Supporting Information

Electrochemical reaction of indole-tethered alkynes enabling stereoselective synthesis of iodovinyl spiroindolenine-cyclopentanes

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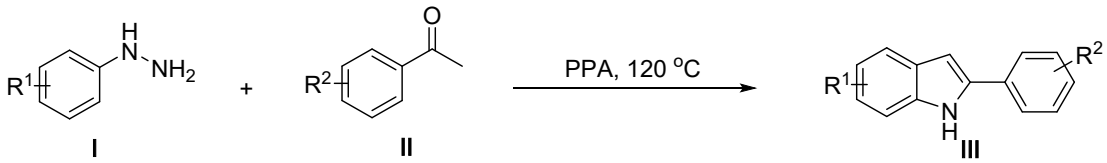
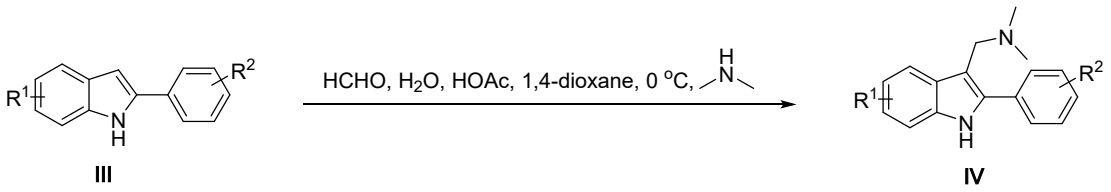
1. General information

All the commercial reagents including solvents were used directly without further purification. All the experiments were monitored by thin layer chromatography (TLC) with UV light. The anode electrode and cathode electrode were platinum flakes (10×10×0.2 mm). The TLC employed 0.25 mm silica gel coated on glass plates. Purification of products was carried out by silica gel 60 F-254 TLC plates of 20 cm × 20 cm. Melting points were recorded without correction on RY-1G of Tianjin Xintianguang instrument company. NMR spectra were recorded on Bruker 400 MHz and 600 MHz spectrometers. High resolution mass spectra (HRMS) were measured on Agilent 6210 ESI/TOF MS instrument. Cyclic voltammetry (CV) was performed on an electrochemical workstation (Chenhua CHI760E).The X-ray data were collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation.

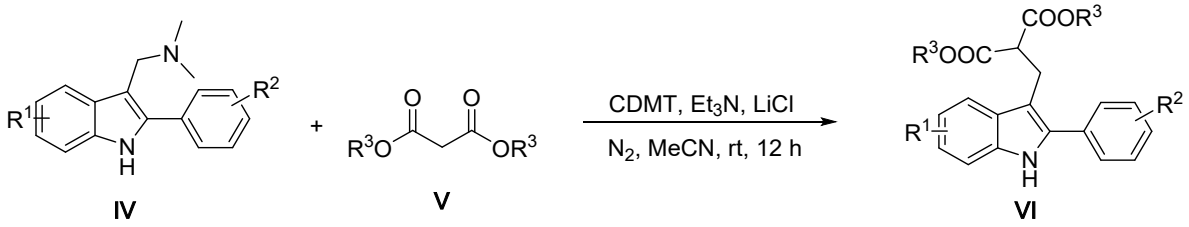
2. Synthesis of indole-tethered alkynes S1



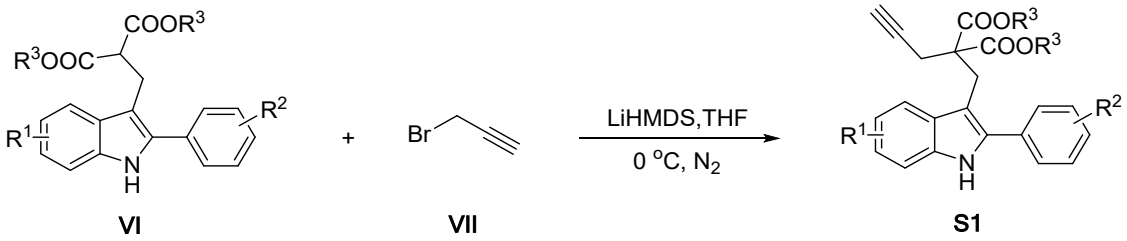
According to a modified literature procedure,[1] a mixture of phenylhydrazine or substituted phenylhydrazine hydrochloride (11 mmol, 1.1 equiv), ketone (10 mmol, 1.0 equiv) and polyphosphoric acid (10 g) was heated to 120 ºC for 3-6 h in a 100 mL three mouth flask. The reaction mixture was cooled to rt, neutralized with an aqueous solution of NaOH. The aqueous layer was extracted with EtOAc (20 mL x 3), dried with Na_2SO_4 and the solvent was evaporated. The crude product was purified by column chromatography to afford the desired product indole **III**.



A three-necked round bottom flask equipped with a magnetic stirring bar and a dropping funnel was charged with a mixture of formaldehyde (37 wt% in water, 2.1 mL, 28 mmol), water (2 mL) and glacial acetic acid (26 mL) in dioxane (24 mL). The reaction mixture was cooled down to 0 °C and dimethylamine (40 wt% in water, 3.5 mL, 28 mmol) was added quickly. Afterwards, phenylindole (5.0 g, 26 mmol) in dioxane (24 mL) was added dropwise via the dropping funnel. Not all phenylindole was dissolved in dioxane and the remaining phenylindole was added slowly as a solid. Following complete addition, the mixture was first stirred for 2 h at 0 °C and then for 12 h at room temperature. In the next step the reaction mixture was diluted with water (32 mL), followed by addition of Celite (1.5 g) and stirring for 10 minutes. The suspension was filtered off over Celite and the filtrate was basified by addition of 2 M NaOH (400 mL) resulting in precipitation of the product. The product was filtered off, washed with water and dried in vacuo yielding **IV** as a pale white solid.[2]



Into a flask were taken gramine **IV** (20 mmol), malonate **V** (50 mmol), CDMT (22 mmol), Et_3N (40 mmol), LiCl (7 mmol), MeCN (75 mL) and the mixture was reacted at room temperature under nitrogen for 12 h. Iced water (150 mL) was added and the organic layer was taken, followed by the evaporation of solvent. Product **VI** was purified by column chromatography using petroleum ether/ acetone (10:1, v/v) as eluent.[3]



Into an oven-dried reaction vial flushed with N_2 were taken compound **VI** (1 mmol) and anhydrous THF (3 mL). The reaction vial was cooled to 0 °C and LiHMDS (1 M in THF, 1.3 mL) was added dropwise with stirring. After 0.5 h at 0 °C, 3-bromopropyne (1.5 mmol) dissolved in anhydrous THF (2 mL) was added dropwise. Stirring was continued at 0 °C for 8 h. Then, the reaction was diluted with H_2O (25 mL) and extracted with DCM (20 mL × 3). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was removed to give the crude product **S1**, which was purified by column chromatography using petroleum ether/ethyl acetate (10:1, v/v) as eluent.

Reference:

1. Liu, Y.; McWhorter, W. W. *J. Am. Chem. Soc*. **2003**, *125*, 4240−4252.

2. Rolka, A. B.; Koenig, B. *Org. Lett.* **2020**, *22*, 5035−5040.

3. Fujita, H.; Nishikawa, R.; Sasamoto, O.; Kitamura, M.; Kunishima, M. *J. Org. Chem.* **2019**, *84*, 8380−8391.

3. General procedure for the electrochemical reaction

An undivided cell connected to a DC power supply was equipped with a Pt anode and a Pt cathode. Into the cell were taken indole derivative **1** (0.2 mmol), *n*-Bu_4NI (2.0 equiv, 0.4 mmol), AcOH (4.0 equiv, 0.8 mmol), MeCN (8 mL) and H_2O (4 mL). The mixture was stirred at a constant current of 10 mA at 80 °C oil bath for 2.5 h. Then, the reaction was diluted with EtOAc (25 mL) and extracted with H_2O (20 mL × 3). The combined organic layers were dried with anhydrous Na_2SO_4, filtered

and concentrated in vacuo. The product **3** was purified by TLC plate of 20 cm × 20 cm using petroleum ether/ethyl acetate (4:1, v/v) as eluent.

4. Procedure for large-scale synthesis

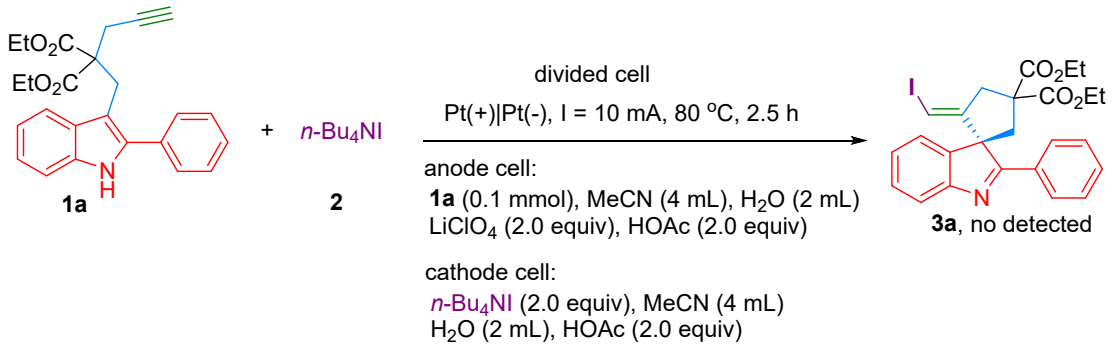
Diethyl 2-((2-phenyl-1*H*-indol-3-yl)methyl)-2-(prop-2-yn-1-yl)malonate (**1a**, 2.5 mmol, 1.008 g), *n*-Bu_4NI (2.0 equiv, 5 mmol, 1.847 g), AcOH (4.0 equiv, 10 mmol, 0.601 g), MeCN (50 mL) and H_2O (25 mL). The mixture was stirred and electrolyzed at a constant current of 10 mA at 80 °C for 15 h. Then, the reaction was diluted with EtOAc (150 mL) and extracted with H_2O (50 mL × 3). The combined organic layers were dried with anhydrous Na_2SO_4, and the solvent was removed to give the crude product **3a**. Purification by column using petroleum ether/ethyl acetate (6:1, v/v) as eluent gave **3a** (1.254 g, 96% yield).

5. Control experiment

a) addition of TEMPO

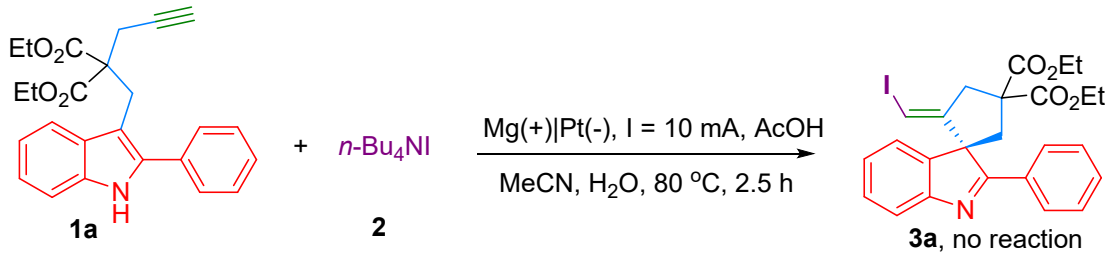
Into a cell were taken alkyne **1a** (0.2 mmol), *n*-Bu_4NI (2.0 equiv, 0.4 mmol), TEMPO (3.0 equiv, 0.6 mmol), AcOH (4.0 equiv, 0.8 mmol), MeCN (8 mL) and H_2O (4 mL). The mixture was stirred under constant current (10 mA) with a Pt anode and a Pt cathode at 80 °C for 2.5 h.

b) reaction conducted in a divided cell



In a divided cell connected to a DC power supply was equipped with a Pt anode and a Pt cathode. Into the anode cell were taken indole derivative **1a** (0.1 mmol), AcOH (2.0 equiv, 0.2 mmol), MeCN (4 mL) and H_2O (2 mL). Into the cathode cell were taken *n*-Bu_4NI (2.0 equiv, 0.2 mmol), AcOH (2.0 equiv, 0.2 mmol), MeCN (4 mL) and H_2O (2 mL). The mixture was stirred at a constant current of 10 mA at 80 °C for 2.5 h. Then, the reaction was diluted with EtOAc (25 mL) and extracted with H_2O (20 mL × 3). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated in vacuo.

c) Mg used as sacrificial anode



An undivided cell connected to a DC power supply was equipped with an Mg anode and a Pt cathode. Into the cell were taken indole derivative **1a** (0.2 mmol), *n*-Bu_4NI (2.0 equiv, 0.4 mmol), AcOH (4.0 equiv, 0.8 mmol), MeCN (8 mL) and H_2O (4 mL). The mixture was stirred at a constant current of 10 mA at 80 °C oil bath for 2.5 h. Then, the reaction was diluted with EtOAc (25 mL) and extracted with H_2O (20 mL × 3). The combined organic layers were dried with anhydrous

Na_2SO_4, filtered and concentrated in vacuo.

6. X-ray crystallography of 3b

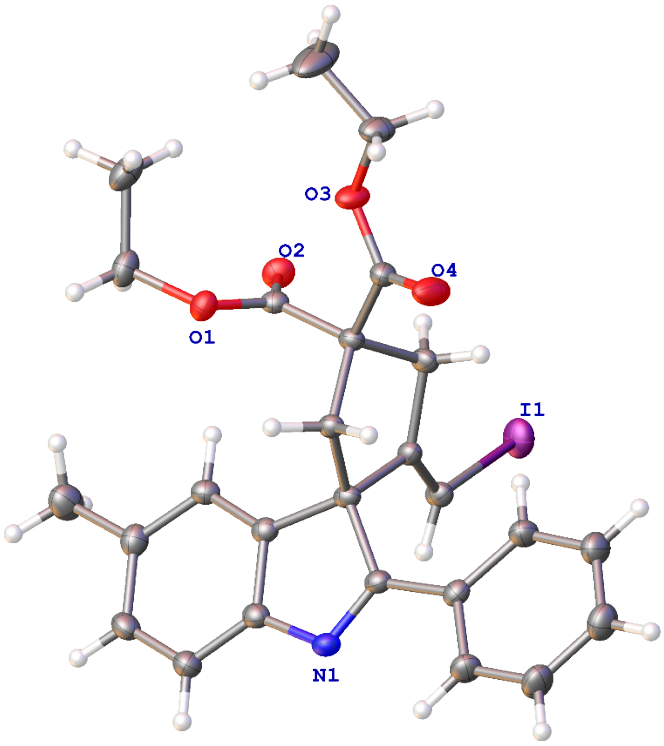


Figure S1. Single crystal x-ray analysis of **3b** (ellipsoid contour 30% probability, CCDC 2425792).

Suitable crystals of compound **3b** were obtained by slowly evaporating a mixture of petroleum ether and ethyl acetate solution at ambient temperature.

7. Cyclic voltammetry (CV) experiment

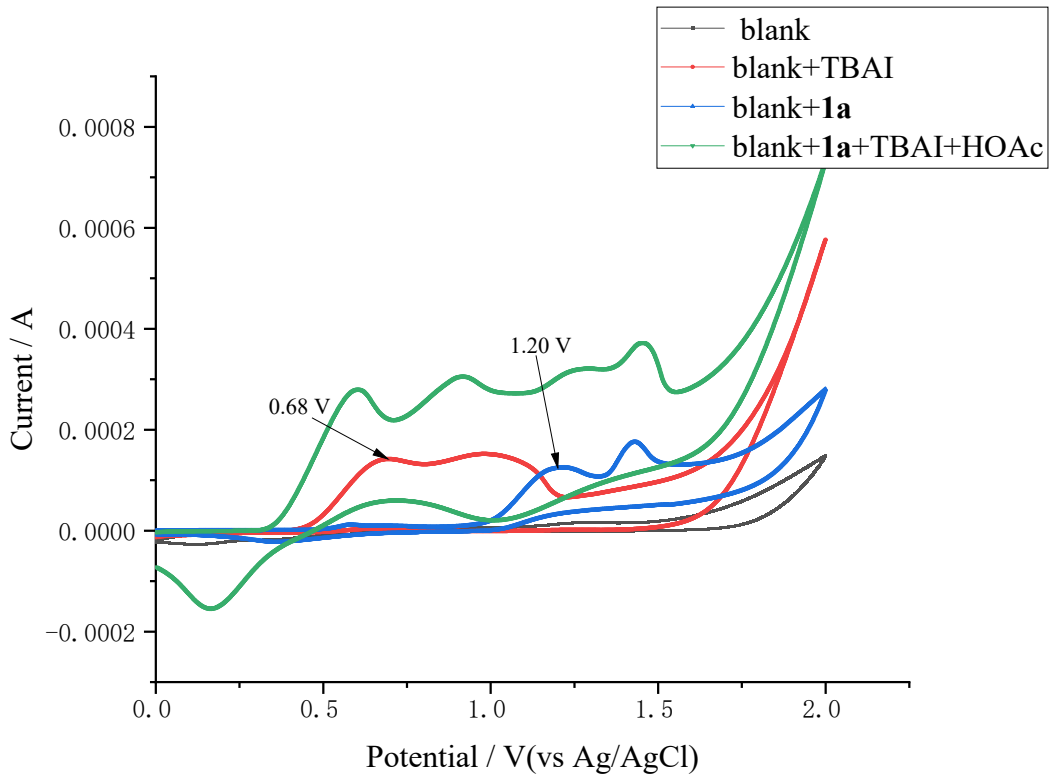


Figure S2. CV experiments.

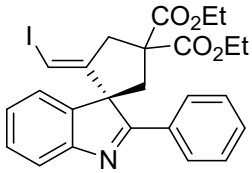
The cyclic voltammetry experiments were carried out with a computer-controlled electrochemical analyzer for electrochemical measurements. The cyclic voltammetry experiments were measured at room temperature. Cyclic voltammetry (CV) was performed on an electrochemical workstation (Chenhua CHI730E). The experiment was performed in a three-electrode cell with MeCN (4 mL) and H_2O (2 mL) as the solvent, $LiClO_4$ (0.2 mmol) as the supporting electrolyte, and the concentration of the **1a** was 16.7 mM; the concentration of the TBAI was 33.3 mM. The scan speed was 150 mV/s. The potential ranges investigated were 0 V to 2.0 V vs. Ag/AgCl (saturated aqueous KCl (3 M)). CV plotting convention is IUPAC.

Working electrode: The working electrode is a 2 mm diameter platinum platter.

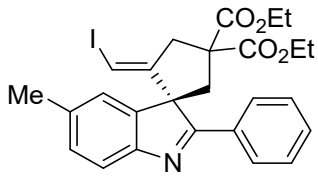
Reference electrode: The reference electrode is Ag/AgCl (saturated aqueous KCl (3 M)).

Counter electrode: The counter electrode is a platinum wire.

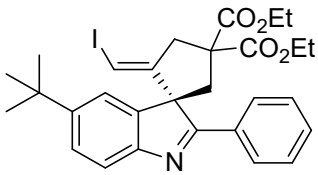
8. Characterization data of compounds 3



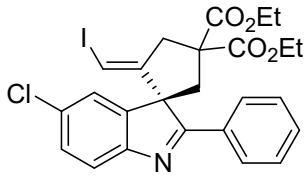
Compound **3a**: 104.5 mg, 99% yield, white solid, mp 162-163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98-7.96 (m, 2H), 7.69 (d, *J* = 7.72 Hz, 1H), 7.51-7.48 (m, 3H), 7.40-7.36 (m, 1H), 7.26-7.20 (m, 2H), 5.74-5.73 (m, 1H), 4.39-4.24 (m, 4H), 3.84-3.78 (m, 1H), 3.49-3.44 (m,1H), 3.42-3.38 (m,1H), 2.91-2.87 (m, 1H), 1.32-1.28 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 179.1, 171.6, 171.4, 153.3, 151.9, 146.4, 131.2, 131.0, 129.0, 128.7, 128.3, 126.5, 121.7, 121.2, 74.5, 68.1, 62.4, 62.3, 58.5, 45.7, 43.9, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{25}INO_4^+$ 530.0823, found 530.0832.



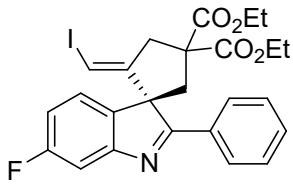
Compound **3b**: 99.6 mg, 92% yield, white solid, mp 142-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96-7.93 (m, 2H), 7.57 (d, *J* = 7.84 Hz, 1H), 7.49-7.48 (m, 3H), 7.19-7.17 (m, 1H), 7.03 (s, 1H), 5.73-5.72 (m, 1H), 4.39-4.24 (m, 4H), 3.84-3.78 (m, 1H), 3.48-3.42 (m,1H), 3.40-3.36 (m,1H), 2.90-2.87 (m, 1H), 2.40 (s, 3H), 1.33-1.28 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 178.2, 171.5, 171.4, 152.0, 151.1, 146.6, 136.5, 131.4, 130.8, 128.9, 128.8, 128.7, 122.5, 120.7, 74.5, 67.9, 62.4, 62.3, 58.6, 45.7, 44.0, 21.7, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{27}INO_4^+$ 544.0979, found 544.0975.



