

## **Controllable Site-selective C-C Bond Cleavage for the Divergent**

### **Synthesis of Imidazo[1,5-a]pyridine Derivatives**

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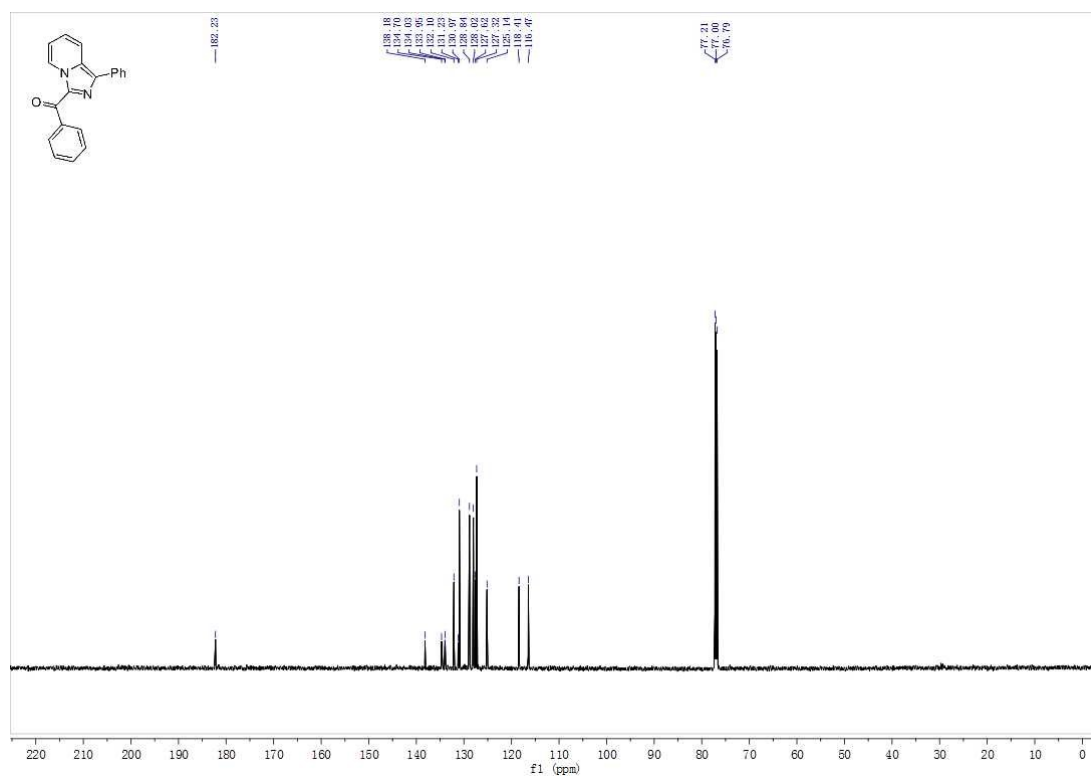
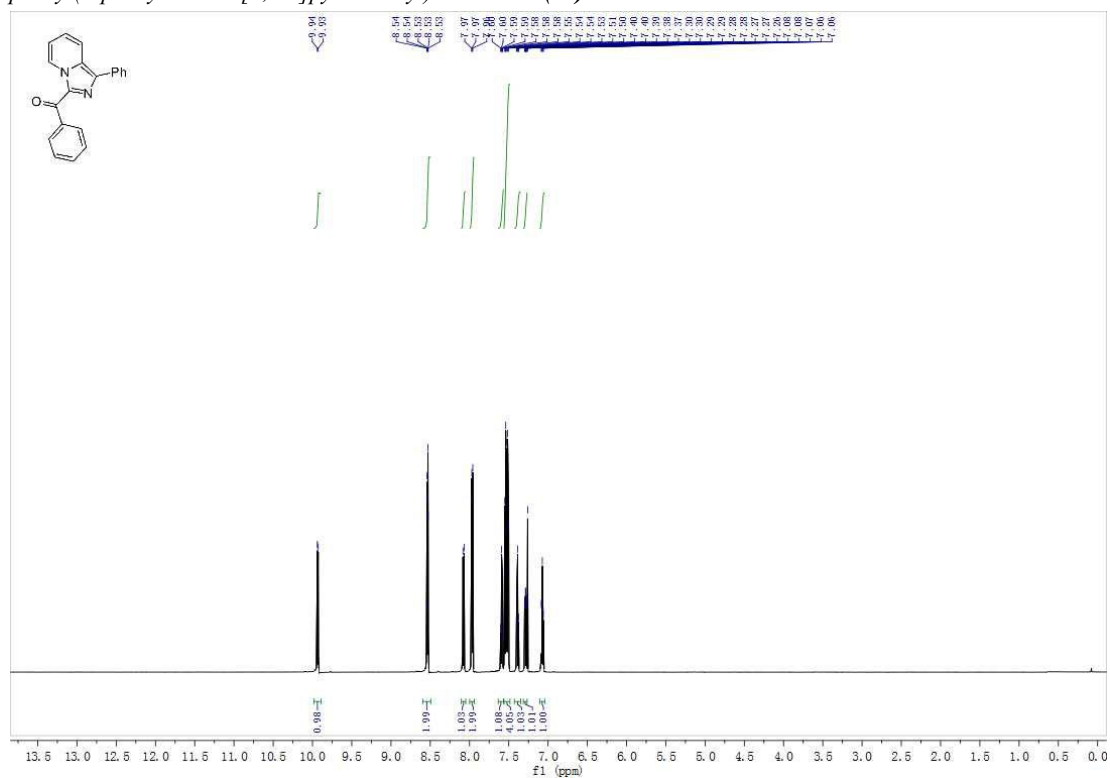
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## **List of Contents**

<b>1. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectrogram</b>	<b>S2-S20</b>
<b>2. Procedure of detection of crucial intermediates by LCMS</b>	<b>S21-S22</b>

# 1. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectrogram

phenyl(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3a**)



**<sup>1</sup>H NMR Spectrum (Top):**

Chemical structure: Cc1cccc(c1)C(=O)Nc2ccccc2

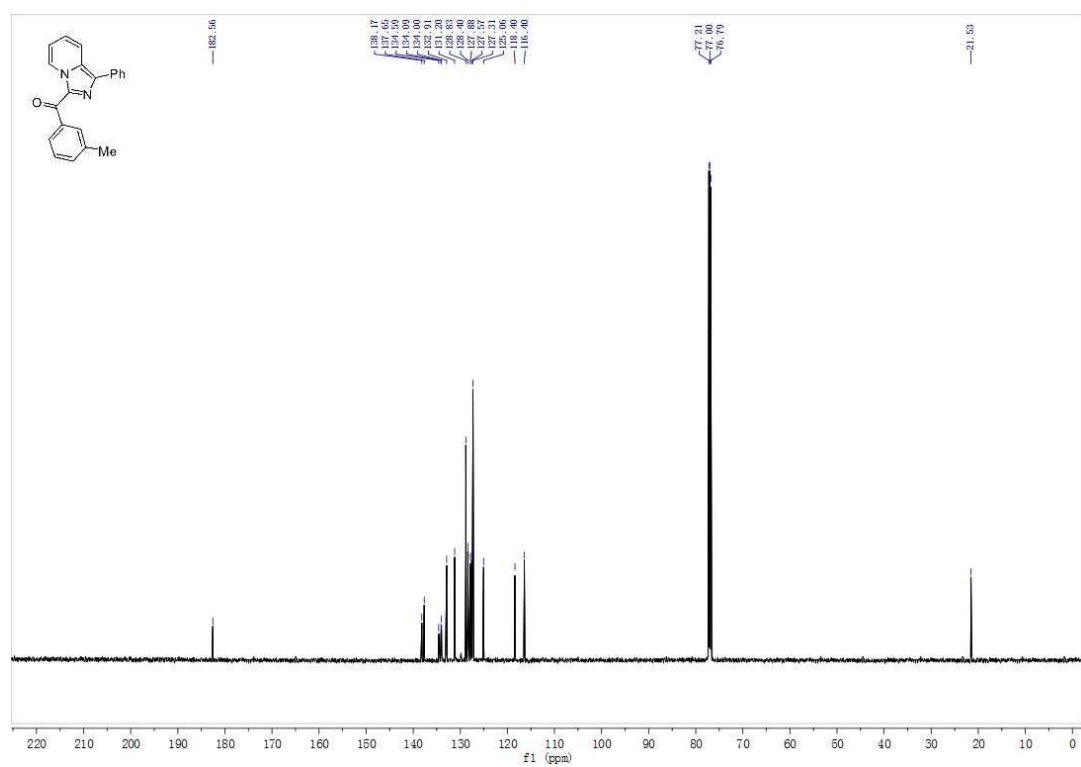
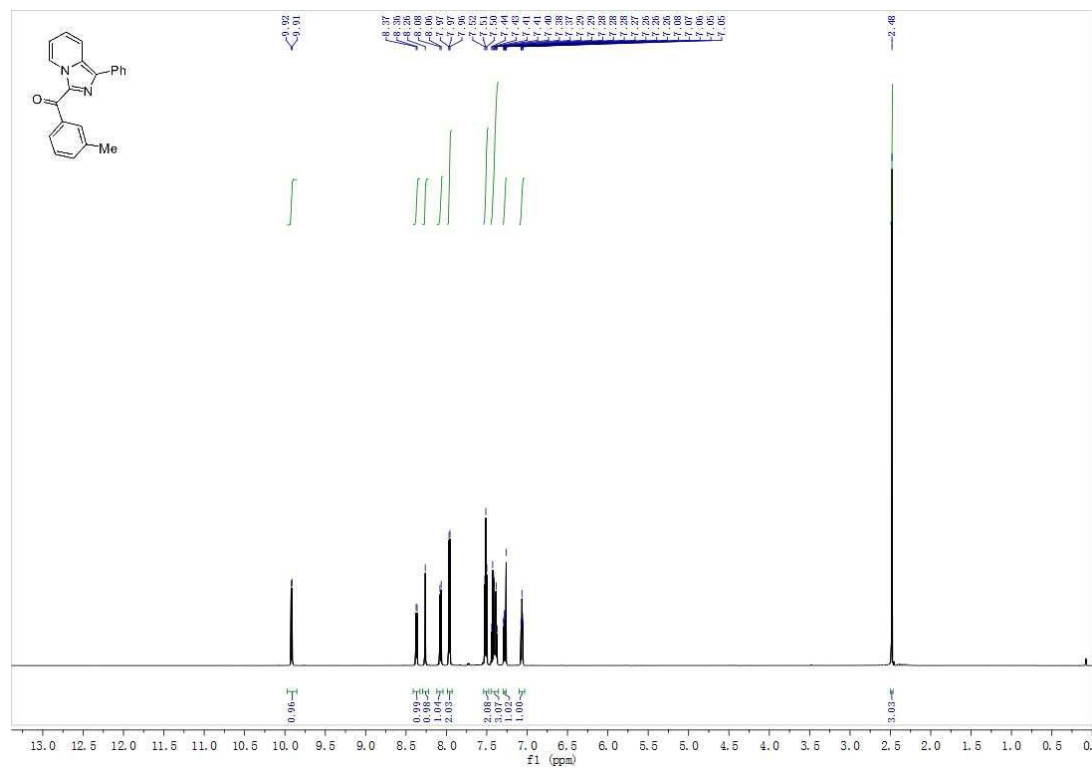
Peak list (ppm): 10.00, 7.80, 7.75, 7.70, 7.65, 7.60, 7.55, 7.50, 7.45, 7.40, 7.35, 7.30, 7.25, 7.20, 7.15, 7.10, 7.05, 7.00, 6.95, 6.90, 6.85, 6.80, 6.75, 6.70, 6.65, 6.60, 6.55, 6.50, 6.45, 6.40, 6.35, 6.30, 6.25, 6.20, 6.15, 6.10, 6.05, 6.00, 5.95, 5.90, 5.85, 5.80, 5.75, 5.70, 5.65, 5.60, 5.55, 5.50, 5.45, 5.40, 5.35, 5.30, 5.25, 5.20, 5.15, 5.10, 5.05, 5.00, 4.95, 4.90, 4.85, 4.80, 4.75, 4.70, 4.65, 4.60, 4.55, 4.50, 4.45, 4.40, 4.35, 4.30, 4.25, 4.20, 4.15, 4.10, 4.05, 4.00, 3.95, 3.90, 3.85, 3.80, 3.75, 3.70, 3.65, 3.60, 3.55, 3.50, 3.45, 3.40, 3.35, 3.30, 3.25, 3.20, 3.15, 3.10, 3.05, 3.00, 2.95, 2.90, 2.85, 2.80, 2.75, 2.70, 2.65, 2.60, 2.55, 2.50, 2.45, 2.40, 2.35, 2.30, 2.25, 2.20, 2.15, 2.10, 2.05, 2.00, 1.95, 1.90, 1.85, 1.80, 1.75, 1.70, 1.65, 1.60, 1.55, 1.50, 1.45, 1.40, 1.35, 1.30, 1.25, 1.20, 1.15, 1.10, 1.05, 1.00, 0.95, 0.90, 0.85, 0.80, 0.75, 0.70, 0.65, 0.60, 0.55, 0.50, 0.45, 0.40, 0.35, 0.30, 0.25, 0.20, 0.15, 0.10, 0.05, 0.00.

