Supporting Information

From Indoles to 3,3'-Biindolin-2-ones: Copper-Catalyzed Oxidative Homocoupling of Indoles

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CONTENTS

1. General Methods

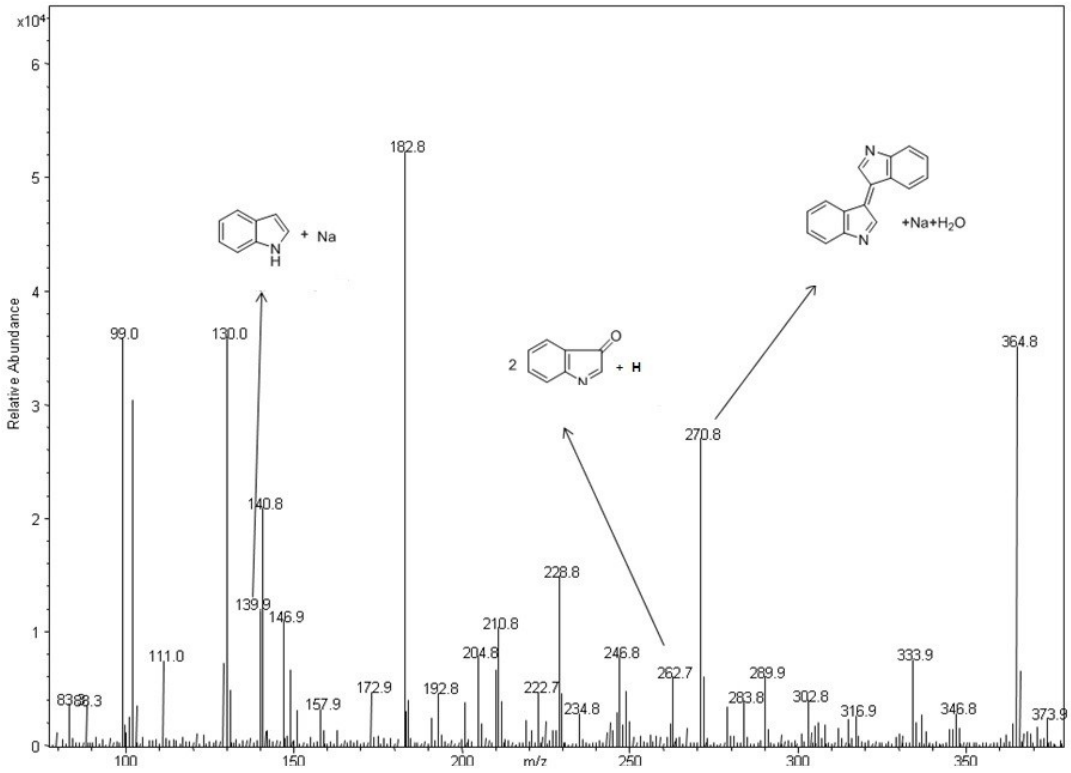
^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometers at 400 and 100 MHz, respectively. Mass spectra were recorded with Bruker Dalton Esquire 3000 plus LC-MS apparatus. Elemental analysis were carried out on a Perkin-Elmer 240B instrument. Silica gel (300-400 mesh) was used for flash column chromatography, eluting (unless otherwise stated) with an ethyl acetate/petroleum ether (PE) (60-90 °C) mixture.

Materials

Commercially available starting materials and solvents were used as supplied, without further purification.

2. ESI-MS Investigation

ESI-MS of crude mixtures after 3 h of the onset of reaction for identifiying the possible intermediates



3. Experimental Section

3.1 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays.

The HepG–2, SCG–7901, MDA–MB–468, MDA–MB–435, Ishikawa cell lines used in this study were all obtained from the Institute of Biochemistry and Cell Biology, China Academy of Sciences. Cells were cultured in RPMI–1640, which supplemented with 10% fetal bovine serum in a humidified atmosphere of 5% CO_2 /95% air at 37 ℃. The 200 μL cell suspensions (4500–5000 cells/mL) was seeded in 96–well plates and incubated for 48 h. All compounds and 5-FU were dissolved in the Phosphate Buffered Saline (PBS) with 1% DMSO to give various concentrations (2.5, 5, 10, 20, 40 μM, respectively) to 96–well plates and control wells contained supplemented media with 1% DMSO. Continue incubating for 48 h at 37 ℃ and in 5% CO_2 atmosphere and then the MTT solution (20 μL, 5 mg/mL) was added into each well and the

cultures were incubated further for 4 h. After removal of the supernatant, DMSO (200 μL) was added to dissolve the formazan crystals. The absorbance was read by enzyme labeling instrument with 570 nm double wavelength measurement. The cytotoxicity was estimated based on the percentage cell survival in a dose dependent manner relative to the negative control. The final IC_{50} (a drug concentration killing 50% cells) values were calculated by the Bliss method (n ¼ 5). All the tests were repeated in at least three independent experiments.

Table S1. IC_{50} (μM) values of compounds after treatment with the six cells for 48 h.

Compounds	HepG-2	SCG-7901	MDA-MB-468	MDA-MB-435	Ishikawa	HUVEC
2a	> 100	> 100	> 100	> 100	> 100	> 100
2b	> 100	> 100	> 100	> 100	> 100	> 100
2c	> 100	> 100	> 100	> 100	> 100	> 100
2d	> 100	> 100	> 100	> 100	> 100	> 100
2e	> 100	> 100	> 100	> 100	> 100	> 100
2f	> 100	> 100	> 100	> 100	> 100	> 100
2g	27.83 ± 0.35	42.36 ± 5.76	70.11 ± 6.78	29.58 ± 0.39	79.95 ± 2.45	> 100
2h	> 100	> 100	> 100	> 100	> 100	> 100
2i	> 100	> 100	> 100	> 100	> 100	> 100
2j	> 100	> 100	> 100	> 100	> 100	> 100
2k	> 100	> 100	> 100	> 100	> 100	> 100
2l	31.26 ± 2.57	65.16 ± 1.40	50.51 ± 0.31	31. 86 ± 2.61	58.37 ± 4.02	27.17 ± 0.18
2m	> 100	> 100	> 100	> 100	> 100	> 100
2n	> 100	> 100	> 100	> 100	> 100	> 100
2o	> 100	> 100	> 100	> 100	> 100	> 100
2p	26.12 ± 1.69	26.52 ± 0.70	31.35 ± 0.84	56.28 ± 1.99	73.21 ± 2.48	36.33 ± 4.26
2q	42.14 ± 1.46	92.81 ± 1.02	> 100	68.34 ± 1.55	> 100	> 100
2r	> 100	> 100	> 100	> 100	> 100	> 100
2s	**10.49 ± 0.41**	18.35 ± 1.31	36.78 ± 0.29	16.02 ± 1.28	14.01 ± 0.74	40.96 ± 0.94
5-FU	49.48 ± 0.53	37.01 ± 4.95	15.65 ± 1.26	> 100	40.27 ± 5.60	> 100

[a]Each data is expressed as means ± SD of three independent experiments. [b]Compounds with IC_{50} (μM) values > 50 μM are considered to be inactive.

3.2 Apoptosis by flow cytometry

Apoptosis was discriminated with the Annexin V-FITC/propidium iodide (BD, Pharmingen) test. The HepG2 cells were seeded in 6-well plates (2×106 cells/well) and cultured for 24 h, then treated with compound **2s** for 24 h. The cells were collected and washed twice with cold PBS and then resuspended in 1×Binding Buffer (0.1 M Hepes/NaOH (pH = 7.4), 1.4 M NaCl, 25 mM $CaCl_2$) at a concentration of 1×106 cells/ml. Transfered 100 μL of the solution (1×105 cells) to 1.5 mL culture tube, then added 5 μL of Annexin V- FITC and 5 μL propidium iodide (PI) to each tube. After incubation for 30 minutes in the dark, the specimens were quantified by flow cytometry on a FACS Canto II (BD Biosciences, USA).

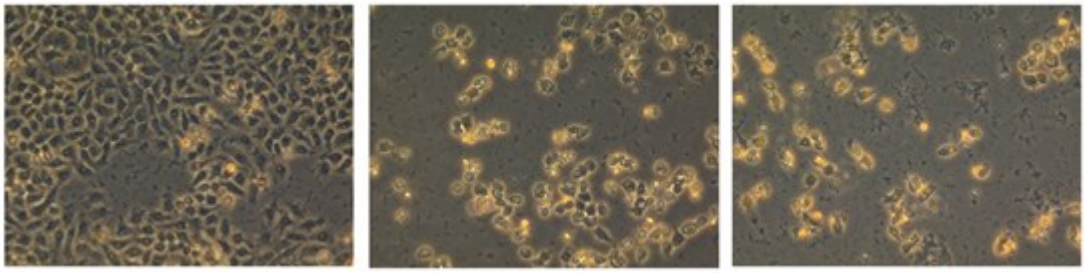
3.3 Induction of cell cycle arrest

Cell cycle distribution analysis Cell cycle distribution was analyzed by propidium iodide (PI) staining and flow cytometry. HepG–2 cells were exposed to compound **2s** at the indicated

concentrations. After 48 h incubation, the cells were collected, washed for twice with ice-cold PBS, fixed with 70% ethanol at 4 °C overnight and treated with RnaseA for 35 min at 37 °C, followed by PI staining for 15 min in the dark. Percentage of cells in different cell cycle phases was measured by flow cytometry using a 488 nm laser (Bection Dickinson FACS Caliber).

3.4 TUNEL assay for apoptosis

The apoptosis of HepG–2 cells induced by compound **2s** was detected by TUNEL assays. After treatment with compound **2s** for 24 h in HepG–2 cells, cells were washed with PBS and permeabilized with 0.2% Triton X–100 for 2 min, then detection of apoptotic in HepG–2 cells according to apoptotic kit steps (DeadEnd™ Colorimetric TUNEL System，Promega). Control and treated cells were observed with fluorescence microscope (Cytation 5 Cell Imaging Multi-Mode Reader, BioTek Instruments, Inc., USA.).



0 μM **20 μM** **40 μM**

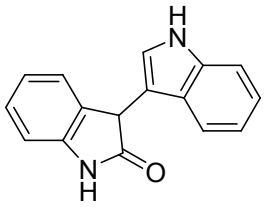
Figure S. Assessment of nuclear morphological changes by TUNEL assay in HepG–2 cells after 24 h.

3.5 General Procedure for the Preparation of 2

To a solution of indole (0.2 mmol), Cu_2O (20 mol %), and TBHP (0.4 mmol) in $CHCl_3$ (1 mL) was added morphline (0.2 mmol) under an O_2 atmosphere and the mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE = 1:2) to yield the corresponding product **2**.

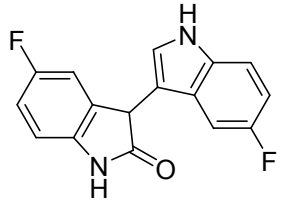
4. Spectroscopic data of the products 2

3,3'-Biindolin-2-one (**2a**)



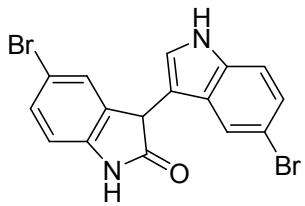
White amorphous solid, 79% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.94 (s, 1H, NH), 10.30 (s, 1H, NH), 7.29 (t, J = 7.6 Hz, 2H, Ar-H), 7.21 (t, J = 7.6 Hz, 1H, Ar-H), 7.19 (dd, J = 7.6, 2.5 Hz, 1H, Ar-H), 7.02 (d, J = 2.5 Hz, 1H, Ar-H), 6.98 (t, J = 7.6 Hz, 1H, Ar-H), 6.91 (t, J = 7.6 Hz, 1H, Ar-H), 6.86 (d, J = 7.6 Hz, 1H, Ar-H), 6.82 (t, J = 7.6 Hz, 1H, Ar-H), 6.31 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.9, 142.1, 137.3, 133.9, 129.5, 125.4, 125.2, 124.0, 122.2, 121.5, 120.8, 118.9, 115.9, 112.0, 110.1, 75.4. MS (ESI): 249 (M+H$^+$, 100). These assignments matched with those previously published.[1]

5,5'-Difluoro-3,3'-biindolin-2-one (**2b**)



White amorphous solid, 63% yield. ^{1}H NMR (400 MHz, DMSO-d6): δ 11.15 (s, 1H, NH), 10.37 (s, 1H, NH), 7.34 (dd, J = 8.9, 4.7 Hz, 1H, Ar-H), 7.19 (dd, J = 10.5, 2.4 Hz, 1H, Ar-H), 7.12 (dt, J = 10.5, 2.4 Hz, 1H, Ar-H), 7.09 (d, J = 8.9 Hz, 1H, Ar-H), 7.06 (d, J = 2.4 Hz, 1H, Ar-H), 6.89 (dt, J = 8.9, 2.4 Hz, 2H, Ar-H), 6.53 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.7, 158.6 (d, J = 237.5 Hz), 157.0 (d, J = 230.3 Hz), 138.3, 135.2 (d, J = 7.1 Hz), 134.0, 129.4 (d, J = 10.6 Hz), 126.1, 115.9 (d, J = 23.2 Hz), 115.4 (d, J = 4.7 Hz), 112.9 (d, J = 2.7 Hz), 112.7, 111.0 (d, J = 7.8 Hz), 109.9 (d, J = 26.1 Hz), 105.7 (d, J = 23.9 Hz), 60.2. MS (ESI): 285 (M+H$^+$, 100). These assignments matched with those previously published.[1]

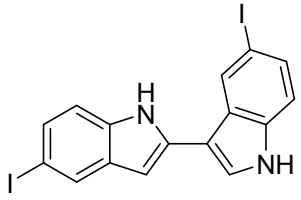
5,5'-Dibromo-3,3'-biindolin-2-one (**2c**)



White amorphous solid, 70% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.24 (d, J = 2.0 Hz, 1H, NH), 10.50 (s, 1H, NH), 7.74 (s, 1H, Ar-H), 7.46 (dd, J = 8.3, 2.0 Hz, 1H, Ar-H), 7.36 (d, J = 2.0 Hz, 1H, Ar-H), 7.33 (d, J = 8.6 Hz, 1H, Ar-H), 7.17 (dd, J = 8.6, 2.0 Hz, 1H, Ar-H), 7.00 (d, J = 2.6 Hz, 1H, Ar-H), 6.87 (d, J = 8.3 Hz, 1H, Ar-H), 6.58 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.1, 141.4, 136.0, 135.7, 132.4, 127.9, 127.2, 125.6, 124.2, 123.5, 114.9, 114.1, 113.9, 112.3,

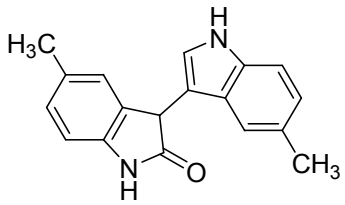
111.8, 75.2. MS (ESI): 404 ($M+H^+$, 50), 406 ($M+H^+$, 100), 408 ($M+H^+$, 50). These assignments matched with those previously published.[1]

5,5'-Diiodo-3'a,7'a-dihydro-1H,1'H-2,3'-biindole (**2d**)



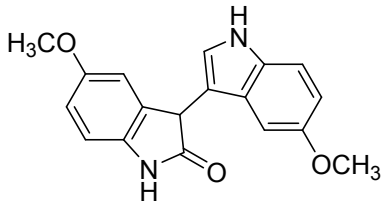
White amorphous solid, 69% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.21 (s, 1H, NH), 10.48 (d, J = 3.0 Hz, 1H, NH), 7.95 (d, J = 3.0 Hz, 1H, Ar-H), 7.62 (t, J = 7.1 Hz, 1H, Ar-H), 7.50 (d, J = 2.8 Hz, 1H, Ar-H), 7.32 (t, J = 8.6 Hz, 1H, Ar-H), 7.24 (t, J = 8.6 Hz, 1H, Ar-H), 6.96 (d, J = 2.8 Hz, 1H, Ar-H), 6.77 (dd, J = 7.1, 4.8 Hz, 1H, Ar-H), 6.55 (d, J = 4.8 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.0, 141.9, 138.2, 136.4, 136.1, 133.4, 129.7, 129.6, 128.2, 125.1, 114.7, 114.6, 112.8, 85.0, 83.1, 75.1. MS (ESI): 501 ($M+H^+$, 100).

