Supporting Information

Transition-Metal-Free Lactamization of C(sp^3)—H Bonds with CO_2: Facile Generation of Pyrido[1,2-a]pyrimidin-4-ones

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General Considerations

All reactions were set up with glovebox and carried out under a carbon dioxide atmosphere in Schlenk tubes. Reaction temperatures were reported as the temperature of the heat transfer medium surrounding the vessel unless otherwise stated. Anhydrous solvent (including diglyme, DMA, THF, DMSO, 1,4-dioxane and DMF, 99.8%, Water < 0.005%) were purchased from J&K Scientific Ltd., and used as received. Commercially available chemicals were obtained from J&K Scientific Ltd., Adamas，Acros Organics, Aldrich Chemical Co., Alfa Aesar, Chengdu Research Accelerators Technology Co., Ltd. and BT Reagent and used as received unless otherwise stated. LiO^{t}Bu (98%, 100 g) was obtained from J&K Scientific Ltd.

^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Brüker Advance 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 101 MHz，^{19}F: 376 MHz). Chemical shifts (δ) for ^{1}H and ^{13}C NMR spectra are given in ppm relative to TMS, The residual solvent signals were used as references for ^{1}H and ^{13}C NMR spectra and the chemical shifts converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm; $(CD_3)_2SO$: δH = 2.50 ppm, δC = 39.52 ppm).

GC-MS was obtained using electron ionization (Agilent Technologies 7890B/GC-System and 5977A/MSD). TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. Exact ESI mass spectra were recorded on a SHIMADZU LCMS-IT-TOF. LRMS are obtained on a Thermo-ITQ. Metal element contents were obtained on a thermo ICP-AES (IRIS Adv.)

Synthesis of Substrates

The substrates in **Table2** were prepared according to procedures described in the literature[S1] reported before.

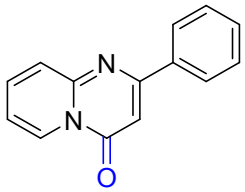
All the protocols were employed without any optimization of the reaction conditions.

General procedure of Products

An oven-dried Schlenk tube (10 mL) containing a stirring bar was charged with the substrate (0.2 mmol). The Schlenk tube was then introduced in a glovebox where it was charged with LiO^{t}Bu (72 mg, 0.9 mmol, 4.5 equiv.). The tube was taken out of the glovebox and connected to a vacuum line where it was evacuated and back-filled under CO_2 flow for at least 3 times. The DMF (2 mL) were added under CO_2 flow. Once added, the tube was closed at atmospheric pressure of CO_2 (1 atm) and stirred for 24 hours at 130 °C. Then, the mixture was cooled to room temperature, quenched with 2 mL water, then concentrated in vacuo. The residue was purified by silica gel flash chromatography (petroleum ether/AcOEt 3/1) to give the pure desired product.

Characterization of Products

2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2a)[S2]



38.3 mg, 0.17 mmol, 86 %;

Orange-red solid;

R_f (PE/EA 3/1): 0.27;

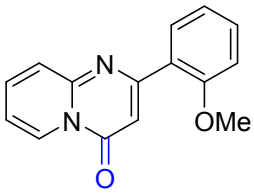
m. p. 146-147 °C（lit: 148 °C）

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (dt, *J* = 7.2, 1.2 Hz, 1H), 8.16 – 8.02 (m, 2H), 7.81 – 7.71 (m, 2H), 7.56 – 7.47 (m, 3H), 7.14 (ddd, *J* = 7.2, 4.8, 3.2 Hz, 1H), 6.92 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.08, 158.64, 151.02, 137.25, 136.17, 130.64, 128.82, 127.41, 127.27, 126.77, 115.21, 100.12.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_{10}N_2OH]^+$: 223.0866, found: 223.0870.

2-(2-methoxyphenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2b)[S3]



24.1 mg, 0.096 mmol, yield 46%; （the substrates is actually delivered 0.208mmol）

Purple solid;

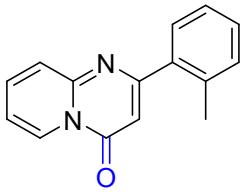
R_f(PE/EA 3/1): 0.21;

m.p 143-144 °C (lit.148-149 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.11 – 9.02 (m, 1H), 7.97 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.71 (dd, *J* = 4.5, 1.2 Hz, 2H), 7.43 (ddd, *J* = 8.4, 7.5, 1.8 Hz, 1H), 7.15 (s, 1H), 7.14 – 7.07 (m, 2H), 7.02 (d, *J* = 8.3 Hz, 1H), 3.90 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.57, 158.42, 157.66, 150.65, 135.60, 131.28, 130.87, 127.12, 126.77, 126.67, 120.86, 114.97, 111.49, 105.37, 55.57.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_2H]^+$: 253.0972, found: 253.0972



2-(*o*-tolyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2c)[S4]

38.4 mg, 0.162 mmol, yield 79%;（the substrates is actually delivered 0.205mmol）White solid;

R_f(PE/EA 3/1): 0.18;

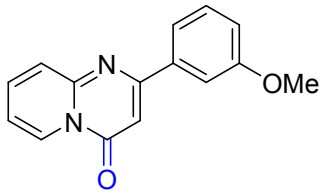
m.p 171-172 °C (lit.160-161.5 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.12 (d, *J* = 7.1 Hz, 1H), 7.83 – 7.65 (m, 2H), 7.53 – 7.41 (m, 1H), 7.32 (dtt, *J* = 11.8, 7.3, 3.5 Hz, 3H), 7.18 (td, *J* = 7.2, 1.6 Hz, 1H), 6.58 (s, 1H), 2.45 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 165.54, 158.10, 150.70, 138.63, 136.19, 135.80, 130.99, 129.22, 129.05, 127.23, 126.64, 126.03, 115.39, 104.39, 20.33.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2OH]^+$: 237.1022, found: 237.1023.

2-(3-methoxyphenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2d)[S3]



39.7 mg, 0.157 mmol, yield 76 %;（the substrates is actually delivered 0.206mmol）

White solid;

R_f(PE/EA 3/1): 0.21;

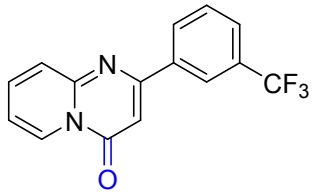
m.p 155-156 °C (lit.156-157 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (dt, *J* = 7.2, 1.1 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.70 – 7.60 (m, 2H), 7.40 (t, *J* = 8.1 Hz, 1H), 7.13 (ddd, *J* = 7.2, 4.7, 3.3 Hz, 1H), 7.03 (ddd, *J* = 8.2, 2.6, 1.0 Hz, 1H), 6.90 (s, 1H), 3.90 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.83, 159.94, 158.59, 150.92, 138.69, 136.15, 129.80, 127.23, 126.75, 119.79, 116.58, 115.22, 112.51, 100.24, 55.39.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_2H]^+$: 253.0972, found: 253.0972

2-(3-(trifluoromethyl)phenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2e)



46.7 mg, 0.161 mmol, yield 77%;（the substrates is actually delivered 0.21mmol）

Light brown solid

R_f(PE/EA 3/1): 0.21;

m.p 143-146 °C

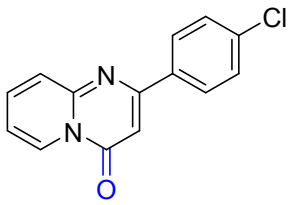
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (d, *J* = 8.0 Hz, 1H), 8.41 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 7.84 – 7.69 (m, 3H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.21 – 7.10 (m, 1H), 6.92 (s, 1H);

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.22, 158.44, 151.10, 138.00, 136.53,131.24 (q, J = 32.4 Hz), 130.41, 129.27, 127.28, 127.07 (q, *J* = 3.7 Hz),126.78, 124.36 (q, *J* = 3.9 Hz), 123.96 (d, *J* = 272.5 Hz).115.54, 100.21.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.66.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_9F_3N_2OH]^+$: 291.0740, found: 291.0738.

2-(4-chlorophenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2f)[S5]



36.9 mg, 0.144 mmol, yield 72%;

White solid;

R$_f$ (PE/EA 3/1): 0.15;

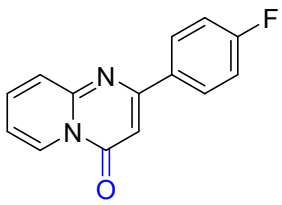
m.p 202-203 °C (lit.203-204 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.05 (d, *J* = 7.1 Hz, 1H), 8.03 (d, *J* = 8.6 Hz, 2H), 7.82 – 7.64 (m, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 7.20 – 7.08 (m, 1H), 6.86 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.70, 158.50, 151.01, 136.86, 136.37, 135.62, 129.01, 128.69, 127.28, 126.71, 115.34, 99.84.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_9ClN_2OH]^+$: 257.0476, found: 257.0474(. calculated m/z for $[C_{14}H_9{}^{37}ClN_2OH]^+$: 259.0447, found: 259.0452

2-(4-fluorophenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2g)[S3]



34.9 mg, 0.145 mmol, yield 72%;

White solid;

R$_f$ (PE/EA 3/1): 0.33;

m.p 189-191 °C（193-195 °C）

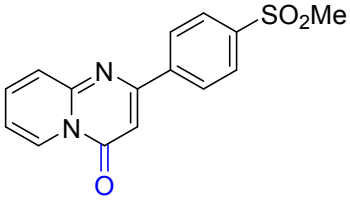
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (d, *J* = 7.1 Hz, 1H), 8.09 (dd, *J* = 8.7, 5.5 Hz, 2H), 7.83 – 7.66 (m, 2H), 7.16 (dt, *J* = 13.0, 7.4 Hz, 3H), 6.85 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.45 (d, *J* = 250 Hz), 159.71 (d, *J* = 236 Hz), 151.99, 136.33, 133.33, 129.46 (d, *J* = 8 Hz), 127.28, 126.67, 115.93, 115.71, 115.26, 99.64;

^{19}F NMR (376 MHz, $CDCl_3$): δ = -110.03.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_9FN_2OH]^+$: 241.0772, found: 241.0773.

2-(4-(methylsulfonyl)phenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2h)



27 mg,0.09 mmol, yield 45%;

Light yellow solid;

R$_f$(PE/EA 1/1): 0.23;

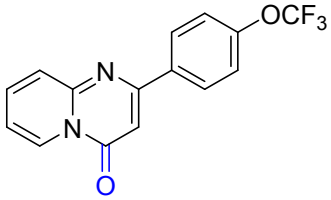
m.p 218-219 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.10 (dd, *J* = 7.1, 2.1 Hz, 1H), 8.40 – 8.17 (m, 2H), 8.13 – 7.93 (m, 2H), 7.90 – 7.69 (m, 2H), 7.21 (ddd, *J* = 7.1, 6.4, 1.7 Hz, 1H), 6.95 (s, 1H), 3.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.78, 158.36, 151.18, 142.51, 141.93, 136.73, 128.34, 127.81, 127.34, 126.86, 115.78, 101.00, 44.49.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_3SNa]^+$: 323.0461, found: 323.0466.

2-(4-(trifluoromethoxy)phenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2i)[S6]



51.1 mg, 0.167mmol, 80%;（the substrates is actually delivered 0.208mmol）

White solid;

R$_f$(PE/EA 3/1): 0.27;

m.p 136-138 °C (lit.152-154 °C)

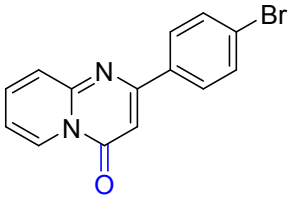
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.08 (d, *J* = 7.1 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 2H), 7.86 – 7.63 (m, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.16 (t, *J* = 6.6 Hz, 1H), 6.88 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.56, 158.49, 151.05, 150.95(t, *J*= 1 Hz), 136.43, 135.76, 129.05, 127.29, 126.72, 120.93(d, *J*= 1 Hz), 120.38(d, *J* = 257 Hz), 115.40, 100.02.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -57.67.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_9F_3N_2O_2H]^+$: 307.0689, found: 307.0687.

2-(4-bromophenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2j)[S5]



28.5 mg, 0.095 mmol, yield 48%;

Yellow solid;

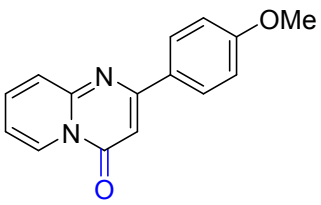
R_f (PE/EA 3/1): 0.25;

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.14 – 9.02 (m, 1H), 8.14 – 8.05 (m, 1H), 8.01 – 7.93 (m, 1H), 7.77 – 7.73 (m, 1H), 7.68 – 7.59 (m, 1H), 7.51 (dd, *J* = 5.1, 1.9 Hz, 2H), 7.19 – 7.10 (m, 1H), 6.90 (d, *J* = 17.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.33, 136.10, 131.97, 130.60, 128.92, 128.78, 127.39, 126.76, 115.30, 115.14, 100.10, 99.83.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_9BrN_2ONa]^+$: 322.9790, found: 322.9787.calculated m/z for $[C_{14}H_9{}^{81}BrN_2ONa]^+$324.9770, found: 324.9751.

2-(4-methoxyphenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2k)[S5]



43.6 mg, 0.173 mmol, yield 86%;

Light yellow solid;

R_f (PE/EA 3/1): 0.12;

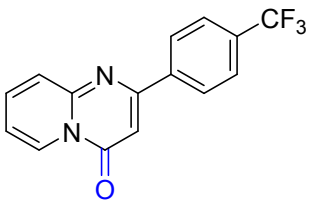
m.p 157-158 °C (lit.157-158 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.03 (d, *J* = 7.1 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 5.8 Hz, 2H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 6.84 (s, 1H), 3.86 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.79, 161.49, 158.59, 150.89, 136.03, 129.51, 128.96, 127.22, 126.57, 114.89, 114.13, 98.77, 55.41.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_2H]^+$: 253.0972, found: 253.0967.

2-(4-(trifluoromethyl)phenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2l)[S7]



43.5 mg, 0.15 mmol, yield 75%;

White solid;

R$_f$(PE/EA 3/1): 0.15;

m.p 173-174 °C (lit.186-188 °C)

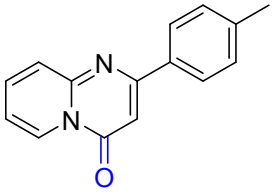
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (d, *J* = 7.2 Hz, 1H), 8.18 (d, *J* = 8.1 Hz, 2H), 7.85 – 7.64 (m, 4H), 7.22 – 7.09 (m, 1H), 6.91 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.35, 158.45, 151.10, 140.61 (q, *J* = 1 Hz), 136.54, 132.17 (q, *J* = 32 Hz), 127.72, 127.29, 126.81, 125.69 (q, *J* = 4 Hz), 123.93 (q, *J* = 271 Hz), 115.59, 100.63.

^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.77.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_9F_3N_2OH]^+$: 291.0740, found: 291.0737.

2-(*p*-tolyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2m)[S5]



33.4 mg, 0.141 mmol, yield 70%;

White solid;

R$_f$(PE/EA 3/1): 0.15;

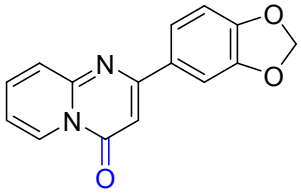
m.p 161-163 °C (lit.161-163 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.05 (d, *J* = 7.1Hz, 1H),7.99 (d, *J* = 8.2Hz，2H), 7.81 – 7.66 (m, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.16 – 7.05 (m, 1H), 6.89 (s, 1H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.98, 158.64, 150.95, 141.03, 136.05, 134.36, 129.54, 127.32, 127.23, 126.69, 115.04, 99.56, 21.45.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2OH]^+$: 237.1022, found: 237.1008.

2-(benzo[d][1,3]dioxol-5-yl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2o)[S4]



38.4 mg, 0.144 mmol, yield 72%;

White solid;

R$_f$(PE/EA 3/1): 0.17;

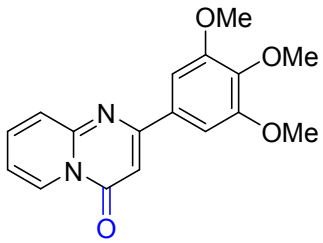
m.p 218-220 °C (lit.222.3-223.8 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.05 (dt, *J* = 7.1, 1.0 Hz, 1H), 7.77 – 7.64 (m, 3H), 7.62 (d, *J* = 1.8 Hz, 1H), 7.12 (ddd, *J* = 7.1, 6.3, 1.8 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.82 (s, 1H), 6.05 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.39, 158.60, 150.89, 149.92, 148.34, 136.14, 131.52, 127.31, 126.66, 122.22, 115.01, 108.53, 107.66, 101.60, 99.15.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{10}N_2O_3Na]^+$: 289.0584, found:289.0597.

2-(3,4,5-trimethoxyphenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2p)[S6]



57.8 mg, 0.185 mmol, yield 89%;（the substrate is actually delivered 0.207mmol）

White solid;

R$_f$(PE/EA 3/1): 0.10 ;

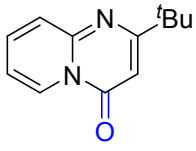
m.p 188-190 °C (lit.188-200 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.06 (d, *J* = 7.1 Hz, 1H), 7.74 (s, 2H), 7.35 (s, 2H), 7.14 (ddd, *J* = 7.6, 5.3, 2.8 Hz, 1H), 6.87 (s, 1H), 3.97 (s, 6H), 3.91 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.64, 158.55, 153.40, 150.85, 140.31, 136.23, 132.59, 127.27, 126.66, 115.20, 104.57, 99.68, 60.96, 56.22.

Exact Mass ESI-MS: calculated m/z for $[C_{17}H_{16}N_2O_4Na]^+$: 335.1002, found: 335.1004.

2-(tert-butyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2q)



31.2 mg, 0.154 mmol, yield 73%;（the substrates is actually delivered 0.21mmol）

White solid;

R$_f$(PE/EA 40/1): 0.41;

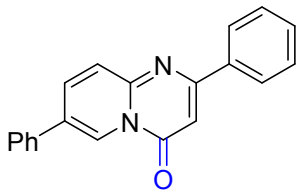
m.p 115-117 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.99 (d, *J* = 7.1 Hz, 1H), 7.72 – 7.49 (m, 2H), 7.05 (td, *J* = 7.2, 1.5 Hz, 1H), 6.52 (s, 1H), 1.35 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 175.95, 158.91, 150.26, 135.28, 126.86, 126.48, 114.65, 99.87, 37.63, 29.16.

ESI-MS: calculated m/z for $[C_{12}H_{14}N_2ONa]^+$: 225.0998, found:225.0996.

2,7-diphenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2r)



47.9 mg, 0.16 mmol, yield 80%;（the substrate is actually delivered 0.202mmol）

Off-white solid;

R$_f$(PE/EA 3/1): 0.5;

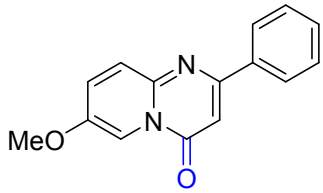
m.p 172-173 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.30 (d, *J* = 1.7 Hz, 1H), 8.17 – 8.07 (m, 2H), 8.04 (dd, *J* = 9.2, 2.2 Hz, 1H), 7.82 (d, *J* = 9.9 Hz, 1H), 7.72 – 7.64 (m, 2H), 7.57 – 7.41 (m, 6H), 6.95 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.81, 158.68, 150.05, 137.24, 136.18, 135.45, 130.63, 129.35, 129.22, 128.86, 128.81, 127.38, 126.87, 126.84, 124.21, 100.07.

Exact Mass ESI-MS: calculated m/z for $[C_{20}H_{14}N_2OH]^+$: 299.1179,found: 299.1177.

7-methoxy-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2s)



31.8 mg, 0.126 mmol, yield 58%; (the substrate is actually delivered 0.217mmol)

Off-white solid;

R$_f$(PE/EA 3/1): 0.23;

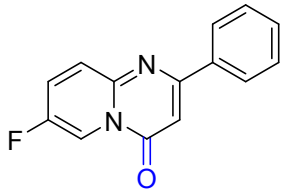
m.p 153-154 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (d, *J* = 2.7 Hz, 1H), 8.08 (dd, *J* = 7.4, 2.2 Hz, 2H), 7.69 (d, *J* = 9.6 Hz, 1H), 7.59 – 7.46 (m, 4H), 6.92 (s, 1H), 3.96 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ =160.83, 158.51, 150.70, 148.10, 137.30, 131.57, 130.40, 128.78, 127.44, 127.24, 106.71, 99.48, 56.46.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_2H]^+$: 253.0972, found: 253.0971.

7-fluoro-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2t)[S2]



9.1 mg, 0.038 mmol, yield 19%;

Yellow solid;

R$_f$ (PE/EA 10/1): 0.42;

m.p 183-185 °C (lit.162 °C)

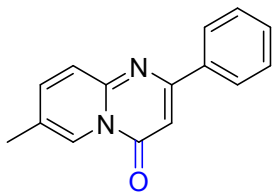
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.98 (dd, *J* = 4.3, 2.9 Hz, 1H), 8.08 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.77 (dd, *J* = 9.7, 5.2 Hz, 1H), 7.67 (ddd, *J* = 9.6, 6.5, 2.8 Hz, 1H), 7.57 – 7.46 (m, 3H), 6.94 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.72, 158.08, 153.94 (d, *J* = 244.1 Hz), 148.94, 136.90, 130.75, 128.83, 128.62,128.56 (d, *J* = 2 Hz), 127.35, 113.36 (*J* = 40.8 Hz), 99.84

^{19}F NMR (376 MHz, $CDCl_3$): δ = -133.06.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_9FN_2ONa]^+$: 263.0591, found: 263.0589.

7-methyl-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2u)[S2]



16.9 mg, 0.072 mmol, yield 36%;

Gray solid;

R$_f$ (PE/EA 10/1): 0.20;

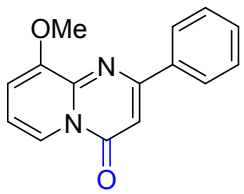
m.p 157-159 °C (lit. 163 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.89 (s, 1H), 8.13 – 8.03 (m, 2H), 7.68 (d, *J* = 9.1 Hz, 1H), 7.61 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.49 (dd, *J* = 5.2, 1.9 Hz, 3H), 6.90 (s, 1H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.67, 158.56, 149.96, 139.14, 137.37, 130.49, 128.79, 127.34, 126.20, 125.54, 124.70, 99.88, 18.37.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2OH]^+$: 237.1022, found: 237.1018.

9-methoxy-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2v)[S4]



40.4 mg, 0.16 mmol, yield 78%;（the substrates is actually delivered 0.207mmol）

Yellow solid;

R_f(PE/EA 3/1): 0.07;

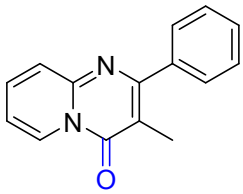
m.p 200-201 °C (lit.192.3-193.9 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (dd, *J* = 6.5, 2.0 Hz, 1H), 8.17 – 8.05 (m, 2H), 7.56 – 7.36 (m, 3H), 7.11 – 6.98 (m, 2H), 6.95 (s, 1H), 4.07 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.98, 158.70, 152.45, 145.37, 137.31, 130.53, 128.78, 127.49, 119.05, 114.16, 111.06, 100.95, 56.81.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2O_2H]^+$: 253.0972, found: 253.0976.

3-methyl-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2w)



29.0 mg, 0.122 mmol, yield 61%;

Light yellow solid;

R_f(PE/EA 3/1): 0.19;

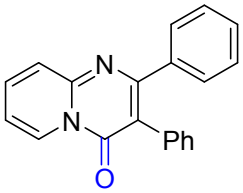
m.p 116-118 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.04 (dt, *J* = 7.1, 1.1 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.59 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.52 – 7.39 (m, 3H), 7.10 (ddd, *J* = 7.7, 4.7, 3.3 Hz, 1H), 2.30 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 161.48, 159.21, 148.35, 139.20, 134.59, 128.88, 128.78, 128.31, 126.83, 126.52, 114.99, 111.83, 13.93.

Exact Mass ESI-MS: calculated m/z for $[C_{15}H_{12}N_2OH]^+$: 237.1022, found:237.1023.

