Supporting Information

Direct Arylation of Pyridines without the Use of Transition Metal Catalyst

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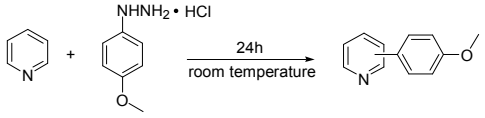
Ⅰ.General information:

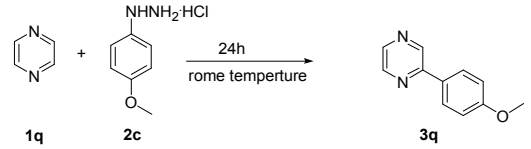
All manipulations were carried out under argon using standard Schlenk techniques. All glassware was oven or flame dried immediately prior to use. Al solvents were purified and dried according to standard methods prior to use, unless stated otherwise.

Unless otherwise, all reagents were obtained from commercial sources and used without further purification. ^{1}H NMR spectra were obtained at 400 MHz and recorded relative to the tetramethylsilane signal (0 ppm) or residual protio-solvent. ^{13}C NMR spectra were obtained at 100 MHz, and chemical shifts were recorded relative to the solvent resonance ($CDCl_3$, 77.0 ppm). Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, br = broad singlet, coupling constant in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High-resolution mass spectra were obtained on a JEOL JMS.DX303HF spectrometer (ESI).

Ⅱ.Experimental Procedure

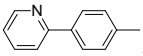


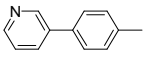
A mixture of pyridine (2 ml)，4-methoxyphenylhydrazine hydrochloride (0.5 mmol), was stirred at rt for 24 h. The reaction mixture was washed with EtOAc, and concentrated in vacuo. The resulting residue was purified by PTLC using hexanes:EtOAc (3:1 to 1:1, depending on different substrates) as the eluent. The isomer ratio was calculated from the isolated yield of isomers. Known compounds are characterized by ^{1}H NMR and their comparison to literature. Unknown compounds are characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

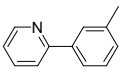


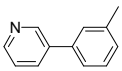
A mixture of pyrazine (500mg, 6.26mmol)，4-methoxyphenylhydrazine hydrochloride (0.5 mmol), and 1Ml DMF was stirred at 25°C for 24h. in sealed tube. The reaction mixture was washed with EtOAc, and concentrated in vacuo. The resulting residue was purified by PTLC using hexanes:EtOAc (3:1 to 1:1, depending on different substrates) as the eluent to yield product (**3**).

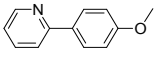
1. Data of products

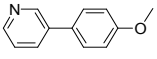

2-p-Tolyl-pyridine **[1]** Yellow oil,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.79 – 7.66 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.20 (ddd, *J* = 6.6, 4.9, 1.7 Hz, 1H), 2.41 (s, 3H).

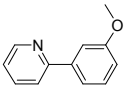

3-p-Tolyl-pyridine[2], Yellow oil,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.57 (d, *J* = 3.7 Hz, 1H), 7.91 – 7.81 (m, 1H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.35 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.29 (d, *J* = 7.9 Hz, 2H), 2.41 (s, 3H).

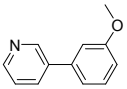

2-m-Tolyl-pyridine[1], Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.6 Hz, 1H), 7.84 (s, 1H), 7.79 – 7.69 (m, 3H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.23 (dd, *J* = 9.1, 4.4 Hz, 2H), 2.44 (s, 3H)

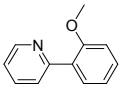

3-m-Tolyl-pyridine[2], Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 1H), 8.61 (d, *J* = 4.3 Hz, 1H), 7.94 – 7.85 (m, 1H), 7.46 – 7.35 (m, 4H), 7.26 (d, *J* = 4.0 Hz, 1H), 2.46 (s, 3H).

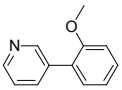

2-(4-Methoxy-phenyl)-pyridine**[1]**, White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 1H), 7.97 (d, *J* = 8.8 Hz, 2H), 7.73 (ddd, *J* = 16.5, 11.4, 4.8 Hz, 2H), 7.22 – 7.16 (m, 1H), 7.01 (t, *J* = 8.2 Hz, 2H), 3.89 (s, 3H).

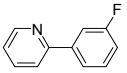

3-(4-Methoxy-phenyl)-pyridine[2], White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 1.7 Hz, 1H), 8.57 – 8.51 (m, 1H), 7.86 – 7.81 (m, 1H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.34 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H).

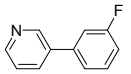
 2-(3-Methoxy-phenyl)-pyridine[5], White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.6 Hz, 1H), 7.79 – 7.69 (m, 2H), 7.59 (s, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 5.0 Hz, 1H), 6.97 (dd, *J* = 8.1, 2.0 Hz, 1H), 3.90 (s, 3H).

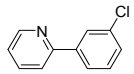
 3-(3-Methoxy-phenyl)-pyridine[6], White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (d, *J* = 1.7 Hz, 1H), 8.59 (d, *J* = 3.9 Hz, 1H), 7.87 (d, *J* = 7.9 Hz, 1H), 7.38 (dt, *J* = 7.8, 6.4 Hz, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.11 (s, 1H), 6.96 (dd, *J* = 8.3, 2.3 Hz, 1H), 3.88 (s, 3H).

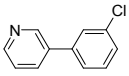
 2-(2-Methoxy-phenyl)-pyridine[3]. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.78 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.73 (td, *J* = 7.8, 1.7 Hz, 1H), 7.43 – 7.37 (m, 1H), 7.23 (dd, *J* = 6.8, 5.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 3.89 (s, 3H).

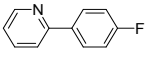
 3-(2-Methoxy-phenyl)-pyridine[4], Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.58 (d, *J* = 4.7 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.45 – 7.31 (m, 3H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 3.85 (s, 3H).

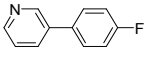
 2-(3-Fluoro-phenyl)-pyridine[7], Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.7 Hz, 1H), 7.83 – 7.71 (m, 3H), 7.46 (dd, *J* = 13.9, 7.9 Hz, 1H), 7.31 – 7.26 (m, 2H), 7.13 (td, *J* = 8.3, 1.8 Hz, 1H).

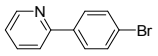
 3-(3-Fluoro-phenyl)-pyridine[2], Brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.62 (s, 1H), 7.90 – 7.82 (m, 1H), 7.48 – 7.41 (m, 1H), 7.41 – 7.34 (m, 2H), 7.28 (dd, *J* = 12.1, 2.0 Hz, 1H), 7.10 (td, *J* = 8.3, 2.0 Hz, 1H).

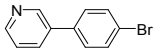
 2-(3-Chloro-phenyl)-pyridine[8], Brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.01 (s, 1H), 7.87 (dd, *J* = 6.5, 2.0 Hz, 1H), 7.78 (td, *J* = 7.9, 1.7 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.27 (d, *J* = 9.4 Hz, 1H).

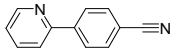
 3-(3-Chloro-phenyl)-pyridine [9], Brown liquid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H), 8.63 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.57 (s, 1H), 7.50 – 7.35 (m, 4H).

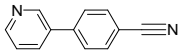
 2-(4-Fluoro-phenyl)-pyridine[10], Brown solid..^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.2 Hz, 1H), 8.03 – 7.93 (m, 2H), 7.75 (td, *J* = 7.9, 1.7 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.23 (dd, *J* = 6.7, 5.5 Hz, 1H), 7.16 (t, *J* = 8.7 Hz, 2H).

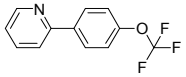
 3-(4-Fluoro-phenyl)-pyridine[11], Brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.59 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.55 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.37 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.18 (t, *J* = 8.6 Hz, 2H).

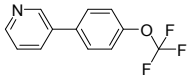
 2-(4-Bromo-phenyl)-pyridine [12], Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.1 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.79 – 7.73 (m, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.28 – 7.23 (m, 1H).

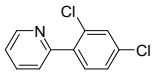
 3-(4-Bromo-phenyl)-pyridine [13], Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.61 (s, 1H), 7.85 (d, *J* = 7.9 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.38 (dd, *J* = 7.5, 4.8 Hz, 1H).

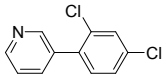
 4-Pyridin-2-yl-benzonitrile [14], Yellow solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.5 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.82 (td, *J* = 7.7, 1.5 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 3H), 7.37 – 7.29 (m, 1H).

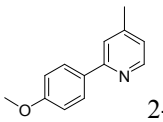
 4-Pyridin-3-yl-benzonitrile [2], Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (d, *J* = 1.7 Hz, 1H), 8.68 (d, *J* = 3.7 Hz, 1H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.43 (dd, *J* = 7.8, 4.9 Hz, 1H).

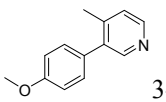
 2-(4-Trifluoromethoxy-phenyl)-pyridine [15], colorless oil,.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.01 (s, 1H), 7.87 (dd, *J* = 6.5, 2.0 Hz, 1H), 7.78 (td, *J* = 7.9, 1.7 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.27 (d, *J* = 10.3 Hz, 1H).

 3-(4-Trifluoromethoxy-phenyl)-pyridine[16] , colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.65 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.59 (s, 1H), 7.53 – 7.37 (m, 4H).

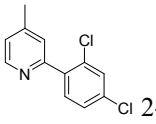
 2-(2,4-Dichloro-phenyl)-pyridine[17] , Brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.8 Hz, 1H), 7.77 (td, *J* = 7.8, 1.7 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 1H), 7.50 (d, *J* = 2.0 Hz, 1H), 7.35 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.33 – 7.28 (m, 1H).

 3-(2,4-Dichloro-phenyl)-pyridine , Brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 – 8.60 (m, 2H), 7.82 – 7.74 (m, 1H), 7.53 (d, *J* = 1.9 Hz, 1H), 7.42 – 7.32 (m, 2H), 7.28 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.81, 149.02, 136.95, 135.43, 134.82, 134.21, 133.54, 131.97, 130.02, 127.54, 123.04. HRMS(ESI-TOF) m/z Calcd for 225.9971 $C_{11}H_7N$ $[M+H]^+$ found 225.9978.

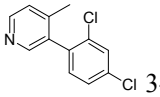
 2-(4-Methoxy-phenyl)-4-methyl-pyridine [19], Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.9 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.51 (s, 1H), 7.02 (t, *J* = 6.1 Hz, 3H), 3.93 – 3.87 (s, 3H), 2.42 (s, 3H).

 3-(4-Methoxy-phenyl)-4-methyl-pyridine, Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 3.1 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 7.18 (d, *J* = 5.0 Hz, 1H), 6.99 (d, *J* = 8.6 Hz, 2H), 3.86 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.16, 150.06, 147.96, 144.63, 137.40,

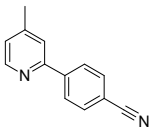
130.42, 130.20, 125.18, 113.89, 55.34, 19.90. HRMS(ESI-TOF) m/z Calcd for 200.1012，$C_{11}H_7N$ $[M+H]^+$ found 200.1016.



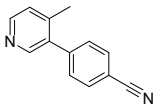
2-(2,4-Dichloro-phenyl)-4-methyl-pyridine, Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 5.0 Hz, 1H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 1.9 Hz, 1H), 7.46 (s, 1H), 7.36 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.15 (d, *J* = 4.6 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.26, 132.92, 132.41, 129.85, 129.01, 128.66, 127.43, 127.31, 125.66, 124.90, 123.70, 29.47, 21.17.HRMS(ESI-TOF) m/z Calcd for 238.1176，$C_{11}H_7N$ $[M+H]^+$ found 238.1178.



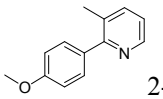
3-(2,4-Dichloro-phenyl)-4-methyl-pyridine, Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 5.0 Hz, 1H), 8.32 (s, 1H), 7.52 (d, *J* = 2.0 Hz, 1H), 7.34 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.21 (d, *J* = 5.0 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.52, 149.12, 145.75, 135.33, 134.76, 134.66, 131.94, 130.35, 129.55, 127.27, 125.67, 29.69, 19.30.HRMS(ESI-TOF) m/z Calcd for 238.1176，$C_{11}H_7N$ $[M+H]^+$ found 238.1178.



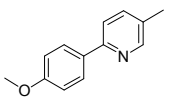
4-(4-Methyl-pyridin-2-yl)-benzonitrile, Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.9 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.61 (s, 1H), 7.17 (d, *J* = 4.6 Hz, 1H), 2.47 (s, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 155.16, 149.81, 148.26, 143.68, 132.52, 127.49, 124.32, 121.99, 118.87, 112.33, 21.25. HRMS (ESI-TOF) m/z Calcd for 195.0900，$C_{11}H_7N$ $[M+H]^+$ found 195.0905.



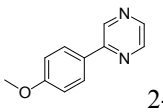
4-(4-Methyl-pyridin-3-yl)-benzonitrile, Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.5 Hz, 1H), 8.43 (s, 1H), 7.76 (d, *J* = 8.1 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 6.8 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.39, 149.20, 142.62, 132.31, 130.09, 128.50, 125.51, 118.54, 111.84, 110.31, 19.73. HRMS (ESI-TOF) m/z Calcd for 195.0900，$C_{11}H_7N$ $[M+H]^+$ found 195.0896.



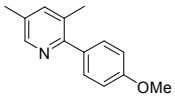
2-(4-Methoxy-phenyl)-3-methyl-pyridine[18], White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.4 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.14 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 3.86 (s, 3H), 2.37 (s, 3H).



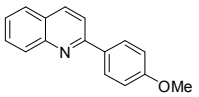
2-(4-Methoxy-phenyl)-5-methyl-pyridine [20], White solid ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.57 (dd, *J* = 18.0, 8.1 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.88 (s, 3H), 2.38 (s, 3H).



2-(4-Methoxy-phenyl)-pyrazine [21], Brown solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.62 (s, 1H), 8.47 (s, 1H), 8.01 (d, *J* = 7.7 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 3.91 (s, 3H).

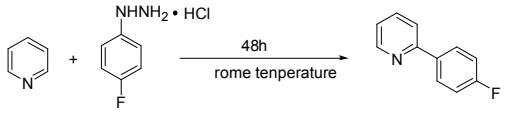


2-(4-Methoxy-phenyl)-3,5-dimethyl-pyridine, White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.38 (s, 1H), 6.97 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 3H), 2.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.29, 155.49, 147.16, 139.33, 132.95, 131.17, 130.28, 130.14, 113.54, 55.32, 20.05, 17.92. HRMS (ESI-TOF) m/z Calcd for 214.0812，$C_{11}H_7N$ $[M+H]^+$ found 214.0810.



2-(4-Methoxy-phenyl)-quinoline [22]， White solid,^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.6 Hz, 1H), 8.14 (d, *J* = 8.8 Hz, 3H), 7.82 (dd, *J* = 13.3, 8.4 Hz, 2H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.1 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H).

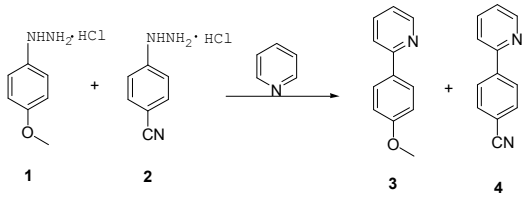
2. Prepared arylation of pyridines on a gram scale



To a 100 mL sealed tube, were added (4-Fluoro-phenyl)hydrazine hydrochloride (1g，6.71mmol)，and pyridine (40 mL). The tube was capped then stirred at 25℃ for 48 h.The reaction mixture was washed with EtOAc, and the filtrate was concentrated invacuo. The resulting residue was purified by silica gel column using hexanes:EtOAc (3:1 to 1:1) as the eluent to give a desired product, 0.38 g (36 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.2 Hz, 1H), 8.03 – 7.93 (m, 2H), 7.75 (td, *J* = 7.9, 1.7 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 1H), 7.23 (dd, *J* = 6.7, 5.5 Hz, 1H), 7.16 (t, *J* = 8.7 Hz, 2H).