Compound **3c**: 111.9 mg, 96% yield, white solid, mp 111-113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00-7.98 (m, 2H), 7.62-7.60 (m, 1H), 7.50-7.48 (m, 3H), 7.43-7.41 (m, 1H), 7.33-7.32 (m, 1H), 5.74-5.73 (m, 1H), 4.44-4.39 (m, 1H), 4.32-4.25 (m, 3H), 3.89-3.83 (m, 1H), 3.48-3.42 (m, 2H), 2.88-2.84 (m, 1H), 1.37 (s, 9H), 1.33-1.28 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 178.3, 171.6, 152.2, 150.9, 150.1, 146.3, 131.3, 130.8, 129.0, 128.6, 125.3, 120.4, 118.8, 74.4, 68.2, 62.4, 62.3, 58.4, 45.5, 44.0, 35.1, 31.7, 14.1. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{29}H_{33}INO_4^+$ 586.1449, found 586.1442.

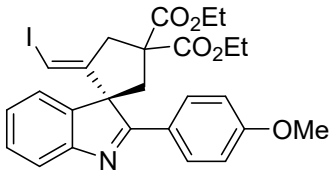


Compound **3d**: 82.0 mg, 73% yield, white solid, mp 134-136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95-7.92 (m, 2H), 7.59 (d, *J* = 8.24 Hz, 1H), 7.52-7.47 (m, 3H), 7.35-7.33 (m, 1H), 7.21-7.20 (m, 1H), 5.78-5.76 (m, 1H), 4.40-4.34 (m, 2H), 4.29-4.24 (m, 2H), 3.82-3.77 (m, 1H), 3.48-3.42 (m,1H), 3.40-3.36 (m,1H), 2.90-2.86 (m, 1H), 1.35-1.27 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 179.5, 171.4, 171.2, 151.9, 151.2, 147.8, 132.1, 131.3, 130.9, 129.0, 128.8, 128.5, 122.5, 122.0, 75.3, 68.2, 62.6, 62.5, 58.6, 45.7, 44.1, 14.0, 13.9. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}ClINO_4^+$ 564.0433, found 564.0433.

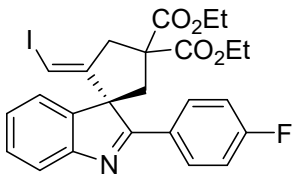


Compound **3e**: 105.9 mg, 97% yield, white solid, mp 173-174 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97-7.94 (m, 2H), 7.52-7.50 (m, 3H), 7.39-7.36 (m, 1H), 7.21-7.17 (m, 1H), 6.94-6.89 (m, 1H), 5.75-5.74 (m, 1H), 4.37-4.24 (m, 4H), 3.82-3.76 (m, 1H), 3.47-3.42 (m, 1H), 3.41-3.37 (m, 1H),

2.87-2.84 (m, 1H), 1.32-1.28 (m, 6H). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$): δ = 181.2, 171.6, 171.2, 163.8 (d, *J* = 243.5 HZ), 154.9 (d, *J* = 11.1 HZ), 151.7, 142.0 (d, *J* = 2.4 HZ), 131.4, 130.9, 129.1, 128.8, 122.5 (d, *J* = 9.5 HZ), 113.0 (d, *J* = 22.8 HZ), 108.8 (d, *J* = 23.8 HZ), 74.8, 67.6, 62.5, 62.4, 58.5, 45.6, 44.1, 14.0, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -113.7 (s). HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}FINO_4^+$ 548.0729, found 548.0735.

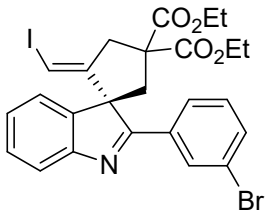


Compound **3f**: 80.7 mg, 72% yield, white solid, mp 140-142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96-7.94 (m, 2H), 7.65-7.63 (m, 1H), 7.37-7.33 (m, 1H), 7.24-7.15 (m, 2H), 7.02-6.99 (m, 2H), 5.71-5.69 (m, 1H), 4.39-4.26 (m, 4H), 3.89 (s, 3H), 3.85-3.80 (m, 1H), 3.49-3.43 (m, 1H), 3.42-3.38 (m, 1H), 2.90-2.86 (m, 1H), 1.33-1.28 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 178.5, 171.6, 171.5, 161.9, 153.4, 152.2, 146.2, 130.9, 128.3, 126.0, 123.6, 121.6, 120.7, 114.1, 74.5, 67.9, 62.5, 62.4, 58.5, 55.4, 45.6, 44.5, 14.0, 13.9. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{27}INO_5^+$ 560.0928, found 560.0936.

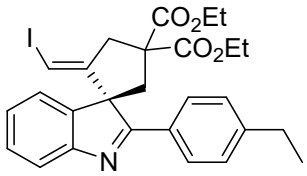


Compound **3g**: 84.0 mg, 77% yield, white solid, mp 164-166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01-7.97 (m, 2H), 7.67 (d, *J* = 7.64 Hz, 1H), 7.39-7.35 (m, 1H), 7.26-7.16 (m, 4H), 5.72-5.71 (m, 1H), 4.39-4.25 (m, 4H), 3.85-3.80 (m, 1H), 3.46-3.40 (m, 1H), 3.38-3.35 (m, 1H), 2.89-2.85 (m, 1H), 1.32-1.28 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 177.8, 171.5, 171.4, 165.7 (d, *J* = 251.4 HZ), 153.1, 151.8, 146.3, 131.3 (d, *J* = 8.6 HZ), 128.4, 127.5 (d, *J* = 3.4 HZ), 126.5, 121.7,

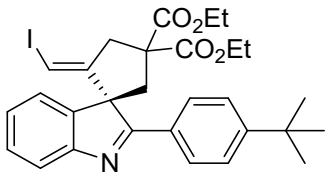
121.2, 116.0 (d, J = 21.6 HZ), 74.6, 68.0, 62.5, 62.4, 58.4, 45.6, 44.0, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -108.3 (s). HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}FINO_4^+$ 548.0729, found 548.0736.



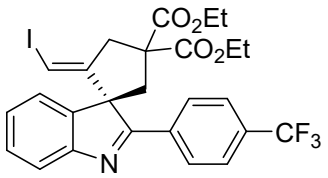
Compound **3h**: 79.1 mg, 65% yield, white solid, mp 133-134 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25-8.23 (m, 1H), 7.79 (d, J = 7.88 Hz, 1H), 7.69 (d, J = 7.68 Hz, 1H), 7.64-7.62 (m, 1H), 7.40-7.34 (m, 2H), 7.26-7.21 (m, 2H), 5.73-5.72 (m, 1H), 4.38-4.26 (m, 4H), 3.84-3.79 (m, 1H), 3.46-3.35 (m, 2H), 2.89-2.85 (m, 1H), 1.32-1.28 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 177.5, 171.5, 171.3, 153.0, 151.5, 146.4, 133.9, 133.2, 131.9, 130.1, 128.5, 127.4, 126.9, 123.0, 121.8, 121.4, 74.7, 68.0, 62.6, 62.4, 58.5, 45.7, 43.7, 14.1, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}BrINO_4^+$ 607.9928, found 607.9922.



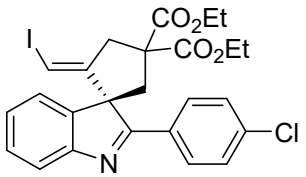
Compound **3i**: 86.8 mg, 78% yield, white solid, mp 94-96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92-7.90 (m, 2H), 7.68 (d, J = 7.68 Hz, 1H), 7.38-7.32 (m, 3H), 7.25-7.17 (m, 2H), 5.72-5.70 (m, 1H), 4.39-4.25 (m, 4H), 3.85-3.80 (m, 1H), 3.50-3.40 (m, 2H), 2.90-2.87 (m, 1H), 2.76 (q, J = 7.60 Hz, 2H), 1.32-1.28 (m, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 179.0, 171.6, 171.5, 153.4, 152.1, 147.7, 146.4, 129.1, 128.5, 128.3, 128.2, 126.3, 121.7, 121.0, 74.5, 68.0, 62.4, 62.3, 58.5, 45.7, 44.2, 28.9, 15.2, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{27}H_{29}INO_4^+$ 558.1136, found 558.1128.



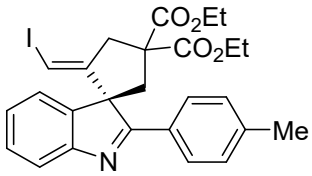
Compound **3j**: 99.9 mg, 85% yield, white solid, mp 65-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94-7.92 (m, 2H), 7.68 (d, *J* = 7.64 Hz, 1H), 7.52-7.50 (m, 2H), 7.38-7.34 (m, 1H), 7.26-7.18 (m, 2H), 5.72-5.71 (m, 1H), 4.39-4.26 (m, 4H), 3.85-3.80 (m, 1H), 3.52-3.47 (m, 1H), 3.45-3.41 (m, 1H), 2.91-2.88 (m, 1H), 1.38 (s, 9H), 1.32 (t, *J* = 7.12 Hz, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 178.9, 171.6, 171.5, 154.5, 153.4, 152.1, 146.4, 128.9, 128.3, 126.2, 125.7, 121.7, 121.0, 74.5, 68.0, 62.4, 62.3, 58.6, 45.7, 44.2, 35.0, 31.2, 14.0, 13.9. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{29}H_{33}INO_4^+$ 586.1449, found 586.1462.



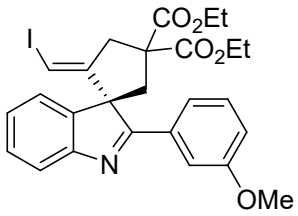
Compound **3k**: 108.7 mg, 91% yield, white solid, mp 127-128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.28 Hz, 2H), 7.77 (d, *J* = 8.40 Hz, 2H), 7.71 (d, *J* = 7.72 Hz, 1H), 7.41-7.37 (m, 1H), 7.29-7.25 (m, 2H), 5.74-5.73 (m, 1H), 4.39-4.25 (m, 4H), 3.87-3.82 (m, 1H), 3.47-3.37 (m, 2H), 2.90-2.87 (m, 1H), 1.32 (t, *J* = 7.08 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 177.4, 171.5, 171.4, 152.9, 151.4, 146.4, 134.5, 132.8 (d, *J* = 32.4 HZ), 129.3, 128.5, 127.9 (d, *J* = 270.7 HZ), 127.2, 125.7 (d, *J* = 3.5 HZ), 121.8, 121.7, 74.6, 68.1, 62.6, 62.5, 58.4, 45.7, 43.5, 14.0, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.9 (s). HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{24}F_3INO_4^+$ 598.0697, found 598.0703.



Compound **3l**: 104.5 mg, 93% yield, white solid, mp 150-153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94-7.92 (m, 2H), 7.68 (d, *J* = 7.68 Hz, 1H), 7.49-7.46 (m, 2H), 7.40-7.36 (m, 1H), 7.24-7.22 (m, 2H), 5.72-5.71 (m, 1H), 4.39-4.26 (m, 4H), 3.85-3.80 (m, 1H), 3.45-3.35 (m, 2H), 2.88-2.84 (m, 1H), 1.33-1.28 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 177.8, 171.5, 171.4, 153.0, 151.7, 146.3, 137.3, 130.3, 129.5, 129.0, 128.4, 126.7, 121.7, 121.3, 74.6, 68.0, 62.6, 62.5, 58.4, 45.6, 43.9, 14.1. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}ClINO_4^+$ 564.0433, found 564.0433.

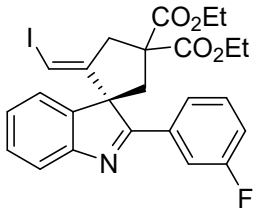


Compound **3m**: 78.9 mg, 73% yield, white solid, mp 139-140 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.22 Hz, 2H), 7.67 (d, *J* = 7.68 Hz, 1H), 7.38-7.35 (m, 1H), 7.31 (d, *J* = 8.10 Hz, 2H), 7.25-7.24 (m, 1H), 7.21-7.18 (m, 1H), 7.02-6.99 (m, 2H), 5.71-5.70 (m, 1H), 4.38-4.26 (m, 4H), 3.84-3.81 (m, 1H), 3.48-3.45 (m, 1H), 3.43-3.40 (m, 1H), 2.89-2.87 (m, 1H), 2.43 (s, 3H), 1.32-1.29 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 179.0, 171.6, 171.5, 153.4, 152.1, 146.4, 141.5, 129.4, 129.0, 128.4, 128.3, 126.3, 121.7, 121.0, 74.5, 68.0, 62.4, 62.3, 58.5, 45.7, 44.2, 21.6, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{27}INO_4^+$ 544.0979, found 544.0996.

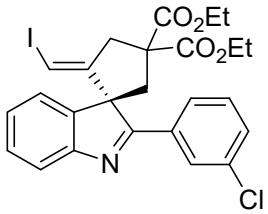


Compound **3n**: 66.2 mg, 59% yield, white solid, mp 145-146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.67 (m, 1H), 7.56-7.55 (m, 1H), 7.50-7.48 (m, 1H), 7.41-7.36 (m, 2H), 7.23-7.21 (m, 2H), 7.08-7.05 (m, 1H), 5.75-5.74 (m, 1H), 4.38-4.25 (m, 4H), 3.92, (s, 3H), 3.83-3.78 (m, 1H), 3.48-3.38 (m, 2H), 2.90-2.87 (m, 1H), 1.32-1.27 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 179.0,

171.5, 171.3, 159.7, 153.2, 151.9, 146.3, 132.6, 129.6, 128.3, 126.5, 121.8, 121.6, 121.2, 118.0, 113.1, 74.7, 68.2, 62.4, 62.3, 58.6, 55.5, 45.8, 44.0, 14.0, 13.9. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{27}INO_5^+$ 560.0928, found 560.0944.

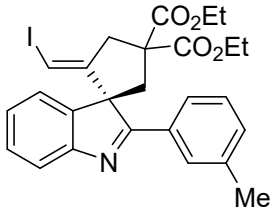


Compound **3o**: 85.5 mg, 78% yield, white solid, mp 159-162 °C. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.77-7.75 (m, 1H), 7.70-7.68 (m, 2H), 7.48-7.44 (m, 1H), 7.39-7.37 (m, 1H), 7.26-7.19 (m, 3H), 5.75-5.70 (m, 1H), 4.38-4.28 (m, 4H), 3.84-3.80 (m, 1H), 3.46-3.43 (m, 1H), 3.41-3.38 (m, 1H), 2.90-2.87 (m, 1H), 1.32-1.29 (m, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ = 177.7, 171.5, 171.3, 163.6 (d, *J* = 245.0 HZ), 153.0, 151.6, 146.4, 133.5 (d, *J* = 7.5 HZ), 130.2 (d, *J* = 8.0 HZ), 128.4, 126.9, 124.7 (d, *J* = 2.8 HZ), 121.7, 121.4, 118.0 (d, *J* = 21.2 HZ), 115.8 (d, *J* = 23.1 HZ), 74.6, 68.0, 62.5, 62.4, 58.5, 45.6, 43.7, 14.0, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -111.6 (s). HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}FINO_4^+$ 548.0729, found 548.0753.

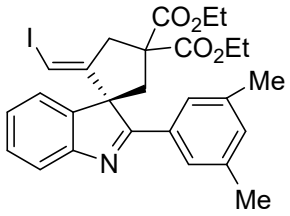


Compound **3p**: 99.2 mg, 88% yield, white solid, mp 150-151 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.09-8.08 (m, 1H), 7.76-7.74 (m, 1H), 7.69 (d, *J* = 7.68 Hz, 1H), 7.49-7.36 (m, 3H), 7.26-7.21 (m, 2H), 5.73-5.72 (m, 1H), 4.39-4.26 (m, 4H), 3.84-3.79 (m, 1H), 3.46-3.36 (m, 2H), 2.89-2.86 (m, 1H), 1.32-1.28 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ = 177.6, 171.5, 171.3, 153.0, 152.9, 151.5, 146.4, 134.9, 133.0, 131.0, 129.9, 129.0, 128.5, 126.9, 121.8, 121.4, 74.7, 68.0, 62.6, 62.5,

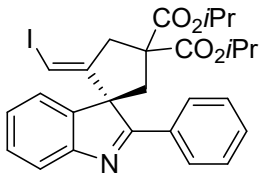
58.4, 45.6, 43.7, 14.1. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{25}H_{24}ClINO_4^+$ 564.0433, found 564.0438.



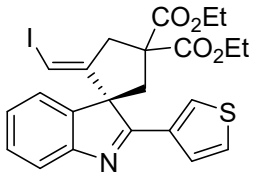
Compound **3q**: 76.1 mg, 70% yield, white solid, mp 146-148 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (s, 1H), 7.70-7.68 (m, 2H), 7.40-7.32 (m, 3H), 7.27-7.22 (m, 2H), 5.73-5.72 (m, 1H), 4.37-4.24 (m, 4H), 3.82-3.77 (m, 1H), 3.51-3.45 (m, 1H), 3.42-3.38 (m, 1H), 2.92-2.88 (m, 1H), 2.46 (s, 3H), 1.32-1.28 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 179.3, 171.6, 171.4, 153.3, 152.0, 146.4, 138.5, 131.8, 131.1, 129.7, 128.5, 128.3, 126.4, 126.1, 121.7, 121.1, 74.5, 68.1, 62.4, 62.3, 58.5, 45.7, 44.0, 21.4, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{26}H_{27}INO_4^+$ 544.0979, found 544.0981.



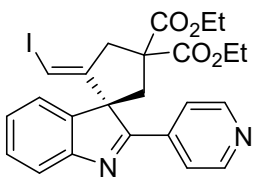
Compound **3r**: 83.9 mg, 75% yield, white solid, mp 140-142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 7.68 Hz, 1H), 7.59 (s, 2H), 7.39-7.35 (m, 1H), 7.28-7.26 (m, 1H), 7.23-7.21 (m, 1H), 7.15 (s, 1H), 5.71-5.70 (m, 1H), 4.37-4.24 (m, 4H), 3.80-3.75 (m, 1H), 3.54-3.48 (m,1H), 3.42-3.38 (m,1H), 2.93-2.90 (m, 1H), 2.41 (s, 6H), 1.32-1.27 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 179.5, 171.6, 171.4, 153.3, 152.0, 146.4, 138.3, 132.8, 130.9, 128.3, 126.9, 126.4, 121.8, 121.0, 74.6, 68.1, 62.4, 62.3, 58.5, 45.8, 44.0, 21.3, 14.1. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{27}H_{29}INO_4^+$ 558.1136, found 558.1131.



Compound **3t**: 55.5 mg, 50% yield, white solid, mp 157-160 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.96 (m, 2H), 7.69 (d, *J* = 7.68 Hz, 1H), 7.51-7.48 (m, 3H), 7.40-7.36 (m, 1H), 7.28-7.26 (m, 1H), 7.23-7.20 (m, 1H), 5.73-5.71 (m, 1H), 5.24-5.18 (m, 1H), 5.14-5.08 (m, 1H), 3.81-3.75 (m, 1H), 3.45-3.36 (m, 2H), 2.87-2.84 (m, 1H), 1.33-1.31 (m, 6H), 1.25-1.22 (m, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 179.1, 171.1, 170.9, 153.3, 152.0, 146.4, 131.3, 131.0, 129.0, 128.7, 128.3, 126.5, 121.8, 121.1, 74.3, 70.1, 70.0, 68.1, 58.6, 45.6, 43.8, 21.7, 21.6, 21.5, 21.4. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{27}H_{29}INO_4^+$ 558.1136, found 558.1134.



Compound **3u**: 79.5 mg, 74% yield, white solid, mp 170-172 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.87 (m, 1H), 7.78-7.77 (m, 1H), 7.67-7.65 (m, 1H), 7.43-7.41 (m, 1H), 7.39-7.35 (m, 1H), 7.25-7.18 (m, 2H), 5.70-5.69 (m, 1H), 4.39-4.27 (m, 4H), 3.85-3.80 (m, 1H), 3.47-3.38 (m, 2H), 2.89-2.86 (m, 1H), 1.34-1.28 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 175.1, 171.9, 171.5, 153.5, 151.7, 145.6, 133.7, 129.0, 128.4, 127.9, 126.3, 126.1, 121.7, 121.1, 75.0, 68.0, 62.6, 62.4, 58.2, 45.6, 44.5, 14.1. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{23}H_{23}INO4_S^+$ 536.0387, found 536.0384.

