Supporting Information

Palladium Catalyzed Divergent Cycloadditions of Vinylidenecyclopropane-diesters with Methyleneindolinones Enabled by Zwitterionic π-Propargyl Palladium Species

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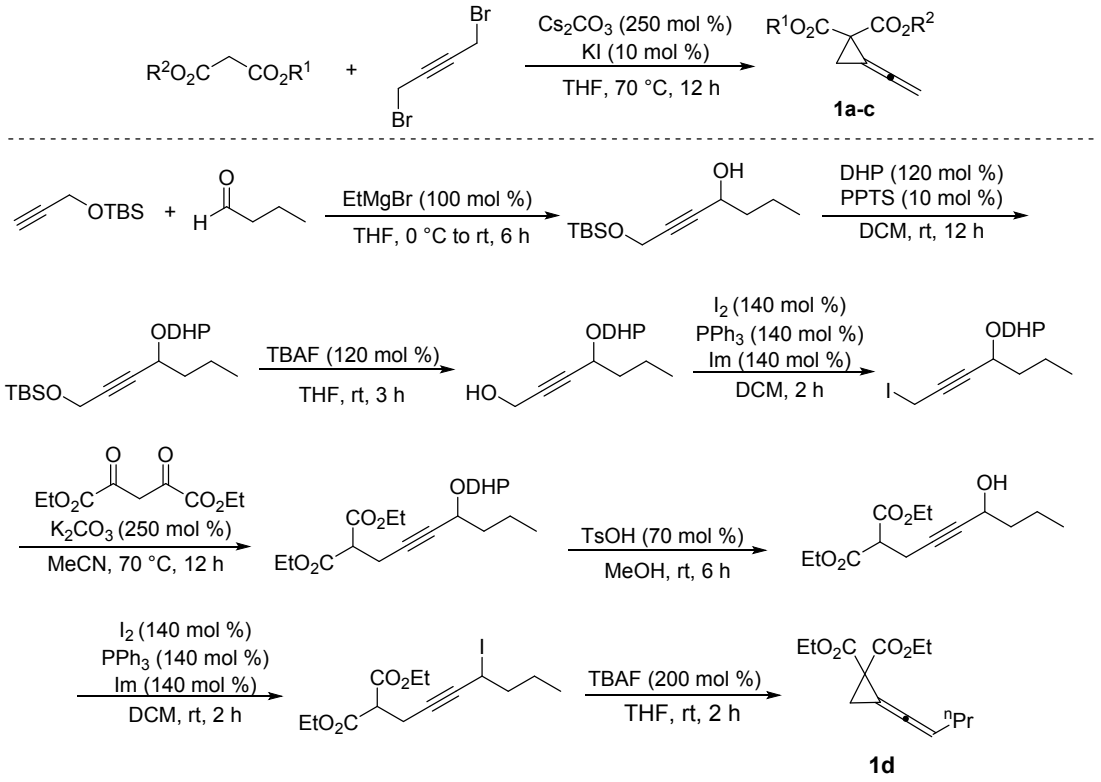
Content

1. General remarks

Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. ^{1}H NMR spectra were measured on a Brucker AC 400 or Agilent (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm referenced to the internal solvent signal (peak at 0.00 ppm in the case of $CDCl_3$ with tetramethylsilane as an internal standard), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet,), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a Brucker AC 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the internal solvent signal (peak at 77.000 ppm in the case of $CDCl_3$). Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Flash column chromatography was performed using 300-400 mesh silica gel. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. Chiral HPLC was performed on a SHIMADZU SPD-10A *vp* series with chiral columns (Chiralpak OD-H, column 4.6 × 250 mm, (Daicel Chemical Ind., Ltd.)). Mass spectra were recorded by ESI, and HRMS was measured on a HP-5989 instrument. The employed solvents were dry up by standard methods when necessary. Commercially obtained reagents were used without further purification.

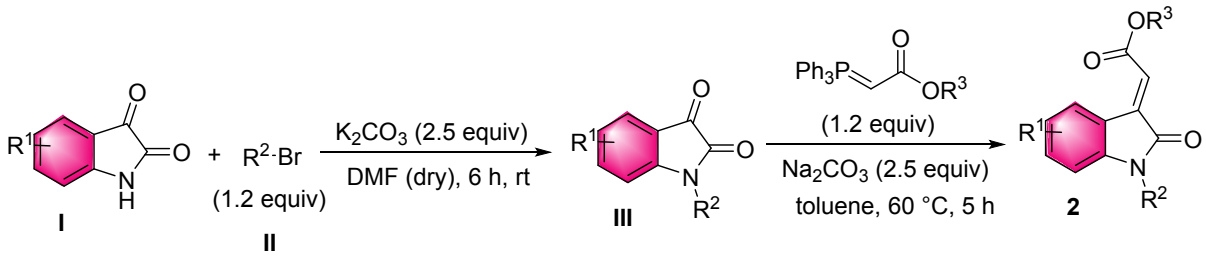
2. Preparation of the starting materials 1 and 2

2.1 Preparation of substrates 1a-d



Vinylidenecyclopropanes **1a-d** were prepared according to previously reported literature.[1]

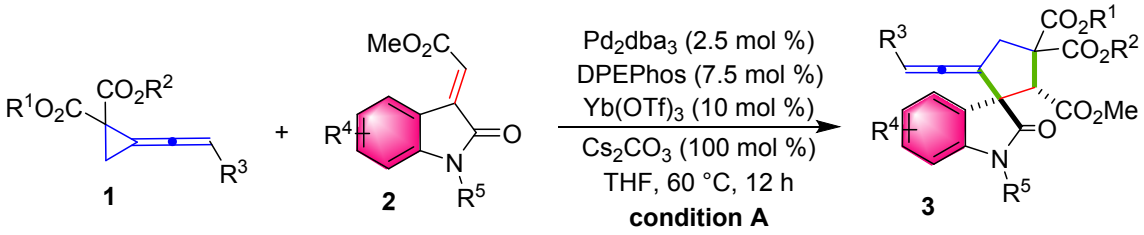
2.1 Preparation of substrates 2



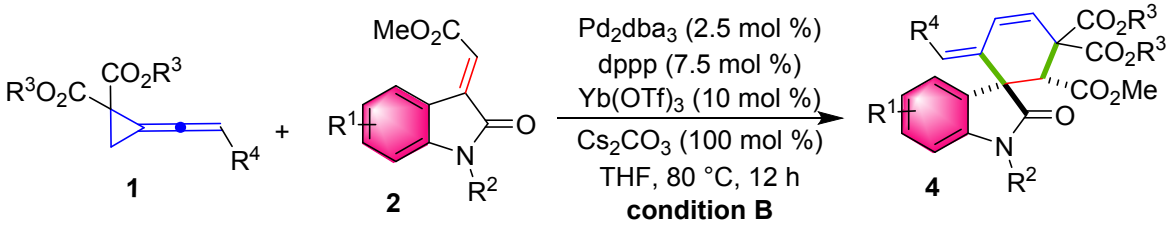
N-alkylated isatin derivatives **III** were prepared from commercially available isatins **I** with different alkyl halides **II** (1.2 equiv) in the presence of K_2CO_3 (2.5 equiv) in DMF at room temperature for 6 h. The reaction was quenched with water and the reaction mixture was extracted with dichloromethane (3 x 20 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude residue was then purified by a column chromatography on silica gel with petroleum ether-ethyl acetate (10/1 to 4/1) to provide compounds **III**.

A solution of *N*-alkylated isatin derivative **III**, ylide (1.2 equiv) and sodium carbonate (2.5 equiv) in toluene was allowed under reflux for 3 hours. Ethyl acetate and water were added to the reaction mixture. After work up, the organic layer was dried over Na_2SO_4, concentrated under reduced pressure and purified using a column chromatography (silica gel, petroleum ether-ethyl acetate 10/1 to 20:1) to obtain **2** as an orange solid in good yield.[2]

3. General procedure for the synthesis of compounds 3 and 4

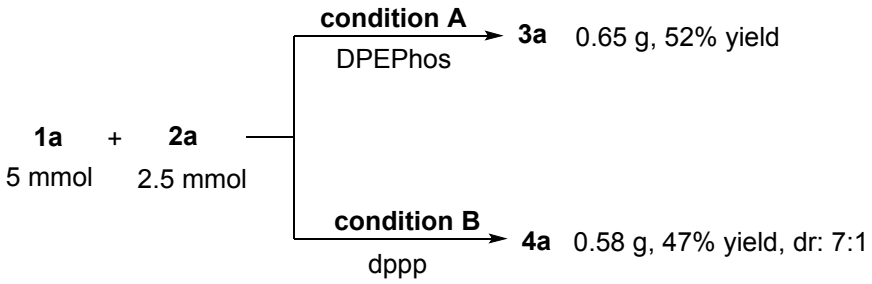


In an oven dried 10 mL Schlenk tube equipped with a magnetic stirring bar, Pd-catalyst (0.005 mmol, 2.5 mol %) and DPEPhos (0.015 mmol, 7.5 mol %) was stirred in THF (degassed) (1.0 mL) for 30 min. After that, vinylidenecyclopropane **1** (0.4 mmol), methyleneindolinone **2** (0.2 mmol), $Yb(OTf)_3$ (0.02 mmol, 10 mol %) and CS_2CO_3 (0.2 mmol, 100 mol %) were added under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 12 h. The reaction solution was diluted by dichloromethane, and then, the solvent was evaporated under vacuum and the residue was purified by a column chromatography (eluent: petroleum ether:ethyl acetate = 4:1 to 6:1) to afford the desired product **3**.



The general procedure for the synthesis of compounds **4** was similar as that of **3**.

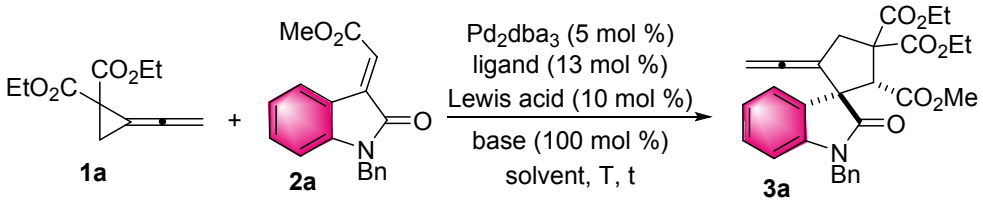
3.1 The general procedure for the scale-up synthesis of compounds 3a and 4a



In an oven dried 25 mL Schlenk tube equipped with a magnetic stirring bar, Pd-catalyst (0.125 mmol, 2.5 mol %) and DPEPhos (0.375 mmol, 7.5 mol %) was stirred in THF (degassed) (10 mL) for 60 min. After that, vinylidenecyclopropane **1a** (5 mmol), methyleneindolinone **2a** (5 mmol), $Yb(OTf)_3$ (0.5 mmol, 10 mol %) and CS_2CO_3 (5 mmol, 100 mol %) were added under nitrogen atmosphere. The reaction mixture was stirred at 60 °C for 15 h. The reaction solution was diluted by dichloromethane, and then, the solvent was evaporated under vacuum and the residue was purified by a column chromatography (eluent: petroleum ether:ethyl acetate = 4:1) to afford the desired product **3a**.

The general procedure for the scale-up synthesis of compound **4a** was similar as that of **3a**.

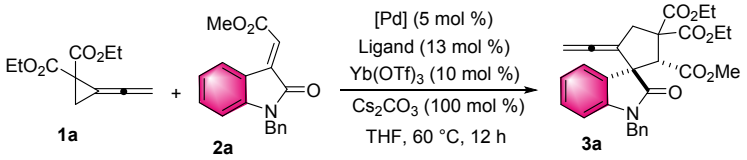
4. The detailed investigation for the synthesis of 3 and 4

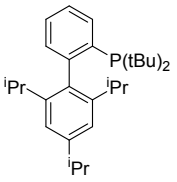


entry[a]	Ligand	Lewis acid	base	solvent	T °C	t/(h)	yield (%)[b]
1	XantPhos	$Yb(OTf)_3$	–	THF	80	12	11
2	XantPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	80	12	36
3	rac-BINAP	$Yb(OTf)_3$	Cs_2CO_3	THF	80	12	complex
4	XPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	80	12	NR
5	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	80	12	42
6	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	60	12	50
7	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	40	12	18
8[c]	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	40	6	20
9	DPEPhos	$Sc(OTf)_3$	Cs_2CO_3	THF	60	12	48
10	DPEPhos	$In(OTf)_3$	Cs_2CO_3	THF	60	12	47
11	DPEPhos	$Gd(OTf)_3$	Cs_2CO_3	THF	60	12	47
12	DPEPhos	$CeCl_3$	Cs_2CO_3	THF	60	12	complex
13	DPEPhos	$Yb(OTf)_3$	K_3PO_4	THF	60	12	47
14	DPEPhos	$Yb(OTf)_3$	K_2HPO_4	THF	60	12	NR
15	DPEPhos	$Yb(OTf)_3$	Li_2CO_3	THF	60	12	Trace
16	DPEPhos	$Yb(OTf)_3$	Na_2CO_3	THF	60	12	23
17	DPEPhos	$Yb(OTf)_3$	2,6-Lutidine	THF	60	12	NR
18	DPEPhos	$Yb(OTf)_3$	DIPEA	THF	60	12	NR
19	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	Dioxane	100	4	complex
20	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	CF_3CH_2OH	60	12	NR
21	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	MeCN	60	12	47
22	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	PhMe	60	12	31
23	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	t-BuOH	60	12	40
24[d]	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	60	12	32
25[e,f]	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	60	12	63
26[g]	DPEPhos	$Yb(OTf)_3$	Cs_2CO_3	THF	60	12	59

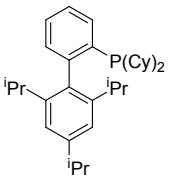
[a] Reaction was run under the following conditions: a solution of **1a** (0.4 mmol), **2a** (0.2 mmol), catalyst (5 mol %), ligand (13 mol %) in dry solvent (2 mL). [b] Isolated yield. [c] Lewis acid was added as 20 mol %. [d] Reaction was performed without $Yb(OTf)_3$. [e] Pd_2dba_3 (2.5 mol %), ligand (7.5 mol %). [f] Degassed THF. [g] DPEPhos (9 mol %).

Scheme S1 Optimization of the reaction conditions for the synthesis of 3





L1

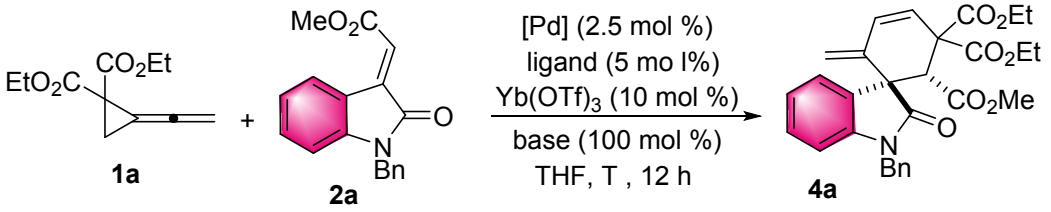


L2

entry	[Pd]	Ligand	yield (%)[a]
1	$Pd(PPh_3)_4$	–	34
2	$Pd(PPh_3)_4$	DPEPhos	46
3	$Pd(PPh_3)_2Cl_2$	DPEPhos	32
4	$Pd(OAc)_2$	DPEPhos	complex
5	Pd_2dba_3	**L1**	NR
6	Pd_2dba_3	**L2**	NR

[a]Isolated yields

Scheme S1 Optimization of the reaction conditions for the synthesis of 3

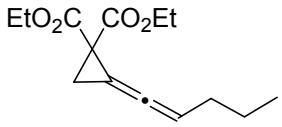


entry	[Pd]	Ligand	base	T(°C)	yield (%)[a]	dr
1	Pd_2dba_3	dppe	Cs_2CO_3	80	54	5:1
2	Pd_2dba_3	dppp	Cs_2CO_3	80	53	7:1
3	Pd_2dba_3	dppe	Cs_2CO_3	60	55	4:1
4	Pd_2dba_3	dppp	Cs_2CO_3	60	52	8:1
5	Pd_2dba_3	dppb	Cs_2CO_3	60	47	9:1
6	Pd_2dba_3	dppp	CsOAc	80	-	-
7	Pd_2dba_3	dppp	K_3PO_4	80	37	5:1
8	Pd_2dba_3	dppp	K_2CO_3	80	31	4:1
9	Pd_2dba_3	dppp	DIPEA	80	-	-
10[b]	Pd_2dba_3	dppp	Cs_2CO_3	80	24	7:1
11[c]	Pd_2dba_3	dppp	Cs_2CO_3	80	54	11:1
12	$[Pd(\eta^3\text{-}C_3H_5)PdCl]_2$	dppp	Cs_2CO_3	80	-	-
13	$Pd(PPh_3)_4$	dppp	Cs_2CO_3	80	45	6:1
14[d]	Pd_2dba_3	dppp	Cs_2CO_3	80	45	5:1
15[e]	Pd_2dba_3	dppp	Cs_2CO_3	80	complex	
16[f]	Pd_2dba_3	dppp	Cs_2CO_3	80	24	4:1
17[g]	Pd_2dba_3	dppp	Cs_2CO_3	80	56	11:1
18[h]	Pd_2dba_3	dppp	Cs_2CO_3	80	55	11:1

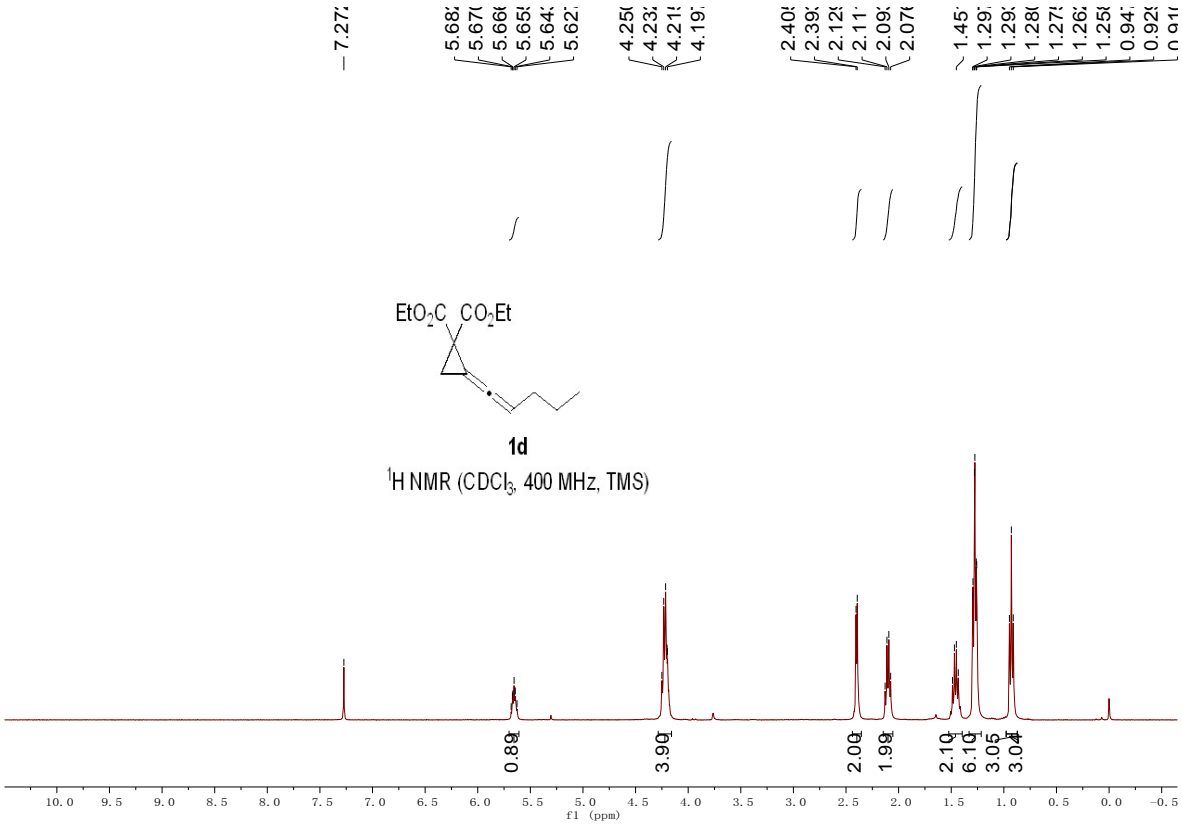
[a] Isolated yields. [b] Cs_2CO_3 (50 mol %). [c] THF (4 mL). [d] The reaction was performed in PhMe. [e] The reaction was performed in MeCN. [f] The reaction was performed in DCE. [g] liagnd (7.5 mol %). [h] dppp (9.0 mol %).

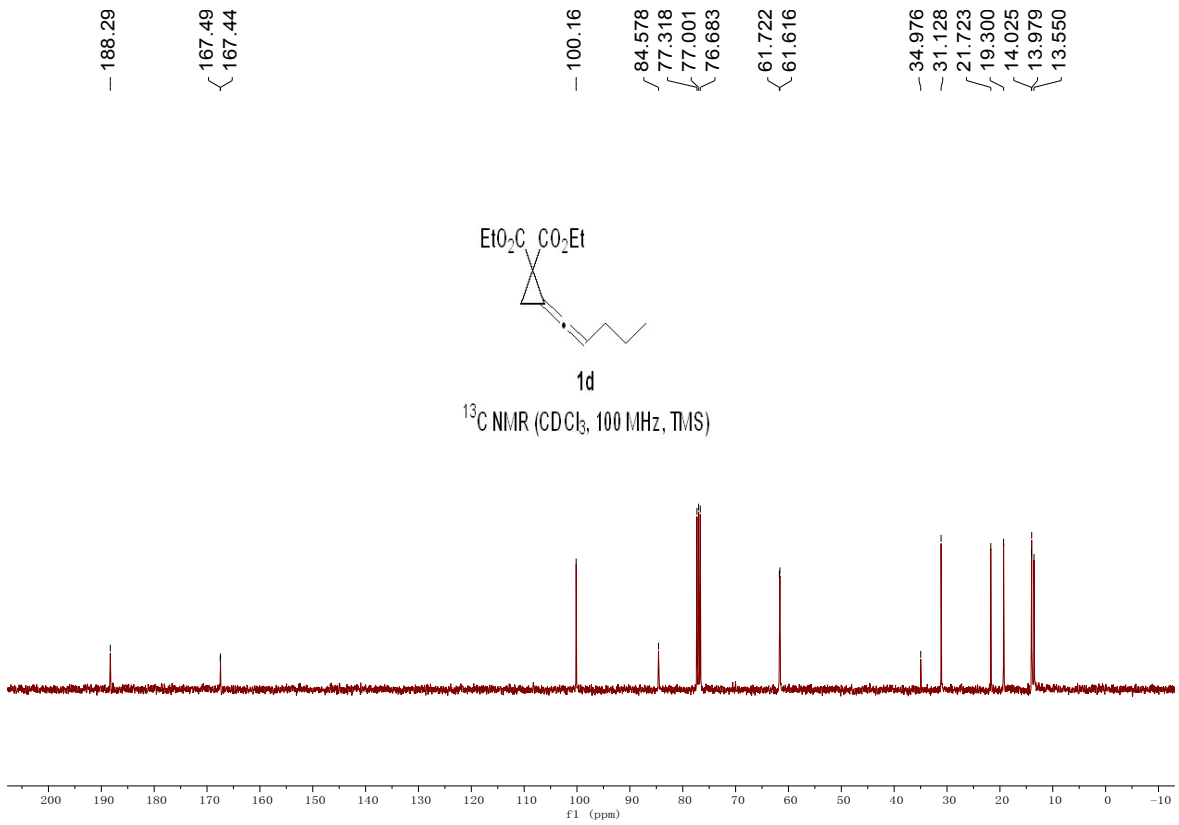
Scheme S2 Optimization of the reaction conditions for the synthesis of 4

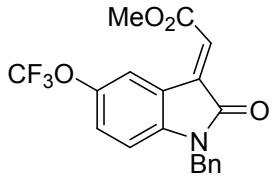
5. Spectroscopic data of the products



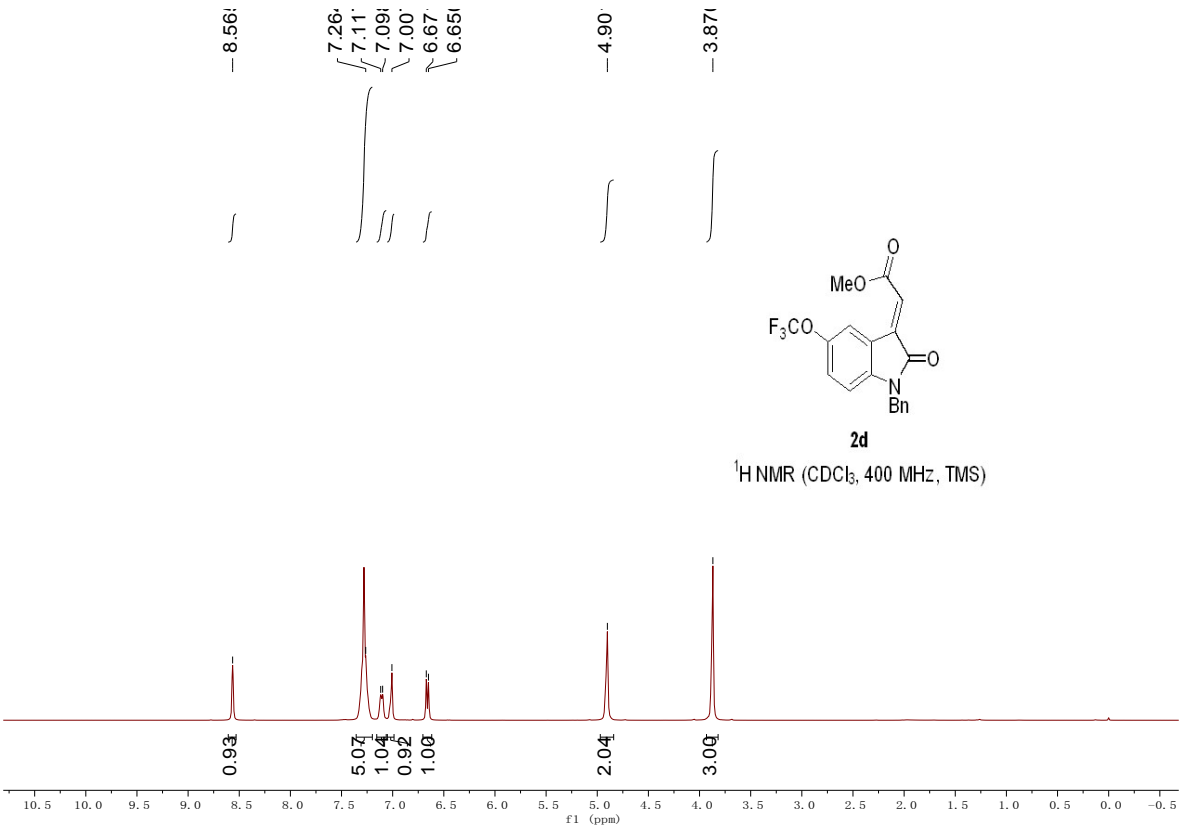
Compound 1d: Yield: 0.8 g, 54%; A colorless liquid; Eluent: petroleum ether:ethyl acetate = 40:1; R_f = 0.4; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.70–5.61 (m, 1H), 4.28–4.16 (m, 4H), 2.40 (d, *J* = 4.4 Hz, 2H), 2.10 (q, *J* = 7.2 Hz, 2H), 1.46 (q, *J* = 7.2 Hz, 2H), 1.33–1.22 (m, 6H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 167.5, 167.4, 100.2, 84.6, 61.7, 61.6, 35.0, 31.1, 21.7, 19.3, 14.0, 13.5; IR (neat): ν 2968, 2929, 2016, 1727, 1299, 1231, 1098 cm^{-1}; HRMS (EI) Calcd. for $C_{14}H_{20}O_4$ $[M]^+$: 252.1361, found: 252.1358.





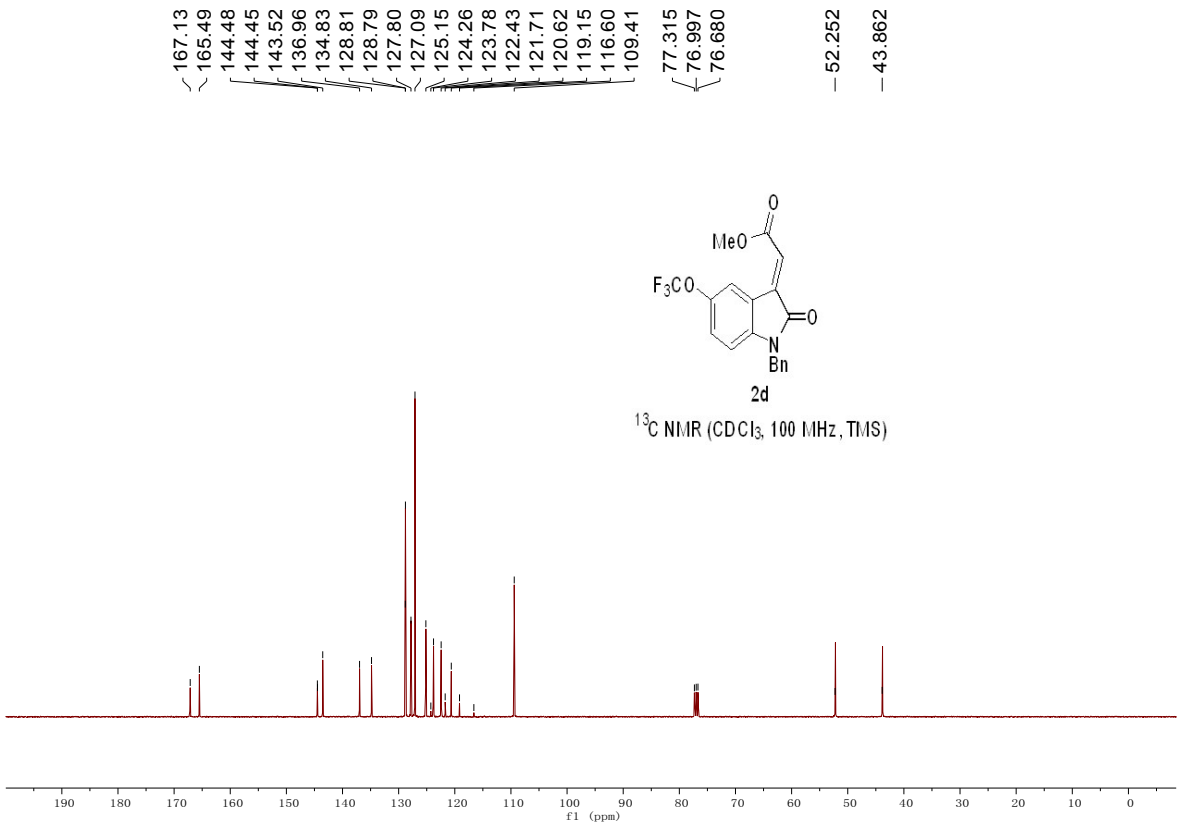


Compound 2d: Yield: 1.4 g, 73%; A yellow solid; Mp: 145-147 °C; Eluent: petroleum ether:ethyl acetate = 10:1; R_f = 0.4; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 7.36–7.20 (m, 5H), 7.16–7.06 (m, 1H), 7.01 (s, 1H), 6.66 (d, *J* = 8.6 Hz, 1H), 4.90 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 165.5, 144.48, 144.45, 143.5, 137.0, 134.8, 128.81, 128.79, 127.8, 127.1, 124.3, 123.8, 122.4, 120.6, 120.4 (q, *J* = 255 Hz), 109.4, 52.3, 43.9; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.3; IR (neat): ν 3118, 1728, 1709, 1476, 1347, 1253, 1206, 722 cm^{-1}; HRMS (ESI) Calcd. for $C_{19}H_{14}NO_4F_3Na$ $[M+H]^+$: 400.0767, found: 400.0765.



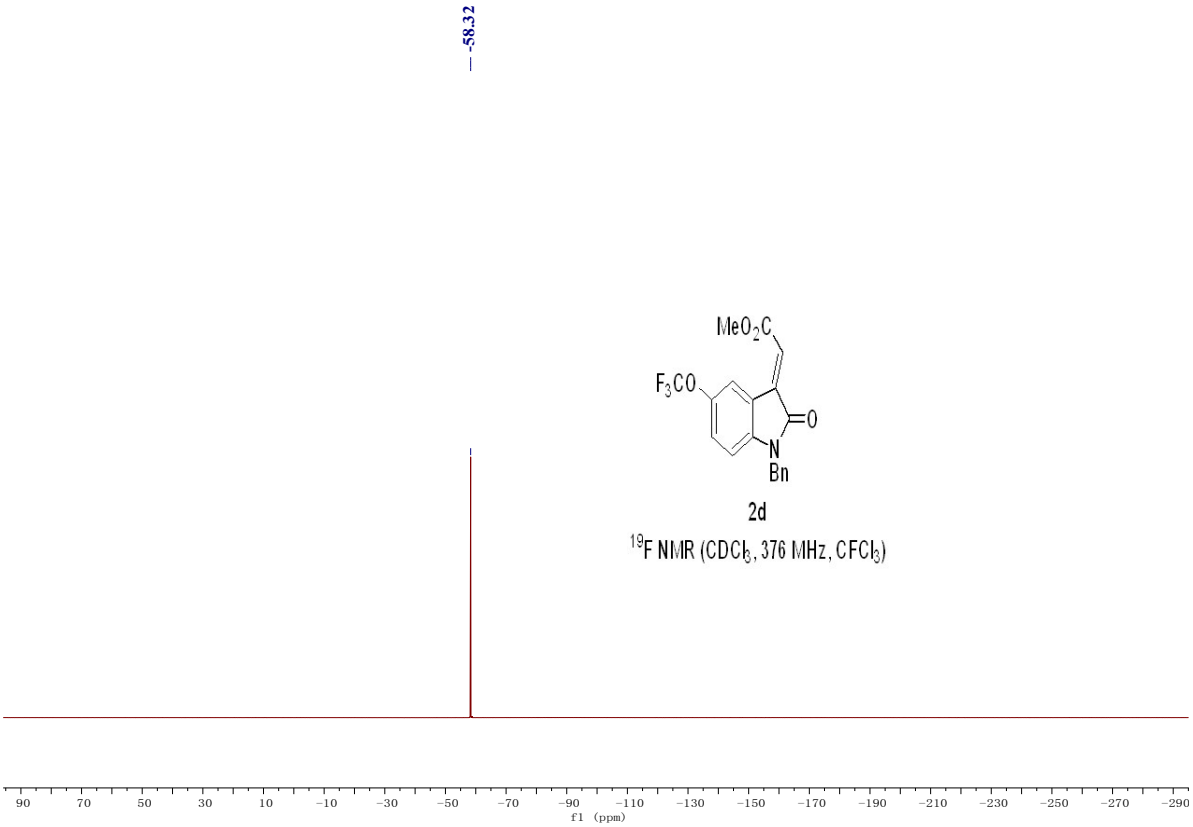
2d

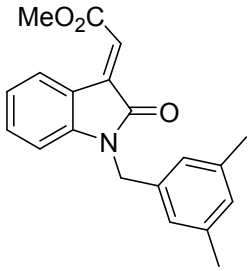
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)



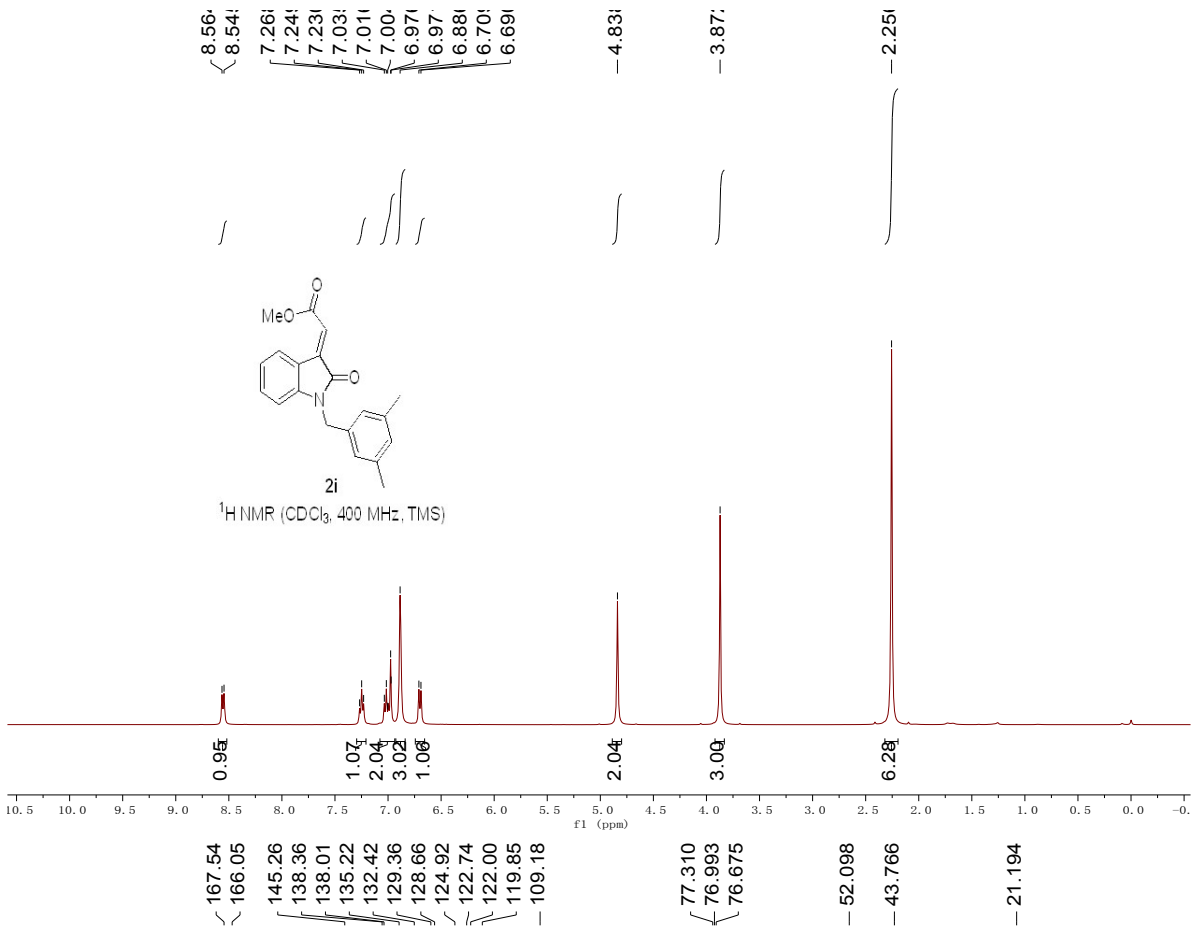
2d

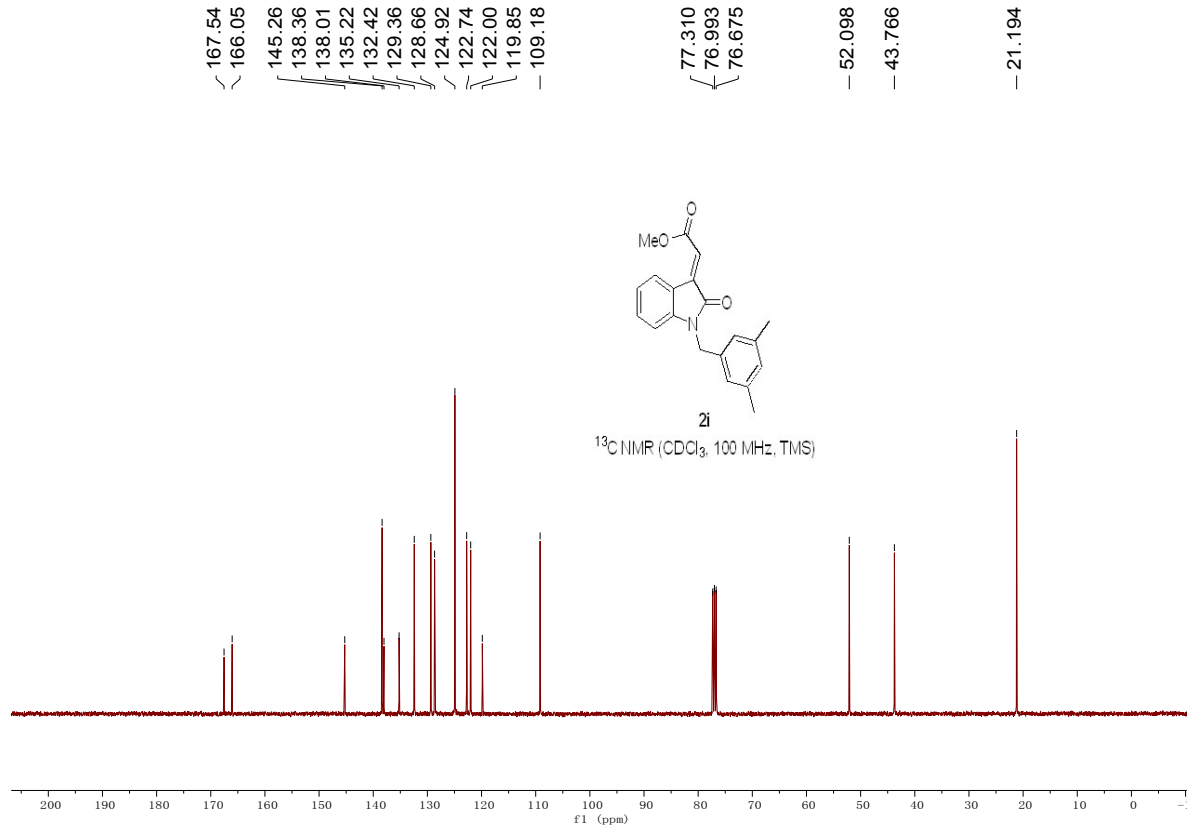
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)

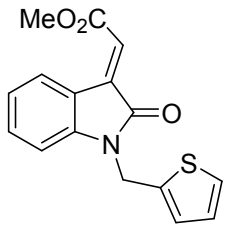




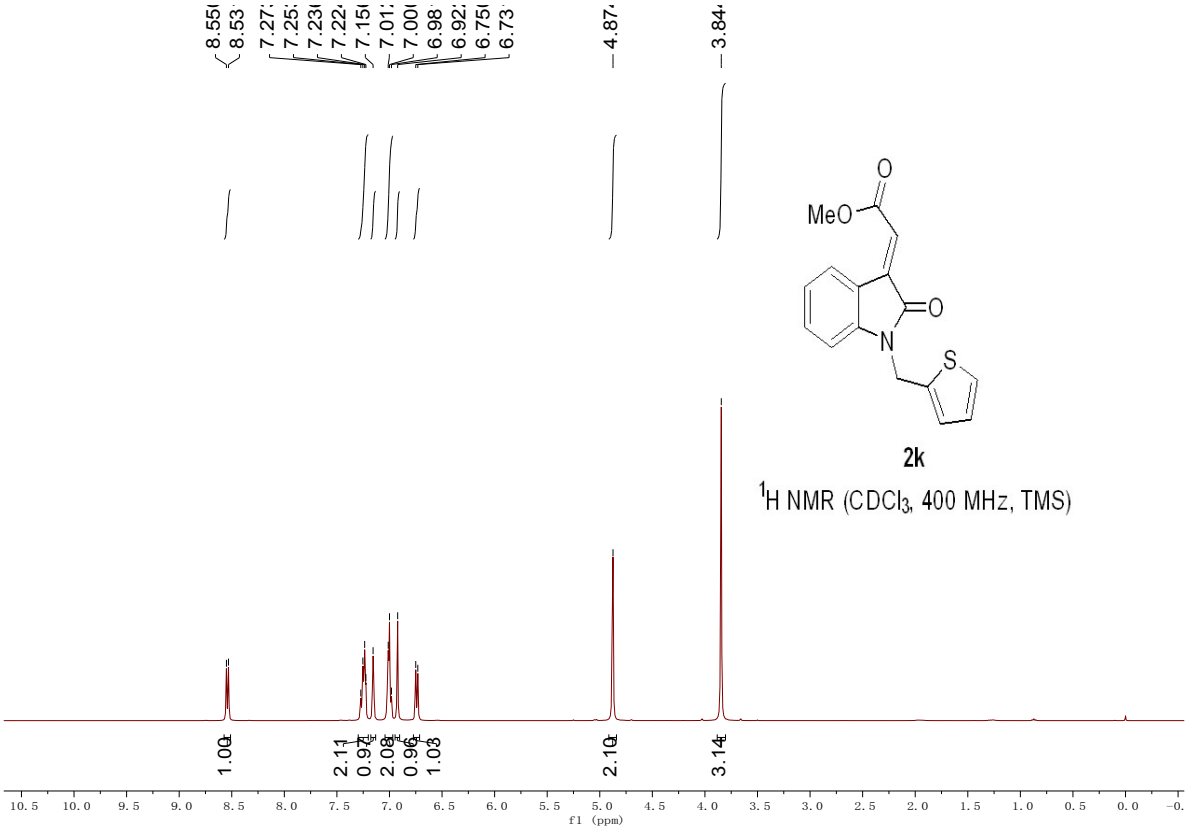
Compound 2i: Yield: 0.98 g, 53%; A yellow solid; Mp: 134-136 ^{o}C; Eluent: petroleum ether:ethyl acetate = 10:1; R_f = 0.5; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 7.6 Hz, 1H), 7.30–7.21 (m, 1H), 7.08–6.94 (m, 2H), 6.89 (s, 3H), 6.70 (d, *J* = 7.6 Hz, 1H), 4.84 (s, 2H), 3.87 (s, 3H), 2.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 166.1, 145.3, 138.4, 138.0, 135.2, 132.4, 129.4, 128.7, 124.9, 122.7, 122.0, 119.9, 109.2, 52.1, 43.8, 21.2; IR (neat): ν 2921, 2848, 1703, 1602, 1359, 1177, 784, 748 cm^{-1}; HRMS (ESI) Calcd. for $C_{20}H_{19}NO_3Na$ $[M+H]^+$: 344.1257, found: 344.1254.