5,5'-Dimethyl-3,3'-biindolin-2-one (**2e**)



White amorphous solid, 84% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.81 (s, 1H, NH), 10.21 (s, 1H, NH), 7.20 (d, J = 8.3 Hz, 1H, Ar-H), 7.17 (s, 1H, Ar-H), 7.03 (d, J = 7.7 Hz, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 6.85 (d, J = 1.0 Hz, 1H, Ar-H), 6.84 (dd, J = 7.7, 1.0 Hz, 1H, Ar-H), 6.77 (d, J = 7.7 Hz, 1H, Ar-H), 6.23 (s, 1H), 2.25 (s, 3H, CH_3), 2.20 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 183.7, 144.4, 140.4, 138.8, 135.6, 134.3, 131.8, 130.5, 130.4, 128.7, 127.8, 125.2, 120.3, 116.3, 114.5, 80.2, 26.6, 25.9. MS (ESI): 277 ($M+H^+$, 100). These assignments matched with those previously published.[1]

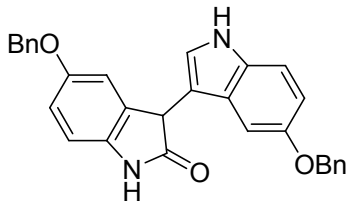
5,5'-Dimethoxy-3,3'-biindolin-2-one (**2f**)



White amorphous solid, 86% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.83 (d, J = 1.8 Hz, 1H, NH), 10.16 (s, 1H, NH), 7.23 (d, J = 8.8 Hz, 1H, Ar-H), 7.02 (d, J = 2.5 Hz, 1H, Ar-H), 6.85 (t, J = 1.8 Hz, 2H, Ar-H), 6.84 (d, J = 2.5 Hz, 2H, Ar-H), 6.70 (dd, J = 8.8, 2.5 Hz, 1H, Ar-H), 6.33 (s, 1H), 3.67 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.8, 155.4, 153.2, 135.4, 135.1, 132.5, 125.8, 124.7, 115.5, 114.1, 112.5, 112.1, 111.3, 110.4, 103.1, 75.8,

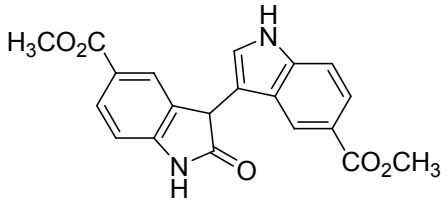
55.9, 55.7. MS (ESI): 309 ($M+H^+$, 100). Anal calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found C, 69.87; H, 5.60; N, 8.96.

5,5'-Bis(benzyloxy)-3,3'-biindolin-2-one (**2g**)



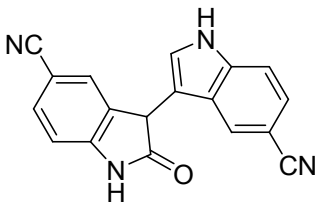
White amorphous solid, 81% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.86 (d, J = 2.4 Hz, 1H, NH), 10.17 (s, 1H, NH), 7.45-7.34 (m, 8H, Ar-H), 7.32 (t, J = 6.7 Hz, 2H, Ar-H), 7.24 (d, J = 8.8 Hz, 1H, Ar-H), 7.02 (d, J = 2.4 Hz, 1H, Ar-H), 6.99 (d, J = 2.4 Hz, 1H, Ar-H), 6.93 (s, 1H, Ar-H), 6.92 (dd, J = 7.1, 2.4 Hz, 1H, Ar-H), 6.83 (dd, J = 7.4, 1.6 Hz, 1H, Ar-H), 6.79 (dd, J = 8.8, 2.4 Hz, 1H, Ar-H), 6.34 (s, 1H), 5.00 (s, 2H, CH_2), 4.94 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.8, 154.4, 152.2, 138.1, 137.7, 135.6, 135.0, 132.7, 128.9, 128.8, 128.7, 128.3, 128.2, 128.1, 128.0, 125.8, 124.8, 115.5, 115.4, 113.1, 112.5, 112.0, 110.5, 104.8, 75.8, 70.3. MS (ESI): 461 ($M+H^+$, 100). These assignments matched with those previously published.[1]

Dimethyl 2-oxo-3,3'-biindoline-5,5'-dicarboxylate (**2h**)



White amorphous solid, 67% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.44 (d, J = 2.3 Hz, 1H, NH), 10.83 (s, 1H, NH), 8.39 (d, J = 1.9 Hz, 1H, Ar-H), 7.96 (dd, J = 8.2, 1.9 Hz, 1H, Ar-H), 7.85 (d, J = 1.9 Hz, 1H, Ar-H), 7.71 (dd, J = 8.6, 1.9 Hz, 1H, Ar-H), 7.44 (d, J = 8.6 Hz, 1H, Ar-H), 7.07 (d, J = 2.3 Hz, 1H, Ar-H), 7.04 (d, J = 8.2 Hz, 1H, Ar-H), 6.68 (s, 1H), 3.82 (s, 3H, CH_3), 3.79 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.8, 167.8, 166.5, 146.9, 140.1, 133.8, 132.2, 126.1, 125.9, 125.2, 124.4, 123.6, 122.8, 120.7, 116.8, 112.1, 110.3, 74.9, 52.4, 52.2. MS (ESI): 365 ($M+H^+$, 100). These assignments matched with those previously published.[1]

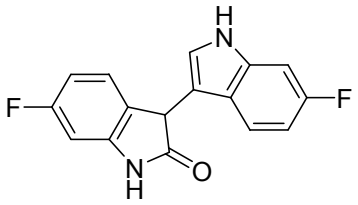
2-Oxo-3,3'-biindoline-5,5'-dicarbonitrile (**2i**)



White amorphous solid, 56% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.67 (d, J = 1.6 Hz, 1H, NH), 10.89 (s, 1H, NH), 8.22 (s, 1H, Ar-H), 7.79 (dd, J = 8.1, 1.6 Hz, 1H, Ar-H), 7.75 (d, J = 2.5 Hz, 1H, Ar-H), 7.53 (d, J = 8.5 Hz, 1H, Ar-H), 7.45 (dd, J = 8.5, 1.6 Hz, 1H, Ar-H), 7.09 (d, J =

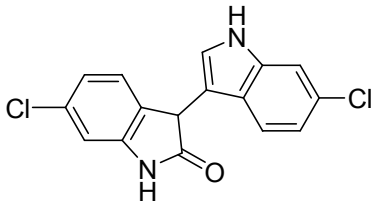
2.5 Hz, 1H, Ar-H), 7.06 (d, J = 8.1 Hz, 1H, Ar-H), 6.78 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.5, 146.6, 139.3, 135.4, 129.8, 129.1, 127.5, 126.9, 125.3, 124.6, 121.0, 119.9, 115.7, 113.7, 111.3, 104.5, 101.4, 74.6. MS (ESI): 299 (M+H$^+$, 100). These assignments matched with those previously published.[1]

6,6'-Difluoro-3,3'-biindolin-2-one (**2j**)



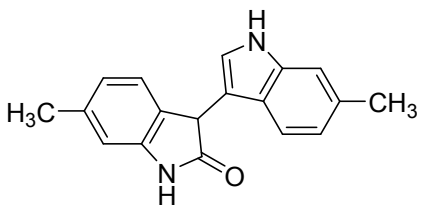
White amorphous solid, 65% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.08 (s, 1H, NH), 10.49 (s,1H, NH), 7.45 (dd, J = 8.8, 5.8 Hz, 1H, Ar-H), 7.25 (dd, J = 8.0, 5.8 Hz, 1H, Ar-H), 7.10 (dd, J = 10.0, 2.2 Hz, 1H, Ar-H), 6.97 (d, J = 2.2 Hz, 1H, Ar-H), 6.79 (dt, J = 9.4, 2.3 Hz, 1H, Ar-H), 6.76 (dt, J = 9.4, 2.3 Hz, 1H, Ar-H), 6.70 (dd, J = 10.0, 2.2 Hz, 1H, Ar-H), 6.44 (s, 1H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.9, 163.1 (d, J = 242.7 Hz), 159.2 (d, J = 234.5 Hz), 143.8 (d, J = 12.4 Hz), 137.2 (d, J = 12.5 Hz), 129.5 (d, J = 2.7 Hz), 126.7 (d, J = 10.0 Hz), 124.7 (d, J = 3.0 Hz), 122.3, 122.1 (d, J = 10.1 Hz), 115.8, 108.2 (d, J = 22.1 Hz), 107.6 (d, J = 24.2 Hz), 98.3 (d, J = 26.9 Hz), 97.9 (d, J = 25.3 Hz), 74.8. MS (ESI): 285 (M+H$^+$, 100). These assignments matched with those previously published.[1]

6,6'-Dichloro-3,3'-biindolin-2-one (**2k**)



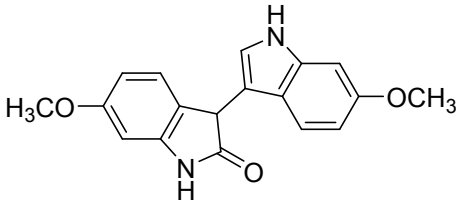
White amorphous solid, 69% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.17 (s, 1H, NH), 10.51 (s, 1H, NH), 7.51 (d, J = 8.6 Hz, 1H, Ar-H), 7.50 (t, J = 8.2 Hz, 1H, Ar-H), 7.38 (d, J = 1.8 Hz, 1H, Ar-H), 7.25 (d, J = 8.2 Hz, 1H, Ar-H), 7.03 (d, J = 1.9 Hz, 1H, Ar-H), 7.02 (t, J = 1.9 Hz, 1H, Ar-H), 6.95 (dd, J = 8.6, 1.9 Hz, 1H, Ar-H), 6.91 (d, J = 1.9 Hz, 1H, Ar-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.6, 143.7, 137.8, 132.4, 129.8, 129.1, 126.7, 125.2, 124.3, 122.5, 122.0, 119.5, 115.6, 111.7, 110.3, 74.8. MS (ESI): 317 (M+H$^+$, 100), 319 (M+H$^+$, 30). These assignments matched with those previously published.[1]

6,6'-Dimethyl-3,3'-biindolin-2-one (**2l**)



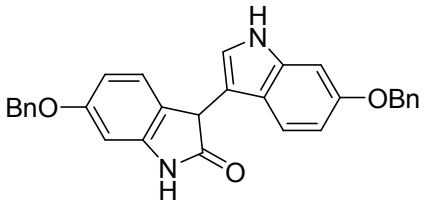
White amorphous solid, 77% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.80 (s, 1H, NH), 10.26 (s, 1H, NH), 7.26 (d, J = 8.1 Hz, 1H, Ar-H), 7.12 (s, 1H, Ar-H), 7.11 (d, J = 8.1 Hz, 1H, Ar-H), 6.97 (d, J = 2.3 Hz, 1H, Ar-H), 6.76 (d, J = 7.6 Hz, 1H), 6.72 (s, 1H, Ar-H), 6.71 (d, J = 7.2 Hz, 1H, Ar-H), 6.23 (s, 1H), 2.35 (s, 3H, CH_3), 2.31 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.2, 142.2, 138.9, 137.7, 131.1, 130.5, 125.0, 123.4, 123.2, 122.5, 120.7, 120.6, 116.0, 111.6, 110.7, 75.2, 21.8, 21.7. MS (ESI): 277 (M+H$^+$, 100). Anal calcd for $C_{18}H_{16}N_2O$: C, 78.24; H, 5.84; N, 10.14. Found C, 78.09; H, 6.16; N, 9.83.

6,6'-Dimethoxy-3,3'-biindolin-2-one (**2m**)



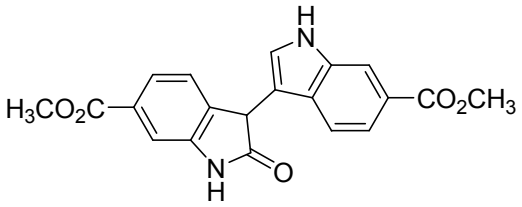
White amorphous solid, 78% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.75 (d, J = 1.8 Hz, 1H, NH), 10.25 (s, 1H, NH), 7.24 (d, J = 8.8 Hz, 1H, Ar-H), 7.12 (d, J = 8.2 Hz, 1H, Ar-H), 6.88 (d, J = 2.3 Hz, 1H, Ar-H), 6.82 (d, J = 2.3 Hz, 1H, Ar-H), 6.55 (dd, J = 8.8, 2.3 Hz, 1H, Ar-H), 6.50 (dd, J = 8.2, 2.3 Hz, 1H, Ar-H), 6.44 (d, J = 2.3 Hz, 1H, Ar-H), 6.18 (s, 1H), 3.76 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.3, 160.6, 155.9, 143.4, 138.0, 126.0, 125.9, 122.6, 121.5, 119.9, 116.3, 109.1, 106.8, 96.8, 94.9, 75.0, 55.7, 55.6. MS (ESI): 309 (M+H$^+$, 100). Anal calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found C, 69.75; H, 5.59; N, 8.81.

6,6'-Bis(benzyloxy)-3,3'-biindolin-2-one (**2n**)



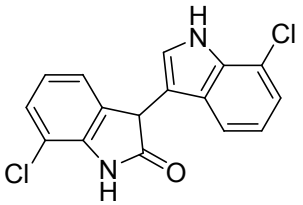
White amorphous solid, 78% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.77 (d, J = 2.0 Hz, 1H, NH), 10.27 (s, 1H, NH), 7.47-7.31 (m, 10H, Ar-H), 7.27 (d, J = 8.8 Hz, 1H, Ar-H), 7.13 (d, J = 8.2 Hz, 1H, Ar-H), 6.89 (dd, J = 4.2, 2.0 Hz, 2H, Ar-H), 6.64 (dd, J = 8.8, 2.2 Hz, 1H, Ar-H), 6.59 (dd, J = 8.2, 2.2 Hz, 1H, Ar-H), 6.53 (d, J = 2.2 Hz, 1H, Ar-H), 6.20 (s, 1H), 5.12 (s, 2H, OCH_2) , 5.09 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.3, 159.7, 154.8, 143.4, 138.1, 137.9, 137.5, 128.9, 128.8, 128.3, 128.0, 127.9, 126.2, 126.0, 125.4, 122.8, 121.6, 120.1, 116.2, 109.8, 107.8, 97.8, 96.4, 75.0, 69.9, 69.8. MS (ESI): 461 (M+H$^+$, 100). These assignments matched with those previously published.[1]

Dimethyl 2-oxo-3,3'-biindoline-6,6'-dicarboxylate (**2o**)



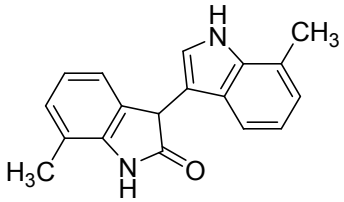
White amorphous solid, 72% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.48 (d, J = 2.3 Hz, 1H, NH), 10.62 (s, 1H, NH), 8.04 (s, 1H, Ar-H), 7.65 (dd, J = 7.7, 1.2 Hz, 1H, Ar-H), 7.59 (t, J = 8.5 Hz, 1H, Ar-H), 7.56 (dt, J = 1.2, 8.5 Hz, 1H, Ar-H), 7.45 (d, J = 1.2 Hz, 1H, Ar-H), 7.42 (d, J = 7.7 Hz, 1H, Ar-H), 7.29 (d, J = 2.3 Hz, 1H, Ar-H), 6.68 (s, 1H), 3.86 (s, 3H, CH_3), 3.84 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.4, 167.6, 166.5, 142.6, 138.7, 136.6, 130.9, 129.0, 128.0, 125.4, 123.9, 122.8, 120.9, 119.8, 115.7, 114.2, 110.3, 75.1, 52.8, 52.3. MS (ESI): 365 (M+H$^+$, 100). These assignments matched with those previously published.[1]

7,7'-Dichloro-3,3'-biindolin-2-one (**2p**)