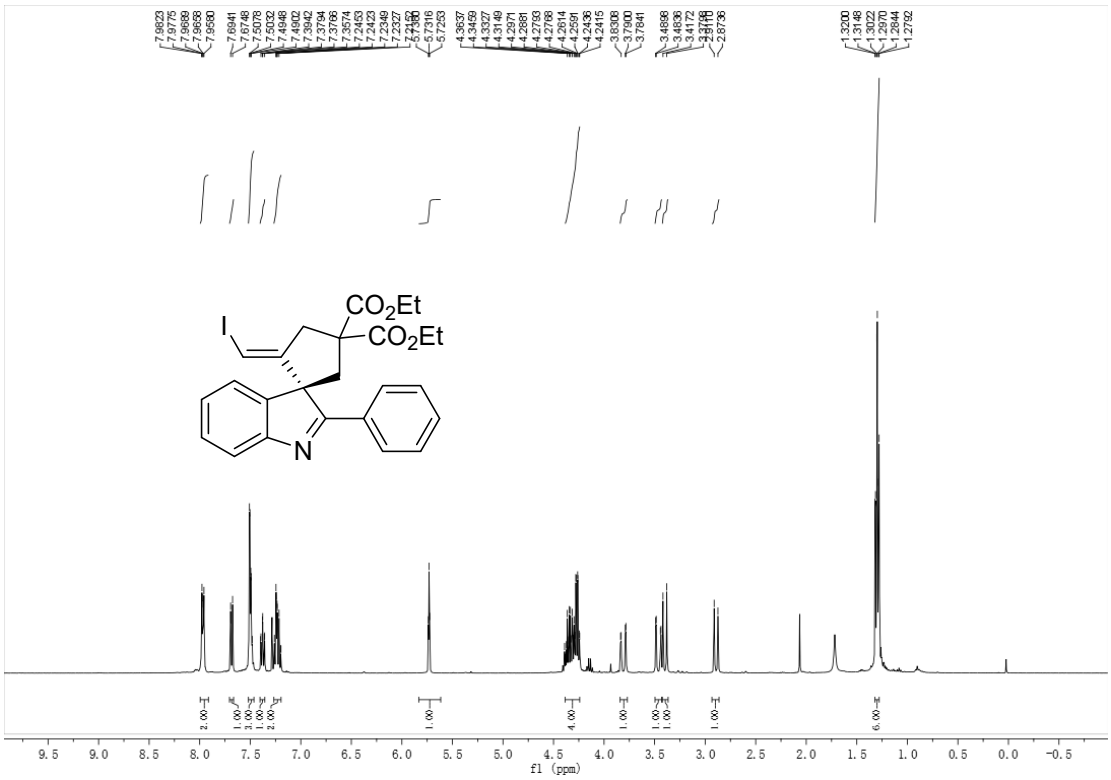


Compound **3v**: 63.9 mg, 60% yield, white solid, mp 155-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ =

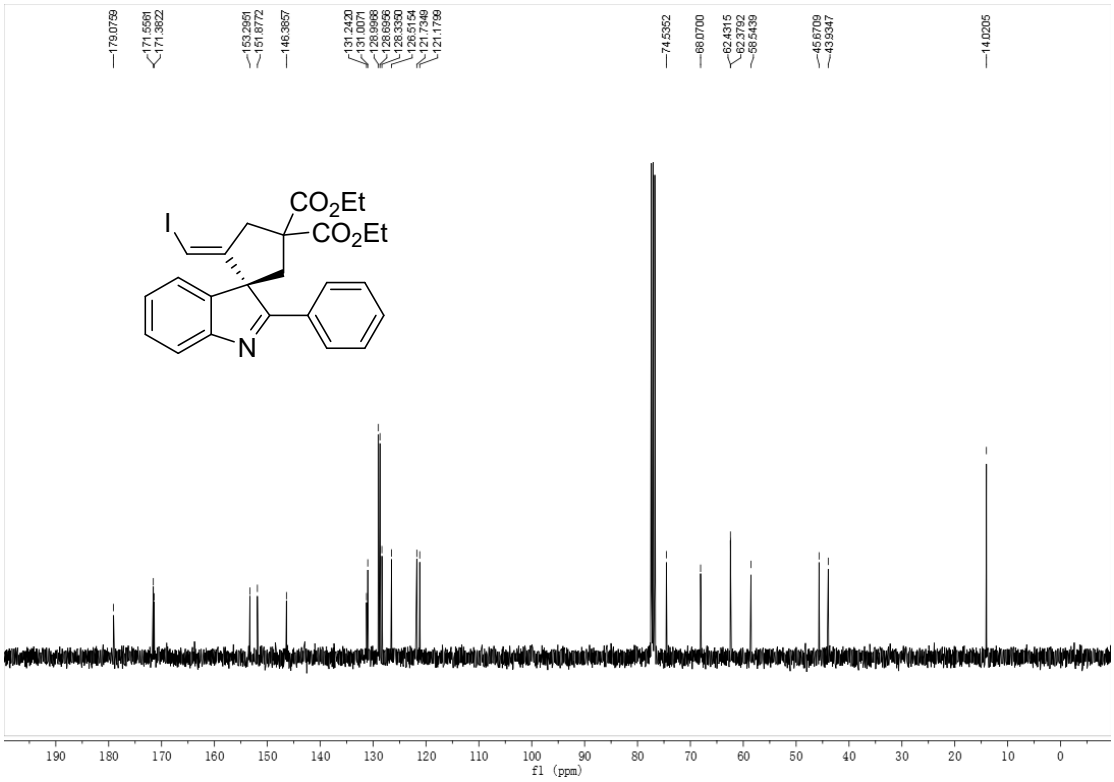
8.77-8.76 (m, 2H), 7.81-7.80 (m, 2H), 7.72 (d, J = 7.64 Hz, 1H), 7.41-7.37 (m, 1H), 7.27-7.26 (m, 2H), 5.71-5.70 (m, 1H), 4.38-4.24 (m, 4H), 3.84-3.79 (m, 1H), 3.44-3.34 (m, 2H), 2.88-2.84 (m, 1H), 1.31-1.27 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ = 176.9, 171.4, 171.3, 152.7, 150.9, 150.5, 146.4, 138.2, 128.6, 127.6, 122.4, 122.0, 121.8, 74.8, 67.9, 62.6, 62.5, 58.4, 45.6, 43.1, 14.0. HRMS (TOF MS ESI) m/z: $[M+H]^+$ calcd for $C_{24}H_{24}IN_2O_4^+$ 531.0775, found 531.0768.

9. ^{1}H, ^{13}C and ^{19}F NMR spectra for compound 3

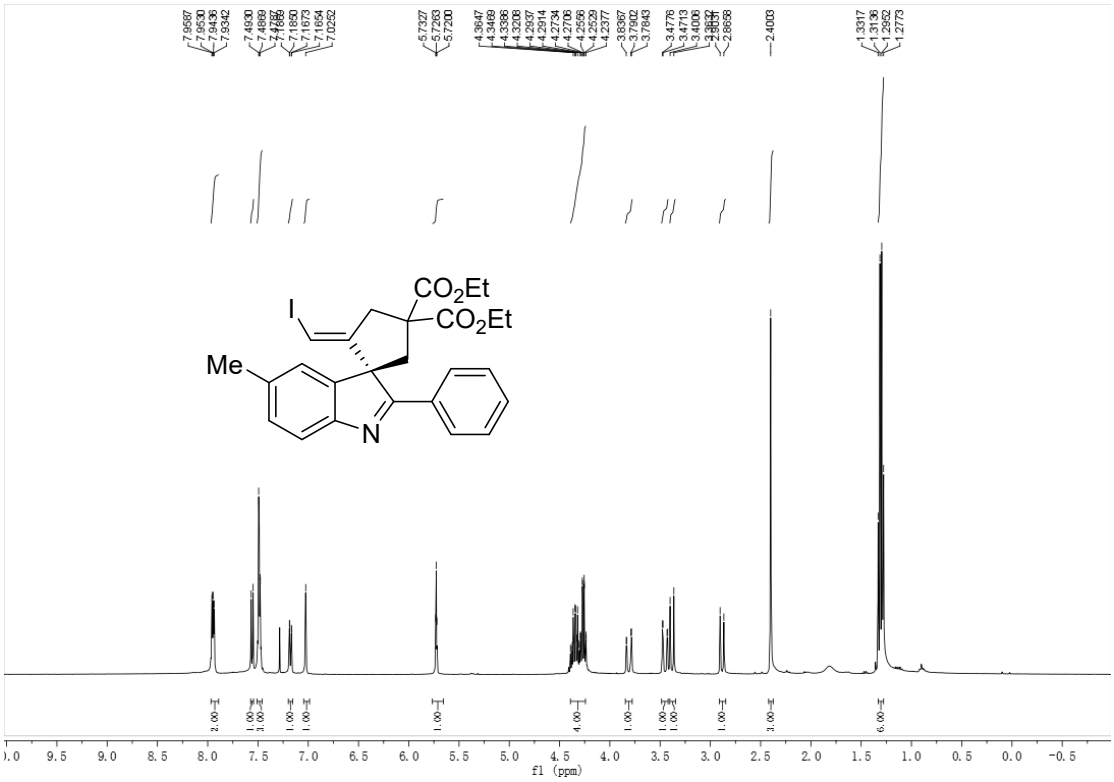
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**:



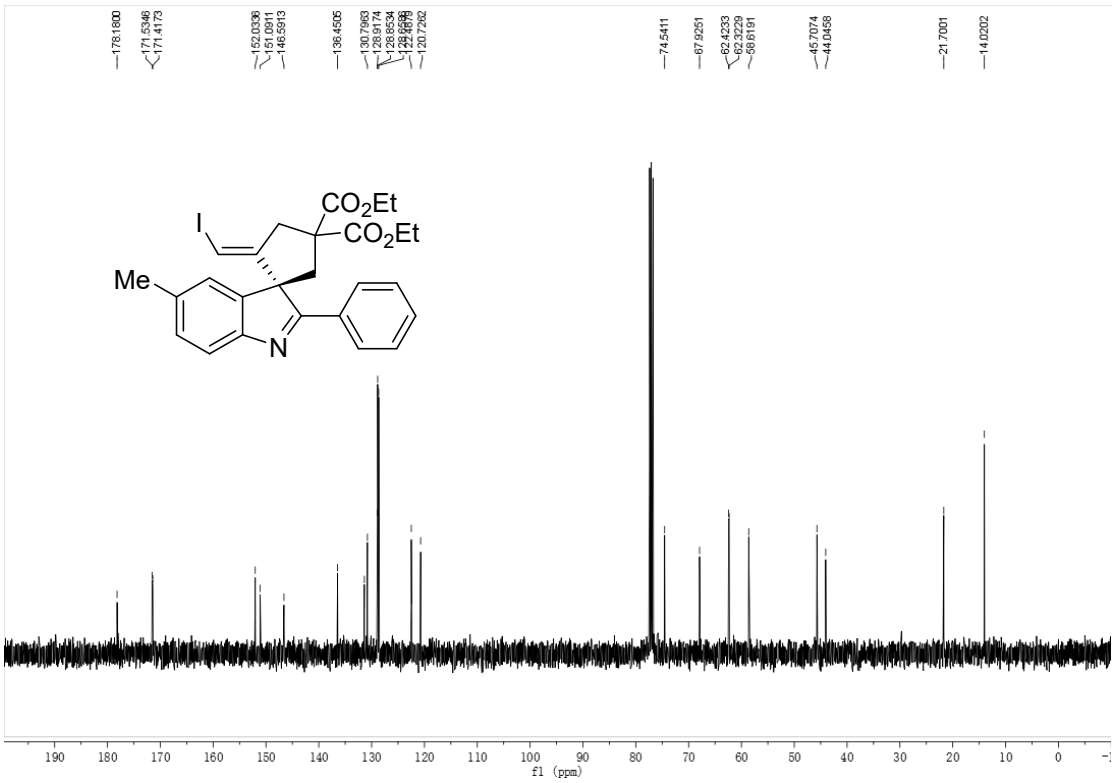
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3a**:



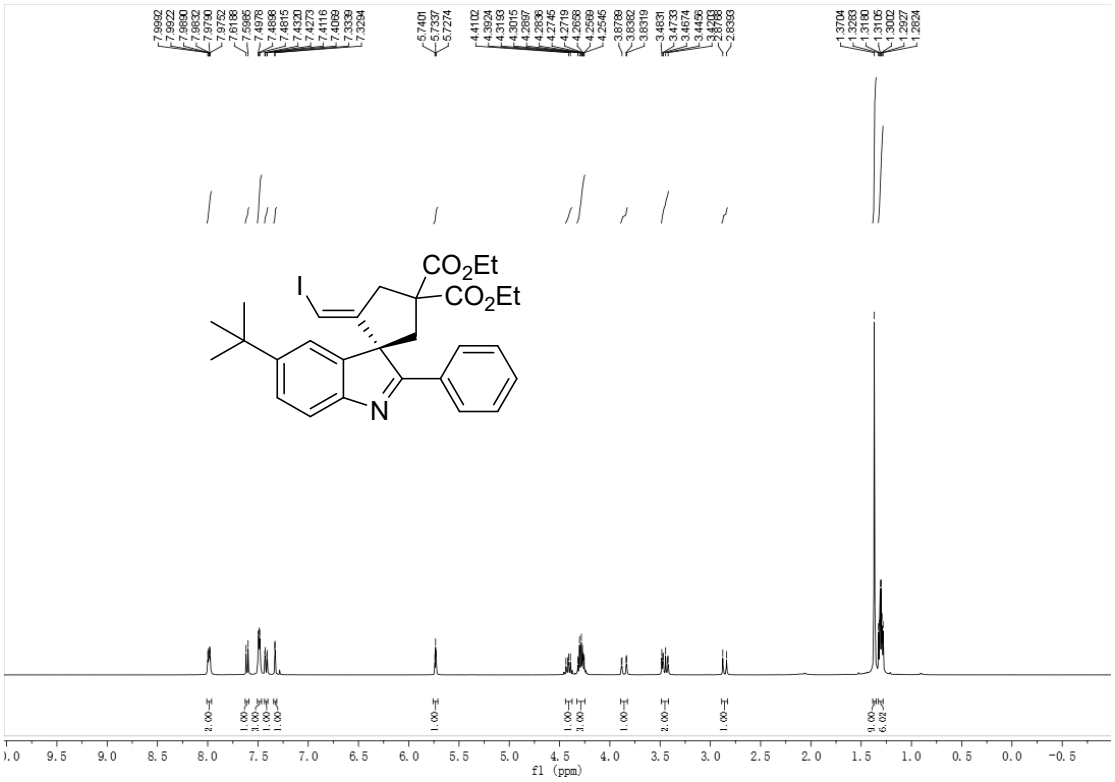
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**:



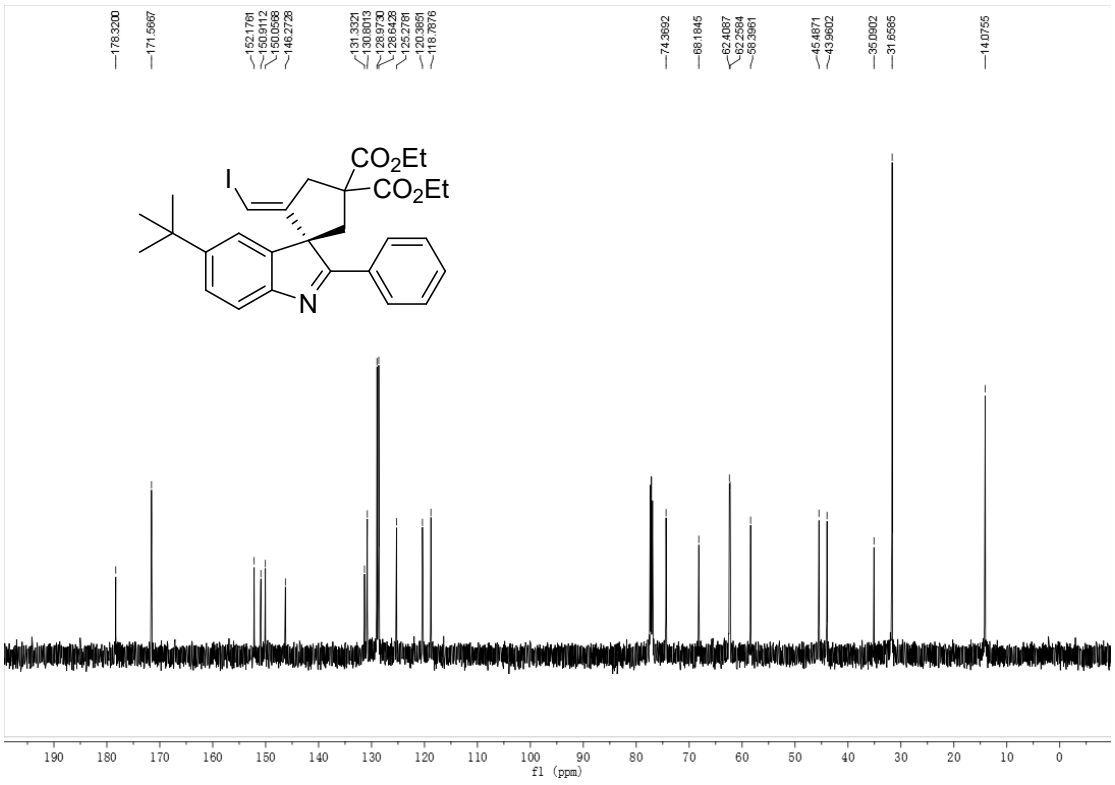
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3b**:



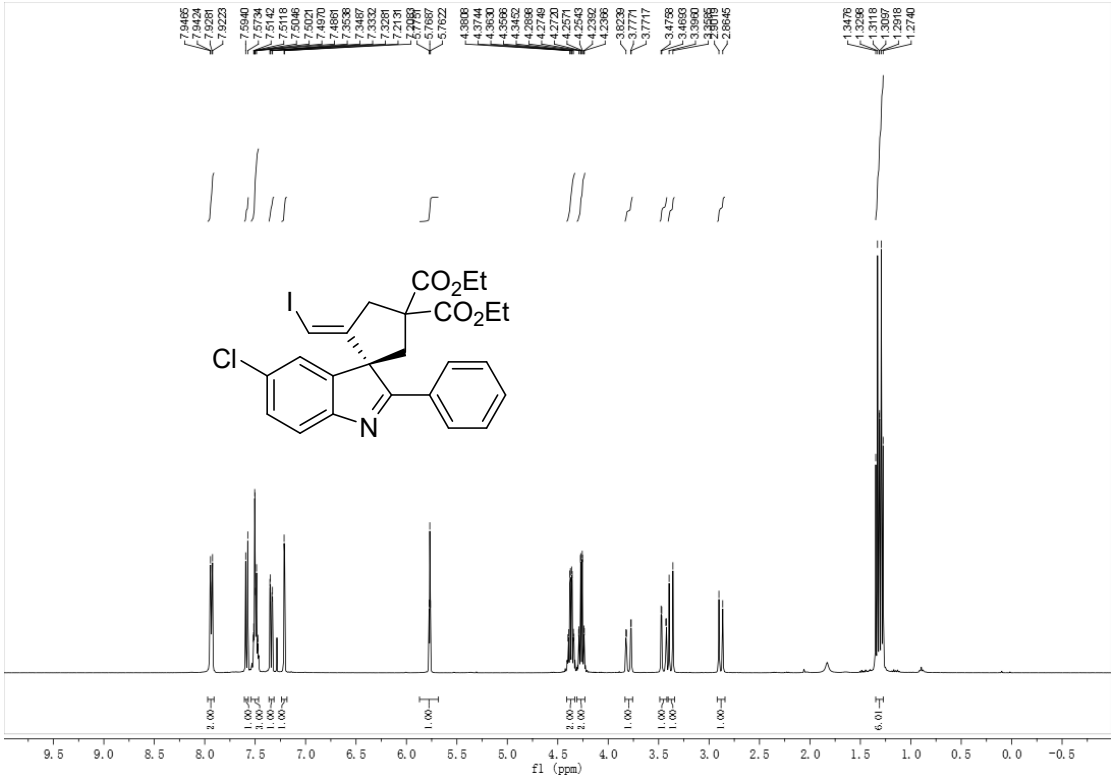
^{1}H NMR (400 MHz, $CDCl_3$) of **3c**:



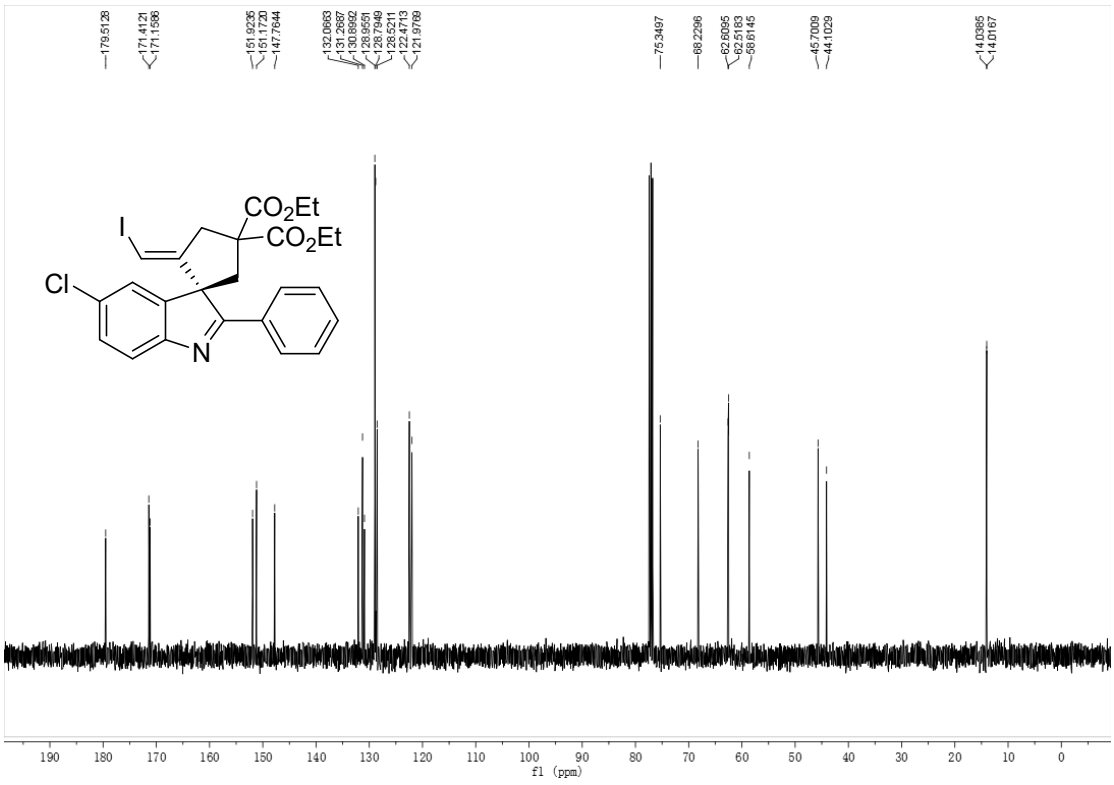
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **3c**:



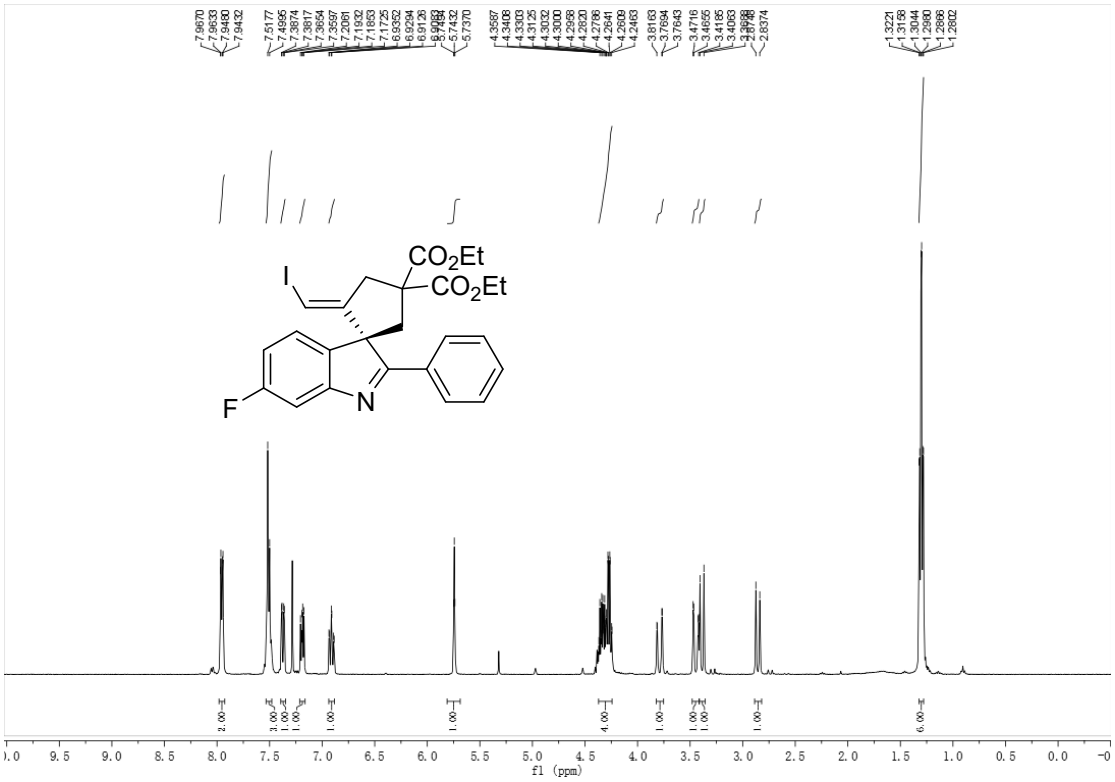
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**:



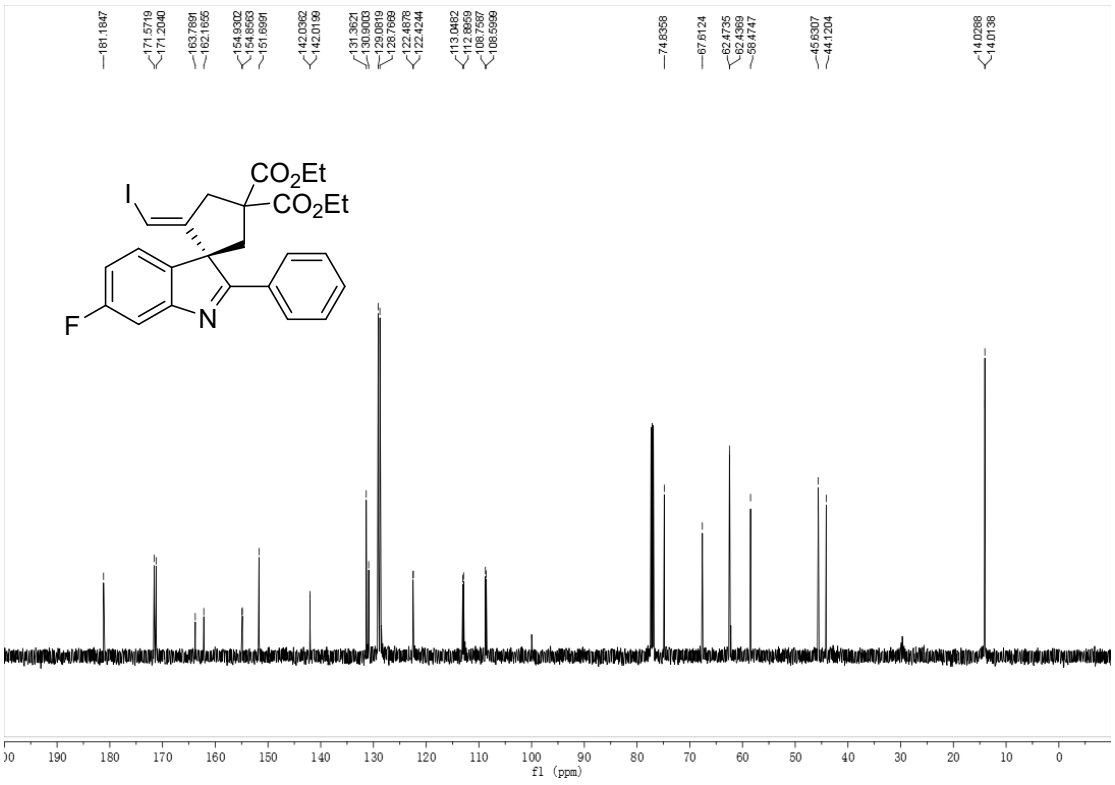
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3d**:



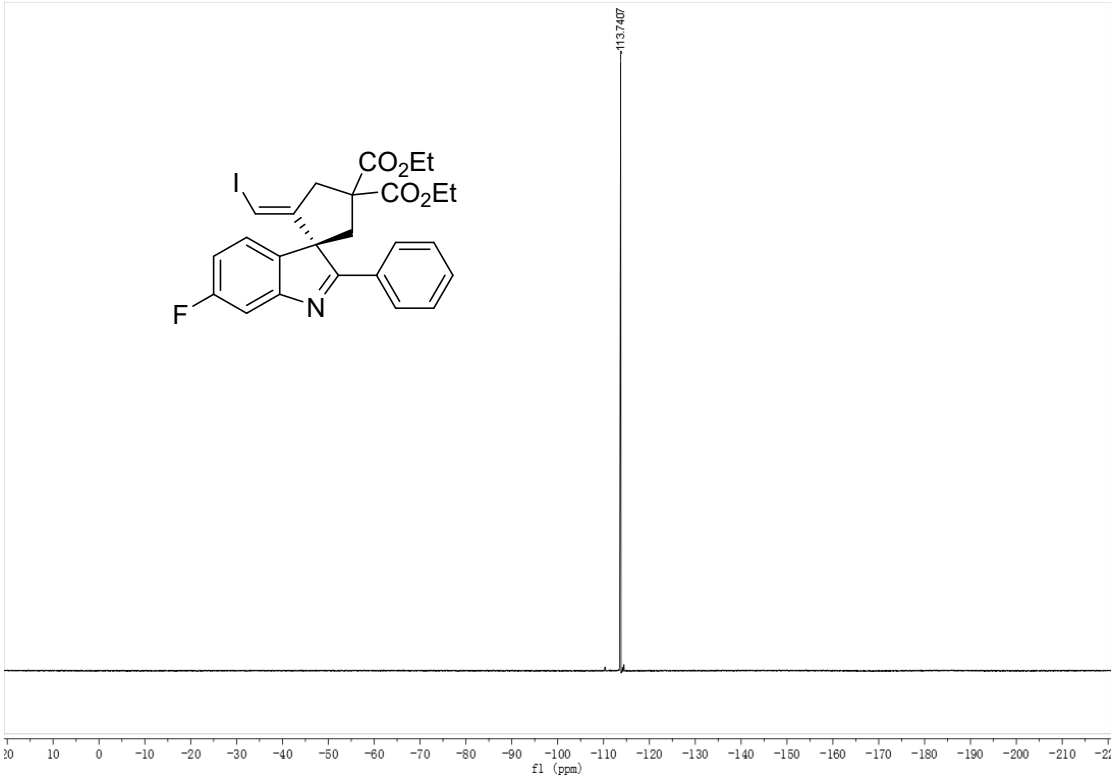
^{1}H NMR (400 MHz, $CDCl_3$) of **3e**:



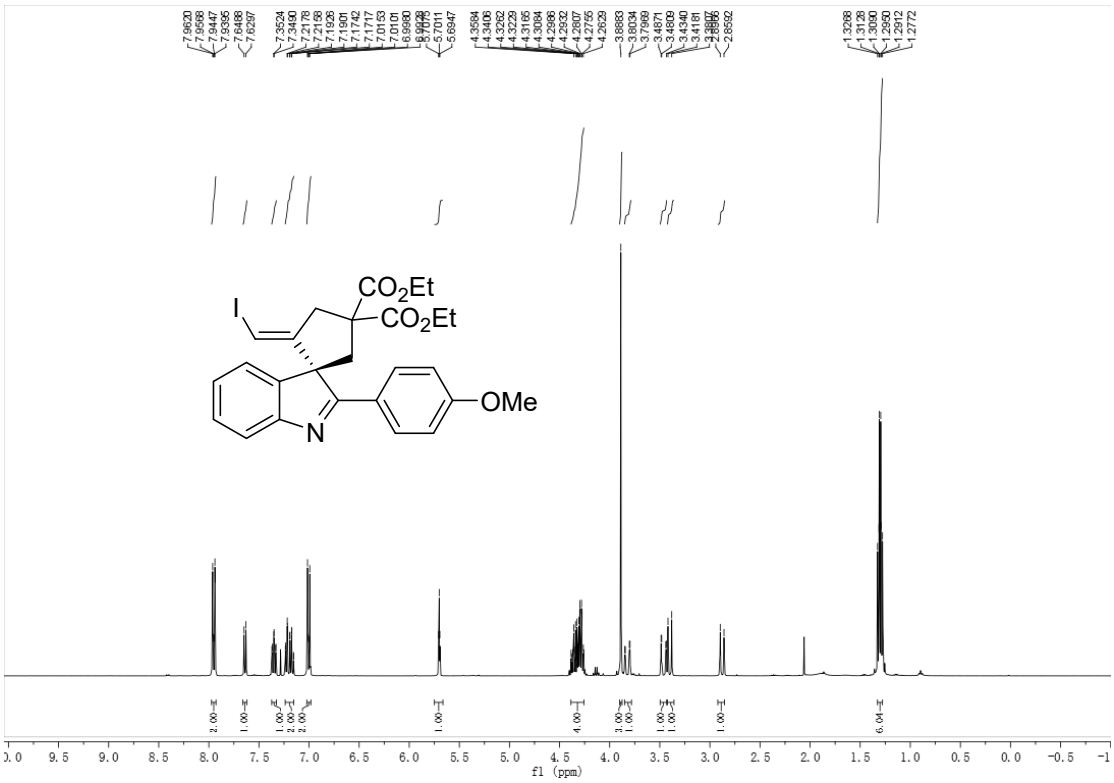
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) of **3e**:



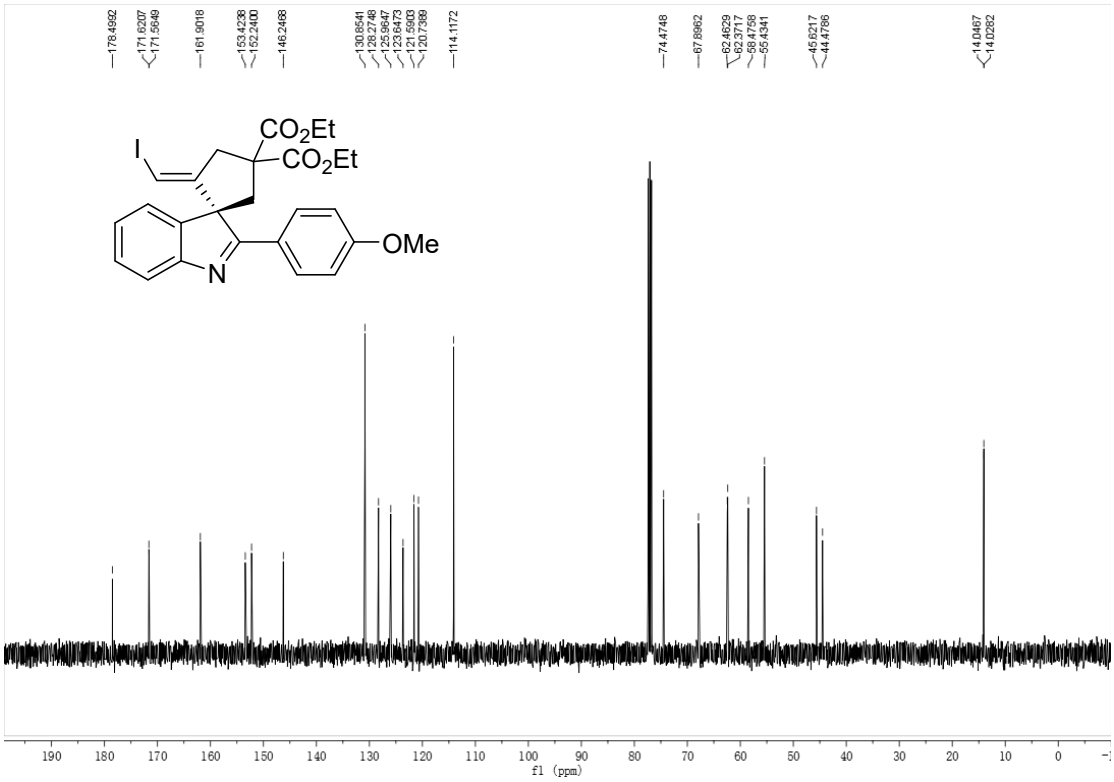
^{19}F NMR (376 MHz, $CDCl_3$) of **3e**:



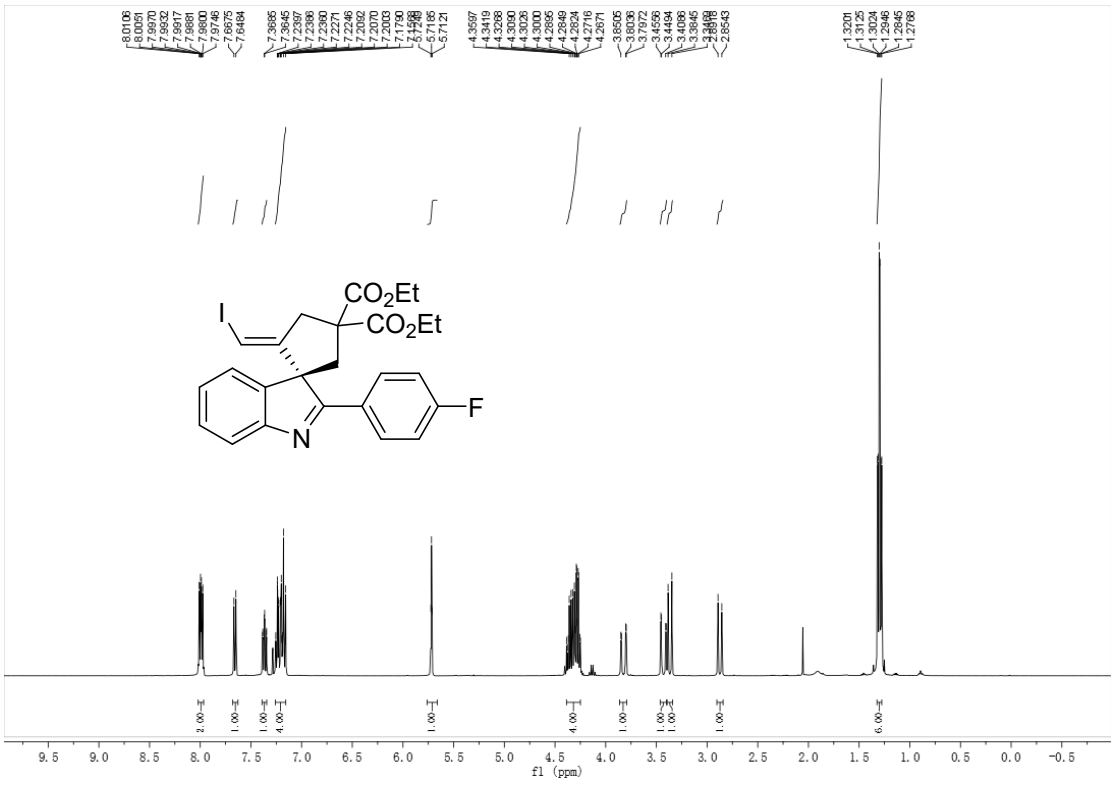
^{1}H NMR (400 MHz, $CDCl_3$) of **3f**:



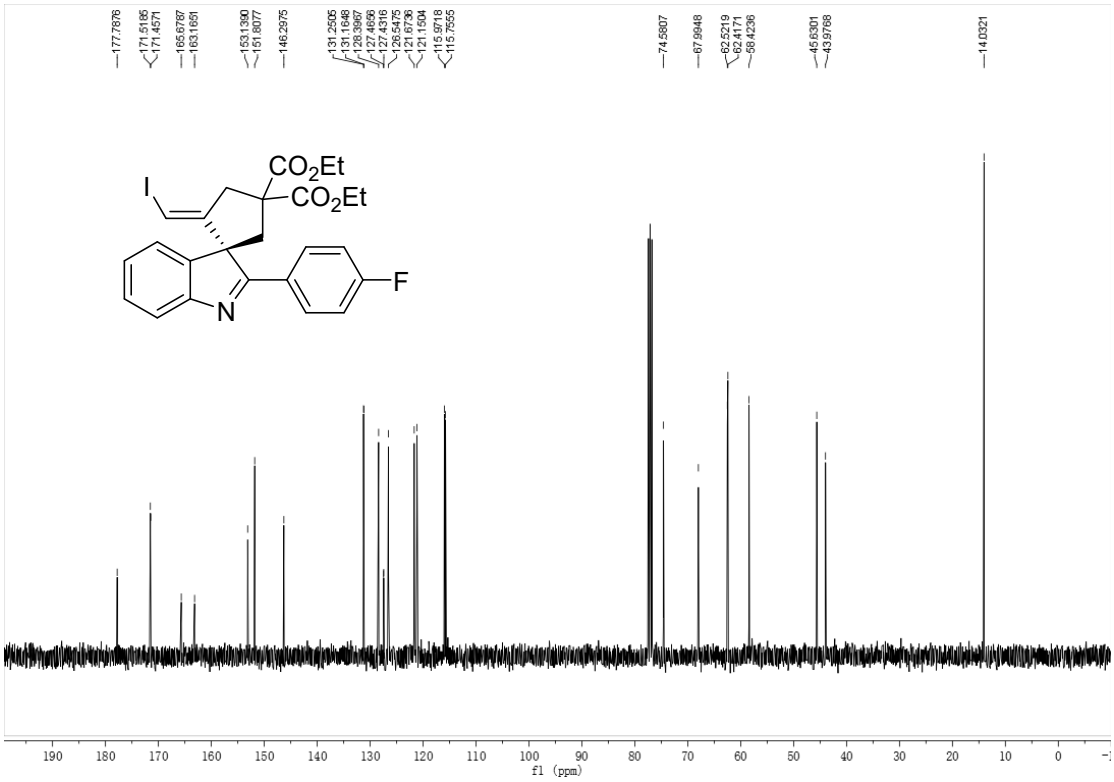
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3f**:



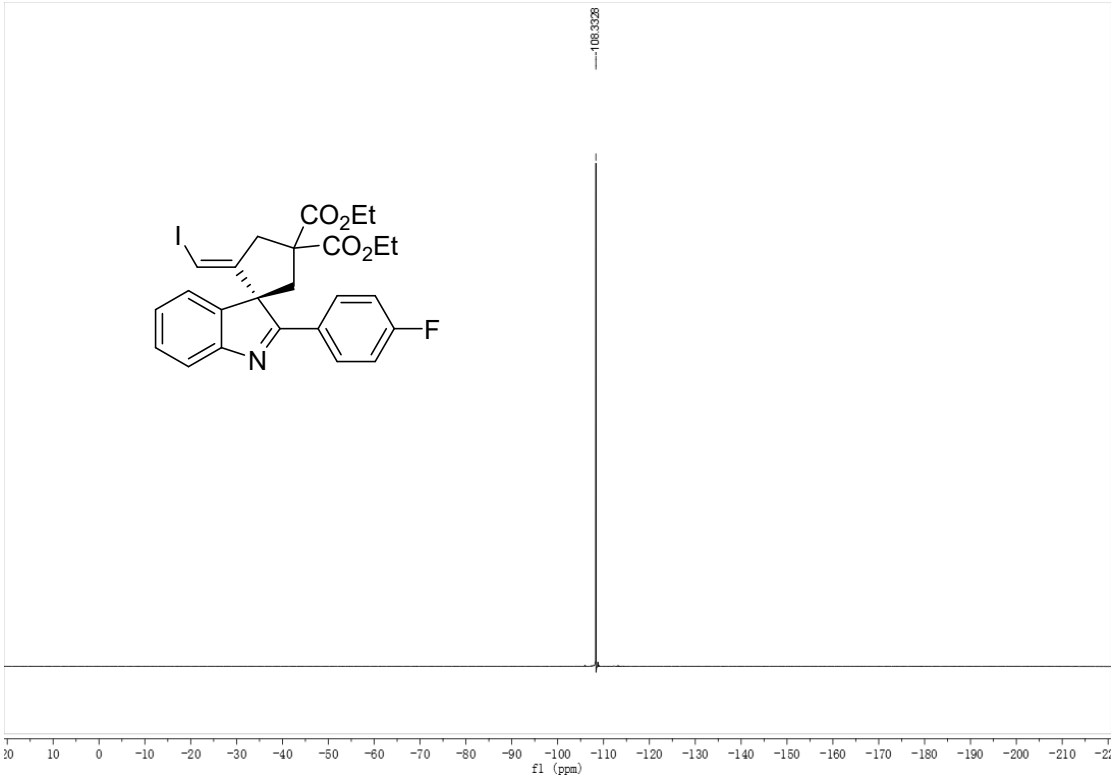
^{1}H NMR (400 MHz, $CDCl_3$) of **3g**:



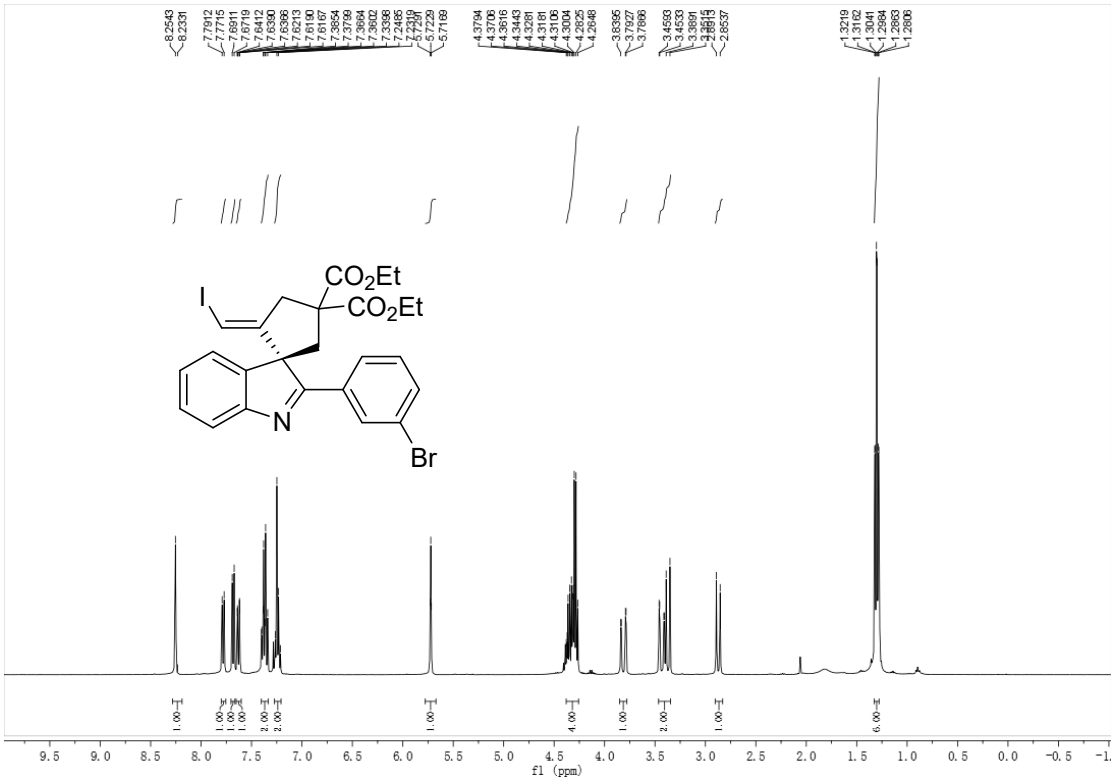
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3g**:



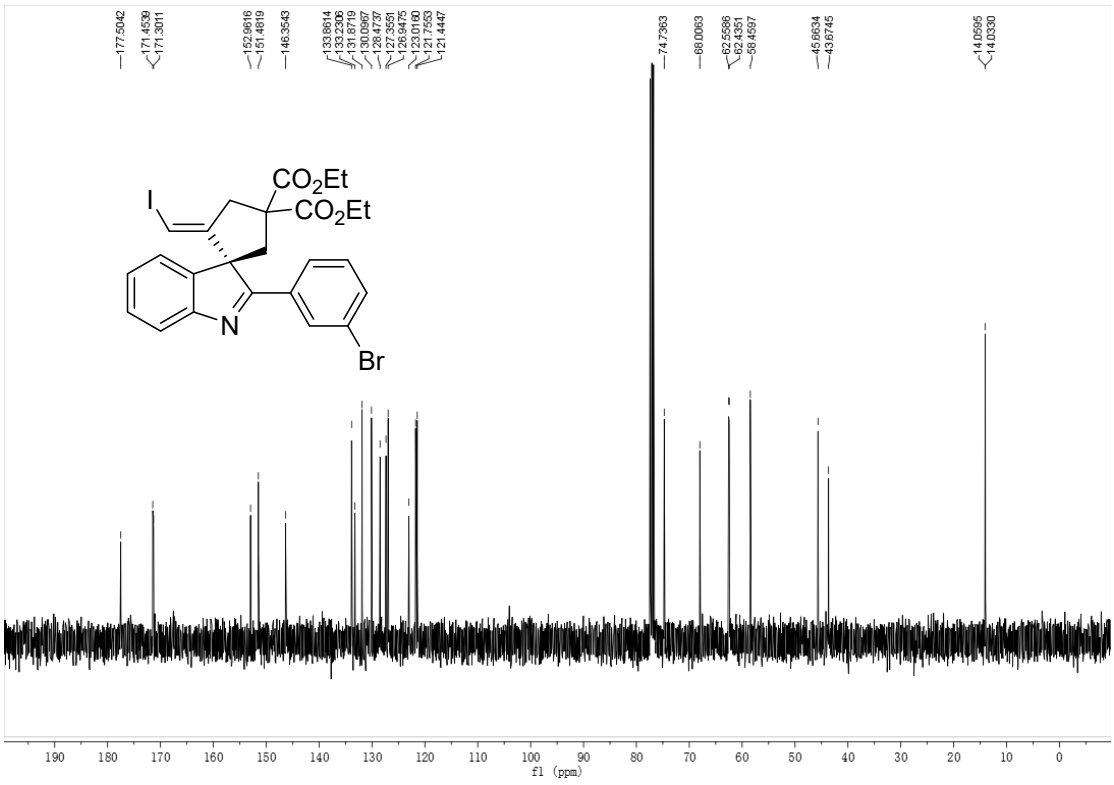
^{19}F NMR (376 MHz, $CDCl_3$) of **3g**:



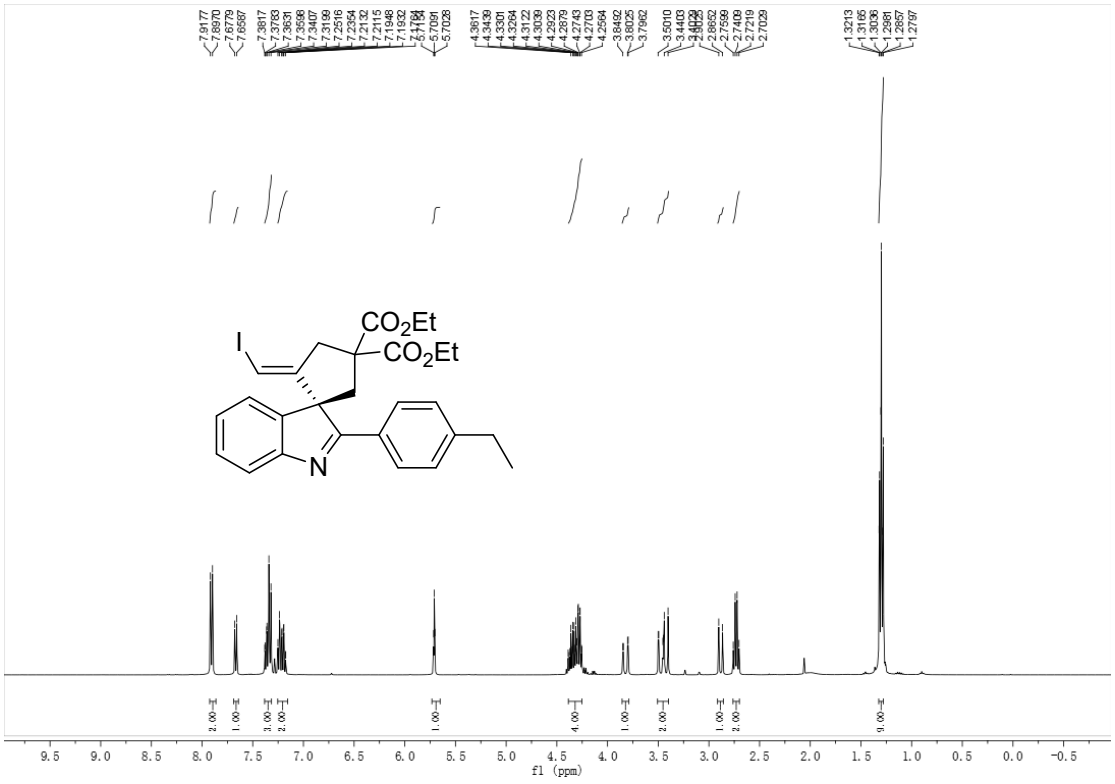
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**:



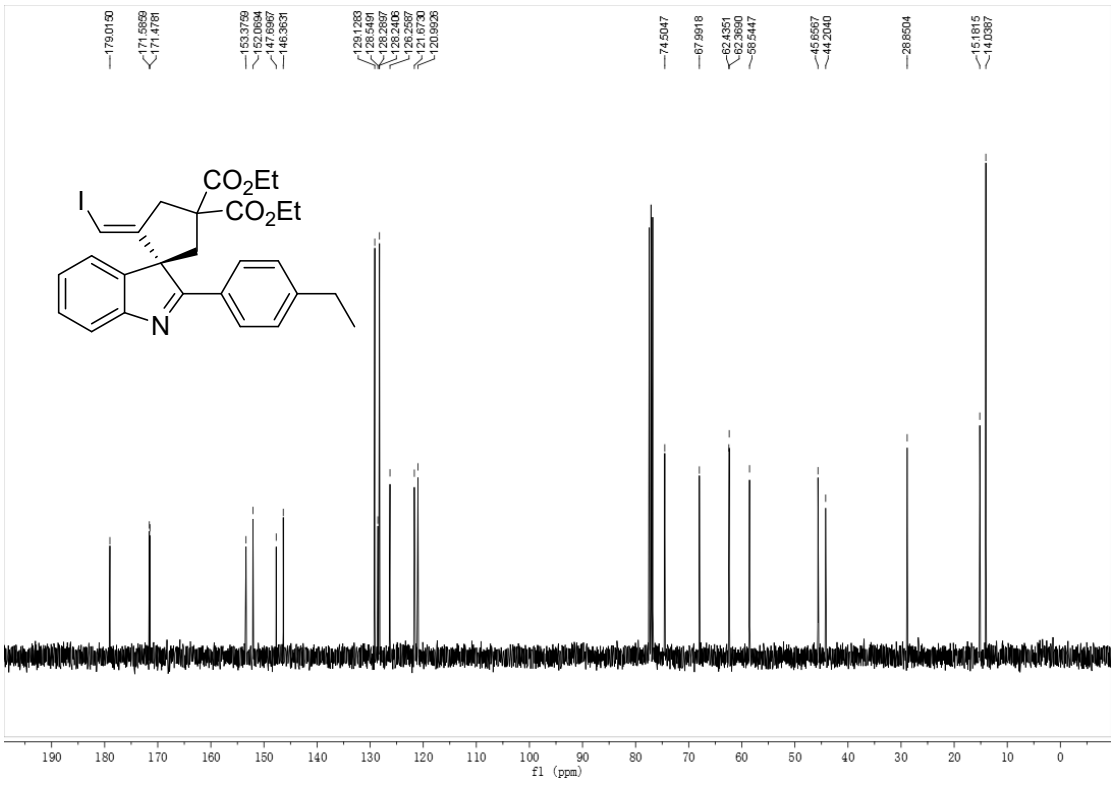
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3h**:



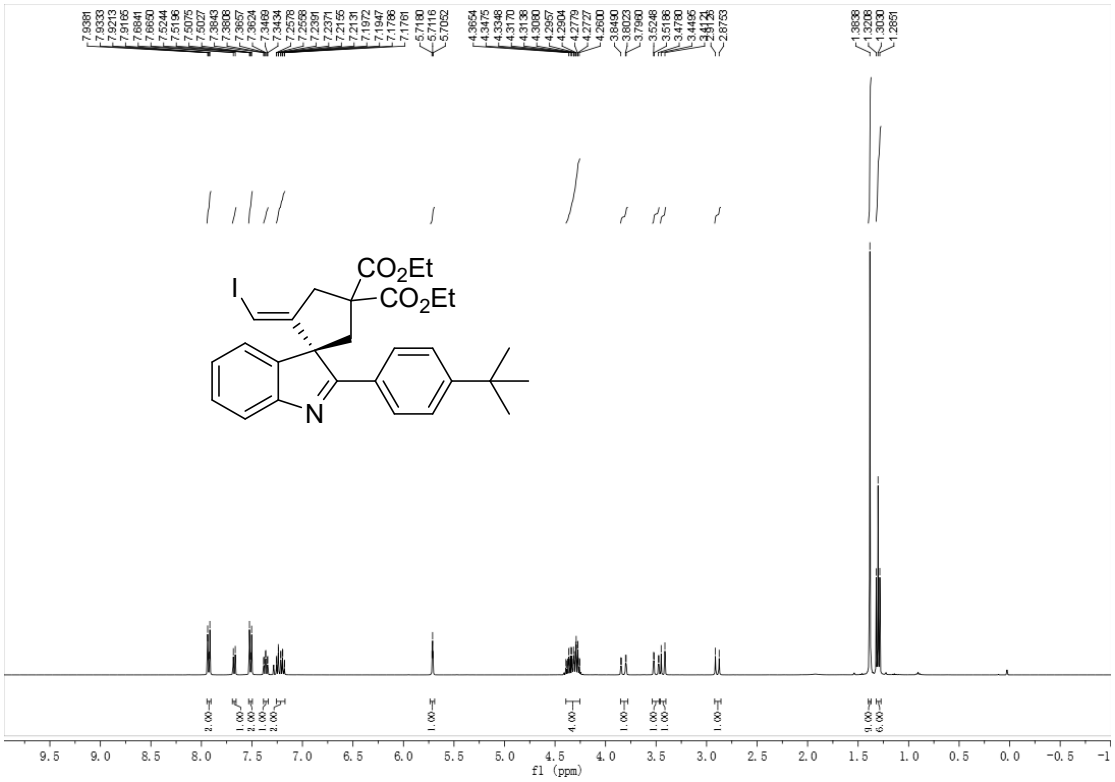
^{1}H NMR (400 MHz, $CDCl_3$) of **3i**:



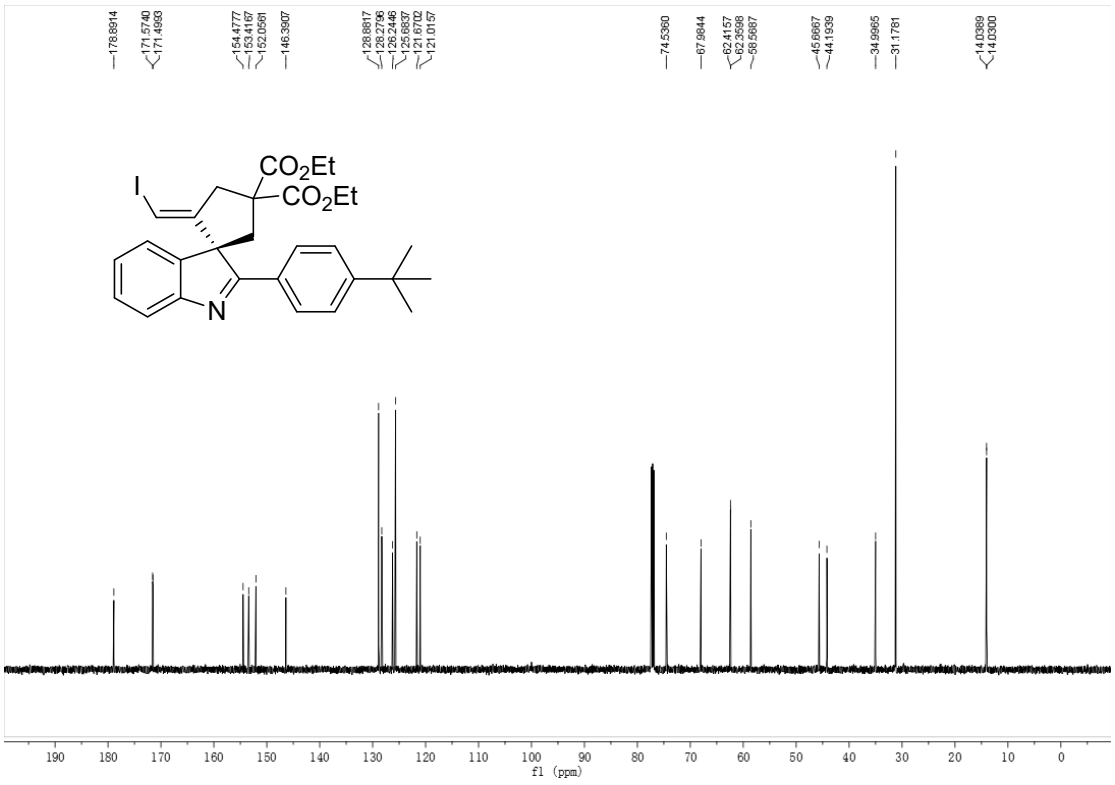
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3i**:



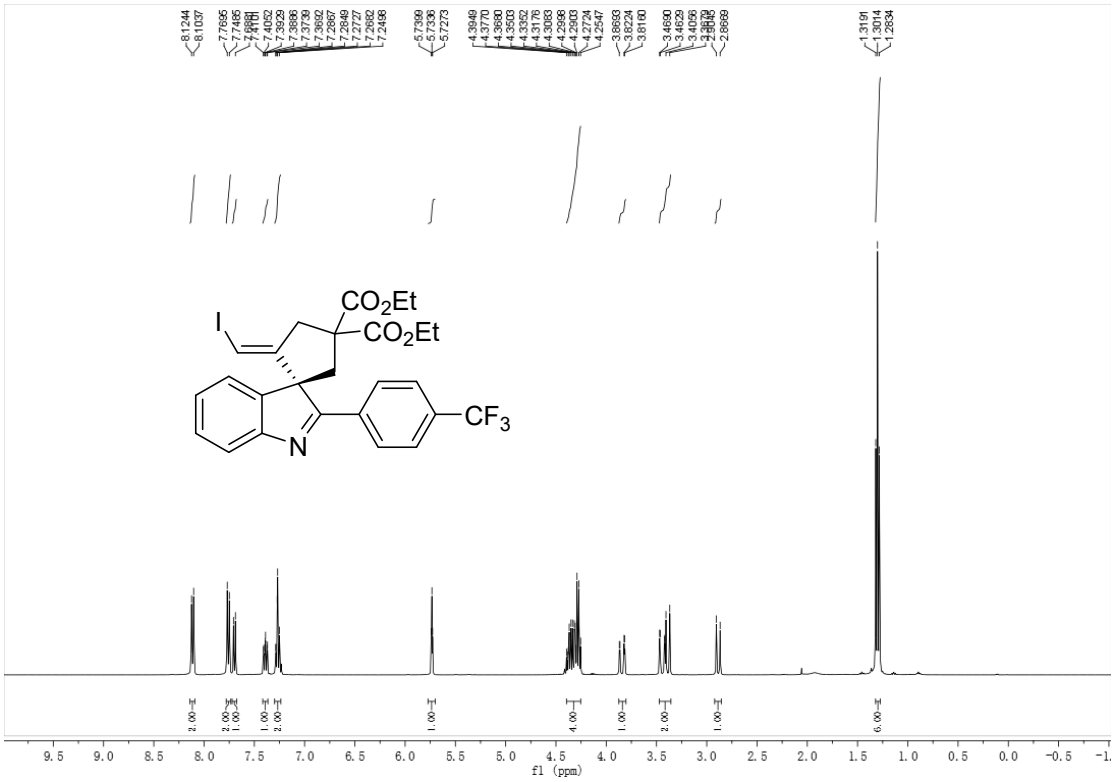
^{1}H NMR (400 MHz, $CDCl_3$) of **3j**:



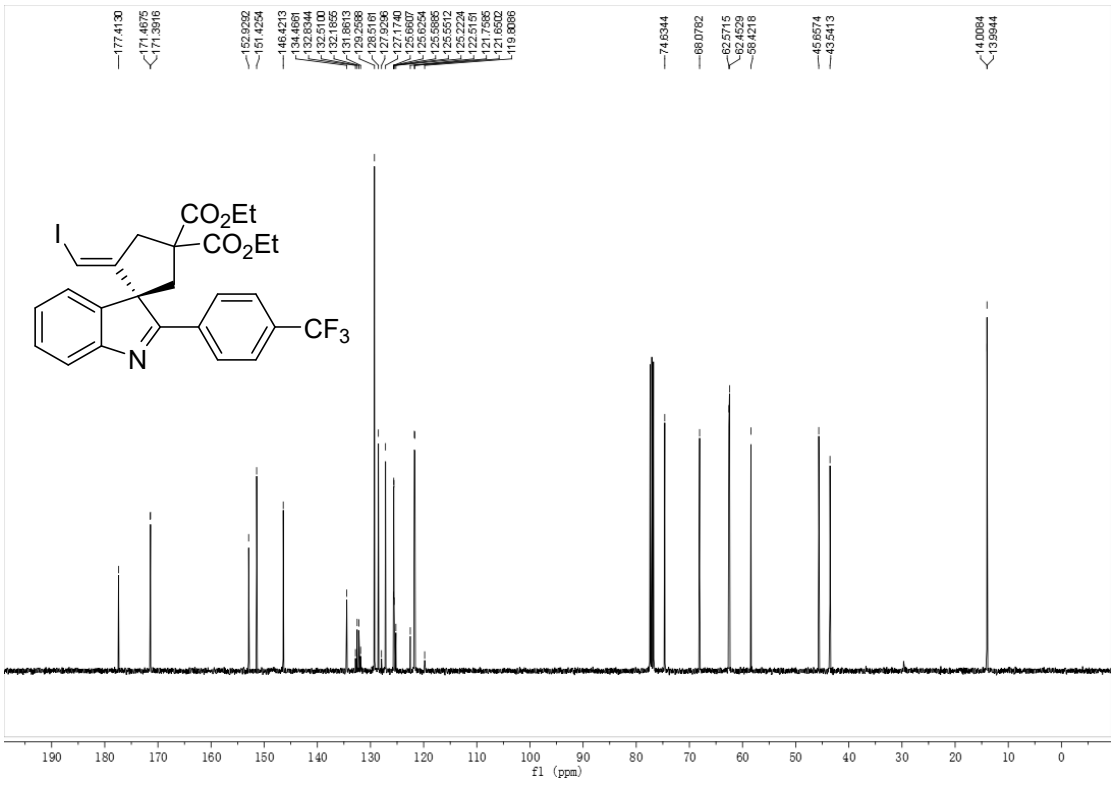
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) of **3j**:



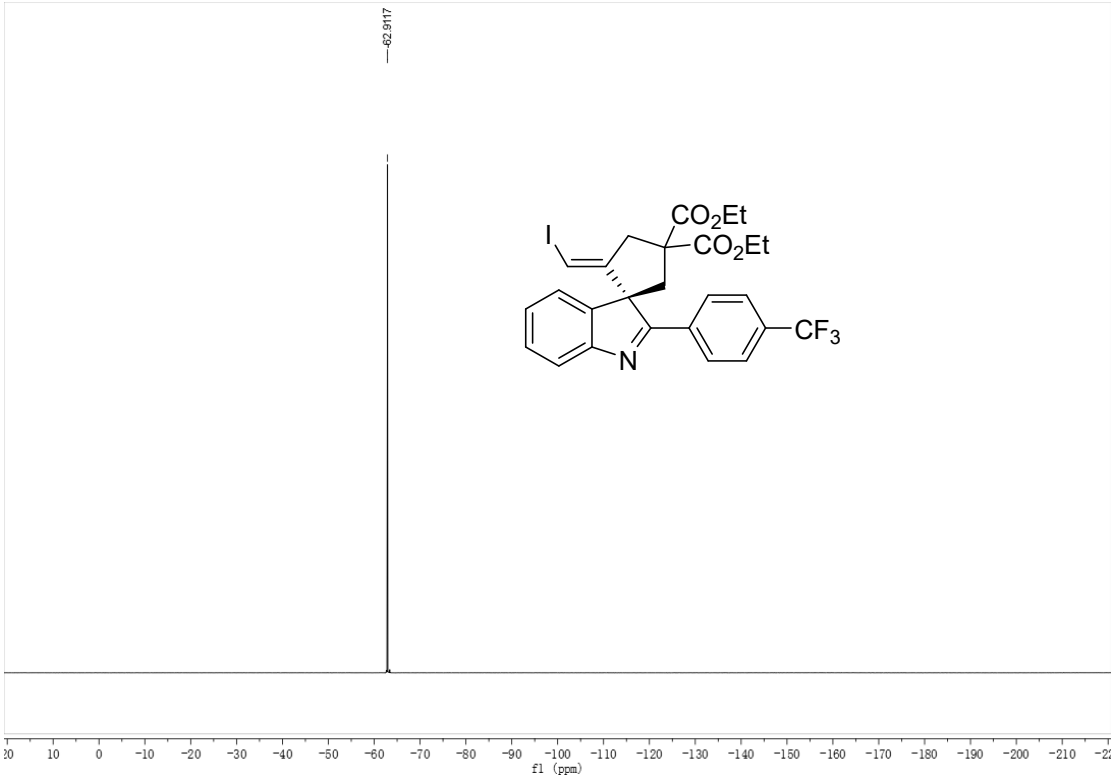
^{1}H NMR (400 MHz, $CDCl_3$) of **3k**:



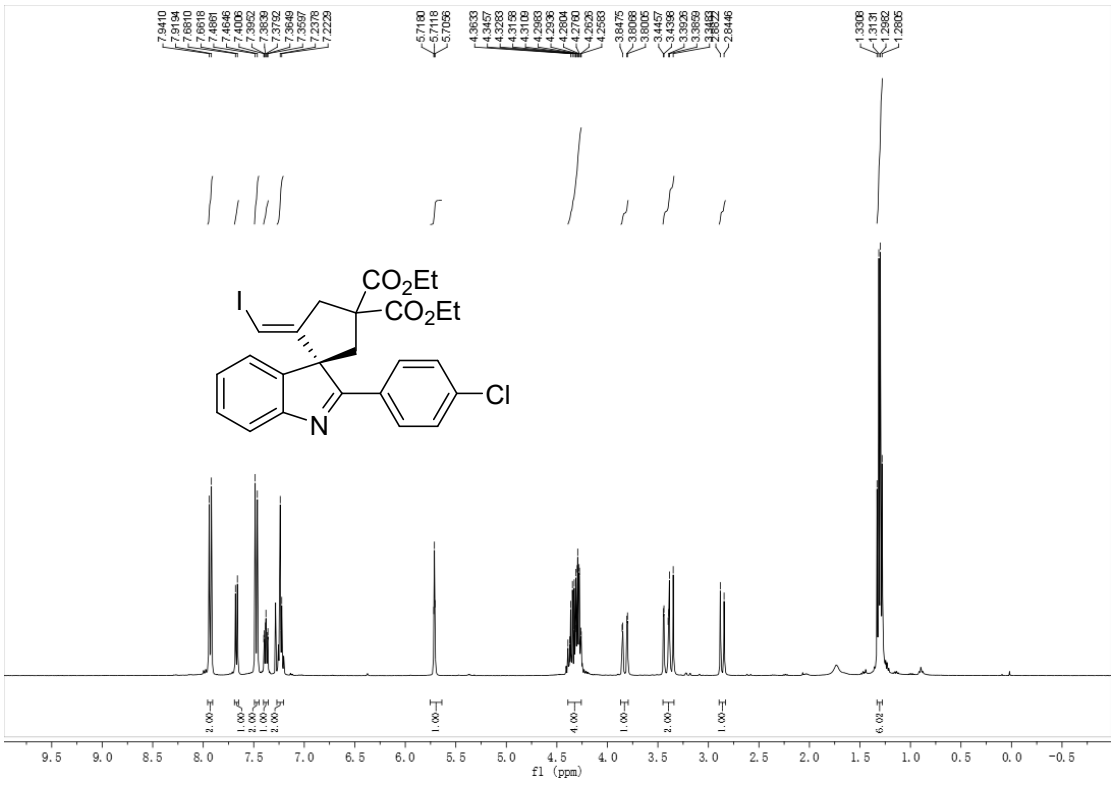
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3k**:



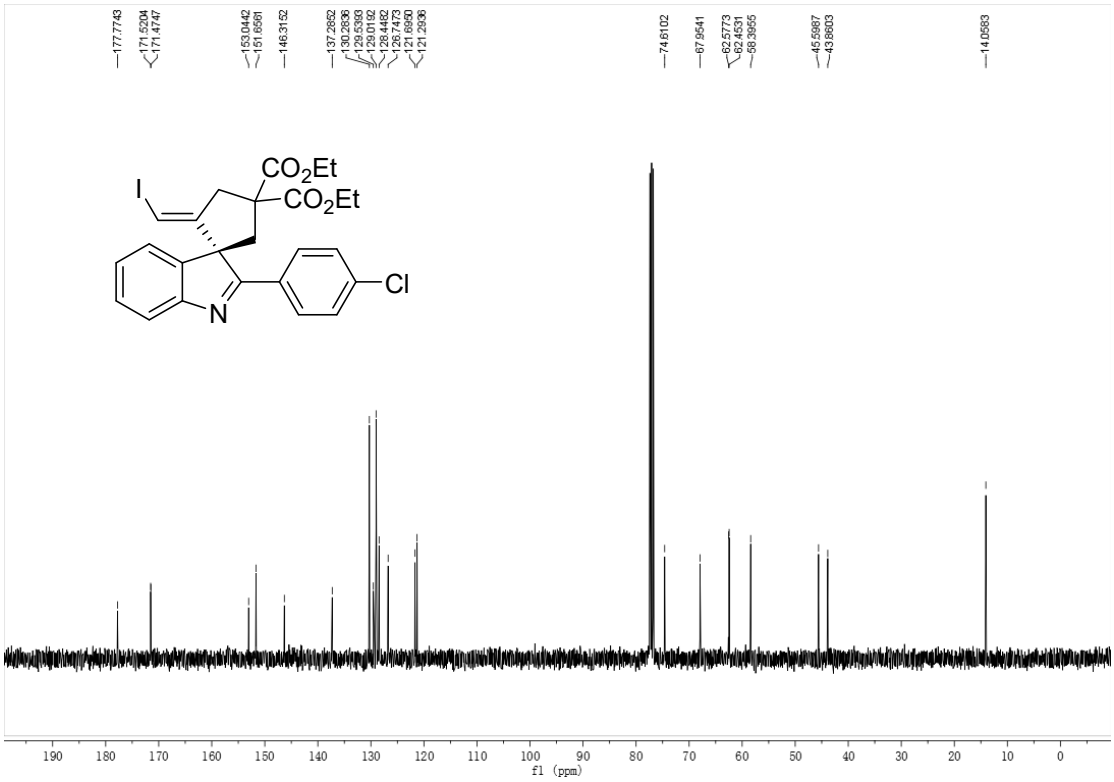
^{19}F NMR (376 MHz, $CDCl_3$) of **3k**:



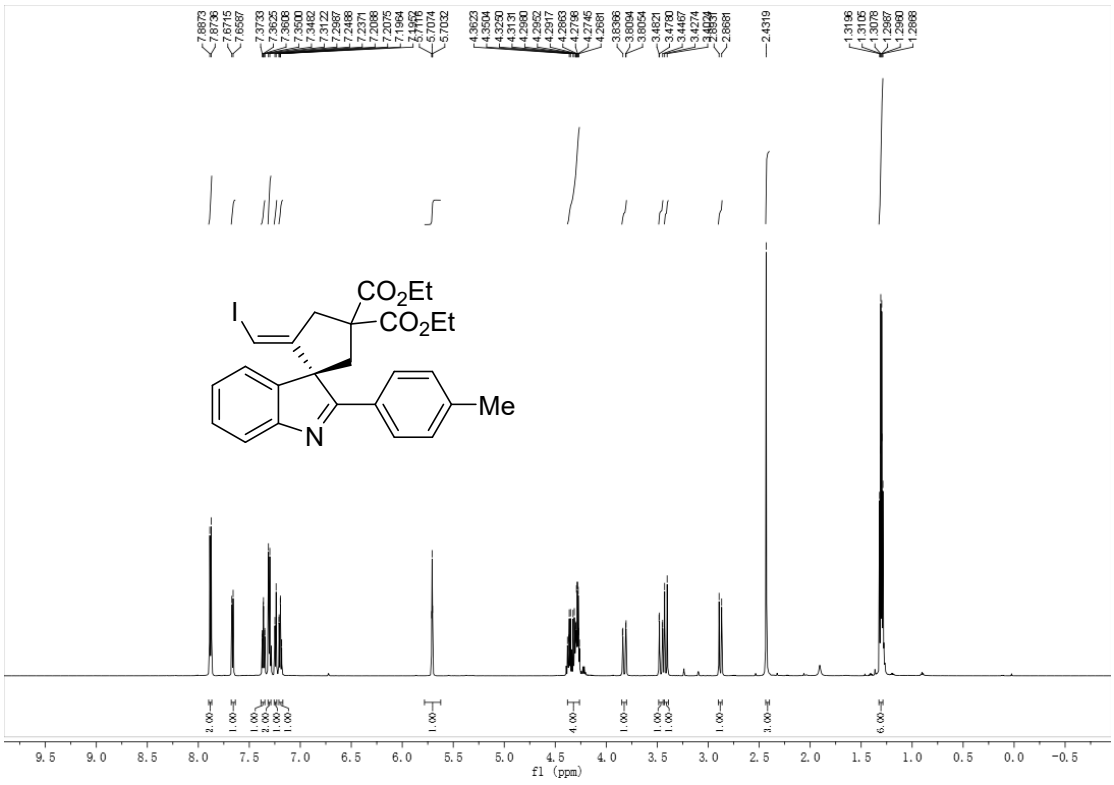
^{1}H NMR (400 MHz, $CDCl_3$) of **3l**:



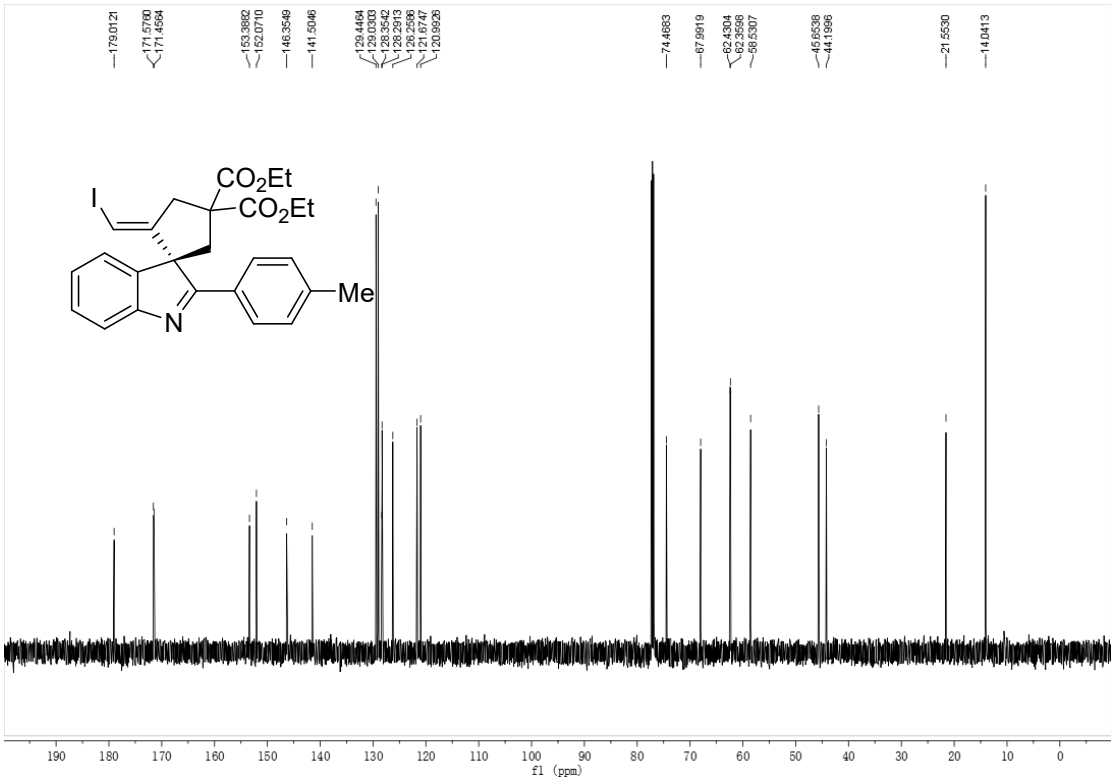
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of **3l**:



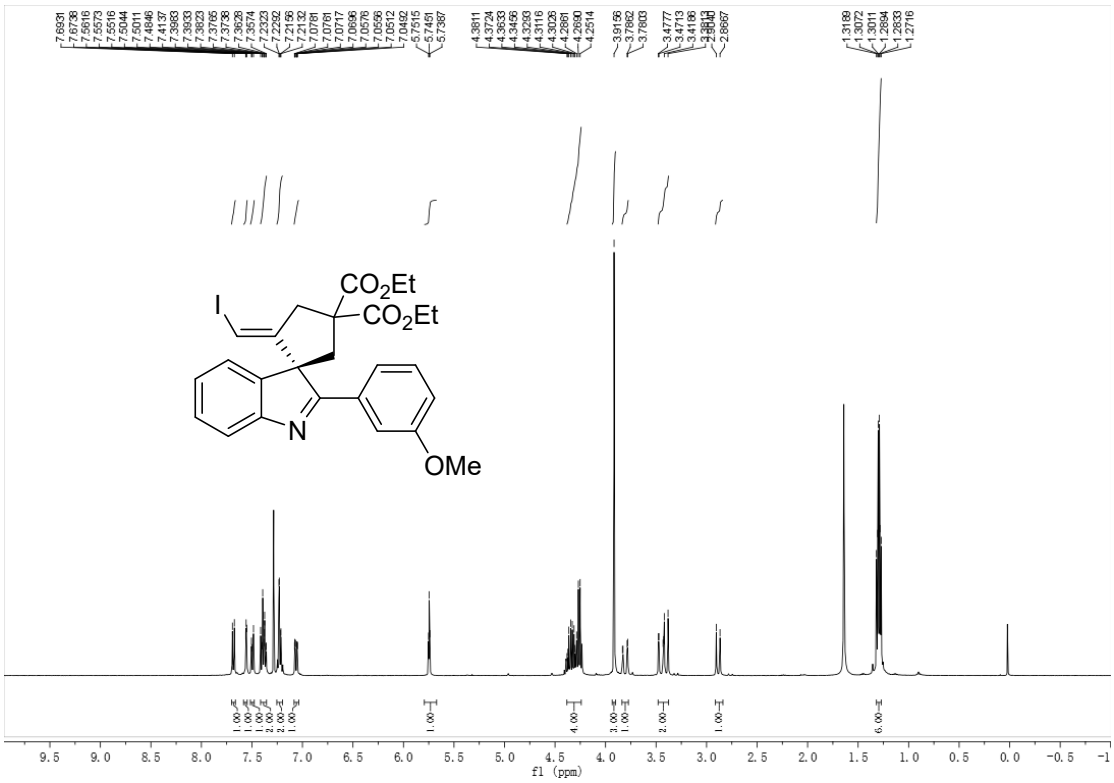
^{1}H NMR (600 MHz, $CDCl_3$) of **3m**:



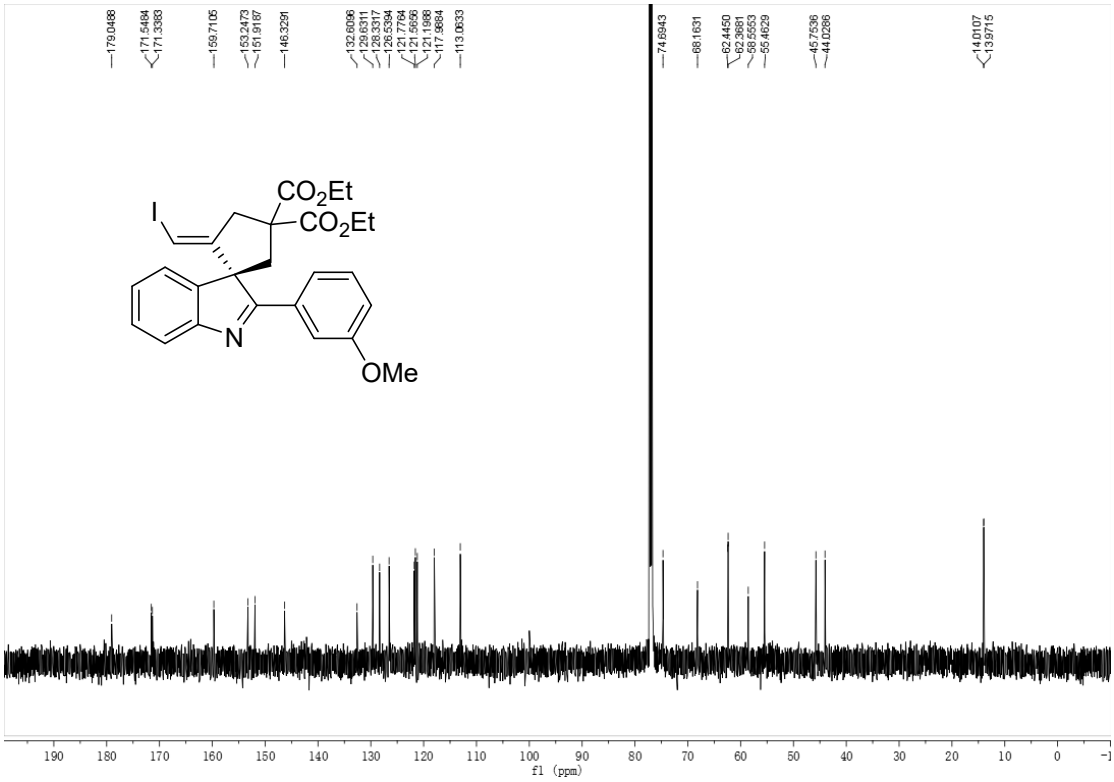
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **3m**:



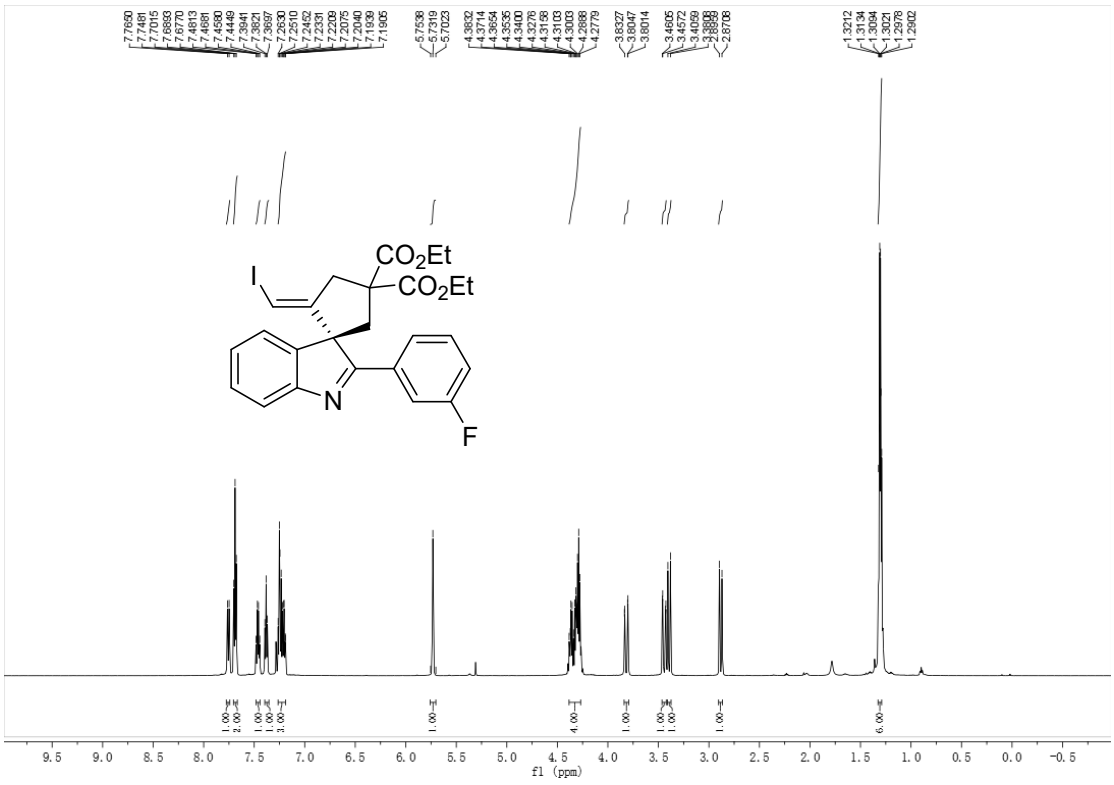
^{1}H NMR (400 MHz, $CDCl_3$) of **3n**:



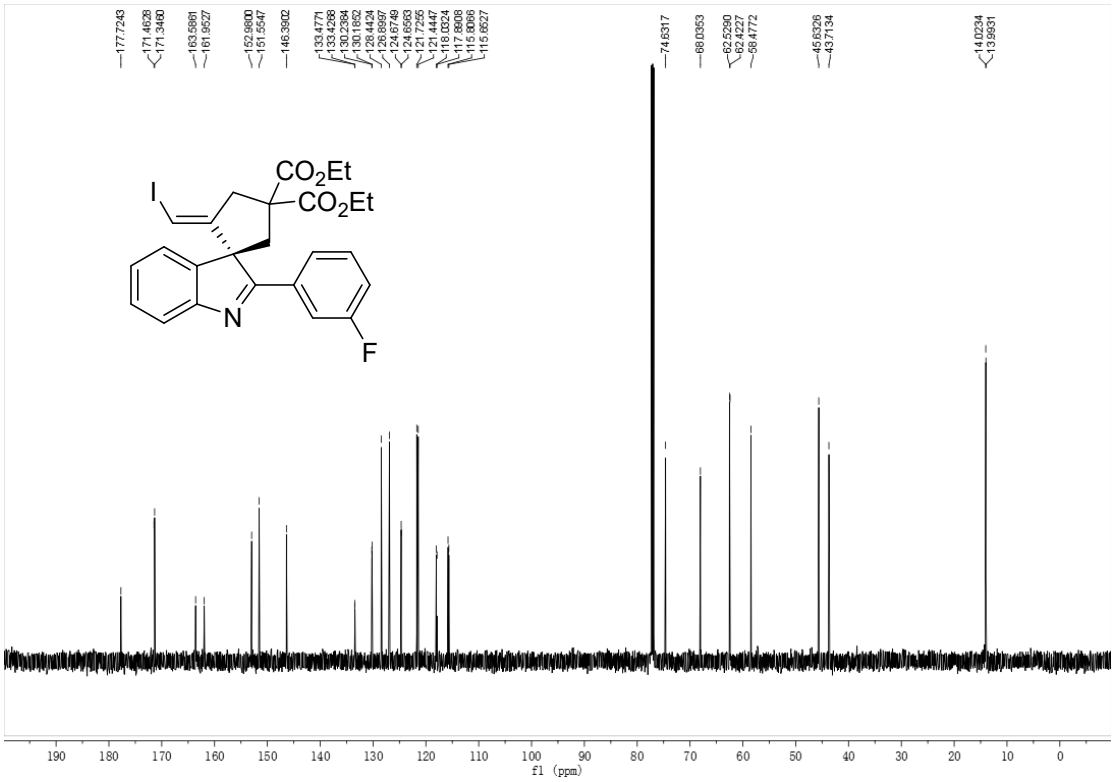
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **3n**:



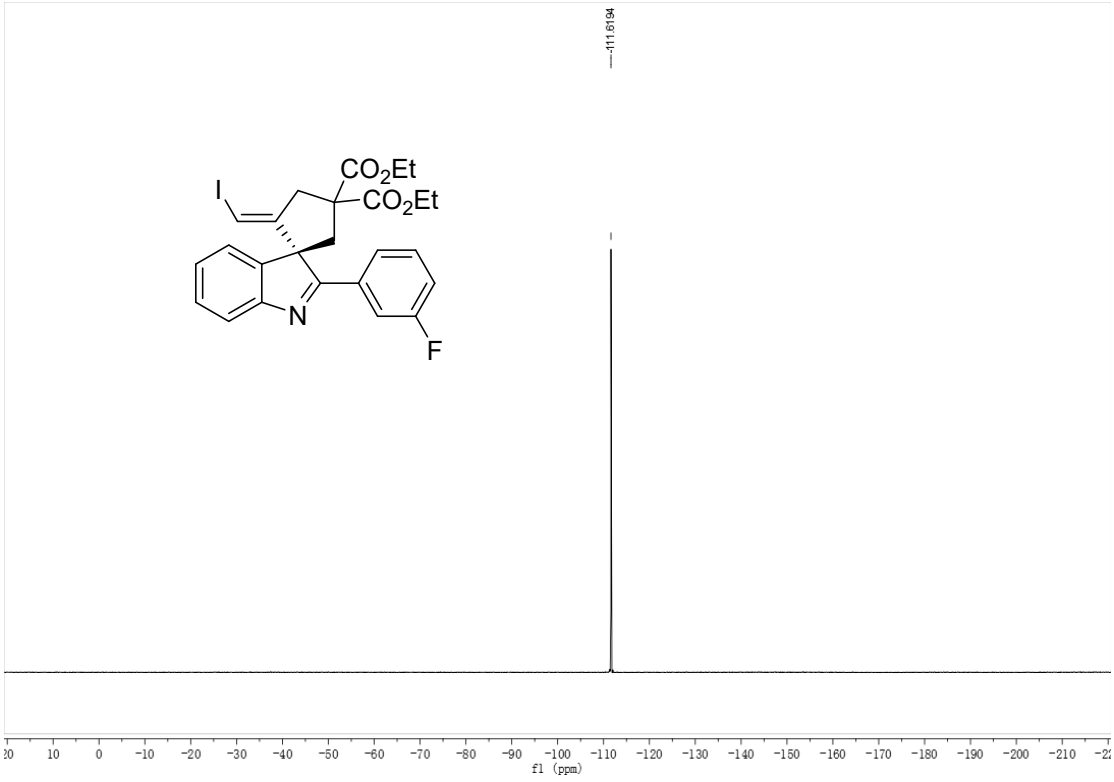
^{1}H NMR (600 MHz, $CDCl_3$) of **3o**:



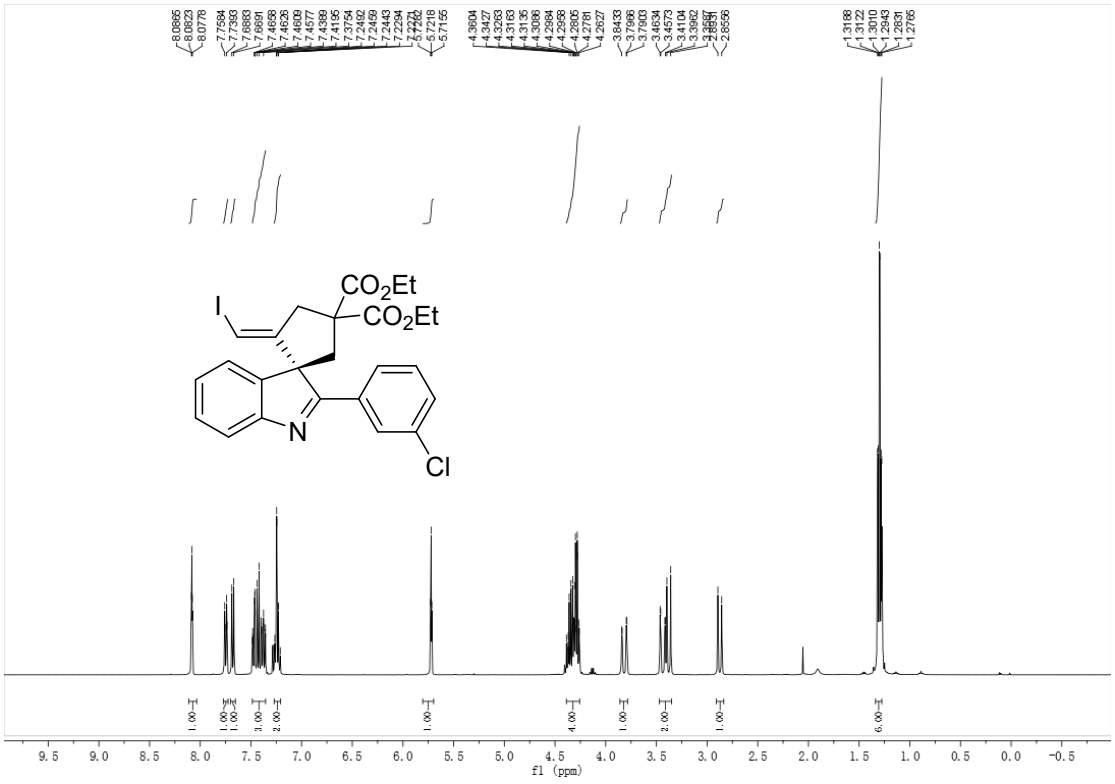
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **3o**:



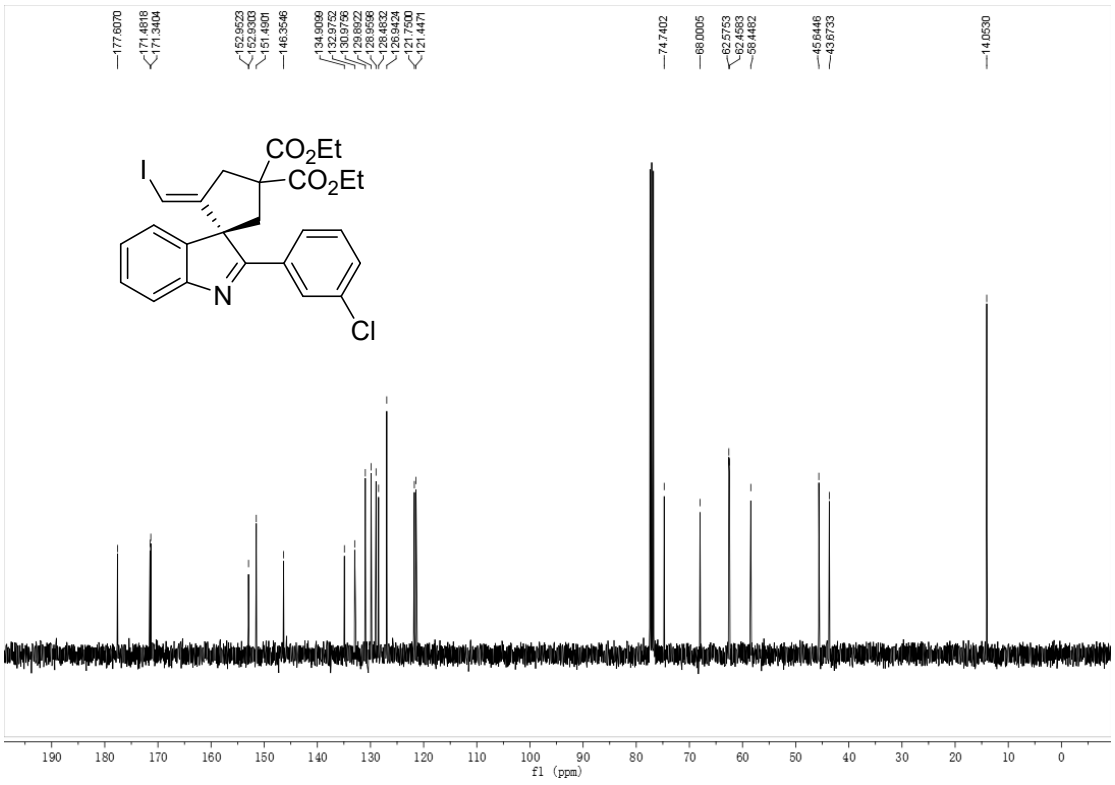
^{19}F NMR (376 MHz, $CDCl_3$) of **3o**:



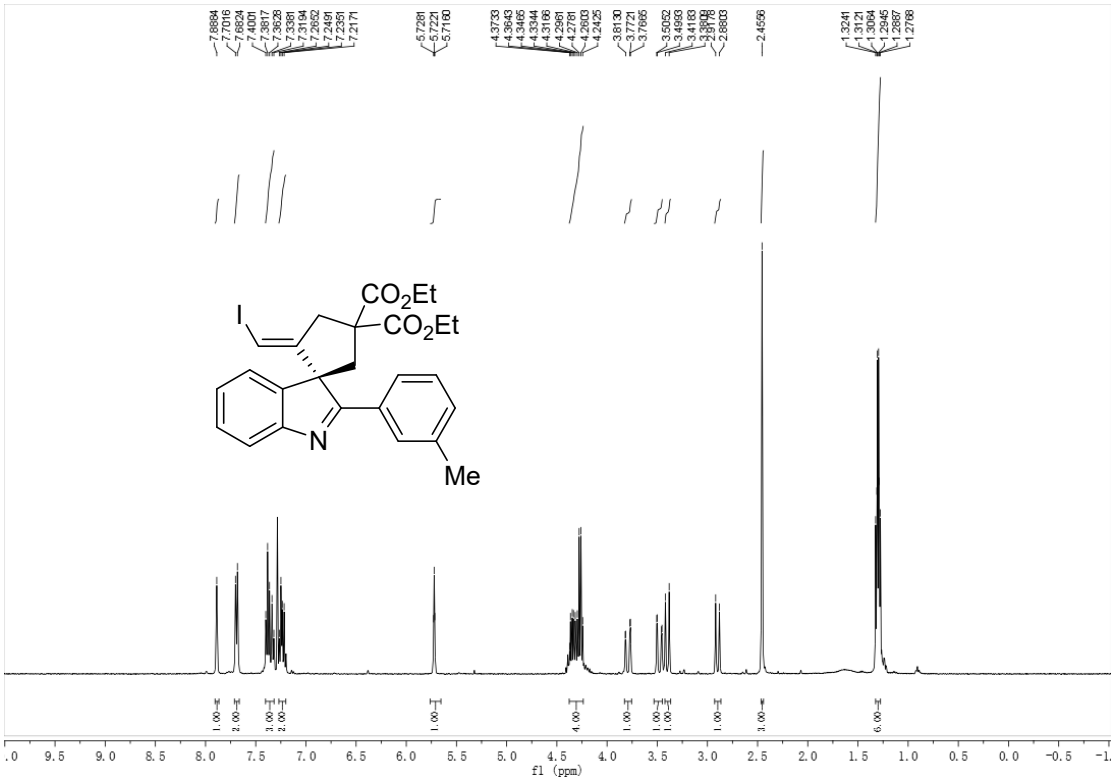
^{1}H NMR (400 MHz, $CDCl_3$) of **3p**:



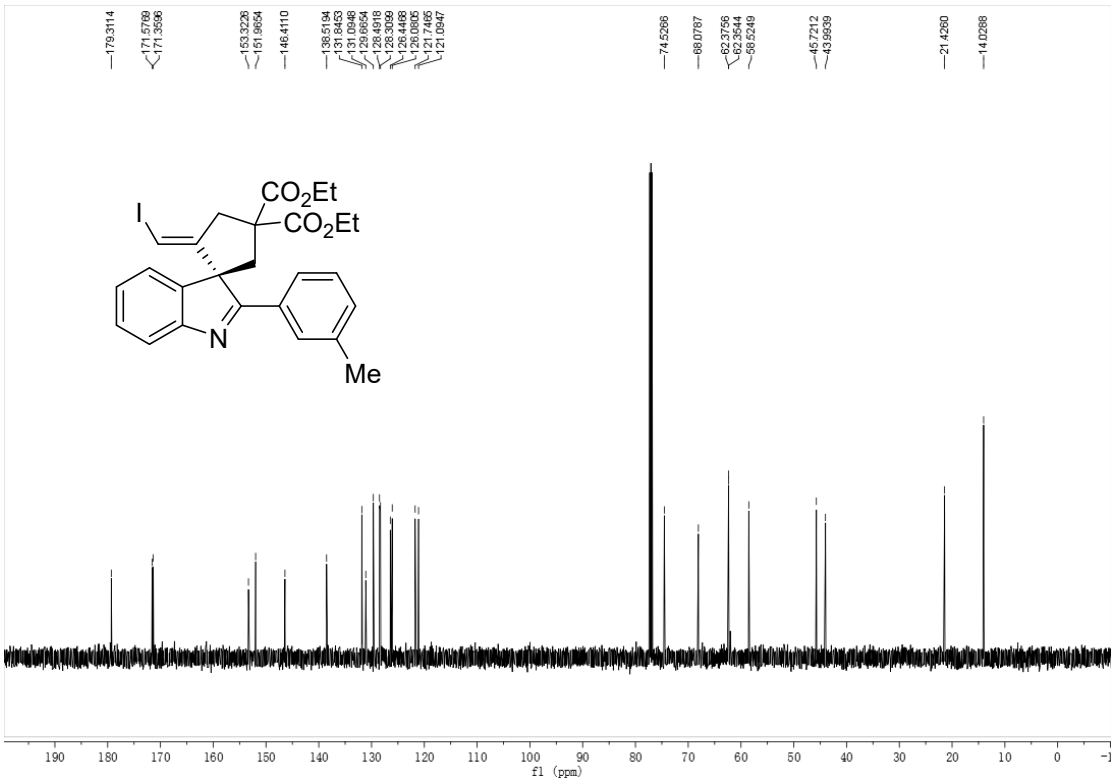
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3p**:



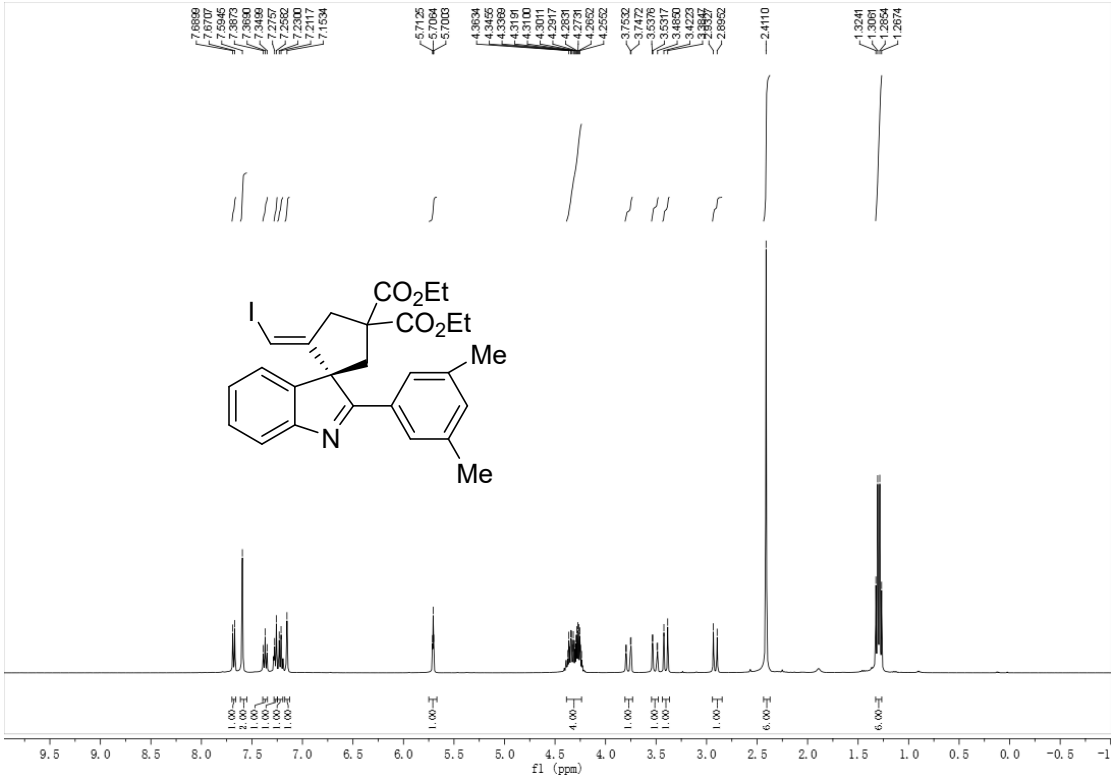
^{1}H NMR (400 MHz, $CDCl_3$) of **3q**:



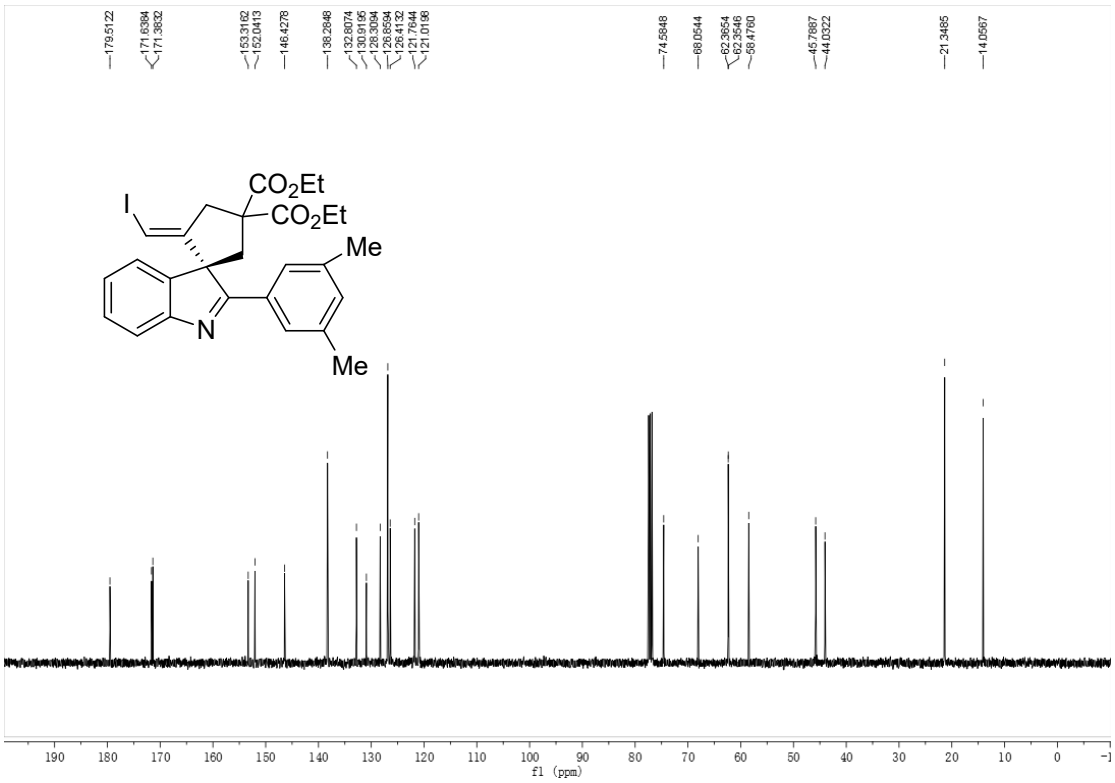
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) of **3q**:



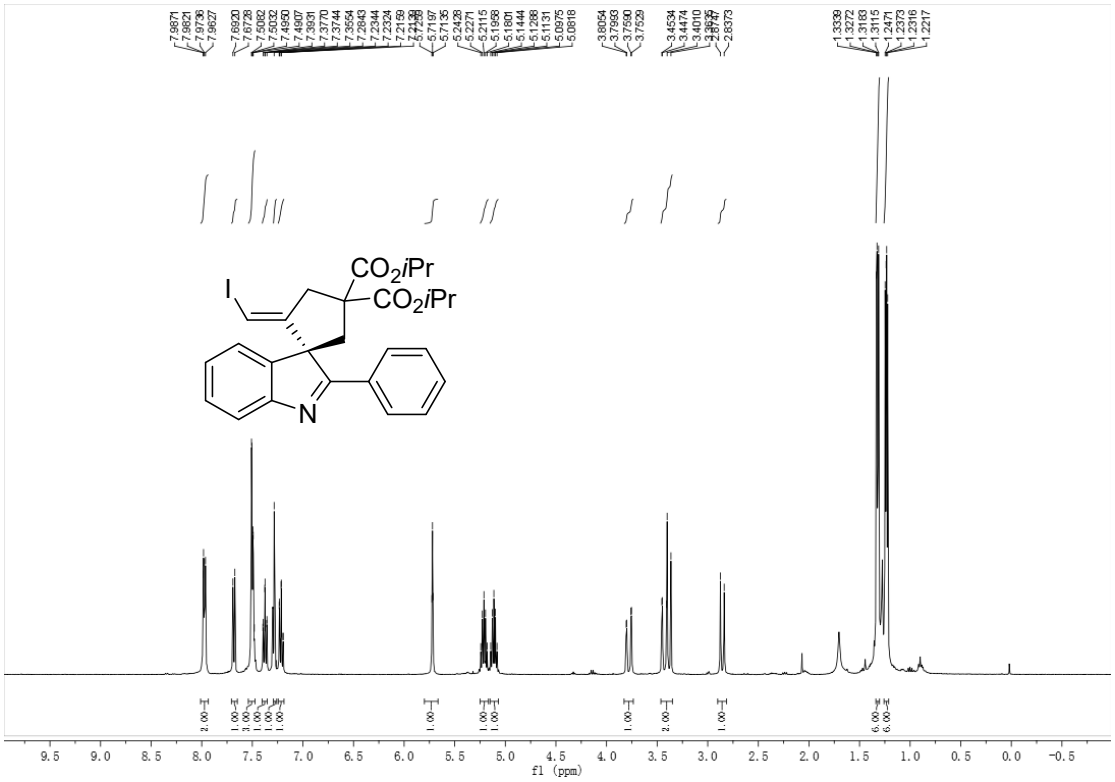
^{1}H NMR (400 MHz, $CDCl_3$) of **3r**:



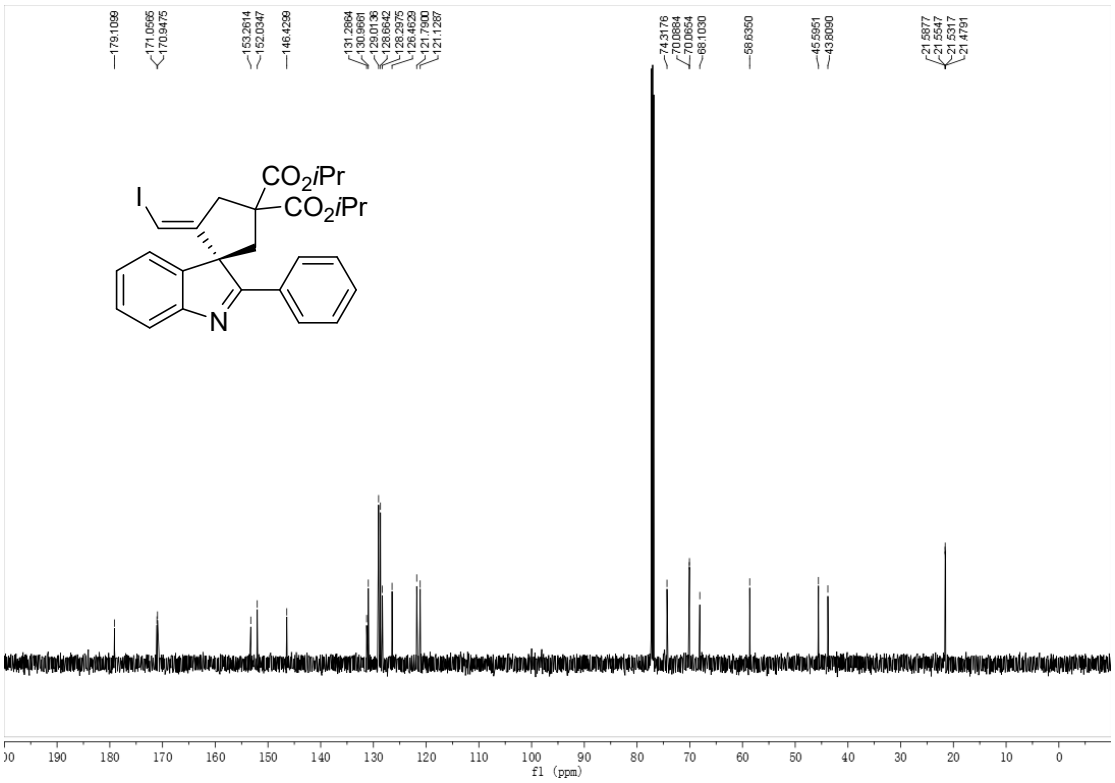
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3r**:



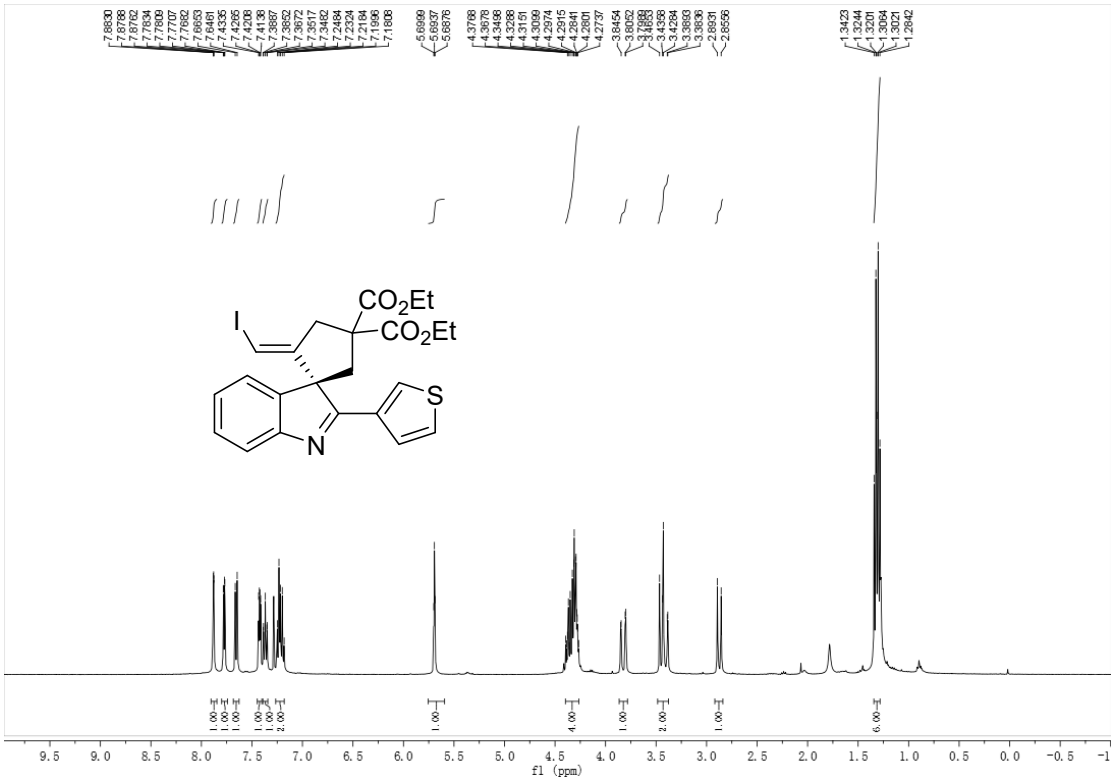
^{1}H NMR (400 MHz, $CDCl_3$) of **3t**:



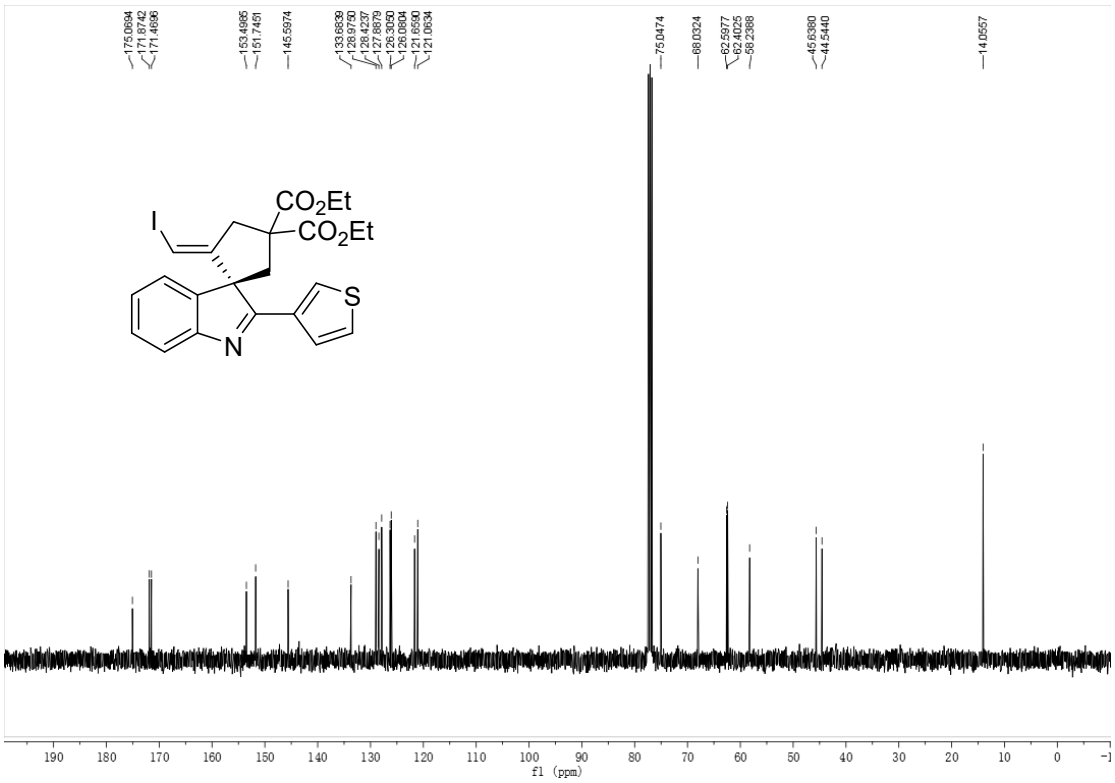
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) of **3t**:



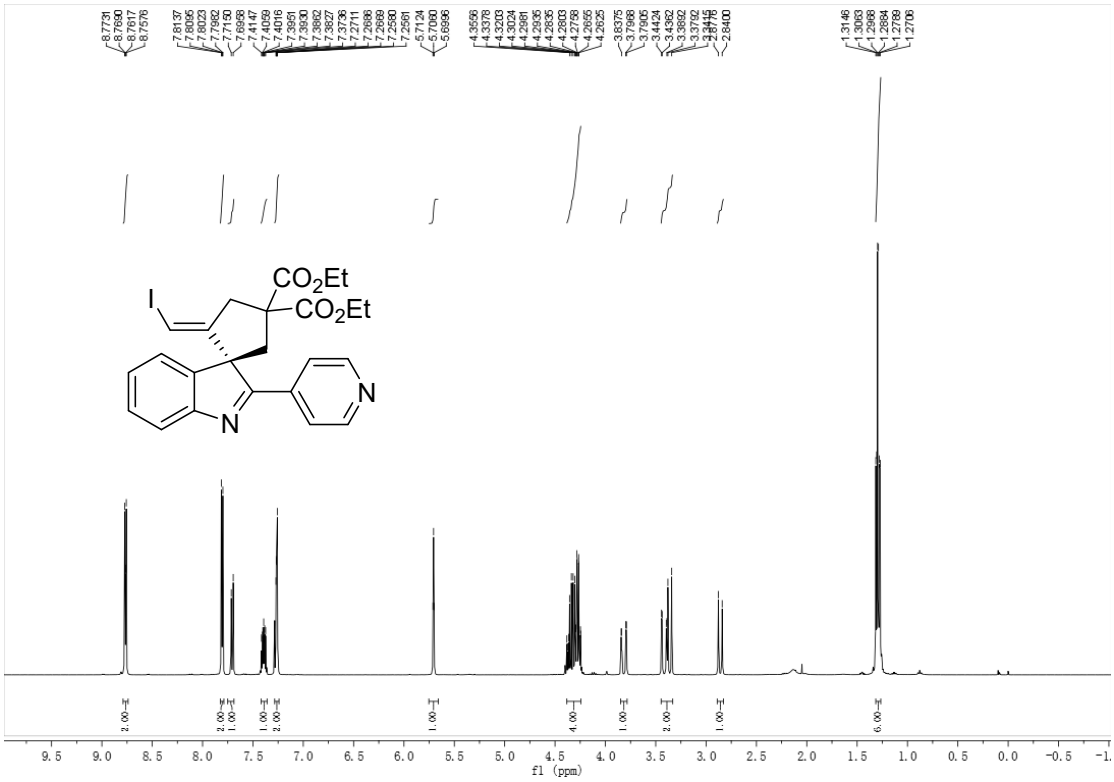
^{1}H NMR (400 MHz, $CDCl_3$) of **3u**:



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3u**:



^{1}H NMR (400 MHz, $CDCl_3$) of **3v**:



^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) of **3v**: