

## The effects of CO<sub>2</sub> pressure and pH on the Suzuki coupling of basic nitrogen containing substrates.

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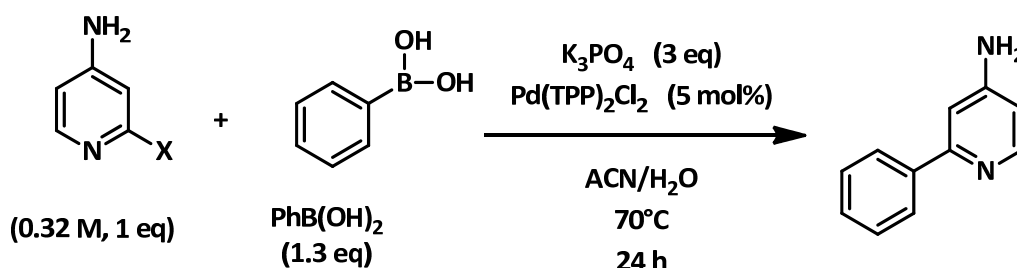
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### Supporting Material

#### Experimental Procedure for Suzuki Coupling Reactions



Scheme 1 - Reaction of 2-halo-4-aminopyridine with phenylboronic acid.

#### I. Reaction of 2-halo-4-aminopyridine with phenylboronic acid under a nitrogen atmosphere.

2-Chloro-4-aminopyridine (2.057 g, 16 mmol, 1 eq) or 4-amino-2-bromopyridine (2.768 g, 16 mmol, 1 eq), phenylboronic acid (2.536 g, 1.3 eq), K<sub>3</sub>PO<sub>4</sub> (10.189 g, 3 eq), and Pd(TPP)<sub>2</sub>Cl<sub>2</sub> (0.562 g, 5 mol%) were added to a 100 mL three-neck Morton flask equipped with a magnetic stirrer. The flask was evacuated and backfilled with nitrogen. Degassed acetonitrile (30 mL) and degassed water (10 mL for 25% v/v reactions; 20 mL for 40% v/v reactions) were added by means of an air-tight syringe. The reaction vessel was insulated with glass wool and heated to reflux at 70°C (monitored by internal thermometer) under an atmosphere of N<sub>2</sub> for 24 h. The initial reaction time (t = 0) was taken when the reaction mixture reached an internal temperature of 70°C; the time to reach this temperature was approximately 10-15 minutes. The reactions were biphasic with two liquid phases.

#### II. Reaction of 2-halo-4-aminopyridine with phenylboronic acid under varying pressures of carbon dioxide.

2-Chloro-4-aminopyridine (2.057 g, 16 mmol, 1 eq) or 4-amino-2-bromopyridine (2.768 g, 16 mmol, 1 eq), phenylboronic acid (2.536 g, 1.3 eq),  $K_3PO_4$  (10.189 g, 3 eq), and  $Pd(TPP)_2Cl_2$  (0.562 g, 5 mol%) were added to a 300 mL stainless steel bomb (Parr reactor). The Parr reactor was then purged with a flow of  $CO_2$  for 15 minutes. Degassed acetonitrile (30 mL) and degassed water (10 mL for 25% v/v reactions; 20 mL for 40% v/v reactions) were then added by means of an air-tight syringe. The Parr reactor was then pressurized with  $CO_2$  via a model 260D or 500D ISCO syringe pump to within  $\sim 6.8$  atm of the desired pressure. The reaction mixture was mechanically stirred by means of a built-in impeller at a stirring rate of 415 rpm and heated to  $70^\circ C$  as monitored by an internal thermocouple. If necessary, additional  $CO_2$  pressure was added to bring the system to the final indicated pressure (2, 6.8, 30.6, or 44.2 atm). The initial reaction time ( $t = 0$ ) was taken when the reaction mixture reached an internal temperature of  $70^\circ C$  and the final  $CO_2$  pressure has been reached; the time to reach this temperature and pressure was approximately 10 minutes. Constant pressure was maintained throughout the reaction by the ISCO pump. The reaction mixture was heated for 24 h. The reactions contain two liquid phases. With 25% water present, an additional solid phase forms upon addition of  $CO_2$ . With 40% water present, solid formation is minimal.

### III. Workup Procedure

After reacting for 24 h the reaction vessel was cooled to room temperature. Depressurization was necessary for the reactions conducted under an atmosphere of  $CO_2$ . Methanol was added ( $\sim 100$  mL) to the reaction mixture which resulted in the precipitation of a solid. At this point the reaction mixture is characterized by two phases- a solid phase and a single liquid phase. The mixture was filtered and the filtrate analyzed by gas chromatography/flame ionization detector (GC-FID) using a Shimadzu GC-2010 gas chromatograph fitted with a Supelco PTA-5 (30m x 0.32 mm x 1.00  $\mu m$ , length x inside diameter x film thickness) capillary column. Product yields were calculated using the calibration curves discussed below. The filtrate was then transferred to a round bottom flask and the solvent removed *in vacuo*. The crude product was analyzed by  $^1H$ -NMR ( $CDCl_3$ ) using a 300 MHz Varian NMR spectrometer and compared to standards to determine NMR yields. The calculation and an example NMR are provided in Section X. GC and NMR yields are listed in Section XI.

### IV. Reaction of 2-halo-4-aminopyridine with phenylboronic acid as a function of time.

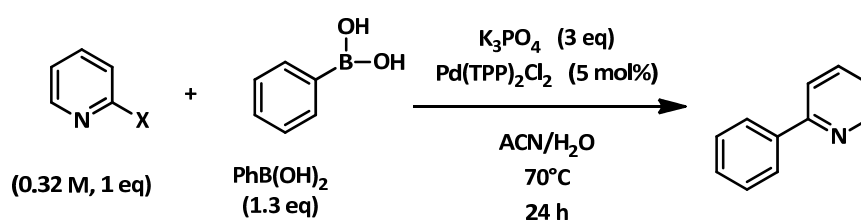
Reactions were set up as described by the procedure in Section II. To monitor the reactions as a function of time, samples were taken from the organic layer for analysis by GC-FID.

### Reactions Under Atmospheric Nitrogen

For reactions conducted under a nitrogen atmosphere the stirring was stopped briefly at specified times in order to allow the acetonitrile and water phases to separate. Air tight syringes were used to remove 0.2 mL samples from the organic phase; stirring was then resumed. The 0.2 mL sample was placed in a vial from which 0.1 mL was transferred to a GC vial by means of an Eppendorf calibrated pipette. Methanol (0.9 mL) was then added to the GC vial by an Eppendorf pipette and the sample analyzed by GC-FID.

## Reactions Under CO<sub>2</sub> Pressure

For reactions conducted under CO<sub>2</sub> pressures, samples were removed through a stainless steel dip tube which extends into the organic phase. Stirring was stopped briefly to allow the acetonitrile and water phases to separate. The valve was opened so that the pressure differential slowly drove the sample out of the reactor into a vial in the form of droplets. After ~0.2 mL was collected the valve was shut and stirring resumed. Then 0.1 mL of the sample was transferred from the vial to a GC vial by means of an Eppendorf pipette. Methanol (0.9 mL) was added to the GC vial by an Eppendorf pipette and the sample was analyzed by GC-FID.



Scheme 2 -Reaction of 2-halopyridine with phenylboronic acid.

