Supporting Information

For

Synthesis of indolizines from pyridiniium 1,4-zwitterionic thiolates and propiolic acid derivatives via a formal [4 + 1] pathway

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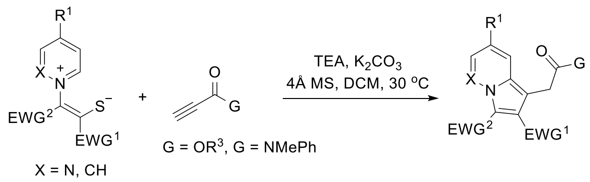
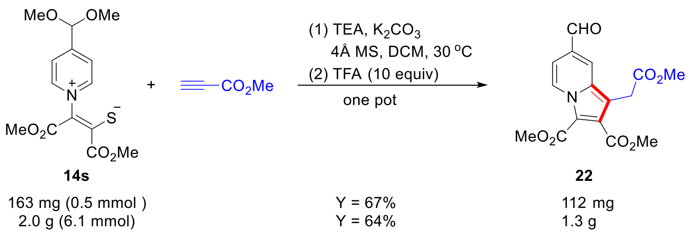
1. General Information

All isolated compounds were characterized on Varian 300, Bruker 400, JEOL 400 MHz spectrometers in $CDCl_3$ or $(CD_3)_2SO$. Chemical shifts were reported as δ values relative to internal $CHCl_3$ (δ 7.26 for ^{1}H NMR and 77.16 for ^{13}C NMR) and $(CH_3)_2SO$ (δ 2.50 for ^{1}H NMR and δ 39.52 for ^{13}C NMR). High-resolution mass spectra (HRMS) were obtained on a 4G mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (QTof). All melting points were measured with the samples after column chromatography and uncorrected. Column chromatography was performed on silica gel. Pyridinium 1,4-zwitterionic thiolates were prepared according to the literature.[1] **12s−16s** are new compounds as shown below.

2. Experimental Procedure



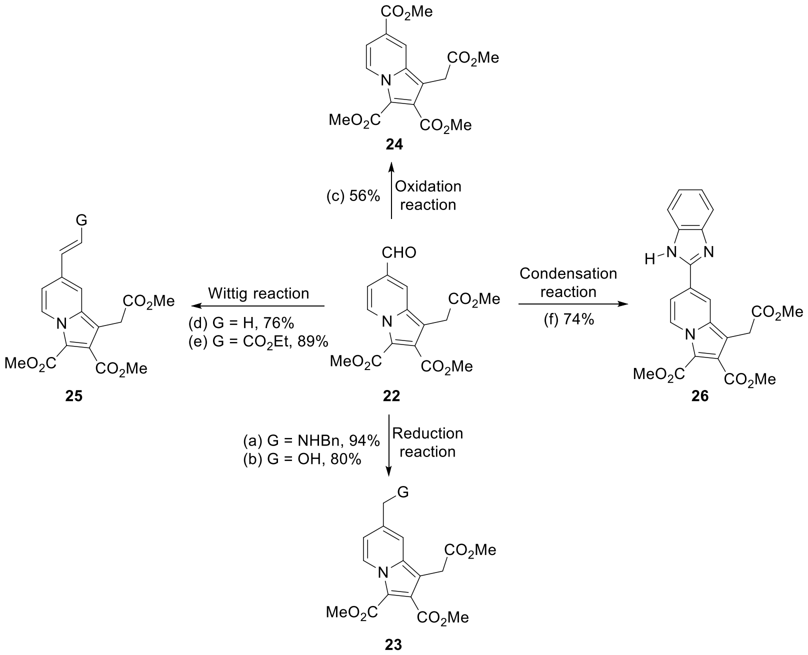
(1) General Experimental Procedure for Indolizines 3−21. To a solution of pyridinium 1,4-zwitterionic thiolate (0.5 mmol) and propiolic acid derivative (2.0 mmol, 4 equiv) in CH_2Cl_2 (5 mL) were added TEA (1.0 mmol, 2 equiv), 4 Å MS (150 mg) and K_2CO_3 (1.0 mmol, 2 equiv) at RT. Then the mixture was stirred at 30 ^{o}C. After completion as monitored by TLC, the crude reaction mixture was directly purified by column chromatography on silica gel to give the corresponding indolizine.



(2) Experimental Procedure of Indolizine 22. To a solution of pyridinium 1,4-zwitterionic thiolate **14s** (164 mg, 0.500 mmol) and methyl propiolate (0.18 mL, 2.0 mmol, 4 equiv) in CH_2Cl_2 (5 mL) were added TEA (0.14 mL, 1.0 mmol, 2 equiv), 4Å MS (150 mg) and K_2CO_3 (138 mg, 1.00 mmol, 2 equiv) at RT. Then the mixture was stirred at 30 ^{o}C. After completion of the cascade annulation reaction as monitored by TLC, TFA (0.37 mL, 5.0 mmol, 10 equiv) was added slowly at RT. After completion of hydrolysis reaction (checked by TLC), the excess of TFA was neutralized with saturated solution of $NaHCO_3$ and then the mixture was extracted with CH_2Cl_2. The combinded organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica gel to afford the indolizine product **22** (112 mg, 67% for 2 steps) as a yellow solid.

Scale-up experiment of 22: To a solution of pyridinium 1,4-zwitterionic thiolate **14s** (2.0 g, 6.1 mmol) and methyl propiolate (2.17 mL, 24.4 mmol, 4 equiv) in DCM (60 mL) were added TEA

(1.70 mL, 12.2 mmol, 2 equiv), 4Å MS (1.8 g) and K_2CO_3 (1.69 g, 12.2 mmol, 2 equiv) at RT. Then the mixture was stirred at 30 ^oC. After completion of pyridinium 1,4-zwitterionic thiolate **14s** as monitored by TLC, TFA (4.4 mL, 60 mmol, 10.0 equiv) was added slowly at RT, after completion of reaction (checked by TLC), the excess of TFA was neutralizad with saturated solution of $NaHCO_3$ and then the mixture was extracted with CH_2Cl_2. The combinded organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified purified by column chromatography on silica gel to afford the indolizine product **22** (1.3 g, 64% for 2 steps) as a yellow solid.



(3) Experimental Procedure for the Preparation of 23a. To a solution of compound **22** (100 mg, 0.300 mmol) in anhydrous MeOH (5.0 mL), benzylamine was added (45 mg, 0.42 mmol, 1.4 equiv) under argon at RT. After stirring for 6 h at RT, the reaction mixture was allowed to cool to 0 ^oC and $NaBH_4$ (16 mg, 0.42 mmol, 1.4 equiv) was added. After an additional 1 h at 0 ^oC, the reaction was quenched with aqueous NH_4Cl (10 mL) and extracted with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to gave product **23a** (119 mg, 94%) as a yellow oil.

(4) Experimental Procedure for the Preparation of 23b. To a solution of compound **22** (100 mg, 0.300 mmol) in MeOH (5 mL), $NaBH_4$ (17 mg, 0.45 mmol, 1.5 equiv) was added at -40 ^oC. The reaction mixture was warmed to 0 ℃ and stirred for 1 h. The reaction was quenched with aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the product **23b** (80 mg, 80%) as a yellow solid.

(5) Experimental Procedure for the Preparation of 24.To a solution of compound **22** (100 mg, 0.300 mmol) in MeOH (4 mL) was added a solution of KOH (44 mg, 0.78 mmol, 2.6 equiv) and iodine (99 mg, 0.39 mmol, 1.3 equiv) in MeOH (2 mL) at 0 ^oC. After completion of reaction (checked by TLC), the reaction was quenched with aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give the product **24** (61 mg, 56%) as a yellow solid.

(6) Experimental Procedure for the Preparation of 25d. To a solution of methyltriphenylphosphonium iodide (182 mg, 0.450 mmol, 1.5 equiv) in THF (5 mL) was added potassium *tert*-butoxide (50 mg, 0.45 mmol, 1.5 equiv) at 0 ^{o}C. The canary yellow mixture was stirred vigorously for 30 min. The compound **22** (100 mg, 0.300 mmol) was added and stirring was continued for 15 min at 0 ^{o}C. The reaction was quenched with aqueous NH_4Cl and extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel to give the product **25d** (75 mg, 76%) as a yellow solid.

(7) Experimental Procedure for the Preparation of 25e. To a solution of compound **22** (100 mg, 0.300 mmol) in toluene (5 mL), ethyl 2-(triphenyl-λ^5-phosphanylidene)acetate (136 mg, 0.390 mmol, 1.3 equiv) was added. The mixture was heated and stirred at 110 ℃ until completion of the reaction (checked by TLC). After cooling, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel to give the product **25e** (108 mg, 89%) as a yellow solid.

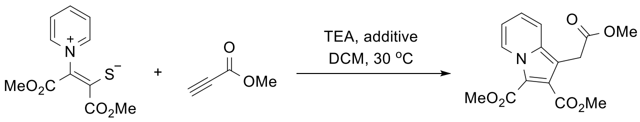
(8) Experimental Procedure for the Preparation of 26. A mixture of *o*-phenylenediamine (32 mg, 0.30 mmol), compound **22** (100 mg, 0.300 mmol), L-proline (41 mg, 0.36 mmol, 1.2 equiv), and 4Å MS (100 mg) in MeCN (2 mL) was stirred under reflux for 8 h. After completion of the reaction (checked by TLC), the reaction mixture was diluted with large amount of CH_2Cl_2 and washed with brine. The organic phase was dried over Na_2SO_4 and concentrated under vacuum. The resulting crude product was purified by column chromatography on silica gel to give the product **26** (93 mg, 74%) as a yellow solid.

3. References

(1) L. Moafi, S. Ahadi, H. R. Khavasi, A. Bazgir, *Synthesis* **2011**, 1399.

4. Optimization Table of the Reaction Conditions

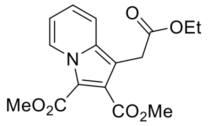
Table S1



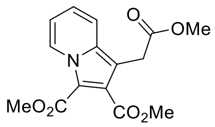
Entry	**1**:**2’**:TEA	Additive	Solvent	Time	4 Å MS	Yield[b] (%)
1	1:4:2	/	DCM	11 h	-	56
2	1:4:2	/	DCM	11 h	+	59
3	1:4:2	CsF	DCM	24 h	+	55
4	1:4:2	KF	DCM	24 h	+	54
5	1:4:2	DBU	DCM	24 h	+	30
6	1:4:2	DABCO	DCM	24 h	+	31
7	1:4:2	pyridine	DCM	11 h	+	61
8	1:4:2	$(^t Bu)_3N$	DCM	24 h	+	64
9	1:4:2	DMAP	DCM	24 h	+	43
10	1:4:2	Na_2CO_3	DCM	24 h	+	64
11	1:4:2	K_2CO_3	DCM	<24 h	+	67
12	1:4:2	Cs_2CO_3	DCM	24 h	+	57
13	1:4:2	$NaHCO_3$	DCM	24 h	+	59
14	1:4:2	KOAc	DCM	24 h	+	62
15	1:4:2	KOH	DCM	24 h	+	55
16	1:4:2	NaOH	DCM	24 h	+	60

[a] Reaction conditions: **1** (0.2 mmol), **2’**, TEA, additive (2 equiv), 4 Å MS (90 mg), Solvent (2 mL), 30 °C, in air. [b]The yields were determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as the internal standard.

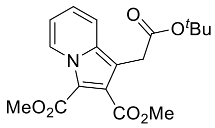
5. Characterization Data



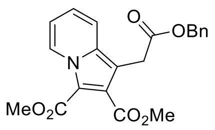
3 (102 mg, Y = 64%, R_f = 0.57 (PE:EA = 2:1)) was isolated as a yellow solid; mp 46–47 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.32 (d, J = 7.2 Hz, 1H), 7.51 (d, J = 9.2 Hz, 1H), 7.04 (ddd, J = 9.2, 6.8, 1.2 Hz, 1H), 6.84 (td, J = 7.0, 1.6 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 3.78 (s, 2H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 165.5, 160.0, 134.2, 126.1, 126.0, 121.6, 116.7, 113.5, 110.4, 106.4, 60.2, 51.5, 50.8, 29.3, 13.5; ESI-HRMS *m/z* calcd for $C_{16}H_{18}NO_6$ $[M + H]^+$ 320.1129, found 320.1123.



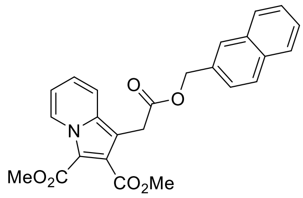
4 (104 mg, Y = 68%, R_f = 0.36 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (d, J = 7.2 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.09–7.02 (m, 1H), 6.85 (t, J = 7.2 Hz, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.80 (s, 2H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 166.5, 161.0, 135.1, 127.3, 126.9, 122.6, 117.5, 114.4, 111.1, 106.7, 52.5, 52.2, 51.6, 30.0; ESI-HRMS *m/z* calcd for $C_{15}H_{16}NO_6$ $[M + H]^+$ 306.0972, found 306.0966.



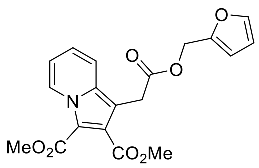
5 (104 mg, Y = 60%, R_f = 0.25 (PE:EA = 5:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (d, J = 6.8 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.06 (t, J = 7.4 Hz,1H), 6.84 (t, J = 6.4 Hz, 1H), 3.93 (s, 3H), 3.87 (s, 3H), 3.69 (s, 2H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 166.6, 161.0, 135.2, 127.3, 127.0, 122.4, 117.8, 114.3, 111.0, 107.6, 81.2, 52.4, 51.6, 31.5, 28.1; ESI-HRMS *m/z* calcd for $C_{18}H_{22}NO_6$ $[M + H]^+$ 348.1442, found 348.1435.



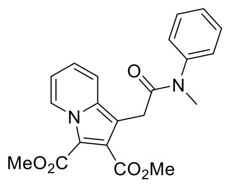
6 (120 mg, Y = 63%, R_f = 0.37 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (d, J = 7.2 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.41–7.26 (m, 5H), 7.04 (t, J = 7.8 Hz, 1H), 6.85 (t, J = 7.0 Hz, 1H), 5.10 (s, 2H), 3.88 (s, 3H), 3.86 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 166.4, 161.0, 135.8, 135.1, 128.5, 128.3, 128.3, 127.2, 127.0, 122.6, 117.6, 114.4, 111.2, 106.7, 66.9, 52.4, 51.6, 30.2; ESI-HRMS *m/z* calcd for $C_{21}H_{20}NO_6$ $[M + H]^+$ 382.1285, found 382.1278.



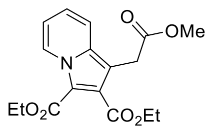
7 (123 mg, Y = 57%, R_f = 0.25 (PE:EA = 5:1)) was isolated as a yellow solid; mp 47–48 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 9.36 (d, J = 7.2 Hz, 1H), 7.84–7.77 (m, 3H), 7.75 (s, 1H), 7.53–7.47 (m, 3H), 7.40 (dd, J = 8.8, 2.0 Hz, 1H), 7.06–7.00 (m, 1H), 6.86 (td, J = 7.2, 1.6 Hz, 1H), 5.27 (s, 2H), 3.89 (s, 2H), 3.89 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 166.5, 161.1, 135.2, 133.3, 133.2, 128.4, 128.1, 127.8, 127.4, 127.3, 127.0, 126.4 (2C), 125.9, 122.7, 117.7, 114.4, 111.3, 106.7, 67.0, 52.5, 51.7, 30.3, (1C peak is merged with other peaks); ESI-HRMS *m/z* calcd for $C_{25}H_{22}NO_6$ $[M + H]^+$ 432.1442, found 432.1435.



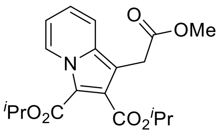
8 (130 mg, Y = 70%, R_f = 0.26 (PE:EA = 3:1)) was isolated as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 9.34 (d, J = 7.2 Hz, 1H), 7.48 (d, J = 9.2 Hz, 1H), 7.40 (s, 1H), 7.06 (t, J = 7.8 Hz, 1H), 6.86 (t, J = 6.8 Hz, 1H), 6.40–6.32 (m, 2H), 5.05 (s, 2H), 3.87 (s, 6H), 3.83 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 166.4, 161.0, 149.4, 143.3, 135.2, 127.3, 127.0, 122.6, 117.6, 114.4, 111.3, 110.9, 110.7, 106.5, 58.7, 52.5, 51.7, 30.0; ESI-HRMS *m/z* calcd for $C_{19}H_{18}NO_7$ $[M + H]^+$ 372.1078, found 372.1087.



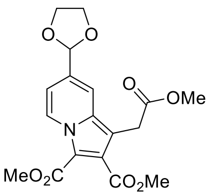
10 (57 mg, Y = 30%, R_f = 0.30 (PE:EA = 1:1)) was isolated as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 7.2 Hz, 1H), 7.42 (t, J = 7.2 Hz, 2H), 7.38–7.29 (m, 2H), 7.22 (d, J = 7.2 Hz, 2H), 6.98 (t, J = 7.2 Hz, 1H), 6.81 (t, J = 6.8 Hz, 1H), 3.86 (s, 3H), 3.86 (s, 3H), 3.63 (s, 2H), 3.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 166.7, 161.1, 144.1, 135.3, 130.0, 128.0, 127.5, 127.1, 127.0, 122.1, 118.0, 114.2, 110.9, 108.3, 52.4, 51.6, 37.9, 29.9; ESI-HRMS *m/z* calcd for $C_{21}H_{21}N_2O_5$ $[M + H]^+$ 381.1445, found 381.1441.



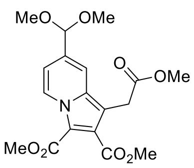
11 (107 mg, Y = 64%, R_f = 0.25 (PE:EA = 5:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 9.0 Hz, 1H), 7.03 (t, J = 6.8 Hz, 1H), 6.82 (t, J = 6.8 Hz, 1H), 4.38 (q, J = 7.2 Hz, 2H), 4.32 (q, J = 7.2 Hz, 2H), 3.78 (s, 2H), 3.63 (s, 3H), 1.37 (t, J = 7.2 Hz, 3H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.0, 160.6, 135.0, 127.2, 122.5, 117.4, 114.2, 111.1, 106.3, 61.4, 60.3, 52.1, 29.9, 14.3, 14.2, (1C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{17}H_{20}NO_6$ $[M + H]^+$ 334.1285, found 334.1280.



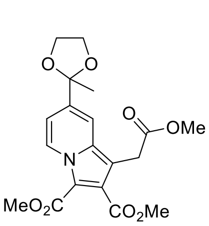
12 (114 mg, Y = 63%, R_f = 0.29 (PE:EA = 5:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.35 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 9.2 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H), 6.80 (t, J = 6.8 Hz, 1H), 5.31–5.18 (m, 2H), 3.76 (s, 2H), 3.63 (s, 3H), 1.39 (d, J = 6.4 Hz, 6H), 1.33 (d, J = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 165.3, 160.1, 135.0, 127.8, 127.2, 122.4, 117.4, 114.0, 111.2, 105.7, 69.2, 68.1, 52.1, 30.0, 22.0, 21.9; ESI-HRMS m/z calcd for $C_{19}H_{24}NO_6$ $[M + H]^+$ 362.1598, found 362.1591.



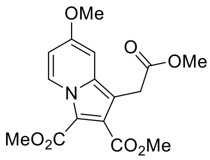
13 (140 mg, Y = 74%, R_f = 0.24 (PE:EA = 5:1)) was isolated as a yellow solid; mp 76–77 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, J = 7.2 Hz, 1H), 7.57 (s, 1H), 6.91 (dd, J = 7.6, 1.2 Hz, 1H), 5.76 (s, 1H), 4.09–3.97 (m, 4H), 3.89 (s, 3H), 3.84 (s, 3H), 3.79 (s, 2H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 166.2, 160.8, 134.3, 132.8, 127.2, 127.0, 115.1, 112.4, 111.6, 107.7, 102.4, 65.4, 52.4, 52.1, 51.6, 29.8; ESI-HRMS m/z calcd for $C_{18}H_{20}NO_8$ $[M + H]^+$ 378.1183, found 378.1176.



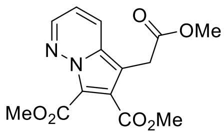
14 (142 mg, Y = 75%, R_f = 0.33 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, J = 7.2 Hz, 1H), 7.58 (s, 1H), 6.90 (d, J = 7.2 Hz, 1H), 5.36 (s, 1H), 3.90 (s, 3H), 3.85 (s, 3H), 3.80 (s, 2H), 3.63 (s, 3H), 3.29 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.3, 160.9, 134.6, 133.0, 127.1, 127.0, 115.3, 113.0, 111.5, 107.5, 101.3, 52.6, 52.4, 52.2, 51.6, 29.8; ESI-HRMS m/z calcd for $C_{18}H_{22}NO_8$ $[M + H]^+$ 380.1340, found 380.1335.



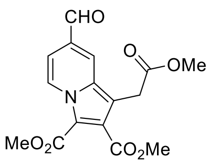
15 (135 mg, Y = 69%, R_f = 0.32 (PE:EA = 2:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, J = 7.6 Hz, 1H), 7.58 (s, 1H), 6.94 (d, J = 7.2 Hz, 1H), 4.06–4.00 (m, 2H), 3.90 (s, 3H), 3.85 (s, 3H), 3.80 (s, 2H), 3.79–3.74 (m, 2H), 3.64 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.3, 160.9, 138.1, 134.6, 127.3, 127.2, 113.2, 112.5, 111.3, 108.0, 107.3, 64.7, 52.4, 52.2, 51.6, 29.8, 26.8; ESI-HRMS *m/z* calcd for $C_{19}H_{22}NO_8$ $[M + H]^+$ 392.1340, found 392.1340.



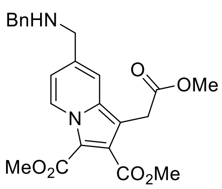
16 (25 mg, Y = 15%, R_f = 0.27 (PE:EA = 2:1)) was isolated as a yellow solid; mp 64–65 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (d, J = 7.6 Hz, 1H), 6.70 (d, J = 2.4 Hz, 1H), 6.58 (dd, J = 7.6, 2.8 Hz, 1H), 3.93 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.73 (s, 2H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 166.7, 160.9, 156.0, 136.8, 128.7, 127.9, 109.8, 109.2, 104.5, 94.5, 55.6, 52.5, 52.2, 51.5, 30.1; ESI-HRMS *m/z* calcd for $C_{16}H_{18}NO_7$ $[M + H]^+$ 336.1078, found 336.1077.



