Supporting Information

Electrochemically Enabled Chemoselective Sulfonylation and Hydrazination of Indoles

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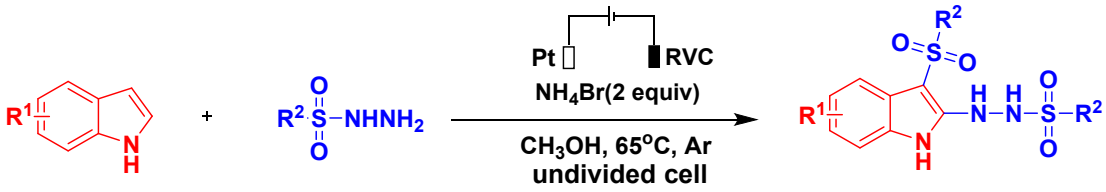
1. General Information

Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. Column chromatography on silica gel (300-400 mesh) was carried out using technical grade 60-90 ^{o}C petroleum ether and analytical grade EtOAc (without further purification). ^{1}H and ^{13}C spectra were recorded on a 400 MHz or 500 MHz spectrometer. Chemical shifts were reported in ppm. ^{1}H NMR spectra were referenced to DMSO (2.5 ppm), and ^{13}C-NMR spectra were referenced to DMSO (39.5 ppm). Peak multiplicities were designated by the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; brs, broad singlet and J, coupling constant in Hz. HRMS spectra were recorded with Micromass QTOF2 Quadrupole/Time-of-Flight Tandem mass spectrometer using electron spray ionization.

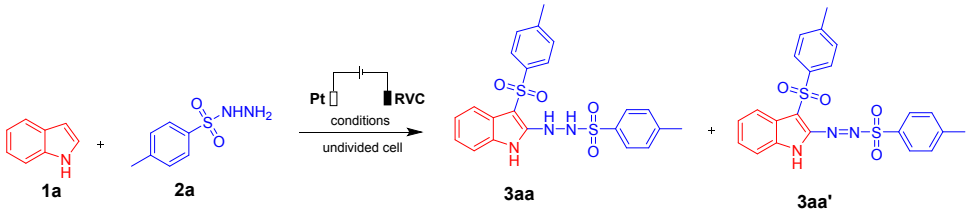
2. Chemical experiment procedure

2.1 Synthesis of sulfonylation and hydrazination products



The indoles (0.5 mmol, 1.0 equiv), benzene sulfonyl hydrazides (1 mmol, 2.0 equiv) and NH_4Br (1 mmol, 2.0 equiv) were placed in a 10 mL three-necked round-bottomed flask. The flask was equipped with a condenser, a platinum plate (1 cm x 1 cm) anode and a RVC (100 PPI, 1 cm x 1 cm x 1.2 cm) cathode. MeOH (8.0 mL) were added. The electrolysis was carried out under Ar at 65 °C using a constant current of 20 mA until complete consumption of the substrate (monitored by TLC, about 5 h). The reaction mixture was concentrated and the residue was chromatographed through silica gel eluting with ethyl acetate/petroleum ether to give the products.

2.2 Table S1. Optimization of reaction conditions.[a,b]



Entry	Catalyst	Solvent	Yield (%)[b]	
			3aa	**3aa′**
1	NH_4Br	CH_3OH	41[c]	0
2	NH_4Br	CH_3OH	74[d]	0
3	NH_4Br	CH_3OH	45[e]	0
4	NH_4Br	CH_3OH	60[f]	0
5	NH_4Br	CH_3OH	32[g]	0

[a]Reaction conditions: Pt plate as anode (1 cm × 1 cm), reticulated vitreous carbon (RVC) as cathode (100 PPI, 1 cm × 1 cm × 1.2 cm), undivided cell, constant current = 20 mA , **1a** (0.5 mmol), **2a** (1 mmol), catalyst (2 eq.), solvent (8 mL), under Ar at 65 °C for 5 h. [b]Isolated yields. [c]Reaction

temperature = 40 °C. [d]Reaction temperature = 80 °C. [e]Catalyst (1 eq.). [f]Catalyst (3 eq.). [g]Constant current = 10 mA.

2.3 Crystal Structure of Compound 3ad

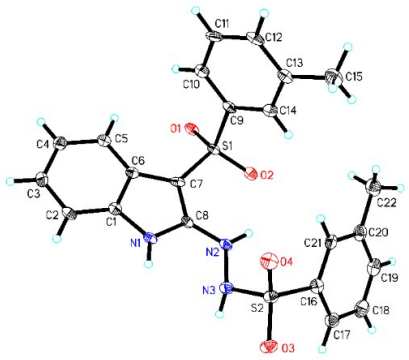


Figure S1. X-ray Structure of **3ad**, CCDC number: 1897802.

2.4 Procedure for cyclic voltammetry (CV):

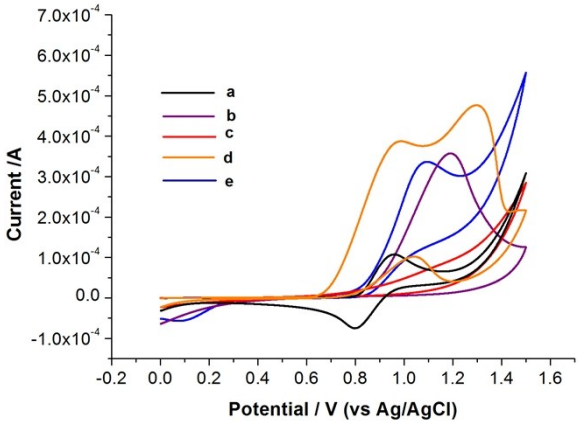


Figure S2. Cyclic voltammograms of reactants and their mixtures in 0.1 M $LiClO_4/CH_3OH$ using a glassy carbon disk working electrode (diameter, 3 mm), Pt disk and Ag/AgCl (0.1 M in CH_3OH) as counter and reference electrode at 100 mV/s scan rate: (a) NH_4Br(4 mmol/L), (b) **1a** (10 mmol/L), (c) **2a** (10 mmol/L), (d) **1a** (10 mmol/L) + NH_4Br(4 mmol/L), (e) **2a** (10 mmol/L) + NH_4Br (4 mmol/L).

3. Study on Anti-Tumor Activity

3.1 Detection of released calcium ions

Ca^{2+} as a death signaling molecule is involved in important life activities, such as cell shrinkage, movement, secretion, and division. When cells are stimulated by specific signals, calcium channels (mitochondria and endoplasmic reticulum) will be opened, resulting in a rapid increase in intracellular calcium concentration. Intracellular Ca^{2+} levels were determined by fluorescence microscope with Fluo-3 AM staining kit, which could pass through the cell membrane and be cut into Fluo-3 by esterase. Fluo-3 could bind to the calcium ions to produce strong green fluorescence. As shown in Fig. S3, after treatment with compound **3ae** (0 and 20 μM) , the green fluorescence intensity increased significantly in T-24 cells. Hence, compound **3ae** can increase the intracellular levels of Ca^{2+}.

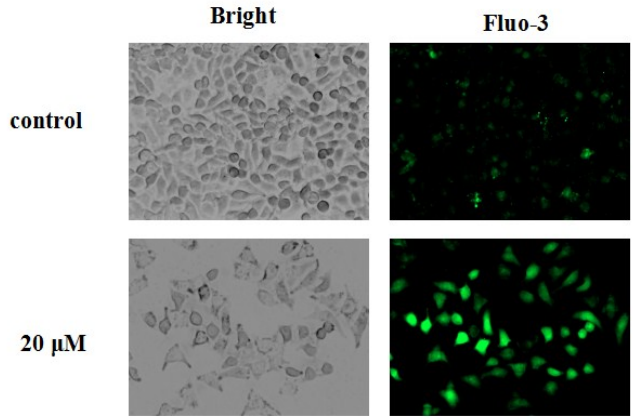


Figure S3. Changes in Ca^{2+} concentration in T-24 cells treated with compound **3ae** determined with a Fluo-3AM staining kit under a fluorescence microscope. Scale bar: 100 μm.

3.2 Intracellular ROS

The DCFH-DA (2′,7′-dichlorofluorescein diacetate) probe was used to detect ROS content in cells. DCFH-DA cannot produce fluorescence but can freely pass through the cell membrane. Upon entry to the cell, DCFH-DA can be hydrolyzed by esterase into DCFH, which will not permeate the cell membrane but accumulate in the cell. ROS in the cells can oxidize the nonfluorescent DCFH to produce a green fluorescent DCF. The intensity of green fluorescence is proportional to the ROS level. Therefore, the green fluorescence intensity can reflect the concentration of ROS in cells.

As shown in Fig. S4, after treatment with compound **3ae** (0 and 20 μM) for 24 h, the green fluorescence in T-24 cells were enhanced compared with that in the untreated controls. Hence, compound **3ae** can increase the level of ROS in T-24 cells, respectively.

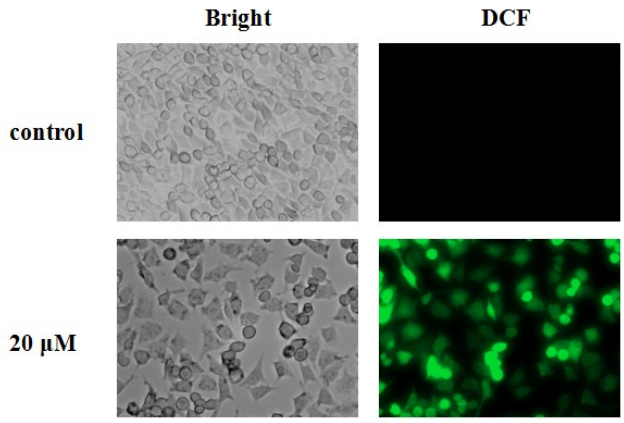


Figure S4. Changes in ROS concentration in T-24 cells treated with compound **3ae** determined with a DCFH-DA staining kit under a fluorescence microscope. Scale bar: 100 μm.

3.3 Hoechst 33342 nucleic acid staining

Hoechst 33342 staining is a fluorescent dye that binds sturdily to nucleus and detect the nuclear damage or chromatin condensation. The Hoechst 33342 stains the apoptotic cells as bright colored owing to the condensed nucleus which is a distinctive apoptotic characteristic. Hence, it was of our interest to detect nuclear damage or chromatin condensation persuaded by the compound **3ae** in T-24 cells. Hoechst 33342 staining technique was performed according to earlier reported method. The results from Fig. S5 illustrated that the nuclear structure of untreated cells was intact whereas compound **3ae** treated cells exhibitedcondensed, or fragmented nuclei.

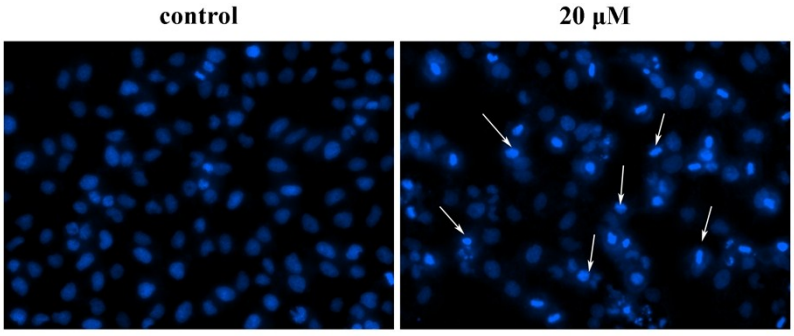


Figure S5. Assessment of nuclear morphological changes by Hoechst 33342 staining in T-24 cells after 24 h. Compound **3ae** treated T-24 cells have displayed nuclear apoptotic characteristics such as nuclear fragmentation and shrunken nuclei.

3.4 Inhibition of polymerization of microfilaments

T-24 cells were treated with compound **3ae** (0 and 20 μM) for 24 h and stained with Hoechst 33342 and anti-β-tubulin antibody. As shown in Fig. S6, cells in the control group exhibited normal filamentous microtubules arrays. However, after treatment with compound **3ae**, the cells showed reduced microtubule networks, indicating the decreased expression of the microtubule protein. Hence, compound **3ae** can inhibit the polymerization of microtubules and disrupt their organization. The result indicated that compound **3ae** induced the collapse of the microtubule network and interfered with the mitosis of T-24 cells.

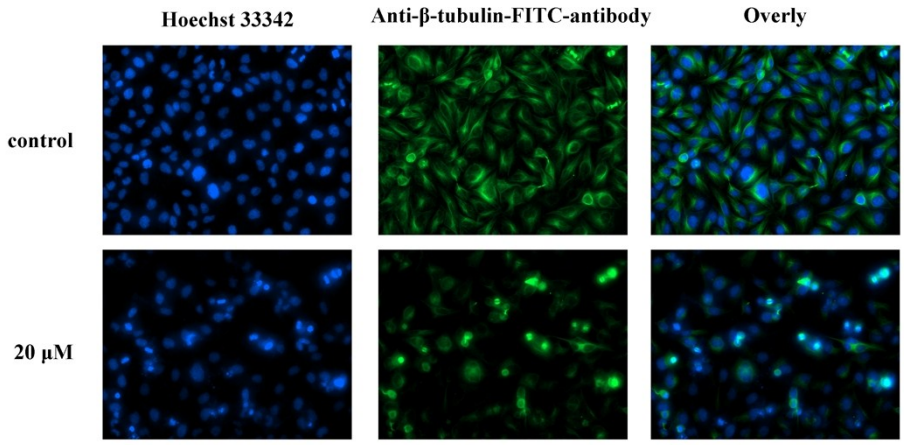


Figure S6. Fluorescence microscopic images of T-24 cells stained with Hoechst 33342 and anti-β-tubulin antibody after treatment with compound **3ae** 24 h.

3.5 Anticancer activity assay

Metastasis is a multistep process involving cancer cell motility and invasion which accounts for more than 90% of cancer related deaths. Microtubule or tubulin network plays an important role in cell motility and migration. As the compound **3ae** inhibits tubulin polymerization, we have investigated their migration inhibition capacity through wound healing assay. In this assay, standardized scratches (wounds) were made in confluent monolayers of T-24 cells and incubated with increasing concentrations of the compound **3ae** (0 and 20 μM). The number of cells migrated in to the wound area were captured using phase contrast microscope after 0 and 24 h incubation. As shown in Fig. S7, the compound **3ae** treatment resulted in significant inhibition of migration capacity of T-24 cells and the effect was more prominent after 24 h. For instance, compound **3ae** treatment at 20 μM concentration led to strong inhibition of migration in to the scratch area in relative comparison to control after 24 h. It can be inferred from the results that the compound **3ae** suppresses the migration potential of the T-24 cells in dose dependent manner.

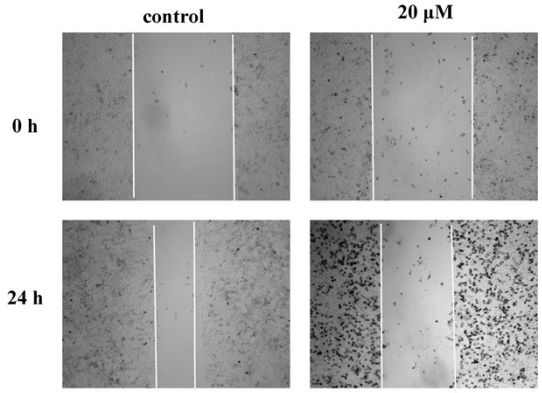


Figure S7. Effect of compound **3ae** on in vitro migration potential of T-24 prostate cancer cells. Scratches were created with sterile 200 m L pipette and images were captured using fluorescence microscopic (Cytation 5 Cell Imaging Multi-Mode Reader, BioTek Instruments, Inc., USA) at 0 h and 24 h after treatment with 20 μM of compound **3ae**.

3.6 Hoechst 33342 nucleic acid staining method

Nuclear morphological changes were observed through Hoechst 33342 staining. After treatment with compound **3ae** for 24 h in T-24 cells, cells were washed with PBS and permeabilized with 0.1% Tween 20 for 10 min followed by staining with Hoechst 33342 (2.5 μg/mL). Control and treated cells were observed with fluorescence microscope (Cytation 5 Cell Imaging Multi-Mode Reader, BioTek Instruments, Inc., USA.).

3.7 Measurement of intracellular reactive oxygen species method

Intracellular reactive oxygen species (ROS) was detected by using fluorescence microscope by with 2′,7′-dichlorofluorescein diacetate (DCHF-DA) staining kit. T-24 cells were seeded at 2×10^6/well in 10% FBS/DMEM into 6-well plates and treated with different concentrations of compound **3ae** (0 and 20 μM) for 24 h, then cells were washed twice with serum free DMEM and incubated with DCHF-DA for 30 minutes at 37 ^{o}C in dark. The fluorescence microscope was used to measure the enhanced green flourescent intensity in cells, the intensity of the microscope is 488 nm, and the emission wavelength is 525 nm.

