

# Novel Recyclable Pd/H-MOR Catalyst for Suzuki-Miyaura Coupling and Application in the Synthesis of Crizotinib

Enmu Zhou<sup>1</sup>, Jianzhong Jin<sup>2\*</sup>, Kai Zheng<sup>2</sup>, Letian Zhang<sup>1</sup>, Hao Xu<sup>2</sup>, Chao Shen<sup>2\*</sup>

<sup>1</sup> College of Petroleum Chemical Industry, Changzhou University, Changzhou 213164; China; [geormochou@outlook.com](mailto:geormochou@outlook.com) (E.Z.); [997485470@QQ.com](mailto:997485470@QQ.com) (L.Z.)

<sup>2</sup> College of Biology and Environmental Engineering, Zhejiang Shuren University, Hangzhou 310015, China; [hzjjz@163.com](mailto:hzjjz@163.com) (J.J.); [zkai86@163.com](mailto:zkai86@163.com) (K.Z.); [xuhao@zju.edu.cn](mailto:xuhao@zju.edu.cn) (H.X.)

\* Correspondence: [shenchaozju@163.com](mailto:shenchaozju@163.com); Tel.: +86-057-188297172

## Supporting Information

### Tables of contents

1. General Information	S2
2. Experimental Section	S2
3. Characterization of Catalyst	S3
4. Characterization of Products	S3
5. References	S6

## 1. General Information

### Materials

All the chemicals were obtained commercially and used without any prior purification. H-MOR Zeolite was provided by Nankai University Catalyst Co., Ltd. Palladium (II) chloride ( $\text{PdCl}_2$ , 59.5%) was provided by J&K Scientific Ltd (Shanghai, China). Ethanol was provided by Anhui Ante Food Co., Ltd (Suzhou, Anhui, China). Potassium hydroxide was provided by Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). Other materials were of analytical grade and used as received.

### Characterization

X-ray diffraction (XRD) measurements were performed at room temperature by using a Rigaku Ultimate VI X-ray diffractometer (40 kV, 40 mA) using  $\text{CuK}\alpha$  ( $\lambda=1.5406 \text{ \AA}$ ). The  $\text{N}_2$  sorption isotherms at the temperature of liquid nitrogen were measured using Micromeritics ASAP 2020. The Pd loading of sample was determined by inductively coupled plasma (ICP) with a Perkin-Elmer 3300DV emission spectrometer. Scanning electron microscopy (SEM) experiments were performed on Hitachi SU-1510 electron microscopes.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Advance 500 spectrometer at ambient temperature with  $\text{CDCl}_3$  or  $\text{DMSO-}d_6$  as solvent and tetramethylsilane (TMS) as the internal standard.

## 2. Experimental Section

### 2.1 Preparation of Pd/H-MOR [1-3]

0.5 g of H-MOR zeolite was added to 50 mL of ethanol in a 100 mL round-bottom flask. This mixture was infiltrated and dispersed by ultrasonic bath for 30 min. After this time of ultrasonic treatment,  $\text{PdCl}_2$  (0.075 g) was added to this solution and dispersed by ultrasonic for 20 min. Then, KOH (0.048 g with 10 mL  $\text{H}_2\text{O}$ ) was added to this solution by a constant pressure dropping funnel for 10 min. This mixture was dispersed by ultrasonic bath for 1 h. After ultrasonic treatment, the product was centrifuged, washed, and was kept constant at 100 °C overnight.

### 2.2 General procedure for the Suzuki coupling reactions

Phenylboronic acid (1.3 mmol), aryl halides (1 mmol),  $\text{K}_2\text{CO}_3$  (2 mmol), Pd/H-MOR (10 mg), 8 mL  $\text{H}_2\text{O}$  and 2 mL ethanol were put into a reaction flask and stirred at 80 °C under air. After the reaction was complete, the reaction was cooled to room temperature. Then the mixture was extracted with ethyl acetate, dried, filtered, and concentrated in vacuo. All products were isolated by short chromatography on a silica gel (200-300 mesh) column using petroleum ether (60-90 °C) and ethyl acetate.

### 2.3 General procedure for catalyst recovery

The 4-iodoanisole (2.5 mmol), phenylboronic acid (3.25 mmol),  $\text{K}_2\text{CO}_3$  (5 mmol), and Pd/H-MOR (50 mg) were mixed in  $\text{H}_2\text{O}$  and ethanol (25 mL, 4:1). The mixture was stirred at 80 °C under air. After the reaction was complete, the catalyst was separated by a centrifuge and washed with ethanol (4×10 mL) twice and water (4×10 mL) once by an ultrasonic cleaner, then dried in 4 centrifugal tubes and used in the next run. The ingredients involved in the cyclic reaction are based on the Pd/H-MOR obtained by separation and are fed in proportion.

### 3. Characterization of Catalyst

**Table S1.** Textural parameters of the synthesized sample.

Sample	$S_{\text{BET}}$ (m <sup>2</sup> /g) <sup>a</sup>	$S_{\text{ext.}}$ (m <sup>2</sup> /g) <sup>b</sup>	$V_{\text{micro.}}$ (cm <sup>3</sup> /g) <sup>c</sup>
H-MOR	464.0223	17.7928	0.210255
Pd/H-MOR	412.1592	13.2391	0.188157

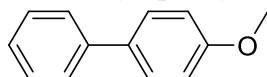
<sup>a</sup> BET surface area.

<sup>b</sup> *t*-Plot External surface area.

<sup>c</sup> Microporous volume.

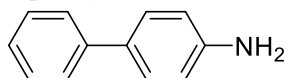
### 4. Characterization of Products

#### 4-Methoxybiphenyl 3a:



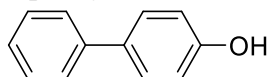
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.54 (d, *J* = 7.5 Hz, 2H), 7.52 (d, *J* = 8.8 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H).

#### Biphenyl-4-amine 3b:



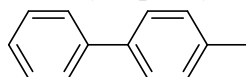
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.53 (d, *J* = 7.1 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.26 (d, *J* = 6.9 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 2H), 3.69 (s, 2H).

#### Biphenyl-4-ol 3c:



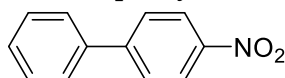
<sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  9.49 (s, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 2H).

#### 4-Methylbiphenyl 3d:



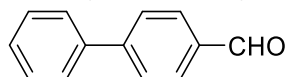
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.57 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.32 (d, *J* = 4.8 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 2H), 2.37 (s, 3H).

#### 4-Nitrobiphenyl 3e:



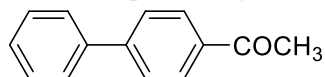
<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.30 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 8.9 Hz, 2H), 7.62 (d, *J* = 7.1 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H).

**4-Phenylbenzaldehyde 3f:**



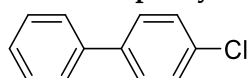
$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  10.06 (s, 1H), 7.95 (d,  $J$  = 8.0 Hz, 2H), 7.75 (d,  $J$  = 7.9 Hz, 2H), 7.64 (d,  $J$  = 7.4 Hz, 2H), 7.48 (t,  $J$  = 7.5 Hz, 2H), 7.42 (t,  $J$  = 7.3 Hz, 1H).

**4-Acetylbiphenyl 3g:**



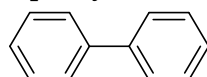
$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 (d,  $J$  = 8.0 Hz, 2H), 7.69 (d,  $J$  = 8.0 Hz, 2H), 7.63 (d,  $J$  = 7.5 Hz, 2H), 7.47 (t,  $J$  = 7.5 Hz, 2H), 7.40 (t,  $J$  = 7.3 Hz, 1H), 2.64 (s, 3H).

**4-Chlorobiphenyl 3h:**



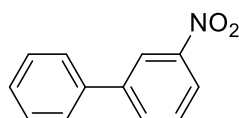
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.53 (dd,  $J$  = 7.9, 16.9 Hz, 4H), 7.47 – 7.39 (m, 4H), 7.35 (t,  $J$  = 7.4 Hz, 1H).

**Biphenyl 3i:**



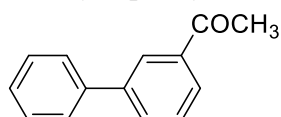
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (d,  $J$  = 7.1 Hz, 4H), 7.40 (t,  $J$  = 7.7 Hz, 4H), 7.31 (t,  $J$  = 7.4 Hz, 2H).

**3-Nitrobiphenyl 3j:**



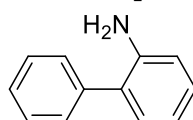
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.44 (s, 1H), 8.19 (d,  $J$  = 9.6 Hz, 1H), 7.91 (d,  $J$  = 7.8 Hz, 1H), 7.63 – 7.58 (m, 3H), 7.49 (d,  $J$  = 15.0 Hz, 2H), 7.42 (t,  $J$  = 7.3 Hz, 1H).

