Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Highly Stereoselective Dearomative [3+2] Cycloadditons of Cyclic Pyridinium Ylides to Access Spiroindolizidine Scaffolds

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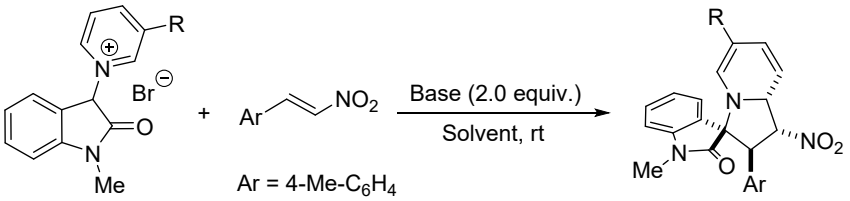
Supporting Information

1. General Methods

NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H-NMR spectra were recorded at 400 MHz, ^{13}C-NMR spectra were recorded at 100 MHz, and ^{19}F-NMR spectra were recorded at 376 MHz. Chemical shifts were reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or $(CD_3)_2SO$ (δ = 2.50 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) or $(CD_3)_2SO$ resonance (δ = 39.52 ppm) for ^{13}C NMR spectroscopy. Coupling constants are given in Hz. UV detection was monitored at 254 nm. TLC was performed on glass-backed silica plates. UV light and I_2 were used to visualize products. Column chromatography was performed using silica gel (200–300 mesh) eluting with EtOAc/petroleum ether. Unless otherwise noted, commercial reagents were used as received and all reactions were carried out directly in air atmosphere. The nitroolefin **2** were obtained according to the literature procedures. [1]

2. Detailed screening conditions for the [3+2]cycloaddition

Table S1, Condition optimizations for [3+2] cycloaddition.[a]



1a, R = CO_2Me
1a', R = H

Ar = 4-Me-C_6H_4
2a

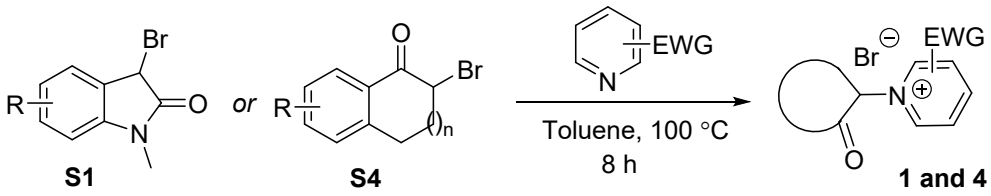
3aa >19:1 d.r.

Entry	Base	Solvent	t (min)	yield (%) [b]
1	Et_3N	toluene	5	59
2[c]	Et_3N	toluene	60	n.r.
3	Et_3N	THF	20	82
4	Et_3N	DCM	5	90
5	Et_3N	EtOH	60	76
6	Et_3N	$CHCl_3$	5	88
7	Et_3N	Et_2O	120	90
8	Et_3N	H_2O	5	59
9	DIPEA	DCM	5	77
10	DBU	DCM	5	79
11	Na_2CO_3	DCM	60	47

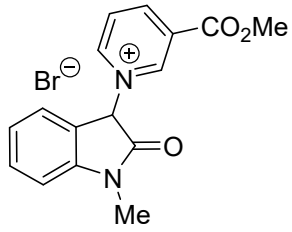
12	K_2CO_3	DCM	60	58
13[d]	Et_3N	DCM	60	25
14[e]	Et_3N	DCM	10	71
15[f]	Et_3N	DCM	5	69
16[g]	**Et_3N**	**DCM**	**5**	**90**

[a] Unless noted otherwise, the reactions were carried out with **1a** (R = CO_2Me, 0.03 mmol), **2a** (0.025 mmol), and base (0.05 mmol) in 0.5 mL of solvent at room temperature. [b] Isolated yield. [c] With **1a'** (R = H, 0.03 mmol). [d] With 0.025 mmol of Et_3N. [e] With 0.03 mmol of Et_3N. [f] With 0.075 mmol of Et_3N. [g] At a 0.1 mmol (**2a**) scale.

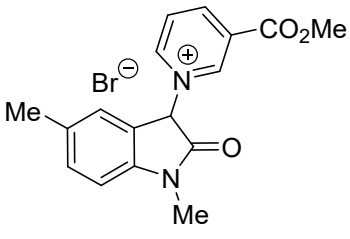
3. General procedure for the preparation of pyridinium salts



A solution of bromo-substrate **S1**[2] or **S4**[3] (1.0 equiv.) and pyridine derivative (1.5 equiv.) in anhydrous toluene under Ar atmosphere was stirred at 100 °C for about 8 hours. After that, the reaction mixture was cooled down to room temperature with generation of vast brown or yellow solid, filtered and washed with ethyl acetate to give the target pyridinium salt as a brown or yellow solid.

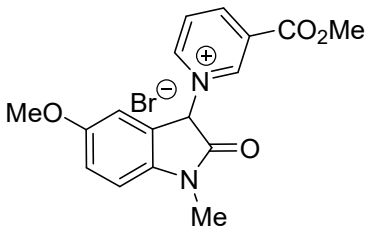


Synthesis of 1a: Following the general procedure, **1a** was obtained as a brown solid in 91% yield; Mp 268–270 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.59 (s, 1H), 9.17–9.12 (m, 2H), 8.39–8.36 (m, 1H), 7.59 (dd, J = 10.6, 4.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.4 Hz, 1H), 7.09 (s, 1H), 3.99 (s, 3H), 3.21 (s, 3H) ppm; ^{13}C NMR (101 MHz, d_6-DMSO): δ 168.9, 162.0, 147.2, 146.9, 146.0, 145.1, 131.8, 130.0, 129.0, 126.1, 123.4, 120.6, 110.3, 68.9, 53.7, 27.1 ppm; ESI-HRMS: calcd. for $C_{16}H_{15}N_2O_3^+$ 283.1077, found 283.1064.

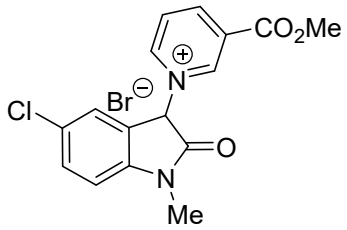


Synthesis of 1b: Following the general procedure, **1b** was obtained as a brown solid in 70% yield; Mp 152–154 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.61 (s, 1H), 9.14–9.12 (m,, 2H), 8.38–8.35 (m, 1H), 7.40–7.38 (m, 2H), 7.17 (d, J = 8.2 Hz, 1H), 7.05 (s, 1H), 4.00 (s, 3H), 3.20 (s, 3H), 2.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.8, 161.9, 147.1, 146.8, 146.1,

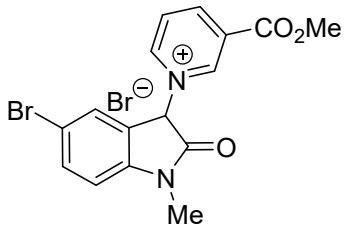
142.6, 132.6, 131.9, 130.0, 129.0, 126.5, 120.7, 110.0, 69.0, 53.6, 27.1, 20.5 ppm; ESI-HRMS: calcd. for $C_{17}H_{17}N_2O_3^+$ 297.1234, found 297.1263.



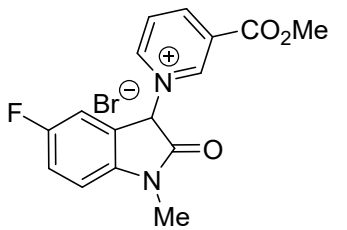
Synthesis of 1c: Following the general procedure, **1c** was obtained as a yellow solid in 52% yield; Mp 197–199 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.61 (s, 1H), 9.14–9.12 (m, 2H), 8.38–8.35 (m, 1H), 7.32 (d, J = 1.7 Hz, 1H), 7.21 (d, J = 8.6 Hz, 1H), 7.16–7.13 (m, 1H), 7.07 (s, 1H), 4.00 (s, 3H), 3.74 (s, 3H), 3.19 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.5, 161.9, 156.0, 147.1, 146.8, 146.1, 138.2, 130.0, 129.0, 121.6, 116.4, 113.0, 110.9, 69.1, 55.8, 53.6, 27.1 ppm; ESI-HRMS: calcd. for $C_{17}H_{17}N_2O_4^+$ 313.1183, found 313.1184.



Synthesis of 1d: Following the general procedure, **1d** was obtained as a brown solid in 77% yield; Mp 276–278 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.65 (s, 1H), 9.18–9.13 (m, 2H), 8.38–8.35 (m, 1H), 7.74 (s, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.12 (s, 1H), 4.01 (s, 3H), 3.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.7, 161.9, 147.3, 146.9, 146.4, 144.0, 131.5, 130.1, 129.0, 127.2, 126.2, 122.6, 111.7, 68.7, 53.6, 27.3 ppm; ESI-HRMS: calcd. for $C_{16}H_{14}ClN_2O_3^+$ 317.0687, found 317.0677.

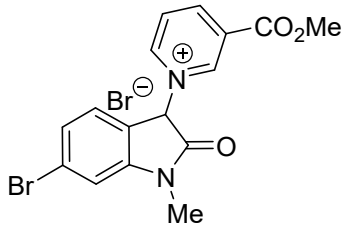


Synthesis of 1e: Following the general procedure, **1e** was obtained as a brown solid in 69% yield; Mp 282–284 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.66 (s, 1H), 9.19–9.13 (m, 2H), 8.39–8.35 (m, 1H), 7.86 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.15 (s, 1H), 4.01 (s, 3H), 3.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.7, 161.9, 147.3, 146.9, 146.4, 144.4, 134.3, 130.0, 129.0, 128.8, 123.0, 114.8, 112.2, 68.6, 53.6, 27.2 ppm; ESI-HRMS: calcd. for $C_{16}H_{14}BrN_2O_3^+$ 361.0182, found 361.0188.

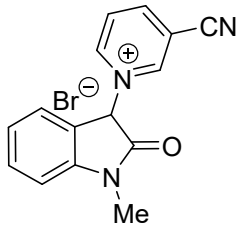


Synthesis of 1f: Following the general procedure, **1f** was obtained as a brown solid in 60% yield; Mp 262–264 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.64 (s, 1H), 9.20–9.13 (m, 2H), 8.40–8.36 (m, 1H), 7.61 (d, J = 6.9 Hz, 1H), 7.48–7.43 (m, 1H), 7.33–7.30 (m, 1H), 7.18 (s, 1H), 4.00 (s, 3H), 3.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.8, 161.9, 158.5 (d, $J_{C\text{-}F}$ = 237.7 Hz), 147.3, 146. 9, 146. 2, 141.4, 130.0, 129.0, 122.0 (d, $J_{C\text{-}F}$ = 9.4 Hz), 118.1 (d, $J_{C\text{-}F}$ = 23.4 Hz), 114.2 (d, $J_{C\text{-}F}$ = 26.3 Hz), 111.4 (d, $J_{C\text{-}F}$ = 8.3 Hz), 68.8, 53.6, 27.3 ppm; ^{19}F NMR (376 MHz,

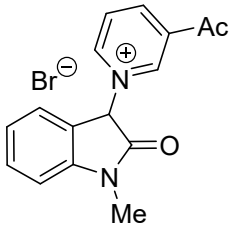
d_6-DMSO):δ -119.38 – -119.44(m) ppm;ESI-HRMS: calcd. for $C_{16}H_{14}FN_2O_3^+$ 301.0983, found 301.0990.



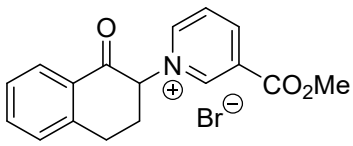
Synthesis of 1g: Following the general procedure, **1g** was obtained as a brown solid in 60% yield; Mp 285–287 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.60 (s, 1H), 9.17–9.12 (m, 2H), 8.38–8.35 (m, 1H), 7.59–7.53 (m, 2H), 7.43 (d, J = 7.5 Hz, 1H), 7.04 (s, 1H), 4.00 (s, 3H), 3.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 169.0, 161.9, 147.3, 146.9, 146.8, 146.1, 129.9, 128.9, 127.8, 125.9, 124.8, 119.9, 113.6, 68.5, 53.6, 27.3 ppm; ESI-HRMS: calcd. for $C_{16}H_{14}BrN_2O_3^+$ 361.0182, found 361.0178.



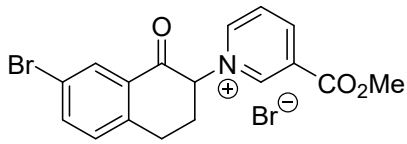
Synthesis of 1h: Following the general procedure, **1h** was obtained as a yellow solid in 73% yield; Mp 251–253 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.74 (s, 1H), 9.38 (d, J = 5.8 Hz, 1H), 9.24 (d, J = 7.9 Hz, 1H), 8.50–8.46 (m, 1H), 7.61–7.56 (m, 2H), 7.29–7.20 (m, 2H), 6.97 (s, 1H), 3.21 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 168.5, 150.3, 148.3, 148.2, 145.1, 131.8, 128.9, 126.4, 123.4, 120.4, 113.6, 113.4, 110.1, 69.2, 27.1 ppm; ESI-HRMS: calcd. for $C_{15}H_{12}N_3O^+$ 250.0975, found 250.0980.



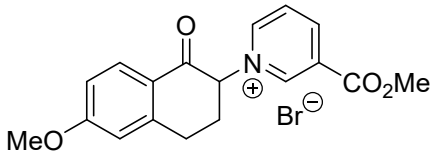
Synthesis of 1i: Following the general procedure, **1i** was obtained as a brown solid in 81% yield; Mp 274–276 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.63 (s, 1H), 9.19 (d, J = 8.1 Hz, 1H), 9.10 (d, J = 6.2 Hz, 1H), 8.40–8.36 (m, 1H), 7.61–7.57 (m 2H), 7.29 (d, J = 7.8 Hz, 1H), 7.24–7.20 (m, 1H), 7.07 (s, 1H), 3.23 (s, 3H), 2.77 (s, 3H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO) δ 194.0, 169.0, 146.4, 146.0, 145.5, 145.0, 135.6, 131.7, 128.8, 125.9, 123.3, 120.9, 110.2, 69.0, 27.3, 27.1 ppm; ESI-HRMS: calcd. for $C_{16}H_{15}N_2O_2^+$ 267.1128, found 267.1130.



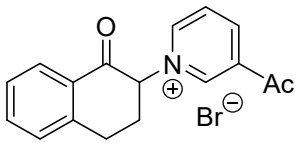
Synthesis of 4a: Following the general procedure, **4a** was obtained as a brown solid in 61% yield; Mp 172–174 °C; ^{1}H NMR (400 MHz, D_2O): δ 9.50 (s, 1H), 9.25–9.22 (m, 1H), 9.19–9.17(m, 1H), 8.43–8.40 (m, 1H), 8.04–8.02 (m, 1H), 7.80–7.76 (m, 1H), 7.56–7.49 (m, 2H), 6.24 (dd, J = 14.0, 4.6 Hz, 1H), 4.12 (s, 3H), 3.60–3.51 (m, 1H), 3.47–3.40 (m, 1H), 3.14–3.03 (m, 1H), 2.97–2.91 (m, 1H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 192.1, 163.2, 147.7, 146.9, 145.9, 144.3, 136.0, 130.8, 130.0, 129.5, 128.6, 127.8, 127.5, 76.2, 54.0, 29.6, 27.9 ppm; ESI-HRMS: calcd. for $C_{17}H_{16}NO_3^+$ 282.1125, found 282.1125.



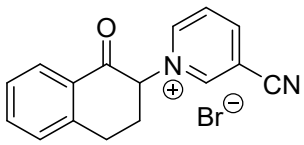
Synthesis of 4b: Following the general procedure, **4b** was obtained as a yellow solid in 33% yield; Mp 224–226 °C; ^{1}H NMR (400 MHz, D_2O): δ 9.49 (s, 1H), 9.24 (d, *J* = 7.3 Hz, 1H), 9.15 (s, 1H), 8.41 (s, 1H), 8.15 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.7 Hz, 1H), 6.23 (d, *J* = 13.9 Hz, 1H), 4.12 (s, 3H), 3.54–3.40 (m, 2H), 3.14–3.05 (m, 1H), 2.94–2.91 (m, 1H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 190.9, 163.2, 147.7, 147.0, 145.9, 143.2, 138.3, 131.5, 131.4, 130.8, 130.1, 128.6, 120.6, 75.9, 54.0, 29.2, 27.5 ppm; ESI-HRMS: calcd. for $C_{17}H_{15}BrNO_3^+$ 360.0230, found 360.0256.



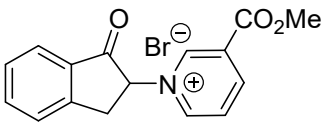
Synthesis of 4c: Following the general procedure, **4c** was obtained as a yellow solid in 74% yield; Mp 156–158 °C; ^{1}H NMR (400 MHz, D_2O): δ 9.48 (s, 1H), 9.23 (d, *J* = 7.8 Hz, 1H), 9.14 (d, *J* = 5.6 Hz, 1H), 8.41–8.37 (m 1H), 8.02 (d, *J* = 8.9 Hz, 1H), 7.04 (s, 2H), 6.14–6.11 (m, 1H), 4.11 (s, 3H), 3.99 (s, 3H), 3.53–3.36 (m, 2H), 3.08–2.91 (m, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 190.5, 165.1, 163.2, 147.7, 147.4, 146.8, 145.9, 130.7, 130.5, 128.5, 123.4, 114.5, 113.1, 76.0, 55.9, 54.0, 29.6, 28.1 ppm; ESI-HRMS: calcd. for $C_{18}H_{18}NO_4^+$ 312.1230, found 312.1202.



Synthesis of 4d: Following the general procedure, **4d** was obtained as a brown solid in 74% yield; Mp 187–189 °C; ^{1}H NMR (400 MHz, D_2O): δ 9.44 (s, 1H), 9.23 (d, *J* = 8.2 Hz, 1H), 9.15 (d, *J* = 6.2 Hz, 1H), 8.44–8.41 (m, 1H), 8.04 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.80–7.76 (m, 1H), 7.56–7.49 (m, 2H), 6.25 (dd, *J* = 14.0, 4.6 Hz, 1H), 3.60–3.52 (m, 1H), 3.47–3.41 (m, 1H), 3.15–3.04 (m, 1H), 2.97–2.92 (m, 1H), 2.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 196.4, 192.2, 147.2, 145.9, 145.2, 144.3, 136.0, 135.9, 130.0, 129.5, 128.7, 127.8, 127.5, 76.2, 29.7, 28.0, 26.7 ppm; ESI-HRMS: calcd. for $C_{17}H_{16}NO_2^+$ 266.1176, found 266.1183.

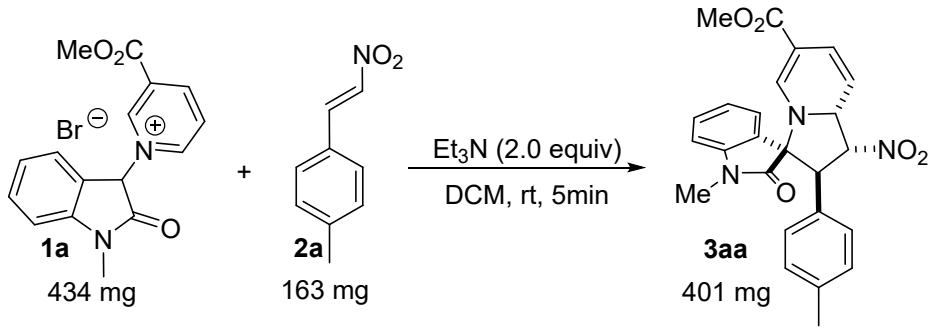


Synthesis of 4e: Following the general procedure, **4e** was obtained as a brown solid in 39% yield; Mp 168–169 °C; ^{1}H NMR (400 MHz, D_2O): δ 9.60 (s, 1H), 9.29–9.27 (m, 1H), 9.18–9.15 (m, 1H), 8.51–8.47 (m, 1H), 8.08–8.06 (m, 1H), 7.81–7.77 (m, 1H), 7.57–7.51 (m, 2H), 6.28 (dd, *J* = 13.9, 4.6 Hz, 1H), 3.61–3.52 (m, 1H), 3.48–3.42 (m, 1H), 3.12–2.93 (m, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 191.6, 150.1, 148.5, 148.4, 144.3, 136.1, 129.9, 129.5, 129.0, 127.9, 127.5, 114.1, 113.3, 76.5, 29.5, 27.9 ppm; ESI-HRMS: calcd. for $C_{16}H_{13}N_2O^+$ 249.1022, found 249.1033.



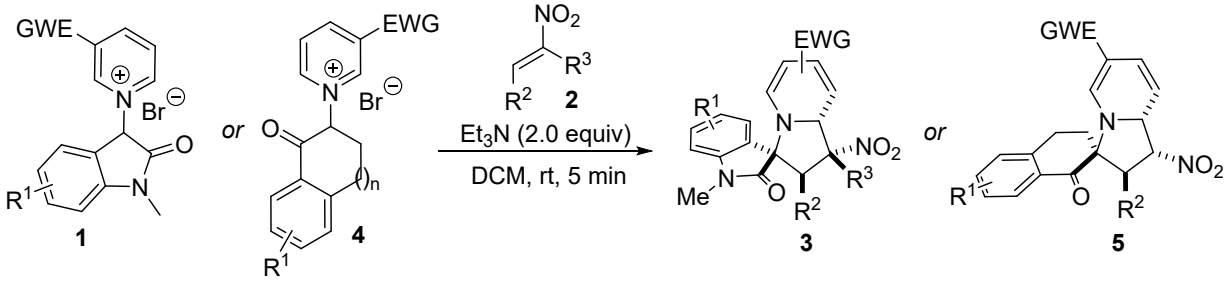
Synthesis of 4f: Following the general procedure, **4f** was obtained as a yellow solid in 45% yield; Mp 235–238 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 9.77 (s, 1H), 9.44 (d, J = 6.2 Hz, 1H), 9.11 (d, J = 8.1 Hz, 1H), 8.42–8.38 (m, 1H), 7.90–7.84 (m, 2H), 7.76 (d, J = 7.7 Hz, 1H), 7.63–7.59 (m, 1H), 6.50–6.46 (m, 1H), 4.08–4.02 (m, 1H), 3.99 (s, 3H), 3.84–3.78 (m, 1H) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 196.9, 162.0, 150.7, 147.9, 146.5, 146.4, 136.7, 132.9, 130.0, 128.8, 128.7, 127.0, 124.3, 73.7, 53.5, 34.1 ppm; ESI-HRMS: calcd. for $C_{16}H_{14}NO_3^+$ 268.0968, found 268.0969.

4. Procedure for the preparation of 3aa at a 1.0 mmol scale

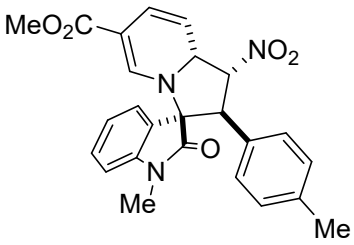


To the solution of pyridinium salt **1a** (434 mg, 1.2 mmol) and nitroolefin **2a** (163 mg, 1.0 mmol) in DCM (10.0 mL) was added Et_3N (202 mg, 2.0 mmol) and stirred at room temperature for 30 minutes. Upon workup, solvent was evaporated under reduced pressure, product **3aa** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (401 mg, 90% yield, > 19:1 d.r.).

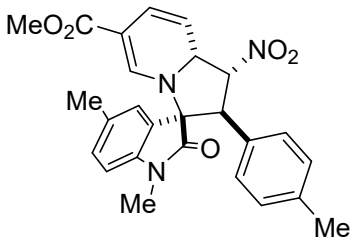
5. General procedure for the [3+2] cycloaddition



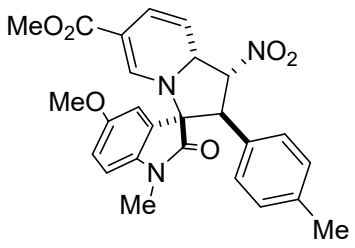
The reaction was carried out with pyridinium salts **1** or **4** (0.12 mmol), nitrolefins **2** (0.1 mmol), and Et_3N (0.2 mmol) in DCM (2.0 mL) at room temperature for about 5 minutes. After completion, the solution was purified by flash chromatography to afford the product **3** or **5**.



Synthesis of 3aa: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3aa** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (40 mg) in 90% yield; Mp 90–91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 7.4 Hz, 1H), 7.42–7.39 (m, 1H), 7.25–7.23 (m, 1H), 6.99 (s, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 10.1 Hz, 1H), 6.10–6.02 (m, 2H), 4.96 (dd, *J* = 10.2, 0.9 Hz, 1H), 4.36 (d, *J* = 6.8 Hz, 1H), 3.62 (s, 3H), 2.85 (s, 3H), 2.22 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 166.3, 144.6, 139.3, 138.5, 131.4, 129.3, 128.2, 128.1, 125.1, 124.9, 124.0, 122.4, 109.2, 106.6, 100.5, 92.9, 75.0, 61.2, 57.1, 50.9, 25.7, 21.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}N_3O_5$ + H^+ 446.1710, found 446.1707.

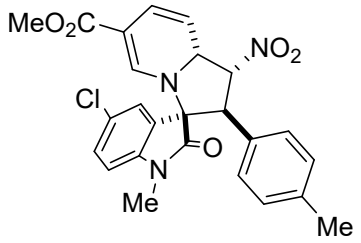


Synthesis of 3ba: pyridinium salt **1b** (37.6 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ba** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (43 mg) in 93% yield; Mp 114–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (s, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.99–6.95 (m, 3H), 6.84 (d, *J* = 7.4 Hz, 2H), 6.62–6.58 (m, 2H), 6.08–6.01 (m, 2H), 4.96 (d, *J* = 10.1 Hz, 1H), 4.35 (d, *J* = 6.5 Hz, 1H), 3.63 (s, 3H), 2.82 (s, 3H), 2.43 (s, 3H), 2.23 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 166.1, 142.1, 139.3, 138.2, 133.6, 131.6, 129.0, 128.0, 128.0, 125.4, 124.7, 122.3, 108.7, 106.3, 100.4, 92.7, 74.8, 61.0, 56.9, 50.7, 25.5, 21.0, 20.8 ppm; ESI-HRMS: calcd. for $C_{26}H_{25}N_3O_5$ + H^+ 460.1867, found 460.1857.

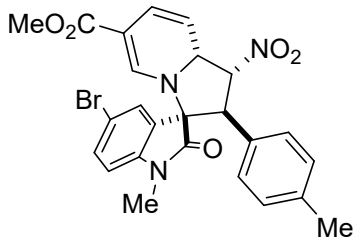


Synthesis of 3ca: pyridinium salt **1c** (39.2 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ca** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (41 mg) in 86% yield; Mp 119–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (s, 1H), 7.00–6.85 (m, 6H), 6.65–6.58 (m, 2H), 6.05–6.03 (m, 2H), 4.96 (d, *J* = 9.8 Hz, 1H), 4.34 (d, *J* = 6.0 Hz, 1H), 3.86 (s, 3H), 3.64 (s, 3H), 2.82 (s, 3H), 2.23 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 166.3, 156.9, 139.3, 138.5,

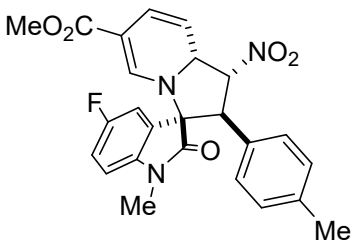
137.9, 129.3, 128.2, 128.1, 124.9, 123.6, 116.0, 111.7, 109.8, 106.6, 100.8, 92.8, 75.1, 61.1, 57.2, 56.0, 51.0, 25.8, 21.0 ppm; ESI-HRMS: calcd. for $C_{26}H_{25}N_3O_6$ + H^+ 476.1816, found 476.1802.



Synthesis of 3da: pyridinium salt **1d** (39.6 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3da** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (44 mg) in 92% yield; Mp 164–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (dd, *J* = 7.3, 2.6 Hz, 1H), 7.12 (td, *J* = 8.7, 2.6 Hz, 1H), 6.99 (s, 1H), 6.96 (d, *J* = 4.4 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.68–6.65 (m, 1H), 6.61–6.58 (m, 1H), 6.06–6.00 (m, 2H), 4.99–4.96 (m, 1H), 4.34 (d, *J* = 6.5 Hz, 1H), 3.65 (s, 3H), 2.84 (s, 3H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 166.2, 138.9, 138.7, 129.4, 128.2, 127.9, 124.9, 118.1, 117.9, 113.3, 113.0, 110.0, 109.9, 106.8, 101.4, 92.6, 74.9, 61.3, 57.4, 51.0, 25.9, 21.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{22}ClN_3O_5$ + H^+ 480.1321, found 480.1308.

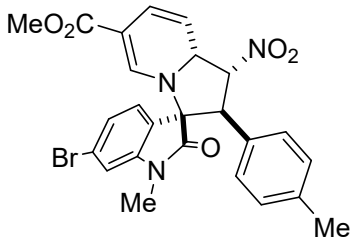


Synthesis of 3ea: pyridinium salt **1e** (44.0 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ea** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (48 mg) in 92% yield; Mp 172–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 1.5 Hz, 1H), 7.54 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.94 (s, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.60 (t, *J* = 8.7 Hz, 2H), 6.04–5.98 (m, 2H), 4.98 (d, *J* = 10.2 Hz, 1H), 4.35 (d, *J* = 6.3 Hz, 1H), 3.65 (s, 3H), 2.83 (s, 3H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 166.1, 143.7, 138.9, 138.8, 134.4, 129.4, 128.2, 128.0, 127.8, 125.0, 124.7, 116.5, 110.6, 106.8, 101.6, 92.5, 74.6, 61.3, 57.4, 51.1, 25.9, 21.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{22}BrN_3O_5$ + H^+ 524.0816, found 524.0810.

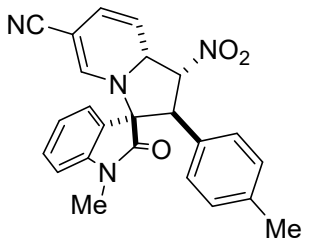


Synthesis of 3fa: pyridinium salt **1f** (38.0 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3fa** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (38 mg) in 82% yield; Mp 150–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (dd, *J* = 7.3, 2.5 Hz, 1H), 7.12 (td, *J* = 8.7, 2.6

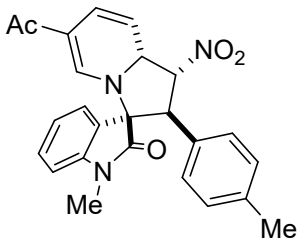
Hz, 1H), 6.99–6.96 (m, 3H), 6.87–6.85 (m, 2H), 6.69–6.66 (m, 1H), 6.62–6.58 (m, 1H), 6.06–6.00 (m, 2H), 4.98 (d, J = 10.1 Hz, 1H), 4.34 (d, J = 6.5 Hz, 1H), 3.64 (s, 3H), 2.84 (s, 3H), 2.24 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 166.1, 159.6 (d, $J_{C\text{-}F}$ = 243.0 Hz), 140.6 (d, $J_{C\text{-}F}$ = 2.2 Hz), 138.9, 138.7, 129.4, 128.2, 127.9, 124.9, 124.2 (d, $J_{C\text{-}F}$ = 7.6 Hz), 118.0 (d, $J_{C\text{-}F}$ = 23.3), 113.1 (d, $J_{C\text{-}F}$ = 25.0 Hz), 110.0 (d, $J_{C\text{-}F}$ = 7.9 Hz), 106.8, 101.4, 92.6, 74.9, 61.3, 57.4, 51.0, 25.9, 21.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ -117.09 – -117.04(m) ppm ESI-HRMS: calcd. for $C_{25}H_{22}FN_3O_5$ + Na^+ 486.1436, found 486.1427



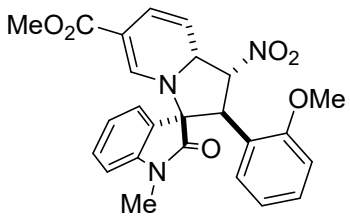
Synthesis of 3ga: pyridinium salt **1g** (44.0 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ga** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (40 mg) in 76% yield; Mp 173–176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (s, 2H), 6.98 (d, J = 7.9 Hz, 2H), 6.91 (d, J = 16.4 Hz, 2H), 6.84 (d, J = 8.1 Hz, 2H), 6.59 (d, J = 10.1 Hz, 1H), 6.07–5.99 (m, 2H), 4.98 (dd, J = 10.1, 1.0 Hz, 1H), 4.33 (d, J = 6.7 Hz, 1H), 3.64 (s, 3H), 2.84 (s, 3H), 2.25 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 166.2, 145.8, 138.9, 138.8, 129.5, 128.2, 127.8, 126.9, 126.4, 125.4, 124.9, 121.4, 112.8, 106.8, 101.0, 92.8, 74.6, 61.3, 57.0, 51.0, 25.9, 21.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{22}BrN_3O_5$ + H^+ 524.0816, found 524.0808.



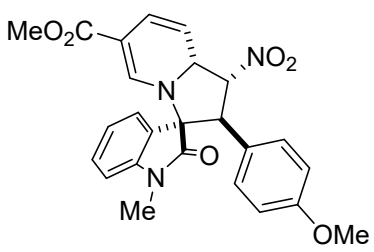
Synthesis of 3ha: pyridinium salt **1h** (32.9 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ha** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (39 mg) in 95% yield; Mp 99–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 7.3 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.30–7.26 (m, 1H), 6.96 (d, J = 7.5 Hz, 2H), 6.84 (d, J = 7.6 Hz, 2H), 6.74 (d, J = 7.7 Hz, 1H), 6.54 (s, 1H), 6.09–6.04 (m, 3H), 5.01 (d, J = 10.7 Hz, 1H), 4.34 (d, J = 6.6 Hz, 1H), 2.86 (s, 3H), 2.23 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 144.6, 140.9, 138.7, 131.8, 129.4, 128.2, 127.6, 125.1, 124.1, 124.0, 121.6, 119.4, 109.4, 108.5, 92.8, 80.6, 74.9, 60.5, 56.6, 25.8, 21.0 ppm; ESI-HRMS: calcd. for $C_{24}H_{20}N_4O_3$ + H^+ 413.1608, found 413.1610.



Synthesis of 3ia: pyridinium salt **1i** (34.6 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ia** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (41 mg) in 96% yield; Mp 96–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.45–7.23 (m, 1H), 7.27–7.26 (m, 1H), 6.97–6.95 (m, 3H), 6.84 (d, *J* = 8.1 Hz, 2H), 6.76–6.70 (m, 2H), 6.12–6.09 (m, 1H), 6.05–6.02 (m, 1H), 5.05 (dd, *J* = 10.2, 1.4 Hz, 1H), 4.37 (d, *J* = 6.9 Hz, 1H), 2.86 (s, 3H), 2.23 (s, 3H), 2.03 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 173.7, 144.7, 139.8, 138.6, 131.6, 129.3, 128.2, 128.0, 125.1, 124.6, 124.0, 122.3, 111.0, 109.4, 107.4, 92.8, 75.2, 61.3, 57.2, 25.8, 24.7, 21.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}N_3O_4 + H^+$ 430.1761, found 430.1752.

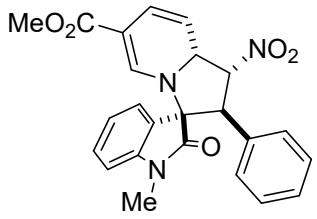


Synthesis of 3ab: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2b** (21.5 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ab** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (44 mg) in 95% yield; Mp 157–158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, *J* = 7.3 Hz, 1H), 7.38–7.34 (m, 1H), 7.23–7.14 (m, 3H), 7.00 (s, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.62 (d, *J* = 8.1 Hz, 1H), 6.60–6.57 (m, 1H), 6.13 (dt, *J* = 7.2, 1.9 Hz, 1H), 5.98–5.92 (m, 1H), 5.09 (d, *J* = 5.8 Hz, 1H), 5.03 (dd, *J* = 10.2, 1.4 Hz, 1H), 3.61 (s, 3H), 3.34 (s, 3H), 2.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 166.3, 157.4, 144.5, 139.6, 130.8, 129.6, 128.9, 126.1, 124.9, 123.4, 123.1, 120.6, 120.5, 110.4, 108.6, 106.8, 99.7, 93.5, 74.7, 62.3, 54.9, 50.9, 49.3, 25.7 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}N_3O_6 + H^+$ 462.1660, found 462.1659.

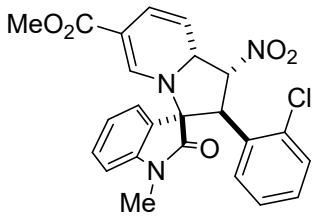


Synthesis of 3ac: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2c** (21.5 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ac** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (42 mg) in 91% yield; Mp 158–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.3 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.4 Hz, 1H), 6.99 (s, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.73–6.66 (m, 3H), 6.59 (d, *J* =

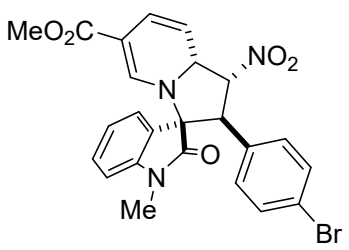
10.0 Hz, 1H), 6.08–6.00 (m, 2H), 4.95 (d, *J* = 10.1 Hz, 1H), 4.34 (d, *J* = 6.8 Hz, 1H), 3.70 (s, 3H), 3.62 (s, 3H), 2.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 166.2, 159.7, 144.6, 139.3, 131.4, 129.5, 125.1, 124.9, 124.0, 122.9, 122.4, 114.0, 109.2, 106.6, 100.6, 93.0, 75.0, 61.0, 56.9, 55.1, 50.9, 25.8 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}N_3O_6$ + H^+ 462.1660, found 462.1665.



Synthesis of 3ad: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2d** (17.9 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ad** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (35 mg) in 82% yield; Mp 74–76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.42–7.39 (m, 1H), 7.27–7.23 (m, 1H), 7.20–7.13 (m, 3H), 7.01 (s, 1H), 6.96–6.94 (m, 2H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 10.1 Hz, 1H), 6.12–6.05 (m, 2H), 4.98 (d, *J* = 10.1 Hz, 1H), 4.40 (d, *J* = 6.6 Hz, 1H), 3.62 (s, 3H), 2.82 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 166.2, 144.6, 139.3, 131.5, 131.2, 128.6, 128.6, 128.3, 125.1, 124.9, 124.0, 122.3, 109.2, 106.6, 100.6, 92.7, 75.1, 61.3, 57.4, 50.9, 25.7 ppm; ESI-HRMS: calcd. for $C_{24}H_{21}N_3O_5$ + H^+ 432.1554, found 432.1561.

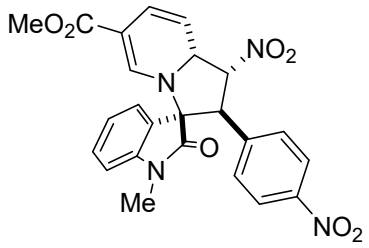


Synthesis of 3ae: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2e** (22.0 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ae** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (41 mg) in 89% yield; Mp 169–171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 7.4 Hz, 1H), 7.46 (d, J = 7.4 Hz, 1H), 7.40 (td, J = 7.8, 0.9 Hz, 1H), 7.25–7.20 (m, 2H), 7.18–7.13 (m, 2H), 6.99 (s, 1H), 6.73 (d, J = 7.8 Hz, 1H), 6.61 (d, J = 10.2 Hz, 1H), 6.18–6.13 (m, 1H), 5.86–5.80 (m, 1H), 5.27 (d, J = 6.1 Hz, 1H), 5.03 (dd, J = 10.2, 1.3 Hz, 1H), 3.63 (s, 3H), 2.91 (s, 3H). ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 166.2, 144.4, 139.3, 135.1, 131.5, 130.3, 130.0, 129.8, 129.7, 127.1, 126.7, 125.2, 123.9, 121.8, 109.0, 106.7, 100.4, 94.6, 74.8, 62.2, 51.4, 51.0, 25.9 ppm; ESI-HRMS: calcd. for $C_{24}H_{20}ClN_3O_5$ + H^+ 466.1164, found 466.1160.

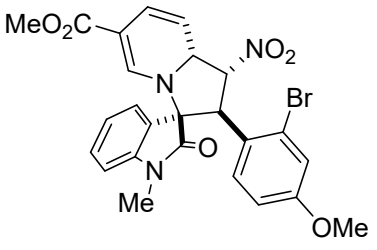


Synthesis of 3af pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2f** (27.2 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon

workup, product **3af** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (46 mg) in 90% yield; Mp 184–186 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 7.4 Hz, 1H), 7.43–7.37 (m, 1H), 7.28 (brs, 1H), 7.25–7.22 (m, 2H), 6.95 (s, 1H), 6.83 (d, J = 8.3 Hz, 2H), 6.73 (d, J = 7.8 Hz, 1H), 6.58 (d, J = 10.1 Hz, 1H), 6.09–5.95 (m, 2H), 4.95 (d, J = 10.1 Hz, 1H), 4.31 (t, J = 9.5 Hz, 1H), 3.61 (s, 3H), 2.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 166.2, 144.6, 139.1, 131.8, 131.7, 130.3, 130.1, 125.1, 125.0, 124.2, 123.0, 121.9, 109.4, 106.6, 100.9, 92.7, 74.8, 61.1, 56.7, 51.0, 25.9 ppm; ESI-HRMS: calcd. for $C_{24}H_{20}BrN_3O_5$ + H^+ 510.0659, found 510.0647.

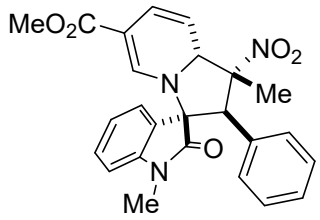


Synthesis of 3ag: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2g** (23.3 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ag** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (38 mg) in 80% yield; Mp 121–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.7 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.48 (td, *J* = 7.8, 0.9 Hz, 1H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.00 (s, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 10.1 Hz, 1H), 6.16–6.08 (m, 2H), 5.03 (dd, *J* = 10.2, 1.1 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 1H), 3.66 (s, 3H), 2.90 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 166.1, 148.0, 144.5, 138.8, 138.8, 132.0, 129.6, 125.2, 125.1, 124.4, 123.7, 121.4, 109.6, 106.7, 101.2, 92.4, 74.9, 61.3, 56.6, 51.1, 25.9 ppm; ESI-HRMS: calcd. for $C_{24}H_{20}N_4O_7$ + H^+ 477.1405, found 477.1412.

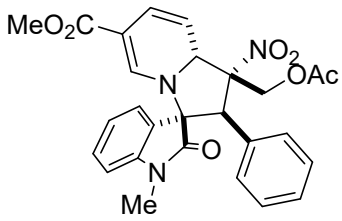


Synthesis of 3ah: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2h** (30.8 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ah** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (43 mg) in 80% yield; Mp 194–196 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.4 Hz, 1H), 7.42–7.35 (m, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.98 (s, 1H), 6.89 (d, *J* = 2.6 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 10.2 Hz, 1H), 6.13 (dt, *J* = 7.5, 1.9 Hz, 1H), 5.76–5.73 (m, 1H), 5.20 (d, *J* = 6.1 Hz, 1H), 5.00 (dd, *J* = 10.2, 1.3 Hz, 1H), 3.72 (s, 3H), 3.62 (s, 3H), 2.94 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 166.2, 159.8, 144.5, 139.3, 131.4, 130.5, 127.0, 126.2,

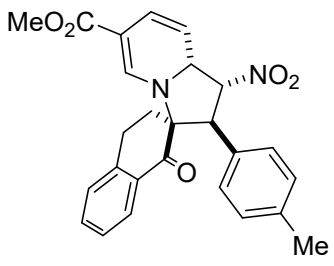
125.1, 123.8, 123.8, 121.8, 118.2, 114.0, 109.0, 106.7, 100.3, 95.1, 74.8, 62.0, 55.4, 53.4, 51.0, 26.0 ppm; ESI-HRMS: calcd. for $C_{25}H_{22}BrN_3O_6 + H^+$ 540.0765, found 540.0761.



Synthesis of 3ai: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2i** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3ai** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (40 mg, 90% yield), d.r. = 1.8:1; Mp 119–122 °C; ^1H NMR_{major} (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.3 Hz, 1H), 7.33 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.19–7.15 (m, 6H), 6.99 (s, 1H), 6.74 (d, *J* = 5.9 Hz, 1H), 6.58–6.54 (m, 1H), 5.85 (t, *J* = 2.1 Hz, 1H), 5.01 (dd, *J* = 10.3, 1.6 Hz, 1H), 4.90 (s, 1H), 3.61 (s, 3H), 3.07 (s, 3H), 1.73 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 173.3, 166.3, 166.0, 144.3, 143.1, 141.0, 139.3, 131.3, 131.1, 130.7, 130.6, 129.5, 129.3, 128.9, 128.6, 128.4, 125.1, 124.9, 124.6, 124.1, 124.0, 123.4, 122.9, 109.2, 108.7, 108.0, 107.6, 101.9, 100.6, 99.3, 94.3, 74.4, 73.7, 69.3, 67.7, 62.9, 61.5, 50.9, 50.9, 26.5, 26.1, 21.3, 16.7 ppm; ESI-HRMS: calcd. for $C_{25}H_{23}N_3O_5 + H^+$ 446.1710, found 446.1709.

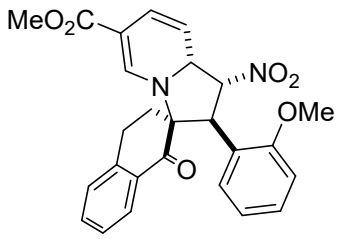


Synthesis of 3aj: pyridinium salt **1a** (36.2 mg, 0.10 mmol) and nitroolefin **2j** (26.5 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **3aj** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (30 mg) in 59% yield; Mp 132–135 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (m, 1H), 7.36 (td, *J* = 7.8, 1.1 Hz, 1H), 7.21–7.15 (m, 4H), 7.11–7.08 (m, 2H), 6.98 (s, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 6.57–6.54 (m, 1H), 6.05 (t, *J* = 2.1 Hz, 1H), 5.05 (dd, *J* = 10.3, 1.5 Hz, 1H), 4.82 (s, 1H), 4.75 (t, *J* = 13.2 Hz, 2H), 3.62 (s, 3H), 3.10 (s, 3H), 1.69 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 169.5, 166.2, 144.5, 138.9, 131.6, 130.3, 129.8, 128.9, 128.8, 125.0, 124.6, 124.2, 122.2, 109.4, 108.7, 100.6, 99.5, 74.0, 65.8, 64.0, 60.3, 50.9, 26.2, 20.0 ppm; ESI-HRMS: calcd. for $C_{27}H_{25}N_3O_7 + H^+$ 504.1765, found 504.1758.

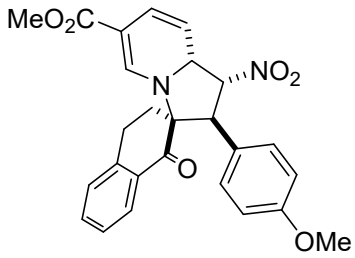


Synthesis of 5aa: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5aa** was obtained by flash chromatography

(EtOAc/petroleum ether = 1/4) as a yellow solid (37 mg) in 83% yield; Mp 102–103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.33–7.29 (m, 1H), 7.08–7.02 (m, 2H), 6.77 (brs, 4H), 6.60 (d, *J* = 10.1 Hz, 1H), 5.76 (d, *J* = 5.8 Hz, 1H), 5.31–5.30 (m, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.25 (d, *J* = 1.8 Hz, 1H), 3.67 (s, 3H), 3.49–3.40 (m, 1H), 3.22 (d, *J* = 17.3 Hz, 1H), 2.76–2.68 (m, 2H), 2.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7, 166.3, 144.1, 141.4, 140.7, 138.2, 133.6, 132.1, 129.2, 128.5, 127.9, 127.6, 126.6, 125.6, 106.3, 100.3, 95.6, 74.9, 65.3, 54.4, 50.9, 33.6, 26.6, 20.7 ppm; ESI-HRMS: calcd. for $C_{26}H_{24}N_2O_5$ + H^+ 445.1758, found 445.1754.

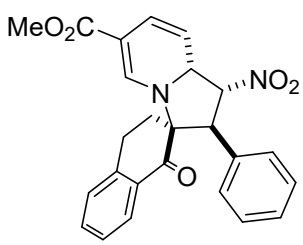


Synthesis of 5ab: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2b** (21.5 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ab** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (43 mg) in 94% yield; Mp 108–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 1H), 7.39 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.28–7.23 (m, 1H), 7.02–6.94 (m, 3H), 6.88 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.66 (td, *J* = 7.6, 1.0 Hz, 1H), 6.60 (ddd, *J* = 10.2, 2.0, 1.3 Hz, 1H), 6.40 (d, *J* = 8.3 Hz, 1H), 5.74 (dt, *J* = 6.1, 1.9 Hz, 1H), 5.28 (dd, *J* = 6.1, 2.4 Hz, 1H), 5.04 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.73 (d, *J* = 2.3 Hz, 1H), 3.68 (s, 3H), 3.64–3.61 (m, 1H), 3.60 (s, 3H), 3.11 (ddd, *J* = 17.9, 5.3, 2.0 Hz, 1H), 2.75–2.60 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 166.4, 156.2, 141.7, 141.0, 133.1, 132.5, 130.1, 129.7, 127.7, 127.1, 126.4, 125.6, 123.7, 120.8, 110.1, 106.4, 100.0, 95.2, 75.1, 64.9, 54.8, 50.8, 48.9, 34.1, 26.3 ppm; ESI-HRMS: calcd. for $C_{26}H_{24}N_2O_6$ + H^+ 461.1707, found 461.1704.