3.8 Measurement of intracellular Ca^{2+} levels method

The intracellular Ca^{2+} levels were determined by fluorescent with Fluo-3 AM staining kit, which could pass through the cell membrane and be cut into Fluo-3 by the esterase. The Fluo-3 could bind with calcium ions to produce strong green fluorescence. T-24 cells were seeded at 2×10^6/well in 10% FBS/DMEM into 6-well plates and incubation for 24 hours. After the cells were treated with compound **3ae** (0 and 20 μM) for 24 h, the Fluo-3 AM (5.0

μM) was added and incubated for 30 min at 37 °C. The fluorescence microscope was used to measure the enhanced green flourescent intensity in cells, the intensity of the microscope is 506 nm, and the emission wavelength is 526 nm.

3.9 Tubulin polymerization assay method

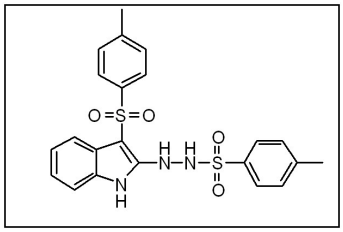
The effects of compound **3ae** on tubulin were detected using a anti-beta tubulin antibody (EPR16774, ab179513). The T-24 cells were seeded in 6-well plates (2×10^6 cells/well) and cultured for 24 h. After treated with compound **3ae** (0 and 20 μM) for 24 h, the cells were fixed with 4% paraformaldehyde for 10 min, and were permeabilized with 0.1% Triton X-100 for 10 min. Then incubation with tubulin proteins (1/1000) at 4 °C overnight. Followed by anti-rabbit Alexa Fluor 488 secondary antibody at 1/5000. Confocal image showing cytoplasmic staining on T-24 cells. The nuclears were stained by Hoechst 33342 (2.5 μg/mL) for 30 min. Fluorescence microscope was used to observed the change of microtubule networks in cells.

3.10 Wound healing assay method

T-24 cells (5×10^5 cells/well) were grown in petridishes for 24 h. Scratches were made in confluent monolayers using 200 mL pipette tip. Then, wounds were washed twice with PBS to remove non-adherent cell debris. The media containing different concentrations (0 and 20 μM) of the compound **3ae** wereadded to the petridishes. Cells which migrated across the wound area were photographed under the fluorescence microscope (Cytation 5 Cell Imaging Multi-Mode Reader, BioTek Instruments, Inc., USA) after 0 and 24 h treatment.

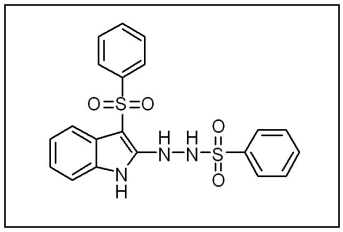
4. ^{1}H, ^{13}C NMR, MP and MS Data of all products

4-methyl-N'-(3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3aa**)



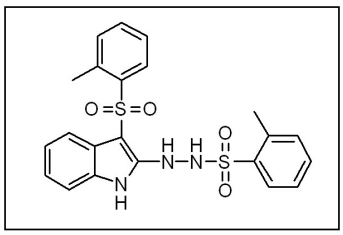
White solid (85%, 193.4 mg). mp: 125.0 – 125.6 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.73 (s, 1H), 9.97 (s, 1H), 7.92 (s, 1H), 7.85 – 7.75 (m, 2H), 7.72 – 7.65 (m, 2H), 7.58 – 7.50 (m, 2H), 7.48 – 7.40 (m, 1H), 7.38 – 7.32 (m, 2H), 7.30 – 7.24 (m, 1H), 7.10 – 6.90 (m, 2H), 2.44 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.3, 144.4, 142.9, 141.2, 133.9, 132.0, 129.9, 129.6, 128.0, 125.3, 124.7, 121.3, 120.7, 116.1, 111.3, 89.8, 21.1, 20.9. HRMS (m/z) (ESI): calcd for $C_{22}H_{22}N_3O_4S_2$ $[M+H]^+$ 456.1052, found 456.1036.

N'-(3-(phenylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ab**)



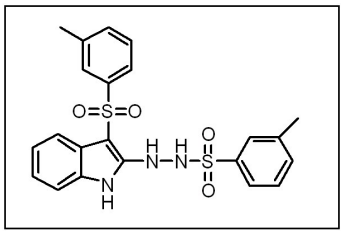
White solid (78%, 166.5 mg). mp: 112.4 – 113.7 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.77 (s, 1H), 10.08 (s, 1H), 8.04 (s, 1H), 7.91 – 7.87 (m, 2H), 7.81 – 7.75 (m, 3H), 7.74 – 7.68 (m, 2H), 7.60 – 7.52(m, 3H), 7.47 – 7.43 (M, 1H), 7.28 – 7.24 (m, 1H), 7.04 – 6.94 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.5, 144.0 , 136.9, 133.9, 132.5, 132.0 , 129.4 , 129.2, 127.9, 125.2, 124.7, 121.3, 120.8, 116.1, 111.3, 89.4. HRMS (m/z) (ESI): calcd for $C_{20}H_{18}N_3O_4S_2$ $[M+H]^+$ 428.0739, found 428.0725.

2-methyl-N'-(3-(o-tolylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ac**)



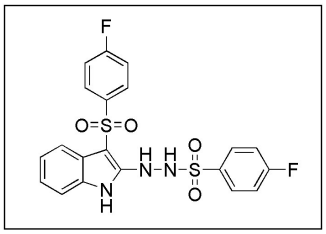
White solid (45%, 102.4 mg). mp: 131.5 – 132.9 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.78 (s, 1H), 10.02 (s, 1H), 8.00-7.90 (m, 1H), 7.82 (s, 1H), 7.75 – 7.70 (m, 2H), 7.52 – 7.45 (m, 3H), 7.44 – 7.38 (m, 1H), 7.34 – 7.28 (m, 2H), 7.14 – 7.08 (m, 1H), 7.02 – 6.88 (m, 2H), 2.42 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.0, 144.3, 141.2, 136.8, 133.9, 132.6, 132.5, 132.0, 129.9, 127.9, 127.8, 126.3, 124.7, 121.2, 120.8, 115.8, 111.4, 87.8, 21.1, 19.4. HRMS (m/z) (ESI): calcd for $C_{22}H_{22}N_3O_4S_2$ $[M+H]^+$ 456.1052, found 456.1038.

methyl-N'-(3-(m-tolylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ad**)



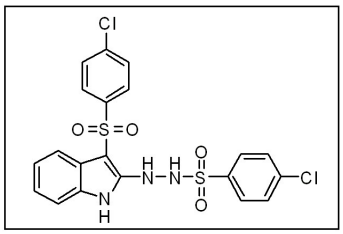
White solid (78%, 177.5 mg). mp: 125.3 – 125.8 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H), 10.04 (s, 1H), 8.01 (s, 1H), 7.77 – 7.66 (m, 3H), 7.65 – 7.61 (m, 1H), 7.62 – 7.53 (m, 2H), 7.47 – 7.37 (m, 3H), 7.31 – 7.25 (m, 1H), 7.06 – 6.97 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.5, 144.0, 139.2, 139.0, 136.8, 134.4, 133.2, 132.1, 129.3, 129.0, 128.1, 125.4, 124.9, 124.7, 122.5, 121.3, 120.9, 116.2, 111.3, 89.5, 20.9, 20.8. HRMS (m/z) (ESI): calcd for $C_{22}H_{22}N_3O_4S_2$ $[M+H]^+$ 456.1052, found 456.1038.

4-fluoro-N'-(3-((4-fluorophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ae**)



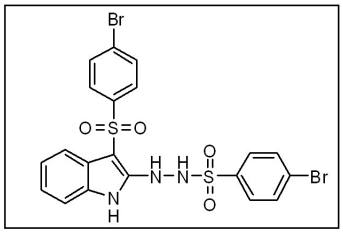
White solid (65%, 150.5 mg). mp: 165.1 – 162.8 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (s, 1H), 10.14 (s, 1H), 8.31 (s, 1H), 7.99 – 7.92 (m, 2H), 7.91 – 7.85 (m, 2H), 7.62 – 7.56 (m, 2H), 7.52 – 7.38 (m, 3H), 7.32 – 7.24 (m, 1H), 7.06 – 6.98 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.7 (d, J = 252.1 Hz), 164.7 (d, J = 251.1 Hz), 148.9, 141.0 (d, J = 3.1 Hz), 133.9 (d, J = 2.7 Hz), 132.4, 131.7 (d, J = 9.9 Hz) , 128.5 (d, J = 9.7 Hz) , 125.1, 121.7, 121.2, 117.0 (d, J = 23.1 Hz), 116.8 (d, J = 22.9 Hz), 116.4, 111.7, 89.69. HRMS (m/z) (ESI): calcd for $C_{20}H_{14}F_2N_3O_4S_2$ $[M-H]^-$ 462.0394, found 462.0395.

4-chloro-N'-(3-((4-chlorophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3af**)



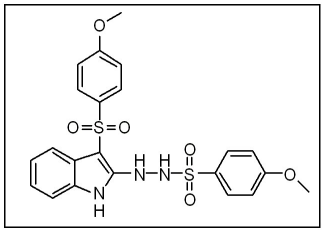
White solid (75%, 175.6 mg). mp: 209.2 – 210.0 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.78 (s, 1H), 10.22 (s, 1H), 8.44 (s, 1H), 7.92 – 7.87 (m, 2H), 7.86 – 7.80 (m, 4H), 7.70 – 7.64 (m, 2H), 7.52 – 7.47 (m, 1H), 7.32 – 7.27 (m, 1H), 7.08 – 6.98 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.8, 143.0, 138.7, 137.5, 136.1, 132.1, 130.0, 129.5, 129.4, 127.1, 124.7, 121.5, 120.9, 116.1, 111.4, 89.1. HRMS (m/z) (ESI): calcd for $C_{20}H_{14}Cl_2N_3O_4S_2$ [M − H]$^-$ 493.9803, found 493.9805.

4-bromo-N'-(3-((4-bromophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ag**)



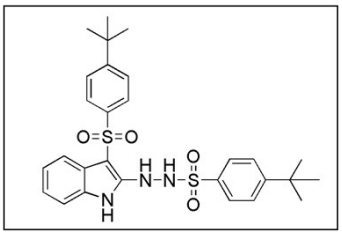
Yellow solid (60%, 175.5 mg). mp: 219.5 – 221.0 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (s, 1H), 10.21 (s, 1H), 8.42 (s, 1H), 7.98 – 7.93 (m, 2H), 7.82 – 7.78 (m, 4H), 7.78 – 7.73 (m, 2H), 7.50 – 7.43 (m, 1H), 7.32 – 7.26 (m, 1H), 7.06 – 6.98 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.8, 143.4, 136.6, 132.4, 132.3, 132.1, 130.0, 127.8, 127.2, 126.4, 124.7, 121.5, 120.9, 116.1, 111.4, 89.0. HRMS (m/z) (ESI): HRMS (m/z) (ESI): calcd for $C_{20}H_{14}Br_2N_3O_4S_2$ [M − H]$^-$ 583.8772, found 583.8774.

4-methoxy-N'-(3-((4-methoxyphenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ah**)



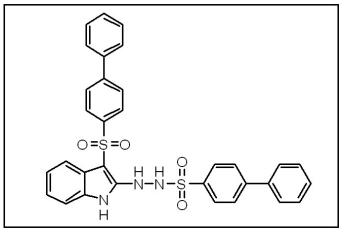
White solid (72%, 175.3 mg). mp: 189.1 – 189.9 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.71 (s, 1H), 9.90 (s, 1H), 7.90 – 7.83 (m, 3H), 7.80 – 7.70 (m, 2H), 7.46 – 7.40 (m, 1H), 7.30 – 7.22 (m, 3H), 7.12 – 7.05 (m, 2H), 7.04 – 6.96 (m, 2H), 3.87 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.3, 162.4, 148.1, 135.9, 132.1, 130.3, 128.2, 127.5, 124.7, 121.2, 120.7, 116.1, 114.7, 114.4, 111.3, 90.2, 55.9, 55.7. HRMS (m/z) (ESI): calcd for $C_{22}H_{22}N_3O_6S_2$ [M+H]$^+$ 488.0950 found 488.0932.

4-(tert-butyl)-N'-(3-((4-(tert-butyl)phenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ai**)



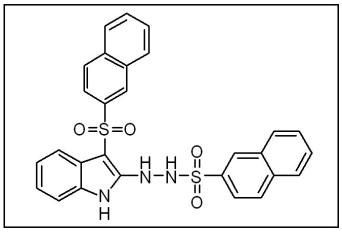
White solid (63%, 169.8 mg). mp: 193.5 – 194.0 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.71 (s, 1H), 10.01 (s, 1H), 8.02 (s, 1H), 7.90 – 7.80 (m, 2H), 7.77 – 7.65 (m, 4H), 7.60 – 7.50 (m, 2H), 7.50 – 7.40 (m, 1H), 7.30 – 7.20 (m, 1H), 7.05 – 6.90 (m, 2H), 1.29 (s, 9H), 1.26 (s, 9H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.9, 155.6, 148.2, 141.2, 134.0, 132.0, 127.9, 126.2 , 126.0, 125.7, 125.5, 125.1, 124.6, 121.2, 120.7, 116.1, 111.3, 89.7, 35.0, 34.8, 34.7, 30.8, 30.7, 30.7. HRMS (m/z) (ESI): calcd for $C_{28}H_{33}N_3O_4S_2$ [M − H]$^-$ 538.1834 found 538.1832.

N'-(3-([1,1'-biphenyl]-4-ylsulfonyl)-1H-indol-2-yl)-[1,1'-biphenyl]-4-sulfonohydrazide (**3aj**)



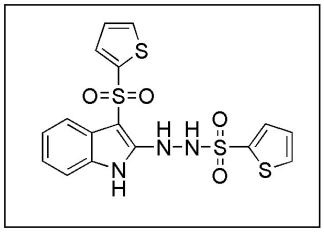
White solid (60%, 173.7 mg). mp: 220.4 – 221.0 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 10.15 (s, 1H), 8.25 (s, 1H), 8.10 – 7.95 (m, 4H), 7.93 – 7.89 (m, 2H), 7.87– 7.83 (m, 2H), 7.80 – 7.76 (m, 2H), 7.71 – 7.67 (m, 2H), 7.57 – 7.49 (m, 4H), 7.48 – 7.39 (m, 4H), 7.35 – 7.25 (m, 1H), 7.10 – 6.95 (m, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.6, 145.2, 144.2, 142.8, 138.5, 138.2, 135.8, 132.1, 129.2, 129.1, 128.8, 128.7, 128.5, 127.5, 127.2, 127.1, 125.9, 124.8, 121.4, 120.9, 116.2, 111.4, 99.5, 89.56. HRMS (m/z) (ESI): calcd for $C_{32}H_{24}N_3O_4S_2$ [M − H]$^-$ 578.1208 found 578.1210.

N'-(3-(naphthalen-2-ylsulfonyl)-1H-indol-2-yl)naphthalene-2-sulfonohydrazide (**3ak**)



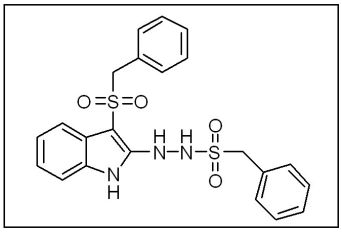
White solid (65%, 171.3 mg). mp: 209.7 – 210.3 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 1H), 10.25 (s, 1H), 8.65 – 8.60 (m, 1H), 8.55 – 8.50 (m, 1H), 8.31 (s, 1H), 8.26 – 8.22 (m, 1H), 8.19 – 8.14 (m, 1H), 8.13 – 8.07 (m, 2H), 8.07 – 8.03 (m, 1H), 8.02 – 7.92 (m, 2H), 7.78 – 7.70 (m, 3H), 7.69 – 7.60 (m, 2H), 7.54 – 7.48 (m, 1H), 7.35 – 7.25 (m, 1H), 7.05 – 6.90 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.8, 140.9, 134.8, 134.2, 132.1, 131.7, 131.7, 129.6, 129.4, 129.4, 129.4, 129.2, 128.7, 128.0, 127.8, 127.6, 125.7, 124.7, 122.9, 121.3, 120.8, 116.1, 111.3, 89.3. HRMS (m/z) (ESI): calcd for $C_{28}H_{21}N_3O_4S_2$ $[M-H]^-$ 526.0895 found 526.0892.