**3-Acetylbiphenyl 3k:**



$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.18 (s, 1H), 7.93 (d,  $J$  = 7.7 Hz, 1H), 7.79 (d,  $J$  = 7.6 Hz, 1H), 7.62 (d,  $J$  = 7.7 Hz, 2H), 7.53 (t,  $J$  = 7.7 Hz, 1H), 7.47 (t,  $J$  = 7.3 Hz, 2H), 7.38 (t,  $J$  = 7.3 Hz, 1H), 2.65 (s, 3H).

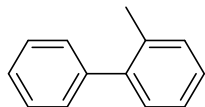
**2-Aminebiphenyl 3l:**



$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 (d,  $J$  = 8.2 Hz, 4H), 7.33 (t,  $J$  = 6.8 Hz, 1H), 7.15 – 7.11 (m, 2H),

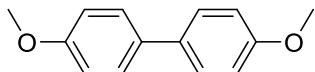
6.82 (t,  $J = 7.4$  Hz, 1H), 6.75 (d,  $J = 8.0$  Hz, 1H), 3.63 (s, 2H).

**2-Methylbiphenyl 3m:**



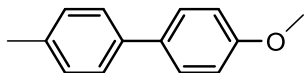
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 (d,  $J = 7.9$  Hz, 1H), 7.45 – 7.41 (m, 2H), 7.40 (d,  $J = 7.4$  Hz, 2H), 7.33 (d,  $J = 7.8$  Hz, 2H), 7.24 (d,  $J = 6.9$  Hz, 2H), 2.27 (s, 3H).

**4,4'-Dimethoxybiphenyl 3n:**



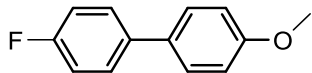
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.45 (m, 2H), 6.97 – 6.94 (m, 2H), 3.84 (s, 3H).

**1-Methoxy-4-(4-methylphenyl)benzene 3o:**



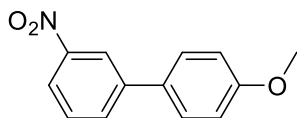
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 (d,  $J = 8.8$  Hz, 2H), 7.46 (d,  $J = 8.1$  Hz, 2H), 7.24 (d,  $J = 7.9$  Hz, 2H), 6.97 (d,  $J = 8.8$  Hz, 2H), 3.85 (s, 3H), 2.39 (s, 3H).

**1-Fluoro-4-(4-methylphenyl)benzene 3p:**



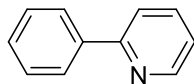
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 – 7.46 (m, 4H), 7.14 – 7.08 (m, 2H), 7.00 – 6.96 (m, 2H), 3.86 (s, 3H).

**1-(4-methoxyphenyl)-3-nitrobenzene 3q:**



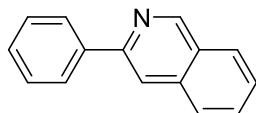
$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.41 (s, 1H), 8.14 (d,  $J = 8.2$  Hz, 1H), 7.87 (d,  $J = 7.7$  Hz, 1H), 7.57 (t,  $J = 7.3$  Hz, 3H), 7.02 (d,  $J = 8.0$  Hz, 2H), 3.87 (s, 3H).

**2-Phenylpyridine 3r:**

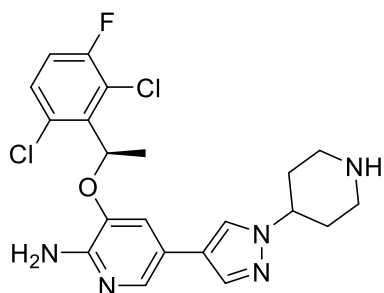


$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  8.69 (d,  $J = 4.6$  Hz, 1H), 7.99 (d,  $J = 7.7$  Hz, 2H), 7.72 (d,  $J = 6.9$  Hz, 2H), 7.47 (t,  $J = 7.5$  Hz, 2H), 7.41 (t,  $J = 7.3$  Hz, 1H), 7.21 (t,  $J = 5.6$  Hz, 1H).

**3-Phenylquinoline 3s:**



$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  9.17 (s, 1H), 8.25 (s, 1H), 8.14 (d,  $J$  = 8.4 Hz, 1H), 7.83 (d,  $J$  = 8.1 Hz, 1H), 7.70 – 7.66 (m, 3H), 7.54 (t,  $J$  = 7.5 Hz, 1H), 7.49 (t,  $J$  = 7.5 Hz, 2H), 7.41 (t,  $J$  = 7.4 Hz, 1H).

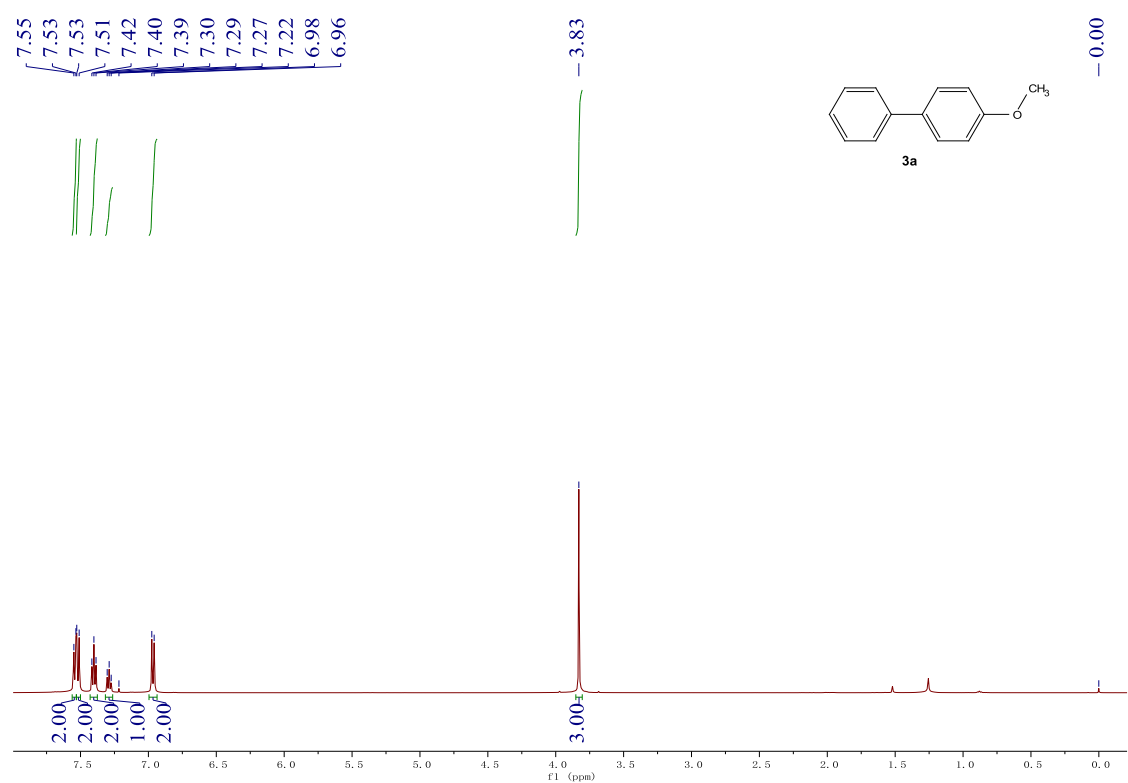


$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.77 (d,  $J$  = 1.7 Hz, 1H), 7.57 (s, 1H), 7.50 (s, 1H), 7.30 (dd,  $J$  = 4.8, 8.8 Hz, 1H), 7.06 – 7.03 (m, 1H), 6.87 (d,  $J$  = 1.6 Hz, 1H), 6.07 (d,  $J$  = 6.7 Hz, 1H), 4.78 (s, 2H), 4.21 (ddd,  $J$  = 4.1, 7.7, 11.7 Hz, 1H), 3.26 (d,  $J$  = 12.6 Hz, 2H), 2.78 (td,  $J$  = 2.2, 12.5 Hz, 2H), 2.18 – 2.15 (m, 2H), 1.92 (td,  $J$  = 4.6, 9.1 Hz, 2H), 1.85 (d,  $J$  = 6.7 Hz, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  149.52, 140.48, 137.64, 136.28, 123.11, 120.55, 119.95, 117.44, 117.29, 115.59, 73.07, 60.41, 46.32, 34.56, 34.54, 19.58.

