

## Supporting Information

### **Application of 2-Aryl Indenylphosphine Ligand in the Buchwald-Hartwig Cross-Coupling Reactions of Aryl and Heteroaryl Chlorides under the Solvent-Free and Aqueous Conditions**

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## 1. General experimental information

### 1.1 General methods

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. (2,6-dimethoxyphenyl)boronic acid,<sup>1</sup> Dicyclohexyl (2-(2,6-dimethoxyphenyl)-1H-inden-3-yl) phosphine<sup>2</sup> were prepared according to the reported procedures. All of the (hetero) aryl chloride was dried over anhydrous magnesium sulfate. All arylamine compounds were dried over anhydrous potassium carbonate. All reactions were performed in a reaction bulb (approx. 4 mL volume) in the presence of a Teflon coated magnetic stirrer bar. Silica gel (200–300 mesh) was used for column chromatography. <sup>1</sup>H and <sup>13</sup>C spectra were recorded on a Mercury-Plus (400 MHz) and (300 MHz) spectrometer. HRMS were obtained on an IonSpec FT-ICR mass spectrometer with ESI resource. All yields reported refer to isolated yields of compounds estimated to be greater than 95% purity as determined <sup>1</sup>H NMR.

### 1.2 General Procedures for Reaction Condition Screenings.

Chlorobenzene (2.5 mmol), aniline (3.0 mmol), <sup>t</sup>BuONa (3.5 mmol), Pd source and phosphine ligand (as indicated in Table 1) was loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The mixture was pumped and refilled with nitrogen three times. The tube was then placed into a preheated oil bath and stirred for the time period as indicated in Table 1. After completion of reaction, the tube was allowed to cool to room temperature. The mixture was purified by column chromatography to afford the desired product.

### 1.3 General procedure for the Buchwald-Hartwig cross-coupling reaction under solvent-free conditions.

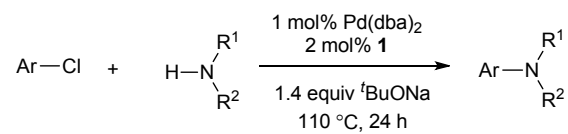
A disposable tube with a screw cap, Teflon septum and stir bar was charged with Pd(dba)<sub>2</sub> (0.0125 mmol), ligand **1** (0.0250 mmol), aryl halide (1.25 mmol), amine (1.50 mmol), <sup>t</sup>BuONa (1.75 mmol). The tube was evacuated and flushed with nitrogen three times, and then placed in a preheated oil bath (110 °C) for 24 h. After completion of reaction, the tube was allowed to cool to room temperature. The mixture was purified by silica gel column chromatography to provide desired compounds.


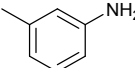
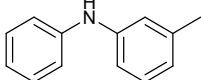

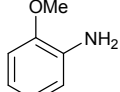
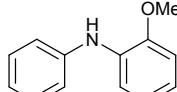

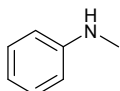
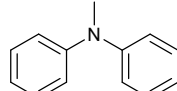


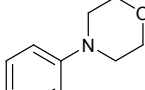

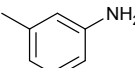
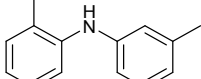

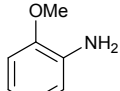
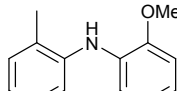

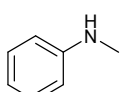
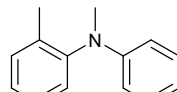


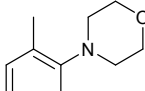
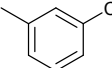
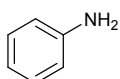
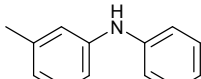
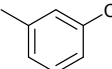
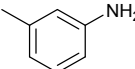
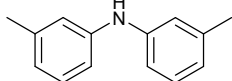
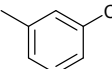
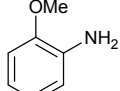
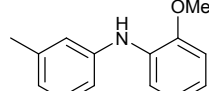
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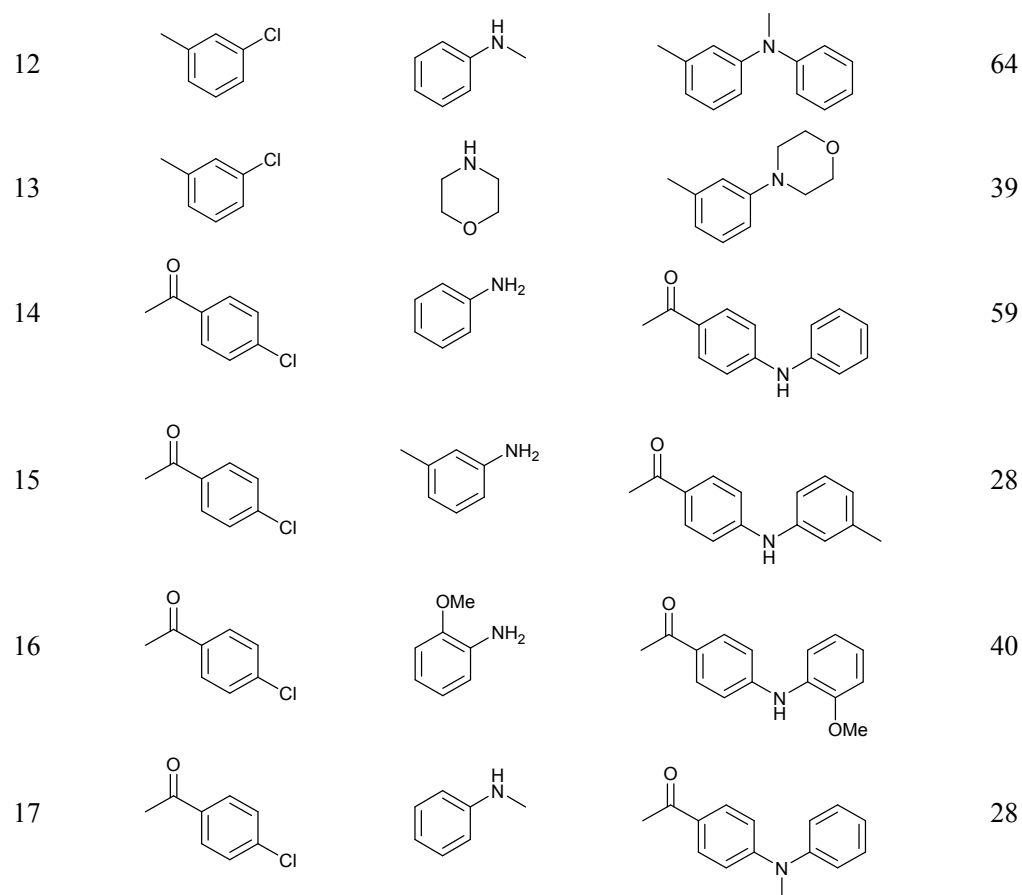
A disposable tube with a screw cap, Teflon septum and stir bar was charged with Pd(dba)<sub>2</sub> (0.0125 mmol), ligand **1** (0.0250 mmol), aryl halide (1.25 mmol), amine (1.50 mmol), <sup>t</sup>BuONa (1.75 mmol) and water (0.05 mL). The tube was evacuated and flushed with nitrogen three times, and then placed in a preheated oil bath (110 °C) for 24 h. After completion of reaction, the tube was allowed to cool to room temperature. Water was drawn with dropper and the mixture was purified by silica gel column chromatography to provide desired compounds.

## 2. Table

**Table 1.** Buchwald-Hartwig cross-coupling reactions of aryl chlorides with amines under solvent-free conditions<sup>a</sup>

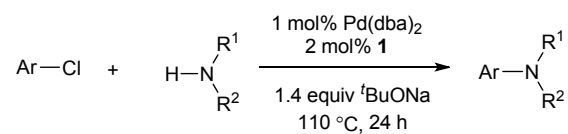



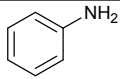
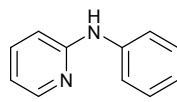

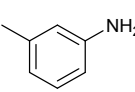
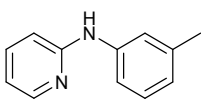

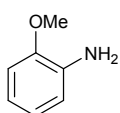
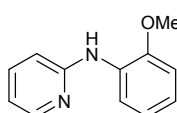

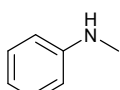
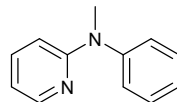

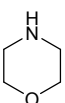
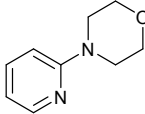

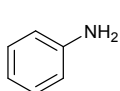
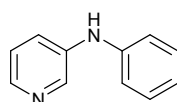

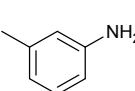
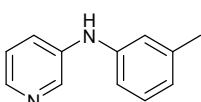

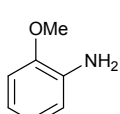
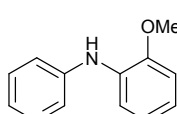

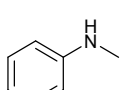
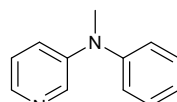

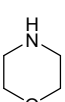
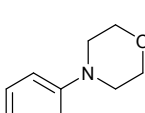
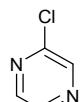
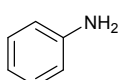
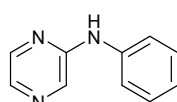
Entry	ArCl	Amine	Product	Yield (%) <sup>b</sup>
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2				52
3				75
4				29
5				73
6				64
7				58
8				62
9				57
10				63
11				62

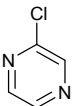
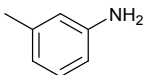
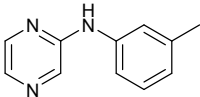
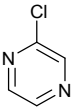
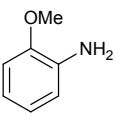
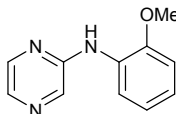
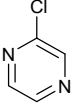
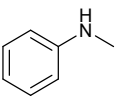
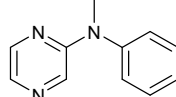
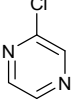

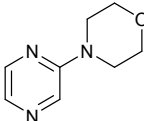
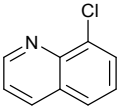
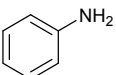
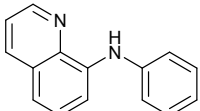
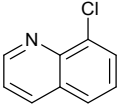
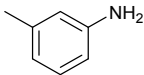
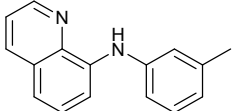
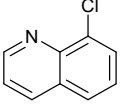
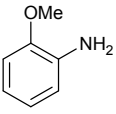
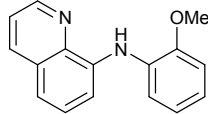
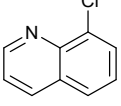

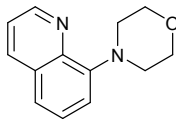


<sup>a</sup>Reaction conditions: ArCl (1.25 mmol), Amines (1.5 mmol), Pd(dba)<sub>2</sub> (1 mol%, 0.0125 mmol), ligand **1** (2 mol%, 0.025 mmol) and <sup>t</sup>BuONa (1.4 equiv, 1.75 mmol) at 110 °C for 24 h. <sup>b</sup>Isolated yield.

**Table 2.** Buchwald-Hartwig cross-coupling reactions of heteroaryl chlorides with amines under solvent-free conditions<sup>a</sup>

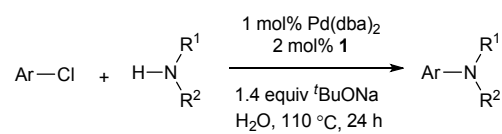


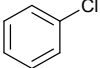
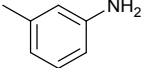
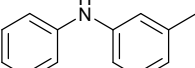
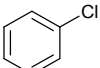
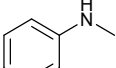
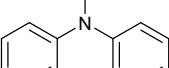
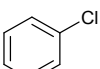

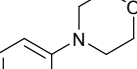
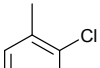
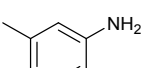
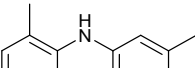
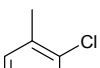
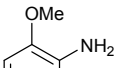
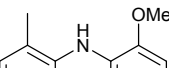
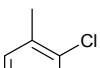

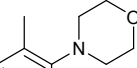
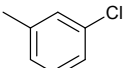
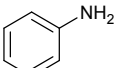
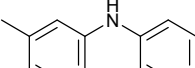
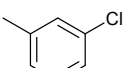
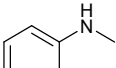
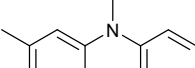
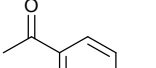
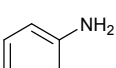
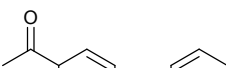
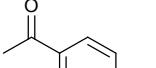
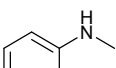
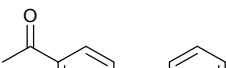
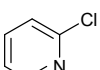
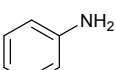
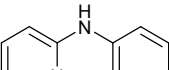
Entry	ArCl	Amine	Product	Yield (%) <sup>b</sup>
1				64
2				59
3				70
4				46
5				58
6				51
7				55
8				49
9				52
10				30
11				78


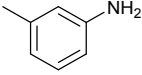
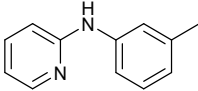

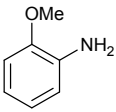
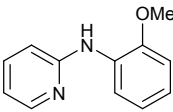

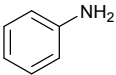
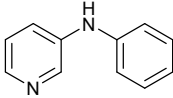

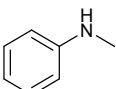
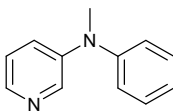
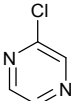
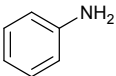
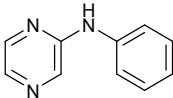

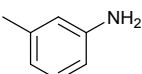
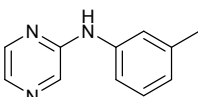
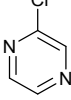
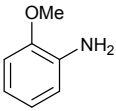
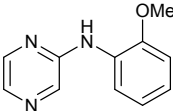
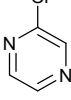
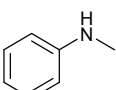
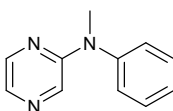


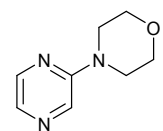
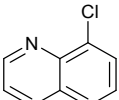
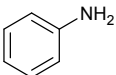
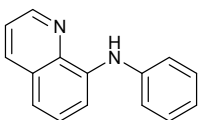
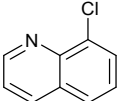
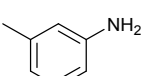
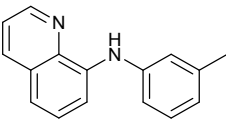
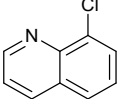
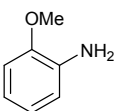
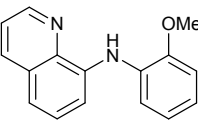
12				82
13				64
14				48
15				75
16				44
17				67
18				65
19				26

<sup>a</sup>Reaction conditions: heteroaryl chlorides (1.25 mmol), Amines (1.5 mmol), Pd(dba)<sub>2</sub> (1 mol%, 0.0125 mmol), ligand **1** (2 mol%, 0.025 mmol) and <sup>t</sup>BuONa (1.4 equiv, 1.75 mmol) at 110 °C for 24 h. <sup>b</sup>Isolated yield.

**Table 3.** Buchwald-Hartwig cross-coupling reactions of amines with aryl and heteroaryl chlorides under aqueous conditions<sup>a</sup>



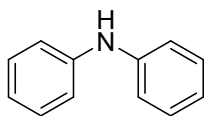
Entry	ArCl	Amine	Product	Yield (%) <sup>c</sup>
1				50
2				79
3				51
4				71
5				61
6				53
7				73
8				73
9				74
10				60
11				65

12				66
13				70
14				77
15				71
16				88
17				87
18				80
19				69
20				73
21				55
22				55
23				58

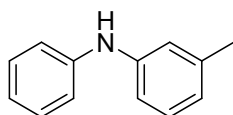
<sup>a</sup>Reaction conditions: H<sub>2</sub>O (0.05 mL), ArCl (1.25 mmol), Amines (1.5 mmol), Pd(dba)<sub>2</sub> (1 mol%, 0.0125 mmol), ligand **1** (2 mol%, 0.025 mmol) and <sup>t</sup>BuONa (1.4 equiv, 1.75 mmol) at 110 °C for 24 h. <sup>b</sup>Isolated yield.



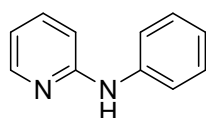
### 3. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectrum for all isolated products



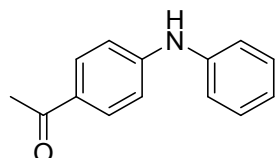
Diphenylamine.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether :  $\text{CH}_2\text{Cl}_2$  = 20 : 1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.26 - 7.21 (m, 4H, Ar-H), 7.06 - 7.03 (m, 4H, Ar-H), 6.92 - 6.88 (m, 2H, Ar-H), 5.68 (s, 1H, NH) ppm.



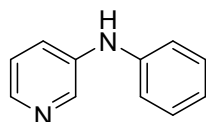
3-methyl-*N*-phenylaniline.<sup>6</sup> The product was purified with silica gel column chromatography (Petroleum ether :  $\text{CH}_2\text{Cl}_2$  = 20 : 1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.25 - 7.20 (m, 2H, Ar-H), 7.12 (t,  $J$  = 8 Hz, 1H, Ar-H), 7.03 (d,  $J$  = 8 Hz, 2H, Ar-H), 6.90 - 6.84 (m, 3H, Ar-H), 6.72 (d,  $J$  = 8 Hz, 1H, Ar-H), 5.62 (s, 1H, NH), 2.29 (s, 3H,  $\text{CH}_3$ ) ppm.



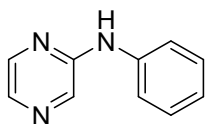
*N*-phenylpyridin-2-amine.<sup>5</sup> The product was purified with silica gel column chromatography (Petroleum ether :  $\text{CH}_2\text{Cl}_2$  = 10 : 1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.16 (d,  $J$  = 4 Hz, 1H, NH), 7.48 - 7.44 (m, 1H, Ar-H), 7.30 - 7.28 (m, 4H, Ar-H), 7.03 - 7.01 (m, 1H, Ar-H), 6.86 (d,  $J$  = 8 Hz, 1H, Ar-H), 6.72 - 6.69 (m, 2H, Ar-H) ppm.



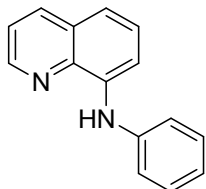
1-(4-(phenylamino)phenyl)ethanone.<sup>7</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.84 (d,  $J$  = 8 Hz, 2H, Ar-H), 7.32 (t,  $J$  = 8 Hz, 2H, Ar-H), 7.16 (d,  $J$  = 8 Hz, 2H, Ar-H), 7.06 (t,  $J$  = 8 Hz, 1H, Ar-H), 6.97 (d,  $J$  = 8 Hz, 2H, Ar-H), 6.10 (s, 1H, NH), 2.52 (s, 1H, CO- $\text{CH}_3$ ) ppm.



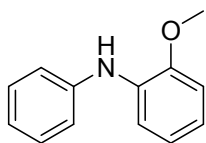
*N*-phenylpyridin-3-amine.<sup>5</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.34 (s, 1H, Ar-H), 8.13 (d,  $J$  = 8 Hz, 1H, Ar-H), 7.38 (d,  $J$  = 8 Hz, 1H, Ar-H), 7.27 (t,  $J$  = 8 Hz, 2H, Ar-H), 7.16 - 7.13 (m, 1H, Ar-H), 7.06 (d,  $J$  = 8 Hz, 2H, Ar-H), 6.97 (t,  $J$  = 8 Hz, 1H, Ar-H), 5.70 (s, 1H, NH) ppm.