2,3-diphenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2x)[S2]



27.4 mg, 0.092 mmol, yield 66%; (the substrate was used crudely without silica gel chromatography due to its instability, and it was quantified as 0.14 mmol by ^{1}H-NMR with CH_2Br_2 as internal standard.)

Yellow solid;

R_f(PE/EA 5/1): 0.20;

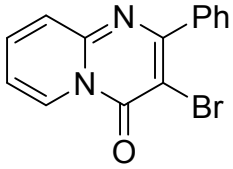
m. p. 186-187 °C (lit.191 °C)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, J = 7.1 Hz, 1H), 7.74 (d, J = 3.4 Hz, 2H), 7.44 – 7.37 (m, 2H), 7.31 – 7.20 (m, 8H), 7.16 (dt, J = 7.6, 4.1 Hz, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.25, 158.22, 149.52, 139.01, 135.73, 134.70, 131.23, 129.75, 128.71, 128.04, 127.88, 127.56, 127.18, 126.66, 115.83, 115.41.

Exact Mass ESI-MS: calculated m/z for $[C_{20}H_{14}N_2OH]^+$: 299.1179, found: 299.1184.

3-bromo-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (3)[S8]



White solid; yield 99% (by ^{1}H-NMR, see the part "The Application of the Reaction")

R_f (PE/EA 3/1): 0.35;

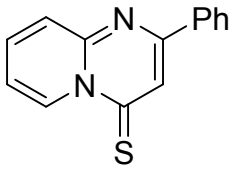
m. p. 175-178 °C (lit.174.5-175.5 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.11 (m, 1H), 7.89 – 7.67 (m, 4H), 7.54 – 7.44 (m, 3H), 7.22 (td, *J* = 7.2, 1.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.59, 155.58, 148.85, 138.68, 136.26, 129.71, 128.99, 128.10, 127.67, 126.53, 116.21, 101.07.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_9{}^{79}BrN_2OH]^+$: 300.9971, found: 300.9973. calculated m/z for $[C_{14}H_9{}^{81}BrN_2OH]^+$: 302.9951, found: 302.9936.

2-phenyl-*4H*-pyrido[1,2-a]pyrimidine-4-thione (4)



Yellow solid; yield 99% (by ^{1}H-NMR, see the part "The Application of the Reaction")

R_f (PE/EA 3/1): 0.6;

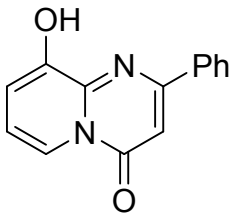
m.p 195-197 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (d, *J* = 7.2 Hz, 1H), 8.27 (s, 1H), 8.21 – 8.17 (m, 2H), 7.99 – 7.86 (m, 2H), 7.57 – 7.51 (m, 3H), 7.44 – 7.37 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.59, 155.60, 150.60, 136.47, 135.86, 133.05, 131.34, 129.05, 127.86, 127.78, 119.67, 117.79.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_{10}N_2SH]^+$: 239.0637, found: 239.0636.

9-hydroxy-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (5)[S9]



39.1 mg, 0.164 mmol, yield 82%;

Yellowish brown solid;

R_f (PE/EA 1/1): 0.6;

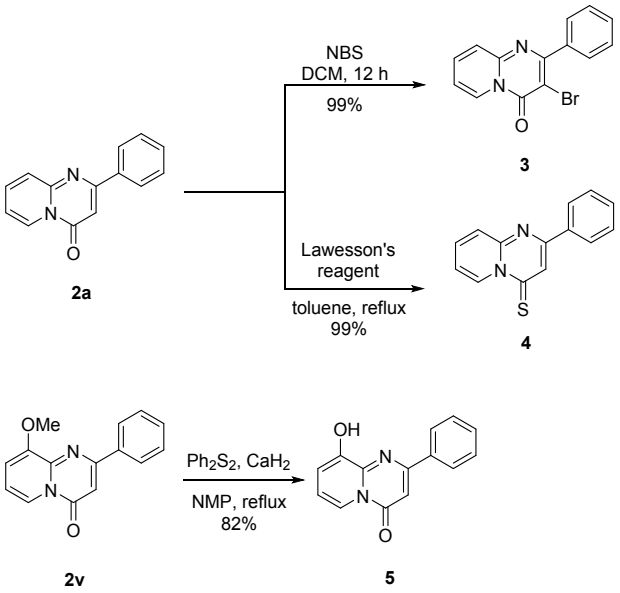
m.p. 227-230 °C (lit. 234-235 °C)

^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.17 (s, 1H), 8.47 (d, J = 7.0 Hz, 1H), 8.43 – 8.34 (m, 2H), 7.53 – 7.45 (m, 3H), 7.30 – 7.24 (m, 1H), 7.22 – 7.16 (m, 1H), 6.99 (s, 1H).

^{13}C NMR (101 MHz, DMSO-d_6): δ = 159.01, 158.27, 150.52, 144.95, 136.75, 131.11, 129.00, 128.09, 117.95, 116.60, 115.99, 98.79.

Exact Mass ESI-MS: calculated m/z for $[C_{14}H_{10}N_2O_2H]^+$: 239.0815, found: 239.0816.

The Application of the Reaction



Synthesis of 3

The lactam **2a** (44.4 mg, 0.2 mmol) and NBS (35.6 mg, 0.22 mmol, 1.2 equiv) were dissolved in 2mL DCM. The solution was stirred at ambient temperature for 12 h. Then the solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give a white solid. The yield of **3** was determined by ^{1}H-NMR (>99%). Further recrystallization using ethanol was carried out to provide **3** as white needle-like crystal (50.6 mg, 84%).

Synthesis of 4

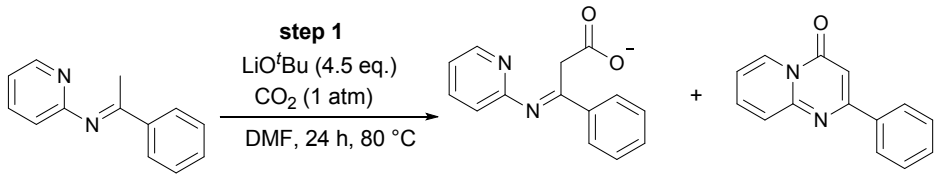
The lactam **2a** (44.4 mg, 0.2 mmol) and Lawesson's reagent (97.1 mg, 0.24 mmol, 1.2 equiv) were dissolved in anhydrous toluene. The mixture was refluxed at 120 ℃ for 3 h. After cooling to ambient temperature, 15 mL sat. $NaHCO_3$ (aq.) was added and the aqueous phase was extracted with DCM (20 mL×3). Combined organic layer was concentrated under reduced pressure and further purified by chromatography on silica gel to afford a yellow solid. The yield was determined by ^{1}H-NMR with CH_2Br_2 as internal standard (>99%).

Synthesis of 5

The reaction was carried out following the procedure described in literature[S10]. To a mixture of Ph_2S_2 (26.2 mg, 0.12 mmol, 0.6 equiv) and CaH_2 (13.5 mg, 0.32 mmol, 1.6 equiv) in NMP (2 mL) under argon was added lactam **2v** (50.5 mg, 0.2 mmol). Then the mixture was heated to reflux for 30 min. After cooling down to room temperature, H_2O was added carefully until no further gas release. After that, the mixture was acidified with 2 M HCl and diluted with 30 mL H_2O. Then the solution was extracted with EA (20 mL×3) and combined organic layer was dried with Na_2SO_4 and filtered, following which the solvent was evaporated under reduced pressure. The residue was subjected to silica gel chromatography to afford a yellow solid (39.1 mg, 82%).

Mechanism studies

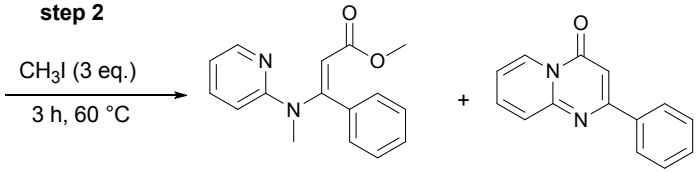
(A)



1a, M.W. 196

possible carboxylate, M.W.239 detected by ESI-MS

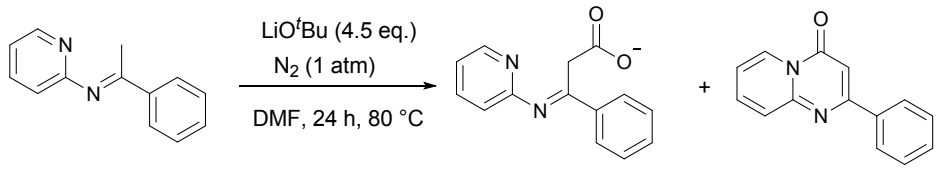
2a, <5% GC yield



possible methyl ester, M.W. 268 detected by ESI-MS

2a, 27% GC yield

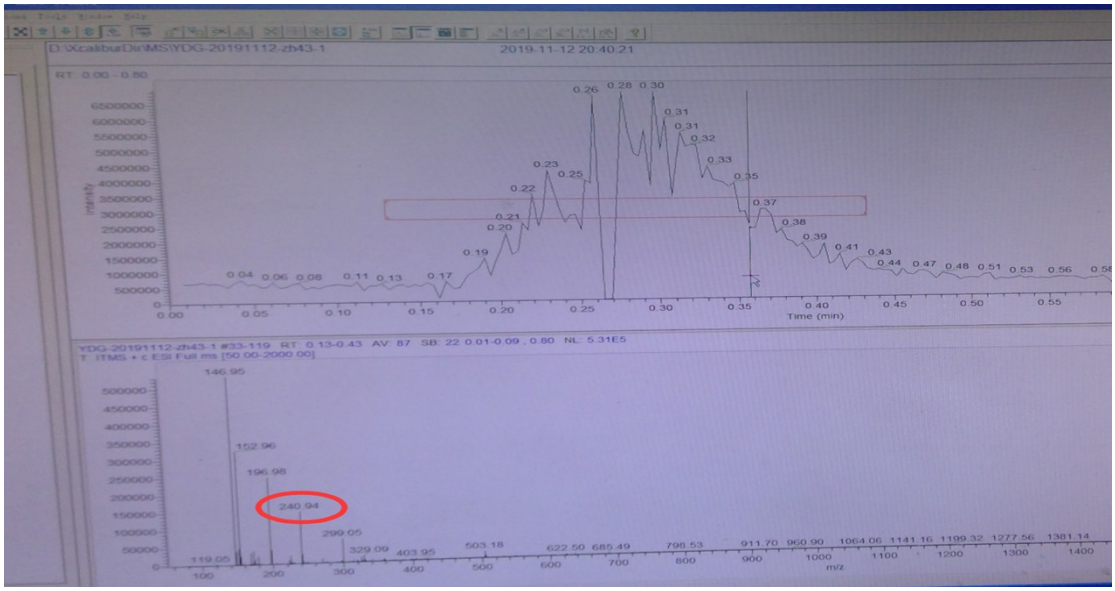
(B)



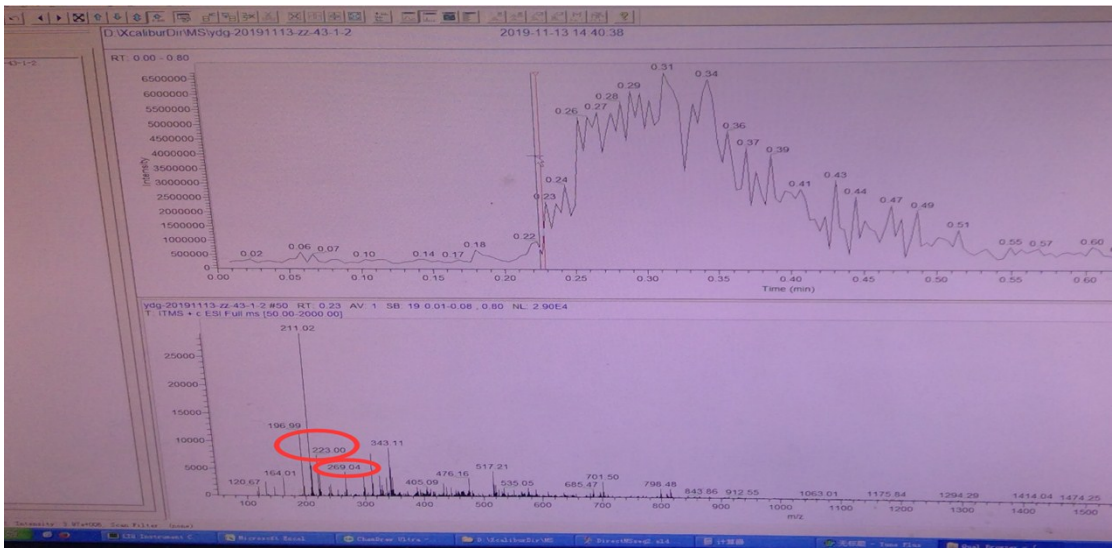
N.D.

N.D.

ESI-MS for the **step 1** of **Reaction A**



ESI-MS for the **step 2** of **Reaction A**



ESI-MS for the **Reaction B**

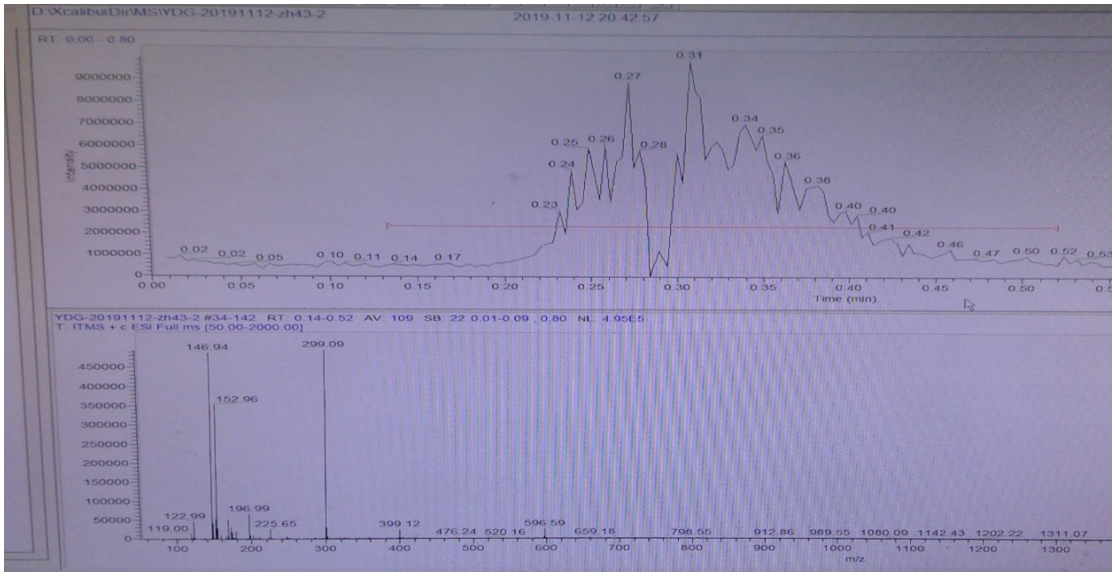


Table 1 entry 1-3

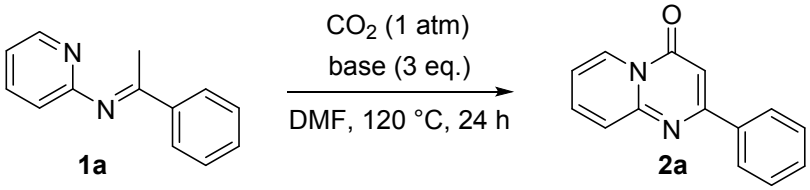
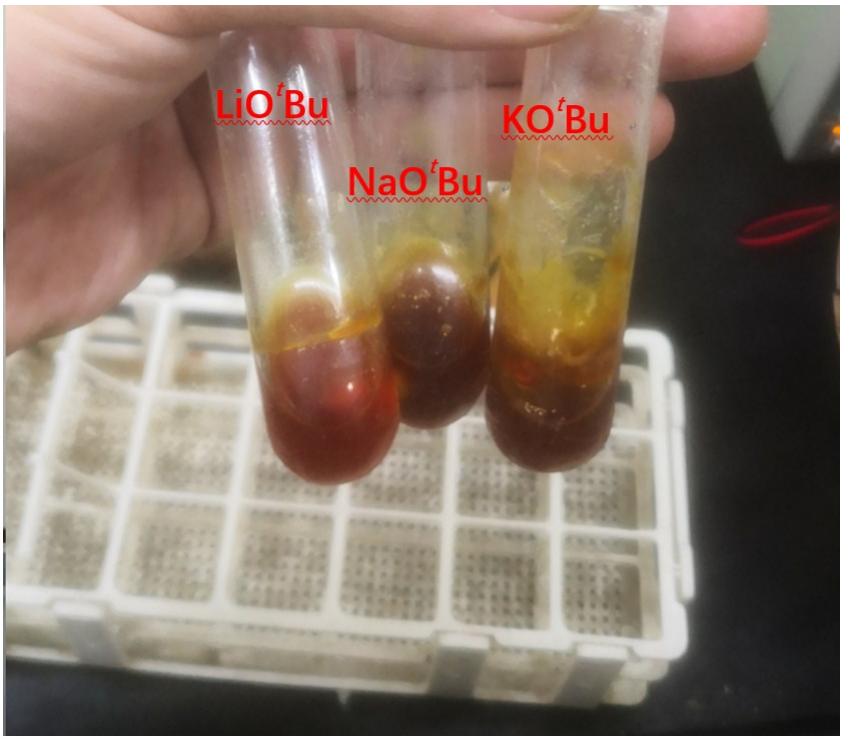
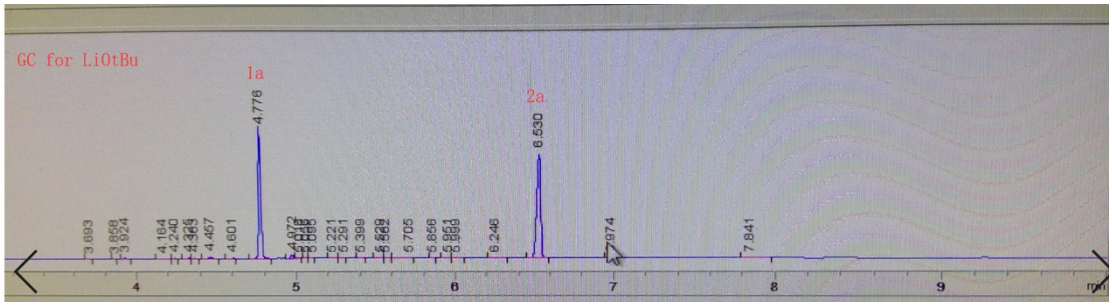
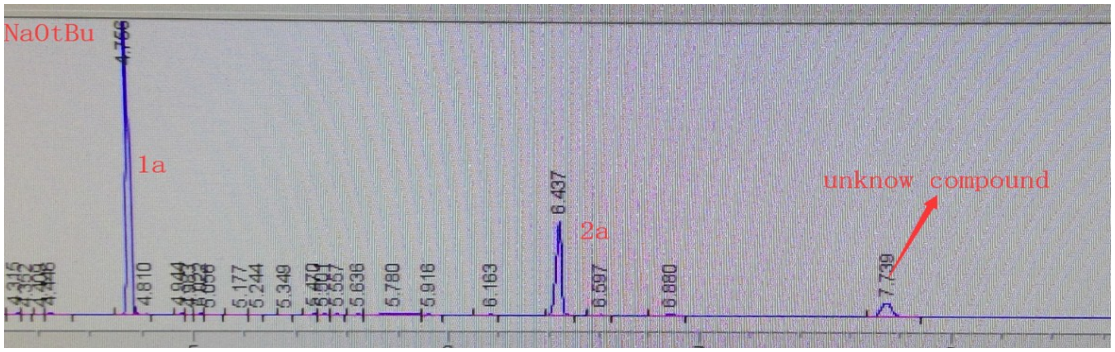


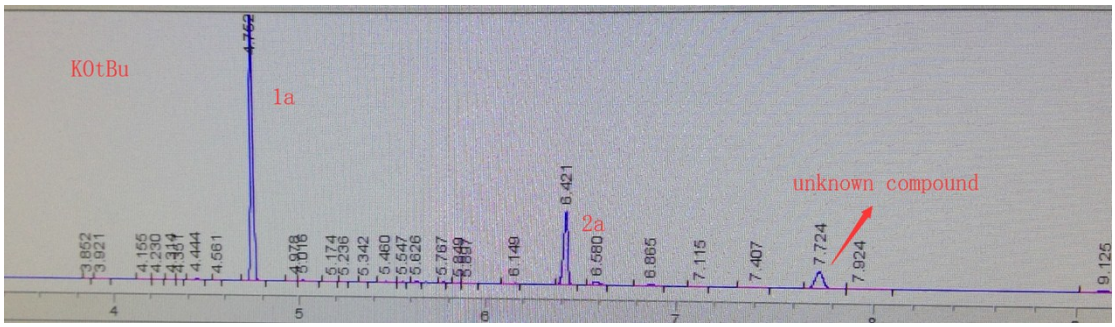
table 1 entry 1, base = LiO^{t}Bu
table 1 entry 2, base = NaO^{t}Bu
table 1 entry 3, base = KO^{t}Bu

20 h after the reaction beginning



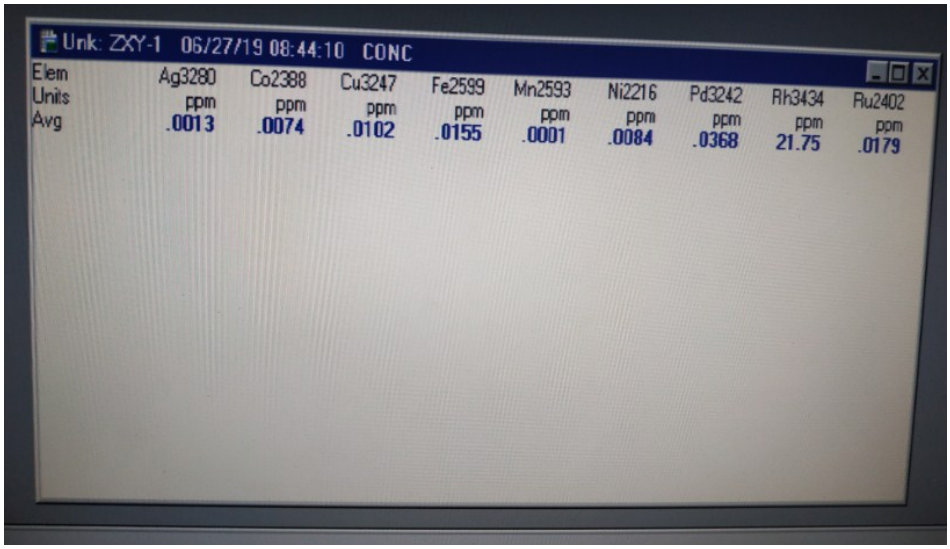






Determination of Metal Element Contents.

Element	Ag3280	Co2388	Cu3247	Fe2599	Mn2593
Units	ppm	ppm	ppm	ppm	ppm
Avg	0.0013	0.0074	0.0102	0.0155	0.0001
Element	Ni2216	Pd3242	Rh3434	Ru2402	
Units	ppm	ppm	ppm	ppm	
Avg	0.0084	0.0386	21.75	0.0179	


Unk: ZXY-1 06/27/19 08:44:10 CONC
Elem Ag3280 Co2388 Cu3247 Fe2599 Mn2593 Ni2216 Pd3242 Rh3434 Ru2402
Units ppm ppm ppm ppm ppm ppm ppm ppm
Avg .0013 .0074 .0102 .0155 .0001 .0084 .0368 21.75 .0179

References

[S1] M. Periasamy, G. Srinivas and P. Bharathi, *J. Org. Chem.,* 1999, **64***,* 4204.

[S2] Y.-F. Liang, R. Steinbock, A. Mnch, D. Stalke and L. Ackermann, *Angew. Chem. Int. Ed.,* 2018, **57**, 5384.

