

**Palladium-Catalyzed Selective [2+2+2] Annulation of  
2-(2-enynyl)-Pyridines with Arynes**

Zongli Xiong,<sup>a</sup> Jingxiang Duan,<sup>a</sup> Xiaoyi Li,<sup>a</sup> Xin Wang,<sup>a</sup> Yesu Addepalli,<sup>a</sup>  
Mengxue Lu,<sup>a</sup> Weijun Yao,<sup>b</sup> Ling He,<sup>\*a</sup> Zhen Wang<sup>\*a</sup>

<sup>a</sup> School of Pharmaceutical Sciences and Chongqing Key Laboratory of Natural Drug Research, Chongqing University, Chongqing 401331, P.R. China.

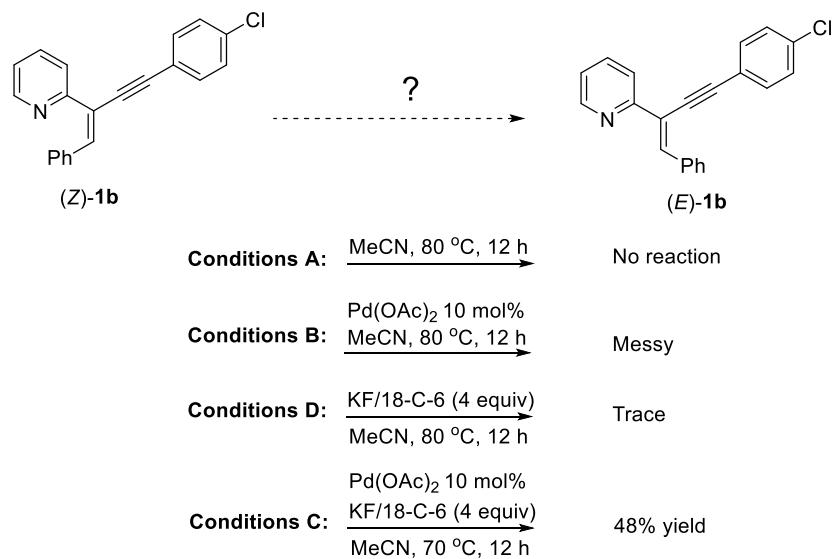
E-mail: heling2015@cqu.edu.cn (Ling He); wangz1114@cqu.edu.cn (Zhen Wang)

<sup>b</sup> Department of Chemistry, Zhejiang Sci-Tech University, Hangzhou, 310018, P. R. China.

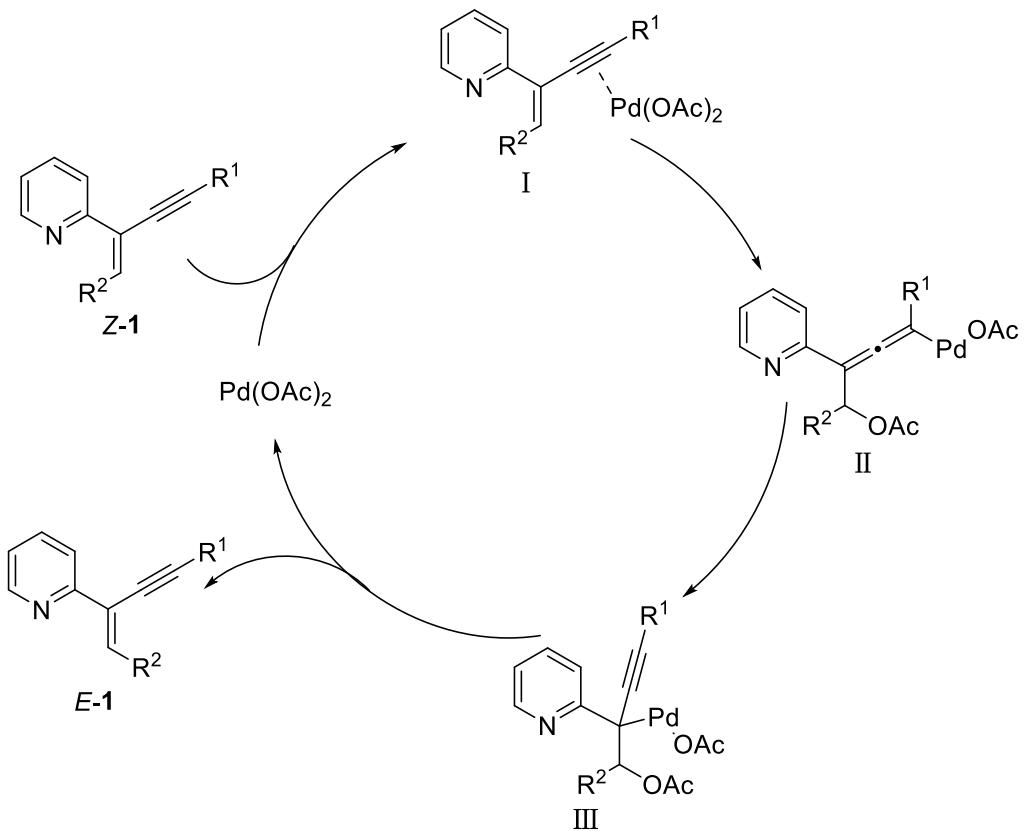
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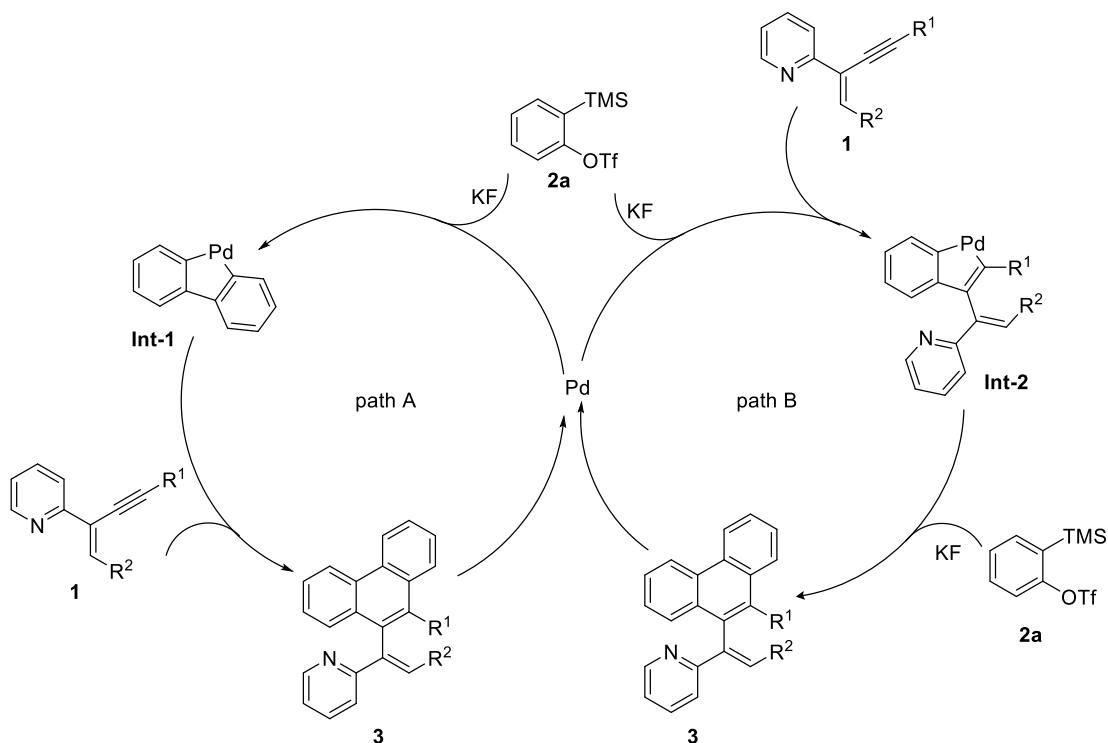
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## 1. Control Experiments

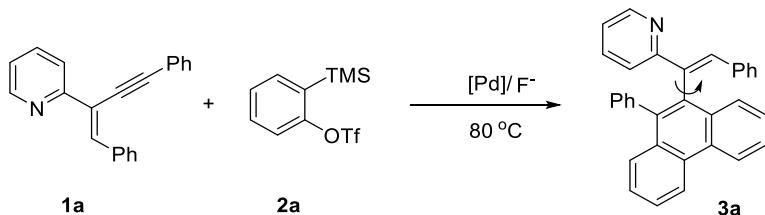


## 2. Proposed mechanism of the isomerization and [2+2+2] annulation reaction





### 3. Exploration of Asymmetric Synthesis of 3a



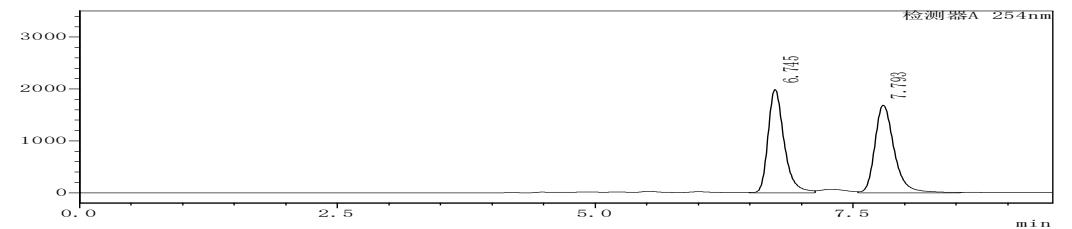
Entry <sup>a</sup>	[Pd]	Ligand	Yield [%] <sup>b</sup>	ee [%] <sup>c</sup>
1	Pd(OAc) <sub>2</sub>	(S)-DTBM-SEGPHOS	28	0
2	Pd(OAc) <sub>2</sub>	(R)-H8-BINAP	24	0
3 <sup>d</sup>	Pd <sub>2</sub> (dba) <sub>3</sub>	(S)-BINAP	30	0
4 <sup>e</sup>	Pd(OAc) <sub>2</sub>	L-Valine	32	0
5 <sup>e</sup>			41	0

<sup>a</sup> Reactions were carried out with **1a** (0.1 mmol), **2a** (0.3 mmol), CsF (0.4 mmol) and palladium catalyst (10 mol%), ligand (10 mol%) in 1.5 mL MeCN at 80 °C for 9 h. <sup>b</sup> Isolated yield. <sup>c</sup> The ee was determined by chiral OD-H column. <sup>d</sup> The reactions were performed in mixture solvent of toluene and MeCN (3:2, v/v, 1.5 mL) and the reaction time was 17 h. <sup>e</sup> Reactions were carried out at 90 °C for 10 h.

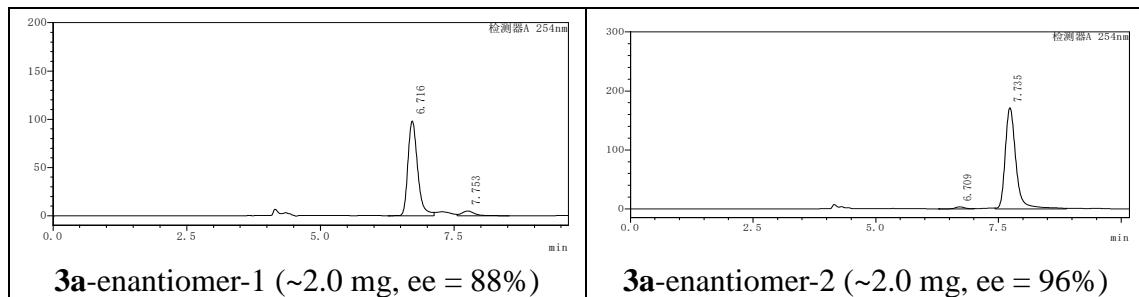
## 4. Separate enantiomers and stability experiments of 3a

### 4.1 Separating enantiomers of 3a

HPLC (chiral ID column), hexane/*i*-PrOH = 95/5, flow rate 0.8 mL/min,  $\lambda = 254$  nm, retention times: 6.75 min, 7.79 min.



	Retention Time	Area	% Area
1	6.745	21632831	49.661
2	7.793	21928270	50.339

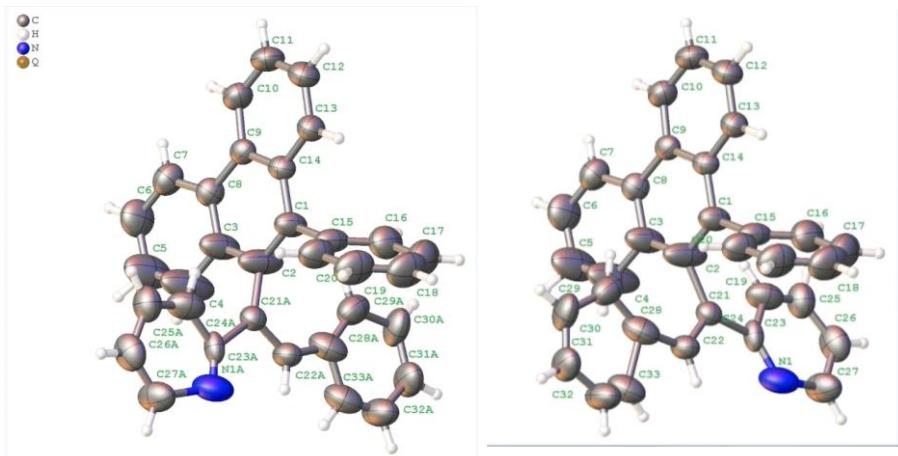


### 4.2 Stability experiments of enantiomers of 3a

Condition A: In 1.0 mL MeCN at 80 °C for 10 h			
3a-enantiomer-1	MeCN, 80 °C 10 h	3a-enantiomer-1	88% ee
Condition B: In the presence of Pd(OAc) <sub>2</sub> (2.0 mg), KF (2.0 mg) and 18-Crown-6 (2.0 mg) in 1.0 mL MeCN at 80 °C for 12 h			
3a-enantiomer-2	Pd(OAc) <sub>2</sub> KF/18-Crown-6 MeCN, 80 °C, 12 h	3a-enantiomer-2	96% ee

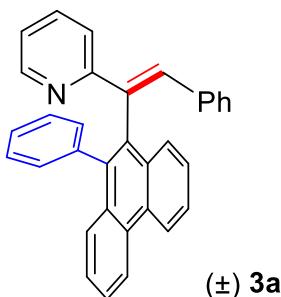
## 5. The Crystallographic Data for 3a

CCDC 2069495 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif). The crystal was prepared by recrystallization in PE/DCM solvent. Single crystal X-ray diffraction measurements were carried out using an Oxford Technologies Exalibur EOS diffractometer. Using Olex2, the structure was solved with the ShelXT structure solution program using Direct Methods and refined with the ShelXL refinement package using Least Squares minimization. All of the non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined by using riding coordinates.



X-Ray of ( $\pm$ )-**3a** (ellipsoids set at 100% probability)

CCDC 2069495



( $\pm$ ) **3a**

Crystallographic Data for C<sub>33</sub>H<sub>23</sub>N.

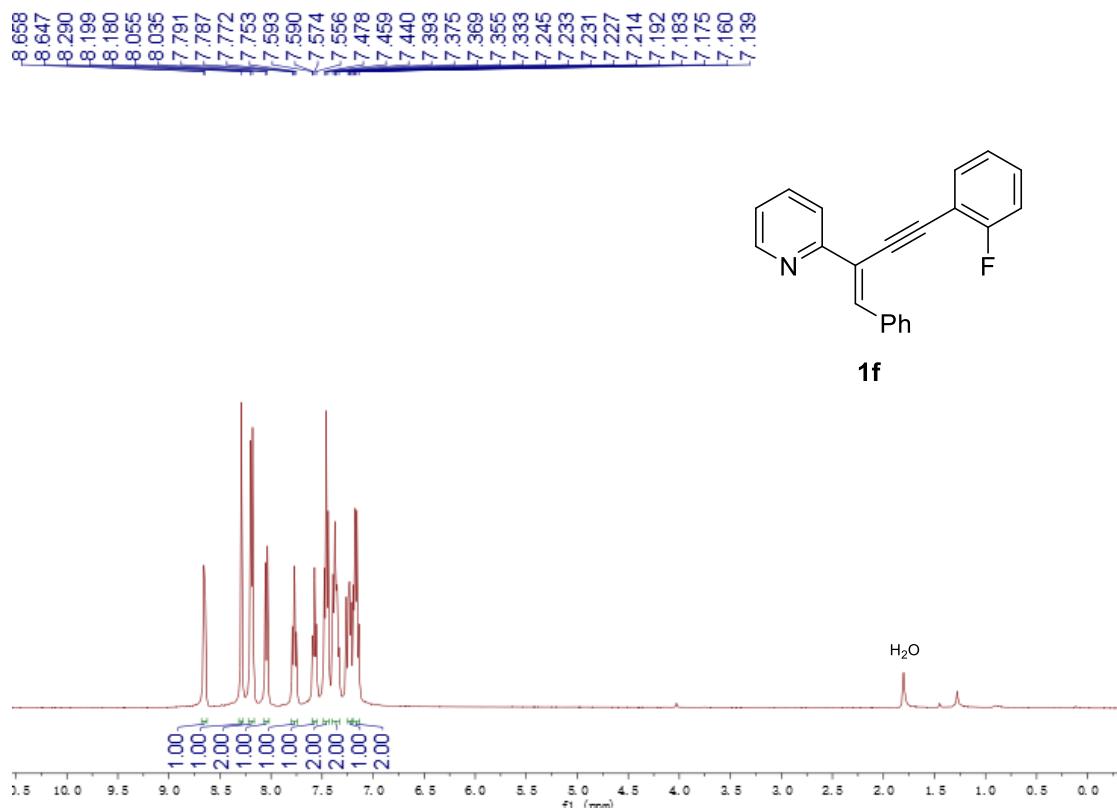
Formula	C <sub>33</sub> H <sub>23</sub> N
Formula mass (amu)	433.52
Space group	P -1
<i>a</i> (Å)	9.9695(9)
<i>b</i> (Å)	10.3713(6)
<i>c</i> (Å)	13.0454(8)
$\alpha$ (deg)	82.395(5)
$\beta$ (deg)	77.803(6)
$\gamma$ (deg)	63.984(7)
<i>V</i> (Å <sup>3</sup> )	1183.60(16)
<i>Z</i>	2
$\lambda$ (Å)	0.71073
<i>T</i> (K)	293 K
$\rho_{\text{calcd}}$ (g cm <sup>-3</sup> )	1.216
$\mu$ (mm <sup>-1</sup> )	0.070
Transmission factors	0.915, 1.000
$2\theta_{\max}$ (deg)	26.367
No. of unique data, including $F_o^2 < 0$	4848
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	2868
No. of variables	378
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ <sup>a</sup>	0.0941
$R_w(F_o^2)$ <sup>b</sup>	0.2359
Goodness of fit	1.087

<sup>a</sup>  $R(F) = \sum ||F_o| - |F_c|| / \sum |F_o|$ .

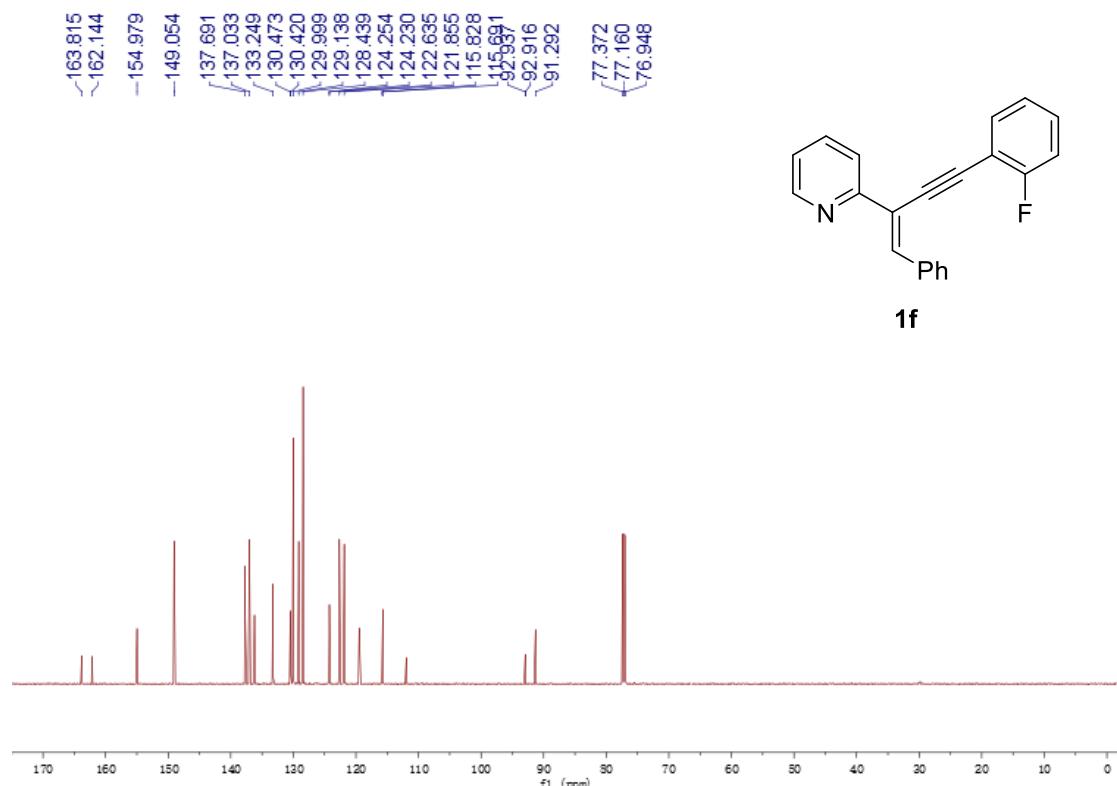
<sup>b</sup>  $R_w(F_o^2) = [\sum [w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$ ;  $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$ , where  $p = [\max(F_o^2, 0) + 2F_c^2] / 3$ .

## 6. Copies of NMR Spectra

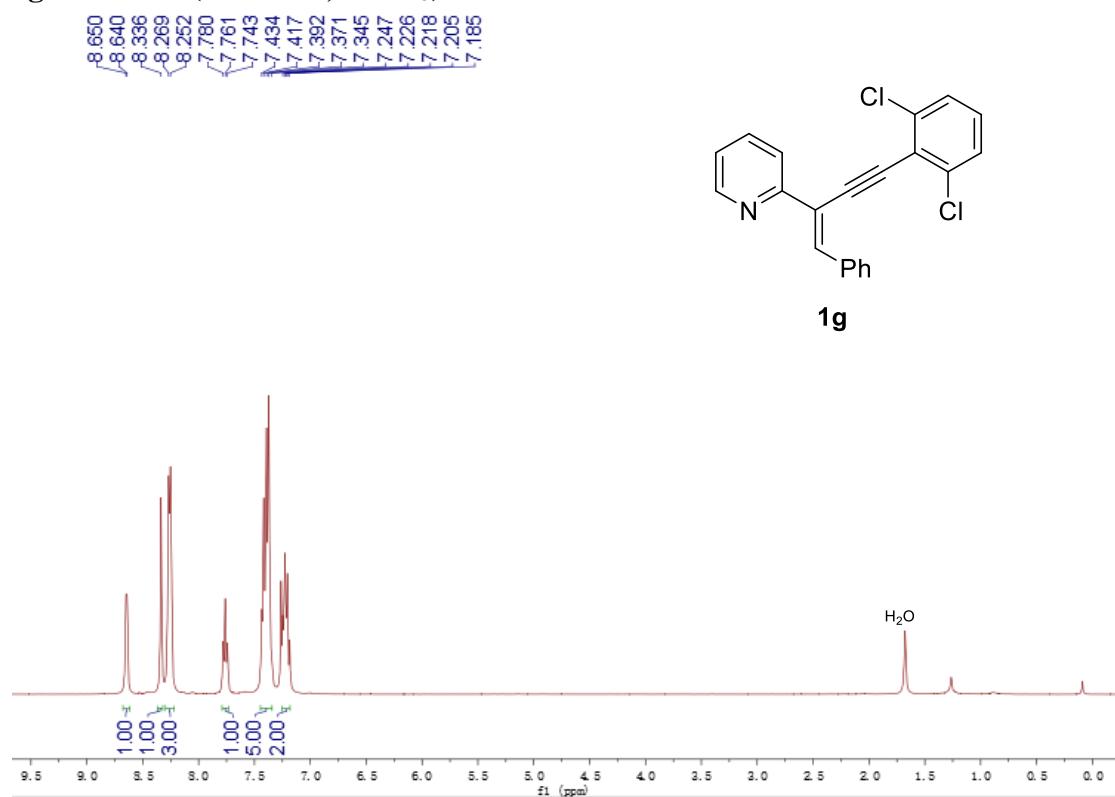
**1f-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



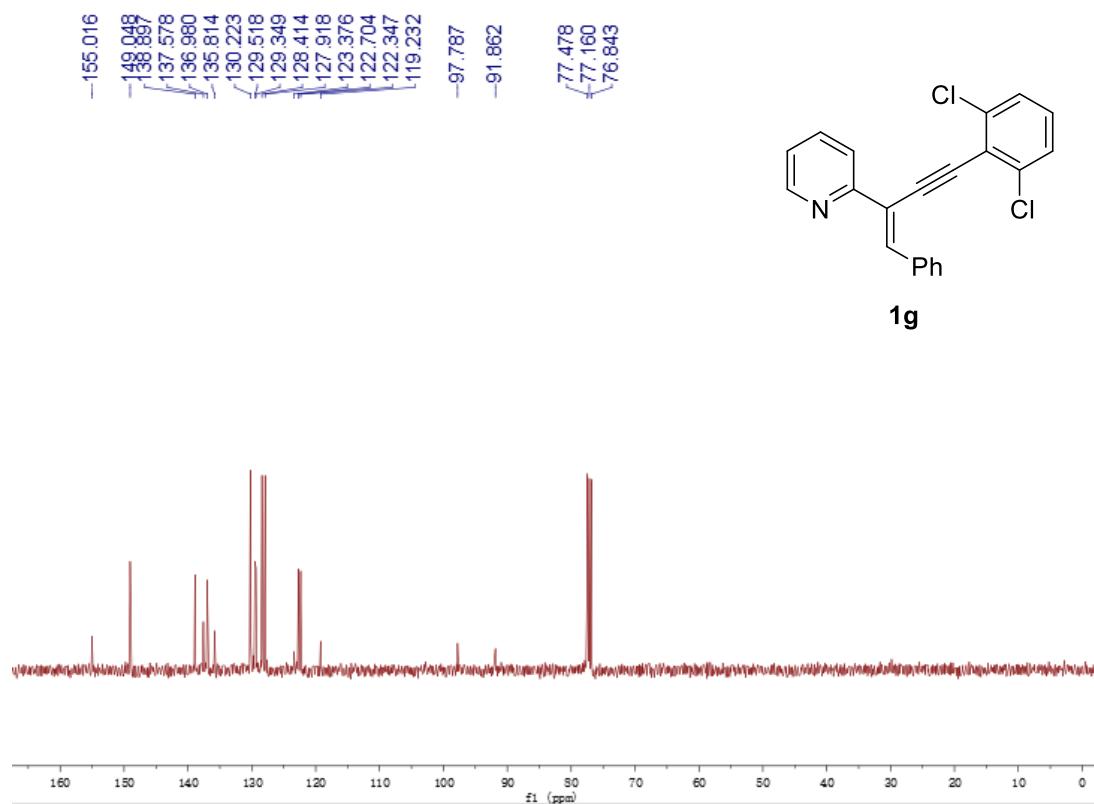
**1f-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



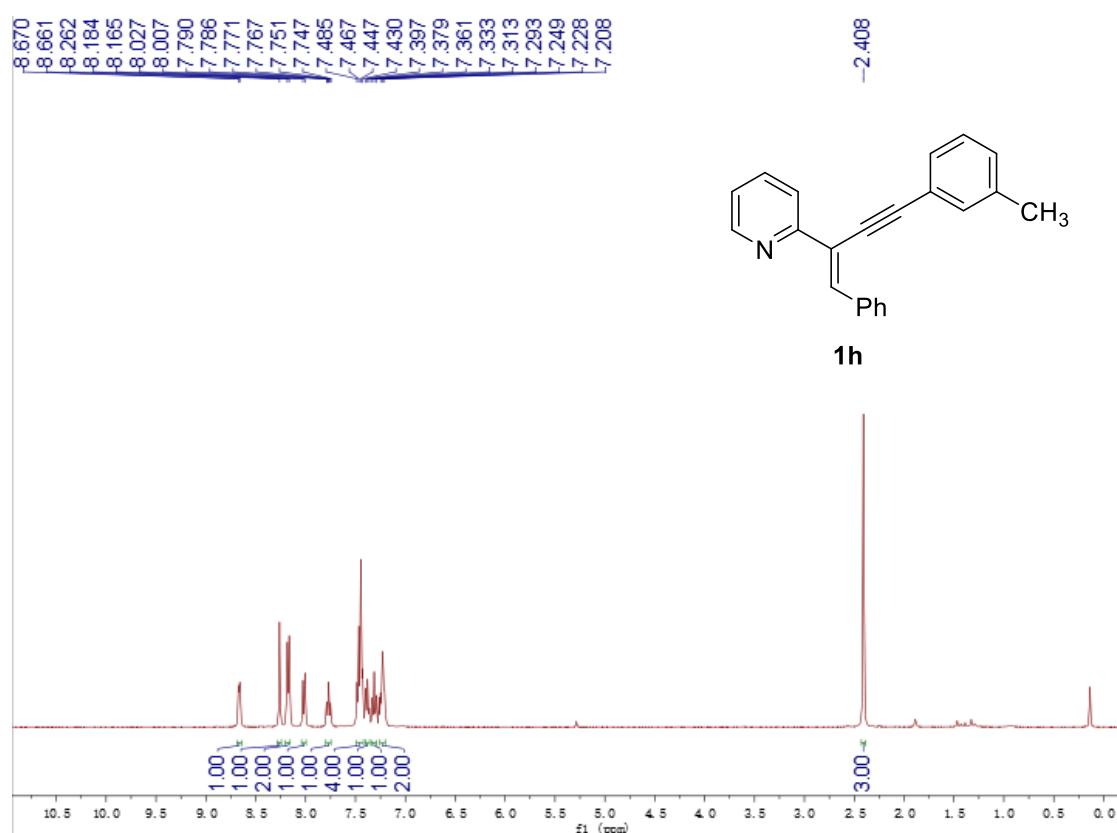
**1g-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



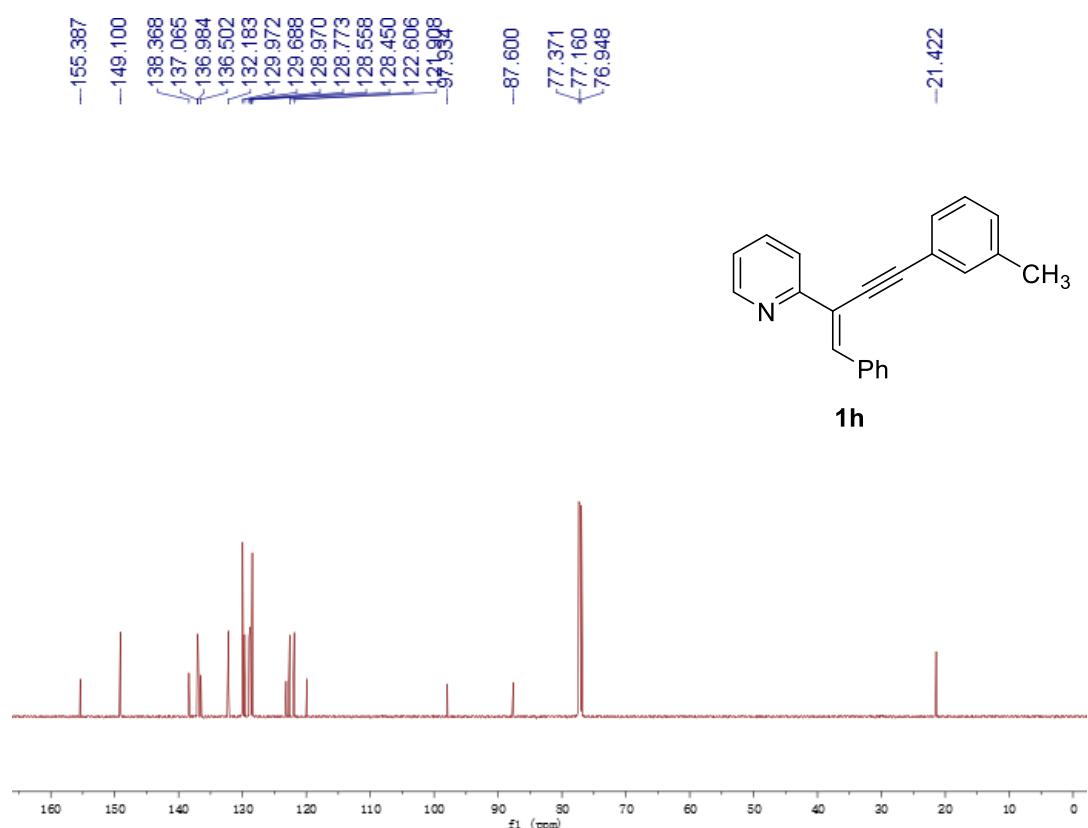
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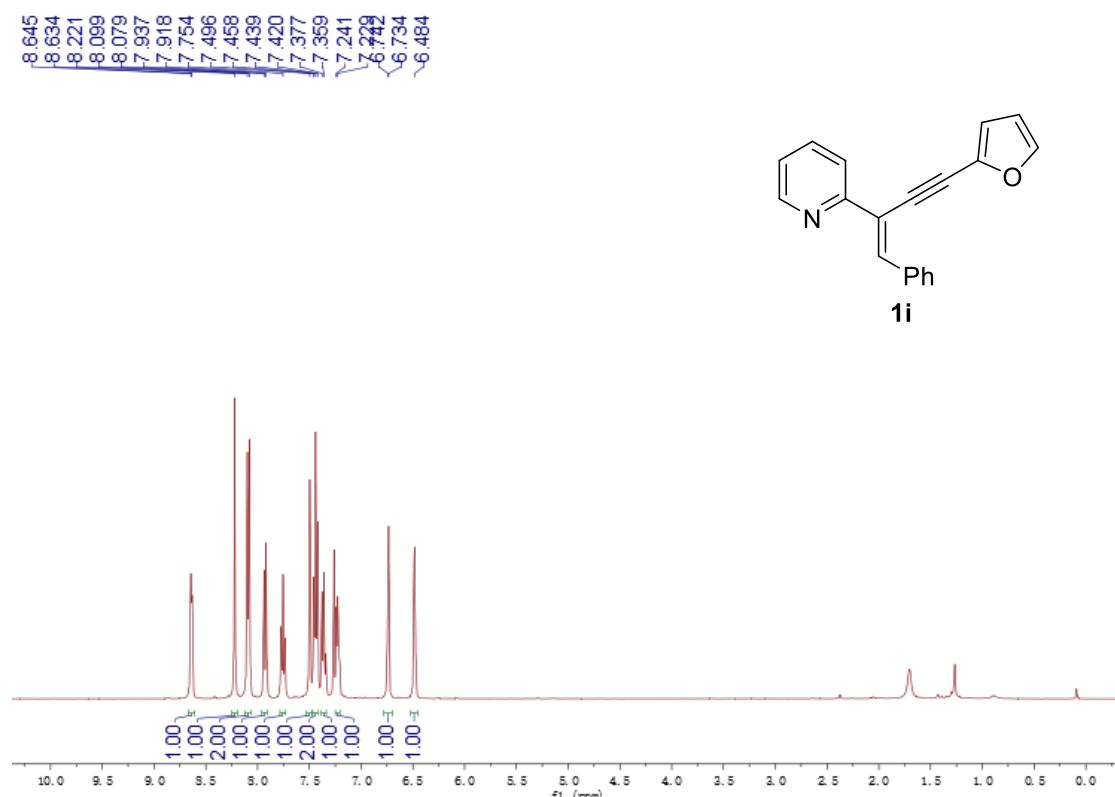
**1h-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



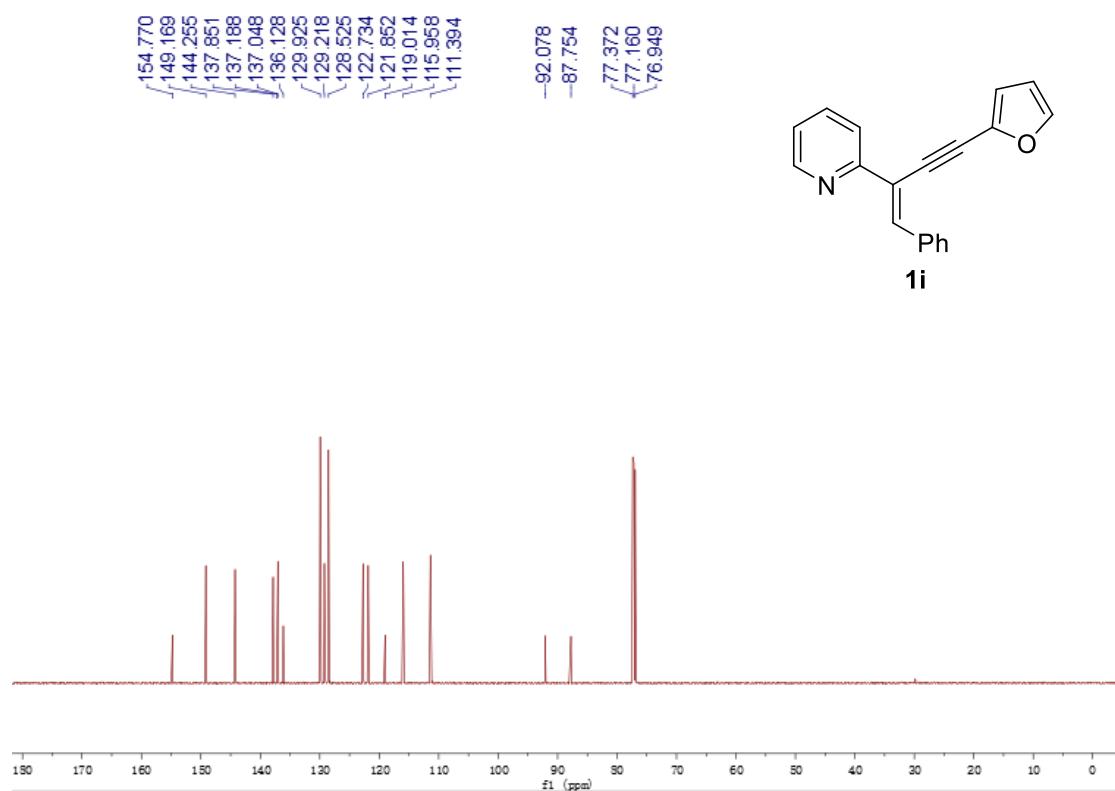
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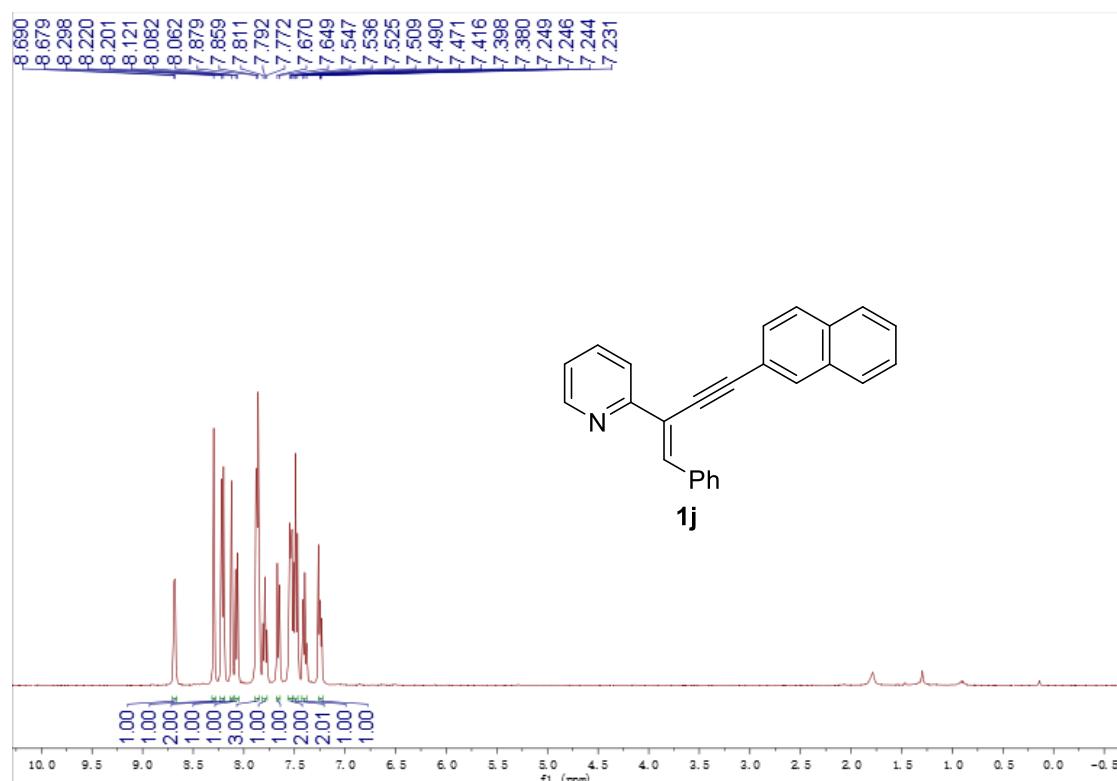
**1i-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



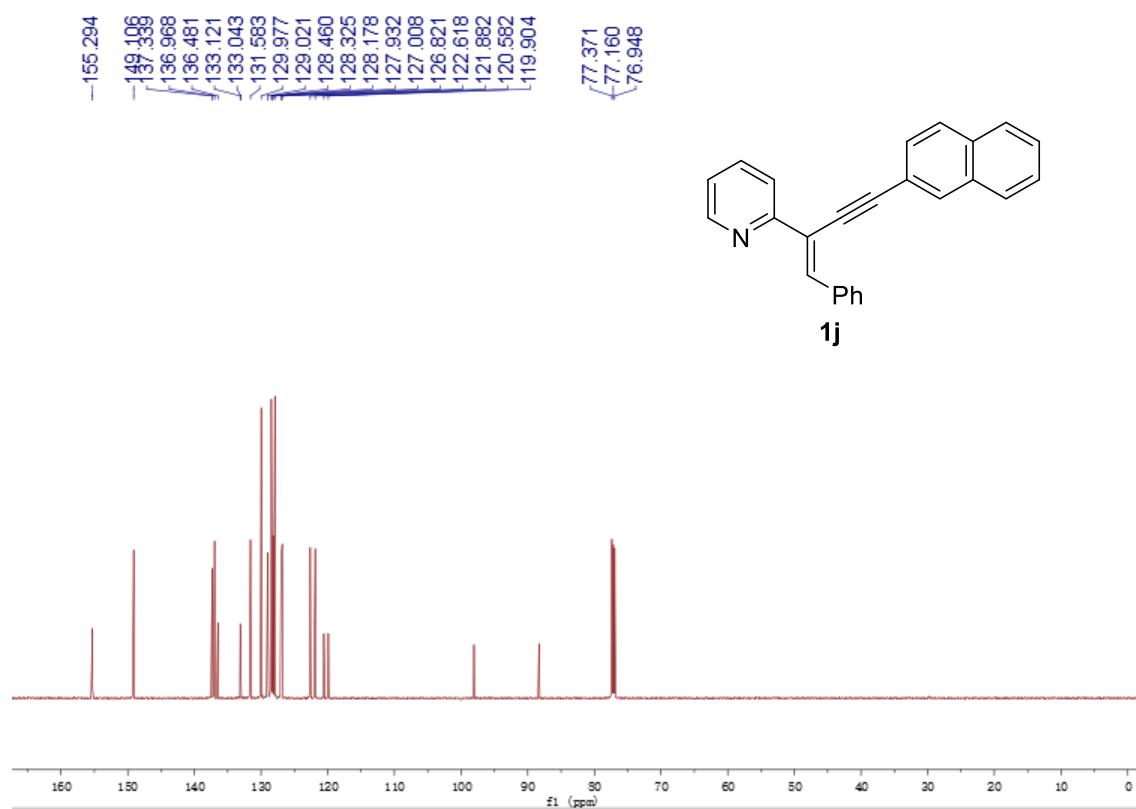
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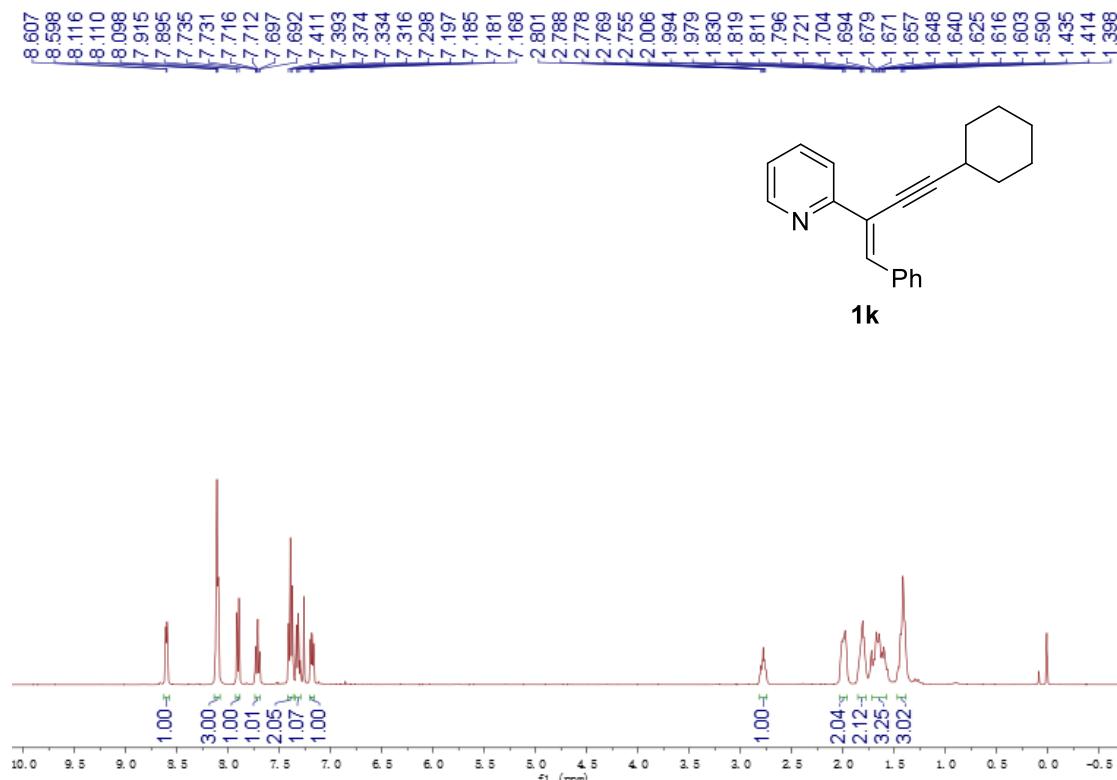
**1j-<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**



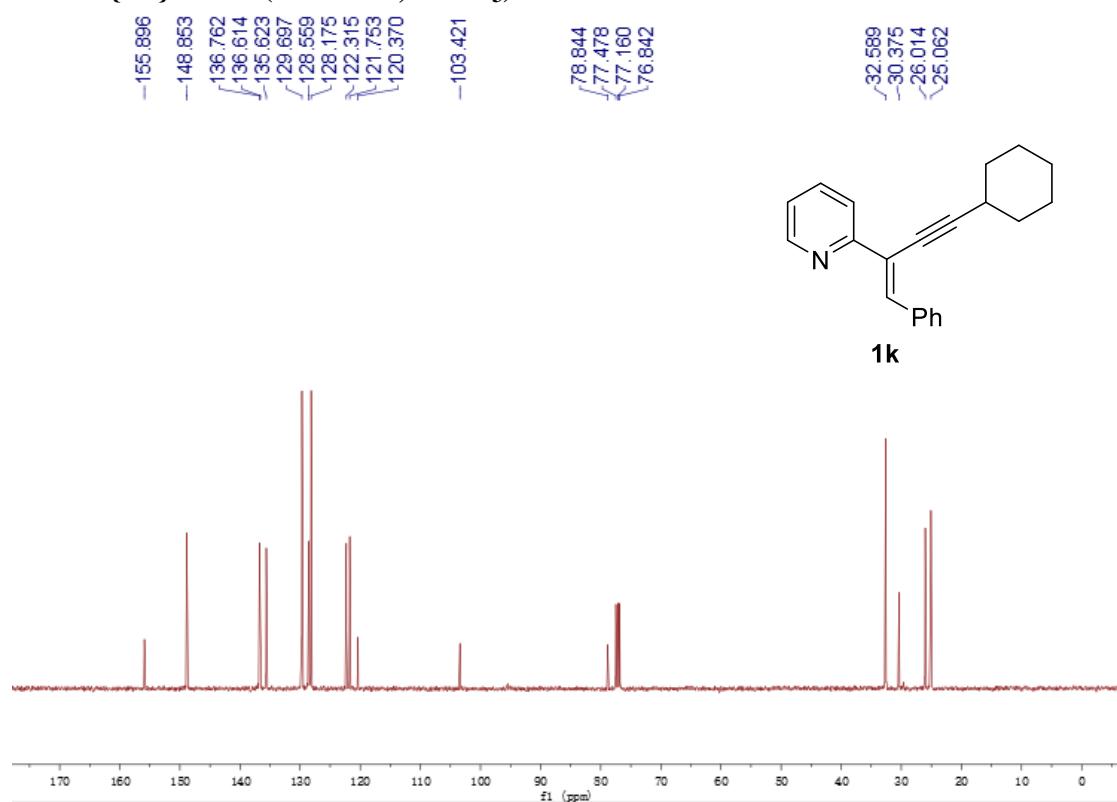
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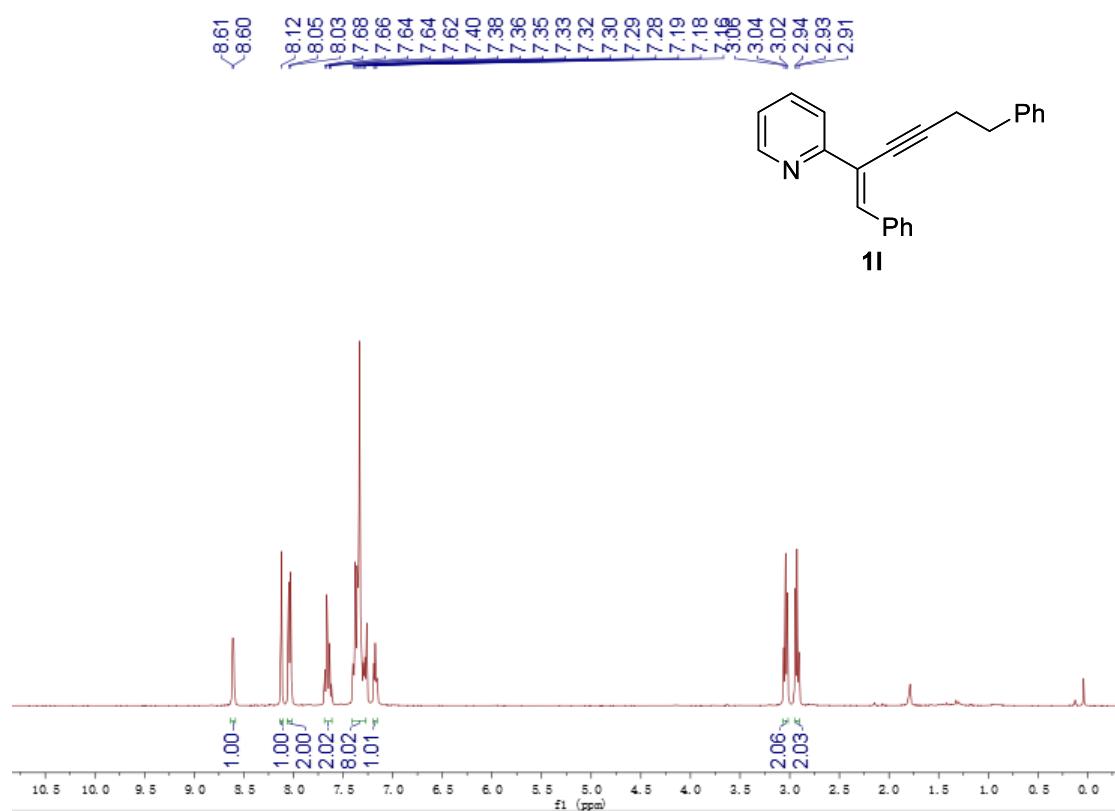
**1k-**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



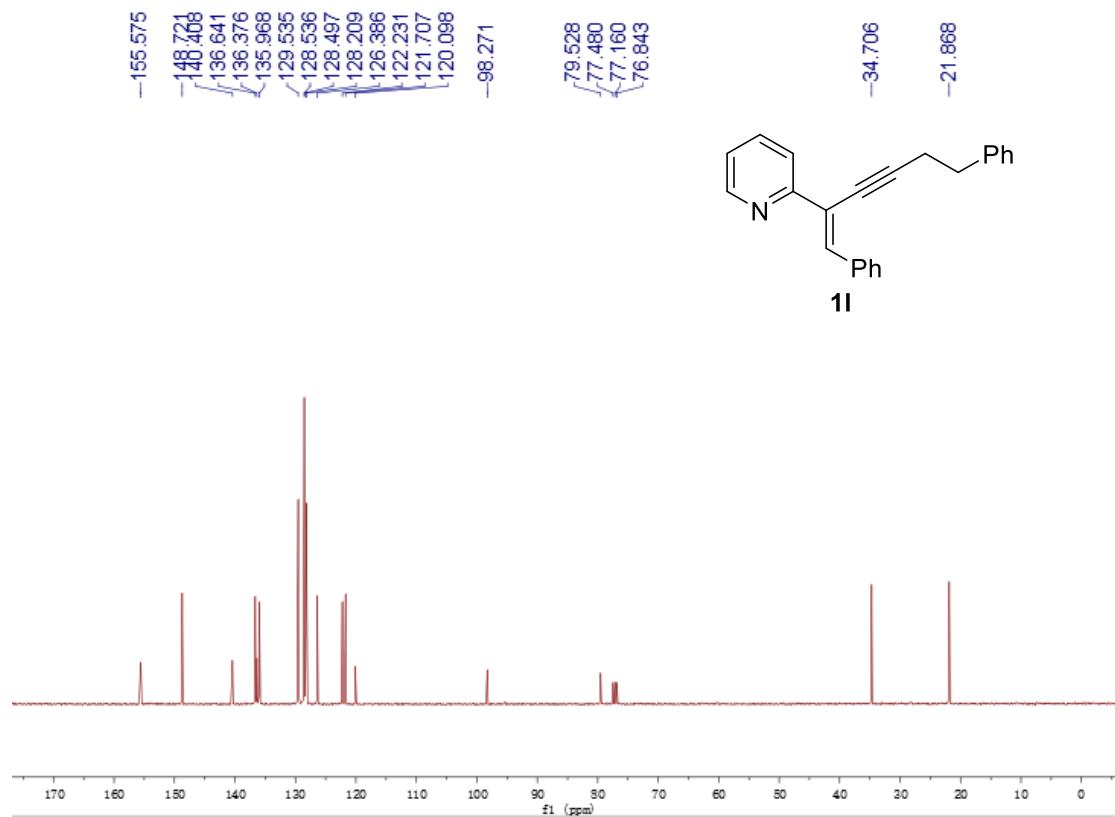
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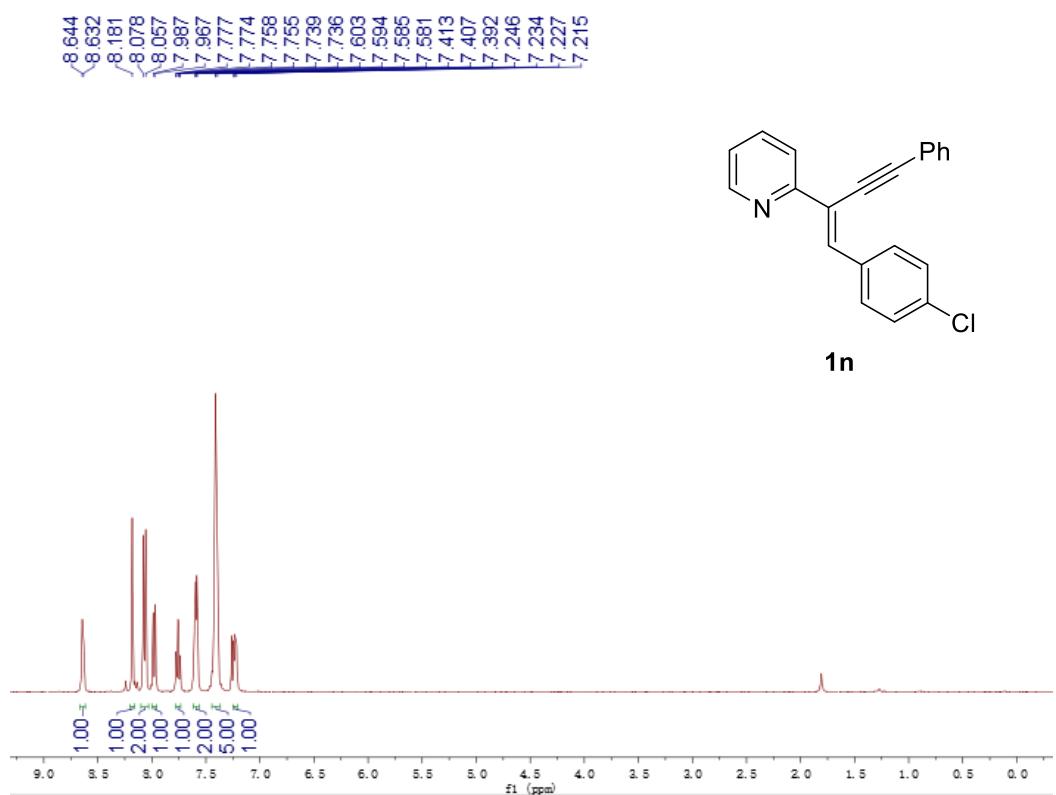
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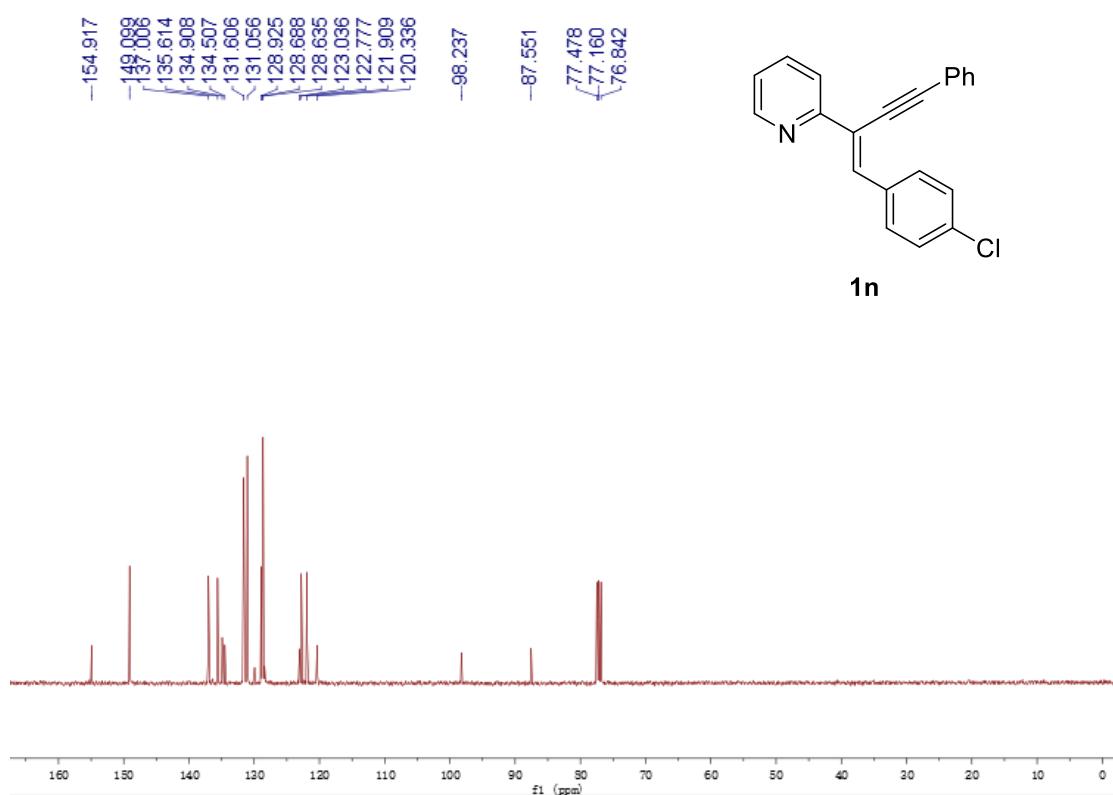
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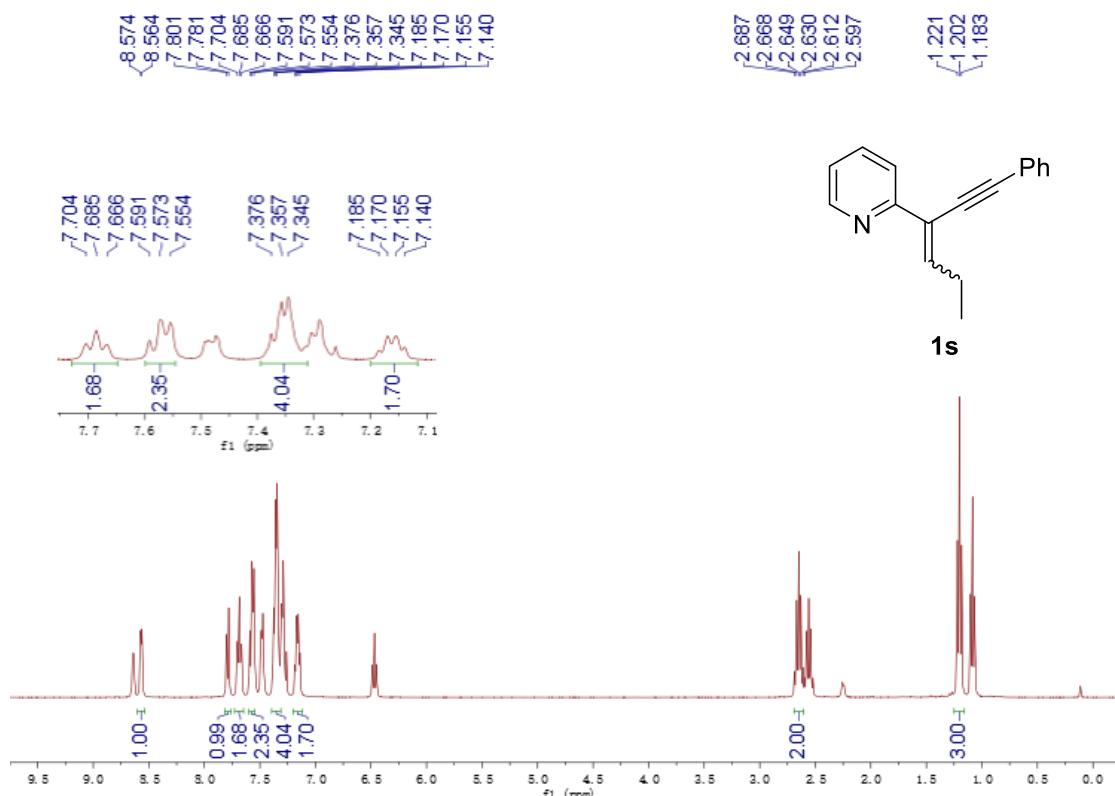
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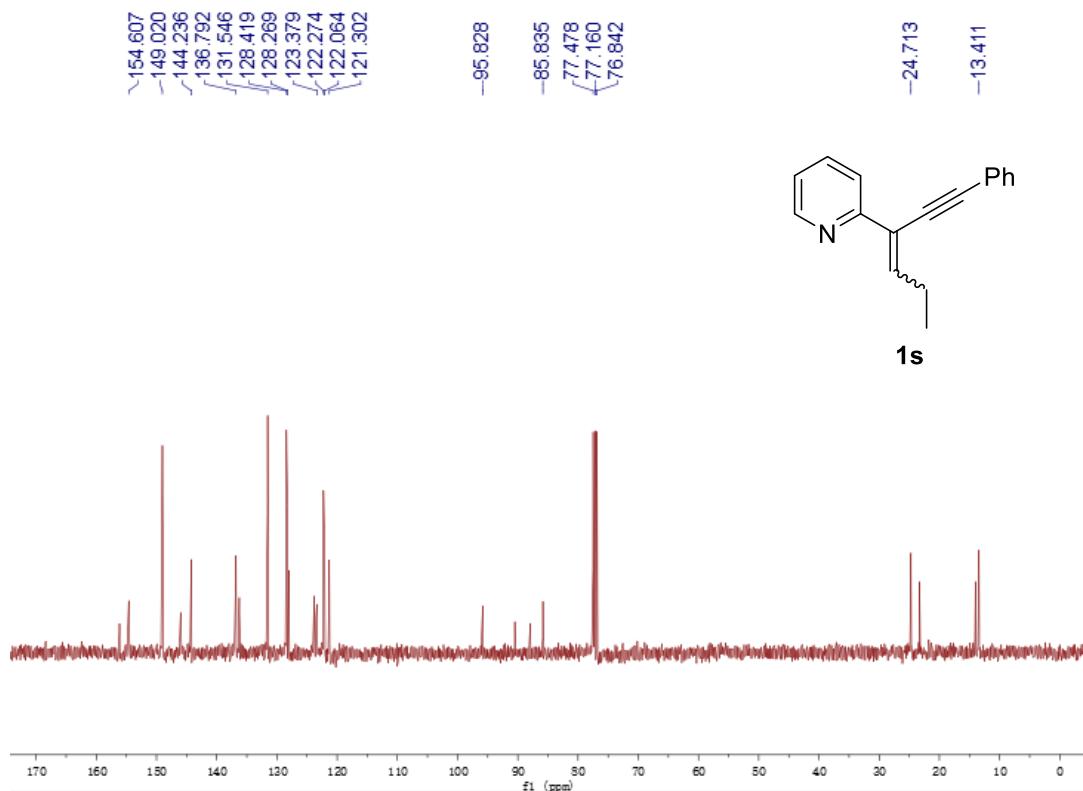
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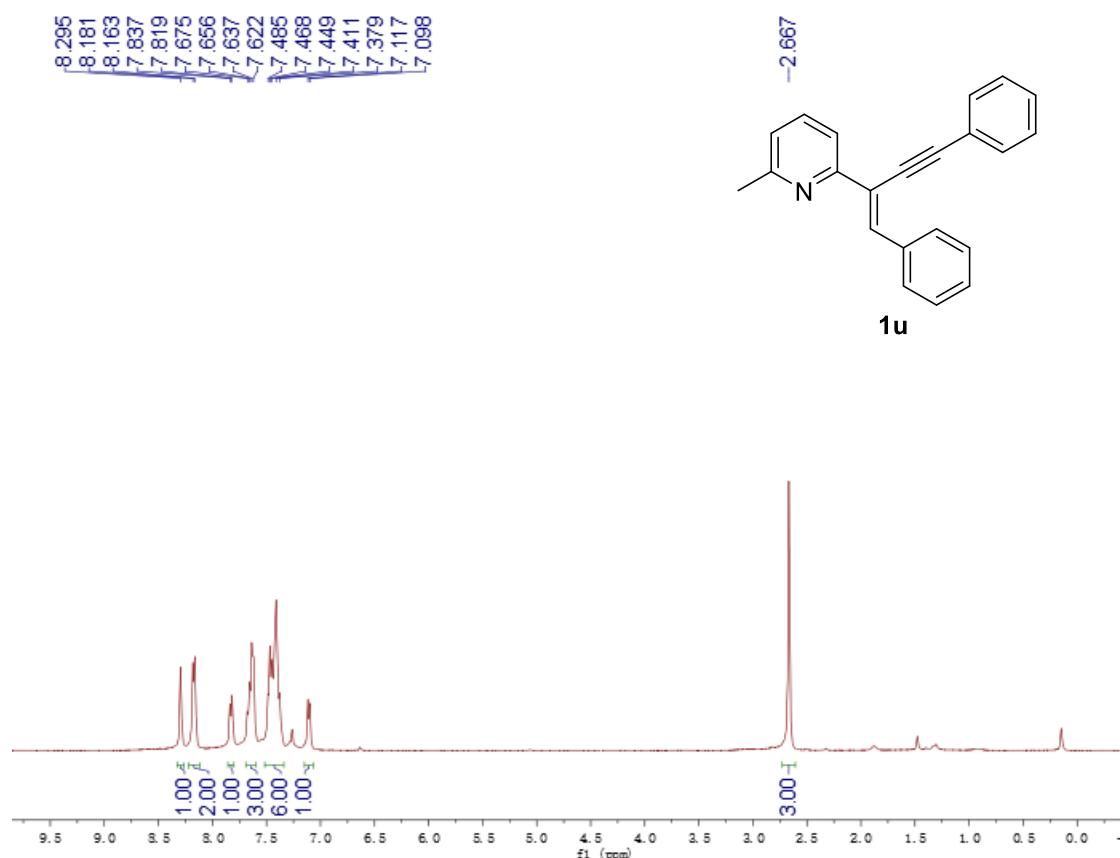
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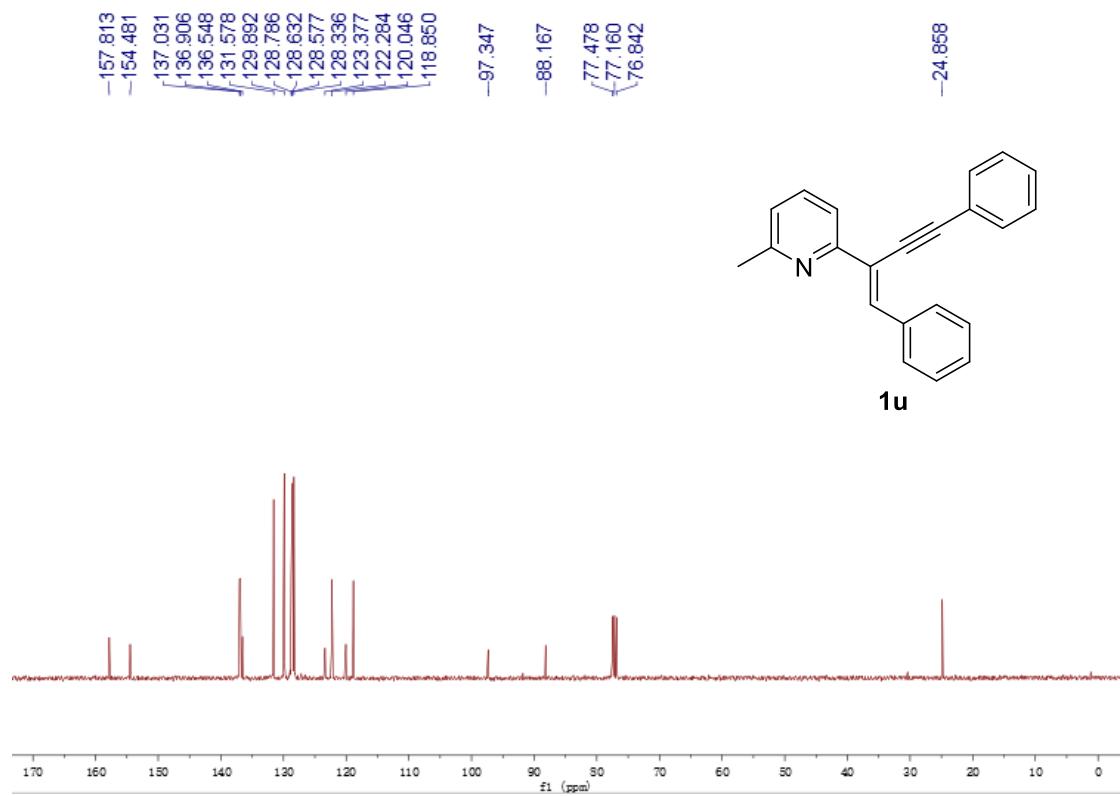
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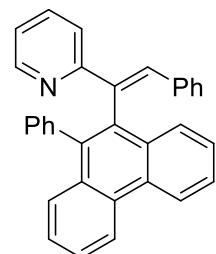
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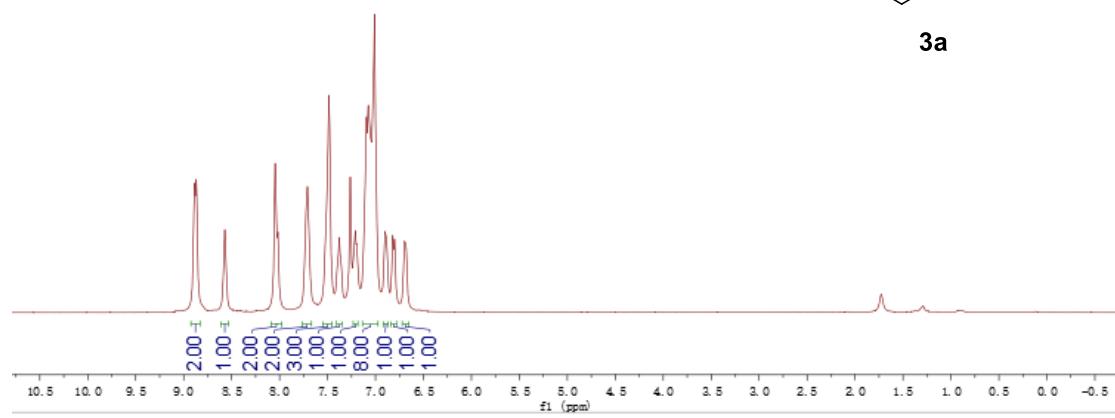
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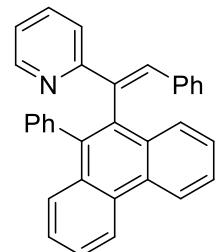
**3a-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



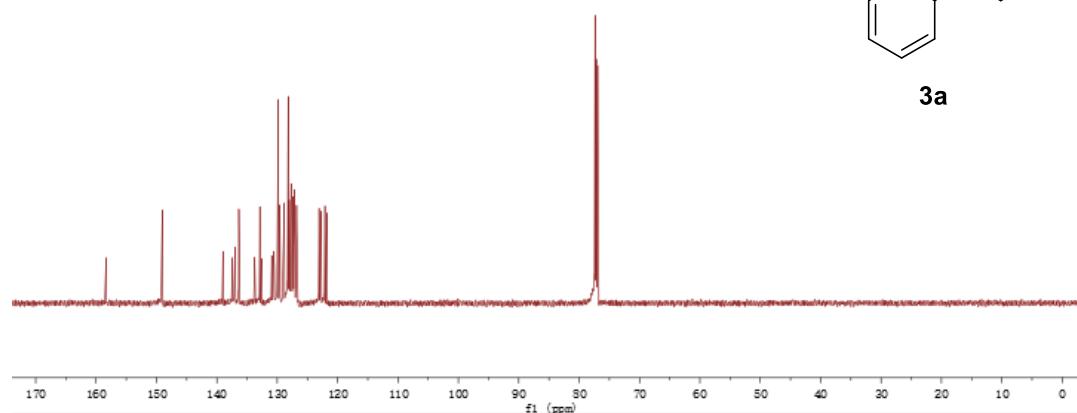
**3a**



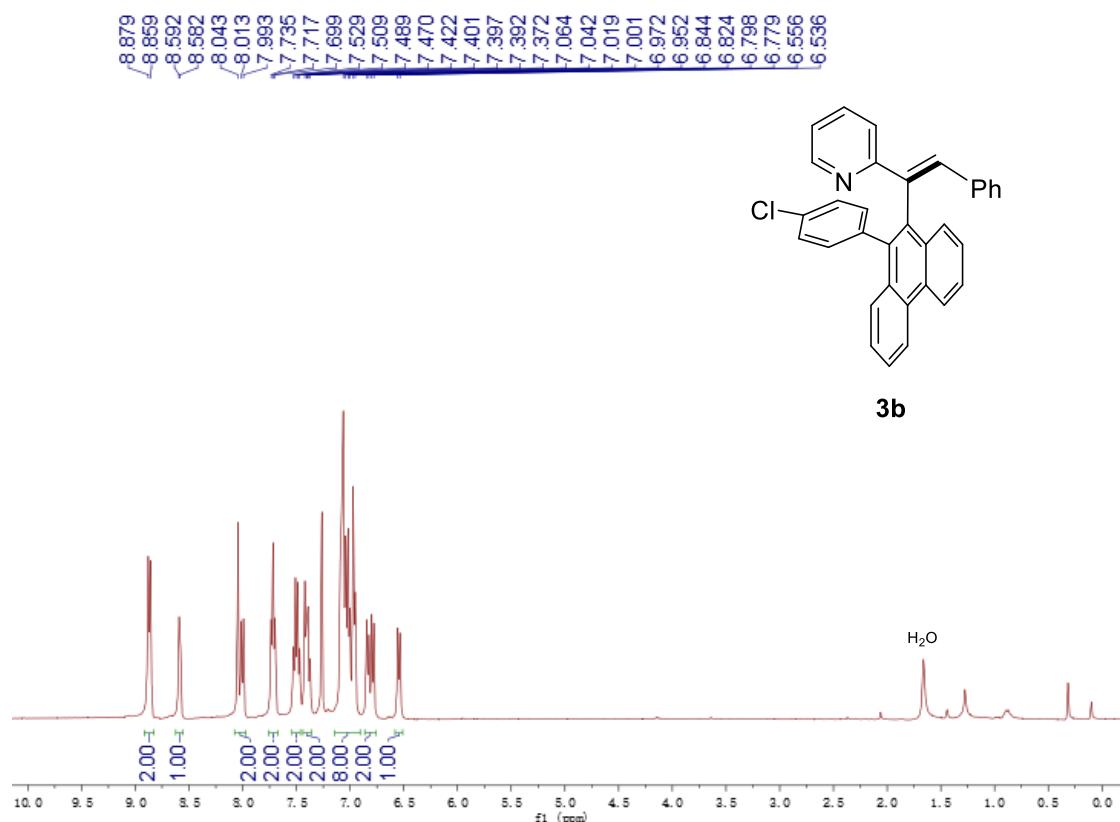
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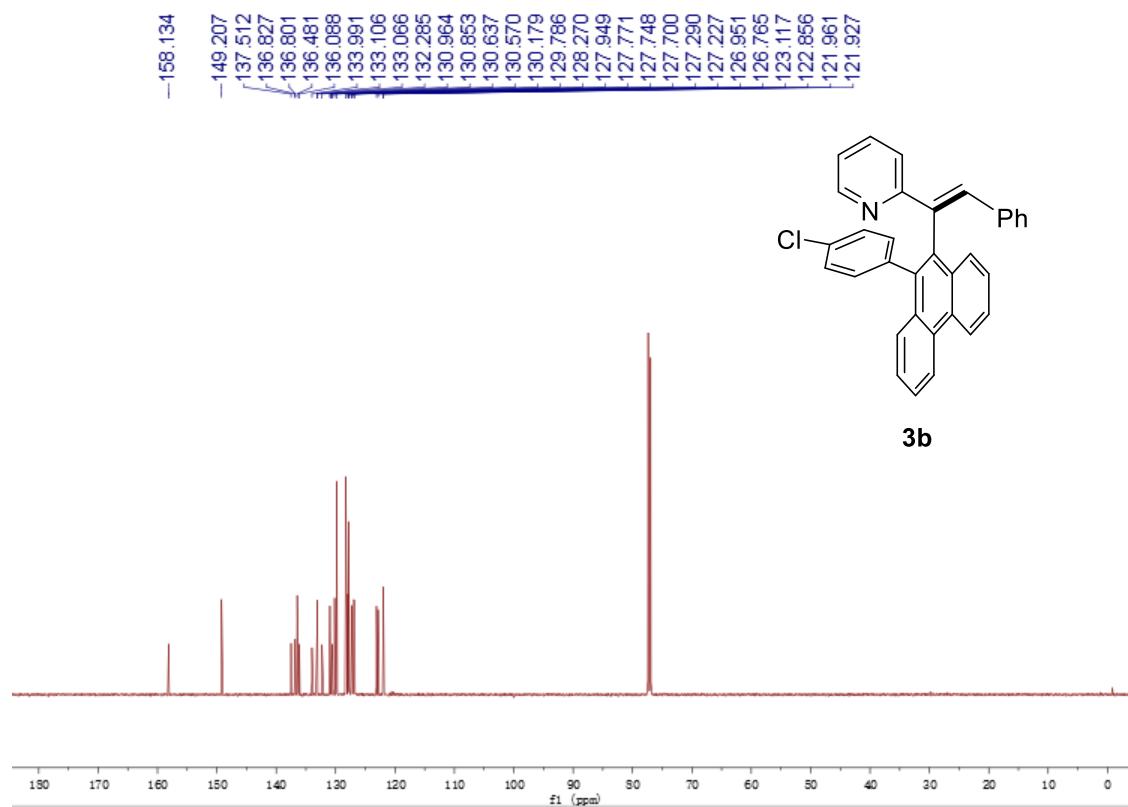
**3a**



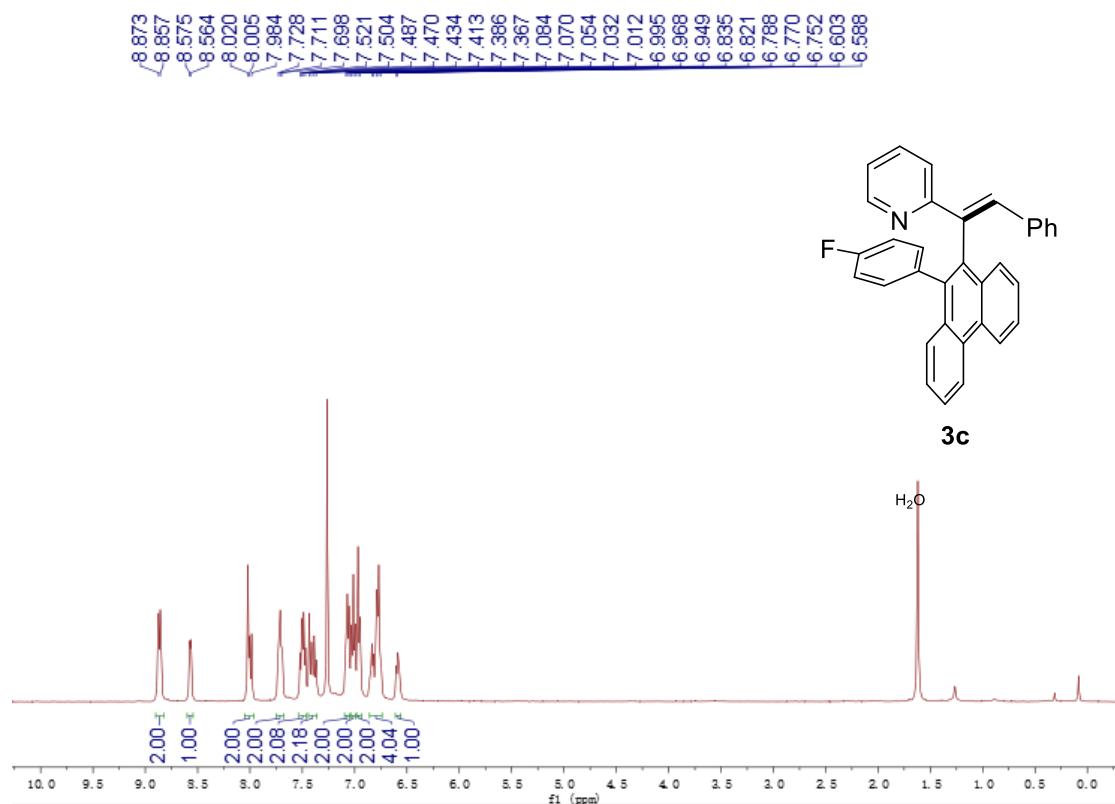
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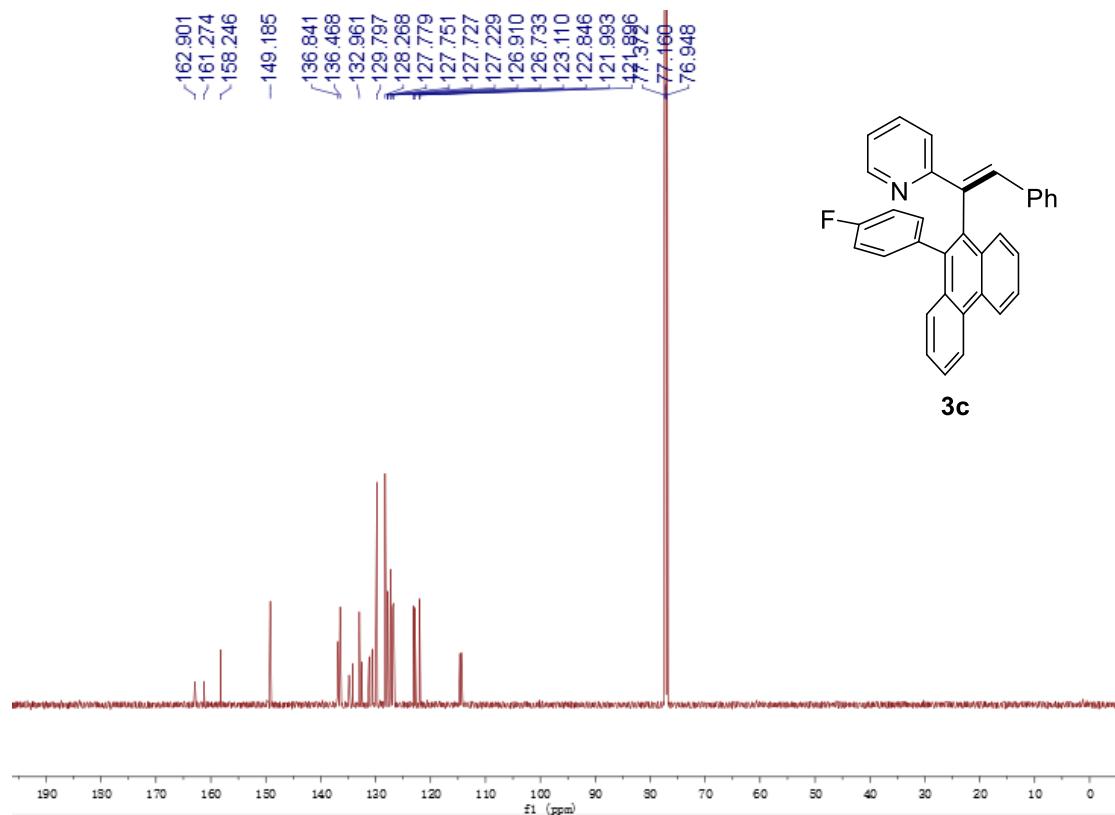
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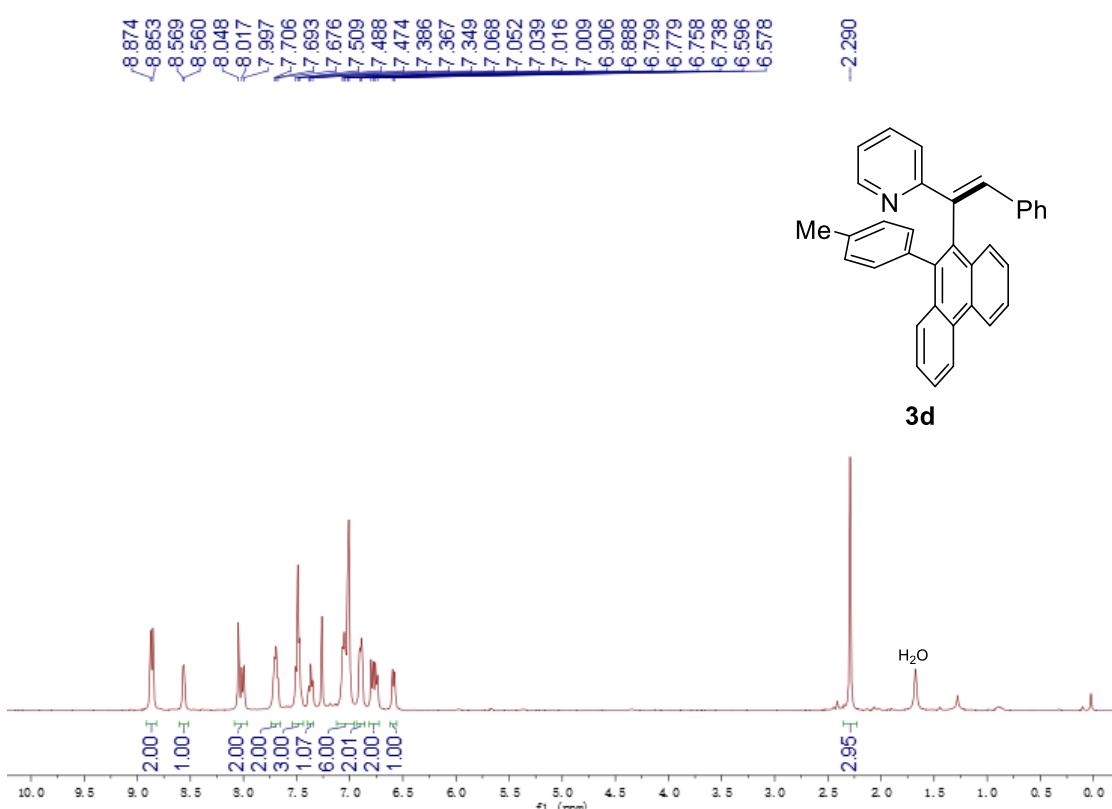
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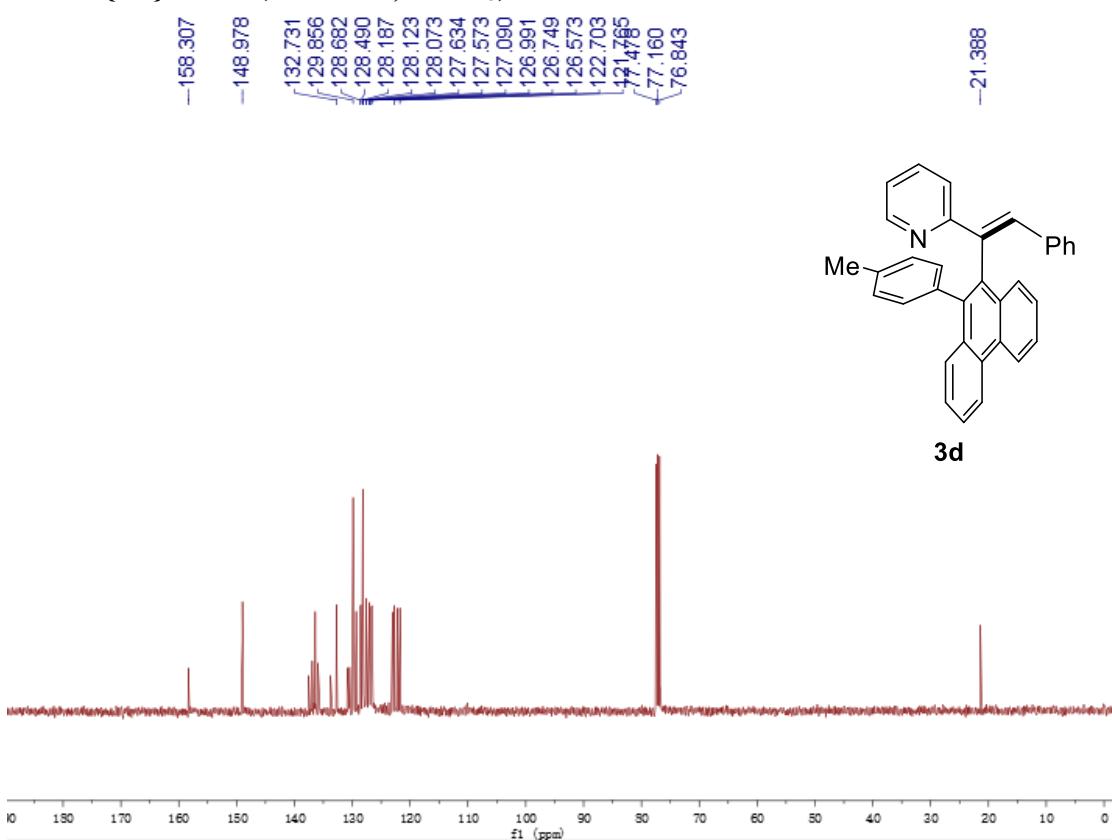
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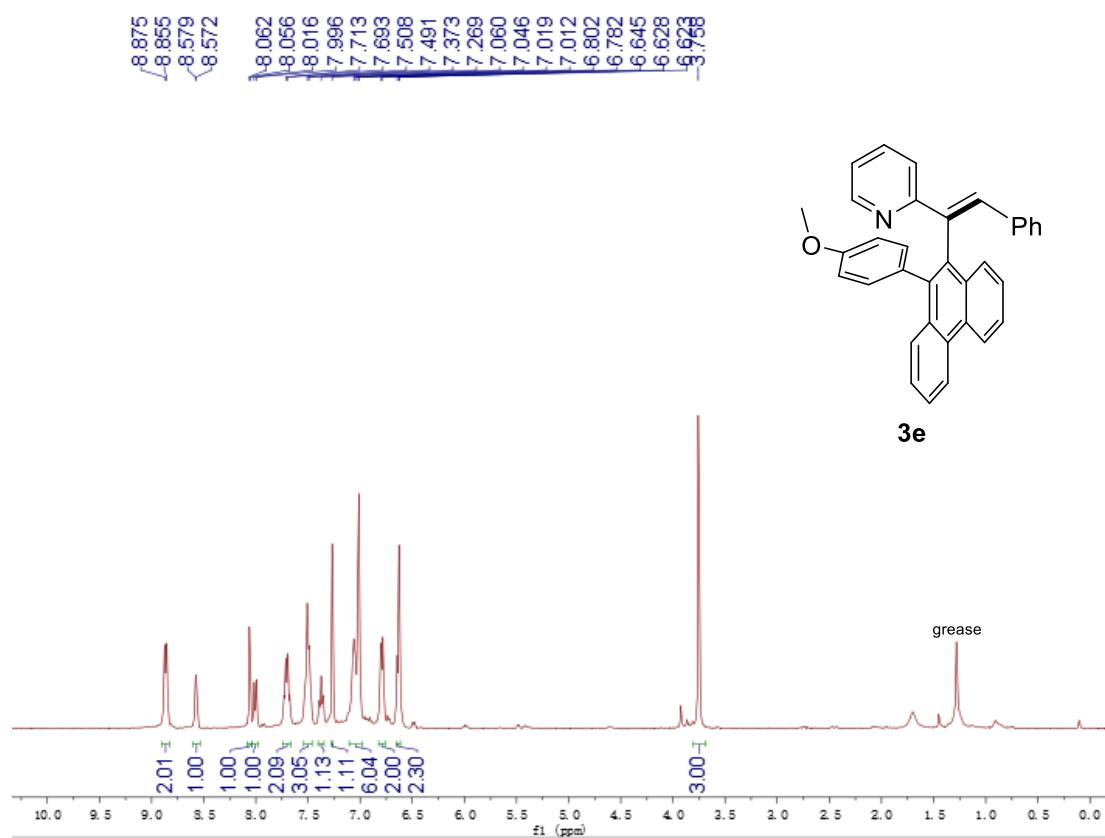
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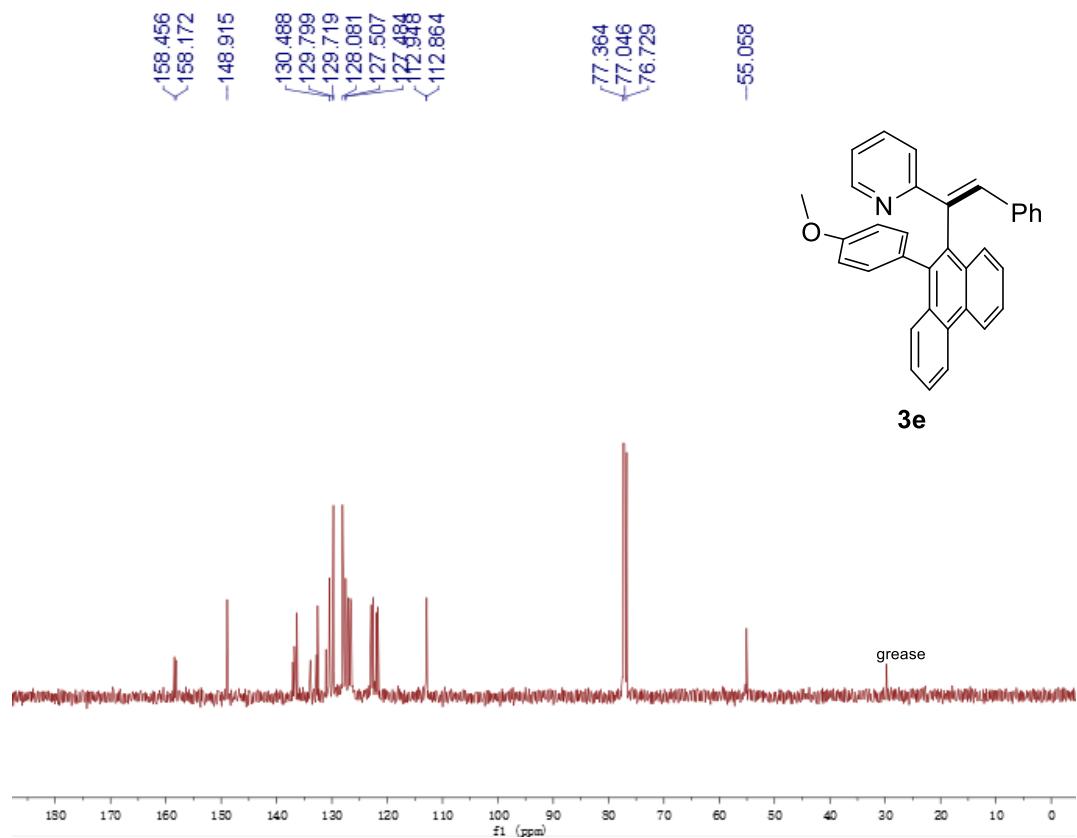
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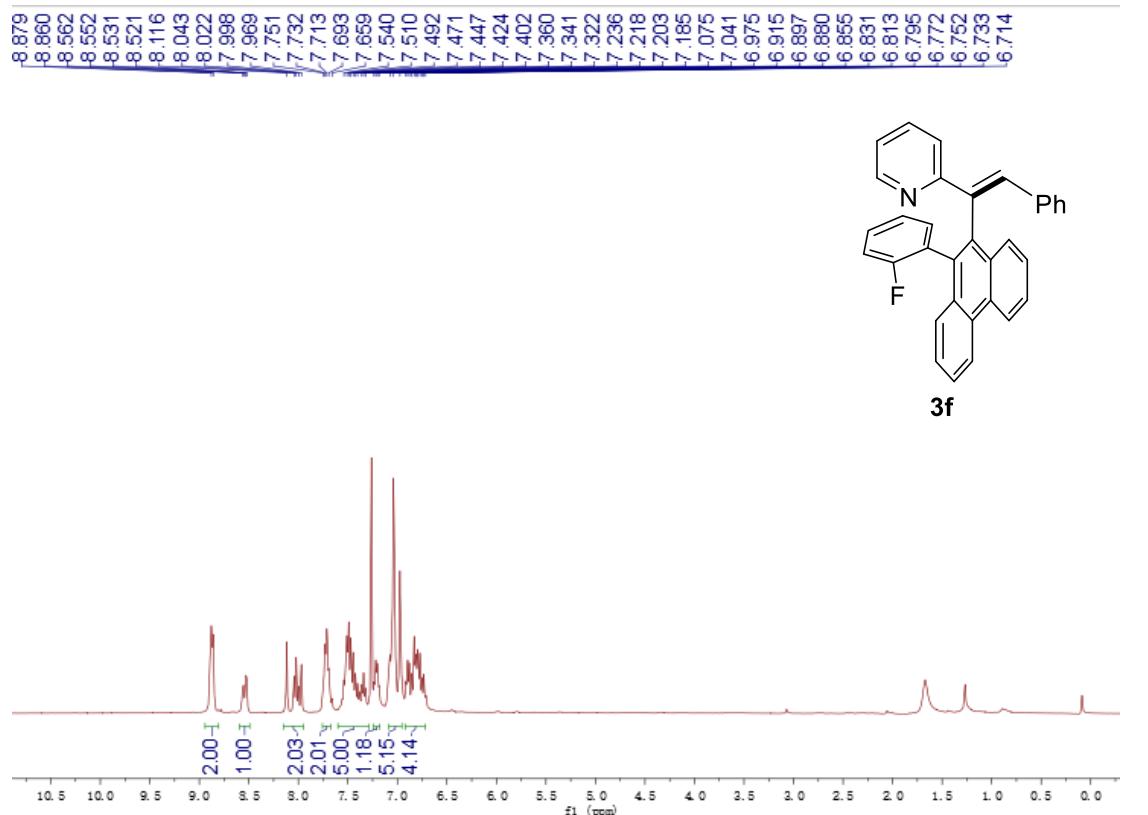
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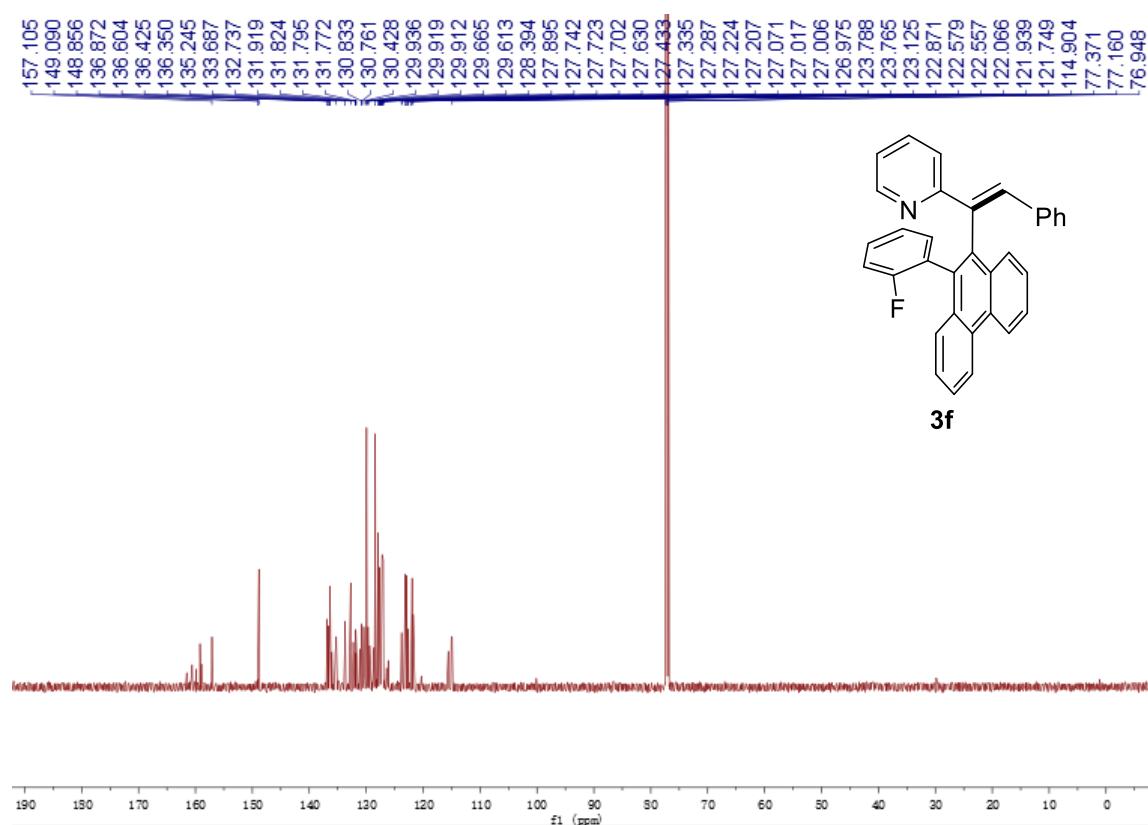
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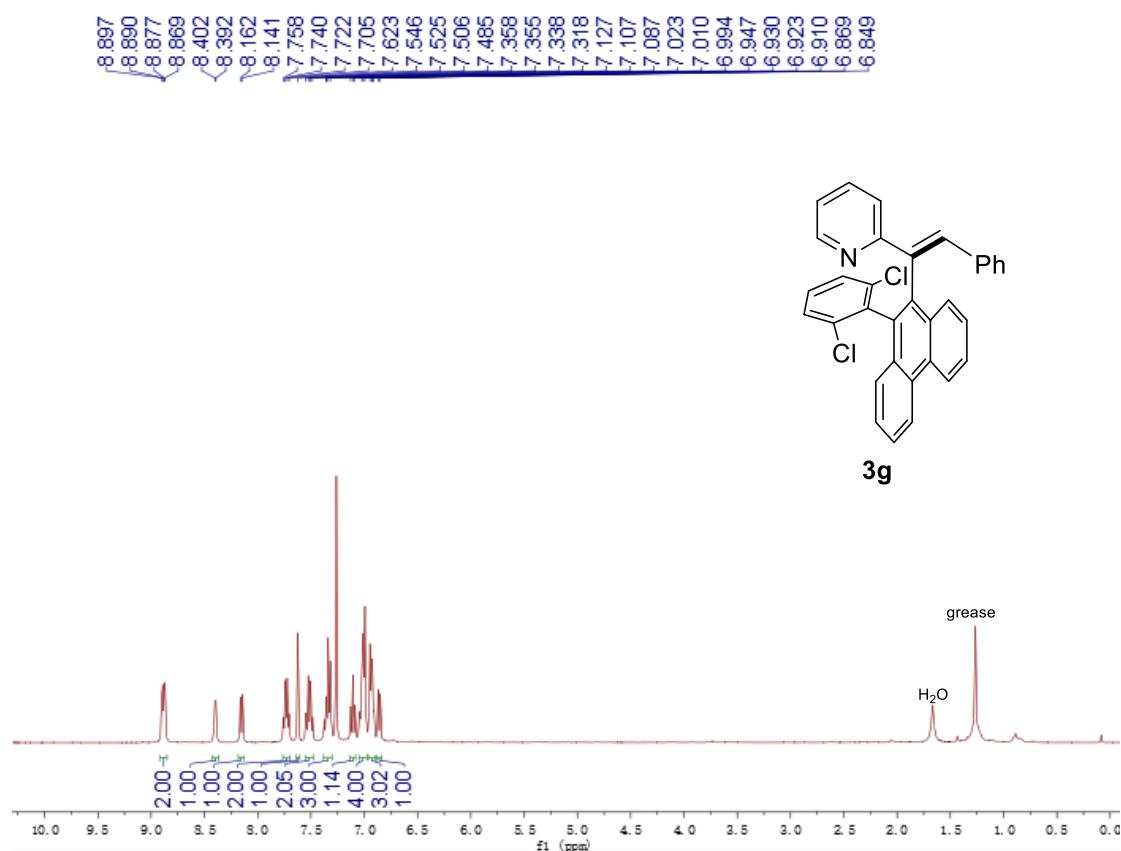
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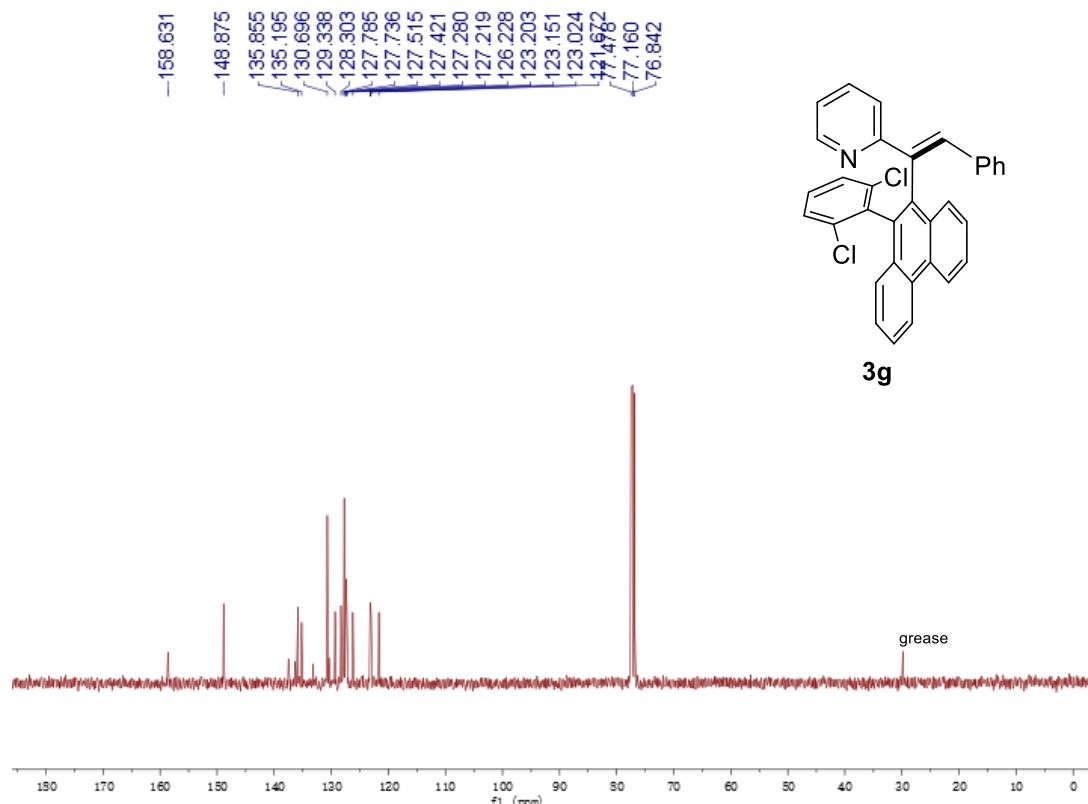
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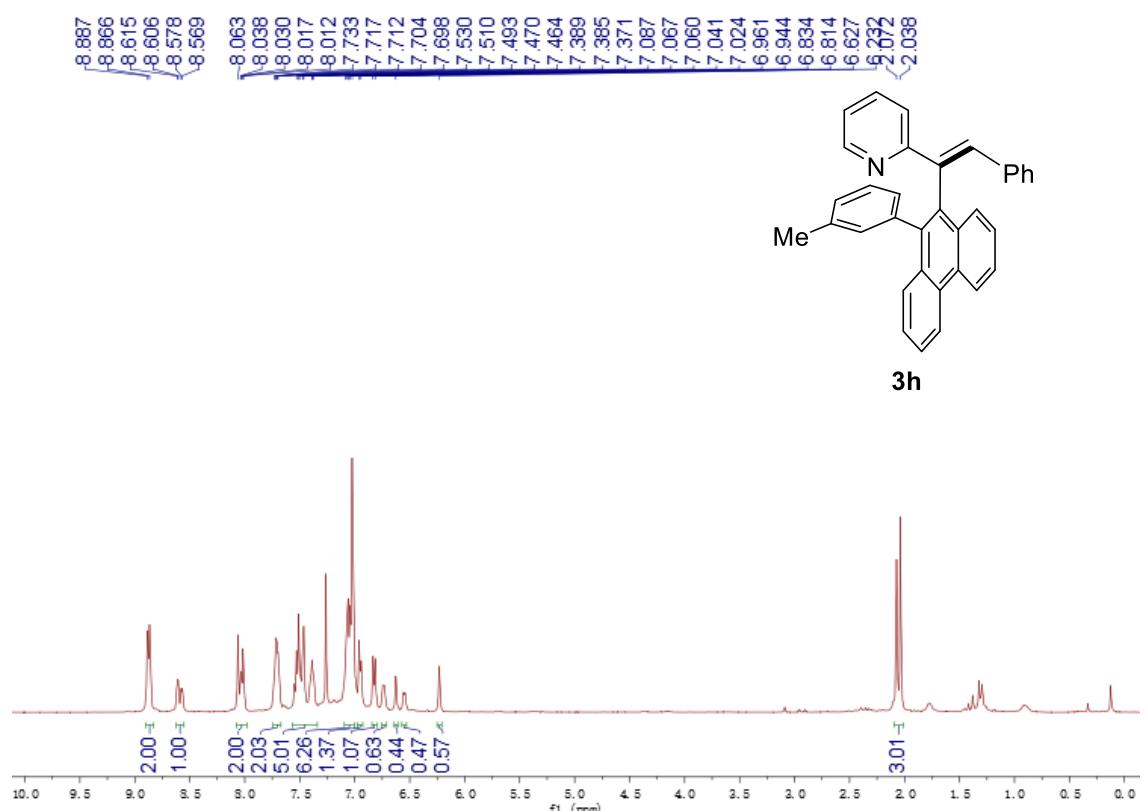
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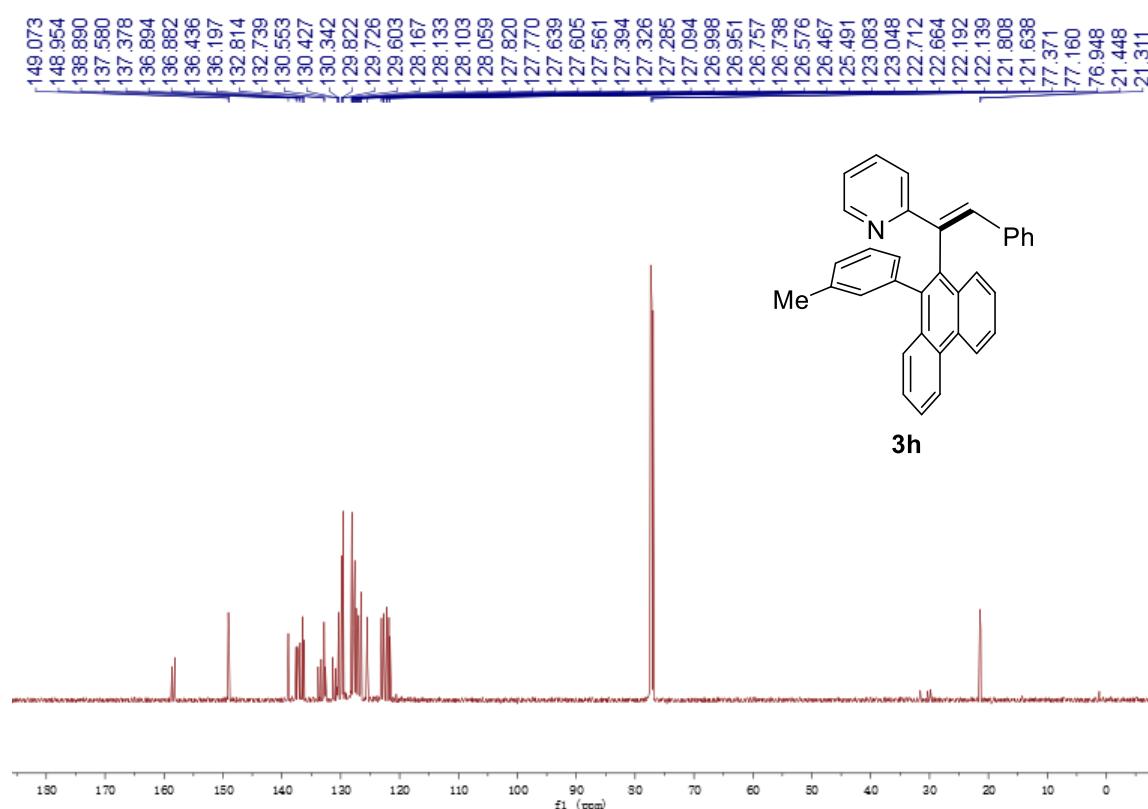
**3g-  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )**