N'-(3-(thiophen-2-ylsulfonyl)-1H-indol-2-yl)thiophene-2-sulfonohydrazide (**3al**)



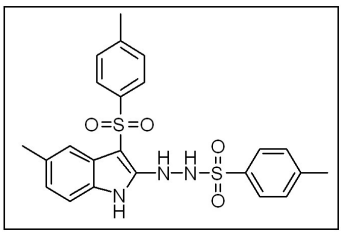
White solid (86%, 188.72 mg). mp: 203.4 – 203.9 °C, ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.82 (s, 1H), 10.21 (s, 1H), 8.18 – 8.12 (m, 2H), 7.89 – 7.83 (m, 1H), 7.79 – 7.73 (m, 1H), 7.67 – 7.63 (m, 1H), 7.52 – 7.46 (m, 1H), 7.37 – 7.32 (m, 1H), 7.32 – 7.27 (m, 1H), 7.16 – 7.11 (m, 1H), 7.10 – 7.00 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 148.2, 145.6, 136.8, 135.2, 134.2, 132.5, 132.1, 130.3, 128.2, 127.8, 124.5, 121.4, 121.0, 116.3, 111.4, 90.1. HRMS (m/z) (ESI): calcd for $C_{16}H_{12}N_3O_4S_4$ $[M-H]^-$ 437.9711 found 437.9712.

N'-(3-(benzylsulfonyl)-1H-indol-2-yl)-1-phenylmethanesulfonohydrazide (**3am**)



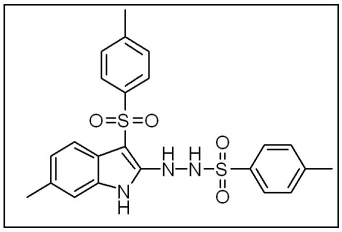
Yellow solid (40%, 91.0 mg). mp: 197.1-198.9 °C, 1H NMR (400 MHz, DMSO-d_6) δ 11.54 (s, 1H), 9.64 (s, 1H), 8.17 (s, 1H), 7.48 – 7.43 (m, 1H), 7.41 – 7.37 (m, 5H), 7.31 – 7.27 (m, 1H), 7.26 – 7.22 (m, 3H), 7.19-7.13 (m, 2H), 7.01 – 6.93 (m, 2H), 4.45-4.40 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.3, 131.7, 131.1, 130.9, 130.8, 129.6, 128.7, 128.6, 128.4, 128.1, 125.8, 121.0, 120.4, 116.4, 111.1, 87.4, 61.7, 55.5. HRMS (m/z) (ESI): calcd for $C_{22}H_{20}N_3O_4S_2$ $[M-H]^-$ 454.0895 found 454.0899.

4-methyl-N'-(5-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3ba**)



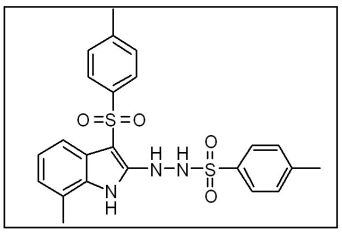
White solid (77%, 180.6 mg). mp:184.3 – 185.2 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 9.93 (s, 1H), 7.85 (s, 1H), 7.82 –7.76 (m, 2H), 7.70 – 7.64 (m, 2H), 7.56 – 7.50 (m, 2H), 7.39 – 7.34 (m, 2H), 7.26 – 7.22 (m, 1H), 7.18 – 7.13 (m, 1H), 6.84 – 6.78 (m, 1H), 2.44 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.3, 144.4, 142.9, 141.3, 133.9, 130.2, 130.0, 129.9, 129.6, 127.9, 125.2, 124.9, 121.9, 116.1, 111.0, 89.4, 21.3, 21.1, 20.9. HRMS (m/z) (ESI): calcd for $C_{23}H_{22}N_3O_4S_2$ $[M-H]^-$ 468.1052 found 468.1053.

4-methyl-N'-(6-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3ca**)



White solid (67%, 157.1 mg). mp: 145.2 – 145.9 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.61 (s, 1H), 9.94 (s, 1H), 7.85 – 7.75 (m, 3H), 7.70 – 7.62 (m, 2H), 7.60 – 7.50 (m, 2H), 7.40 – 7.25 (m, 3H), 7.08 (s, 1H), 6.90 – 6.80 (m, 1H), 2.43 (s, 3H), 2.33 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.0, 144.4, 142.9, 141.2, 133.9, 132.4, 129.9, 129.9, 129.6, 128.0, 125.2, 122.5, 122.4, 115.9, 111.4, 89.5, 21.2, 21.1, 20.9. HRMS (m/z) (ESI): calcd for $C_{23}H_{24}N_3O_4S_2$ $[M+H]^+$ 470.1208 found 470.1198.

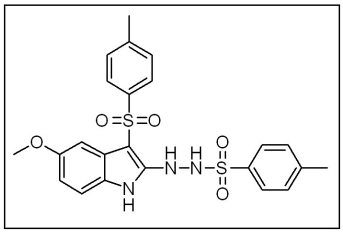
4-methyl-N'-(7-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3da**)



White solid (58%, 136.0 mg). mp: 134.3 – 135.0 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.32 (s, 1H), 9.86 (s, 1H), 7.83 (s, 1H), 7.80 – 7.73 (m, 2H), 7.72 – 7.65 (m, 2H), 7.50 – 7.42 (m, 2H), 7.40 – 7.32 (m, 2H), 7.30 – 7.20 (m, 1H), 6.95 – 6.87 (m, 1H), 6.85 – 6.75 (m, 1H), 2.38 (s, 6H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.2, 144.4, 143.0, 141.0, 134.0, 131.0, 129.8, 129.6, 127.9, 125.3,

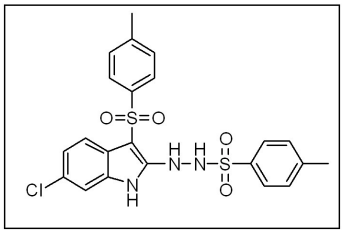
124.4, 122.3, 121.5, 120.8, 113.8, 90.4, 21.1, 20.9, 17.0. HRMS (m/z) (ESI): calcd for $C_{23}H_{22}N_3O_4S_2$ $[M-H]^-$ 468.1052 found 468.1054.

N'-(5-methoxy-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3ea**)



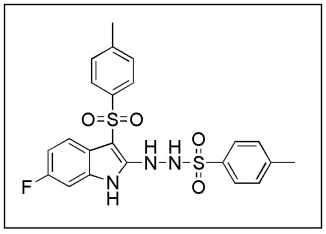
White solid (54%, 131.0 mg). mp: 156.9 – 157.6 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.57 (s, 1H), 9.94 (s, 1H), 7.87 (s, 1H), 7.83 – 7.77 (m, 2H), 7.72 – 7.66 (m, 2H), 7.57 – 7.50 (m, 2H), 7.40 – 7.34 (m, 2H), 7.20 – 7.14 (m, 1H), 6.99 – 6.93 (m, 1H), 6.67 – 6.57(m, 1H), 3.72 (s, 3H), 2.44 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 154.9, 148.5, 144.4, 143.0, 141.2, 134.0, 129.9, 129.6, 128.0, 126.6, 125.6, 125.2, 112.0, 108.6, 100.2, 89.9, 55.4 , 21.1, 20.9. HRMS (m/z) (ESI): calcd for $C_{23}H_{22}N_3O_5S_2$ $[M-H]^-$ 484.1001, found 484.1003.

N'-(6-chloro-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3fa**)



White solid (75%, 183.4 mg). mp: 132.3 – 132.9 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (s, 1H), 10.03 (s, 1H), 8.12 (s, 1H), 7.81 – 7.76 (m, 2H), 7.72 – 7.67 (m, 2H), 7.58 – 7.50 (m, 2H), 7.46 – 7.41 (m, 1H), 7.39 – 7.34 (m, 2H), 7.29 – 7.26 (m, 1H), 7.08 – 7.02 (m, 1H), 2.44 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.9, 144.4, 143.2, 140.9, 133.9, 132.7, 129.8, 129.7, 128.0, 125.3, 125.0, 123.6, 121.4, 117.3, 111.0, 89.9, 21.1, 20.9. HRMS (m/z) (ESI): calcd for $C_{22}H_{19}ClN_3O_4S_2$ $[M-H]^-$ 488.0505, found 488.0508.

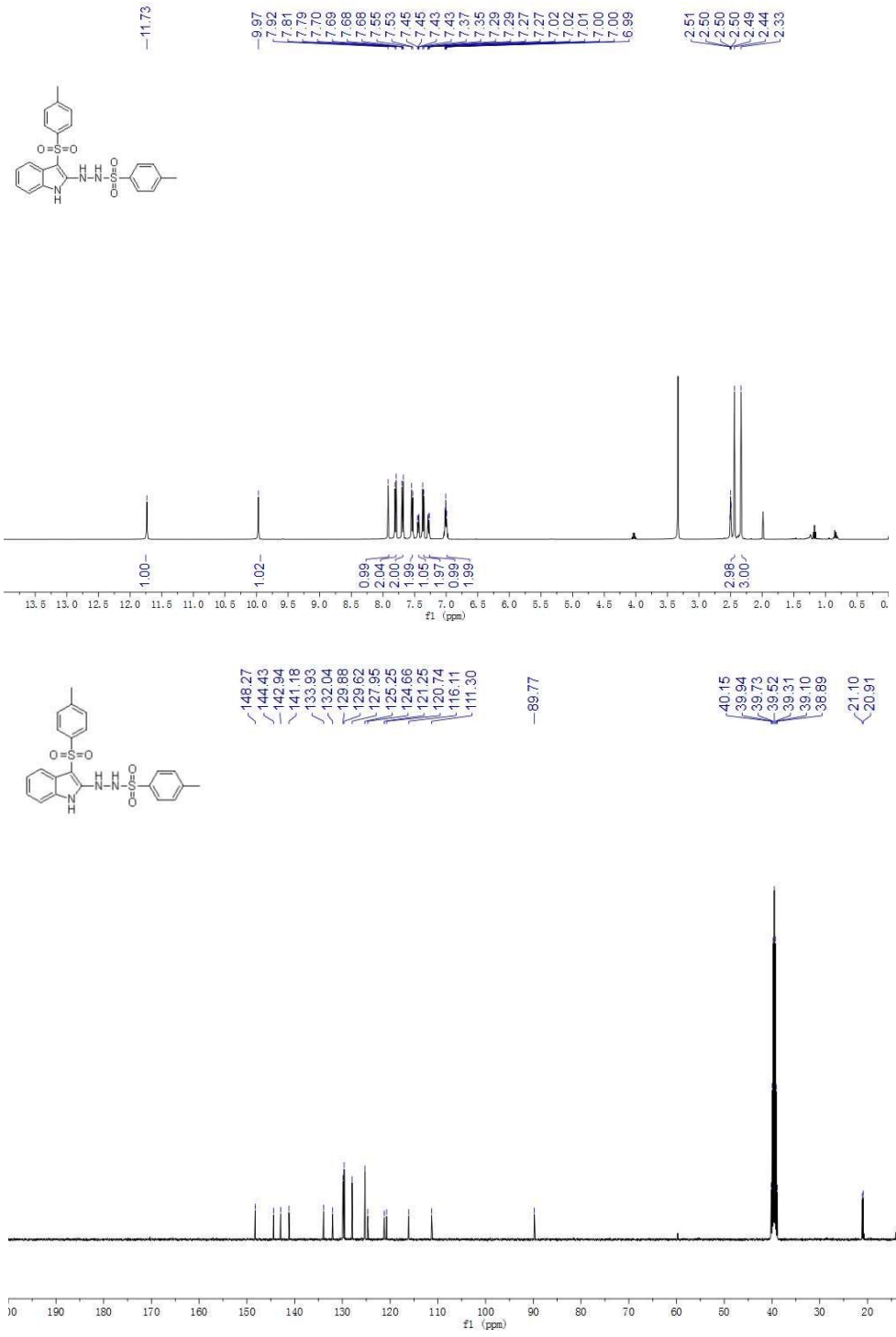
N'-(6-fluoro-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3ga**)



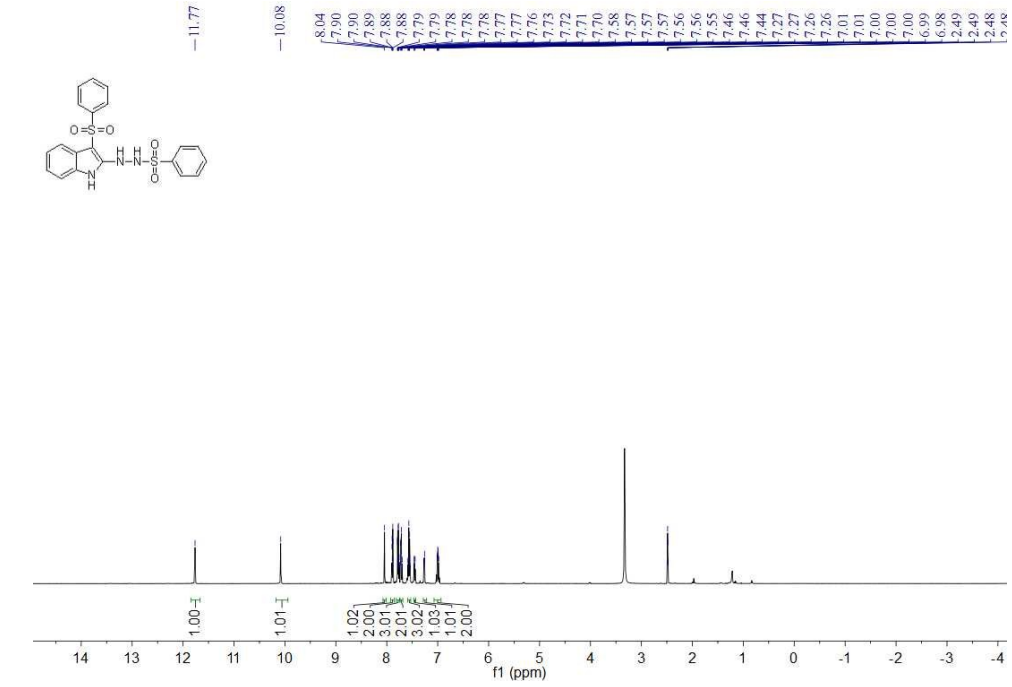
White solid (55%, 130.1 mg). mp:127.5 – 128.2 °C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.80 (s, 1H), 9.99 (s, 1H), 8.00 (s, 1H), 7.81– 7.76 (m, 2H), 7.72 – 7.65 (m, 2H), 7.60 – 7.50 (m, 2H), 7.44 – 7.34 (m, 3H), 7.10 – 7.00 (m, 1H), 6.92 – 6.84 (m, 1H), 2.44 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.5 (d, J = 234.6 Hz), 157.3, 149.3 (d, J = 1.8 Hz), 144.8, 143.5, 141.4, 134.4, 132.7 (d, J = 12.5 Hz), 130.3, 130.1, 128.4, 125.7, 121.6, 117.3 (d, J = 9.7 Hz), 109.2 (d, J = 23.5 Hz) , 98.7 (d, J = 26.9 Hz), 90.00, 21.5, 21.3. HRMS (m/z) (ESI): calcd for $C_{22}H_{19}FN_3O_4S_2$ $[M-H]^-$ 472.0801, found 472.0802.

