Supporting Information

Small Molecule-Mediated Induction of Endoplasmic Reticulum Stress in Cancer Cells

Shalini Pandey[†‡], Virender Kumar Sharma[Ψ], Ankur Biswas[†], Mayurika Lahiri[Ψ], Sudipta Basu[‡]*

† Department of Chemistry, Indian Institute of Science Education and Research (IISER)-Pune, Homi Bhabha Road, Pashan, Pune, 411008, India

Ψ Department of Biology, Indian Institute of Science Education and Research (IISER)-Pune, Homi Bhabha Road, Pashan, Pune, 411008, India

‡ Discipline of Chemistry, Indian Institute of Technology (IIT), Gandhinagar, Palaj, Gandhinagar, Gujarat, 382355, India

* Corresponding author. Email: Sudipta.basu@iitgn.ac.in

MATERIAL AND METHODS

Materials

All the chemicals were purchased from commercial suppliers unless otherwise noted. Reactions were performed in the oven-dried glassware without inert gas. Analytical thin-layer chromatography (TLC) was performed using pre-coated silica gel aluminium sheets 60 F254 bought from EMD Millipore Laboratories. Compounds were purified by column chromatography using silica gel 100-200 mesh as the stationary phase. ^{1}H, ^{13}C, spectra were recorded on a Bruker Avance III HD Ascend 9.4 Tesla/400 MHz with autosampler and/or Jeol 9.4 Tesla/400 MHz with autosampler spectrometer. Chemical shifts are mentioned in parts per million (ppm) and referred to residual protons on the corresponding deuterated solvent. Mass spectrometry was performed in Water Acquity Instrument with Synapt G2 HD MS, C18 Reverse Phase column, 3 kV Capillary Voltage and 40 V Cone Voltage. UV- Visible spectra was recorded on Shimadzu. DMEM media and 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) was purchased from HiMedia. Nunc® Lab-Tek® II chambered cover glass, 4-phenyl butyric acid (4-PBA), Oil-Red-O solution and Sodium dodecyl sulfate (SDS) was purchased from Sigma-Aldrich. ER Tracker Red was purchased from Invitrogen. AnnexinV-FITC and PI staining Kit was purchased from Roche. Flow Cytometry analysis was recorded on BD- Accuri. Western blot analysis was performed on Las ImageQuant 400.

Details of the antibodies used:

CHOP: Cat# sc-7351, Lot# I1317, mouse monoclonal from Santa Cruz Biotechnology

IRE-1α: Cat# sc-390960, Lot# B0917, mouse monoclonal from Santa Cruz Biotechnology

GRP78: Cat #MA5-27687, Lot# UA2698821, mouse monoclonal from Invitrogen

PERK: Cat# sc-377400, Lot# H2917, mouse monoclonal from Santa Cruz Biotechnology

Caspase-12: Cat# sc-515103, Lot# J0317, mouse monoclonal from Santa Cruz Biotechnology

LC3B: Cat# 2775S, Lot#10, rabbit monoclonal from Invitrogen

Beclin: Cat# sc-48341, Lot# K2217, mouse monoclonal from Santa Cruz Biotechnology

GAPDH: Cat# 919501, Lot# B205145, mouse monoclonal from Biolegend

Methods

Synthesis of sulfonohydrazides. The sulfonohydrazides were prepared according to a previous reported procedure.[1] Briefly, to a solution of sulfonyl chloride (1 eq.) in THF at -30ºC, hydrazine monohydrate (5 eq.) was added dropwise. The solution was then allowed to stir for about 30 minutes. Progress of reaction was monitored through TLC and after it was over ethyl acetate was added to the cold reaction mixture. It was washed multiple times with ice cold 10% brine solution. The organic layer was collected, dried over Na_2SO_4 and the solvent was then

evaporated using rotavap. The solid obtained was washed with pentane three times and the product was stored at 4^{o}C for further use.

Synthesis of sulfonohydrazide-hydrazones. To a solution of sulfonohydrazide (1 eq.) in ethanol, aldehyde was added (1 eq.) along with catalytic amount of *p*-toulene sulfonic acid and the reaction was allowed to stir at room temperature overnight. Extent of reaction was monitored by TLC. On completion, the solvent ethanol was evaporated, and the residue obtained was dissolved in organic solvents (DCM/ ethyl acetate). The organic layer was washed with water, collected and evaporated. The residue obtained was then purified using column chromatography. The procedure was utilized to generate a library of 66 small molecules.

Cell Viability assay. 100 µL of 4000 HeLa cells, 4000 A549 cells, 5000 MCF-7 cells and 7000 MDA-MB-231 cells in DMEM media were seeded per well in 96-well microtiter plate and incubated for 16 h in a 5% CO_2 incubator at 37^{o}C. Cells were treated with different concentrations of the nanoparticles and incubated for 24 h. After the said time point, media was removed and 100 µL of MTT in DMEM (0.5 mg/mL) was added. After 4h, the media was carefully removed without disturbing the formazan crystals and 100 µL of DMSO was added to solubilize the formazan crystals. Absorbance was then recorded at 570 nm on Perkin Elmer Ensight.

Cellular Internalization. 2 x 10^4 cells were seeded in a 8-well LabTek chamber. Cells were incubated with the Compound 1 for the mentioned time points. Cells were washed with cold PBS and costained with ER Tracker Red and incubated for 20 mins. Cells were then washed with DPBS at least three times and then visualised using Leica TCS SP8 confocal microscope.

Oil-Red-O staining. HeLa cells were seeded on 24 well plates and were incubated overnight. Cells were then treated with compound 1 at 9 µM concentration and were then incubated for 24 h. After 24 h prior treatment cells were washed with PBS thrice and fixed with 10% formaldehyde for 15 minutes at R.T. After fixation cells were stained with filtered Oil-Red O solution (1 part Oil Red O in 2 parts ddH_2O for 45 minutes.at R.T. Cells were then washed with PBS twice to remove unbound Oil Red O. Cells were then visualised using Perkin Elmer Operetta.

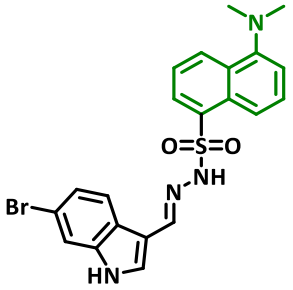
General Protocol for Immunostaining: HeLa cells at a density of 5x 10^4 were allowed to attach on coverslips in a six well plate for overnight. The cells were then treated with compound 1 at IC_{50} concentration. 24 h after treatment, cells were washed with PBS once and then fixed with 4% paraformaldehyde for 10 mins. Cells were then washed twice followed by incubation with PBST (0.1% Tween-20 in PBS) for 10 minutes. Cells were then blocked with 1% BSA in PBS for 30 mins at 37^{o}C. Cells were then incubated with primary antibody diluted in 1% BSA in PBST for 4 h at 37^{o}C. After incubation cells were washed and then incubated with Alexa Fluor tagged secondary antibody diluted in 1% BSA in PBST for 1 h in dark at room temperature. Cells were then washed thrice with PBS and coverslips were carefully mounted on glass slides using Diamond antifade with DAPI. Cells were then imaged using confocal microscopy.

Flow Cytometry analysis. 2 x 10^6 HeLa cells were seeded in a 6-well plate and allowed to attach in a 5% CO_2 incubator overnight. Cells were the treated with compound 1 at IC_{50} and allowed to incubate for 24 h. Cells were then trypsinized and washed with PBS. Cells were

then suspended in Annexin V binding buffer and then incubated with Annexin V- FITC and PI according to the manufacturer's protocol. Apoptotic and necrotic cells were then quantified using BD FACS Caliber.

Western Blot analysis. 1x 10^6 cells were seeded in a 6-well plate and treated with Compound 1 for 24 h. Cells were then lysed. Sodium Dodecyl Sulphate Polyacrylamide Gel Electrophoresis (SDS-PAGE) was used to resolve the different proteins.and transferred to Proteins were then transferred to Immobilon-P Polyvinylidene Difluoride (PVDF) membrane. The blot was developed using clarity Enhanced Chemiluminescence (ECL) substrate and was visualized using ImageQuant LAS 4000. ImageJ software was used to process the blots and intensity calculations. Composition of the cell lysis buffer is: for 6 X Sample Buffer (10 mL), 1 M Tris pH 6.8 = 3.5 mL, Glycerol = 3.6 mL, DTT = 0.93 g, 1% Bromophenol Blue = 0.6 mL and SDS = 1.1 g were used. The final volume was made to 10 mL after mixing the ingredients.

N'-((6-bromo-1H-indol-3-yl) methylene)-5-(dimethylamino) naphthalene-1-sulfonohydrazide (1)

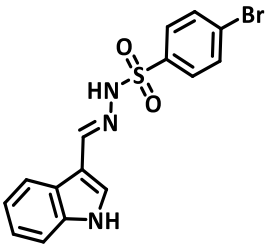


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.55 (s, 1H), 11.41 (s, 1H), 8.52 (d, *J* = 8.7 Hz, 1H), 8.47 (d, *J* = 8.5 Hz, 1H), 8.32 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.05 (s, 1H), 7.70 (dd, *J* = 11.4, 5.2 Hz, 3H), 7.59 (dd, *J* = 8.6, 7.6 Hz, 1H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.26 – 7.16 (m, 2H), 2.77 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 151.27, 143.09, 137.71, 135.07, 131.03, 130.03, 130.00, 129.41, 128.96, 127.99, 123.63, 123.18, 123.16, 122.86, 119.38, 115.18, 114.40, 111.17, 45.02.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{21}H_{19}BrN_4O_2S$ 471.0490; found 471.0489.

N'-((1H-indol-3-yl) methylene)-4-bromobenzenesulfonohydrazide (2)

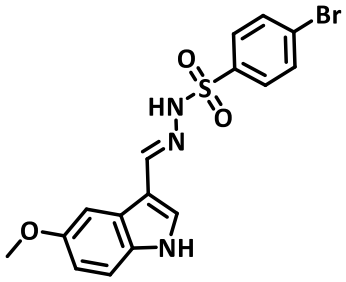


^{1}H NMR (400 MHz, Acetone-d_6, δ): 10.64 (s, 1H), 9.76 (s, 1H), 8.27 – 8.12 (m, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 6.7 Hz, 2H), 7.67 (s, 1H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.19 (p, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, Acetone-d_6, δ): 146.91, 139.73, 138.23, 132.93, 130.90, 130.59, 127.83, 125.41, 123.79, 122.98, 121.71, 112.81, 112.49.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{12}BrN_3O_2S$ 377.9912; found: 377.9912

(4-bromo-N'-((5-methoxy-1H-indol-3-yl) methylene)benzenesulfonohydrazide (3)

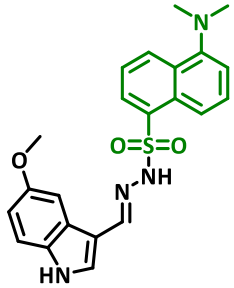


^{1}H NMR (400 MHz, Acetone-d6, δ): 10.55 (s, 1H), 9.77 (s, 1H), 8.22 (s, 1H), 7.95 (d, *J* = 8.6 Hz, 2H), 7.84 – 7.77 (m, 2H), 7.67 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 2.9 Hz, 1H), 7.33 (d, *J* = 8.9 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.85 (s, 3H).

^{13}C NMR (100 MHz, Acetone-d_6, δ): 156.14, 147.50, 139.83, 133.00, 131.39, 130.56, 127.82, 126.05, 121.62, 114.16, 113.27, 112.59, 104.36, 55.83.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}BrN_3O_3S$ 408.0017; found 408.0020

5-(dimethylamino)-N'-((5-methoxy-1H-indol-3-yl)methylene)naphthalene-1-sulfonohydrazide (4)

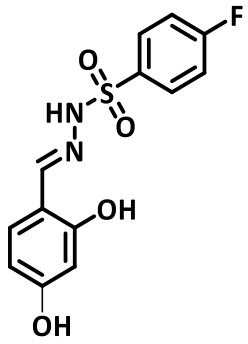


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.34 (d, *J* = 10.8 Hz, 2H), 8.47 (d, *J* = 8.4 Hz, 2H), 8.35 (d, *J* = 4.9 Hz, 1H), 8.07 (d, *J* = 3.6 Hz, 1H), 7.70 – 7.54 (m, 3H), 7.30 (s, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 1H), 3.69 (s, 3H), 2.79 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 154.24, 151.33, 143.96, 134.83, 131.73, 130.54, 130.23, 129.94, 129.25, 128.97, 127.95, 124.33, 123.51, 119.15, 115.19, 112.52, 112.40, 110.76, 103.15, 55.23, 45.22.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{22}H_{22}N_4O_3S$ 423.1494; found 423.1496

N'-(2,4-dihydroxybenzylidene)-4-fluorobenzenesulfonohydrazide (5)

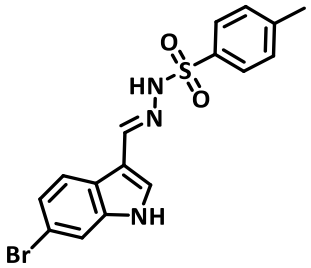


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.25 (s, 1H), 10.19 (s, 1H), 9.87 (s, 1H), 8.06 (s, 1H), 7.90 (dd, *J* = 9.0, 5.2 Hz, 2H), 7.47 (t, *J* = 8.9 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 1H), 6.26 (dt, *J* = 3.7, 2.2 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 165.79, 163.28, 160.84, 158.42, 147.97, 135.13, 135.11, 130.34, 130.24, 129.32, 116.70, 116.47, 110.68, 107.88, 102.39.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}FN_2O_4S$ 311.0502; found 311.0495

N'-((6-bromo-1H-indol-3-yl)methylene)-4-methylbenzenesulfonohydrazide (6)

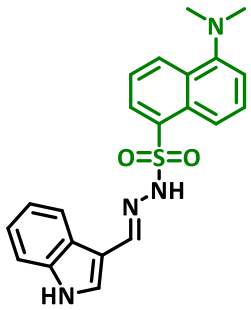


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.61 (s, 1H), 10.93 (s, 1H), 8.05 (s, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 2.6 Hz, 1H), 7.59 (s, 1H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 1H), 2.33 (s, 3H).

^{13}C NMR (10 MHz, DMSO-d_6, δ): 144.35, 143.21, 137.77, 136.16, 131.18, 129.49, 127.37, 123.42, 123.16, 123.00, 115.24, 114.47, 111.21, 20.97.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}BrN_3O_2S$ 392.0068; found 392.0065

N'-((1H-indol-3-yl)methylene)-5-(dimethylamino)naphthalene-1-sulfonohydrazide (7)



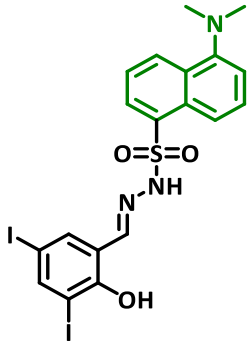
^{1}H NMR (400 MHz, CD_3CN-d_3 , δ): 9.53 (s, 1H), 9.06 (s, 1H), 8.54 (dd, *J* = 8.7, 3.8 Hz, 2H), 8.43 (dd, *J* = 7.4, 1.2 Hz, 1H), 8.02 (s, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.63 (ddd, *J* = 17.4, 8.6,

7.6 Hz, 2H), 7.40 (dd, *J* = 14.4, 5.5 Hz, 2H), 7.24 – 7.15 (m, 2H), 7.11 – 7.08 (m, 1H), 2.79 (s, 6H).

^{13}C NMR (100 MHz, CD_3CN-d_3, δ) 152.89, 145.71, 137.92, 135.44, 132.01, 131.62, 130.86, 130.77, 130.52, 129.28, 125.01, 124.44, 124.02, 122.76, 121.84, 120.31, 116.35, 112.67, 112.42, 45.66

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{21}H_{20}N_4O_2S$ 393.1385; found 393.1382.

5-(dimethylamino)-N'-(2-hydroxy-3,5-diiodobenzylidene)naphthalene-1-sulfonohydrazide (8)

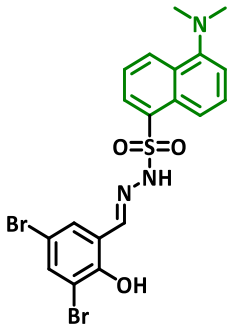


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.56 (s, 1H), 11.09 (s, 1H), 8.52 (d, *J* = 8.5 Hz, 1H), 8.29 (dd, *J* = 26.3, 8.0 Hz, 2H), 8.04 – 7.94 (m, 2H), 7.74 – 7.60 (m, 3H), 7.27 (d, *J* = 7.6 Hz, 1H), 2.81 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 155.50, 151.57, 146.60, 145.59, 137.94, 133.90, 130.76, 129.81, 129.06, 128.98, 128.42, 123.80, 120.76, 118.57, 115.47, 88.17, 82.82, 45.07.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{19}H_{17}I_2N_3O_3S$ 621.9158; found 621.9161.

N'-(3,5-dibromo-2-hydroxybenzylidene)-5-(dimethylamino)naphthalene-1-sulfonohydrazide (9)

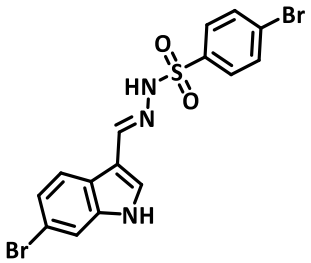


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.54 (s, 1H), 10.89 (s, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.31 (dd, *J* = 30.2, 7.8 Hz, 2H), 8.09 (s, 1H), 7.82 – 7.52 (m, 4H), 7.27 (d, *J* = 7.4 Hz, 1H), 2.81 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 152.40, 151.51, 144.52, 135.47, 134.00, 130.67, 130.57, 129.81, 129.03, 128.99, 128.30, 123.77, 121.87, 118.64, 115.40, 111.75, 110.98, 44.91.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{19}H_{17}Br_2N_3O_3S$ 527.9415; found 527.9409.

4-bromo-N'-((6-bromo-1H-indol-3-yl)methylene)benzenesulfonohydrazide (10)

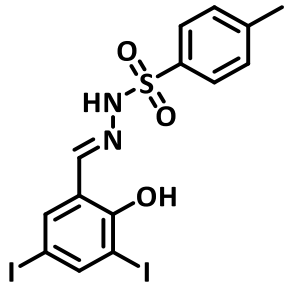


^{1}H NMR (400 MHz, Acetone-d_6 δ): 10.76 (s, 1H), 9.85 (s, 1H), 8.21 (s, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 7.7 Hz, 2H), 7.67 (d, *J* = 18.2 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 1H).

^{13}C NMR (100 MHz, Acetone-d_6, δ) 146.14, 139.65, 139.05, 133.00, 131.61, 130.60, 127.93, 124.80, 124.47, 124.39, 116.82, 115.45, 112.96.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{11}Br_2N_3O_2S$ 457.8996; found 457.8991.

N'-(2-hydroxy-3, 5-diiodobenzylidene)-4-methylbenzenesulfonohydrazide (11)

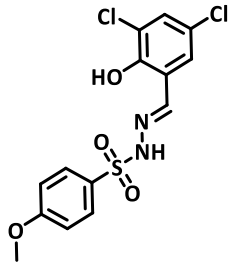


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.06 (s, 1H), 11.32 (s, 1H), 8.05 – 8.00 (m, 2H), 7.74 (ddd, *J* = 10.3, 6.7, 2.0 Hz, 3H), 7.45 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 155.77, 147.29, 146.82, 144.23, 138.39, 135.37, 130.11, 127.07, 120.44, 88.01, 82.77, 21.09.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{12}I_2N_2O_3S$ 542.8736; found 542.8740

N'-(3,5-dichloro-2-hydroxybenzylidene)-4-methoxybenzenesulfonohydrazide (12)

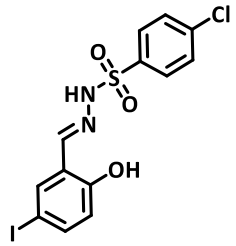


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.91 (s, 1H), 10.98 (s, 1H), 8.13 (s, 1H), 7.79 (d, *J* = 8.9 Hz, 2H), 7.59 (s, 1H), 7.51 (d, *J* = 2.5 Hz, 1H), 7.16 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 162.94, 151.21, 145.48, 130.32, 129.83, 129.31, 126.93, 123.45, 121.88, 121.55, 114.72, 55.74.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{12}Cl_2N_2O_4S$ 374.9973; found 374.9974.

4-chloro-N'-(2-hydroxy-5-iodobenzylidene)benzenesulfonohydrazide (13)

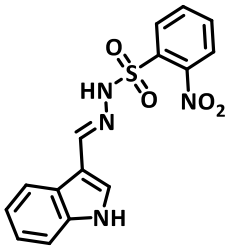


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.72 (s, 1H), 10.43 (s, 1H), 8.10 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.72 (s, 2H), 7.70 (s, 1H), 7.51 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.71 (s, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.15, 143.71, 139.55, 138.13, 137.65, 134.26, 129.56, 129.02, 122.04, 118.89, 81.58.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}ClIN_2O_3S$ 436.9223; found 436.9220

N'-((1H-indol-3-yl)methylene)-2-nitrobenzenesulfonohydrazide (14)

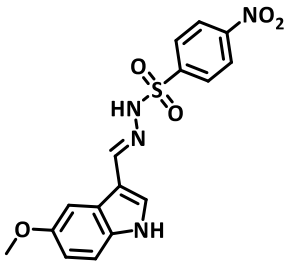


^{1}H NMR (400 MHz, Acetone-d_6, δ): 10.69 (s, 1H), 9.80 (s, 1H), 8.44 (s, 1H), 8.38 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.99 – 7.86 (m, 3H), 7.72 (d, *J* = 2.8 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.18 (ddd, *J* = 14.9, 13.5, 7.1 Hz, 2H).

^{13}C NMR (100 MHz, Acetone-d_6, δ): 147.58, 138.28, 135.36, 133.32, 133.07, 132.43, 131.25, 125.51, 125.38, 123.82, 123.07, 121.73, 112.68, 112.51, 112.46.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{12}N_4O_4S$ 345.0657; found 345.0661

N'-((5-methoxy-1H-indol-3-yl)methylene)-4-nitrobenzenesulfonohydrazide (15)

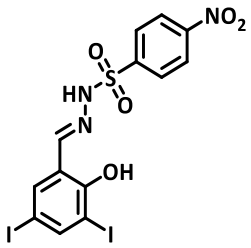


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.43 (s, 1H), 11.27 (s, 1H), 8.44 (d, *J* = 8.8 Hz, 2H), 8.21 – 8.09 (m, 3H), 7.70 (d, *J* = 2.6 Hz, 1H), 7.38 (s, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 154.46, 149.84, 146.87, 144.57, 131.77, 131.31, 128.87, 124.45, 112.60, 110.52, 103.03, 55.15

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}N_4O_5S$ 375.0763; found 375.0765.

N'-(2-hydroxy-3,5-diiodobenzylidene)-4-nitrobenzenesulfonohydrazide (16)

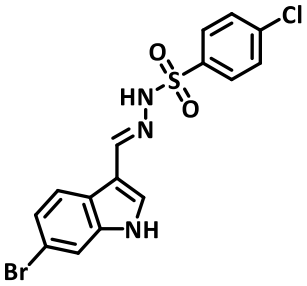


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.49 (s, 1H), 11.10 (s, 1H), 8.50 – 8.41 (m, 2H), 8.11 (dt, *J* = 3.5, 2.0 Hz, 3H), 8.03 (d, *J* = 2.1 Hz, 1H), 7.78 (d, *J* = 2.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 155.71, 150.21, 147.82, 147.03, 143.68, 138.02, 128.64, 124.96, 120.71, 88.43, 83.00.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9I_2N_3O_5S$ 573.8430; found 573.8426

N'-((6-bromo-1H-indol-3-yl)methylene)-4-chlorobenzenesulfonohydrazide (17)

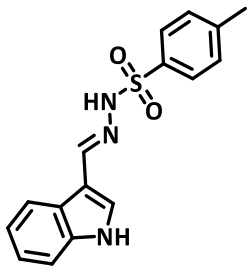


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.64 (s, 1H), 11.10 (s, 1H), 8.08 (d, *J* = 1.0 Hz, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.86 (d, *J* = 8.7 Hz, 1H), 7.77 (d, *J* = 2.7 Hz, 1H), 7.70 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 1.3 Hz, 1H), 7.29 (dd, *J* = 8.5, 1.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d6, δ): 145.10, 137.82, 137.80, 137.78, 131.50, 129.29, 129.28, 123.54, 123.07, 122.96, 115.27, 114.51, 111.04.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{11}BrClN_3O_2S$ 411.9522; found 411.9519

N'-((1H-indol-3-yl)methylene)-4-methylbenzenesulfonohydrazide (18)

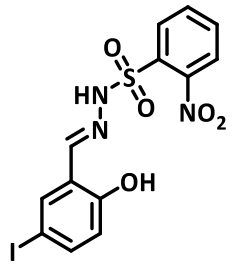


^{1}H NMR (400 MHz, CD_3CN-d_3, δ): 9.60 (s, 1H), 8.67 (s, 1H), 8.04 (d, *J* = 7.2 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 2.8 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.21 (dtd, *J* = 17.5, 7.2, 1.2 Hz, 2H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, CD_3CN-d_3, δ): 146.76, 145.18, 138.01, 136.84, 131.07, 130.49, 128.89, 125.12, 124.10, 122.73, 122.04, 112.71, 112.43, 21.51.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{15}N_3O_2S$ 314.0963; found 314.0967

N'-(2-hydroxy-5-iodobenzylidene)-2-nitrobenzenesulfonohydrazide (19)

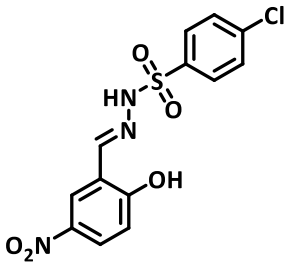


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.19 (s, 1H), 10.40 (s, 1H), 8.24 (d, *J* = 1.8 Hz, 1H), 8.03 (dd, *J* = 9.0, 4.6 Hz, 2H), 7.94 – 7.86 (m, 2H), 7.76 (s, 1H), 7.51 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.71 (d, *J* = 8.6 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.21, 147.89, 143.46, 139.68, 134.92, 134.09, 132.69, 130.81, 130.35, 124.61, 122.12, 118.91, 81.62.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}IN_3O_5S$ 447.9464; found 447.9456

4-chloro-N'-(2-hydroxy-5-nitrobenzylidene)benzenesulfonohydrazide (20)

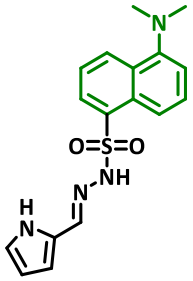


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.79 (s, 2H), 8.33 (d, *J* = 2.9 Hz, 1H), 8.21 (s, 1H), 8.12 (dd, *J* = 9.1, 2.7 Hz, 1H), 7.91 – 7.83 (m, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 9.1 Hz, 1H).

^{13}C NMR (101 MHz, DMSO-d_6, δ): 161.84, 142.43, 139.93, 138.18, 137.69, 129.61, 129.02, 126.80, 121.78, 120.21, 116.86.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}ClN_3O_5S$ 356.0108; found 356.0109

N'-((1H-pyrrol-2-yl)methylene)-5-(dimethylamino)naphthalene-1-sulfonohydrazide (21)

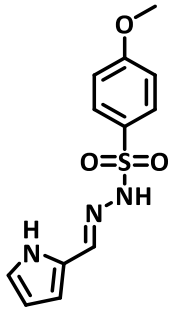


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.44 (s, 1H), 11.15 (s, 1H), 8.46 (t, *J* = 9.7 Hz, 2H), 8.21 (d, *J* = 7.2 Hz, 1H), 7.78 (s, 1H), 7.63 (dd, *J* = 16.1, 11.6 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 1H), 6.80 (s, 1H), 6.30 (s, 1H), 6.03 (s, 1H), 6.03 (s, 1H), 2.80 (s, 6H).

^{13}C NMR (10 MHz, DMSO- d_6, δ): 151.28, 139.44, 135.25, 129.93, 129.50, 129.26, 128.96, 127.97, 126.37, 123.67, 122.17, 119.37, 115.23, 112.63, 109.08, 45.07.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{17}H_{18}N_4O_2S$ 343.1228; found 343.1228

N'-((1H-pyrrol-2-yl)methylene)-4-methoxybenzenesulfonohydrazide (22)

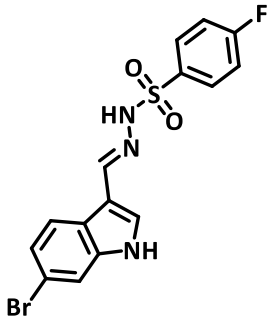


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.26 (s, 1H), 10.84 (s, 1H), 7.85 – 7.80 (m, 2H), 7.73 (s, 1H), 7.09 (d, *J* = 9.0 Hz, 2H), 6.84 (dd, *J* = 4.1, 2.7 Hz, 1H), 6.37 – 6.33 (m, 1H), 6.06 (dd, *J* = 5.9, 2.4 Hz, 1H), 3.81 (s, 3H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 162.46, 140.43, 130.81, 129.45, 126.50, 122.23, 114.23, 112.95, 109.08, 55.64.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{12}H_{13}N_3O_3S$ 280.0756; found 280.0761

N'-((6-bromo-1H-indol-3-yl)methylene)-4-fluorobenzenesulfonohydrazide (23)

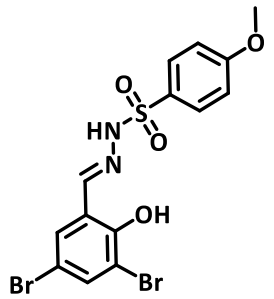


^{1}H NMR (400 MHz, Acetone- d_6, δ): 10.76 (s, 1H), 9.80 (s, 1H), 8.20 (s, 1H), 8.15 – 8.03 (m, 3H), 7.70 (d, *J* = 2.5 Hz, 1H), 7.65 (s, 1H), 7.43 – 7.29 (m, 3H).

^{13}C NMR (100 MHz, Acetone- d_6, δ): 167.19, 164.69, 145.97, 139.05, 136.70, 136.67, 131.51, 124.70, 124.45, 124.37, 116.93, 116.74, 116.70, 115.42, 112.95.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{11}BrFN_3O_2S$ 395.9818 found 395.9813

N'-(3,5-dibromo-2-hydroxybenzylidene)-4-methoxybenzenesulfonohydrazide (24)

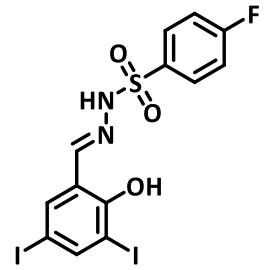


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.97 (s, 1H), 11.15 (s, 1H), 8.11 (s, 1H), 7.82 – 7.76 (m, 3H), 7.67 (d, *J* = 2.2 Hz, 1H), 7.17 (t, *J* = 5.9 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 162.98, 152.67, 146.23, 135.69, 131.11, 129.74, 129.29, 121.45, 114.76, 111.59, 110.96, 55.75.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{12}Br_2N_2O_4S$ 464.8942: found 464.8939.

4-fluoro-N'-(2-hydroxy-3,5-diiodobenzylidene)benzenesulfonohydrazide (25)

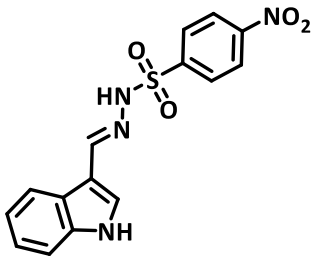


^{1}H NMR (400 MHz, Acetone- d_6, δ): 11.51 (s, 1H), 10.87 (s, 1H), 8.12 (s, 1H), 8.08 – 7.99 (m, 3H), 7.69 (d, *J* = 2.0 Hz, 1H), 7.44 (t, *J* = 8.8 Hz, 2H).

^{13}C NMR (100 MHz, Acetone- d_6, δ) 167.68, 165.16, 157.61, 149.55, 148.53, 140.45, 135.72, 135.69, 131.51, 131.42, 120.57, 117.69, 117.46, 86.85, 81.38.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9FI_2N_2O_3S$ 546.8486; found 546.8491.

N'-((1H-indol-3-yl)methylene)-4-nitrobenzenesulfonohydrazide (26)

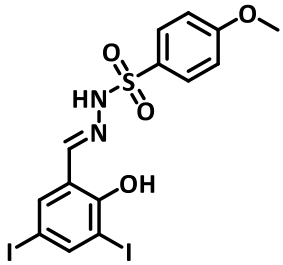


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.56 (s, 1H), 11.30 (s, 1H), 8.44 (d, *J* = 8.6 Hz, 2H), 8.23 – 8.04 (m, 3H), 7.93 (d, *J* = 7.5 Hz, 1H), 7.75 (d, *J* = 2.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.01 (m, 2H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 149.84, 146.27, 144.50, 136.92, 130.98, 128.93, 124.43, 123.96, 122.65, 121.48, 120.71, 111.86, 110.78.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{12}N_4O_4S$ 345.0657; found 345.0659.

N'-(2-hydroxy-3,5-diiodobenzylidene)-4-methoxybenzenesulfonohydrazide (27)

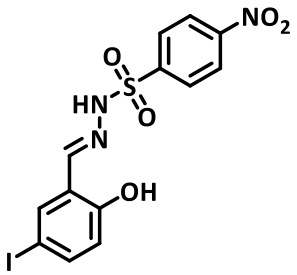


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.98 (s, 1H), 11.37 (s, 1H), 8.02 (d, *J* = 5.6 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 3H), 7.16 (d, *J* = 7.6 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 163.00, 155.74, 147.10, 146.72, 138.35, 129.70, 129.26, 120.41, 114.79, 87.94, 82.72, 55.77.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{12}I_2N_2O_4S$ 558.8685; found 558.8687.

N'-(2-hydroxy-5-iodobenzylidene)-4-nitrobenzenesulfonohydrazide (28)

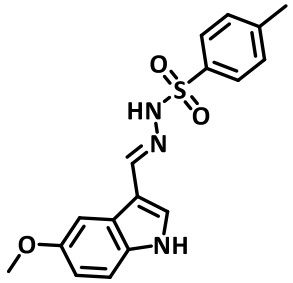


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.96 (s, 1H), 10.41 (s, 1H), 8.44 (d, *J* = 8.6 Hz, 2H), 8.12 (s, 2H), 8.10 (s, 1H), 7.75 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 6.69 (s, 1H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 156.18, 150.01, 144.17, 143.98, 139.71, 134.04, 128.70, 124.74, 122.02, 118.88, 81.61.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}IN_3O_5S$ 447.9464; found 447.9461.

N'-((5-methoxy-1H-indol-3-yl)methylene)-4-methylbenzenesulfonohydrazide (29)

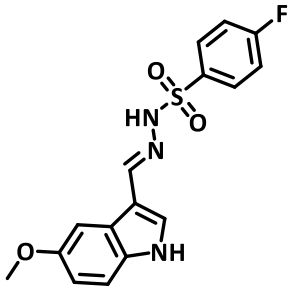


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.38 (s, 1H), 10.84 (s, 1H), 8.07 (d, *J* = 2.9 Hz, 1H), 7.81 (dd, *J* = 8.2, 2.1 Hz, 2H), 7.69 – 7.63 (m, 1H), 7.45 (s, 1H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.28 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.79 (dt, *J* = 8.8, 2.0 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 154.39, 145.57, 143.20, 136.31, 131.76, 130.80, 129.47, 127.39, 124.49, 112.66, 112.53, 110.86, 103.13, 55.15, 39.52, 20.96.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{17}H_{17}N_3O_3S$ 344.1069; found 344.1068.

4-fluoro-N'-((5-methoxy-1H-indol-3-yl)methylene)benzenesulfonohydrazide (30)

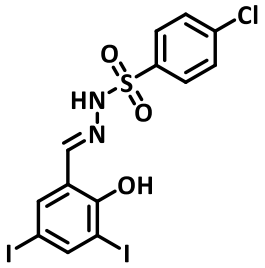


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.41 (s, 1H), 10.95 (s, 1H), 8.10 (d, *J* = 2.3 Hz, 1H), 7.97 (ddd, *J* = 7.3, 5.1, 1.9 Hz, 2H), 7.68 (d, *J* = 1.5 Hz, 1H), 7.45 (dd, *J* = 18.2, 9.4 Hz, 3H), 7.29 (dd, *J* = 8.8, 1.1 Hz, 1H), 6.80 (d, *J* = 8.9 Hz, 1H), 3.74 (d, *J* = 0.9 Hz, 3H).

^{13}C NMR (100 MHz, DMSO- d_6, δ): 165.61, 163.11, 154.41, 146.20, 135.56, 135.53, 131.79, 131.03, 130.36, 130.26, 124.47, 116.40, 116.17, 112.63, 112.55, 110.70, 103.03, 55.15.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}FN_3O_3S$ 348.0818; found 348.0822.

4-chloro-N'-(2-hydroxy-3,5-diiodobenzylidene)benzenesulfonohydrazide (31)

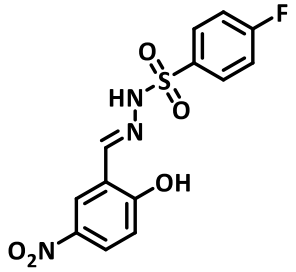


^{1}H NMR (400 MHz, DMSO- $d_{6,}$ δ): 12.23 (s, 1H), 11.20 (s, 1H), 8.06 (s, 1H), 8.02 (s, 1H), 7.85 (d, *J* = 8.6 Hz, 2H), 7.78 (d, *J* = 1.7 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 2H).

^{13}C NMR (100 MHz, DMSO- $d_{6,}$ δ): 155.76, 147.65, 146.95, 138.59, 138.26, 137.13, 129.86, 128.97, 120.55, 88.24, 82.92, 39.52.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9ClI_2N_2O_3S$ 562.8190; found 562.8184.

4-fluoro-N'-(2-hydroxy-5-nitrobenzylidene) benzenesulfonohydrazide (32)

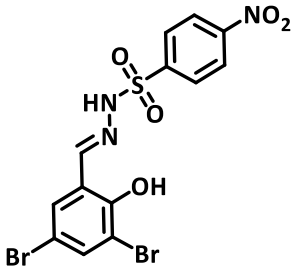


^{1}H NMR (400 MHz, Acetone-$d_{6,}$ δ): 11.30 (s, 2H), 8.39 (s, 1H), 8.35 (d, *J* = 2.8 Hz, 1H), 8.19 (dd, *J* = 9.1, 2.8 Hz, 1H), 8.04 (dd, *J* = 9.0, 5.1 Hz, 2H), 7.44 (t, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 9.1 Hz, 1H).

^{13}C NMR (100 MHz, Acetone-$d_{6,}$ δ): 167.61, 165.09, 163.56, 148.79, 141.52, 135.79, 131.55, 131.45, 127.60, 126.94, 119.08, 118.28, 117.58, 117.35.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}FN_3O_5S$ 340.0403; found 340.0403.

N'-(3,5-dibromo-2-hydroxybenzylidene)-4-nitrobenzenesulfonohydrazide (33)

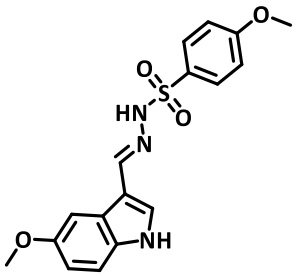


^{1}H NMR (400 MHz, DMSO- $d_{6,}$ δ): 12.44 (s, 1H), 10.88 (s, 1H), 8.45 (d, *J* = 8.8 Hz, 2H), 8.17 (s, 1H), 8.12 (d, *J* = 8.8 Hz, 2H), 7.80 (s, 1H), 7.67 (d, *J* = 2.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-$d_{6,}$ δ): 152.60, 150.17, 146.60, 143.75, 135.96, 130.47, 128.66, 124.90, 121.96, 112.05, 111.19.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Br_2N_3O_5S$ 479.8687; found 479.8684.

4-methoxy-N'-((5-methoxy-1H-indol-3-yl)methylene)benzenesulfonohydrazide (34)

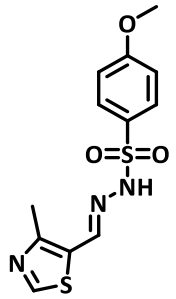


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.37 (s, 1H), 10.75 (s, 1H), 8.07 (s, 1H), 7.85 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 2.6 Hz, 1H), 7.45 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 8.9 Hz, 2H), 6.79 (dd, *J* = 8.8, 2.0 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 205.95, 162.43, 154.35, 145.46, 131.78, 130.84, 130.73, 129.48, 124.48, 114.19, 112.59, 112.48, 110.85, 103.12, 55.63, 55.15.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{17}H_{17}N_3O_4S$ 360.1018; found 360.1014.

4-methoxy-N'-((4-methylthiazol-5-yl)methylene)benzenesulfonohydrazide (35)

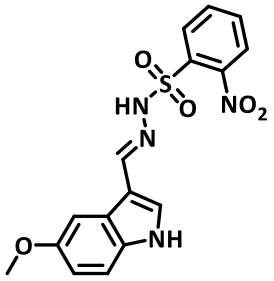


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.36 (s, 1H), 8.99 (s, 1H), 8.13 (s, 1H), 7.76 (d, *J* = 7.7 Hz, 2H), 7.12 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 162.67, 154.72, 153.76, 139.87, 130.32, 129.39, 126.84, 114.38, 55.68, 15.26.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{12}H_{13}N_3O_3S_2$ 312.0477; found 312.0481.

N'-((5-methoxy-1H-indol-3-yl)methylene)-2-nitrobenzenesulfonohydrazide (36)

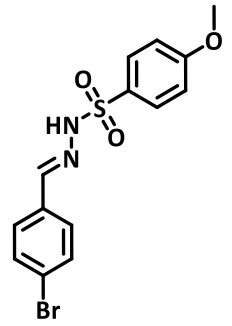


^{1}H NMR (400 MHz, Acetone-d_6, δ): 10.60 (s, 1H), 9.81 (s, 1H), 8.43 (s, 1H), 8.38 – 8.33 (m, 1H), 7.97 – 7.88 (m, 2H), 7.66 (dd, *J* = 14.7, 2.7 Hz, 2H), 7.33 (d, *J* = 8.9 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.5 Hz, 1H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, Acetone-d_6, δ) 156.17, 149.46, 148.02, 135.38, 133.13, 133.09, 132.49, 131.65, 125.90, 125.63, 114.17, 113.24, 112.43, 104.30, 55.85.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}N_4O_5S$ 375.0763; found 375.0758.

N'-(4-bromobenzylidene)-4-methoxybenzenesulfonohydrazide (37)

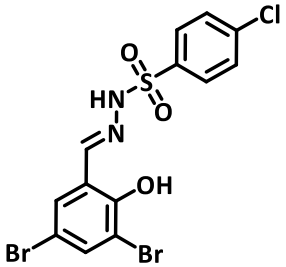


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.47 (s, 1H), 7.88 (s, 1H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H).

^{13}C NMR (101 MHz, DMSO-d_6, δ): 162.62, 145.57, 132.98, 131.78, 130.52, 129.38, 128.58, 123.25, 114.40, 55.66.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{13}BrN_2O_3S$ 368.9908; found 368.9909.

4-chloro-N'-(3,5-dibromo-2-hydroxybenzylidene)benzenesulfonohydrazide (38)

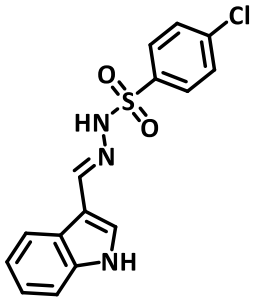


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.22 (s, 1H), 10.99 (s, 1H), 8.14 (s, 1H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.80 (s, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.66 (s, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 152.68, 146.60, 138.56, 137.19, 135.92, 130.85, 129.83, 129.02, 121.72, 111.88, 111.14.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Br_2ClN_2O_3S$ 468.8447; found 468.8436

N'-((1H-indol-3-yl)methylene)-4-chlorobenzenesulfonohydrazide (39)

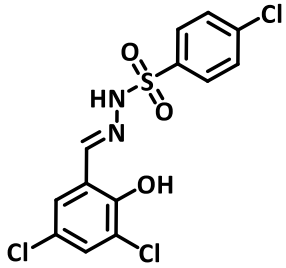


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.53 (s, 1H), 11.01 (s, 1H), 8.10 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 3H), 7.71 (dd, *J* = 14.0, 5.7 Hz, 3H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.20 – 7.09 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 145.73, 137.95, 137.73, 136.91, 130.71, 129.27, 129.22, 123.94, 122.60, 121.47, 120.59, 111.84, 110.90.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{12}ClN_3O_2S$ 334.0417; found 334.0418.

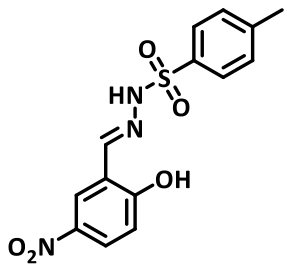
4-chloro-N'-(3,5-dichloro-2-hydroxybenzylidene)benzenesulfonohydrazide (40)



^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.13 (s, 1H), 10.83 (s, 1H), 8.17 (s, 1H), 7.87 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 2H), 7.59 (s, 1H), 7.50 (s, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 151.17, 145.69, 138.43, 137.25, 130.47, 129.74, 129.00, 126.53, 123.56, 122.10, 121.81.
HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Cl_3N_2O_3S$ 378.9477; found 378.9477.

N'-(2-hydroxy-5-nitrobenzylidene)-4-methylbenzenesulfonohydrazide (41)

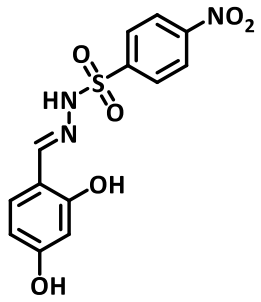


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.74 (s, 1H), 11.68 (s, 1H), 8.33 (d, *J* = 2.9 Hz, 1H), 8.19 (s, 1H), 8.12 (dd, *J* = 9.1, 2.9 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 9.1 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 161.81, 143.77, 142.05, 139.95, 135.95, 129.88, 127.14, 126.72, 121.91, 120.29, 116.88, 21.04.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{13}N_3O_5S$ 336.0654; found 336.0657

N'-(2,4-dihydroxybenzylidene)-4-nitrobenzenesulfonohydrazide (42)

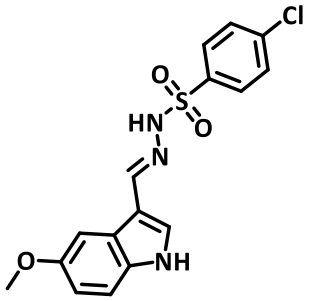


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.54 (s, 1H), 10.12 (s, 1H), 9.88 (s, 1H), 8.47 – 8.40 (m, 2H), 8.11 – 8.07 (m, 3H), 7.30 (d, *J* = 8.9 Hz, 1H), 6.31 – 6.22 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 160.94, 158.34, 149.96, 147.82, 144.21, 128.79, 124.65, 110.69, 107.90, 102.31.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}N_3O_6S$ 338.0447; found 338.0445

4-chloro-N'-((5-methoxy-1H-indol-3-yl)methylene)benzenesulfonohydrazide (43)

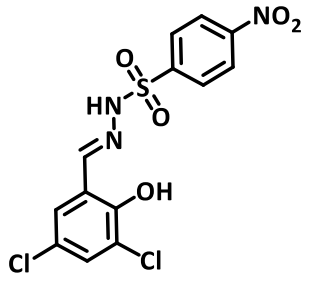


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.43 (s, 1H), 11.02 (s, 1H), 8.10 (s, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.6 Hz, 3H), 7.39 (s, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 6.80 (dd, *J* = 8.8, 2.4 Hz, 1H), 3.73 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 154.44, 146.42, 138.00, 137.80, 131.81, 131.16, 129.30, 129.28, 124.47, 112.69, 112.62, 110.67, 102.97, 55.15.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}ClN_3O_3S$ 364.0522; found 364.0521

N'-(3,5-dichloro-2-hydroxybenzylidene)-4-nitrobenzenesulfonohydrazide (44)

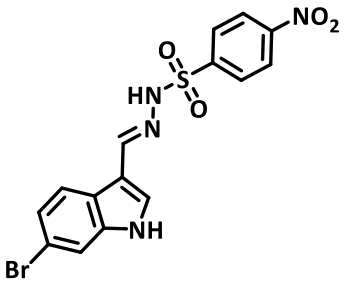


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.35 (s, 1H), 10.74 (s, 1H), 8.48 – 8.42 (m, 2H), 8.19 (s, 1H), 8.15 – 8.09 (m, 2H), 7.59 (d, *J* = 2.6 Hz, 1H), 7.51 (d, *J* = 2.5 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ) 151.14, 150.14, 145.70, 143.81, 130.56, 128.70, 126.16, 124.87, 123.65, 122.26, 122.08

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Cl_2N_3O_5S$ 389.9718; found 389.9719

N'-((6-bromo-1H-indol-3-yl)methylene)-4-nitrobenzenesulfonohydrazide (45)

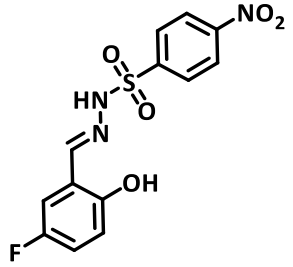


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.65 (s, 1H), 11.36 (s, 1H), 8.44 (d, *J* = 8.8 Hz, 2H), 8.21 – 8.09 (m, 3H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.78 (d, *J* = 2.7 Hz, 1H), 7.60 (d, *J* = 1.3 Hz, 1H), 7.30 (dd, *J* = 8.5, 1.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 149.88, 145.64, 144.33, 137.77, 131.75, 128.92, 124.46, 123.66, 123.08, 122.92, 115.29, 114.51, 110.90.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{15}H_{11}BrN_4O_4S$ 422.9763; found 422.9766

N'-(5-fluoro-2-hydroxybenzylidene)-4-nitrobenzenesulfonohydrazide (46)

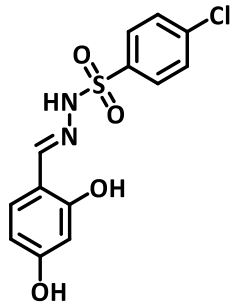


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.93 (s, 1H), 10.13 (s, 1H), 8.46 – 8.41 (m, 2H), 8.17 (s, 1H), 8.15 – 8.10 (m, 2H), 7.26 (dd, *J* = 9.4, 3.2 Hz, 1H), 7.09 (td, *J* = 8.6, 3.2 Hz, 1H), 6.85 (dd, *J* = 9.0, 4.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.58, 154.24, 152.81, 150.03, 144.32, 144.09, 128.82, 124.73, 120.26, 120.19, 118.54, 118.31, 117.61, 117.53, 111.44, 111.20.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}FN_3O_5S$ 340.0403; found 340.0401.

4-chloro-N'-(2,4-dihydroxybenzylidene)benzenesulfonohydrazide (47)

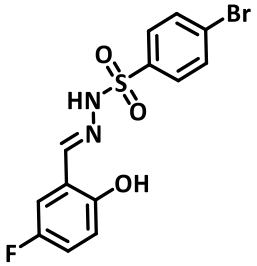


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.30 (s, 1H), 10.17 (s, 1H), 9.88 (s, 1H), 8.07 (s, 1H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 1H), 6.30 – 6.23 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 160.85, 158.38, 148.03, 138.05, 137.57, 129.49, 129.25, 129.11, 110.63, 107.87, 102.37.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}ClN_2O_4S$ 327.0206; found 327.0209.

4-bromo-N'-(5-fluoro-2-hydroxybenzylidene)benzenesulfonohydrazide (48)

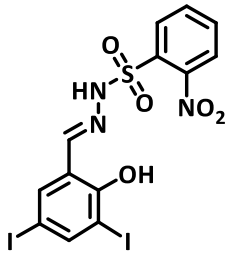


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.68 (s, 1H), 10.12 (s, 1H), 8.15 (s, 1H), 7.82 (dd, *J* = 26.1, 8.6 Hz, 4H), 7.23 (dd, *J* = 9.4, 3.2 Hz, 1H), 7.08 (td, *J* = 8.6, 3.2 Hz, 1H), 6.86 (dd, *J* = 9.0, 4.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.55, 154.21, 152.75, 152.74, 144.10, 137.99, 132.47, 129.15, 127.16, 120.24, 120.17, 118.36, 118.12, 117.59, 117.51, 111.61, 111.37.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}BrFN_2O_3S$ 372.9658; found 372.9658.

N'-(2-hydroxy-3,5-diiodobenzylidene)-2-nitrobenzenesulfonohydrazide (49)

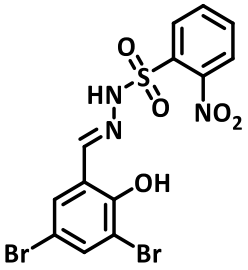


^{1}H NMR (400 MHz, CD_3CN-d_3, δ):11.17 (s, 1H), 9.93 (s, 1H), 8.17 – 8.12 (m, 1H), 8.07 (d, *J* = 2.1 Hz, 1H), 8.04 (s, 1H), 7.91 (ddd, *J* = 6.3, 3.6, 2.1 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.65 (d, *J* = 2.1 Hz, 1H).

^{13}C NMR (100 MHz, CD3CN-d_3 δ): 157.57, 150.82, 148.98, 140.92, 136.46, 134.12, 132.36, 131.41, 126.33, 120.30, 86.88, 81.58.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9I_2N_3O_5S$ 573.8431; found 573.8429.

N'-(3,5-dibromo-2-hydroxybenzylidene)-2-nitrobenzenesulfonohydrazide (50)

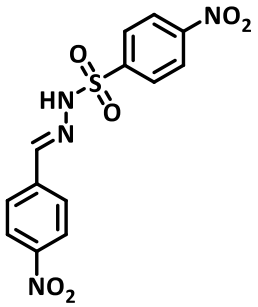


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.65 (s, 1H), 10.76 (s, 1H), 8.26 (s, 1H), 8.10 – 8.01 (m, 2H), 7.96 – 7.88 (m, 2H), 7.80 (d, *J* = 2.3 Hz, 1H), 7.69 (d, *J* = 2.4 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 152.55, 147.82, 145.99, 135.93, 135.17, 132.92, 130.59, 130.47, 130.24, 124.77, 122.14, 112.12, 111.22.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Br_2N_3O_5S$ 479.8687; found 479.8680.

4-nitro-N'-(4-nitrobenzylidene)benzenesulfonohydrazide (51)

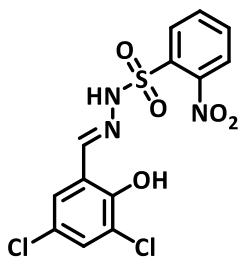


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.32 (s, 1H), 8.46 – 8.41 (m, 2H), 8.23 (d, *J* = 8.6 Hz, 2H), 8.18 – 8.13 (m, 2H), 8.08 (s, 1H), 7.88 – 7.83 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 150.07, 148.04, 145.79, 144.04, 139.47, 128.81, 127.95, 124.73, 124.02.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}N_4O_6S$ 351.0399; found 351.0398

N'-(3,5-dichloro-2-hydroxybenzylidene)-2-nitrobenzenesulfonohydrazide (52)

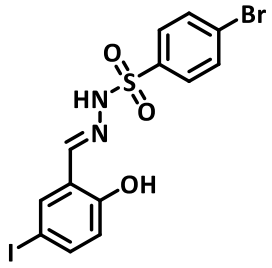


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.58 (s, 1H), 10.66 (s, 1H), 8.29 (s, 1H), 8.05 (ddd, *J* = 9.3, 4.7, 2.2 Hz, 2H), 7.97 – 7.86 (m, 2H), 7.55 (dd, *J* = 29.4, 2.5 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 151.09, 147.80, 145.12, 135.11, 132.85, 130.58, 130.49, 130.33, 126.14, 124.70, 123.63, 122.29, 122.21.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Cl_2N_3O_5S$ 389.9718; found 389.9718.

4-bromo-N'-(2-hydroxy-5-iodobenzylidene)benzenesulfonohydrazide (53)

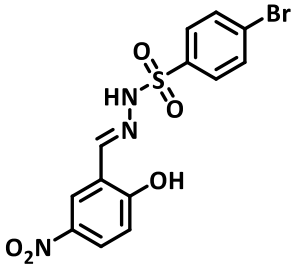


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.72 (s, 1H), 10.42 (s, 1H), 8.10 (s, 1H), 7.85 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.51 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.17, 143.75, 139.58, 138.06, 134.27, 132.52, 129.09, 127.18, 122.04, 118.90, 81.59.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}BrIN_2O_3S$ 480.8718; found 480.8718.

4-bromo-N'-(2-hydroxy-5-nitrobenzylidene)benzenesulfonohydrazide (54)

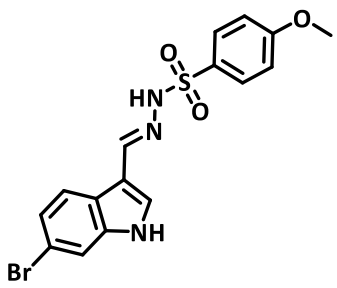


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.80 (d, *J* = 73.7 Hz, 2H), 8.33 (d, *J* = 2.9 Hz, 1H), 8.21 (s, 1H), 8.13 (dd, *J* = 9.0, 2.9 Hz, 1H), 7.89 – 7.75 (m, 4H), 7.04 (d, *J* = 9.1 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 161.83, 142.45, 139.94, 138.06, 132.57, 129.09, 127.24, 126.83, 121.77, 120.21, 116.87.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}BrN_3O_5S$ 399.9603; found 399.9600

N'-((6-bromo-1H-indol-3-yl)methylene)-4-methoxybenzenesulfonohydrazide (55)

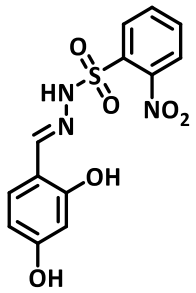


^{1}H NMR (400 MHz, DMSO- $d_{6,}$ δ): 11.60 (s, 1H), 10.85 (s, 1H), 8.05 (d, *J* = 2.0 Hz, 1H), 7.87 (ddd, *J* = 24.4, 8.7, 2.0 Hz, 3H), 7.74 (d, *J* = 2.3 Hz, 1H), 7.59 (s, 1H), 7.31 – 7.26 (m, 1H), 7.12 (dd, *J* = 6.9, 5.0 Hz, 2H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, DMSO-$d_{6,}$ δ): 162.49, 144.27, 137.77, 131.14, 130.69, 129.52, 123.43, 123.19, 123.02, 115.24, 114.46, 114.24, 111.24, 55.64.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{14}BrN_3O_3S$ 408.0017; found 408.0030

N'-(2,4-dihydroxybenzylidene)-2-nitrobenzenesulfonohydrazide (56)

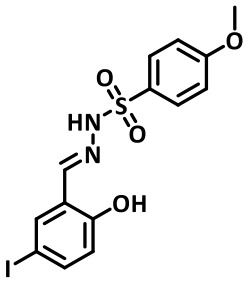


^{1}H NMR (400 MHz, DMSO-$d_{6,}$ δ): 11.78 (s, 1H), 10.05 (s, 1H), 9.87 (s, 1H), 8.21 (s, 1H), 8.04 – 7.98 (m, 1H), 7.91 – 7.86 (m, 1H), 7.30 – 7.25 (m, 1H), 6.28 – 6.23 (m, 1H).

^{13}C NMR (100 MHz, DMSO-$d_{6,}$ δ): 160.95, 158.35, 148.00, 147.56, 134.74, 132.59, 130.85, 130.35, 128.94, 110.68, 107.91, 102.35.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}N_3O_6S$ 338.0447; found 338.0453

N'-(2-hydroxy-5-iodobenzylidene)-4-methoxybenzenesulfonohydrazide (57)

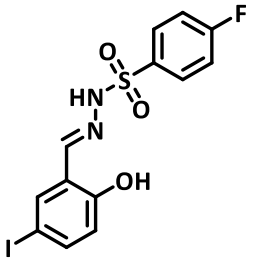


^{1}H NMR (400 MHz, DMSO- d_6, δ): 11.49 (s, 1H), 10.43 (s, 1H), 8.07 (s, 1H), 7.79 – 7.75 (m, 2H), 7.73 (d, *J* = 2.3 Hz, 1H), 7.50 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.16 – 7.11 (m, 2H), 6.69 (d, *J* = 8.6 Hz, 1H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6 δ): 162.73, 156.12, 143.43, 139.37, 134.59, 130.30, 129.31, 122.09, 118.88, 114.53, 81.53, 55.70

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{13}IN_2O_4S$ 432.9719; found 432.9724.

4-fluoro-N'-(2-hydroxy-5-iodobenzylidene)benzenesulfonohydrazide (58)

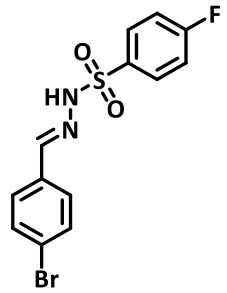


^{1}H NMR (400 MHz, CD_3CN-d_3, δ): 10.30 (s, 1H), 9.80 (s, 1H), 7.98 – 7.91 (m, 3H), 7.65 – 7.51 (m, 2H), 7.41 – 7.22 (m, 2H), 6.71 (d, *J* = 8.7 Hz, 1H).

^{13}C NMR (100 MHz, CD_3CN-d_3, δ): 158.49, 156.36, 150.83, 141.20, 140.07, 135.20, 131.70, 131.64, 131.57, 120.95, 120.11, 120.07, 117.76, 117.51, 117.50, 80.96.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}FIN_2O_3S$ 420.9519; found 420.9521

N'-(4-bromobenzylidene)-4-fluorobenzenesulfonohydrazide (59)

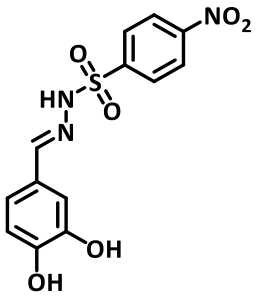


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.65 (s, 1H), 7.93 (ddd, *J* = 8.4, 5.2, 2.7 Hz, 3H), 7.64 – 7.56 (m, 2H), 7.55 – 7.49 (m, 2H), 7.49 – 7.41 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 165.74, 163.24, 146.30, 135.26, 135.23, 133.40, 132.80, 132.08, 131.81, 130.32, 130.22, 128.68, 123.45, 116.62, 116.40.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}BrFN_2O_2S$ 356.9708; found 356.9708.

N'-(3, 4-dihydroxybenzylidene)-4-nitrobenzenesulfonohydrazide (60)

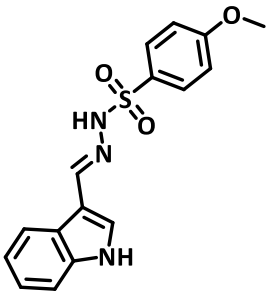


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.52 (s, 1H), 9.42 (s, 1H), 9.19 (s, 1H), 8.50 – 8.38 (m, 2H), 8.17 – 8.04 (m, 2H), 7.77 (s, 1H), 7.02 (d, *J* = 1.9 Hz, 1H), 6.89 – 6.64 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 150.00, 149.15, 148.24, 145.69, 144.51, 128.82, 124.83, 124.60, 120.52, 115.53, 112.65.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{11}N_3O_6S$ 338.0447; found 338.0454.

N'-((1H-indol-3-yl)methylene)-4-methoxybenzenesulfonohydrazide (61)

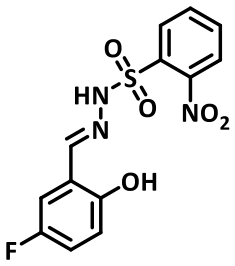


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.49 (s, 1H), 10.76 (s, 1H), 8.08 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 2H), 7.70 (d, *J* = 2.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.13 (ddd, *J* = 10.3, 9.0, 4.5 Hz, 4H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 162.44, 144.93, 136.90, 130.84, 130.35, 129.49, 124.01, 122.56, 121.59, 120.49, 114.19, 111.79, 111.11, 55.62.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{16}H_{15}N_3O_3S$ 330.0912; found 330.0911.

N'-(5-fluoro-2-hydroxybenzylidene)-2-nitrobenzenesulfonohydrazide (62)

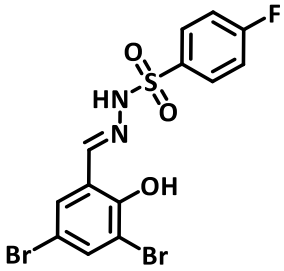


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.27 – 12.02 (m, 1H), 10.11 (s, 1H), 8.29 (d, *J* = 1.5 Hz, 1H), 8.14 – 7.97 (m, 2H), 7.95 – 7.83 (m, 2H), 7.23 (dd, *J* = 9.4, 3.2 Hz, 1H), 7.08 (td, *J* = 8.6, 3.2 Hz, 1H), 6.86 (dd, *J* = 9.0, 4.7 Hz, 1H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 156.57, 154.23, 152.83, 147.88, 143.92, 134.91, 132.66, 130.71, 130.56, 124.53, 120.34, 120.26, 118.47, 118.24, 117.64, 117.55, 111.44, 111.20.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}FN_3O_5S$ 340.0403; found 340.0410

N'-(3,5-dibromo-2-hydroxybenzylidene)-4-fluorobenzenesulfonohydrazide (63)

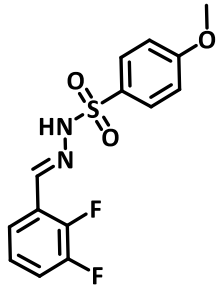


^{1}H NMR (400 MHz, DMSO-d_6, δ): 12.15 (s, 1H), 11.01 (s, 1H), 8.14 (s, 1H), 7.93 (dd, *J* = 8.8, 5.1 Hz, 2H), 7.79 (s, 1H), 7.67 (d, *J* = 2.1 Hz, 1H), 7.50 (t, *J* = 8.8 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 165.98, 163.47, 152.65, 146.49, 135.84, 134.70, 134.68, 130.87, 130.24, 130.14, 121.66, 116.99, 116.76, 111.80, 111.08.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_9Br_2FN_2O_3S$ 450.8763; found 450.8761

N'-(2,3-difluorobenzylidene)-4-methoxybenzenesulfonohydrazide (64)

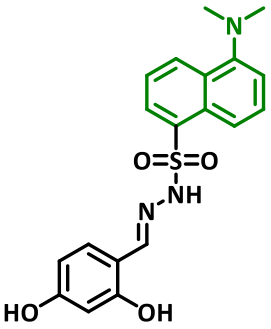


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.70 (s, 1H), 8.06 (s, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.52 – 7.40 (m, 2H), 7.23 (dd, *J* = 13.0, 6.8 Hz, 1H), 7.13 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 162.80, 151.20, 151.08, 149.59, 149.45, 148.76, 148.64, 147.08, 146.94, 138.51, 130.38, 129.46, 125.30, 125.25, 125.23, 125.18, 123.62, 123.55, 121.52, 121.50, 118.67, 118.51, 114.55, 55.74.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{14}H_{12}F_2N_2O_3S$ 327.0615; found 327.0620

N'-(2,4-dihydroxybenzylidene)-5-(dimethylamino)naphthalene-1-sulfonohydrazide (65)

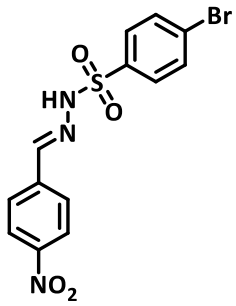


^{1}H NMR (400 MHz, DMSO-d_6, δ): 11.66 (s, 1H), 10.08 (t, *J* = 1.5 Hz, 1H), 9.82 (s, 1H), 8.49 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 8.7 Hz, 1H), 8.26 – 8.17 (m, 1H), 8.04 (s, 1H), 7.71 – 7.58 (m, 2H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 6.25 – 6.17 (m, 2H), 2.80 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6, δ): 160.57, 158.18, 151.40, 146.28, 134.53, 130.25, 129.81, 129.23, 129.18, 129.01, 128.10, 123.71, 119.00, 115.31, 110.66, 107.76, 102.34, 45.07.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{19}H_{19}N_3O_4S$ 386.1174; found 386.1169

4-bromo-N'-(4-nitrobenzylidene)benzenesulfonohydrazide (66)



^{1}H NMR (400 MHz, CD_3CN-d_3, δ): 9.53 (s, 1H), 9.53 (s, 1H), 9.53 (s, 1H), 8.20 (d, *J* = 8.8 Hz, 2H), 7.93 (s, 1H), 7.86 – 7.82 (m, 2H), 7.80 – 7.72 (m, 4H).

^{13}C NMR (101 MHz, CD_3CN-d_3, δ): 149.69, 146.70, 140.56, 138.74, 133.44, 130.46, 128.81, 124.94.

HRMS (ESI-TOF): m/z: [M + H] calculated for $C_{13}H_{10}BrN_3O_4S$ 383.9653; found 383.9656.

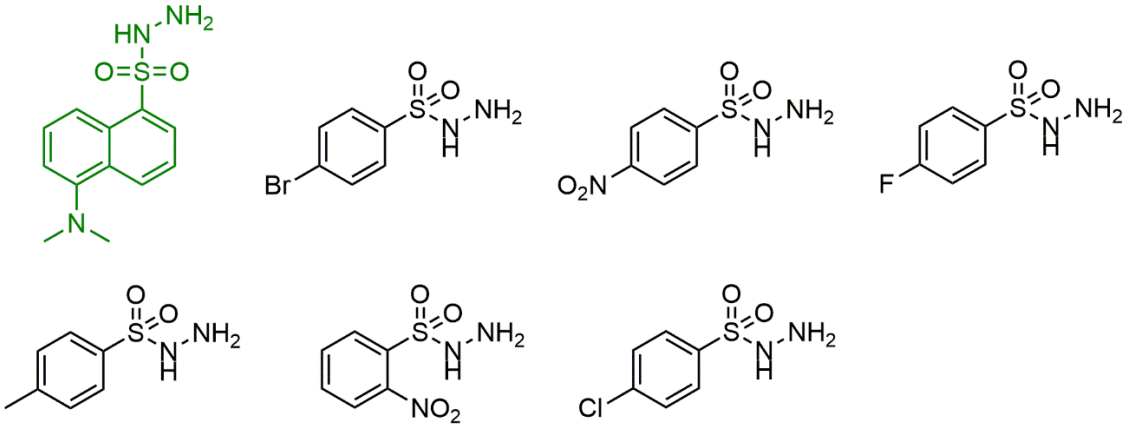
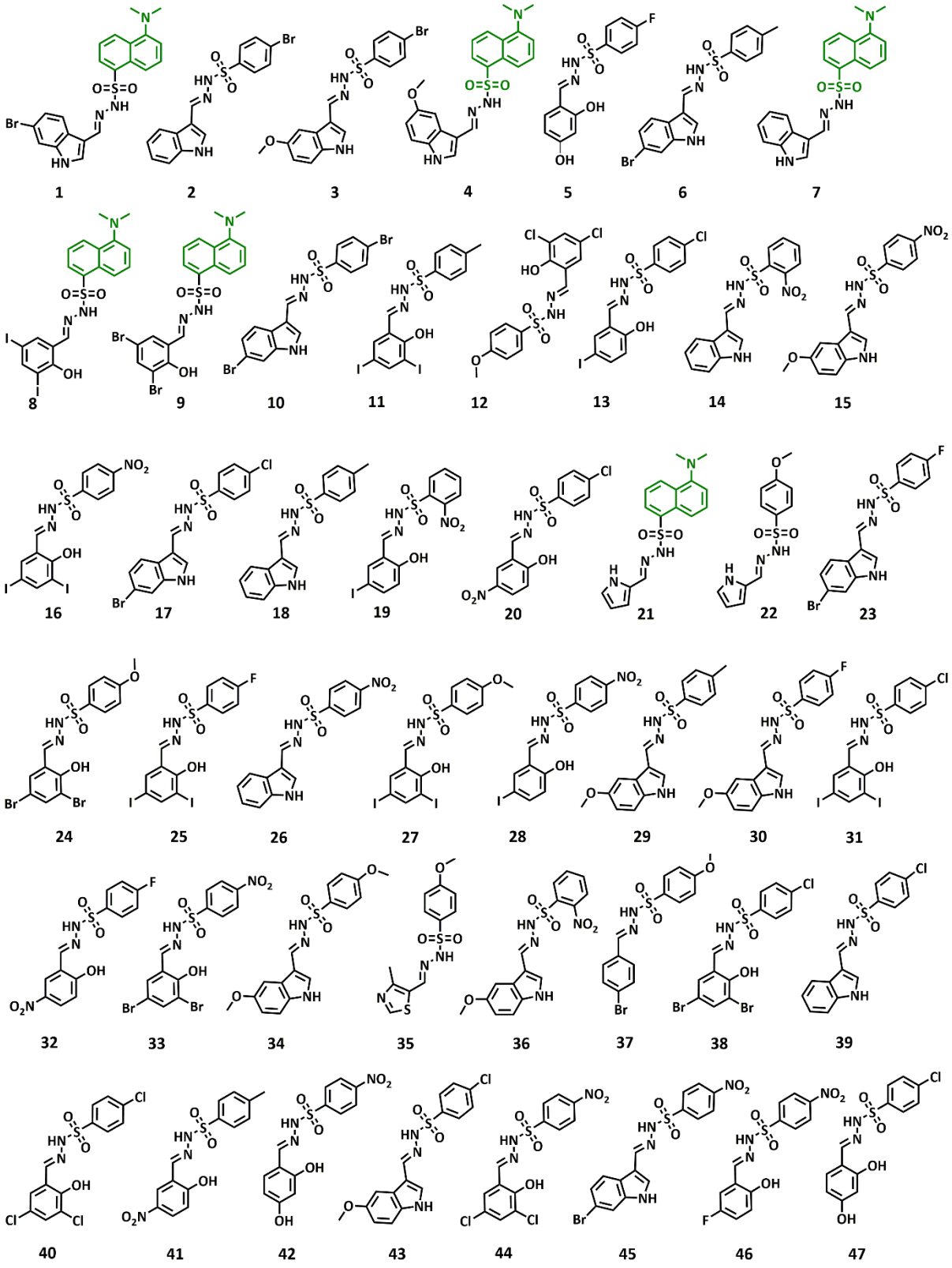


Fig. S1: Structure of synthesised sulfonohydrazides.



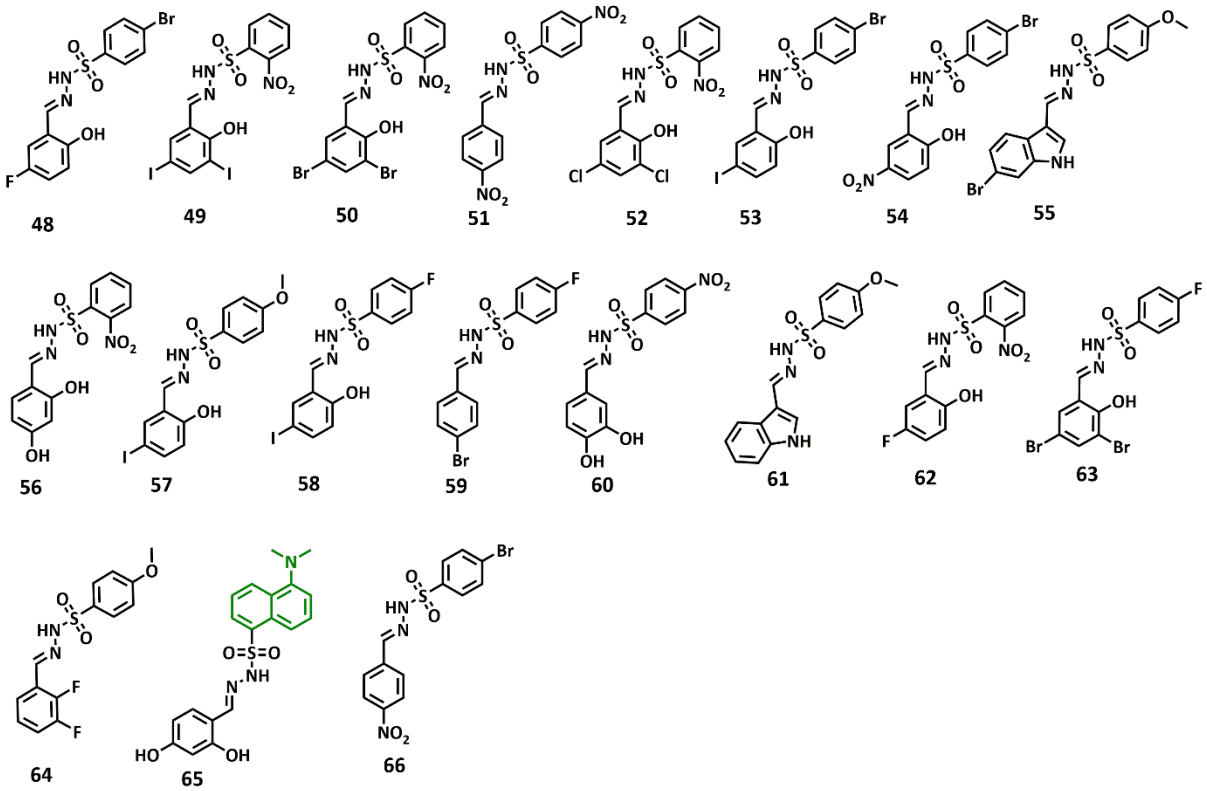


Fig. S2: Structure of 66 sulfonohydrazide- hydrazone based small molecules.

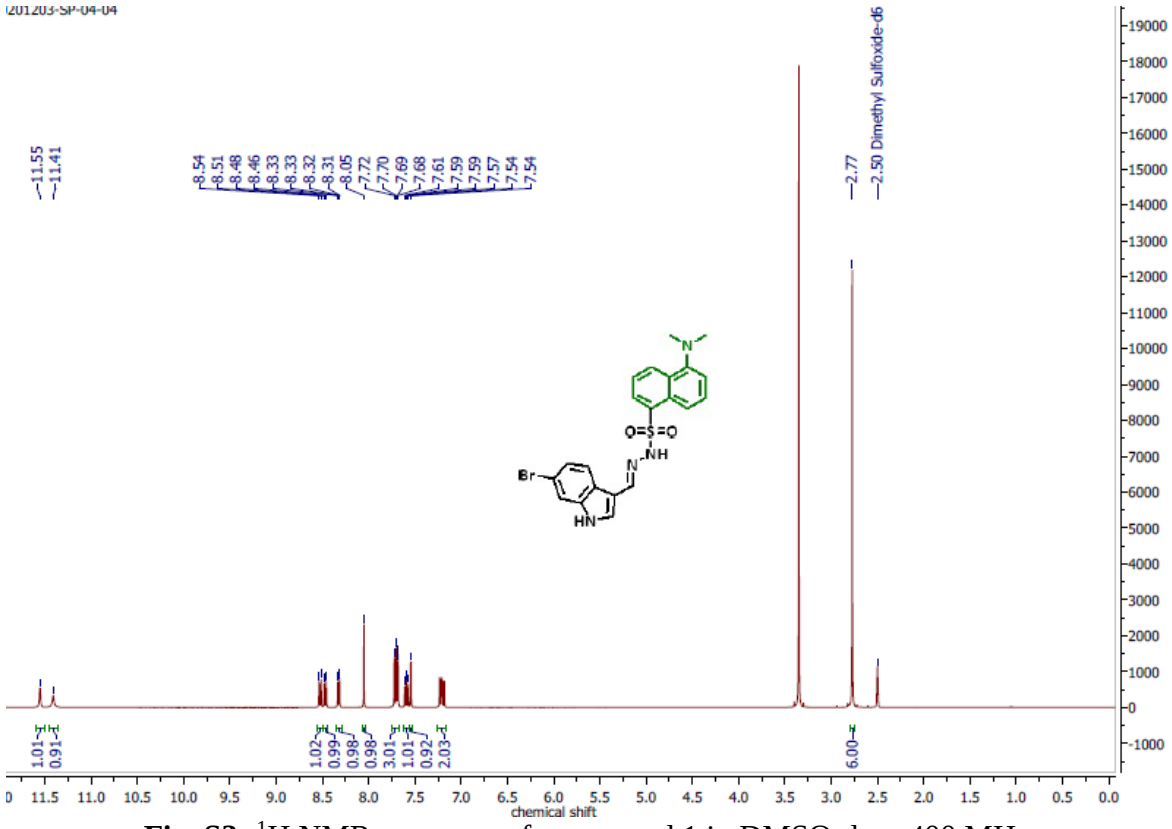


Fig. S3: ^{1}H NMR spectrum of compound 1 in DMSO-d_6 at 400 MHz.

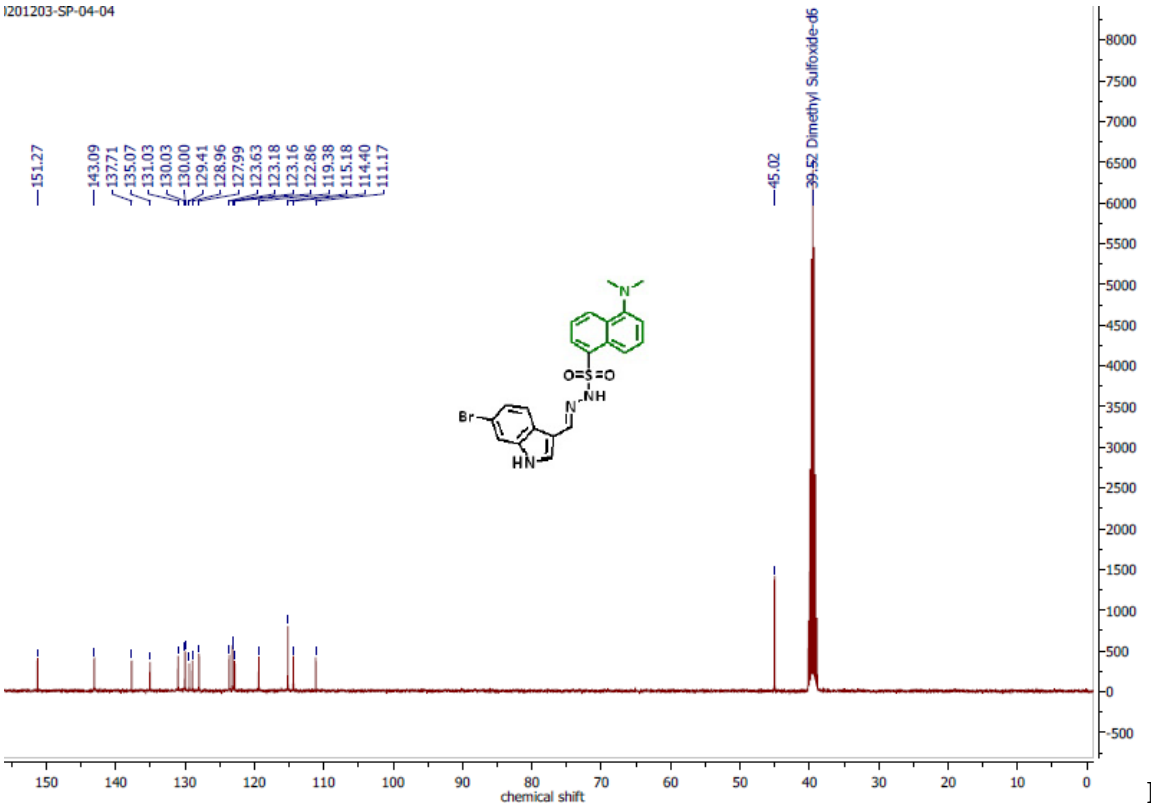


Fig. S4: ^{13}CNMR spectrum of compound 1 in DMSO-d_6 at 100 MHz.

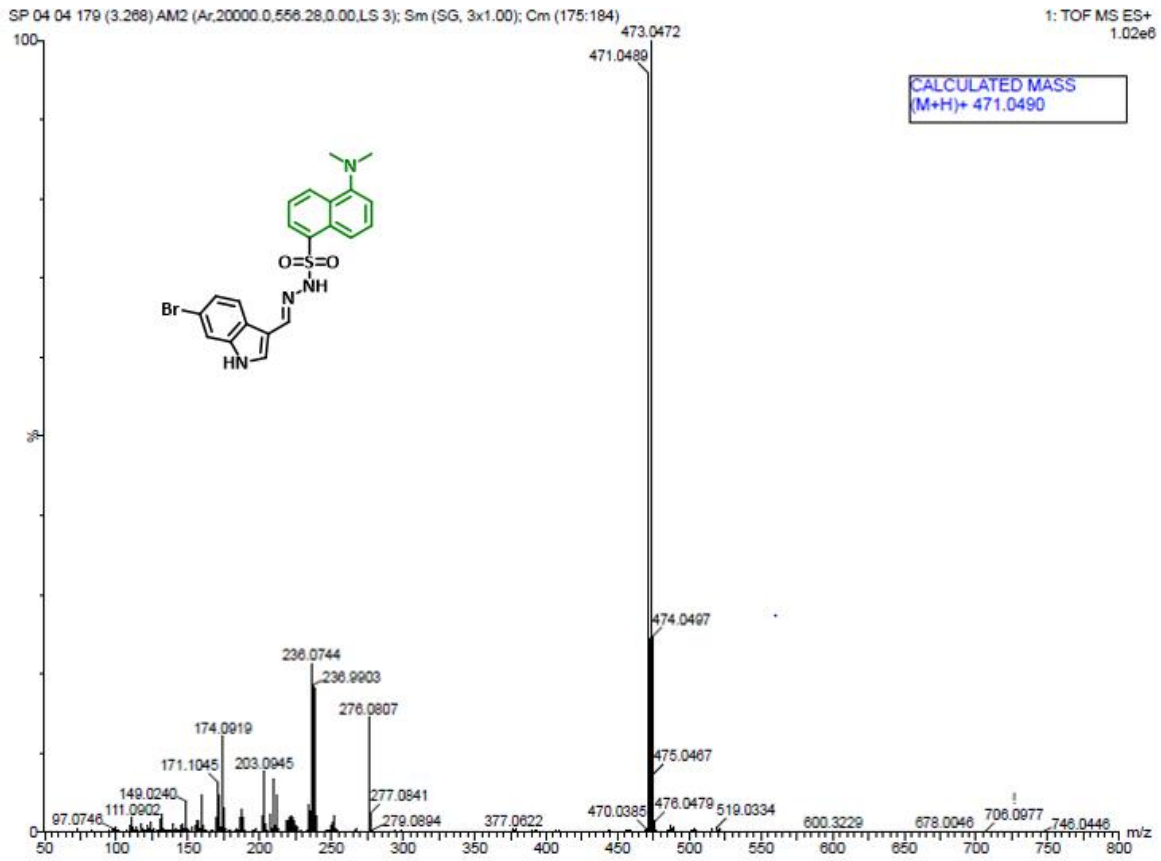


Fig. S5: HRMS spectrum of compound 1

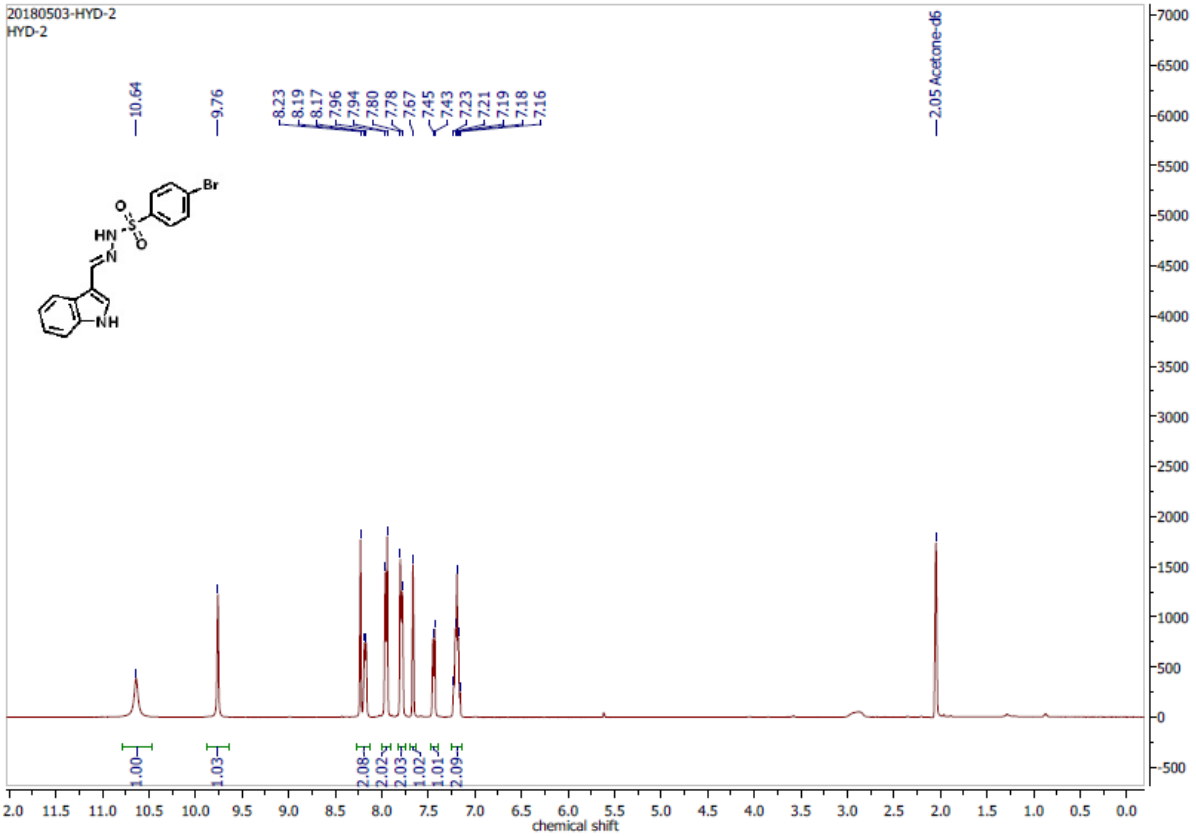


Fig. S6: ^{1}H NMR spectrum of compound 2 in Acetone-d_6 at 400 MHz.

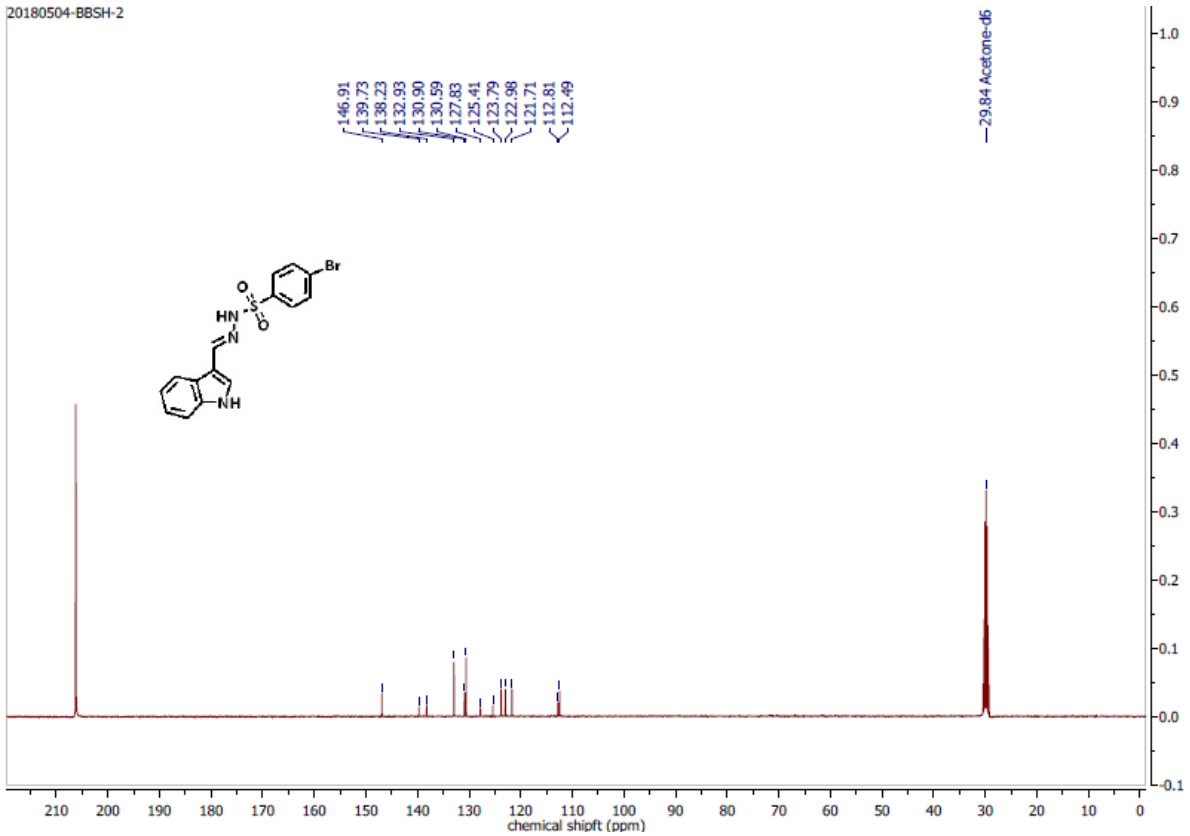


Fig. S7: ^{13}C NMR spectrum of compound 2 in Acetone-d_6 at 100 MHz.