### V. Reaction of 2-halopyridine with phenylboronic acid under a nitrogen atmosphere.

Phenylboronic acid (2.536 g, 1.3 eq), K<sub>3</sub>PO<sub>4</sub> (10.189 g, 3 eq), and Pd(TPP)<sub>2</sub>Cl<sub>2</sub> (0.562 g, 5 mol%) were added to a 100 mL three-neck Morton flask equipped with a magnetic stirrer. The flask was evacuated and backfilled with nitrogen. 2-Chloropyridine (1.817 g, 16 mmol, 1 eq) or 2-bromopyridine (2.528 g, 16 mmol, 1 eq), followed by degassed acetonitrile (30 mL) and then degassed water (10 mL for 25% v/v reactions; 20 mL for 40% v/v reactions) were added by means of an air-tight syringe. The reaction vessel was insulated with glass wool and heated to reflux at 70°C (monitored by internal thermometer) under an atmosphere of N<sub>2</sub> for 24 h. The initial reaction time (t = 0) was taken when the reaction mixture reached an internal temperature of 70°C; the time to reach this temperature was approximately 10-15 minutes. The reactions were biphasic with two liquid phases.

### VI. Reaction of 2-halopyridine with phenylboronic acid under varying pressures of carbon dioxide.

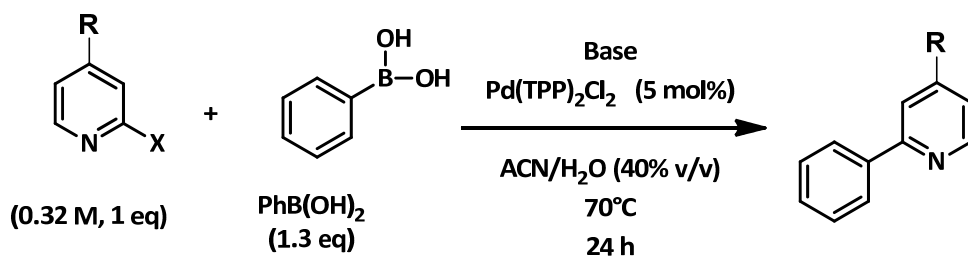
Phenylboronic acid (2.536 g, 1.3 eq), K<sub>3</sub>PO<sub>4</sub> (10.189 g, 3 eq), and Pd(TPP)<sub>2</sub>Cl<sub>2</sub> (0.562 g, 5 mol%) were added to a 300 mL stainless steel bomb (Parr reactor). The Parr reactor was then purged with a flow of CO<sub>2</sub> for 15 minutes. 2-Chloropyridine (1.817 g, 16 mmol, 1 eq) or 2-bromopyridine (2.528 g, 16 mmol, 1 eq) followed by degassed acetonitrile (30 mL) and then degassed water (10 mL for 25% v/v reactions; 20 mL for 40% v/v reactions) were then added by means of an air-tight syringe. The Parr reactor was then pressurized with CO<sub>2</sub> via a model 260D or 500D ISCO syringe pump to within ~6.8 atm of the desired pressure. The reaction mixture was mechanically stirred by means of a built-in impeller at a stirring rate of 415 rpm and heated to 70°C as monitored by an internal thermocouple. If necessary, additional CO<sub>2</sub> pressure was then added to bring the system to the final indicated pressure (2, 6.8, 30.6, or 44.2 atm). The initial reaction time (t = 0) was taken when the reaction mixture reached an internal temperature of

70°C and the final CO<sub>2</sub> pressure has been reached; the time to reach this temperature and pressure was approximately 10 minutes. Constant pressure was maintained throughout the reaction by the ISCO pump. The reaction mixture was heated for 24 h. The reactions contain two liquid phases. With 25% water present, an additional solid phase forms upon addition of CO<sub>2</sub>. With 40% water present, solid formation is minimal.

#### VII. Workup Procedure

Workup was conducted in the same manner as described above for the 4-amino-2-halopyridines (Section III).

Reaction of 2-halopyridine with phenylboronic acid as a function of time. The reaction was set up as described in Section VI. Sampling was conducted in the same manner as described above for the 4-amino-2-halopyridines (Section IV).



**Scheme 3 - Reaction scheme for the coupling of 4-amino-2-halopyridines and 2-halopyridines with phenylboronic acid under various buffered systems.**

#### VIII. Reactions of 4-amino-2-halopyridines and 2-halopyridines in buffered systems (pH vs yield)

Following the procedures outlined above, 4-amino-2-halopyridines (16 mmol, procedure: Section I) and 2-halopyridine (16 mmol, procedure: Section V) were coupled with phenylboronic acid (1.3 eq) in the presence of PdTPP<sub>2</sub>Cl<sub>2</sub> (5 mol%), ACN/H<sub>2</sub>O (60/40 v/v%) and the bases listed in the tables below (Table 1-Table 4). The equivalents of base with respect to the halopyridine are outlined in the table. The pH of the reaction system was measured via a pH meter both before and after reaction. The pH values reported in the manuscript are the pH values after reaction had completed. On average the pH shifted approximately 1 pH unit during the reaction. Yields were calculated by GC-FID.

Table 1 - Reaction of 2-bromo-4-aminopyridine under various buffered systems.

4-NH <sub>2</sub> -2-BrPyr, 40% H <sub>2</sub> O				
Base	Equiv.	Yield (%)	pH before	pH after
K <sub>3</sub> PO <sub>4</sub>	3	23±4	13	13
K <sub>4</sub> P <sub>2</sub> O <sub>7</sub>	3	50±1	10.58	9.67
K <sub>2</sub> HPO <sub>4</sub> /KHCO <sub>3</sub>	1/2	79±3	9.2	8.8
K <sub>2</sub> HPO <sub>4</sub> /KHCO <sub>3</sub>	3/3	51±3	9.64	9.6
K <sub>2</sub> HPO <sub>4</sub>	3	90±2	9.5	7.95
K <sub>3</sub> PO <sub>4</sub> , 30 psi CO <sub>2</sub>	3	83±0	N/A	7.7
K <sub>3</sub> PO <sub>4</sub> , 100 psi CO <sub>2</sub>	3	91±8	N/A	7.9
K <sub>2</sub> HPO <sub>4</sub> /KHCO <sub>3</sub> /KH <sub>2</sub> PO <sub>4</sub>	2.4/3.5/0.6	51±4	8.4	9.85
precond. K <sub>3</sub> PO <sub>4</sub> *	3	76±6	8	8.3
pre-cond. SM. and K <sub>3</sub> PO <sub>4</sub> *	3	75±2	7.9	8.1
CsF	3	95±4	8.97	8.1

Table 2 - Reaction of 2-bromopyridine under various buffered systems

2-BrPyr, 40% H <sub>2</sub> O				
Base	Equiv.	Yield	Initial pH	final pH
K <sub>3</sub> PO <sub>4</sub>	3	92±5	12.8±0.3	11.6±0.5
K <sub>3</sub> PO <sub>4</sub> , 450 psi CO <sub>2</sub>	3	15±0.3	12.8±0.3	7.8±0.5
K <sub>2</sub> HPO <sub>4</sub>	3	26±2	9.4±0.1	8.4±0.3
K <sub>2</sub> HPO <sub>4</sub> /KHCO <sub>3</sub>	1/2	36±8	9.2±0.1	9.6±0.3
KH <sub>2</sub> PO <sub>4</sub>	3	23±4	5.2±0.0	3.4±0.1
K <sub>2</sub> CO <sub>3</sub>	3	66±1	11.9±0.1	10.5±0.2
KHCO <sub>3</sub>	3	64±5	8.9±0.1	9.6±0.3
K <sub>2</sub> HPO <sub>4</sub> /KHCO <sub>3</sub> /KH <sub>2</sub> PO <sub>4</sub>	2.4/3.5/0.6	25±2	8.5±0.1	9.2±0.1
CsF	3	29±7	N/A	8.6±0.2
KOH	3	69±6	14.75±0.07	11.7±0.0