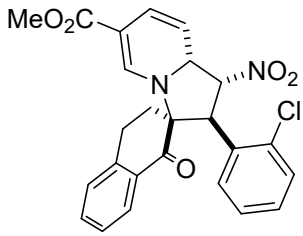


Synthesis of 5ac: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2c** (21.5 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ac** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (44 mg) in 96% yield; Mp 104–105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47–7.46 (m, 1H), 7.41 (s, 1H), 7.32 (td, *J* = 7.6, 1.4 Hz, 1H), 7.08 (d, *J* = 9.2 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 6.60 (ddd, *J* = 10.2, 2.0, 1.3 Hz, 1H), 6.51 (d, *J* = 8.8 Hz, 2H), 5.75 (dt, *J* = 6.1, 2.0 Hz, 1H), 5.30 (dd, *J* = 6.1, 2.5 Hz, 1H), 5.05 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.25 (d, *J* = 2.6 Hz, 1H), 3.67 (s, 3H), 3.62 (s, 3H), 3.47–3.38 (m, 1H), 3.26–3.19 (m, 1H), 2.73–2.68 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.8, 166.3, 159.3, 141.4, 140.6,

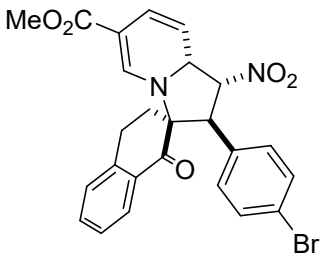
133.7, 132.1, 129.9, 128.0, 127.5, 127.0, 126.8, 125.6, 114.0, 106.3, 100.4, 95.6, 74.7, 65.1, 55.2, 54.1, 50.8, 33.6, 26.6 ppm; ESI-HRMS: calcd. for $C_{26}H_{24}N_2O_6$+ H^+ 461.1707, found 461.1701.



Synthesis of 5ad: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2d** (17.9 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ad** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (41 mg) in 95% yield; Mp 88–90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.42 (m, 2H), 7.30 (td, *J* = 7.6, 1.3 Hz, 1H), 7.07–7.02 (m, 2H), 7.00–6.98 (m, 3H), 6.91– 6.89(m, 2H), 6.60 (ddd, *J* = 10.2, 2.0, 1.3 Hz, 1H), 5.78 (dt, *J* = 6.0, 1.9 Hz, 1H), 5.32 (dd, *J* = 6.0, 2.3 Hz, 1H), 5.06 (dd, *J* = 10.2, 1.1 Hz, 1H), 4.30 (d, *J* = 2.3 Hz, 1H), 3.67 (s, 3H), 3.50–3.41 (m, 1H), 3.26–3.20 (m, 1H), 2.79–2.66 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.6, 166.3, 141.3, 140.6, 135.3, 133.7, 132.1, 128.7, 128.6, 128.3, 127.9, 127.6, 126.7, 125.7, 106.4, 100.4, 95.5, 74.9, 65.4, 54.7, 50.8, 33.7, 26.6 ppm; ESI-HRMS: calcd. for $C_{25}H_{22}N_2O_5$ + H^+ 431.1601, found 431.1597.

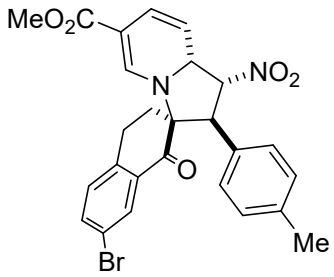


Synthesis of 5ae: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2e** (22.0 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ae** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (36 mg) in 78% yield; 7.1:1 d.r.; Mp 144–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.45 (s, 1H), 7.32 (td, *J* = 7.6, 1.4 Hz, 1H), 7.10–7.04 (m, 3H), 7.00–6.91 (m, 3H), 6.61 (ddd, *J* = 10.1, 2.1, 1.2 Hz, 1H), 5.76 (dt, *J* = 6.5, 2.0 Hz, 1H), 5.23 (dd, *J* = 6.5, 3.4 Hz, 1H), 5.04 (d, *J* = 3.4 Hz, 1H), 5.01 (dd, *J* = 10.1, 1.3 Hz, 1H), 3.68 (s, 3H), 3.65–3.56 (m, 1H), 3.16 (ddd, *J* = 18.1, 5.1, 3.1 Hz, 1H), 2.80–2.66 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.1, 166.3, 141.9, 140.4, 134.2, 133.9, 133.2, 132.1, 129.9, 129.8, 129.3, 128.3, 127.5, 127.3, 126.7, 125.7, 106.2, 101.0, 95.4, 75.5, 64.4, 50.9, 50.0, 33.6, 26.3 ppm; ESI-HRMS: calcd. for $C_{25}H_{21}ClN_2O_5$ + H^+ 465.1212, found 465.1205.

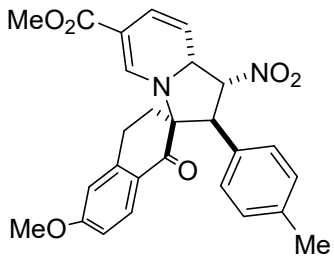


Synthesis of 5af: pyridinium salt **4a** (36.1 mg, 0.10 mmol) and nitroolefin **2f** (27.2 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5af** was obtained by flash chromatography

(EtOAc/petroleum ether = 1/4) as a yellow solid (47 mg) in 93% yield; Mp 156–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* = 7.9 Hz, 1H), 7.41 (s, 1H), 7.37 (td, *J* = 7.5, 1.3 Hz, 1H), 7.14–7.08 (m, 4H), 6.79 (d, *J* = 8.5 Hz, 2H), 6.60 (ddd, *J* = 10.2, 1.9, 1.3 Hz, 1H), 5.73 (dt, *J* = 6.1, 1.9 Hz, 1H), 5.29 (dd, *J* = 6.1, 2.6 Hz, 1H), 5.06 (dd, *J* = 10.2, 1.3 Hz, 1H), 4.24 (d, *J* = 2.6 Hz, 1H), 3.67 (s, 3H), 3.42–3.34 (m, 1H), 3.25 (dt, *J* = 17.9, 4.4 Hz, 1H), 2.74–2.69 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.3, 166.2, 141.2, 140.3, 134.2, 134.1, 131.92, 131.7, 130.4, 128.1, 127.7, 127.0, 125.7, 122.5, 106.4, 100.7, 95.2, 74.8, 65.2, 54.2, 50.9, 33.4, 26.5 ppm; ESI-HRMS: calcd. for $C_{25}H_{21}BrN_2O_5$ + H^+ 509.0707 found 509.0705.

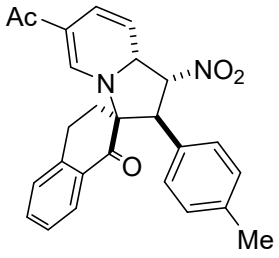


Synthesis of 5ba: pyridinium salt **4b** (43.9 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ba** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (38 mg) in 73% yield; Mp 163–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (dd, *J* = 18.6, 10.4 Hz, 3H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 7.9 Hz, 2H), 6.60 (d, *J* = 10.1 Hz, 1H), 5.73 (d, *J* = 5.7 Hz, 1H), 5.29 (d, *J* = 4.5 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 4.24 (s, 1H), 3.67 (s, 3H), 3.42–3.34 (m, 1H), 3.20 (d, *J* = 16.0 Hz, 1H), 2.77–2.62 (m, 2H), 2.17 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.7, 166.2, 140.4, 139.9, 138.7, 136.2, 133.7, 131.9, 130.1, 129.6, 129.3, 128.5, 125.7, 120.7, 106.5, 100.6, 95.3, 74.8, 65.5, 54.1, 50.9, 33.2, 26.2, 20.8 ppm; ESI-HRMS: calcd. for $C_{26}H_{23}BrN_2O_5$ + H^+ 523.0863, found 523.0854.

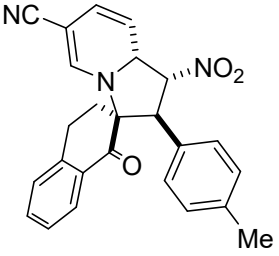


Synthesis of 5ca: pyridinium salt **4c** (39.1 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ca** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (44 mg) in 93% yield; Mp 88–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.8 Hz, 1H), 7.42 (s, 1H), 6.83 (s, 4H), 6.59 (d, *J* = 9.3 Hz, 2H), 6.51 (s, 1H), 5.77 (d, *J* = 6.0 Hz, 1H), 5.34 (dd, *J* = 5.8, 2.5 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), 4.20 (d, *J* = 2.4 Hz, 1H), 3.79 (s, 3H), 3.67 (s, 3H), 3.39–3.31 (m, 1H), 3.16–3.12 (m, 1H), 2.69–2.66 (m, 2H), 2.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.1, 166.4, 163.9, 144.1, 140.6, 138.1, 132.2, 130.2, 129.2, 128.6, 125.7, 125.5, 113.6, 111.7, 106.4, 100.3,

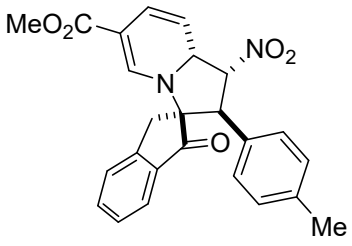
95.7, 74.4, 65.0, 55.4, 55.1, 50.8, 33.8, 26.9, 20.8 ppm; ESI-HRMS: calcd. for $C_{27}H_{26}N_2O_6$ + H^+ 475,1864, found 475.1858.



Synthesis of 5da: pyridinium salt **4d** (34.5 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5da** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (41 mg) in 96% yield; Mp 110–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.36 (s, 1H), 7.32 (td, *J* = 7.6, 1.3 Hz, 1H), 7.10–7.02 (m, 2H), 6.80–6.72 (m, 5H), 5.75 (dt, *J* = 5.9, 1.9 Hz, 1H), 5.29 (dd, *J* = 6.0, 2.2 Hz, 1H), 5.13 (dd, *J* = 10.2, 1.3 Hz, 1H), 4.29 (d, *J* = 2.2 Hz, 1H), 3.52–3.43 (m, 1H), 3.24 (ddd, *J* = 17.8, 5.0, 2.7 Hz, 1H), 2.81–2.69 (m, 2H), 2.14 (s, 3H), 2.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7, 191.6, 141.3, 141.3, 138.3, 133.7, 132.1, 132.0, 129.2, 128.5, 127.9, 127.6, 126.7, 125.3, 111.3, 107.1, 95.3, 75.1, 65.4, 54.3, 33.8, 26.6, 24.5, 20.7 ppm; ESI-HRMS: calcd. for $C_{26}H_{24}N_2O_4$+ H^+ 429.1809, found 429.1808.



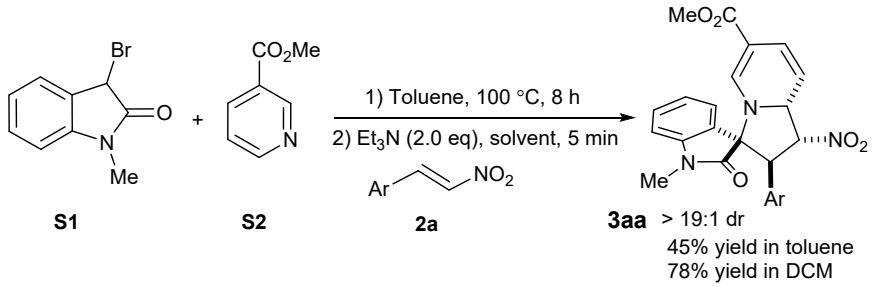
Synthesis of 5ea: pyridinium salt **4e** (32.8 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5ea** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (34 mg) in 83% yield; Mp 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.8 Hz, 1H), 7.34–7.30 (m, 1H), 7.08–7.01 (m, 2H), 6.91 (s, 1H), 6.78–6.72 (m, 4H), 6.07 (d, *J* = 10.0 Hz, 1H), 5.72 (dd, *J* = 4.1, 1.9 Hz, 1H), 5.29 (dd, *J* = 6.0, 2.2 Hz, 1H), 5.09 (d, *J* = 10.1 Hz, 1H), 4.25 (d, *J* = 2.2 Hz, 1H), 3.48–3.40 (m, 1H), 3.25–3.18 (m, 1H), 2.76–2.70 (m, 1H), 2.55 (td, *J* = 12.5, 5.3 Hz, 1H), 2.10 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.4, 142.4, 141.2, 138.3, 133.8, 131.9, 131.7, 129.2, 128.4, 127.9, 127.5, 126.7, 124.7, 120.0, 108.2, 95.2, 80.7, 75.1, 64.4, 54.0, 33.6, 26.5, 20.7 ppm; ESI-HRMS: calcd. for $C_{25}H_{21}N_3O_3$ + H^+ 412.1656, found 412.1652.



Synthesis of 5fa: pyridinium salt **4f** (34.7 mg, 0.10 mmol) and nitroolefin **2a** (19.6 mg, 0.12 mmol) were dissolved in DCM (2.0 mL), Et_3N was added and stirred at room temperature for 5 minutes. Upon workup, product **5fa** was obtained by flash chromatography

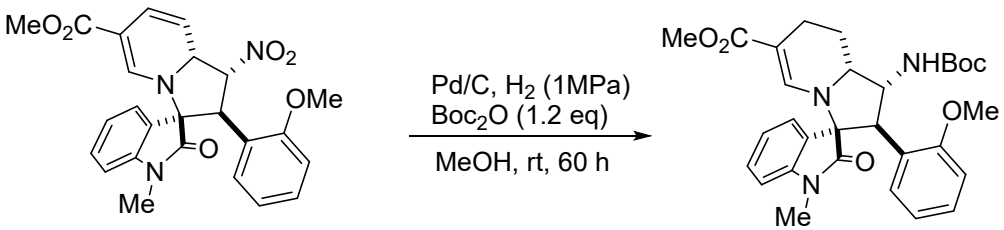
(EtOAc/petroleum ether = 1/4) as a yellow solid (28 mg) in 65% yield; Mp 91–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (t, J = 7.5 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.1 Hz, 3H), 6.56 (d, J = 9.8 Hz, 1H), 6.01 (dd, J = 11.4, 8.8 Hz, 1H), 5.28–5.20 (m, 2H), 4.25 (d, J = 11.4 Hz, 1H), 3.68 (s, 2H), 3.65 (s, 3H), 2.17 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.5, 166.2, 150.2, 139.3, 138.7, 136.2, 134.0, 129.5, 128.4, 128.3, 126.7, 125.8, 124.7, 124.0, 108.2, 103.8, 87.6, 75.8, 62.2, 56.6, 51.0, 38.5, 20.9 ppm. ESI-HRMS: calcd. for $C_{25}H_{22}N_2O_5$ + Na^+ 453.1421, found 453.1449.

6. The procedure of three-component one-pot sequential reaction



Procedure: A solution of **S1** (34 mg, 0.15 mmol) and **S2** (28 mg, 0.2 mmol) was stirred in anhydrous toluene (1.0 mL) at 100 °C for 8 h for the generation of pyridinum salt **1a**. After cooled down to room temperature, nitroolefin **2a** (16.3 mg, 0.1 mmol) and Et_3N (20 mg, 0.2 mmol) were added in sequential. The reaction was stirred for further 5 min to reach the consumption. The solvent was evaporated in vacuo and product **3aa** was obtained by flash chromatography (EtOAc/petroleum ether = 1/4) as a yellow solid (18 mg, 40% yield, > 19:1 d.r.). Alternatively, after the generation of salt **1a**, toluene was evaporated in vacuo and DCM (1.0 mL) was added followed by the addition of nitroolefin **2a** (16.3 mg, 0.1 mmol) and Et_3N (20 mg, 0.2 mmol) in sequential at room temperature for 5 min. The product **3aa** was obtained as a yellow solid in good yield by the above operation (32 mg, 72% yield, > 19:1 d.r.).

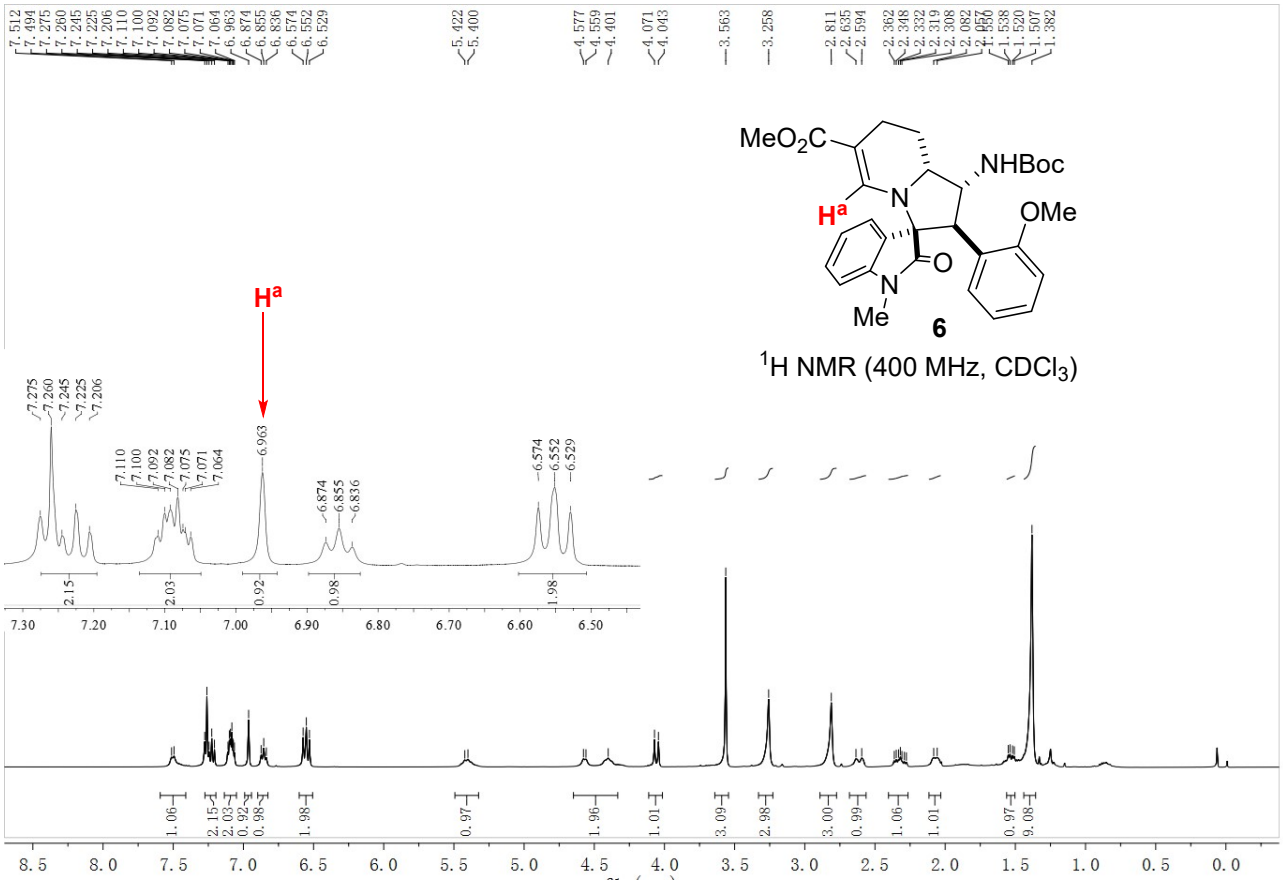
7. Synthetic transformations

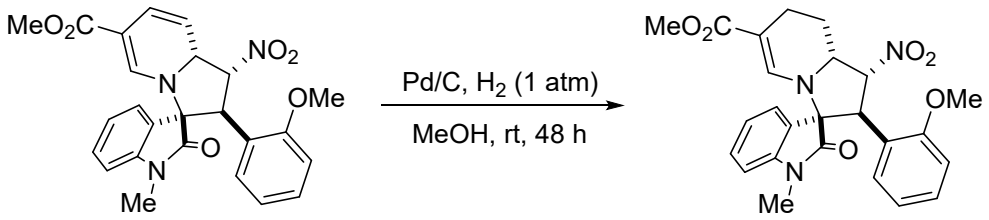


3ab **6**

Synthesis of 6: In an autoclave, cycloadduct **3ab** (46.1 mg, 0.10 mmol) in MeOH (2.0 ml) was added Pd/C (5 mg) and Boc_2O (26.2 mg, 0.12 mmol), and stirred for 60 h at room temperature under hydrogen atmosphere at 1.0 MPa. Upon workup, the mixture was filtered through celite and the filtrate was concentrated and purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/3) to give product **6** as a yellow solid (43 mg, 80% yield); Mp 132–134 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.0 Hz, 1H), 7.28–7.21 (m, 2H), 7.11–7.06 (m, 2H), 6.96 (s, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.57–6.53 (m, 2H), 5.41 (d, *J* = 9.1 Hz, 1H), 4.58–4.40 (m, 2H), 4.06 (d, *J* = 11.3 Hz, 1H), 3.56 (s, 3H), 3.26 (s, 3H), 2.81 (s, 3H), 2.61 (d, *J* = 16.5 Hz, 1H), 2.36–2.28 (m, 1H), 2.07 (d, *J* = 9.9 Hz, 1H), 1.53 (dd, *J* = 12.2, 5.0 Hz, 1H), 1.38 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 168.7, 157.9, 155.6, 144.3, 140.1, 129.8, 128.8, 128.5, 125.2, 124.7, 122.4, 120.9, 120.6, 109.9, 108.1, 97.8, 79.7, 73.6, 58.2, 54.7, 53.1, 50.5, 50.3, 28.2, 25.6, 22.8, 21.2 ppm; ESI-HRMS: calcd. for $C_{30}H_{35}N_3O_6 + H^+$ 534.2599, found 534.2587.

Structure characterization of 6: Based on the ^{1}H-NMR spectra of **3ab** and other prepared cycloadducts, the H-shift of H^a, which is the only singlet at aromatic region in the spectra, is easily identified at about δ 7.0. After the hydrogenation under the catalysis of palladium, the ^{1}H-spectra of the observed product **6** still retained the singlet at δ 6.96, which implied the conjugated C=C bond remained rather than the other C=C bond on the pyridine moiety. Meanwhile, the other H-shifts and the C-shifts are reasonable in accordance with the structure **6**.

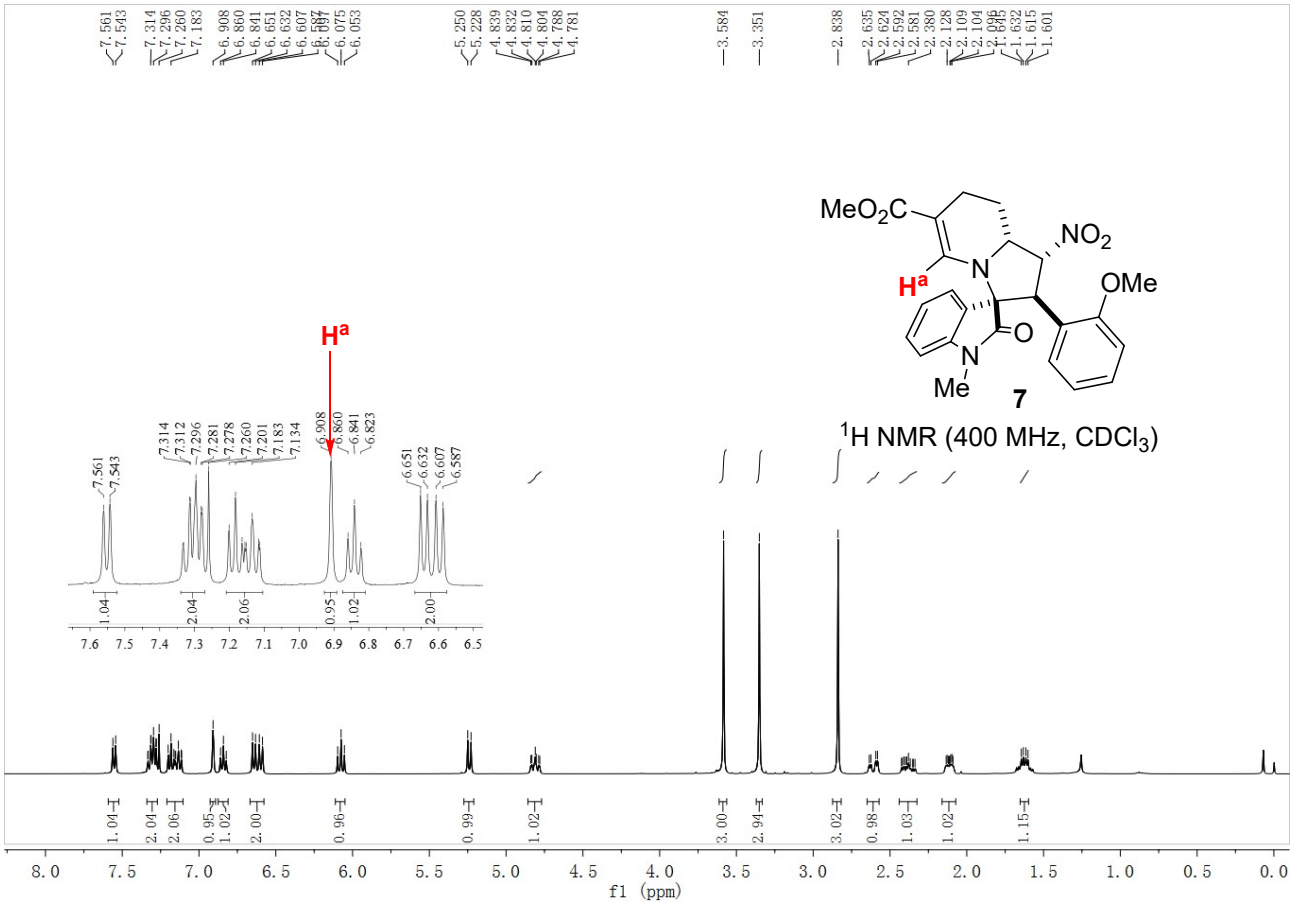

MeO2C
NHBoc
Ha
N
OMe
O
N
Me
6
1H NMR (400 MHz, CDCl3)
Ha

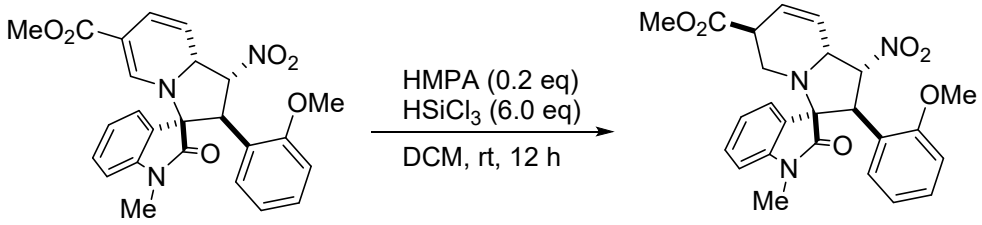


3ab **7**

Synthesis of 7: In an autoclave, cycloadduct **3ab** (46.1 mg, 0.10 mmol) in MeOH (2.0 ml) was added Pd/C (5 mg) and stirred for 48 h at room temperature under hydrogen atmosphere at 1.0 atm. Upon workup, the mixture was filtered through celite and the filtrate was concentrated and purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/4) to give product **7** as a yellow solid (42.6 mg, 92% yield); Mp 145–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.2 Hz, 1H), 7.33–7.28 (m, 2H), 7.15 (ddd, *J* = 15.7, 11.8, 4.4 Hz, 2H), 6.91 (s, 1H), 6.84 (t, *J* = 7.4 Hz, 1H), 6.65–6.59 (m, 2H), 6.07 (t, *J* = 8.8 Hz, 1H), 5.24 (d, *J* = 8.7 Hz, 1H), 4.84–4.78 (m, 1H), 3.58 (s, 3H), 3.35 (s, 3H), 2.84 (s, 3H), 2.61 (dd, *J* = 17.1, 4.4 Hz, 1H), 2.43–2.34 (m, 1H), 2.13–2.09 (m, 1H), 1.62 (dd, *J* = 12.1, 5.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 168.2, 157.7, 144.5, 138.4, 130.5, 129.5, 128.3, 125.8, 123.7, 123.1, 120.5, 120.2, 110.6, 108.4, 99.7, 89.6, 74.2, 57.5, 55.0, 50.8, 49.0, 25.7, 22.7, 20.7 ppm; ESI-HRMS: calcd. for $C_{25}H_{25}N_3O_6$+ H^+ 464.1816, found 464.1813.

Structure characterization of 7: As above discussion, the H^a of structure **7** was observed as an obvious singlet at δ 6.908, which implied the structure **7** was reasonable. Additionally, the other H-shifts and the C-shifts are reasonable in accordance with the structure **7**.

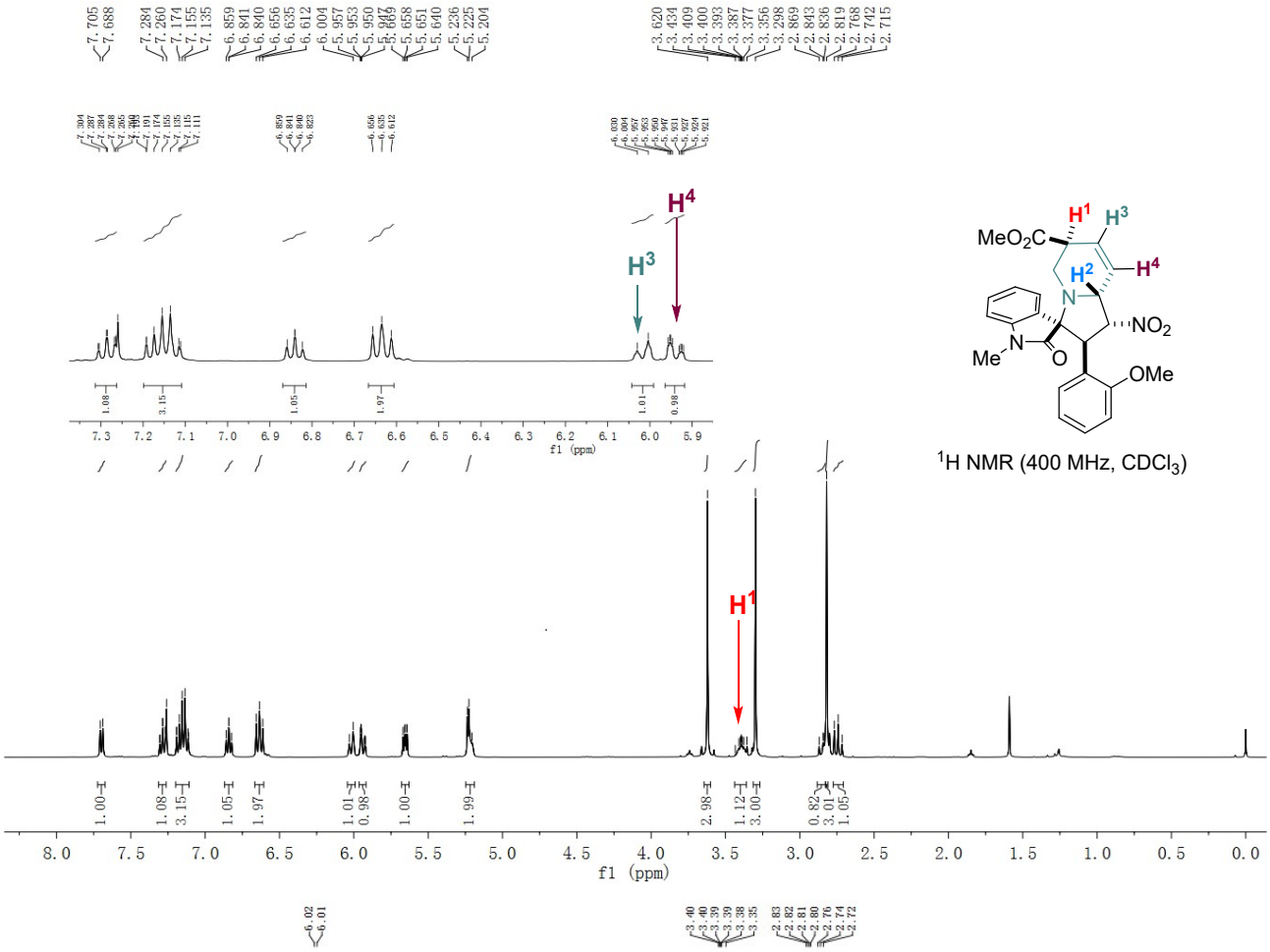

MeO2C
NO2
Ha
OMe
N
O
N
Me
7
1H NMR (400 MHz, CDCl3)
f1 (ppm)



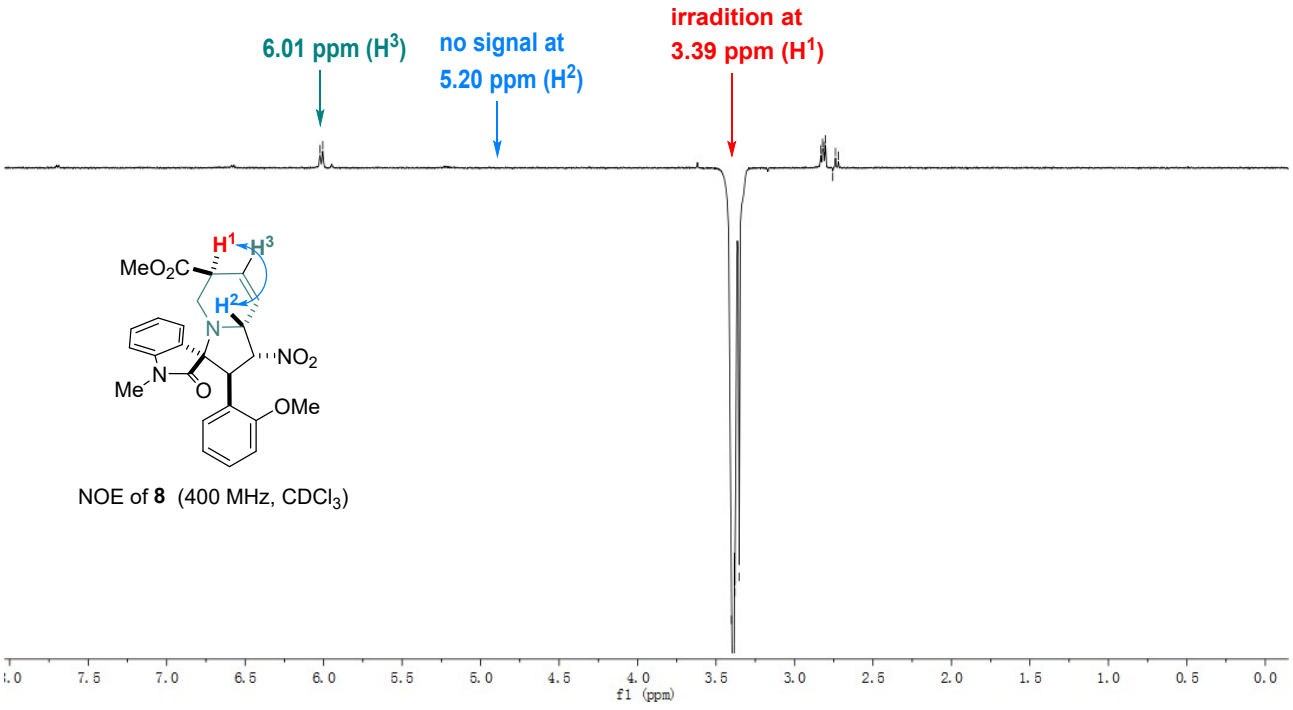
3ab **8**

Synthesis of 8: Cycloadduct **3ab** (46.1 mg, 0.1 mmol) in DCM (2.0 ml) was added HMPA (3.6 mg, 0.02mmol) and $HSiCl_3$ (81.3 mg, 0.6 mmol), then stirred at room temperature for 12 h. Upon workup, the mixture was cooled to 0 ^oC and saturated $NaHCO_3$ was slowly added until pH = 7, then extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum, then purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/6) to give product **8** as a yellow solid (27.8 mg, 60% yield); Mp 139–141 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 6.8 Hz, 1H), 7.31–7.27 (m, 1H), 7.19–7.11 (m, 3H), 6.84 (dd, *J* = 7.5, 6.9 Hz, 1H), 6.66– 6.61(m, 2H), 6.02 (d, *J* = 10.3 Hz, 1H), 5.94 (ddd, *J* = 10.4, 2.6, 1.5 Hz, 1H), 5.65 (dd, *J* = 7.2, 4.3 Hz, 1H), 5.24–5.20 (m, 2H), 3.62 (s, 3H), 3.43–3.36 (m, 1H), 3.30 (s, 3H), 2.87–2.84 (m, 1H), 2.82 (s, 3H), 2.74 (t, *J* = 10.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 171.9, 157.4, 144.3, 129.4, 129.3, 128.9, 127.5, 126.8, 125.0, 124.9, 123.0, 122.8, 120.4, 110.3, 107.5, 91.5, 74.8, 60.6, 54.9, 51.9, 50.8, 44.4, 42.4, 25.4 ppm; ESI-HRMS: calcd. for $C_{25}H_{25}N_3O_6$+ H^+ 464.1816, found 464.1803.

Structure characterization of 8: As above discussion, there is no singlet at aromatic region in the ^1H-spectra of the obtained product **8**, and the appearance of a couple of olefin hydrogen H^3 and H^4 at δ 6.00 and 5.93 implied the conjugated C=C bond was reduced. Meanwhile, the rest H shift and C shift were reasonable in accordance with the structure **8**. Additionally, the relative configuration of the resulting generated ester group was determined via the NOE of **8**.

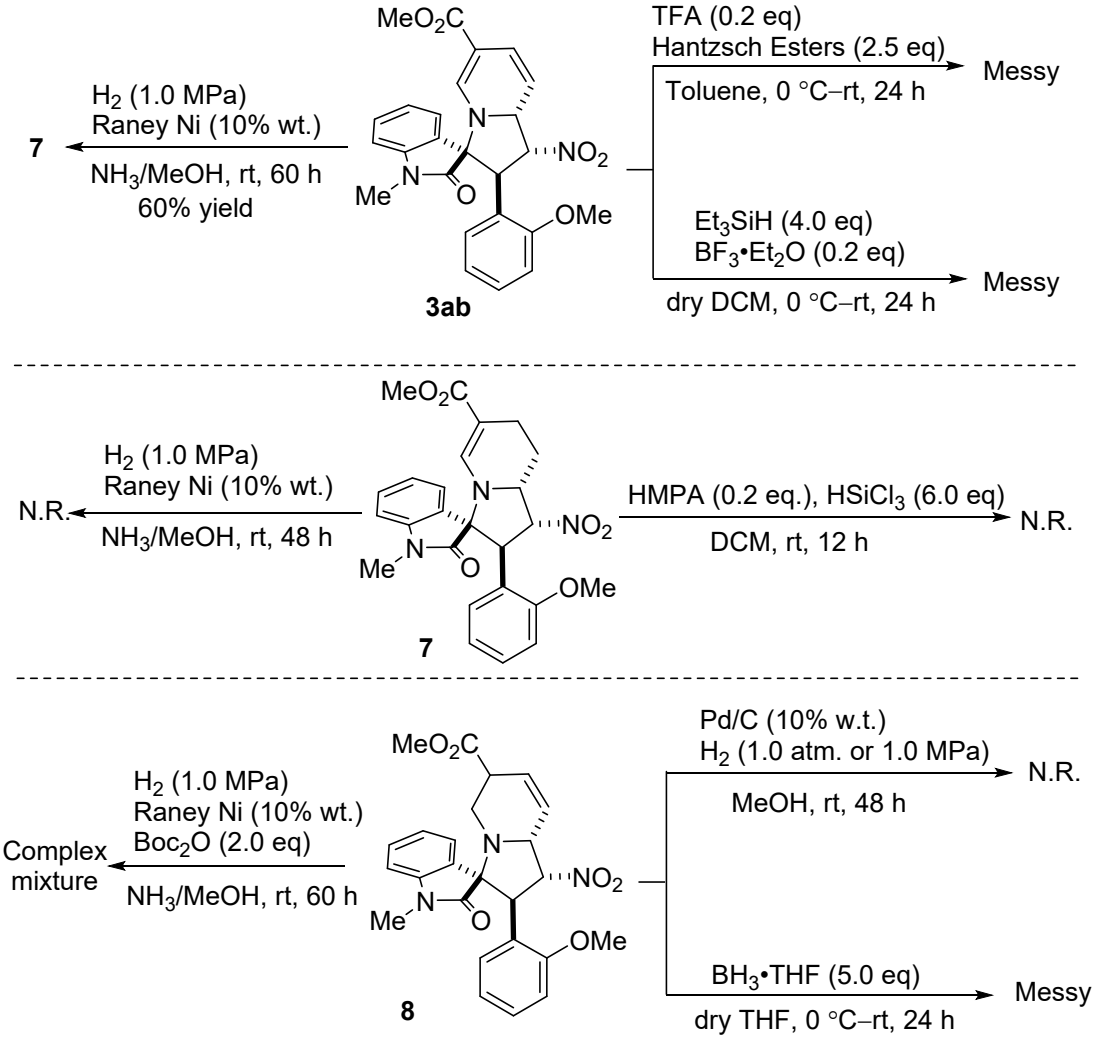


^{1}H NMR (400 MHz, $CDCl_3$)



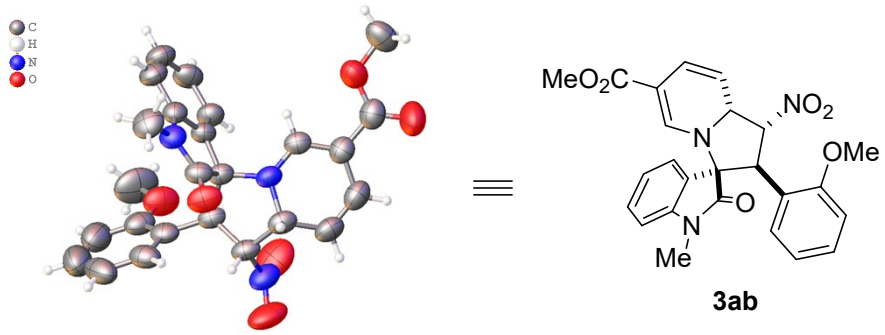
NOE of **8** (400 MHz, $CDCl_3$)

8. Attempts for the hydrogenation of the both C=C bond on the pyridine moiety with product 3ab.



9. Crystal data and structure refinement for 3ab and 5ba

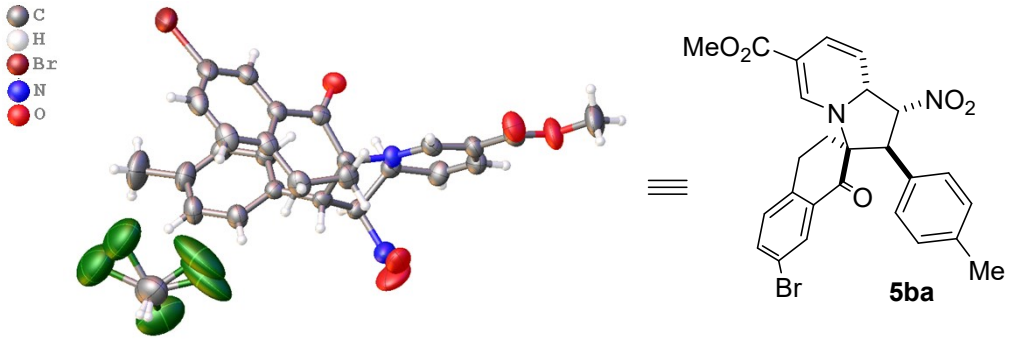
Crystallization of 3ab: The pure product **3ab** (40 mg) was dissolved in the mixture solvent of $CHCl_3$ and *iso*-propanol (3 mL, 1:2, v/v) in a 10 mL vial. Then, the solution was allowed for slow evaporation to afford the crystal of **3ab** in a good quality for the crystallography analysis.



Identification code	**3ab**
Empirical formula	$C_{26}H_{24}Cl_3N_3O_6$
Formula weight	580.83
Temperature/K	290.0
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	15.6783(5)
b/Å	8.3762(2)
c/Å	21.0950(6)
α/°	90
β/°	101.617(2)
γ/°	90
Volume/Å^3	2713.54(13)
Z	4
ρ_{calc}g/cm^3	1.422
μ/mm^{-1}	3.452
F(000)	1200.0
Crystal size/mm^3	0.4 × 0.2 × 0.1
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.442 to 127.872
Index ranges	$-18 \le h \le 18$, $-9 \le k \le 8$, $-24 \le l \le 24$
Reflections collected	27635

Independent reflections	4459 [R_{int} = 0.0734, R_{sigma} = 0.0437]
Data/restraints/parameters	4459/0/376
Goodness-of-fit on F^2	1.058
Final R indexes [I>=2σ (I)]	R_1 = 0.0836, wR_2 = 0.2221
Final R indexes [all data]	R_1 = 0.1055, wR_2 = 0.2474
Largest diff. peak/hole / e $Å^{-3}$	0.78/-0.37

Crystallization of 5ba: The pure product **5ba** (30 mg) was dissolved in the mixture solvent of $CHCl_3$ and petroleum ether (3 mL, 1:1, v/v) in a 10 mL vial. Then, the solution was allowed for slow evaporation to afford the crystal of **5ba** in a good quality for the for the crystallography analysis.



Identification code	**5ba**
Empirical formula	$C_{27}H_{24}BrCl_3N_2O_5$
Formula weight	642.74
Temperature/K	293.15
Crystal system	monoclinic
Space group	P21/c
a/Å	13.953(2)
b/Å	12.3736(16)
c/Å	16.418(3)
α/°	90
β/°	102.001(17)
γ/°	90
Volume/Å3	2772.7(8)
Z	4

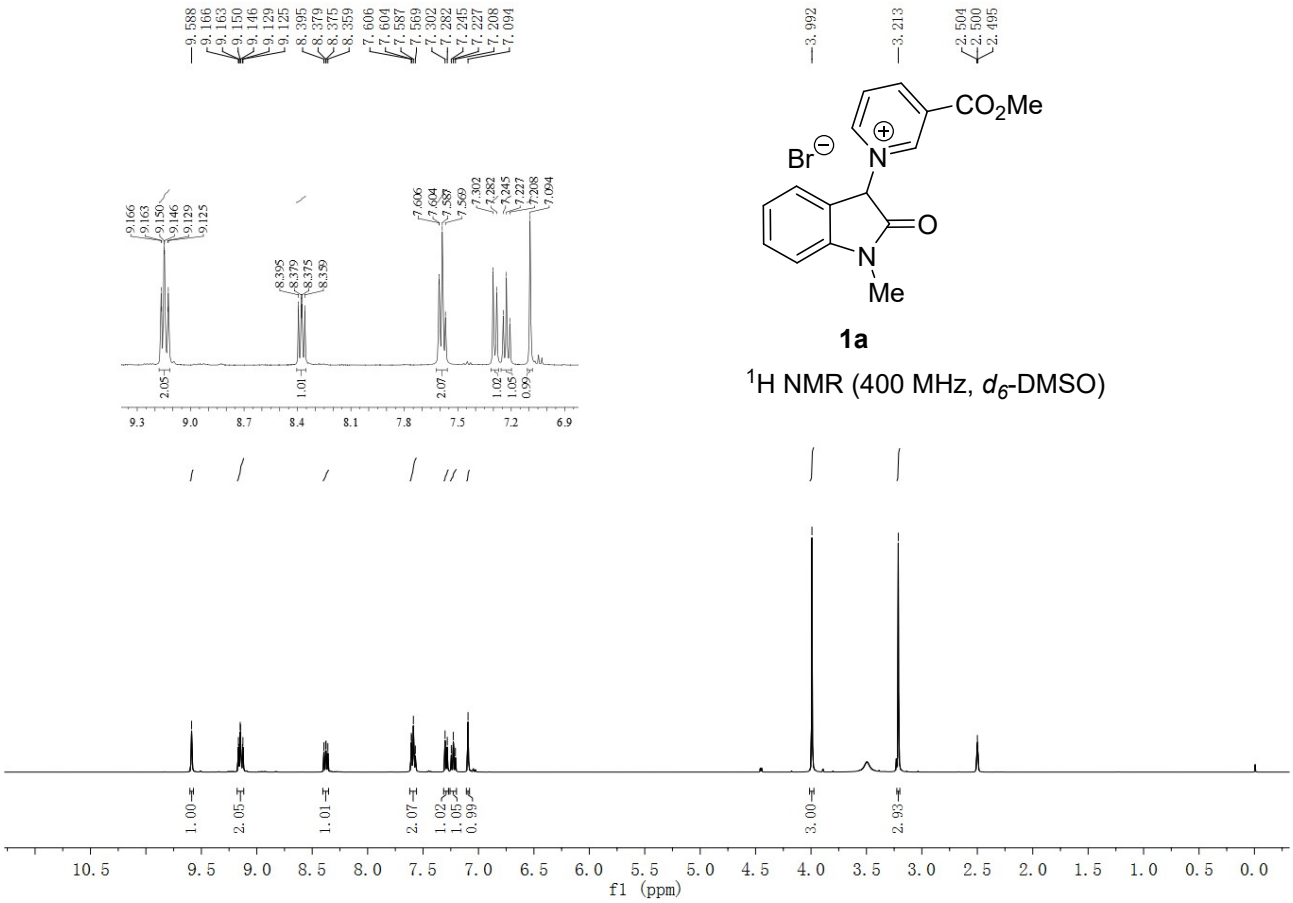
ρcalcg/cm3	1.540
μ/mm-1	1.812
F(000)	1304.0
Crystal size/mm3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.97 to 52.744
Index ranges	-14 ≤ h ≤ 17, -14 ≤ k ≤ 15, -16 ≤ l ≤ 20
Reflections collected	12437
Independent reflections	5673 [Rint = 0.0262, Rsigma = 0.0518]
Data/restraints/parameters	5673/0/352
Goodness-of-fit on F2	1.044
Final R indexes [I>=2σ (I)]	R1 = 0.0639, wR2 = 0.1622
Final R indexes [all data]	R1 = 0.1126, wR2 = 0.1907
Largest diff. peak/hole / e Å-3	0.82/-0.80

[1] A. F. McAnda, K. D. Roberts, A. J. Smallridge, A. Ten and M. A. Trewhella, Mechanism of the yeast mediated reduction of nitrostyrenes in light petroleum, *J. Chem. Soc., Perkin Trans. 1*, **1998**, *29*, 501.