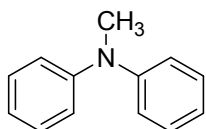
*N*-phenylpyrazin-2-amine.<sup>8</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.21 (s, 1H, Ar-H), 8.08 (s, 1H, Ar-H), 7.95 (d, *J* = 4 Hz, 1H, Ar-H), 7.40 (d, *J* = 8 Hz, 2H, Ar-H), 7.34 (t, *J* = 8 Hz, 2H, Ar-H), 7.08 (d, *J* = 8 Hz, 1H, Ar-H), 6.59 (s, 1H, NH) ppm.



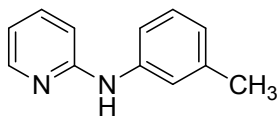
*N*-phenylquinolin-8-amine.<sup>9</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.72 - 8.71 (dd, *J* = 4 Hz, 1H, NH), 8.22 (s, 1H, Ar-H), 8.04 - 8.02 (dd, *J* = 8 Hz, 1H, Ar-H), 7.45 (d, *J* = 8 Hz, 1H, Ar-H), 7.36 - 7.30 (m, 6H, Ar-H), 7.15 (d, *J* = 8 Hz, 1H, Ar-H), 7.09 (t, *J* = 8 Hz, 1H, Ar-H) ppm.



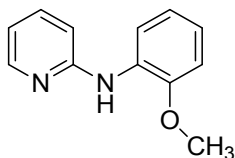
2-methoxy-*N*-phenylaniline.<sup>7</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.28 - 7.22 (m, 3H, Ar-H), 7.11 (d, *J* = 8 Hz, 2H, Ar-H), 6.90 (t, *J* = 8 Hz, 1H, Ar-H), 6.86 - 6.81 (m, 3H, Ar-H), 6.11 (s, 1H, NH), 3.85 (s, 3H, OCH<sub>3</sub>) ppm.



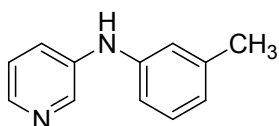
*N*-methyl-*N*-phenylaniline.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.24 - 7.20 (m, 4H, Ar-H), 6.99 - 6.97 (m, 4H, Ar-H), 6.93 - 6.89 (m, 2H, Ar-H), 3.27 (s, 3H, CH<sub>3</sub>) ppm.



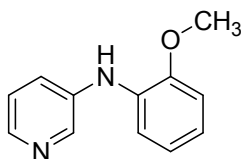
*N*-(*m*-tolyl)pyridin-2-amine.<sup>10</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.14 (d, *J* = 4 Hz, 1H, NH), 7.45 - 7.41 (m, 1H, Ar-H), 7.20 - 7.16 (m, 1H, Ar-H), 7.09 - 7.08 (m, 3H, Ar-H), 6.87 - 6.82 (m, 2H, Ar-H), 6.68 - 6.65 (m, 1H, Ar-H), 2.32 (s, 3H, CH<sub>3</sub>) ppm.



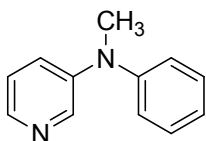
*N*-(2-methoxyphenyl)pyridin-2-amine.<sup>8</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.19 (d, *J* = 4 Hz, 1H, NH), 8.02 - 8.00 (m, 1H, Ar-H), 7.47 - 7.43 (m, 1H, Ar-H), 6.94 - 6.91 (m, 3H, Ar-H), 6.88 - 6.85 (m, 1H, Ar-H), 6.82 (d, *J* = 8 Hz, 1H, Ar-H), 6.71 - 6.68 (m, 1H, Ar-H), 3.86 (s, 3H, OCH<sub>3</sub>) ppm.



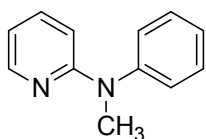
*N*-(*m*-tolyl)pyridin-3-amine.<sup>11</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.34 (s, 1H, Ar-H), 8.12 (d, *J* = 8 Hz, 1H, Ar-H), 7.39 - 7.35 (m, 1H, Ar-H), 7.18 - 7.12 (m, 2H, Ar-H), 6.87 (d, *J* = 8 Hz, 2H, Ar-H), 6.79 (d, *J* = 8 Hz, 1H, Ar-H), 5.70 (s, 1H, NH), 2.31 (s, 3H, CH<sub>3</sub>) ppm.



*N*-(2-methoxyphenyl)pyridin-3-amine.<sup>12</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.40 (d, *J* = 4 Hz, 1H, Ar-H), 8.13 (d, *J* = 4 Hz, 1H, Ar-H), 7.45 (d, *J* = 12 Hz, 1H, Ar-H), 7.22 (s, 1H, Ar-H), 7.17 - 7.14 (m, 1H, Ar-H), 6.89 - 6.86 (m, 3H, Ar-H), 6.11 (s, 1H, NH), 3.89 (s, 3H, OCH<sub>3</sub>) ppm.

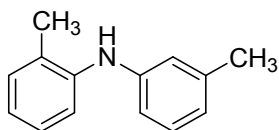


*N*-methyl-*N*-phenylpyridin-3-amine.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.27 (d, *J* = 4 Hz, 1H, Ar-H), 8.10 - 8.09 (m, 1H, Ar-H), 7.30 (t, *J* = 8 Hz, 2H, Ar-H), 7.20 - 7.17 (m, 1H, Ar-H), 7.11 (d, *J* = 8 Hz, 1H, Ar-H), 7.08 - 7.02 (m, 3H, Ar-H), 3.31 (s, 3H, CH<sub>3</sub>) ppm.

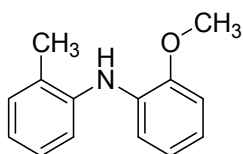


*N*-methyl-*N*-phenylpyridin-2-amine.<sup>13</sup> The product was purified with silica gel column

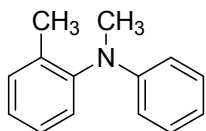
chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.19 (d, *J* = 4 Hz, 1H, Ar-H), 7.36 (t, *J* = 8 Hz, 2H, Ar-H), 7.29 - 7.22 (m, 3H, Ar-H), 7.18 (d, *J* = 8 Hz, 1H, Ar-H), 6.59 - 6.56 (m, 1H, Ar-H), 6.50 (d, *J* = 8 Hz, 1H, Ar-H), 3.46 (s, 3H, CH<sub>3</sub>) ppm.



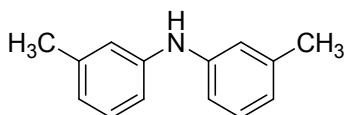
2-methyl-*N*-(*m*-tolyl)aniline.<sup>14</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.19 (d, *J* = 8 Hz, 1H, Ar-H), 7.14 (d, *J* = 4 Hz, 1H, Ar-H), 7.09 (t, *J* = 8 Hz, 2H, Ar-H), 6.88 (t, *J* = 8 Hz, 1H, Ar-H), 6.73 (d, *J* = 8 Hz, 2H, Ar-H), 6.68 (d, *J* = 8 Hz, 1H, Ar-H), 5.28 (s, 1H, NH), 2.28 (s, 3H, CH<sub>3</sub>), 2.22 (s, 3H, CH<sub>3</sub>) ppm.



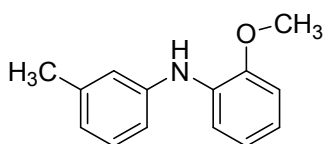
2-methoxy-*N*-(*o*-tolyl)aniline.<sup>15</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.28 (d, *J* = 8 Hz, 1H, Ar-H), 7.17 (d, *J* = 8 Hz, 1H, Ar-H), 7.13 (t, *J* = 8 Hz, 1H, Ar-H), 7.01 - 6.99 (m, 1H, Ar-H), 6.91 (t, *J* = 8 Hz, 1H, Ar-H), 6.87 - 6.76 (m, 3H, Ar-H), 5.84 (s, 1H, NH), 3.88 (s, 3H, OCH<sub>3</sub>), 2.26 (s, 3H, CH<sub>3</sub>) ppm.



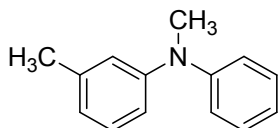
*N*,2-dimethyl-*N*-phenylaniline.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.24 (d, *J* = 8 Hz, 1H, Ar-H), 7.19 (d, *J* = 8 Hz, 1H, Ar-H), 7.16 - 7.09 (m, 4H, Ar-H), 6.67 (t, *J* = 8 Hz, 1H, Ar-H), 6.50 (d, *J* = 8 Hz, 2H, Ar-H), 3.19 (s, 3H, CH<sub>3</sub>), 2.13 (s, 3H, CH<sub>3</sub>) ppm.



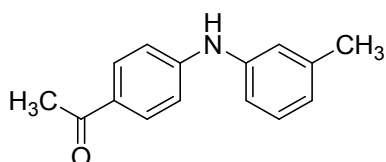
di-*m*-tolylamine.<sup>16</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.11 (t, *J* = 8 Hz, 2H, Ar-H), 6.84 (d, *J* = 8 Hz, 4H, Ar-H), 6.71 (d, *J* = 8 Hz, 2H, Ar-H), 5.55 (s, 1H, NH), 2.29 (s, 6H, CH<sub>3</sub>) ppm.



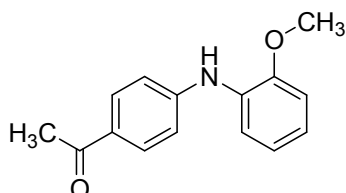
2-methoxy-*N*-(*m*-tolyl)aniline.<sup>14</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.28 - 7.25 (m, 1H, Ar-H), 7.13 (t, *J* = 8 Hz, 1H, Ar-H), 6.94 (s, 2H, Ar-H), 6.86 - 6.80 (m, 3H, Ar-H), 6.73 (d, *J* = 8 Hz, 1H, Ar-H), 6.08 (s, 1H, NH), 3.85 (s, 3H, OCH<sub>3</sub>), 2.30 (s, 3H, CH<sub>3</sub>) ppm.



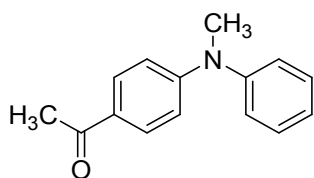
*N*,3-dimethyl-*N*-phenylaniline.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.24 - 7.18 (m, 2H, Ar-H), 7.13 (t, *J* = 8 Hz, 1H, Ar-H), 6.94 (d, *J* = 8 Hz, 2H, Ar-H), 6.90 (t, *J* = 8 Hz, 1H, Ar-H), 6.81 (d, *J* = 8 Hz, 2H, Ar-H), 6.75 (d, *J* = 4 Hz, 1H, Ar-H), 3.27 (s, 3H, CH<sub>3</sub>), 2.28 (s, 3H, CH<sub>3</sub>) ppm.



1-(4-(*m*-tolylamino)phenyl)ethanone.<sup>15</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.83 (d, *J* = 8 Hz, 2H, Ar-H), 7.23 - 7.18 (m, 1H, Ar-H), 6.97 - 6.93 (m, 4H, Ar-H), 6.87 (d, *J* = 8 Hz, 1H, Ar-H), 6.07 (s, 1H, NH), 2.52 (s, 3H, COCH<sub>3</sub>), 2.34 (s, 3H, CH<sub>3</sub>) ppm.

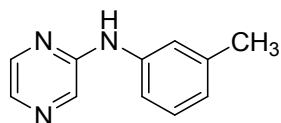


1-(4-((2-methoxyphenyl)amino)phenyl)ethanone. The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.84 (d, *J* = 8 Hz, 2H, Ar-H), 7.37 (d, *J* = 8 Hz, 1H, Ar-H), 7.04 (d, *J* = 8 Hz, 2H, Ar-H), 6.99 - 6.88 (m, 3H, Ar-H), 6.41 (s, 1H, NH), 3.85 (s, 3H, OCH<sub>3</sub>), 2.52 (s, 3H, COCH<sub>3</sub>) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 196.11 (CO), 149.55, 147.72, 130.21, 129.85, 128.59, 122.36, 120.40, 118.02, 114.57, 110.72 (Ar), 55.27 (COCH<sub>3</sub>), 25.80 (CH<sub>3</sub>) ppm. HRMS (ESI): [M+H]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub>: 242.1175. found: 242.1167.

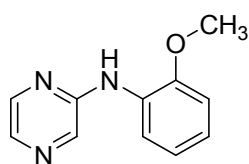


1-(4-(methyl(phenyl)amino)phenyl)ethanone.<sup>17</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.79

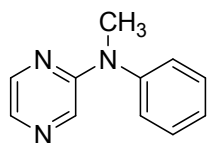
(d,  $J = 8$  Hz, 2H, Ar-H), 7.38 (d,  $J = 8$  Hz, 2H, Ar-H), 7.23 - 7.18 (m, 3H, Ar-H), 6.73 (d,  $J = 8$  Hz, 2H, Ar-H), 3.36 (s, 3H, CH<sub>3</sub>), 2.50 (s, 3H, CO-CH<sub>3</sub>) ppm.



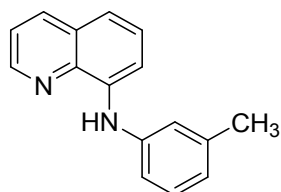
*N*-(*m*-tolyl)pyrazin-2-amine. The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 30 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.20 (s, 1H, NH), 8.05 (d,  $J = 4$  Hz, 1H, Ar-H), 7.91 (d,  $J = 4$  Hz, 1H, Ar-H), 7.23 - 7.09 (m, 4H, Ar-H), 6.88 (t,  $J = 4$  Hz, 1H, Ar-H), 2.33 (s, 3H, CH<sub>3</sub>) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 152.52, 141.64, 139.20, 138.92, 133.84, 132.96, 128.88, 124.00, 120.62, 117.11 (Ar), 21.28 (CH<sub>3</sub>) ppm. HRMS (ESI): [M+H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>: 186.1025. found: 186.1023.



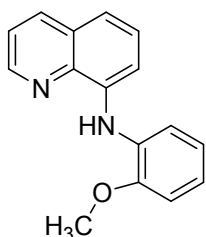
*N*-(2-methoxyphenyl)pyrazin-2-amine. The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 30 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.21 - 8.18 (m, 2H, Ar-H), 8.09 (d,  $J = 4$  Hz, 1H, Ar-H), 7.92 (s, 1H, NH), 7.09 (s, 1H, Ar-H), 6.99 - 6.94 (m, 2H, Ar-H), 6.90 - 6.88 (m, 1H, Ar-H), 3.90 (s, 3H, OCH<sub>3</sub>) ppm. <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 151.81, 148.27, 141.19, 134.09, 128.78, 122.08, 120.61, 118.35, 109.93 (Ar), 55.30 (OCH<sub>3</sub>) ppm. HRMS (ESI): [M+H]<sup>+</sup> Calcd for C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O: 202.0974. found: 202.0970.



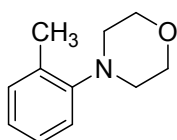
*N*-methyl-*N*-phenylpyrazin-2-amine.<sup>18</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 30 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.05 (d,  $J = 4$  Hz, 1H, Ar-H), 7.91 (s, 1H, Ar-H), 7.79 (s, 1H, Ar-H), 7.41 (t,  $J = 8$  Hz, 2H, Ar-H), 7.27 - 7.23 (m, 3H, Ar-H), 3.44 (s, 3H, CH<sub>3</sub>) ppm.



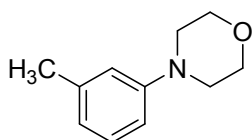
*N*-(*m*-tolyl)quinolin-8-amine.<sup>9</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.71 (s, 1H, NH), 8.19 (s, 1H, Ar-H), 8.04 - 8.01 (m, 1H, Ar-H), 7.45 - 7.43 (m, 1H, Ar-H), 7.36 - 7.32 (m, 2H, Ar-H), 7.23 - 7.14 (m, 4H, Ar-H), 6.82 (d,  $J = 8$  Hz, 1H, Ar-H), 2.35 (s, 3H, CH<sub>3</sub>) ppm.



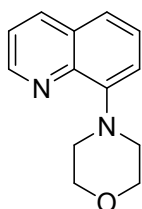
*N*-(2-methoxyphenyl)quinolin-8-amine. The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.79 (d, *J* = 8 Hz, 1H, Ar-H), 8.49 (s, 1H, NH), 8.08 - 8.06 (dd, *J* = 8 Hz, 1H, Ar-H), 7.63 (t, *J* = 4 Hz, 1H, Ar-H), 7.52 (d, *J* = 8 Hz, 1H, Ar-H), 7.40 - 7.36 (m, 2H, Ar-H), 7.19 (t, *J* = 8 Hz, 1H, Ar-H), 6.97 - 6.94 (m, 3H, Ar-H), 3.93 (s, 3H, OCH<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 149.55, 146.93, 139.21, 138.58, 135.51, 130.87, 128.35, 126.69, 120.93, 120.81, 120.08, 116.65, 116.09, 110.22, 107.57 (Ar), 55.10 (OCH<sub>3</sub>) ppm. HRMS (ESI): [M+H]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O: 251.1178. found: 251.1177.



4-(*o*-tolyl)morpholine.<sup>19</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 30 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.14 (t, *J* = 4 Hz, 2H, Ar-H), 6.99 - 6.95 (m, 2H, Ar-H), 3.82 (t, *J* = 4 Hz, 4H, CH<sub>2</sub>), 2.89 (t, *J* = 4 Hz, 4H, CH<sub>2</sub>), 2.30 (s, 3H, CH<sub>3</sub>) ppm.

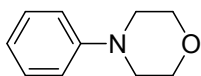


4-(*m*-tolyl)morpholine.<sup>20</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 30 : 1 to 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.13 (t, *J* = 8 Hz, 1H, Ar-H), 6.68 (t, *J* = 8 Hz, 3H, Ar-H), 3.82 (t, *J* = 8 Hz, 4H, CH<sub>2</sub>), 3.12 (t, *J* = 8 Hz, 4H, CH<sub>2</sub>), 2.31 (s, 3H, CH<sub>3</sub>) ppm.

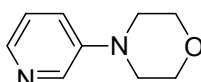


4-(quinolin-8-yl)morpholine.<sup>22</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.85 - 8.84 (dd, *J* = 4 Hz, 1H, Ar-H), 8.10 - 8.08 (dd, *J* = 8 Hz, 1H, Ar-H), 7.43 - 7.40 (m, 2H, Ar-H),

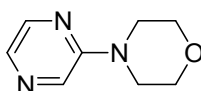
7.37 - 7.33 (m, 1H, Ar-H), 7.11 (t,  $J = 4$  Hz, 1H, Ar-H), 4.04 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>), 3.41 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>), 1.81 (s, 3H, CH<sub>3</sub>) ppm.



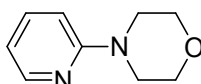
4-phenylmorpholine.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 50 : 1 to 30 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.27 - 7.22 (m, 2H, Ar-H), 6.90 - 6.84 (m, 3H, Ar-H), 3.85 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>), 3.14 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>) ppm.



4-(pyridin-3-yl)morpholine.<sup>23</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 5 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.26 (s, 1H, Ar-H), 8.09 (t,  $J = 4$  Hz, 1H, Ar-H), 7.14 (d,  $J = 4$  Hz, 2H, Ar-H), 3.85 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>), 3.17 (t,  $J = 4$  Hz, 4H, CH<sub>2</sub>) ppm.