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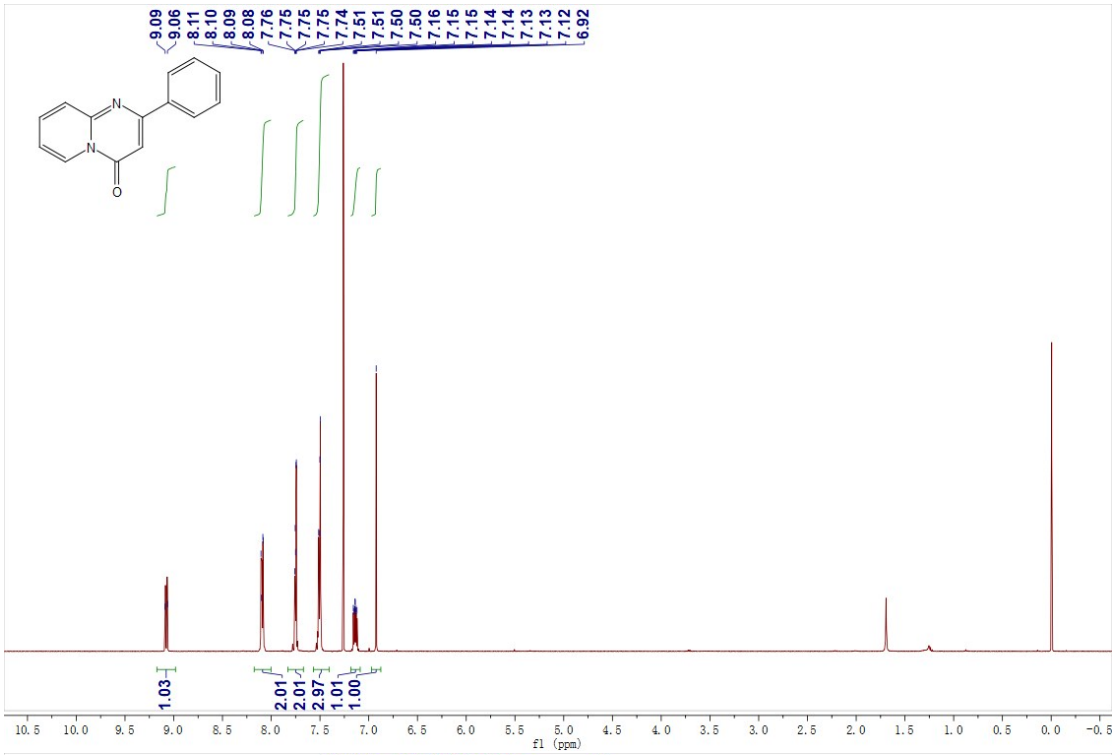
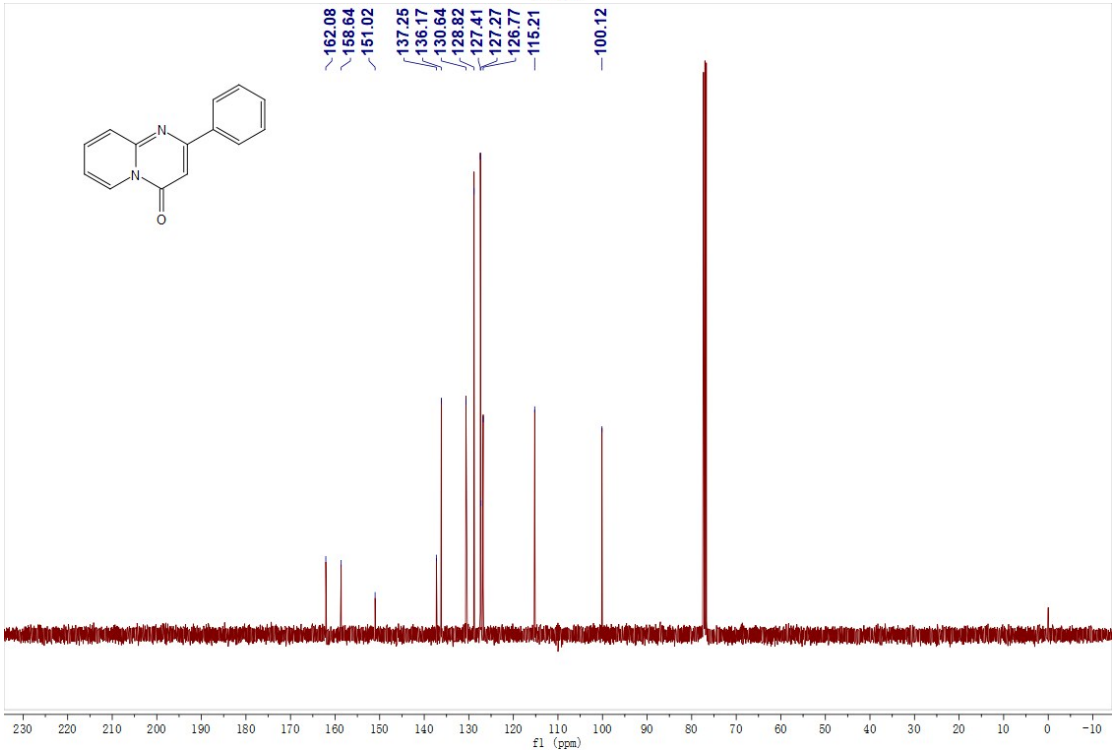
Copies of NMR Spectra

2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2a)





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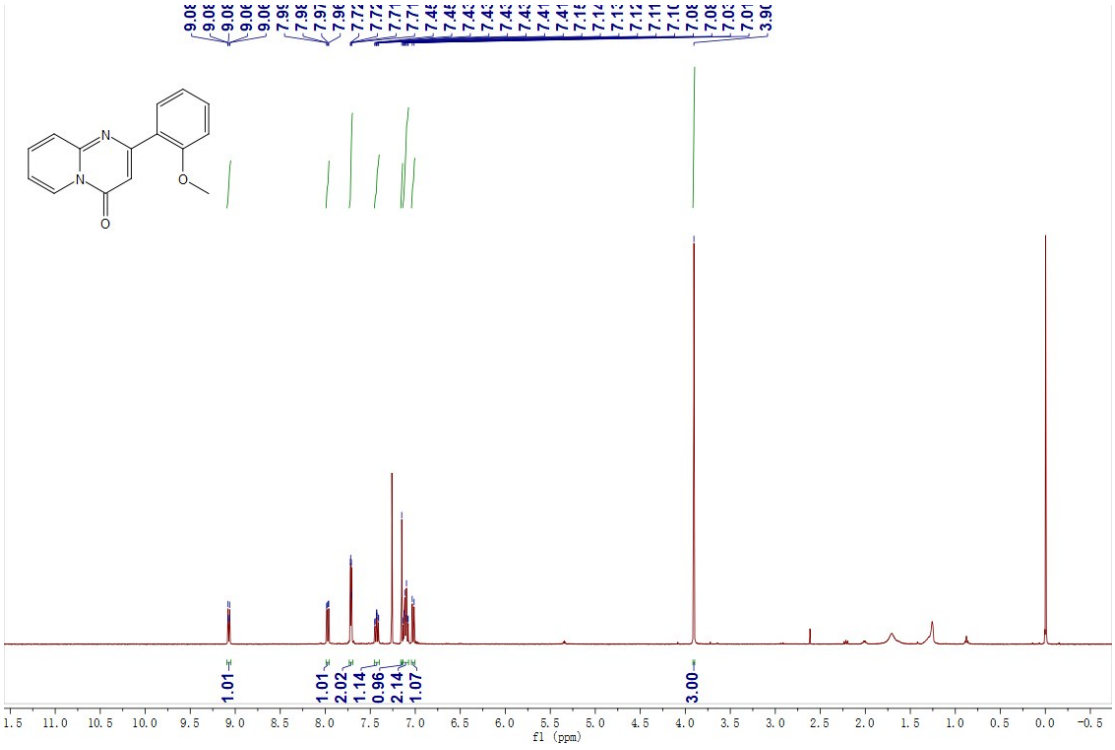

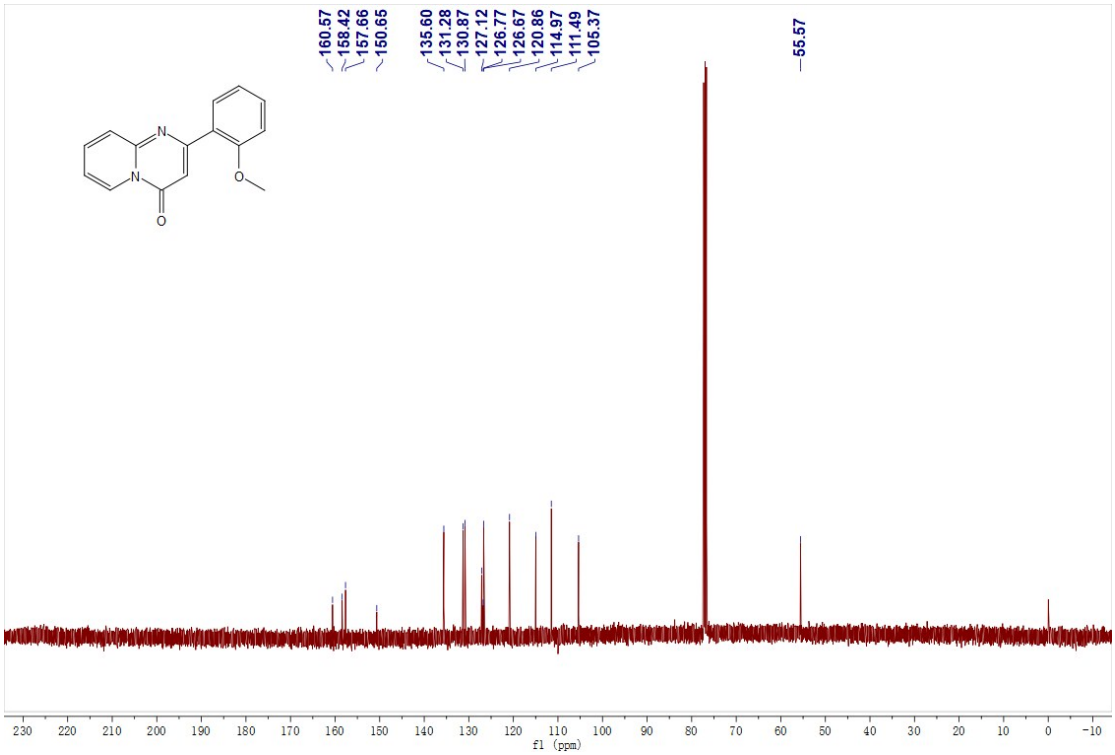

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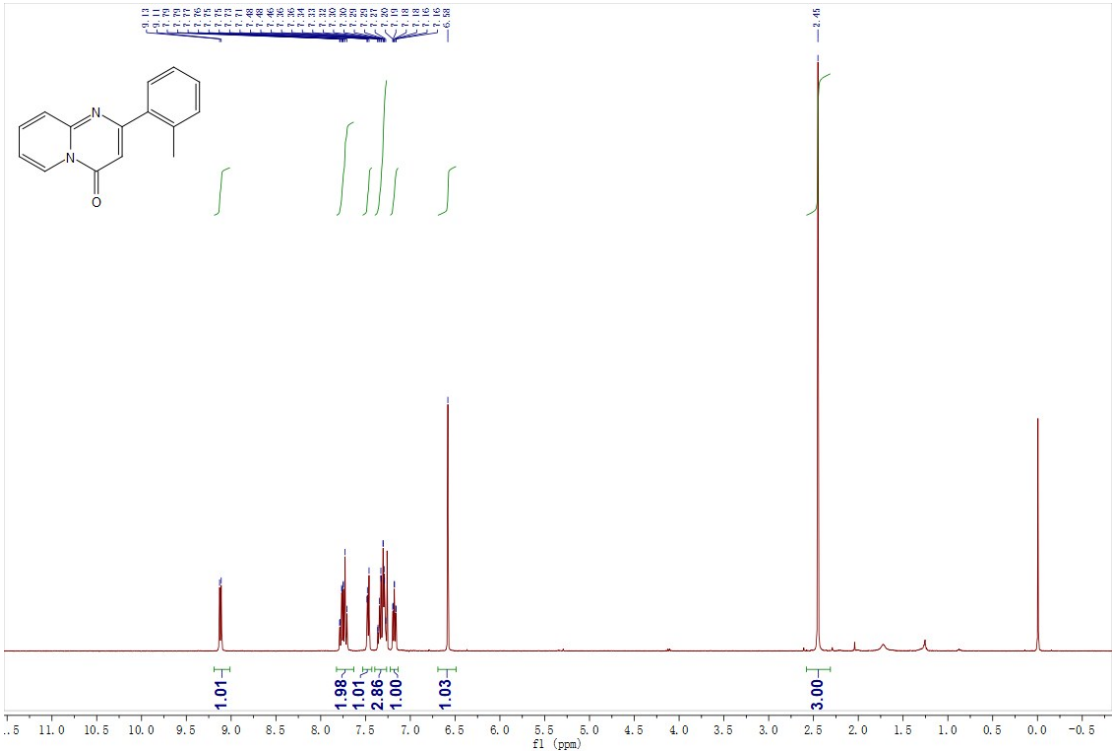

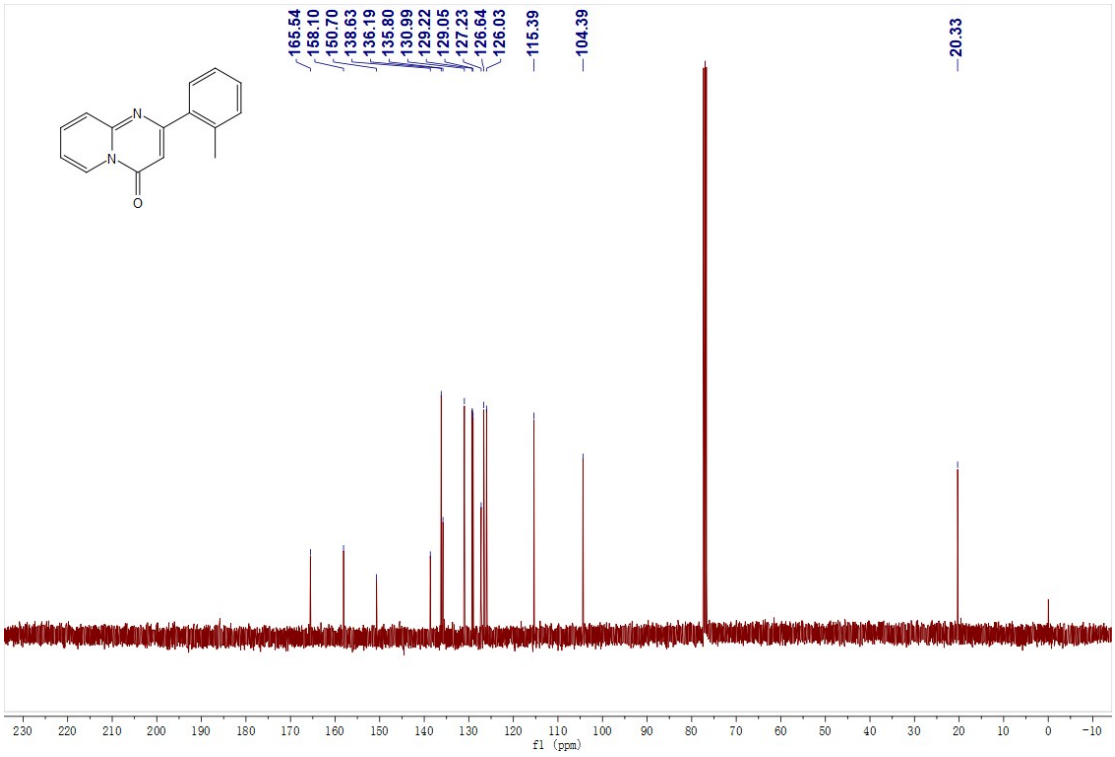

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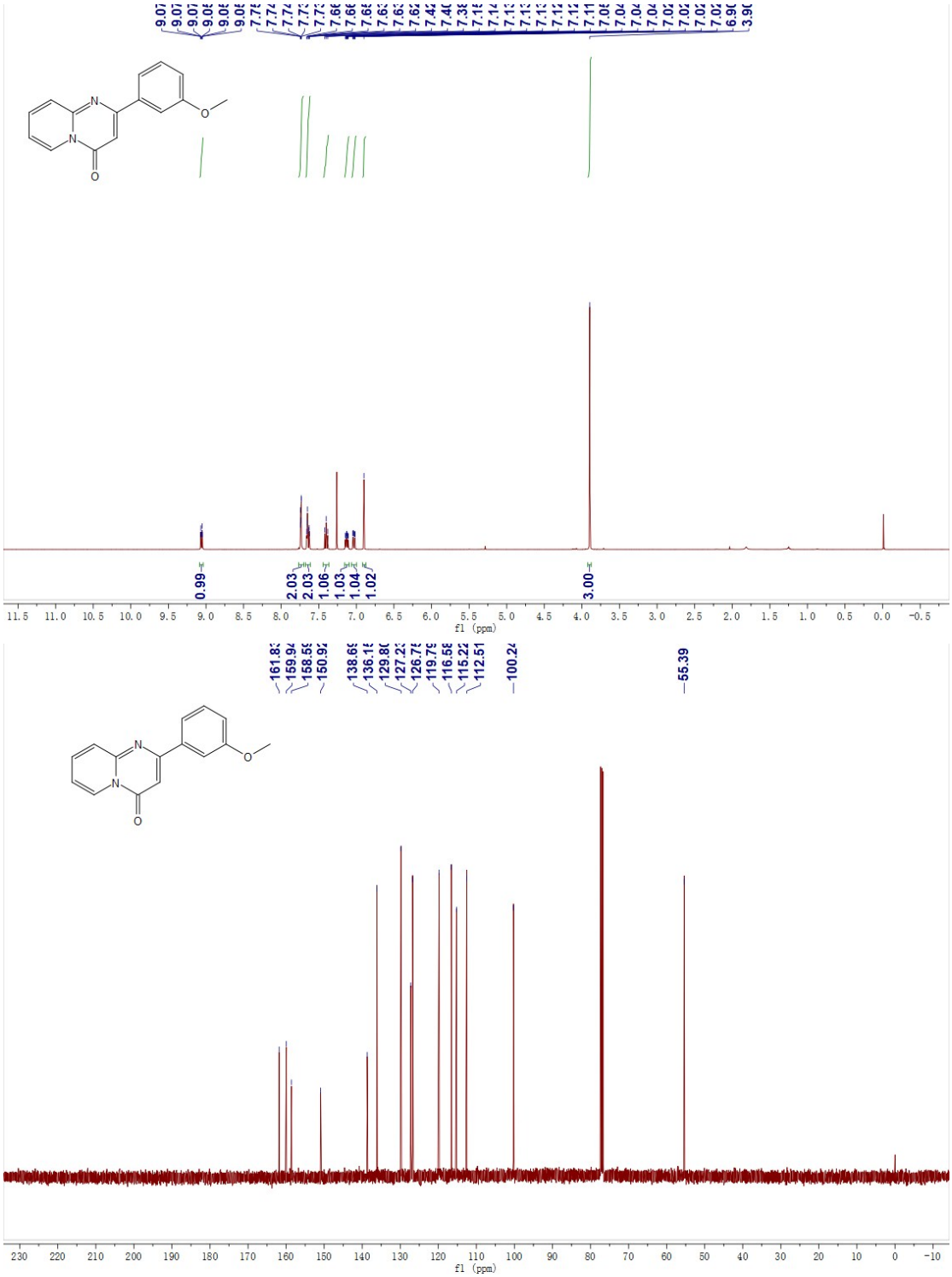

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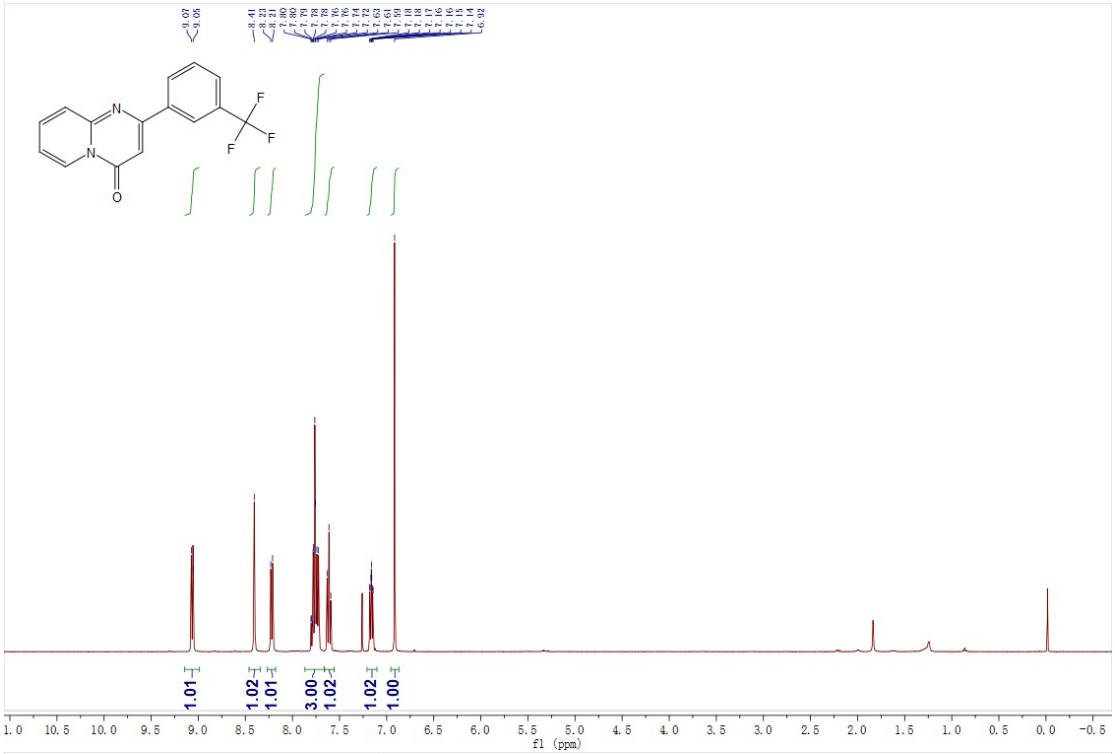