3. Competition Experiments and Hydrochloride or Kinetic Isotope Effects

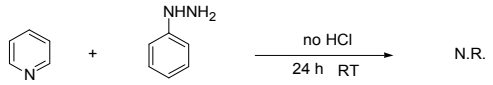
3.1 Competition Reaction



To a 20 mL sealed tube, were added 4-methoxyphenylhydrazine hydrochloride(50 mg，0.28mmol) and 4-cyanophenylhydrazine hydrochloride（47.6mg，0.28mmol） and pyridine (3 mL). The tube was capped then stirred at 25℃ for 24 h. The reaction mixture was washed with EtOAc, and the filtrate was concentrated invacuo. The resulting residue was purified by silica gel column using hexanes:EtOAc (3:1 to 1:1) as the eluent. The product ratio was determined by isolated yield.

3.2 Hydrochloride or Kinetic Isotope Effects

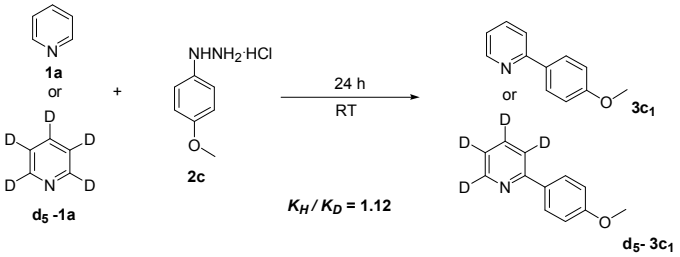
3.2.1 Hydrochloride Effects



To a 20 mL sealed tube, were added phenylhydrazine (50 mg，0.46mmol) and pyridine (2 mL). The tube was capped then stirred at 25℃ for 24 h. The reaction mixture was washed with EtOAc, and the filtrate was concentrated invacuo. However，trace amounts of the desired product was observed.

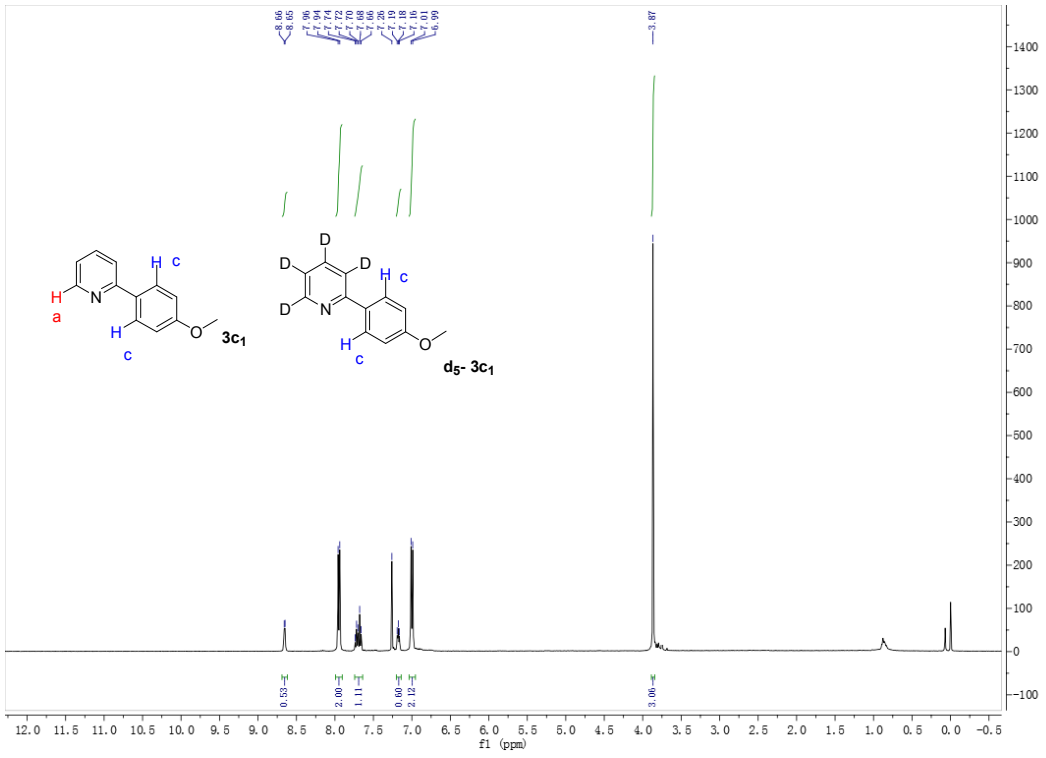
To a 20 mL sealed tube, were added phenylhydrazine (50 mg，0.46mmol) ,Tempo(54mg,,0.46mmol) and pyridine (2 mL). The tube was capped then stirred at 25℃ for 24 h. The reaction mixture was washed with EtOAc, and the filtrate was concentrated invacuo. However，trace amounts of the desired product was observed.

3.2.2 Kinetic Isotope Effects



To a 20 mL sealed tube, were added 4-methoxyphenylhydrazine hydrochloride(50 mg，0.28mmol), pyridine (1.5 mL, 18.75 mmol) and d_5- pyridine (1.5 mL, 18.75 mmol). The tube was capped then stirred at 25 °C for 24 h. The reaction mixture was washed with EtOAc, and the filtrate was concentrated invacuo. The resulting residue was purified by PTLC using hexanes : EtOAc (3:1) as the eluent. The 2-(4-Methoxy-phenyl)-pyridine ratio ($3c_1$ and d4-$3c_1$) was analyzed by ^{1}H NMR. The yield of **$3c_1$**,was determined by integration of the H_a signal of **$3c_1$**, which appeared as a doublets (approximately 8.65 ppm). The total yield of **$3c_1$** and **d_4-$3c_1$**, was determined by integration of **H_c** of **$3c_1$** and **d_4-$3c_1$**, which appeared as doublets at the same chemical shift (7.95 ppm for both **$3c_1$** and **d_4-$3c_1$**). The yield of **d_4-$3c_1$** could then be determined from the following formula: **d_4-$3c_1$**=·**X_{total}** –**$3c_1$**.