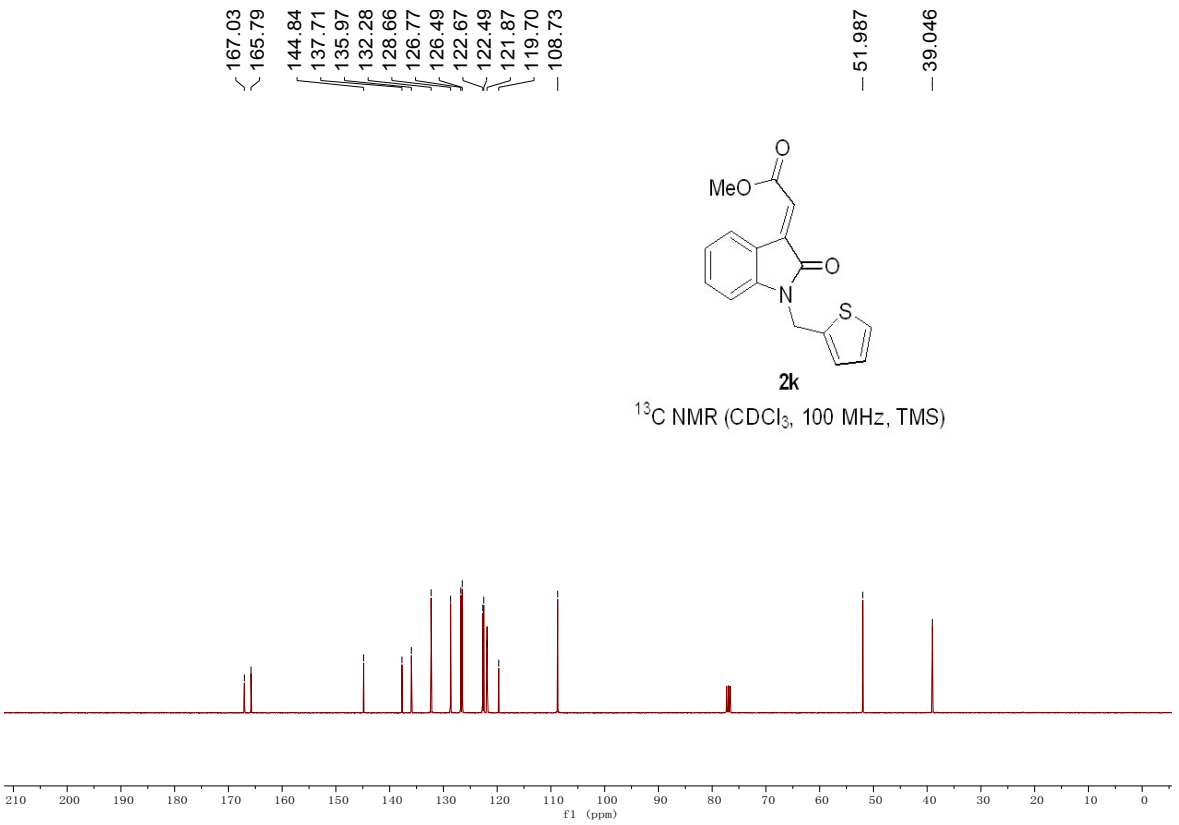

8.56
8.54
7.26
7.24
7.23
7.03
7.01
7.00
6.97
6.97
6.88
6.70
6.69
4.83
3.87
2.25
MeO
O
O
N
2i
^{1}H NMR (CDCl$_3$, 400 MHz, TMS)
0.95
1.07
2.04
3.02
1.06
2.04
3.00
6.28
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

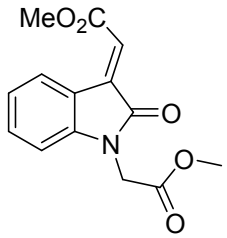

167.54
166.05
145.26
138.36
138.01
135.22
132.42
129.36
128.66
124.92
122.74
122.00
119.85
109.18
77.310
76.993
76.675
52.098
43.766
21.194
MeO
O
O
N
2i
^{13}C NMR (CDCl$_3$, 100 MHz, TMS)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



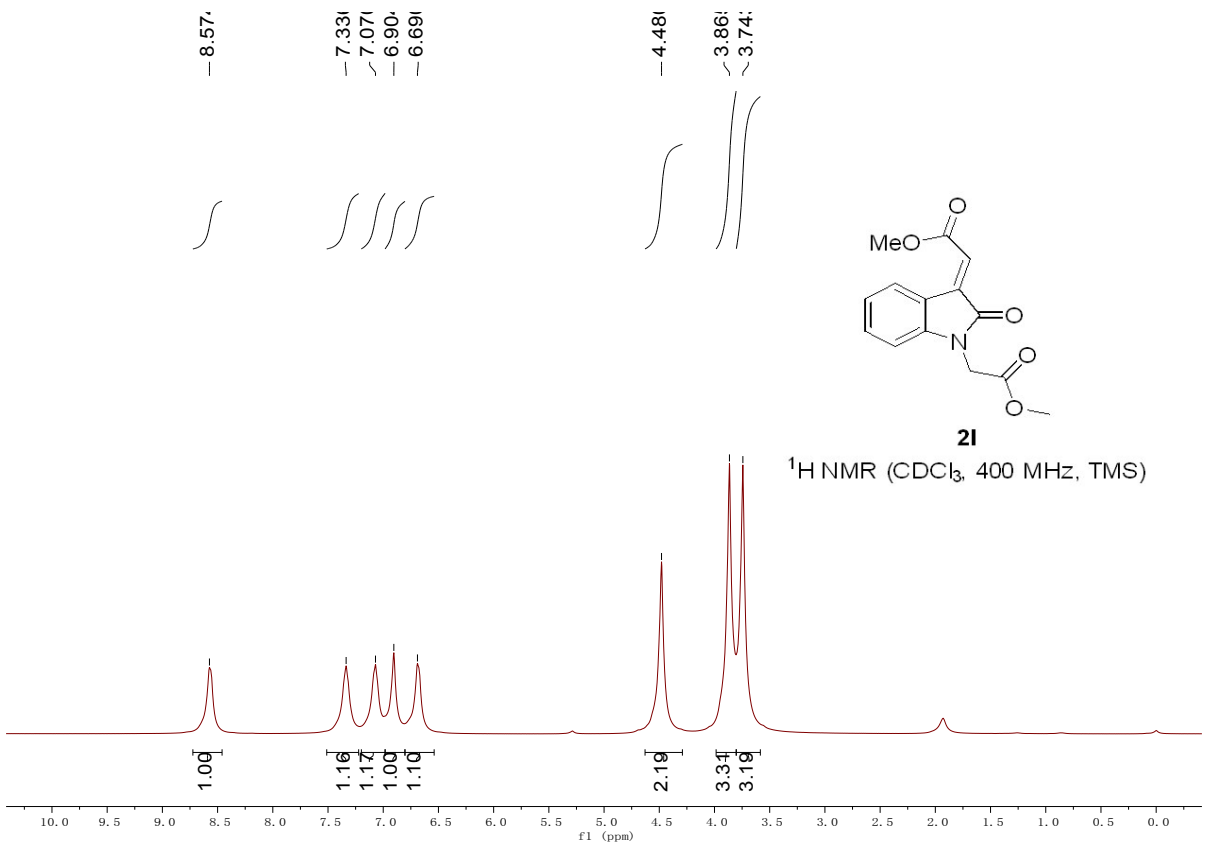
Compound 2k: Yield: 2.1 g, 83%; A yellow solid; Mp: 121-123 °C; Eluent: petroleum ether:ethyl acetate = 15:1; R_f = 0.4; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 (d, *J* = 7.6 Hz, 1H), 7.30–7.20 (m, 2H), 7.16 (s, 1H), 7.04–6.97 (m, 2H), 6.92 (s, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 4.87 (s, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 165.8, 144.8, 137.7, 136.0, 132.3, 128.7, 126.8, 126.5, 122.7, 122.5, 121.9, 119.7, 108.7, 52.0, 39.0; IR (neat): ν 2958, 2924, 1704, 1440, 1210, 1160, 750, 683 cm^{-1}; HRMS (ESI) Calcd. for $C_{16}H_{13}NO_3NaS$ $[M+H]^+$: 322.0508, found: 322.0502.





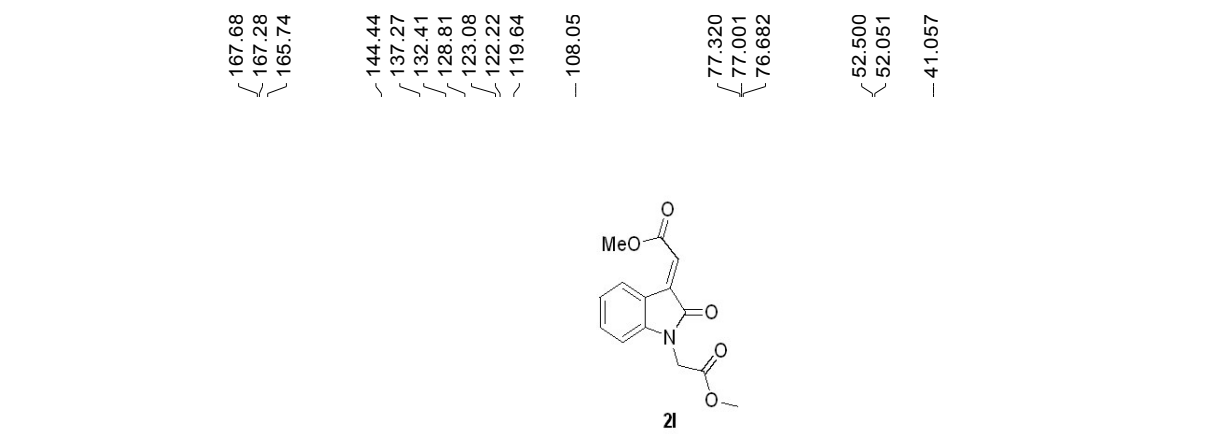


Compound 2l: Yield: 1.2 g, 57%; A yellow solid; Mp: 143-144 °C; Eluent: petroleum ether:ethyl acetate = 10:1; R_f = 0.6; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.57 (s, 1H), 7.34 (s, 1H), 7.07 (s, 1H), 6.90 (s, 1H), 6.69 (s, 1H), 4.48 (s, 2H), 3.86 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 167.3, 165.7, 144.4, 137.3, 132.4, 128.8, 123.1, 122.2, 119.6, 108.1, 52.5, 52.1, 41.1; IR (neat): ν 3078, 2958, 1630, 1602, 1348, 1206, 907, 749 cm^{-1}; HRMS (ESI) Calcd. for $C_{14}H_{13}NO_5Na$ $[M+H]^+$: 298.0685, found: 298.0678.



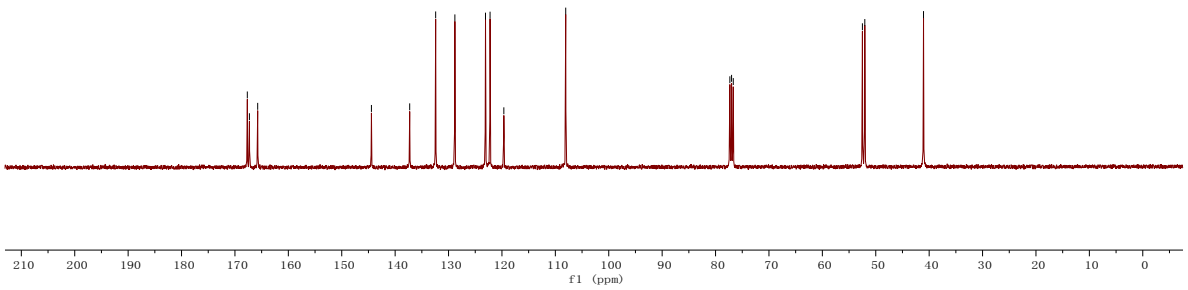
2l

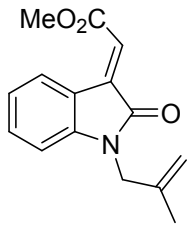
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)



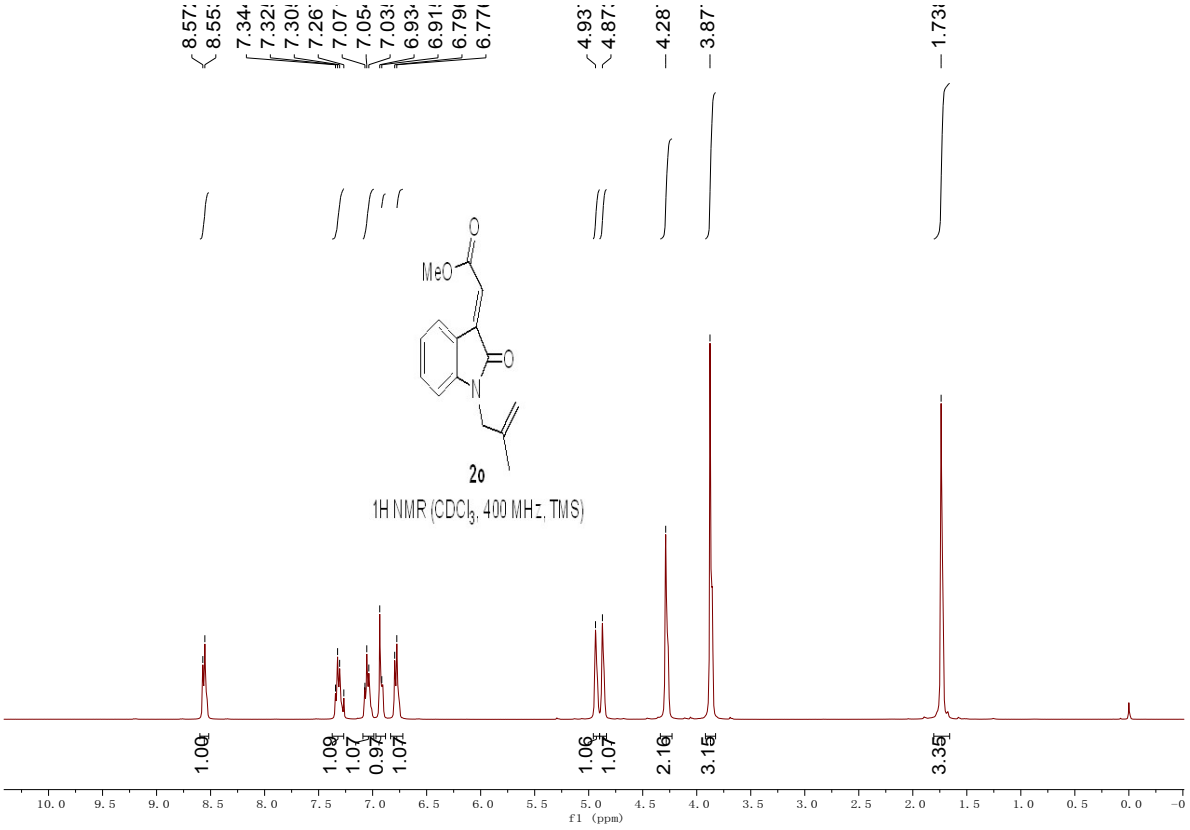
2l

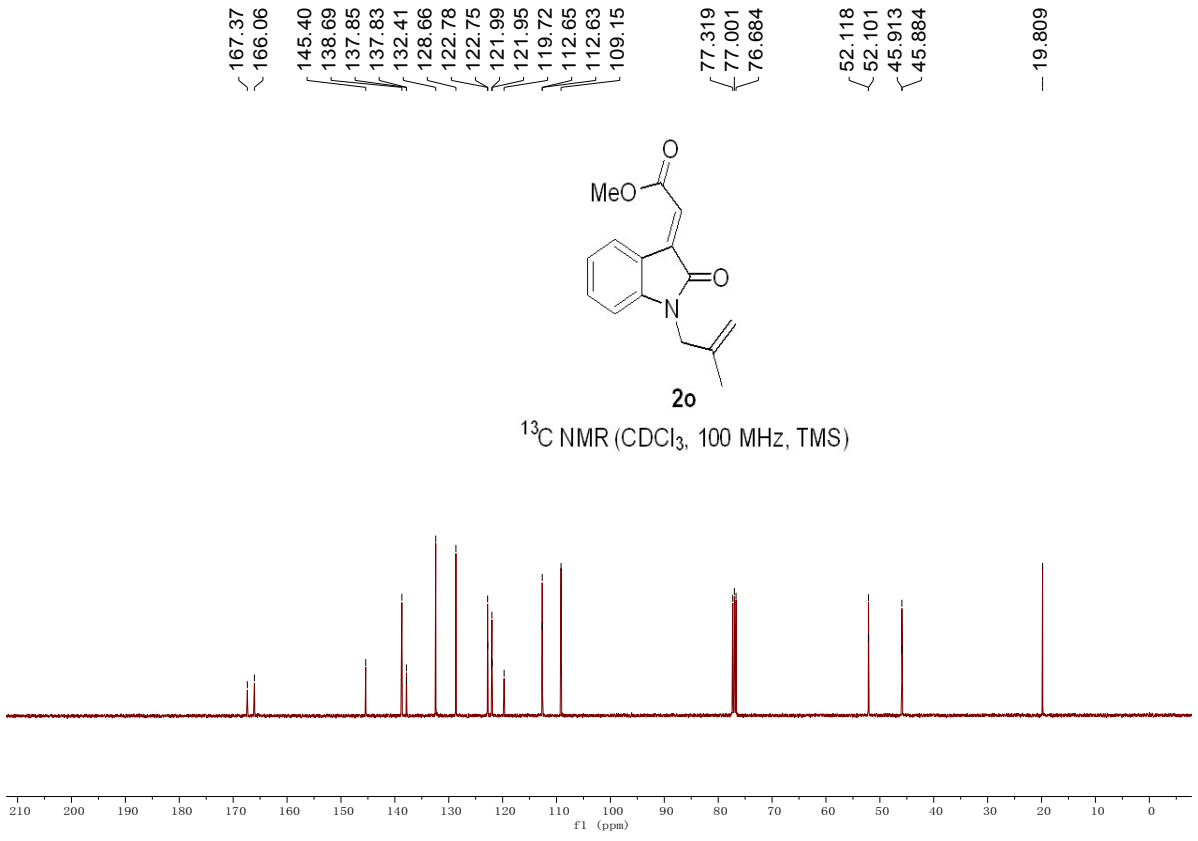
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)

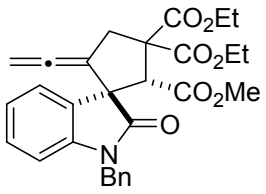




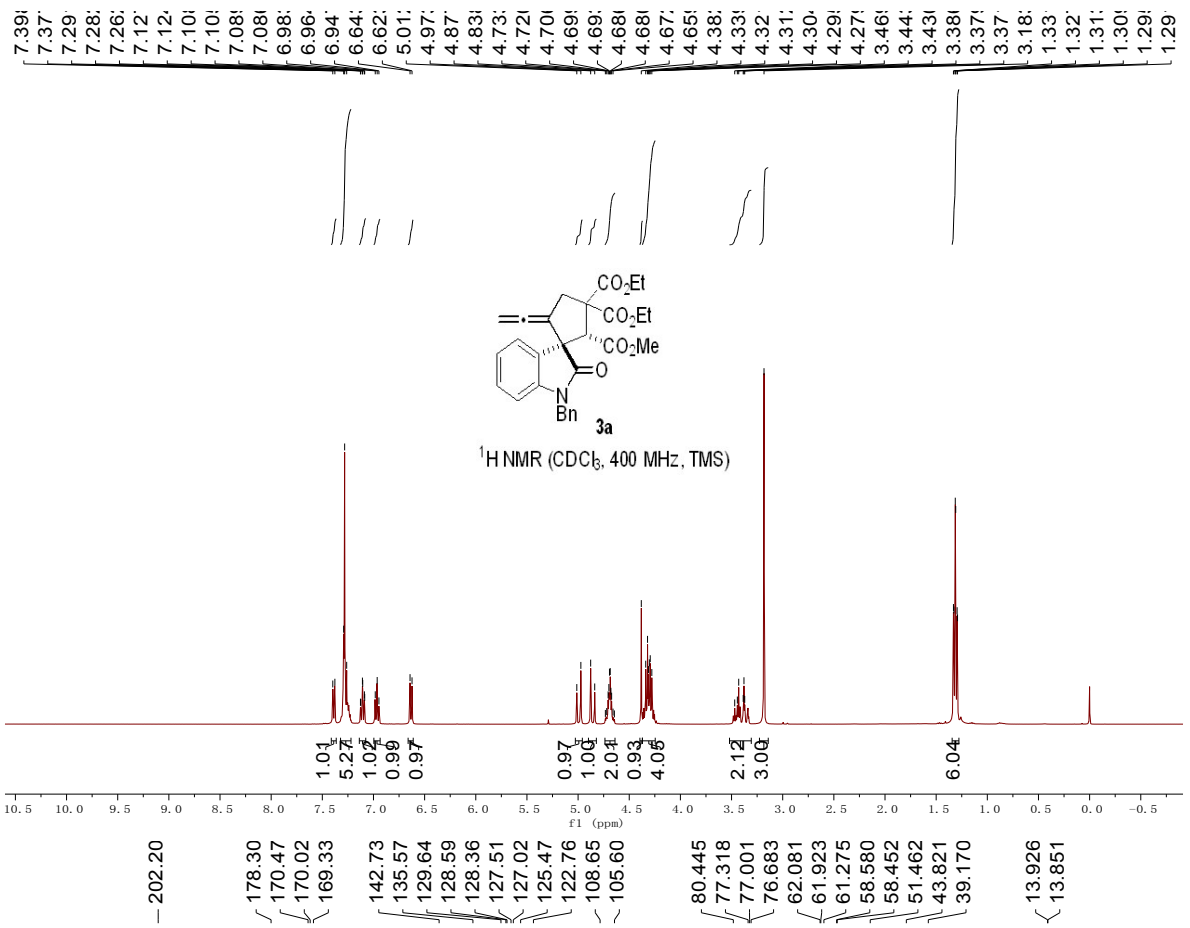
Compound 2o: Yield: 1.6g, 88%; A yellow solid; Mp: 113-115 °C; Eluent: petroleum ether:ethyl acetate = 10:1; R_f = 0.6; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.56 (d, *J* = 7.6 Hz, 1H), 7.37–7.27 (m, 1H), 7.09–6.99 (m, 1H), 6.97–6.88 (m, 1H), 6.83–6.72 (m, 1H), 4.94 (s, 1H), 4.87 (s, 1H), 4.29 (s, 2H), 3.88 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 166.1, 145.4, 138.7, 137.9, 137.8, 132.4, 128.7, 122.78, 122.75, 121.99, 121.95, 119.7, 112.7, 112.6, 109.2, 52.1, 45.9, 19.8; IR (neat): ν 3076, 2947, 1703, 1602, 1348, 1206, 907, 749 cm^{-1}; HRMS (ESI) Calcd. for $C_{15}H_{16}NO_3Na$ $[M+H]^+$: 258.1124, found: 258.1123.

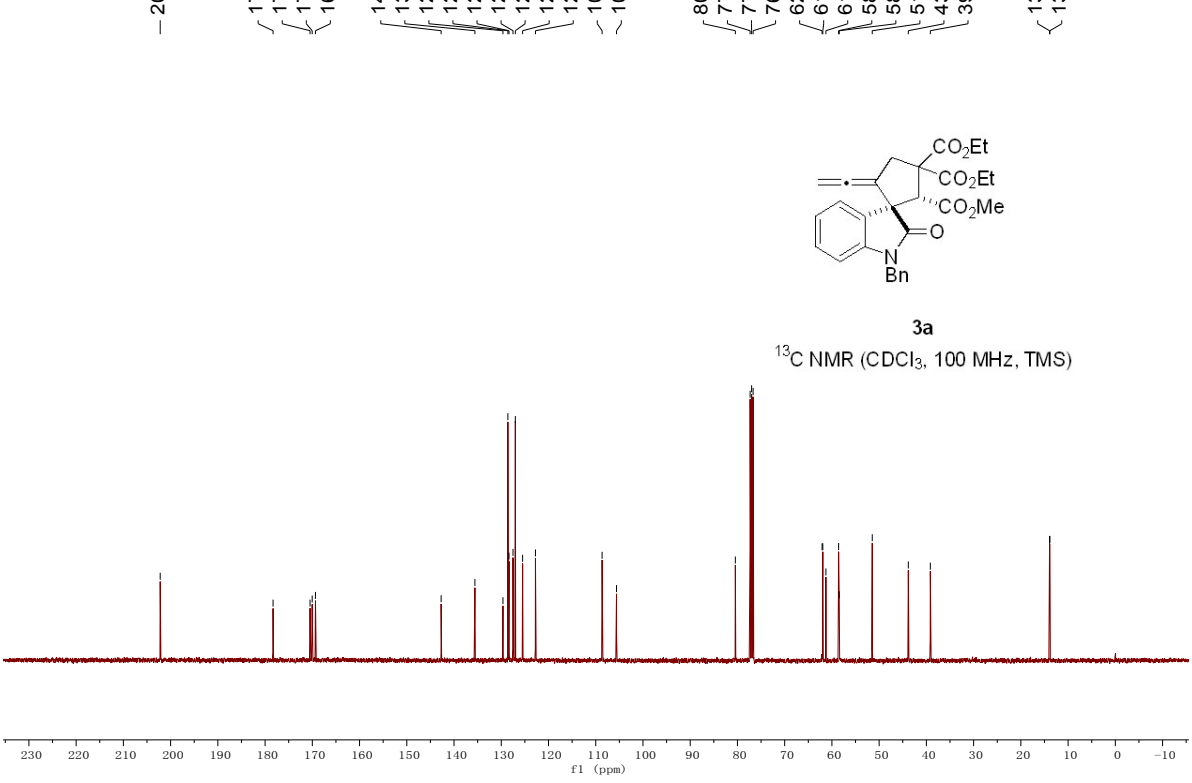


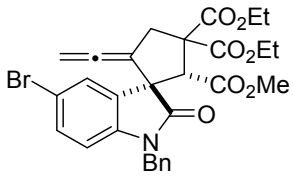




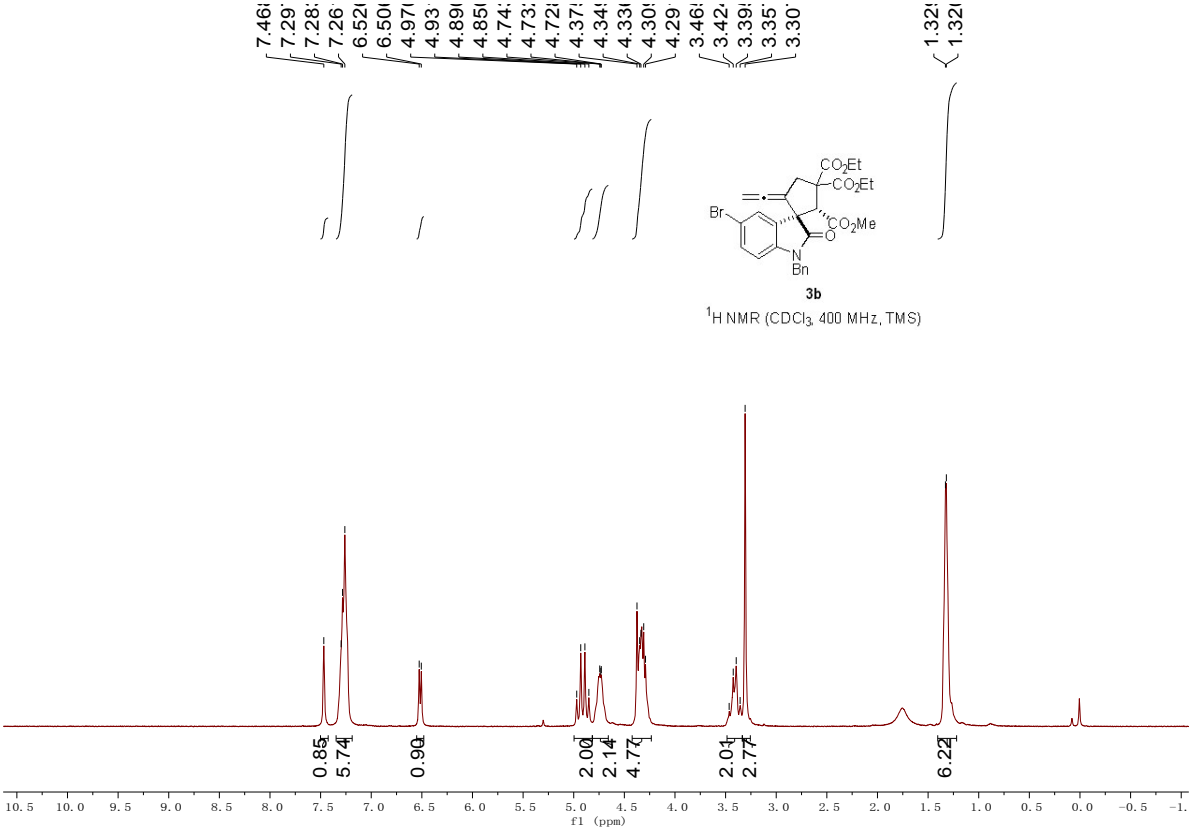
Compound 3a: Yield: 63 mg, 63%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 123-125 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 7.6 Hz, 1H), 7.32–7.22 (m, 5H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 6.8 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.74–4.64 (m, 2H), 4.38 (s, 1H), 4.37–4.25 (m, 4H), 3.52–3.31 (m, 2H), 3.18 (s, 3H), 1.34–1.28 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.3, 170.5, 170.0, 169.3, 142.7, 135.6, 129.6, 128.6, 128.4, 127.5, 127.0, 125.5, 122.8, 108.7, 105.6, 80.4, 62.1, 61.9, 61.3, 58.6, 58.5, 51.5, 43.8, 39.2, 13.92, 13.85; IR (neat): ν 2989, 2929, 2005, 1966, 1488, 1364, 747, 669 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{29}NO_7Na$ $[M+H]^+$: 526.1836, found: 526.1830.

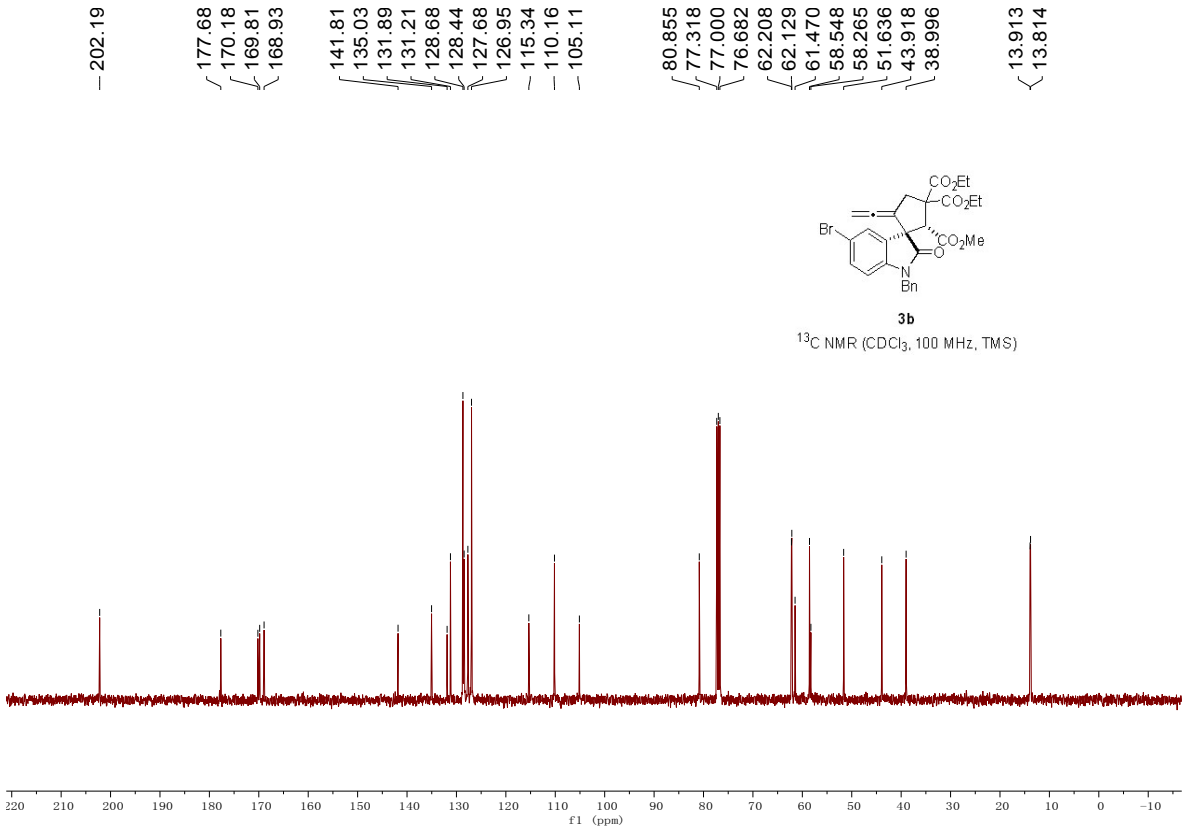

CO2Et
CO2Et
CO2Me
O
N
Bn
3a
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)

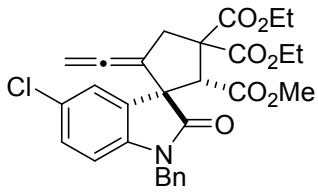

CO2Et
CO2Et
CO2Me
O
N
Bn
3a
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)



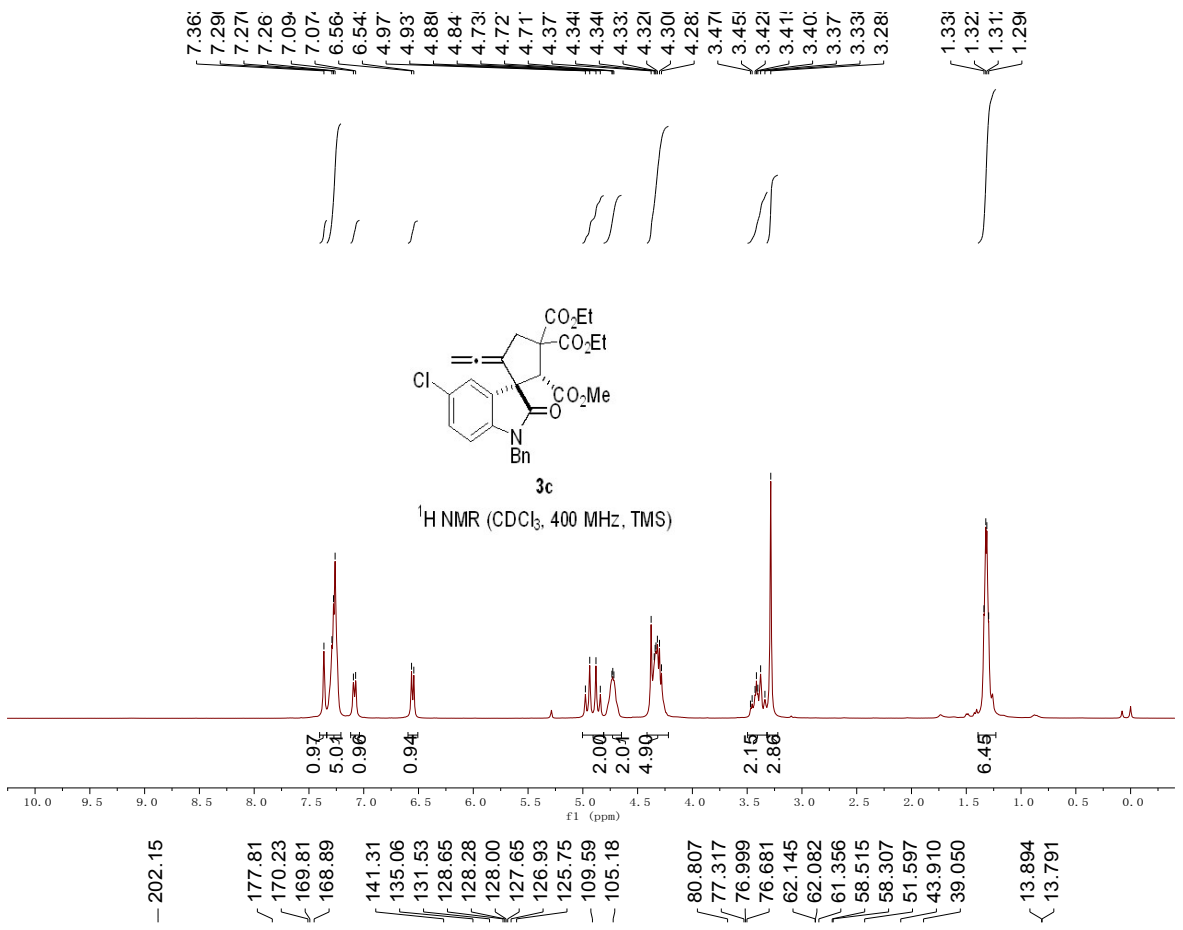
Compound 3b: Yield: 72 mg, 62%; A colorless solid; Mp: 177-179 ^{o}C; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (s, 1H), 7.35–7.19 (m, 6H), 6.52 (d, *J* = 8.0 Hz, 1H), 4.91 (q, *J* = 15.6 Hz, 2H), 4.81–4.66 (m, 2H), 4.42–4.23 (m, 5H), 3.49–3.34 (m, 2H), 3.31 (s, 3H), 1.40–1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 177.7, 170.2, 169.8, 168.9, 141.8, 135.0, 131.9, 131.2, 128.7, 128.4, 127.7, 127.0, 115.3, 110.2, 105.1, 80.9, 62.2, 62.1, 61.5, 58.5, 58.3, 51.6, 43.9, 39.0, 13.9, 13.8; IR (neat): ν 3389, 2912, 2844, 1958, 1739, 1480, 815, 702 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaBr$ $[M+H]^+$: 604.0941, found: 604.0932.