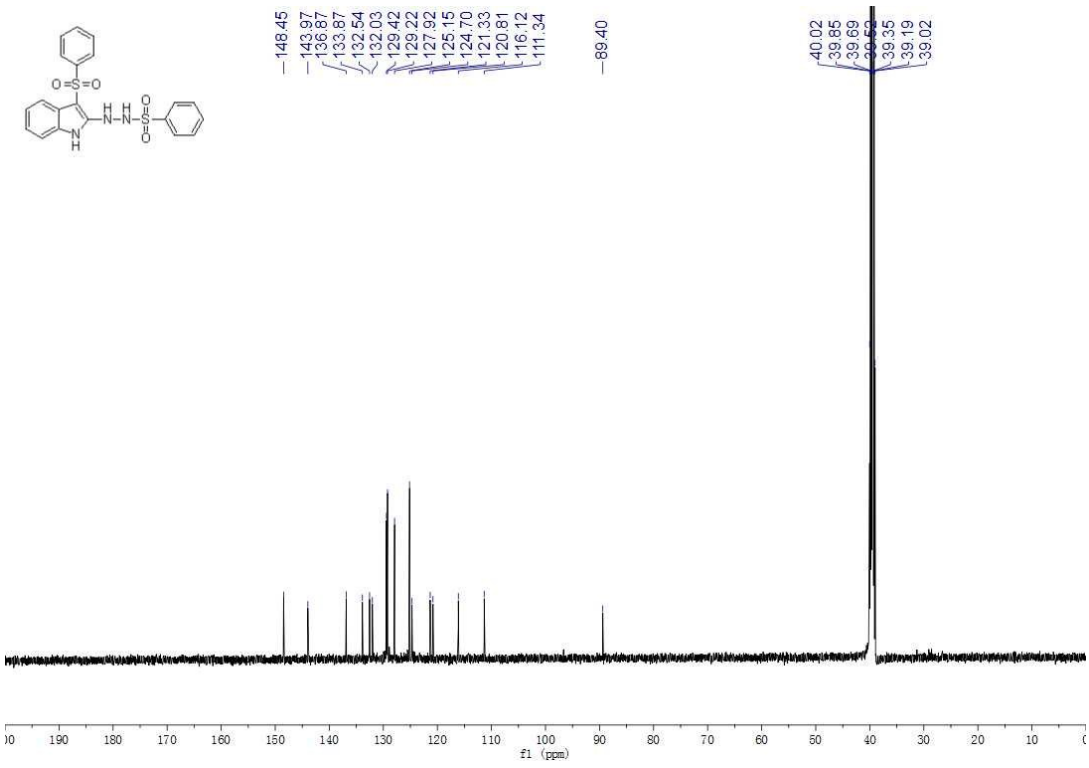
5. Copies of ^{13}C and ^{1}H NMR spectra for all products

4-methyl-N'-(3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3aa**)

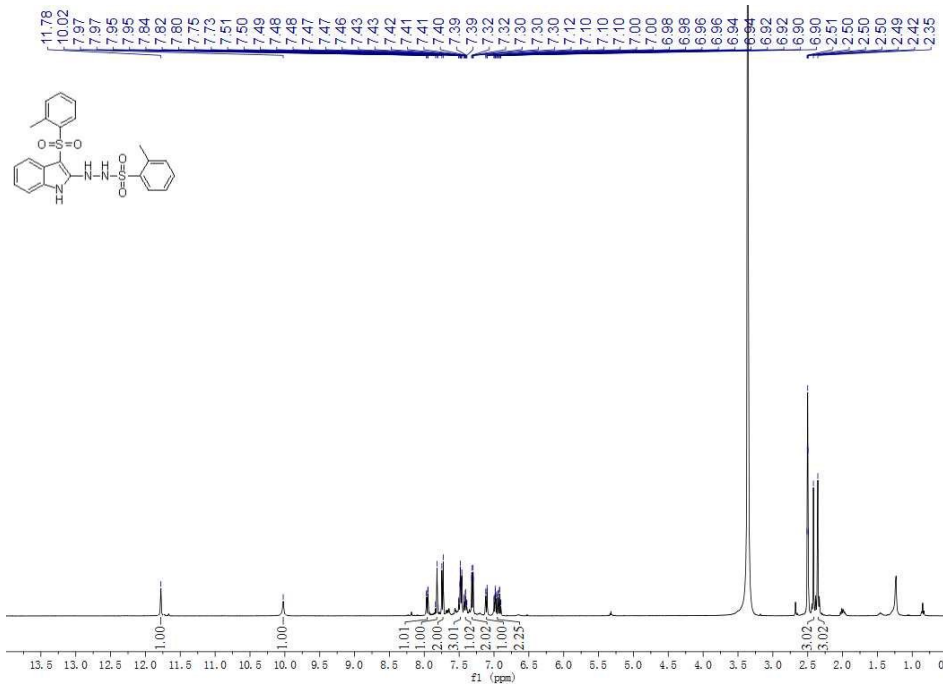


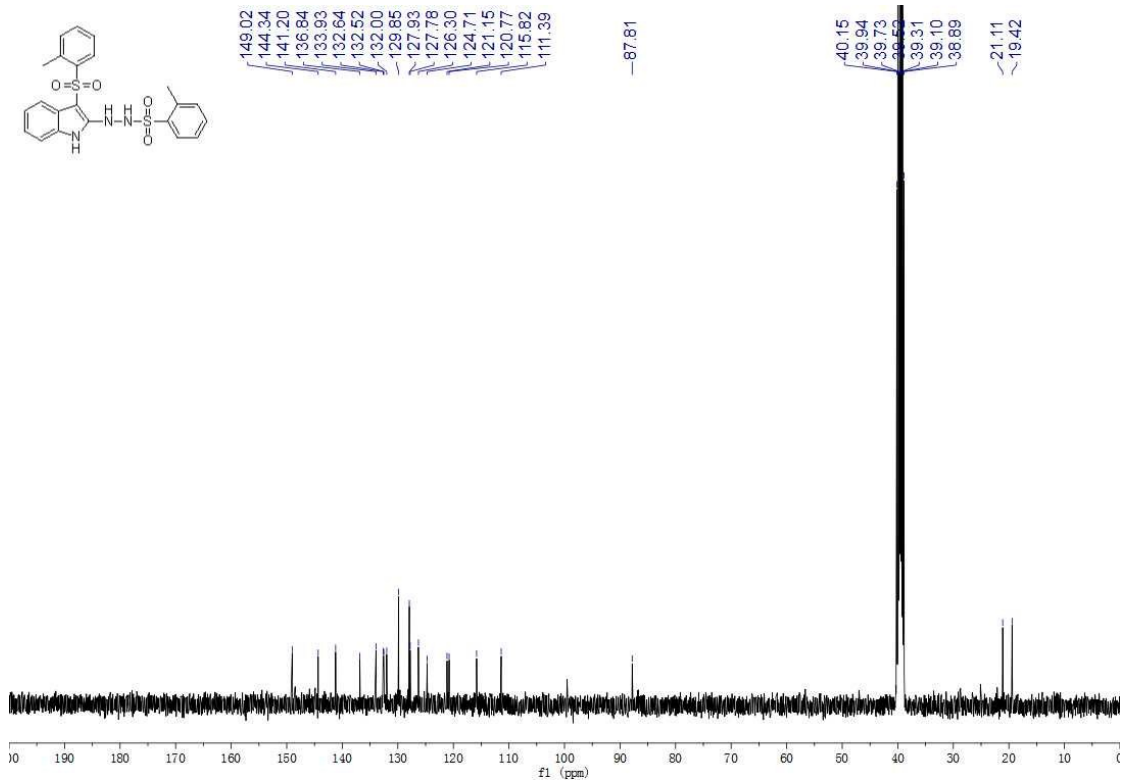
N'-(3-(phenylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ab**)



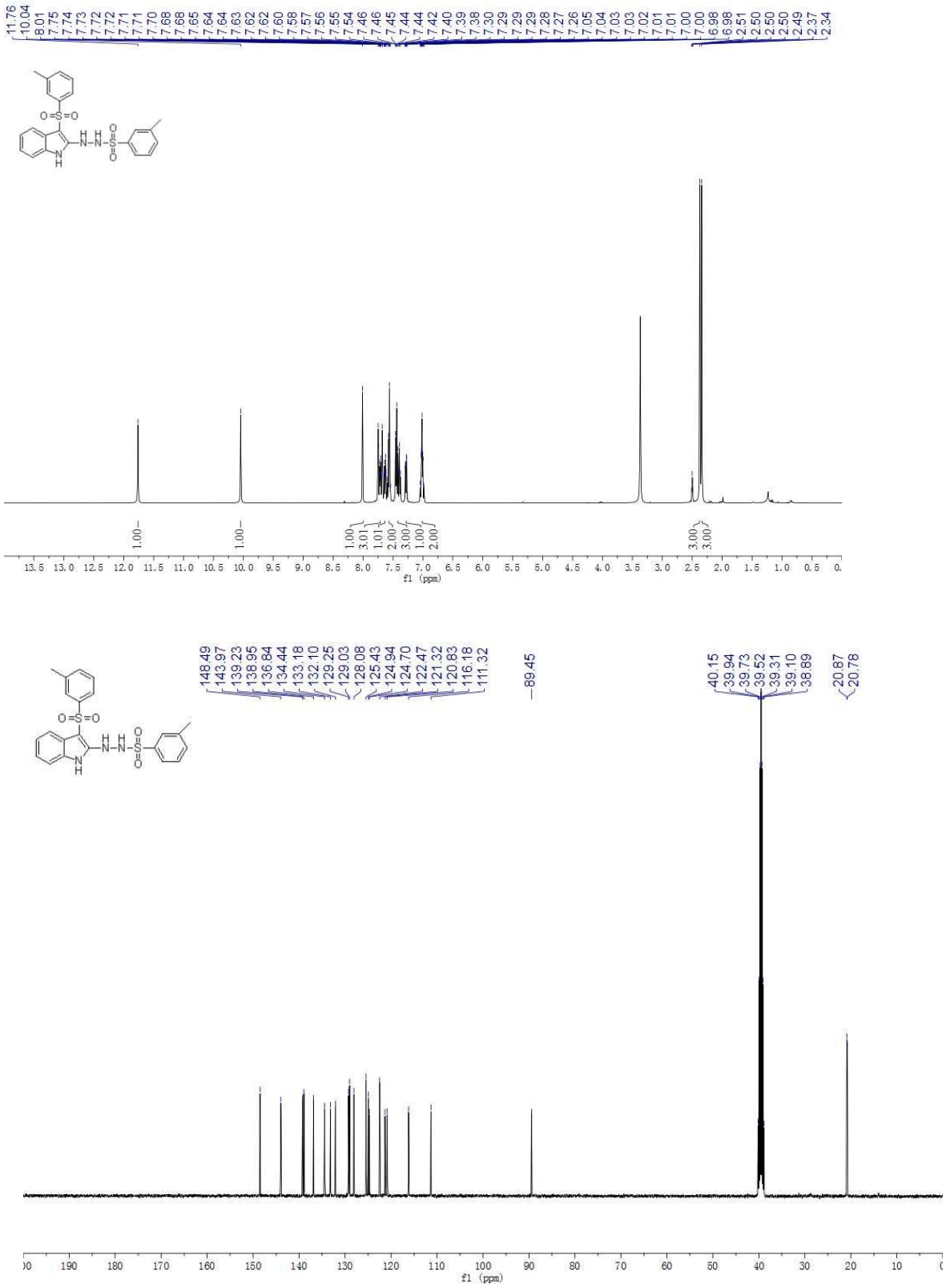


2-methyl-N'-(3-(o-tolylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ac**)

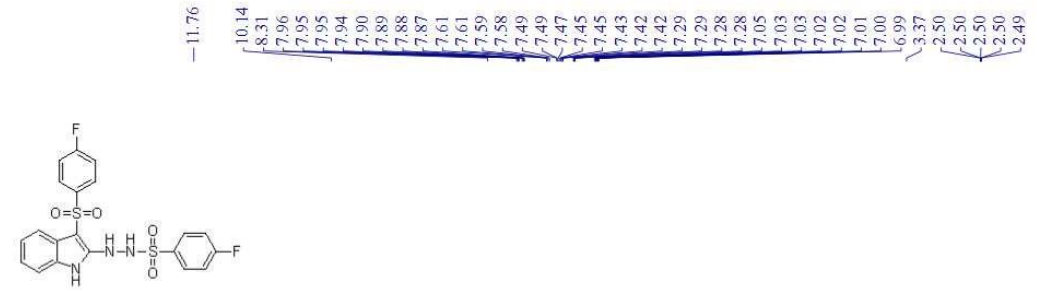


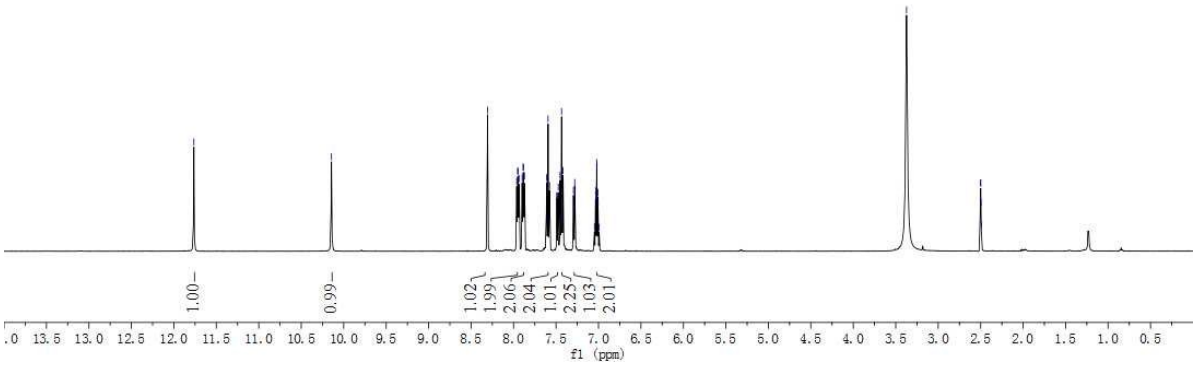


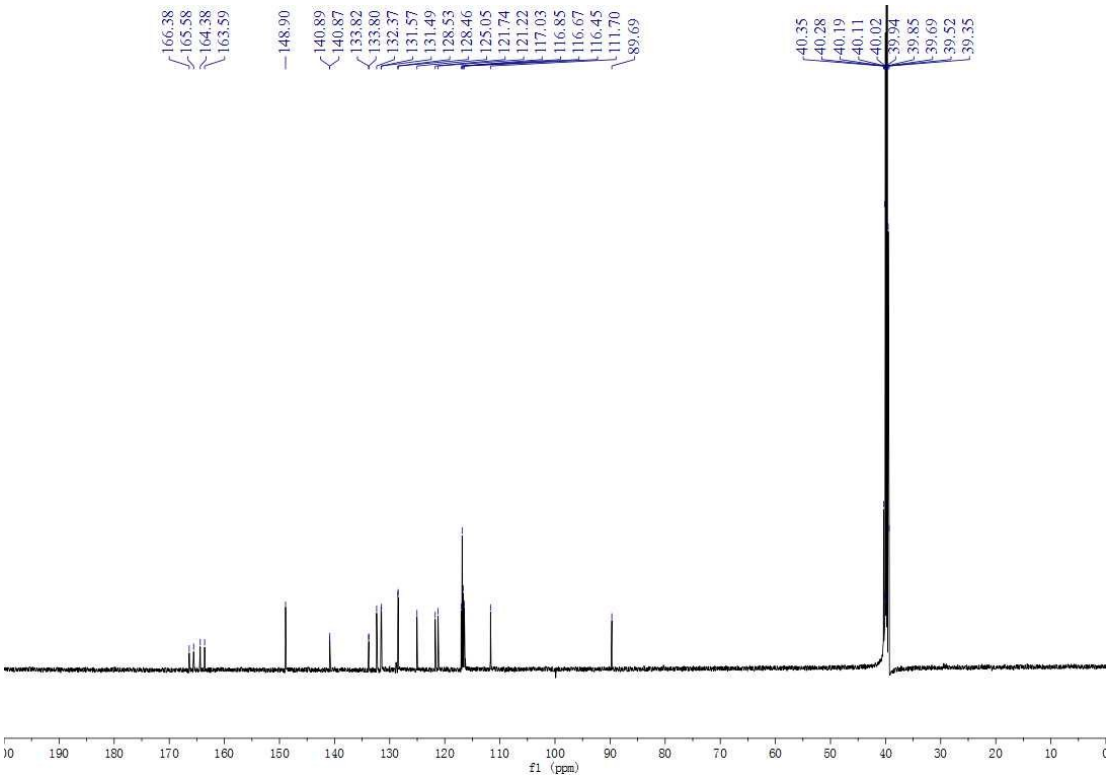
3-methyl-N'-(3-(m-tolylsulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ad**)



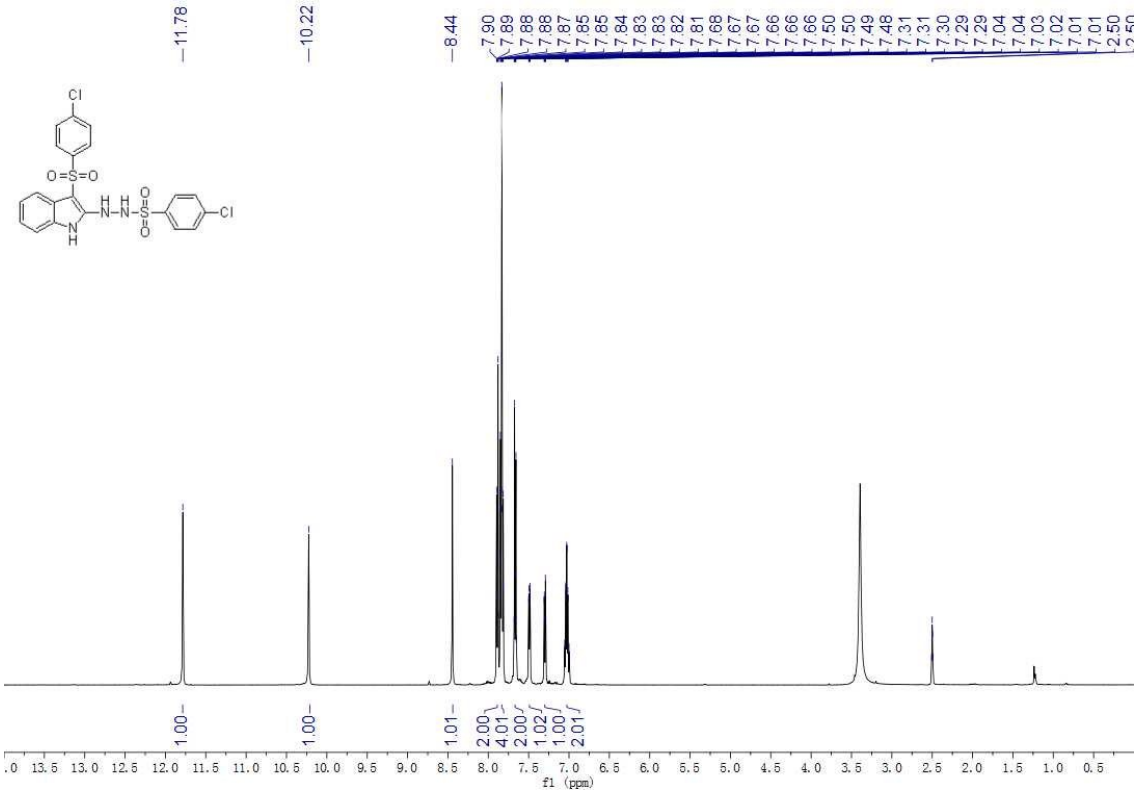
4-fluoro-N'-(3-((4-fluorophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ae**)