[2] P.-F. Zheng, Q. Ouyang, S.-L. Niu, L. Shuai, Y. Yuan, K. Jiang, T.-Y. Liu, and Y.-C. Chen, Enantioselective [4 + 1] Annulation Reactions of α-Substituted Ammonium Ylides To Construct Spirocyclic Oxindoles, *J. Am. Chem. Soc.*, **2015**, *137*, 9390.

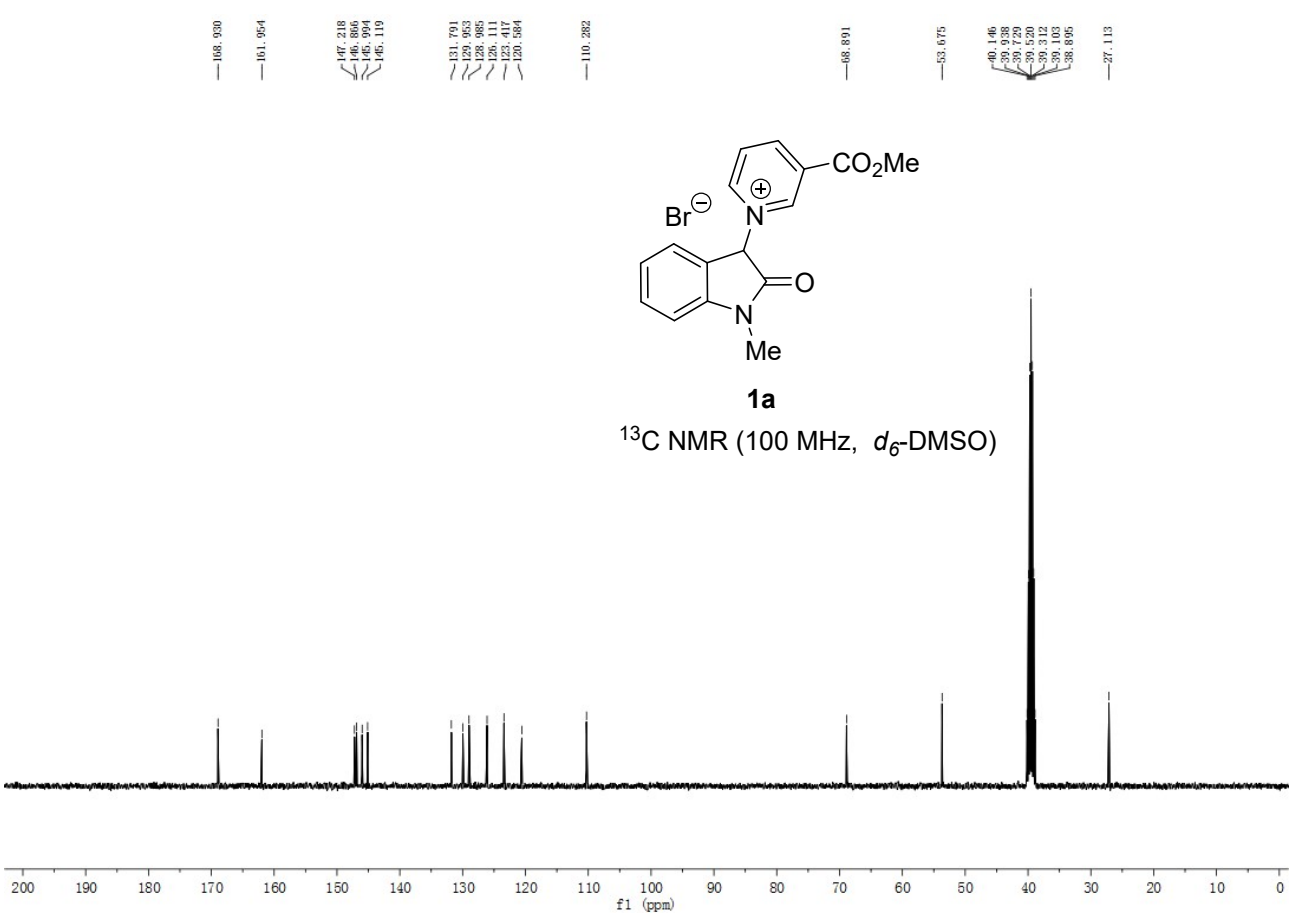
[3] K. Tanemura, T. Suzuki, Y. Nishida, K. Satsumabayashia and T. Horaguchib, A mild and efficient procedure for α-bromination of ketones using *N*-bromosuccinimide catalysed by ammonium acetate, *Chem. Commun.*, **2004**, *35*, 470.

10. NMR spectra



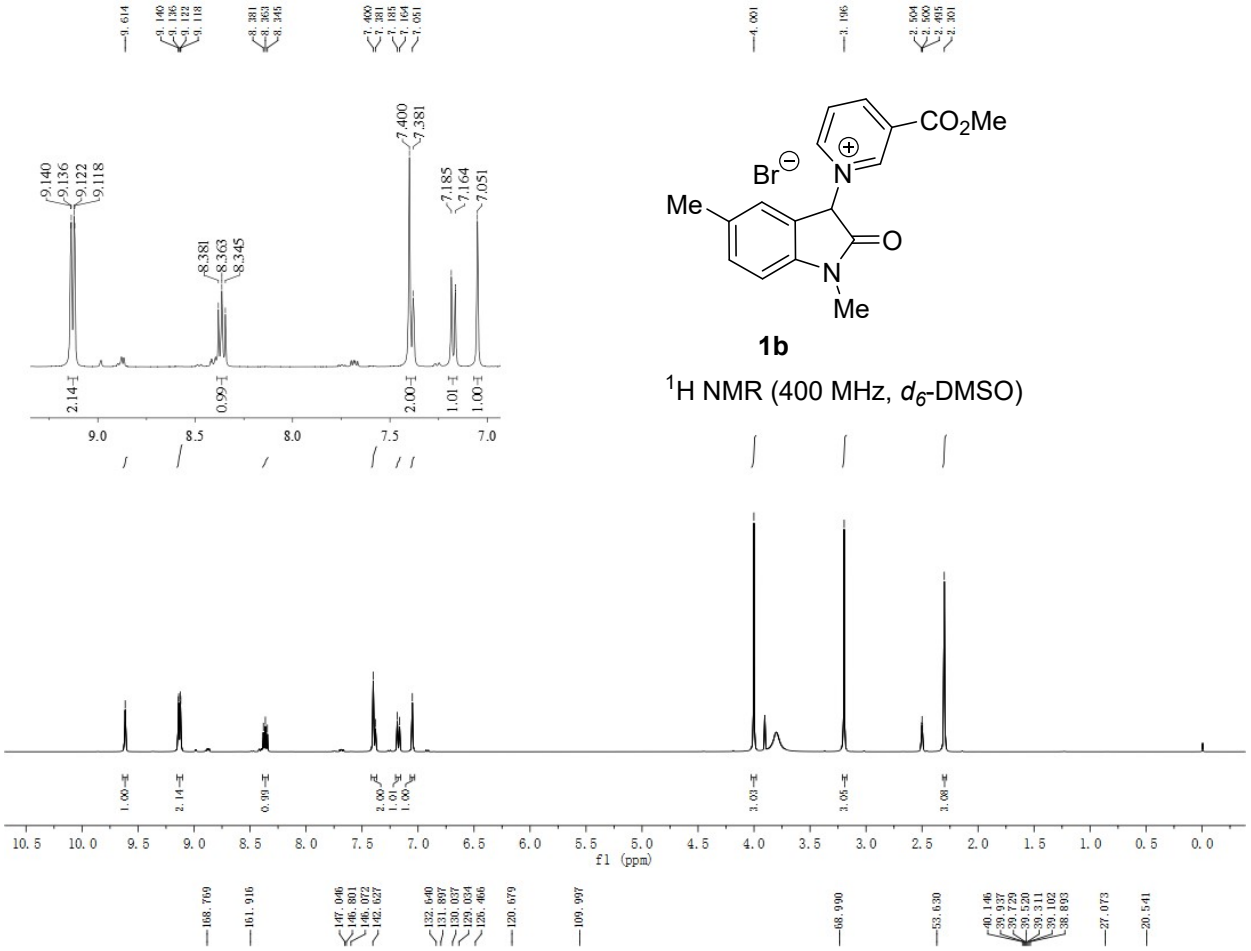
1a

^{1}H NMR (400 MHz, d_6-DMSO)



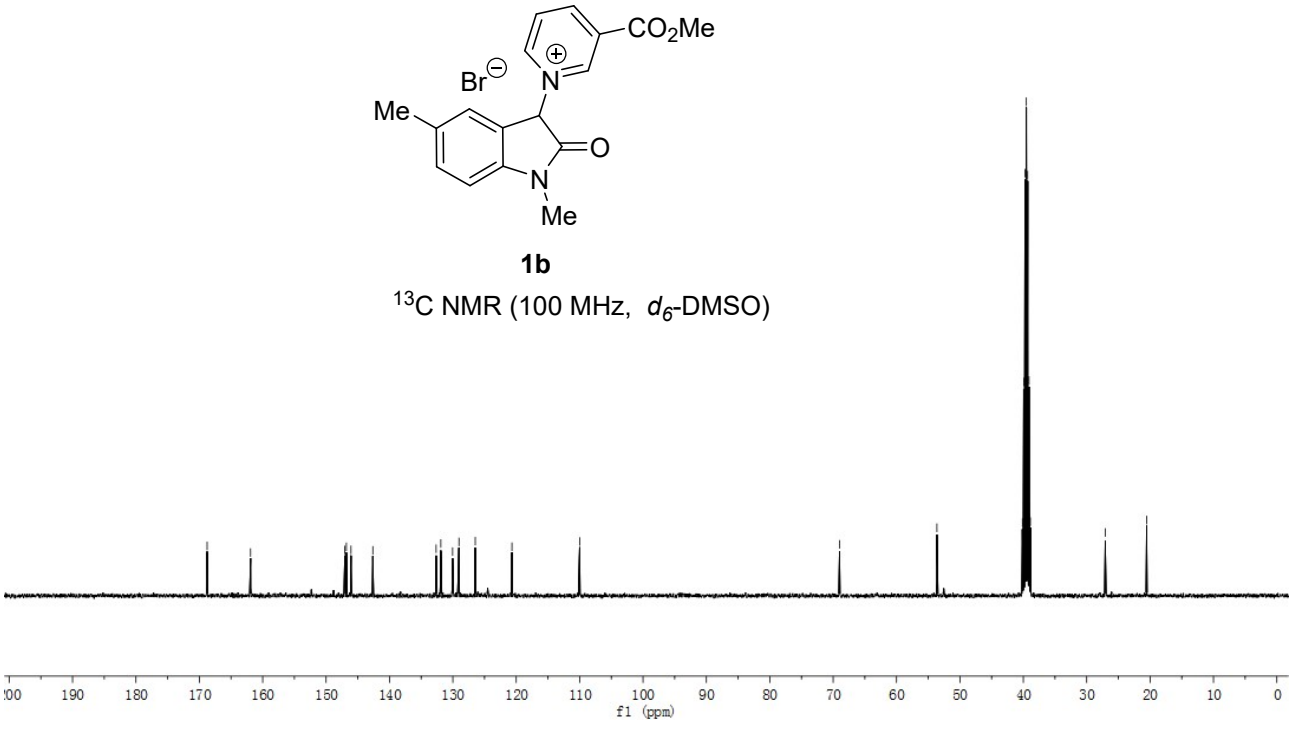
1a

^{13}C NMR (100 MHz, d_6-DMSO)



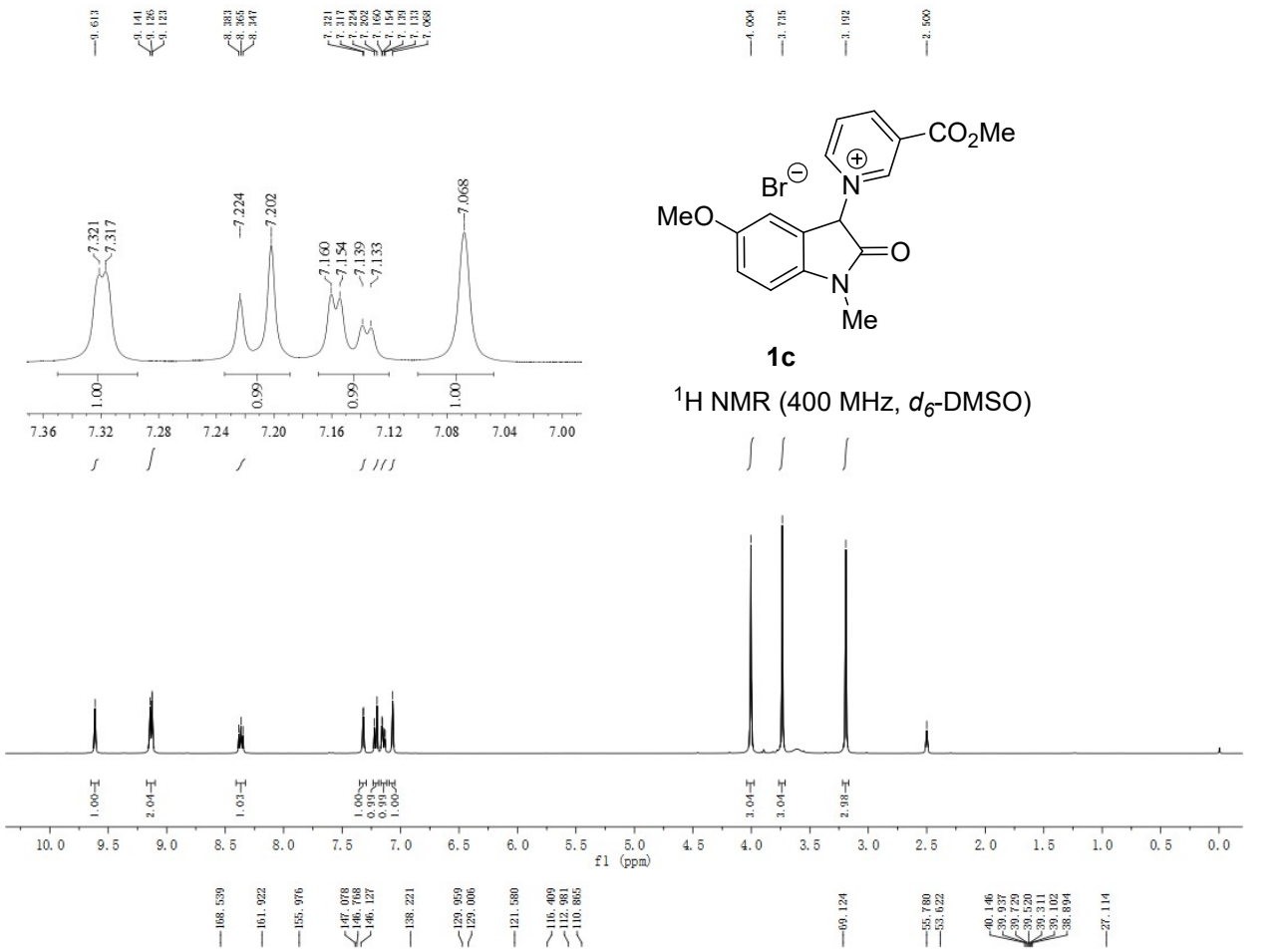
1b

^{1}H NMR (400 MHz, d_6-DMSO)



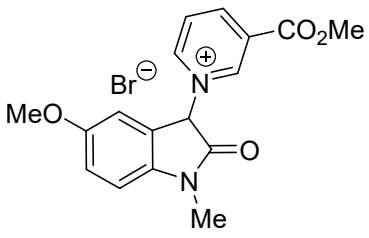
1b

^{13}C NMR (100 MHz, d_6-DMSO)



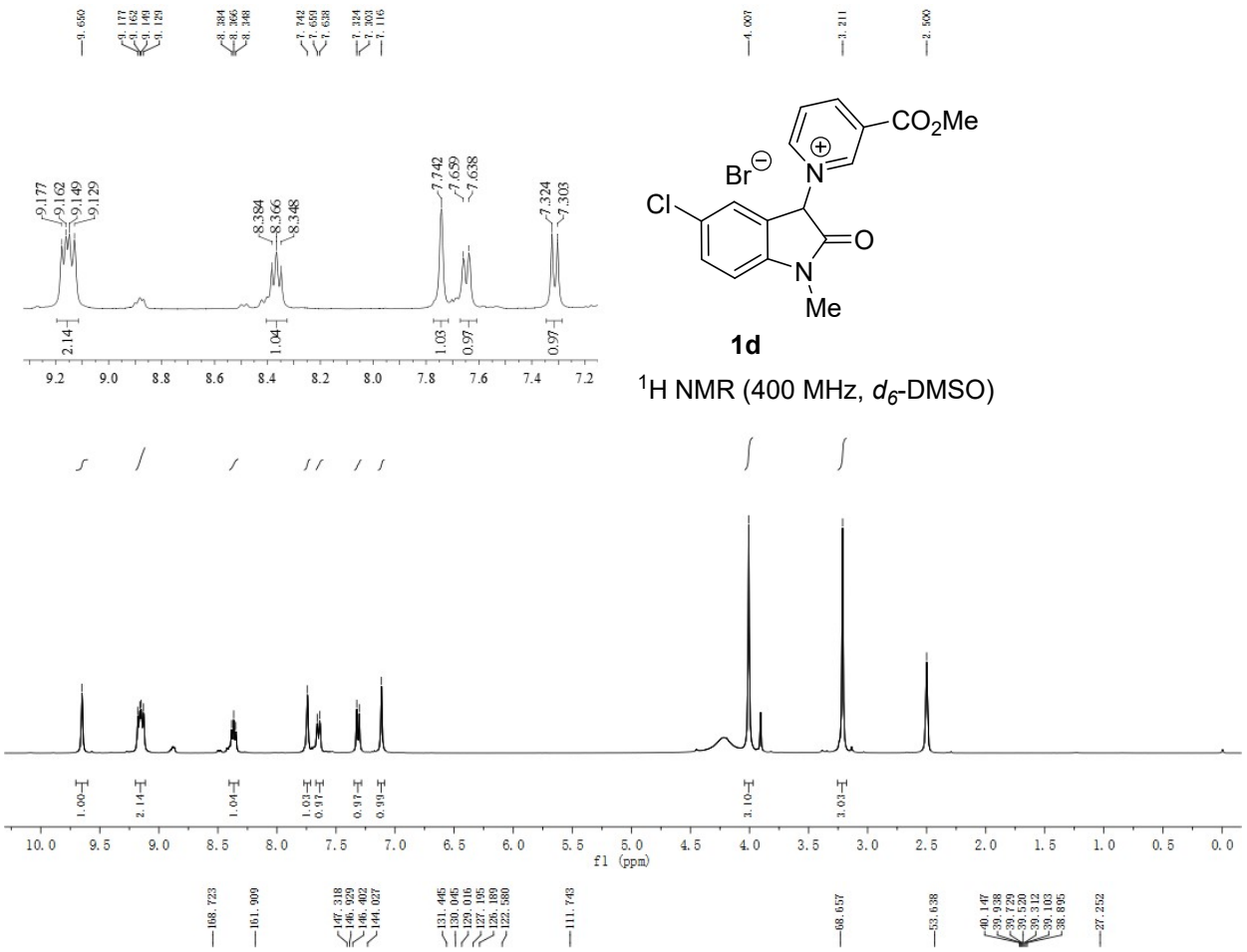
1c

^{1}H NMR (400 MHz, d_6-DMSO)



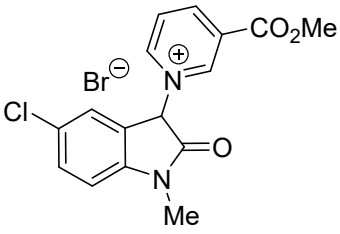
1c

^{13}C NMR (100 MHz, d_6-DMSO)



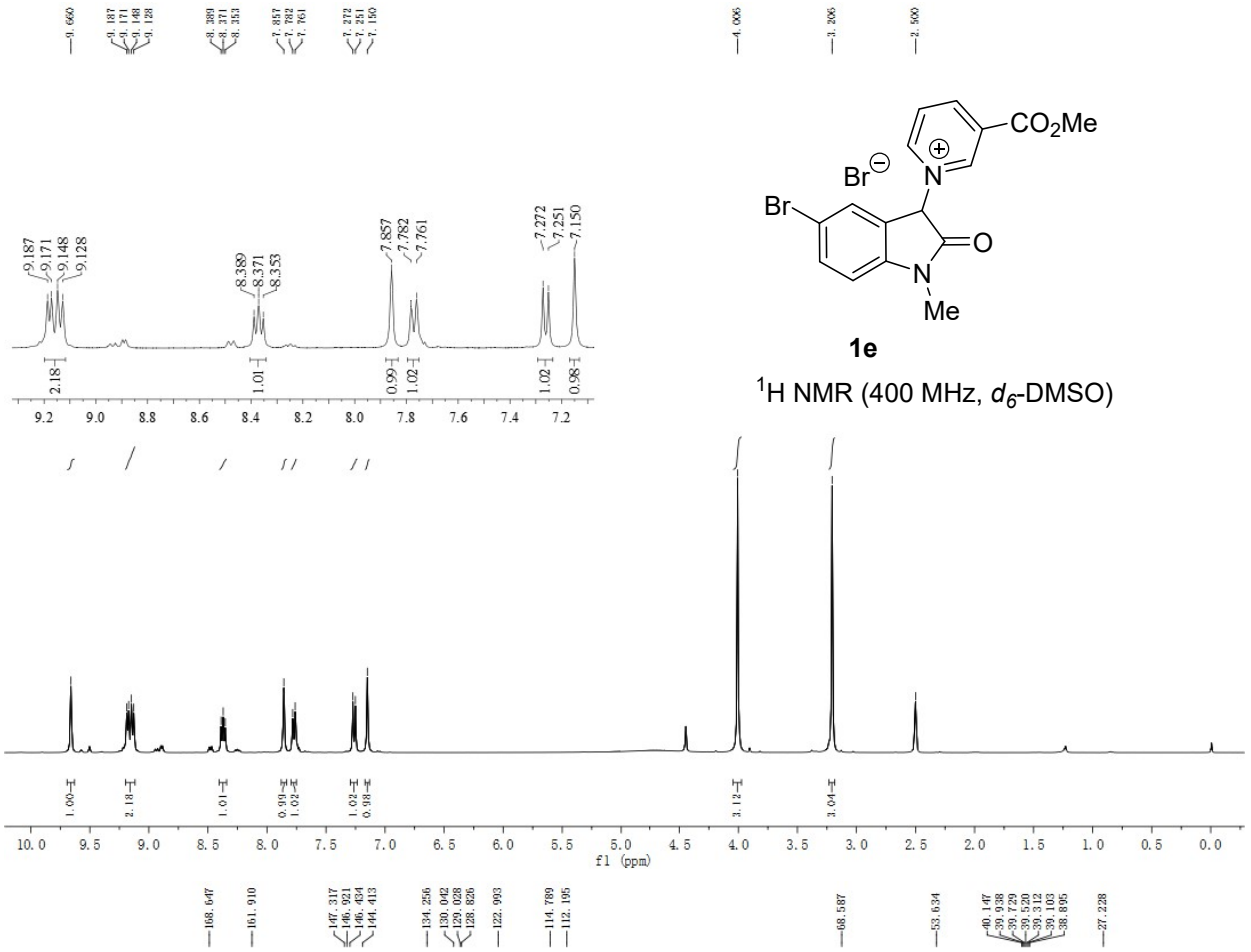
1d

^{1}H NMR (400 MHz, d_6-DMSO)



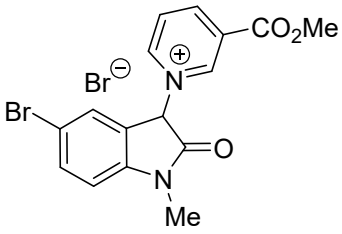
1d

^{13}C NMR (100 MHz, d_6-DMSO)



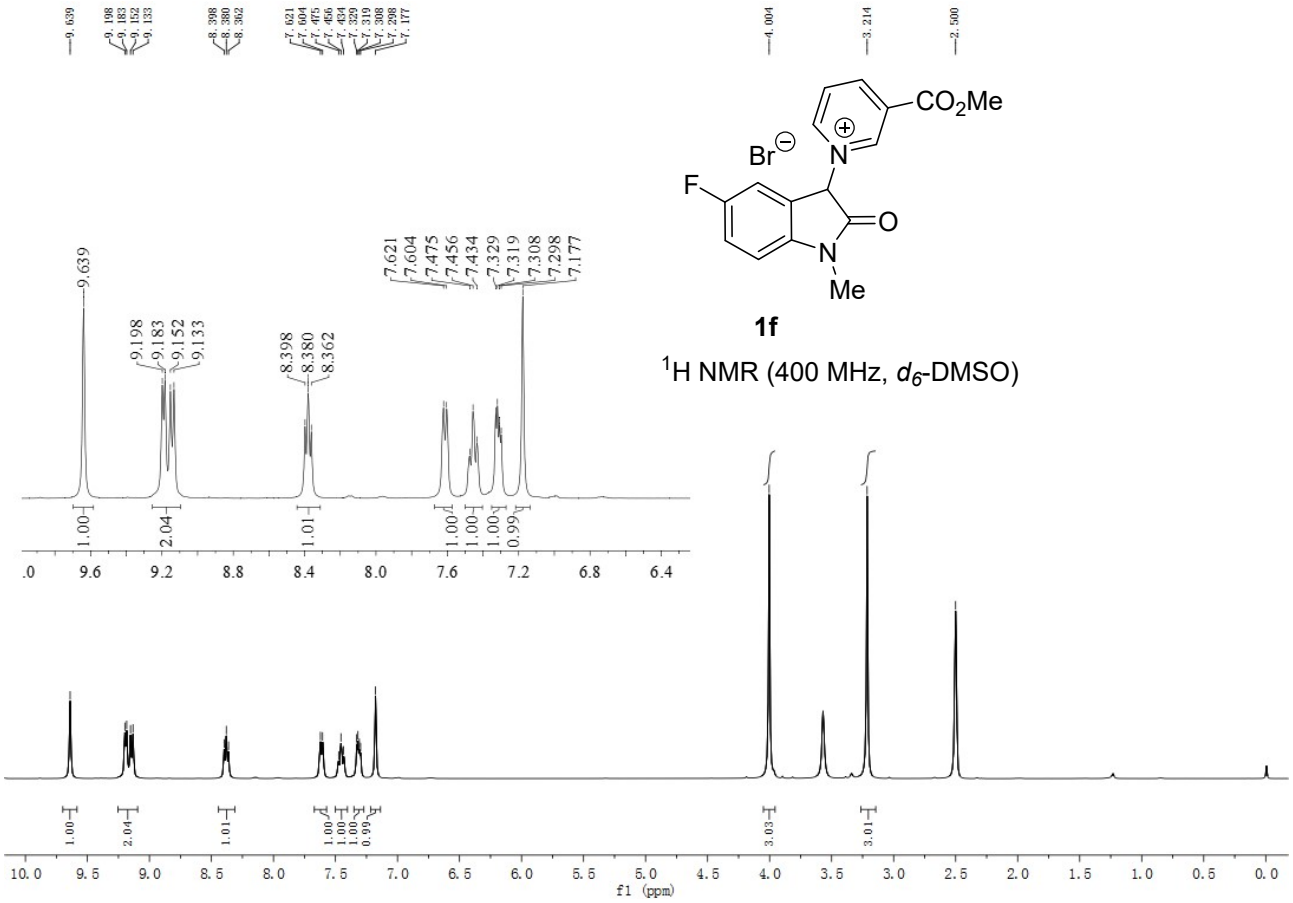
1e

^{1}H NMR (400 MHz, d_6-DMSO)



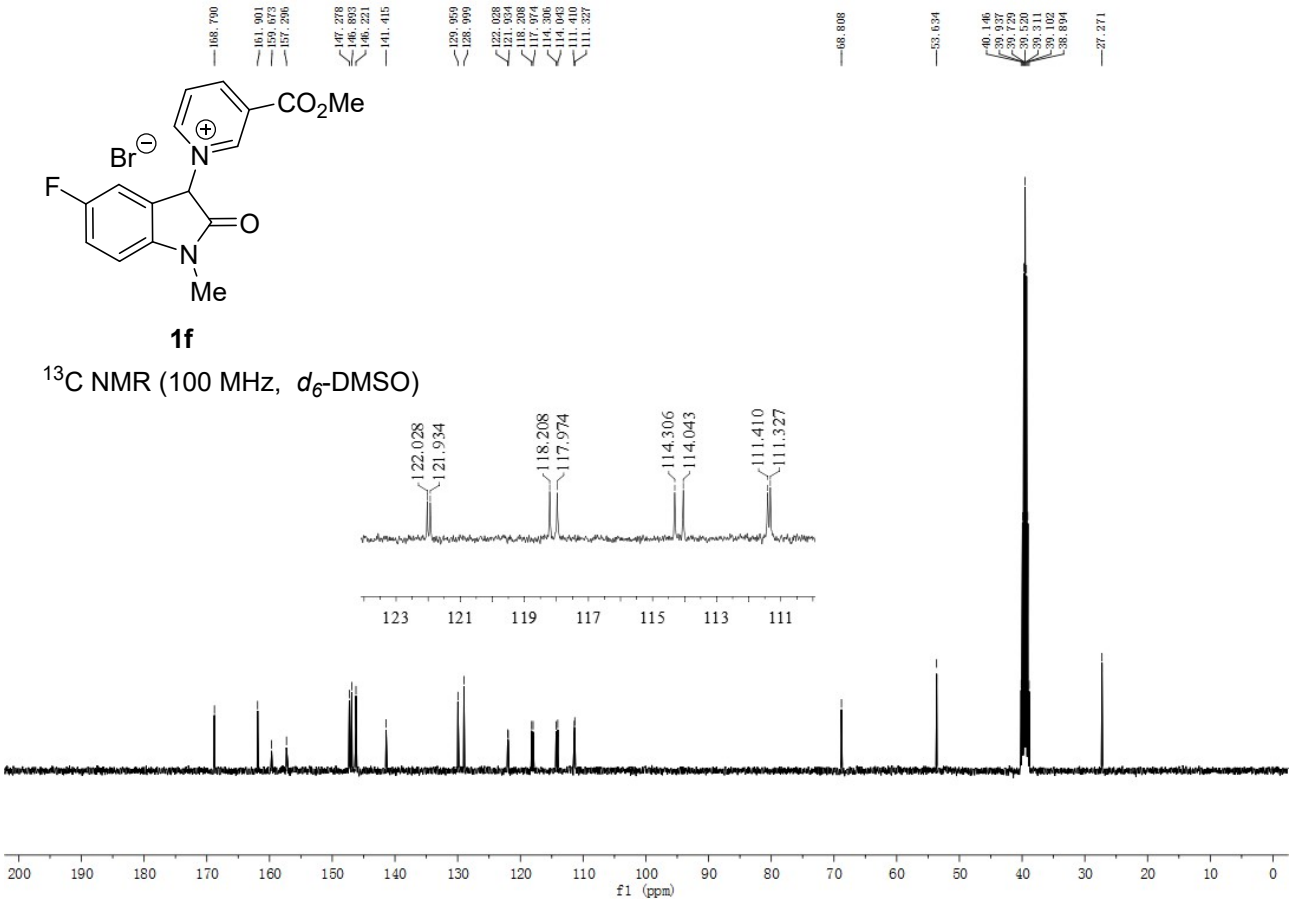
1e

^{13}C NMR (100 MHz, d_6-DMSO)



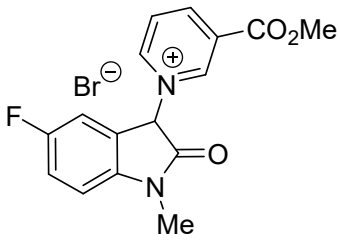
1f

^{1}H NMR (400 MHz, d_6-DMSO)



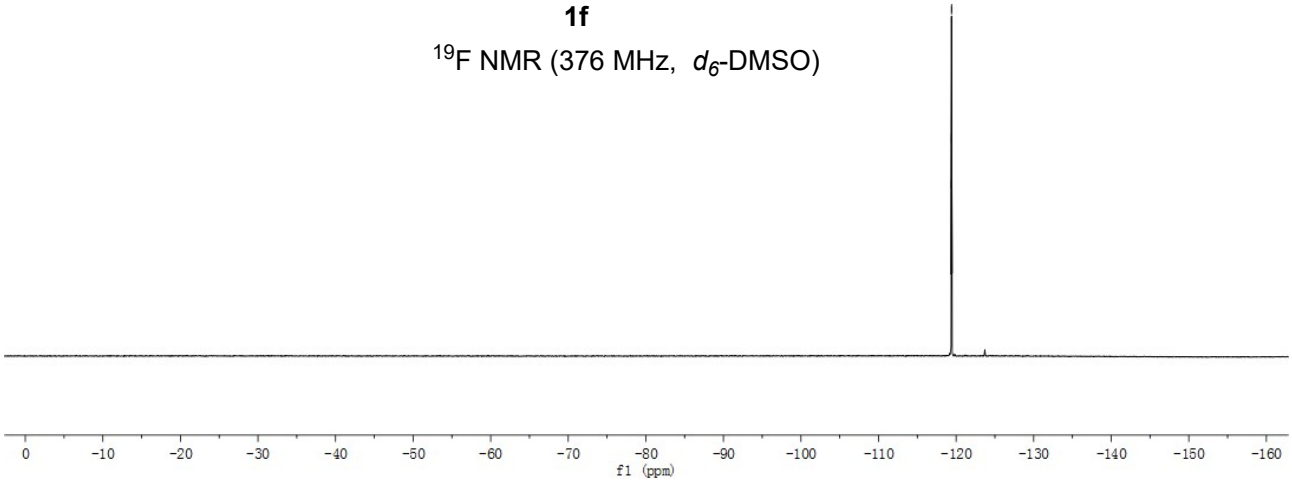
1f

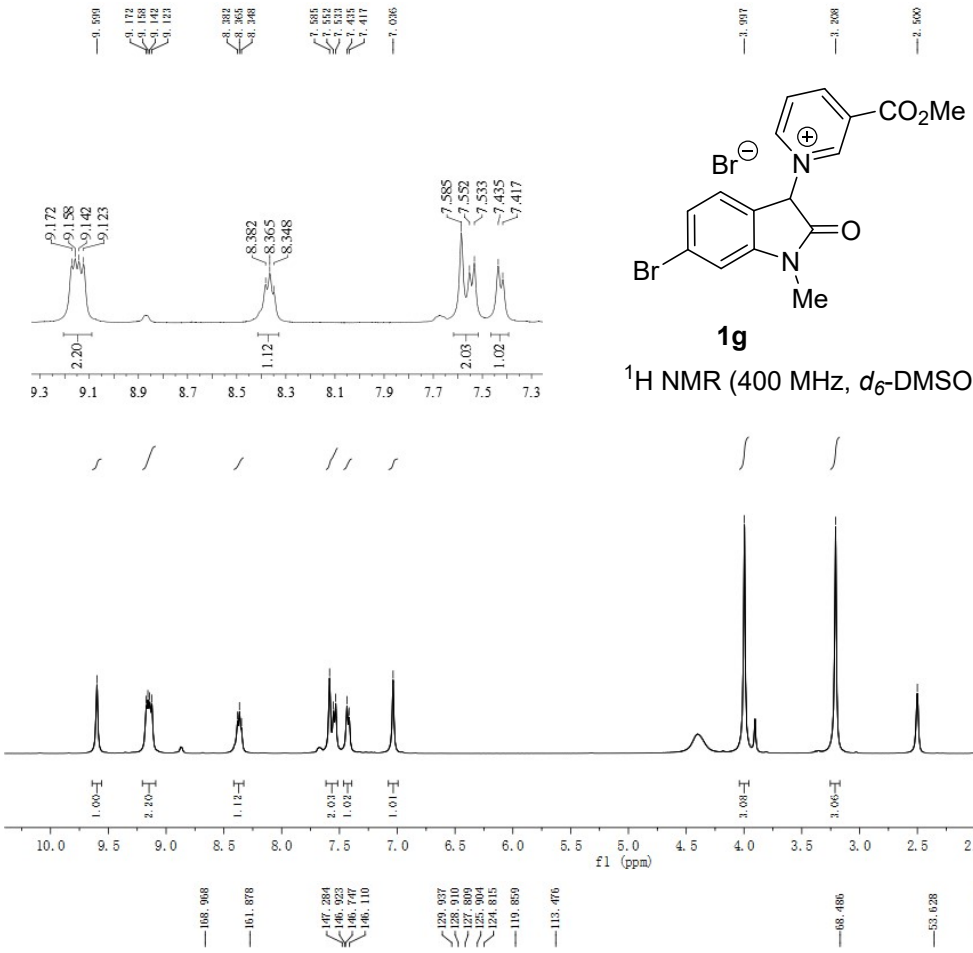
^{13}C NMR (100 MHz, d_6-DMSO)



1f

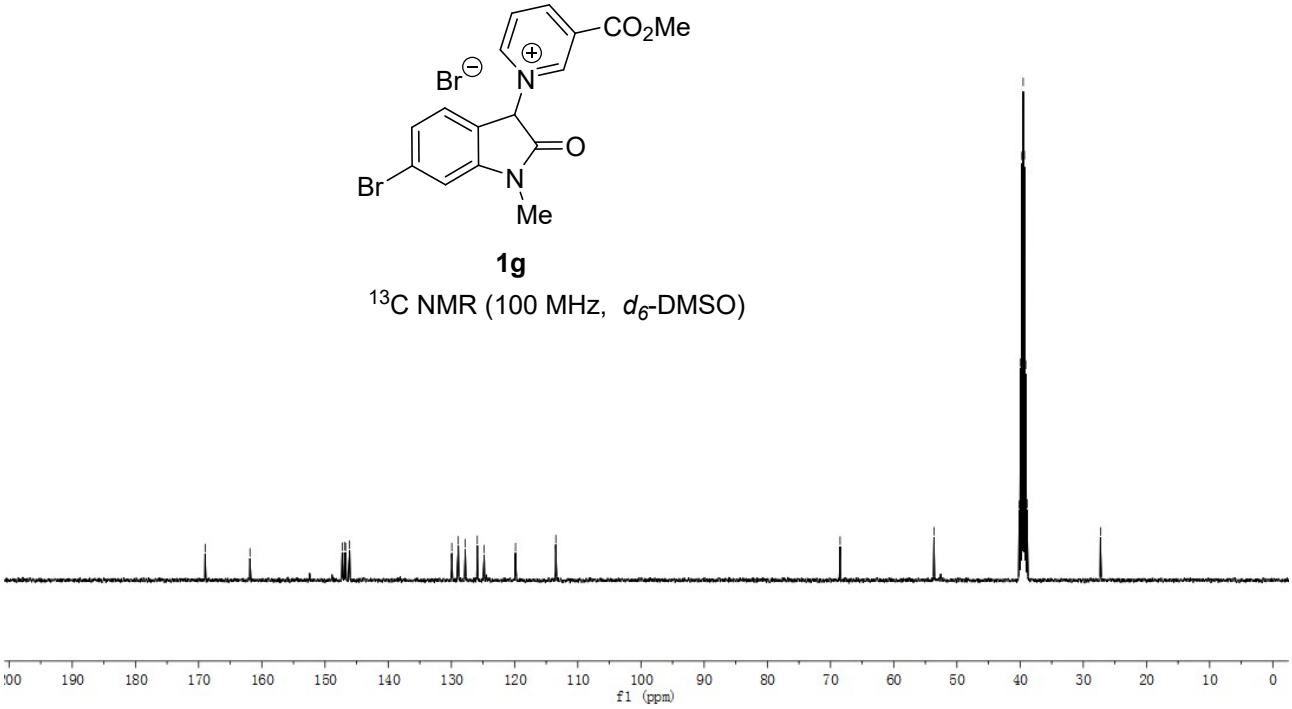
^{19}F NMR (376 MHz, d_6-DMSO)





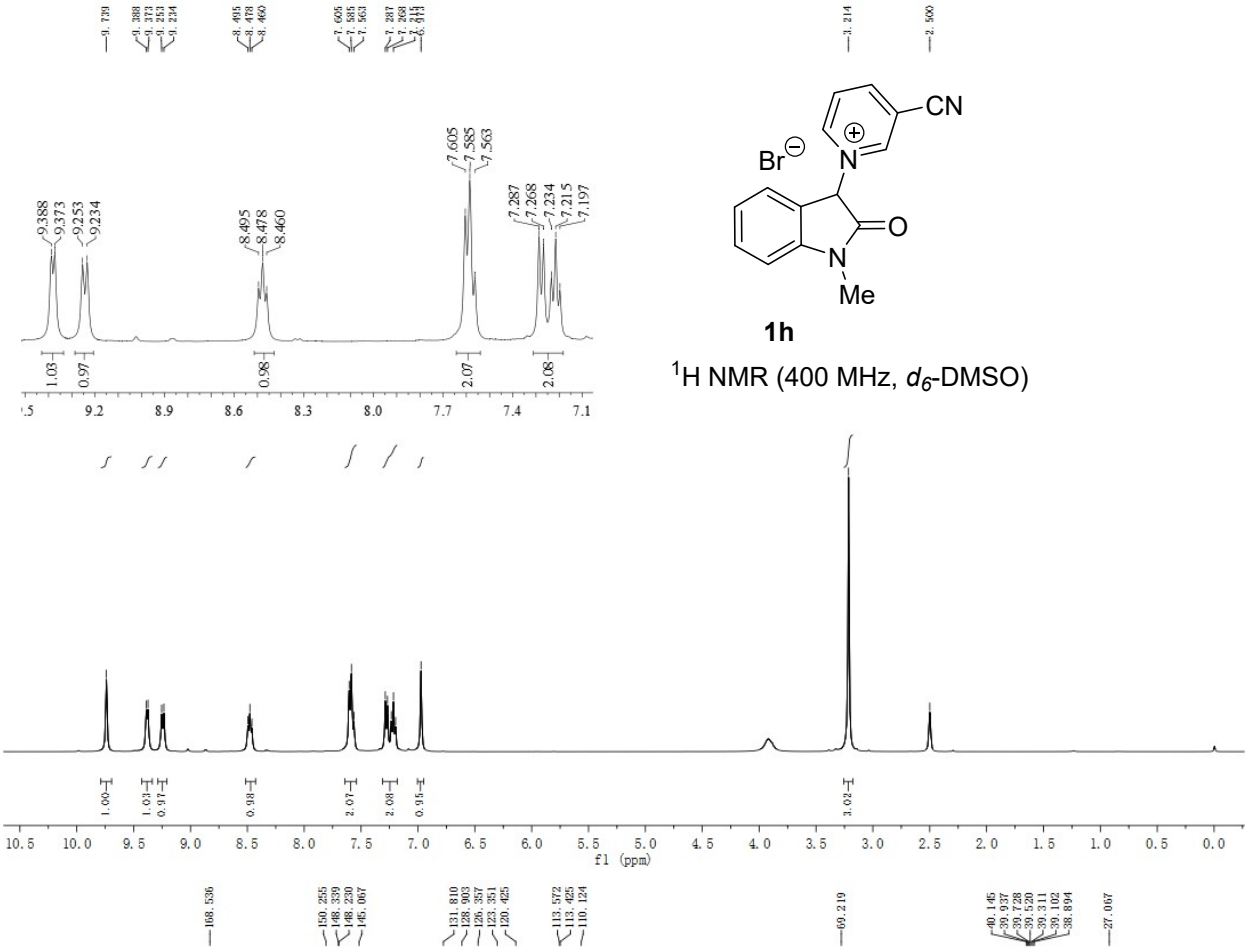
1g

^{1}H NMR (400 MHz, d_6-DMSO)



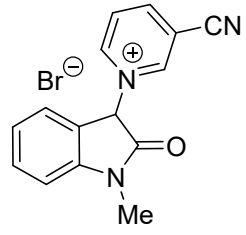
1g

^{13}C NMR (100 MHz, d_6-DMSO)



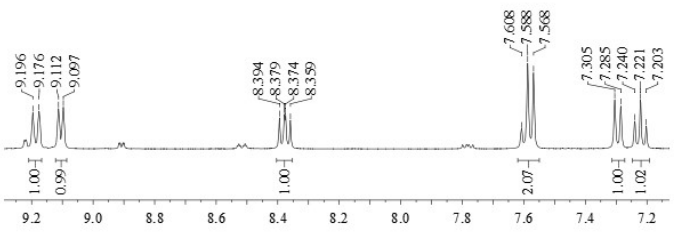
1h

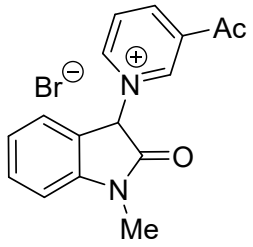
^{1}H NMR (400 MHz, d_6-DMSO)



1h

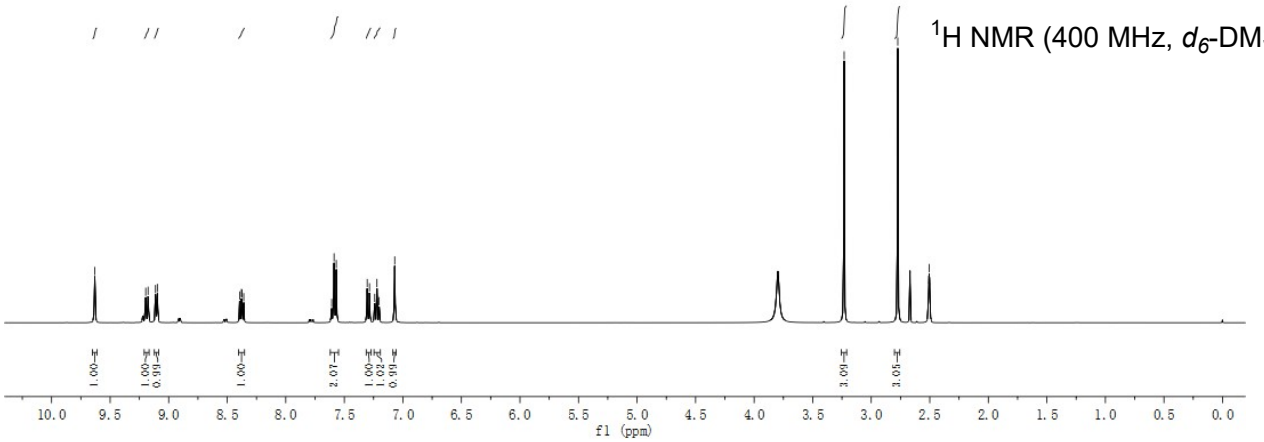
^{13}C NMR (100 MHz, d_6-DMSO)

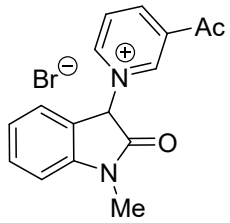




1i

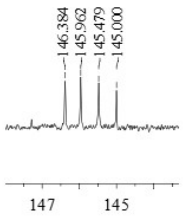
^{1}H NMR (400 MHz, d_6-DMSO)

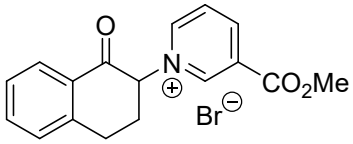




1i

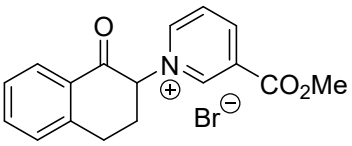
^{13}C NMR (100 MHz, d_6-DMSO)





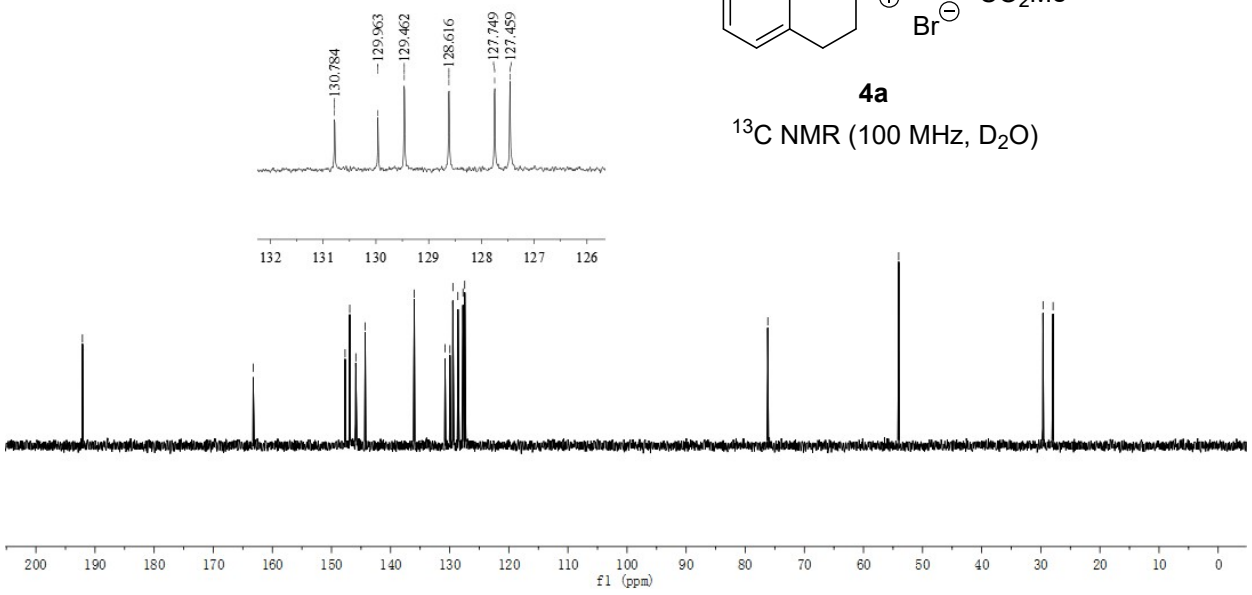
4a

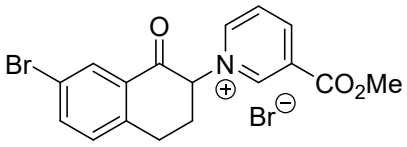
^{1}H NMR (400 MHz,D_2O)



