Controllable Site-selective C-C Bond Cleavage for the Divergent Synthesis of Imidazo[1,5-a]pyridine Derivatives

Qiang Wang*, Xinyu Song, Shujun Qin, Wenya Dong, Pingjing Xue, Jiayi Wu, and Haibo Wang

College of biomedical and Health Sciences, Anhui Science and Technology University, Fengyang 233100, PR China.

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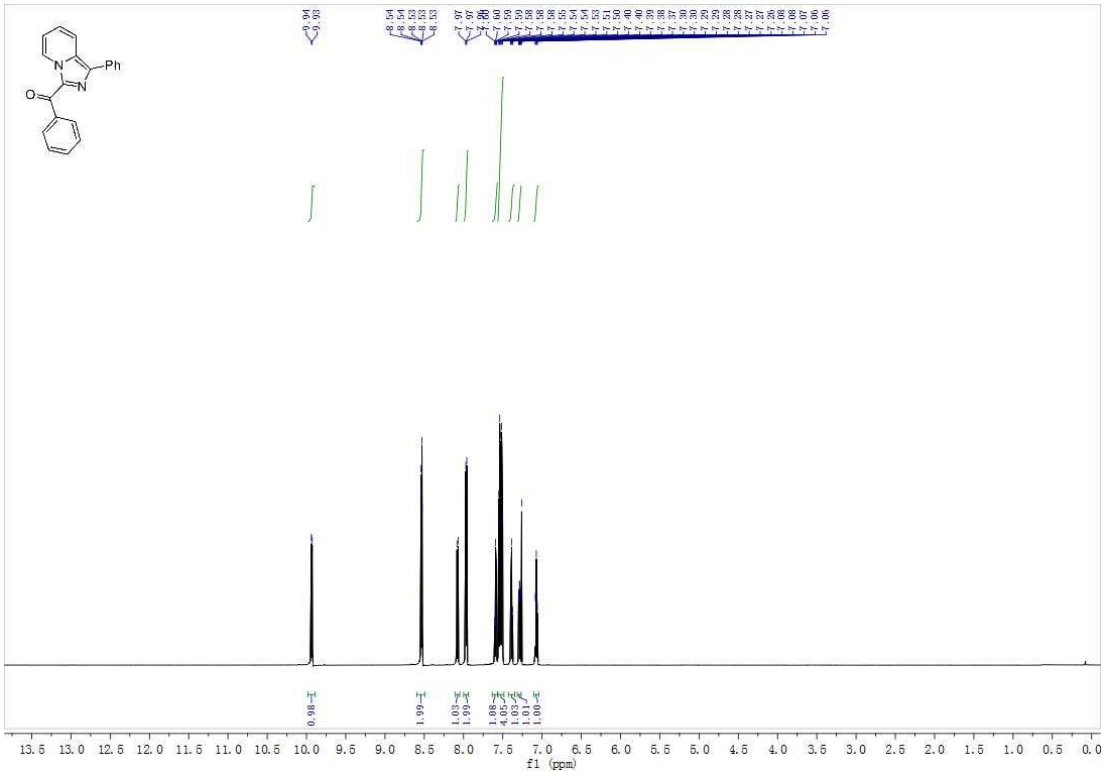
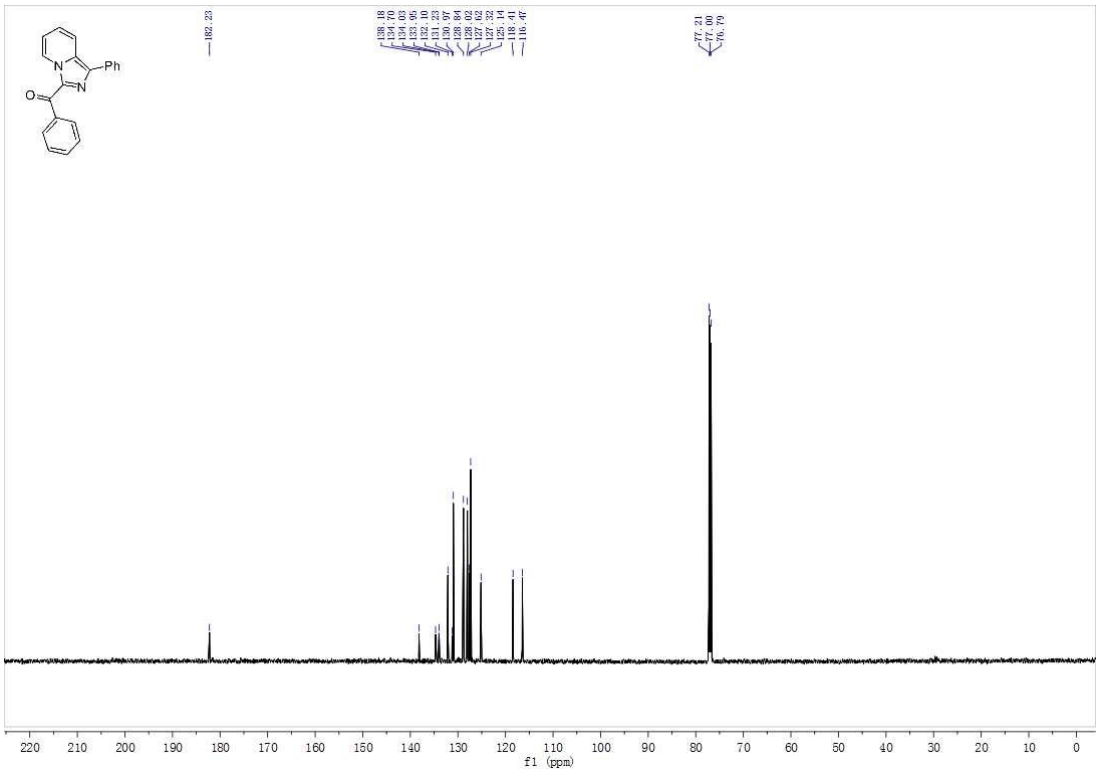
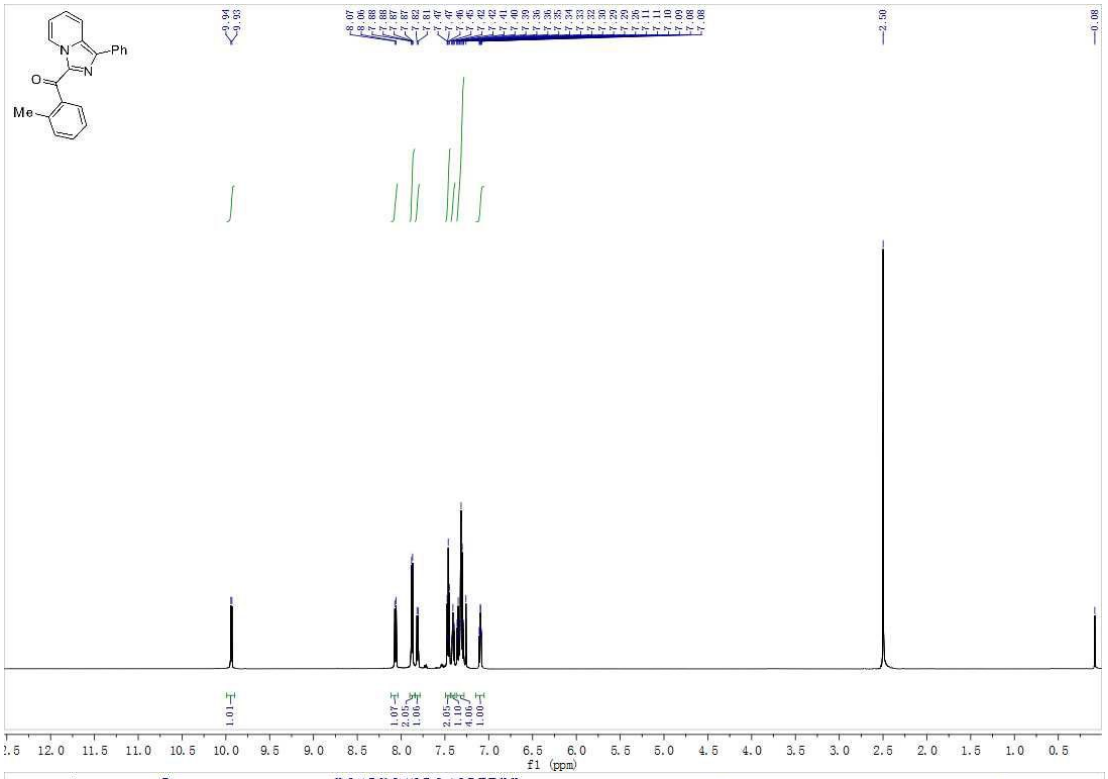
1. ^{1}H NMR and ^{13}C NMR spectrogram

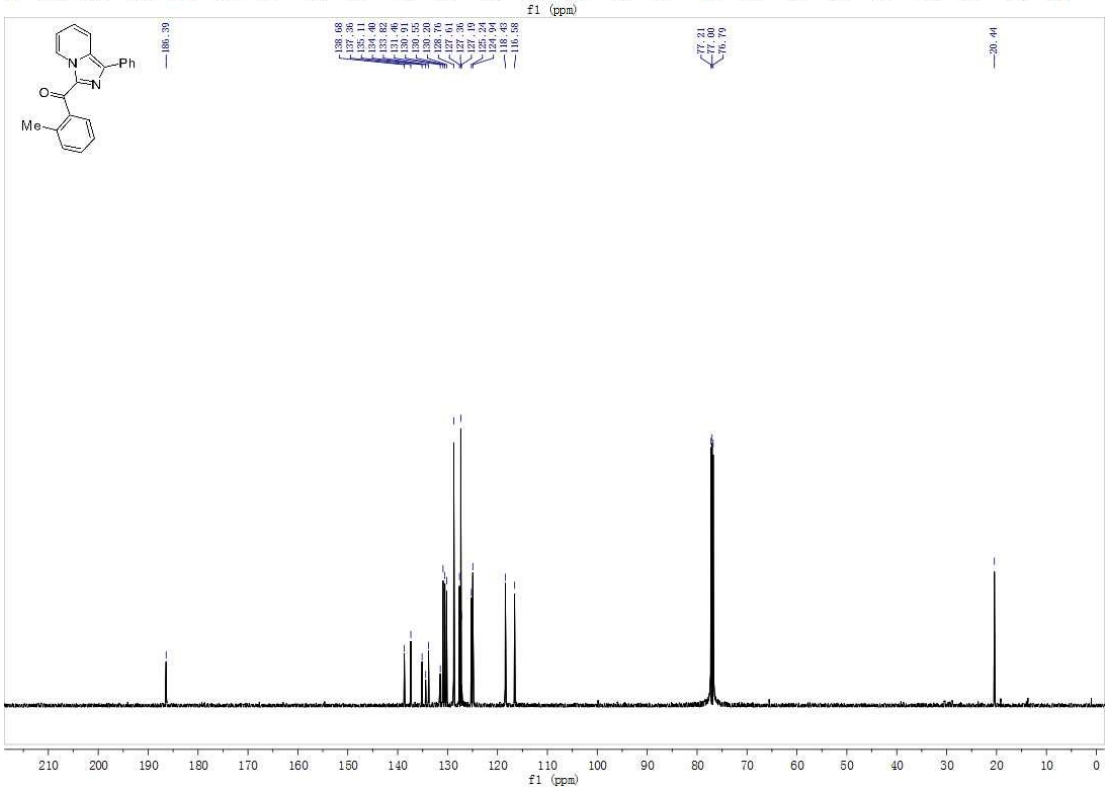
phenyl(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone ***(3a)***





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





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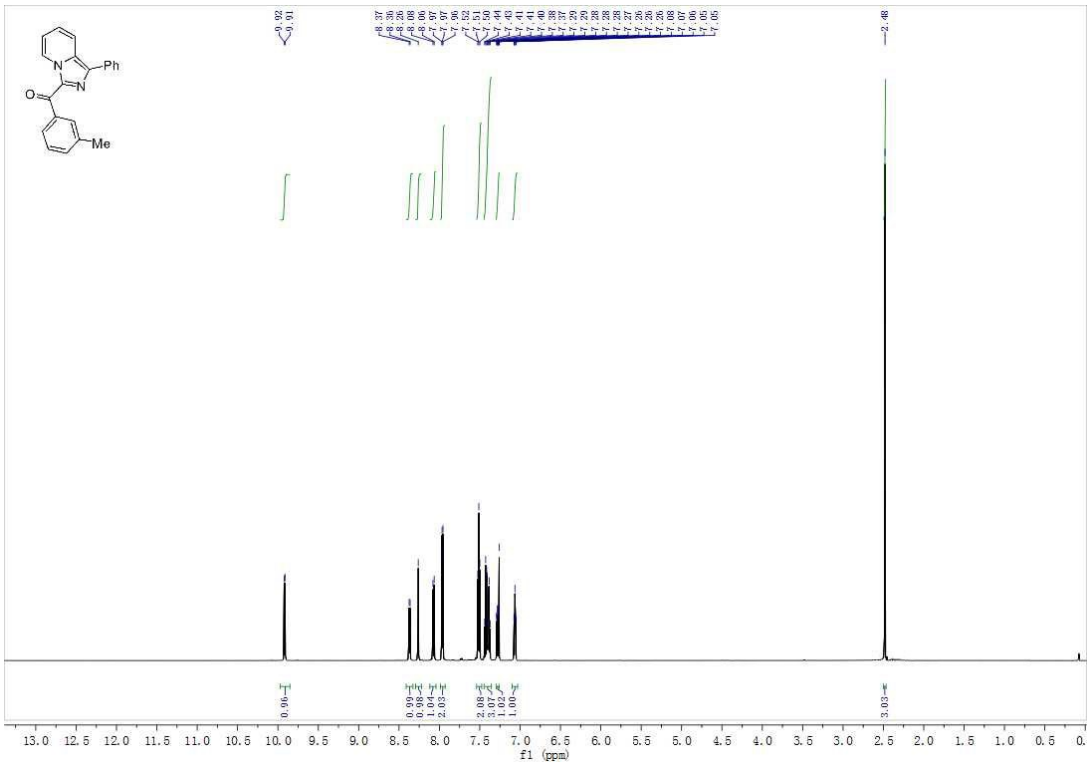