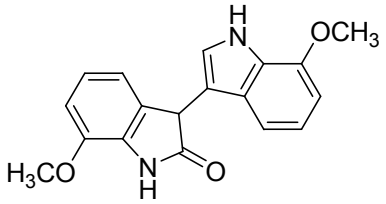
White amorphous solid, 66% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.45 (d, J = 2.3 Hz, 1H, NH), 10.84 (s, 1H, NH), 7.40 (d, J = 7.9 Hz, 1H, Ar-H), 7.35 (dd, J = 7.9, 1.0 Hz, 1H, Ar-H), 7.22 (d, J = 7.6 Hz, 1H, Ar-H), 7.15 (dd, J = 7.6, 1.0 Hz, 1H, Ar-H), 7.07 (d, J = 2.3 Hz, 1H, Ar-H), 7.01 (dd, J = 7.6, 1.0 Hz, 1H, Ar-H), 6.95 (t, J = 7.9 Hz, 1H, Ar-H), 6.64 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.5, 139.8, 133.3, 129.7, 129.6, 129.0, 125.2, 123.8, 123.7, 121.2, 120.2, 119.9, 116.7, 116.4, 114.5, 75.7. MS (ESI): 317 (M+H$^+$, 100), 319 (M+H$^+$, 30). These assignments matched with those previously published.[1]

7,7'-Dimethyl-3,3'-biindolin-2-one (**2q**)



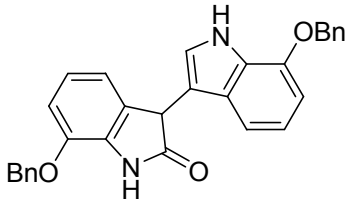
White amorphous solid, 86% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.93 (s, 1H, NH), 10.37 (s, 1H, NH), 7.15 (d, J = 7.8 Hz, 1H, Ar-H), 7.06 (d, J = 7.5 Hz, 1H, Ar-H), 7.05 (d, J = 2.6 Hz, 1H, Ar-H), 7.03 (d, J = 7.5 Hz, 1H, Ar-H), 6.86 (t, J = 7.6 Hz, 1H, Ar-H), 6.82 (d, J = 7.6 Hz, 1H, Ar-H), 6.77 (t, J = 7.6 Hz, 1H, Ar-H), 6.28 (s, 1H), 2.42 (s, 3H, CH_3), 2.27 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 179.4, 140.7, 136.7, 133.6, 130.7, 125.1, 123.6, 122.6, 122.1, 121.9, 120.9, 119.3, 119.1, 118.4, 116.5, 75.6, 17.2, 16.9. MS (ESI): 277 (M+H$^+$, 100). These assignments matched with those previously published.[1]

7,7'-Dimethoxy-3,3'-biindolin-2-one (**2r**)



White amorphous solid, 89% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.07 (d, J = 2.0 Hz, 1H, NH), 10.36 (s, 1H, NH), 6.98 (dd, J = 7.3, 1.1 Hz, 1H, Ar-H), 6.96 (s, 1H, Ar-H), 6.91 (t, J = 8.0 Hz, 1H, Ar-H), 6.90 (d, J = 8.0 Hz, 1H, Ar-H), 6.84 (dd, J = 7.3, 1.1 Hz, 1H, Ar-H), 6.78 (t, J = 8.0 Hz, 1H, Ar-H), 6.59 (d, J = 7.3 Hz, 1H, Ar-H), 6.32 (s, 1H), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.9, 146.5, 144.1, 134.6, 130.6, 127.3, 126.8, 123.5, 122.8, 119.5, 117.5, 116.5, 113.6, 112.6, 102.0, 75.7, 56.2, 55.6. MS (ESI): 309 ($M+H^+$, 100). These assignments matched with those previously published.[1]

7,7'-Bis(benzyloxy)-3,3'-biindolin-2-one (**2s**)



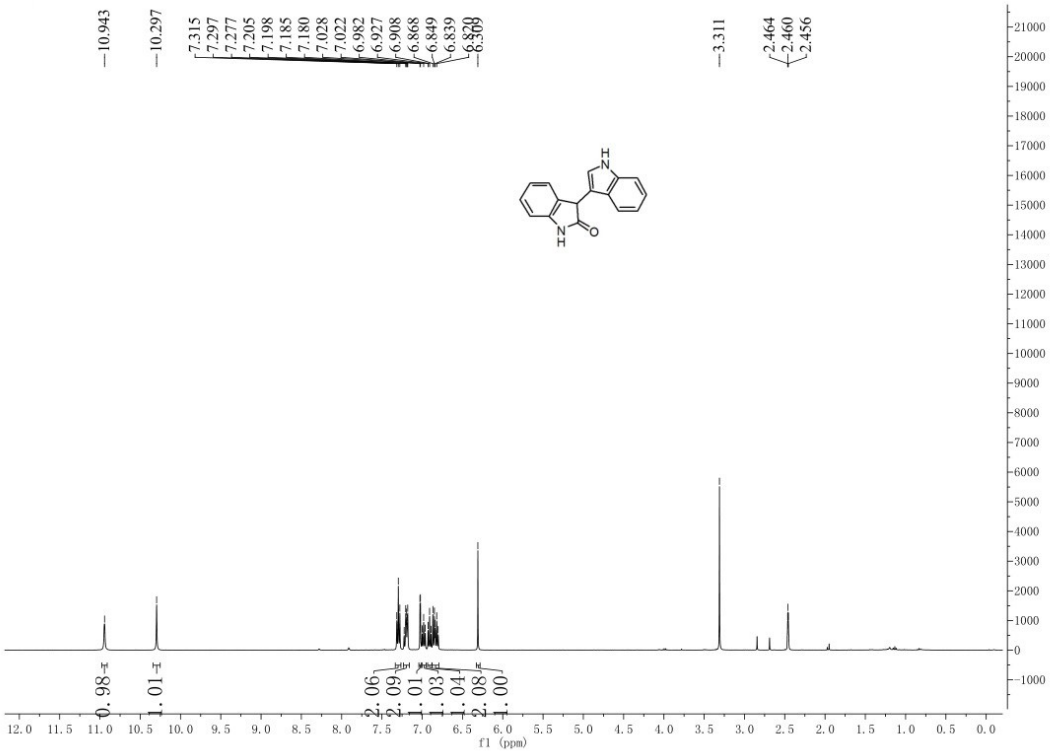
White amorphous solid, 84% yield. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.11 (s, 1H, NH), 10.50 (s, 1H, NH), 7.57 (d, J = 7.5 Hz, 2H, Ar-H), 7.54 (d, J = 7.5 Hz, 2H, Ar-H), 7.40 (t, J = 7.5 Hz, 4H, Ar-H), 7.34 (d, J = 7.5 Hz, 2H, Ar-H), 7.05 (d, J = 7.8 Hz, 1H, Ar-H), 7.01 (d, J = 2.5 Hz, 1H, Ar-H), 6.88 (dt, J = 2.5, 7.8 Hz, 2H, Ar-H), 6.84 (d, J = 7.8 Hz, 1H, Ar-H), 6.75 (t, J = 7.8 Hz, 1H, Ar-H), 6.68 (d, J = 7.8 Hz, 1H, Ar-H), 6.35 (s, 1H), 5.23 (s, 2H, OCH_2) , 5.21 (s, 2H, OCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 178.9, 145.4, .142.8, 137.8, 137.6, 134.9, 131.2, 129.0, 128.8, 128.7, 128.2, 128.1, 127.9, 127.8, 127.6, 123.6, 122.6, 119.4, 117.8, 116.5, 114.3, 113.8, 103.4, 75.7, 70.1, 69.6. MS (ESI): 461 ($M+H^+$, 100). These assignments matched with those previously published.[1]

