Supporting Information

Copper- and DMF-Mediated Switchable Oxidative C-H Cyanation and Formylation of Imidazo[1,2-a]pyridines Using Ammonium Iodide

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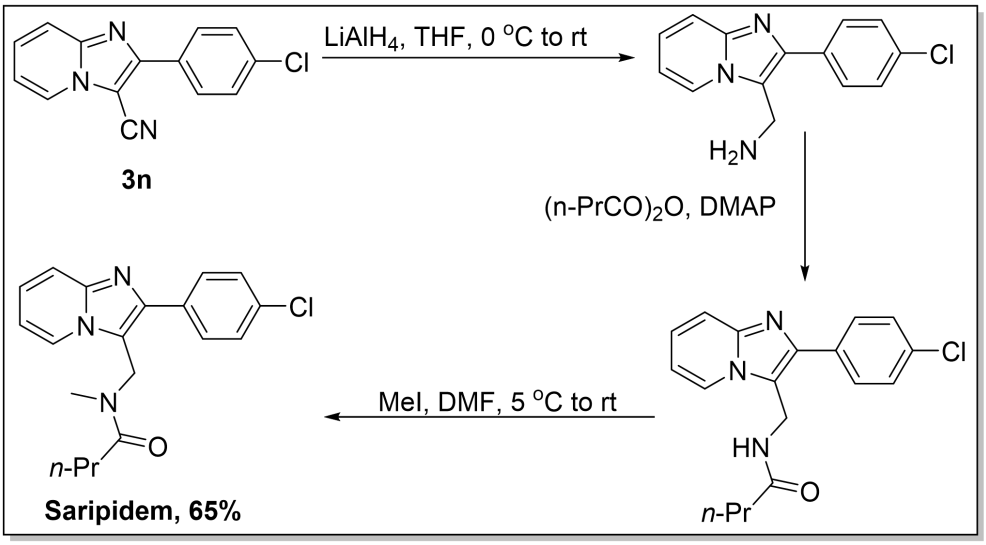
A. Synthesis of Saripidem

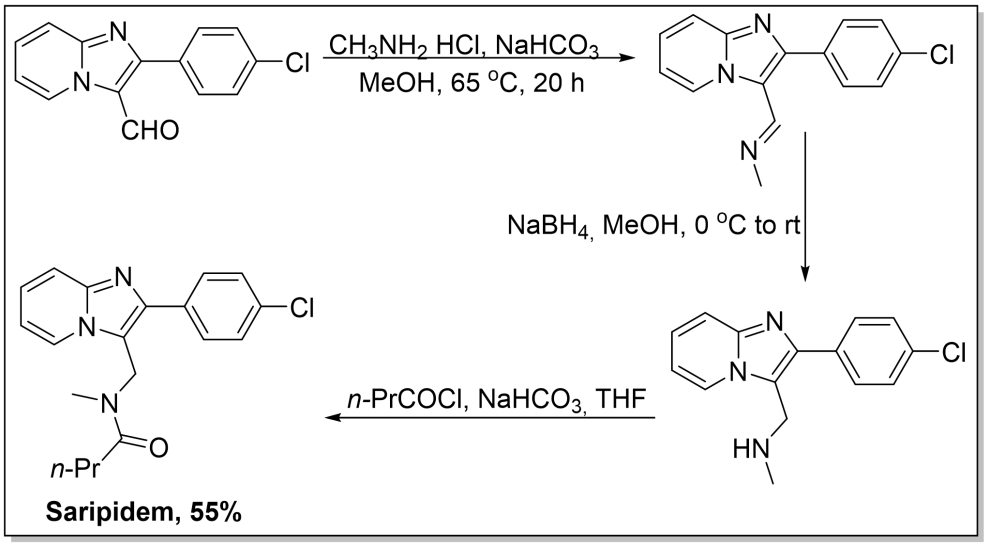


(1) A mixture of **3n** (51 mg, 0.2 mmol) was dissolved in dry THF (2 mL/mmol), a stirred suspension of $LiAlH_4$ (10 mg, 0.24 mmol) in THF (2 mL/mmol) was added slowly at 0 °C in an ice bath under nitrogen atmosphere. Then the reaction mixture was stirred for 3 hours at room temperature. Upon completion, the solution was cooled and added NaOH (15%, 0.2 mL/mmol) and H_2O (0.2 mL/mmol) slowly. The resulting solution was stirred for 0.5 h and filtered through Celite. The filtrate was extracted with EtOAc. The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford the crude product, which was directly subjected to the following step.

The crude product obtained above was dissolved in DCM (5 mL/mmol). To the solution was added triethylamine (101 mg, 1.0 mmol) and dimethylaminopyridine (24.4mg, 0.2 mmol) at 0 °C. Then butyric anhydride (47 mg, 0.3 mmol) was added dropwise, and the mixture was stirred for 10 min at 0 °C in an ice bath and 30 min at

room temperature. The reaction was poured into saturated aqueous $NaHCO_3$, and extracted with DCM. The organic phase was collected, dried and concentrated under reduced pressure.The residue was purified by flash column chromatography to afford the crude product, which was directly subjected to the following step.

The crude product obtained above was dissolved in DMF (5 mL/mmol). To the solution was added MeI (43 mg, 0.3 mmol) slowly at 5 °C for 1 hour and 6 hour at room temperature. After the reaction was completed (monitored by TLC), the resulting mixture were cooled to room temperature and diluted with EtOAc and aqueous NH_3 solution (3 M). Two layers were separated and aqueous layer was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. The desired product Saripidem was obtained in 65% yield.



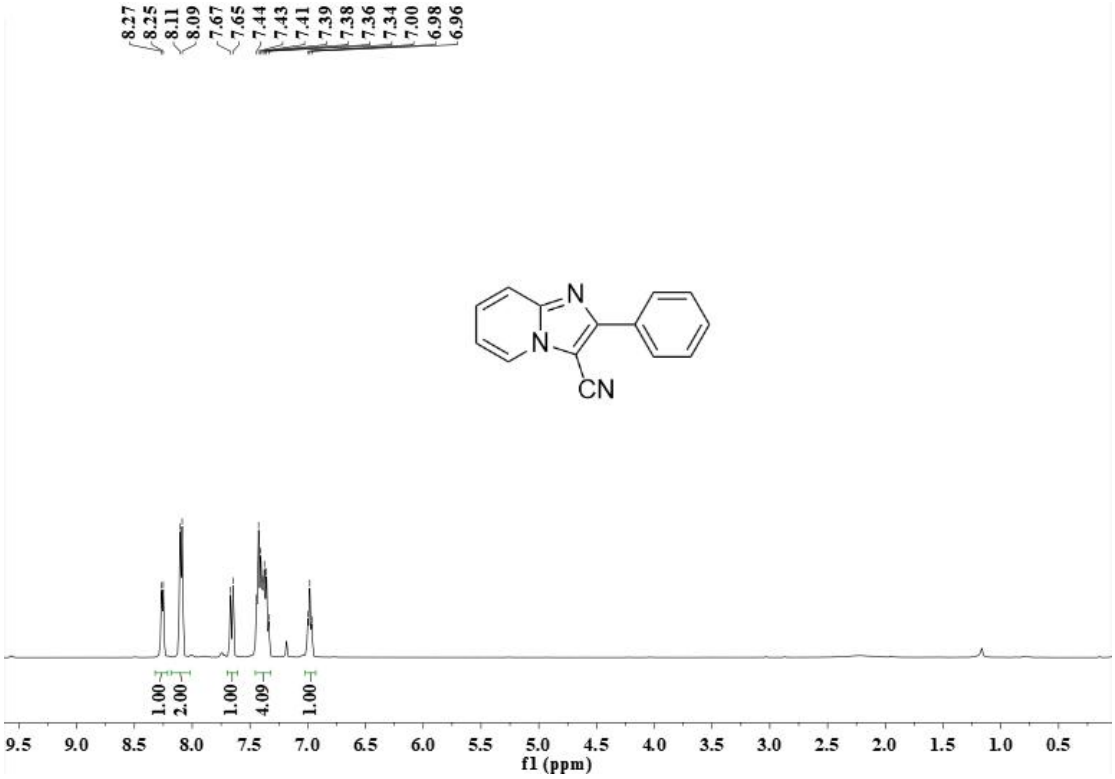
(2) A mixture of **3e** (51 mg, 0.2 mmol), methylamine hydrochloride (40 mg, 0.6 mmol) and $NaHCO_3$ (50 mg, 0.6 mmol) in MeOH (4 mL/mmol) was stirred at 65 °C. The reaction mixture was cooled to 0 °C before addition of $NaBH_4$ (23 mg, 0.6 mmol) in portion. The resulting mixture was warmed to rt and stirred for another 1 h. The solvent was evaporated under reduced pressure. Saturated aqueous Na_2CO_3 (15

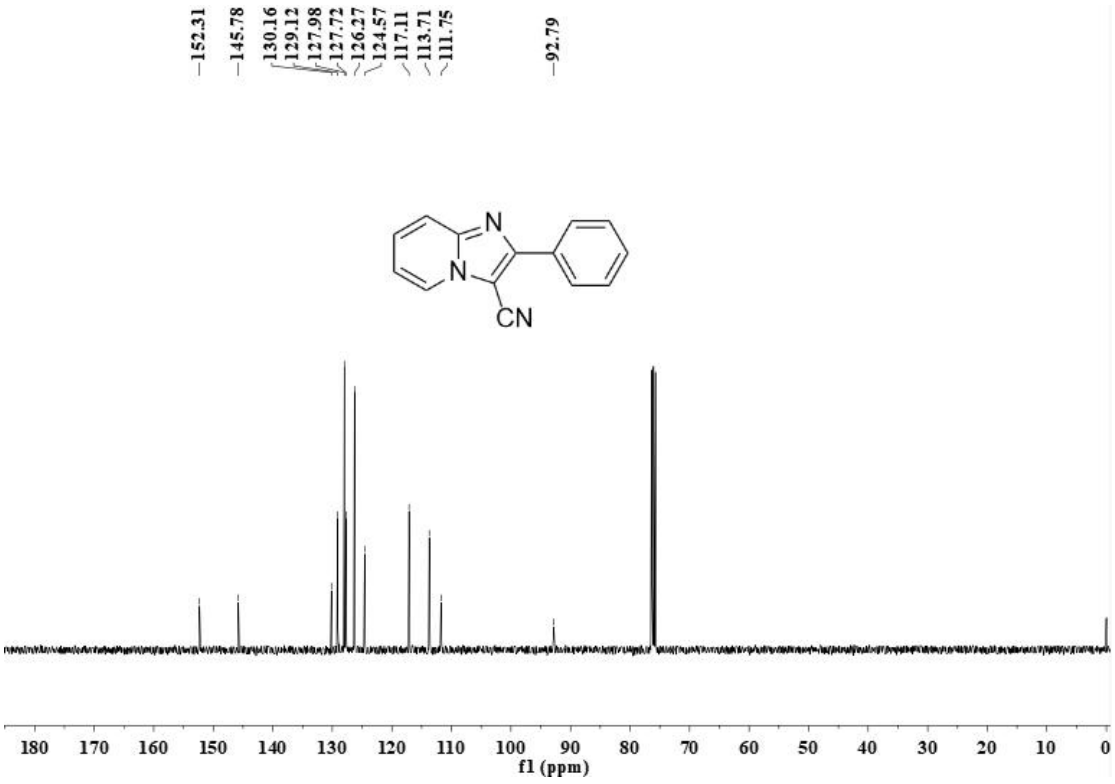
mL/mmol) was added and the mixture was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. The concentrated crude product was subjected to the next step without further purification.

To a mixture of the above crude product, $NaHCO_3$ (49.8 mg, 0.6 mmol) was added in anhydrous THF (5 mL/mmol), *n*-butyryl chloride (42.2 mg, 0.4 mmol) was added dropwise. The resulting mixture was stirred at rt for 30 min. Saturated aqueous $NaHCO_3$ (20 mL) and EtOAc (15 mL/mmol) was added to the reaction mixture. Two layers were separated and aqueous layer was extracted with EtOAc (3×10 mL). The combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum. The desired product Saripidem was obtained in 55% yield.

B. Copies of ^{1}H and ^{13}C NMR spectra

2-phenylimidazo[1,2-a]pyridine-3-carbonitrile (2a)





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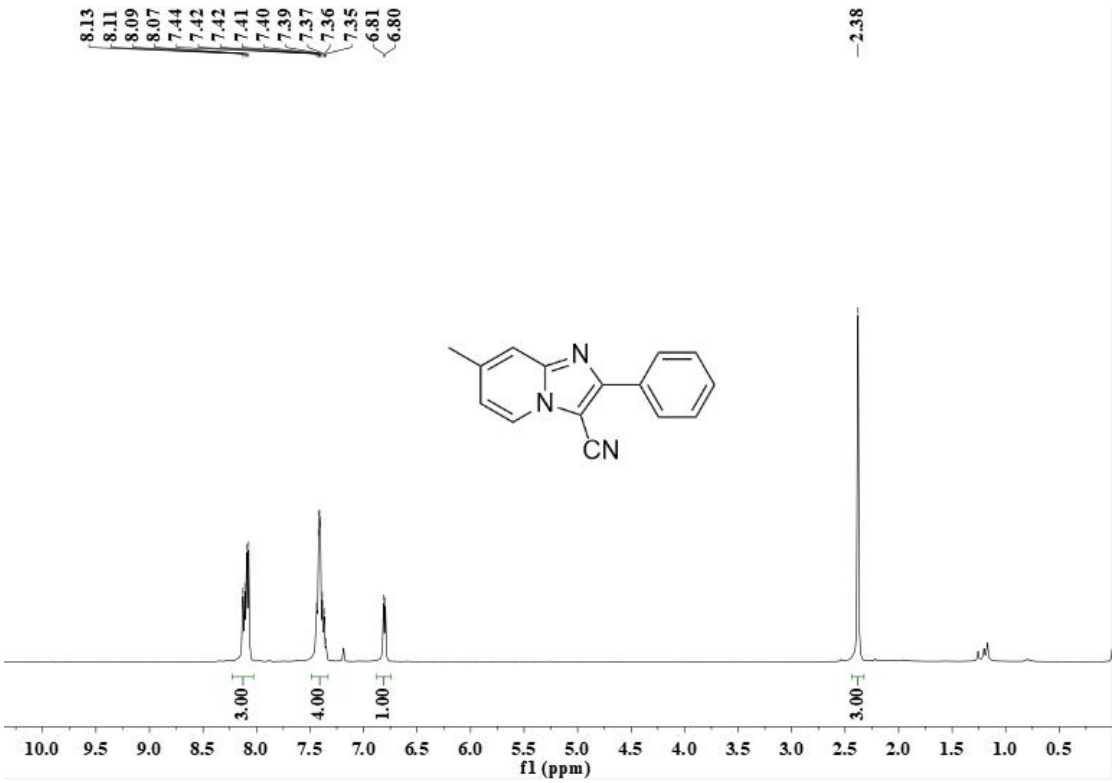

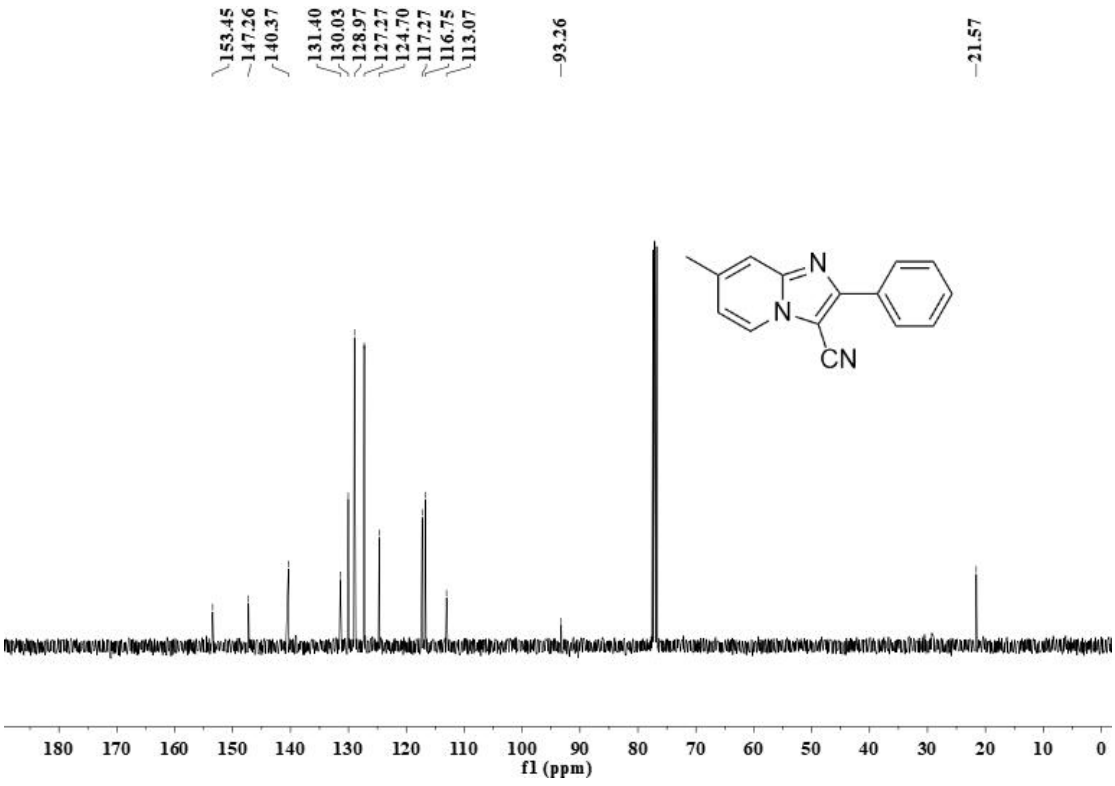

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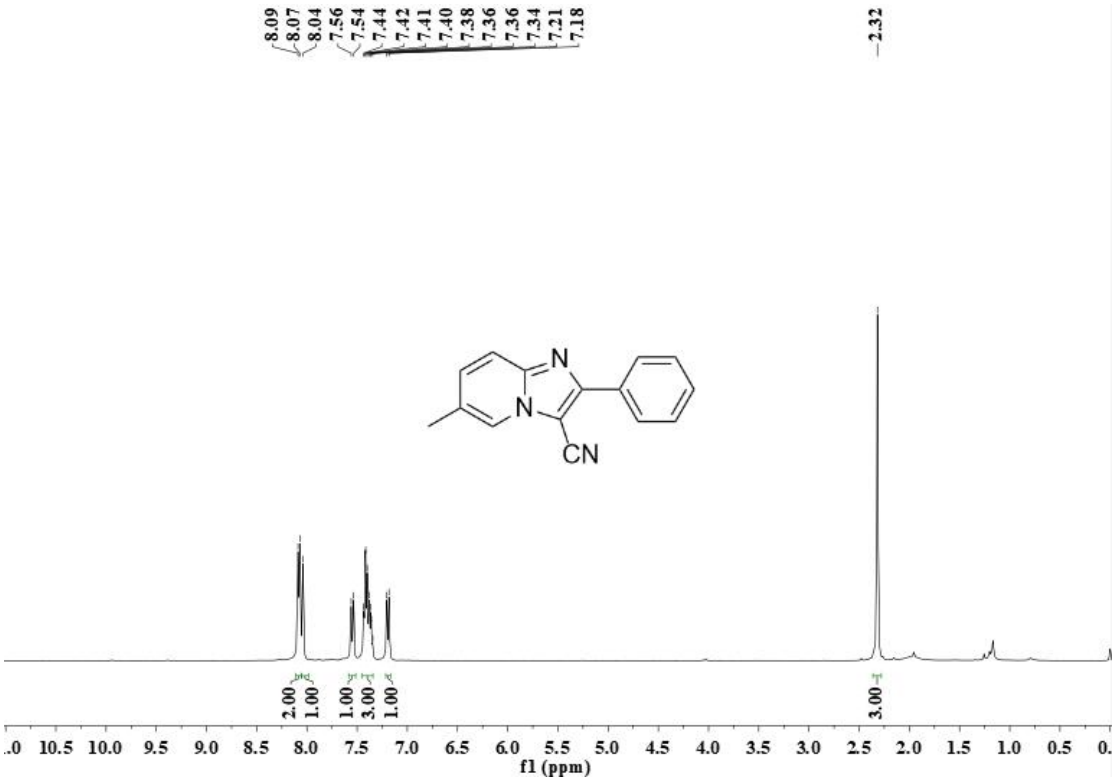

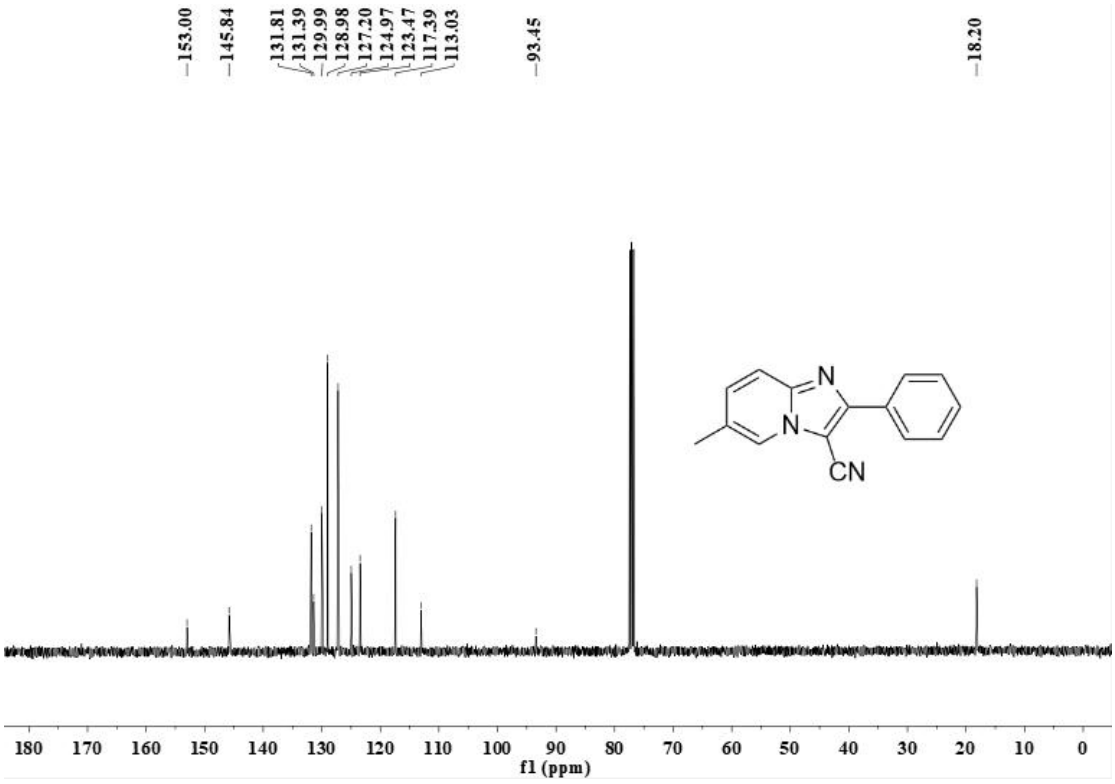

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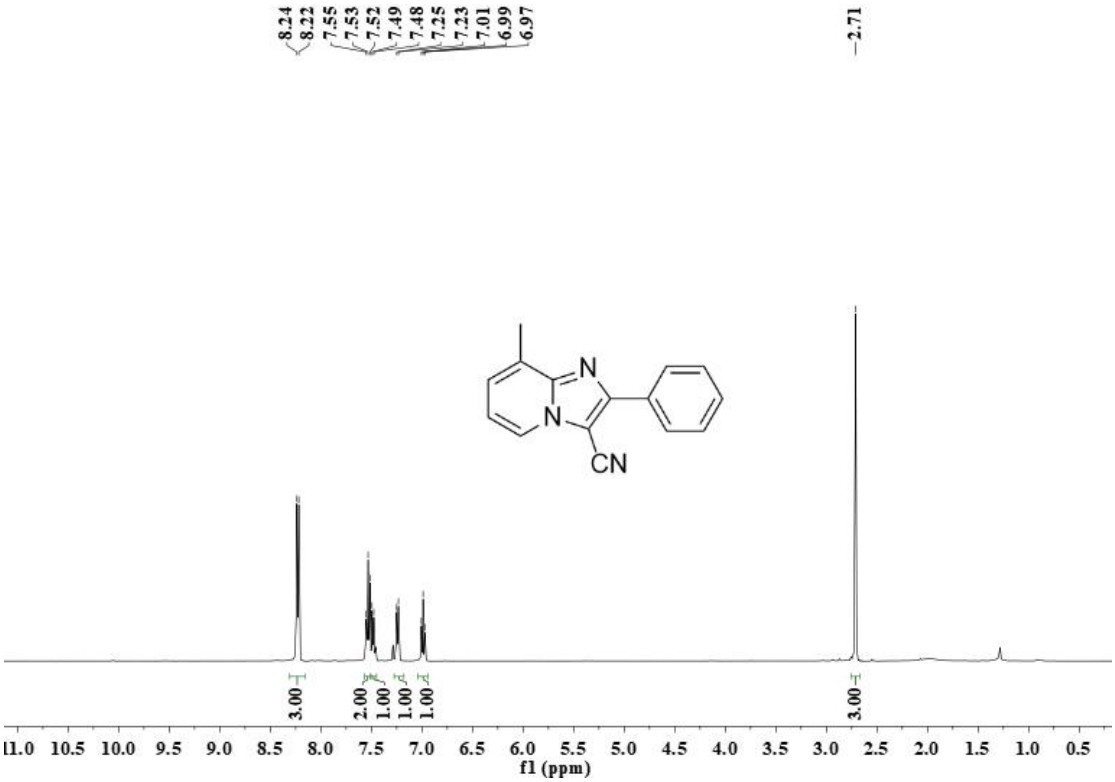

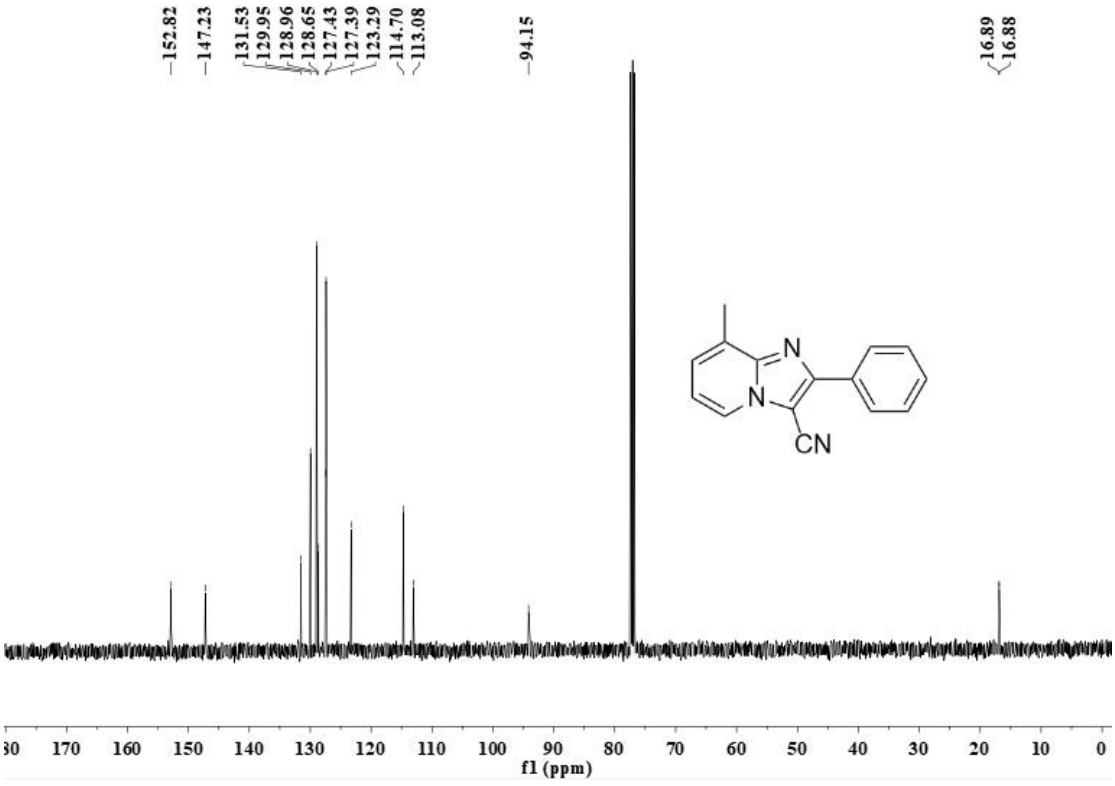

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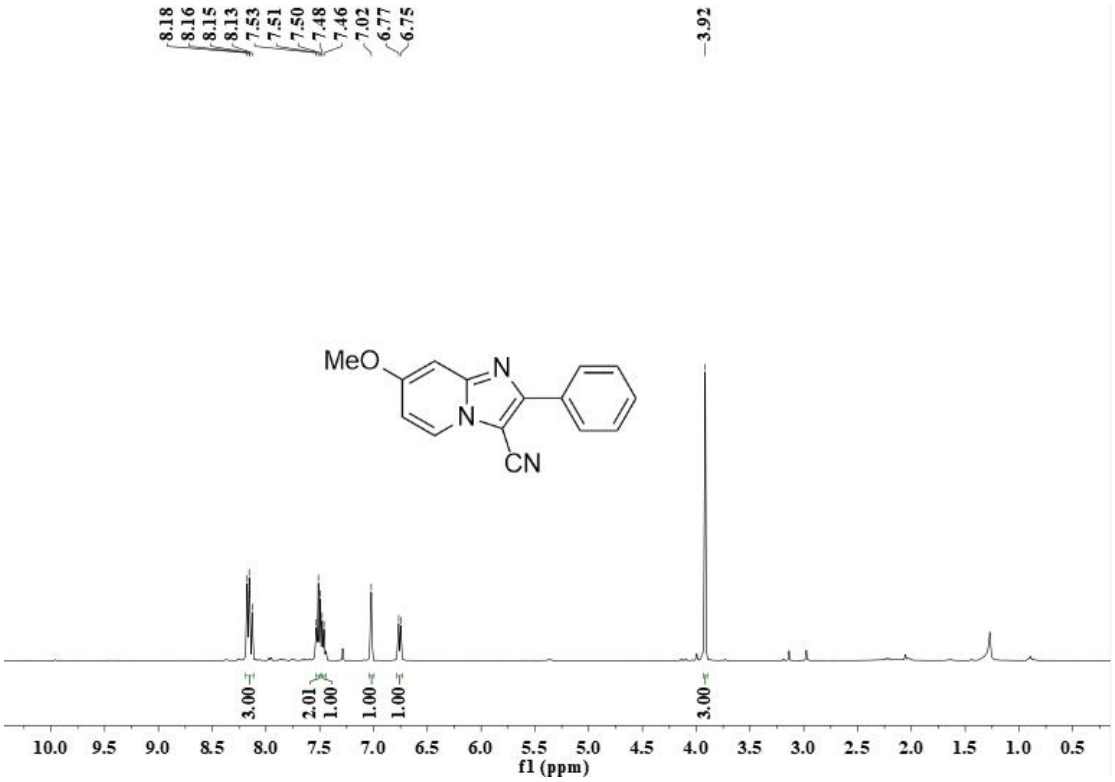