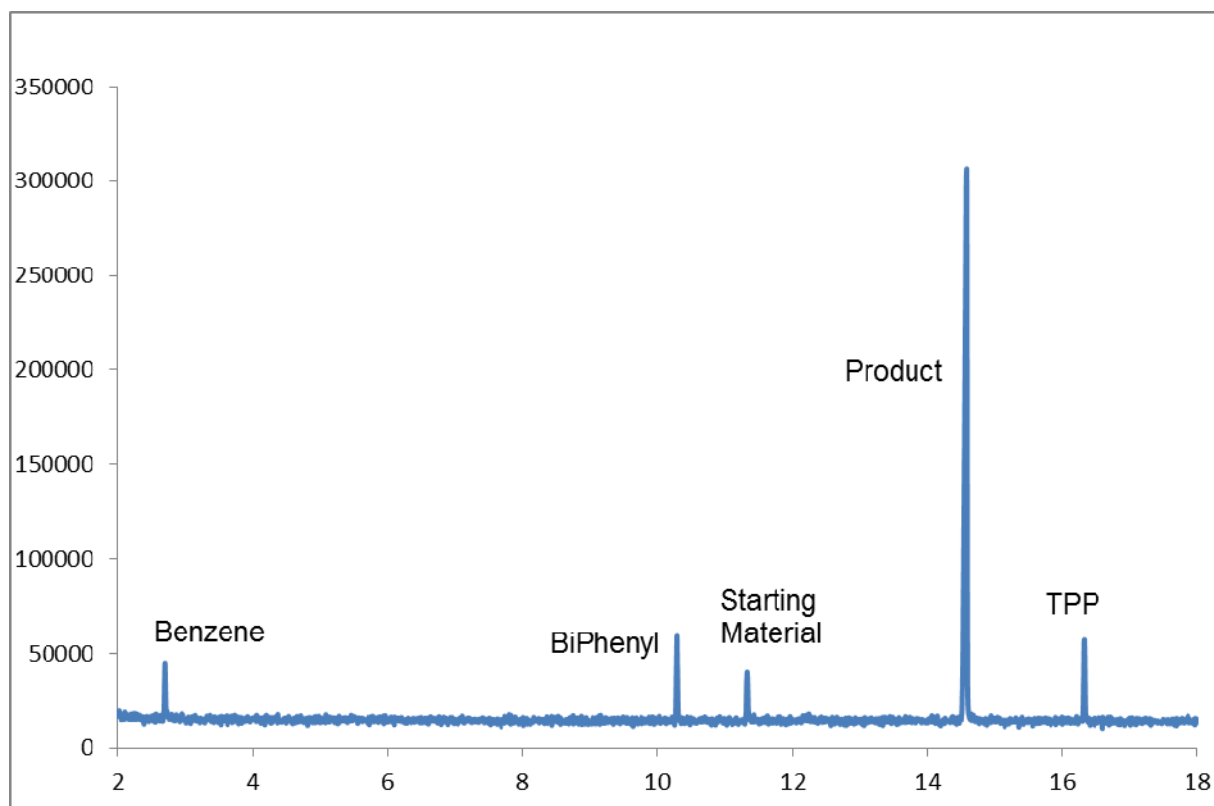
**Table 3 - Reaction of 2-chloro-4-aminopyridine under various buffered systems.**

<b>4-NH<sub>2</sub>-2-ClPyr, 40% H<sub>2</sub>O</b>					
<b>Base</b>	<b>Equiv.</b>	<b>yield</b>	<b>st. dev</b>	<b>pH before</b>	<b>pH after</b>
K <sub>3</sub> PO <sub>4</sub>	3	30±2	2	N/A	12.635
K <sub>2</sub> HPO <sub>4</sub>	3	64±2	2	9.533333	8.2
K <sub>3</sub> PO <sub>4</sub> , 30 psi CO <sub>2</sub>	3	93±3	3	N/A	7.95
K <sub>3</sub> PO <sub>4</sub> , 100 psi CO <sub>2</sub>	3	98±3	3	N/A	7.625

**Table 4 - Reaction of 2-chloropyridine under various buffered systems.**

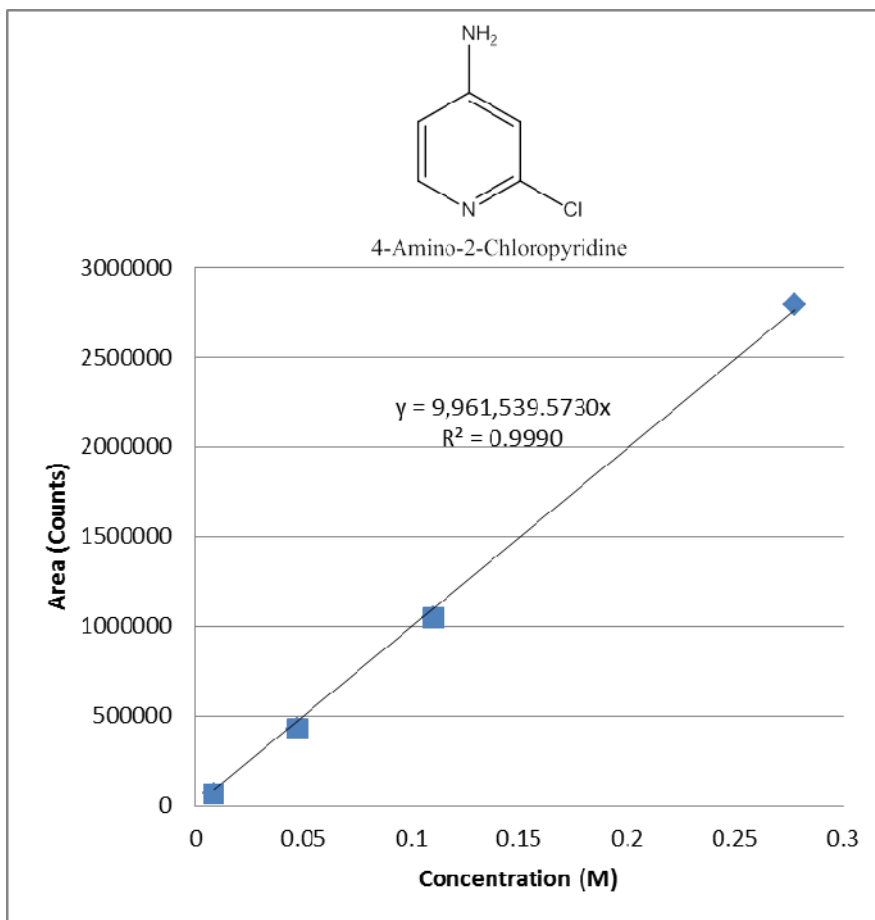
<b>2-ClPyr, 40% H<sub>2</sub>O</b>				
<b>Base</b>	<b>Equiv.</b>	<b>Yield</b>	<b>pH before</b>	<b>pH after</b>
K <sub>3</sub> PO <sub>4</sub>	3	79±1	13.2±0.1	11.6±0.1
K <sub>3</sub> PO <sub>4</sub> , 450 psi CO <sub>2</sub>	3	32±6	13.2±0.1	7.6±0.1
K <sub>2</sub> HPO <sub>4</sub>	3	42±9	9.3±0.1	8.3±0.1
K <sub>2</sub> CO <sub>3</sub>	3	94±2	11.7±0.1	10.5±0.0