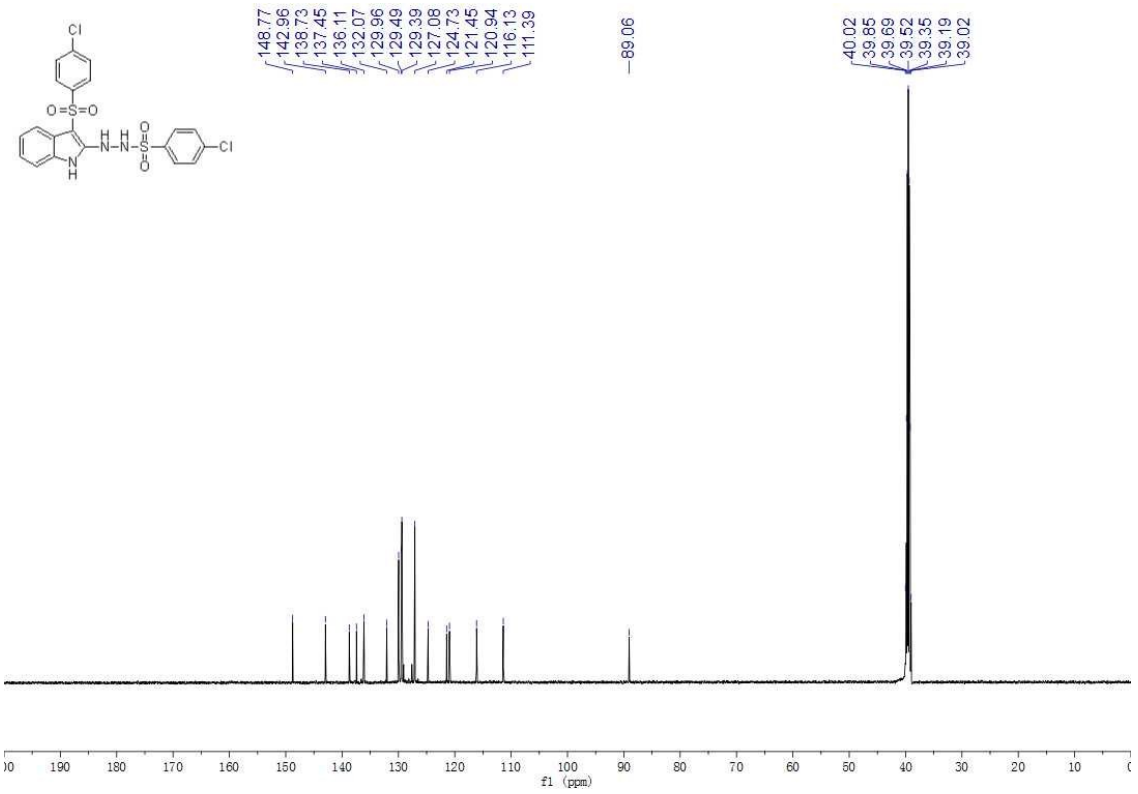




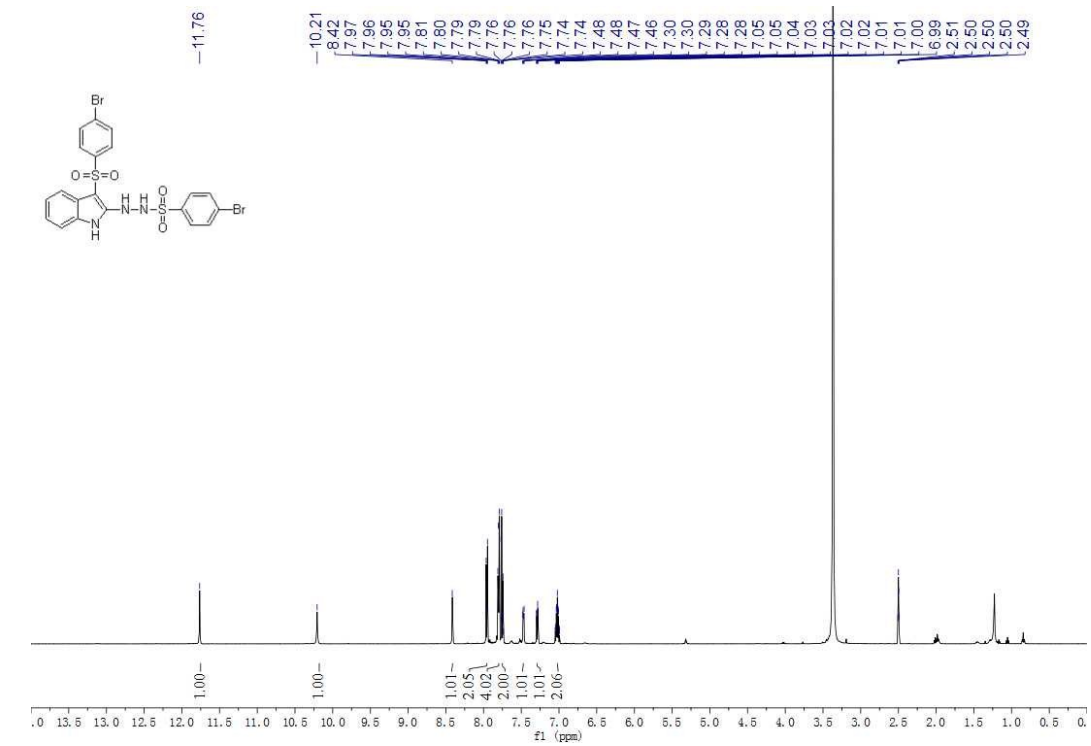


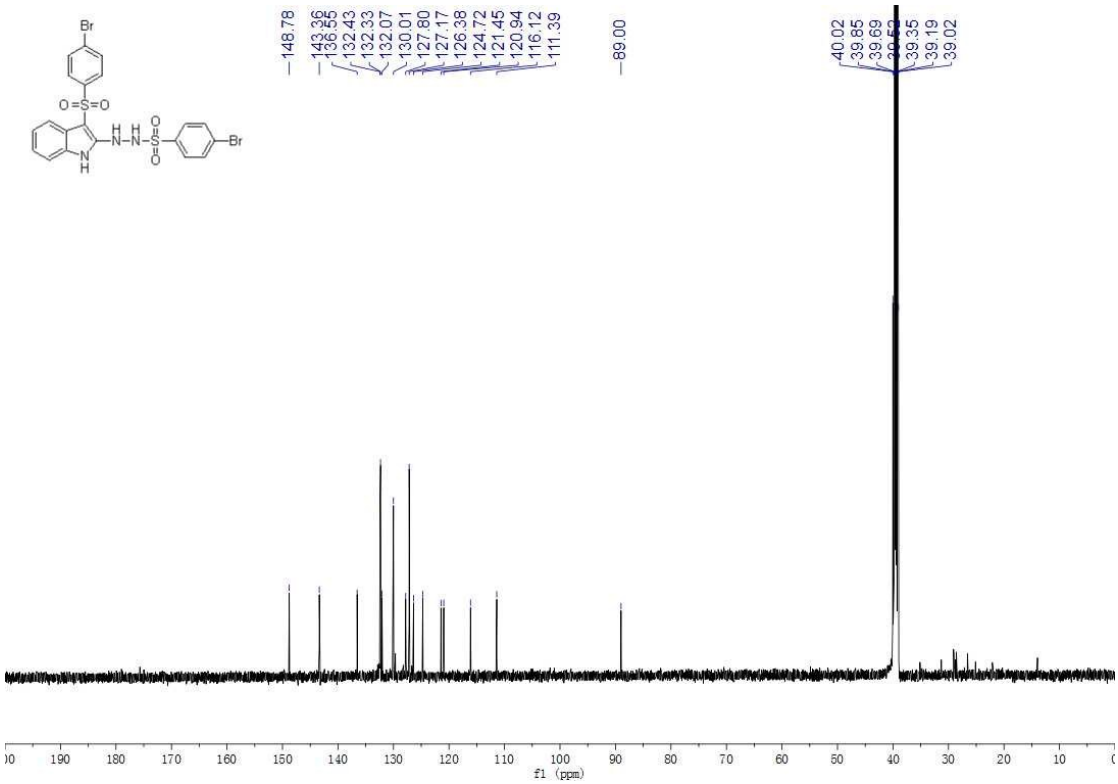
4-chloro-N'-(3-((4-chlorophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3af**)



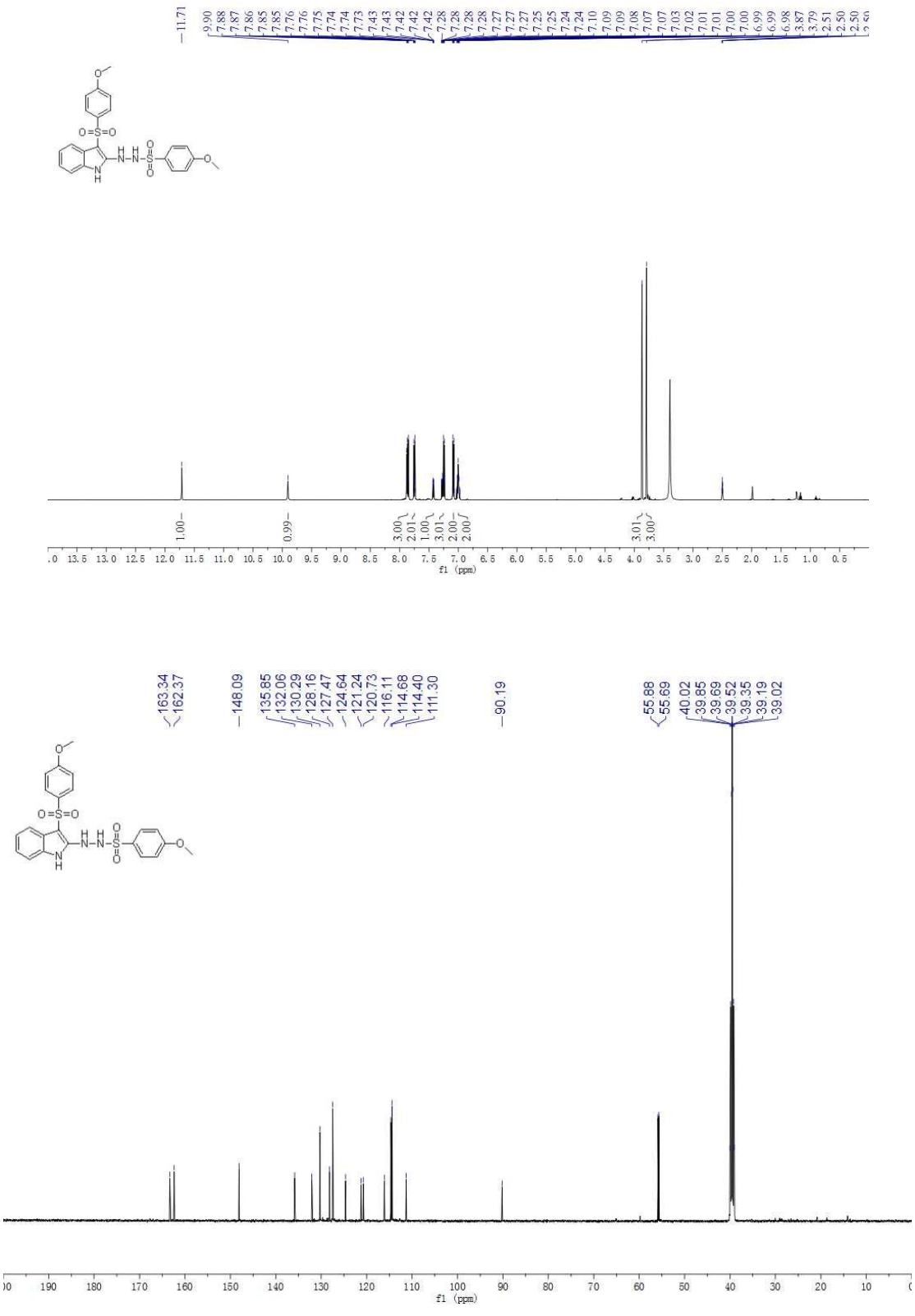


4-bromo-N'-(3-((4-bromophenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ag**)

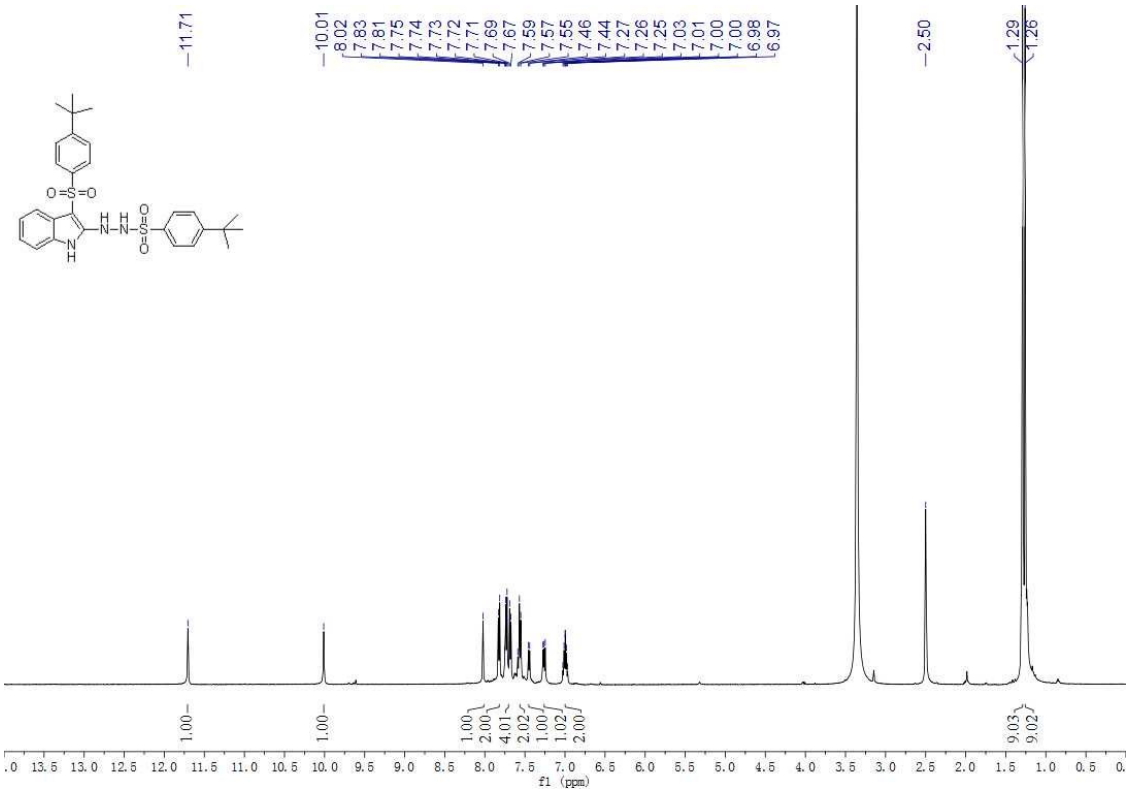


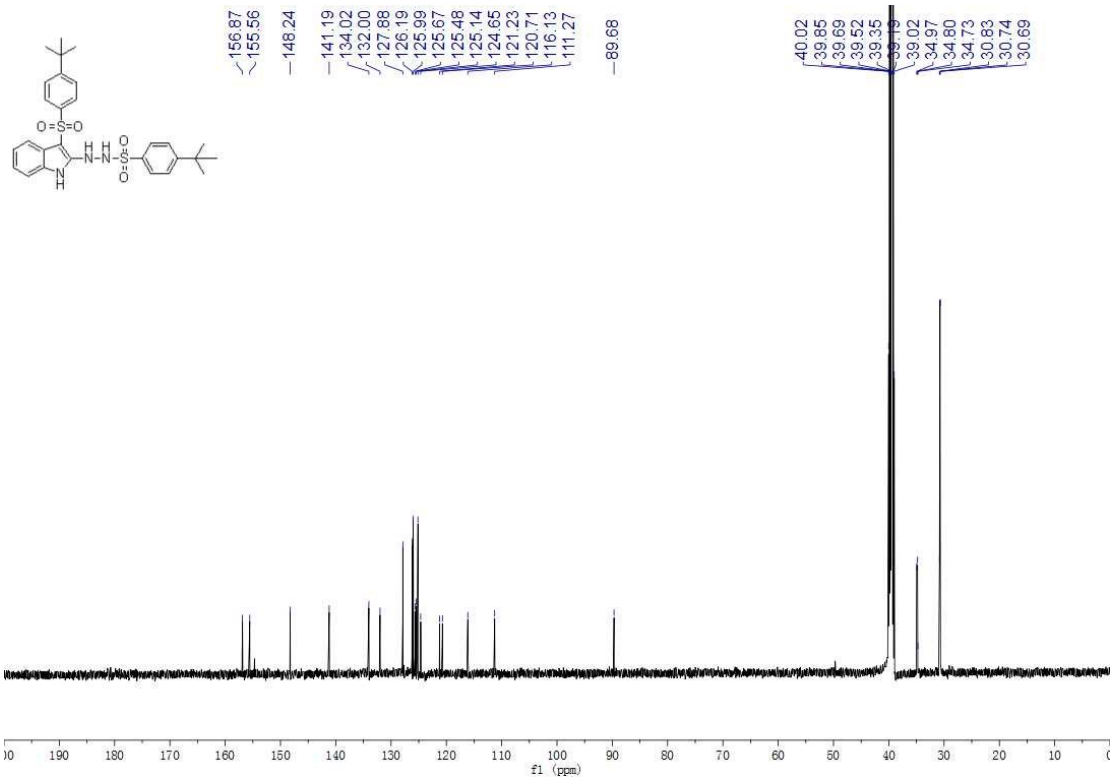


4-methoxy-N'-(3-((4-methoxyphenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ah**)