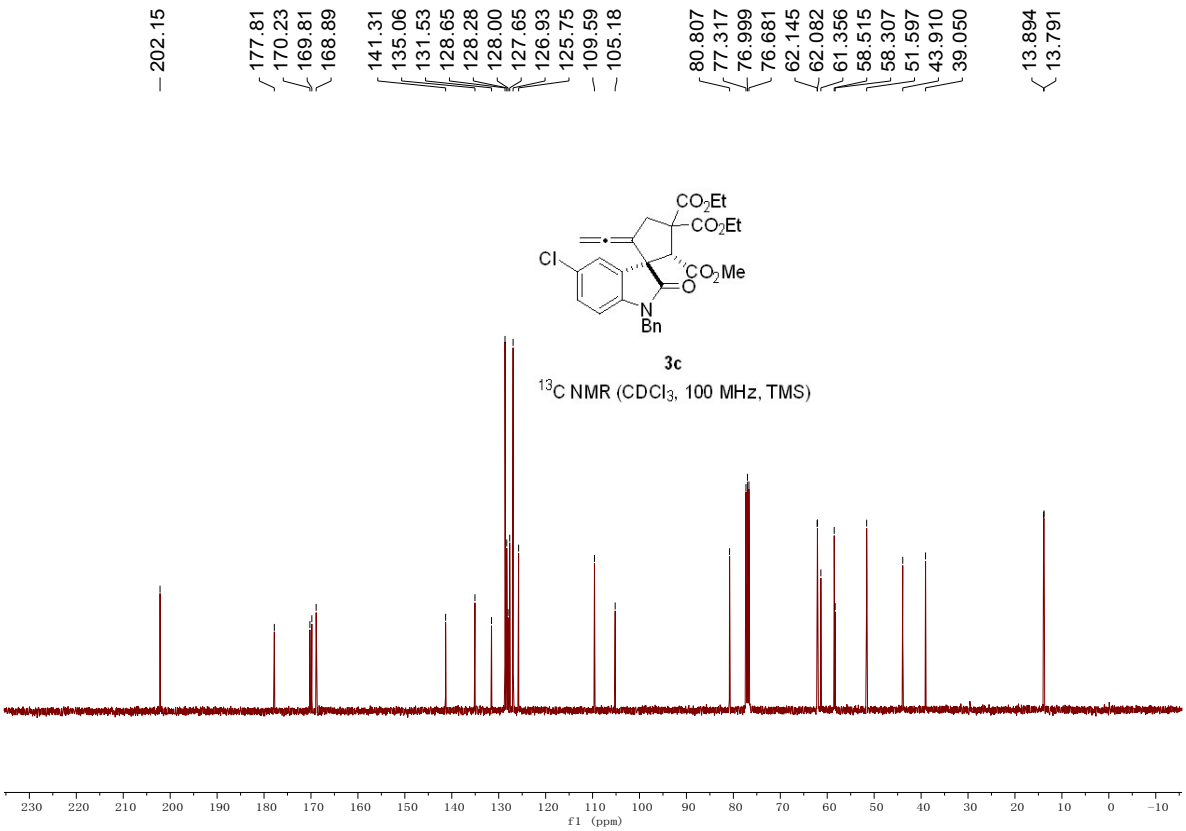


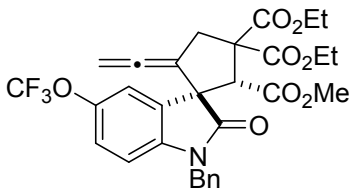




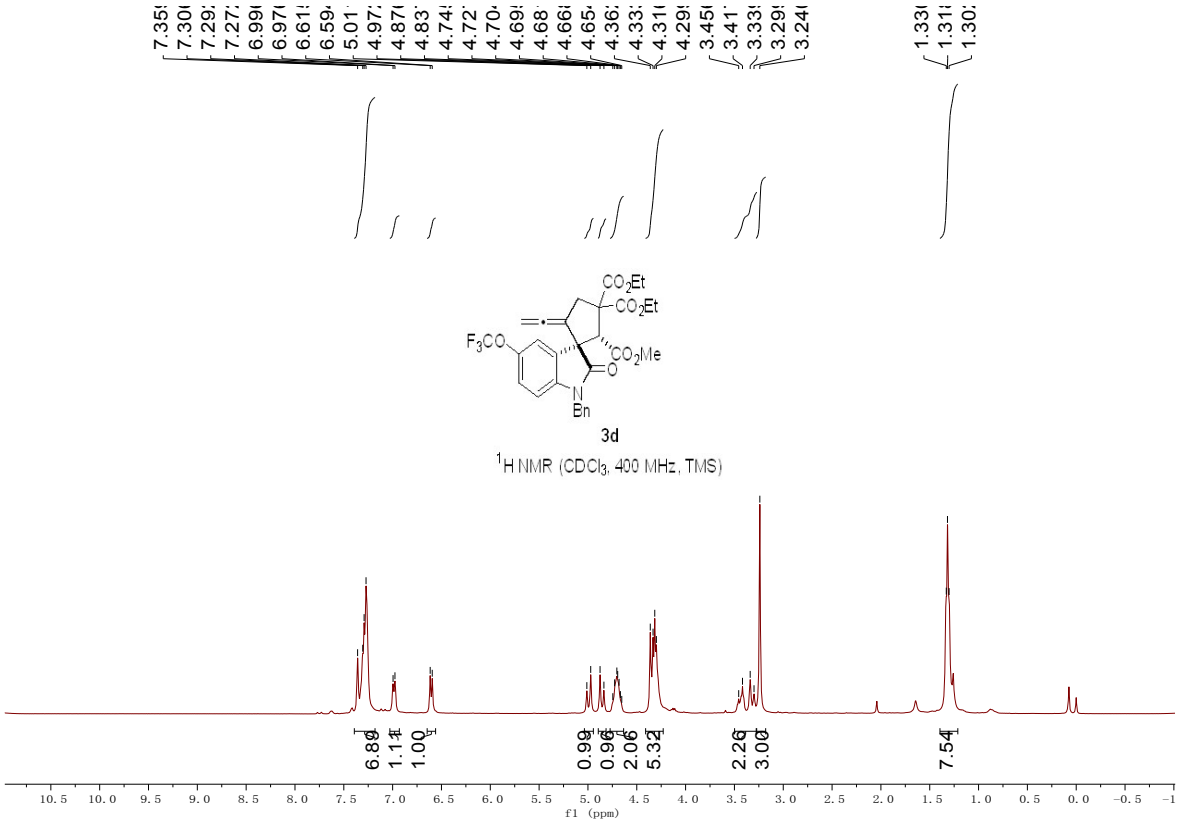
Compound 3c: Yield: 59 mg, 56%; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 165-167 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (s, 1H), 7.34–7.21 (m, 5H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.81–4.65 (m, 2H), 4.41–4.22 (m, 5H), 3.50–3.32 (m, 2H), 3.28 (s, 3H), 1.39–1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 177.8, 170.2, 169.8, 168.9, 141.3, 135.1, 131.5, 128.7, 128.3, 128.0, 127.7, 126.9, 125.8, 109.6, 105.2, 80.8, 62.14, 62.10, 61.08, 58.5, 58.3, 51.6, 43.9, 39.0, 13.9, 13.8; IR (neat): ν 2925, 2844, 1962, 1739, 1290, 1193, 817, 702 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaCl$ $[M+H]^+$: 560.1446, found: 560.1439.

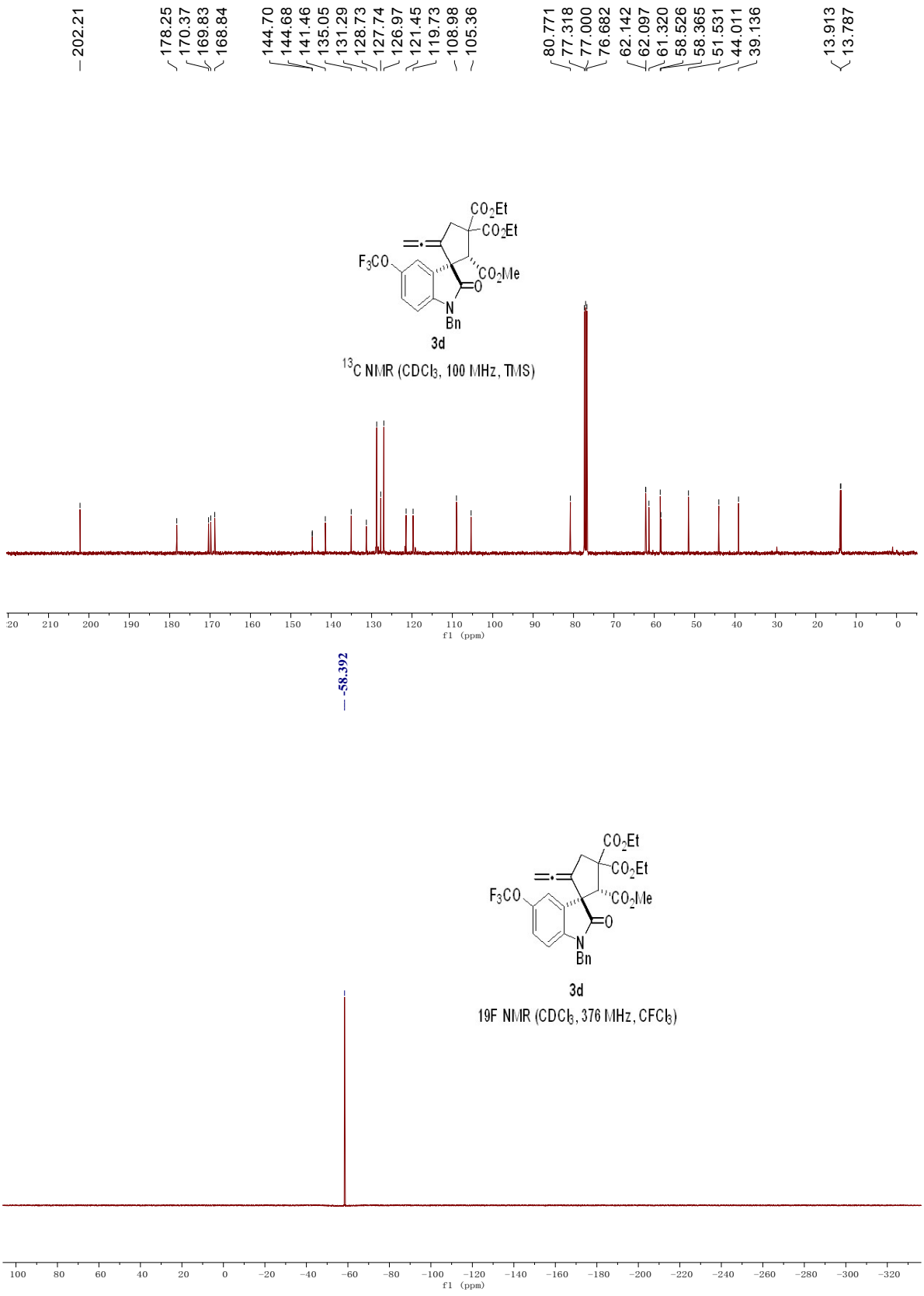

7.36
7.29
7.27
7.26
7.09
7.07
6.56
6.54
4.97
4.93
4.88
4.84
4.73
4.72
4.71
4.37
4.34
4.34
4.33
4.32
4.30
4.28
3.47
3.45
3.42
3.41
3.40
3.37
3.33
3.28
1.33
1.32
1.31
1.29
CO2Et
CO2Et
Cl
CO2Me
O
N
Bn
3c
1H NMR (CDCl3, 400 MHz, TMS)
0.97
5.01
0.96
0.94
2.00
2.04
4.90
2.15
2.86
6.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

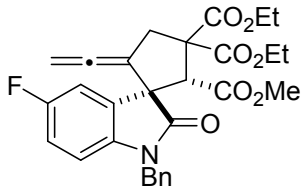

202.15
177.81
170.23
169.81
168.89
141.31
135.06
131.53
128.65
128.28
128.00
127.65
126.93
125.75
109.59
105.18
80.807
77.317
76.999
76.681
62.145
62.082
61.356
58.515
58.307
51.597
43.910
39.050
13.894
13.791
CO2Et
CO2Et
Cl
CO2Me
O
N
Bn
3c
13C NMR (CDCl3, 100 MHz, TMS)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)



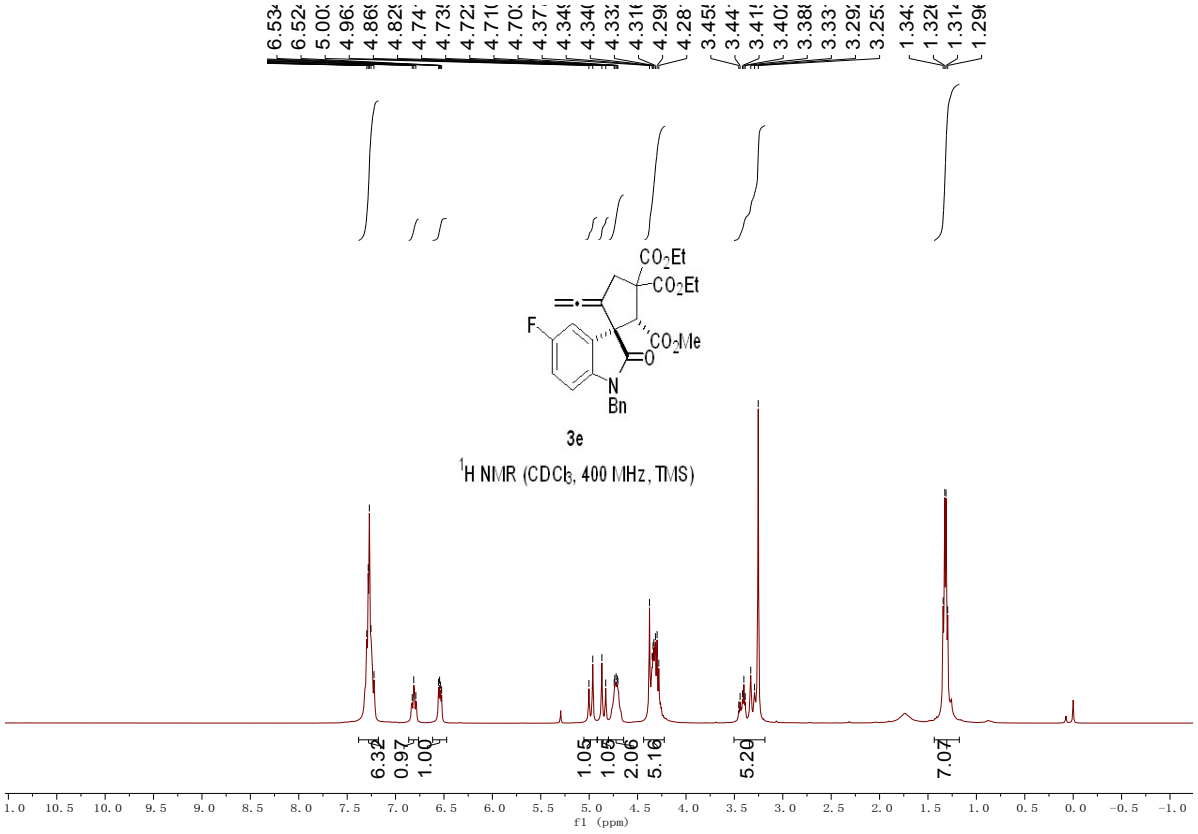
Compound 3d: Yield: 67 mg, 57%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 10:1; R_f = 0.4; Mp: 133-135 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39–7.18 (m, 6H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.77–4.63 (m, 2H), 4.41–4.23 (m, 5H), 3.50–3.27 (m, 2H), 3.24 (s, 3H), 1.40–1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.3, 170.4, 169.8, 168.8, 144.70, 144.68, 141.5, 135.1, 131.3, 128.7, 127.7, 127.0, 121.5, 119.7, 109.0, 105.4, 80.8, 62.14, 62.09, 61.3, 58.5, 58.4, 51.5, 44.0, 39.1, 13.9, 13.8; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -58.4; IR (neat): ν 2987, 2914, 1964, 1739, 1270, 1175, 1084, 741, 698 cm^{-1}; HRMS (ESI) Calcd. for $C_{30}H_{28}NO_8F_3Na$ $[M+H]^+$: 610.1659, found: 610.1650.

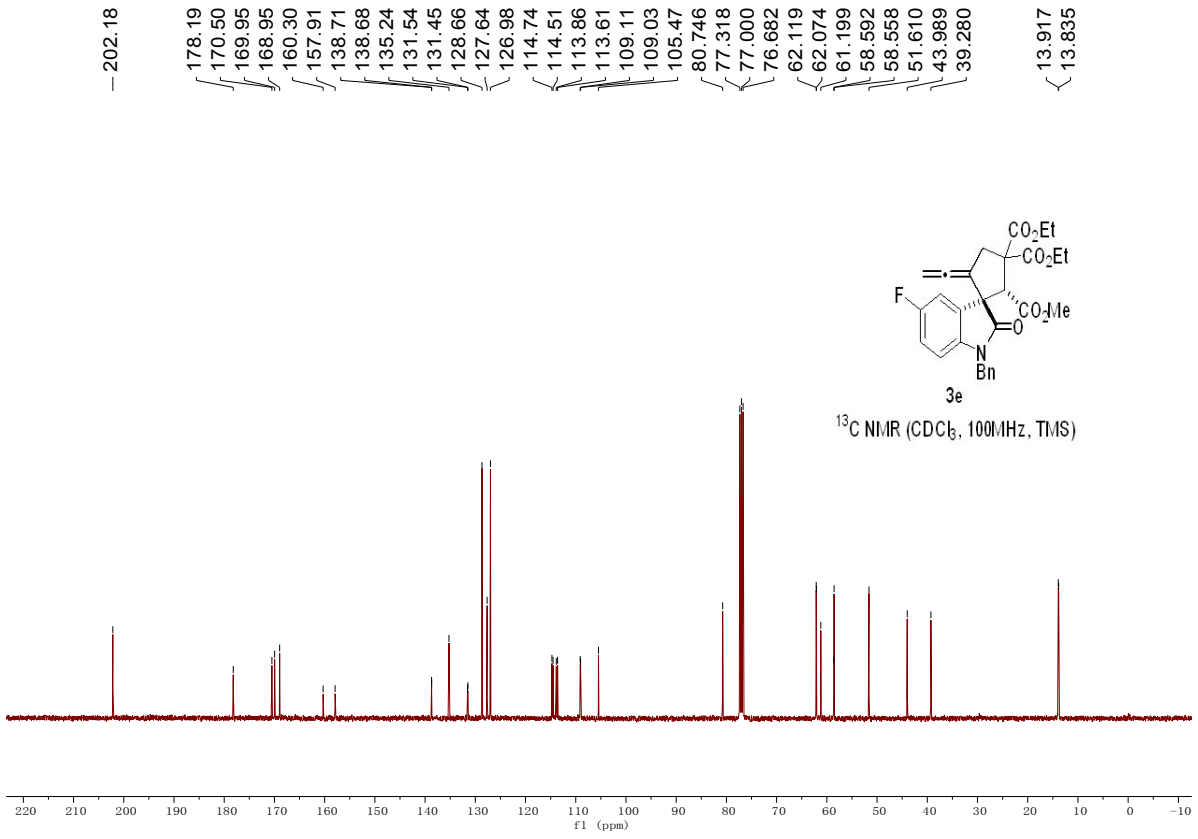


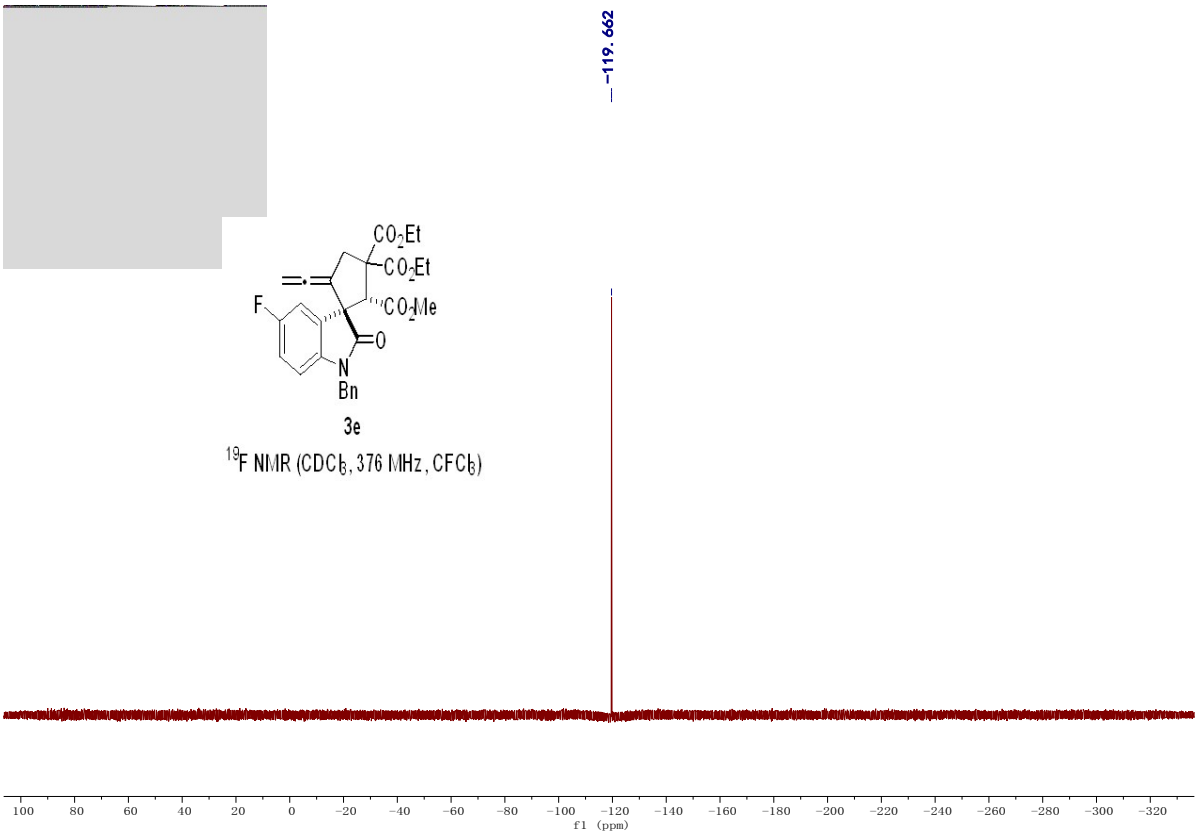

202.21
178.25
170.37
169.83
168.84
144.70
144.68
141.46
135.05
131.29
128.73
127.74
126.97
121.45
119.73
108.98
105.36
80.771
77.318
77.000
76.682
62.142
62.097
61.320
58.526
58.365
51.531
44.011
39.136
13.913
13.787
CO2Et
CO2Et
F3CO
CO2Me
O
N
Bn
3d
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)
-58.392
CO2Et
CO2Et
F3CO
CO2Me
O
N
Bn
3d
19F NMR (CDCl3, 376 MHz, CFCl3)
f1 (ppm)

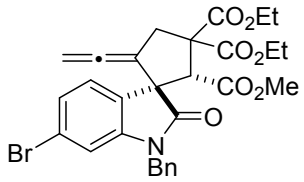


Compound 3e: Yield: 59 mg, 57%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 8:1; R_f = 0.4; Mp: 149-151 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36–7.18 (m, 6H), 6.87–6.77 (m, 1H), 6.59–6.51 (m, 1H), 4.98 (d, *J* = 15.6 Hz, 1H), 4.85 (d, *J* = 15.6 Hz, 1H), 4.79–4.65 (m, 2H), 4.42–4.22 (m, 5H), 3.49–3.20 (m, 5H), 1.41–1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.2, 170.5, 170.0, 169.0, 159.1 (d, *J* = 238.7 Hz), 138.71, 138.68, 135.2, 131.5 (d, *J* = 8.6 Hz), 128.7, 127.6, 127.0, 114.6 (d, *J* = 23.5 Hz), 113.7 (d, *J* = 25.9 Hz), 109.1 (d, *J* = 8.2 Hz), 105.5, 80.7, 62.11, 62.07, 61.2, 58.6, 58.59, 51.55, 44.0, 39.3, 13.9, 13.8; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -119.7; IR (neat): ν 2927, 2849, 1959, 1709, 1191, 696 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_9FNa$ $[M+H]^+$: 544.1742, found: 544.1735.

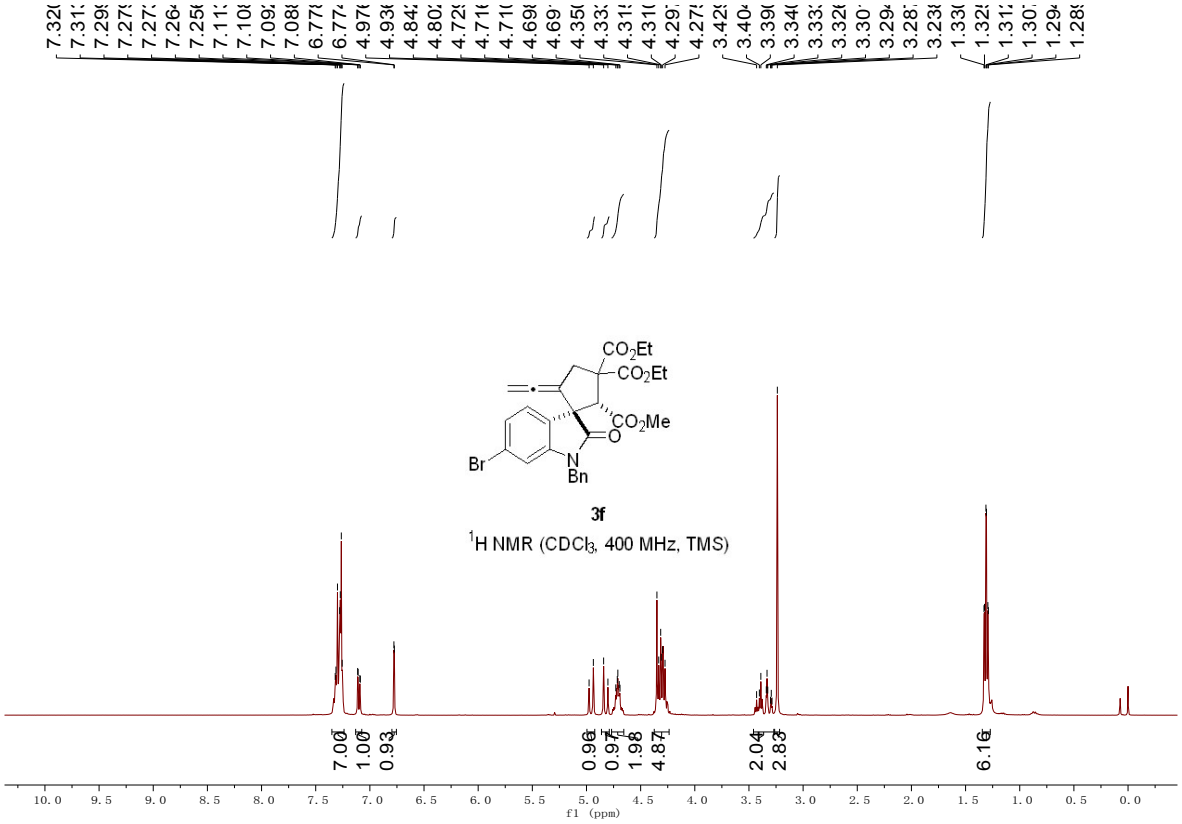


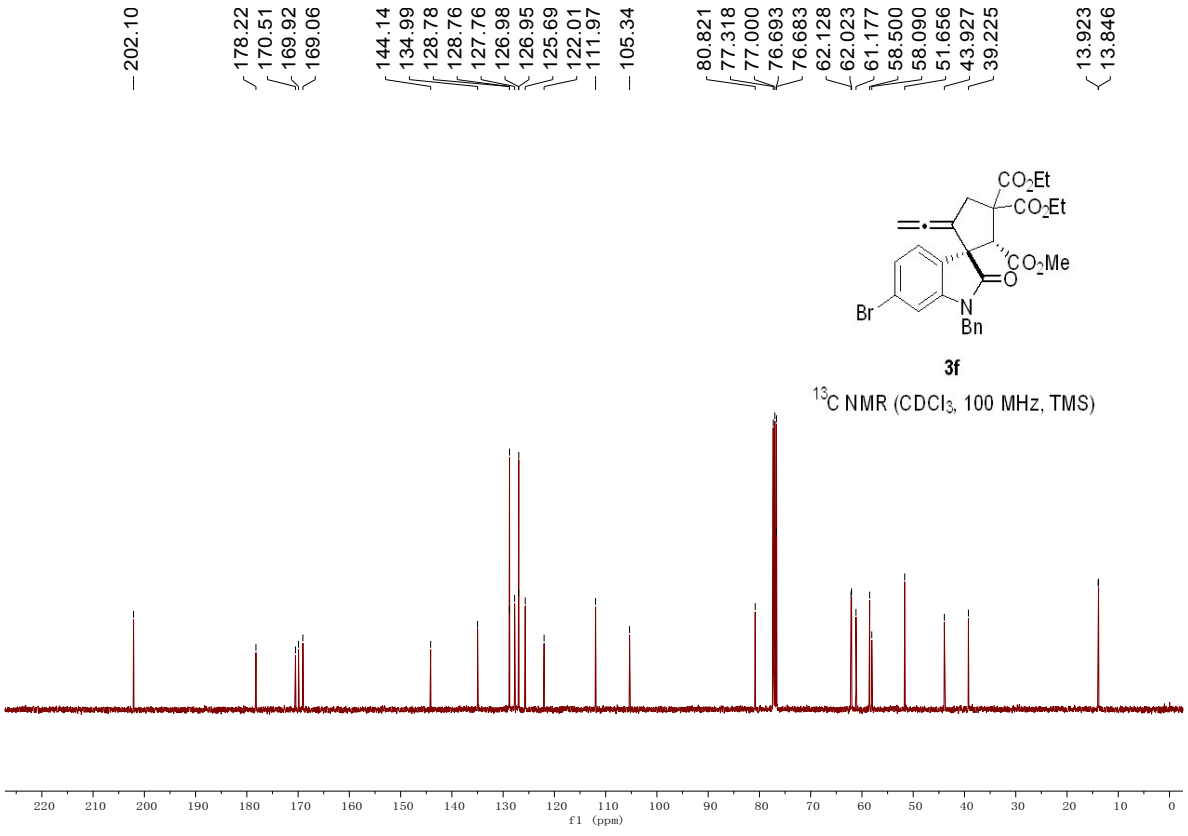

202.18
178.19
170.50
169.95
168.95
160.30
157.91
138.71
138.68
135.24
131.54
131.45
128.66
127.64
126.98
114.74
114.51
113.86
113.61
109.11
109.03
105.47
80.746
77.318
77.000
76.682
62.119
62.074
61.199
58.592
58.558
51.610
43.989
39.280
13.917
13.835
CO2Et
CO2Et
CO2Me
F
O
N
Bn
3e
13C NMR (CDCl3, 100MHz, TMS)
f1 (ppm)

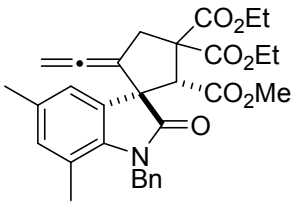

-119.662
CO2Et
CO2Et
CO2Me
F
O
N
Bn
3e
19F NMR (CDCl3, 376 MHz, CFCl3)
f1 (ppm)



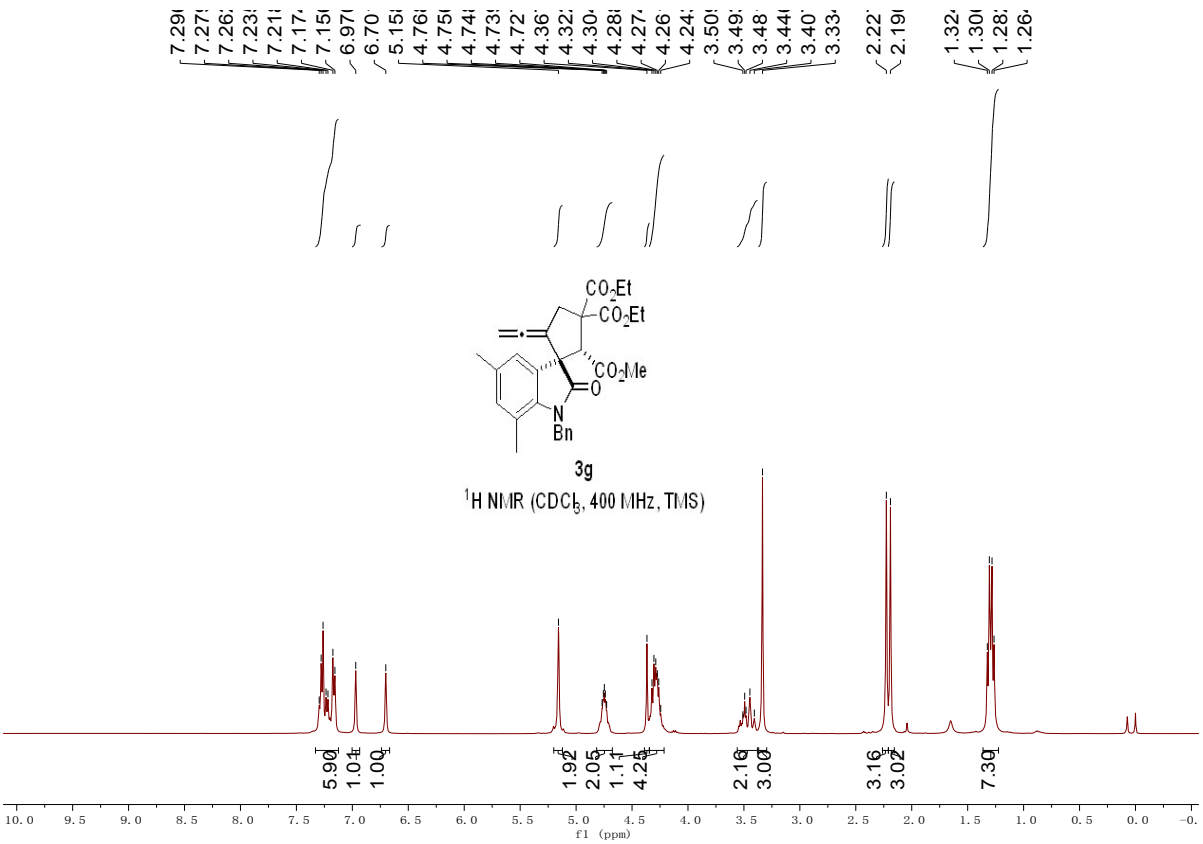
Compound 3f: Yield: 60 mg, 52%; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 113-115 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35–7.24 (m, 6H), 7.10 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 6.78 (d, *J* = 1.6 Hz, 1H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.82 (d, *J* = 15.6 Hz, 1H), 4.77–4.66 (m, 2H), 4.37–4.24 (m, 5H), 3.46–3.27 (m, 2H), 3.24 (s, 3H), 1.35–1.27 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 178.2, 170.5, 169.9, 169.1, 144.1, 135.0, 128.78, 128.76, 127.8, 127.0, 126.9, 125.7, 122.0, 112.0, 105.3, 80.8, 62.1, 62.0, 61.2, 58.5, 58.1, 51.7, 43.9, 39.2, 13.9, 13.8; IR (neat): ν 2930, 2849, 1944, 1739, 1270, 1179, 877, 698 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaBr$ $[M+H]^+$: 604.0941, found: 604.0926.





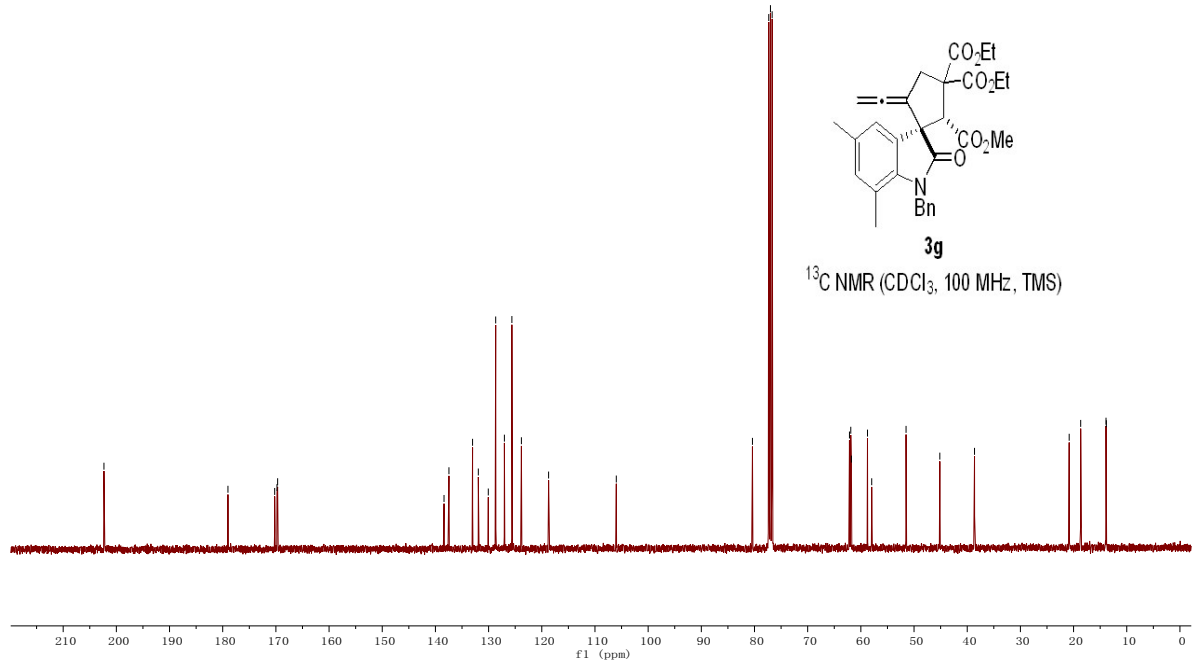


Compound 3g: Yield: 61 mg, 58%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 143-145 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33–7.12 (m, 5H), 6.97 (s, 1H), 6.70 (s, 1H), 5.16 (s, 2H), 4.82–4.68 (m, 2H), 4.37 (s, 1H), 4.35–4.21 (m, 4H), 3.56–3.38 (m, 2H), 3.33 (s, 3H), 2.23 (s, 3H), 2.19 (s, 3H), 1.36–1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3, 179.0, 170.2, 169.8, 169.7, 138.4, 137.5, 133.0, 131.9, 130.1, 128.7, 127.0, 125.6, 123.8, 118.7, 106.0, 80.4, 62.1, 61.9, 61.8, 58.8, 58.0, 51.5, 45.1, 38.6, 20.8, 18.7, 13.9, 13.8; IR (neat): ν 2992, 1962, 1708, 1617, 1354, 1175, 1022, 758, 735 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{33}NO_7Na$ $[M+H]^+$: 554.2149, found: 554.2149.



