Electronic Supplementary Information

for

Electrochemical C3-methylthiolation of imidazopyridines with dimethyl sulfoxide

Zhaoyue Feng, Yingsibing Fan, Congcong Qiang, Ping Liu* and Peipei Sun*

School of Chemistry and Materials Science, Jiangsu Provincial Key Laboratory of Material Cycle Processes and Pollution Control, Jiangsu Collaborative Innovation Center of Biomedical Functional Materials, Nanjing Normal University, Nanjing 210023, China.

pingliu@njnu.edu.cn; sunpeipei@njnu.edu.cn

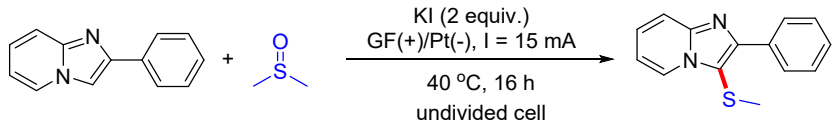
Contents

1 General information

All reagents were obtained from commercial suppliers and used without further purification. Reactions were monitored by thin layer chromatography. Column chromatography was performed using silica gel (300−400 mesh). The NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) in $CDCl_3$ using tetramethylsilane as the internal standard. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublet, dt = doublet of triplet, td = triplet of doublet, q = quartet, m = multiplet. High-resolution mass spectra were obtained with an AB Triple 5600 mass spectrometer by ESI on a TOF mass analyzer. Melting points are uncorrected.

2 Experimental procedures

2.1 General procedure for the electrochemical reactions



1a **2a**

In an undivided three-necked flask (25 mL), 2-phenylimidazo[1,2-*a*]pyridine (**1a**, 97.1mg, 0.5 mmol), KI (166.0 mg, 1.0 mmol), and DMSO (10 mL) were continuously added. The flask was equipped with a graphite felt electrode (30 mm × 10 mm × 2 mm) as the anode and a platinum plate electrode (10 mm × 10 mm × 1 mm) as the cathode (Figure S1). The distance between the electrodes was 10 mm. The reaction mixture was stirred and electrolyzed at a constant current (15 mA) under air at 40 °C for 16 h. After being cooled to room temperature, the resulting solution was diluted with EtOAc (10 mL). The organic layer was washed with water (10 mL). The aqueous phase was re-extracted with EtOAc (10 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. Subsequently, the crude residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1, v/v) as eluent to afford the desired product **2a**.

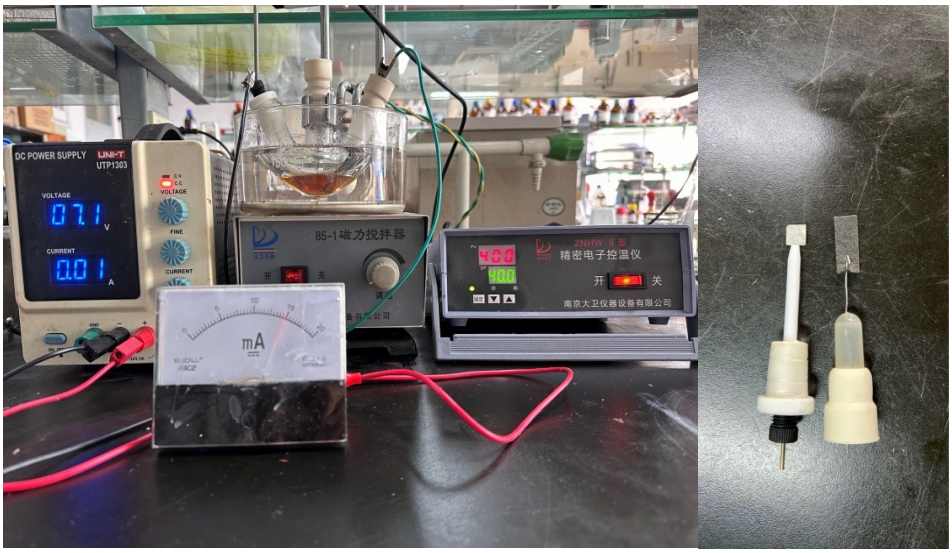
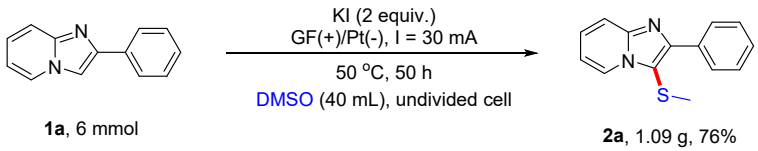


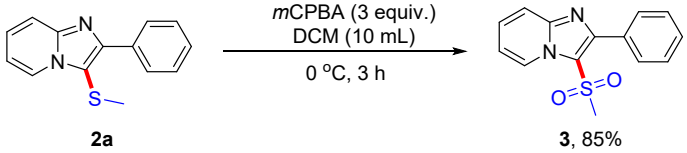
Figure S1. The electrochemical reaction setup.

2.2 Gram-scale synthesis of 2a



In an undivided three-necked flask (100 mL), 2-phenylimidazo[1,2-*a*]pyridine (**1a**, 1.16 g, 6 mmol), KI (1.99 g, 12 mmol), and DMSO (40 mL) were continuously added. The flask was equipped with a graphite felt electrode as the anode and a platinum plate electrode (15 mm × 15 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current (30 mA) under air at 50 °C for 50 h. After being cooled to room temperature, the resulting solution was diluted with EtOAc (50 mL). The organic layer was washed with water (50 mL). The aqueous phase was re-extracted with EtOAc (50 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. Subsequently, the crude residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1, v/v) as eluent to afford the desired product **2a**.

2.3 The transformation of 2a to 3



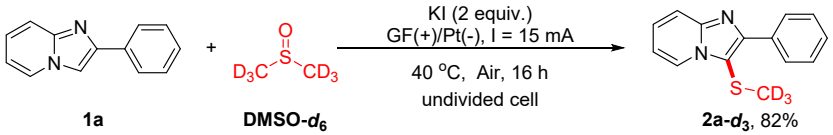
In a Schlenk flask (25 mL), **2a** (0.5 mmol, 120.0 mg), *m*CPBA (1.5 mmol, 258.9 mg) and DCM (10 mL) were added in sequence. After stirring for 3 h at 0 °C, the mixture was quenched with

water, and extracted with ethyl acetate, and the combined organic phases were dried over anhydrous Na_2SO_4, filtered, concentrated in *vacuo*. Subsequently, the crude residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (1:1, v/v) as eluent to afford the desired product **3**.

3 Mechanistic studies

3.1 Control experiments

3.1.1 Deuteration experiments



In an undivided three-necked flask (25 mL), 2-phenylimidazo[1,2-*a*]pyridine (**1a**, 97.1mg, 0.5 mmol), KI (166.0 mg, 1.0 mmol), and dimethyl sulfoxide-d_6 (10 mL) were continuously added. The flask was equipped with a graphite felt electrode as the anode and a platinum plate electrode (10 mm × 10 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current (15 mA) under air at 40 °C for 16 h. After being cooled to room temperature, the resulting solution was diluted with EtOAc (10 mL). The organic layer was washed with water (10 mL). The aqueous phase was re-extracted with EtOAc (10 mL × 2). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. Subsequently, the crude residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (5:1, v/v) as eluent to afford the desired product **2a-*d*$_3$**.

3.1.2 HRMS analysis of the homo-coupling product 1,2-bis(methylsulfinyl)ethane (4)

4, HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_4H_{11}O_2S_2^+$, 155.0195; found 155.0198. (Figure S2)

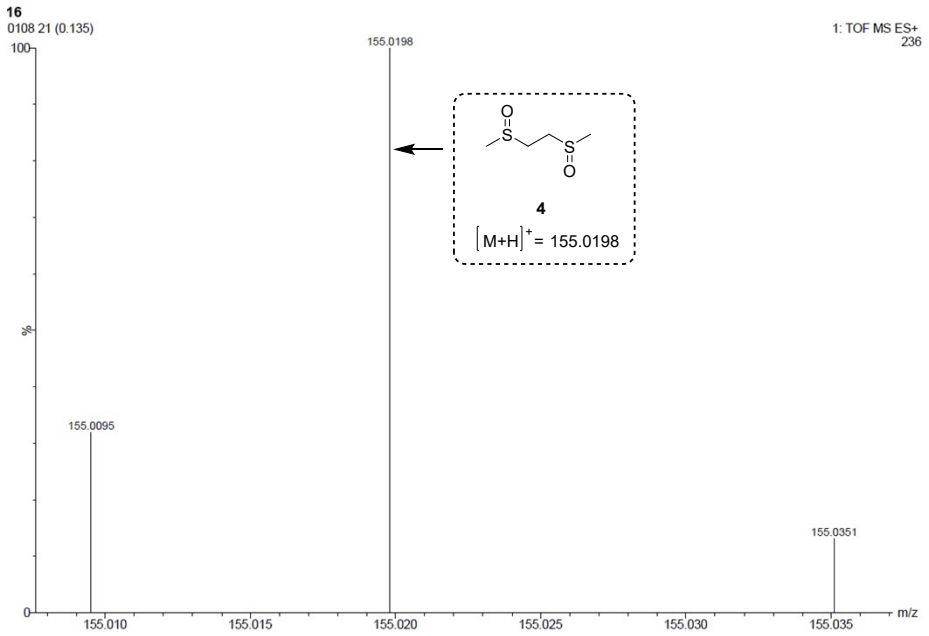
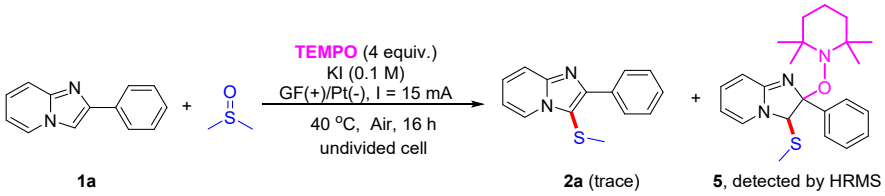


Figure S2. HRMS analysis of the homo-coupling product **4**.

3.1.3 Reaction in the presence of TEMPO



In an undivided three-necked flask (25 mL), 2-phenylimidazo[1,2-*a*]pyridine (**1a**, 97.1mg, 0.5 mmol), KI (166.0 mg, 1.0 mmol), TEMPO (312.5 mg, 2.0 mmol) and DMSO (10 mL) were continuously added. The flask was equipped with a graphite felt electrode as the anode and a platinum plate electrode (10 mm × 10 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current (15 mA) under air at 40 °C for 16 h. The reaction was obviously suppressed by the addition of TEMPO, and a trapping product **5** was detected through the HRMS analysis from the reaction solution (Figure S3).

5, HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_{23}H_{32}N_3OS^+$, 398.2261; found 398.2264.

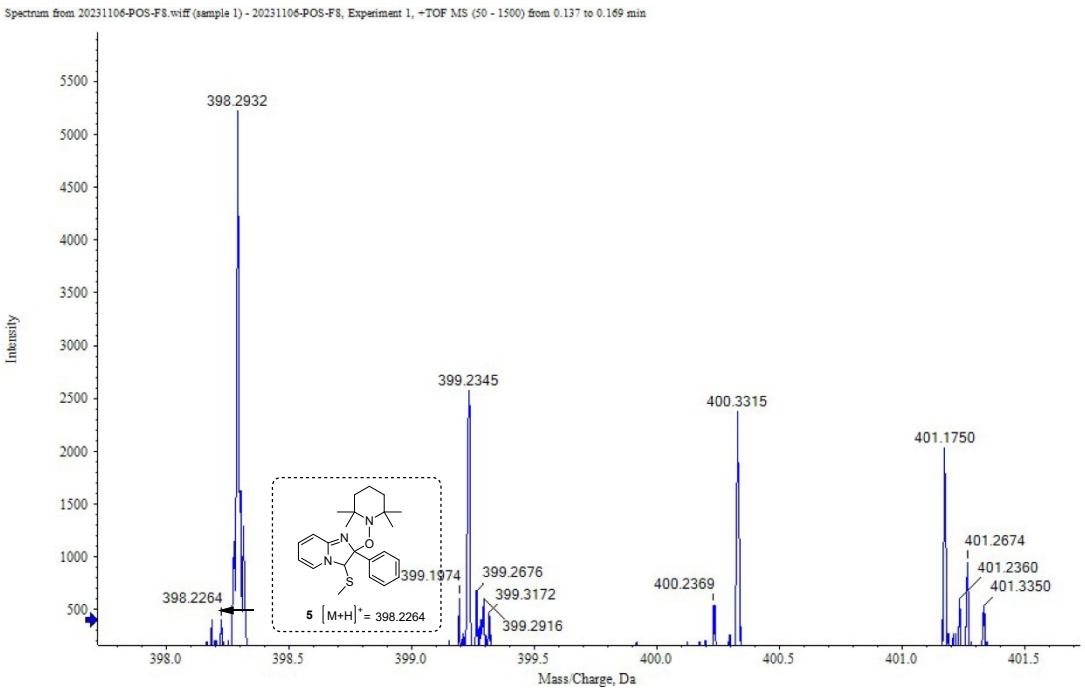
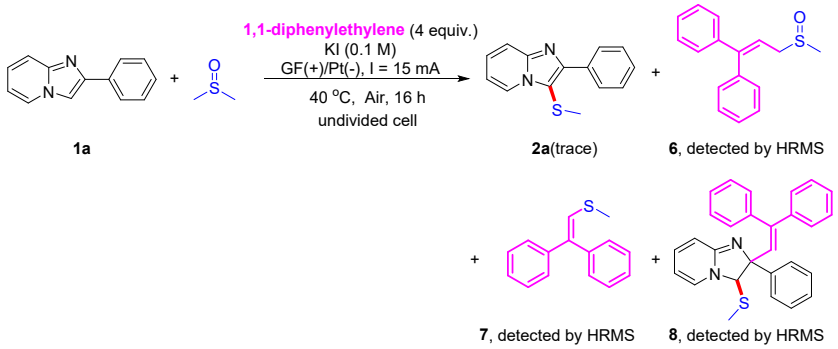


Figure S3. HRMS analysis of the radical-trapping product **5**.

3.1.4 Reaction in the presence of 1,1-diphenylethylene



In an undivided three-necked flask (25 mL), 2-phenylimidazo[1,2-*a*]pyridine (**1a**, 97.1mg, 0.5 mmol), KI (166.0 mg, 1.0 mmol), DMSO (10 mL) and 1,1-diphenylethylene (360.5 mg, 353.1 μL, 2.0 mmol) were continuously added. The flask was equipped with a graphite felt electrode as the anode and a platinum plate electrode (10 mm × 10 mm) as the cathode. The reaction mixture was stirred and electrolyzed at a constant current (15 mA) under air at 40 °C for 16 h. The reaction was obviously suppressed by the addition of 1,1-diphenylethylene, and trapping products **6, 7** and **8** were observed through the HRMS analysis from the reaction solution (Figure S4-S6).

6, HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_{16}H_{17}OS^+$, 257.0095; found 257.0094.

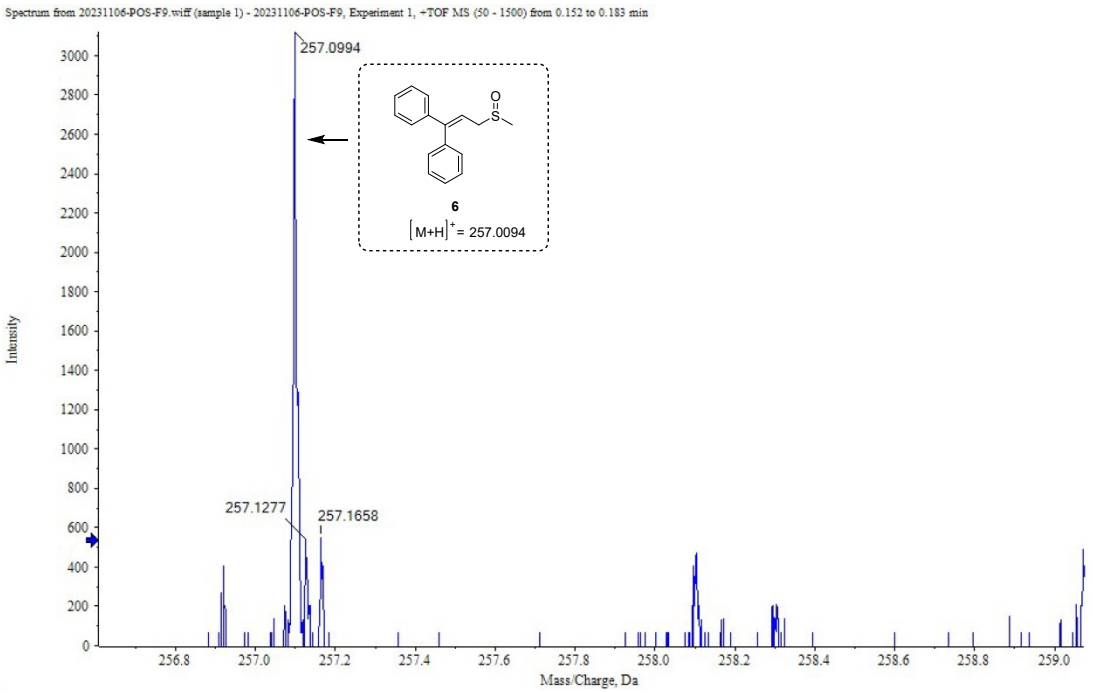


Figure S4. HRMS analysis of the radical-trapping product **6**.

7, HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_{15}H_{15}S^+$, 227.0889; found 227.0876.

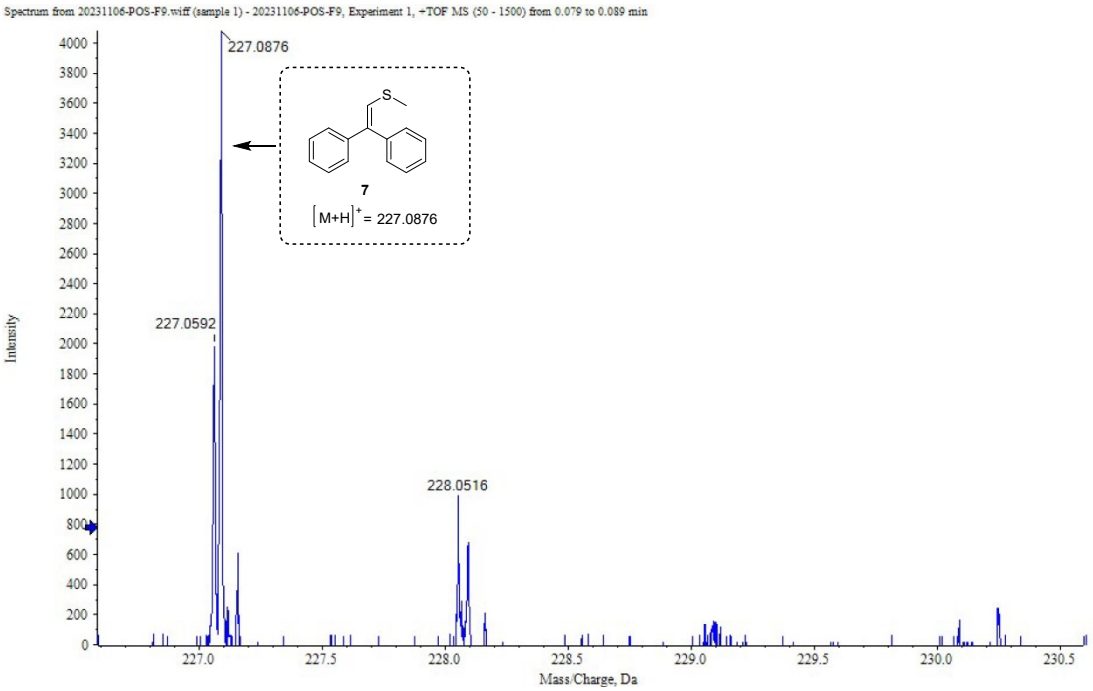


Figure S5. HRMS analysis of the radical-trapping product **7**.

8, HRMS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_{28}H_{25}N_2S^+$, 421.1773; found 421.1772.

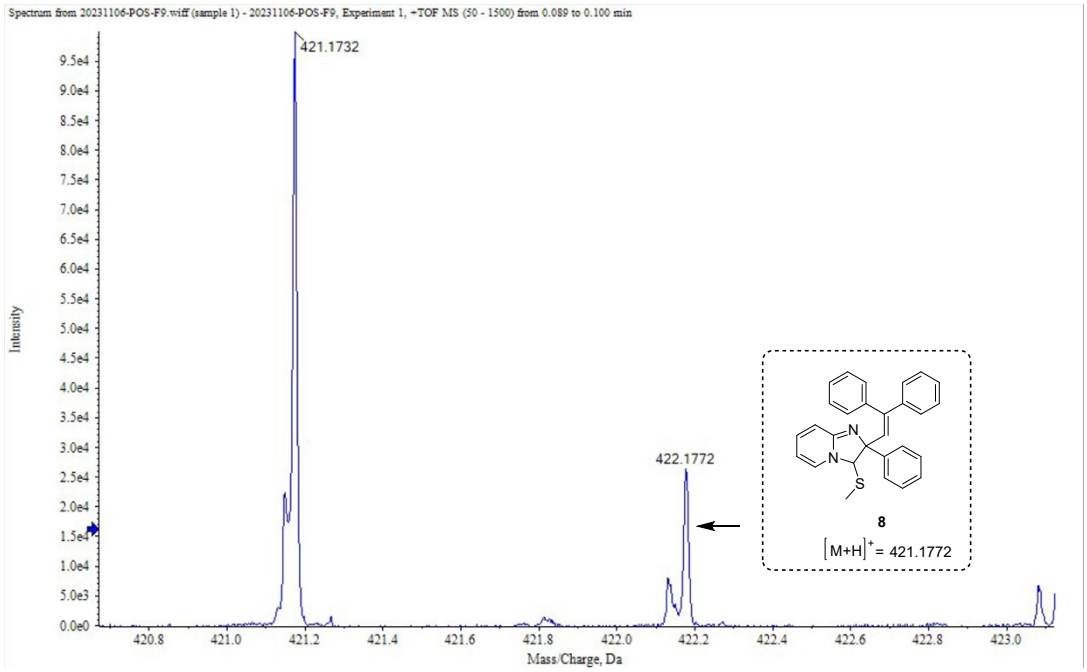


Figure S6. HRMS analysis of the radical-trapping product **8**.

3.2 Cyclic voltammetry analysis

Cyclic voltammetry was performed in a three electrodes cell in a three-necked flask at room temperature. The working electrode was a 3 mm diameter glassy carbon disc electrode, and the counter electrode was a Pt wire. The reference was silver/silver chloride electrode (Ag/AgCl) submerged in saturated aqueous KCl solution. As shown in the Figure S7, DMSO gave an oxidation peak at 1.18 V vs. Ag/AgCl in the range of 0–2.0 V, which indicated that DMSO could be oxidized under the electrochemical conditions (Figure S7).

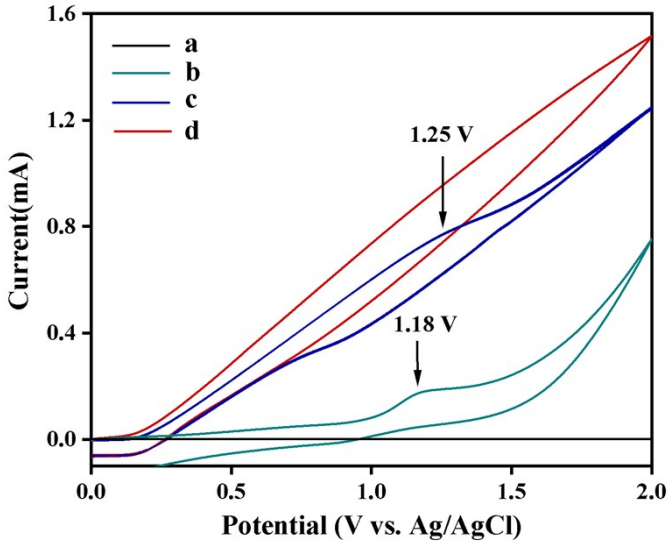
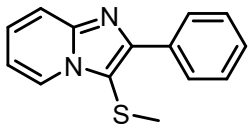


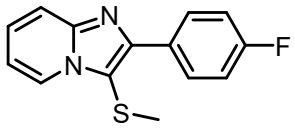
Figure S7 CV scans (scan rate 100 mV s^{-1}) of DMSO (10 mL) at room temperature. (a) Blank experiment (black curve); (b) $^{n}Bu_4NBF_4$ (0.02 M) (green curve); (c) KI (0.1 M) (blue curve); (d)

KI (0.1 M) and 2-phenylimidazo[1,2-*a*]pyridine (**1a**) (0.01 M) (red curve).

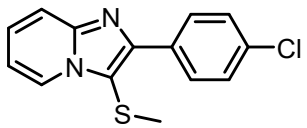
4 Experimental data for the products 2 and 3



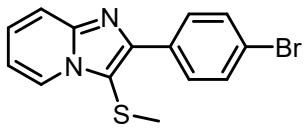
3-(Methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2a**).[1] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Brown oil (206.5 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.45 (d, J = 6.8 Hz, 1H), 8.28 (d, J = 7.3 Hz, 2H), 7.70 (d, J = 9.0 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.29–7.26 (m, 1H), 6.91 (t, J = 6.8 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.43, 146.10, 133.49, 128.42, 128.38, 128.30, 126.29, 124.28, 117.43, 112.97, 111.56, 18.15.



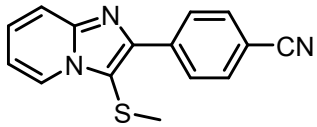
2-(4-Fluorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2b**).[2] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Yellow solid (203.9 mg, 79%), mp 88−90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40 (d, J = 6.8 Hz, 1H), 8.27–8.23 (m, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.25 (t, J = 7.9 Hz, 1H), 7.12 (t, J = 8.6 Hz, 2H), 6.89 (t, J = 6.8 Hz, 1H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.85 (d, J = 248.0 Hz), 147.27, 145.92, 130.04 (d, J = 8.1 Hz), 129.56 (d, J = 3.2 Hz), 126.52, 124.28, 117.26, 115.32 (d, J = 21.5 Hz), 113.09, 111.28, 18.05.



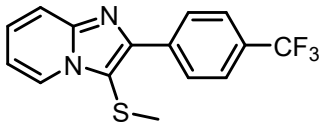
2-(4-Chlorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2c**).[3] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v).Yellow solid (213.7 mg, 78%), mp 102−104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.43 (d, J = 6.9 Hz, 1H), 8.26 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 9.0 Hz, 1H), 7.43 (d, J = 8.3 Hz, 2H), 7.29–7.25 (m, 1H), 6.91 (t, J = 6.8 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.46, 146.27, 134.15, 132.32, 129.44, 128.57, 126.21, 124.25, 117.57, 112.91, 111.53, 18.10.



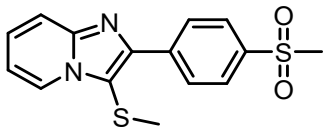
2-(4-Bromophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2d**).[1] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Yellow solid (256.0 mg, 80%), mp 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (d, J = 6.8 Hz, 1H), 8.22 (d, J = 8.2 Hz, 2H), 7.67 (d, J = 9.0 Hz, 1H), 7.61 (d, J = 8.2 Hz, 2H), 7.33–7.29 (m, 1H), 6.96 (t, J = 6.8 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.57, 146.33, 132.78, 131.55, 129.75, 126.24, 124.28, 122.54, 117.65, 112.94, 111.59, 18.14.



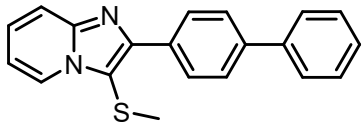
4-(3-(Methylthio)imidazo[1,2-*a*]pyridin-2-yl)benzonitrile (**2e**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Yellow solid (206.8 mg, 78%), mp 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.53–8.48 (m, 3H), 7.80–7.76 (m, 2H), 7.71 (dt, J = 8.8, 1.2 Hz, 1H), 7.39–7.35 (m, 1H), 7.02 (td, J = 6.8, 1.2 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 146.47, 146.35, 138.29, 132.22, 128.54, 126.76, 124.37, 119.08, 117.91, 113.40, 112.98, 111.51, 18.20.



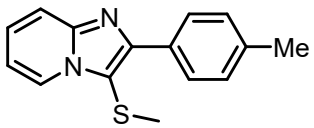
3-(Methylthio)-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-*a*]pyridine (**2f**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (219.6 mg, 72%), mp 102−104 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.50–8.44 (m, 3H), 7.73 (d, J = 8.0 Hz, 2H), 7.68 (dt, J = 9.2, 1.2 Hz, 1H), 7.34–7.30 (m, 1H), 6.96 (td, J = 6.8, 1.2 Hz, 1H), 2.26 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.09, 146.43, 137.38, 129.89 (q, J = 32.4 Hz), 128.34, 126.40, 125.29 (q, J = 3.9 Hz), 124.32, 124.31 (q, J = 272.1 Hz), 117.81, 113.11, 112.40, 18.14. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}F_3N_2S^+$ 309.0668; Found 309.0663.



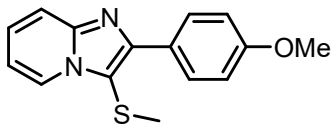
2-(4-(Methylsulfonyl)phenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2g**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (1:1, v/v). Yellow solid (235.4 mg, 74%), mp 129−131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.57 (d, J = 8.1 Hz, 2H), 8.51 (d, J = 6.9 Hz, 1H), 8.05 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 9.0 Hz, 1H), 7.38–7.34 (m, 1H), 7.01 (t, J = 6.8 Hz, 1H), 3.12 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 145.72, 145.19, 139.82, 138.19, 129.02, 128.01, 127.55, 124.74, 117.23, 114.19, 113.79, 44.60, 18.35. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}N_2O_2S_2^+$ 318.0497; Found 319.0570.



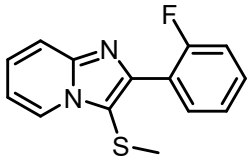
2-([1,1'-Biphenyl]-4-yl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2h**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow oil (240.2 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.82 (s, 1H), 8.52–8.49 (m, 2H), 8.00–7.96 (m, 2H), 7.90–7.88 (m, 1H), 7.74 (dt, J = 9.2, 1.2 Hz, 1H), 7.54–7.49 (m, 2H), 7.35–7.31 (m, 1H), 6.96 (td, J = 6.8, 1.2 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 145.79, 143.82, 138.38, 138.24, 130.24, 126.29, 126.08, 124.88, 124.57, 124.56, 123.56, 121.74, 115.07, 110.29, 108.98, 15.68. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{17}N_2S^+$ 317.1107; Found 317.1104.



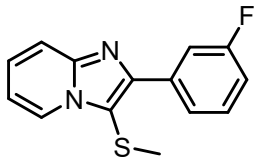
3-(Methylthio)-2-(p-tolyl)imidazo[1,2-*a*]pyridine (2i).[1] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (208.4 mg, 82%), mp 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.46 (dt, J = 6.8, 1.2 Hz, 1H), 8.23–8.21 (m, 2H), 7.67 (dt, J = 9.2, 1.2 Hz, 1H), 7.32–7.25 (m, 3H), 6.90 (td, J = 6.8, 1.2 Hz, 1H), 2.42 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.92, 146.29, 138.14, 131.00, 129.14, 128.15, 125.83, 124.20, 117.50, 112.62, 111.00, 21.39, 18.13.



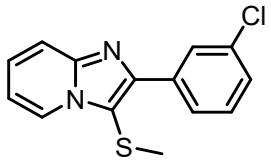
2-(4-Methoxyphenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2j**).[2] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Yellow oil (183.7 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (d, J = 6.8 Hz, 1H), 8.26 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8.9 Hz, 1H), 7.32–7.28 (m, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.94 (t, J = 6.8 Hz, 1H), 3.87 (s, 3H), 2.25 (d, J = 1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.86, 148.19, 145.94, 129.59, 126.26, 125.96, 124.23, 117.15, 113.87, 112.87, 110.61, 55.31, 18.11.



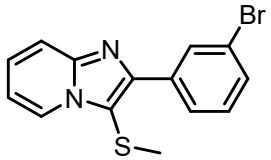
2-(2-Fluorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2k**).[3] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (3:1, v/v). Yellow solid (203.9 mg, 79%), mp 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.48 (d, J = 6.9 Hz, 1H), 7.76–7.70 (m, 2H), 7.46–7.41 (m, 1H), 7.38–7.34 (m, 1H), 7.30–7.26 (m, 1H), 7.25–7.20 (m, 1H), 7.01 (td, J = 6.8, 1.1 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 160.24 (d, J = 249.4 Hz), 146.46, 145.39, 132.18 (d, J = 3.0 Hz), 130.31 (d, J = 8.3 Hz), 126.14, 124.32, 124.03 (d, J = 3.6 Hz), 121.79 (d, J = 14.2 Hz), 117.86, 115.97 (d, J = 22.3 Hz), 113.96, 113.12, 17.89 (d, J = 2.5 Hz).