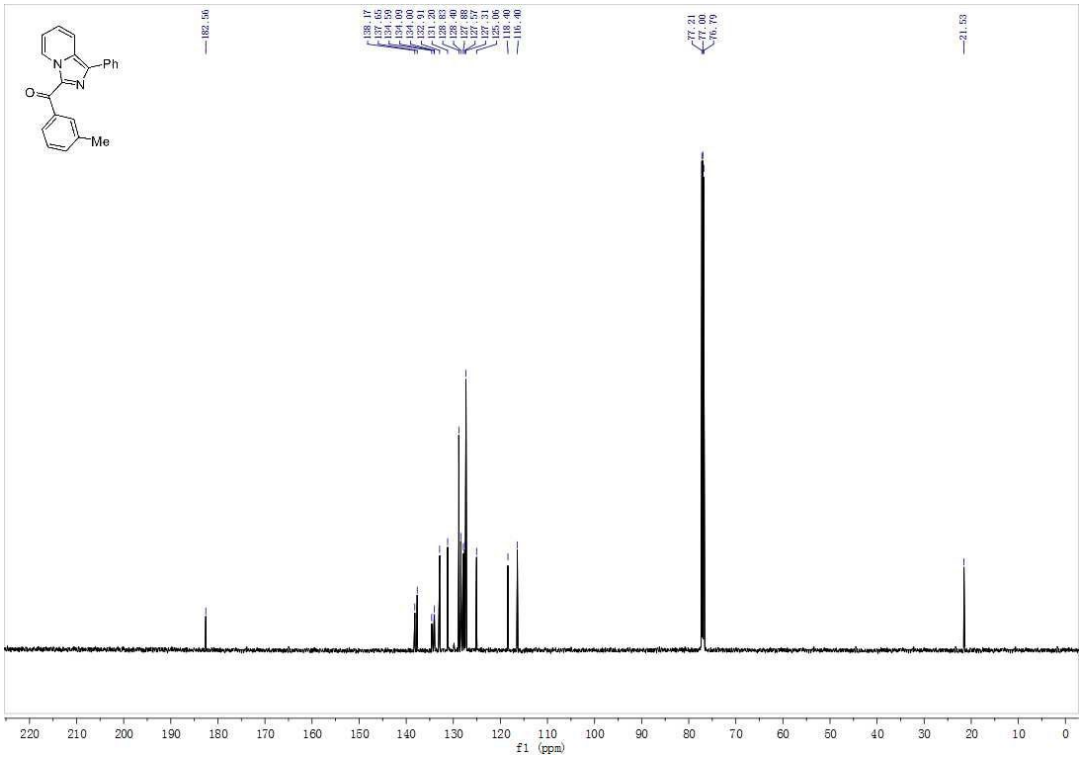

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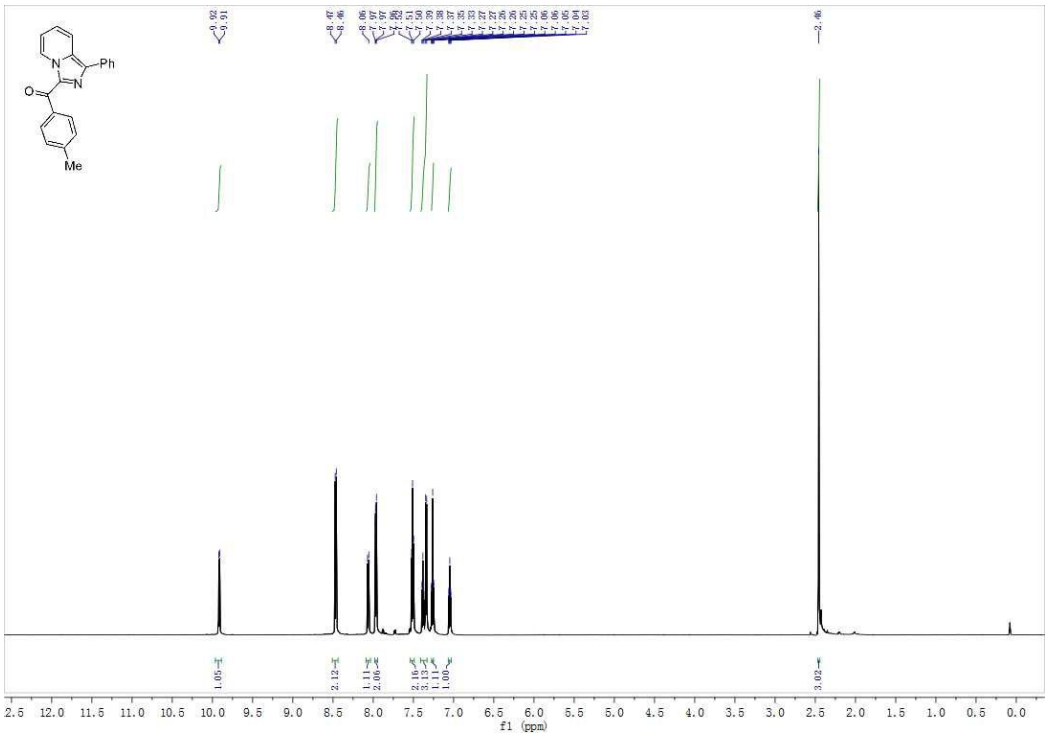

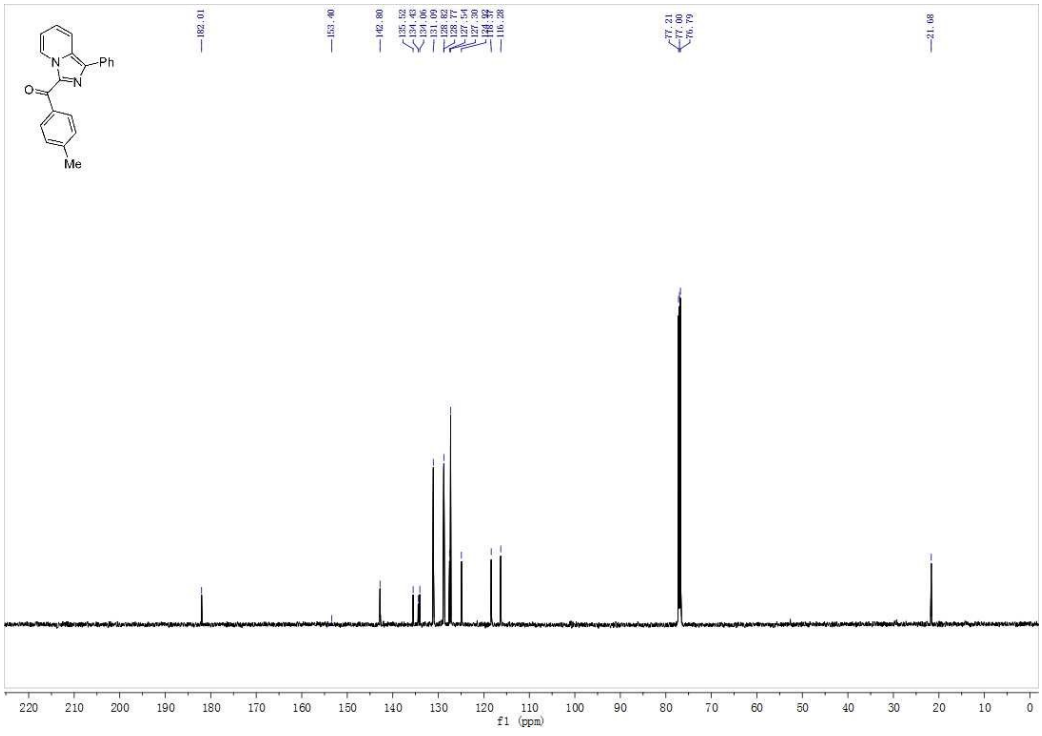

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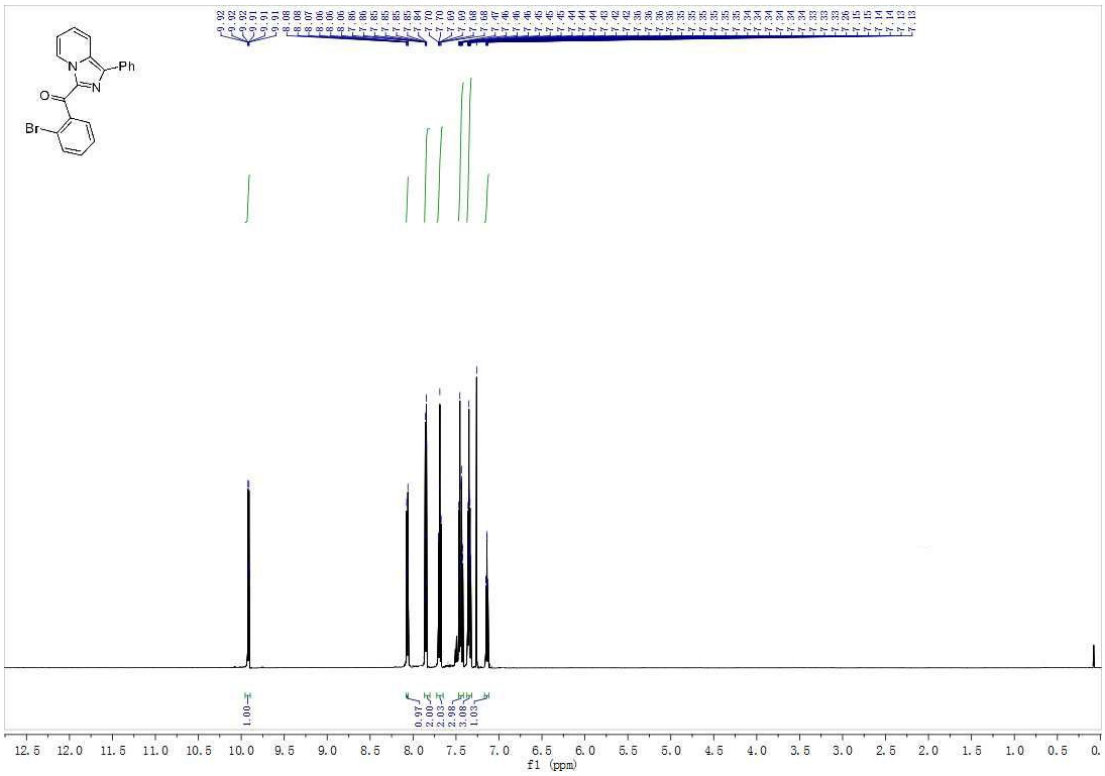
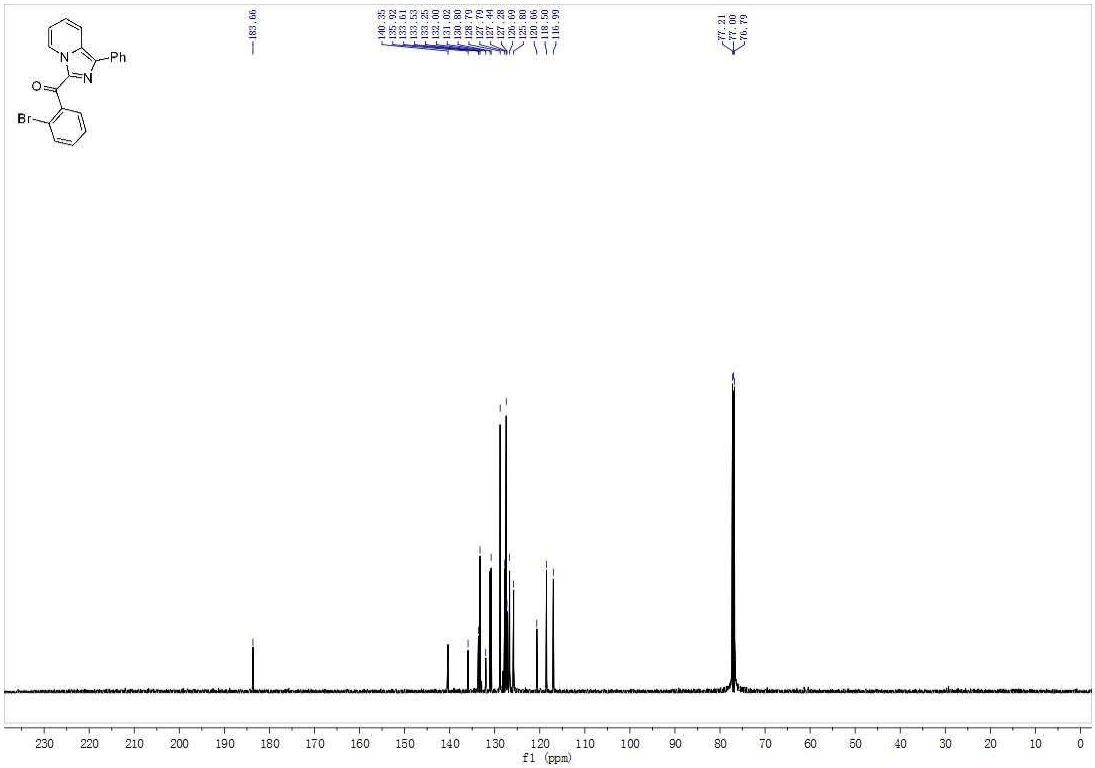
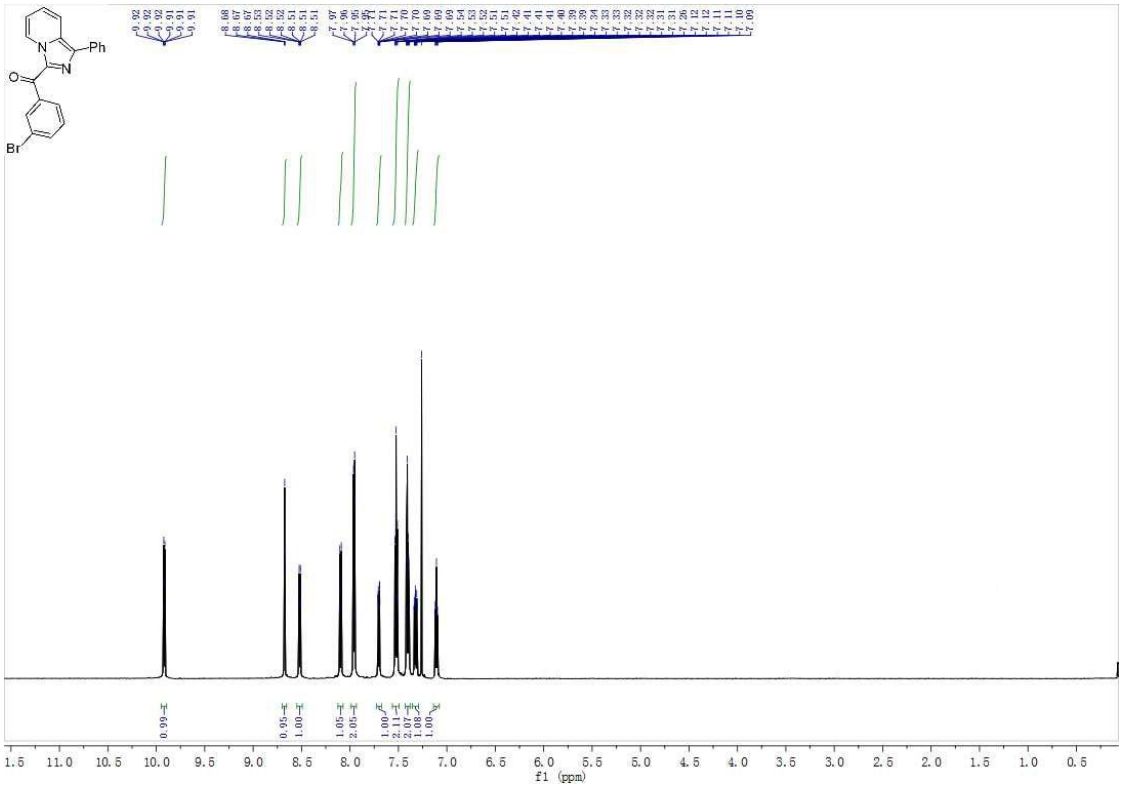
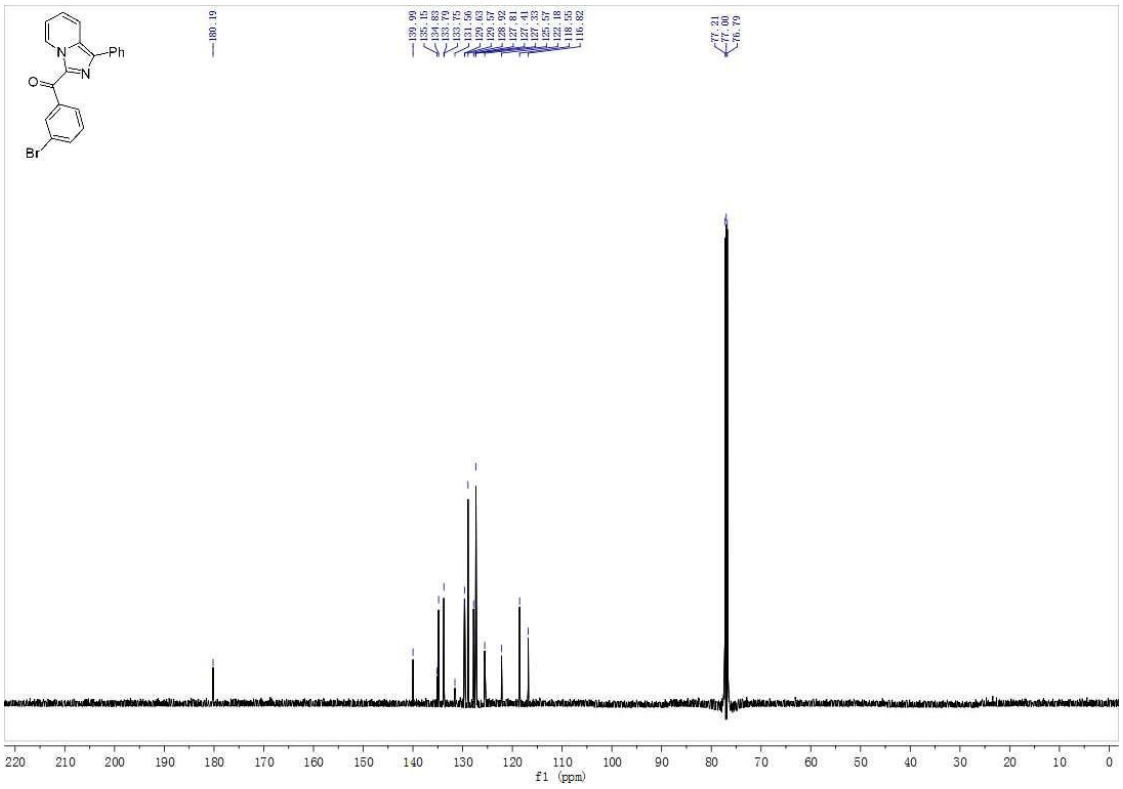