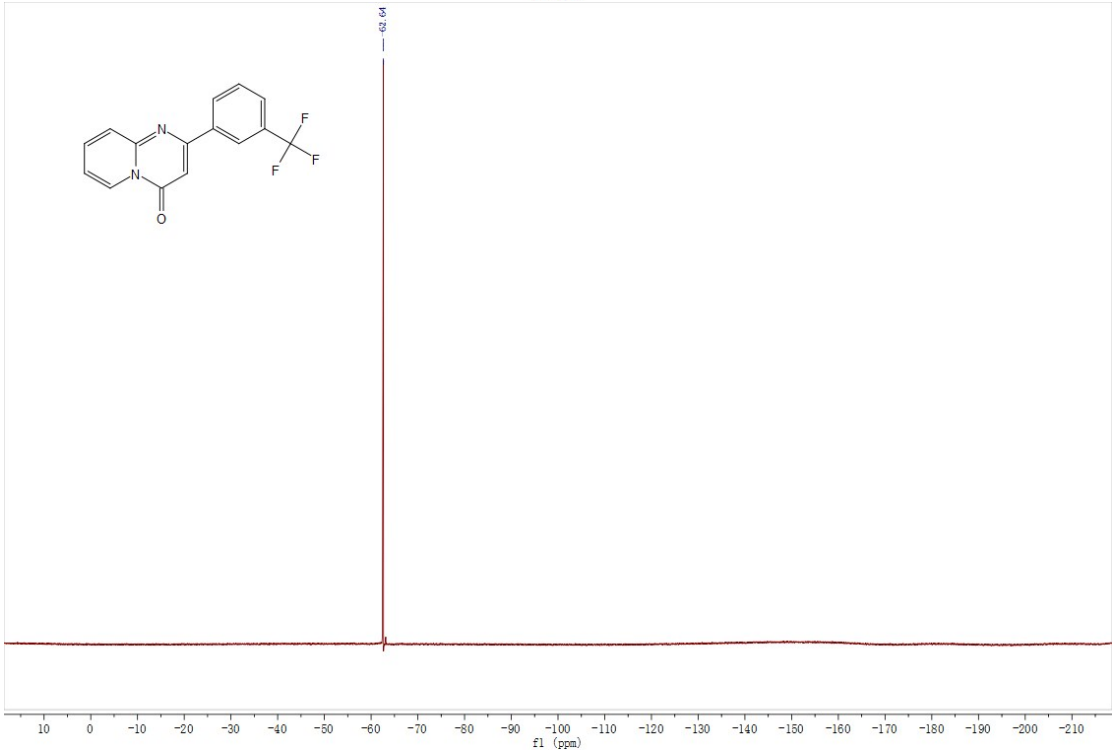

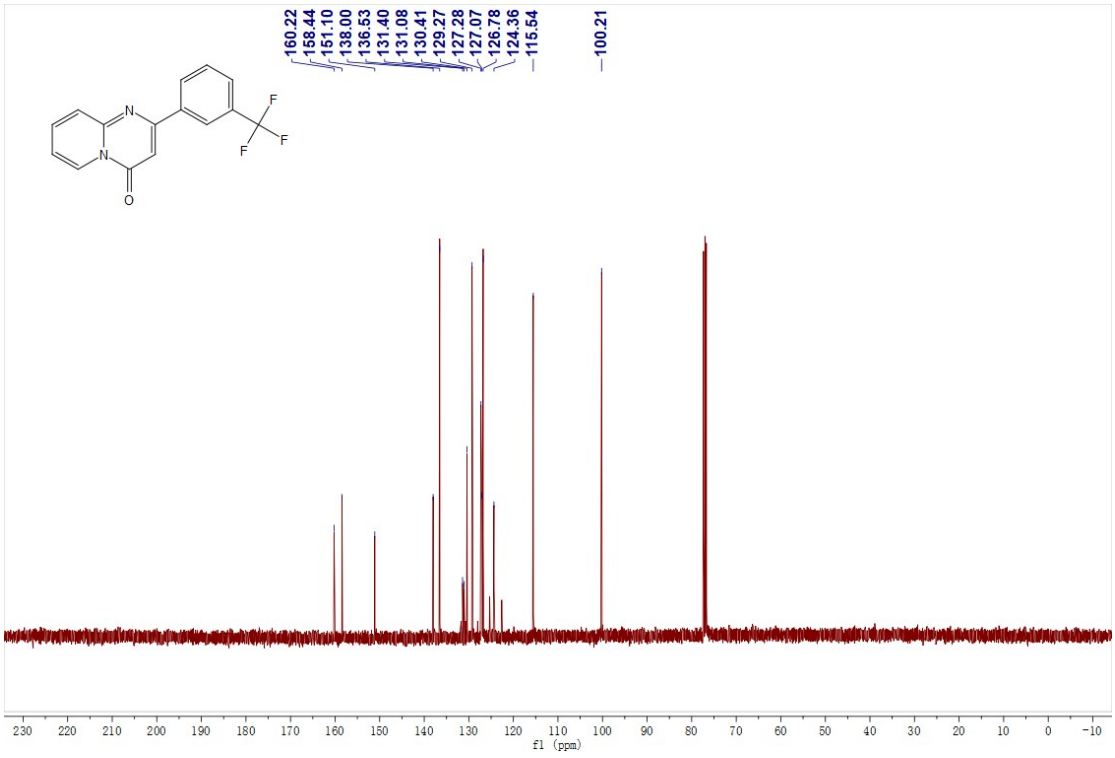

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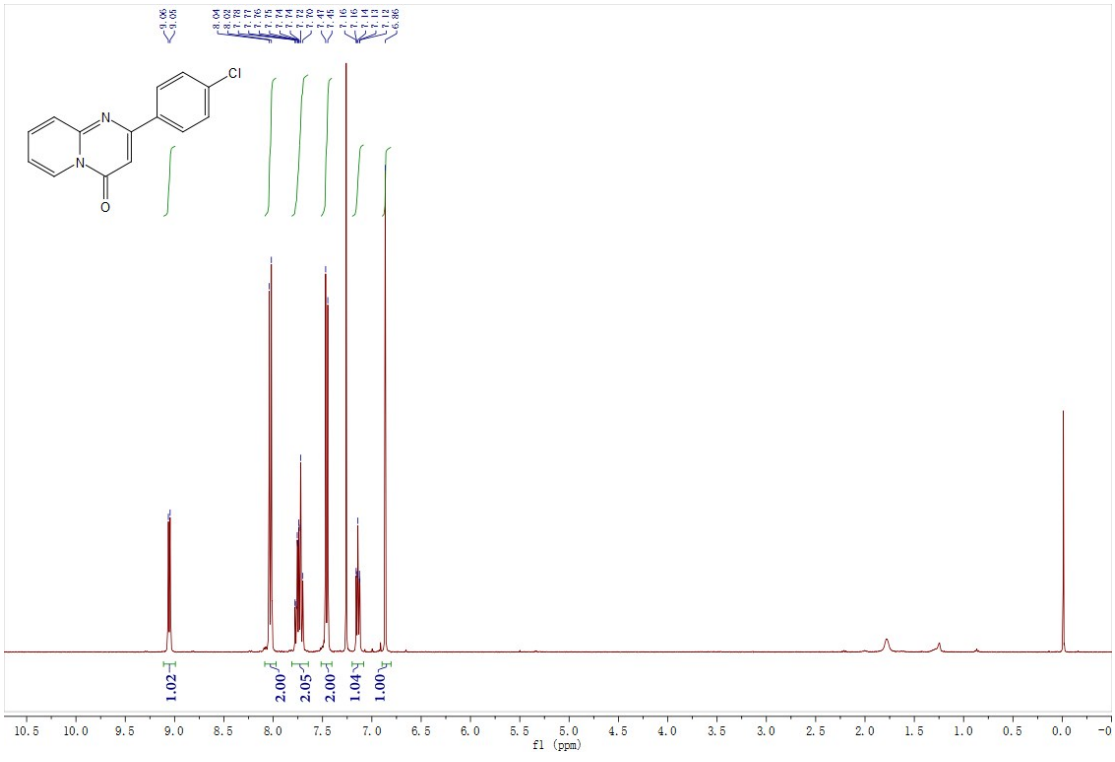

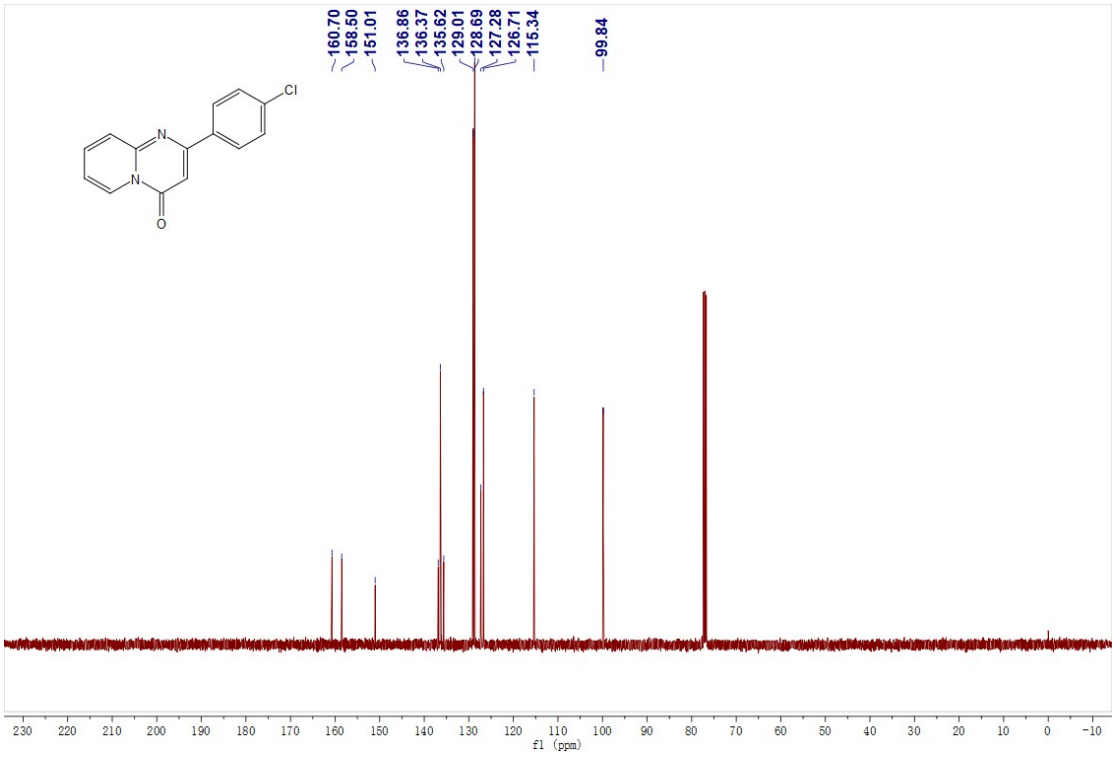

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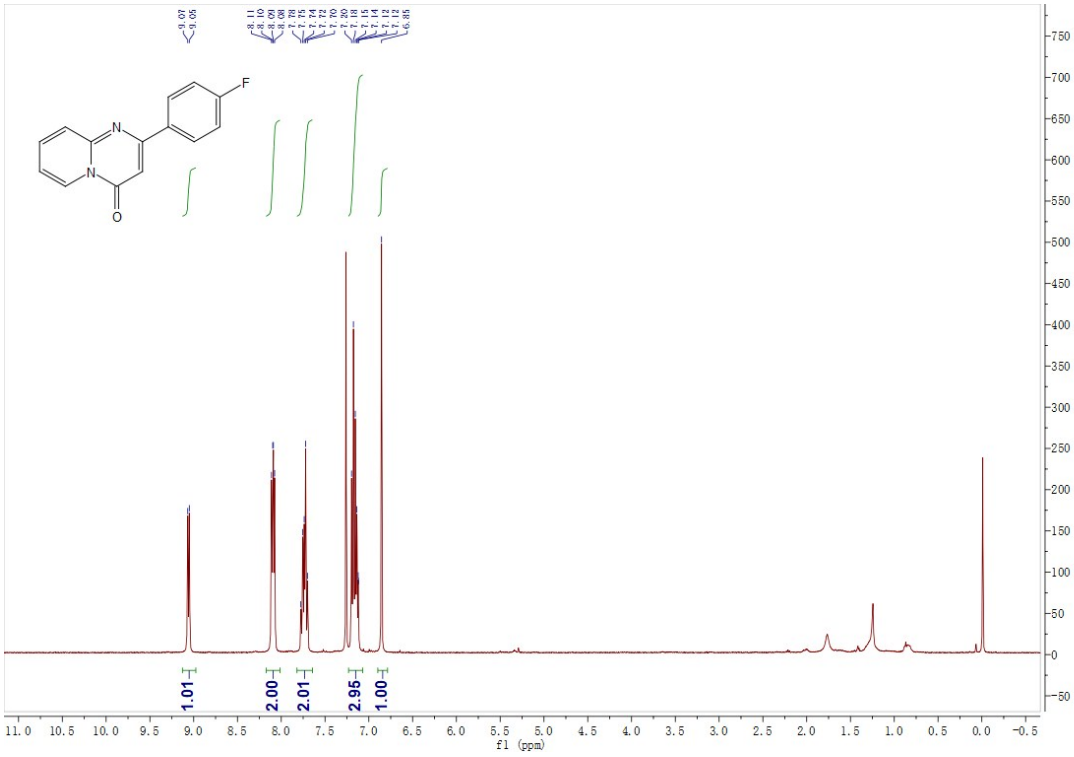

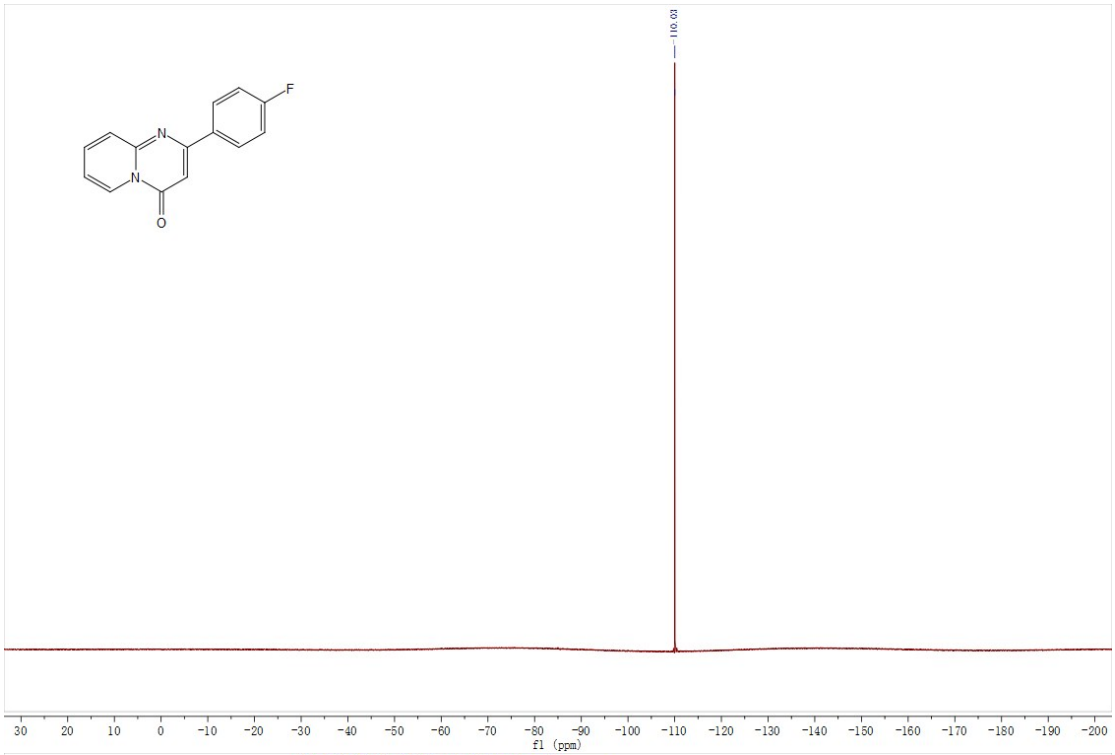
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N
O
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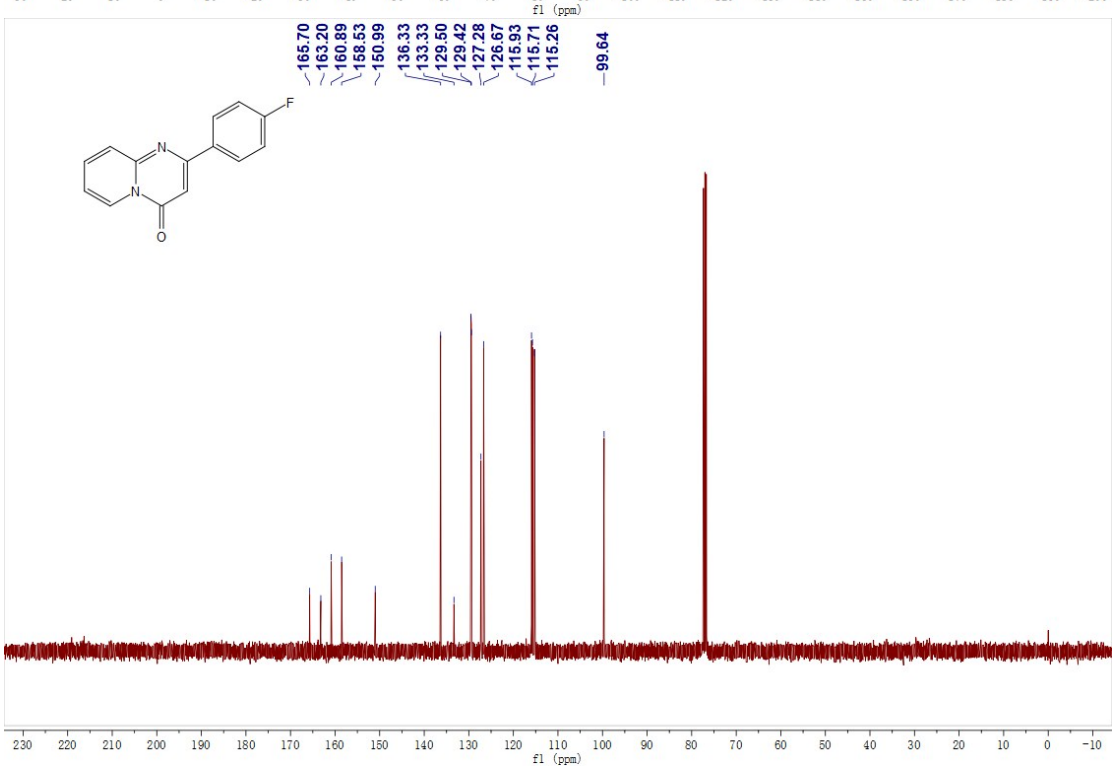
f1 (ppm)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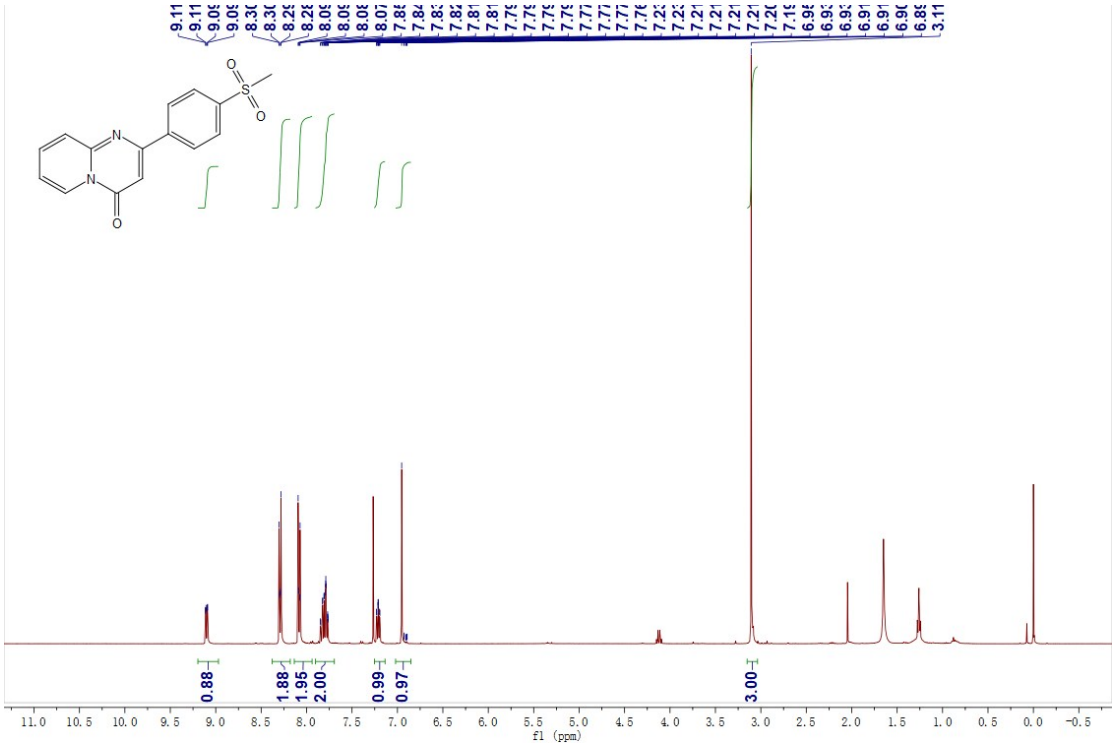
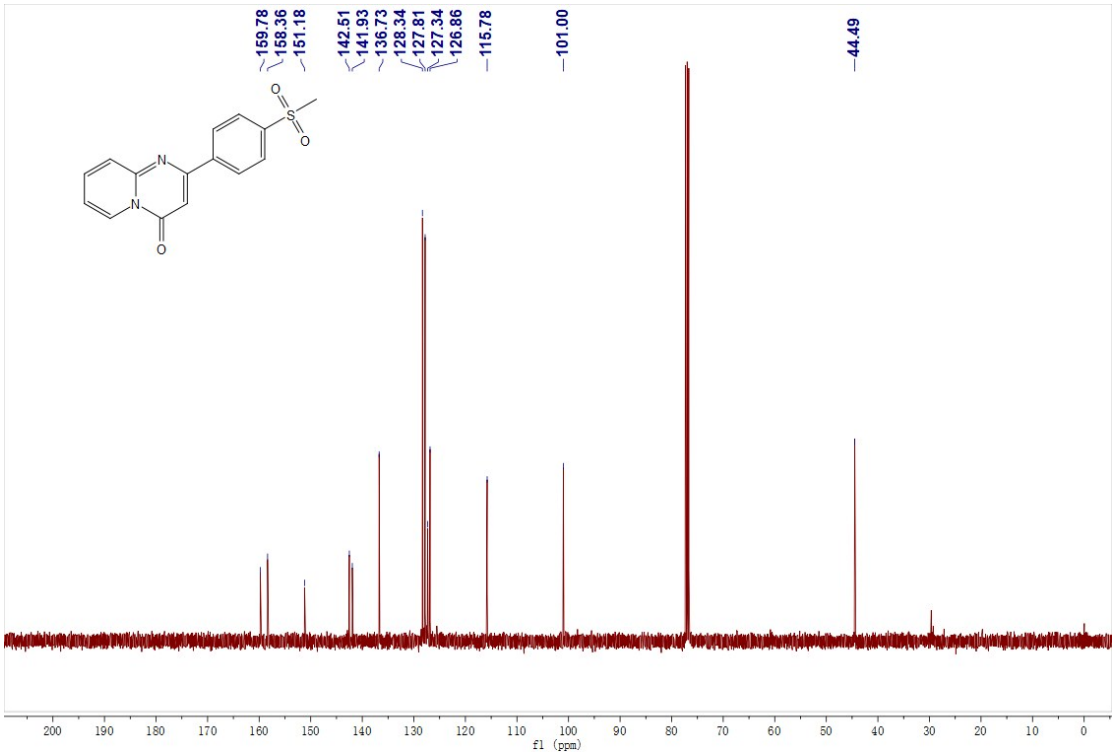
115.71
115.26
99.64
F
N
N
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2-(4-(methylsulfonyl)phenyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2h)





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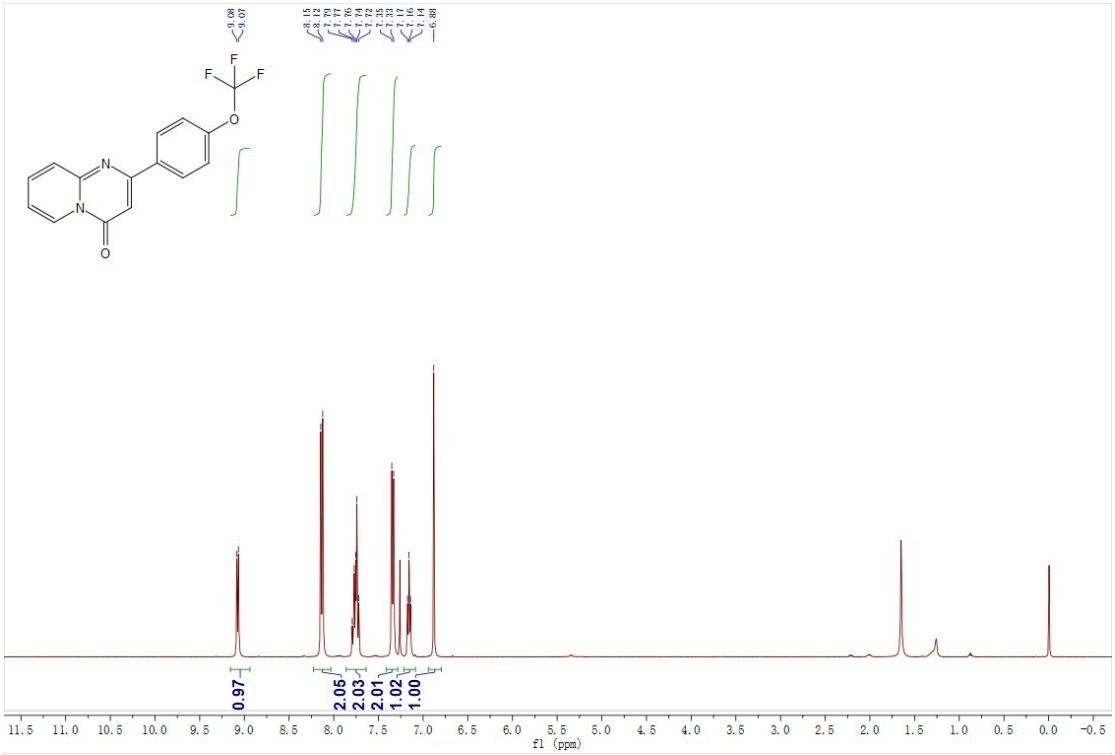