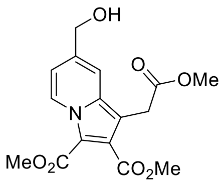
21 (57 mg, Y = 37%, R_f = 0.35 (PE:EA = 1:1)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.22 (m, 1H), 7.82 (d, J = 9.2 Hz, 1H), 6.73 (dd, J = 9.2, 4.4 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 2H), 3.88 (s, 3H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 164.8, 161.0, 144.8, 126.8, 126.7, 120.3, 120.2, 112.8, 107.6, 52.6, 52.3, 52.2, 29.7; ESI-HRMS *m/z* calcd for $C_{14}H_{15}N_2O_6$ $[M + H]^+$ 307.0921, found 307.0921.



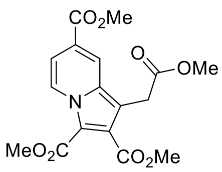
22 (112 mg, Y = 67%, R_f = 0.33 (PE:EA = 2:1)) was isolated as a yellow solid; mp 137–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 9.26 (d, J = 7.6 Hz, 1H), 8.04–8.00 (m, 1H), 7.29 (dd, J = 7.6, 1.6 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.90 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5, 170.7, 165.5, 160.6, 133.3, 130.0, 127.4 (2C), 124.4, 114.8, 112.5, 110.1, 52.7, 52.5, 52.2, 30.1; ESI-HRMS *m/z* calcd for $C_{16}H_{16}NO_7$ $[M + H]^+$ 334.0921, found 334.0919.



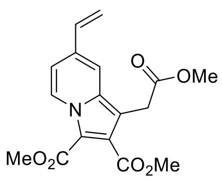
23a (119 mg, Y = 94%, R_f = 0.33 (EA)) was isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (d, J = 7.6 Hz, 1H), 7.46 (s, 1H), 7.34 (d, J = 4.4 Hz, 4H), 7.29–7.25 (m, 1H), 6.91 (dd, J = 7.6, 2.0 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.82 (s, 4H), 3.81 (s, 2H), 3.67 (s, 3H), 1.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 166.6, 161.0, 139.9, 135.8, 135.3, 128.6, 128.3, 127.3, 127.2, 115.3, 111.0, 106.4, 53.2, 52.5, 52.3, 52.2, 51.6, 30.0, (2C peak is merged with other peaks); ESI-HRMS *m/z* calcd for $C_{23}H_{25}N_2O_6$ $[M + H]^+$ 425.1707, found 425.1706.



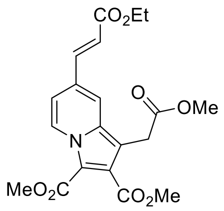
23b (80 mg, Y = 80%, R_f = 0.21 (PE:EA = 1:1)) was isolated as a yellow solid; mp 107–108 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, J = 7.2 Hz, 1H), 7.35 (s, 1H), 6.67 (d, J = 7.6 Hz, 1H), 4.61 (s, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 3.72 (s, 2H), 3.65 (s, 3H), 2.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 166.8, 160.9, 136.7, 135.0, 127.0, 126.8, 113.3 (2C), 110.9, 106.6, 63.7, 52.6, 52.2, 51.7, 29.8; ESI-HRMS *m/z* calcd for $C_{16}H_{18}NO_7$ $[M + H]^+$ 336.1078, found 336.1079.



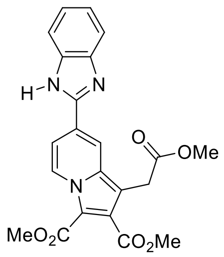
24 (61 mg, Y = 56%, R_f = 0.19 (PE:EA = 3:1)) was isolated as a yellow soild; mp 128–129 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (d, J = 7.6 Hz, 1H), 8.28–8.23 (m, 1H), 7.38 (dd, J = 7.2, 1.6 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 3.88 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 165.9, 165.5, 160.8, 133.7, 127.4, 126.7, 123.7, 120.7, 113.7, 113.2, 111.0, 52.7, 52.6, 52.4, 52.1, 30.0; ESI-HRMS *m/z* calcd for $C_{17}H_{18}NO_8$ $[M + H]^+$ 364.1027, found 364.1029.



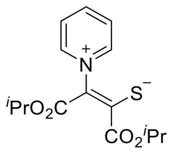
25d (75 mg, Y = 76%, R_f = 0.31 (PE:EA = 3:1)) was isolated as a yellow soild; mp 106–107 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, J = 7.6 Hz, 1H), 7.34 (s, 1H), 7.00 (dd, J = 7.6, 1.6 Hz, 1H), 6.66 (dd, J = 17.6, 10.8 Hz, 1H), 5.78 (d, J = 17.6 Hz, 1H), 5.36 (d, J = 10.8 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.79 (s, 2H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 166.3, 160.9, 135.1, 134.8, 132.3, 127.3, 127.0, 116.0, 115.5, 111.7, 111.4, 107.7, 52.5, 52.2, 51.7, 30.0; ESI-HRMS *m/z* calcd for $C_{17}H_{18}NO_6$ $[M + H]^+$ 332.1129, found 332.1123.



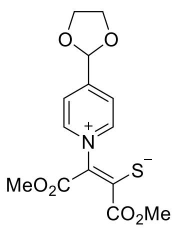
25e (108 mg, Y = 89%, R_f = 0.32 (PE:EA = 2:1)) was isolated as a yellow solid; mp 147–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 16.0 Hz, 1H), 7.54 (s, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.41 (d, J = 16 Hz, 1H), 4.26 (q, J = 7.2 Hz, 2H), 3.92 (s, 3H), 3.87 (s, 3H), 3.81 (s, 2H), 3.66 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 166.6, 165.9, 160.8, 141.9, 134.4, 128.9, 127.4, 127.2, 119.8, 119.3, 113.0, 111.2, 109.6, 60.8, 52.5, 52.3, 51.9, 30.0, 14.4; ESI-HRMS m/z calcd for $C_{20}H_{22}NO_8$ $[M + H]^+$ 404.1340, found 404.1337.



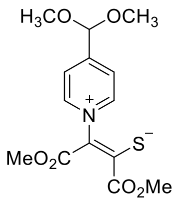
26 (93 mg, Y = 74%, R_f = 0.17 (PE:EA = 1:1)) was isolated as a yellow solid; mp 107–108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, J = 7.2 Hz, 1H), 7.97 (s, 1H), 7.50 (br s, 1H), 7.28–7.13 (m, 4H), 3.89 (s, 3H), 3.83 (s, 3H), 3.75 (s, 2H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 166.2, 159.9, 149.0, 134.3, 126.8 (2C), 123.8, 123.0, 114.7, 112.4, 112.1, 108.5, 52.8, 52.6, 51.6, 29.7, (5C peak is merged with other peaks); ESI-HRMS m/z calcd for $C_{22}H_{20}N_3O_6$ $[M + H]^+$ 422.1347, found 422.1344.



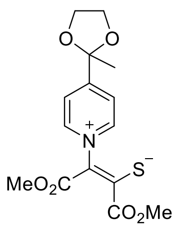
12s (R_f = 0.33 (EA)) was obtained as a yellow solid; mp 142–143 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.92–8.85 (m, 2H), 8.64–8.56 (m, 1H), 8.15–8.08 (m, 2H), 5.04–4.95 (m, 1H), 4.93–4.84 (m, 1H), 1.27 (d, J = 6.4 Hz, 6H), 1.12 (d, J = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 178.1, 167.8, 159.2, 148.8, 145.7, 127.5, 125.0, 67.6, 67.4, 21.6, 21.4; ESI-HRMS m/z calcd for $C_{15}H_{20}NO_4S$ $[M + H]^+$ 310.1108, found 310.1107.



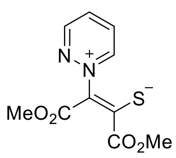
13s (R_f = 0.33 (EA)) was obtained as a yellow solid; mp 195–196 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.94 (d, *J* = 6.8 Hz, 2H), 8.15 (d, *J* = 6.8 Hz, 2H), 6.14 (s, 1H), 4.12–4.04 (m, 4H), 3.72 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 178.2, 168.9, 160.0, 156.2, 149.2, 125.0, 124.6, 99.8, 65.5, 51.9, 51.5; ESI-HRMS *m/z* calcd for $C_{14}H_{16}NO_6S$ $[M + H]^+$ 326.0693, found 326.0692.



14s (R_f = 0.40 (EA)) was obtained as a yellow solid; mp 155–156 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.91 (d, *J* = 6.4 Hz, 2H), 8.08 (d, *J* = 6.8 Hz, 2H), 5.74 (s, 1H), 3.72 (s, 3H), 3.56 (s, 3H), 3.39 (s, 6H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 178.3, 168.9, 160.0, 156.1, 149.0, 125.3, 124.5, 100.2, 54.0, 51.9, 51.5; ESI-HRMS *m/z* calcd for $C_{14}H_{18}NO_6S$ $[M + H]^+$ 328.0849, found 328.0846.



15s (R_f = 0.40 (EA)) was obtained as a yellow solid; mp 175–176 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.90 (d, *J* = 6.8 Hz, 2H), 8.12 (d, *J* = 6.8 Hz, 2H), 4.14–4.06 (m, 2H), 3.85–3.79 (m, 2H), 3.72 (s, 3H), 3.56 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 178.3, 168.9, 160.8, 160.1, 149.1, 124.4, 124.1, 106.7, 65.1, 51.9, 51.6, 25.8; ESI-HRMS *m/z* calcd for $C_{15}H_{18}NO_6S$ $[M + H]^+$ 340.0849, found 340.0849.



1' (R_f = 0.17 (EA)) was obtained as a yellow solid; mp 175–176 °C. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 9.90 (d, *J* = 6.0 Hz, 1H), 9.71 (d, *J* = 4.4 Hz, 1H), 8.77–8.70 (m, 1H), 8.64–8.57 (m, 1H), 3.73 (s, 3H), 3.56 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 178.3, 168.7, 159.9, 155.1, 154.3, 136.8, 135.4, 127.0, 52.1, 51.5; ESI-HRMS *m/z* calcd for $C_{10}H_{11}N_2O_4S$ $[M + H]^+$ 255.0434, found 255.0435.

6. NMR spectra

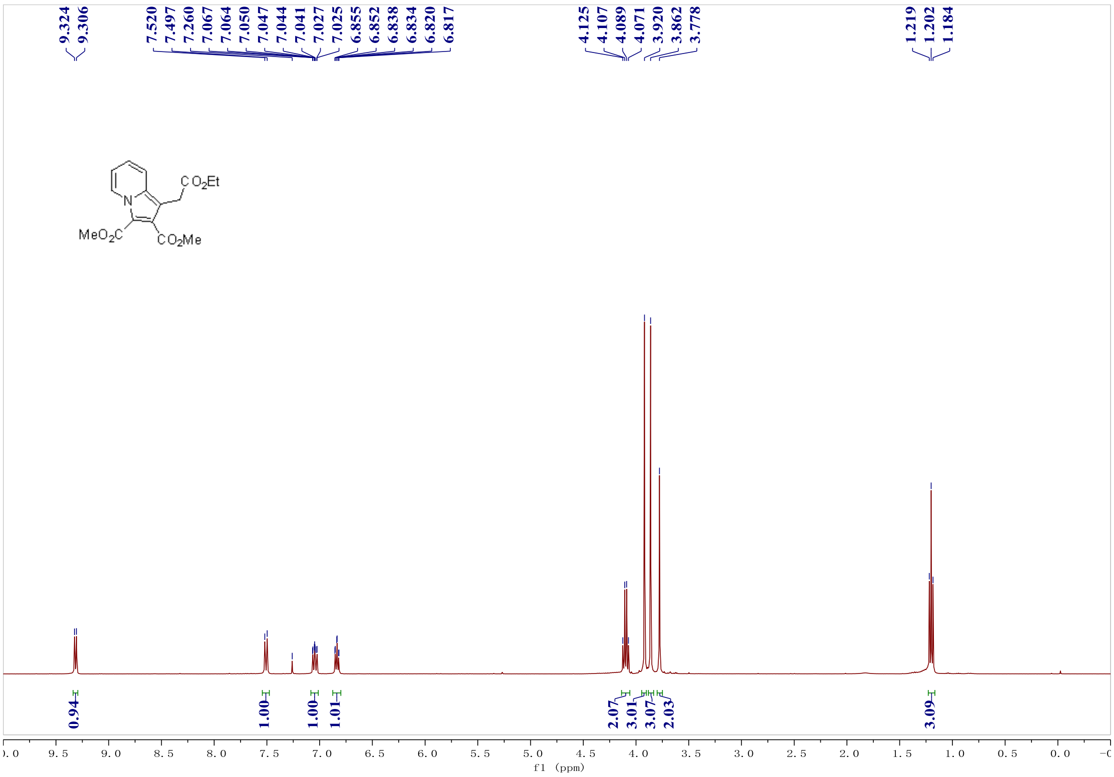


Fig. S1 ^{1}H NMR of compound **3** (300 MHz, $CDCl_3$)

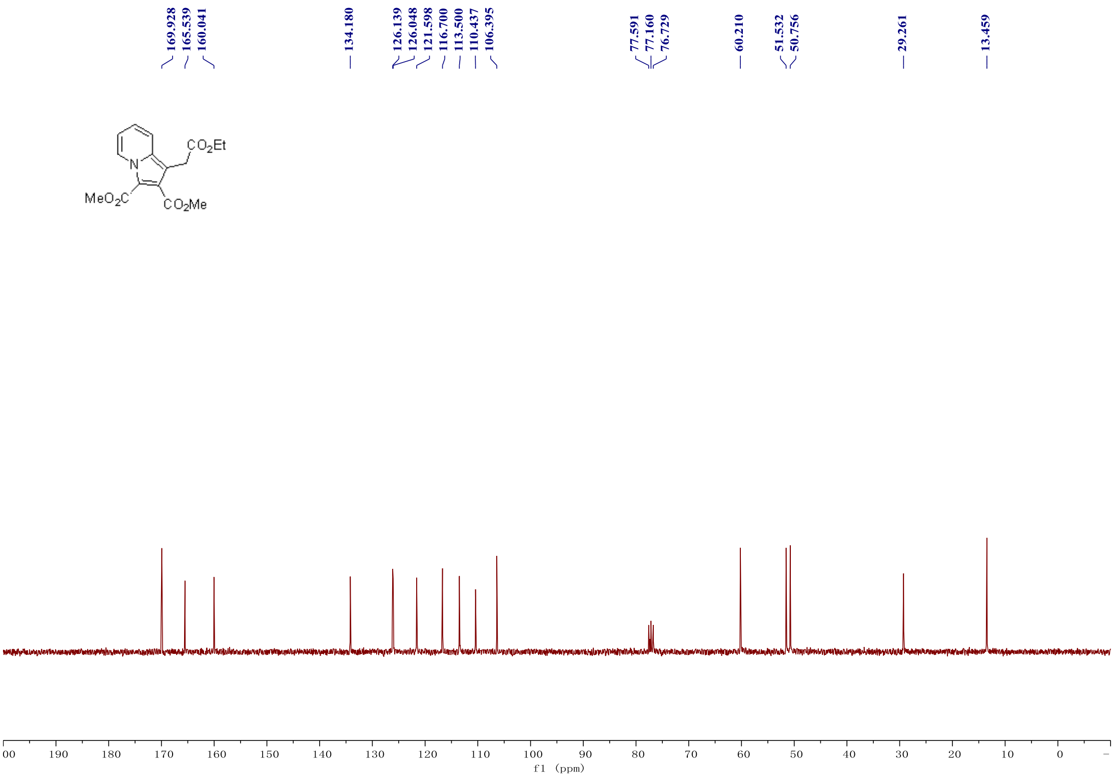


Fig. S2 ^{13}C NMR of compound **3** (75 MHz, $CDCl_3$)

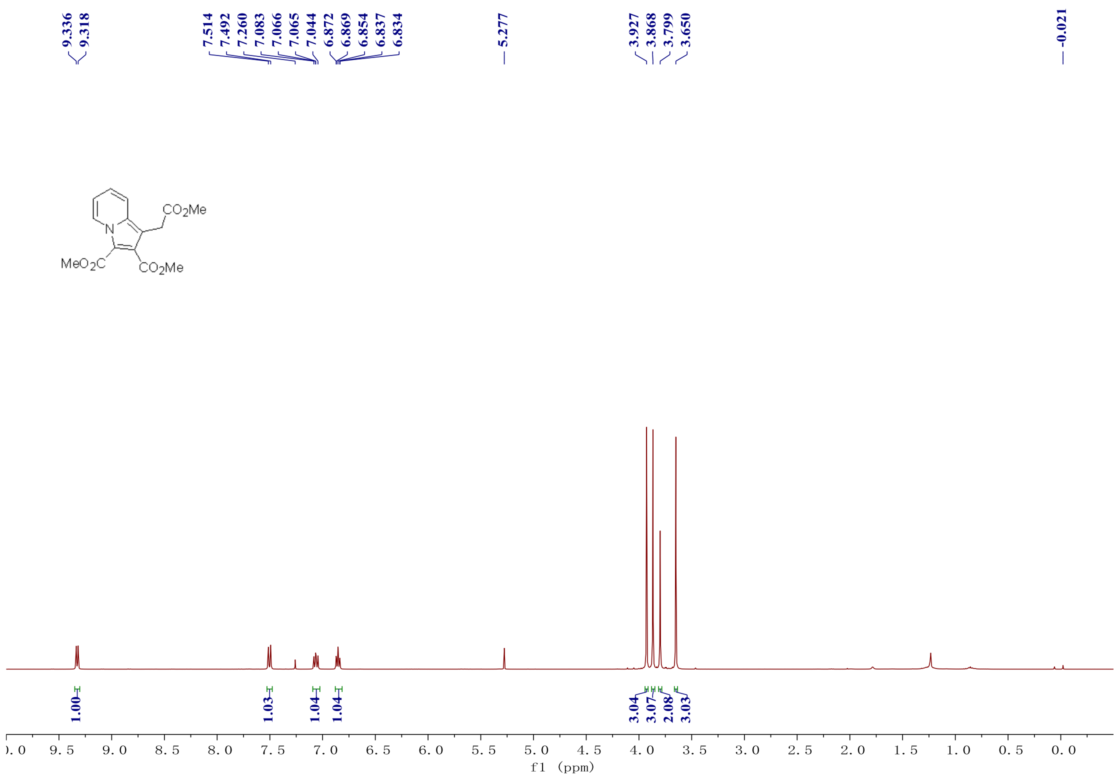


Fig. S3 ^{1}H NMR of compound **4** (400 MHz, $CDCl_3$)

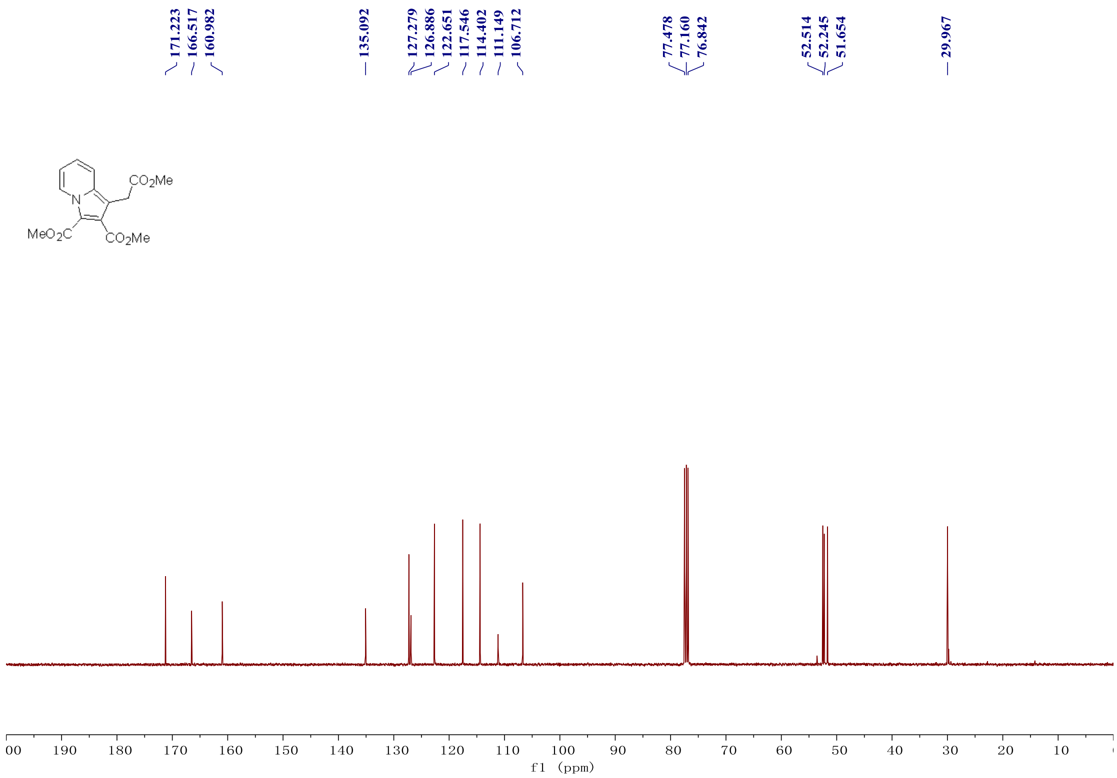


Fig. S4 ^{13}C NMR of compound **4** (100 MHz, $CDCl_3$)