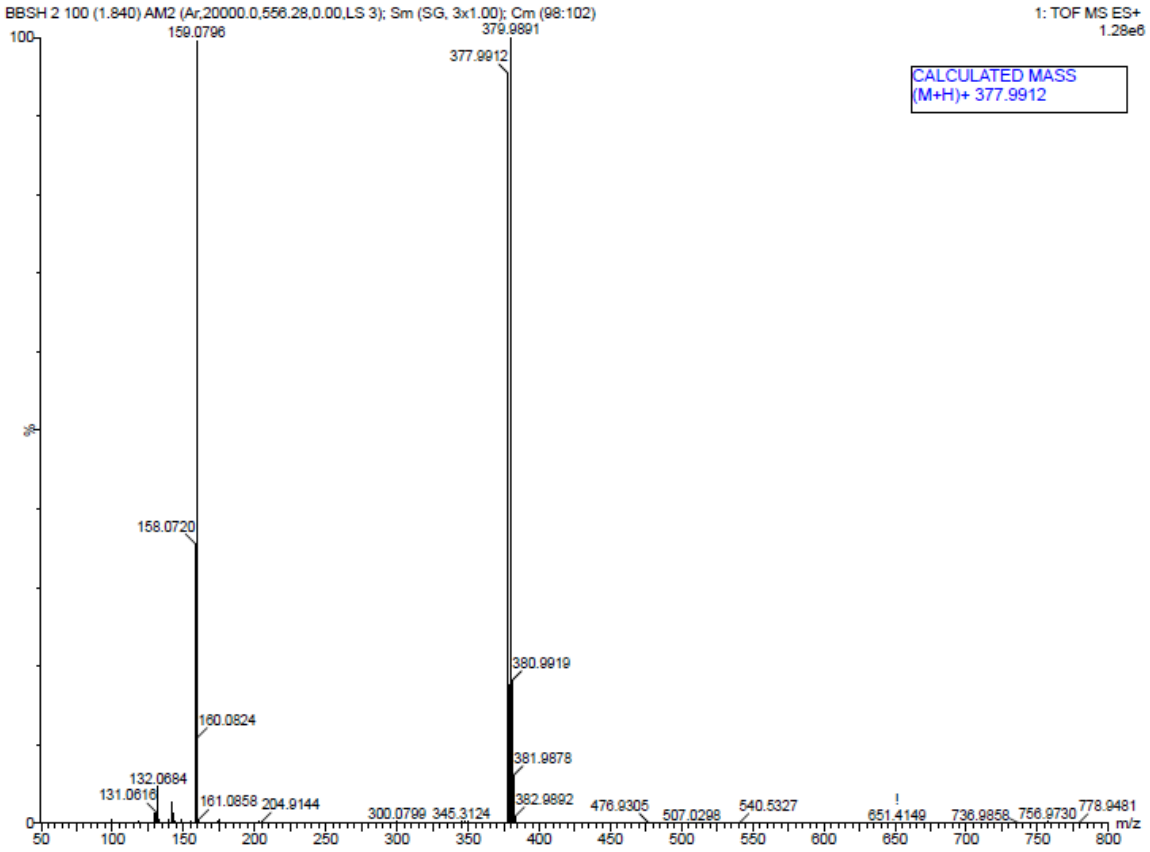


Fig. S8: HRMS spectrum of compound 2.

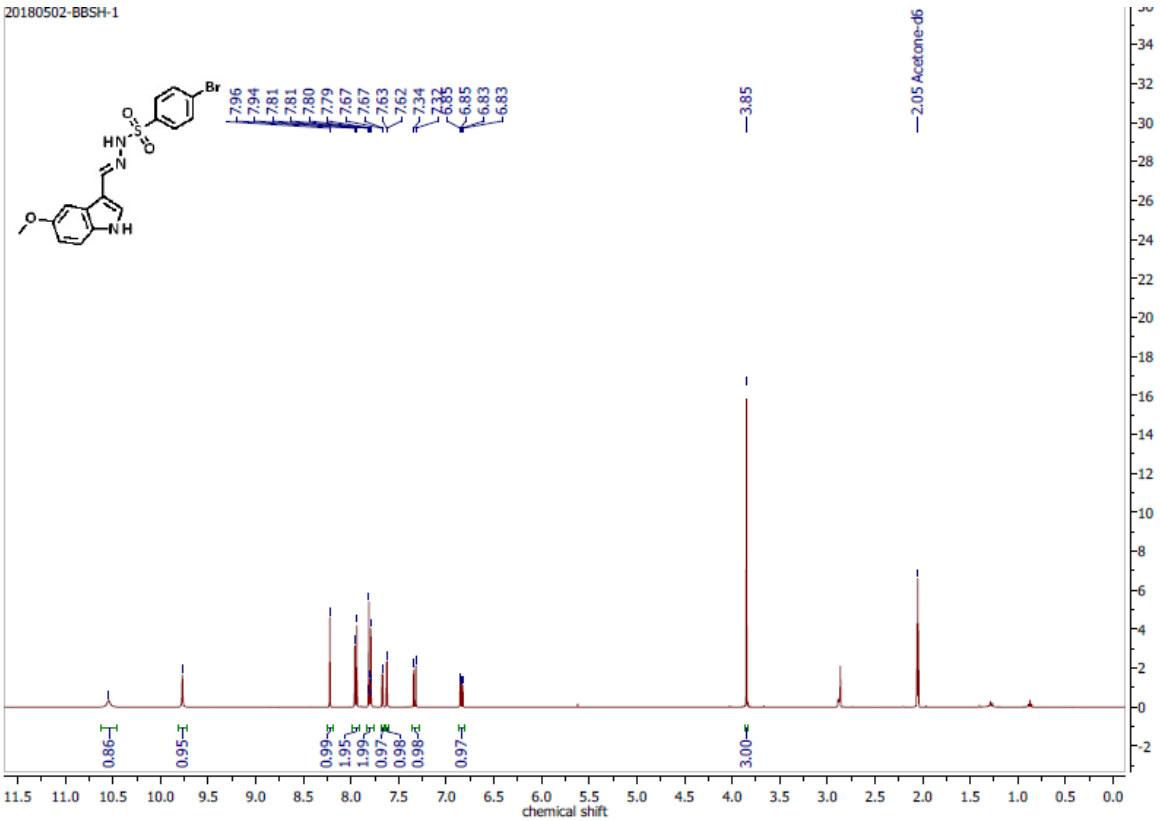


Fig. S9: ^{1}H NMR spectrum of compound 3 in Acetone-d_6 at 400 MHz.

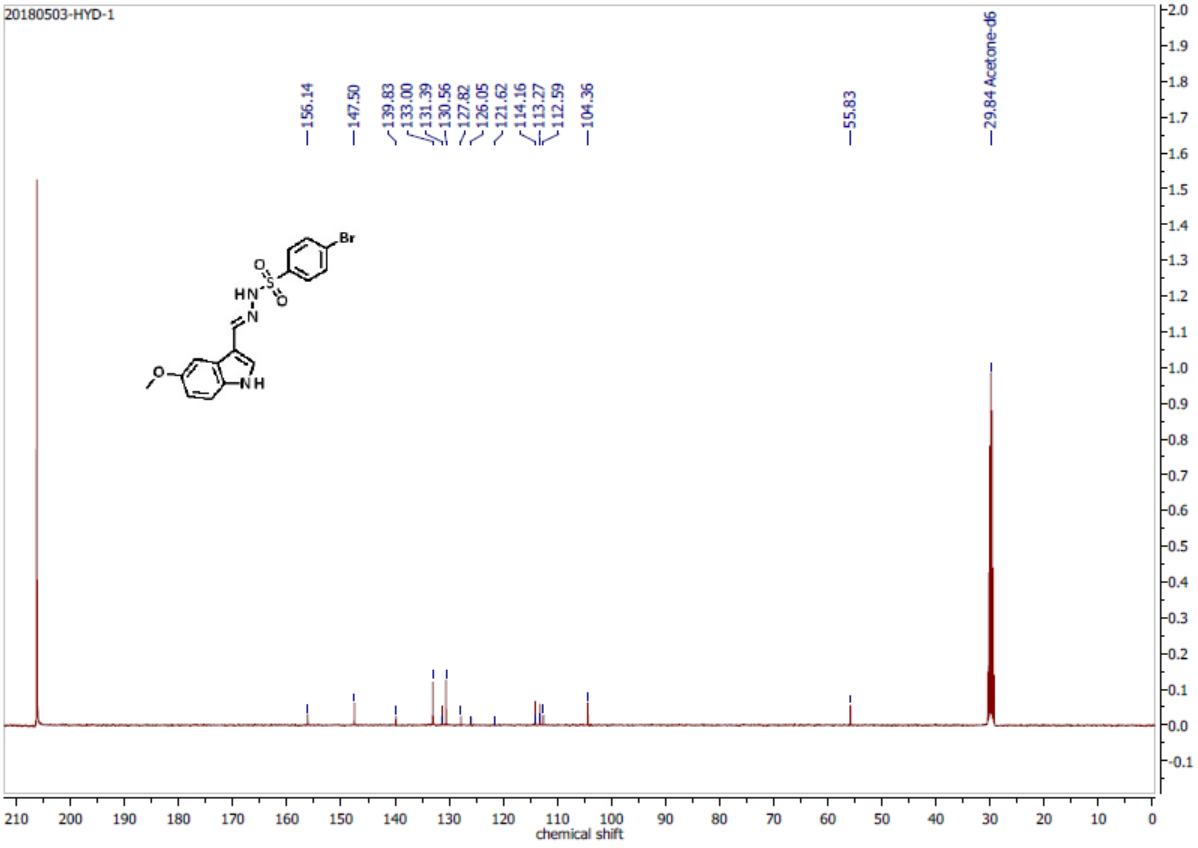


Fig. S10: ^{13}C NMR spectrum of compound 3 in Acetone-d_6 at 100 MHz.

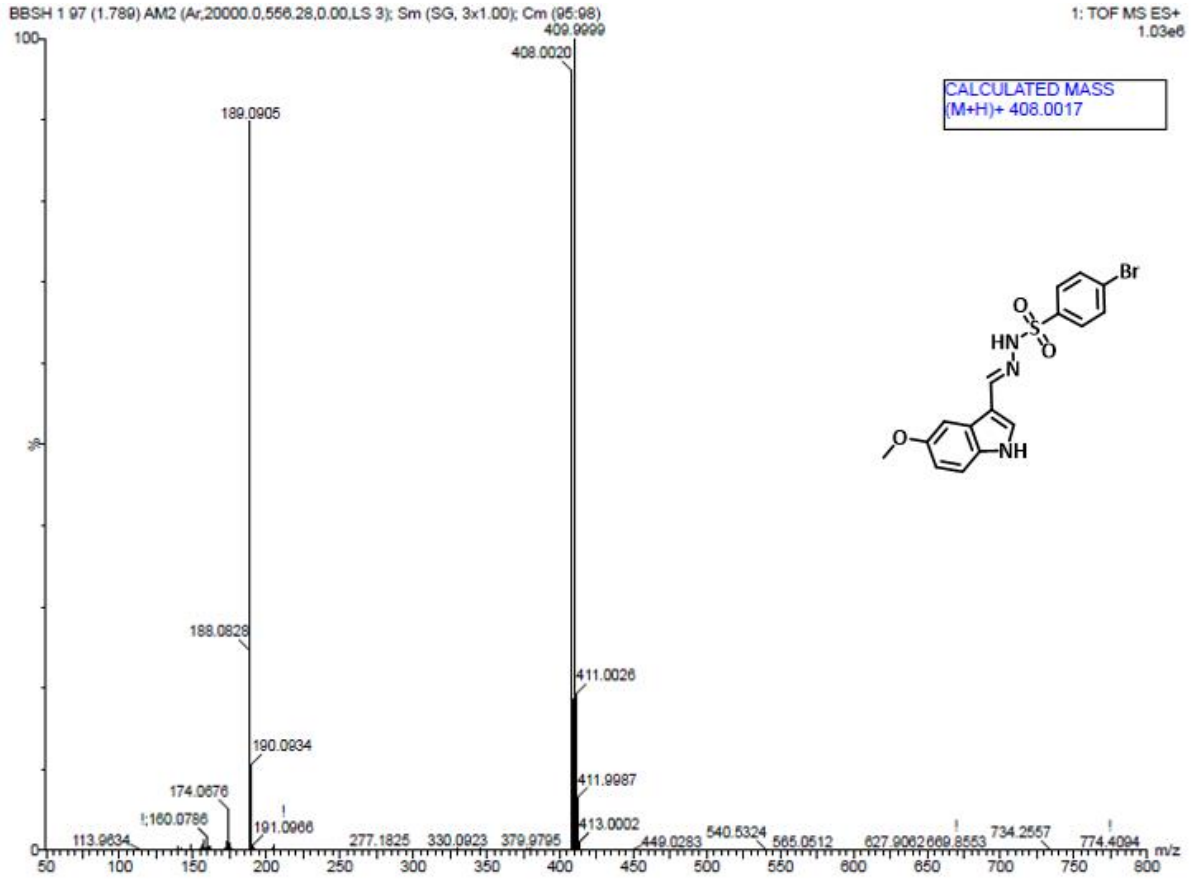


Fig. S11: HRMS spectrum of compound 3.

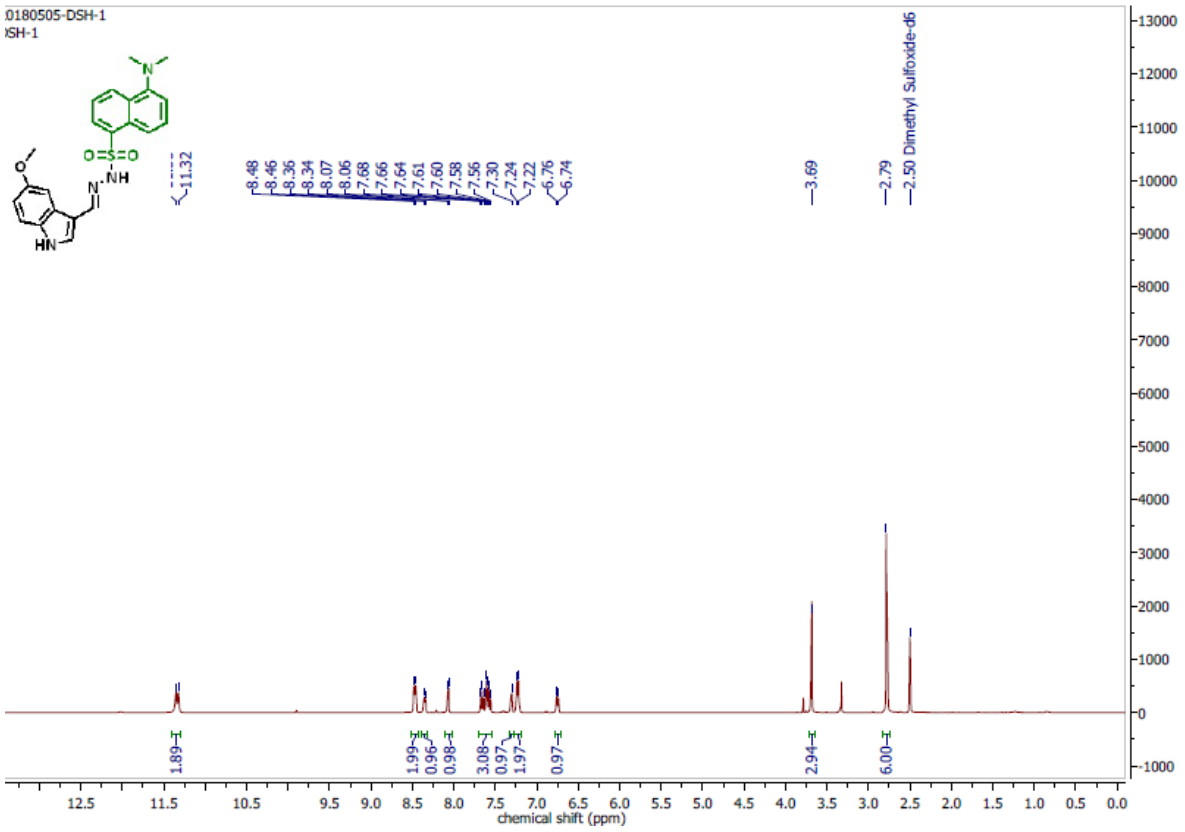


Fig. S12: ^{1}H NMR spectrum of compound 4 in DMSO-d_6 at 400 MHz.

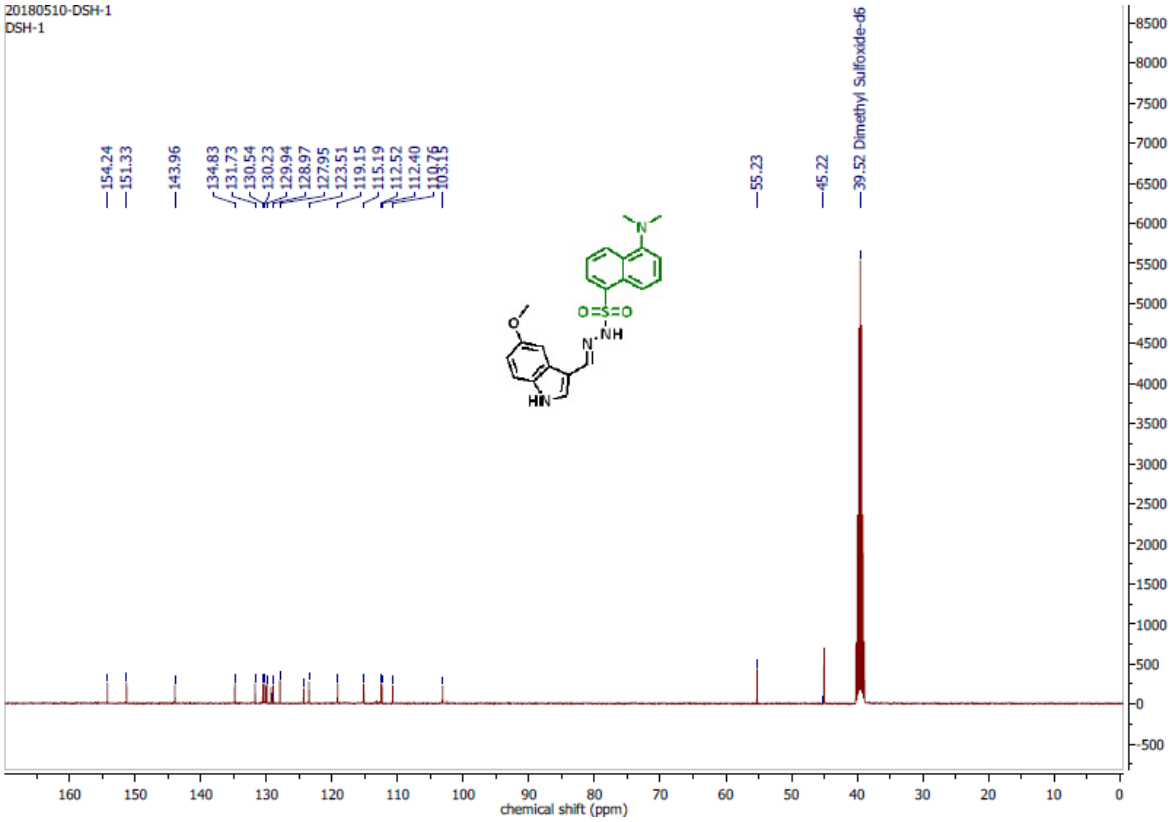


Fig. S13: ^{13}C NMR spectrum of compound 4 in DMSO-d_6 at 100 MHz.

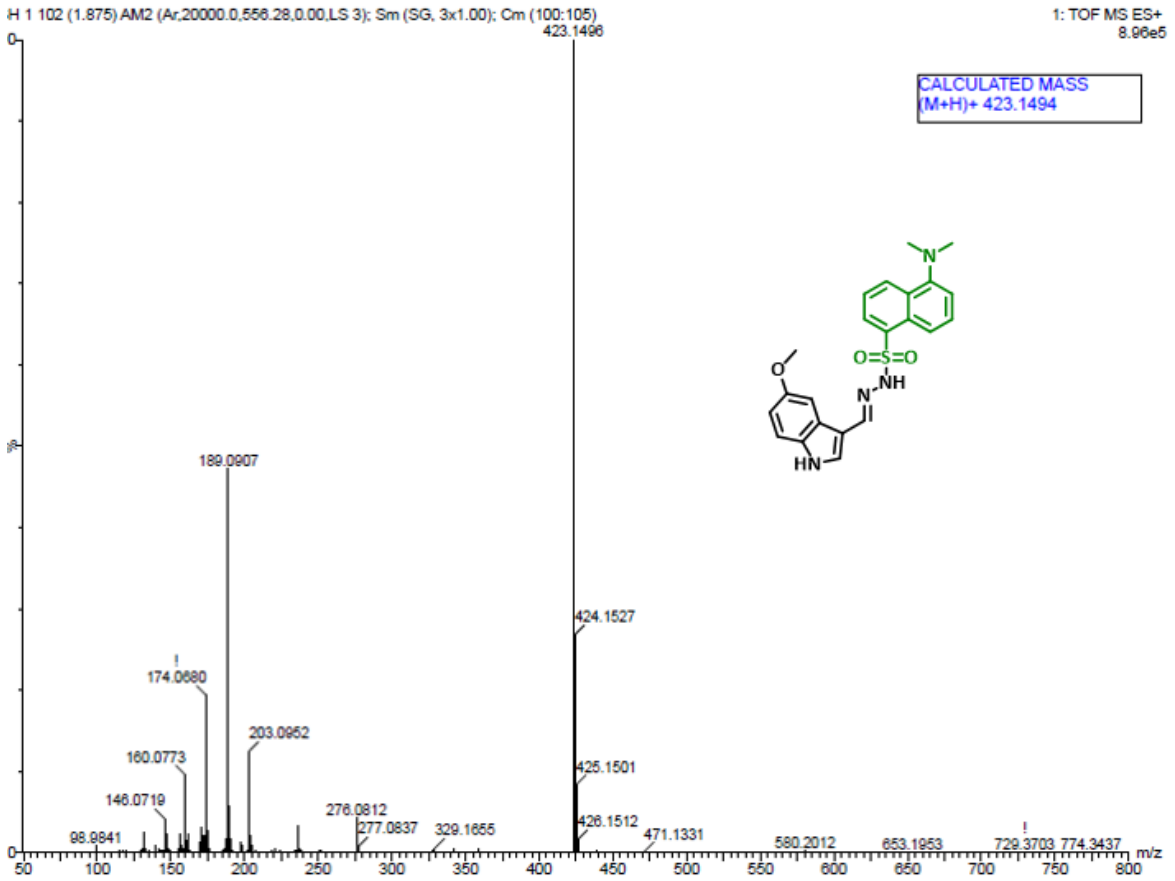


Fig. S14: HRMS spectrum of compound 4.

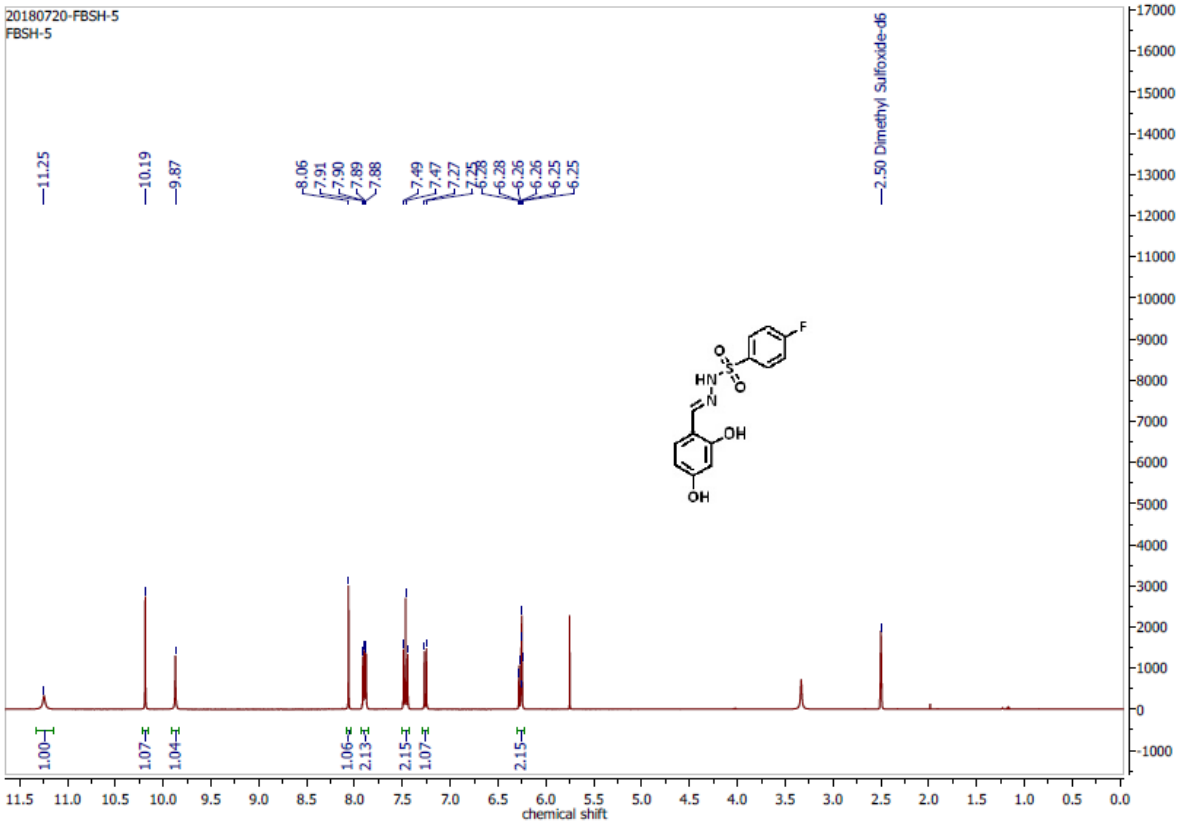


Fig. S15: ^{1}H NMR spectrum of compound 5 in DMSO-d_6 at 400 MHz.

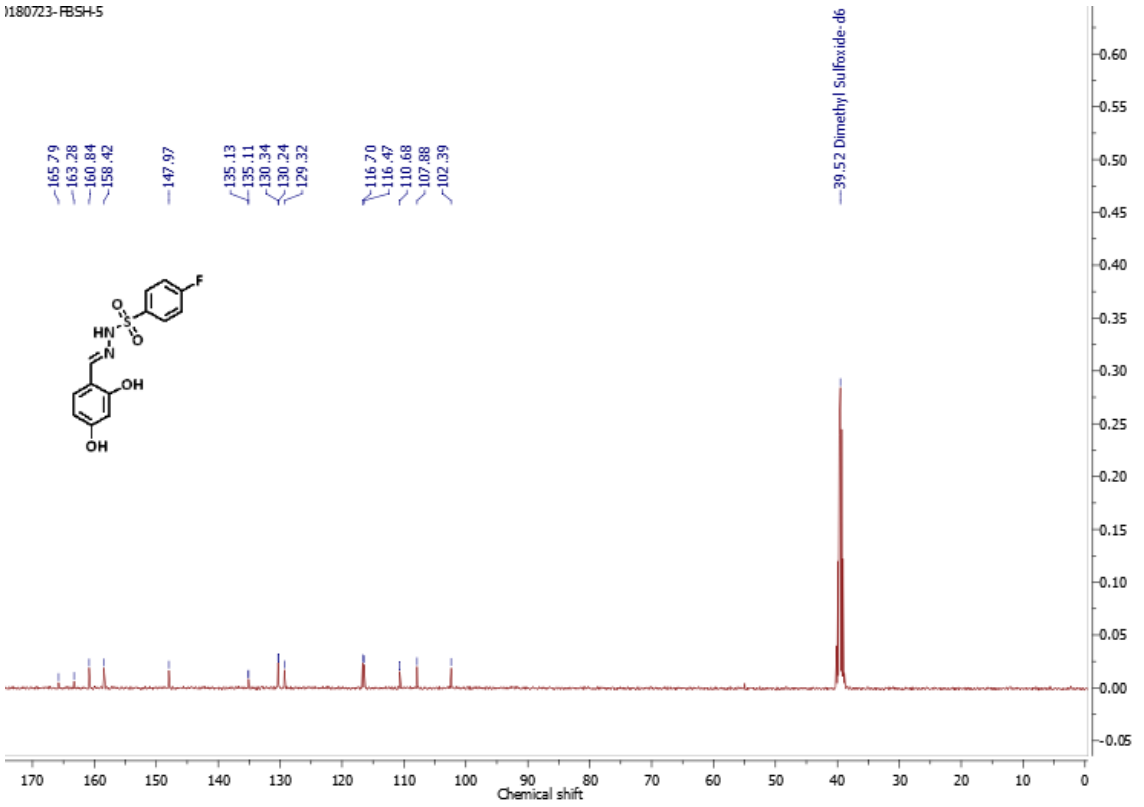


Fig. S16: ^{13}C NMR spectrum of compound 5 in DMSO-d_6 at 100 MHz.

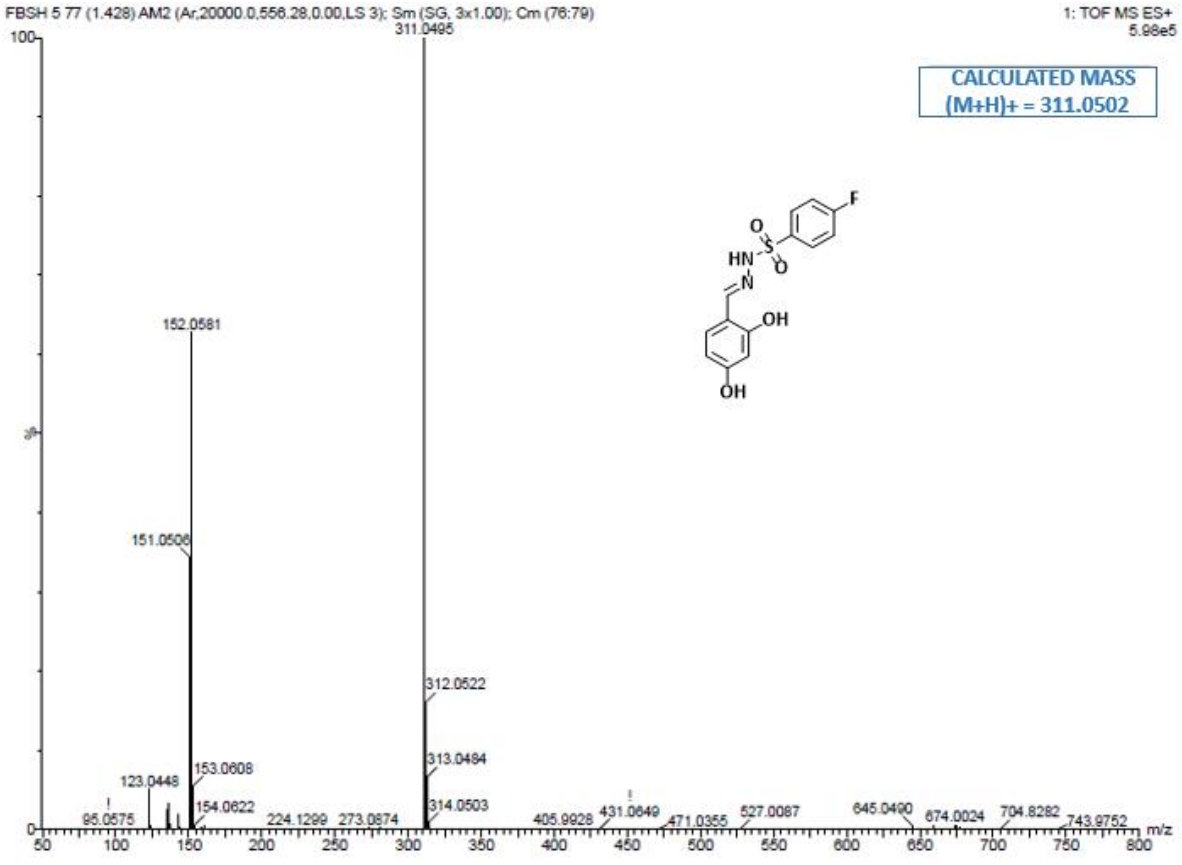


Fig. S17: HRMS spectrum of compound 5.

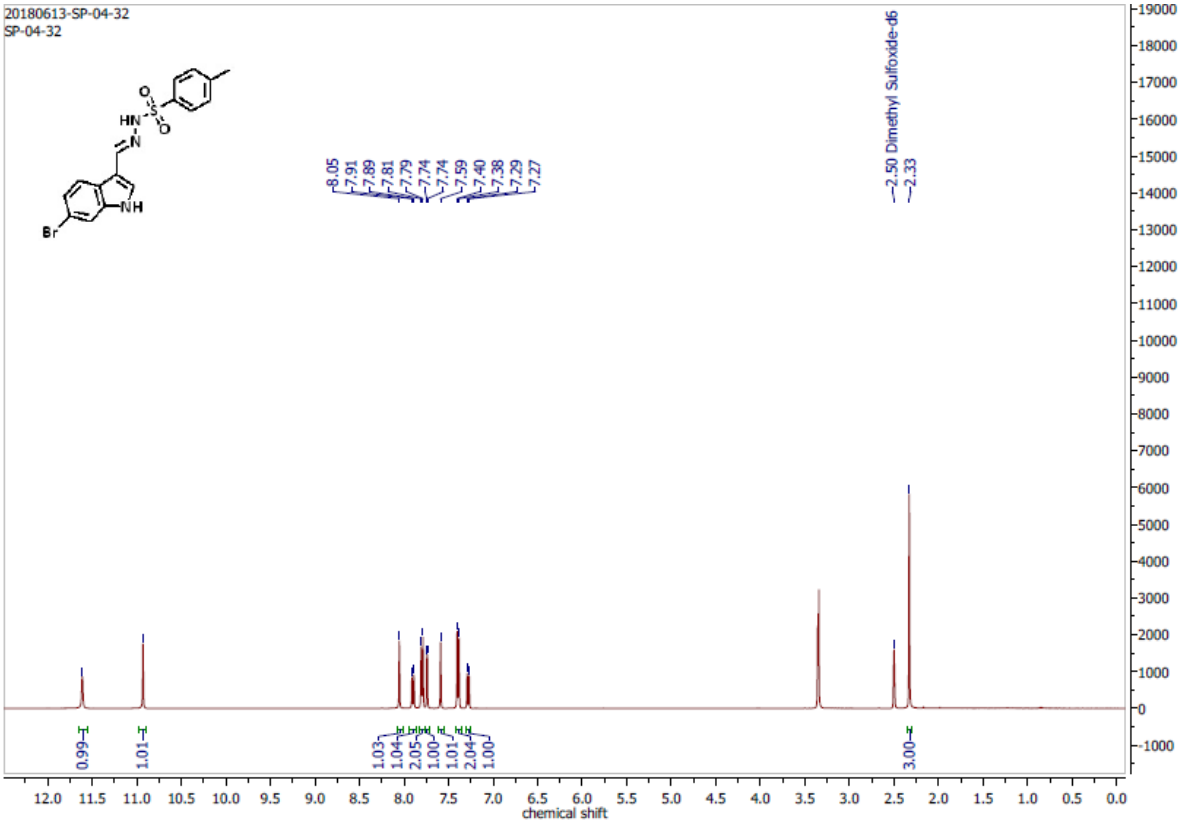


Fig. S18: ^{1}H NMR spectrum of compound 6 in DMSO-d_6 at 400 MHz.

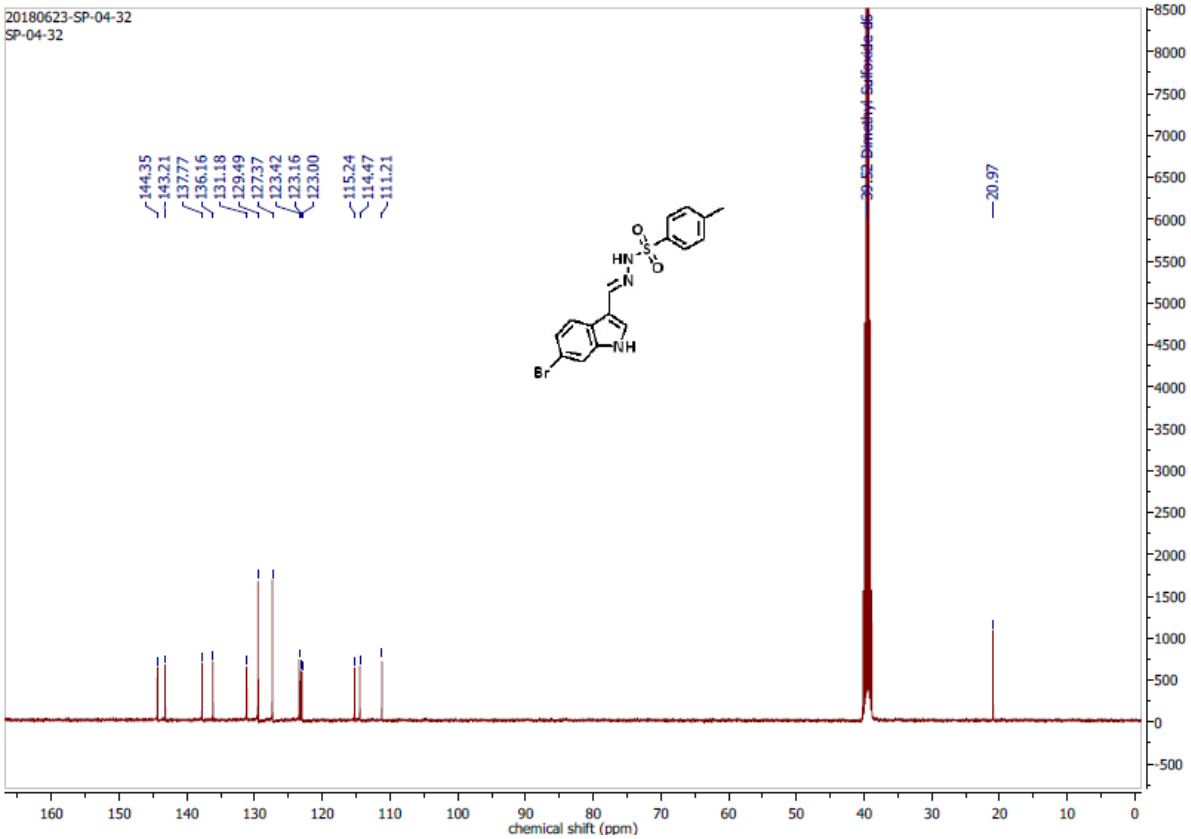


Fig. S19: ^{13}C NMR spectrum of compound 6 in DMSO-d_6 at 100 MHz.

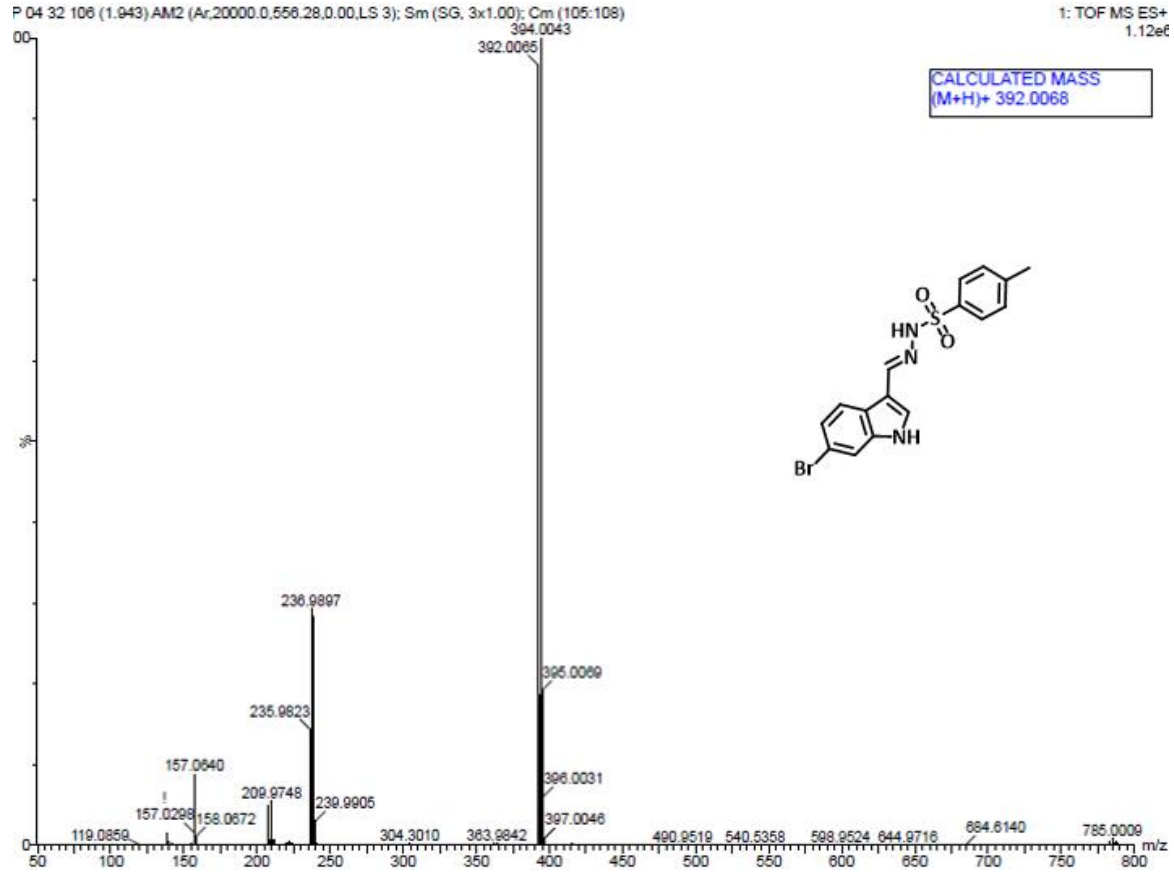


Fig. S20: HRMS spectrum of compound 6.

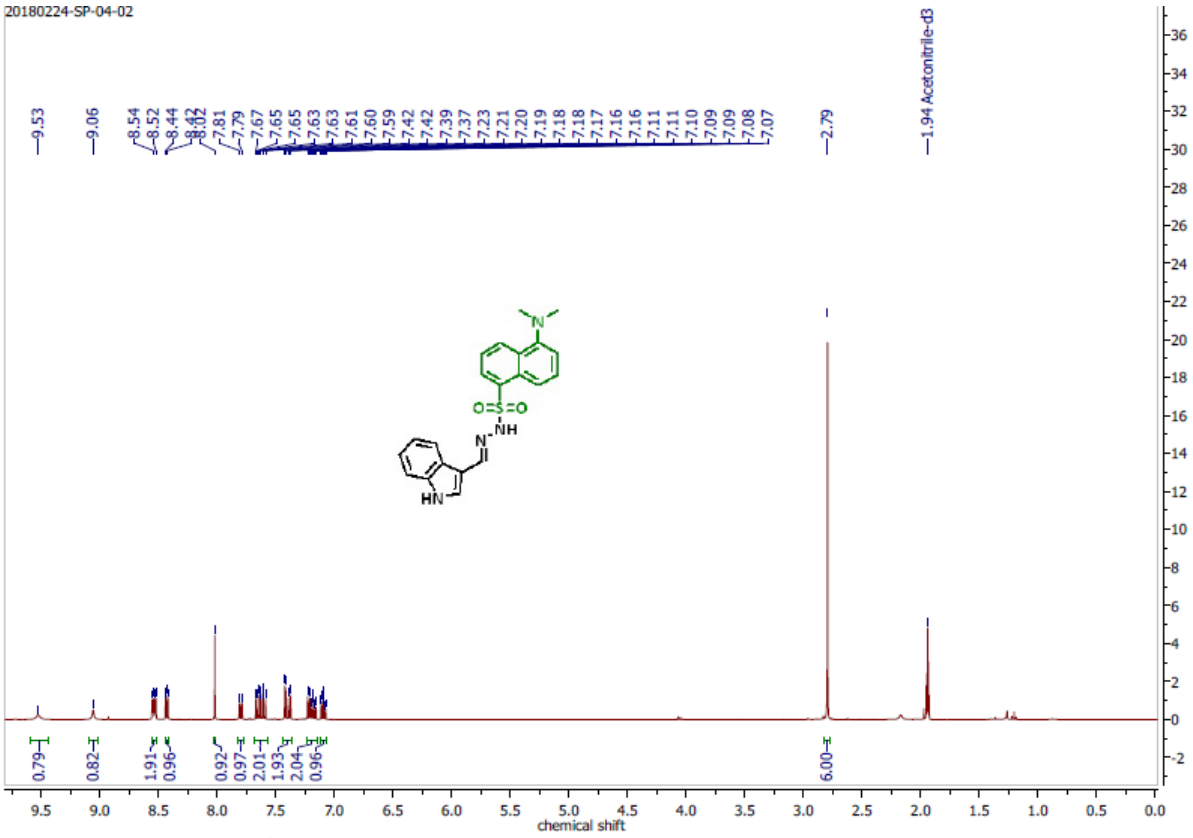


Fig. S21: ^{1}H NMR spectrum of compound 7 in CD_3CN-d_3 at 400 MHz.

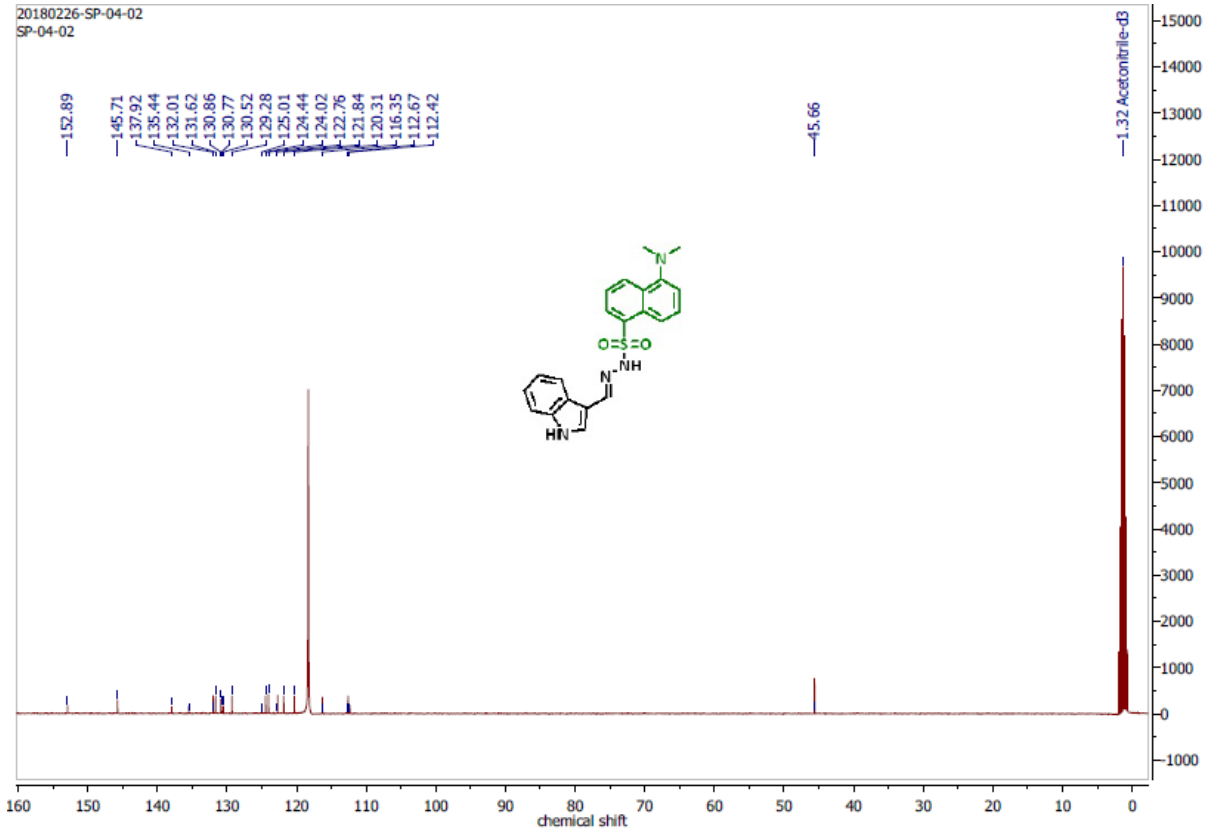


Fig. S22: ^{13}C NMR spectrum of compound 7 in CD_3CN-$d_3$at 100 MHz.

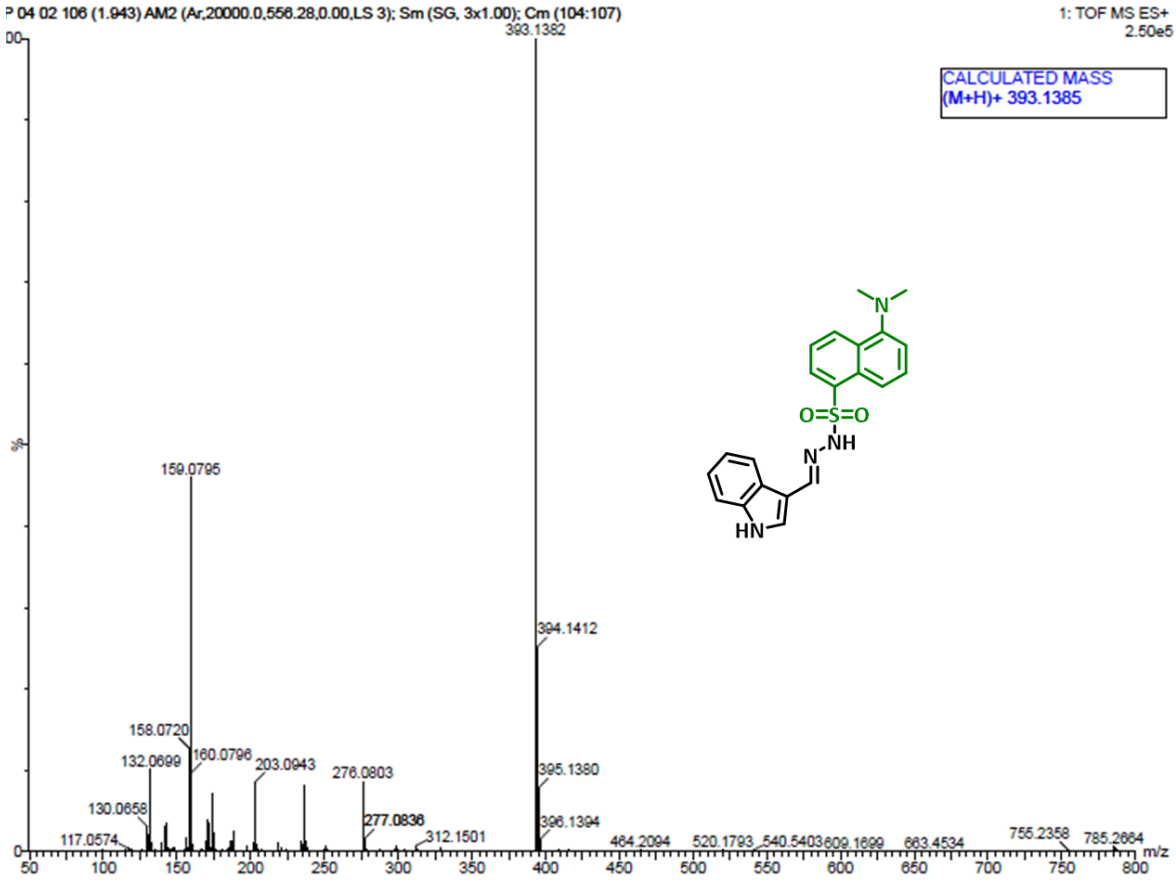


Fig. S23: HRMS spectrum of compound 7.

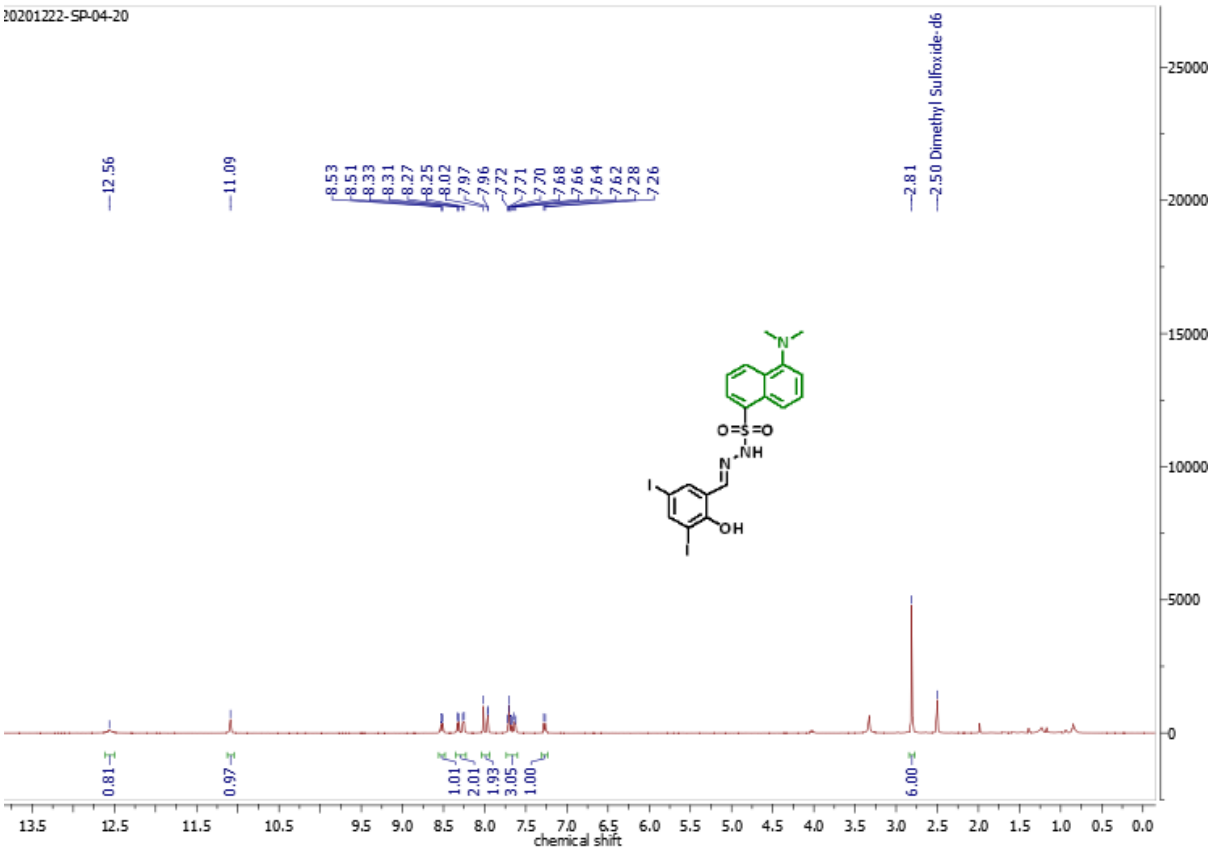


Fig. S24: ^{1}H NMR spectrum of compound 8 in DMSO-d_6 at 400 MHz.

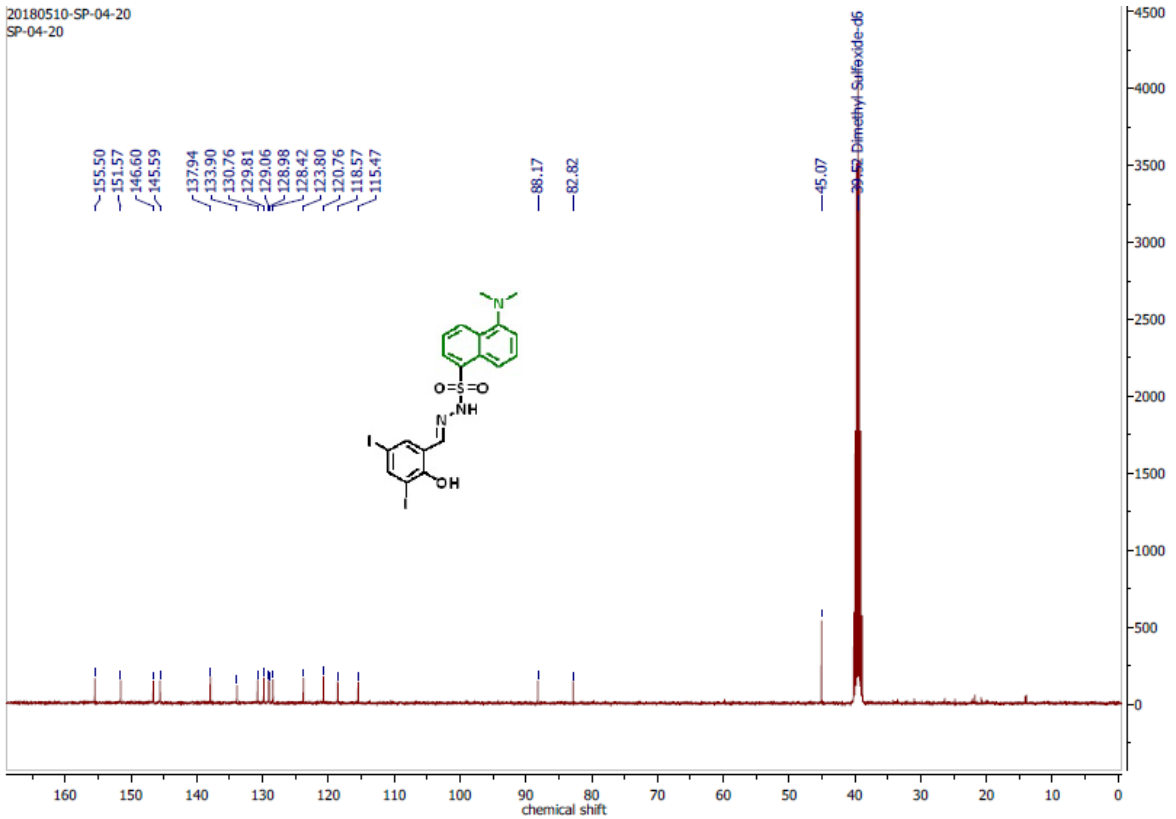


Fig. S25: ^{13}C NMR spectrum of compound 8 in DMSO-d_6 at 100 MHz

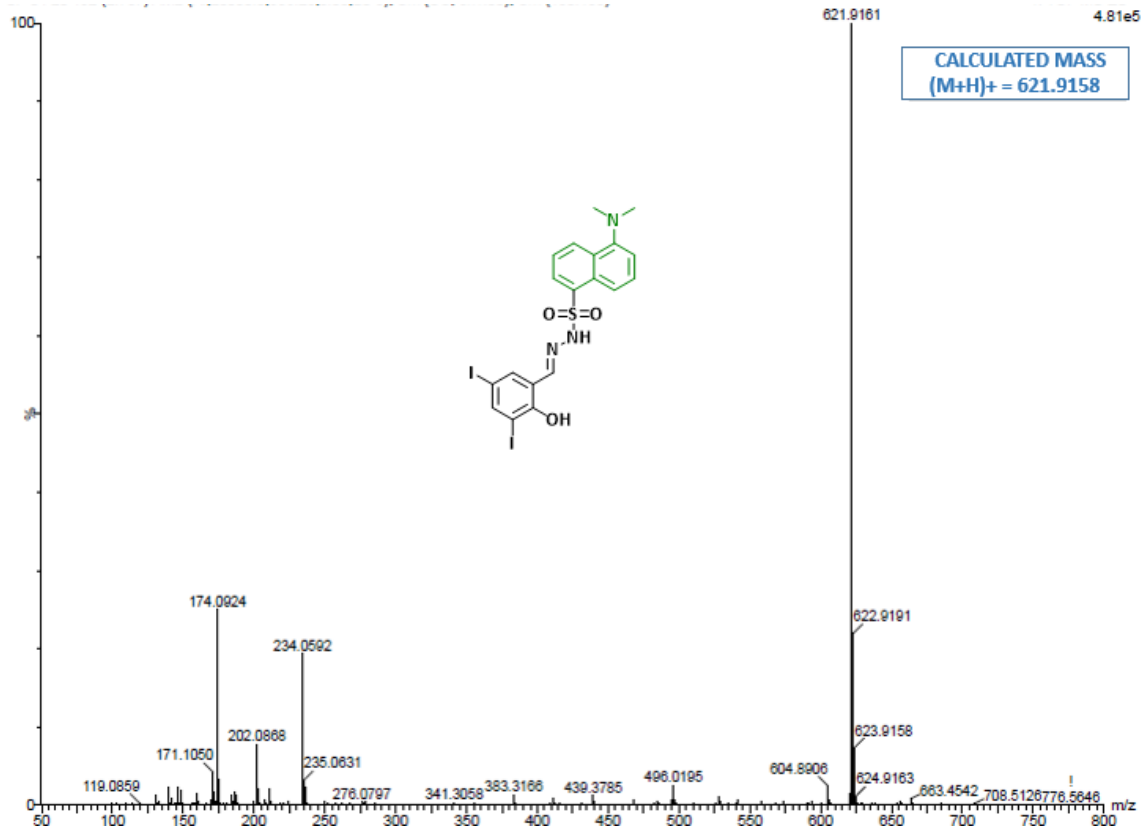


Fig. S26: HRMS spectrum of compound 8.

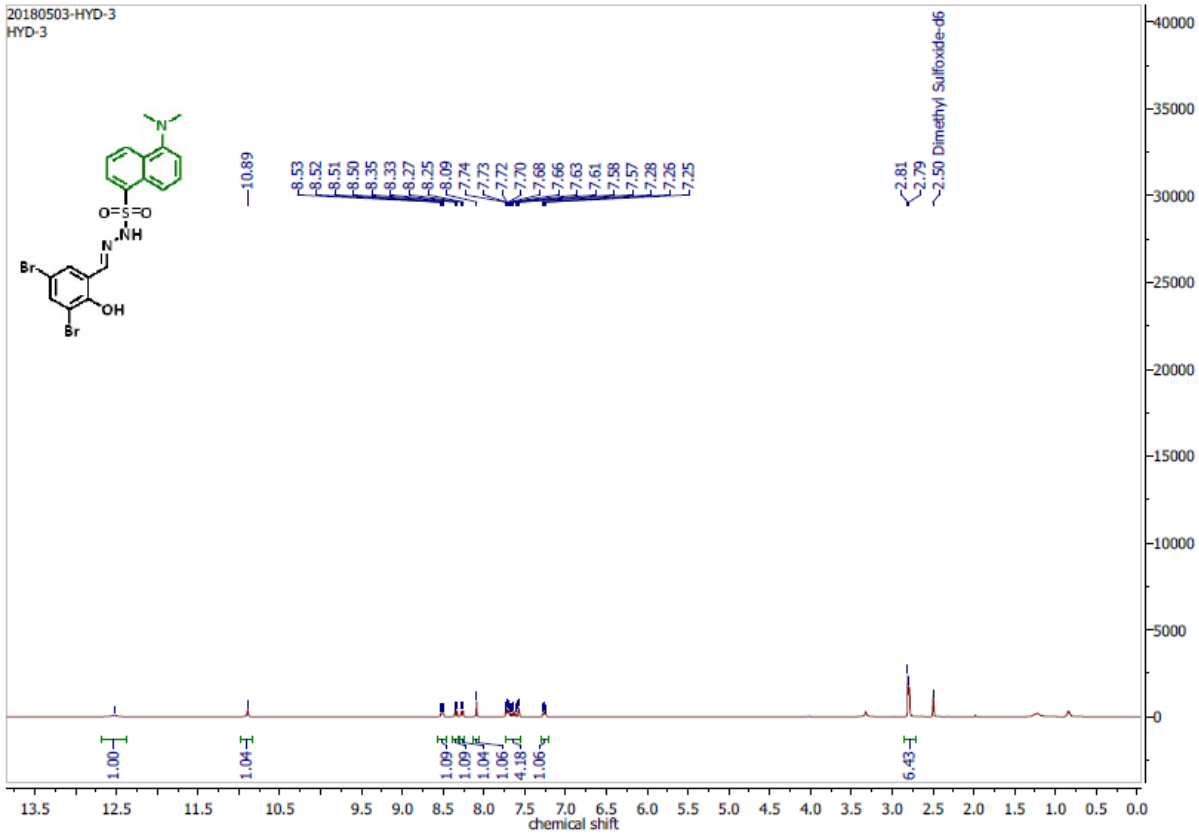


Fig. S27: ^{1}H NMR spectrum of compound 9 in DMSO-d_6 at 400 MHz.

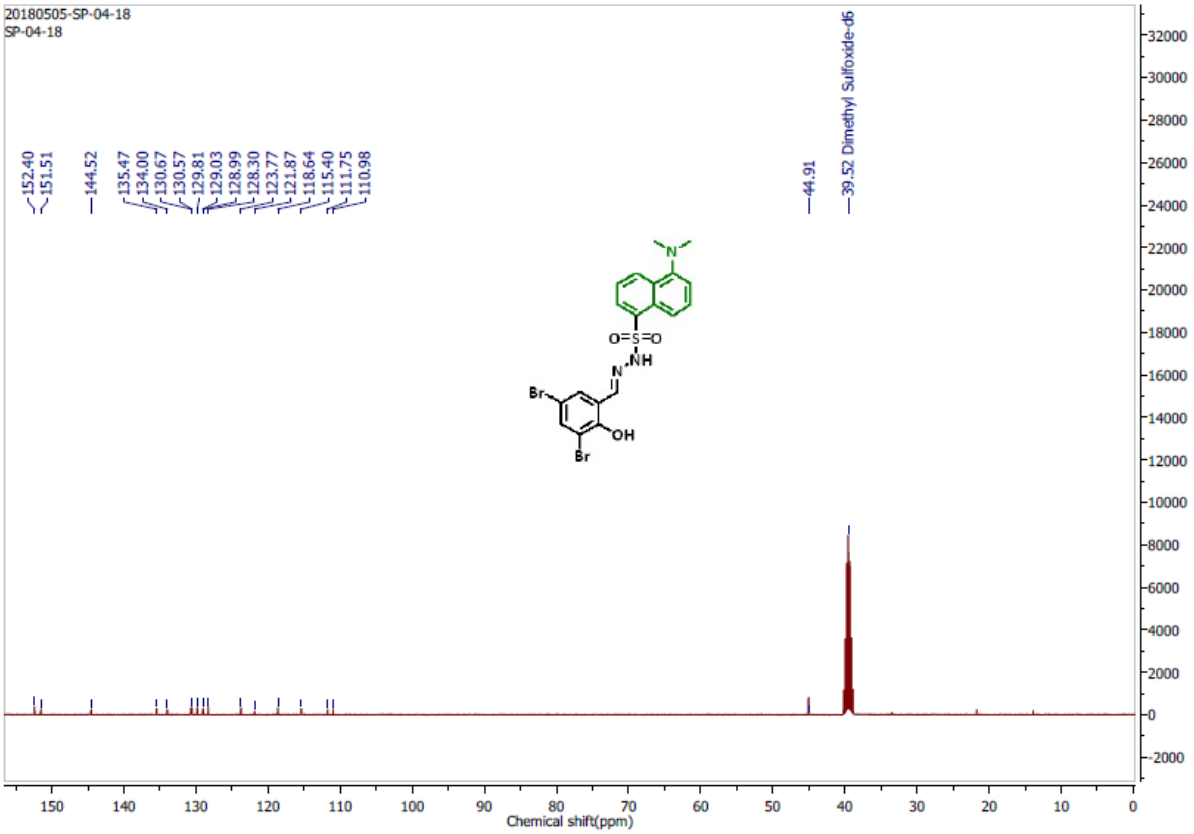


Fig. S28: ^{13}C NMR spectrum of compound 9 in DMSO-d_6 at 100 MHz.

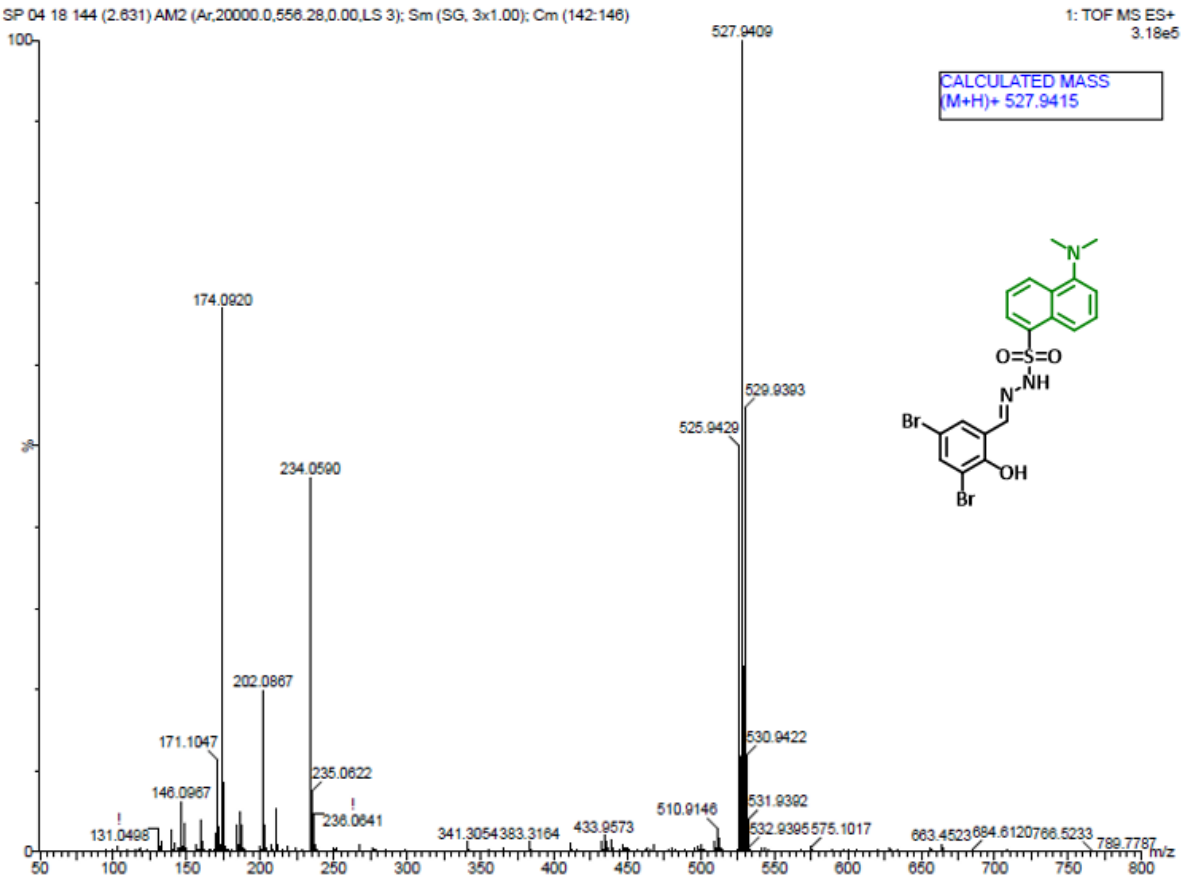


Fig. S29: HRMS spectrum of compound 9.

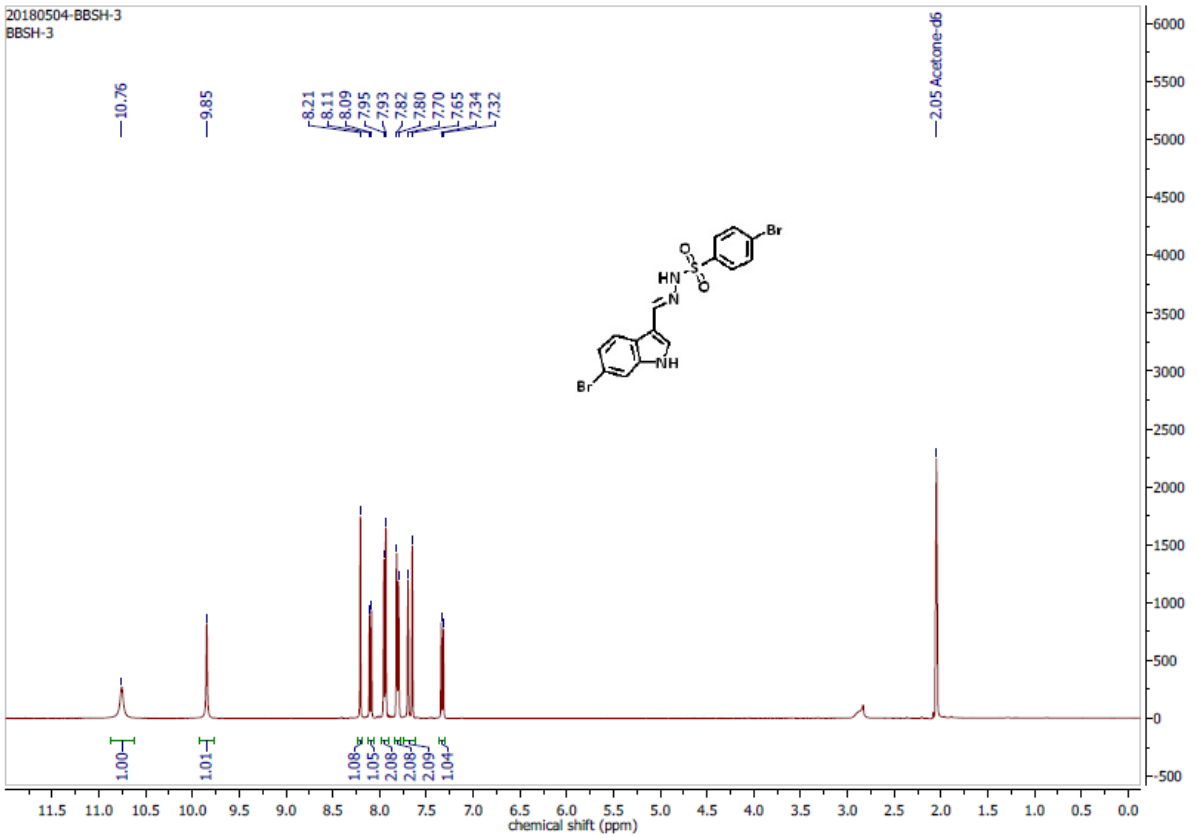


Fig. S30: ^{1}H NMR spectrum of compound 10 in Acetone-$d_6$at 400 MHz.

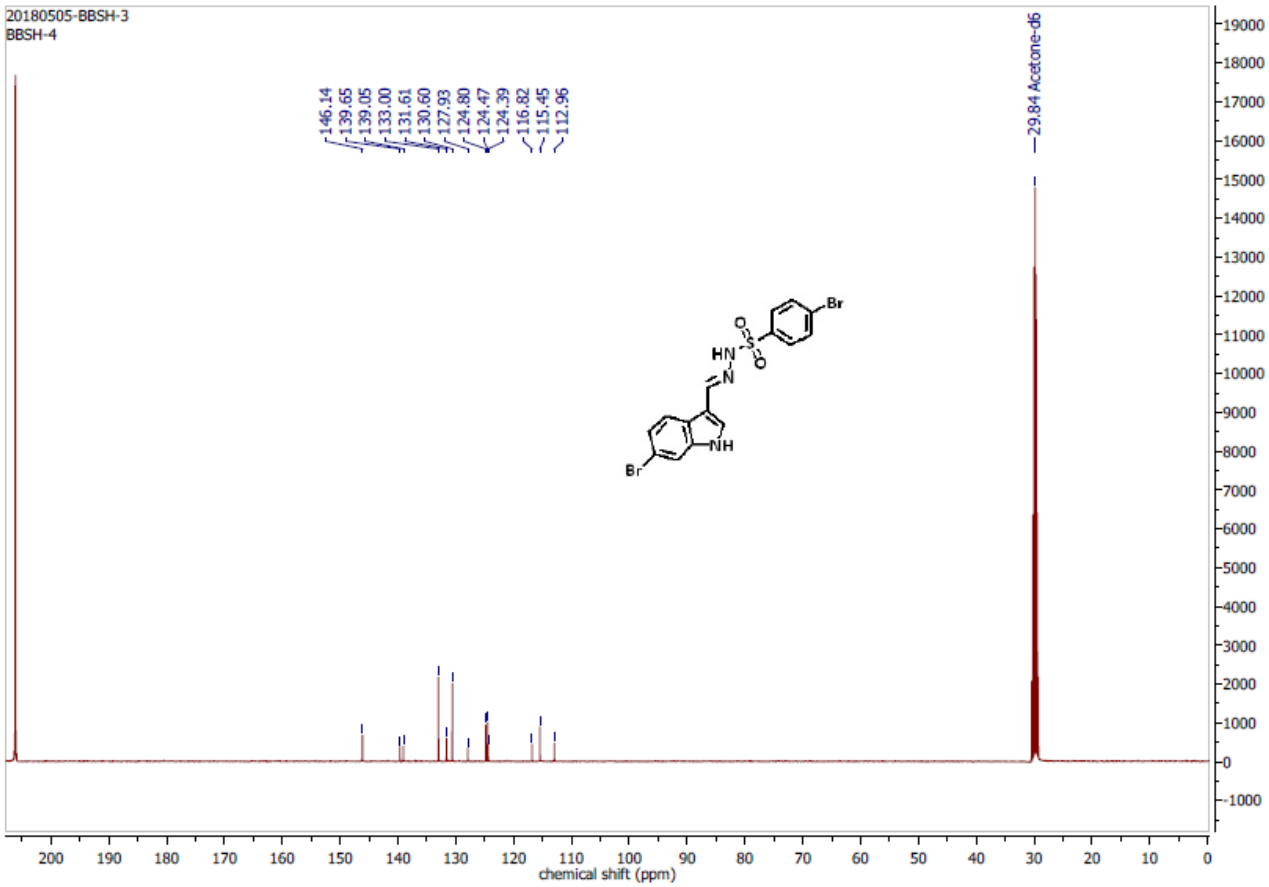


Fig. S31: ^{13}C NMR spectrum of compound 10 in Acetone-d_6 at 100 MHz.

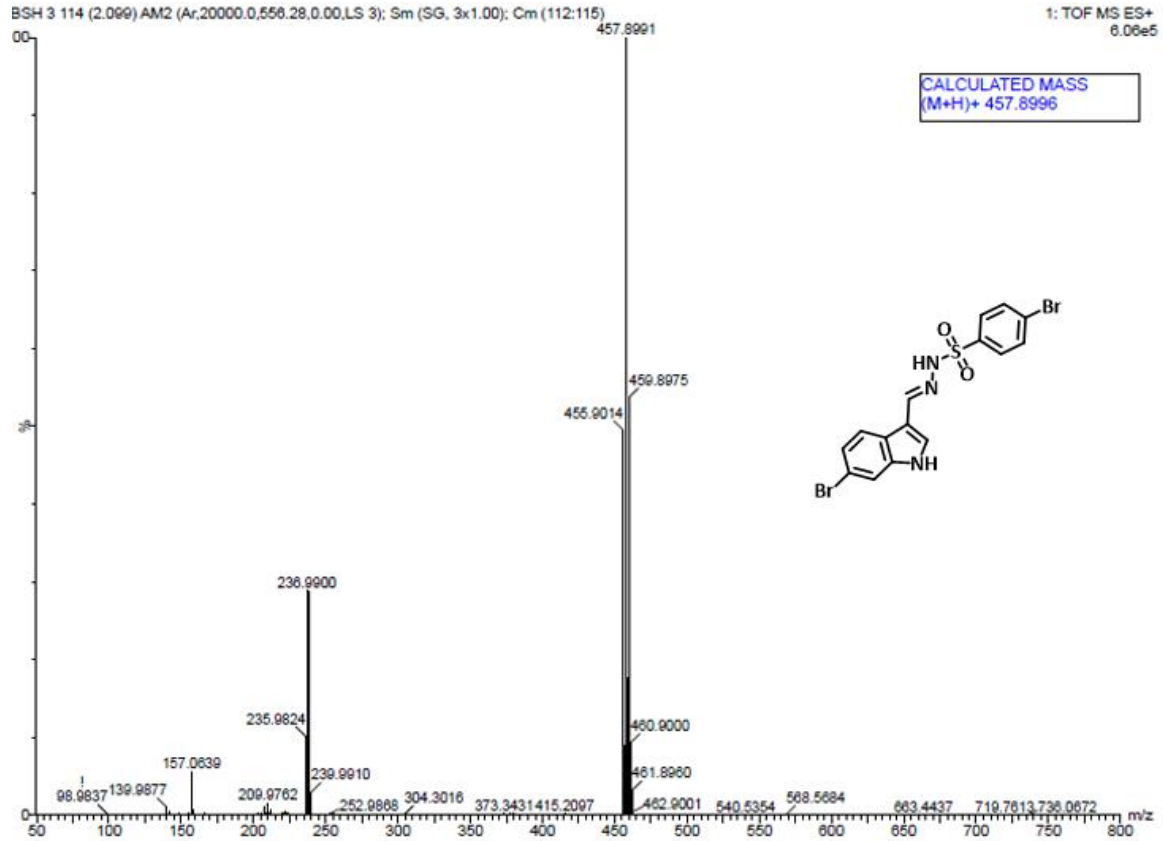


Fig. S32: HRMS spectrum of compound 10.

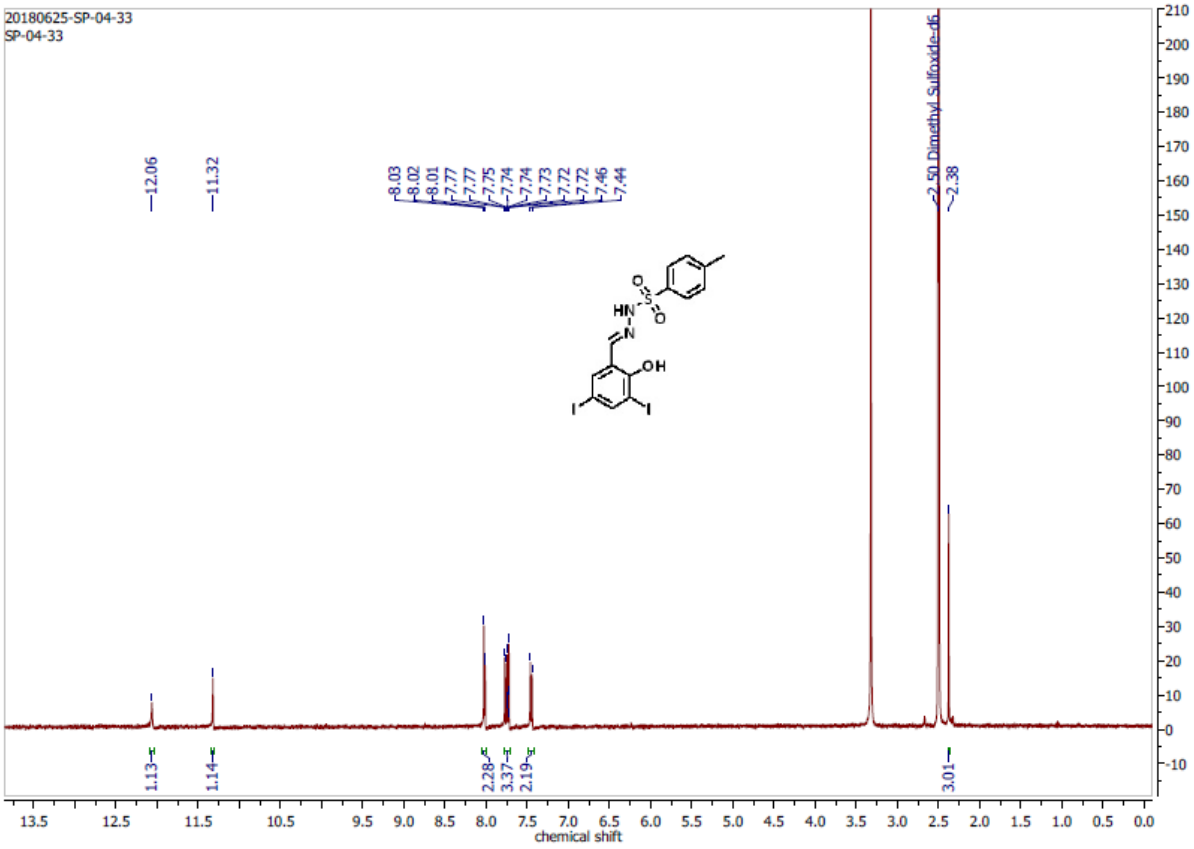


Fig. S33: ^{1}H NMR spectrum of compound 11 in DMSO-d_6 at 400 MHz.

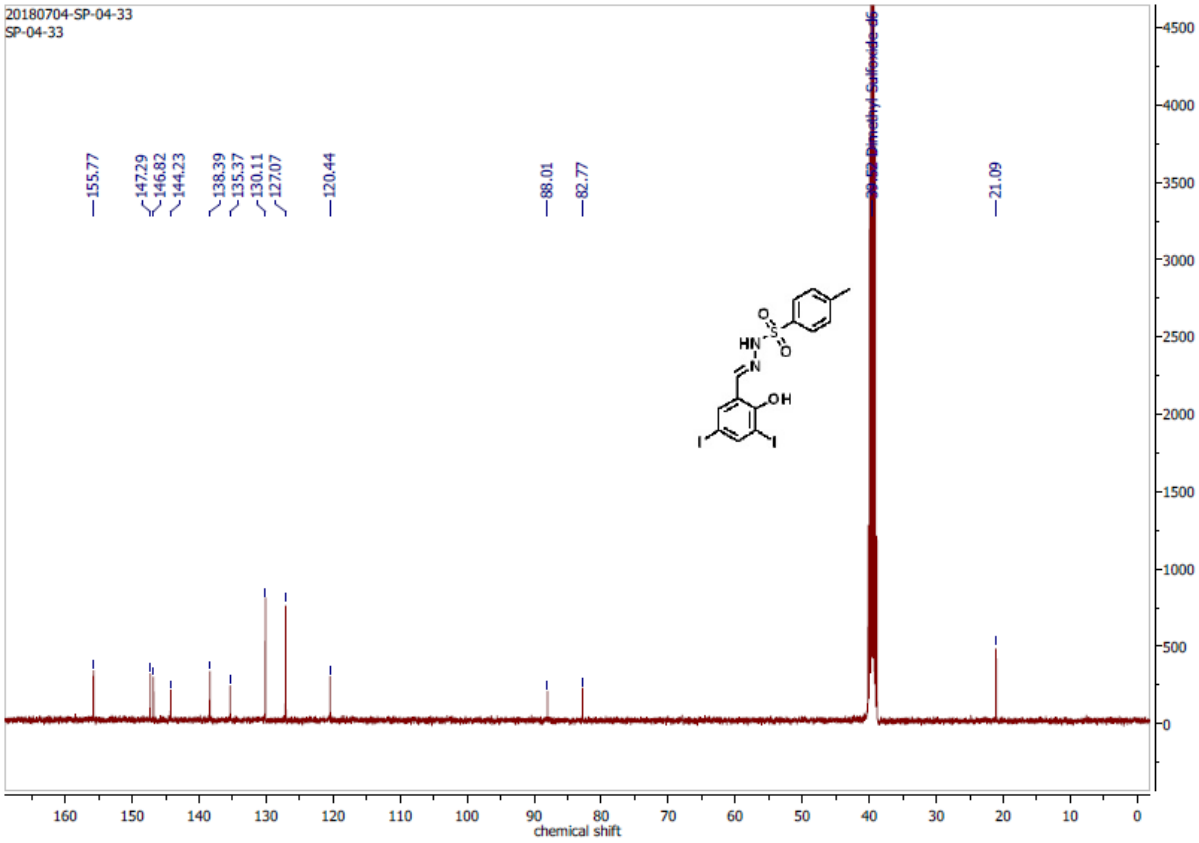


Fig. S34: ^{13}C NMR spectrum of compound 11 in DMSO-d_6 at 100 MHz.

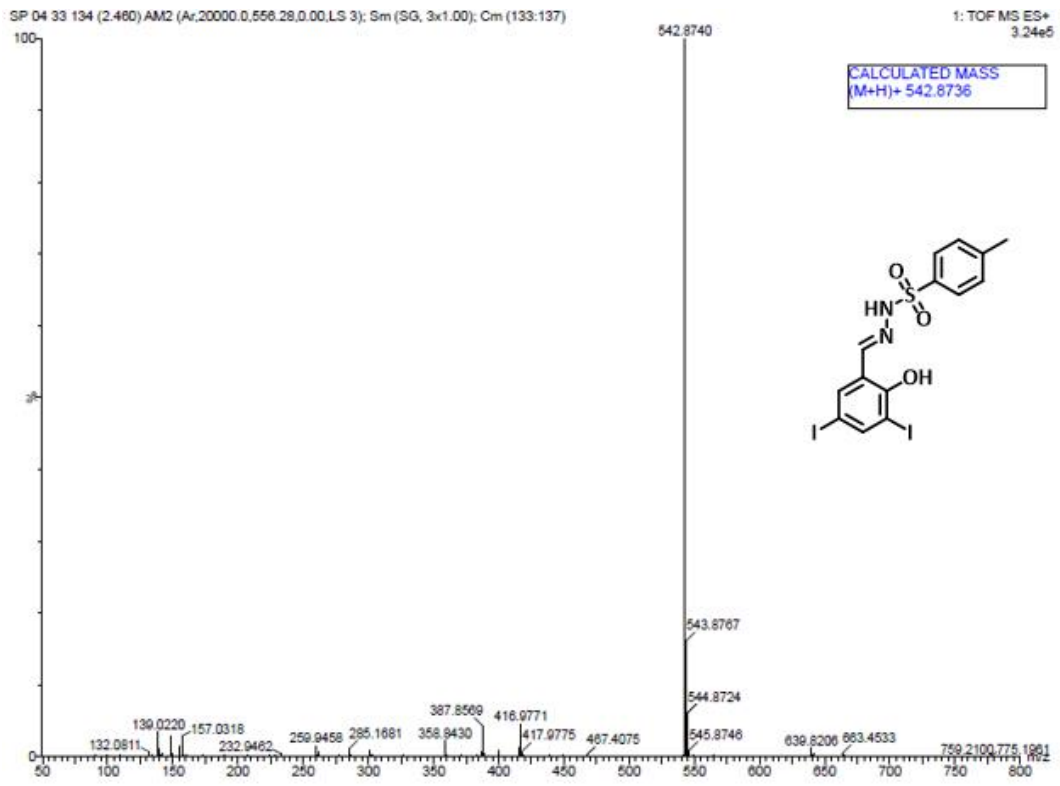


Fig. S35: HRMS spectrum of compound 11.