4a

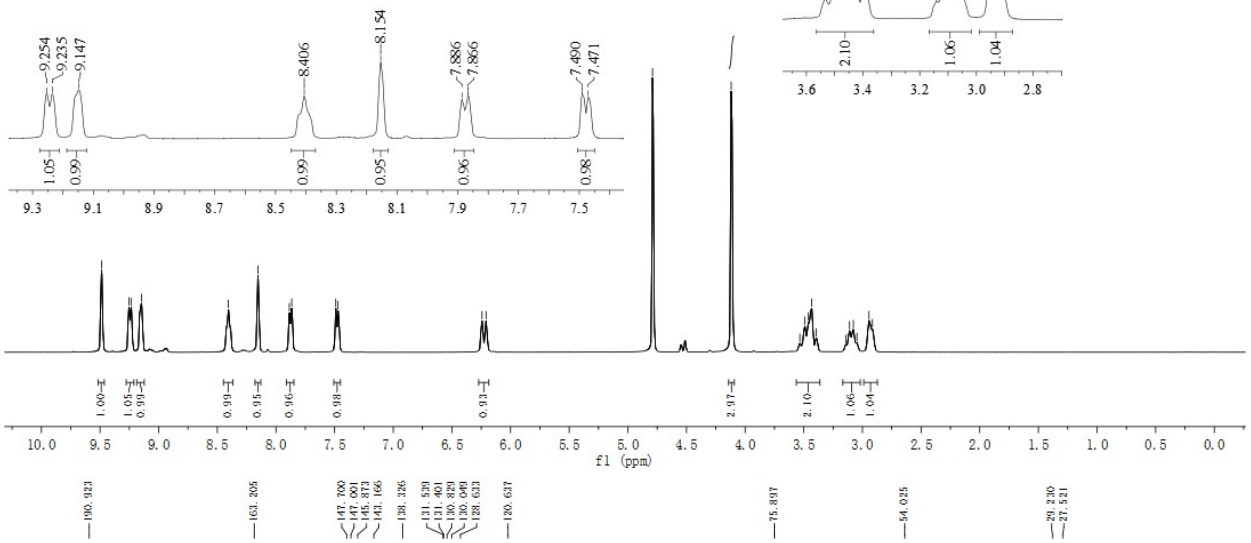
^{13}C NMR (100 MHz, D_2O)

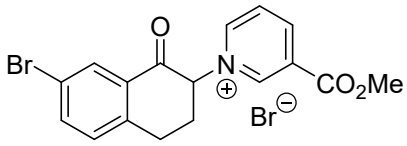




4b

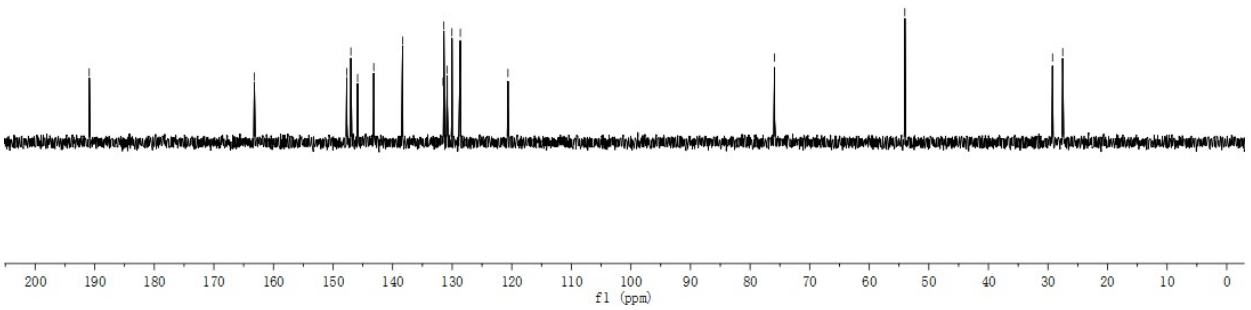
^{1}H NMR (400 MHz,D_2O)

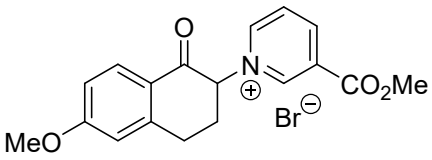




4b

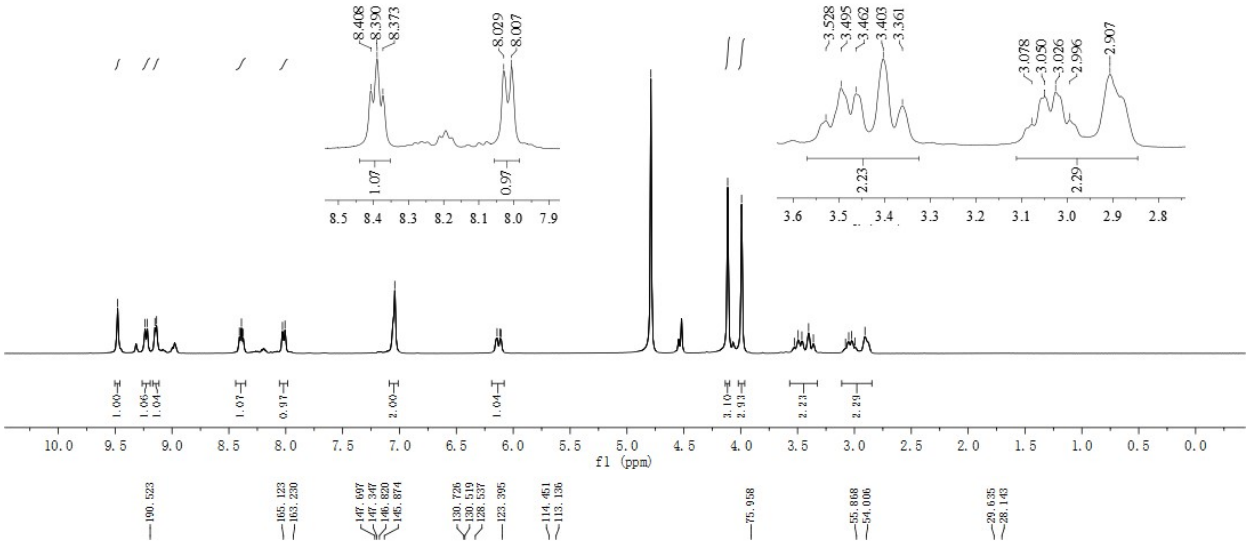
^{13}C NMR (100 MHz, D_2O)

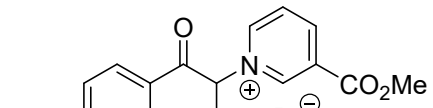




4c

^{1}H NMR (400 MHz,D_2O)





4c

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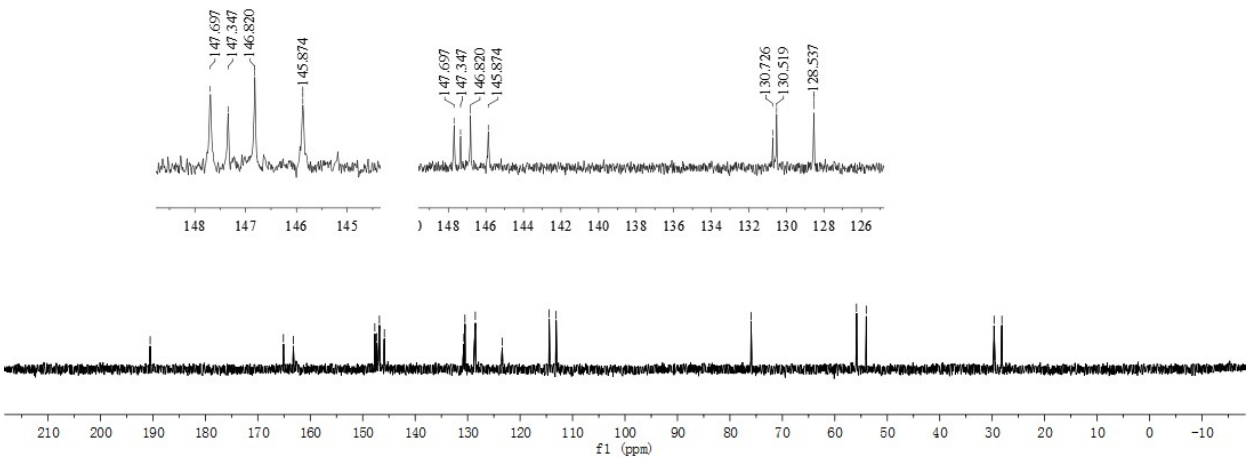

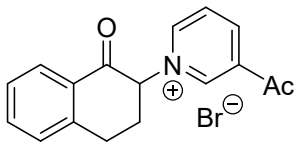

4d

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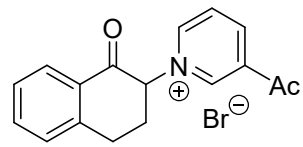

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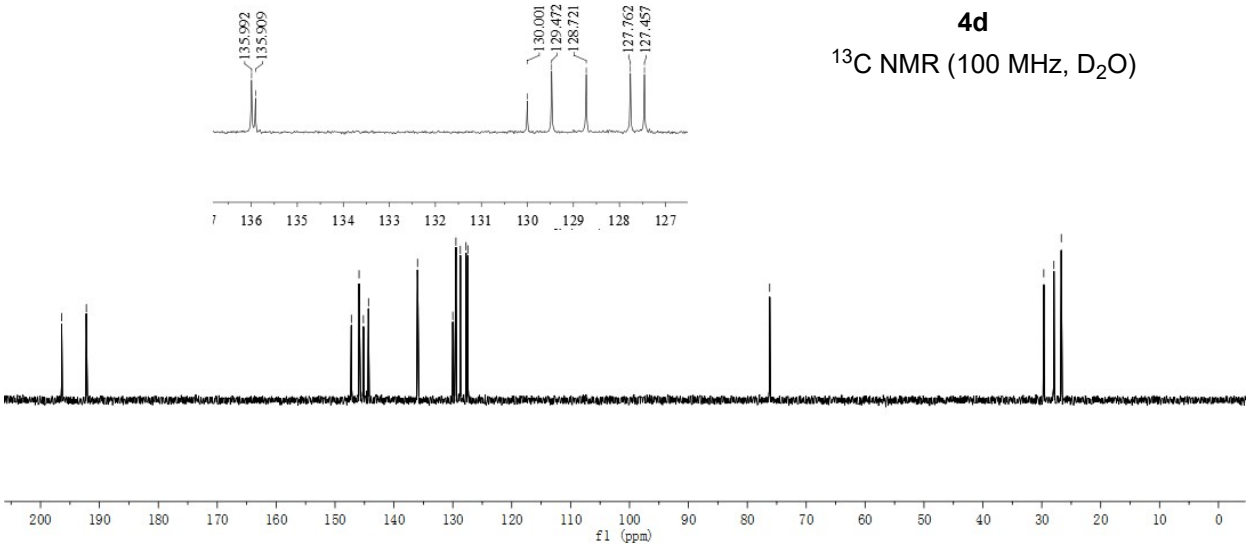

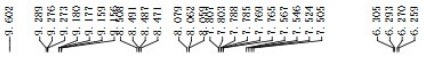

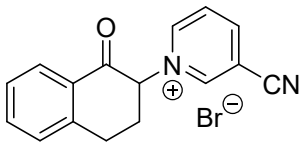

4e

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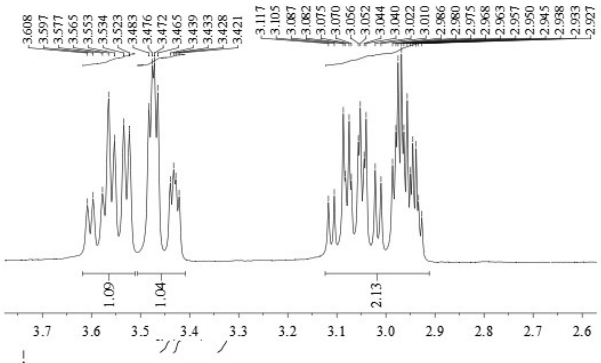
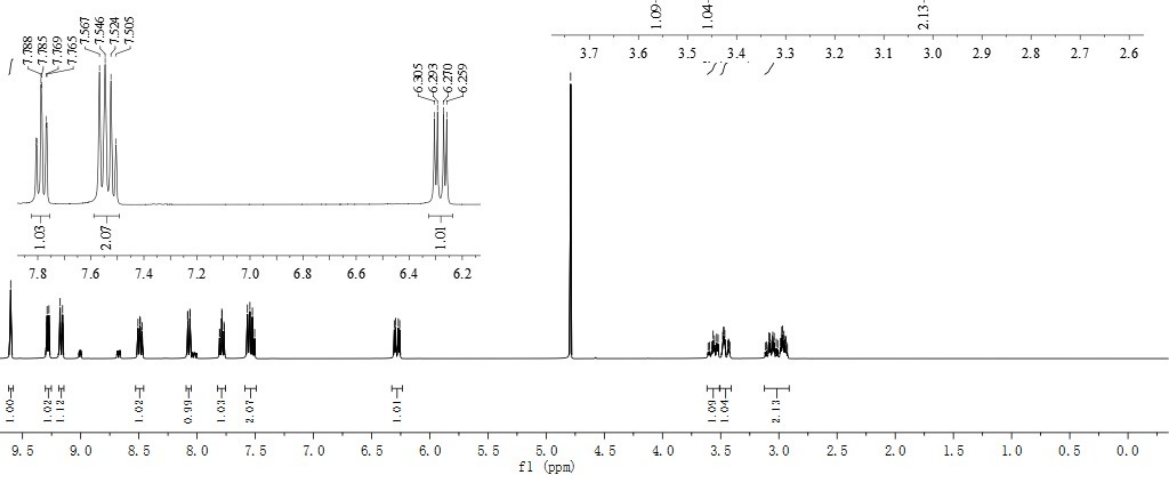
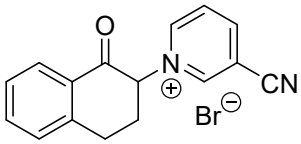
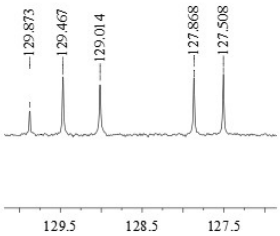


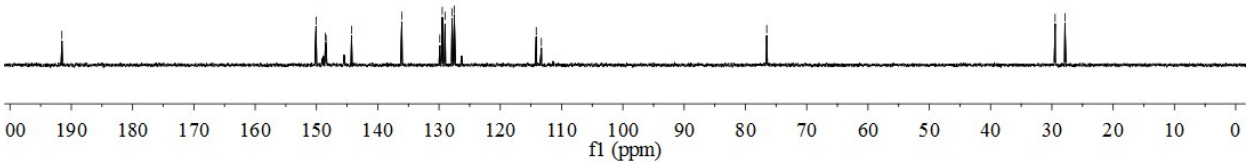


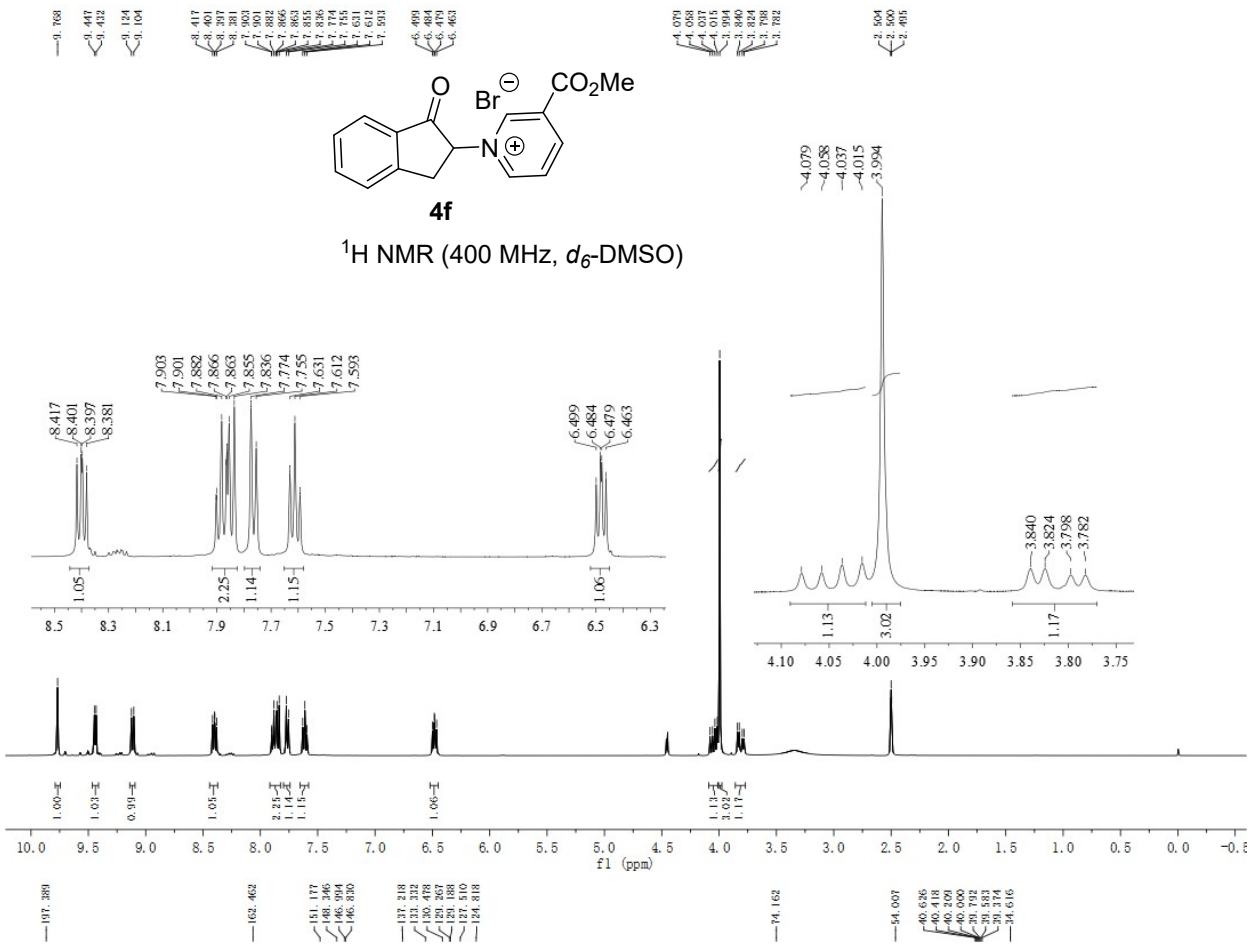


4e

^{13}C NMR (100 MHz, D_2O)

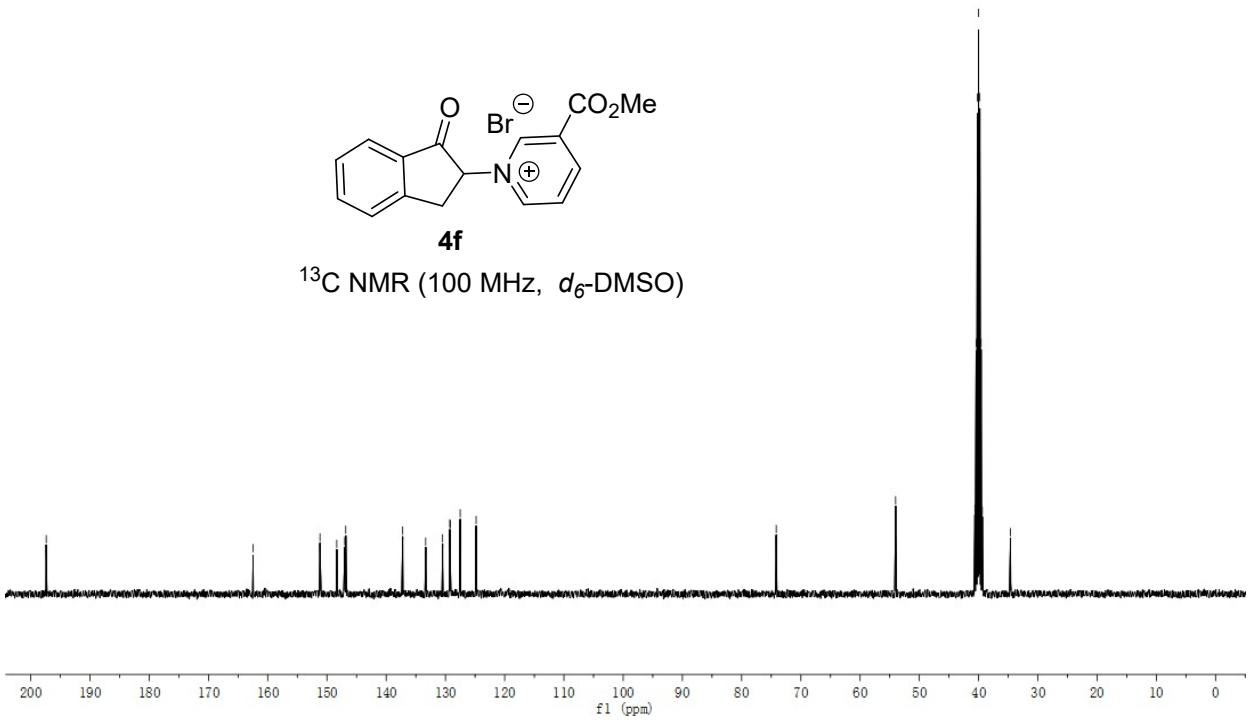






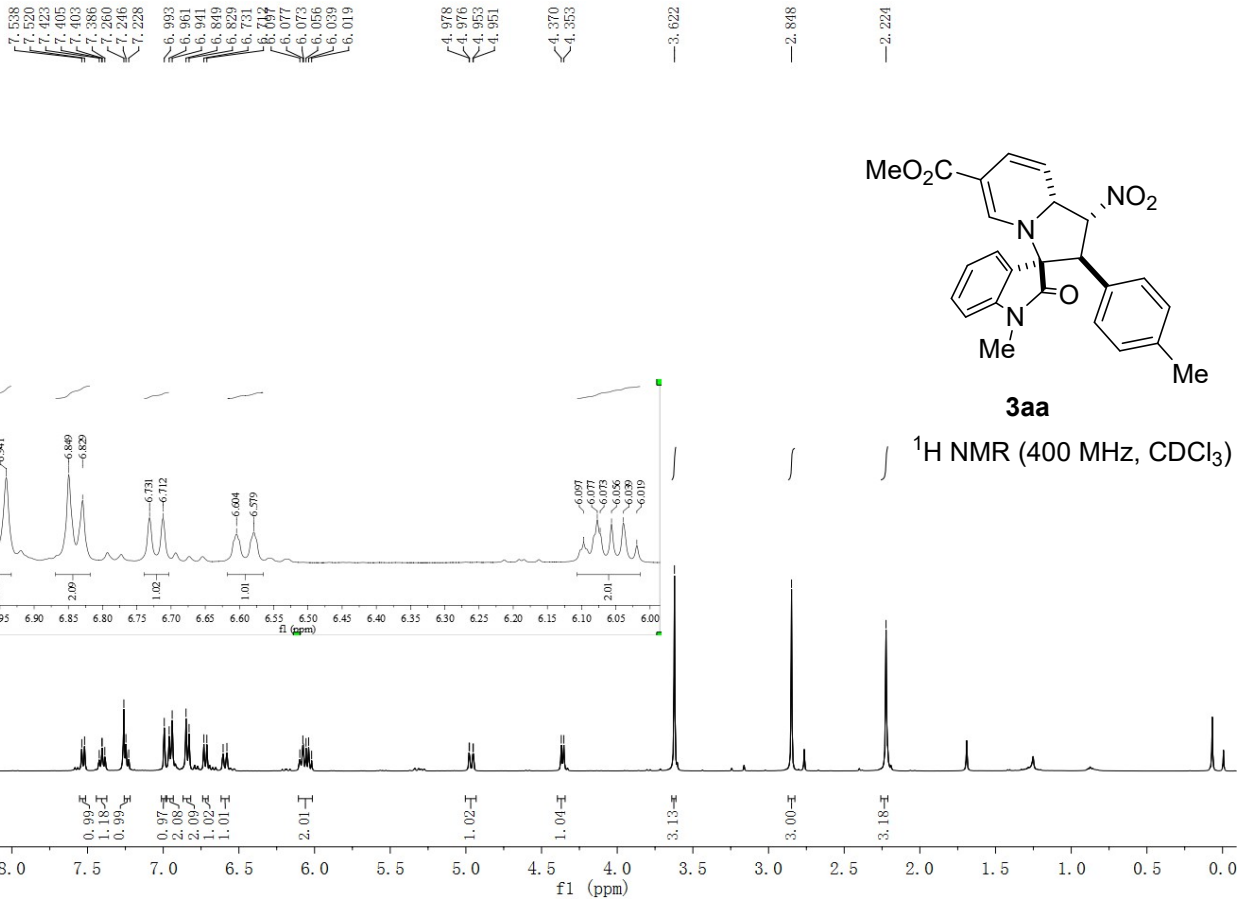
4f

^{1}H NMR (400 MHz, d_6-DMSO)



4f

^{13}C NMR (100 MHz, d_6-DMSO)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7.246
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6.961
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6.731
6.712
6.097
6.077
6.073
6.056
6.039
6.019
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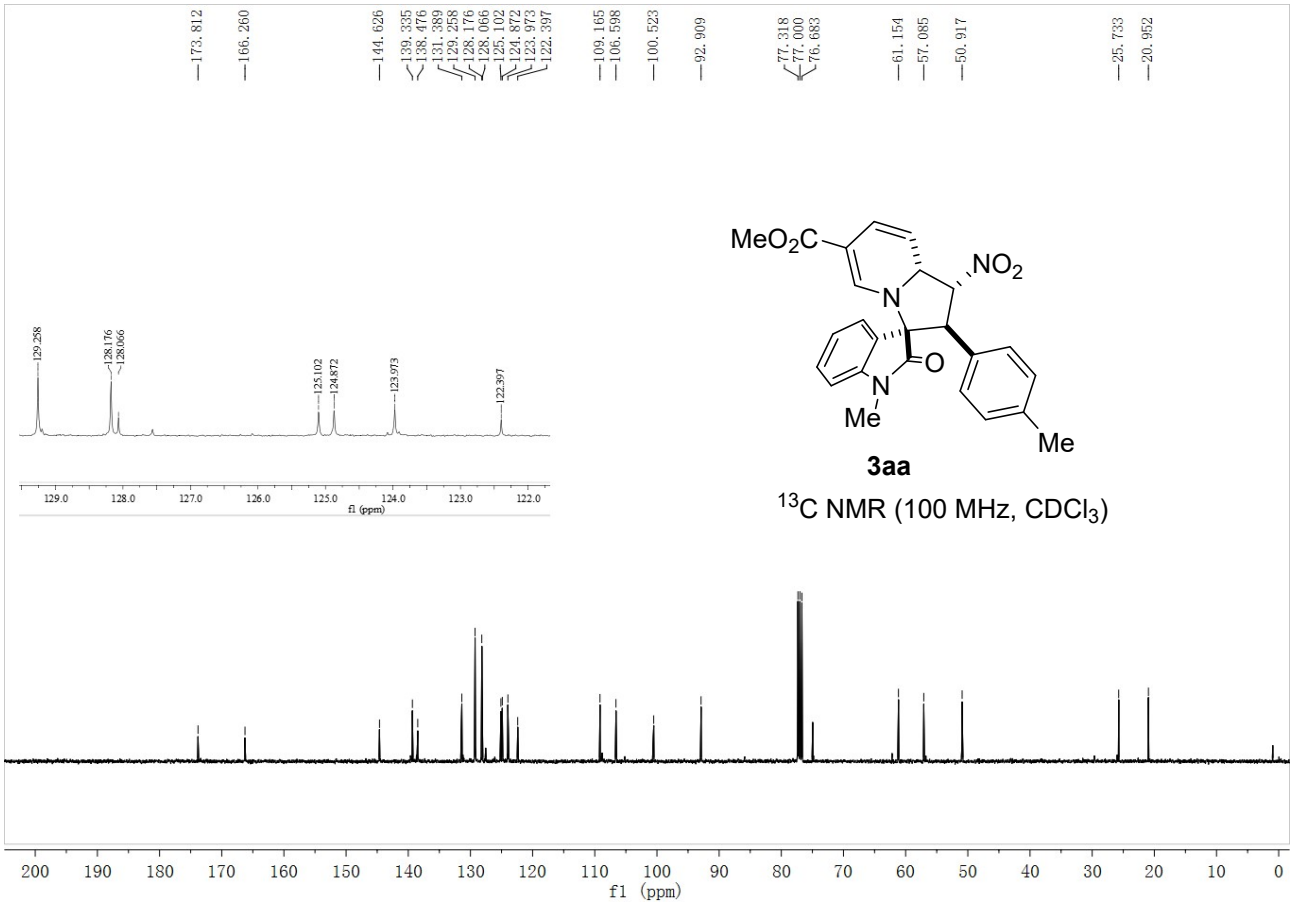
4.976
4.953
4.951
4.370
4.353
3.622
2.848
2.224
MeO2C
NO2
N
O
N
Me
Me
3aa
1H NMR (400 MHz, CDCl3)
f1 (ppm)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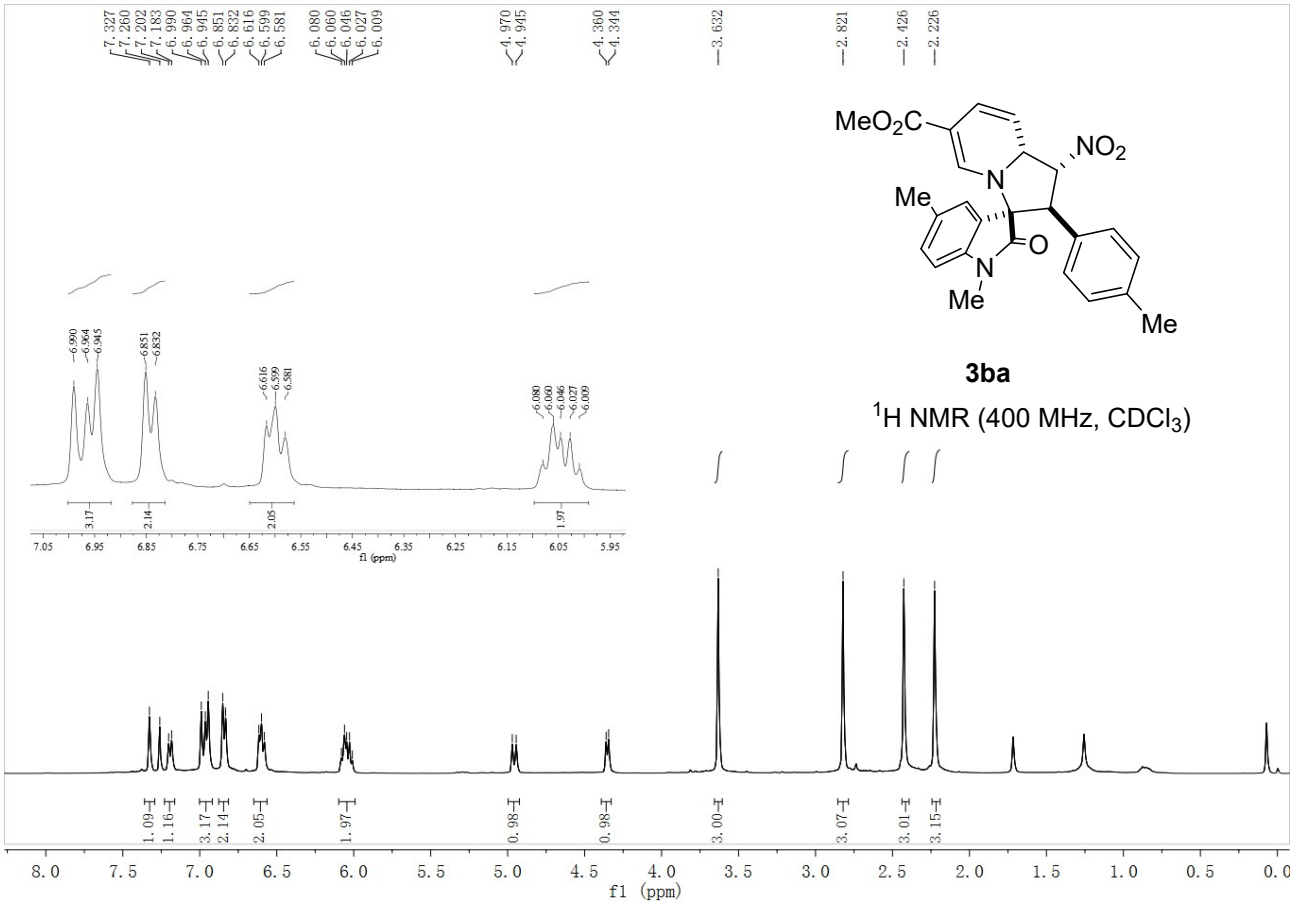
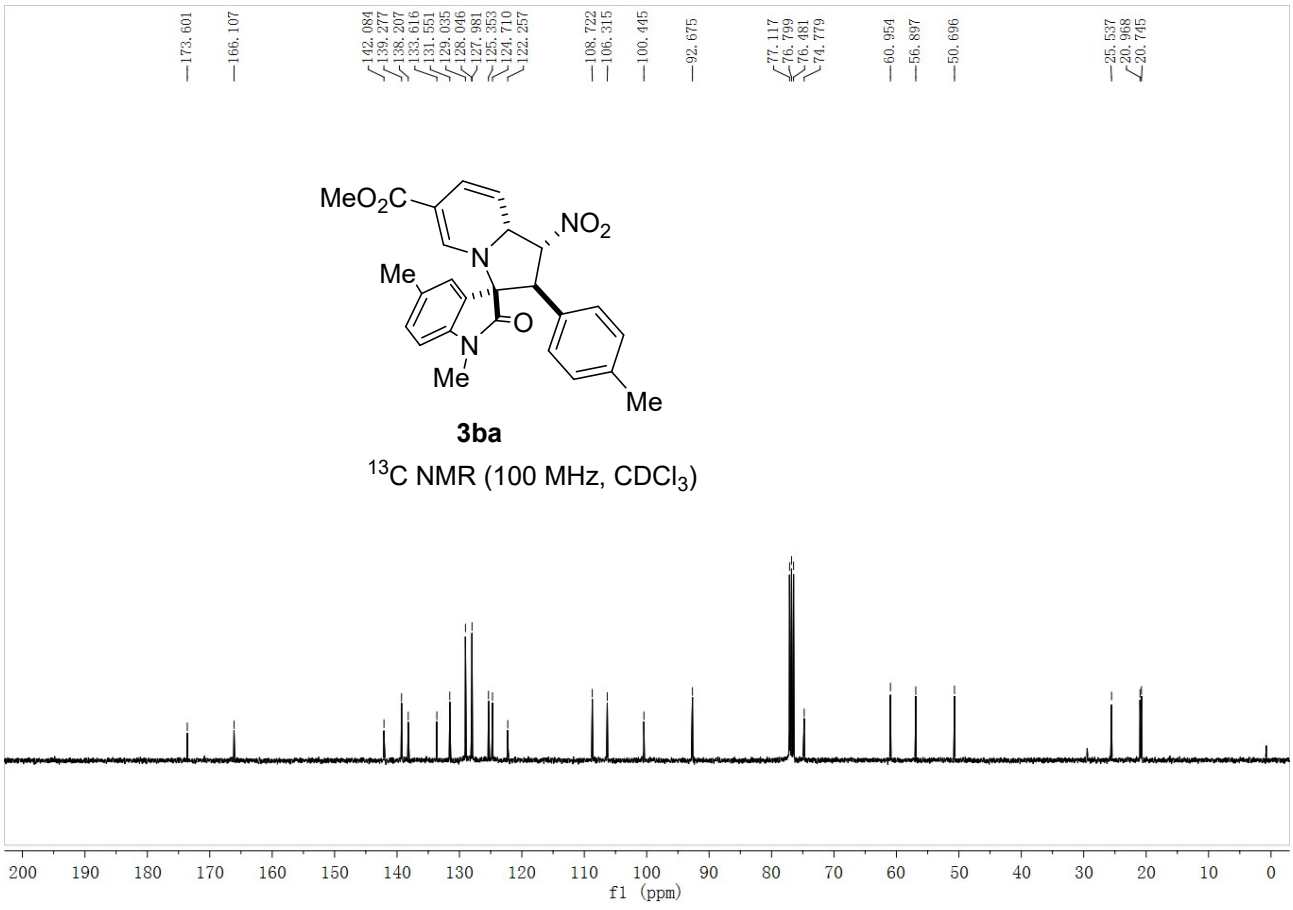
166.260
144.626
139.335
138.476
131.389
129.258
128.176
128.066
125.102
124.872
123.973
122.397
109.165
106.598
100.523
92.909
77.318
77.000
76.683
61.154
57.085
50.917
25.733
20.952
MeO2C
NO2
N
O
N
Me
Me
3aa
13C NMR (100 MHz, CDCl3)
f1 (ppm)



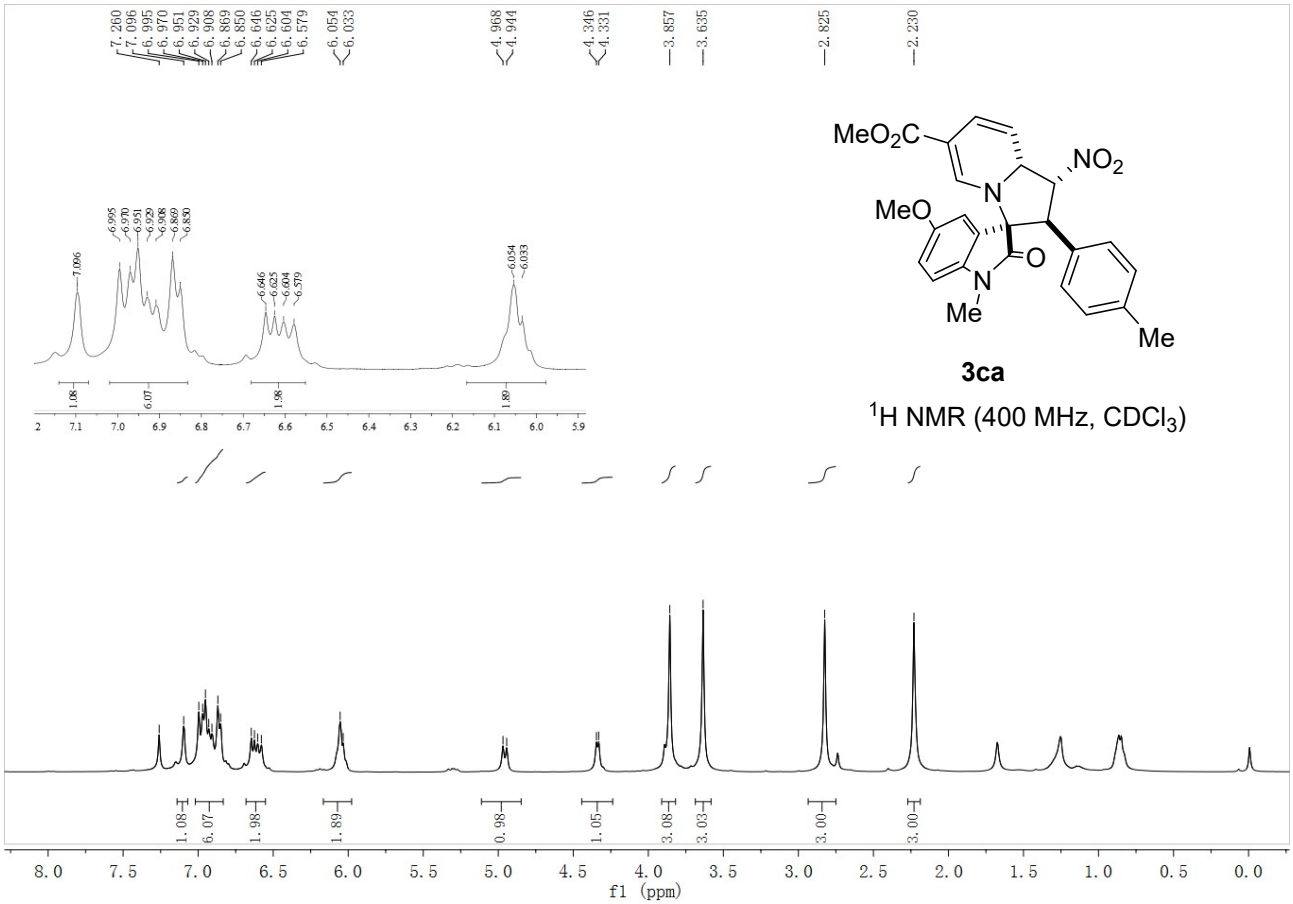
3ba

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



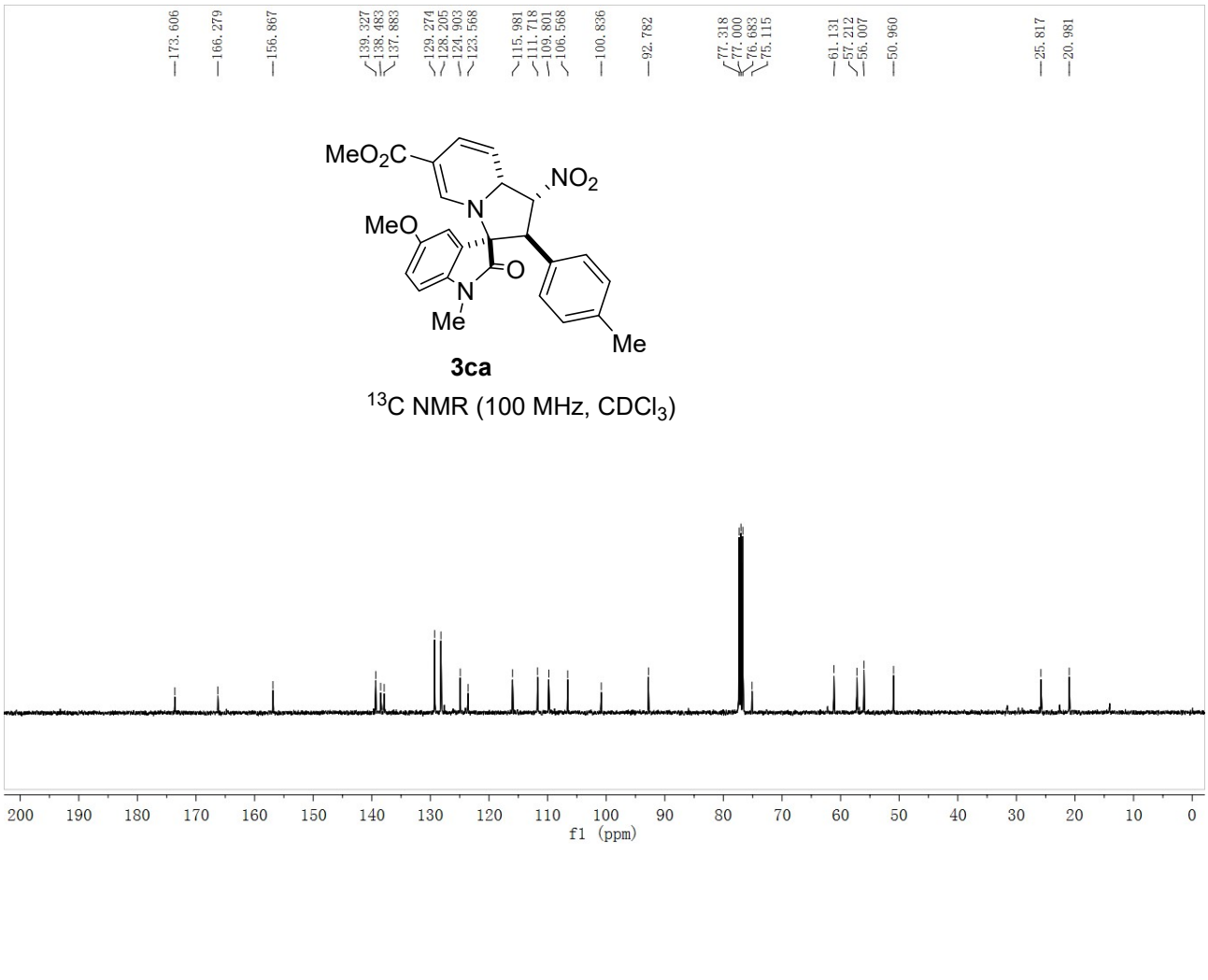
3ba

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



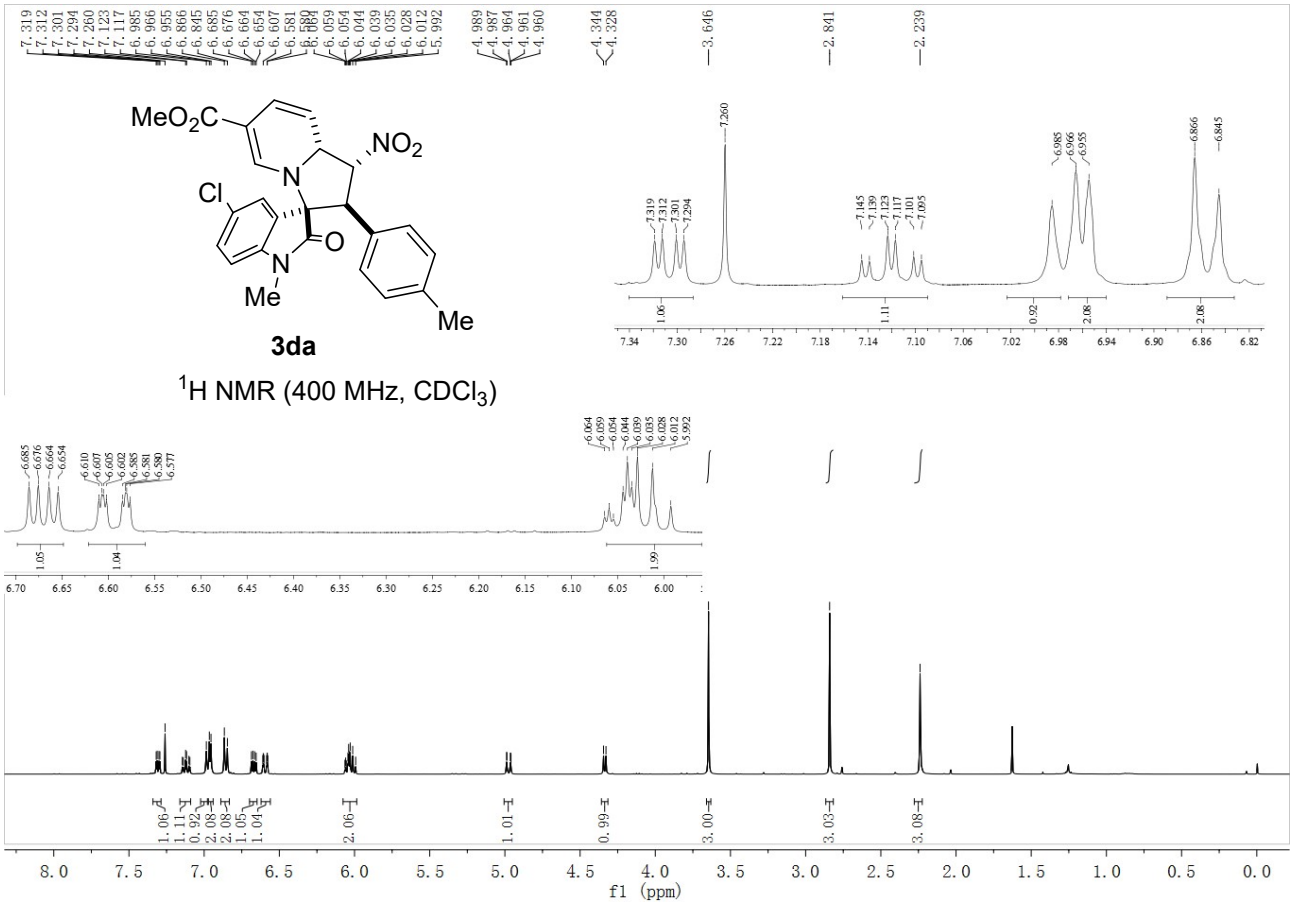
3ca

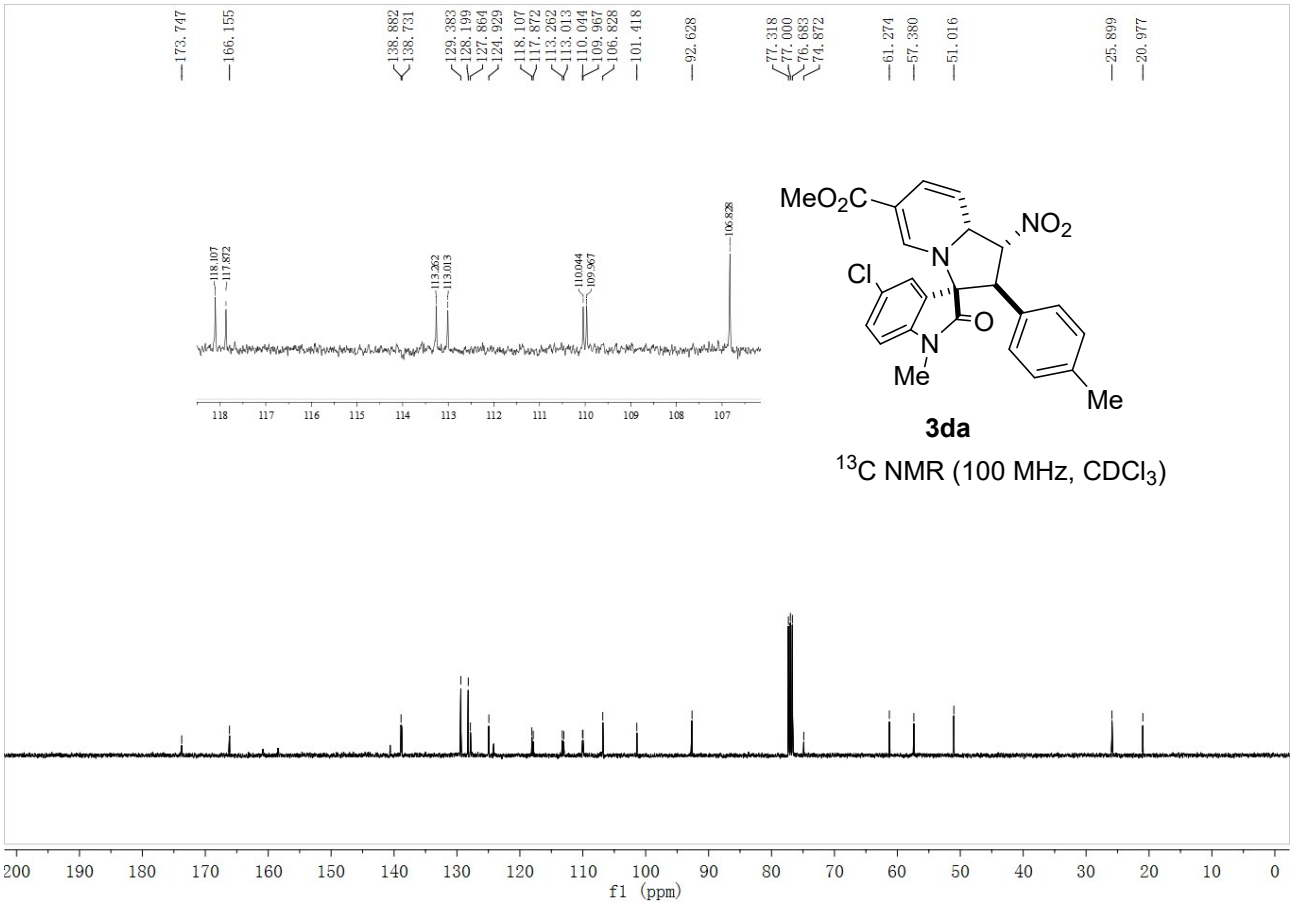
^{1}H NMR (400 MHz, $CDCl_3$)