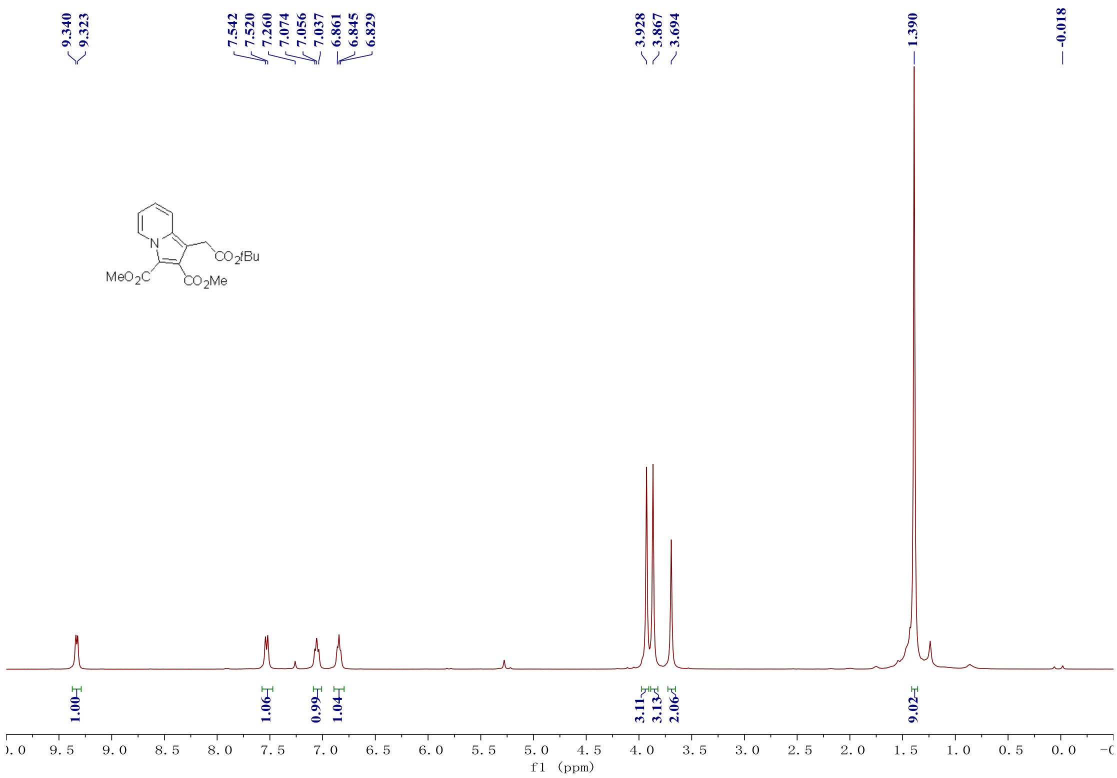


Fig. S5 ^{1}H NMR of compound **5** (400 MHz, $CDCl_3$)

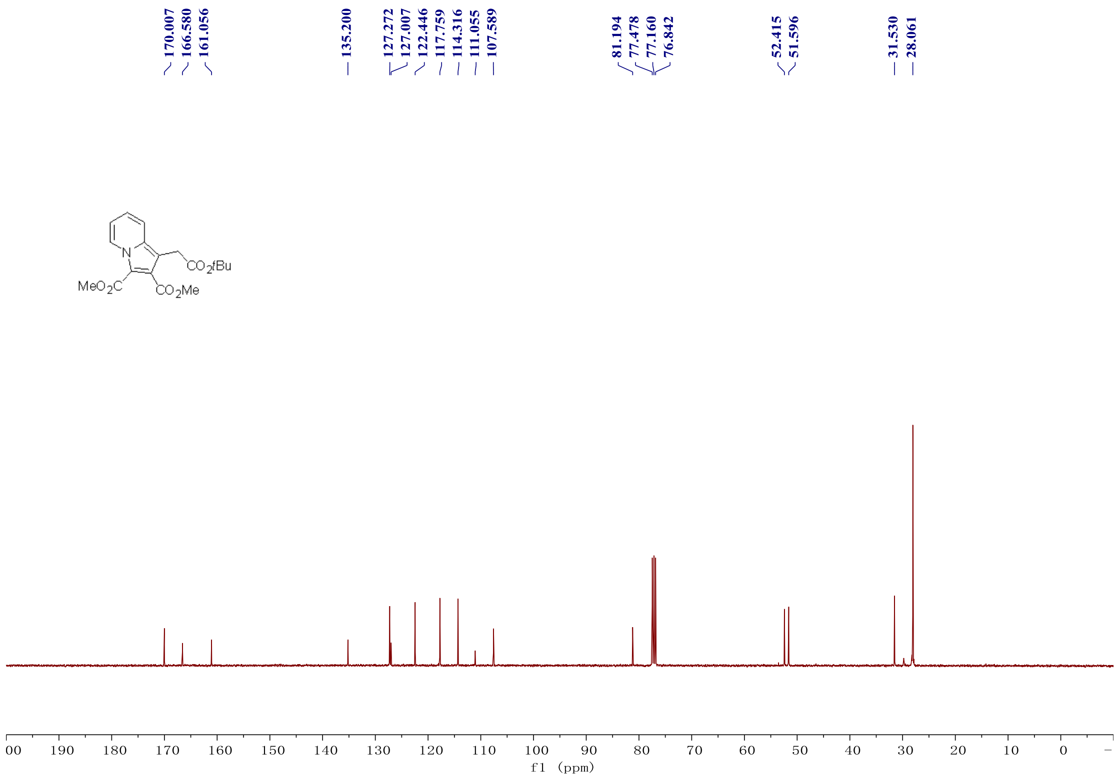


Fig. S6 ^{13}C NMR of compound **5** (100 MHz, $CDCl_3$)

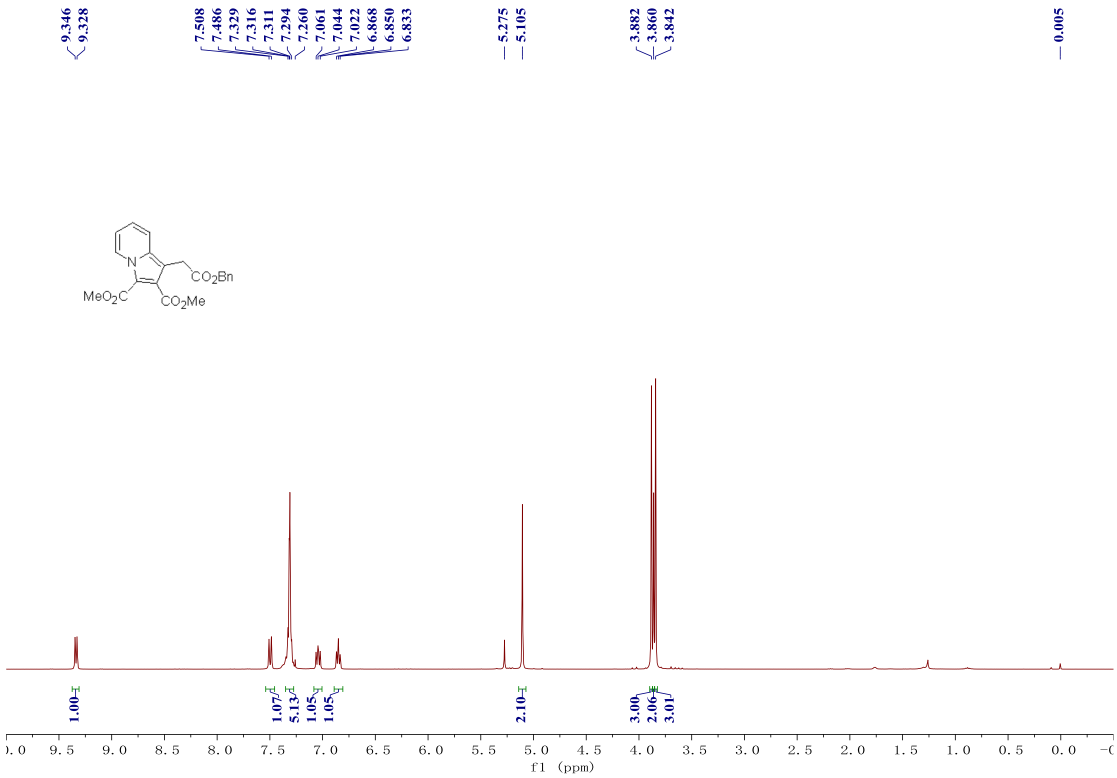


Fig. S7 ^{1}H NMR of compound **6** (400 MHz, $CDCl_3$)

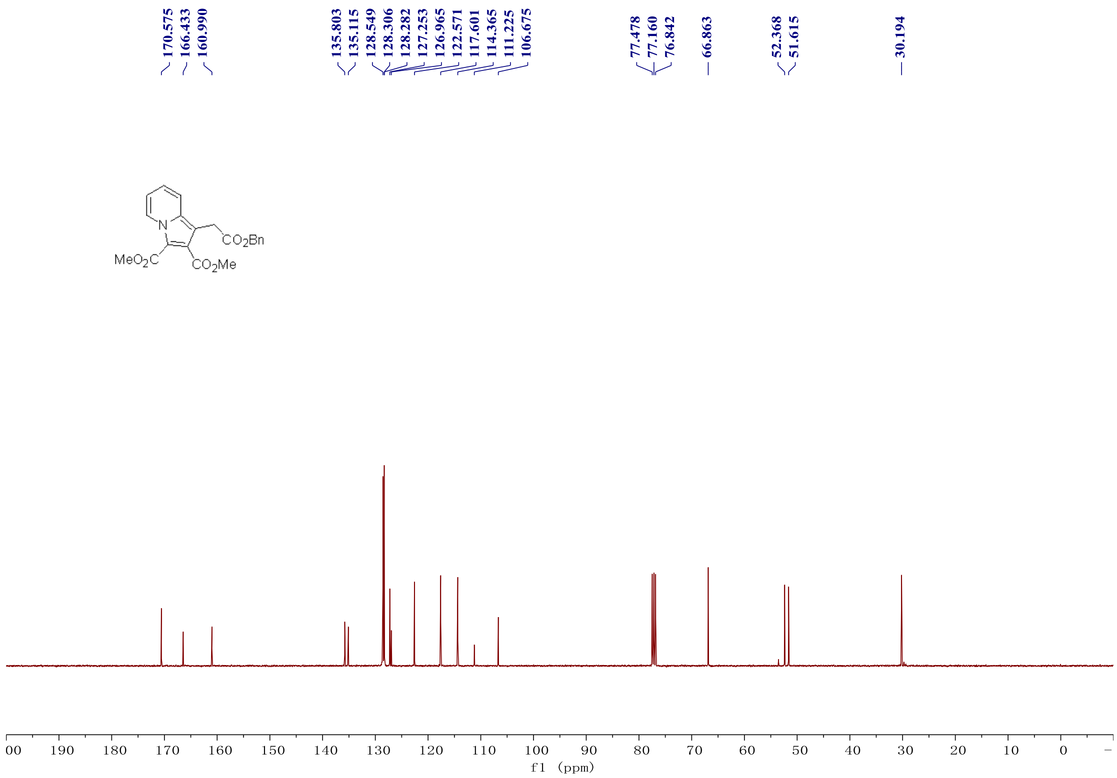


Fig. S8 ^{13}C NMR of compound **6** (100 MHz, $CDCl_3$)

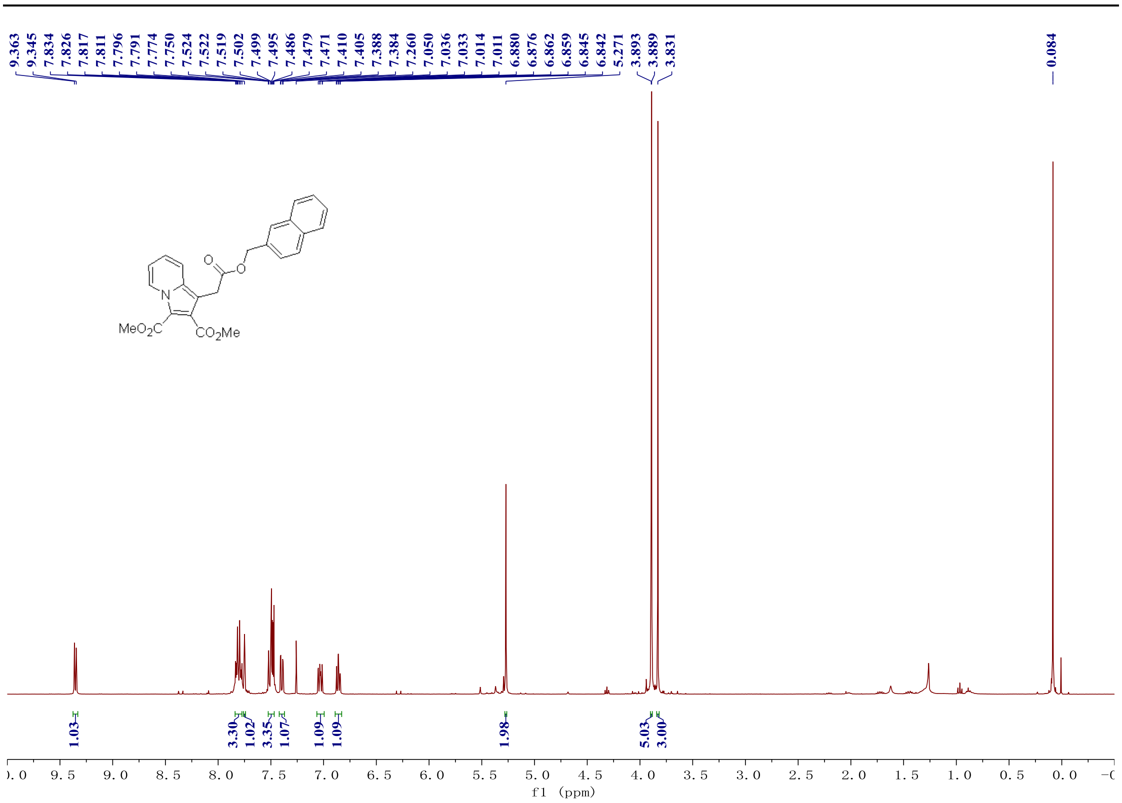


Fig. S9 ^{1}H NMR of compound **7** (400 MHz, $CDCl_3$)

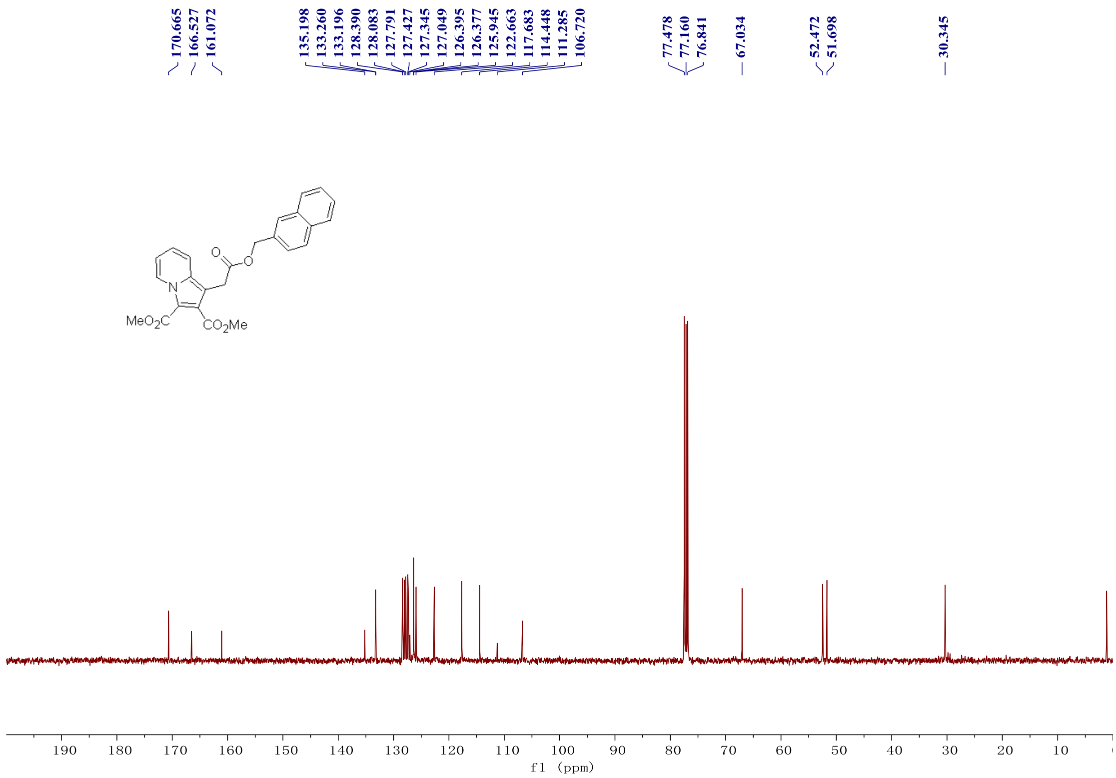


Fig. S10 ^{13}C NMR of compound **7** (100 MHz, $CDCl_3$)

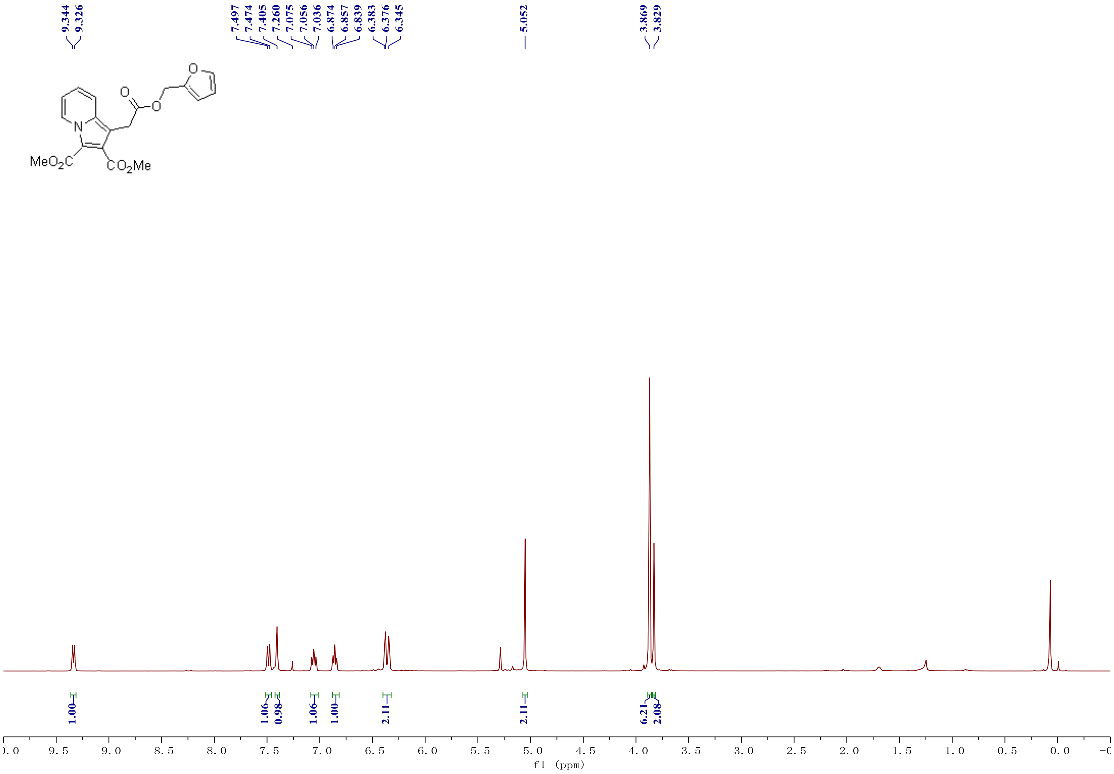


Fig. S11 ^{1}H NMR of compound **8** (400 MHz, $CDCl_3$)

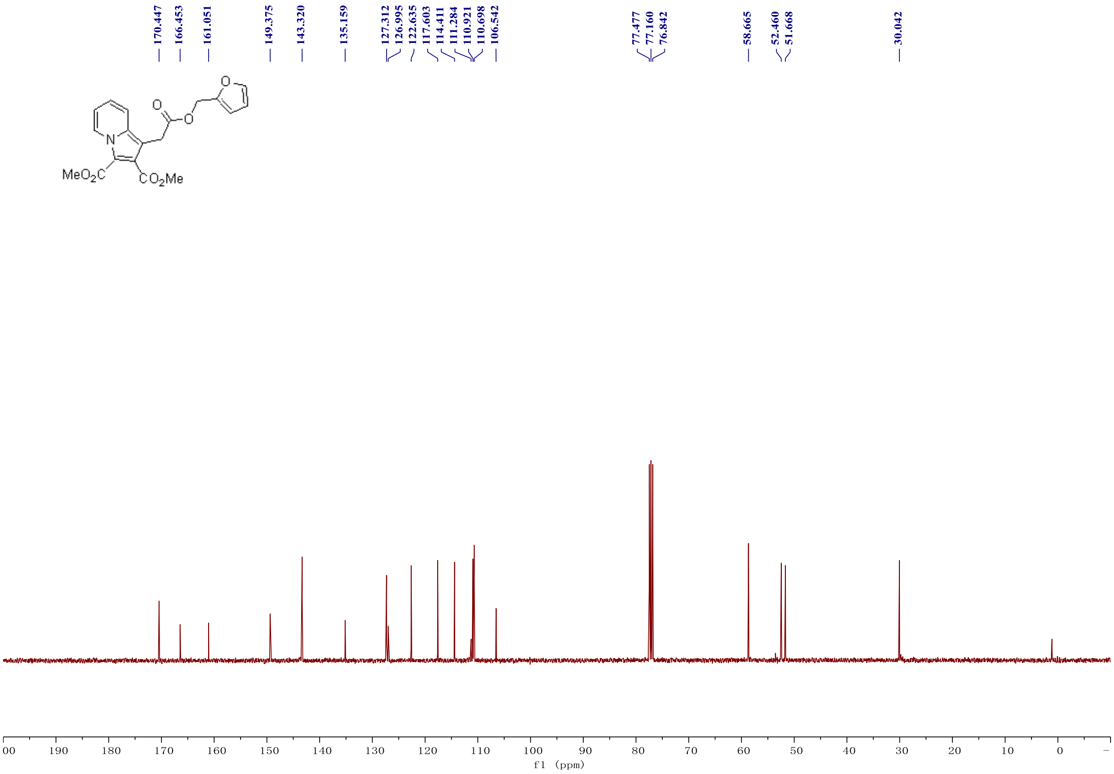


Fig. S12 ^{13}C NMR of compound **8** (100 MHz, $CDCl_3$)

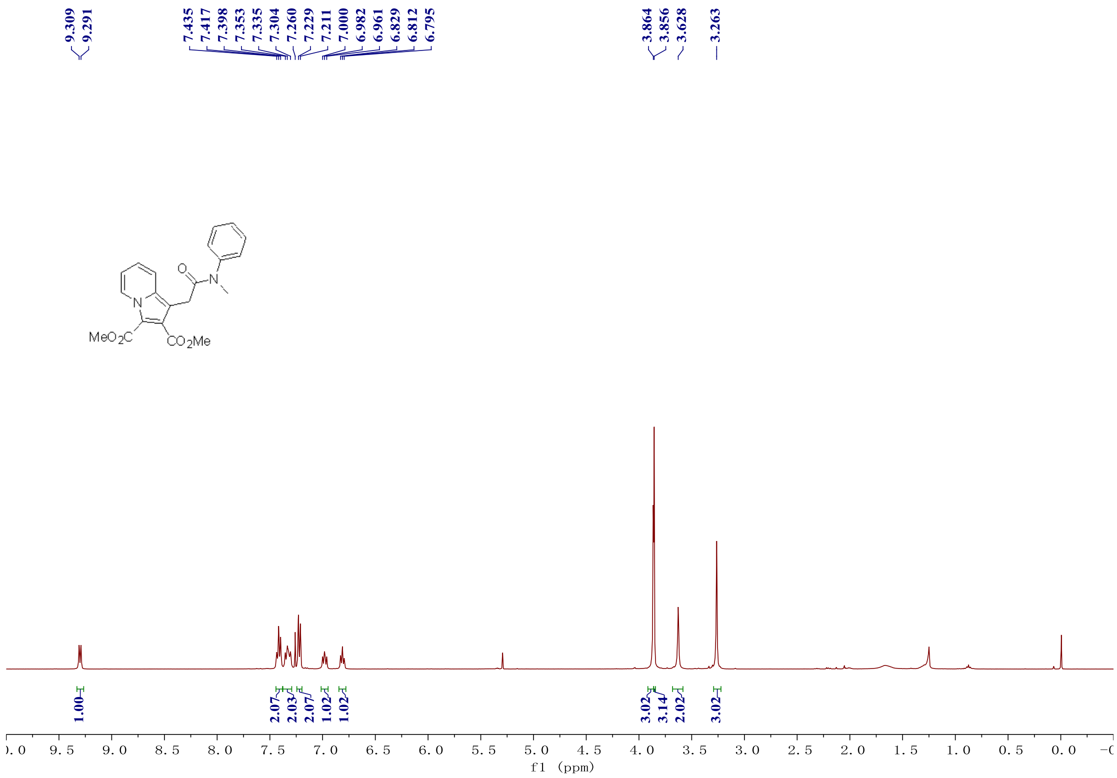


Fig. S13 [1]H NMR of compound **10** (400 MHz, $CDCl_3$)

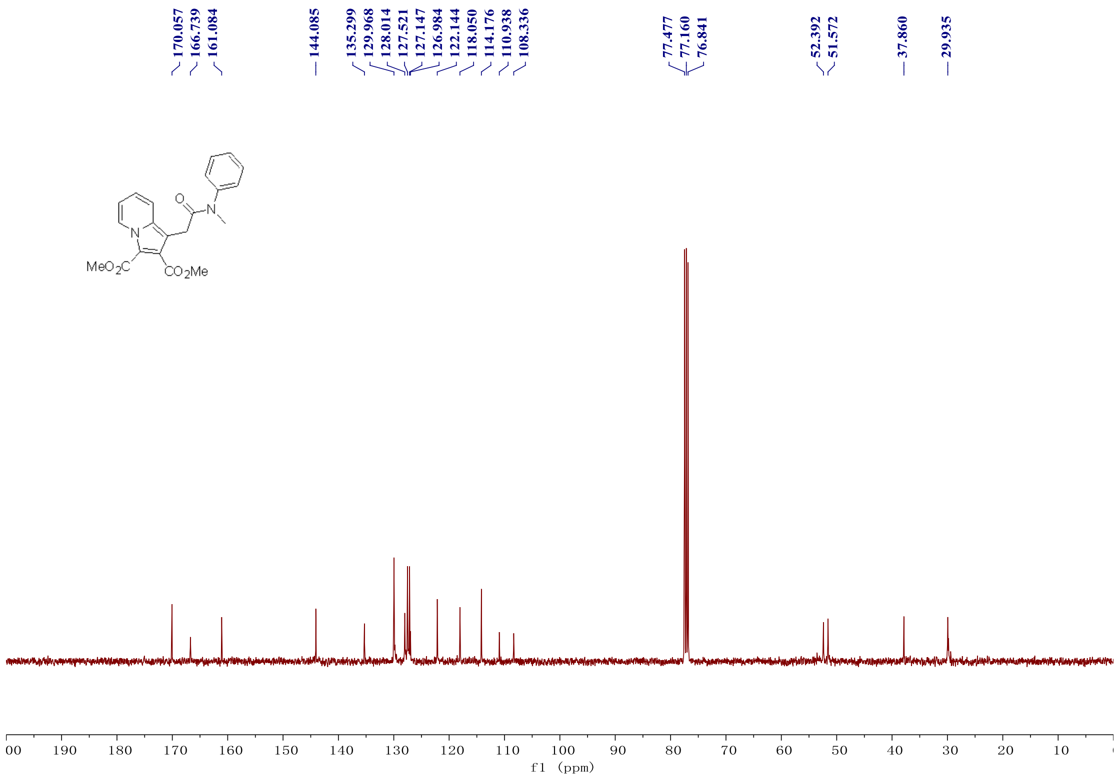


Fig. S14 [13]C NMR of compound **10** (100 MHz, $CDCl_3$)

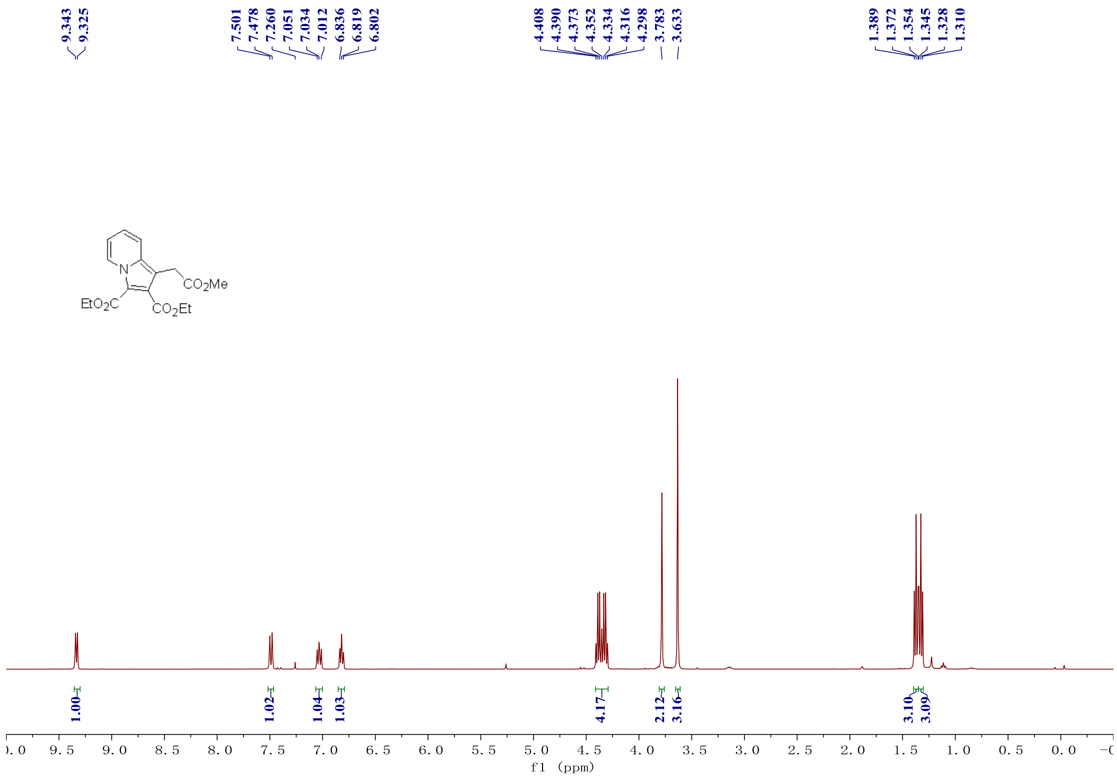


Fig. S15 ^{1}H NMR of compound **11** (400 MHz, $CDCl_3$)

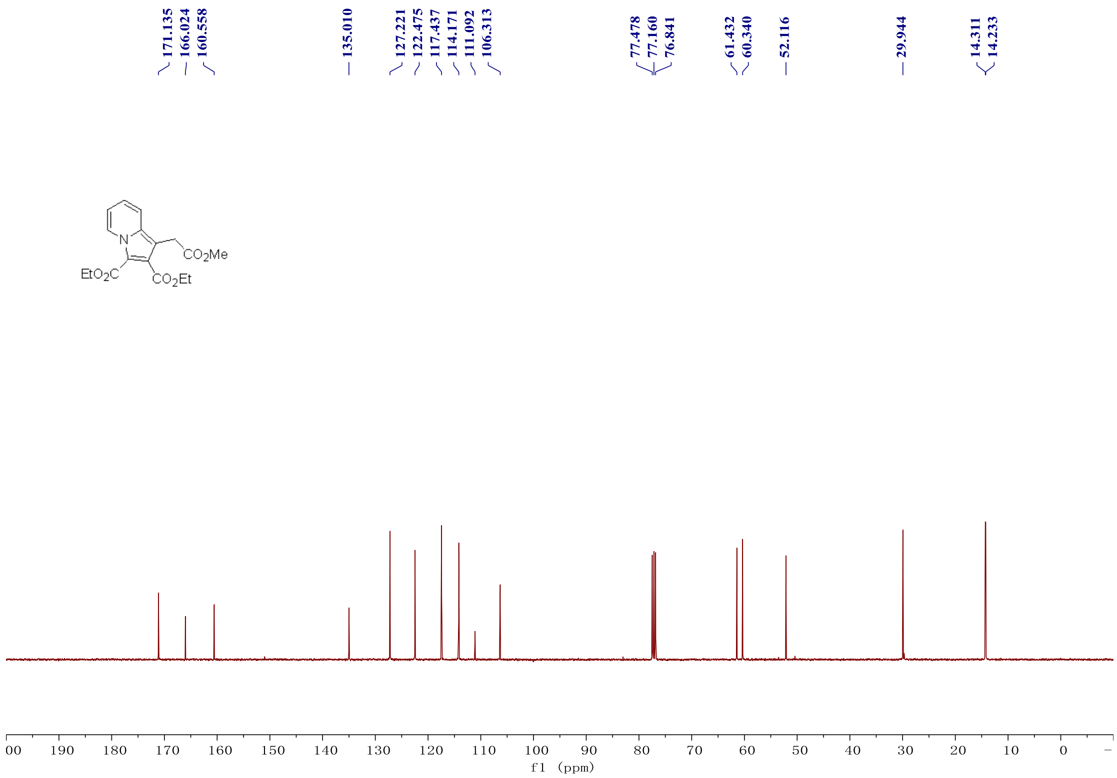


Fig. S16 ^{13}C NMR of compound **11** (100 MHz, $CDCl_3$)

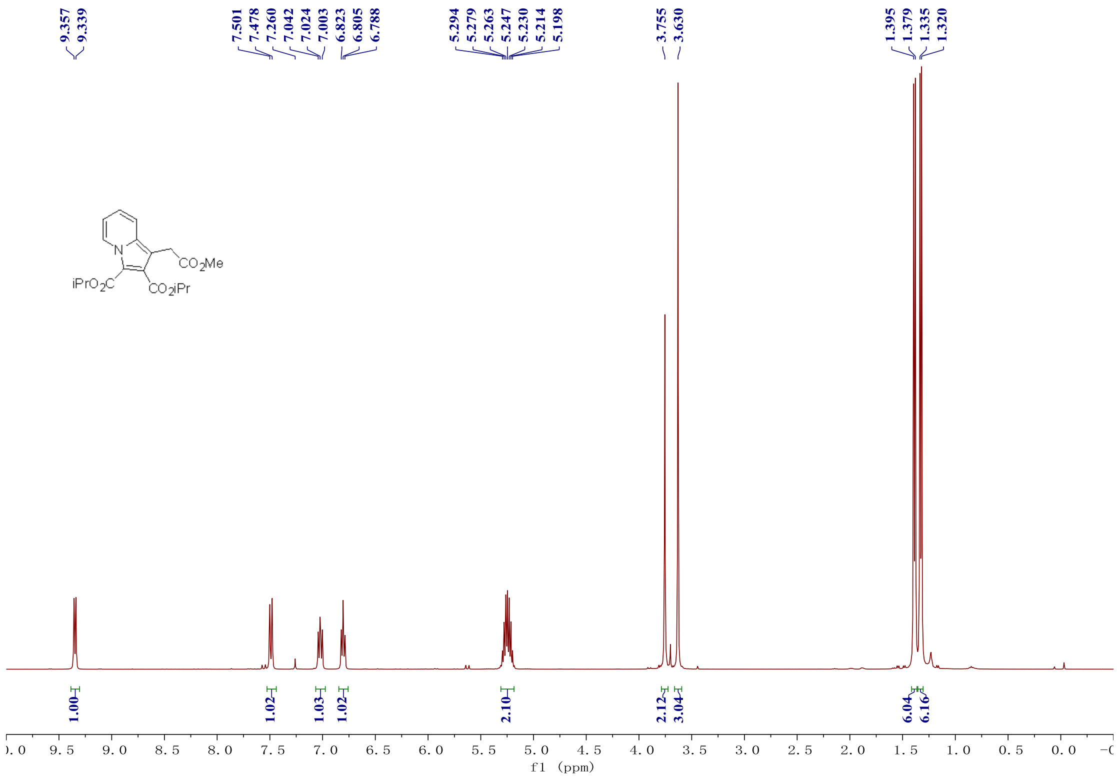


Fig. S17 ^{1}H NMR of compound **12** (400 MHz, $CDCl_3$)

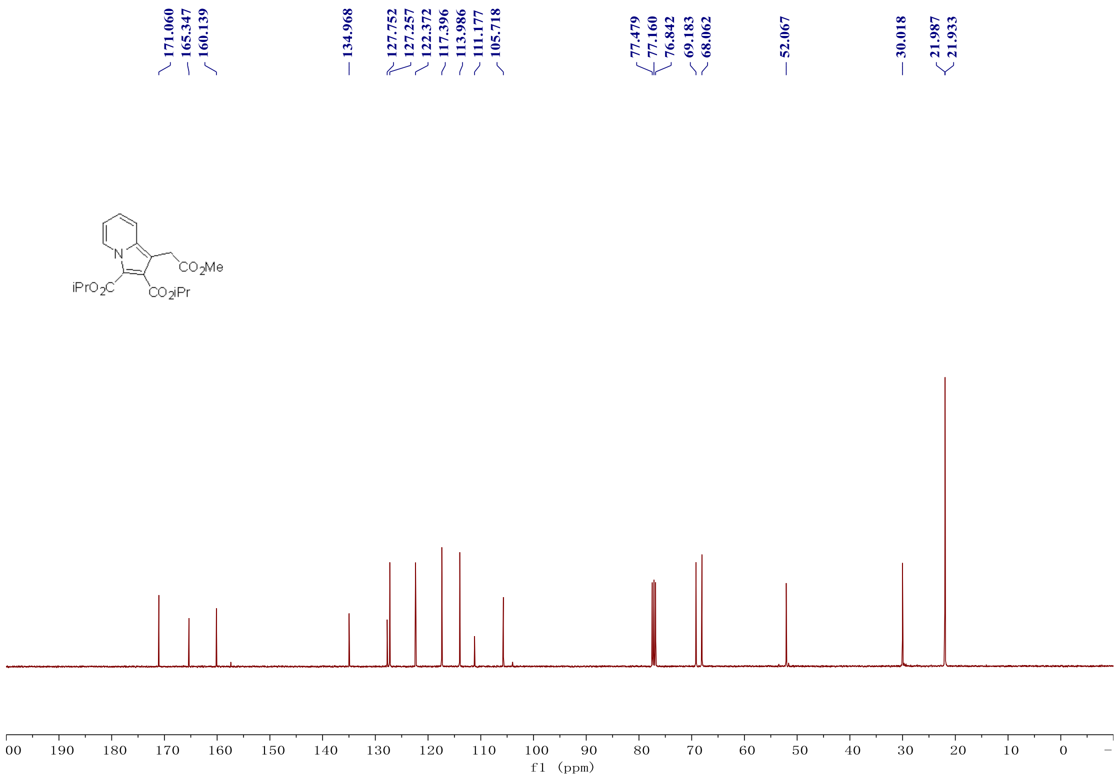


Fig. S18 ^{13}C NMR of compound **12** (100 MHz, $CDCl_3$)

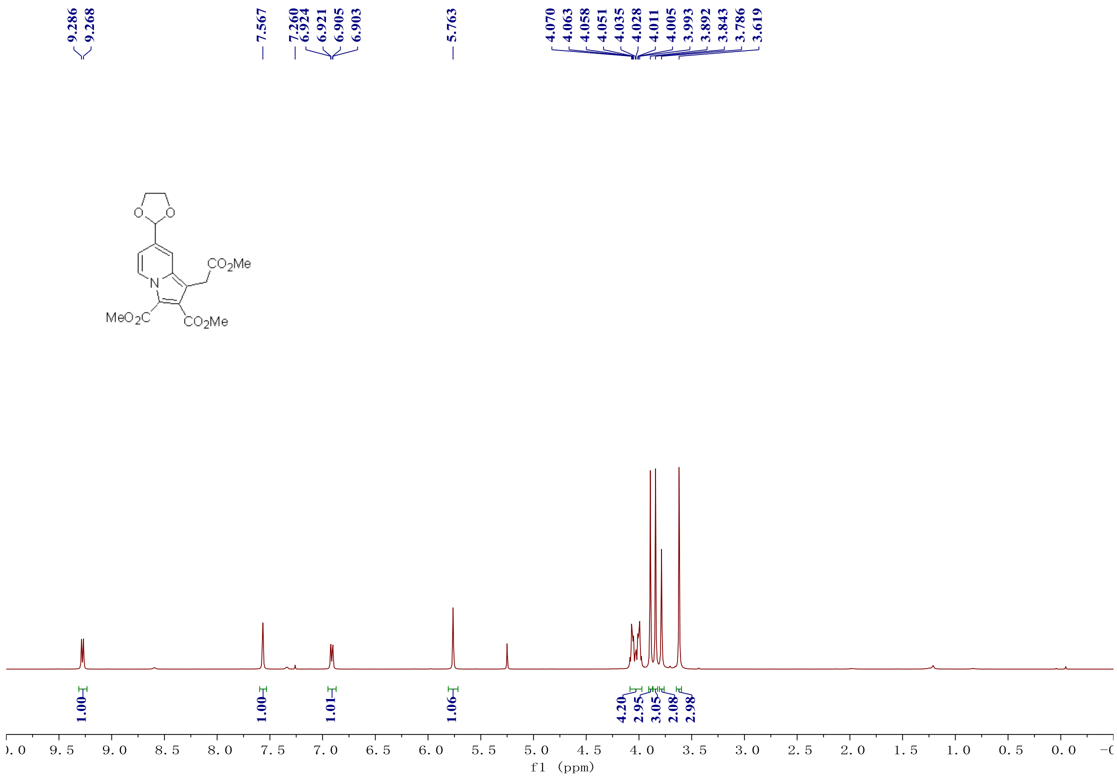


Fig. S19 ^{1}H NMR of compound **13** (400 MHz, $CDCl_3$)

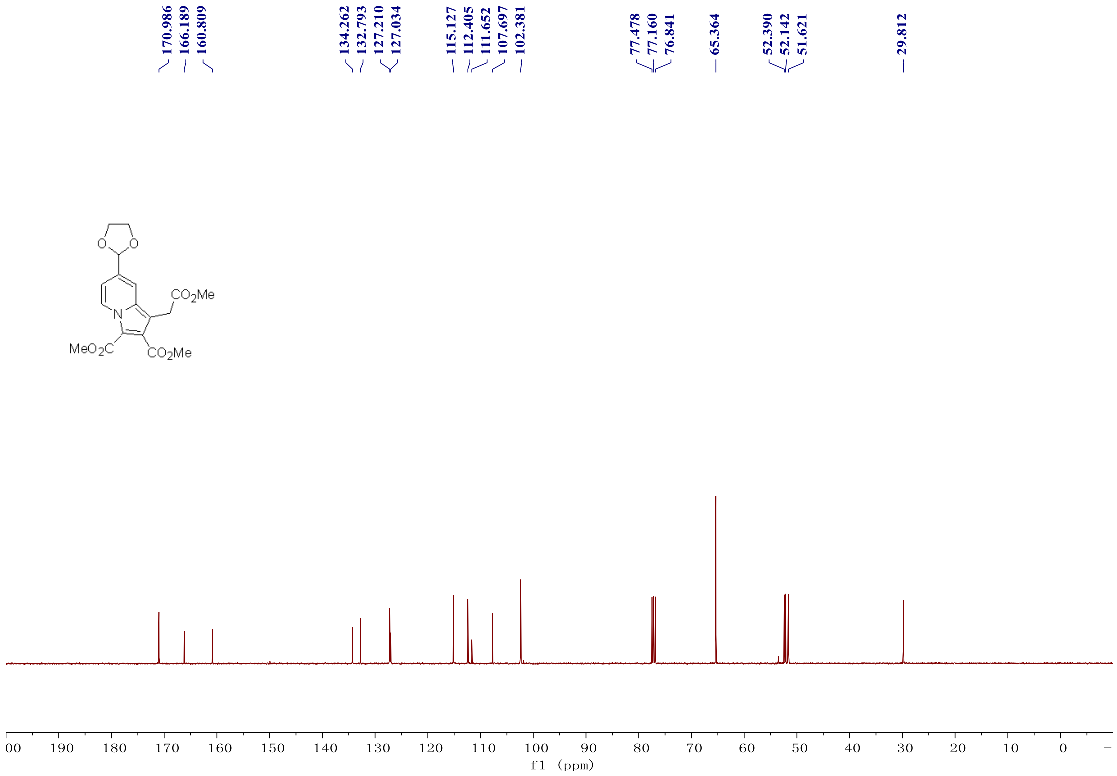


Fig. S20 ^{13}C NMR of compound **13** (100 MHz, $CDCl_3$)

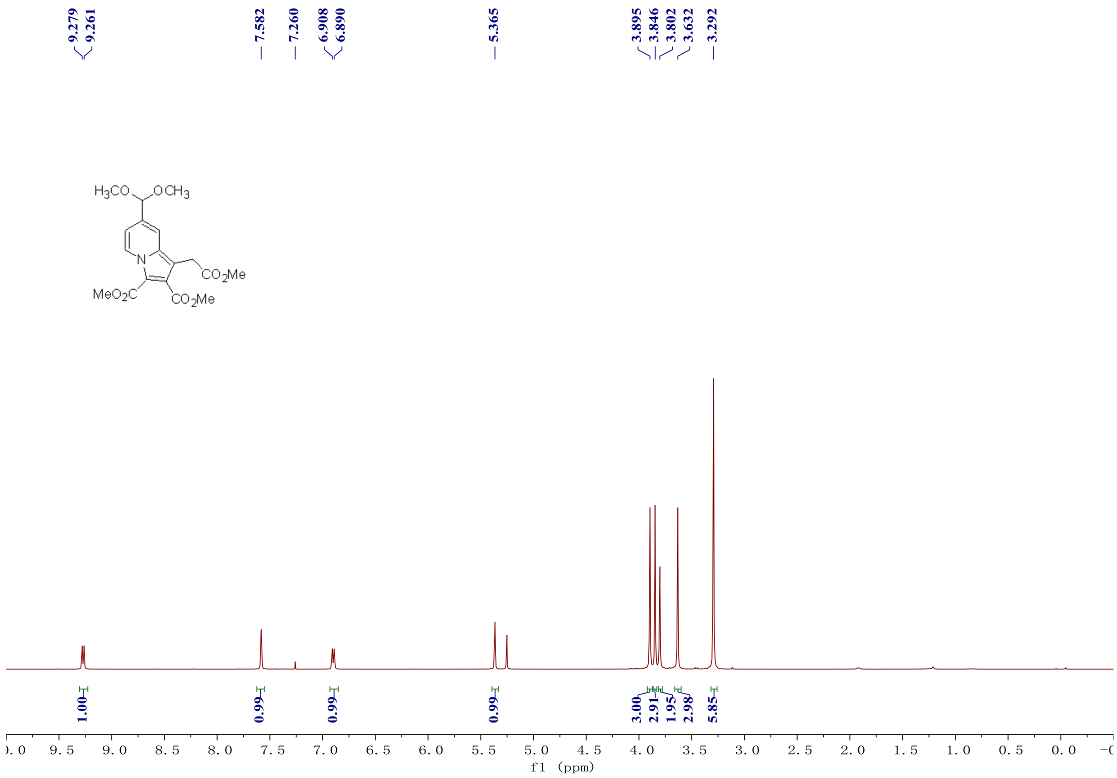


Fig. S21 ^{1}H NMR of compound **14** (400 MHz, $CDCl_3$)

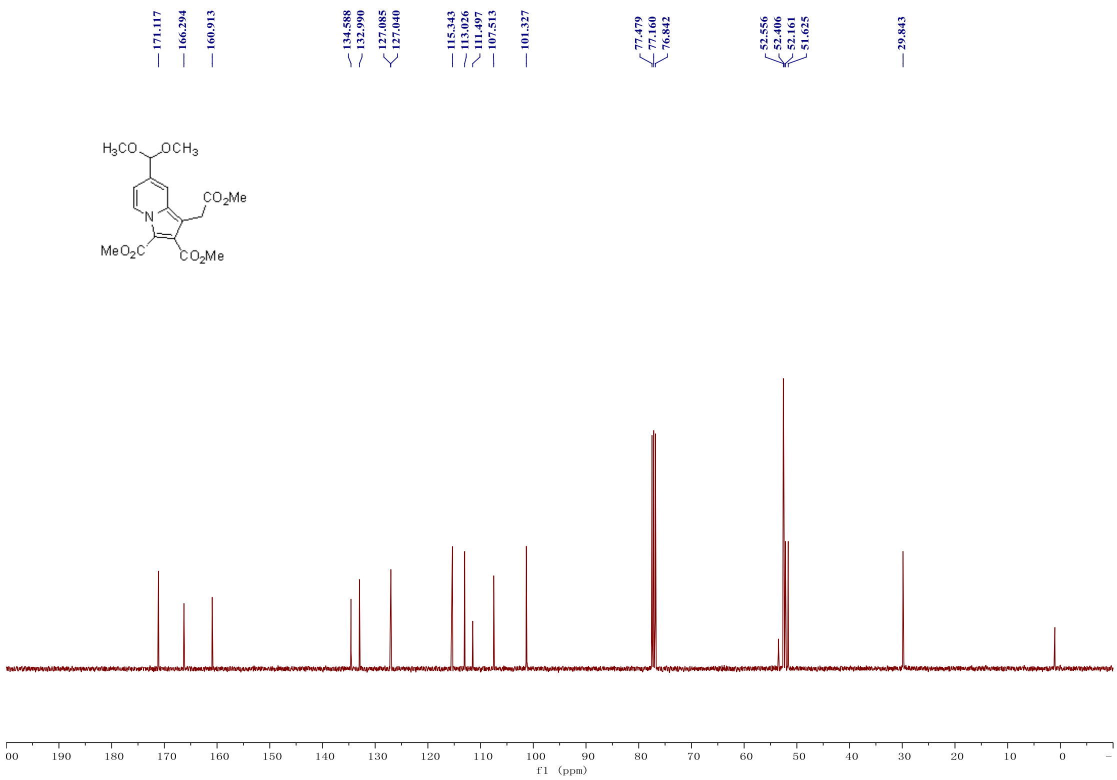


Fig. S22 ^{13}C NMR of compound **14** (100 MHz, $CDCl_3$)

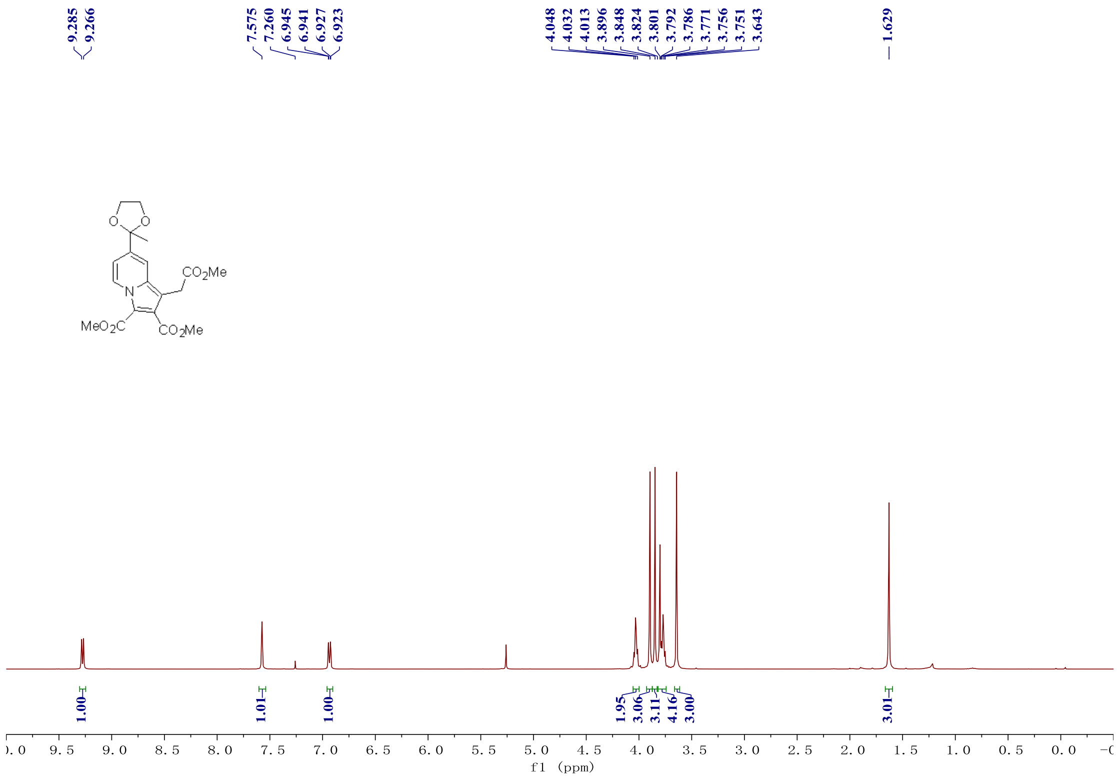


Fig. S23 ^{1}H NMR of compound **15** (400 MHz, $CDCl_3$)

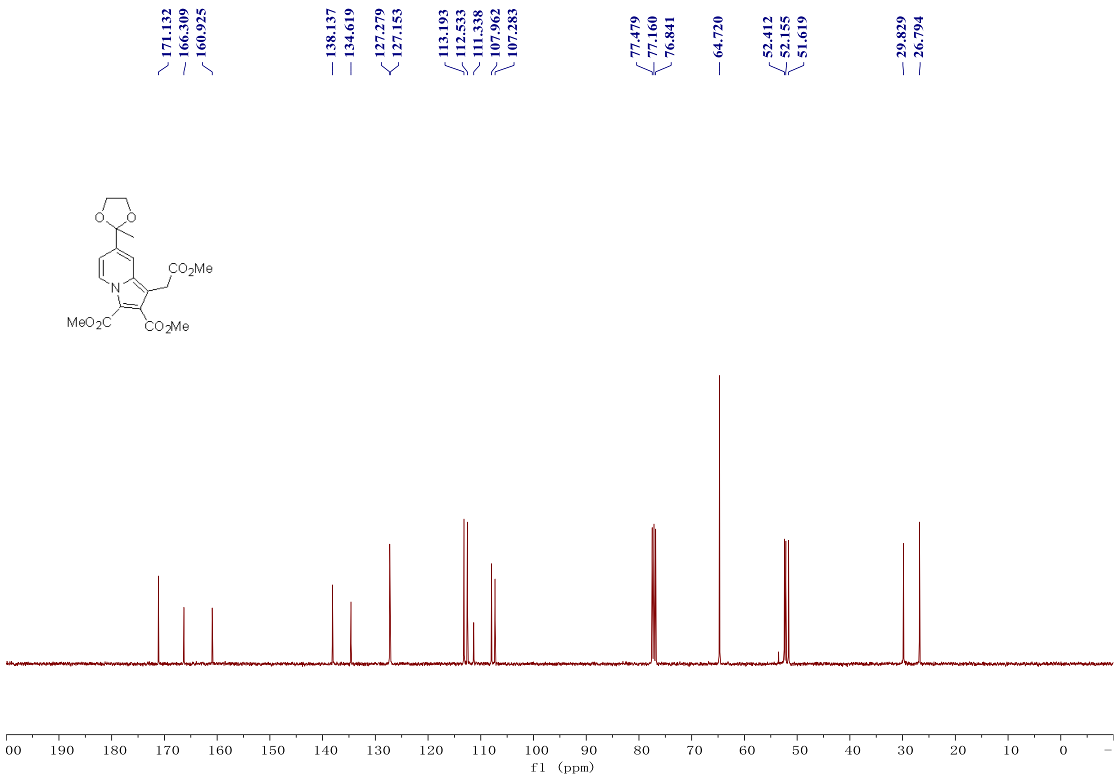


Fig. S24 ^{13}C NMR of compound **15** (100 MHz, $CDCl_3$)

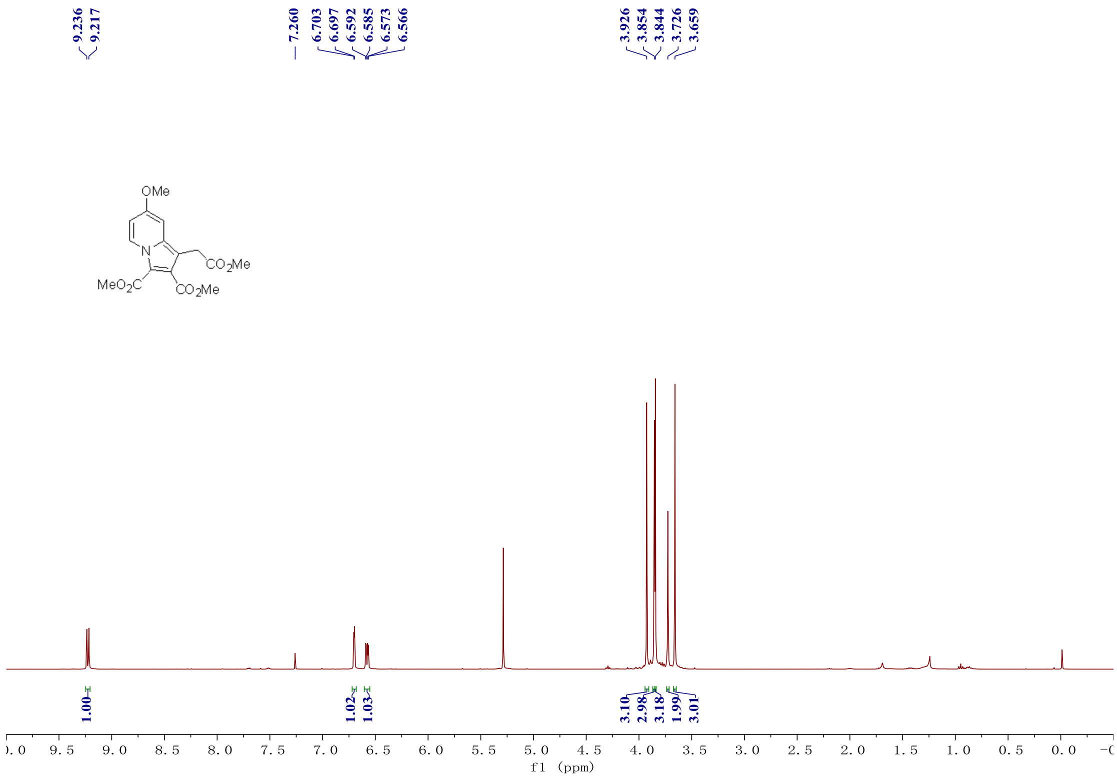


Fig. S25 ^{1}H NMR of compound **16** (400 MHz, $CDCl_3$)

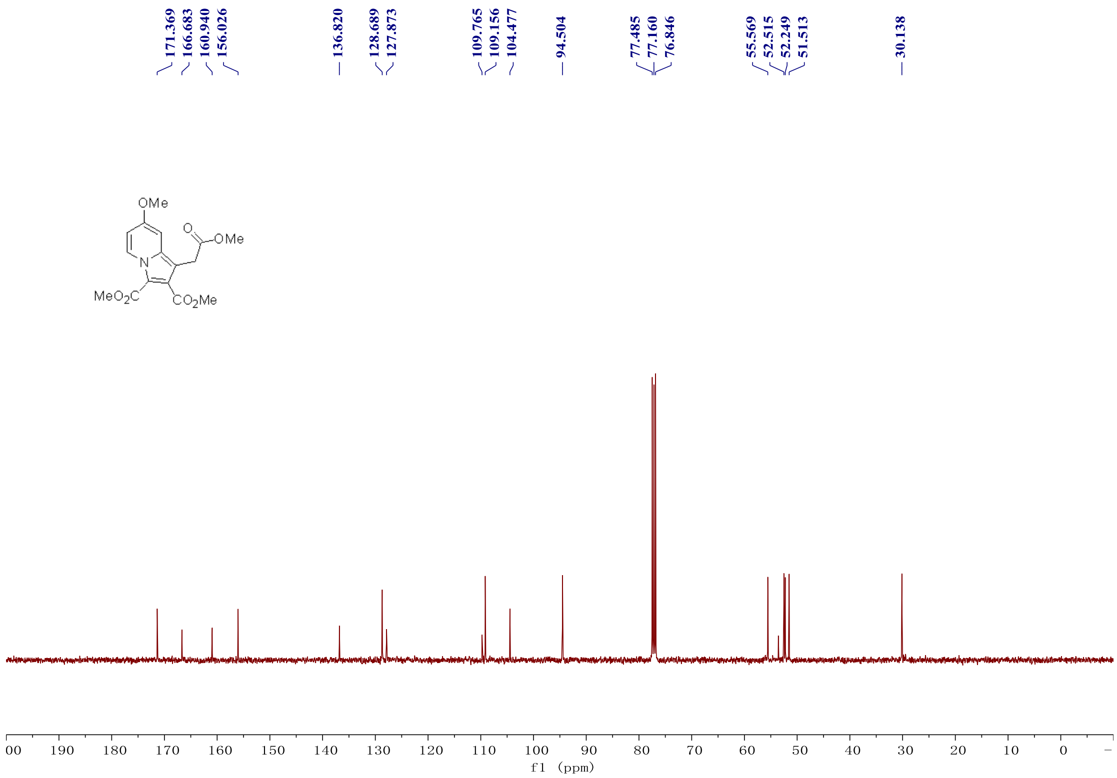


Fig. S26 ^{13}C NMR of compound **16** (100 MHz, $CDCl_3$)

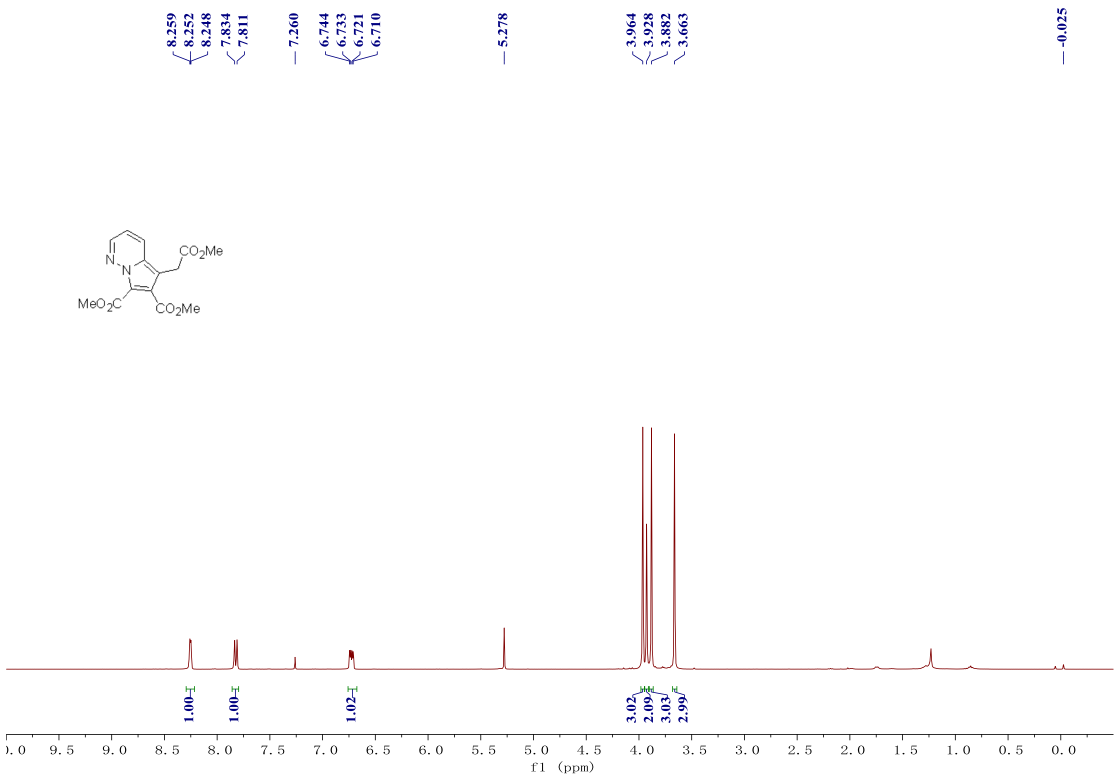


Fig. S27 ^{1}H NMR of compound **21** (400 MHz, $CDCl_3$)

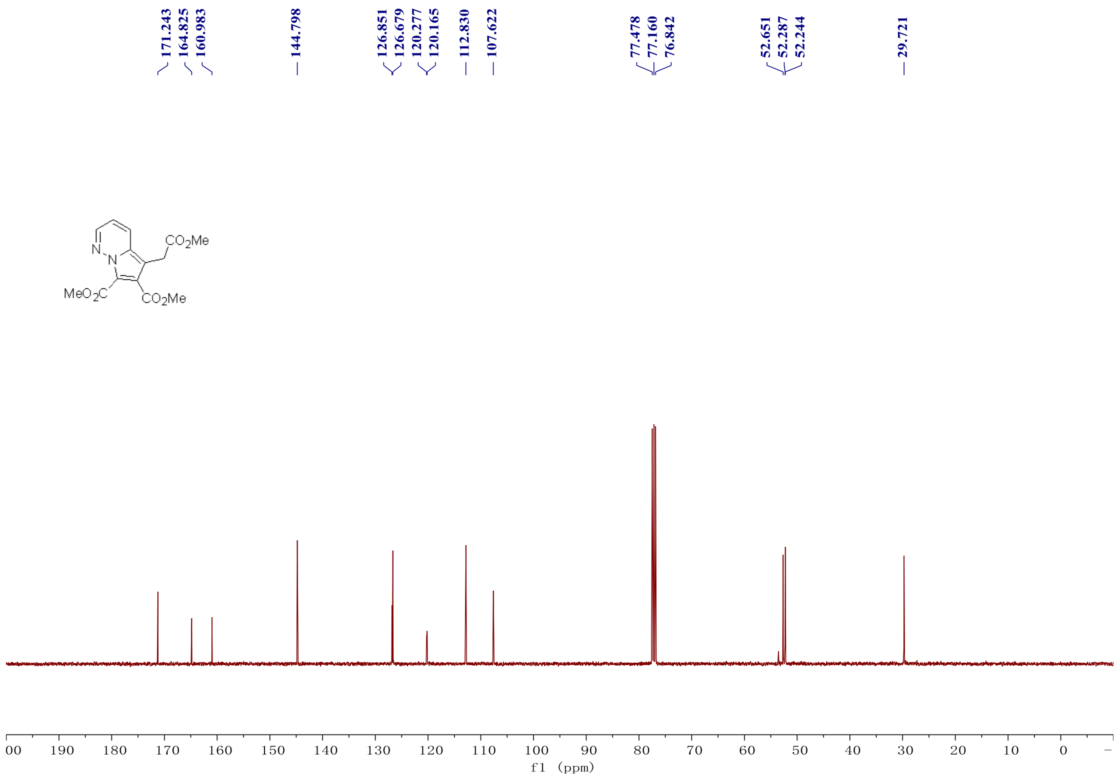


Fig. S28 ^{13}C NMR of compound **21** (100 MHz, $CDCl_3$)

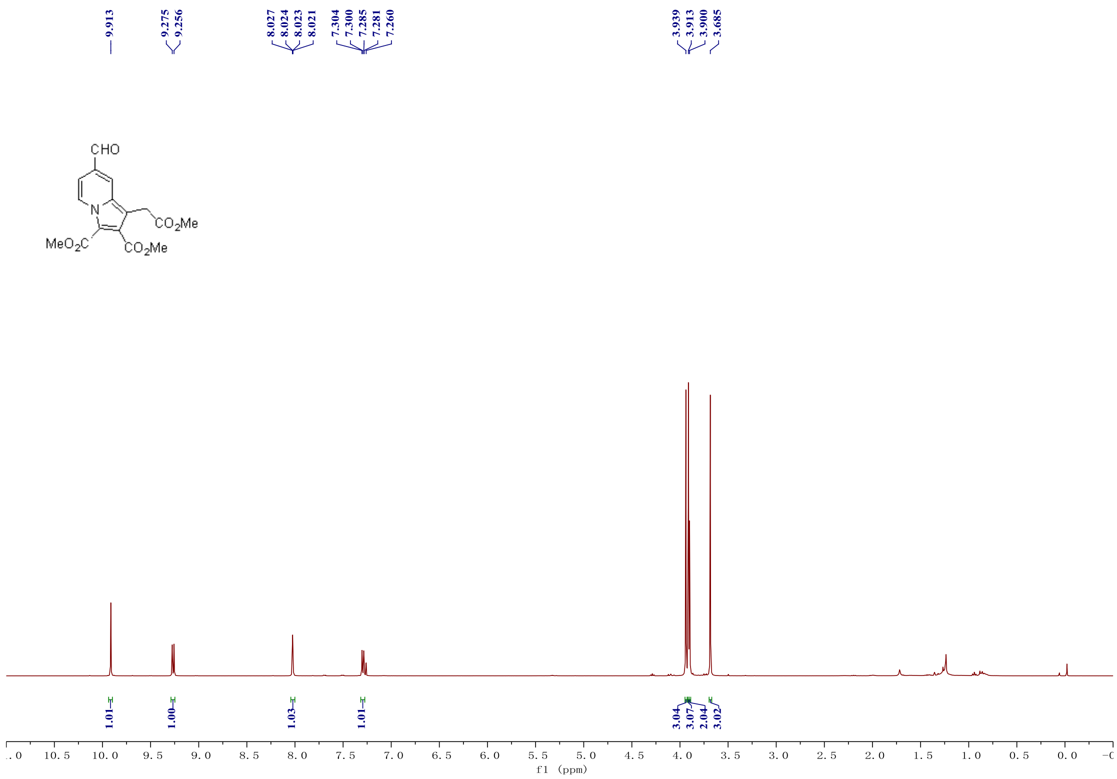


Fig. S29 ^{1}H NMR of compound **22** (400 MHz, $CDCl_3$)

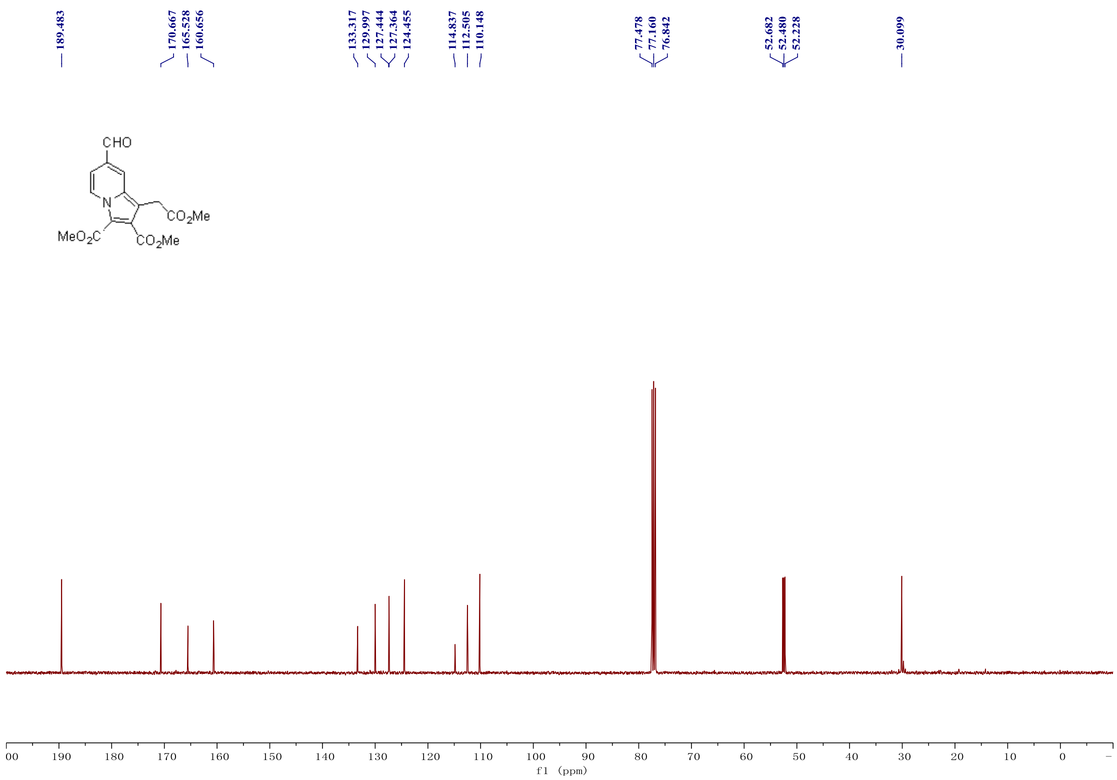


Fig. S30 ^{13}C NMR of compound **22** (100 MHz, $CDCl_3$)

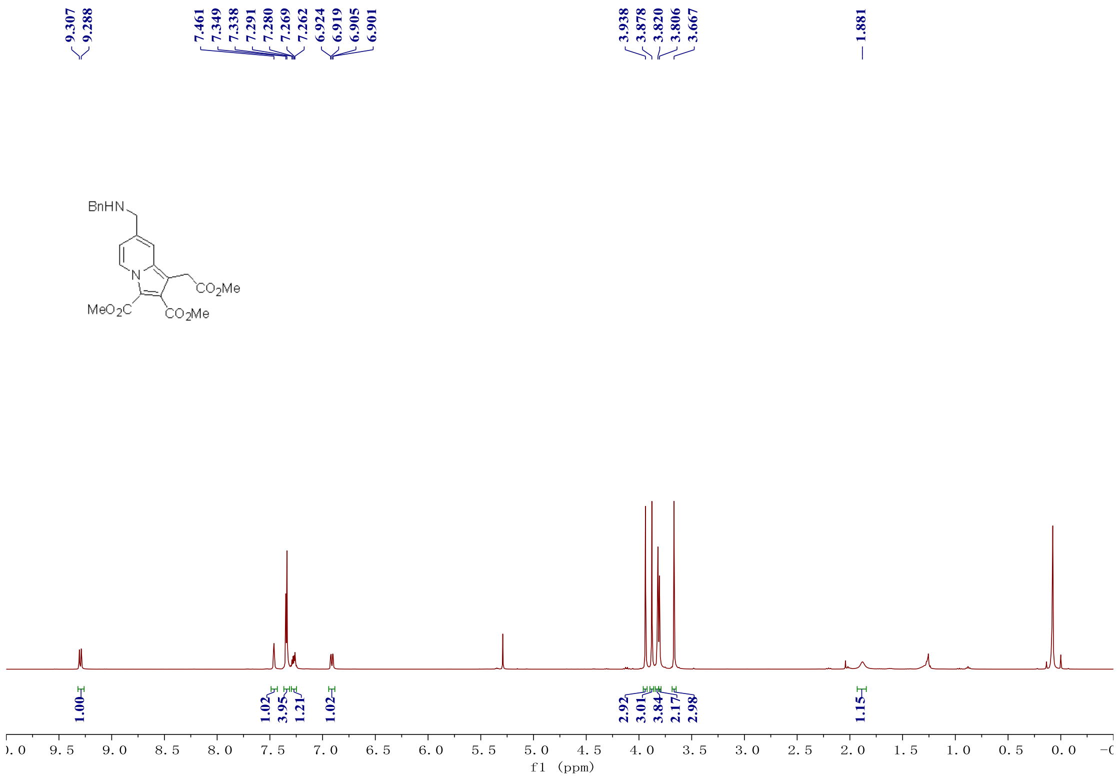


Fig. S31 ^{1}H NMR of compound **23a** (400 MHz, $CDCl_3$)

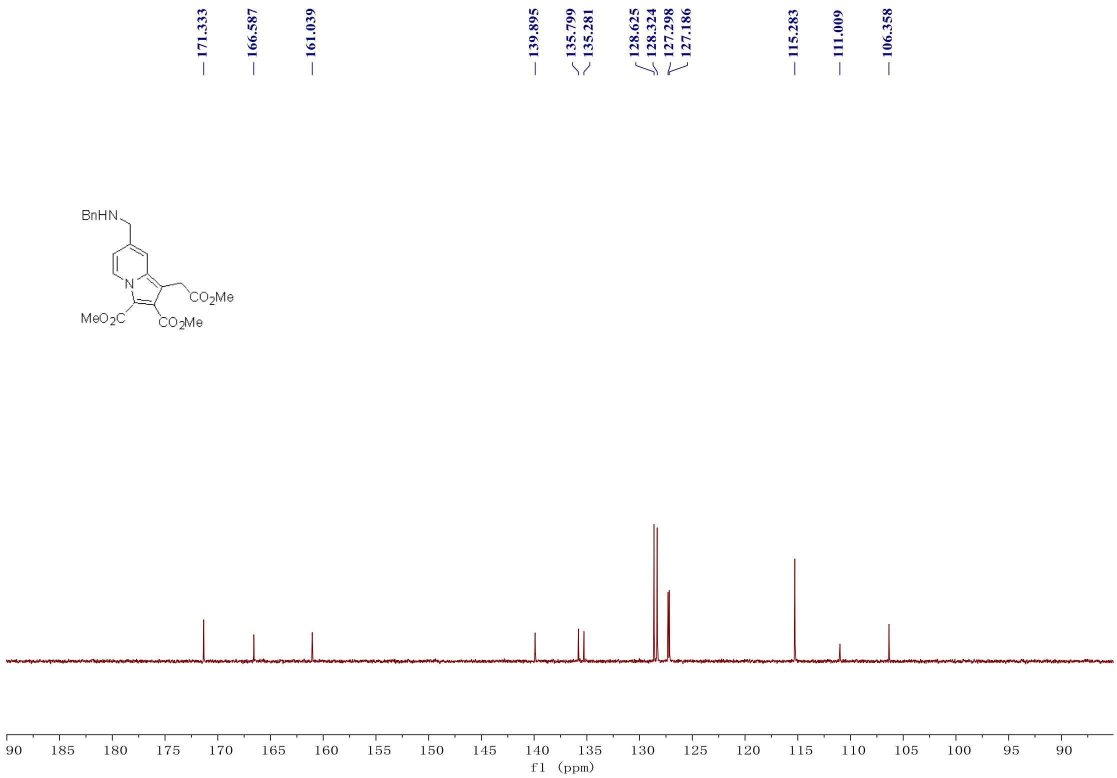


Fig. S32 ^{13}C NMR of compound **23a** (100 MHz, $CDCl_3$)

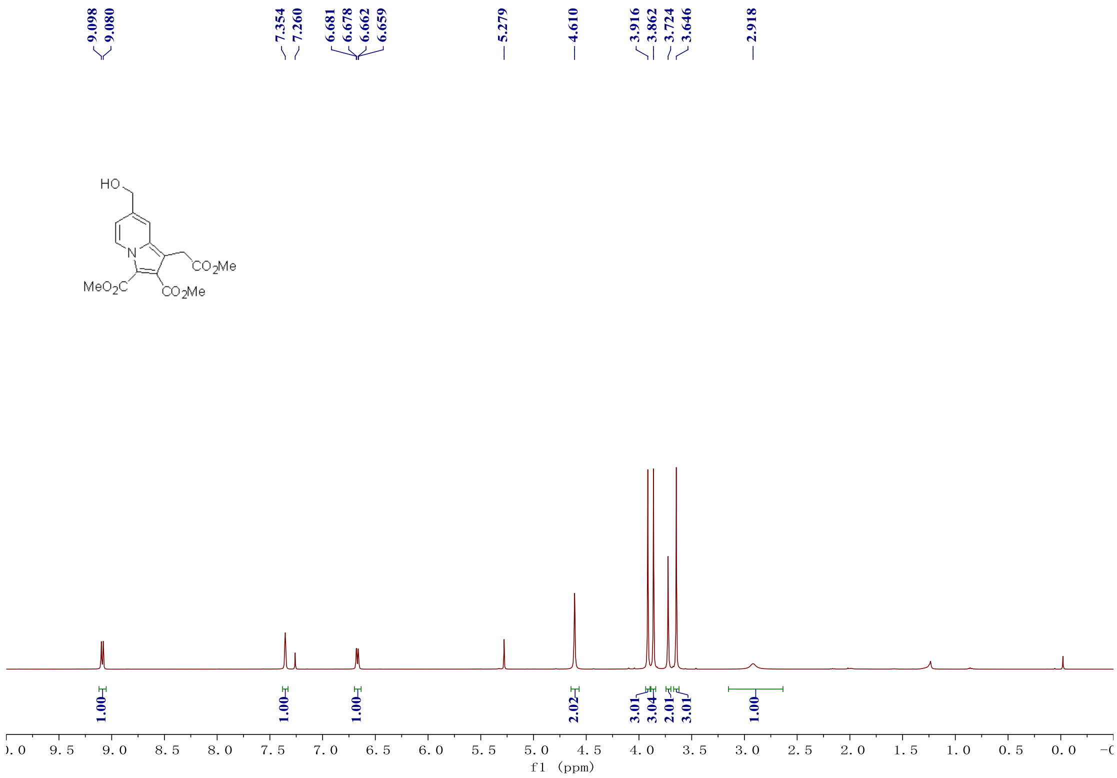


Fig. S33 ^{1}H NMR of compound **23b** (400 MHz, $CDCl_3$)

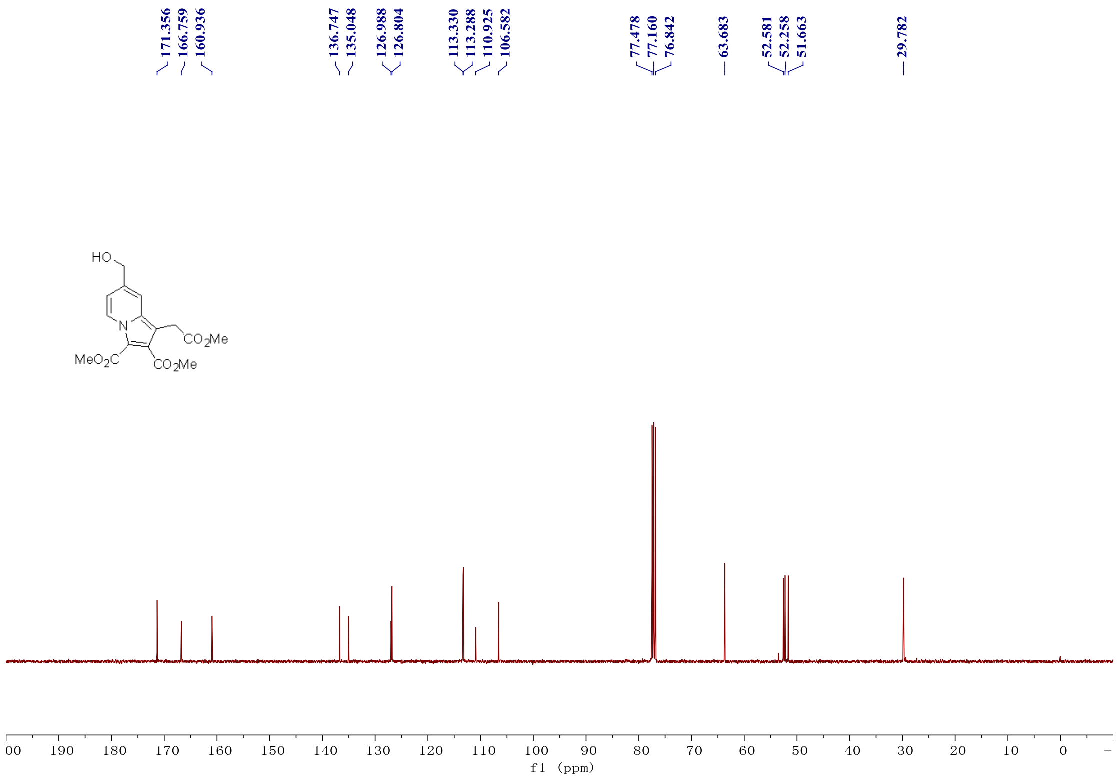


Fig. S34 ^{13}C NMR of compound **23b** (100 MHz, $CDCl_3$)

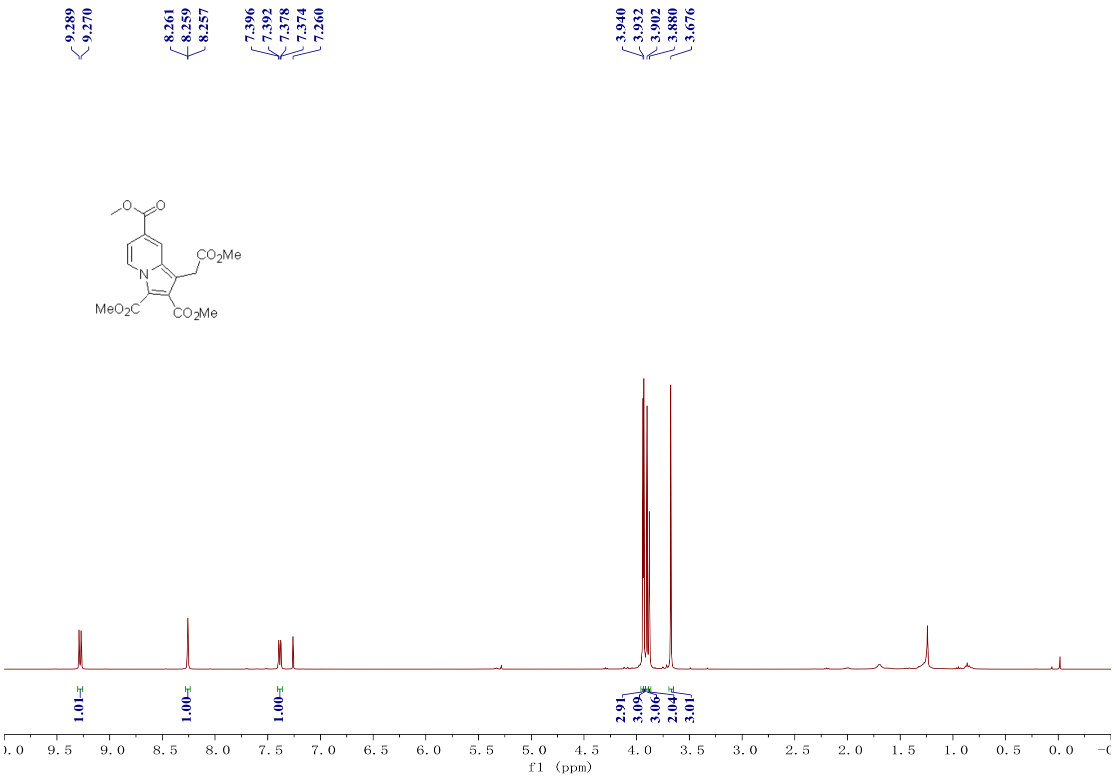


Fig. S35 ^{1}H NMR of compound **24** (400 MHz, $CDCl_3$)

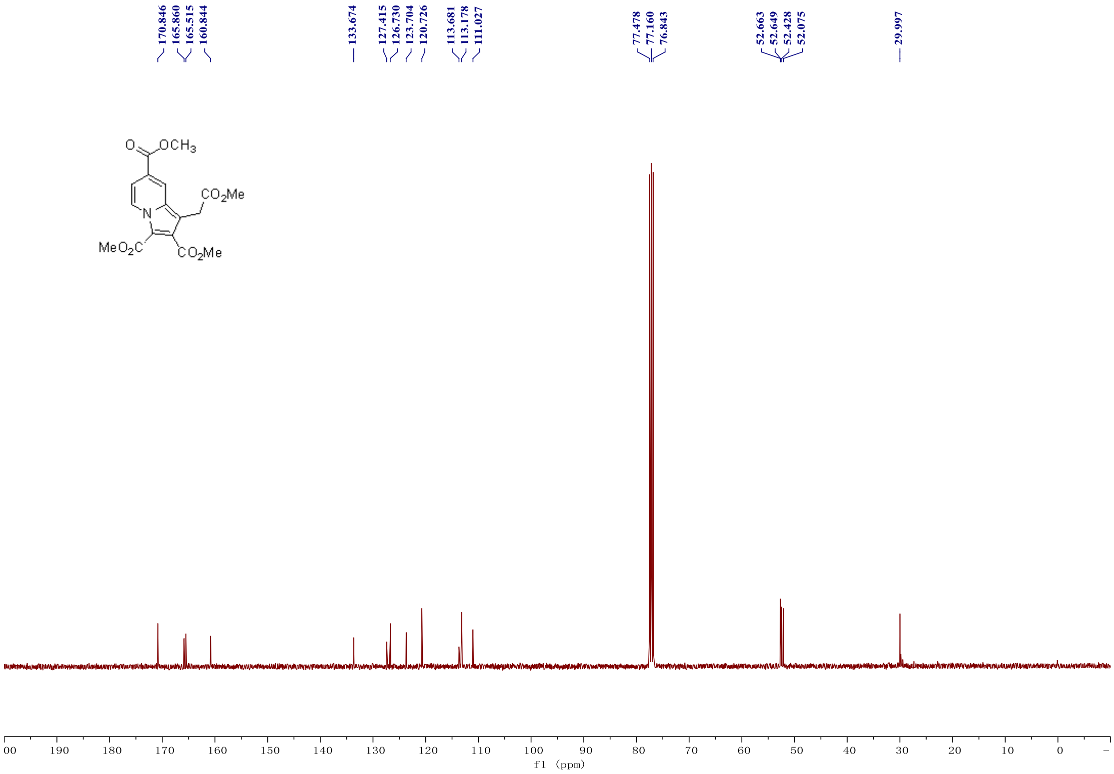


Fig. S36 ^{13}C NMR of compound **24** (100 MHz, $CDCl_3$)

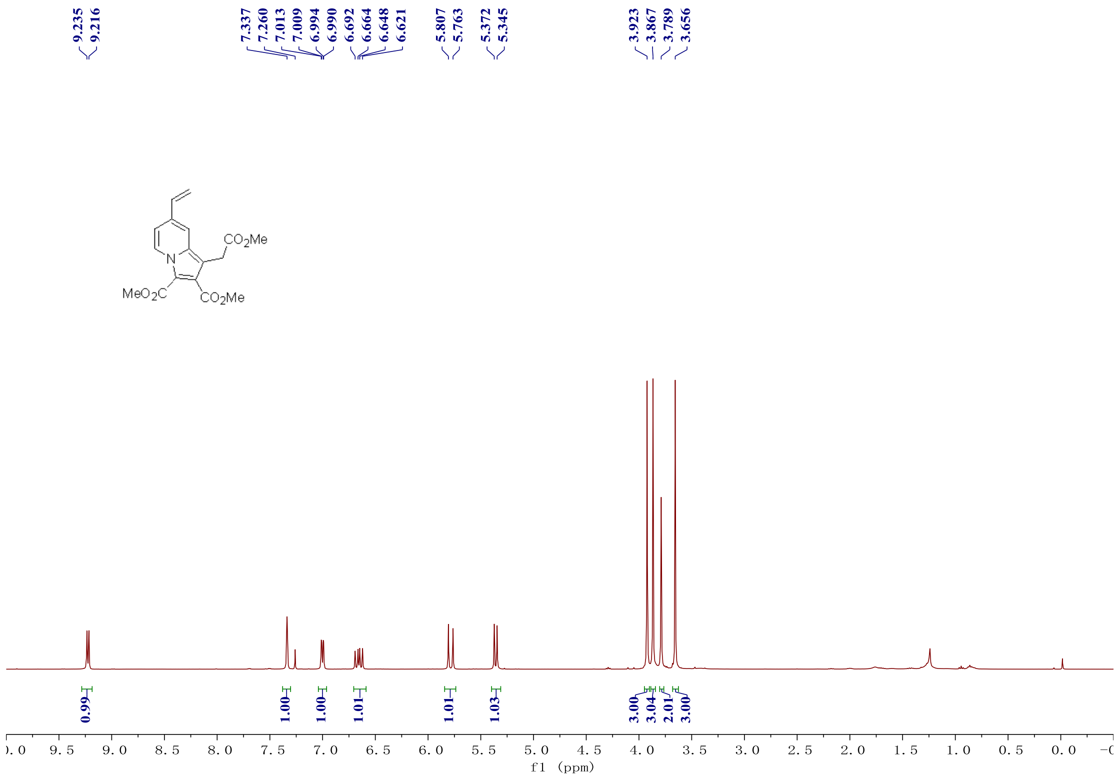


Fig. S37 ^{1}H NMR of compound **25d** (400 MHz, $CDCl_3$)

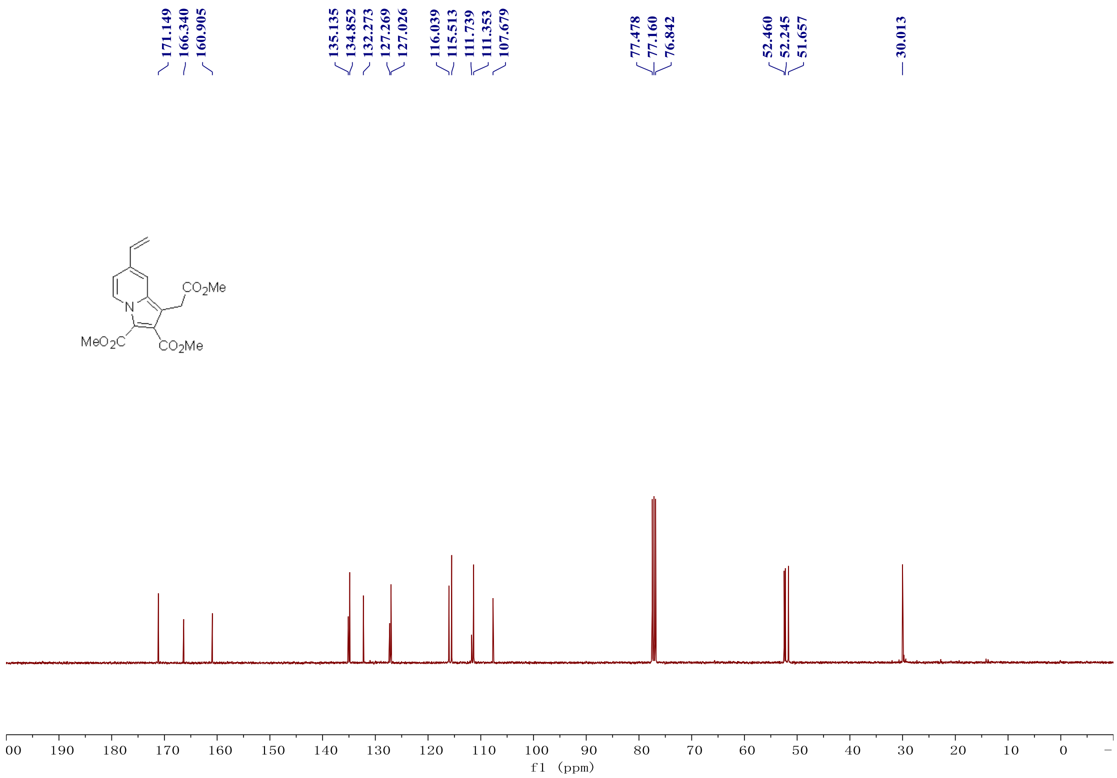


Fig. S38 ^{13}C NMR of compound **25d** (100 MHz, $CDCl_3$)

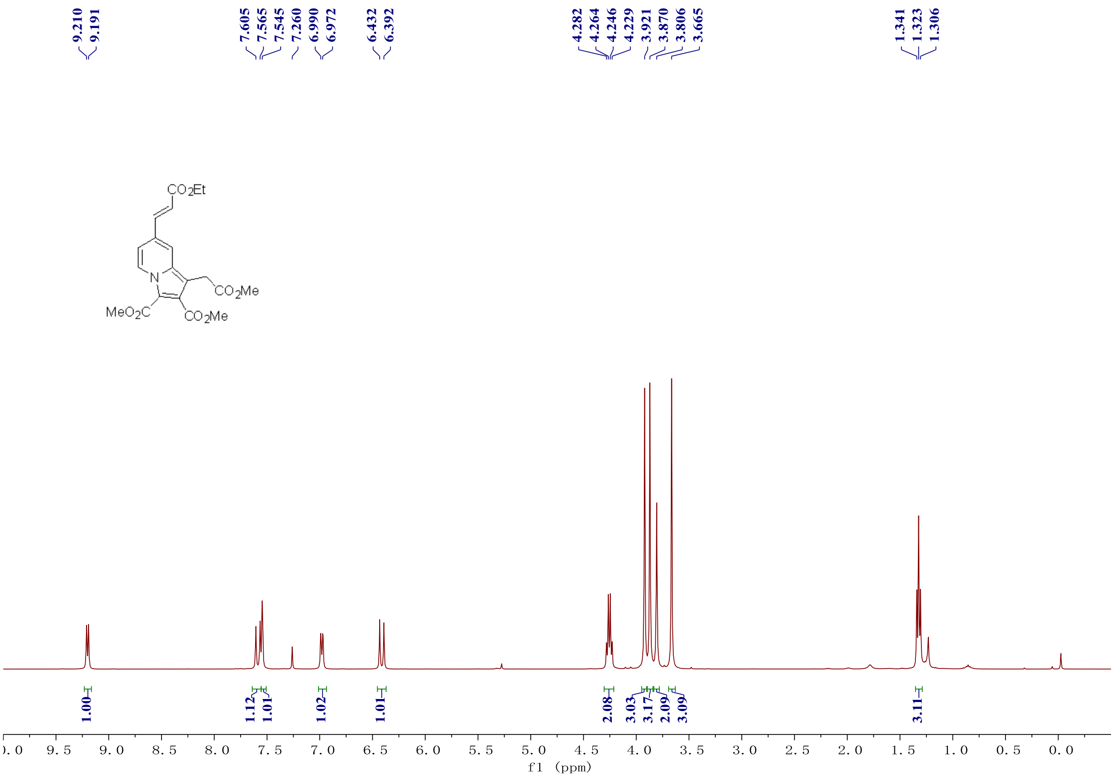


Fig. S39 ^{1}H NMR of compound **25e** (400 MHz, $CDCl_3$)

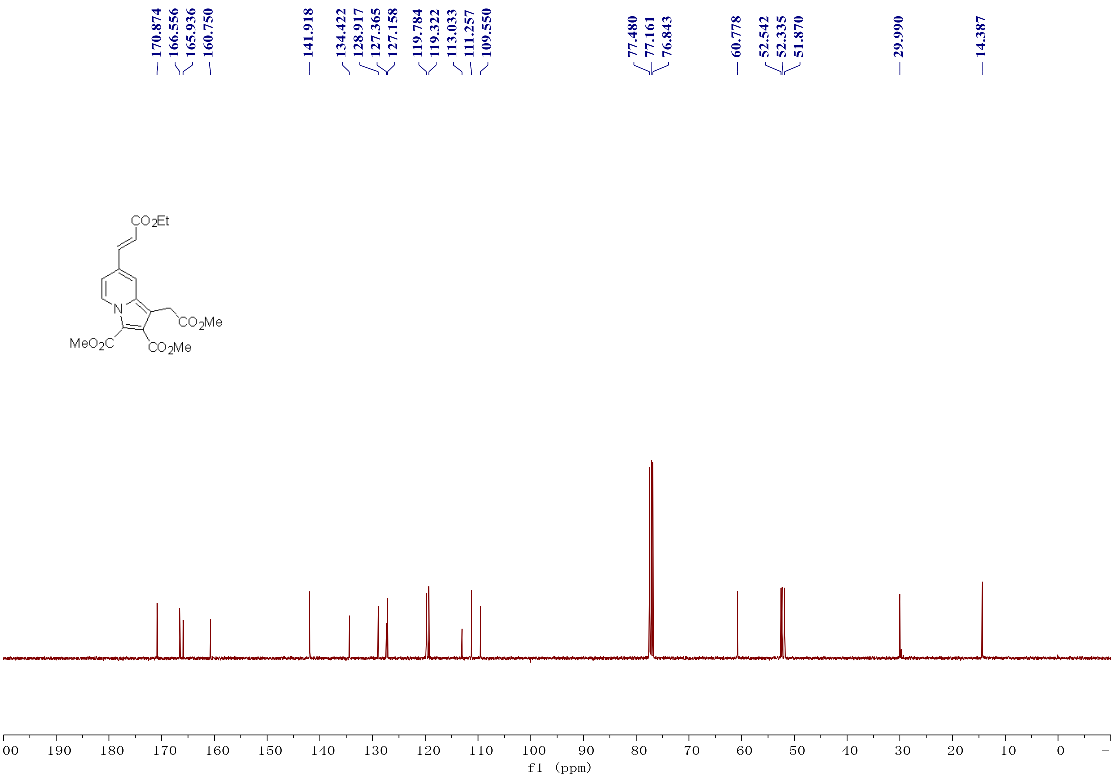


Fig. S40 ^{13}C NMR of compound **25e** (100 MHz, $CDCl_3$)

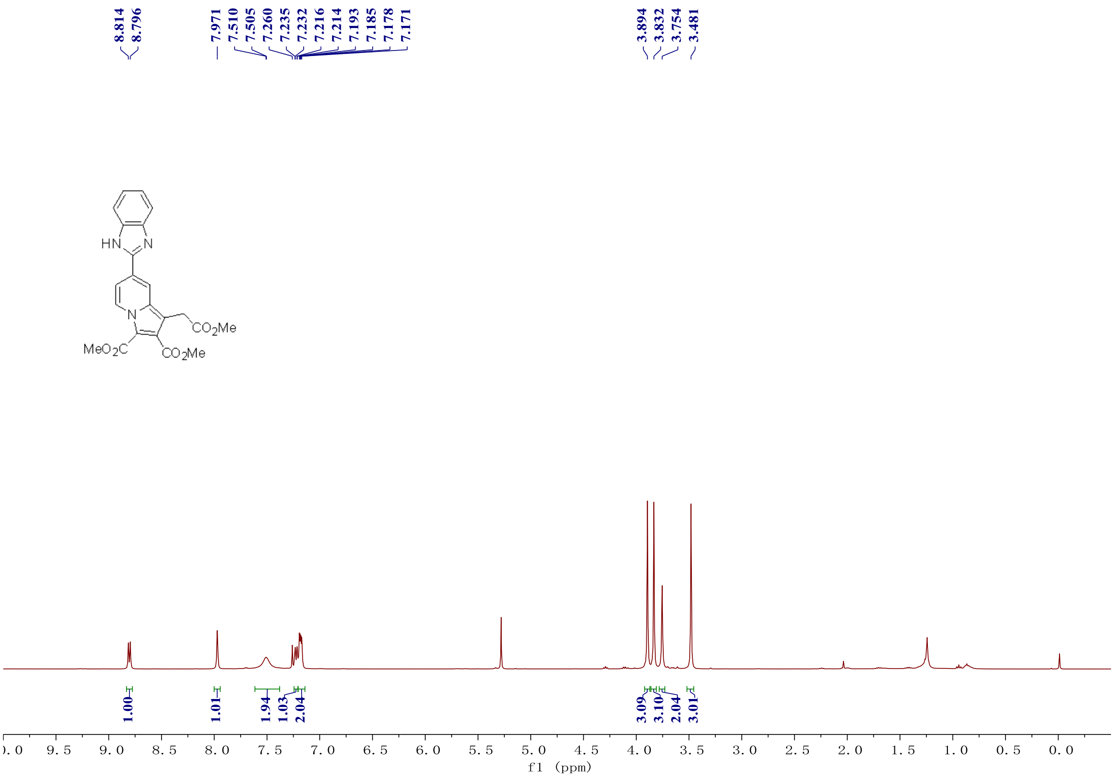


Fig. S41 ^{1}H NMR of compound **26** (400 MHz, $CDCl_3$)

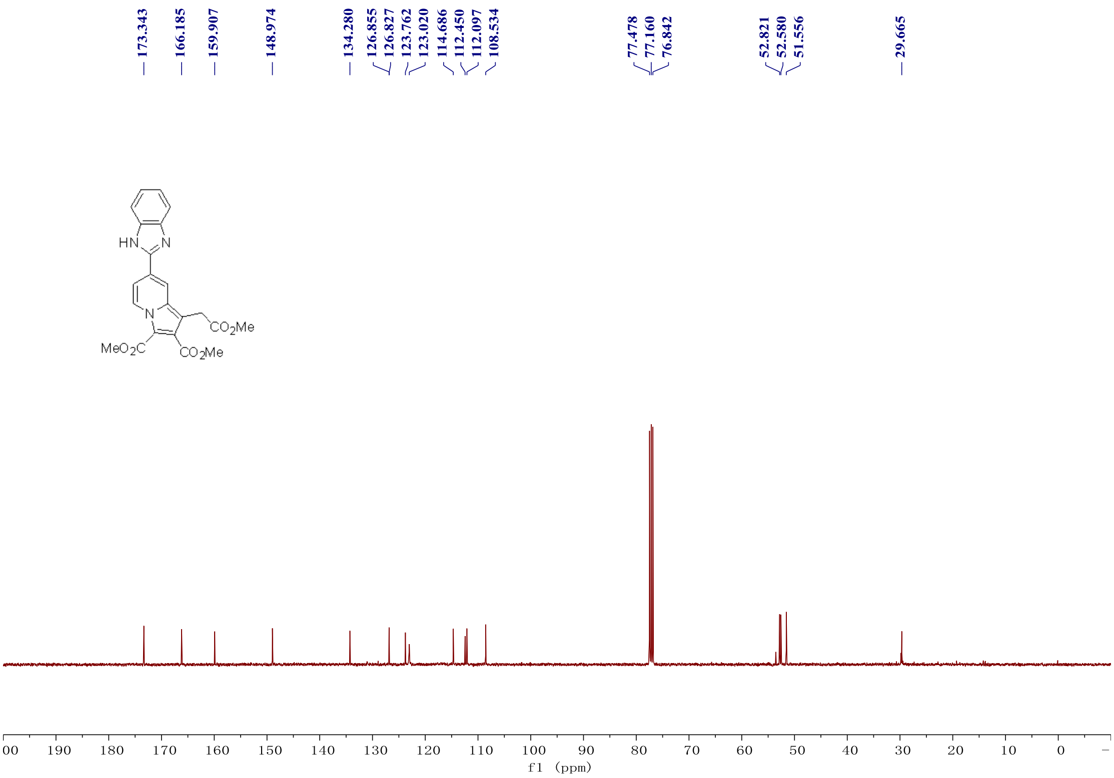


Fig. S42 ^{13}C NMR of compound **26** (100 MHz, $CDCl_3$)

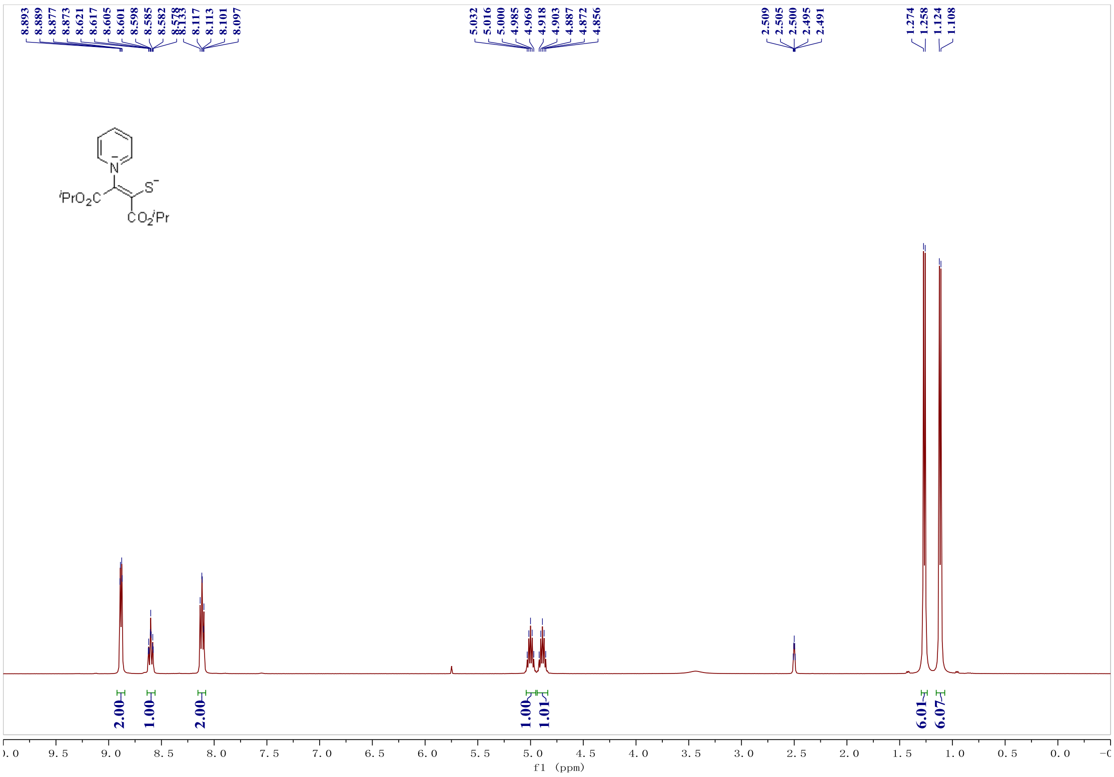


Fig. S43 ^{1}H NMR of compound **12s** (400 MHz, $(CD_3)_2SO$)

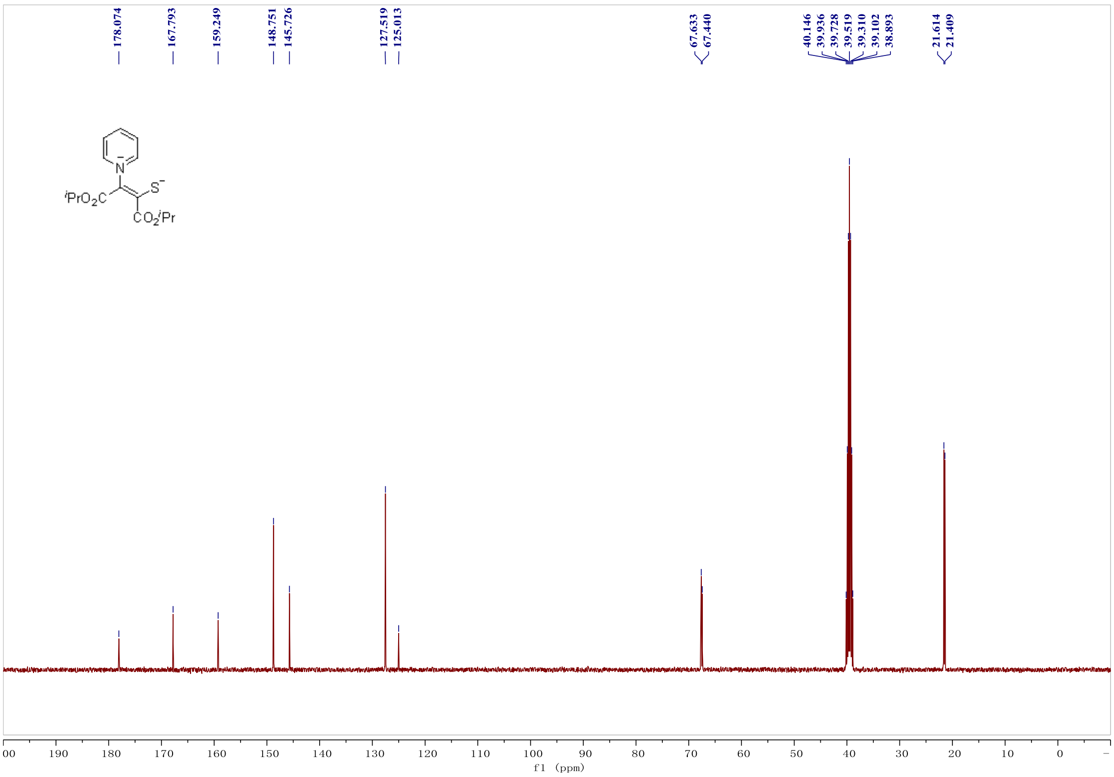


Fig. S44 ^{13}C NMR of compound **12s** (100 MHz, $(CD_3)_2SO$)

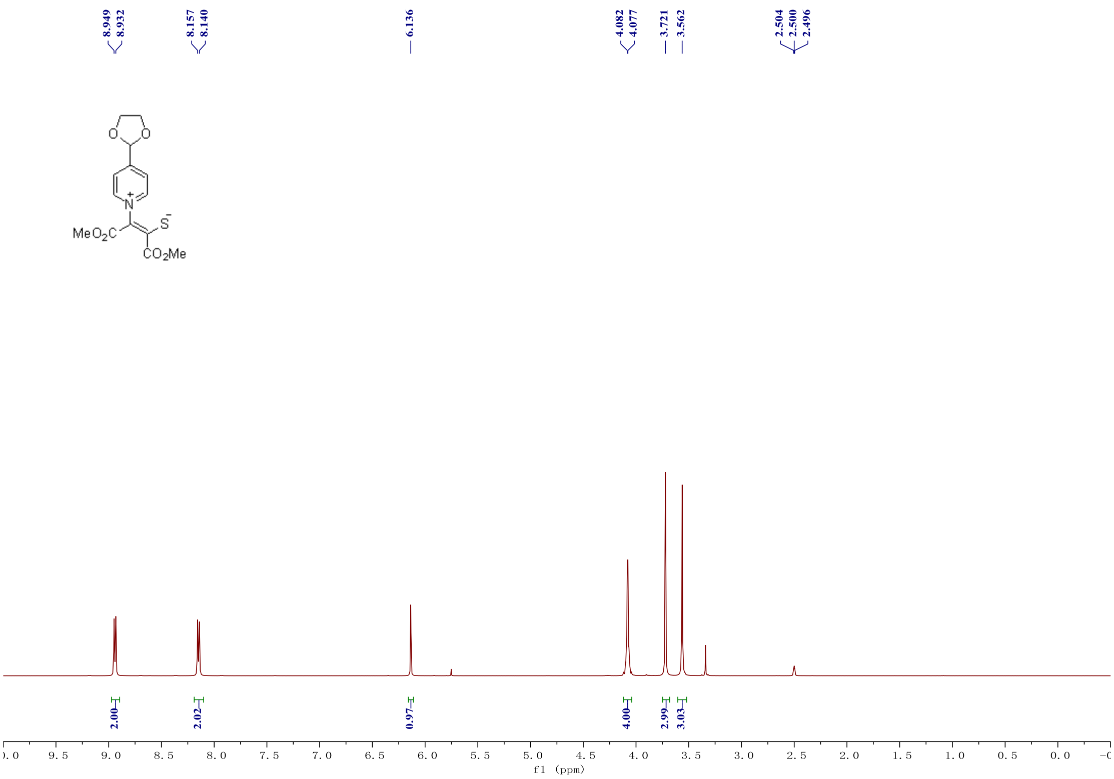


Fig. S45 ^{1}H NMR of compound **13s** (400 MHz, $(CD_3)_2SO$)

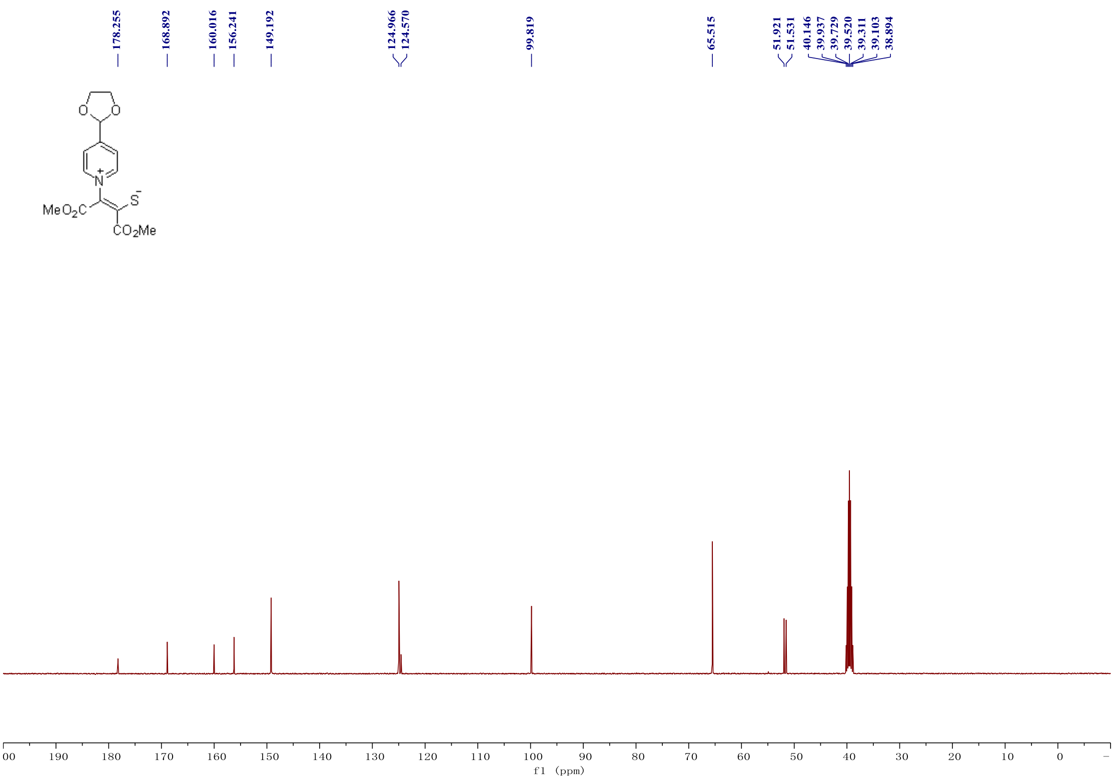


Fig. S46 ^{13}C NMR of compound **13s** (100 MHz, $(CD_3)_2SO$)

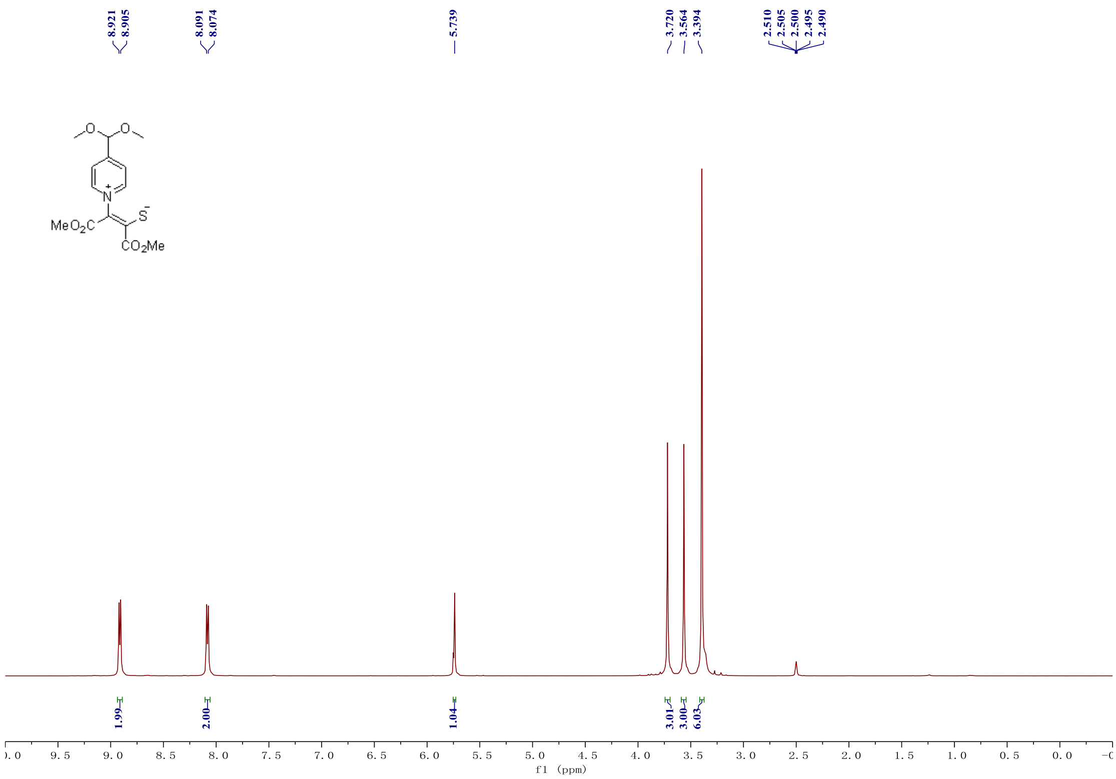


Fig. S47 ^{1}H NMR of compound **14s** (400 MHz, $(CD_3)_2SO$)

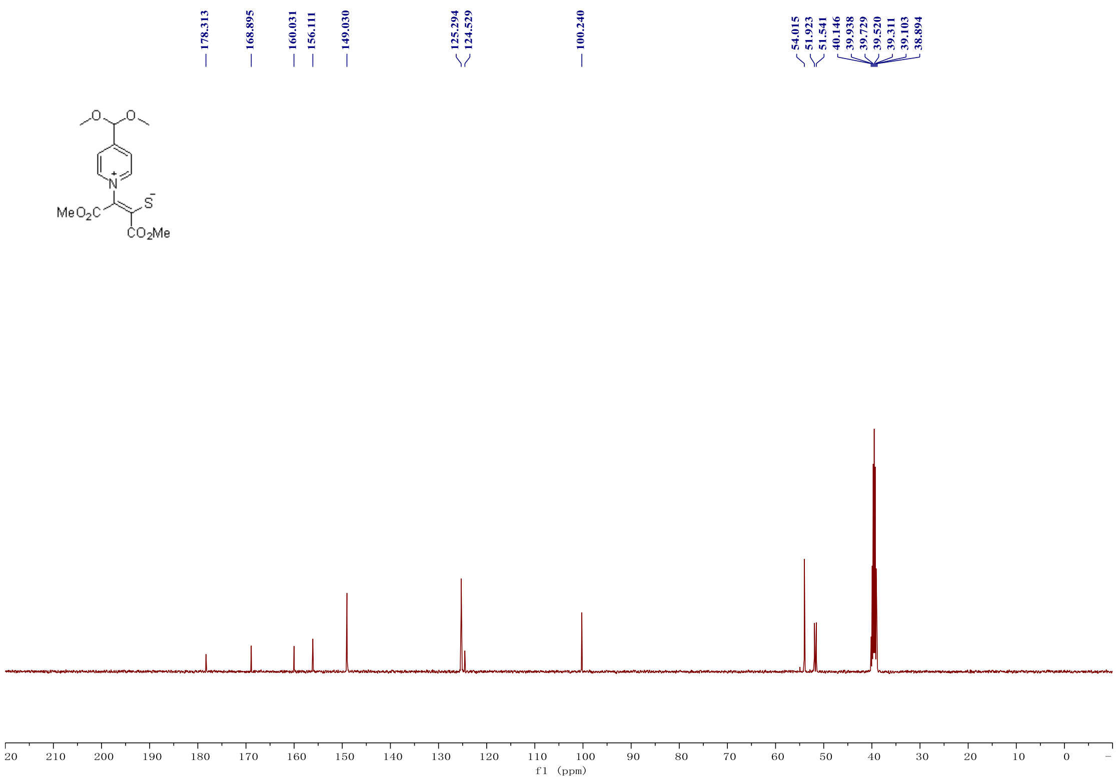


Fig. S48 ^{13}C NMR of compound **14s** (100 MHz, $(CD_3)_2SO$)

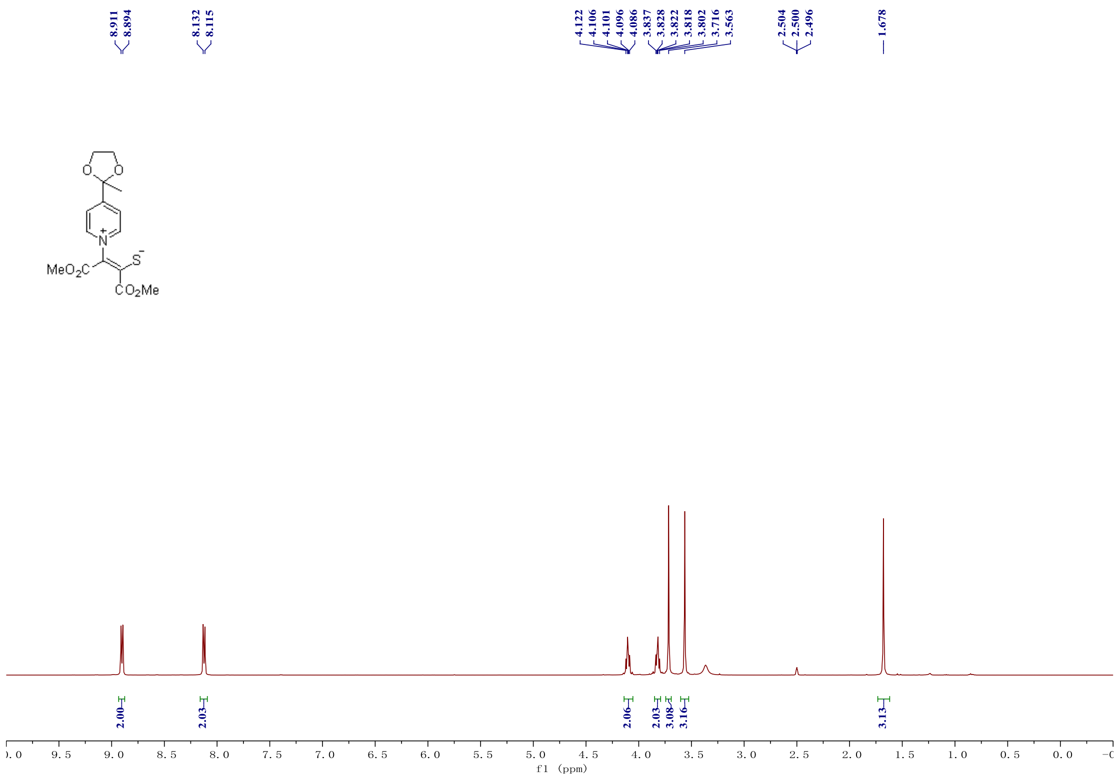


Fig. S49 ^{1}H NMR of compound **15s** (400 MHz, $(CD_3)_2SO$)

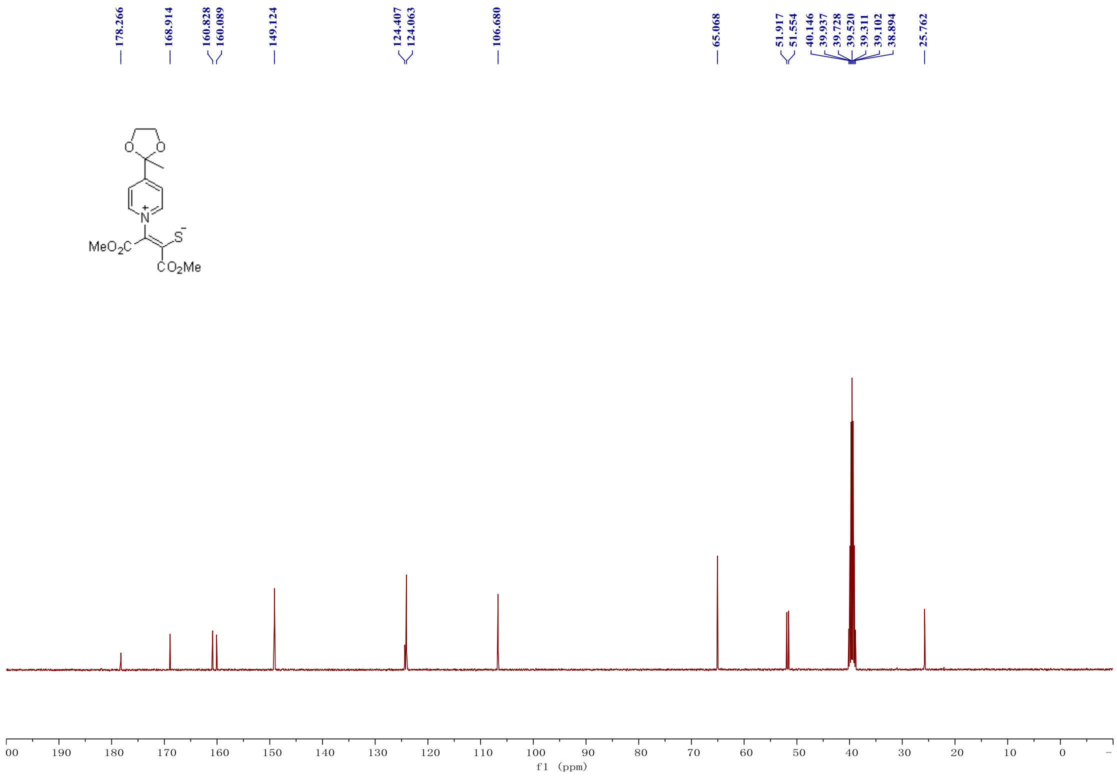


Fig. S50 ^{13}C NMR of compound **15s** (100 MHz, $(CD_3)_2SO$)

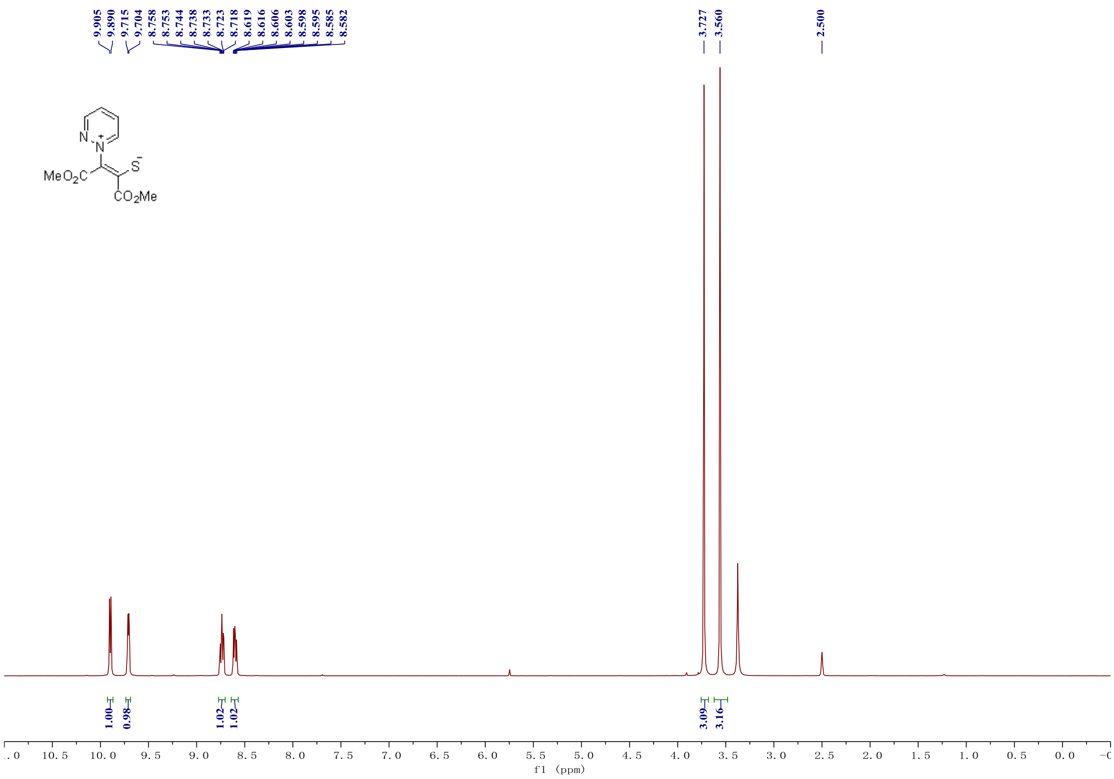


Fig. S51 [1]H NMR of compound **1'** (400 MHz, $(CD_3)_2SO$)

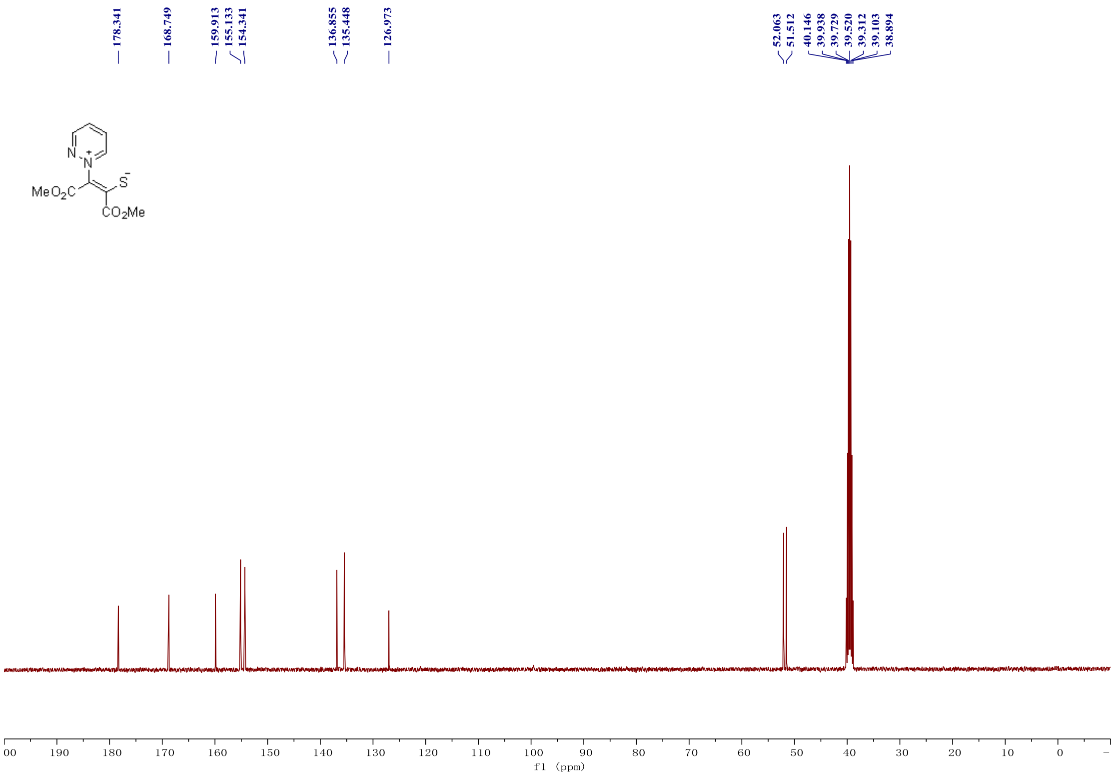


Fig. S52 [13]C NMR of compound **1'** (100 MHz, $(CD_3)_2SO$).