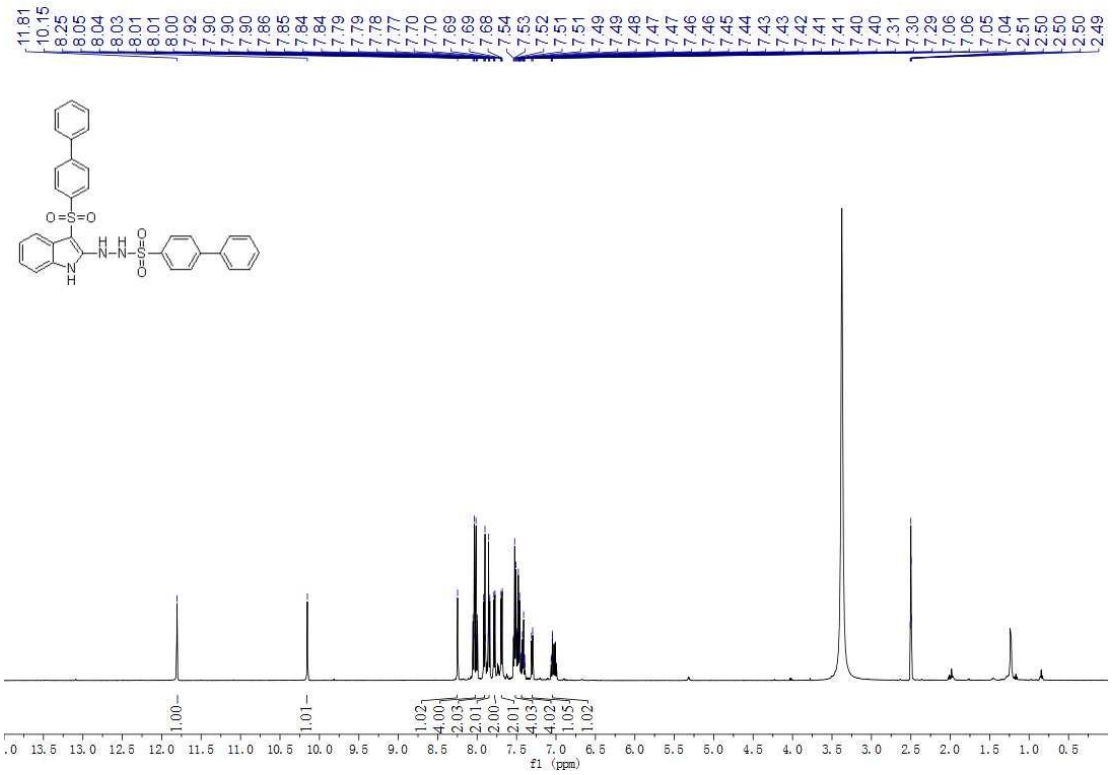


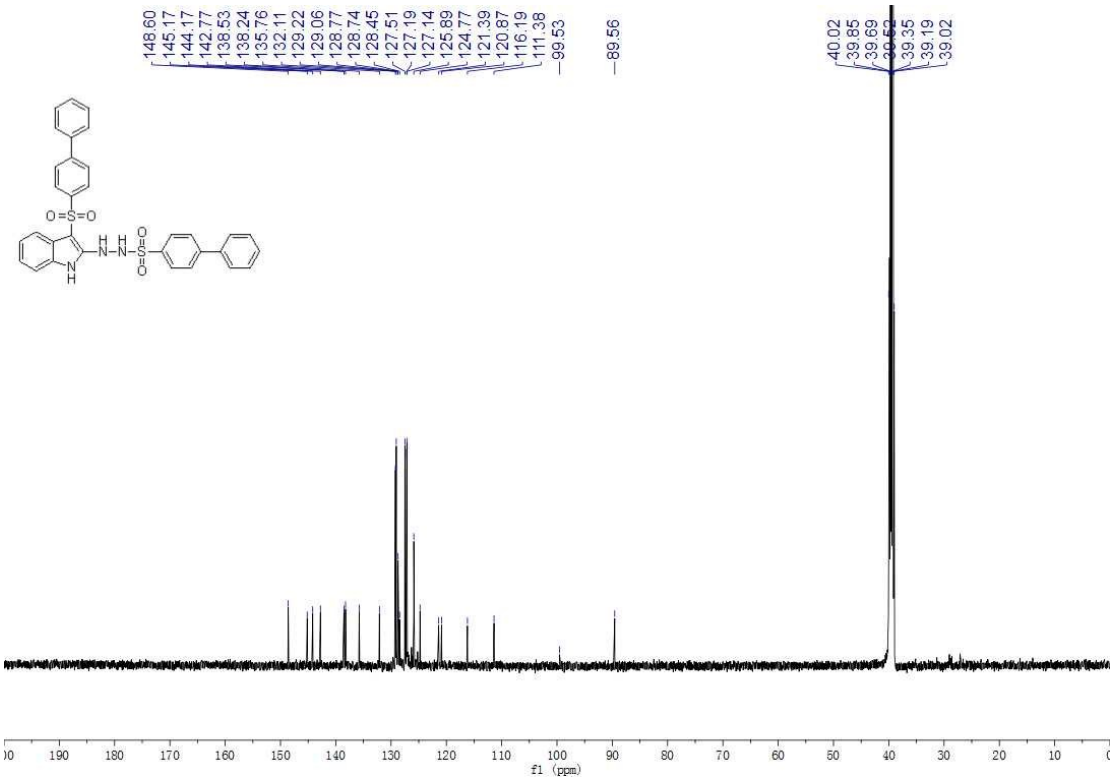
4-(tert-butyl)-N'-(3-((4-(tert-butyl)phenyl)sulfonyl)-1H-indol-2-yl)benzenesulfonohydrazide (**3ai**)



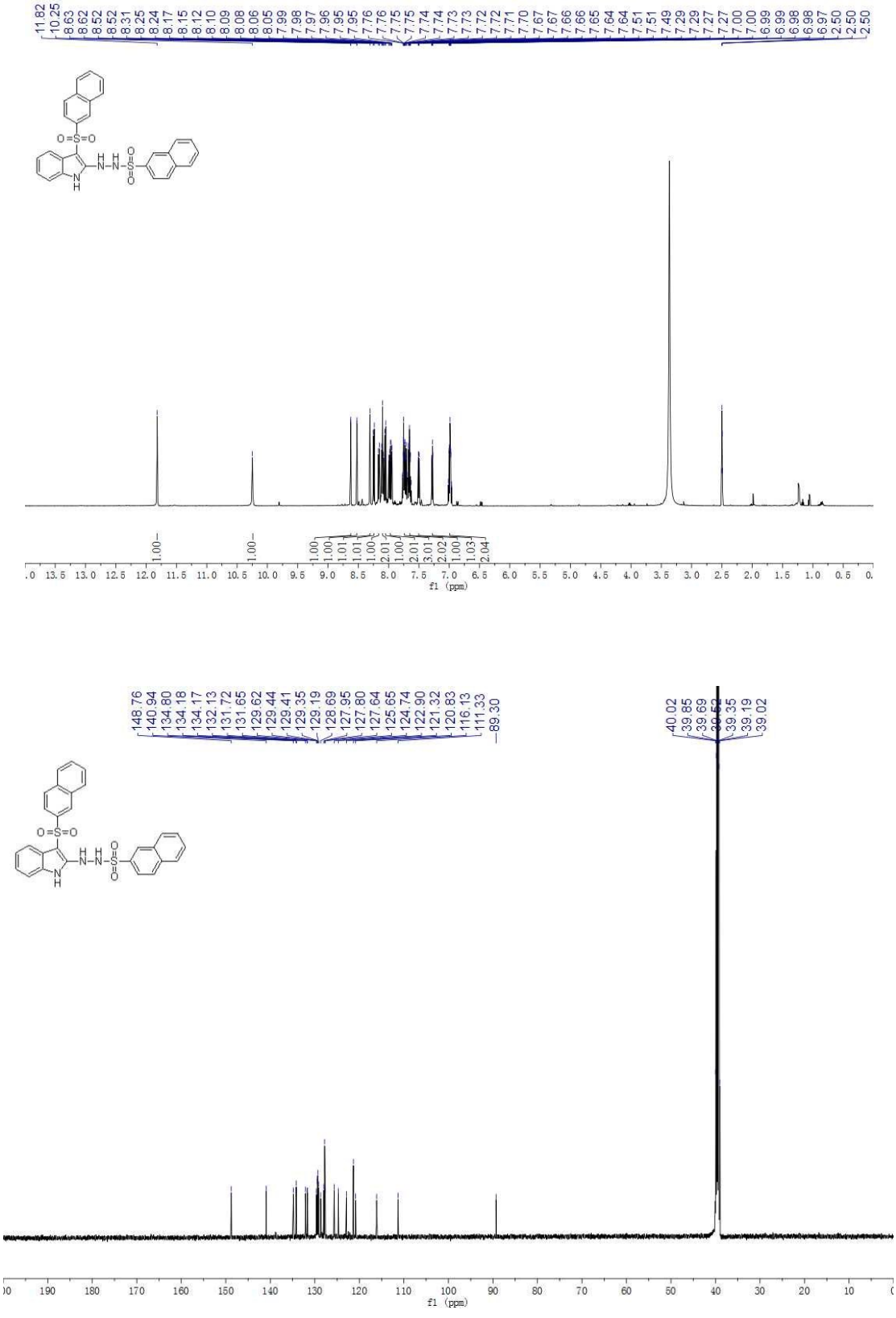


N'-(3-([1,1'-biphenyl]-4-ylsulfonyl)-1H-indol-2-yl)-[1,1'-biphenyl]-4-sulfonohydrazide (**3aj**)

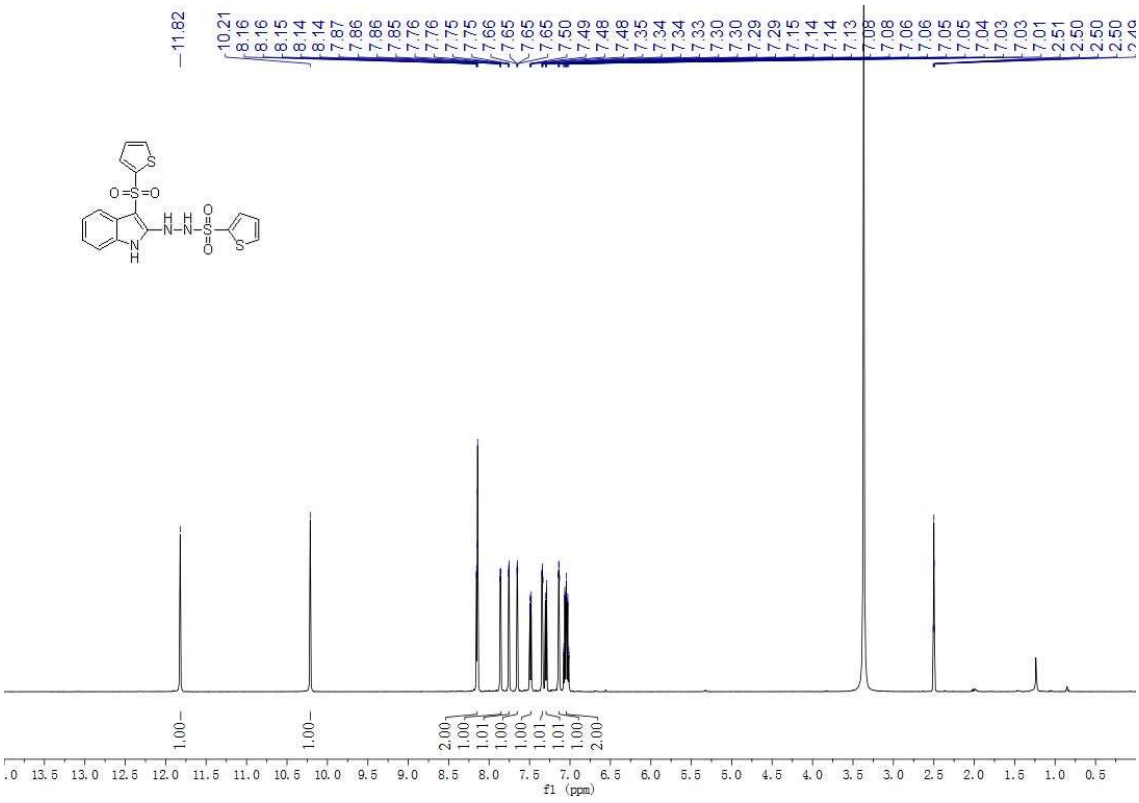


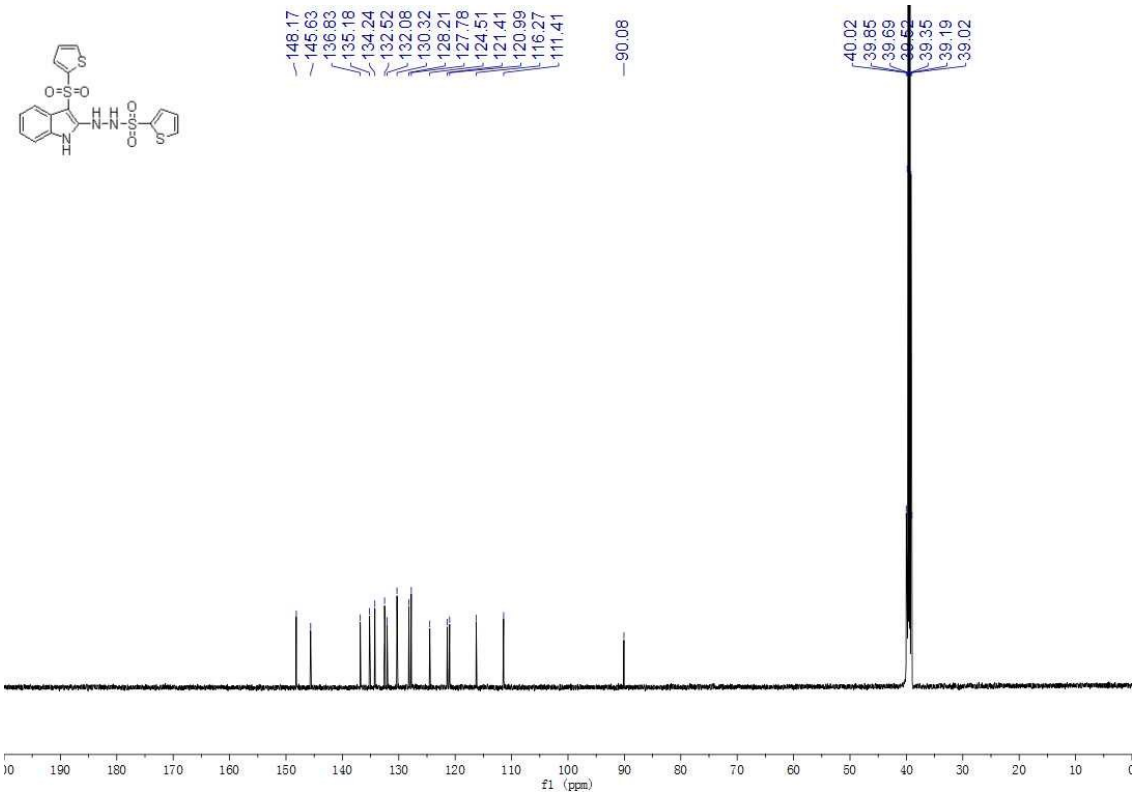


N'-(3-(naphthalen-2-ylsulfonyl)-1H-indol-2-yl)naphthalene-2-sulfonohydrazide (**3ak**)