## IX. GC-FID Chromatograms and Calibration Curves



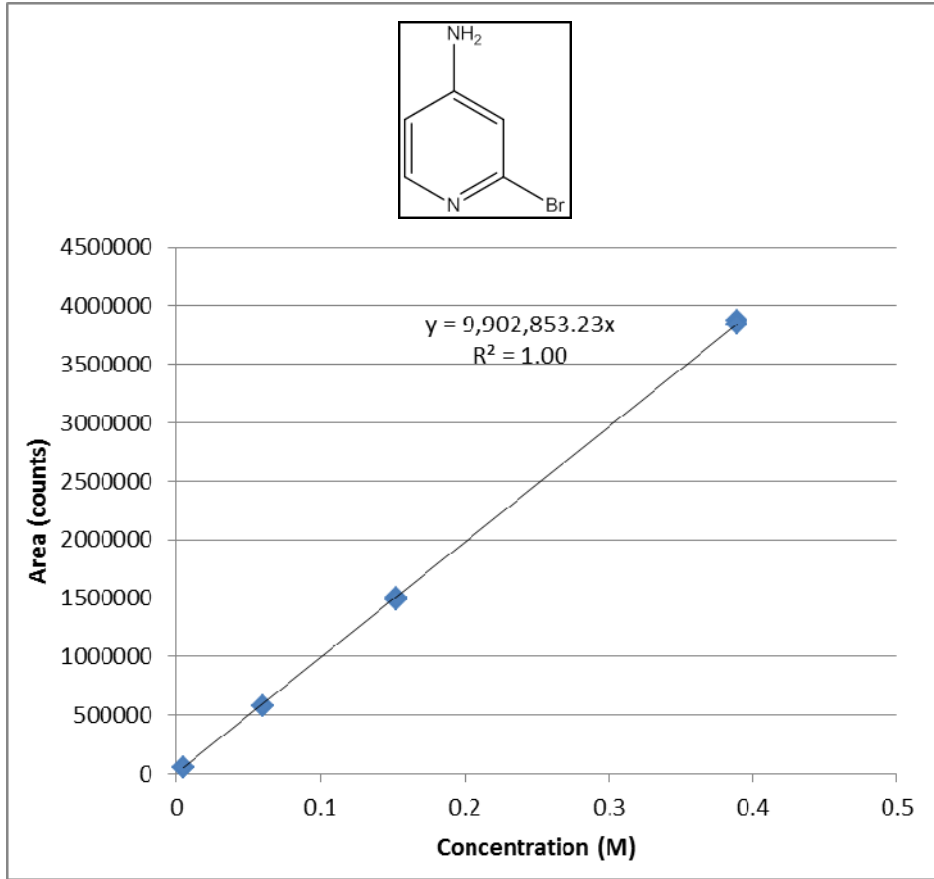
**Figure 1** Example GC-FID spectra: reaction of 4-amino-2-bromopyridine with phenylboronic acid under 2 atm CO<sub>2</sub> and 40% water after 24 h after workup. Calibration curves are used to relate the area of each peak to a concentration, which is then used to calculate yield and conversion.

Calibration curves were created from pure substrate and product standards. Stock solutions (1 M) were made using a 75/15/10 mixture of methanol/acetonitrile/water to mimic the solvent system of the reaction systems after workup. Multiple samples of concentrations between 0.01 M and 0.5 M were then made from dilution of the stock solution with the same solvent mixture and analyzed by GC-FID using a Shimadzu GC-2010 gas chromatograph fitted with a Supelco PTA-5 (30m x 0.32 mm x 1.00  $\mu$ m, length x inside diameter x film thickness) capillary column. Plots of concentration versus area were created for each compound using Microsoft Excel and a trendline analysis used to provide the calibration curve and confirm that the plot followed a straight line. Calibration curves for 2-chloro-4-aminopyridine, 2-bromo-4-aminopyridine, and 2-phenyl-4-aminopyridine are shown in Figures 2-4. Calibration curves for 2-chloropyridine, 2-bromopyridine and 2-phenylpyridine are shown in Figures 5-7.