Then K_H/K_D = 0.53/0.47=1.13



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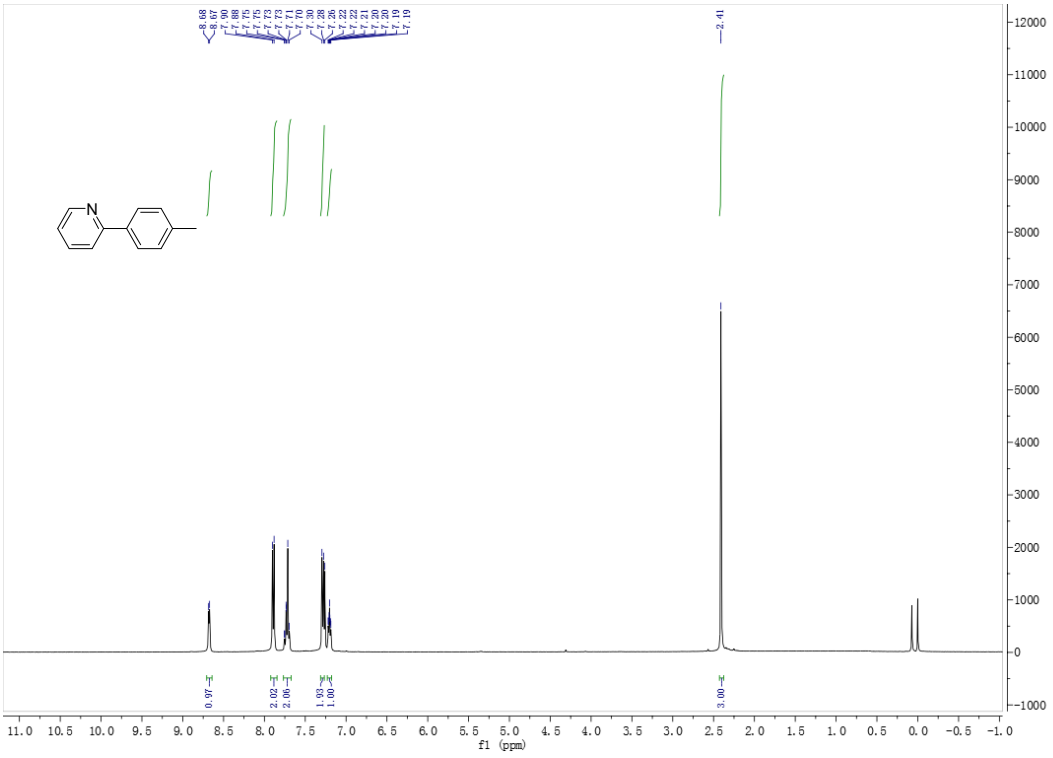
Ⅳ. ^{1}H NMR Spectra of the compounds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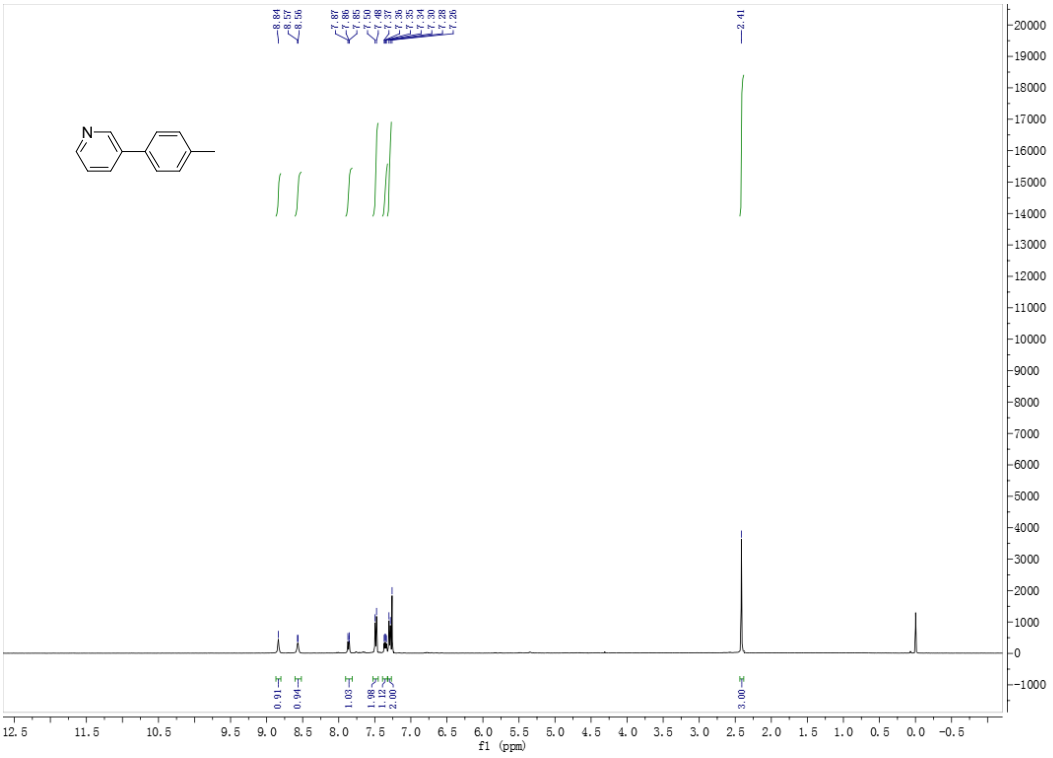
7.90
7.88
7.76
7.75
7.73
7.73
7.71
7.70
7.30
7.28
7.26
7.22
7.21
7.20
7.20
7.19
2.41
0.97
2.02
2.06
1.93
1.00
3.00
f1 (ppm)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7.28
7.26
2.41
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0.94
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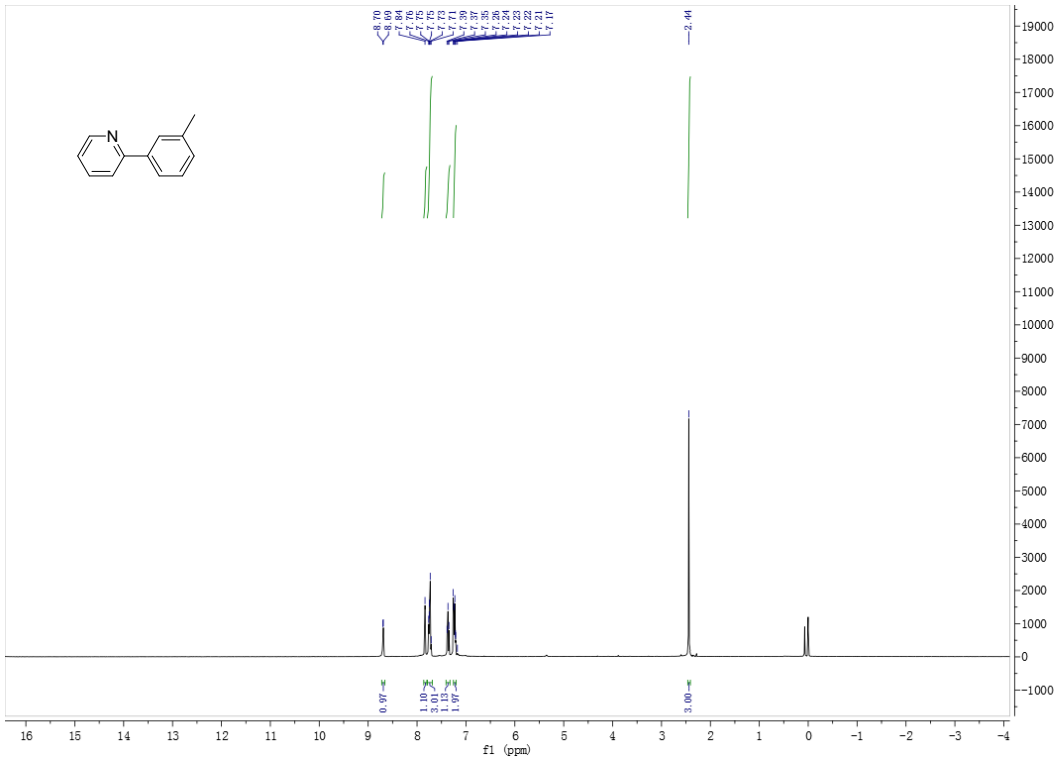
1.98
1.12
2.00
3.00
f1 (ppm)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7.75
7.75
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7.24
7.23
7.22
7.21
7.17
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1.10
3.01
1.13
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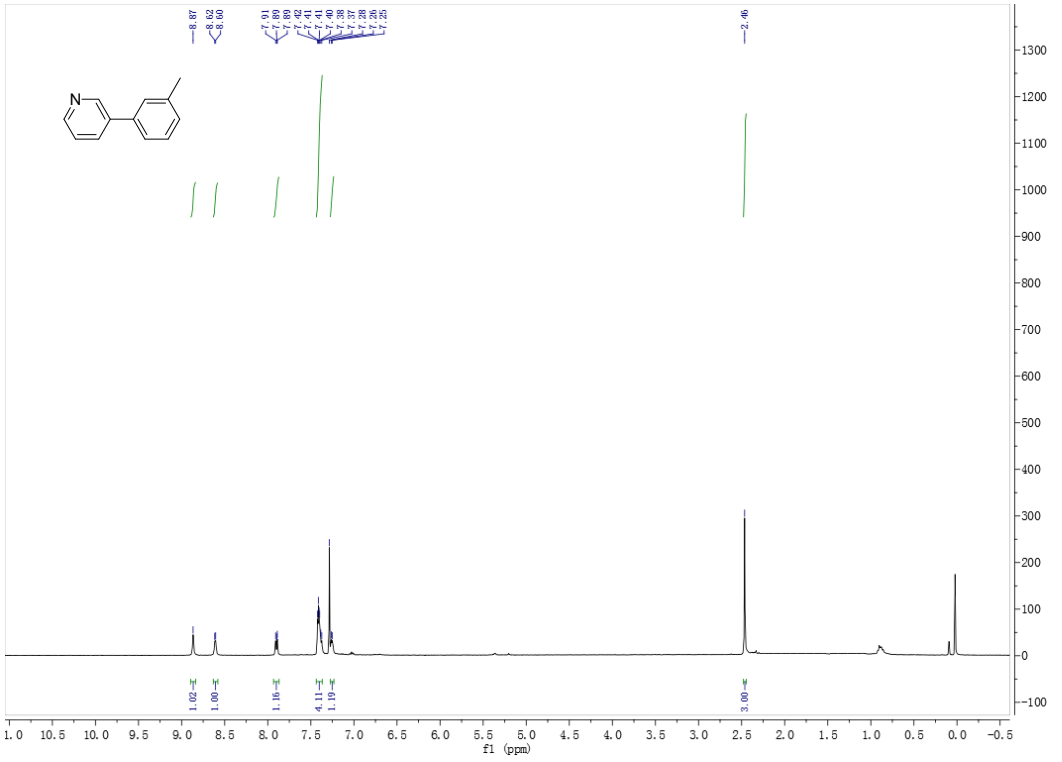
3.00
f1 (ppm)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7.40
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7.26
7.25
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1.00
1.16
4.11
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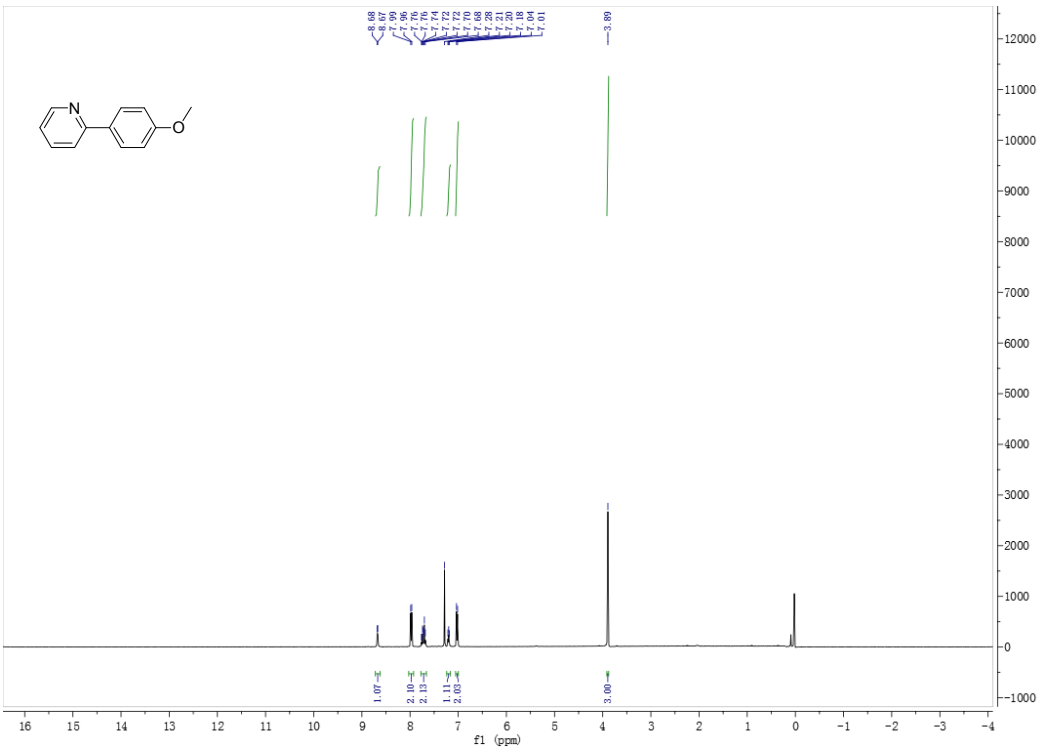
3.00
f1 (ppm)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7.01
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2.13
1.11
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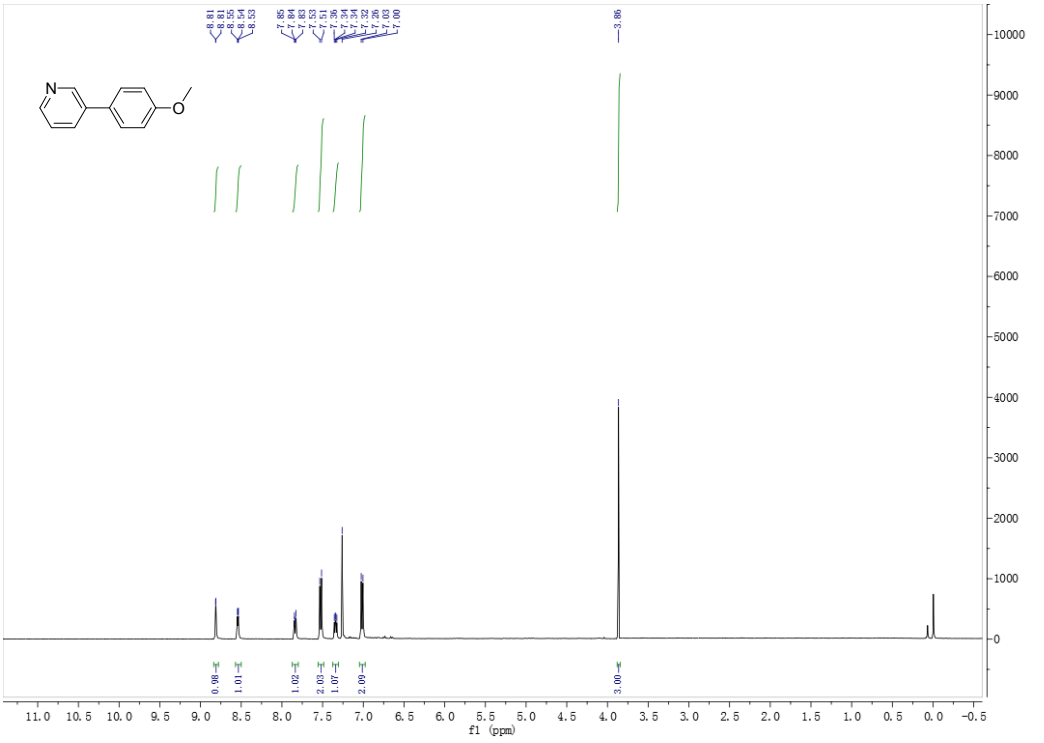
f1 (ppm)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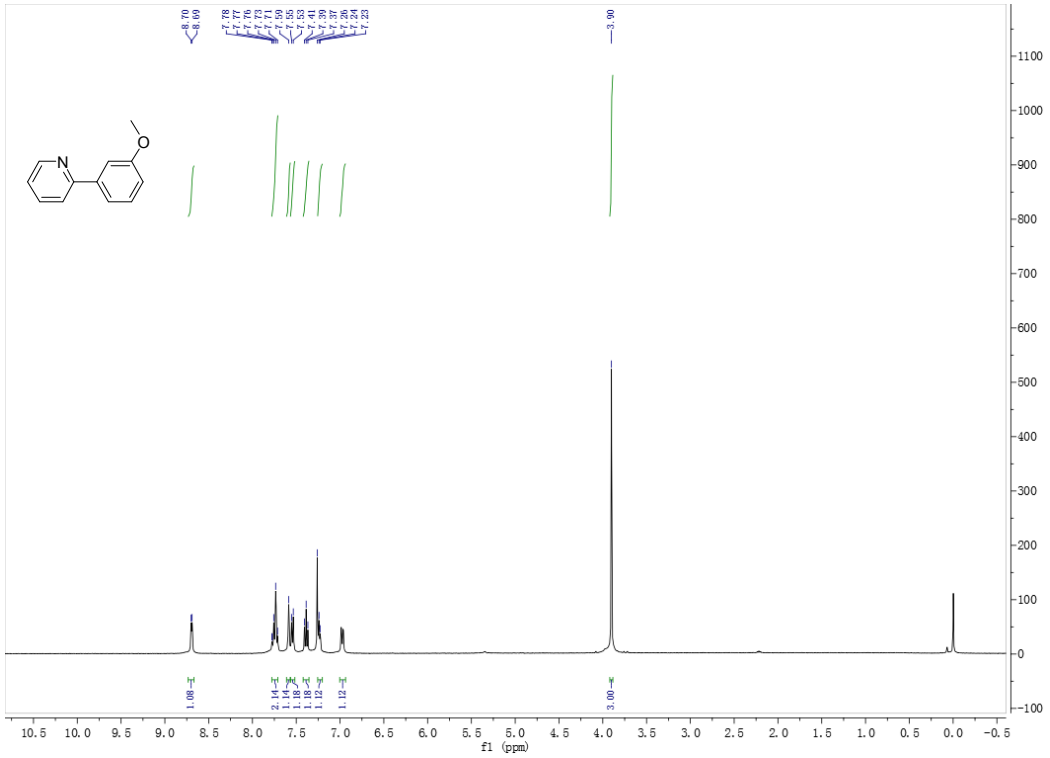
f1 (ppm)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7.53
7.41
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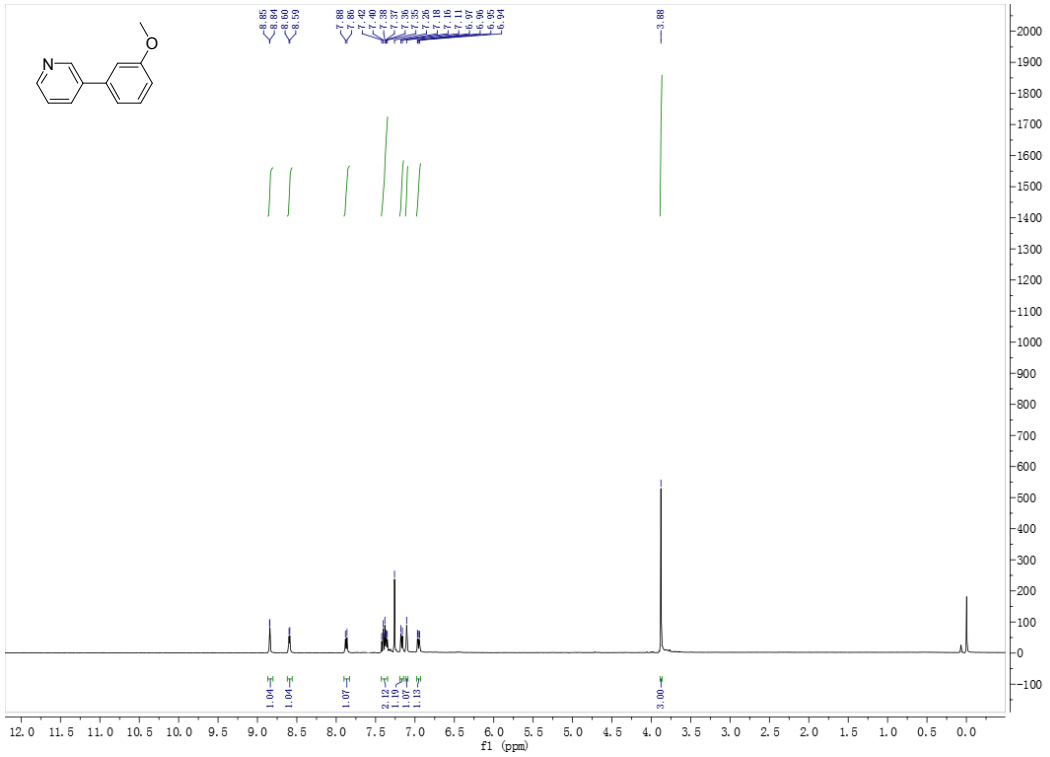
7.26
7.24
7.23
3.90
f1 (ppm)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7.37
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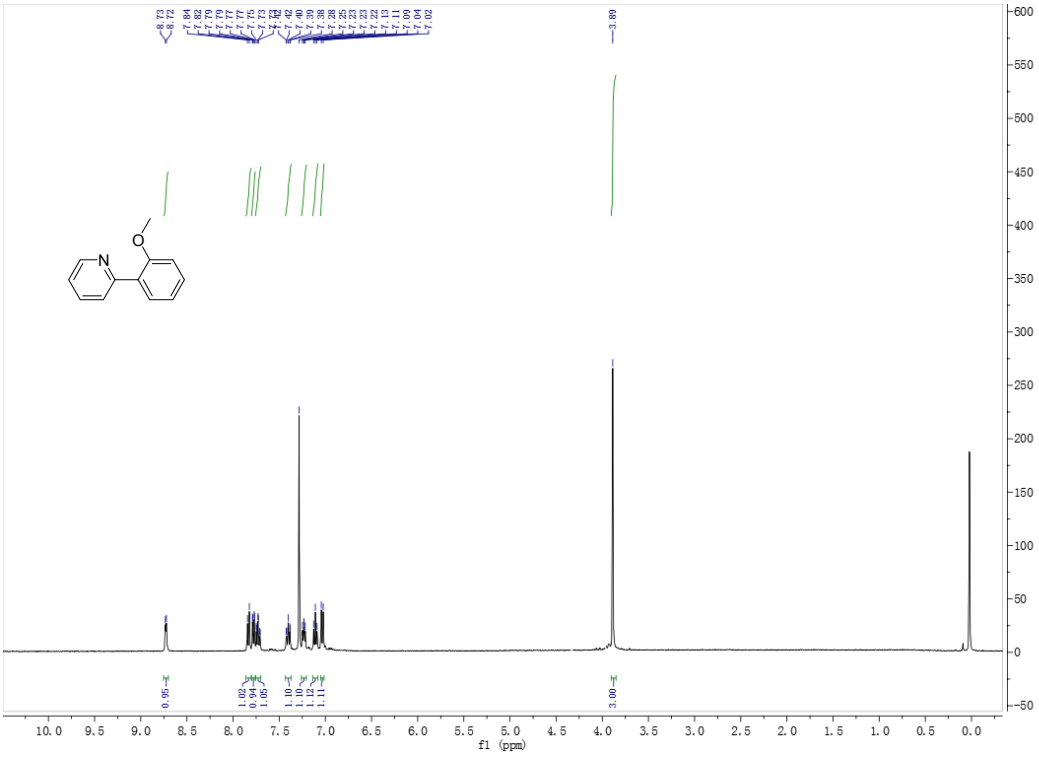
6.96
6.95
6.94
3.88
f1 (ppm)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7.73
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7.39
7.38
7.38
7.25
7.23
7.23
7.22
7.13
7.11
7.09
7.04
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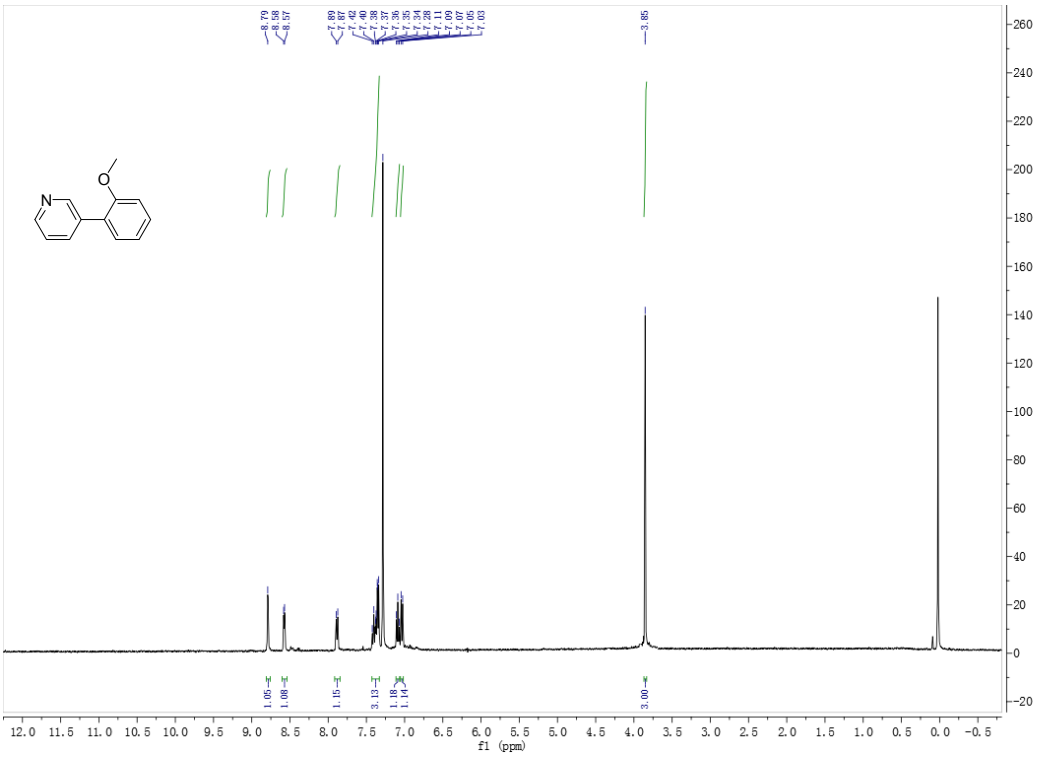
0.94
1.05
1.10
1.10
1.12
1.11
3.00
f1 (ppm)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7.11
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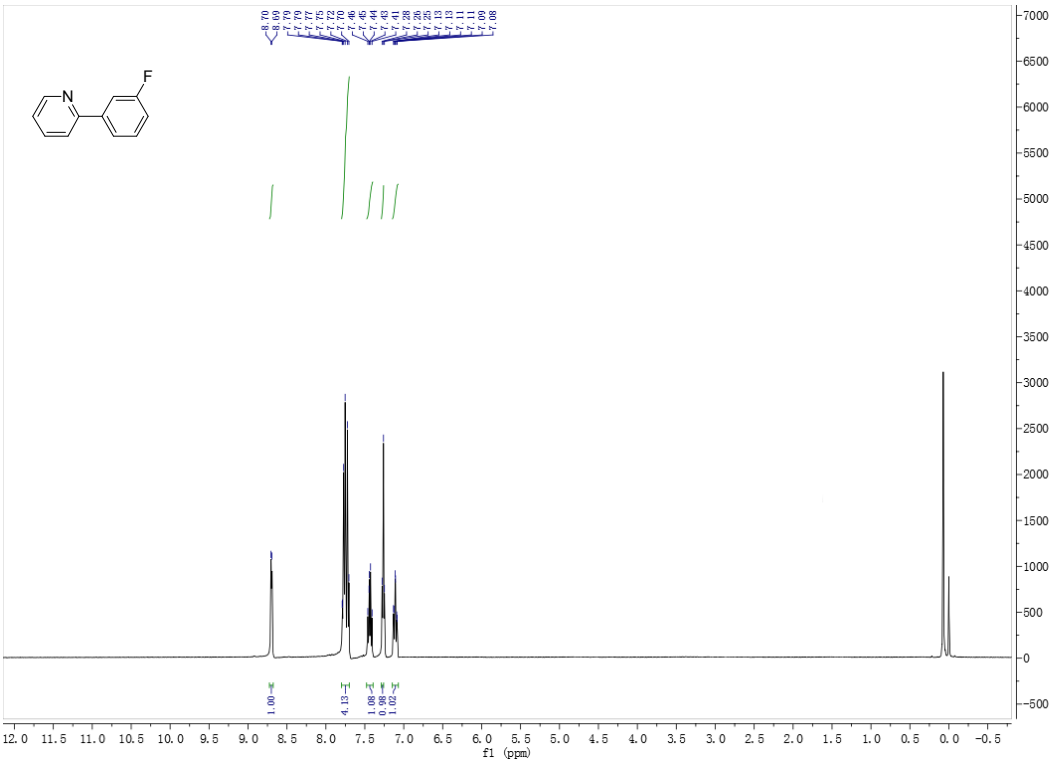
f1 (ppm)