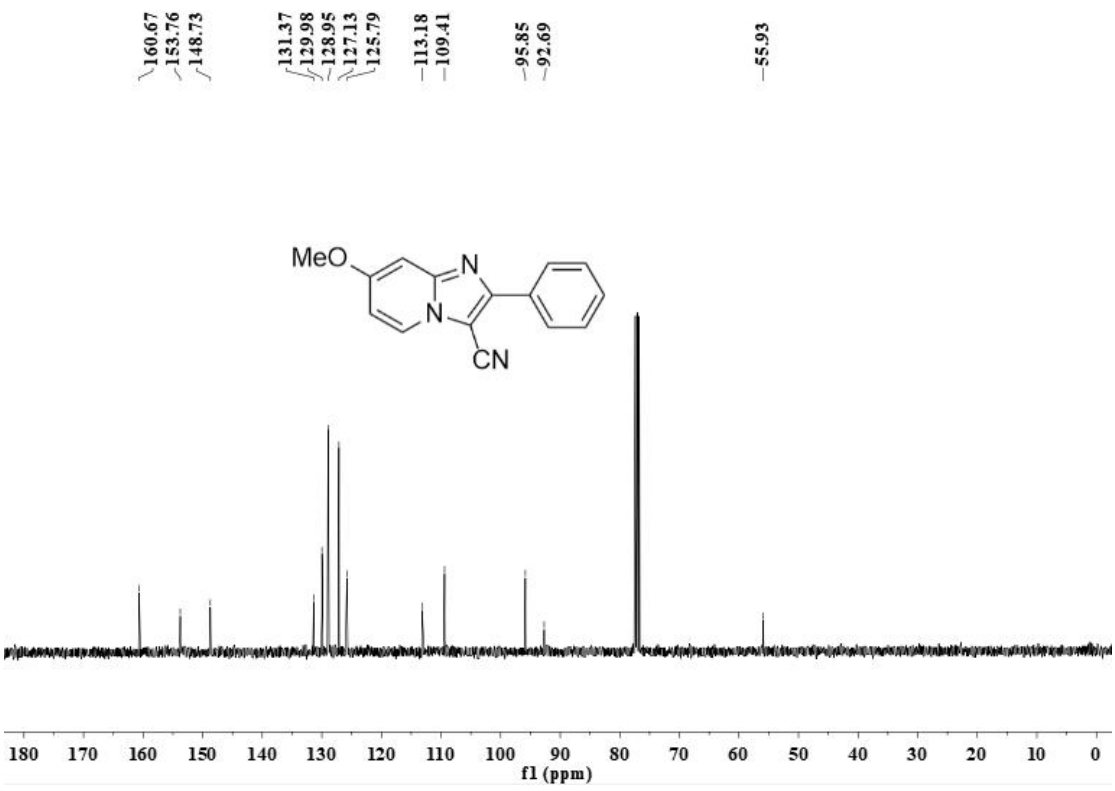

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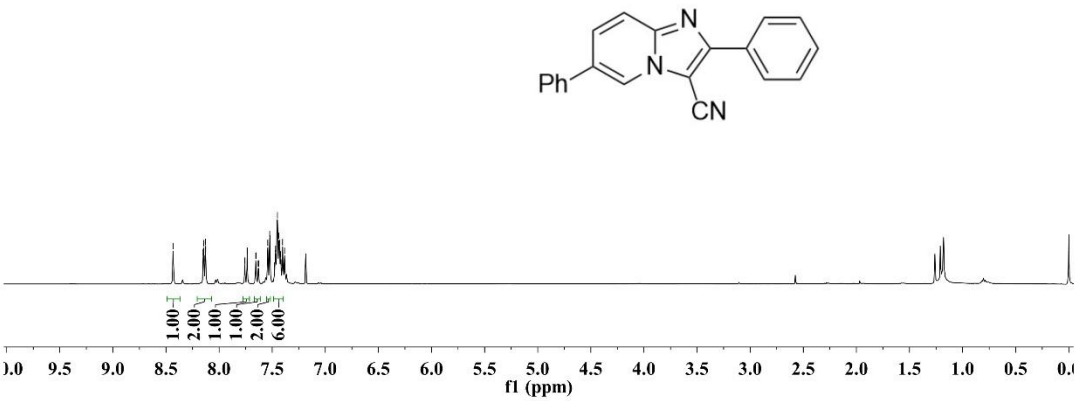

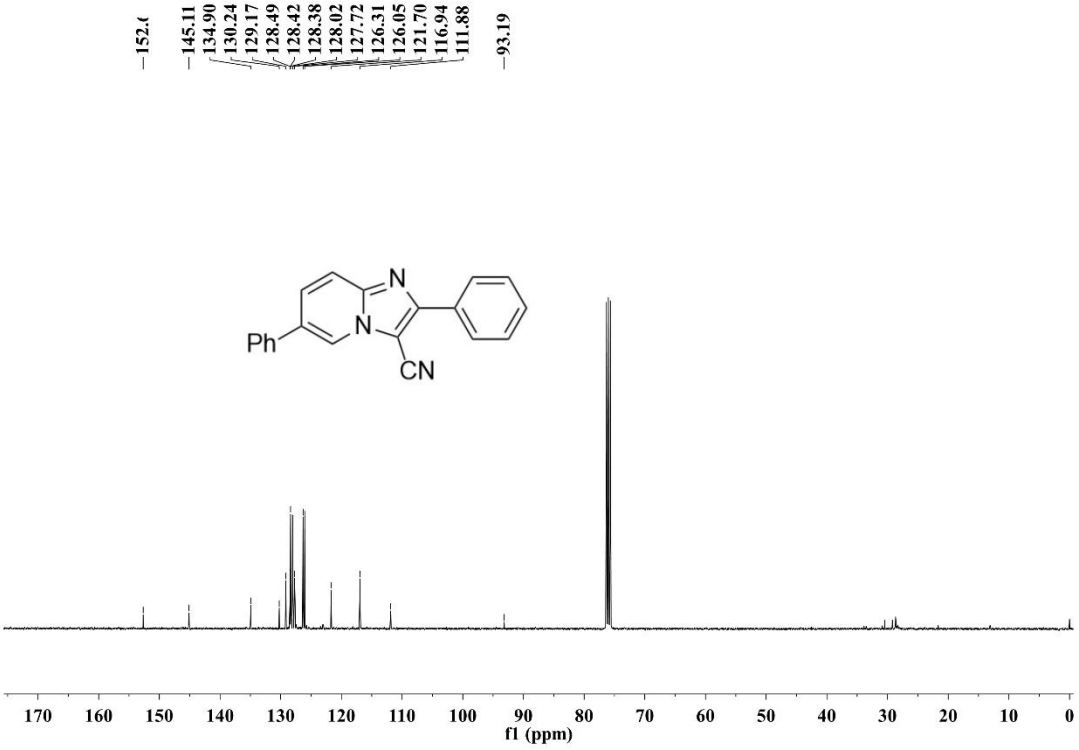

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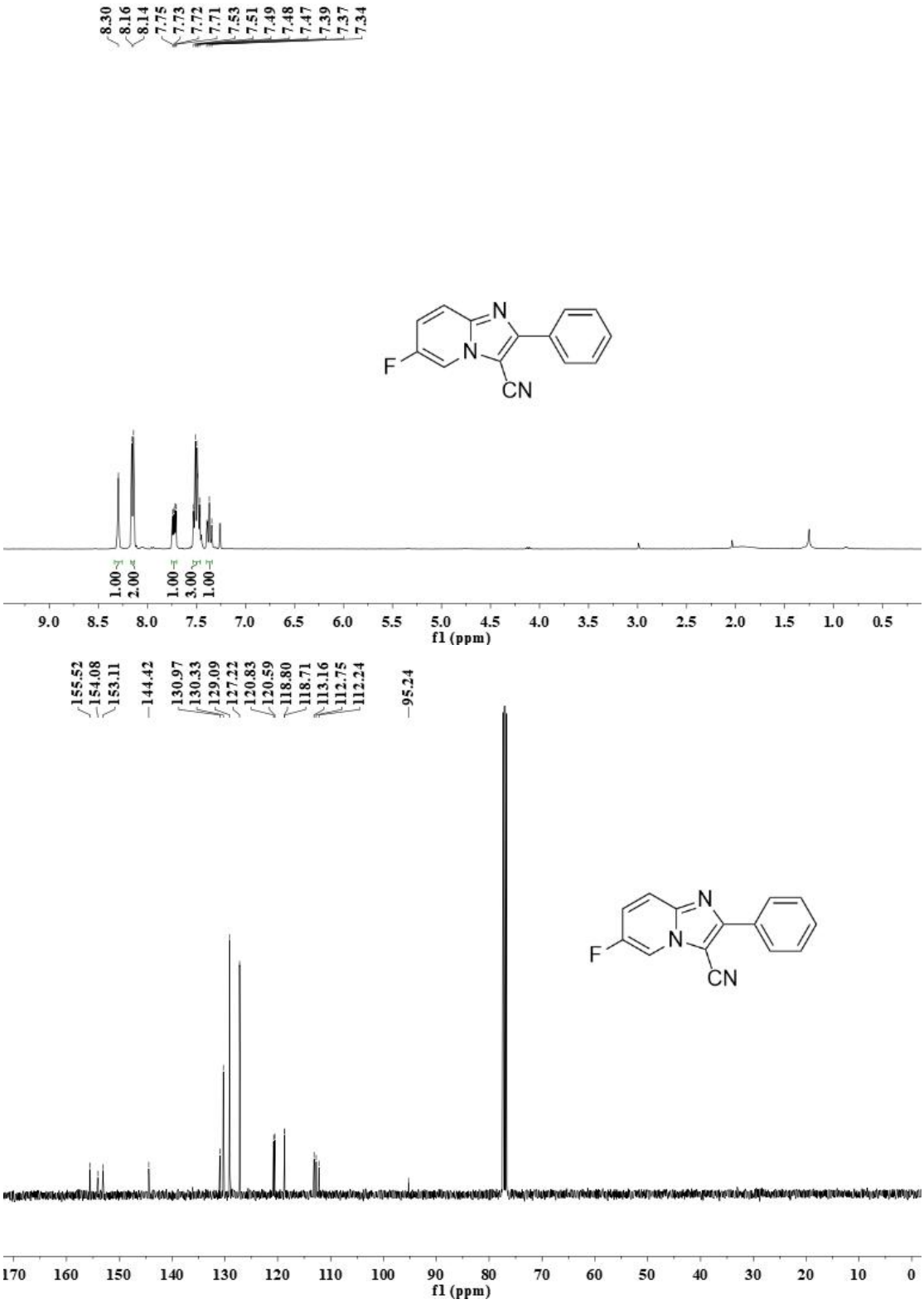

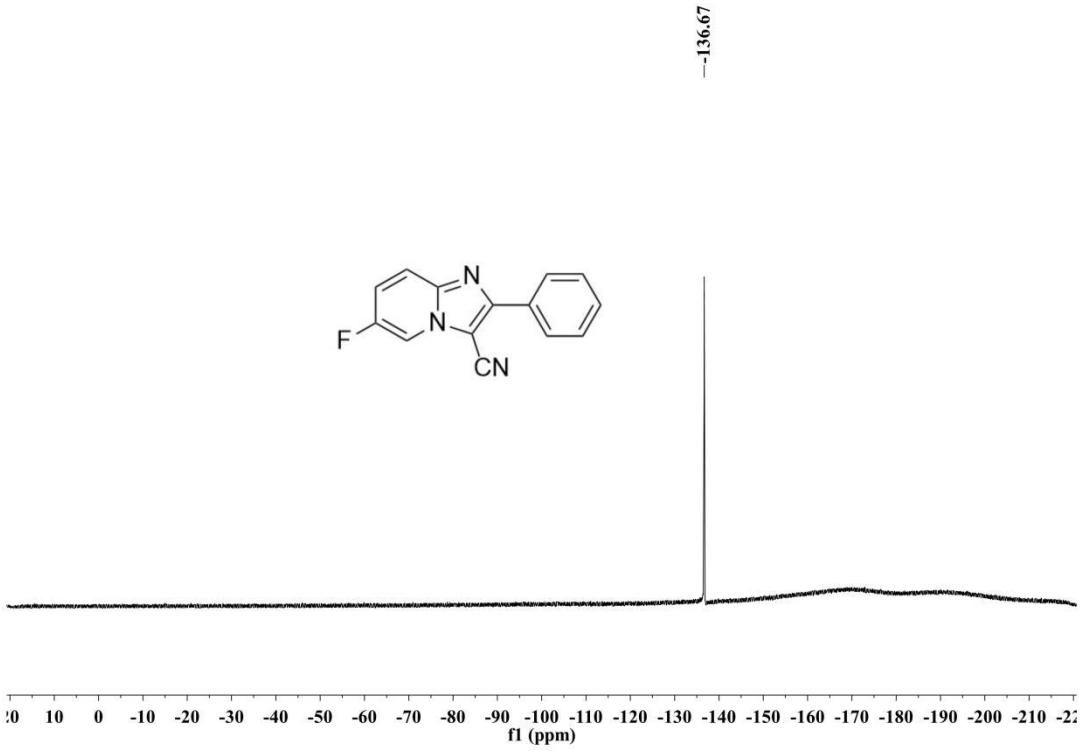

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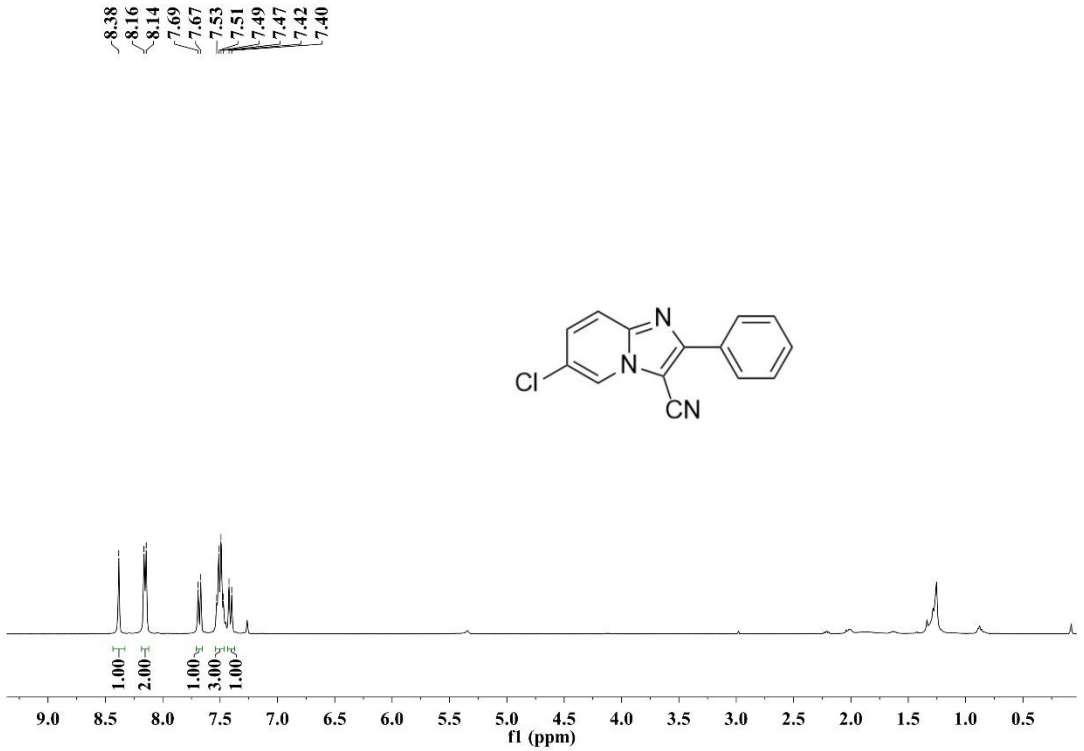

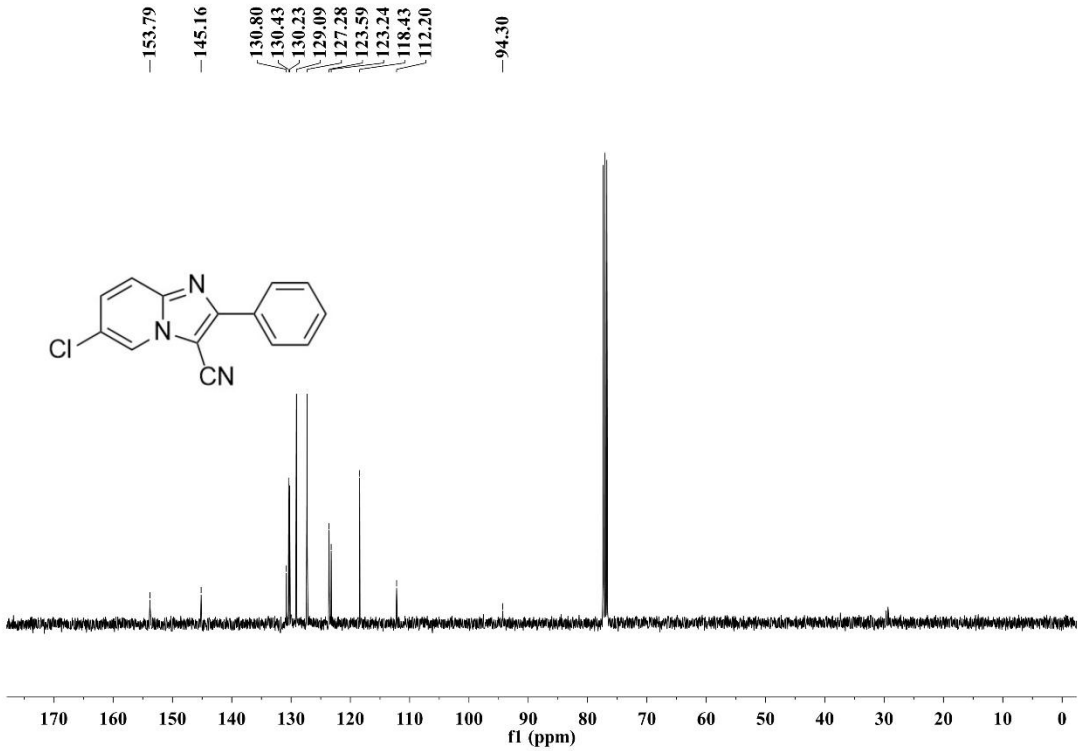

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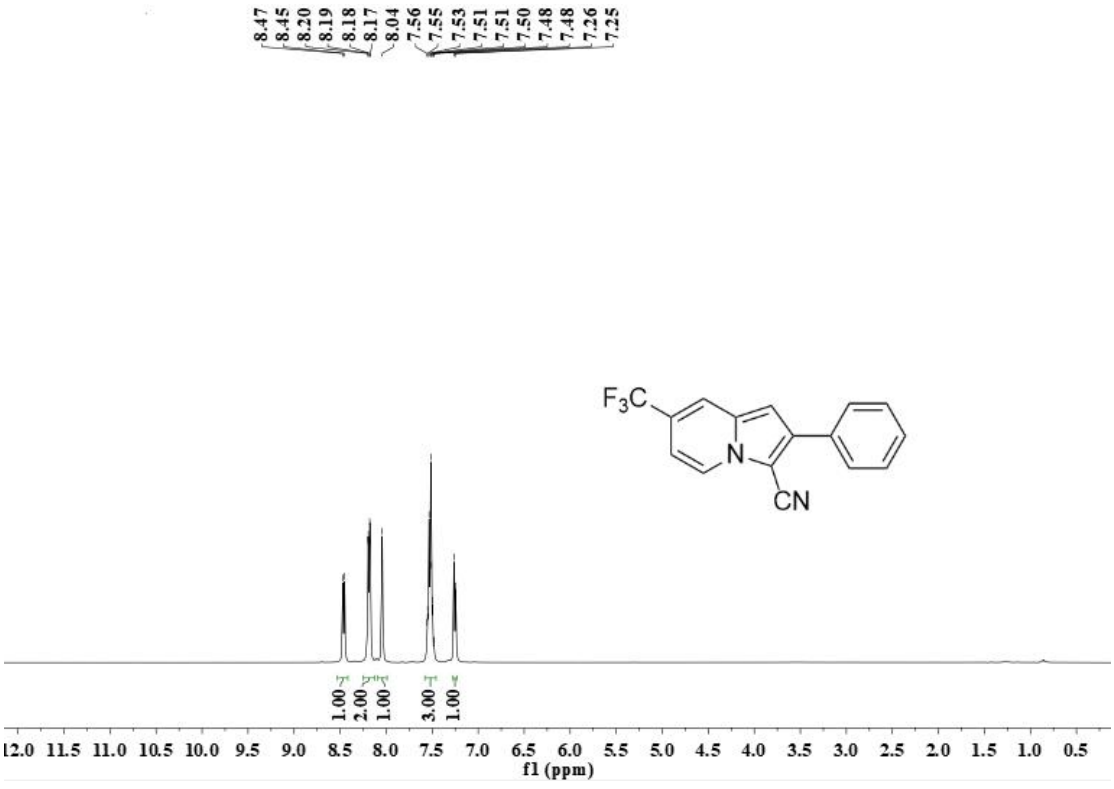

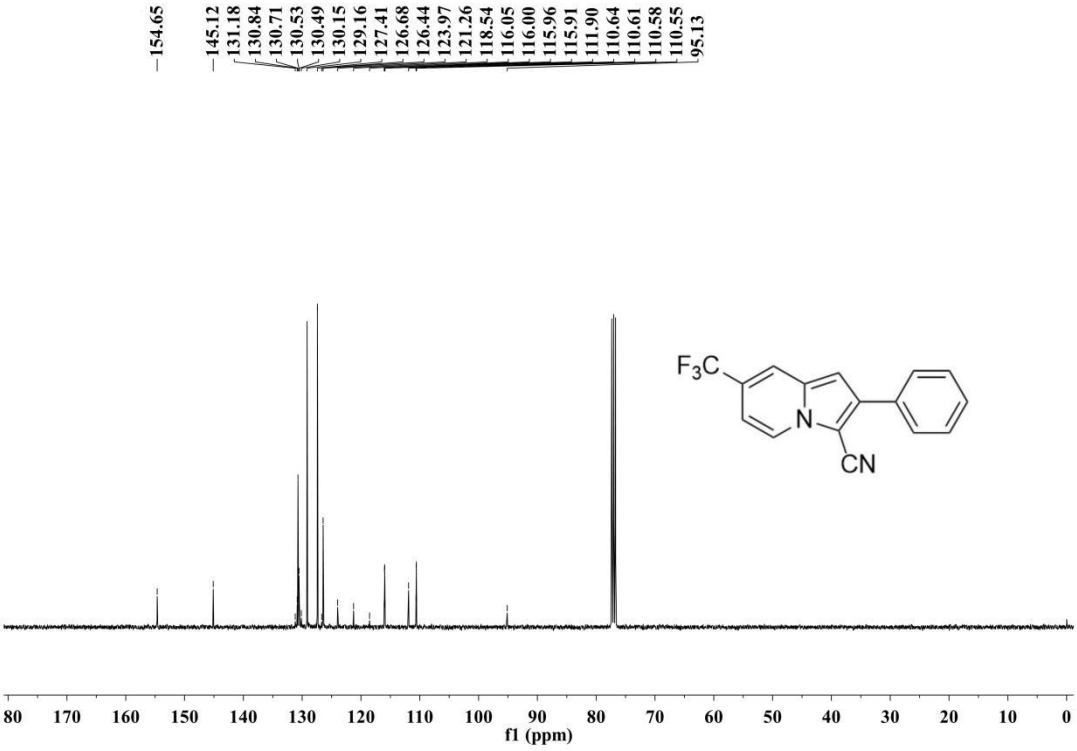
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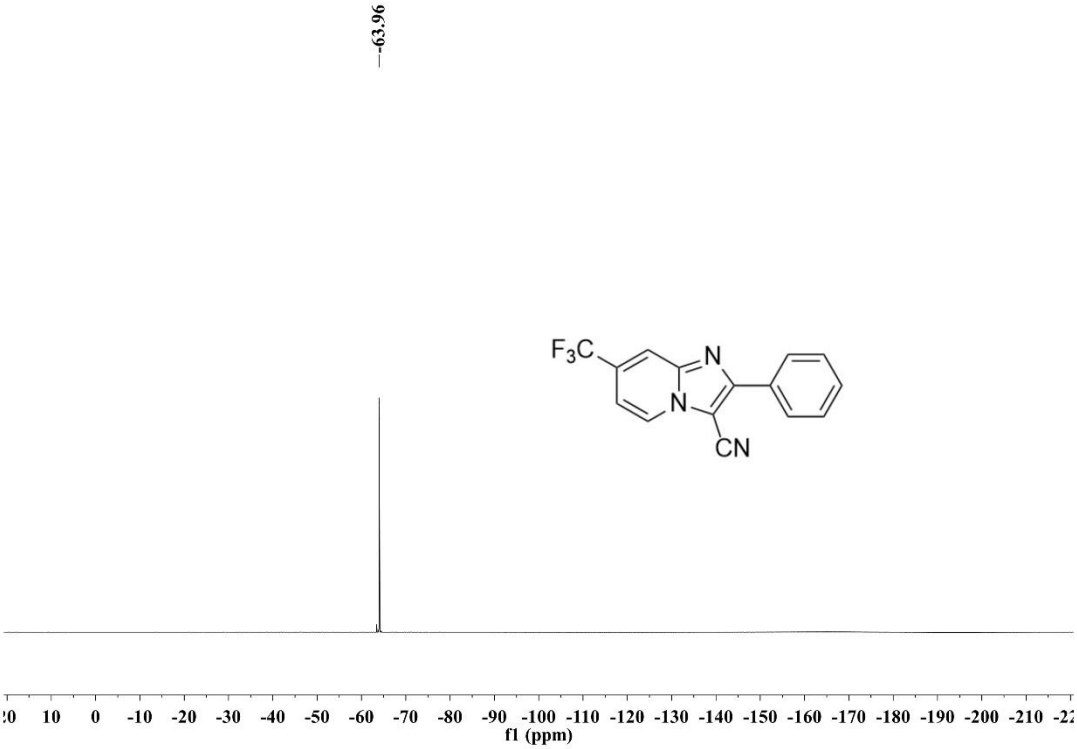
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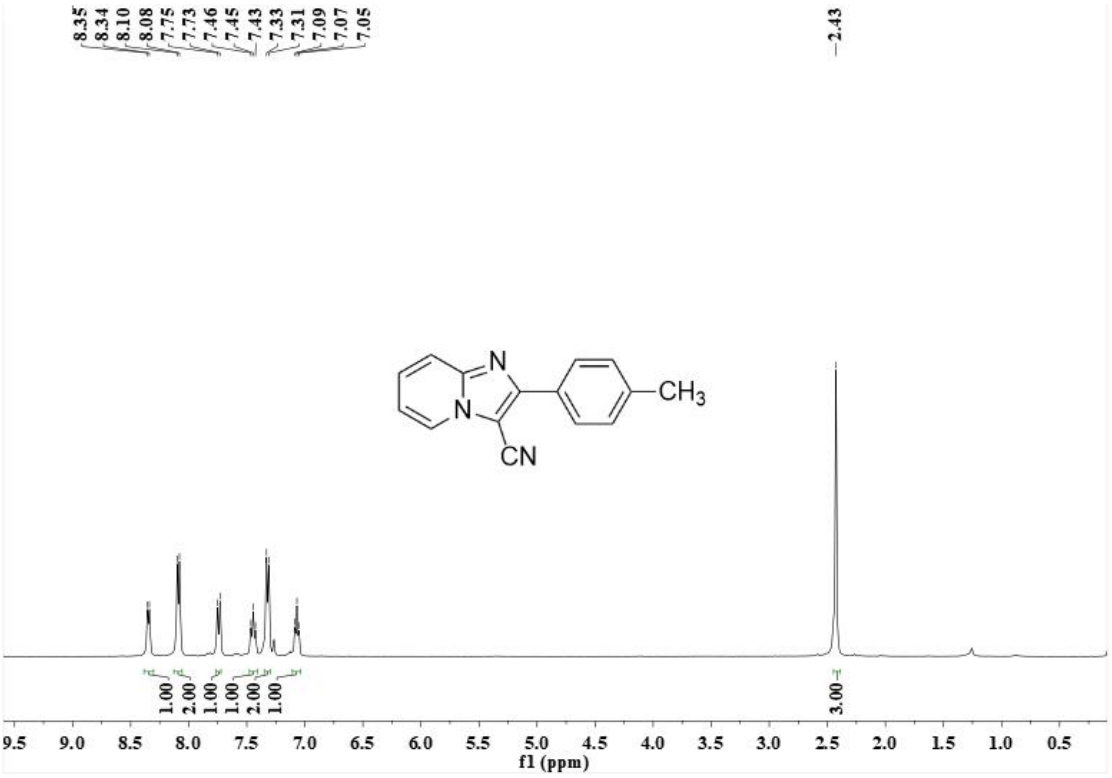