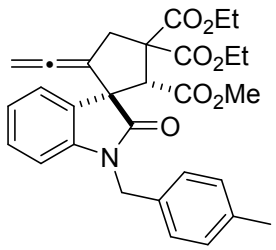
3g

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

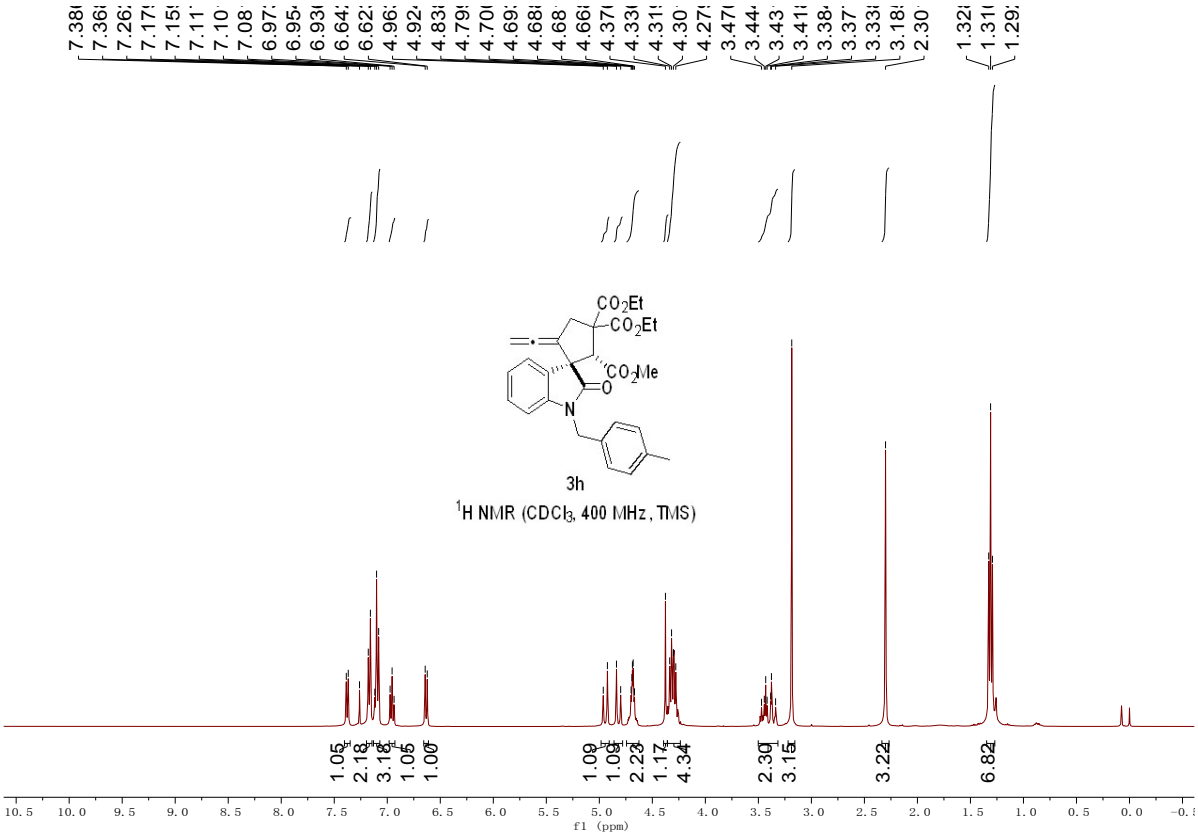


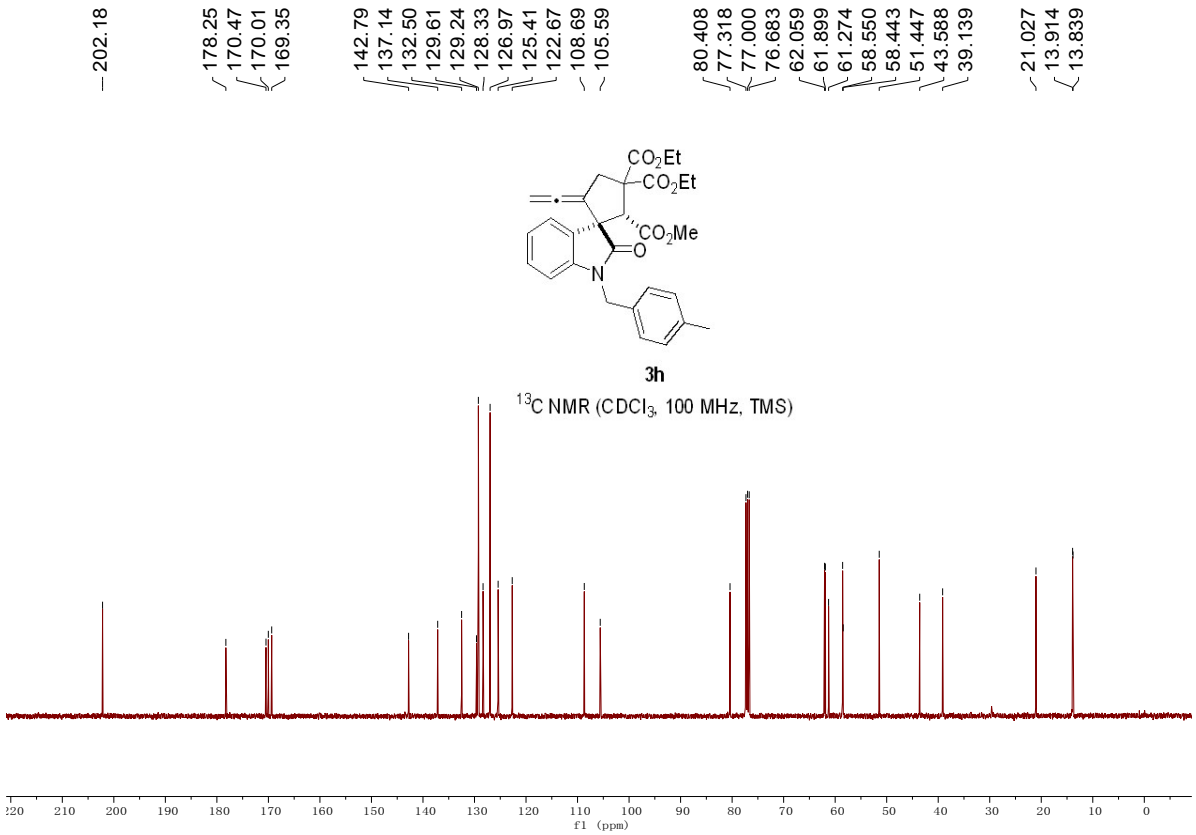
3g

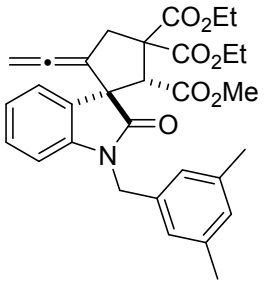
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



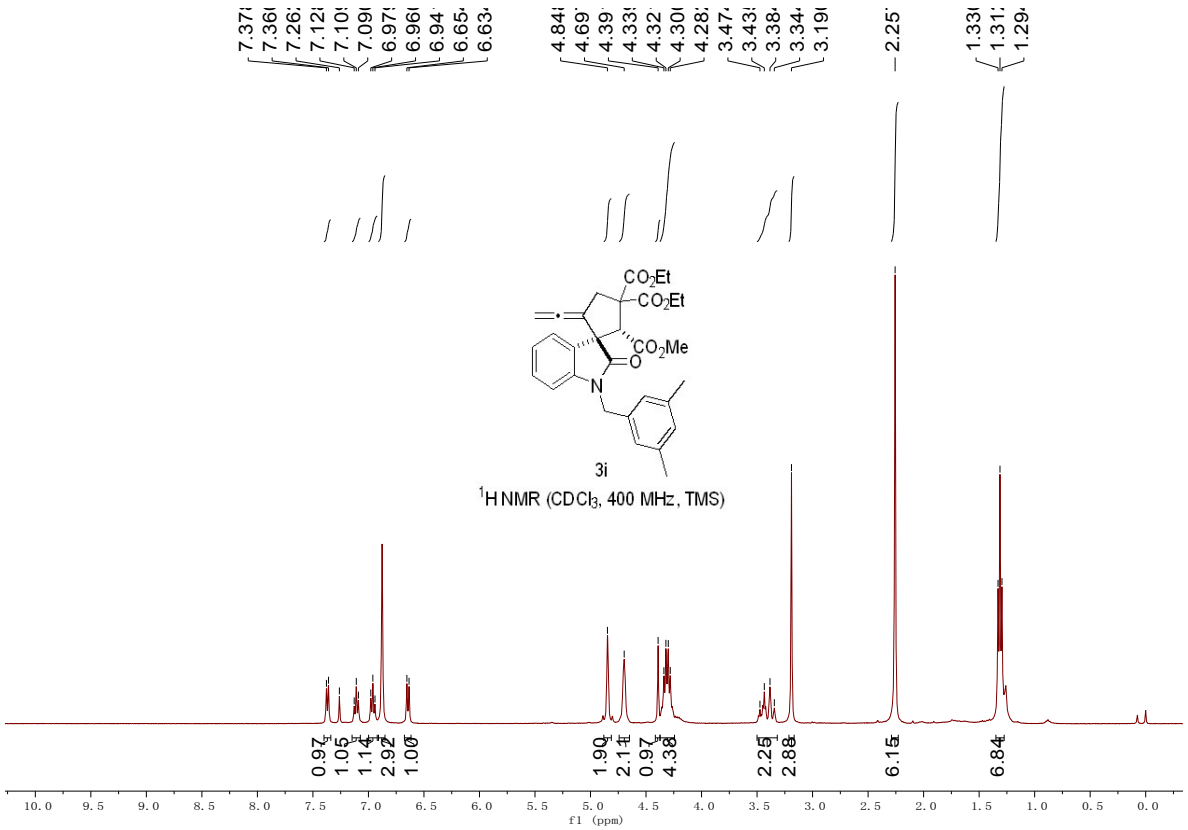
Compound 3h: Yield: 58 mg, 57%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 132-133 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.13–7.07 (m, 3H), 6.95 (t, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.80 (d, *J* = 15.6 Hz, 1H), 4.74–4.63 (m, 2H), 4.38 (s, 1H), 4.36–4.24 (m, 4H), 3.50–3.32 (m, 2H), 3.19 (s, 3H), 2.30 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.3, 170.5, 170.0, 169.4, 142.8, 137.1, 132.5, 129.6, 129.2, 128.3, 127.0, 125.4, 122.7, 108.7, 105.6, 80.4, 62.1, 61.9, 61.3, 58.5, 58.4, 51.4, 43.6, 39.1, 21.0, 13.9, 13.8; IR (neat): ν 3392, 2921, 1964, 1602, 1190, 1019, 760 cm^{-1}; HRMS (ESI) Calcd. for $C_{30}H_{31}NO_7Na$ $[M+H]^+$: 540.1992, found: 540.2003.





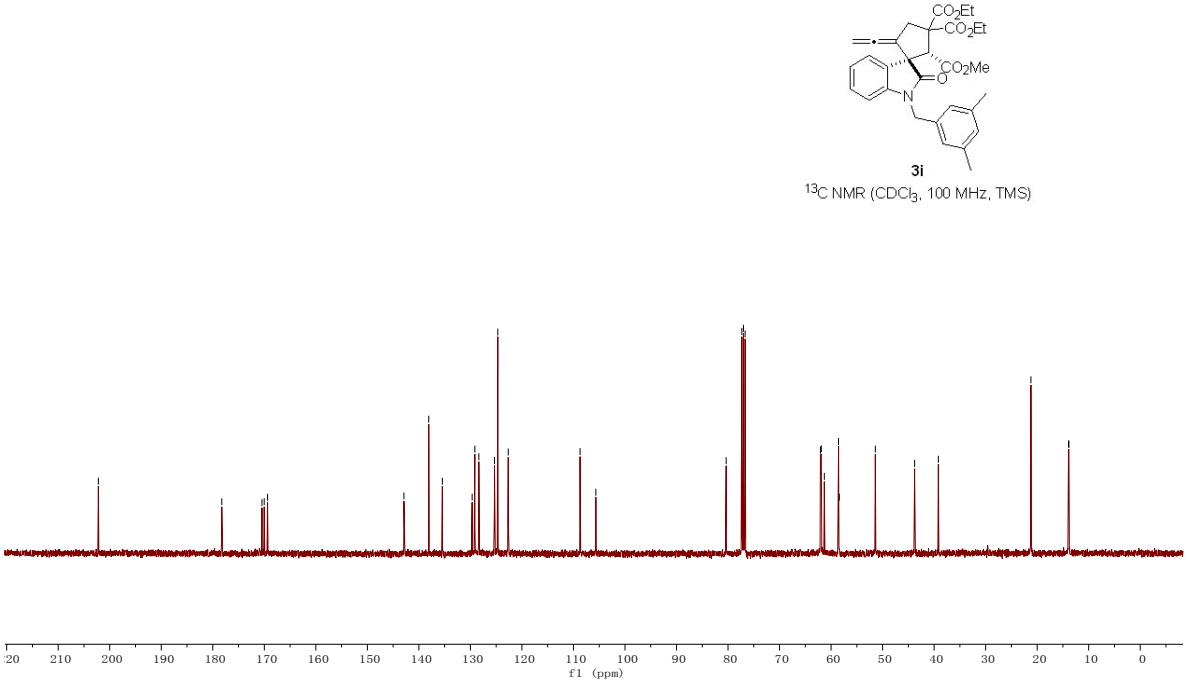


Compound 3i: Yield: 67 mg, 63%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 90-93 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 7.6 Hz, 1H), 6.88 (s, 3H), 6.64 (d, *J* = 7.6 Hz, 1H), 4.85 (s, 2H), 4.70 (s, 2H), 4.39 (s, 1H), 4.37–4.24 (m, 4H), 3.50–3.32 (m, 2H), 3.19 (s, 3H), 2.26 (s, 6H), 1.31 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.3, 170.5, 170.0, 169.4, 142.9, 138.1, 135.4, 129.7, 129.1, 128.4, 125.3, 124.7, 122.7, 108.7, 105.7, 80.4, 62.1, 61.9, 61.3, 58.5, 58.4, 51.4, 43.8, 39.2, 21.2, 13.9, 13.8; IR (neat): ν 2922, 2849, 1956, 1609, 1014, 755, 692 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{33}NO_7Na$ $[M+H]^+$: 554.2149, found: 554.2149.



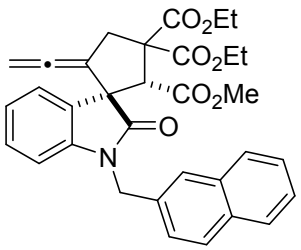
3i

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

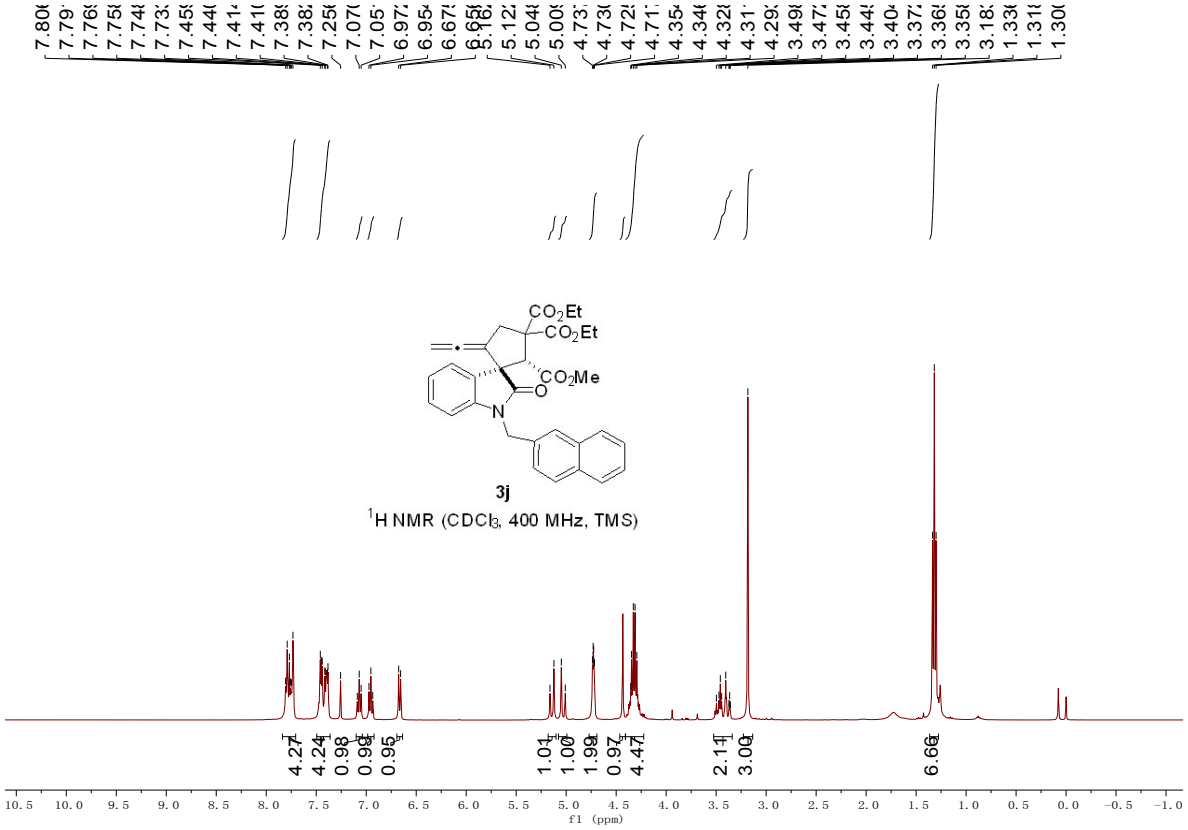


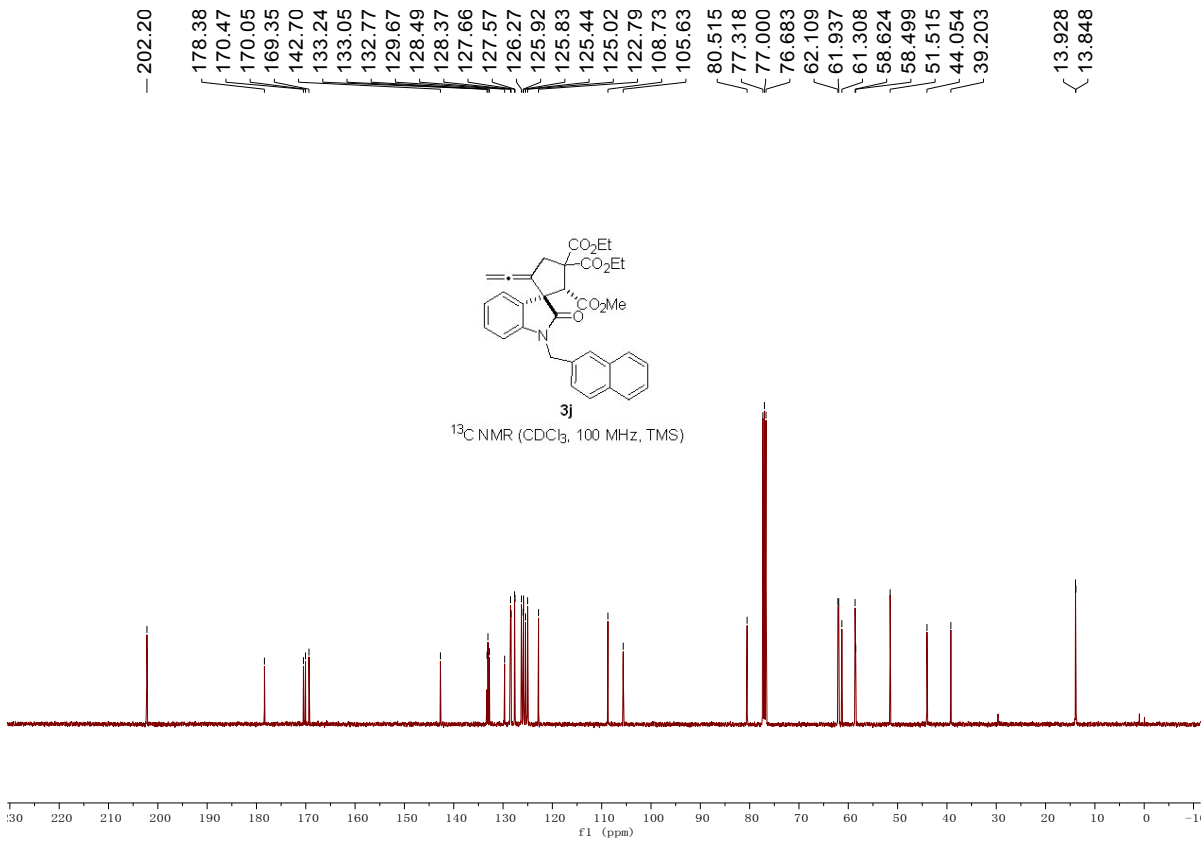
3i

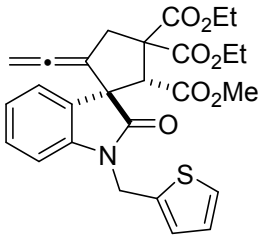
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



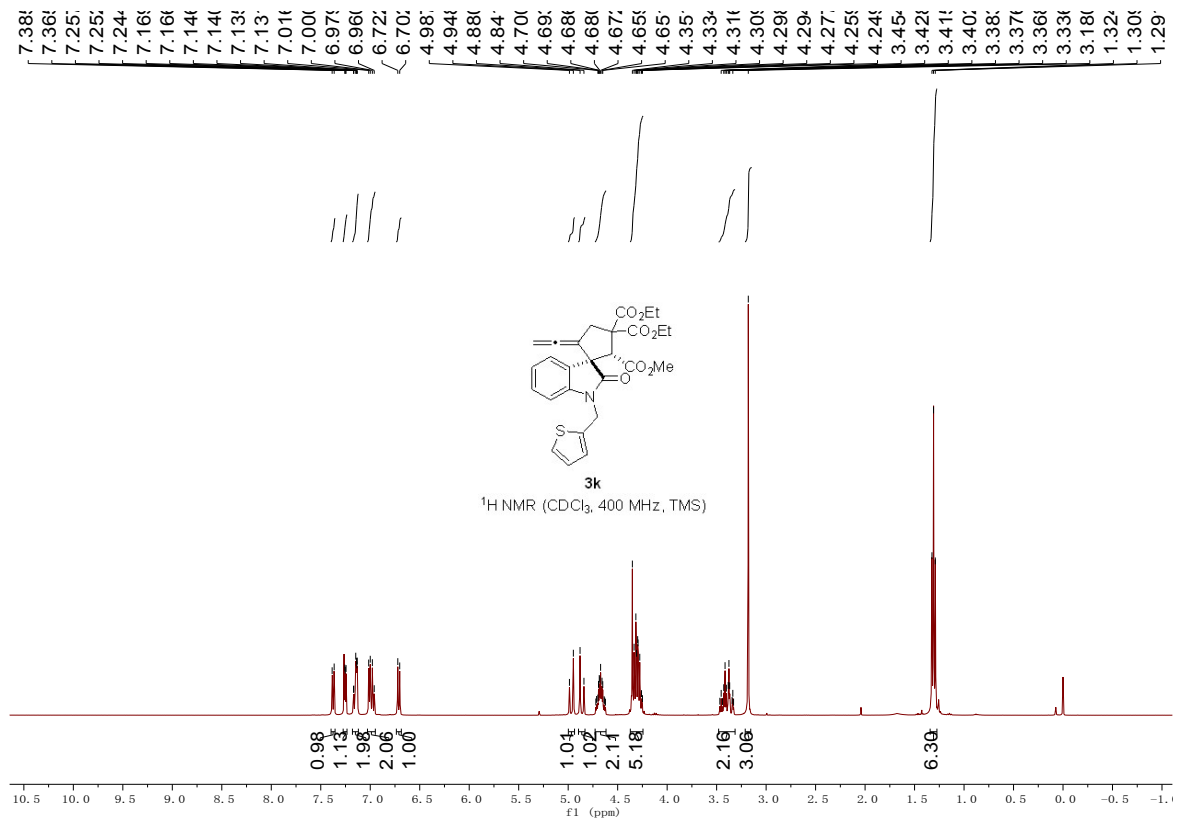
Compound 3j: Yield: 64 mg, 58%; A colorless solid; Eluent: petroleum ether:ethyl acetate = 3:1; R_f = 0.4; Mp: 131-133 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84–7.71 (m, 4H), 7.49–7.36 (m, 4H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 5.14 (d, *J* = 15.6 Hz, 1H), 5.03 (d, *J* = 15.6 Hz, 1H), 4.77–4.69 (m, 2H), 4.43 (s, 1H), 4.41–4.22 (m, 4H), 3.52–3.34 (m, 2H), 3.18 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.4, 170.5, 170.1, 169.4, 142.7, 133.2, 133.1, 132.8, 129.7, 128.5, 128.4, 127.7, 127.6, 126.3, 125.9, 125.8, 125.4, 125.0, 122.8, 108.7, 105.6, 80.5, 62.1, 61.9, 61.3, 58.6, 58.5, 51.5, 44.1, 39.2, 13.9, 13.8; IR (neat): ν 3394, 2919, 1962, 1711, 1271, 1175, 753 cm^{-1}; HRMS (ESI) Calcd. for $C_{33}H_{31}NO_7Na$ $[M+H]^+$: 576.1992, found: 576.1983.

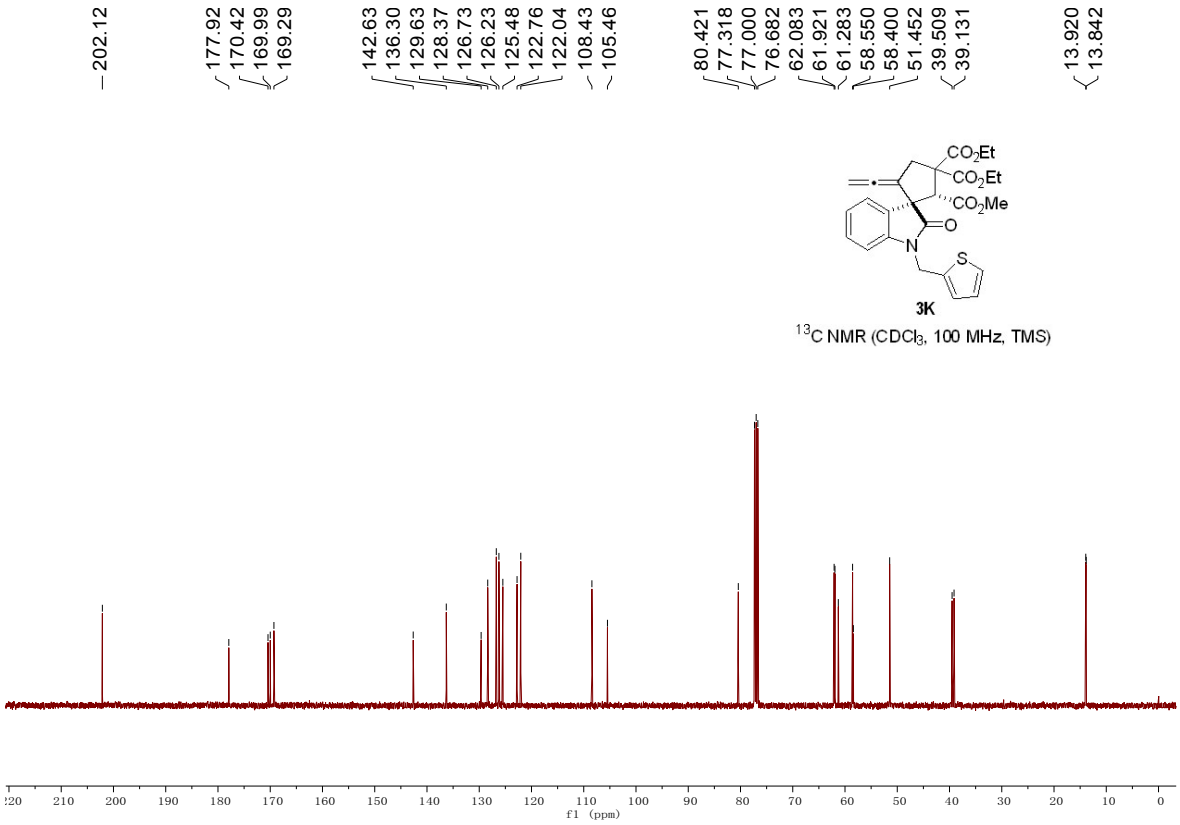


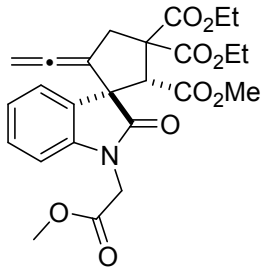




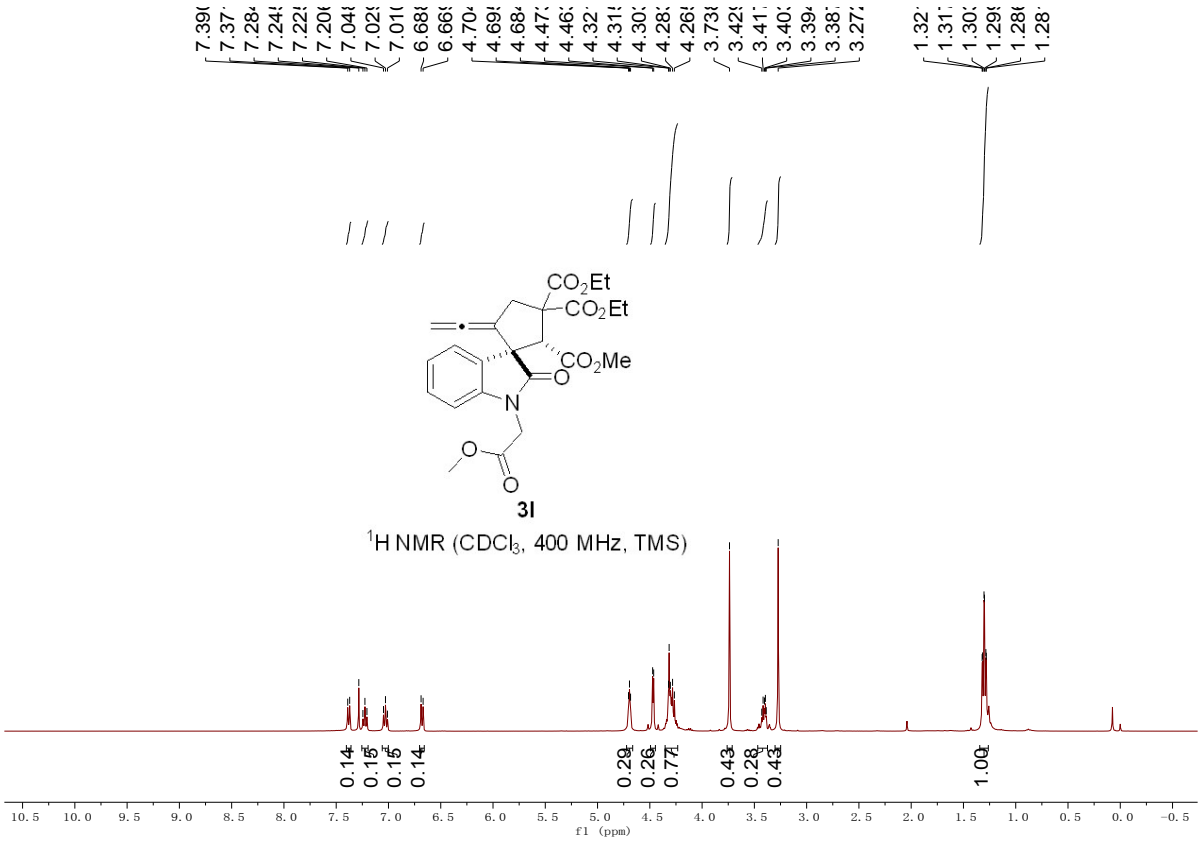
Compound 3k: Yield: 57 mg, 56%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 143-145 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 8.0 Hz, 1H), 7.27–7.23 (m, 1H), 7.18–7.12 (m, 2H), 7.03–6.95 (m, 2H), 6.71 (d, *J* = 8.0 Hz, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.73–4.62 (m, 2H), 4.37–4.24 (m, 5H), 3.48–3.31 (m, 2H), 3.18 (s, 3H), 1.34–1.27 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 177.9, 170.4, 170.0, 169.3, 142.6, 136.3, 129.6, 128.4, 126.7, 126.2, 125.5, 122.8, 122.0, 108.4, 105.5, 80.4, 62.1, 61.9, 61.3, 58.5, 58.4, 51.5, 39.5, 39.1, 13.9, 13.8; IR (neat): ν 2951, 2849, 1954, 1711, 1354, 1024, 745 cm^{-1}; HRMS (ESI) Calcd. for $C_{27}H_{27}NO_7NaS$ $[M+H]^+$: 532.1400, found: 532.1390.

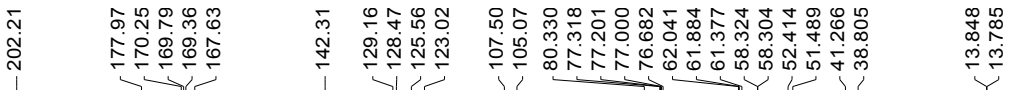

CO2Et
CO2Et
CO2Me
O
N
S
3k
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)

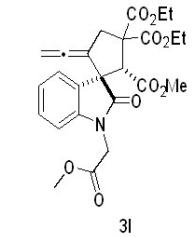

CO2Et
CO2Et
CO2Me
O
N
S
3K
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)



Compound 3l: Yield: 46 mg, 48%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 134-136 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 4.72–4.66 (m, 2H), 4.47 (d, *J* = 4.0 Hz, 2H), 4.35–4.23 (m, 5H), 3.74 (s, 3H), 3.47–3.37 (m, 2H), 3.27 (s, 3H), 1.34–1.26 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.0, 170.3, 169.8, 169.4, 167.6, 142.3, 129.2, 128.5, 125.6, 123.0, 107.5, 105.1, 80.3, 62.0, 61.9, 61.4, 58.32, 58.30, 52.4, 51.5, 41.3, 38.8, 13.84, 13.78; IR (neat): ν 2995, 2984, 1962, 1723, 1177, 733 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{27}NO_9Na$ $[M+H]^+$: 508.1578, found: 508.1561.

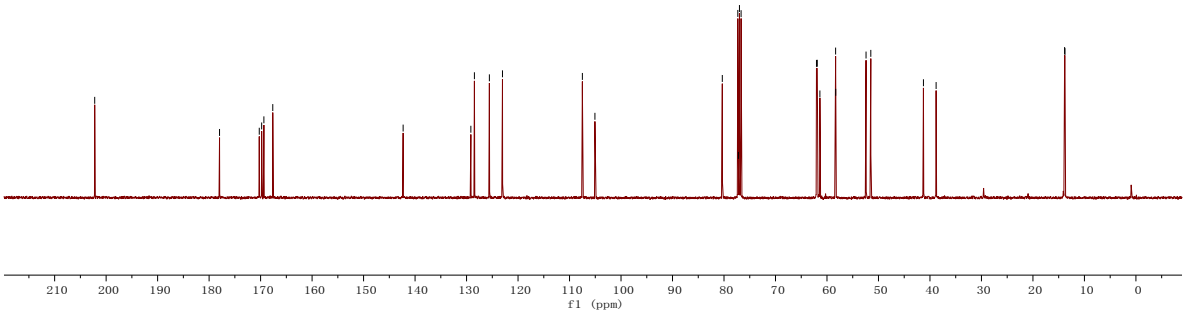


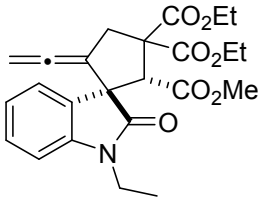




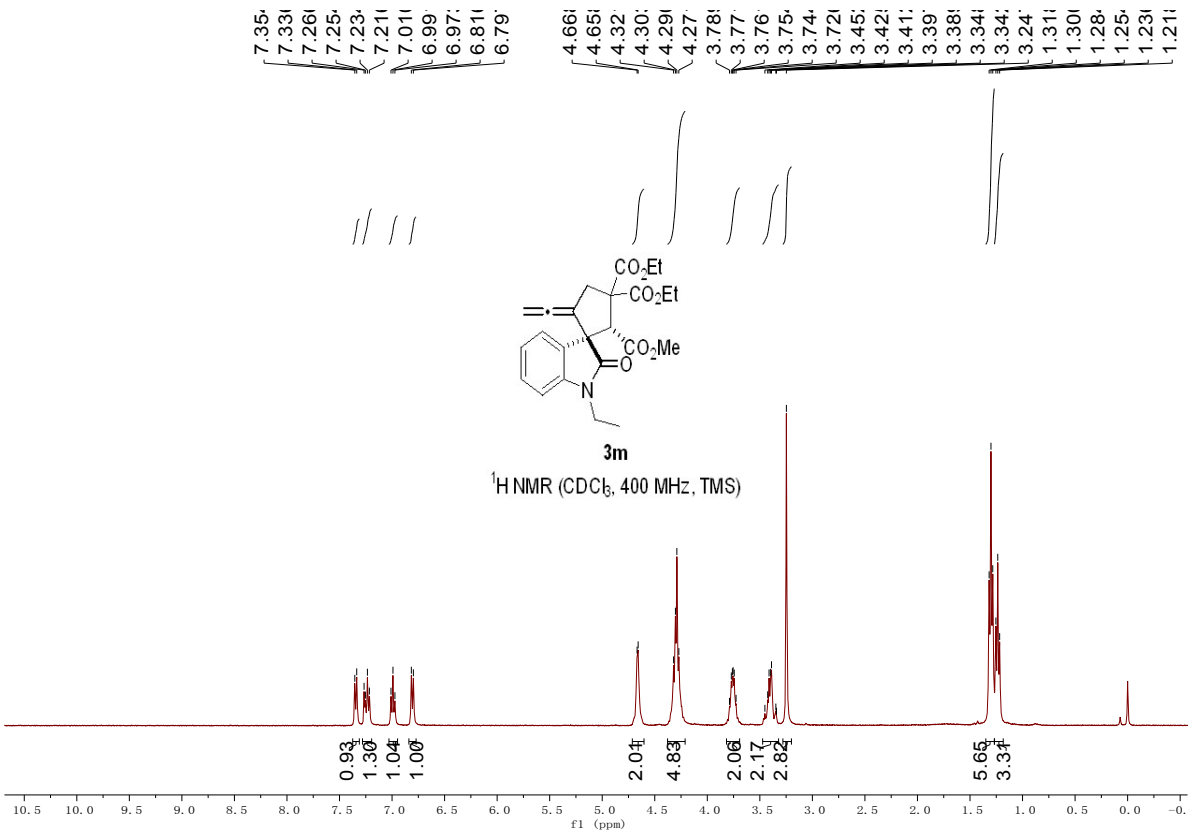
3l

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



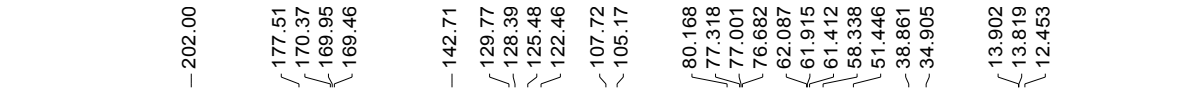


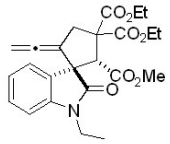
Compound 3m: Yield: 37 mg, 42%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 100-102 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 7.2 Hz, 1H), 7.28–7.19 (m, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 4.71–4.60 (m, 2H), 4.38–4.21 (m, 5H), 3.82–3.69 (m, 2H), 3.47–3.32 (m, 2H), 3.25 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 6H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 177.5, 170.4, 170.0, 169.5, 142.7, 129.8, 128.4, 125.5, 122.5, 107.7, 105.2, 80.2, 62.1, 61.9, 61.4, 58.3, 51.4, 38.9, 34.9, 13.9, 13.8, 12.5; IR (neat): ν 3390, 2193, 1963, 1700, 1225, 872, 695 cm^{-1}; HRMS (ESI) Calcd. for $C_{24}H_{27}NO_7Na$ $[M+H]^+$: 464.1679, found: 464.1668.