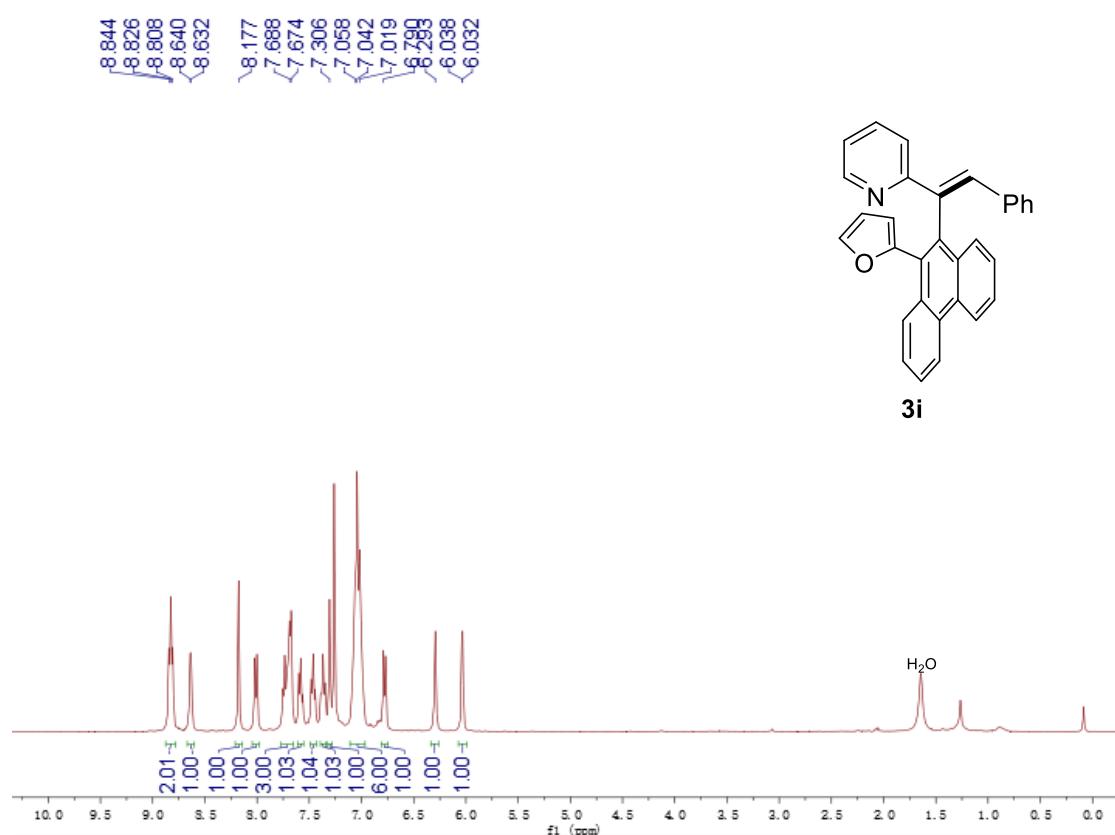
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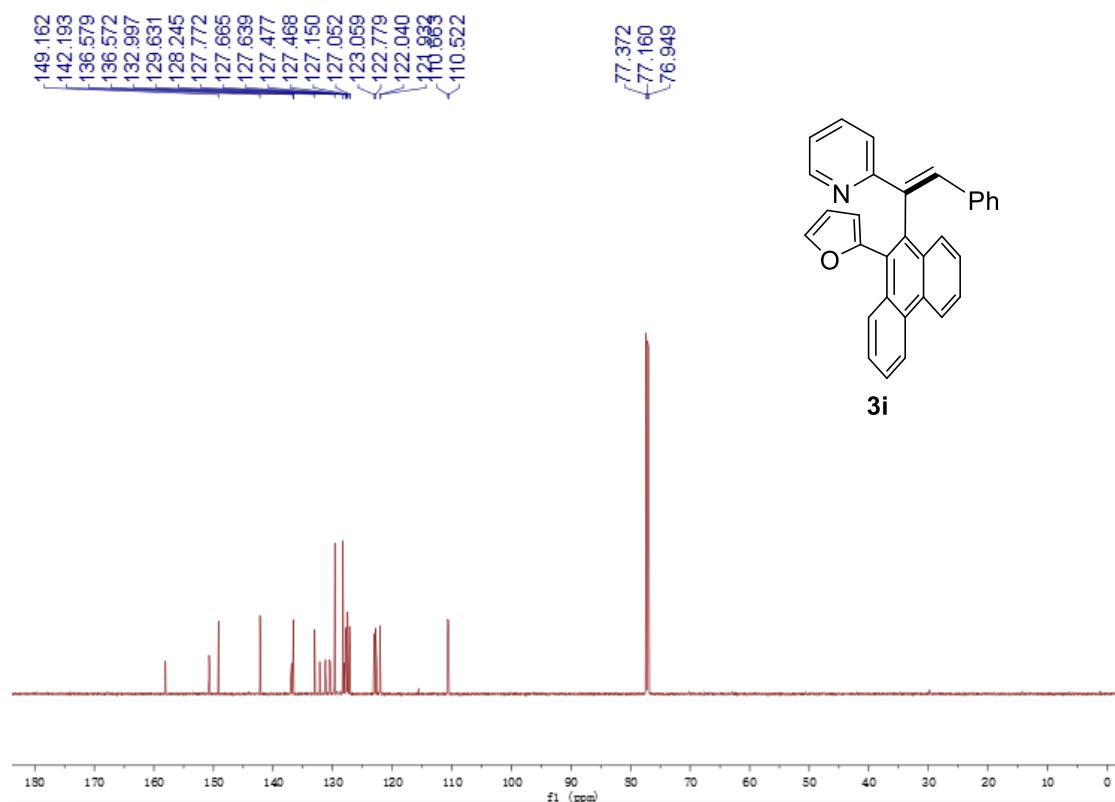
**3h-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



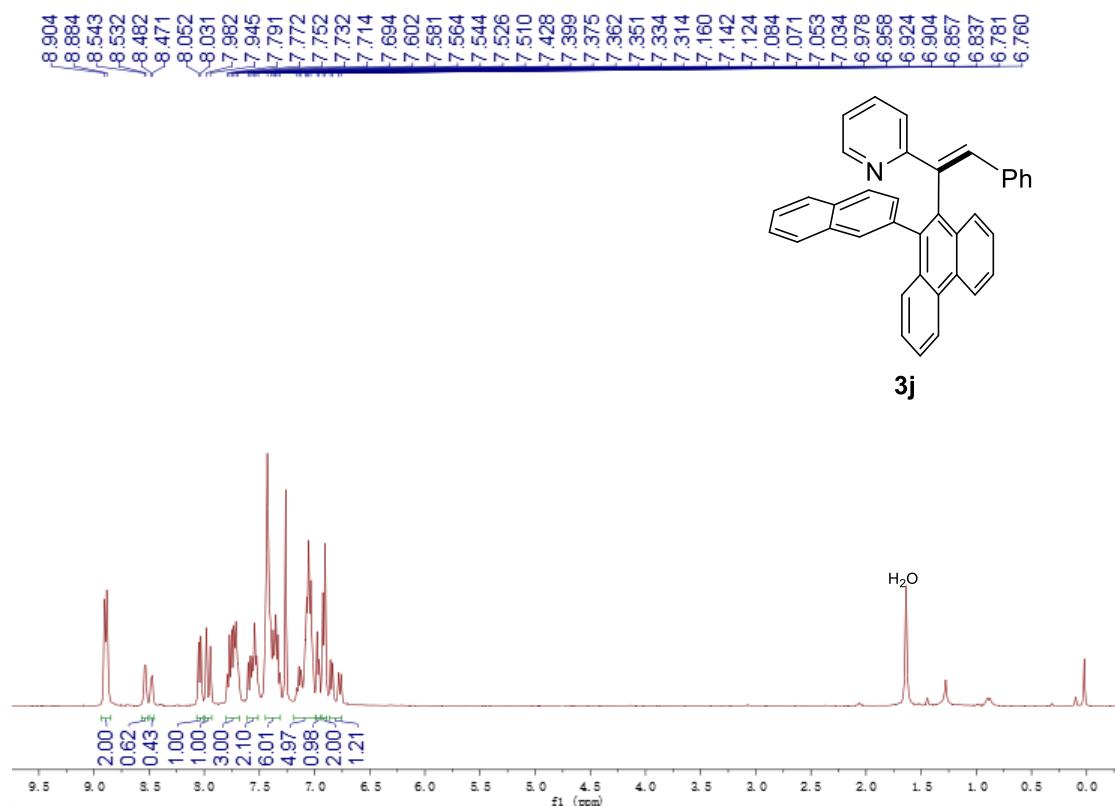
**3i-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



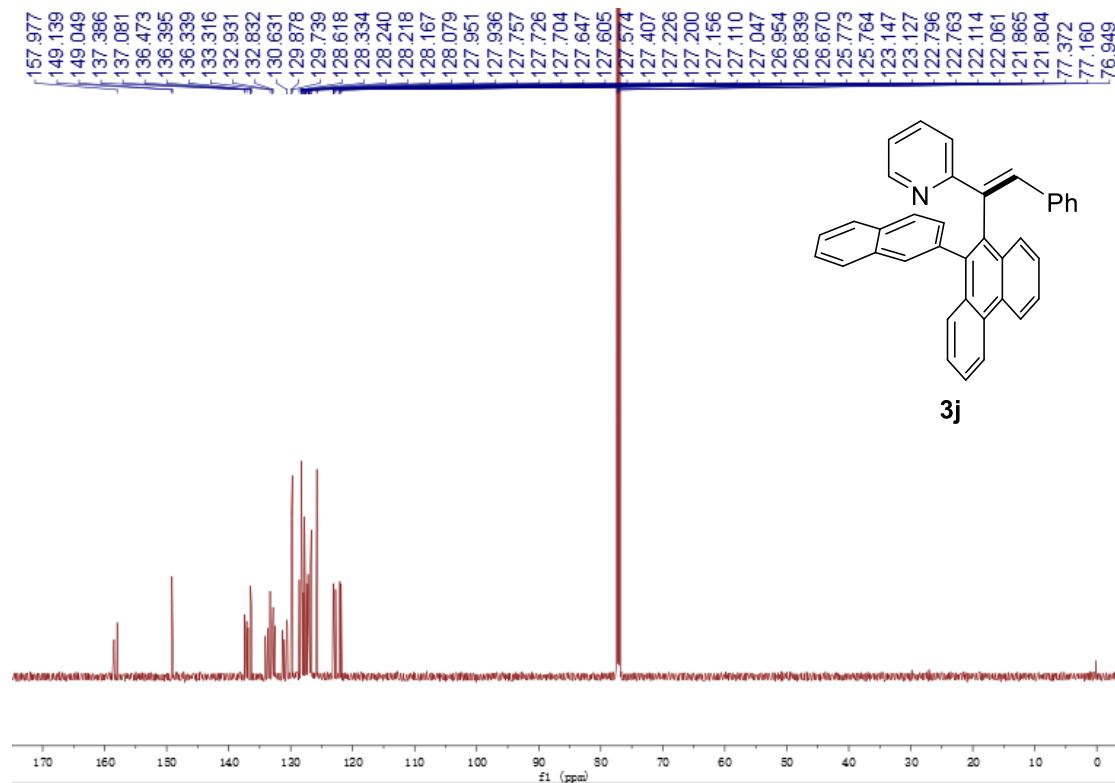
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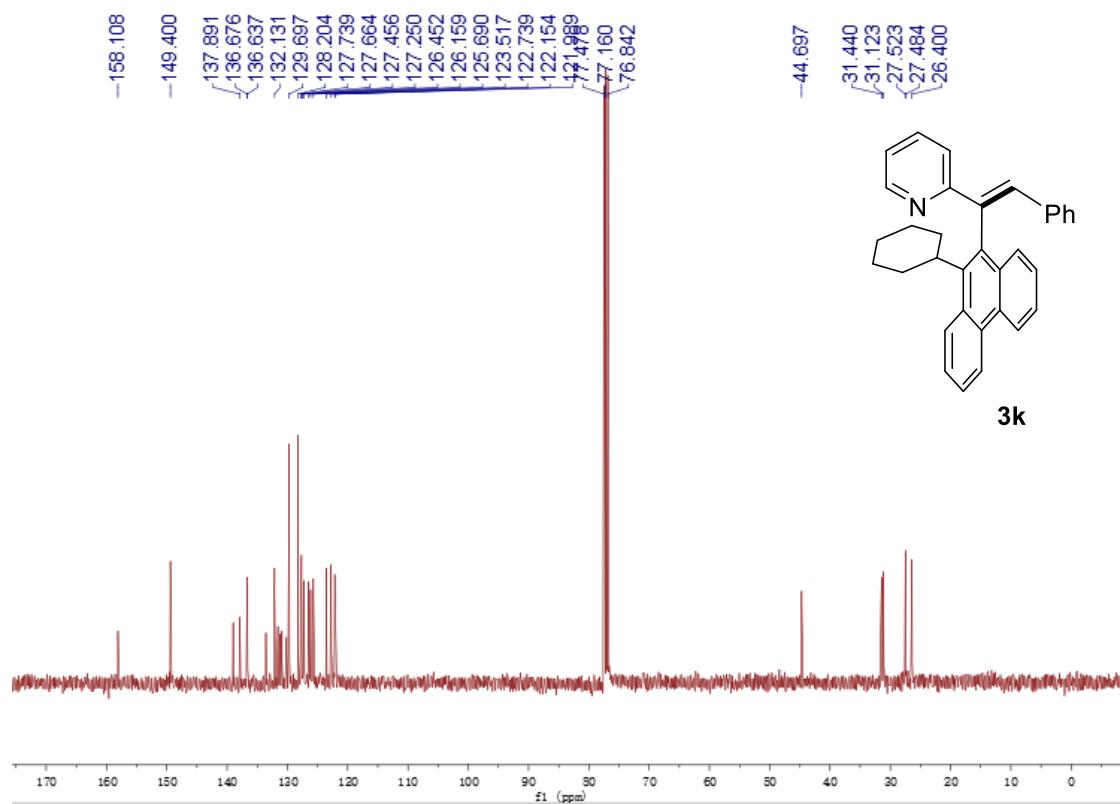
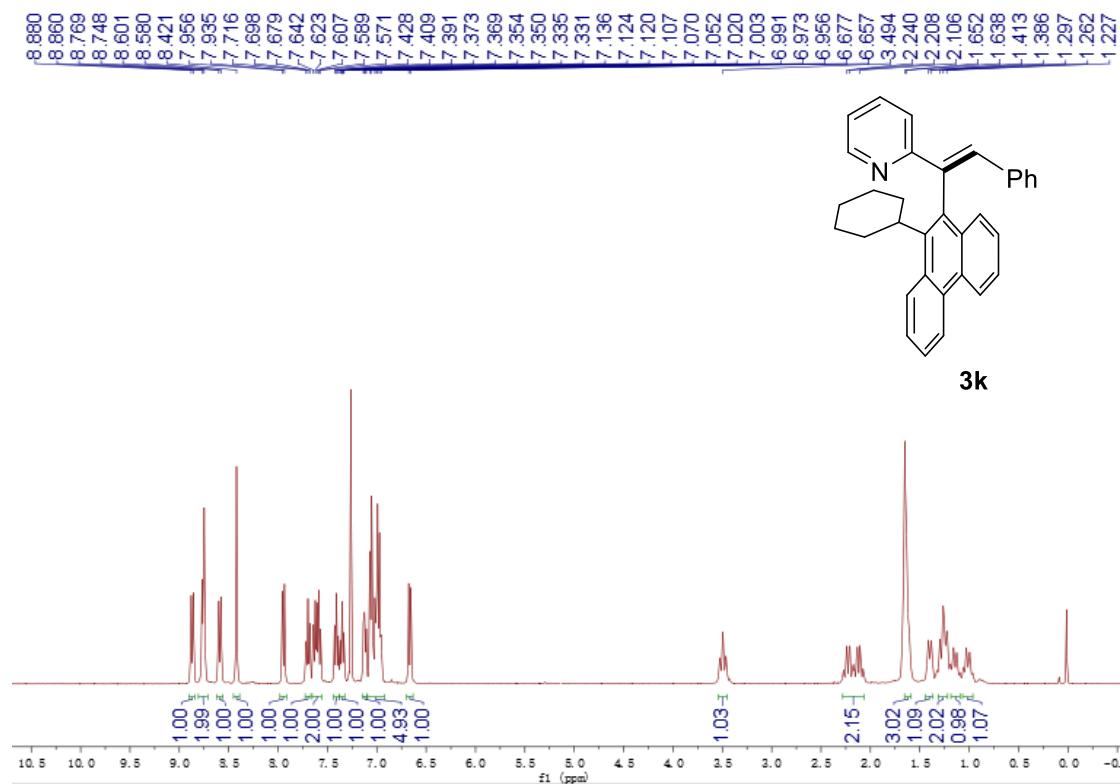
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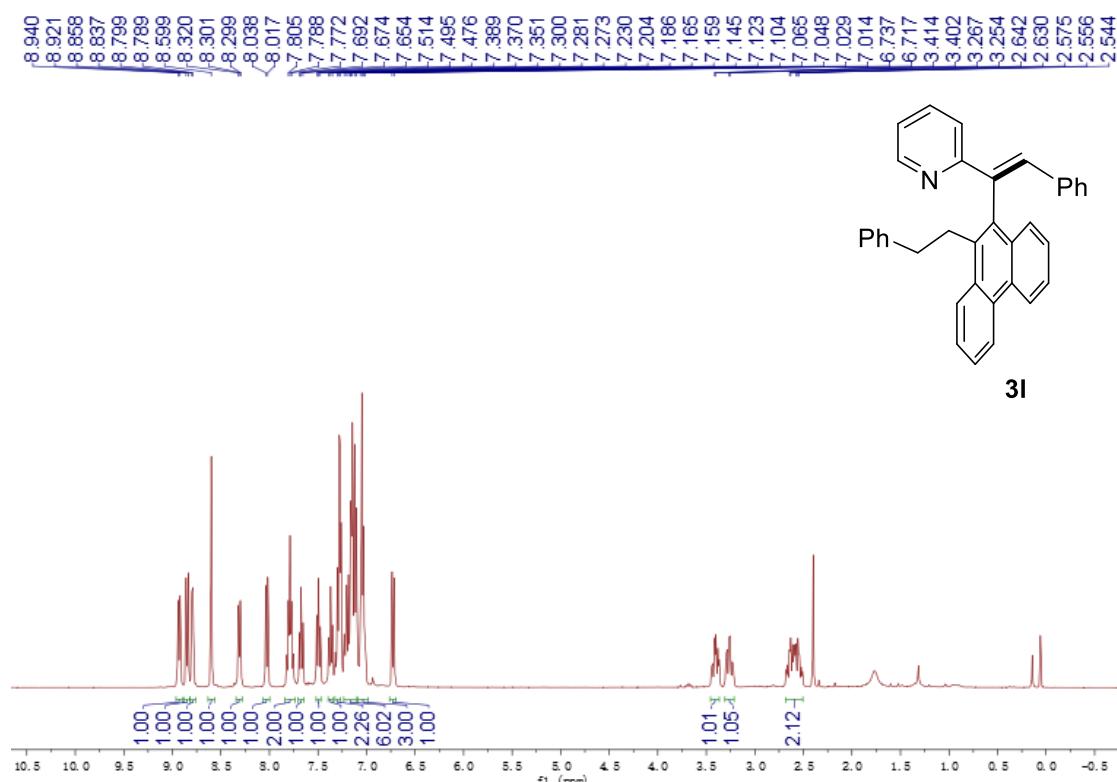
**3j-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