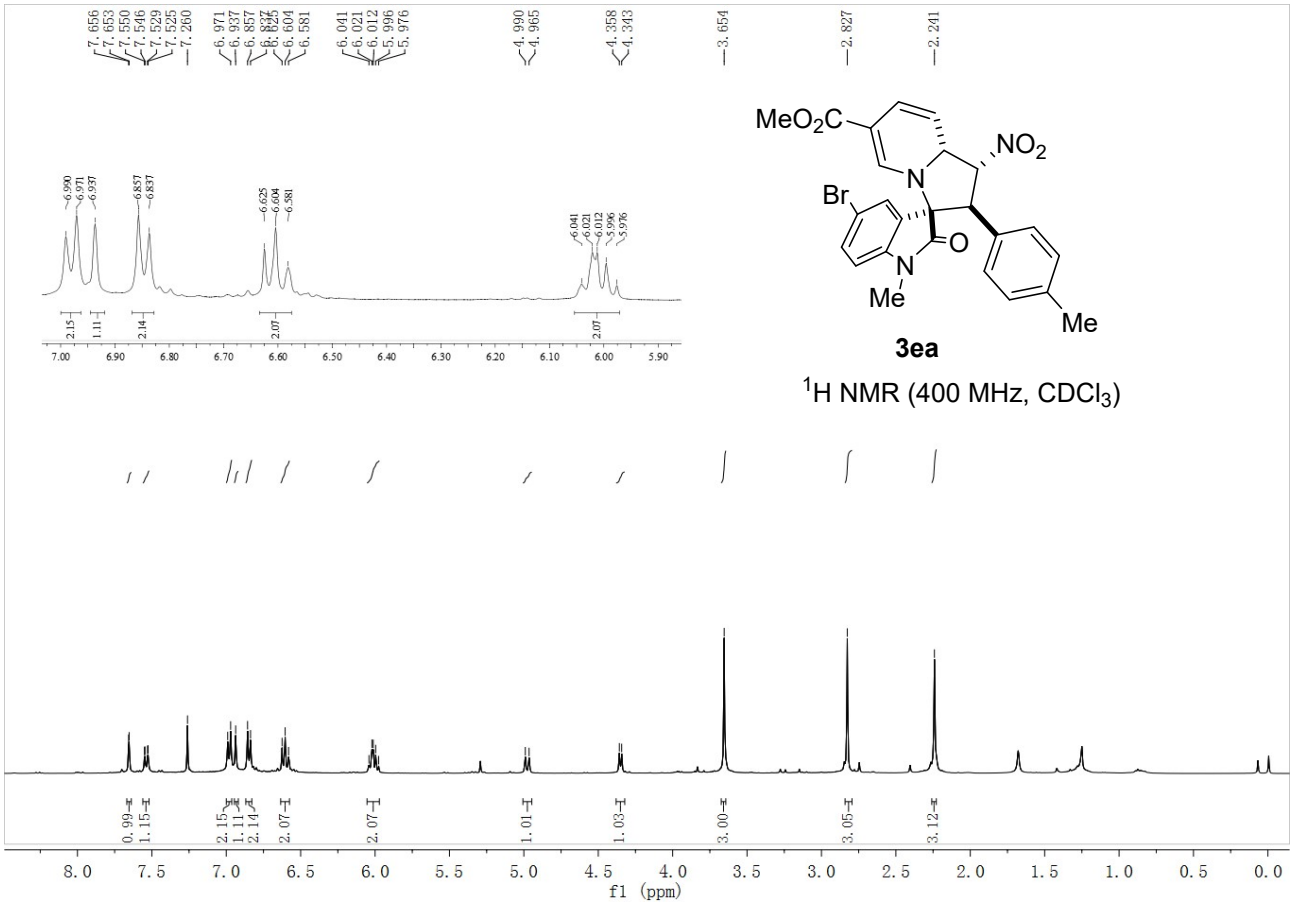


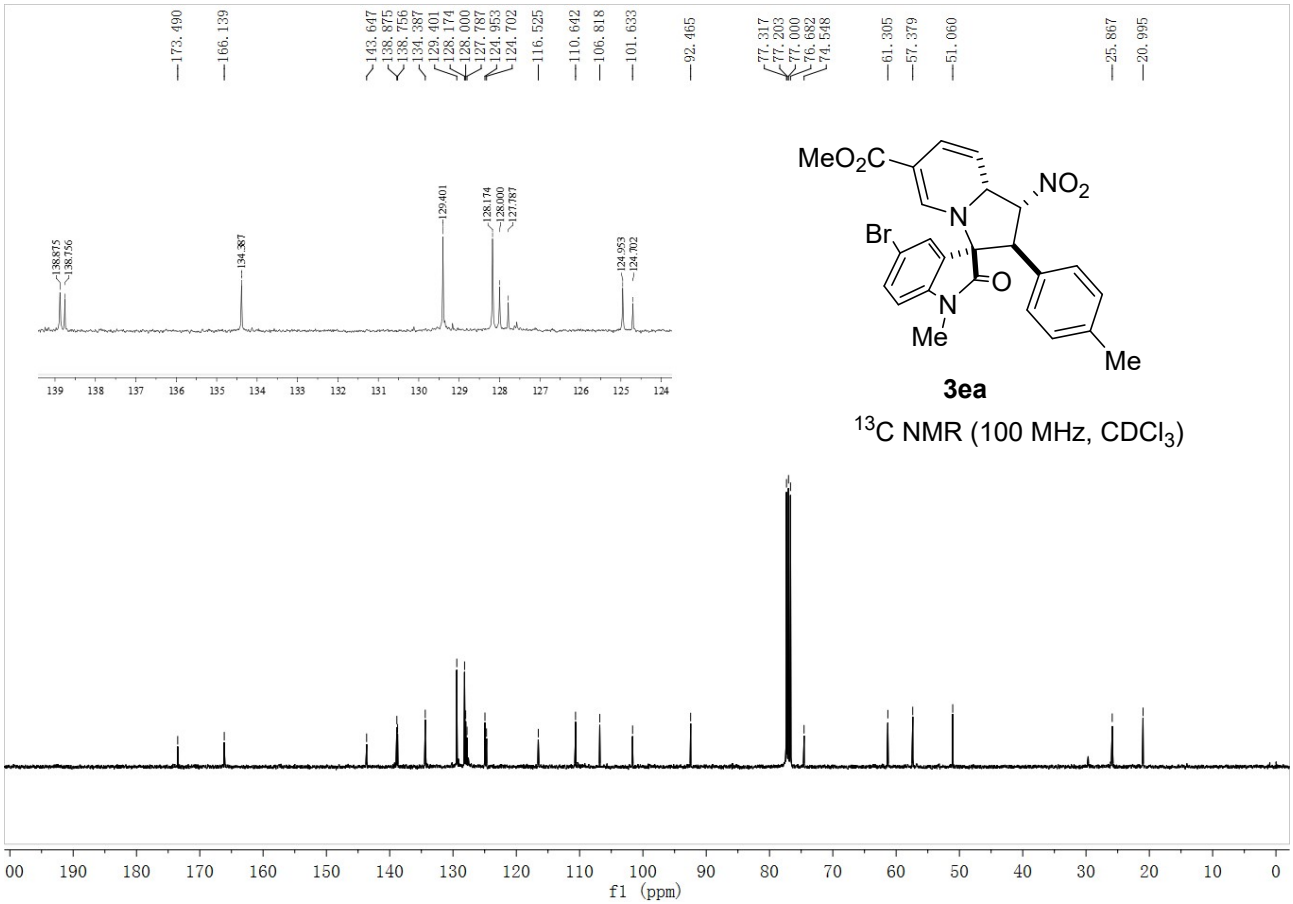
3ca

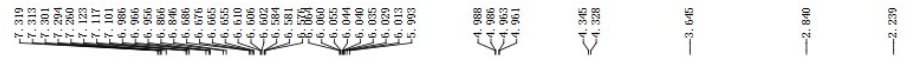
^{13}C NMR (100 MHz, $CDCl_3$)

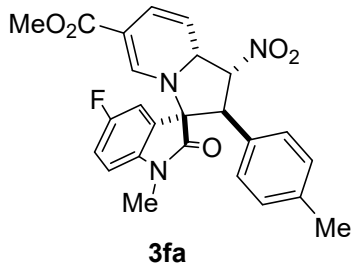

MeO2C
NO2
Cl
N
O
N
Me
Me
3da
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
Cl
N
O
N
Me
Me
3da
13C NMR (100 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
Br
N
O
N
Me
Me
3ea
1H NMR (400 MHz, CDCl3)
f1 (ppm)

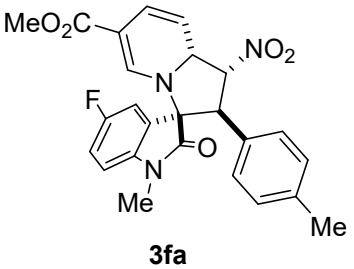

MeO2C
NO2
Br
N
O
N
Me
Me
3ea
13C NMR (100 MHz, CDCl3)
f1 (ppm)





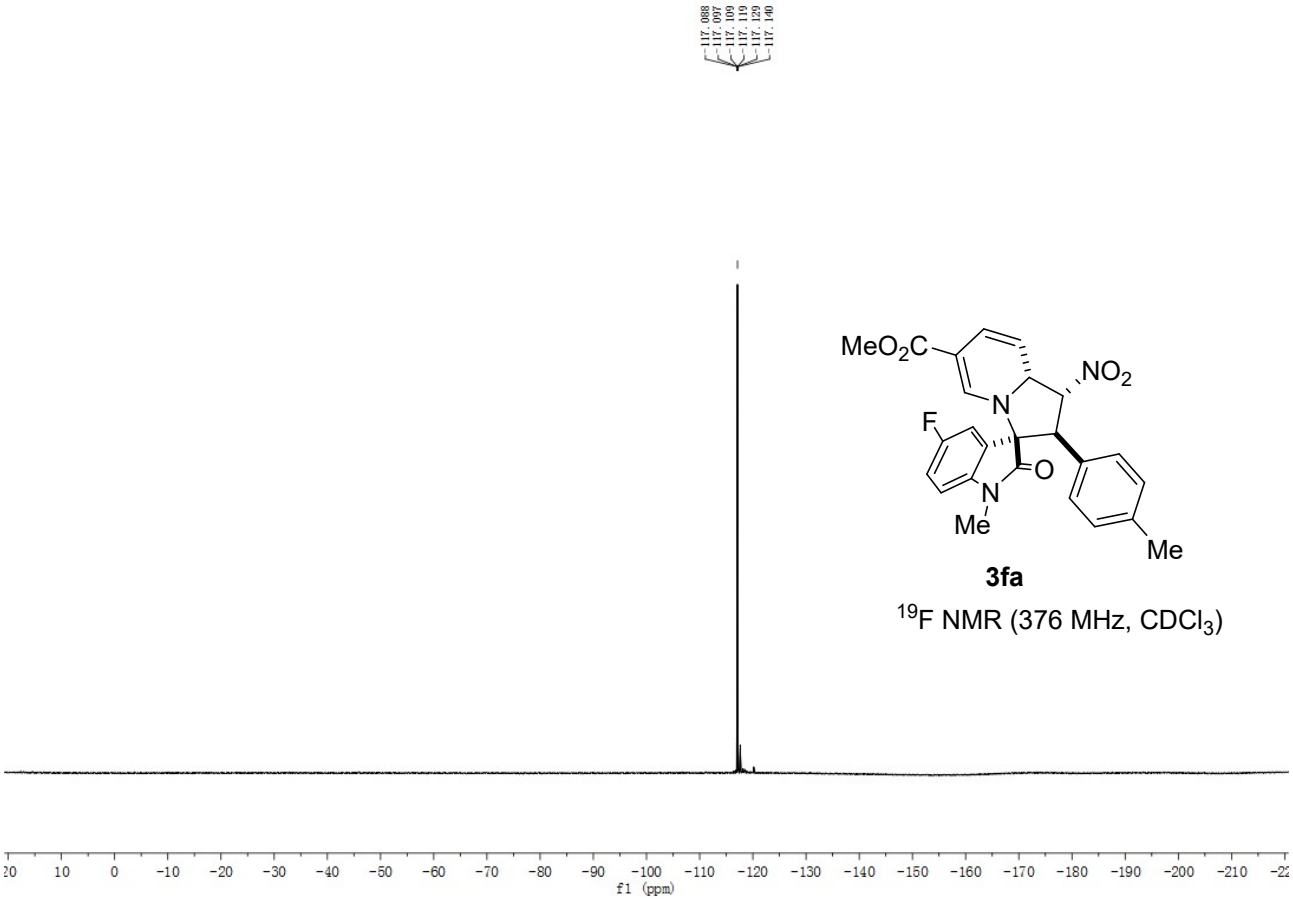
3fa

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



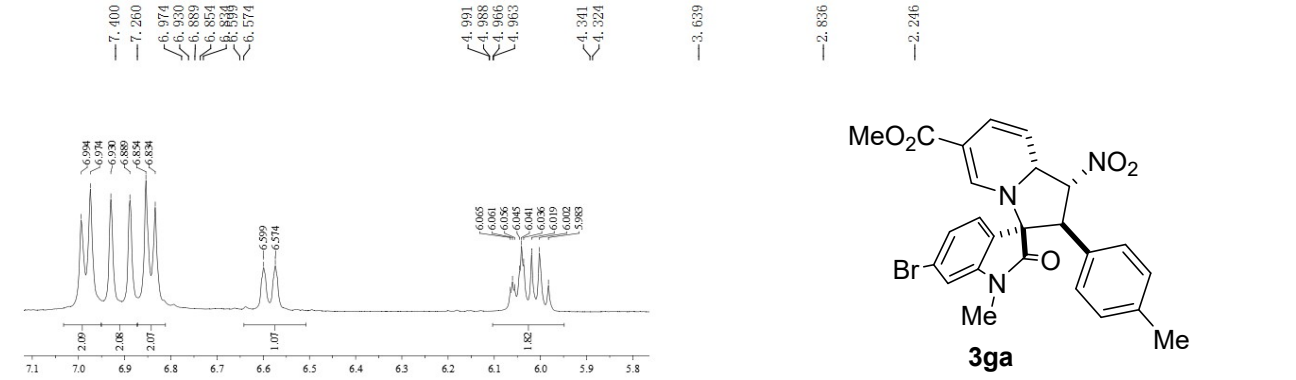
3fa

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



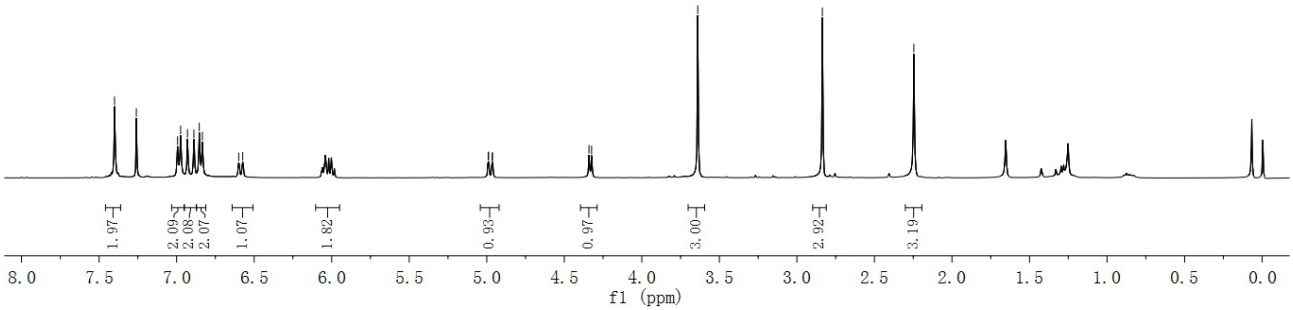
3fa

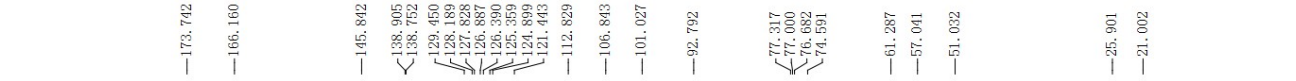
^{19}F NMR (376 MHz, $CDCl_3$)

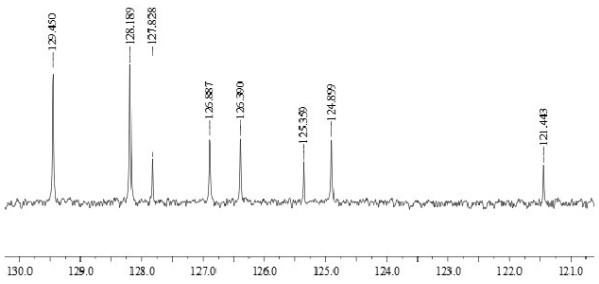


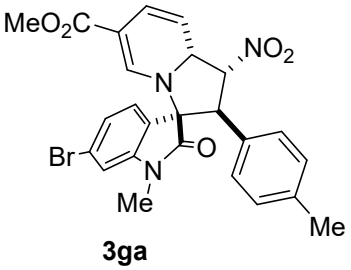
3ga

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



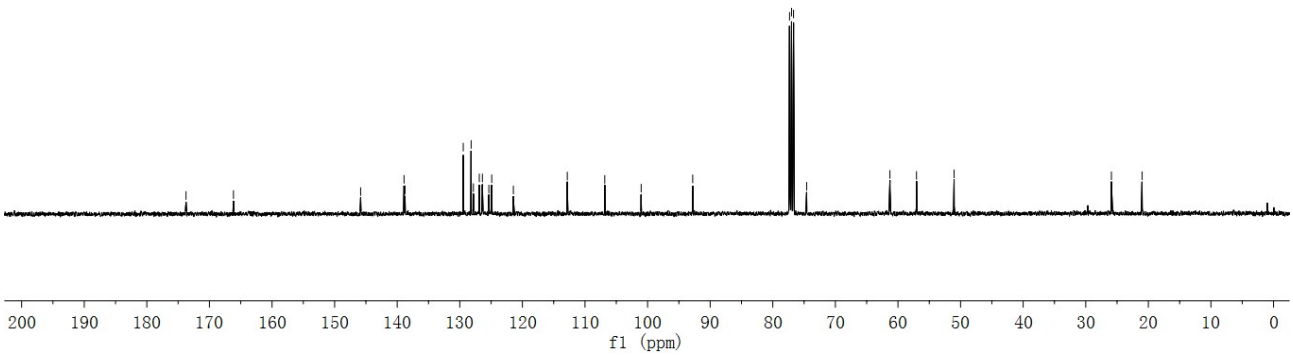


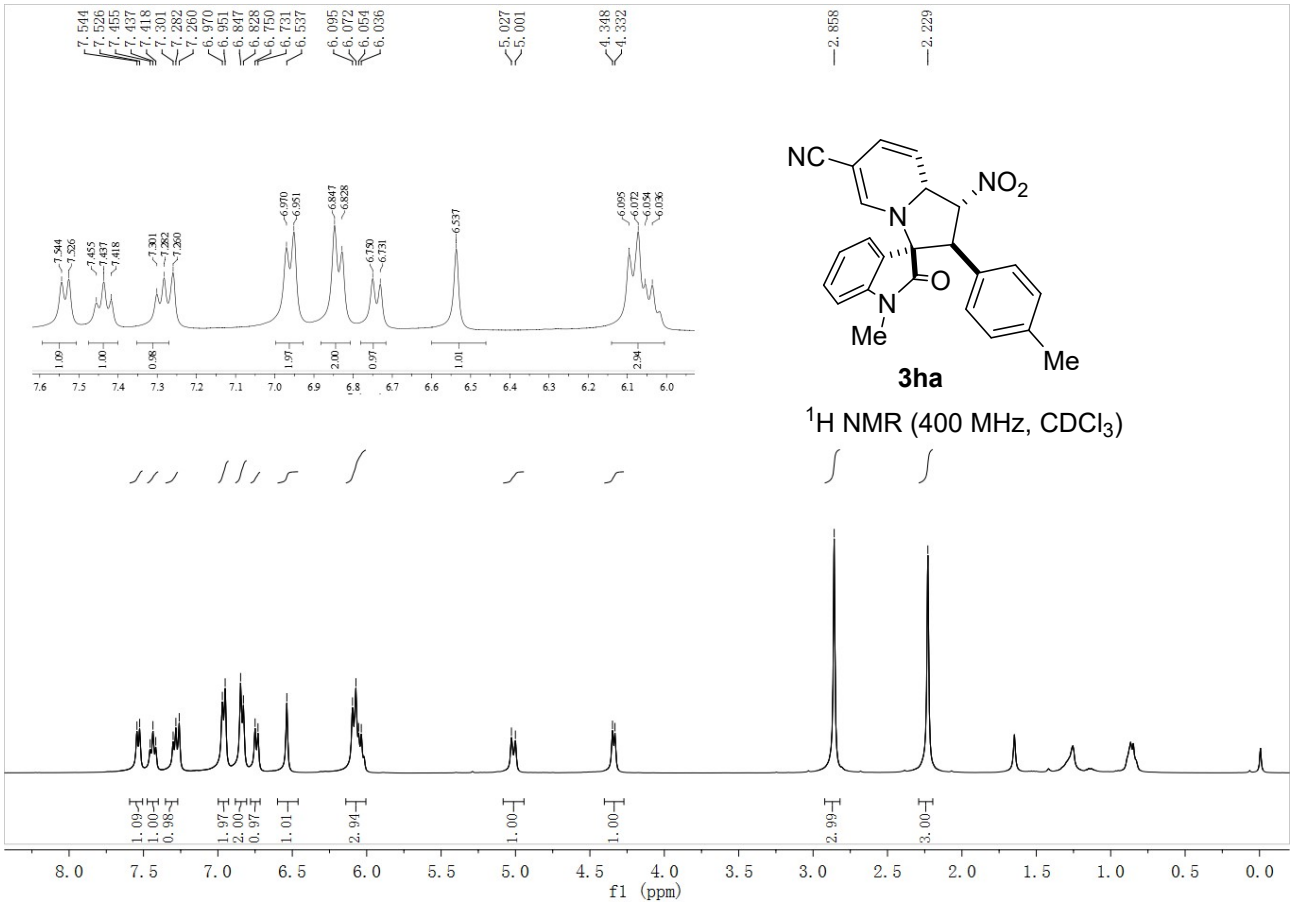




3ga

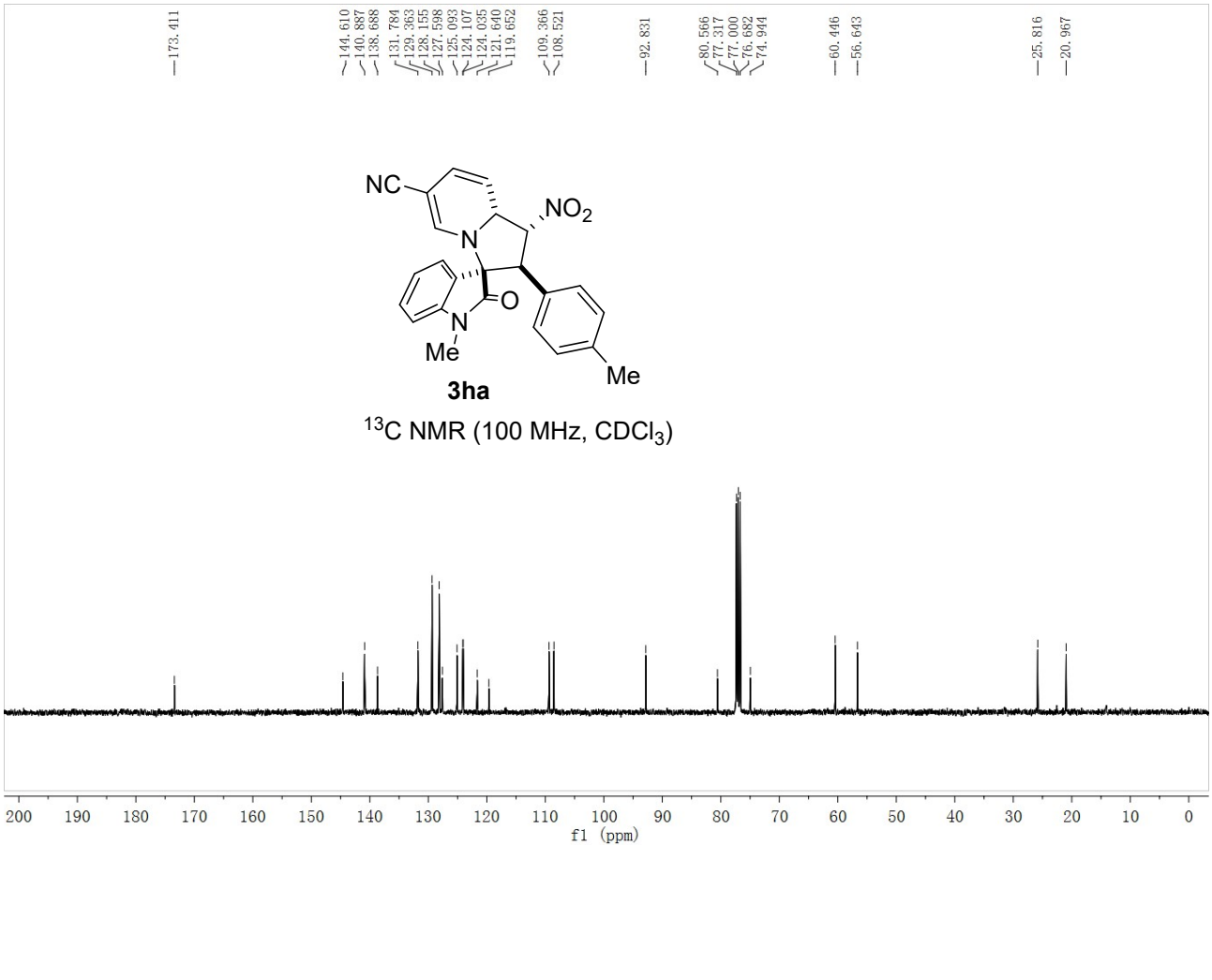
^{13}C NMR (100 MHz, $CDCl_3$)





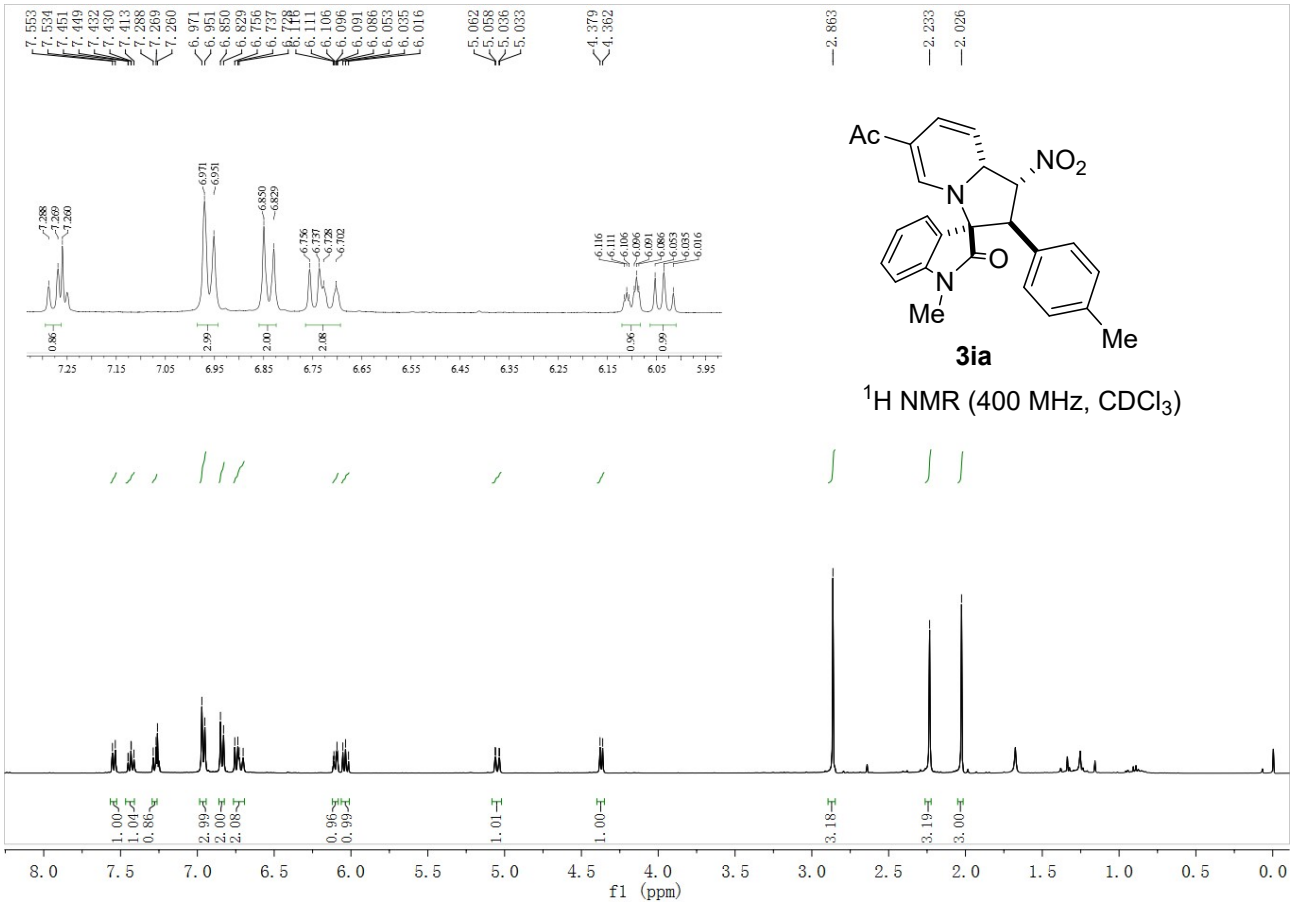
3ha

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

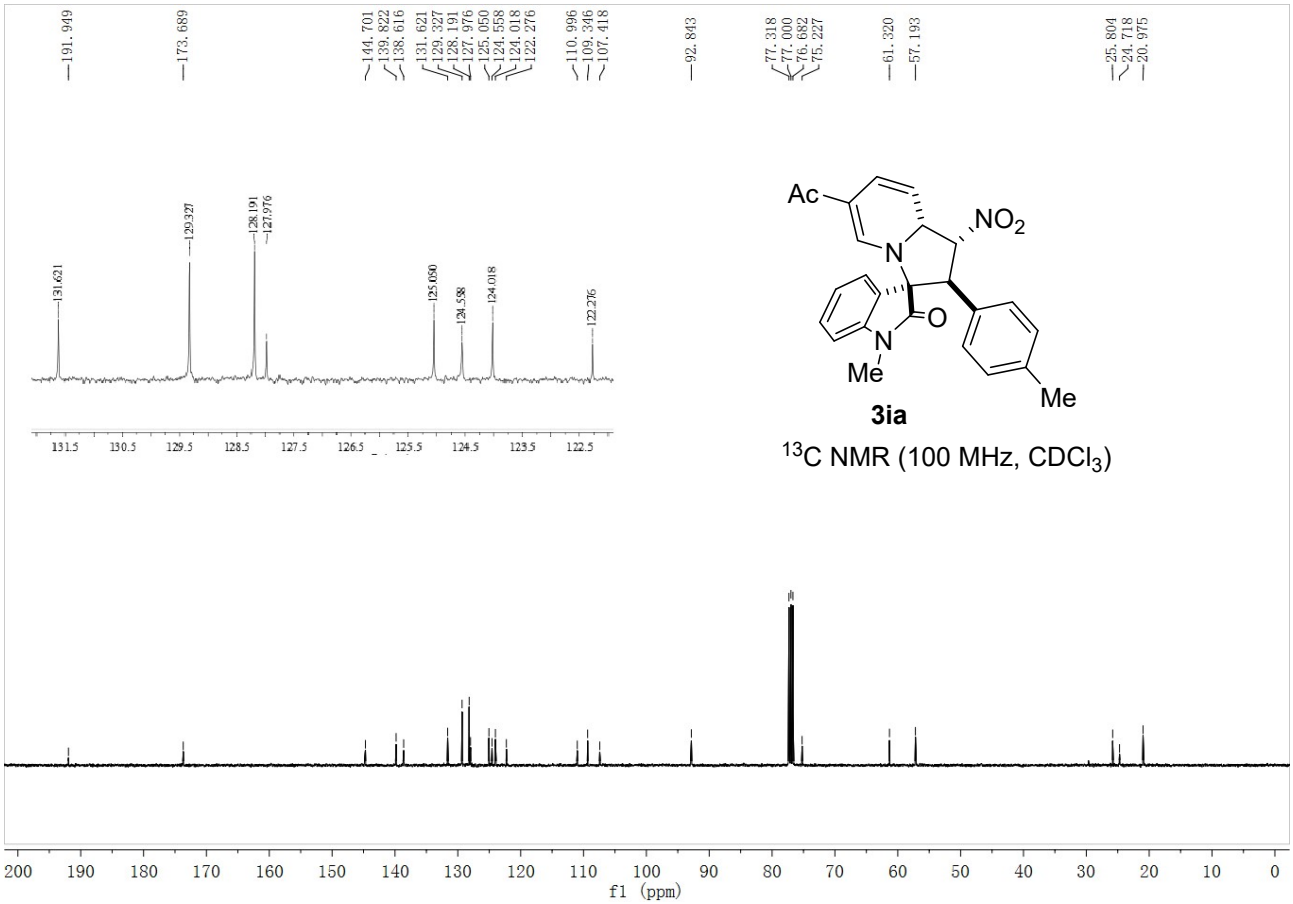


3ha

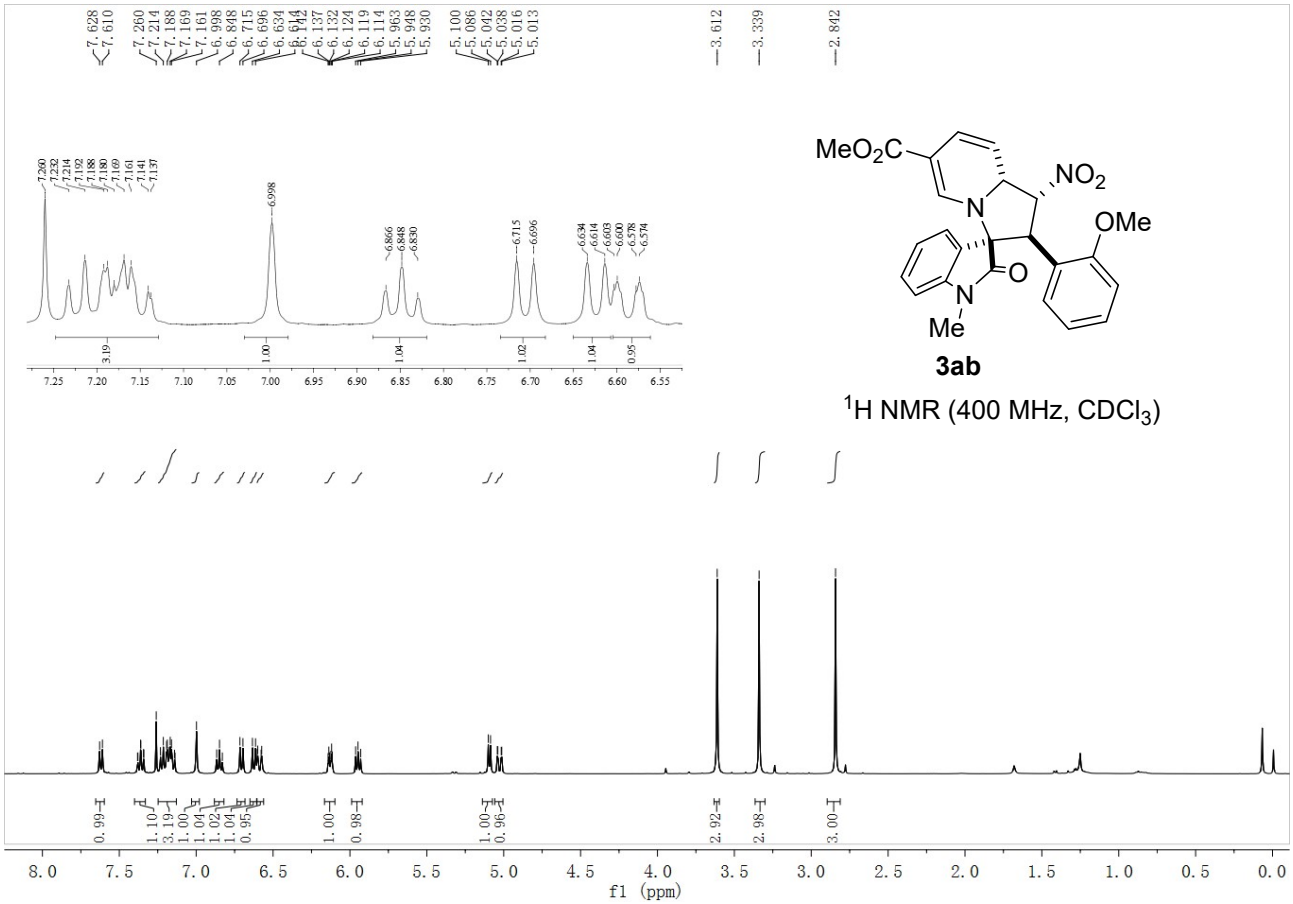
^{13}C NMR (100 MHz, $CDCl_3$)



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

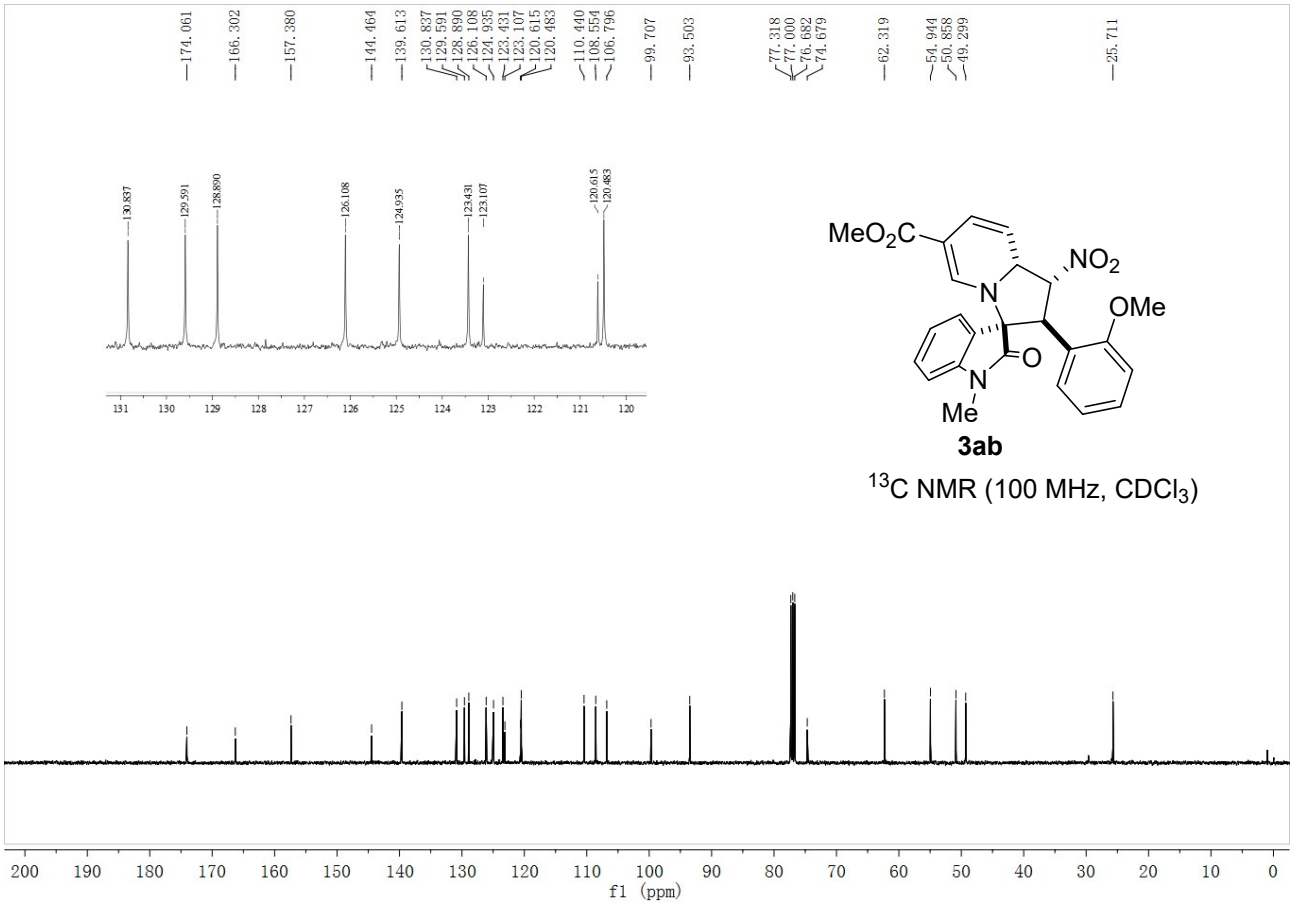


^{13}C NMR (100 MHz, $CDCl_3$)



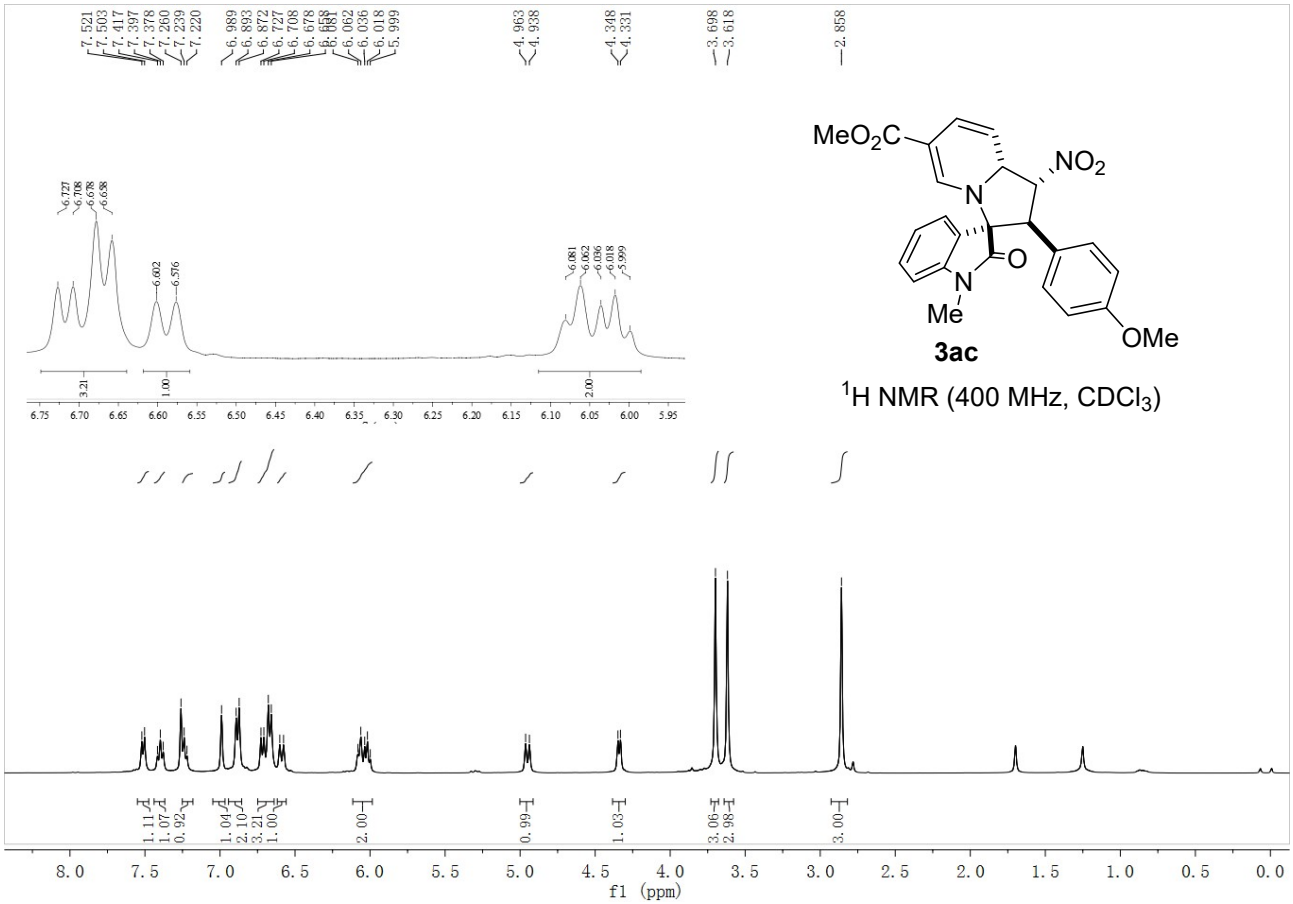
3ab

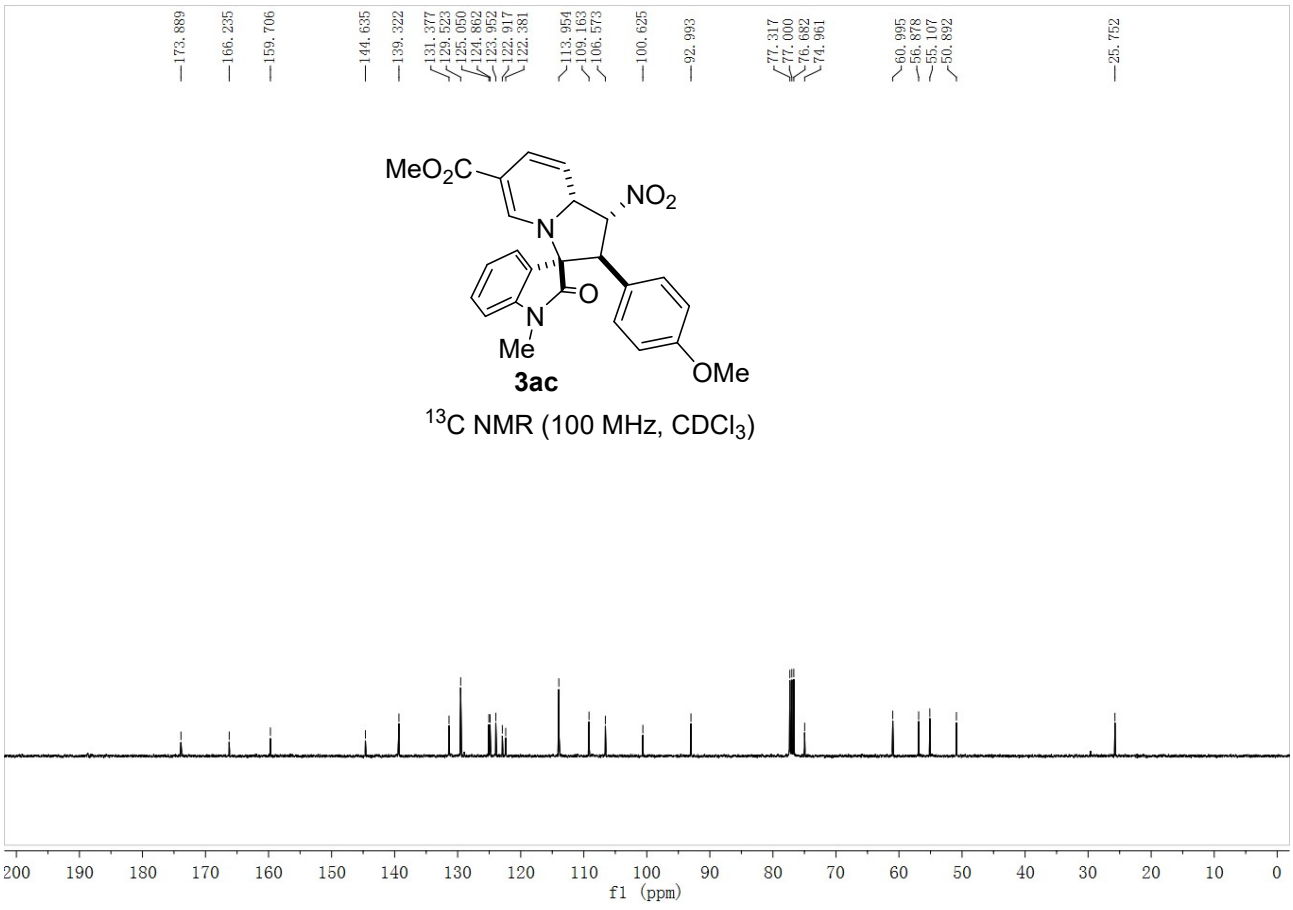
^{1}H NMR (400 MHz, $CDCl_3$)

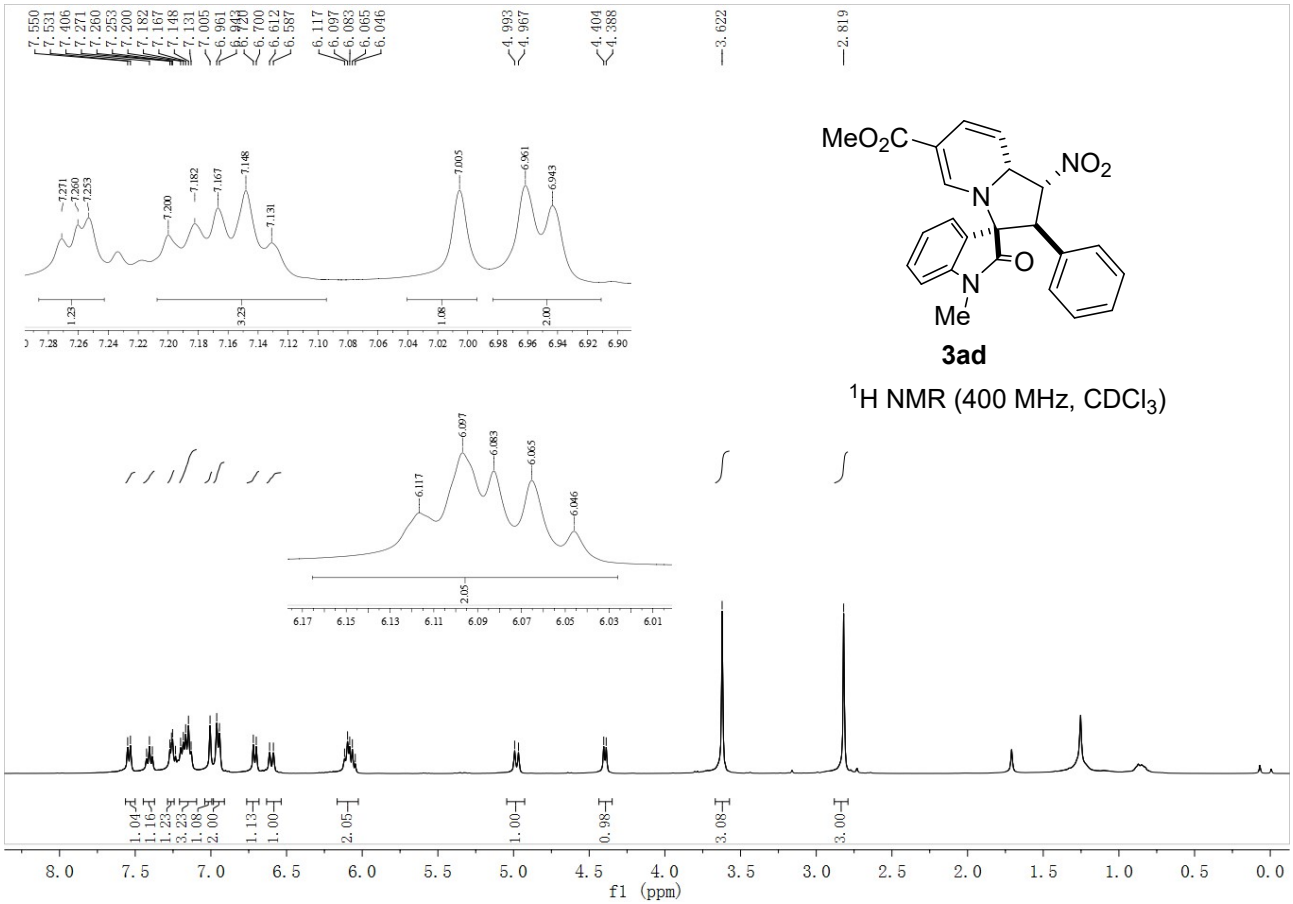


3ab

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

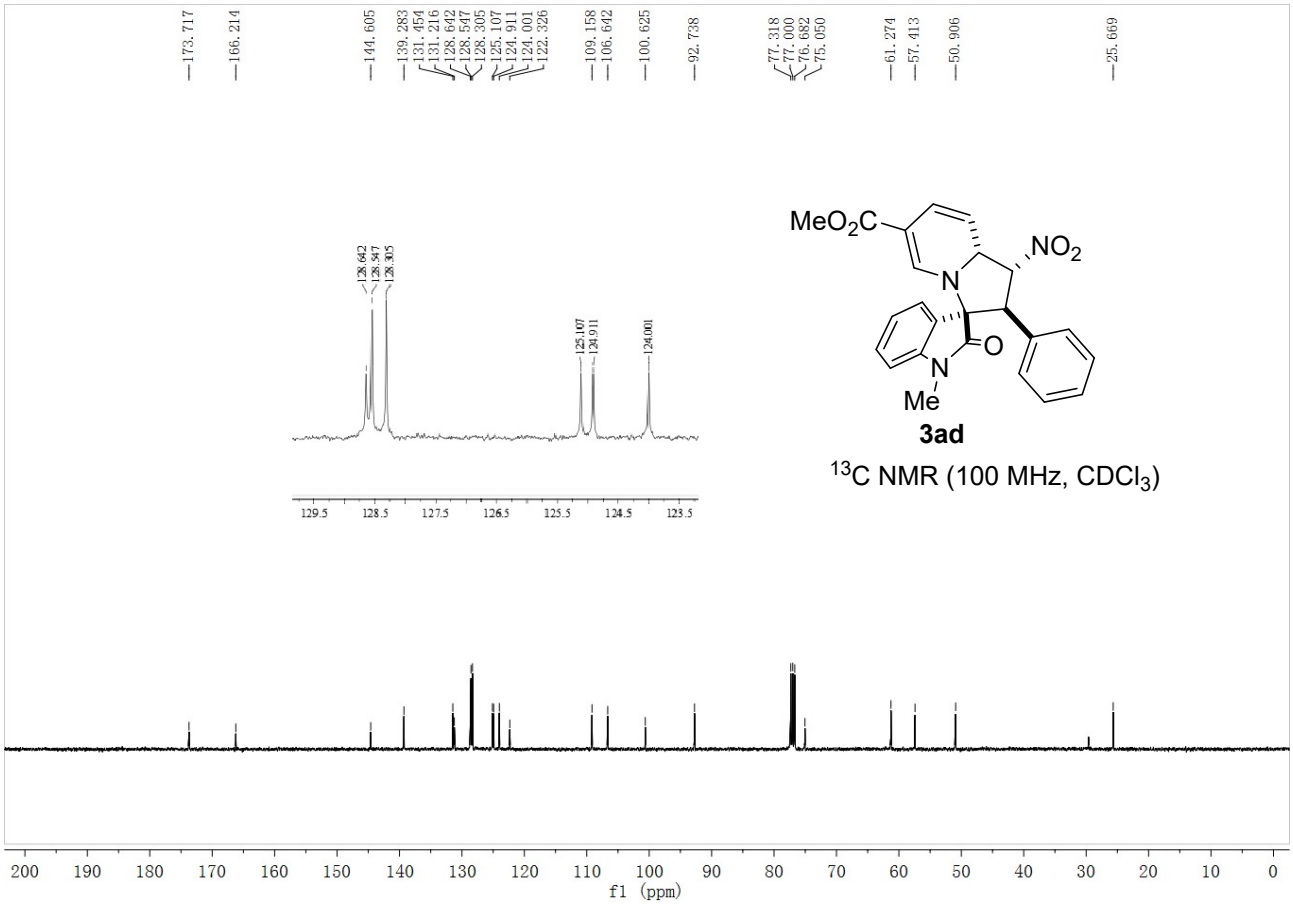

7.521
7.503
7.417
7.397
7.378
7.260
7.239
7.220
6.989
6.893
6.872
6.727
6.708
6.678
6.062
6.036
6.018
5.999
4.963
4.938
4.348
4.331
3.698
3.618
2.858
6.727
6.708
6.678
6.658
6.602
6.576
6.081
6.062
6.036
6.018
5.999
3.21
1.00
2.00
MeO2C
NO2
N
O
N
Me
OMe
3ac
1H NMR (400 MHz, CDCl3)
1.11
1.07
0.92
1.04
2.10
3.21
1.00
2.00
0.99
1.03
3.06
2.98
3.00
f1 (ppm)


173.889
166.235
159.706
144.635
139.322
131.377
129.523
125.050
124.862
123.952
122.917
122.381
113.954
109.163
106.573
100.625
92.993
77.317
77.000
76.682
74.961
60.995
56.878
55.107
50.892
25.752
MeO2C
NO2
N
O
N
Me
OMe
3ac
13C NMR (100 MHz, CDCl3)
f1 (ppm)



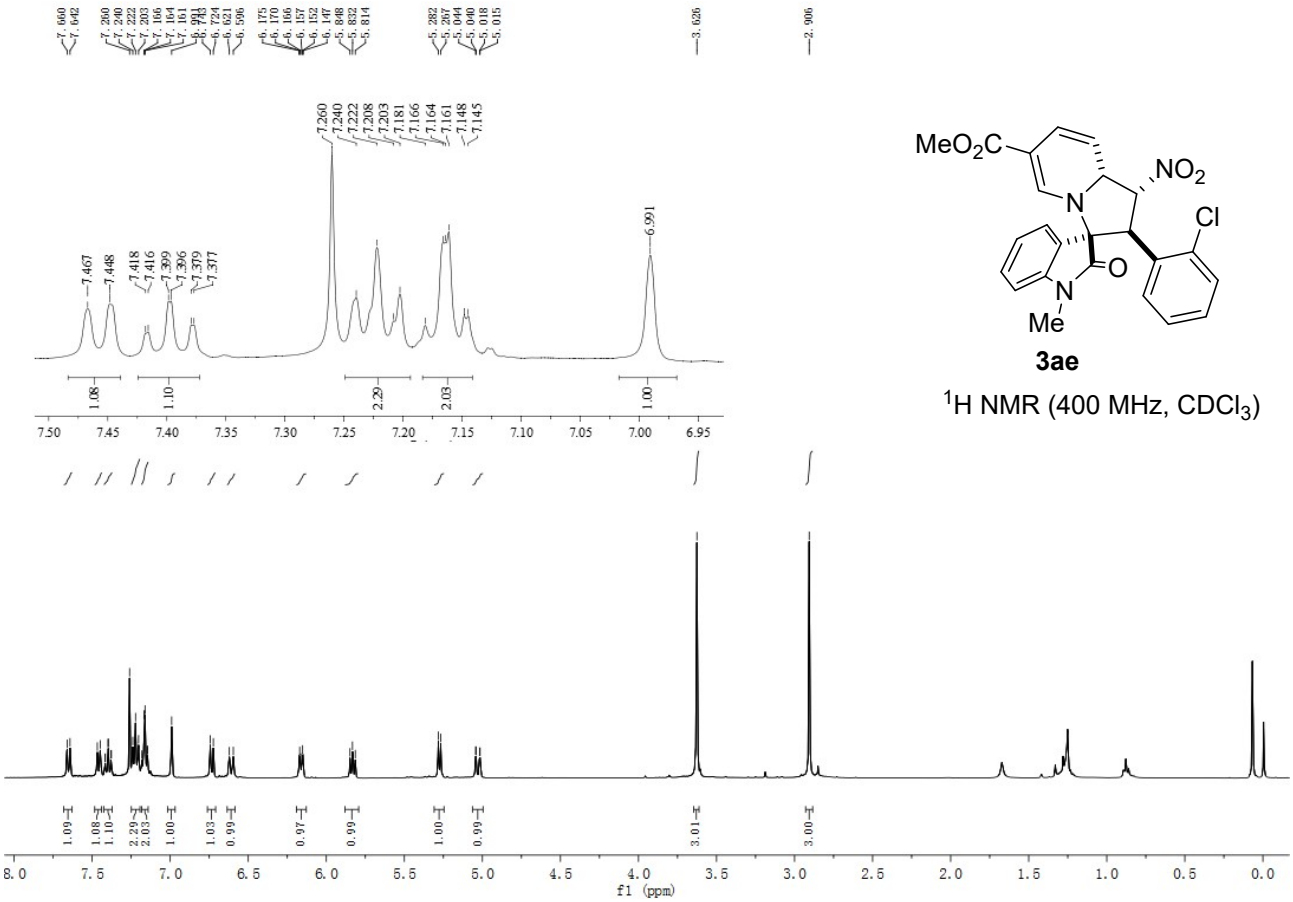
3ad

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



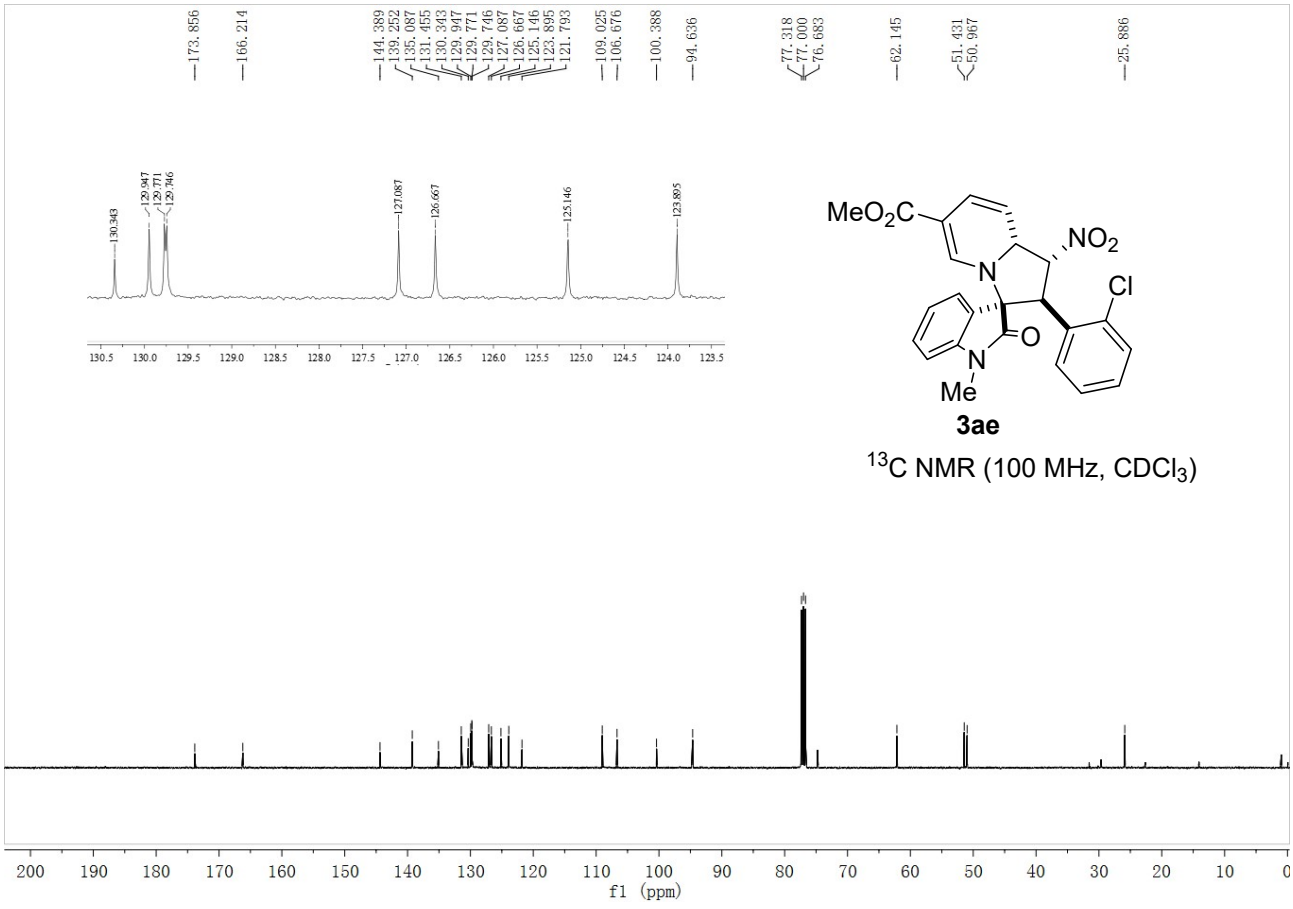
3ad

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



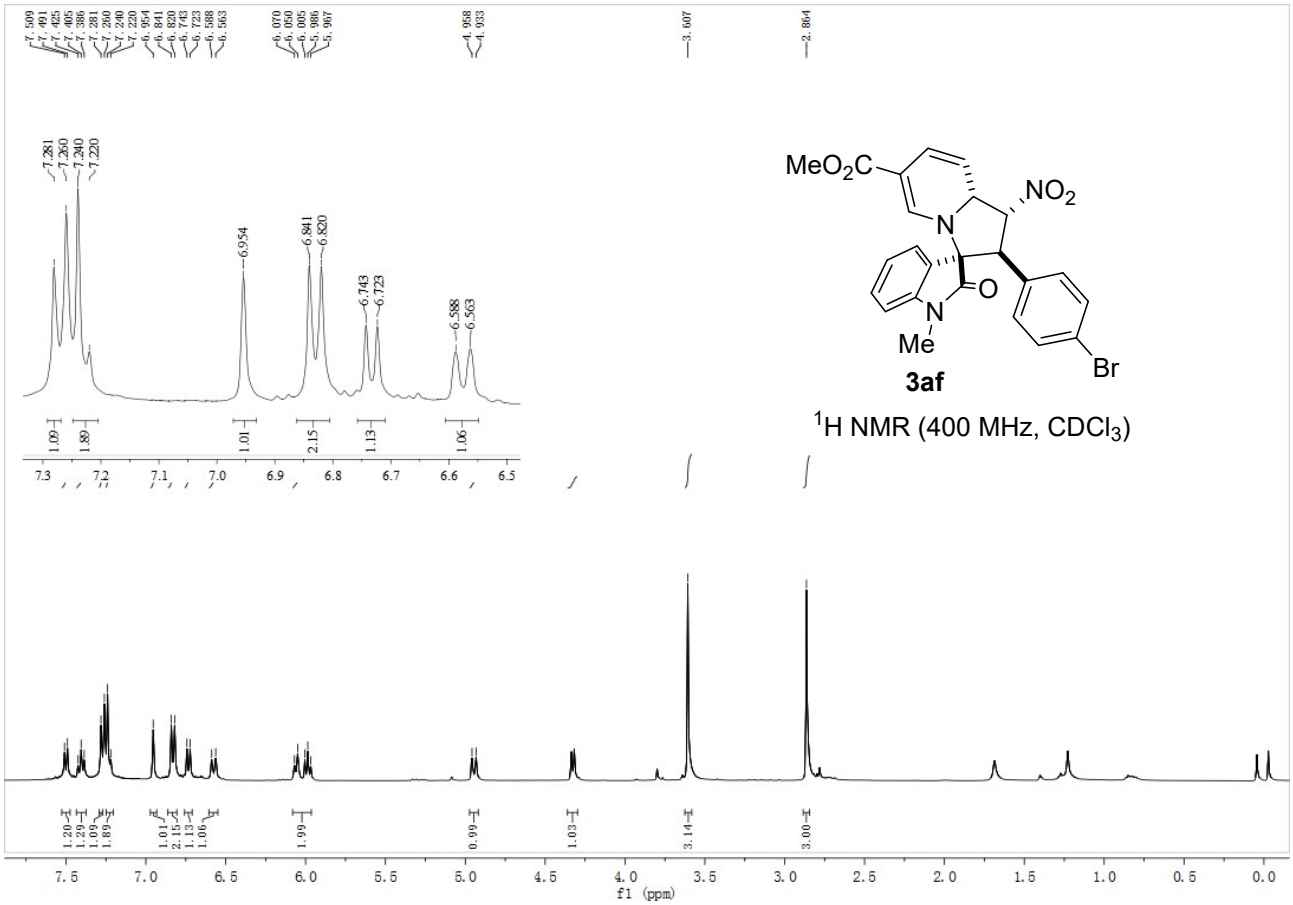
3ae

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



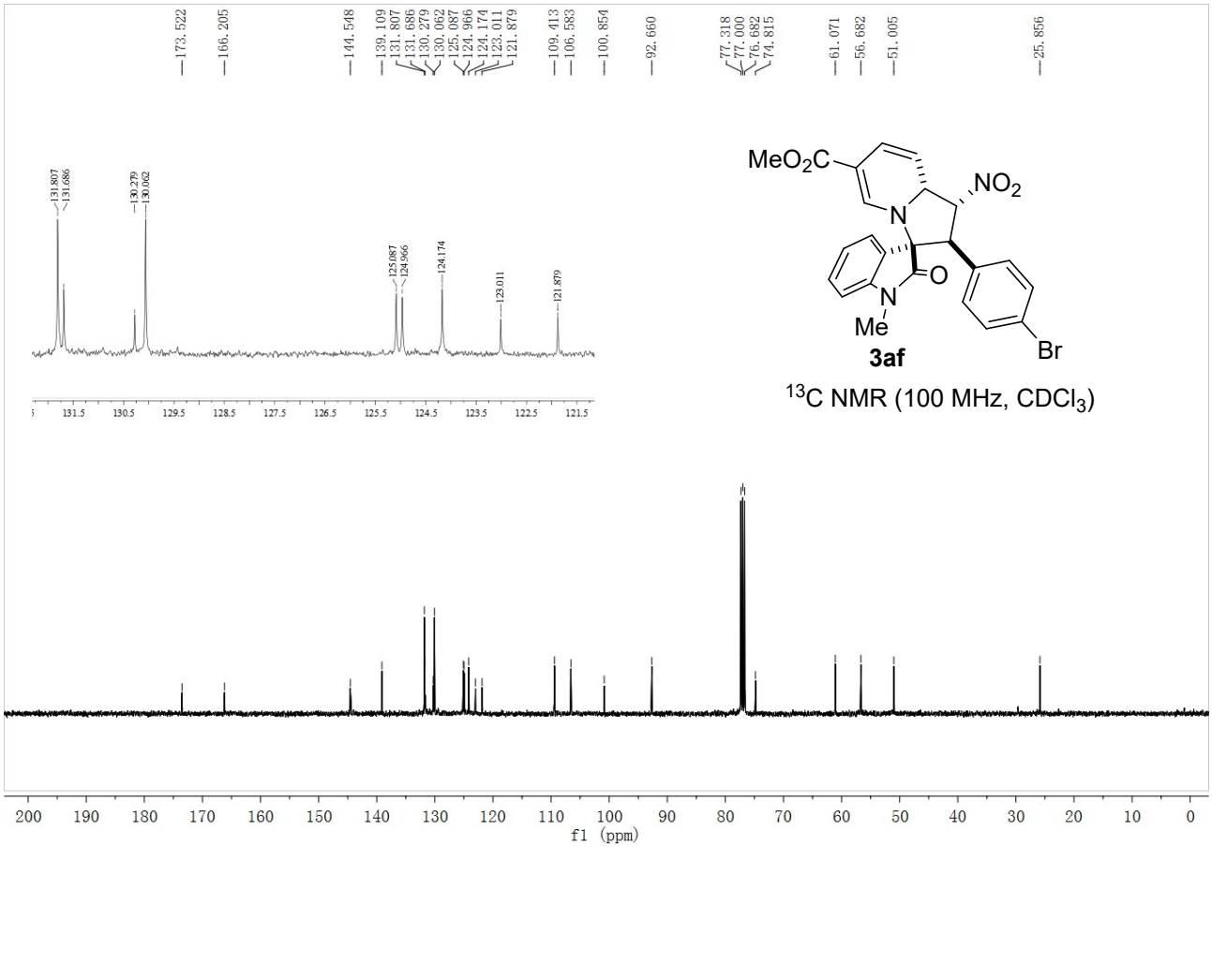
3ae

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



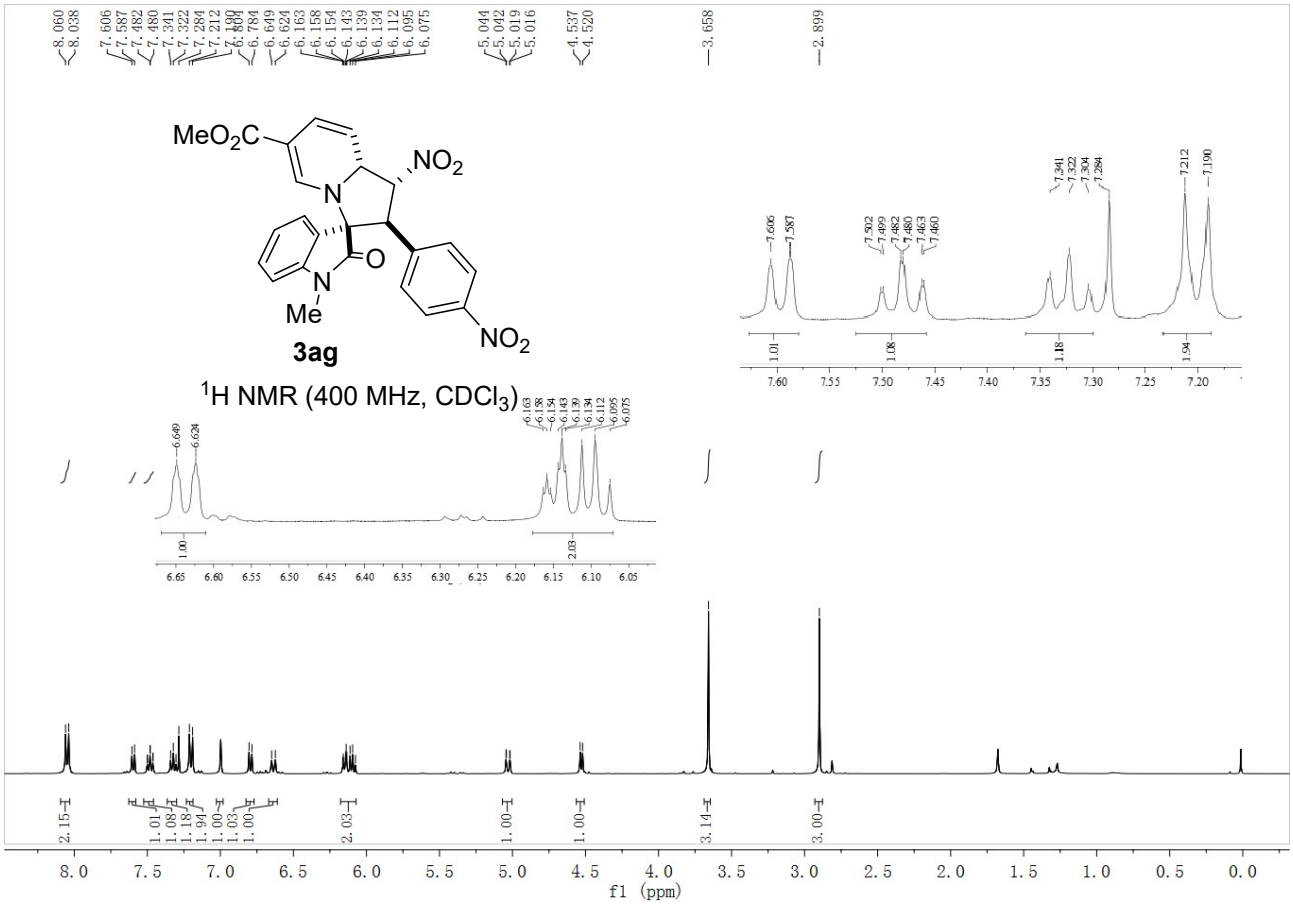
3af

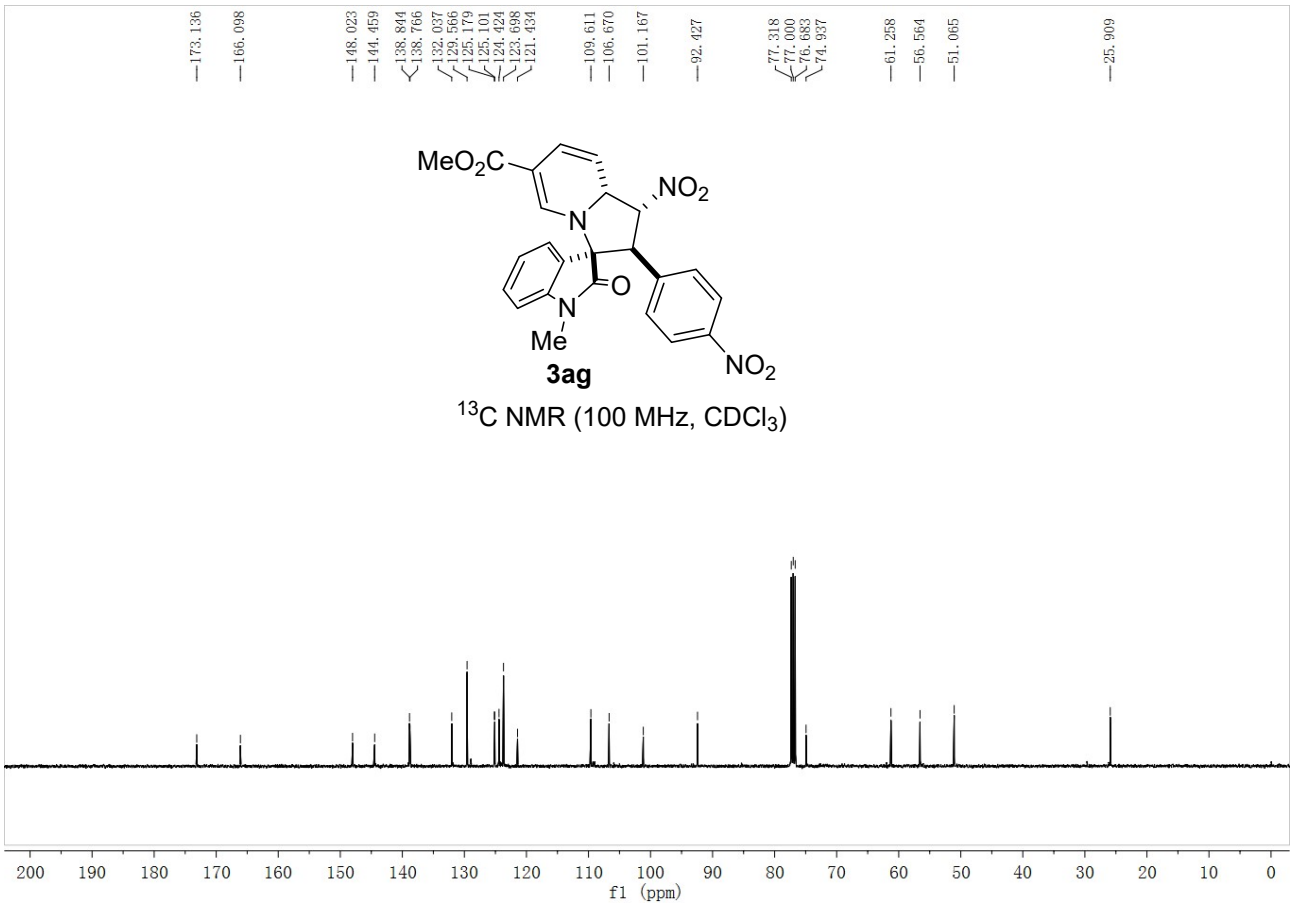
^{1}H NMR (400 MHz, $CDCl_3$)

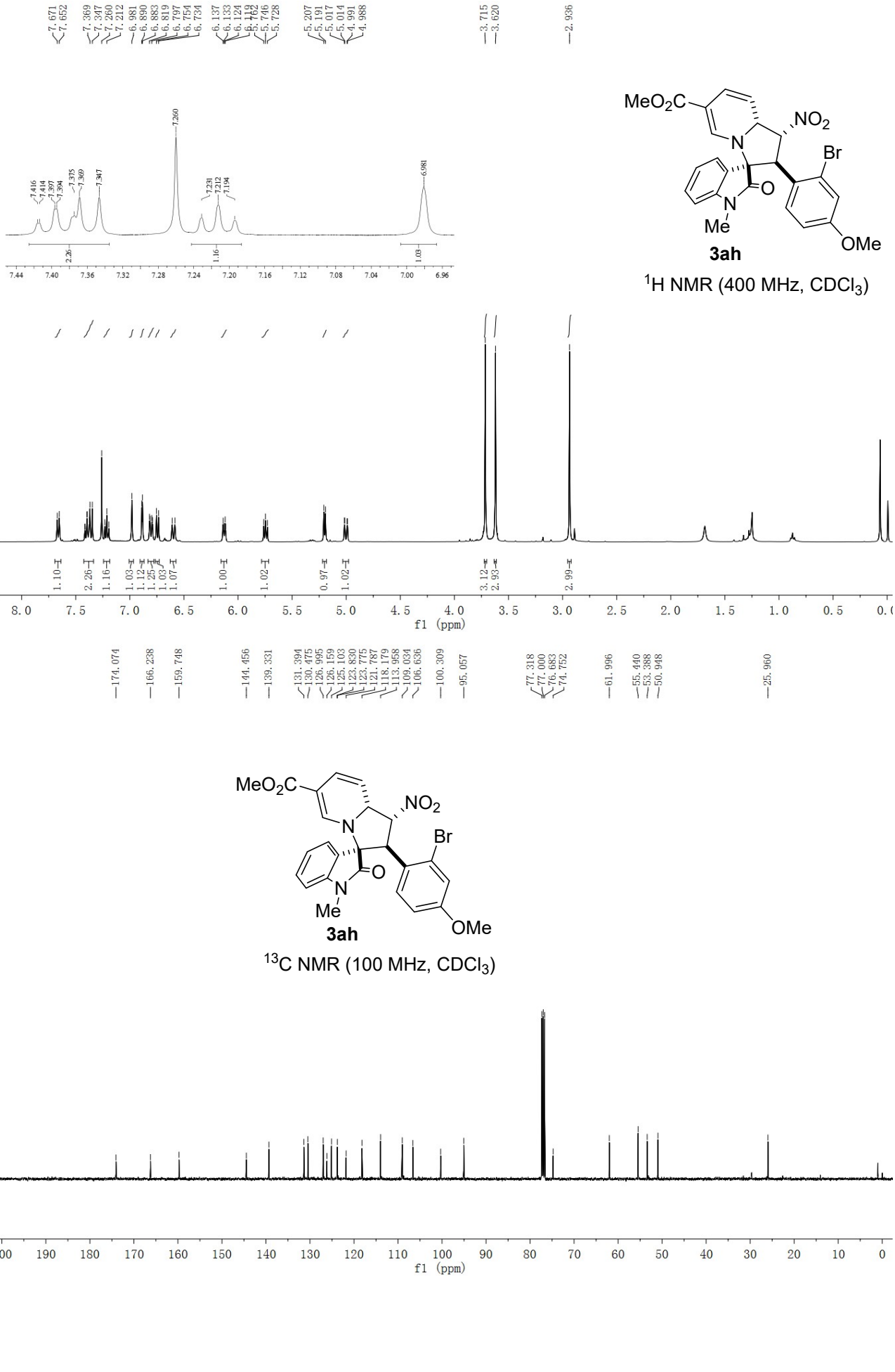


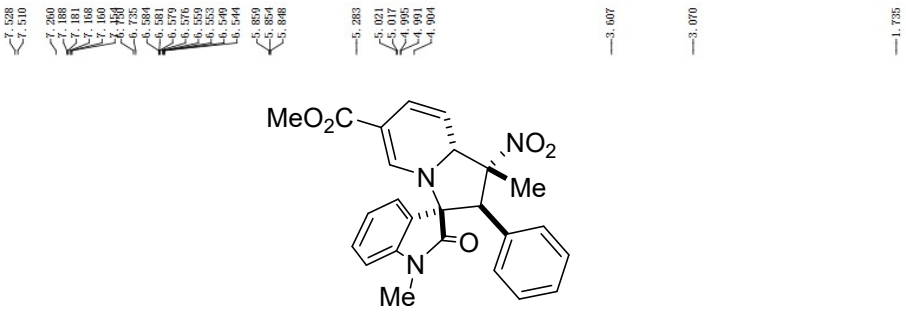
3af

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


MeO2C
NO2
N
O
N
Me
NO2
3ag
1H NMR (400 MHz, CDCl3)
f1 (ppm)

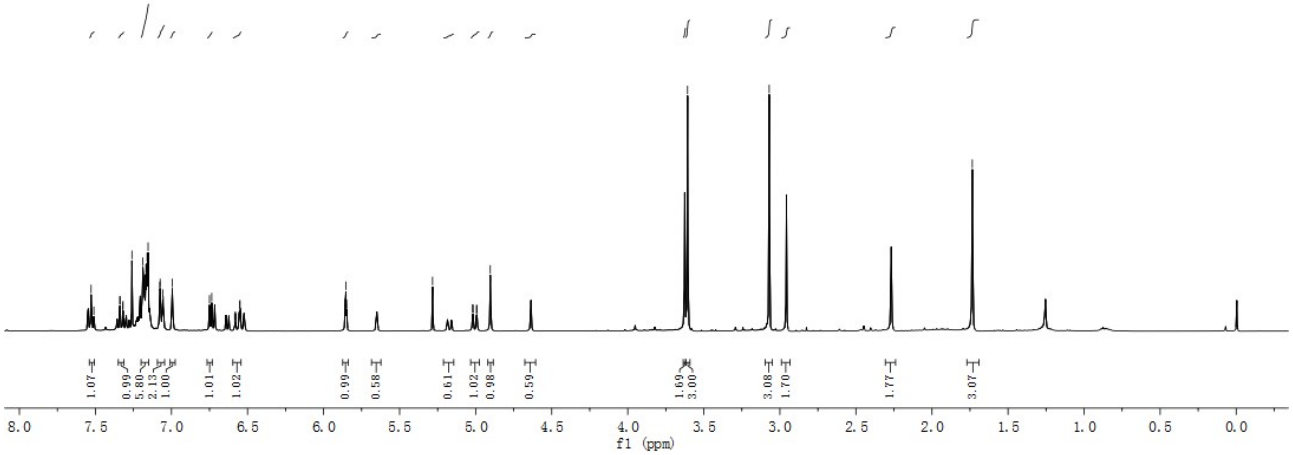

MeO2C
NO2
N
O
N
Me
NO2
3ag
13C NMR (100 MHz, CDCl3)
f1 (ppm)

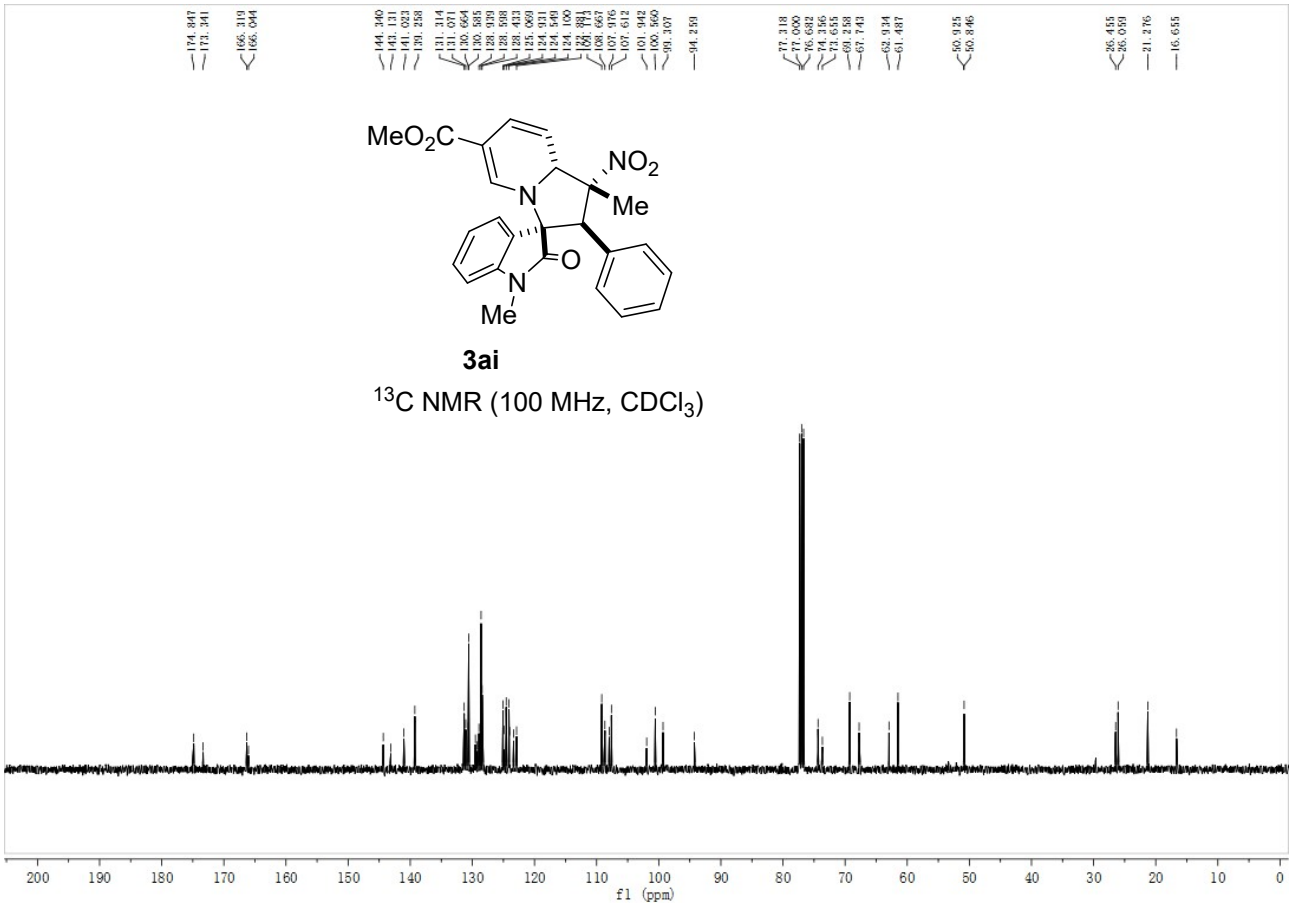

MeO2C
NO2
Br
N
O
N
Me
OMe
3ah
1H NMR (400 MHz, CDCl3)
f1 (ppm)
13C NMR (100 MHz, CDCl3)



3ai

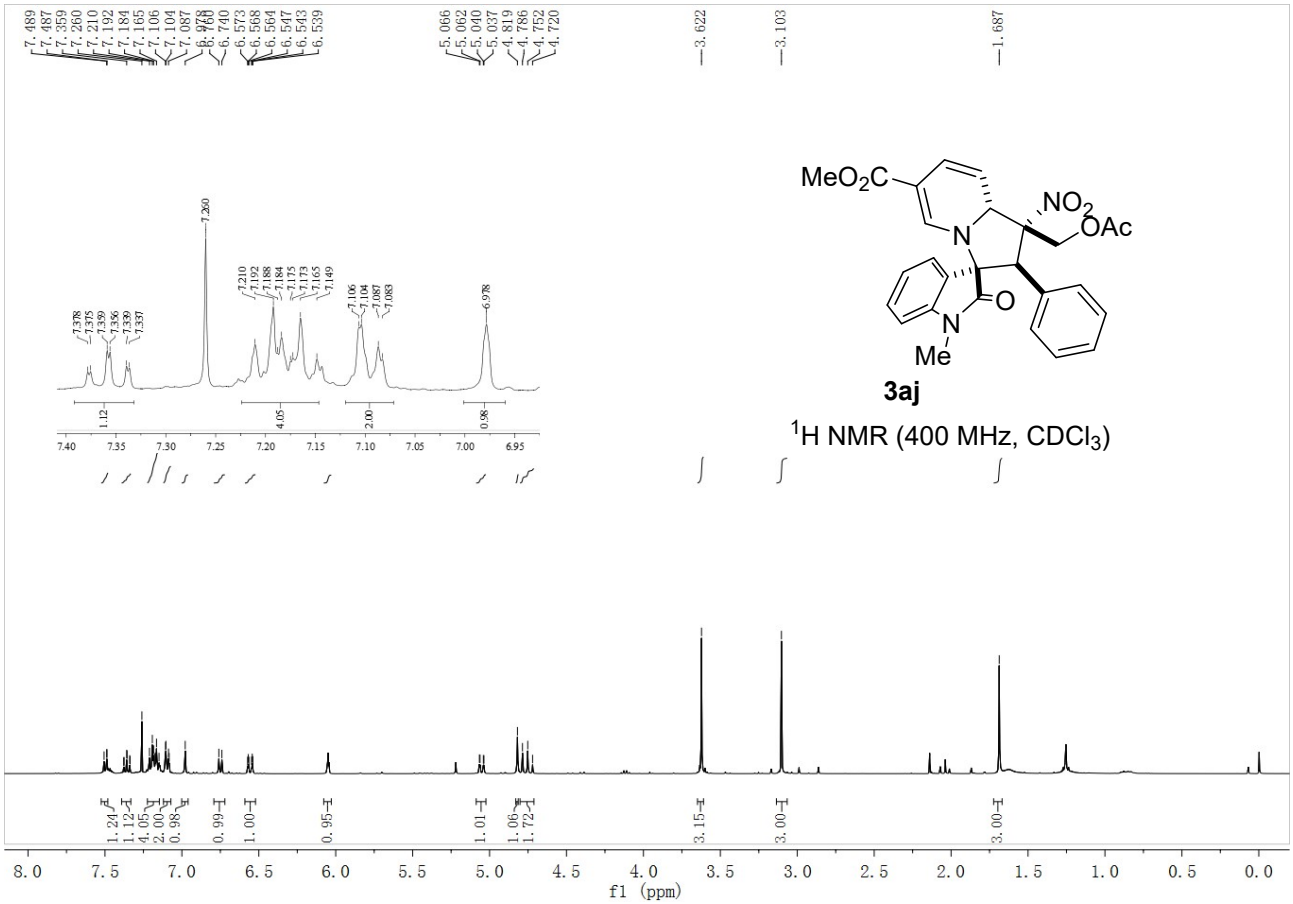
^{1}H NMR (400 MHz, $CDCl_3$)