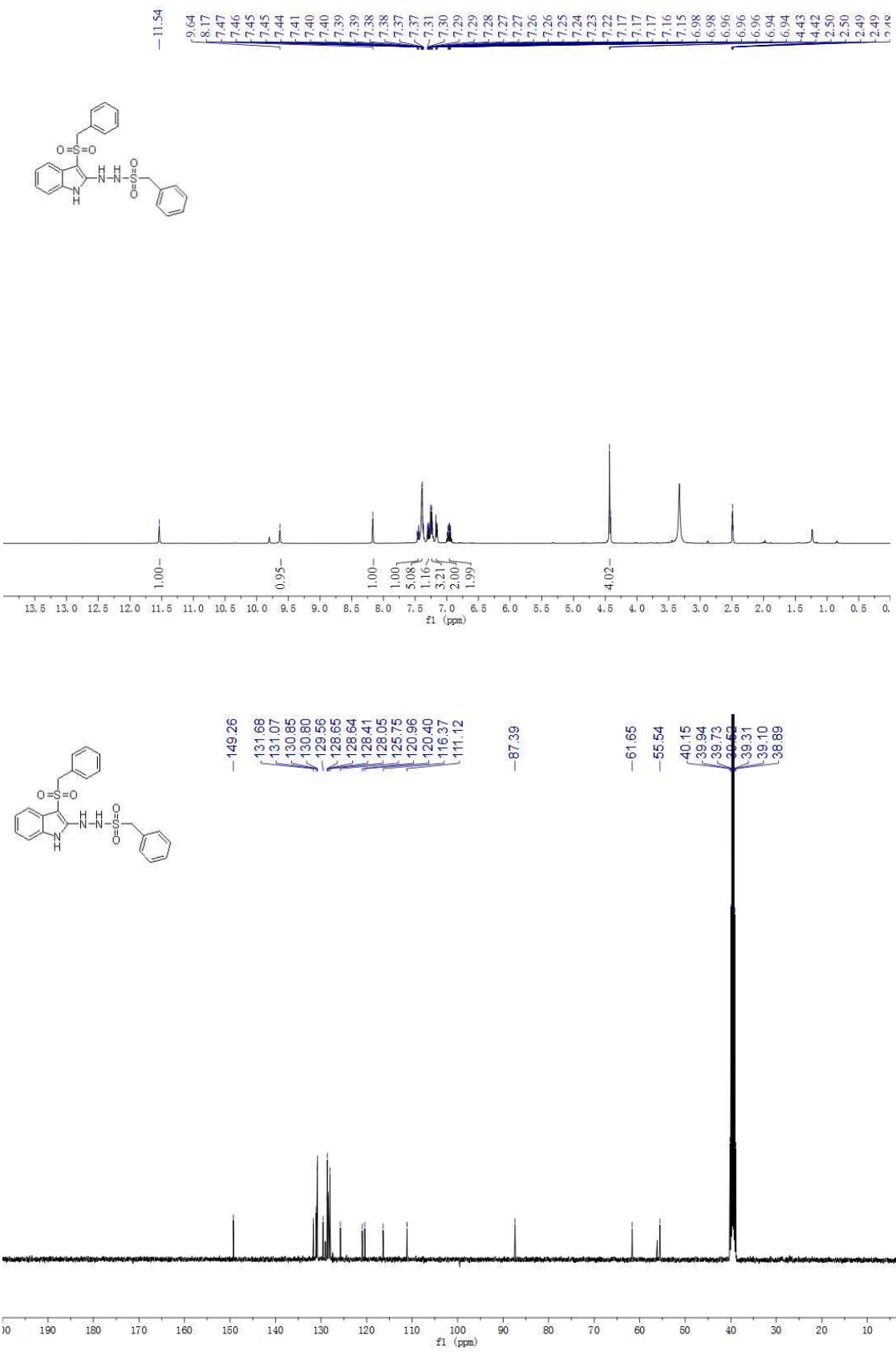


N'-(3-(thiophen-2-ylsulfonyl)-1H-indol-2-yl)thiophene-2-sulfonohydrazide (**3al**)

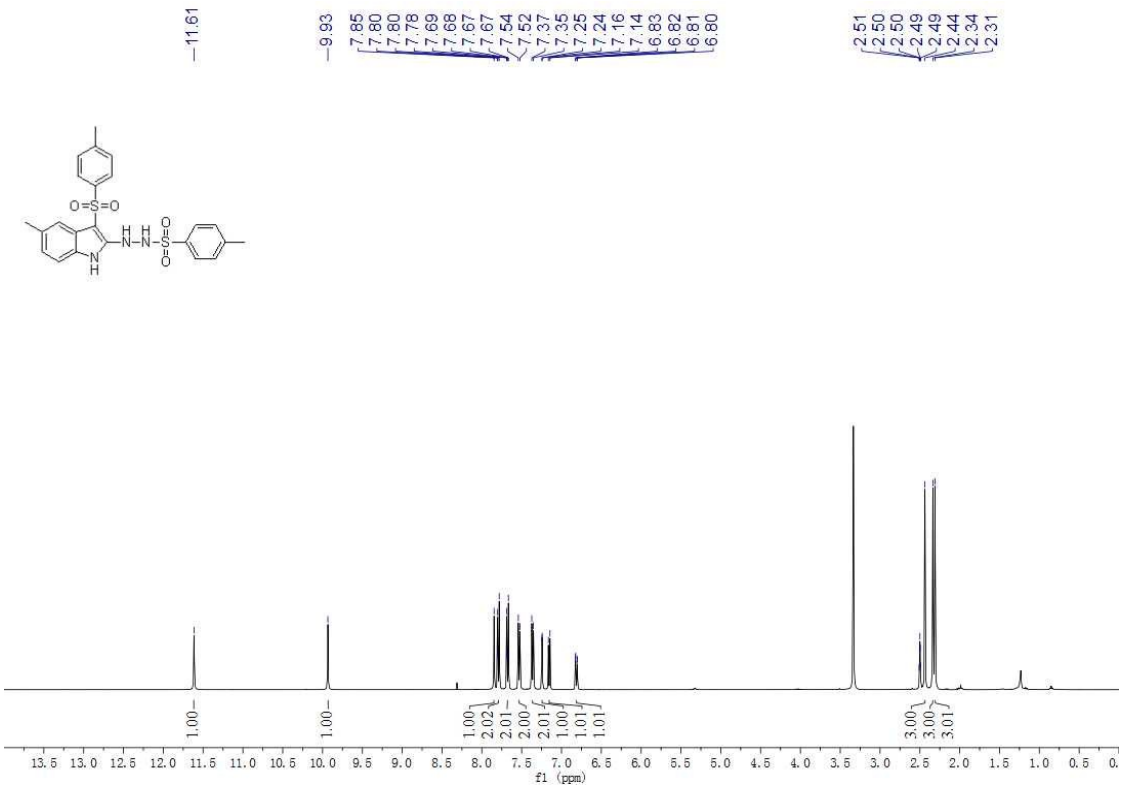


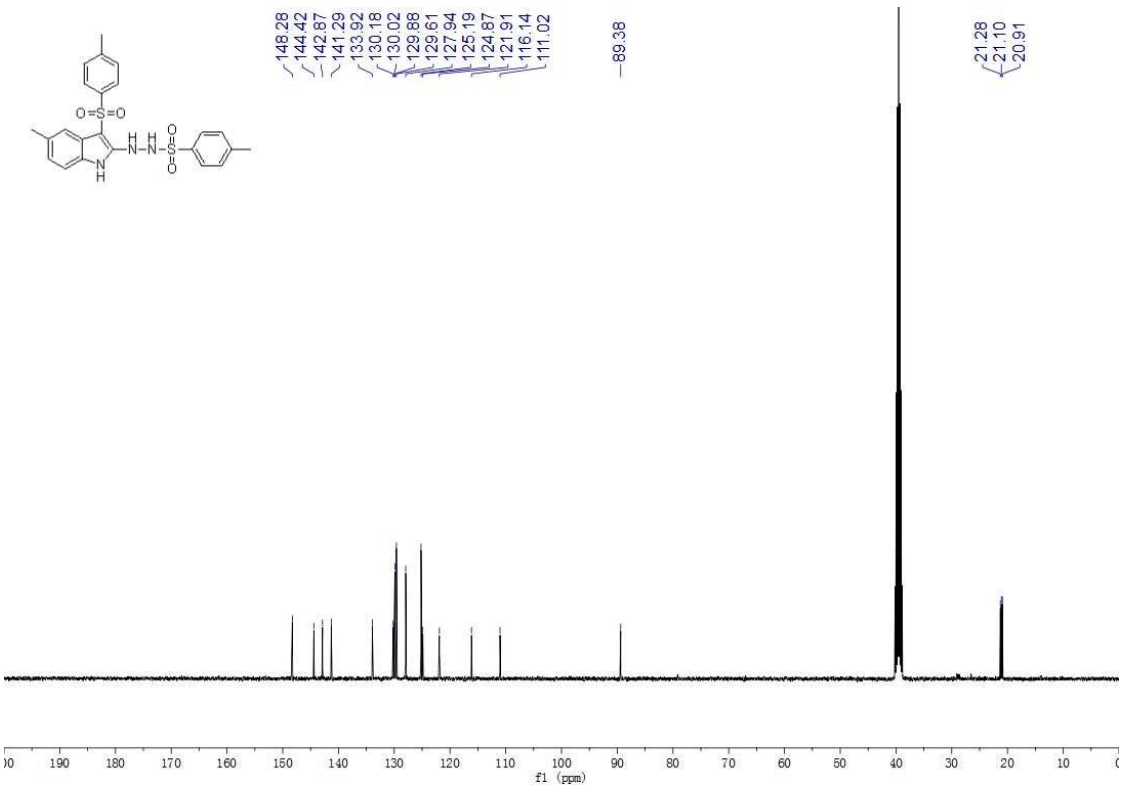


N'-(3-(benzylsulfonyl)-1H-indol-2-yl)-1-phenylmethanesulfonohydrazide (**3am**)

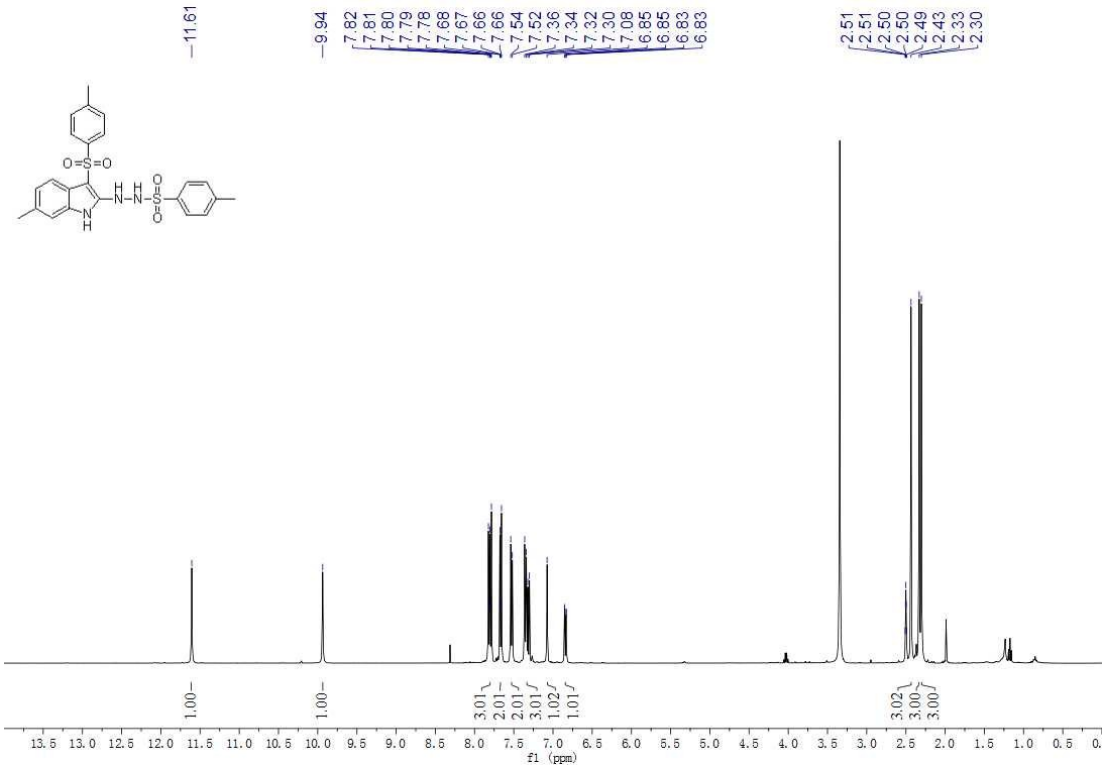


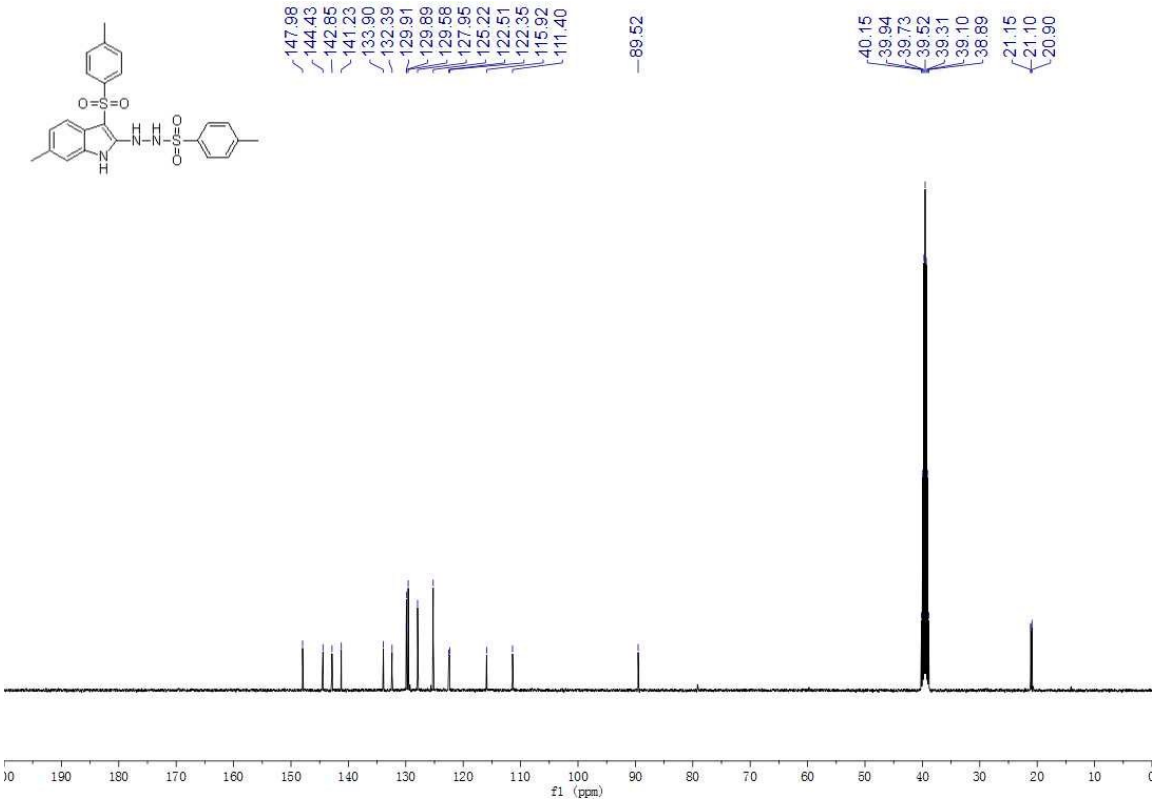
4-methyl-N'-(5-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3ba**)