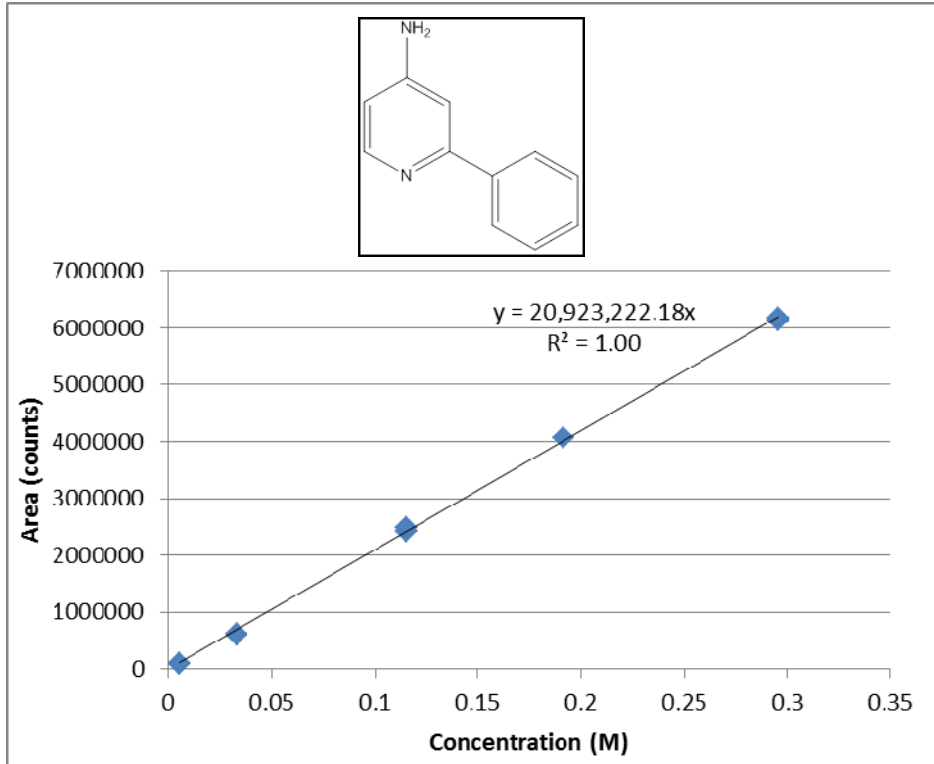


**Figure 2.** GC-FID calibration curve of 2-chloro-4-aminopyridine.





**Figure 3.** GC-FID Calibration Curve for 2-bromo-4-aminopyridine.



**Figure 4.** GC-FID Calibration Curve for 2-phenyl-4-aminopyridine

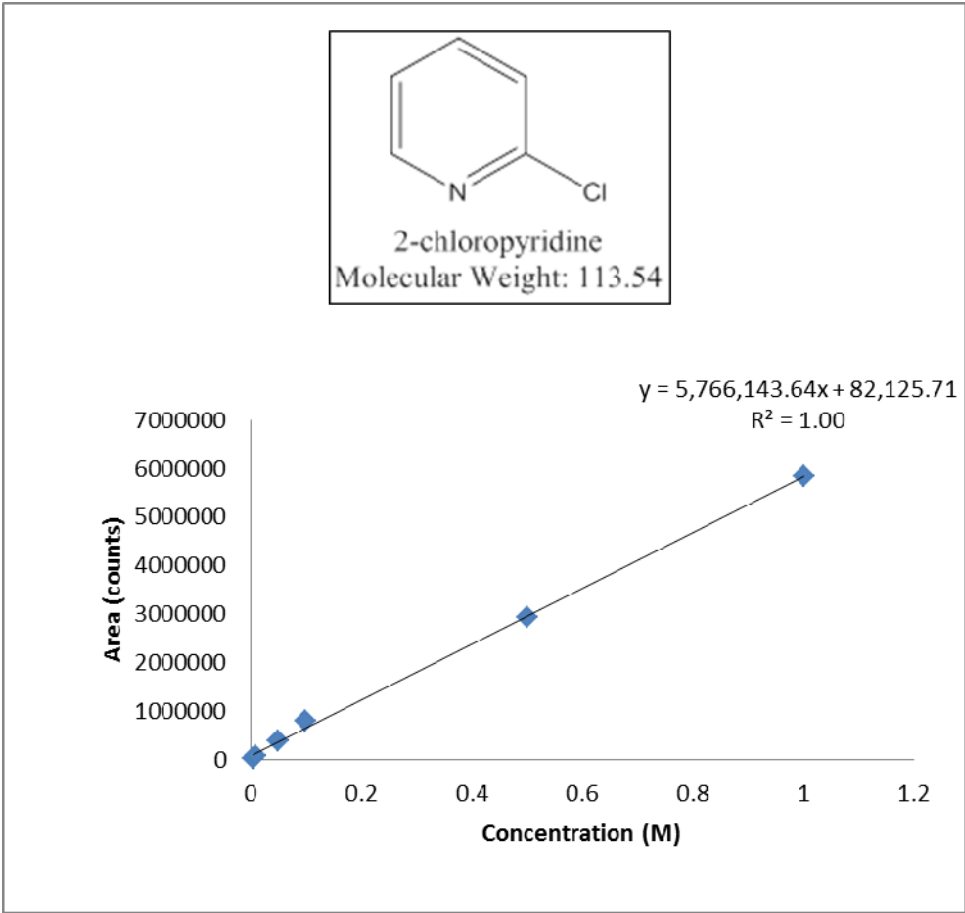
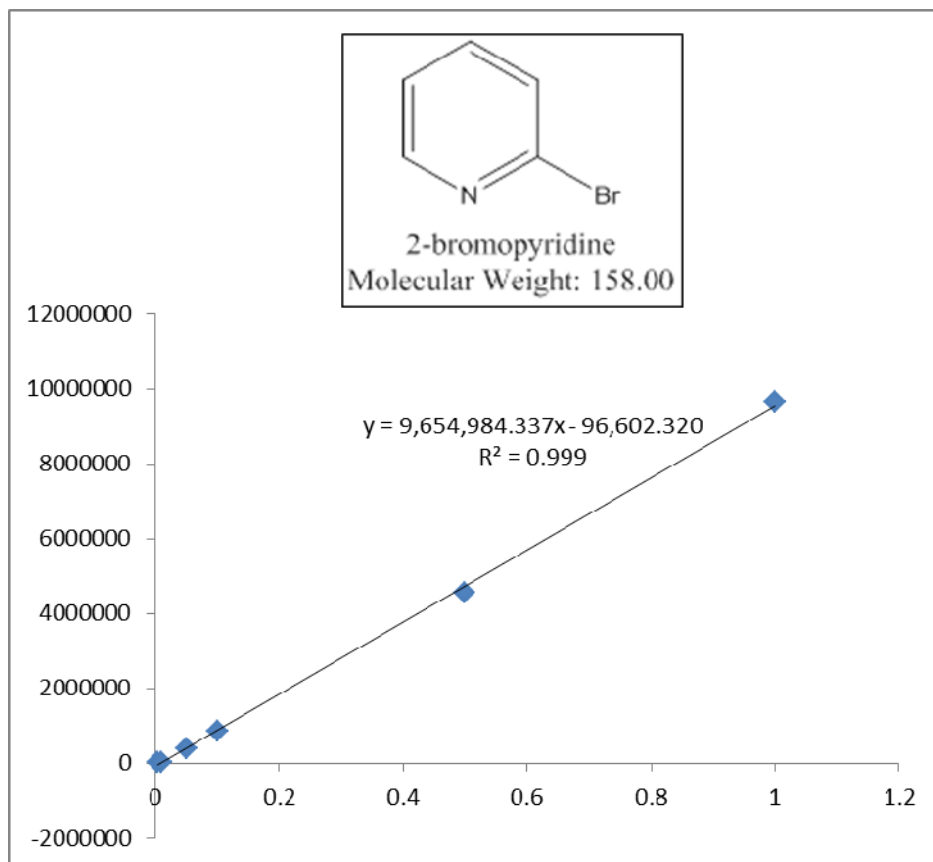
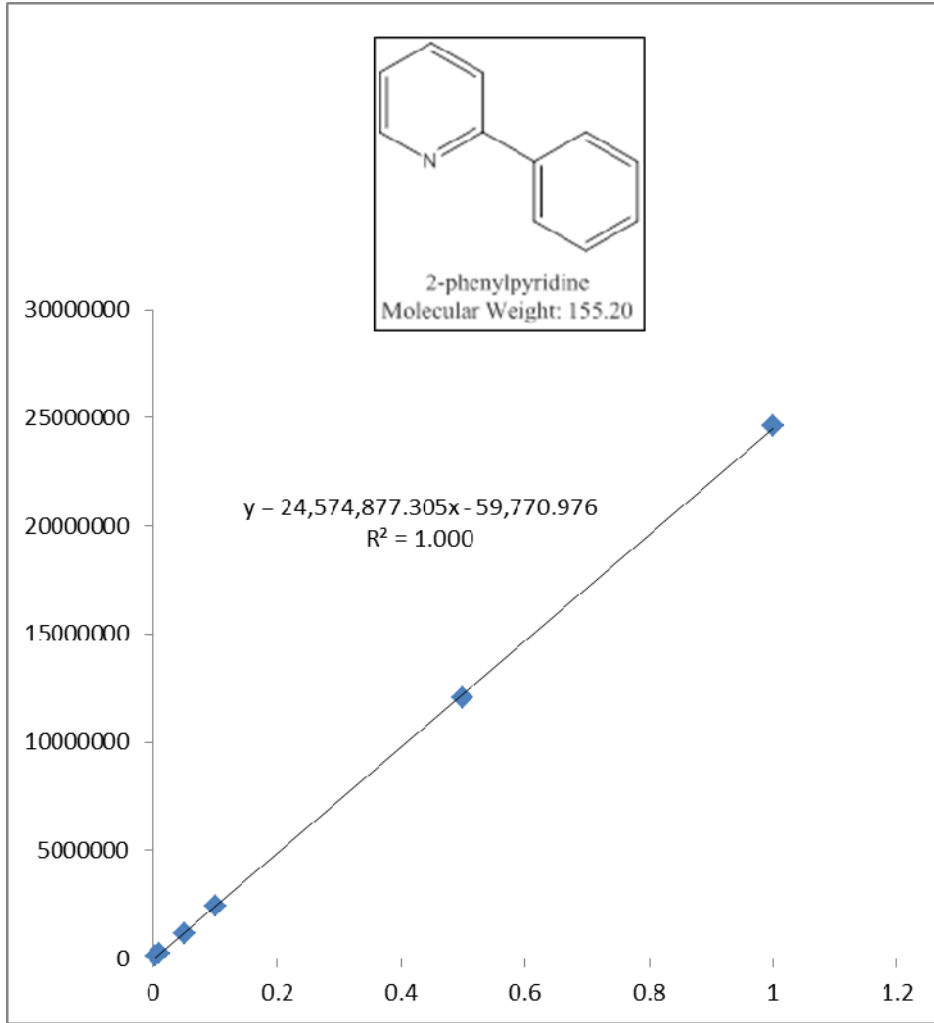


Figure 5 - GC-FID Calibration Curve for 2-chloropyridine.