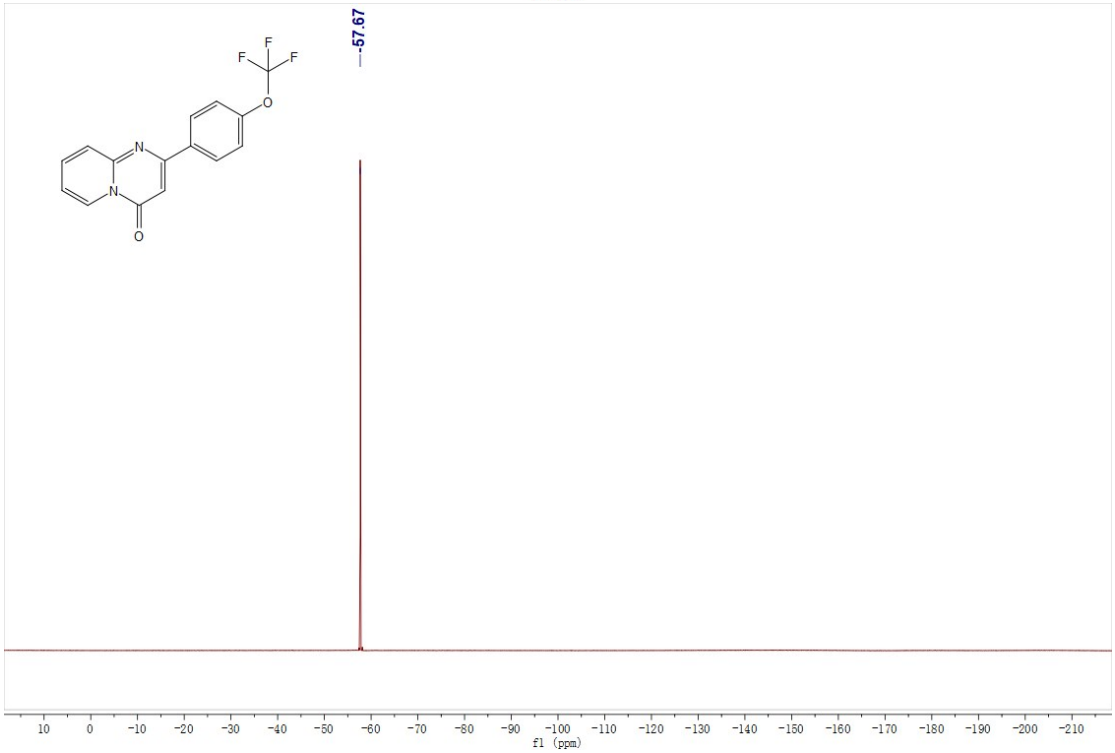

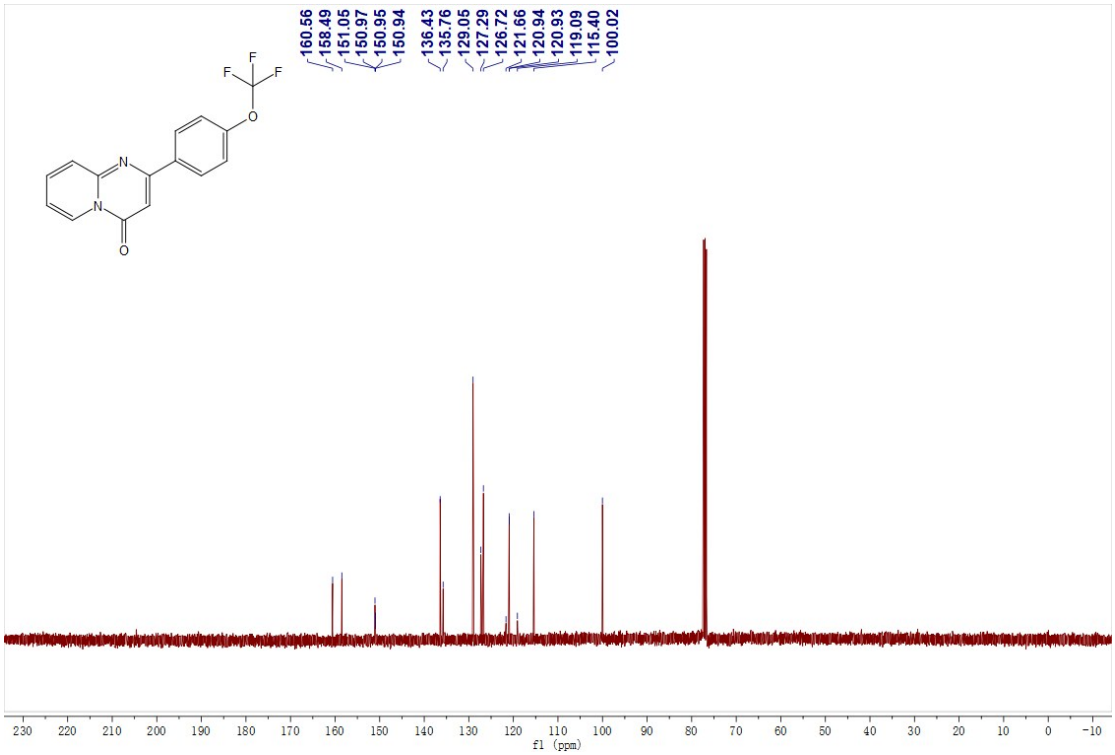

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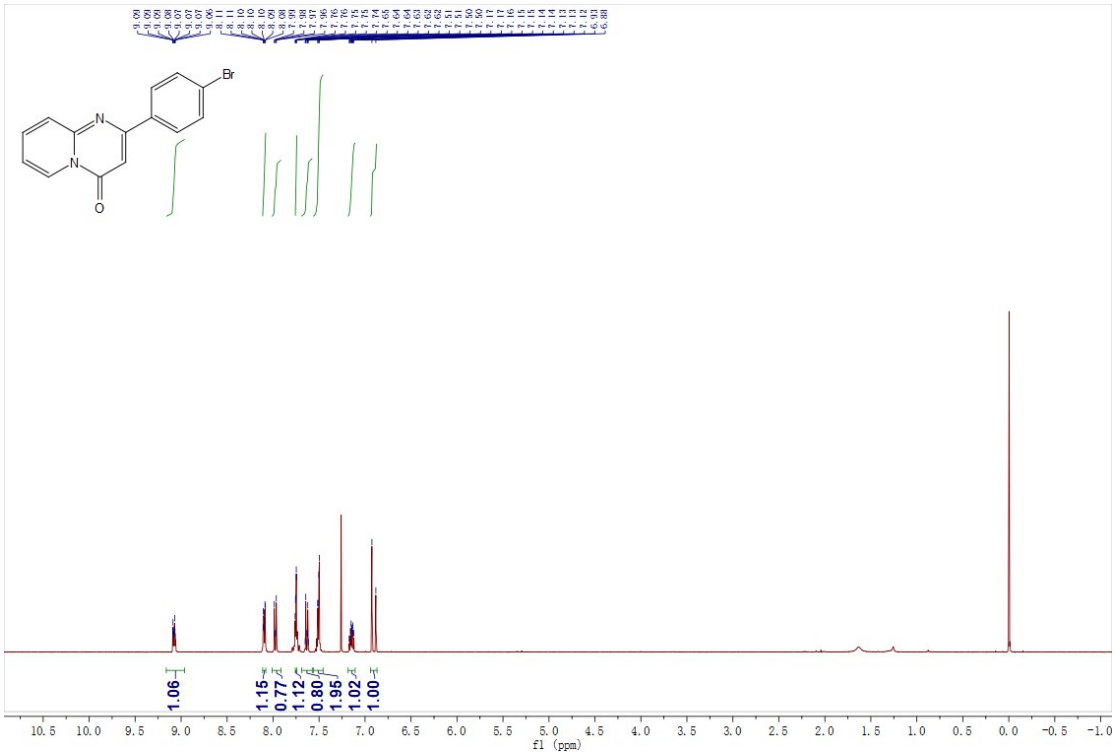

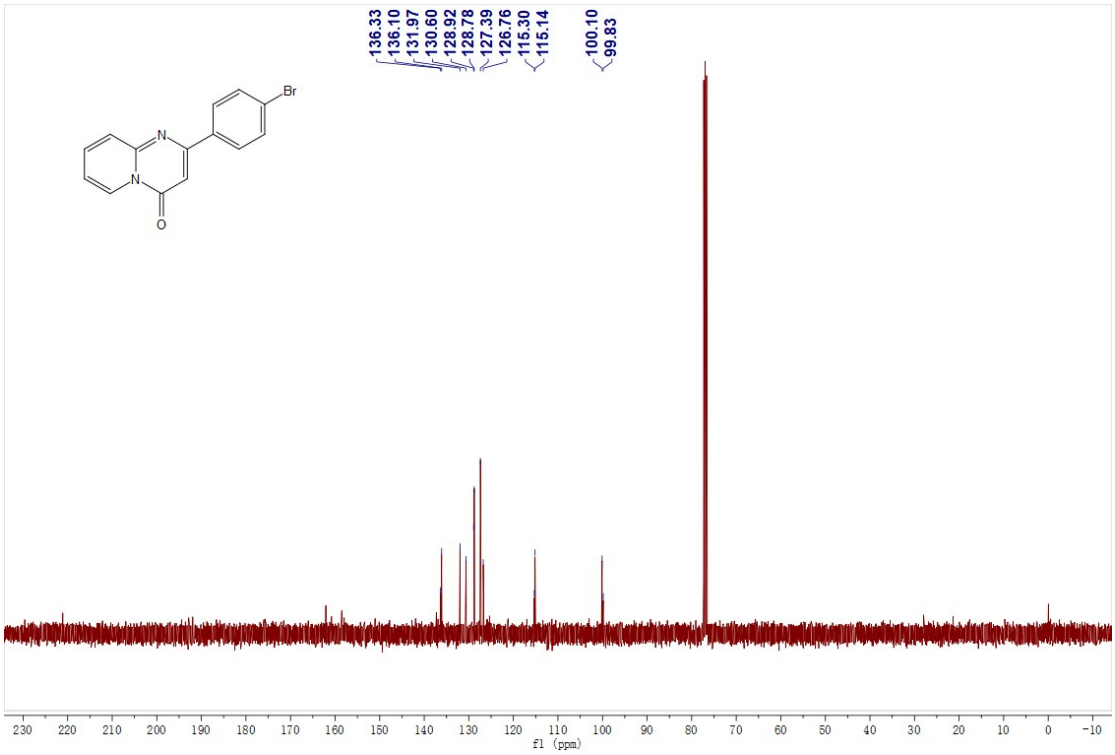

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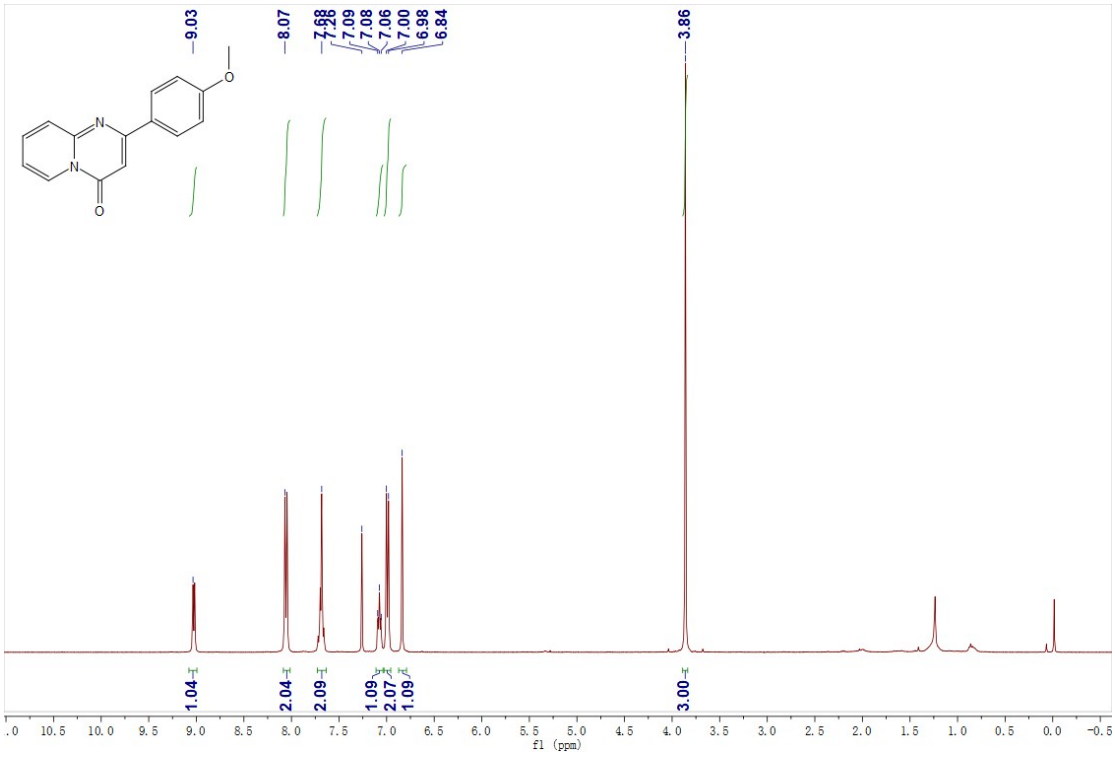

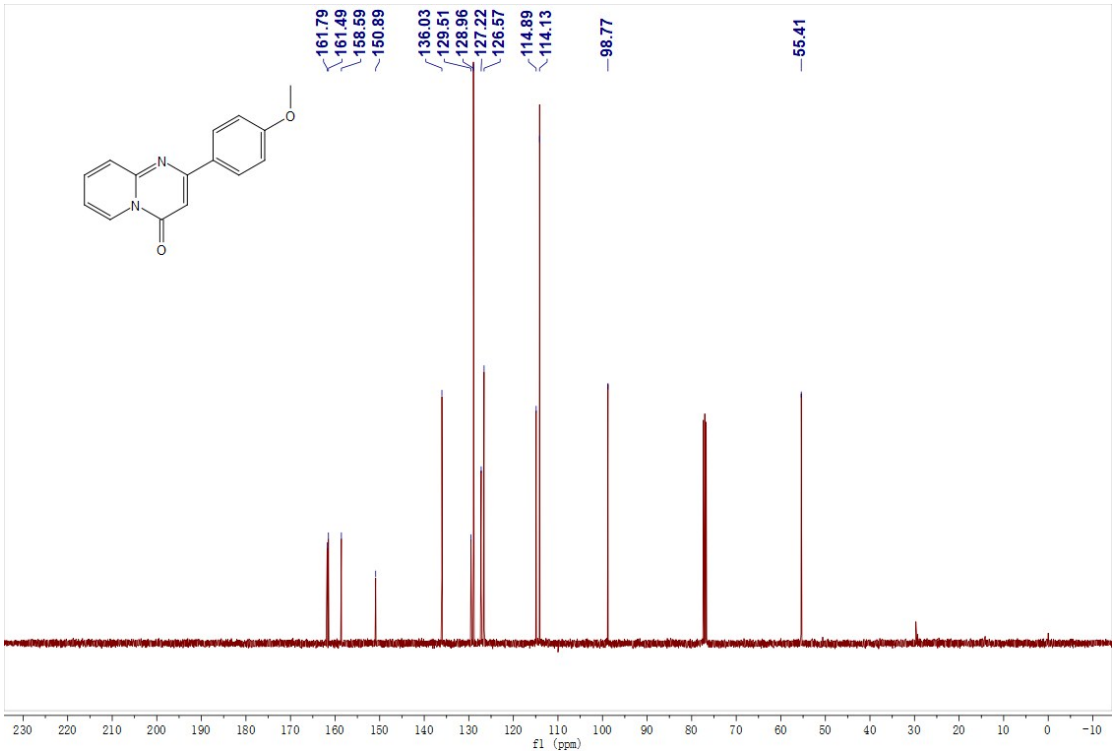

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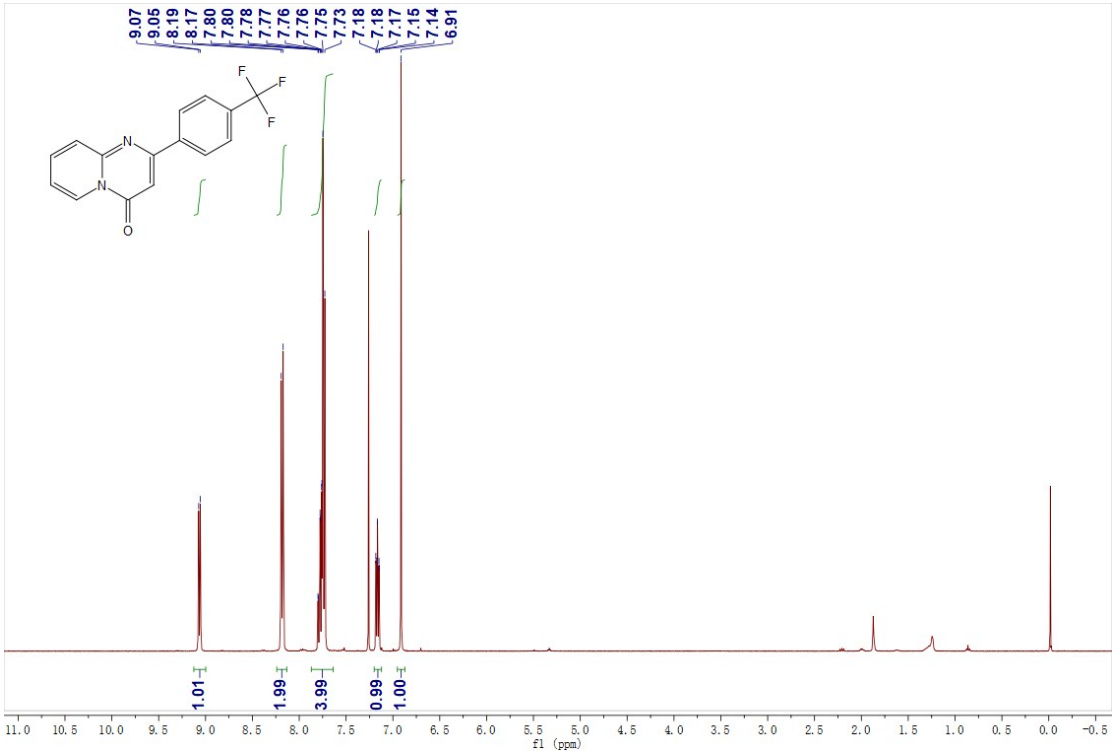