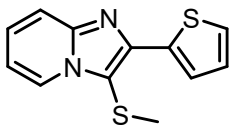
2-(3-Fluorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2l**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (10:1, v/v). Yellow solid (188.4 mg, 73%), mp 96−98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.50 (dt, J = 6.8, 1.2 Hz, 1H), 8.16–8.08 (m, 2H), 7.68 (d, J = 9.0 Hz, 1H), 7.48–7.43 (m, 1H), 7.35–7.31 (m, 1H), 7.12–7.07 (m, 1H), 6.97 (td, J = 6.8, 1.2 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.94 (d, J = 244.3 Hz), 147.35, 146.29, 136.05 (d, J = 8.2 Hz), 129.86 (d, J = 8.2 Hz), 126.24, 124.29, 123.81 (d, J = 2.8 Hz), 117.74, 115.08 (d, J = 21.2 Hz), 114.99 (d, J = 23.2 Hz), 112.97, 111.88, 18.15. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}FN_2S^+$ 259.0700; Found 259.0699.



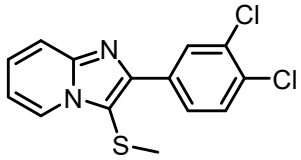
2-(3-Chlorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2m**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (208.3 mg, 76%), mp 100−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.48 (dt, J = 6.8, 1.2 Hz, 1H), 8.34 (t, J = 1.9 Hz, 1H), 8.24 (dt, J = 7.6, 1.6 Hz, 1H), 7.67 (dt, J = 8.8, 1.2 Hz, 1H), 7.42 (t, J = 7.8 Hz, 1H), 7.38–7.29 (m, 2H), 6.95 (td, J = 6.8, 1.2 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.22, 146.32, 135.68, 134.39, 129.64, 128.24, 128.17, 126.26, 126.25, 124.30, 117.73, 112.99, 111.92, 18.17. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}ClN_2S^+$ 275.0404; Found 275.0401.



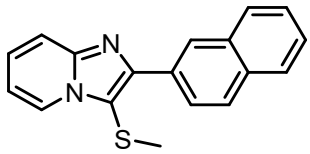
2-(3-Bromophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2n**).[5] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (222.6 mg, 70%), mp 103−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.51–8.49 (m, 2H), 8.30–8.27 (m, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.53 (dt, J = 7.6, 1.6 Hz, 1H), 7.38–7.32 (m, 2H), 6.98 (td, J = 6.8, 1.1 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 147.03, 146.27, 135.83, 131.21, 131.09, 129.92, 126.71, 126.37, 124.32, 122.62, 117.71, 113.07, 111.99, 18.19.



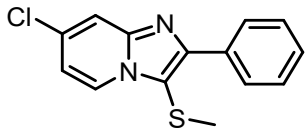
3-(Methylthio)-2-(thiophen-2-yl)imidazo[1,2-*a*]pyridine (**2o**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow oil (182.1 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.43 (dt, J = 6.8, 1.2 Hz, 1H), 8.07 (dd, J = 3.6, 1.2 Hz, 1H), 7.64 (d, J = 9.1 Hz, 1H), 7.40 (dd, J = 5.2, 1.2 Hz, 1H), 7.30–7.26 (m, 1H), 7.16 (dd, J = 5.2, 4.0 Hz, 1H), 6.91 (td, J = 6.8, 1.2 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 146.39, 144.61, 136.71, 127.66, 126.44, 126.24, 126.20, 124.15, 117.31, 112.82, 110.26, 17.84.



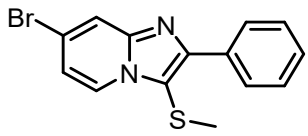
2-(3,4-Dichlorophenyl)-3-(methylthio)imidazo[1,2-*a*]pyridine (**2p**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (212.5 mg, 69%), mp 85−87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.48–8.46 (m, 2H), 8.22 (dd, J = 8.4, 2.0 Hz, 1H), 7.66 (dt, J = 8.8, 1.2 Hz, 1H), 7.54 (d, J = 8.5 Hz, 1H), 7.35–7.31 (m, 1H), 6.97 (td, J = 6.8, 1.2 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 143.79, 143.64, 131.39, 130.04, 129.61, 127.79, 127.30, 124.70, 123.92, 121.75, 115.19, 110.58, 109.46, 15.60. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}Cl_2N_2S^+$ 309.0015; Found 309.0008.



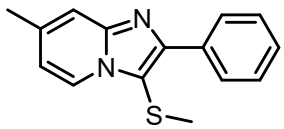
3-(Methylthio)-2-(naphthalen-2-yl)imidazo[1,2-*a*]pyridine (**2q**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow oil (220.5 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.82 (s, 1H), 8.52–8.49 (m, 2H), 8.00–7.96 (m, 2H), 7.90– 7.88 (m, 1H), 7.74 (dt, J = 9.2, 1.2 Hz, 1H), 7.54–7.49 (m, 2H), 7.35–7.31 (m, 1H), 6.96 (td, J = 6.8, 1.2 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.47, 146.32, 133.46, 133.25, 131.12, 128.67, 127.94, 127.66, 127.62, 126.33, 126.27, 126.13, 125.94, 124.32, 117.53, 112.93, 111.90, 18.26.



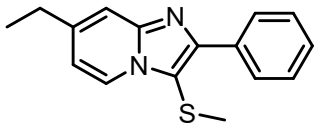
7-Chloro-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2r**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (197.3 mg, 72%), mp 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.39 (d, J = 7.2 Hz, 1H), 8.29–8.27 (m, 2H), 7.67 (d, J = 2.0 Hz, 1H), 7.52–7.48 (m, 2H), 7.43–7.39 (m, 1H), 6.91 (dd, J = 7.2, 2.0 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 149.56, 145.97, 133.40, 132.53, 128.54, 128.47, 128.19, 124.61, 116.46, 114.32, 111.89, 18.24. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}ClN_2S^+$ 275.0405; Found 275.0399.



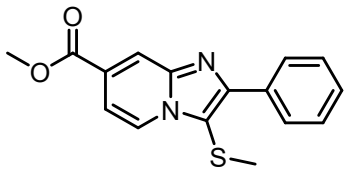
7-Bromo-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2s**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (10:1, v/v). Yellow solid (232.1 mg, 73%), mp 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.37 (d, J = 7.2 Hz, 1H), 8.30–8.27 (m, 2H), 7.89 (d, J = 1.8 Hz, 1H), 7.53–7.49 (m, 2H), 7.45–7.41 (m, 1H), 7.08 (dd, J = 7.2, 2.0 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 149.10, 146.10, 133.05, 128.69, 128.53, 128.25, 124.65, 120.28, 119.73, 116.88, 112.14, 18.22. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{12}BrN_2S^+$ 318.9900; Found 318.9903.



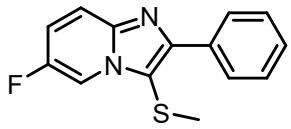
7-Methyl-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2t**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (203.3 mg, 80%), mp 116−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.38 (d, J = 7.0 Hz, 1H), 8.31–8.29 (m, 2H), 7.52–7.46 (m, 3H), 7.42–7.38 (m, 1H), 6.80 (dd, J = 7.2, 2.0 Hz, 1H), 2.47 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.48, 146.62, 137.28, 133.81, 128.37, 128.22, 128.20, 123.46, 116.08, 115.45, 110.70, 21.39, 18.32.



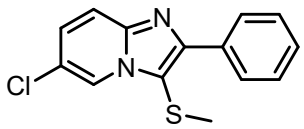
7-Ethyl-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2u**).[3] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (10:1, v/v). Yellow oil (211.8 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.38 (d, J = 7.0 Hz, 1H), 8.31–8.29 (m, 2H), 7.51–7.47 (m, 3H), 7.41–7.37 (m, 1H), 6.81 (dd, J = 6.8, 1.6 Hz, 1H), 2.75 (q, J = 7.5 Hz, 2H), 2.26 (s, 3H), 1.32 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.63, 146.81, 143.28, 133.97, 128.35, 128.19, 128.14, 123.61, 114.66, 114.40, 110.66, 28.42, 18.33, 14.44.



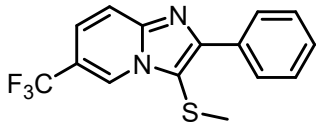
Methyl 3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine-7-carboxylate (**2v**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (199.7 mg, 67%), mp 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.55 (dd, J = 7.2, 1.2 Hz, 1H), 8.44 (t, J = 1.2 Hz, 1H), 8.34–8.31 (m, 2H), 7.58 (dd, J = 7.2, 1.6 Hz, 1H), 7.55–7.51 (m, 2H), 7.47–7.43 (m, 1H), 4.01 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 165.51, 144.98, 132.94, 128.86, 128.58, 128.34, 127.58, 124.00, 119.87, 113.76, 112.27, 52.73, 18.08. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{15}N_2O_2S^+$ 299.0849; Found 299.0831.



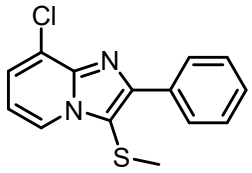
6-Fluoro-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2w**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (10:1, v/v). Yellow solid (191.0 mg, 74%), mp 135−137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.42–8.40 (m, 1H), 8.30–8.27 (m, 2H), 7.66–7.62 (m, 1H), 7.52–7.47 (m, 2H), 7.42–7.38 (m, 1H), 7.23–7.18 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 153.79 (d, J = 237.6 Hz), 150.02 (d, J = 2.4 Hz), 143.85, 133.58, 128.45, 128.44, 128.10, 118.15 (d, J = 8.7 Hz), 117.78 (d, J = 25.6 Hz), 112.91, 111.11 (d, J = 41.5 Hz), 18.03.



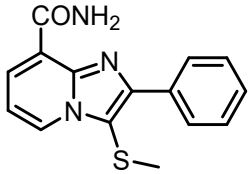
6-Chloro-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2x**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (194.6 mg, 71%), mp 164−166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.54 (dd, J = 2.0, 0.8 Hz, 1H), 8.31–8.29 (m, 2H), 7.64 (dd, J = 9.6, 0.8 Hz, 1H), 7.53–7.49 (m, 2H), 7.44–7.40 (m, 1H), 7.28 (dd, J = 9.2, 2.0 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 149.58, 144.60, 133.33, 128.58, 128.50, 128.18, 127.37, 122.31, 121.32, 118.01, 112.24, 18.23.



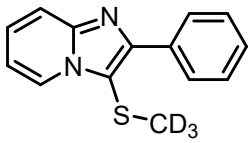
3-(Methylthio)-2-phenyl-6-(trifluoromethyl)imidazo[1,2-*a*]pyridine (**2y**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (215.6 mg, 70%), mp 140−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.86 (s, 1H), 8.35–8.32 (m, 2H), 7.79 (d, J = 9.3 Hz, 1H), 7.53 (t, J = 7.4 Hz, 2H), 7.48–7.43 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 150.45, 146.05, 133.03, 128.86, 128.56, 123.63 (q, J = 271.2 Hz), 123.32 (q, J = 5.5 Hz), 121.89 (q, J = 2.9 Hz), 118.30, 117.26 (q, J = 34.3 Hz), 113.35, 18.34.



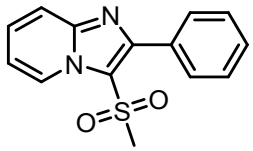
8-Chloro-3-(methylthio)-2-phenylimidazo[1,2-*a*]pyridine (**2z**).[4] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow solid (205.5 mg, 75%), mp 110−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.40 (dd, J = 6.8, 0.8 Hz, 1H), 8.34–8.32 (m, 2H), 7.52–7.48 (m, 2H), 7.41 (t, J = 7.3 Hz, 1H), 7.35 (dd, J = 7.2, 1.2 Hz, 1H), 6.86 (t, J = 7.1 Hz, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 149.48, 143.55, 133.39, 128.80, 128.52, 128.39, 124.85, 123.38, 123.07, 113.40, 112.30, 18.22.



3-(Methylthio)-2-phenylimidazo[1,2-*a*]pyridine-8-carboxamide (**2aa**). The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (1:1, v/v). Yellow solid (164.2 mg, 58%), mp 182−184 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.16 (s, 1H), 8.68 (d, J = 6.7 Hz, 1H), 8.37–8.33 (m, 3H), 7.56–7.51 (m, 2H), 7.48–7.44 (m, 1H), 7.15 (t, J = 7.0 Hz, 1H), 6.11 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 164.96, 148.12, 144.35, 133.00, 129.89, 128.82, 128.54, 128.30, 127.28, 120.75, 112.62, 18.29. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}N_3OS^+$ 284.0852; Found 284.0856.



3-((Methyl-d_3)thio)-2-phenylimidazo[1,2-*a*]pyridine (2a-d_3).[2] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (5:1, v/v). Yellow oil (199.3 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.51 (d, J = 6.8 Hz, 1H), 8.33–8.30 (m, 2H), 7.71 (d, J = 9.0 Hz, 1H), 7.53–7.49 (m, 2H), 7.44–7.39 (m, 1H), 7.35–7.31 (m, 1H), 6.99–6.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.69, 146.25, 133.69, 128.42, 128.34, 128.28, 126.07, 124.29, 117.61, 112.83, 112.67.



3-(Methylsulfonyl)-2-phenylimidazo[1,2-*a*]pyridine (3).[6] The product was purified by silica gel column chromatography with petroleum ether/ethyl acetate (1:1, v/v). Yellow solid (231.3 mg, 85 %), mp 185−187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.08 (d, J = 6.8 Hz, 1H), 7.83 (d, J = 6.8 Hz, 2H), 7.79 (d, J = 9.0 Hz, 1H), 7.52–7.43 (m, 4H), 7.02 (t, J = 6.8 Hz, 1H), 3.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 148.86, 147.57, 132.24, 129.29, 129.24, 128.72, 127.72, 126.90, 118.33, 116.09, 113.79, 37.96.

5 References

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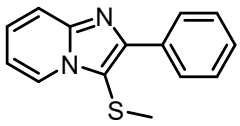
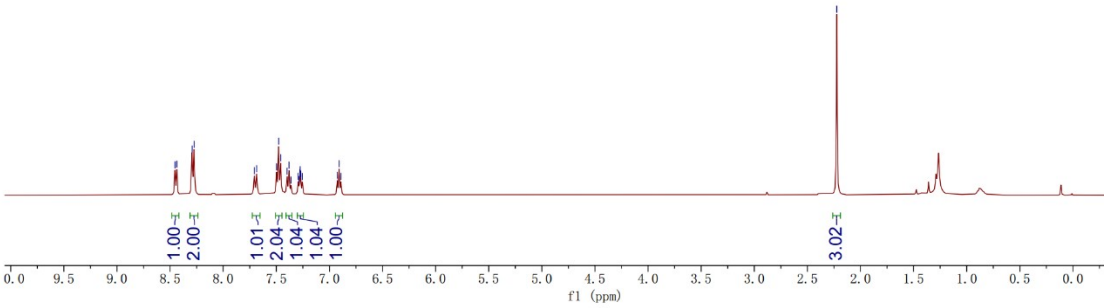
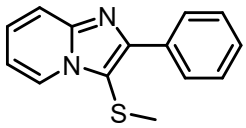
6 ^{1}H and ^{13}C NMR spectra of the products 2 and 3

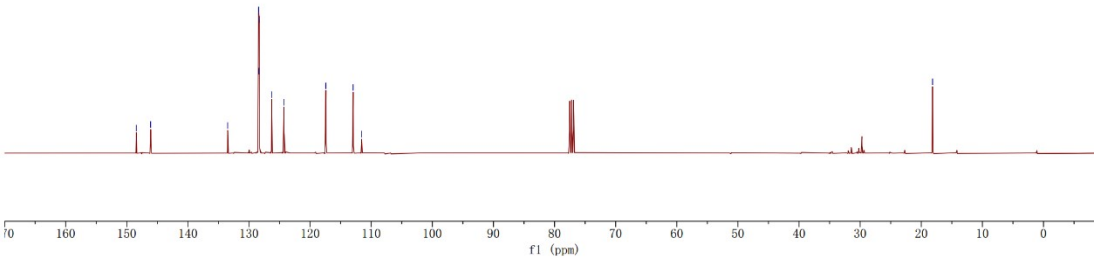


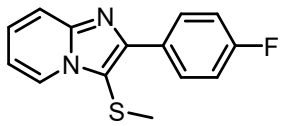
2a (^{1}H NMR) (400 MHz, $CDCl_3$)





2a (^{13}C NMR) (100 MHz, $CDCl_3$)





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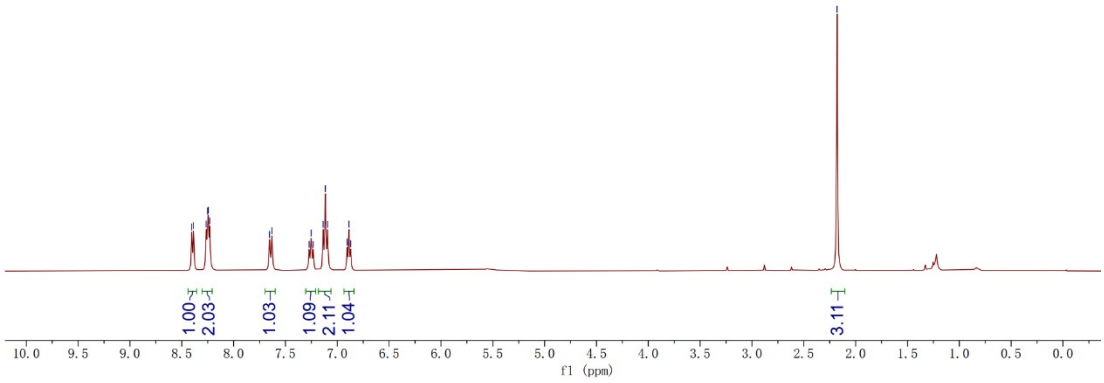

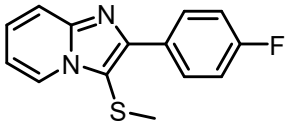

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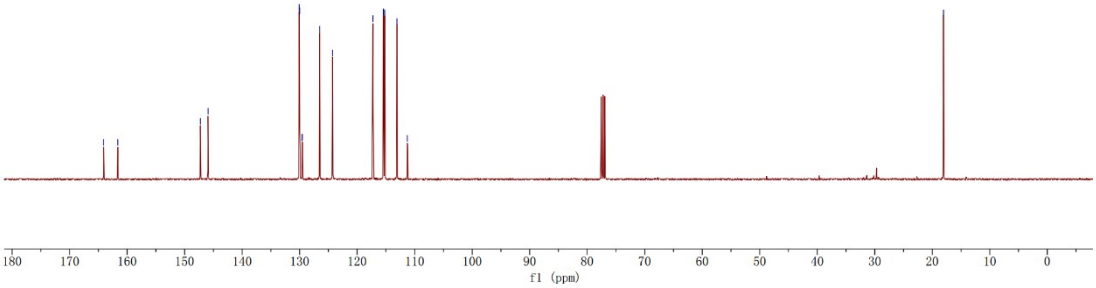

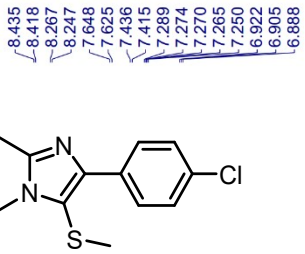

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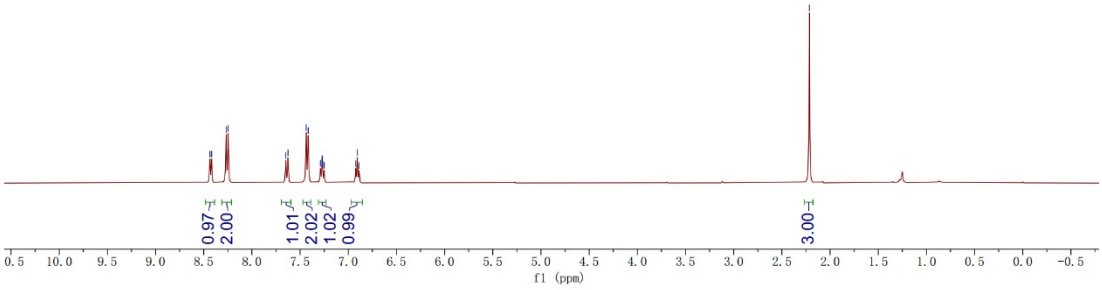

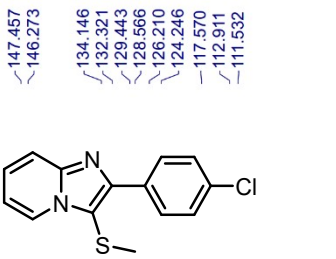

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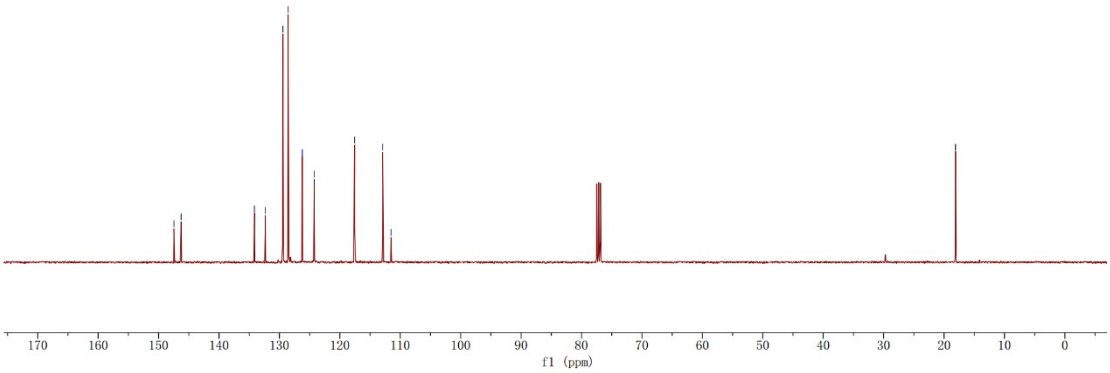

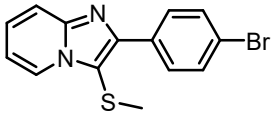

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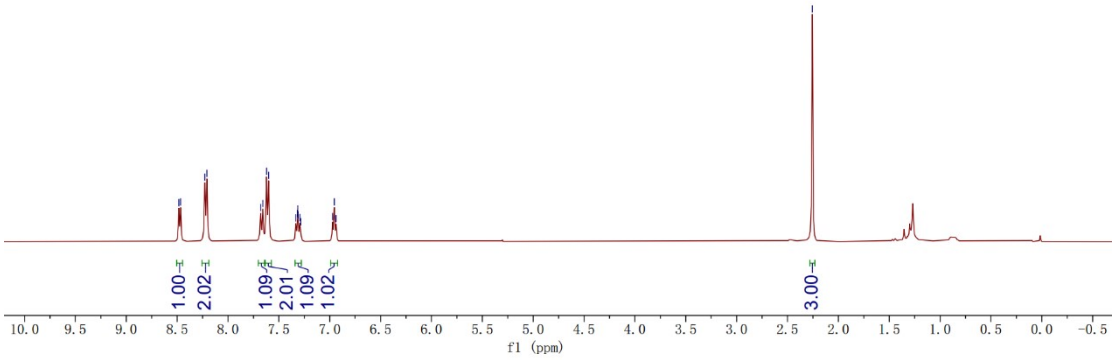

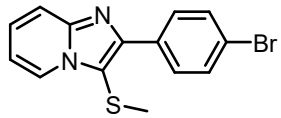

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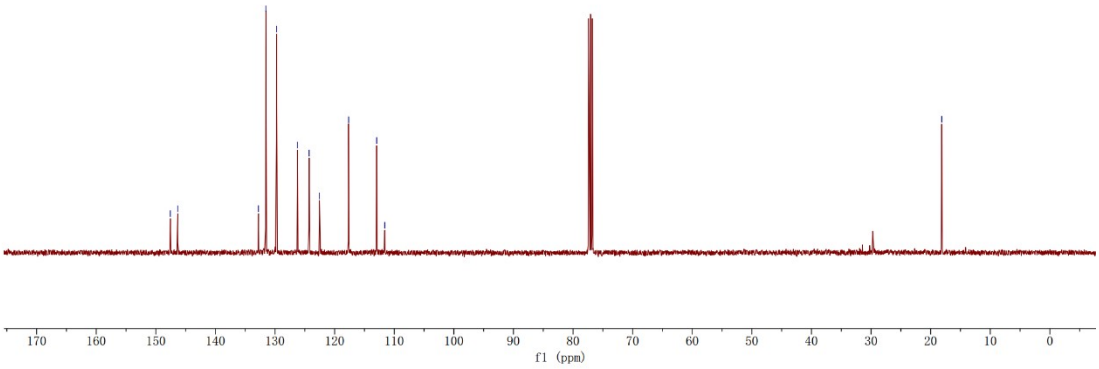

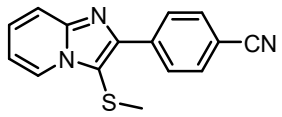

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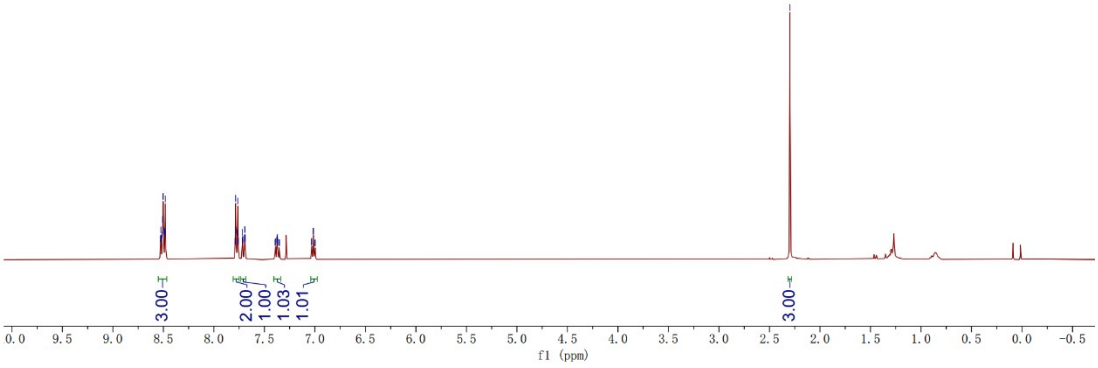

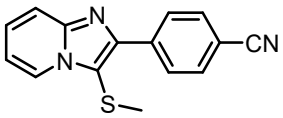

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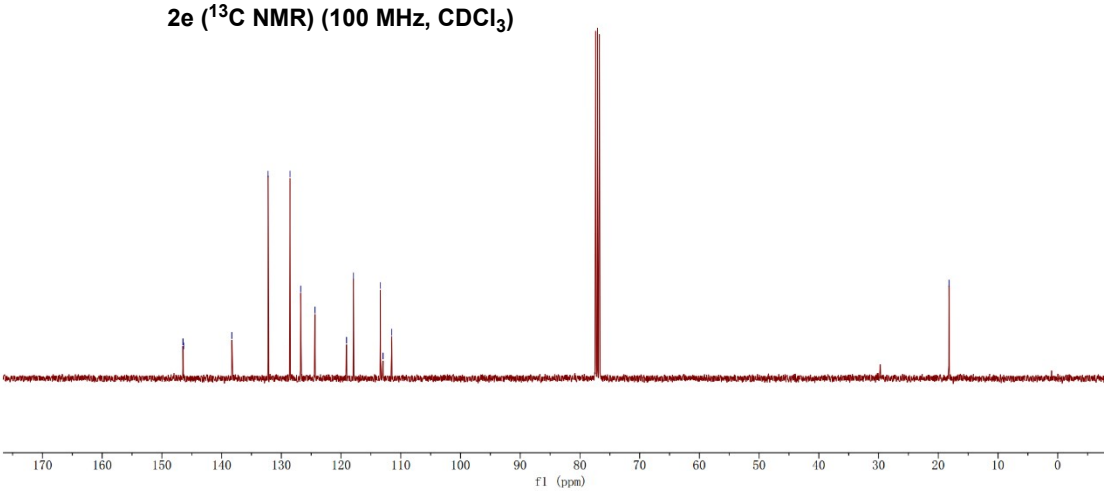

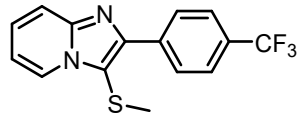

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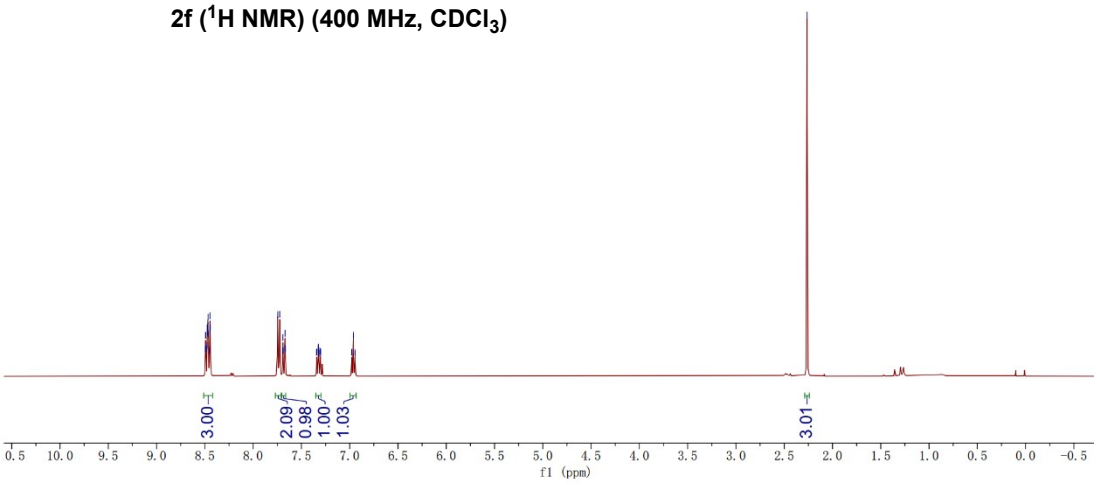

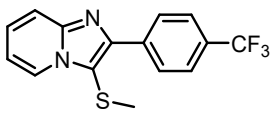

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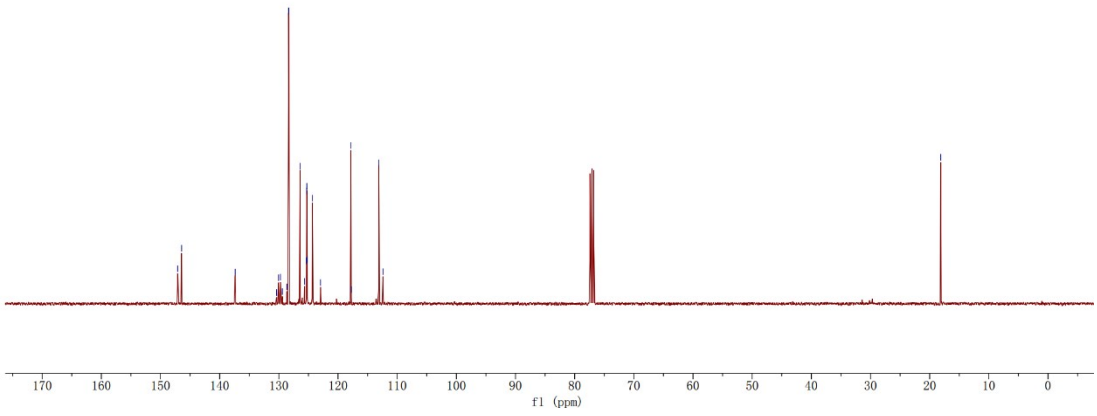

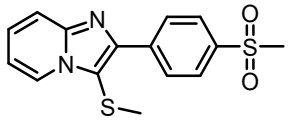

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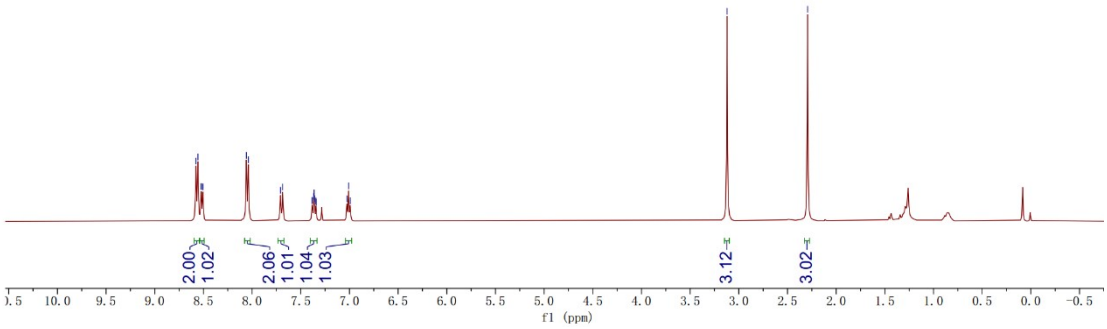

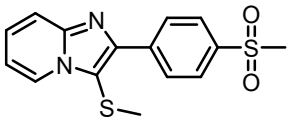

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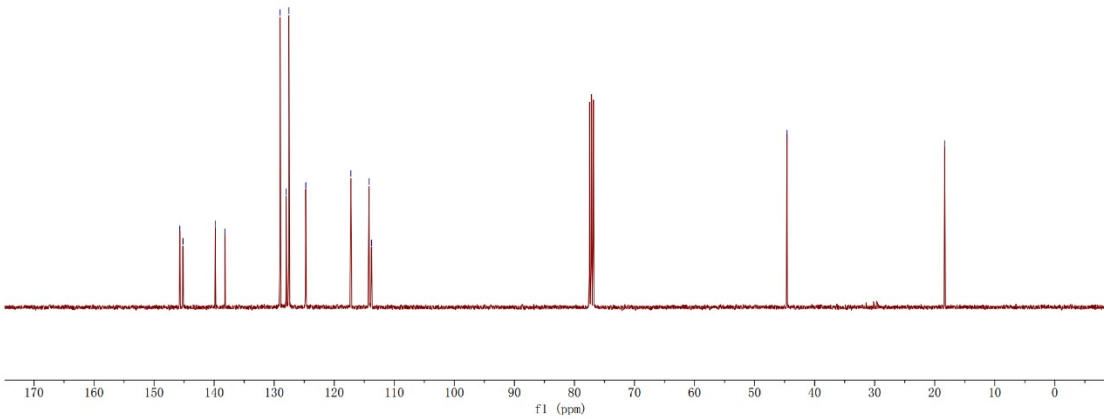

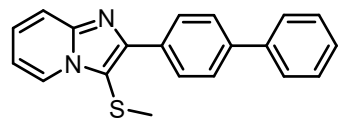

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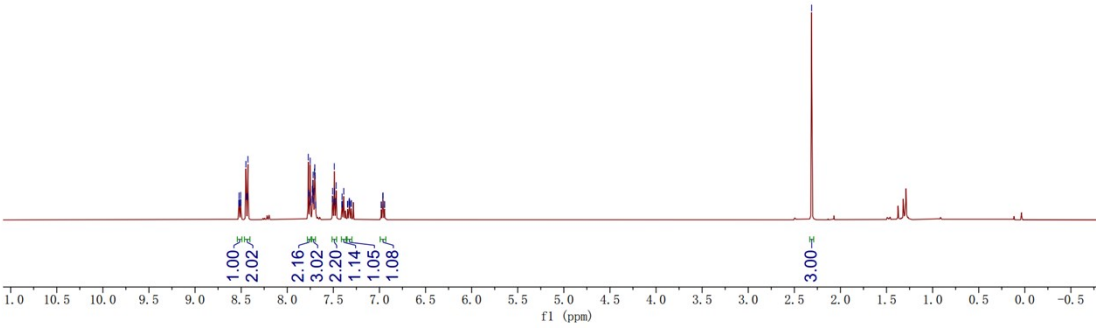

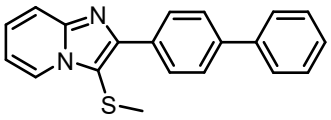

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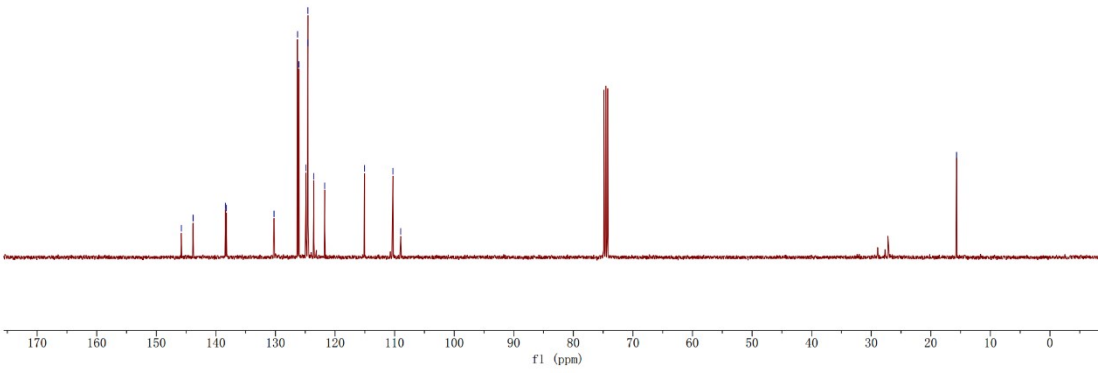

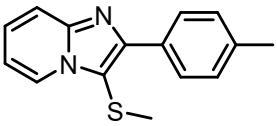

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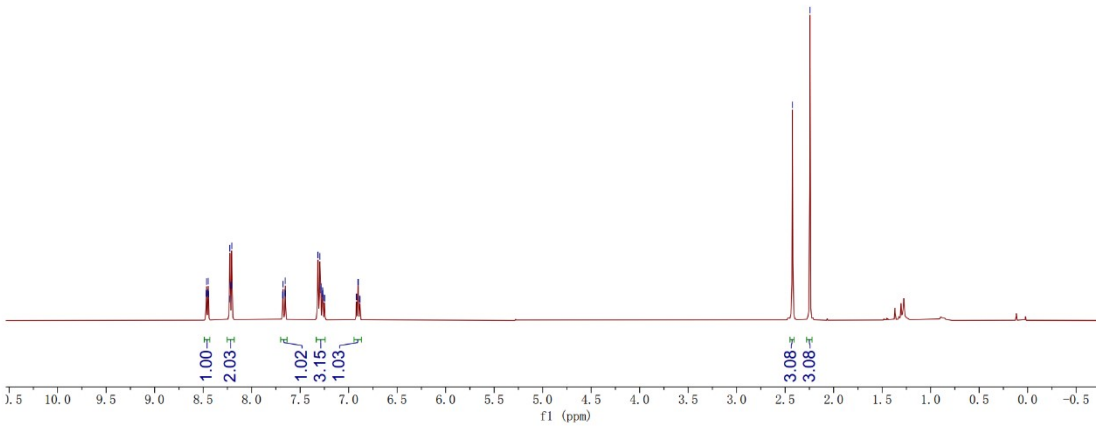

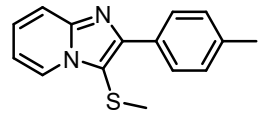

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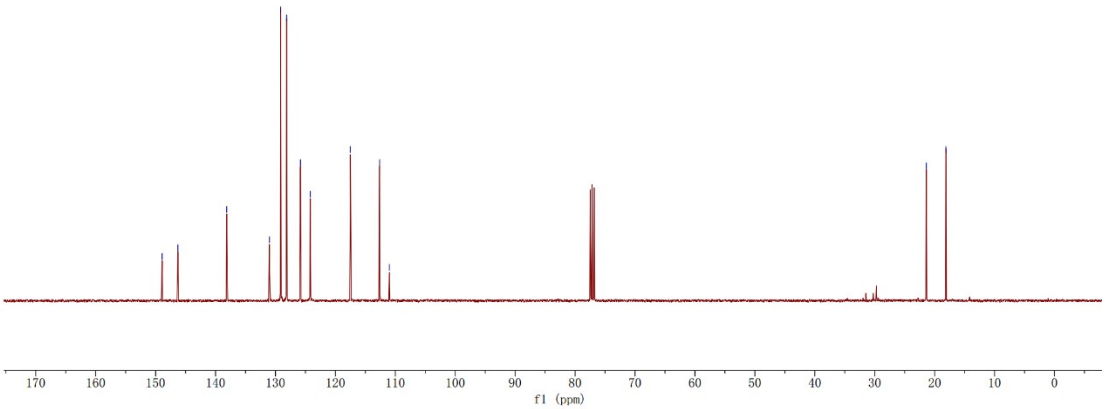

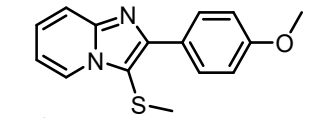

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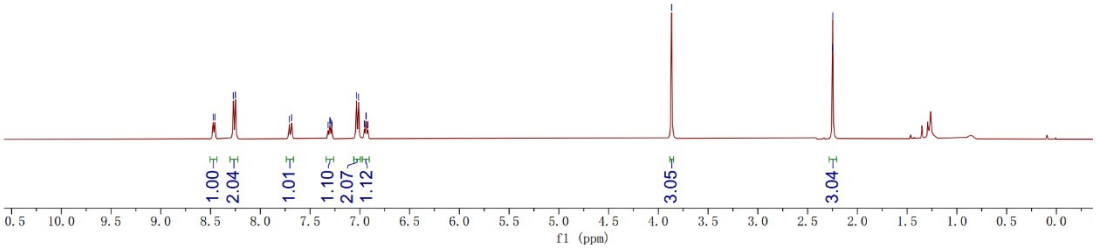

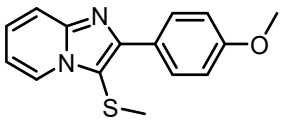

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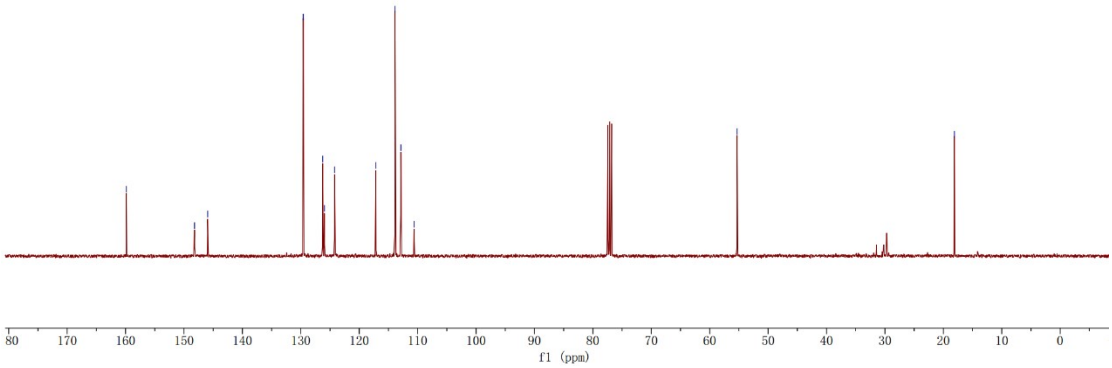

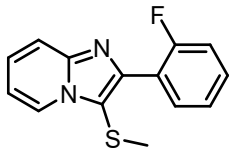

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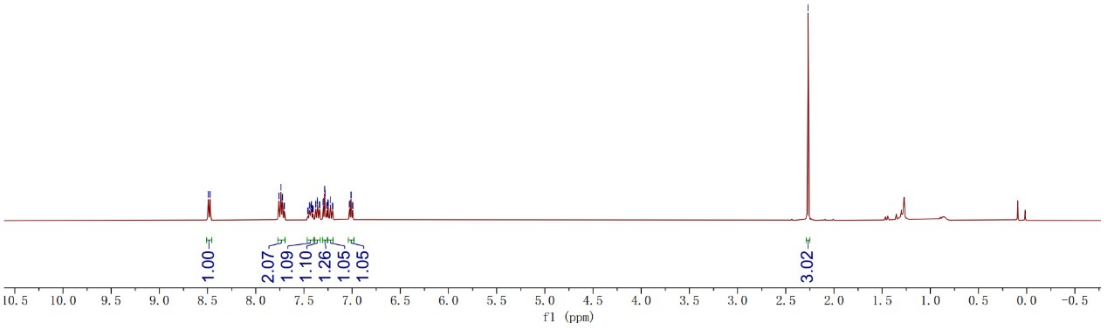

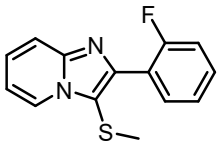

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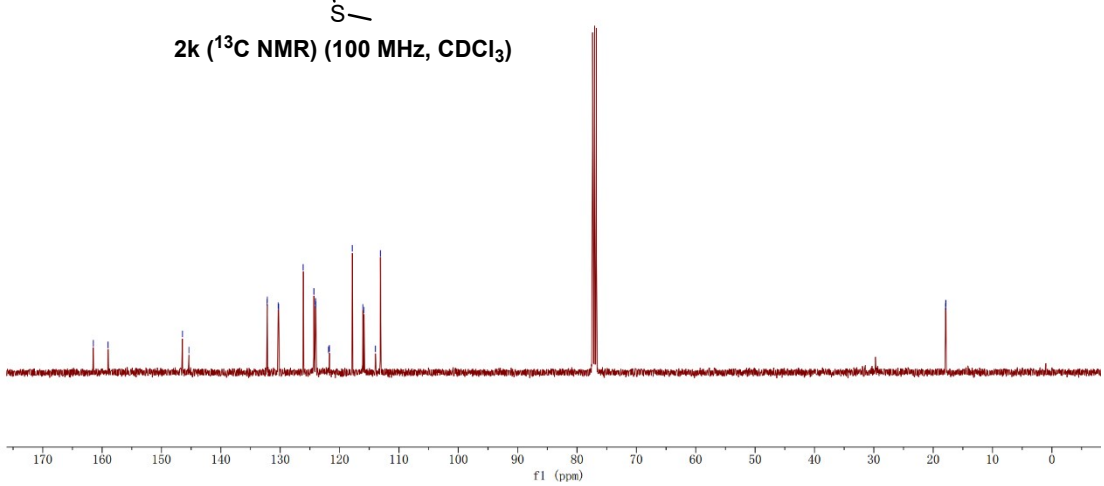

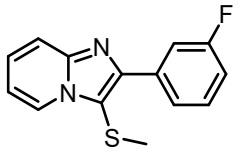

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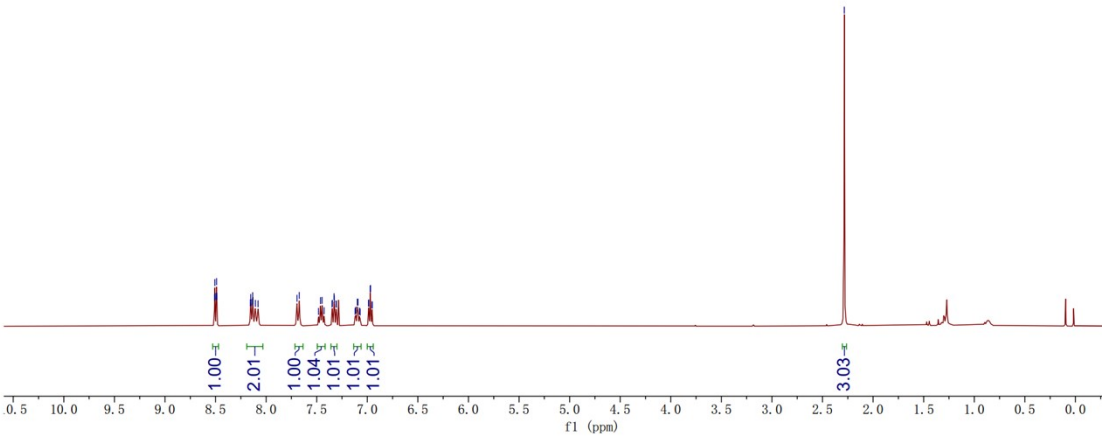
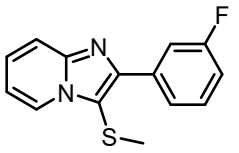
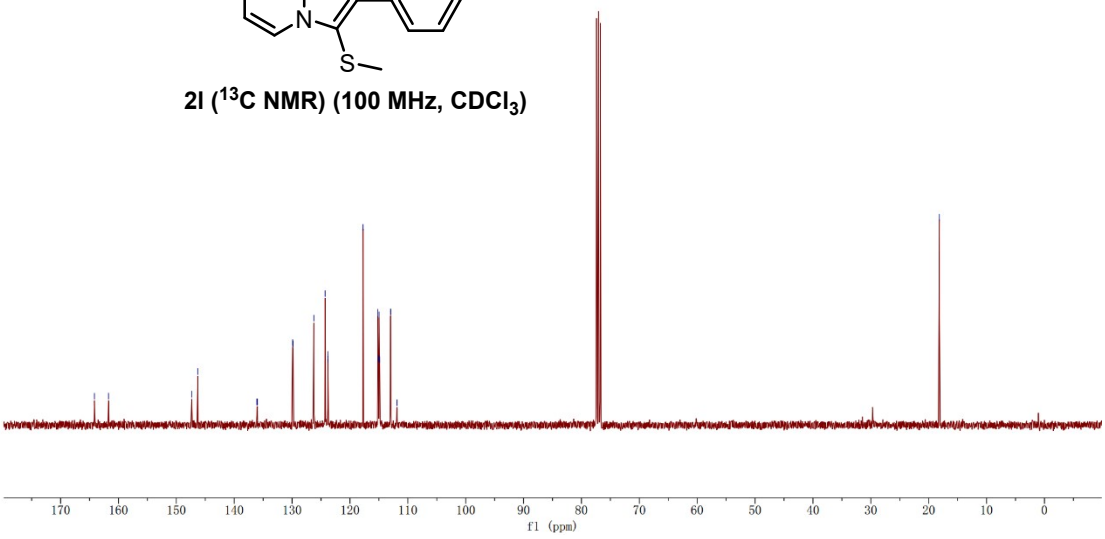
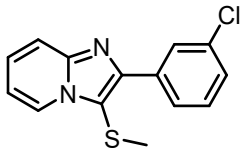




2l (^{13}C NMR) (100 MHz, $CDCl_3$)





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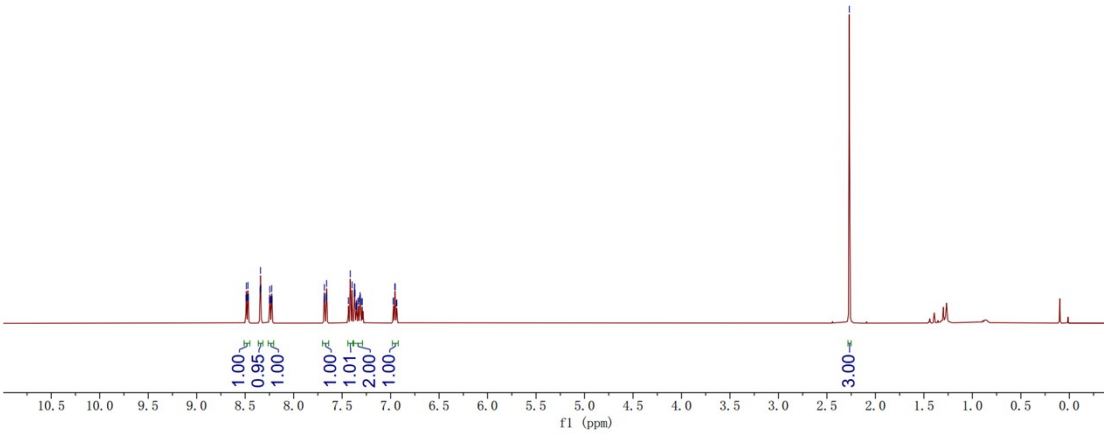
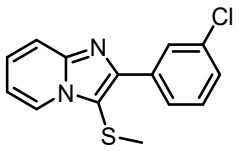
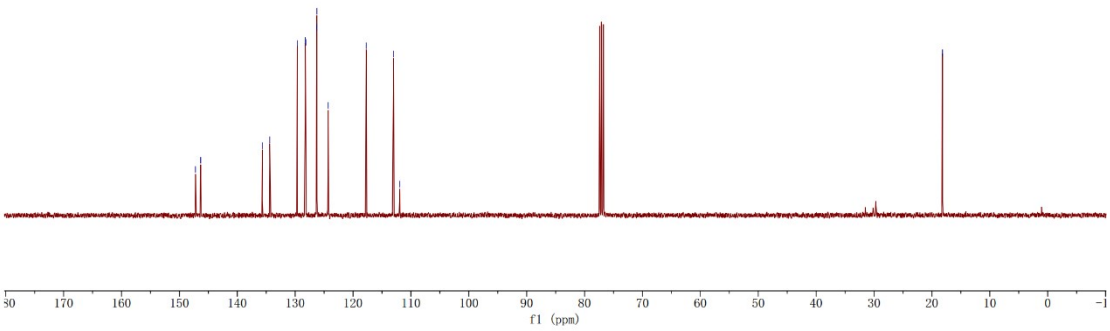
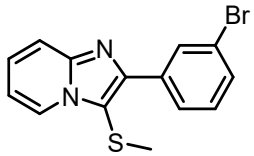


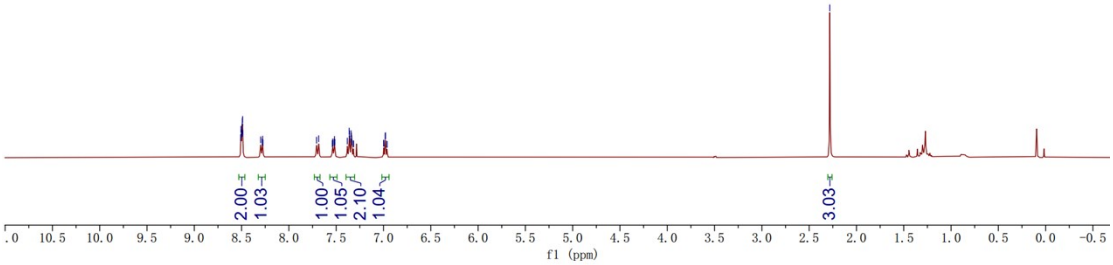


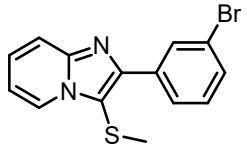
2m (^{13}C NMR) (100 MHz, $CDCl_3$)



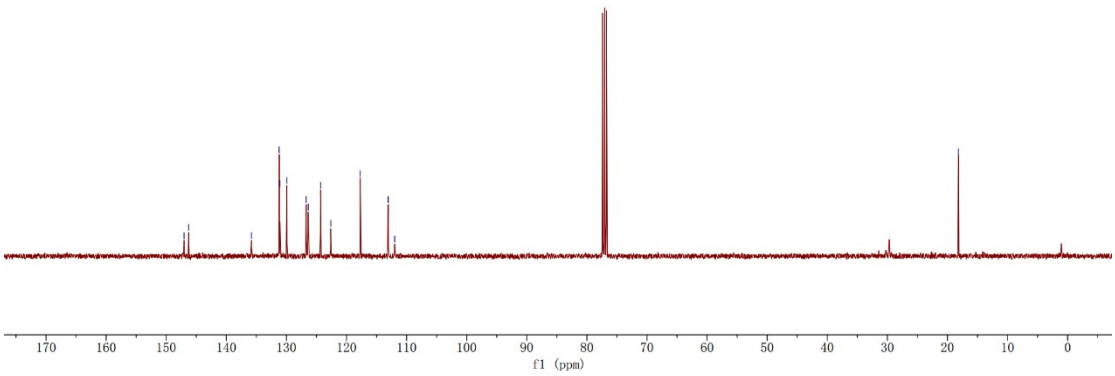


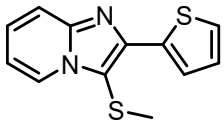
2n (^{1}H NMR) (400 MHz, $CDCl_3$)



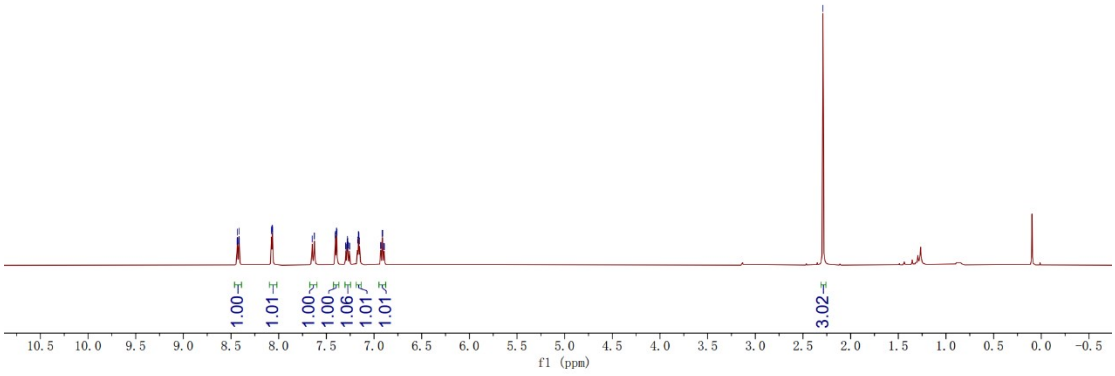


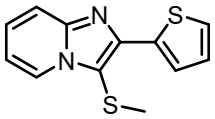
2n (^{13}C NMR) (100 MHz, $CDCl_3$)



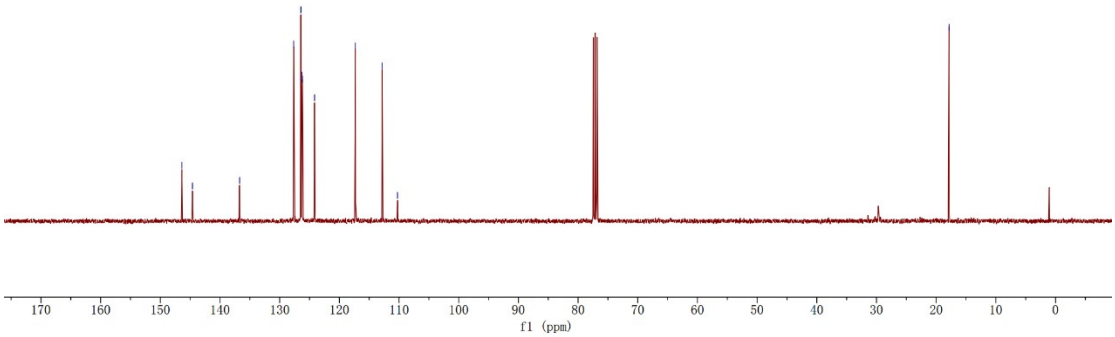


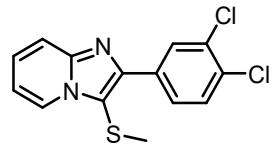
2o (^{1}H NMR) (400 MHz, $CDCl_3$)



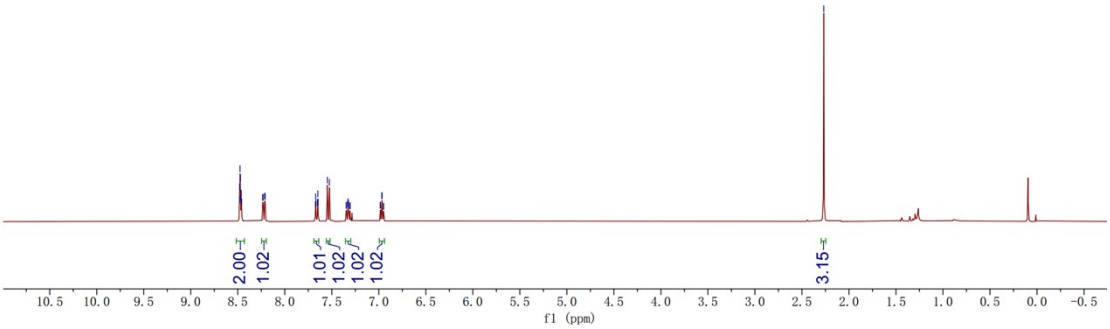


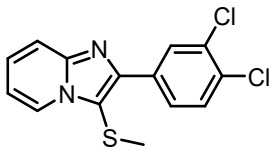
2o (^{13}C NMR) (100 MHz, $CDCl_3$)



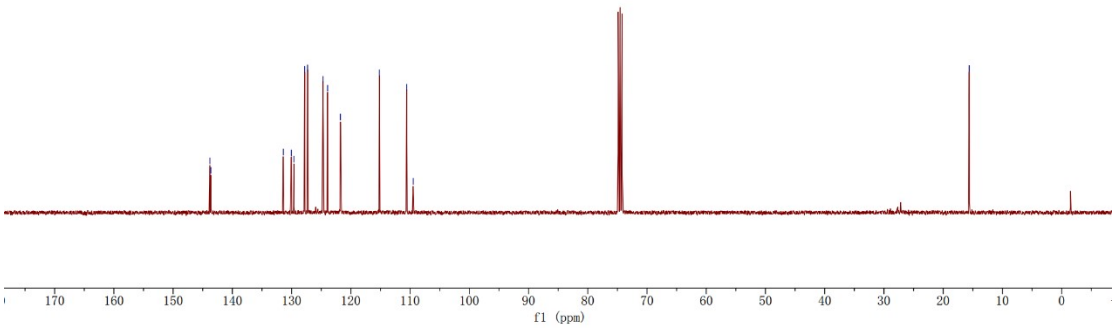


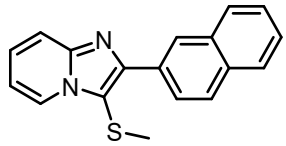
2p (^{1}H NMR) (400 MHz, $CDCl_3$)



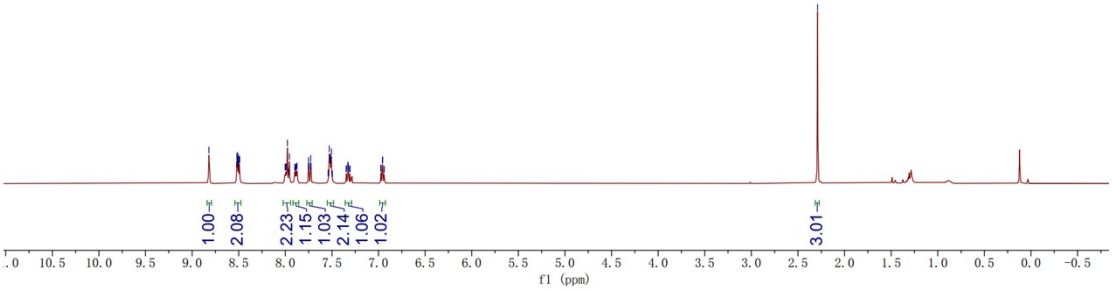


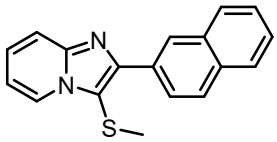
2p (^{13}C NMR) (100 MHz, $CDCl_3$)



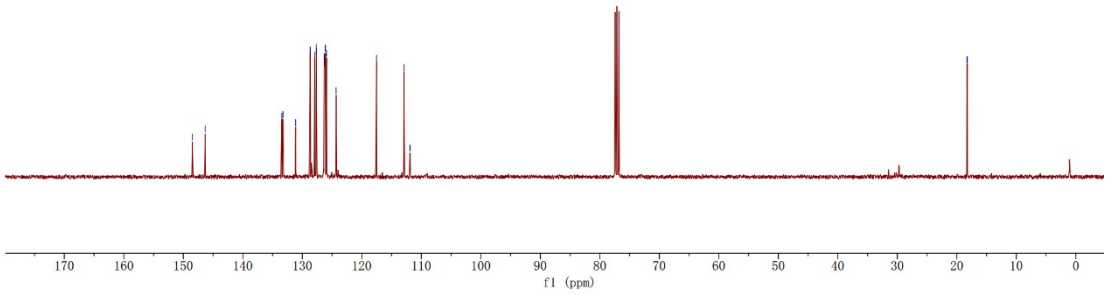


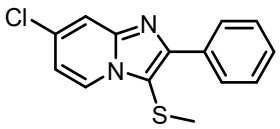
2q (^{1}H NMR) (400 MHz, $CDCl_3$)



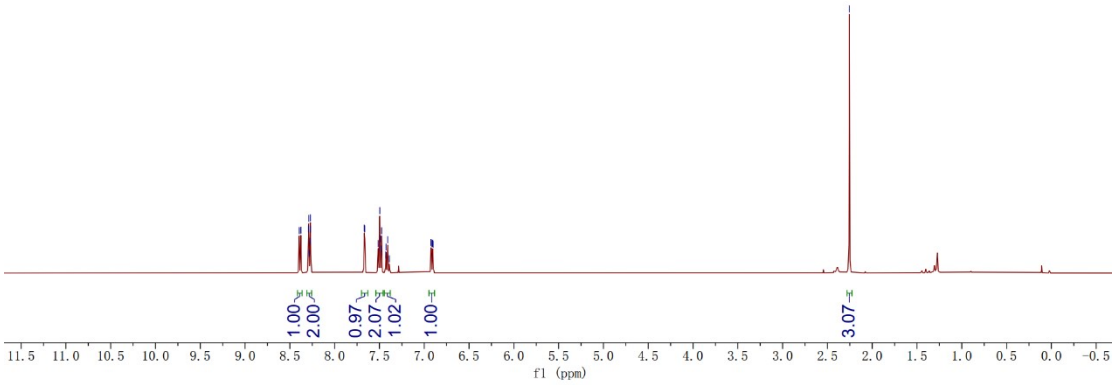


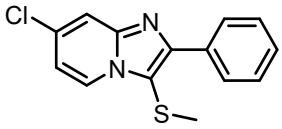
2q (^{13}C NMR) (100 MHz, $CDCl_3$)



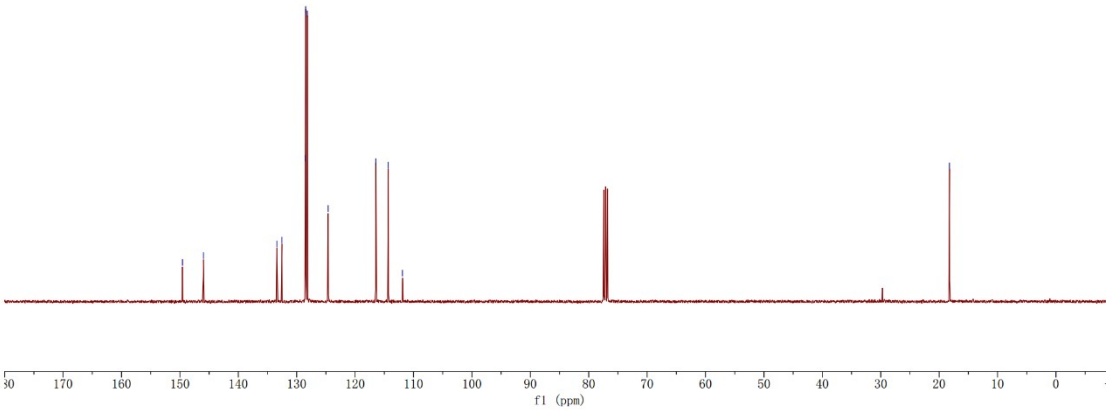


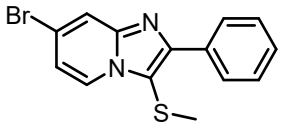
2r (^{1}H NMR) (400 MHz, $CDCl_3$)





2r (^{13}C NMR) (100 MHz, $CDCl_3$)





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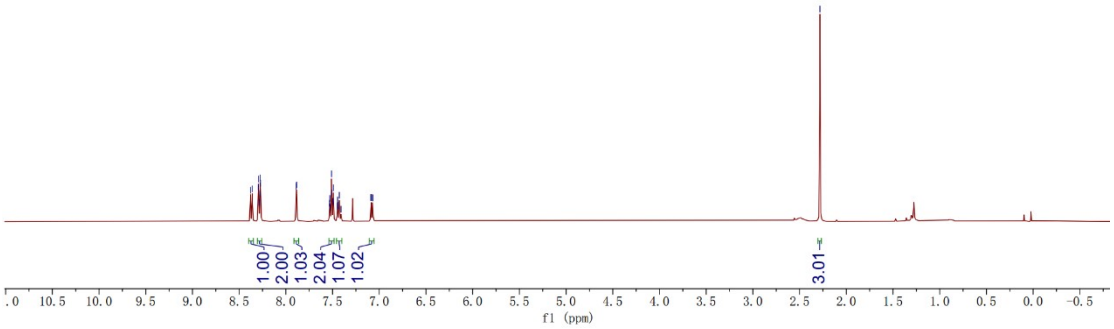
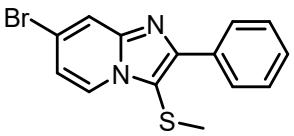
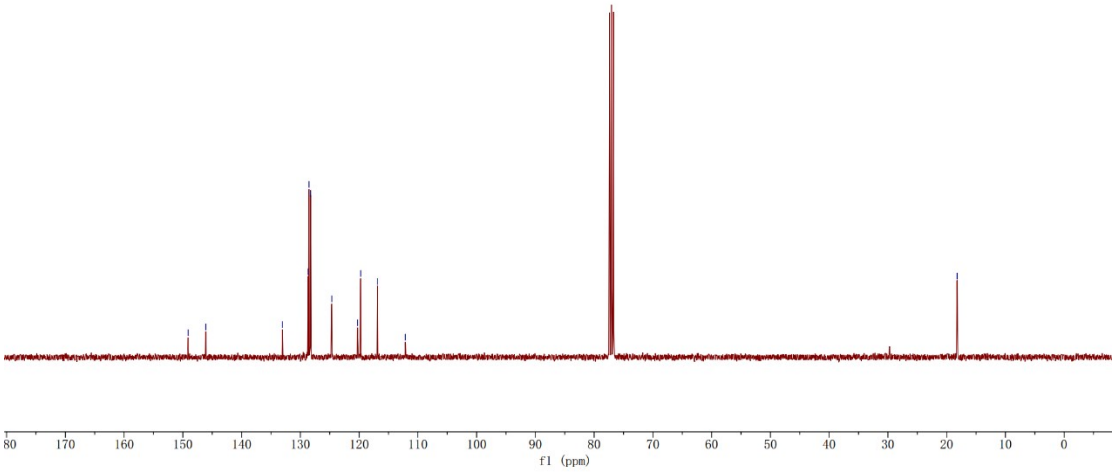
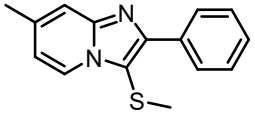


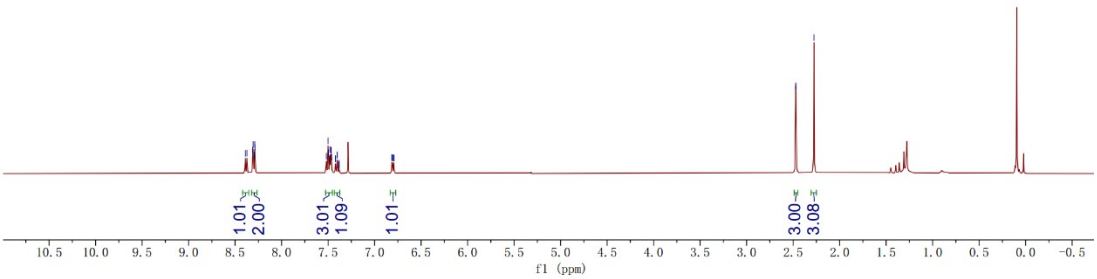


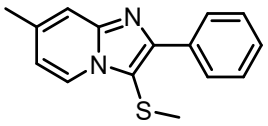
2s (^{13}C NMR) (100 MHz, $CDCl_3$)



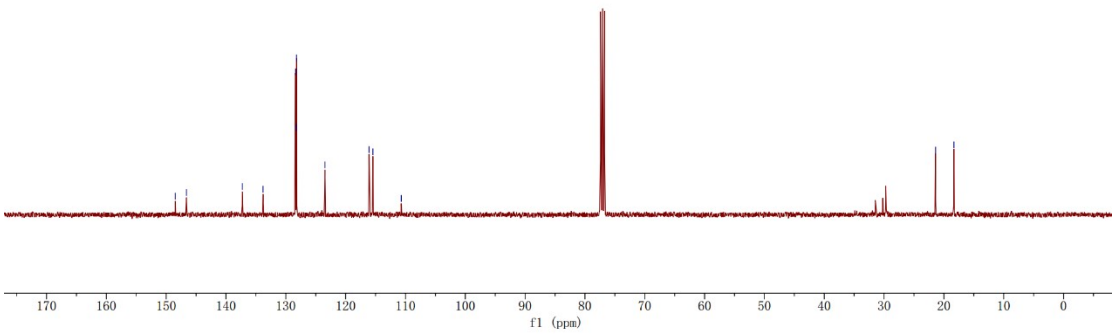


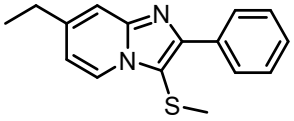
2t (^{1}H NMR) (400 MHz, $CDCl_3$)



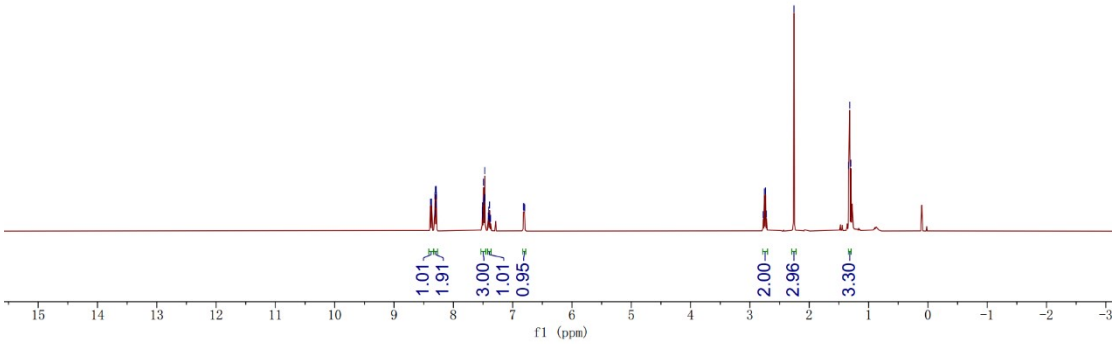


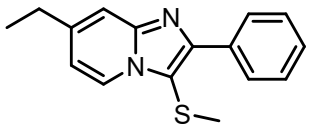
2t (^{13}C NMR) (100 MHz, $CDCl_3$)



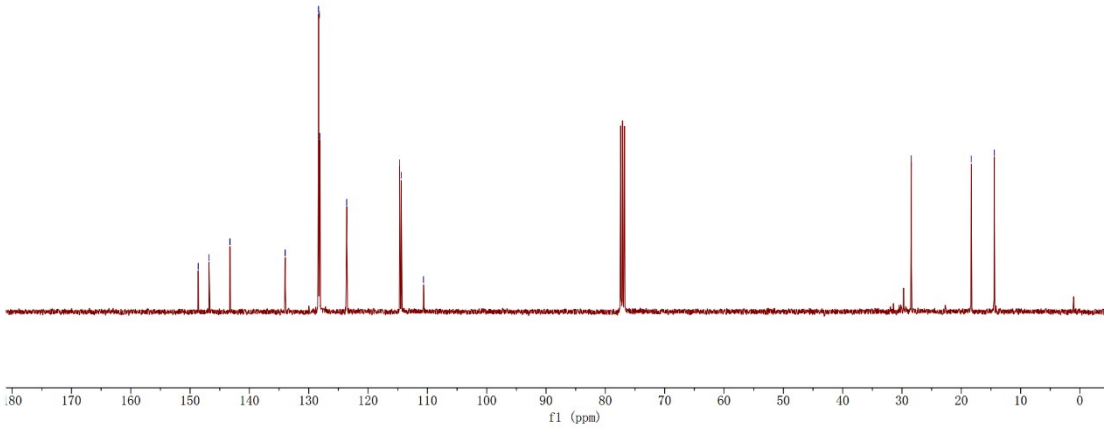


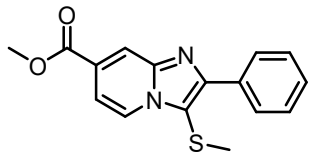
2u (^{1}H NMR) (400 MHz, $CDCl_3$)



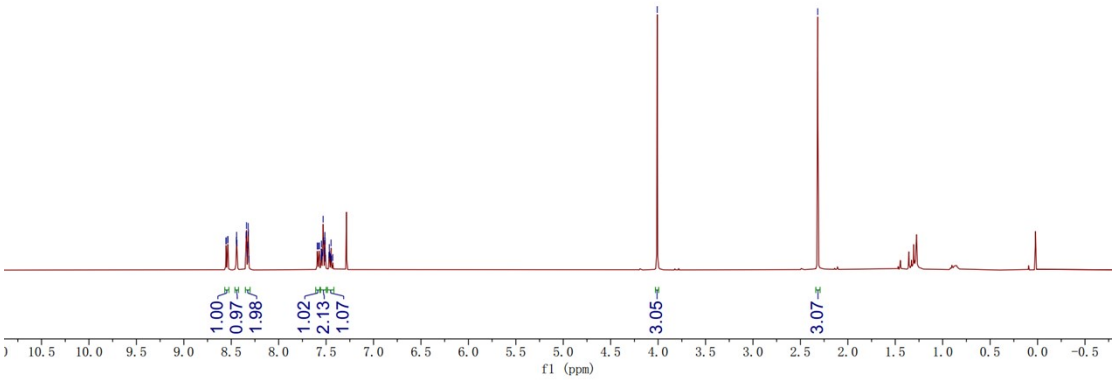


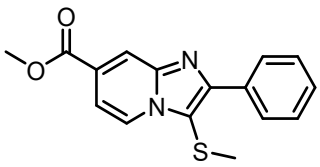
2u (^{13}C NMR) (100 MHz, $CDCl_3$)



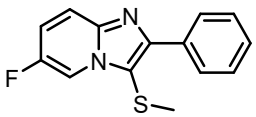


2v (^{1}H NMR) (400 MHz, $CDCl_3$)

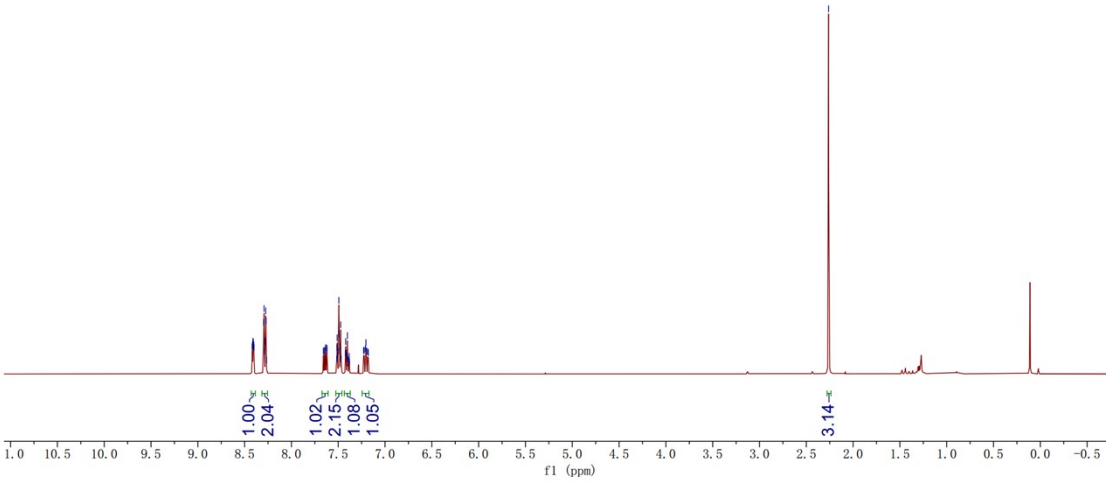


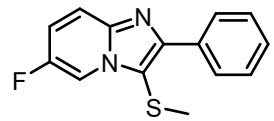


2v (^{13}C NMR) (100 MHz, $CDCl_3$)

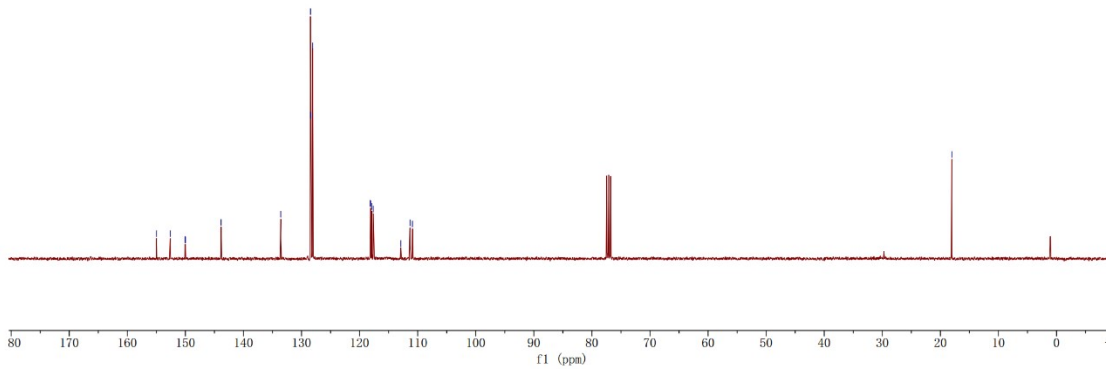


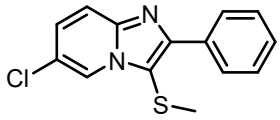
2w (^{1}H NMR) (400 MHz, $CDCl_3$)