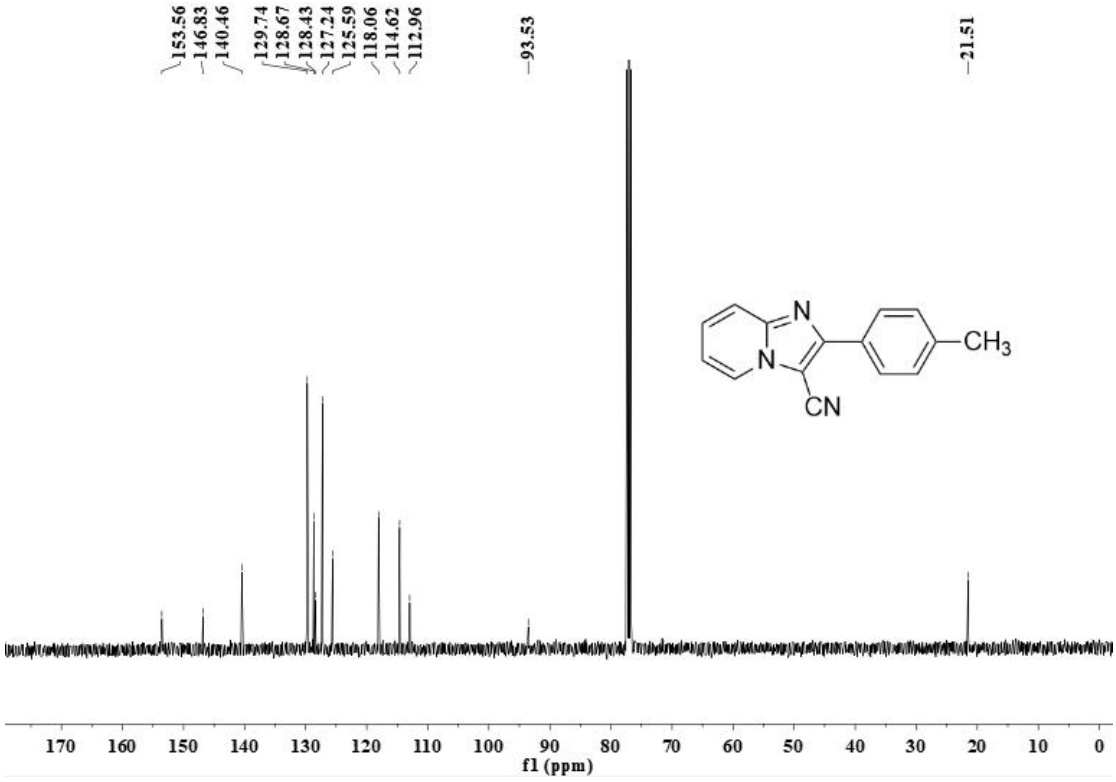

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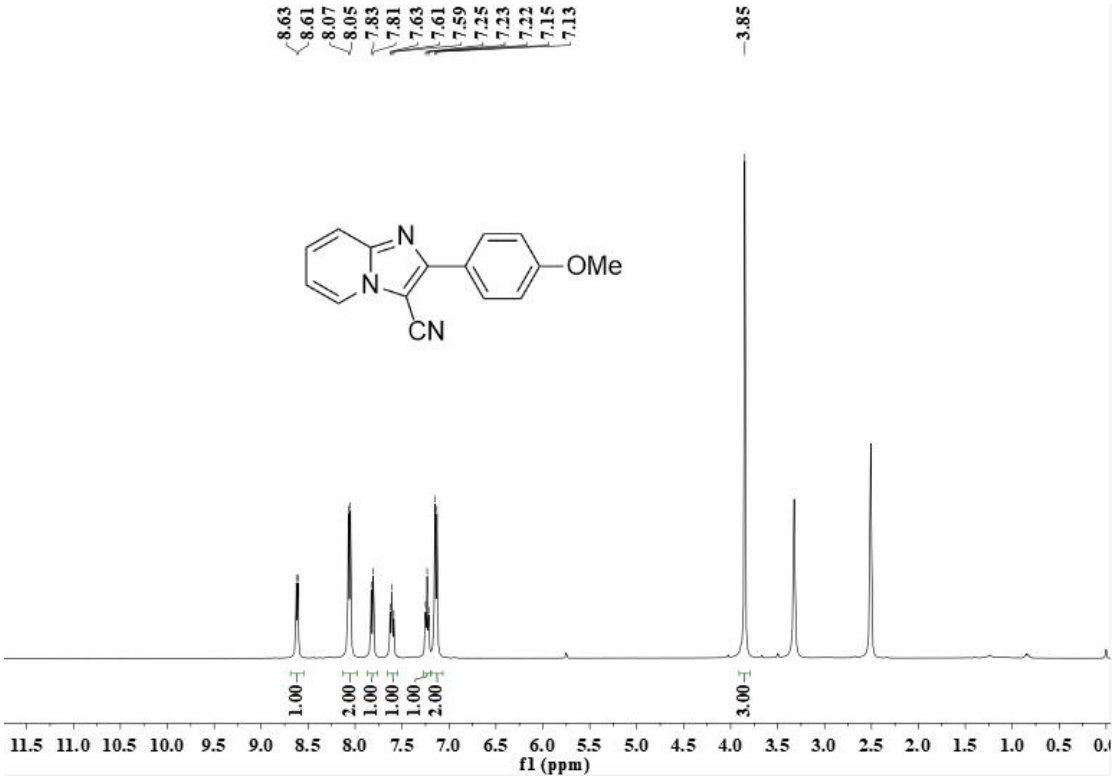

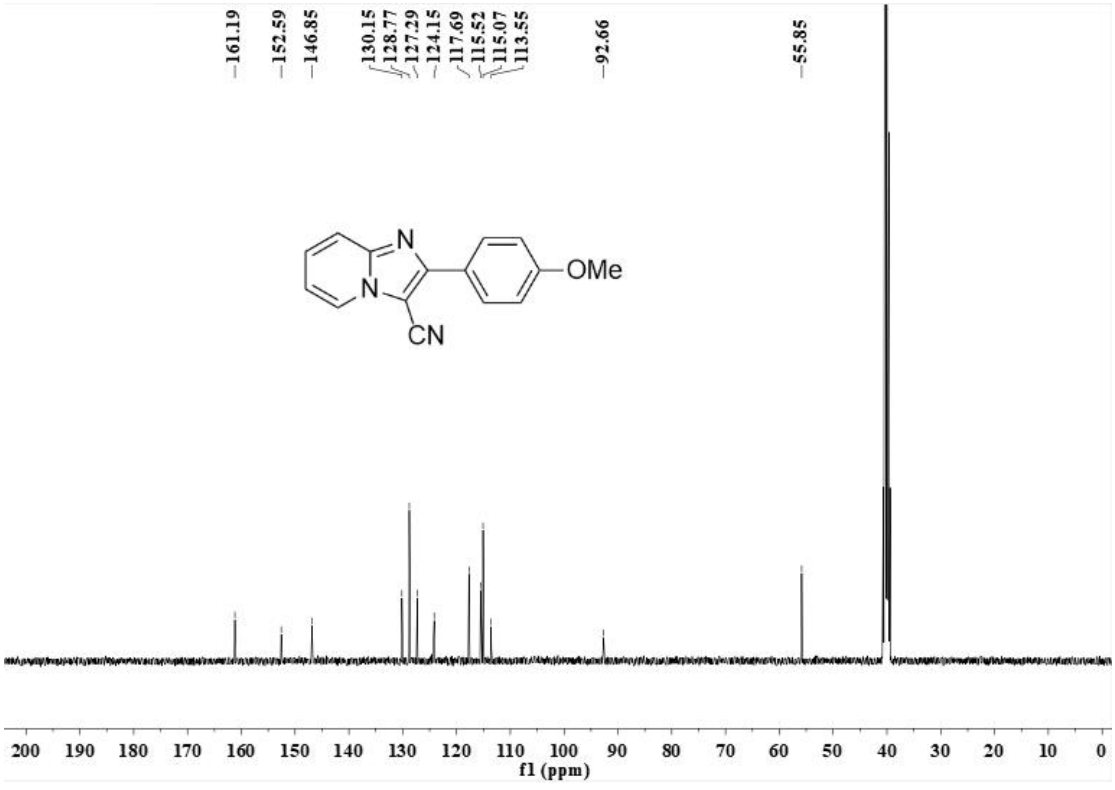

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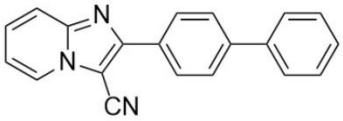

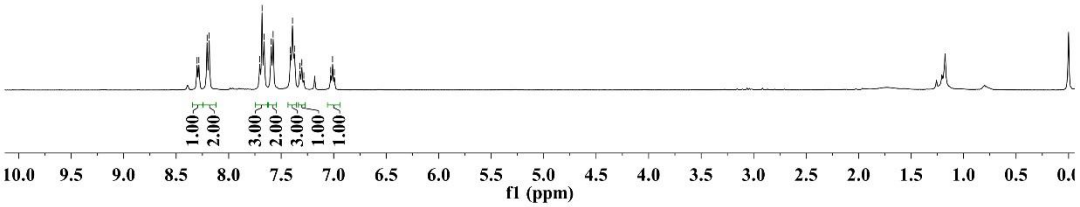

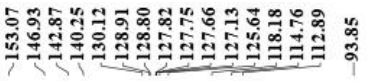

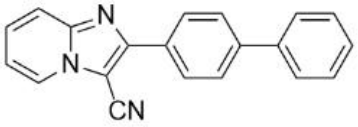

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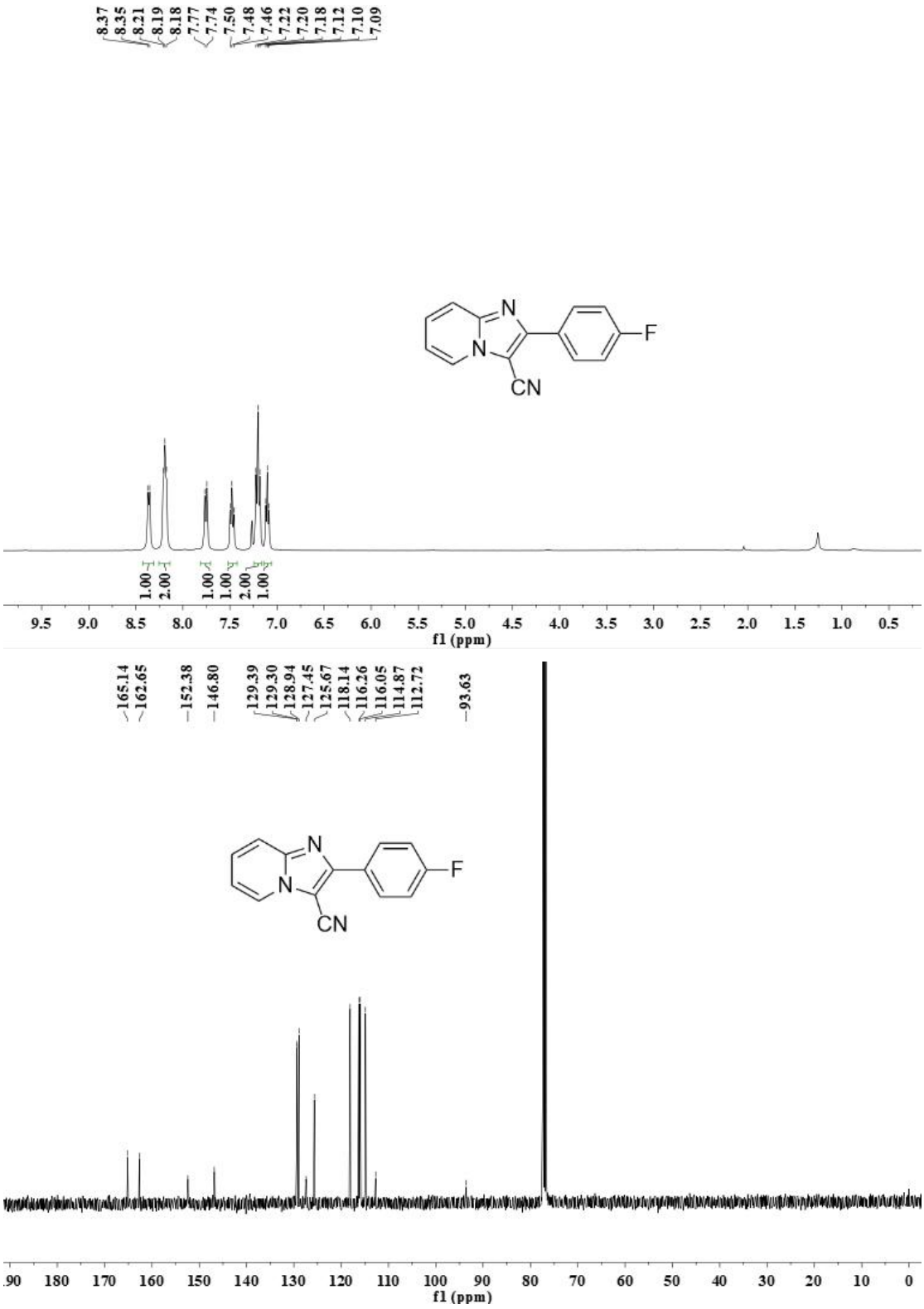

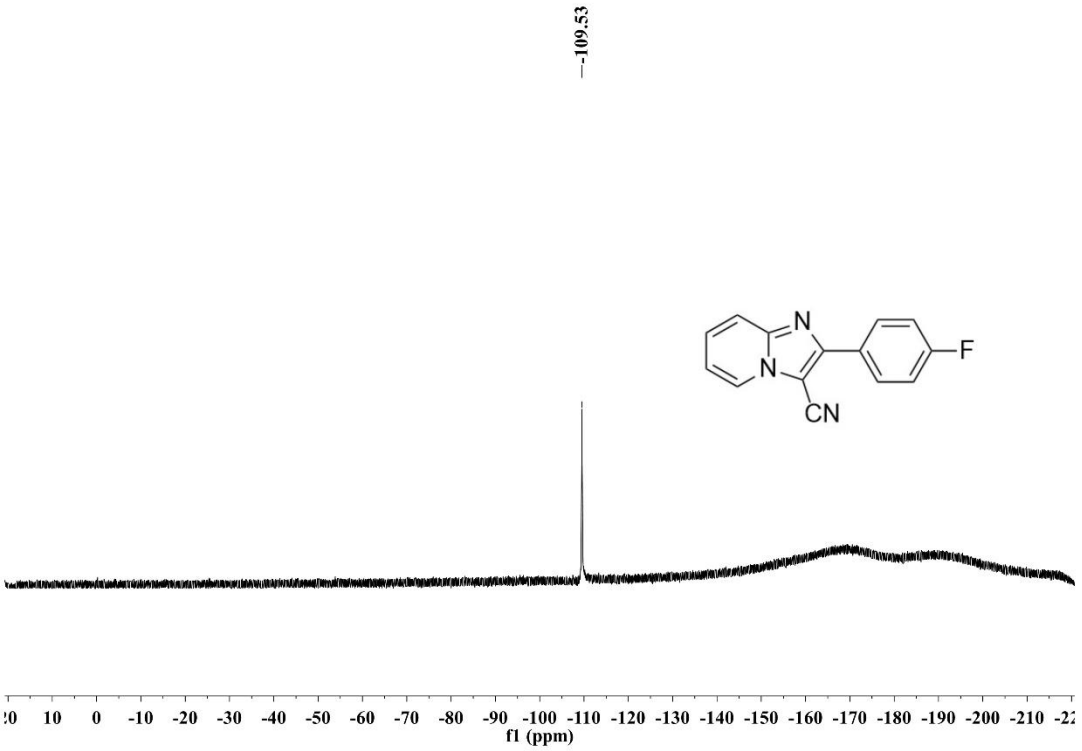

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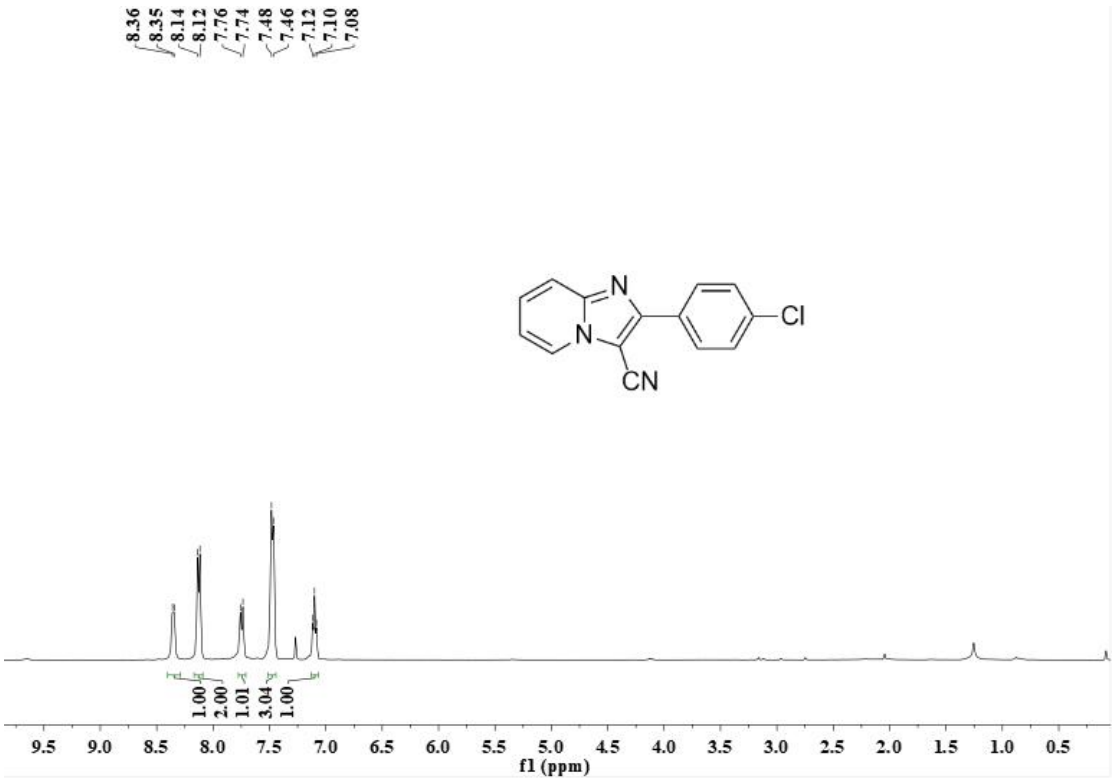

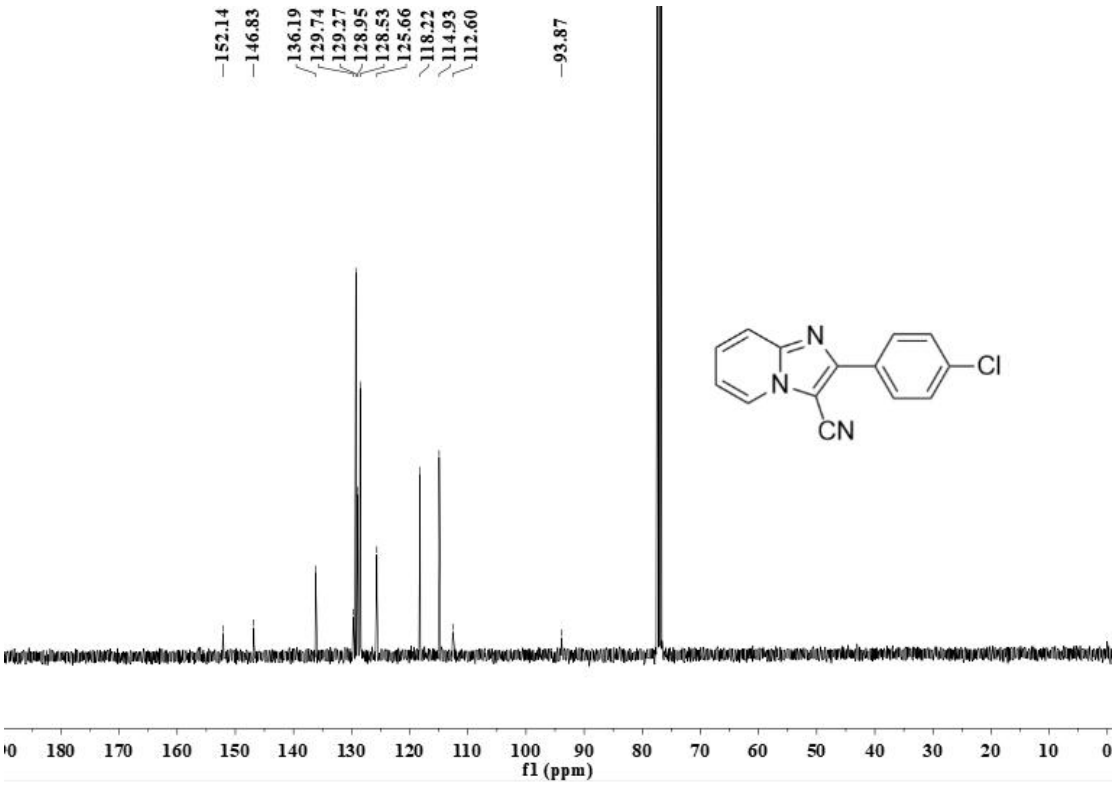

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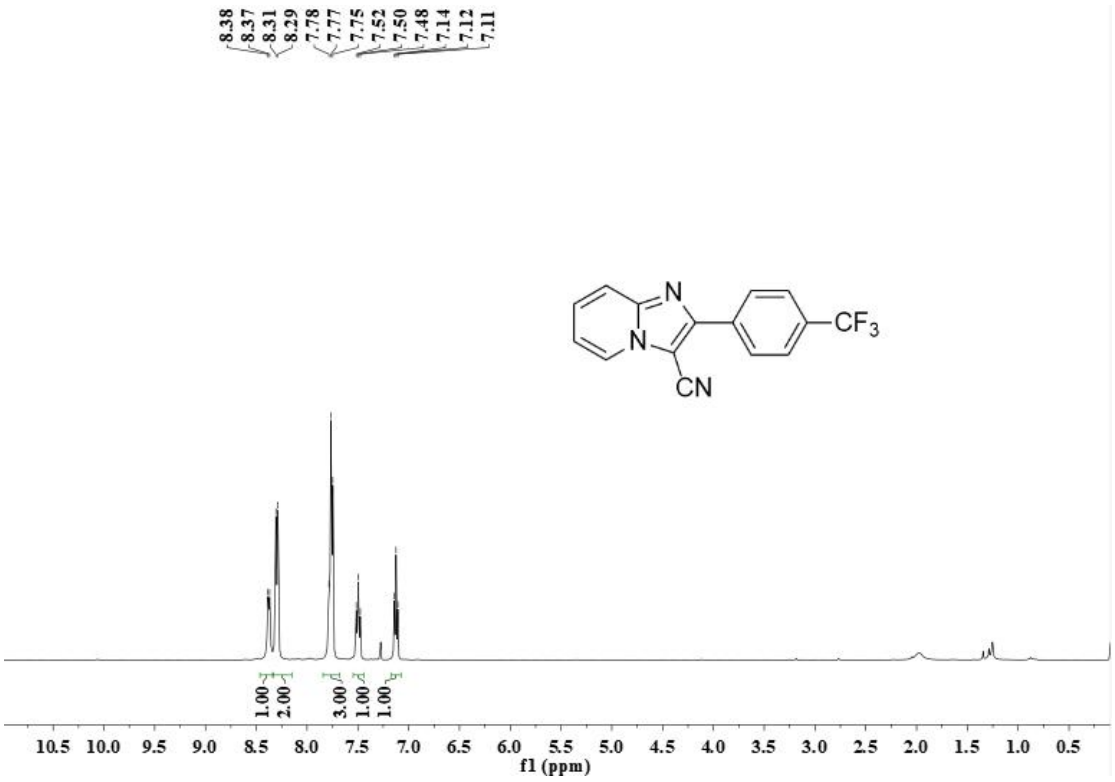