F
N
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7.45
7.44
7.43
7.41
7.28
7.26
7.25
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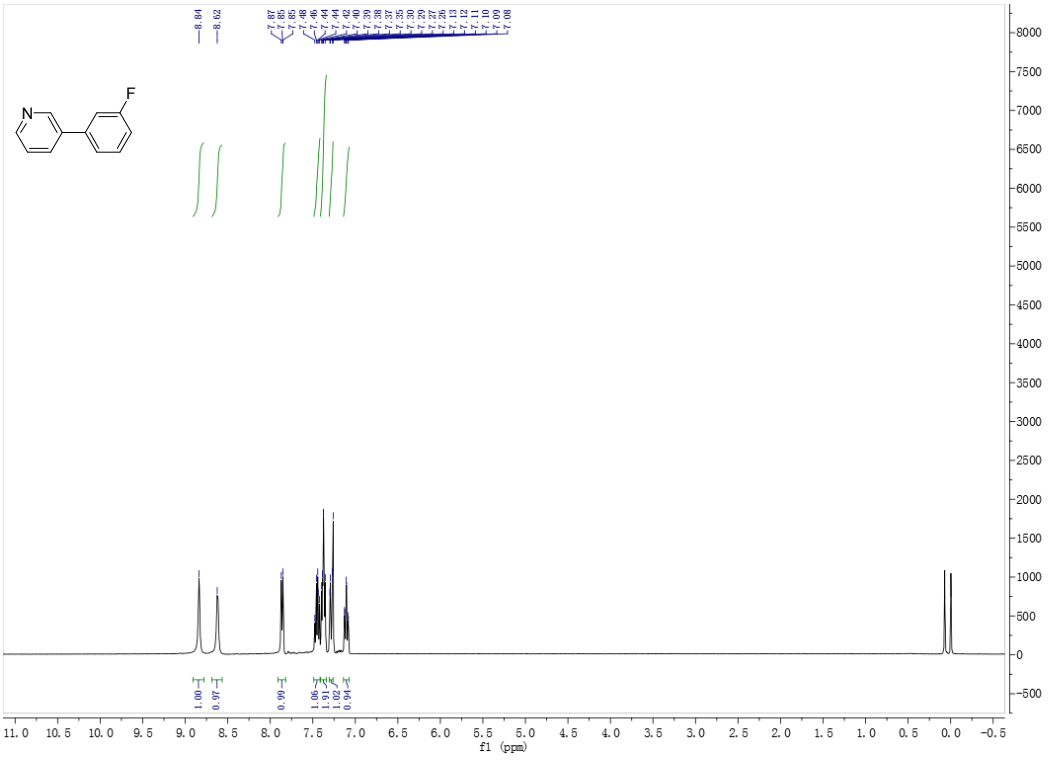
7.11
7.11
7.09
7.08
1.00
4.13
1.08
0.98
1.02
f1 (ppm)


F
N
8.84
8.82
7.87
7.85
7.85
7.46
7.44
7.44
7.42
7.40
7.39
7.38
7.37
7.35
7.30
7.29
7.27
7.26
7.13
7.12
7.11
7.10
7.09
7.08
1.00
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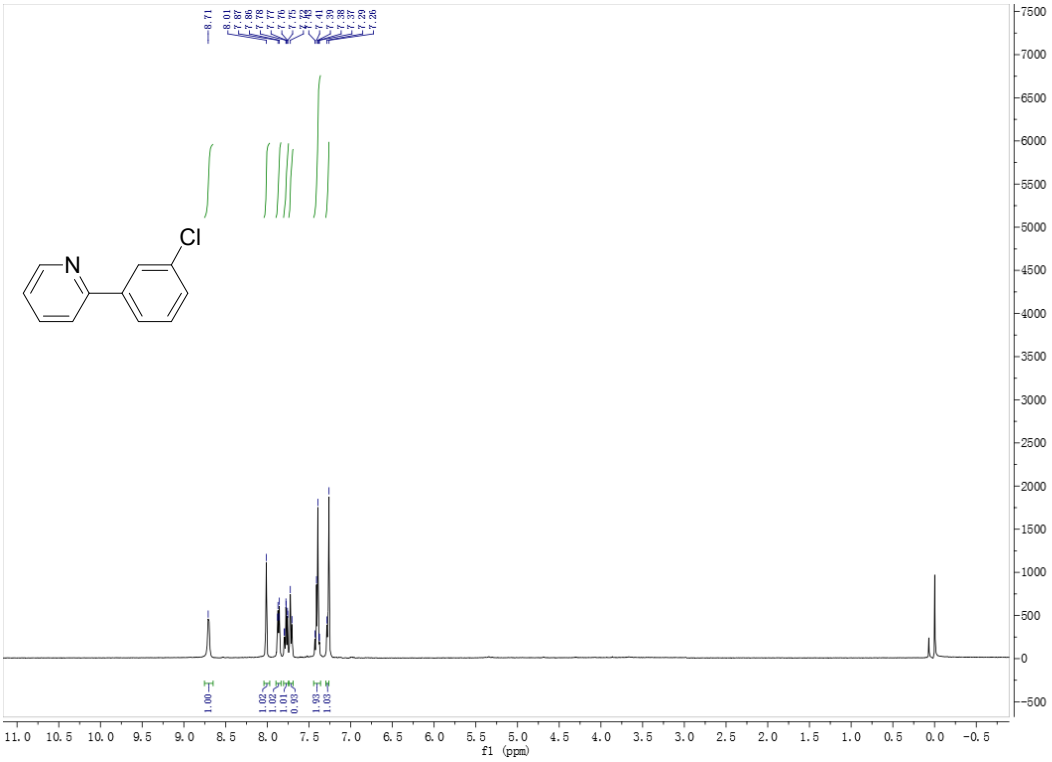
0.99
1.06
1.91
1.02
0.94
f1 (ppm)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8.01
7.87
7.86
7.78
7.77
7.76
7.75
7.43
7.41
7.39
7.38
7.37
7.29
7.26
Cl
N
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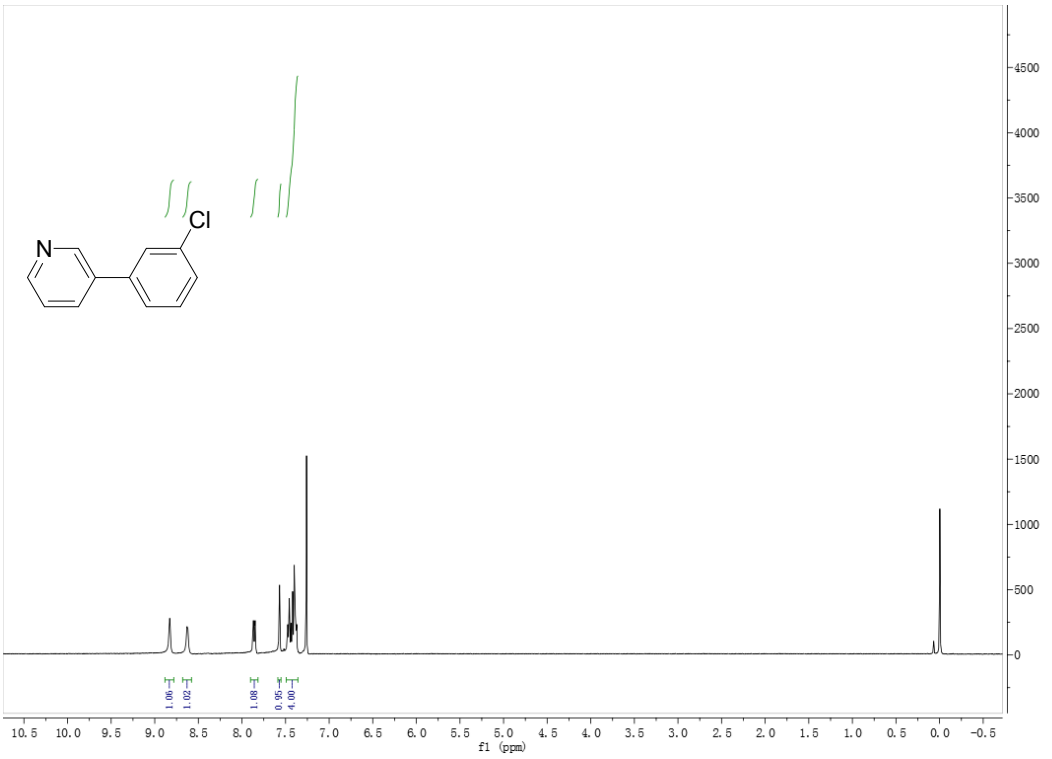
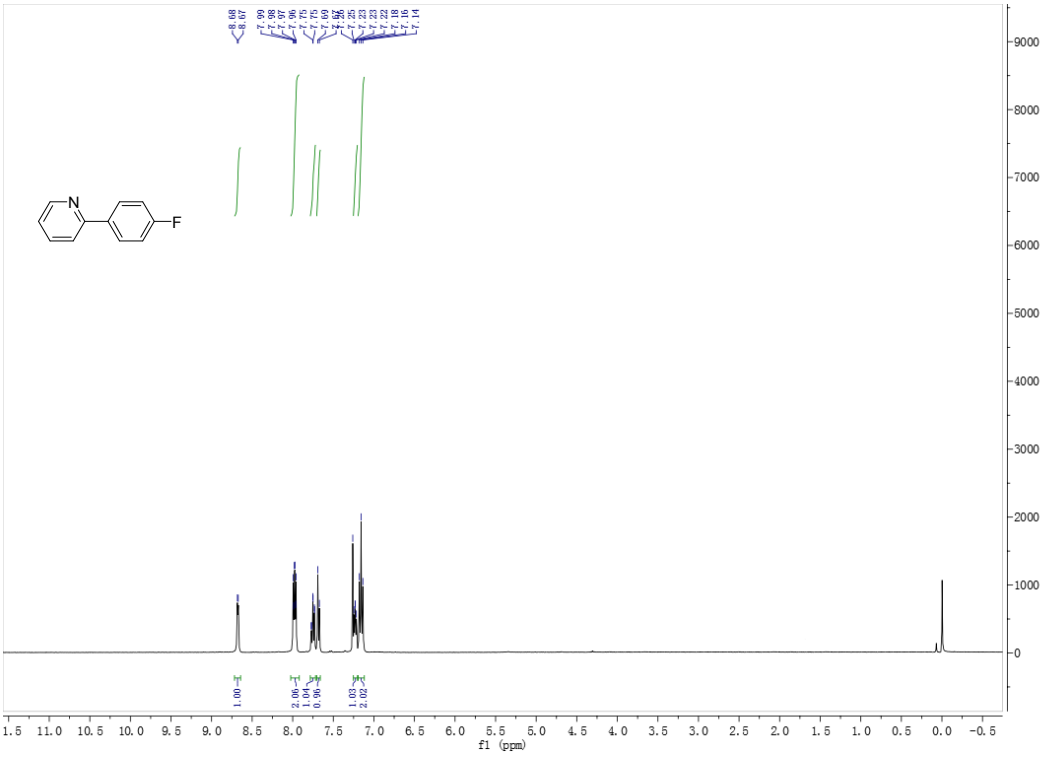
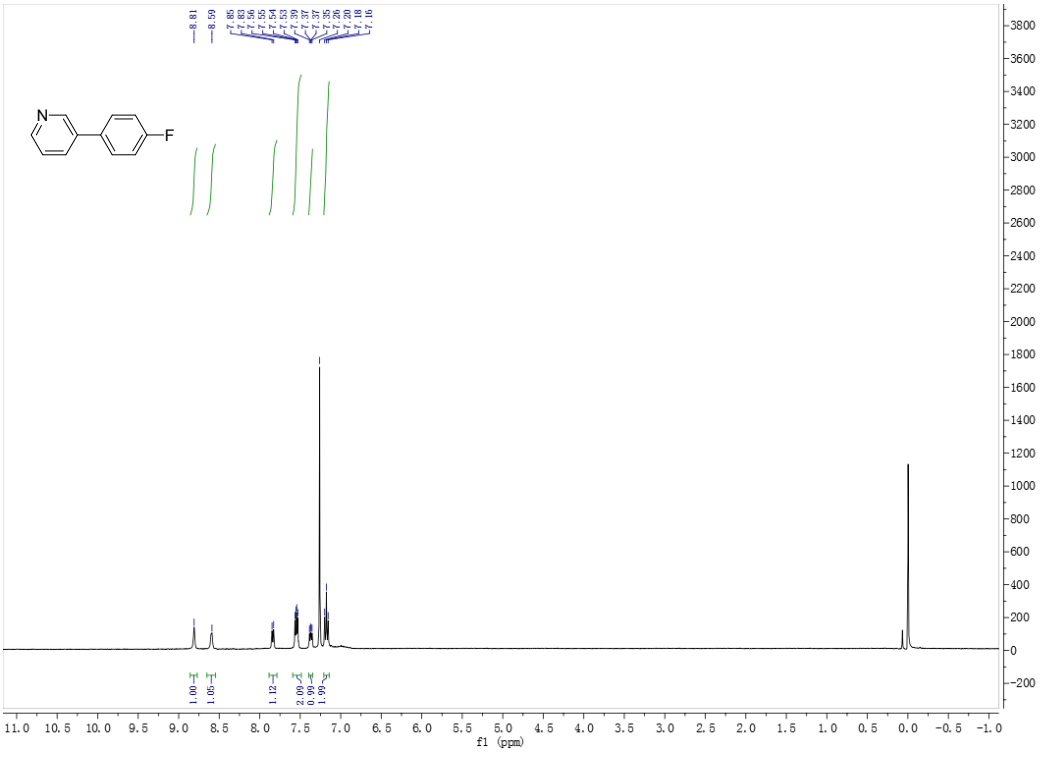
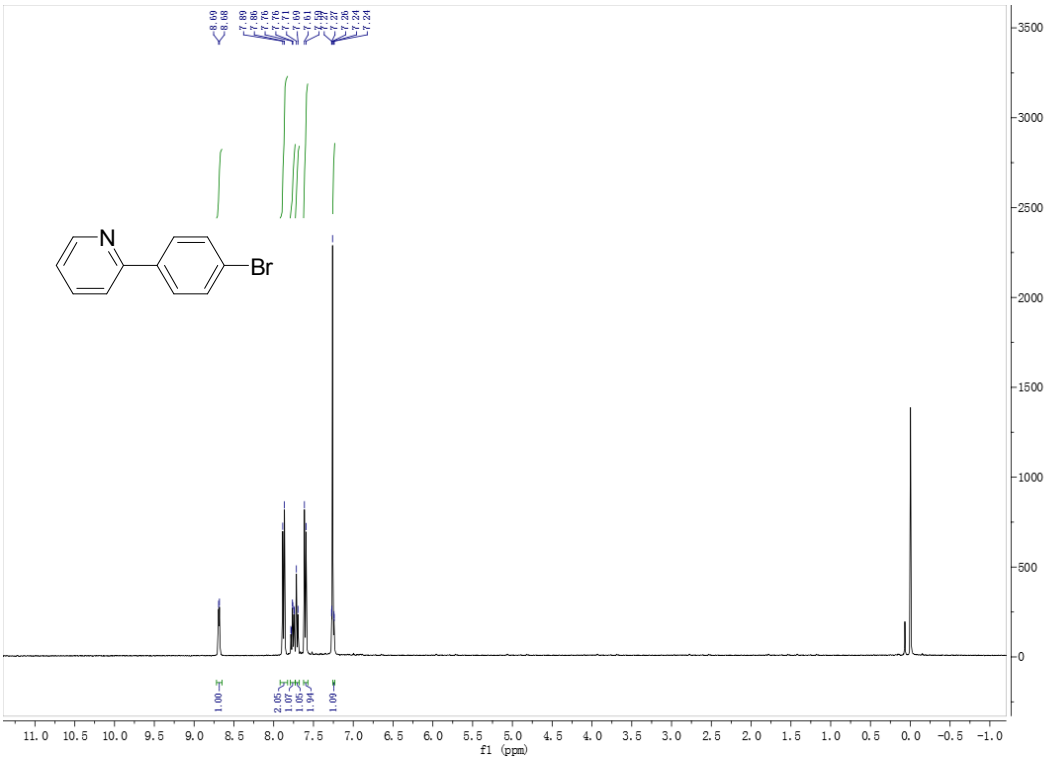
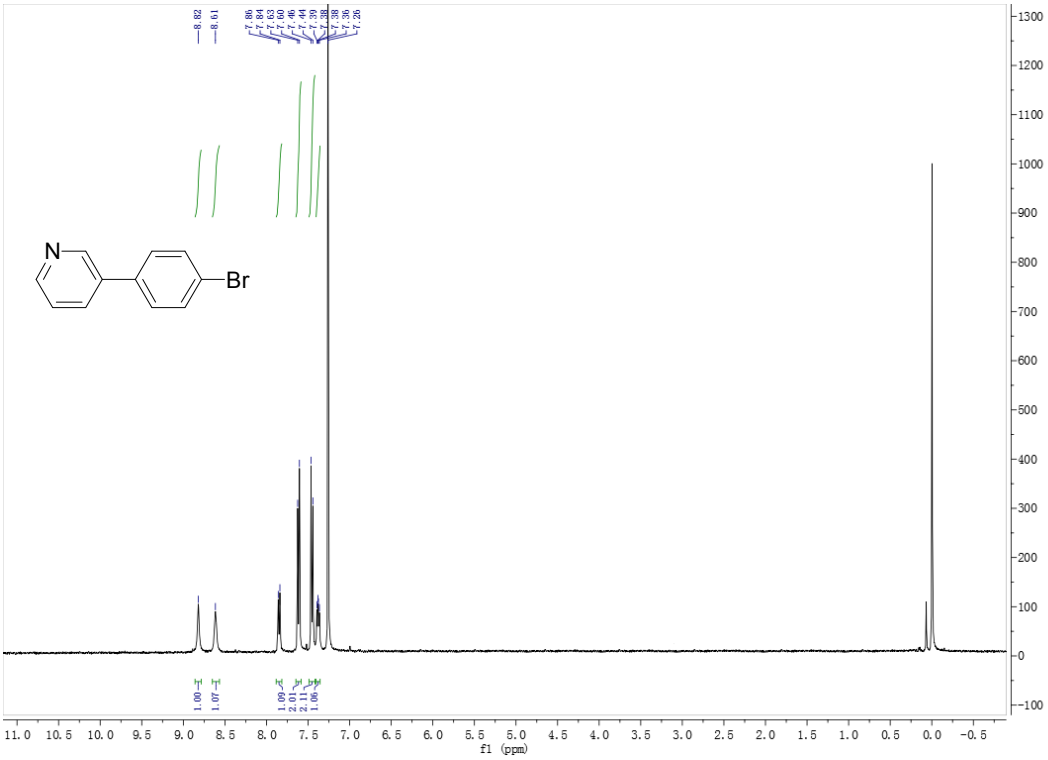
1.02
1.02
1.01
0.93
1.93
1.03
f1 (ppm)