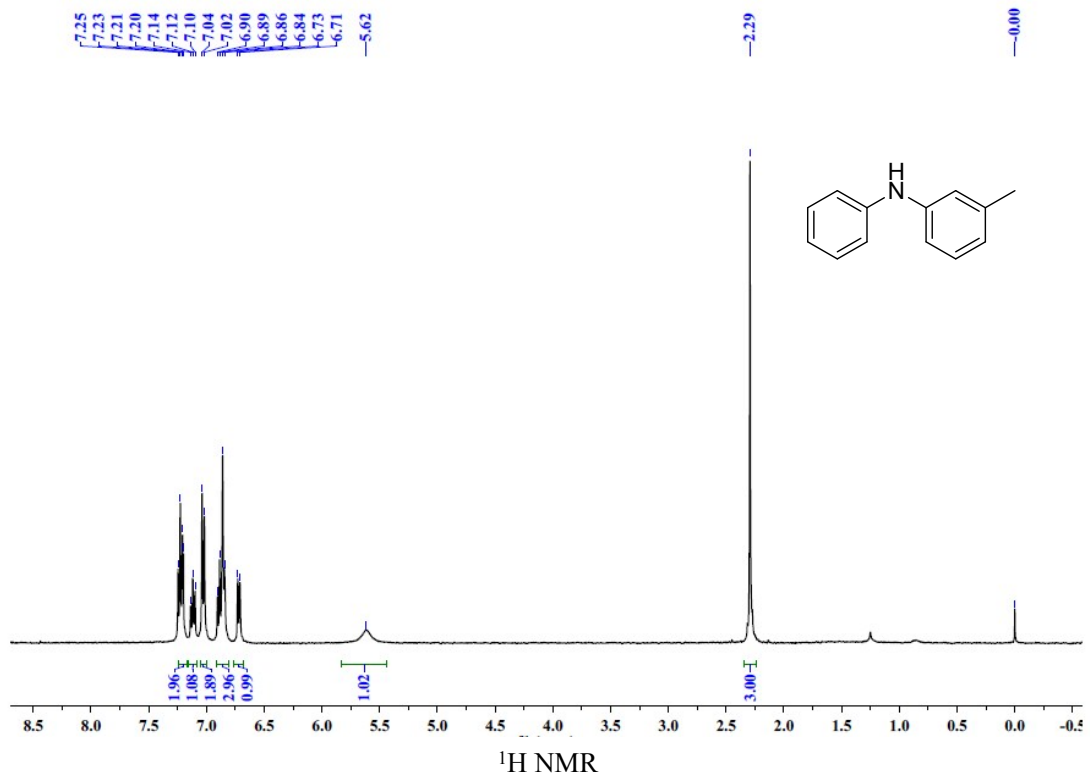
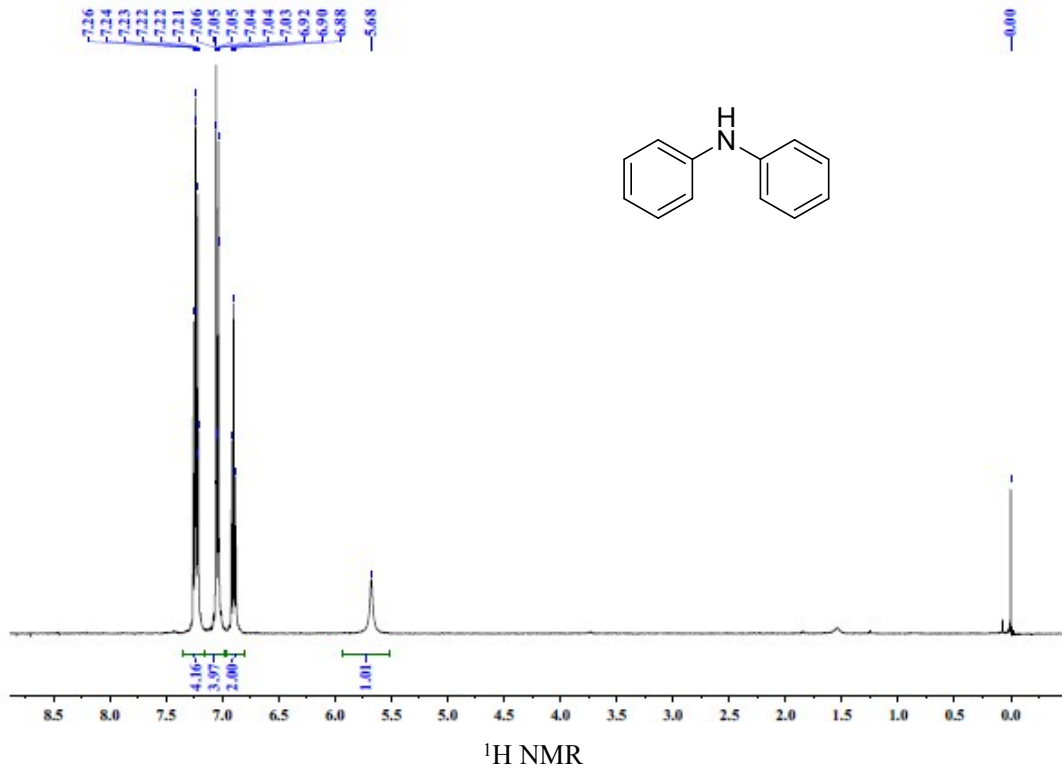


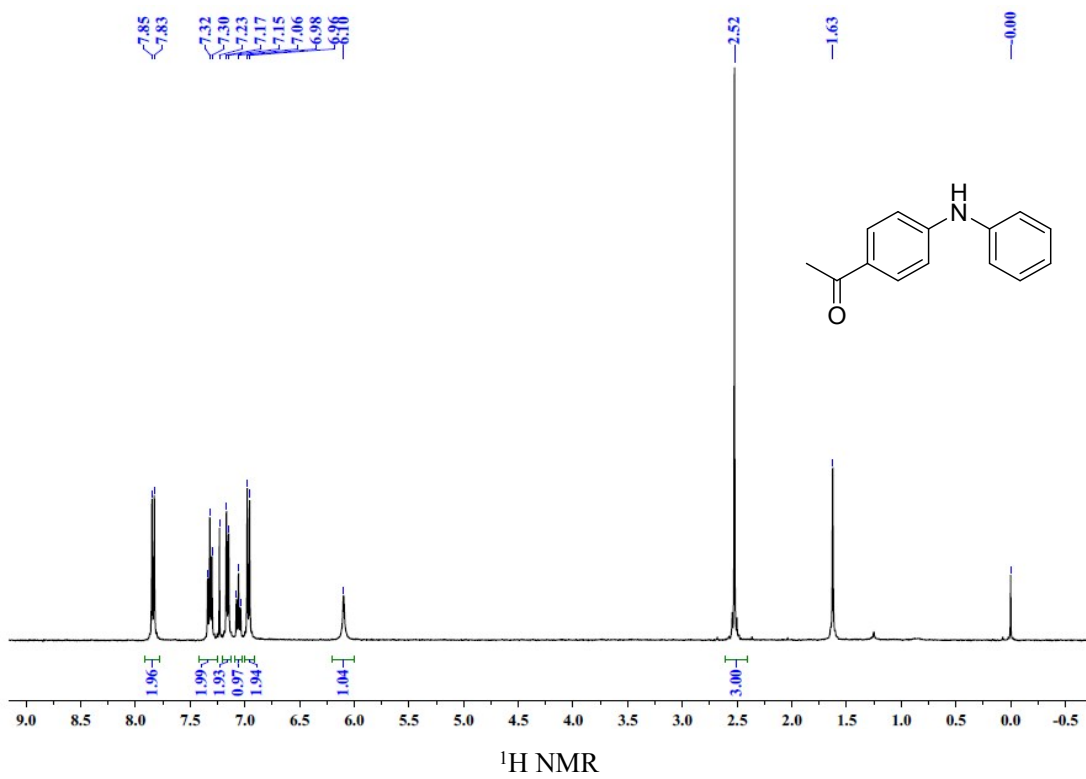
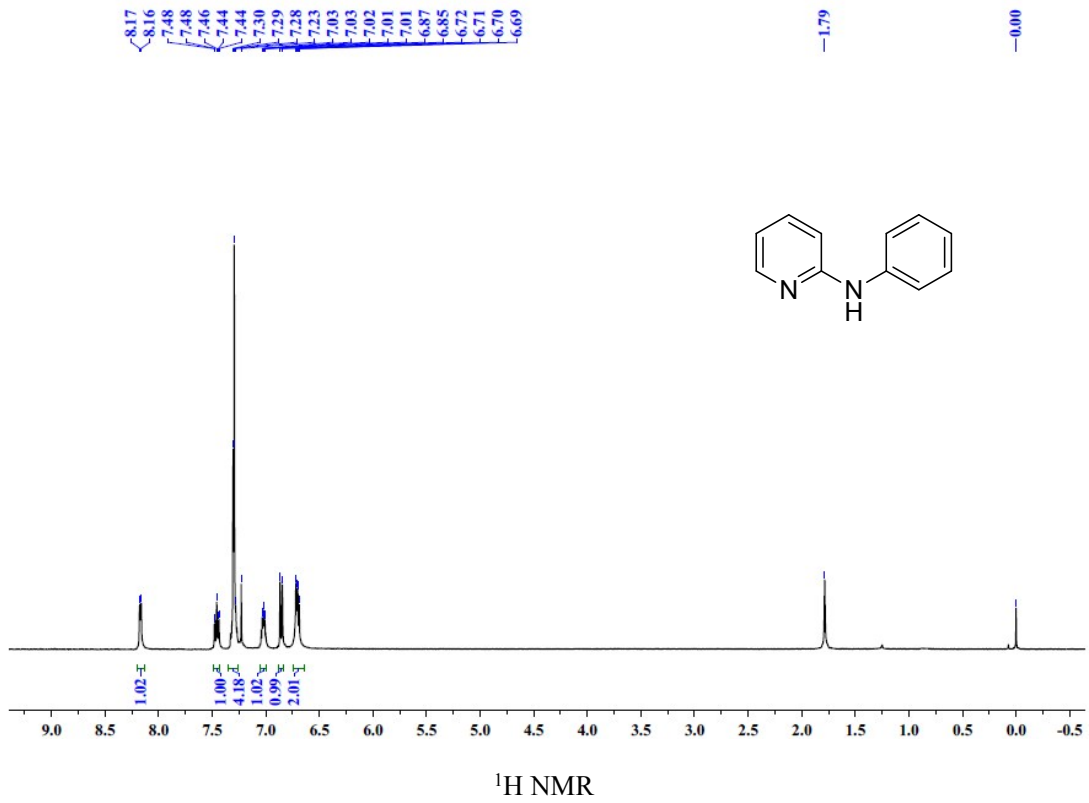
4-(pyrazin-2-yl)morpholine.<sup>18</sup> The product was purified with silica gel column chromatography (Petroleum ether : Ethyl acetate = 10 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.10 (d,  $J = 0.8$  Hz, 1H, Ar-H), 8.06 - 8.05 (m, 1H, Ar-H), 7.86 (d,  $J = 0.8$  Hz, 1H, Ar-H), 3.82 (t,  $J = 4$  Hz, 4H, O-CH<sub>2</sub>), 3.55 (t,  $J = 4$  Hz, 4H, N-CH<sub>2</sub>) ppm.

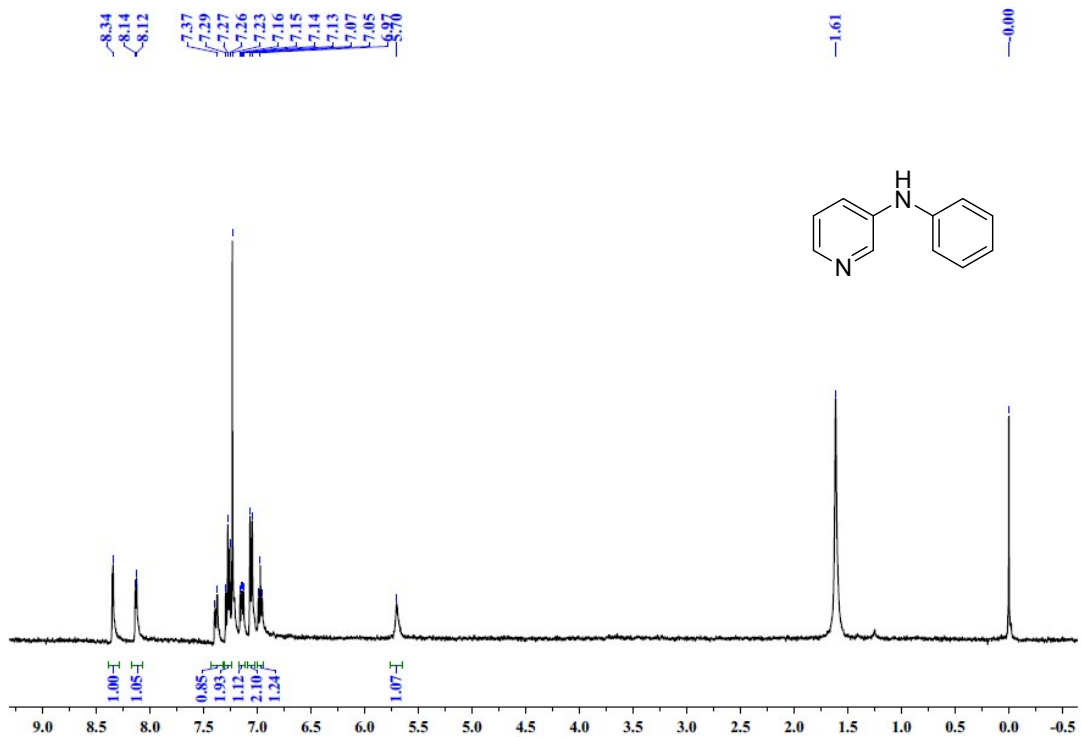


4-(pyridin-2-yl)morpholine.<sup>3</sup> The product was purified with silica gel column chromatography (Petroleum ether : CH<sub>2</sub>Cl<sub>2</sub> = 20 : 1). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.16 (d,  $J = 4$  Hz, 1H, Ar-H), 7.48 - 7.44 (m, 1H, Ar-H), 6.64 - 6.59 (m, 2H, Ar-H), 3.80 (t,  $J = 8$  Hz, 4H, CH<sub>2</sub>), 3.48 (t,  $J = 8$  Hz, 4H, CH<sub>2</sub>) ppm.

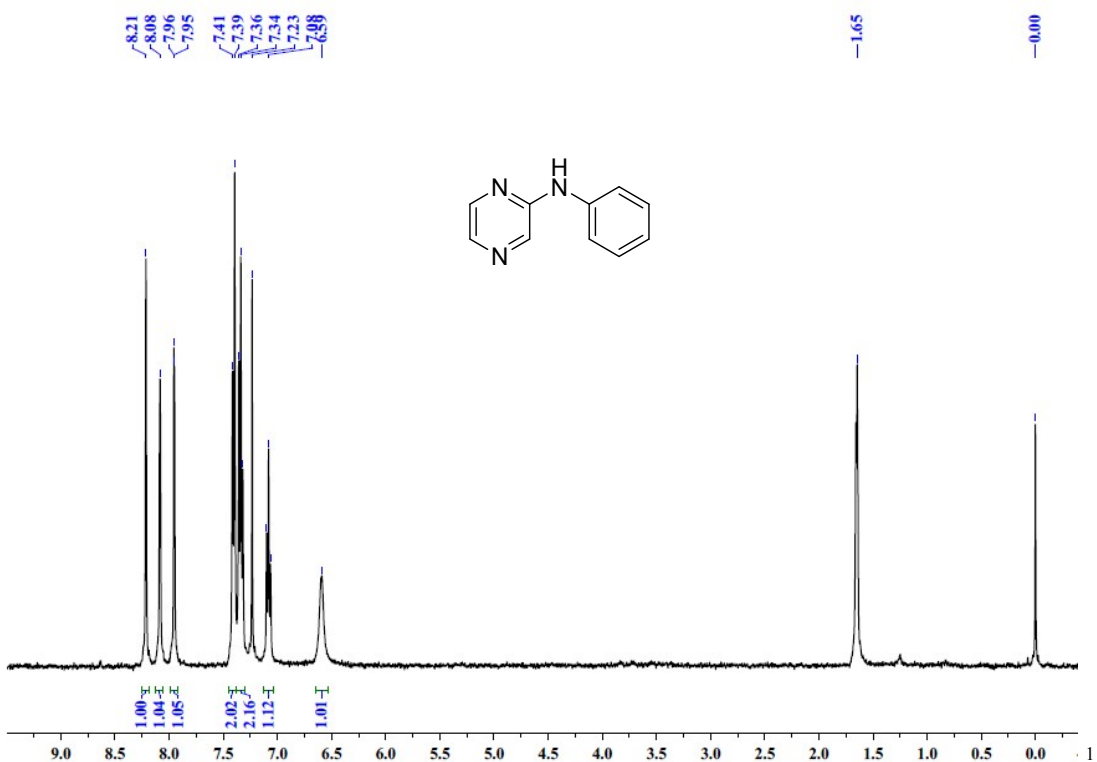




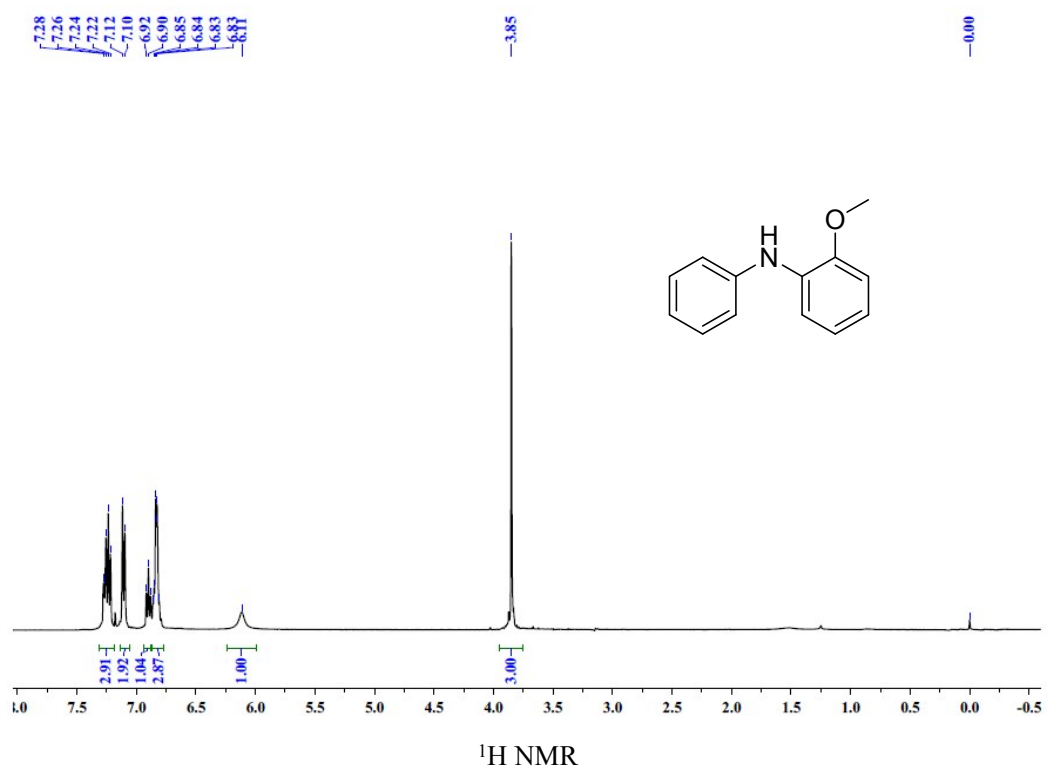
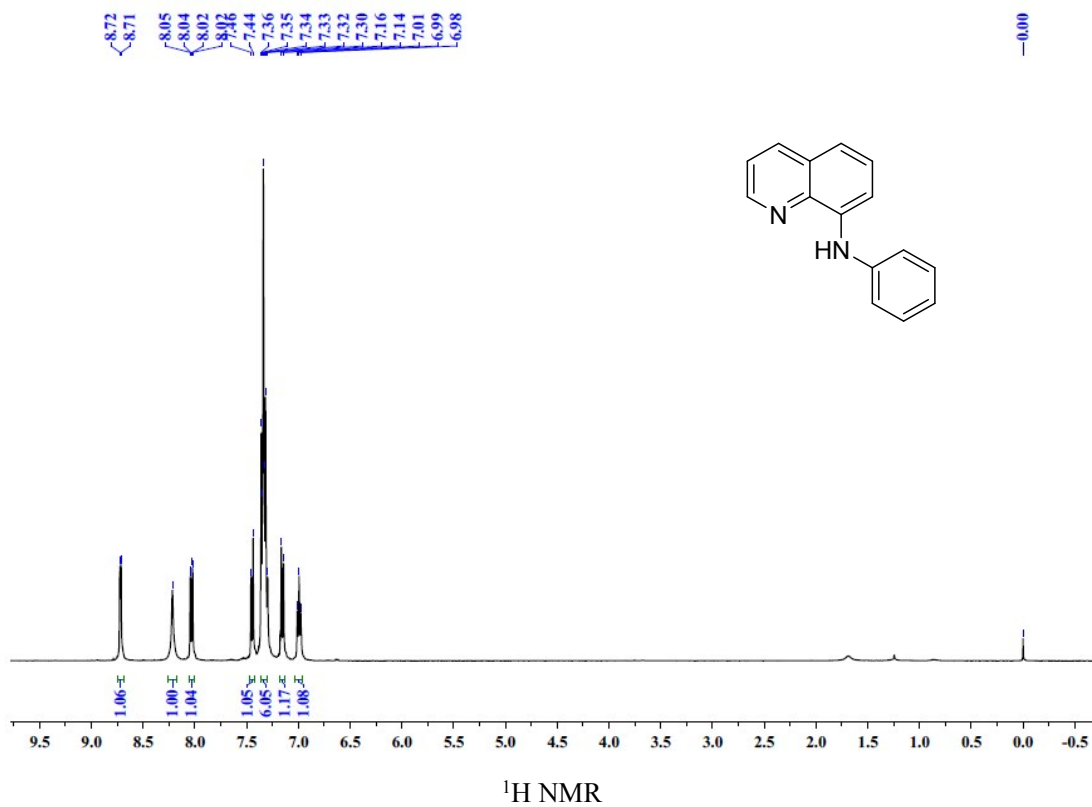