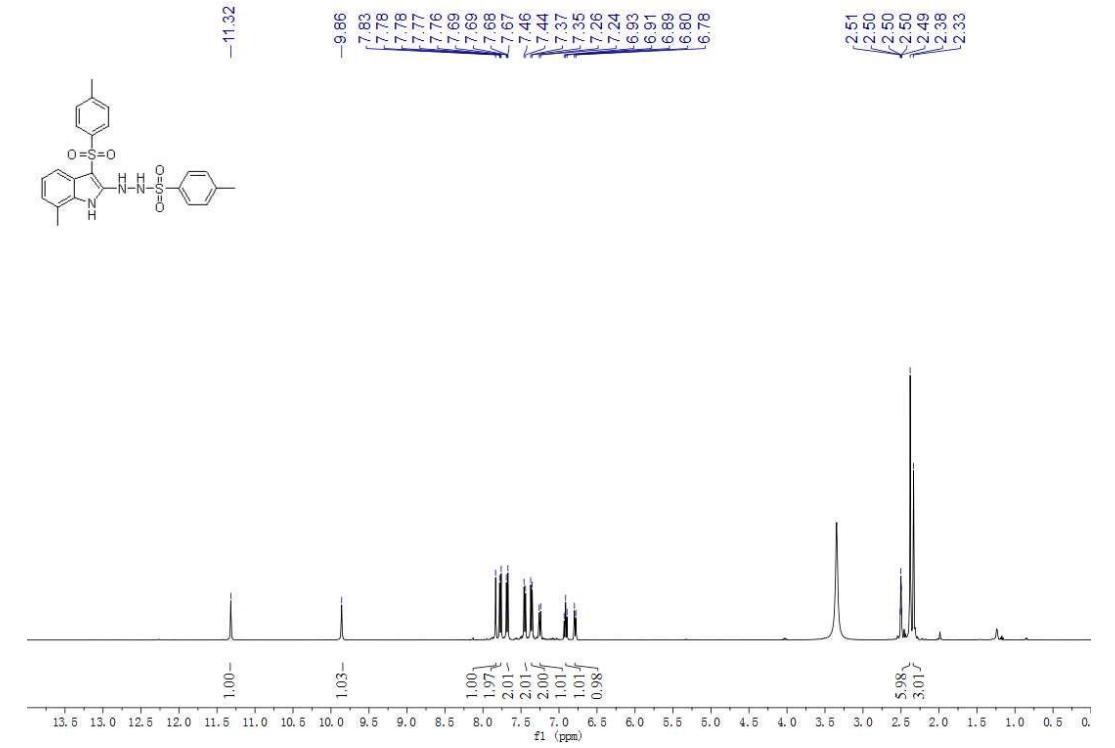


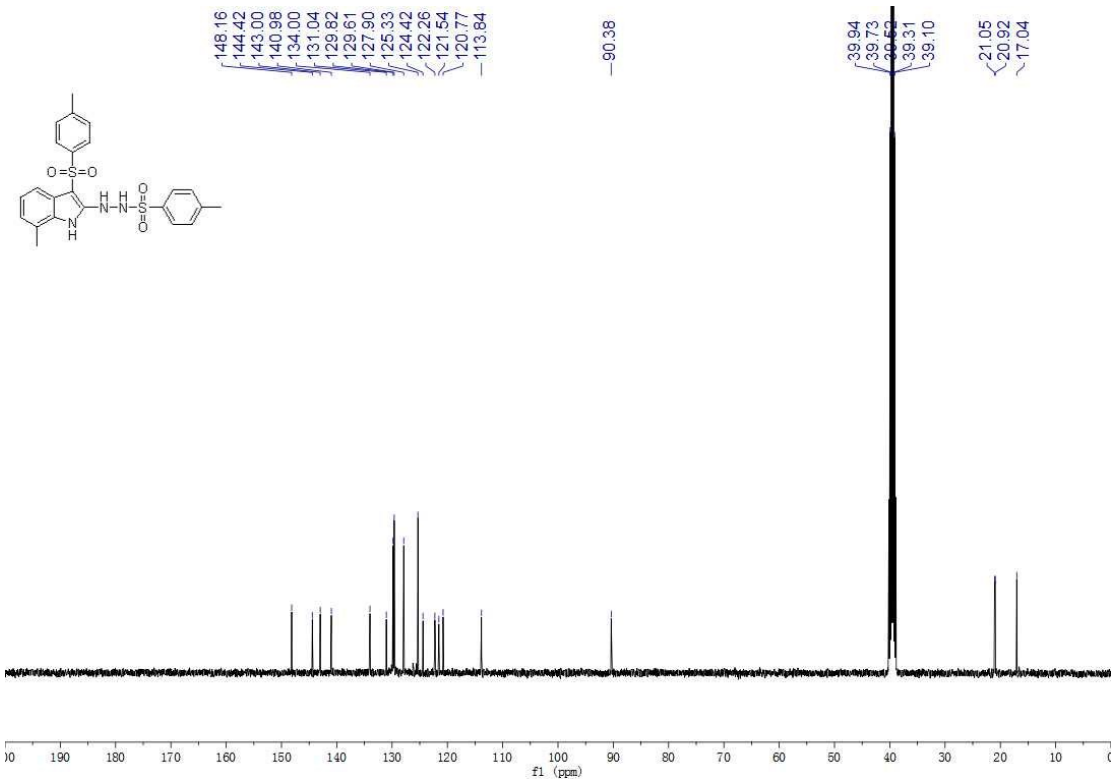
4-methyl-N'-(6-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3ca**)



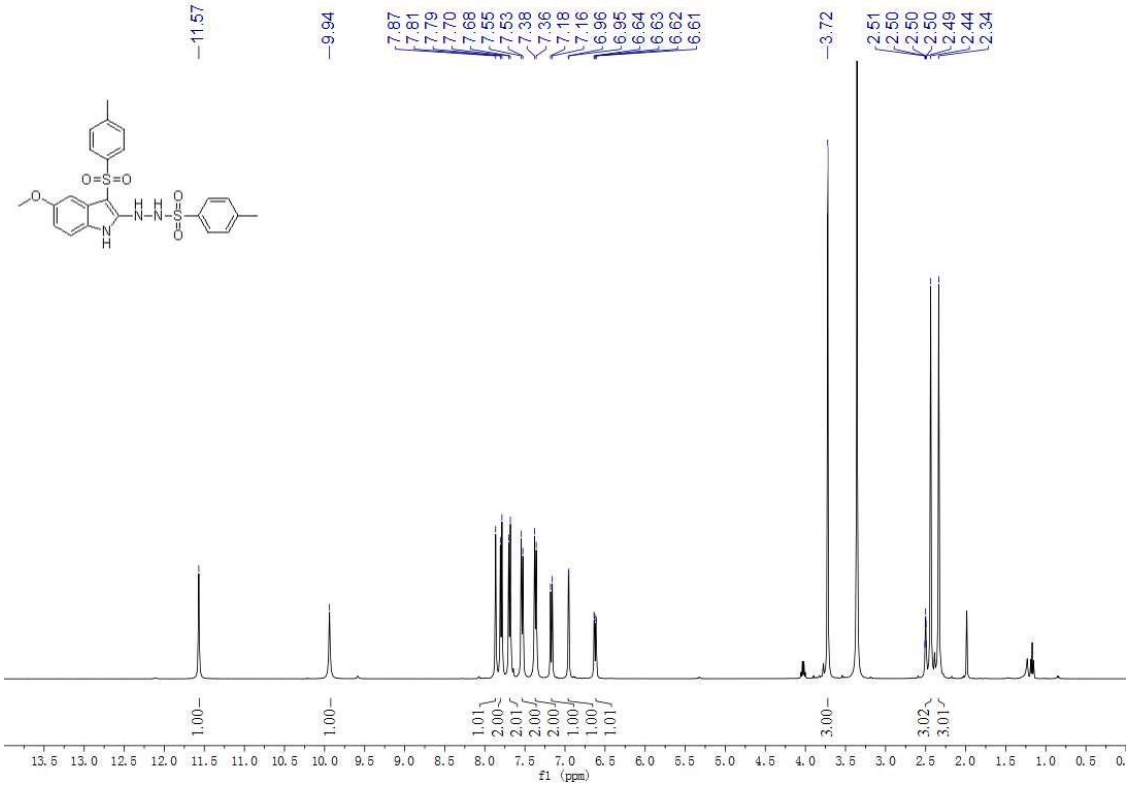


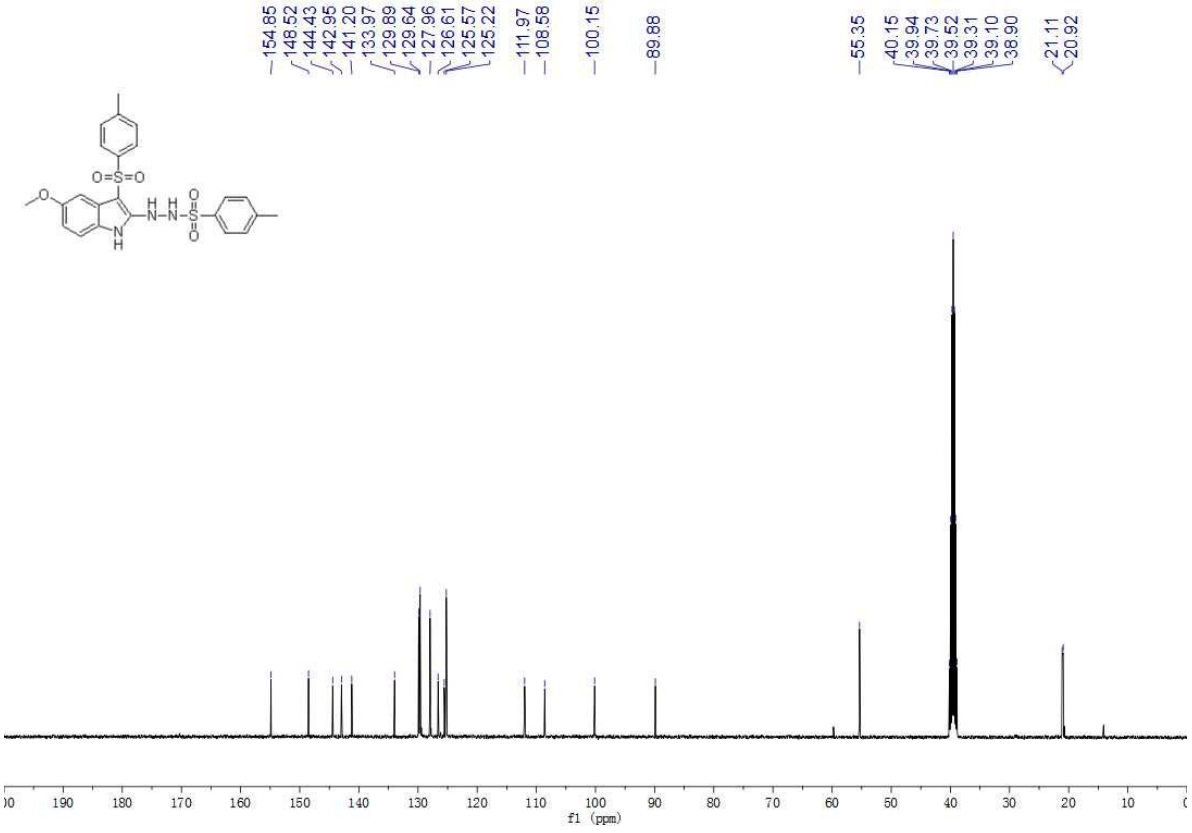
4-methyl-N'-(7-methyl-3-tosyl-1H-indol-2-yl)benzenesulfonohydrazide (**3da**)



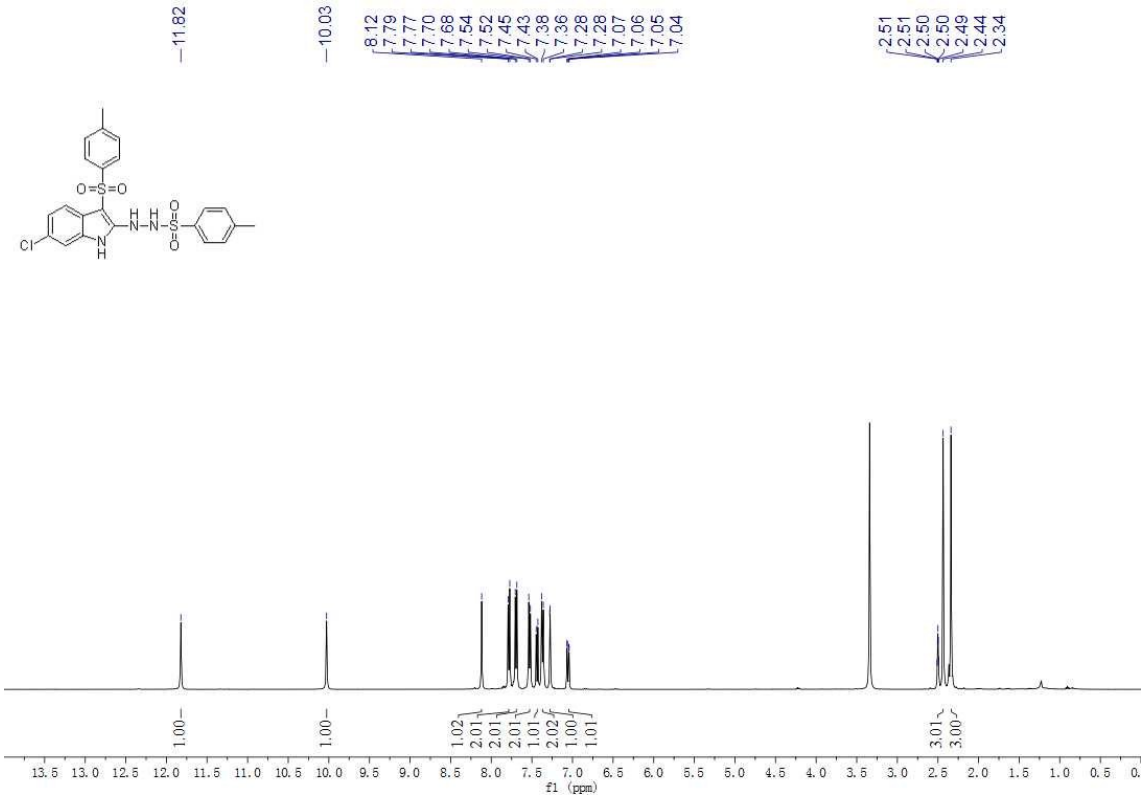


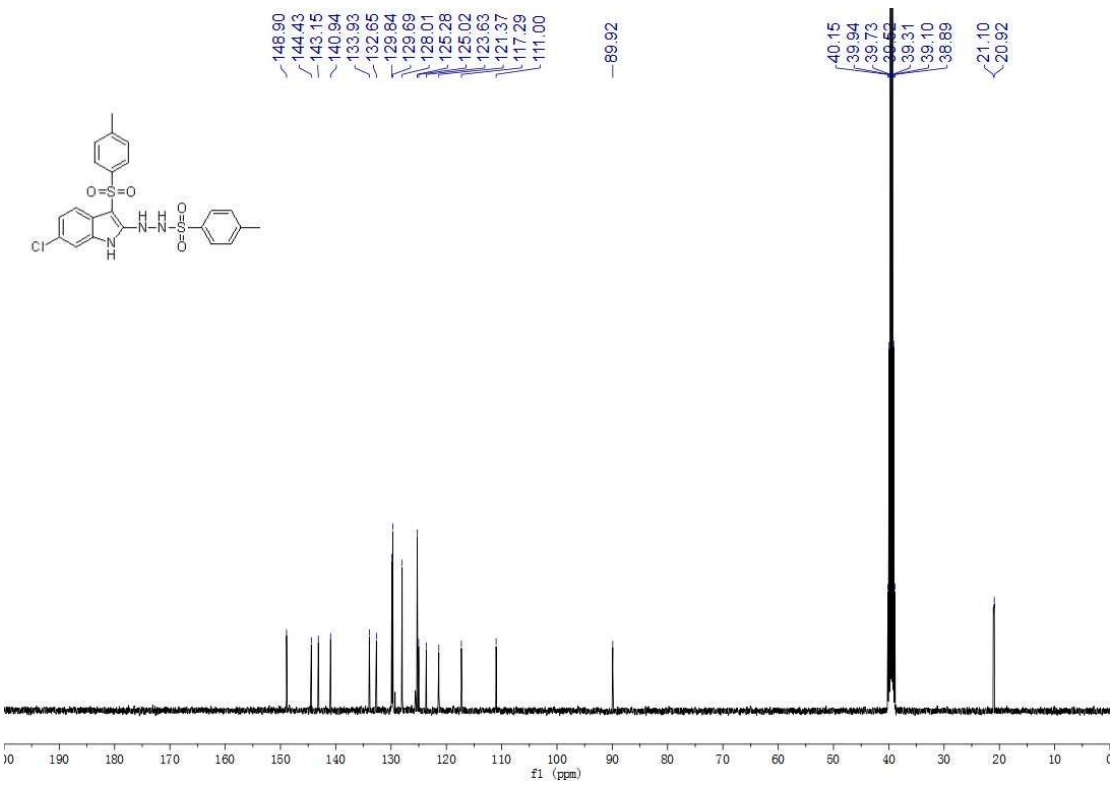
N'-(5-methoxy-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3ea**)





N'-(6-chloro-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3fa**)





N'-(6-fluoro-3-tosyl-1H-indol-2-yl)-4-methylbenzenesulfonohydrazide (**3ga**)