Cl
N
1.06
1.02
1.08
0.95
4.00
f1 (ppm)


N
F
f1 (ppm)


N
F
f1 (ppm)


8.69
8.68
7.89
7.86
7.76
7.75
7.71
7.69
7.61
7.59
7.27
7.26
7.24
N
Br
1.00
2.05
1.07
1.05
1.94
1.09
f1 (ppm)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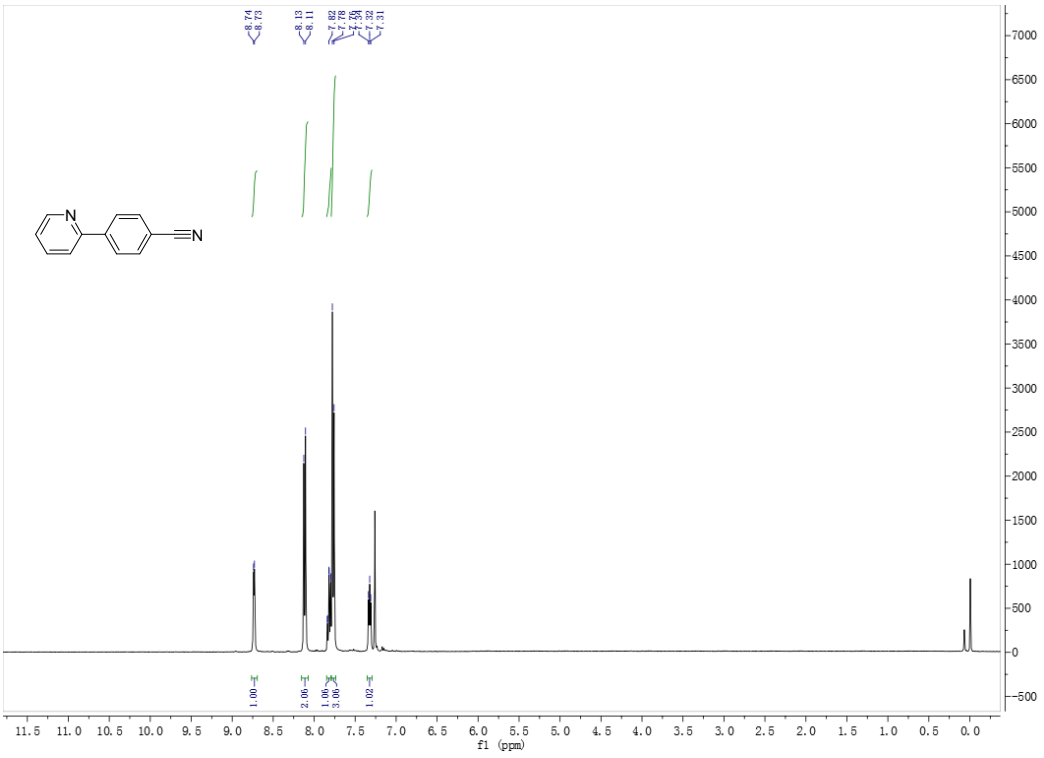
8.61
7.86
7.84
7.63
7.60
7.46
7.44
7.39
7.38
7.36
7.26
N
Br
1.00
1.07
1.09
2.01
1.11
1.06
f1 (ppm)


8.74
8.73
8.13
8.11
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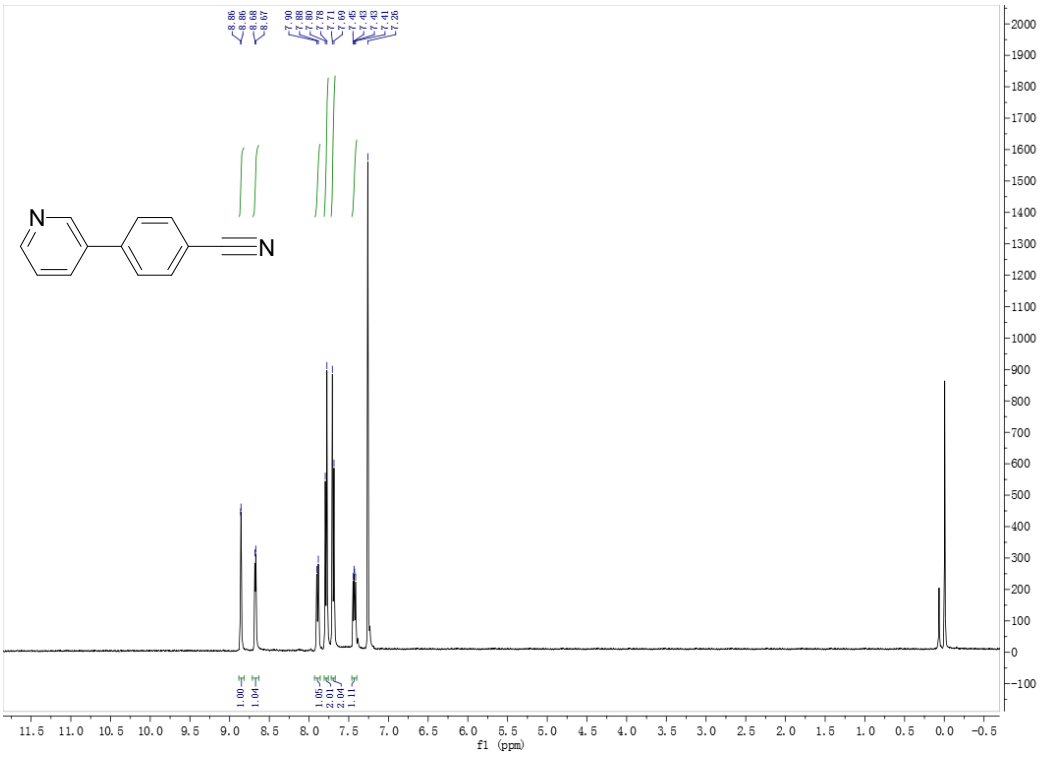
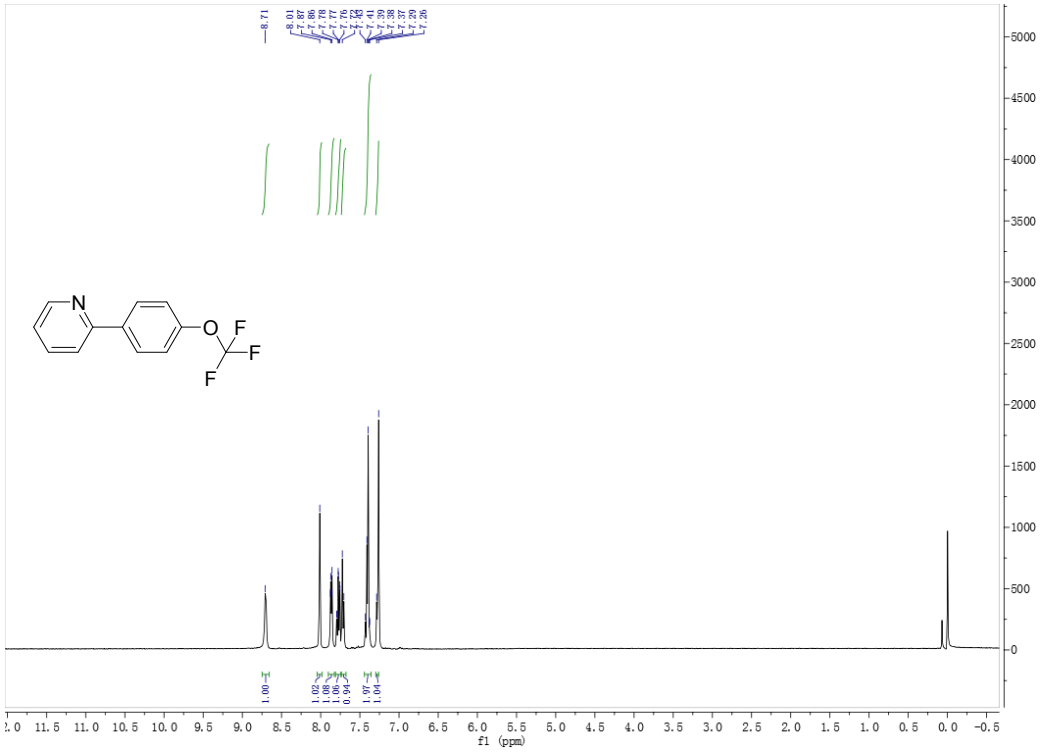
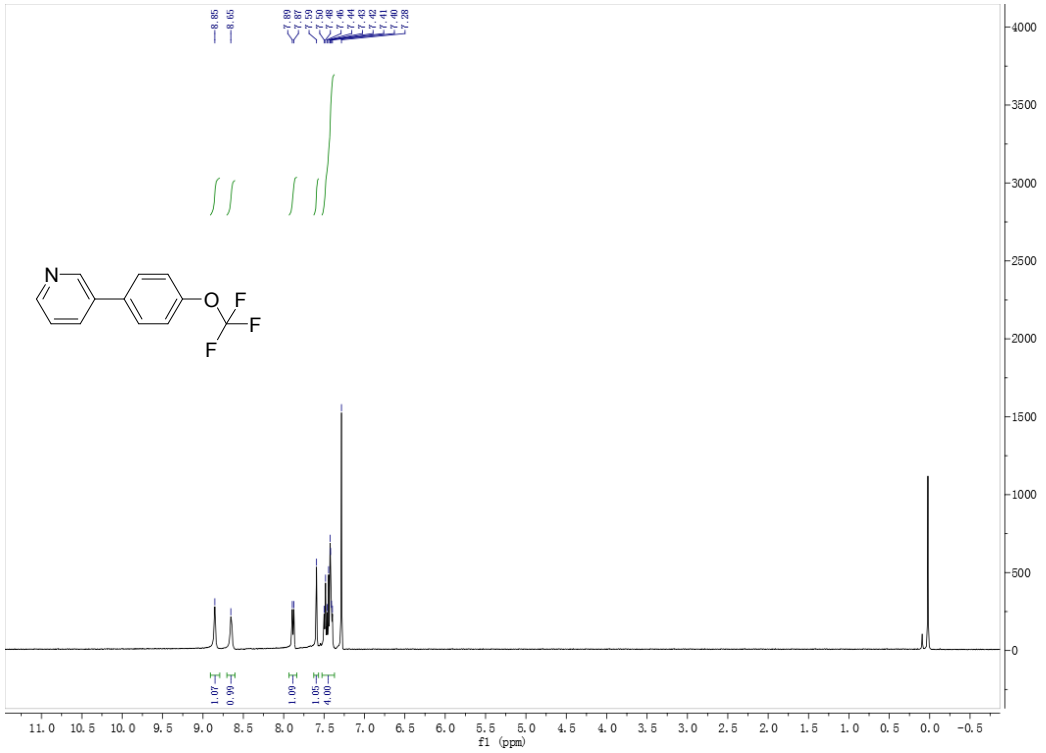
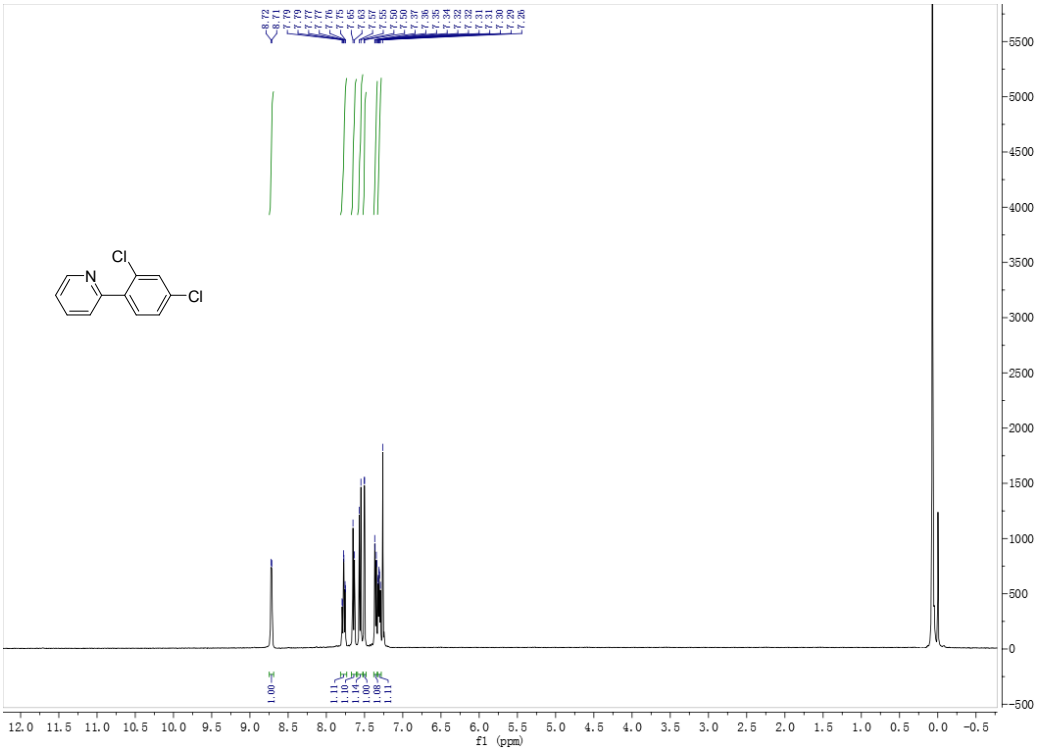
7.31
N
N
1.00
2.06
1.00
3.06
1.02
f1 (ppm)