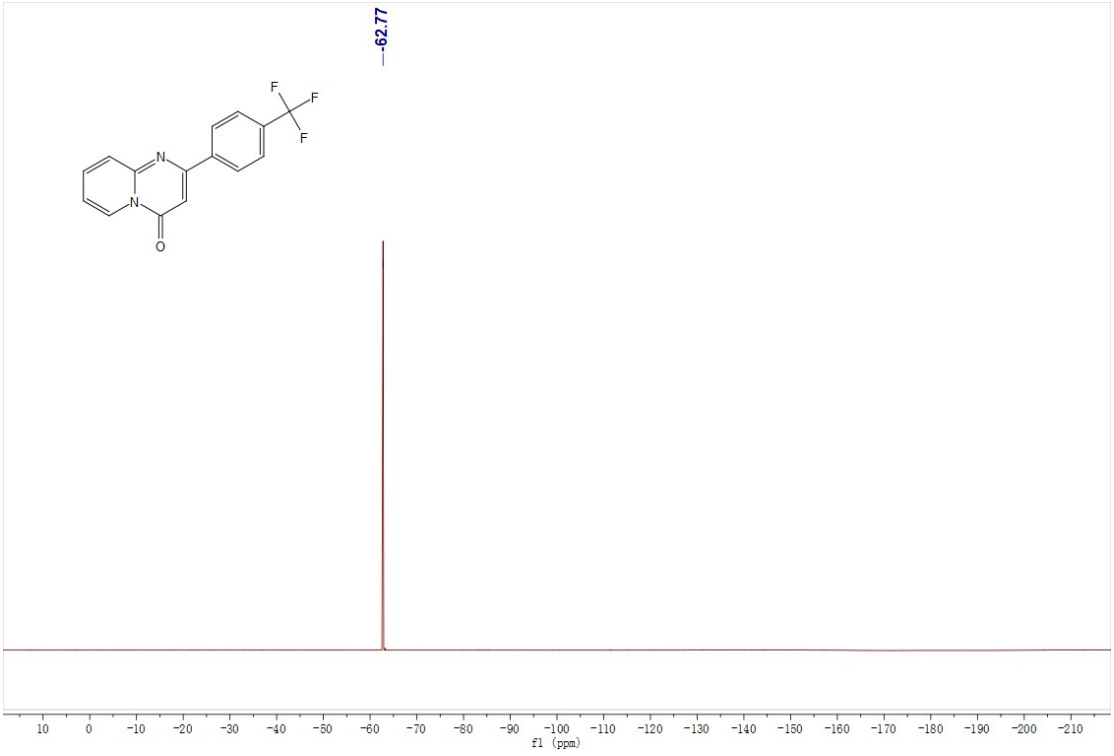
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F
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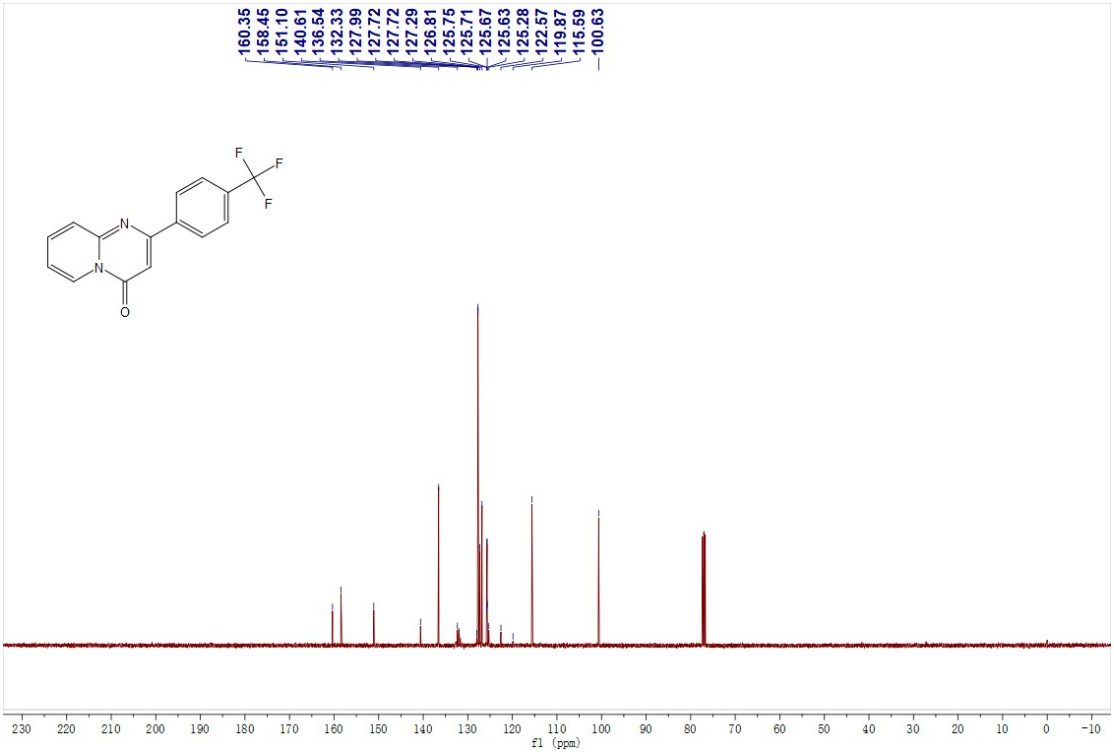
f1 (ppm)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125.67
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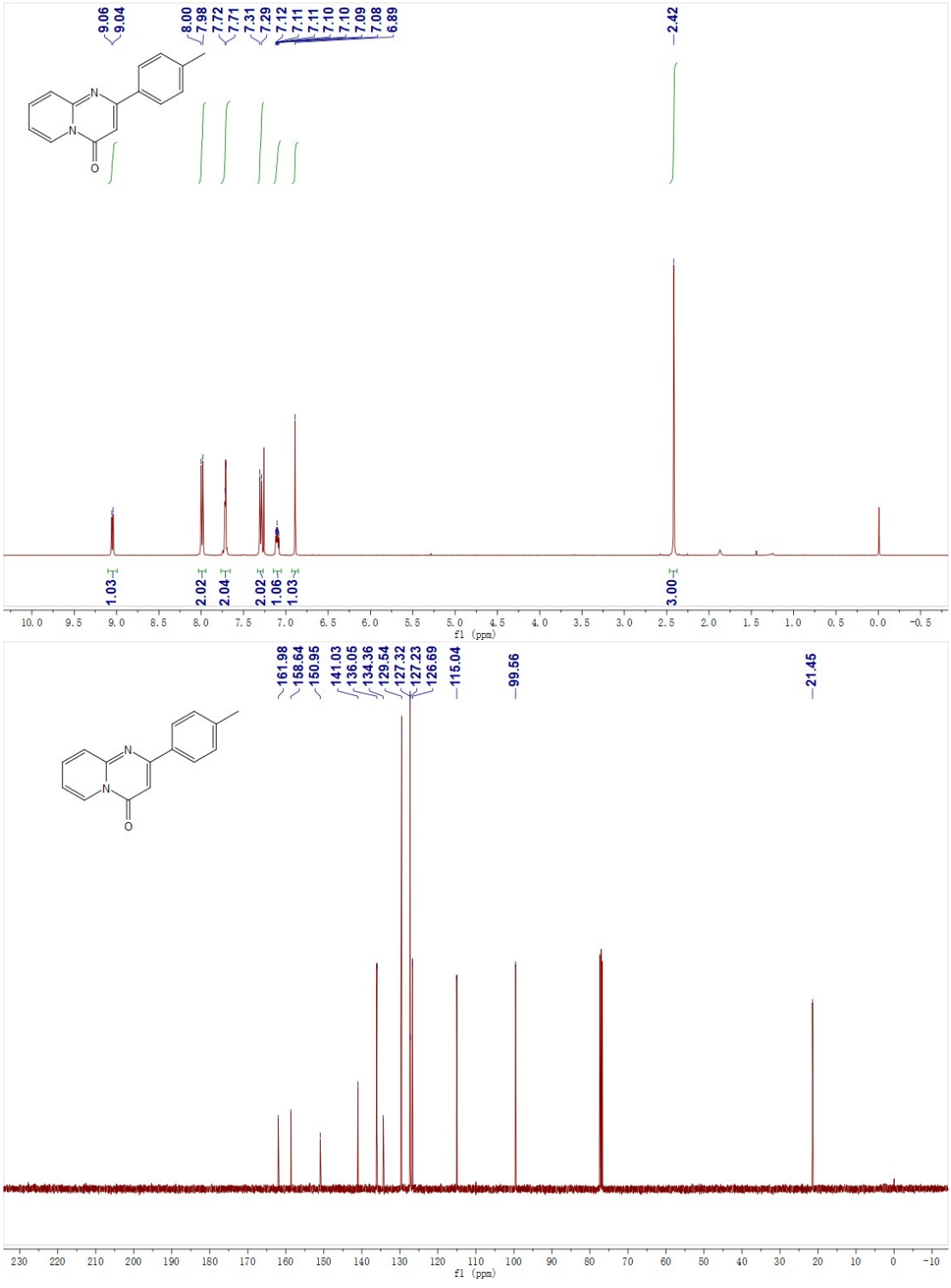
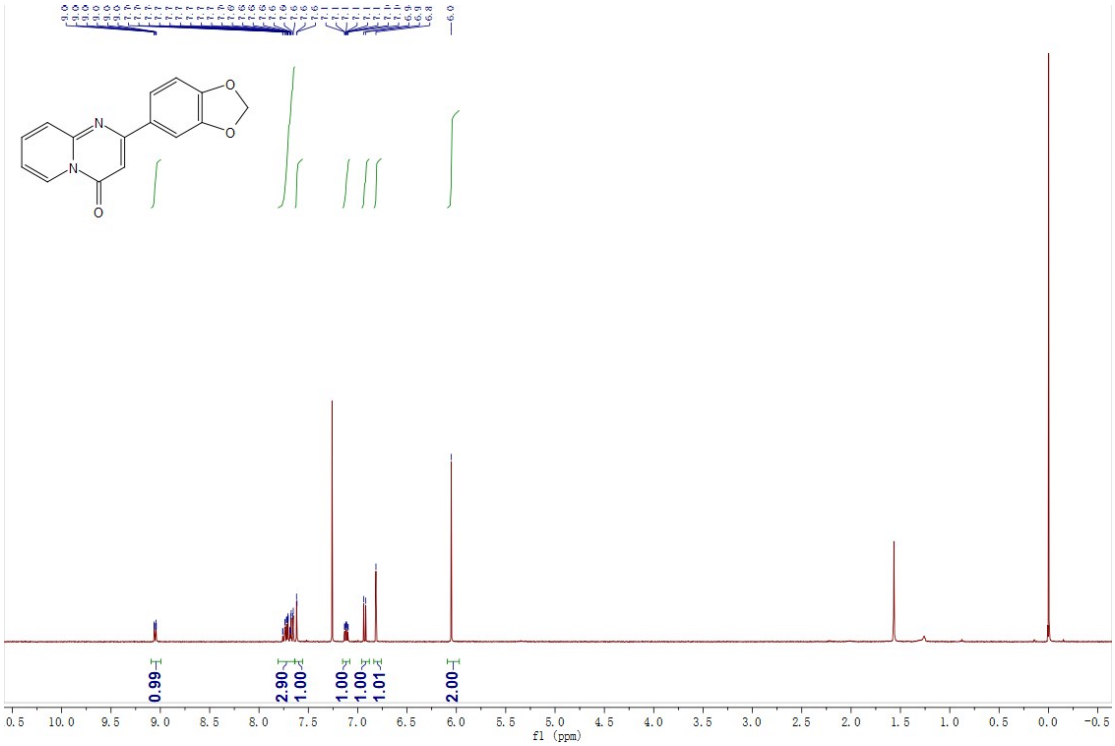
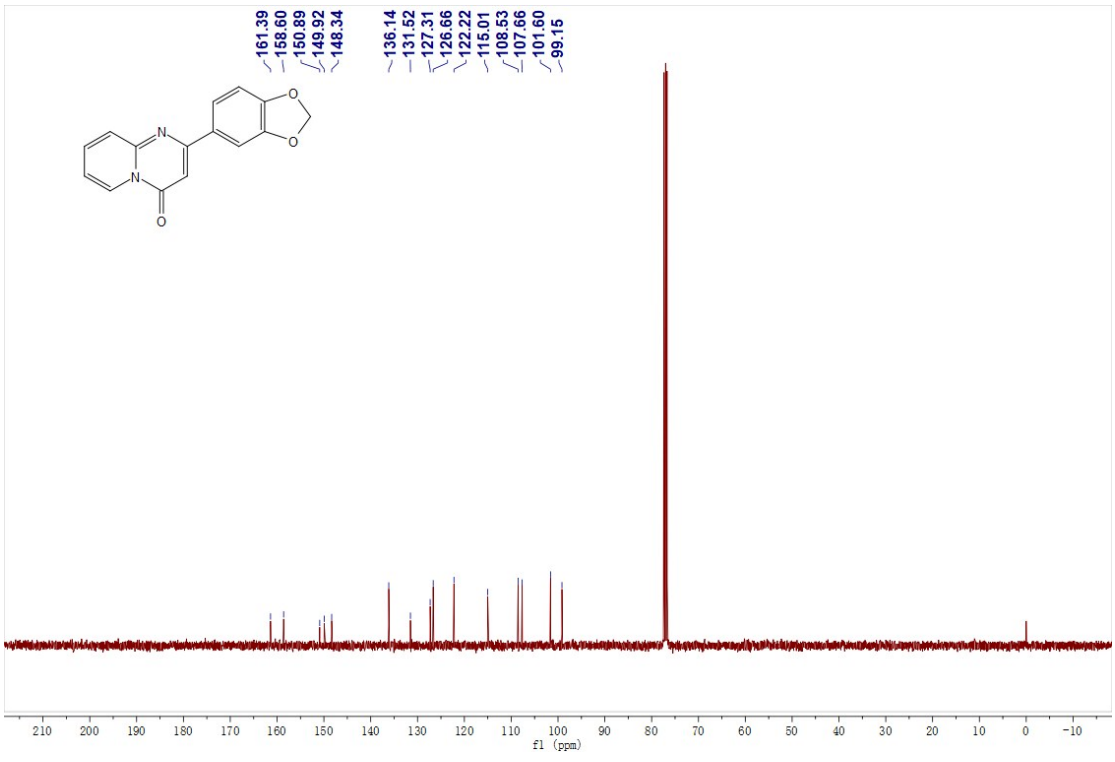
125.28
122.57
119.87
115.59
100.63
F
F
F
N
N
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

2-(p-tolyl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2m)



2-(benzo[d][1,3]dioxol-5-yl)-*4H*-pyrido[1,2-a]pyrimidin-4-one (2o)





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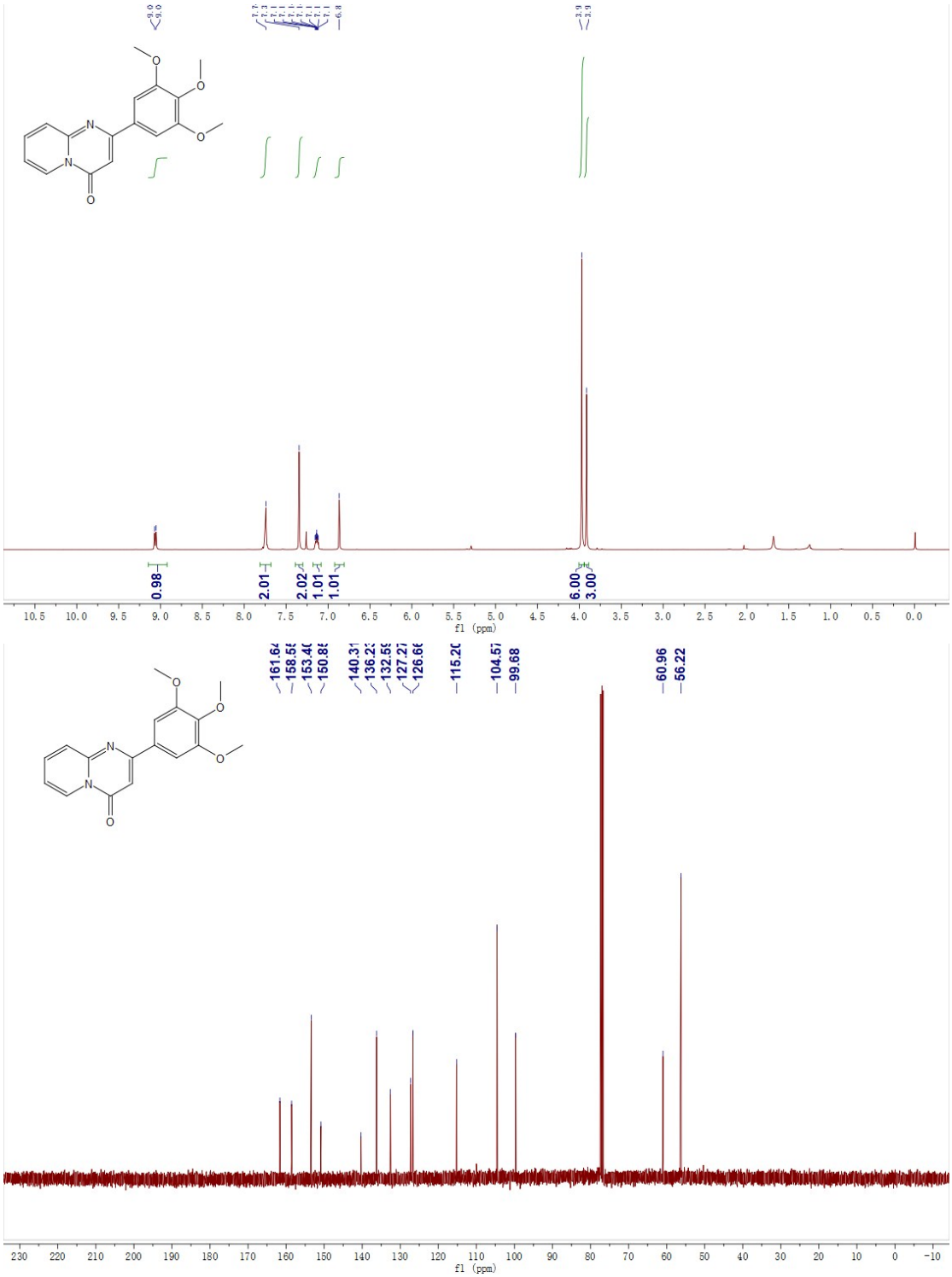

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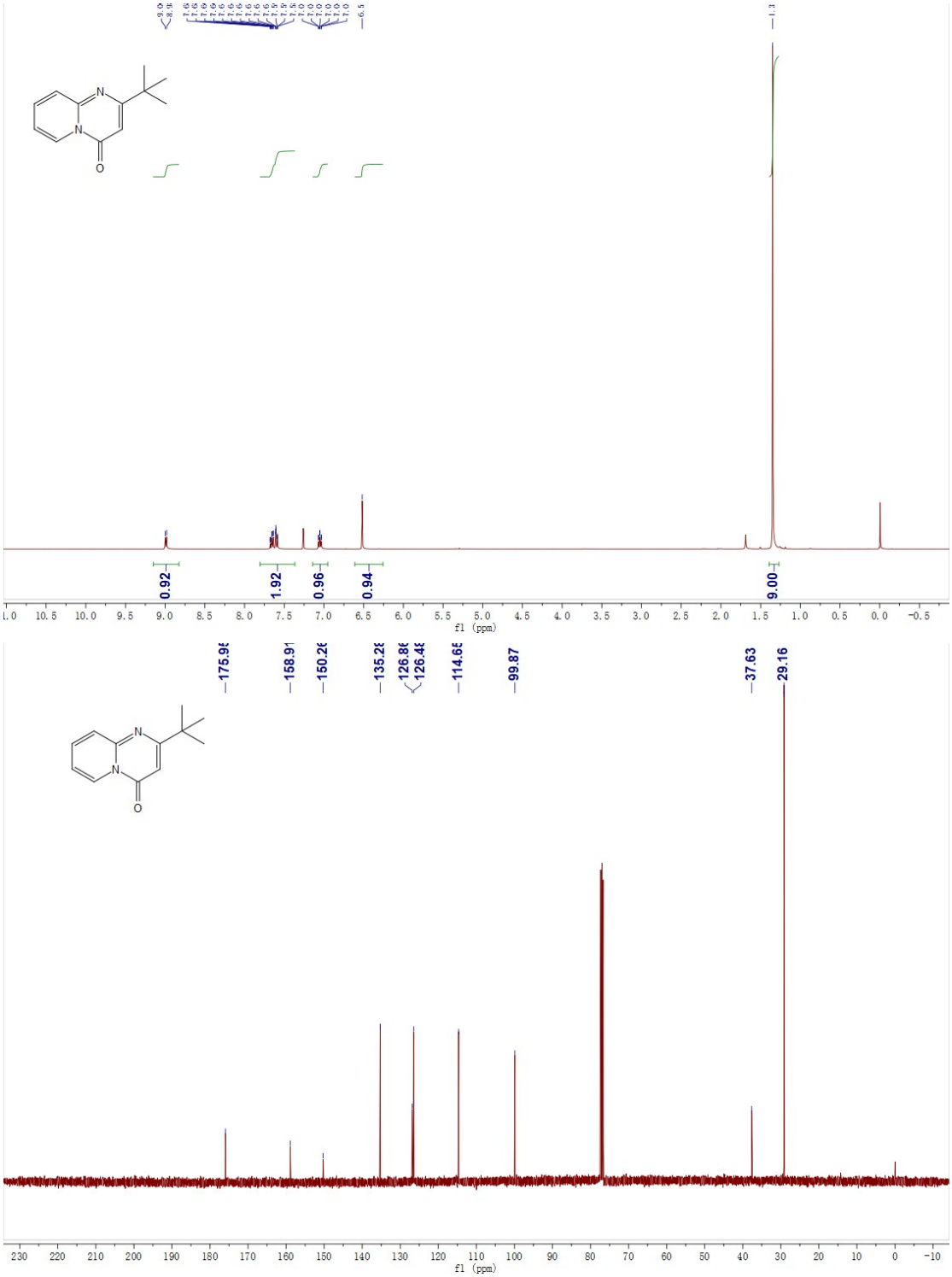

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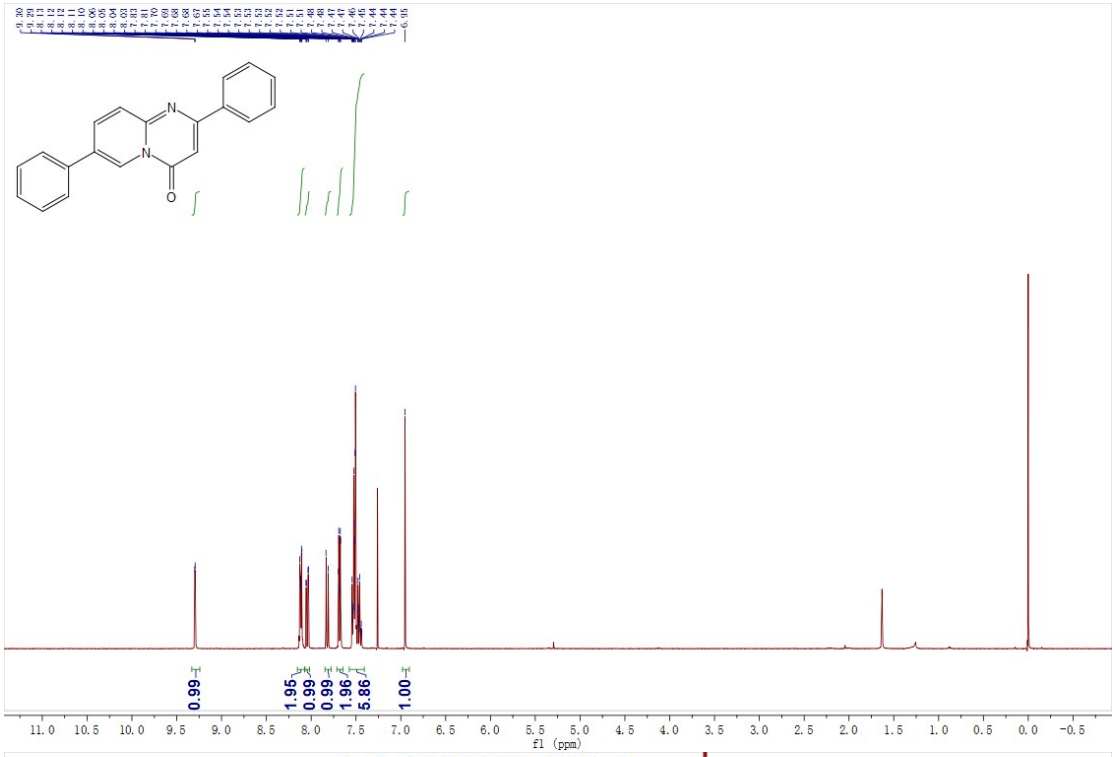
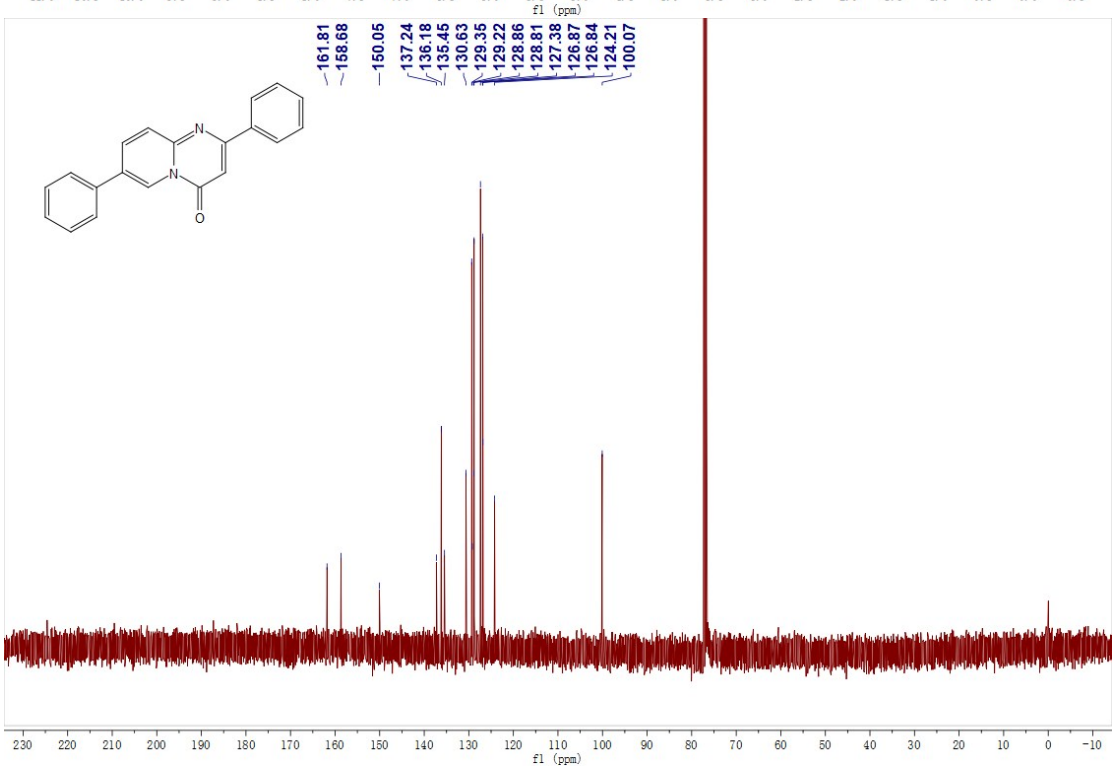
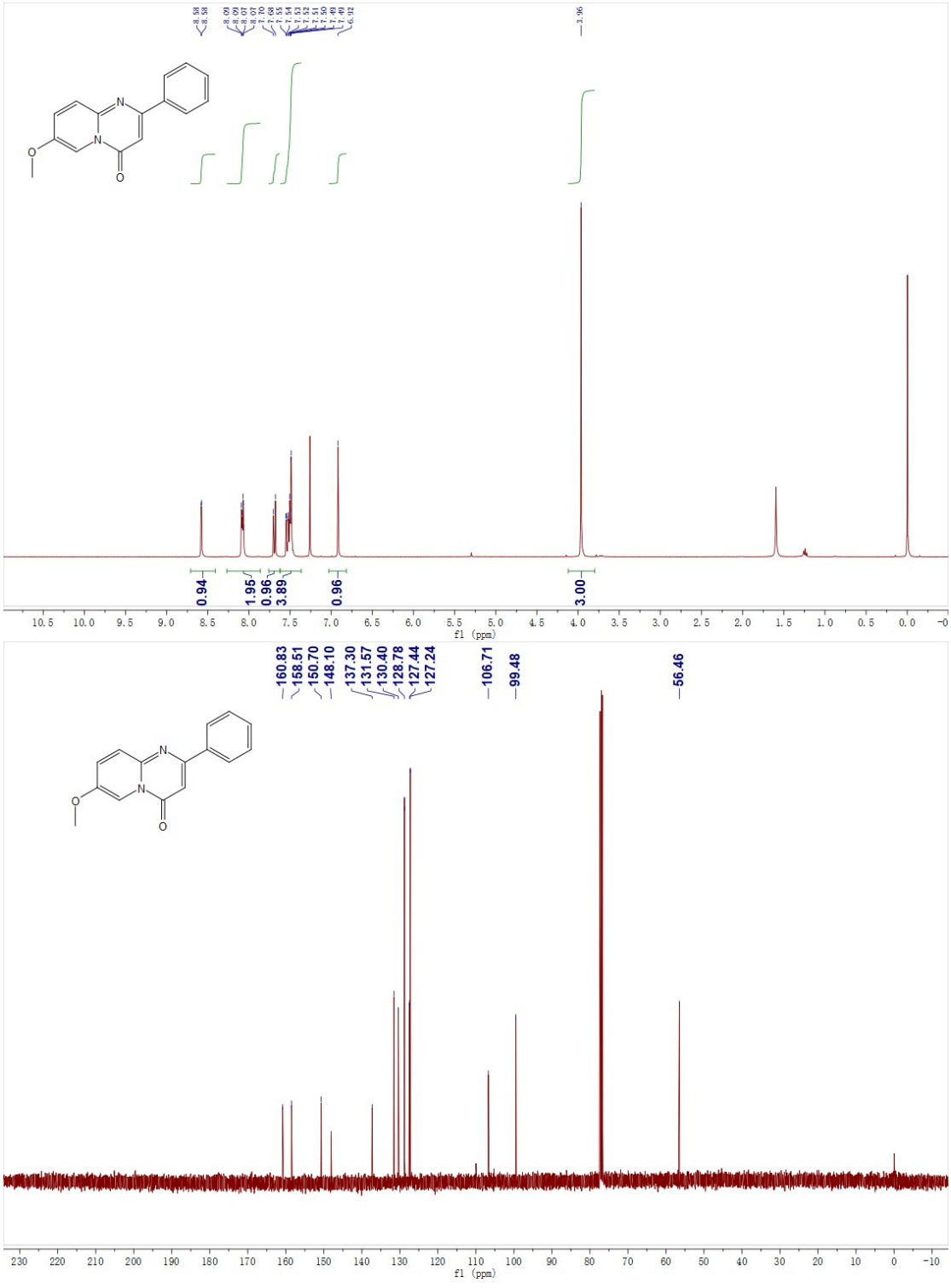
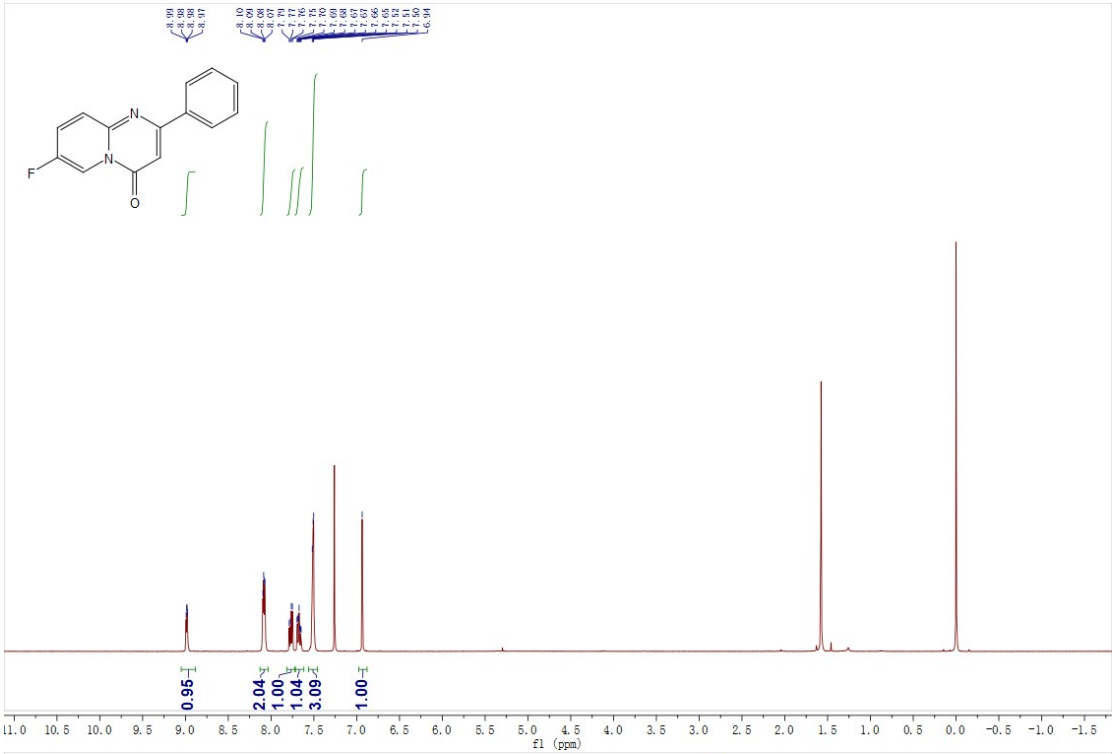