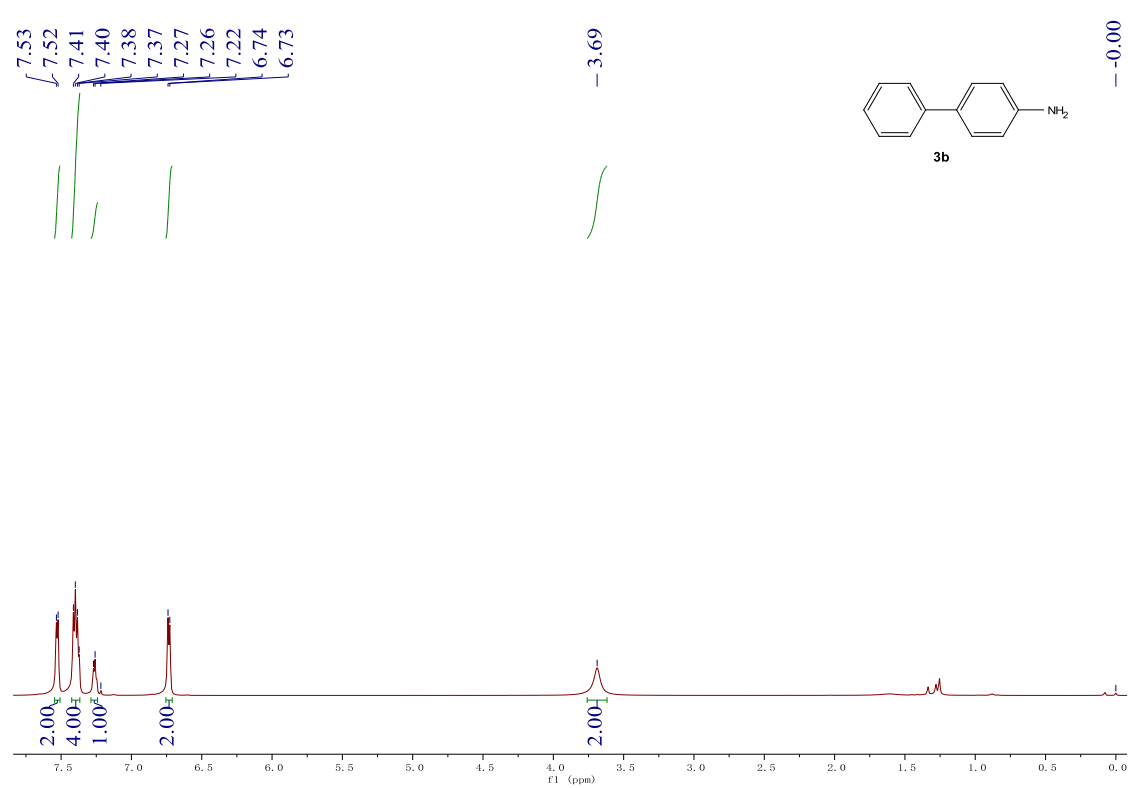
## 5. References

1. Tadjarodi, A.; Dehghani, M.; Imani, M. Green synthesis and characterization of palladium nanoparticles supported on zeolite Y by sonochemical method, powerful and efficient catalyst for Suzuki-Miyaura coupling of aryl halides with phenylboronic acid. *Appl. Organomet. Chem.* **2018**, 32, e4594.
2. Dehghani, M.; Tadjarodi, A.; Chamani, S. Synthesis and characterization of magnetic zeolite Y-Palladium-Nickel Ferrite by ultrasonic irradiation and investigating its catalytic activity in Suzuki-Miyaura Cross-Coupling reactions. *ACS Omega*. **2019**, 4, 10640-10648.
3. Padilla, R.H.; Priece, P.; Lin, M.; Lopez-Sanchez, J.A.; Zhong, Z. A versatile sonication-assisted deposition-reduction method for preparing supported metal catalysts for catalytic applications. *Ultrason. Sonochem.* **2017**, 35, 631-639.