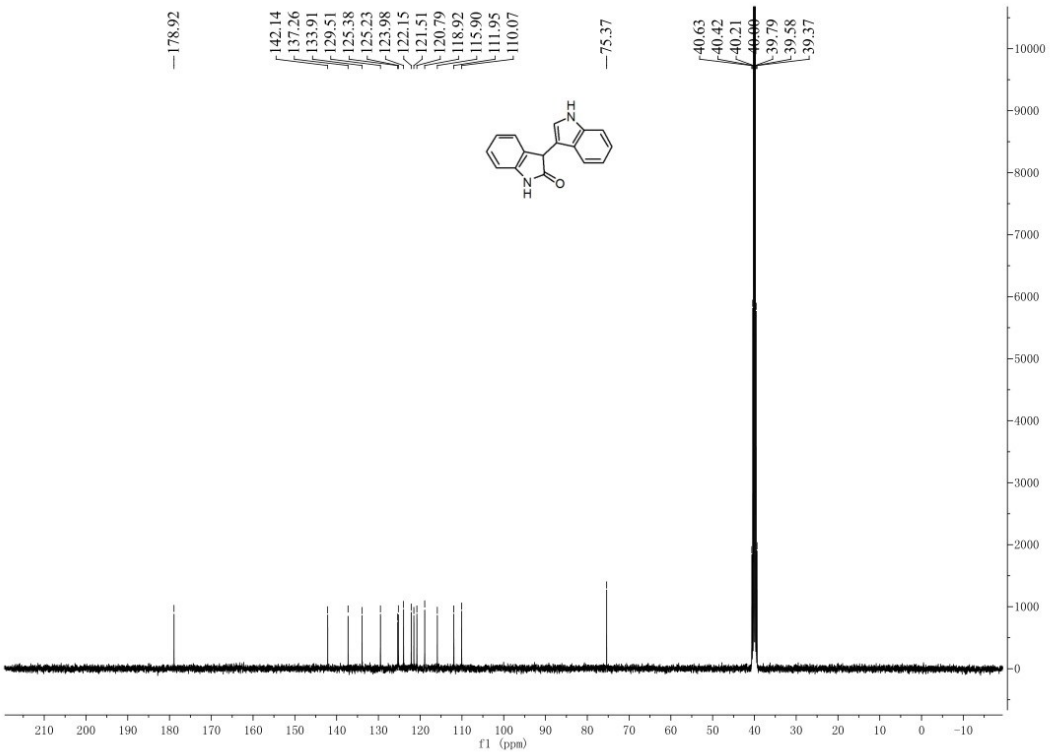
References

1. F. Lin, Y. Chen, B. Wang, W. Qin and L. Liu, *RSC Adv.*, **2015**, *5*, 37018–37022.

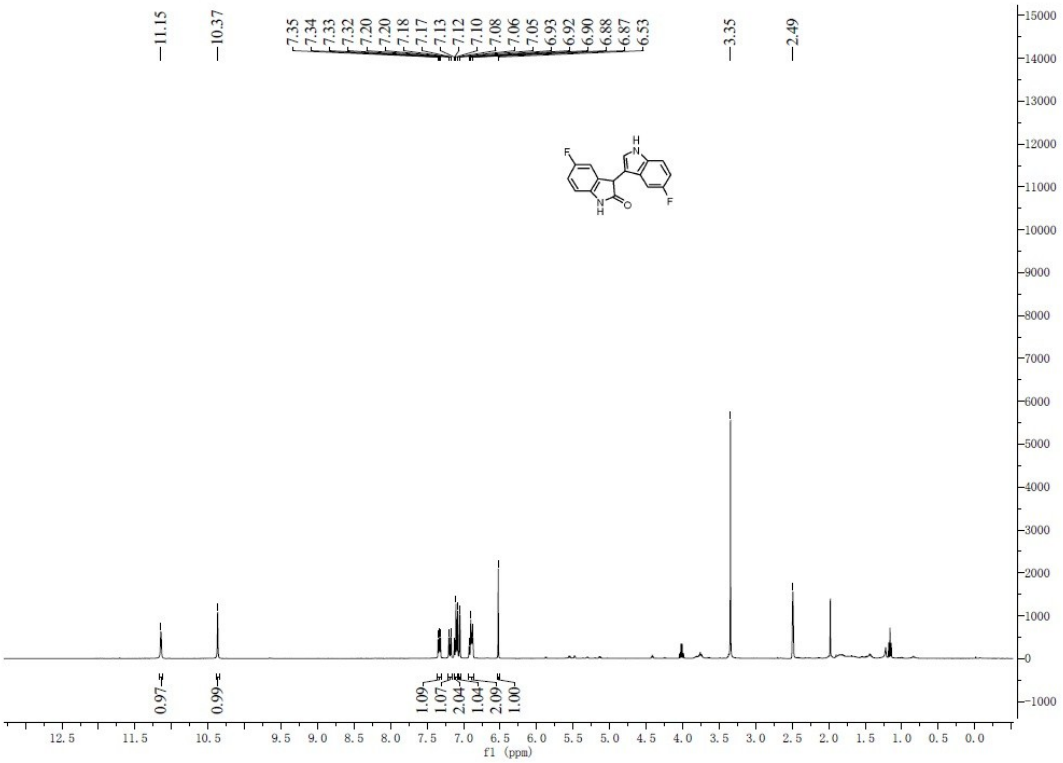
5. Copies of ^{1}H and ^{13}C Spectra

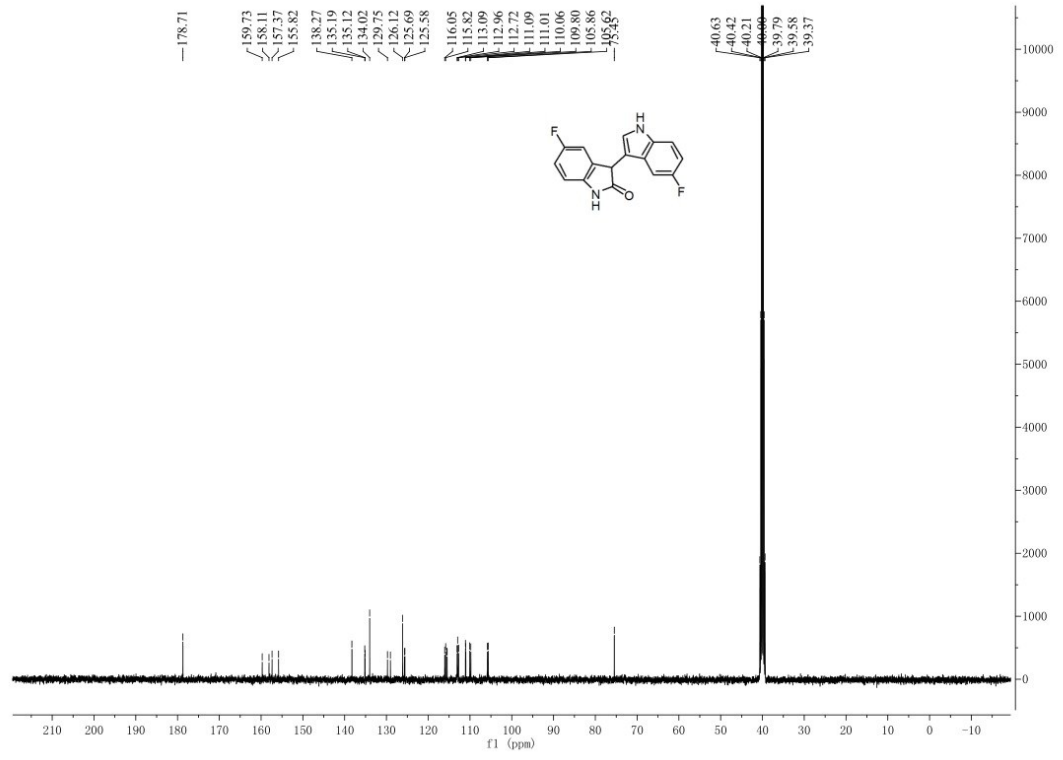
^{1}H and ^{13}C NMR Spectra for **2a**



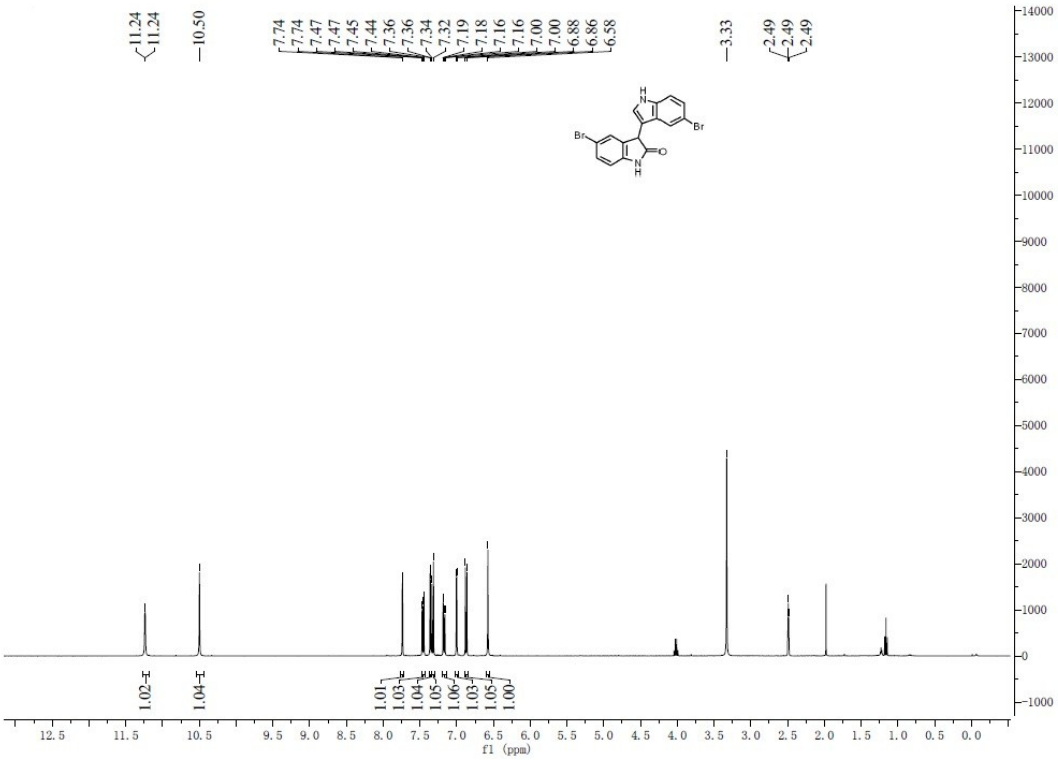


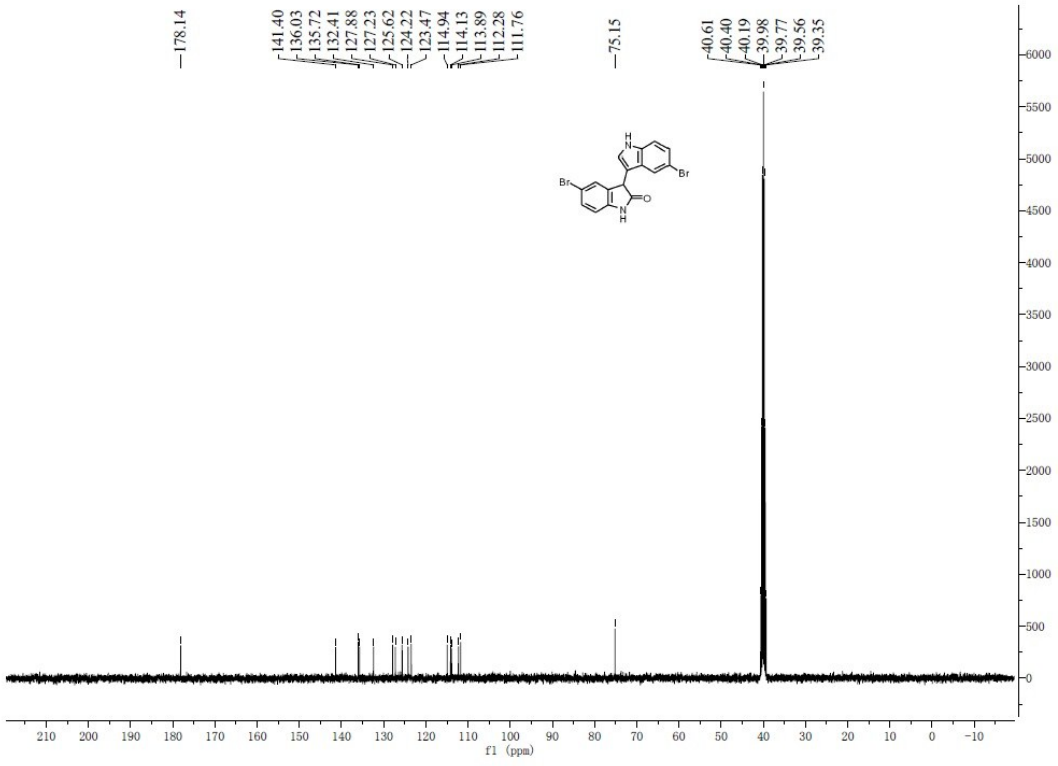
^{1}H and ^{13}C NMR Spectra for **2b**



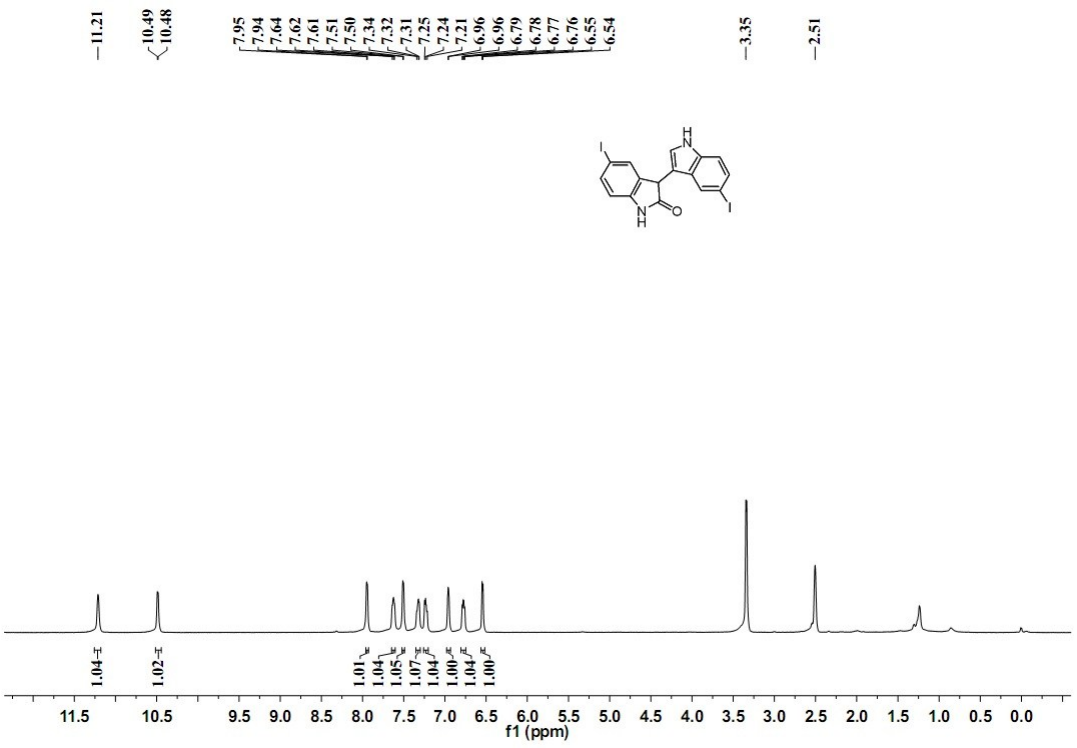