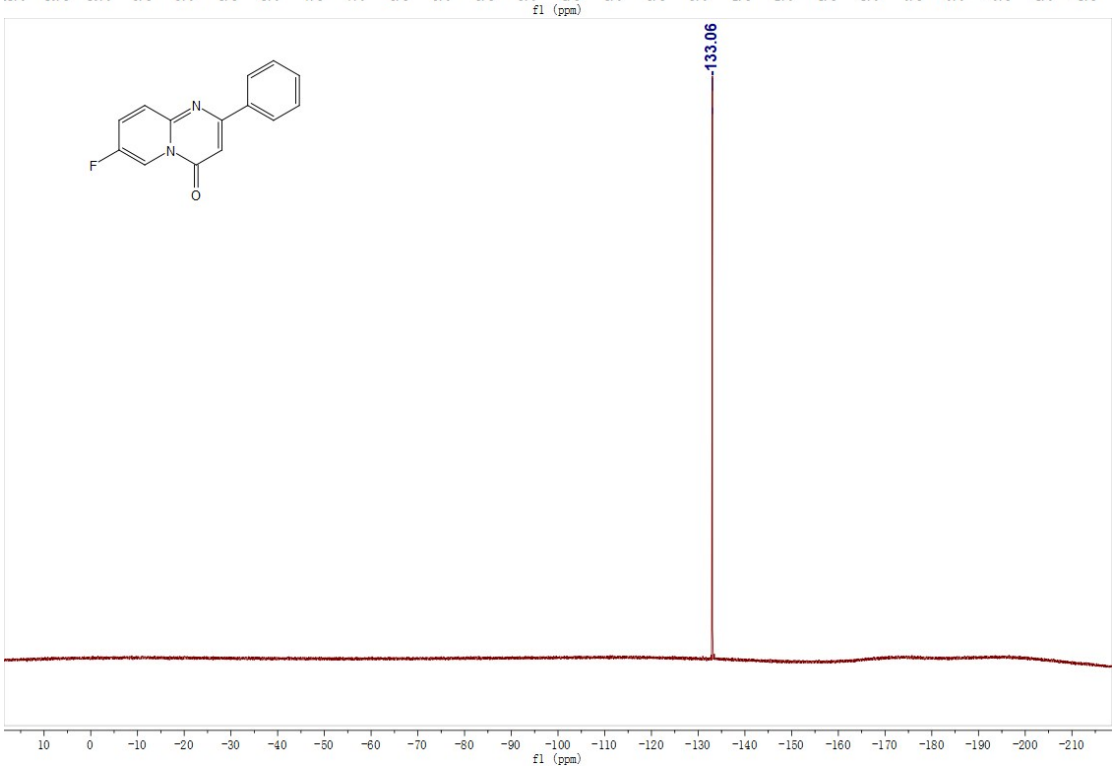


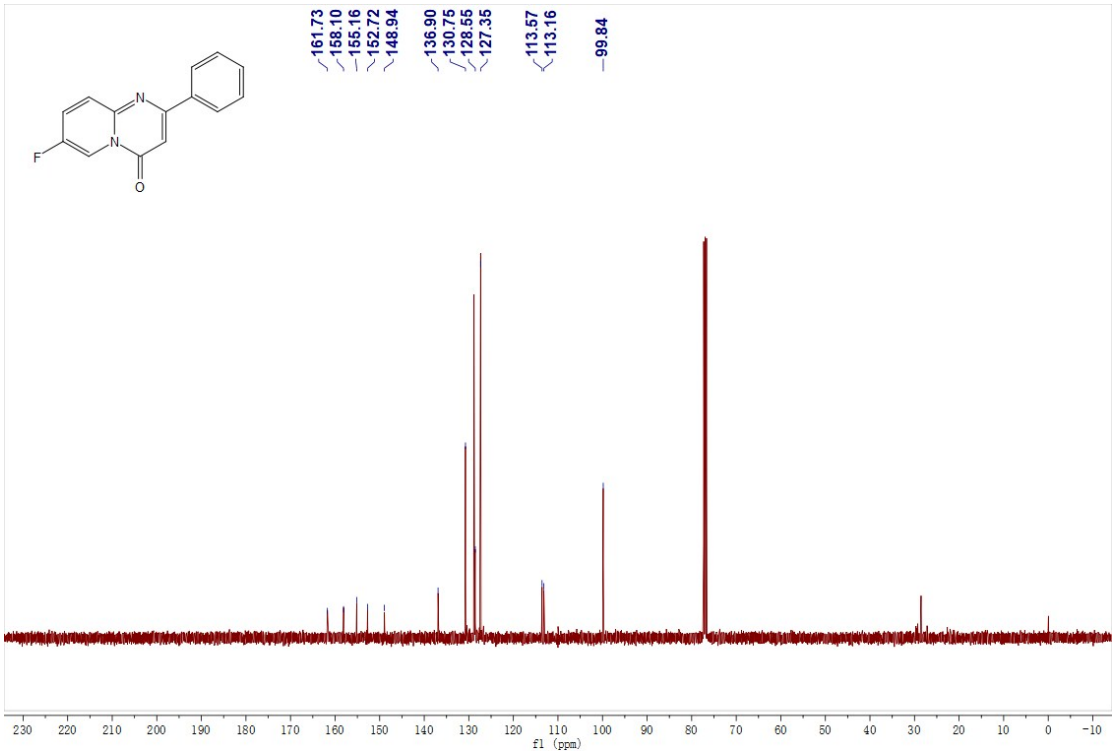
7-methoxy-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2s)



7-fluoro-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2t)







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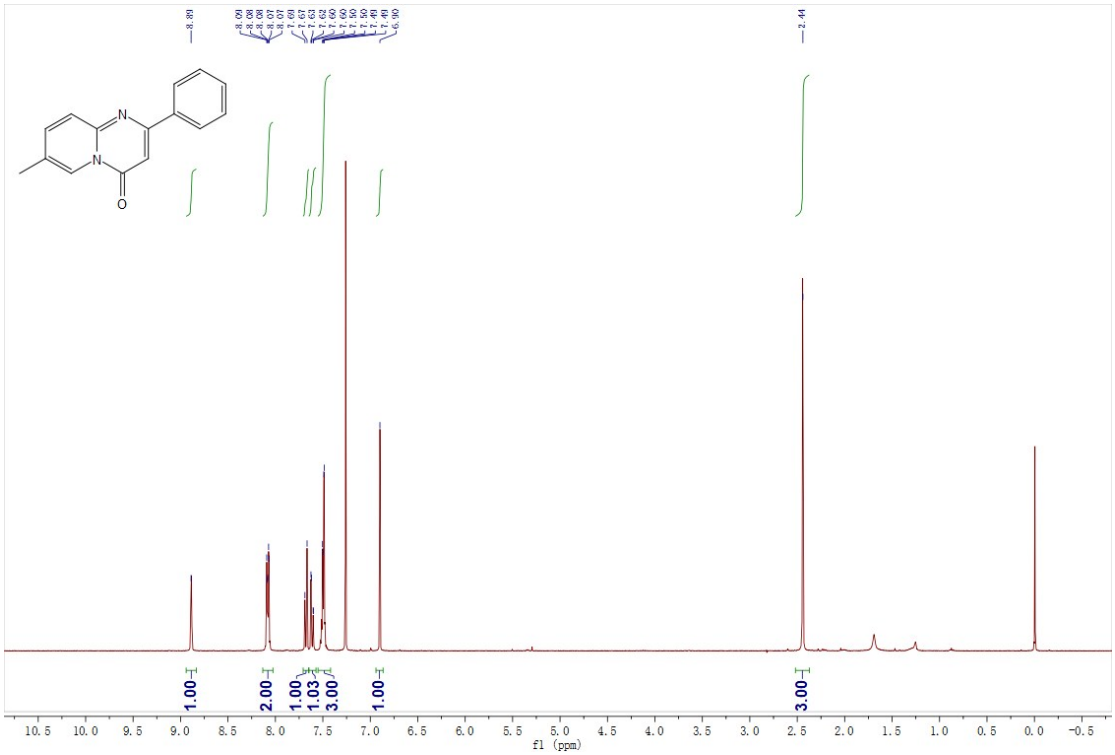

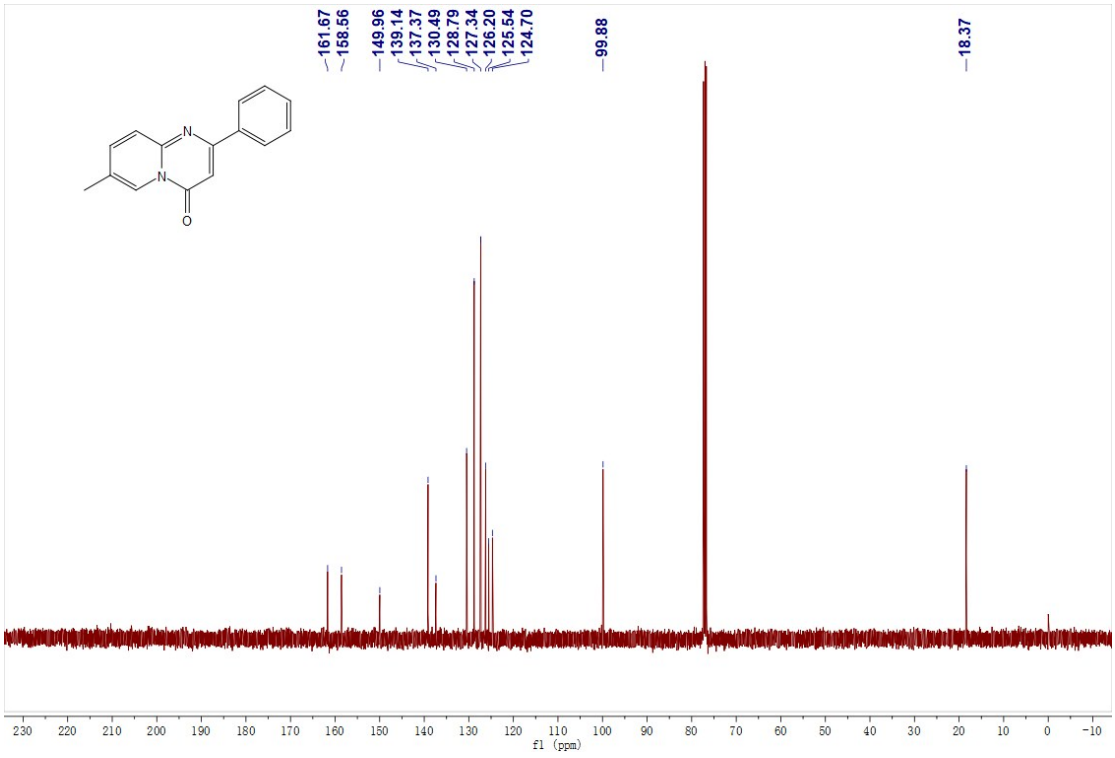

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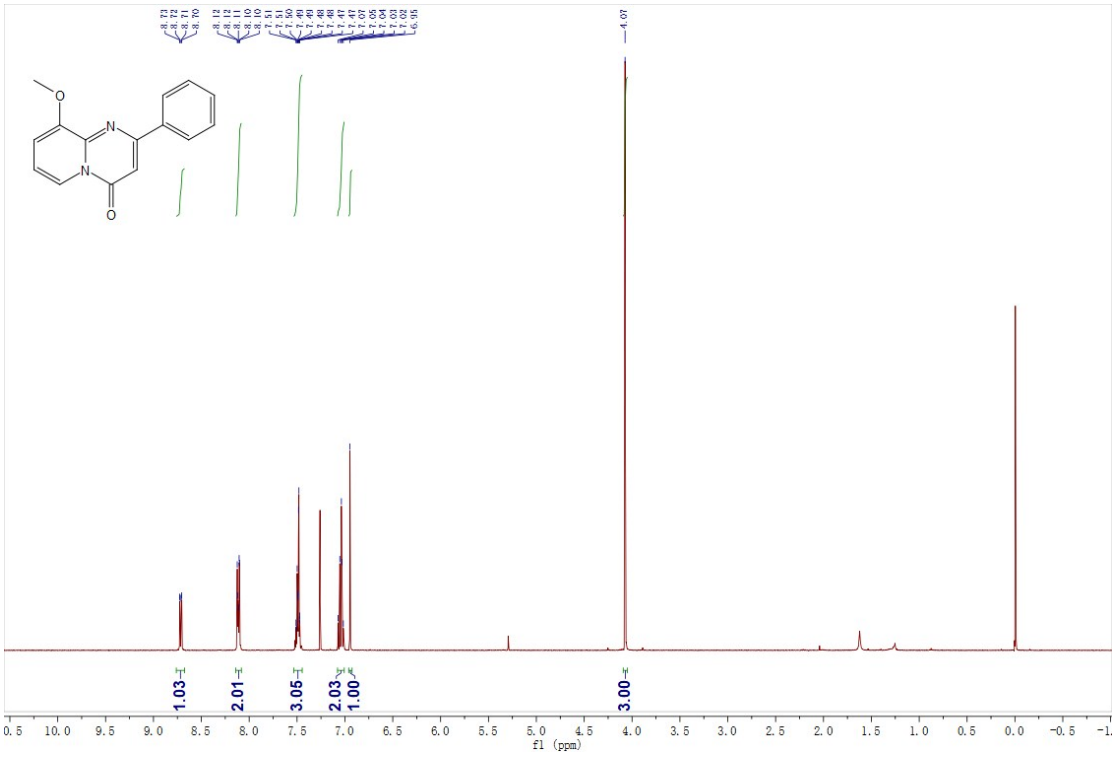
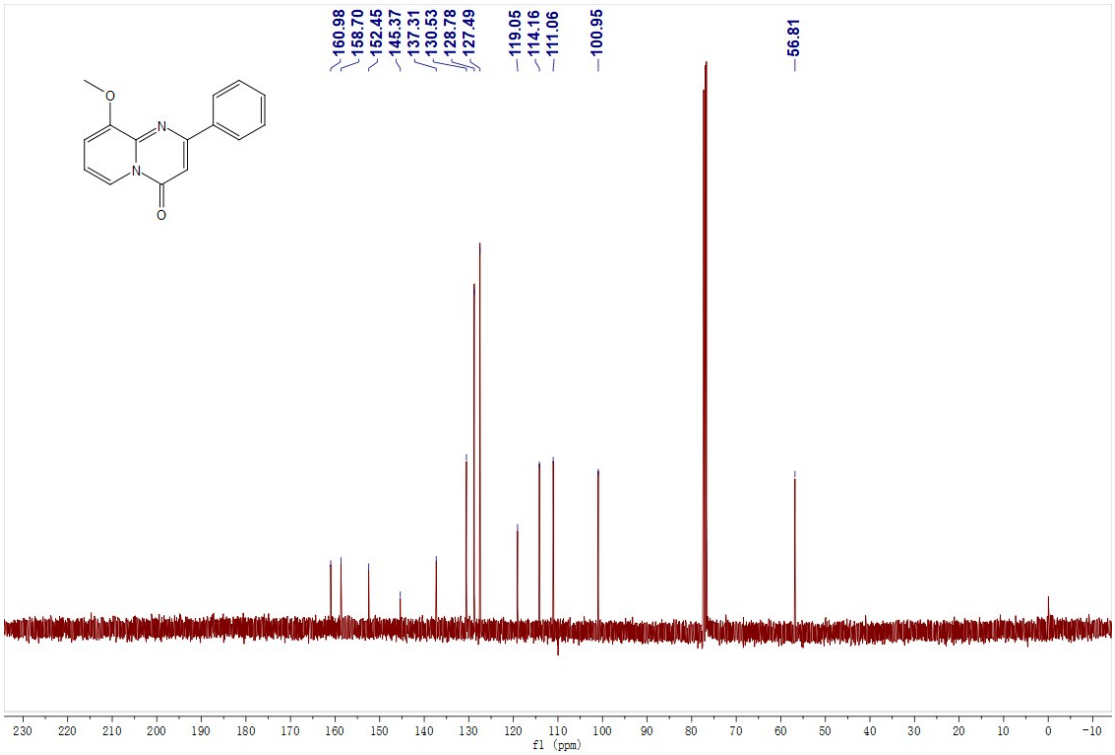
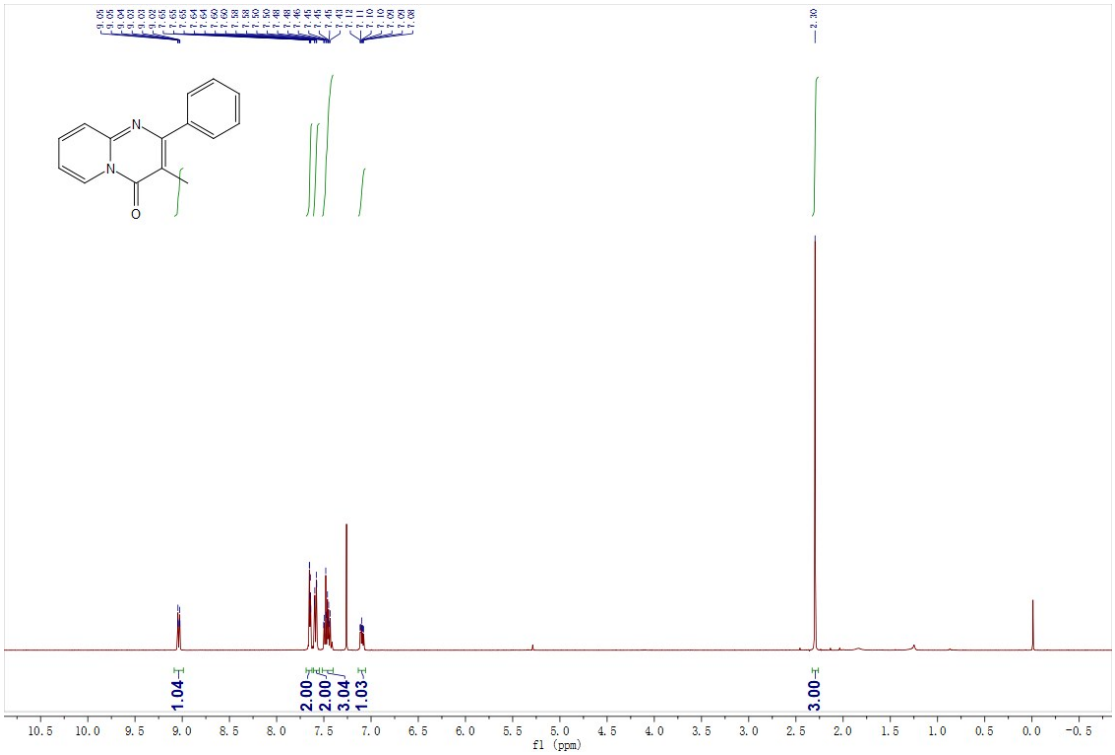
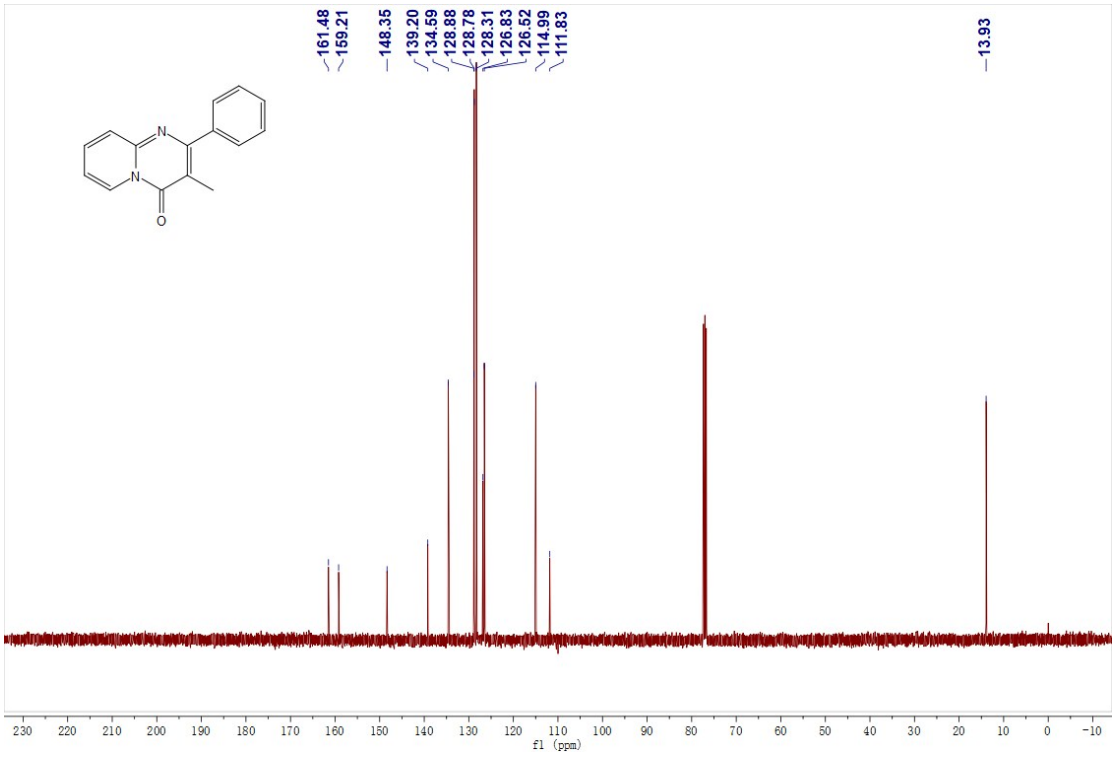