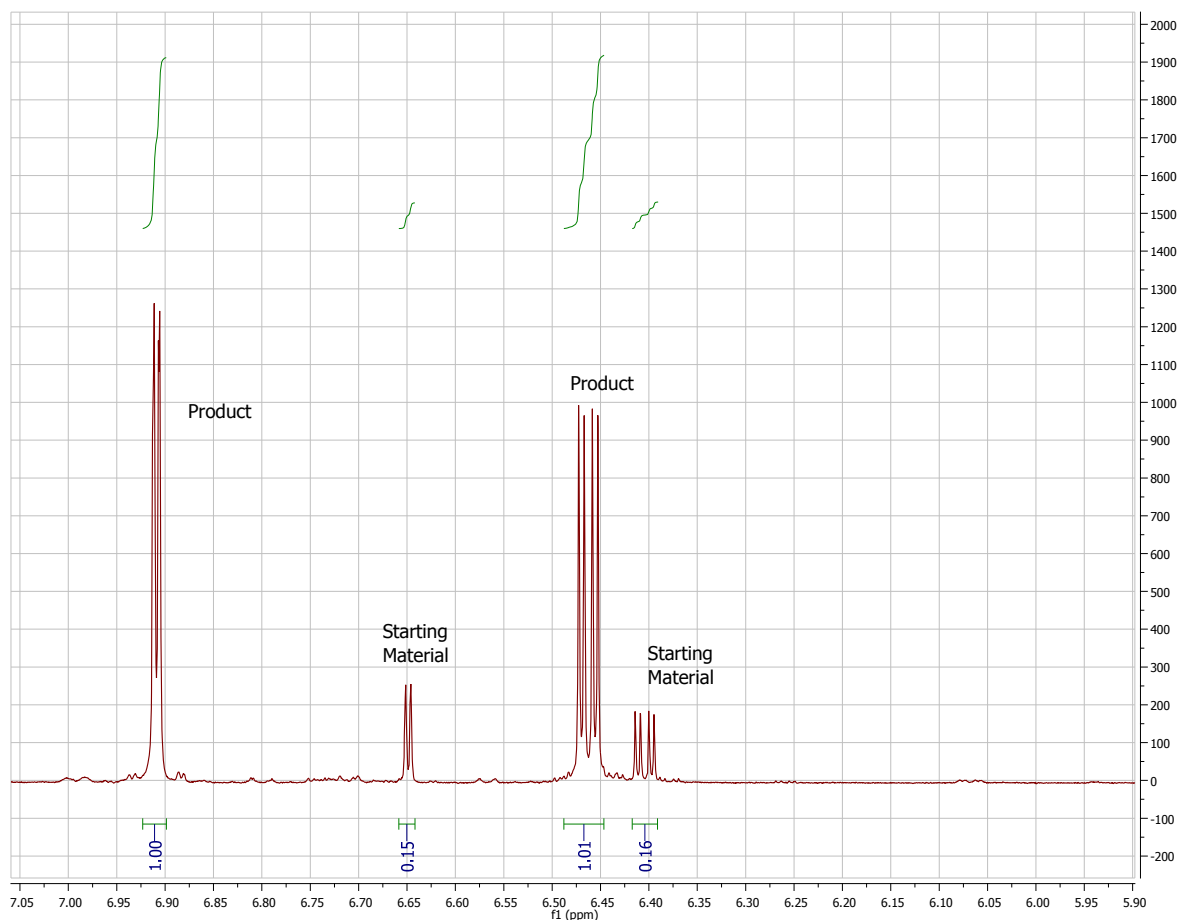


**Figure 6** - GC-FID Calibration Curve for 2-bromopyridine.



**Figure 7** - GC-FID Calibration Curve for 2-phenylpyridine.

## X. NMR Example



**Figure 8.** Example NMR spectra: reaction of 2-bromo-4-aminopyridine with phenylboronic acid under 2 atm CO<sub>2</sub> with 40% water, 24 h, after workup.

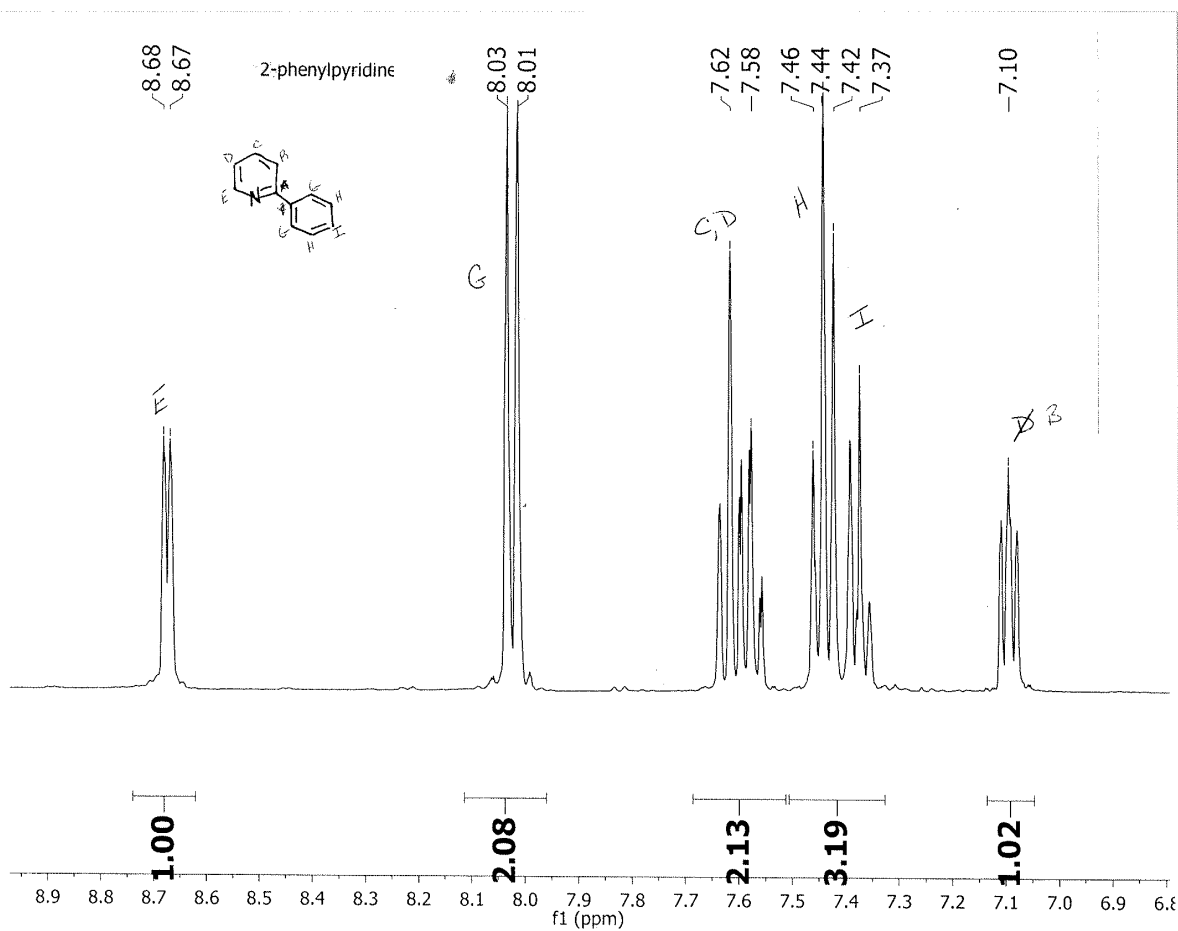
NMR spectra were used to determine amount of starting material and product in reaction mixtures after workup by comparison to standards of each compound. NMR Yields were calculated according to the following:

$$\text{NMR Yield} = \frac{I_{\text{prod.}}}{I_{\text{SM}} + I_{\text{prod.}}}$$

Where  $I_{\text{prod.}}$  and  $I_{\text{SM}}$  denote the area integrals of the product and substrate respectively.