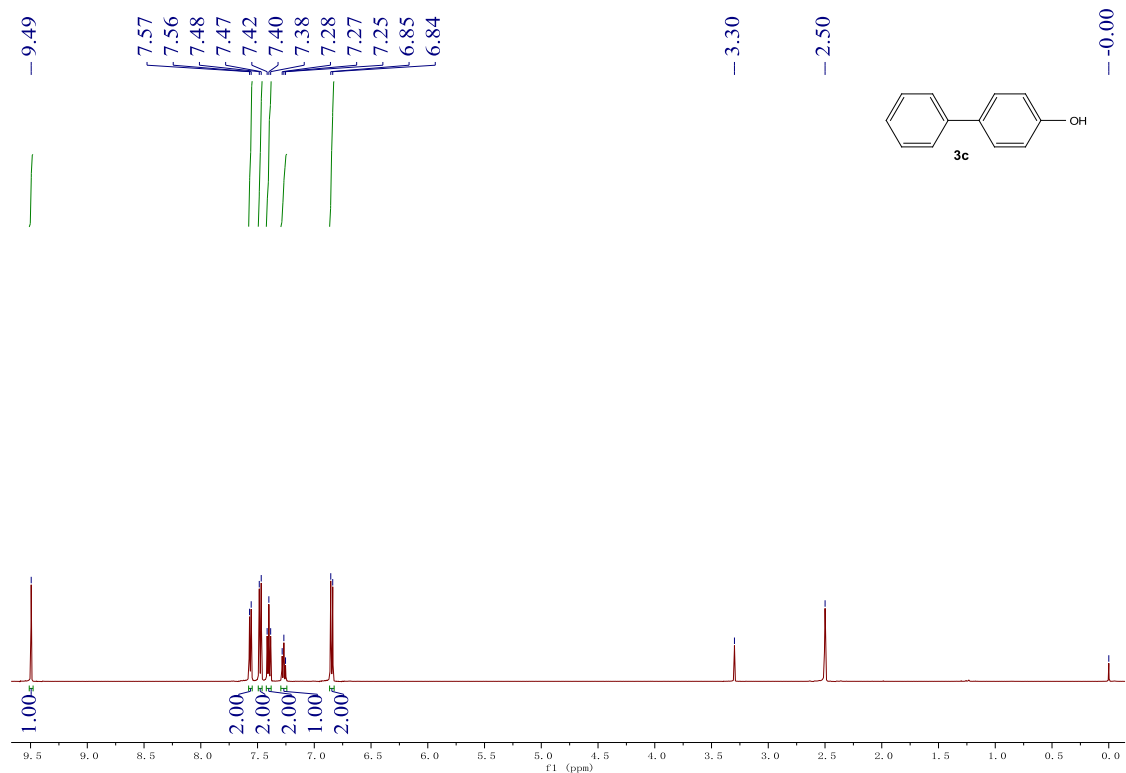
<sup>1</sup>H NMR



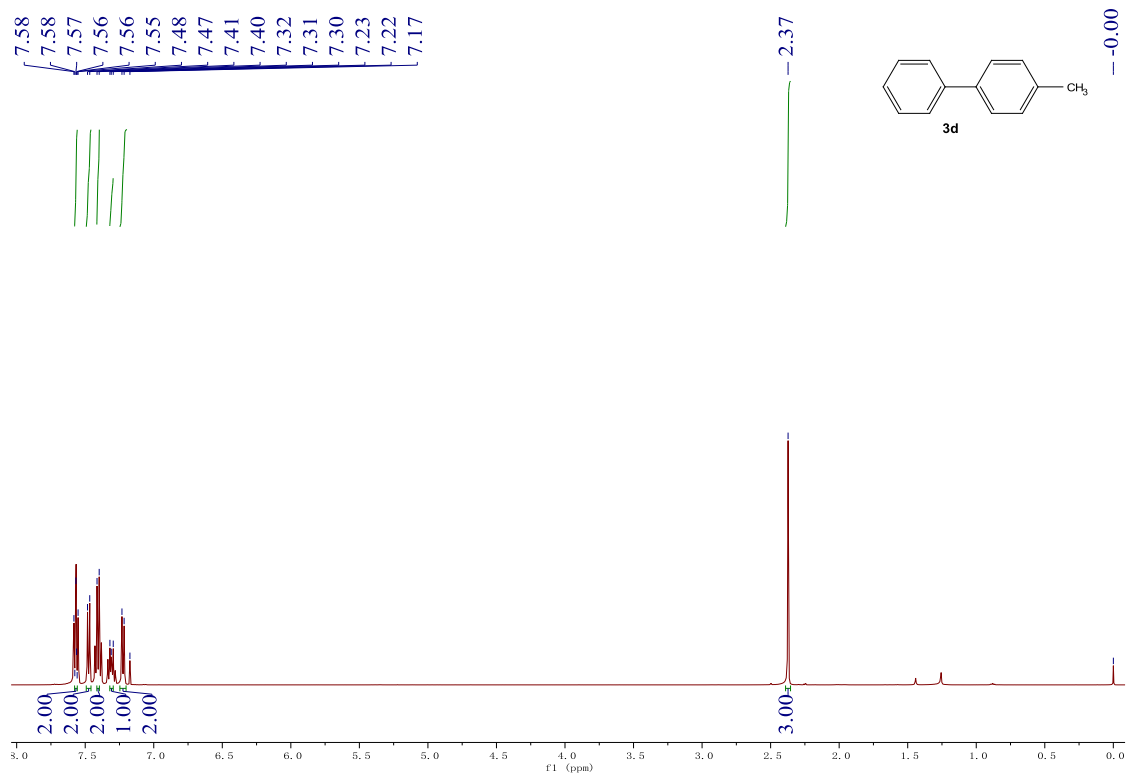
<sup>1</sup>H NMR



<sup>1</sup>H NMR

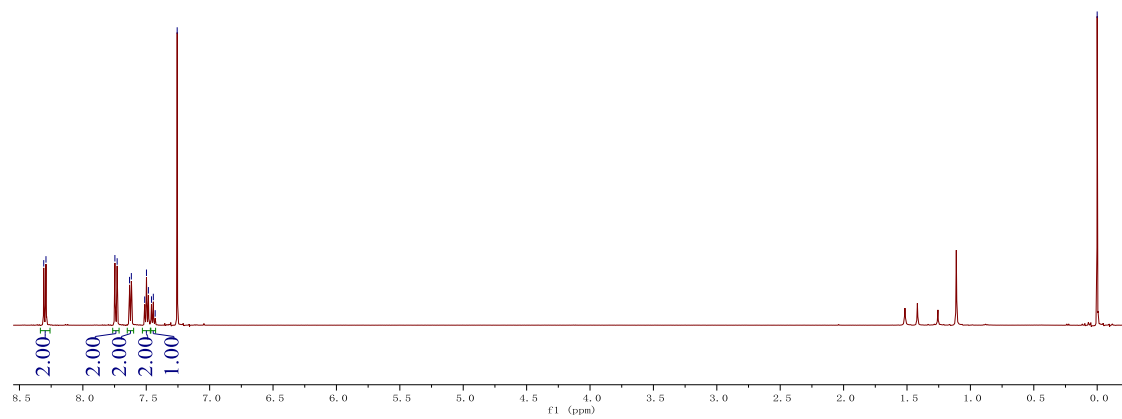
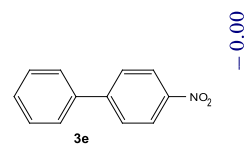
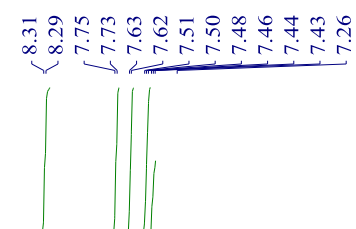


<sup>1</sup>H NMR

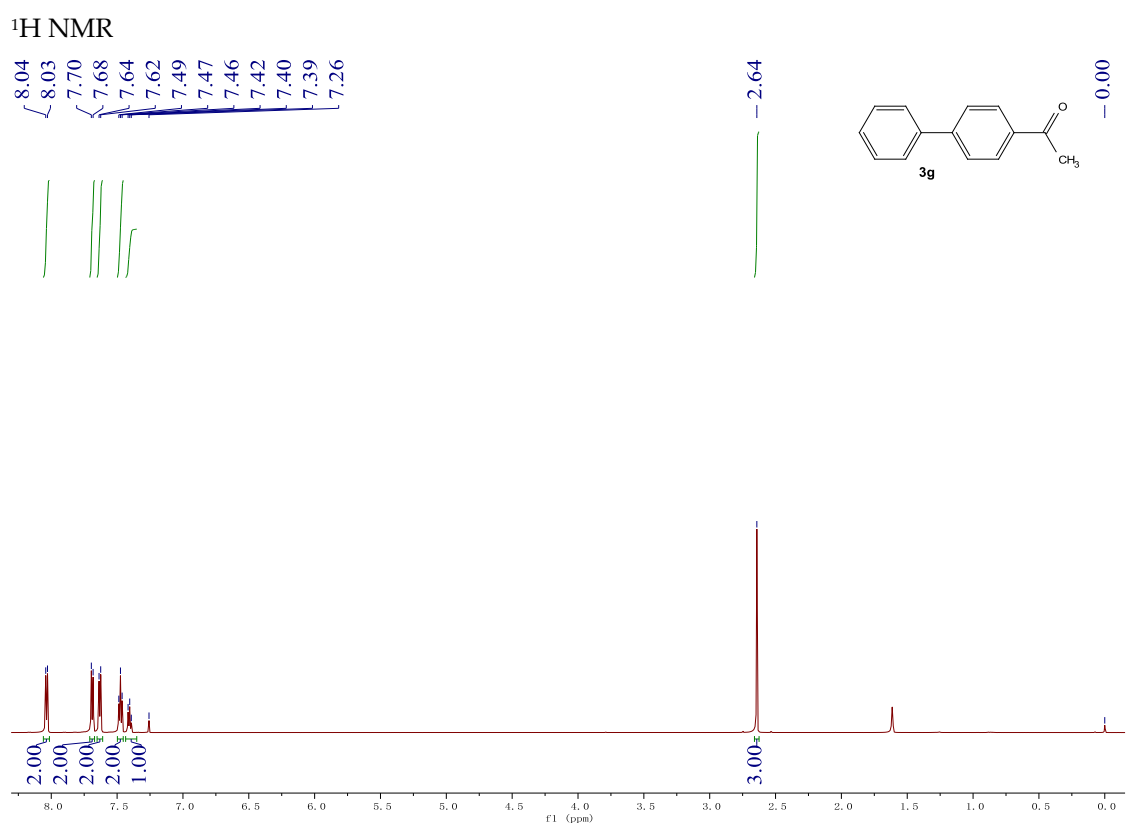
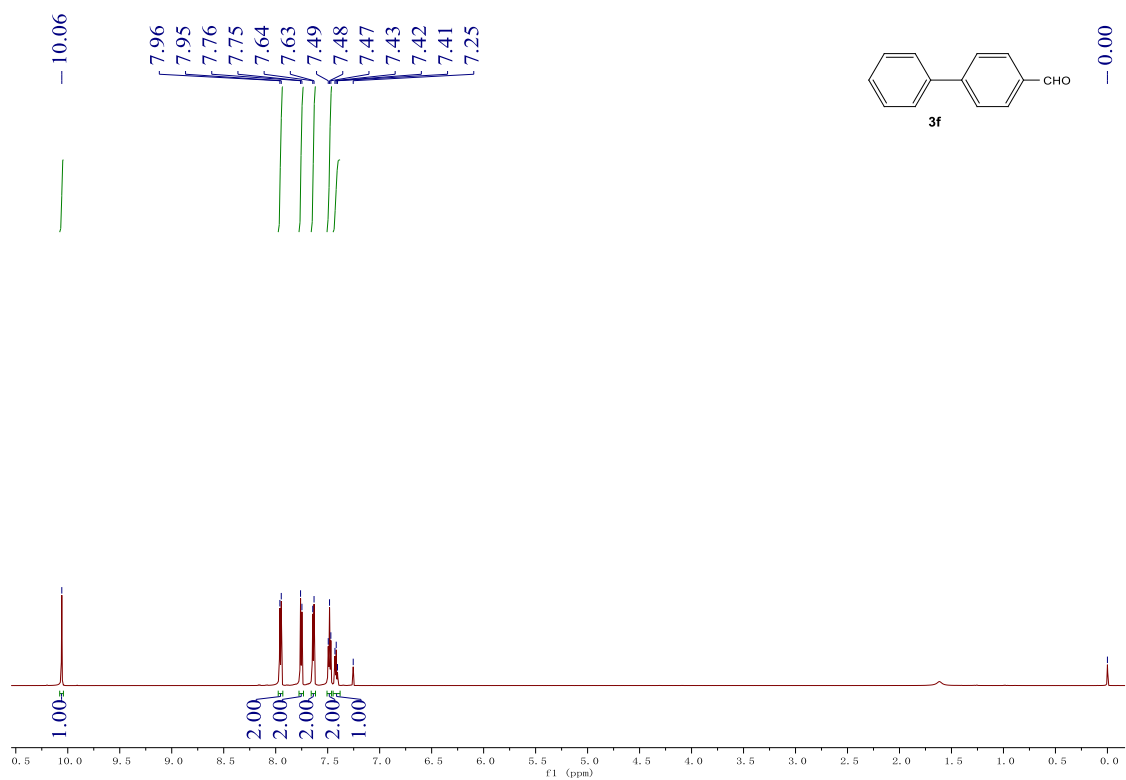