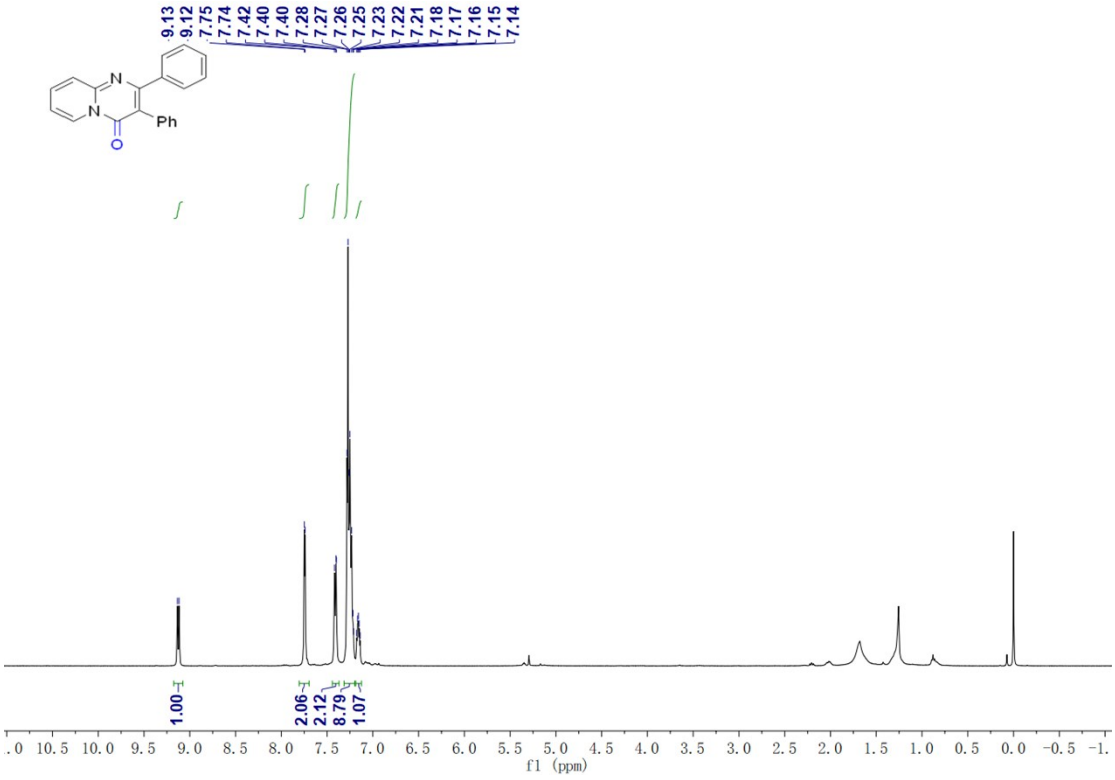


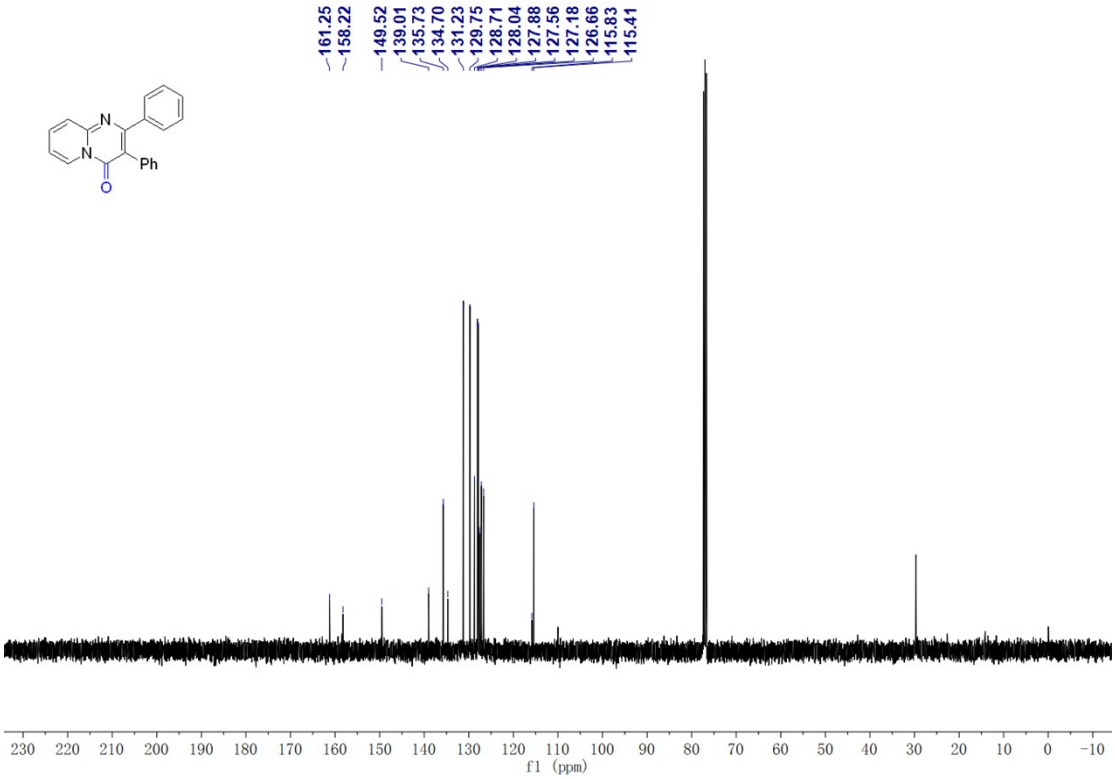
3-methyl-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2w)



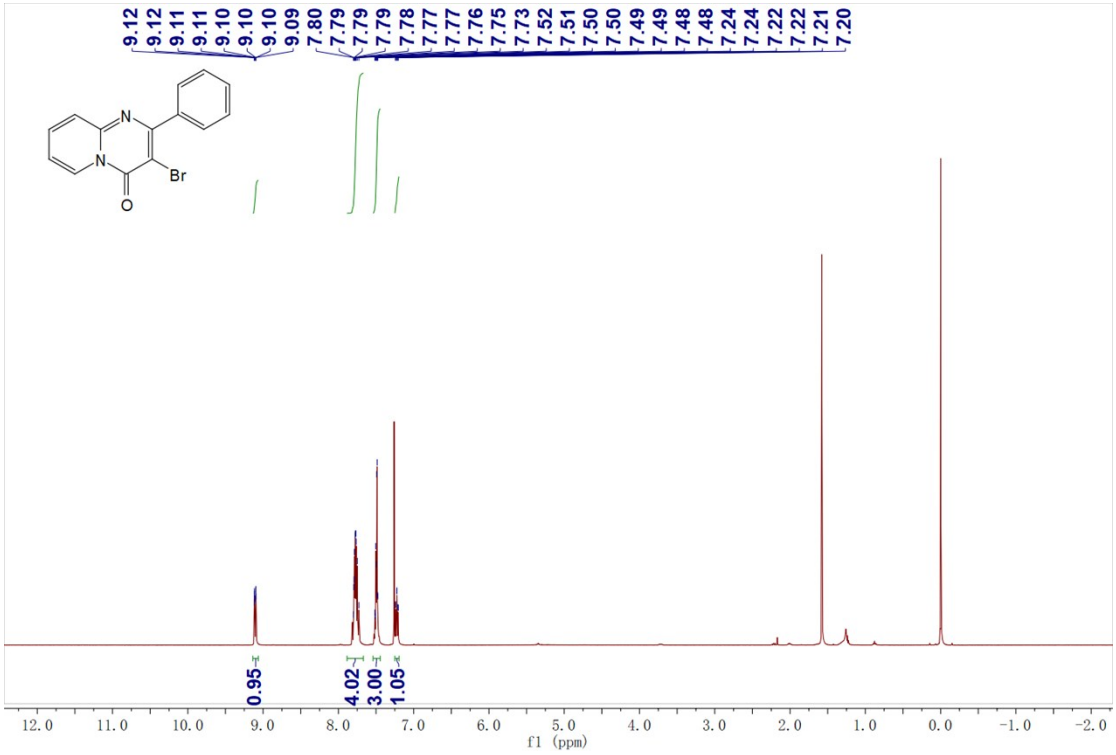


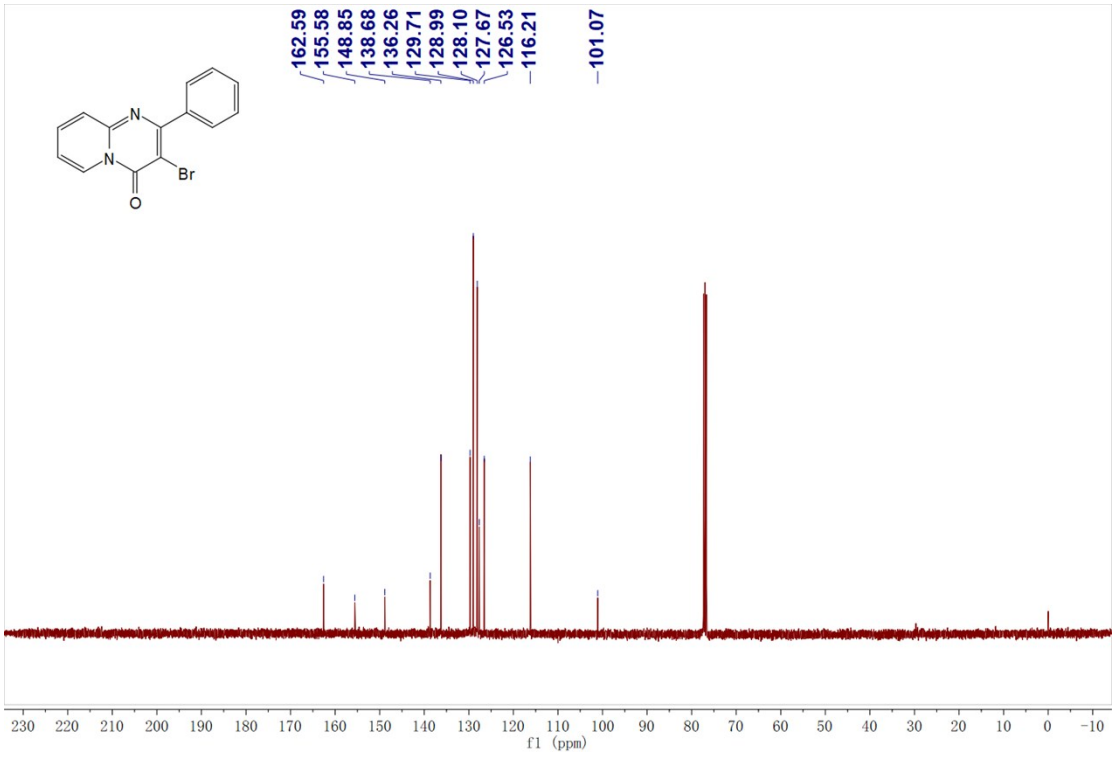
2,3-diphenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (2x)



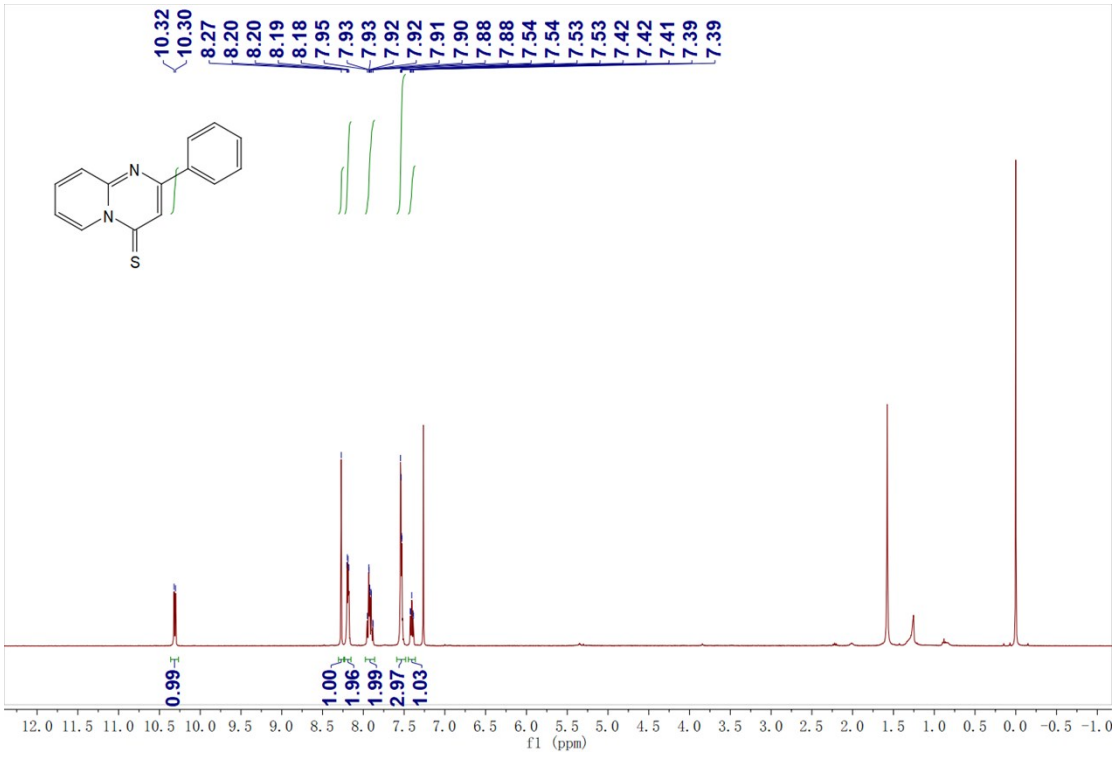


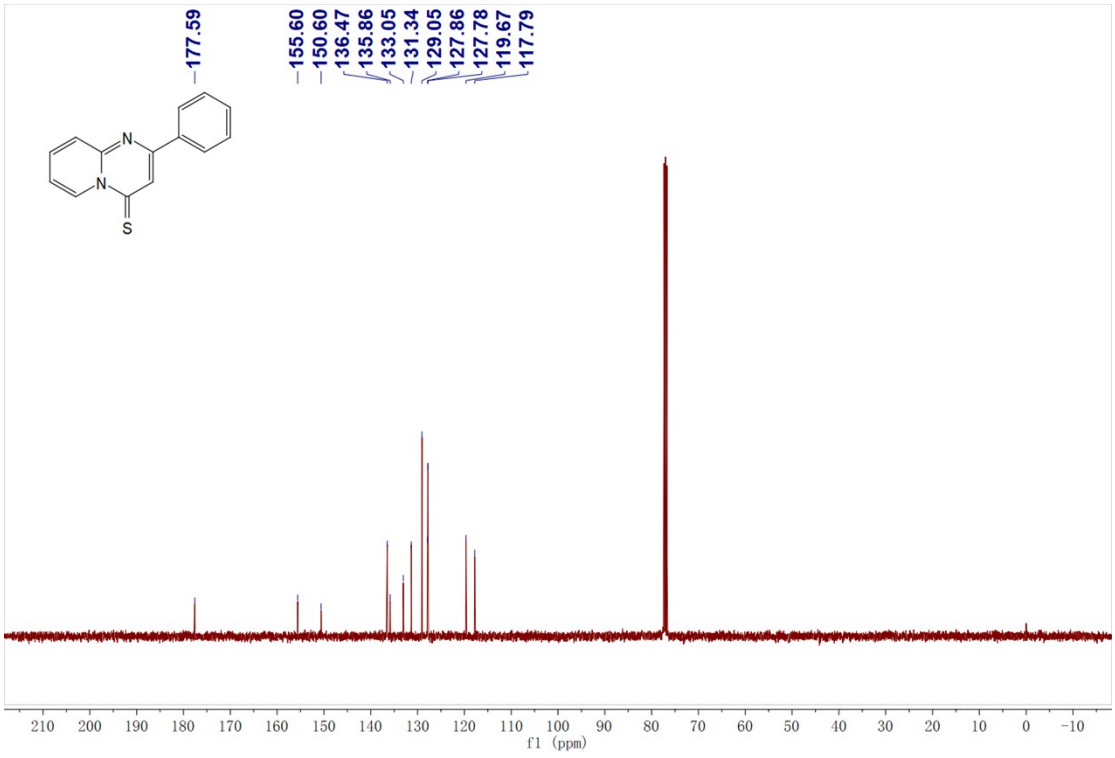
3-bromo-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (3)



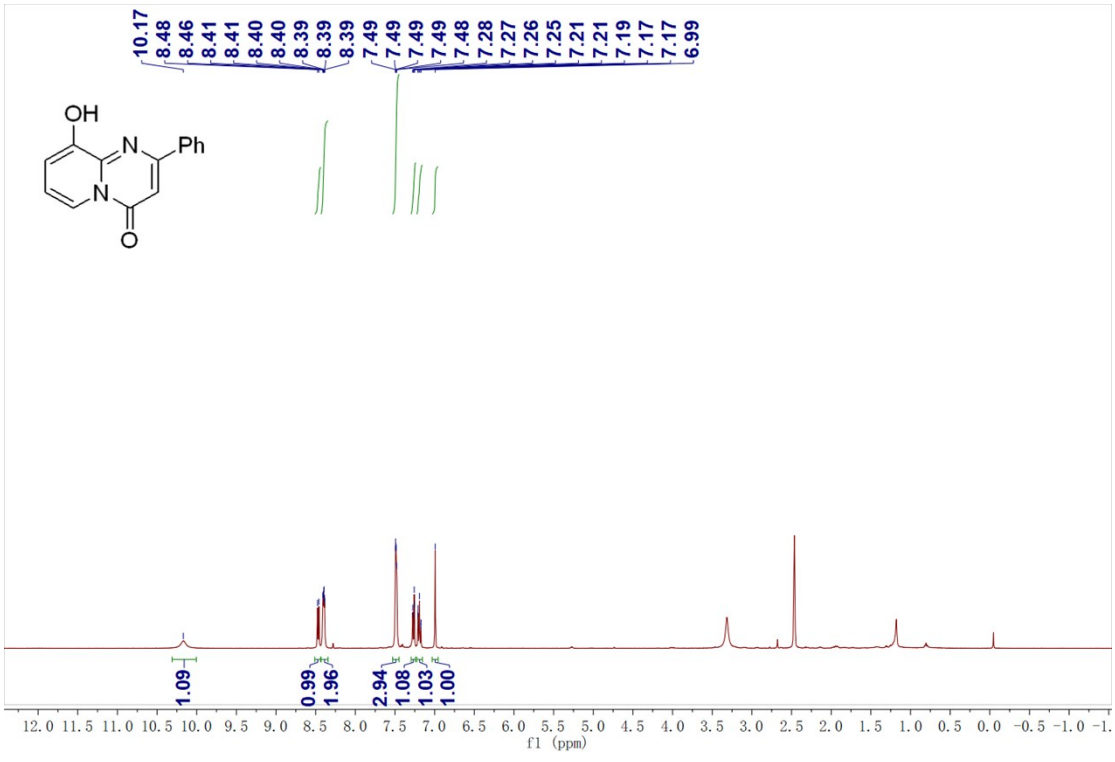


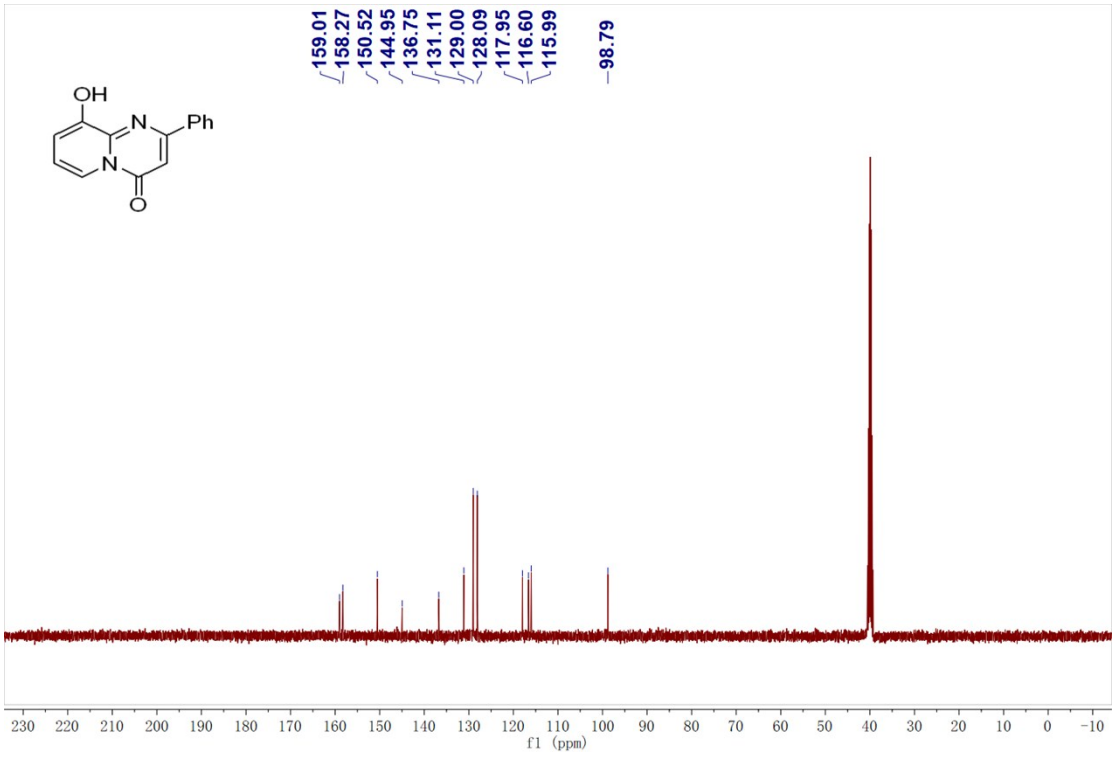
2-phenyl-*4H*-pyrido[1,2-a]pyrimidine-4-thione (4)





9-hydroxy-2-phenyl-*4H*-pyrido[1,2-a]pyrimidin-4-one (5)




159.01
158.27
150.52
144.95
136.75
131.11
129.00
128.09
117.95
116.60
115.99
98.79
OH
N
Ph
N
O
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)