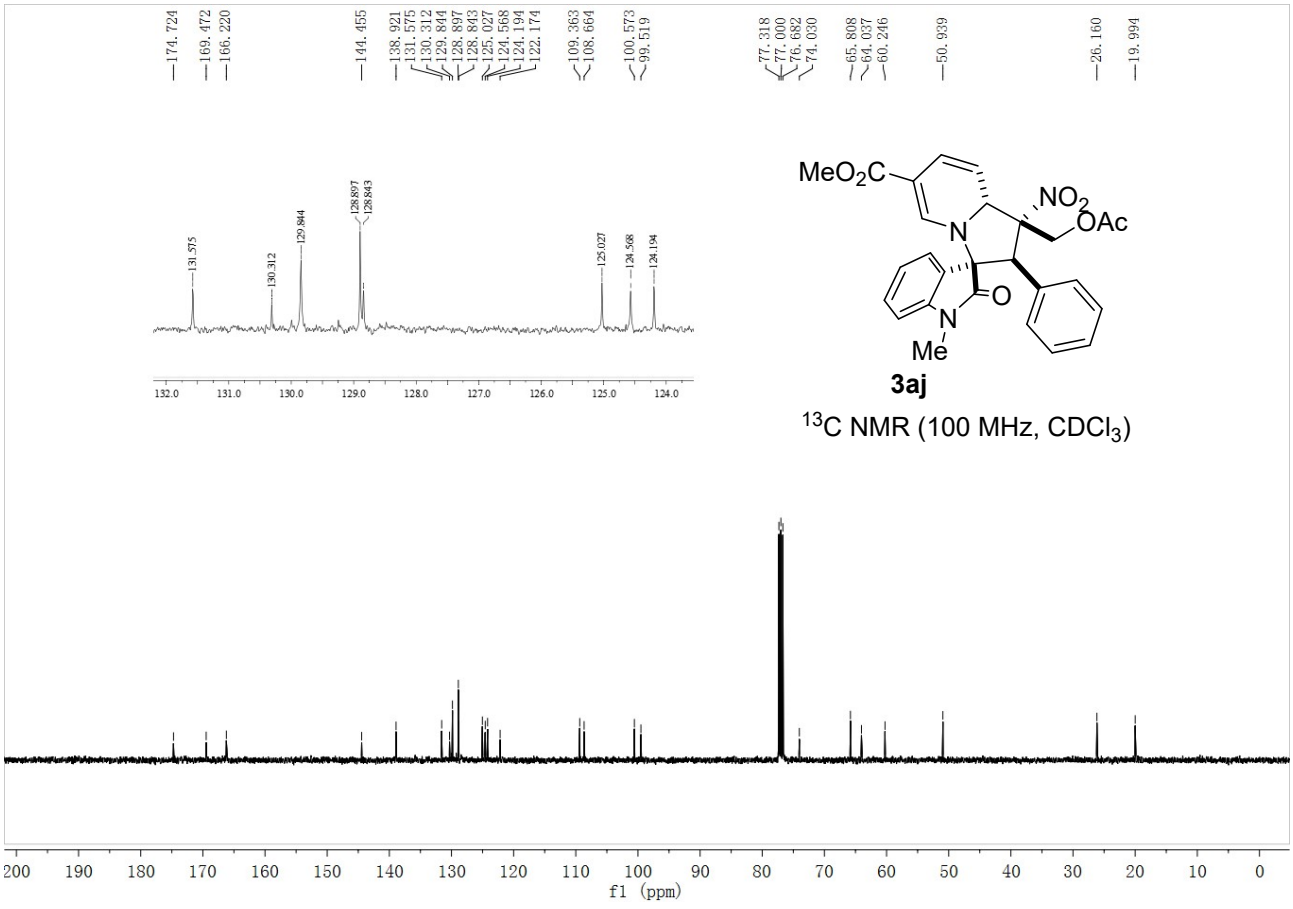


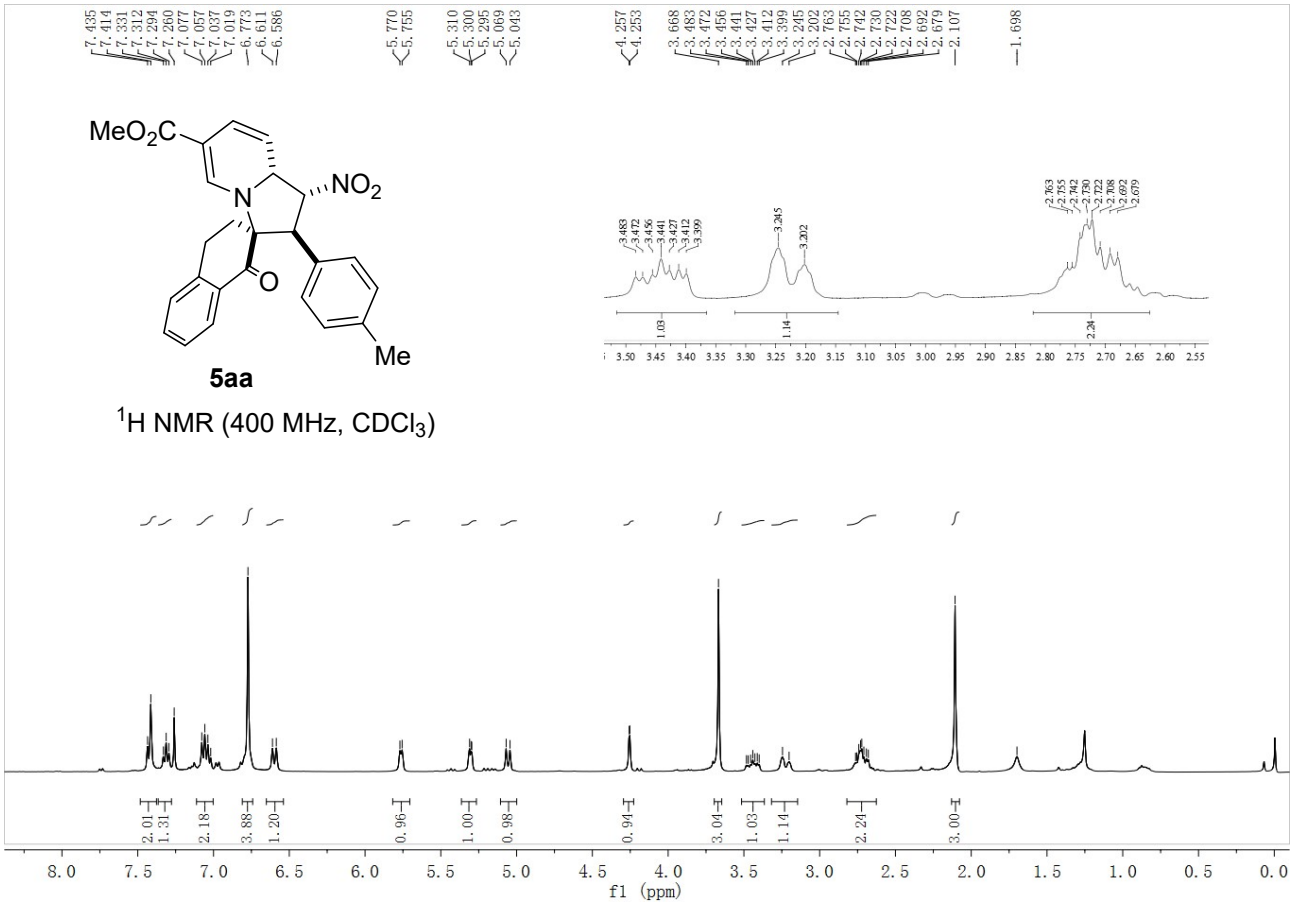


3ai

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


MeO2C
NO2
OAc
N
O
N
Me
3aj
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
OAc
N
O
N
Me
3aj
13C NMR (100 MHz, CDCl3)
f1 (ppm)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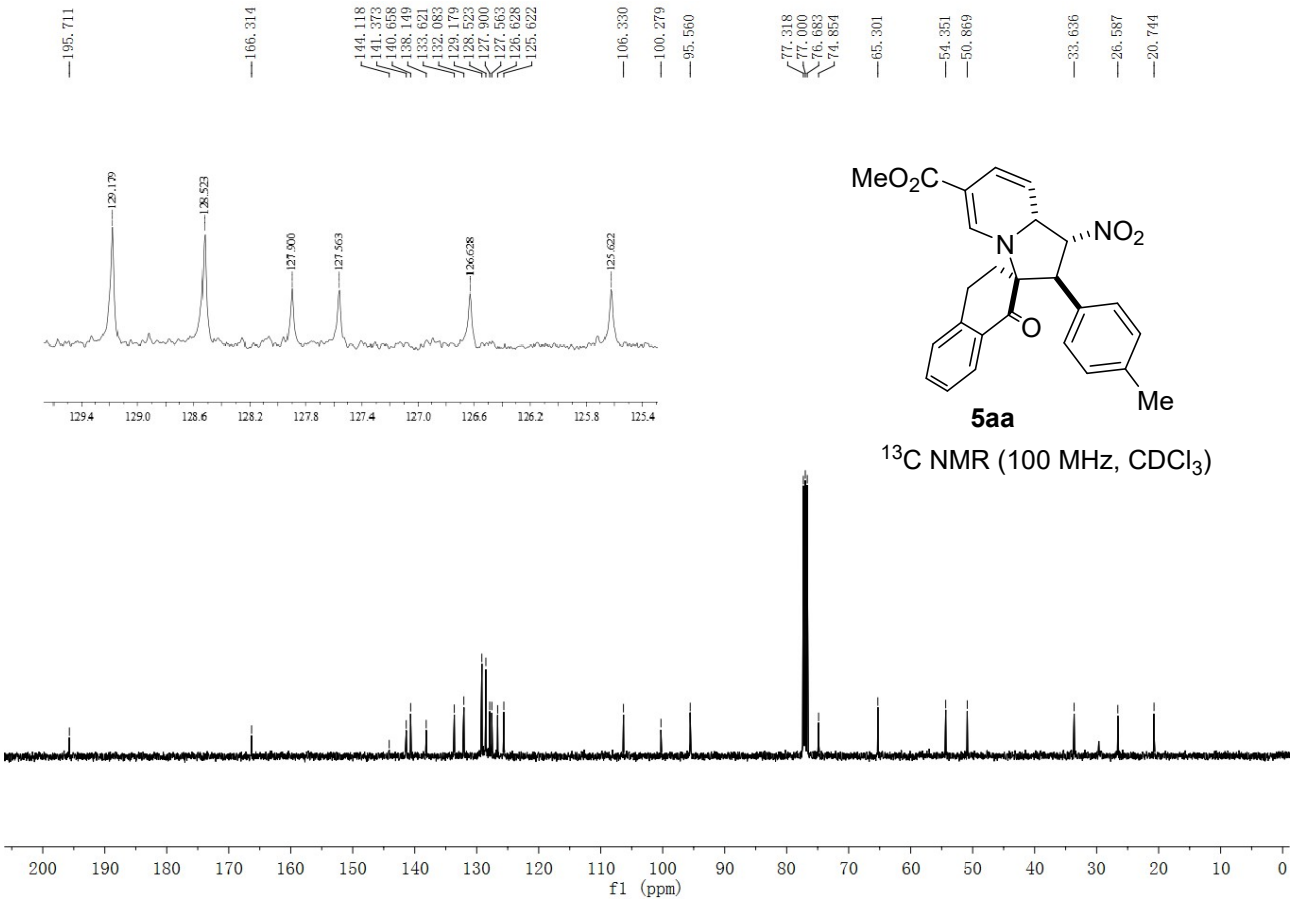
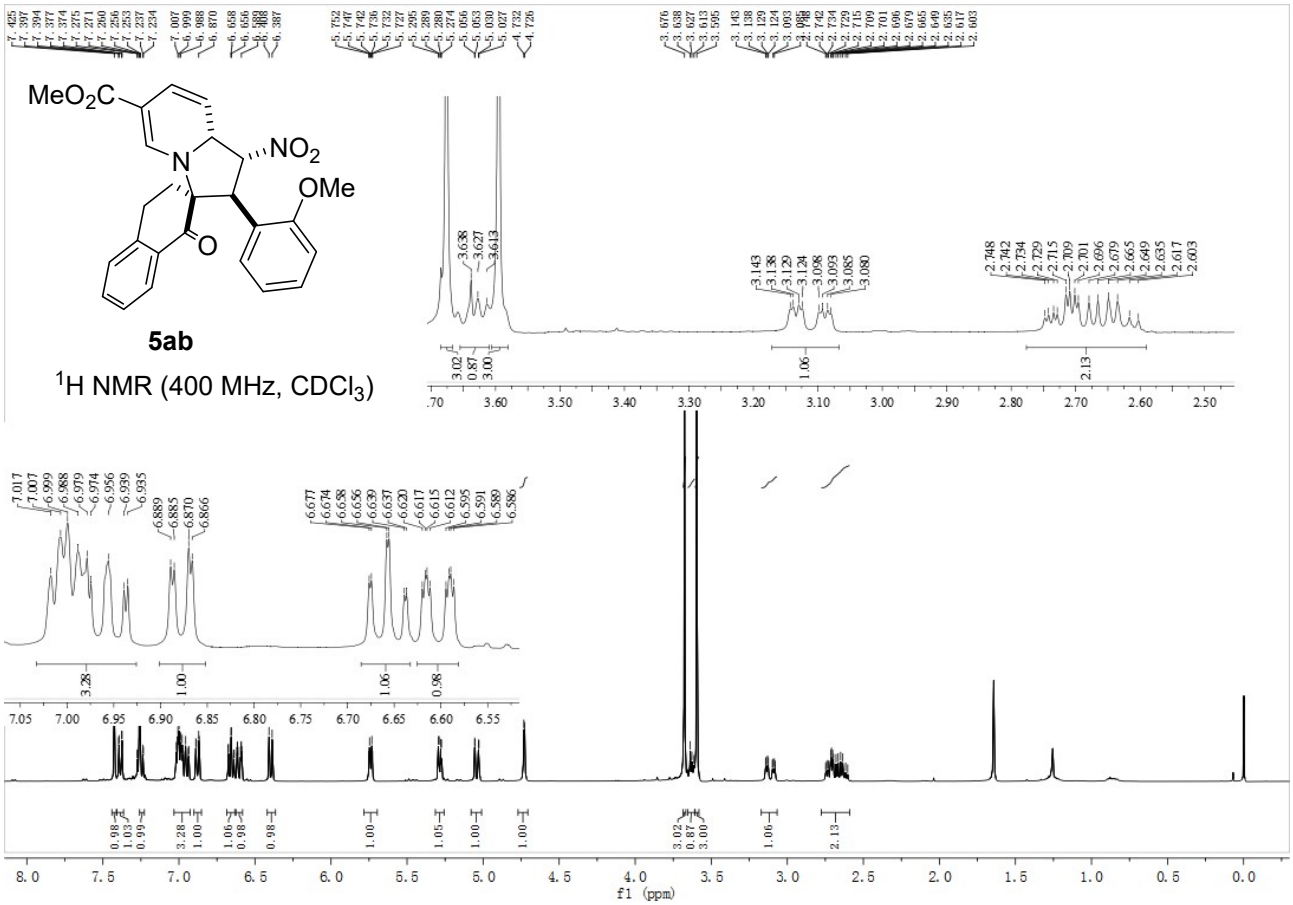
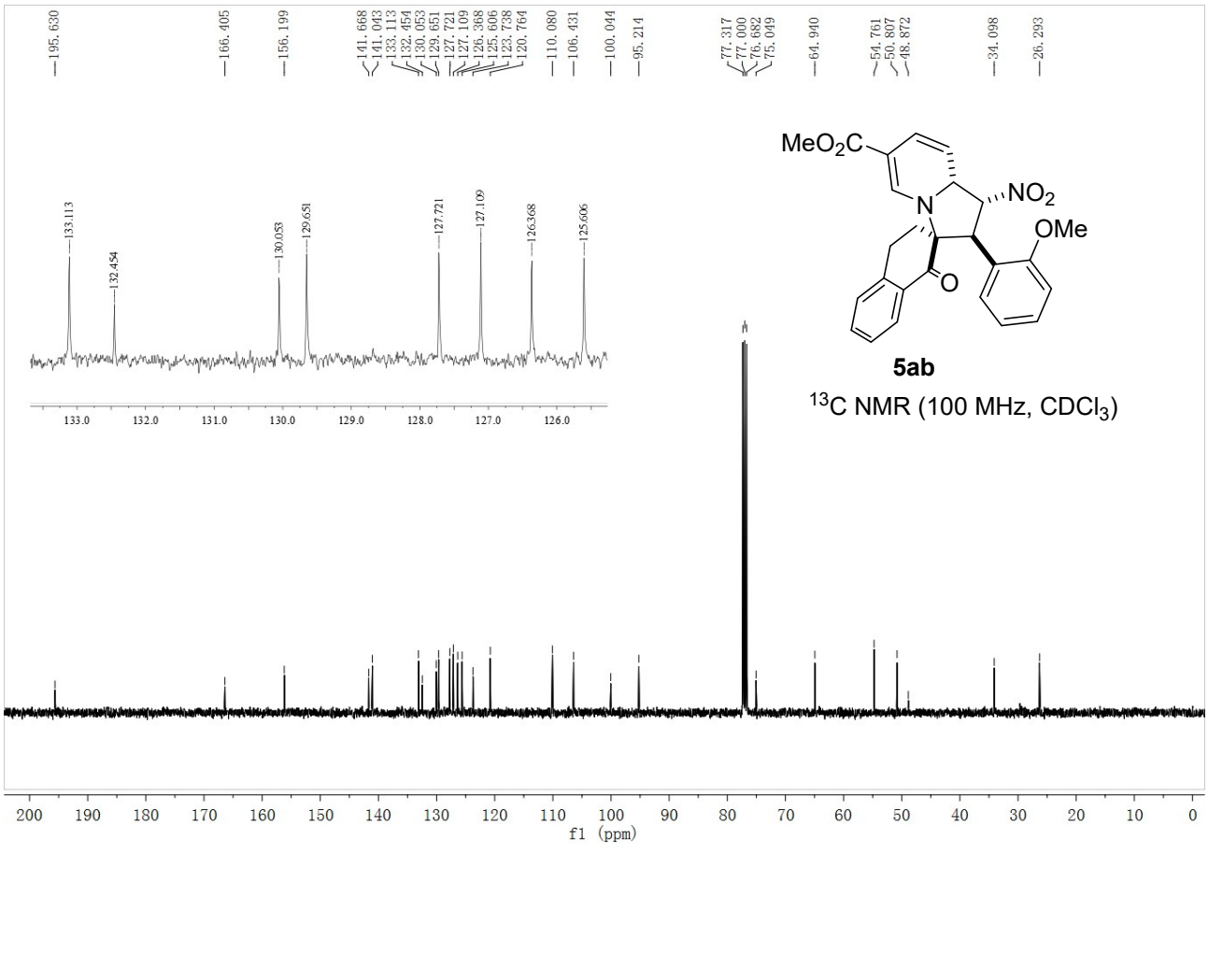
NO2
N
O
Me
5aa
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
N
O
Me
5aa
13C NMR (100 MHz, CDCl3)
f1 (ppm)



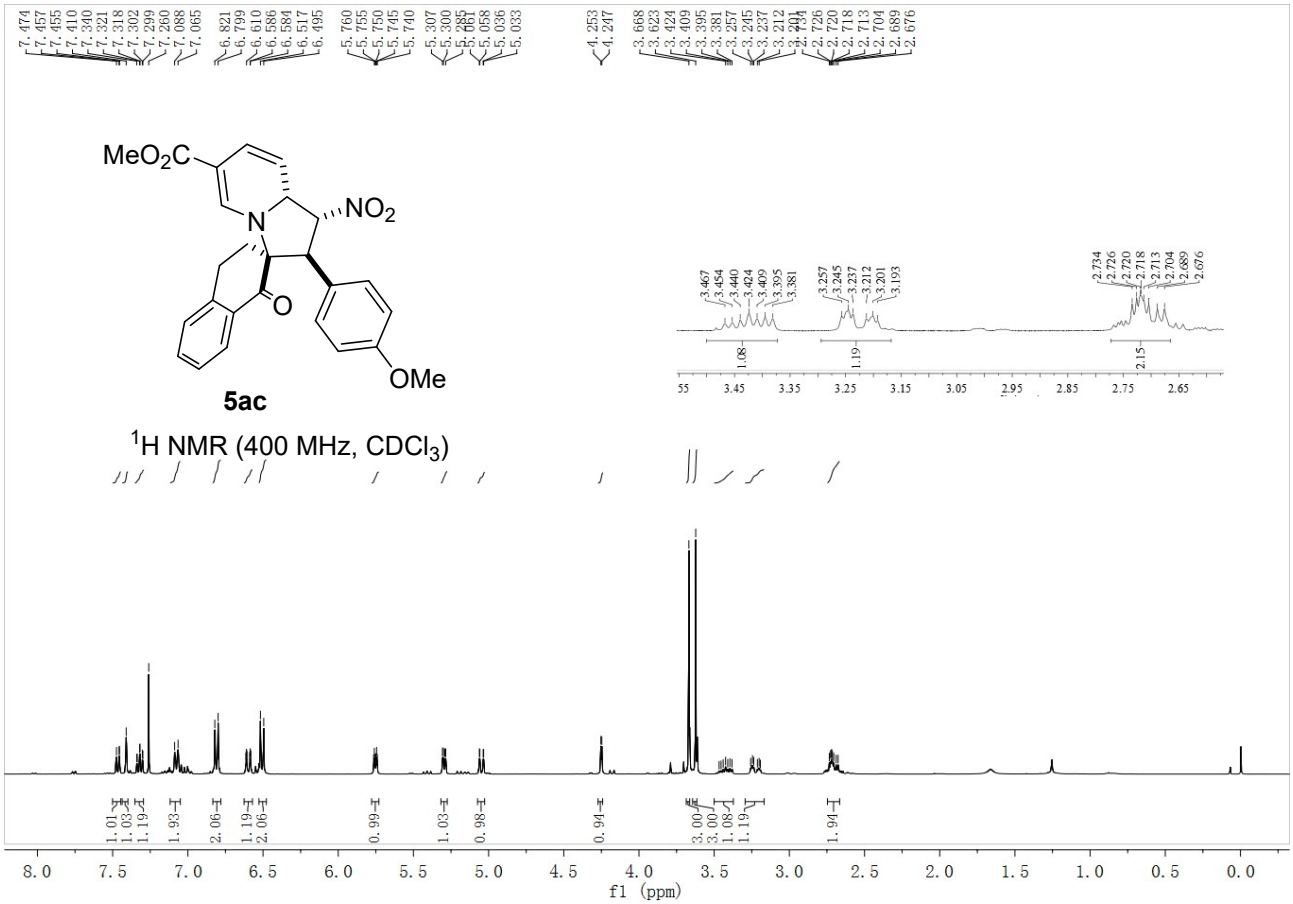
5ab

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



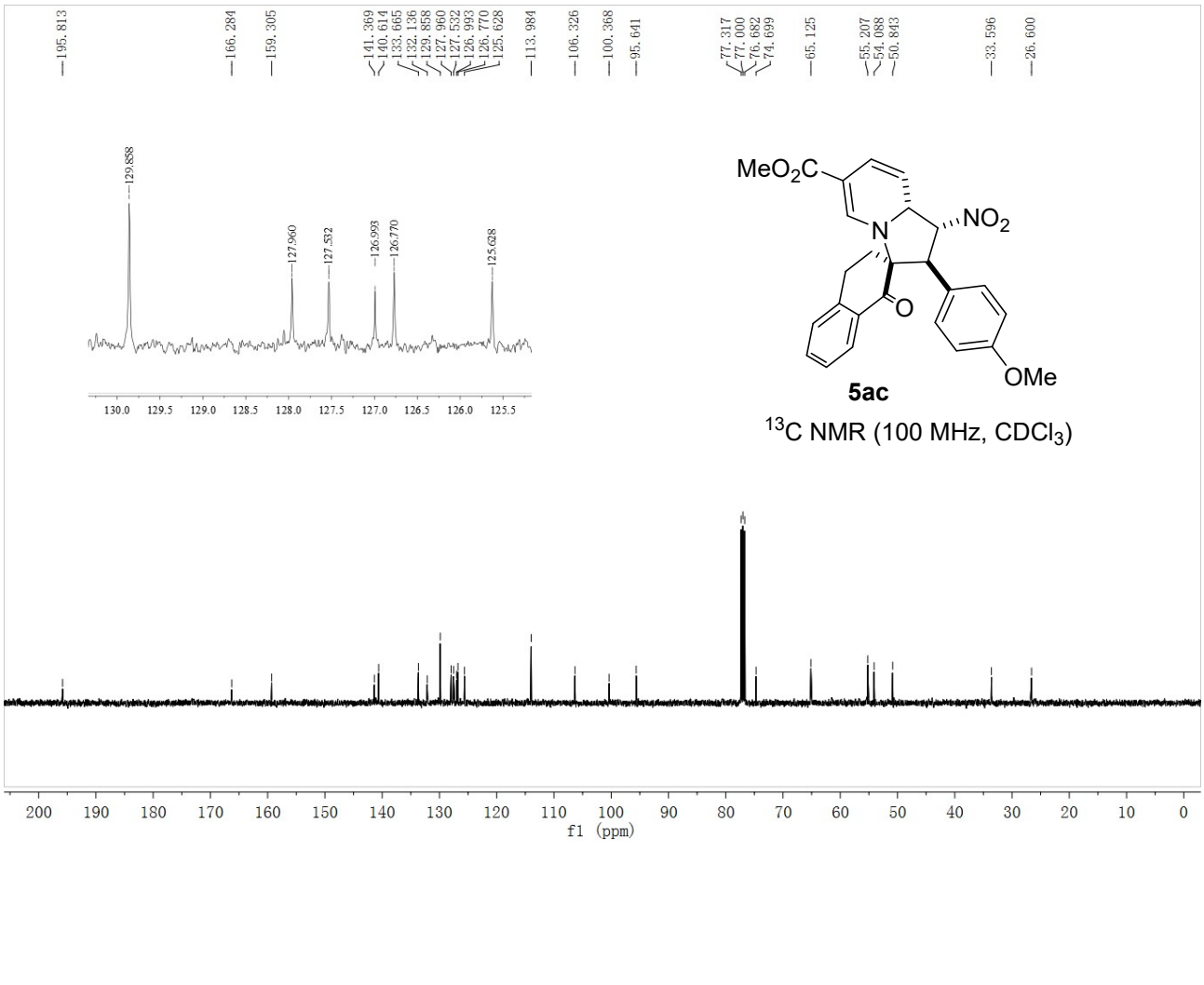
5ab

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



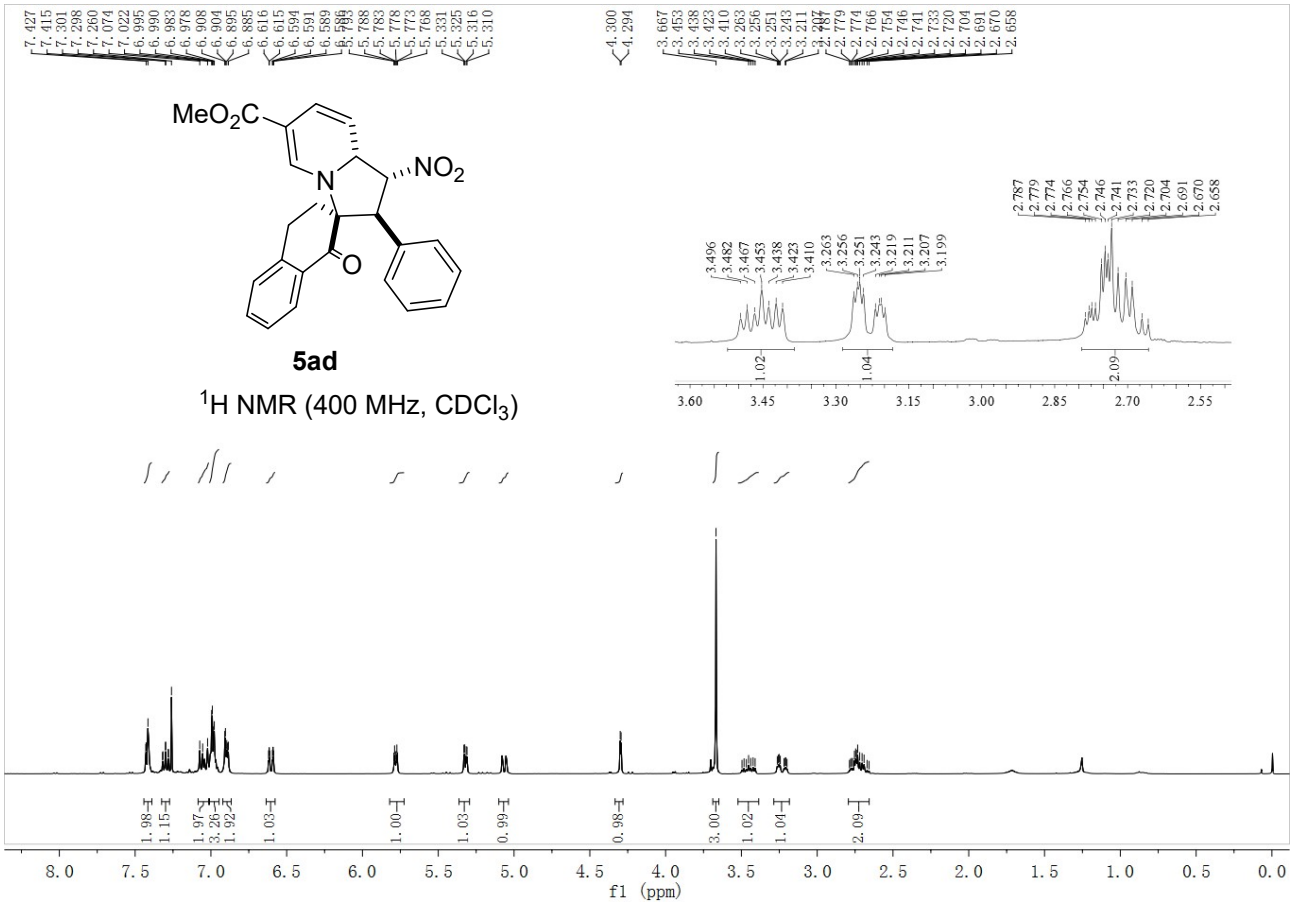
5ac

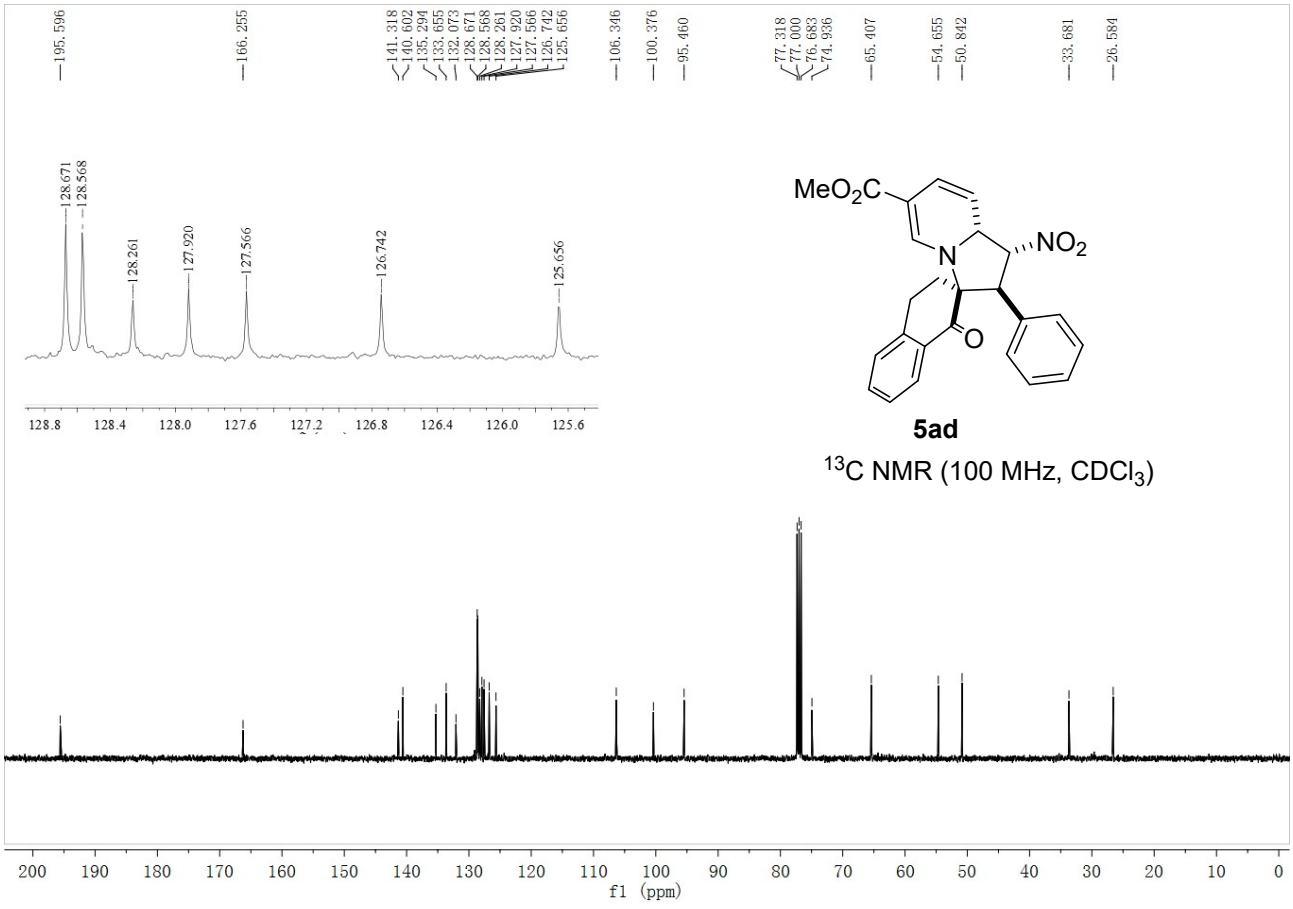
^{1}H NMR (400 MHz, $CDCl_3$)

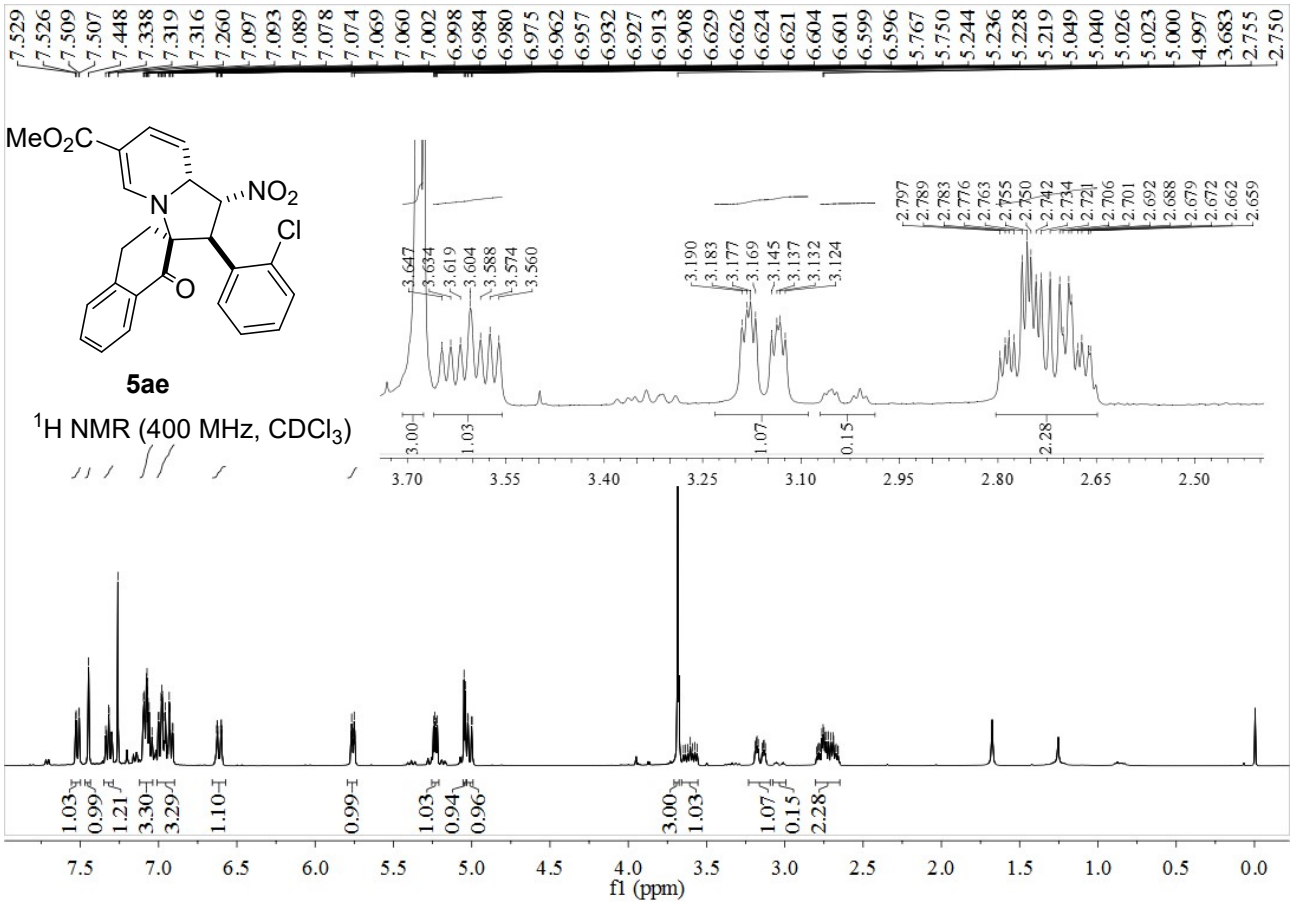


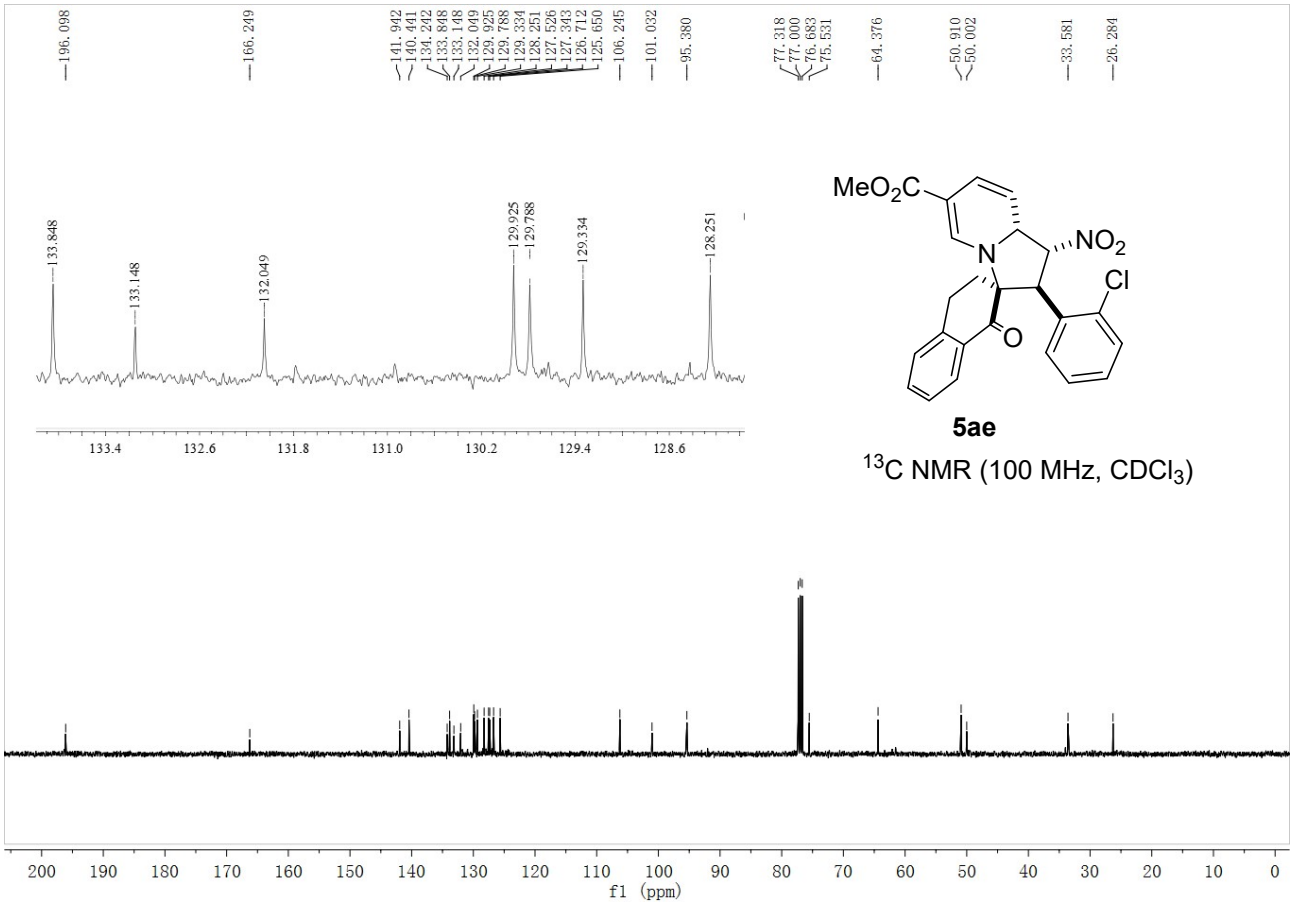
5ac

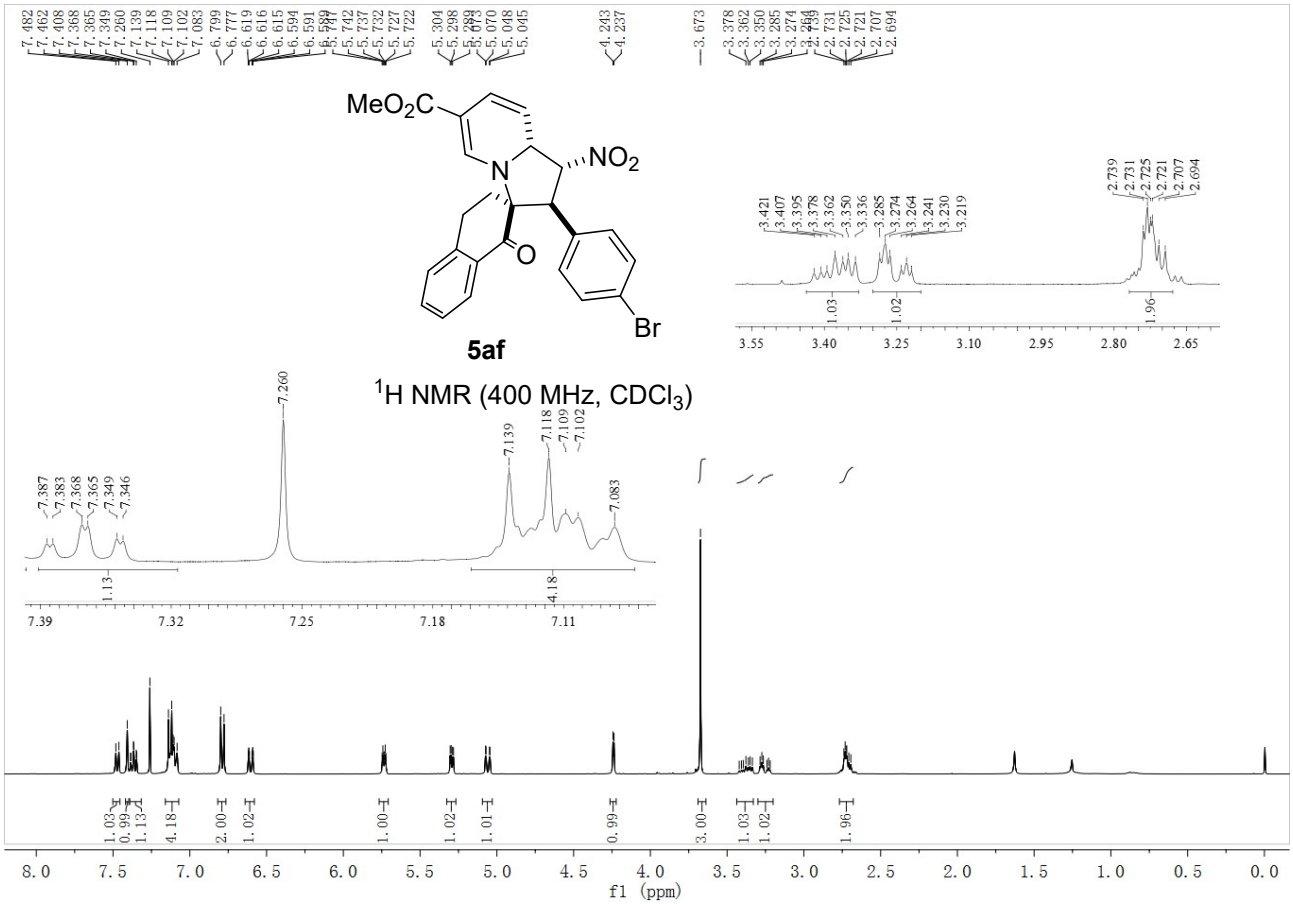
^{13}C NMR (100 MHz, $CDCl_3$)

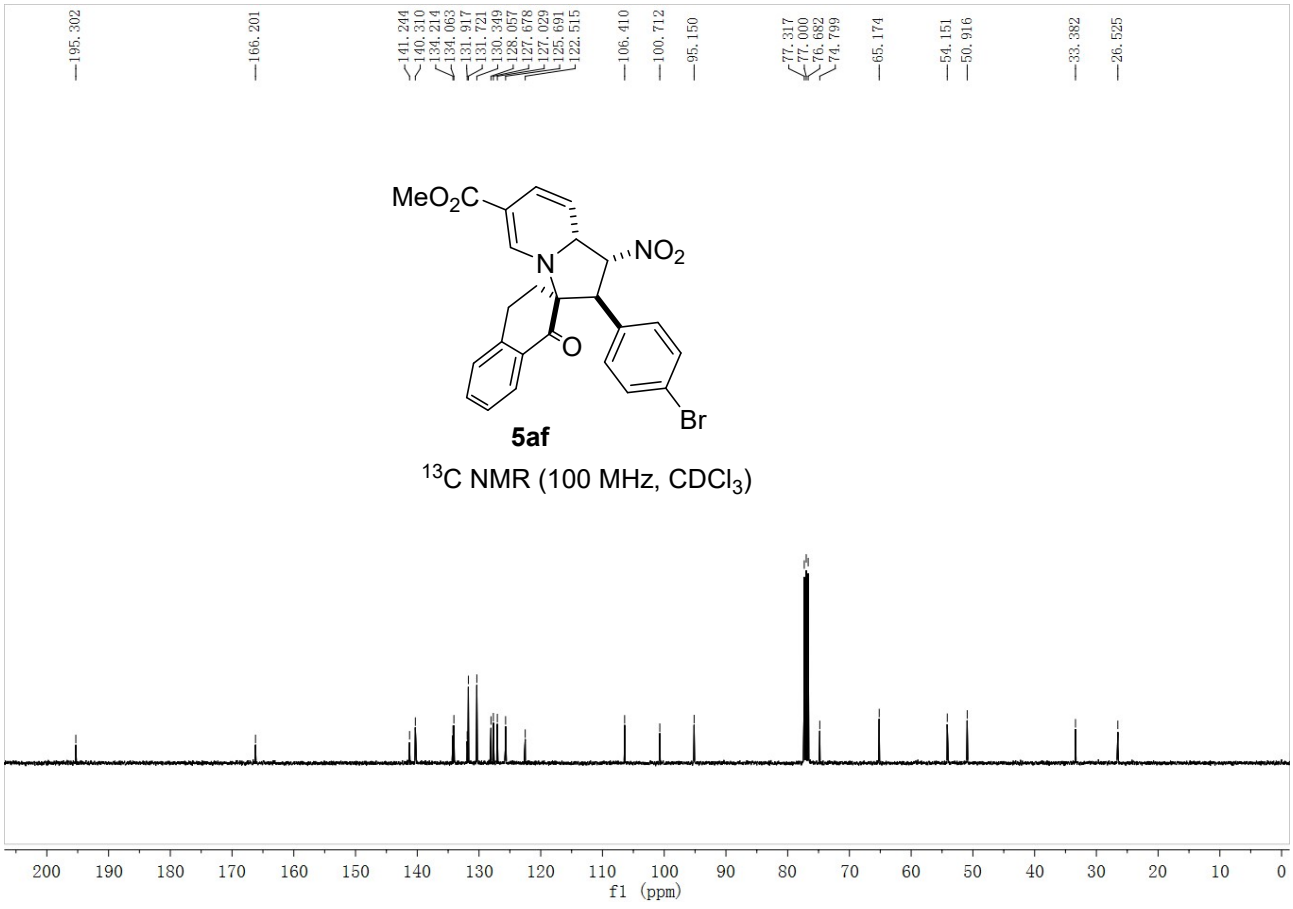

MeO2C
NO2
N
O
5ad
1H NMR (400 MHz, CDCl3)
f1 (ppm)

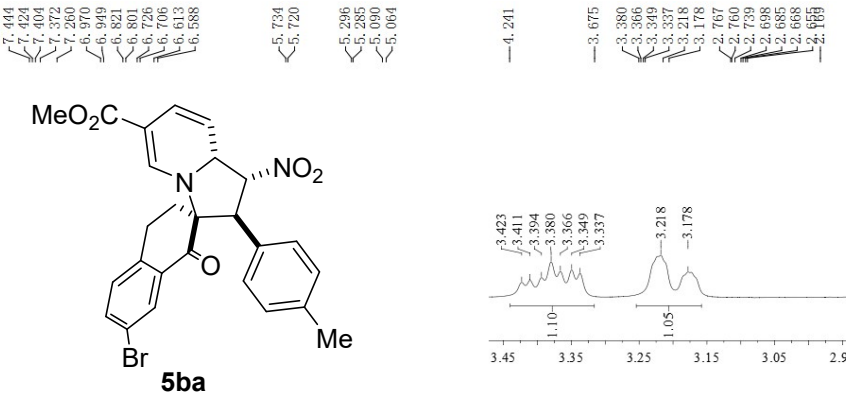

MeO2C
NO2
N
O
5ad
13C NMR (100 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
Cl
O
N
5ae
1H NMR (400 MHz, CDCl3)
f1 (ppm)

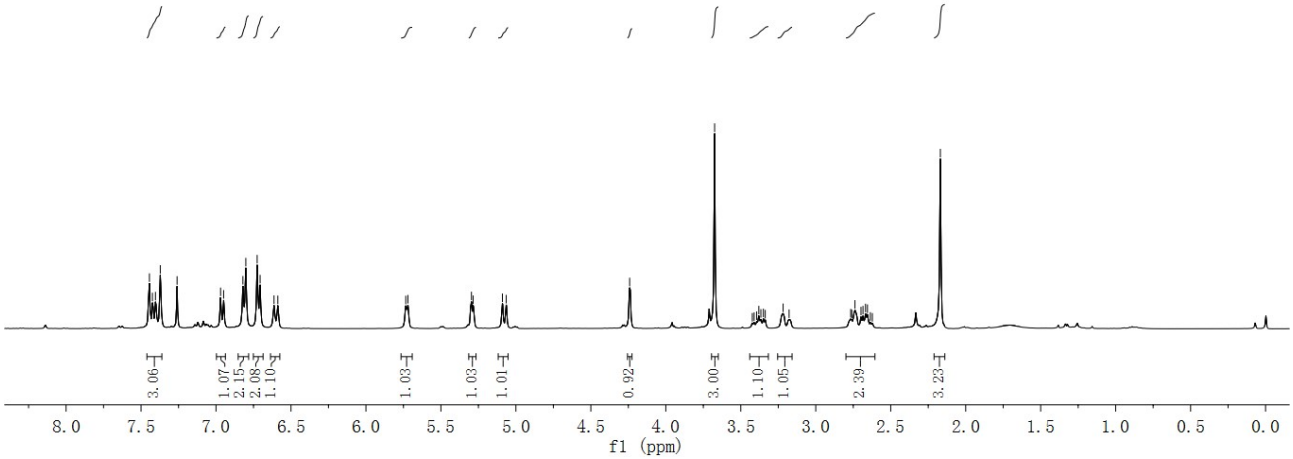

MeO2C
NO2
Cl
O
N
5ae
13C NMR (100 MHz, CDCl3)
f1 (ppm)