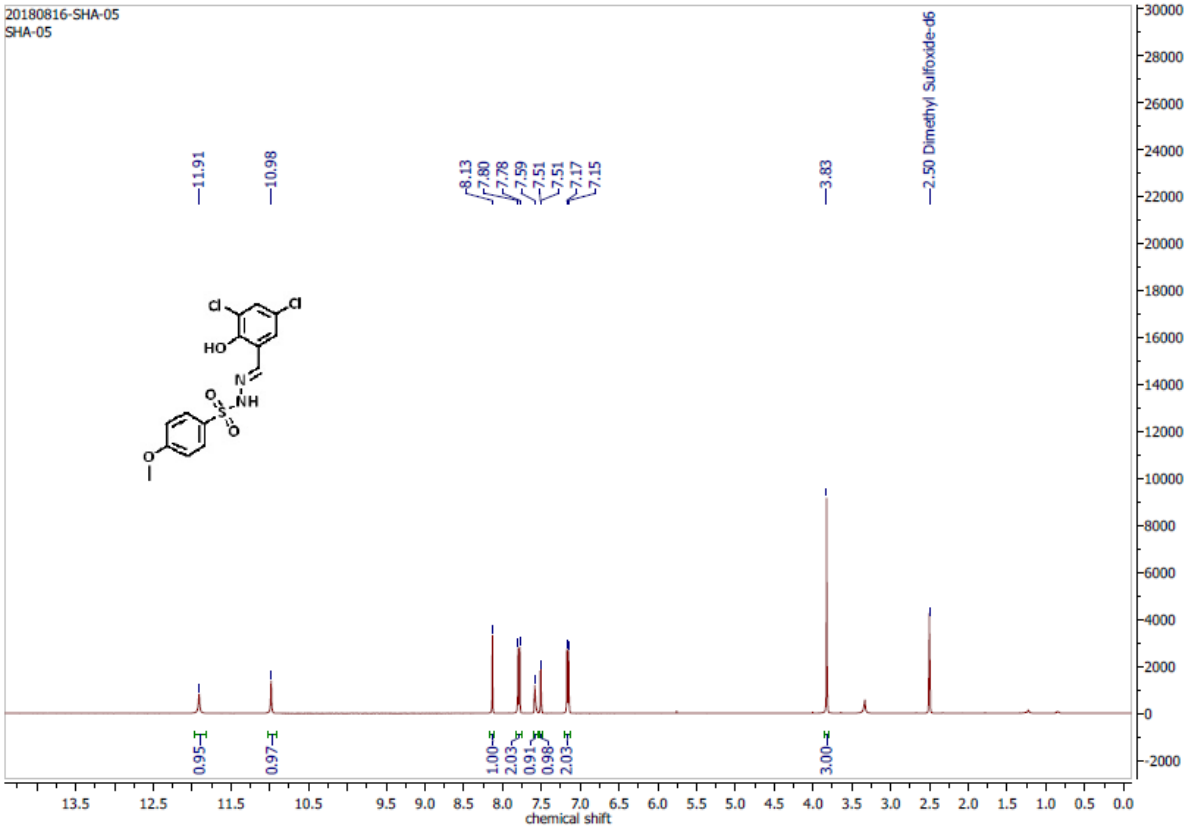


Fig. S36: ^{1}H NMR spectrum of compound 12 in DMSO-d_6 at 400 MHz.

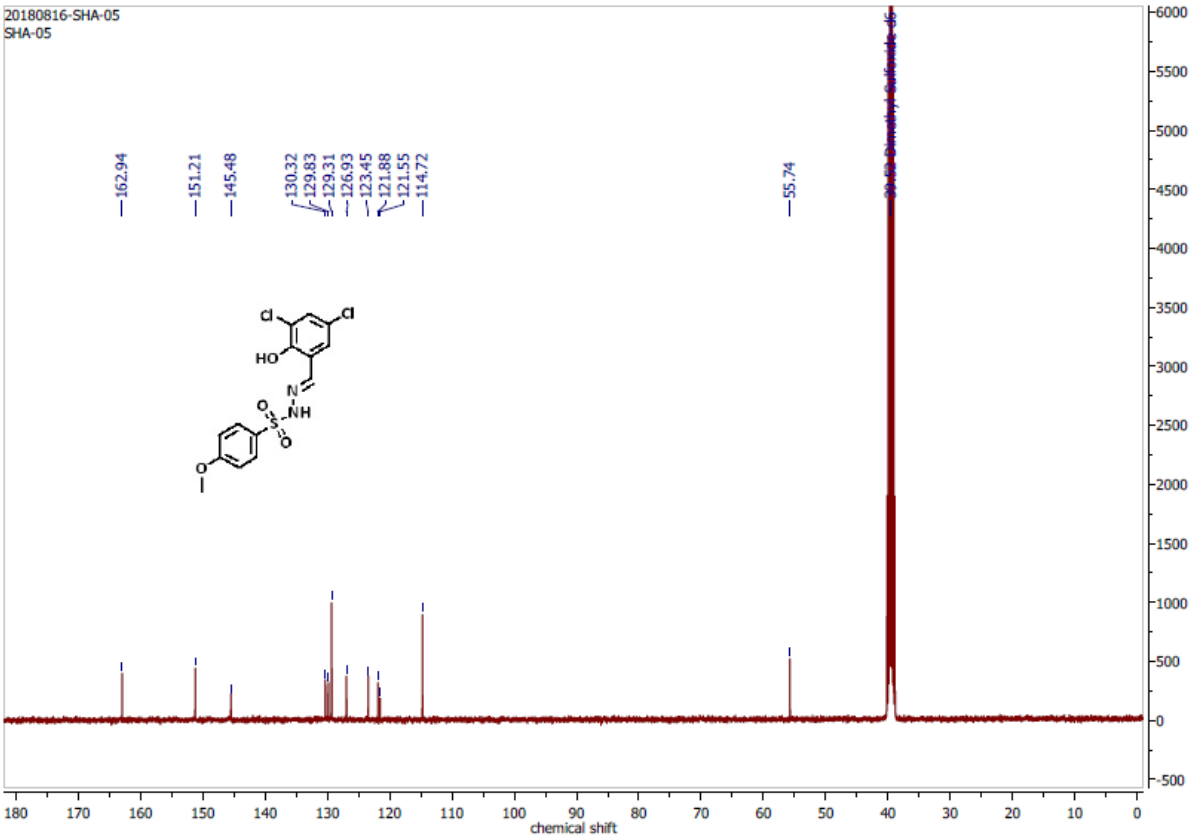


Fig. S37: ^{13}C NMR spectrum of compound 12 in DMSO-d_6 at 100 MHz.

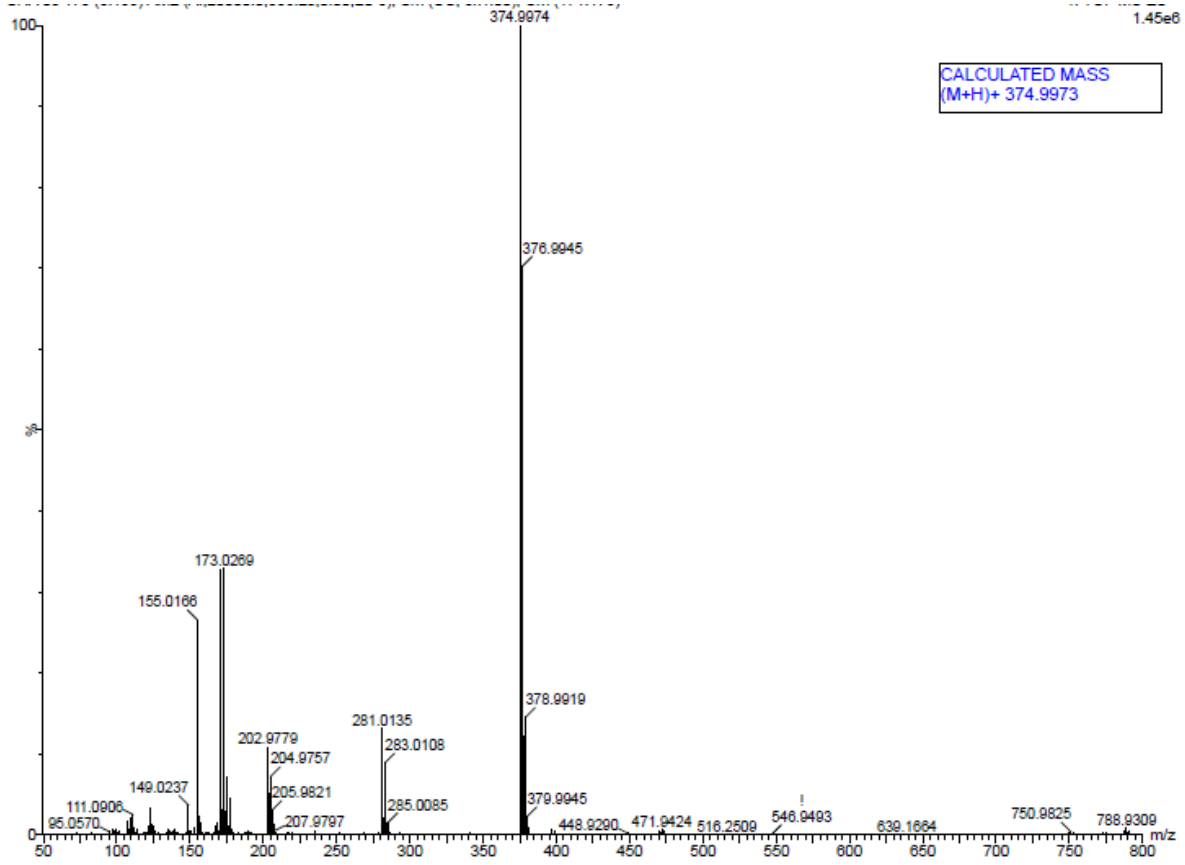


Fig. S38: HRMS spectrum of compound 12.

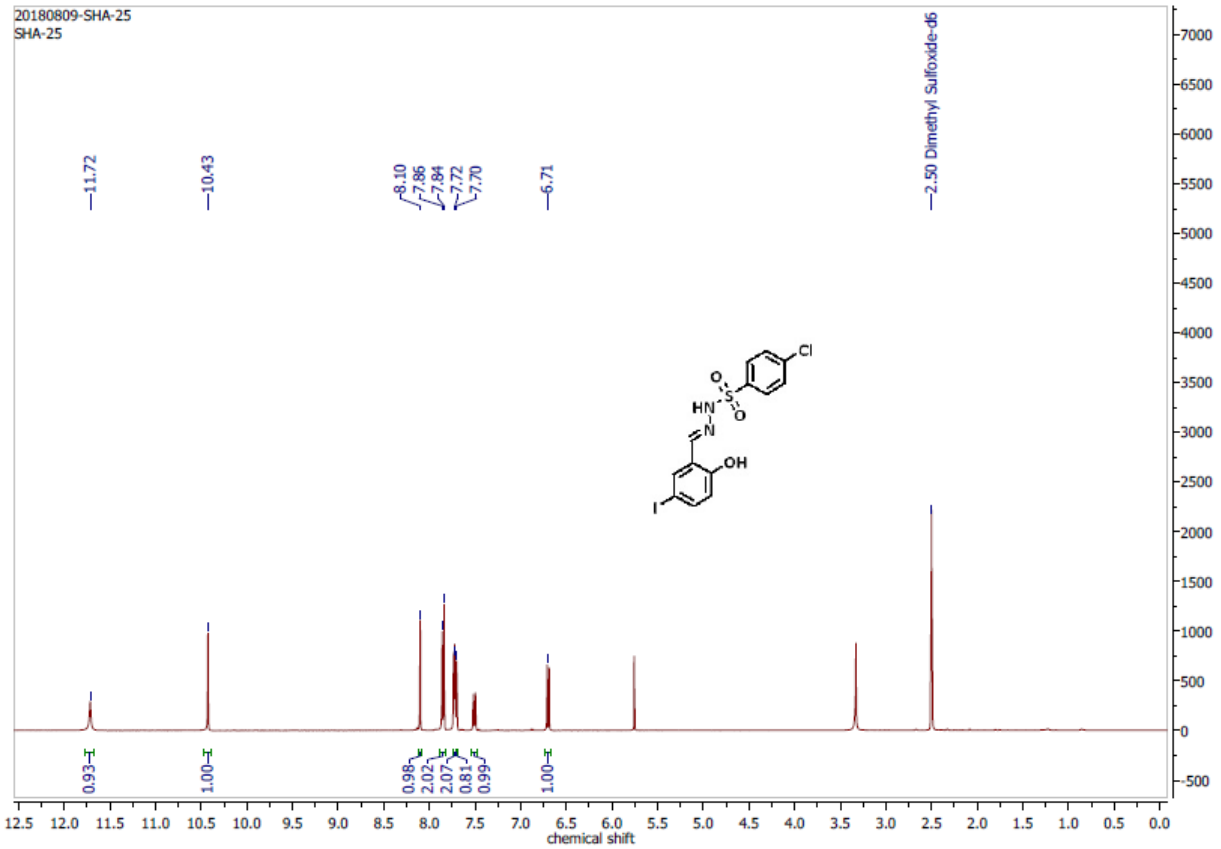


Fig. S39: ^{1}H NMR spectrum of compound 13 in DMSO-d_6 at 400 MHz.

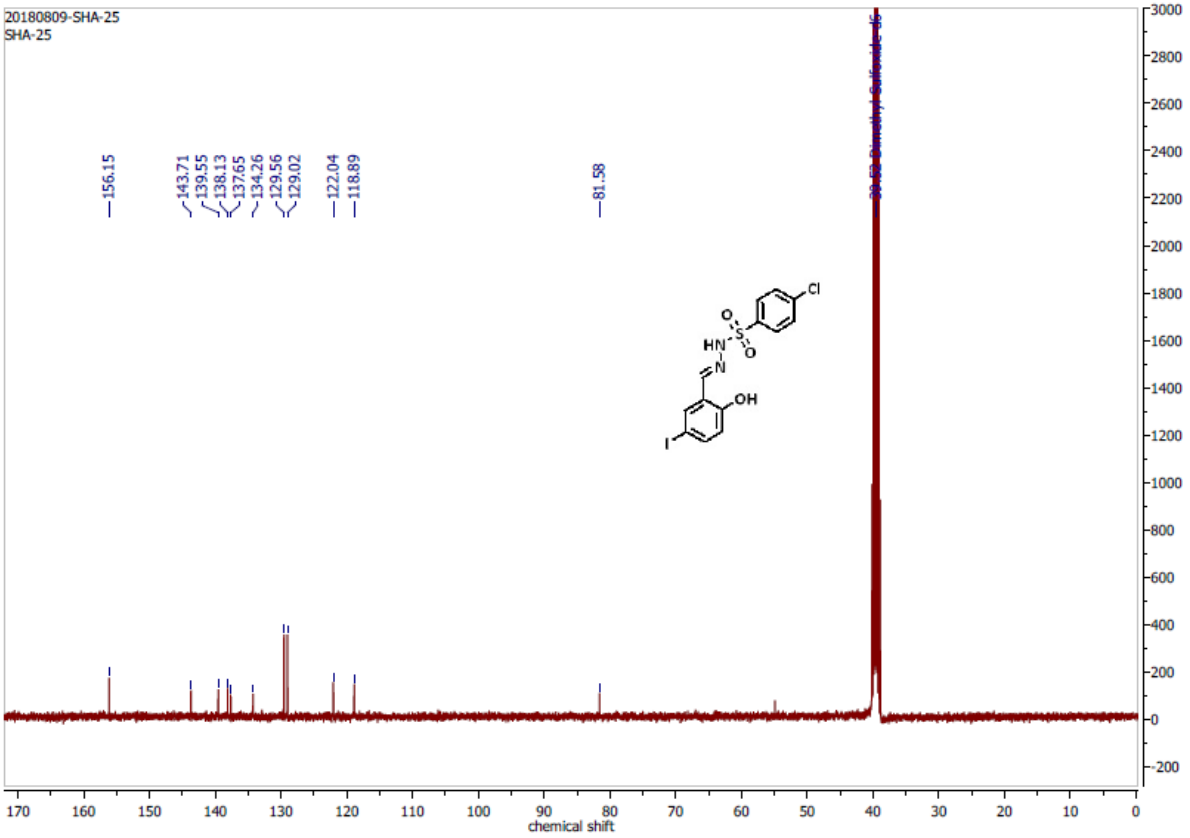


Fig. S40: ^{13}C NMR spectrum of compound 13 in DMSO-d_6 at 100 MHz.

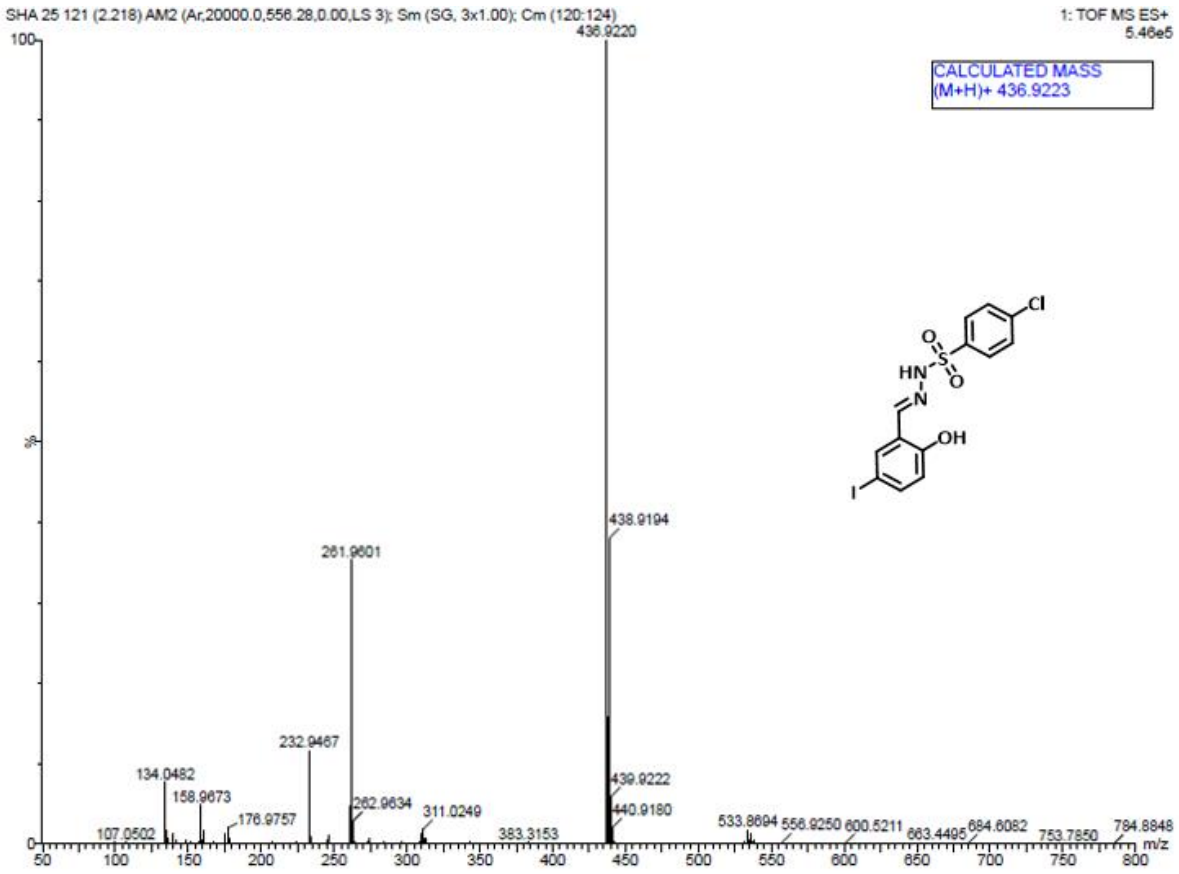


Fig. S41: HRMS spectrum of compound 13.

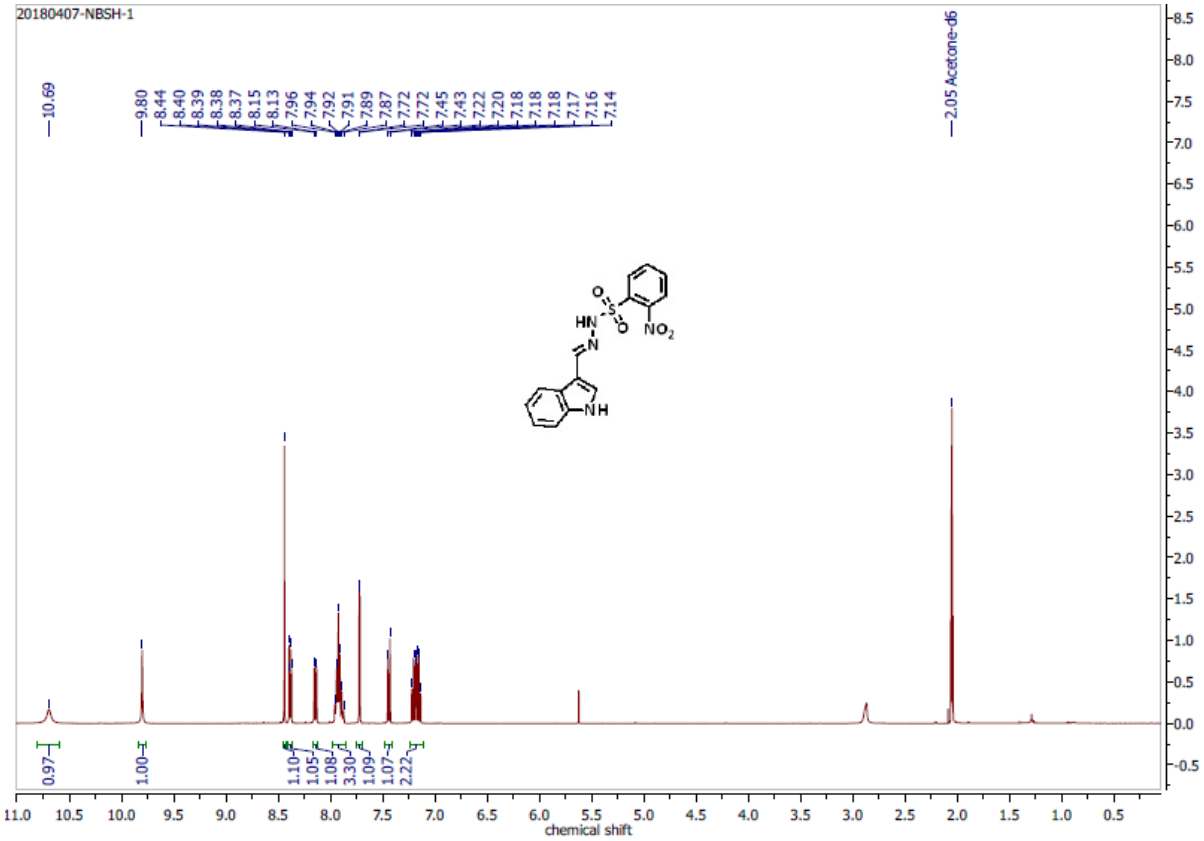


Fig. S42: ^{1}H NMR spectrum of compound 14 in Acetone-d_3 at 400 MHz.

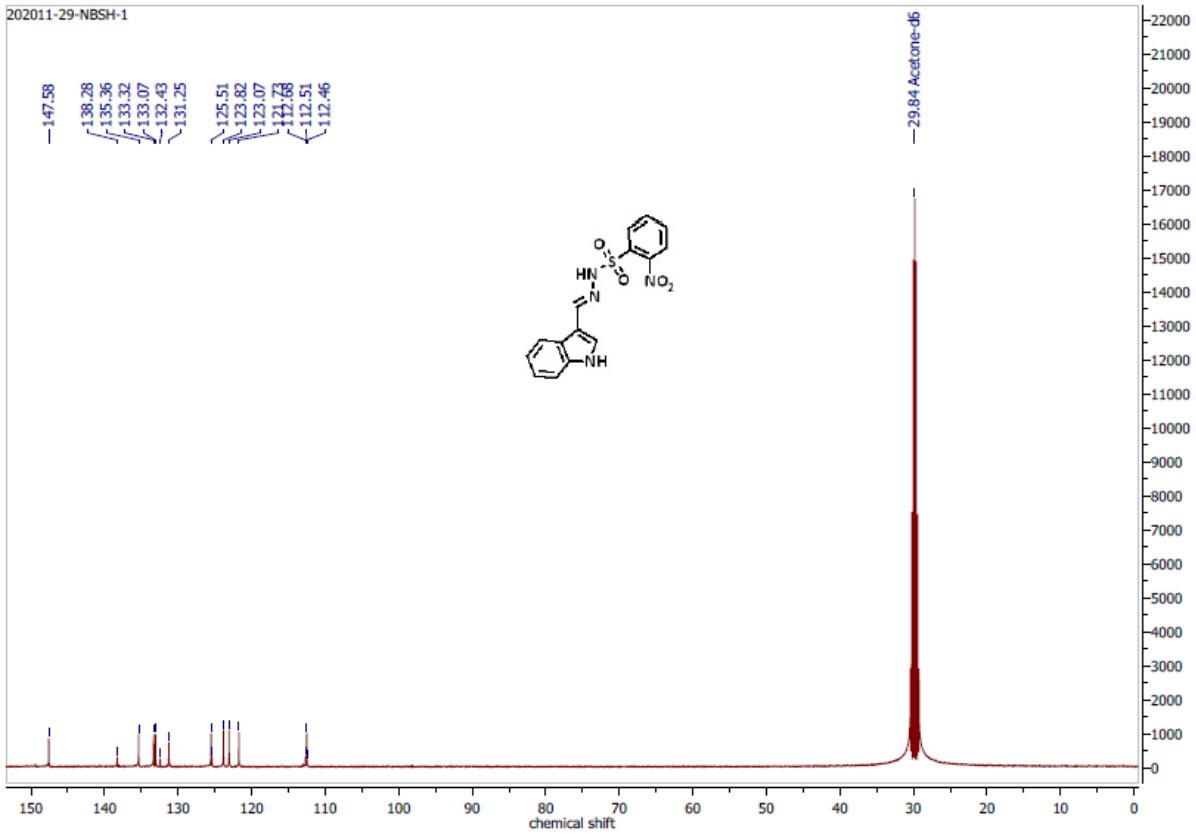


Fig. S43: ^{13}C NMR spectrum of compound 14 in Acetone-d_3 at 100 MHz.

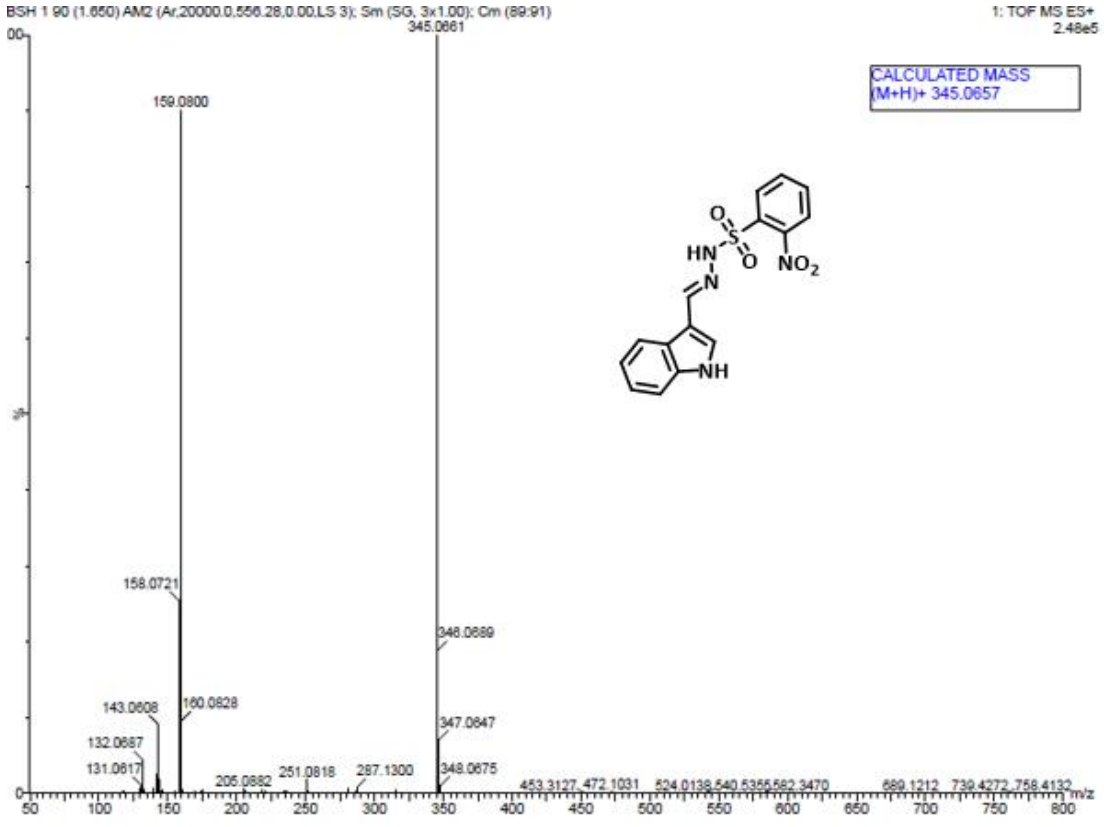


Fig. S44: HRMS spectrum of compound 14.

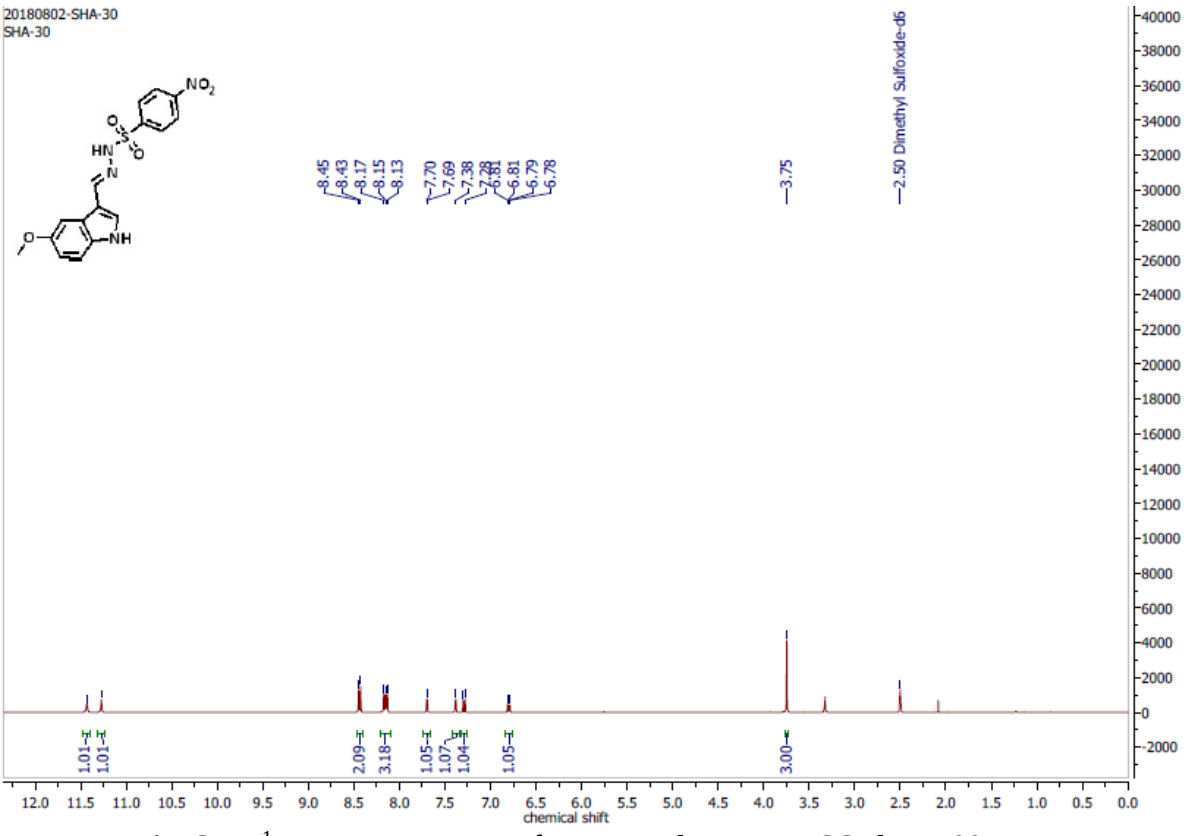


Fig. S45: [1] H NMR spectrum of compound 15 in DMSO-d_6 at 400 MHz.

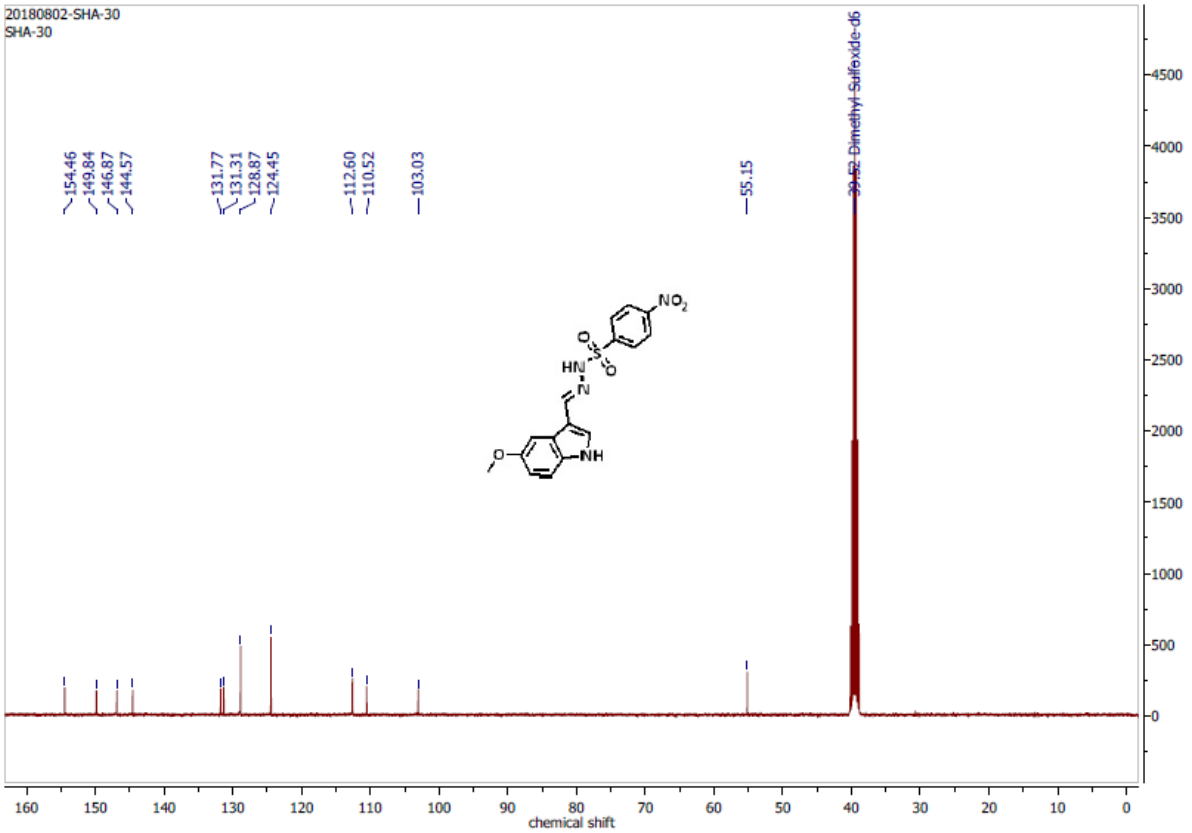


Fig. S46: ^{13}C NMR spectrum of compound 15 in DMSO-d_6 at 100 MHz.

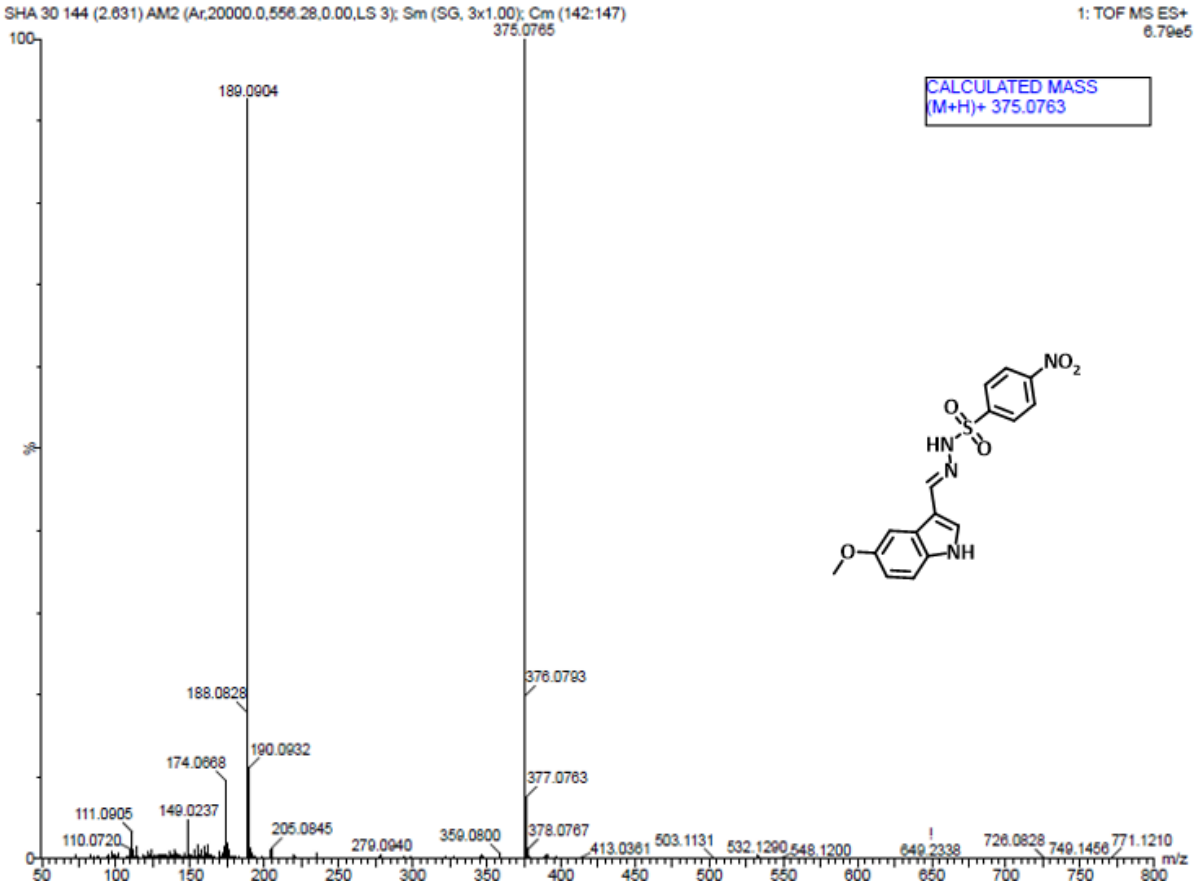


Fig. S47: HRMS spectrum of compound 15

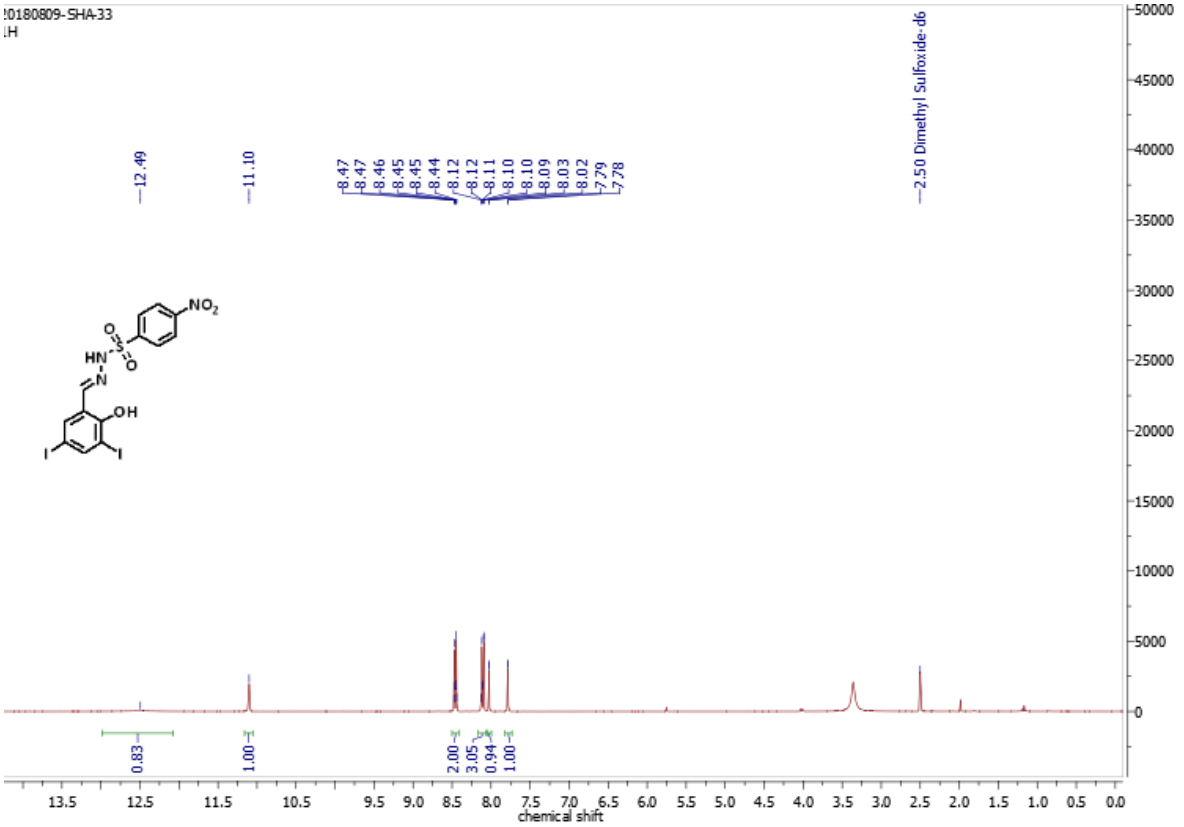


Fig. S48: ^{1}H NMR spectrum of compound 16 in DMSO-d_6 at 400 MHz.

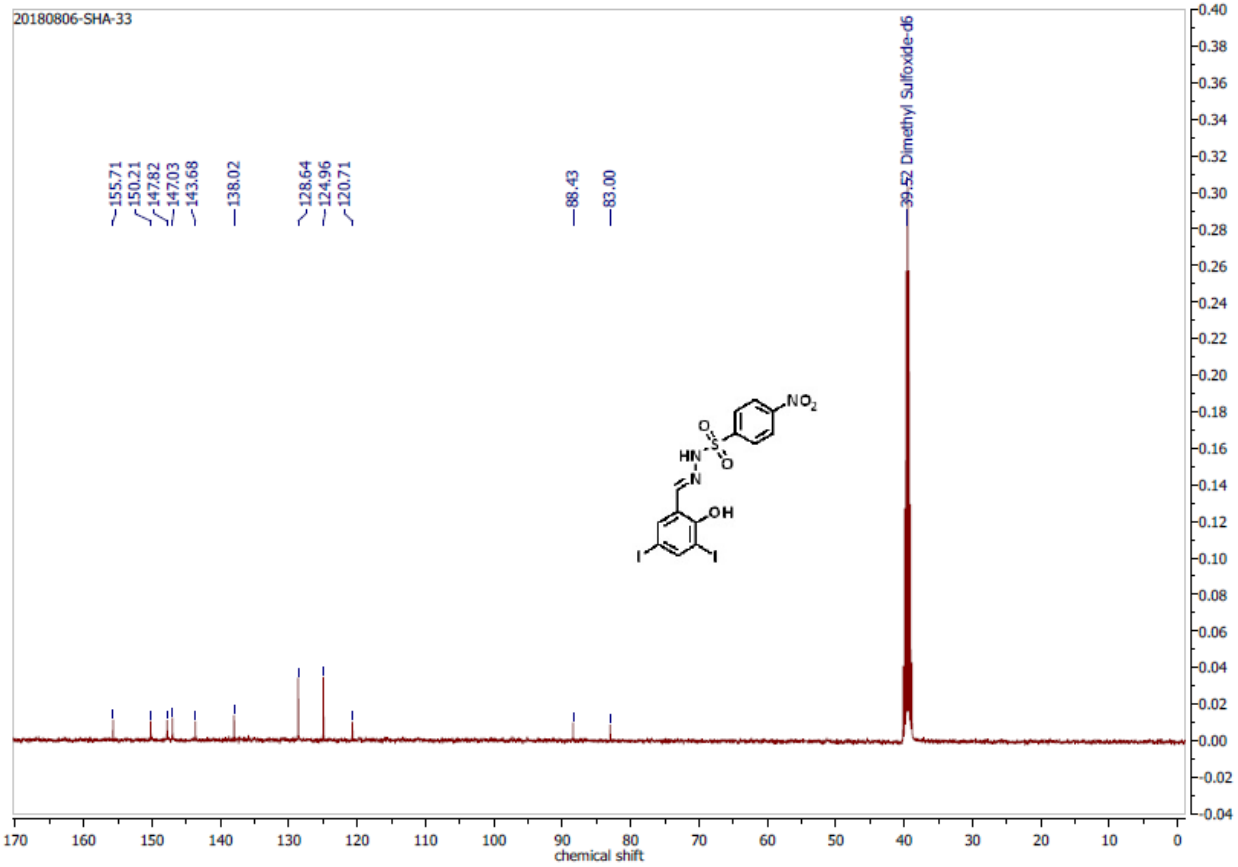


Fig. S49: ^{13}C NMR spectrum of compound 16 in DMSO-d_6 at 100 MHz.

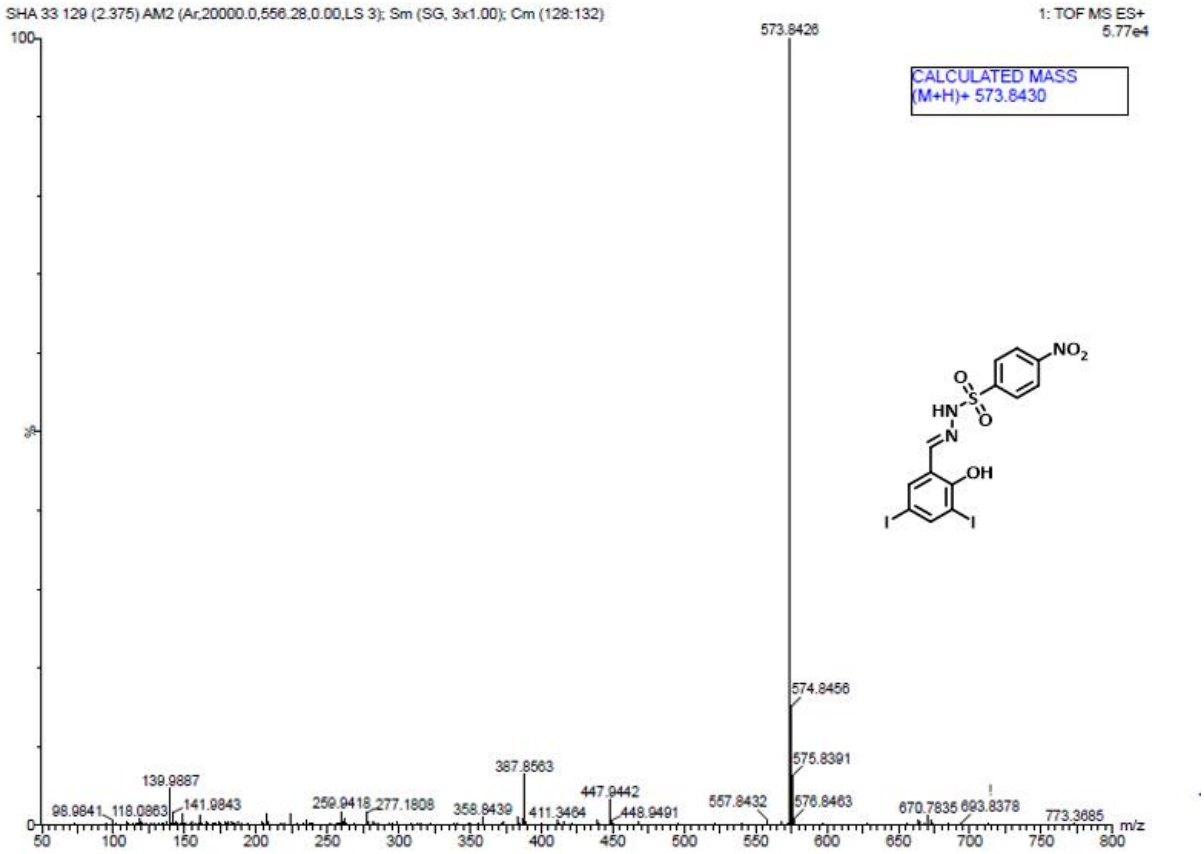


Fig. S50: HRMS spectrum of compound 16.

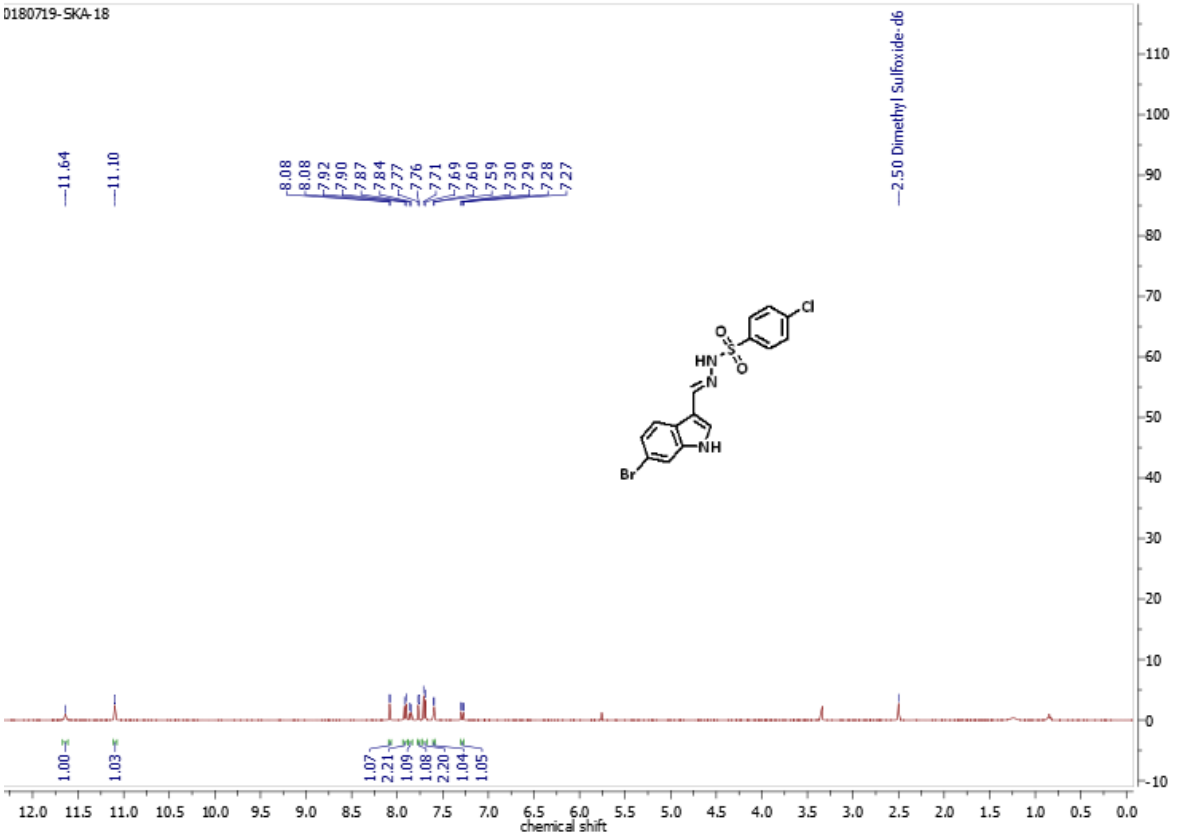


Fig. S51: ^{1}H NMR spectrum of compound 17 in DMSO-d_6 at 400 MHz.

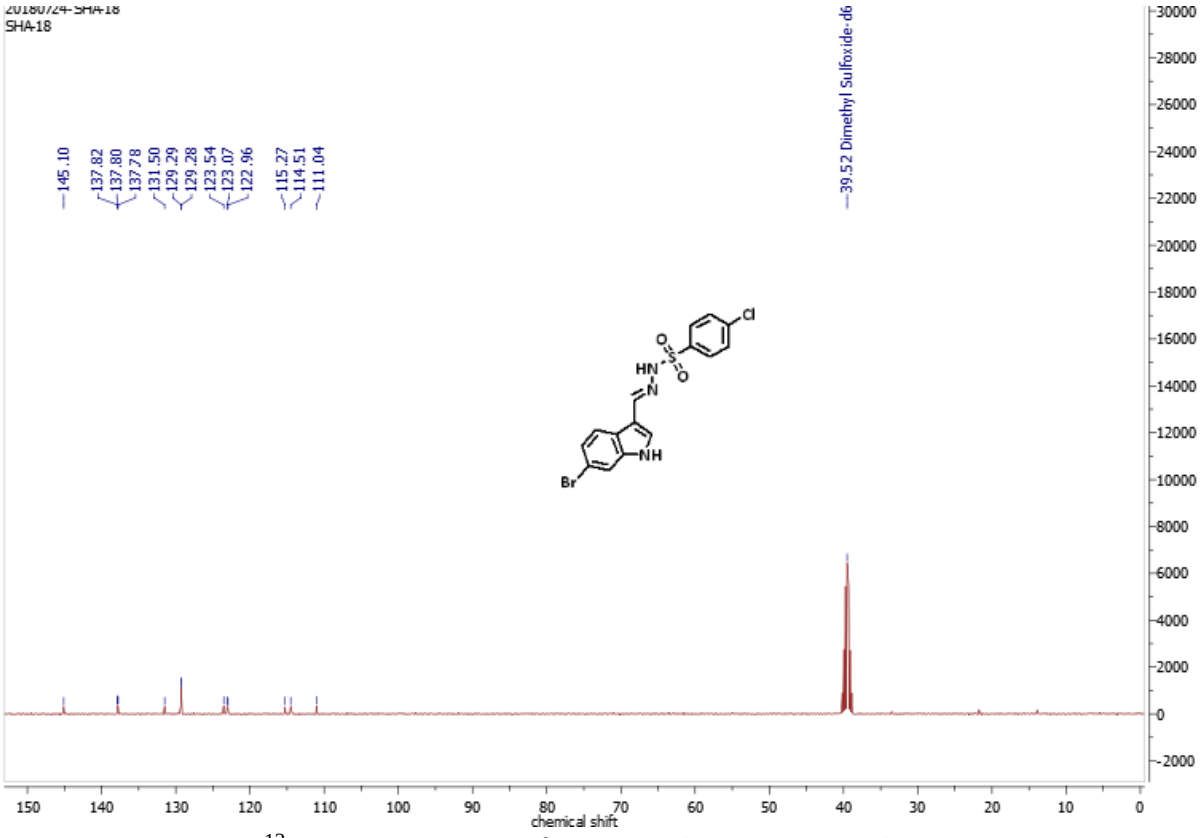


Fig. S52: ^{13}C NMR spectrum of compound 17 in DMSO-d_6 at 100 MHz

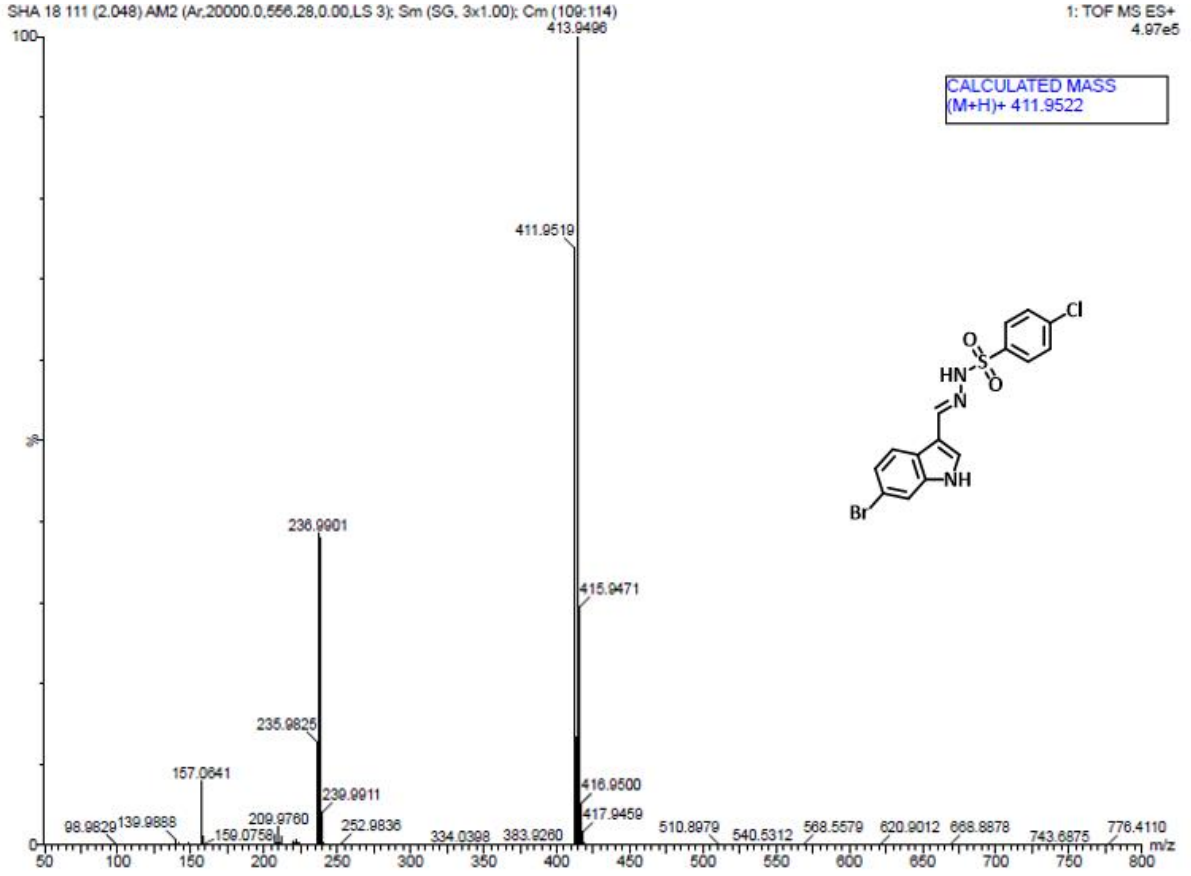


Fig. S53: HRMS spectrum of compound 17.

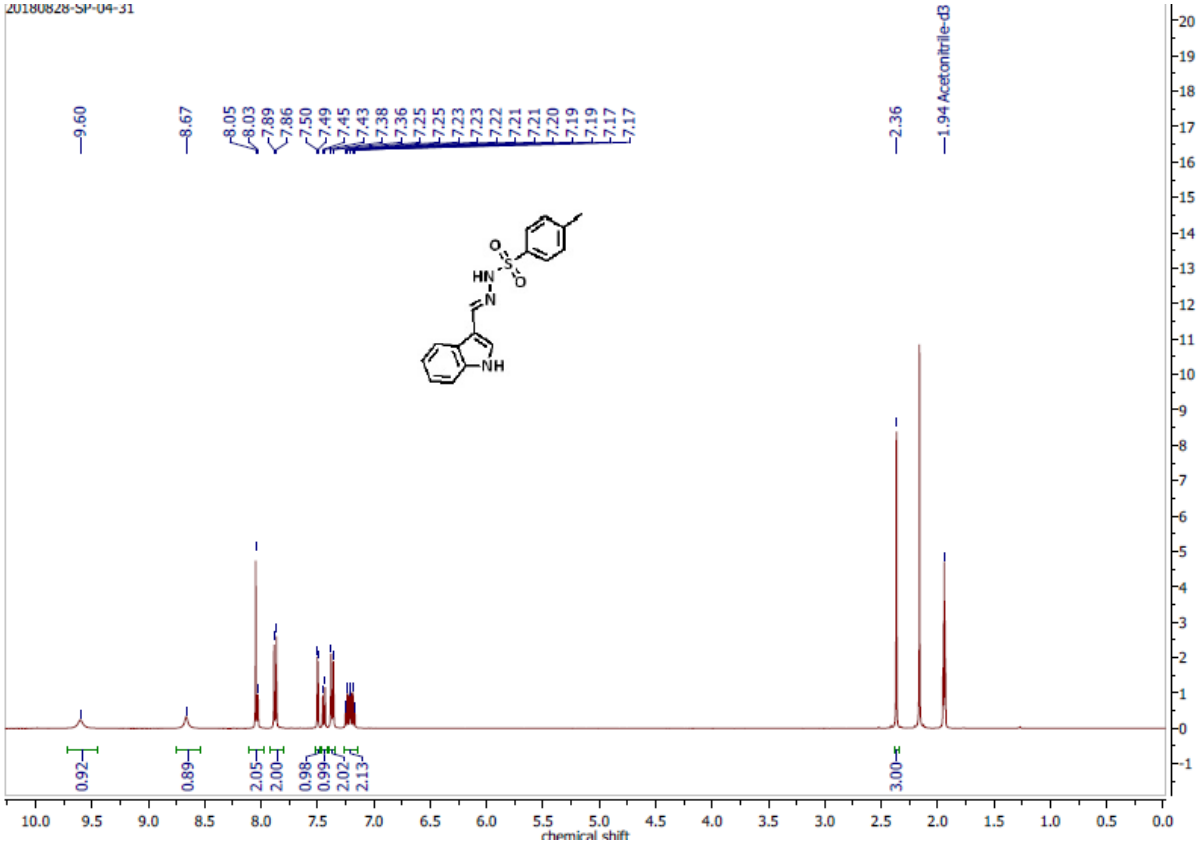


Fig. S54: ^{1}H NMR spectrum of compound 18 in CD_3CN-d_3 at 400 MHz.

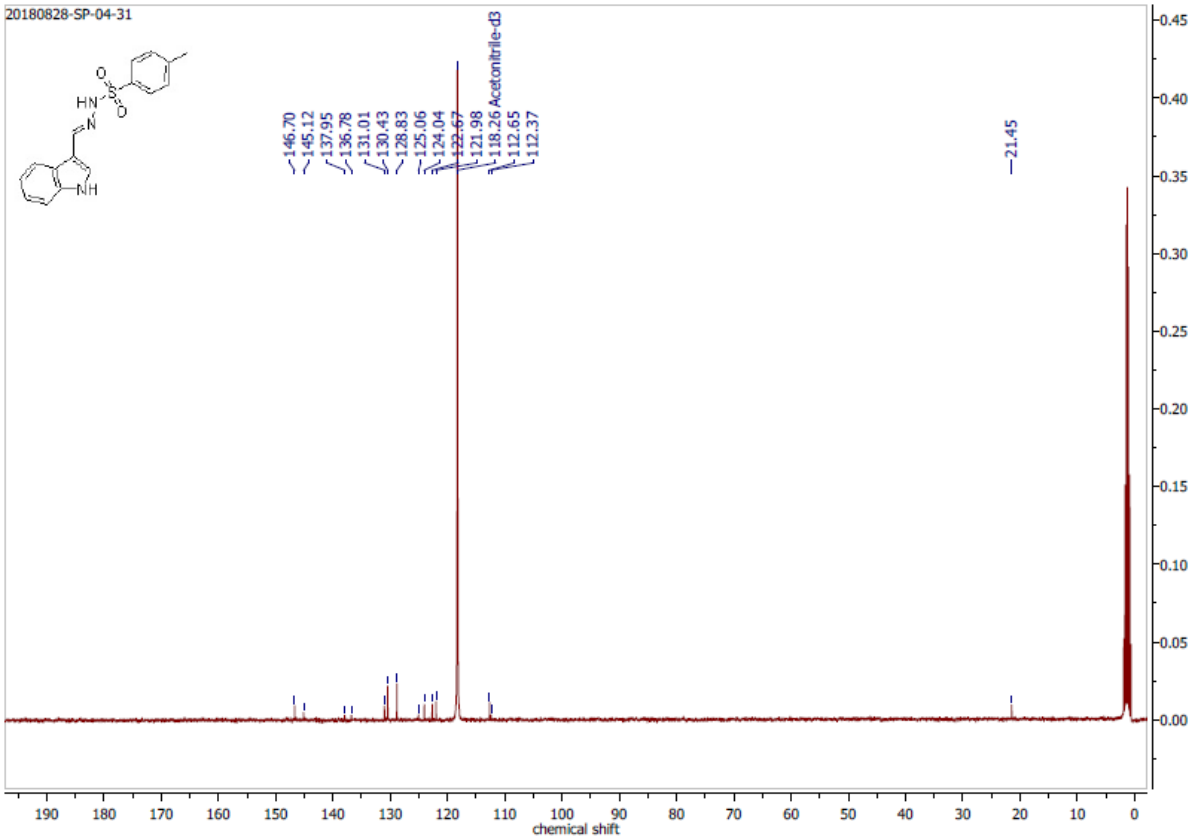


Fig. S55: ^{13}C NMR spectrum of compound 18 in CD_3CN-d_3 at 100 MHz.

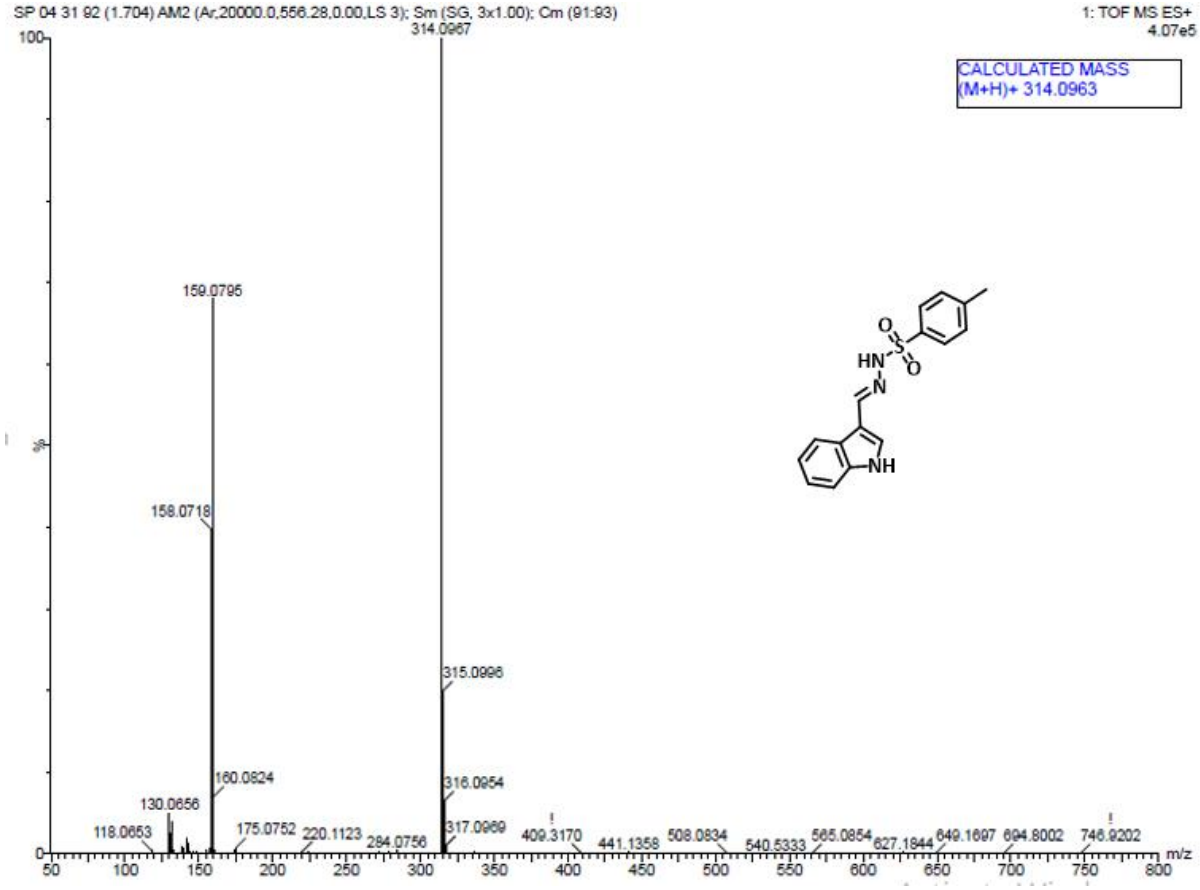


Fig. S56: HRMS spectrum of compound 18.

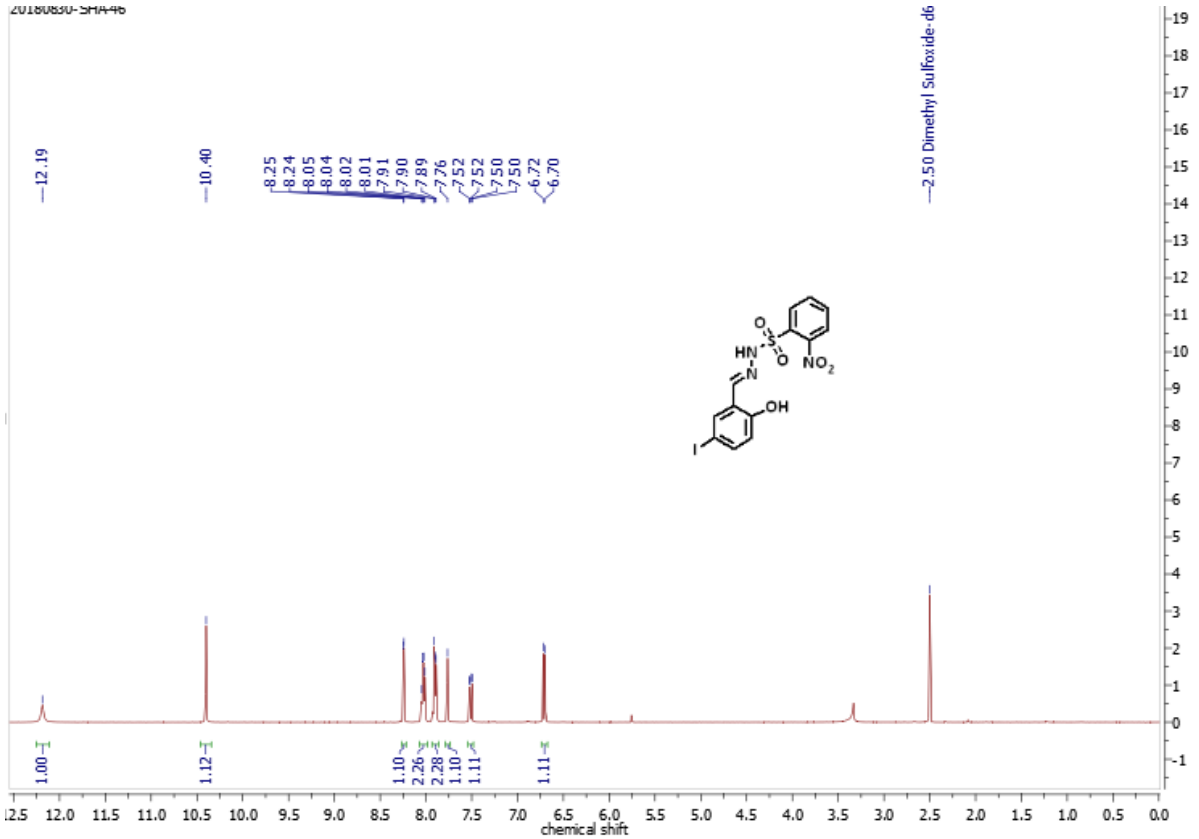


Fig. S57: ^{1}H NMR spectrum of compound 19 in DMSO-d_6 at 400 MHz.

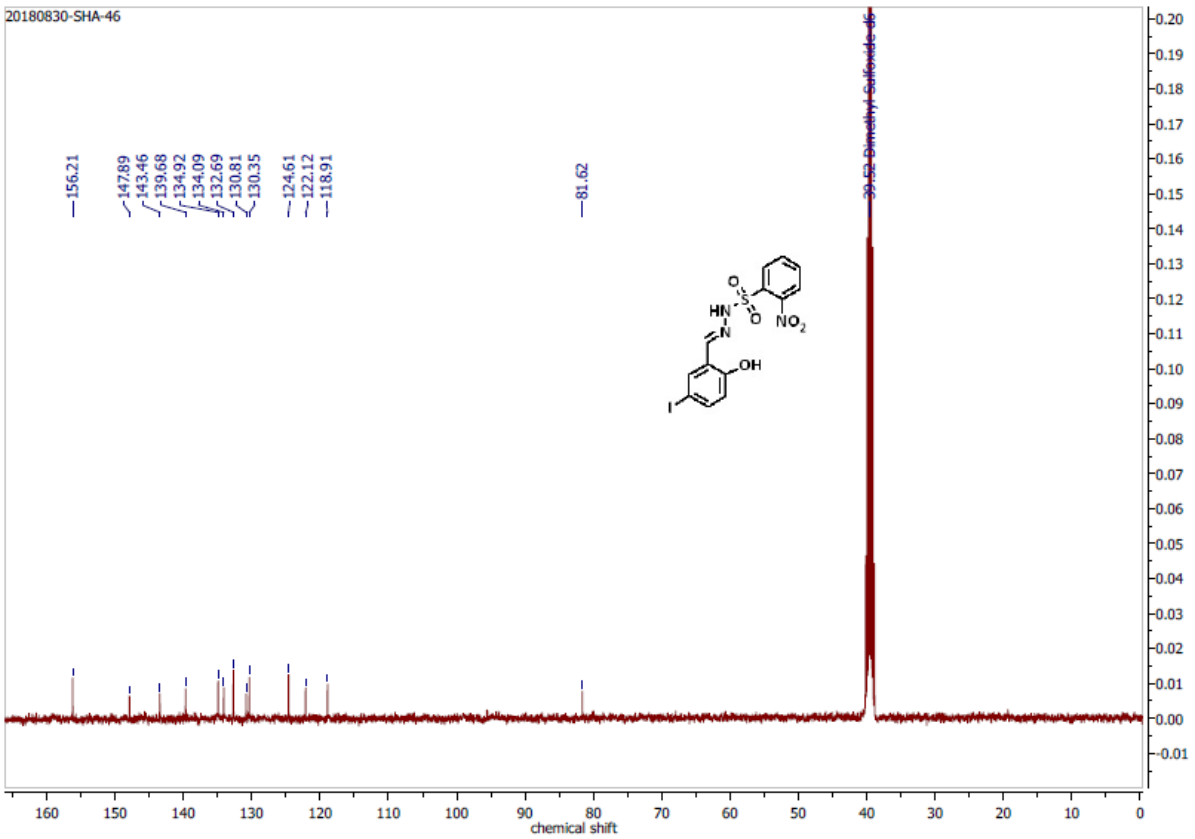


Fig. S58: ^{13}C NMR spectrum of compound 19 in DMSO-d_6 at 100 MHz.

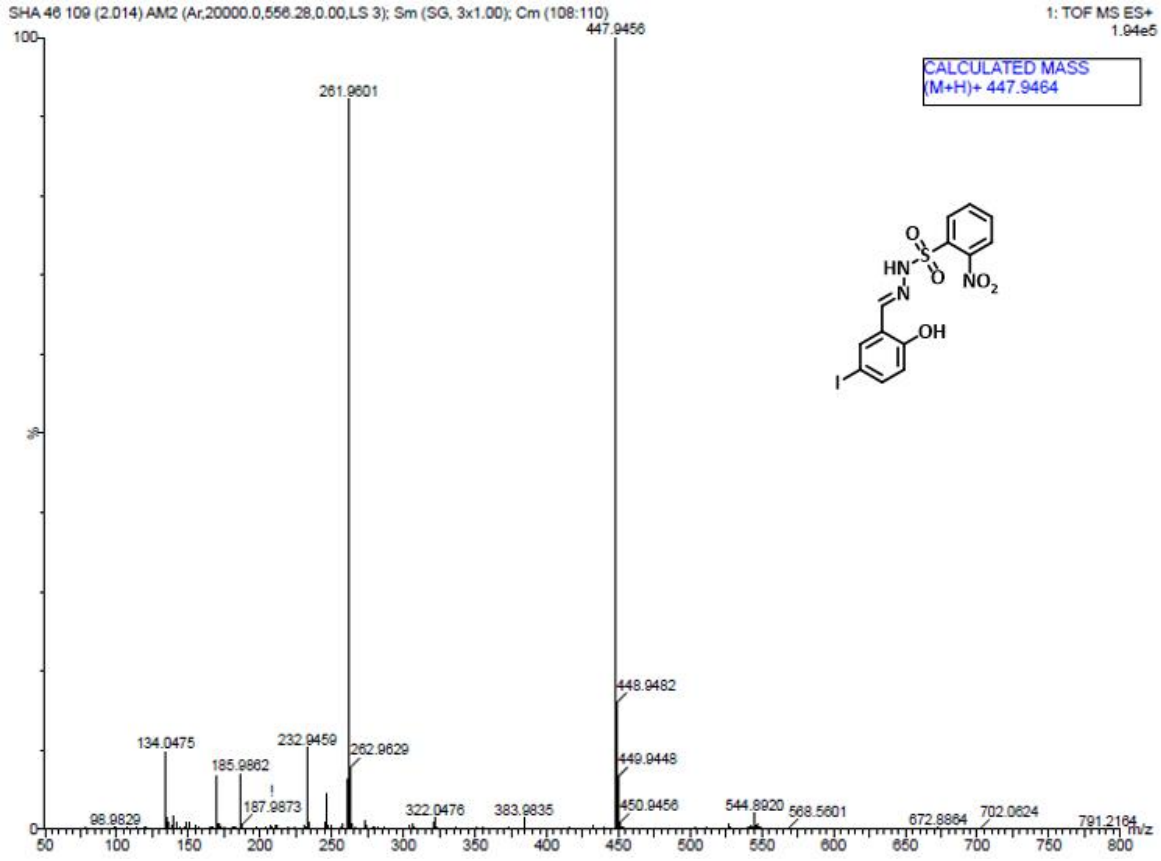


Fig. S59: HRMS spectrum of compound 19.

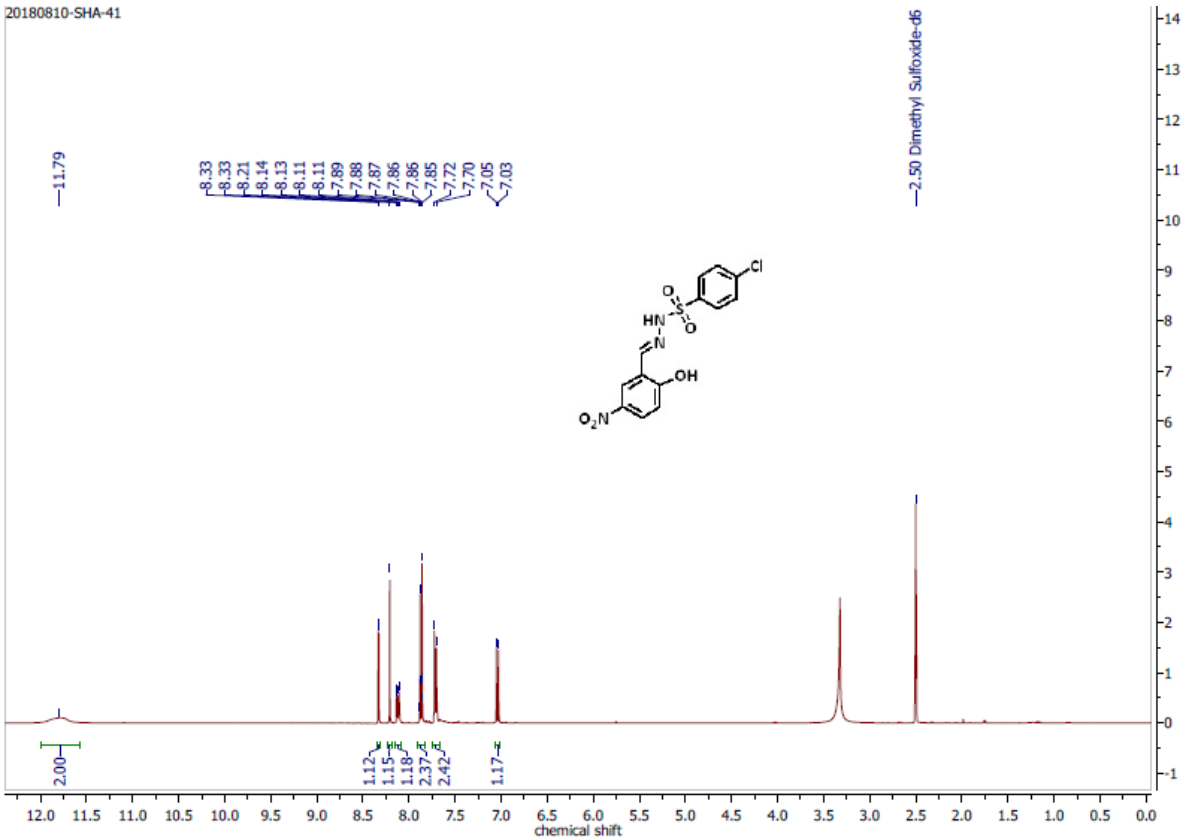


Fig. S60: ^{1}H NMR spectrum of compound 20 in DMSO-d_6 at 400 MHz.

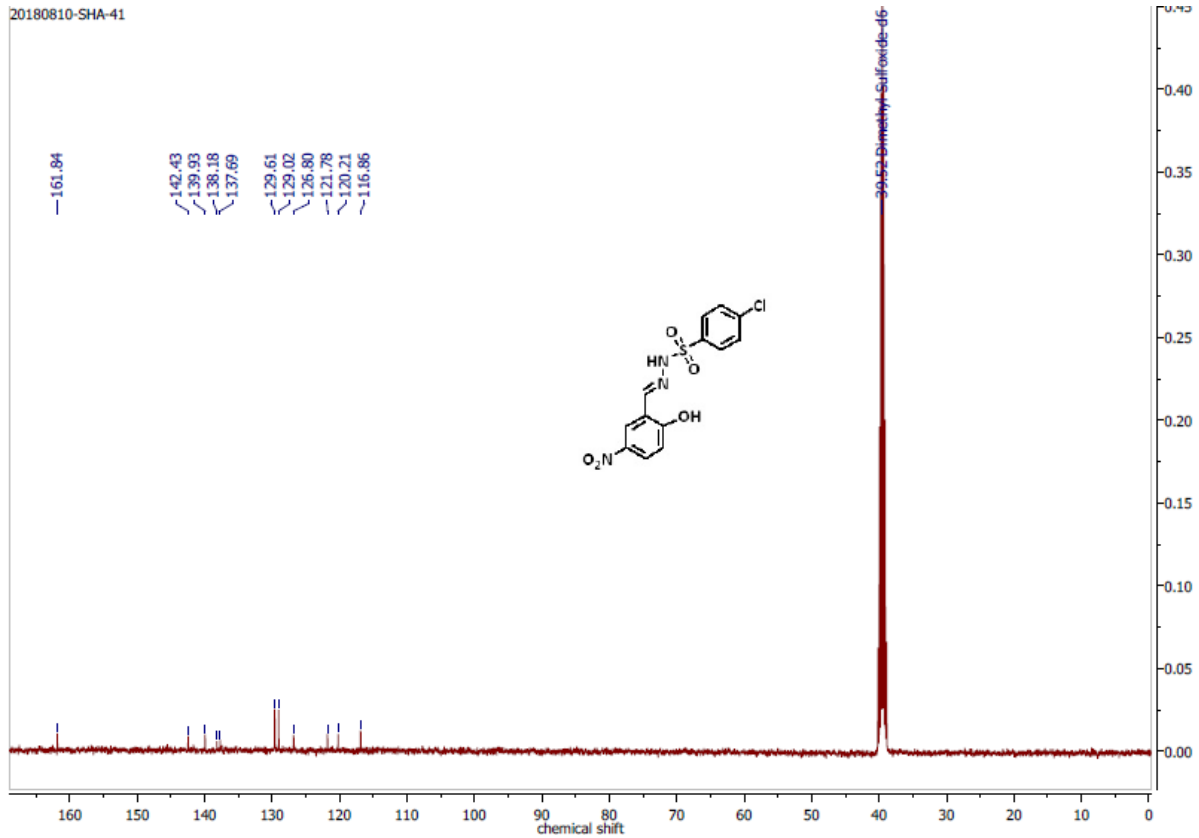


Fig. S61: ^{13}C NMR spectrum of compound 20 in DMSO-d_6 at 100 MHz.

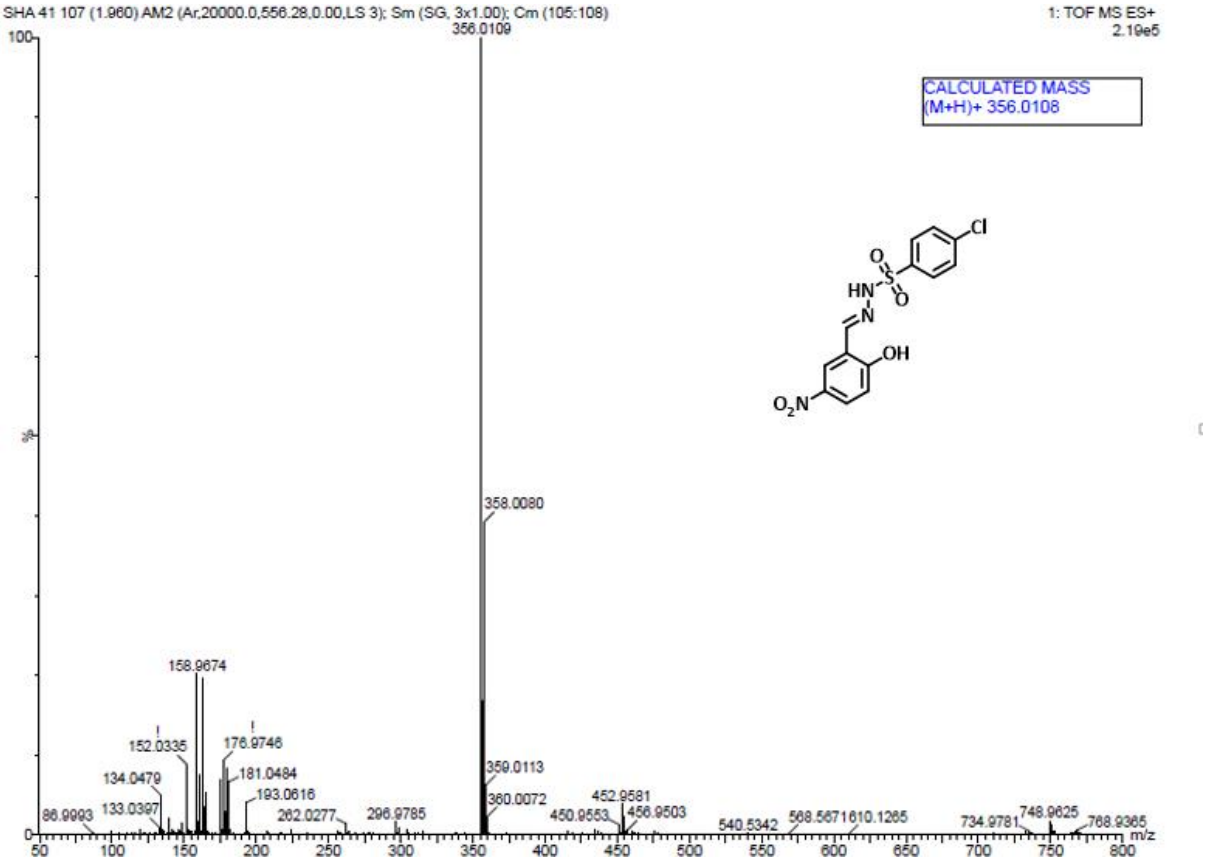


Fig. S62: HRMS spectrum of compound 20.

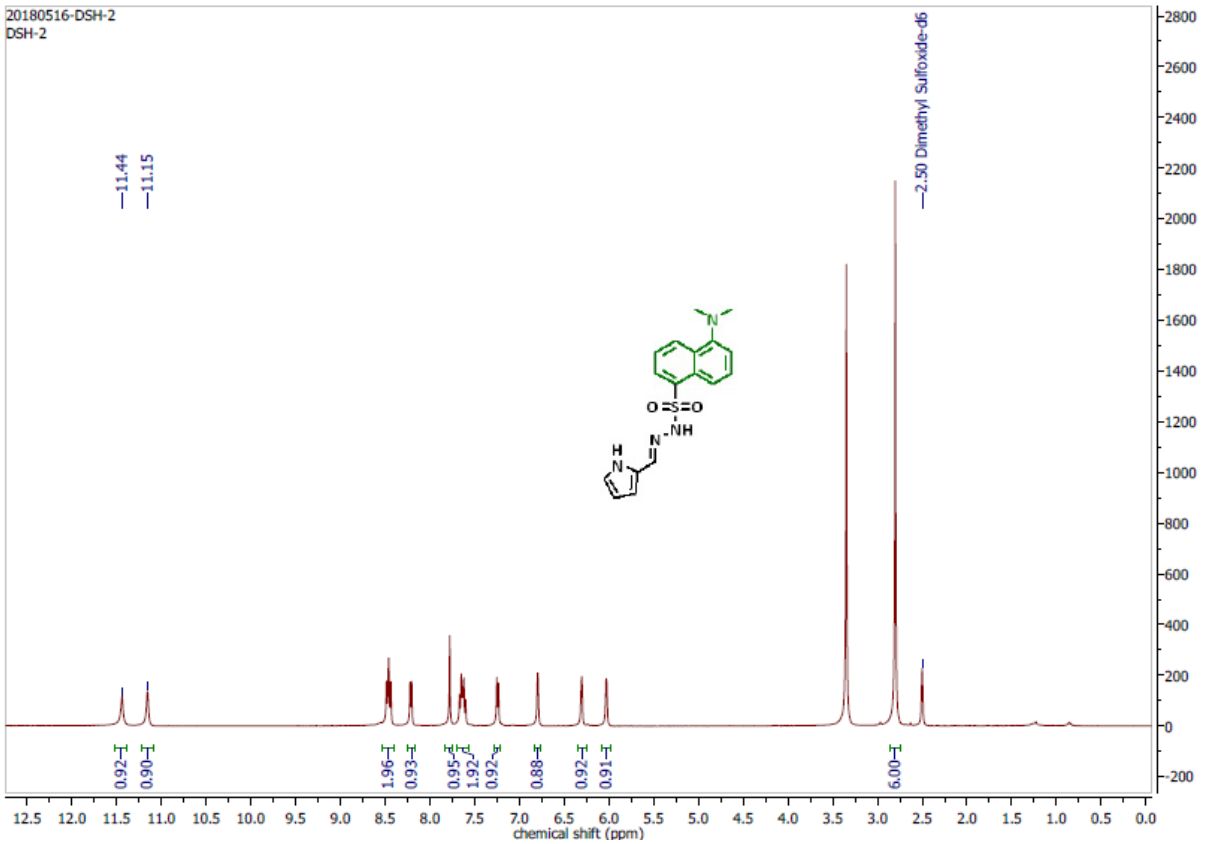


Fig. S63: ^{1}H NMR spectrum of compound 21 in DMSO-d_6 at 400 MHz.

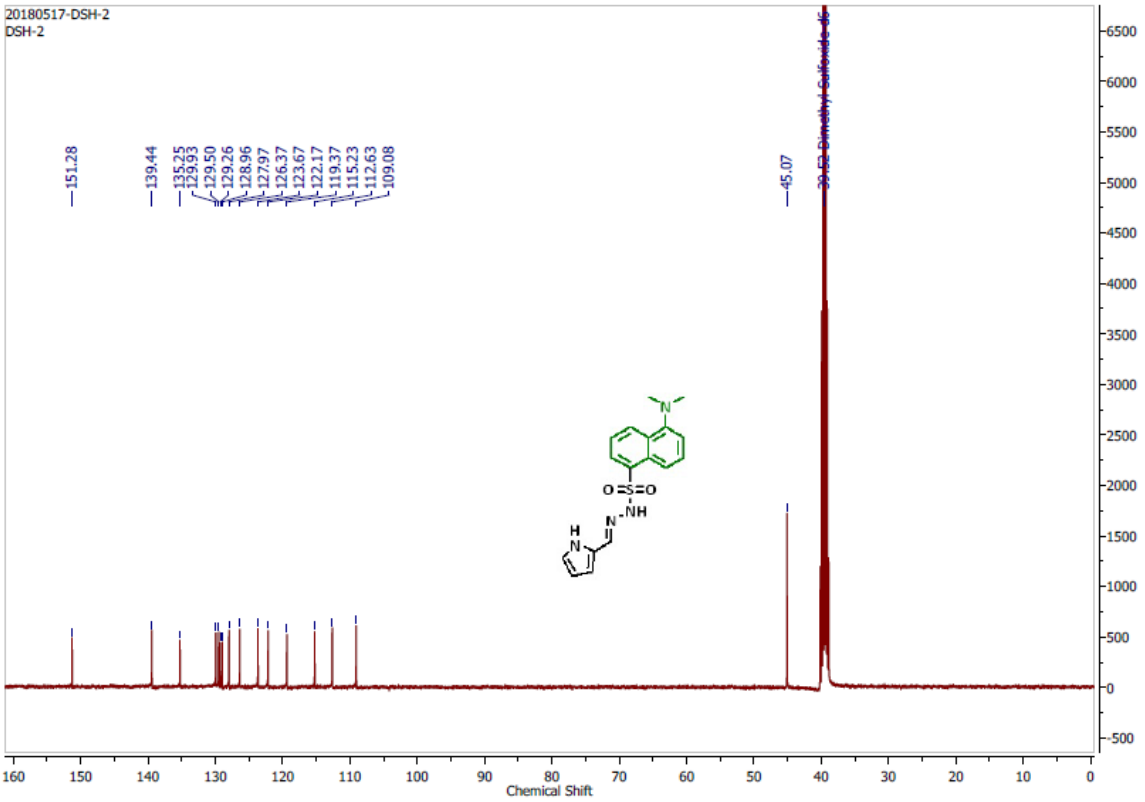


Fig. S64: ^{13}C NMR spectrum of compound 21 in DMSO-d_6 at 100 MHz.

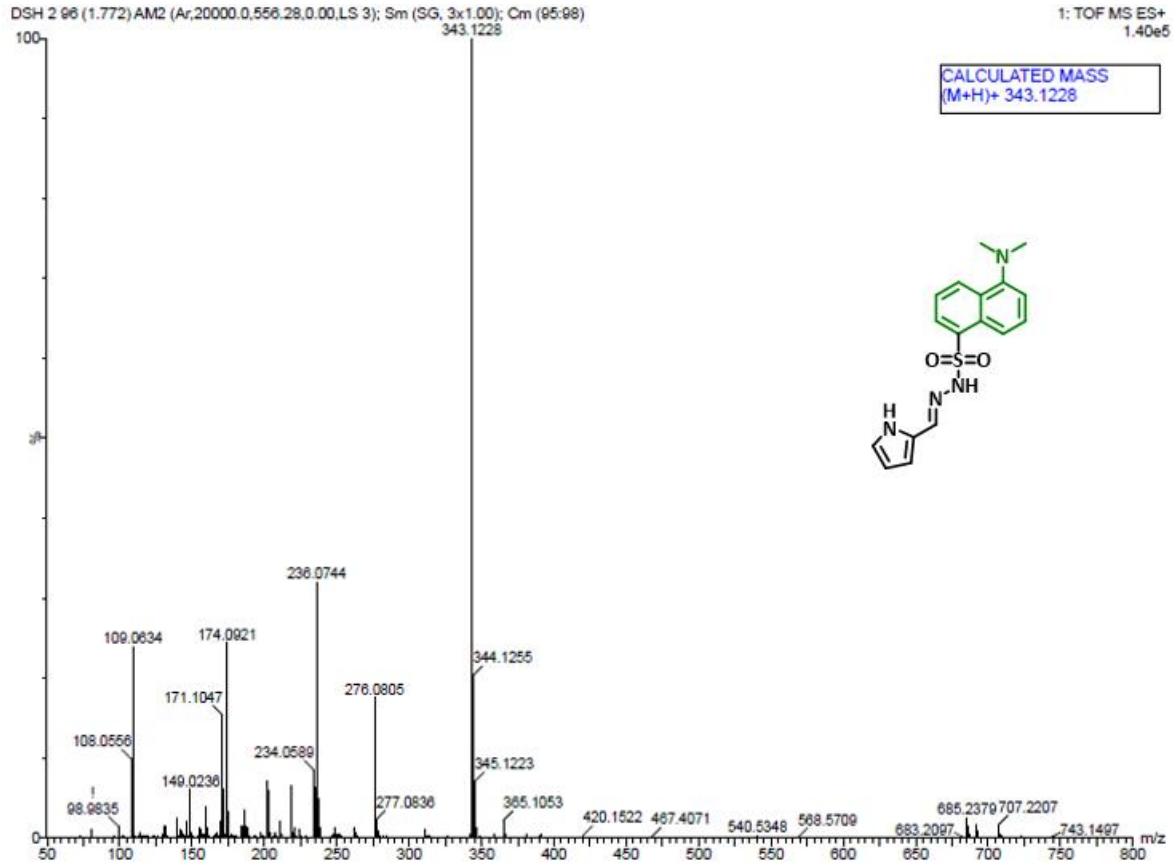


Fig. S65: HRMS spectrum of compound 21.

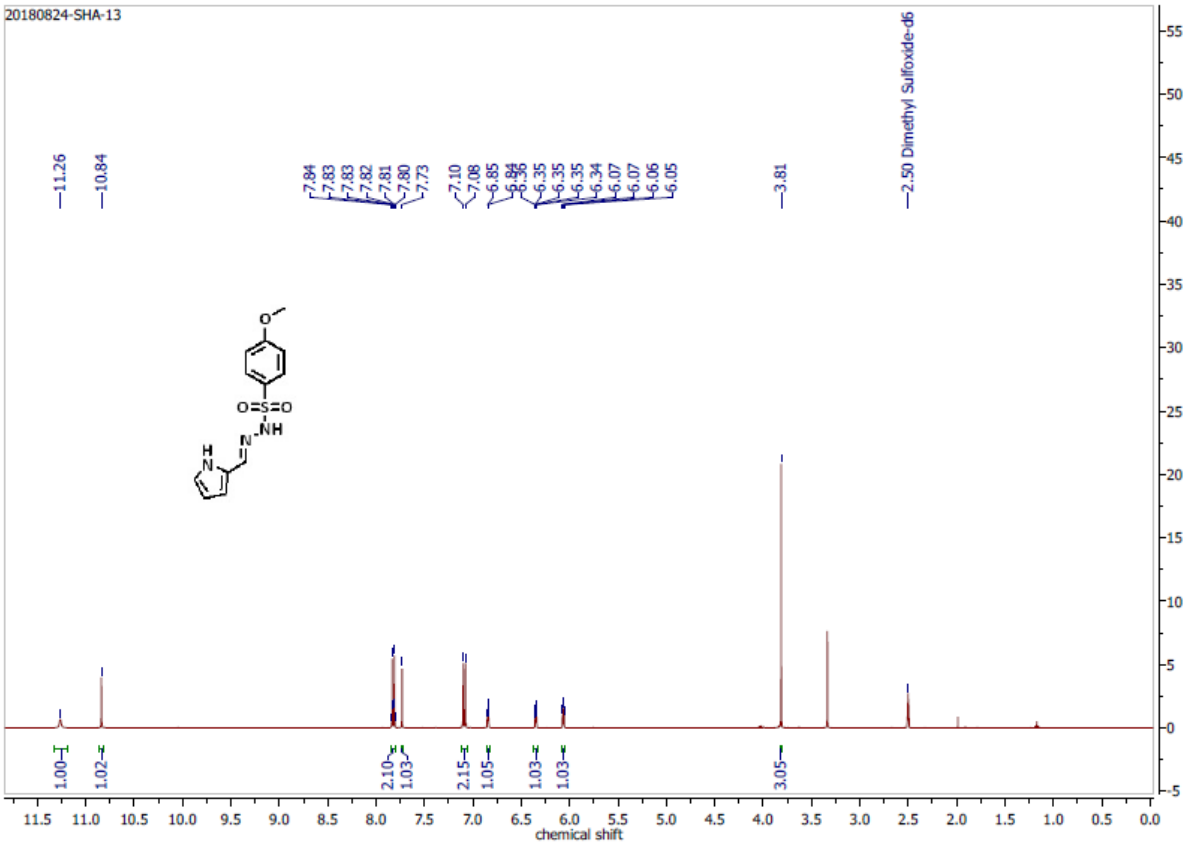


Fig. S66: ^{1}H NMR spectrum of compound 22 in DMSO-d_6 at 400 MHz.

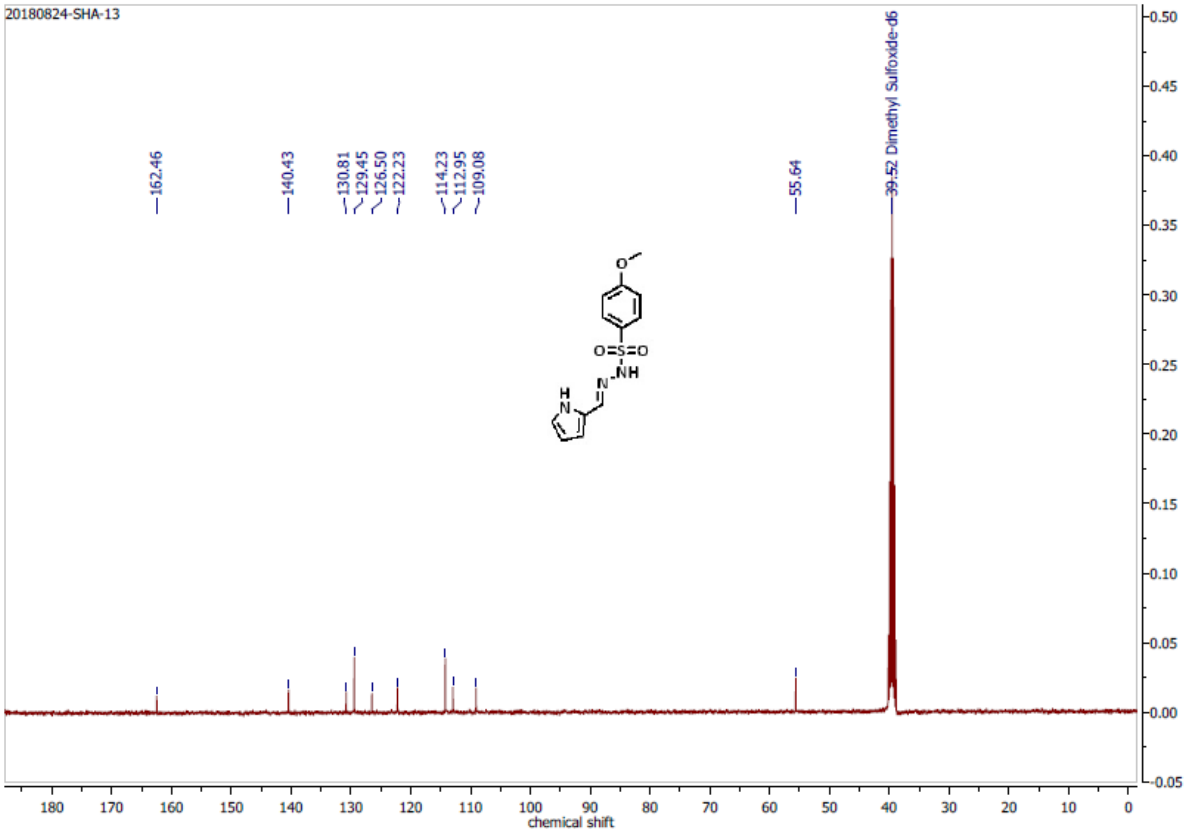


Fig. S67: ^{13}C NMR spectrum of compound 22 in DMSO-d_6 at 100 MHz.

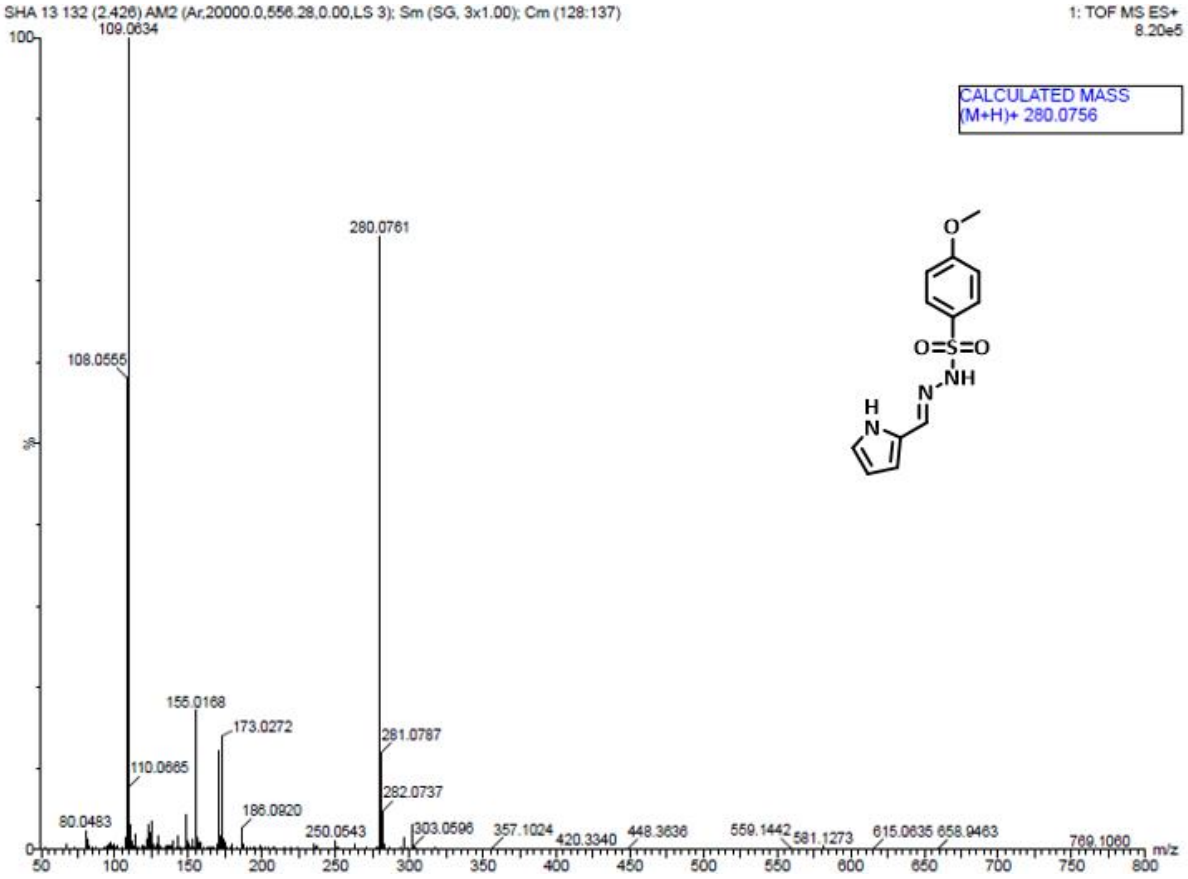


Fig. S68: HRMS spectrum of compound 22.

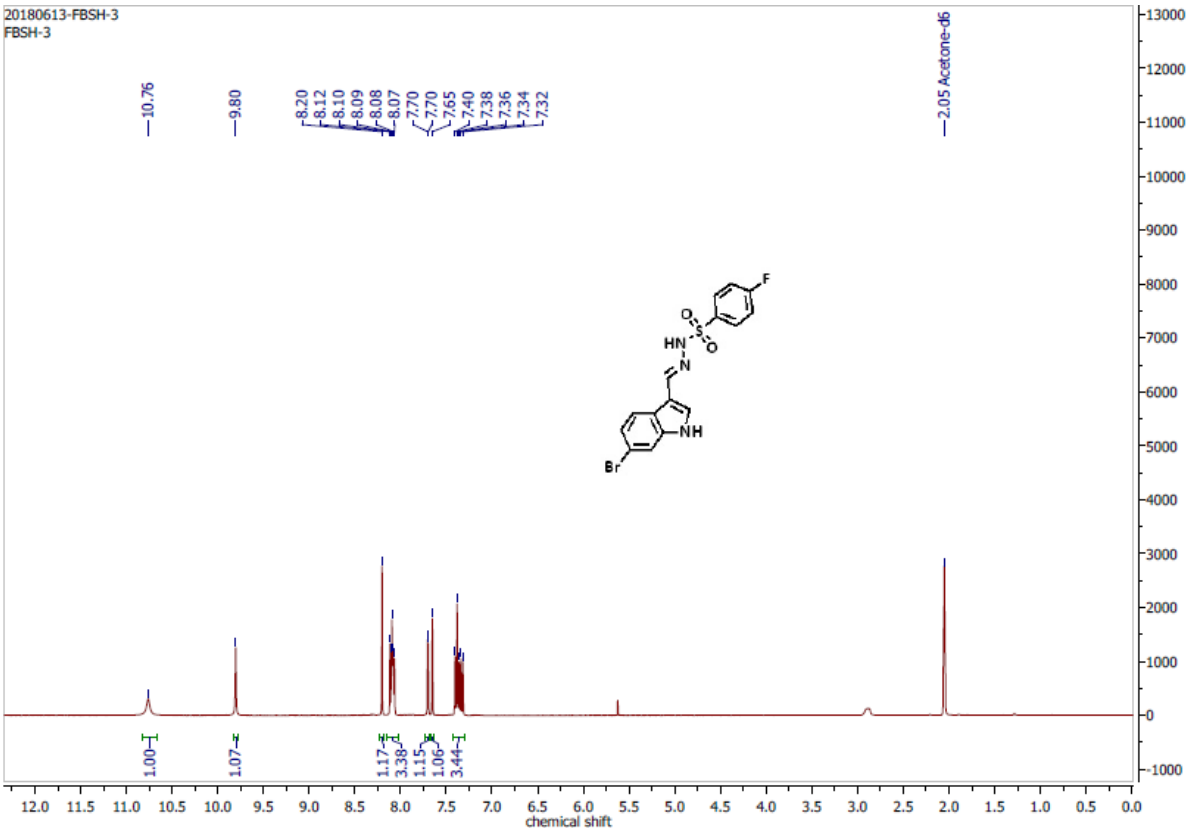


Fig. S69: [1] H NMR spectrum of compound 23 in DMSO-d_6 at 400 MHz.

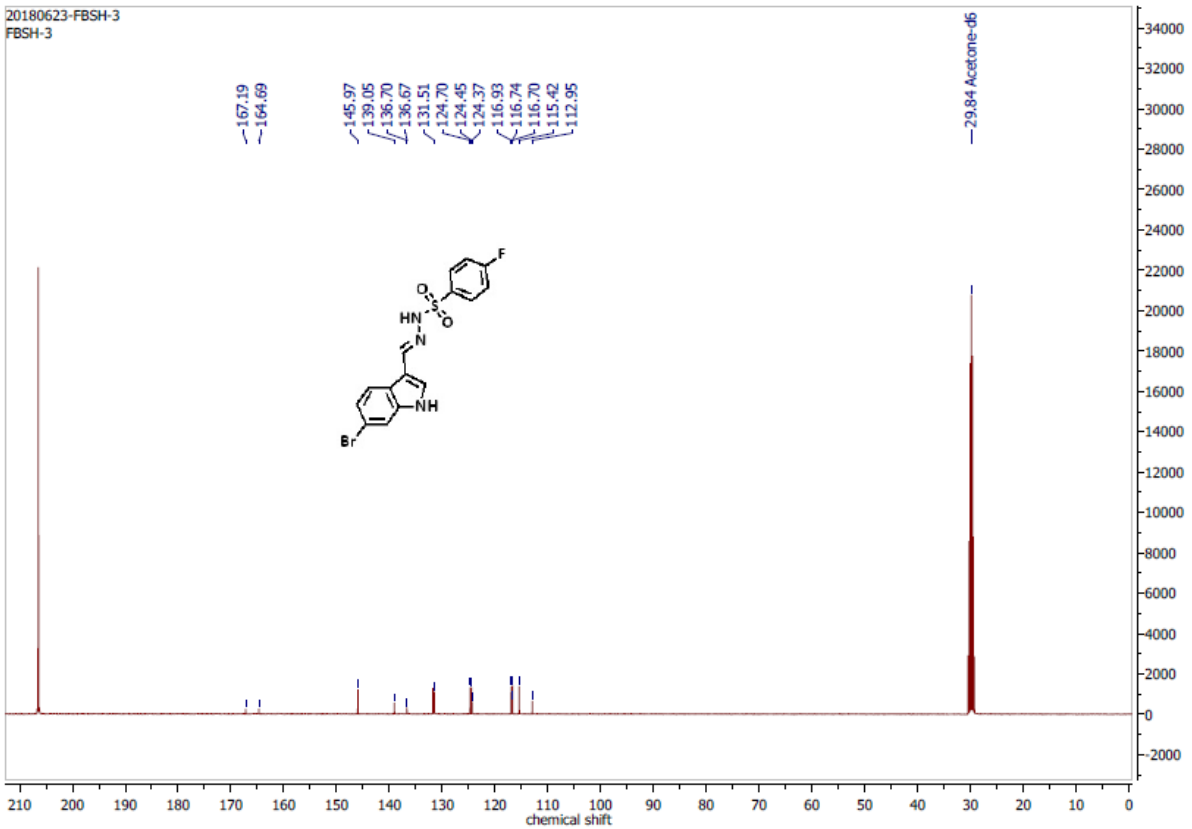


Fig. S70: ^{13}C NMR spectrum of compound 23 in DMSO-d_6 at 100 MHz.

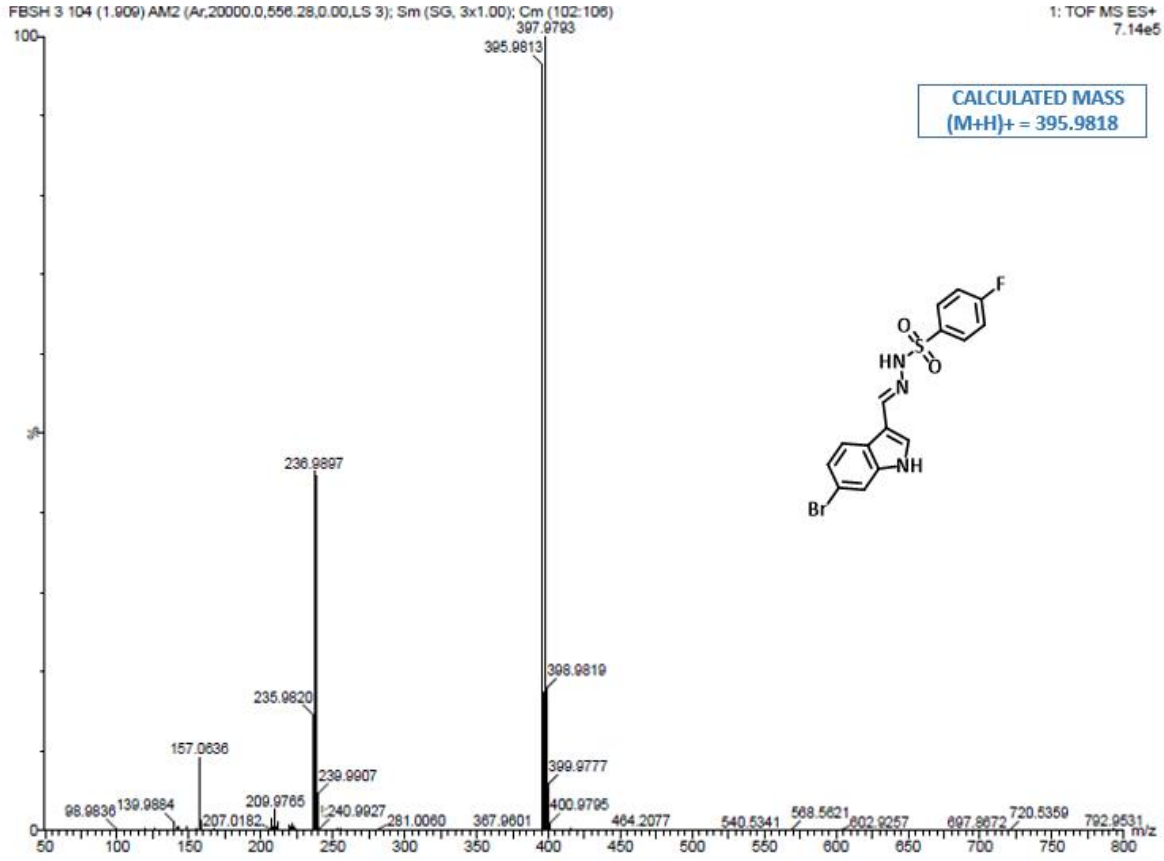


Fig. S71: HRMS spectrum of compound 23.

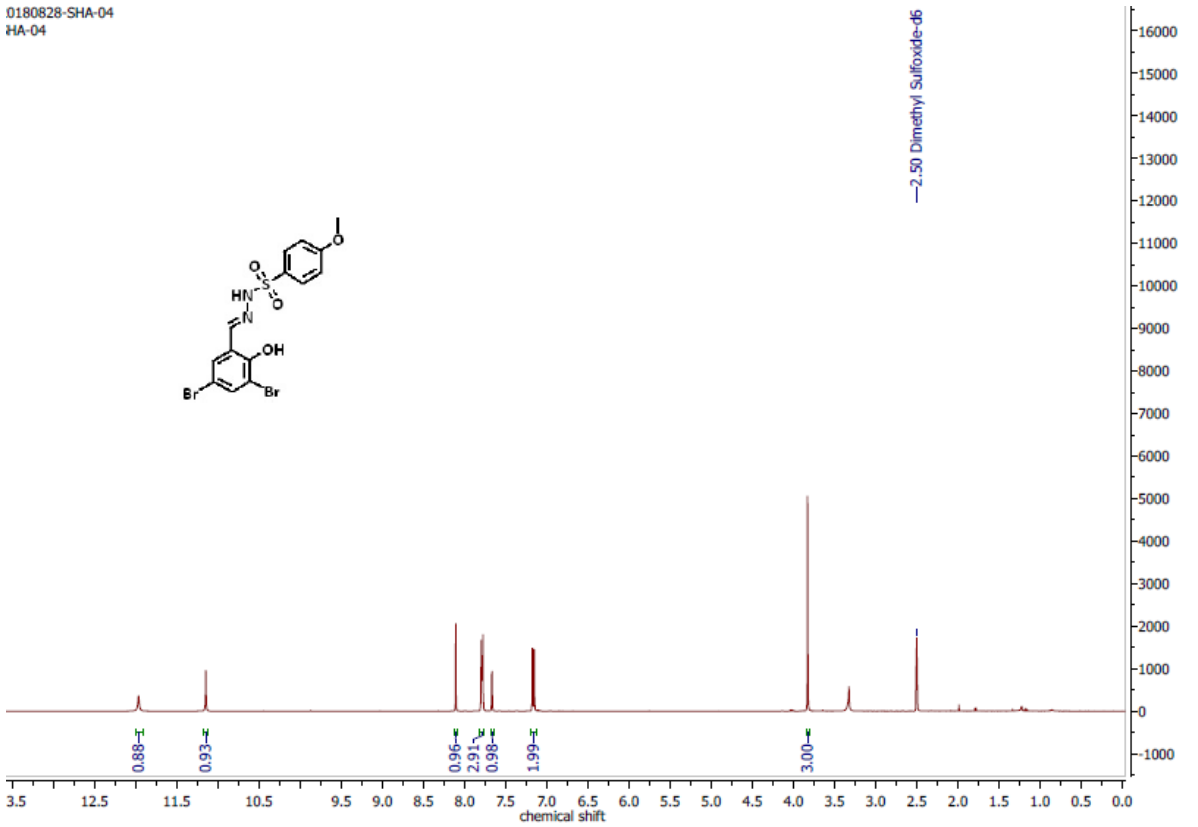


Fig. S72: [1] H NMR spectrum of compound 24 in DMSO-d_6 at 400 MHz.

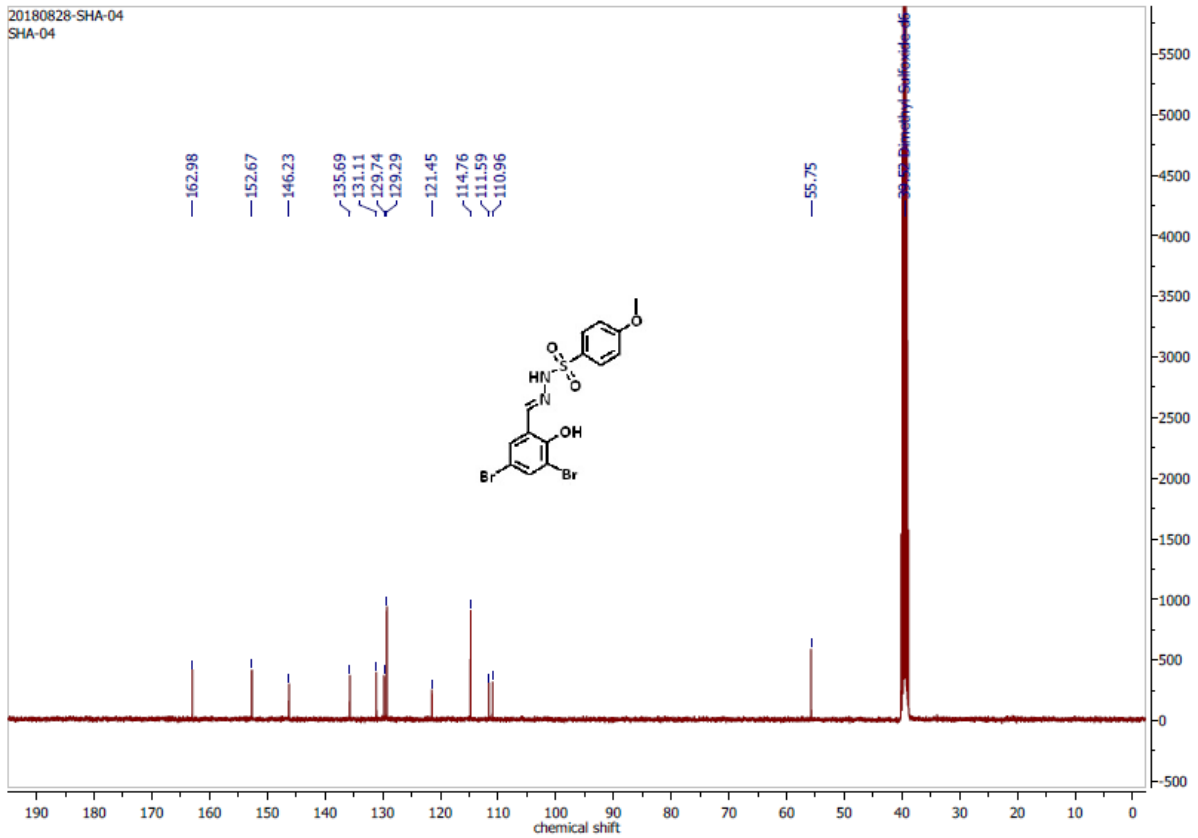


Fig. S73: [13]C NMR spectrum of compound 24 in DMSO-d_6 at 100 MHz.

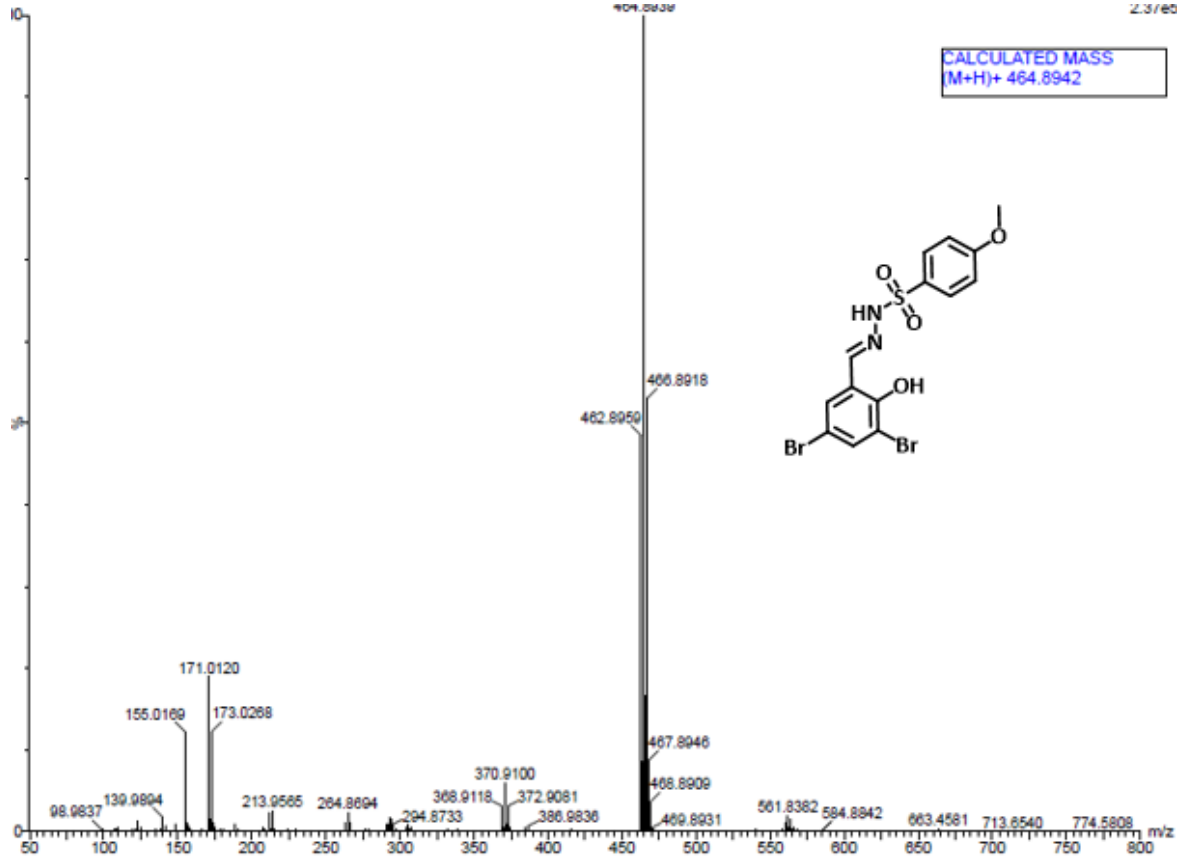


Fig. S74: HRMS spectrum of compound 24.

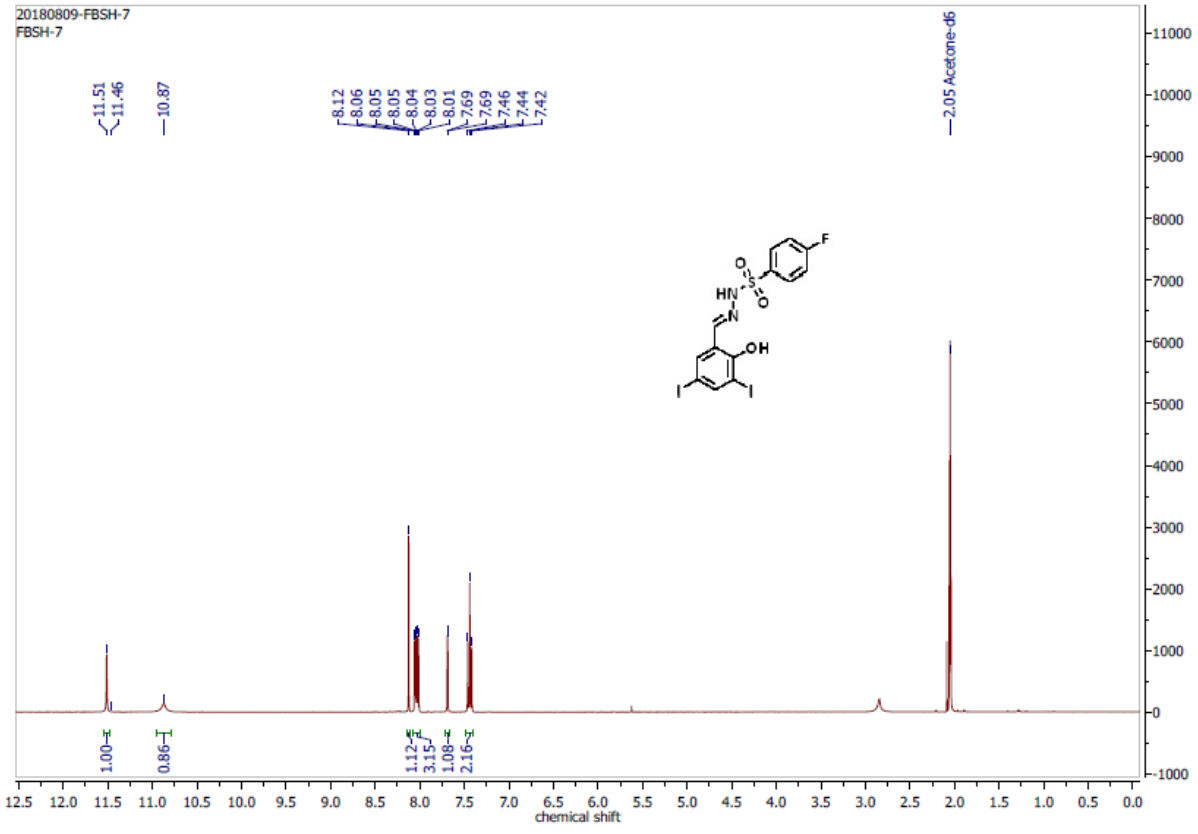


Fig. S75: ^{1}H NMR spectrum of compound 25 in Acetone-d_6 at 400 MHz.

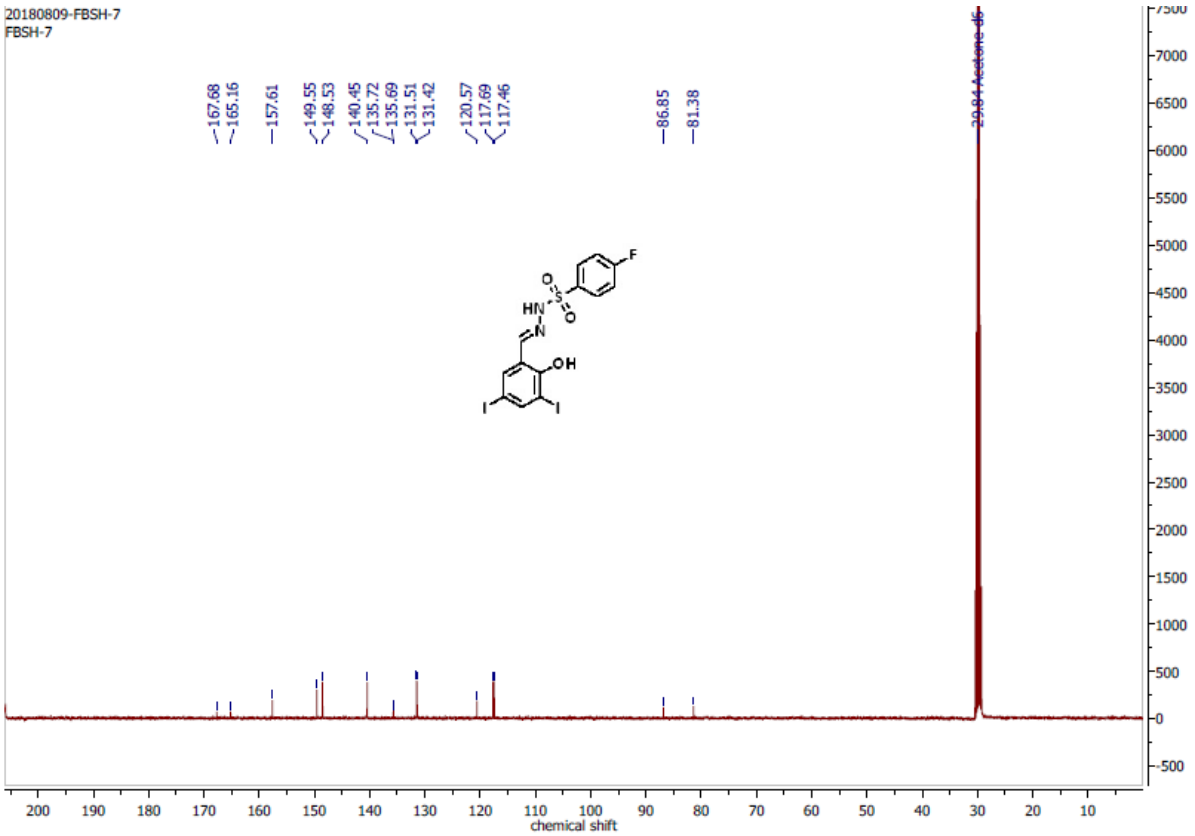


Fig. S76: ^{13}C NMR spectrum of compound 25 in Acetone-d_6 at 100 MHz.

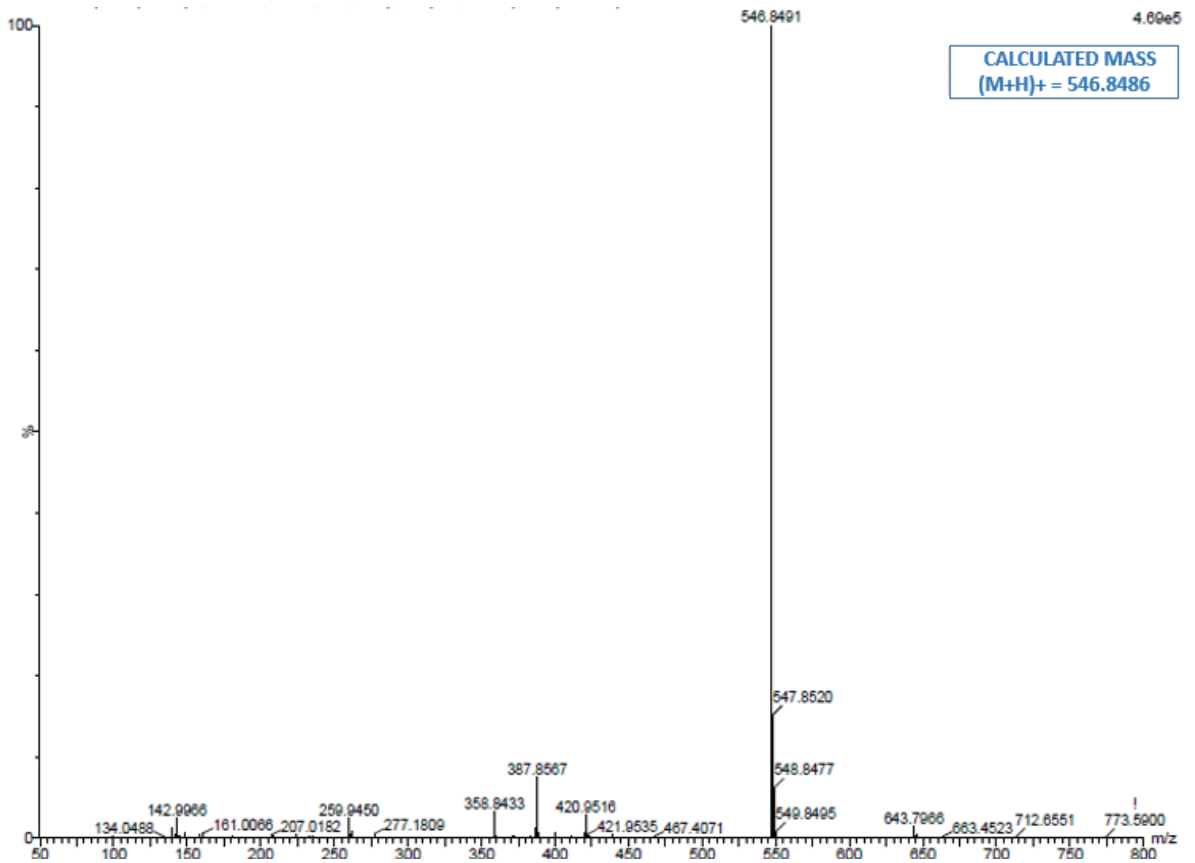


Fig. S77: HRMS spectrum of compound 25.

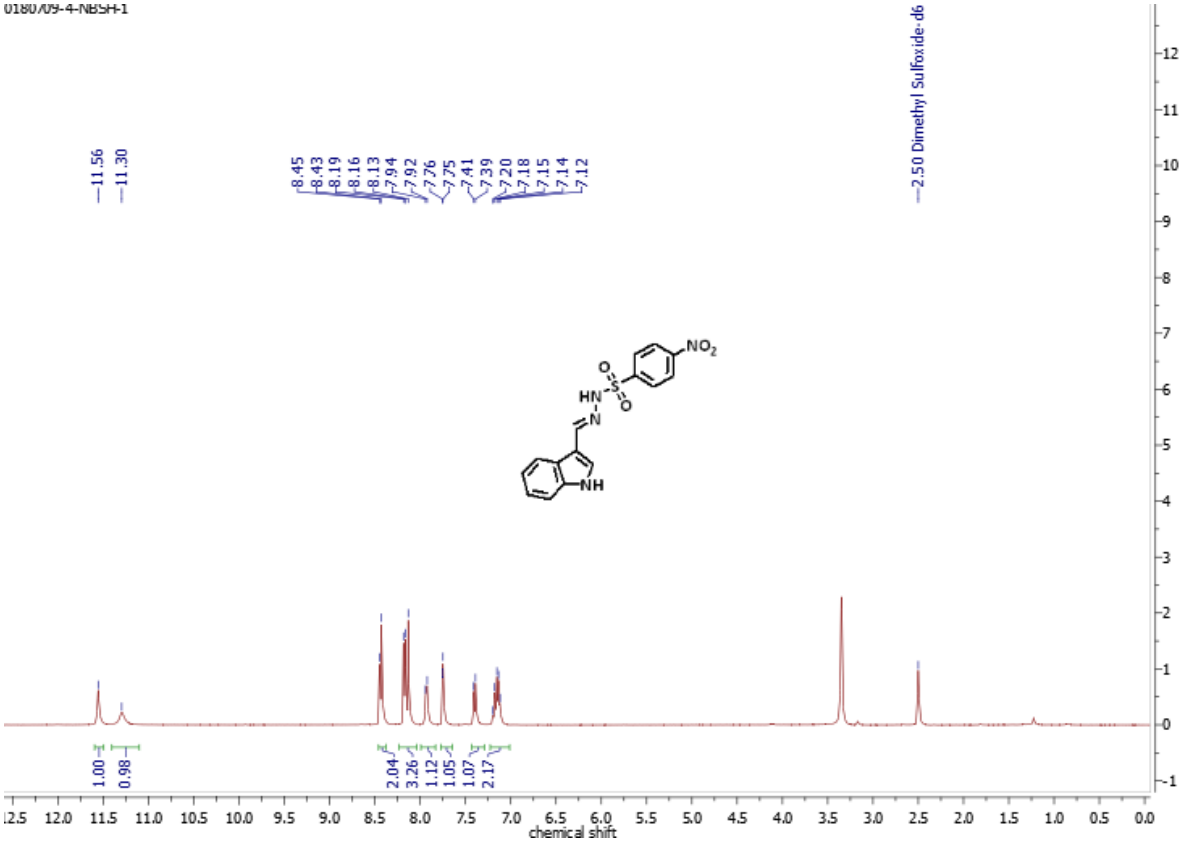


Fig. S78: [1] H NMR spectrum of compound 26 in DMSO-d_6 at 400 MHz.

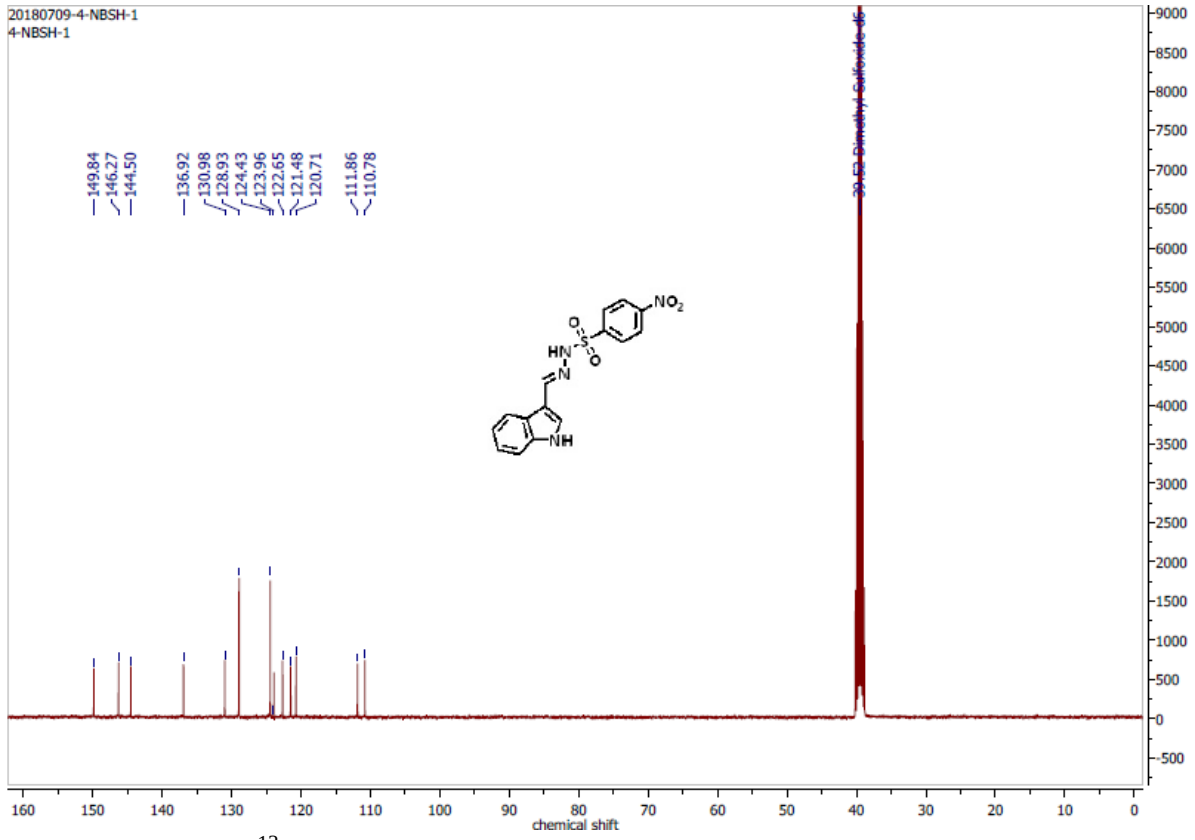


Fig. S79: [13] C NMR spectrum of compound 26 in DMSO-d_6 at 100 MHz.

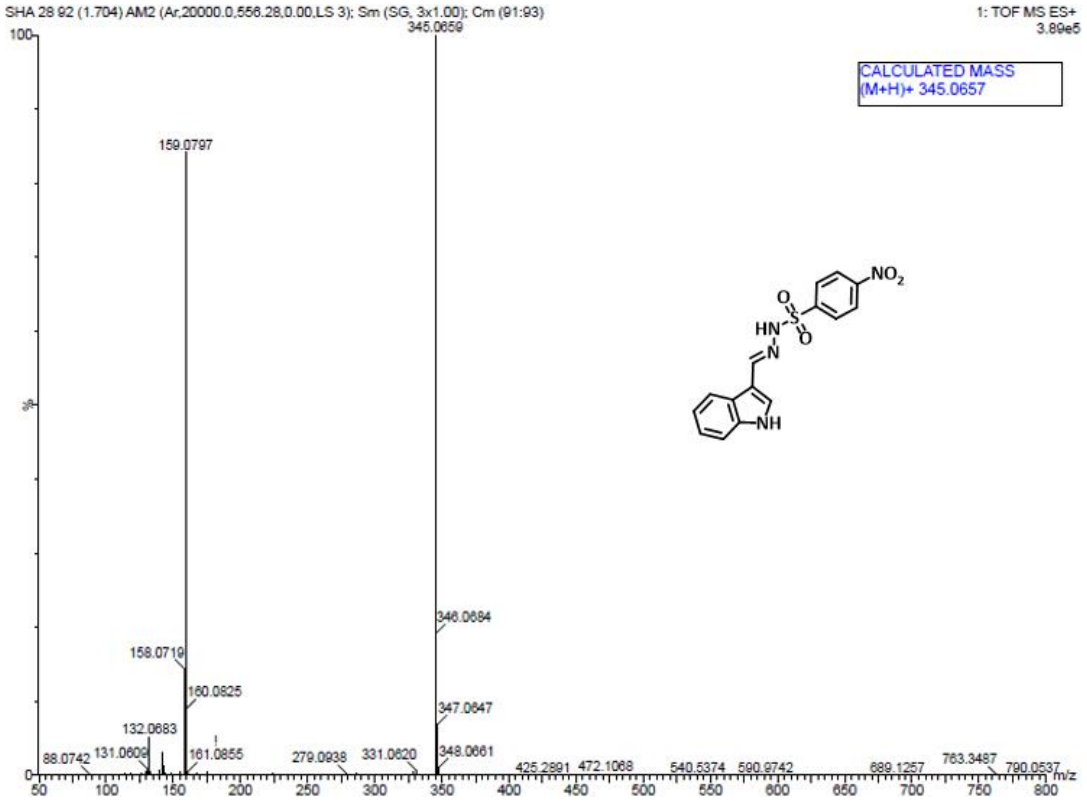


Fig. S80: HRMS spectrum of compound 26.

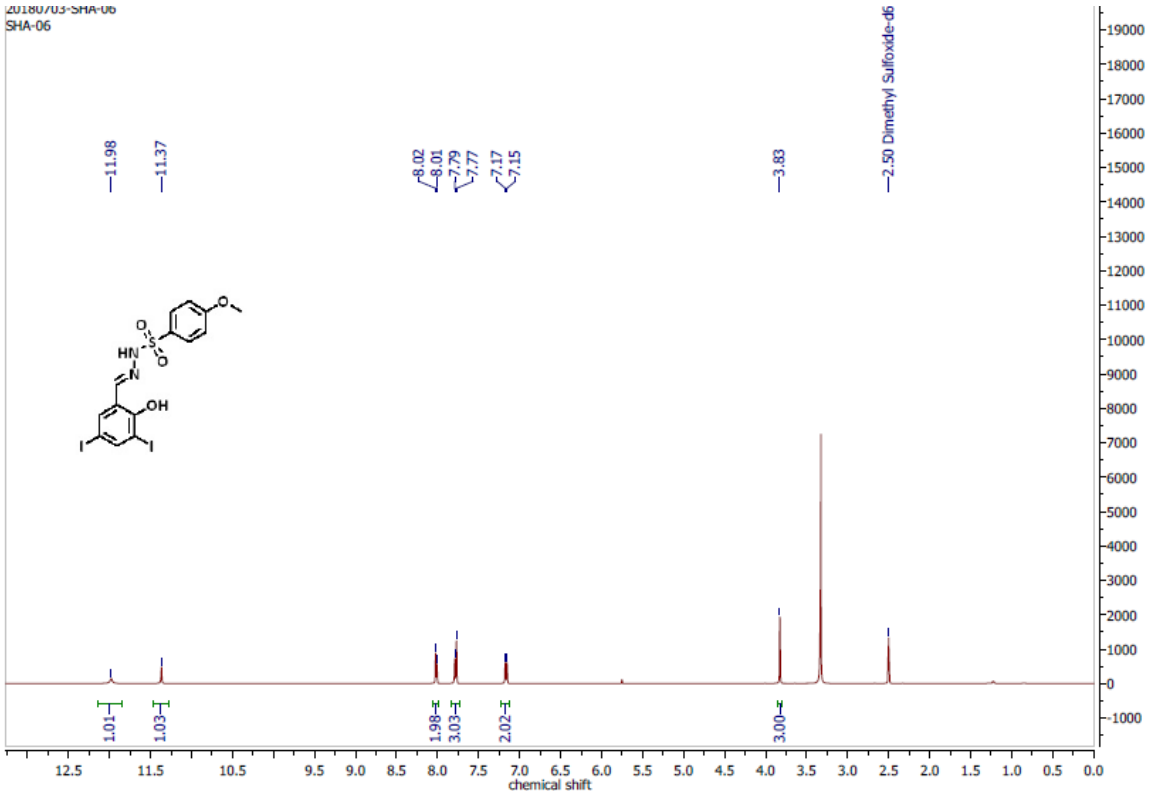


Fig. S81: [1] H NMR spectrum of compound 27 in DMSO-d_6 at 400 MHz.

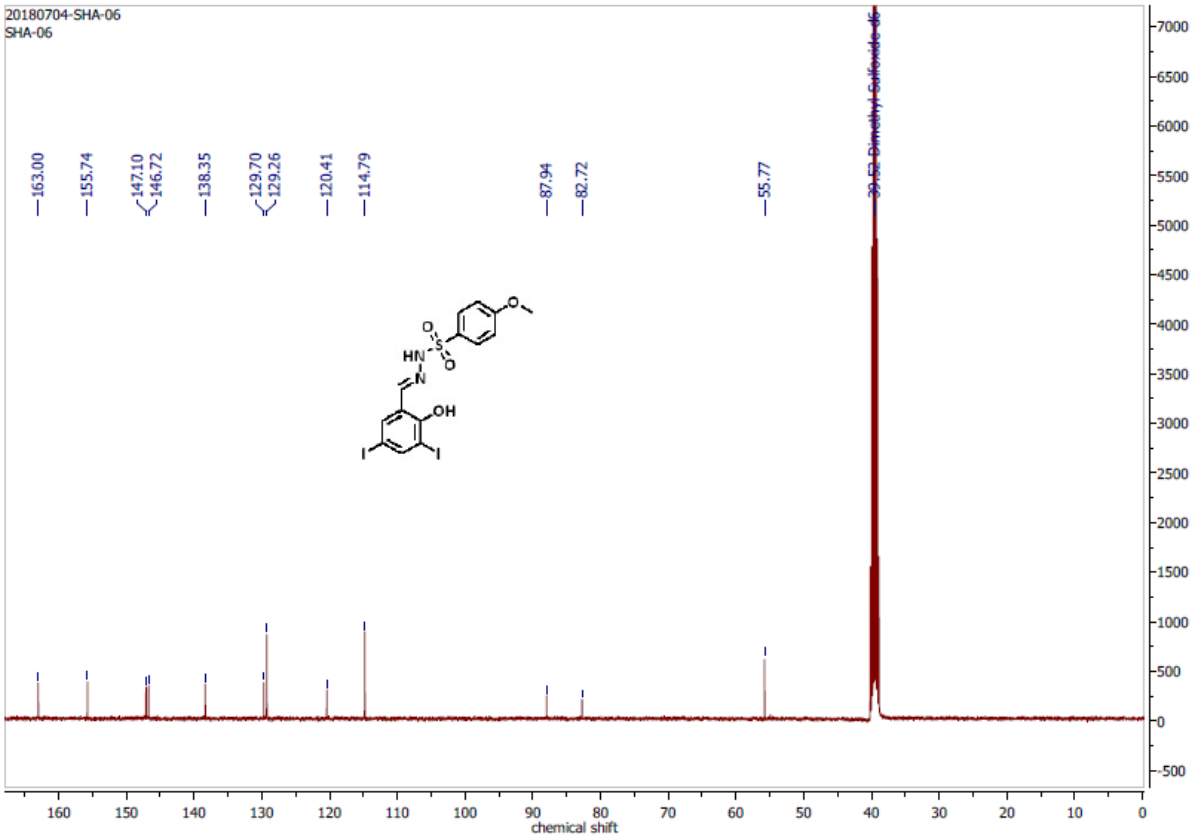


Fig. S82: ^{13}CNMR spectrum of compound 27 in DMSO-d_6 at 100 MHz.

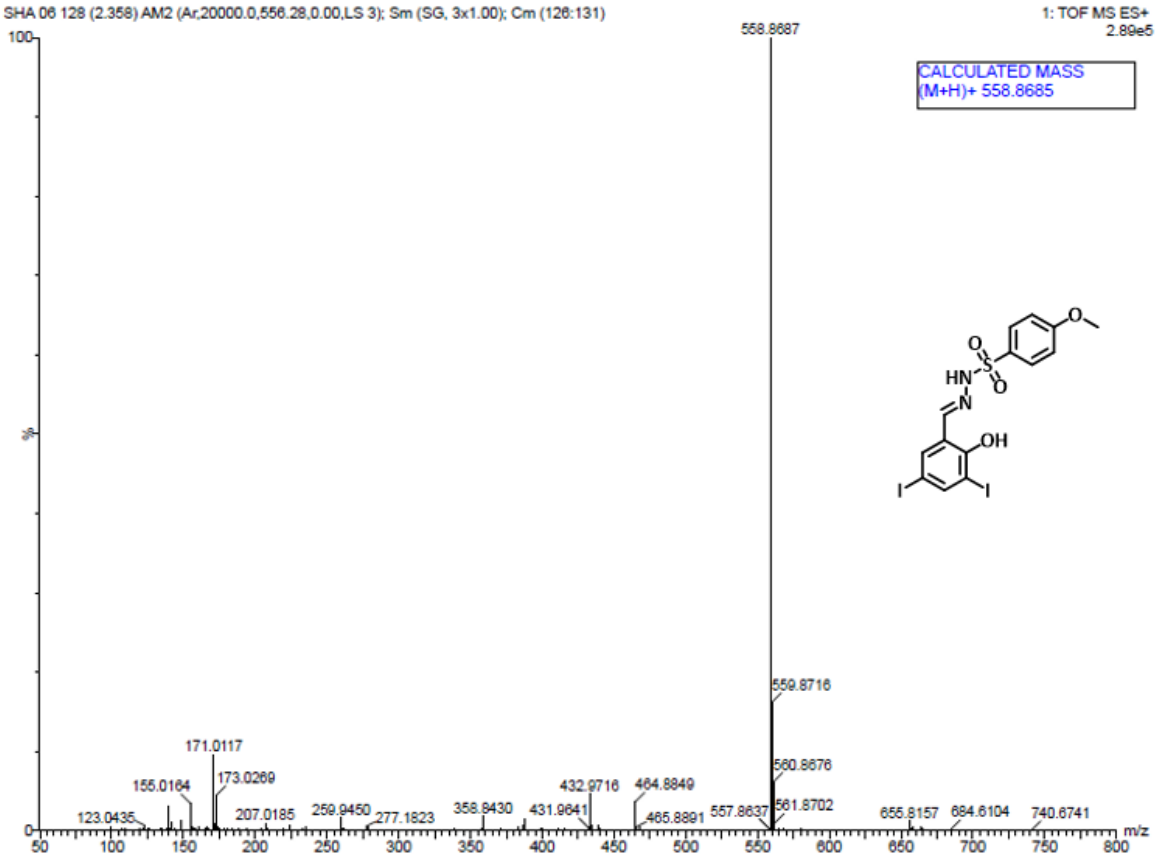


Fig. S83: HRMS spectrum of compound 27.

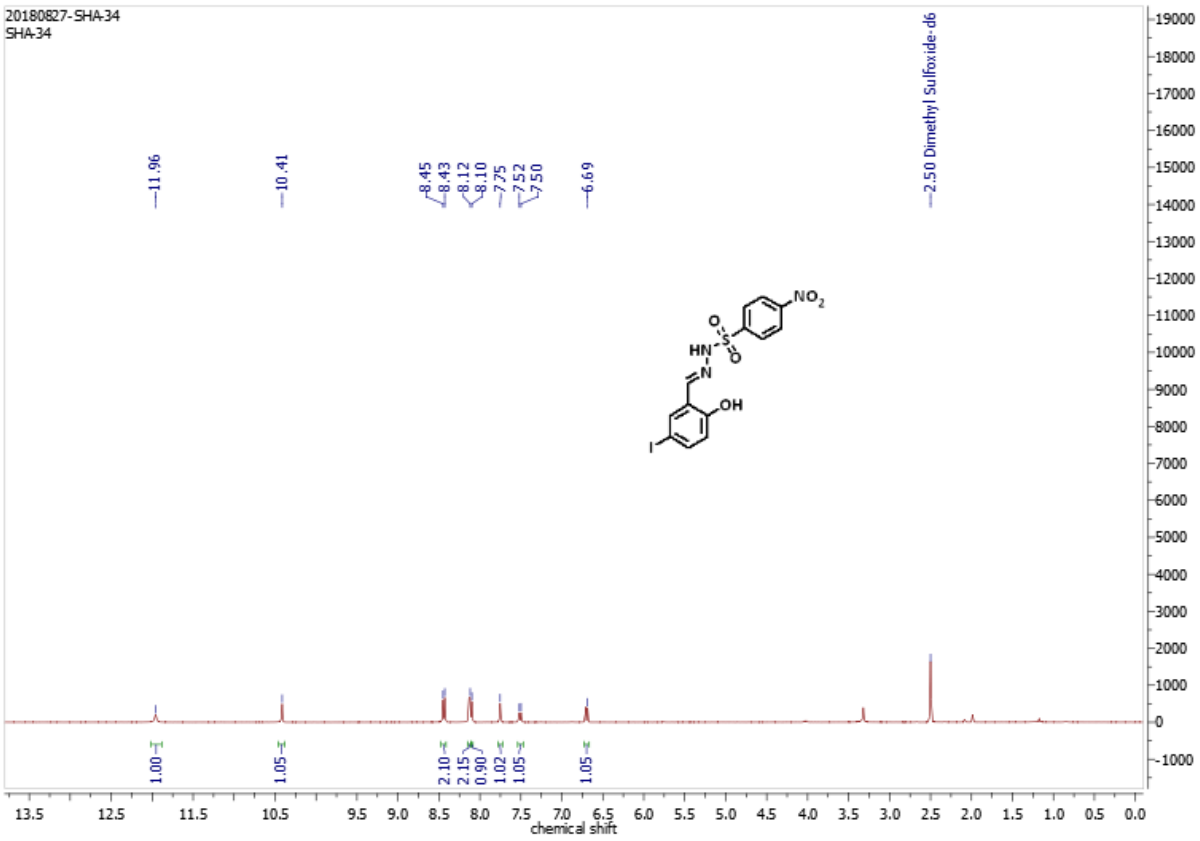


Fig. S84: [1] H NMR spectrum of compound 28 in DMSO-d_6 at 400 MHz.

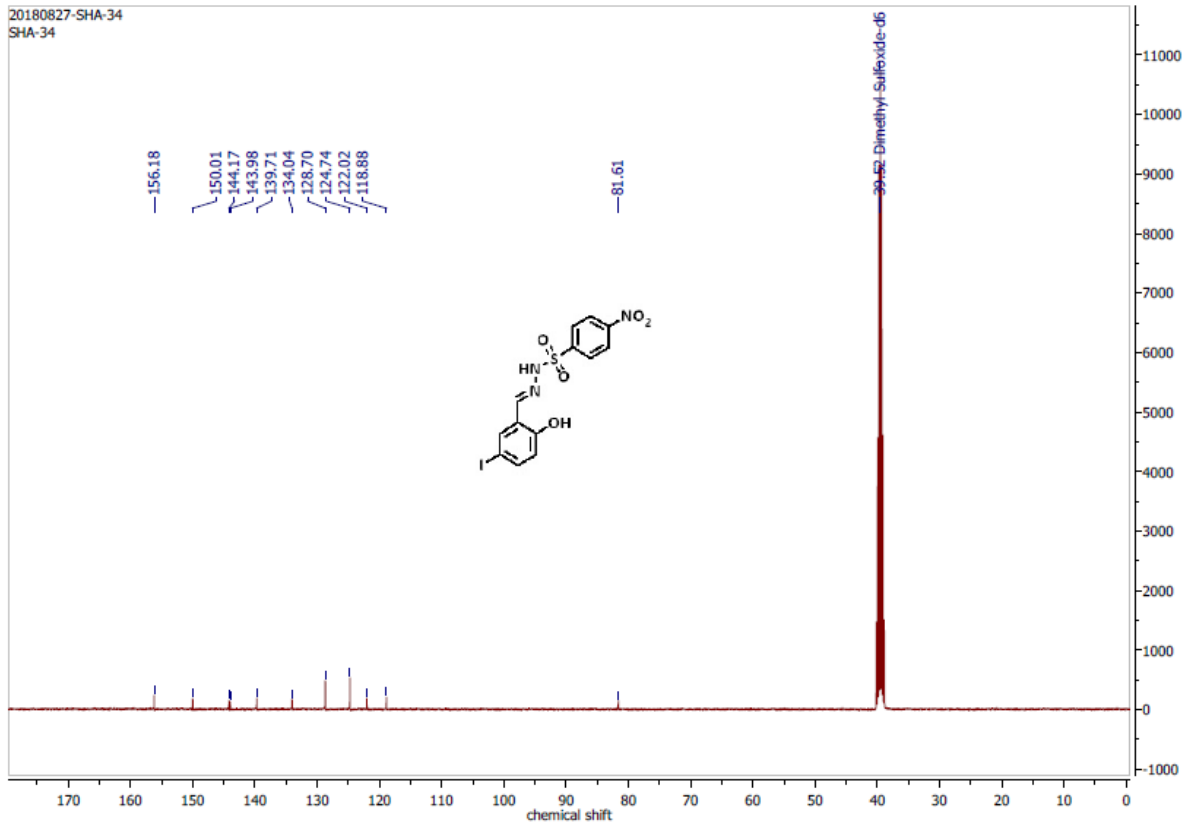


Fig. S85: [13] C NMR spectrum of compound 28 in DMSO-d_6 at 100 MHz.

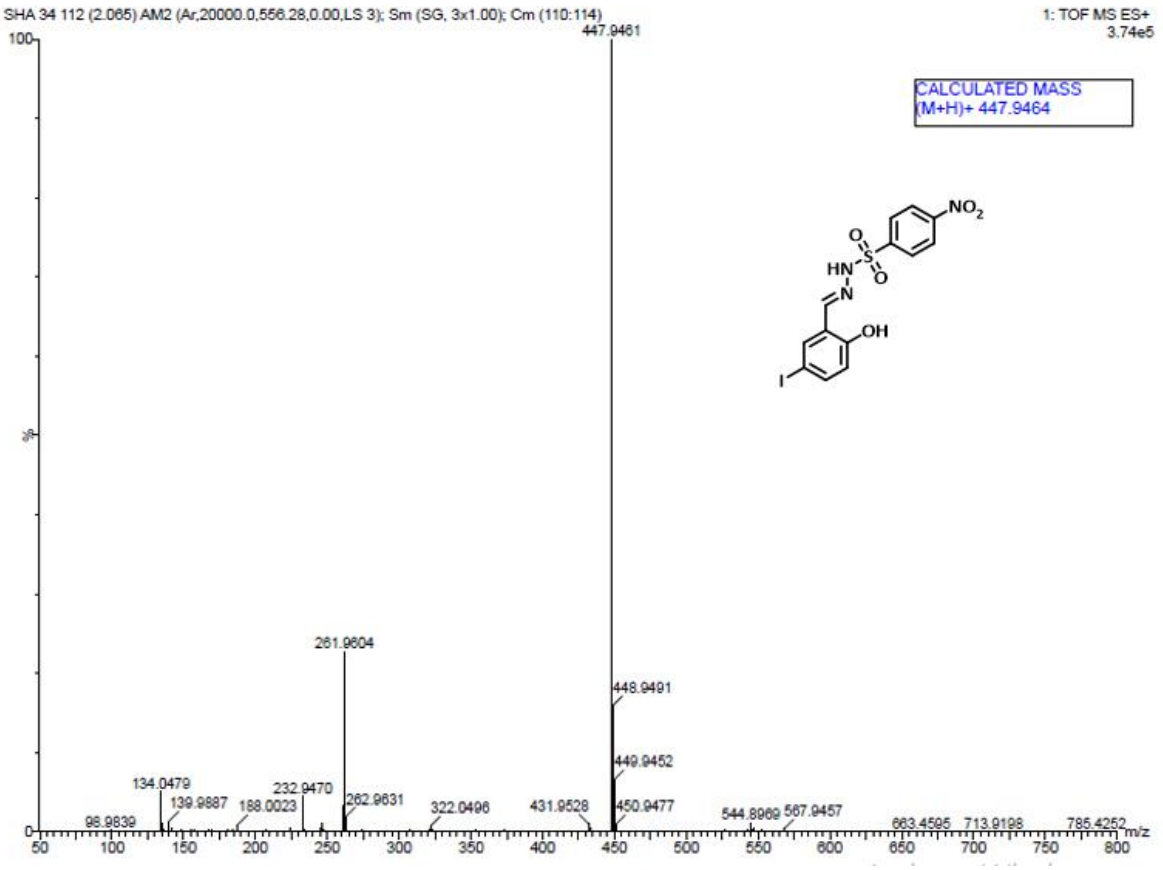


Fig. S86: HRMS spectrum of compound 28.

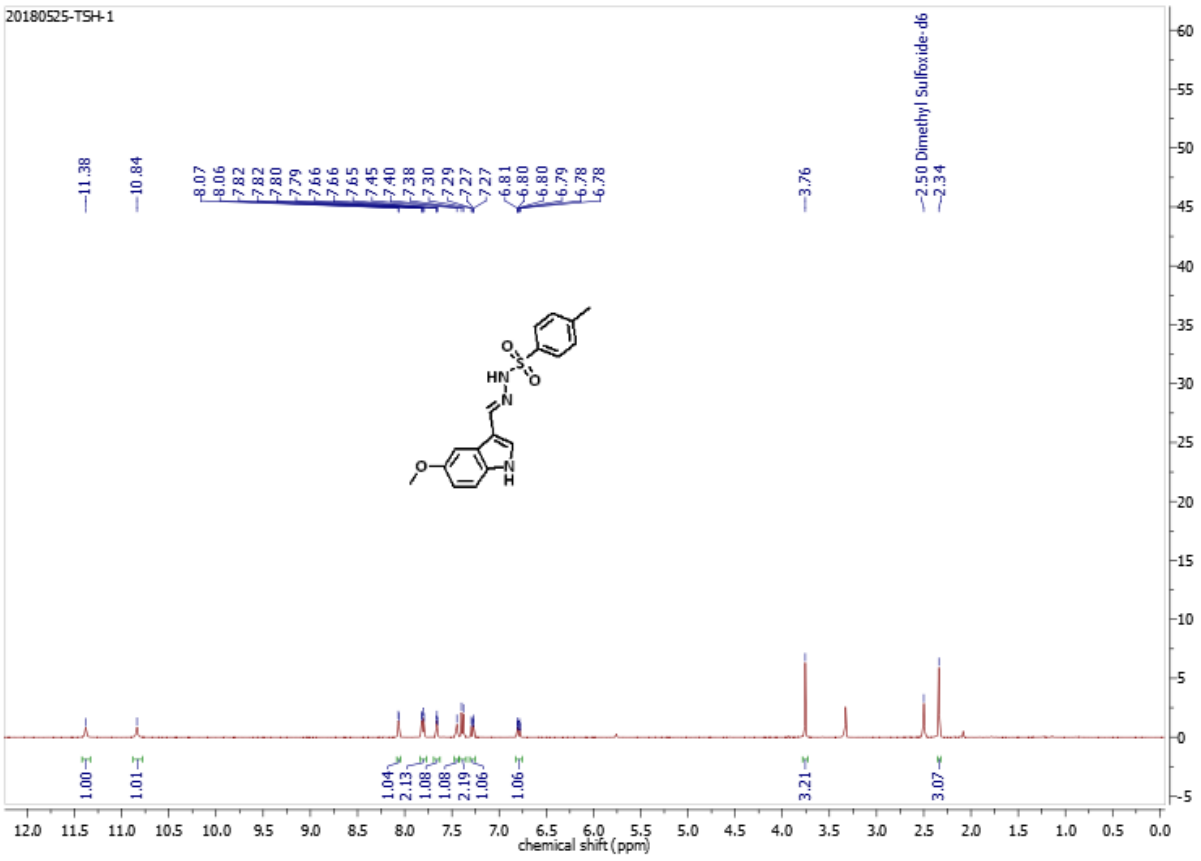


Fig. S87: ^{1}H NMR spectrum of compound 29 in DMSO-d_6 at 400 MHz.

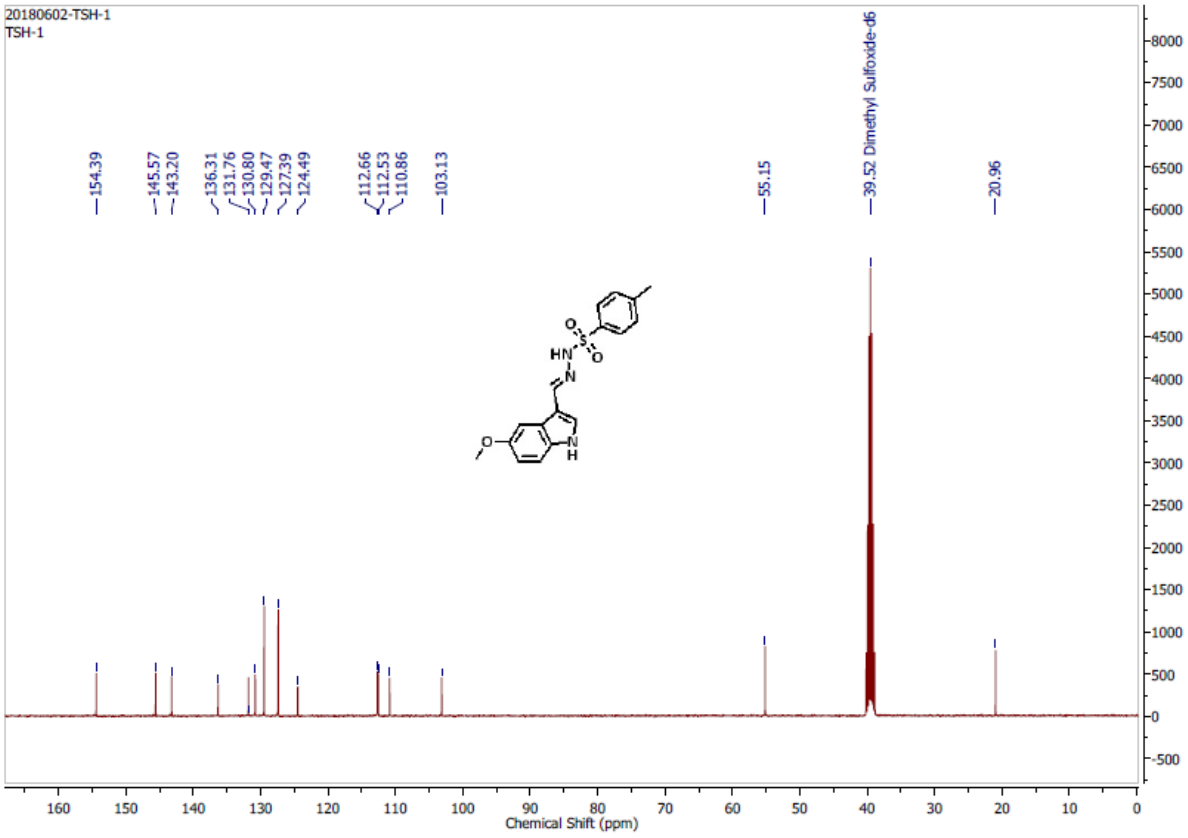


Fig. S88: ^{13}C NMR spectrum of compound 29 in DMSO-d_6 at 100 MHz.

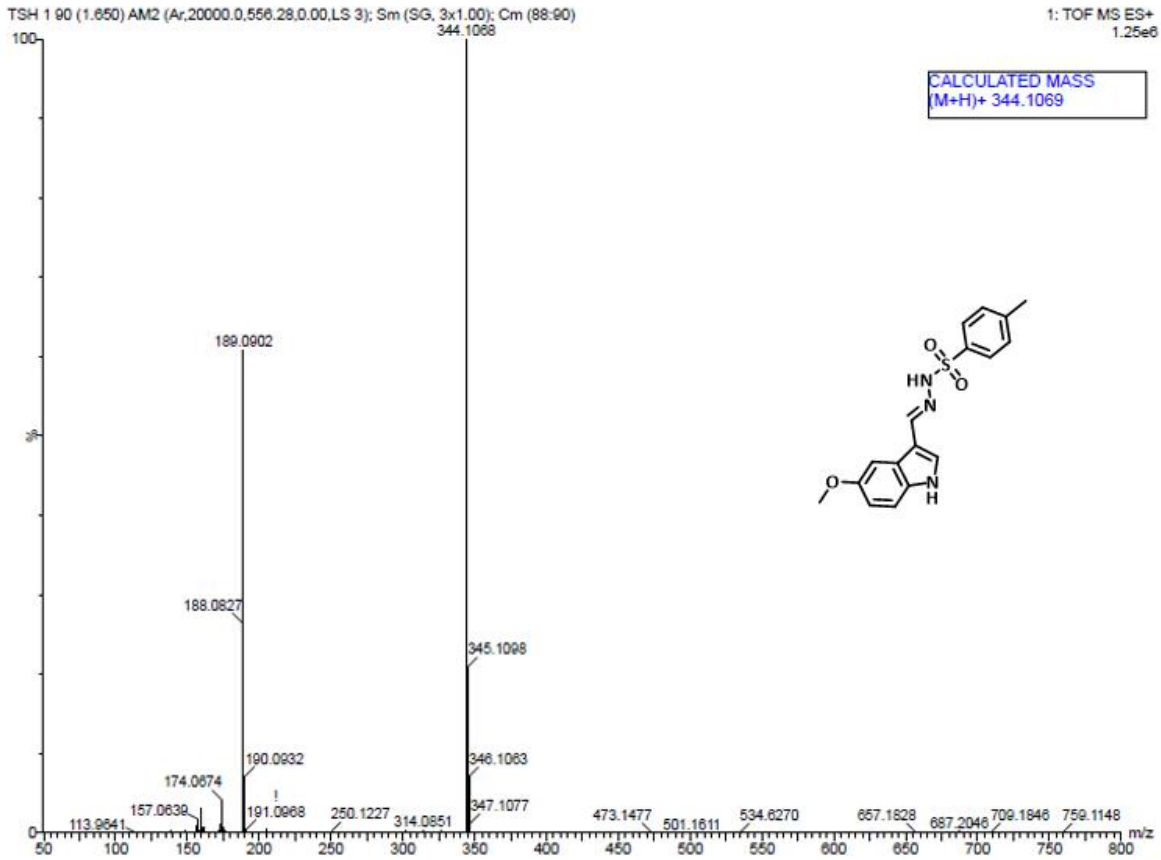


Fig. S89: HRMS spectrum of compound 29.

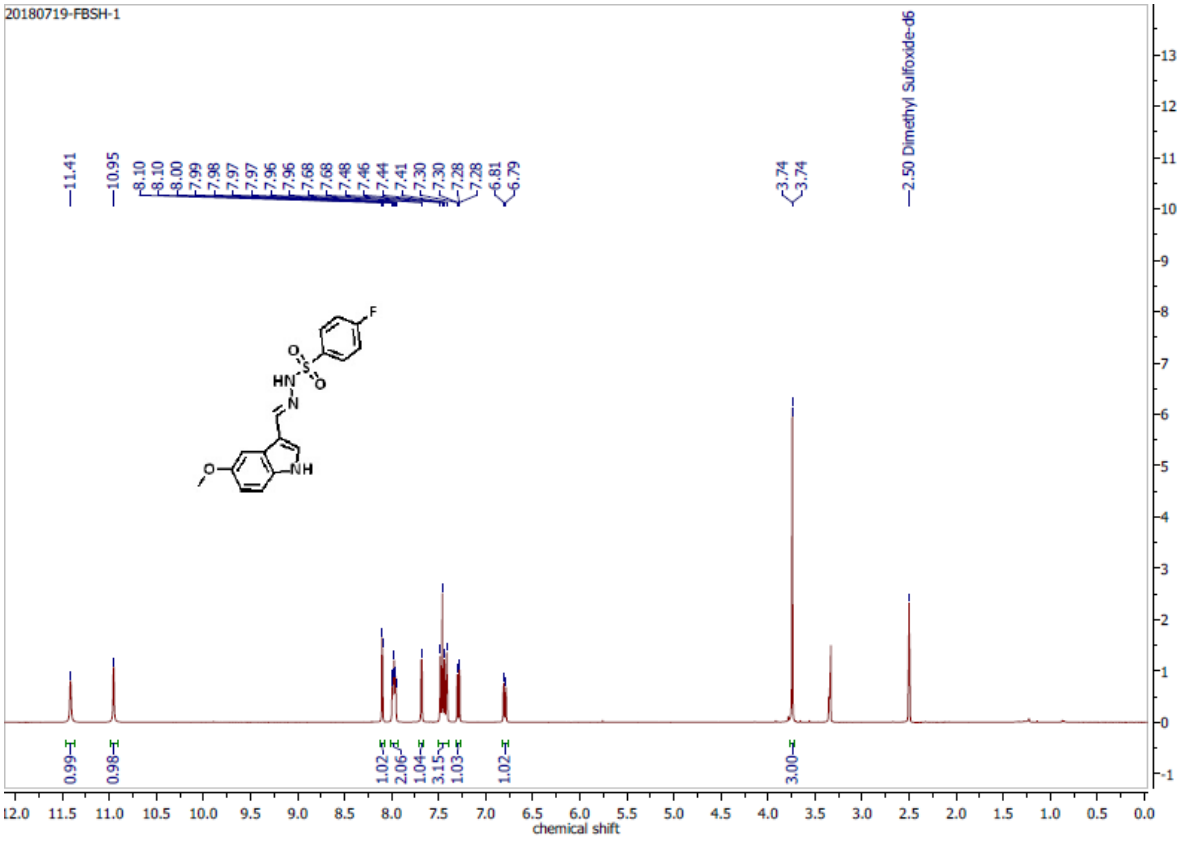


Fig. S90: [1] H NMR spectrum of compound 30 in DMSO-d_6 at 400 MHz.

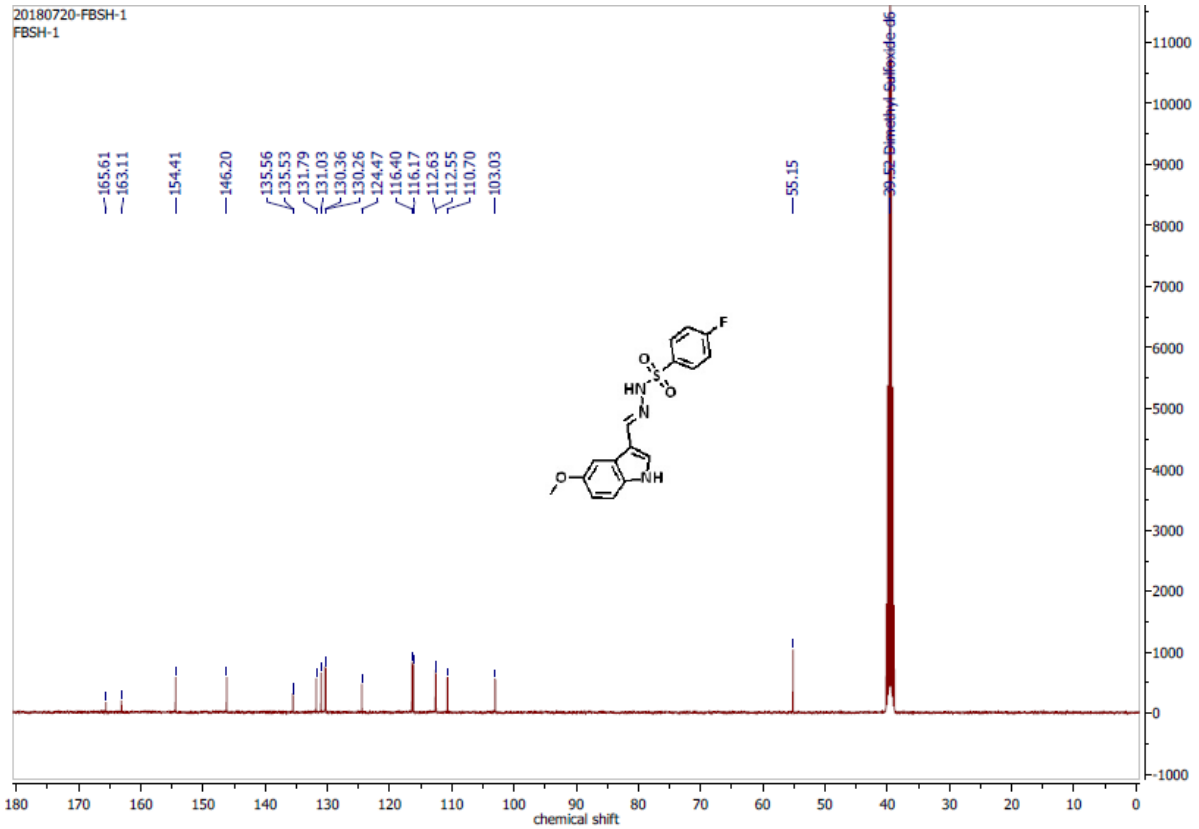


Fig. S91: [13] C NMR spectrum of compound 30 in DMSO-d_6 at 100 MHz.

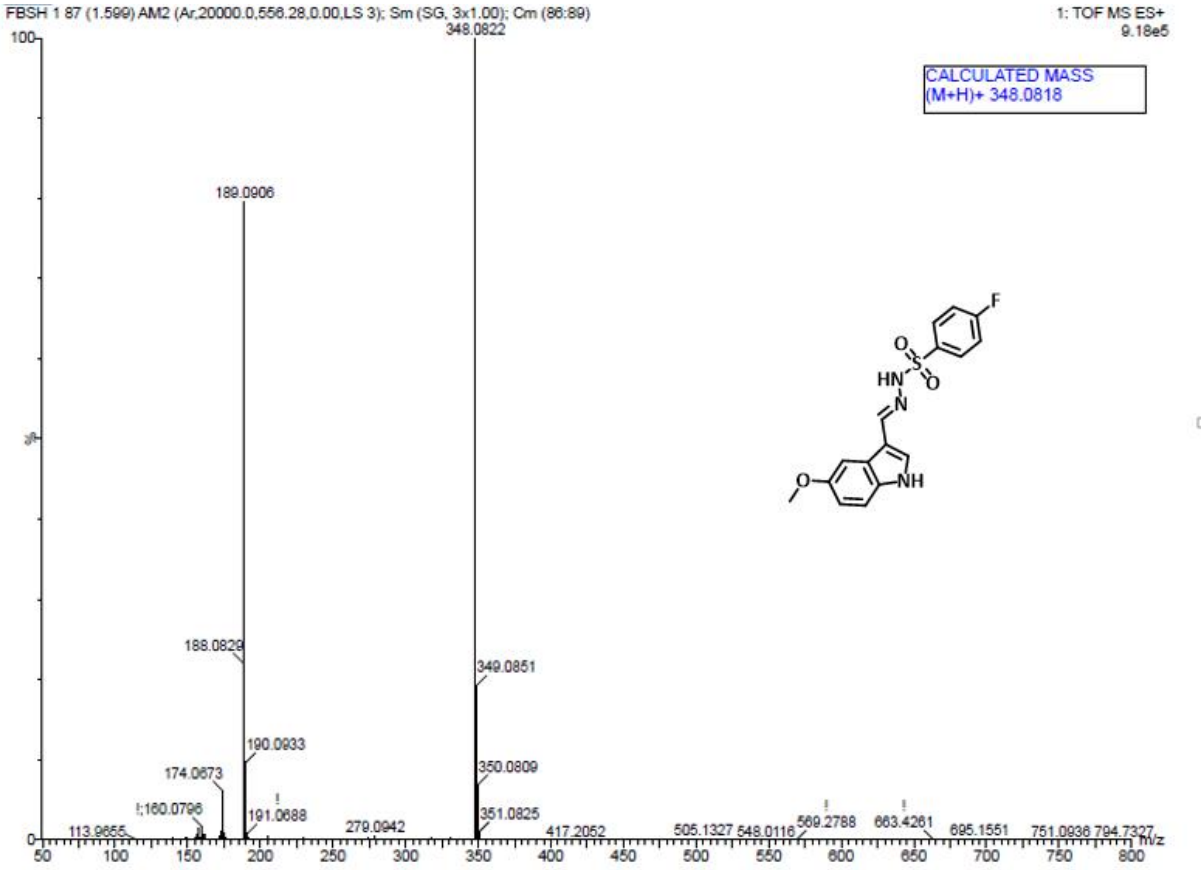


Fig. S92: HRMS spectrum of compound 30.

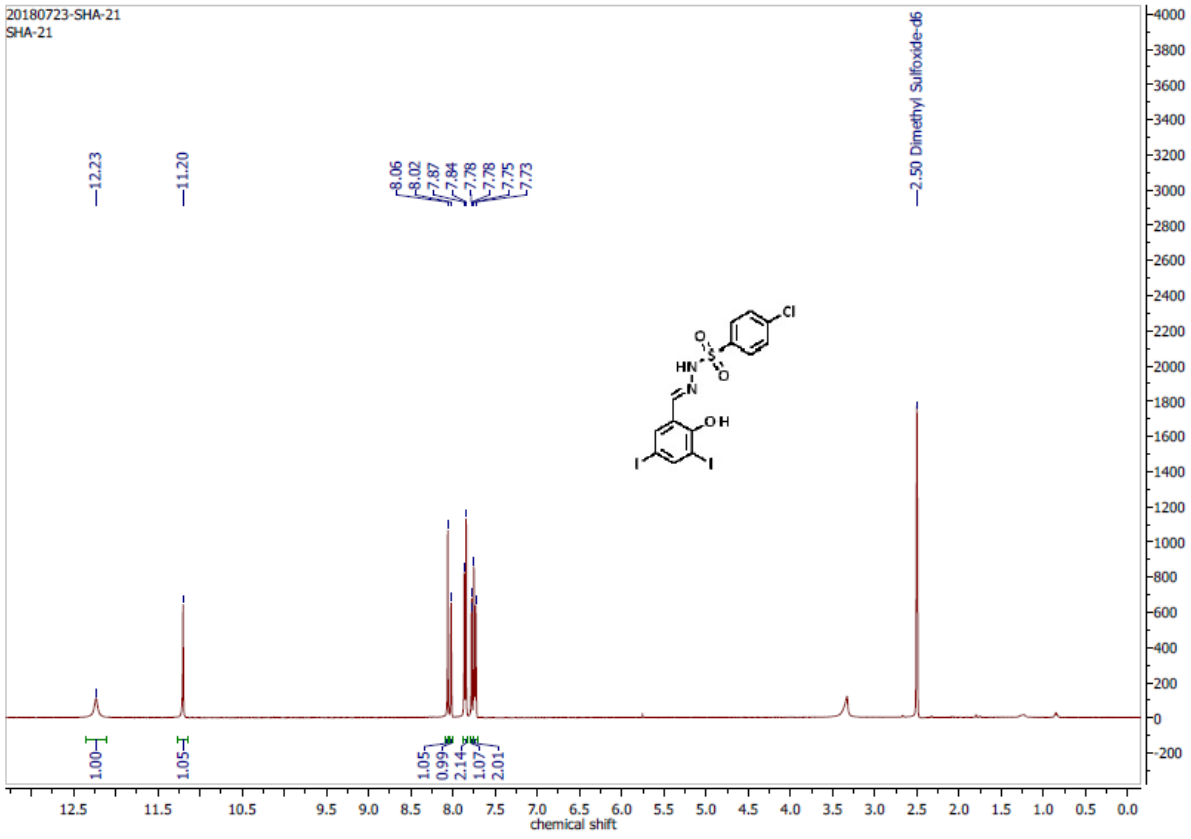


Fig. S93: [1] H NMR spectrum of compound 31 in DMSO-d_6 at 400 MHz.

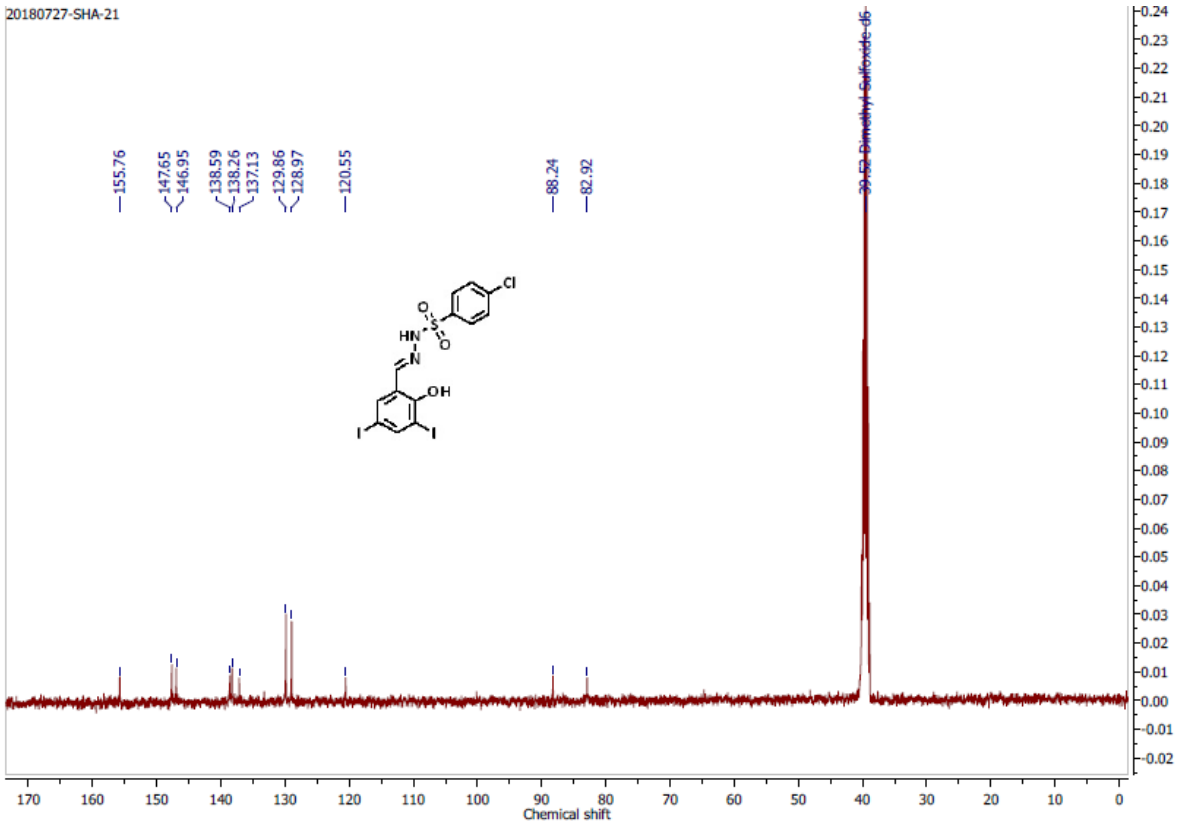


Fig. S94: ^{13}C NMR spectrum of compound 31 in DMSO-d_6 at 100 MHz.

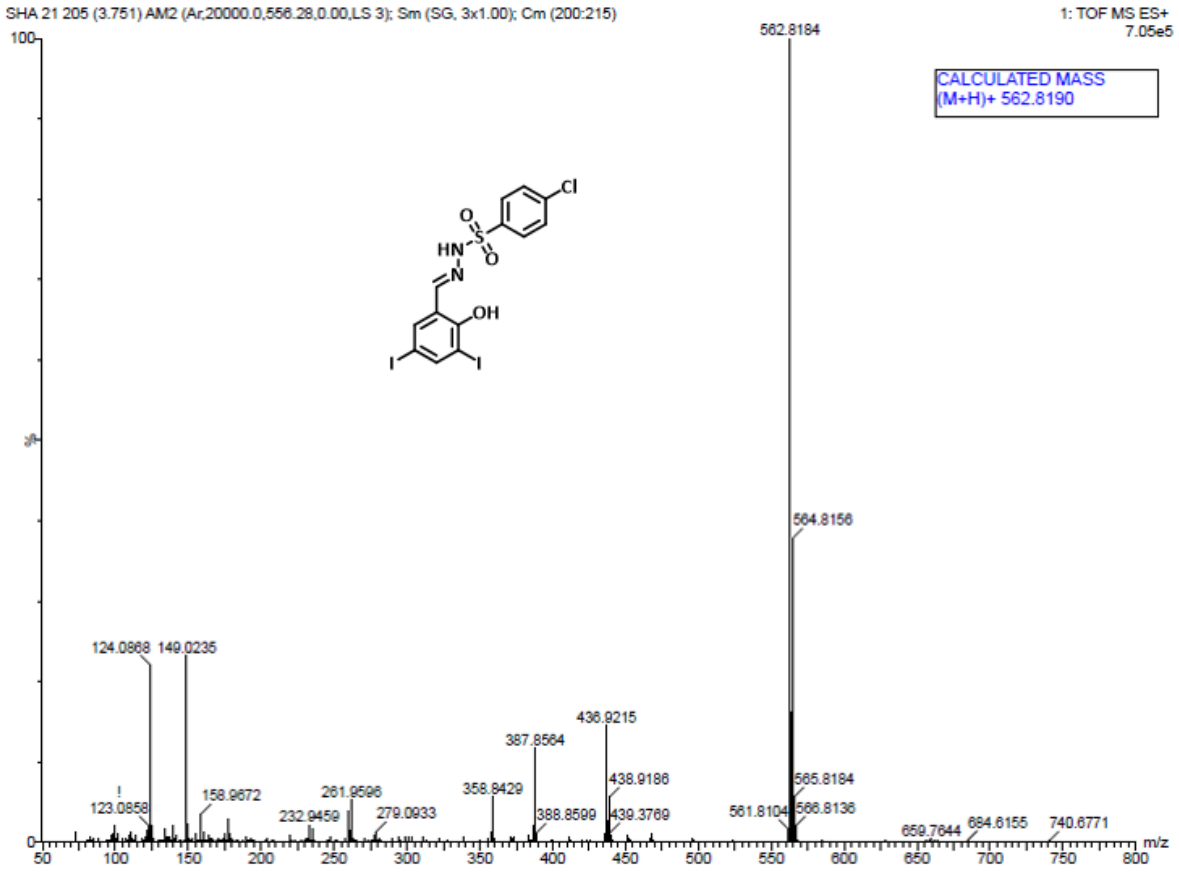


Fig. S95: HRMS spectrum of compound 31.

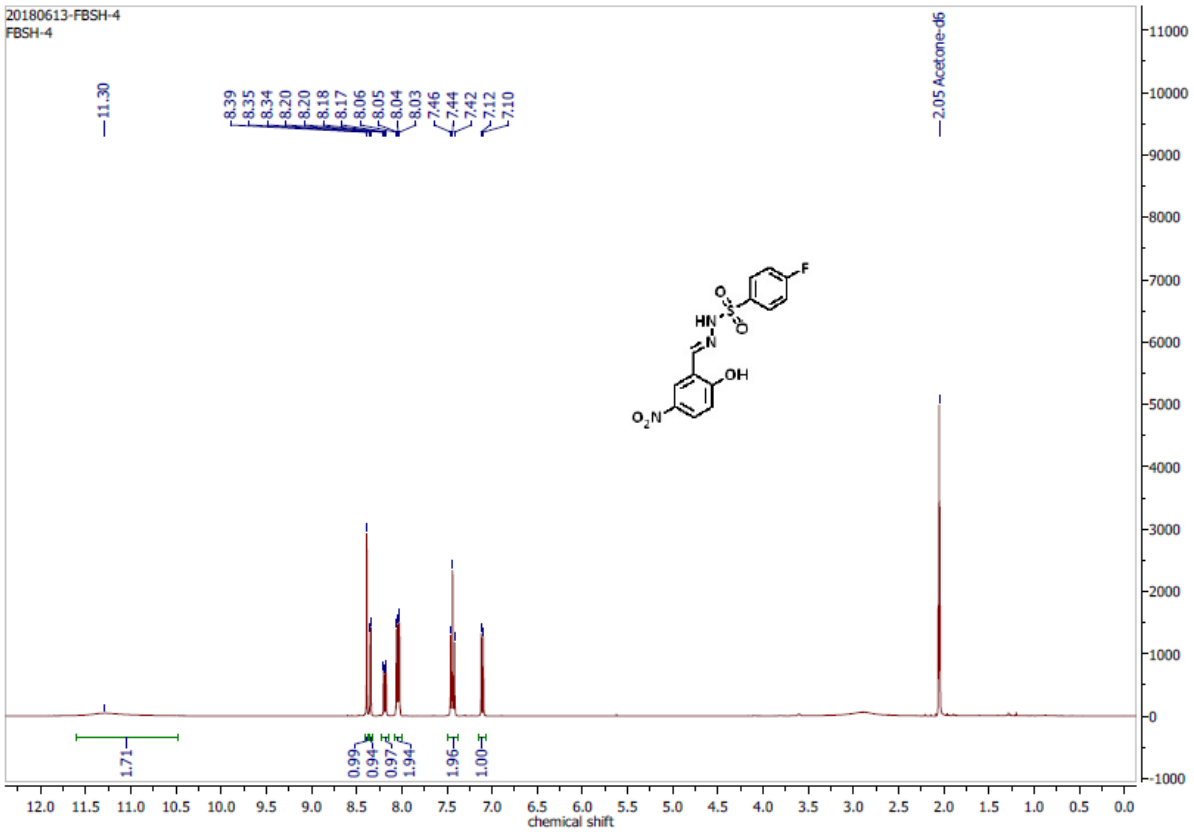


Fig. S96: [1] H NMR spectrum of compound 32 in DMSO-d_6 at 400 MHz.

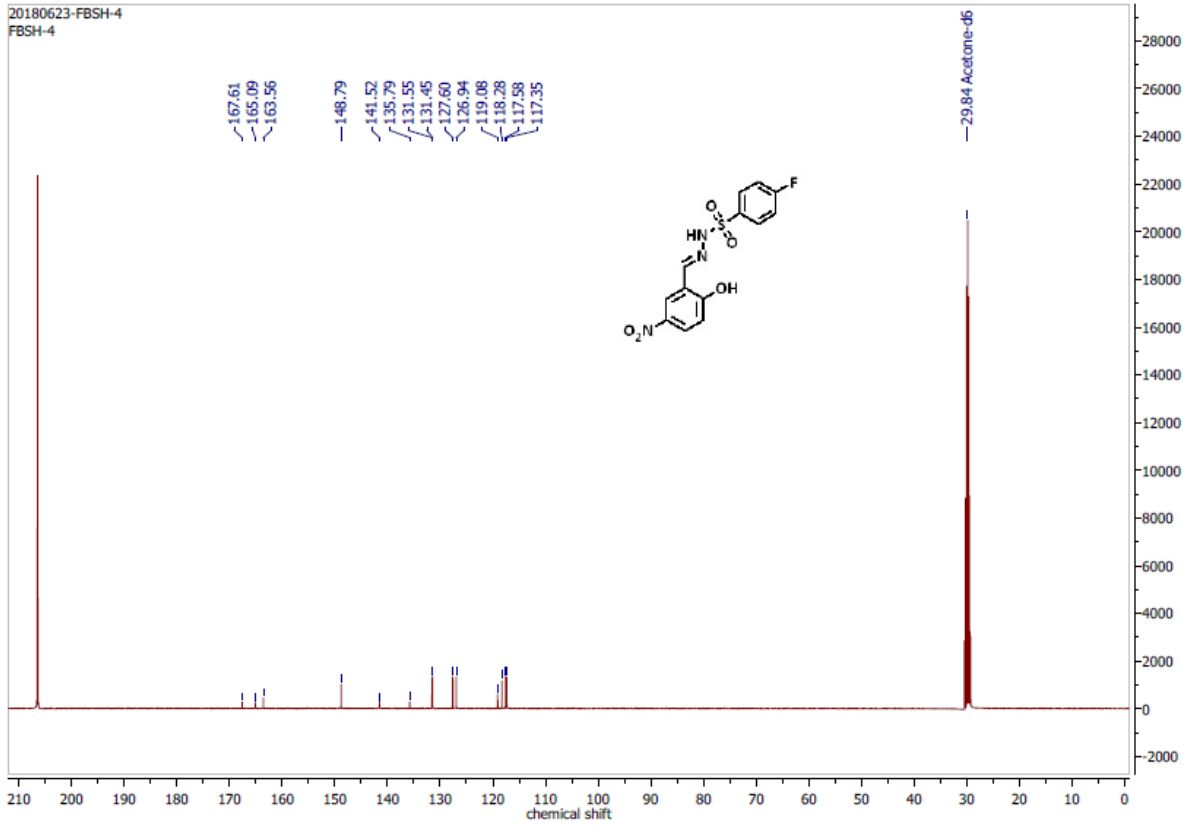


Fig. S97: [13] C NMR spectrum of compound 32 in DMSO-d_6 at 100 MHz.

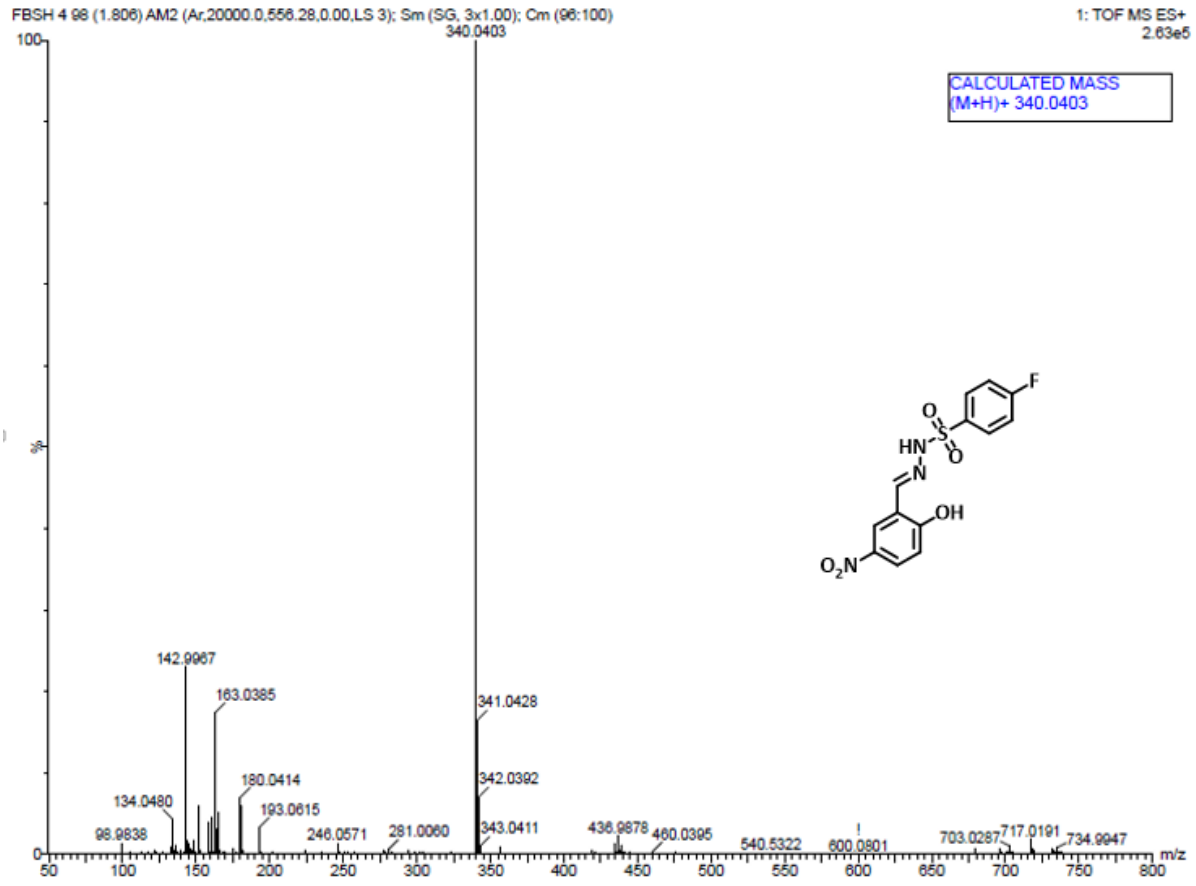


Fig. S98: HRMS spectrum of compound 32.

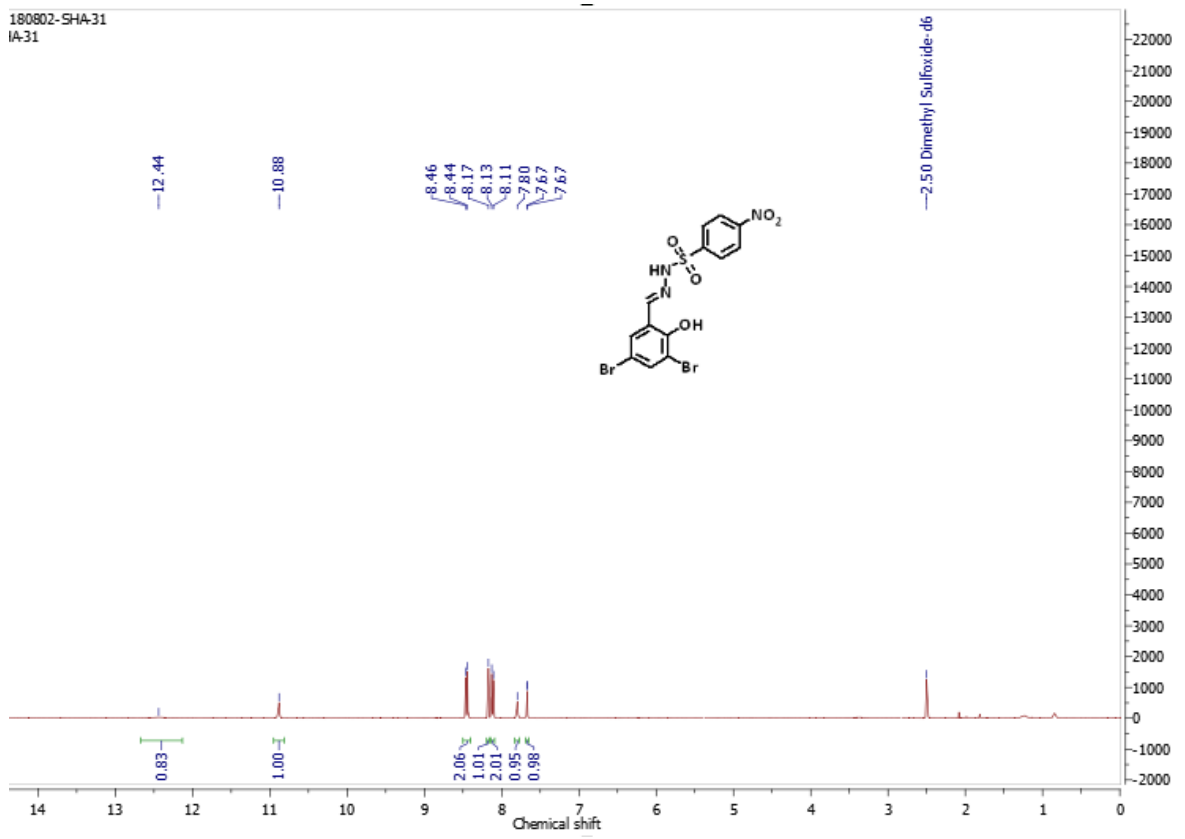


Fig. S99: ^{1}H NMR spectrum of compound 33 in DMSO-d_6 at 400 MHz.

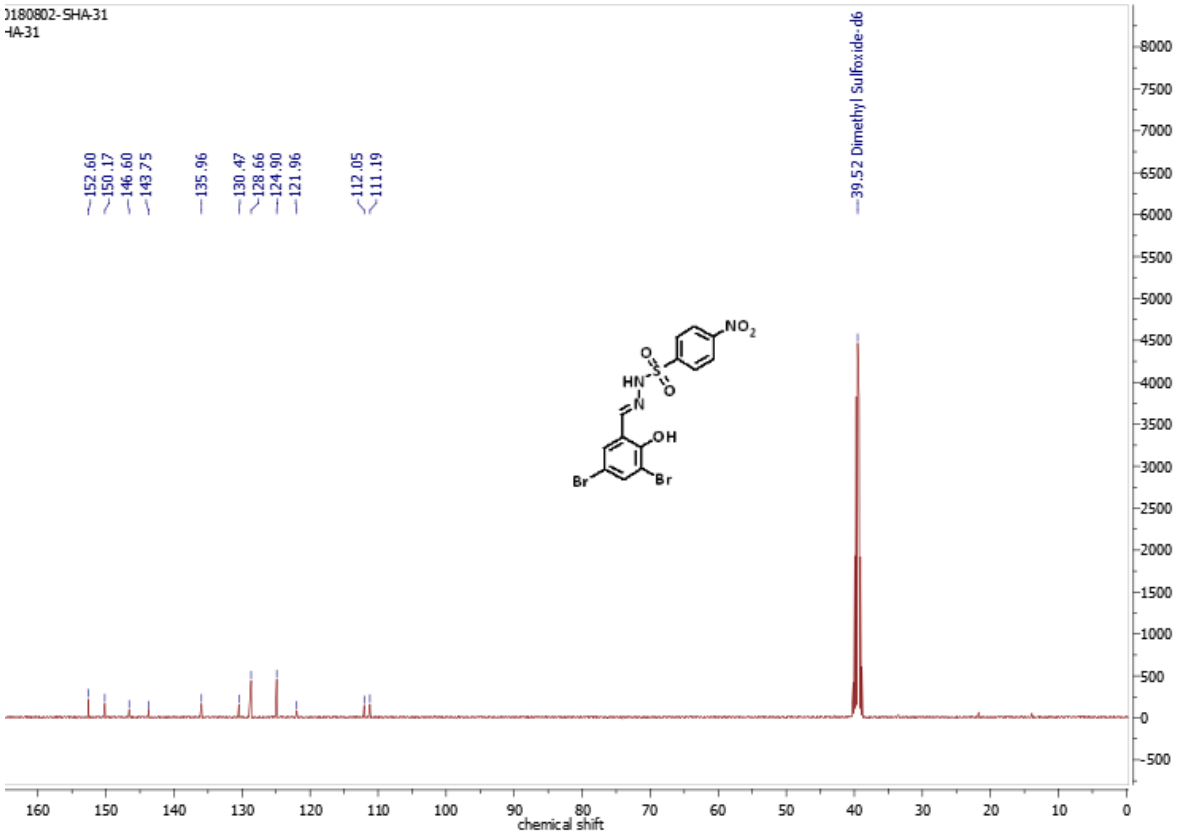


Fig. S100: ^{13}C NMR spectrum of compound 33 in DMSO-d_6 at 100 MHz.

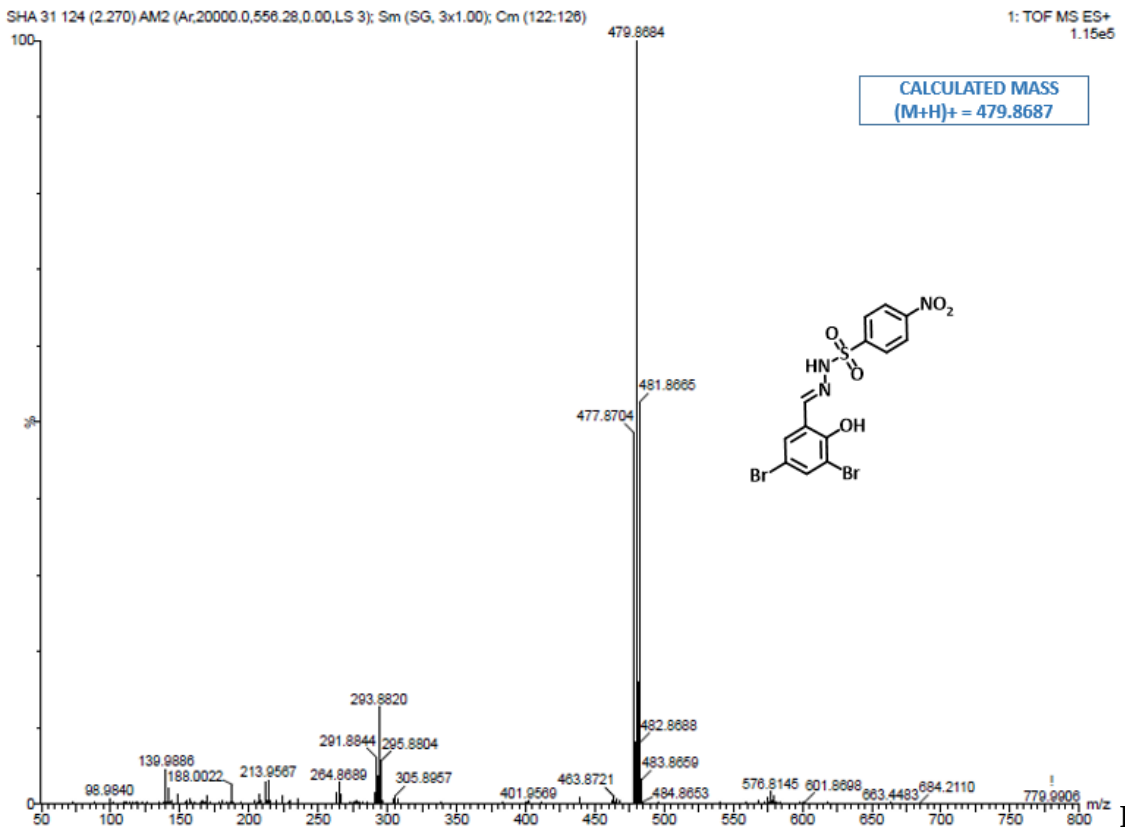


Fig. S101: HRMS spectrum of compound 33.

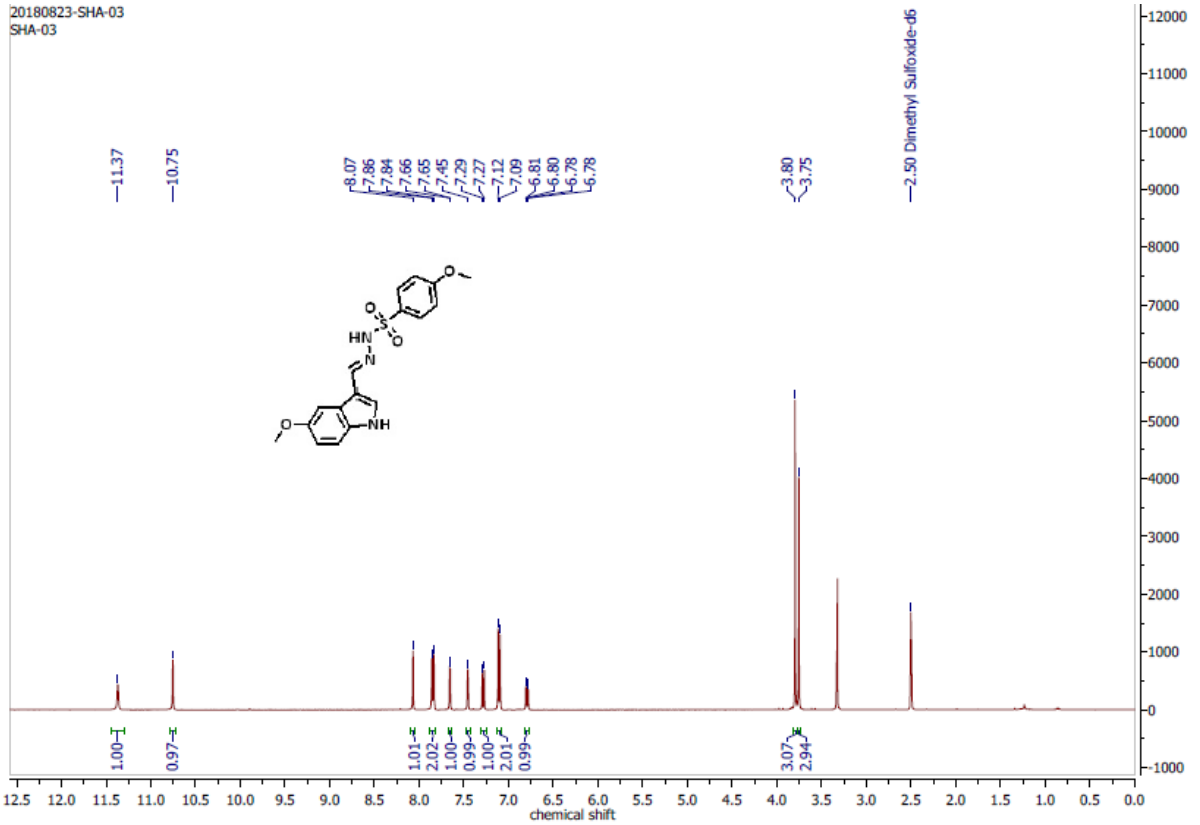


Fig. S102: [1] H NMR spectrum of compound 34 in D DMSO-d_6 at 400 MHz.

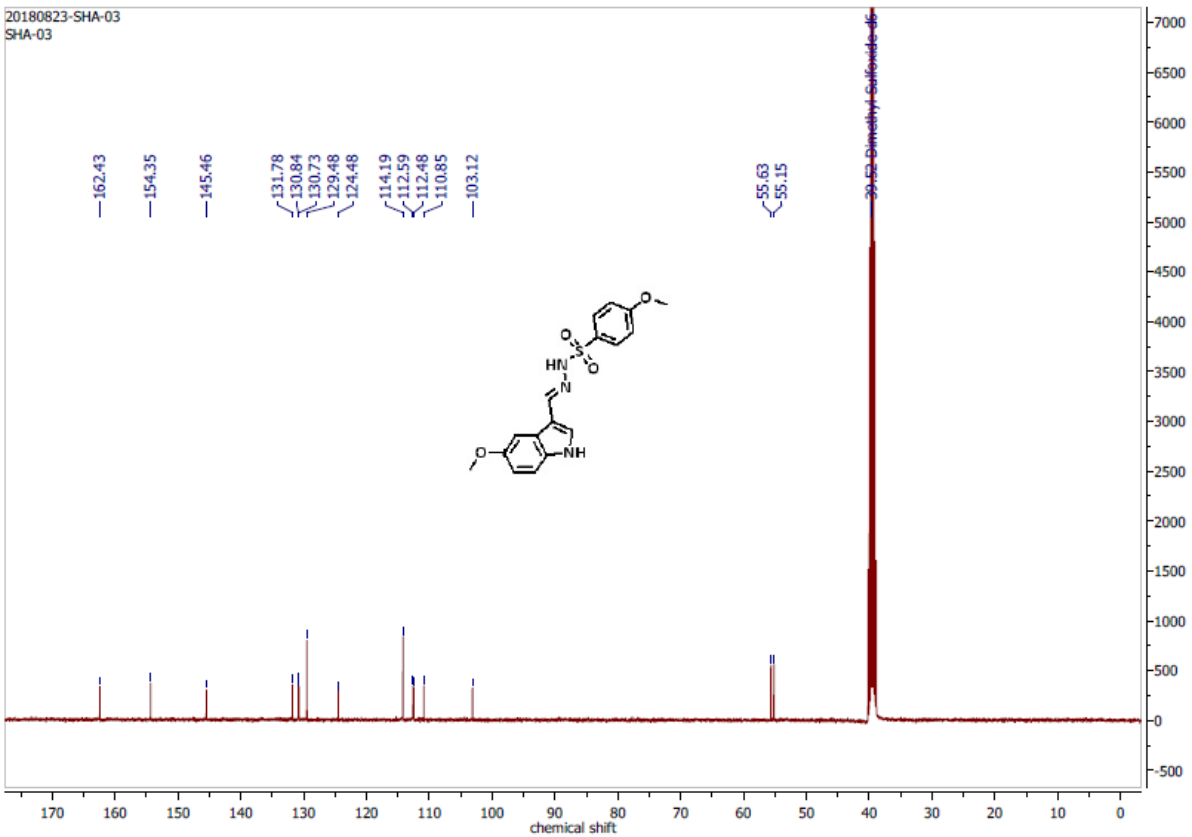


Fig. S103: [13] C NMR spectrum of compound 34 in DMSO-d_6 at 100 MHz.

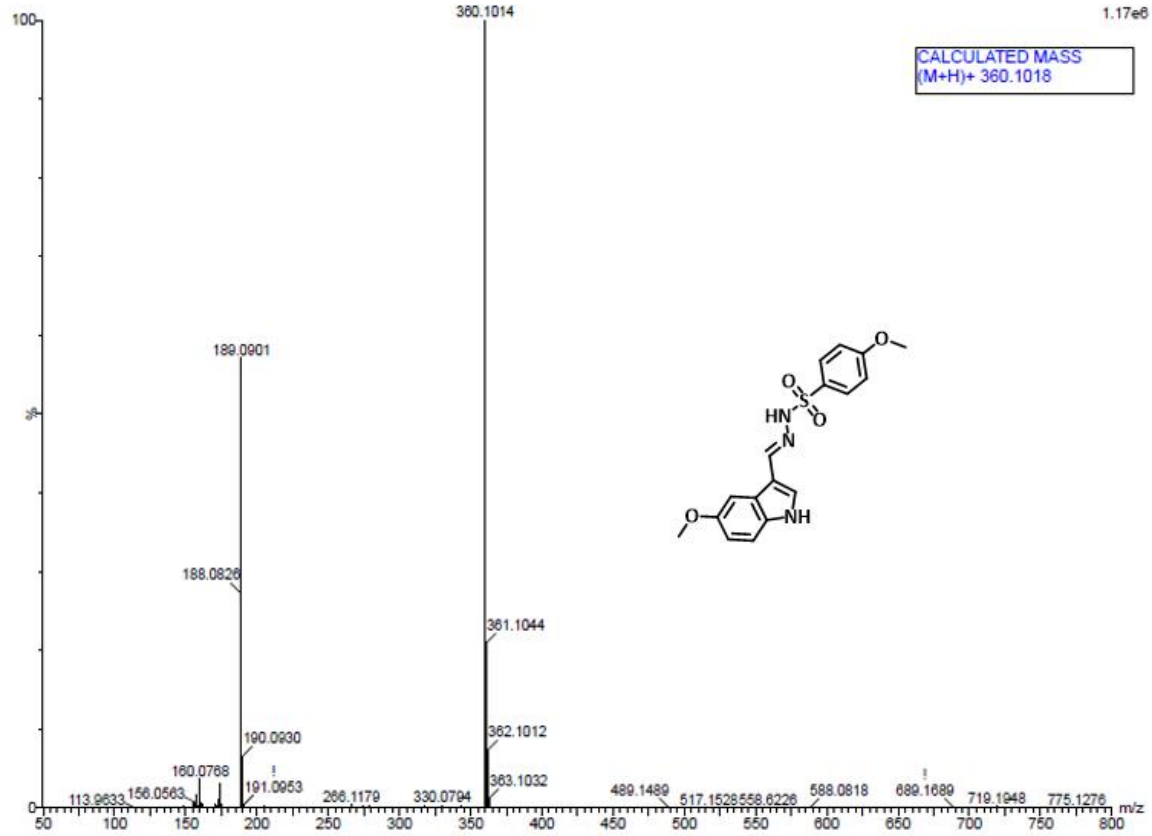


Fig. S104: HRMS spectrum of compound 34.

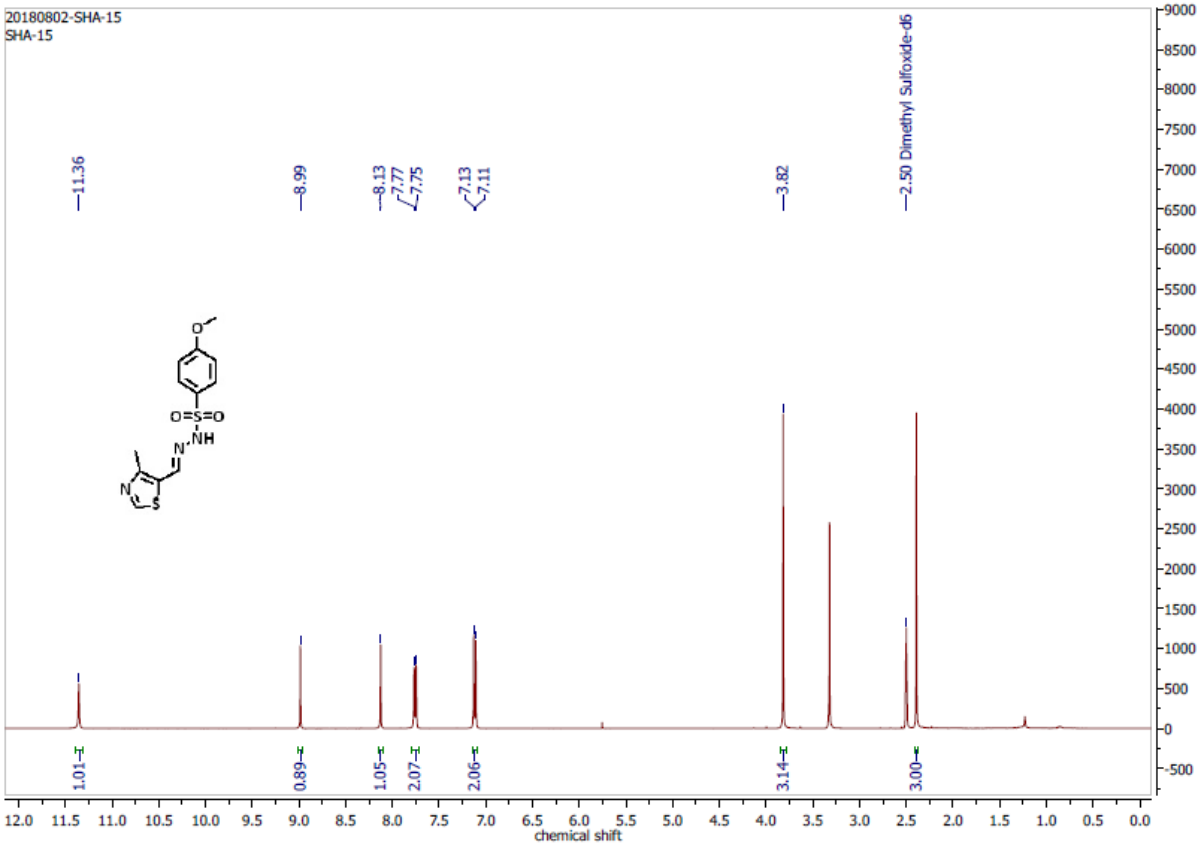


Fig. S105: [1] H NMR spectrum of compound 35 in DMSO-d_6 at 400 MHz.

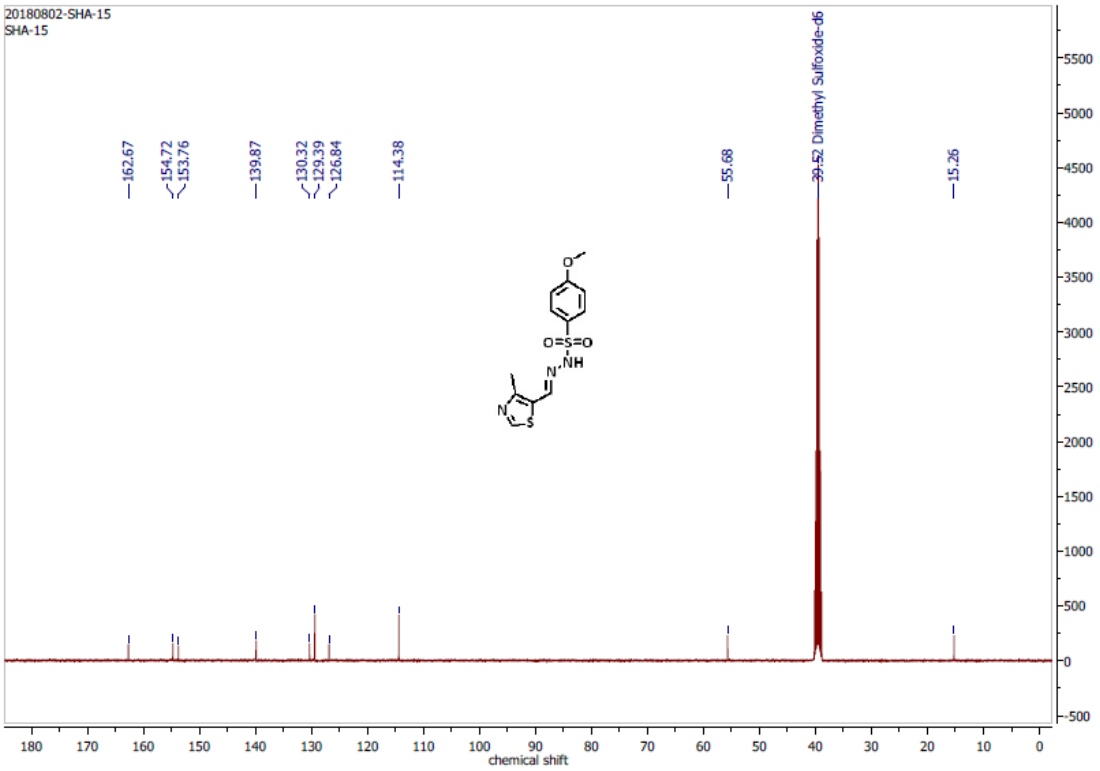


Fig. S106: ^{13}C NMR spectrum of compound 35 in DMSO-d_6 at 100 MHz.

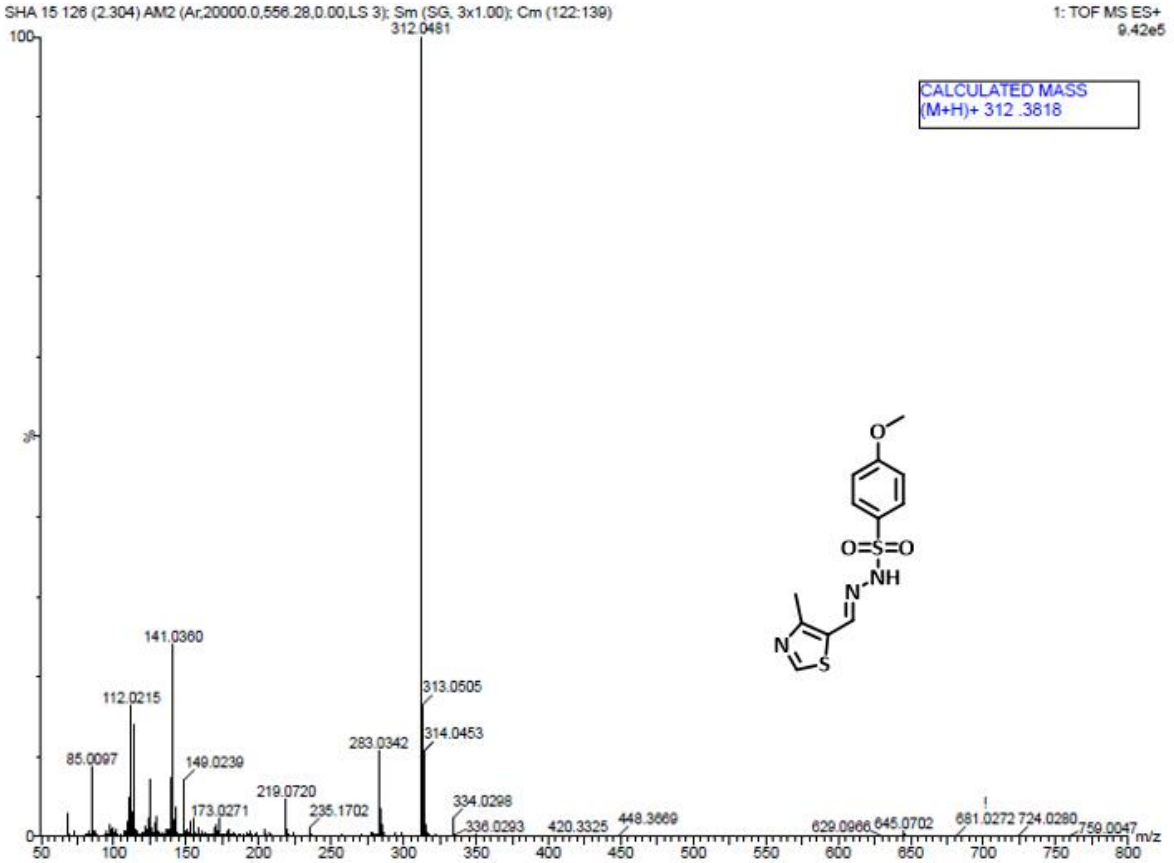


Fig. S107: HRMS spectrum of compound 35.

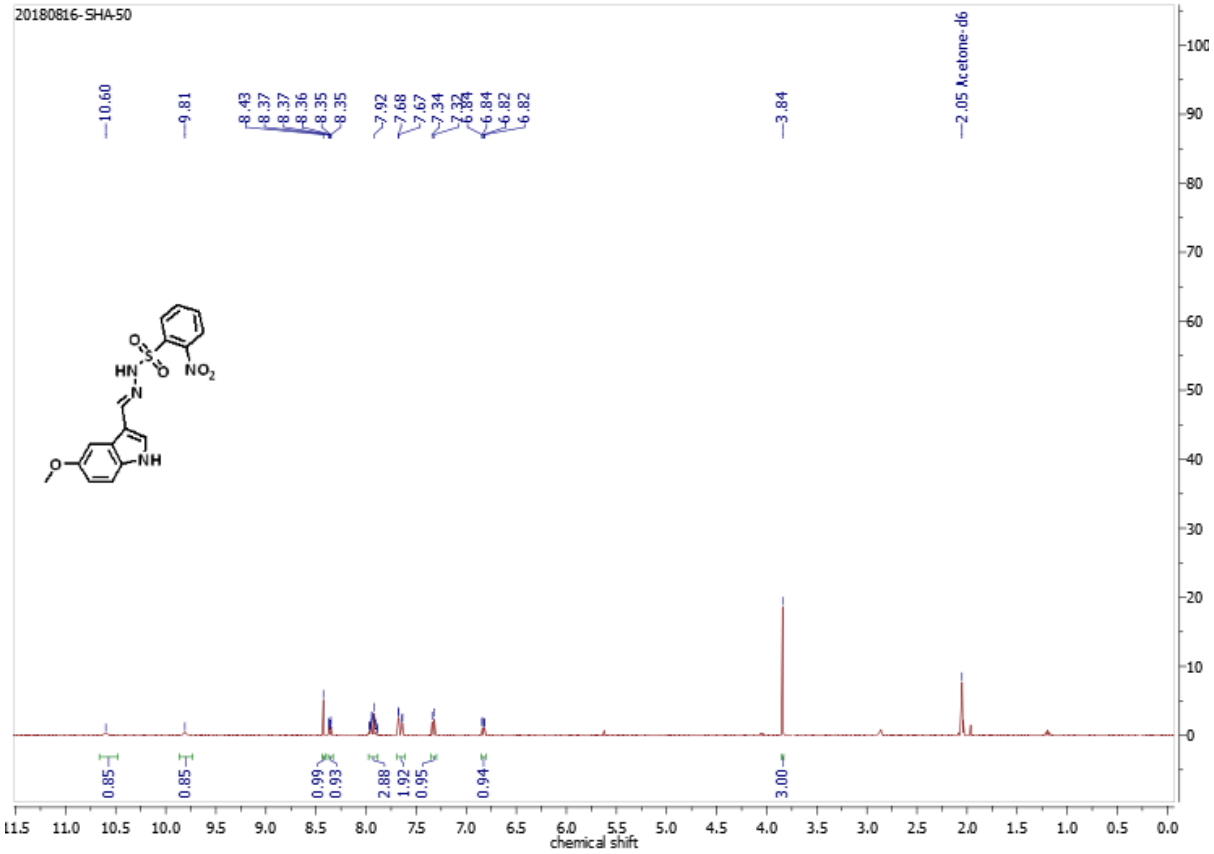


Fig. S108: [1] H NMR spectrum of compound 36 in Acetone-d_6 at 400 MHz.

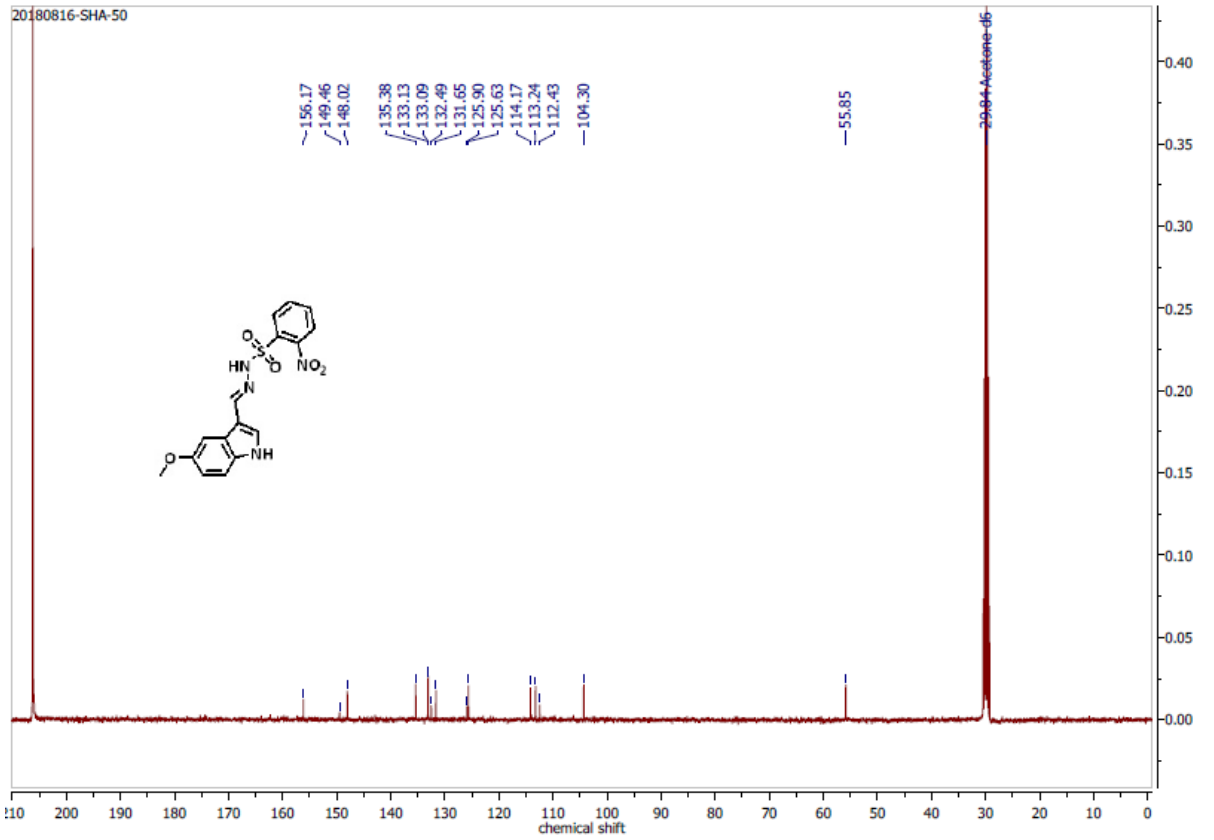


Fig. S109: [13] C NMR spectrum of compound 36 in Acetone-d_6 at 100 MHz.

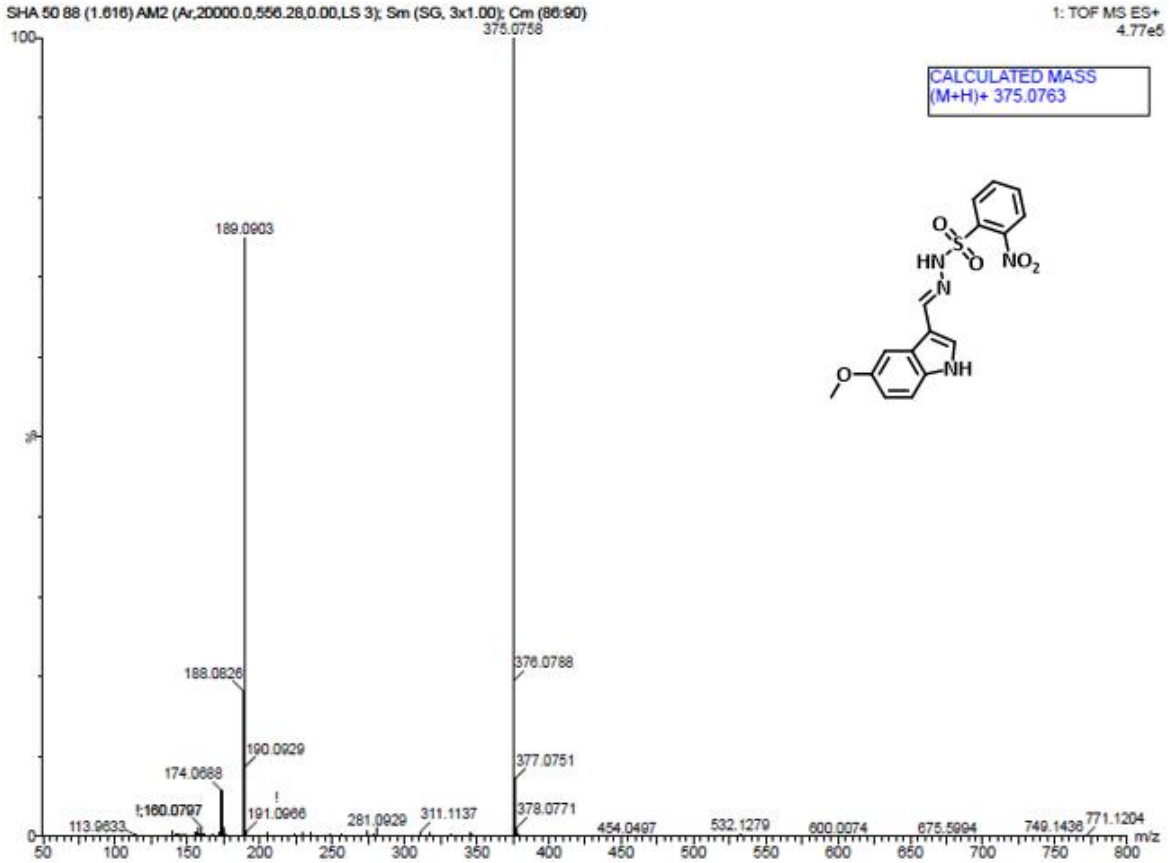


Fig. S110: HRMS spectrum of compound 36.

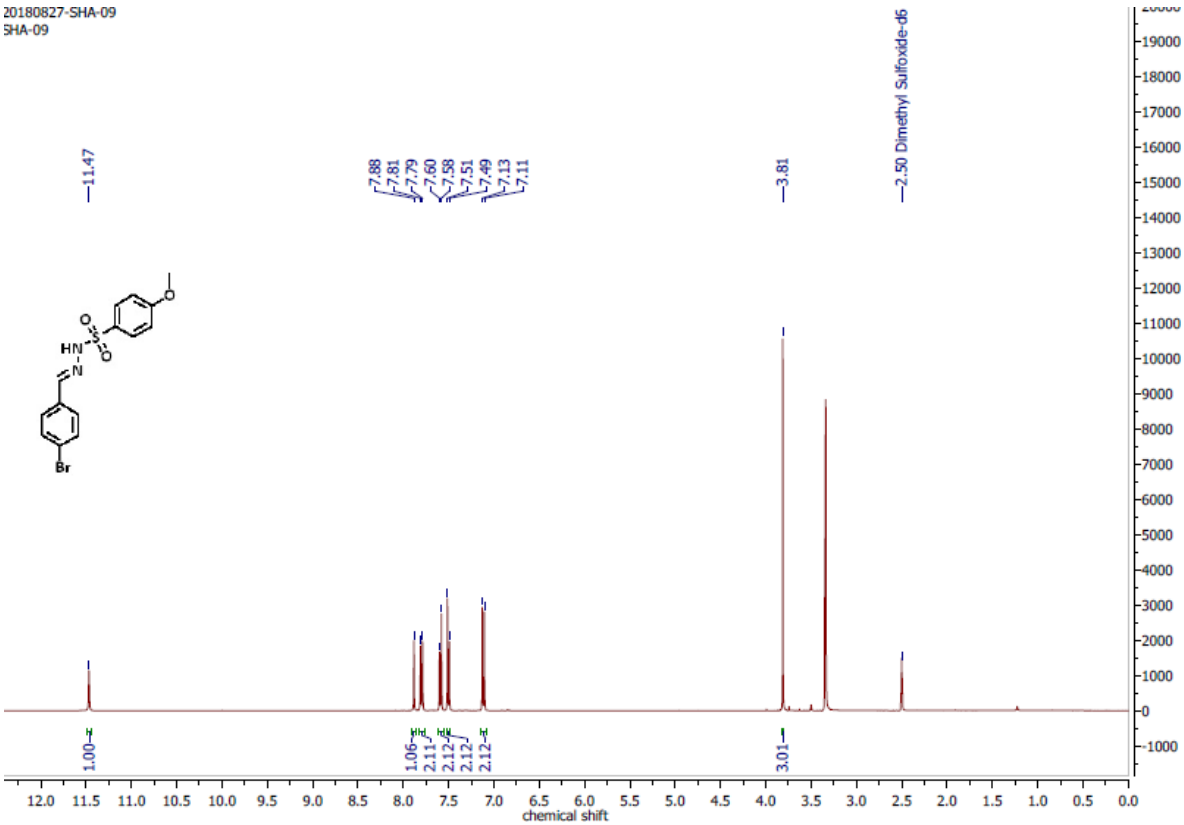


Fig. S111: [1] H NMR spectrum of compound 37 in DMSO-d_6 at 400 MHz.

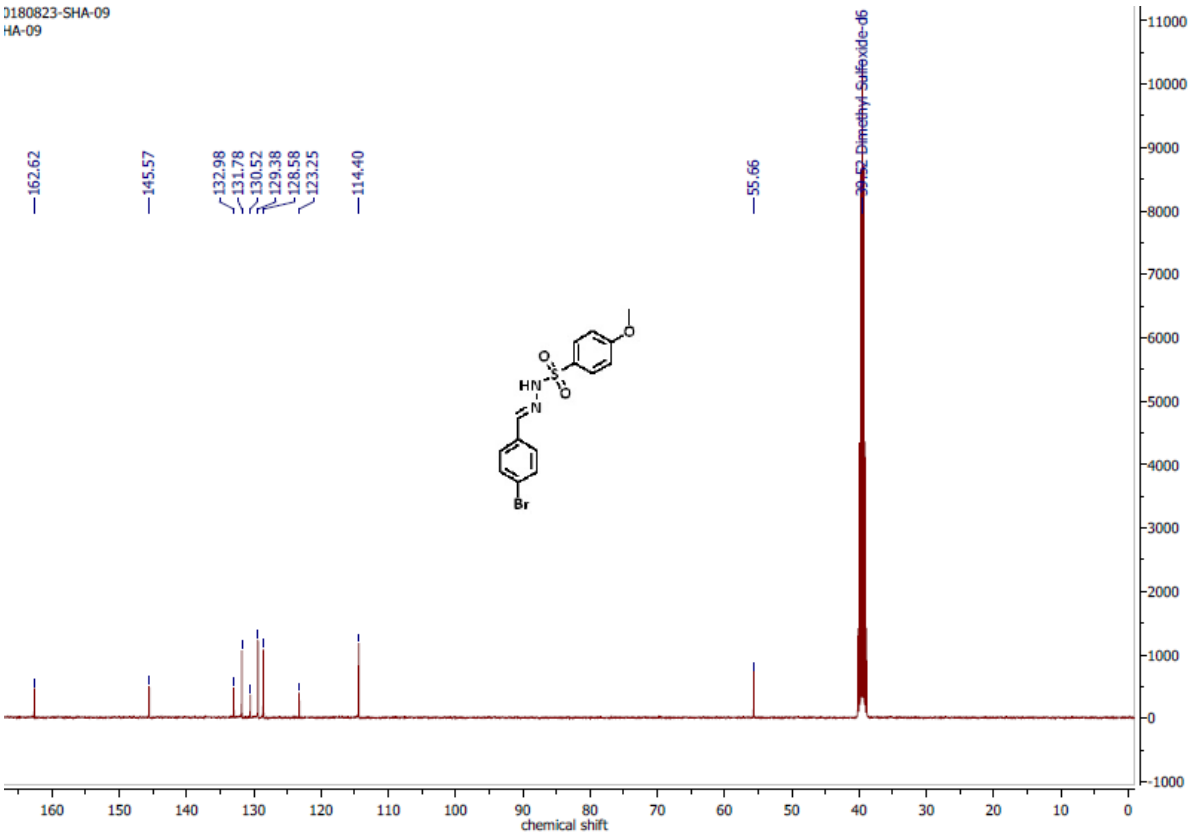


Fig. S112: ^{13}C NMR spectrum of compound 37 in DMSO-d_6 at 100 MHz.

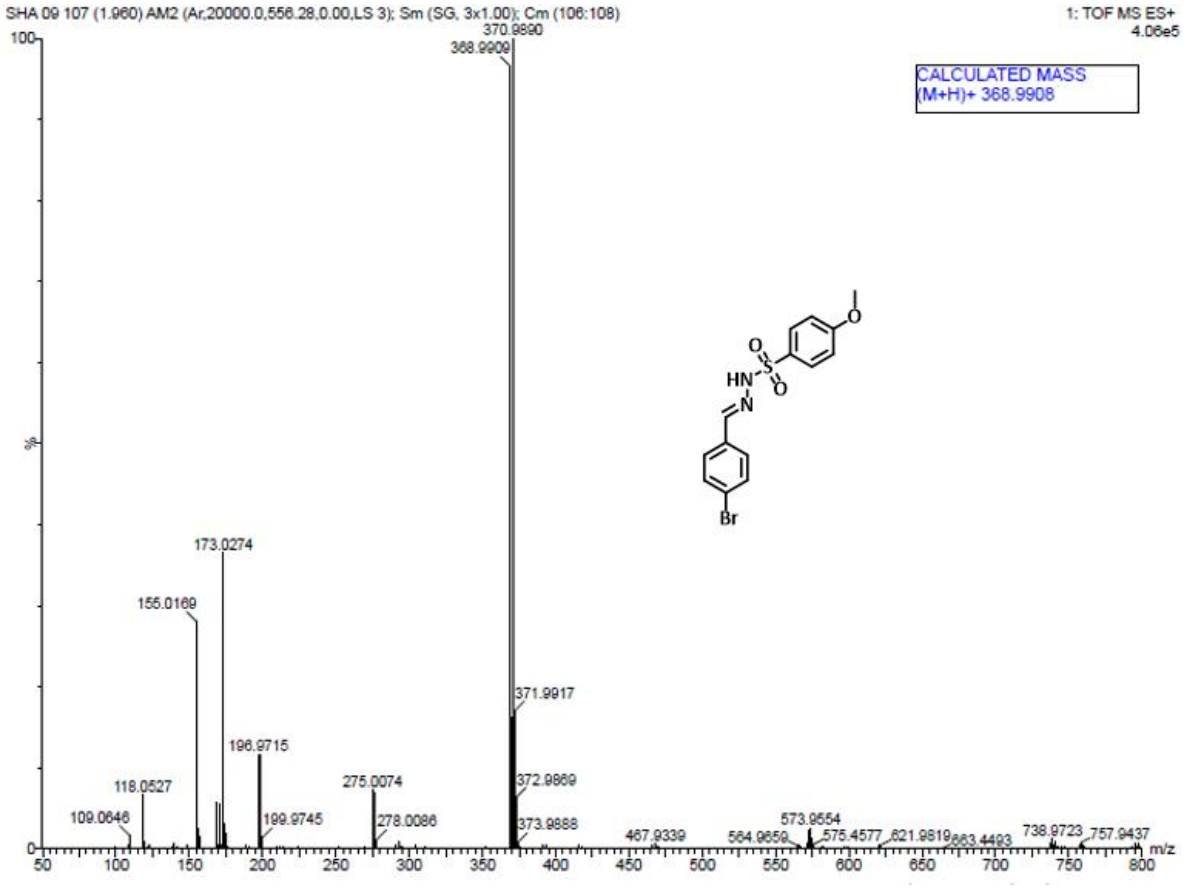


Fig. S113: HRMS spectrum of compound 37.

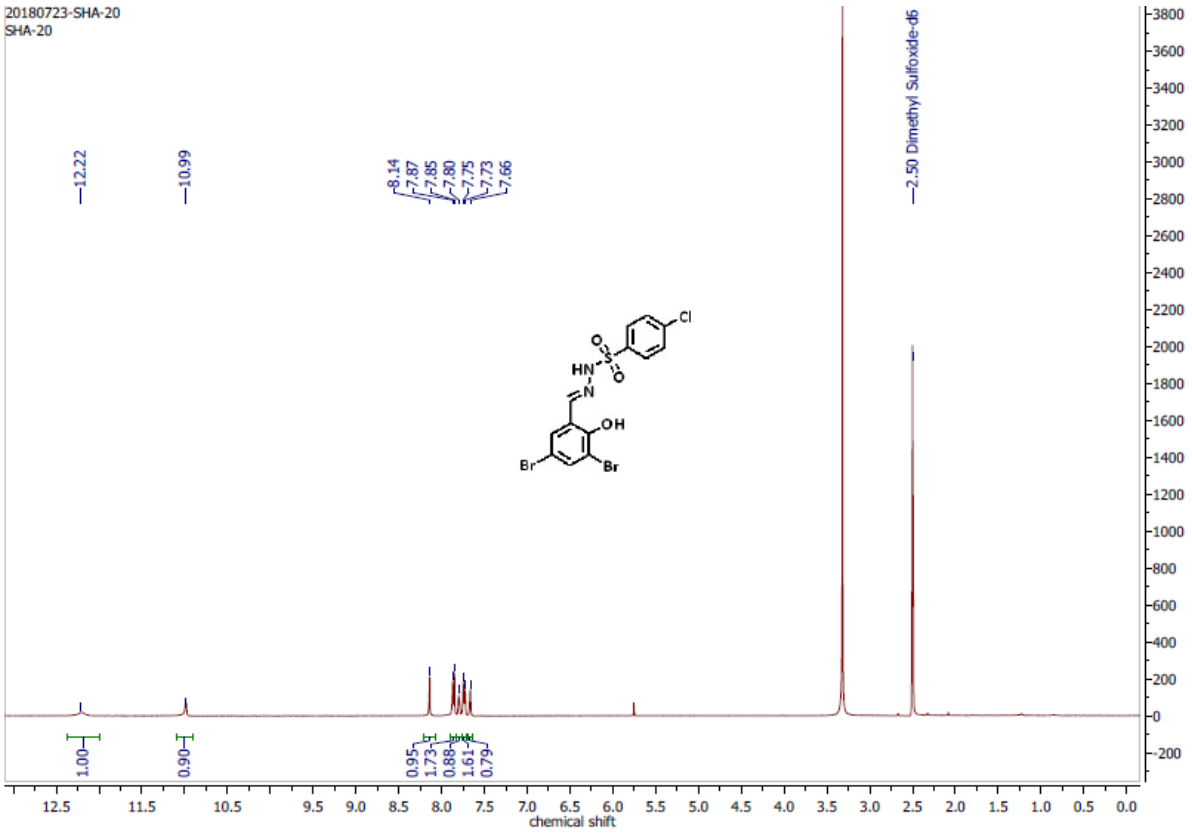


Fig. S114: [1] H NMR spectrum of compound 38 in DMSO-d_6 at 400 MHz.

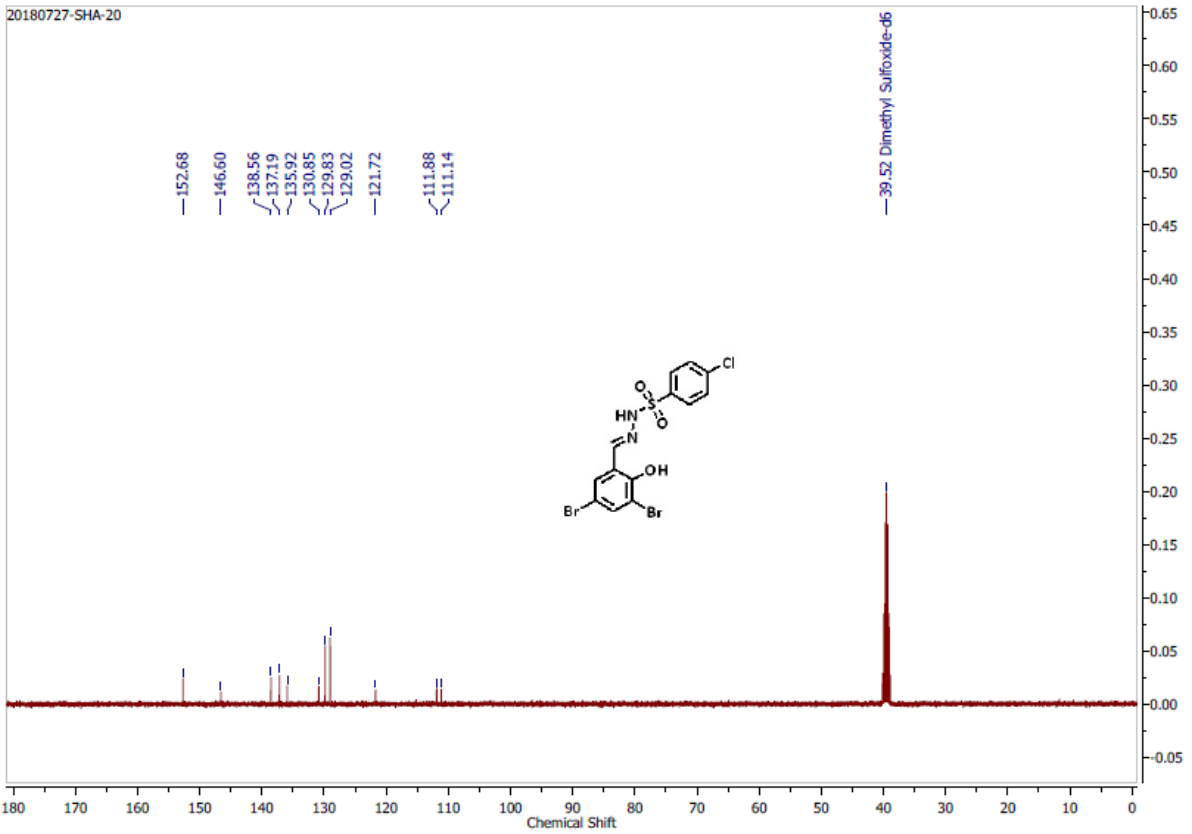


Fig. S115: [13] C NMR spectrum of compound 38 in DMSO-d_6 at 100 MHz.

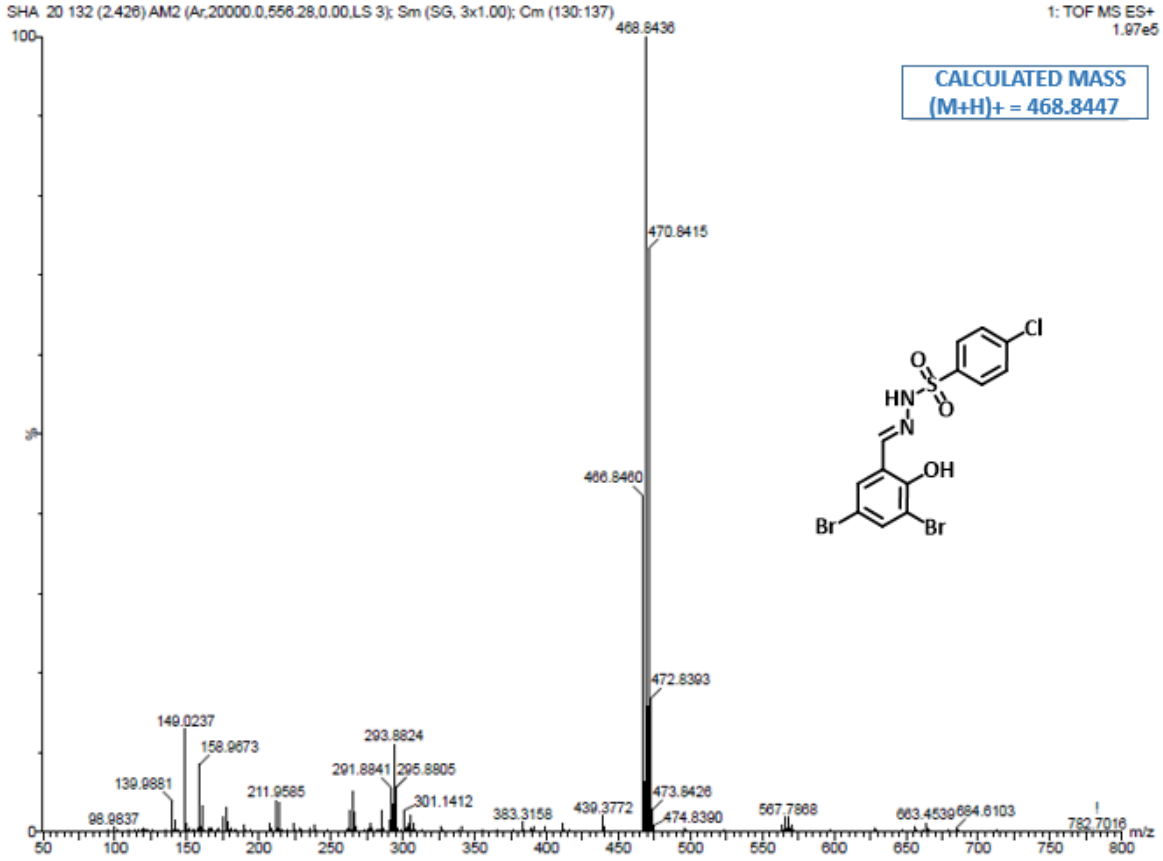


Fig. S116: HRMS spectrum of compound 38.

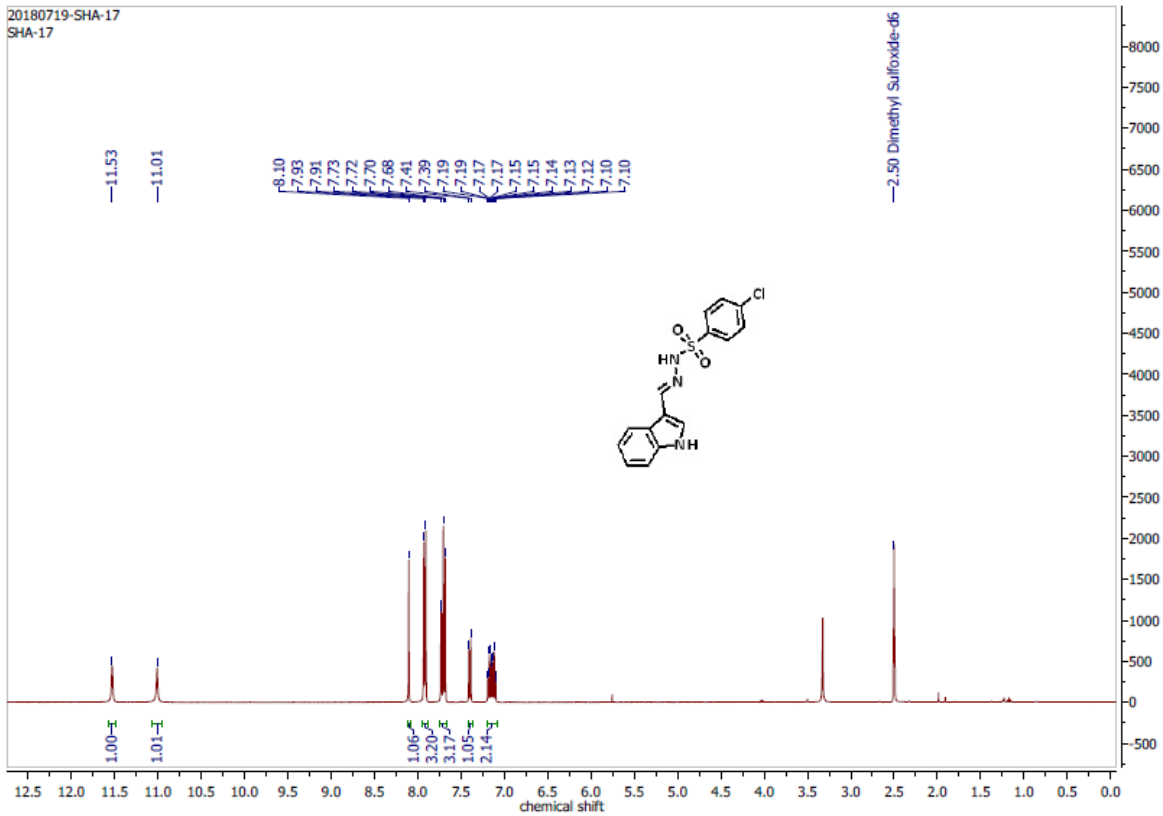


Fig. S117: [1] H NMR spectrum of compound 39 in DMSO-d_6 at 400 MHz.

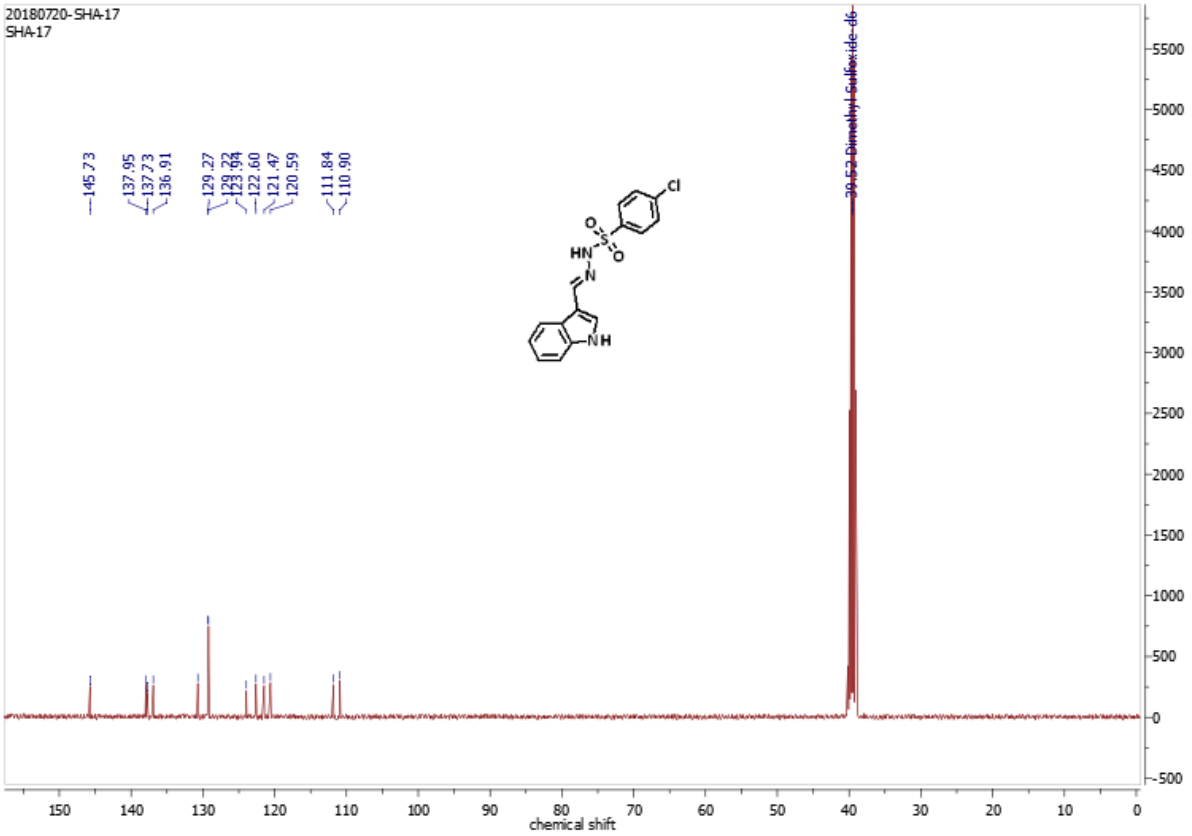


Fig. S118: ^{13}C NMR spectrum of compound 39 in DMSO-d_6 at 100 MHz.

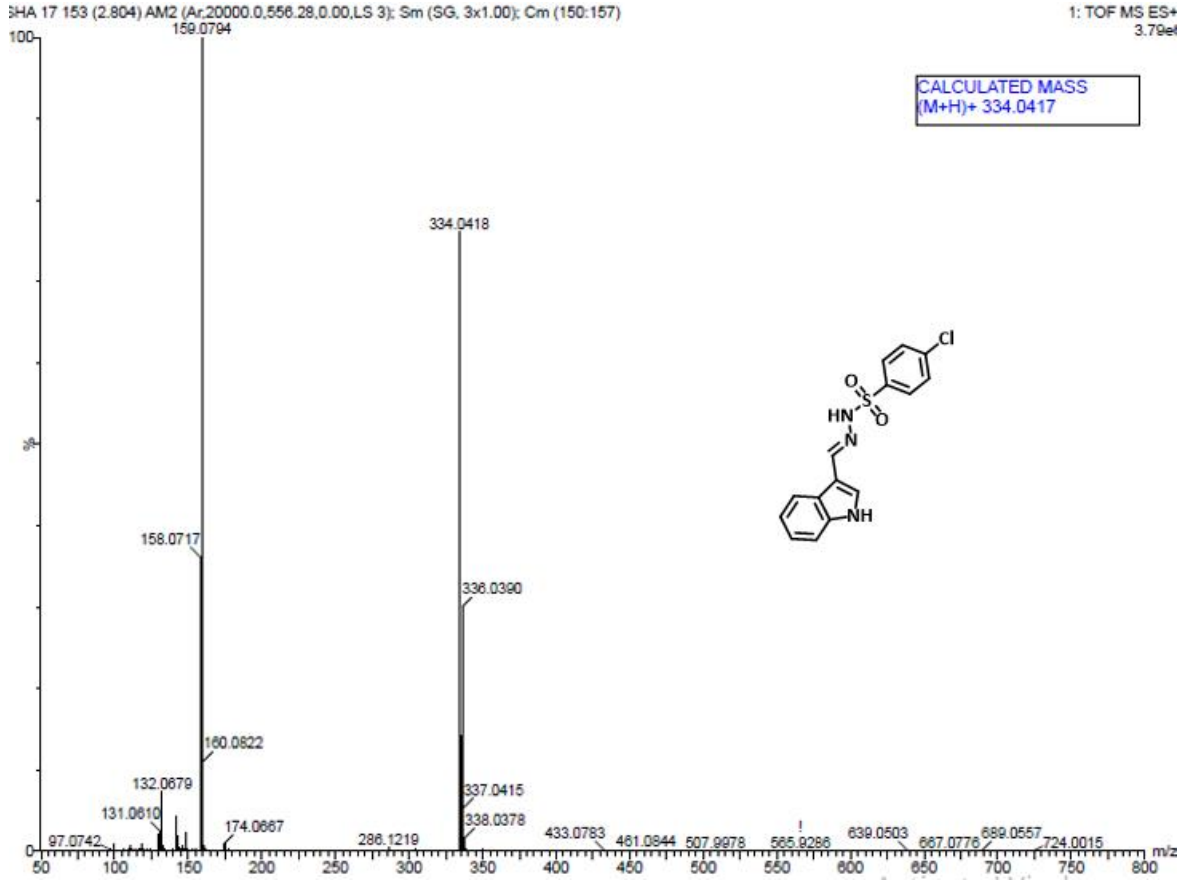


Fig. S119: HRMS spectrum of compound 39.

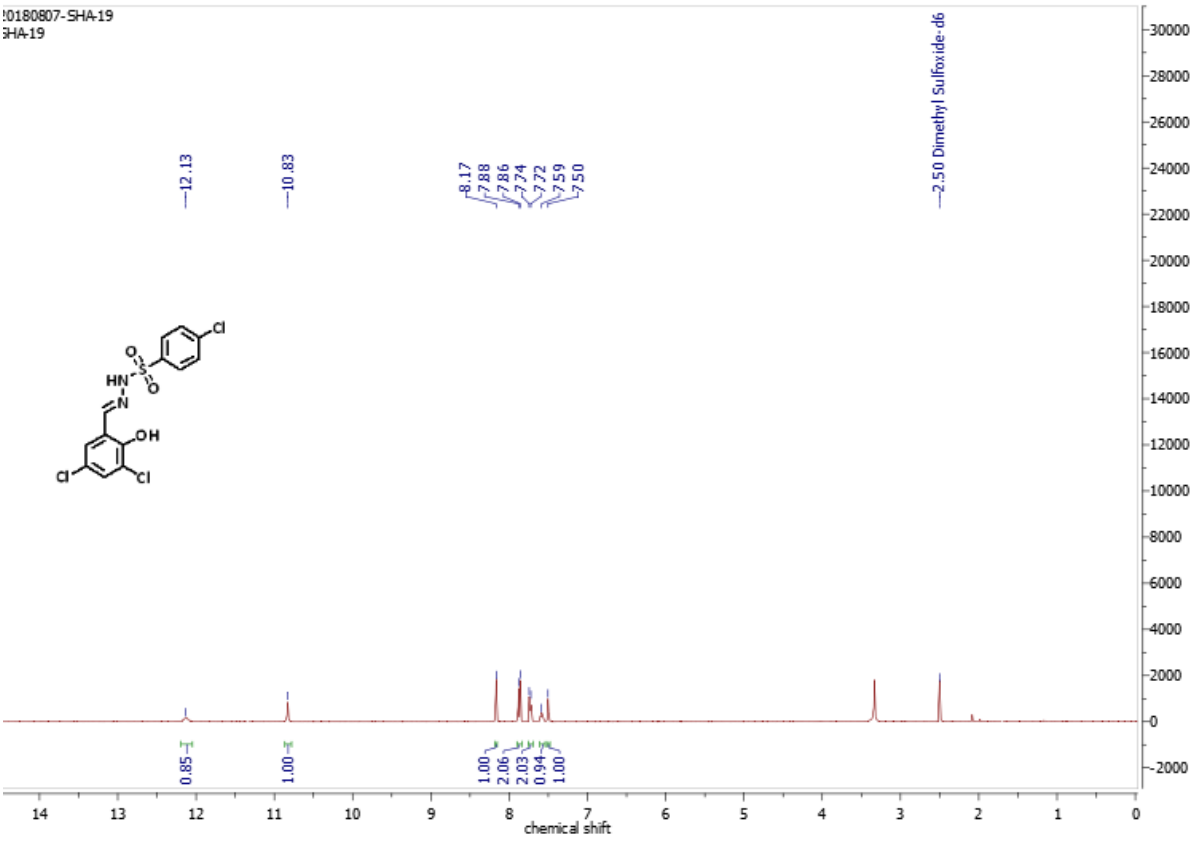


Fig. S120: [1] H NMR spectrum of compound 40 in DMSO-d_6 at 400 MHz.

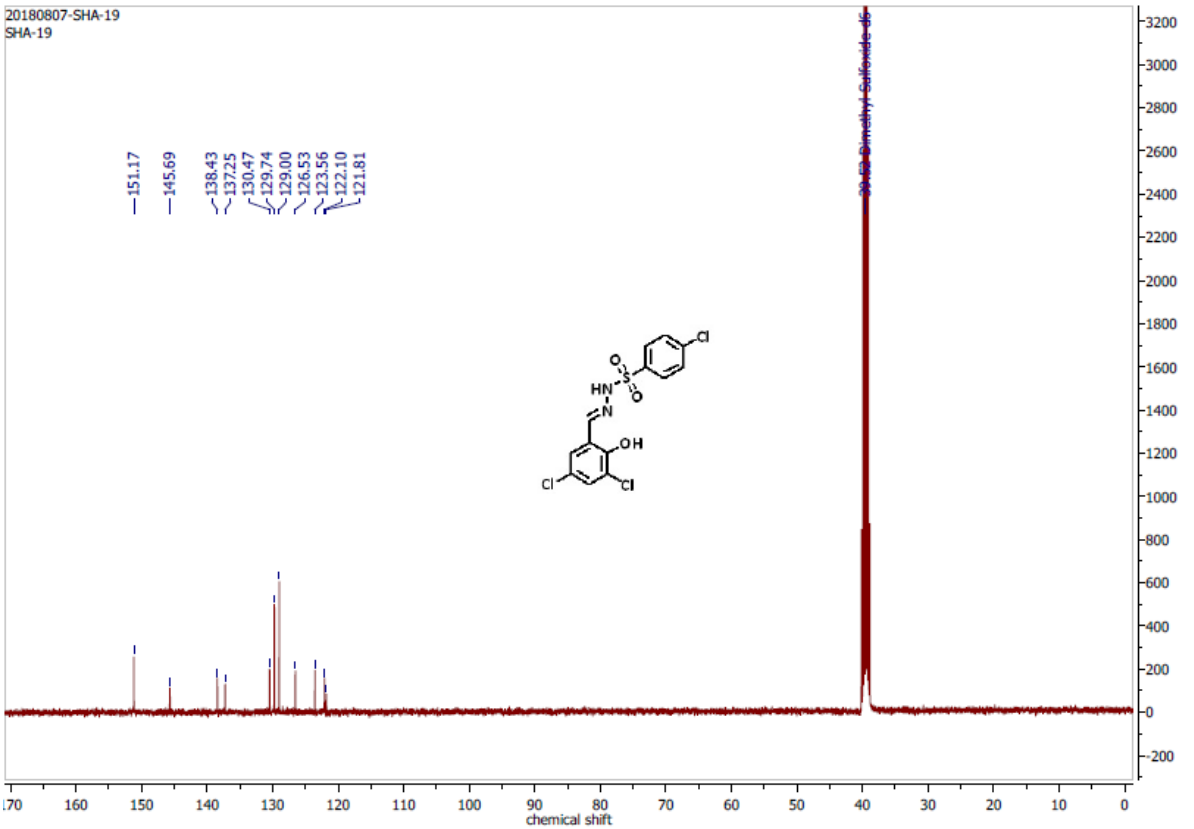


Fig. S121: [13] C NMR spectrum of compound 40 in DMSO-d_6 at 100 MHz.

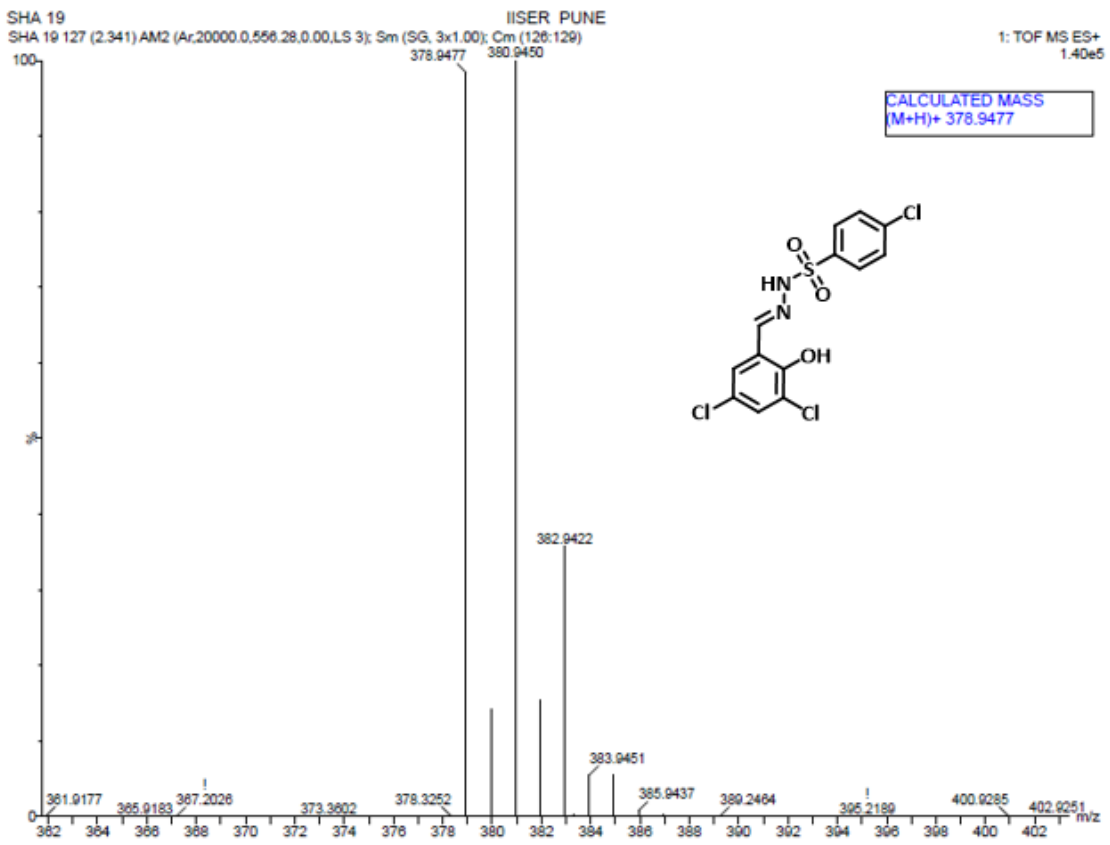


Fig. S122: HRMS spectrum of compound 40.

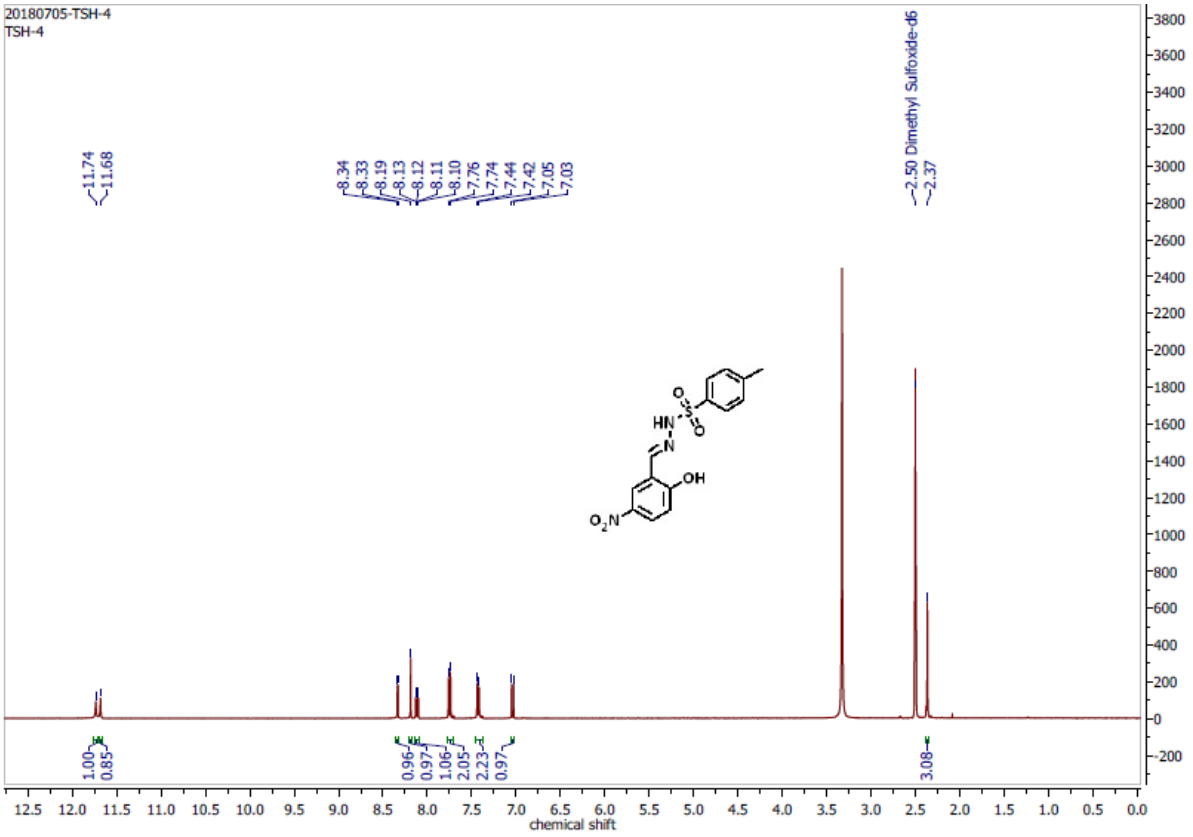


Fig. S123: ^{1}H NMR spectrum of compound 41 in DMSO-d_6 at 400 MHz.

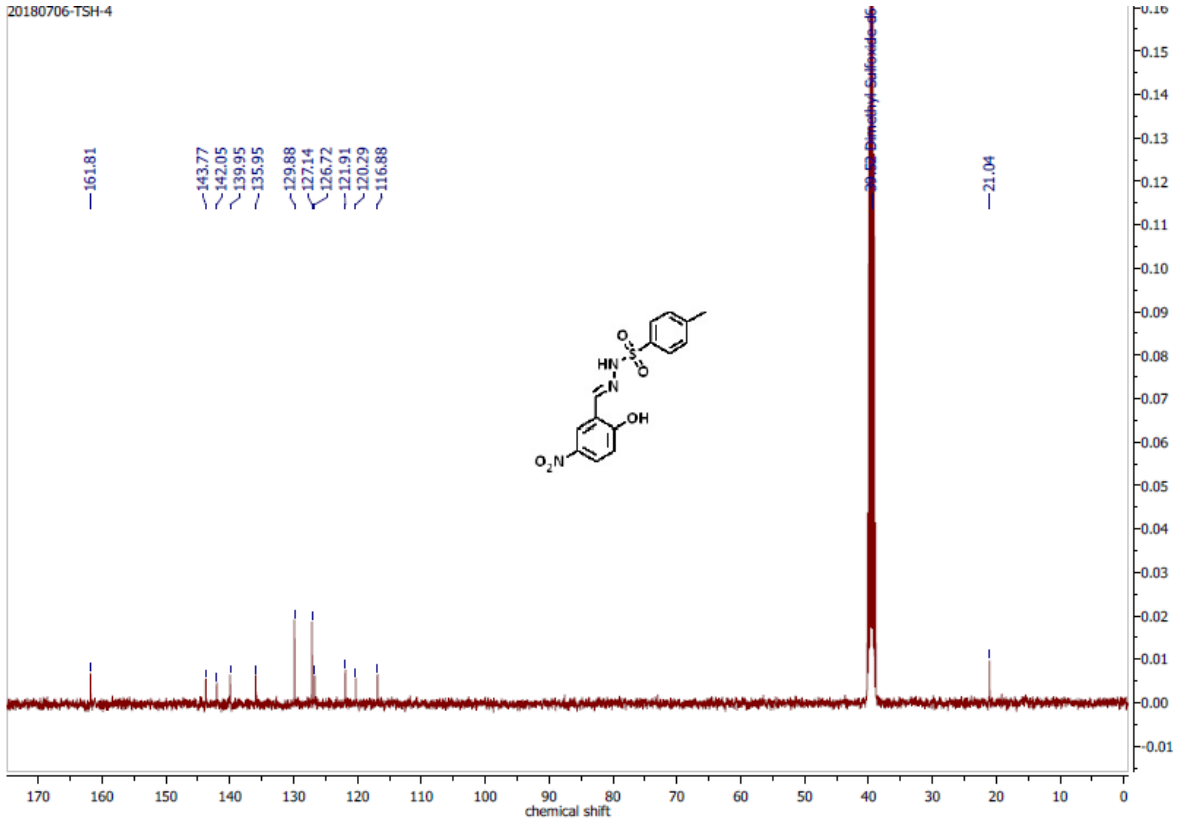


Fig. S124: ^{13}C NMR spectrum of compound 41 in DMSO-d_6 at 100 MHz.

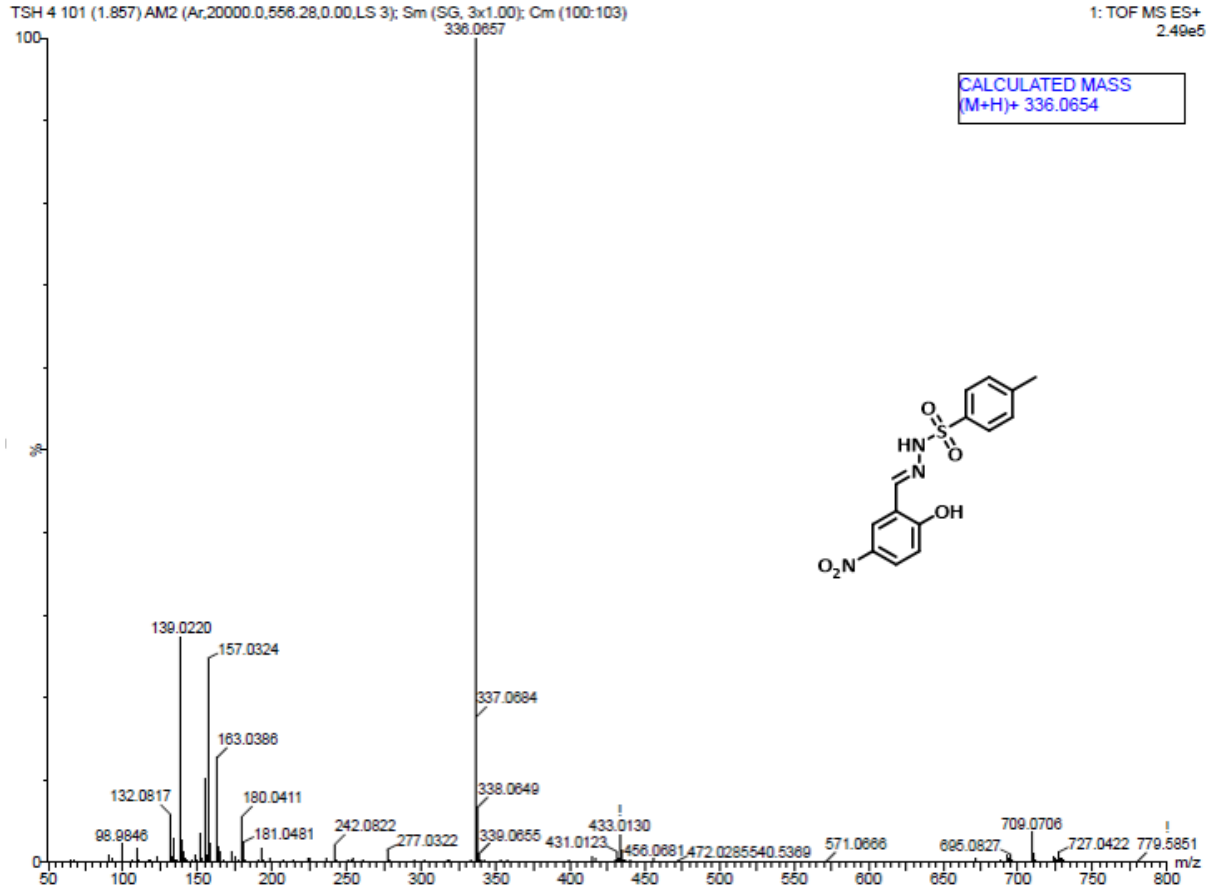


Fig. S125: HRMS spectrum of compound 41.

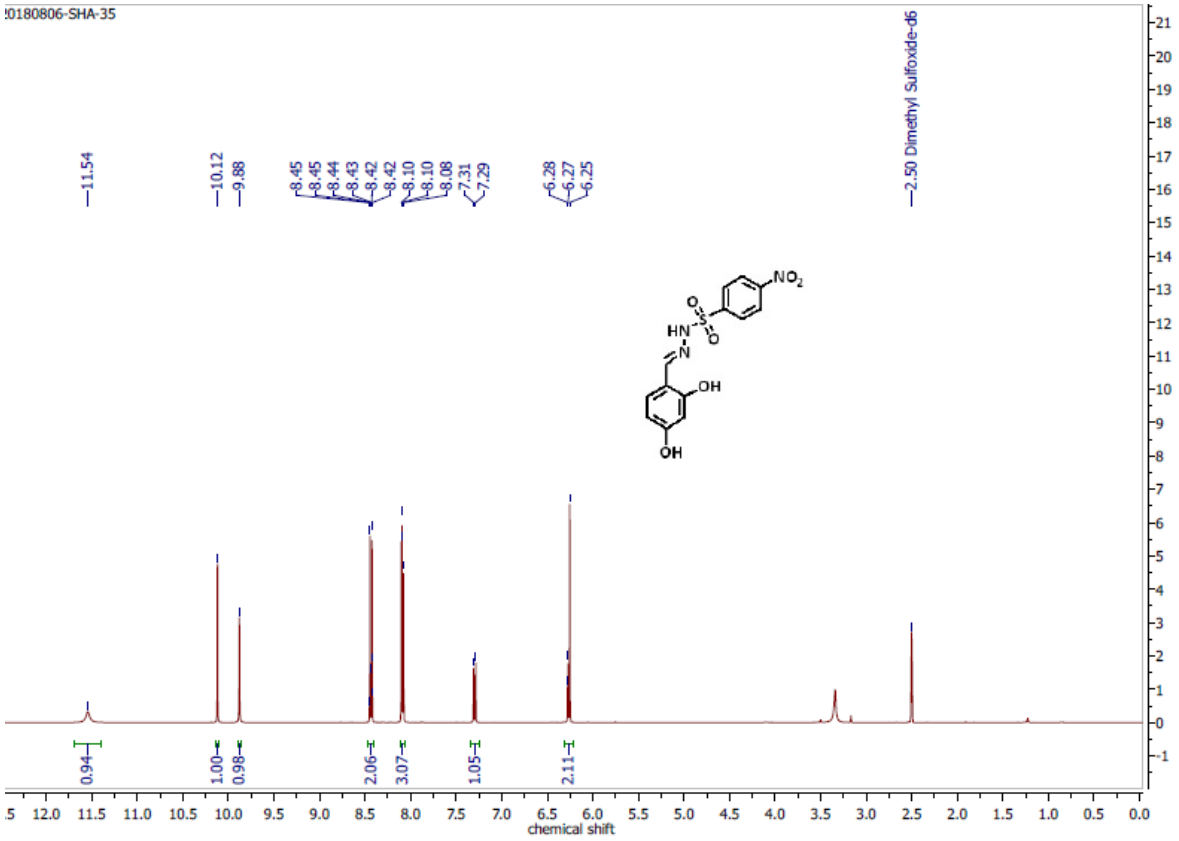


Fig. S126: [1] H NMR spectrum of compound 42 in DMSO-d_6 at 400 MHz.

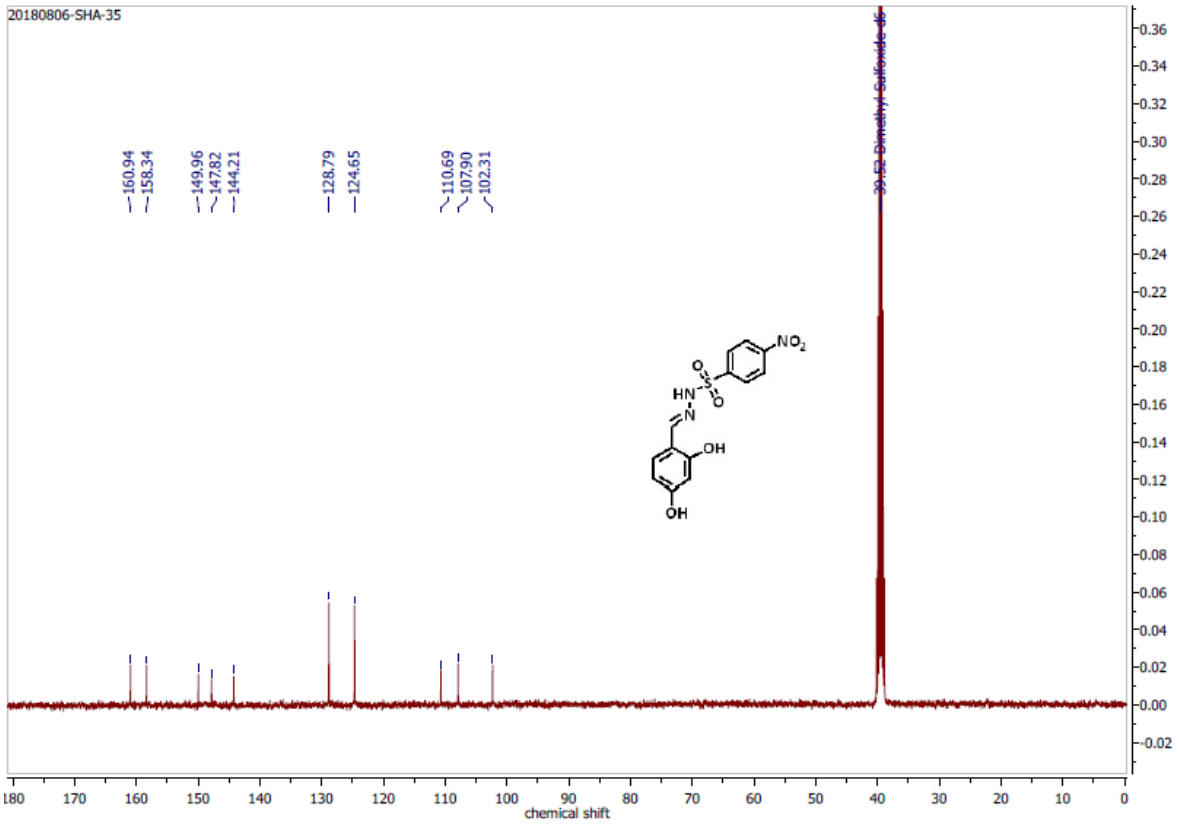


Fig. S127: [13] C NMR spectrum of compound 42 in DMSO-d_6 at 100 MHz.

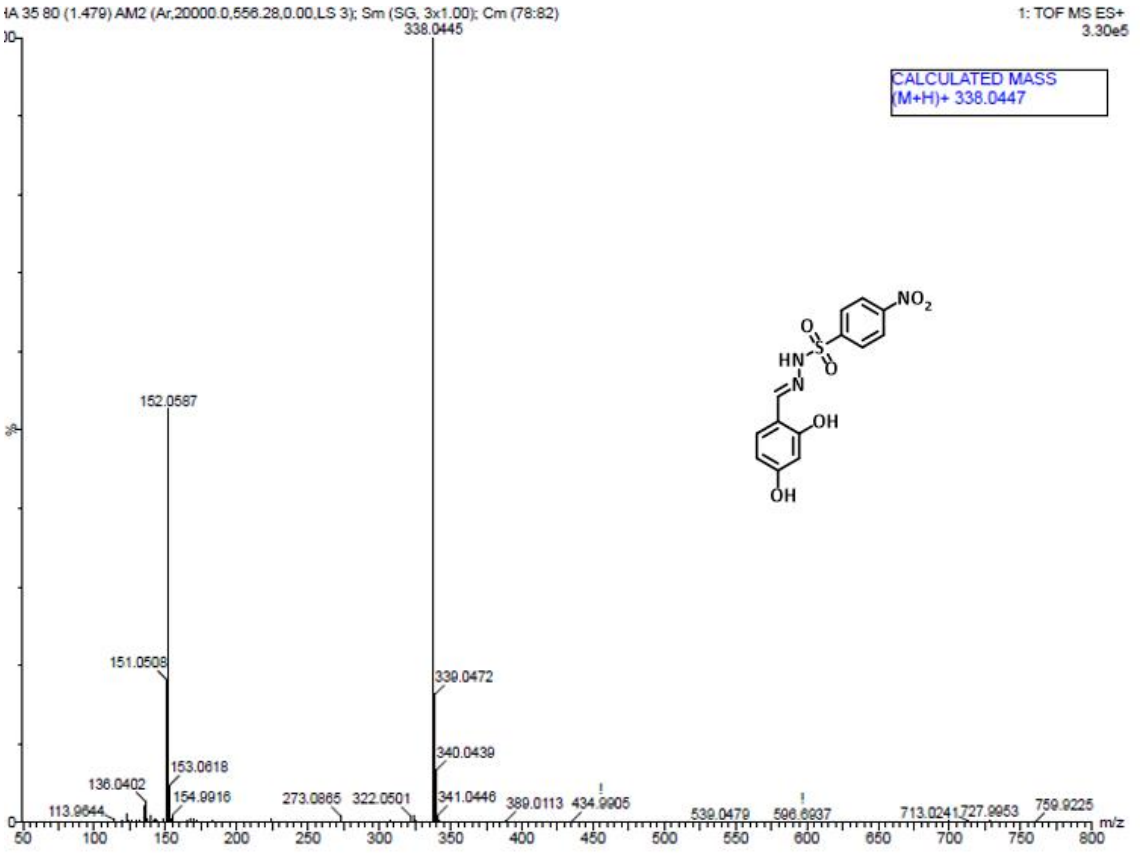


Fig. S128: HRMS spectrum of compound 42.

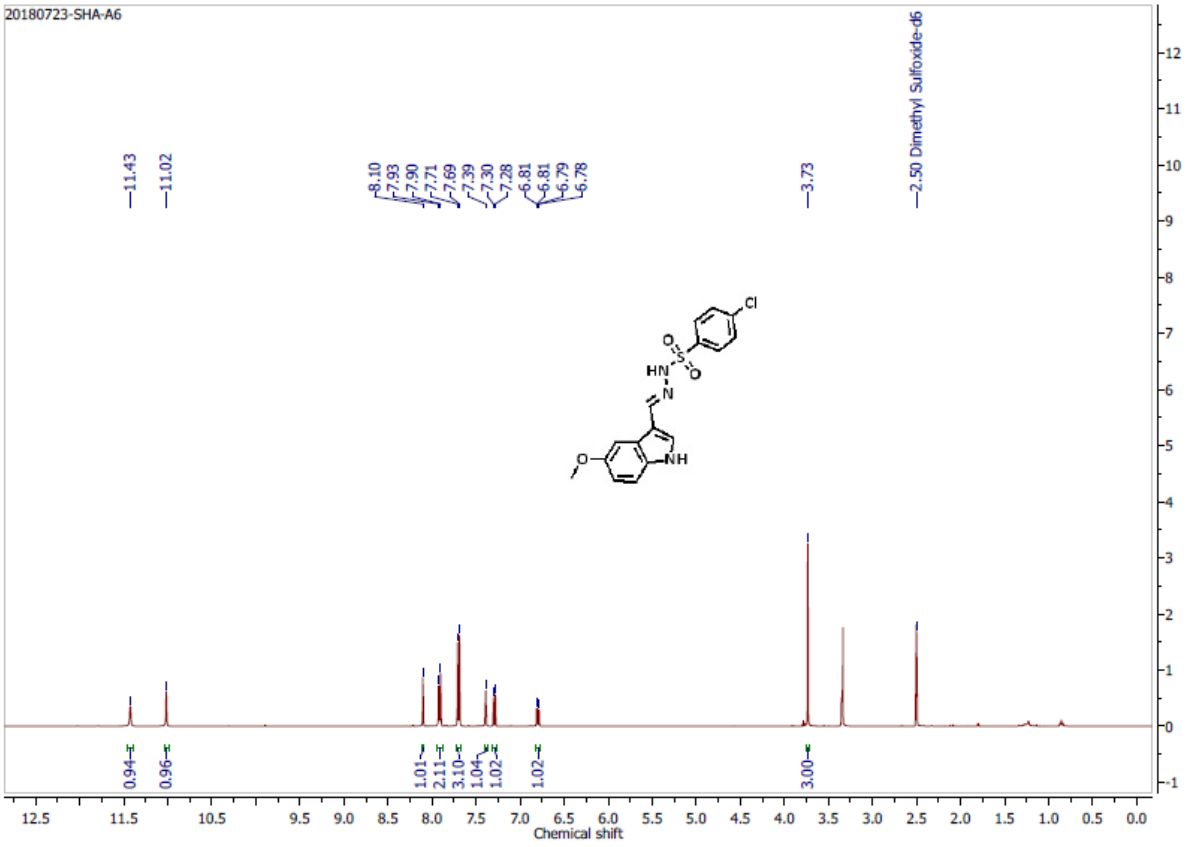


Fig. S129: [1] H NMR spectrum of compound 43 in DMSO-d_6 at 400 MHz.

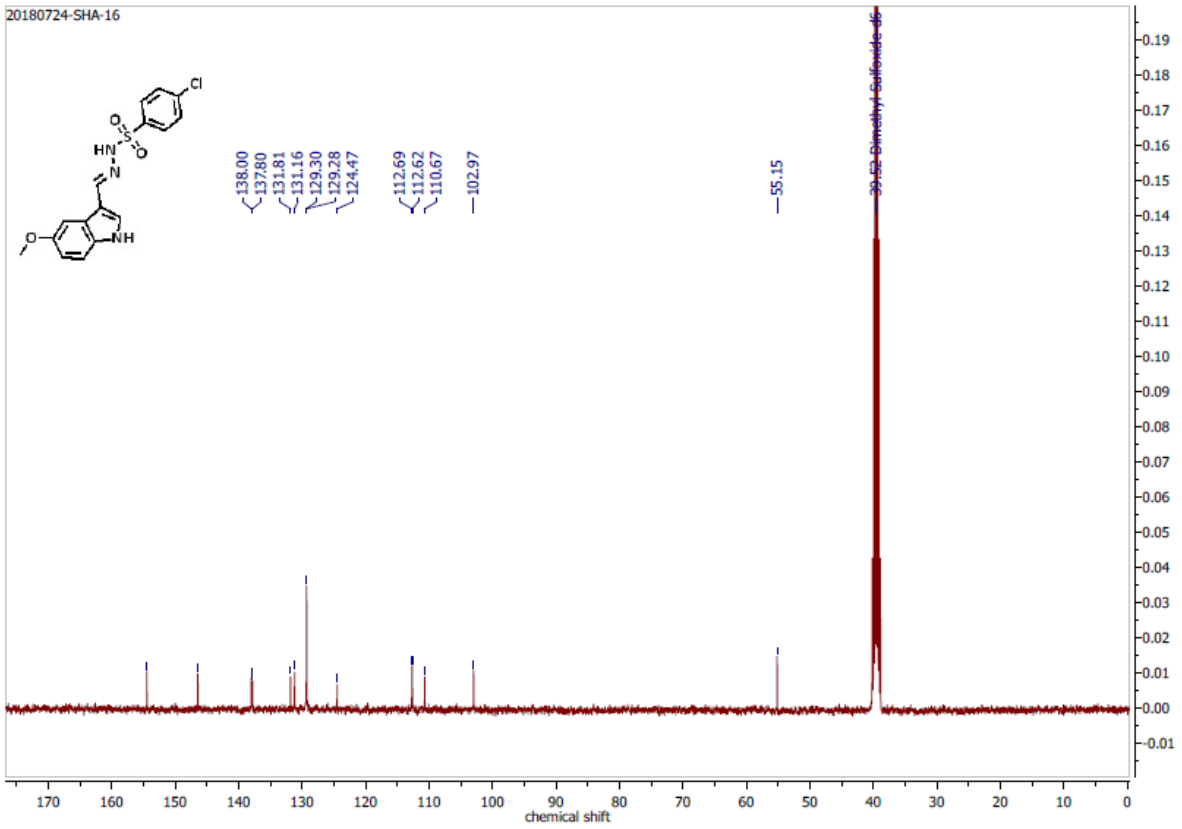


Fig. S130: ^{13}C NMR spectrum of compound 43 in DMSO-d_6 at 100 MHz.

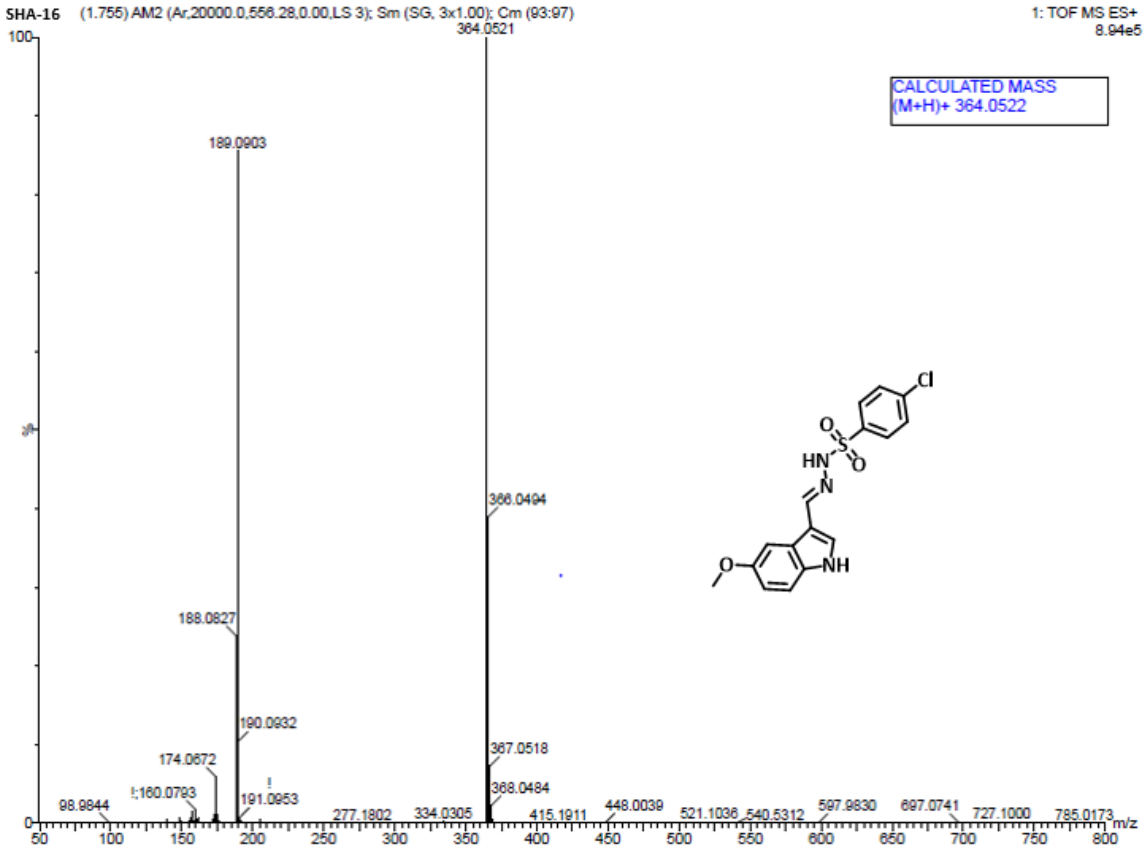


Fig. S131: HRMS spectrum of compound 43.

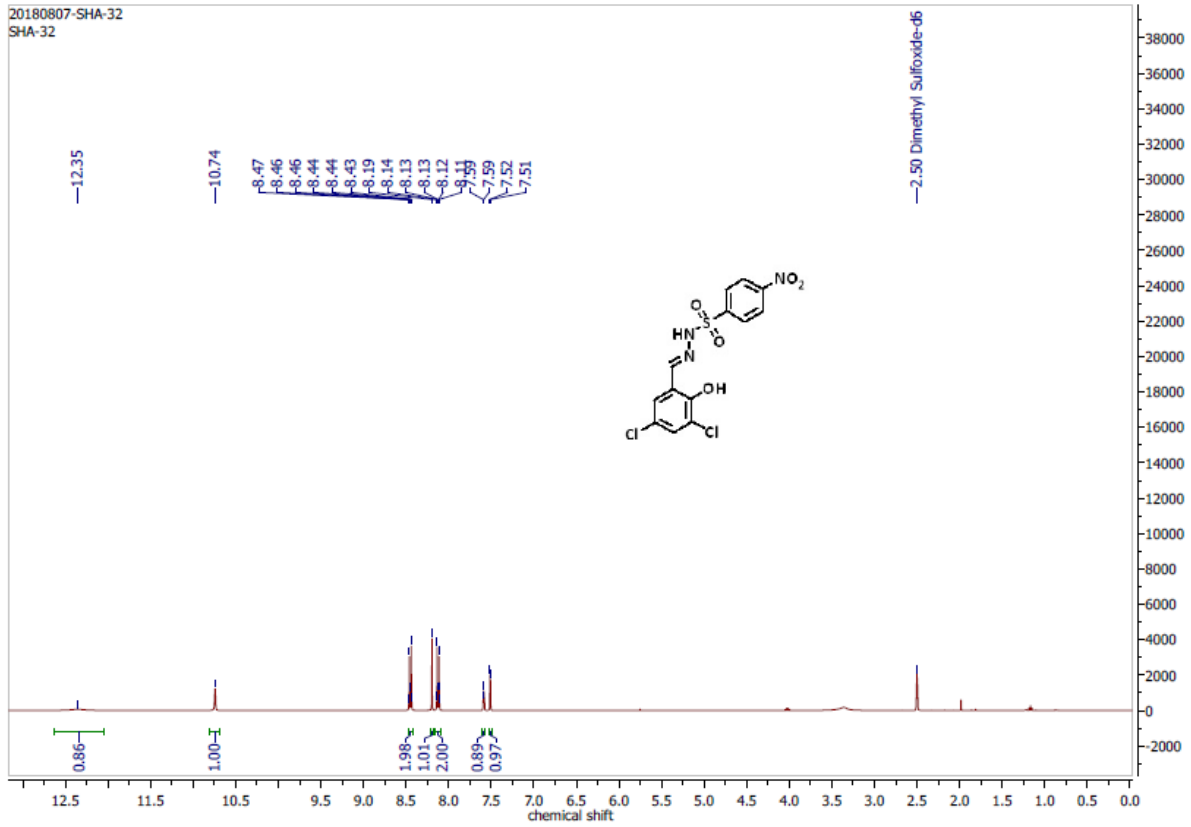


Fig. S132: [1] H NMR spectrum of compound 44 in DMSO-d_6 at 400 MHz.

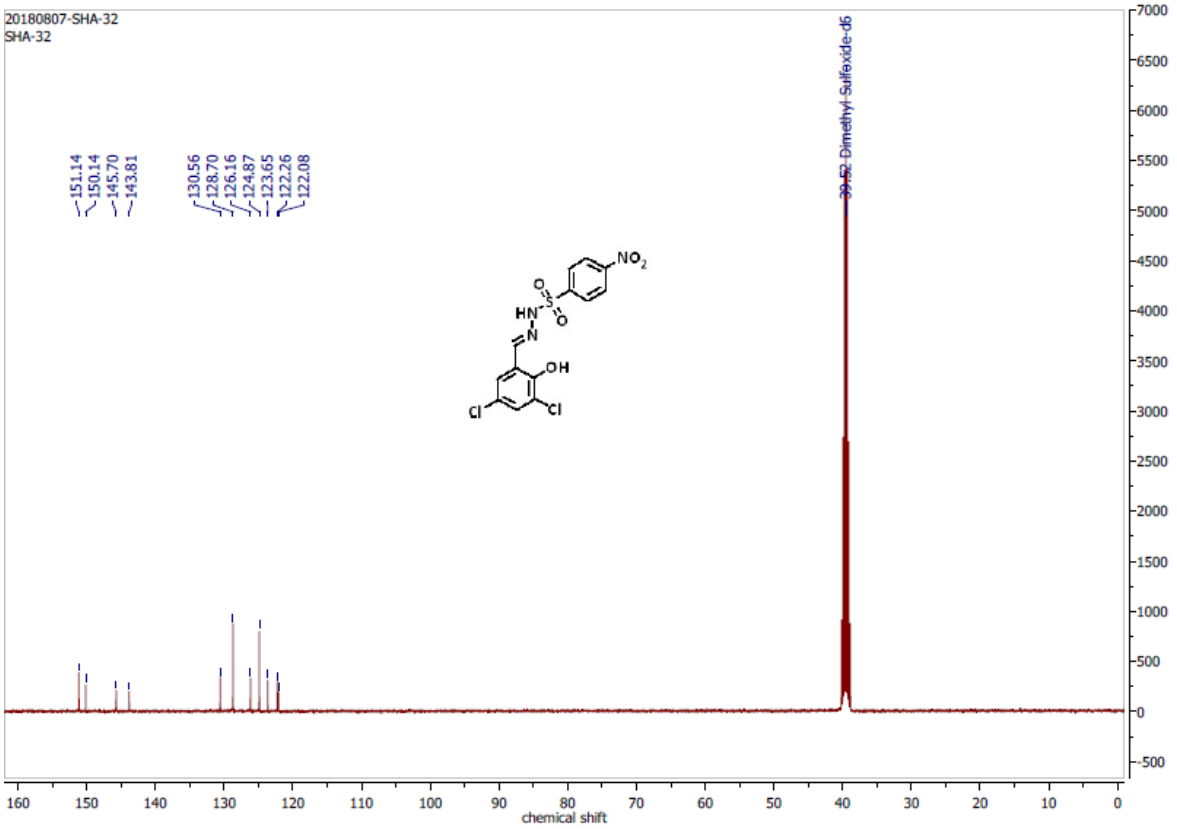


Fig. S133: [13] C NMR spectrum of compound 44 in DMSO-d_6 at 100 MHz.

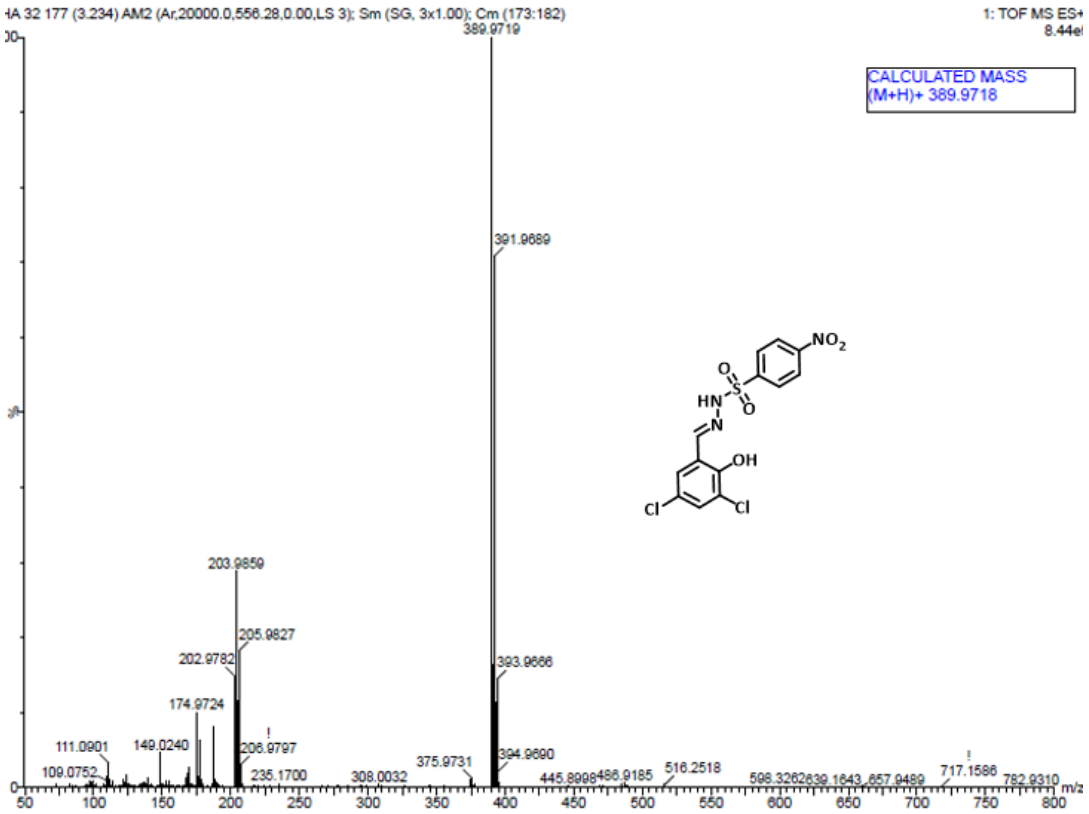


Fig. S134: HRMS spectrum of compound 44.

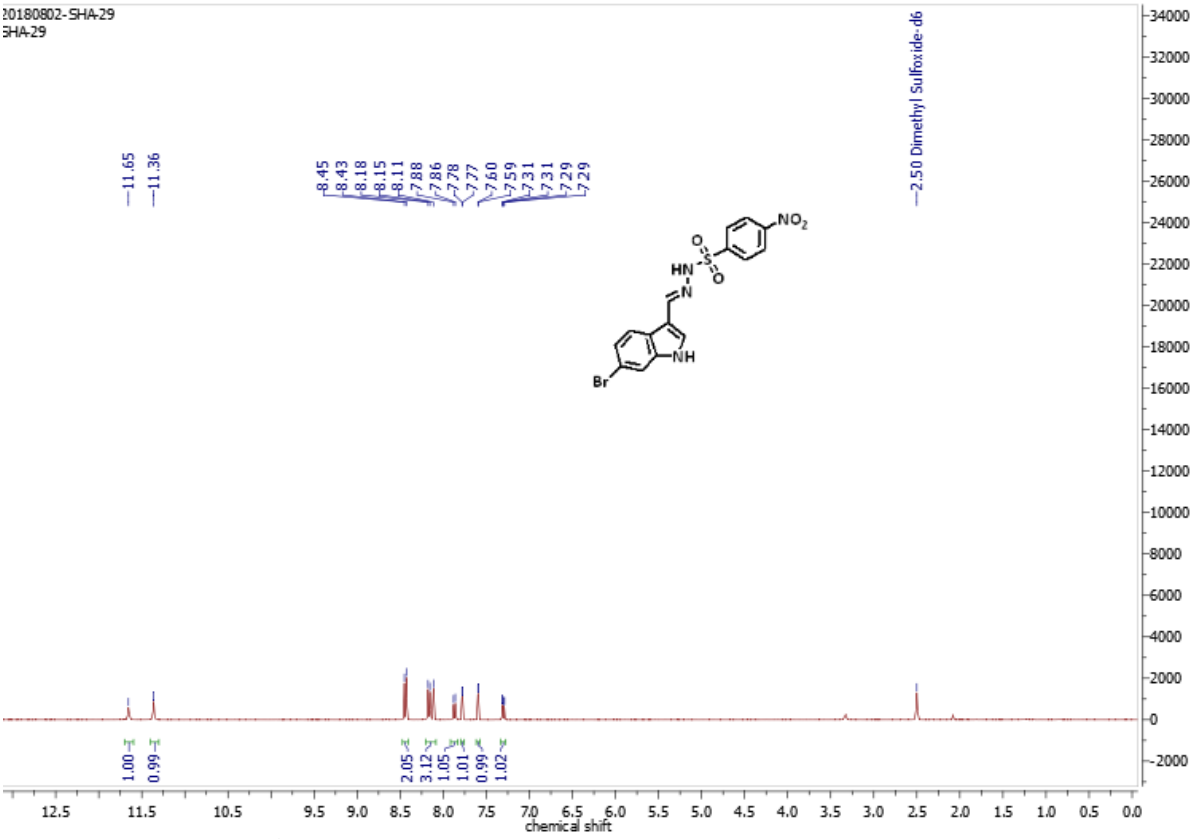


Fig. S135: [1] H NMR spectrum of compound 45 in DMSO-d_6 at 400 MHz.

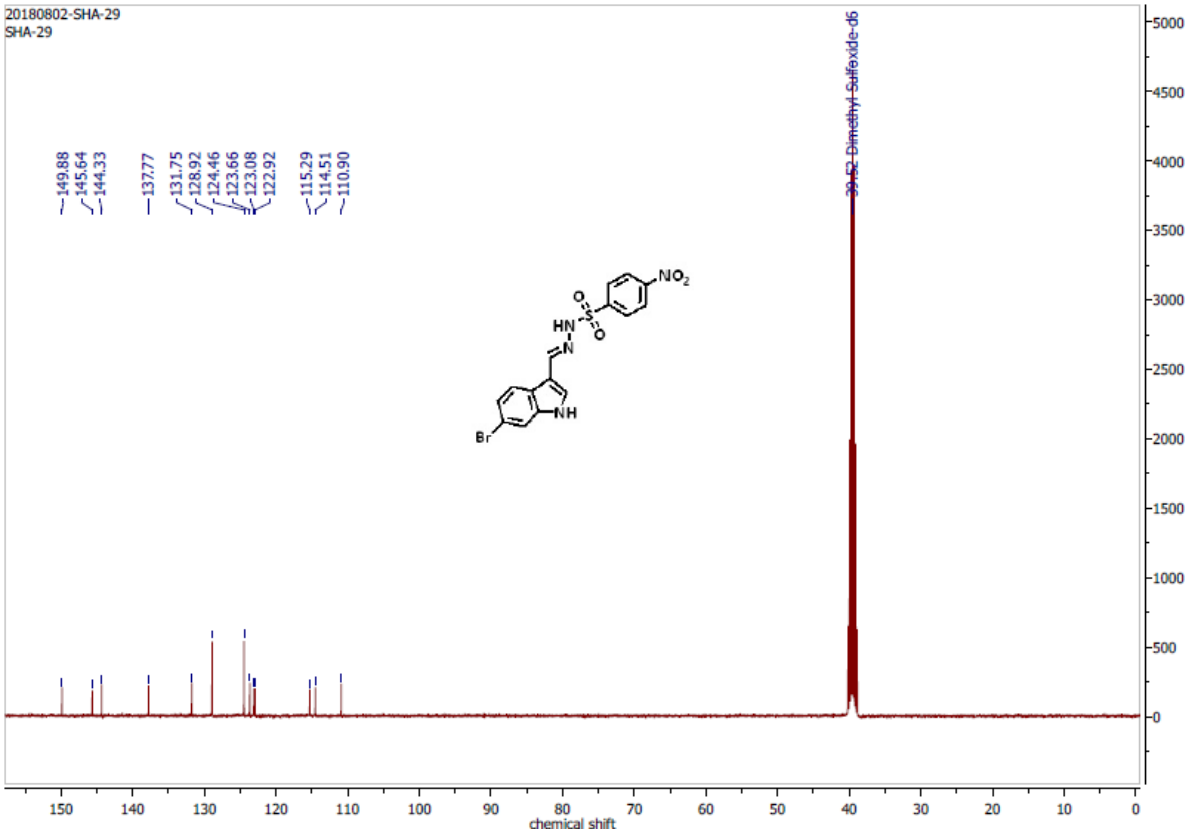


Fig. S136: ^{13}C NMR spectrum of compound 45 in DMSO-d_6 at 100 MHz.

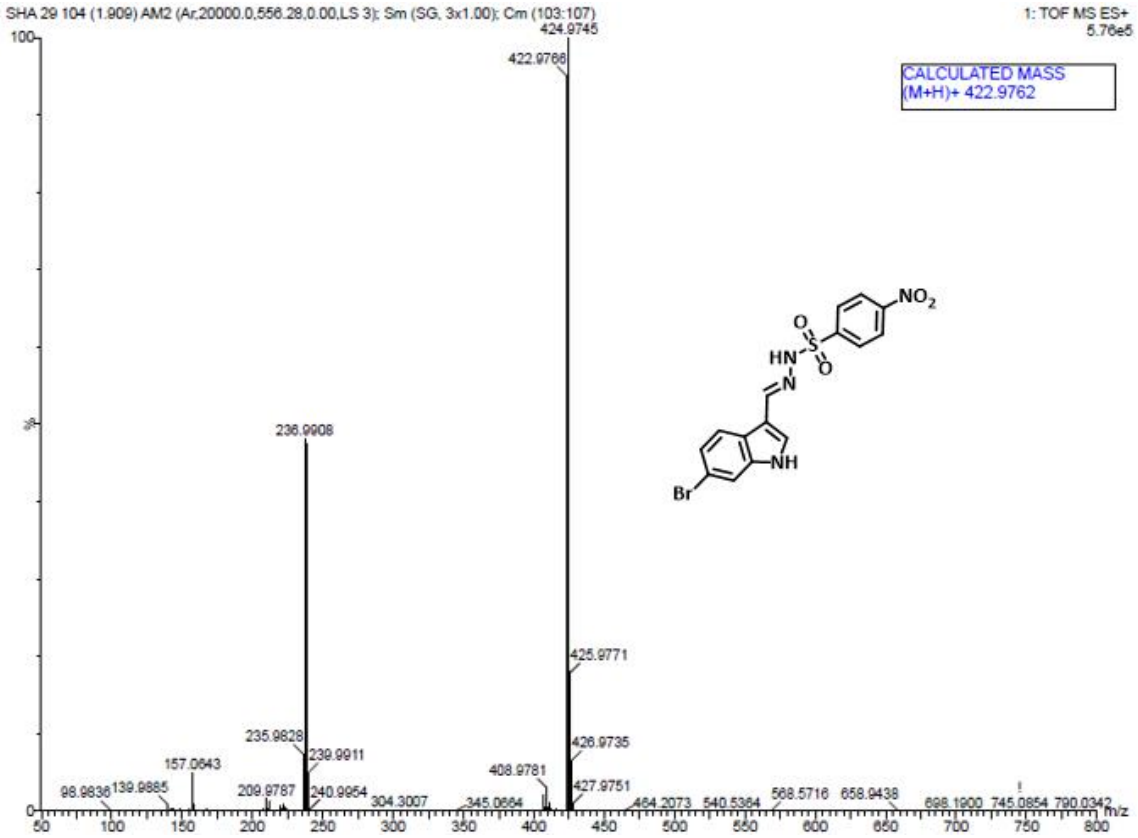


Fig. S137: HRMS spectrum of compound 45.

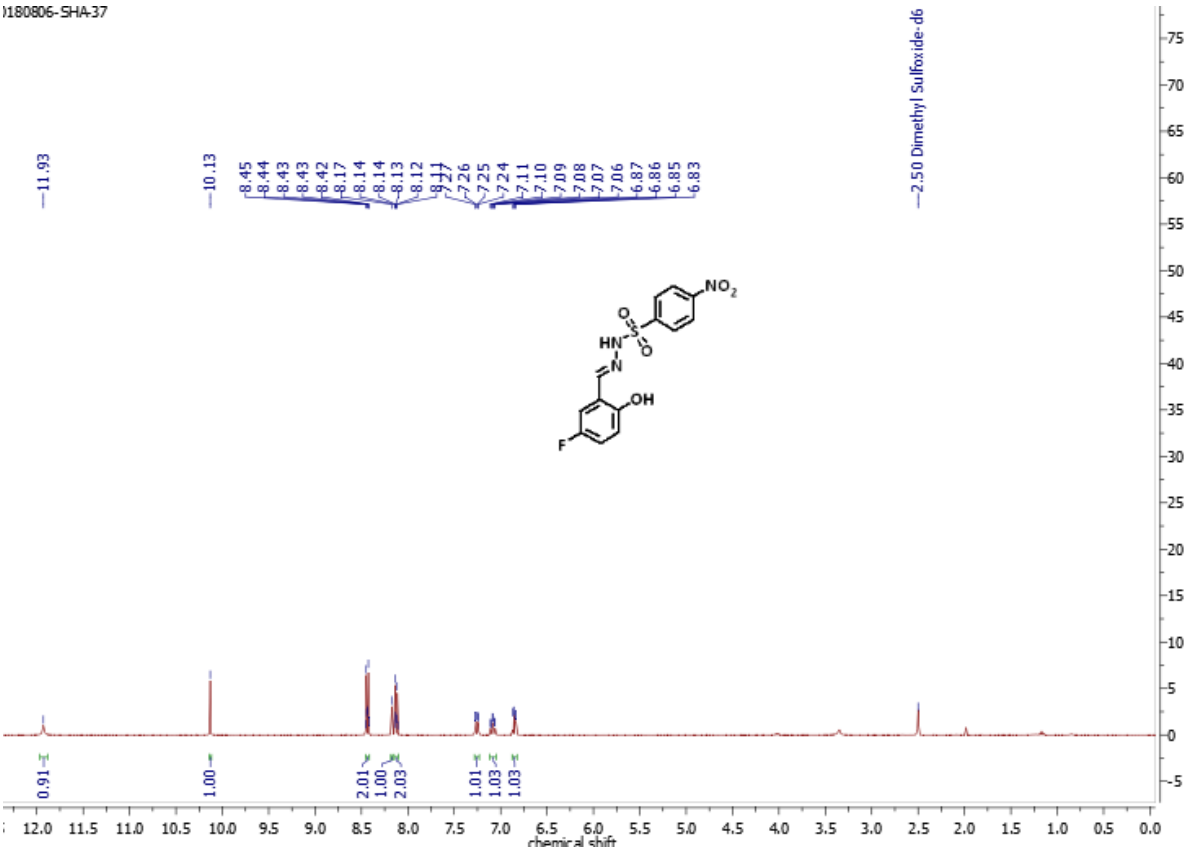


Fig. S138: [1] H NMR spectrum of compound 46 in DMSO-d_6 at 400 MHz.

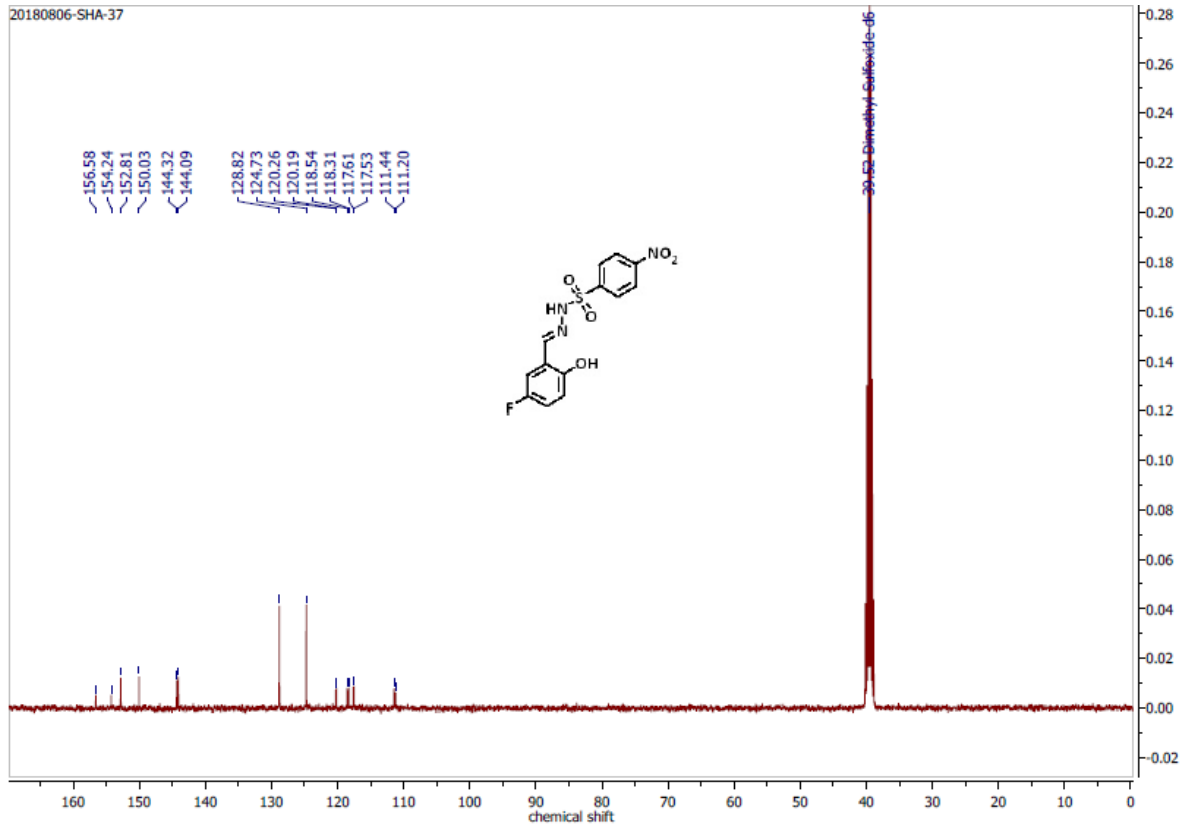


Fig. S139: [13] C NMR spectrum of compound 46 in DMSO-d_6 at 100 MHz.

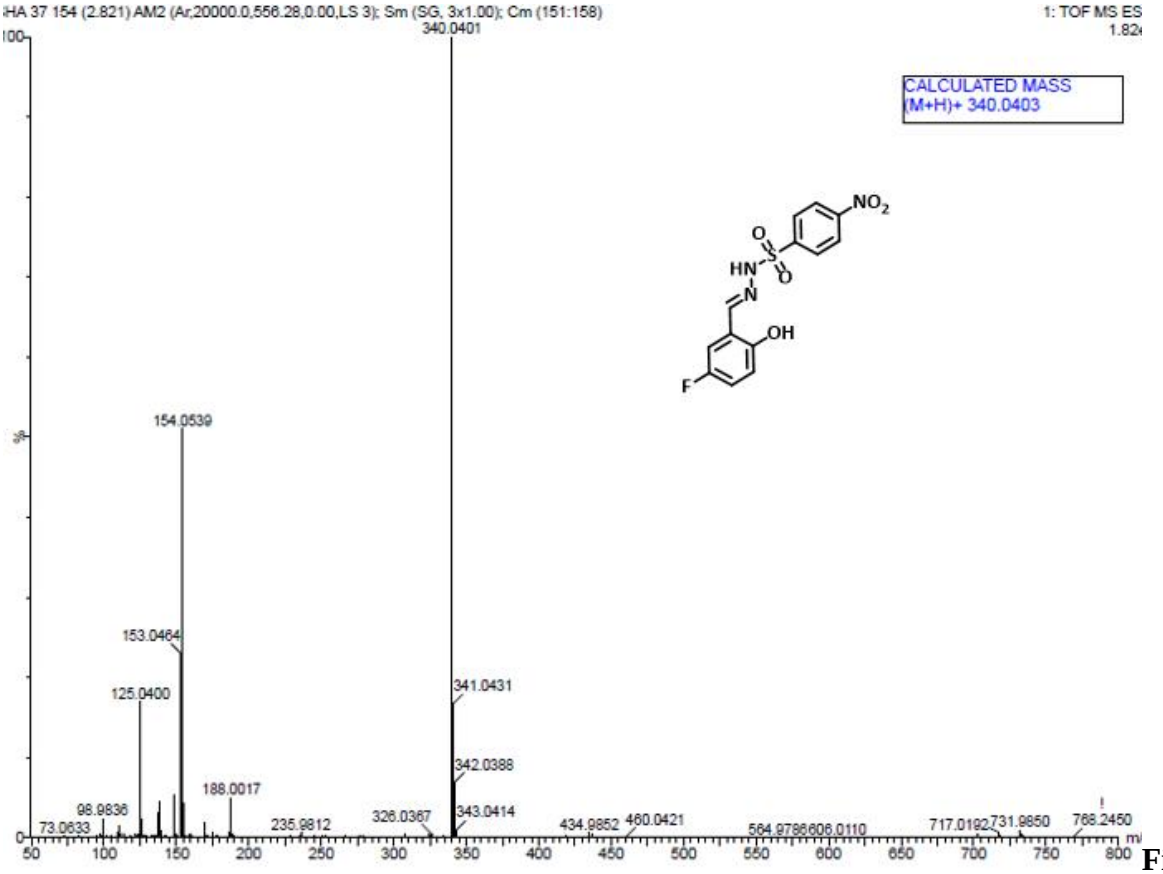


Fig. S140: HRMS spectrum of compound 46.

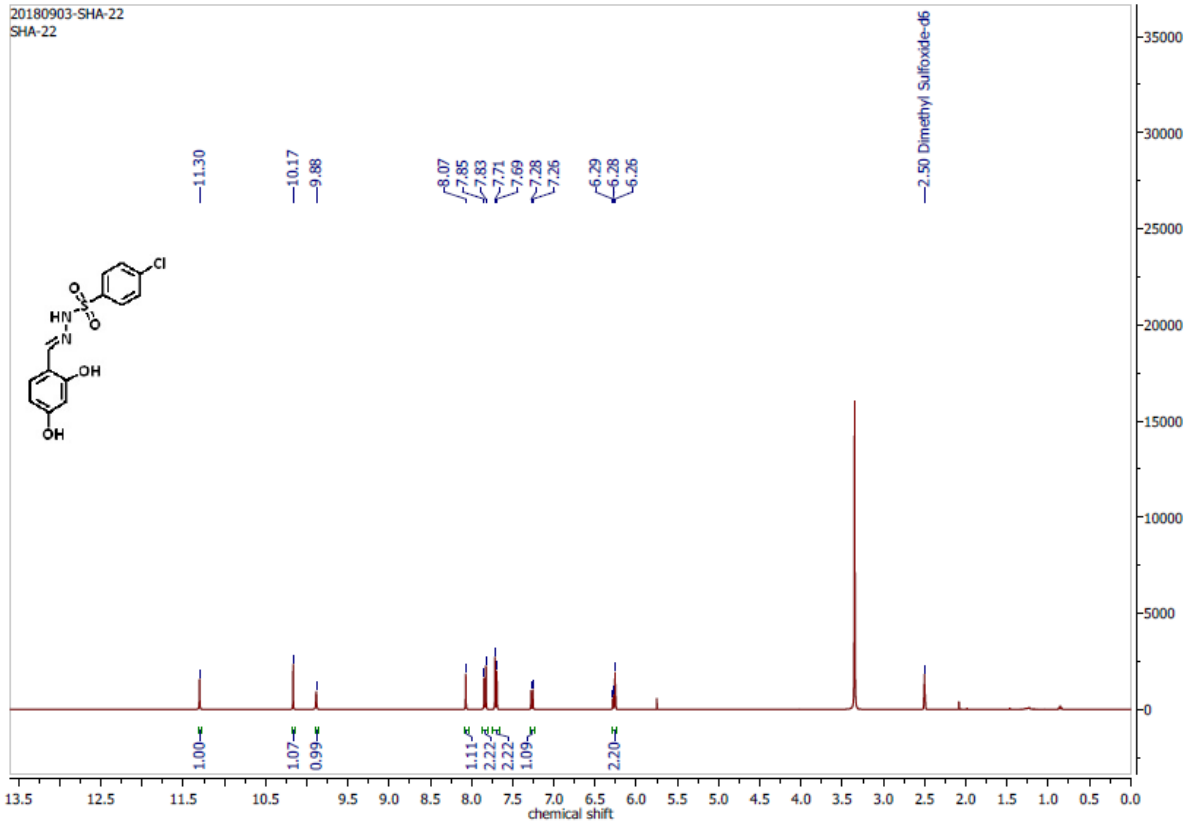


Fig. S141: [1] H NMR spectrum of compound 47 in DMSO-d_6 at 400 MHz.

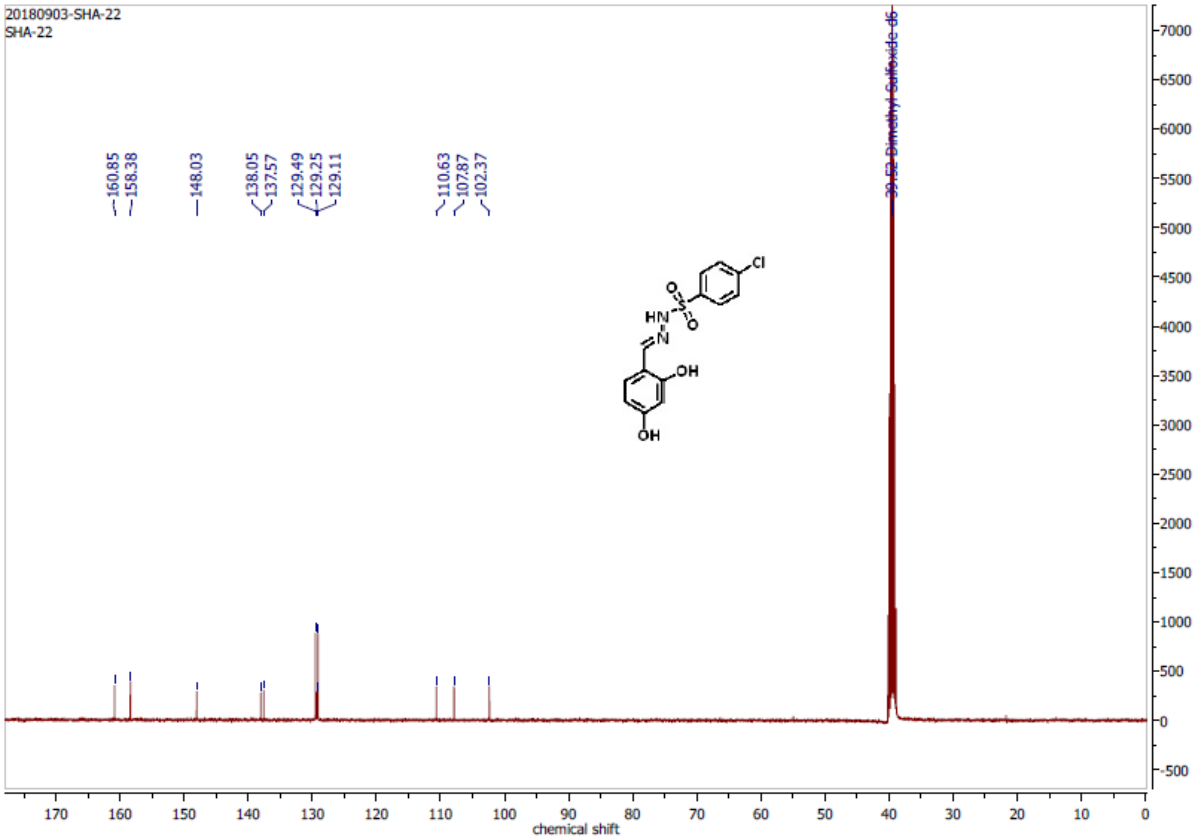


Fig. S142: ^{13}C NMR spectrum of compound 47 in DMSO-d_6 at 100 MHz.

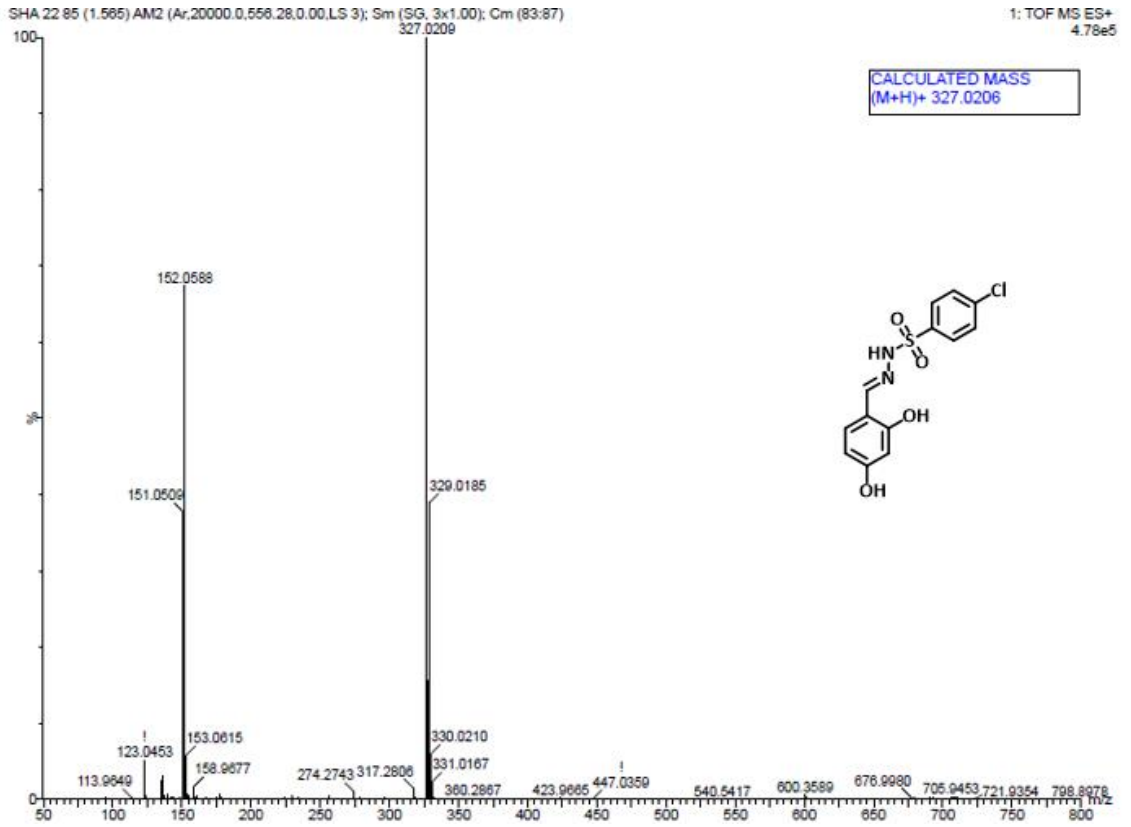


Fig. S143: HRMS spectrum of compound 47.

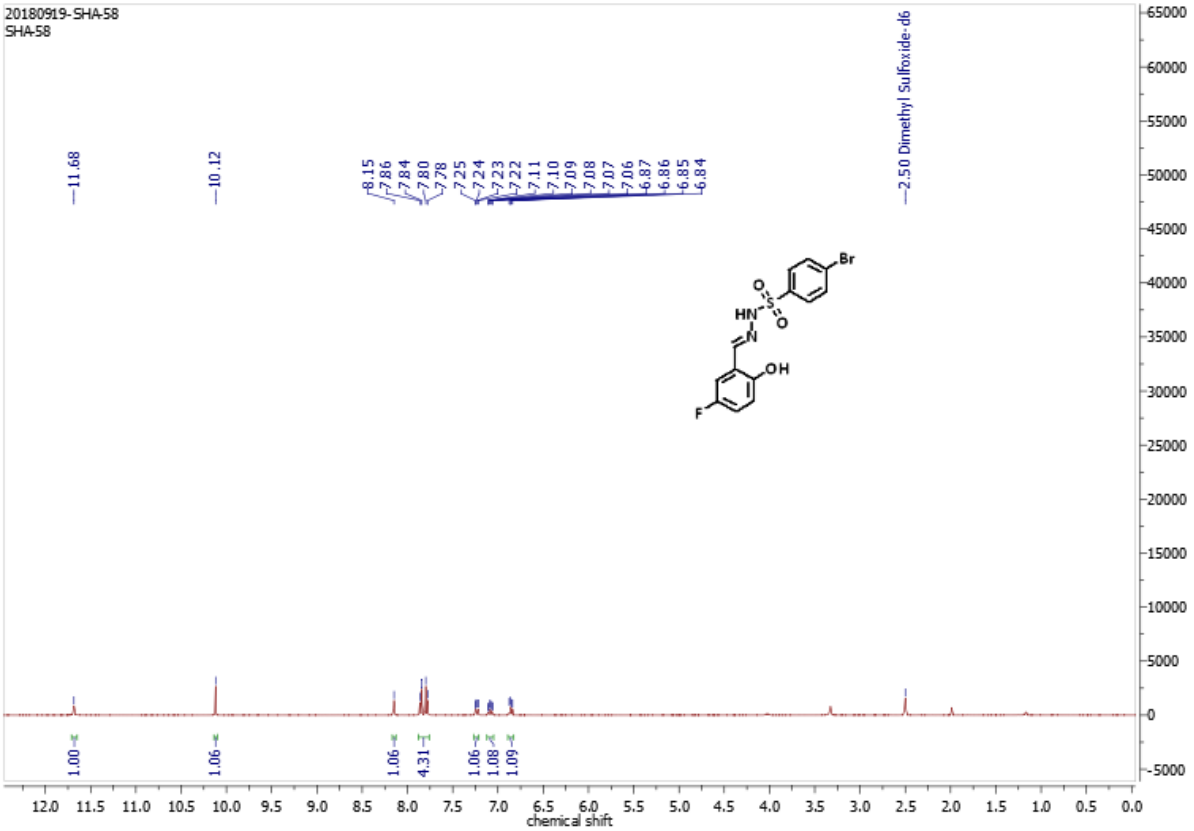


Fig. S144: [1] H NMR spectrum of compound 48 in DMSO-d_6 at 400 MHz.

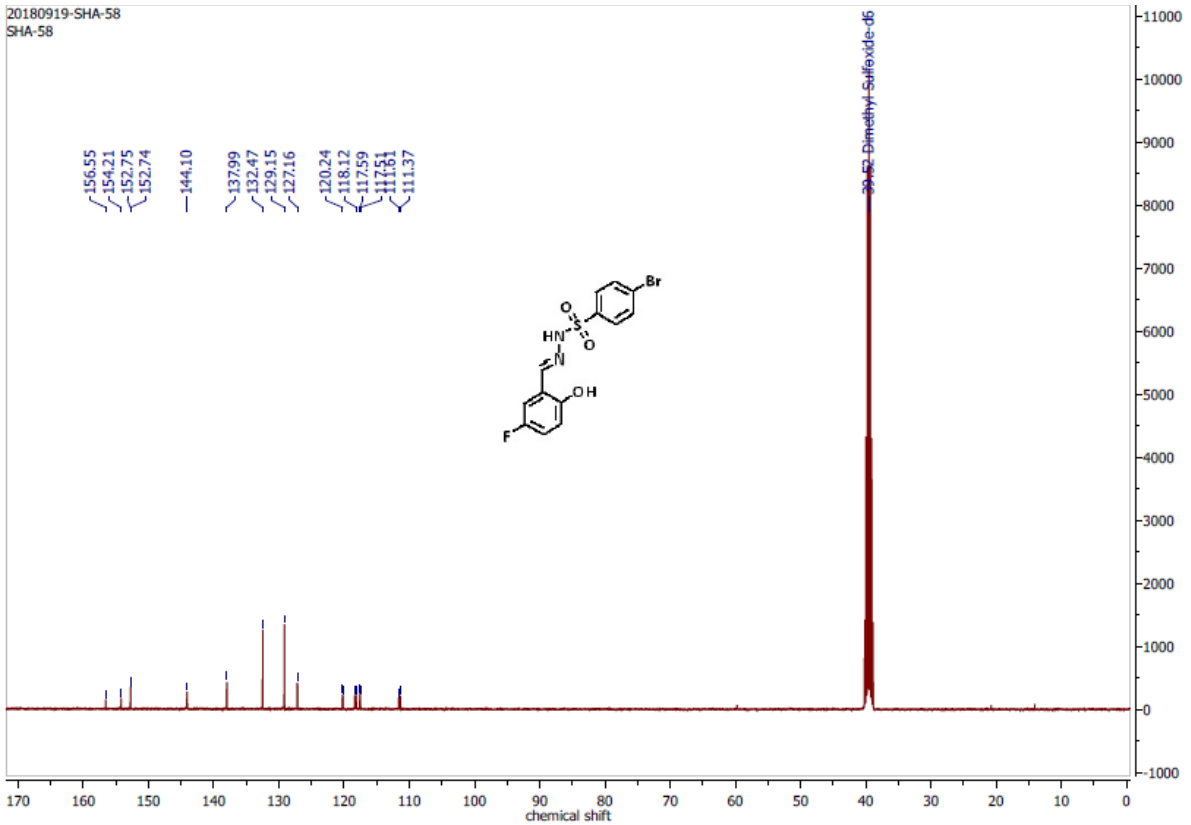


Fig. S145: [13] C NMR spectrum of compound 48 in DMSO-d_6 at 100 MHz.

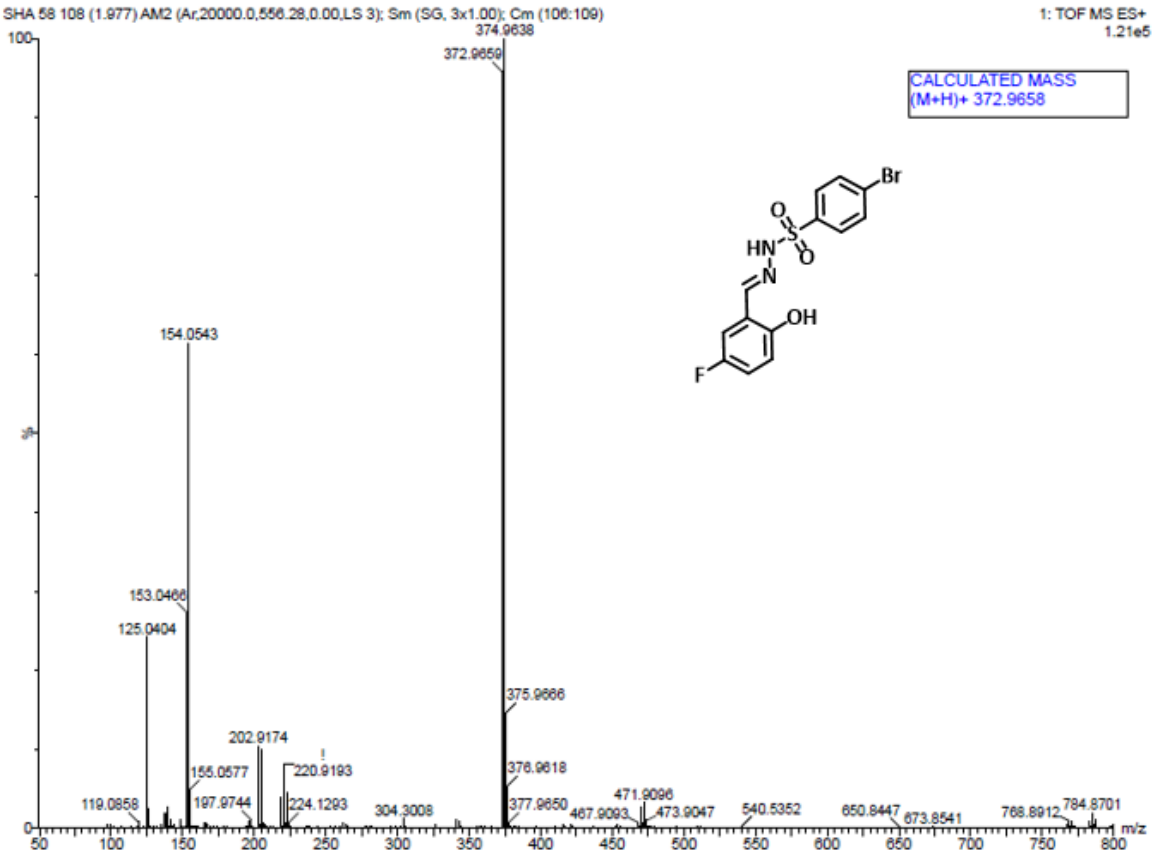


Fig. S146: HRMS spectrum of compound 48.

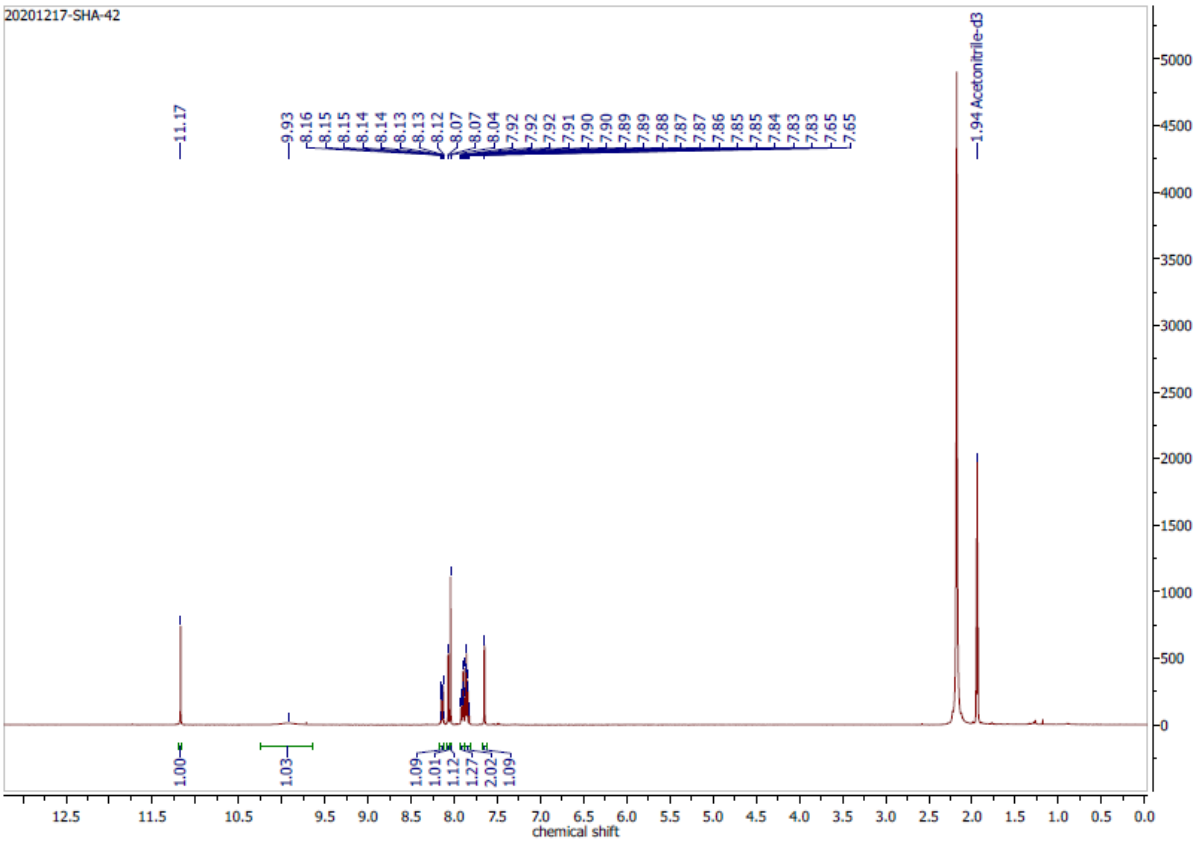


Fig. S147: [1] H NMR spectrum of compound 49 in CD_3CN-d_3 at 400 MHz.

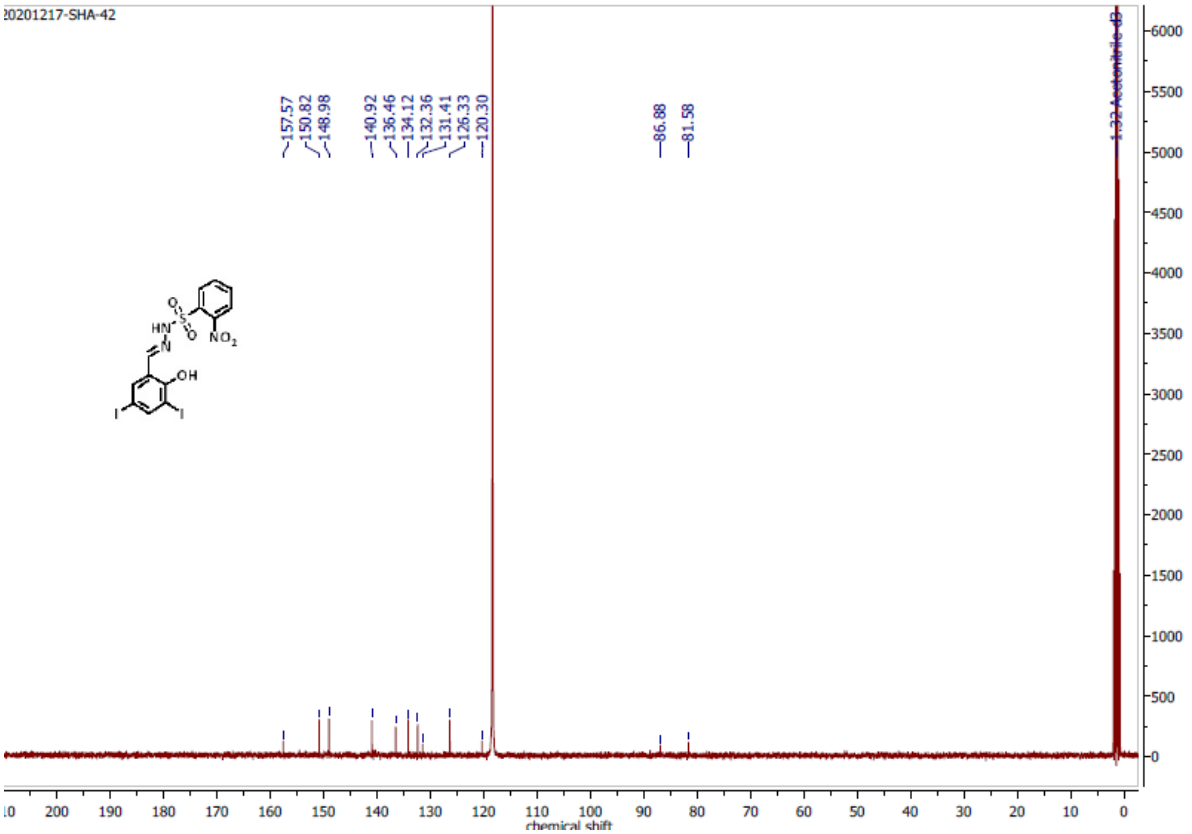


Fig. S148: ^{13}C NMR spectrum of compound 49 in CD_3CN-d_3 at 100 MHz.

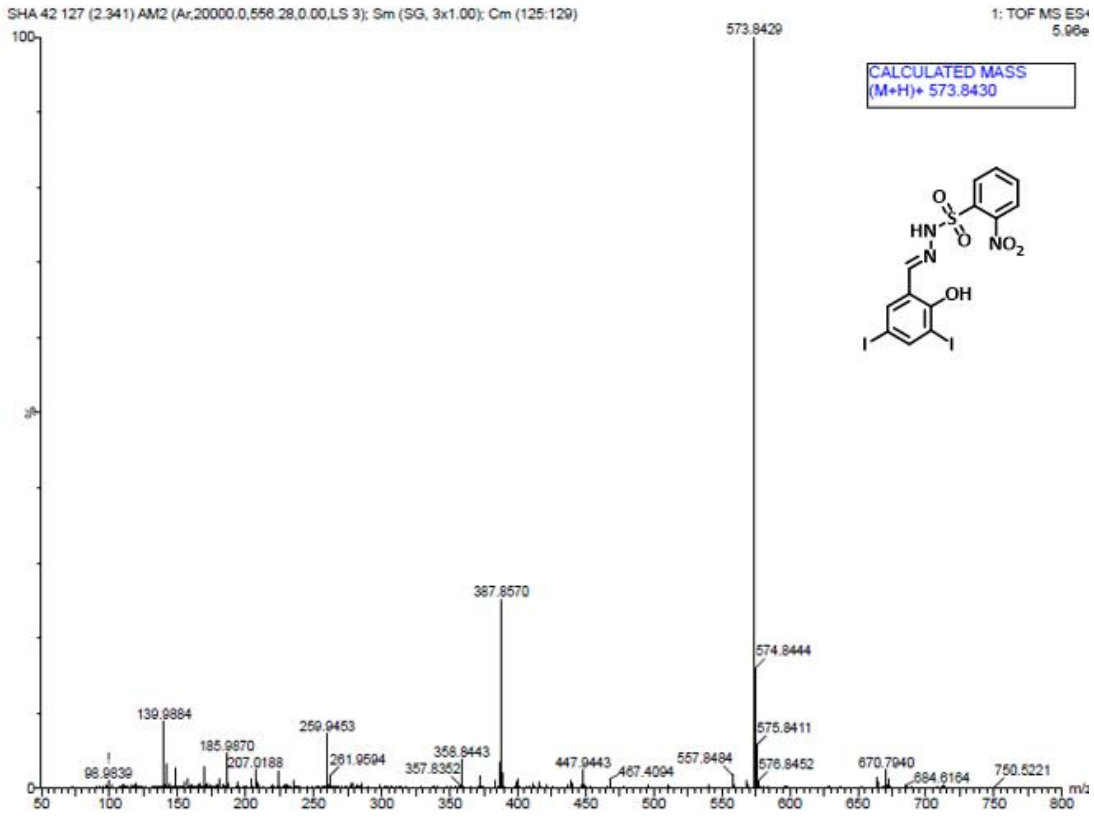


Fig. S149: HRMS spectrum of compound 49.

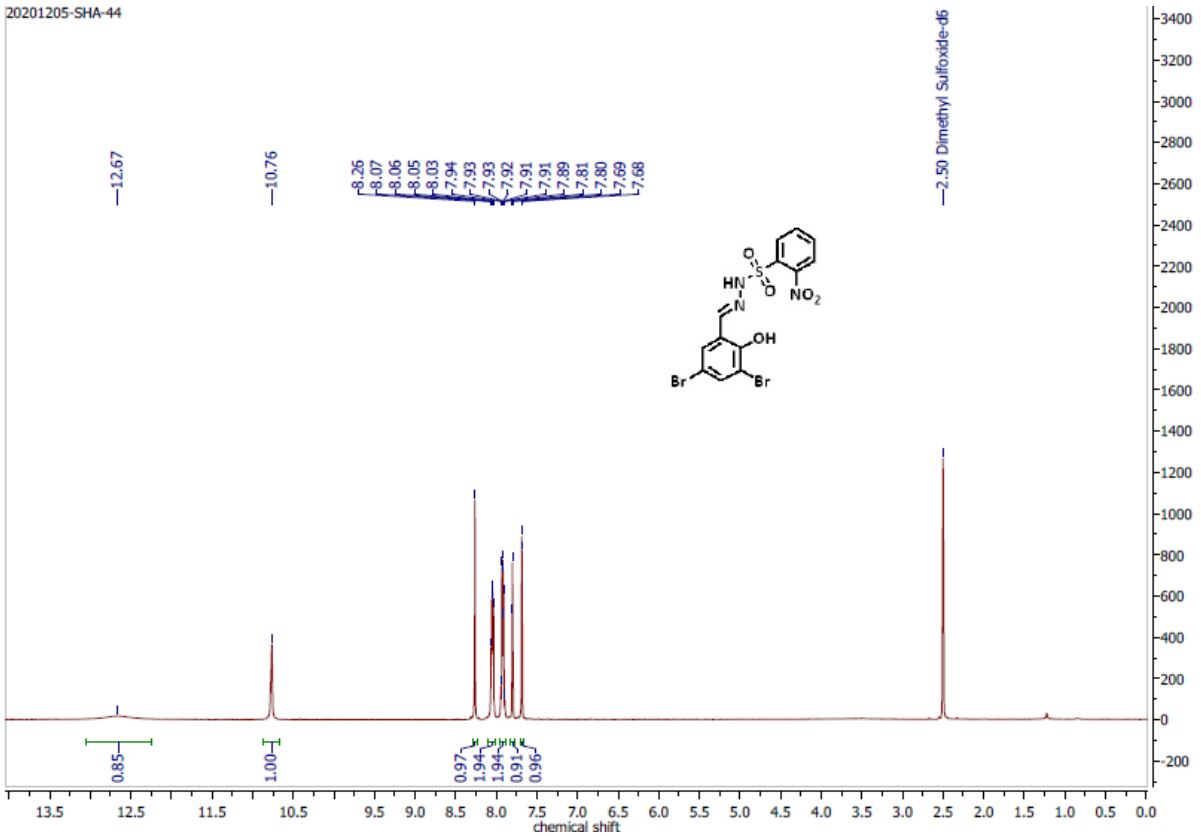


Fig. S150: [1] H NMR spectrum of compound 50 in DMSO-d_6 at 400 MHz.

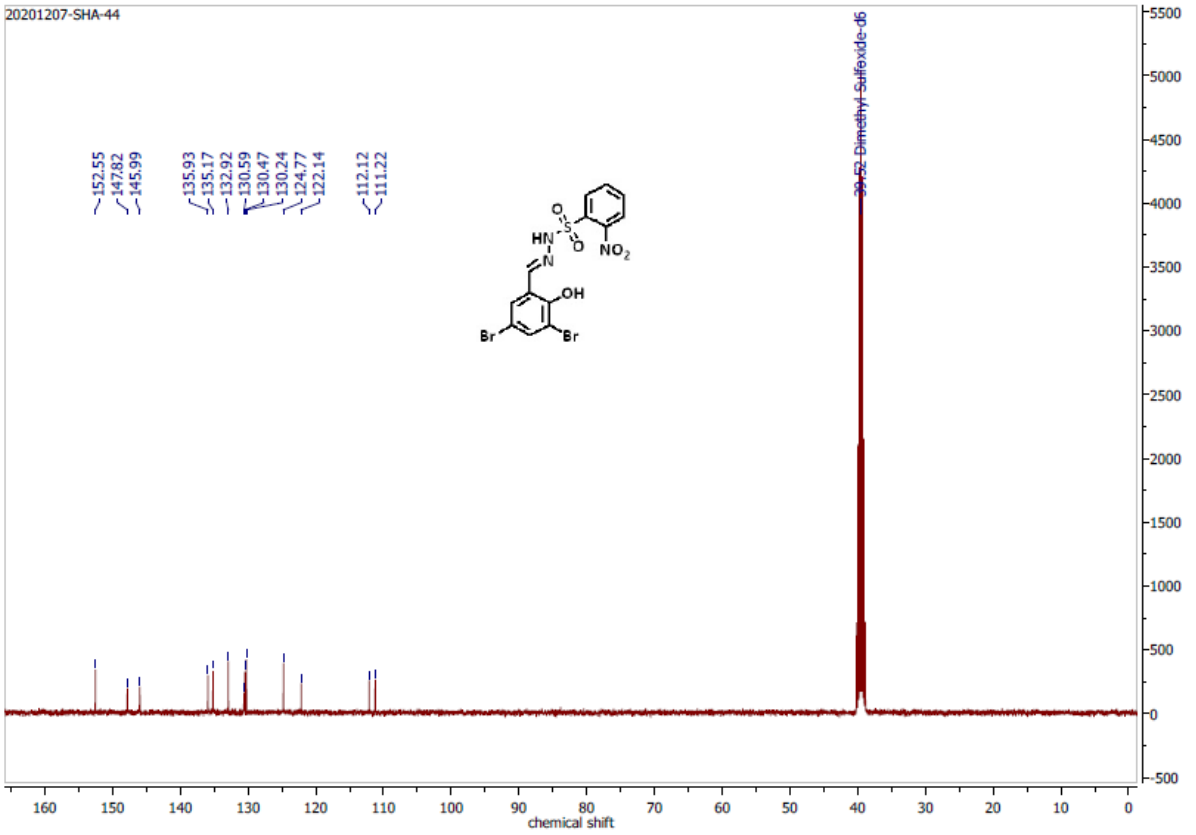


Fig. S151: [13] C NMR spectrum of compound 50 in DMSO-d_6 at 100 MHz.

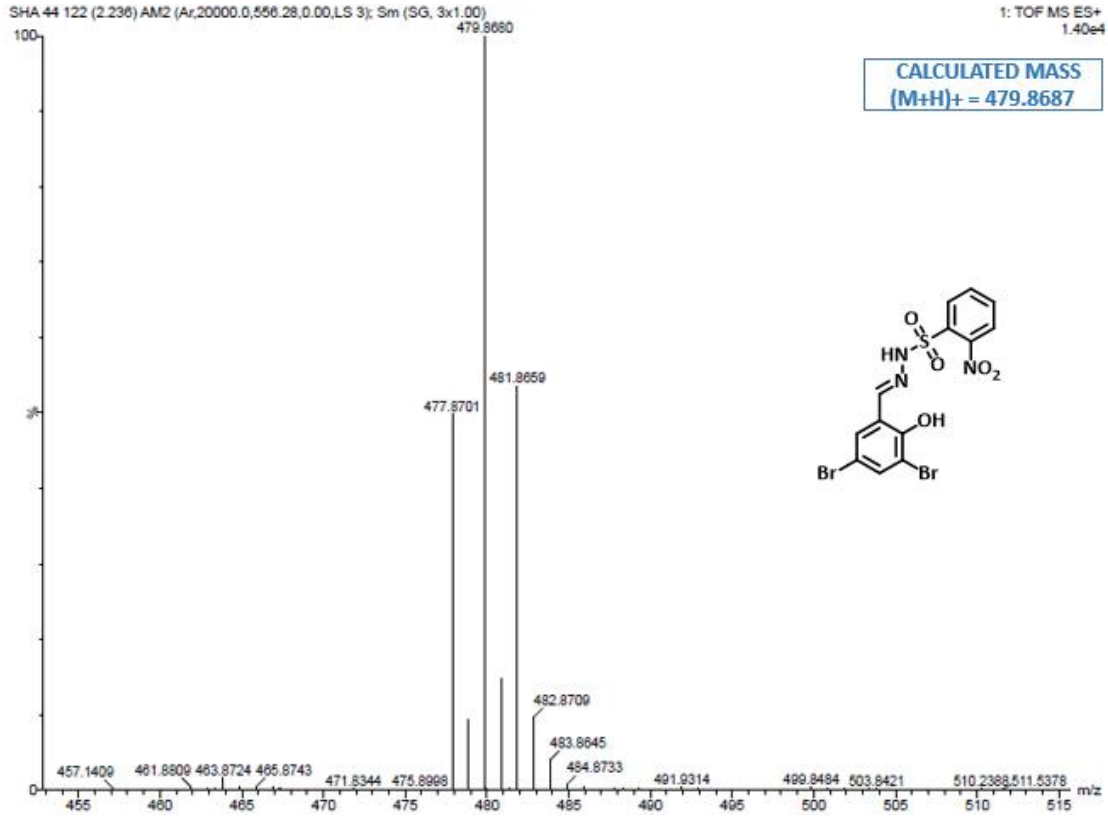


Fig. S152: HRMS spectrum of compound 50.

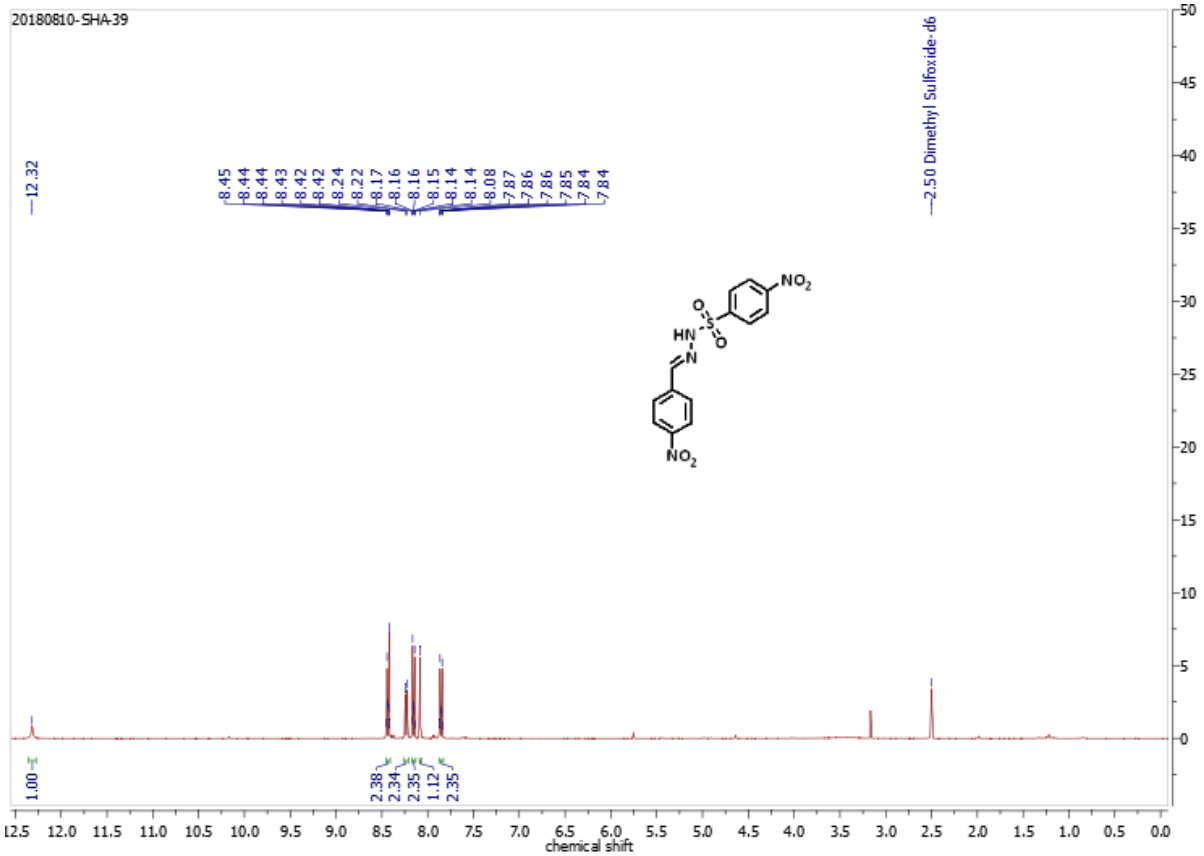


Fig. S153: [1] H NMR spectrum of compound 51 in DMSO-d_6 at 400 MHz.

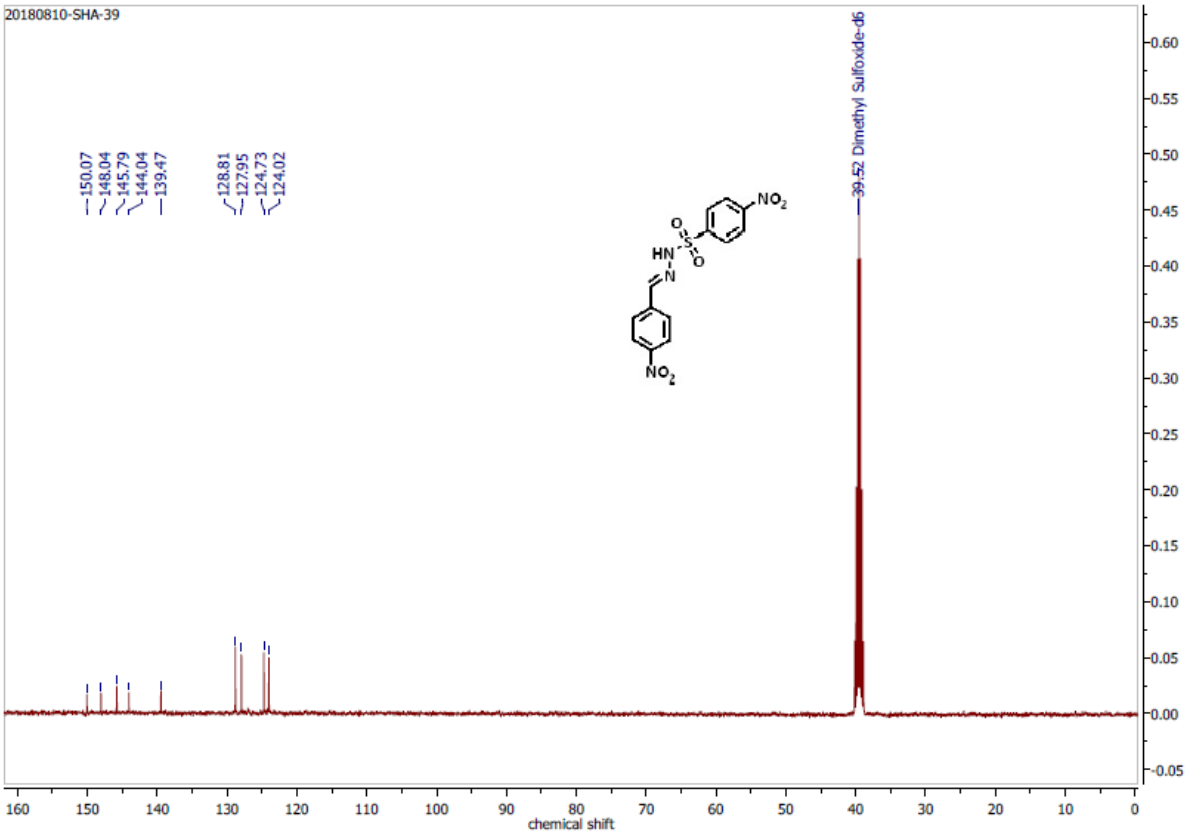


Fig. S154: ^{13}C NMR spectrum of compound 51 in DMSO-d_6 at 100 MHz.

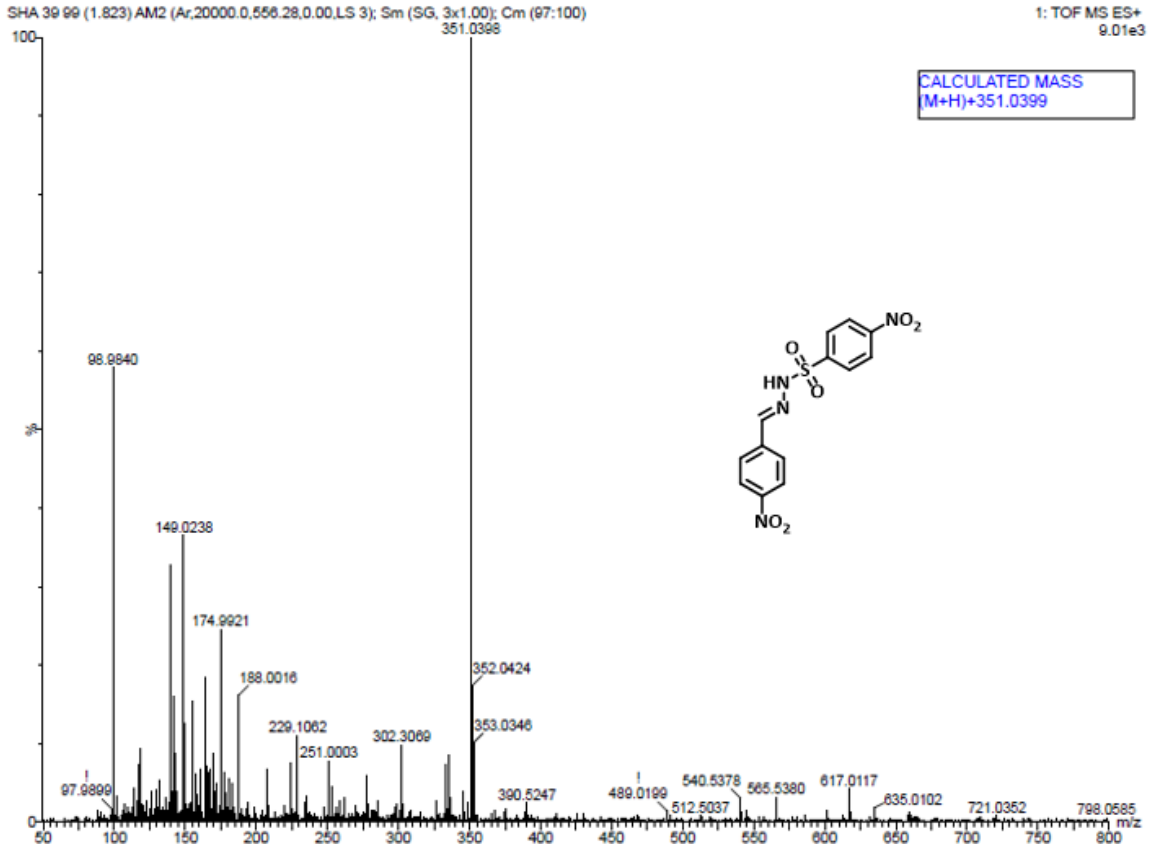


Fig. S155: HRMS spectrum of compound 51.

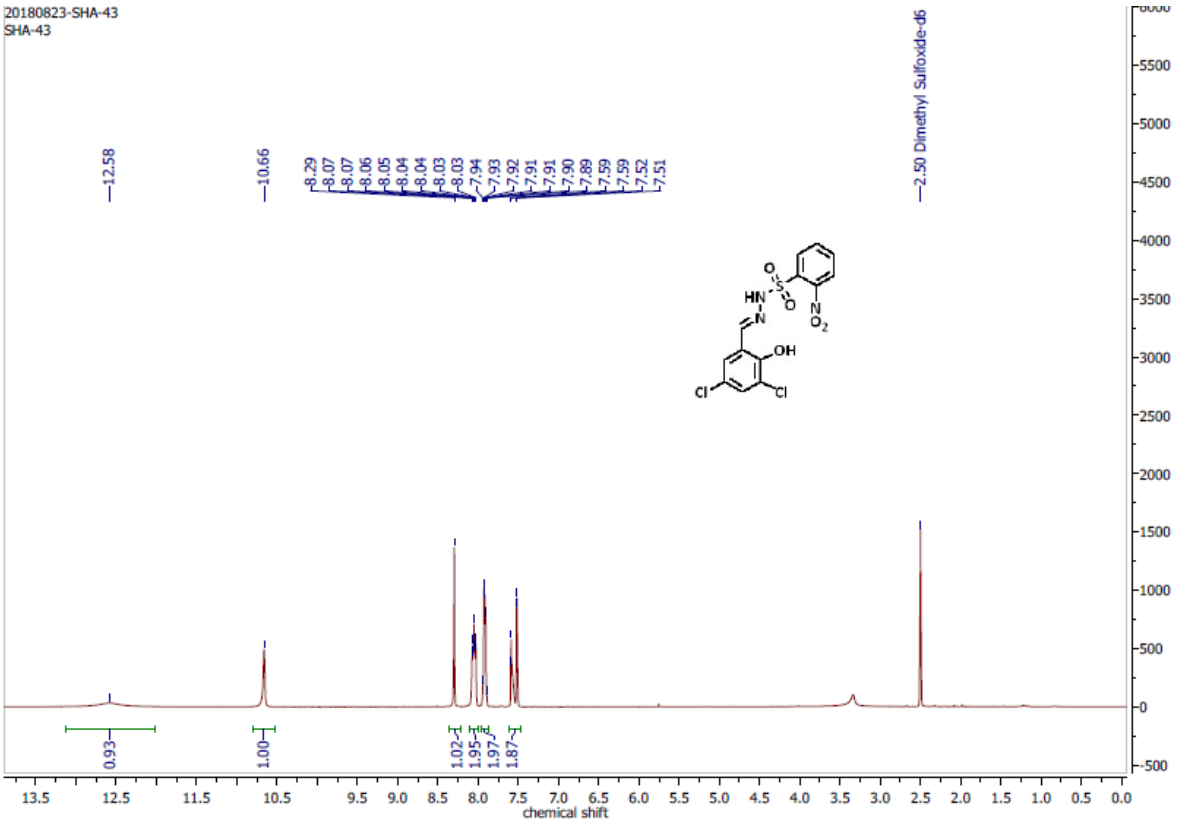


Fig. S156: [1] H NMR spectrum of compound 52 in DMSO-d_6 at 400 MHz.

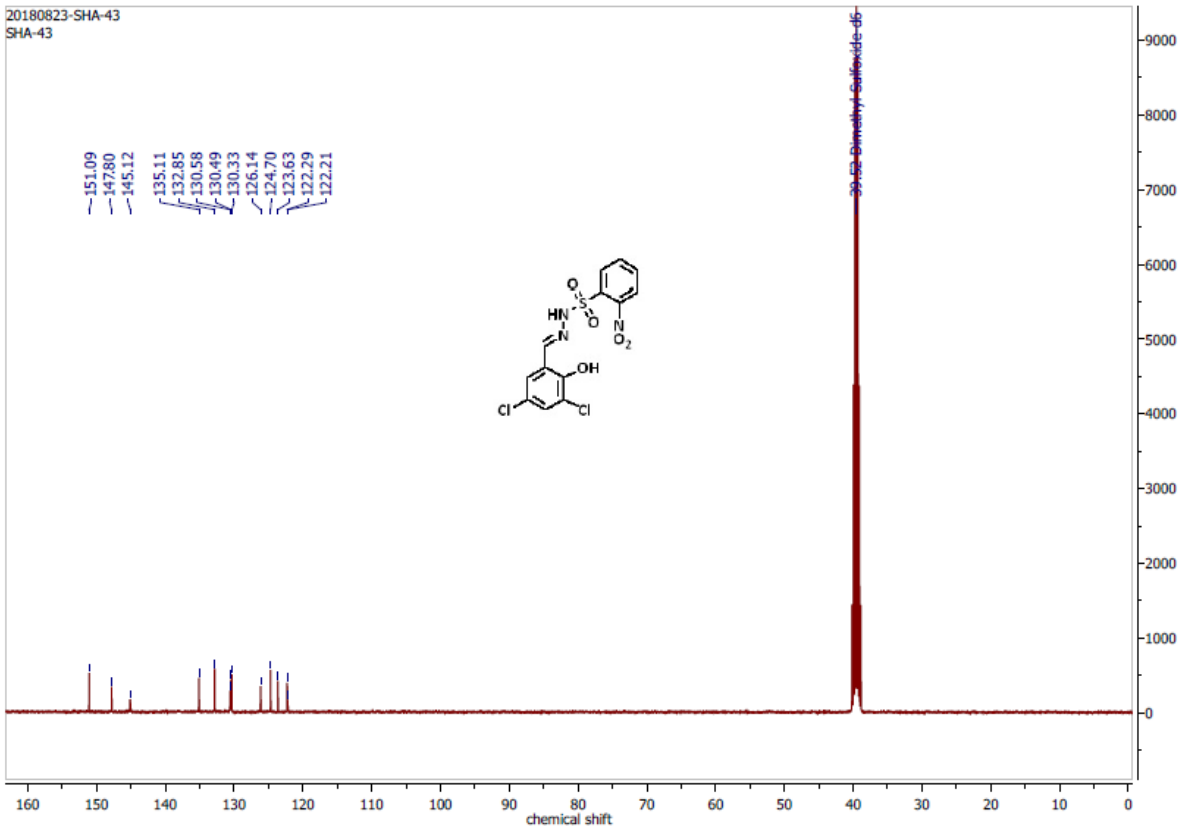


Fig. S157: [13] C NMR spectrum of compound 52 in DMSO-d_6 at 100 MHz.

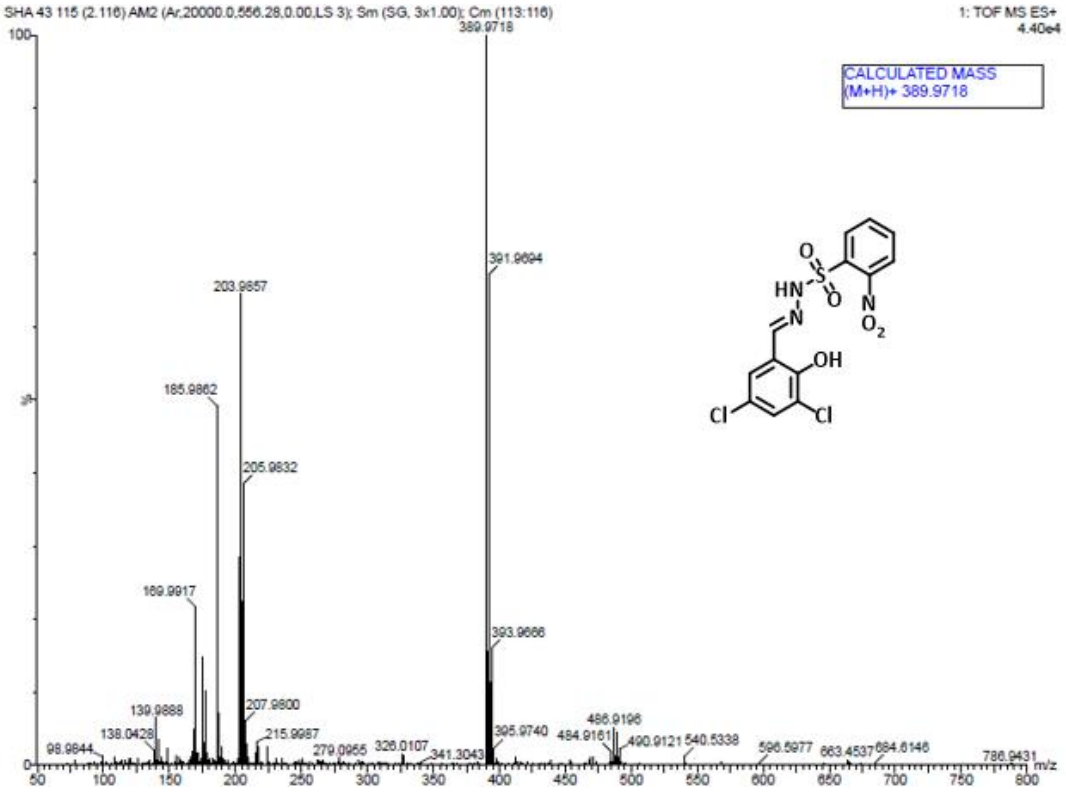


Fig. S158: HRMS spectrum of compound 52.

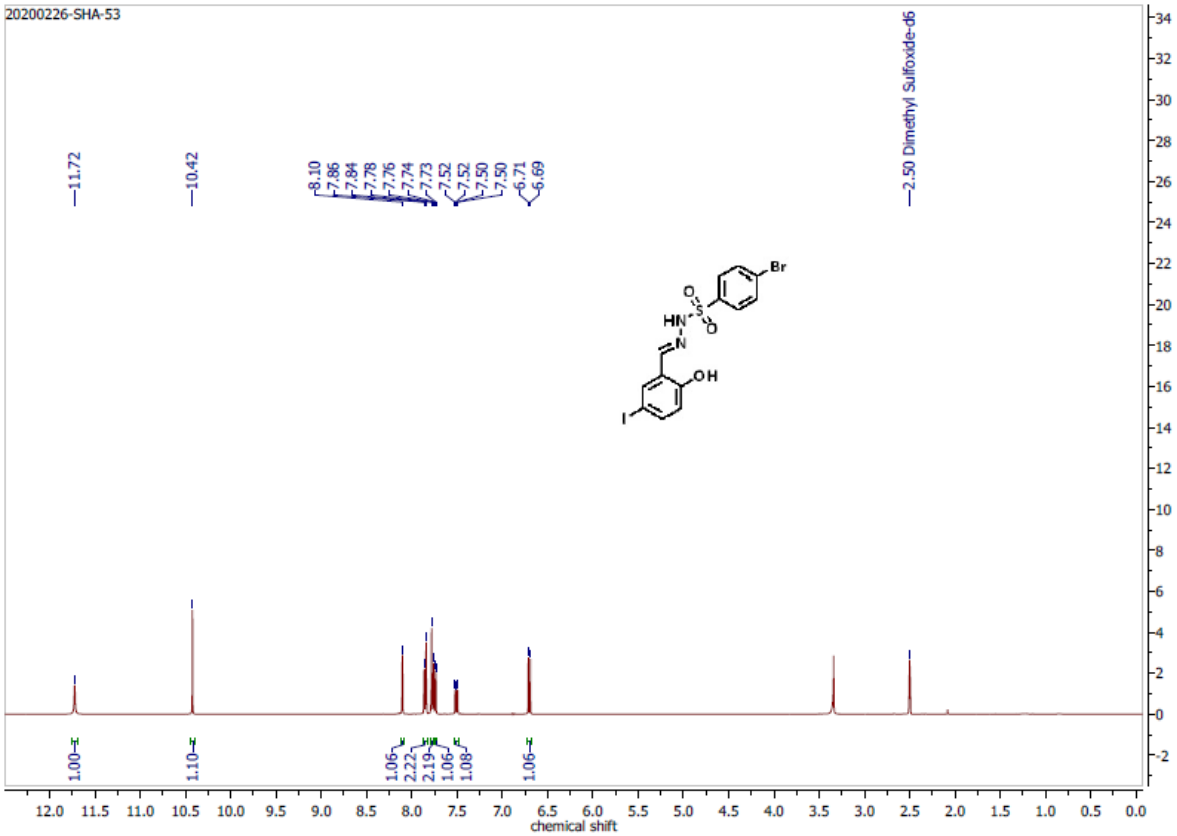


Fig. S159: [1] H NMR spectrum of compound 53 in DMSO-d_6 at 400 MHz.

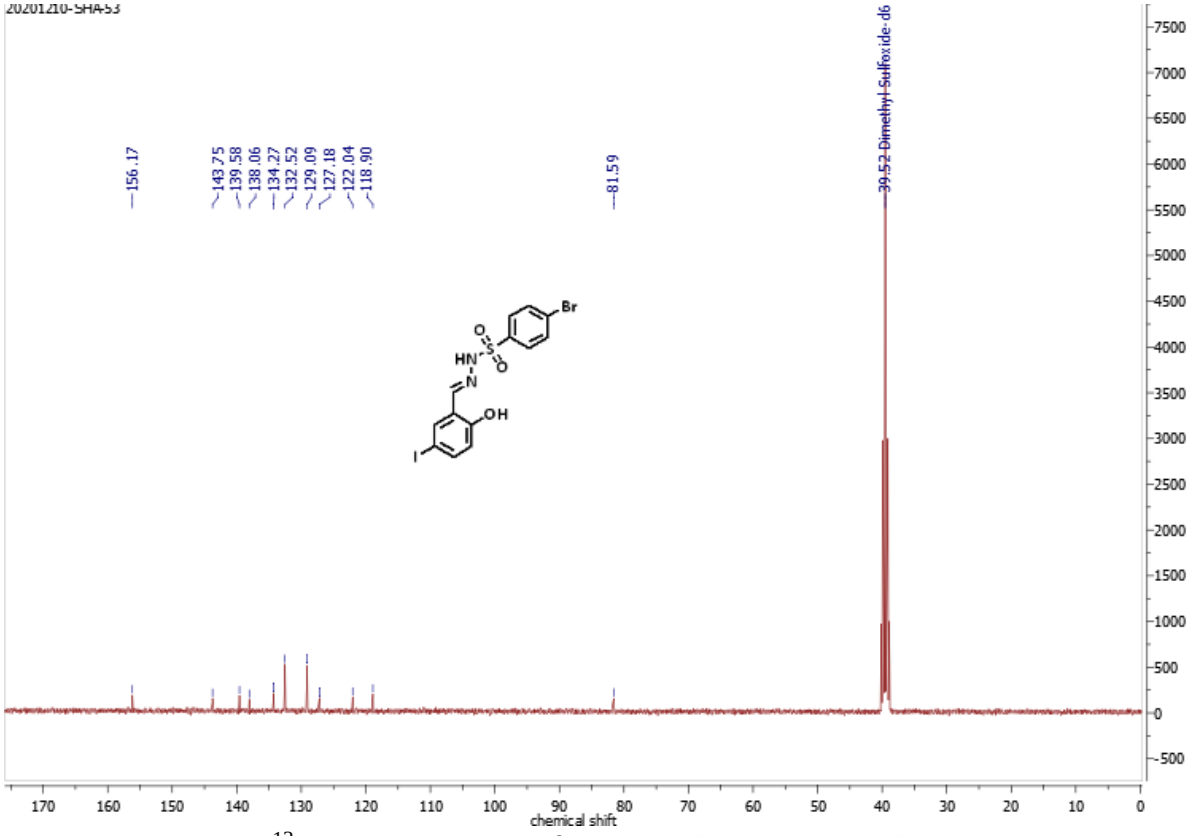


Fig. S160: ^{13}C NMR spectrum of compound 53 in DMSO-d_6 at 100 MHz.

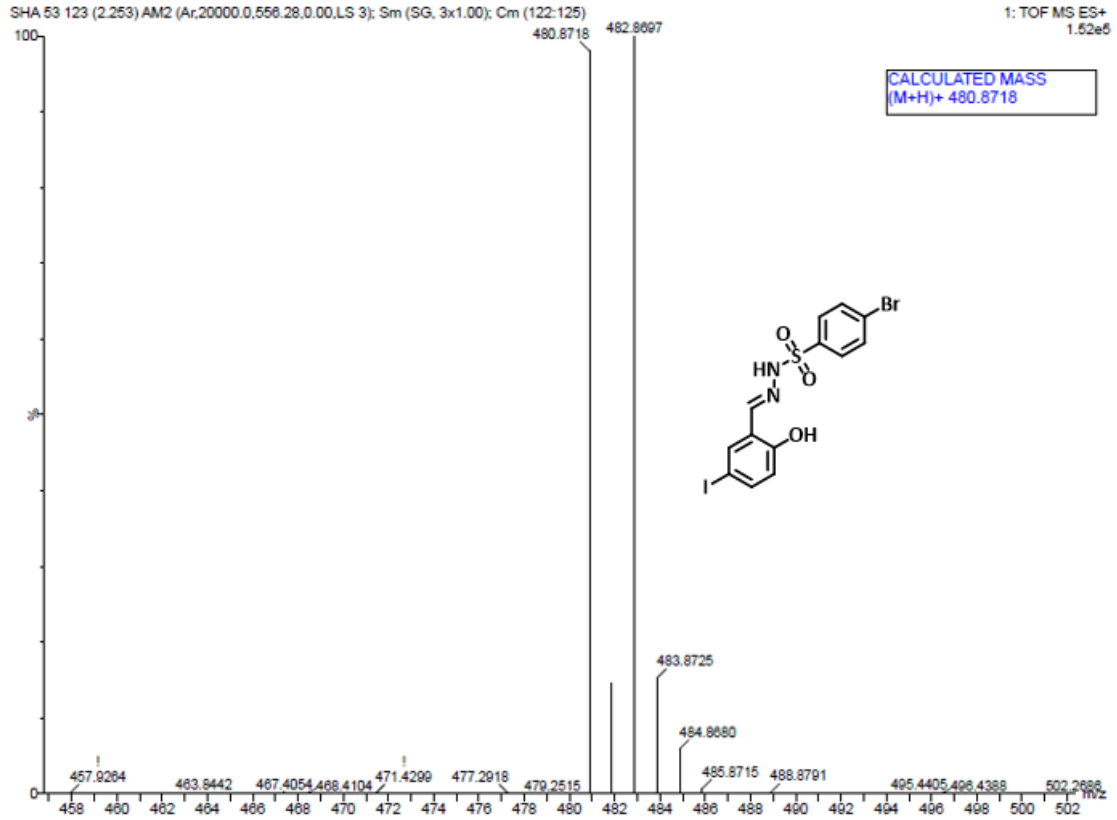


Fig. S161: HRMS spectrum of compound 53.

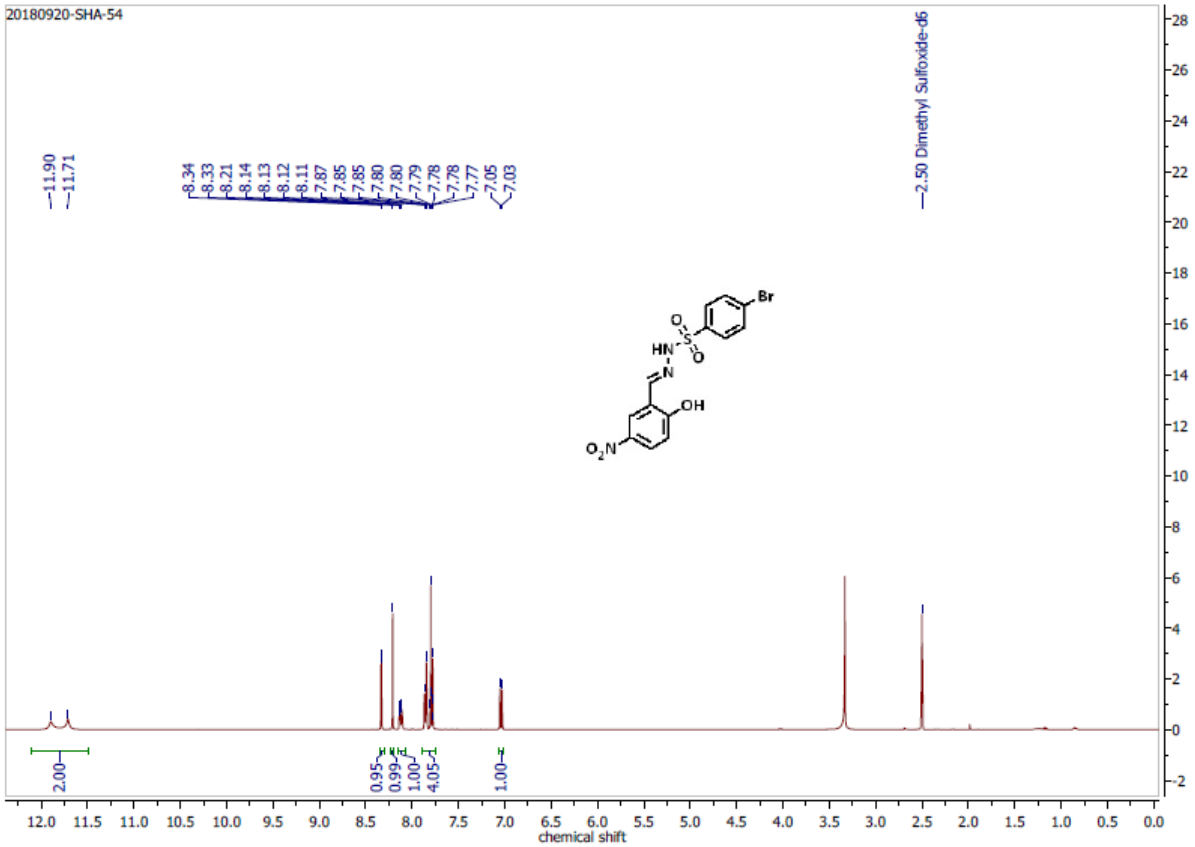


Fig. S162: [1] H NMR spectrum of compound 54 in DMSO-d_6 at 400 MHz.

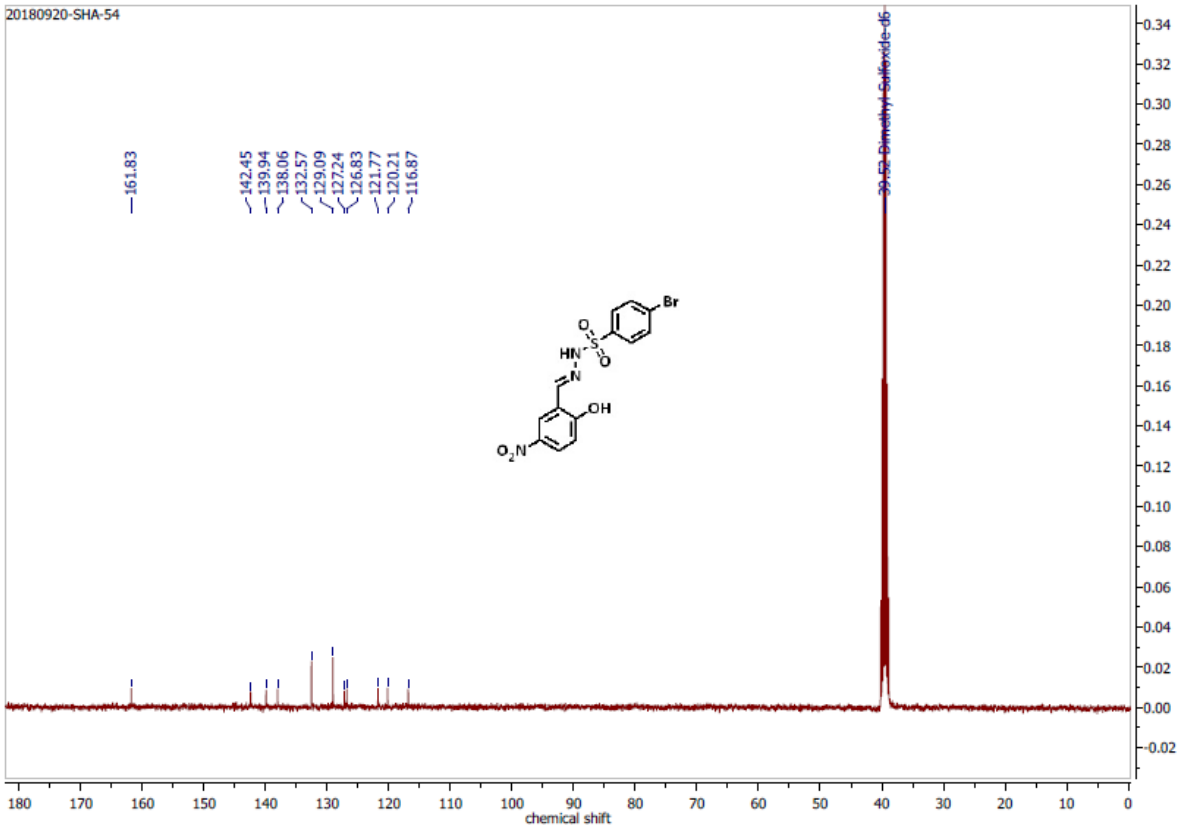


Fig. S163: [13] C NMR spectrum of compound 54 in DMSO-d_6 at 100 MHz.

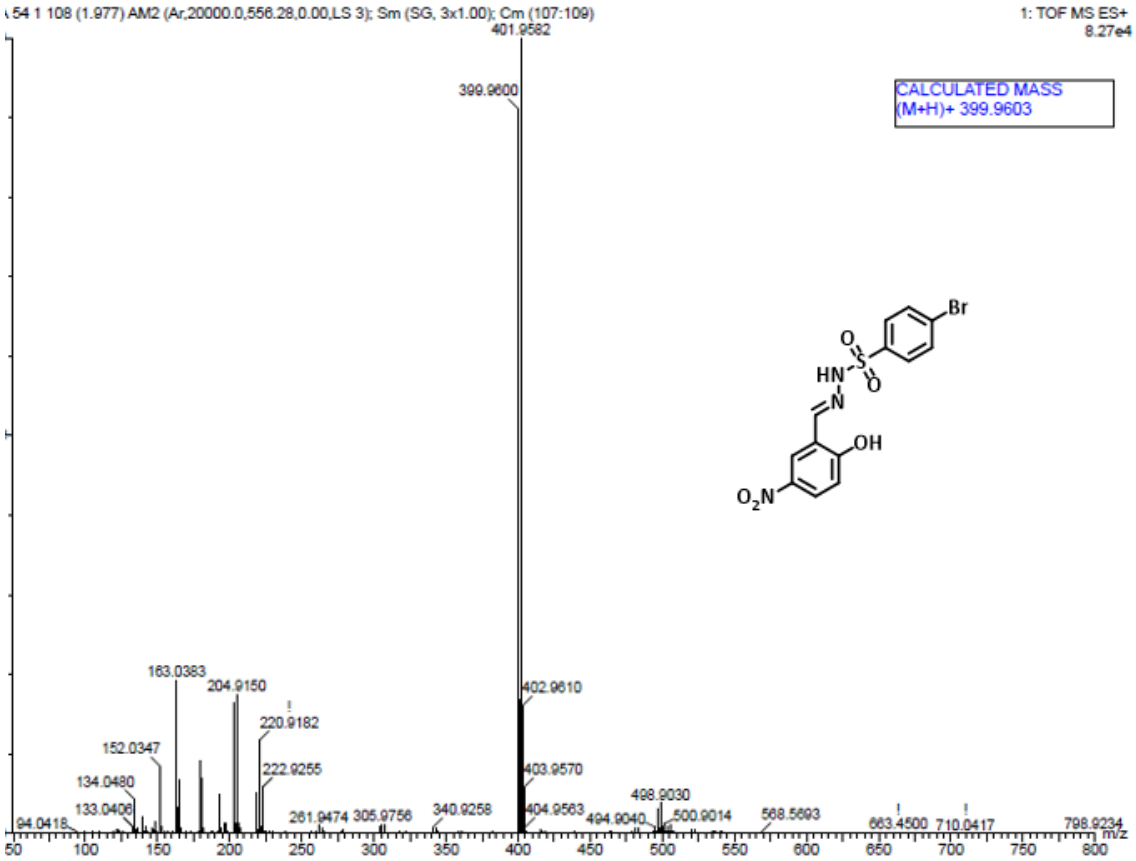


Fig. S164: HRMS spectrum of compound 54.

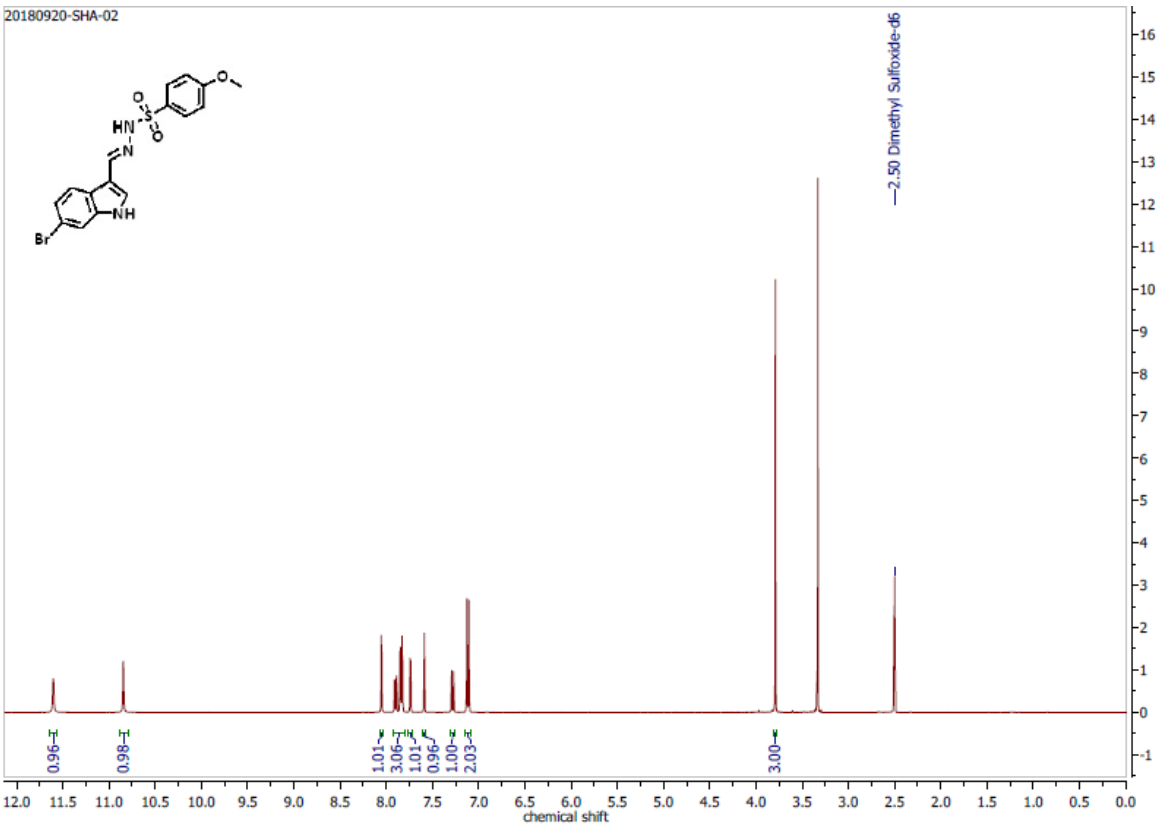


Fig. S165: [1] H NMR spectrum of compound 55 in DMSO at 400 MHz.

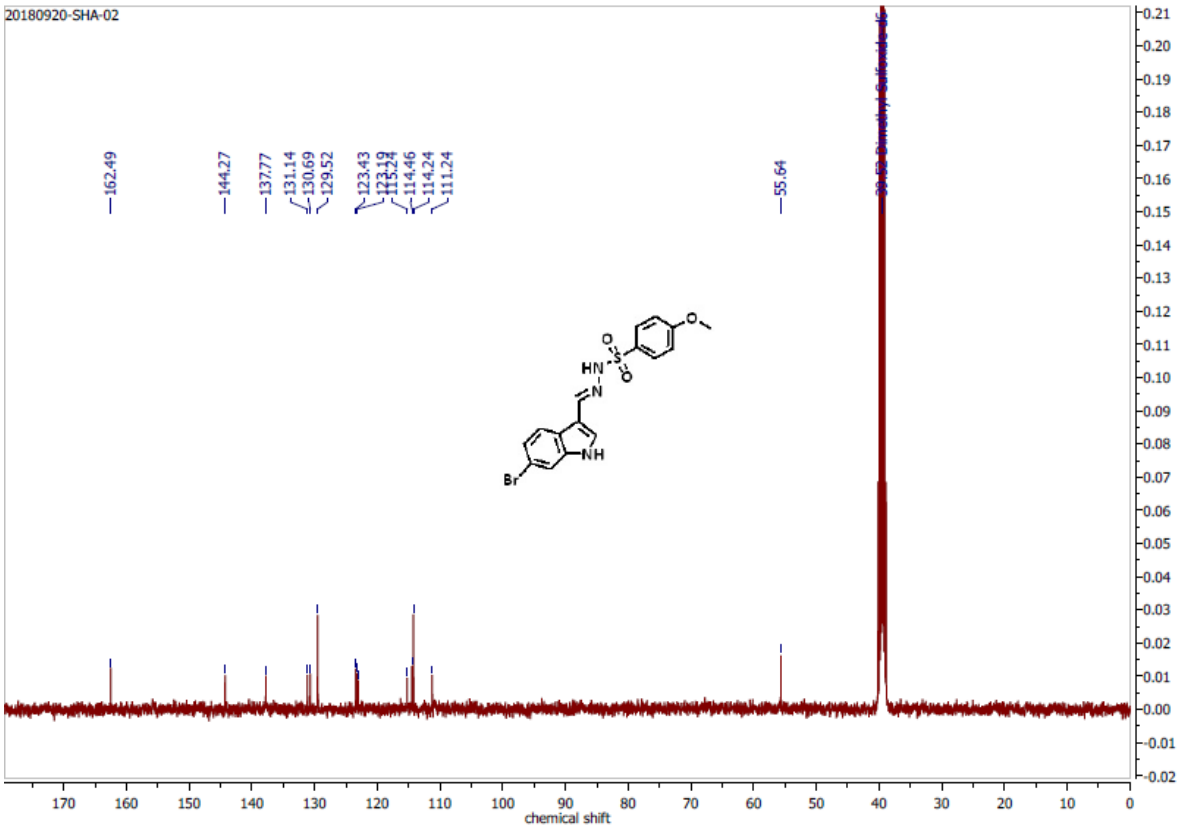


Fig. S166: ^{13}C NMR spectrum of compound 55 in DMSO-d_6 at 100 MHz.

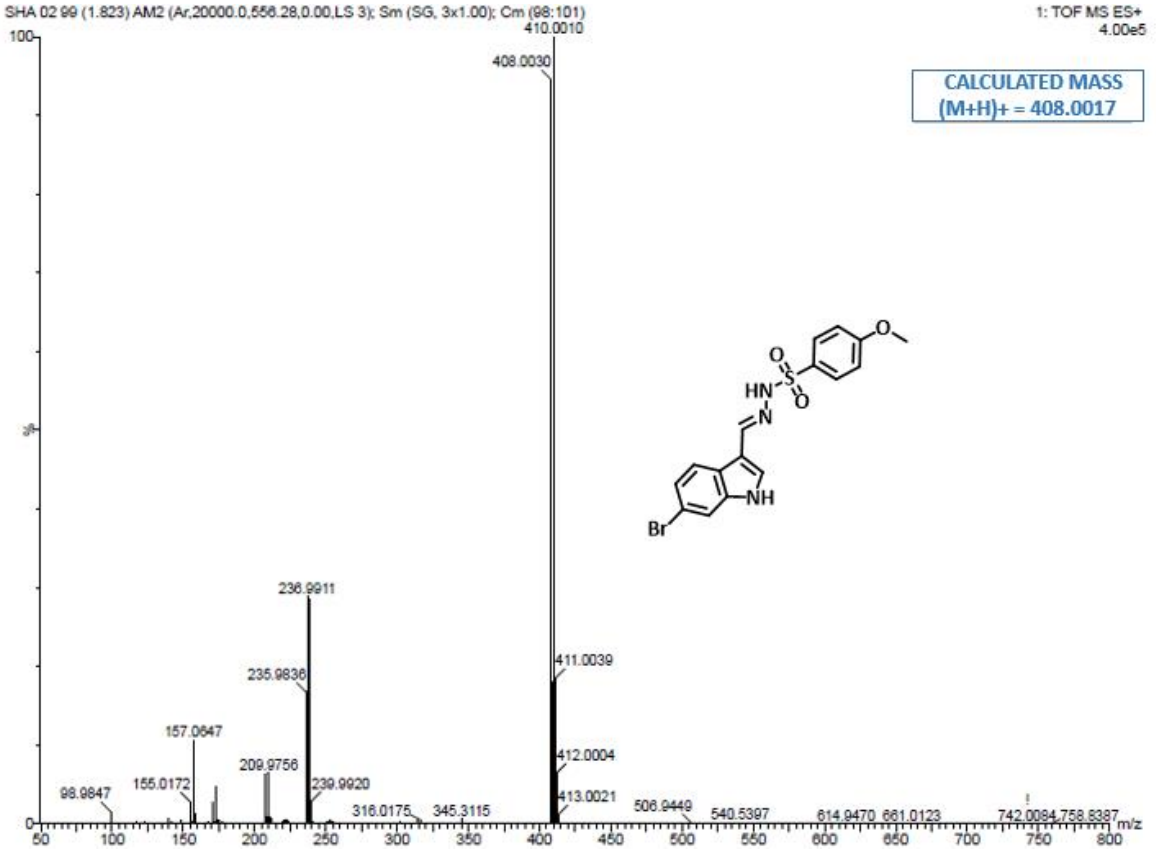


Fig. S167: HRMS spectrum of compound 55.

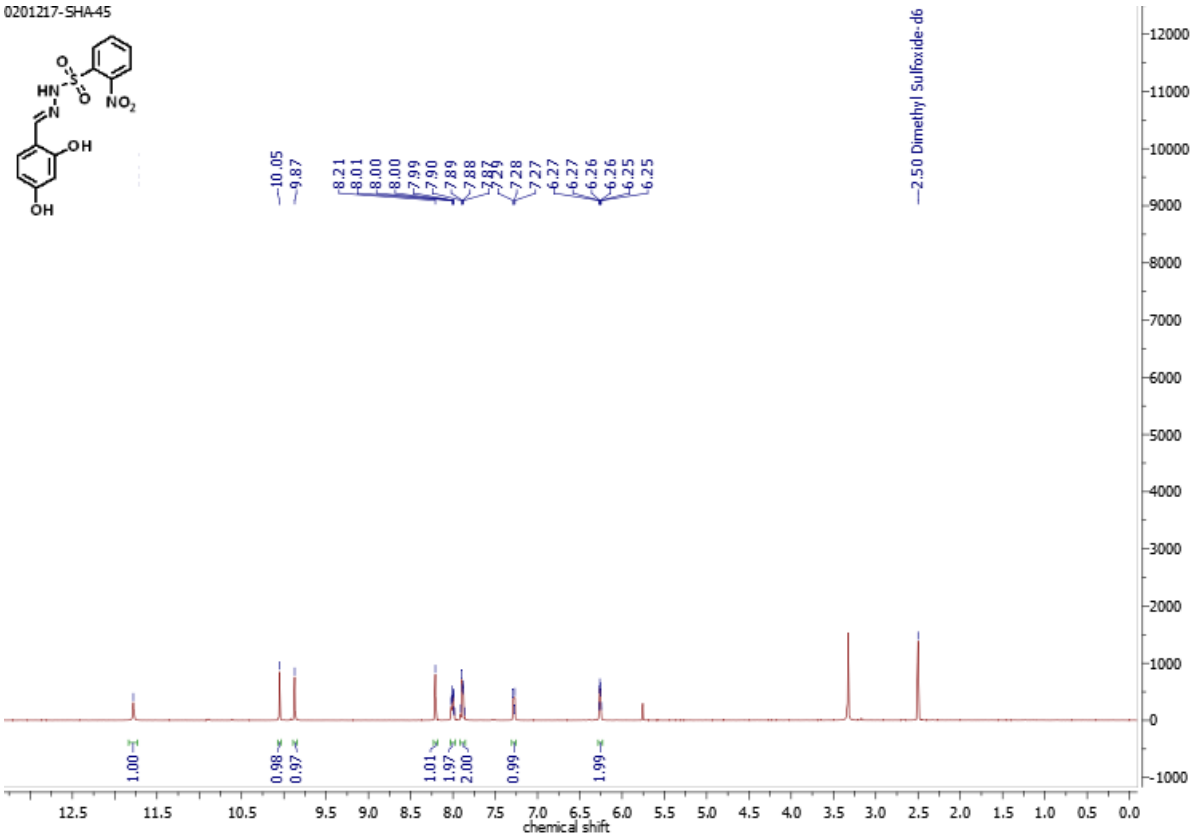


Fig. S168: [1] H NMR spectrum of compound 56 in DMSO-d_6 at 400 MHz.

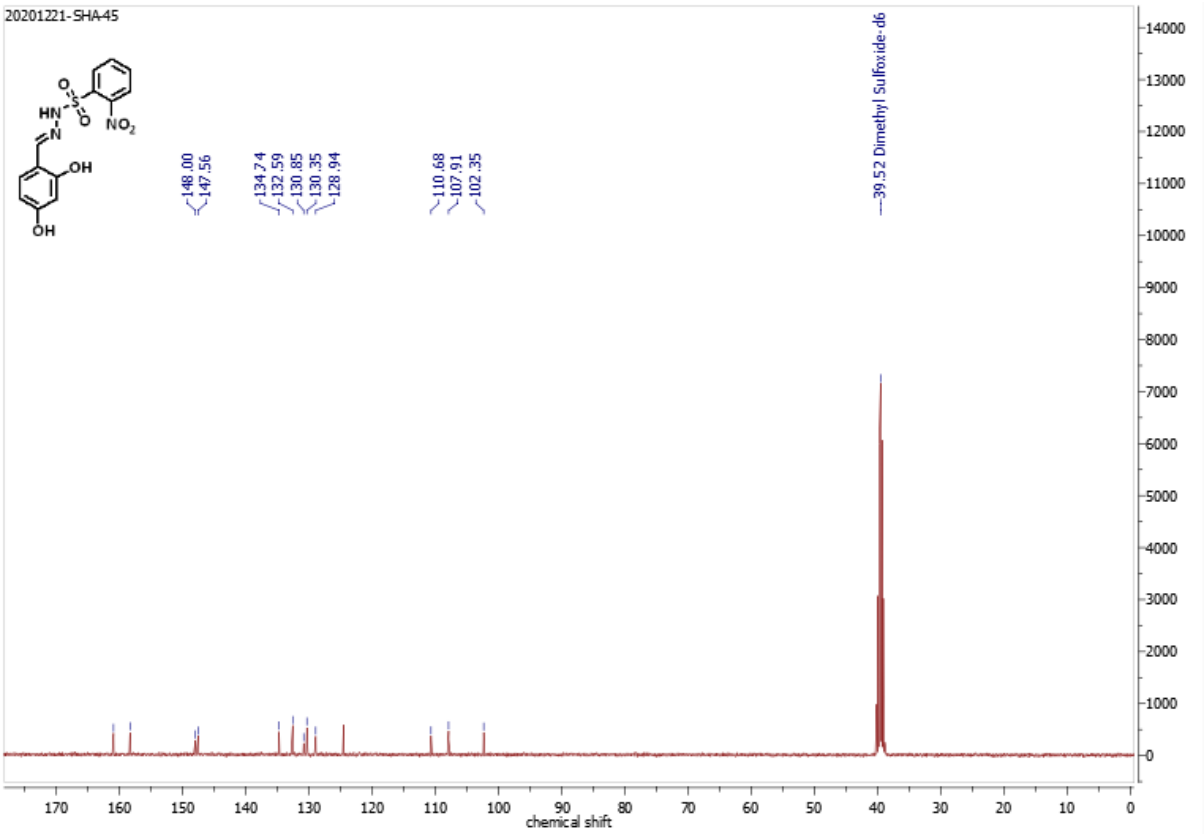


Fig. S169: [13] C NMR spectrum of compound 56 in DMSO-d_6 at 100 MHz.

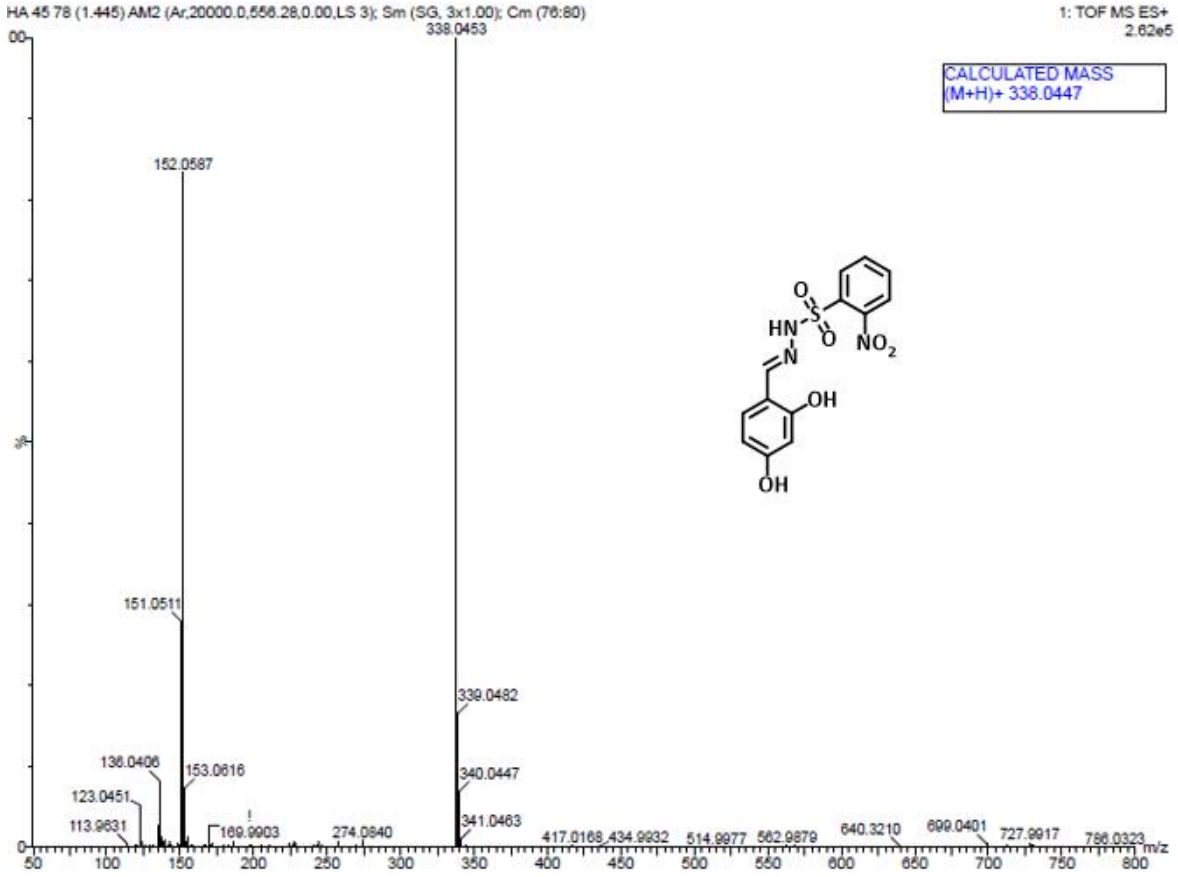


Fig. S170: HRMS spectrum of compound 56.

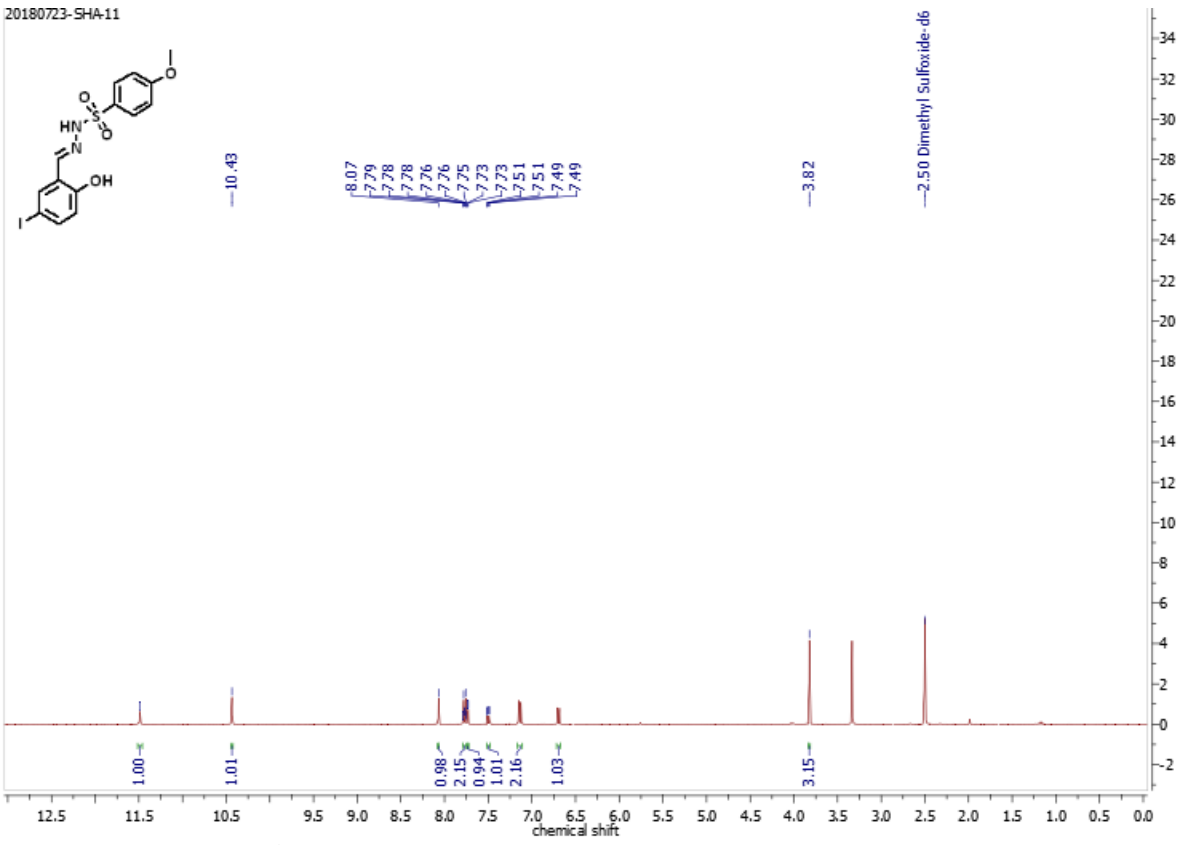


Fig. S171: [1] H NMR spectrum of compound 57 in DMSO-d_6 at 400 MHz.

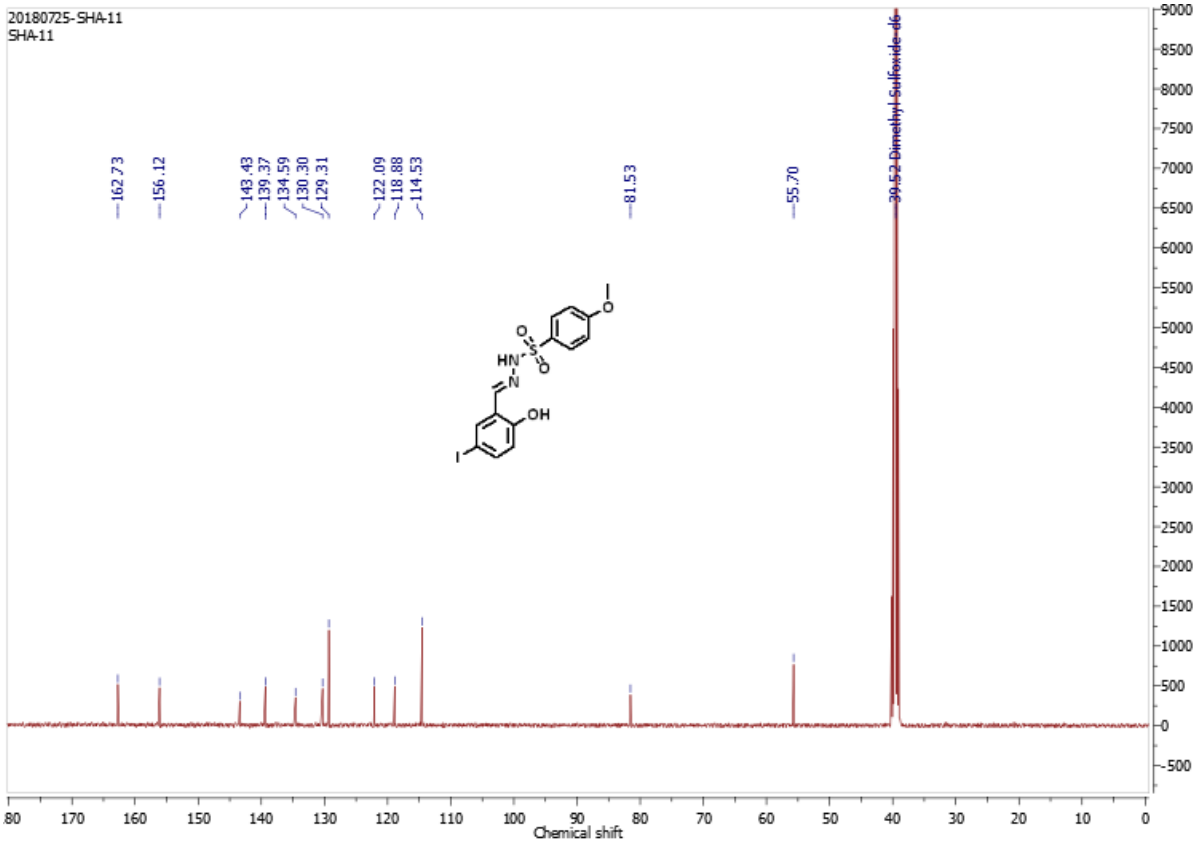


Fig. S172: ^{13}C NMR spectrum of compound 57 in DMSO-d_6 at 100 MHz.

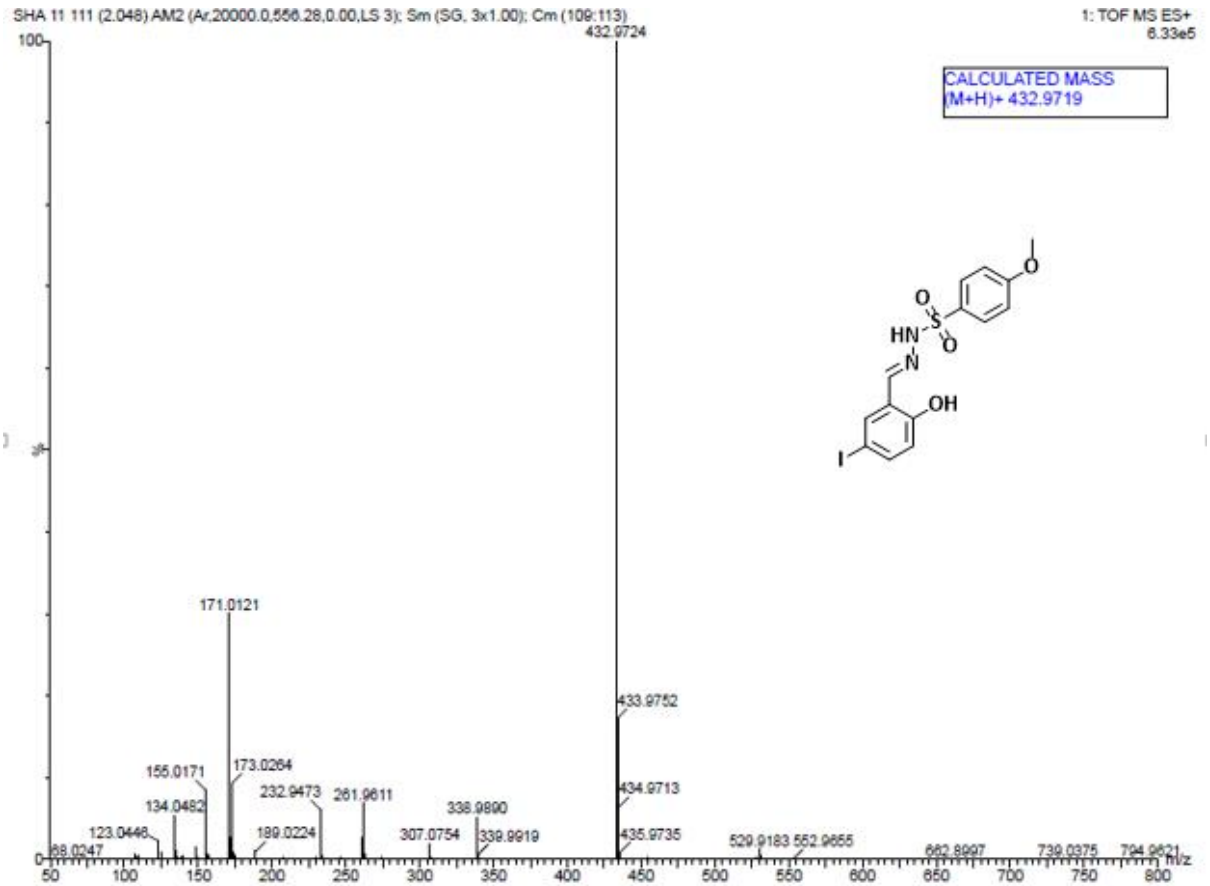


Fig. S173: HRMS spectrum of compound 57.

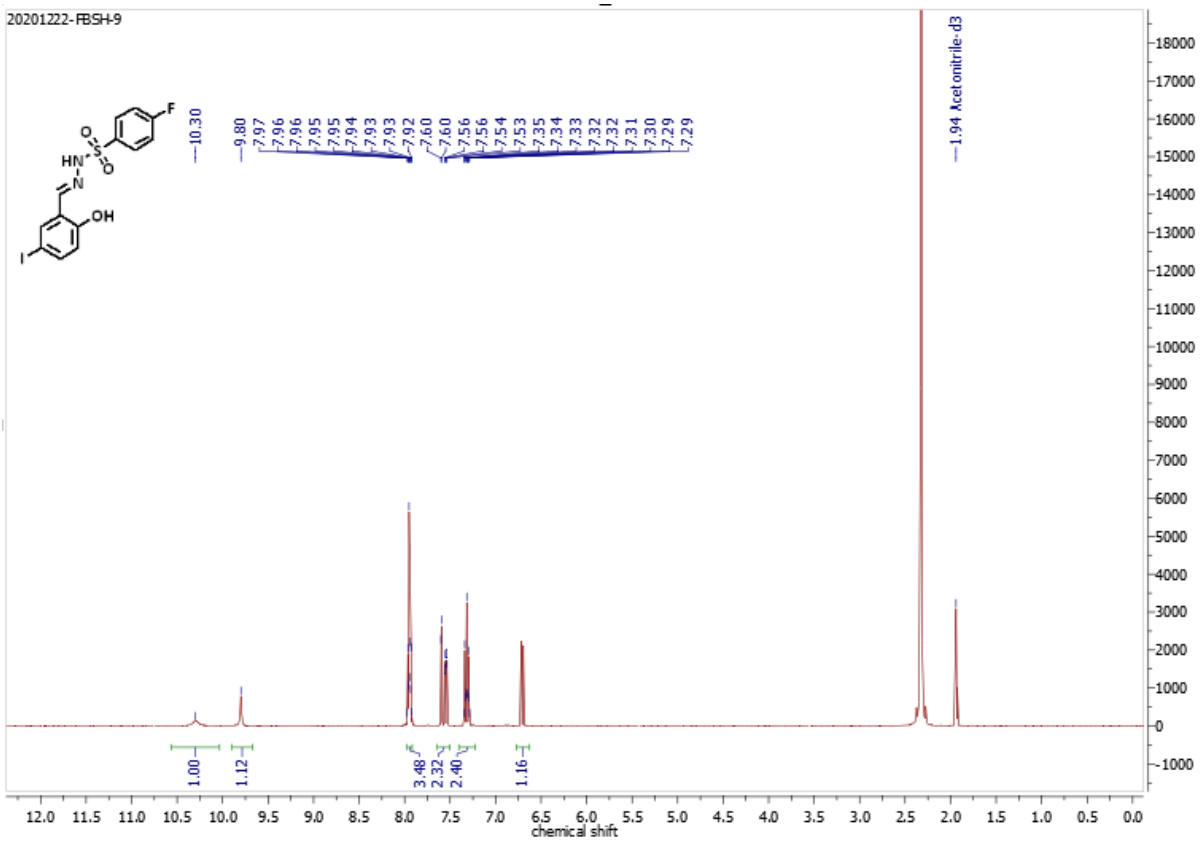


Fig. S174: [1] H NMR spectrum of compound 58 in CD_3CN-d_3 at 400 MHz.

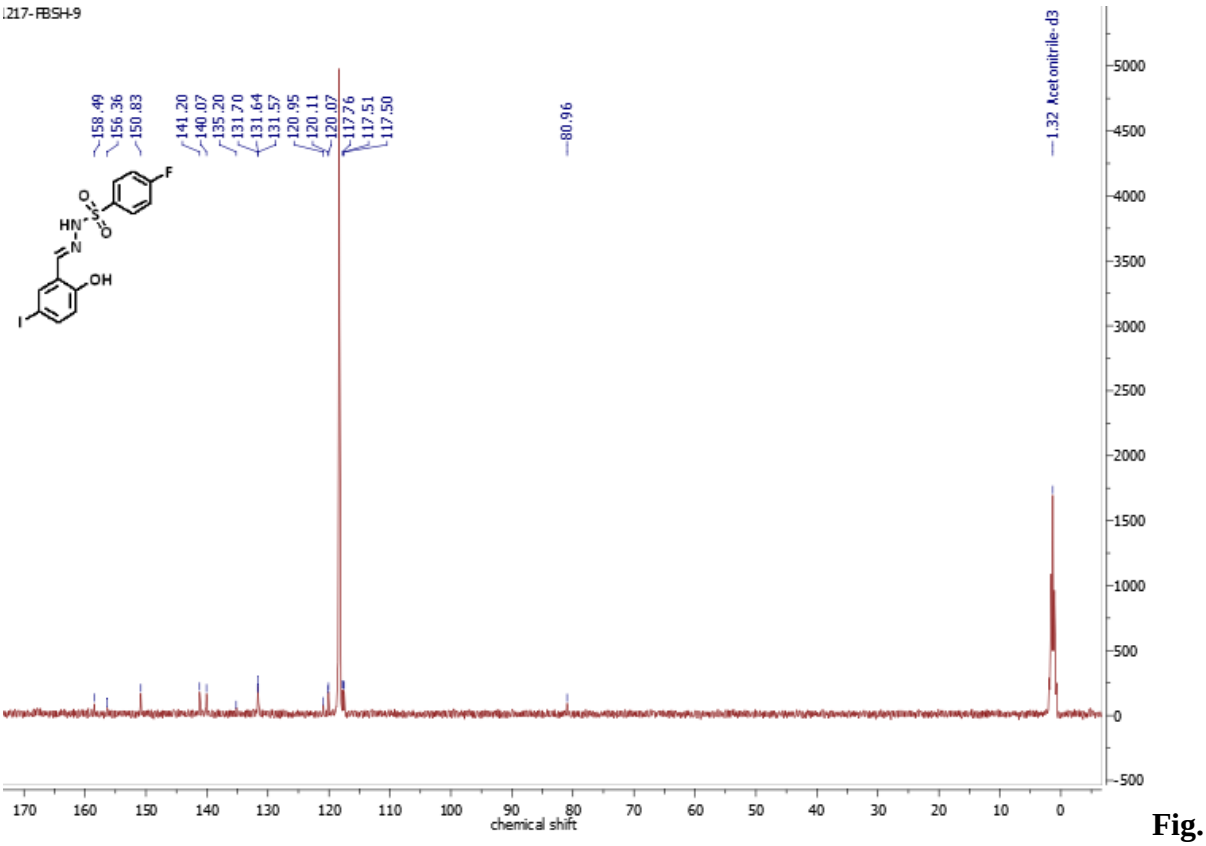


Fig. S175: [13] C NMR spectrum of compound 58 in CD_3CN-d_3 at 100 MHz.

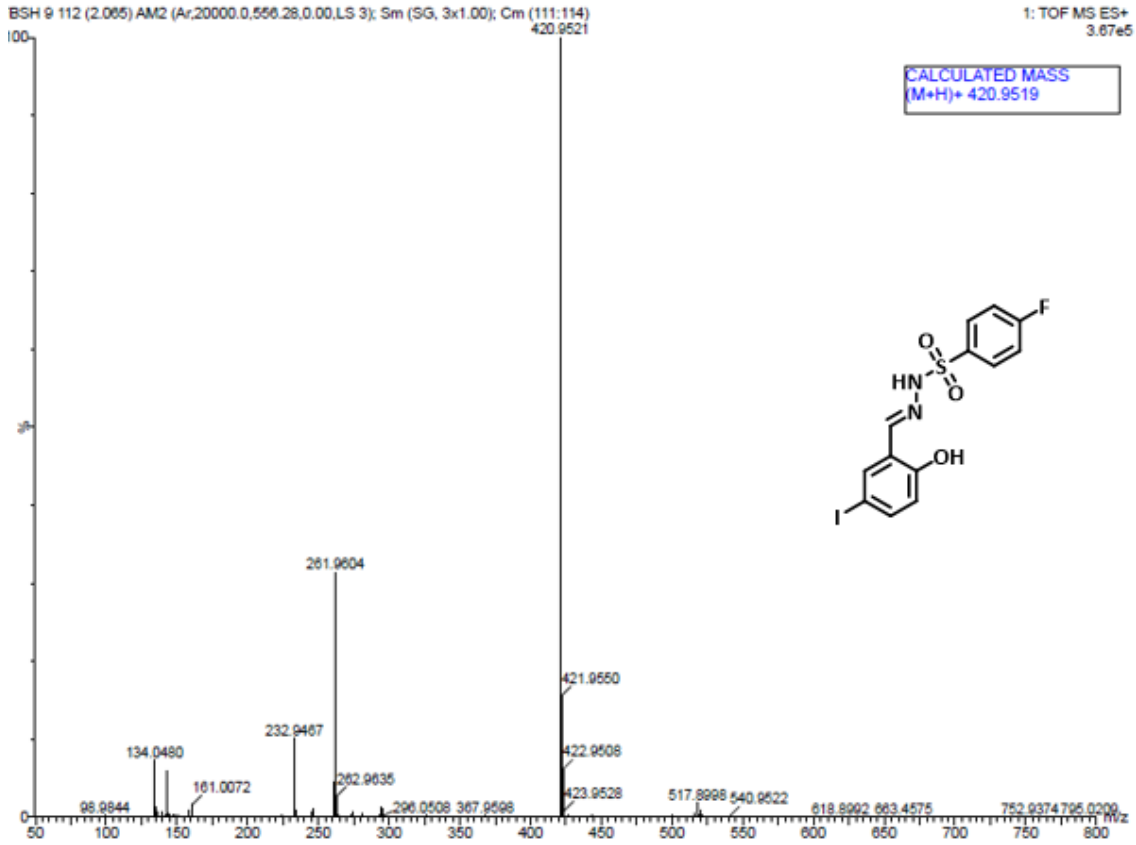


Fig. S176: HRMS spectrum of compound 58.

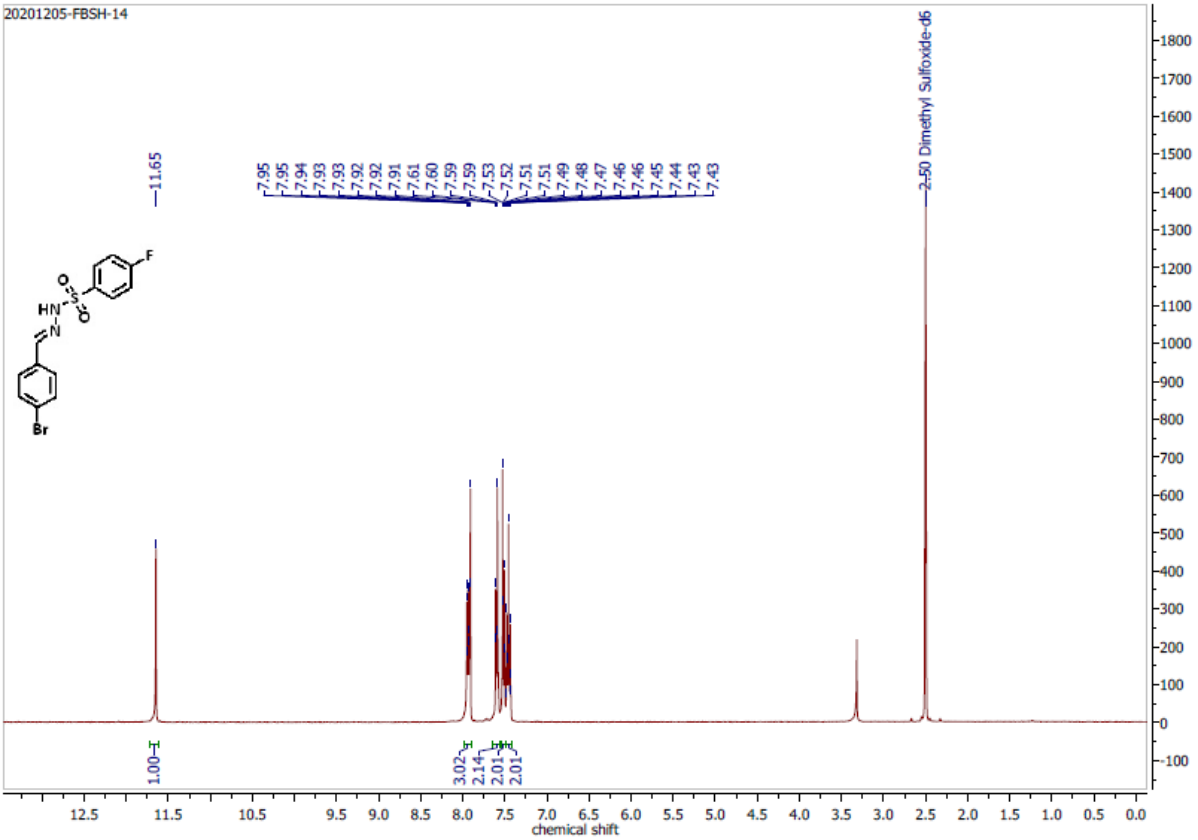


Fig. S177: [1] H NMR spectrum of compound 59 in DMSO-d_6 at 400 MHz.

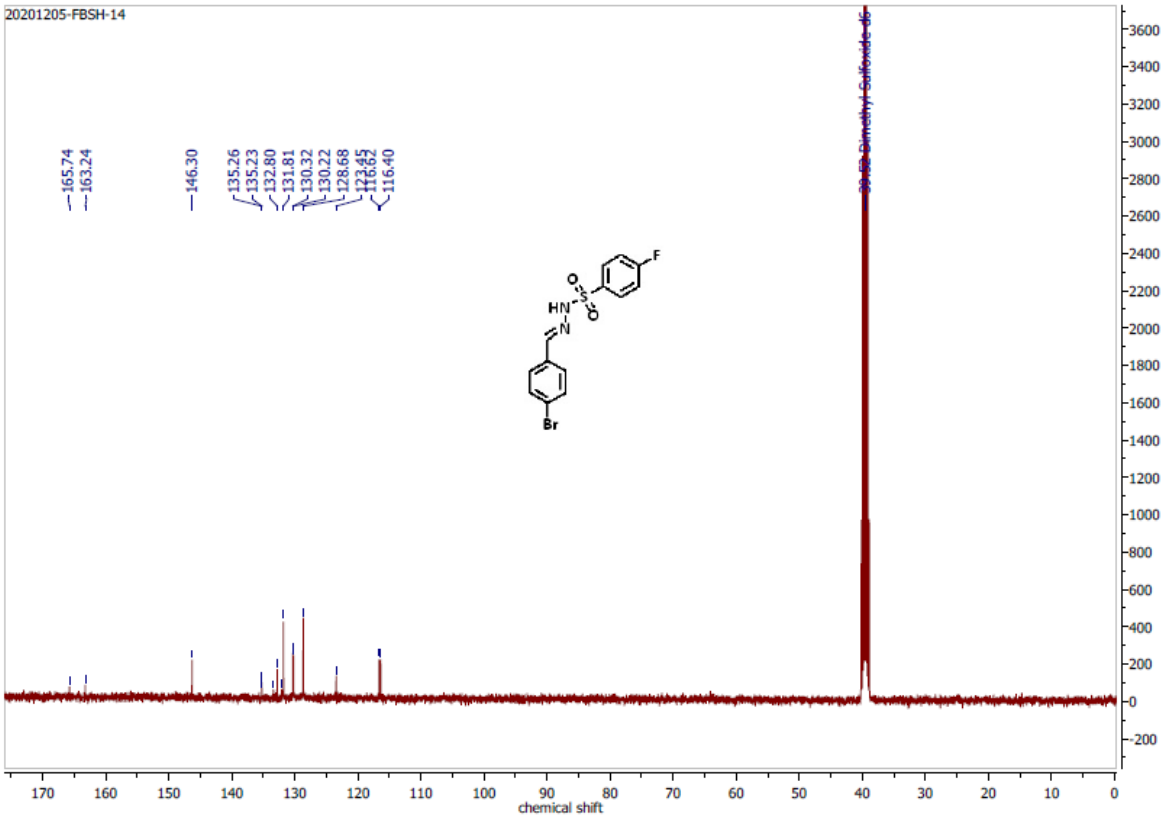


Fig. S178: ^{13}C NMR spectrum of compound 59 in DMSO-d_6 at 100 MHz.

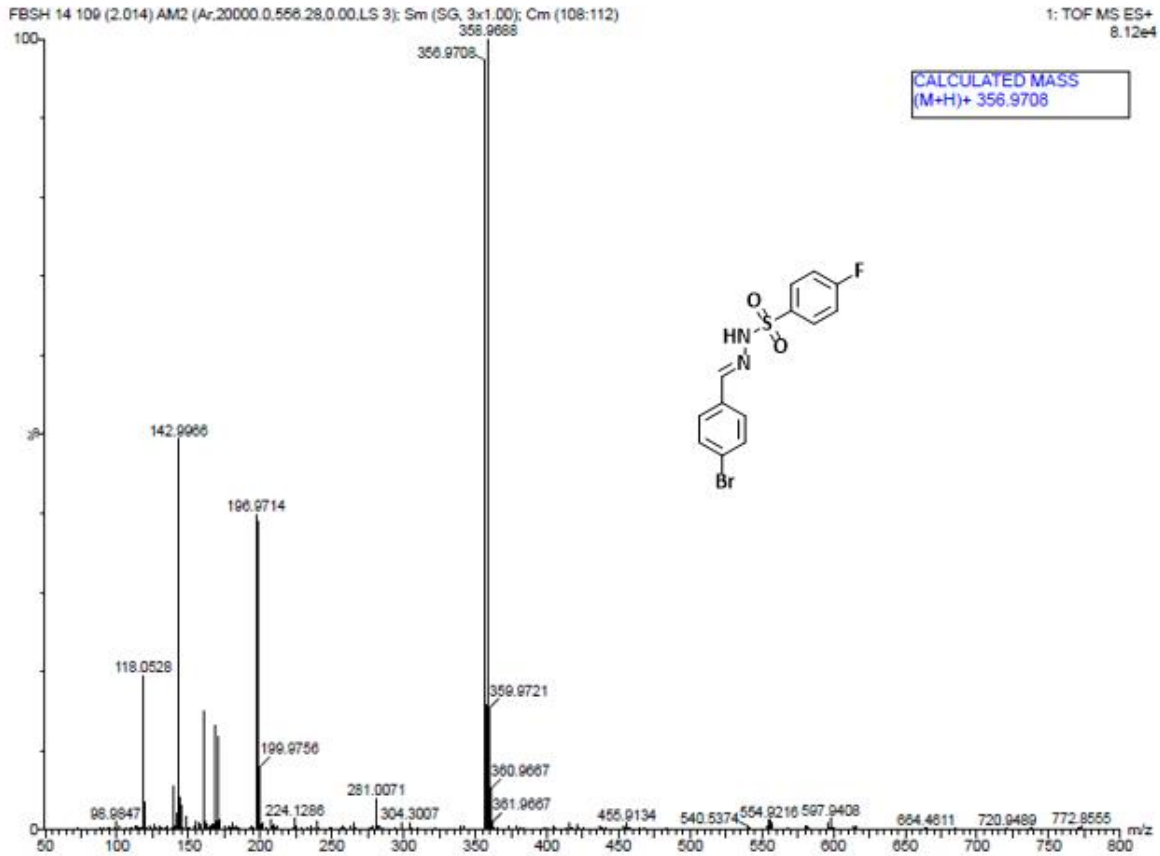


Fig. S179: HRMS spectrum of compound 59

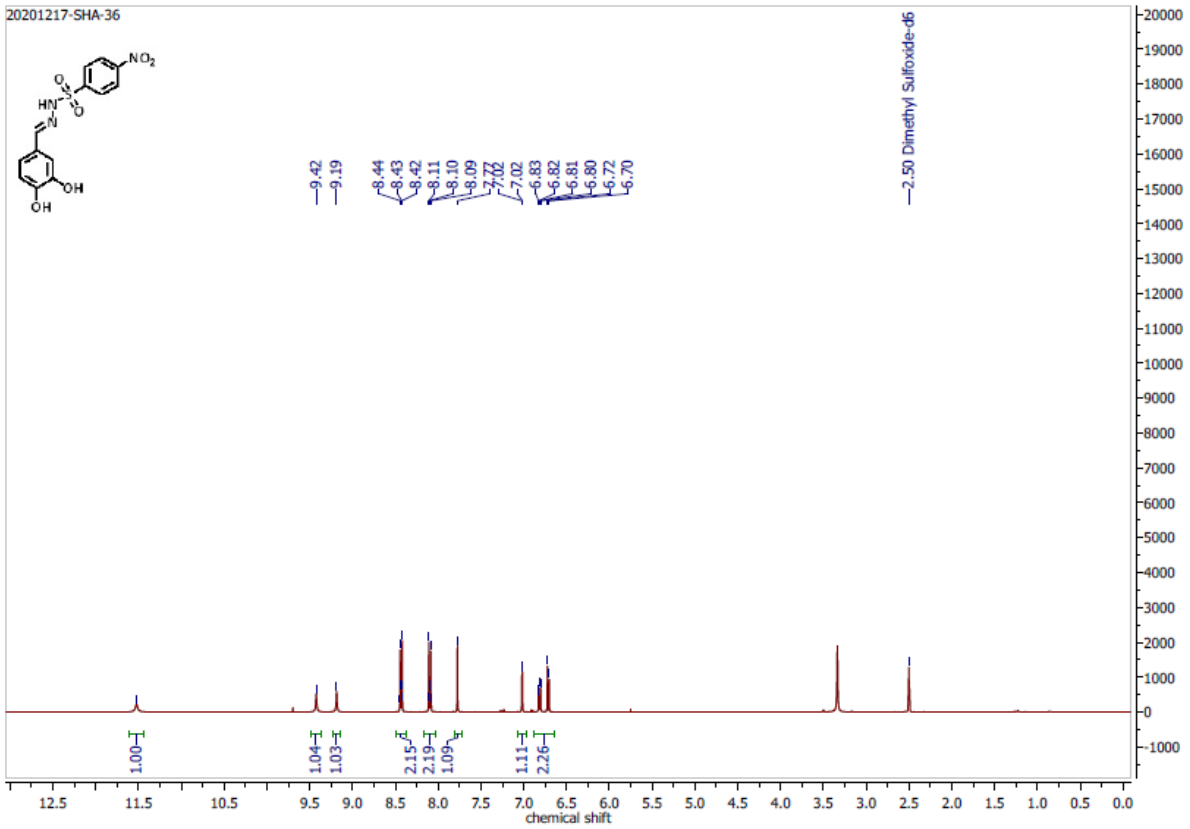


Fig. S180: [1] H NMR spectrum of compound 60 in DMSO-d_6 at 400 MHz.

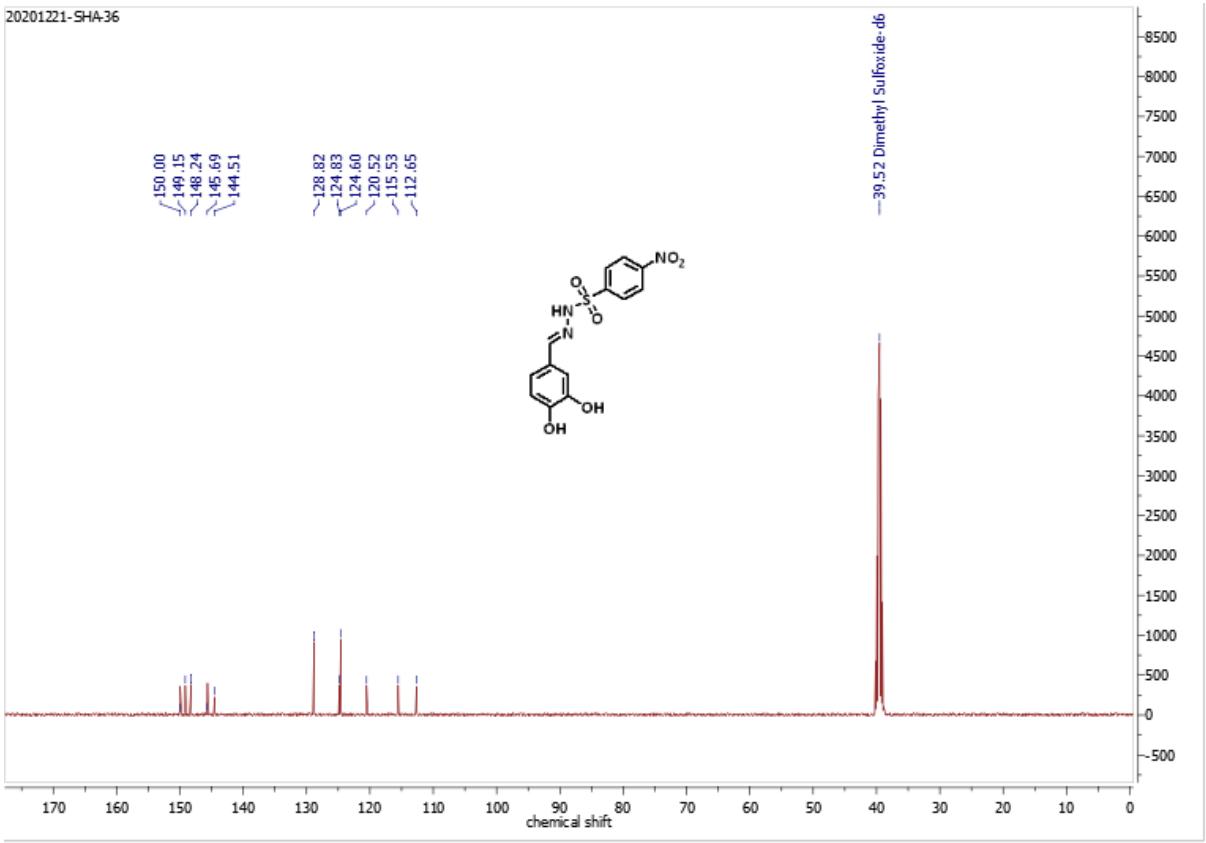


Fig. S181: [13] C NMR spectrum of compound 60 in DMSO-d_6 at 100 MHz.

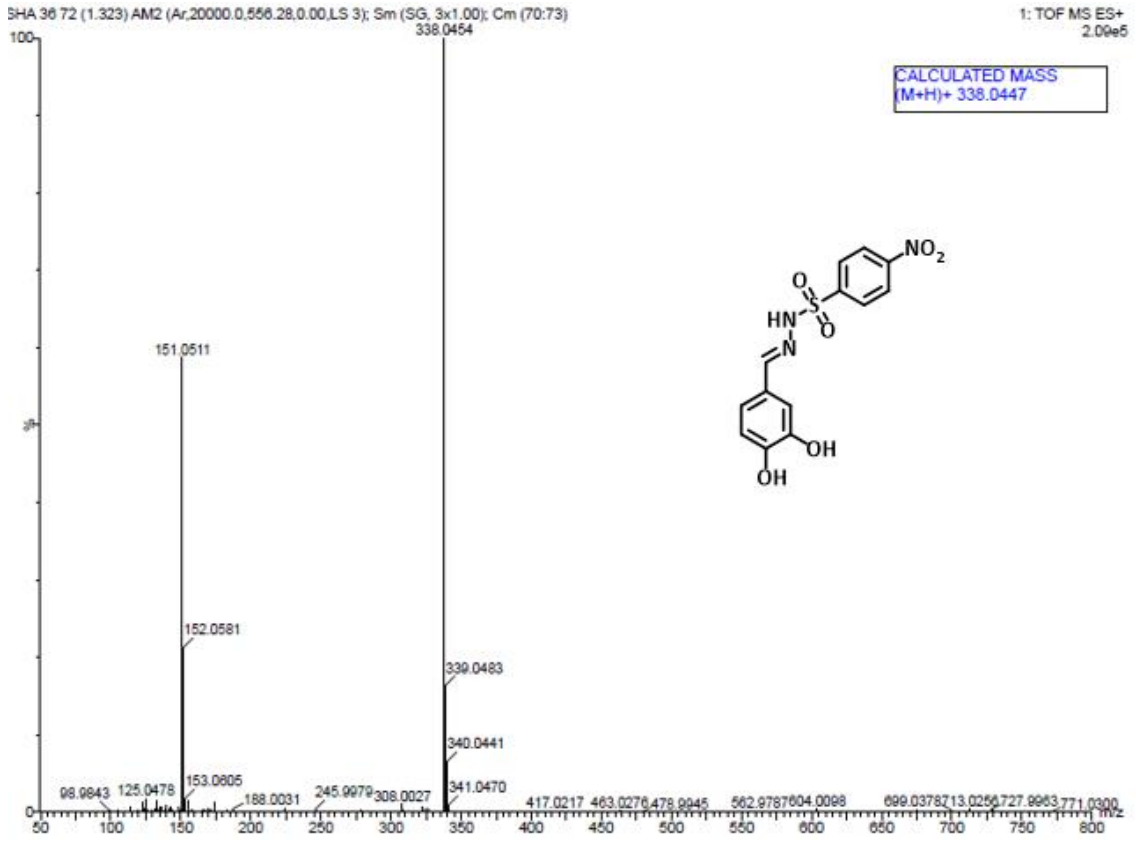


Fig. S182: HRMS spectrum of compound 60

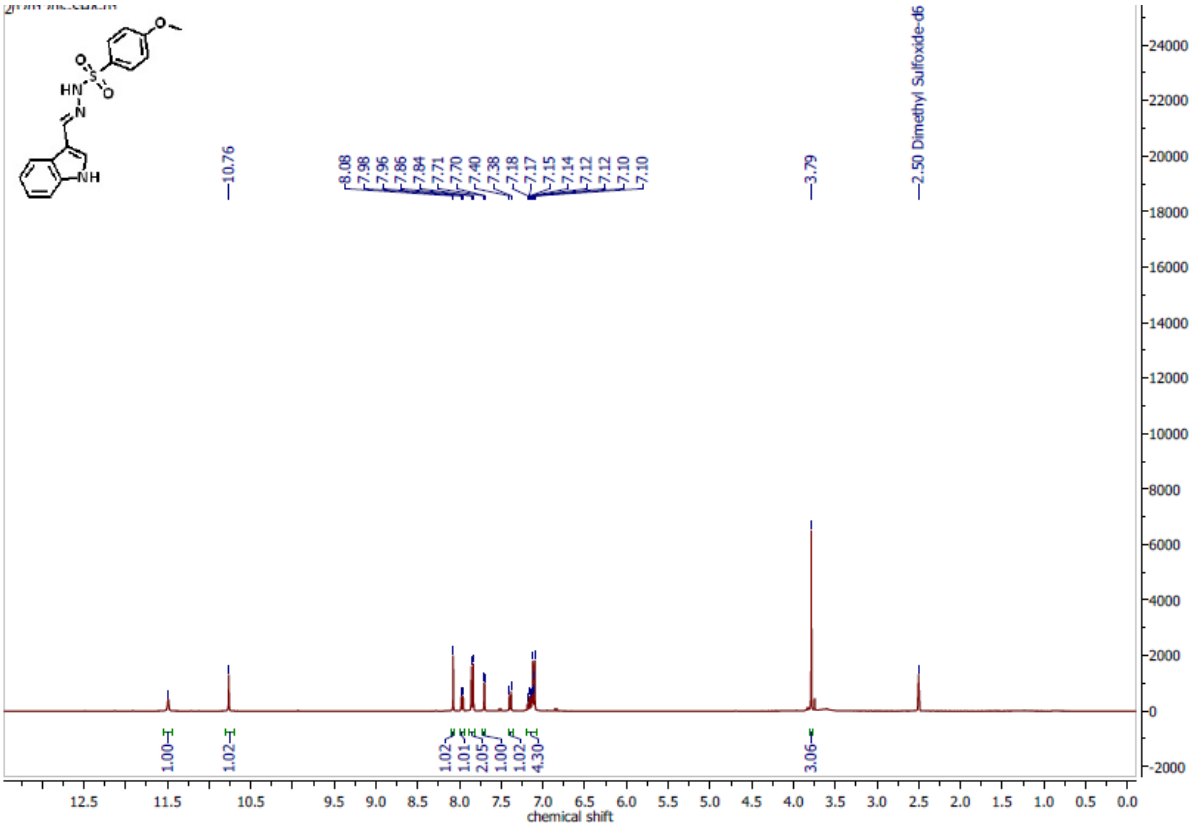


Fig. S183: ^{1}H NMR spectrum of compound 61 in DMSO-d_6 at 400 MHz

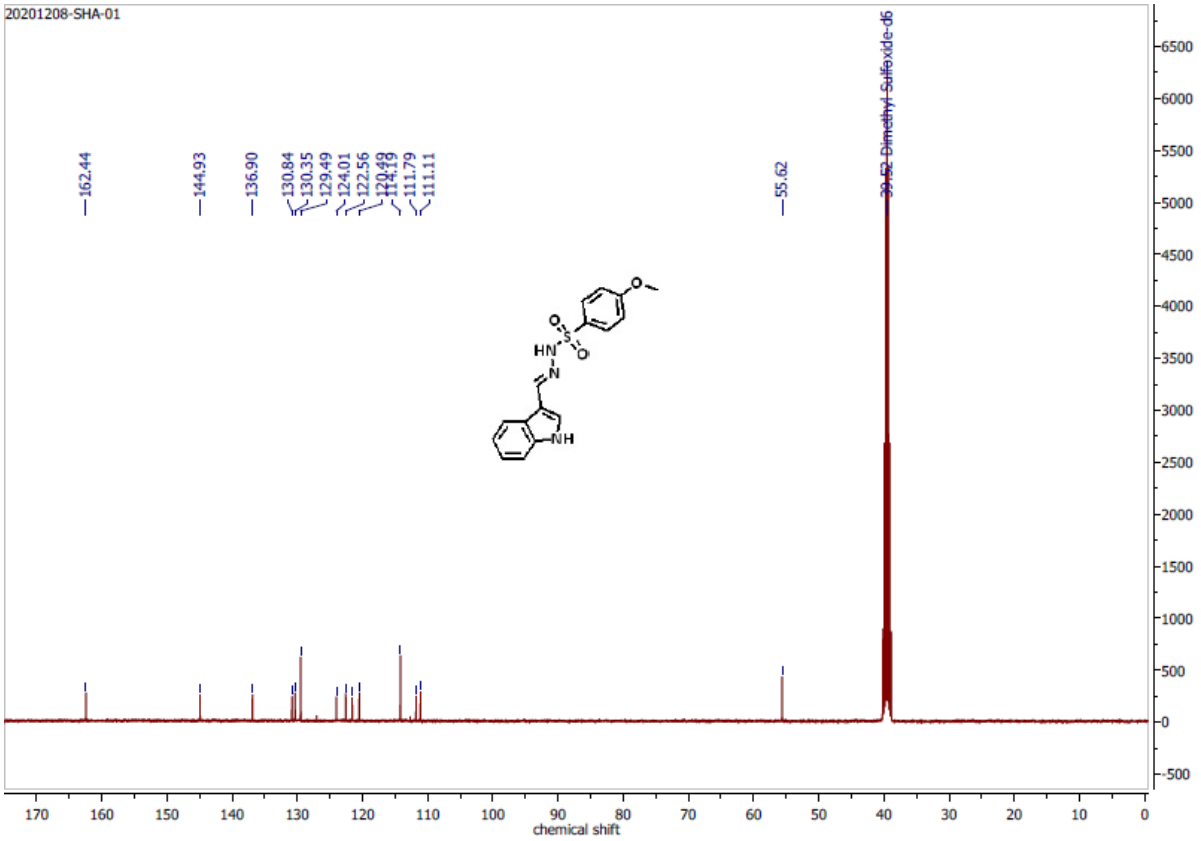


Fig. S184: ^{13}C NMR spectrum of compound 61 in DMSO-d_6 at 100 MHz

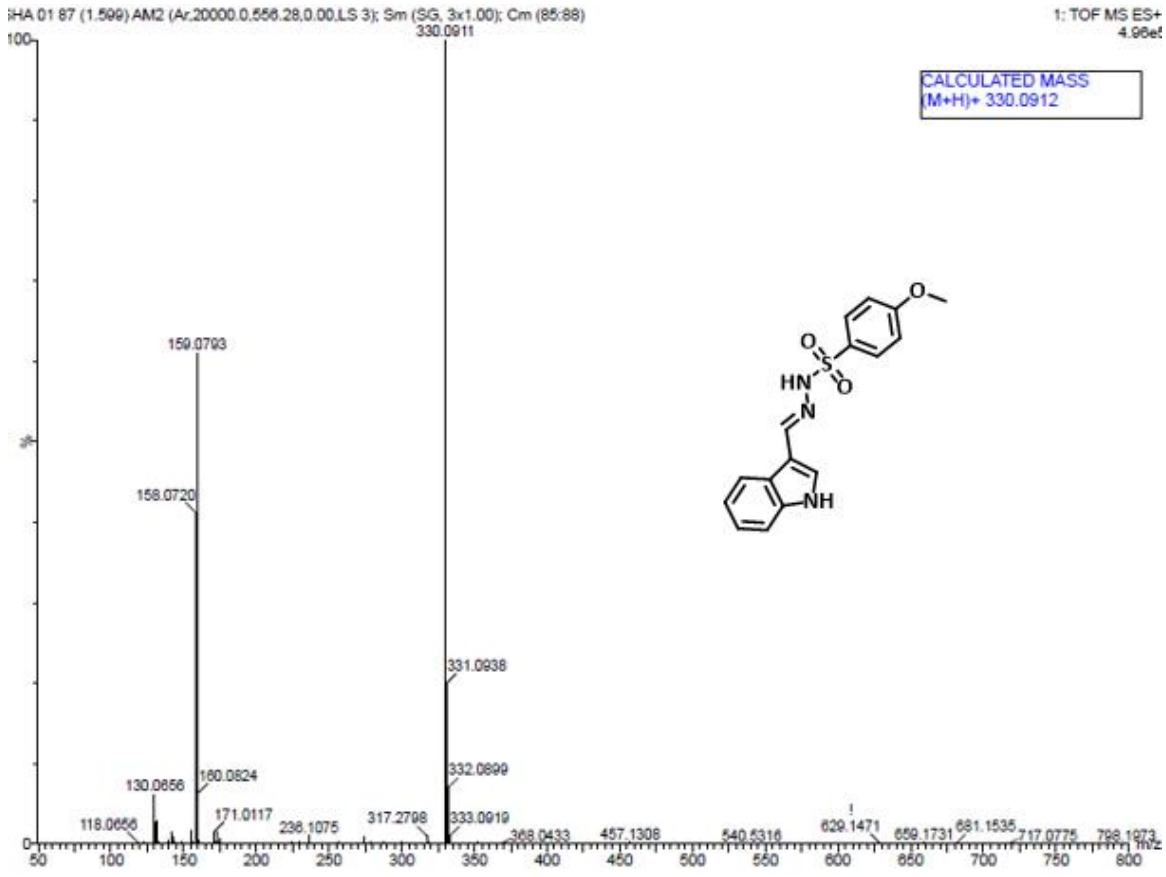


Fig. S185: HRMS spectrum of compound 61

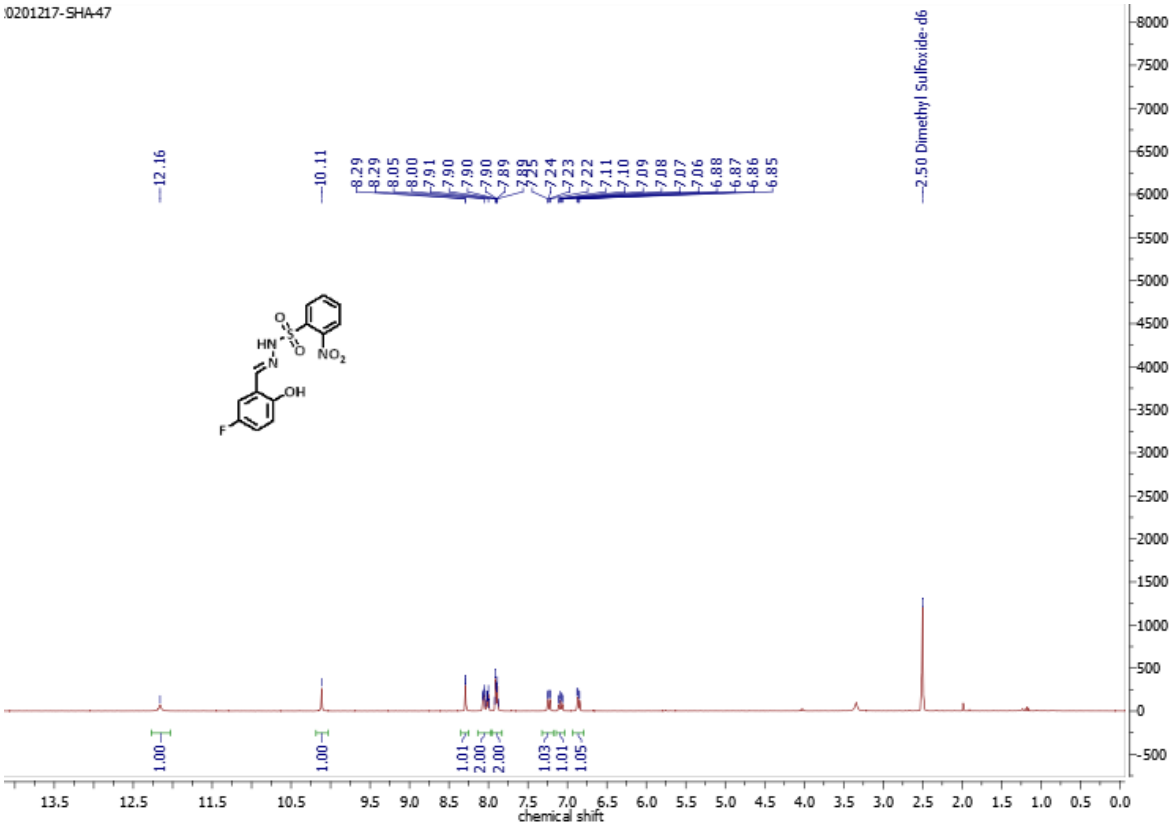


Fig. S186: [1] H NMR spectrum of compound 62 in DMSO-d_6 at 400 MHz

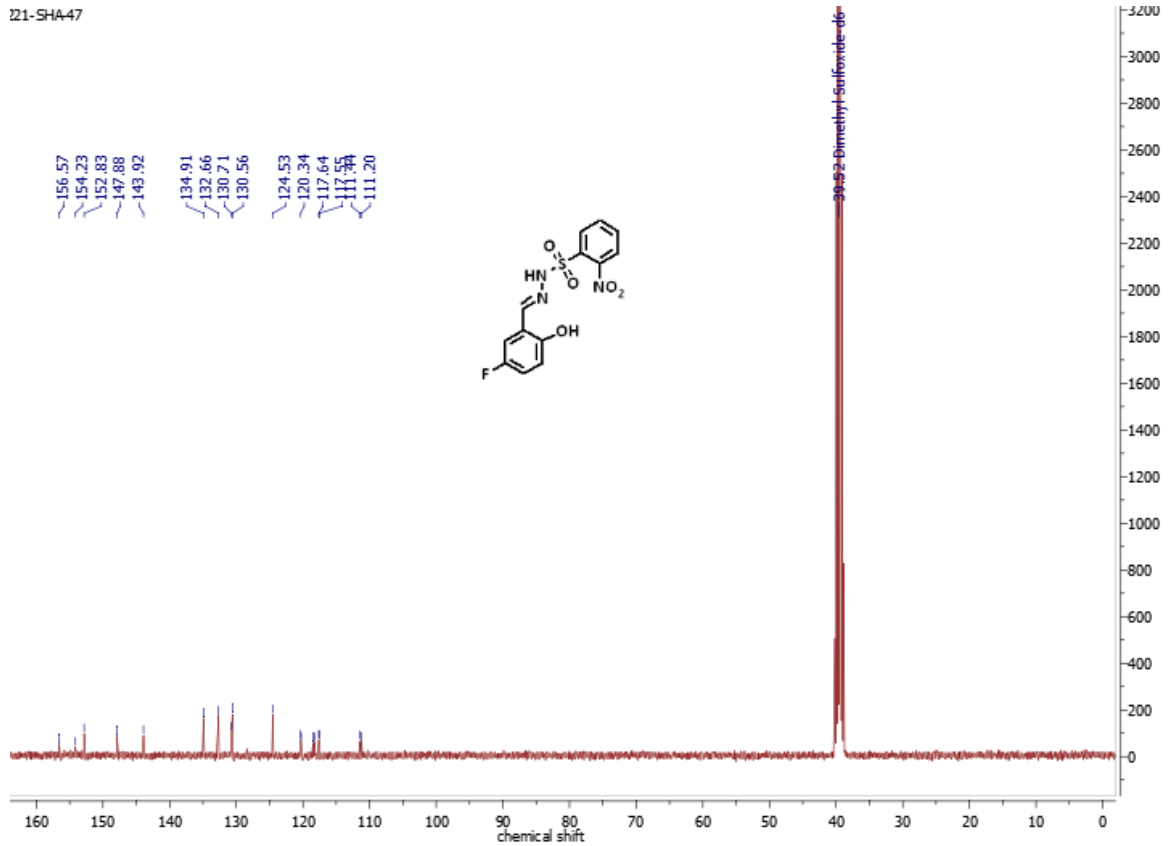


Fig. S187: [13] C NMR spectrum of compound 62 in DMSO-d_6 at 100 MHz

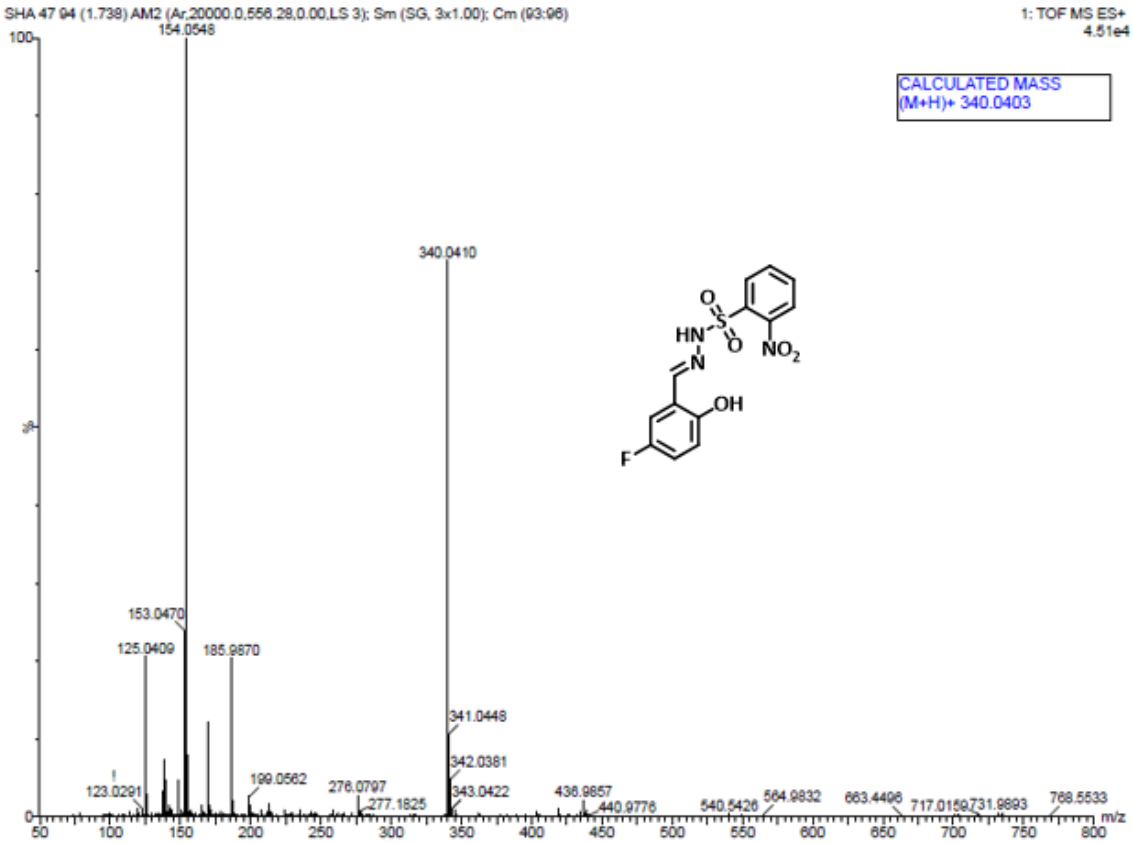


Fig. S188: HRMS spectrum of compound 62

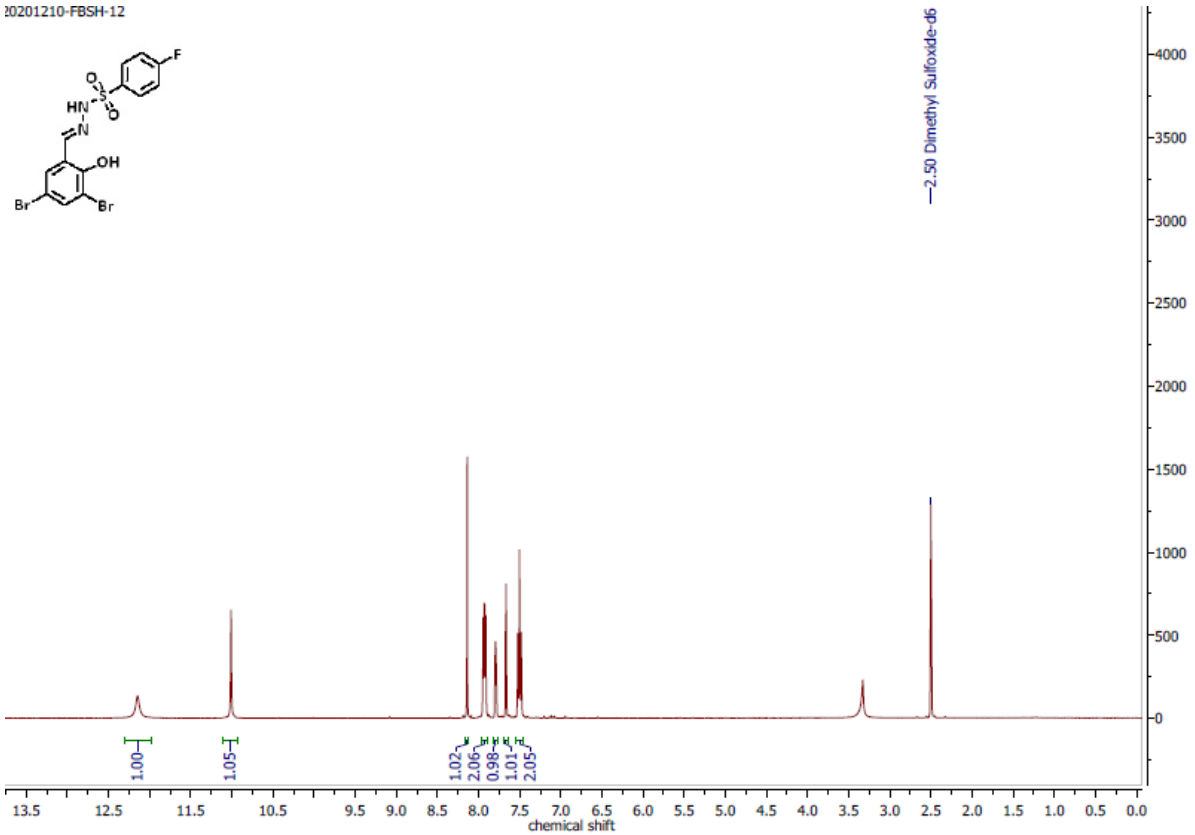


Fig. S189: ^{1}H NMR spectrum of compound 63 in DMSO-d_6 at 400 MHz

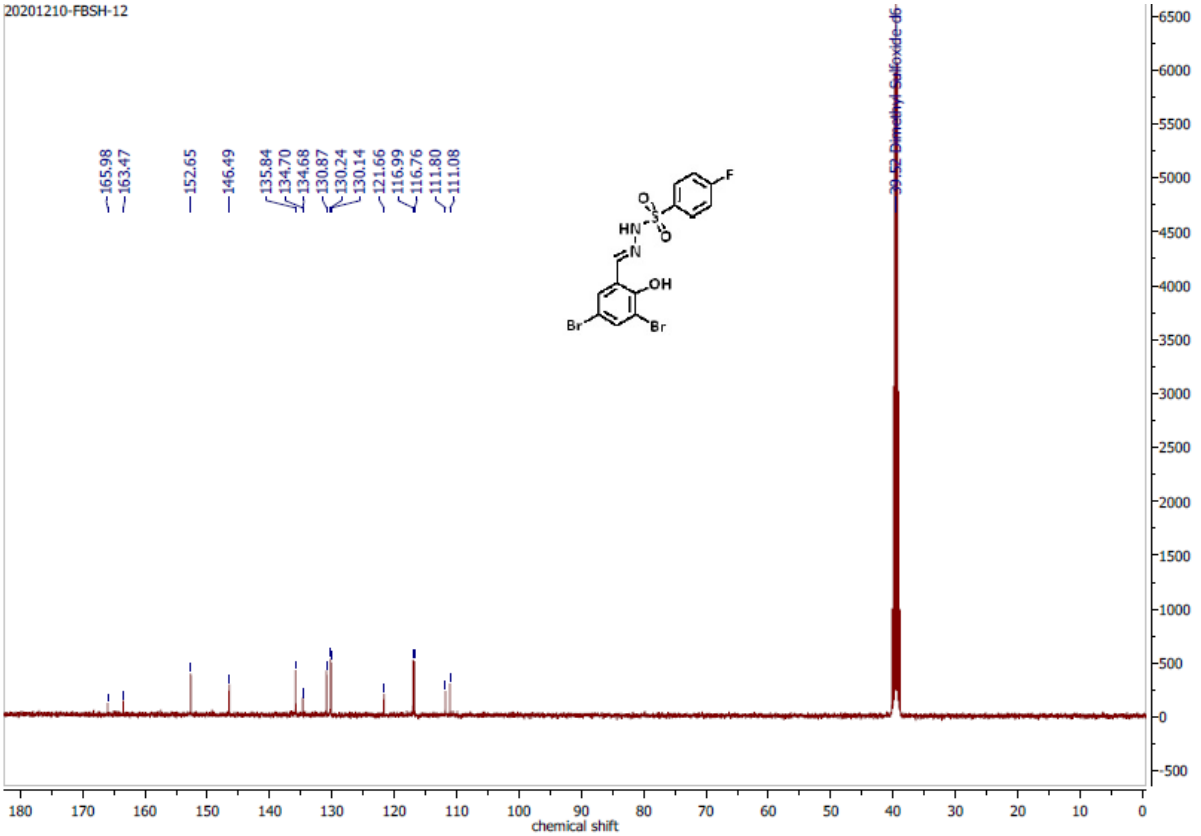


Fig. S190: ^{13}C NMR spectrum of compound 63 in DMSO-d_6 at 100 MHz

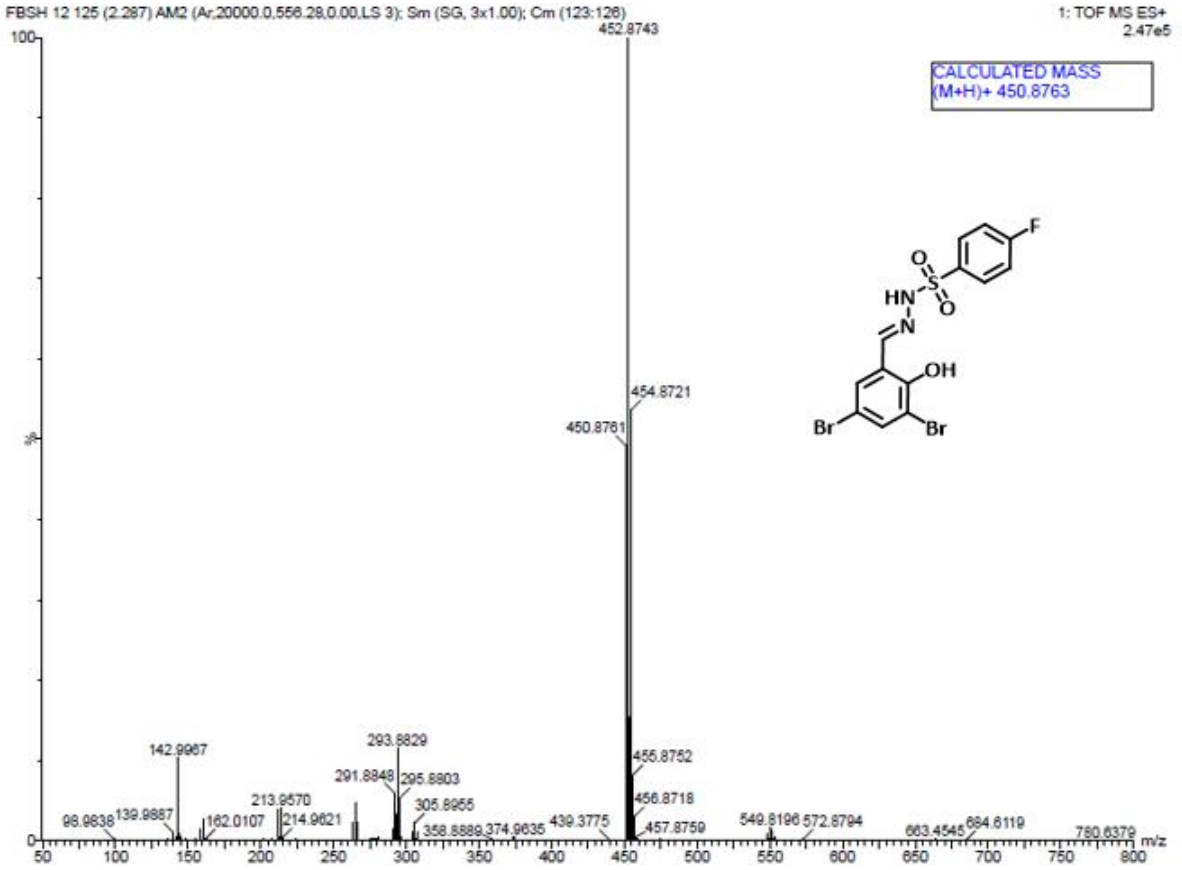


Fig. S191: HRMS spectrum of compound 63

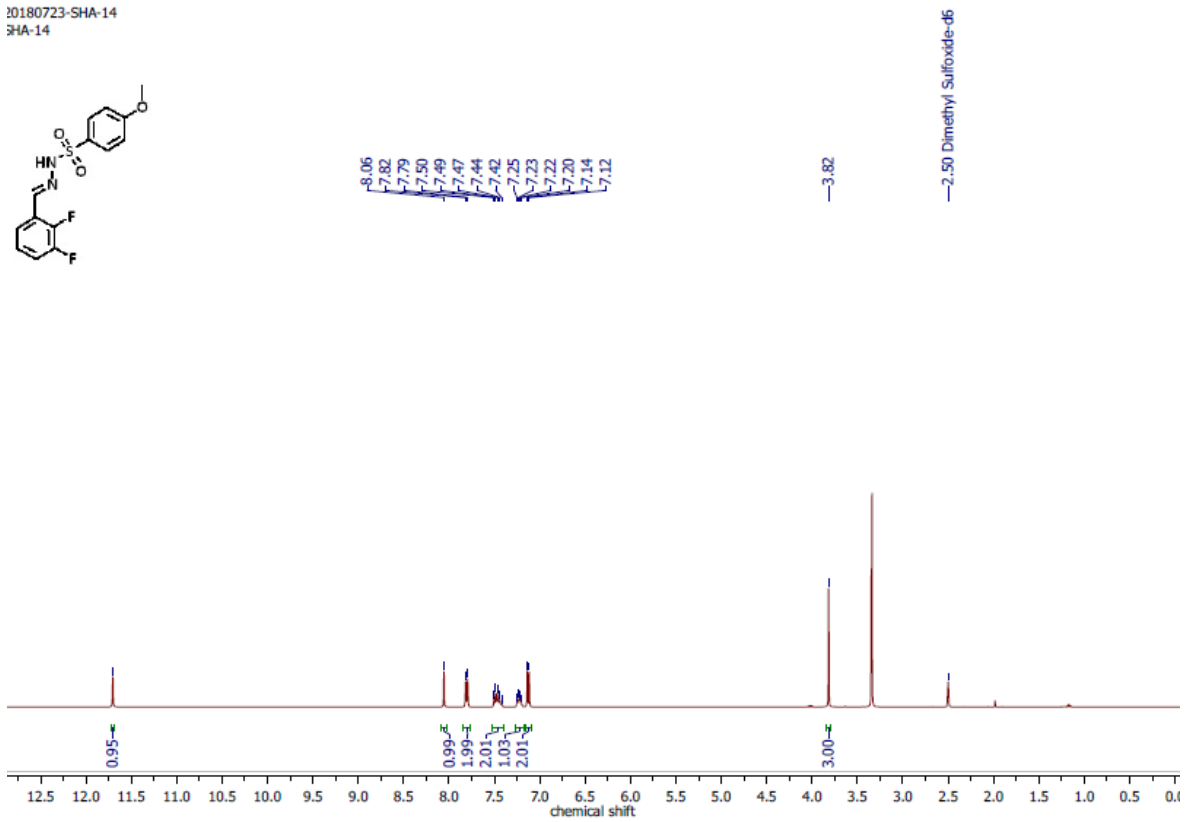


Fig. S192: [1] H NMR spectrum of compound 64 in DMSO-d_6 at 400 MHz.

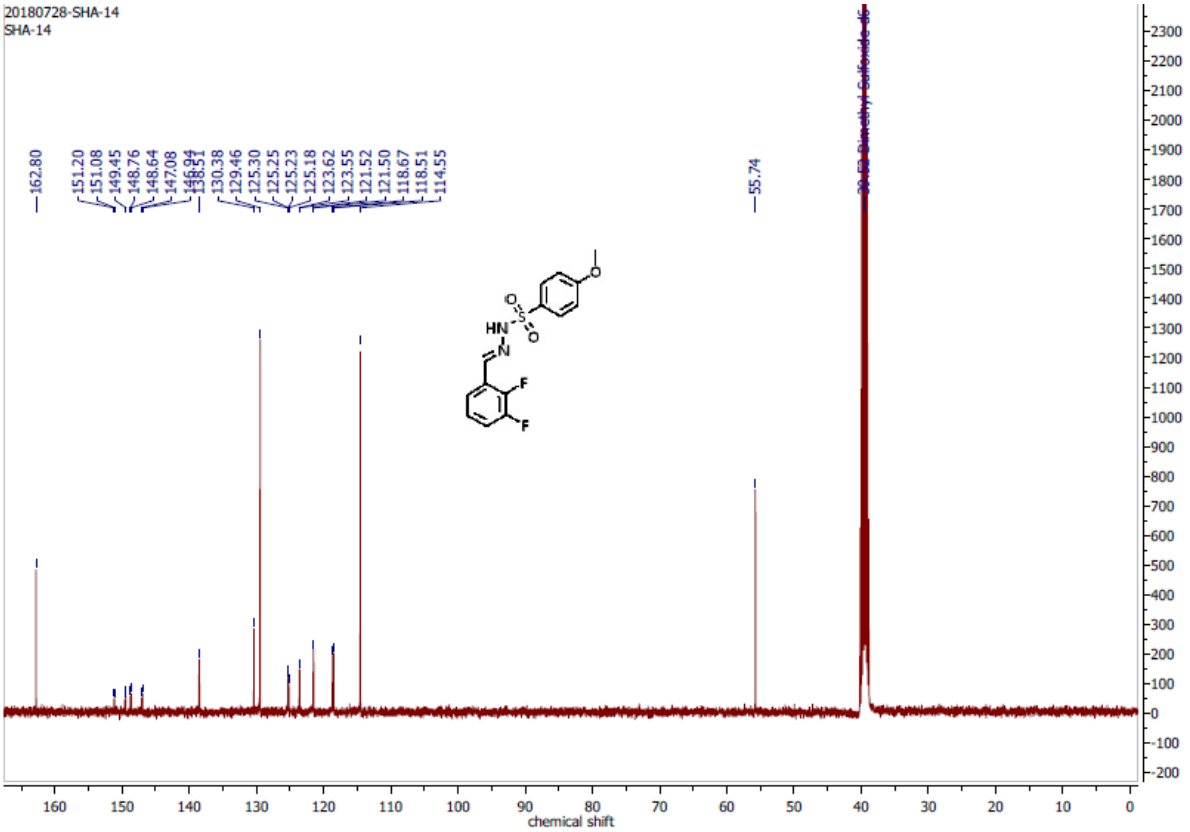


Fig. S193: [13] C NMR spectrum of compound 64 in DMSO-d_6 at 100 MHz

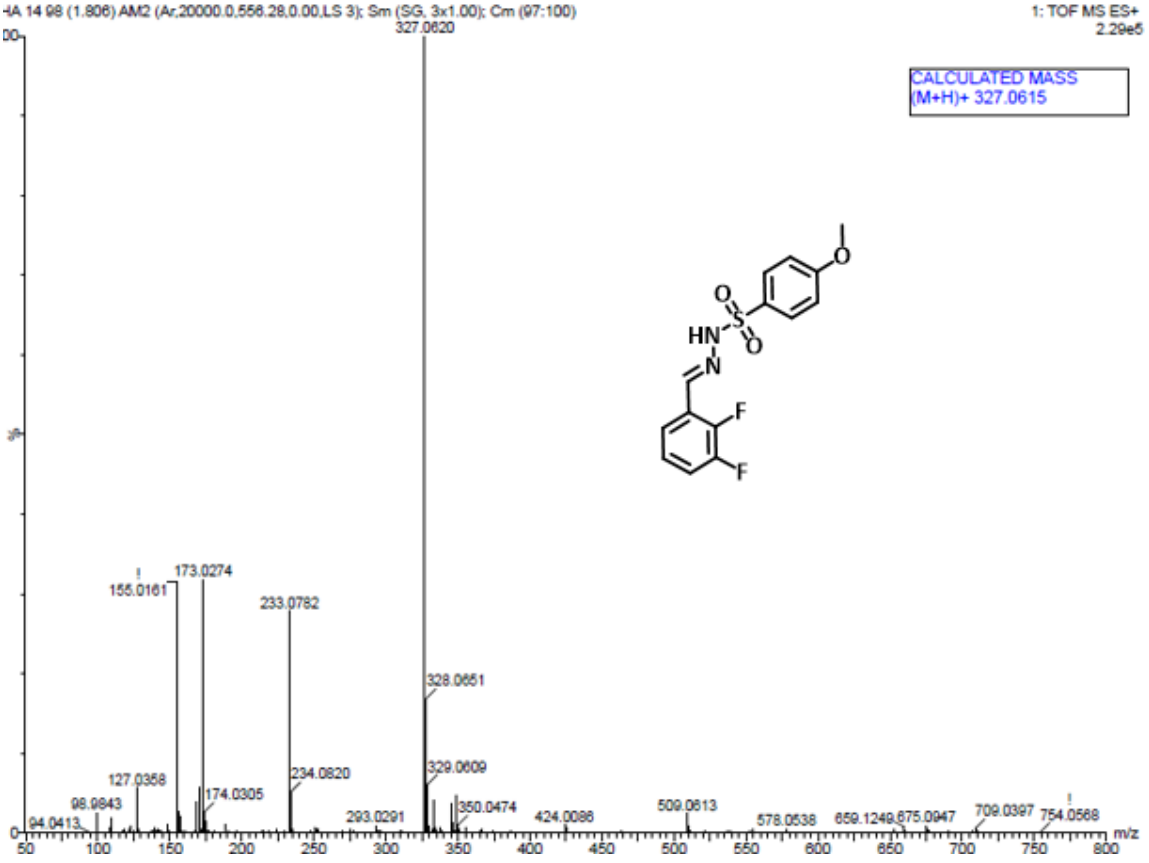


Fig. S194: HR-MS spectrum of compound 64

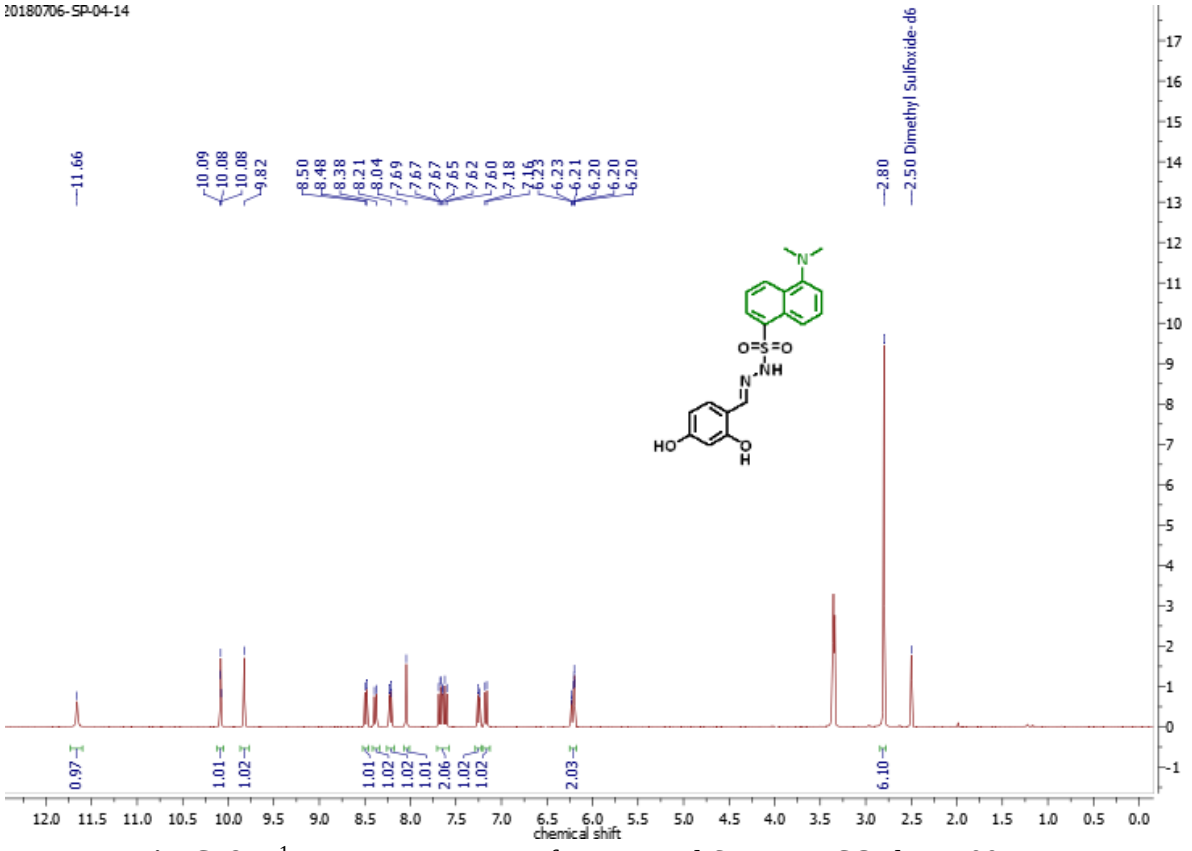


Fig. S195: [1] H NMR spectrum of compound 65 in DMSO-d_6 at 400 MHz

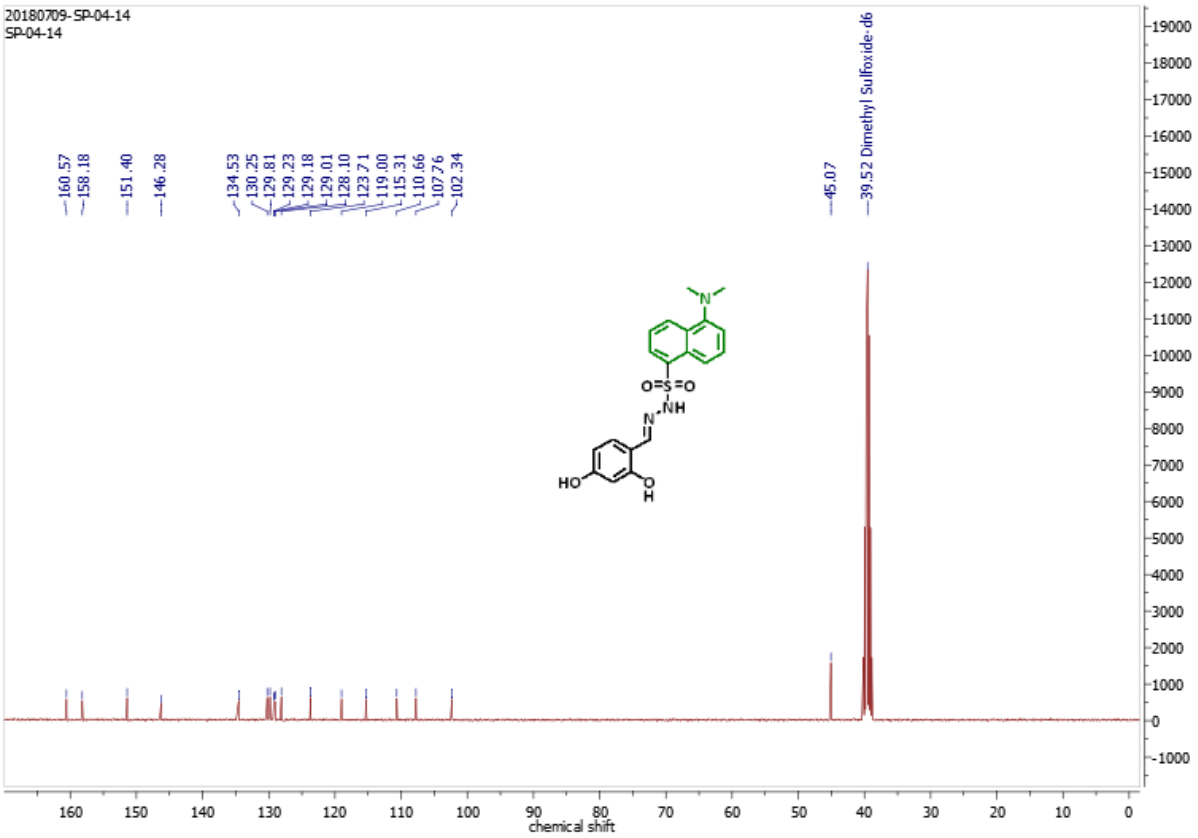


Fig. S196: ^{13}C NMR spectrum of compound 65 in DMSO-d_6 at 100 MHz

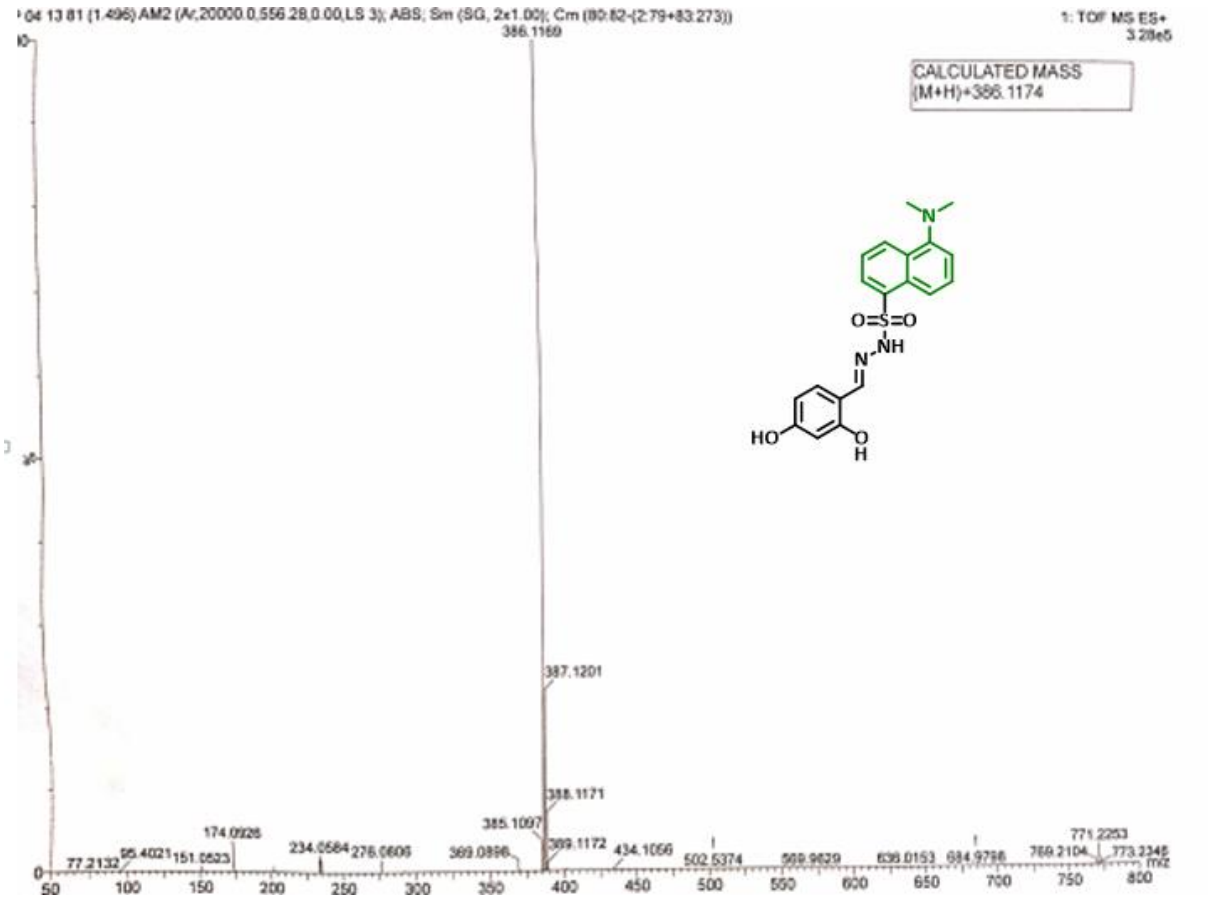


Fig. S197: HR-MS spectrum of compound 65

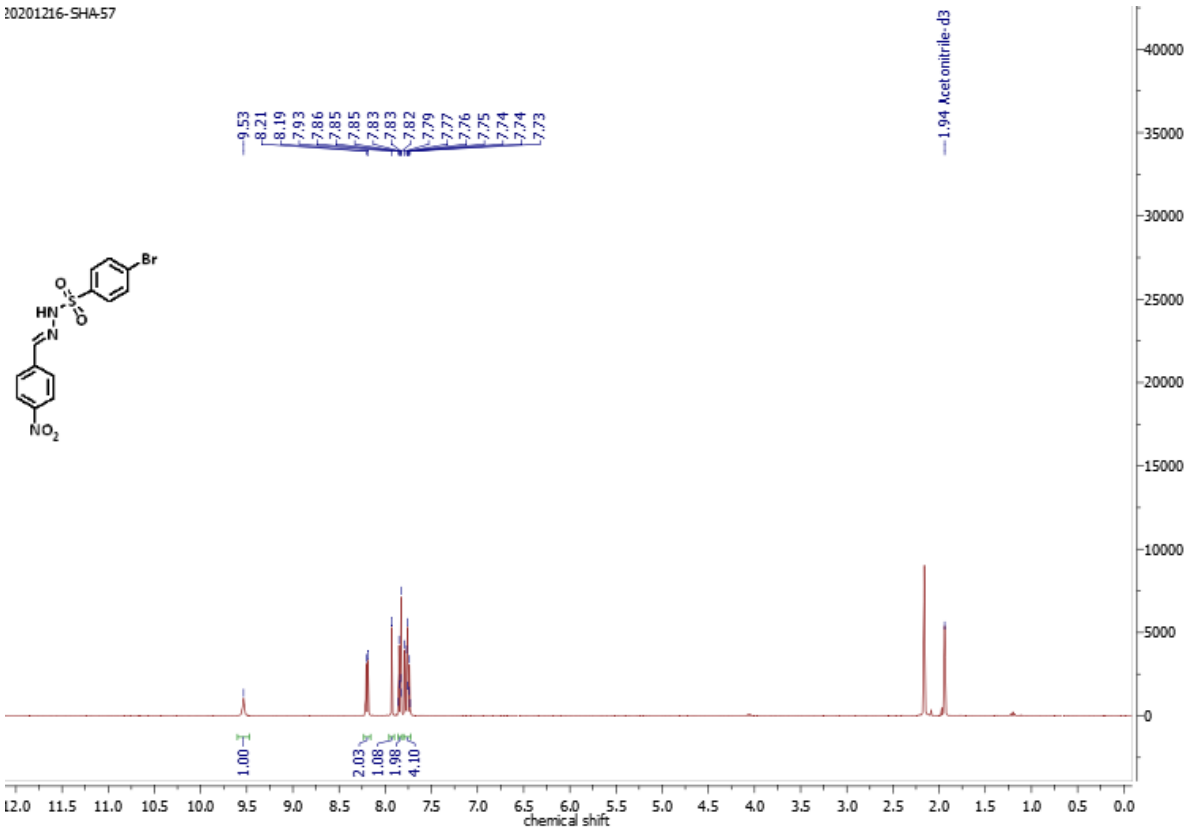


Fig. S198: [1] H NMR spectrum of compound 66 in CD_3CN-d_3 at 400 MHz.

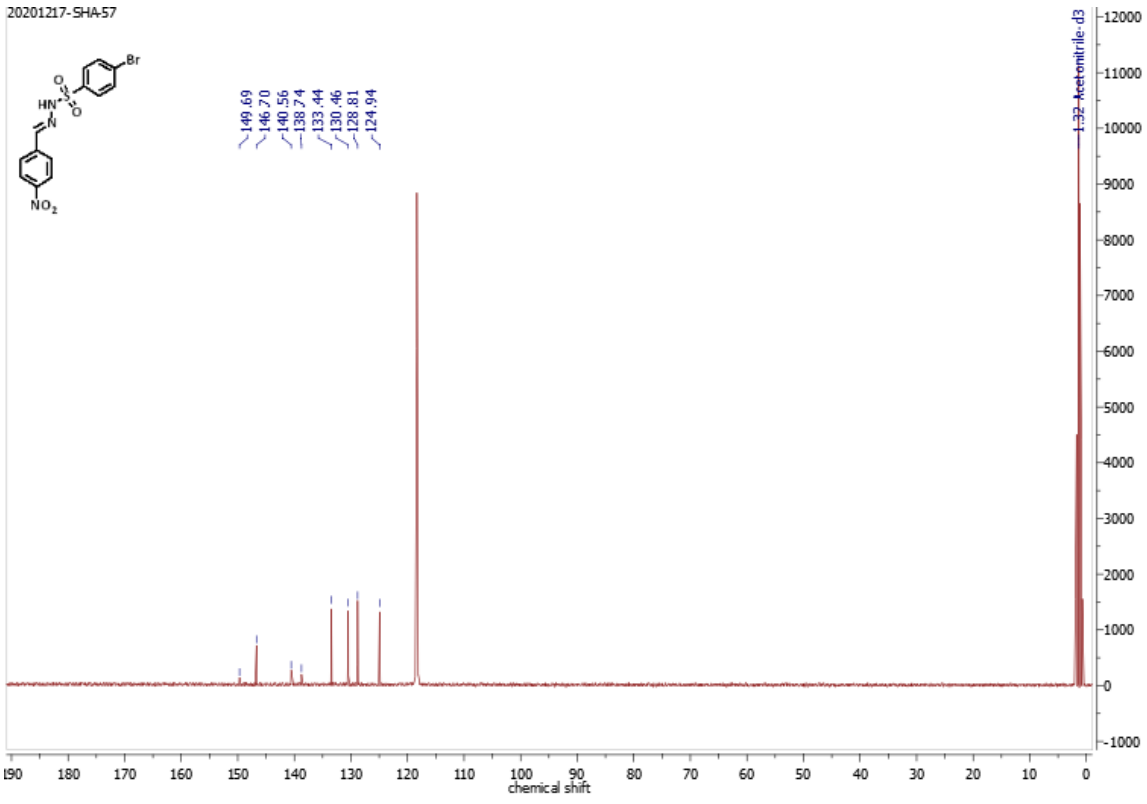


Fig. S199: [13] C NMR spectrum of compound 66 in CD_3CN-d_3 at 100 MHz.

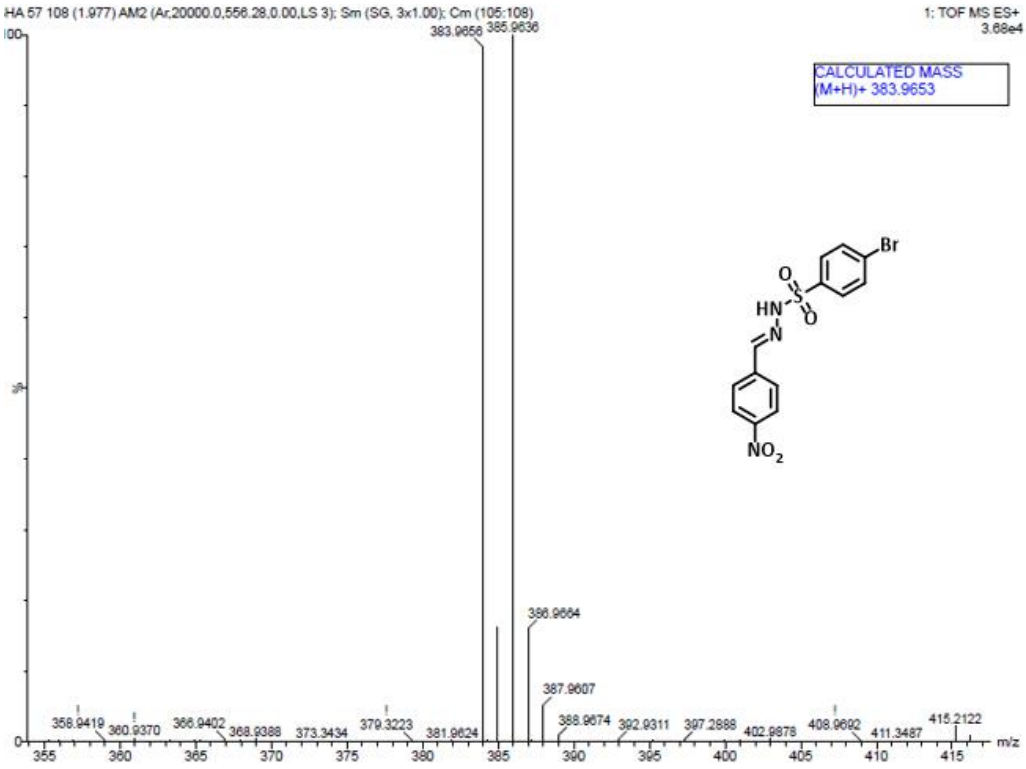


Fig. S200: HRMS spectrum of compound 66

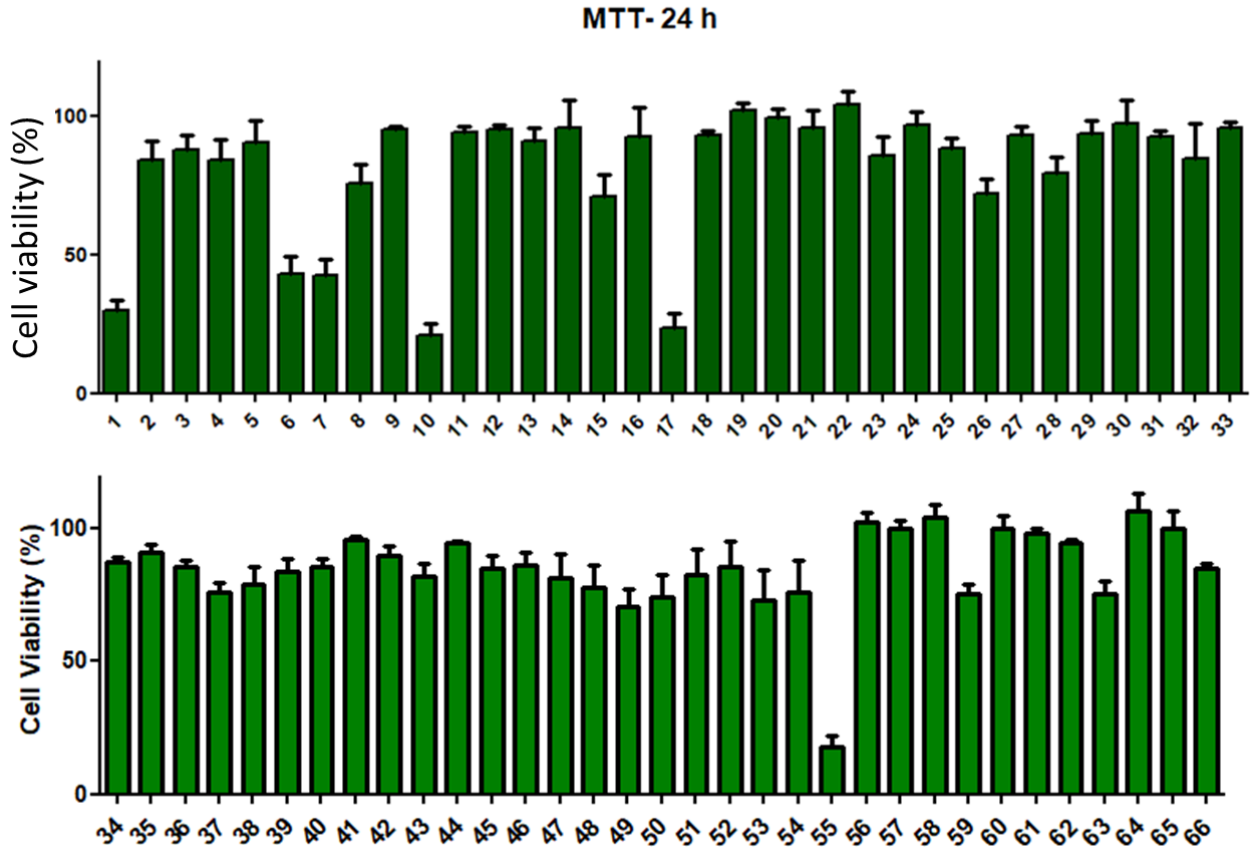


Fig. S201: Screening of 66 molecules in HeLa cell line at 30 μM for 24 h.

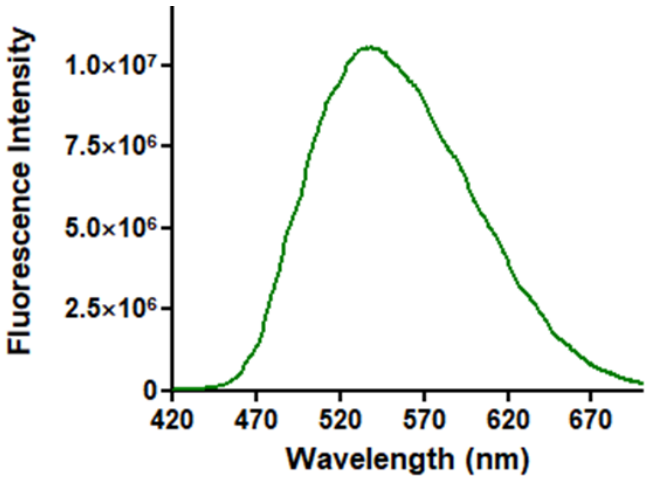


Fig. S202: Fluorescence spectra of compound 1 at $\lambda_{excitation}$ = 400 nm.

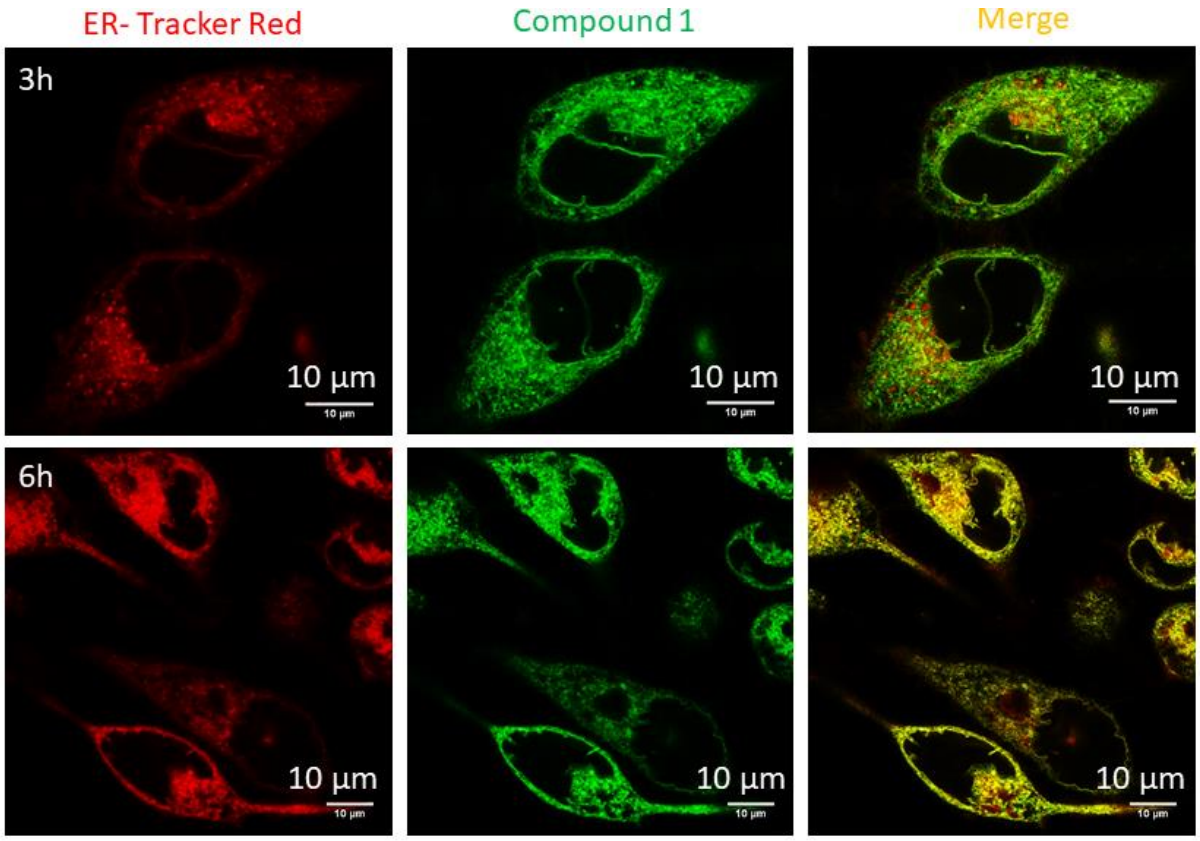


Fig. S203: Confocal microscopy images of HeLa cells at 3h and 6h post-incubation with compound 1 (green fluorescence). Cells were counter stained with ER-Tracker Red dye. Scale bar = 10 µm.

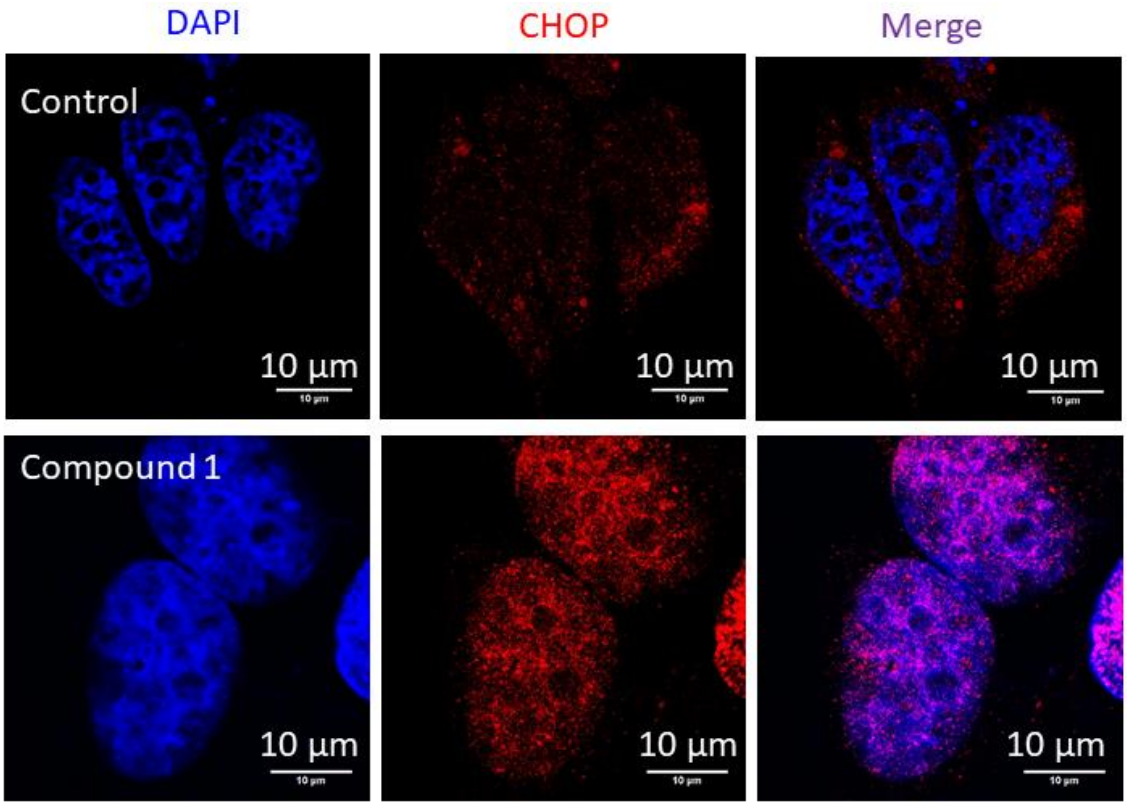


Fig. S204: Confocal images of HeLa cells after treatment with compound 1 for 24h followed by treatment with CHOP primary antibody and Alexa Fluor 594-tagged secondary antibody (red). Nuclei were stained with DAPI (blue). Scale bar = 10 µm.

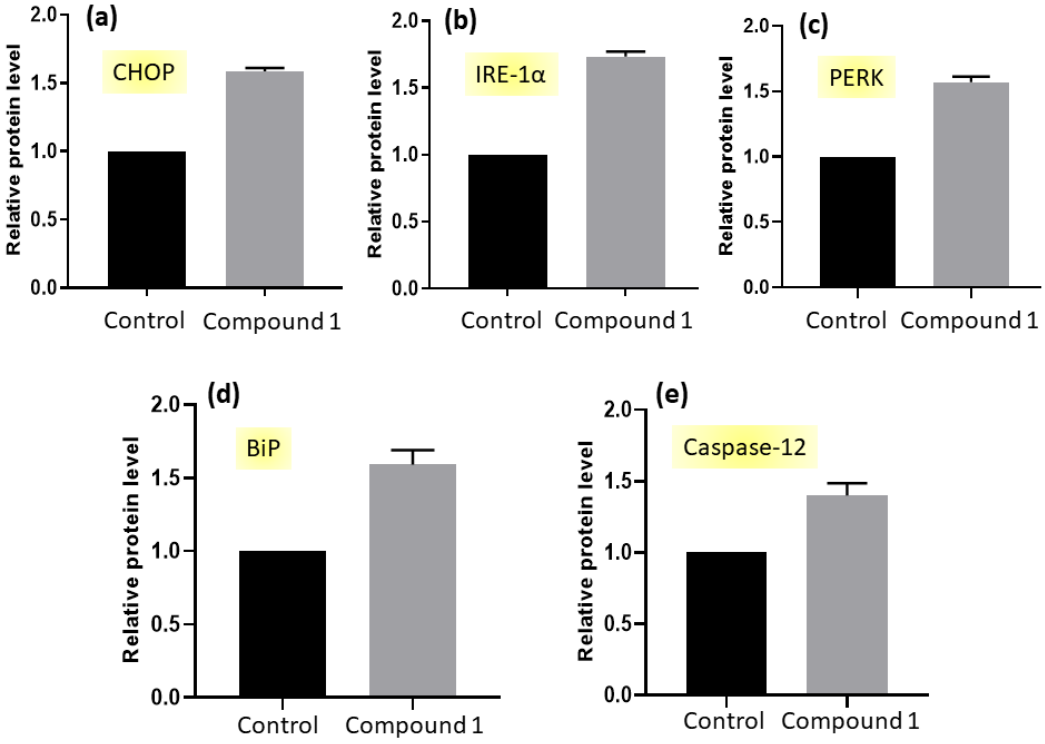


Fig. S205: Quantification of (a) CHOP (SD = ± 0.1) (b) IRE-1α (SD = ± 0.2) (c) PERK (SD = ± 0.2) (d) BiP (SD = ± 0.4) and (e) Caspase-12 (SD = ± 0.4) from western blot analysis after treatment of HeLa cells with Compound 1. SD: Standard deviation, n = 3.

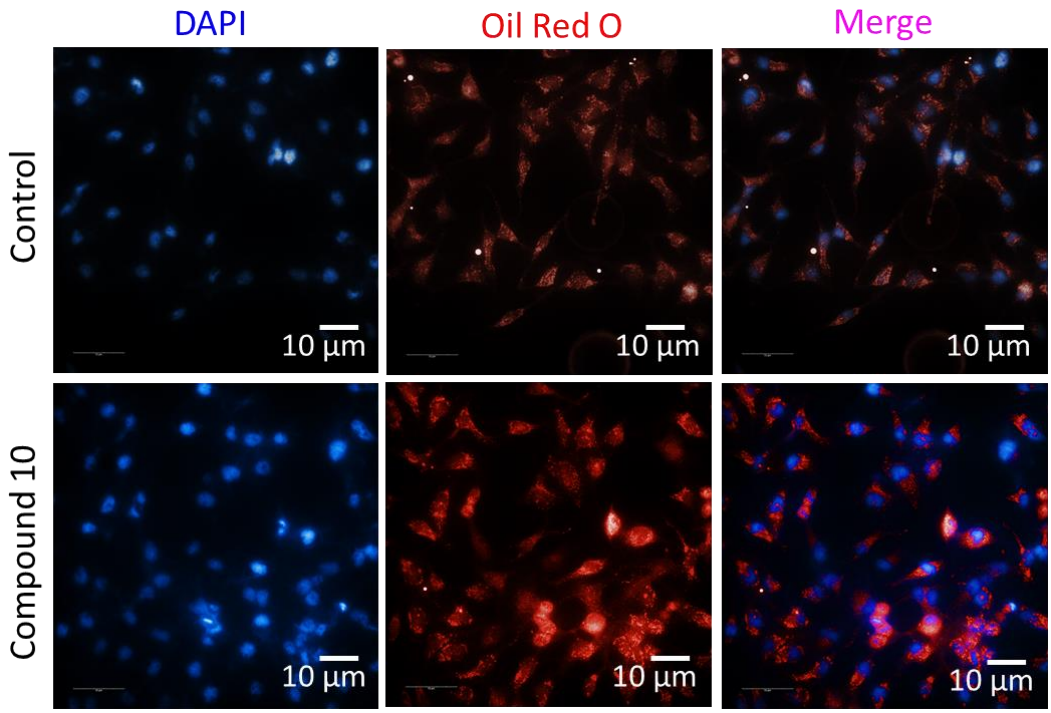


Fig. S206: The confocal microscopy images of HeLa cells after incubation with compound 10 for 24h followed by the Oil Red O dye (red) and DAPI. Scale bar = 10 µm.

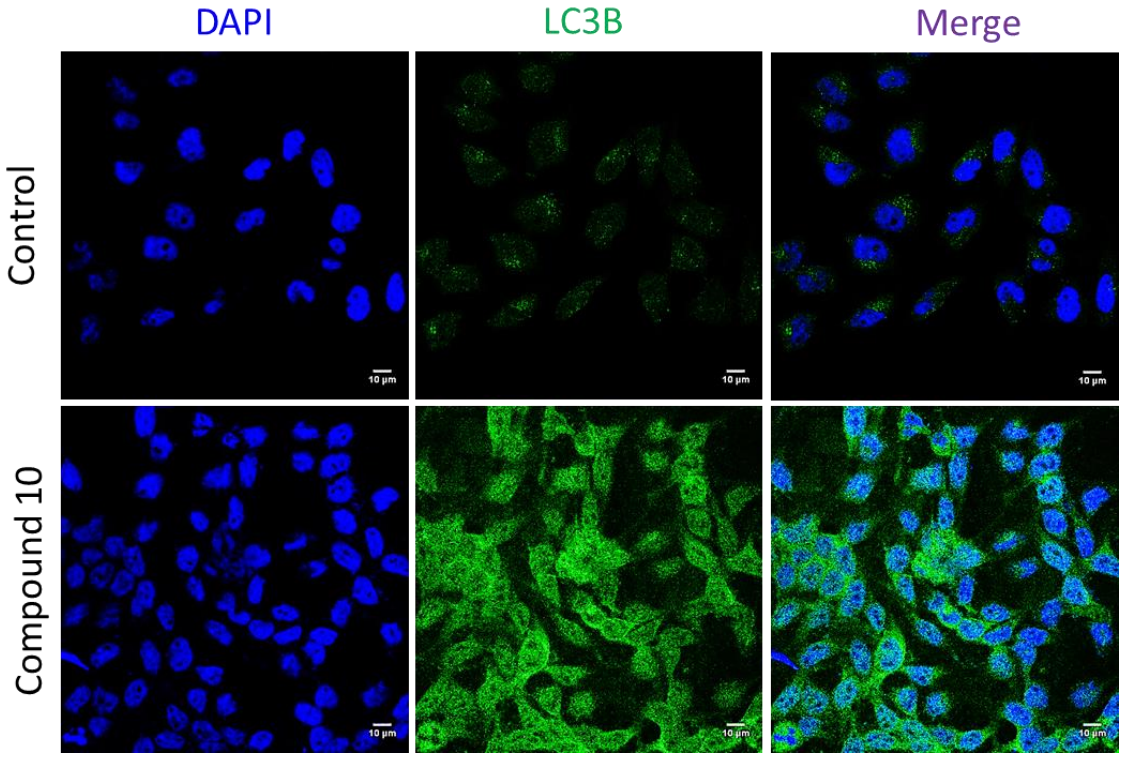


Fig. S207: Confocal images of HeLa cells after treatment with compound 10 for 24h followed by LC3B specific primary antibodies followed by Alexa Fluor 488 tagged secondary antibody (green). Scale bar = 10 µm.

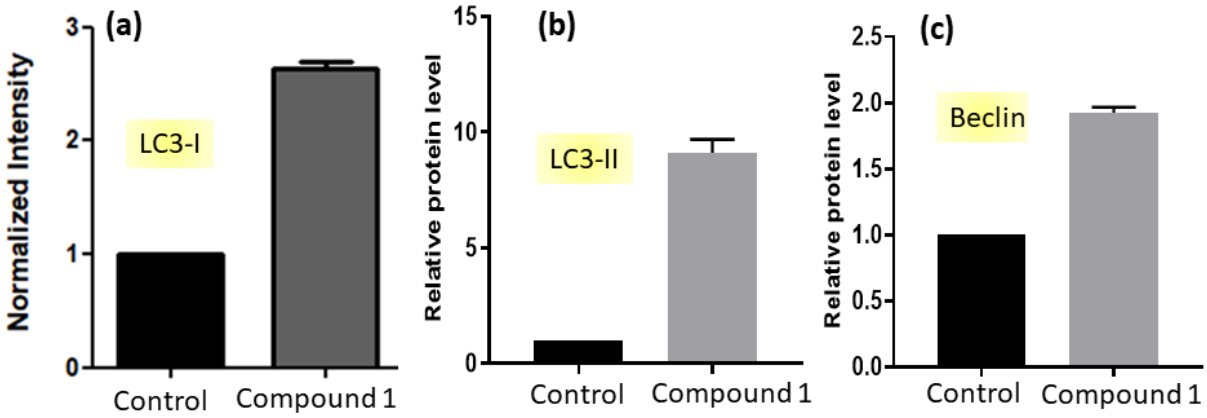


Fig. S208: Quantification of (a) LC3-I (SD = ± 0.1), (b) LC3-II (SD = ± 0.9) and (c) Beclin (SD = ± 0.1) from western blot analysis after treatment of HeLa cells with Compound 1. SD: Standard Deviations, n = 3.

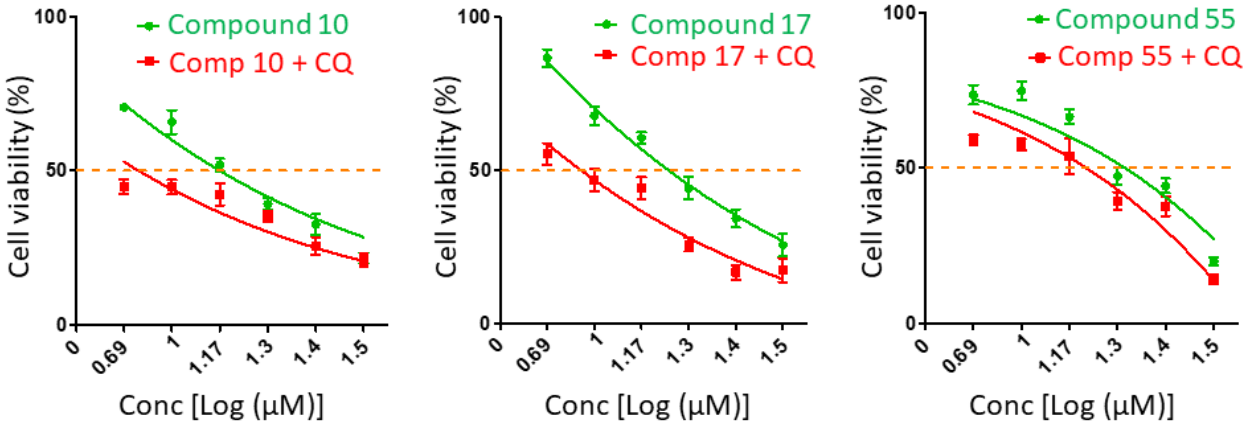


Fig. S209: Cell viability assays of compound 10,17 and 55 in combination with CQ in HeLa cells at 24h.

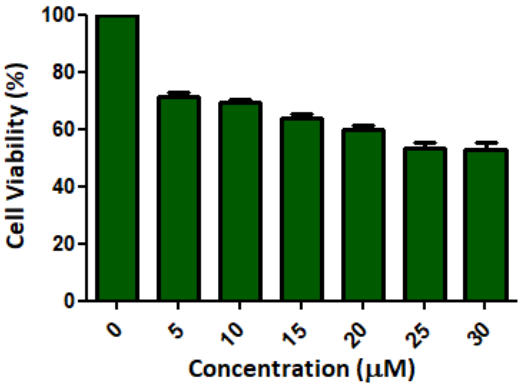


Fig. S210: Cell Viability assay for compound 1 on HEK-293 at 24 h.

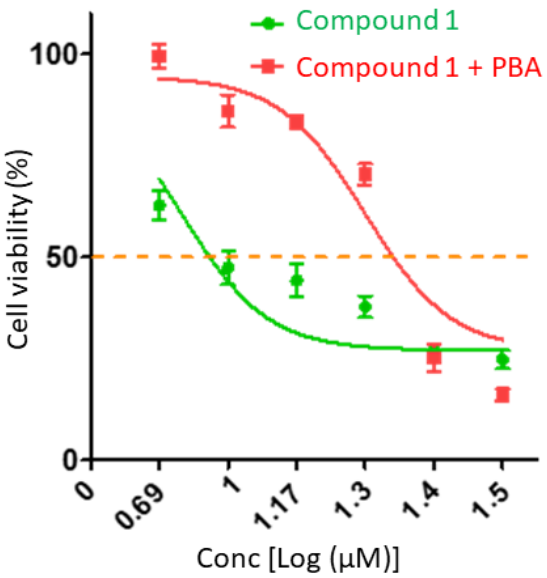


Fig. S211: Cell viability assay of compound 1 in combination with 4-phenyl butyric acid in HeLa cells for 24h.

Treatment Time		3 h	6 h
Image Channels		C1 (red) C2 (green)	C1 (red) C2 (green)
Pearsons' Correlation Coeffecient		0.8497	0.8666
Manders Coeffecients	M1 (fraction of C1 overlapping C2)	0.9830	0.9763
	M2 (fraction of C2 overlapping C1)	1	0.9866

Table S1: Quantification of co-localization of Compound 1 in ER of HeLa cells at 3 h and 6 h from CLSM.

References.

1. A.G. Myers, B. Zheng, M. Movassaghi *J. Org. Chem.* 1997, 62, 21, 7507