*(3- bromophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3f**)*





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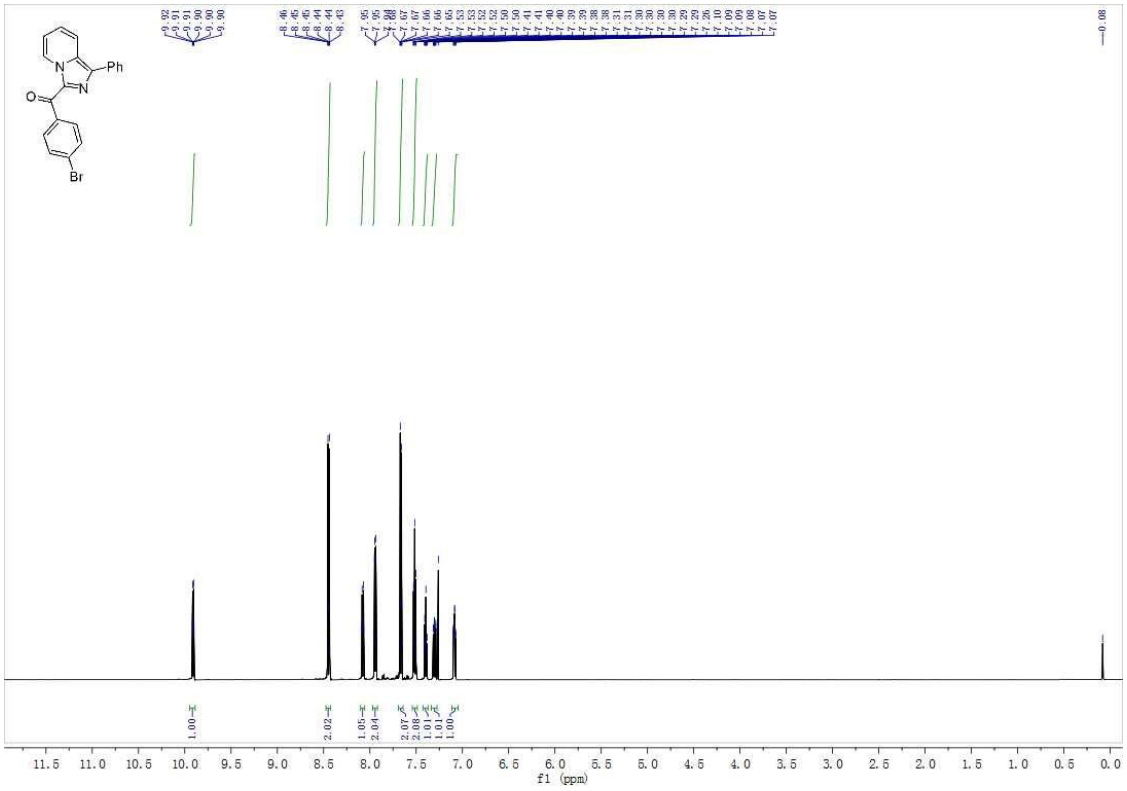
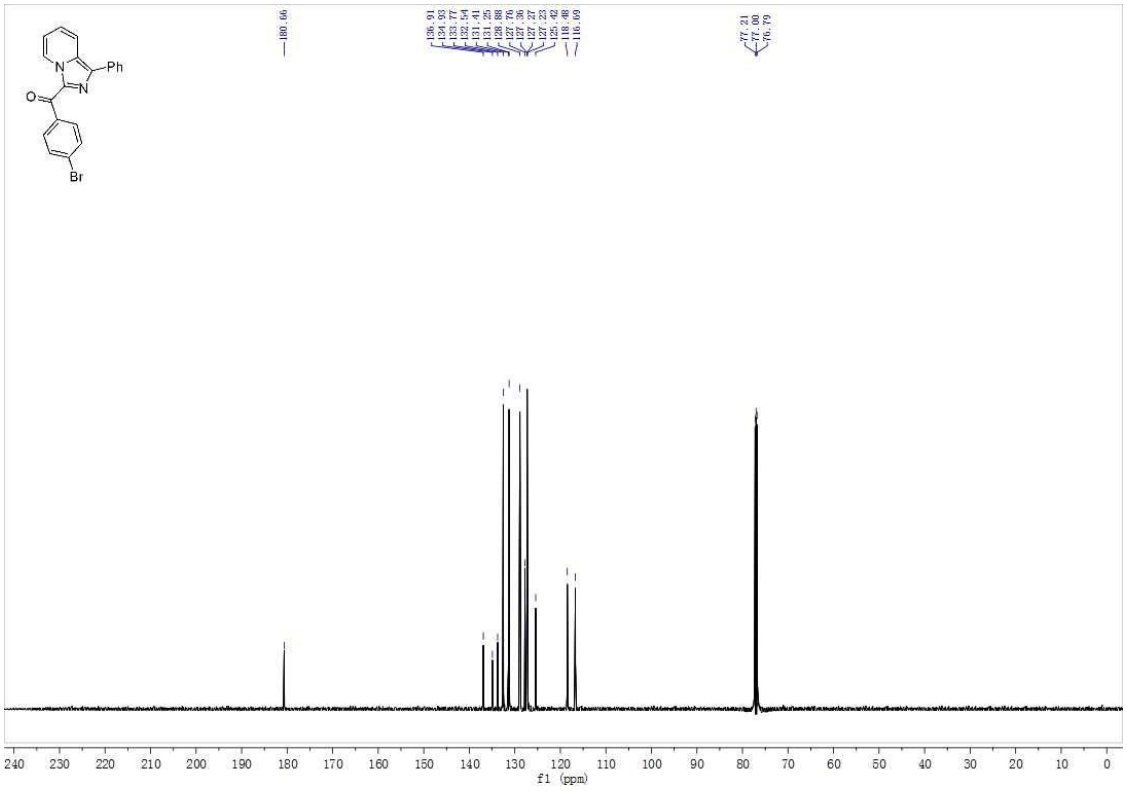
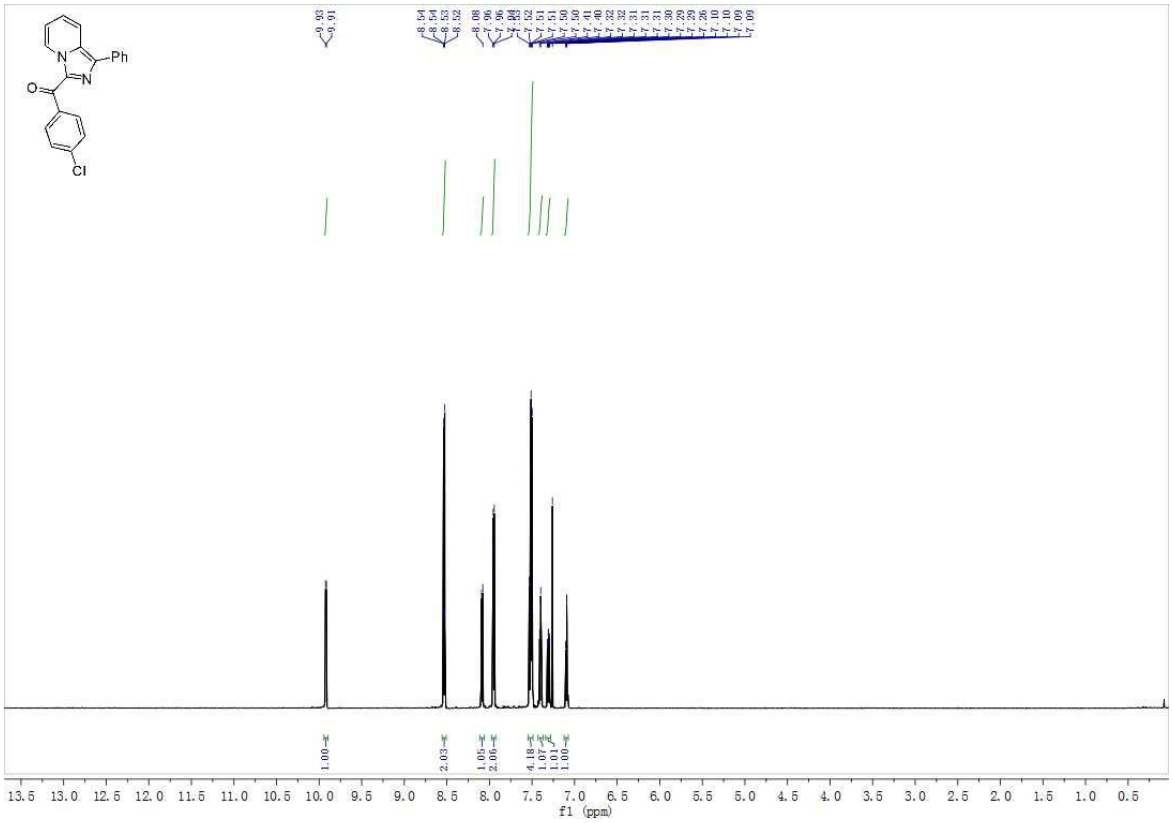
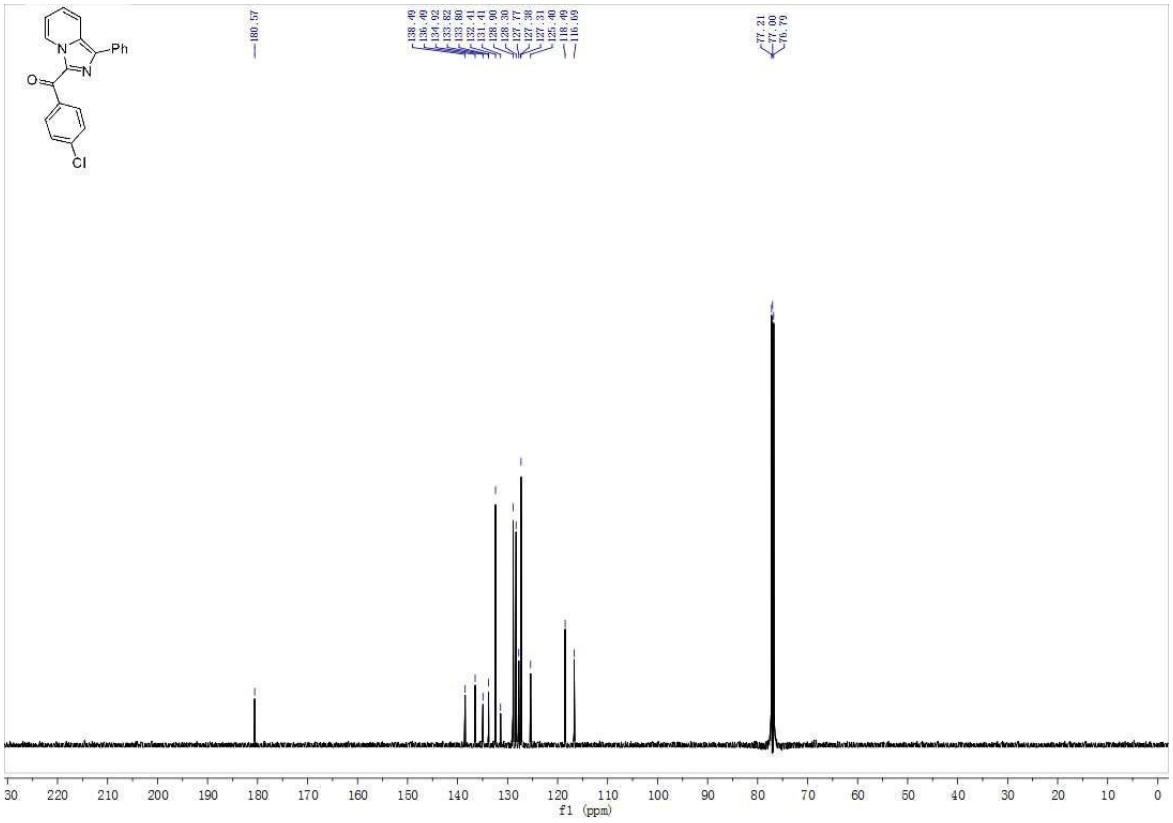