The chemical shifts for each product and starting material were confirmed via prepared standards and are consistent to reports in the literature.<sup>1,2</sup> The NMR yield of 2-phenylpyridine was determined from the <sup>1</sup>H NMR areas of the following signals (CDCl<sub>3</sub>): Starting material (2-bromopyridine) – 8.36 ppm, 1H (d); Product (2-phenylpyridine) – 8.66 ppm, 1H (d).

2-phenylpyridine:



$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 8.68 (d, 1H), 8.02 (d, 2H), 7.62 (d, 1H), 7.58 (t, 1H), 7.44 (t, 2H), 7.10 (t, 1H), 7.14 (t, 1H) ppm.

$^{13}\text{C}$  (100 MHz,  $\text{CDCl}_3$ ): 156.91, 149.22, 139.00, 136.22, 128.54, 128.32, 126.50, 121.64, 119.98 ppm.

#### XI. Data with NMR yields included

Table 5 -2-halo-4-aminopyridine reactions (Scheme 1). Reactions run for 24 hours with 25% v/v of  $\text{H}_2\text{O}$ . a) Yield calculated from GC-FID calibration curve. b) Reaction was run in 3-neck, 100mL Morton flask.

X=	Pressure of $\text{CO}_2$ (atm)	GC Yield(%) <sup>a</sup>	NMR Yield(%)
Br	6.8	50±4	42
Br	30.6	55±6	56±7
Br	44.2	57±2	50±1
Br <sup>b</sup>	$\text{N}_2$ , 1 atm	17±4	22±1
Cl	30.6	71±3	83±2
Cl <sup>b</sup>	$\text{N}_2$ , 1 atm	21±2	23±2

**Table 6 - 2-halo-4-aminopyridine reactions (Scheme 1). Reactions run for 24 hours with 40% v/v of H<sub>2</sub>O. a) Yield calculated from GC-FID calibration curve. b) Reaction was run in 3-neck, 100mL Morton flask.**

X=	Pressure of CO <sub>2</sub> (atm.)	GC Yield(%) <sup>a</sup>	NMR Yield(%)
Br	2.0	83±0	84±3
Br	6.8	91±8	92±12
Br	30.6	99±2	100±0
Br <sup>b</sup>	N <sub>2</sub> , 1 atm.	23±4	26±2
Cl	2.0	93±3	93±5
Cl	6.8	98±3	96±2
Cl <sup>b</sup>	N <sub>2</sub> , 1 atm.	30±2	32±2

**Table 7 – 2-halopyridine reactions run for 24 hours with 25% v/v of H<sub>2</sub>O (Scheme 2). a) Yield calculated from GC-FID calibration curve. b) Reaction was run in 3-neck, 100mL Morton flask.**

Entry	X=	Atmosphere	Pressure (atm)	GC Yield (%) <sup>a</sup>	NMR Yield (%)
1 <sup>b</sup>	Br	N <sub>2</sub>	1	87±3	94±2
2	Br	CO <sub>2</sub>	30.6	7±0.3	10±1

**Table 8 - 2-halopyridine reactions run for 24 hours with 40% v/v of H<sub>2</sub>O (Scheme 2). a) Yield calculated from GC-FID calibration curve. b) Reaction was run in 3-neck, 100mL Morton flask.**

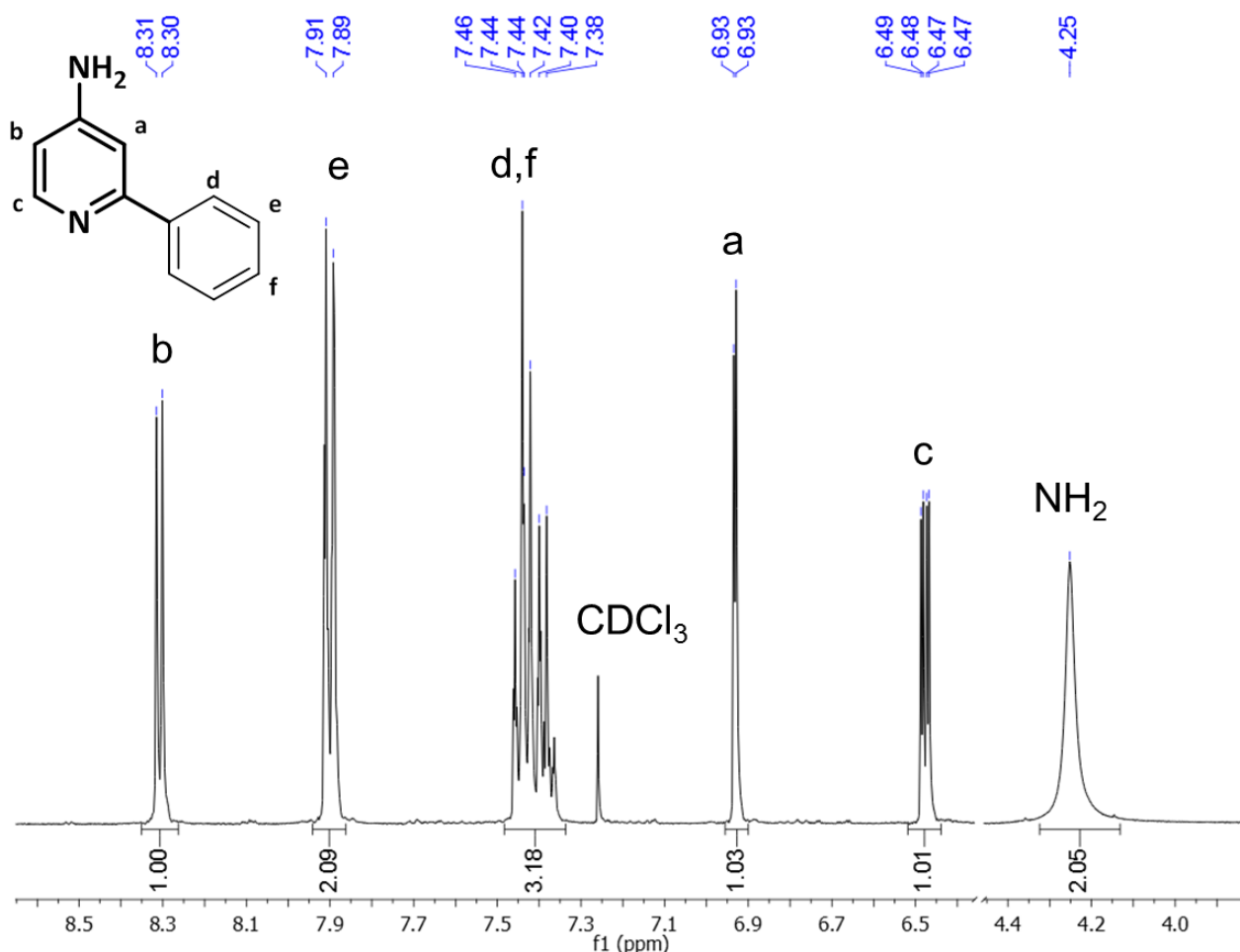
Entry	X=	Atmosphere	Pressure (atm.)	GC Yield (%) <sup>a</sup>	NMR Yield (%)
8 <sup>b</sup>	Br	N <sub>2</sub>	1	92±5	94±4
9	Br	CO <sub>2</sub>	30.6	15±0.3	19±1
10 <sup>b</sup>	Cl	N <sub>2</sub>	1	91±1	89±2
11	Cl	CO <sub>2</sub>	30.6	32±6	33±4

**XII. Isolation of 4-amino-2-phenylpyridine from the reaction of 4-amino-2-bromopyridine with phenylboronic acid under CO<sub>2</sub> pressure.**