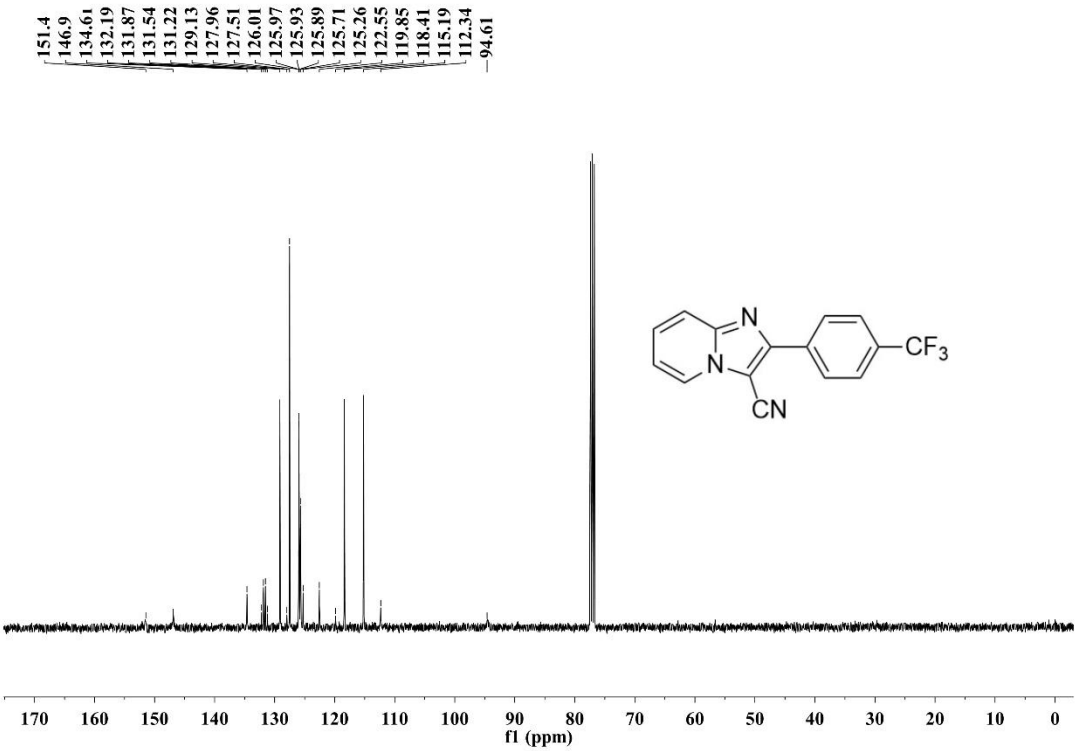
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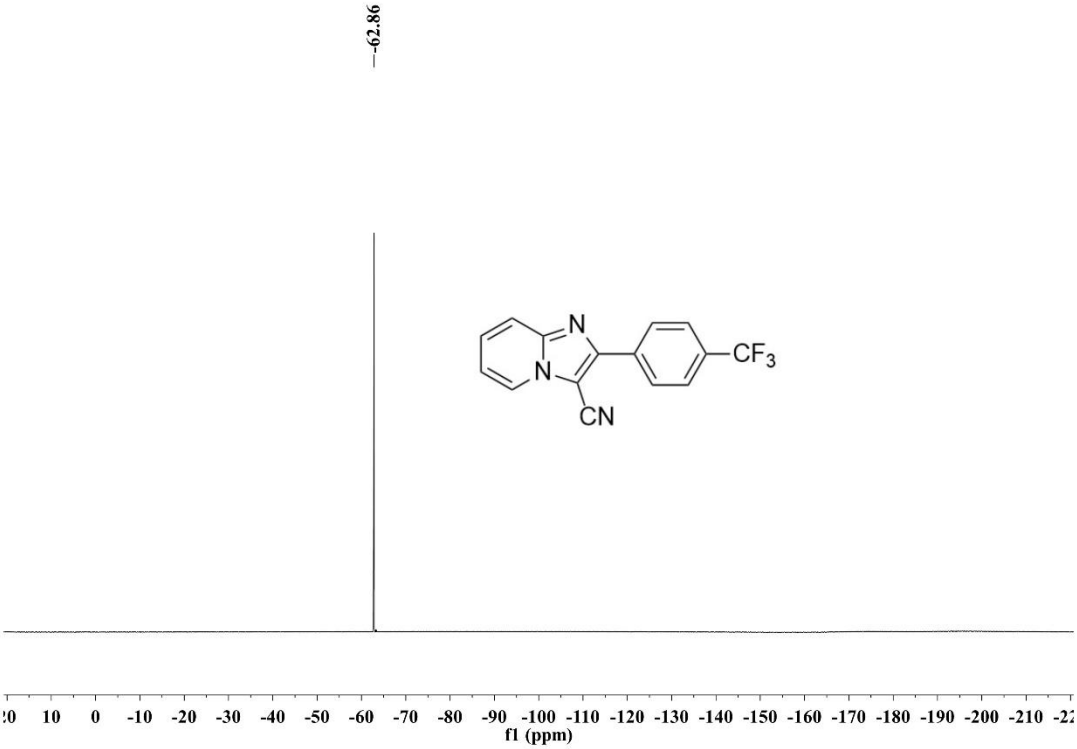
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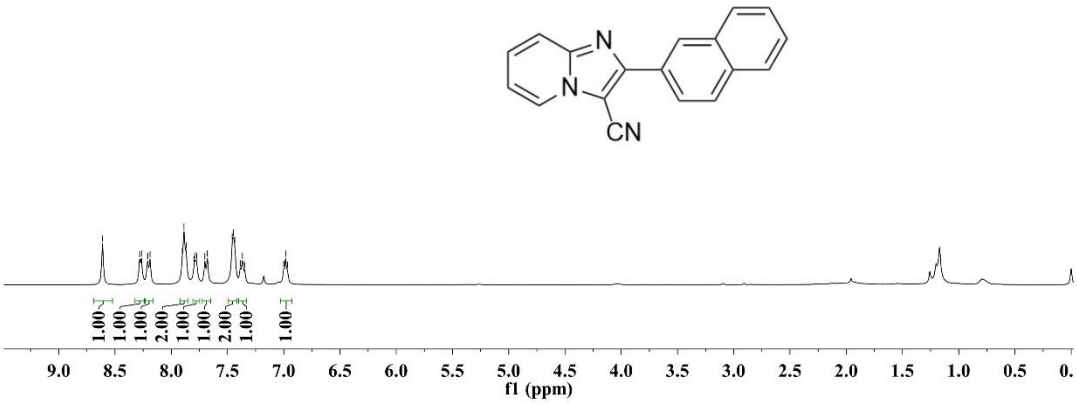
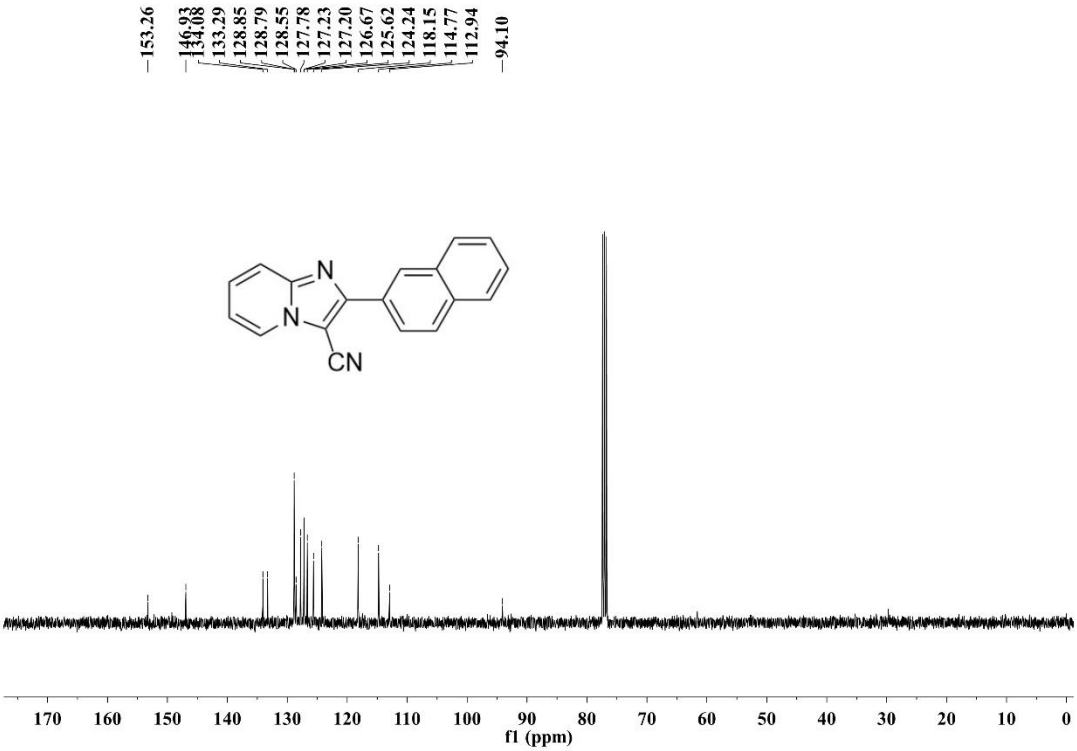
2-(naphthalen-2-yl)imidazo[1,2-a]pyridine-3-carbonitrile (2p)





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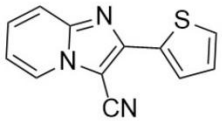

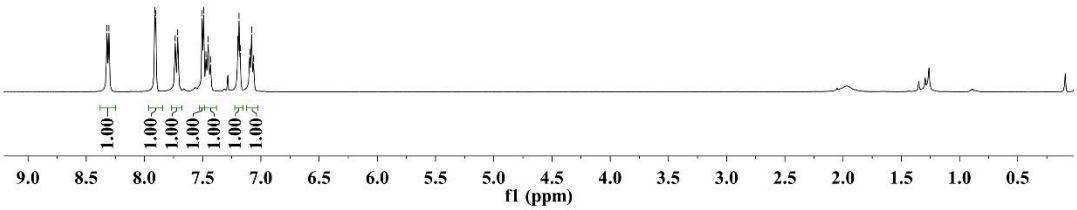

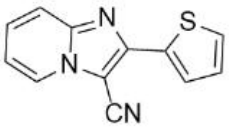

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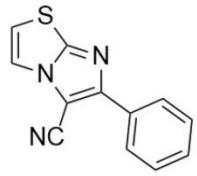
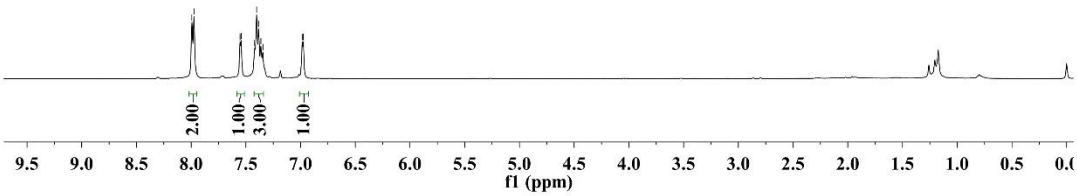
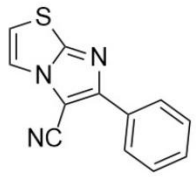
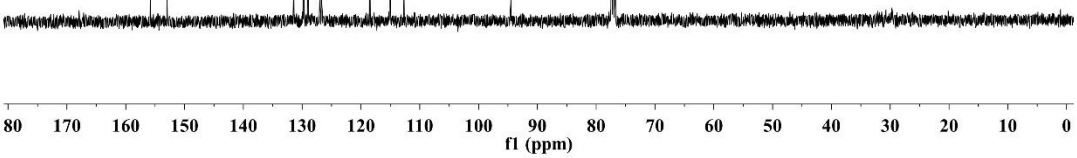
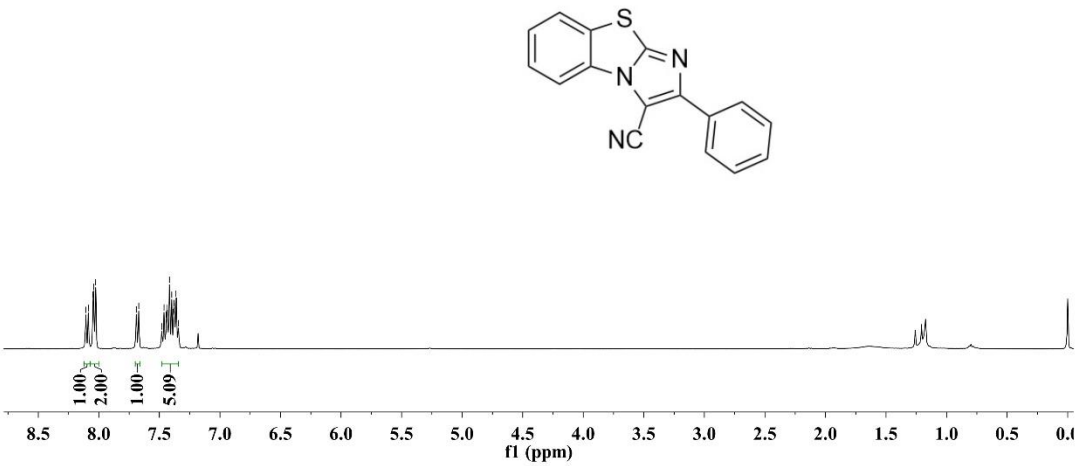


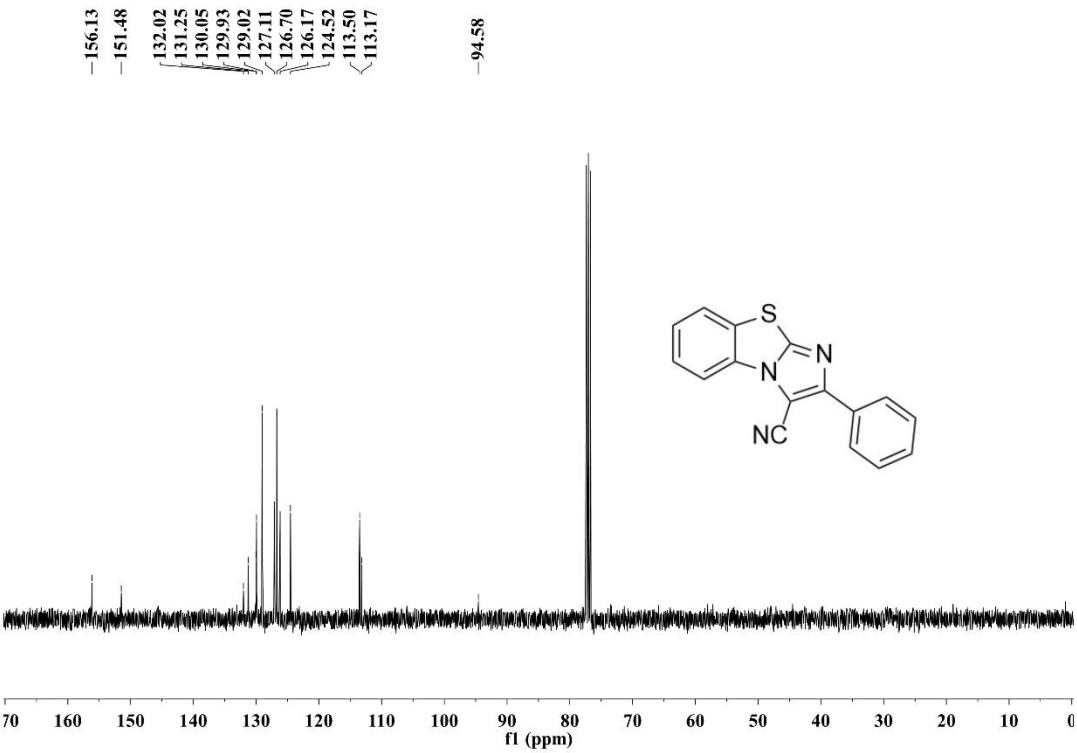




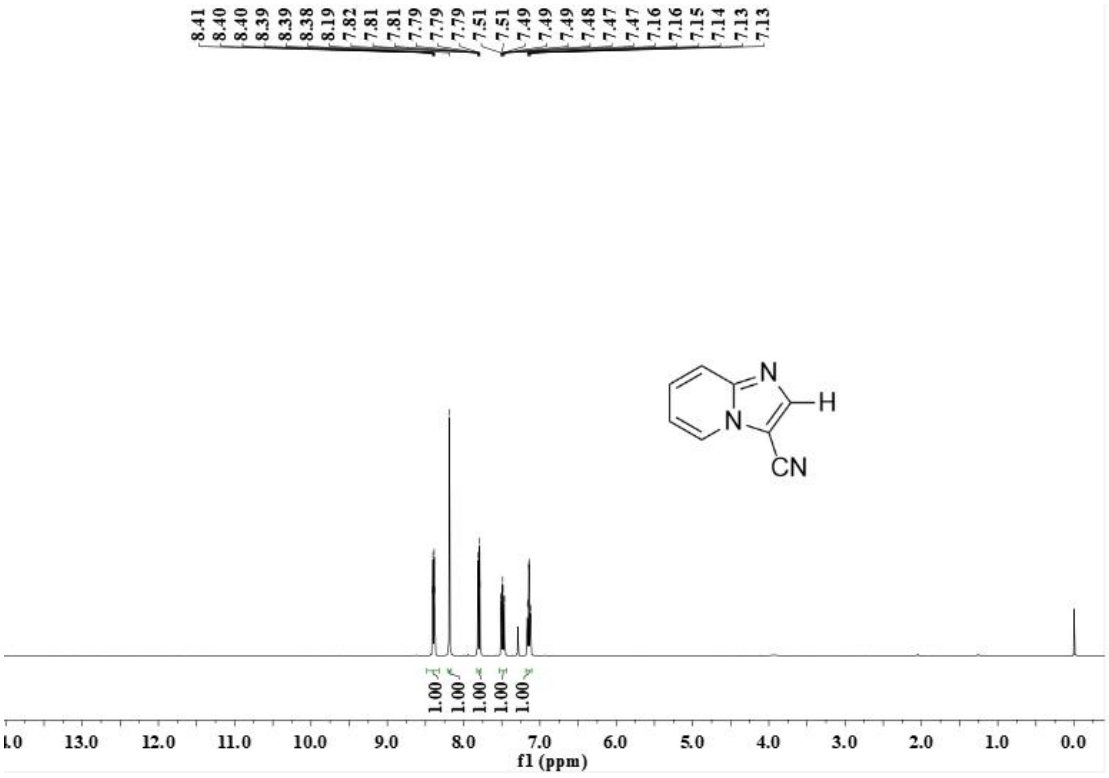


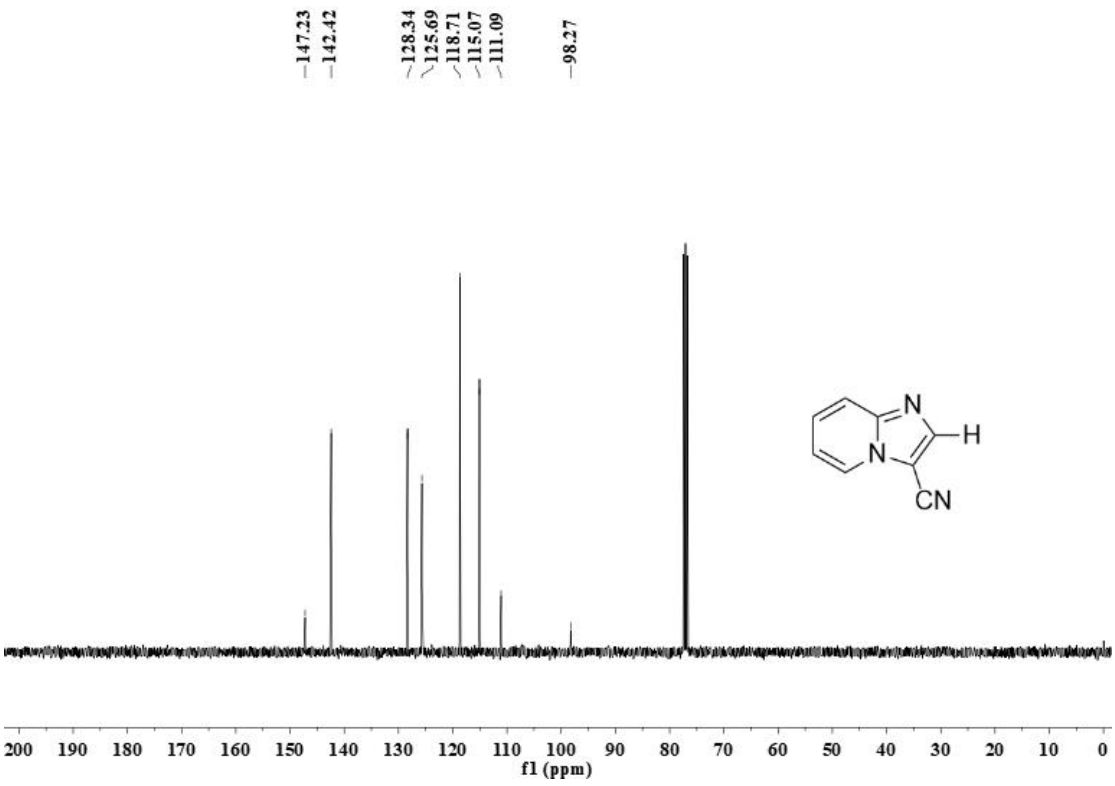
2-phenylbenzo[d]imidazo[2,1-b]thiazole-3-carbonitrile (2s)



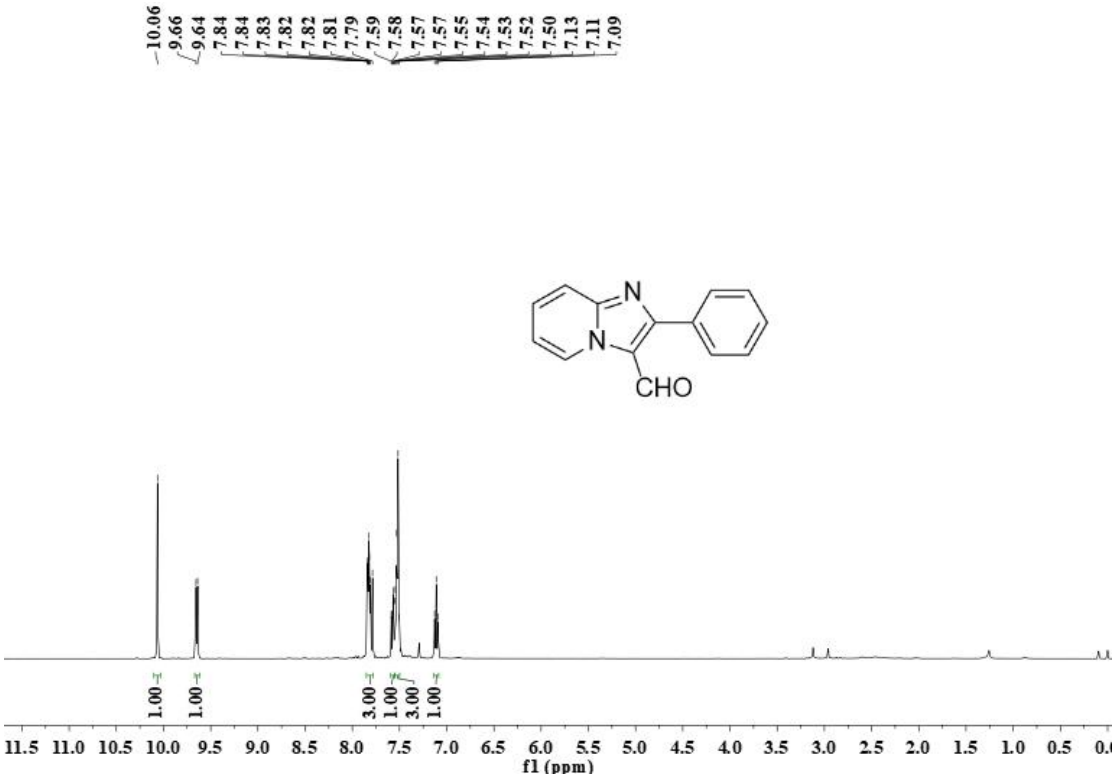


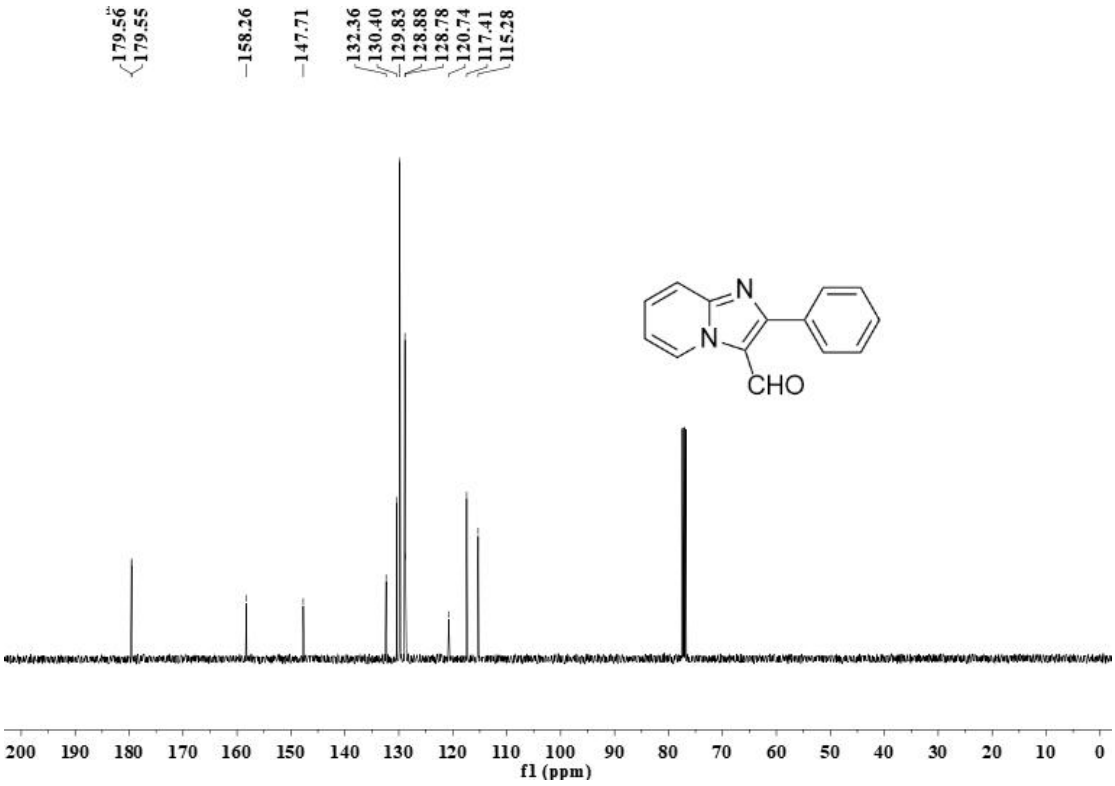
imidazo[1,2-a]pyridine-3-carbonitrile (2t)



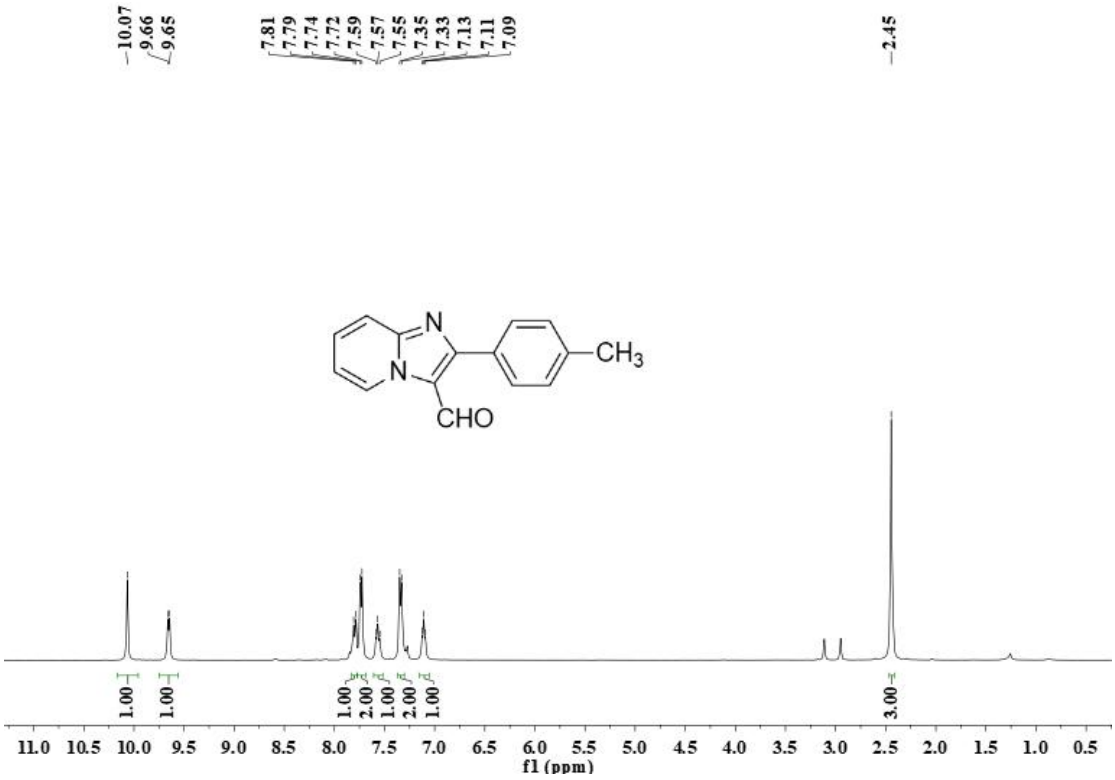


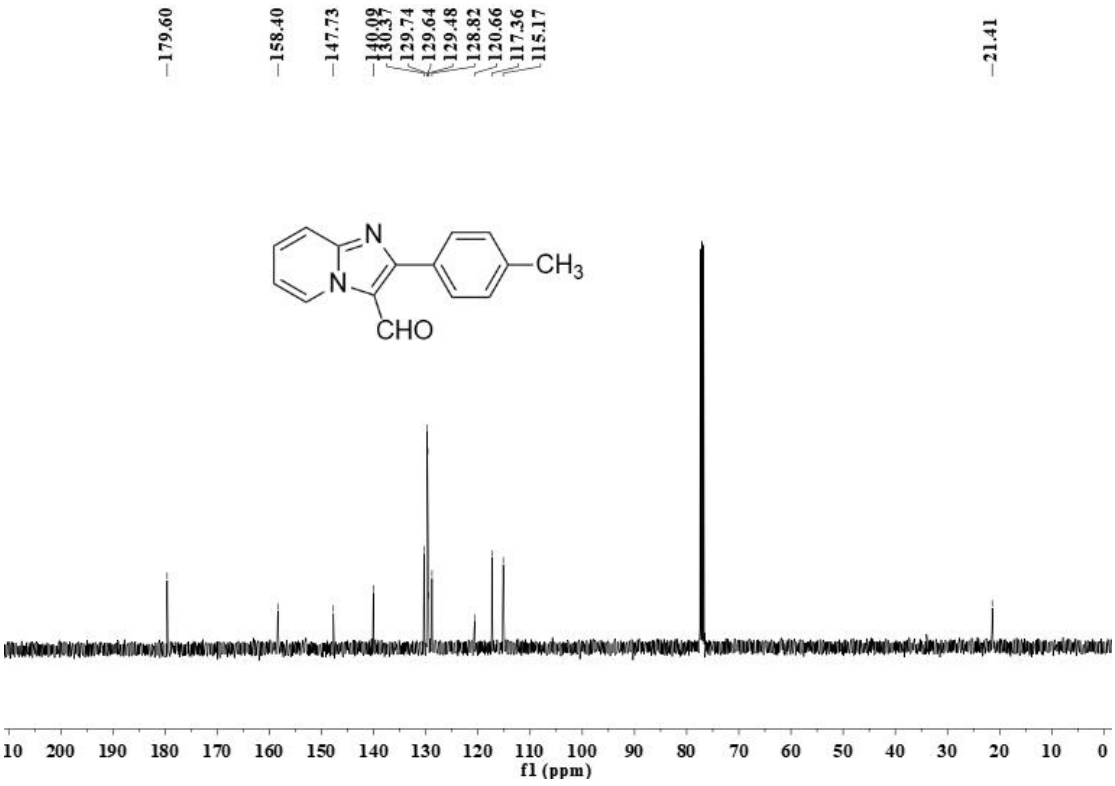
2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (3a)