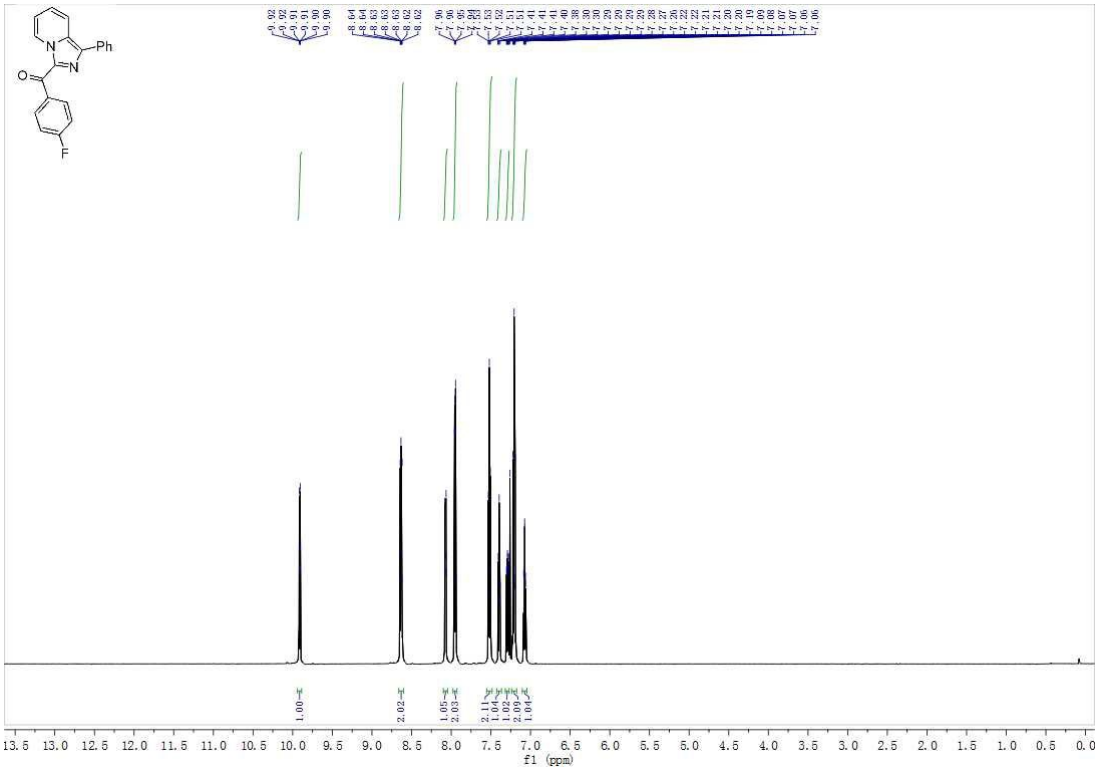


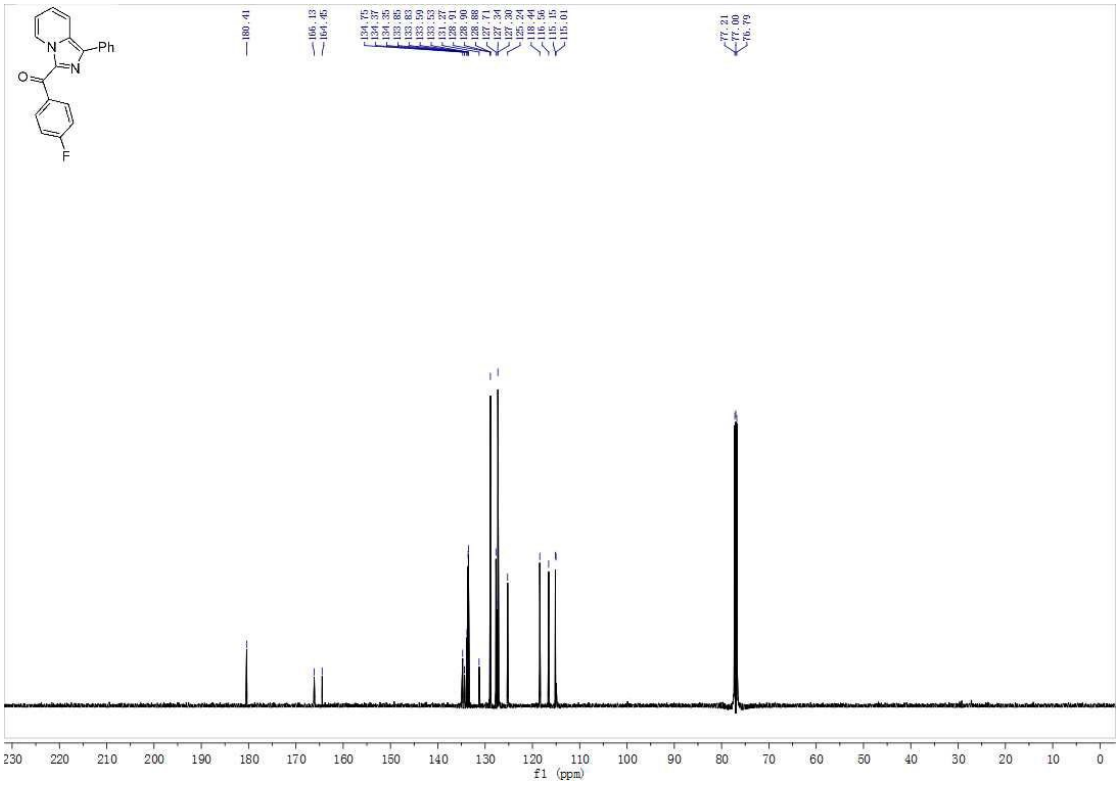
*(4-chlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3h**)*