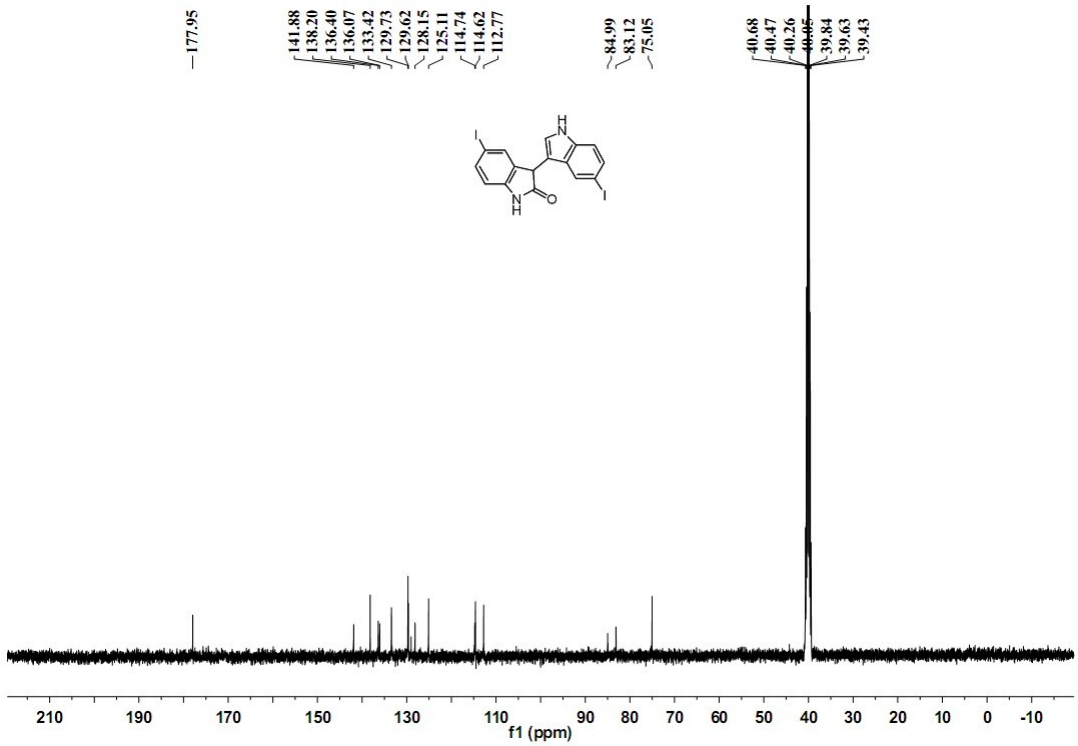
^{1}H and ^{13}C NMR Spectra for **2c**



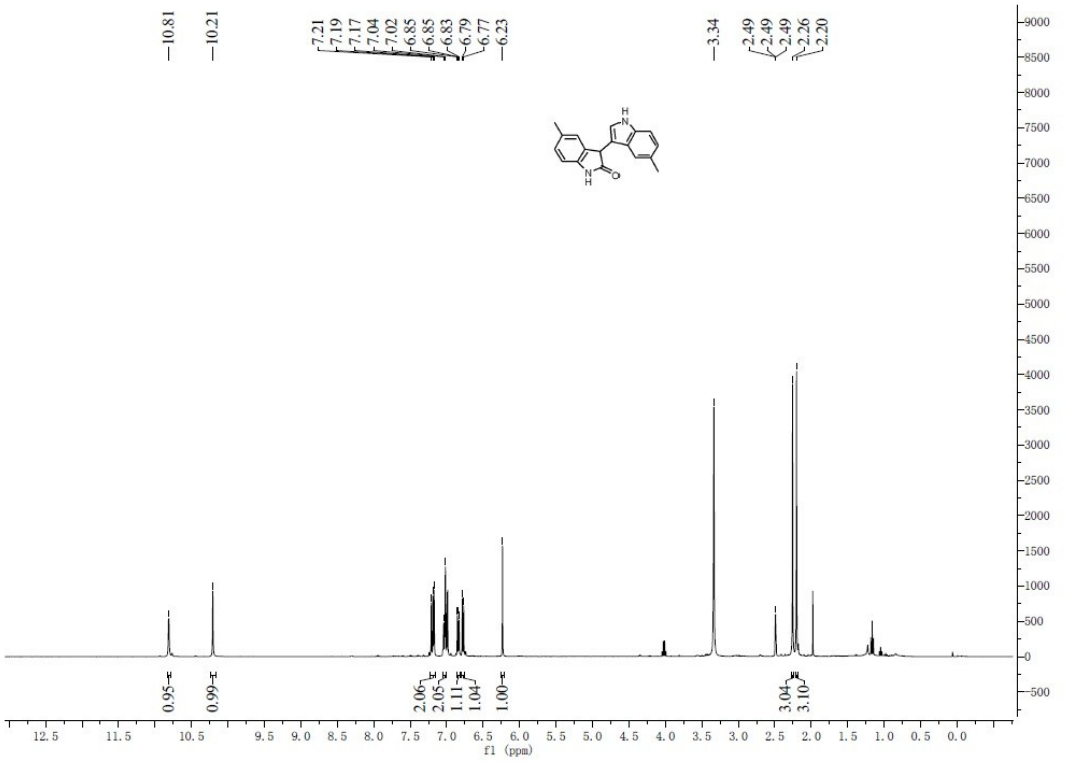


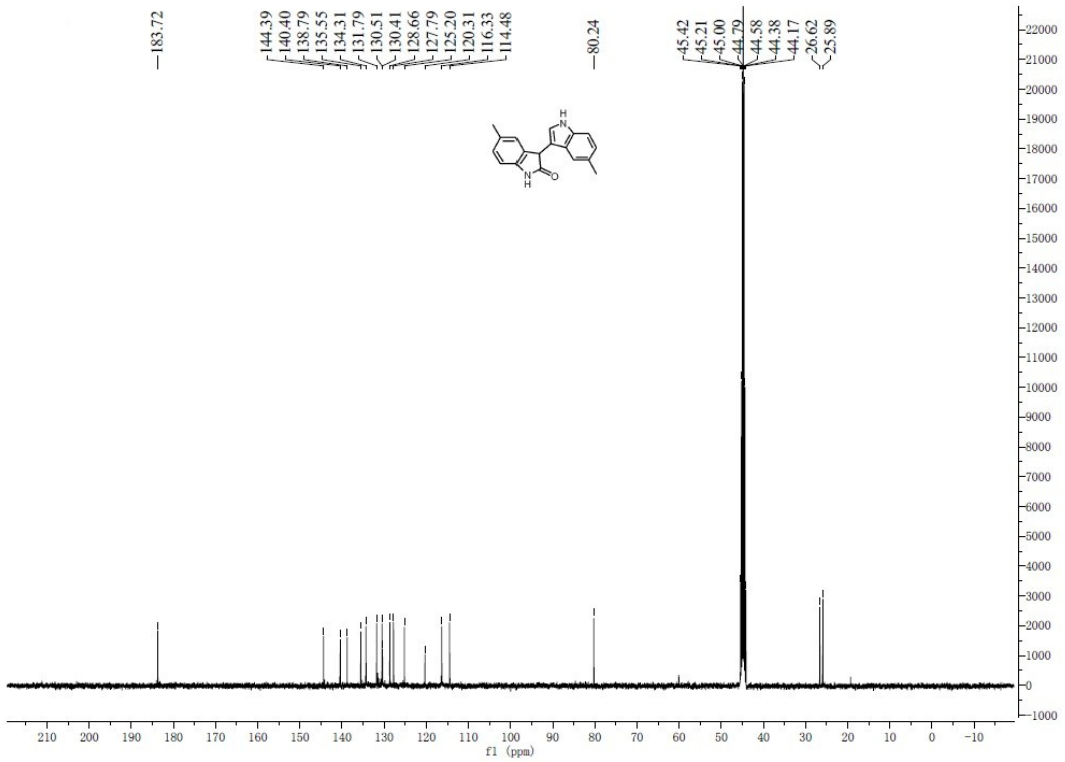
^{1}H and ^{13}C NMR Spectra for **2d**



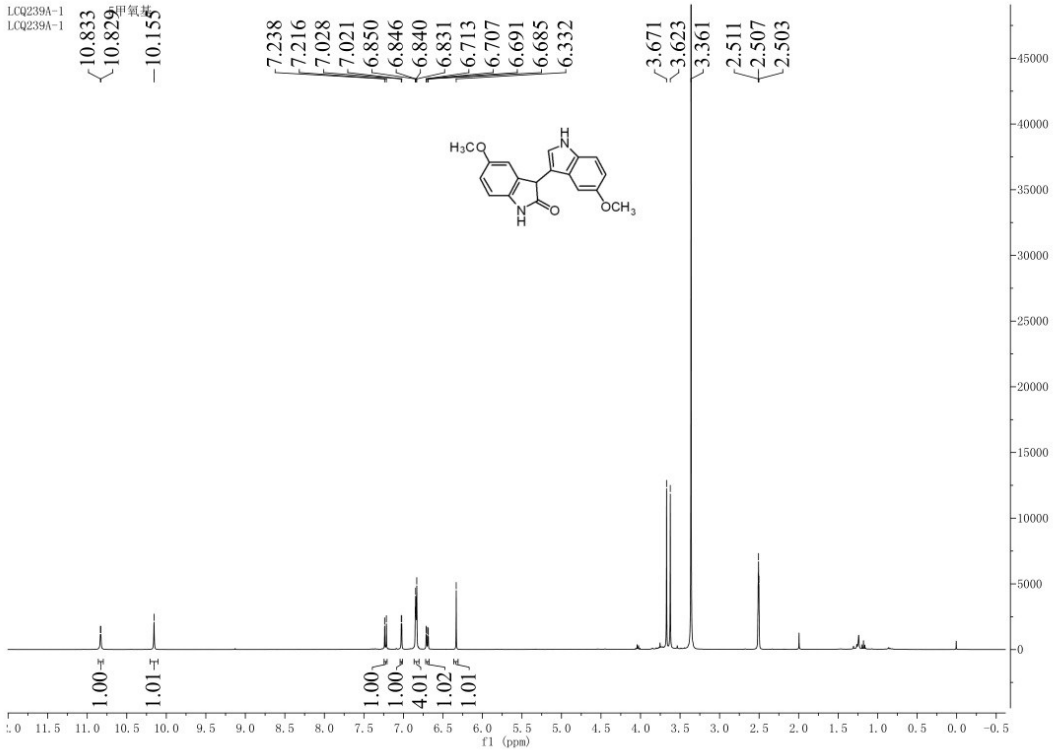


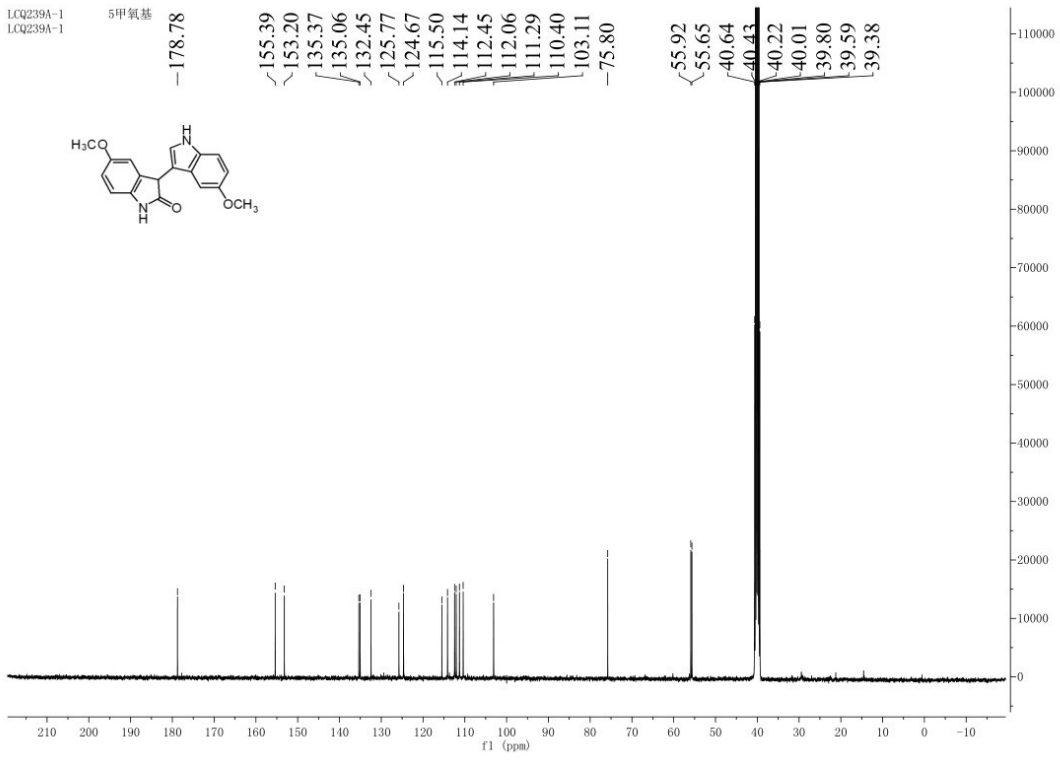
^{1}H and ^{13}C NMR Spectra for **2e**



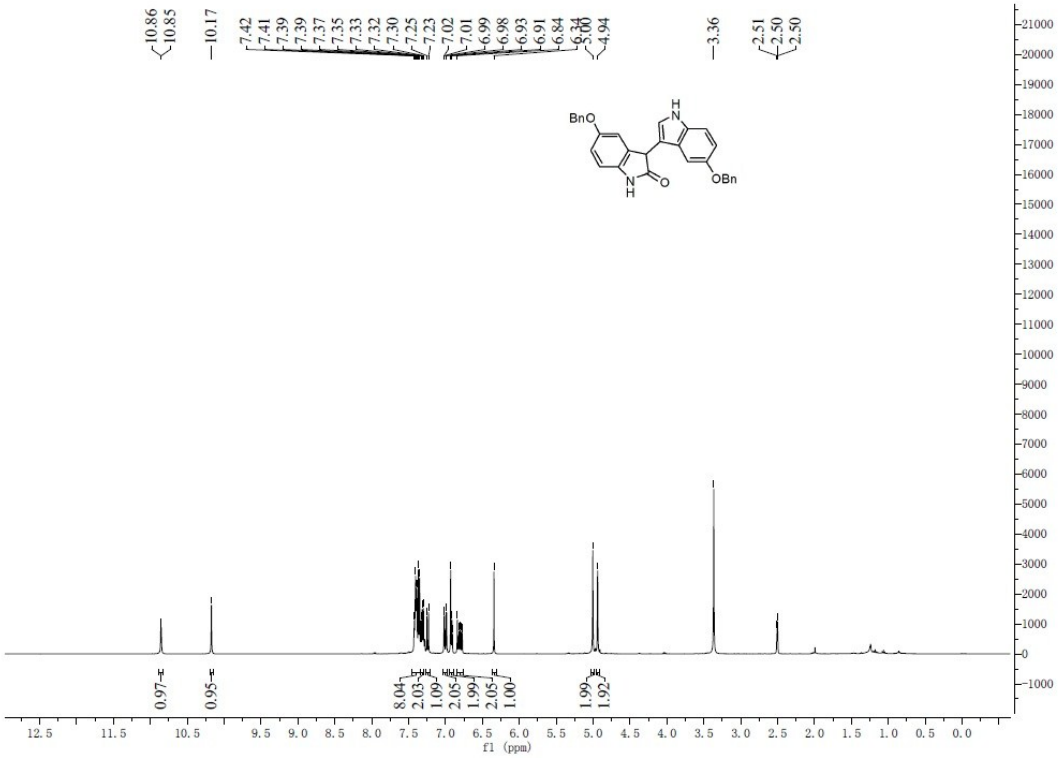


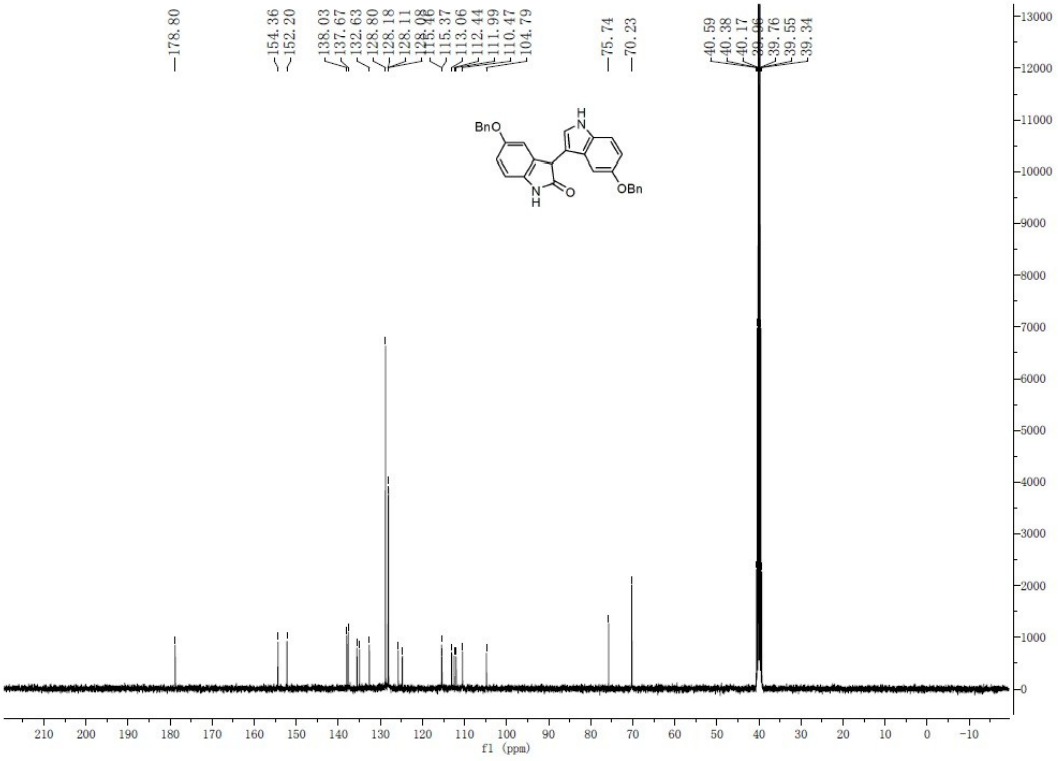
^{1}H and ^{13}C NMR Spectra for **2f**



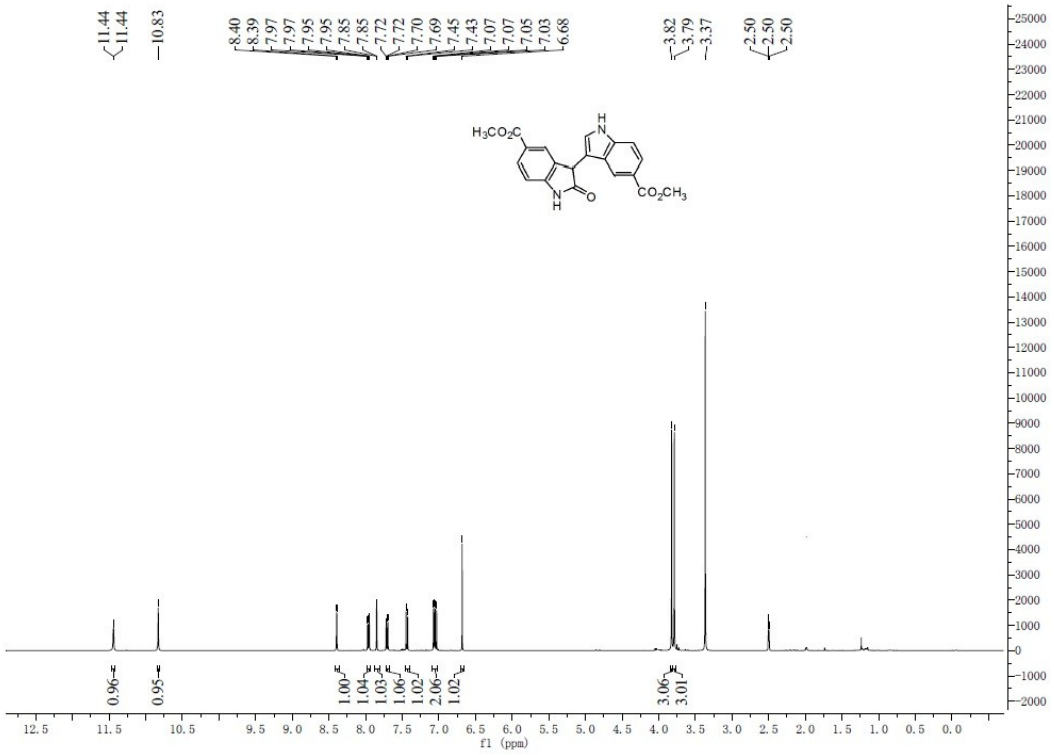