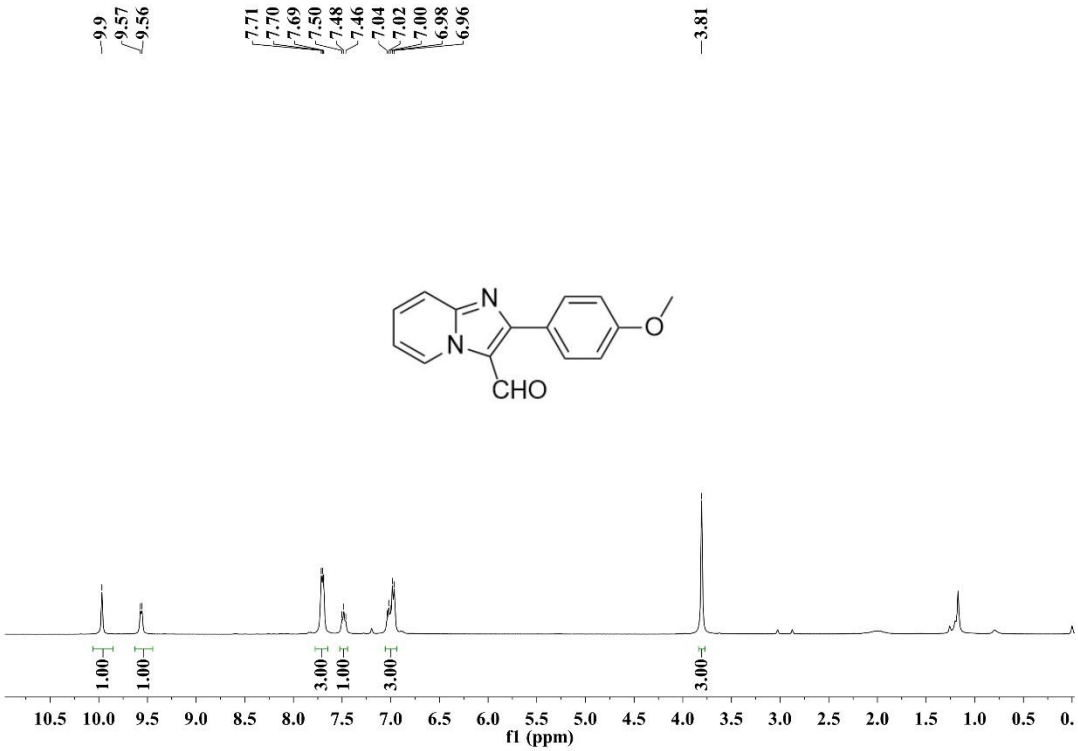


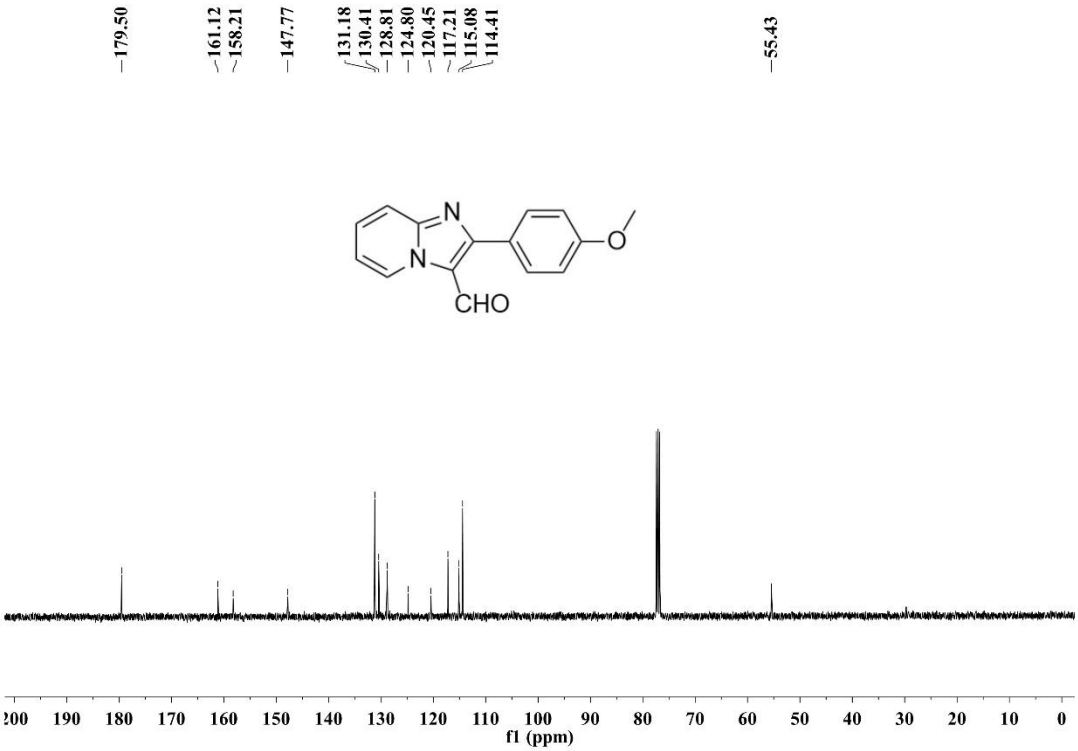
2-(p-tolyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3b)



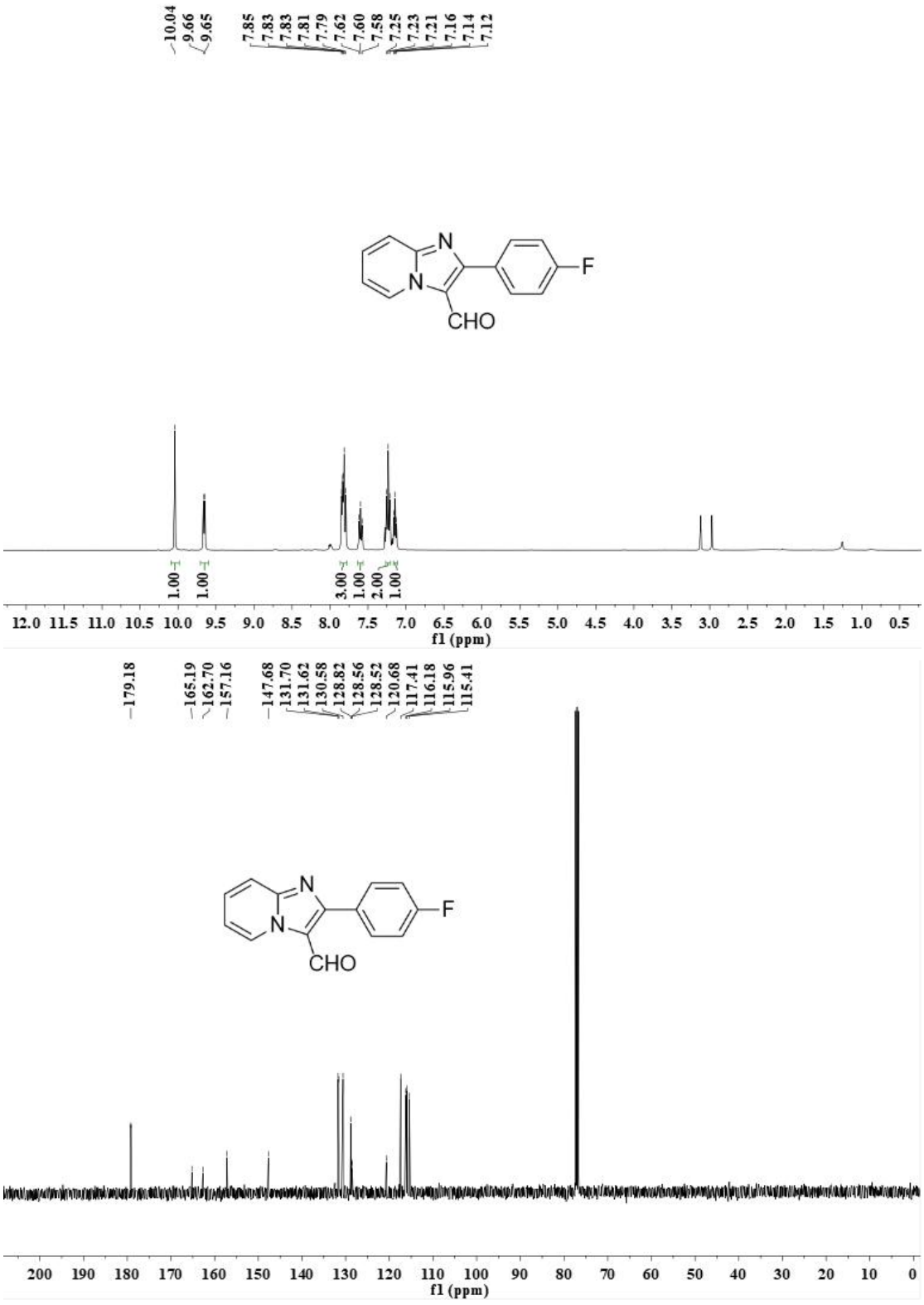


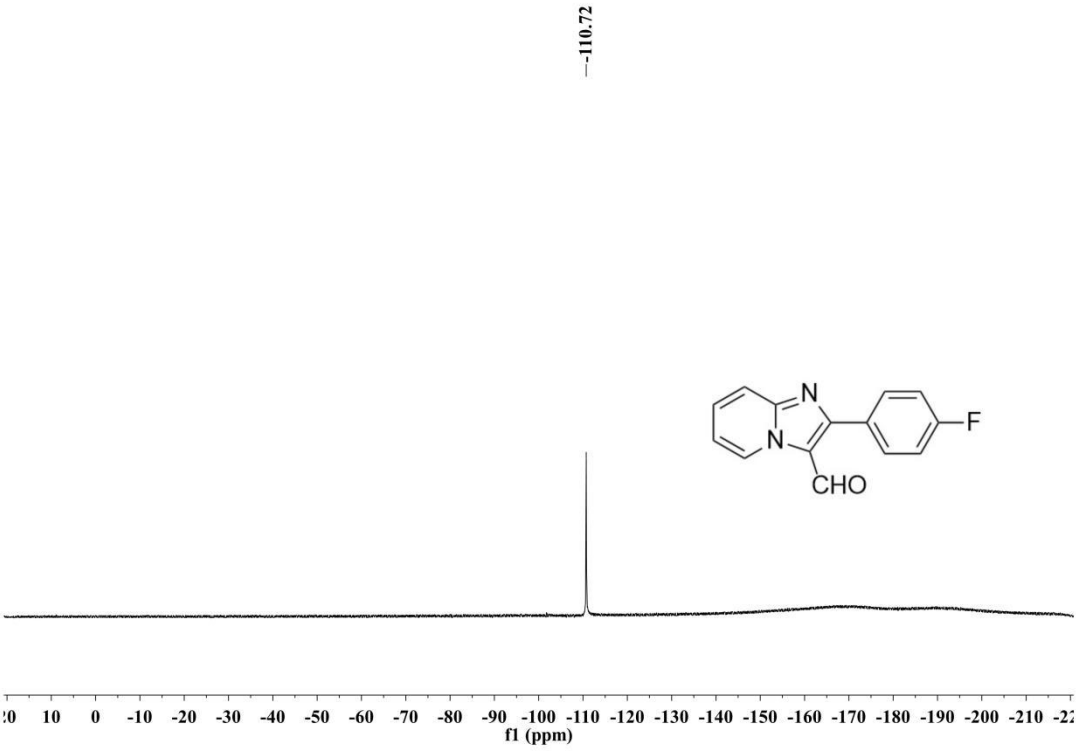
2-(4-methoxyphenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3c)



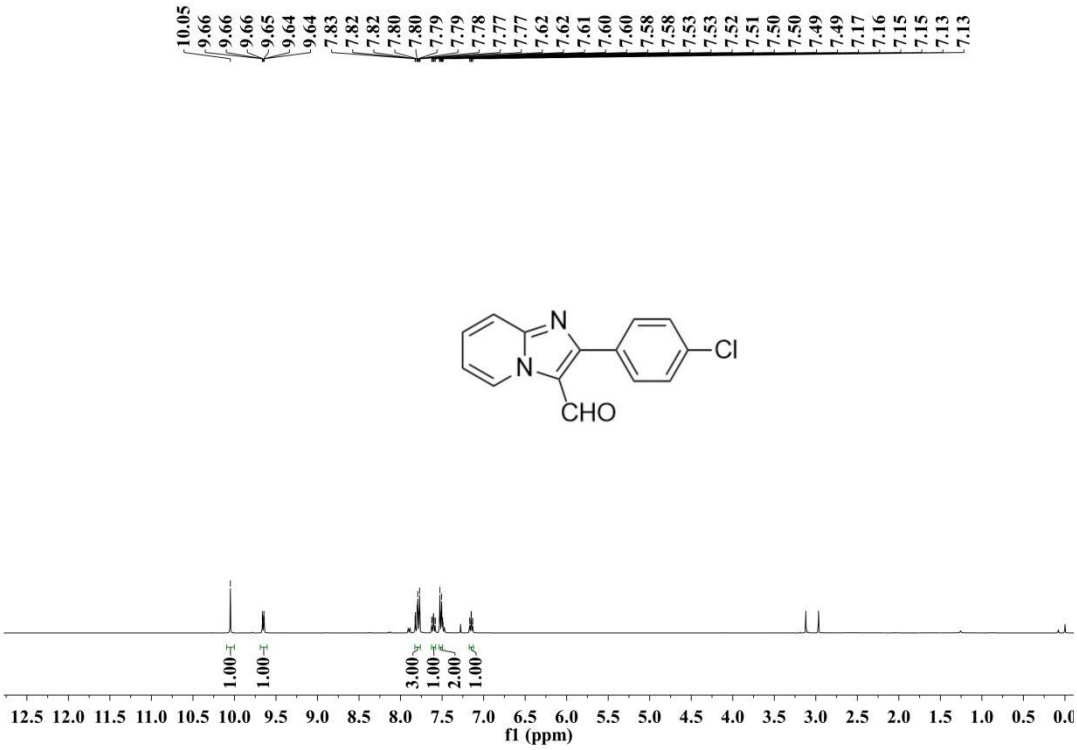


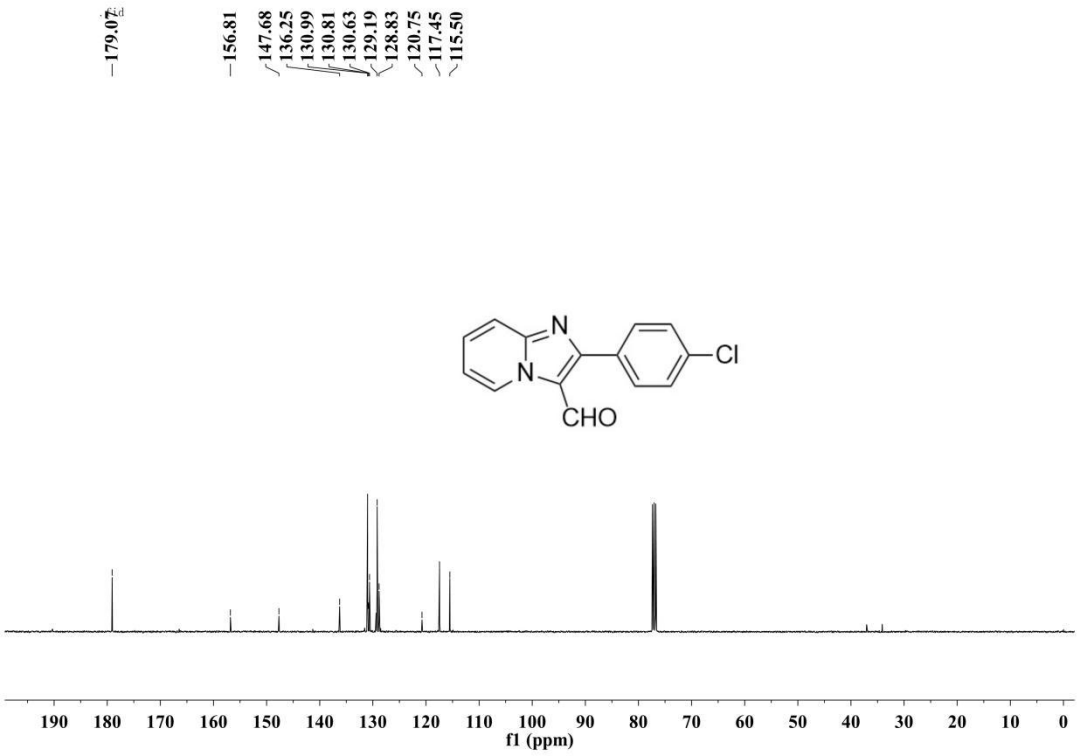
2-(4-fluorophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3d)



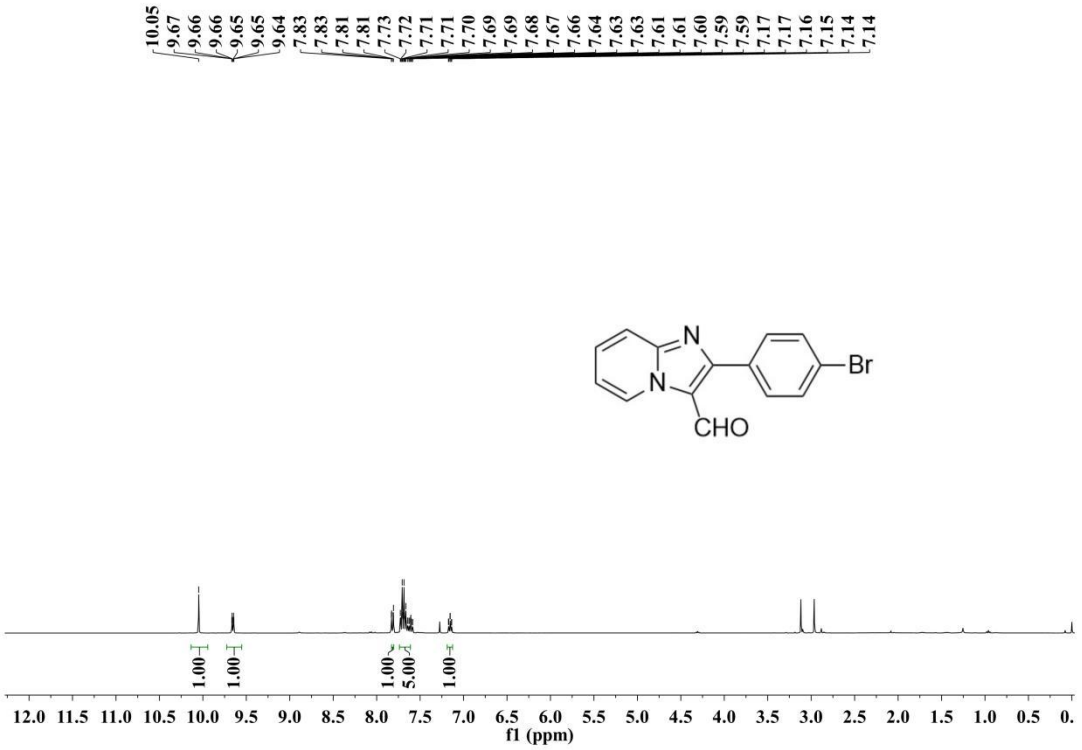


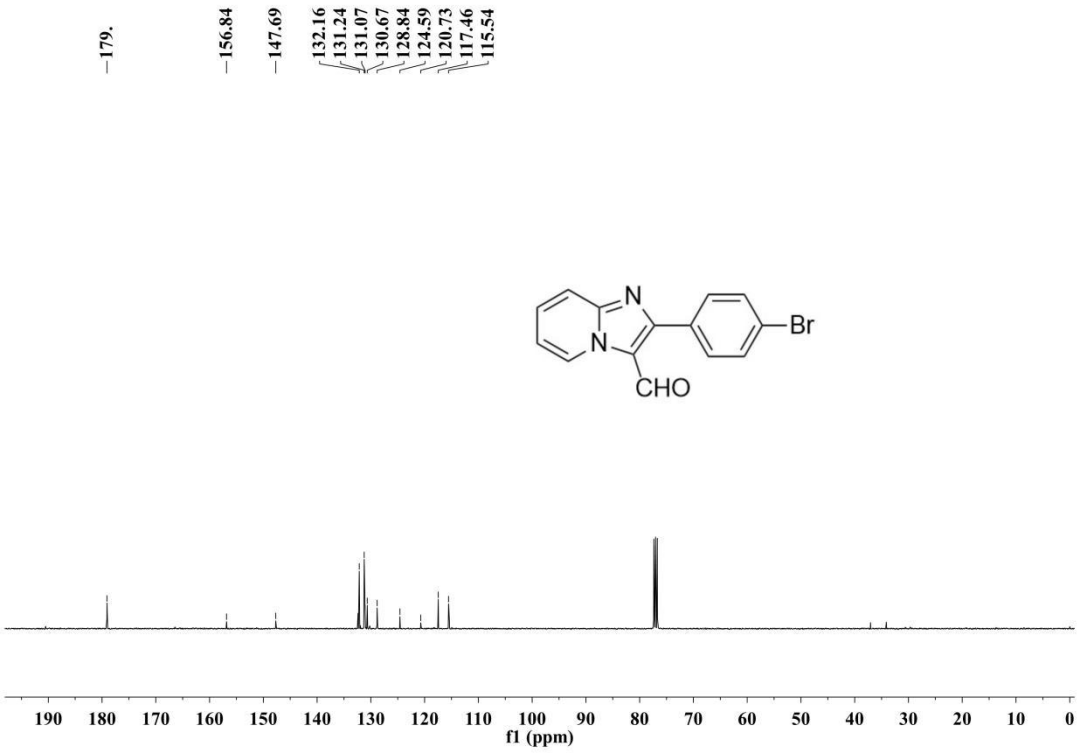
2-(4-chlorophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3e)



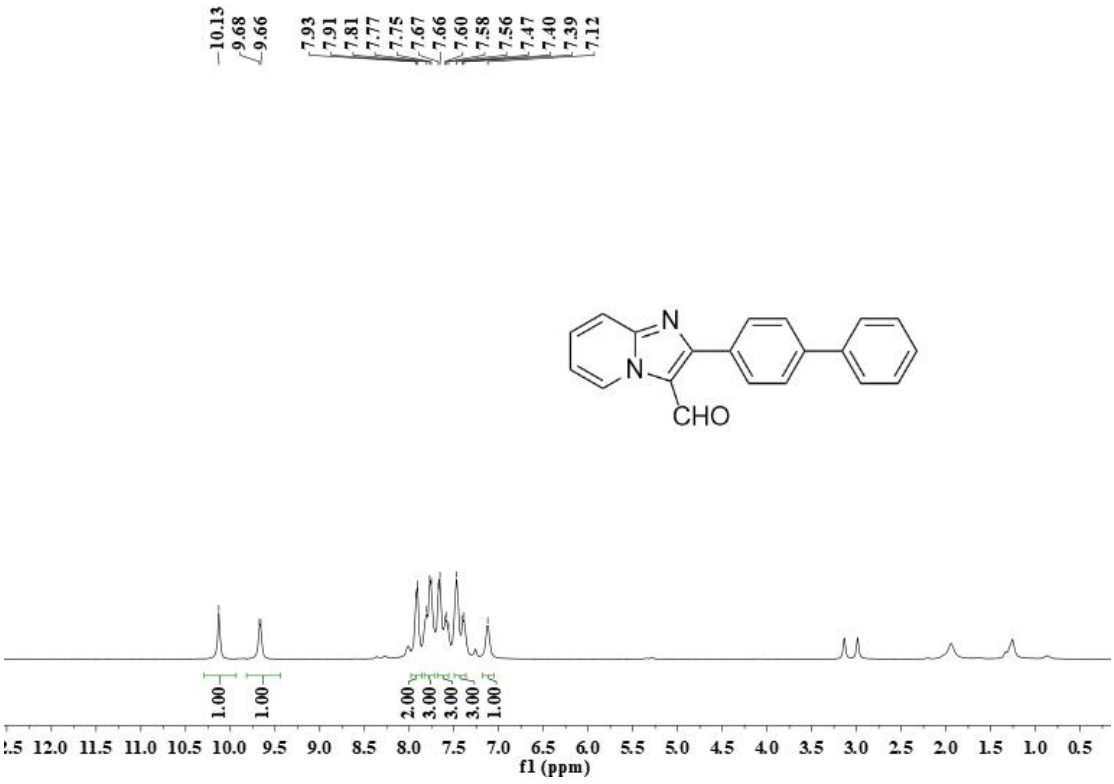


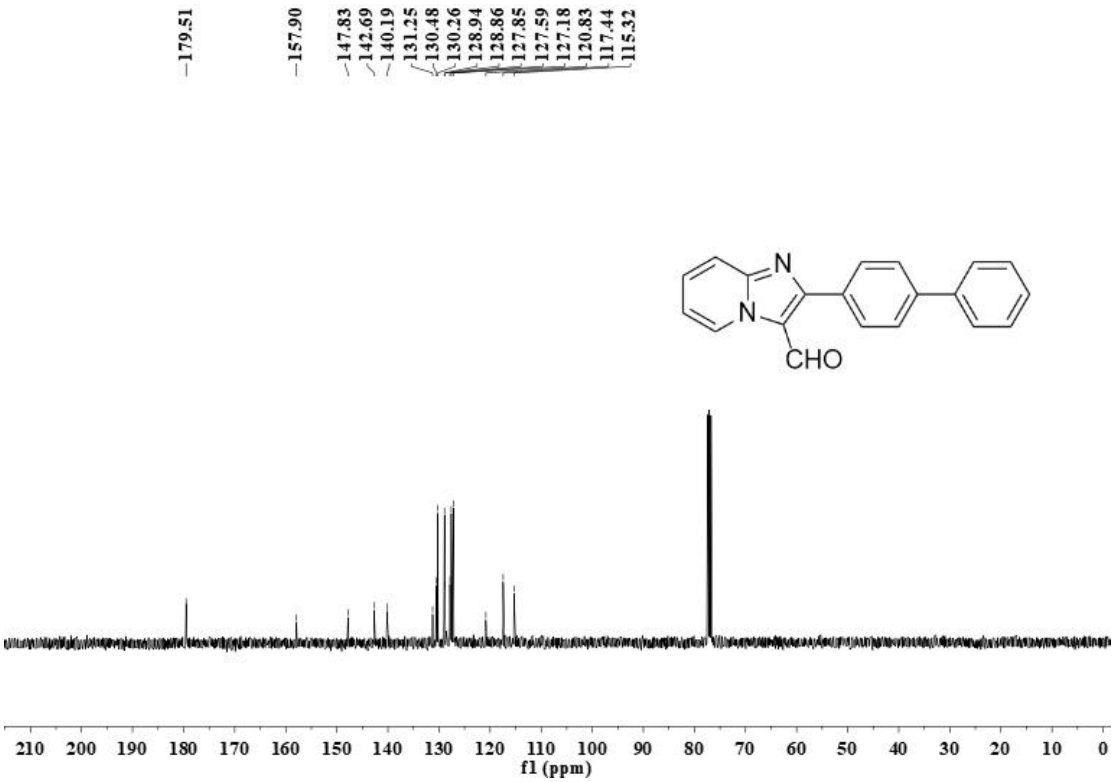
2-(4-bromophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3f)