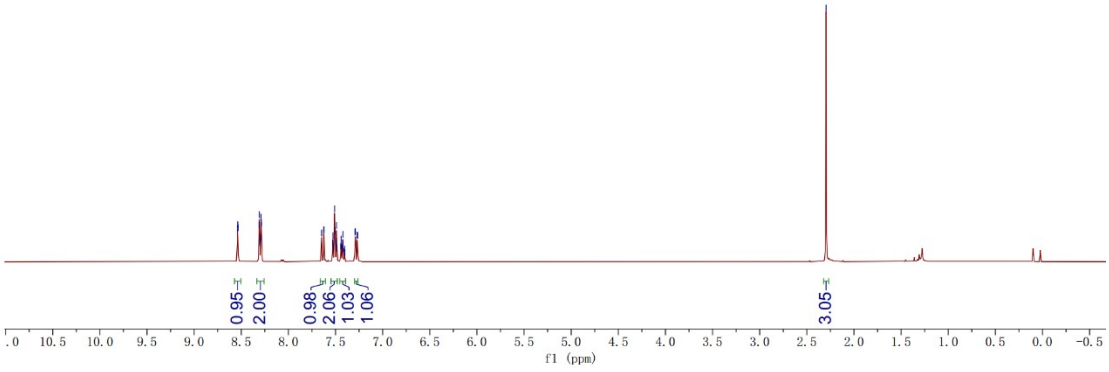


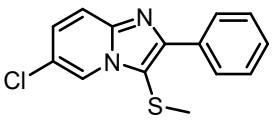
2w (^{13}C NMR) (100 MHz, $CDCl_3$)



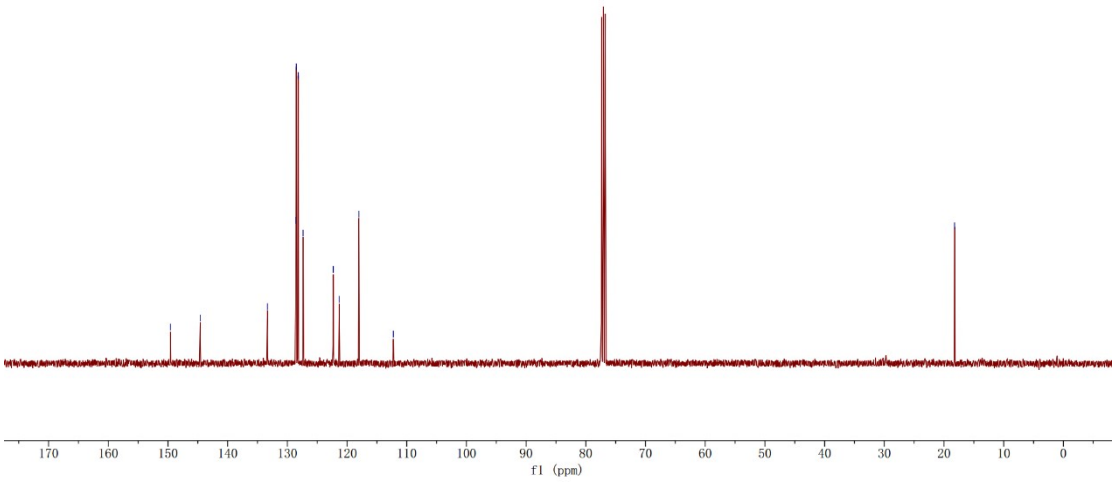


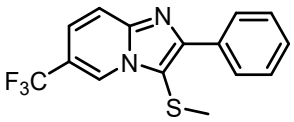
2x (^{1}H NMR) (400 MHz, $CDCl_3$)



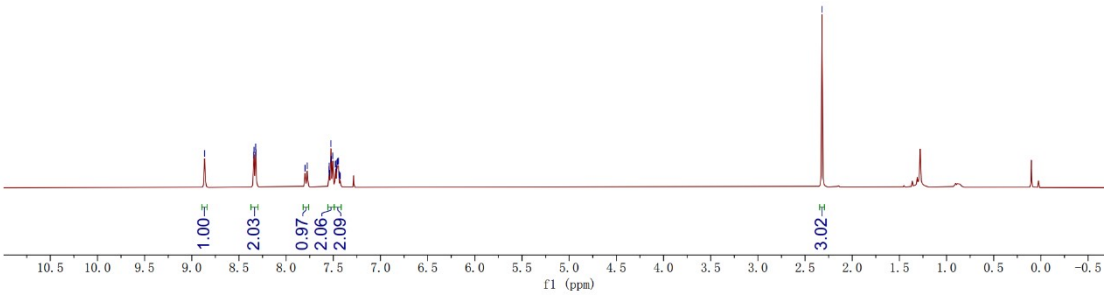


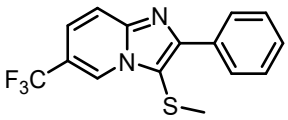
2x (^{13}C NMR) (100 MHz, $CDCl_3$)



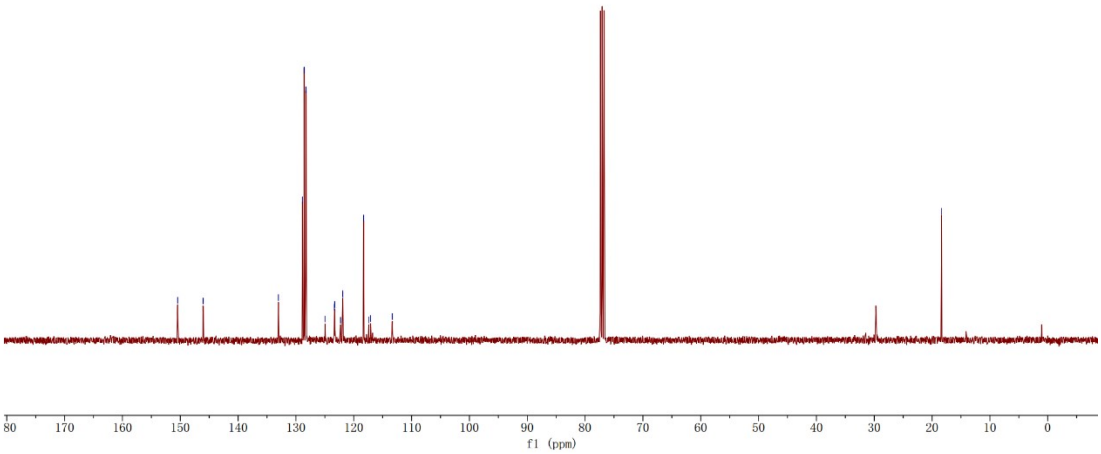


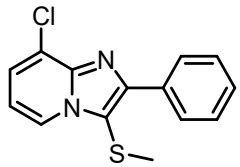
2y (^{1}H NMR) (400 MHz, $CDCl_3$)



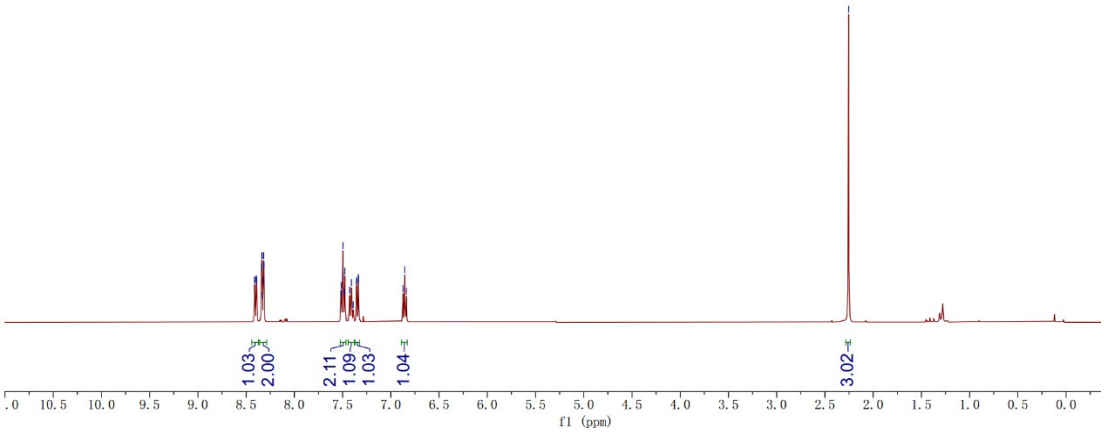


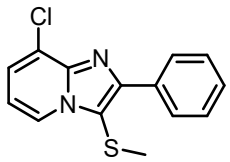
2y (^{13}C NMR) (100 MHz, $CDCl_3$)



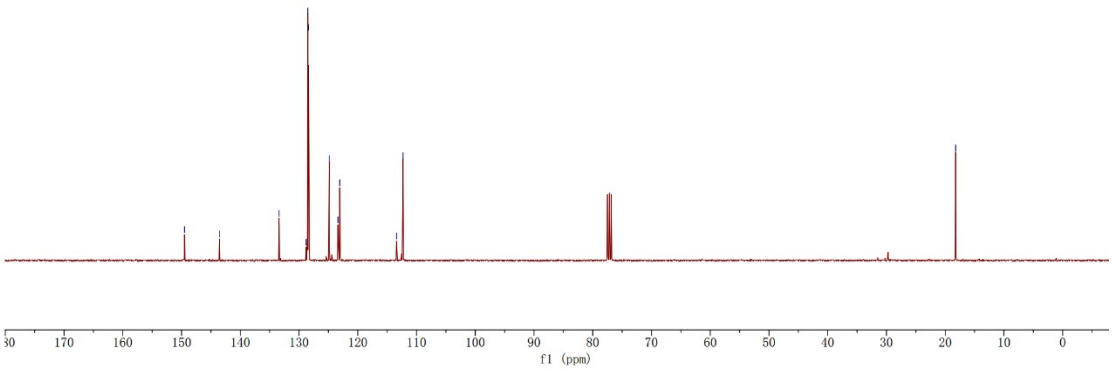


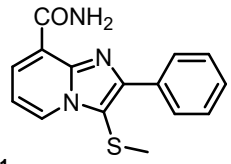
2z (^{1}H NMR) (400 MHz, $CDCl_3$)



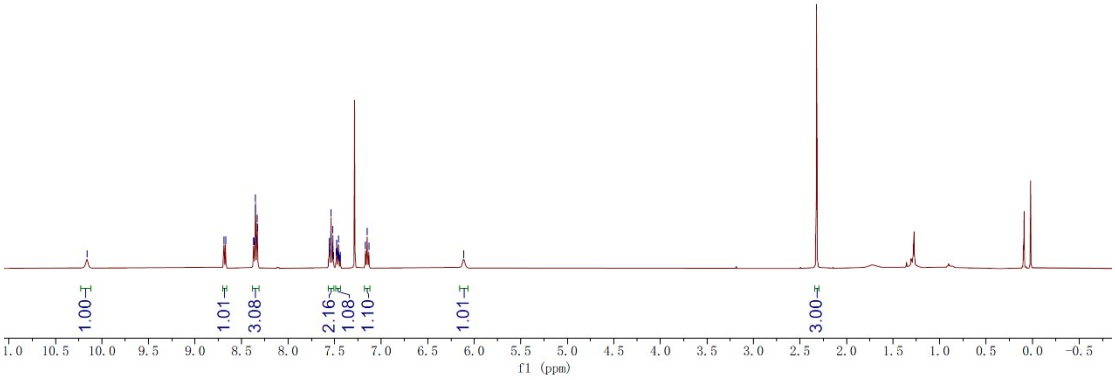


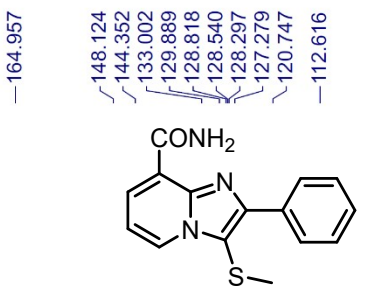
2z (^{13}C NMR) (100 MHz, $CDCl_3$)



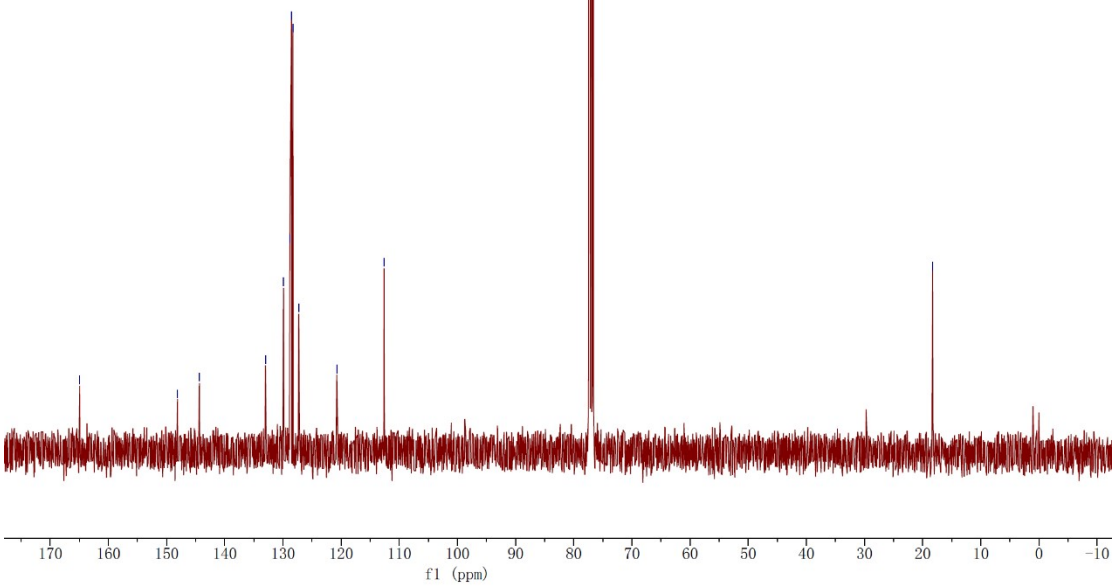


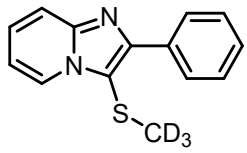
2aa (^{1}H NMR) (400 MHz, $CDCl_3$)



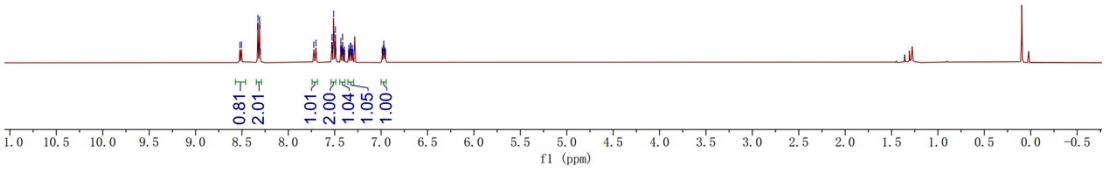


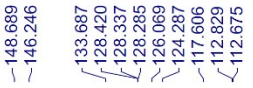
2aa (^{13}C NMR) (100 MHz, $CDCl_3$)

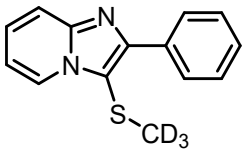




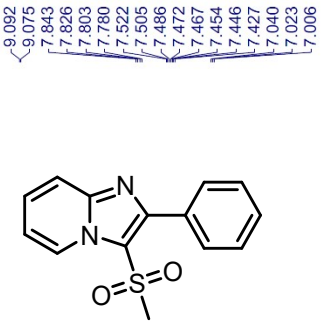
2a-d_3 (^{1}H NMR) (400 MHz, $CDCl_3$)



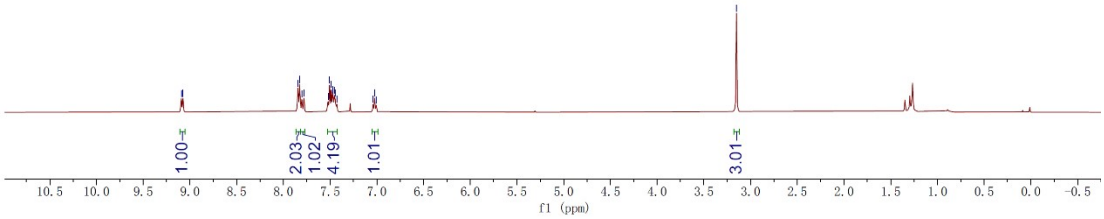


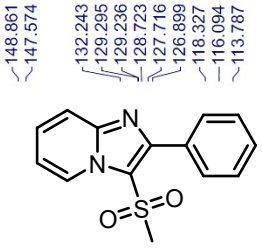


2a-d_3 (^{13}C NMR) (100 MHz, $CDCl_3$)



3 (^{1}H NMR) (400 MHz, $CDCl_3$)





3 (^{13}C NMR) (100 MHz, $CDCl_3$)