3m

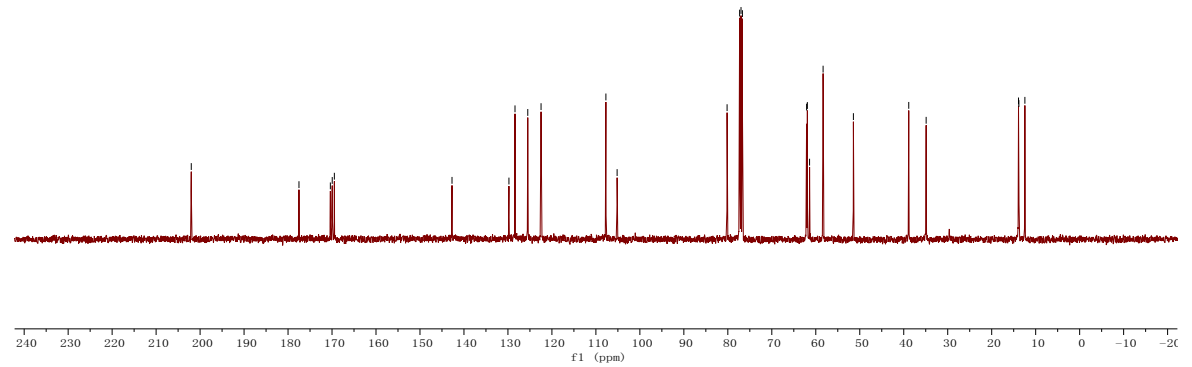
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)

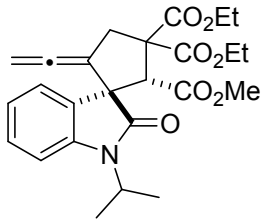




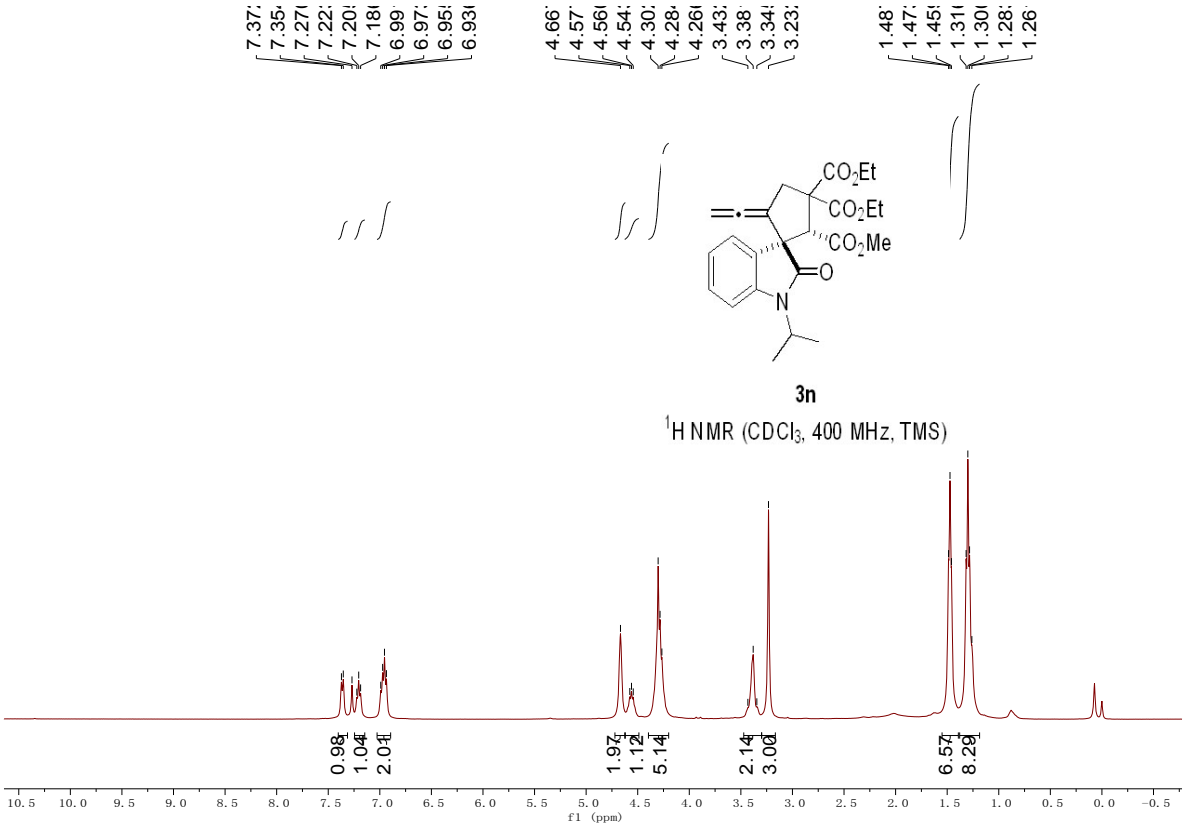
3m

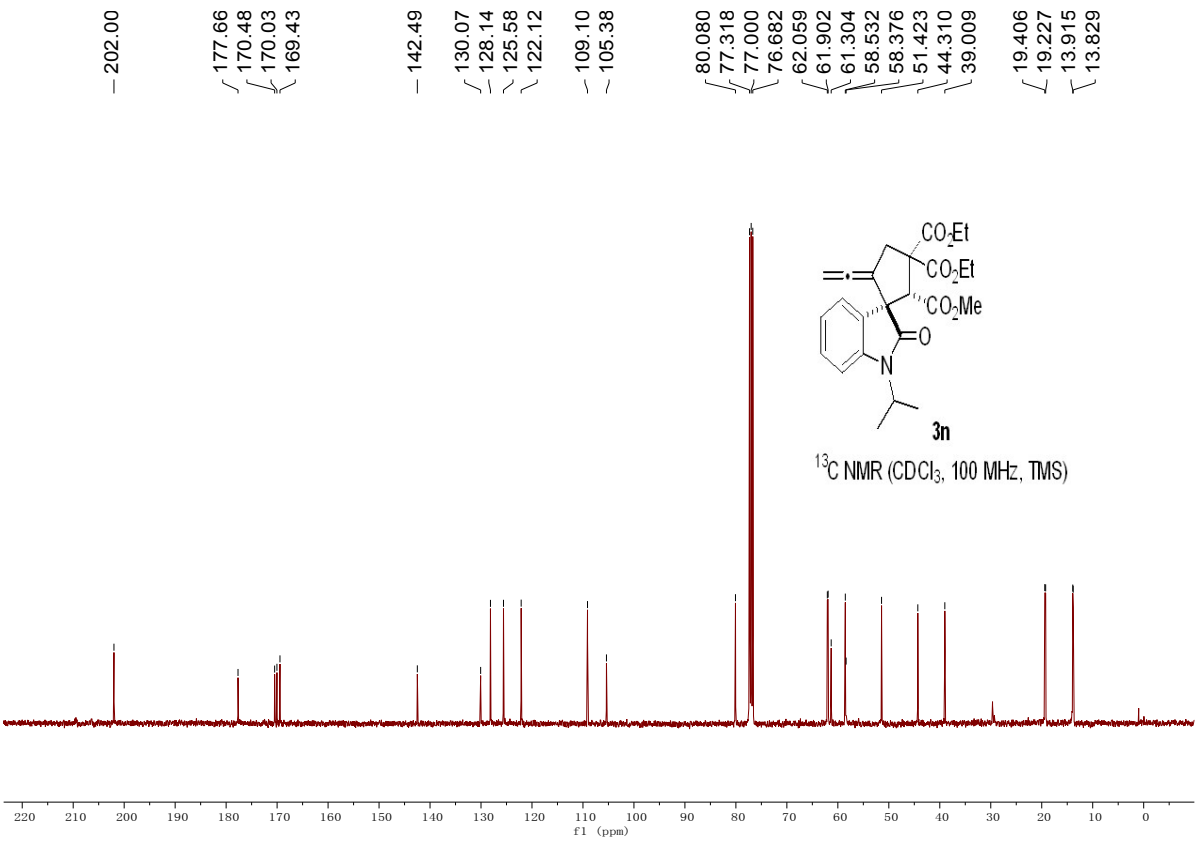
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)

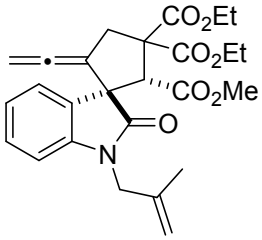




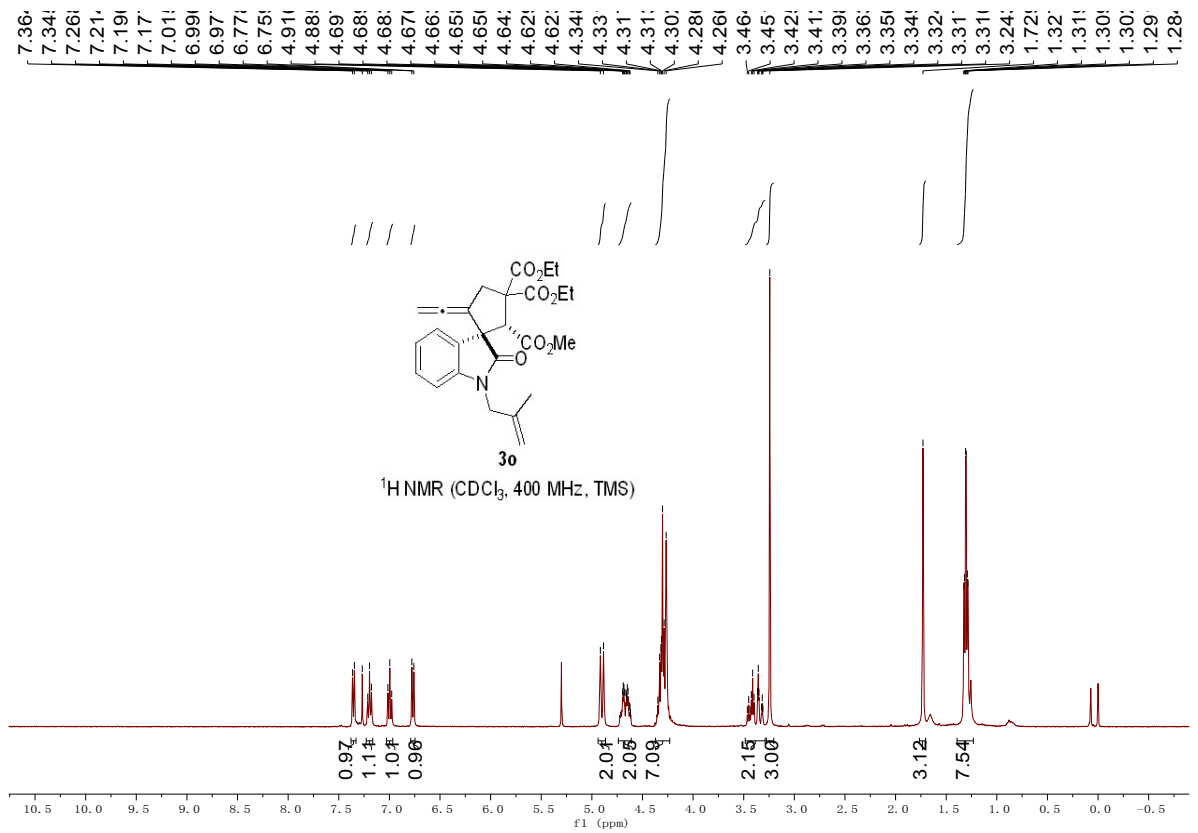
Compound 3n: Yield: 39 mg, 45%; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 103-105 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.03–6.90 (m, 2H), 4.67 (s, 2H), 4.63–4.49 (m, 1H), 4.40–4.20 (m, 5H), 3.47–3.30 (m, 2H), 3.23 (s, 3H), 1.55–1.39 (m, 6H), 1.38–1.19 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 177.7, 170.5, 170.0, 169.4, 142.5, 130.1, 128.1, 125.6, 122.1, 109.1, 105.4, 80.1, 62.1, 61.9, 61.3, 58.5, 58.4, 51.4, 44.3, 39.0, 19.4, 19.2, 13.9, 13.8; IR (neat): ν 3394, 2919, 1964, 1699, 1284, 1058, 756 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{29}NO_7Na$ $[M+H]^+$: 478.1836, found: 478.1840.

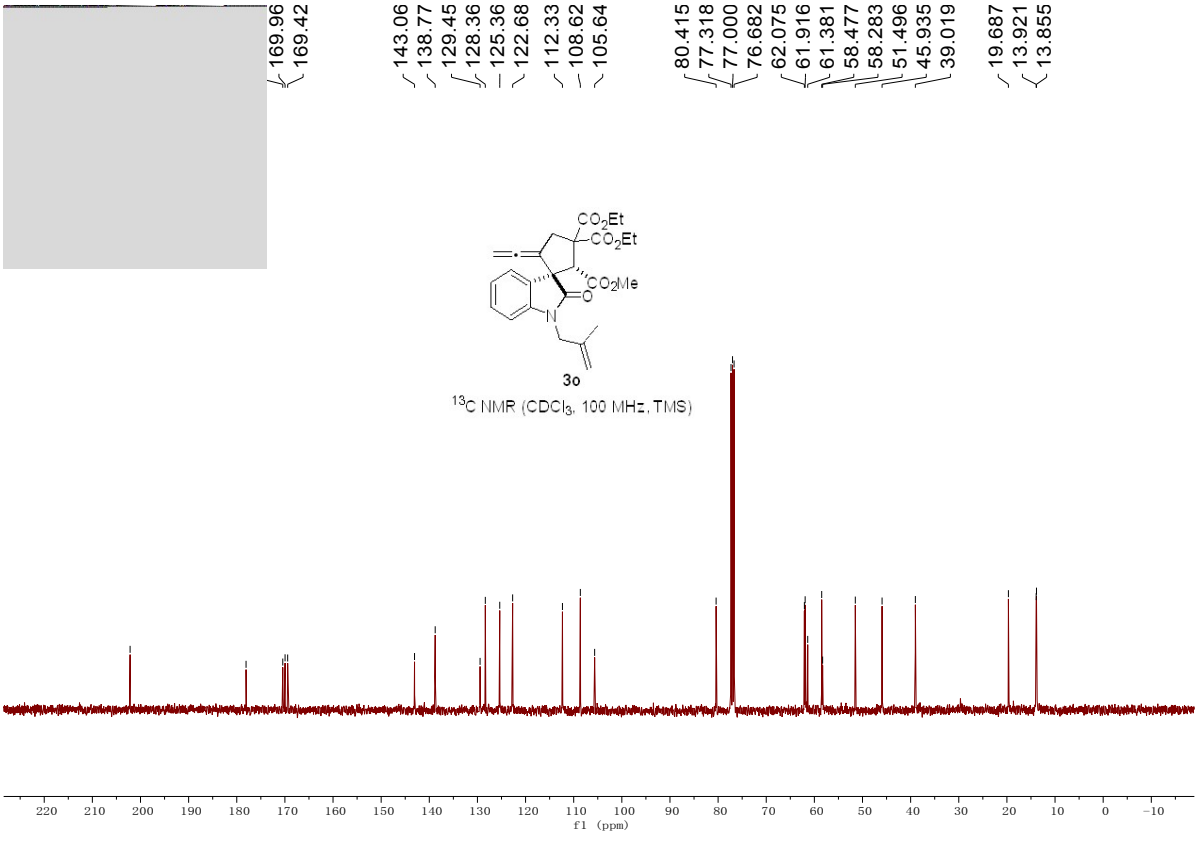


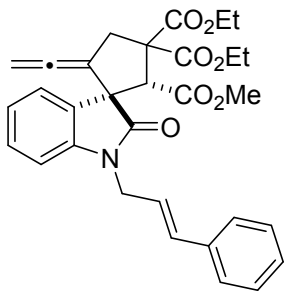




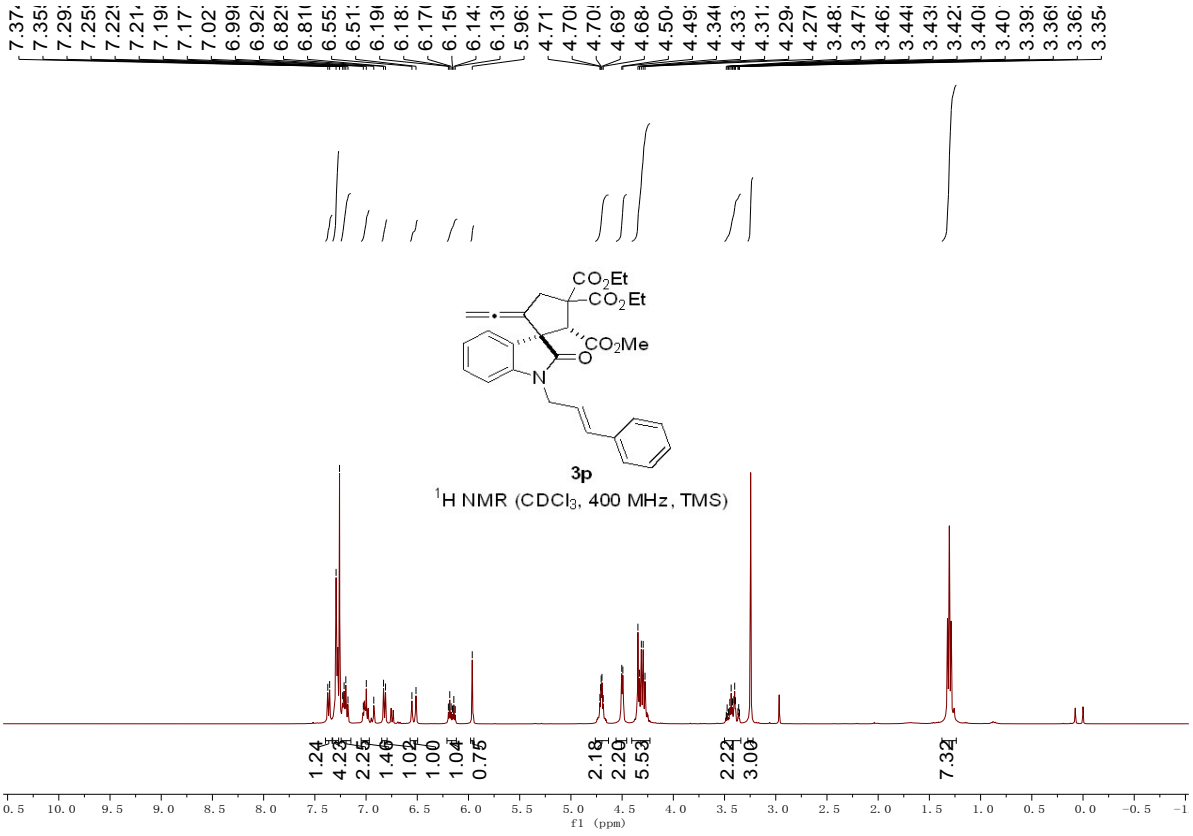
Compound 3o: Yield: 52 mg, 56%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.5; Mp: 125-127 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 7.2 Hz, 1H), 7.23–7.16 (m, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 4.90 (d, *J* = 12.4 Hz, 2H), 4.74–4.61 (m, 2H), 4.37–4.23 (m, 7H), 3.48–3.29 (m, 2H), 3.24 (s, 3H), 1.73 (s, 3H), 1.41–1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.1, 170.4, 170.0, 169.4, 143.1, 138.8, 129.5, 128.4, 125.4, 122.7, 112.3, 108.6, 105.6, 80.4, 62.1, 61.9, 61.4, 58.5, 58.3, 51.5, 45.9, 39.0, 19.7, 13.92, 13.85; IR (neat): ν 2927, 1957, 1740, 1604, 1174, 1024, 758 cm^{-1}; HRMS (ESI) Calcd. for $C_{26}H_{29}NO_7Na$ $[M+H]^+$: 490.1836, found: 490.1829.

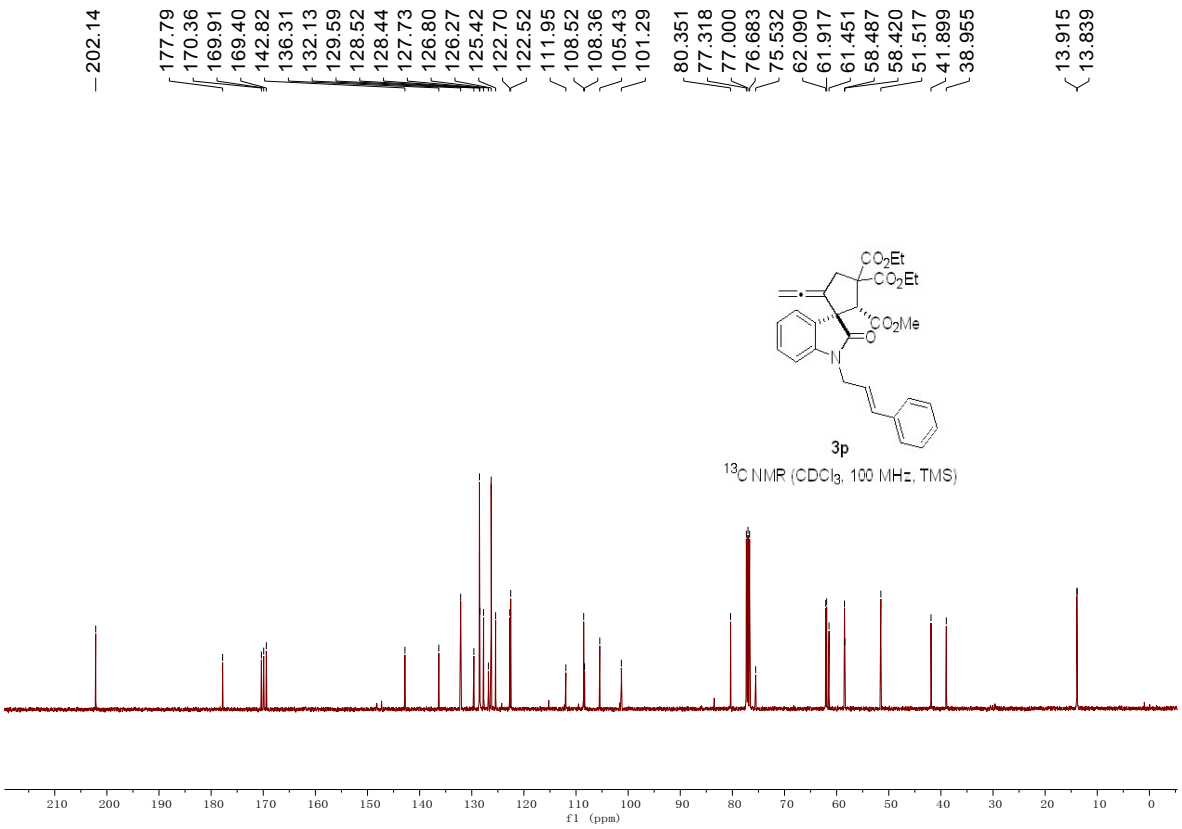

CO2Et
CO2Et
CO2Me
O
N
3o
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)

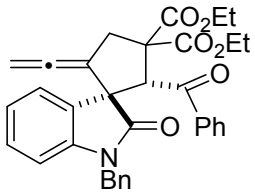

CO2Et
CO2Et
CO2Me
O
N
3o
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)



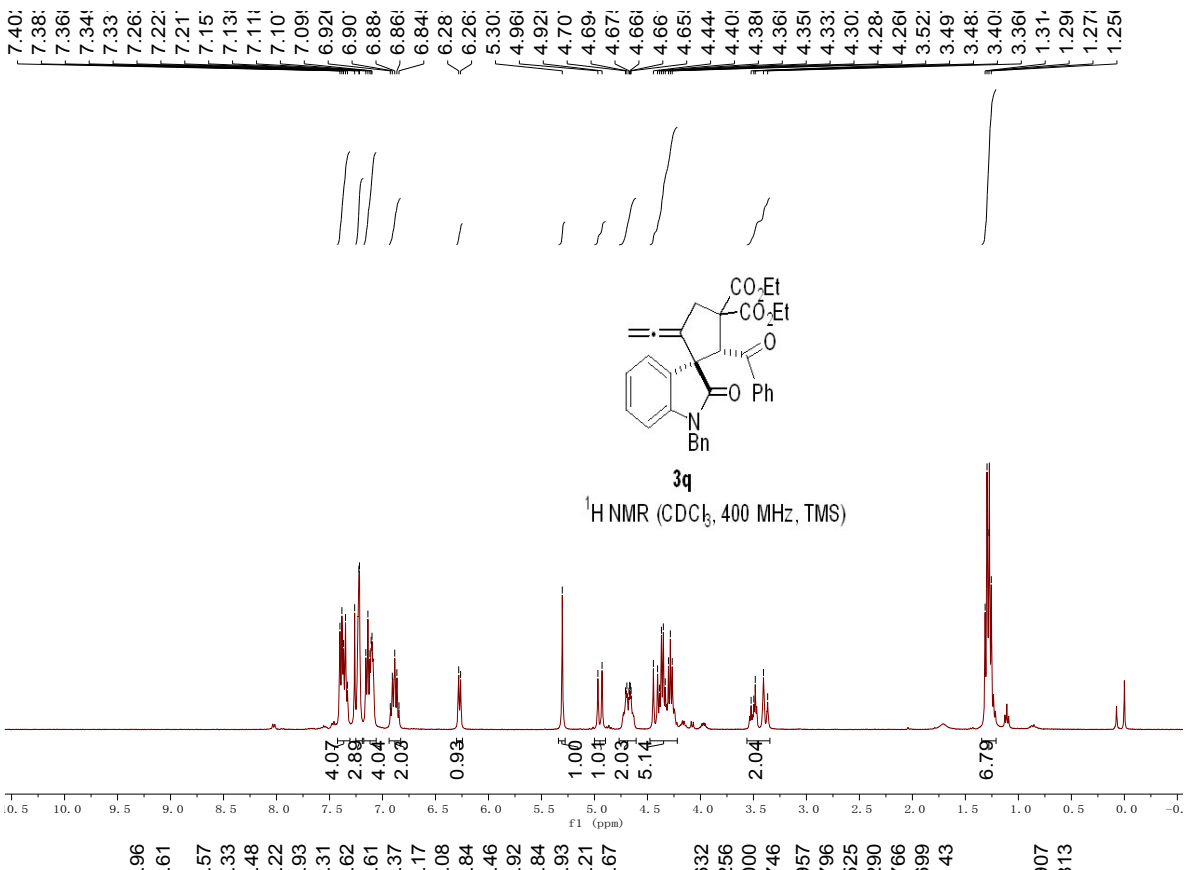
Compound 3p: Yield: 56 mg, 53%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 82-84 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 7.6 Hz, 1H), 7.33–7.27 (m, 3H), 7.24–7.15 (m, 2H), 7.05–6.97 (m, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 16.0 Hz, 1H), 6.16 (dt, *J* = 16.0 Hz, *J* = 4.8 Hz, 1H), 5.96 (s, 1H), 4.76–4.63 (m, 2H), 4.50 (d, *J* = 4.0 Hz, 2H), 4.41–4.23 (m, 5H), 3.50–3.34 (m, 2H), 3.25 (s, 3H), 1.38–1.24 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 177.8, 170.4, 169.9, 169.4, 142.8, 136.3, 132.1, 129.6, 128.5, 128.4, 127.7, 126.8, 126.3, 125.4, 122.7, 122.5, 112.0, 108.5, 108.4, 105.4, 101.3, 80.4, 75.5, 62.1, 61.9, 61.5, 58.5, 58.4, 51.5, 41.9, 39.0, 13.9, 13.8; IR (neat): ν 2951, 2849, 1954, 1711, 1354, 1024, 745 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{31}NO_7Na$ $[M+H]^+$: 552.1992, found: 552.1978.





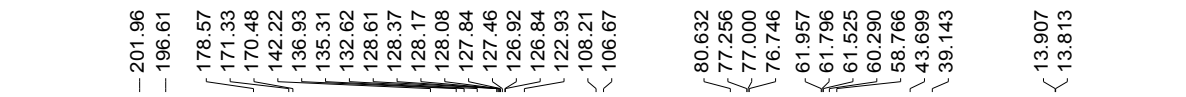


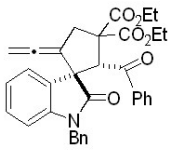
Compound 3q: Yield: 50 mg, 46%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 6:1; R_f = 0.4; Mp: 123-125 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42–7.31 (m, 4H), 7.25–7.19 (m, 3H), 7.18–7.06 (m, 4H), 6.94–6.83 (m, 2H), 6.27 (d, *J* = 7.2 Hz, 1H), 5.30 (s, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.77–4.61 (m, 2H), 4.48–4.22 (m, 5H), 3.56–3.34 (m, 2H), 1.35–1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 196.6, 178.6, 171.3, 170.5, 142.2, 136.9, 135.3, 132.6, 128.6, 128.4, 128.2, 128.1, 127.8, 127.5, 126.9, 126.8, 122.9, 108.2, 106.7, 80.6, 62.0, 61.8, 61.5, 60.3, 58.8, 43.7, 39.1, 13.9, 13.8; IR (neat): ν 3060, 2981, 1963, 1724, 1708, 1610, 1270, 733 cm^{-1}; HRMS (ESI) Calcd. for $C_{34}H_{31}NO_6Na$ $[M+H]^+$: 572.2043, found: 572.2026.



3q

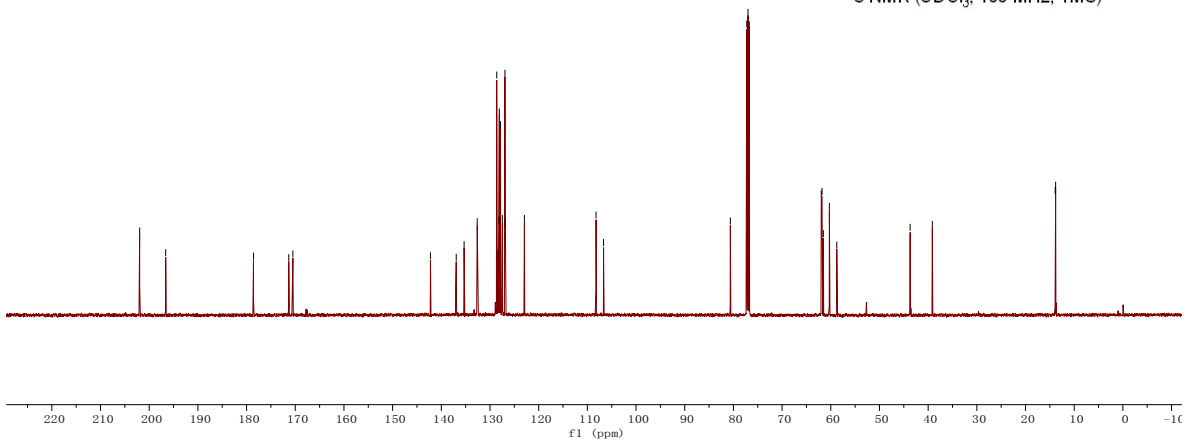
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)

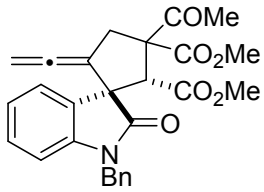




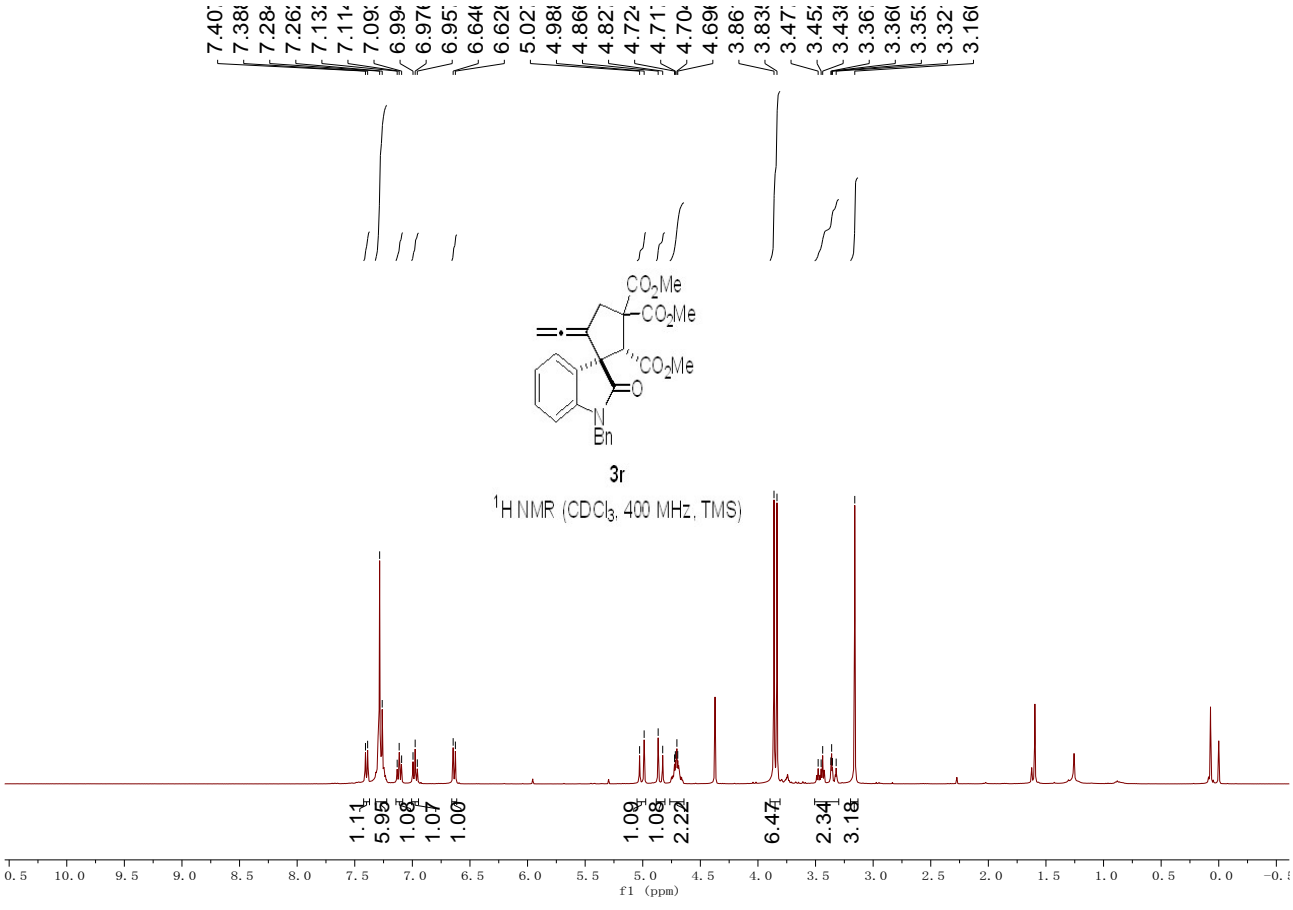
3q

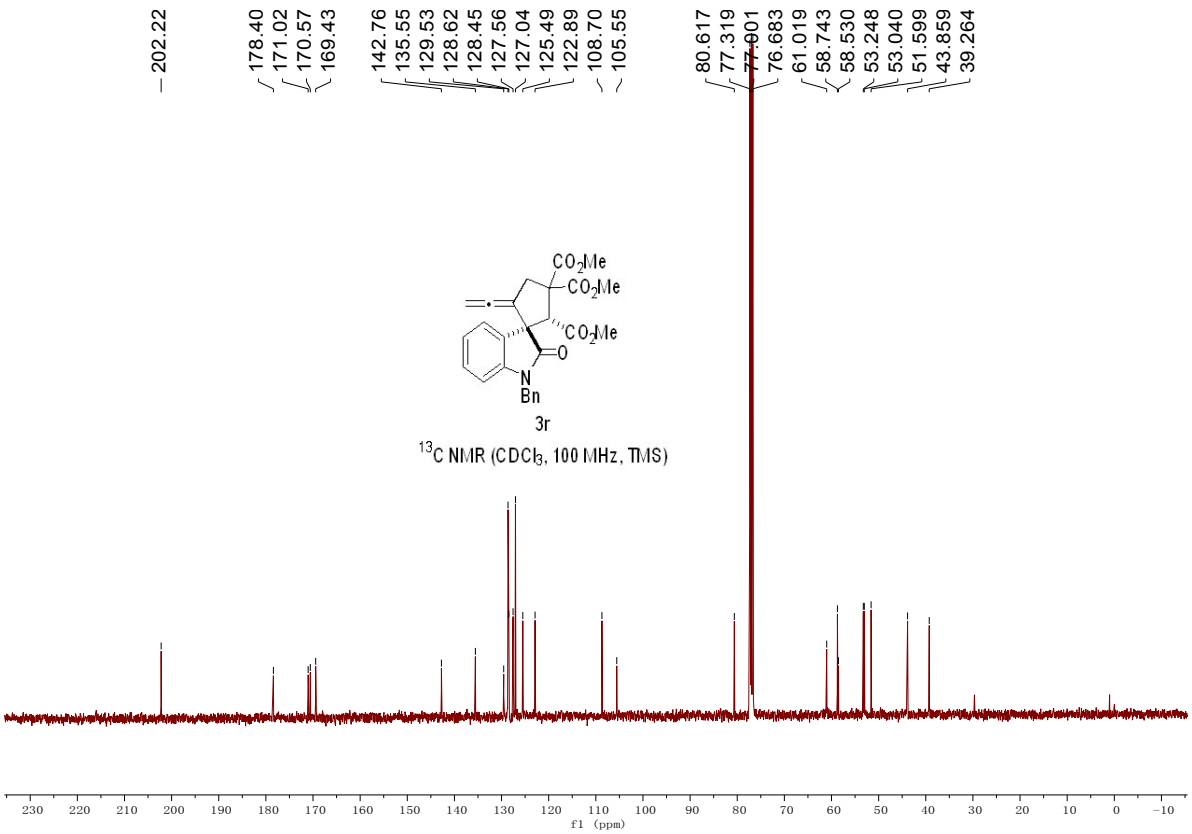
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)

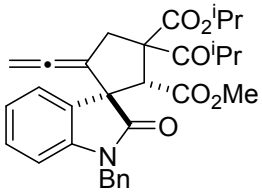




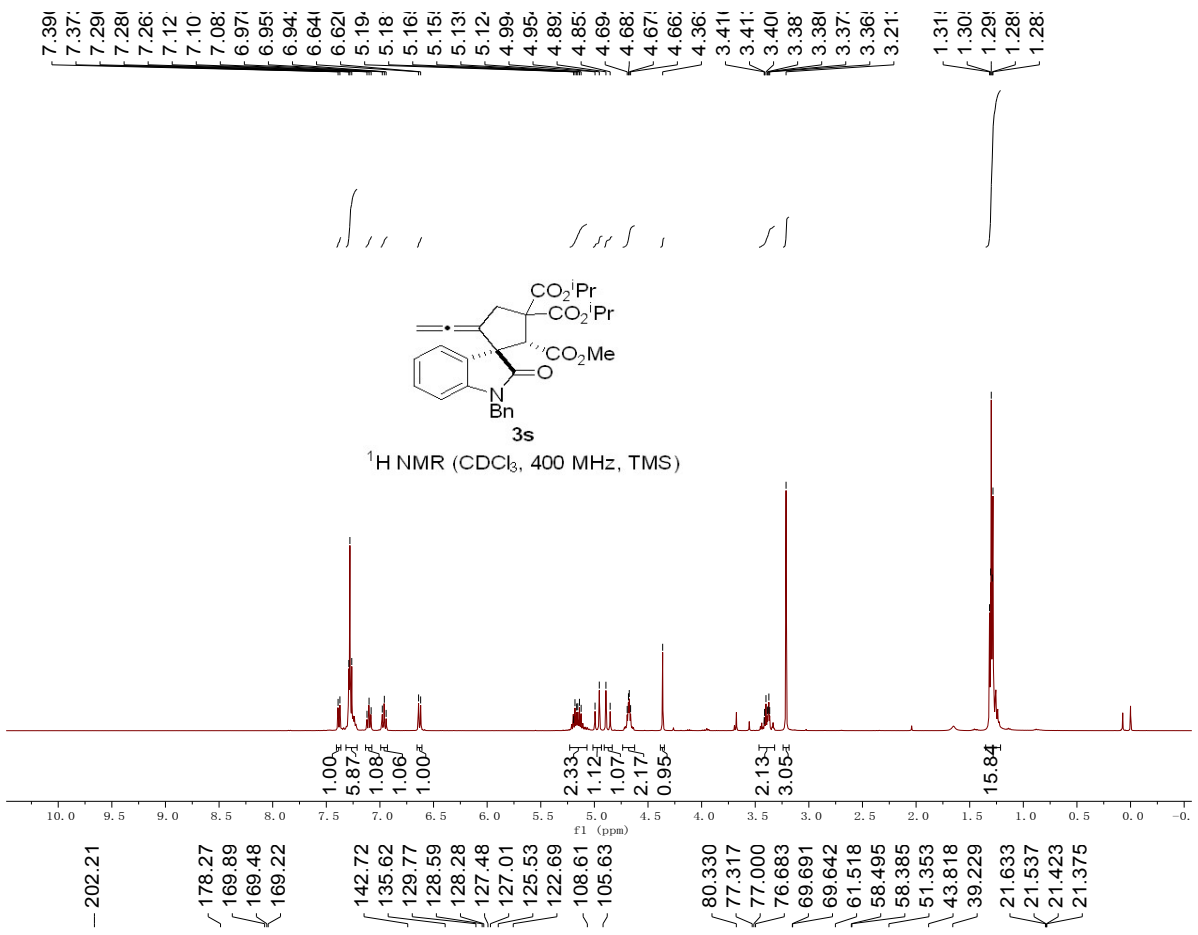
Compound 3r: Yield: 55 mg, 54%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 6:1; R_f = 0.4; Mp: 102-104 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 7.6 Hz, 1H), 7.32–7.22 (m, 5H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 4.85 (d, *J* = 15.6 Hz, 1H), 4.77–4.64 (m, 2H), 3.86 (s, 3H), 3.83 (s, 3H), 3.51–3.30 (m, 2H), 3.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.4, 171.0, 170.6, 169.4, 142.8, 135.6, 129.5, 128.6, 128.5, 127.6, 127.0, 125.5, 122.9, 108.7, 105.6, 80.6, 61.0, 58.7, 58.5, 53.2, 53.0, 51.6, 43.9, 39.3; IR (neat): ν 2919, 2849, 1740, 1722, 1107, 1010, 748, 707 cm^{-1}; HRMS (ESI) Calcd. for $C_{27}H_{25}NO_7Na$ $[M+H]^+$: 498.1523, found: 498.1519.

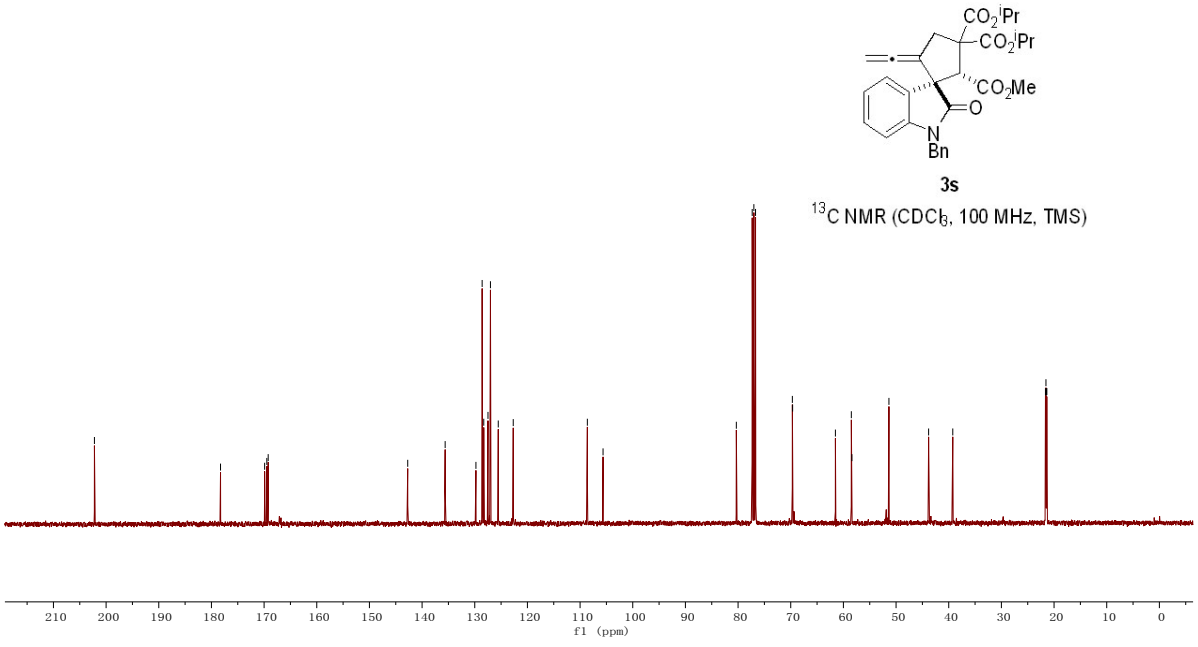


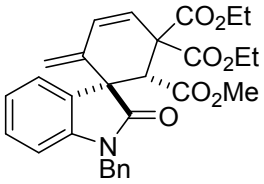




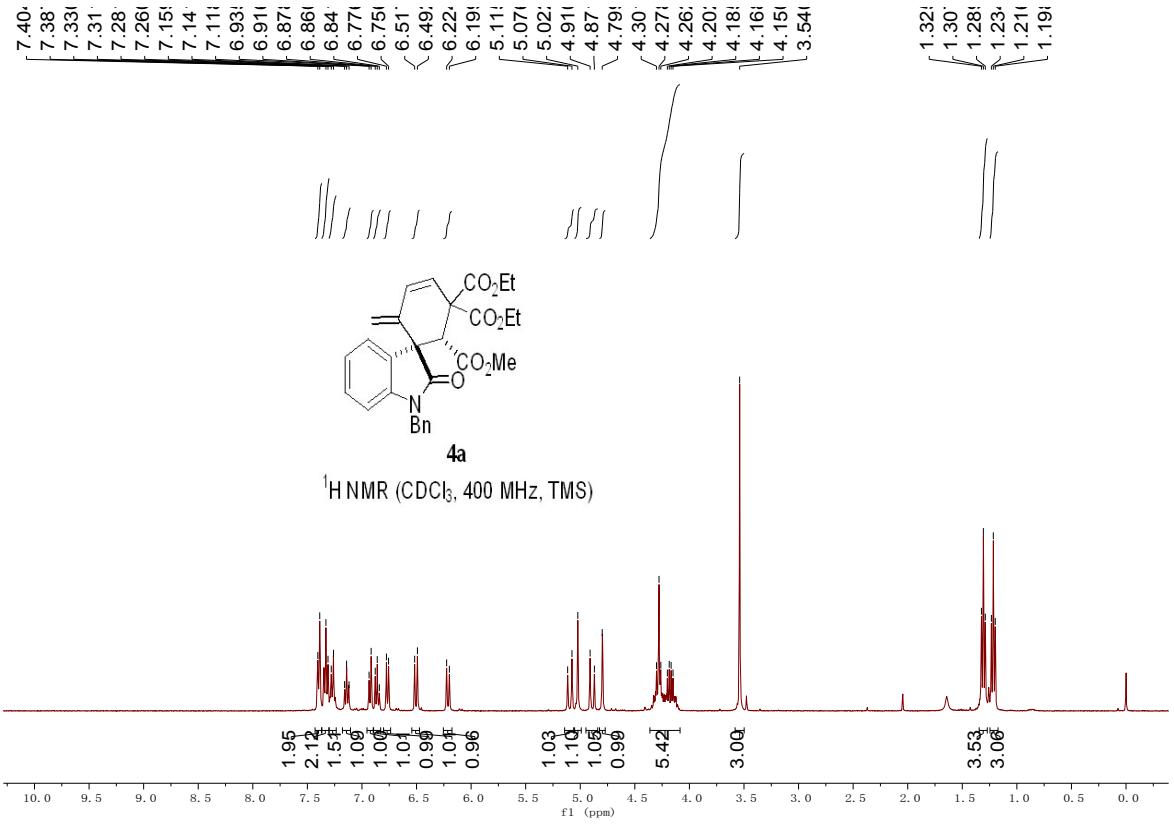
Compound 3s: Yield: 56 mg, 52%; A yellow solid; Eluent: petroleum ether:ethyl acetate = 6:1; R_f = 0.4; Mp: 115-117 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 6.8 Hz, 1H), 7.32–7.21 (m, 6H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 5.23–5.07 (m, 2H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.74–4.62 (m, 2H), 4.36 (s, 1H), 3.46–3.32 (m, 2H), 3.21 (s, 3H), 1.35–1.21 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 178.3, 169.9, 169.5, 169.2, 142.7, 135.6, 129.8, 128.6, 128.3, 127.5, 127.0, 125.5, 122.7, 108.6, 105.6, 80.3, 69.7, 69.6, 61.5, 58.5, 58.4, 51.4, 43.8, 39.2, 21.6, 21.5, 21.42, 21.37; IR (neat): ν 2985, 2853, 1736, 1461, 874, 755, 748, 707 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{33}NO_7Na$ $[M+H]^+$: 554.2149, found: 554.2155.

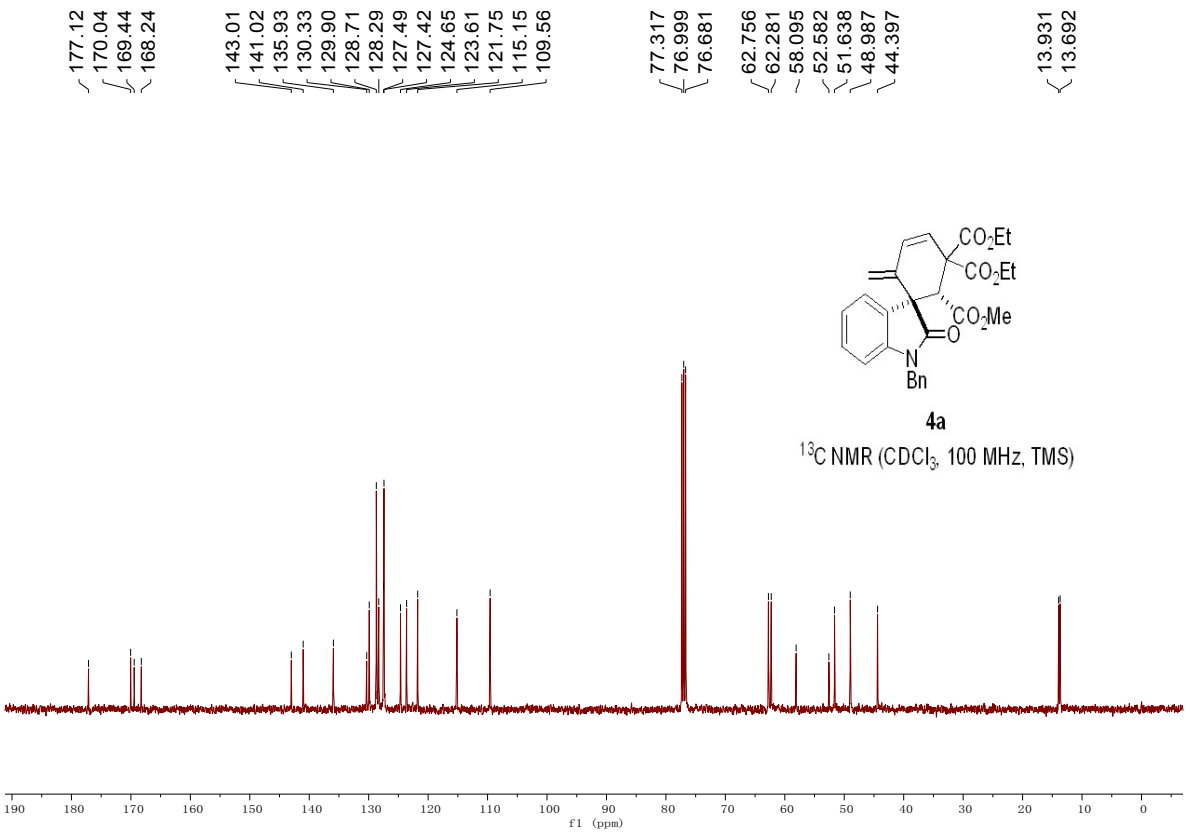

CO2iPr
CO2iPr
CO2Me
O
N
Bn
3s
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)

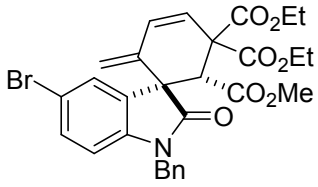

CO2iPr
CO2iPr
CO2Me
O
N
Bn
3s
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)



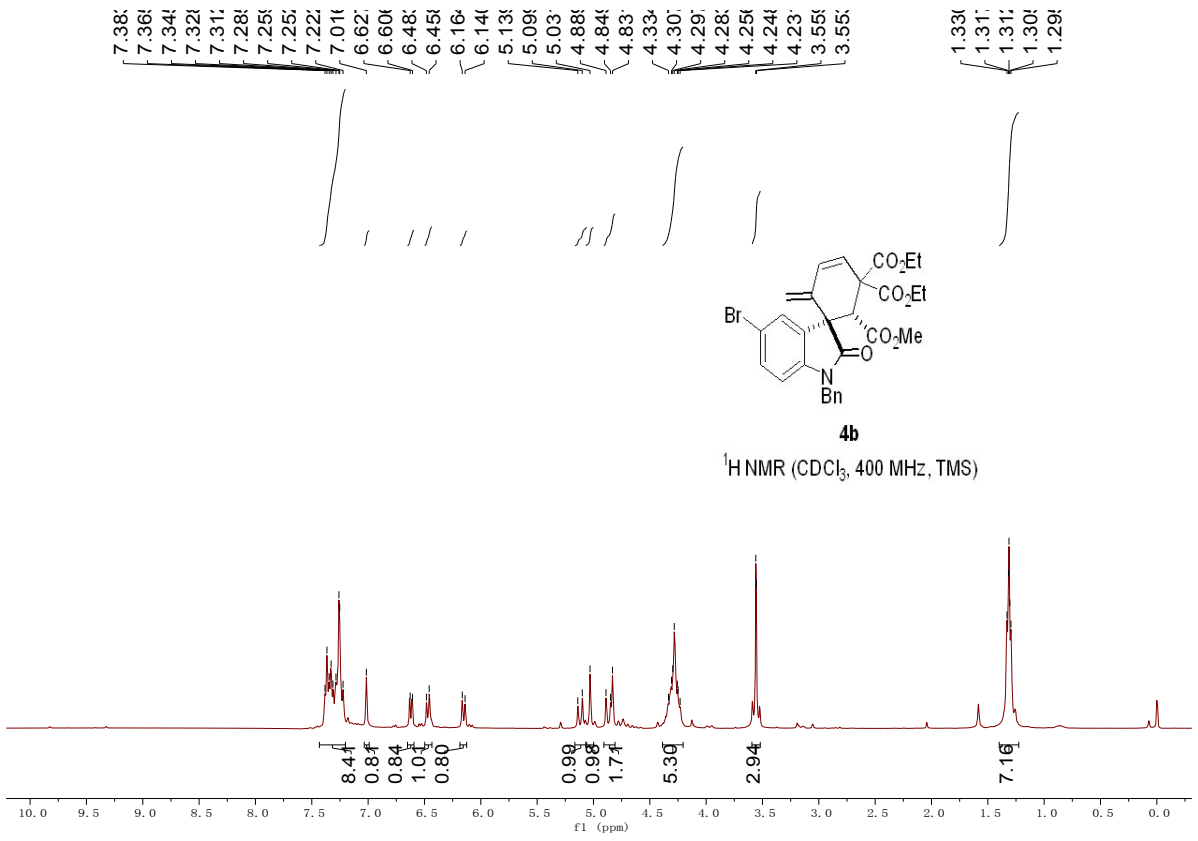
Compound 4a: Yield: 56 mg, 56%, dr: 11:1; A yellow solid; Eluent: petroleum ether:ethyl acetate = 6:1; R_f = 0.3; Mp: 108-111 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 6.8 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.86 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 10.0 Hz, 1H), 6.21 (d, *J* = 10.0 Hz, 1H), 5.10 (d, *J* = 15.6 Hz, 1H), 5.02 (s, 1H), 4.89 (d, *J* = 15.6 Hz, 1H), 4.80 (s, 1H), 4.36–4.09 (m, 5H), 3.54 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 170.0, 169.4, 168.2, 143.0, 141.0, 135.9, 130.3, 129.9, 128.7, 128.3, 127.5, 127.4, 124.6, 123.6, 121.8, 115.2, 109.6, 62.8, 62.3, 58.1, 52.6, 51.6, 49.0, 44.4, 13.9, 13.7; IR (neat): ν 2984, 2942, 1609, 1488, 1466, 1364, 1096, 1028, 747, 698, 672 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{29}NO_7Na^+$: 526.1836, found: 526.1818.

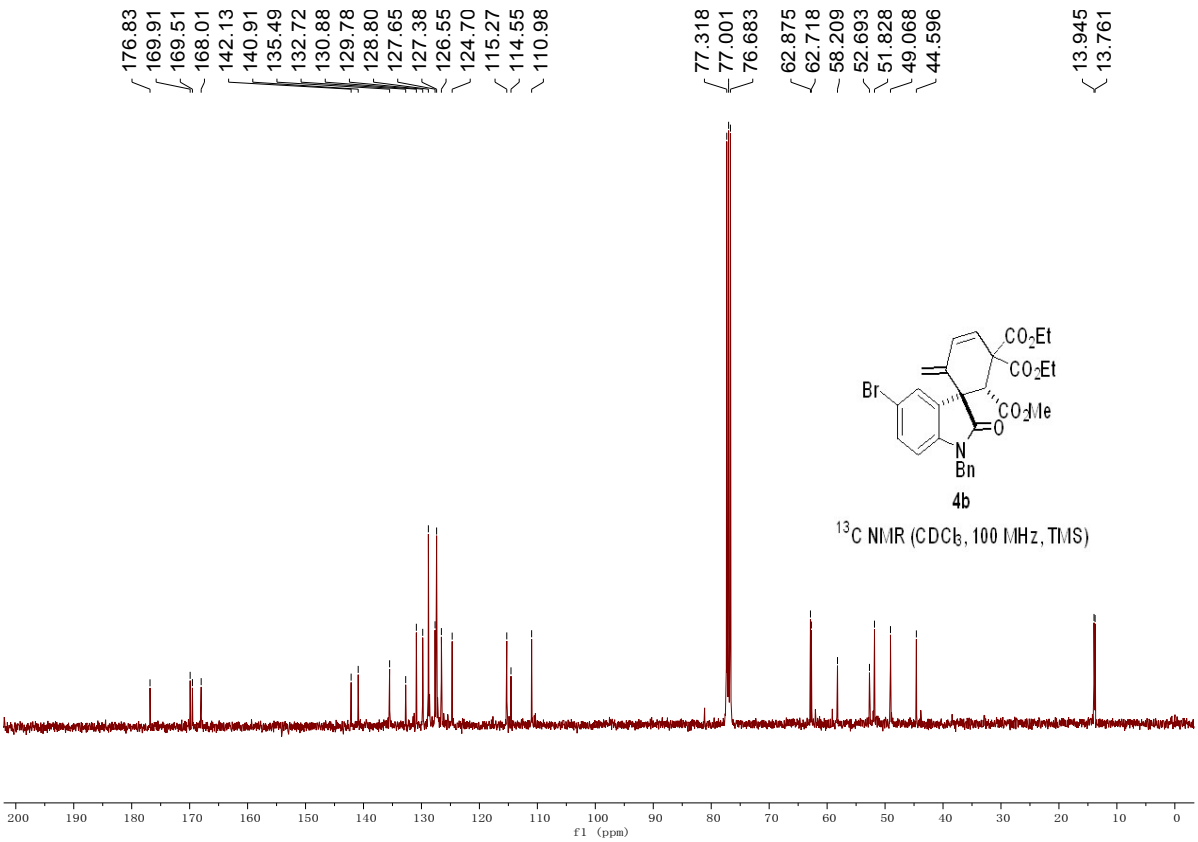


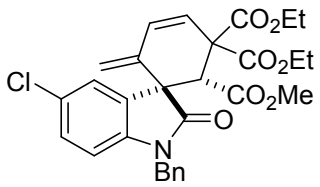




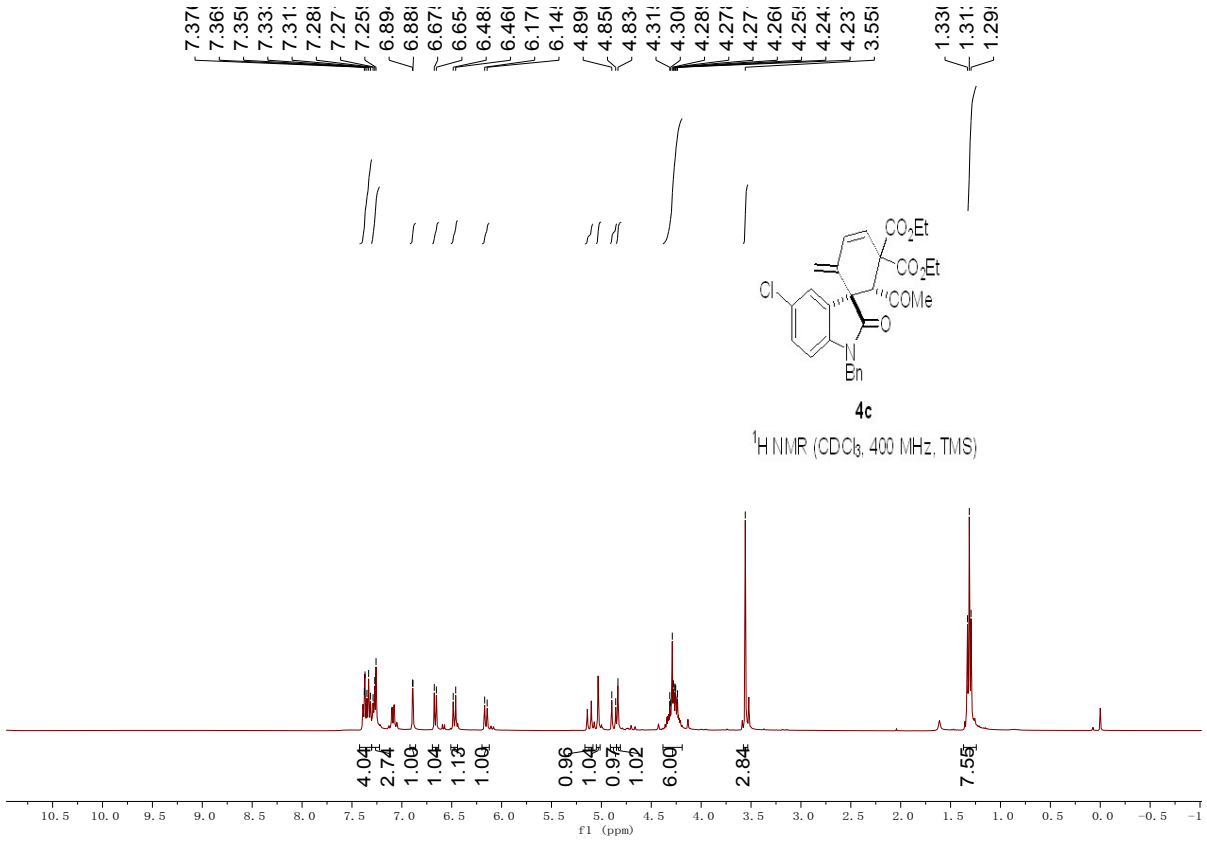
Compound 4b: Yield: 63 mg, 55%, dr: 9:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 6:1; R_f = 0.3; Mp: 148-150 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.43–7.20 (m, 6H), 7.02 (s, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 10.0 Hz, 1H), 6.15 (d, *J* = 9.6 Hz, 1H), 5.12 (d, *J* = 16.0 Hz, 1H), 5.03 (s, 1H), 4.91–4.81 (m, 2H), 4.39–4.20 (m, 5H), 3.56 (s, 3H), 1.40–1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 169.9, 169.5, 168.0, 142.1, 140.9, 135.5, 132.7, 130.9, 129.8, 128.8, 127.7, 127.4, 126.6, 124.7, 115.3, 114.6, 111.0, 62.9, 62.7, 58.2, 52.7, 51.8, 49.1, 44.6, 13.9, 13.8; IR (neat): ν 2979, 2943, 1748, 1735, 1712, 1602, 1479, 1304, 1198, 699 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaBr$ $[M+H]^+$: 604.0941, found: 604.0927.

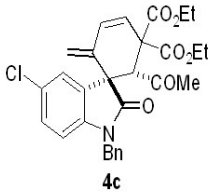

CO2Et
CO2Et
CO2Me
Br
O
N
Bn
4b
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)


CO2Et
CO2Et
CO2Me
Br
O
N
Bn
4b
13C NMR (CDCl3, 100 MHz, TMS)
f1 (ppm)



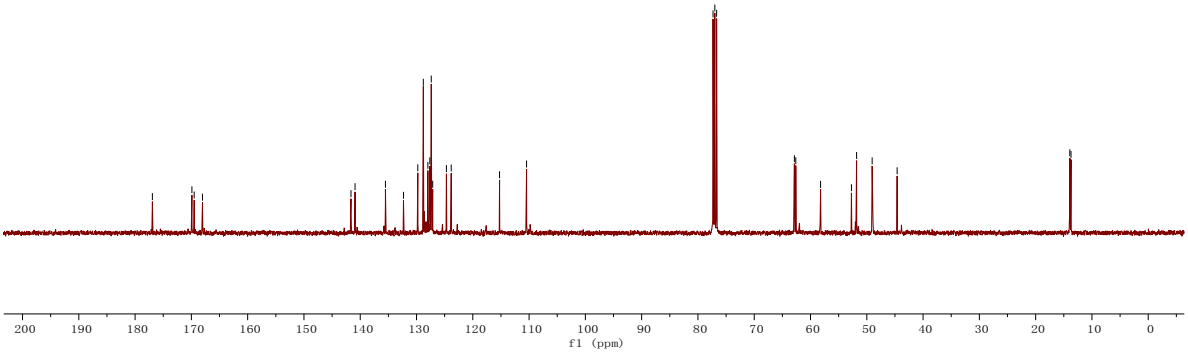
Compound 4c: Yield: 66 mg, 62%, dr: 6:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 125-127 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42–7.30 (m, 4H), 7.30–7.22 (m, 2H), 6.89 (s, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 10.0 Hz, 1H), 6.16 (d, *J* = 10.0 Hz, 1H), 5.12 (d, *J* = 16.0 Hz, 1H), 5.03 (s, 1H), 4.88 (d, *J* = 16.0 Hz, 1H), 4.83 (s, 1H), 4.38–4.19 (m, 5H), 3.56 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 169.9, 169.5, 168.0, 141.6, 140.9, 135.5, 132.3, 129.8, 128.8, 128.0, 127.6, 127.4, 127.1, 124.7, 123.8, 115.2, 110.4, 62.9, 62.6, 58.2, 52.7, 51.8, 49.0, 44.6, 13.9, 13.7; IR (neat): ν 2982, 2938, 1749, 1711, 1269, 1217, 1199, 823, 756 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaCl$ $[M+H]^+$: 560.1446, found: 560.1443.

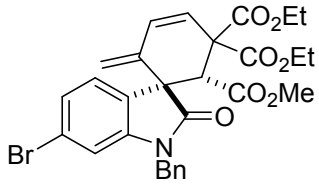




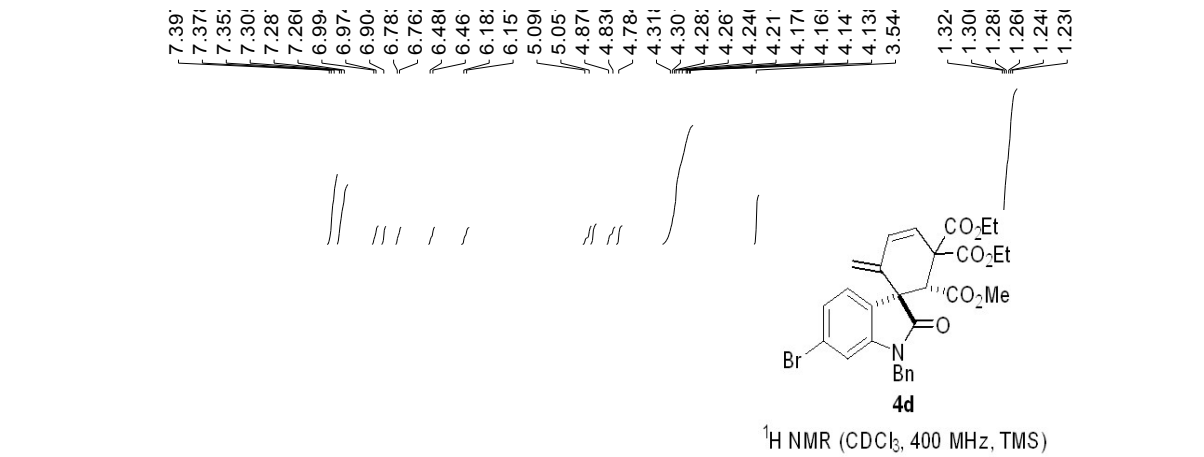
4c

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



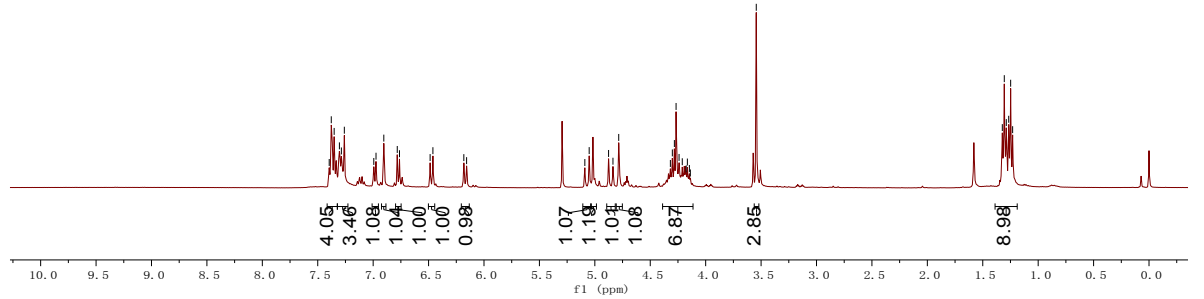


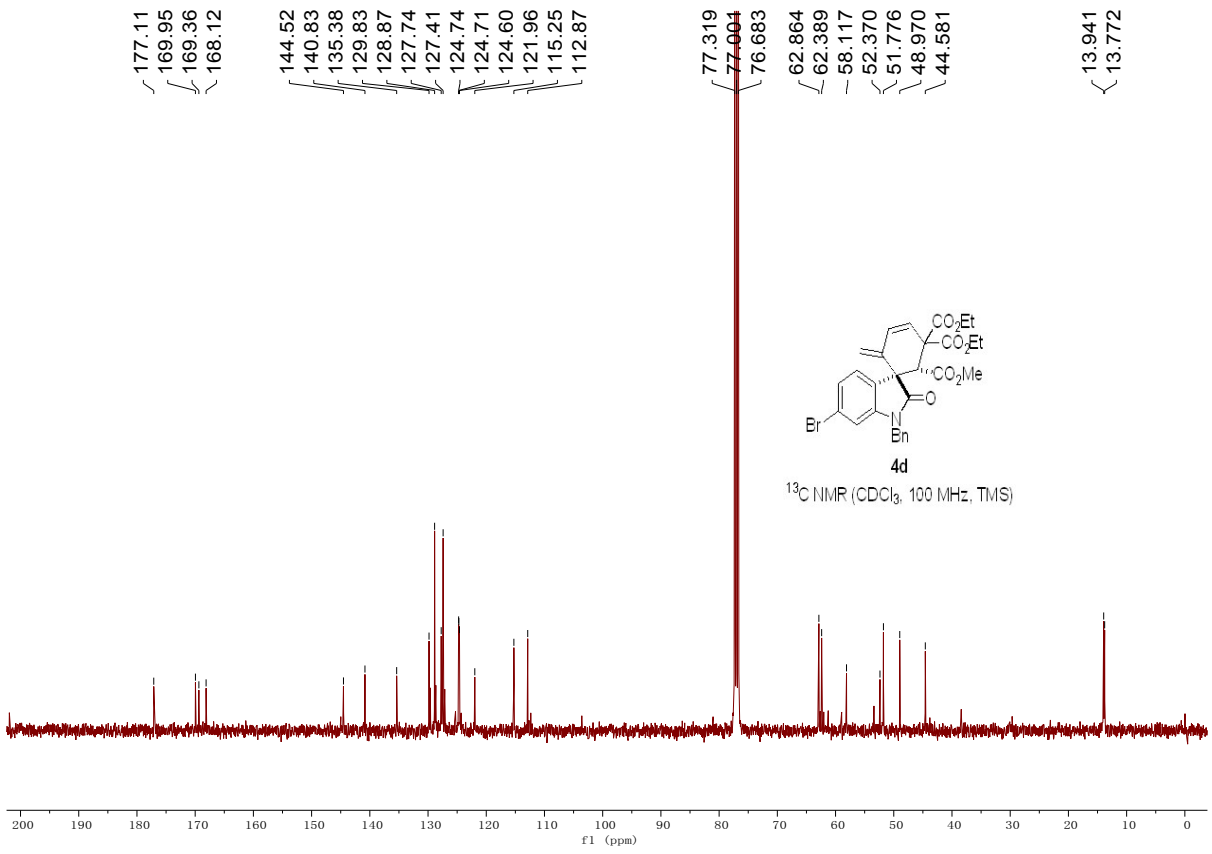
Compound 4d: Yield: 67 mg, 57%, dr: 9:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 115-117 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42–7.32 (m, 3H), 7.32–7.23 (m, 2H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.90 (s, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 5.07 (d, *J* = 15.6 Hz, 1H), 5.01 (d, *J* = 7.2 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.78 (s, 1H), 4.39–4.11 (m, 5H), 3.54 (s, 3H), 1.28 (dt, *J* = 24.0 Hz, *J* = 7.2 Hz, 6H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 170.0, 169.4, 168.1, 144.5, 140.8, 135.4, 129.8, 128.9, 127.7, 127.4, 124.74, 124.71, 124.6, 122.0, 115.3, 112.9, 62.9, 62.4, 58.1, 52.4, 51.8, 49.0, 44.6, 13.9, 13.8; IR (neat): ν 2982, 1720, 1600, 1275, 1197, 1070, 1025, 700 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{28}NO_7NaBr$ $[M+H]^+$: 604.0941, found: 604.0927.



4d

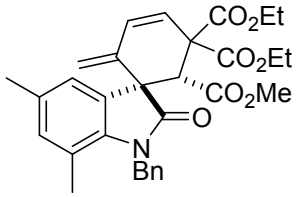
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)



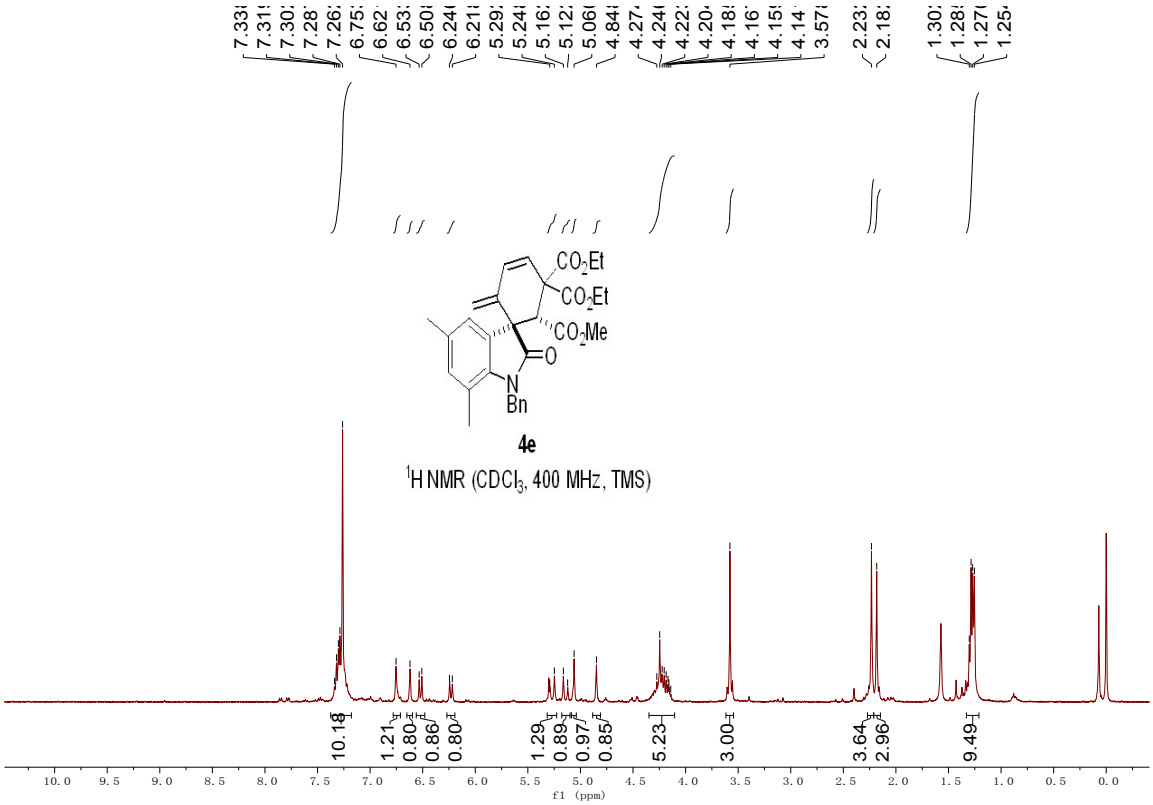


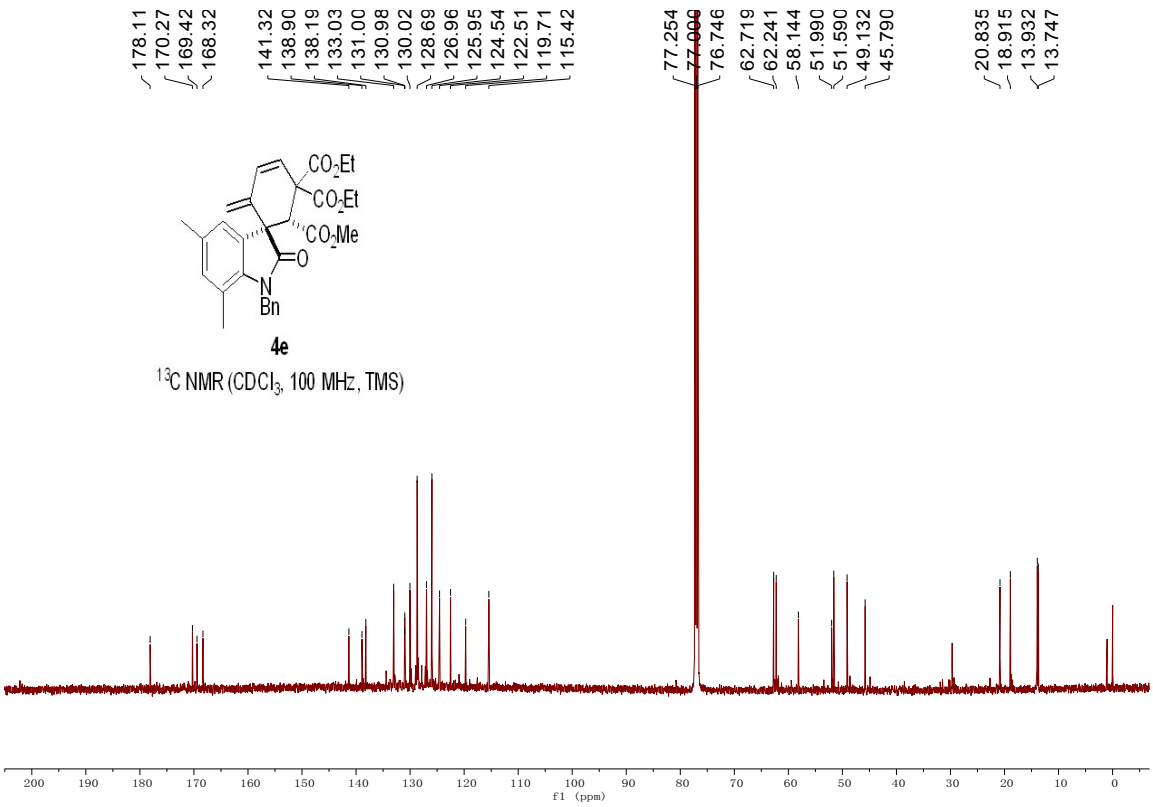
4d

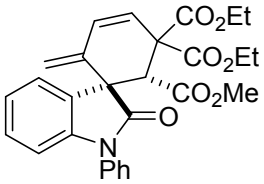
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



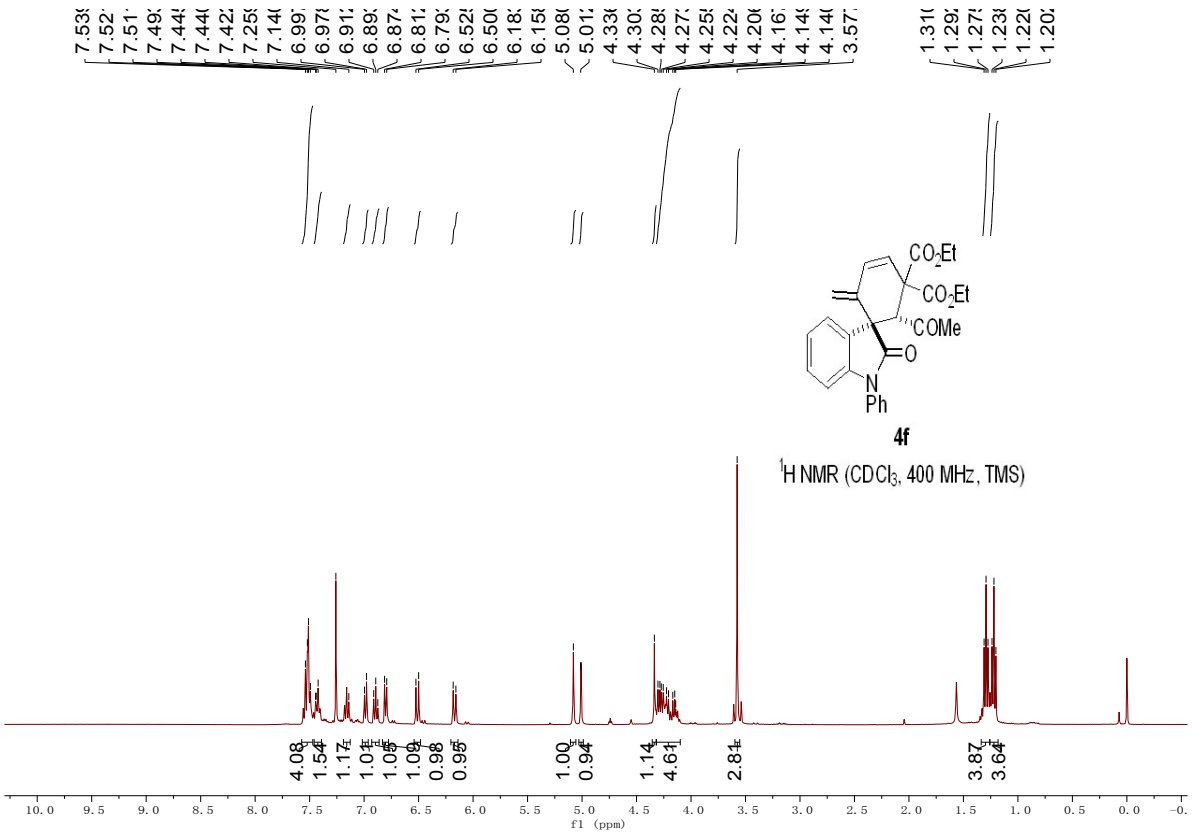
Compound 4e Yield: 50 mg, 48%, dr: 6:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 145-147 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37–7.18 (m, 5H), 6.75 (s, 1H), 6.62 (s, 1H), 6.52 (d, *J* = 10.0 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.27 (d, *J* = 16.8 Hz, 1H), 5.14 (d, *J* = 16.8 Hz, 1H), 5.06 (s, 1H), 4.85 (s, 1H), 4.37–4.10 (m, 5H), 3.58 (s, 3H), 2.23 (s, 3H), 2.18 (s, 3H), 1.3– 1.19 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 170.3, 169.4, 168.3, 141.3, 138.9, 138.2, 133.0, 131.0, 130.0, 128.7, 127.0, 125.9, 124.5, 122.5, 119.7, 115.4, 62.7, 62.2, 58.1, 52.0, 51.6, 49.1, 45.8, 20.8, 18.9, 13.9, 13.7.; IR (neat): ν 3379, 1748, 1735, 11712, 1267, 1176, 1102, 738, 674 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{34}NO_7$ $[M+H]^+$: 532.2329, found: 532.2138.





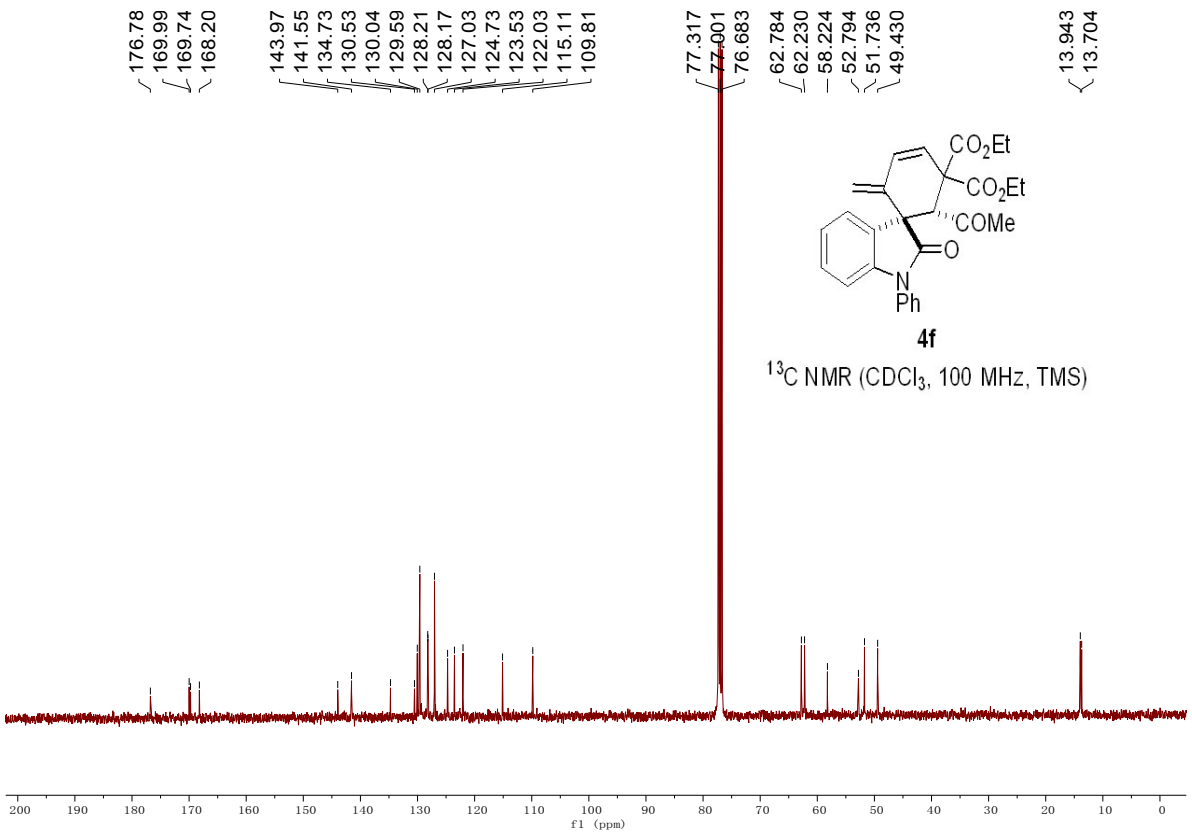


Compound 4f: Yield: 37 mg, 38%, dr: 7:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 185-187 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57–7.47 (m, 4H), 7.46–7.39 (m, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.51 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 5.08 (s, 1H), 5.01 (s, 1H), 4.34 (s, 1H), 4.32–4.10 (m, 4H), 3.58 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 170.0, 169.7, 168.2, 144.0, 141.5, 134.7, 130.5, 130.0, 129.6, 128.21, 128.17, 127.0, 124.7, 123.5, 122.0, 115.1, 109.8, 62.8, 62.2, 58.2, 52.8, 51.7, 49.4, 13.9, 13.7; IR (neat): ν 3379, 3337, 1739, 1722, 1604, 1372, 1202, 757, 738, 674 cm^{-1}; HRMS (ESI) Calcd. for $C_{28}H_{27}NO_7Na$ $[M+H]^+$: 512.1679, found: 512.1671.



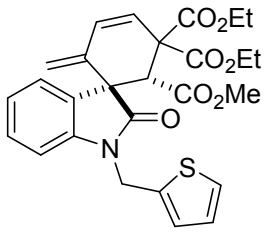
4f

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

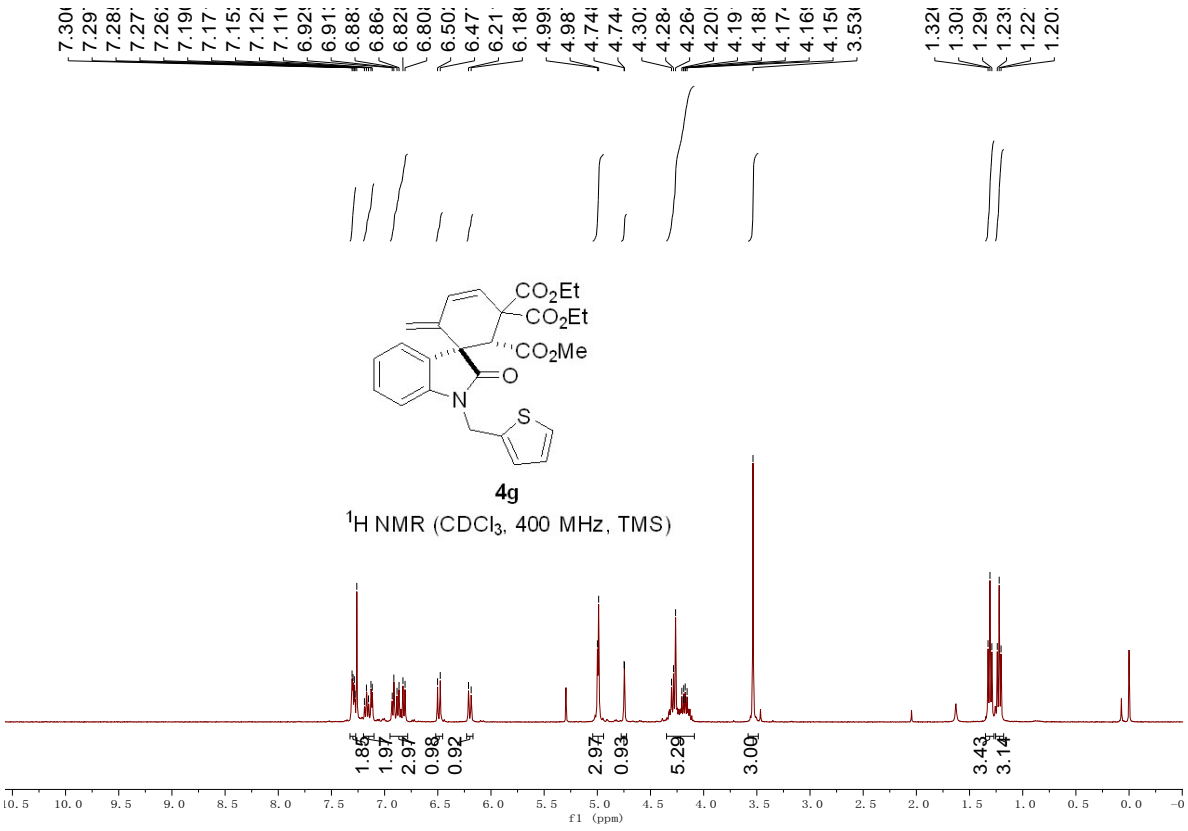


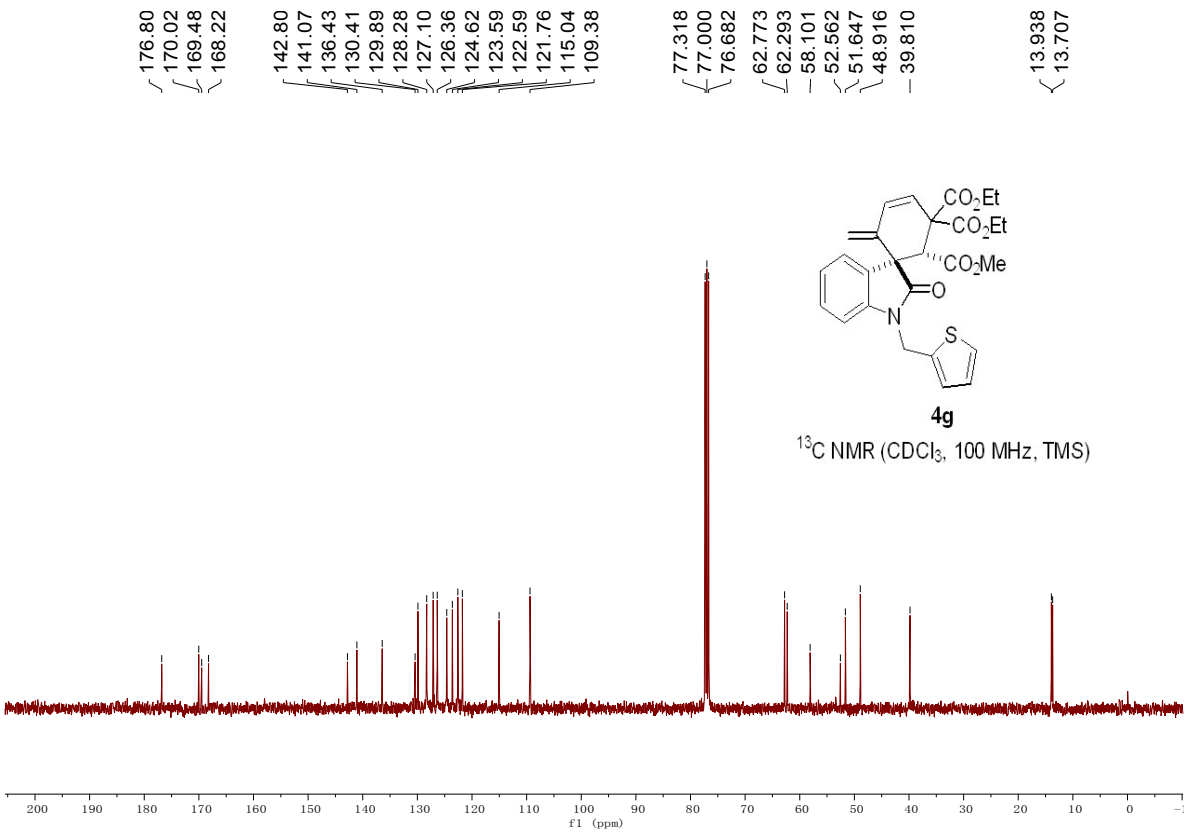
4f

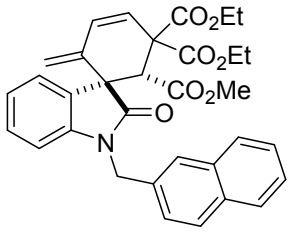
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



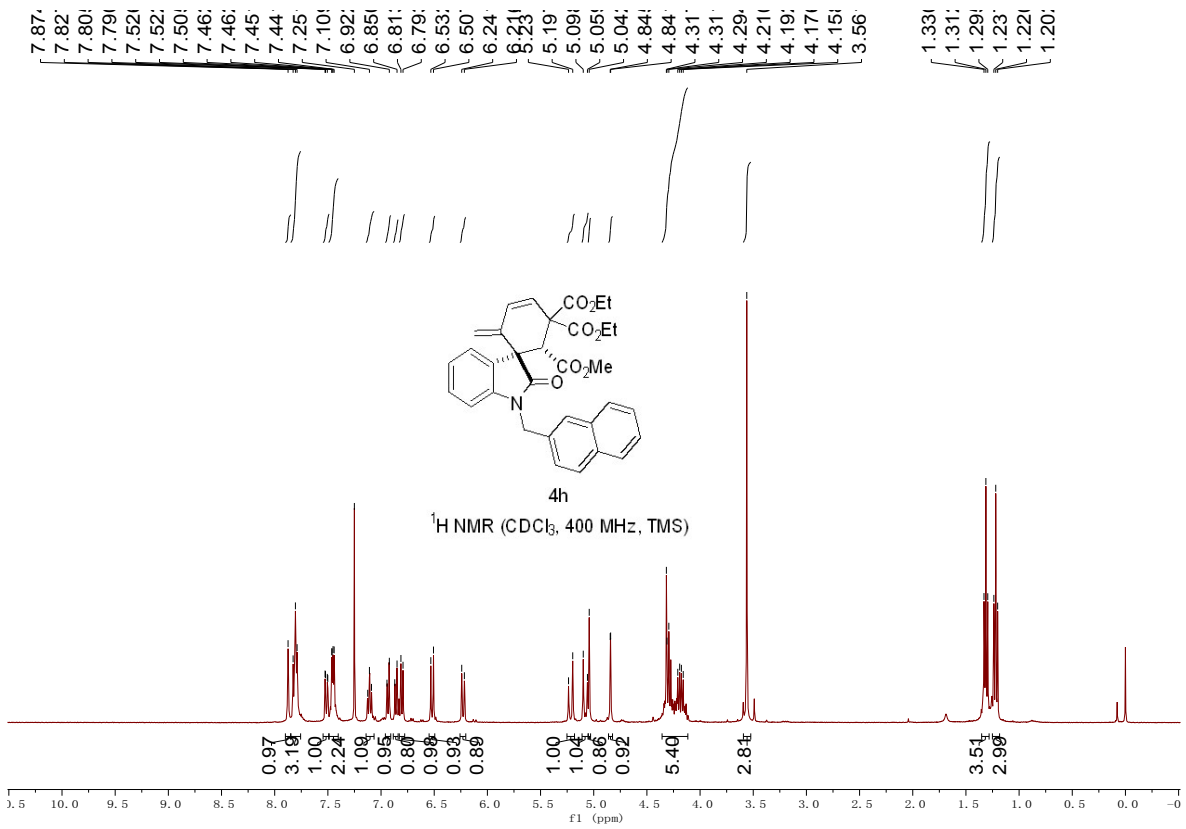
Compound 4g: Yield: 54 mg, 53%, dr: 9:1; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 110-112 °C; ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.33–7.27 (m, 2H), 7.20–7.10 (m, 2H), 6.95–6.78 (m, 3H), 6.49 (d, *J* = 10.0 Hz, 1H), 6.20 (d, *J* = 10.0 Hz, 1H), 5.04–4.94 (m, 3H), 4.75 (d, *J* = 1.6 Hz, 1H), 4.35–4.09 (m, 5H), 3.54 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 176.8, 170.0, 169.5, 168.2, 142.8, 141.1, 136.4, 130.4, 129.9, 128.3, 127.1, 126.4, 124.6, 123.6, 122.6, 121.8, 115.0, 109.4, 62.8, 62.3, 58.1, 52.6, 51.6, 48.9, 39.8, 13.9, 13.7; IR (neat): ν 3381, 2977, 1711, 1604, 1487, 1196, 1068, 688, 670 cm^{-1}; HRMS (ESI) Calcd. for $C_{27}H_{27}NO_7NaS$ $[M+H]^+$: 532.1400, found: 532.1385.





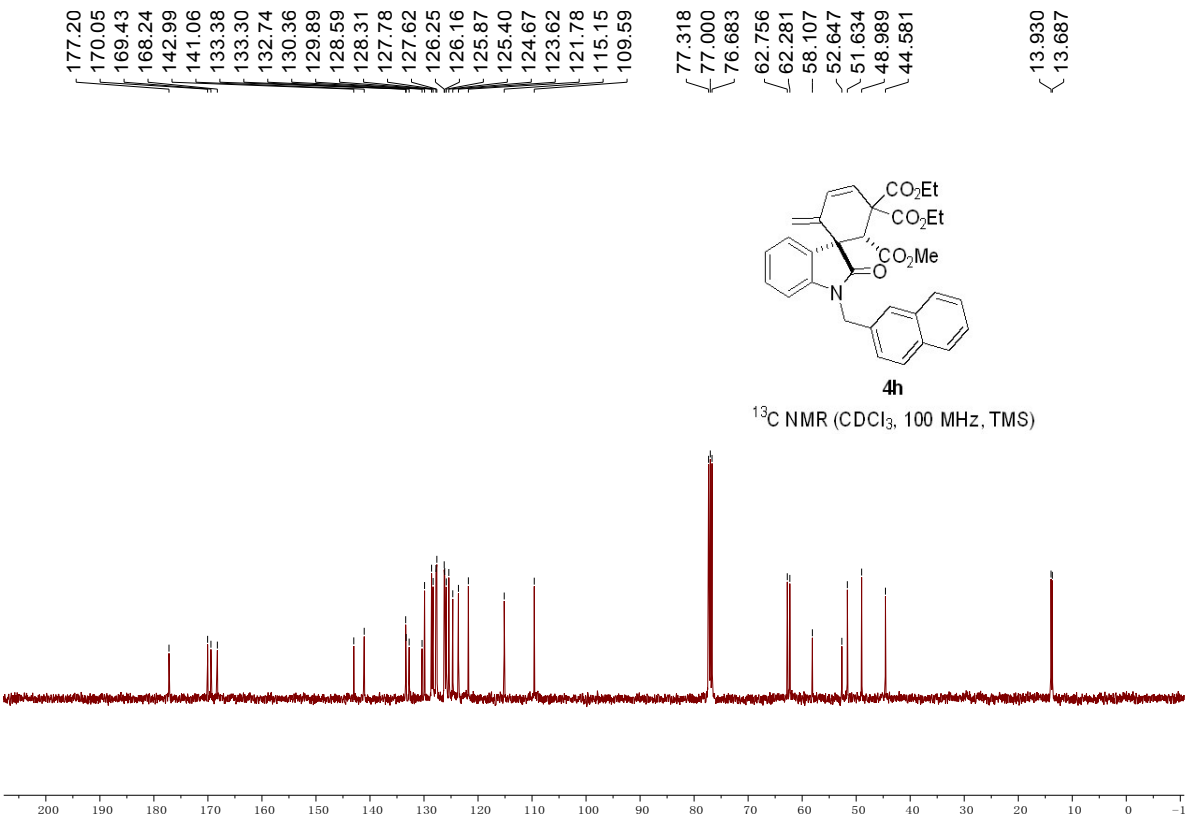


Compound 4h: Yield: 68 mg, 52%, dr:8:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 97-98 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.87 (s, 1H), 7.85–7.76 (m, 3H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.49–7.40 (m, 2H), 7.11 (t, *J* = 6.4 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 10.0 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.22 (d, *J* = 16.0 Hz, 1H), 5.08 (d, *J* = 16.0 Hz, 1H), 5.04 (s, 1H), 4.84 (s, 1H), 4.36–4.11 (m, 5H), 3.56 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 170.1, 169.4, 168.2, 143.0, 141.1, 133.4, 133.3, 132.7, 130.4, 129.9, 128.6, 128.3, 127.8, 127.6, 126.3, 126.2, 125.9, 125.4, 124.7, 123.6, 121.8, 115.2, 109.6, 62.8, 62.3, 58.1, 52.6, 51.6, 49.0, 44.6, 13.9, 13.7; IR (neat): ν 2977, 2943, 17732, 1712, 1608, 1487, 1197, 747 cm^{-1}; HRMS (ESI) Calcd. for $C_{33}H_{31}NO_7Na$ $[M+H]^+$: 576.1992, found: 576.2001.



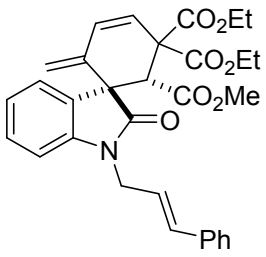
4h

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

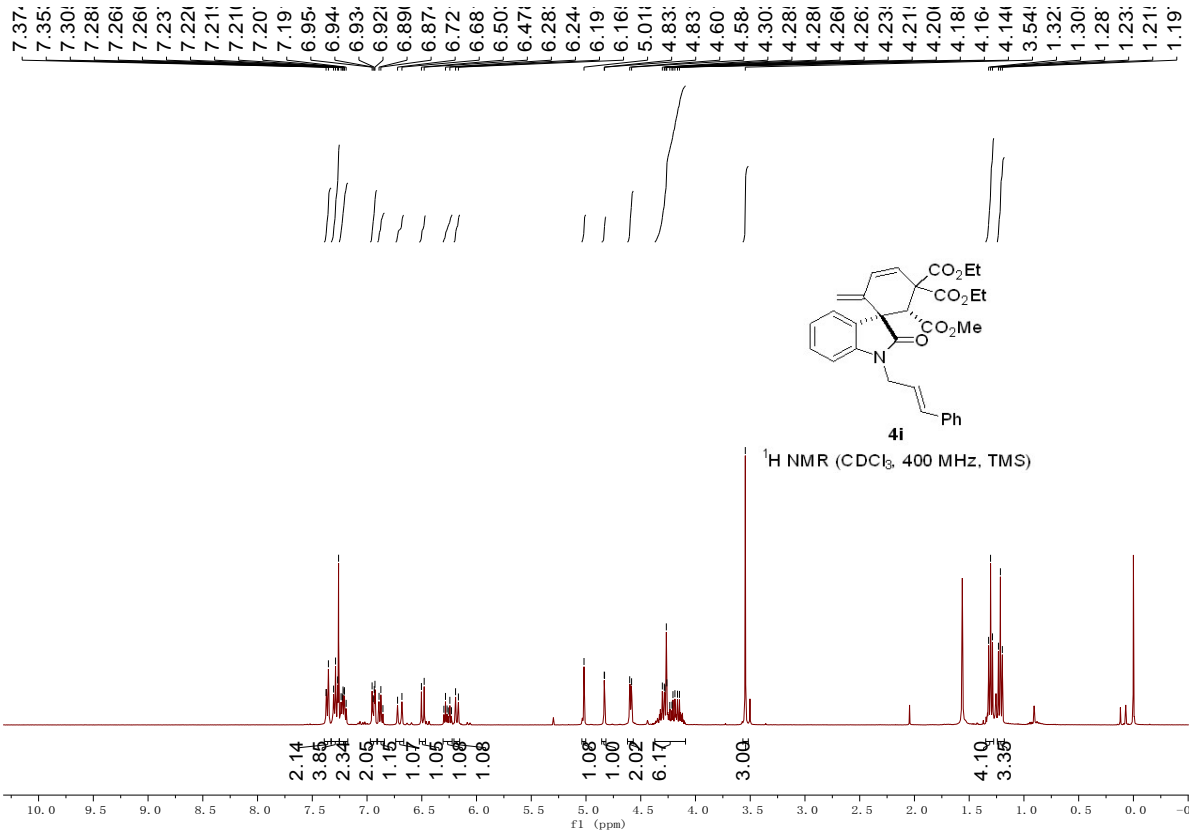


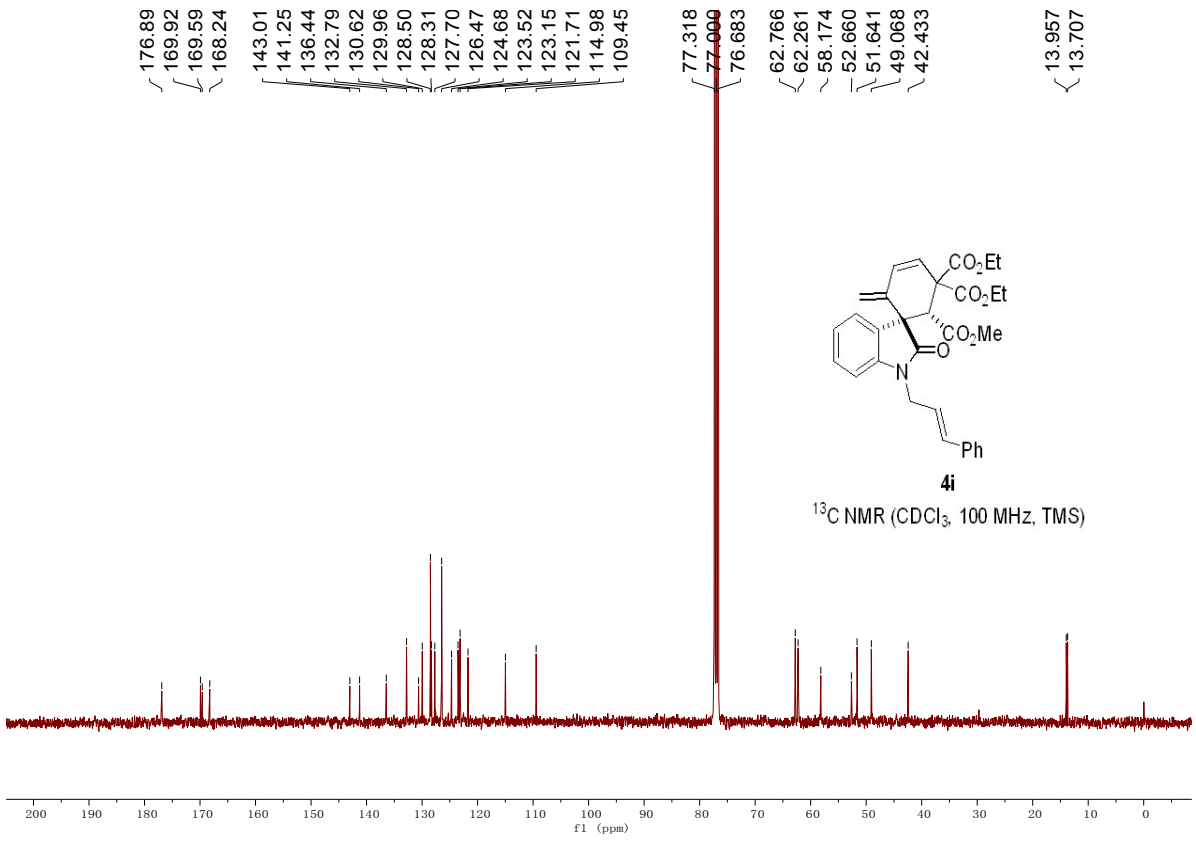
4h

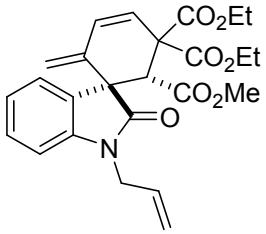
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



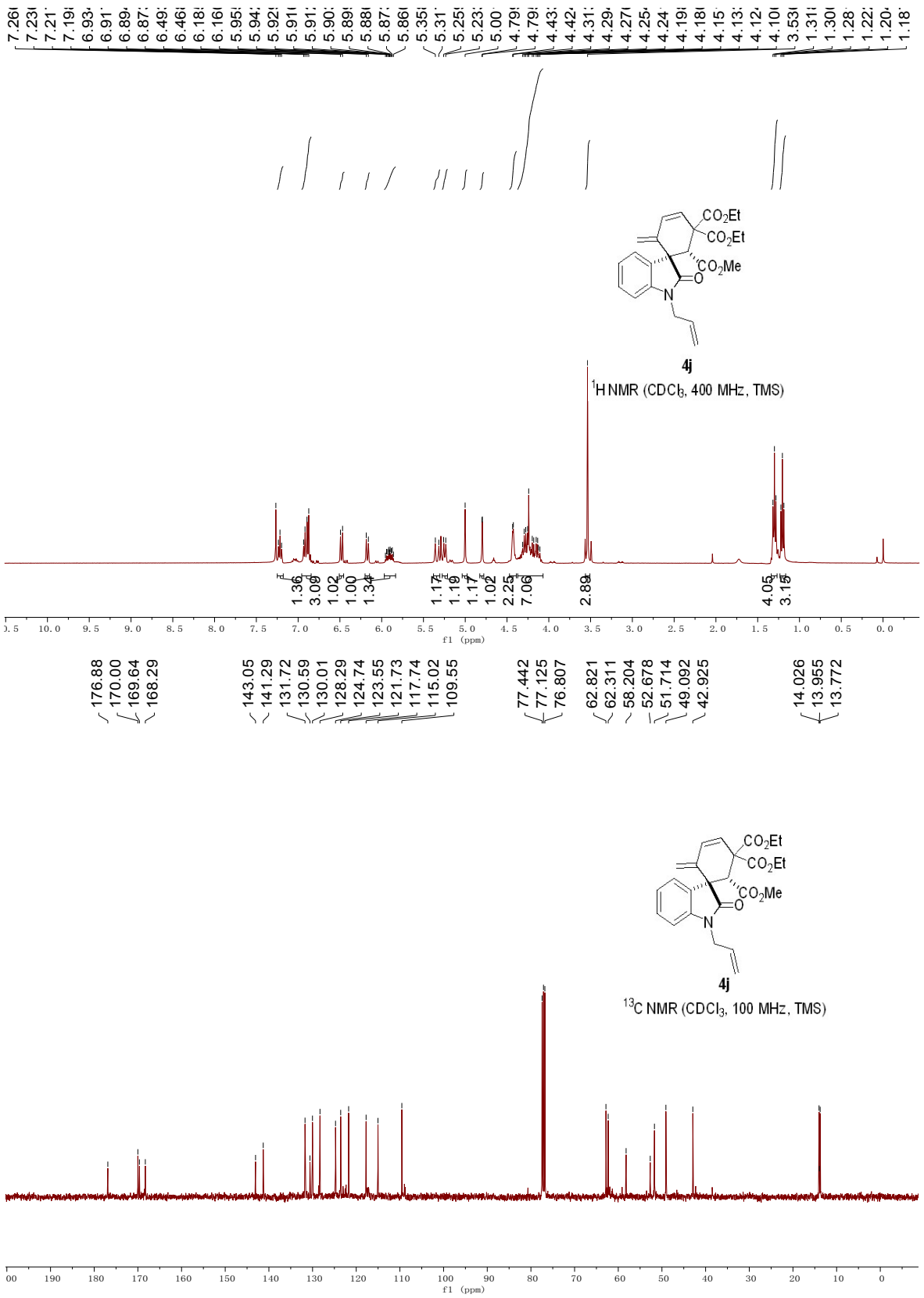
Compound 4i: Yield: 54 mg, 51%, dr: 4:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 111-113 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39–7.33 (m, 2H), 7.33–7.25 (m, 2H), 7.25–7.18 (m, 2H), 6.97–6.91 (m, 2H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.49 (d, *J* = 10.0 Hz, 1H), 6.31–6.22 (m, 1H), 6.18 (d, *J* = 10.0 Hz, 1H), 5.02 (s, 1H), 4.83 (d, *J* = 0.8 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 2H), 4.37–4.09 (m, 6H), 3.54 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 4H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 169.9, 169.6, 168.2, 143.0, 141.3, 136.4, 132.8, 130.6, 130.0, 128.5, 128.3, 127.7, 126.5, 124.7, 123.5, 123.1, 121.7, 115.0, 109.5, 62.8, 62.3, 58.2, 52.7, 51.6, 49.1, 42.4, 14.0, 13.7; IR (neat): ν 3135, 2933, 1687, 1514, 1389, 1150, 1049, 1066 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{31}NO_7Na$ $[M+H]^+$: 552.1992, found: 552.1984.

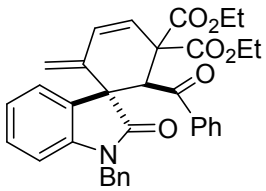




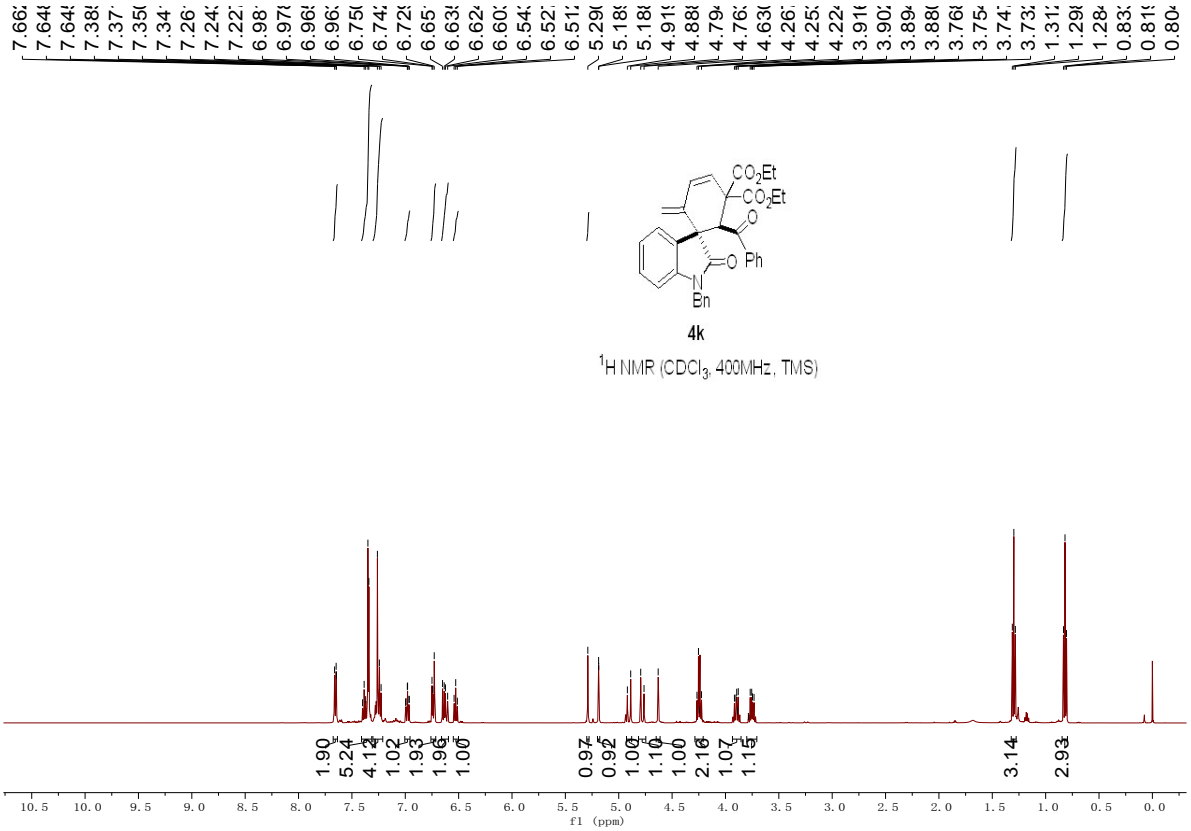


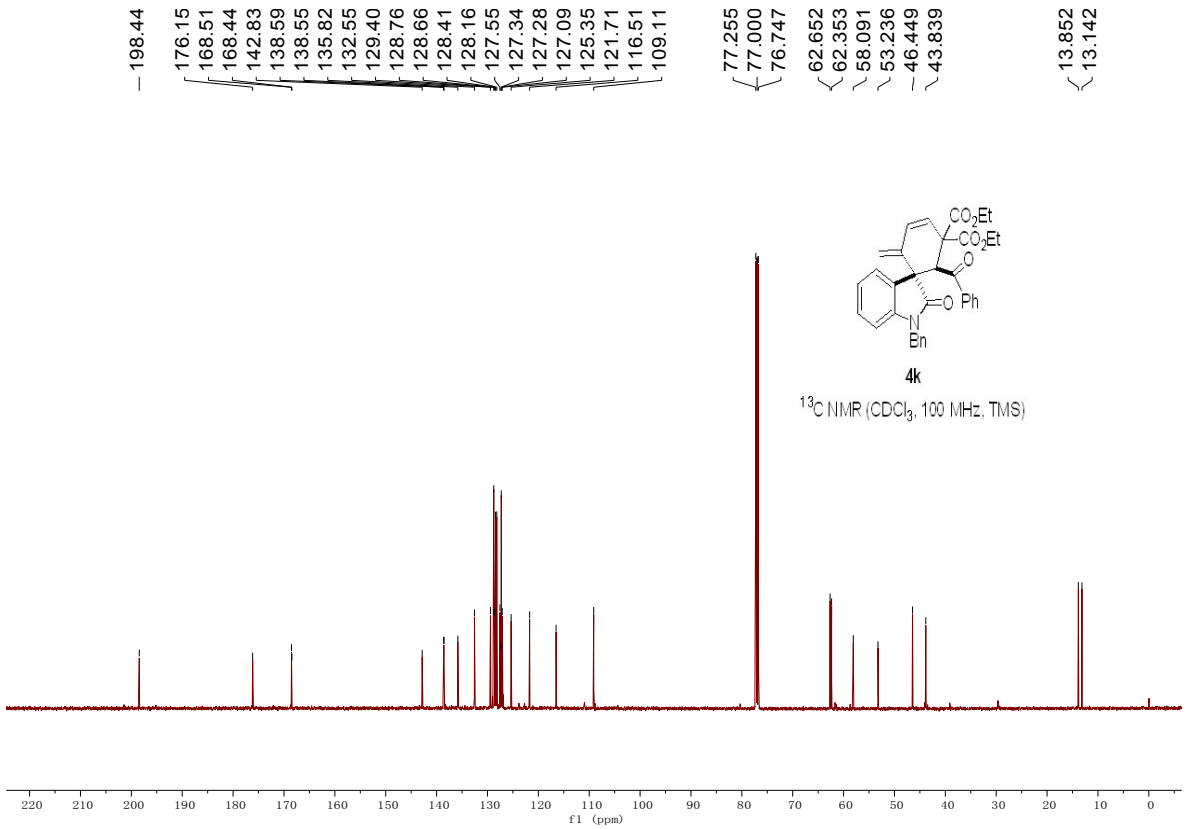
Compound 4j: Yield: 40 mg, 44%, dr: 7:1; A yellow solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 103-105 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (t, *J* = 7.6 Hz, 1H), 6.96–6.84 (m, 3H), 6.48 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 5.97–5.83 (m, 1H), 5.34 (d, *J* = 16.4 Hz, 1H), 5.25 (d, *J* = 10.0 Hz, 1H), 5.00 (s, 1H), 4.80 (s, 1H), 4.43 (s, 2H), 4.37–4.07 (m, 5H), 3.54 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 169.9, 169.5, 168.2, 142.9, 141.2, 131.6, 130.5, 129.9, 128.2, 124.6, 123.4, 121.6, 117.6, 114.9, 109.4, 62.7, 62.2, 58.1, 52.6, 51.6, 49.0, 42.8, 13.9, 13.6; IR (neat): ν 3111, 2231, 1842, 1605, 1362, 1142, 1071, 765 cm^{-1}; HRMS (ESI) Calcd. for $C_{25}H_{27}NO_7Na$ $[M+H]^+$: 476.1679, found: 476.1689.

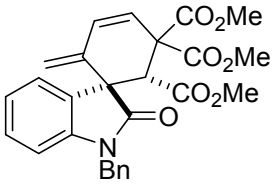

CO2Et
CO2Et
CO2Me
O
N
4j
1H NMR (CDCl3, 400 MHz, TMS)
f1 (ppm)
13C NMR (CDCl3, 100 MHz, TMS)



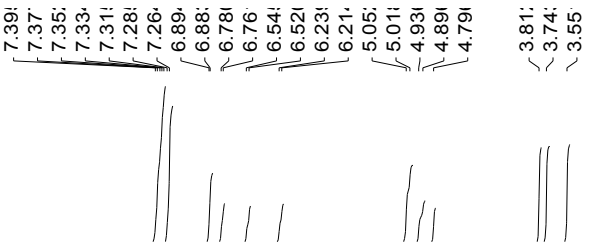
Compound 4k: Yield: 62 mg, 57%, dr: 7:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 155-157 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68–7.64 (m, 2H), 7.41–7.31 (m, 5H), 7.30–7.21 (m, 4H), 7.00–6.96 (m, 1H), 6.76–6.71 (m, 2H), 6.66–6.60 (m, 2H), 6.55–6.50 (m, 1H), 5.29 (s, 1H), 5.19 (s, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.78 (d, *J* = 15.6 Hz, 1H), 4.63 (s, 1H), 4.29–4.21 (m, 2H), 3.93–3.85 (m, 1H), 3.80–3.71 (m, 1H), 1.30 (t, *J* = 7.2 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 176.2, 168.5, 168.4, 142.8, 138.59, 138.55, 135.8, 132.6, 129.4, 128.8, 128.7, 128.4, 128.2, 127.6, 127.34, 127.28, 127.1, 125.4, 121.7, 116.5, 109.1, 62.7, 62.4, 58.1, 53.2, 46.4, 43.8, 13.9, 13.1; IR (neat): ν 3057, 2981, 2927, 1712, 1682, 1237, 1029, 744 cm^{-1}; HRMS (ESI) Calcd. for $C_{34}H_{31}NO_6Na$ $[M+H]^+$: 572.2043, found: 572.2052.

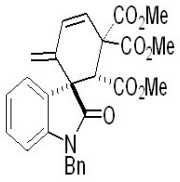






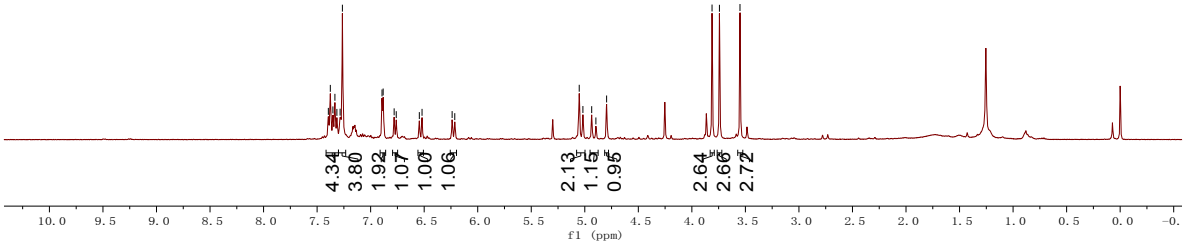
Compound 4l: Yield: 53 mg, 56%, dr: 8:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.3; Mp: 175-176 °C; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.42–7.30 (m, 4H), 7.29 (s, 2H), 6.89 (d, *J* = 3.6 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 10.0 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.05– 5.00 (m, 2H), 4.92 (d, *J* = 16.0 Hz, 1H), 4.80 (s, 1H), 4.25 (s, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 170.1, 169.8, 168.7, 143.1, 140.6, 135.9, 130.1, 130.0, 128.7, 128.5, 127.5, 127.4, 124.2, 123.7, 121.9, 115.6, 109.6, 58.1, 53.6, 53.2, 52.5, 51.9, 49.1, 44.4; IR (neat): ν 2922, 2851, 1744, 1719, 1607, 1200, 1012, 736 cm^{-1}; HRMS (ESI) Calcd. for $C_{29}H_{29}NO_7Na$ $[M+H]^+$: 526.1836, found: 526.1823.

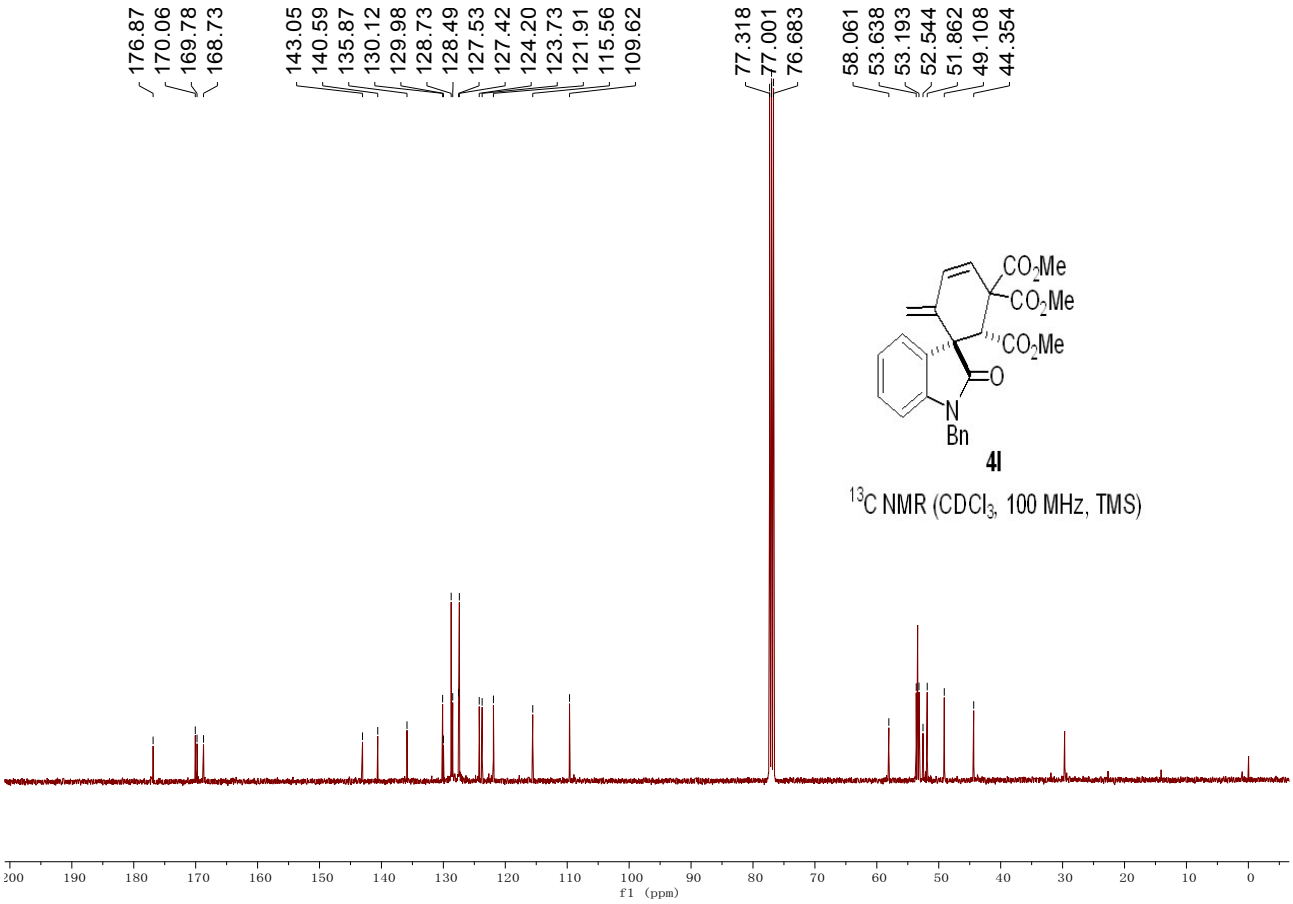




4l

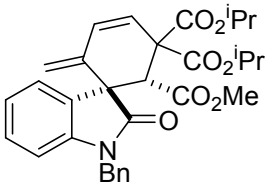
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)



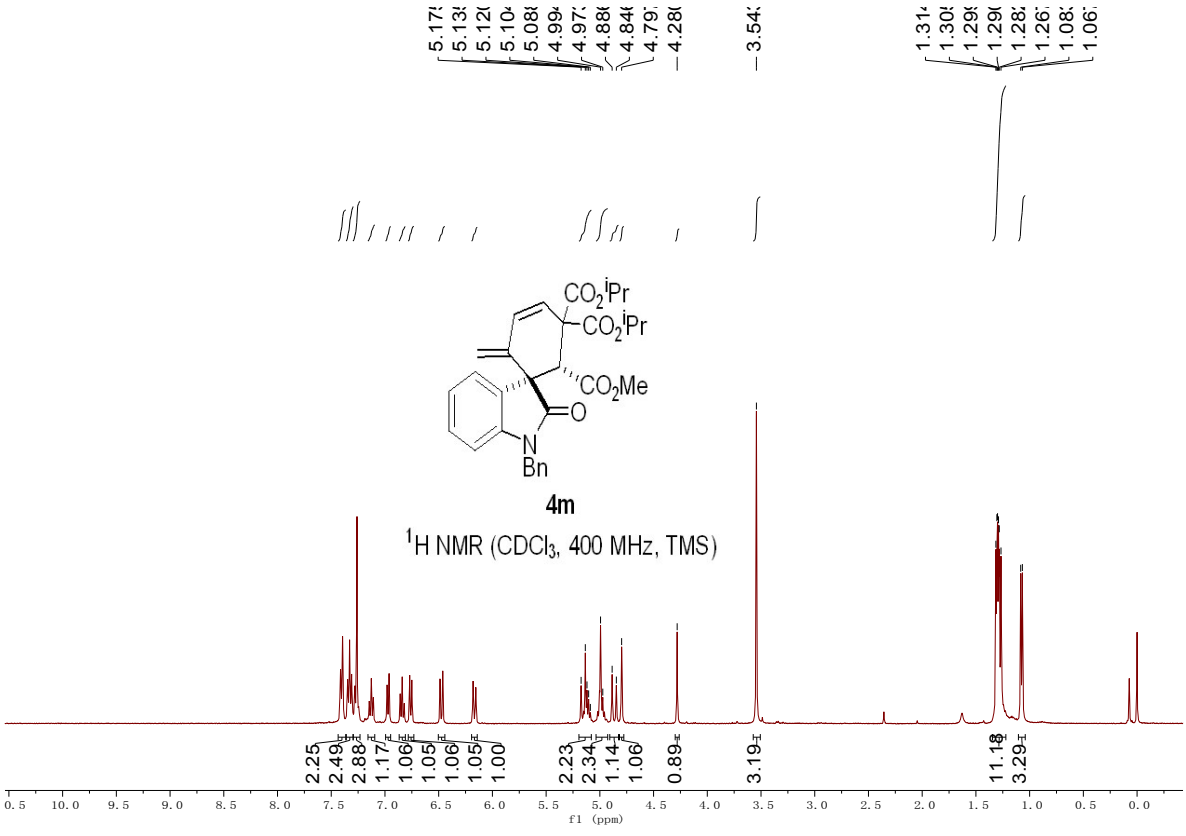


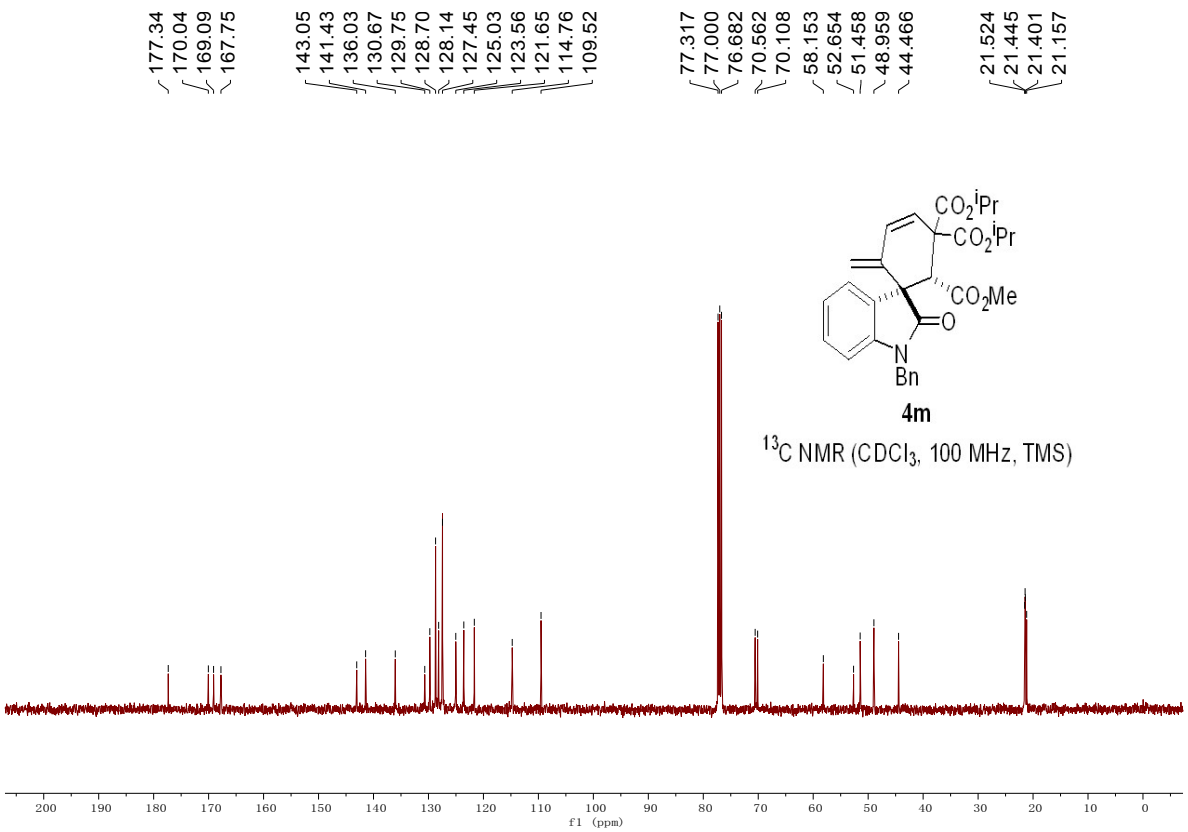
4l

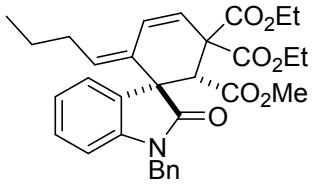
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



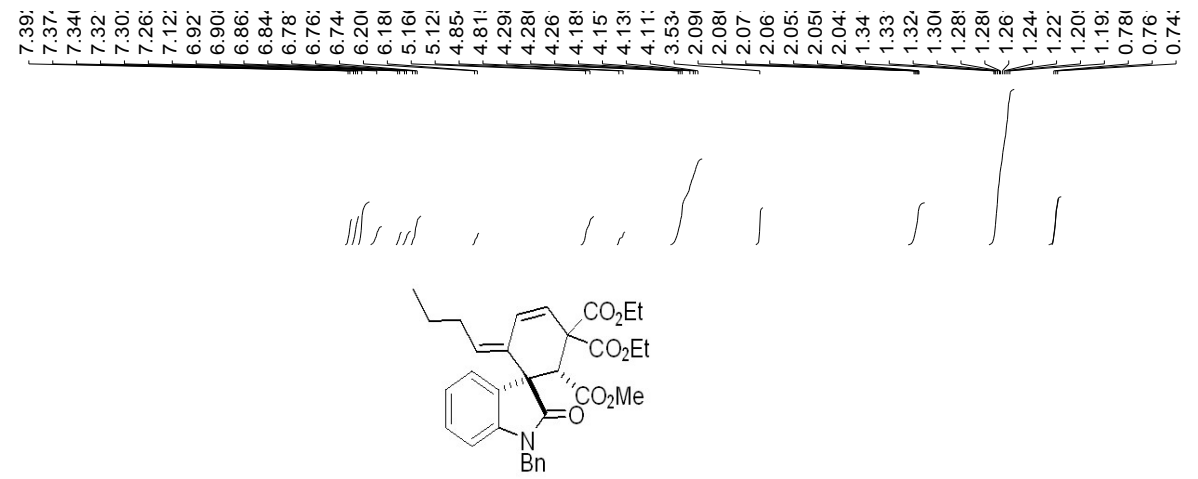
Compound 4m: Yield: 58 mg, 55%, dr: 7:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 125-127 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 7.2 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.30–7.23 (m, 3H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.47 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 10.0 Hz, 1H), 5.19–5.08 (m, 2H), 5.00–4.93 (m, 2H), 4.87 (d, *J* = 16.0 Hz, 1H), 4.80 (s, 1H), 4.28 (s, 1H), 3.54 (s, 3H), 1.35–1.22 (m, 9H), 1.08 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 170.0, 169.1, 167.8, 143.1, 141.4, 136.0, 130.7, 129.8, 128.7, 128.1, 127.5, 125.0, 123.6, 121.7, 114.8, 109.5, 70.6, 70.1, 58.2, 52.7, 51.5, 49.0, 44.5, 21.5, 21.44, 21.40, 21.2; IR (neat): ν 3324, 1698, 1614, 1489, 1173, 1153, 766, 697 cm^{-1}; HRMS (ESI) Calcd. for $C_{31}H_{33}NO_7Na$ $[M+H]^+$: 554.2149, found: 554.2157.





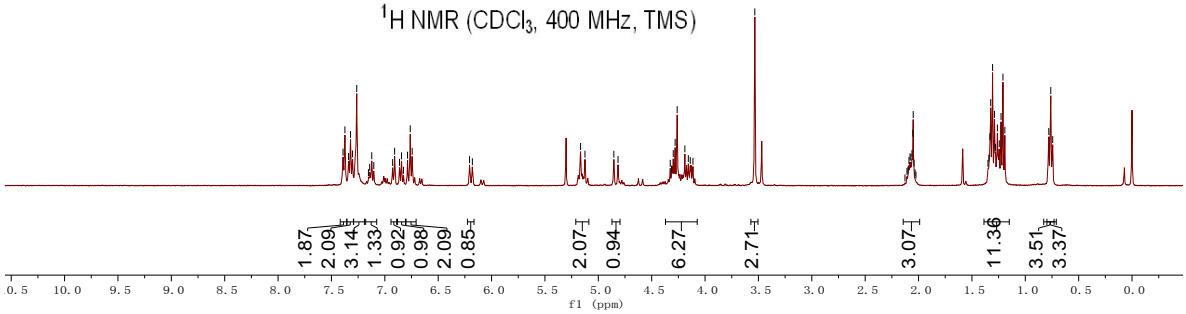


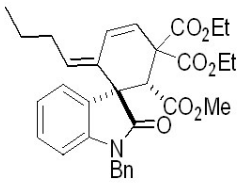
Compound 4n: Yield: 51 mg, 47%, dr: 3:1; A colorless solid; Eluent: petroleum ether:ethyl acetate = 4:1; R_f = 0.4; Mp: 101-103 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.33– 7.29 (m, 2H), 7.26 (s, 1H), 7.10–7.08 (m, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.88–6.81 (m, 1H), 6.80–6.71 (m, 2H), 6.19 (d, *J* = 10.0 Hz, 1H), 5.21–5.09 (m, 2H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.37–4.07 (m, 5H), 3.53 (s, 3H), 2.14–1.99 (m, 2H), 1.39–1.15 (m, 8H), 0.76 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 170.2, 169.6, 168.4, 142.9, 136.1, 132.3, 130.1, 128.6, 128.5, 128.0, 127.4, 127.2, 124.9, 123.6, 123.5, 121.6, 109.4, 62.6, 62.2, 58.2, 53.4, 53.0, 51.5, 49.4, 44.2, 22.3, 13.9, 13.7, 13.5; IR (neat): ν 2961, 2861, 1712, 1201, 1068, 1027, 733, 698 cm^{-1}; HRMS (ESI) Calcd. for $C_{32}H_{36}NO_7Na$ $[M+H]^+$: 546.2486, found: 546.2489.



4n

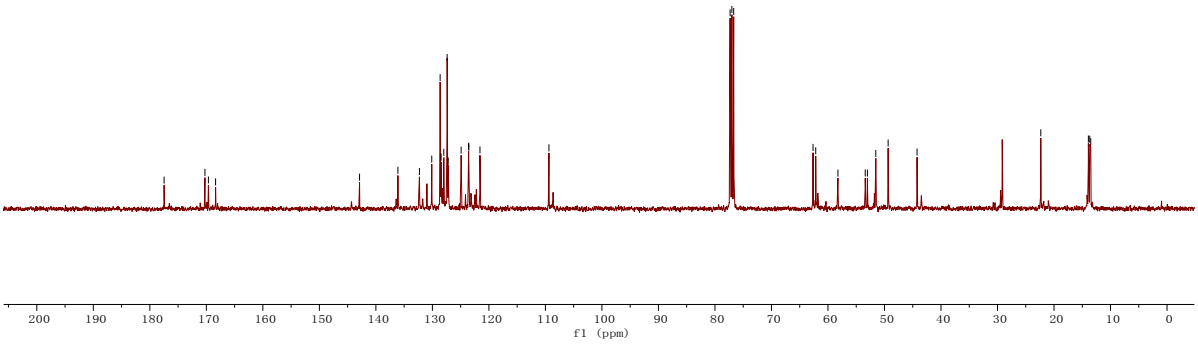
^{1}H NMR ($CDCl_3$, 400 MHz, TMS)





4n

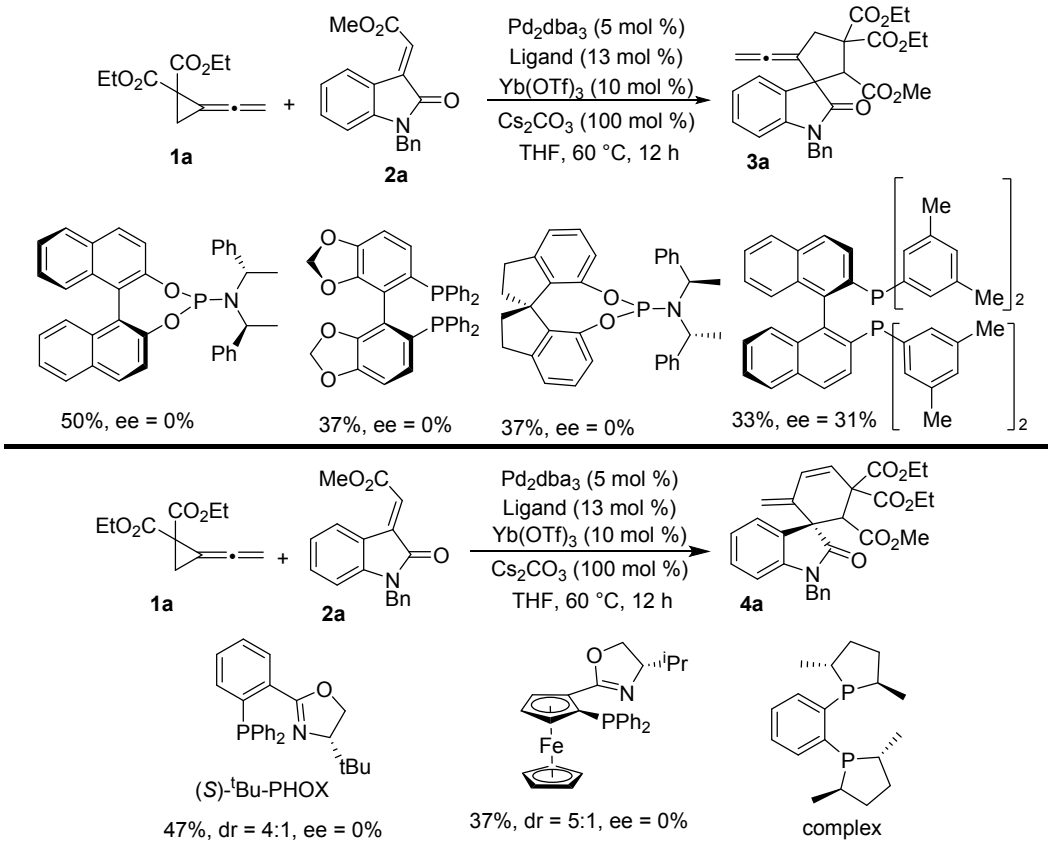
^{13}C NMR ($CDCl_3$, 100 MHz, TMS)



5 Asymmetric studies

5.1 Screening of the chiral ligand

Table S1: The investigation of catalytic asymmetric version

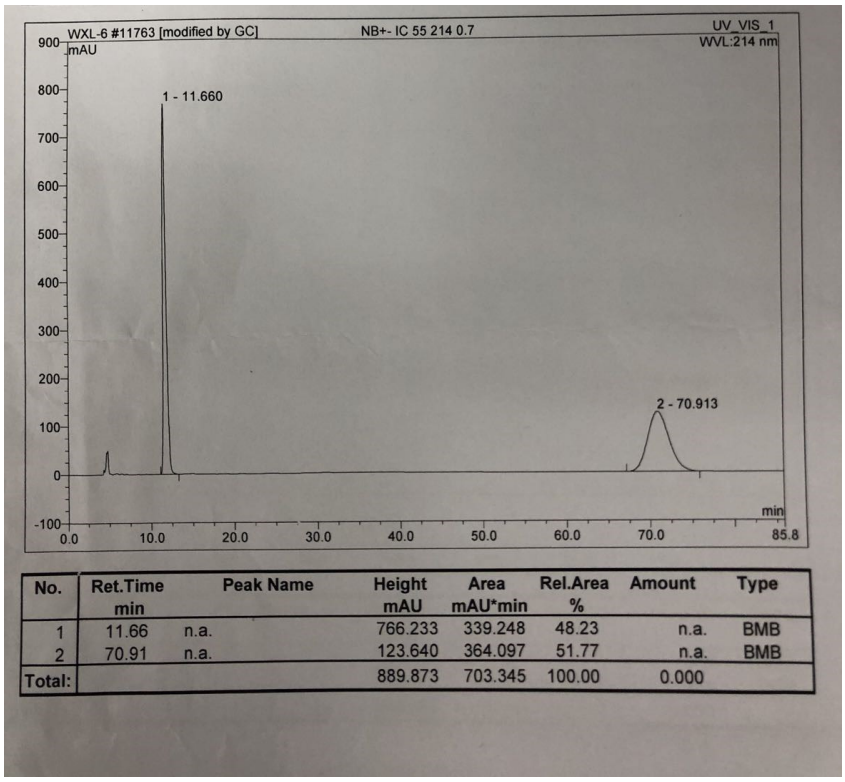


[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), catalyst (5 mol %), ligand (13 mol %) and solvent (2 mL) were used and the ee values were determined by HPLC on a chiral stationary phase.

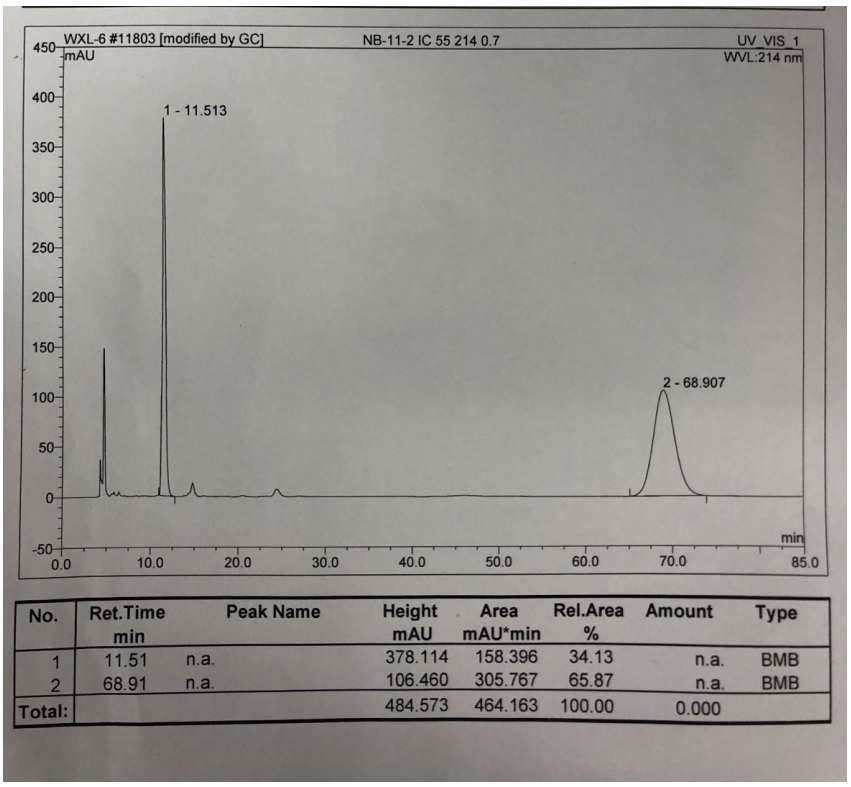
5.2 Reaction procedure and HPLC spectra

In an oven dried 10 mL Schlenk tube equipped with a magnetic stirring bar, (Pd_2dba_3) (0.01 mmol, 5 mol %), and chiral ligand (0.026 mmol, 13 mol %) were added into THF (1.0 mL) under nitrogen atmosphere. The reaction mixture was stirred for 1 h at room temperature. Then, methyleneindolinone **1a** (0.2 mmol), vinylidenecyclopropane **1** (0.4 mmol, 200 mol %), $Yb(OTf)_3$ (0.02 mmol, 10 mol %) and CS_2CO_3 (0.2 mmol, 100 mol %) were added and the reaction mixture was stirred for another 12 h at 60 °C. Then, the solvent was evaporated under vacuum and the residue was purified by a column chromatography (Eluent: petroleum ether:ethyl acetate = 4:1) to afford the corresponding product **3a**.

Product (**3a**): a Chiralcel IC column; λ = 214 nm; Eluent: Hexane/Isopropanol = 98/2; Flow rate: 0.70 mL/min; t_R = 11.51 min (minor), t_R = 68.91 min (major), enantiomeric ratio: 65.87:34.13. $[\alpha]_D^{20}$ = +13.4 (c = 0.370, CH_2Cl_2), Mp: 122-123 °C.



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.66	n.a.	766.233	339.248	48.23	n.a.	BMB
2	70.91	n.a.	123.640	364.097	51.77	n.a.	BMB
Total:			889.873	703.345	100.00	0.000	

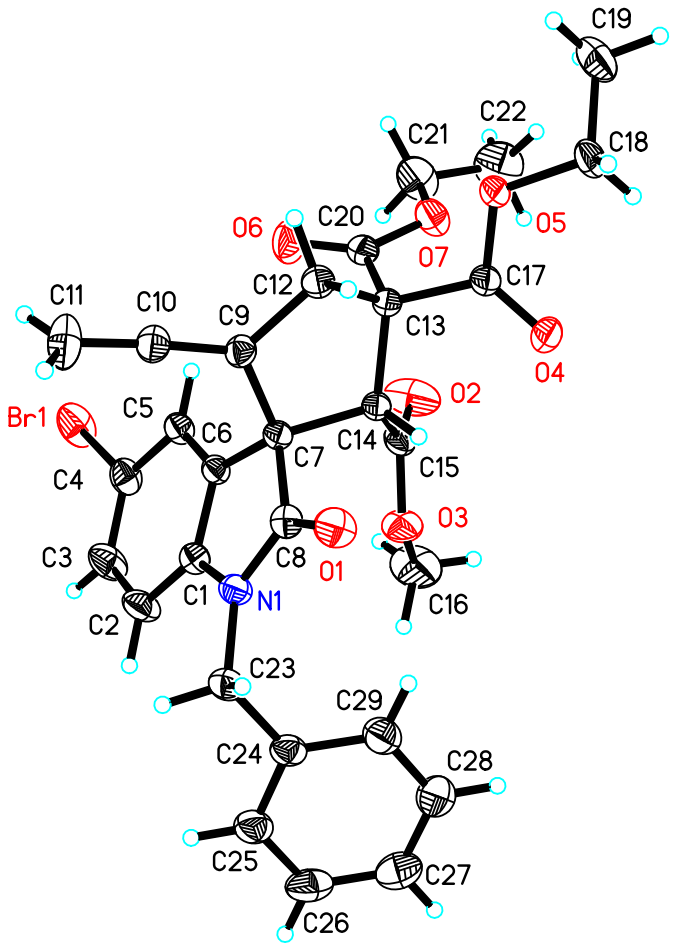


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.51	n.a.	378.114	158.396	34.13	n.a.	BMB
2	68.91	n.a.	106.460	305.767	65.87	n.a.	BMB
Total:			484.573	464.163	100.00	0.000	

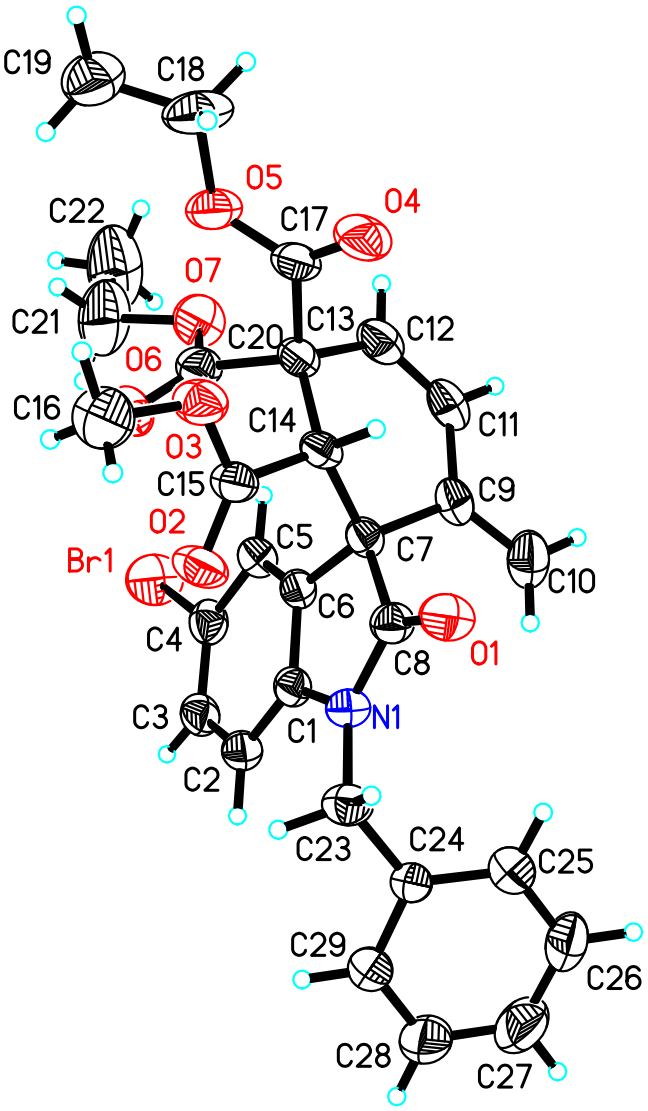
6 X-ray crystal data of compounds 3b and 4b

Single crystals suitable for XRD were obtained by evaporation experiment:

Compounds **3b** and **4b** (50 mg) were dissolved in 0.5 mL of dichloromethane, and then 5 mL n-pentane was added, allowing this mixed solution evaporate slowly in a dry environment. Crystals were obtained in about 3-5 days with the evaporation of the solvent.



The crystal data of **3b** have been deposited in CCDC with number 2014790. Empirical Formula: $C_{29}H_{28}BrNO_7$; Formula Weight: 582.43; Crystal Color, Habit: colorless, Crystal Dimensions: 0.180 x 0.150 x 0.130 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 13.1045(3)Å, b = 14.6076(4)Å, c = 14.4910(4)Å, α = 90°, β = 103.3330(10)°, γ = 90°, V = 2699.18(12)$Å^3$; Space group: P 21/c; Z = 4; Dcalc= 1.433 g/cm^3; F000 = 1200; Final R indices [I>2sigma(I)] R1 = 0.0382, wR2 = 0.0868.



The crystal data of **4b** have been deposited in CCDC with number 2024031. Empirical Formula: $C_{29}H_{28}BrNO_7$; Formula Weight: 582.43; Crystal Color, Habit: colorless, Crystal Dimensions: 0.180 x 0.150 x 0.100 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 9.4920(5)Å, b = 11.5335(6)Å, c = 26.1458(16)Å, α = 90°, β = 97.433(2)°, γ = 90°, V = 2838.3(3)$Å^3$; Space group: P 21/c; Z = 4; D_{calc}= 1.363 g/cm^3; F_{000} = 1200; Final R indices [I>2sigma(I)] R1 = 0.0532, wR2 = 0.1270

7. Reference

[1] Chen, J.; Gao, S.; Chen, M. Cu-Catalyzed Silylation and Borylation of Vinylidene Cyclopropanes. *Org. Lett*. **2019**, *21*, 8800-8804.

[2] Suman, K.; Srinu, L.; Thennarasu, S. Lewis Acid Catalyzed Unprecedented [3+2] Cycloaddition Yields 3,3′-Pyrrolidinyldispirooxindoles Containing Four Contiguous Chiral Stereocenters with Two Contiguous Quaternary Spirostereocenters. *Org. Lett*. **2014**, *16*, 3732-3735.