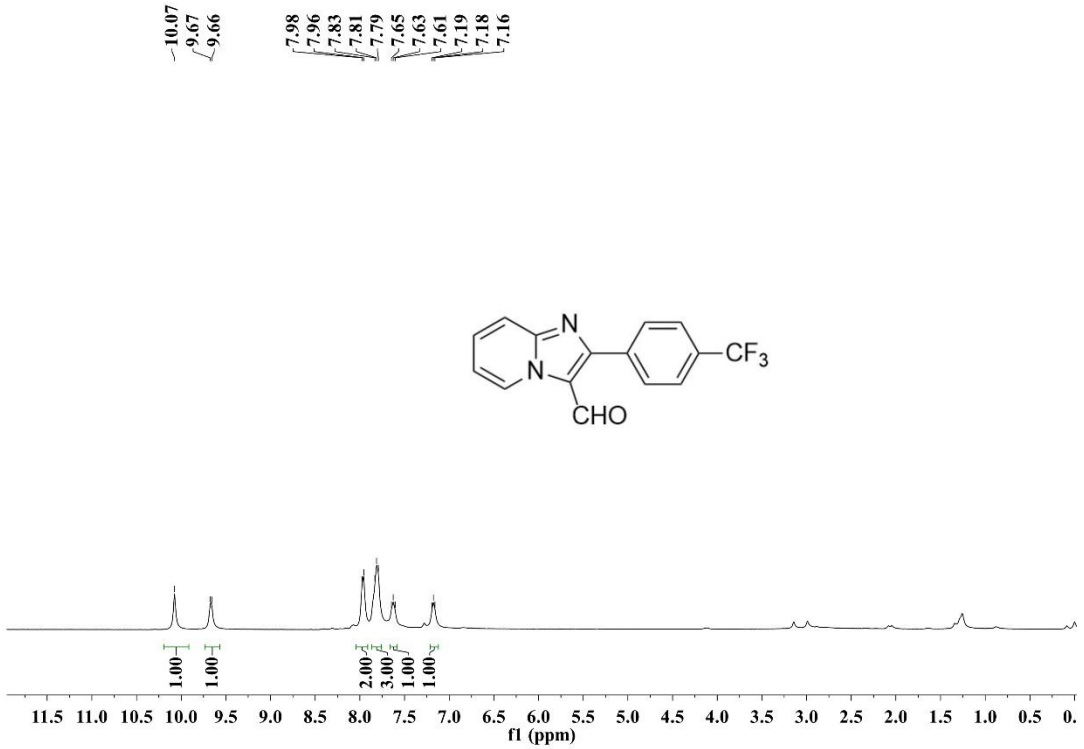


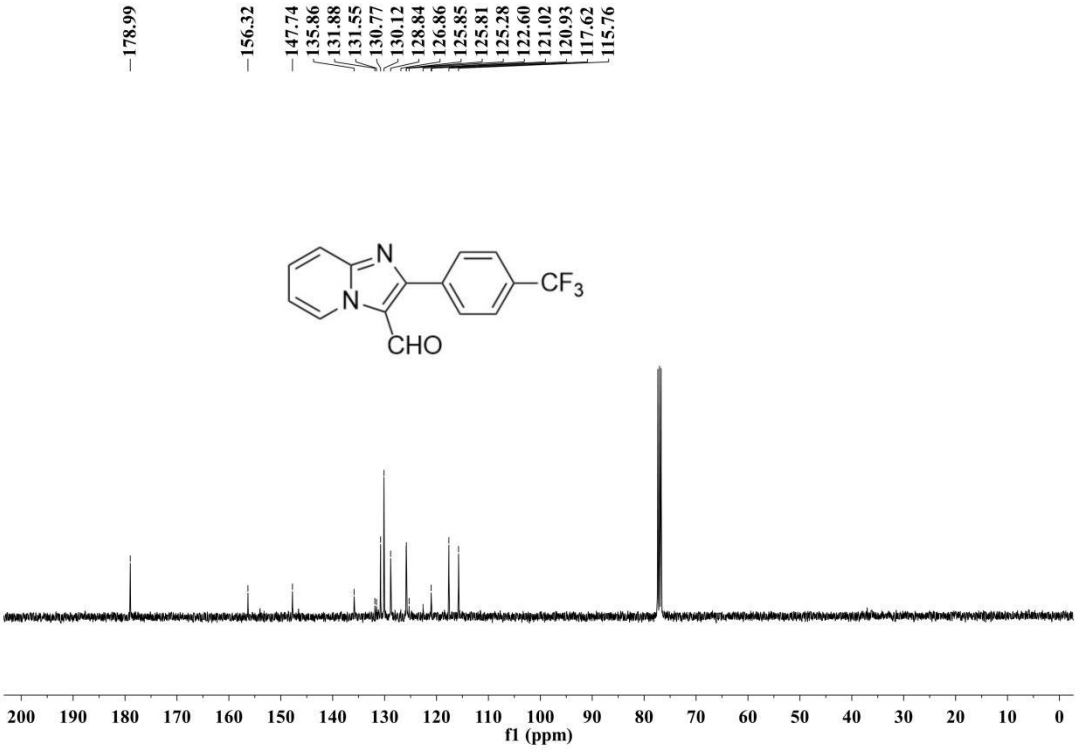
2-([1,1'-biphenyl]-4-yl)imidazo[1,2-a]pyridine-3-carbaldehyde (3g)

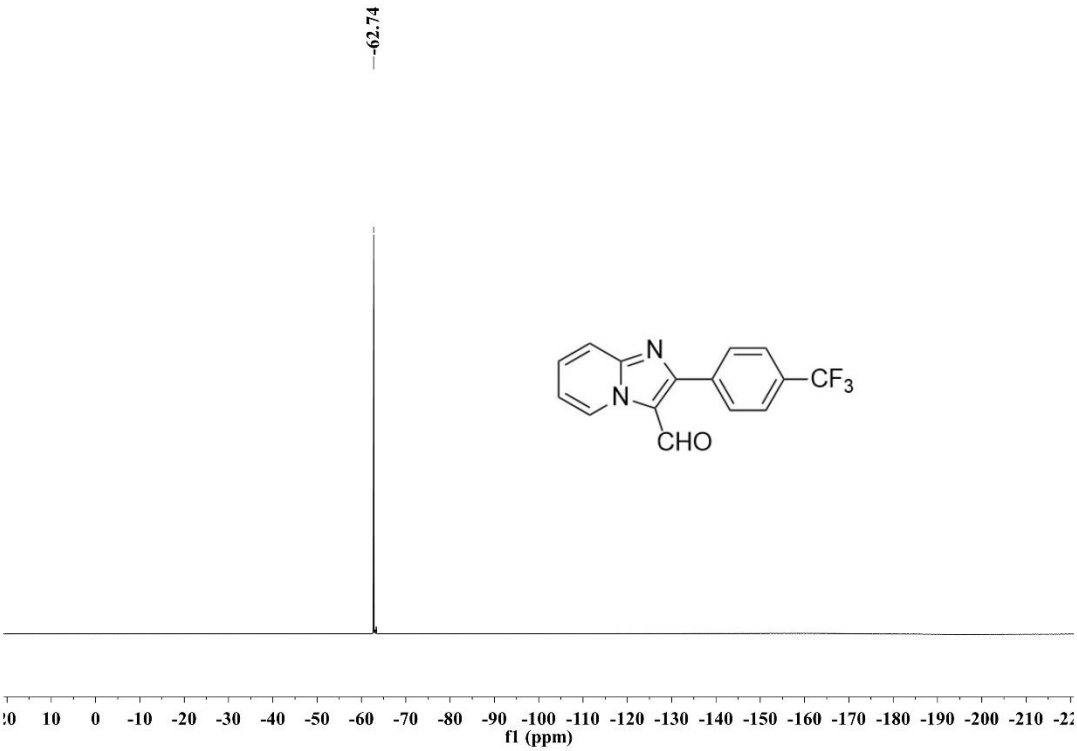




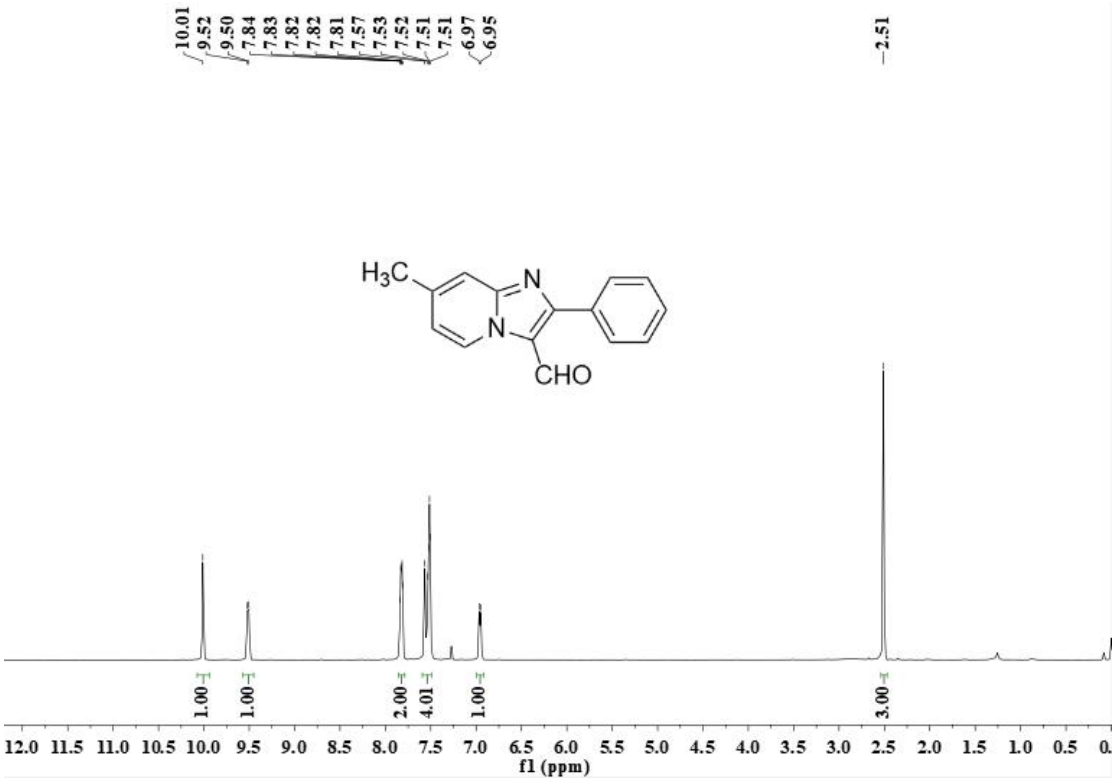
2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3h)

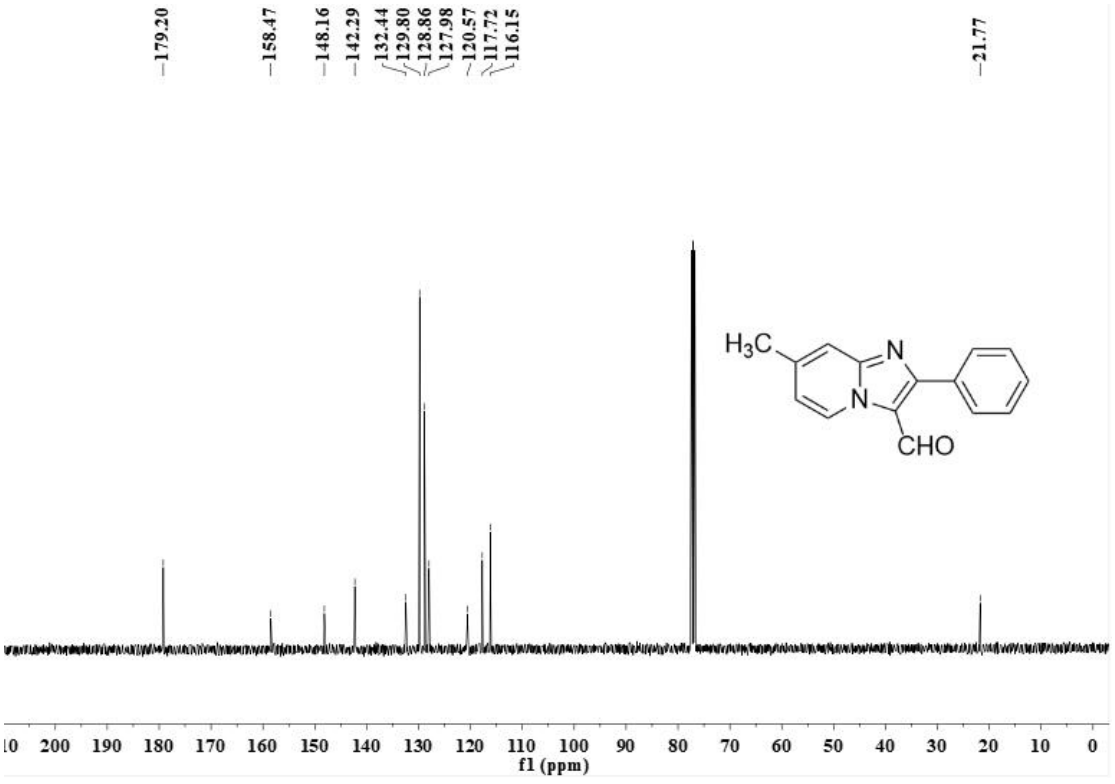



178.99
156.32
147.74
135.86
131.88
131.55
130.77
130.12
128.84
126.86
125.85
125.81
125.28
122.60
121.02
120.93
117.62
115.76
N
N
CF3
CHO
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

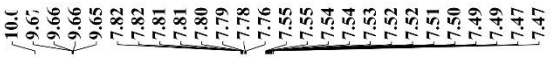

-62.74
N
N
CF3
CHO
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

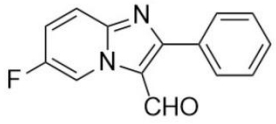
7-methyl-2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (3i)

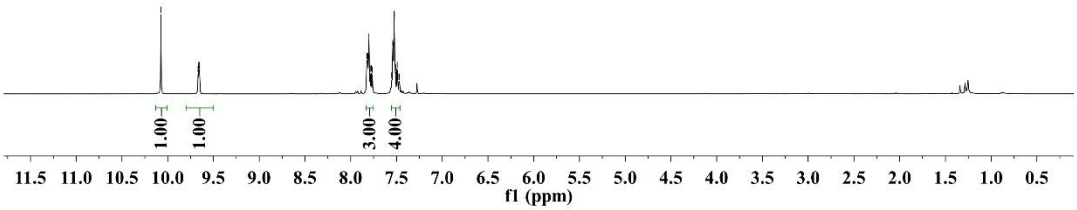


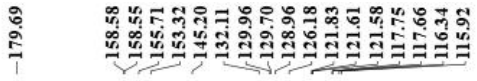


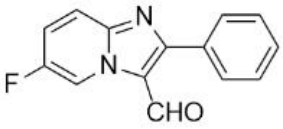
6-fluoro-2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (3j)

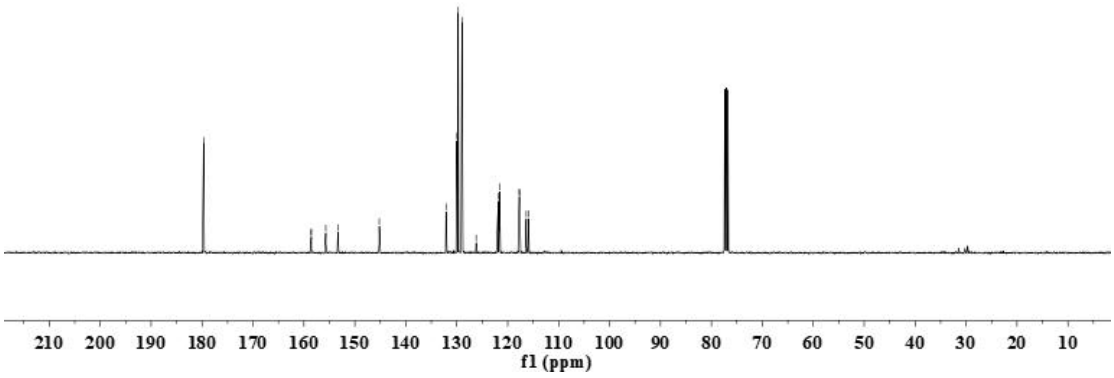


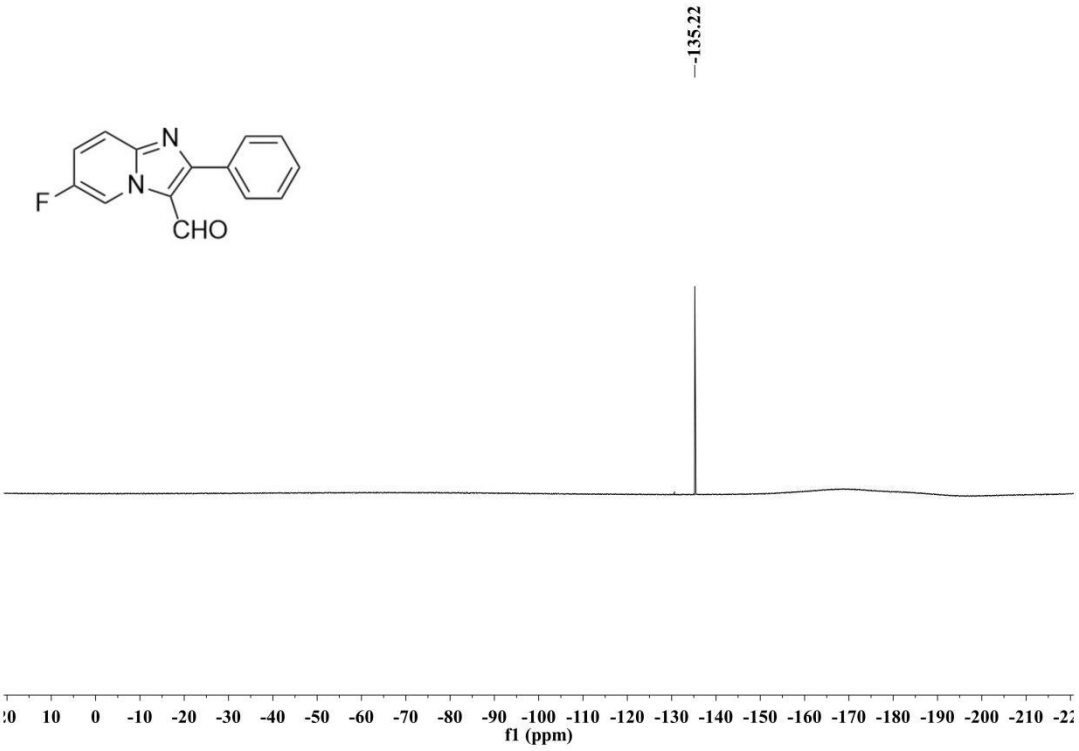




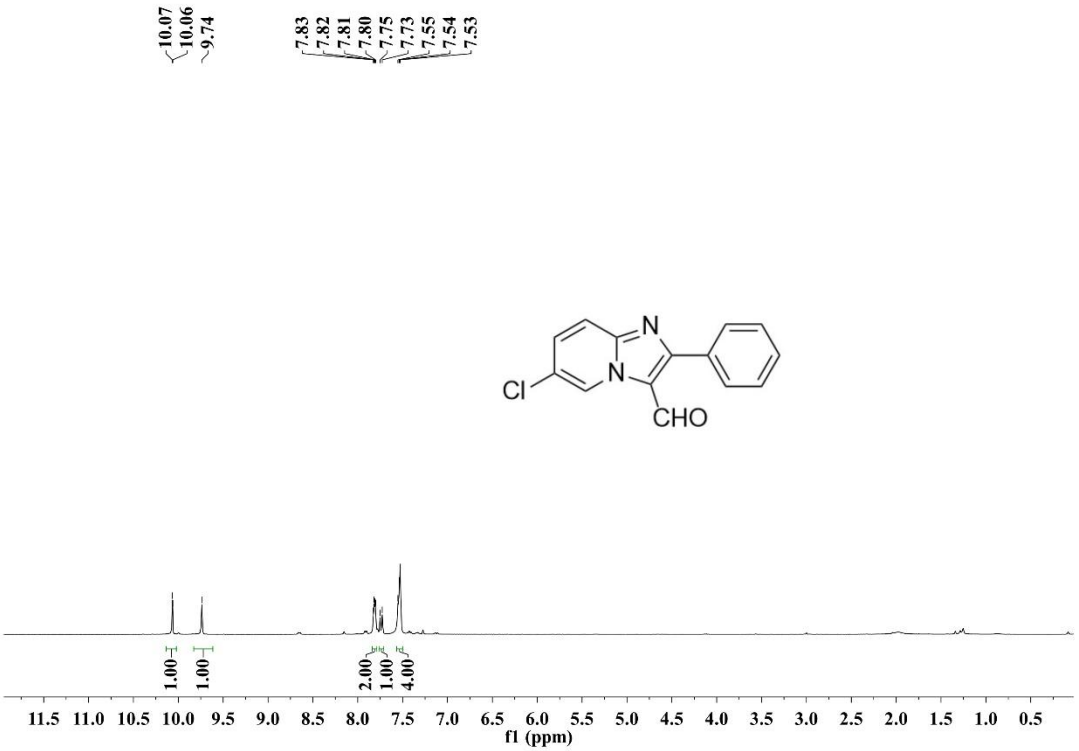


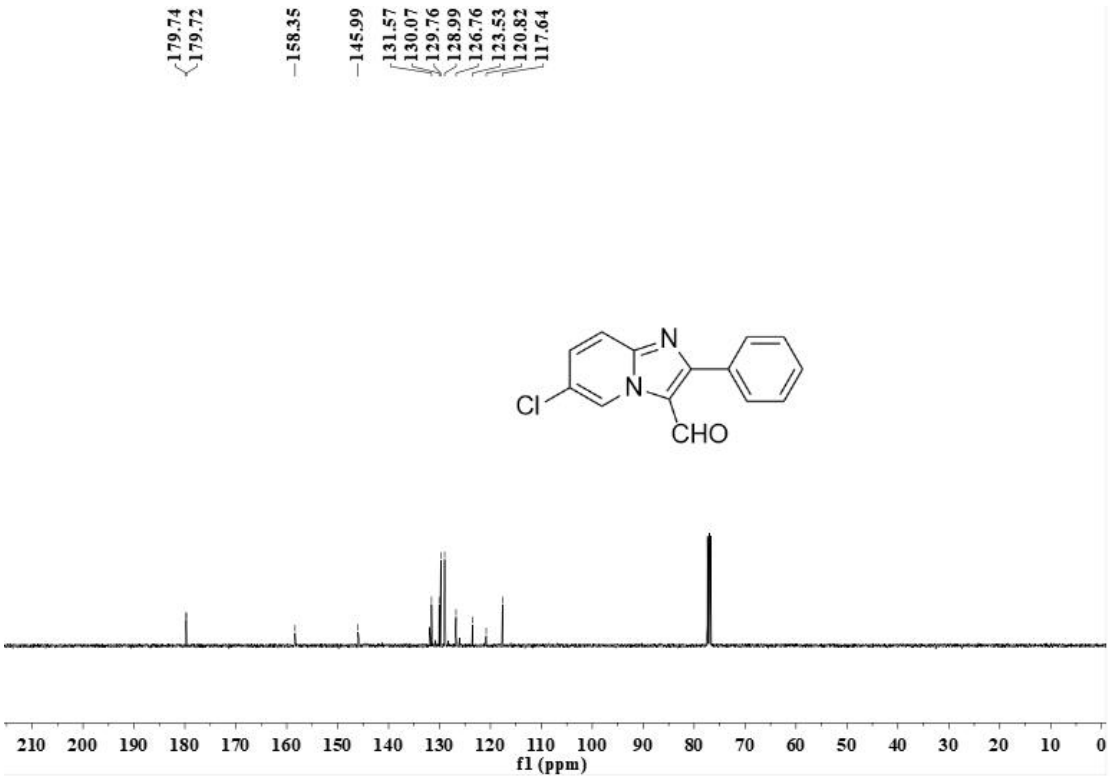




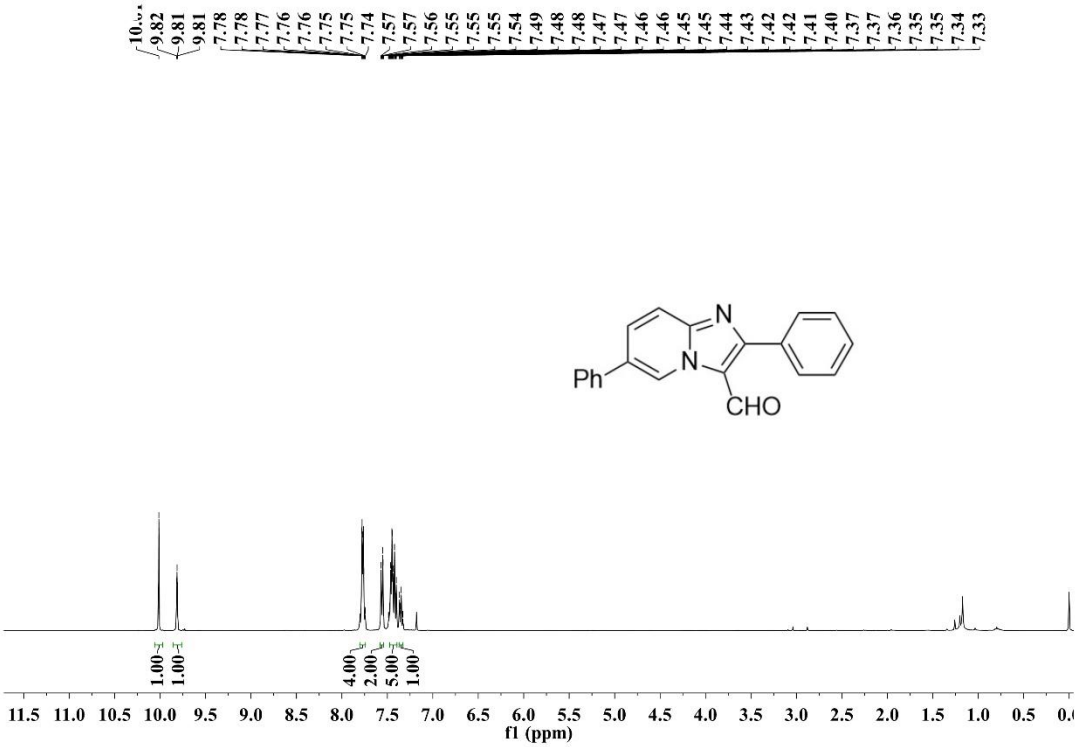


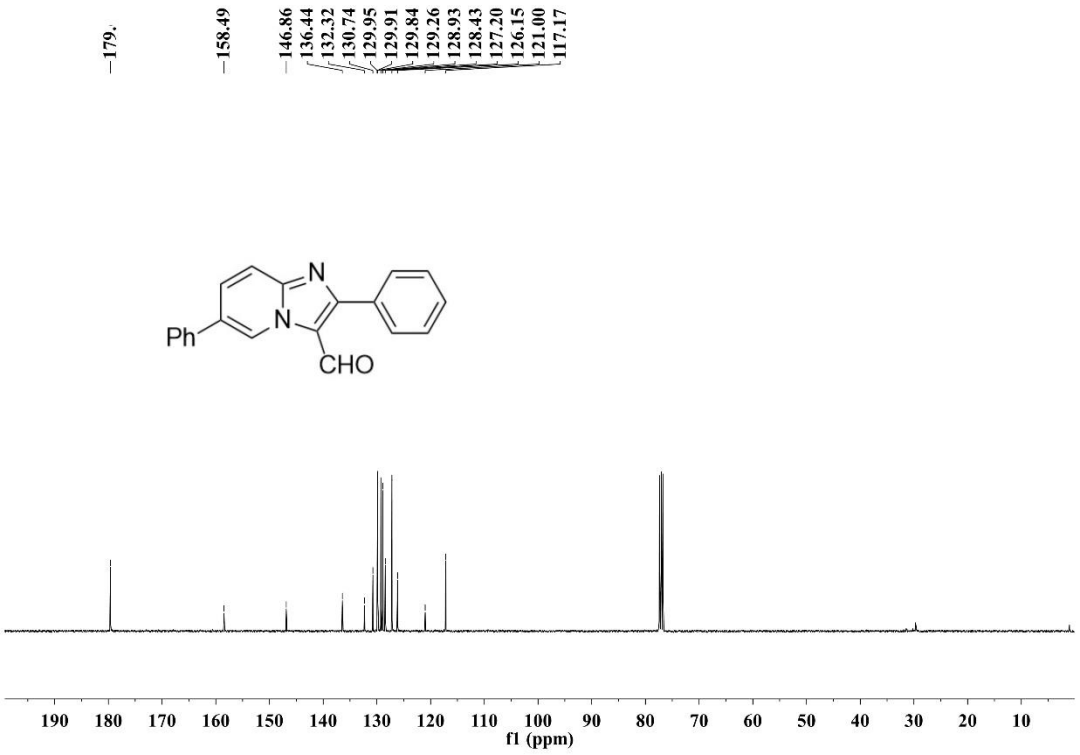
6-chloro-2-phenylimidazo[1,2-a]pyridine-3-carbaldehyde (3k)