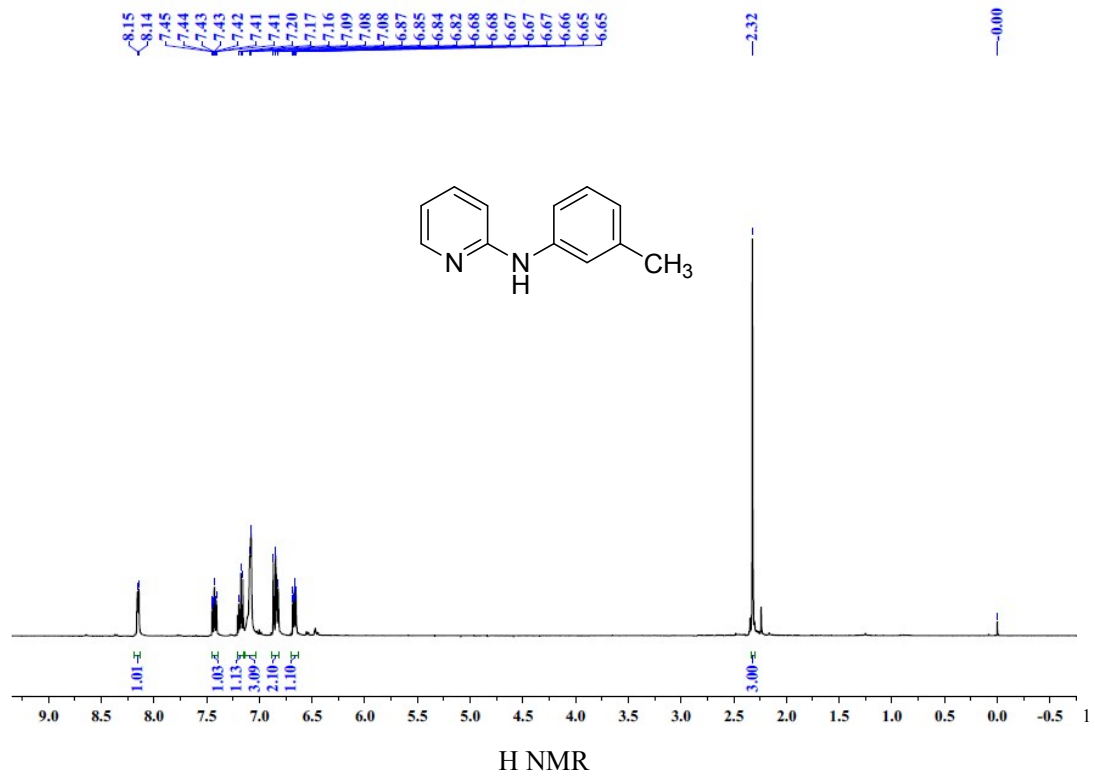
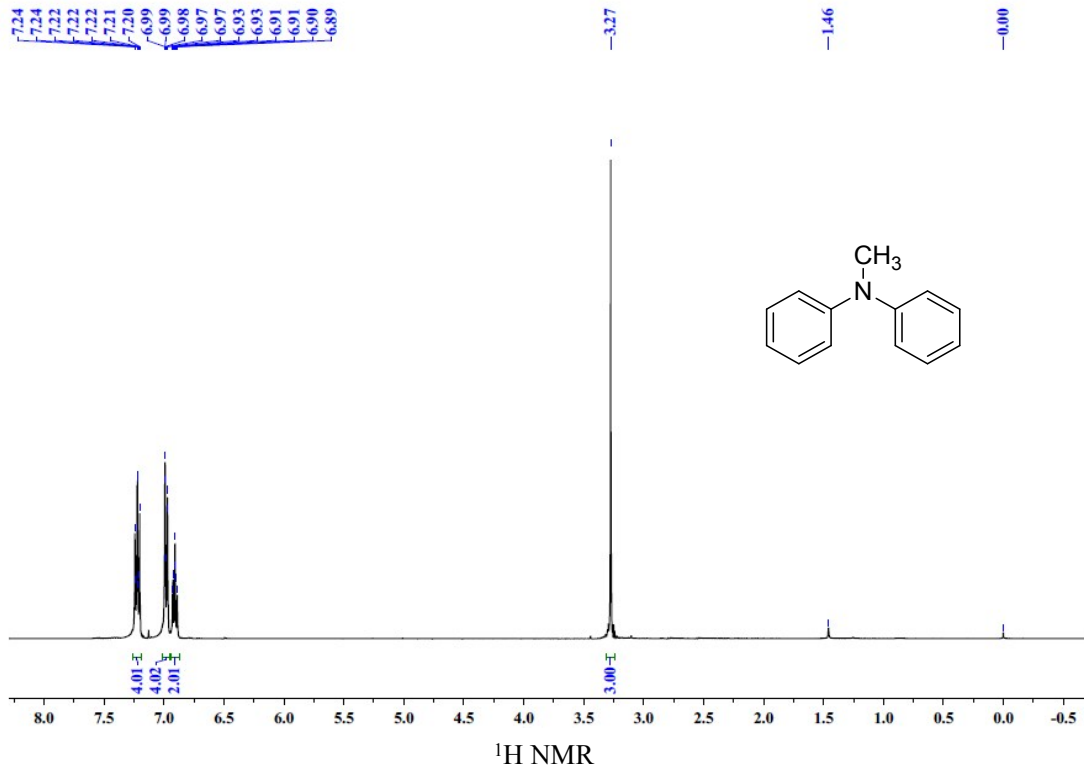


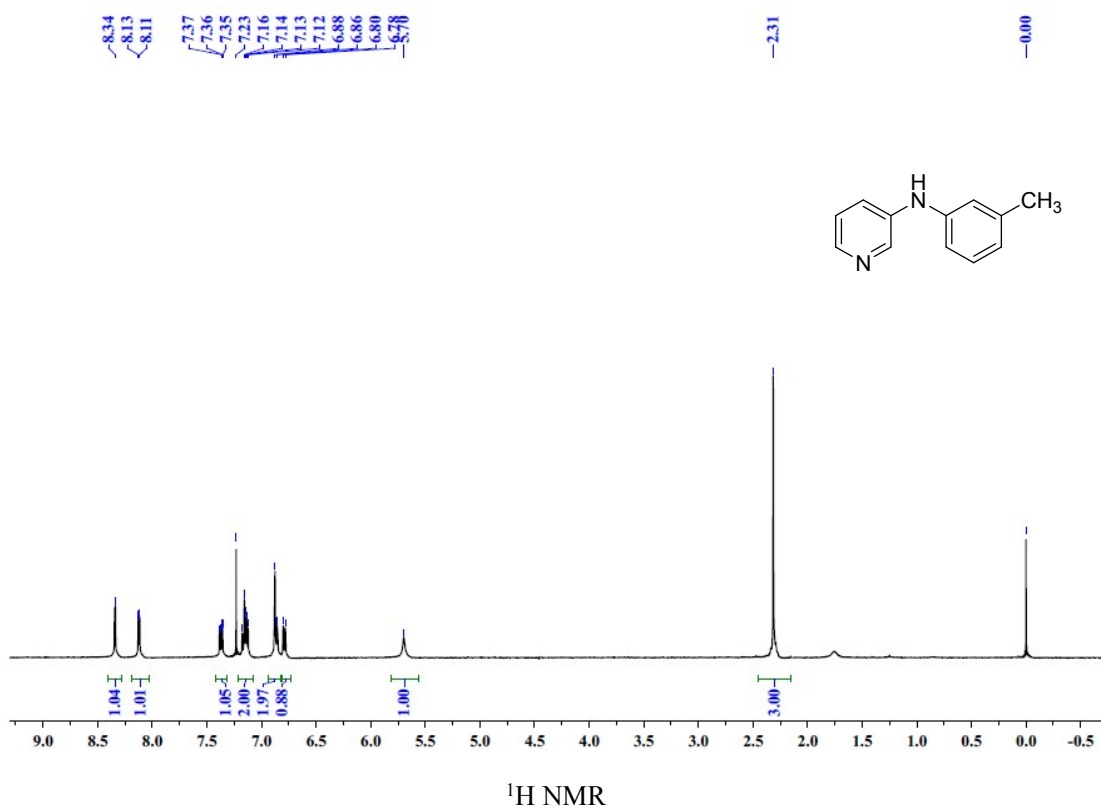
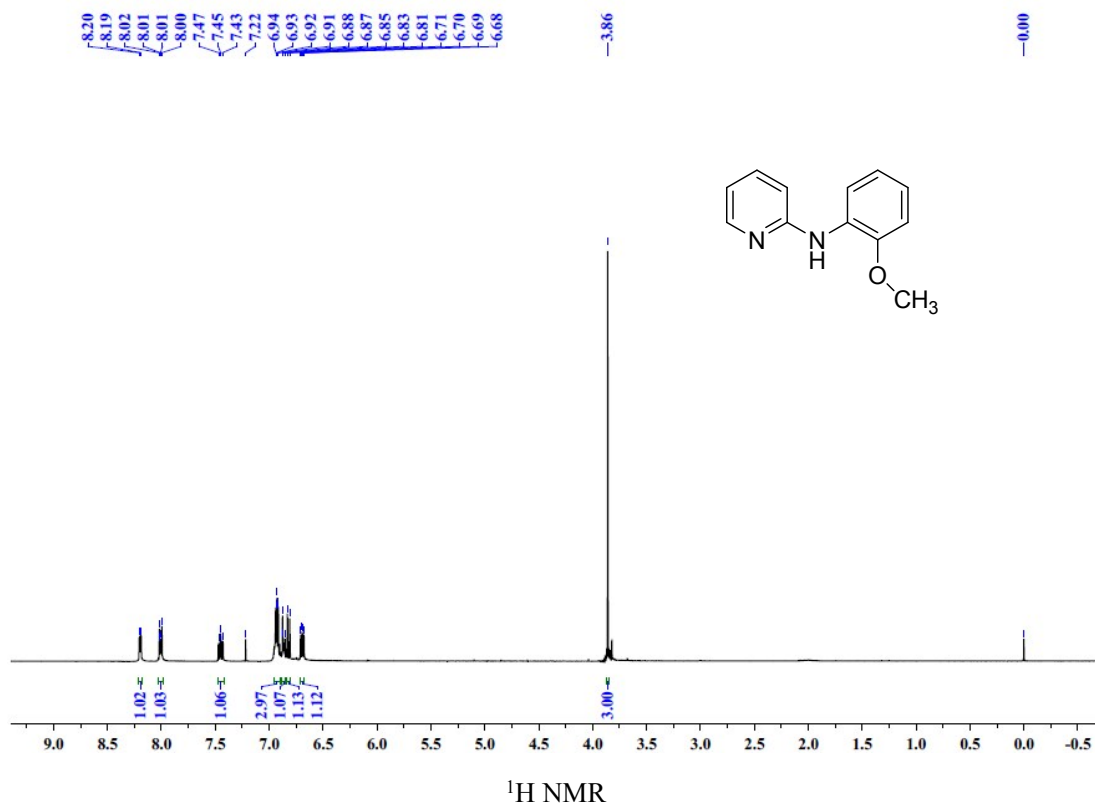
<sup>1</sup>H NMR

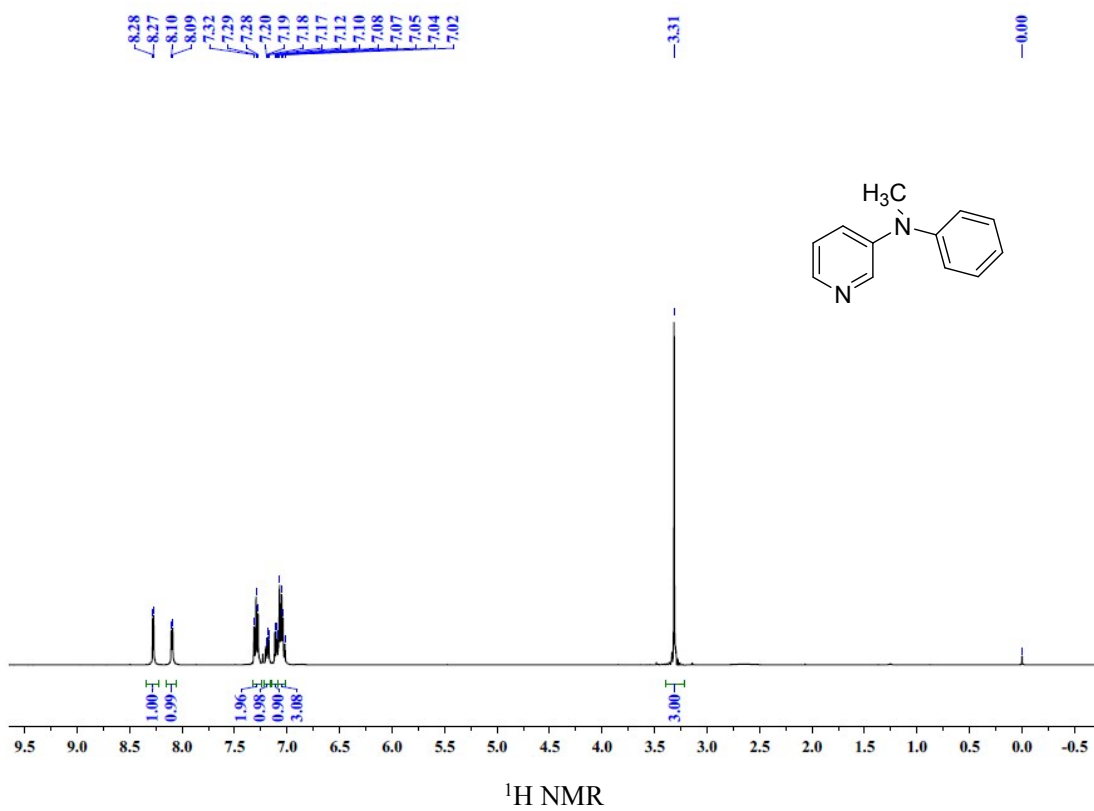
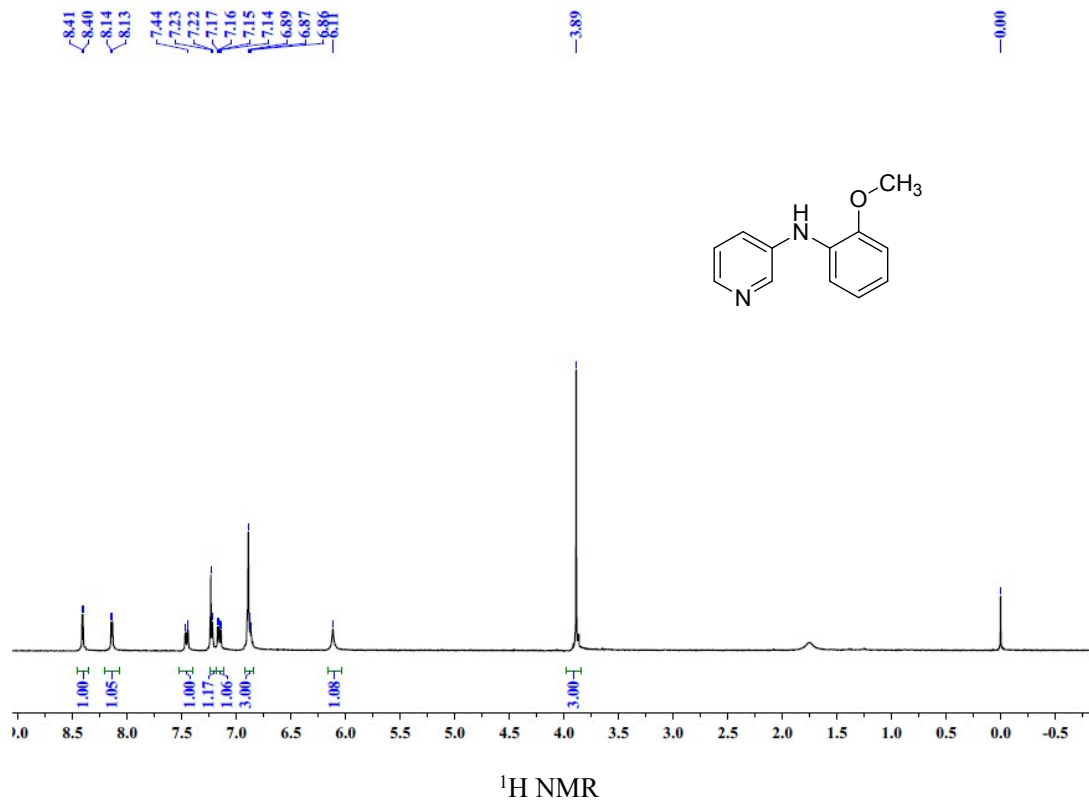