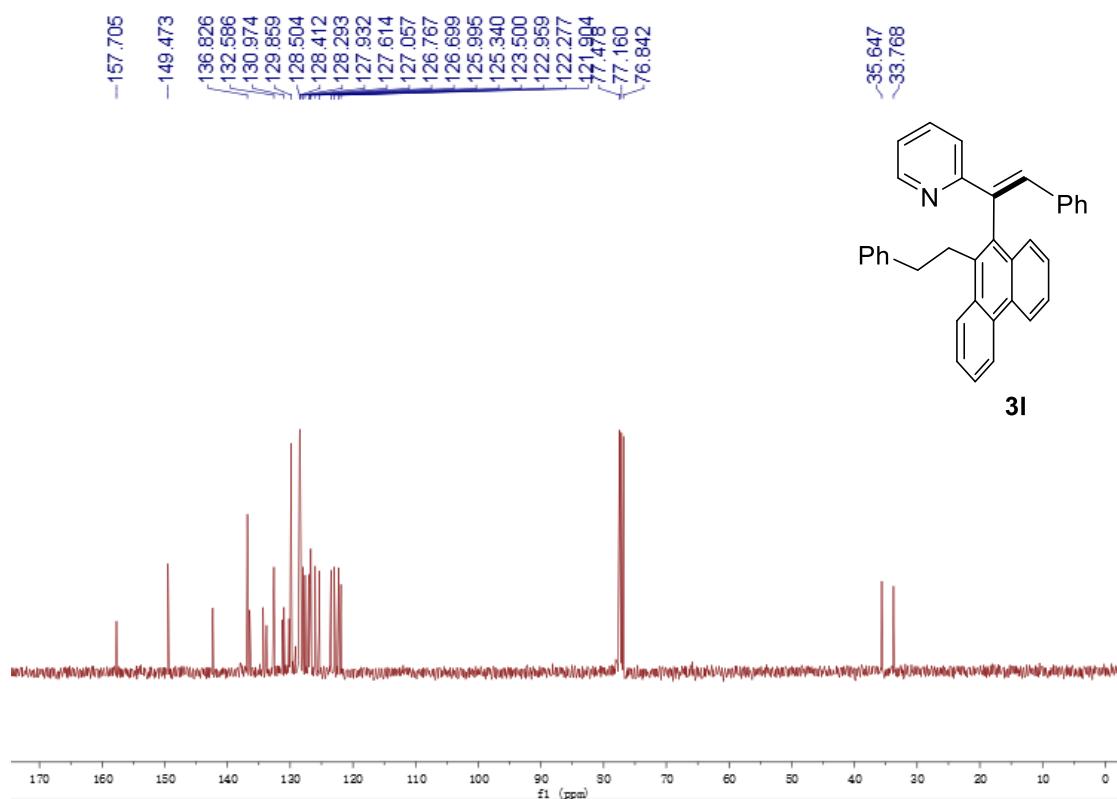
**3k-<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**



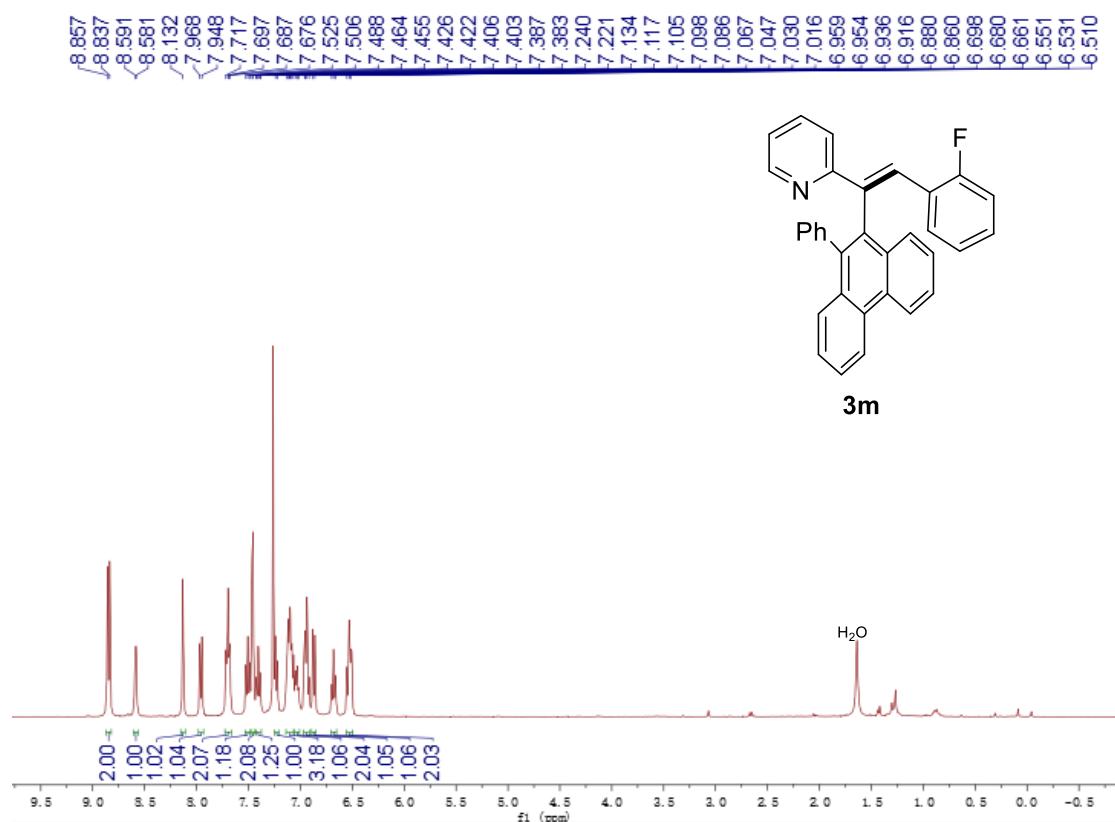
**3l-<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**



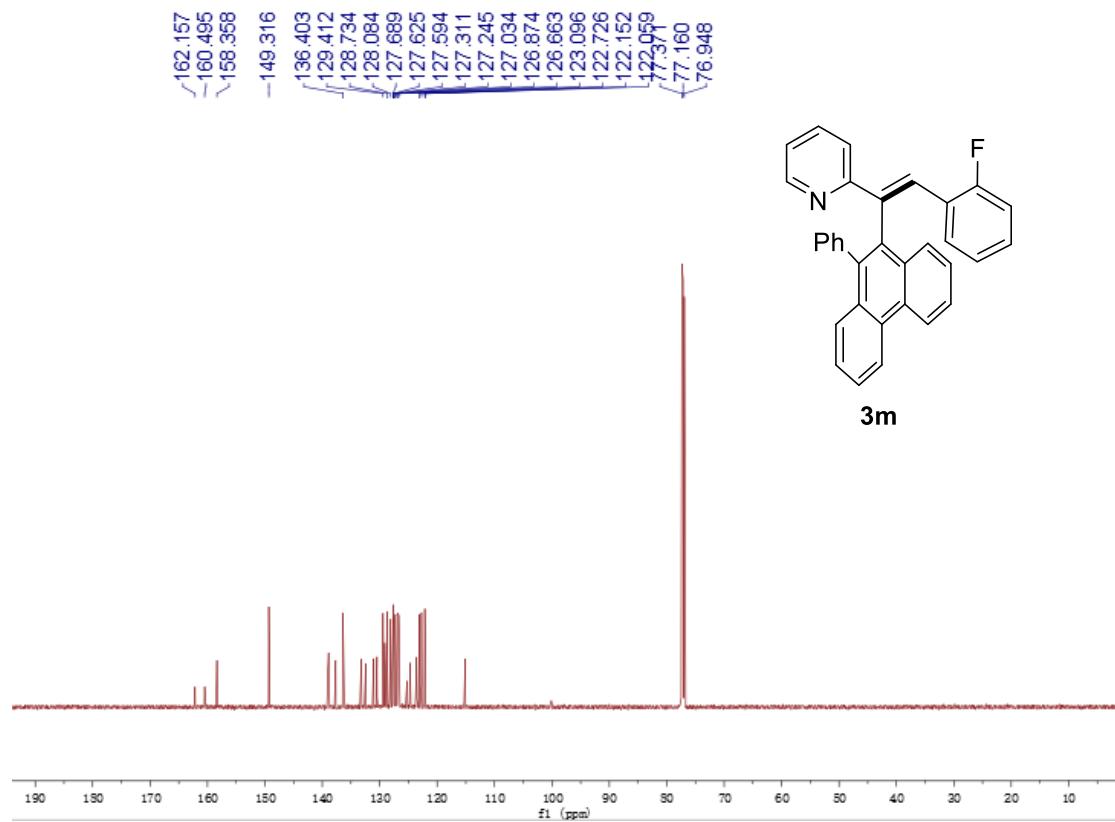
**3l- <sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, CDCl<sub>3</sub>)**



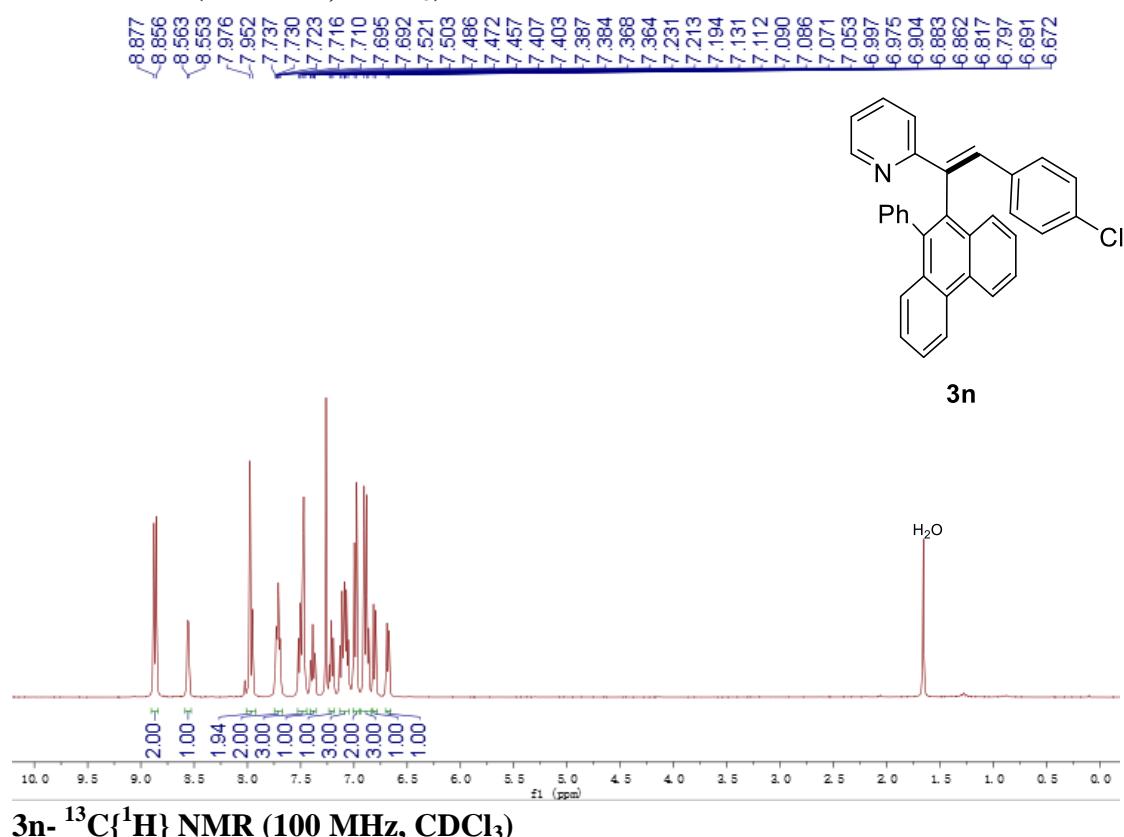
**3m-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



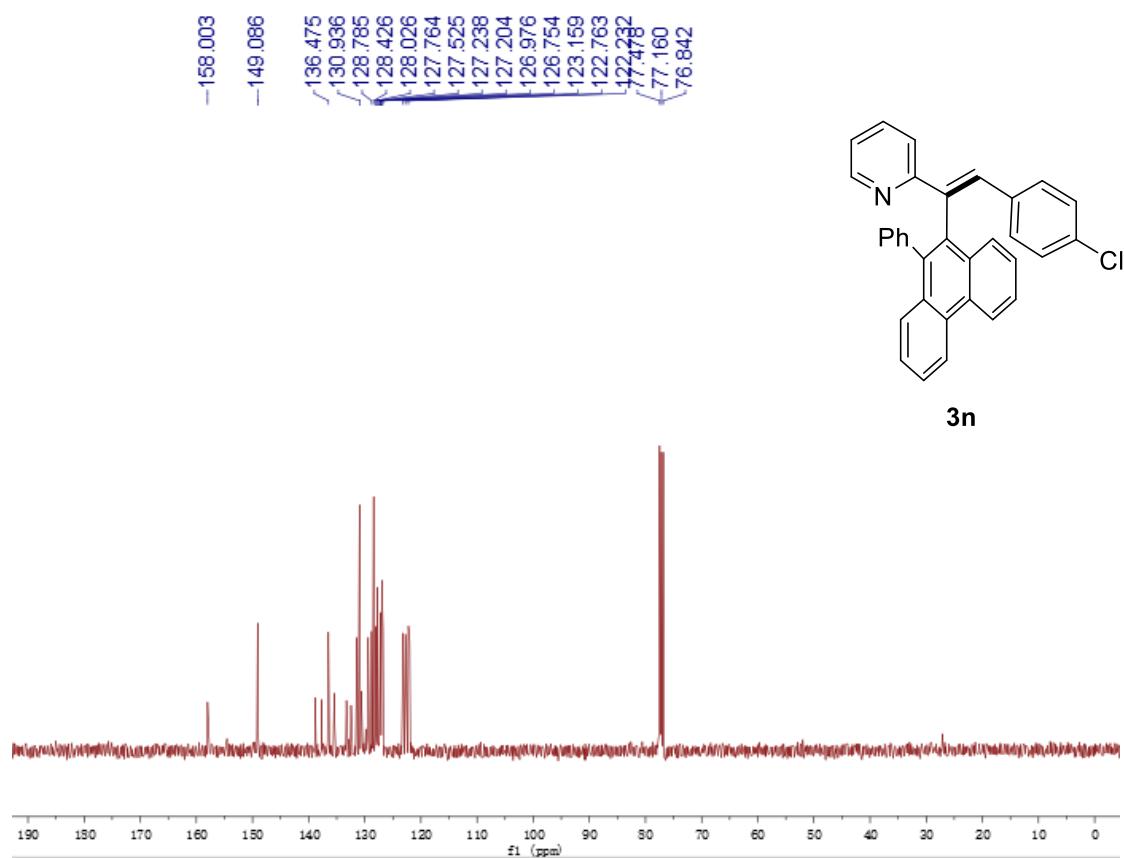
**3m-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



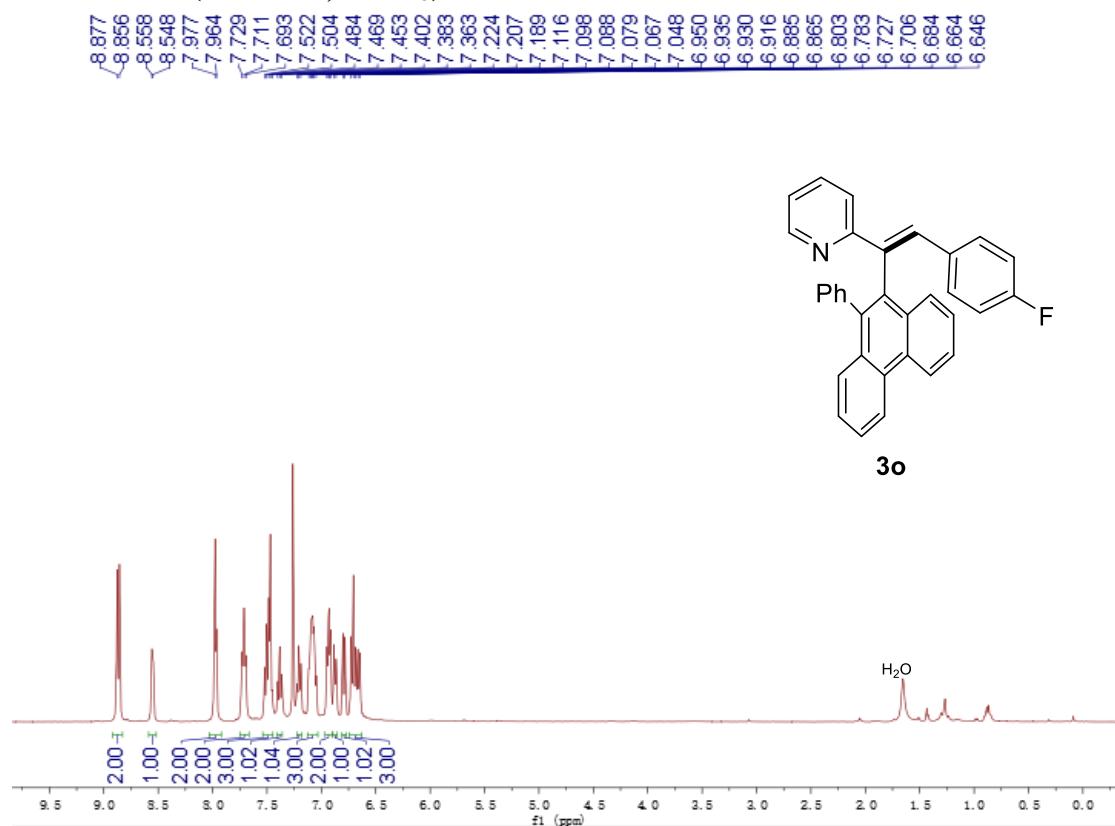
**3n-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



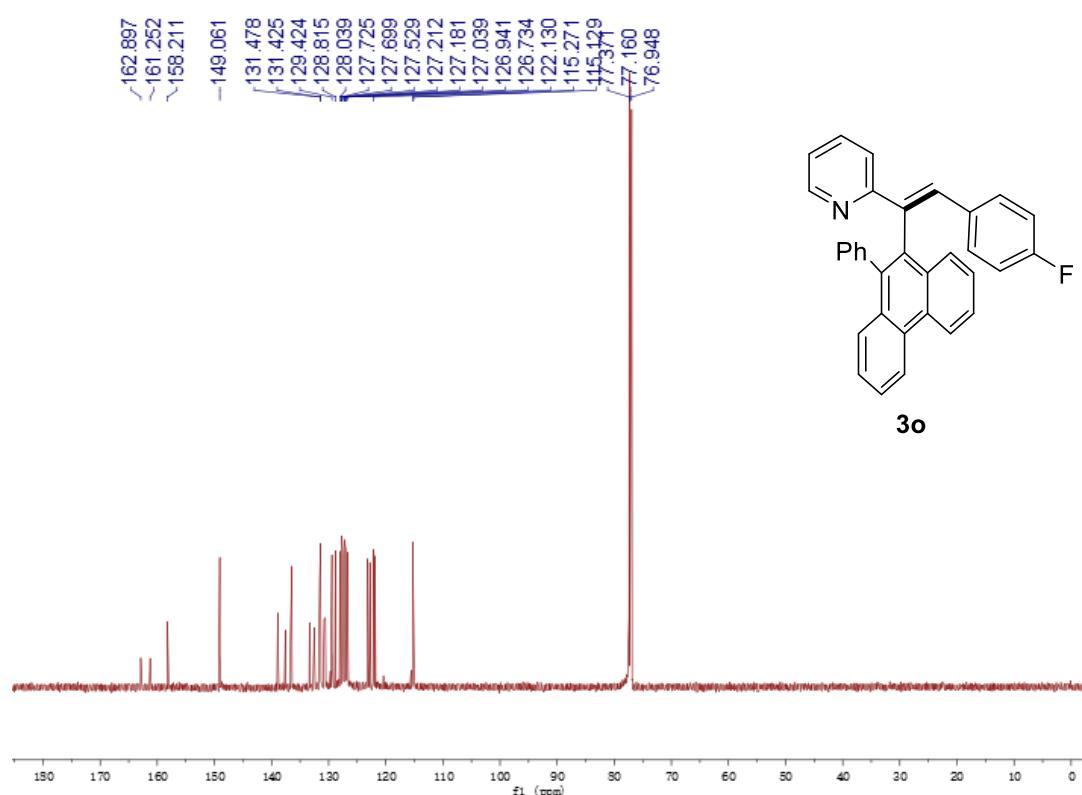
**3n-  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )**



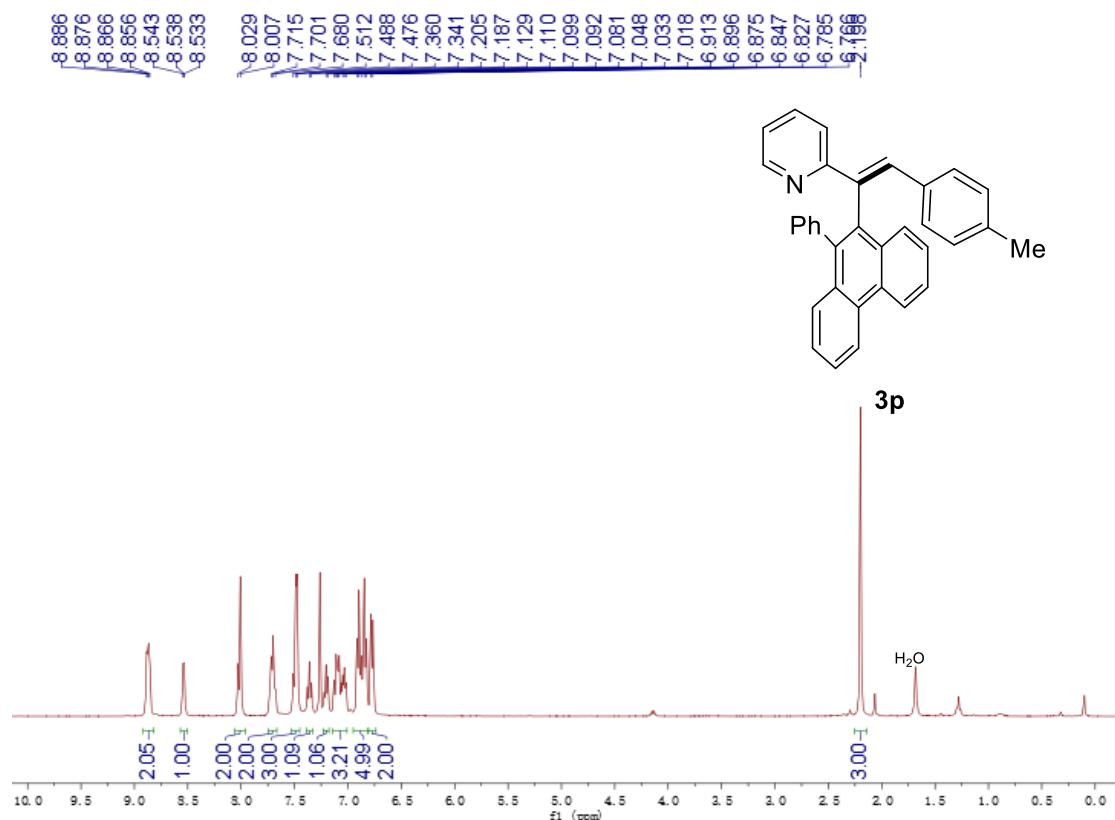
**3o-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