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





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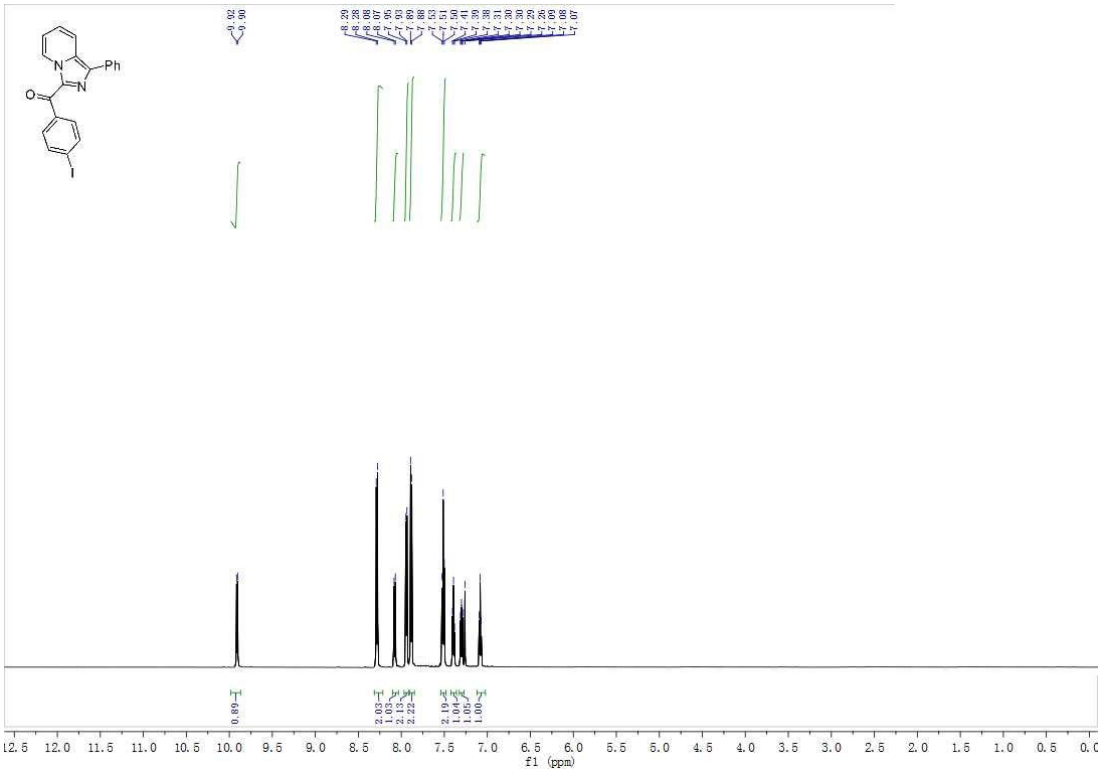
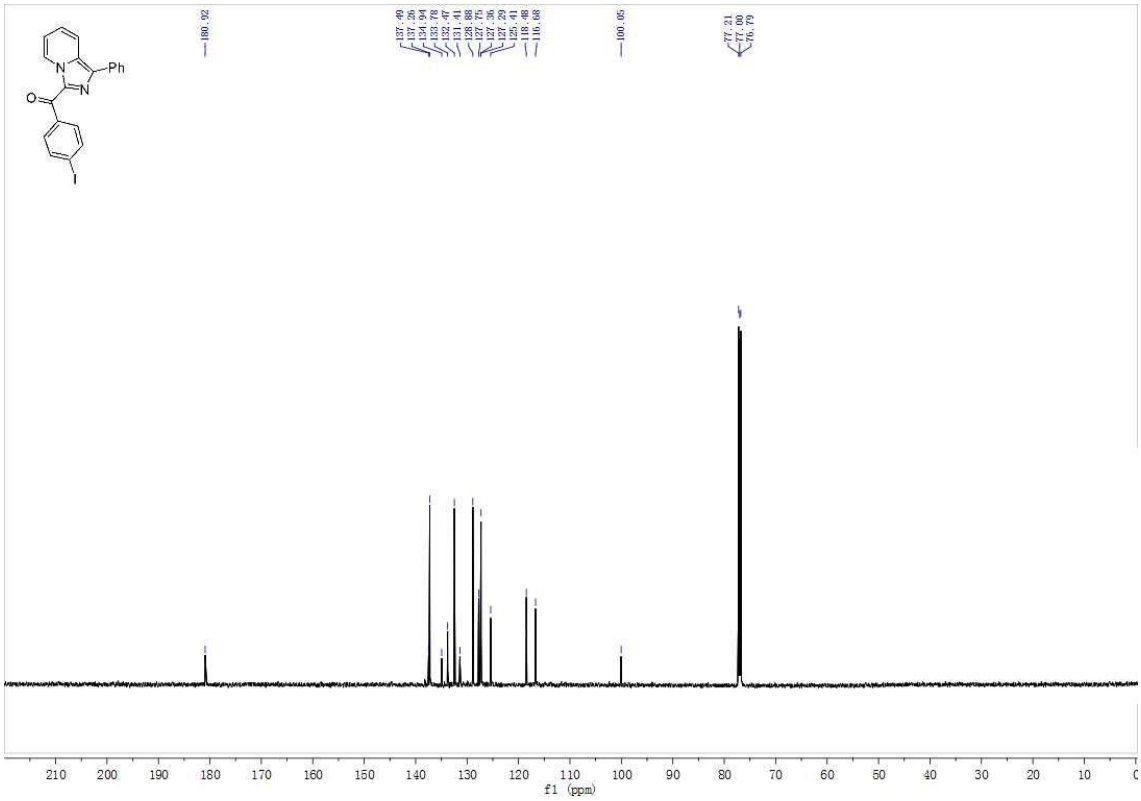
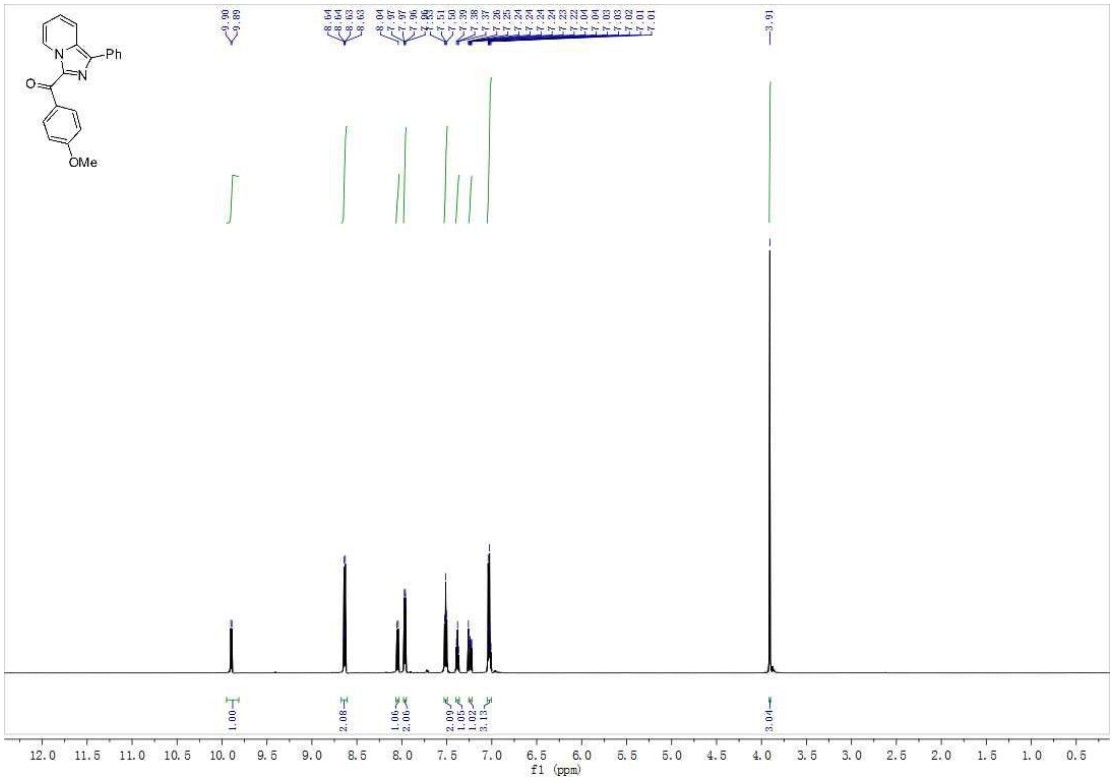
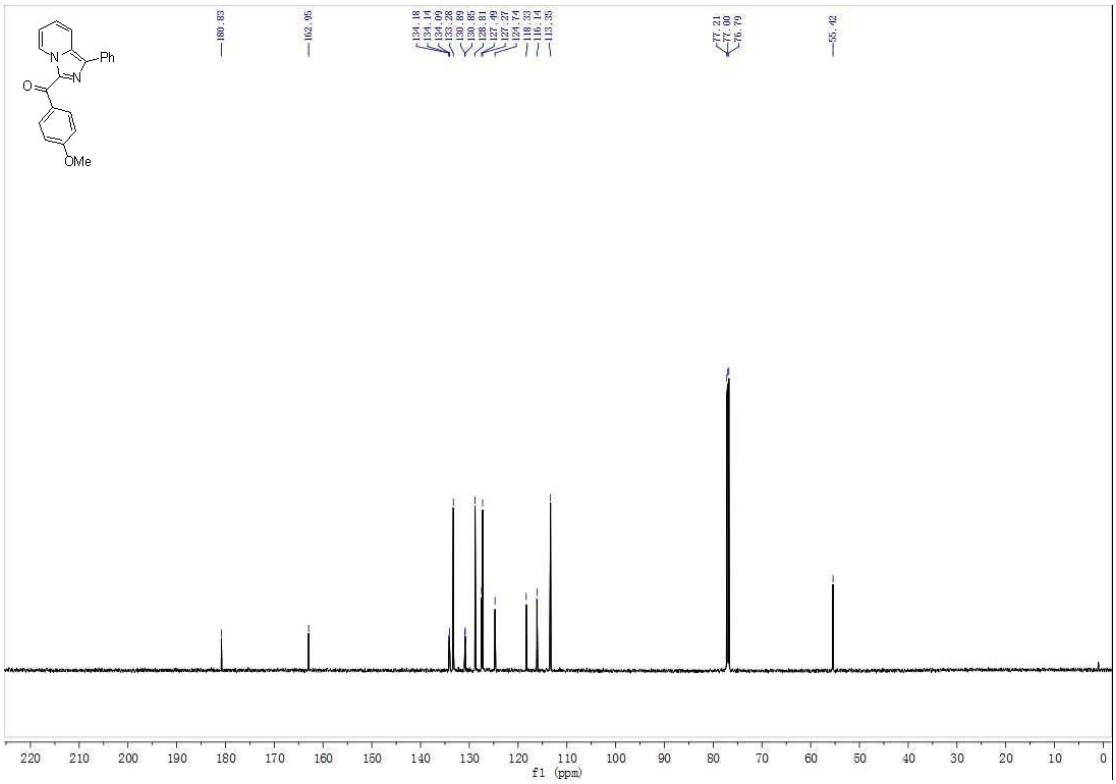
*(4-iodophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3j**)*



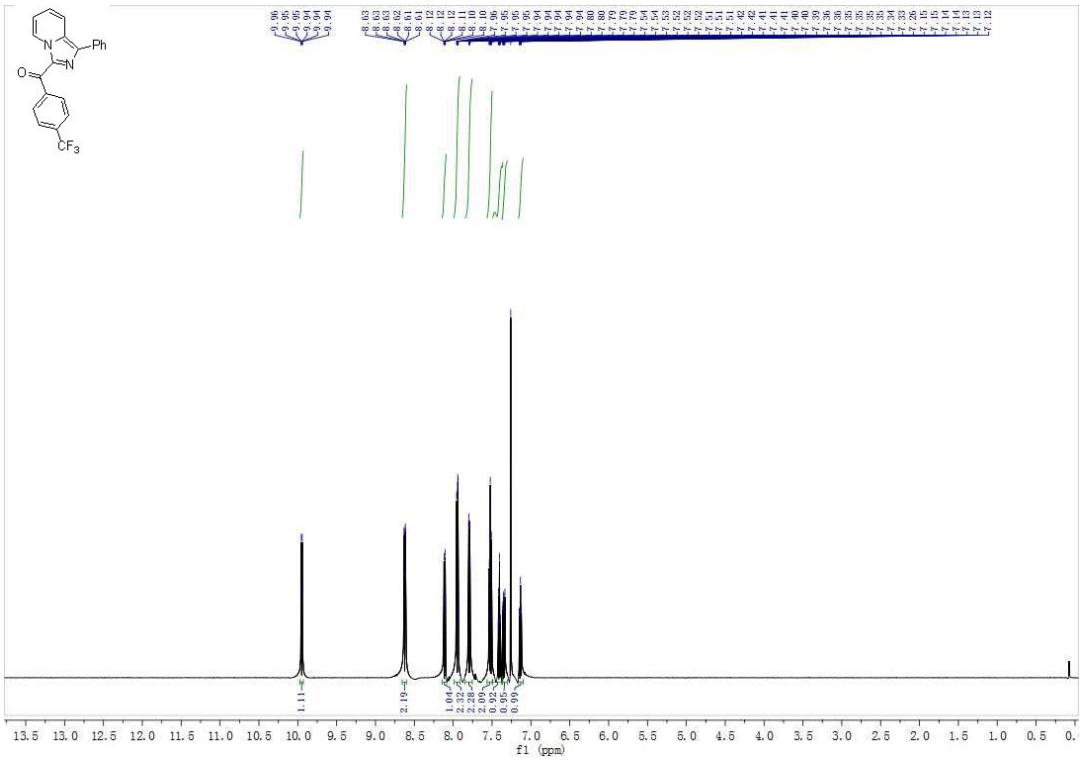


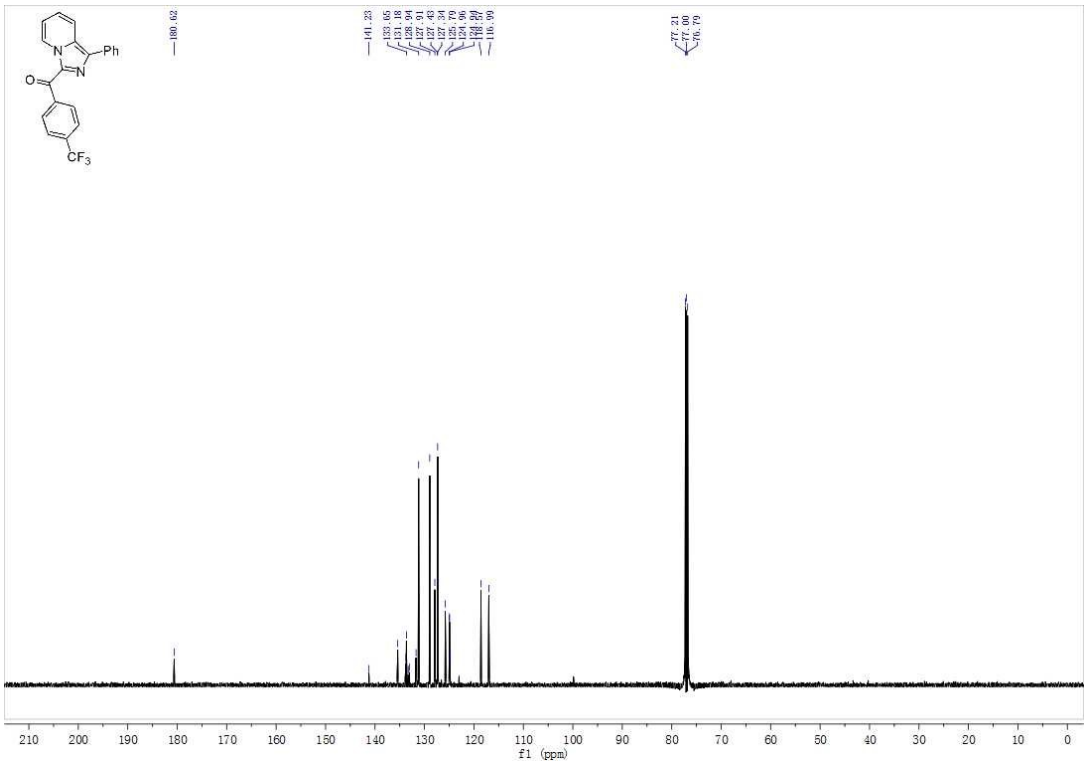
(4-methoxyphenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone ***(3k)***