8.86
8.86
8.68
8.67
7.90
7.88
7.80
7.78
7.71
7.69
7.45
7.43
7.42
7.41
7.26
N
N
1.00
1.04
1.05
2.01
2.04
1.11
f1 (ppm)


N
O
F
F
F
f1 (ppm)


N
O
F
F
F
f1 (ppm)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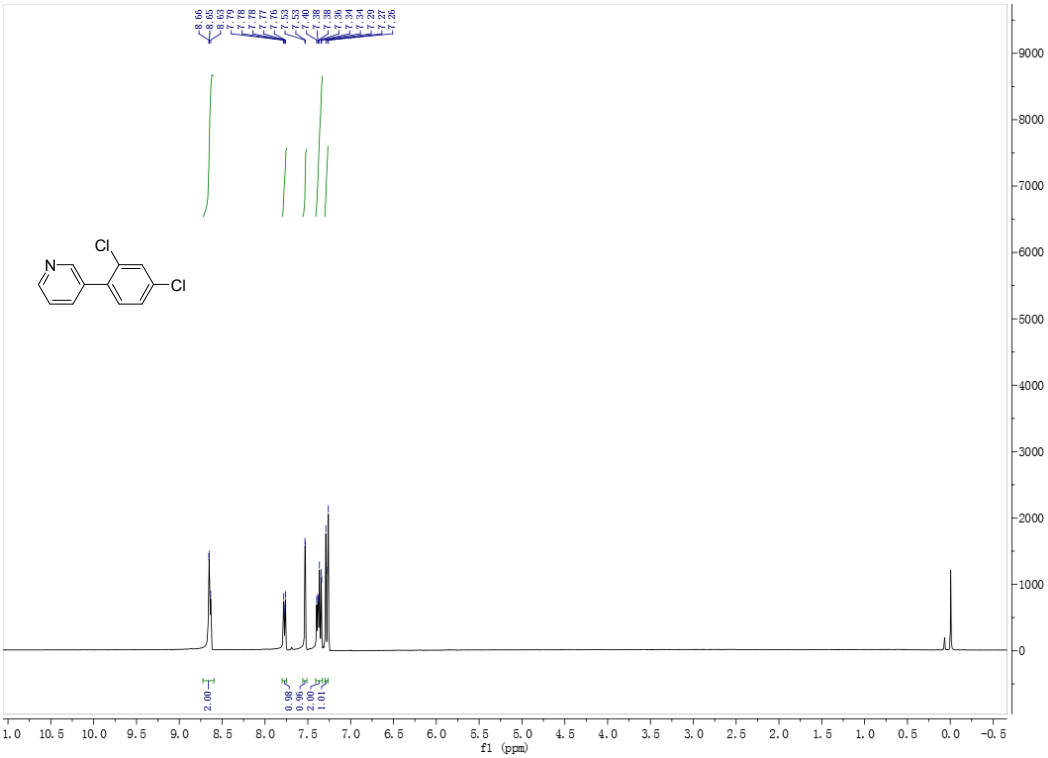
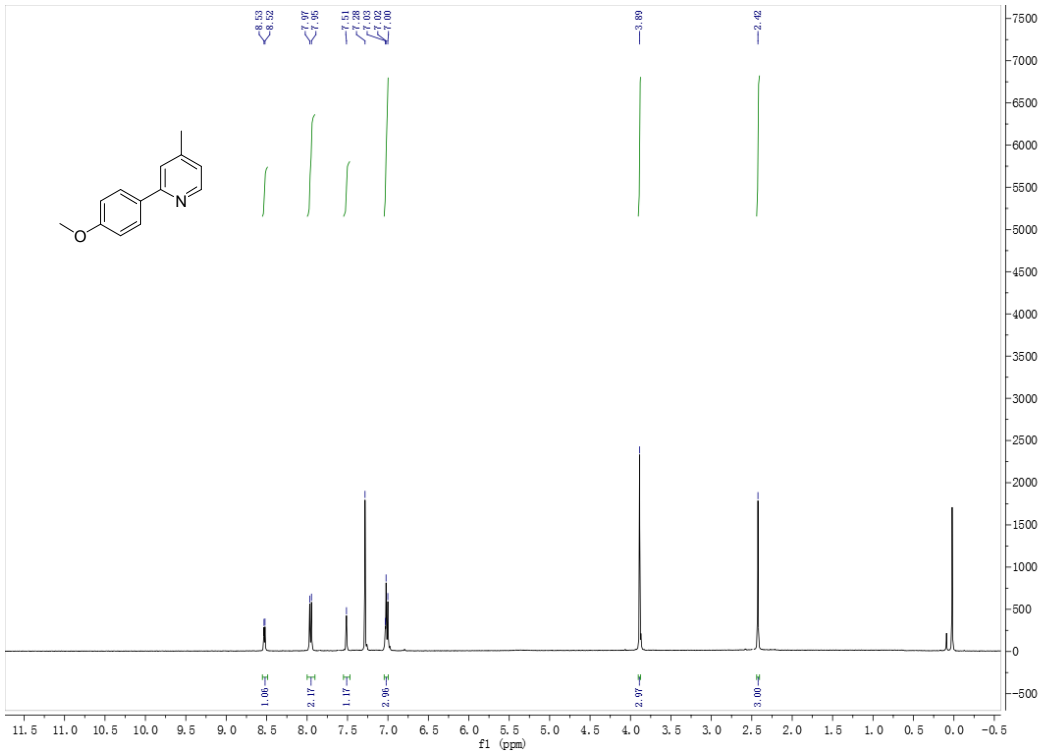
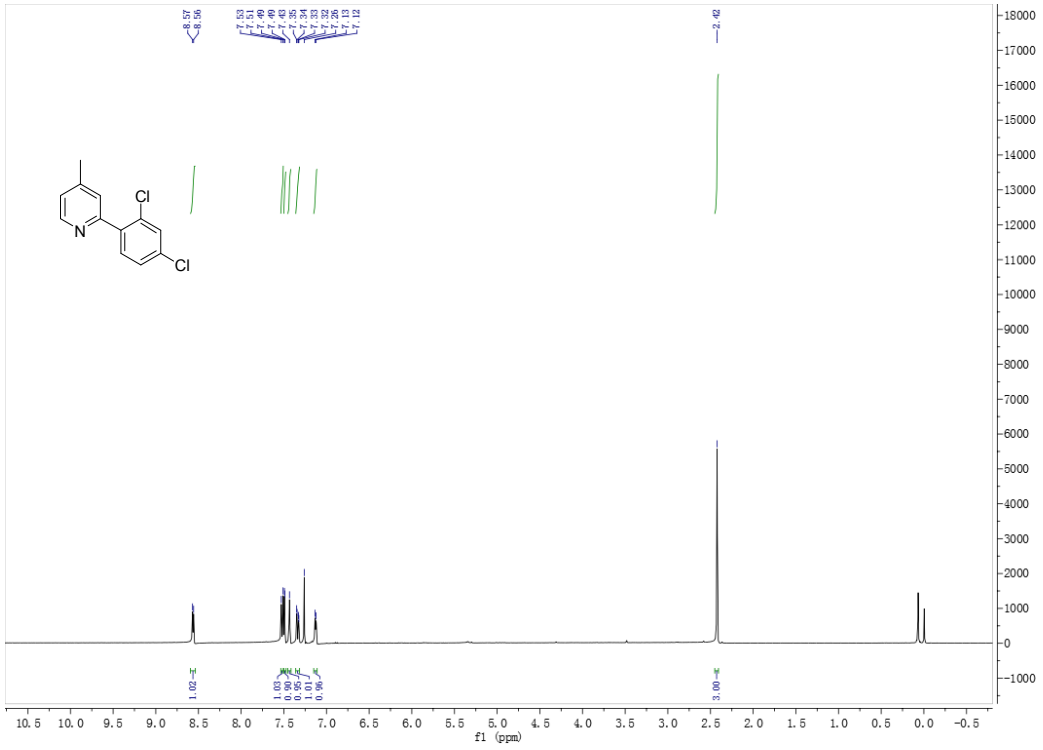
8.71
7.79
7.77
7.76
7.75
7.65
7.63
7.57
7.55
7.50
7.39
7.37
7.36
7.35
7.34
7.32
7.31
7.30
7.29
7.26
Cl
N
Cl
1.00
1.11
1.10
1.14
1.00
1.08
1.14
f1 (ppm)


8.66
8.65
8.63
7.79
7.78
7.77
7.76
7.53
7.40
7.38
7.36
7.34
7.30
7.29
7.27
7.26
Cl
N
Cl
2.00
0.98
0.96
2.00
1.01
f1 (ppm)


8.53
8.52
7.97
7.95
7.51
7.28
7.03
7.02
7.00
3.89
2.42
N
O
1.00
2.17
1.17
2.06
2.97
3.00
f1 (ppm)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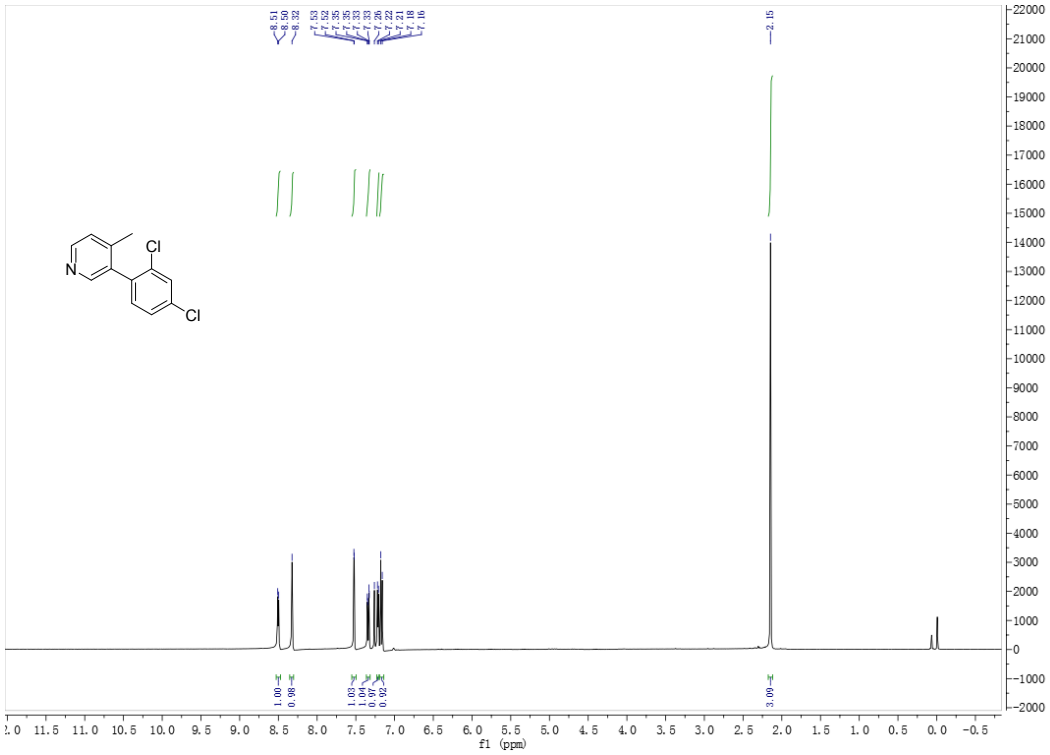
8.56
7.53
7.51
7.49
7.49
7.45
7.35
7.34
7.33
7.32
7.26
7.13
7.12
2.42
N
Cl
Cl
1.02
1.03
0.90
0.95
1.01
0.96
3.00
f1 (ppm)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8.50
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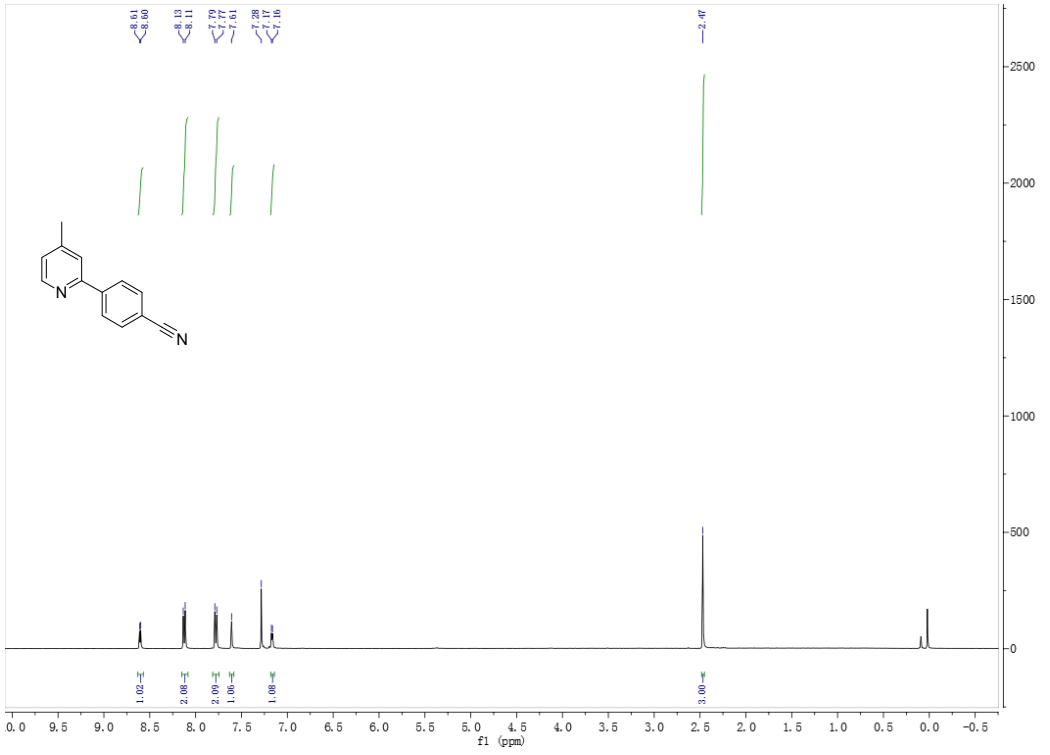
7.52
7.35
7.35
7.33
7.33
7.26
7.22
7.21
7.18
7.16
2.15
Cl
Cl
N
1.00
0.98
1.03
1.04
0.97
0.92
3.09
f1 (ppm)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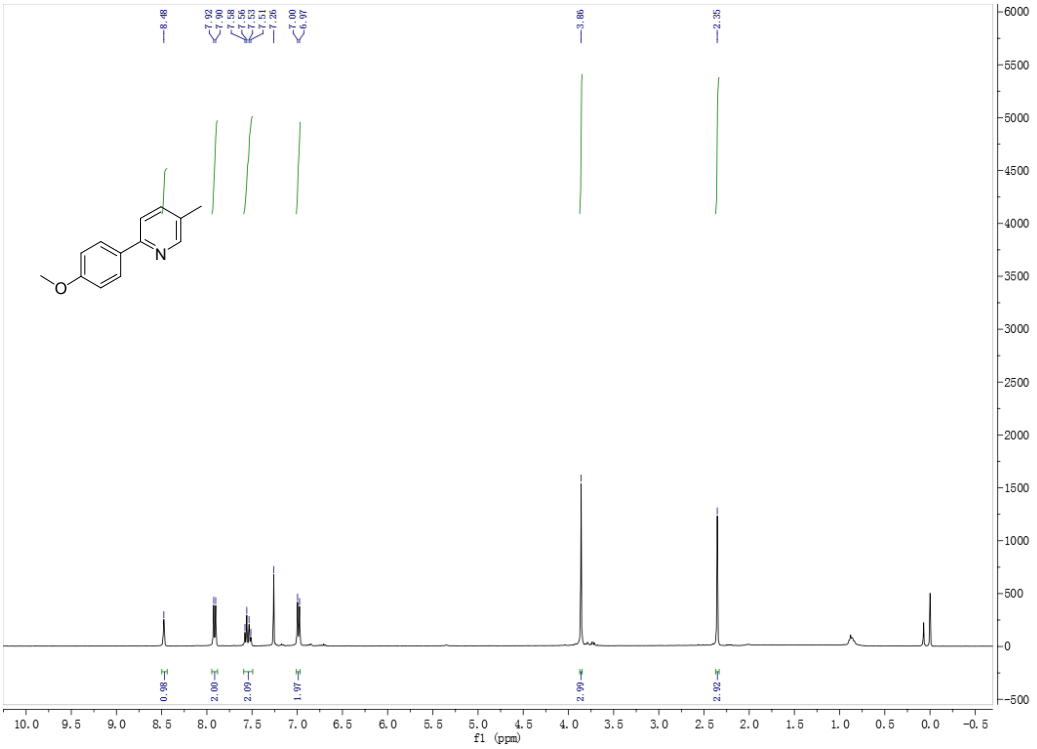
8.60
8.13
8.11
7.79
7.77
7.61
7.28
7.17
7.16
2.47
N
N
1.02
2.08
2.09
1.06
1.08
3.00
f1 (ppm)