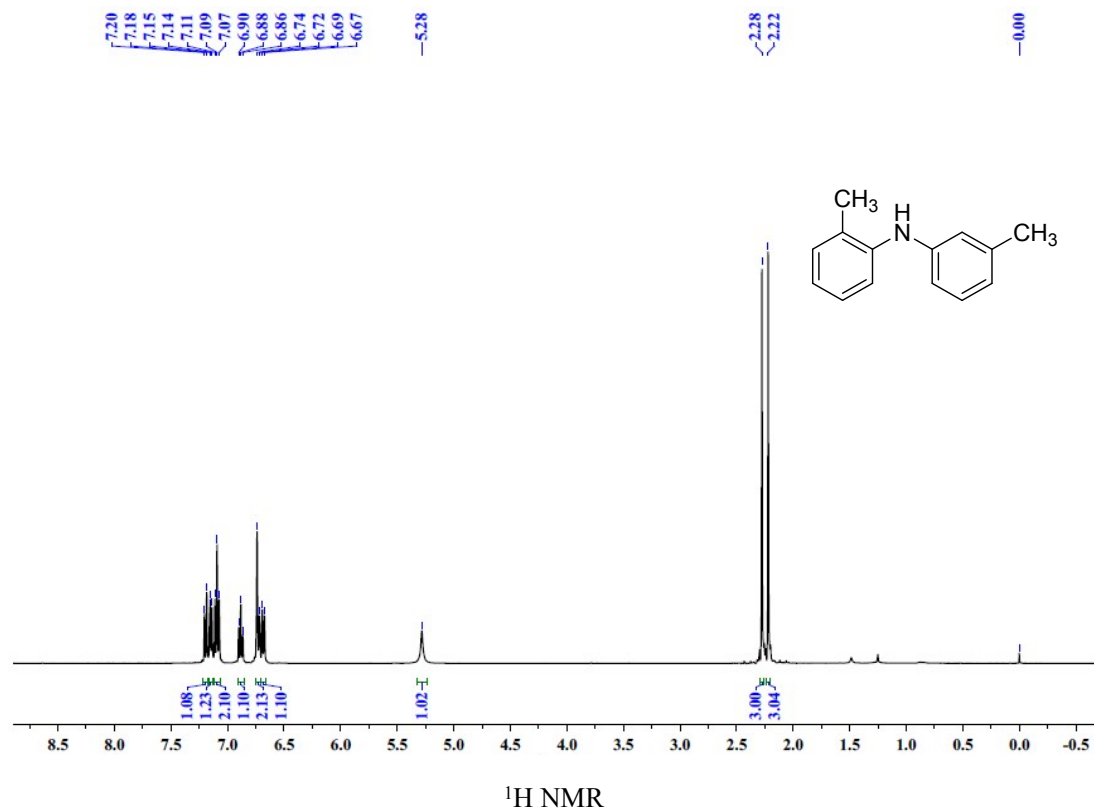
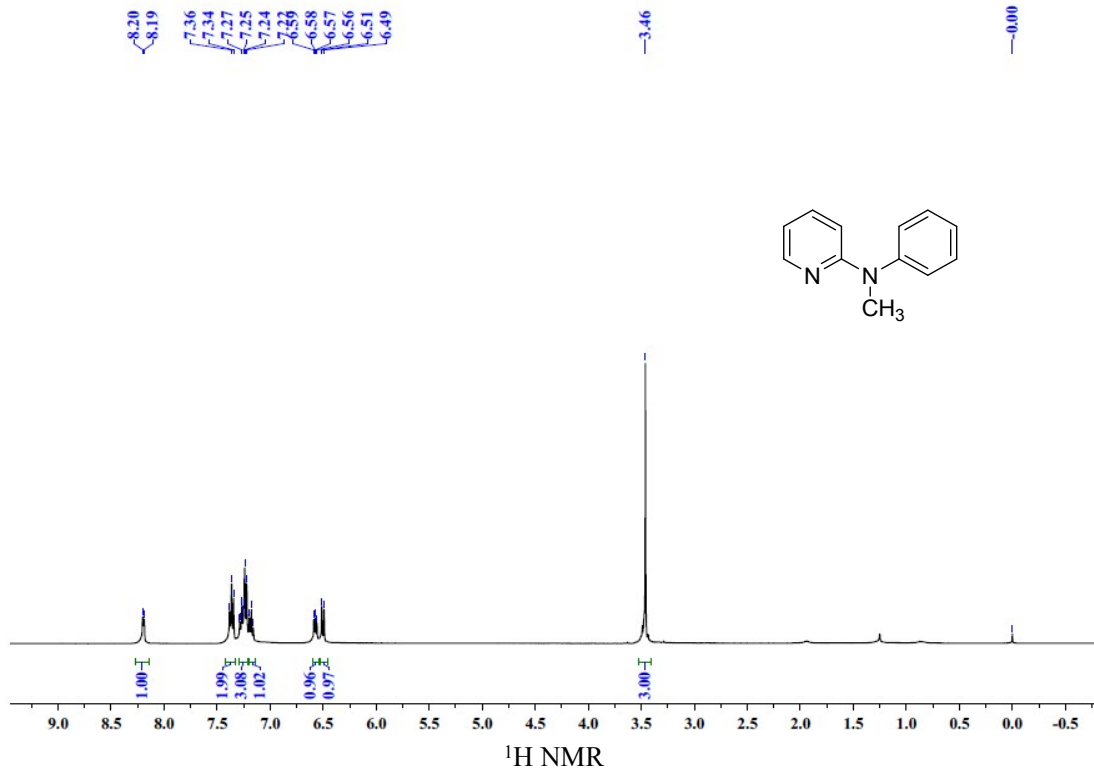
<sup>1</sup>H NMR



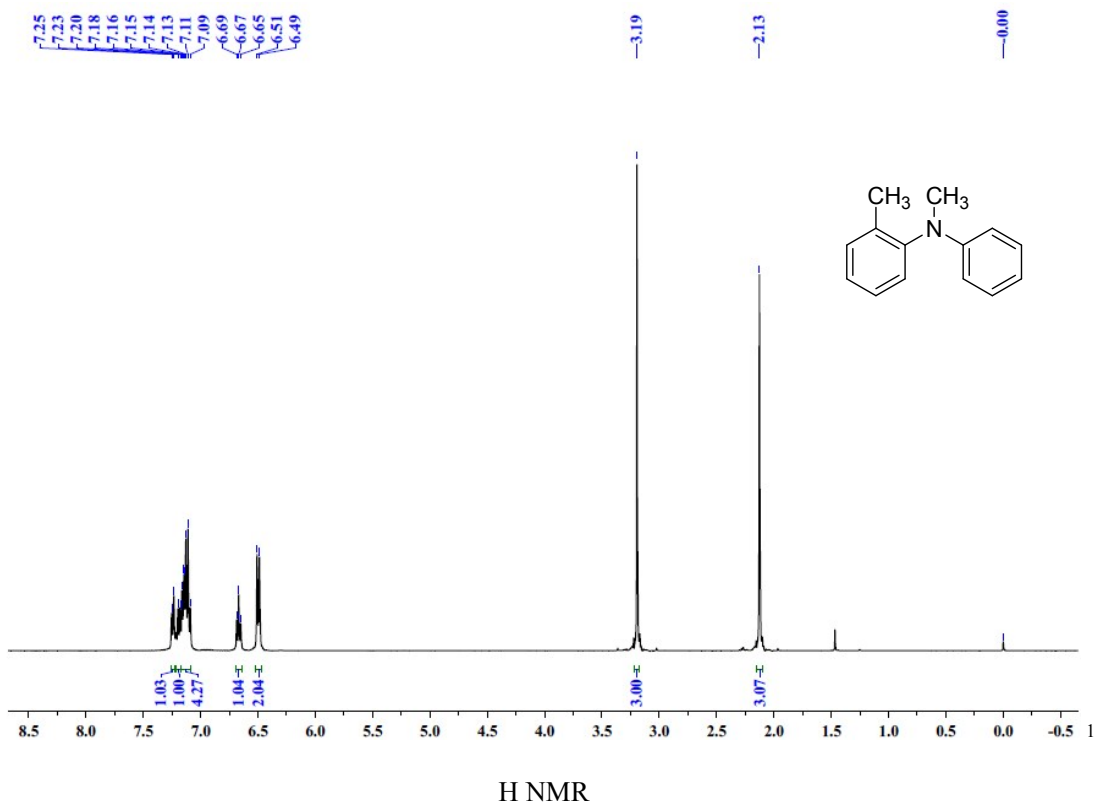
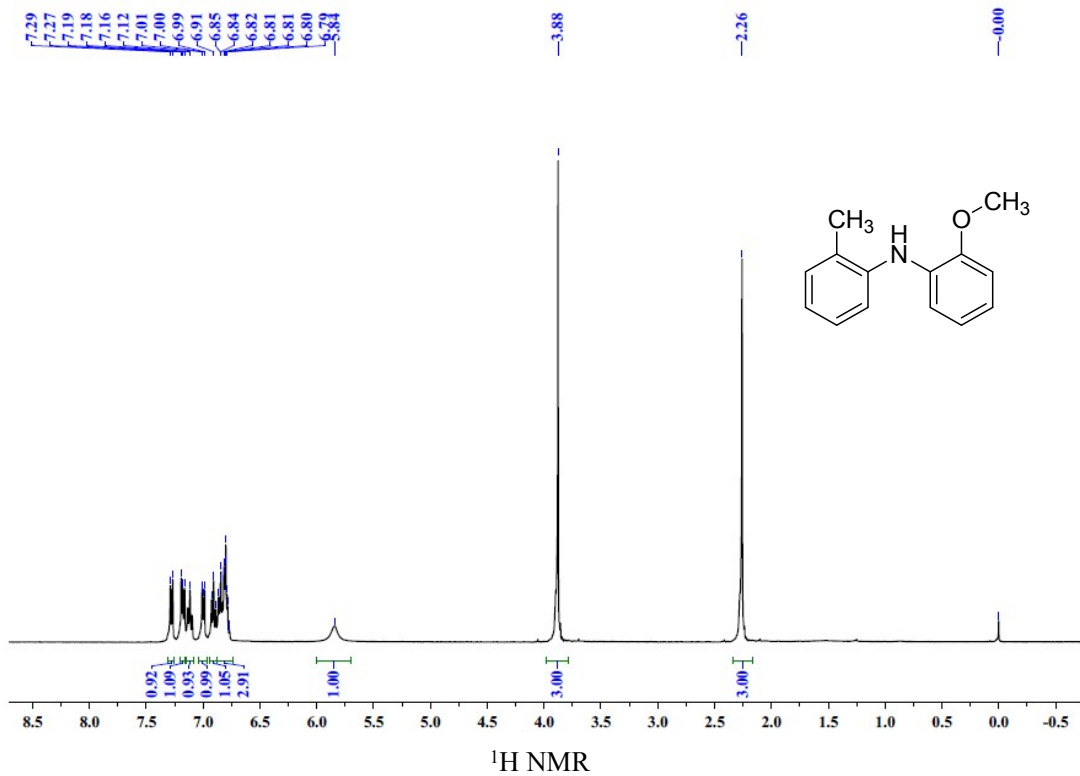


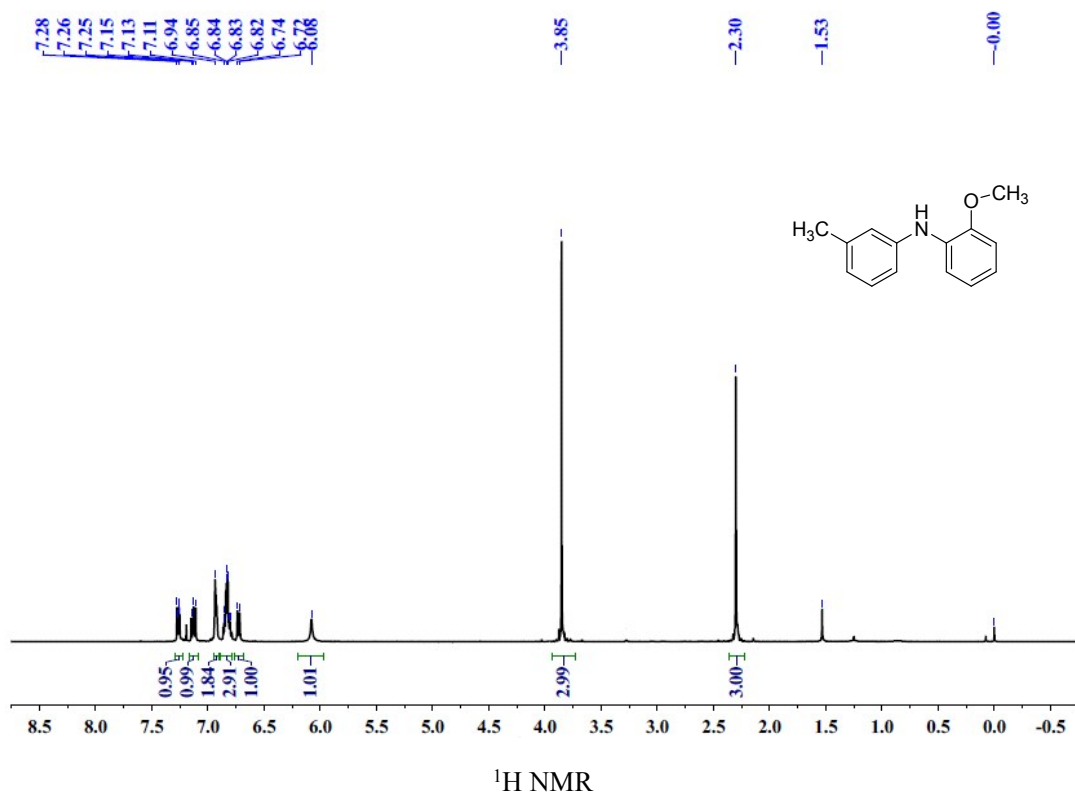
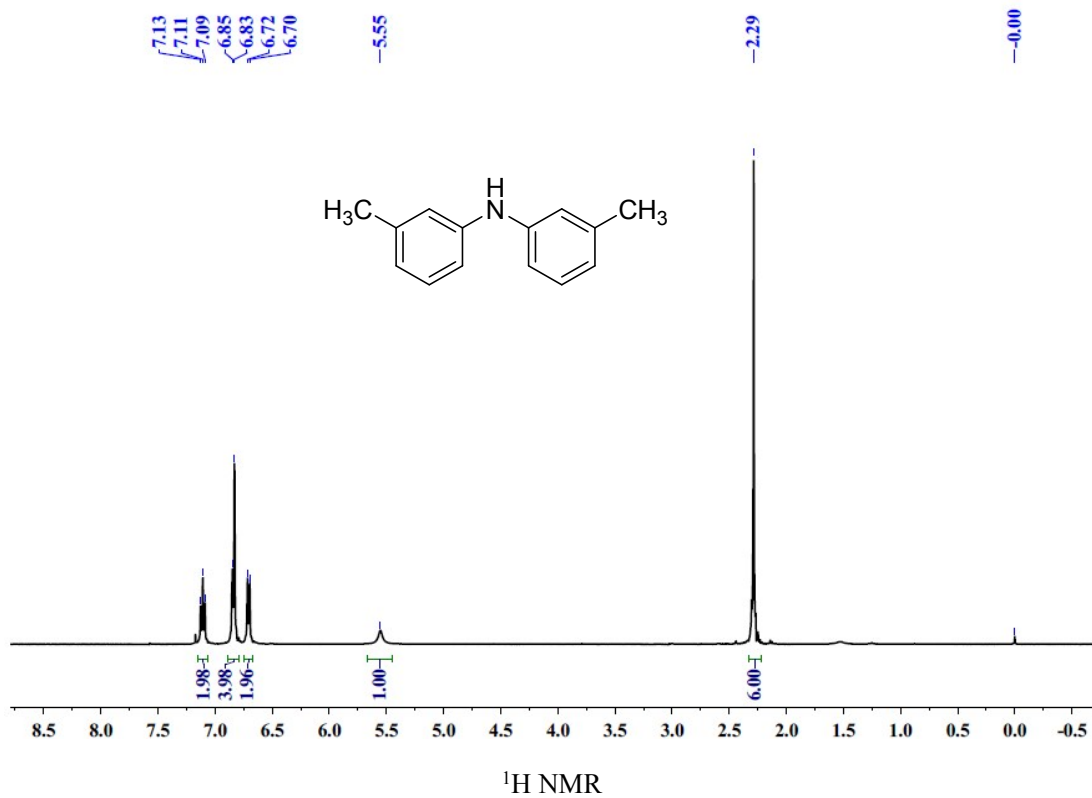


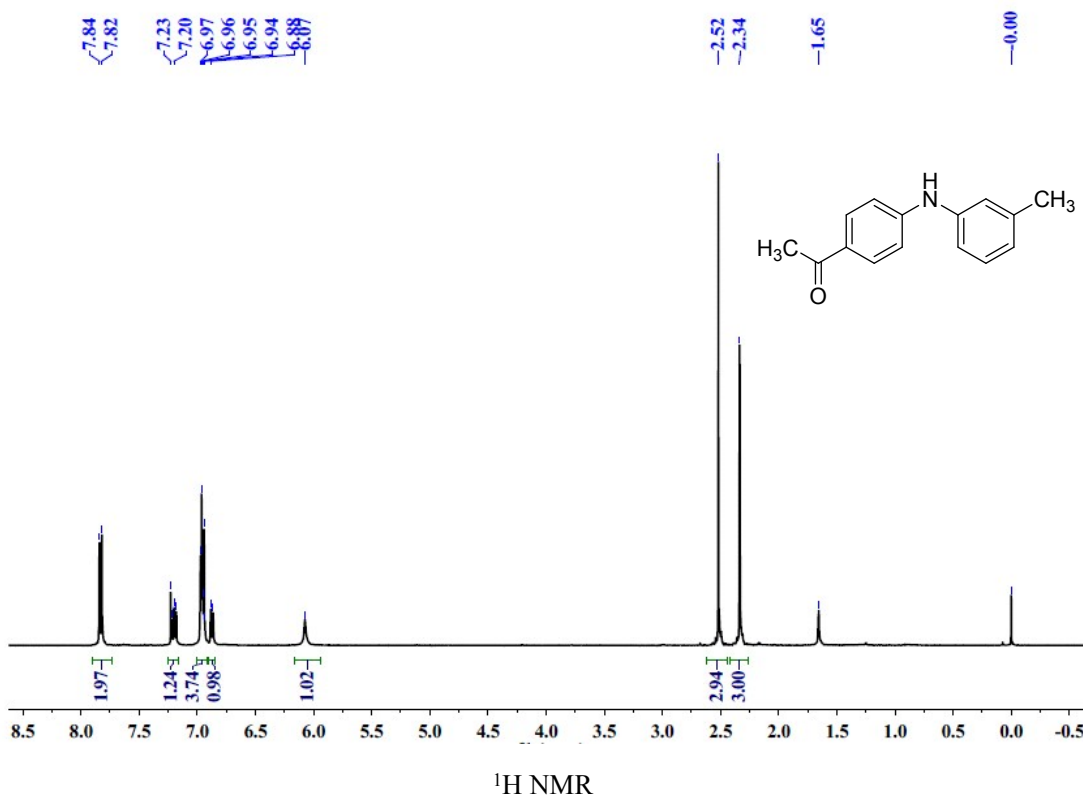
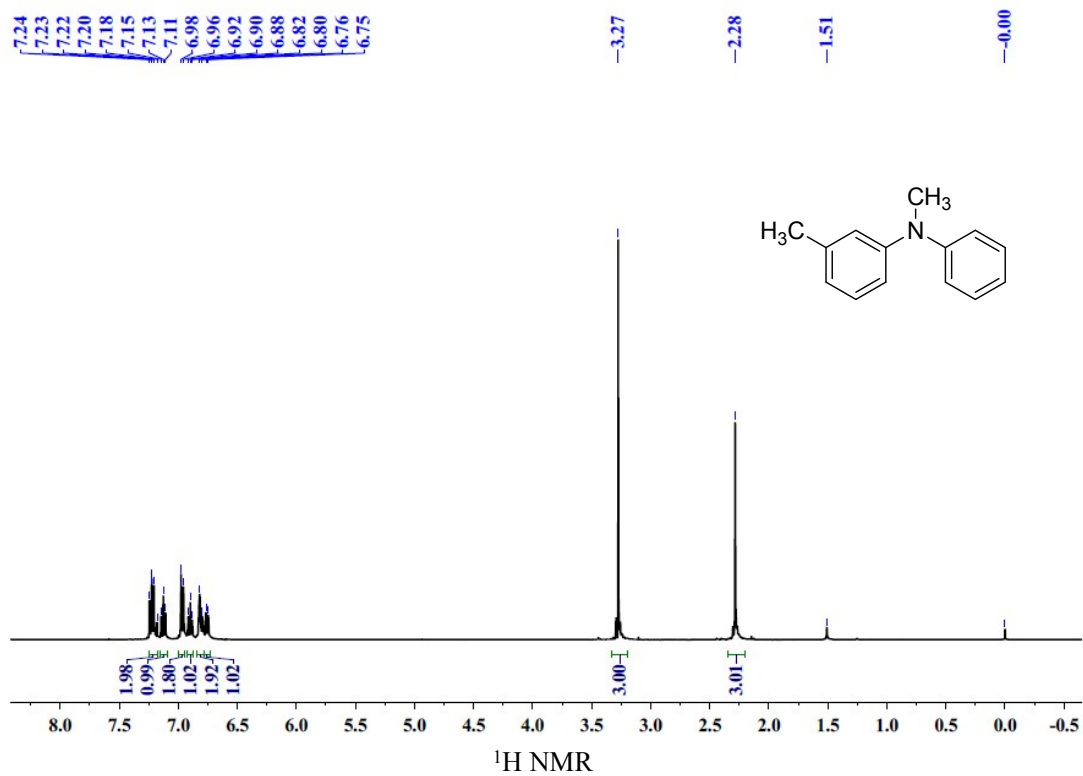


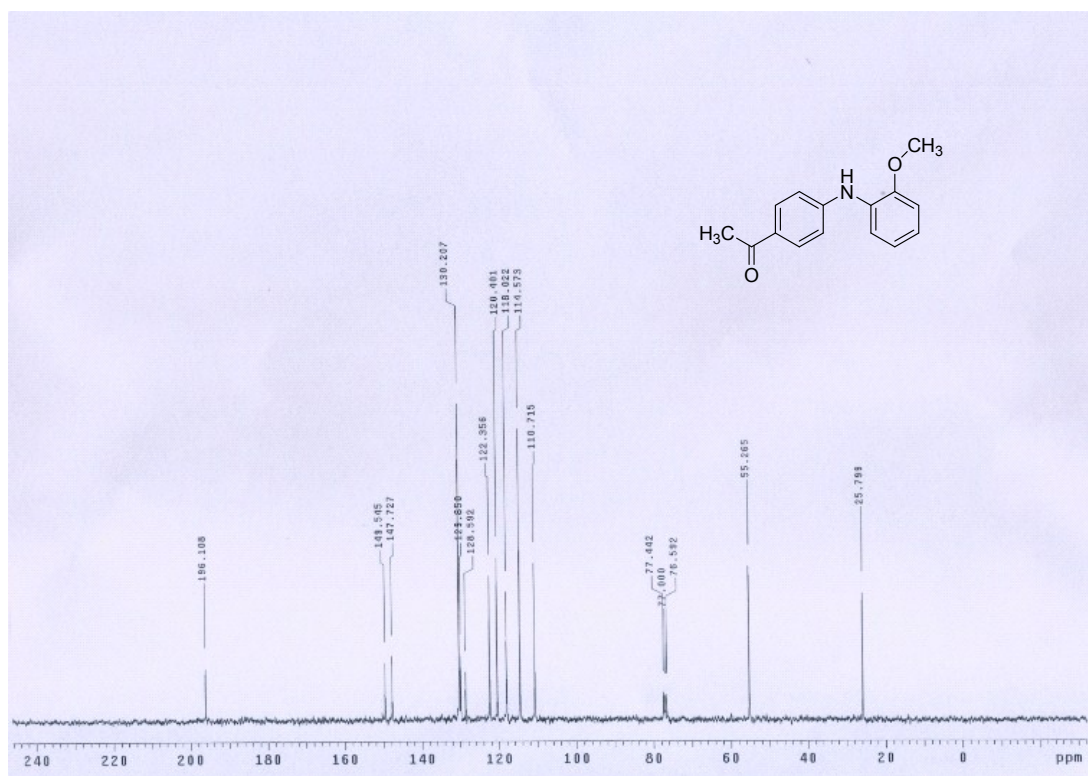
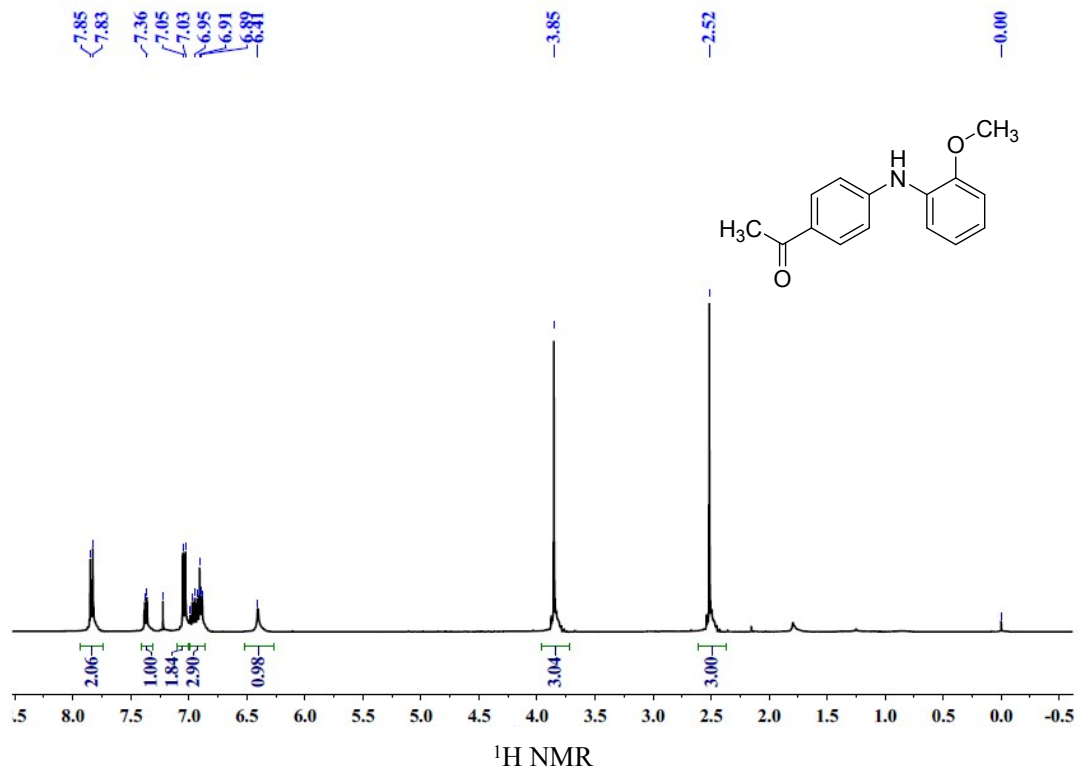


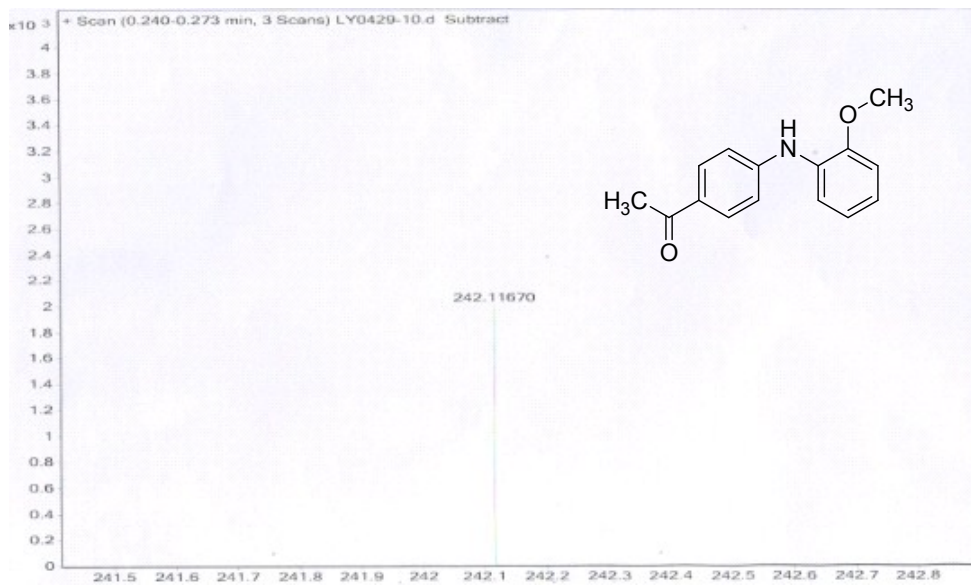




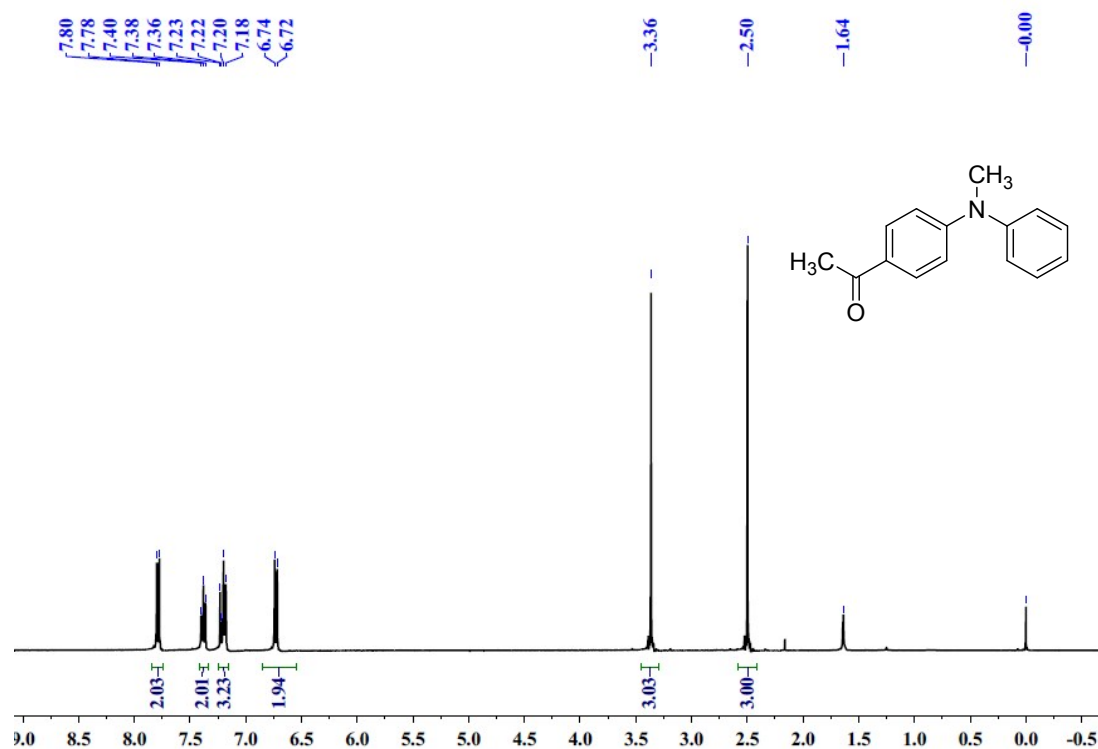




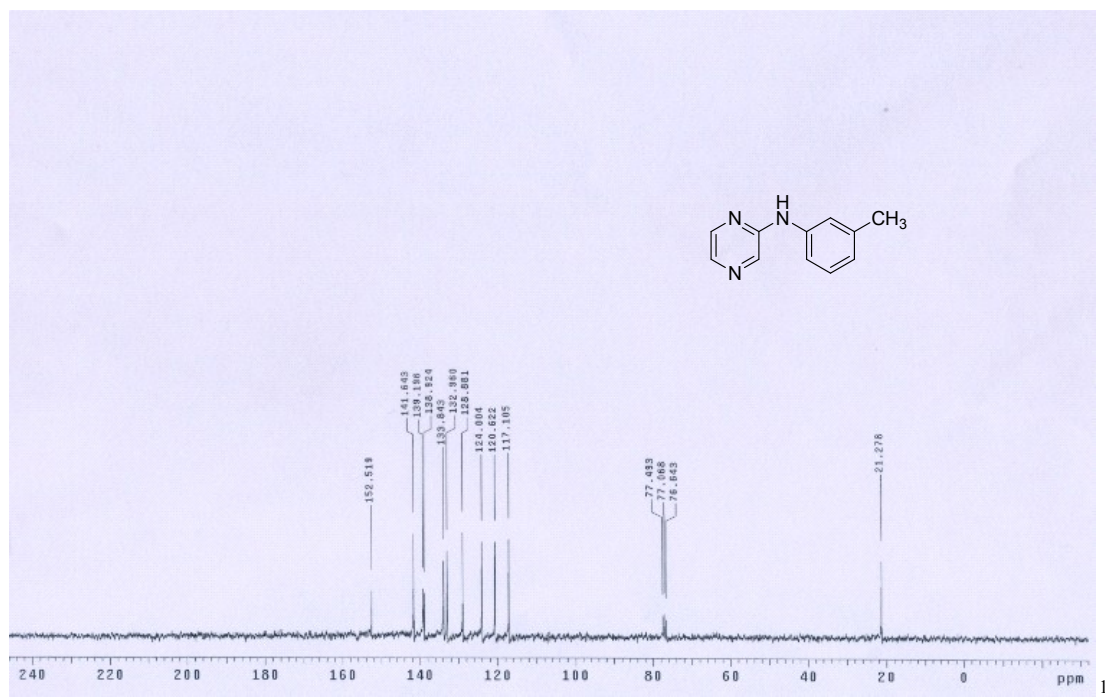
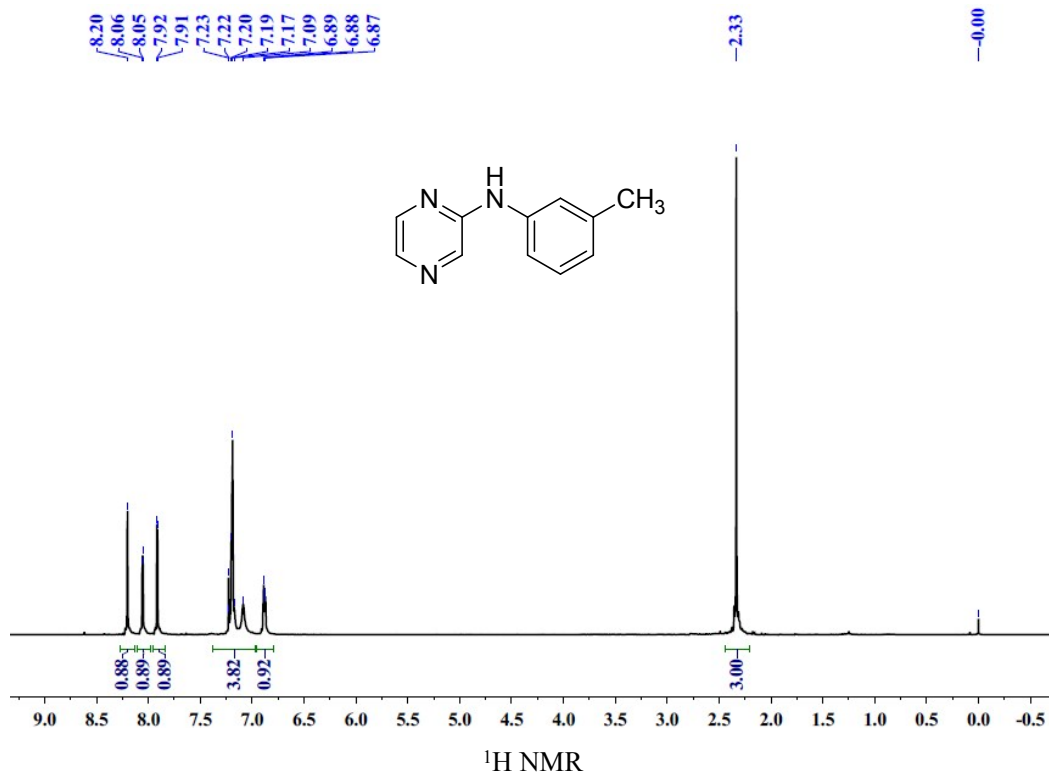


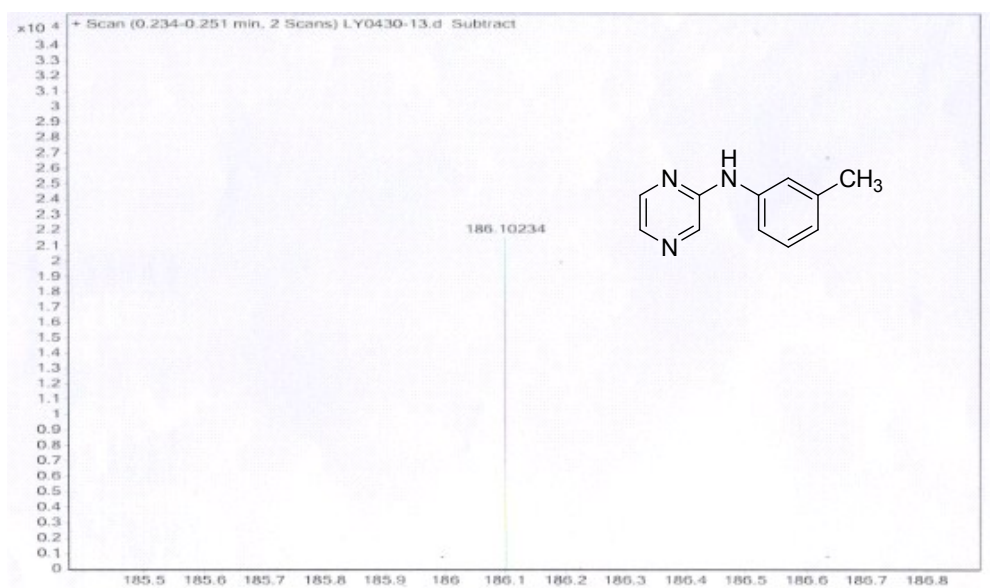


HRMS

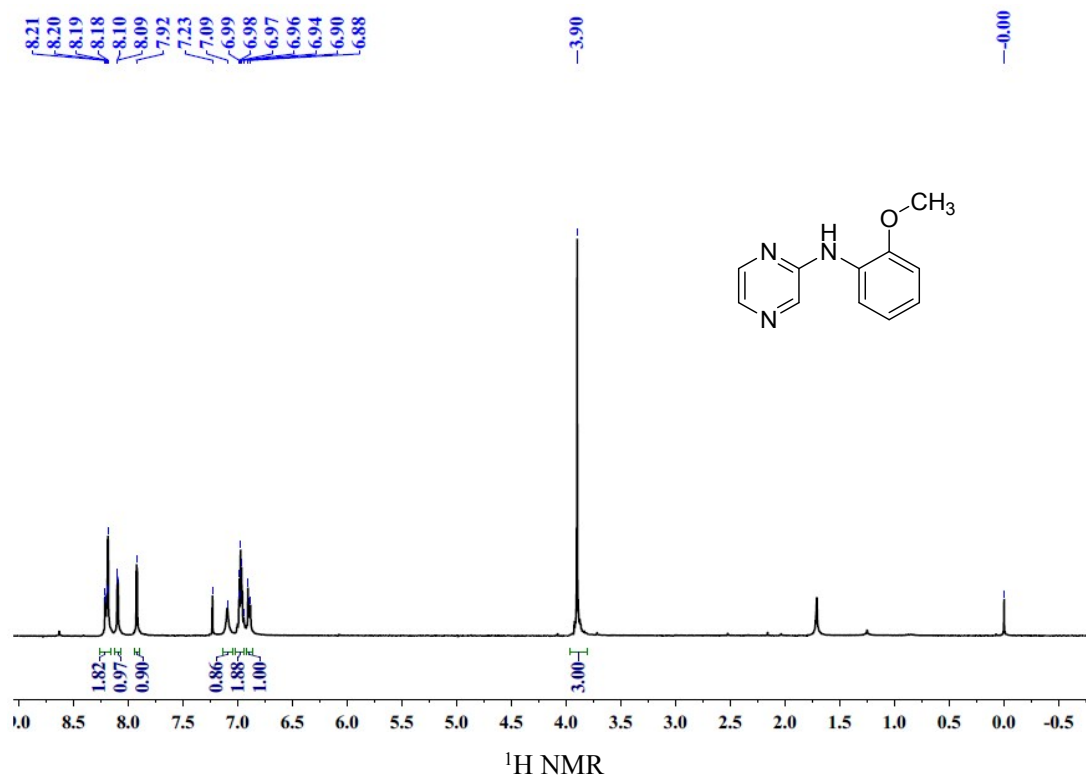


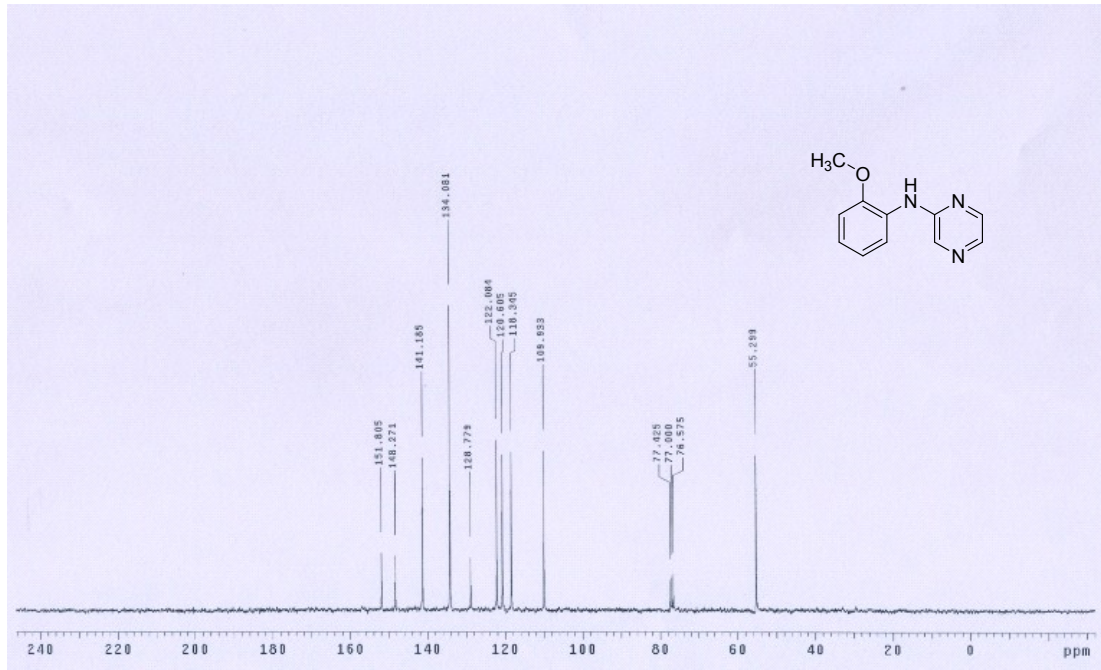
<sup>1</sup>H NMR



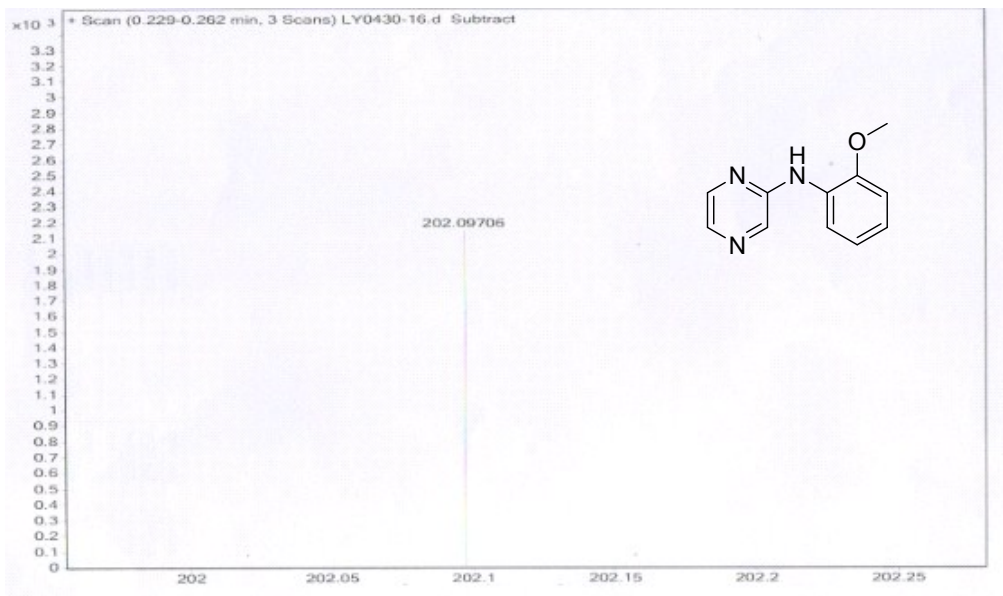


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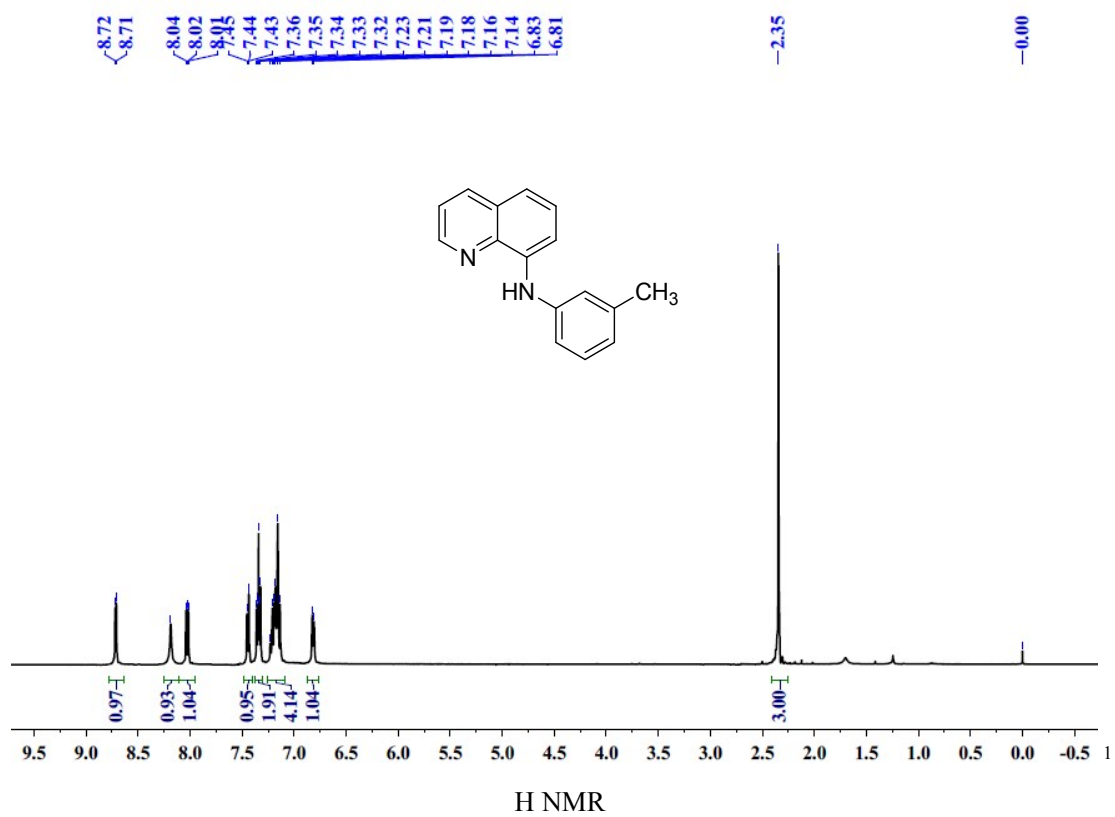
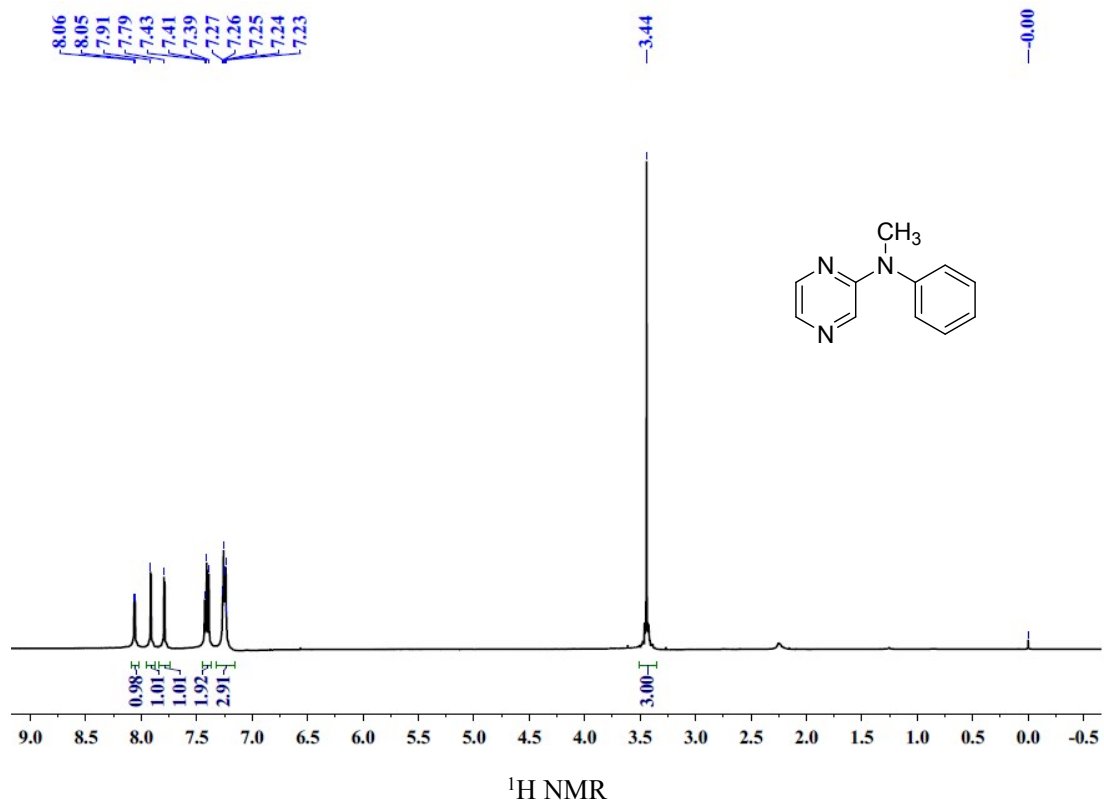


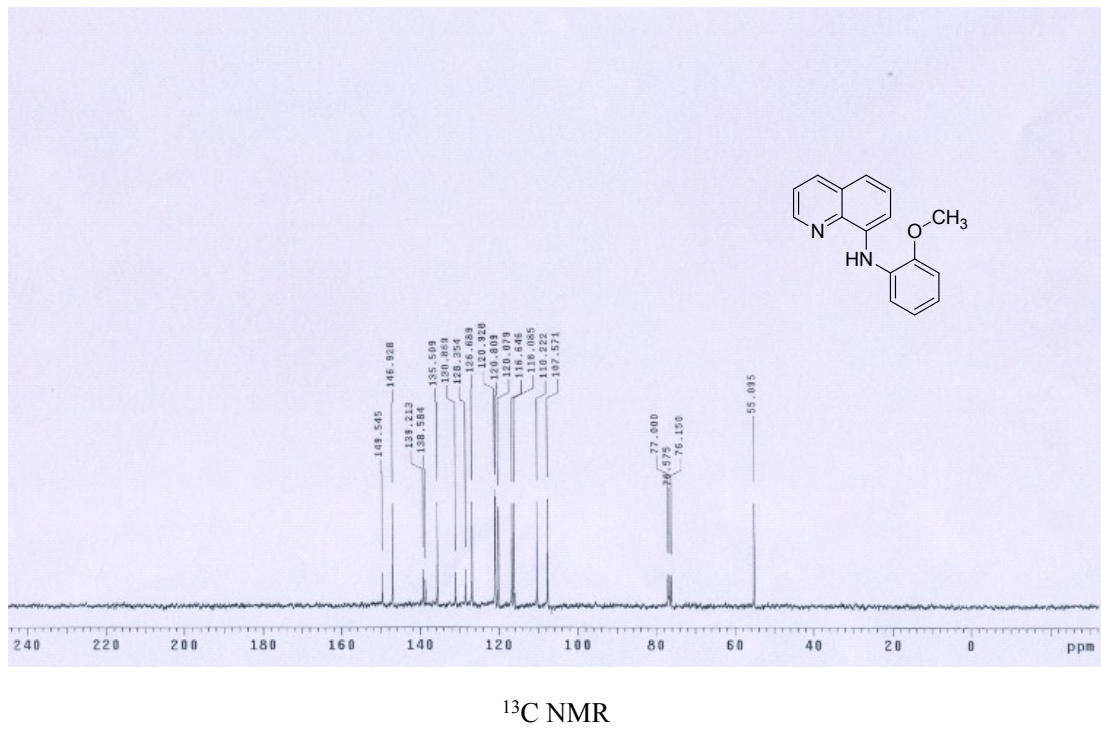
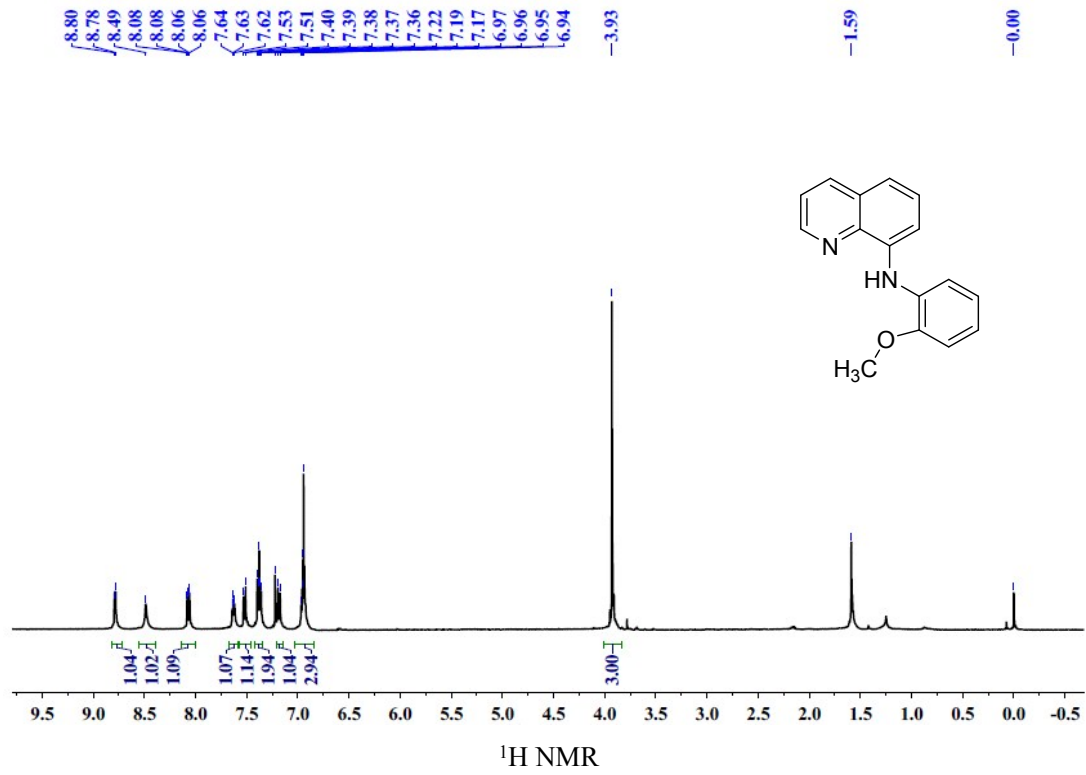
<sup>13</sup>C NMR

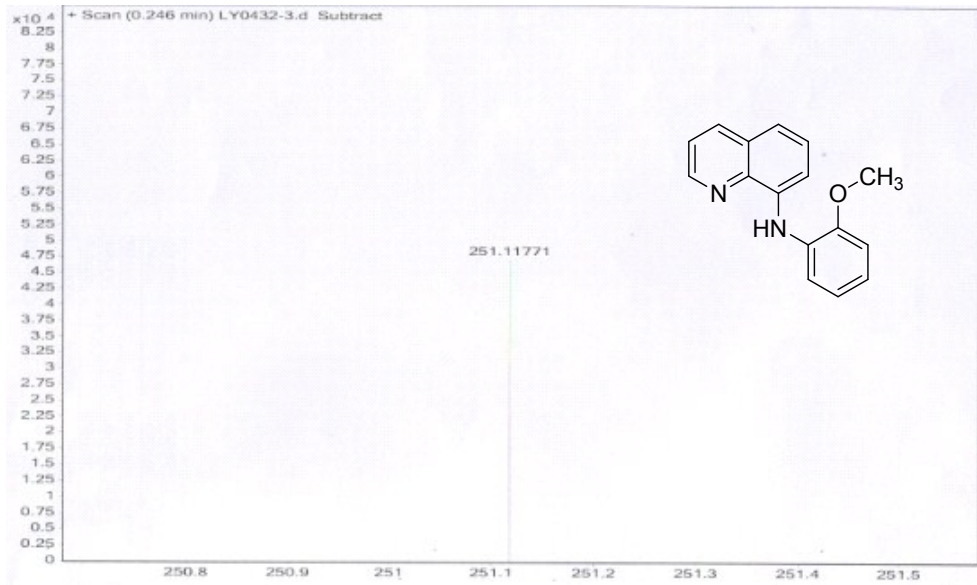


HRMS

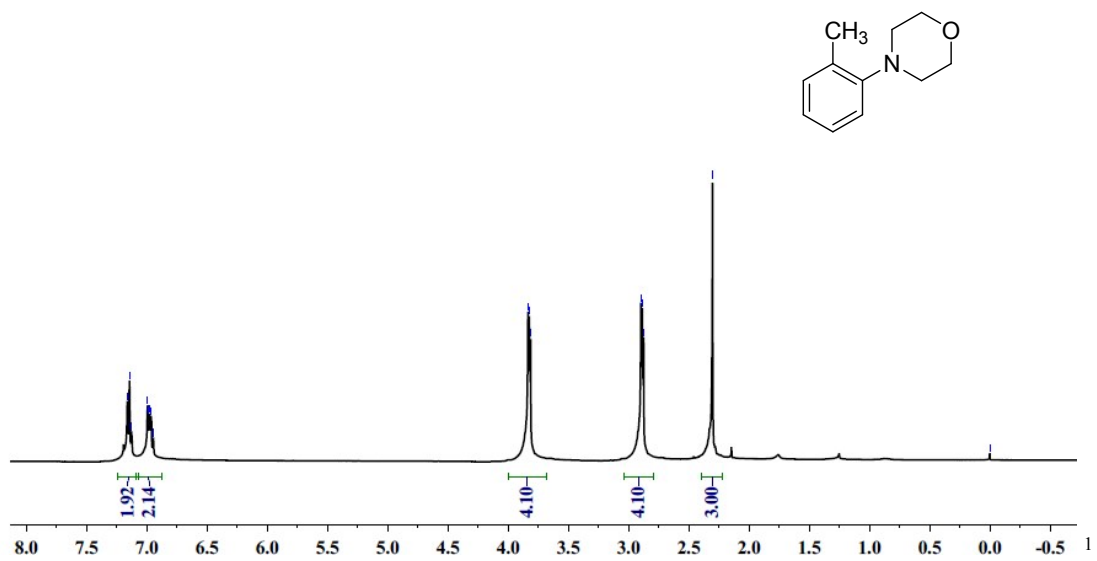




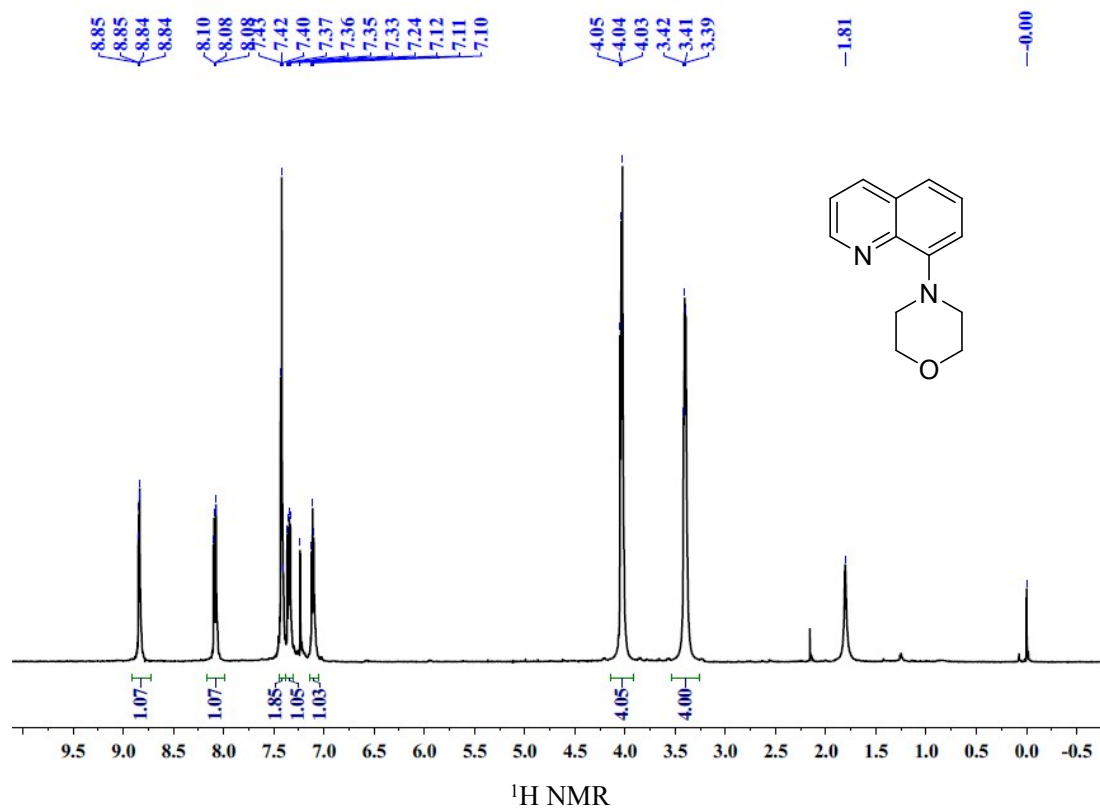
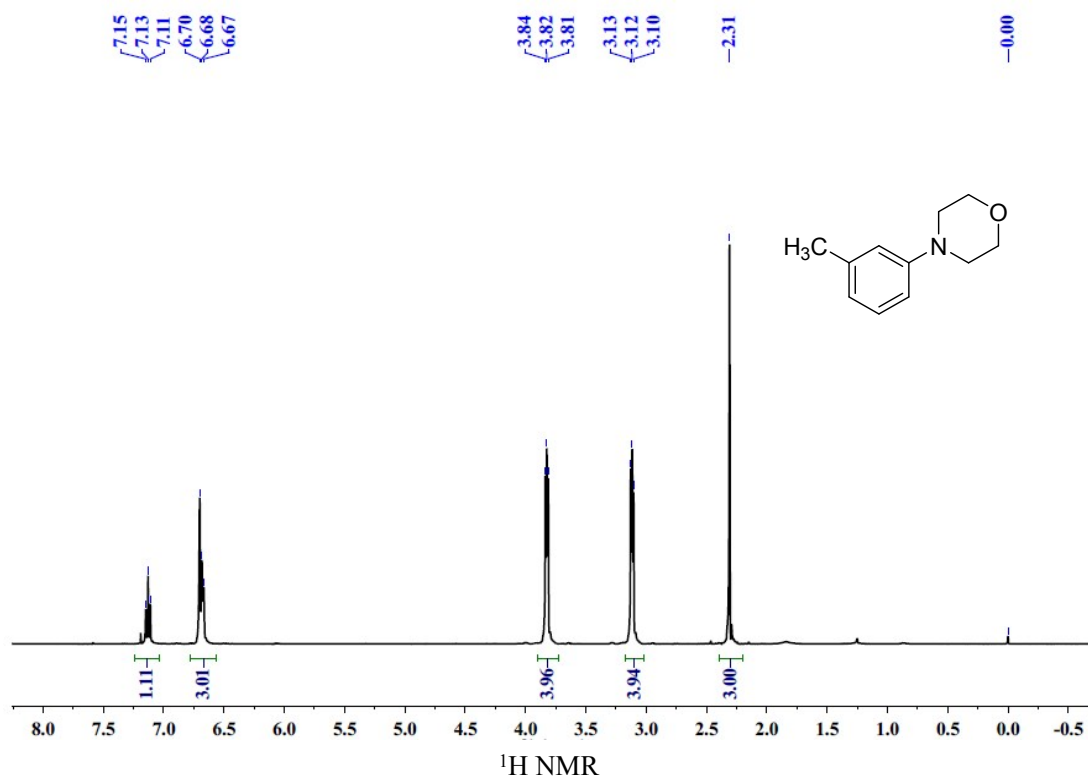


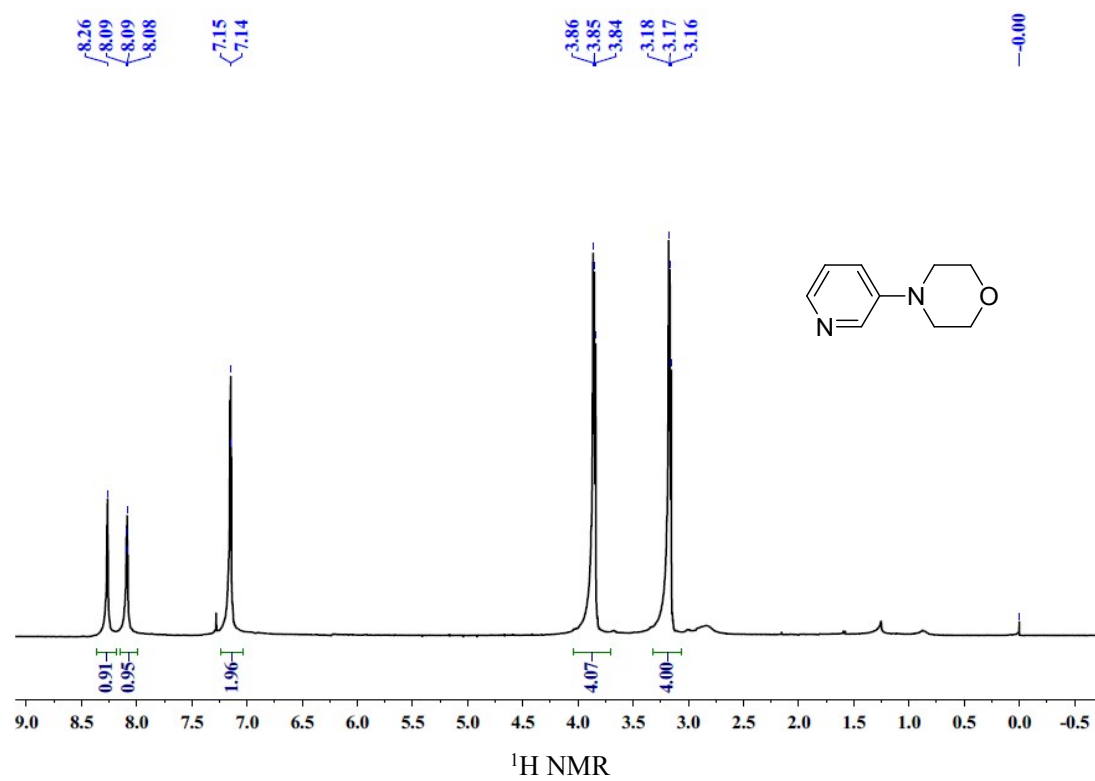
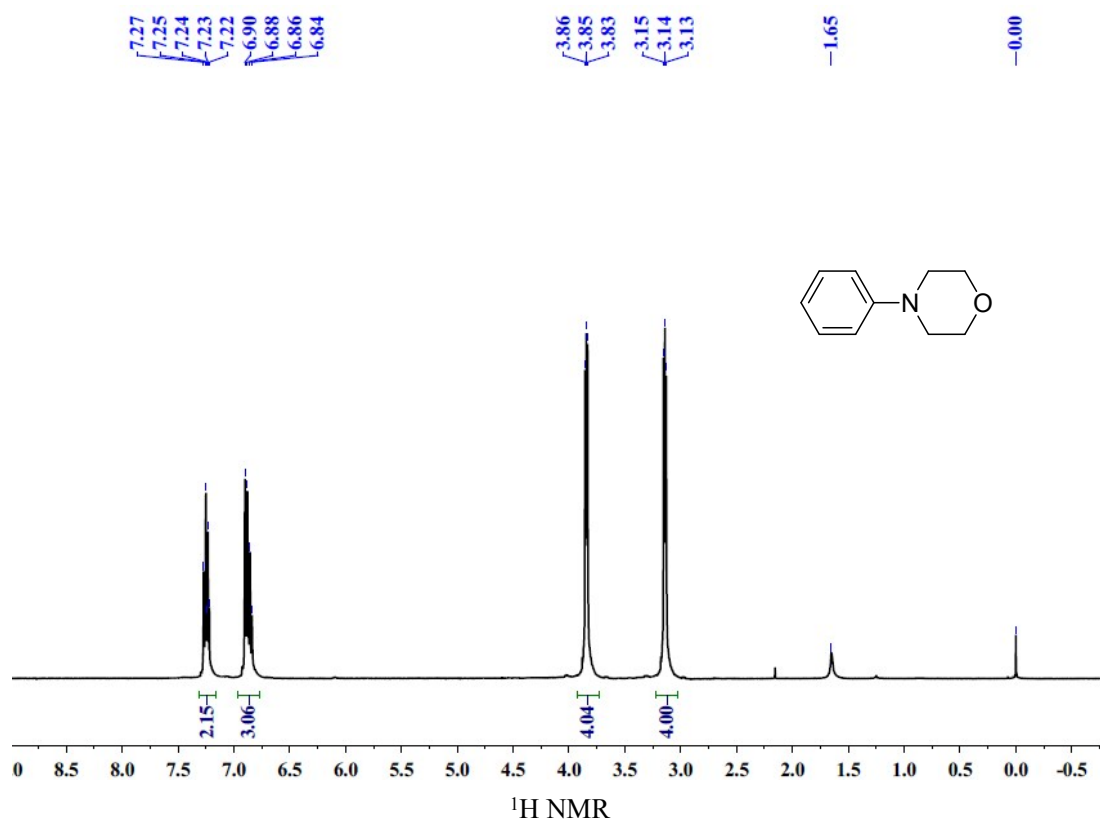


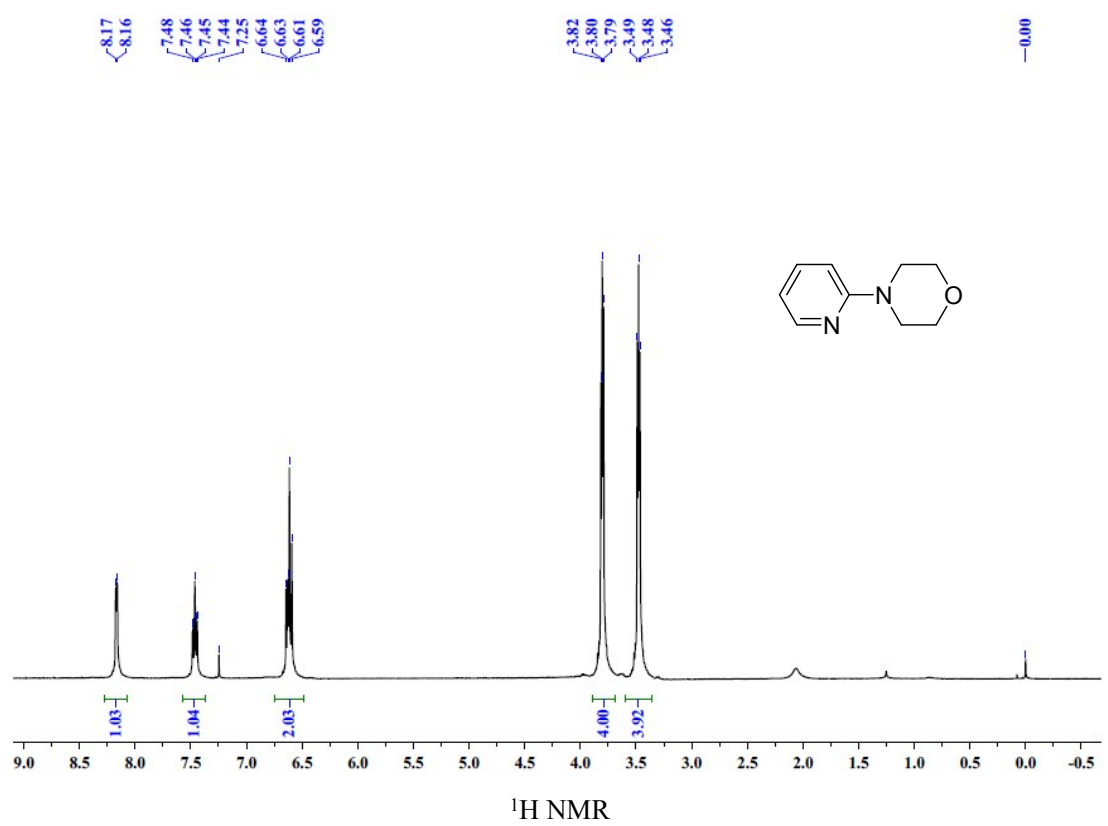
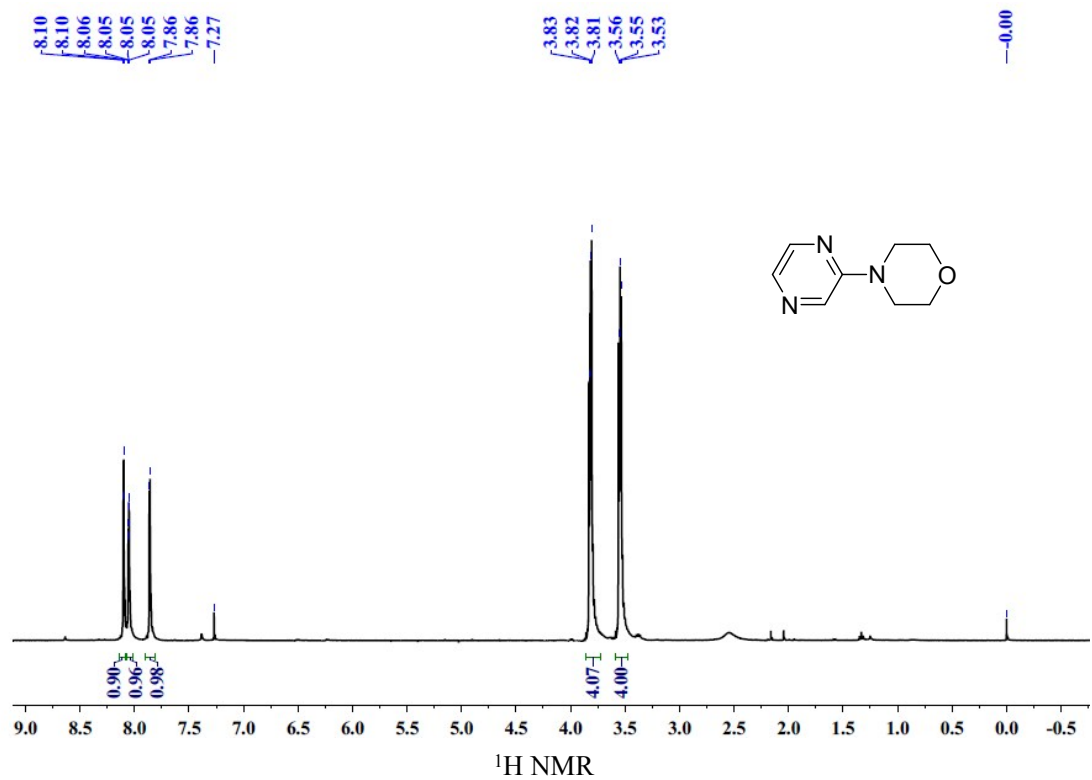
HRMS



<sup>1</sup>H NMR







#### 4. References

- 1 T. Tu, Z. Sun, W. Fang, M. Xu and Y. Zhou, *Org. Lett.*, 2012, **14**, 4250-4253.
- 2 Y. Liu, H. Peng, J. Yuan, M.-Q. Yan, X. Luo, Q.-G. Wu, S.-H. Liu, J. Chen and G.-A. Yu, *Org. Biomol. Chem.*, 2016, **14**, 4664-4668.
- 3 F. Rataboul, A. Zapf, R. Jackstell, S. Harkal, T. Riermeier, A. Monsees, U. Dingerdissen and M. Beller, *Chem. Eur. J.*, 2004, **10**, 2983-2990.
- 4 S. Keesara, *Tetrahedron Lett.*, 2015, **56**, 6685-6688.
- 5 J. C. Vantourout, R. P. Law, A. I. Llobet, S. J. Atkinson and A. J. B. Watson, *J. Org. Chem.*, 2016, **81**, 3942-3950.
- 6 Anuradha, S. Kumari and D. D. Pathak, *Tetrahedron Lett.*, 2015, **56**, 4135-4142.
- 7 S. Pradhan, A. Bhattacharyya and R. P. John, *Tetrahedron Lett.*, 2016, **57**, 1532-1536.
- 8 D.-P. Wang, D.-Z. Kuang, F.-X. Zhang, Y. Liu and S.-H. Ning, *Tetrahedron Lett.*, 2014, **55**, 7121-7123.
- 9 P. Puthiaraj and K. Pitchumani, *Chem. Eur. J.*, 2014, **20**, 8761-8770.
- 10 J.-B. Chen, K. Natte, Nikki Y.-T. Man, S. G. Stewart and X.-F. Wu, *Tetrahedron Lett.*, 2015, **56**, 4843-4847.
- 11 C. Salomé, P. Wagner, M. Bollenbach, F. Bihel, J. J. Bourguignon and M. Schmitt, *Tetrahedron*, 2014, **70**, 3413-3421.
- 12 T. K. Mazu, J. R. Etukala, X.-Y. Zhu, M. R. Jacob, S. I. Khan, L. A. Walker and S. Y. Ablordeppy, *Bioorg. Med. Chem.*, 2011, **19**, 524-533.
- 13 M. E. Daniel, G. O. Rodrigo, O. Cecilia, N. S. Guillermo E, A. H. Alejandro, B. H. Claudia I and S. C. Oscar R, *J. Organomet. Chem.*, 2016, **803**, 142-149.
- 14 R. A. Altman, K. W. Anderson and S. L. Buchwald, *J. Org. Chem.*, 2008, **73**, 5167-5169.
- 15 J. P. Wolfe, H. Tomori, J. P. Sadighi, J.-J. Yin and S. L. Buchwald, *J. Org. Chem.*, 2000, **65**, 1158-1174.
- 16 A. Tlili, F. Monnier and M. Taillefer, *Chem. Commun.*, 2012, **48**, 6408-6410.
- 17 S. Dastgir, K. S. Coleman, A. R. Cowley and M. L. H. Green, *Organometallics*, 2010, **29**, 4858-4870.
- 18 B. J. Tardiff and M. Stradiotto, *Eur. J. Org. Chem.*, 2012, **2012**, 3972-3977.
- 19 N. Kataoka, Q. Shelby, J. P. Stambuli and J. F. Hartwig, *J. Org. Chem.*, 2002, **67**, 5553-5566.
- 20 R. J. Lundgren, A. S. Kumankumah and M. Stradiotto, *Chem. Eur. J.*, 2010, **16**, 1983-1991.
- 21 M. A. Topchiy, A. F. Asachenko and M. S. Nechaev, *Eur. J. Org. Chem.*, 2014, **2014**, 3319-3322.
- 22 N. F. F. Nathel, J. Y. Kim, L. Hie, X.-Y. Jiang and N. K. Garg, *ACS Catal.*, 2014, **4**, 3289-3293.
- 23 Y. Zhang, V. César, G. Storch, N. Lugan and G. Lavigne, *Angew. Chem., Int. Ed.*, 2014, **53**, 6482-6486.
- 24 W.-J. Sheng, Q. Ye, W.-B. Yu, R.-R. Liu, M. Xu, J.-R. Gao and Y.-X. Jia, *Tetrahedron Lett.*, 2015, **56**, 599-601.