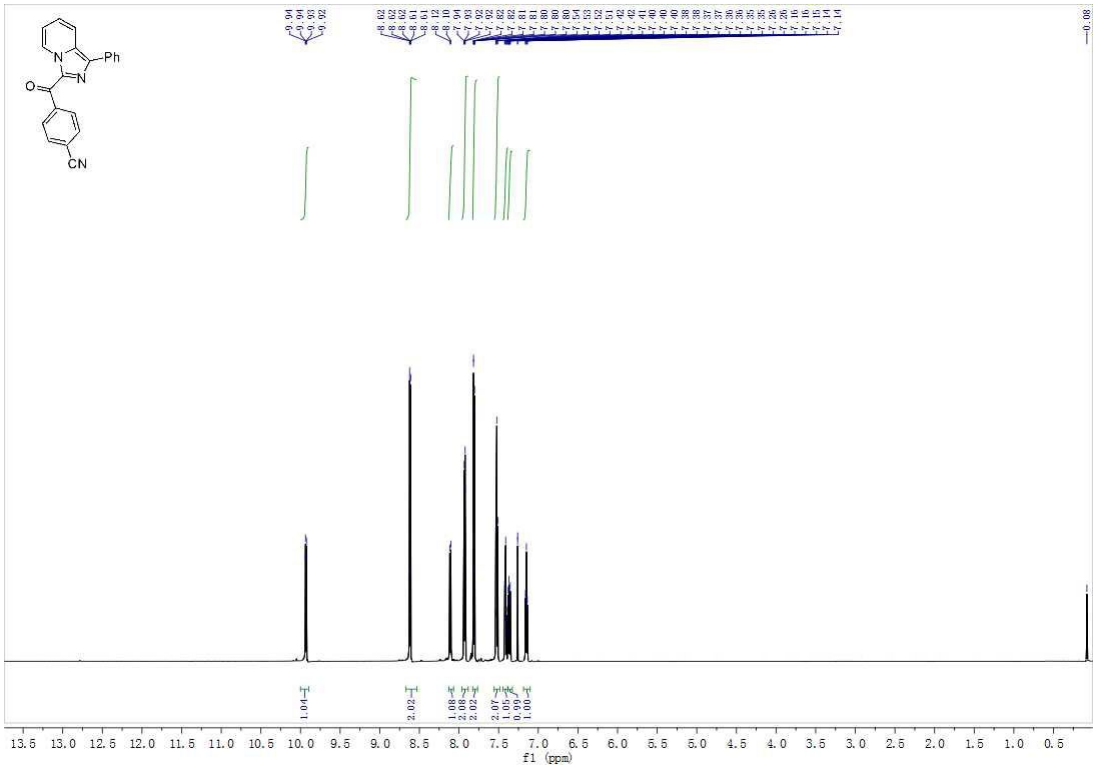


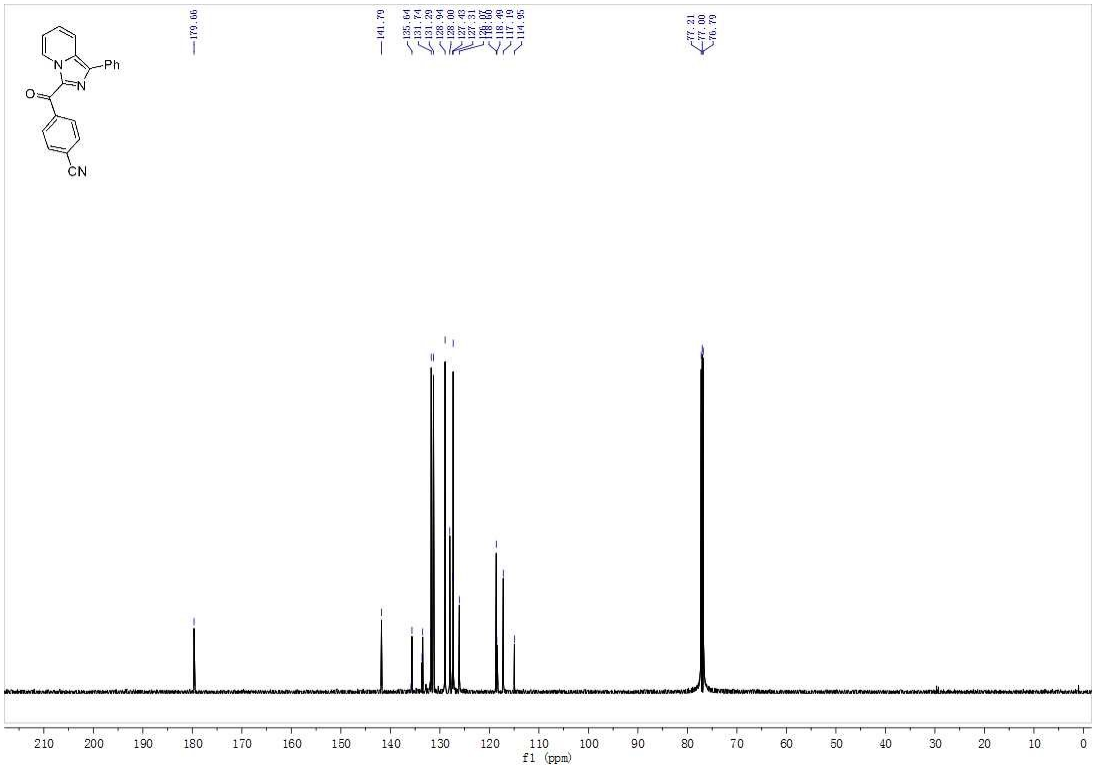
*(1-phenylimidazo[1,5-a]pyridin-3-yl)(4-(trifluorome-thyl)phenyl)methanone (**3l**)*



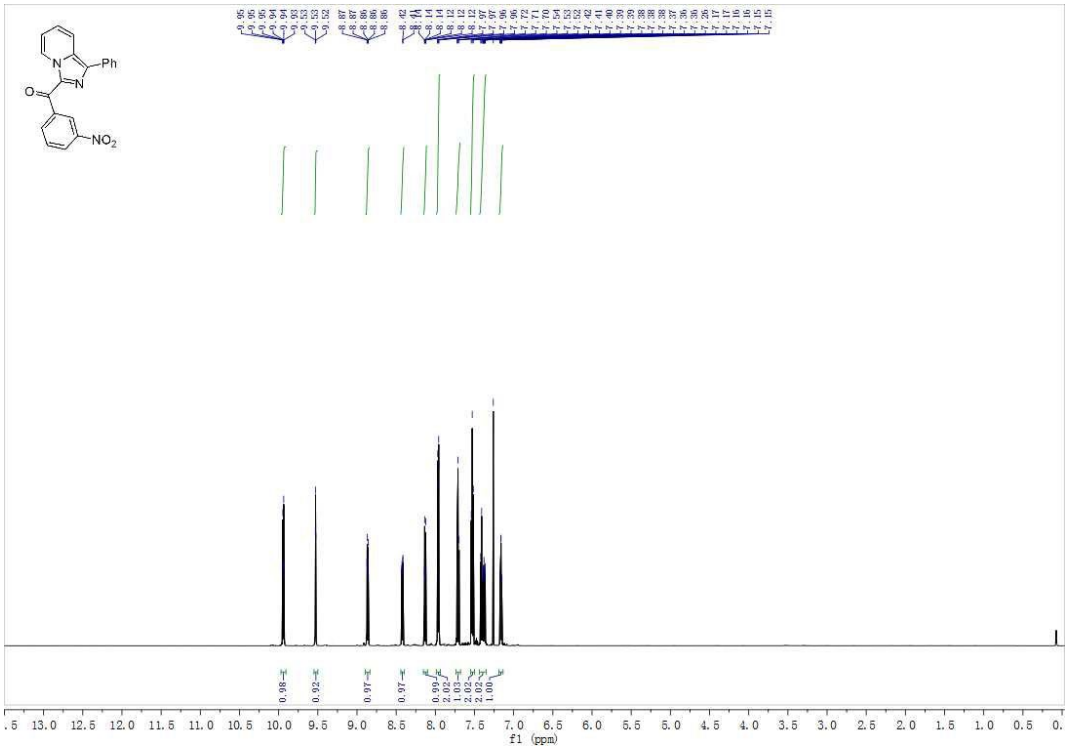


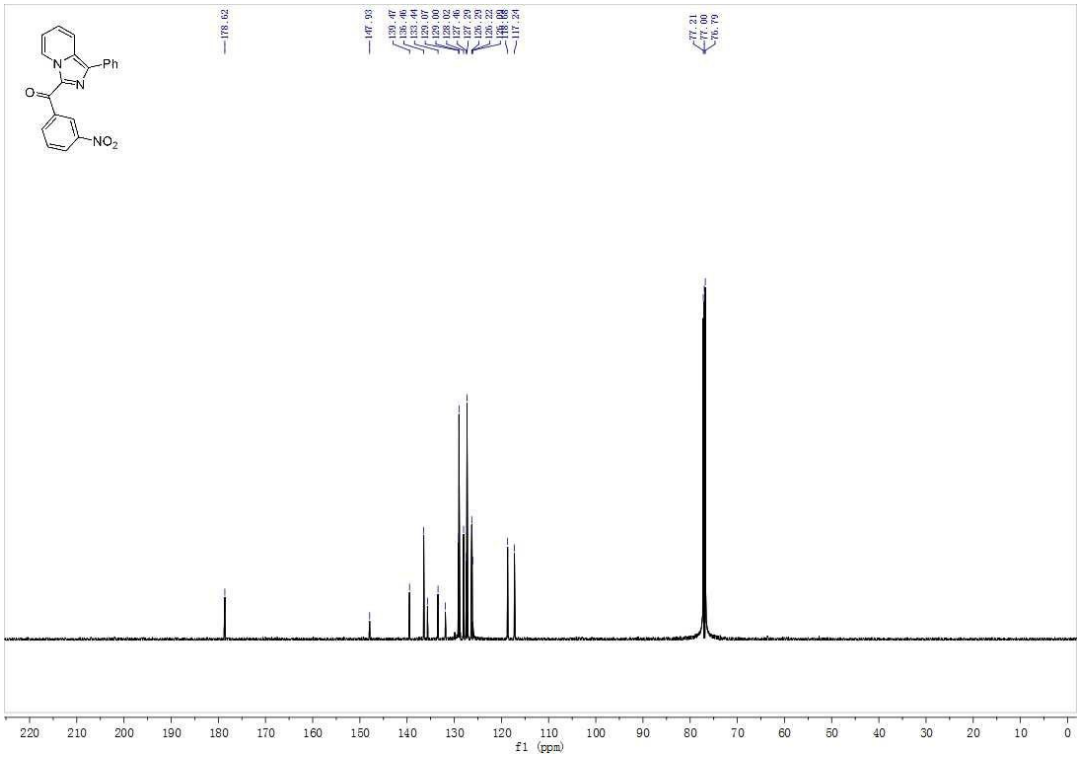
*4-(1-phenylimidazo[1,5-a]pyridine-3-carbonyl)benzonitrile (**3m**)*



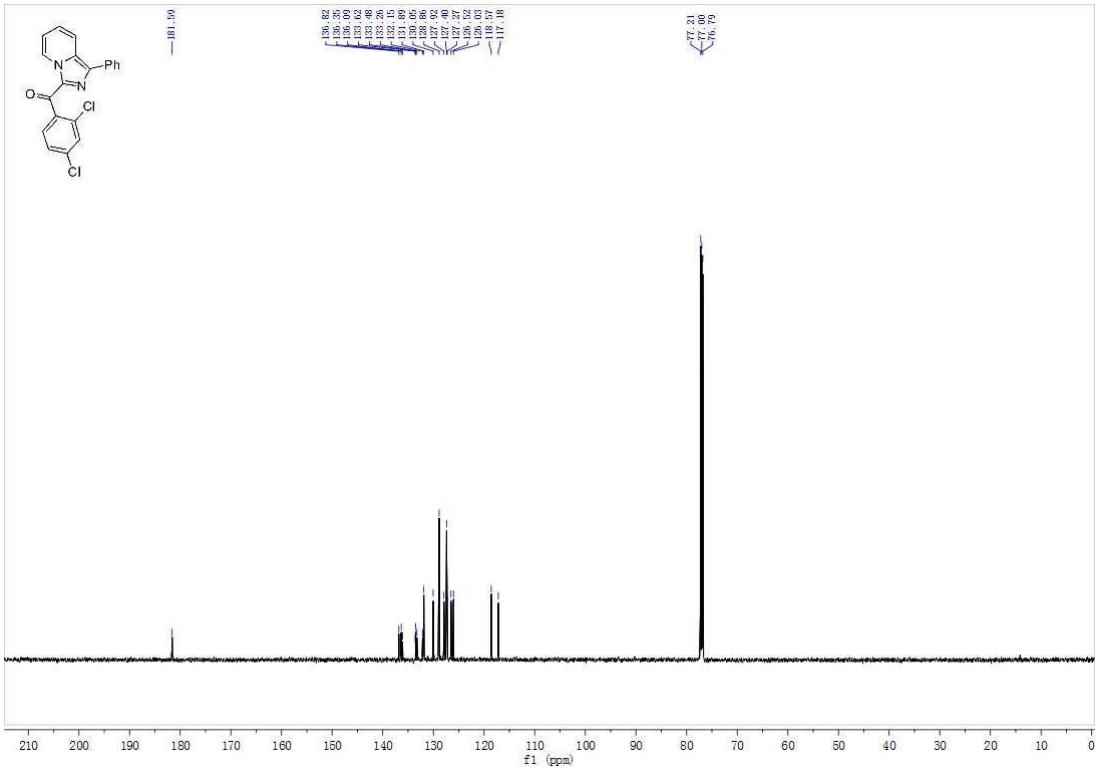


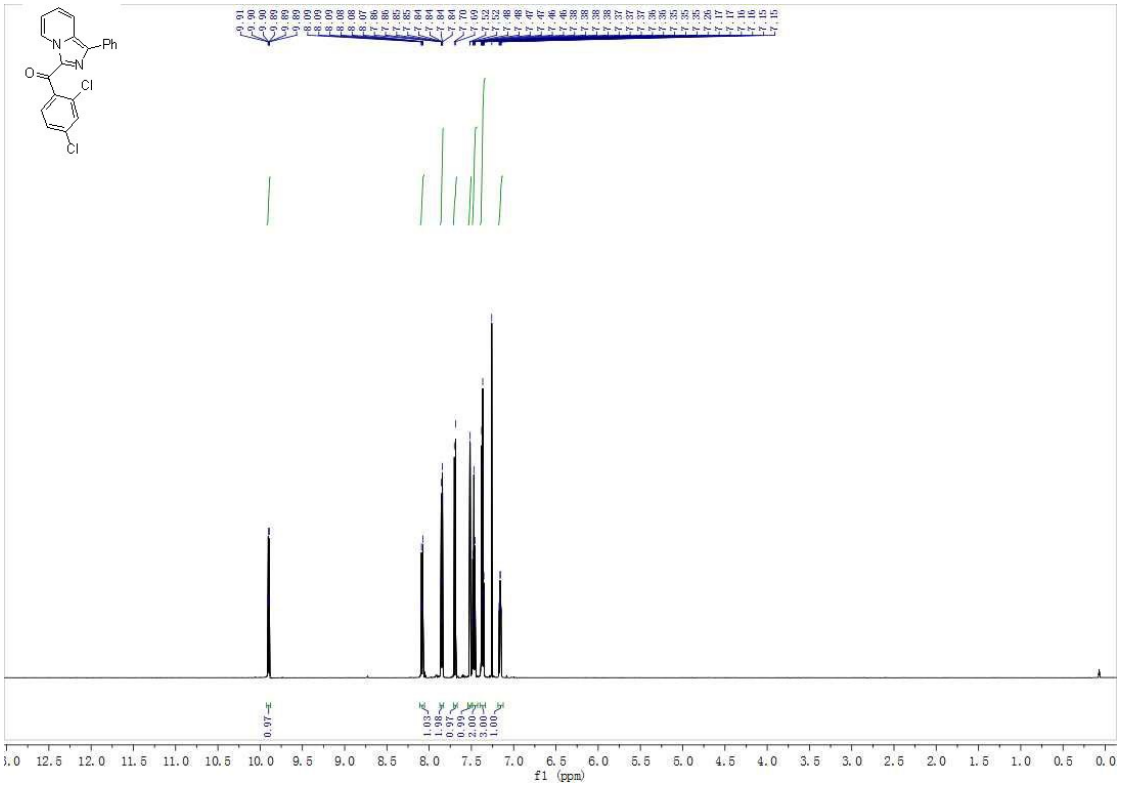
*(3-nitrophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3n**)*



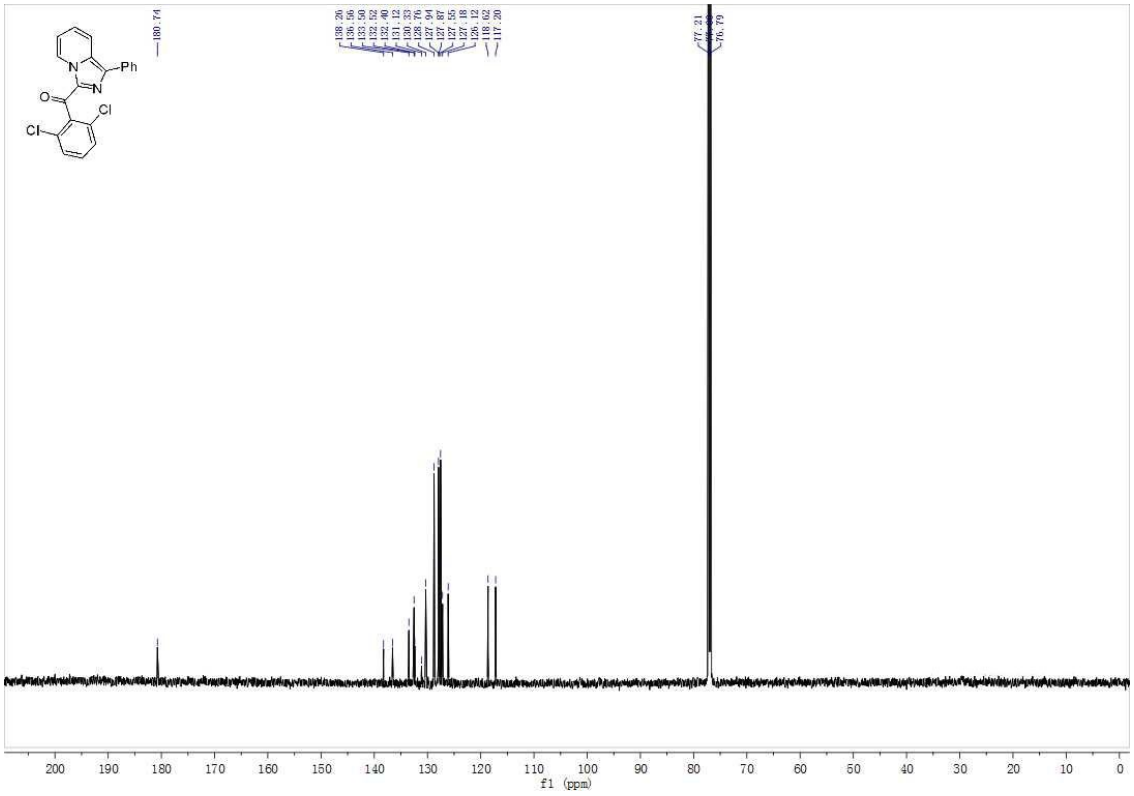


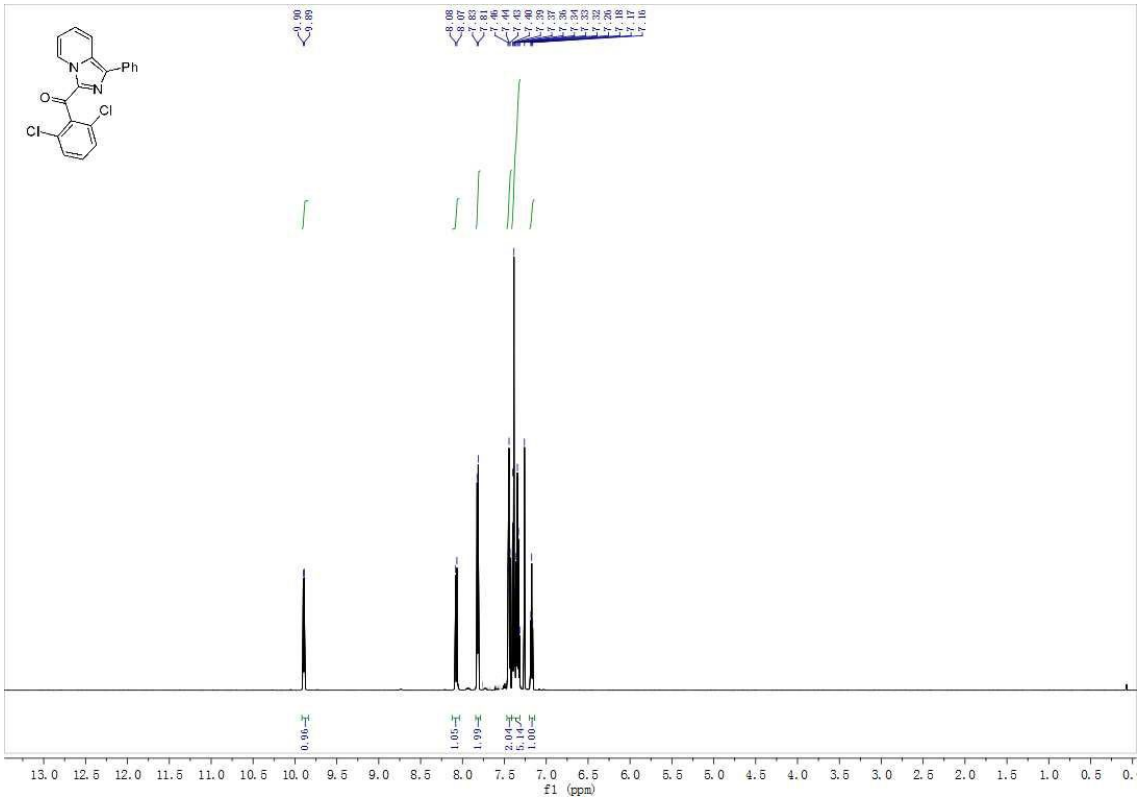
*(2,4-dichlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3p**)*



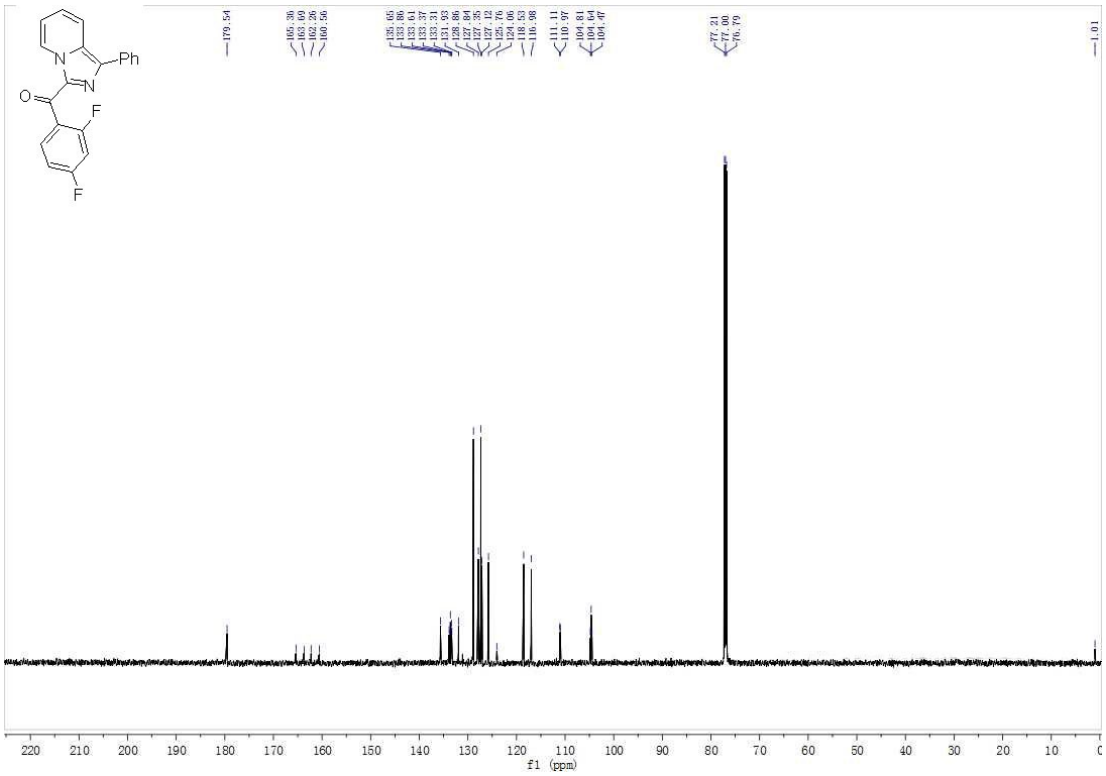


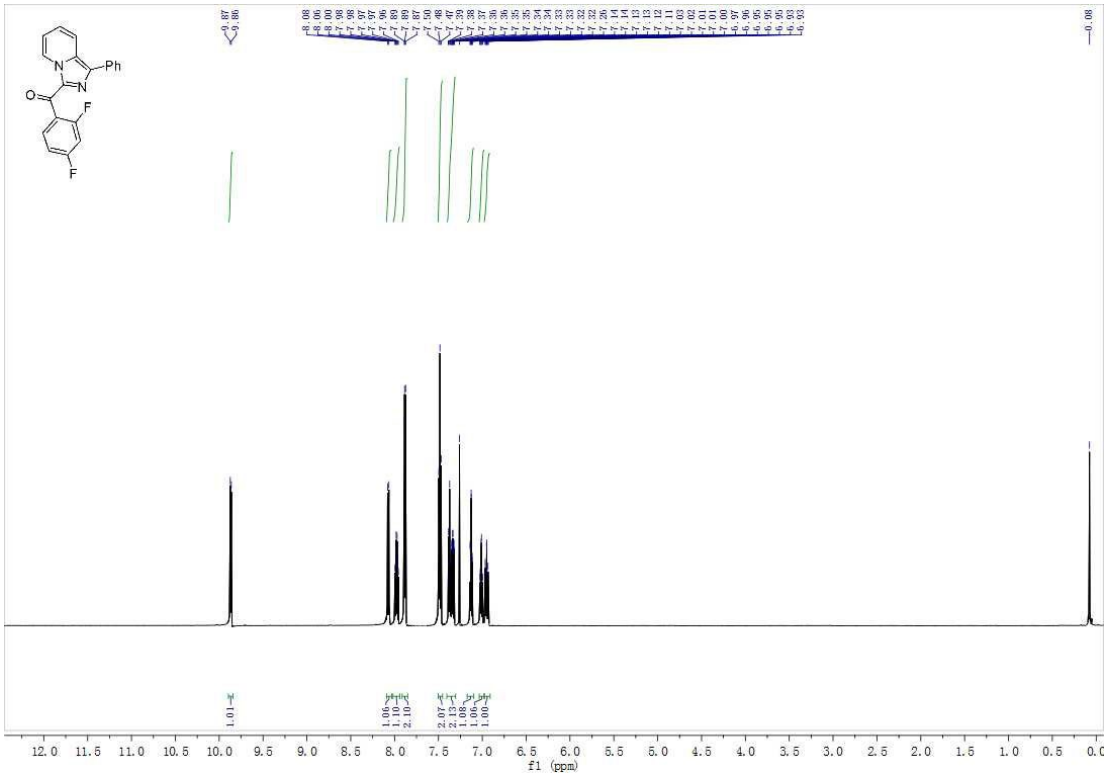
*(2,6-dichlorophenyl)(1-phenylimidazo[1,5-a]pyridin-3-yl)methanone (**3q**)*





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





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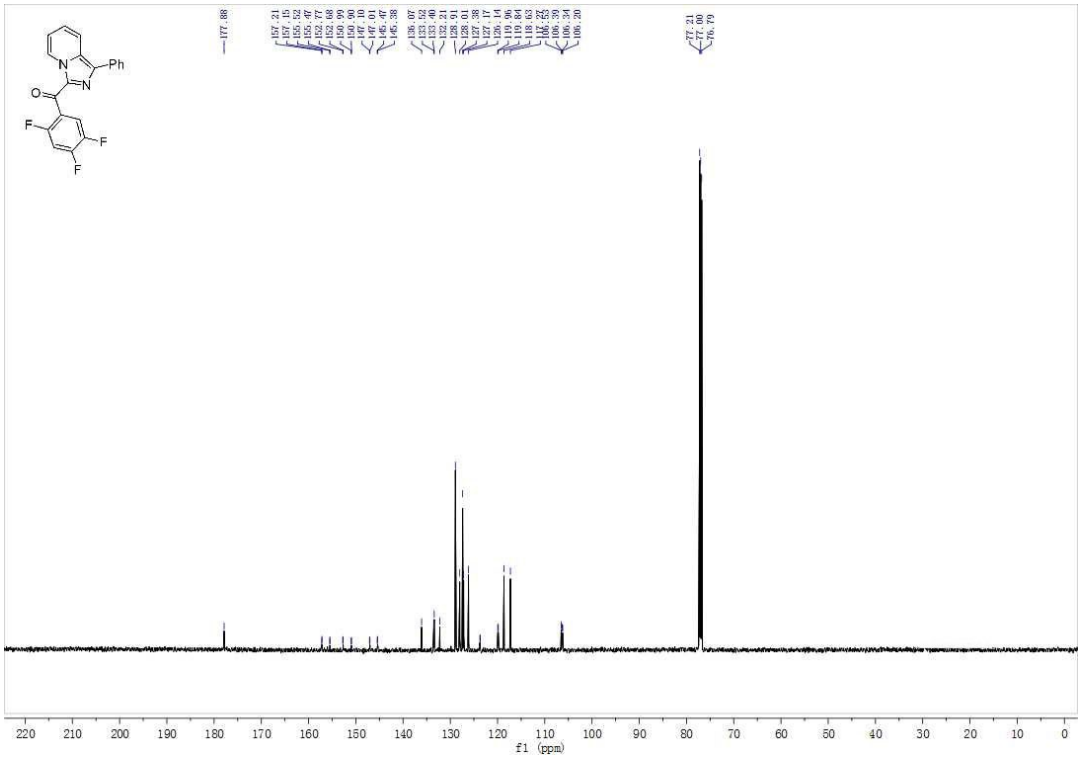
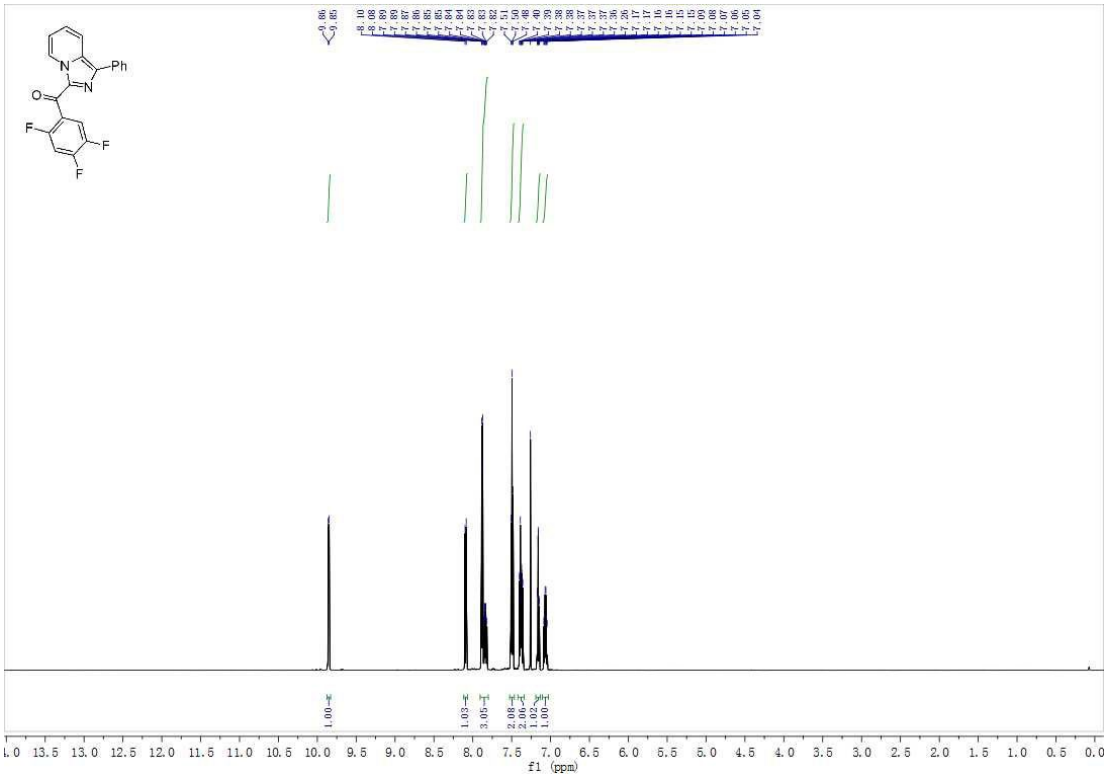
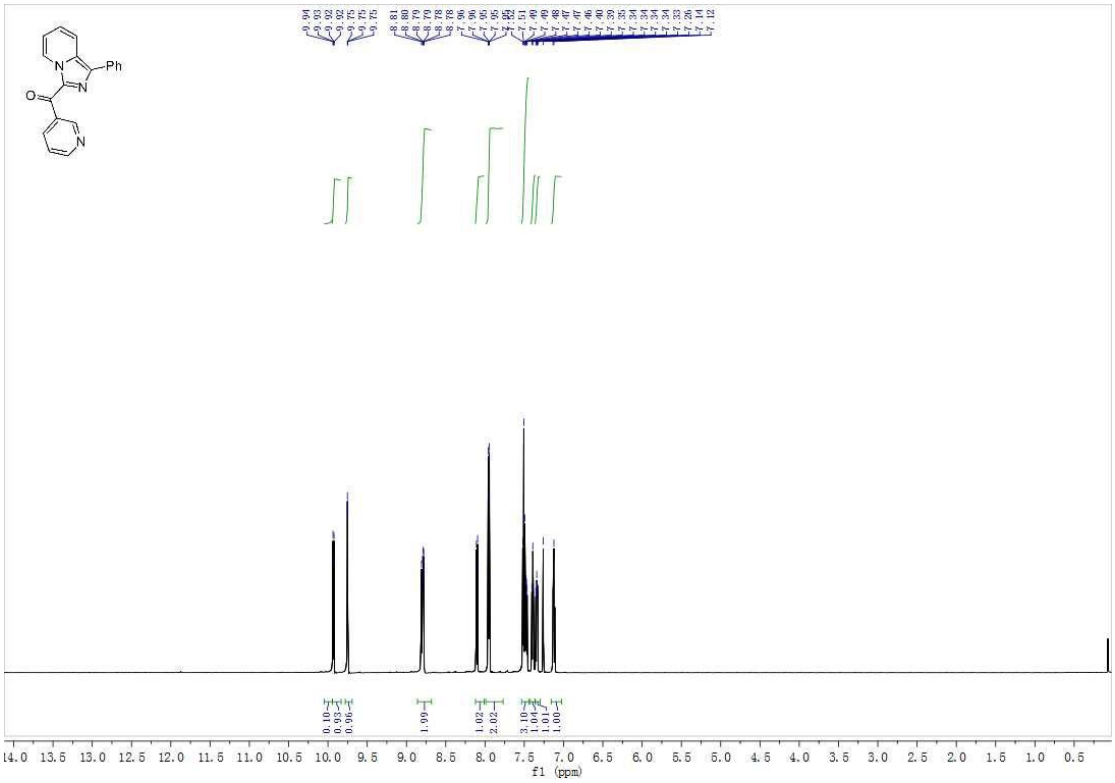
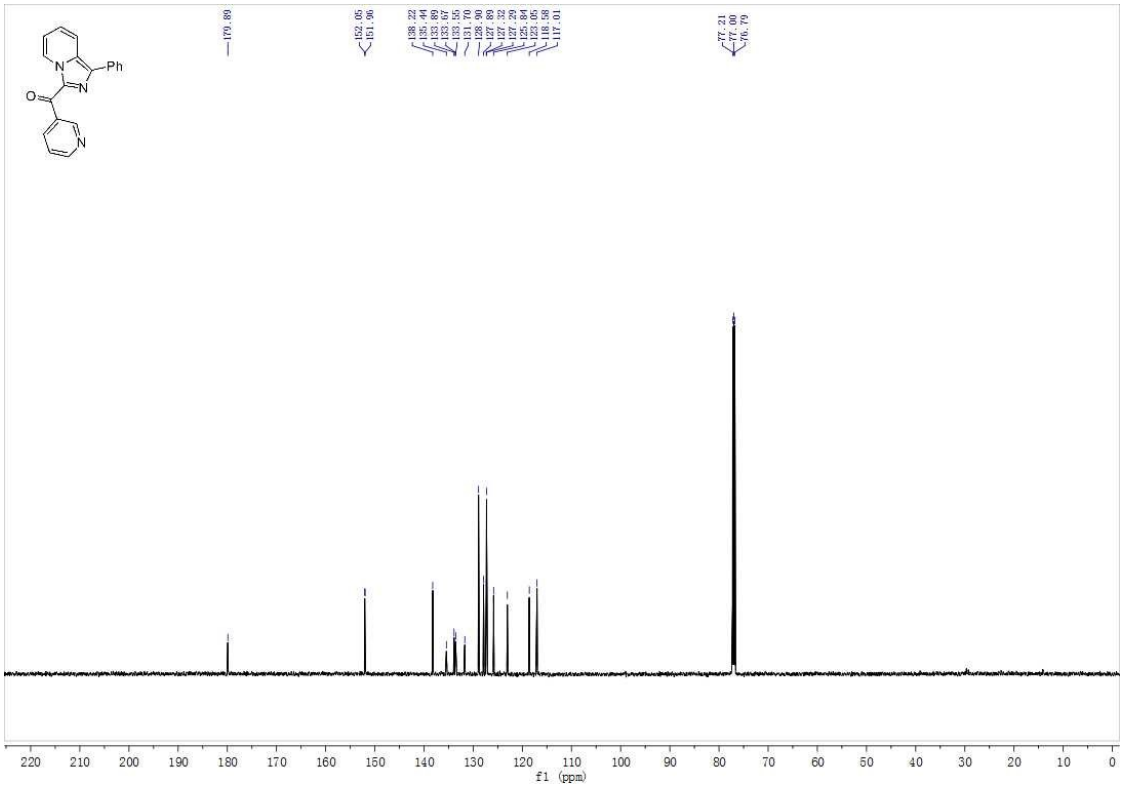




*(1-phenylimidazo[1,5-a]pyridin-3-yl)(pyridin-3-yl)methanone (**3t**)*





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

Sample preparation

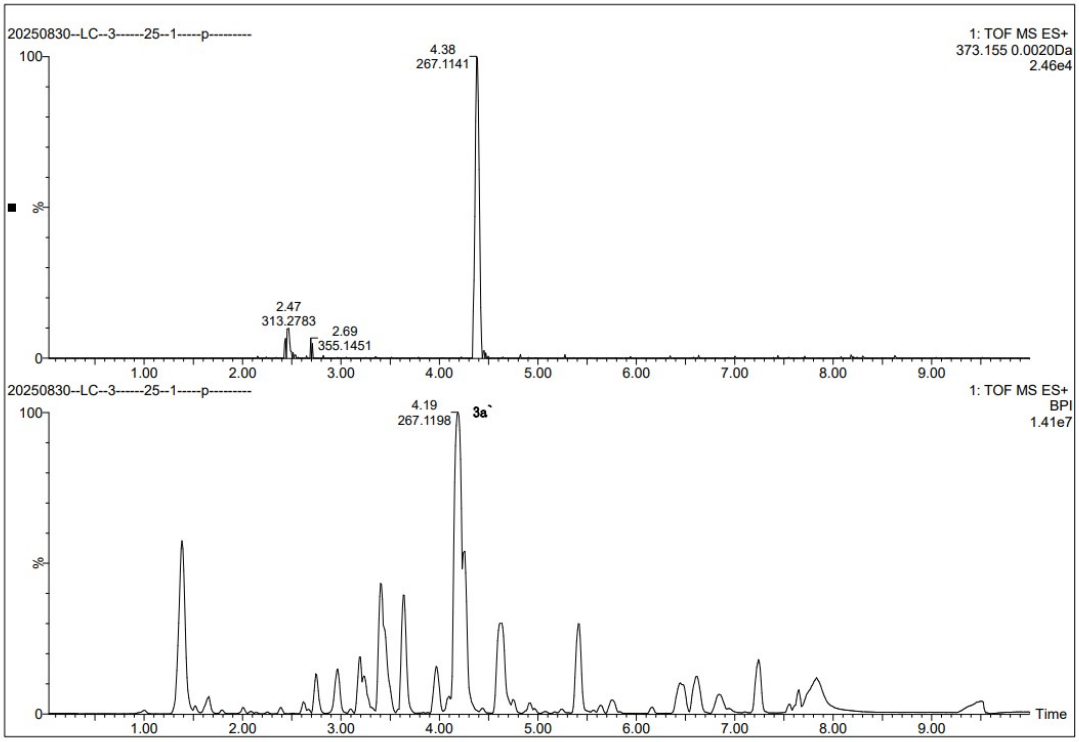
To a solution of ethyl 3-oxo-3-phenylpropanoate (0.2 mmol, 1 equiv.), phenyl(pyridin-2-yl)methanamine (0.25 mmol, 1.25 equiv.) in 2mL of DMSO in a tube was added I_2 (0.6 mmol, 3equiv.) and H_2O (0.6 mmol), and the tube was heated at 75℃ and for 2 hours with oil bath. The system was cooled to room temperature, 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_2O; B: 0.1% formate in acetonitrile. Chromatographic column: waters BEH C18 1.7um 2.1*50mm. Column temperature: 40℃.

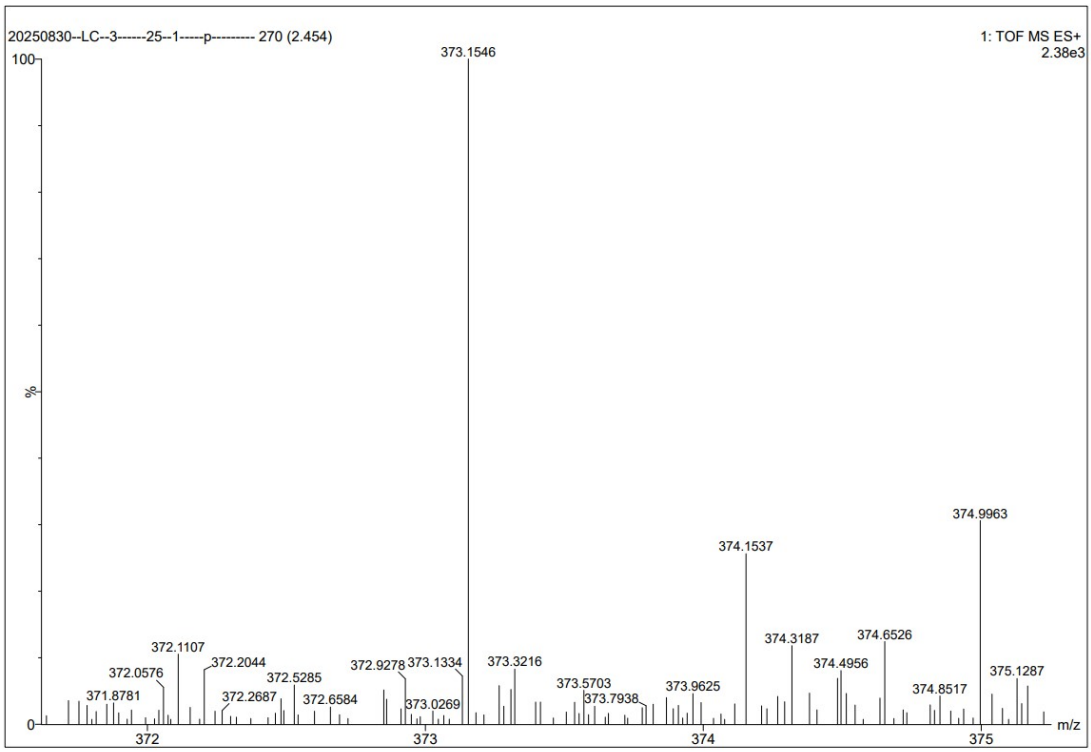
Time (min)	Flow rate（mL/min）	A(%)	B(%)
0	0.4	95	5
1	0.4	95	5
7	0.4	2	98
10	0.4	2	98

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 $C_{23}H_{20}N_2O_3$ (**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