8.48
7.92
7.90
7.58
7.56
7.53
7.51
7.26
7.00
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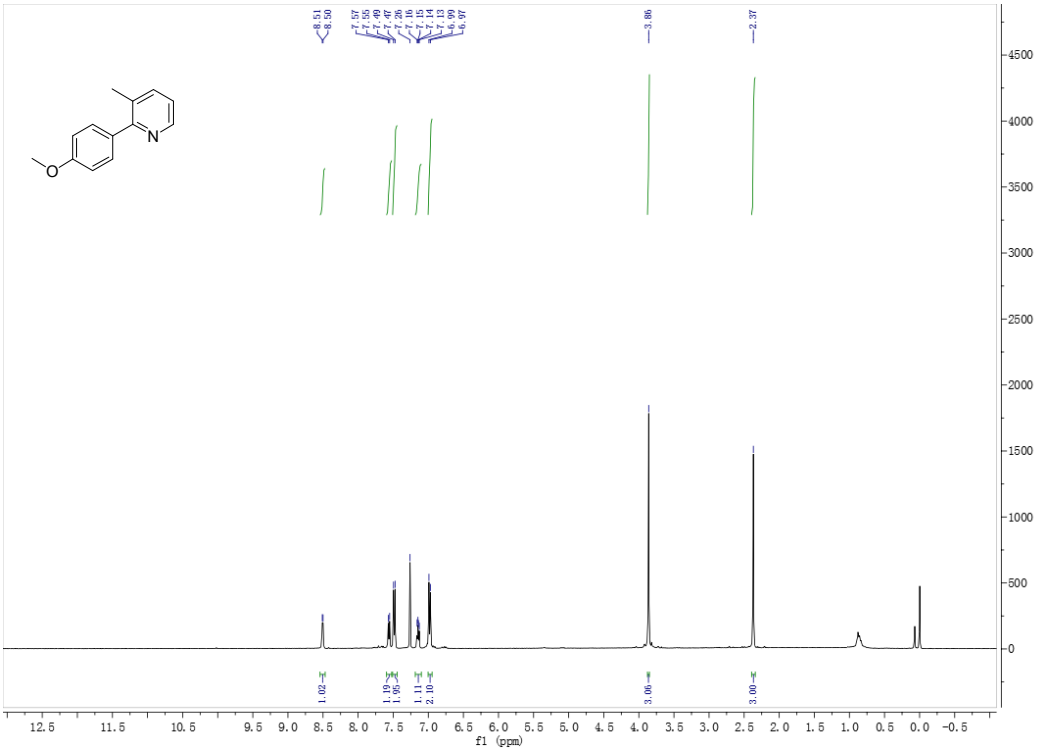
3.86
2.35
0.98
2.00
2.09
1.97
2.99
2.92
f1 (ppm)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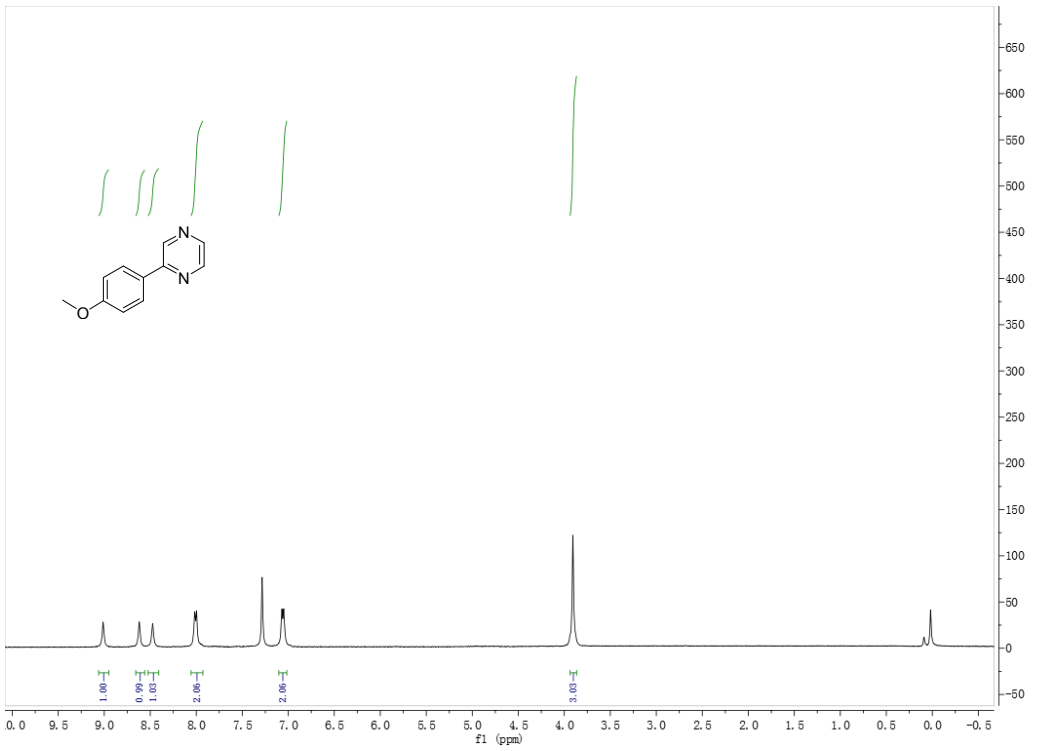
8.50
7.57
7.55
7.49
7.47
7.26
7.16
7.15
7.14
7.13
6.99
6.97
3.86
2.37
1.02
1.19
1.95
1.11
2.10
3.06
3.00
f1 (ppm)


N
N
O
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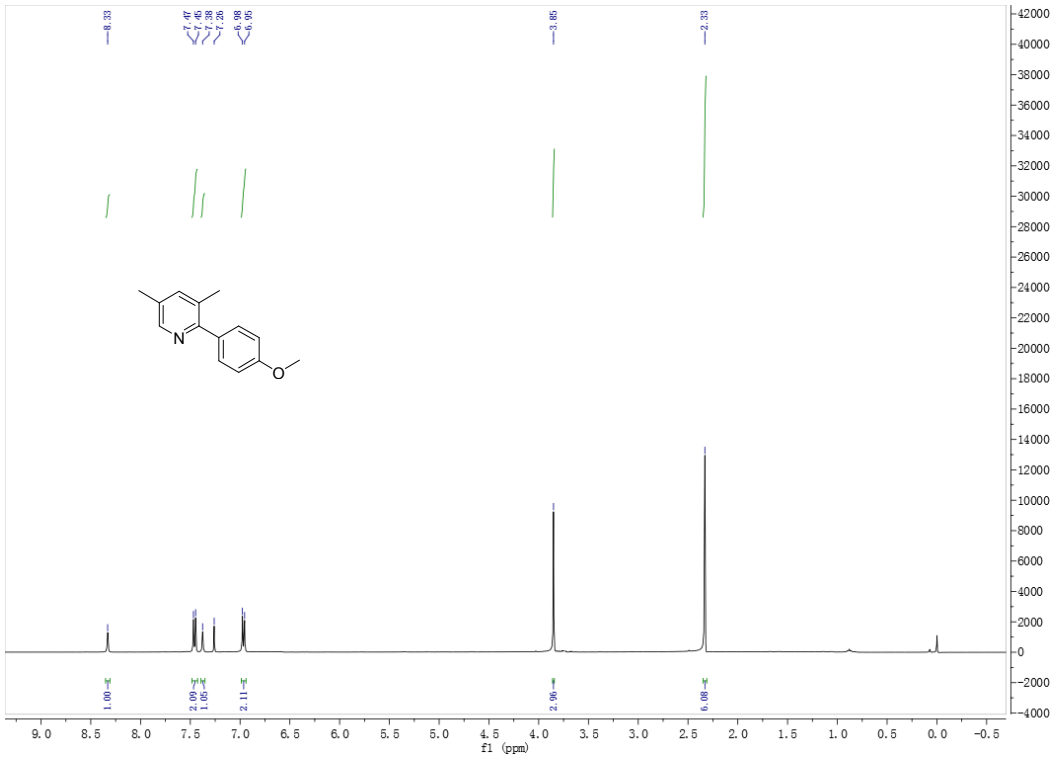
0.99
1.83
2.06
2.06
3.03
f1 (ppm)


8.33
7.47
7.45
7.38
7.26
6.98
6.95
3.85
2.33
N
O
1.00
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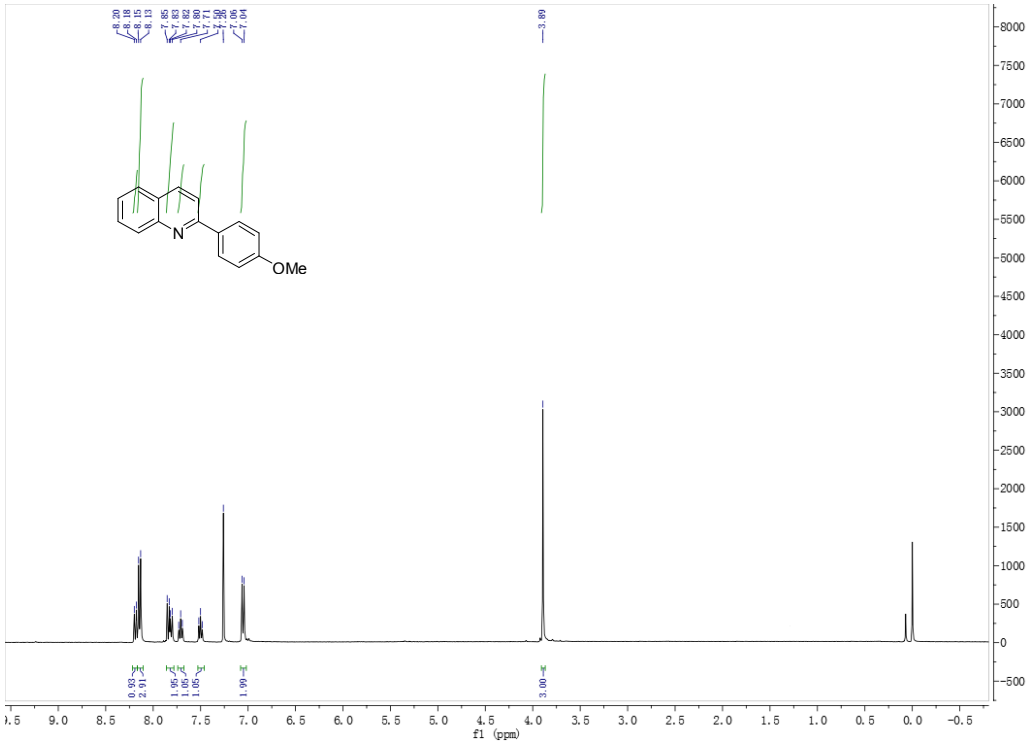
1.05
2.11
2.96
6.08
f1 (ppm)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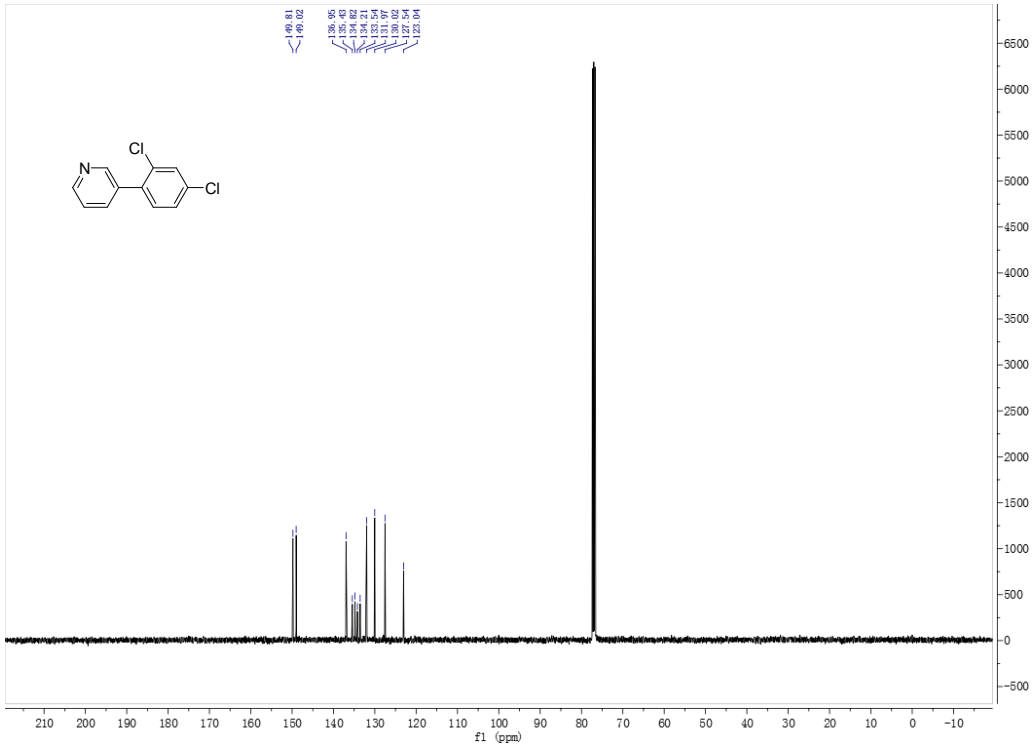
8.18
8.15
8.13
7.85
7.83
7.82
7.80
7.77
7.75
7.06
7.04
3.89
OMe
N
0.93
2.91
1.95
1.05
1.05
1.99
3.00
f1 (ppm)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149.02
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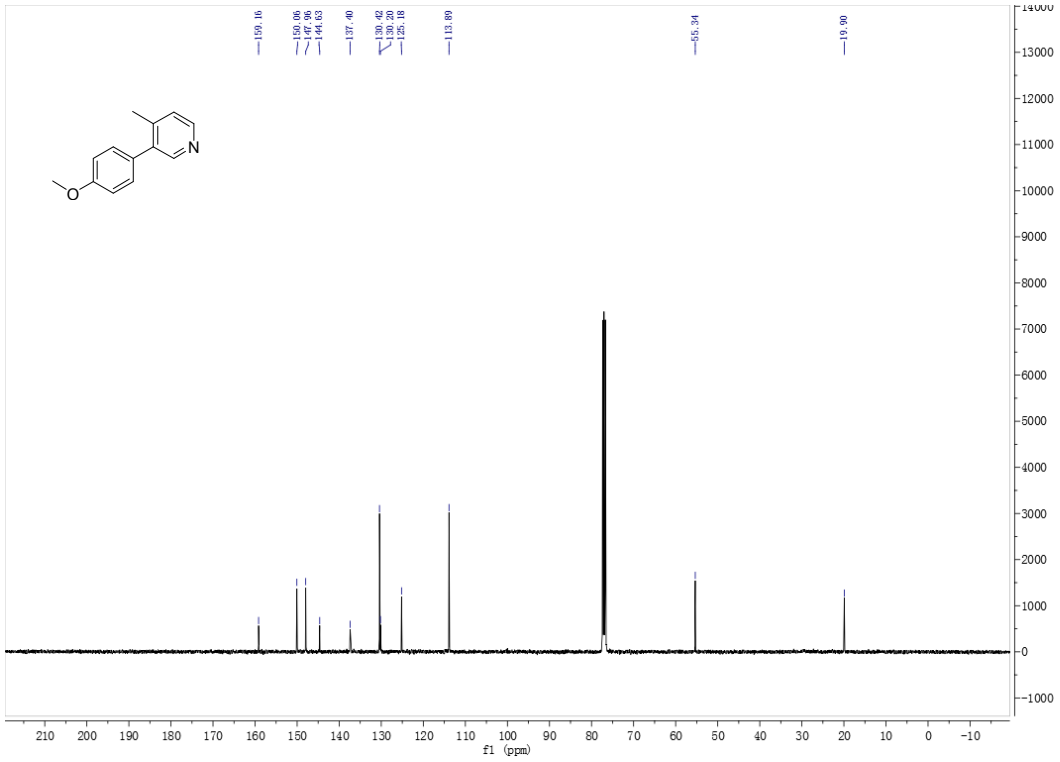
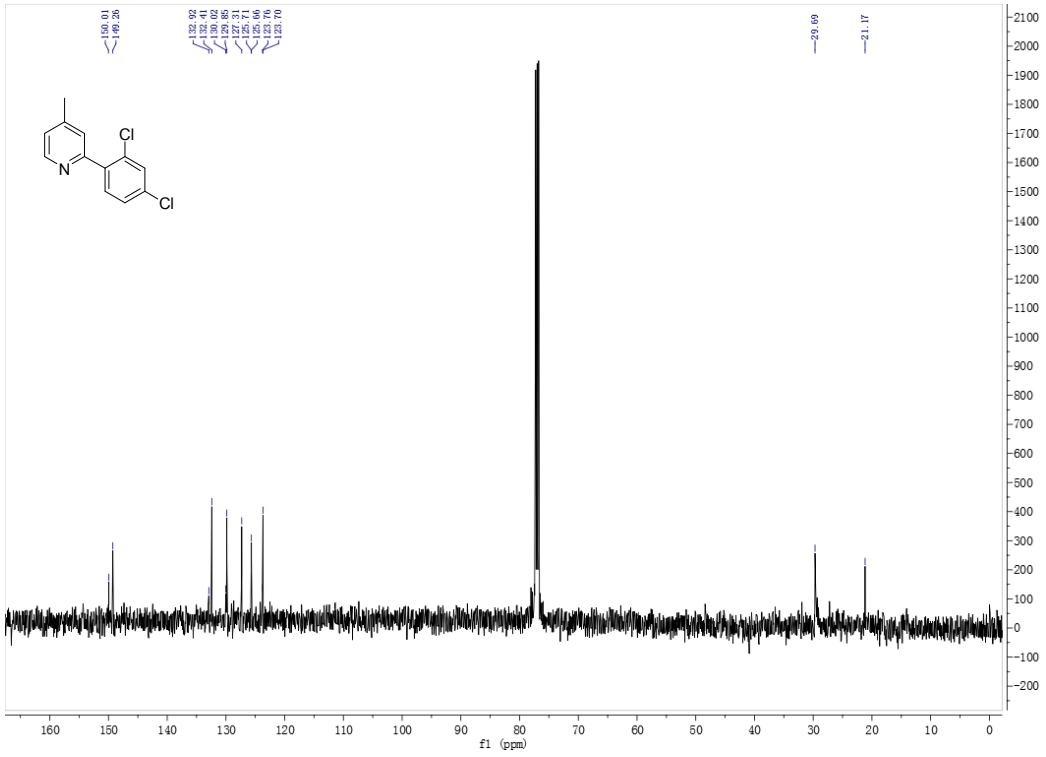
135.43
134.62
133.21
132.54
131.97
130.02
127.54
123.04
Cl
N
Cl
f1 (ppm)