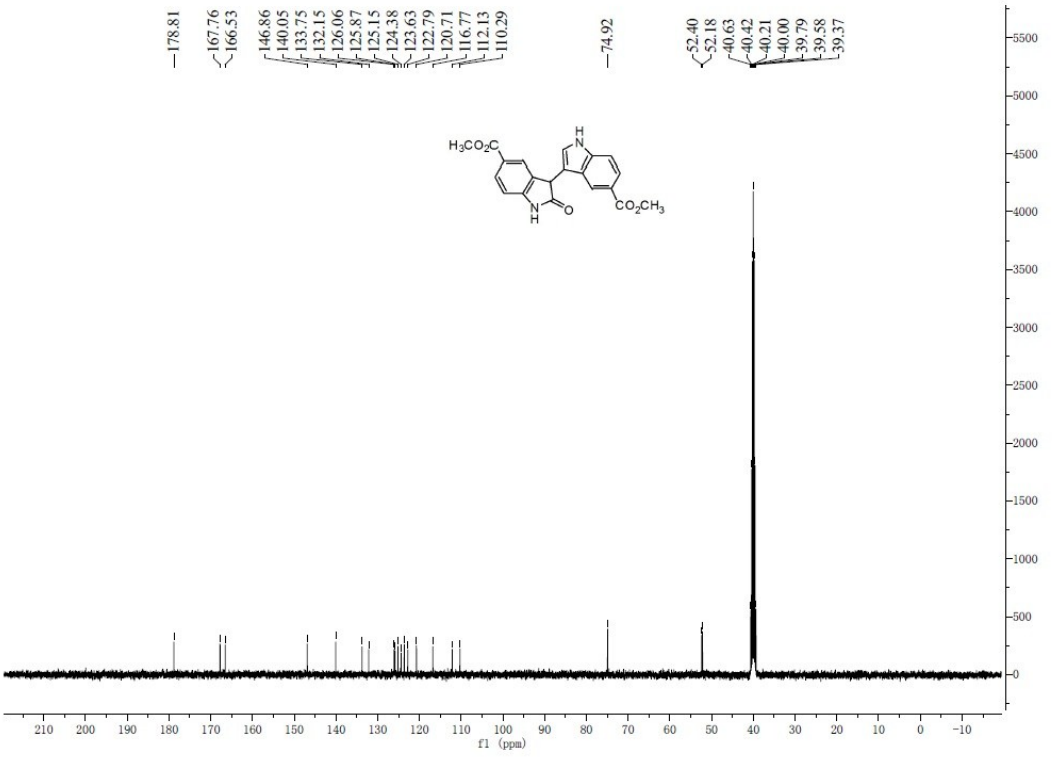
^{1}H and ^{13}C NMR Spectra for **2g**



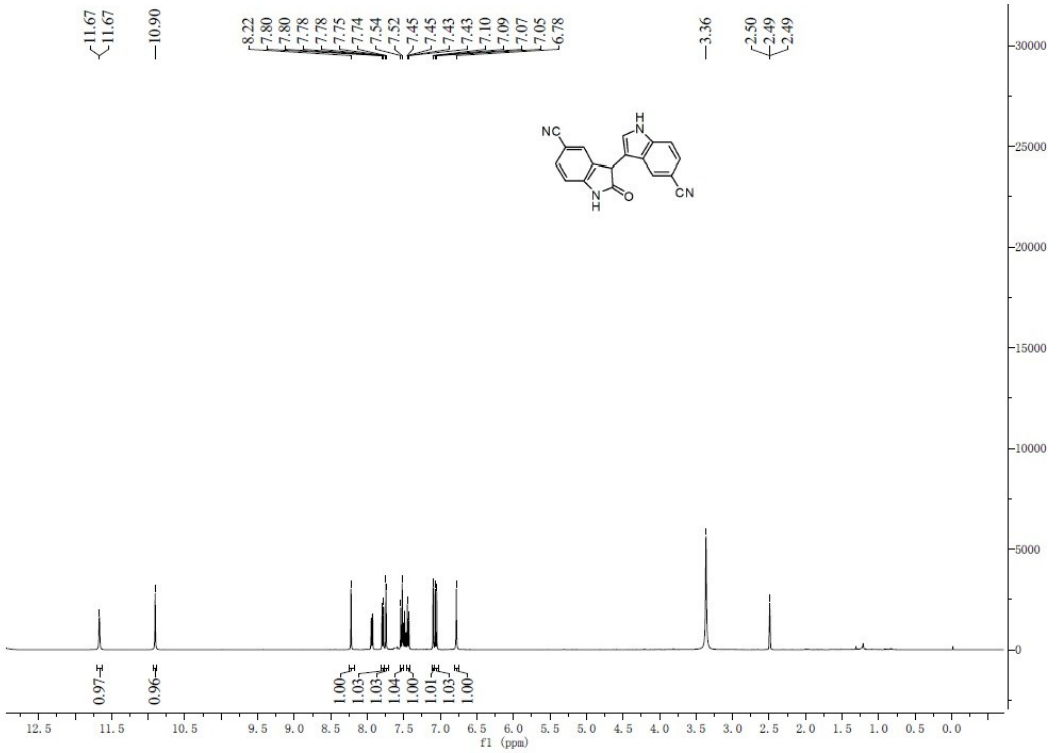


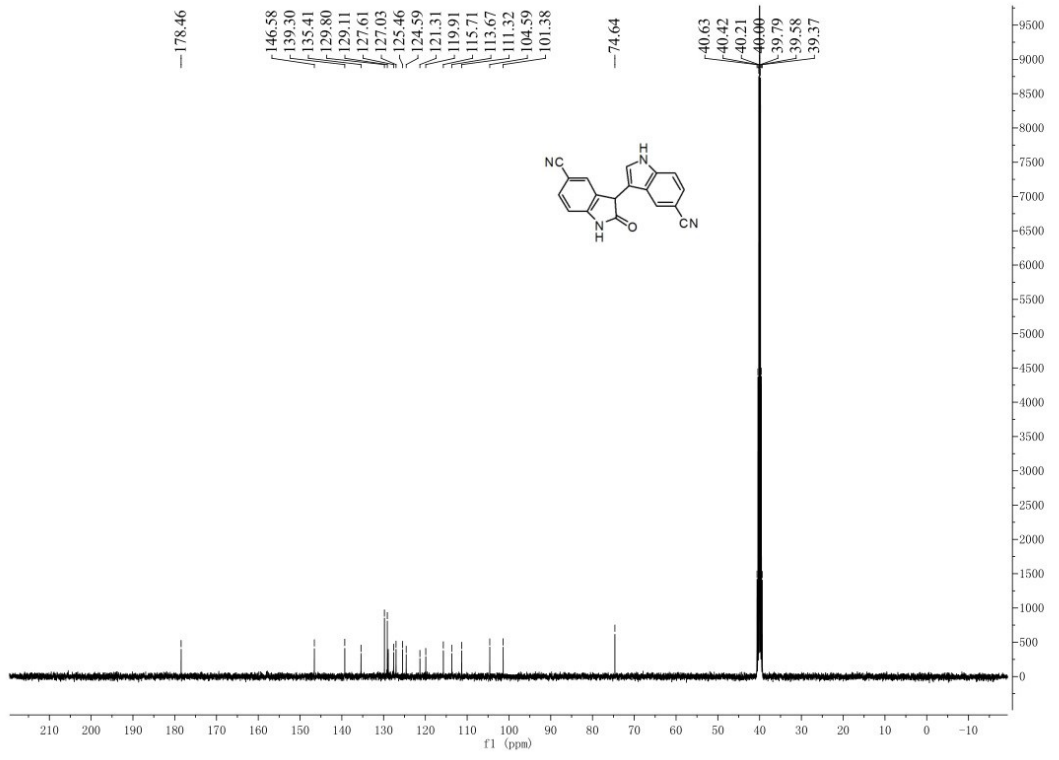
^{1}H and ^{13}C NMR Spectra for **2h**



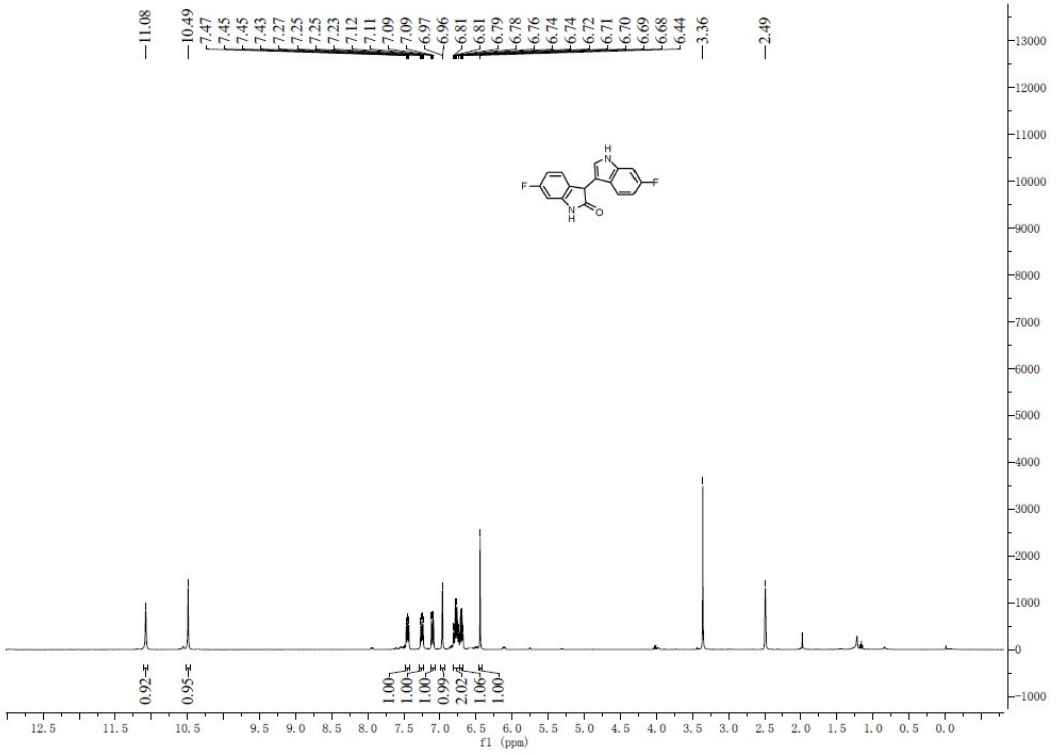


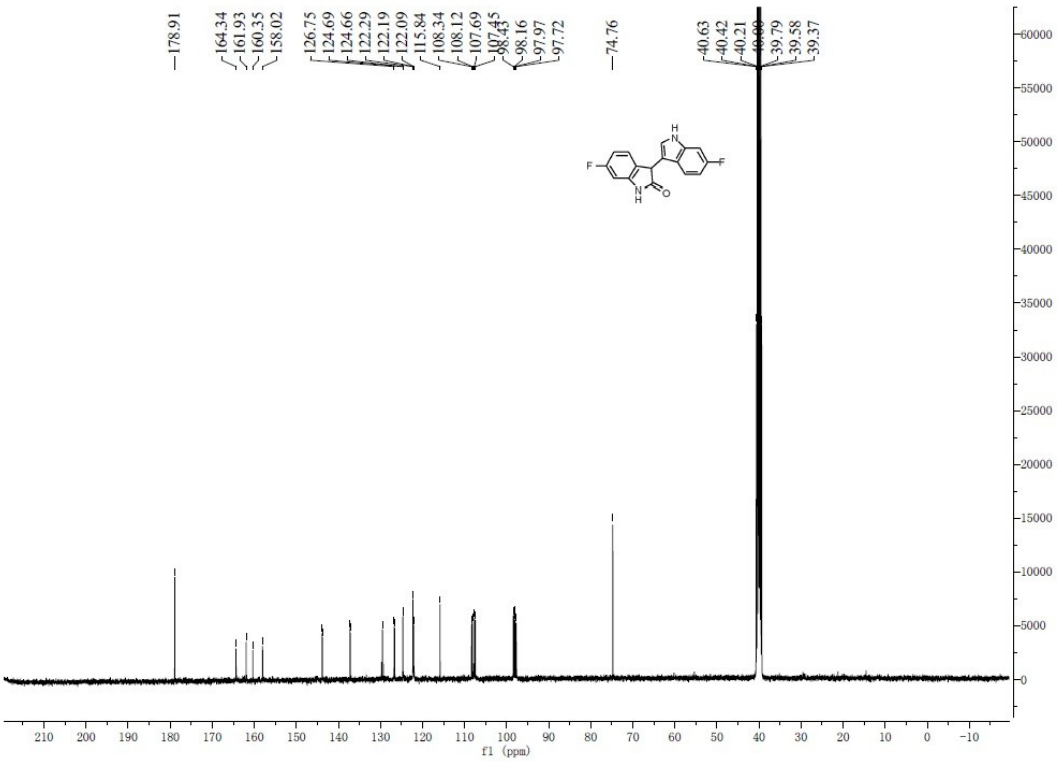
^{1}H and ^{13}C NMR Spectra for **2i**



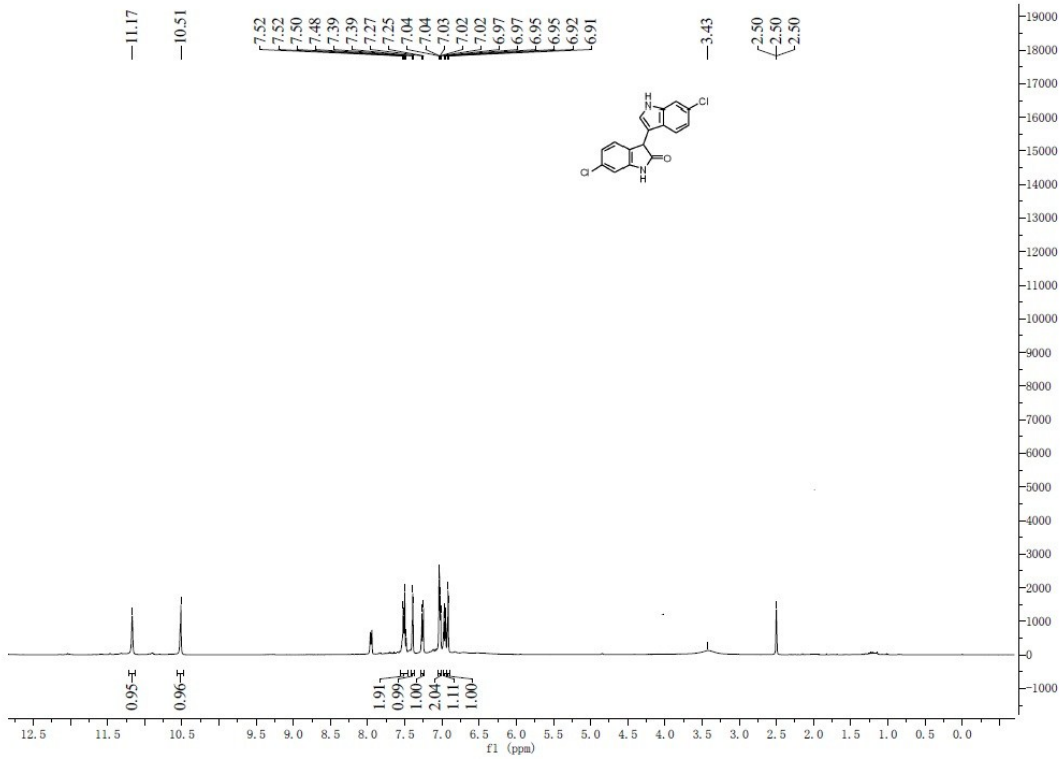


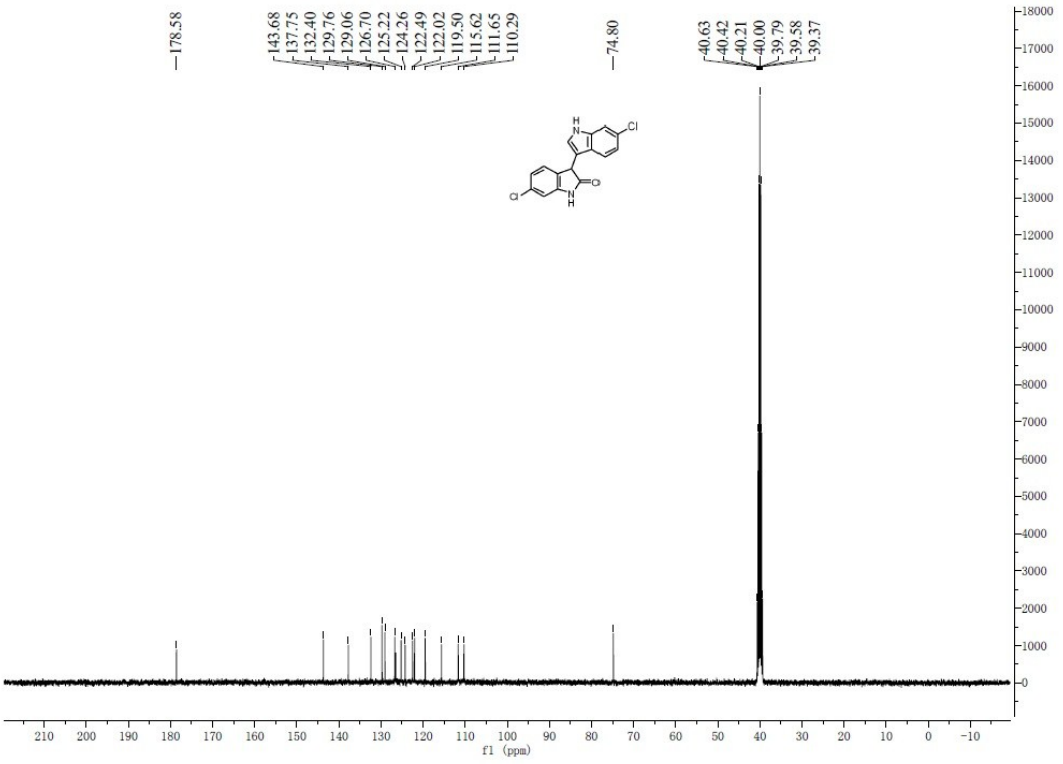
^{1}H and ^{13}C NMR Spectra for **2j**