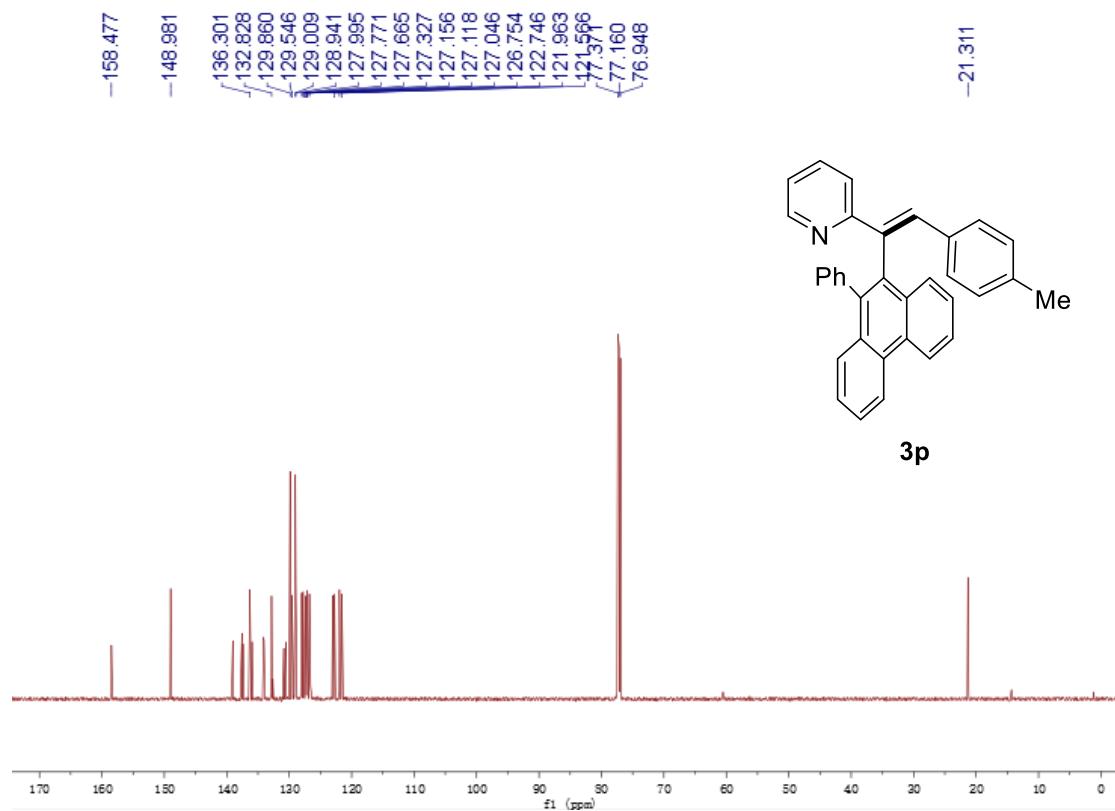
**3o-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



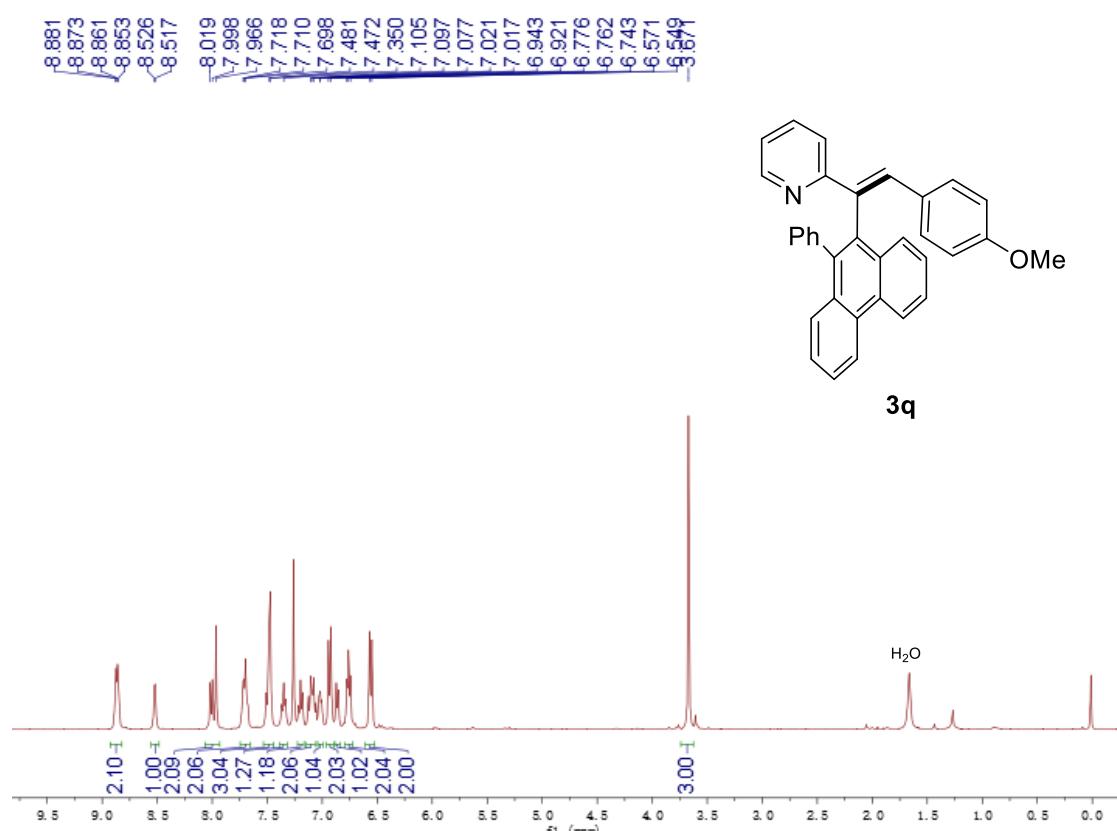
**3p-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



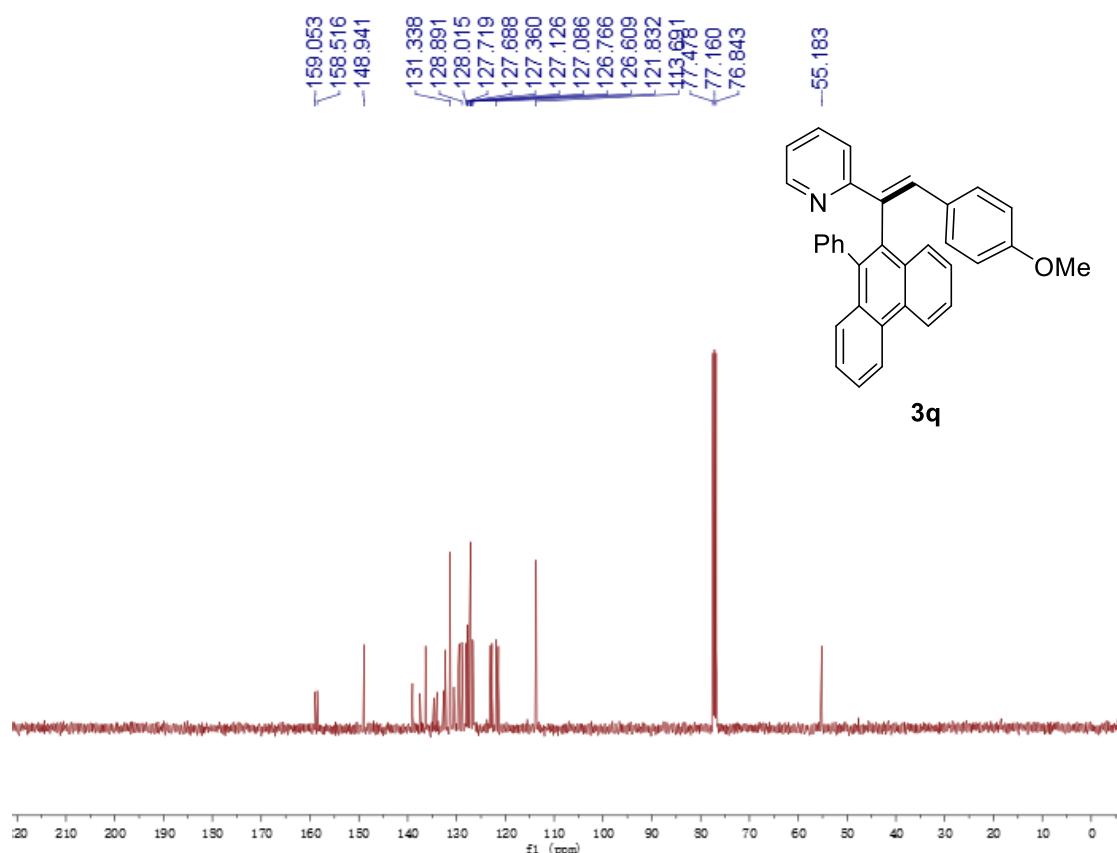
**3p-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



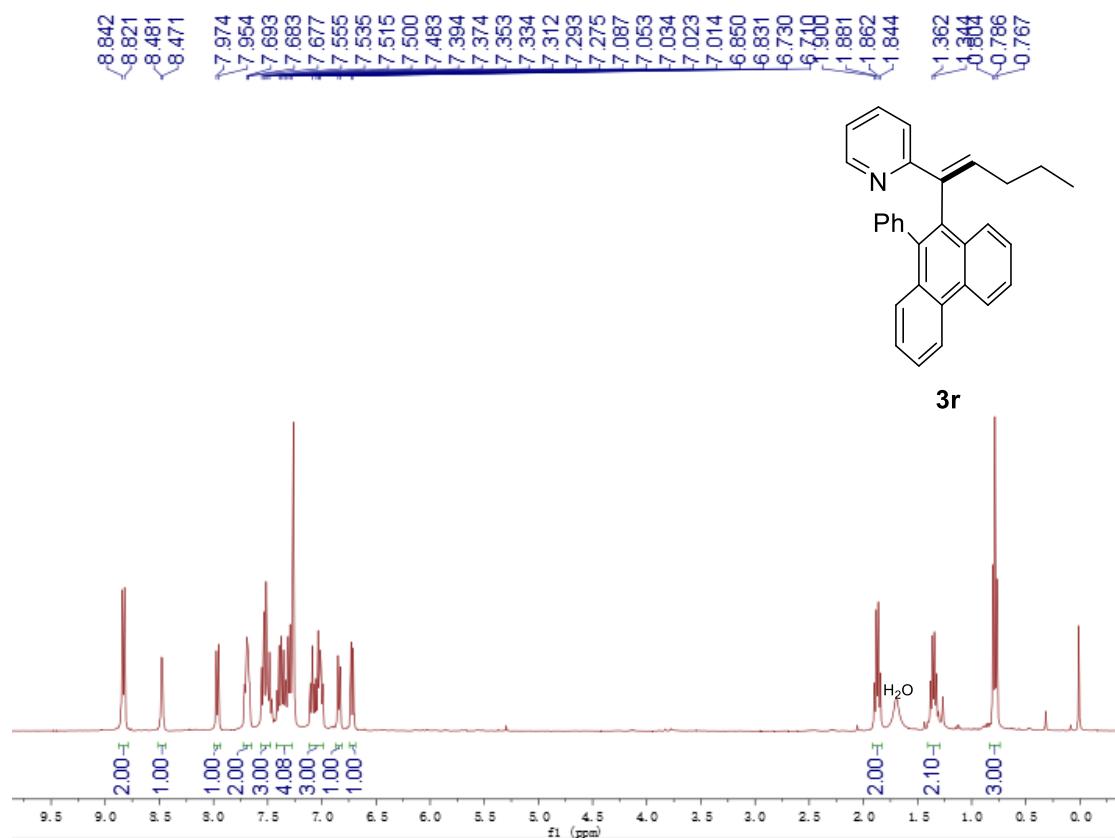
**3q-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



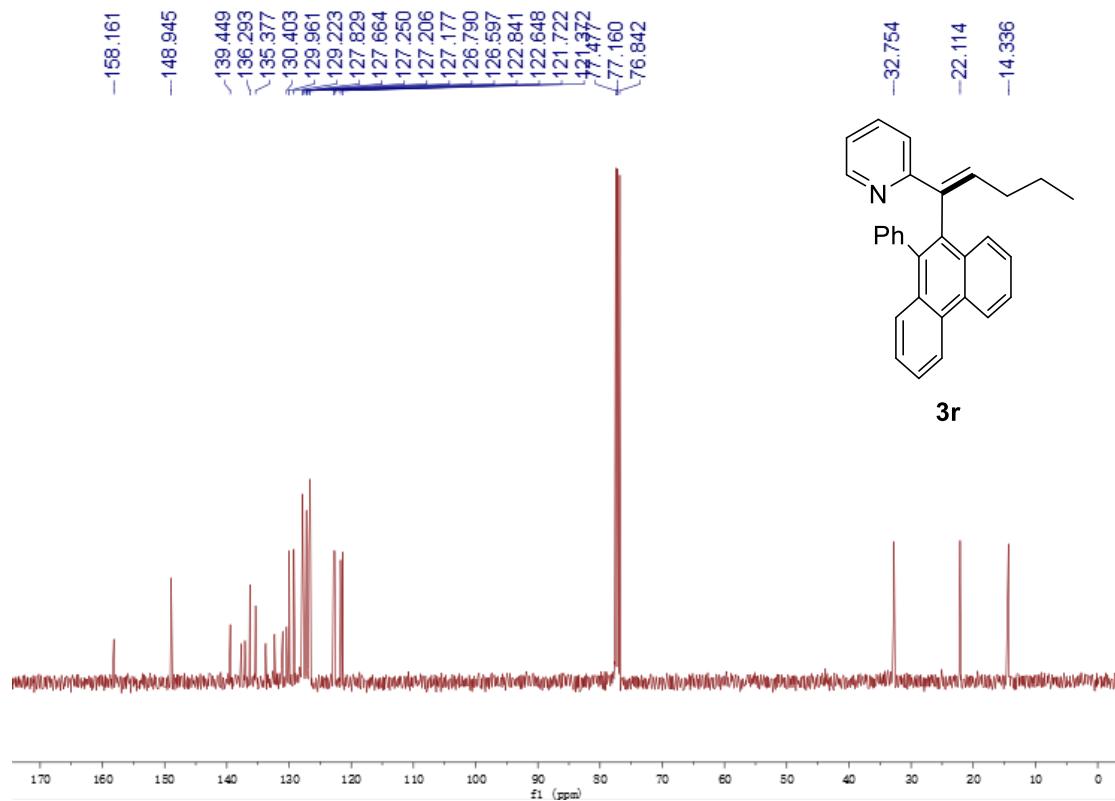
**3q-  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )**



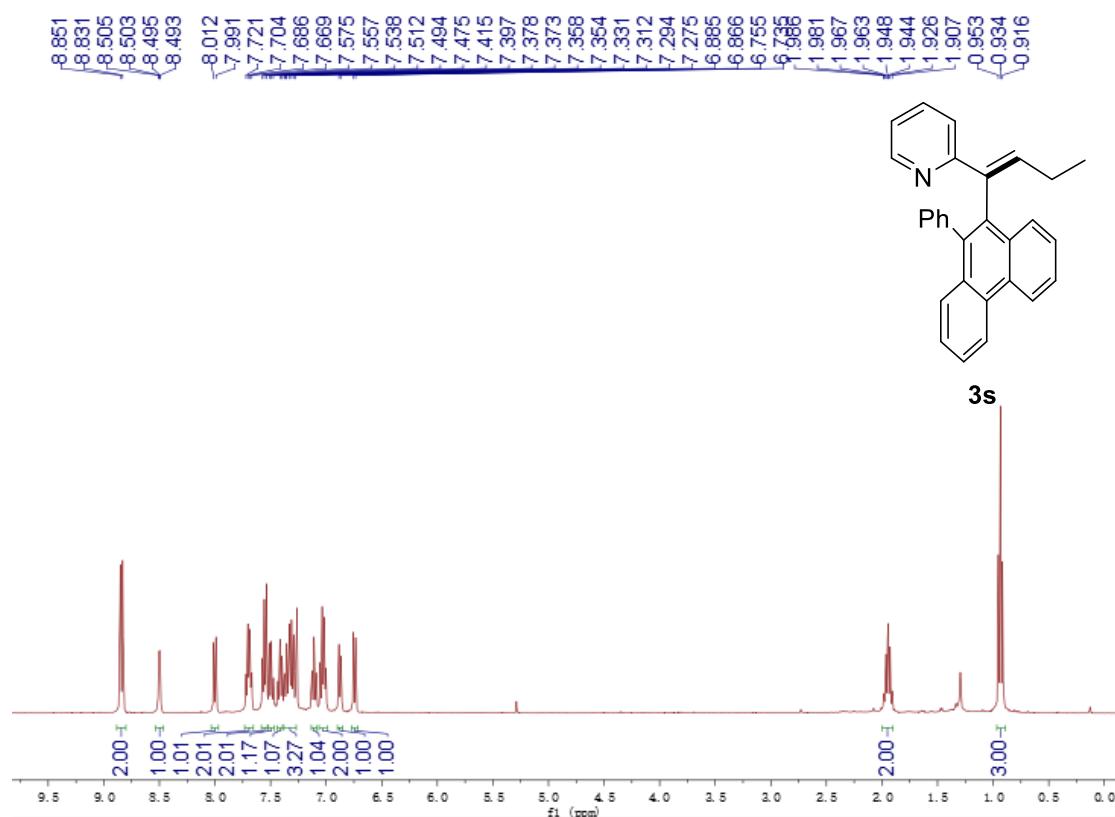
**3r-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



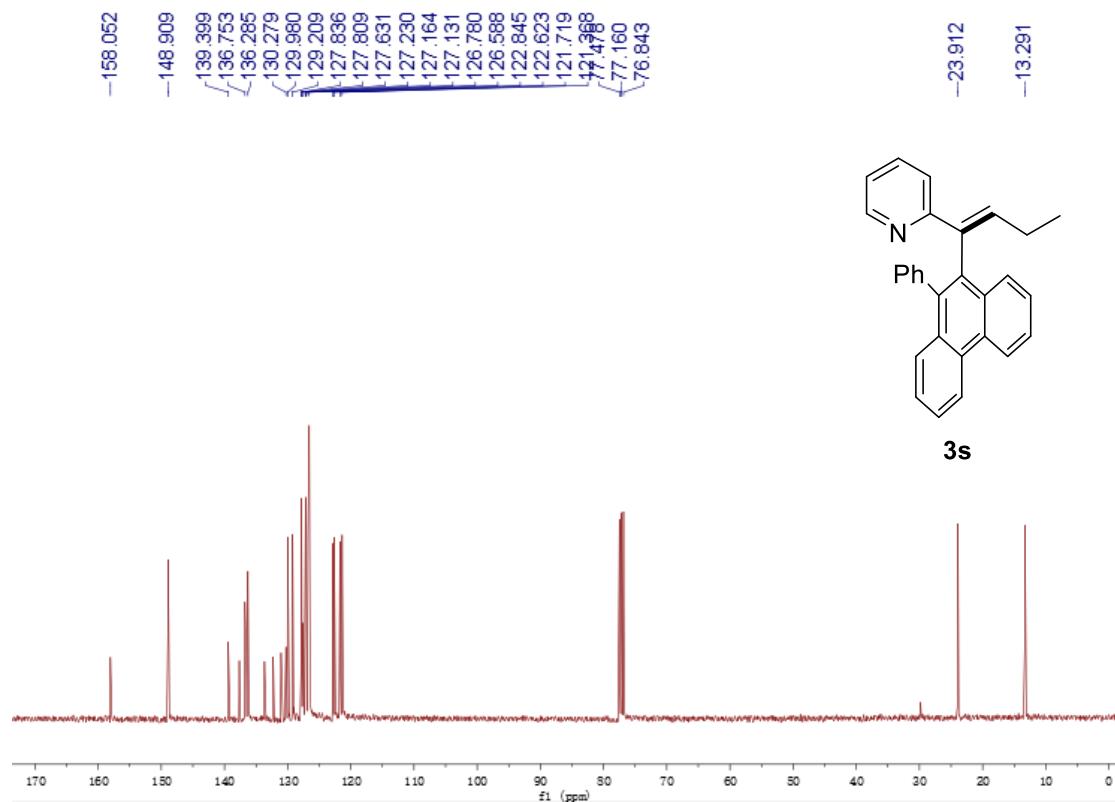
**3r-  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )**



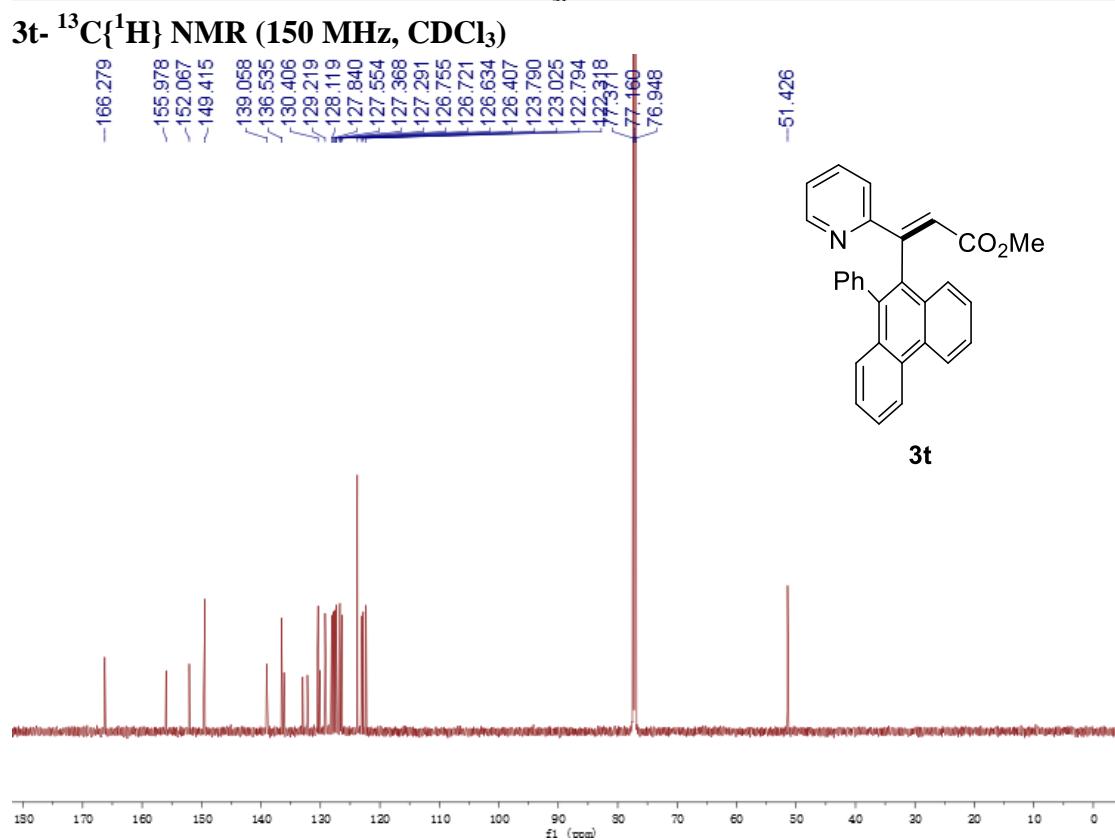
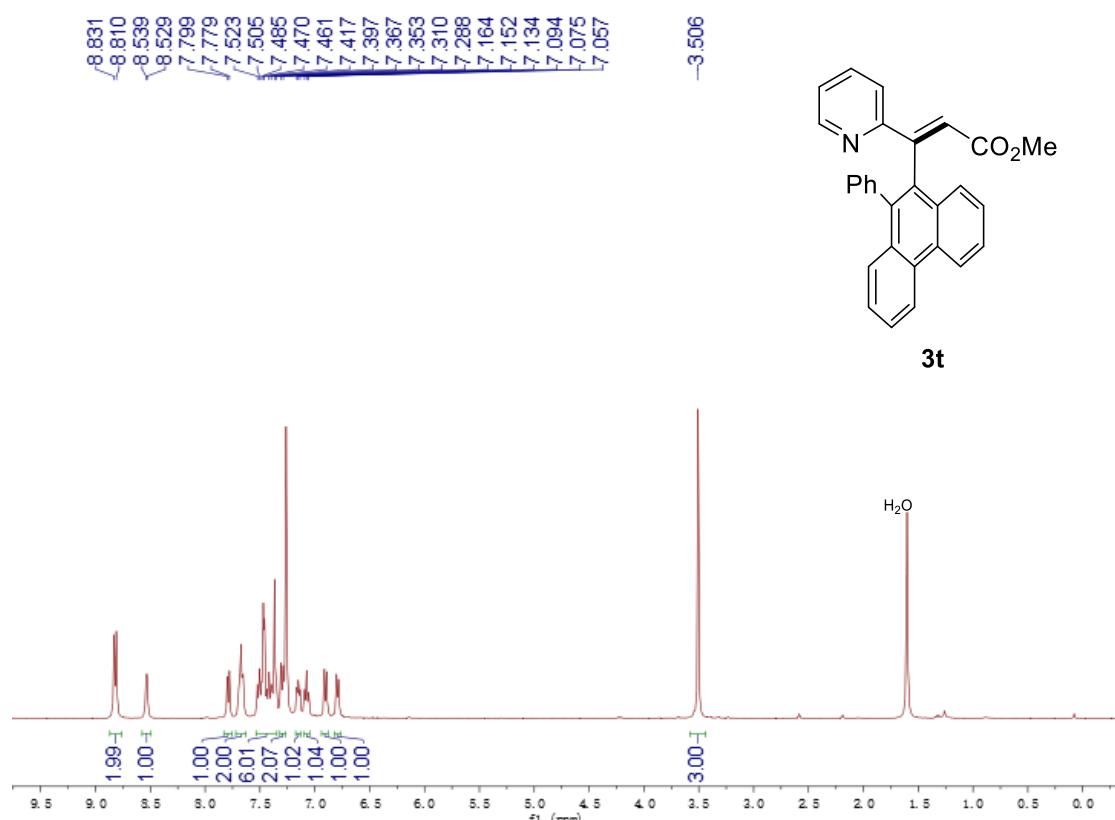
**3s-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



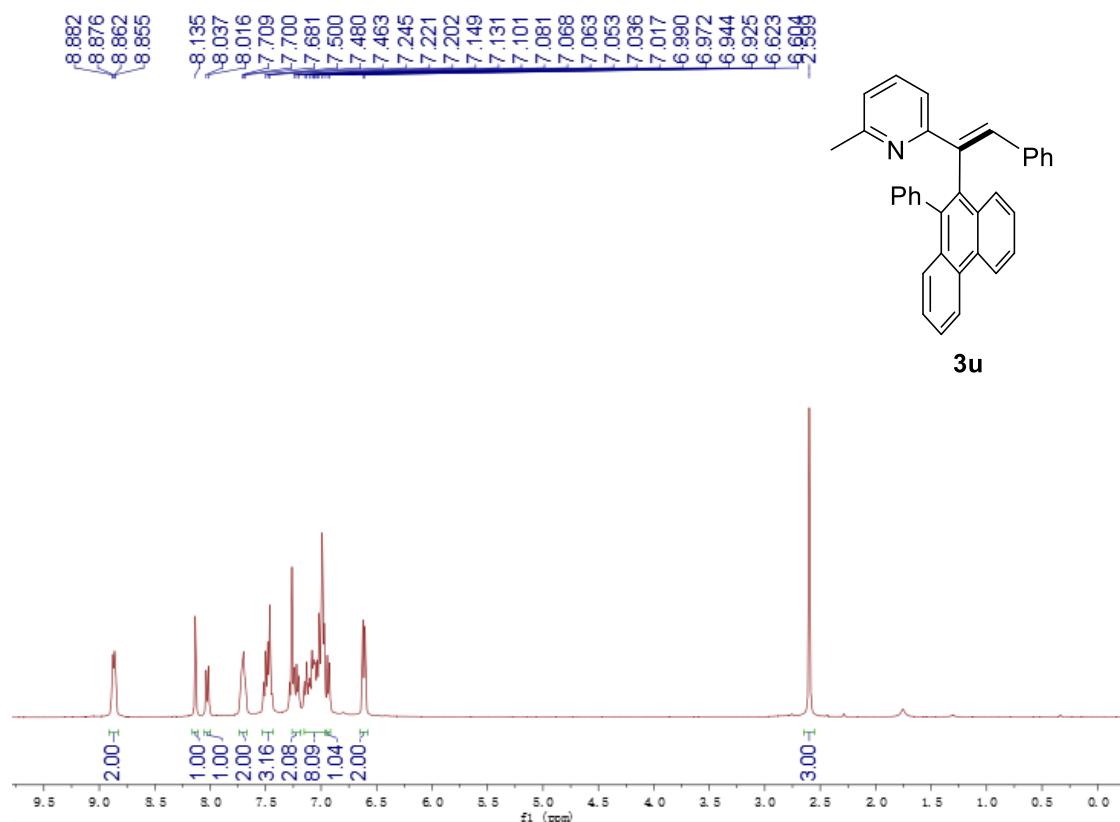
**3s-  $^{13}\text{C}\{^1\text{H}\}$  NMR (100 MHz,  $\text{CDCl}_3$ )**



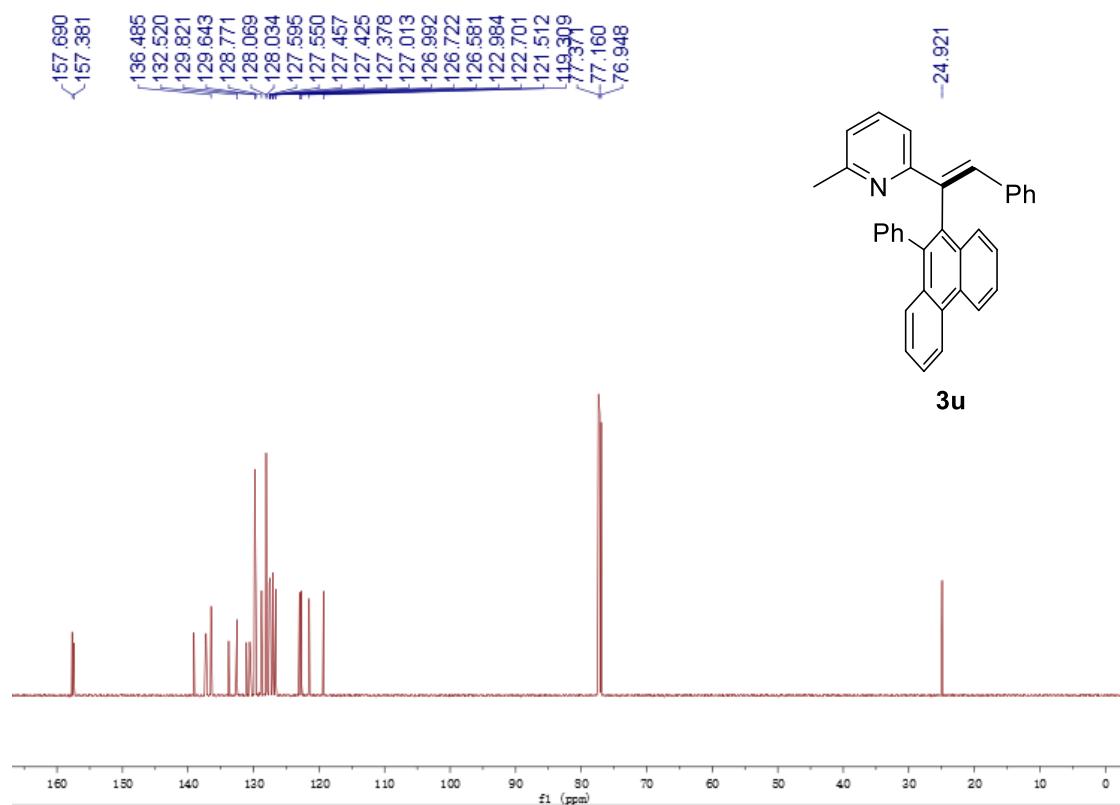
**3t-<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**



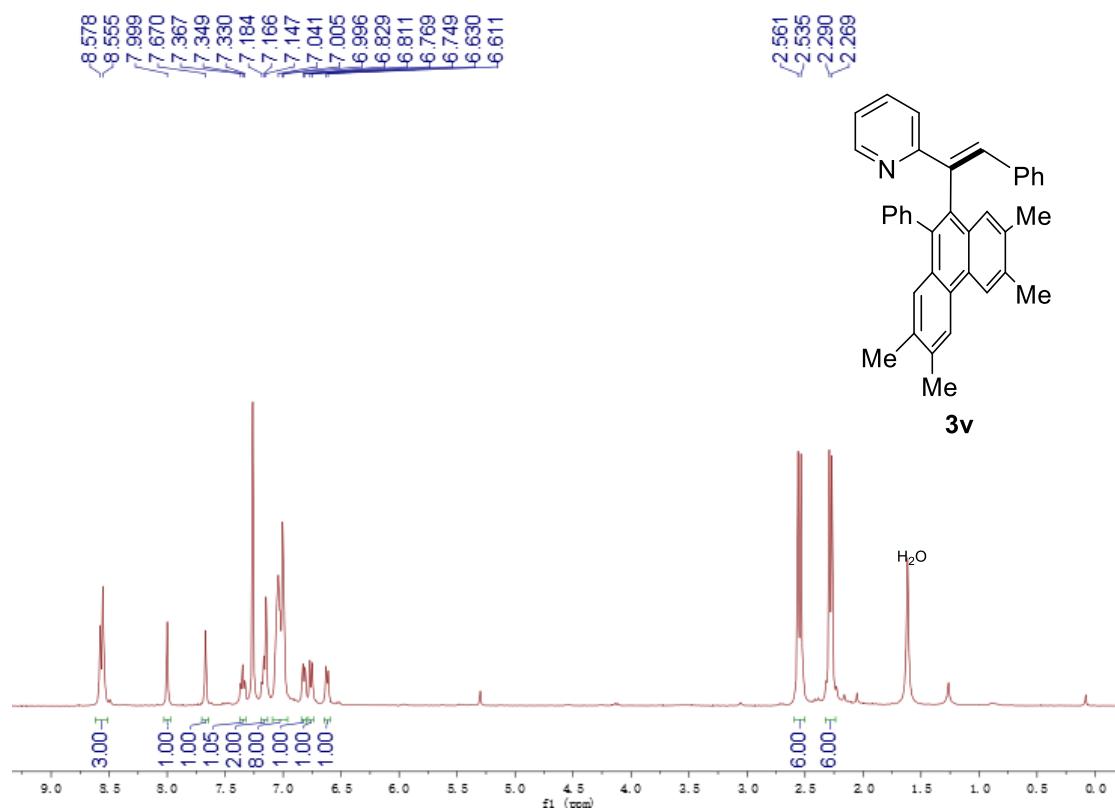
**3u-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



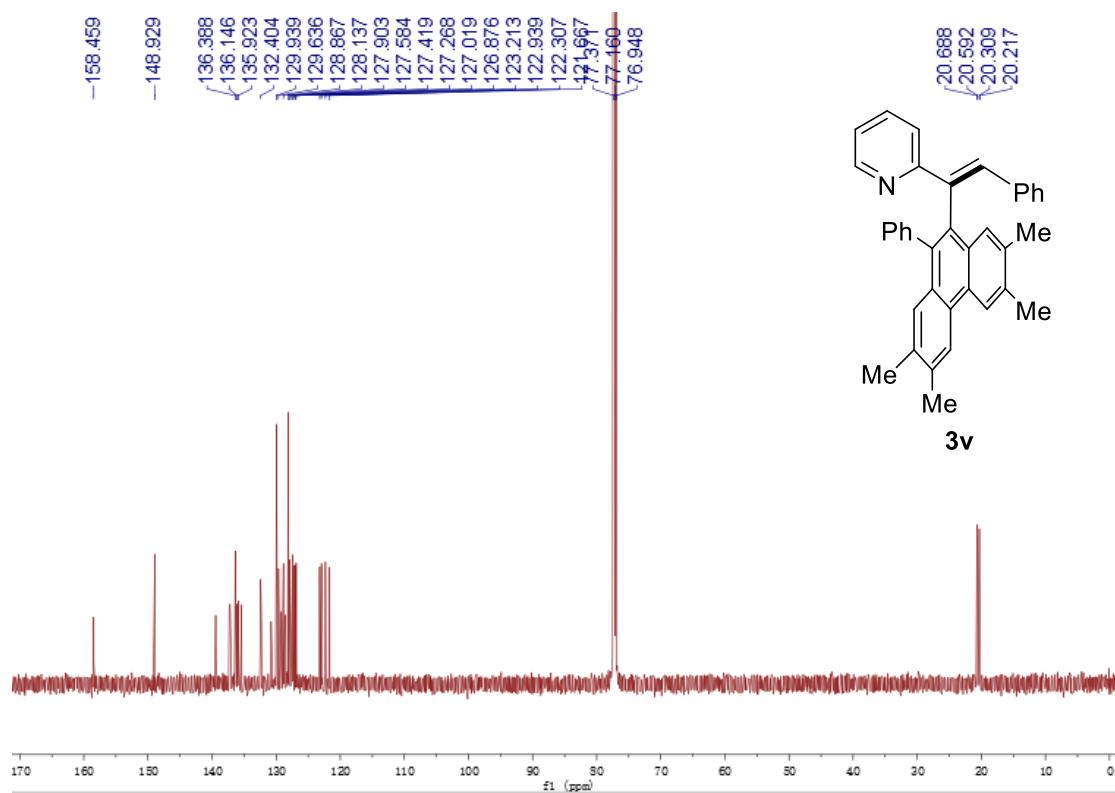
**3u-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



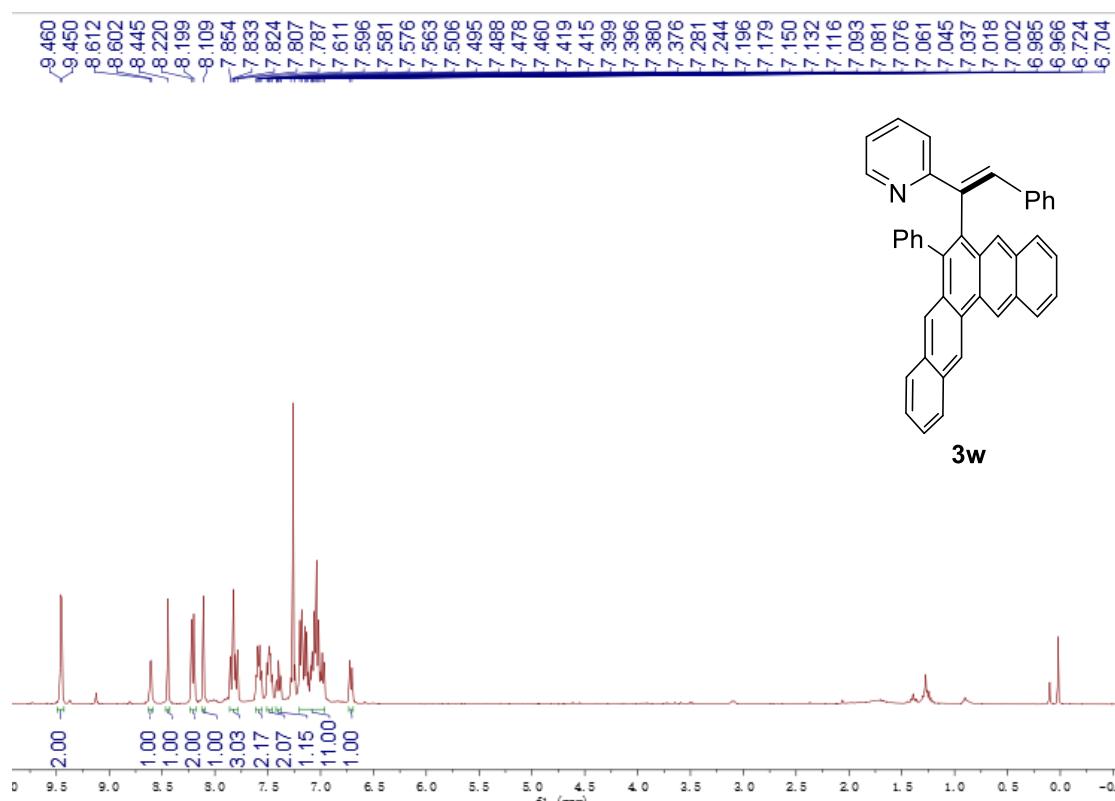
**3v-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



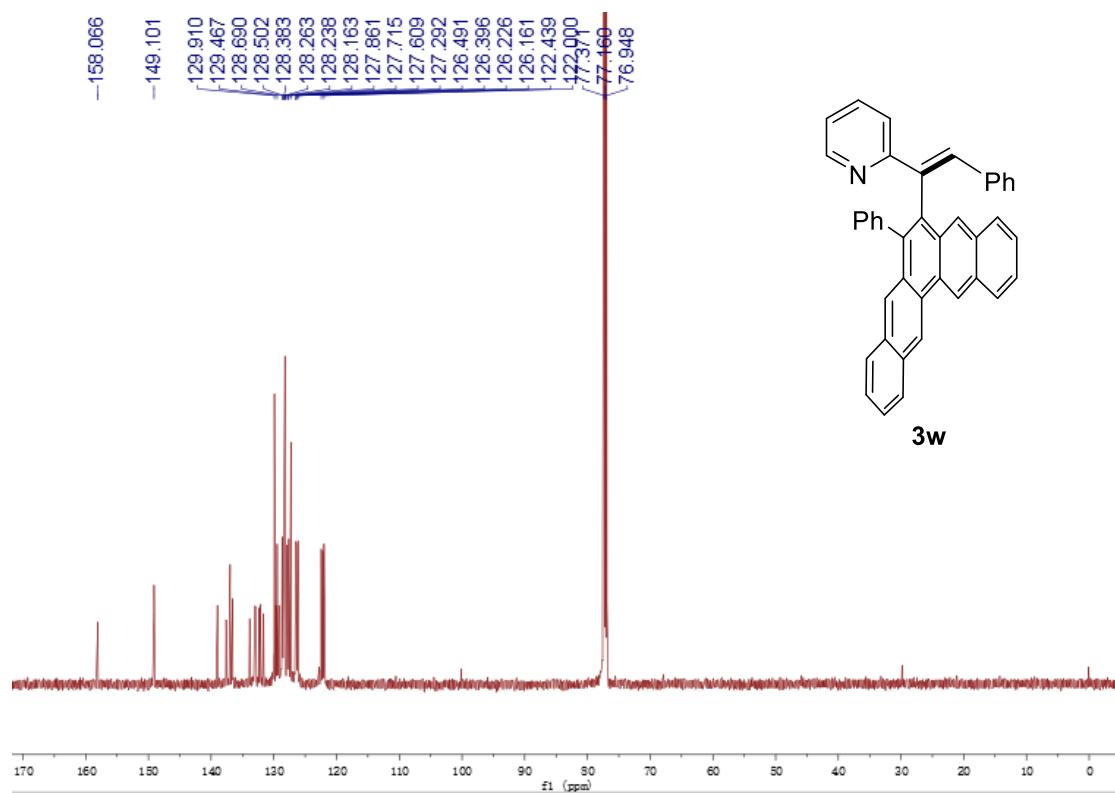
**3v-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



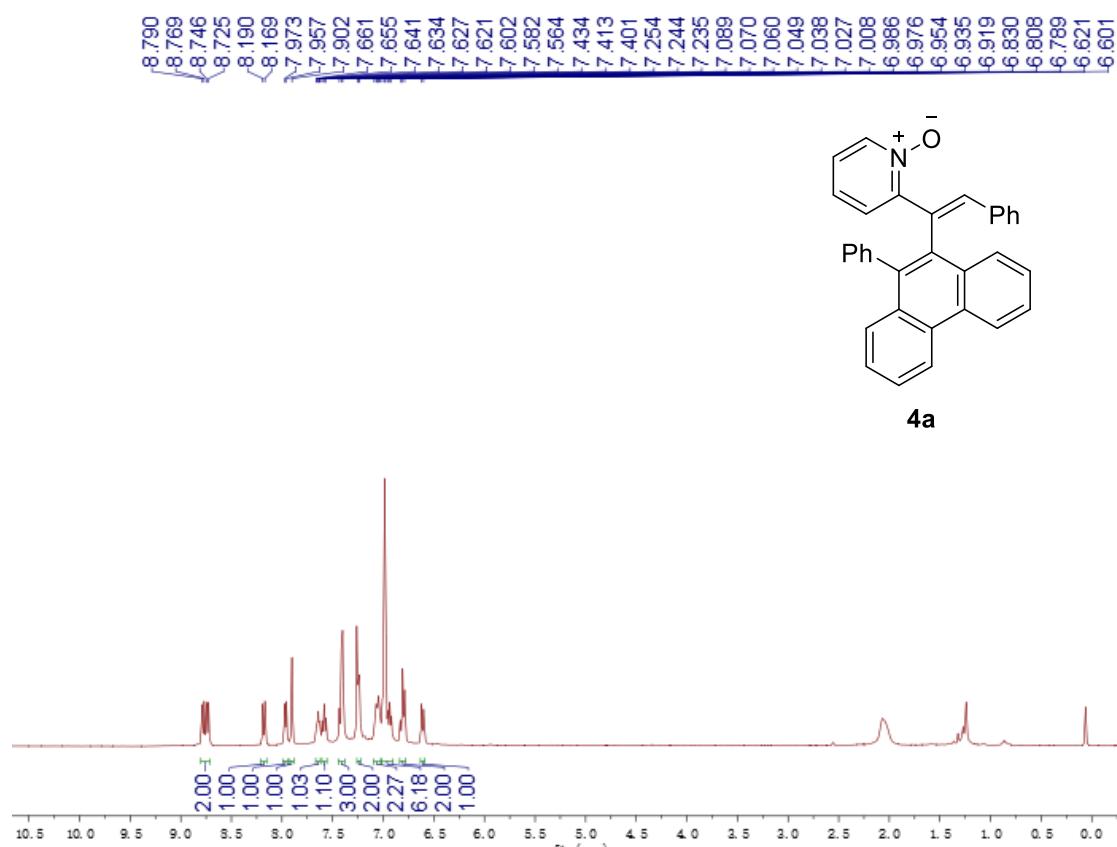
**3w-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



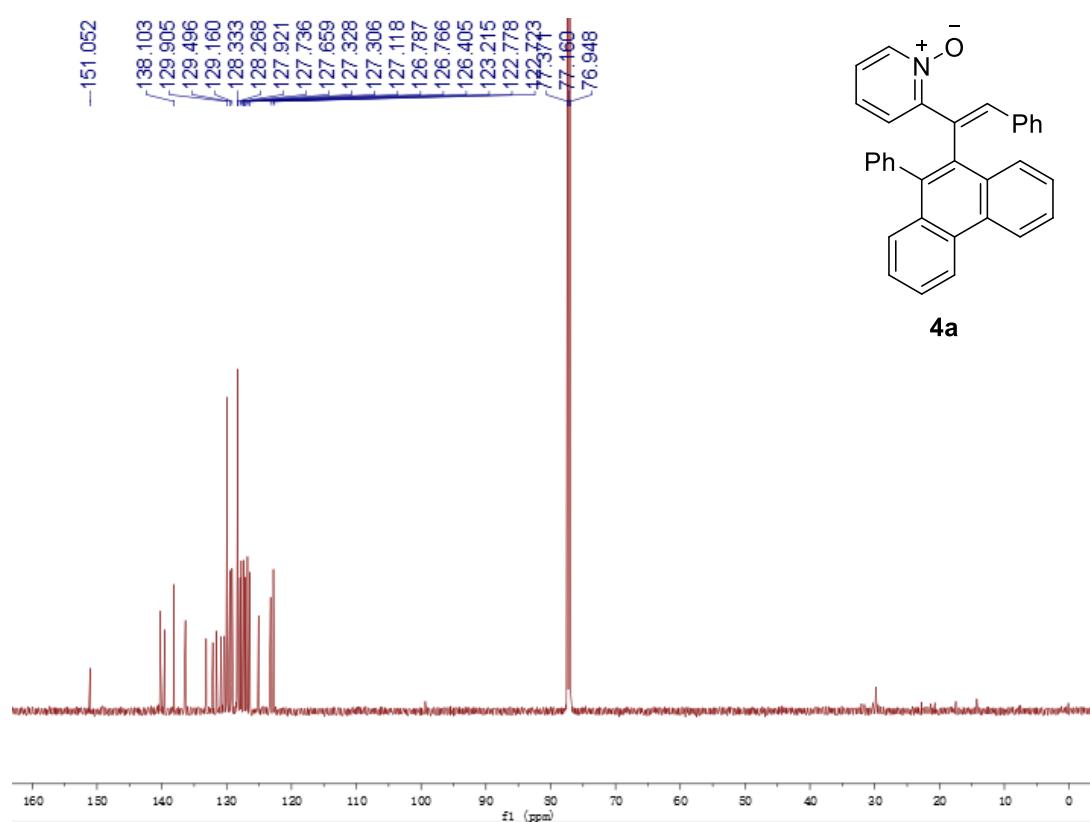
**3w-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



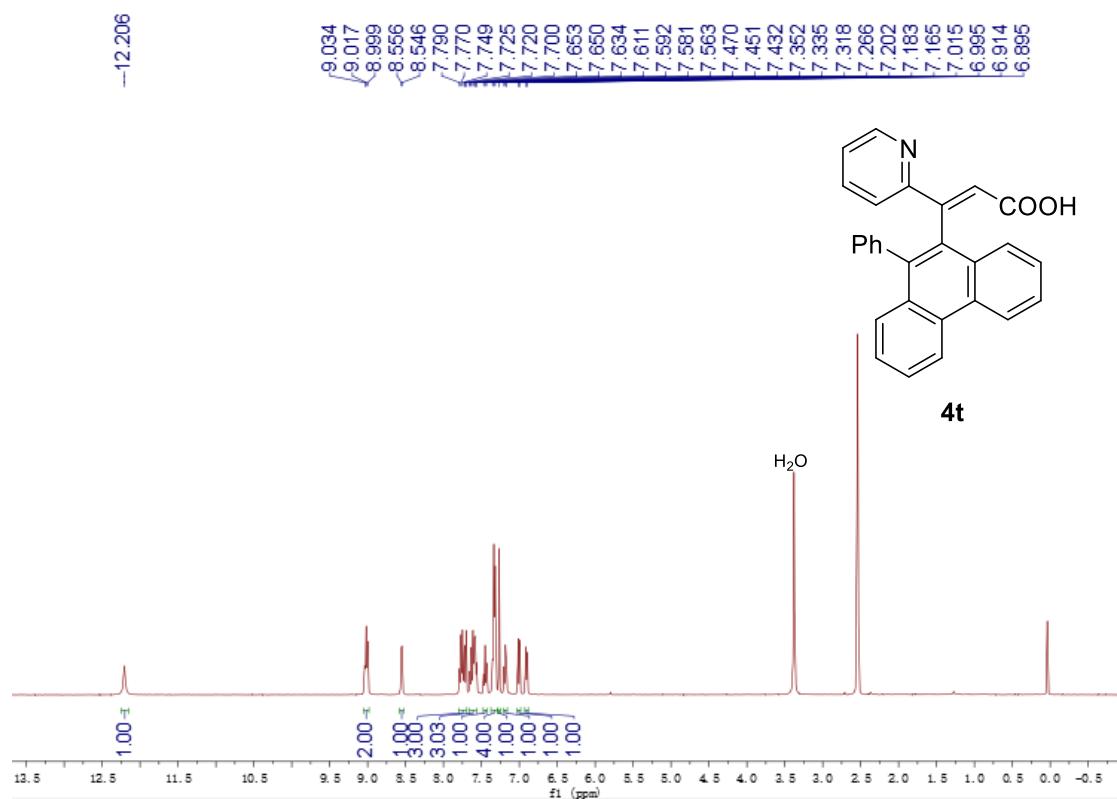
**4a-  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**



**4a-  $^{13}\text{C}\{^1\text{H}\}$  NMR (150 MHz,  $\text{CDCl}_3$ )**



**4t-<sup>1</sup>H NMR (400 MHz, DMSO)**



**4t-<sup>13</sup>C{<sup>1</sup>H} NMR (100 MHz, DMSO)**