4-Amino-2-bromopyridine (2.761 g, 15.96 mmol, 1 eq), phenylboronic acid (2.536 g, 1.3 eq), K<sub>3</sub>PO<sub>4</sub> (10.189 g, 3 eq), and Pd(TPP)<sub>2</sub>Cl<sub>2</sub> (0.562 g, 5 mol%) were added to a 300 mL stainless steel bomb (Parr reactor). The Parr was then purged with a flow of CO<sub>2</sub> for 15 minutes. Degassed acetonitrile (30 mL) and degassed water (20 mL) were then added by air-tight syringe. The Parr was then pressurized with CO<sub>2</sub> by means of a model 500D ISCO syringe pump to ~24 atm CO<sub>2</sub>. The reaction mixture was mechanically stirred by means of a built-in impeller at a stirring rate of 415 rpm and heated to 70°C as monitored by an internal thermocouple. The pressure was then increased to 30.6 atm CO<sub>2</sub>. The initial reaction time (t = 0) was taken when the reaction mixture reached an internal temperature of 70°C and the final CO<sub>2</sub> pressure has been reached; this took approximately 10 minutes. Constant pressure was maintained throughout the reaction by the ISCO pump. The reaction mixture was heated for 24 h.



After 24 h the Parr reactor was cooled to room temperature and depressurized. Methanol was added (~100 mL) to the reaction mixture which resulted in the precipitation of a solid. At this point the reaction mixture is characterized by two phases- a solid phase and a single liquid phase. The mixture was filtered and the filtrate analyzed by GC-FID using a Shimadzu GC-2010 gas chromatograph fitted with a Supelco PTA-5 (30m x 0.32 mm x 1.00  $\mu$ m, length x inside diameter x film thickness) capillary column. Using the above described calibration curves, the yield of 2-phenyl-4-aminopyridine was calculated to be 99%; the conversion was 100%. The filtrate was transferred to a round bottom flask and the solvent was removed *in vacuo* leaving a brown solid. The crude mixture was loaded onto neutral silica (~10 g) then added to a column packed with neutral silica (pH~7). A hexanes/ethyl acetate (EtOAc) gradient was used. Biphenyl was removed first under 100% hexanes. The EtOAc concentration was gradually increased to 50% and then held at 50% until the product had completely eluted from the column as indicated by TLC. The product fractions were combined and the solvent removed *in vacuo* to yield 94% 4-amino-2-phenylpyridine as yellow crystalline solid (2.54 g, 14.992 mmol).  $^1\text{H}$  and  $^{13}\text{C}$  NMR of the pure product are shown below (Figure 6 and 7) and are consistent to the literature reports.<sup>3</sup>



**Figure 9.**  $^1\text{H}$  NMR of 2-phenyl-4-aminopyridine.

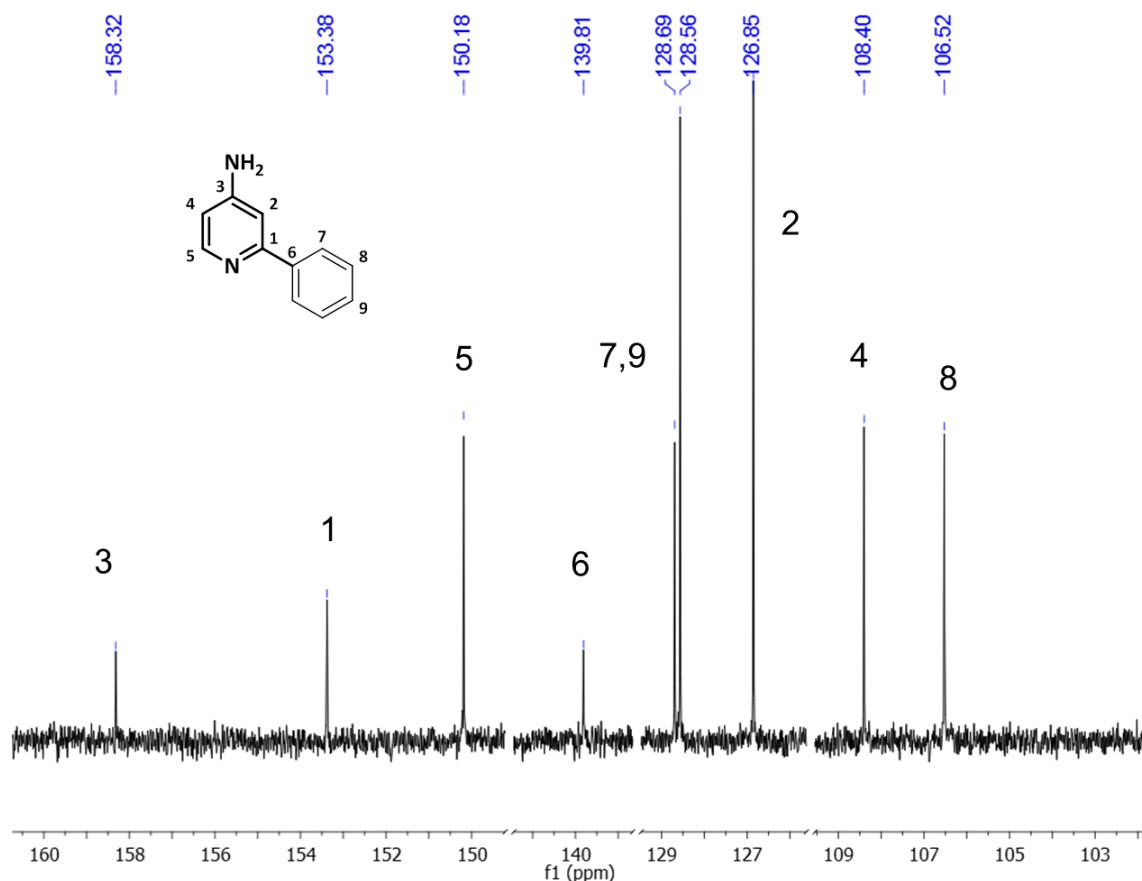


Figure 10 - <sup>13</sup>C NMR of 4-amino-2-phenylpyridine.

### XIII. Partitioning of 2-bromo-4-aminopyridine as a function of pH.

2-bromo-4-aminopyridine (2.768 g, 16 mmol, 1 eq.) was added to a 60/40 (v/v%) acetonitrile (30mL) and water (20mL) solvent mixture. The pH of the aqueous phase was controlled by adding different amounts of phosphate buffers. Three separate solutions were made with 3 eq. of either K<sub>2</sub>HPO<sub>4</sub>, K<sub>4</sub>P<sub>2</sub>O<sub>7</sub>, or K<sub>3</sub>PO<sub>4</sub>. Additionally, a fourth solution was made containing 1.5 eq. K<sub>2</sub>HPO<sub>4</sub> and 6 eq. of NaCl. In order to account for differences in ionic strength between each system (3 eq. of K<sub>2</sub>HPO<sub>4</sub> produces 6 K<sup>+</sup> ions and 3 eq. of K<sub>4</sub>P<sub>2</sub>O<sub>7</sub> produces 12 K<sup>+</sup> ions when fully dissociated), two additional solutions were prepared. The first contained 3/2 eq. of K<sub>4</sub>P<sub>2</sub>O<sub>7</sub> and the second contained 2 eq. of K<sub>3</sub>PO<sub>4</sub>. The pH of the aqueous phase of each sample was measured. Overall, these six separate samples comprised a pH range of 7-14. Samples were then taken from each phase and the amount of starting material was determined quantitatively by GC-FID. In every case, >99% of starting material was found to be in the organic phase.

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