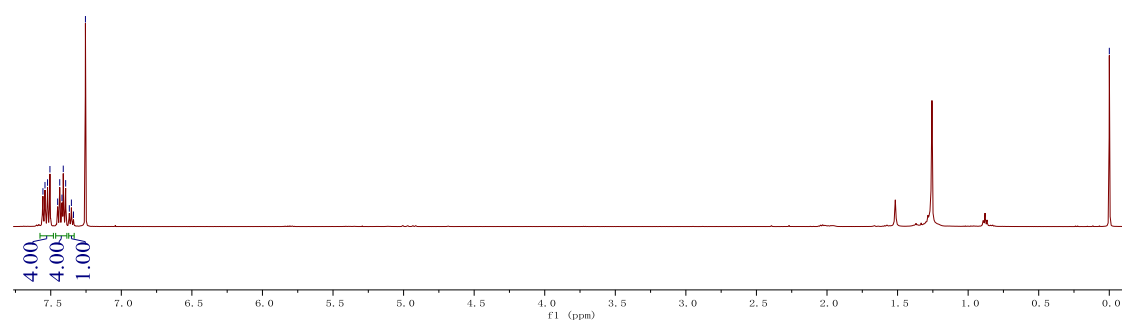
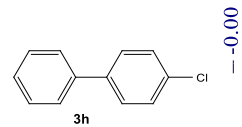
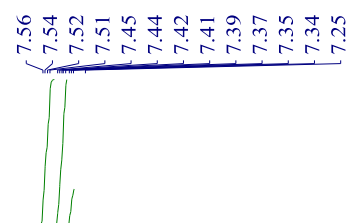
<sup>1</sup>H NMR



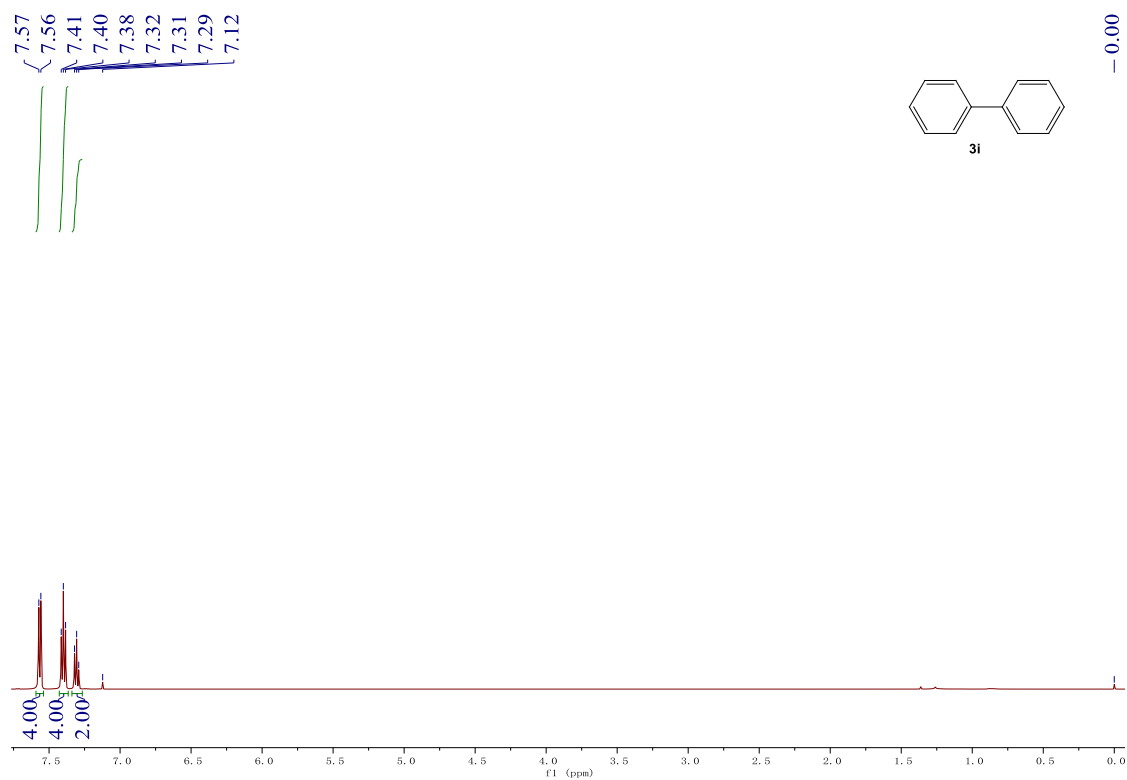
<sup>1</sup>H NMR



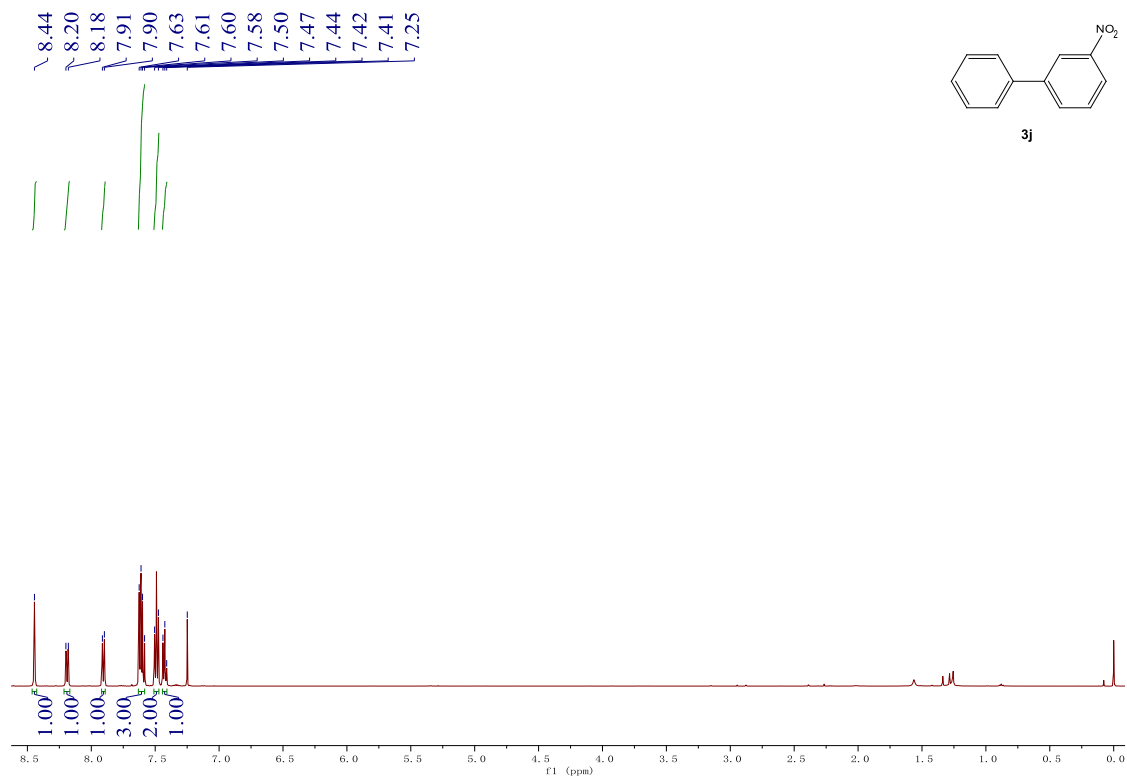
<sup>1</sup>H NMR



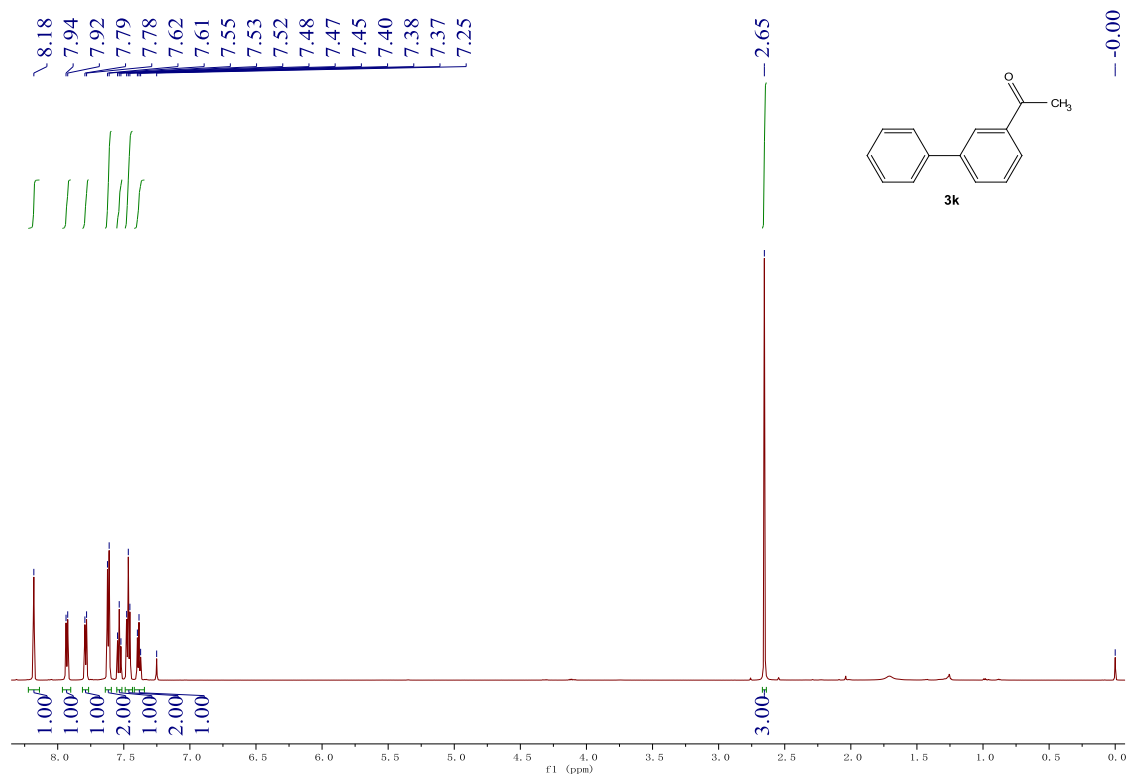
<sup>1</sup>H NMR



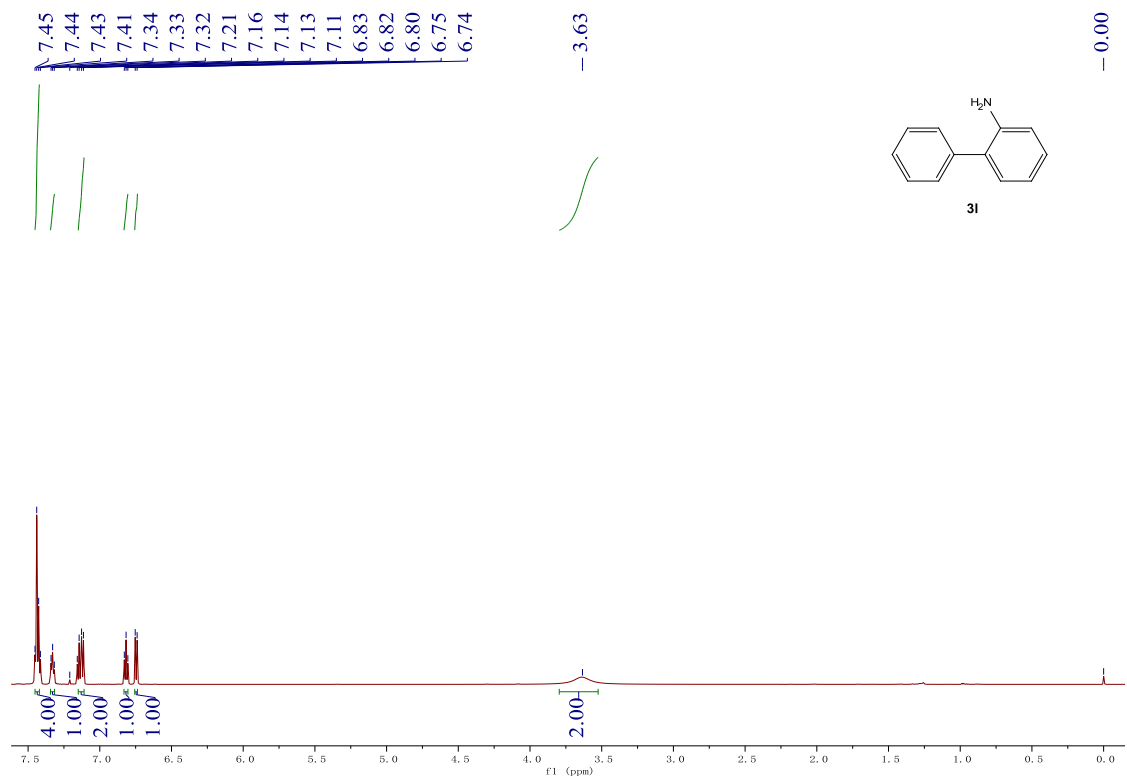
<sup>1</sup>H NMR



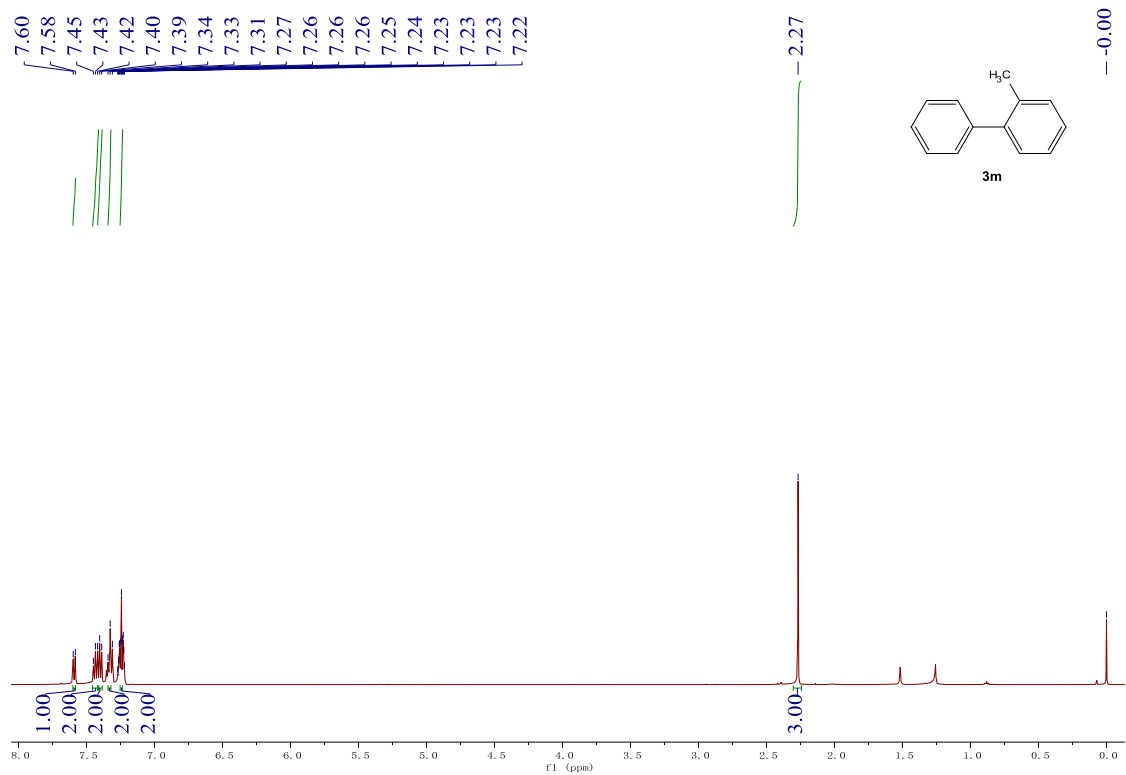
<sup>1</sup>H NMR



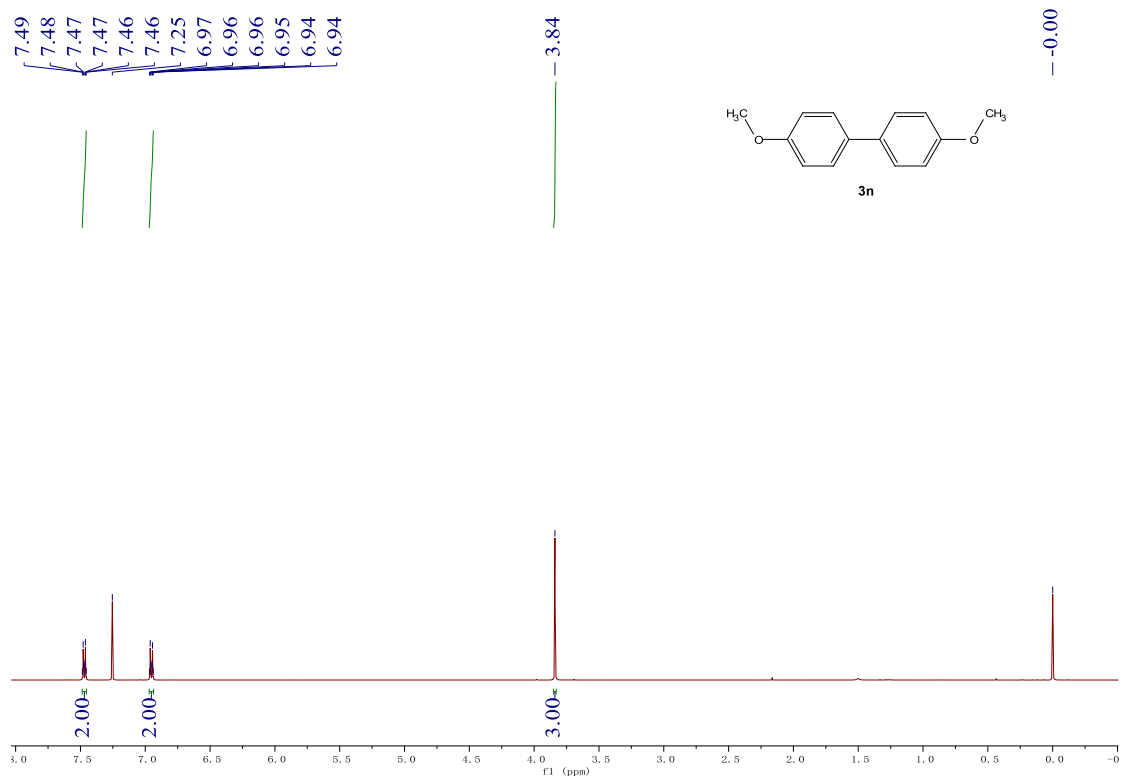
<sup>1</sup>H NMR



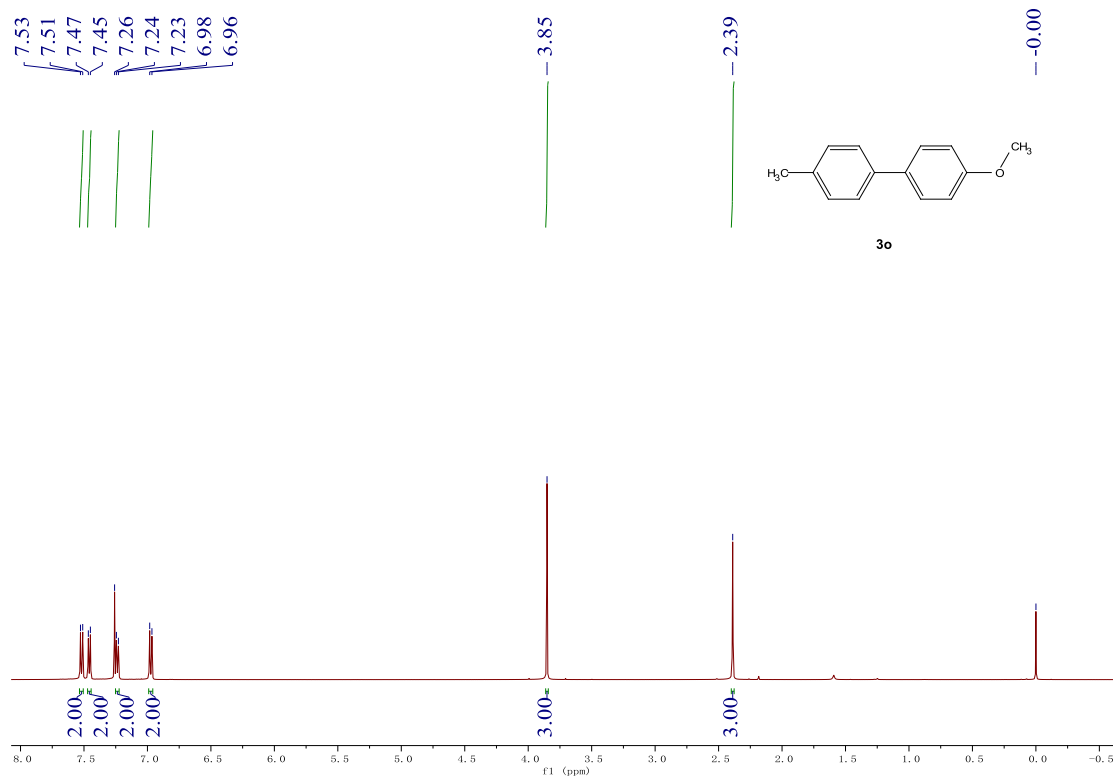
<sup>1</sup>H NMR



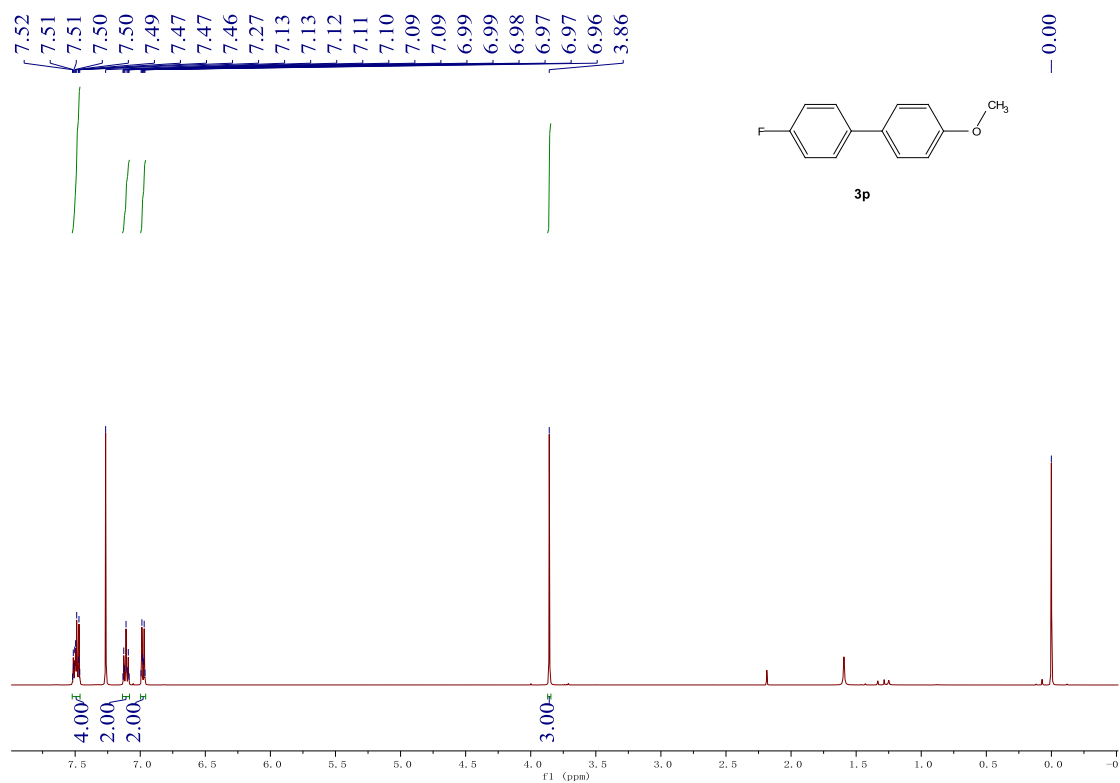
<sup>1</sup>H NMR



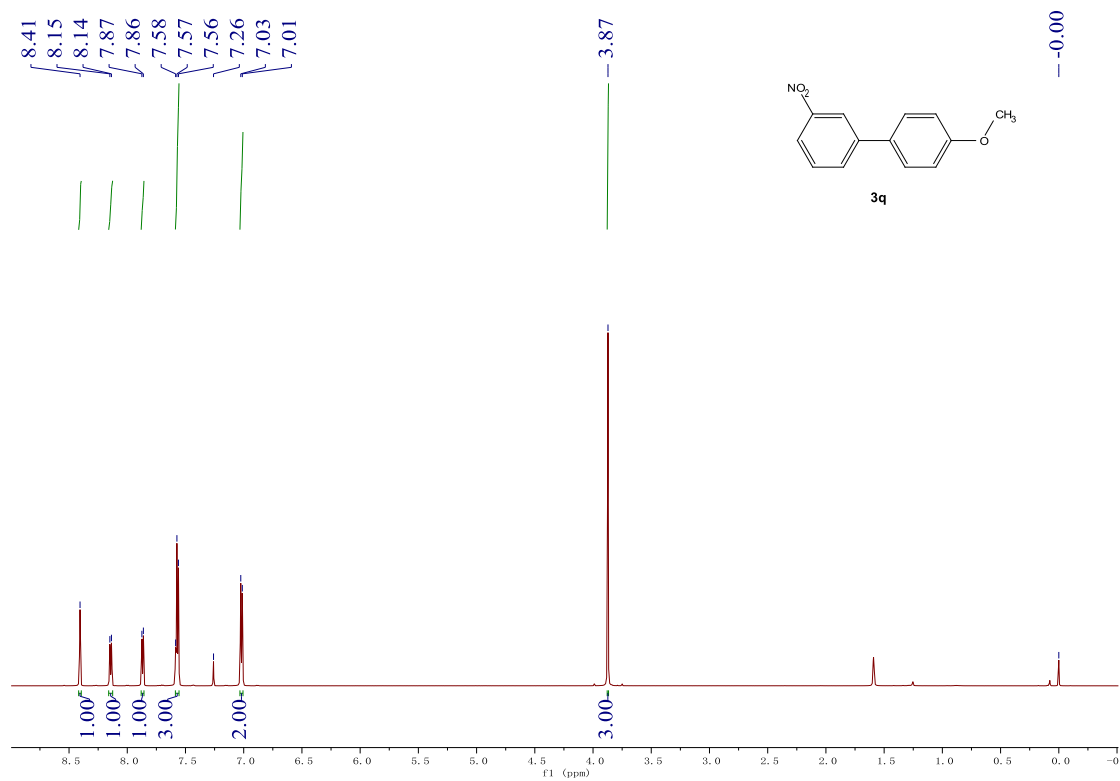
<sup>1</sup>H NMR



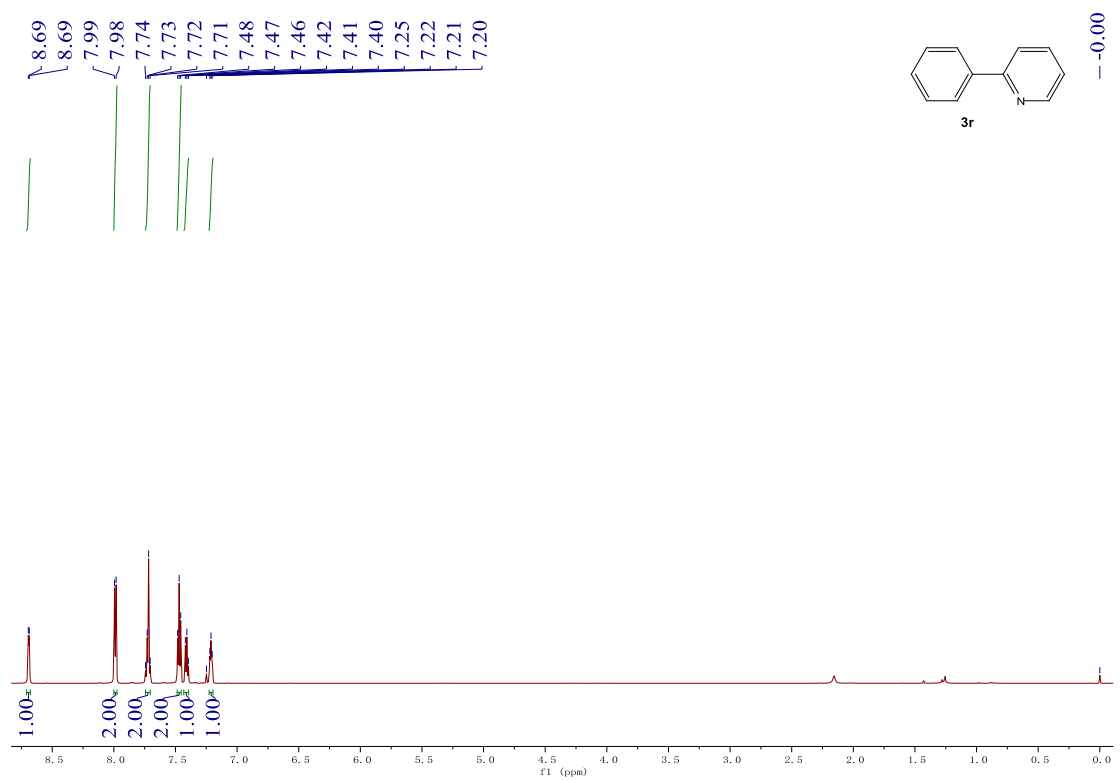
<sup>1</sup>H NMR



<sup>1</sup>H NMR

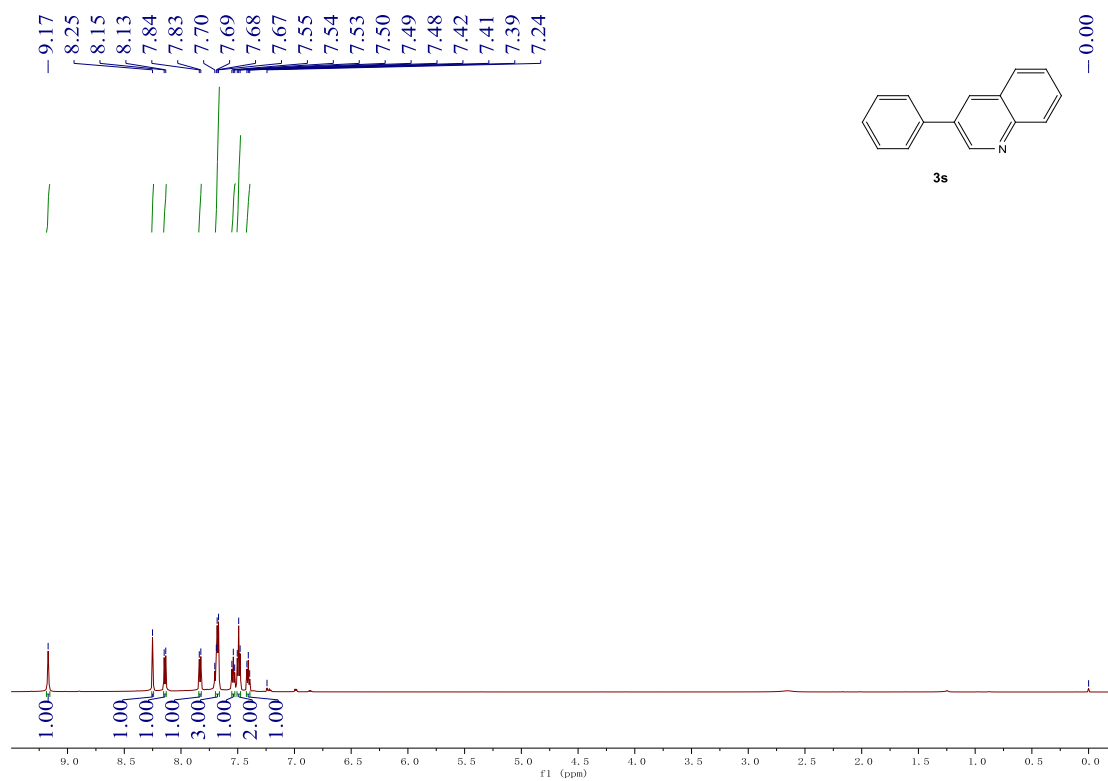


<sup>1</sup>H NMR

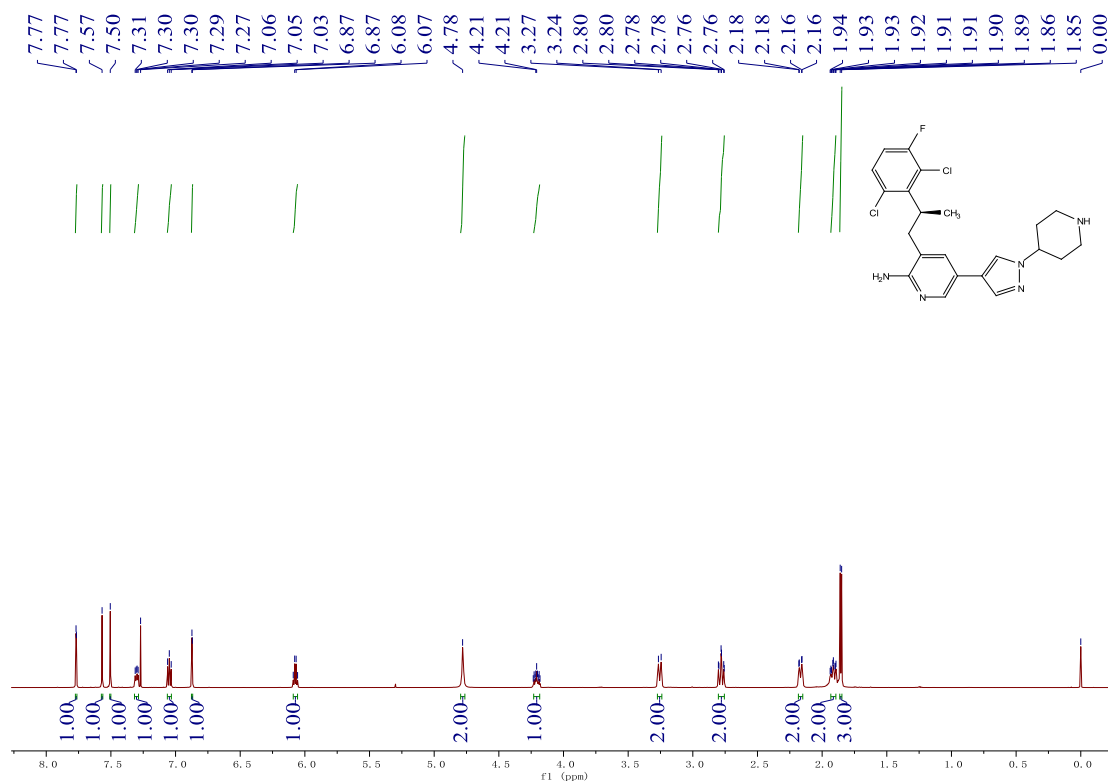




<sup>1</sup>H NMR



<sup>1</sup>H NMR



<sup>13</sup>C NMR