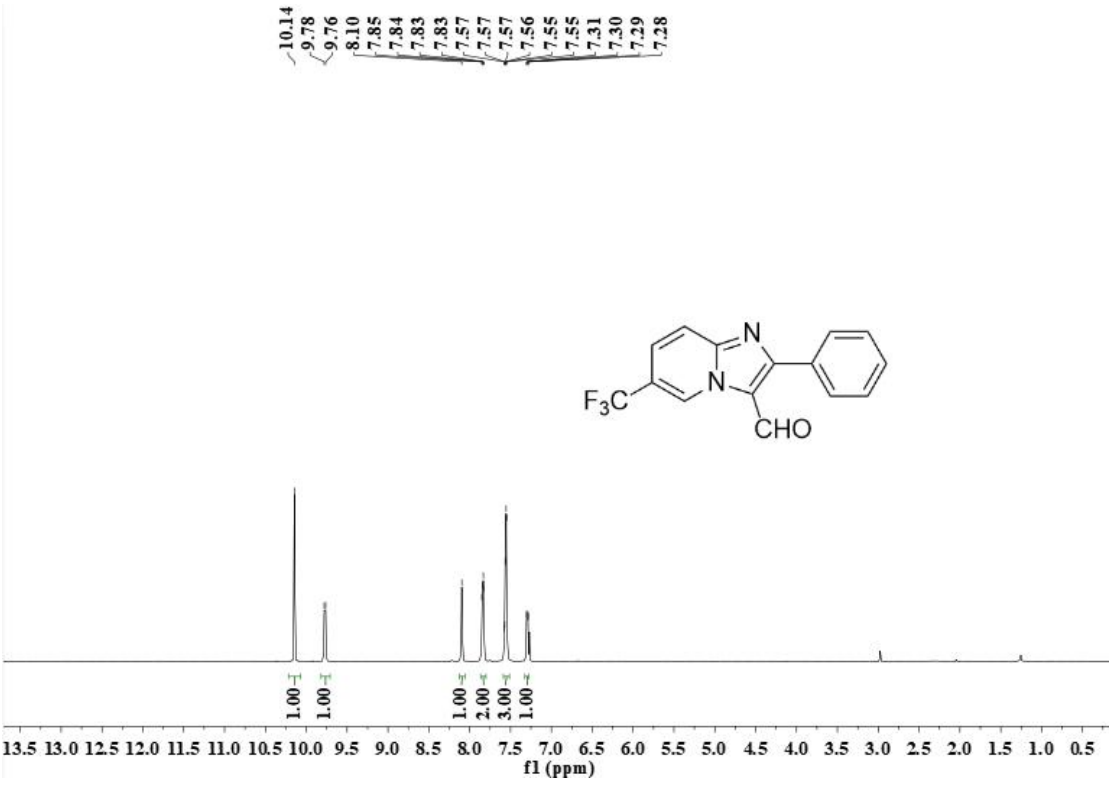


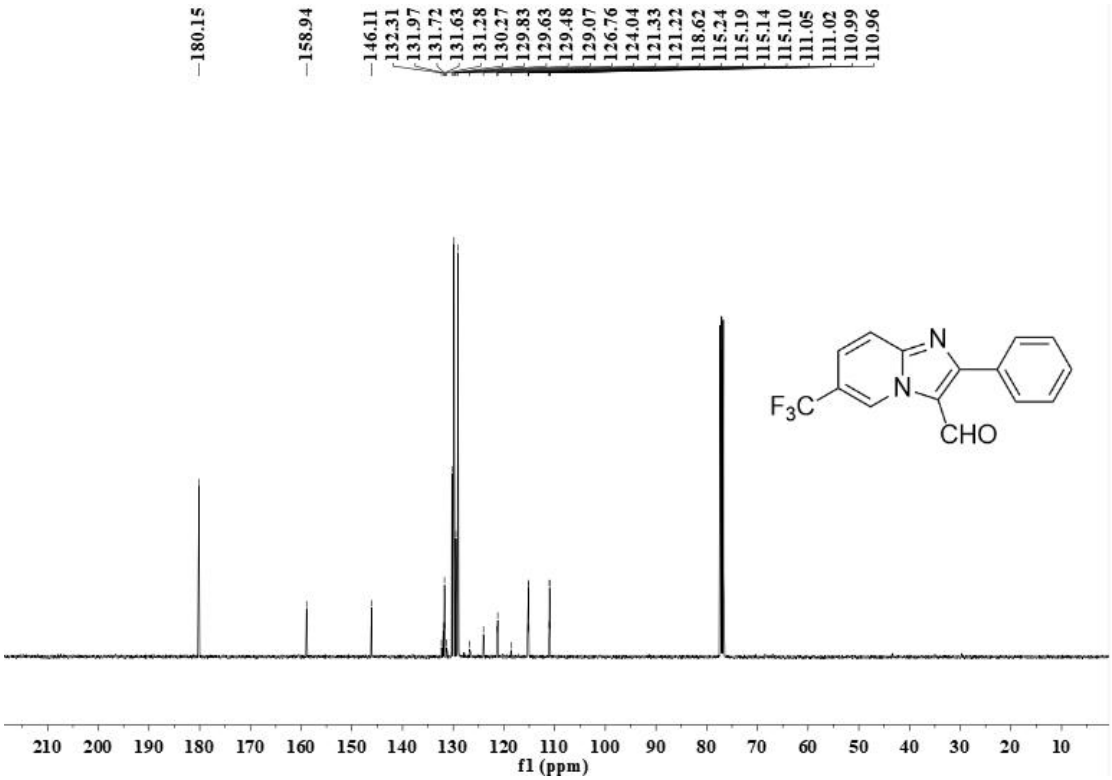
2,6-diphenylimidazo[1,2-a]pyridine-3-carbaldehyde (3l)

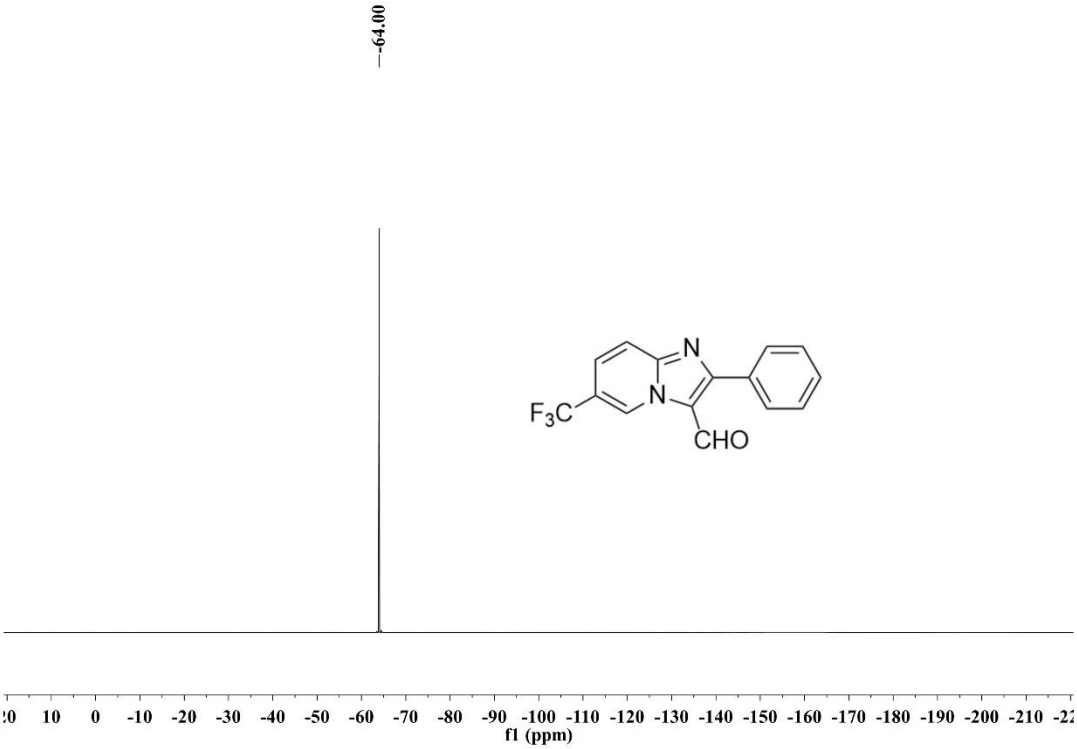




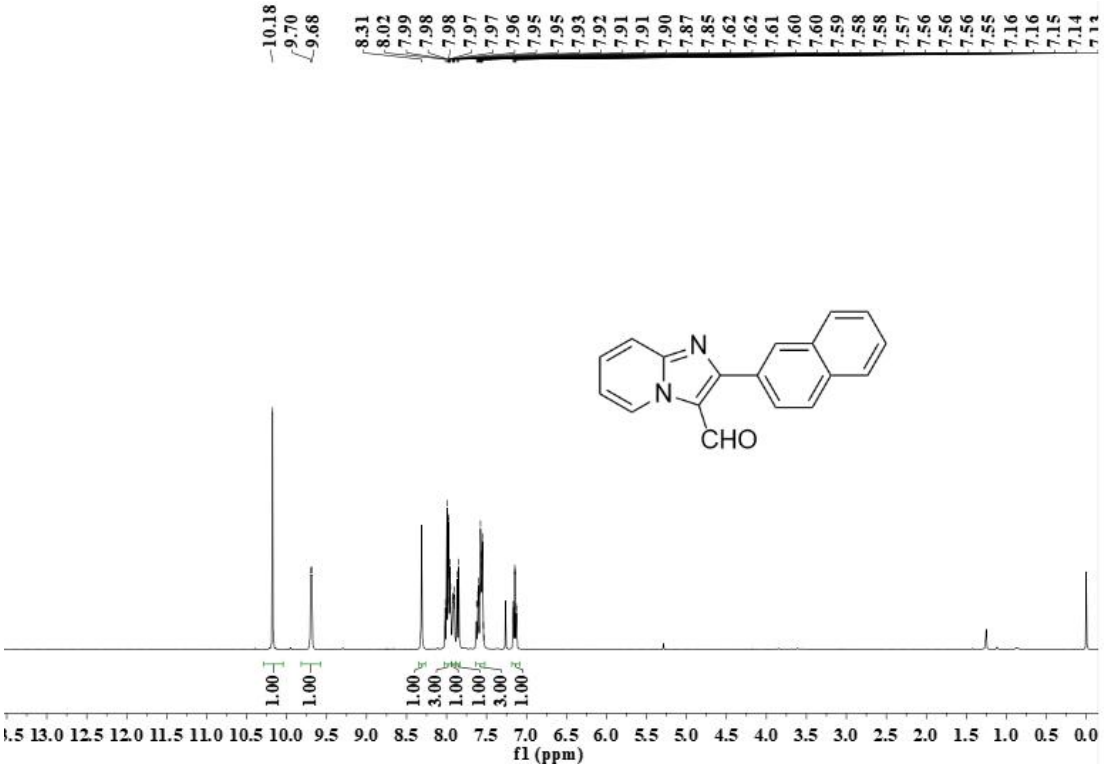
2-phenyl-6-(trifluoromethyl)imidazo[1,2-a]pyridine-3-carbaldehyde (3m)

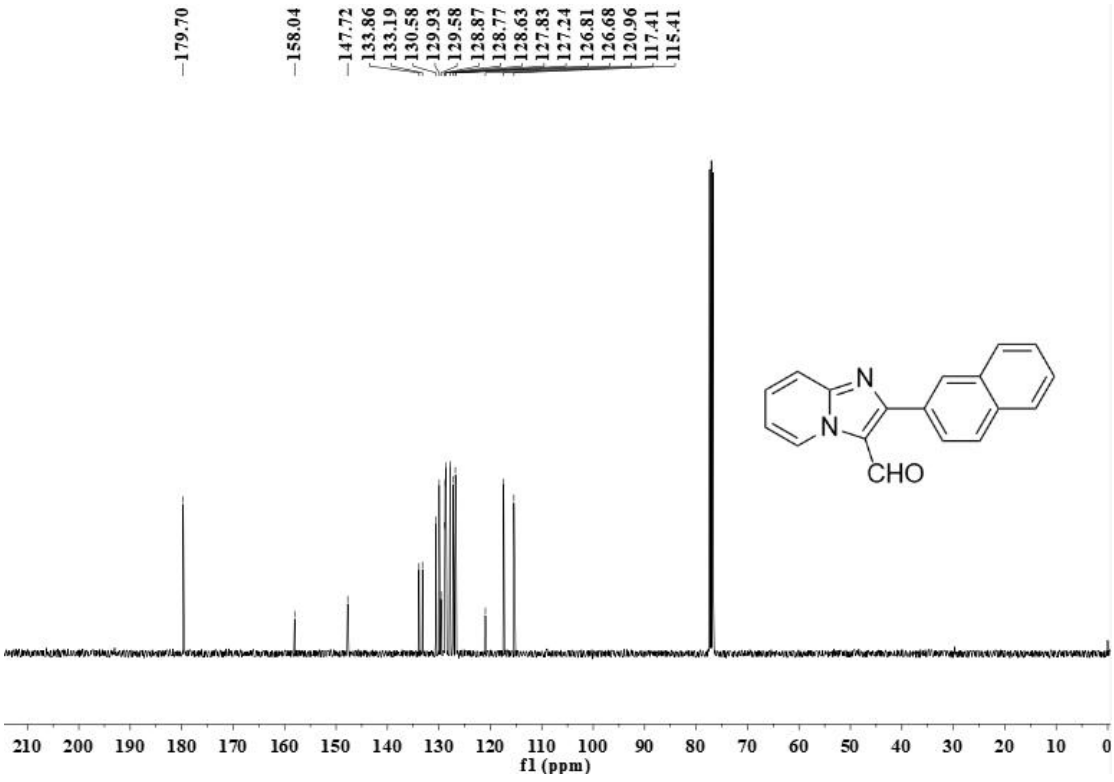



180.15
158.94
146.11
132.31
131.97
131.72
131.63
131.28
130.27
129.83
129.63
129.48
129.07
126.76
124.04
121.33
121.22
118.62
115.24
115.19
115.14
115.10
111.05
111.02
110.99
110.96
N
N
F3C
CHO
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

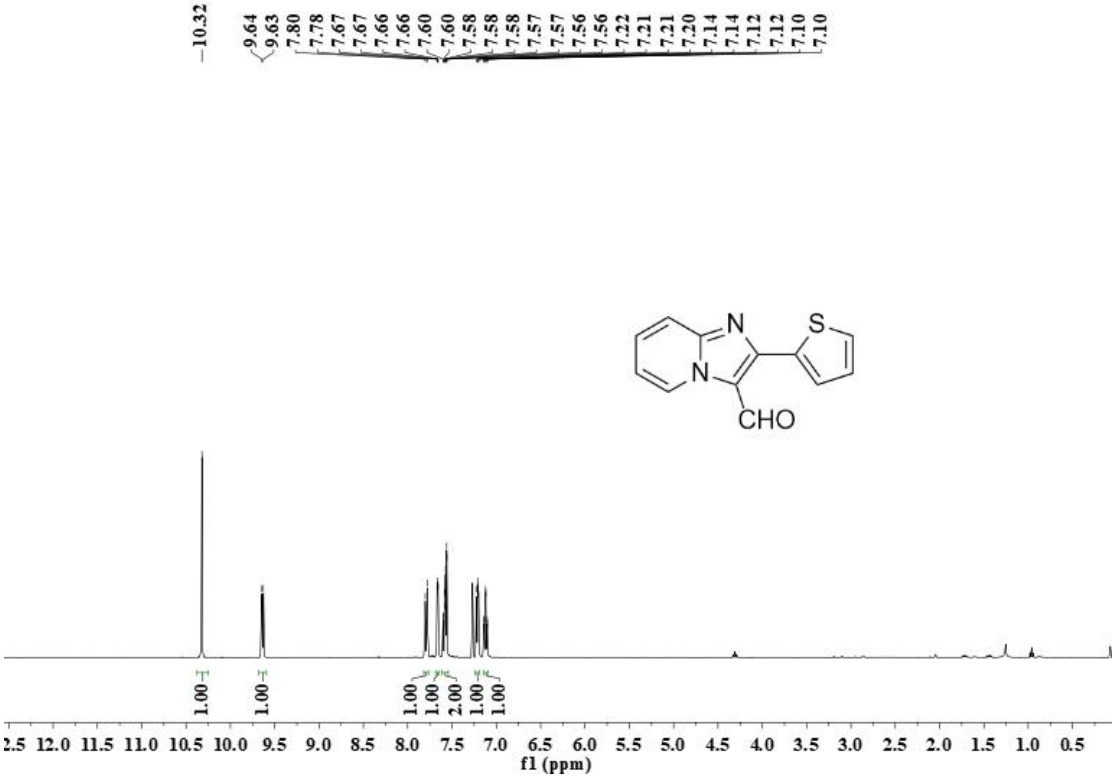

-64.00
N
N
F3C
CHO
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

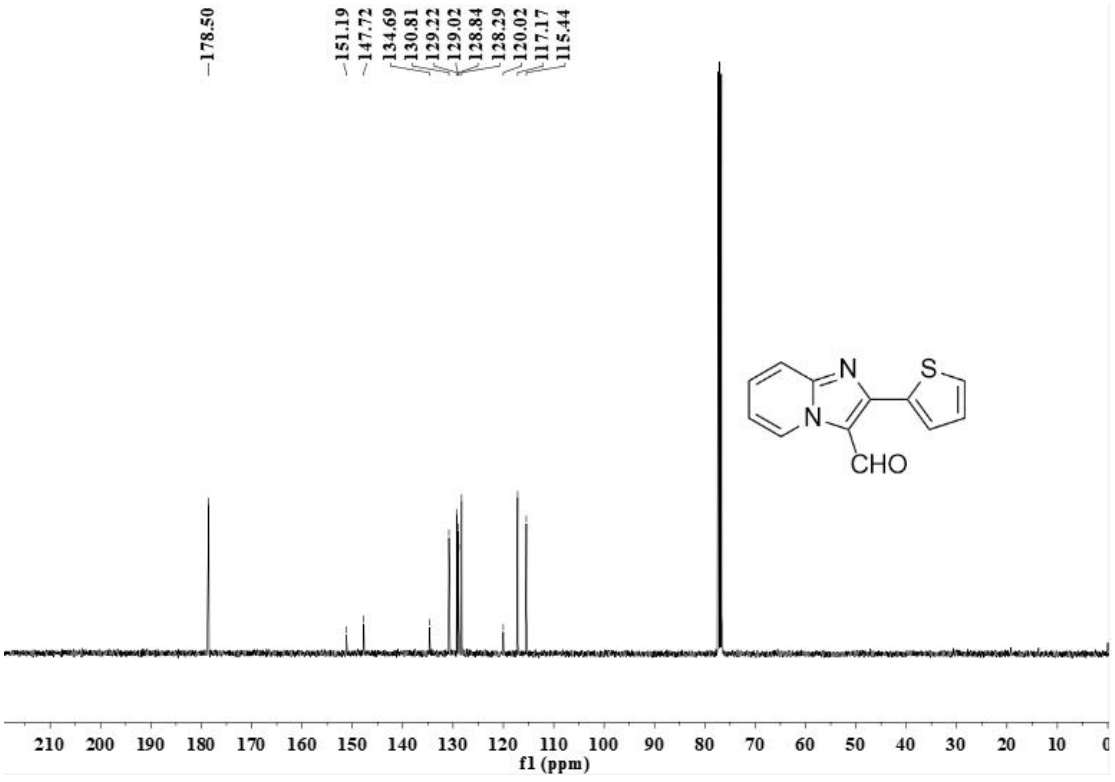
2-(naphthalen-2-yl)imidazo[1,2-a]pyridine-3-carbaldehyde (3n)



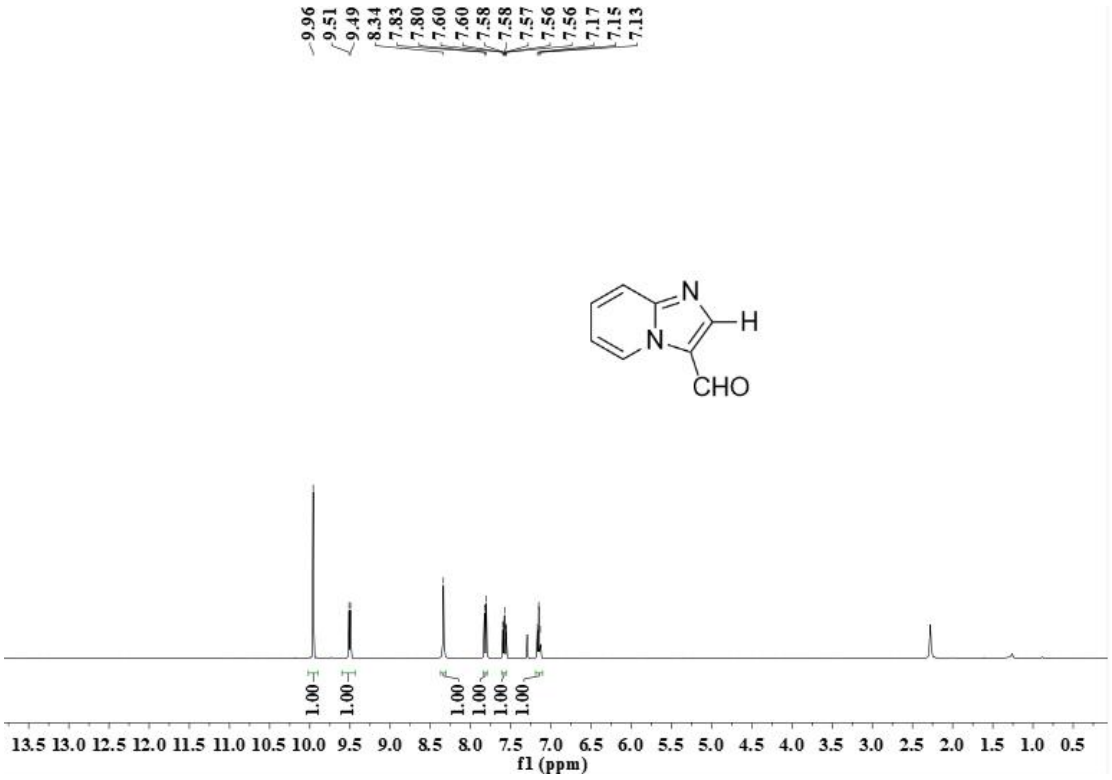


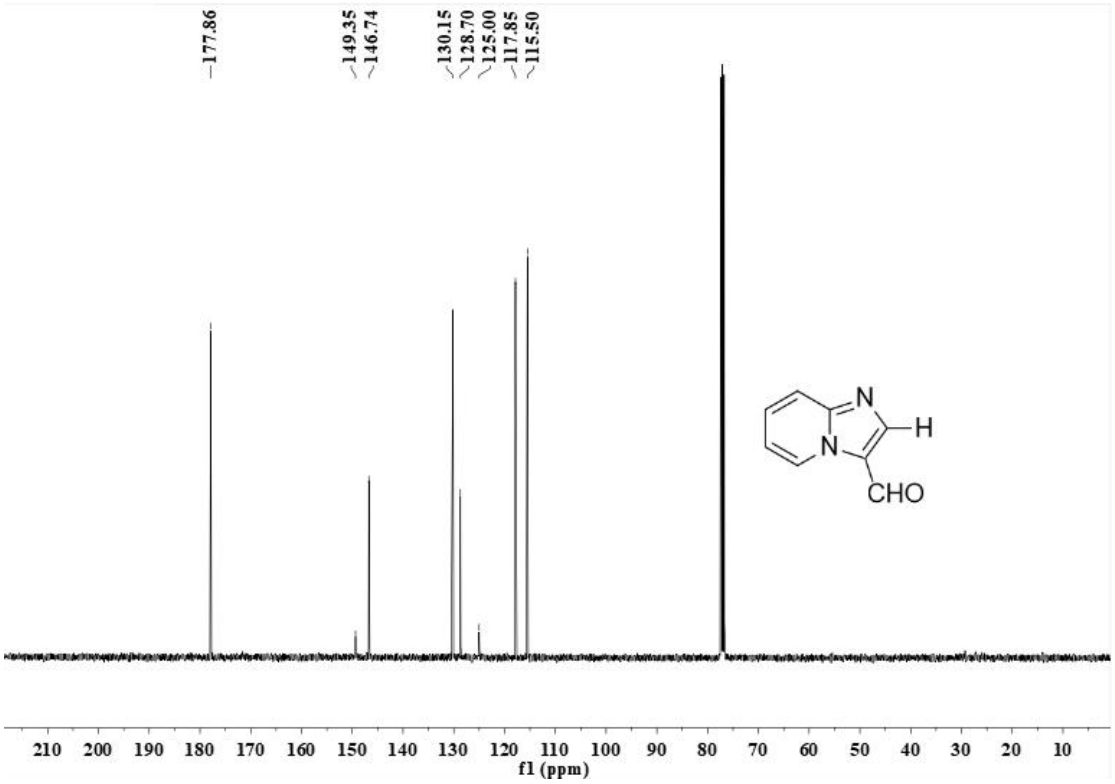
2-(thiophen-2-yl)imidazo[1,2-a]pyridine-3-carbaldehyde (3o)