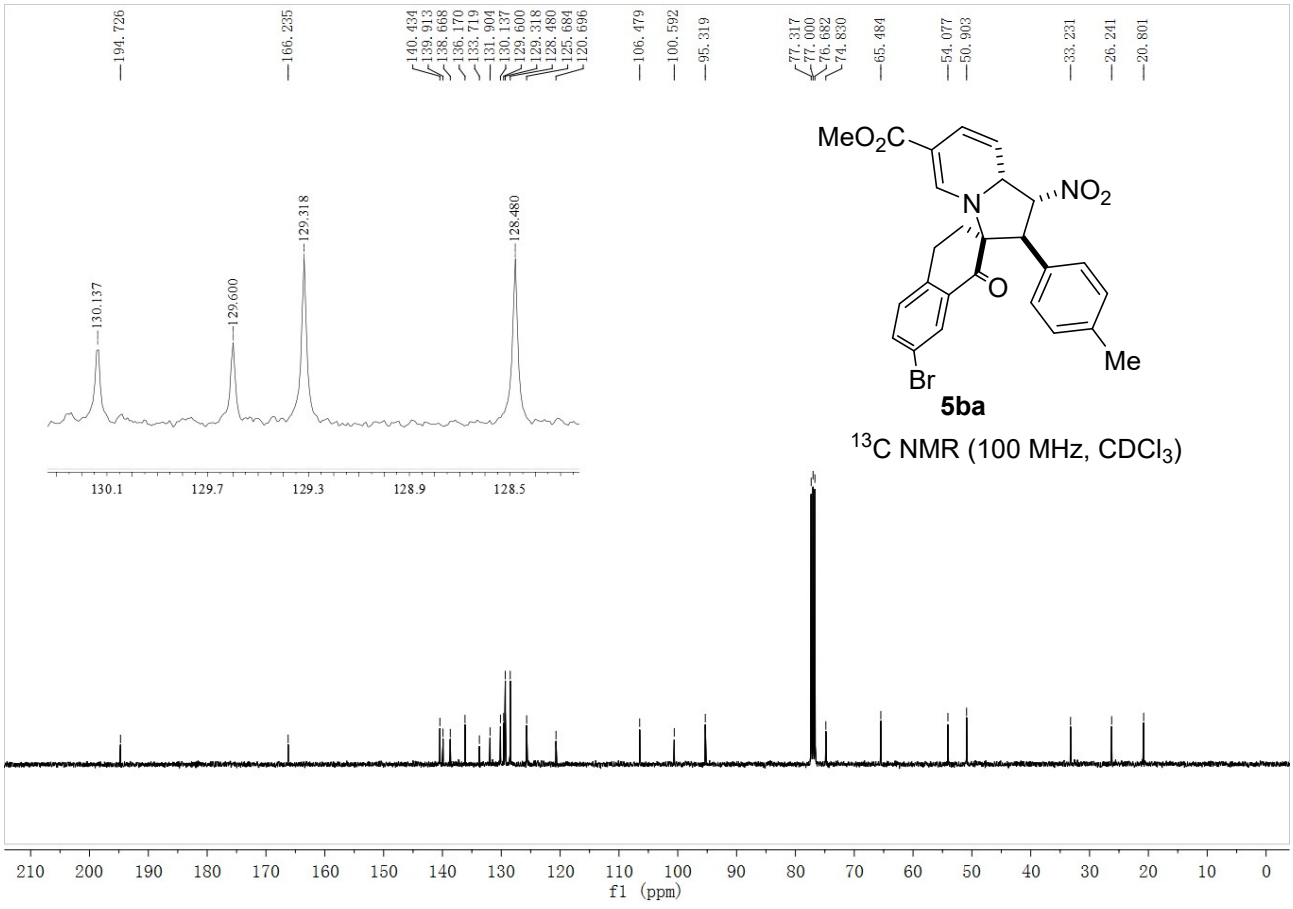

MeO2C
NO2
N
O
Br
5af
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
N
O
Br
5af
13C NMR (100 MHz, CDCl3)
f1 (ppm)

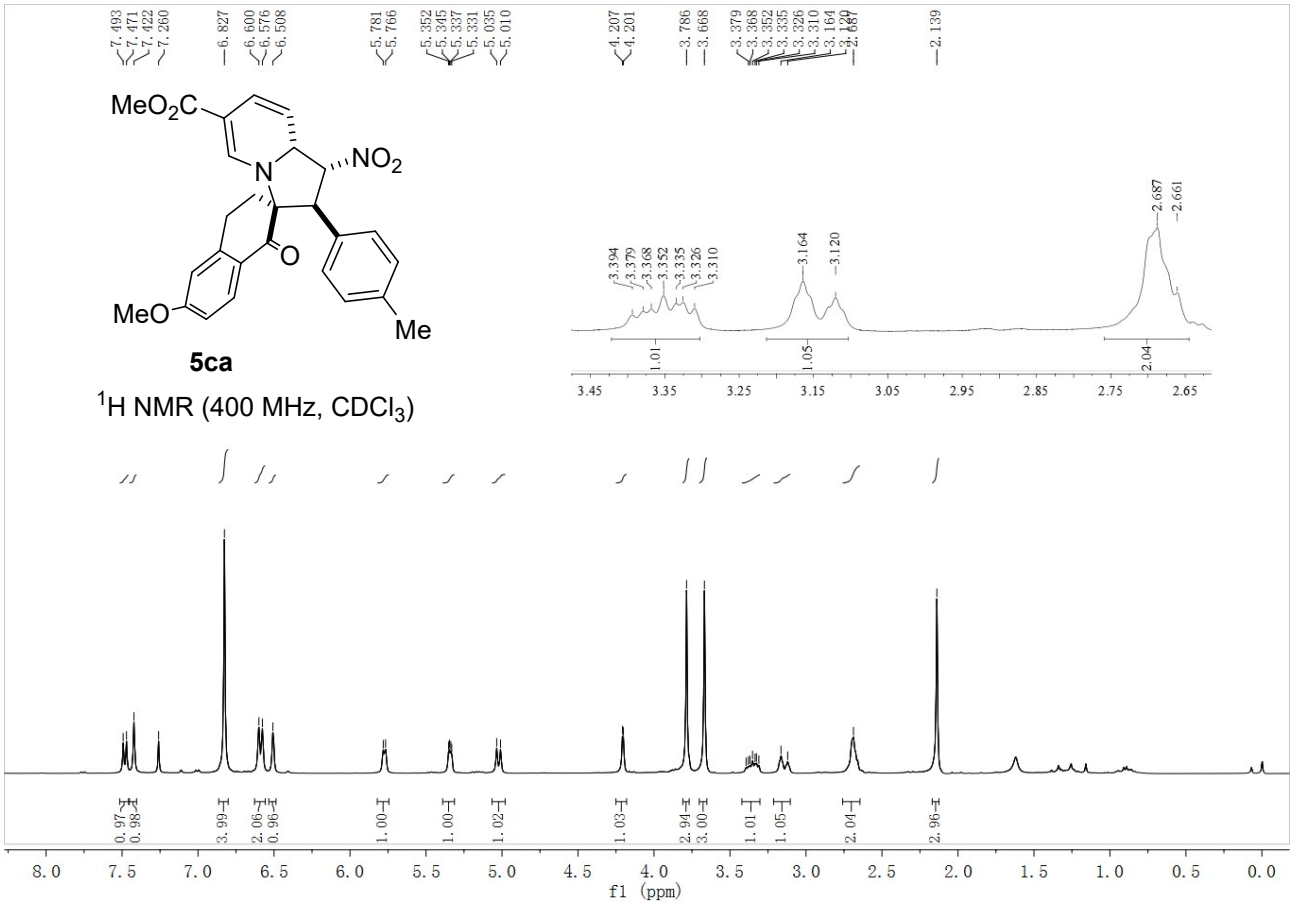


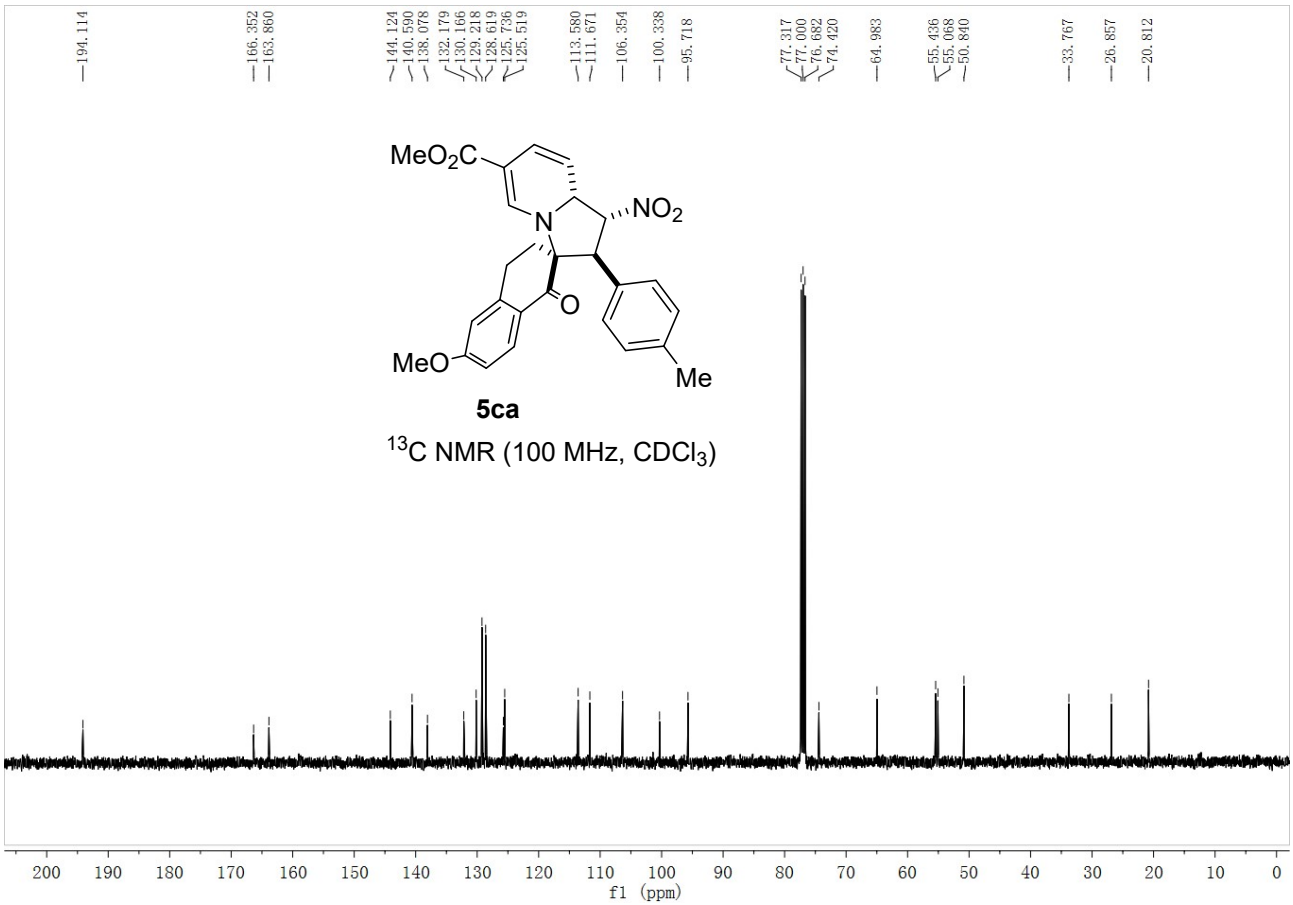
^{1}H NMR (400 MHz, $CDCl_3$)

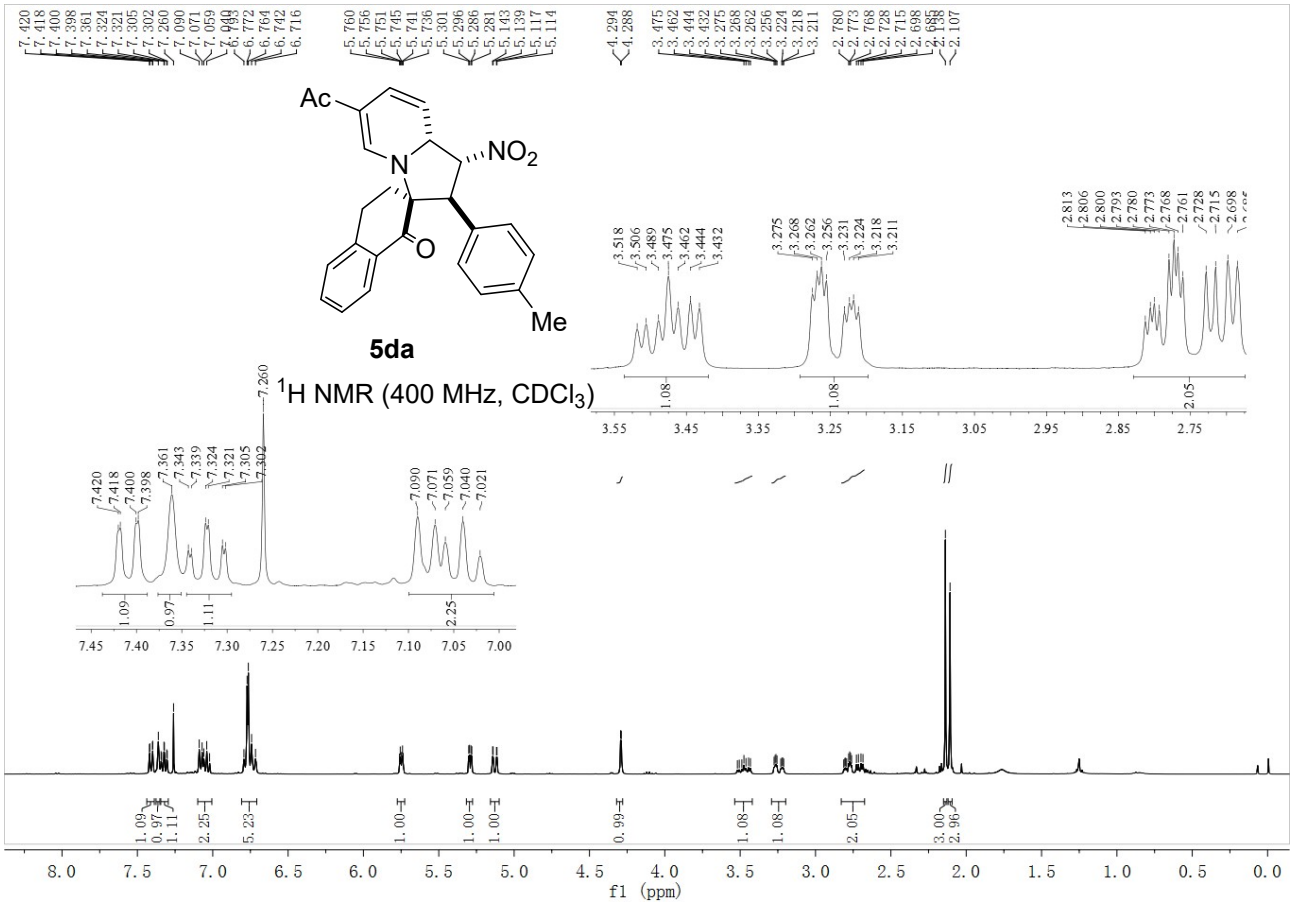




^{13}C NMR (100 MHz, $CDCl_3$)

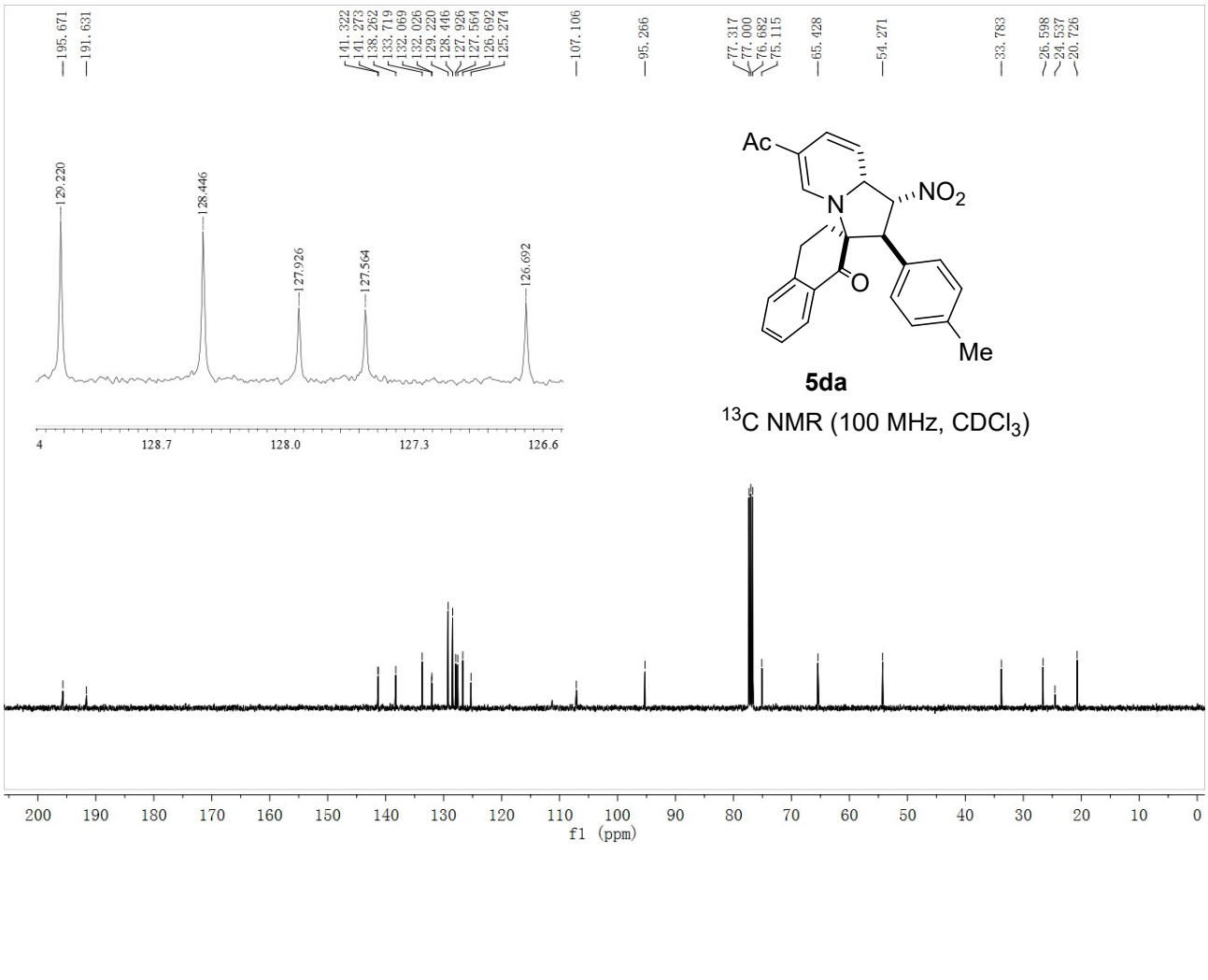

MeO2C
NO2
N
O
MeO
Me
5ca
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
N
O
MeO
Me
5ca
13C NMR (100 MHz, CDCl3)
f1 (ppm)

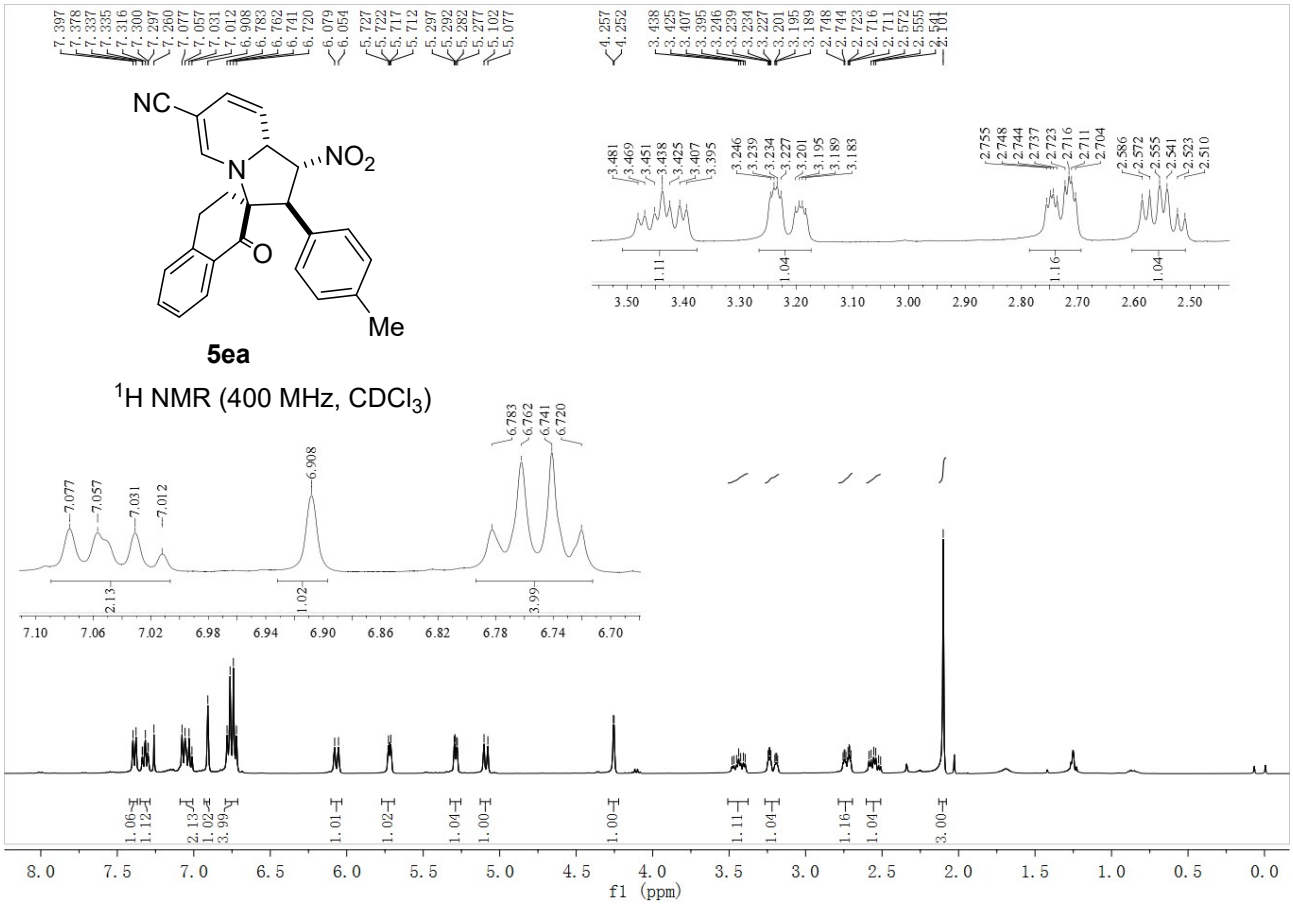


5da

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

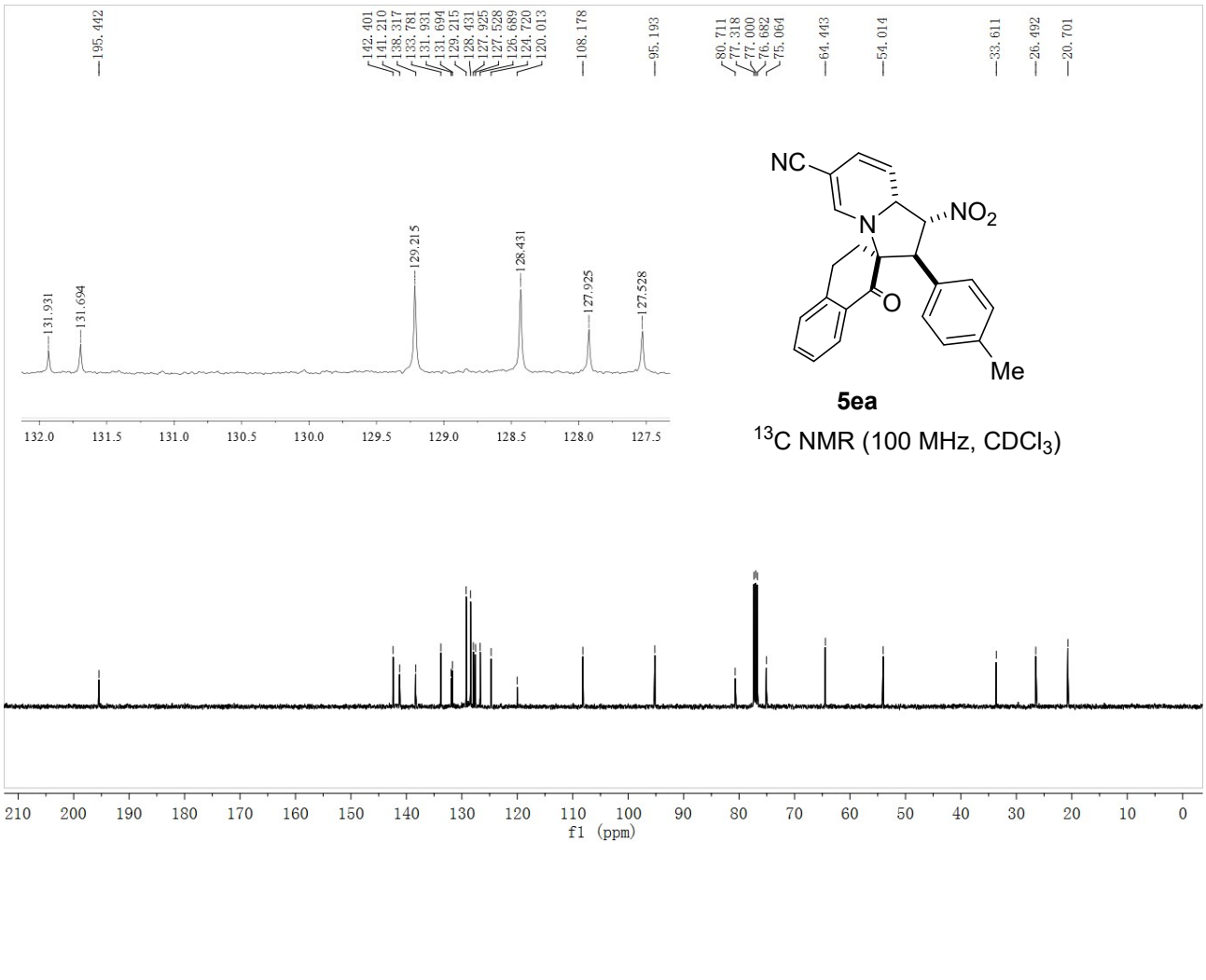


^{13}C NMR (100 MHz, $CDCl_3$)



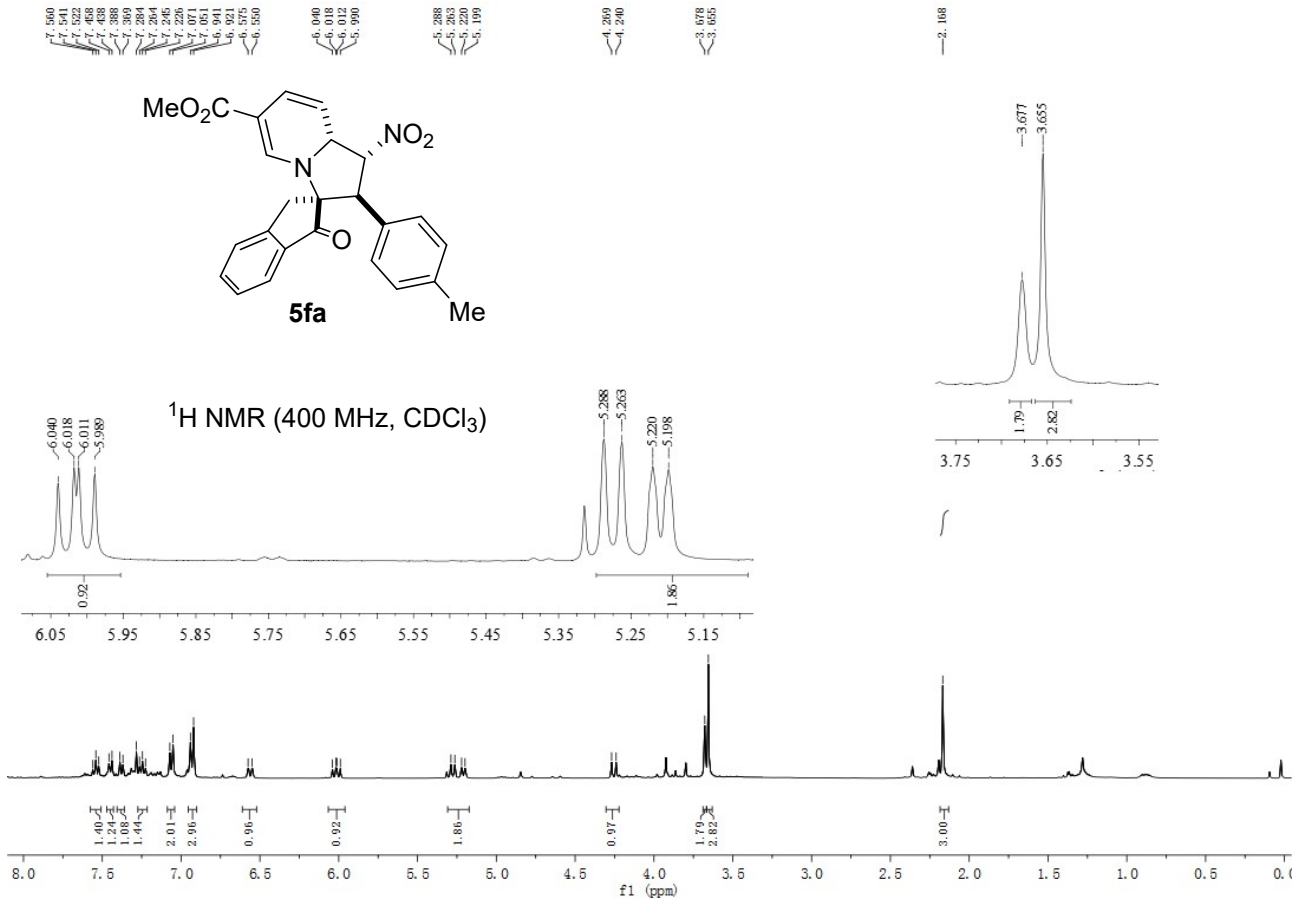
5ea

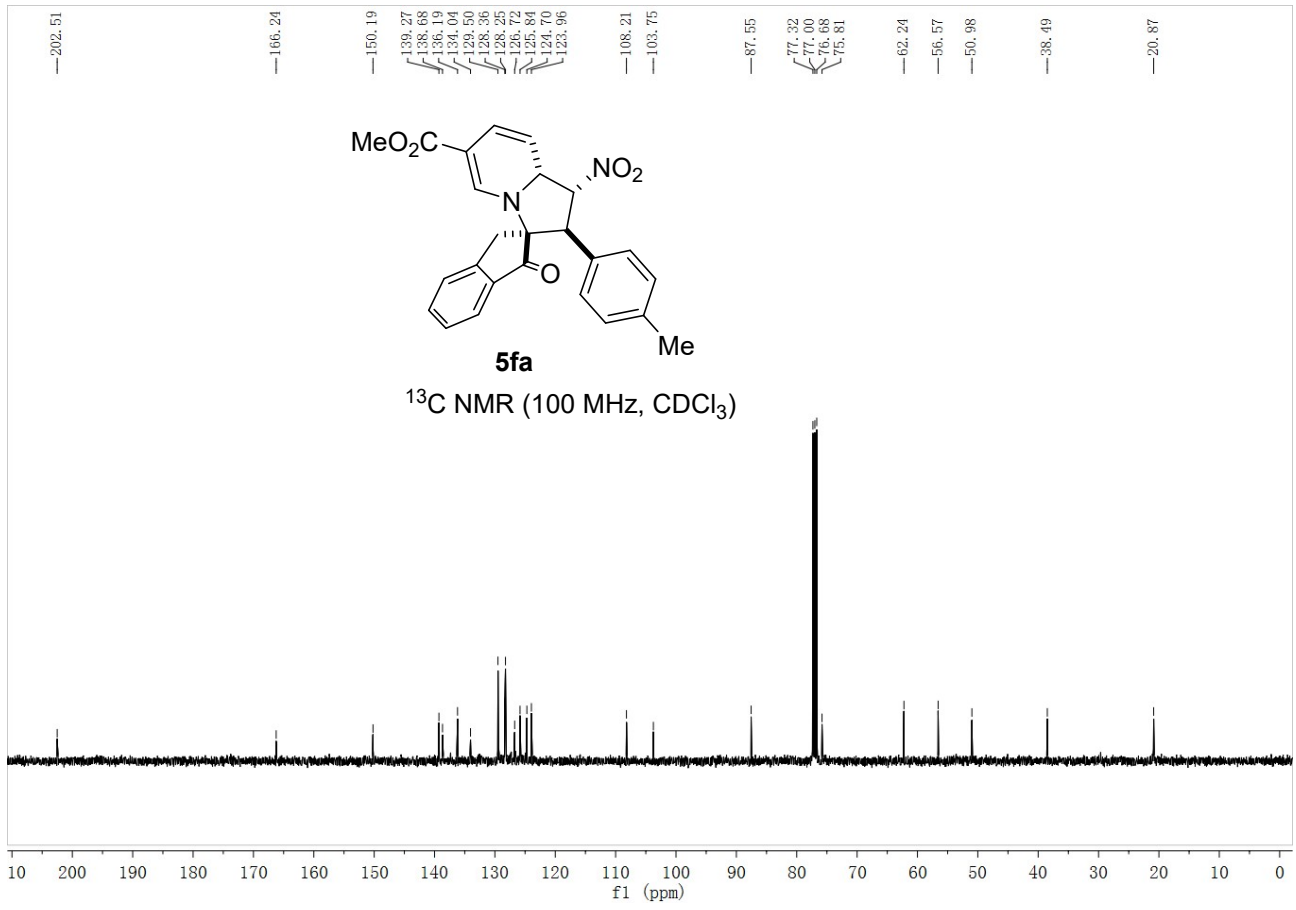
^{1}H NMR (400 MHz, $CDCl_3$)

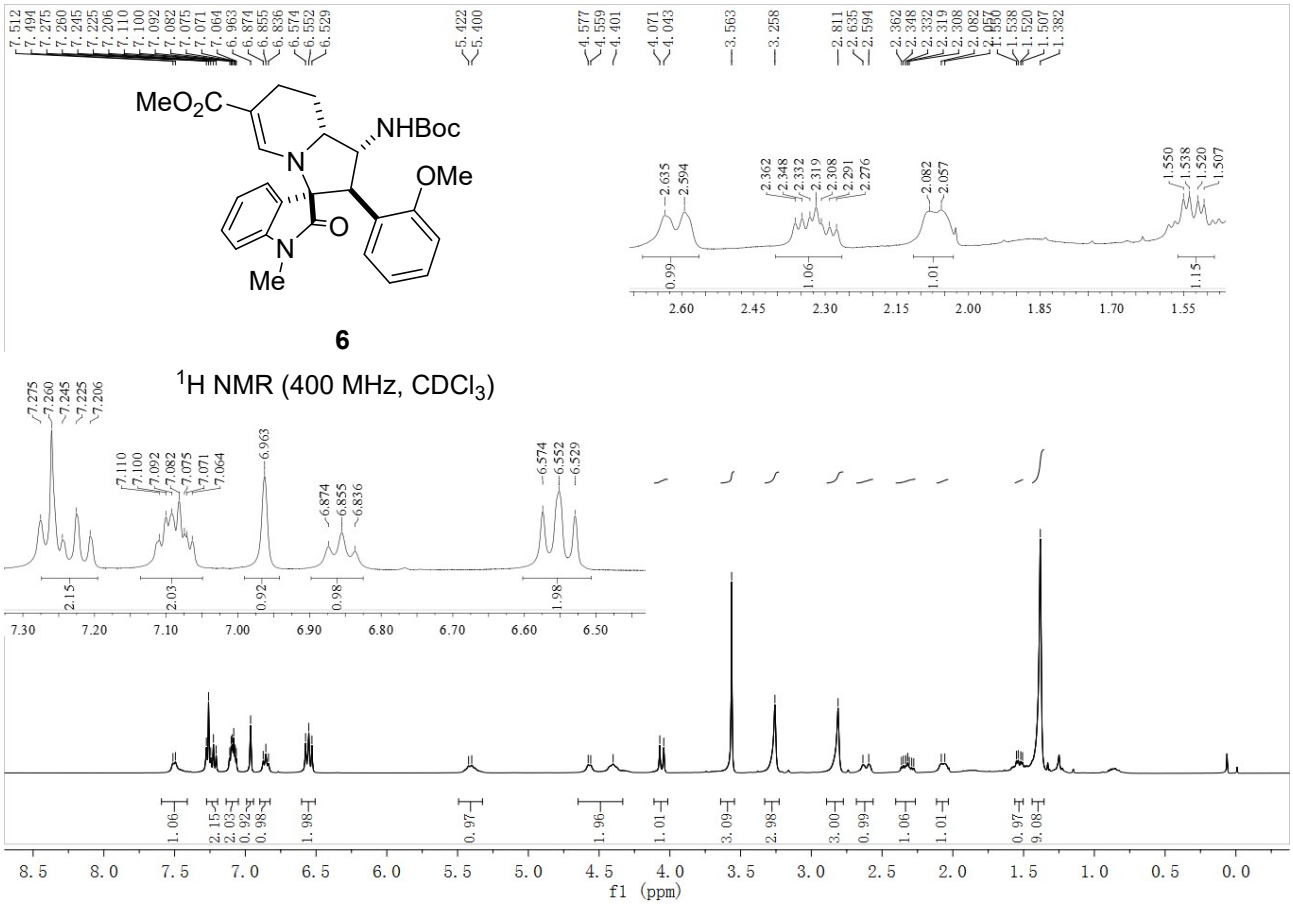


5ea

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

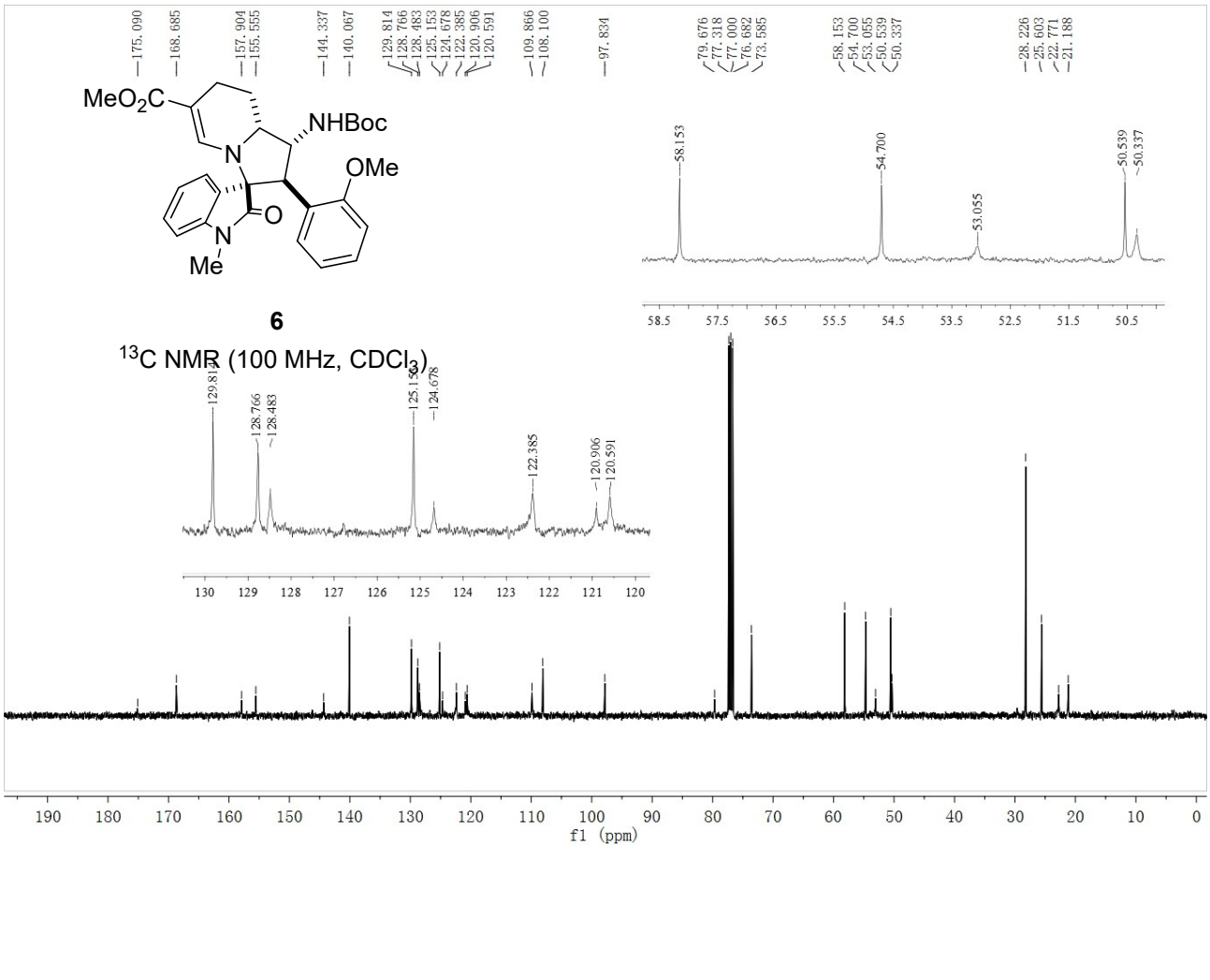

MeO2C
NO2
N
O
Me
5fa
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
N
O
Me
5fa
13C NMR (100 MHz, CDCl3)
f1 (ppm)



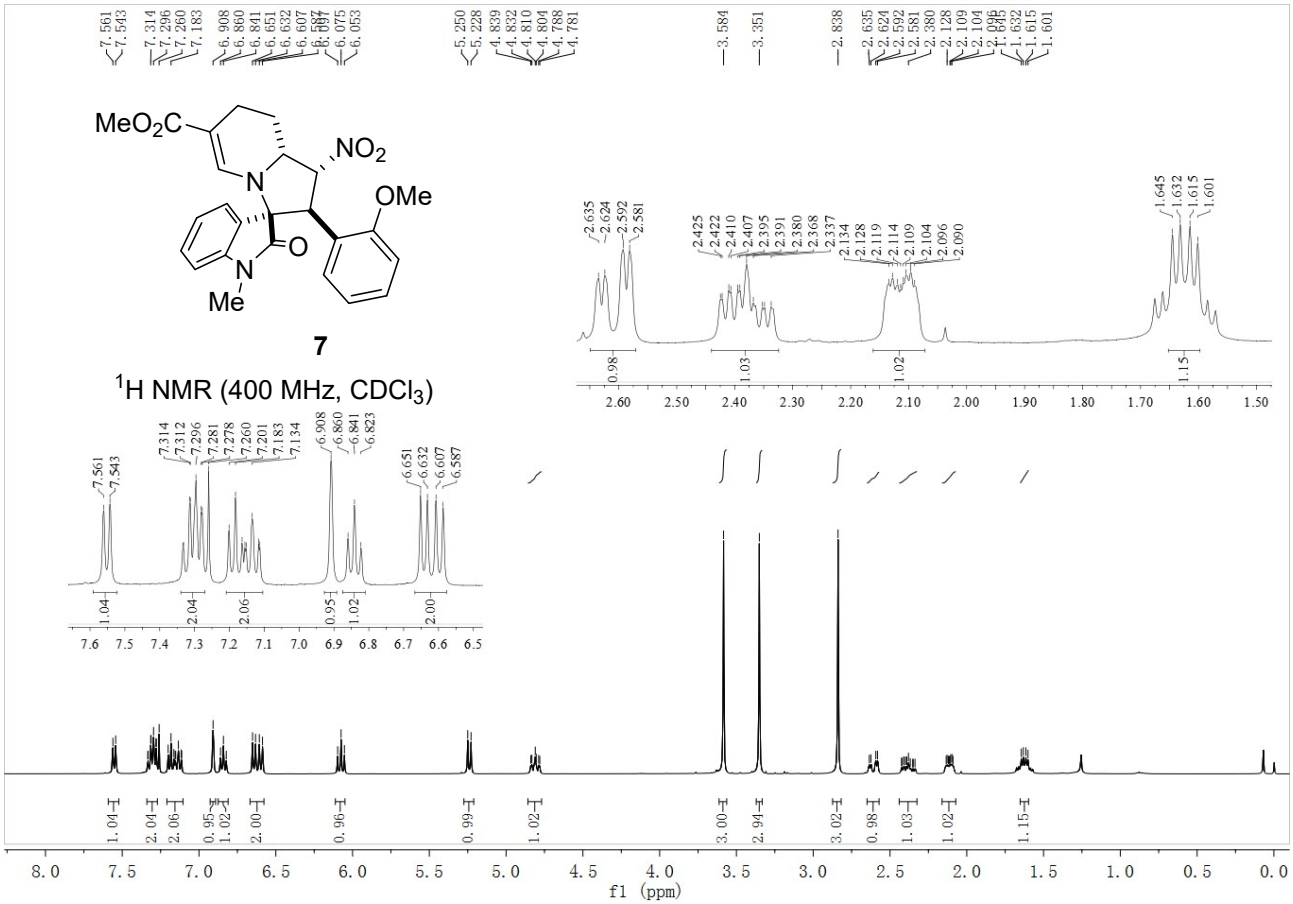
6

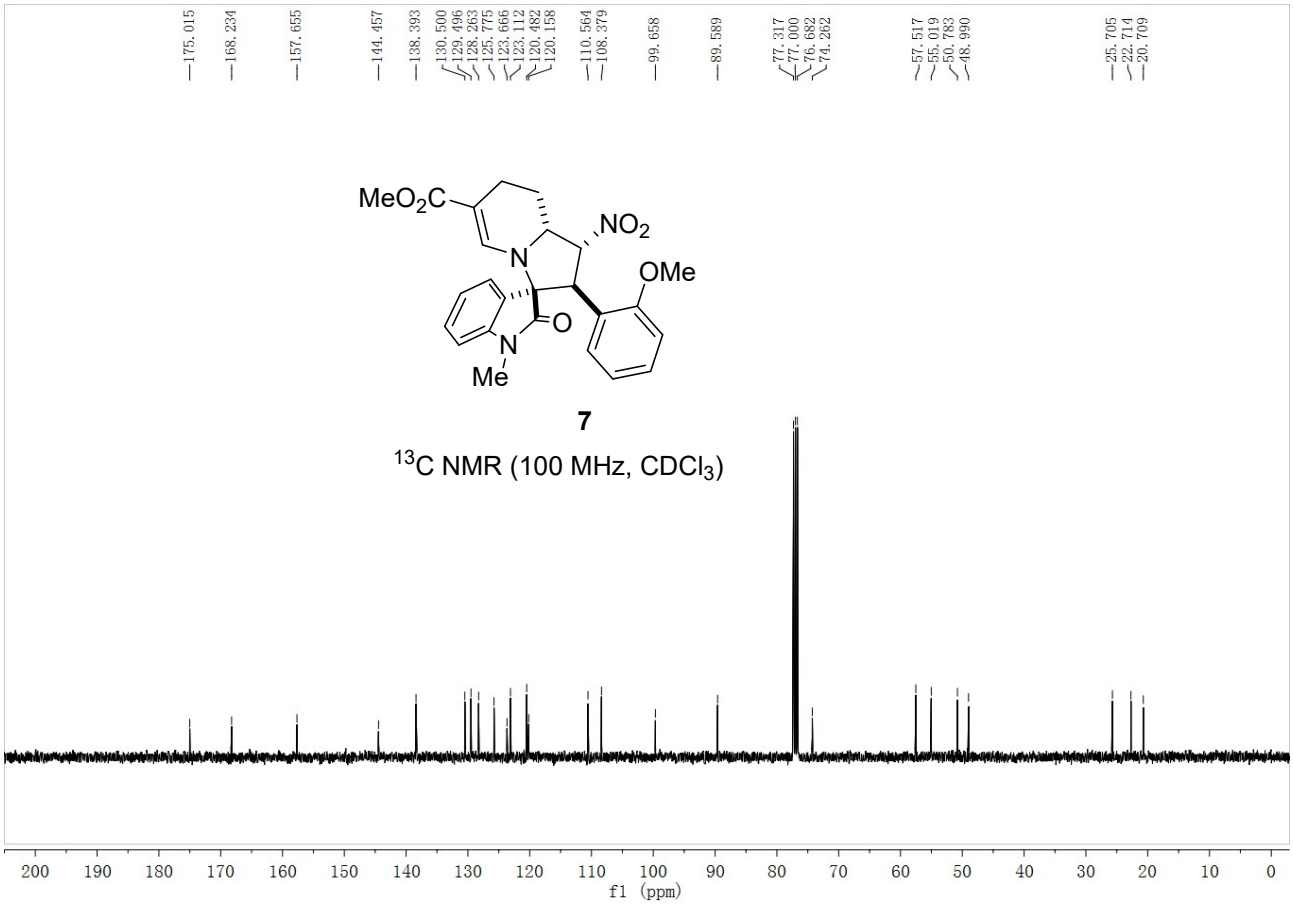
^{1}H NMR (400 MHz, $CDCl_3$)

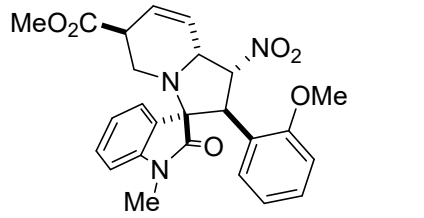


6

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


MeO2C
NO2
OMe
N
O
N
Me
7
1H NMR (400 MHz, CDCl3)
f1 (ppm)


MeO2C
NO2
OMe
N
O
N
Me
7
13C NMR (100 MHz, CDCl3)
f1 (ppm)



8

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

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