159.16
150.06
147.95
144.63
137.40
130.42
130.03
125.18
113.89
55.34
19.90
O
N
f1 (ppm)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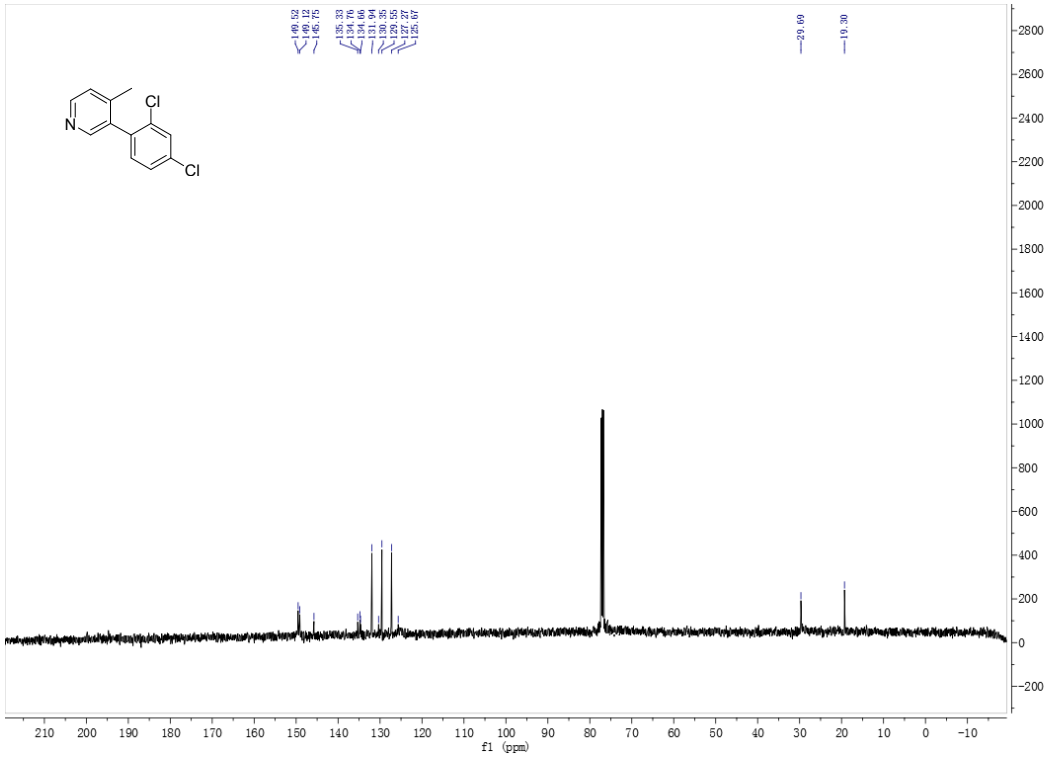
149.26
132.92
132.41
130.02
129.85
127.31
125.71
125.66
123.76
123.70
29.69
21.17
Cl
Cl
N
f1 (ppm)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149.12
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135.33
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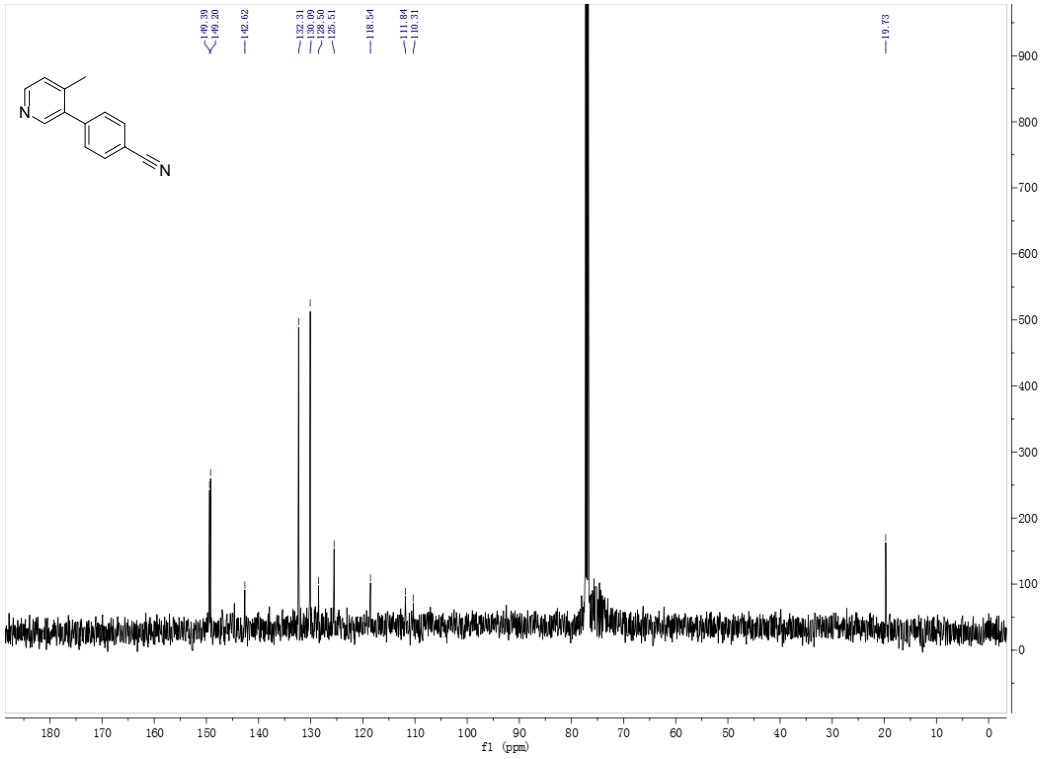
134.46
131.94
130.35
129.55
127.27
125.67
29.69
19.30
Cl
Cl
N
f1 (ppm)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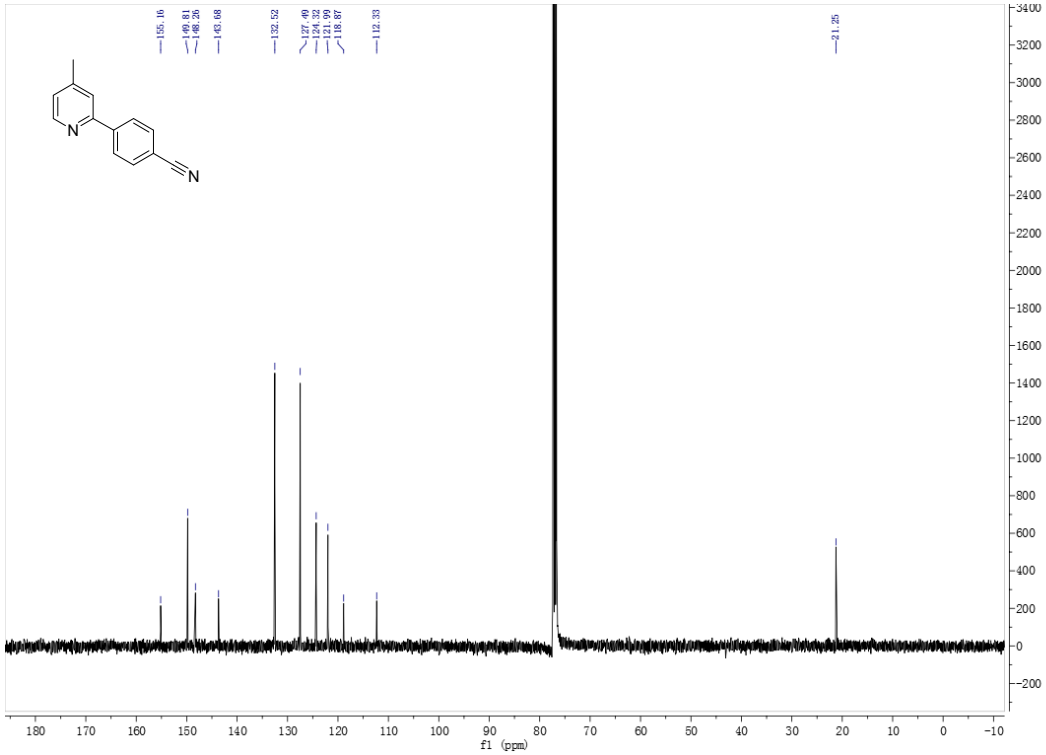
149.20
142.62
132.31
130.09
128.50
125.51
118.54
111.84
110.31
19.73
N
N
f1 (ppm)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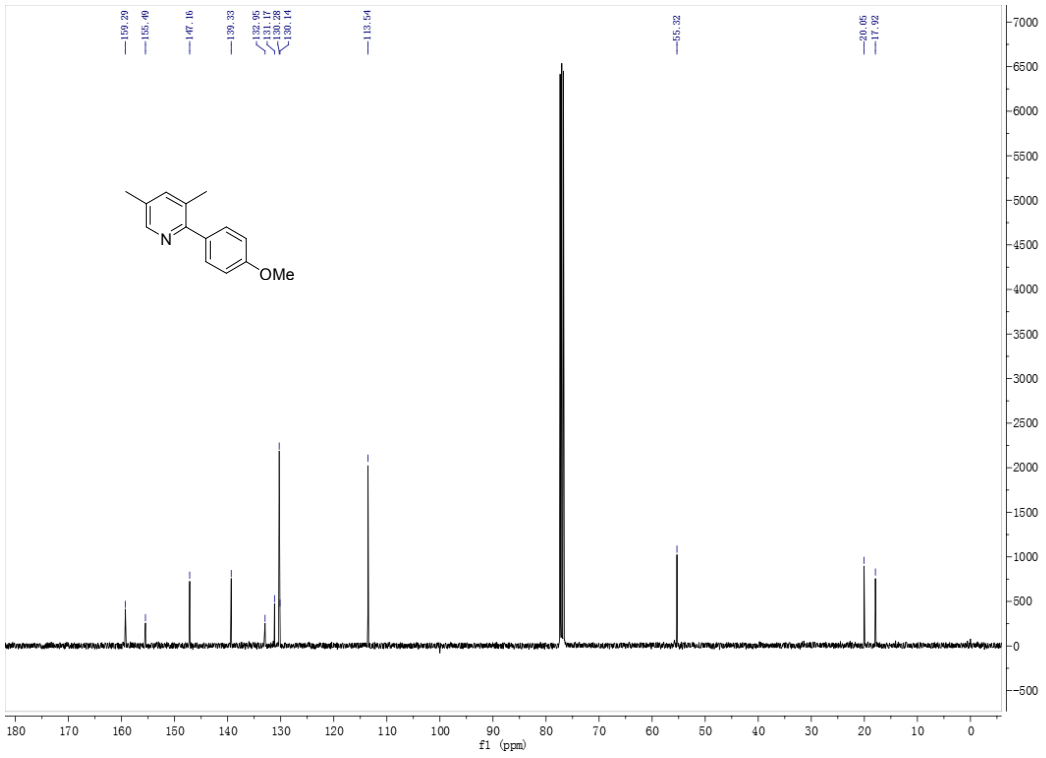
132.52
127.49
124.32
121.99
118.87
112.33
21.25
N
N
f1 (ppm)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155.49
147.16
139.33
132.95
131.17
130.98
130.14
113.154
55.32
20.05
17.92
N
OMe
f1 (ppm)