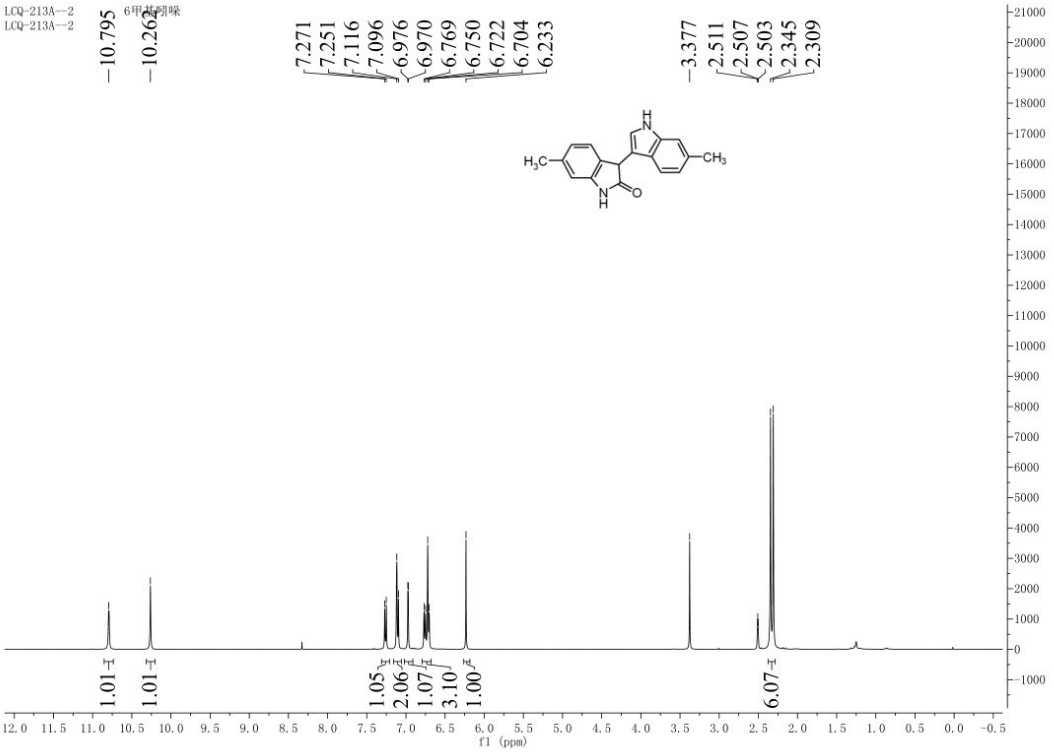


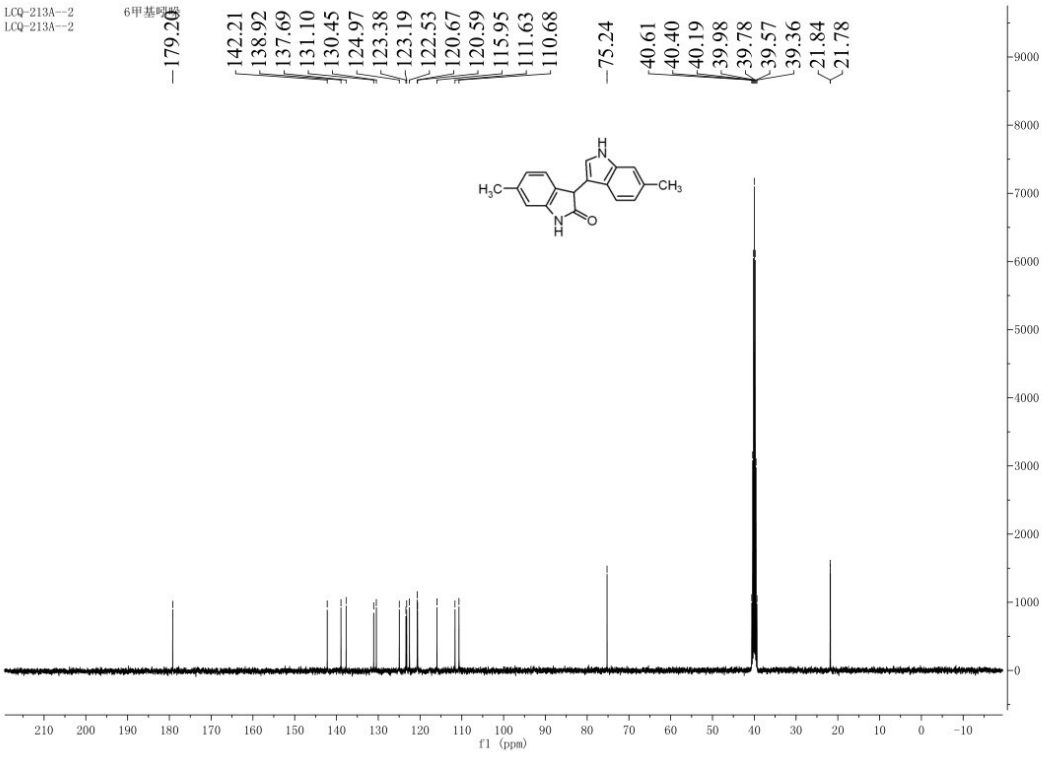
^{1}H and ^{13}C NMR Spectra for **2k**



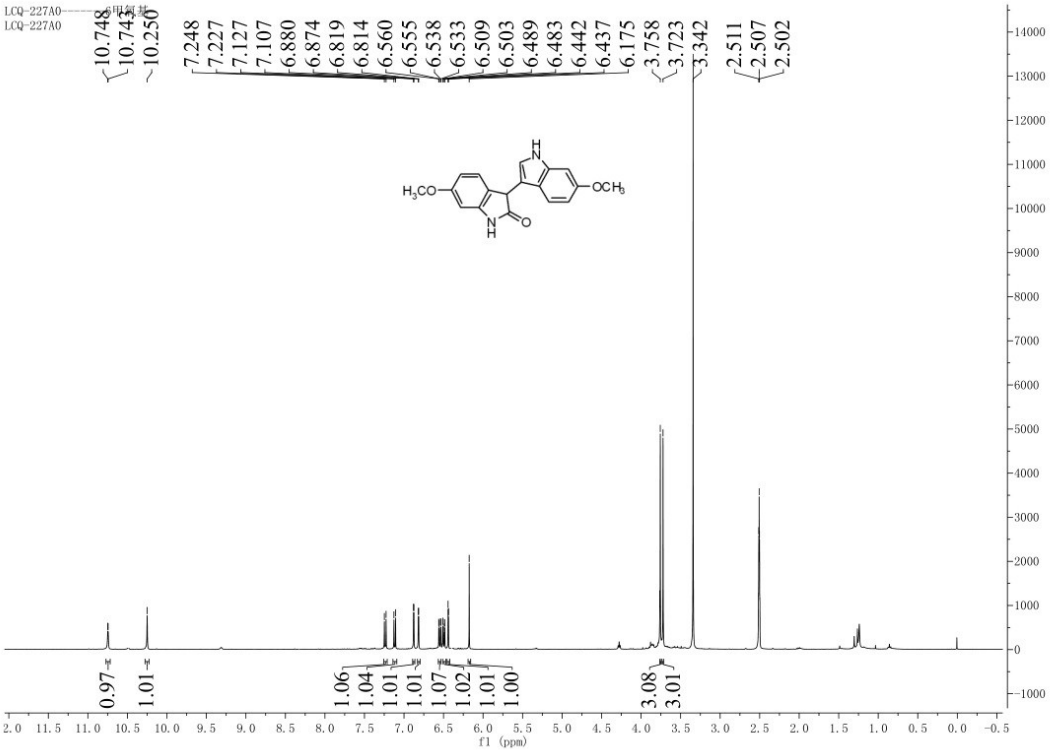


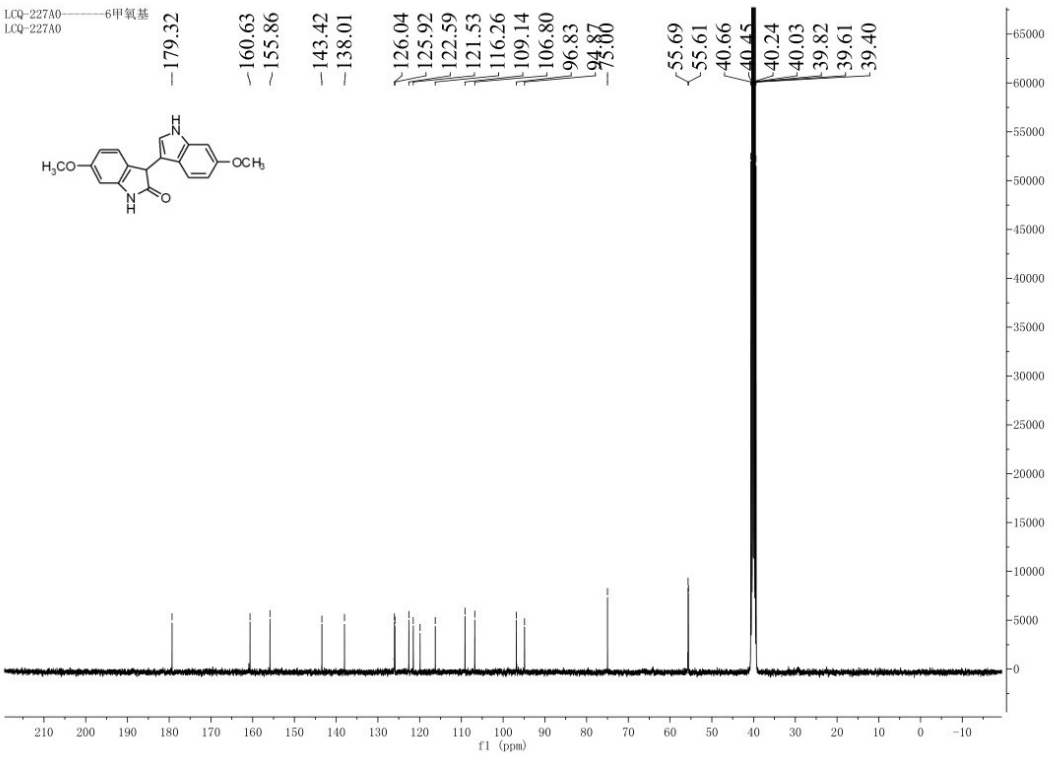
^{1}H and ^{13}C NMR Spectra for **2l**



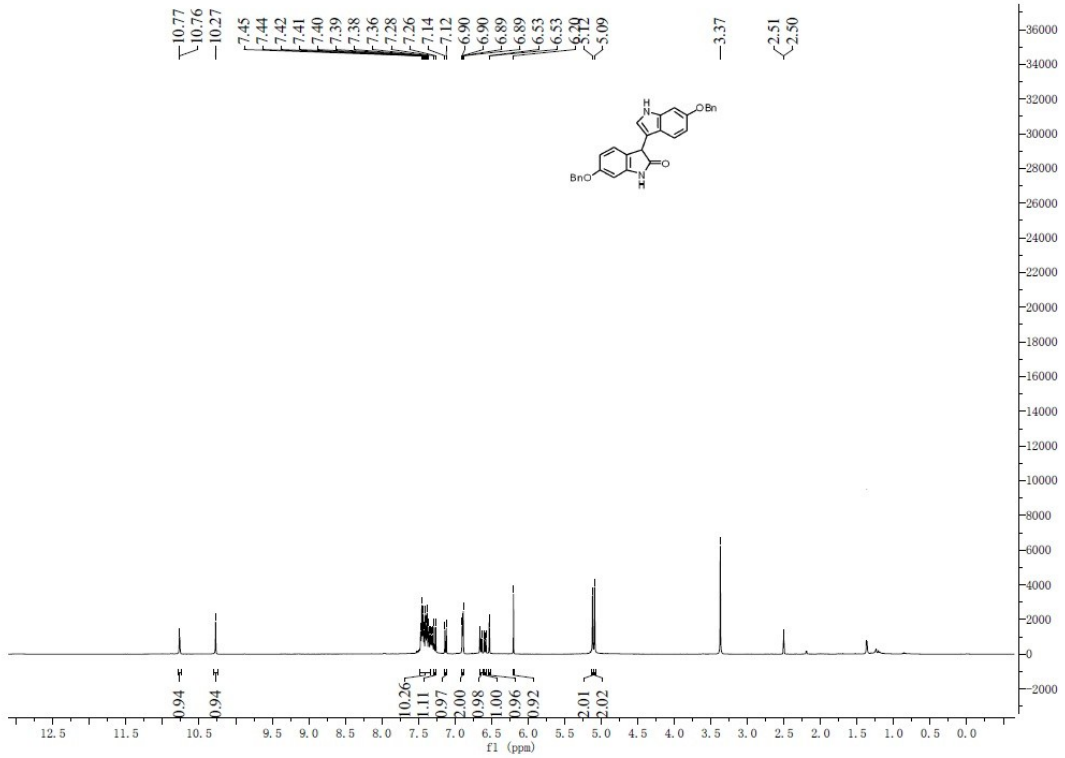


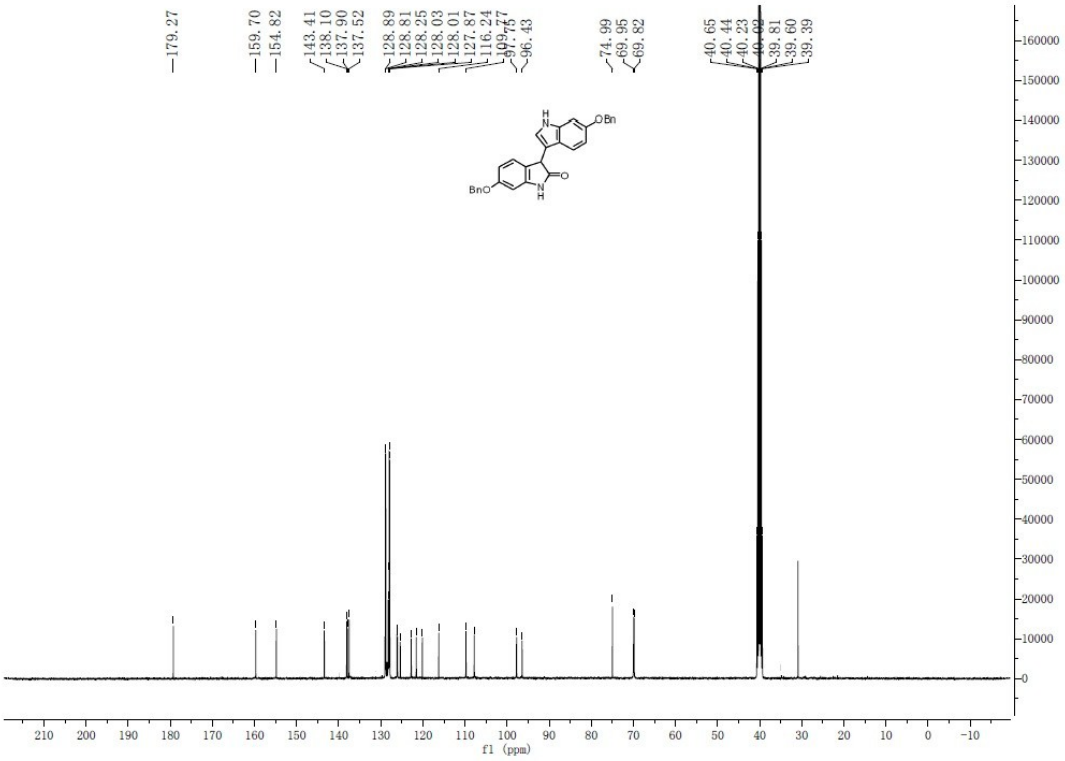
^{1}H and ^{13}C NMR Spectra for **2m**



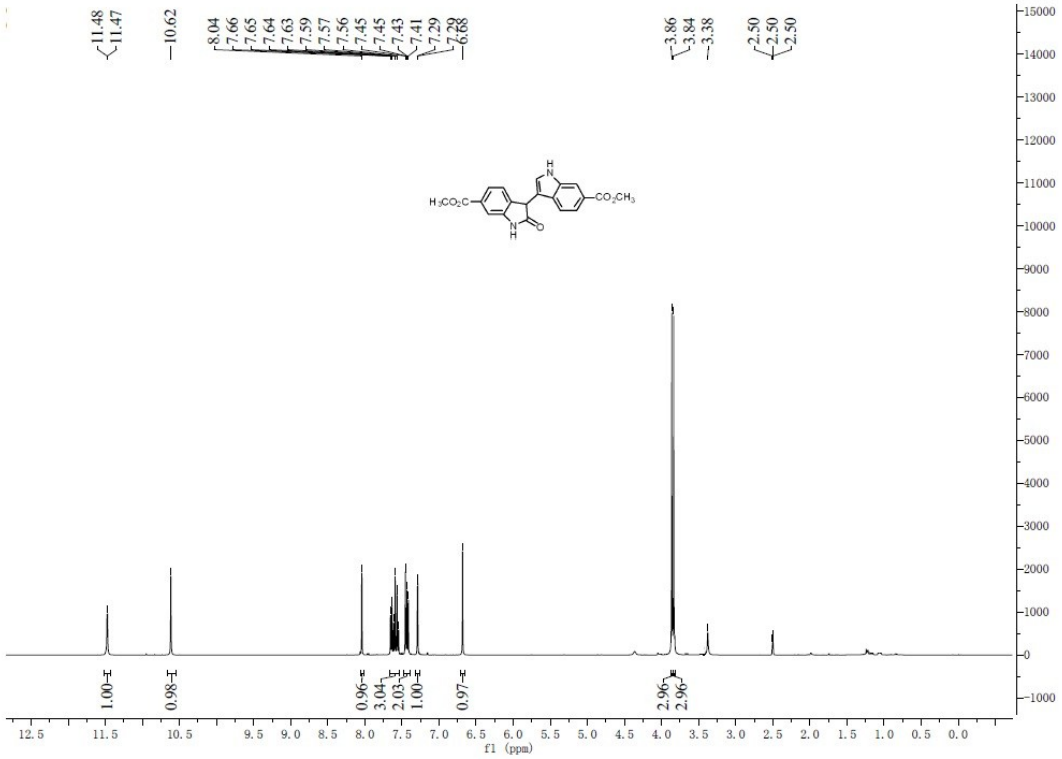


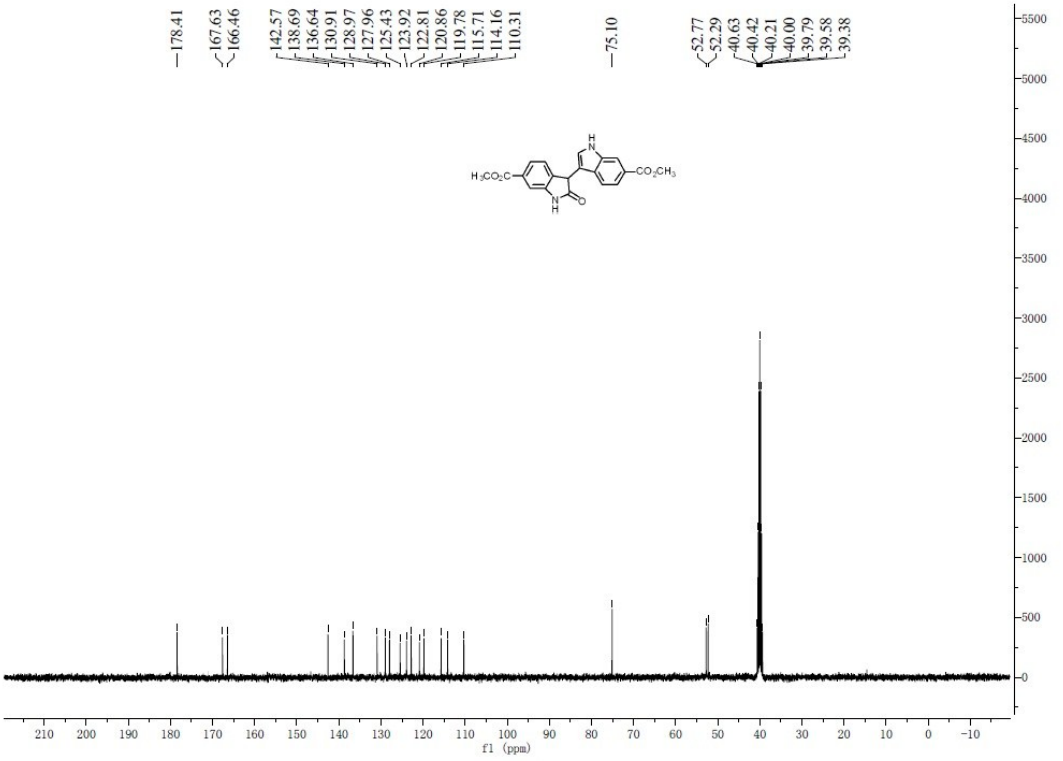
^{1}H and ^{13}C NMR Spectra for **2n**