**<sup>13</sup>C NMR Spectrum (Bottom):**

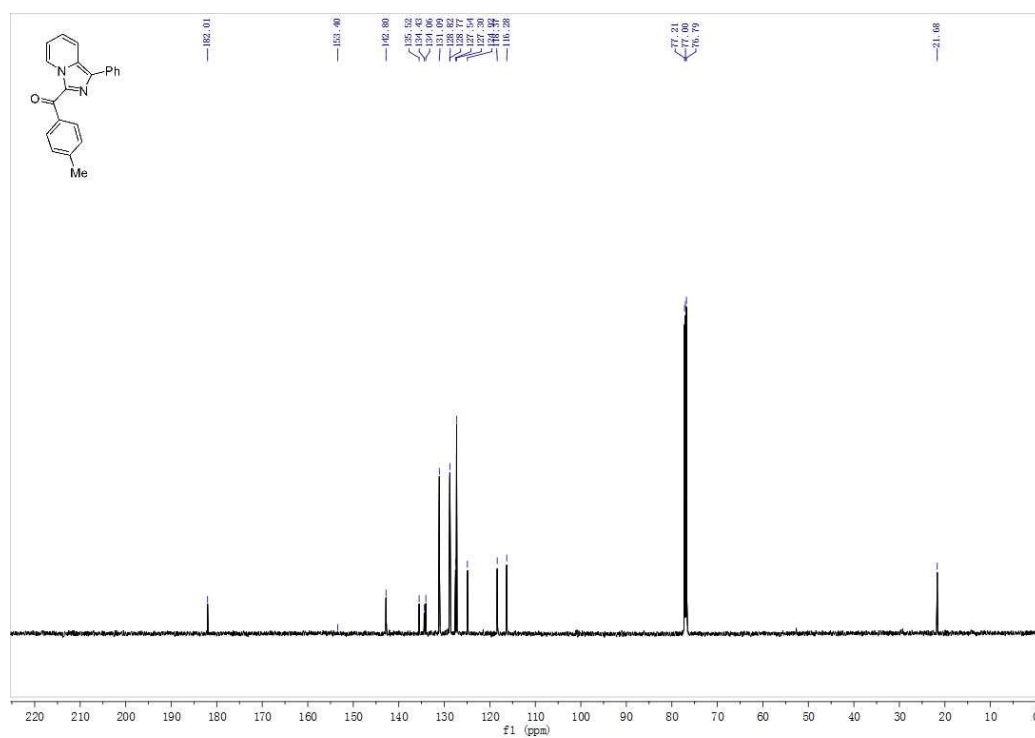
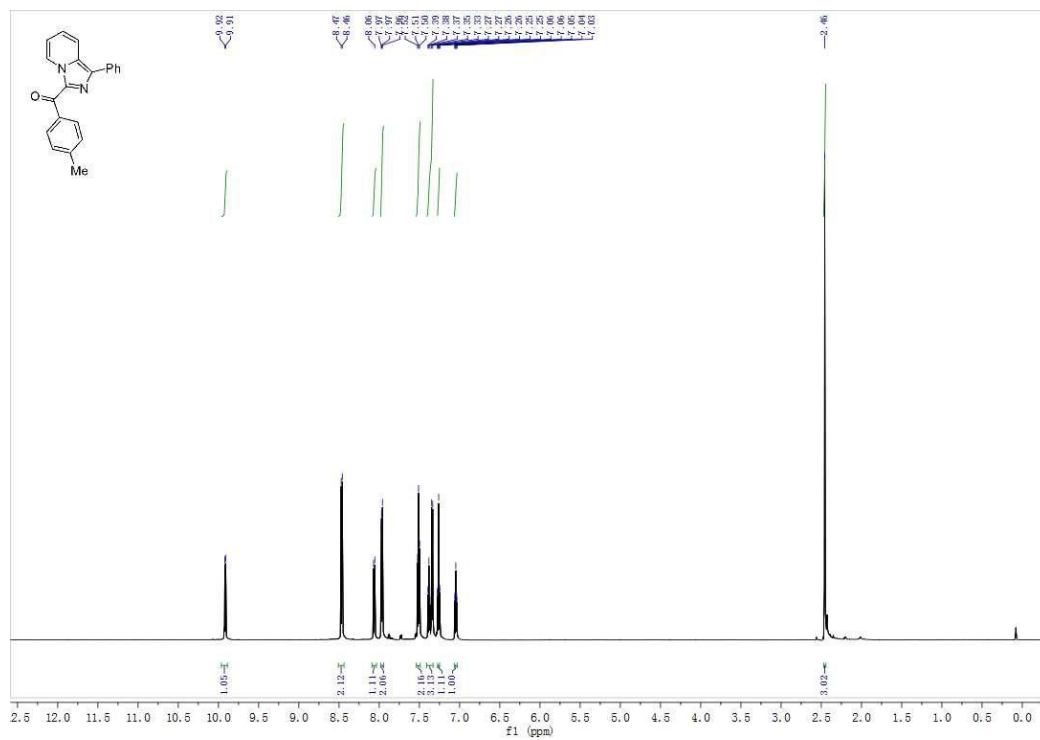
Chemical structure: Cc1cccc(c1)C(=O)Nc2ccccc2

Peak list (ppm): 186.39, 138.08, 137.36, 135.14, 133.62, 131.46, 130.55, 130.20, 127.61, 127.36, 125.24, 124.94, 116.58, 77.21, 76.79, 20.44.

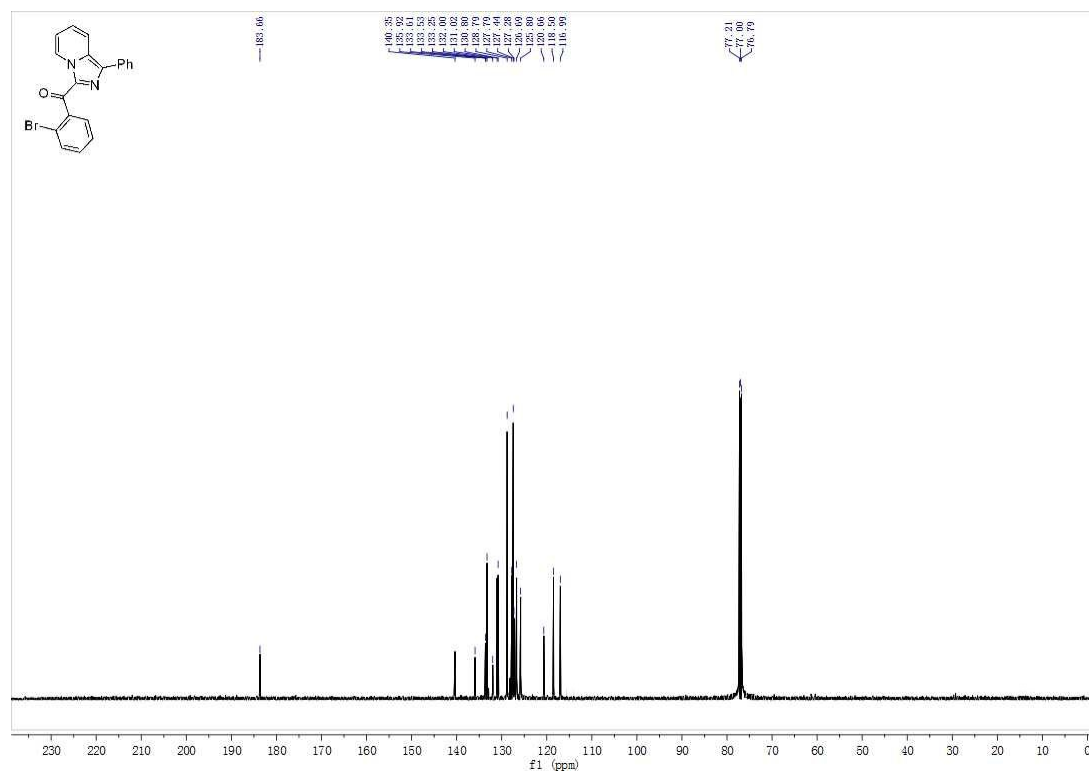
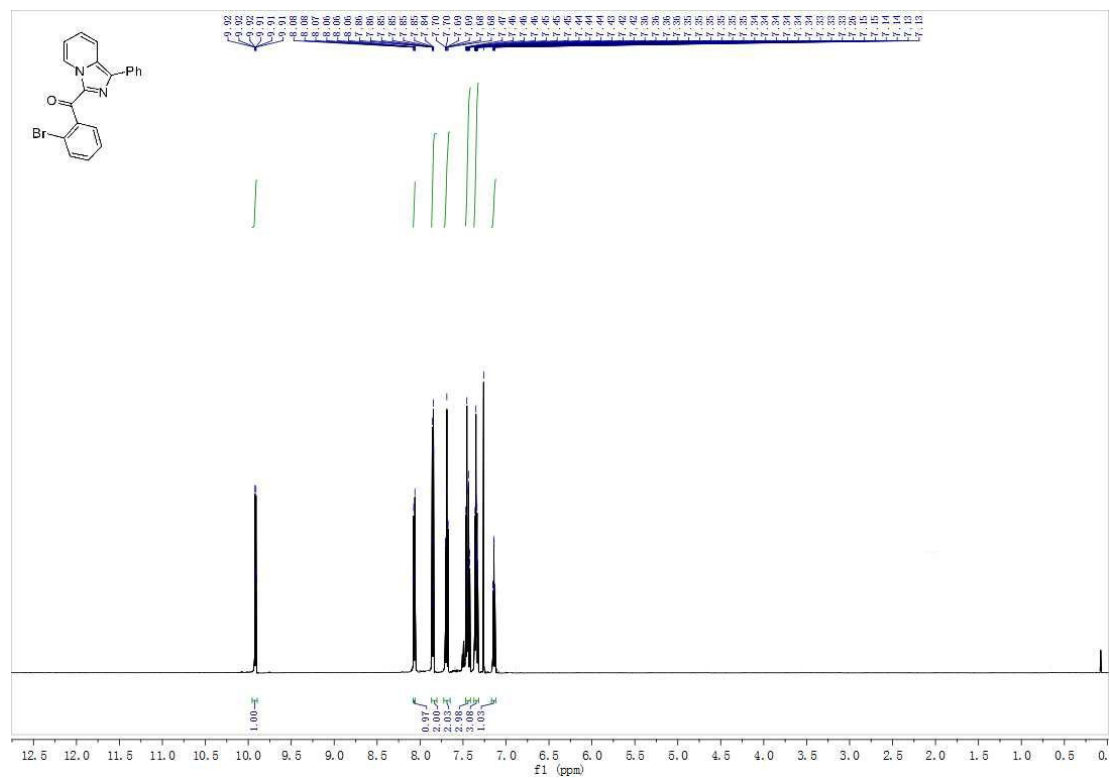
(1- phenylimidazo[1,5-a]pyridin-3-yl)(*m*-tolyl)methanone (**3c**)



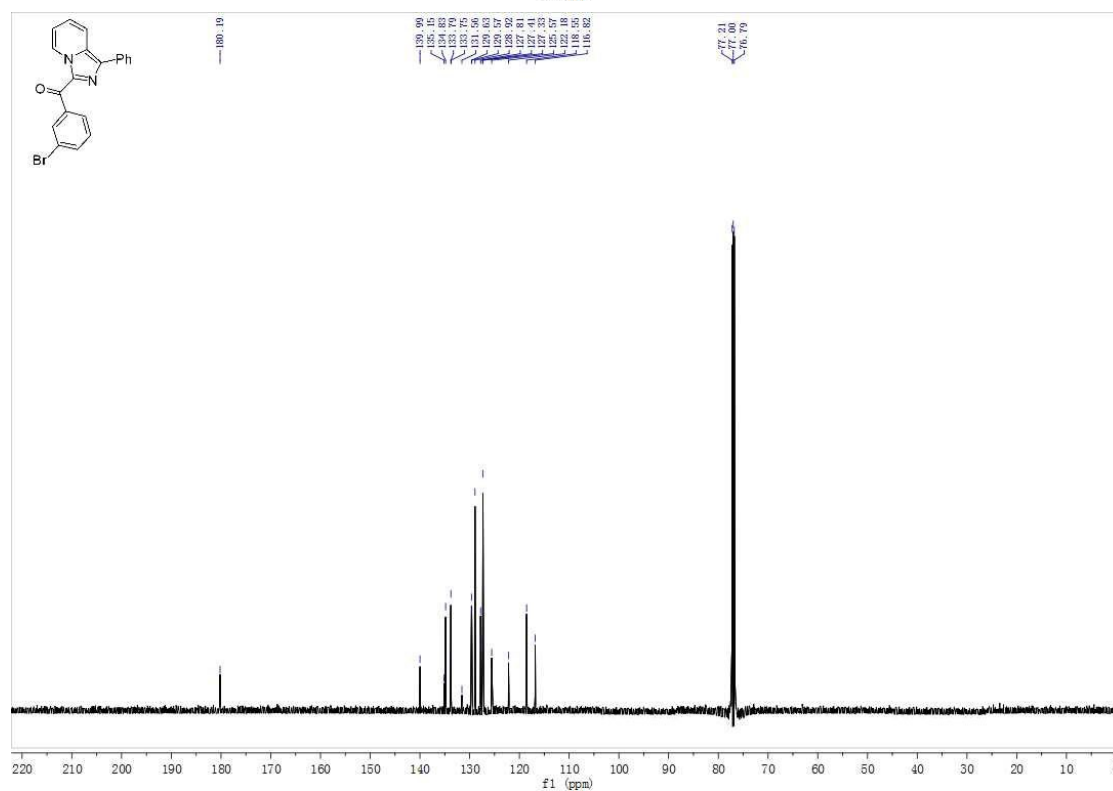
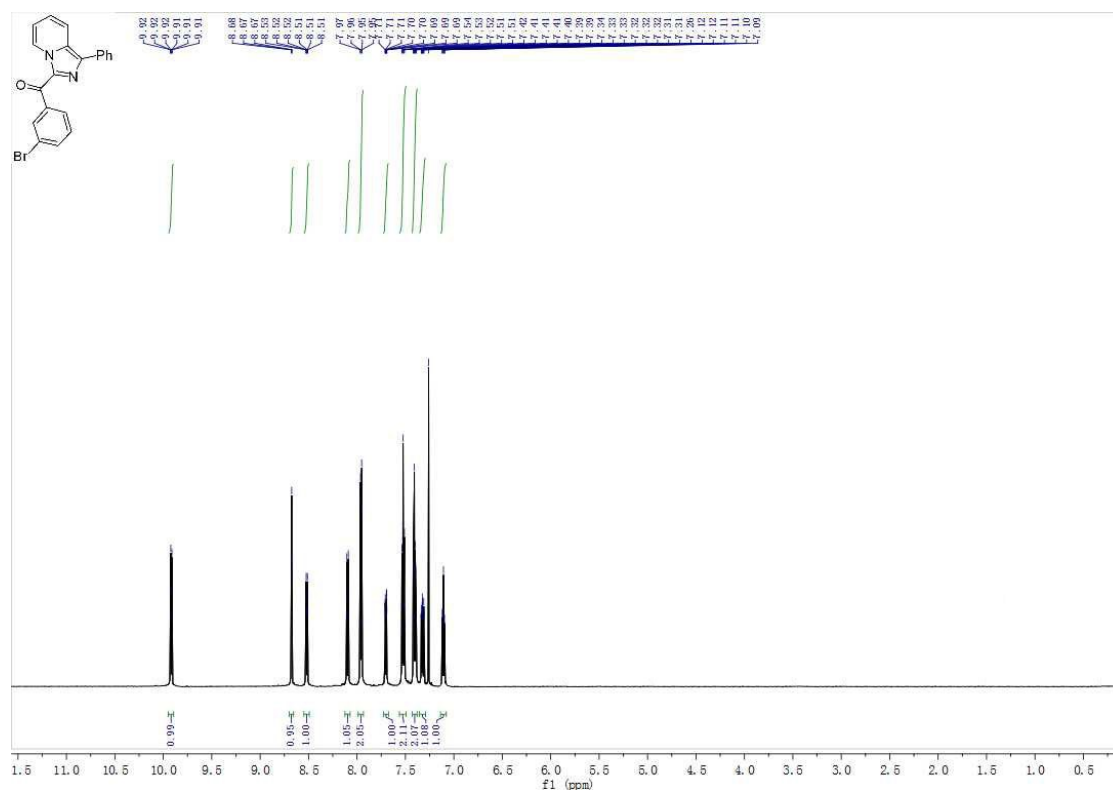
(1- phenylimidazo[1,5-a]pyridin-3-yl)(p-tolyl)methanone (3d)



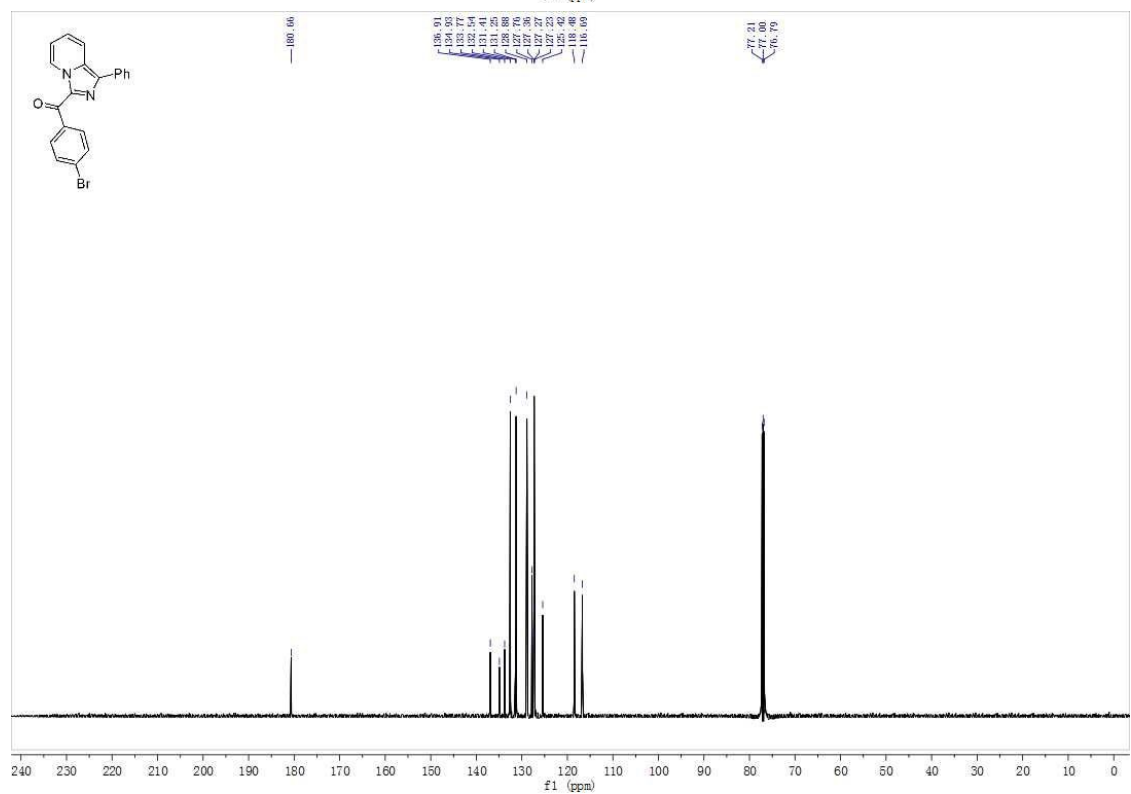
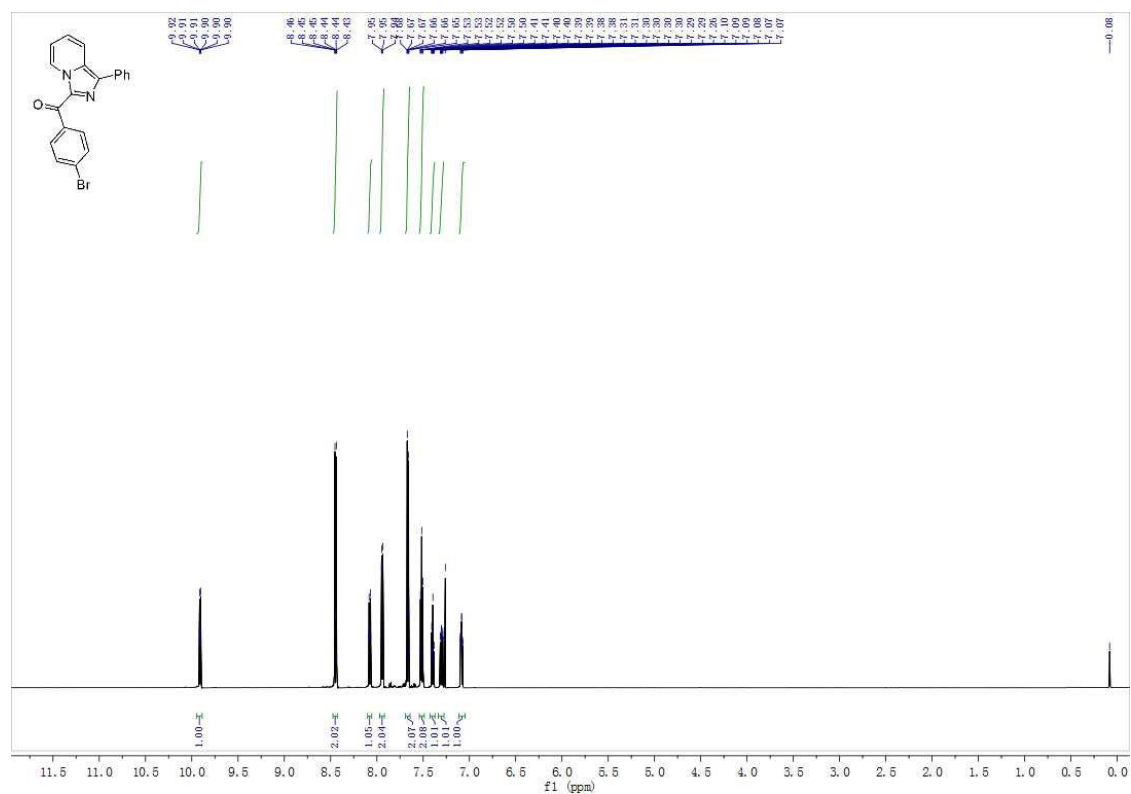
(2-bromophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3e**)



(3- bromophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3f**)

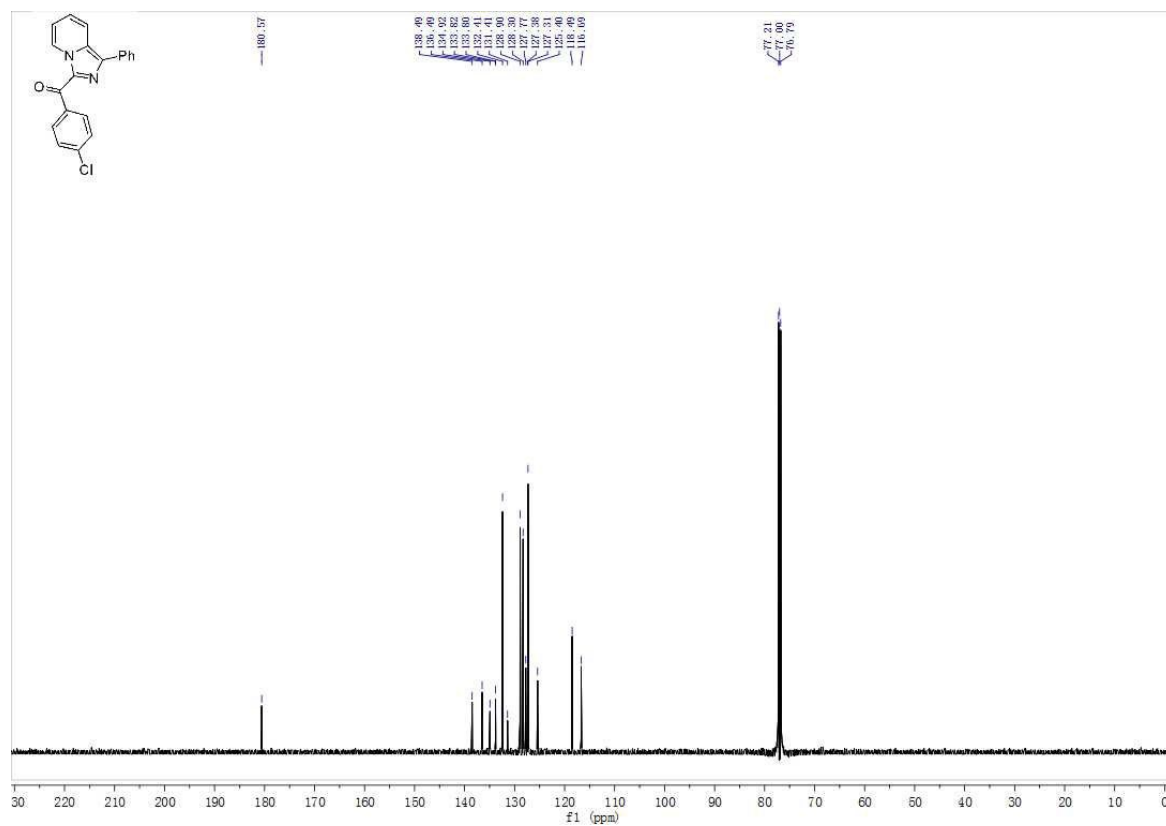
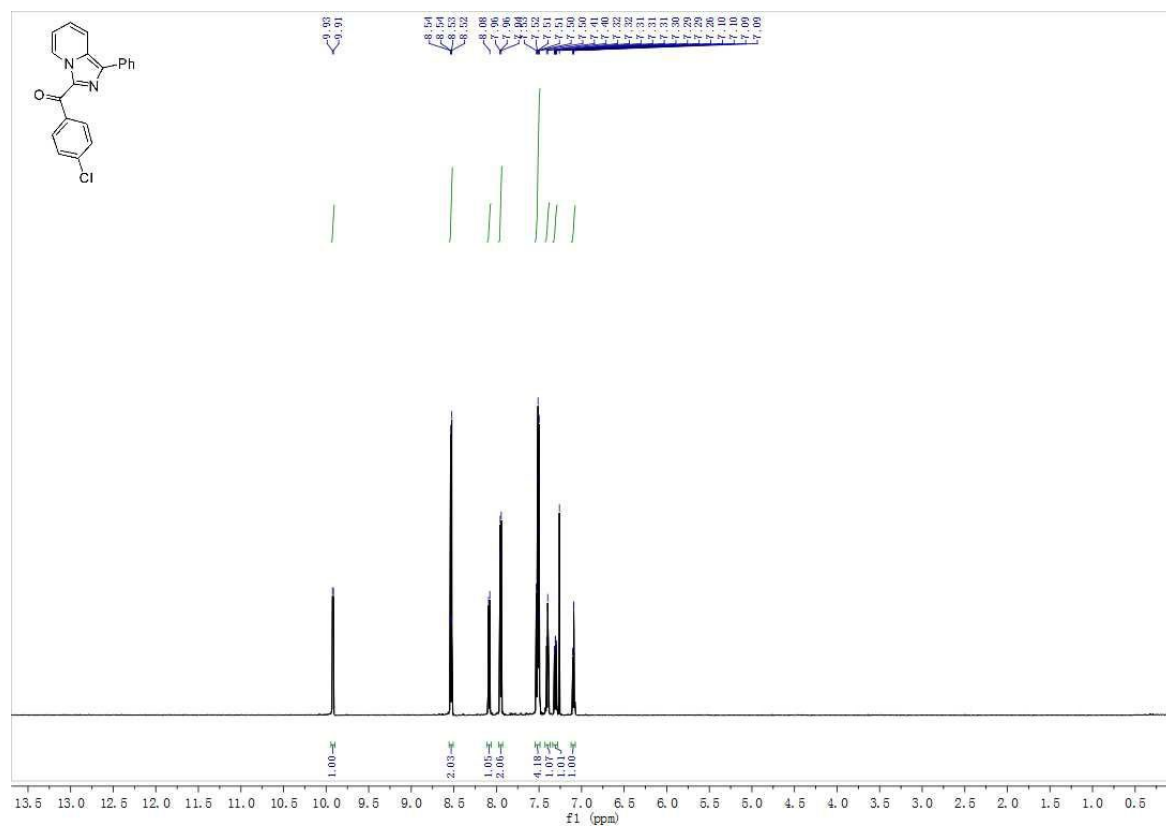


(4-bromophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3g**)

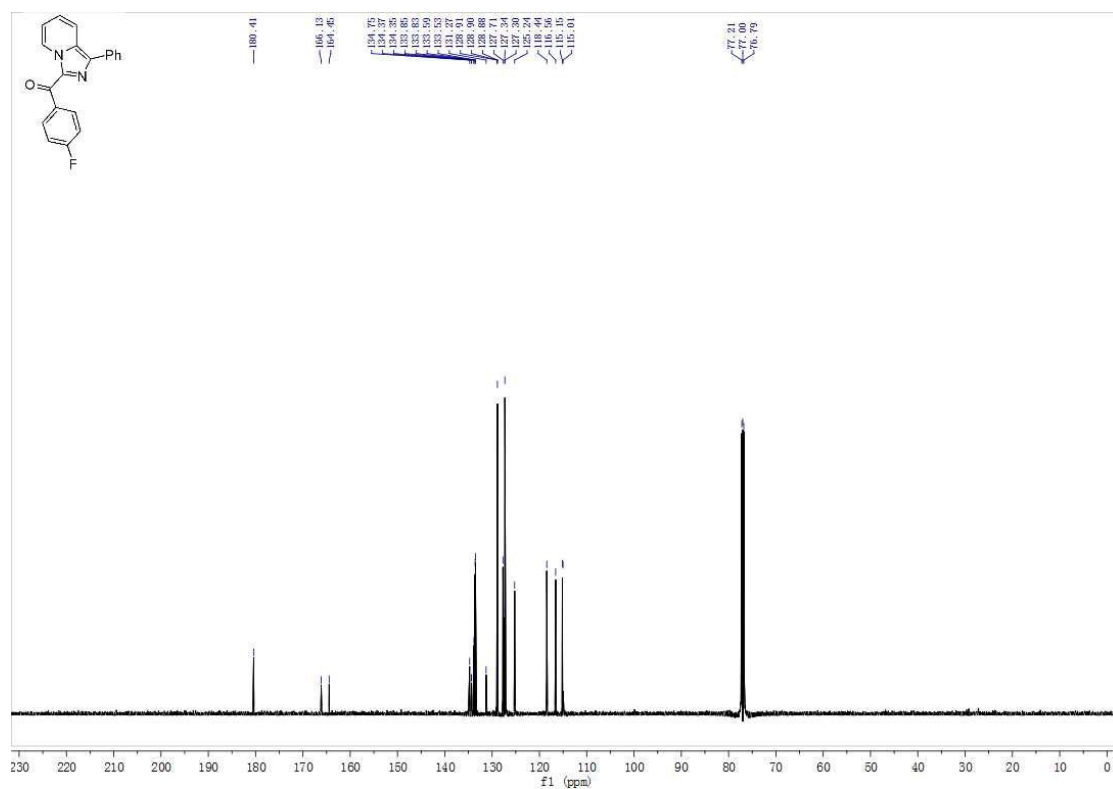
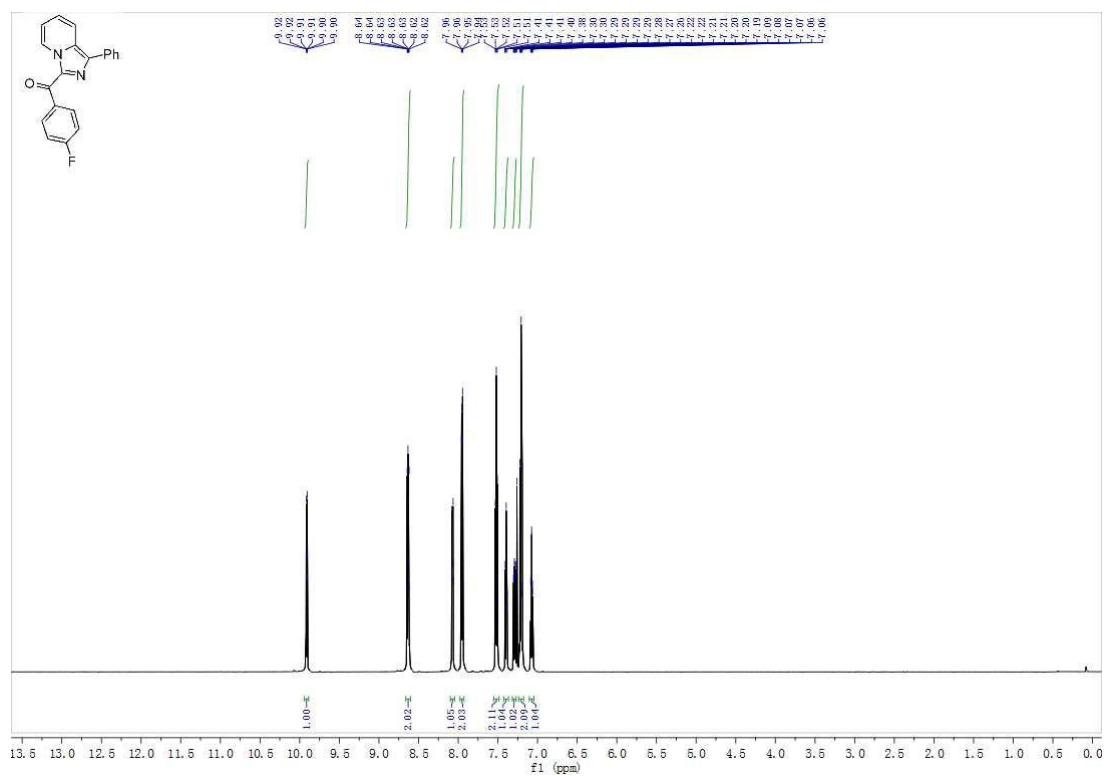




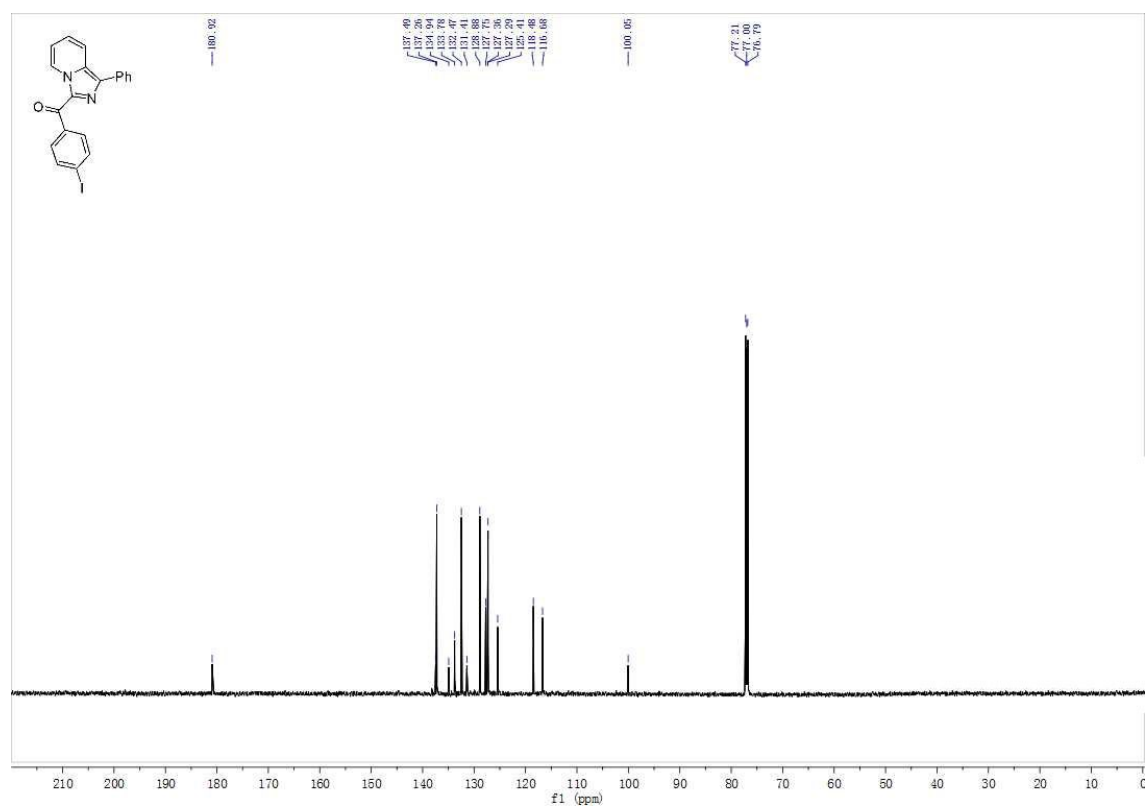
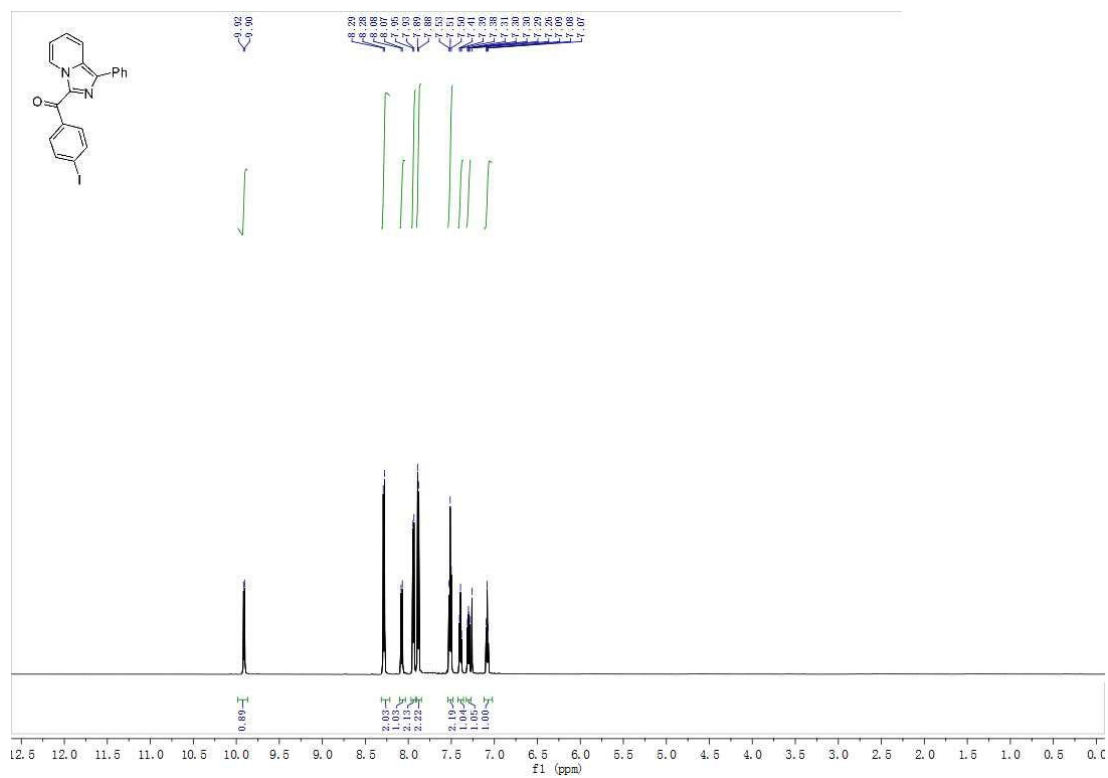
(4-chlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3h**)



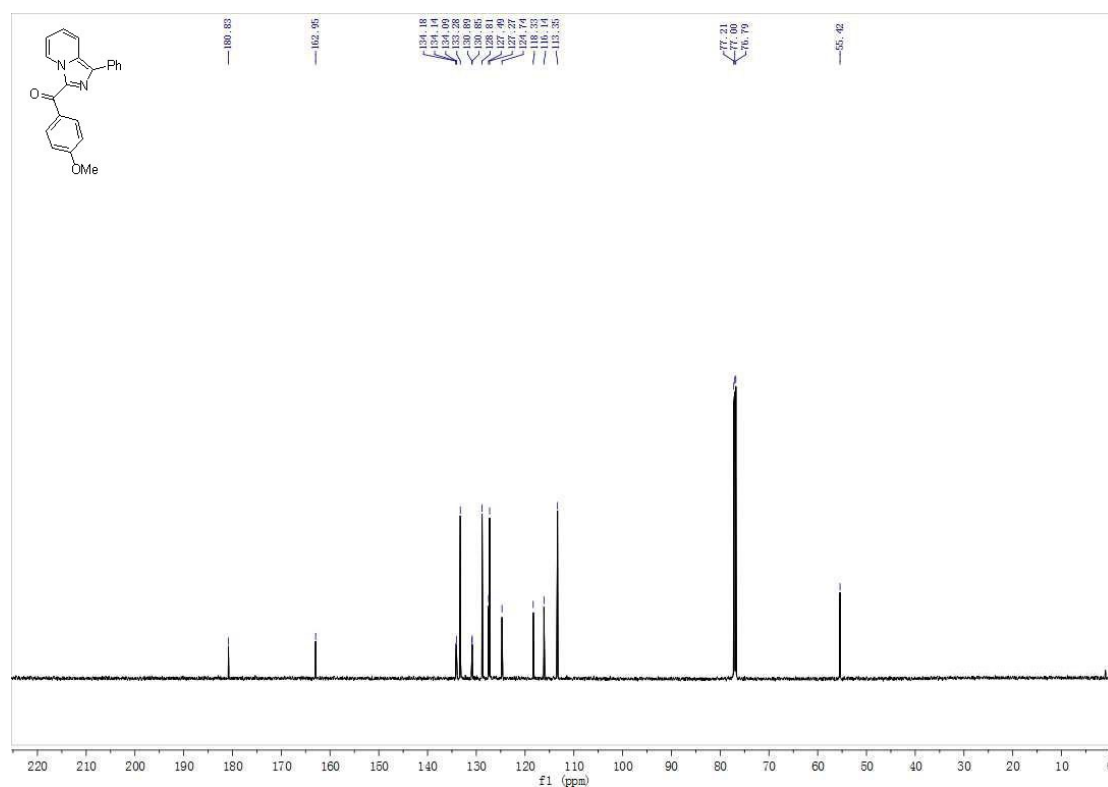
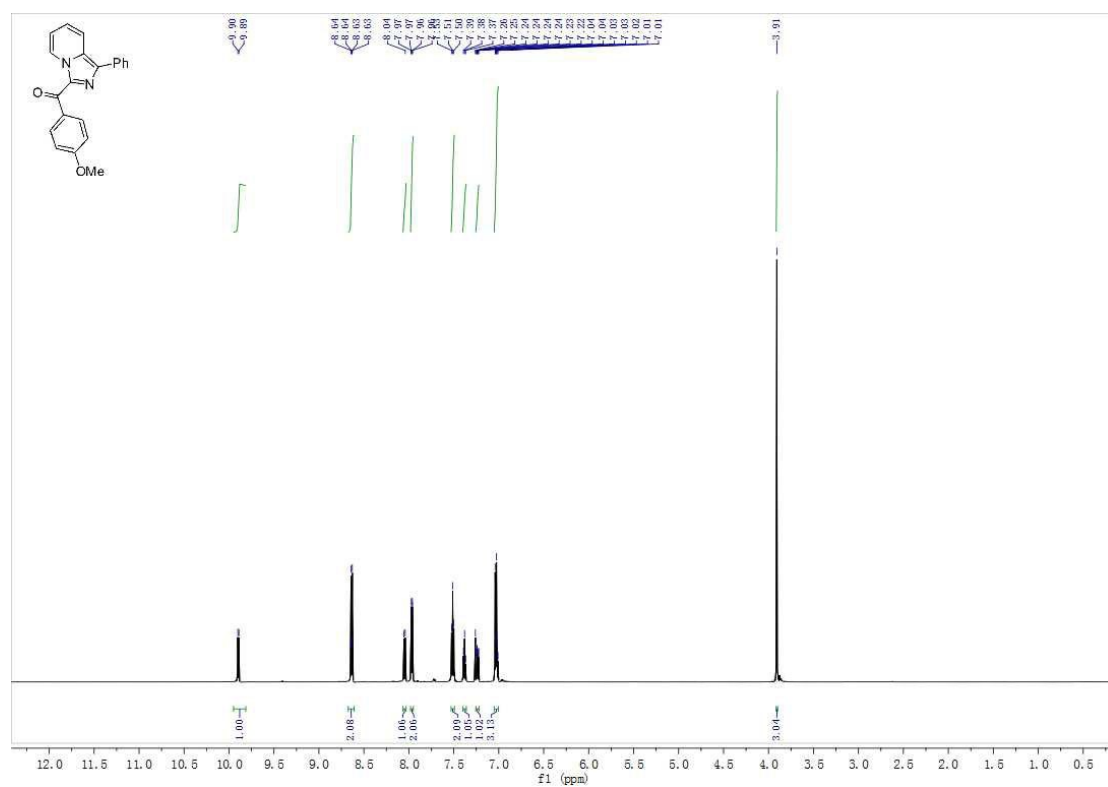
(4-fluorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3i**)



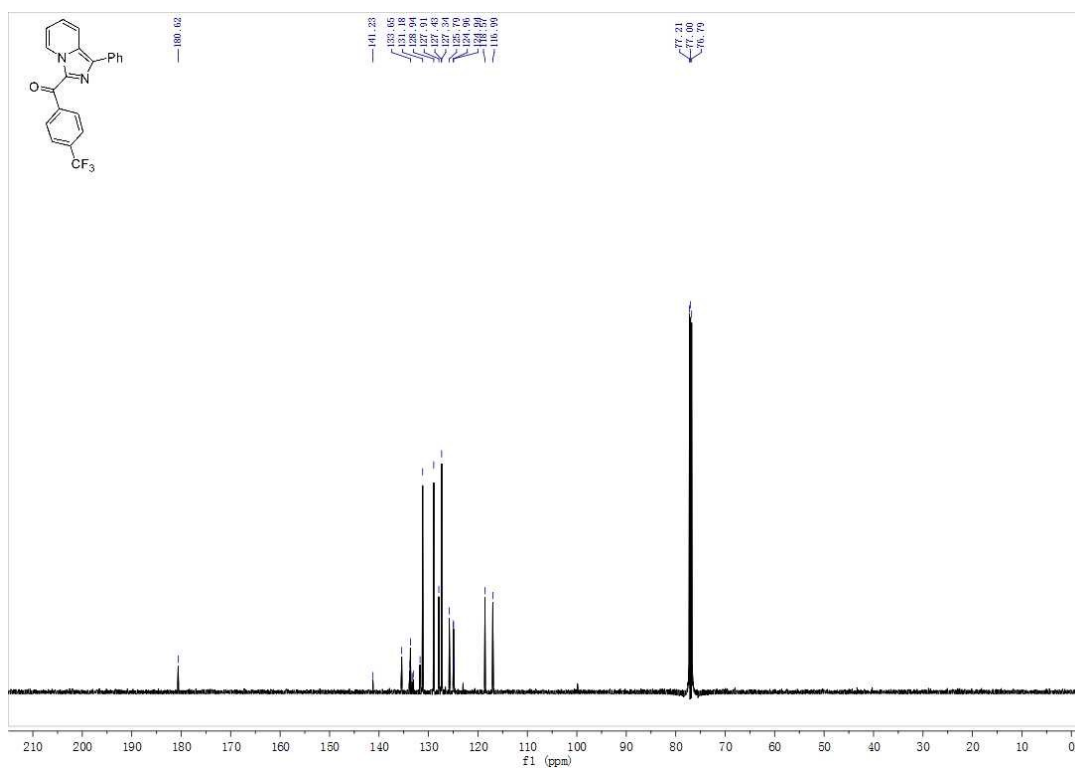
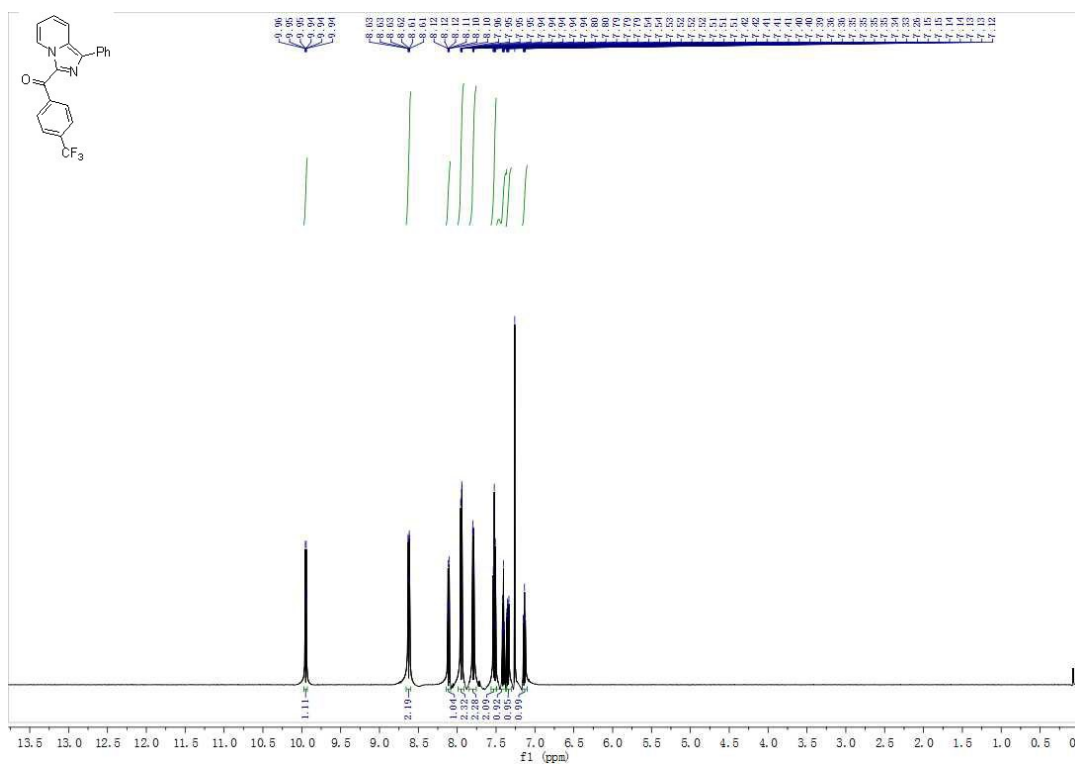
(4-iodophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3j**)



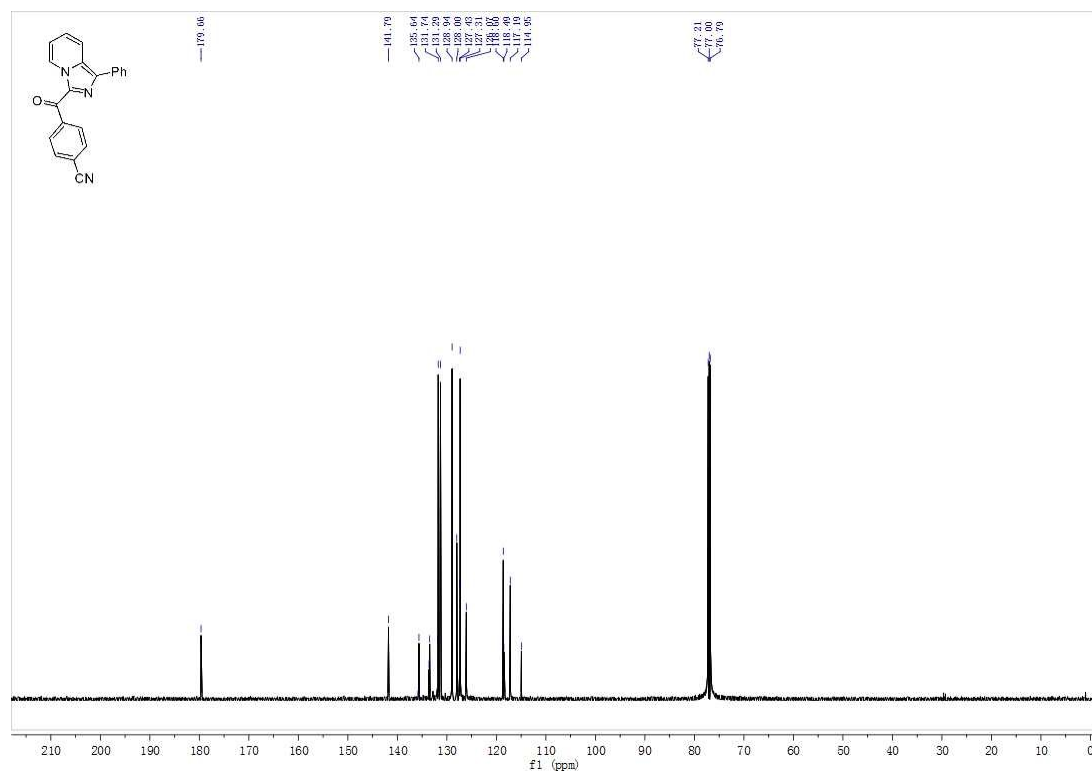
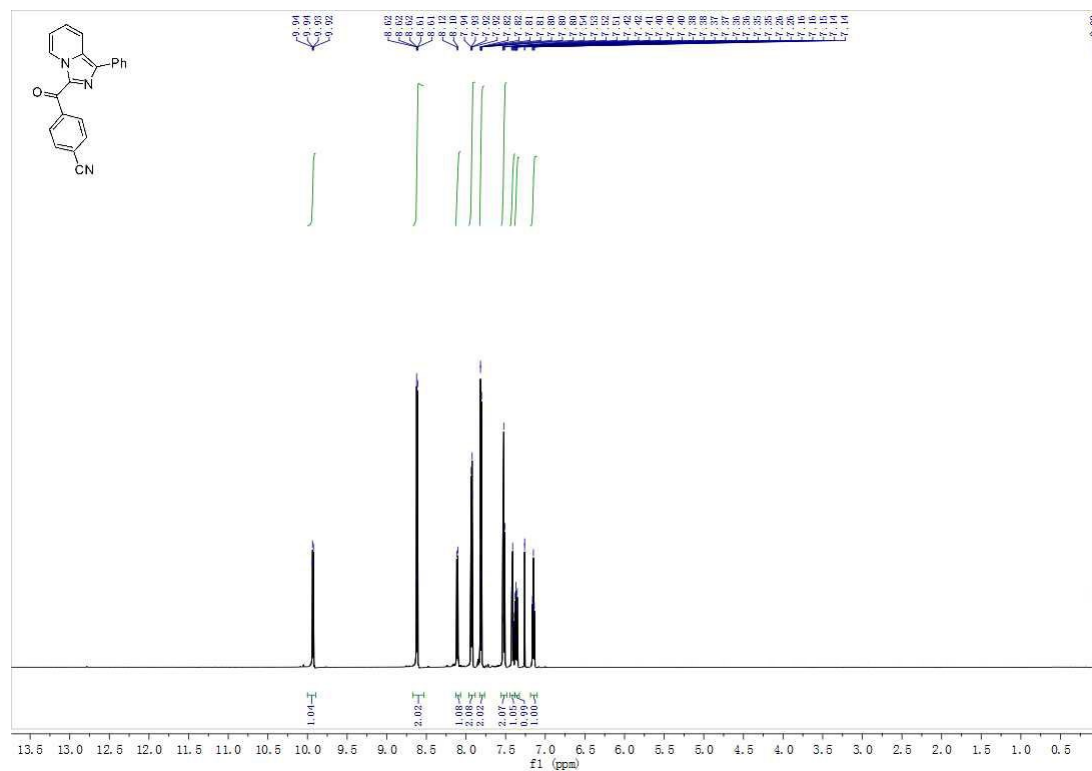
(4-methoxyphenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3k**)



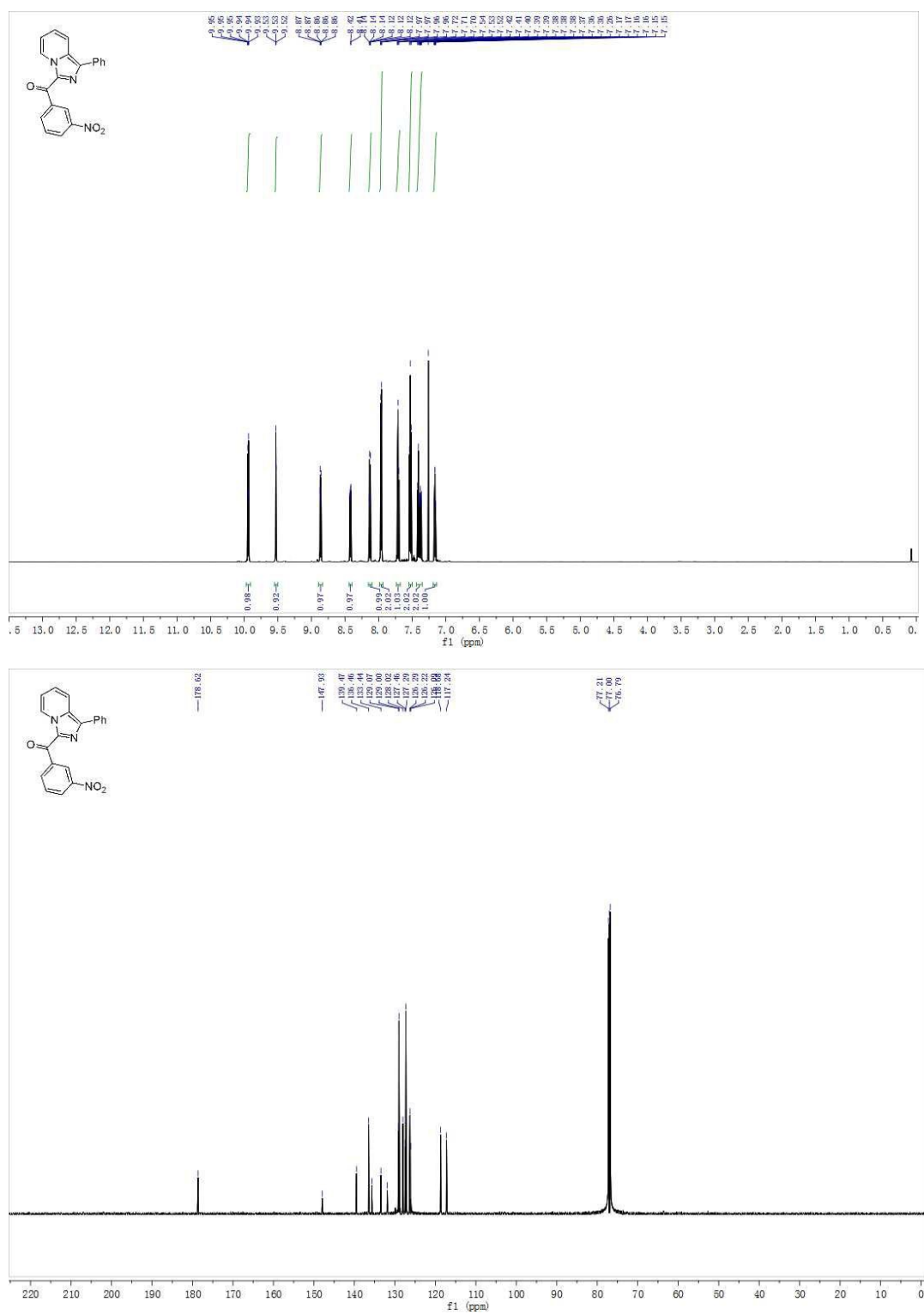
(1-phenylimidazo[1,5-a]pyridin-3-yl)(4-(trifluoromethyl)phenyl)methanone (**3l**)



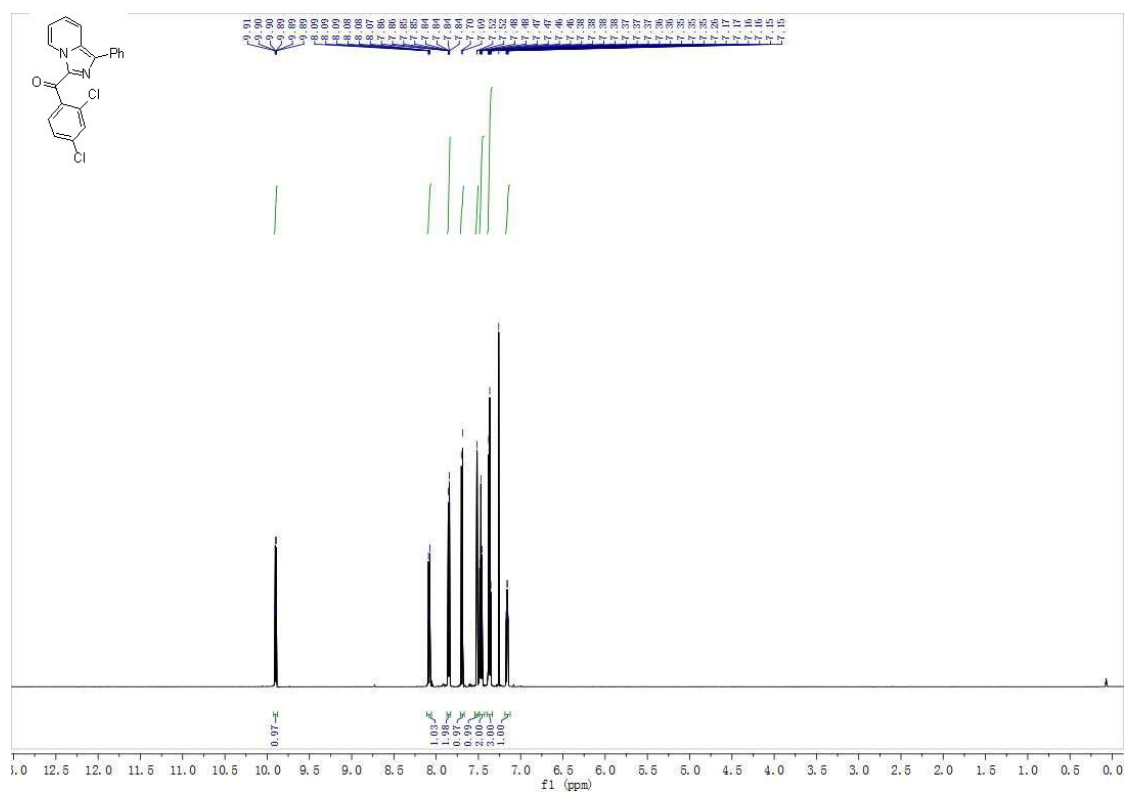
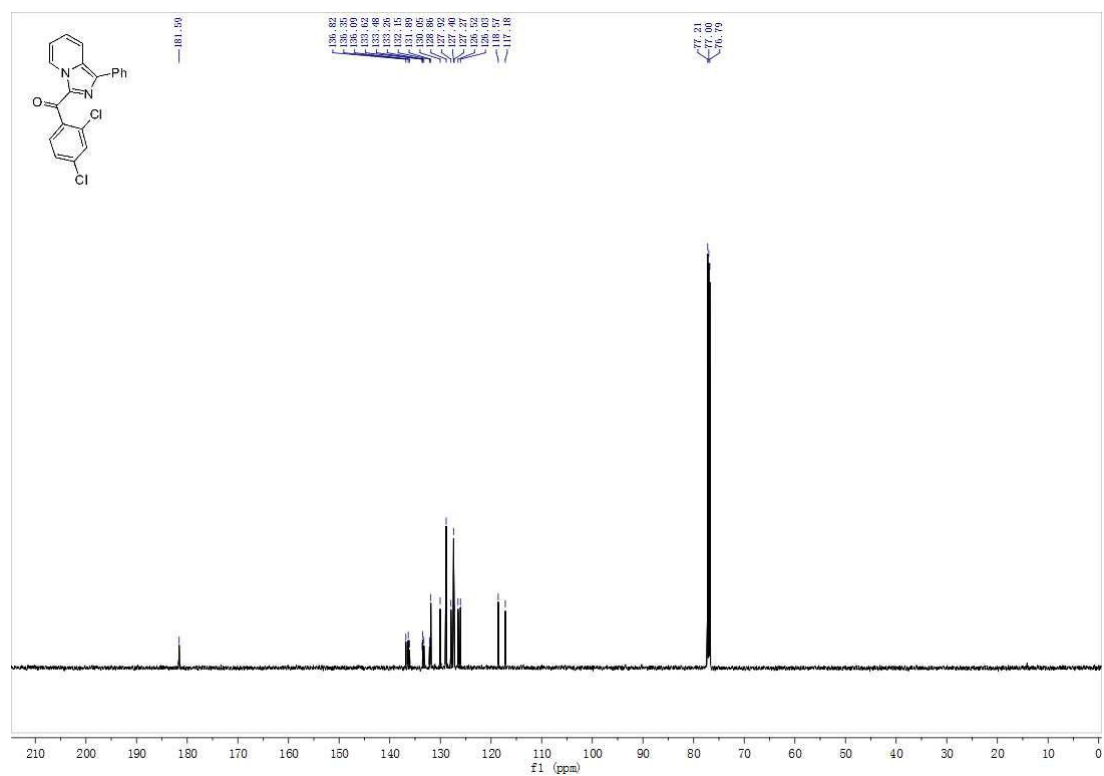
4-(1-phenylimidazo[1,5-a]pyridine-3-carbonyl)benzonitrile (**3m**)



(3-nitrophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3n**)

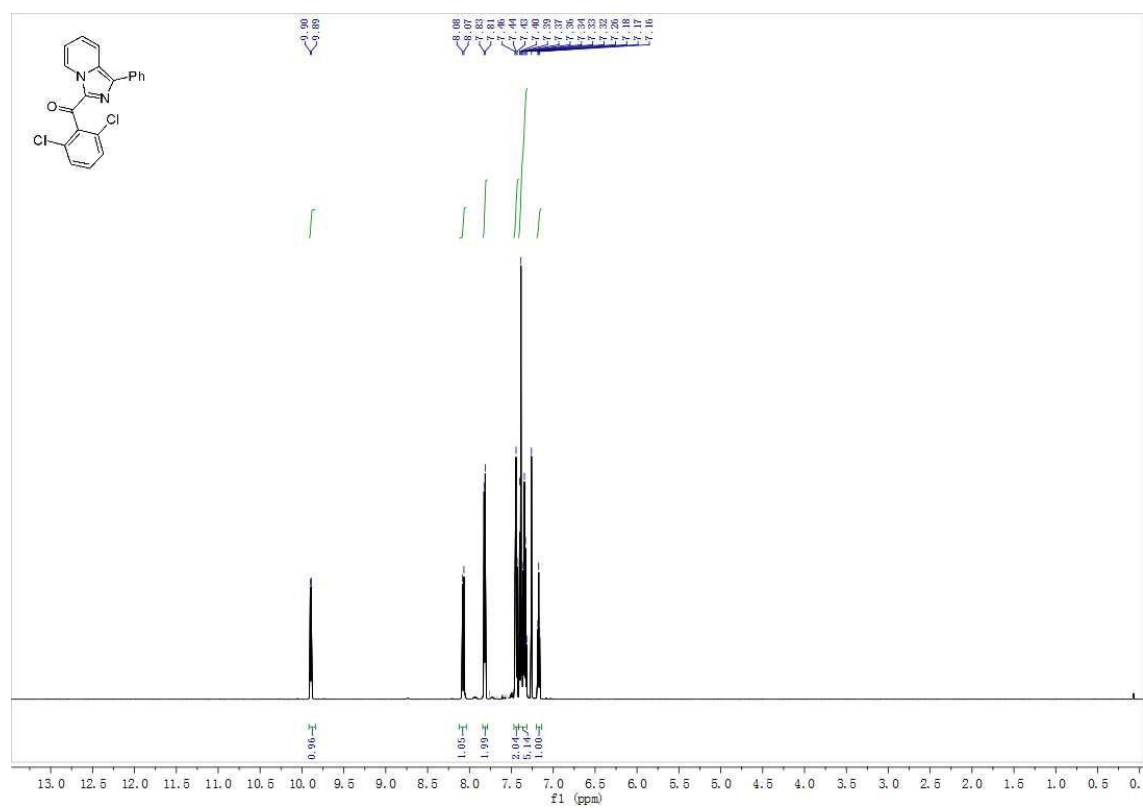
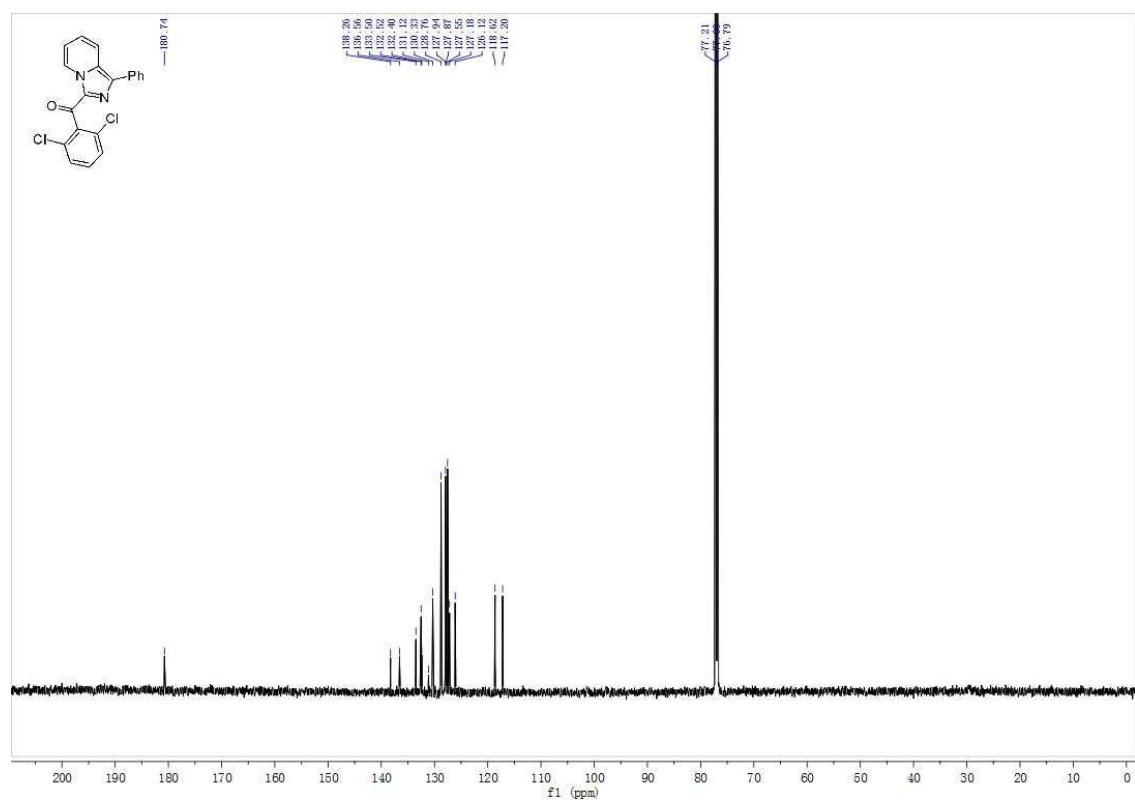


(2,4-dichlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3p**)

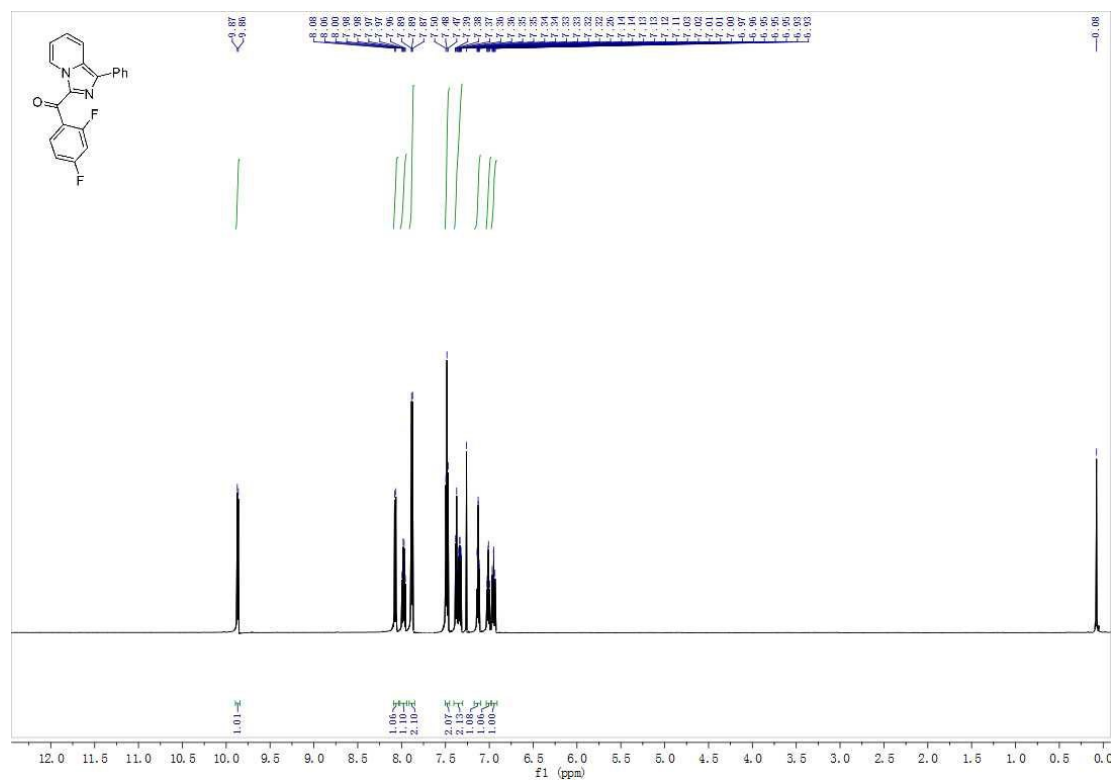




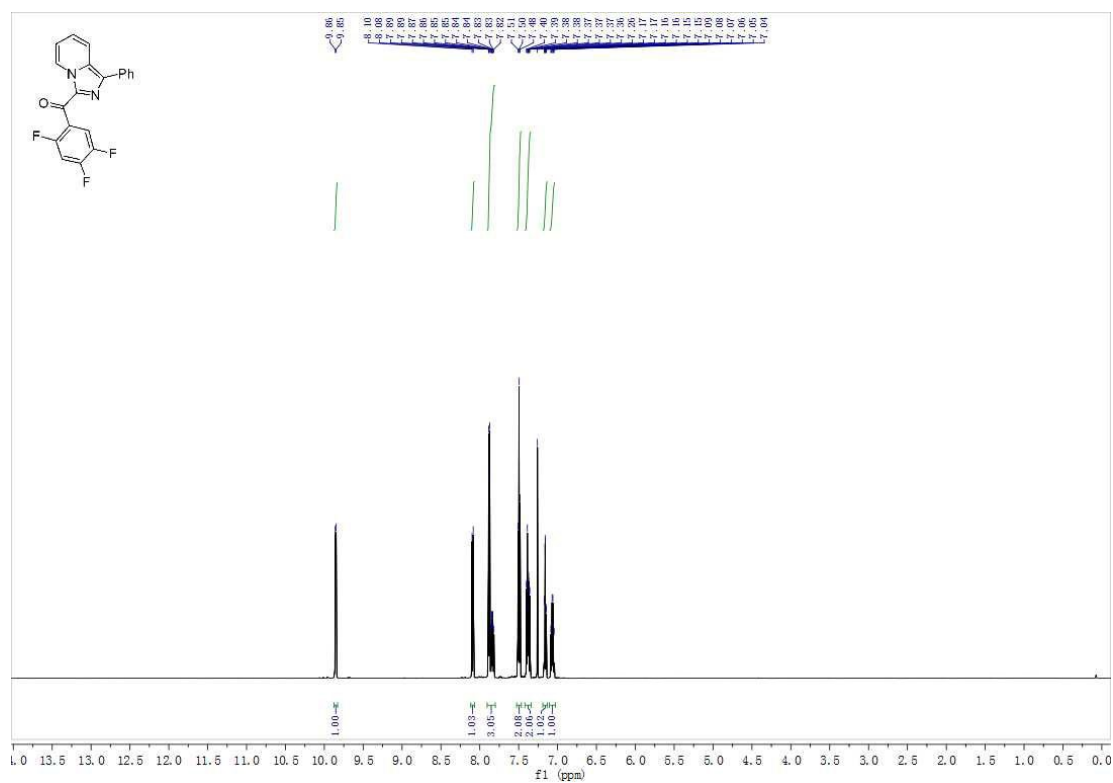
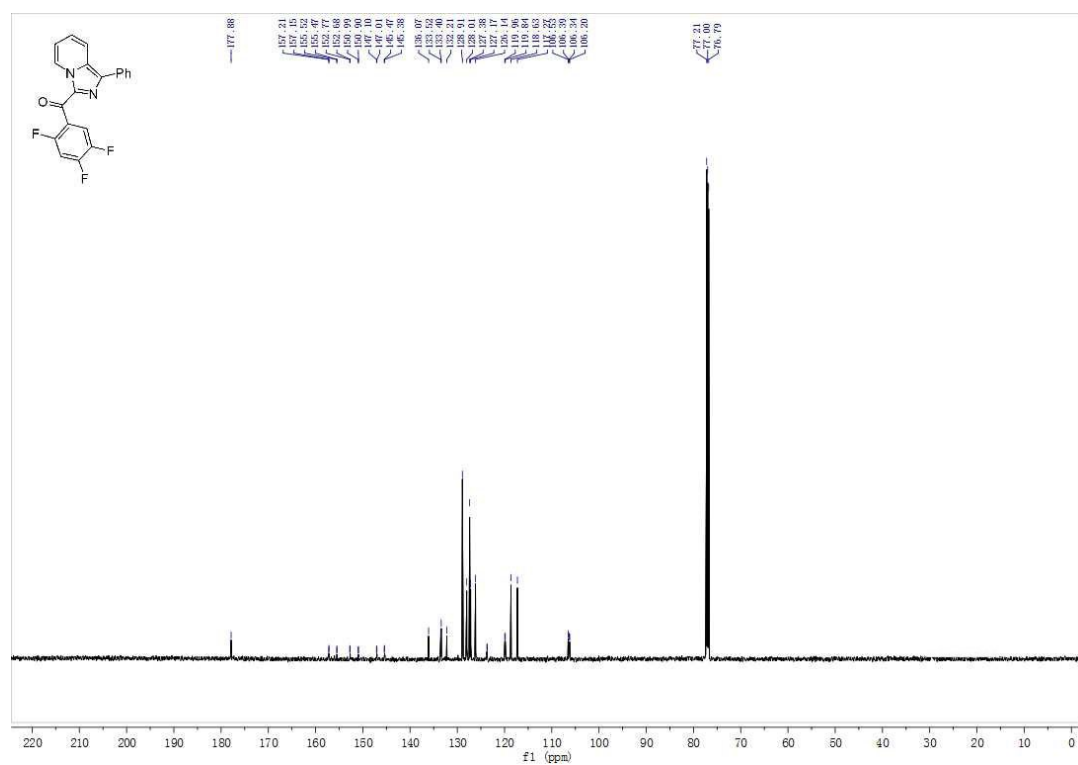
(2,6-dichlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3q**)



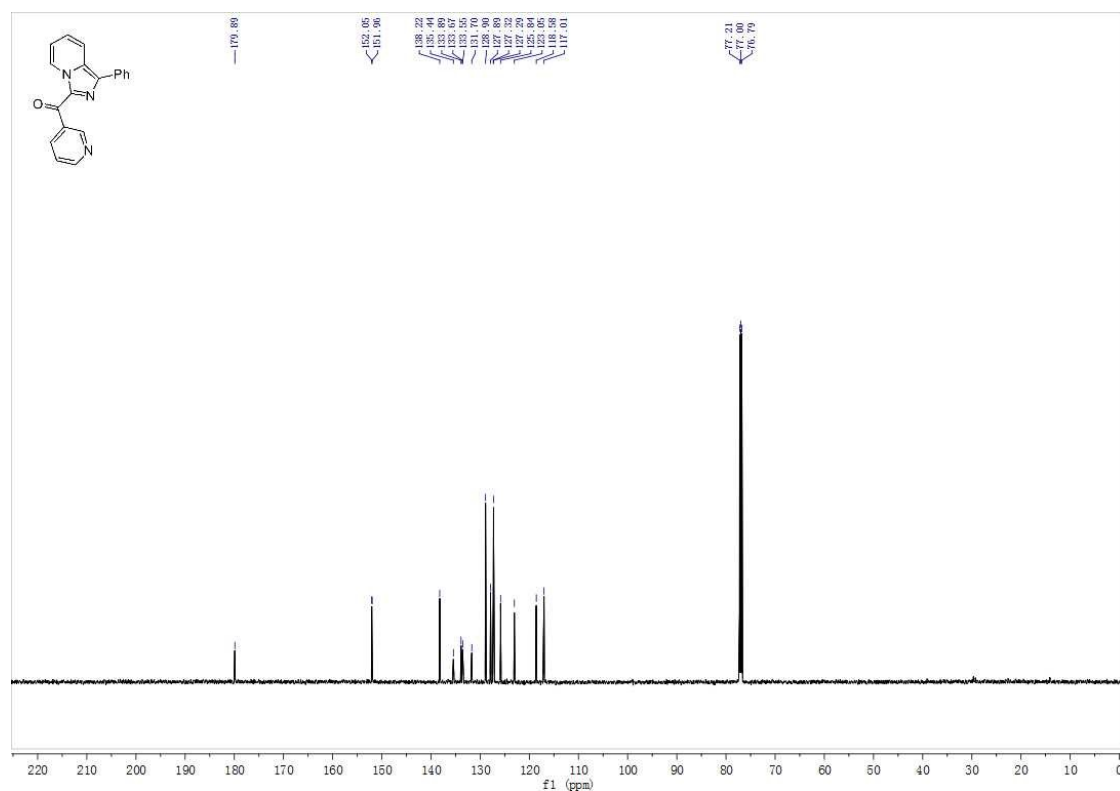
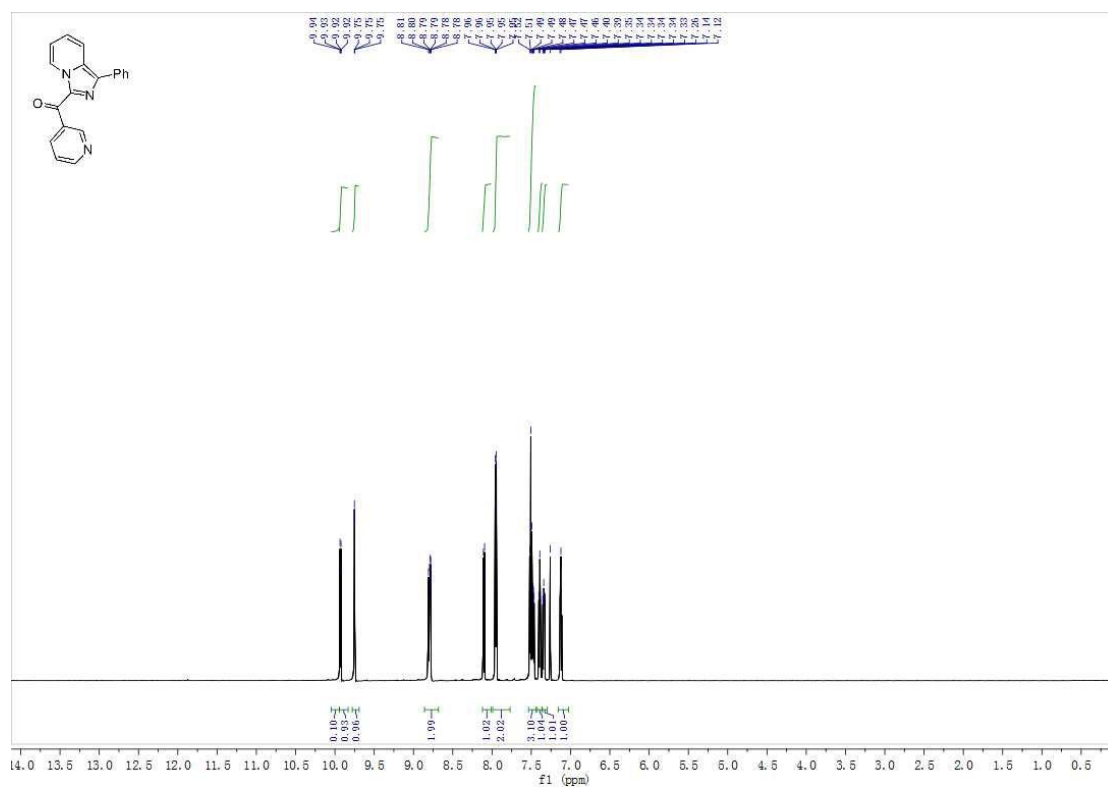
Chemical structure of 2-phenyl-2-(2,4-difluorophenyl)-1H-imidazo[1,2-a]pyridine is shown. The <sup>13</sup>C NMR spectrum (CDCl<sub>3</sub>) displays the following peak values (ppm): 179.54, 165.30, 165.09, 164.56, 160.50, 135.65, 133.86, 133.61, 133.41, 133.31, 133.31, 131.93, 129.94, 129.64, 127.84, 127.35, 127.12, 125.76, 124.06, 118.53, 116.38, 111.11, 109.81, 109.64, 109.47, 77.21, 76.85, 76.79.



(1-phenylimidazo[1,5-a]pyridin-3-yl)(2,4,5-trifluorophenyl)methanone (3s)



(1-phenylimidazo[1,5-a]pyridin-3-yl)(pyridin-3-yl)methanone (**3t**)



## 2. Procedure of detection of crucial intermediates by LC-MS

### Sample preparation

To a solution of ethyl 3-oxo-3-phenylpropanoate (0.2 mmol, 1 equiv.), phenyl(pyridin-2-yl)methanamine (0.25 mmol, 1.25 equiv.) in 2mL of DMSO in a tube was added I<sub>2</sub> (0.6 mmol, 3equiv.) and H<sub>2</sub>O (0.6 mmol), and the tube was heated at 75°C and for 2 hours with oil bath. The system was cooled to room temperature, water (10 mL) was added and the aqueous solution was extracted with ethyl acetate (3 x 30 mL), the combined organic phase was washed with saturated brine and concentrated under reduced pressure, the residue was dissolved by MeOH and tested by LC-MS (Instrument: Waters HClass).

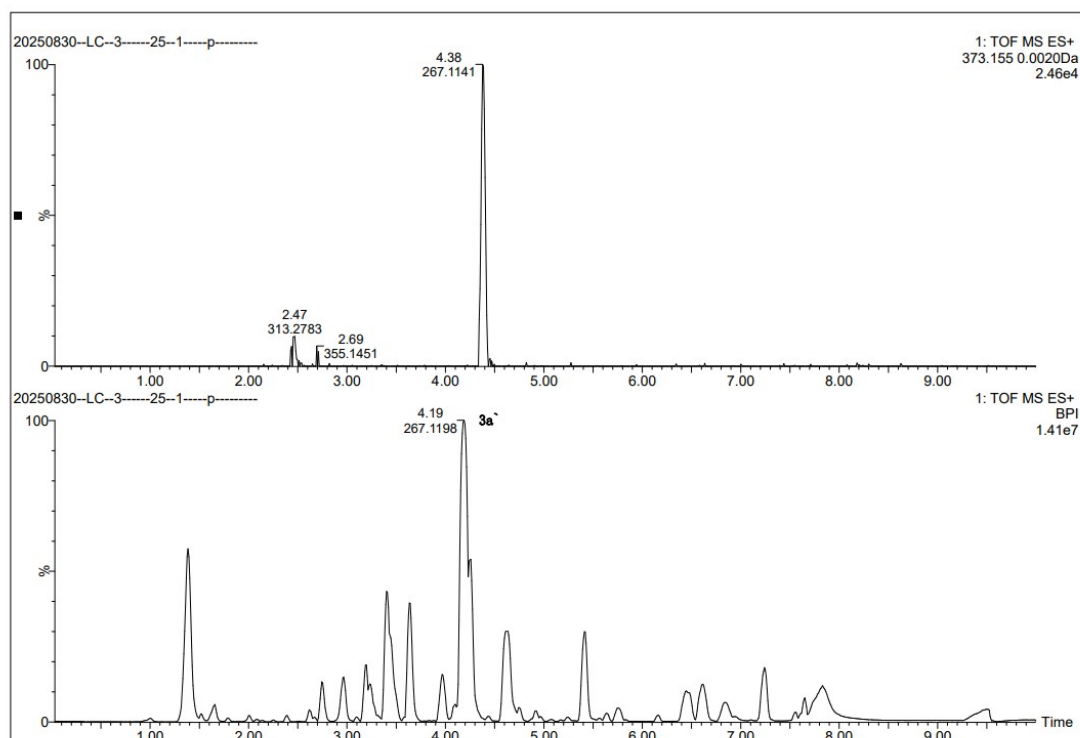
LC-MS detecting condition: Mobile phase A: 0.1% formic acid in H<sub>2</sub>O; B: 0.1% formate in acetonitrile.

Chromatographic column: waters BEH C18 1.7um 2.1\*50mm. Column temperature: 40°C.

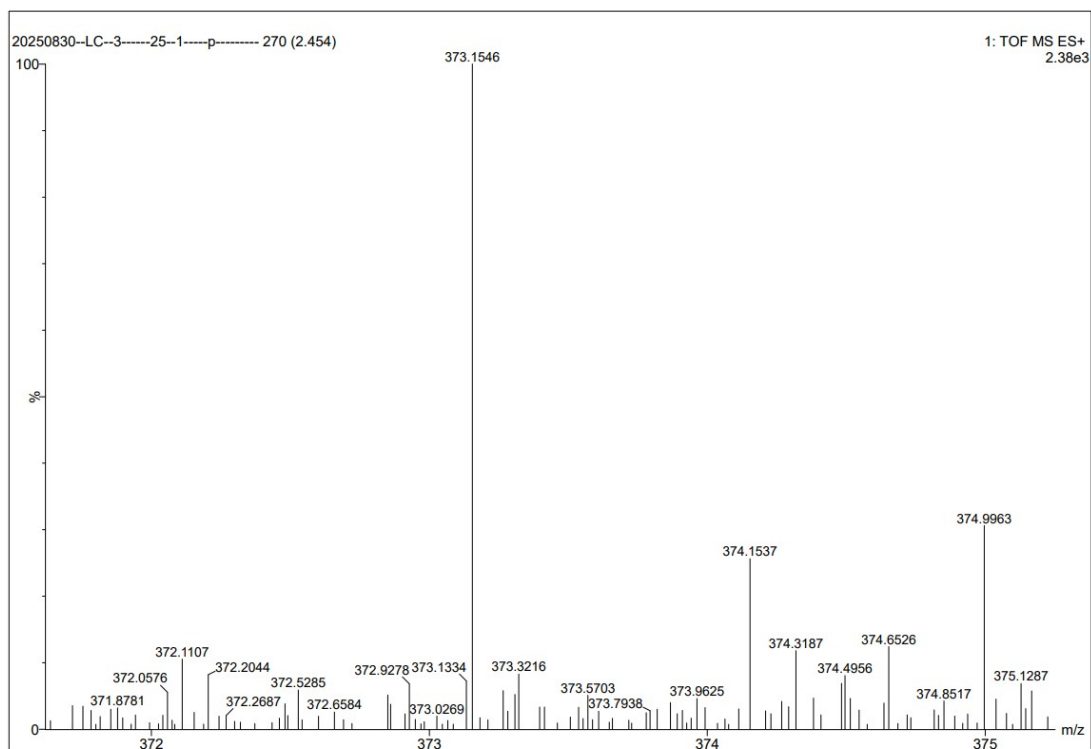
Time (min)	Flow rate (mL/min)	A(%)	B(%)
0	0.4	95	5
1	0.4	95	5
7	0.4	2	98
10	0.4	2	98

### Results and explanations

**II** and **III** are isomeride, target molecular ion peak appeared twice at two different retention time would be reasonable. **II** and **III** were indeed detected at retention time of 2.47 and 4.38.  $m/z$   $[M+H]^+$  calcd for C<sub>23</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub> (**II** and **III**), 373.1552, found 373.1546 and 373.1548. This evidence can only to some extent explain the rationality of mechanism, for the isomerides of **II** and **III** are uncertain.



(1) Retention time of 2.47, m/z found 373.1546



(2) Retention time of 4.38, m/z found 373.1548