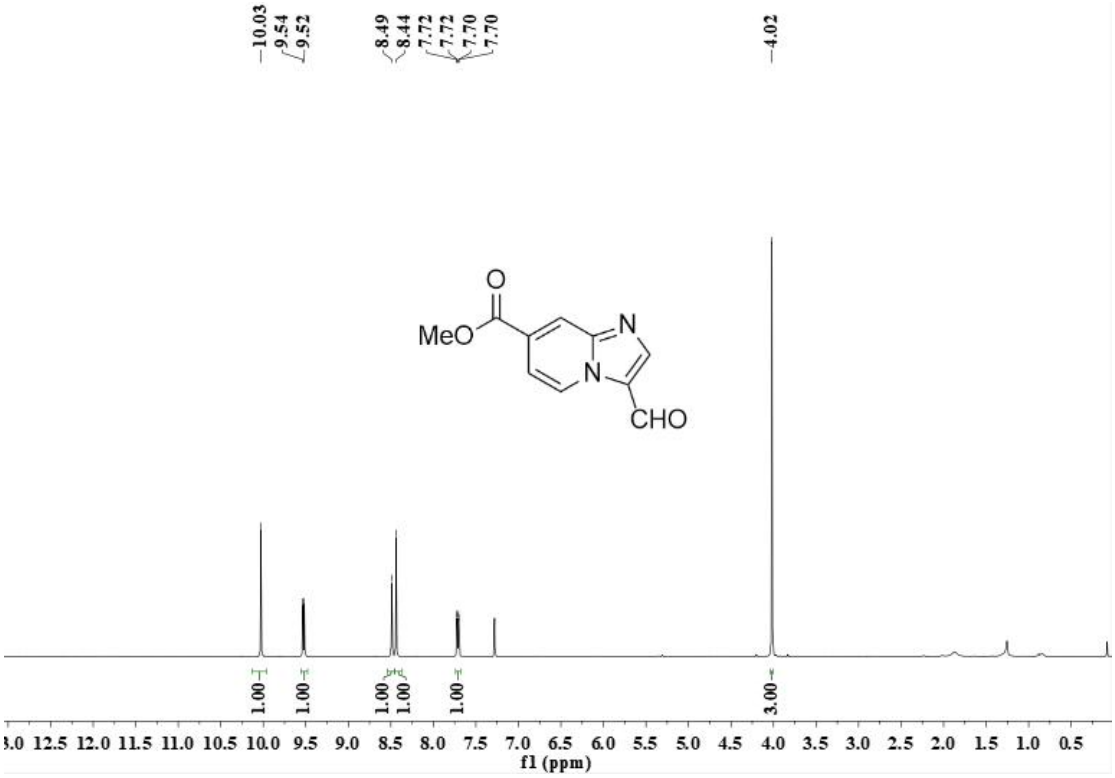


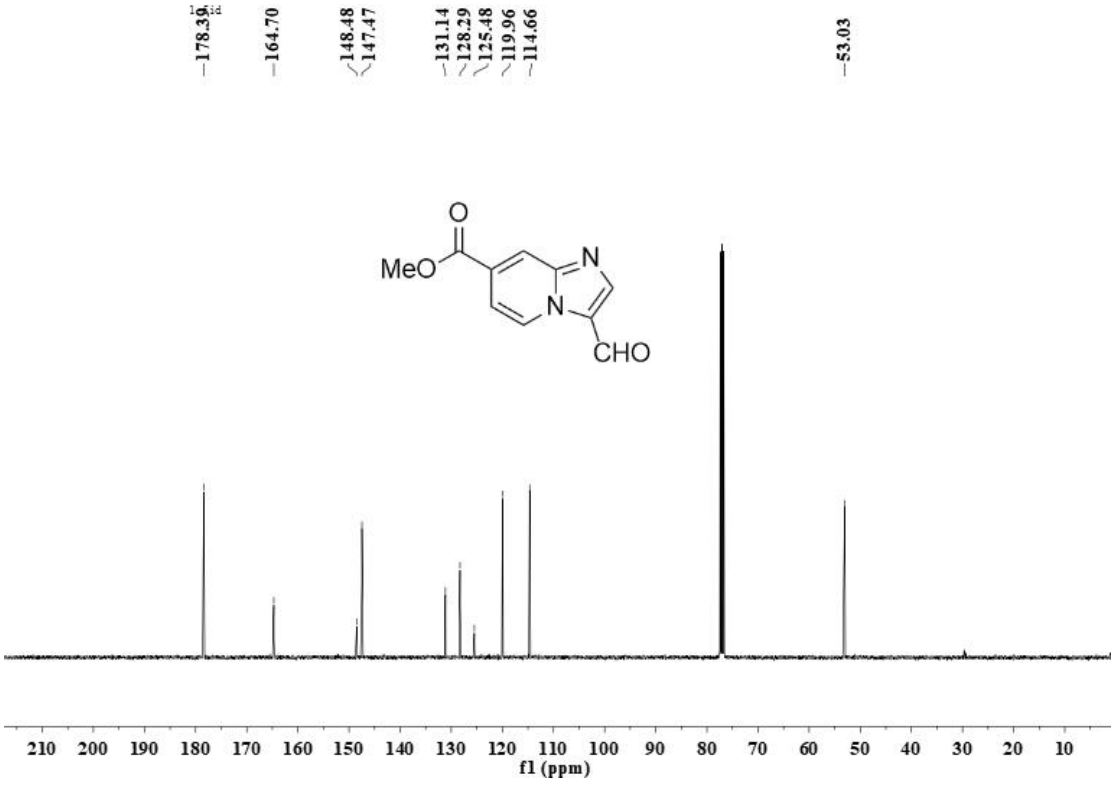
imidazo[1,2-a]pyridine-3-carbaldehyde (3p)



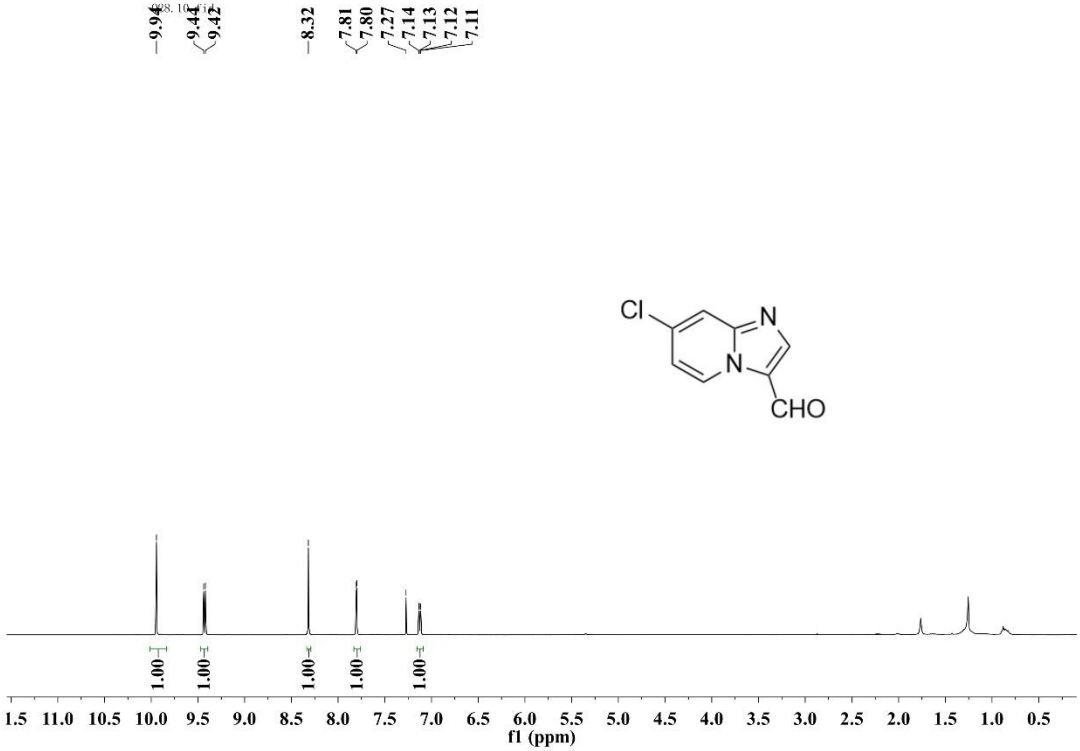


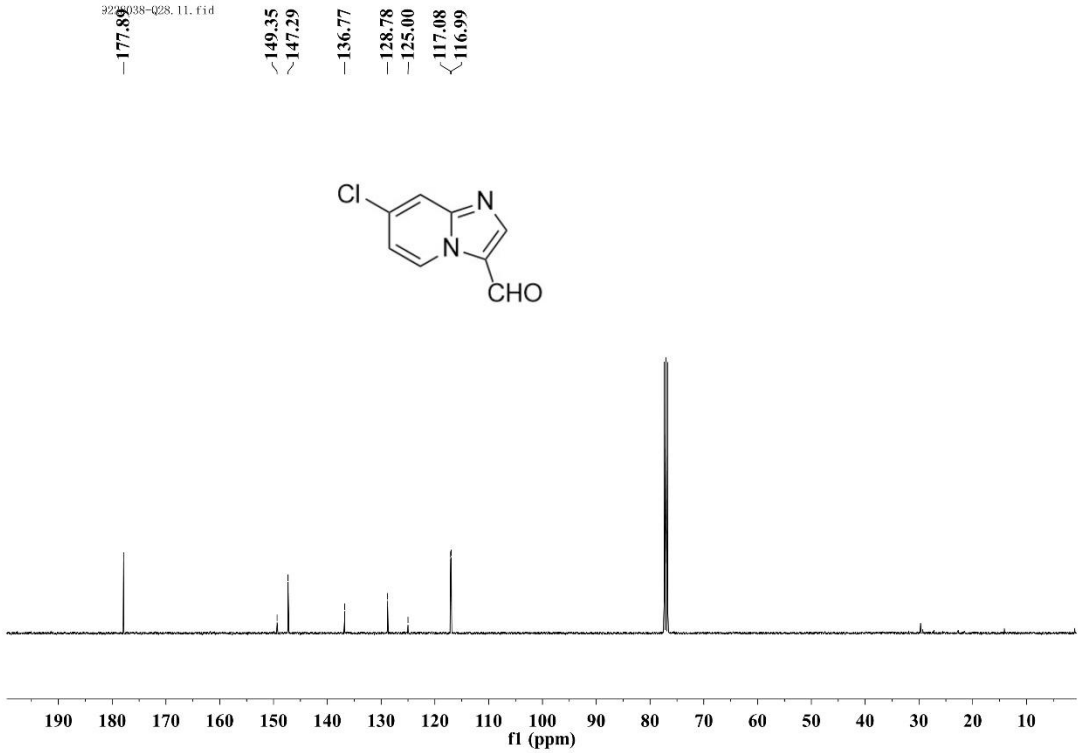
methyl 3-formylimidazo[1,2-a]pyridine-7-carboxylate (3q)



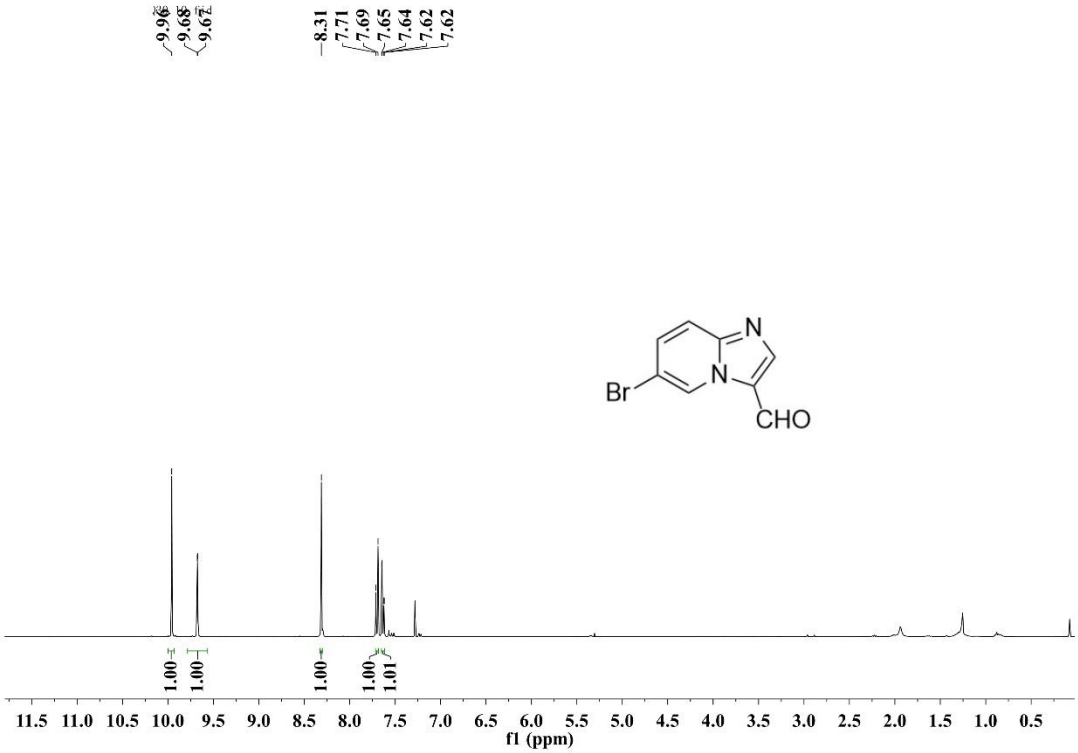


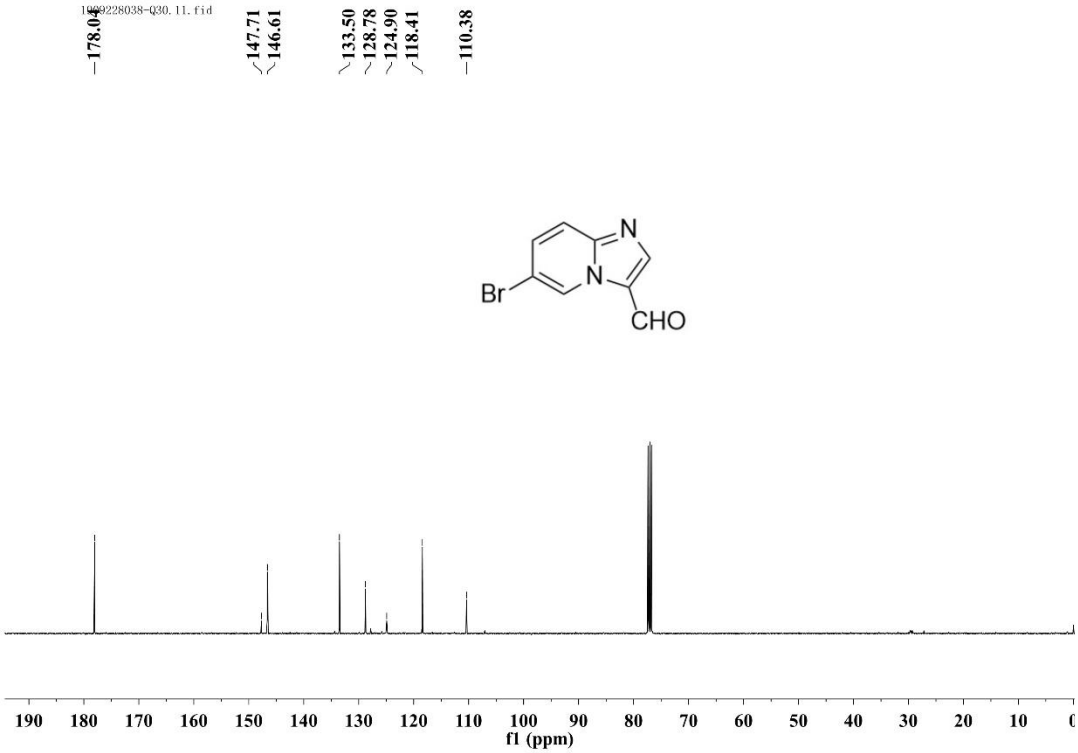
7-chloroimidazo[1,2-a]pyridine-3-carbaldehyde (3r)



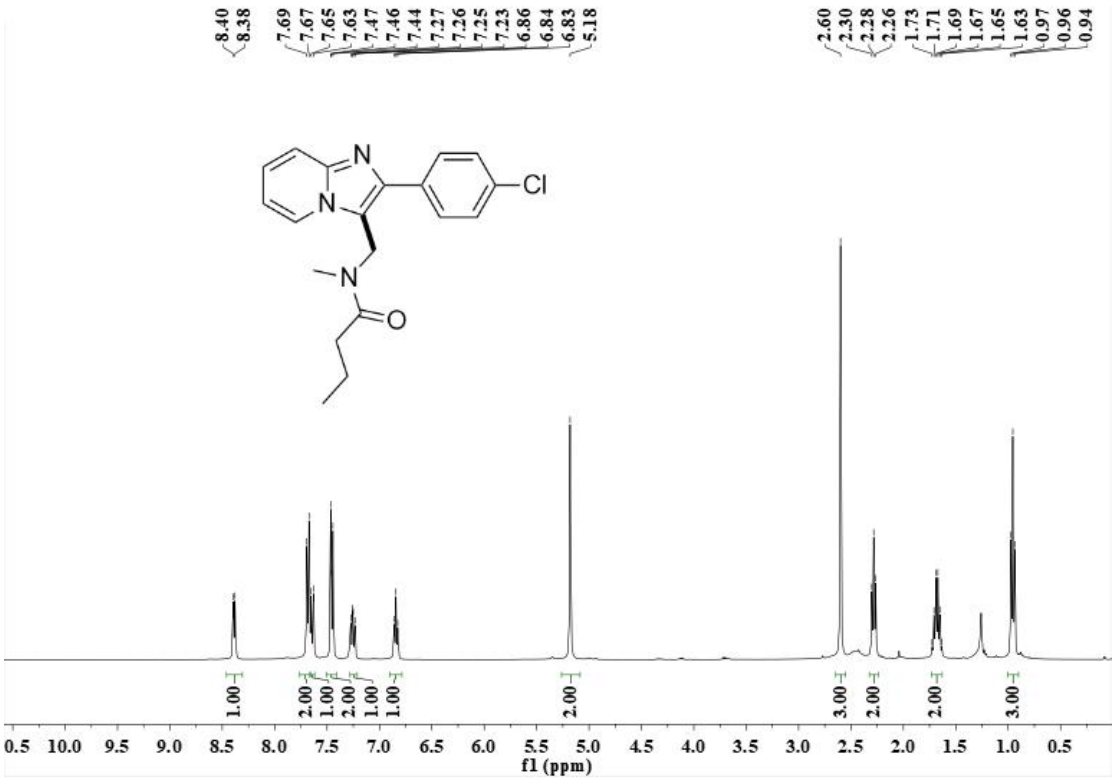


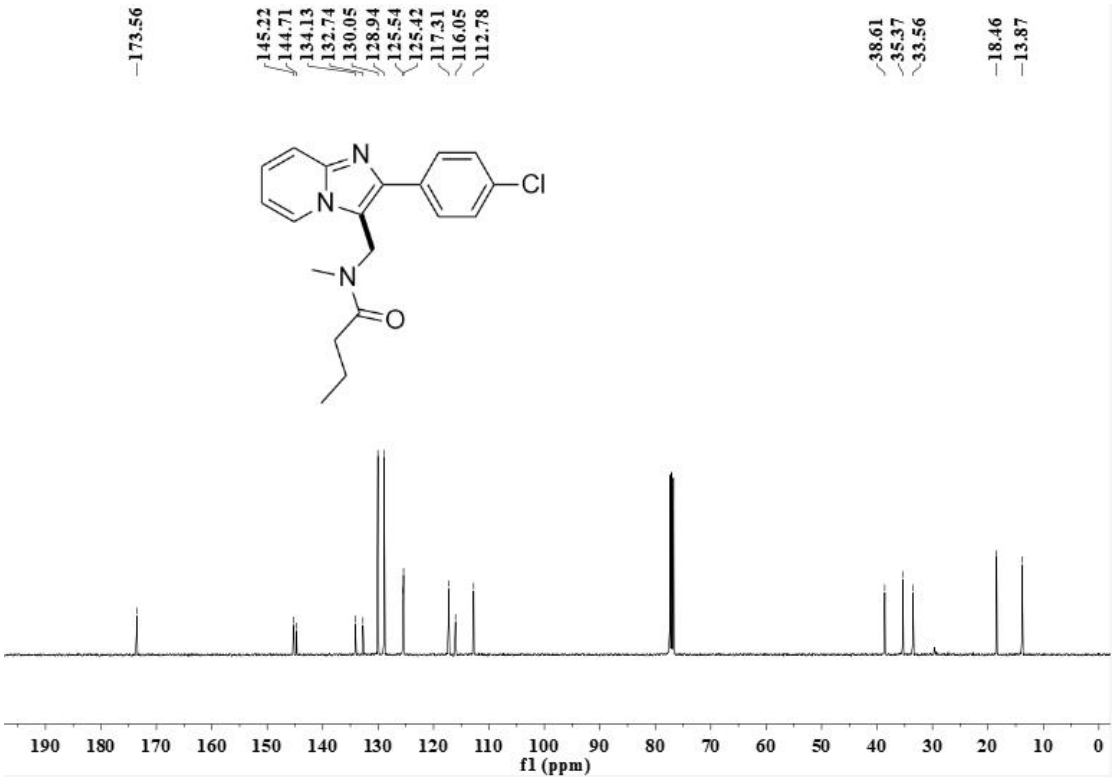
6-bromoimidazo[1,2-a]pyridine-3-carbaldehyde (3s)



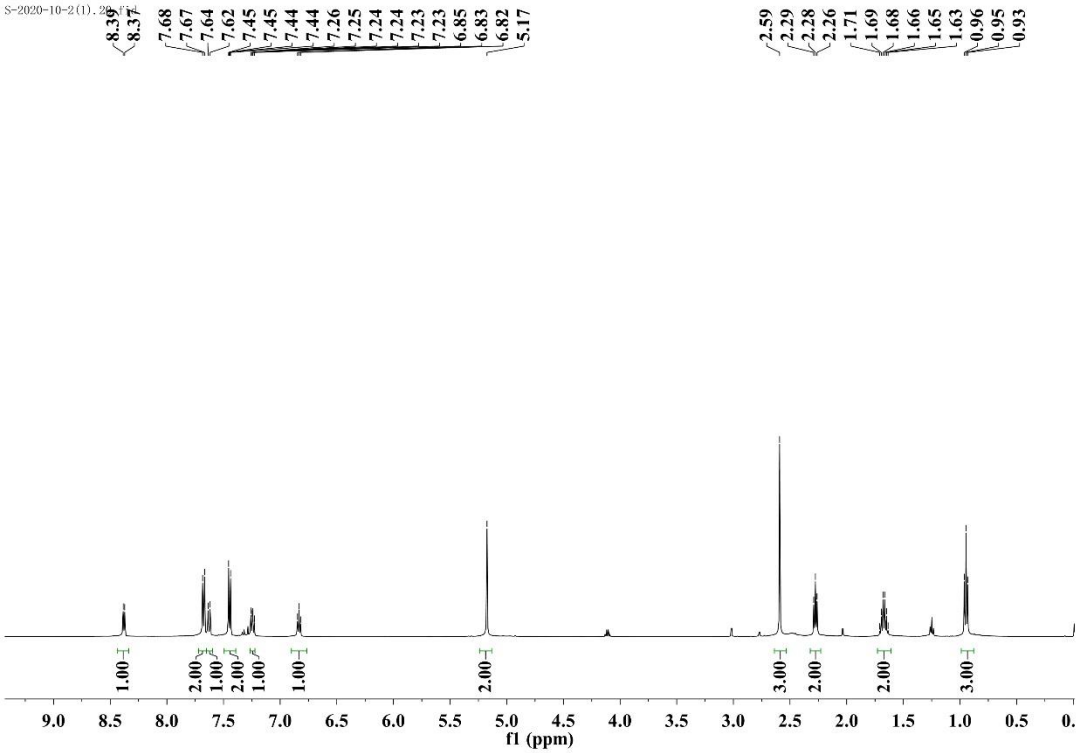


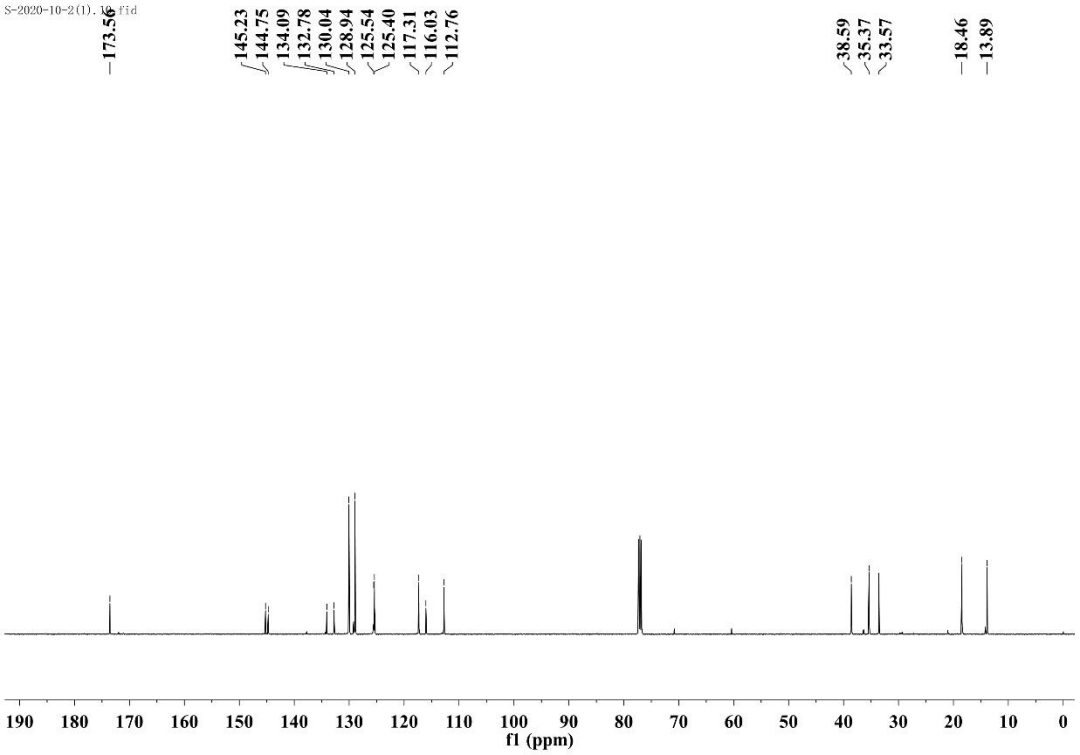
Saripidem from 2n



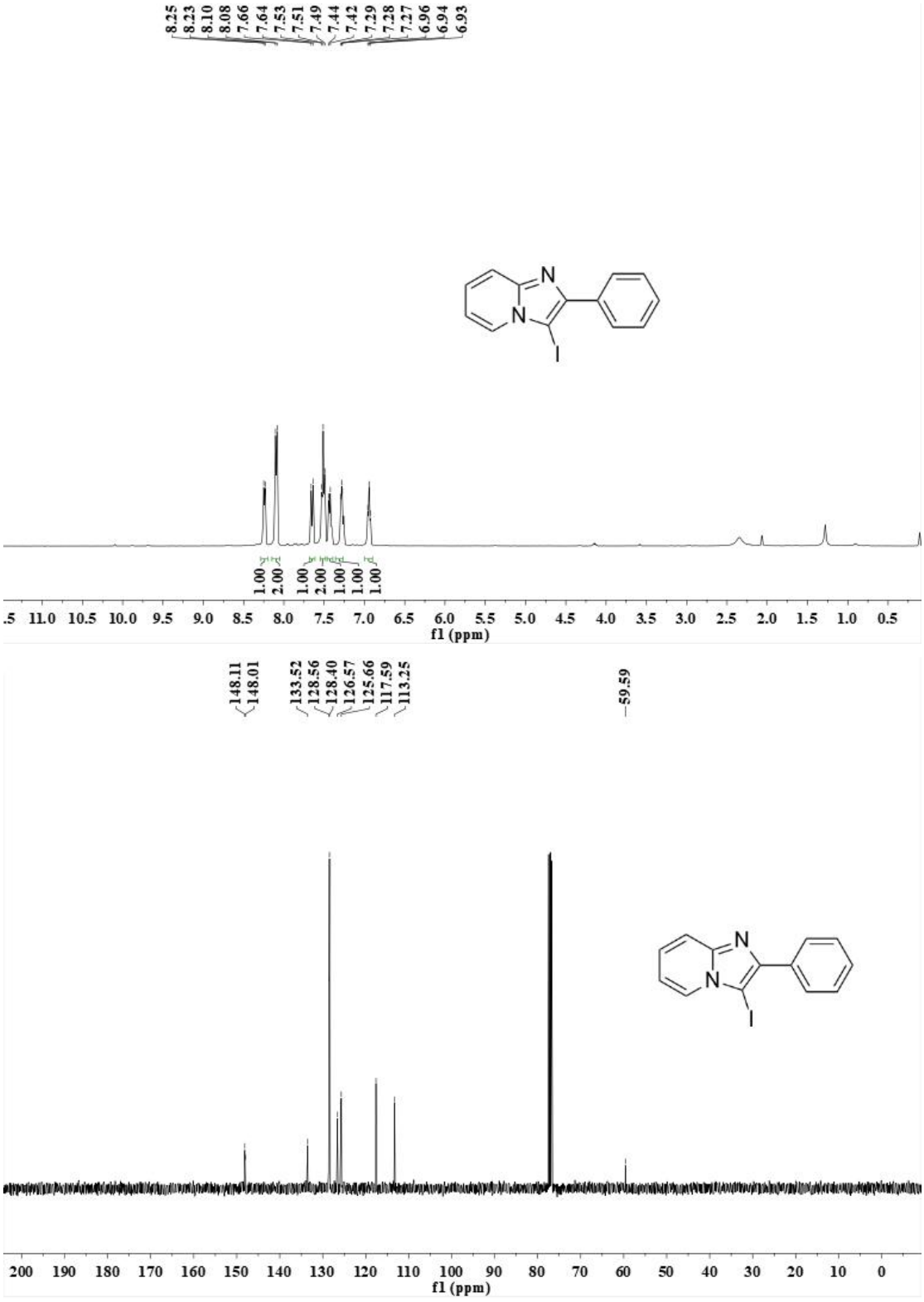


Saripidem from 3e





3-iodo-2-phenylimidazo[1,2-a]pyridine



2k from gram-scale