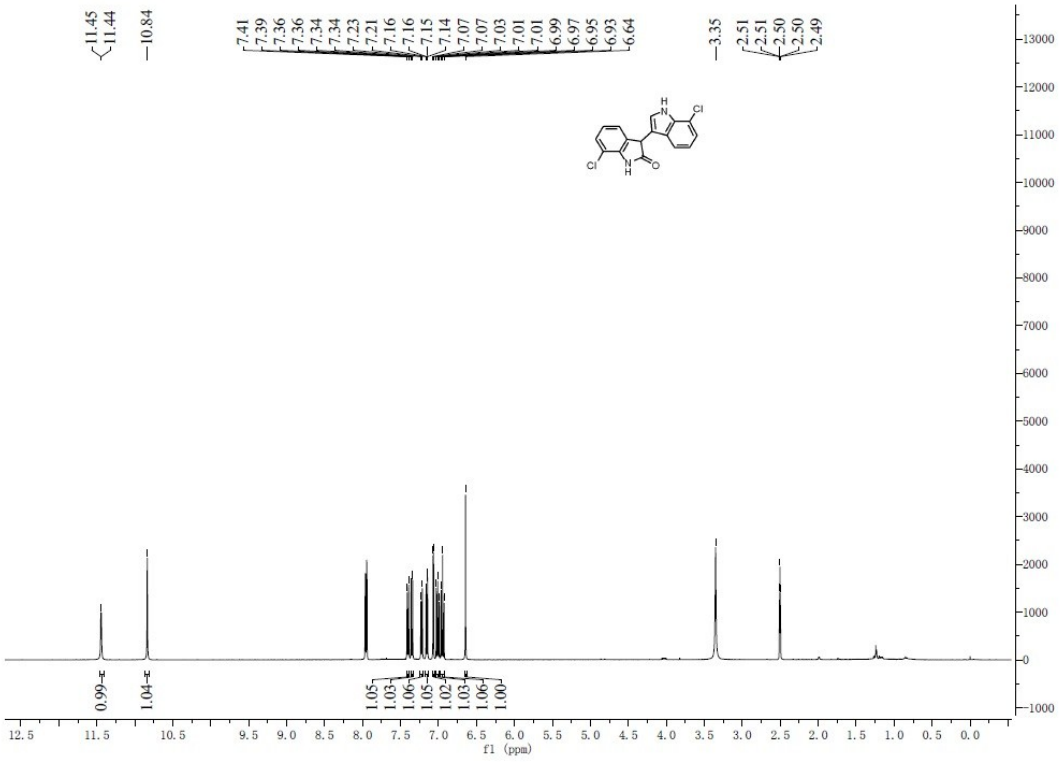


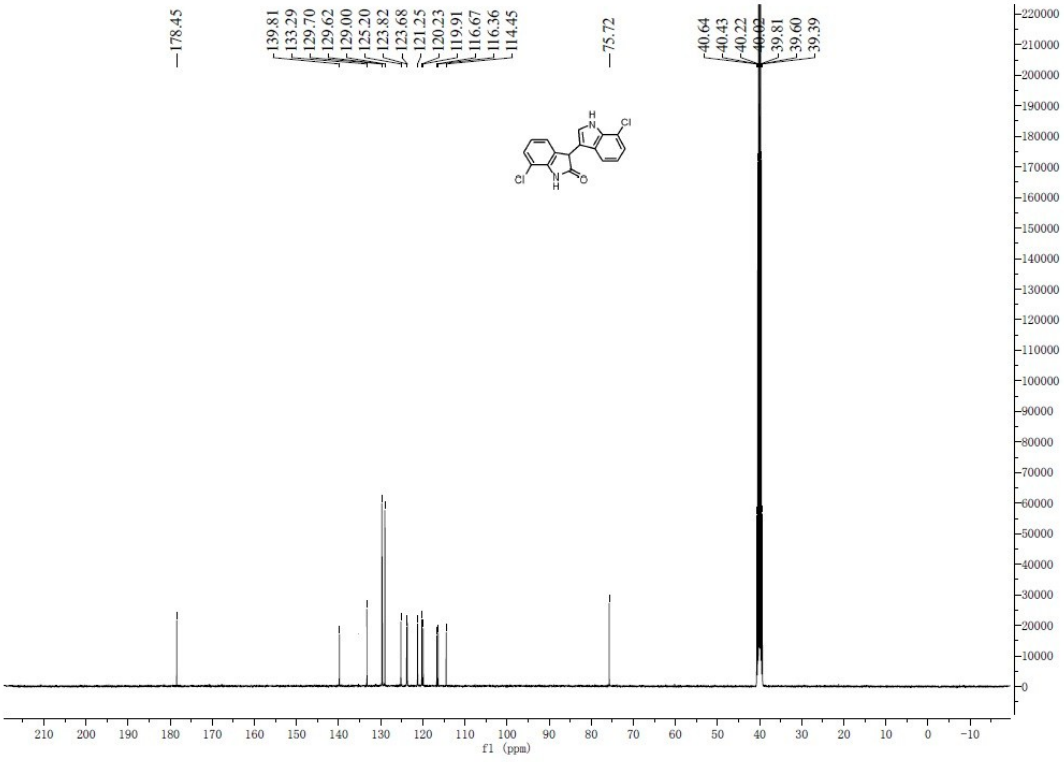
^{1}H and ^{13}C NMR Spectra for **2o**



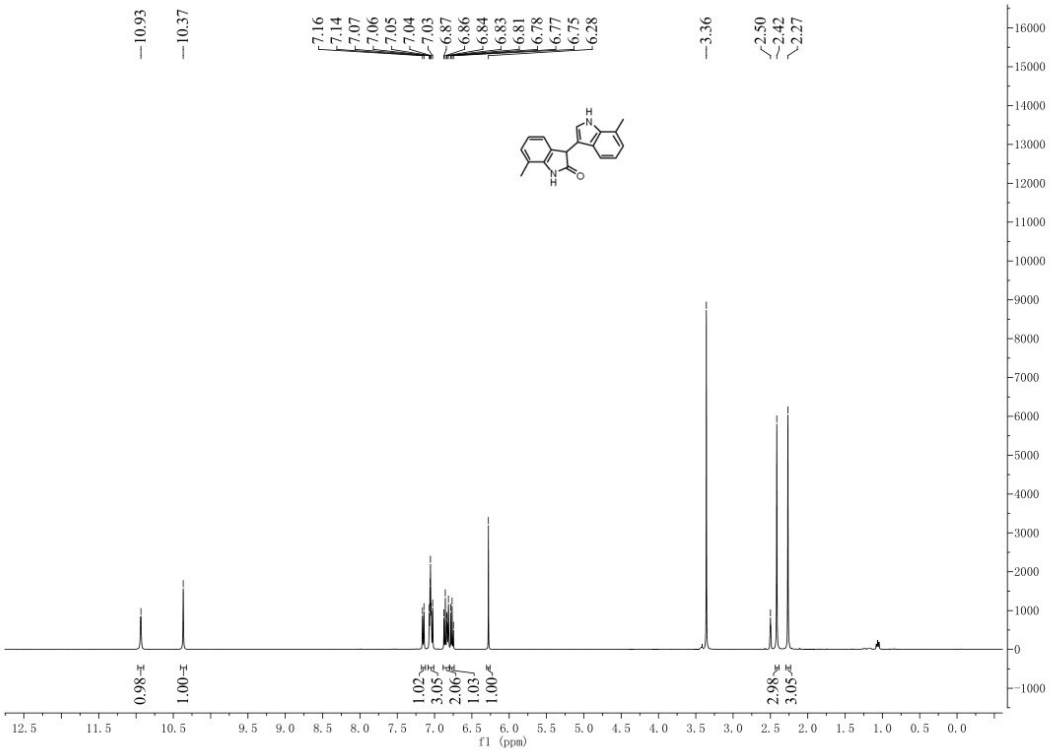


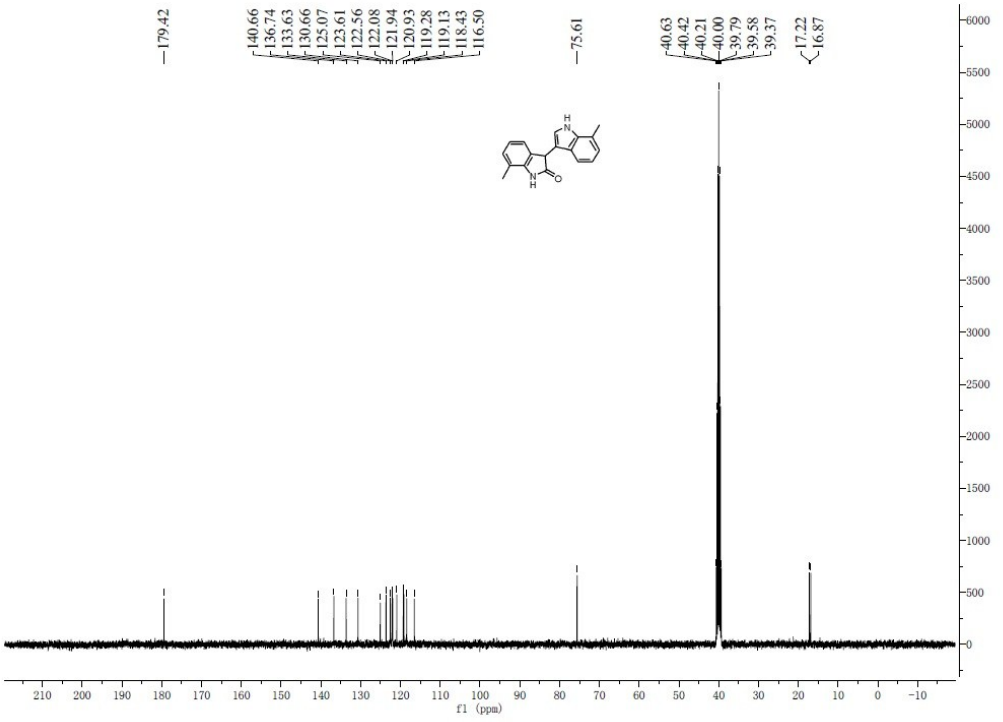
^{1}H and ^{13}C NMR Spectra for **2p**



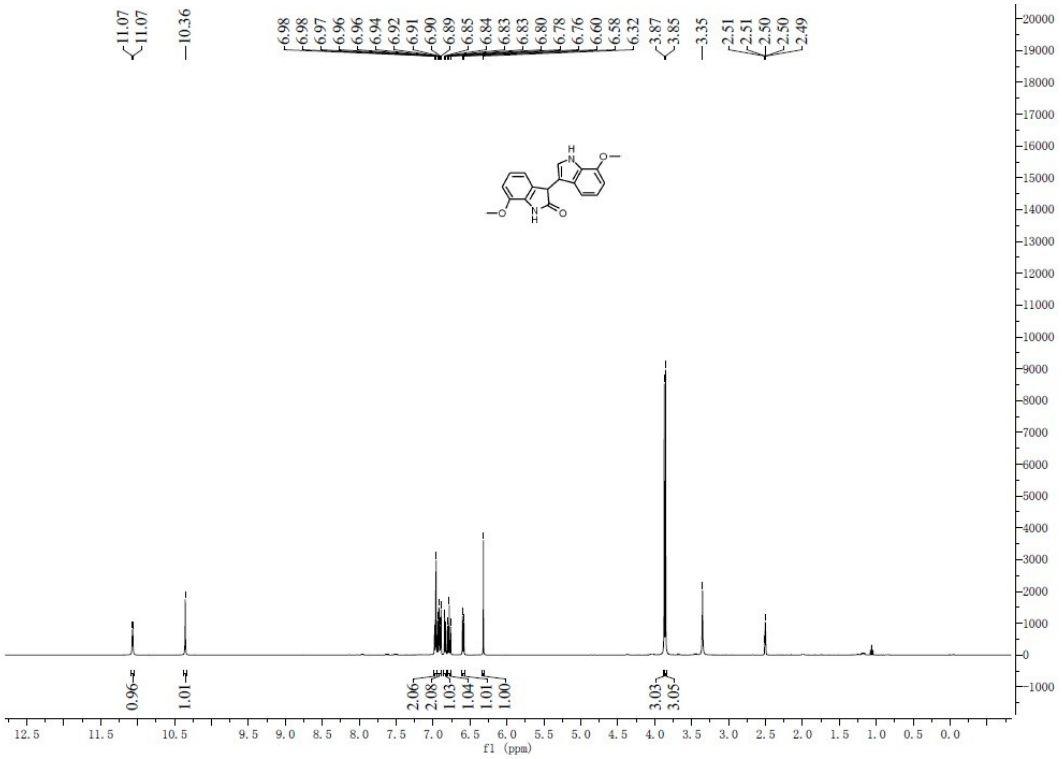


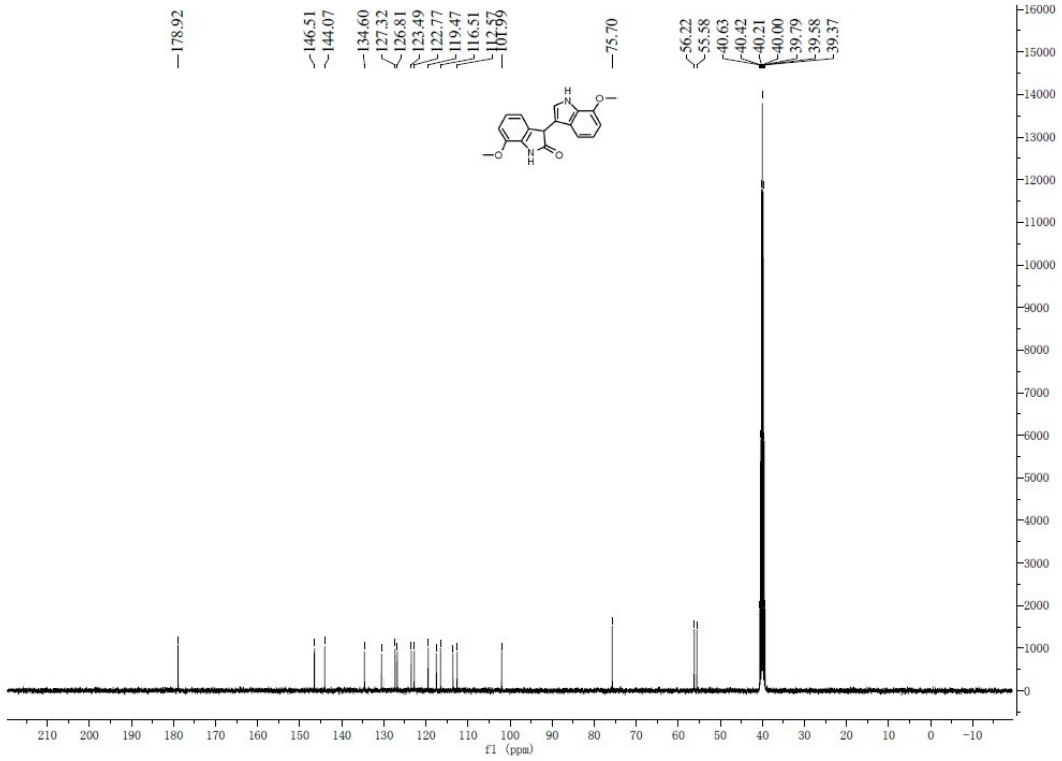
^{1}H and ^{13}C NMR Spectra for **2q**





^{1}H and ^{13}C NMR Spectra for **2r**





^{1}H and ^{13}C NMR Spectra for **2s**