Supporting Information

Transition metal-free one-pot tandem reductive cyclization of 3/5-(2-nitrophenyl)-1*H*-pyrazoles using sodium dithionite

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Table of Contents

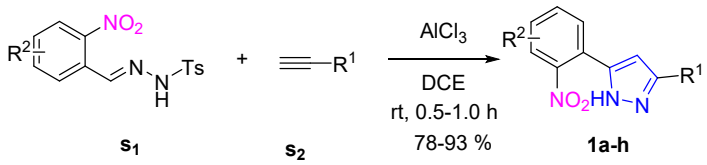
1. General information

The solvents and reagents used for the synthesis were procured from commercial vendors and were utilized without additional purification. Thin layer chromatography (TLC) manufactured by Merck was used to monitor the completion of the reaction. The ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on Bruker Avance III AV500 MHz using Tetramethylsilane (TMS) as the internal standard. Chemical shift values (δ=ppm) and coupling constants values (J =HZ) are reported. Agilent QTOF mass spectrometer 6540 was used to determine the compounds' mass spectra. The Stuart MP2 melting point instrument was utilized to ascertain the purity of the compounds. All the IUPAC names and chemical structures of the compounds were generated through PerkinElmer's Chem Draw 22.0.

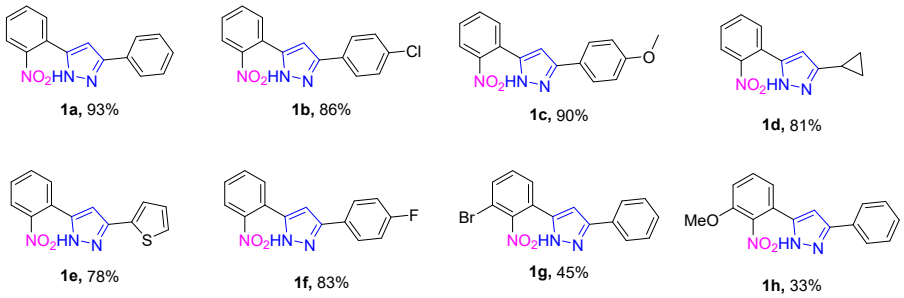
2. Preparation of starting precursors

2.1 General procedure for the synthesis of substituted 5-(2-nitrophenyl)-1*H*-pyrazoles (1a-f)

Substituted 5-(2-nitrophenyl)-1*H*-pyrazole derivatives were prepared according to the modified procedure of the previous literature report.[1]

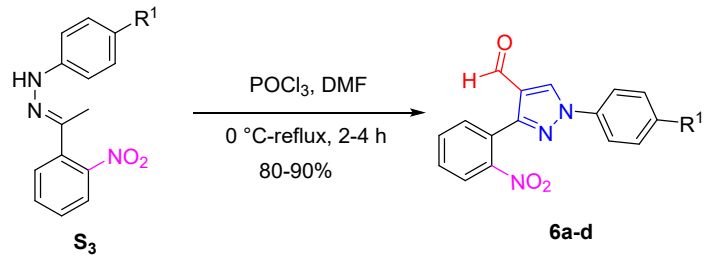


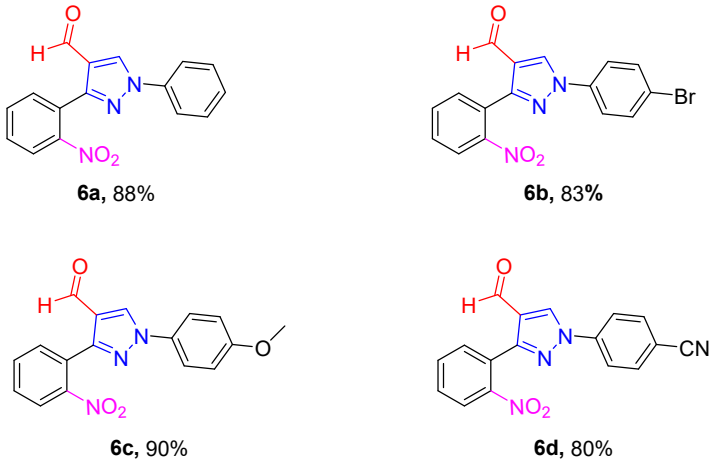
A solution of substituted 2-nitrobenzaldehyde (1.0 equiv., 6.62 mmol, 1.0g) and 4-methylbenzenesulfonohydrazide (1.1 equiv., 7.28 mmol, 1.36g) in tetrahydrofuran (THF) was stirred at room temperature for 1 hour. Upon completion of the reaction, crushed ice was added to the reaction mixture, resulting in the formation of a thick precipitate. The obtained precipitate was then filtered to yield the 2-nitrobenzaldehyde tosylhydrazone (**s_1**). The intermediate 2-nitrobenzaldehyde tosylhydrazone (**s_1**) (1.0 equiv., 3.13 mmol, 1.0 g) was then reacted with alkynes (**s_2**) (2.5 equiv., 7.83 mmol) and aluminum chloride ($AlCl_3$) (2.5 equiv., 7.83 mmol, 1.04 g) in dichloroethane (DCE) under an argon atmosphere. The reaction was stirred at room temperature for 0.5-1 hour. After completion of the reaction, the reaction mixture was quenched with water and extracted with dichloromethane (DCM), and evaporated under reduced pressure to afford the 5-(2-nitrophenyl)-1*H*-pyrazoles **1a-h**.



2.2 General procedure for the synthesis of 3-(2-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehydes (6a-d).

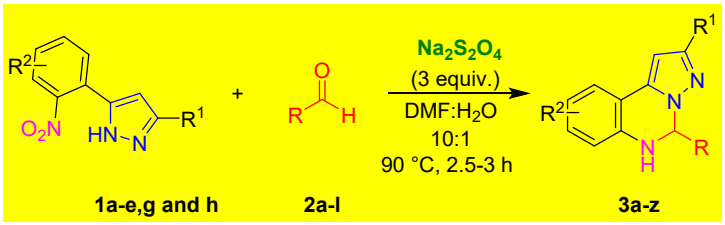
3-(2-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehydes (**6a-d**) were synthesized according to the previous literature reports.[2]





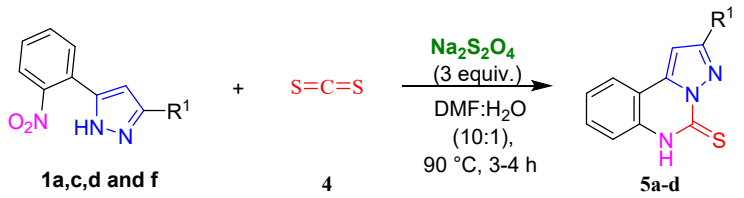
3. General procedure for the synthesis of **pyrazolo[1,5-*c*]quinazolines and pyrazolo[4,3-*c*]quinolines**

3.1 **General procedure for the synthesis of pyrazolo[1,5-*c*]quinazoline product (3a-z)**



To a stirred solution of substituted 5-(2-nitrophenyl)-1*H*-pyrazole derivatives **1a-e, g** and **h** (1.0 equiv., 0.56 mmol), in DMF: water (10:1 v/v), were added aldehyde derivatives **2a-l** (1.1 equiv.), and sodium dithionite ($Na_2S_2O_4$, 3.0 equiv., 1.7 mmol). The reaction mixture was heated at 90 °C for 2.5–3 hours. Upon completion of the reaction, the reaction mixture was poured into crushed ice and the resultant precipitate was filtered. The resulting crude residue was purified by column chromatography (silica gel 100-200 mesh) using a mixture of hexane and ethyl acetate as the eluent to afford the desired products **3a-z**.

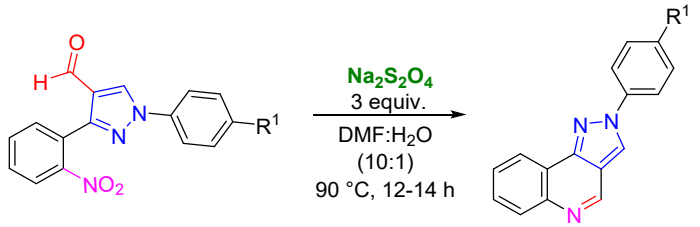
3.2 General procedure for the synthesis of **pyrazolo[1,5-c]quinazoline-5(6*H*)-thione (5a-d)**



1a,c,d and f **4** **5a-d**

A solution of 5-(2-nitrophenyl)-1*H*-pyrazoles **1a, c, d, and f** (1.0 equiv., 0.56 mmol), carbon disulfide **4** (2.0 equiv., 1.13 mmol) and $Na_2S_2O_4$ (3.0 equiv., 1.7 mmol) in DMF: water (10:1 v/v) was heated at 90 °C for 3–4 h. Upon completion of the reaction, the reaction mixture was allowed to cool to room temperature, then diluted with cold water and extracted with ethyl acetate (3 x50 mL). The organic layer was concentrated under reduced pressure and the resulting crude residue was purified by column chromatography (silica gel 100-200 mesh) using a mixture of hexane and ethyl acetate as the eluent to afford the desired products **5a-d**.

3.3 **General procedure for the synthesis of pyrazolo[4,3-*c*]quinolines (7a-d)**



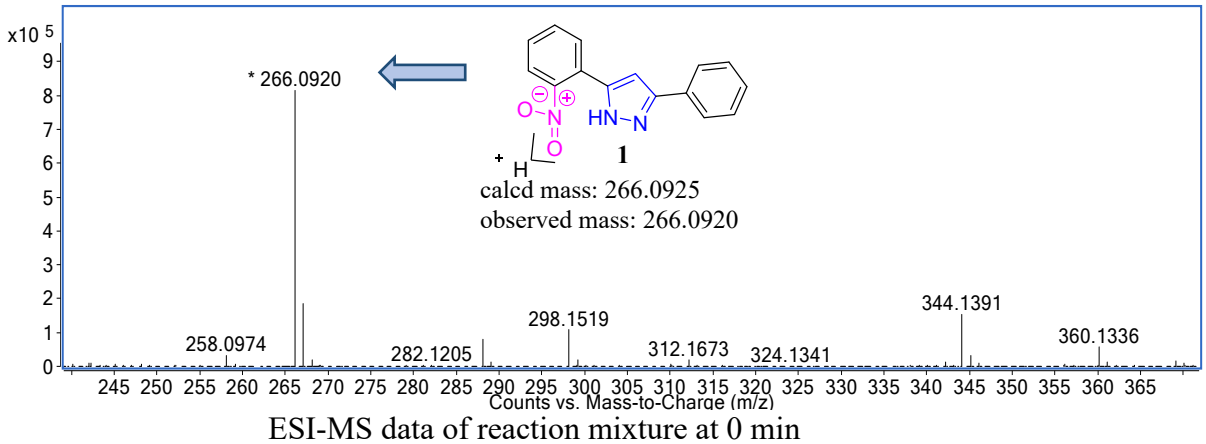
6a-d **7a-d**

The compounds **7a-d** were synthesized through *in situ* reduction followed by intramolecular cyclization of the intermediates **6a-d** using sodium dithionite. A solution of 3-(2-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde derivatives **6a-d** (1.0 equiv., 0.5 mmol) and $Na_2S_2O_4$ (3.0 equiv., 1.5 mmol) in DMF: water (10:1 v/v) was heated at 90 °C for 12–14 h. Upon completion of the reaction, the reaction mixture was poured into crushed ice and the resultant precipitate was filtered. The obtained crude residue was purified by column chromatography

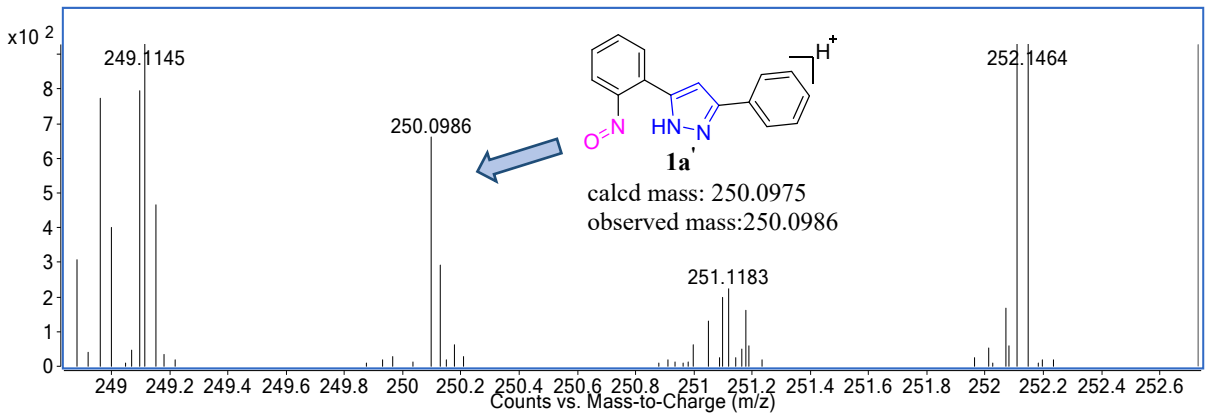
(silica gel 100-200 mesh) using a gradient of ethyl acetate and hexane to afford the desired products **7a-d**.

4. ESI-MS studies of pyrazolo[1,5-*c*]quinazolines

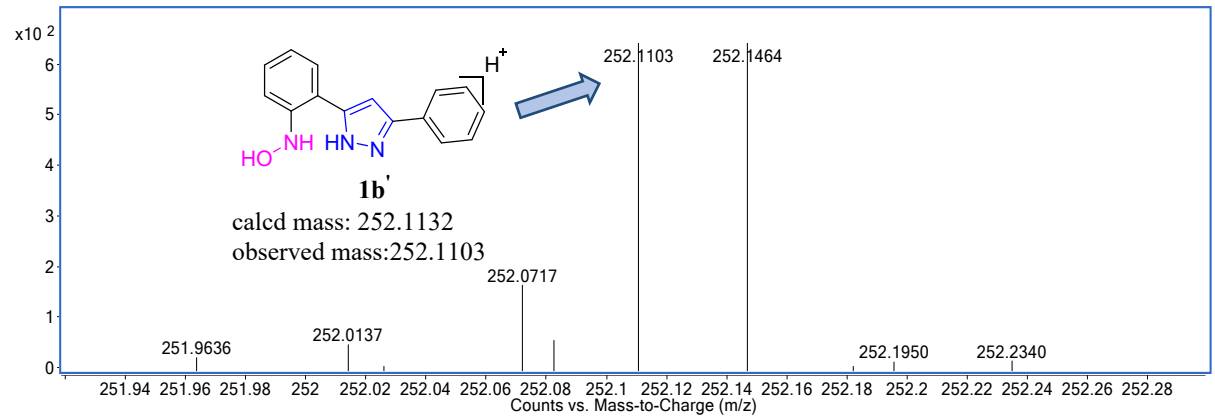
In order to identify the potential intermediates to support the proposed mechanism, we performed ESI-MS experiments with samples collected during the reaction process. The samples were withdrawn from the reaction tube, and the mass of the crude mixture was recorded at subsequent time intervals (0 sec, 30 sec, 1 min., 2 min., 5 min., and 10 min.) to predict the intermediates of the catalytic cycle. Initially, the mass peak of starting material **1** was observed at m/z 266.0920 $[M + H]^+$. Subsequently, *in situ* reduction and cyclization of 5-(2-nitrophenyl)-3-phenyl-1*H*-pyrazole **1a** was observed by the mass peaks of intermediates of **1a'** m/z 250.0986 $[M + H]^+$, **1b'** 252.1103 $[M + H]^+$, **1c'** 236.1166 $[M + H]^+$ and **1d'** 324.1468 $[M + H]^+$. Finally, the compound **3a** peak was observed at m/z 324.1468 $[M + H]^+$. In another instance, compound **1a** was reacted with carbon disulfide **4** and observed similar intermediates till the onward formation of intermediate **2d′**, which was observed at m/z 278.0736 $[M + H]^+$. Finally, the compound **5a** peak was observed at m/z 278.0736 $[M + H]^+$ **Fig. s1.**



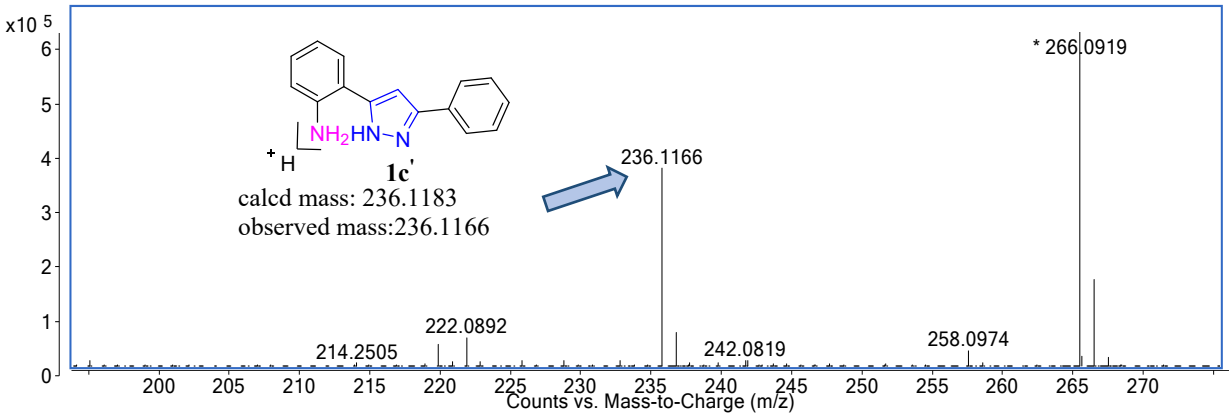
ESI-MS data of reaction mixture at 0 min



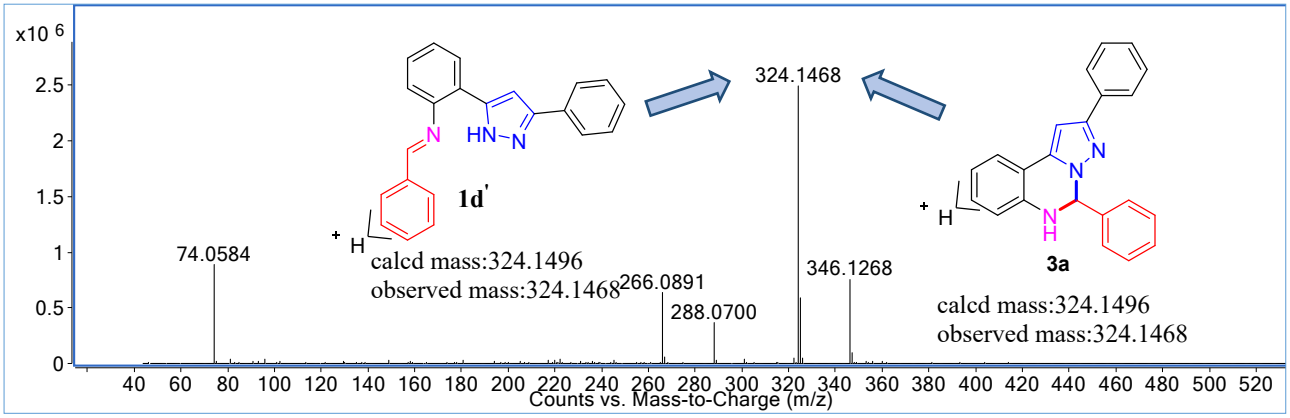
ESI-MS data of reaction mixture after 30 sec



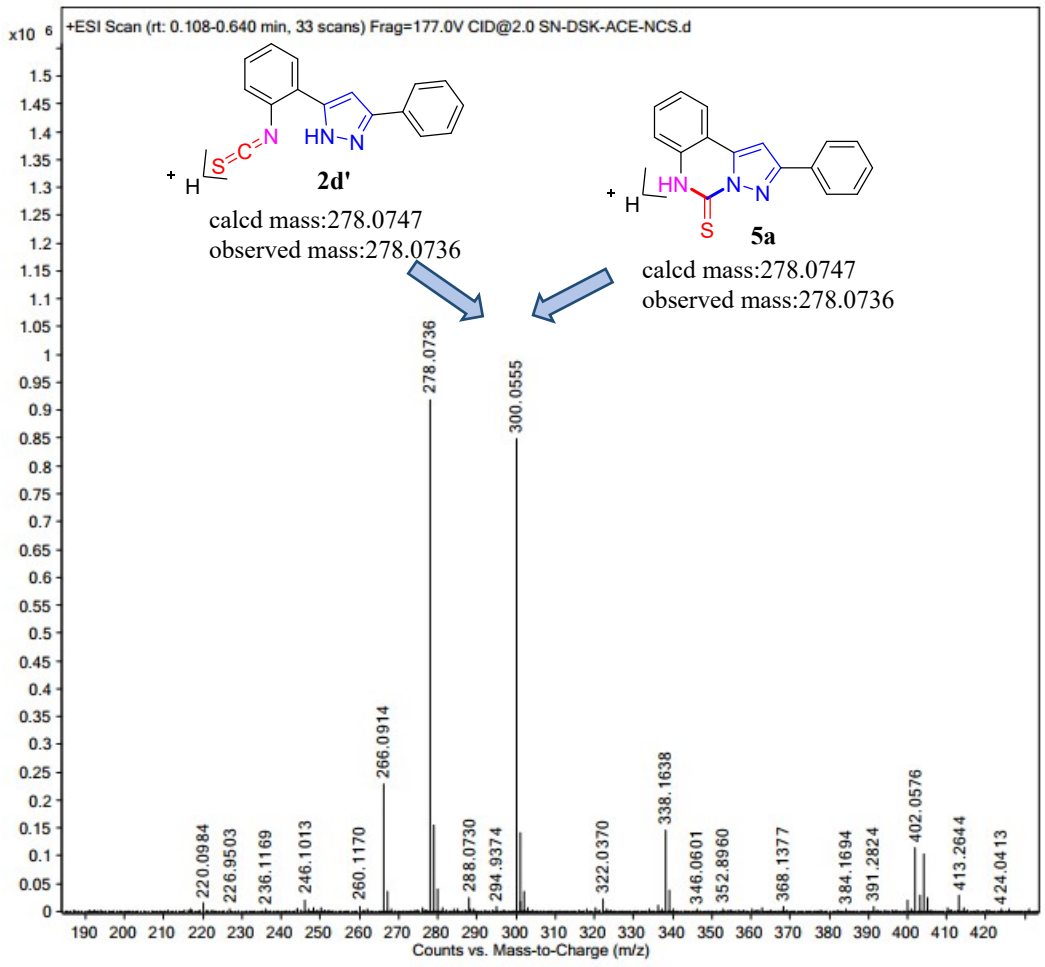
ESI-MS data of reaction mixture after 1min



ESI-MS data of reaction mixture after 2min



ESI-MS data of reaction mixture after 5min and 10 min



ESI-MS data of reaction mixture after 5min. and 10 min.

Figure S1: Trapping of key intermediates for the synthesis of compounds 3a and 5a by ESI- MS study.

5. DFT

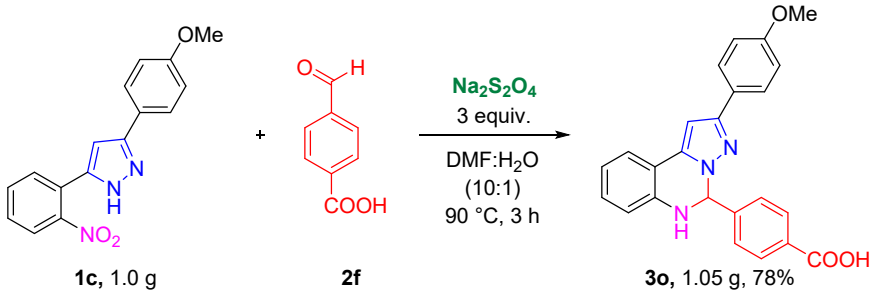
Table S1: Total energies of Pyrazolo[1,5-*c*]quinazoline intermediates

Structure	**E_0+G_{corr} (au)**
Reactant	-892.851
1a'	-817.649
1b'	-818.884

1c'	-743.716
1d'	-1012.409
3a(product)	-1012.433

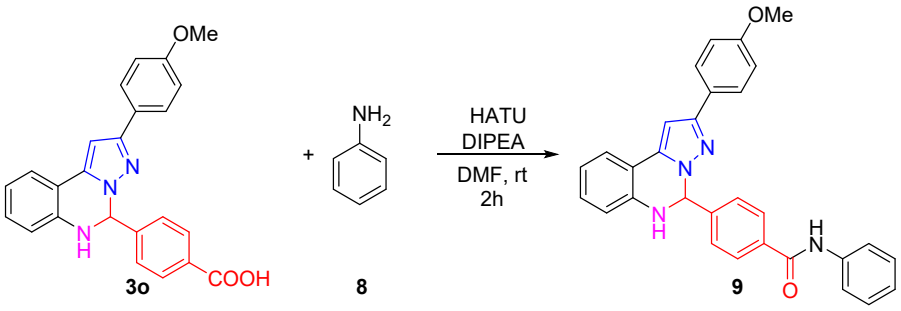
6. Gram scale synthesis and synthetic transformation of compound 1c

6.1 Gram scale synthesis



An oven-dried screw cap vial equipped with a magnetic stir bar was charged with 2-nitrophenyl pyrazole derivative **1c** (1.0 equiv., 3.39 mmol, 1 g), aldehyde derivative **2f** (1.1 equiv., 3.73 mmol, 0.559 g) and $Na_2S_2O_4$ (3.0 equiv., 10.16 mmol, 1.77 g) in DMF: water (11 mL,10:1 v/v) was heated at 90 °C for 3 hours. Upon completion of the reaction, the reaction mixture was poured into crushed ice and the resultant precipitate was filtered. The resulting crude residue was purified by column chromatography on silica gel (100-200 mesh) using a gradient of ethyl acetate and hexane (40:60) to afford the desired product **3o** (1.05 g, 78%)

6.2 Synthetic transformation of pyrazolo[1,5-c]quinazoline product 3o



A solution of 4-(2-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazolin-5-yl)benzoic acid **3o** (1.0 equiv., 0.25 mmol, 0.1 g) and hexafluorophosphate azabenzotriazole tetramethyluranium (HATU) (1.2 equiv., 0.30 mmol, 0.11 g) in dimethylformamide (DMF) for 20 min. Subsequently, aniline **8** (0.035g, 0.37 mmol, 1.5 equiv.) was added along with

diisopropylethylamine (DIPEA) (2.0 equiv., 0.50 mmol, 0.08 mL,), and the solution was stirred again for 2 hours at ambient temperature. After the completion of the reaction, crushed ice was added to the reaction mixture to get a thick precipitate to afford the desired product 4-[2-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*] quinazolin-5-yl]-*N*-phenylbenzamide **9** (0.11 g, 92%).

7. Photophysical study

The emission experiments were performed in a 3.0 mL quartz cuvette in an Agilent F-4700 fluorescence spectrophotometer (HITACHI). The emission slit widths were 10 nm each, while the scanning speed was 1200 nm per minute with 10 millisecond integration time. The resulting data were plotted as fluorescence intensity versus wavelength plots. The fluorescence emission spectrum of compounds at 5 µM was recorded in ACN and MeOH. The emission wavelength for pyrazolo[1,5-*c*]quinazoline compounds **3a**, **3c**,**3d** and **3f** in ACN and MeOH ranged from 388.8-399.2 nm and 399.2-401.8nm. Whereas pyrazolo[4,3-*c*]quinoline compounds **7a**, **7b**, **7c** and **7d** in ACN and MeOH ranged from 385.8-473.4 nm and 368.8-482.4 nm respectively.

8. Antibiotic susceptibility testing against ESKAP pathogen panel (Anti-bacterial activity)

Antibiotic susceptibility testing was carried out on the newly synthesized compounds by determining the Minimum Inhibitory Concentration (MIC) according to the standard CLSI guidelines.[3,4] MIC is defined as the minimum concentration of compound at which visible bacterial growth is inhibited. Bacterial cultures were grown in Mueller-Hinton cation supplemented broth (CA-MHB). Optical density (OD600) of the cultures was measured, followed by dilution for ~106 CFU/mL. This inoculum was added into a series of test wells in a microtitre plate that contained various concentrations of the compound under test ranging from 64-0.03 μg/mL. Controls i.e., cells alone and media alone (without compound+cells) and Levofloxacin (LVX) used as a reference standard. Plates were incubated at 37 °C for 16-18 h followed by observations of MIC values by the absence or presence of visible growth. For each compound, MIC determinations were performed independently thrice using duplicate samples each time.

9. X-ray Crystallographic studies

Crystal structure determination of compound **3l**

Single crystals of compound **3l** ($C_{23}H_{19}N_3O$) were obtained at room temperature by slow solvent evaporation from the ethanol solution, in which the compound was saturated earlier. A suitable block shaped crystal was selected and mounted on nylon cryoloop using paratone oil and the data was collected on a Bruker D8 Quest diffractometer equipped with Iμs3.0 Mo microfocus source and Photon III C14 CPAD detector. The crystal was kept at rt (~298 K) during data collection. Using Olex2[5], the structure was solved with the olex2[6].solve structure solution program using Charge Flipping and refined with the ShelXL refinement package using Least Squares minimisation.

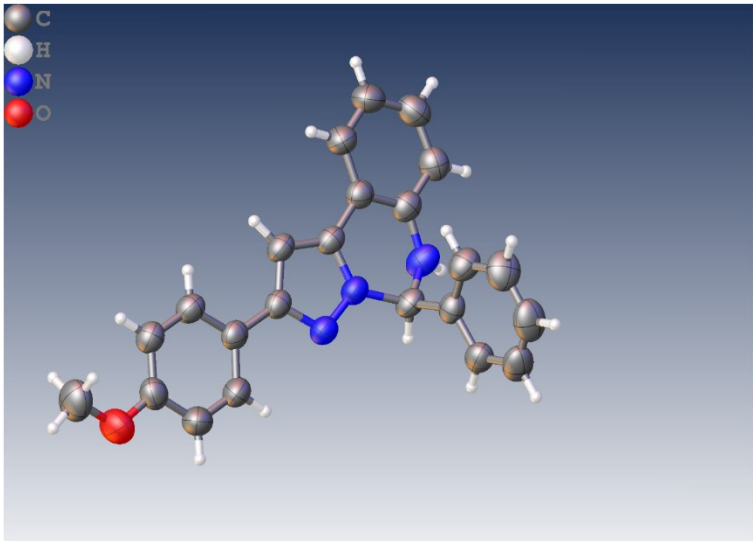


Figure S2. View of three-dimensional molecular structure of **3l** (ORTEP with 50 % probability ellipsoids).

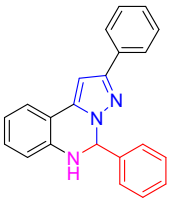
Table S3 Crystal data and structure refinement for compound 3l.

CCDC deposition number	2409299
Identification code	**3l**
Empirical formula	$C_{23}H_{19}N_3O$
Formula weight	353.41
Temperature/K	298
Crystal system	triclinic
Space group	P-1
a/Å	11.5160(10)
b/Å	13.0682(12)
c/Å	13.6833(14)
α/°	71.107(3)
β/°	77.855(3)

γ/°	71.037(3)
Volume/Å^3	1829.8(3)
Z	4
ρ_{calc}g/cm^3	1.283
μ/mm^{-1}	0.080
F(000)	744.0
Crystal size/mm^3	0.694 × 0.203 × 0.095
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.974 to 49.998
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 15, -16 ≤ l ≤ 16
Reflections collected	74168
Independent reflections	6439 [Rint = 0.0604, Rsigma = 0.0313]
Data/restraints/parameters	6439/0/489
Goodness-of-fit on F^2	1.106
Final R indexes [I>=2σ (I)]	R1 = 0.0470, wR2 = 0.1427
Final R indexes [all data]	R1 = 0.0623, wR2 = 0.1563
Largest diff. peak/hole / e Å^{-3}	0.22/-0.36

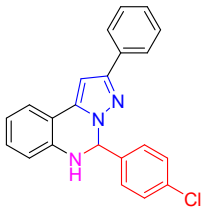
10. Experimental data

2,5-Diphenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3a)



Benzaldehyde (66mg, 0.41mmol) was used to synthesize compound **3a**; purification: hexane: ethyl acetate (85:15); color: white solid; yield: 94% (115mg); m.p. 152-154 °C. ^{1}H NMR (500 MHz, DMSO-d_6) ^{1}H NMR (500 MHz, DMSO) δ 7.81 (d, J = 7.8 Hz, 2H), 7.58 (d, J = 7.5 Hz, 1H), 7.44 (s, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.34 – 7.27 (m, 4H), 7.22 (d, J = 1.7 Hz, 2H), 7.21 (s, 1H), 7.13 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.1 Hz, 1H), 6.79 (d, J = 7.5 Hz, 1H), 6.77 (s, 1H).; ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) 150.8, 141.1, 140.2, 138.5, 133.1, 129.6, 128.8, 128.5, 128.5, 127.8, 126.1, 125.3, 124.0, 118.4, 114.9, 112.8, 96.8, 70.9. HRMS (ESI): *m/z* calculated for $C_{22}H_{17}N_3$ 324.1496[M + H]$^+$; found 324.1508.

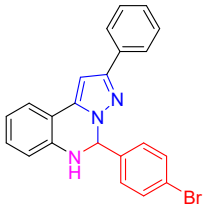
5-(4-Chlorophenyl)-2-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3b)



4-Chlorobenzaldehyde (58mg, 0.41mmol) was used to synthesize compound **3b**; purification: hexane: ethyl acetate (88:12); color: off-white solid; yield: 86% (117mg); m.p. 124-126 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.81 (d, J = 6.7 Hz, 2H), 7.58 (d, J = 9.2 Hz, 1H), 7.47 (d, J = 2.3 Hz, 1H), 7.44 –7.38 (m, 4H), 7.35 – 7.28 (m, 1H), 7.24 (s, 1H)7.23 (d, J = 8.7 Hz, 2H), 7.14 (t, J = 8.5 Hz, 1H), 6.87 (d, J = 6.9 Hz, 1H), 6.83-6.77 (m, 2H); ^{13}C {^{1}H} NMR

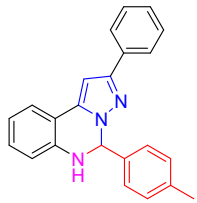
(125 MHz, DMSO-d_6): δ 150.9, 140.0, 139.9, 138.4, 133.1, 133.0, 129.6, 128.7, 128.5, 128.1, 127.8, 125.2, 123.9, 118.5, 114.9, 112.8, 96.9, 70.1. HRMS (ESI): *m/z* calculated for $C_{22}H_{16}ClN_3$ 358.1106 $[M+H]^+$; found 358.1097.

5-(4-Bromophenyl)-2-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3c)



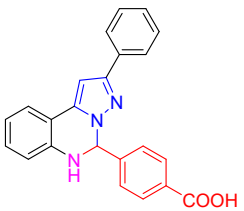
4-Bromobenzaldehyde (77mg, 0.41mmol) was used to synthesize compound **3c**; purification: hexane: ethyl acetate (90:10); color: brown solid; yield: 82% (125mg); m.p. 132-134 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 7.6 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 2.3 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 6.7 Hz, 1H), 7.22 (s, 1H), 7.17 (d, J = 8.5 Hz, 2H), 7.13 (d, J = 8.1 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 6.79 (d, J = 1.4 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 151.0, 140.4, 140.0, 138.5, 133.0, 131.5, 129.7, 129.0, 128.4, 127.9, 125.3, 124.0, 121.8, 118.7, 115.0, 112.8, 96.9, 70.3; HRMS (ESI): *m/z* calculated for $C_{22}H_{16}BrN_3$ 402.0600 $[M+H]^+$; found 402.0568 $[M+H]^+$, 404.0551 [M + 2].

2-Phenyl-5-(p-tolyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3d)



4-Methylbenzaldehyde (50mg, 0.41mmol) was used to synthesize compound **3d**; purification: hexane: ethyl acetate (80:20); color: off-white solid; yield: 95% (121mg); m.p. 174-176 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 (d, J = 8.7 Hz,2H), 7.57 (d, J = 9.2 Hz,1H), 7.41 (d, J = 7.5 Hz, 2H), 7.39 (d, J = 2.3 Hz, 1H), 7.31 (t, J = 7.3 Hz, 1H), 7.19 (s, 1H), 7.15 – 7.07 (m, 5H), 6.85 (d, J = 7.9 Hz, 1H), 6.78 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 1.1 1H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 150.6, 140.3, 138.4, 138.2, 137.7, 133.1, 129.5, 129.0, 129.0, 127.7, 126.0, 125.2, 123.8, 118.3, 114.8, 112.8, 96.7, 70.8, 20.7; HRMS (ESI): *m/z* calculated for $C_{23}H_{19}N_3$ 338.1652 $[M+H]^+$; found 338.1669.

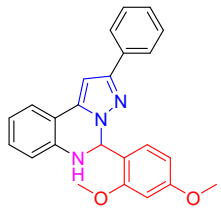
4-(2-Phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazolin-5-yl) benzoic acid (3e)



4-Formylbenzoic acid (62mg, 0.41mmol) was used to synthesize compound **3e**; purification: hexane: ethyl acetate (55:45); color: buff solid; yield: 79% (110mg); m.p. 263-265 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.96 (s, 1H), 7.89 (d, J = 8.4 Hz, 2H), 7.81 (d, J = 6.7 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.32 (d, J = 8.4 Hz, 3H), 7.24 (s, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.87 (d, J = 3.1 Hz, 1H), 6.86 (d, J = 1.2 Hz, 1H), 6.80 (t, J =

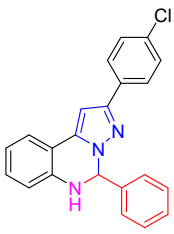
7.5 Hz, 1H); 13C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 166.9, 150.9, 145.5, 139.9, 138.5, 133.0, 130.9, 129.6, 129.6, 128.7, 127.8, 126.3, 125.2, 123.9, 118.5, 114.9, 112.7, 96.9, 70.4; HRMS (ESI): *m/z* calculated for $C_{23}H_{17}N_3O_2$ 368.1394 $[M+H]^+$; found 368.1380.

5-(2,4-Dimethoxyphenyl)-2-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3f)



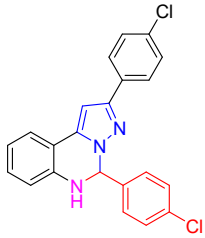
2,4-Dimethoxybenzaldehyde (69mg, 0.41mmol) was used to synthesize compound **3f**; purification: hexane: ethyl acetate (60:40); color: white solid; yield: 92% (133mg); m.p. 193-195 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (d, J = 9.6 Hz, 2H), 7.57 (d, J = 9.3 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.36 (d, J = 2.1 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.19 (s,1H), 7.16 – 7.09 (m, 1H), 7.01 (d, J = 2.1 Hz,1H), 6.86 (t, J = 8.5 Hz,2H), 6.78 (d, J = 6.3 Hz, 1H), 6.67 (d, J = 2.0 Hz,1H), 6.59 (d, J = 10.5 Hz, 1H), 3.68 (s, 3H), 3.67 (s, 3H); 13C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 151.0, 149.3, 149, 140.9, 138.9, 133.7, 133.6, 129.9, 129.2, 128.2, 125.6, 124.3, 118.8, 118.7, 115.3, 113.4, 111.9, 110.7, 97.1, 71.2, 57.0, 56.0; HRMS (ESI): *m/z* calculated for $C_{24}H_{21}N_3O_2$ 384.1707 $[M+H]^+$; found 384.1697.

2-(4-Chlorophenyl)-5-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3g)



Benzaldehyde (39mg, 0.36mmol) was used to synthesize compound **3g**; purification: hexane: ethyl acetate (90:10); color: white solid; yield: 87% (104mg); m.p. 124-126 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (d, J = 6.7 Hz, 2H), 7.58 (d, J = 9.2 Hz, 1H), 7.47 (d, J = 2.3 Hz, 1H), 7.35 – 7.28 (m, 4H) , 7.32 (t, J= 7.3 Hz, 1H), 7.23 (d, J = 6.4 Hz, 3H), 7.14 (t, J = 8.5 Hz, 1H), 6.87 (d, J = 6.9 Hz, 1H), 6.81 (d, J = 7.3 Hz, 1H), 6.79 (d, J = 6.3 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 150.9, 140.0, 139.9, 138.4, 133.1, 133.0, 129.6, 128.7, 128.5, 128.1, 127.8, 125.2, 123.9, 118.5, 114.9, 112.8, 97.0, 70.1; HRMS (ESI): *m/z* calculated for $C_{22}H_{16}ClN_3$ 358.1106 $[M+H]^+$; found 358.1097.

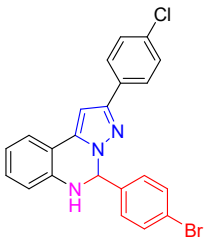
2,5-Bis(4-Chlorophenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3h)



4-Chlorobenzaldehyde (52mg, 0.36mmol) was used to synthesize compound **3h**; purification: hexane: ethyl acetate (95:5); color: yellow solid; yield: 84% (110mg); m.p. 168-170 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.82 (d, J = 8.5 Hz, 2H), 7.57 (d, J = 7.6 Hz, 1H), 7.47 (d, J= 8.7 Hz, 3H), 7.41 (d, J = 8.5 Hz, 2H), 7.25 (t, J = 8.1 Hz, 3H), 7.14 (t, J = 7.7 Hz,

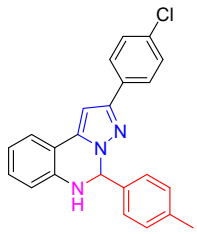
1H), 6.87 (d, J = 8.2 Hz, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.79 (d, J = 2.0 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 150.2, 140.5, 140.2, 139.1, 133.6, 132.7, 132.4, 130.2, 129.2, 129.0, 129.0, 127.4, 124.4, 119.0, 115.4, 113.1, 97.5, 70.7; HRMS (ESI): *m/z* calculated for $C_{22}H_{15}Cl_2N_3$ 392.0704 $[M + H]^+$, found 392.0705.

5-(4-Bromophenyl)-2-(4-chlorophenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3i)



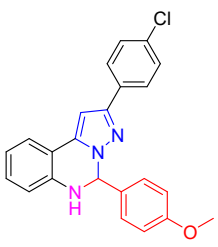
4-Bromobenzaldehyde (68mg, 0.36mmol) was used to synthesize compound **3i**; purification: hexane: ethyl acetate (95:5); color: white solid; yield: 79% (115mg); m.p. 190-192 °C; ^{1}H NMR (500 MHz, DMSO- d_6) δ 7.82 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 7.4 Hz, 1H), 7.54 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 8.3 Hz, 3H), 7.25 (s, 1H), 7.18 (d, J = 8.3 Hz, 2H), 7.14 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.78 (d, J = 7.6 Hz, 1H); 13C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 149.7, 140.1, 140.0, 138.6, 132.2, 131.9, 131.4, 129.7, 128.7, 128.4, 126.9, 123.9, 121.7, 118.5, 114.9, 112.6, 97.0, 70.2; HRMS (ESI): *m/z* calculated for $C_{22}H_{15}BrClN_3$ 436.0216 $[M + H]^+$, found 436.0201.

2-(4-Chlorophenyl)-5-(p-tolyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3j)



4-Methylbenzaldehyde (44mg, 0.36mmol) was used to synthesize compound **3j**; purification: hexane: ethyl acetate (90:10); color: off-white solid; yield: 88% (104mg); m.p. 175-177 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 9.2 Hz, 1H), 7.46 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 2.1 Hz, 1H), 7.22 (s, 1H), 7.13 (d, J = 8.2 Hz, 1H), 7.11 (d, J = 8.2 Hz, 4H), 6.86 (d, J = 7.6 Hz, 1H), 6.78 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 2.0 Hz, 1H), 2.24 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 149.5, 140.3, 138.6, 137.9, 137.8, 132.1, 132.0, 129.5, 128.9, 128.7, 126.8, 126.1, 123.8, 118.3, 114.8, 112.7, 96.8, 70.8, 20.7; HRMS (ESI): *m/z* calculated for $C_{23}H_{18}ClN_3$ 372.1268 $[M + H]^+$, found 372.1251.

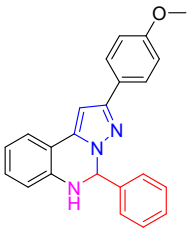
2-(4-Chlorophenyl)-5-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3k)



4-Methoxybenzaldehyde (50mg, 0.36mmol) was used to synthesize compound **3k**; purification: hexane: ethyl acetate (80:20); color: off-white solid; yield: 91% (118 mg); m.p. 195-197 °C; ^{1}H NMR (500 MHz, DMSO- d_6) δ 7.81 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 6.4 Hz, 1H), 7.46 (d, J = 8.5 Hz, 2H), 7.36 (s, 1H), 7.21 (s, 1H), 7.17 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.9 Hz, 1H), 6.87 (t, J =

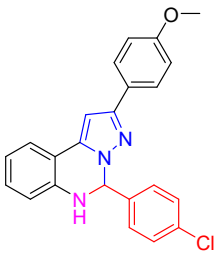
8.2 Hz, 3H), 6.79 (t, J = 7.6 Hz, 1H), 6.68 (s, 1H), 3.70 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 159.4, 149.4, 140.4, 138.5, 132.8, 132.1, 132.0, 129.5, 128.7, 127.6, 126.82, 123.8, 118.3, 114.8, 113.8, 112.6, 96.8, 70.7, 55.1. HRMS (ESI): *m/z* calculated for $C_{23}H_{18}ClN_3O$ 388.1212, found 388.1201$[M+H]^+$.

2-(4-Methoxyphenyl)-5-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3l)



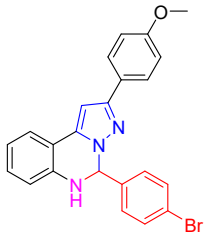
Benzaldehyde (40mg, 0.37mmol) was used to synthesize compound **3l**; purification: hexane: ethyl acetate (80:20); color: white solid; yield: 91% (109mg); m.p. 150-152 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.73 (d, J = 8.9 Hz, 2H), 7.56 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 2.3 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.20 (d, J = 9.9 Hz, 2H), 7.12 (s, 1H), 6.97 (d, J = 9.0 Hz,2H), 6.85 (d, J = 9.3 Hz, 1H), 6.78 (t, J = 6.1 Hz, 1H), 6.73 (d, J = 2.1 Hz, 1H), 3.77 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 159.0, 150.6, 141.2, 140.2, 138.3, 129.4, 128.4, 128.4, 126.5, 126.1, 125.8, 123.8, 118.3, 114.7, 114.1, 112.8, 96.1, 70.8, 55.1. HRMS (ESI): *m/z* calculated for $C_{23}H_{19}N_3O$ 354.1601 $[M+H]^+$; found 354.1602.

5-(4-Chlorophenyl)-2-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3m)



4-Chlorobenzaldehyde (52mg, 0.37mmol) was used to synthesize compound **3m**; purification: hexane: ethyl acetate (85:15); color: buff solid; yield: 79% (104 mg); m.p. 193-195 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.73 (d, J = 8.9 Hz, 2H), 7.56 (d, J = 9.3 Hz, 1H), 7.44 (d, J = 2.4 Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.7 Hz, 2H), 7.14-7.10 (m, 2H), 6.97 (d, J = 8.9 Hz, 2H), 6.85 (d, J = 8.1 Hz, 1H), 6.80 (d, J = 7.5 Hz, 1H), 6.77 (d, J = 2.1 Hz, 1H), 3.78 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.0, 150.8, 140.0, 140.0, 138.3, 133.0, 129.5, 128.5, 128.1, 126.5, 125.7, 123.9, 118.5, 114.8, 114.1, 112.8, 96.3, 70.1, 55.1; HRMS (ESI): *m/z* calculated for $C_{23}H_{18}ClN_3O$ 388.1212, found 388.1201$[M+H]^+$.

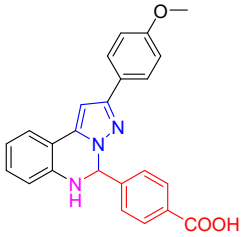
5-(4-Bromophenyl)-2-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3n)



4-Bromobenzaldehyde (69mg, 0.37mmol) was used to synthesize compound **3n**; purification: hexane: ethyl acetate (90:10); color: off-white solid: yield: 85% (124mg); m.p. 163-165 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.73 (d, J = 9.0 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.53 (d, J = 8.5 Hz, 2H), 7.44 (d, J

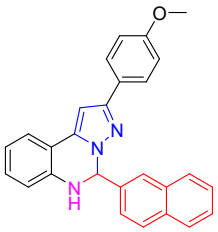
= 2.3 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.13 (s, 1H), 7.11 (d, *J* = 1.5 Hz, 1H), 6.97 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.75 (d, *J* = 2.3 Hz, 1H), 3.78 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 159.0, 150.8, 140.4, 139.9, 138.3, 131.4, 129.5, 128.4, 126.5, 125.7, 123.9, 121.7, 118.5, 114.8, 114.1, 112.8, 96.3, 70.1, 55.1; HRMS (ESI): *m/z* calculated for $C_{23}H_{18}BrN_3O$ 432.0706 $[M+H]^+$; found 432.0695.

4-(2-(4-Methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazolin-5-yl) benzoic acid (3o)



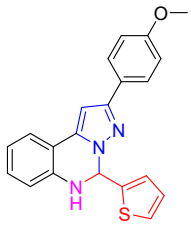
4-Formylbenzoic acid (56 mg, 0.37mmol) was used to synthesize compound **3o**; purification: hexane: ethyl acetate (40:60); color: buff solid; yield: 83% (112mg); m.p. 250-252 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.97 (s, 1H), 7.89 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 6.7 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 2.3 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.14 (s, 1H), 7.13 – 7.10 (m, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 1H), 6.83 (d, *J* = 2.1 Hz, 1H), 6.79 (t, *J* = 8.1 Hz, 1H), 3.77 (s, 3H); 13C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 166.9, 159.1, 150.9, 145.6, 139.9, 138.4, 130.9, 129.6, 129.5, 126.6, 126.3, 125.7, 123.9, 118.5, 114.8, 114.1, 112.8, 70.4, 55.1; HRMS (ESI): *m/z* calculated for $C_{24}H_{19}N_3O_3$ 398.1499 $[M+H]^+$; found 398.1488.

2-(4-Methoxyphenyl)-5-(naphthalen-2-yl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3p)



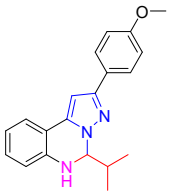
Napthaldehyde (58mg, 0.37mmol) was used to synthesize compound **3p**; purification: hexane: ethyl acetate (90:10); color: white solid; yield: 92% (122mg); m.p. 164-166 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (d, *J* = 7.5 Hz, 1H), 7.95 (dd, *J* = 21.9, 8.4 Hz, 2H), 7.63 (d, *J* = 8.9 Hz, 3H), 7.61-7.53 (m, 2H), 7.47 (s, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.33 (s, 1H), 7.19 (s, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.80 (t, *J* = 7.2 Hz, 1H) 6.79 (d, *J* = 2.4 Hz, 1H), 3.74 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 158.9, 150.7, 140.3, 139.0, 135.5, 133.7, 130.1, 129.4, 129.2, 128.6, 126.4, 126.3, 125.9, 125.7, 125.2, 124.7, 124.2, 123.9, 118.2, 114.8, 114.0, 112.6, 96.0, 69.3, 55.1; HRMS (ESI): *m/z* calculated for $C_{27}H_{21}N_3O$ 404.1757 $[M+H]^+$; found 404.1746.

2-(4-Methoxyphenyl)-5-(thiophen-3-yl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3q)



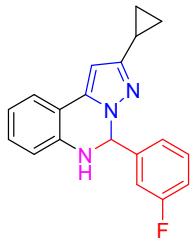
Thiophene-2-carbaldehyde (92mg, 0.37mmol) was used to synthesize compound **3q**; purification: hexane: ethyl acetate (70:30); color: yellow solid: yield: 75% (92 mg); m.p. 176-178 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.75 (d, J = 9.0 Hz, 2H), 7.56 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 2.4 Hz, 1H), 7.38 (dd, J = 5.0, 1.3 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.09 (s, 1H), 7.07 (d, J = 3.5 Hz, 1H), 7.02 (d, J = 2.0 Hz, 1H), 6.98 (d, J = 8.9 Hz, 2H), 6.94 – 6.90 (m, 2H), 6.82 (t, 1H), 3.78 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 159.1, 150.8, 144.3, 139.8, 137.8, 129.5, 126.6, 126.5, 126.4, 125.8, 125.5, 123.8, 118.8, 115.2, 114.1, 113.0, 96.4, 67.2, 55.2. HRMS (ESI): *m/z* calculated for $C_{21}H_{17}N_3OS$ 360.1165 $[M+H]^+$; found 360.1157.

5-Isopropyl-2-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3r)



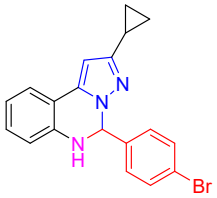
Isobutyraldehyde (55mg, 0.76mmol) was used to synthesize compound **3r**; purification: hexane: ethyl acetate (90:10); color: white solid. HRMS (ESI): *m/z* calculated for $C_{20}H_{21}N_3O$ 320.1758 $[M+H]^+$; found 320.1779. Due to the extremely low yield of compound **3r**, we are unable to perform the ^{1}H and ^{13}C NMR studies.

2-Cyclopropyl-5-(3-fluorophenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3s)



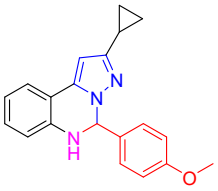
3-Fluorobenzaldehyde (60mg, 0.47mmol) was used to synthesize compound **3s**; purification: hexane: ethyl acetate (85:15); color: white solid; yield: 79% (105mg); m.p. 145-146 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.48 (d, J = 7.8 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.26 (d, J = 8.2 Hz, 1H), 7.22 (d, J = 8.9 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 11.7 Hz, 1H), 6.80 – 6.77 (m, 3H), 6.74 (t, J = 7.5 Hz, 1H), 6.41 (s, 1H), 1.87 – 1.75 (m, 1H), 0.85 (q, J = 2.6 Hz, 2H), 0.63 (q, J = 2.7 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.2 (d, J = 245 Hz, $^{1}J_{C\text{-}F}$), 155.3, 139.8, 138.0, 130.6 (d, J = 8.75 Hz, $^{2}J_{C\text{-}F}$), 129.2, 127.9 (d, J = 12.5 Hz, $^{3}J_{C\text{-}F}$), 127.5 (d, J = 3.75 Hz, $^{4}J_{C\text{-}F}$) , 124.5 (d, J = 3.75 Hz, $^{5}J_{C\text{-}F}$), 123.7, 118.3, 115.8 (d, J = 21.25 Hz, $^{6}J_{C\text{-}F}$) , 114.6, 112.6, 95.4, 65.3 (d, J = 5 Hz, $^{7}J_{C\text{-}F}$) , 9.2, 8.1, 8.0. HRMS (ESI): *m/z* calculated for $C_{19}H_{16}FN_3$ 306.1401 $[M+H]^+$; found 306.1416.

5-(4-Bromophenyl)-2-cyclopropyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3t)



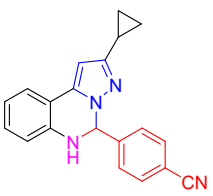
4-Bromobenzaldehyde (89mg, 0.47mmol) was used to synthesize compound **3t**; purification: hexane: ethyl acetate (90:10); color: white solid; yield: 73% (117mg); m.p. 178-180 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.52 (d, J = 8.5 Hz, 2H), 7.44 (dd, J = 7.7, 1.6 Hz, 1H), 7.31 (d, J = 2.3 Hz, 1H), 7.11 – 7.04 (m, 3H), 6.80 (dd, J = 8.1, 1.2 Hz, 1H), 6.73 (td, J = 7.5, 1.2 Hz, 1H), 6.57 (d, J = 2.1 Hz, 1H), 6.40 (s, 1H), 1.90 – 1.77 (m, 1H), 0.86 (q, J = 2.4 Hz, 2H), 0.65 (q, J = 2.5 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 155.3, 140.6, 134.0, 137.7, 131.5, 129.4, 128.5, 123.9, 121.8, 118.6, 114.9, 113.0, 95.9, 70.1, 9.4, 8.2. HRMS (ESI): *m/z* calculated for $C_{19}H_{16}BrN_3$ 366.0600 $[M+H]^+$; found 366.0591.

2-Cyclopropyl-5-(4-methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3u)



4-Methoxybenzaldehyde (65mg, 0.47mmol) was used to synthesize compound **3u**; purification: hexane: ethyl acetate (75:25); color: off-white solid; yield: 85% (118 mg); m.p. 167-169 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.42 (d, J = 6.1 Hz, 1H), 7.21 (d, J = 2.0 Hz, 1H), 7.10 – 7.03 (m, 3H), 6.86 (d, J = 8.7 Hz, 2H), 6.79 (dd, J = 8.1, 1.2 Hz, 1H), 6.71 (td, J = 7.5, 1.2 Hz, 1H), 6.48 (d, J = 1.9 Hz, 1H), 6.36 (s, 1H), 3.70 (s, 3H), 1.90 – 1.80 (m, 1H), 0.85 (q, J = 2.4 Hz, 2H), 0.64 (q, J = 2.4 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.3, 154.7, 140.3, 137.4, 133.3, 129.1, 127.5, 123.6, 118.1, 114.6, 113.7, 113.0, 95.4, 70.4, 55.1, 9.3, 8.0, 8.0; HRMS (ESI): *m/z* calculated for $C_{20}H_{19}N_3O$ 318.1601 $[M+H]^+$; found 318.1596.

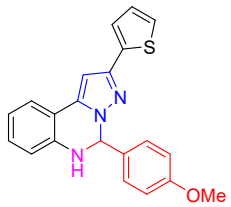
4-(2-Cyclopropyl-5,6-dihydropyrazolo[1,5-*c*]quinazolin-5-yl) benzonitrile (3v)



4-Cyanobenzaldehyde (63mg, 0.47mmol) was used to synthesize compound **3v**; purification: hexane: ethyl acetate (40:60); color: white solid; yield: 68% (93 mg); m.p. 217-219 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 (d, J = 8.5 Hz, 2H), 7.45 (d, J = 7.6 Hz, 1H), 7.42 (d, J = 2.4 Hz, 1H), 7.28 (d, J = 8.2

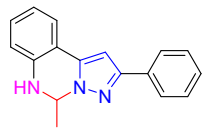
Hz, 2H), 7.11 – 7.05 (m, 1H), 6.80 (d, J = 1.2 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 2.3 Hz, 1H), 6.43 (s, 1H), 1.91–1.84 (m, 1H), 0.87 (q, J = 2.4 Hz, 2H), 0.66 (q, J = 2.1 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 156.1, 146.6, 139.8, 138.1, 133.0, 130.0, 127.4, 124.3, 119.3, 119.0, 115.3, 113.2, 111.6, 96.4, 70.3, 9.6, 8.7, 8.6. HRMS (ESI): *m/z* calculated for $C_{20}H_{16}N_4$ 313.1448 $[M + H]^+$; found 313.1439.

5-(4-Methoxyphenyl)-2-(thiophen-2-yl)-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3w)



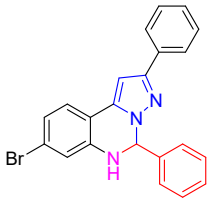
4-Methoxybenzaldehyde (55mg, 0.47mmol) was used to synthesize compound **3w**; purification: hexane: ethyl acetate (60:40); color: brown solid; yield: 82% (109mg); m.p. 194-196 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.55 (d, J = 9.3 Hz, 1H), 7.46 (dd, J = 5.1, 1.1 Hz, 1H), 7.43 (dd, J = 3.5, 1.2 Hz, 1H), 7.36 (d, J = 2.1 Hz, 1H), 7.13 (d, J = 8.9 Hz, 2H), 7.11 (d, J = 3.1 Hz, 1H), 7.10 – 7.08 (m, 1H), 7.07 (s, 1H), 6.87 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 9.3 Hz, 1H), 6.77 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 3.70 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 159.3, 146.3, 140.4, 138.4, 136.3, 133.0, 127.7, 127.4, 125.0, 124.1, 123.9, 118.2, 114.8, 113.8, 112.5, 96.50 70.5, 55.1; HRMS (ESI): *m/z* calculated for $C_{21}H_{17}N_3OS$ 360.1165 $[M + H]^+$; found 360.1157.

5-Methyl-2-phenyl-5,6-dihydropyrazolo[1,5-*c*]quinazoline (3x)



Acetaldehyde (27mg, 0.62mmol) was used to synthesize compound **3x**; purification: hexane: ethyl acetate (95:05); color: white solid; yield: 40% (59mg); m.p. 108-110 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.86 – 7.82 (m, 2H), 7.53 (dd, J = 7.6, 1.5 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.34 – 7.29 (m, 1H), 7.16 – 7.12 (m, 1H), 7.11 (s, 1H), 6.87 – 6.82 (m, 2H), 6.79 (td, J = 7.5, 1.1 Hz, 1H), 5.59 (qd, J = 5.7, 1.2 Hz, 1H), 1.67 (d, J = 5.8 Hz, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO- d_6) δ 150.20, 141.13, 137.99, 133.31, 129.26, 128.62, 127.54, 125.09, 123.78, 118.32, 114.66, 113.15, 96.68, 65.52, 20.61. HRMS (ESI): *m/z* calculated for $C_{17}H_{15}N_3$ 262.1339 $[M + H]^+$; found 262.1340.

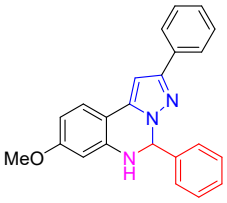
8-Bromo-2,5-diphenyl-5,6-dihydropyrazolo[1,5-*c*] quinazoline (3y)



Benzaldehyde (51mg, 0.48mmol) was used to synthesize compound **3x**; purification: hexane: ethyl acetate (95:05); color: off-white solid; yield: 33% (58mg); m.p. 151-153 °C ; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.83 – 7.75 (m, 2H), 7.68 (d, J = 2.3 Hz, 1H), 7.54 (d, J = 8.2 Hz, 1H), 7.41 (t, J = 7.6 Hz,

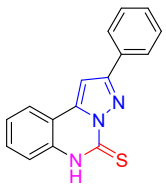
2H), 7.37 – 7.29 (m, 4H), 7.26 (s, 1H), 7.21 (dd, J = 8.2, 1.6 Hz, 2H), 7.05 (d, J = 2.0 Hz, 1H), 6.95 (dd, J = 8.2, 1.9 Hz, 1H), 6.83 (d, J = 2.0 Hz, 1H).; ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 151.41, 142.09, 141.18, 138.03, 133.37, 129.16, 129.08, 129.05, 128.31, 126.49, 126.08, 125.66, 122.59, 121.31, 117.26, 112.31, 97.62, 71.08. HRMS (ESI): *m/z* calculated for $C_{22}H_{16}BrN_3$ 402.0601 $[M+H]^+$; found 402.0602.

8-Methoxy-2,5-diphenyl-5,6-dihydropyrazolo[1,5-*c*] quinazoline (3y)



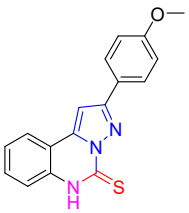
Benzaldehyde (38mg, 0.35mmol) was used to synthesize compound **3y**; purification: hexane: ethyl acetate (80:20); color: brown solid; HRMS (ESI): *m/z* calculated for $C_{23}H_{19}N_3O$ 354.1601 $[M+H]^+$; found 354.1608. Due to the extremely low yield of compound 3r, we are unable to perform the ^{1}H and ^{13}C NMR studies.

2-Phenylpyrazolo[1,5-*c*]quinazoline-5(6*H*)-thione (5a)



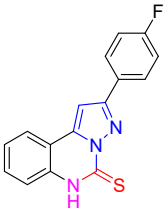
Purification: hexane: ethyl acetate (85:15) was used to synthesize compound **5a**; color: buff solid; yield: 88% (92mg); m.p. 272-274 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.54 (s, 1H), 8.14 (d, J = 7.9 Hz, 1H), 8.07 (d, J = 7.5 Hz, 2H), 7.92 (s, 1H), 7.65 – 7.58 (m, 2H), 7.56 (t, J = 7.6 Hz, 2H), 7.51 – 7.44 (m, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 167.5, 155.9, 138.5, 133.0, 131.5, 130.7, 129.6, 129.0, 126.5, 125.1, 124.0, 116.0, 114.0, 99.0; HRMS (ESI): *m/z* calculated for $C_{16}H_{11}N_3S$ 278.0746 $[M+H]^+$; found 278.0736.

2-Cyclopropylpyrazolo[1,5-*c*]quinazoline-5(6*H*)-thione (5b)



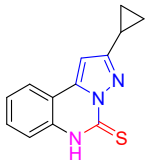
Purification: hexane: ethyl acetate (75:25) was used to synthesize compound **5b**; color: buff solid; yield: 91% (95mg); m.p. 242-244 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.34 (s, 1H), 7.85 (s, 1H), 7.75 (d, J = 8.5 Hz, 2H), 7.67 – 7.58 (m, 3H), 7.05 (d, J = 8.5 Hz, 2H), 6.77 (t, J = 7. Hz, 1H), 3.81 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 160.4, 159.3, 138.5, 133.0, 130.7, 128.0, 127.4, 126.7, 124.0, 119.5, 117.8, 116.7, 114.5, 99.5, 55.3. HRMS (ESI): m/z calculated for $C_{17}H_{13}N_3OS$ 308.0853 $[M+H]^+$; found 308.0830.

2-(4-Fluorophenyl) pyrazolo[1,5-*c*]quinazoline-5(6*H*)-thione (5c)



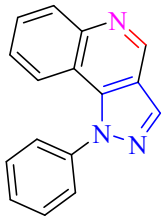
Purification: hexane: ethyl acetate (80:20) was used to synthesize compound **5c**; color: brown solid; yield: 82% (89mg); m.p. 266-268 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.54 (s, 1H), 8.11 (s, 3H), 7.90 (s, 1H), 7.61 (s, 2H), 7.43 (d, J = 34.6 Hz, 3H); 13C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 167.3, 163.7, 161.8, 154.8, 138.5, 132.9, 130.6, 128.5, 128.0, 125.0, 123.9, 116.0, 115.8, 113.8, 98.8. HRMS (ESI): *m/z* calculated for $C_{16}H_{10}FN_3S$ 296.0653 $[M+H]^+$; found 296.0654.

2-Cyclopropylpyrazolo[1,5-*c*]quinazoline-5(6*H*)-thione (5d)



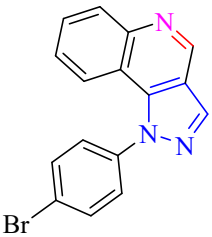
Purification: hexane: ethyl acetate (70:30) was used to synthesize compound **5d**; color: yellow solid; yield: 76% (80mg); m.p. 284-286 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.35 (s, 1H), 8.01 (d, J = 7.5 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.40 (t, J = 6.4 Hz, 1H), 7.09 (s, 1H), 2.20 – 2.12 (m, 1H), 1.08 (q, J = 2.4 Hz, 2H), 0.88 (q, J = 2.4 Hz, 2H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 167.3, 161.9, 137.8, 133.0, 130.6, 125.1, 124.0, 116.0, 113.9, 98.2, 9.7, 9.1; HRMS (ESI): *m/z* calculated for $C_{13}H_{11}N_3S$ 242.0746 $[M+H]^+$; found 242.0740.

1-Phenyl-1*H*-pyrazolo[4,3-*c*]quinoline (7a)



Purification: hexane: ethyl acetate (80:20) was used to synthesize compound **7a**; color: buff solid; yield: 92% (115mg); m.p. 217-219 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.44 (s, 1H), 9.28 (s, 1H), 8.49 (d, J = 9.5 Hz, 1H), 8.16 (d, J = 8.2 Hz, 2H), 8.06 (d, J = 8.1 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.72-7.63 (m, 3H), 7.50 (t, J = 7.4 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) 147.0, 146.6, 143.8, 139.0, 129.2, 129.0, 128.3, 127.7, 126.6, 124.7, 121.3, 119.9, 119.1, 116.4. HRMS (ESI): *m/z* calculated for $C_{16}H_{11}N_3$ 246.1026 $[M+H]^+$; found 246.1025.

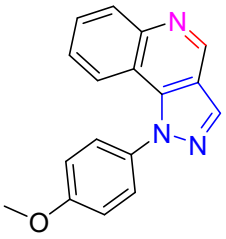
1-(4-Bromophenyl)-1*H*-pyrazolo[4,3-*c*]quinoline (7b)



Purification: hexane: ethyl acetate (90:10) was used to synthesize compound **7b**; color: white solid; yield: 87% (114mg); m.p. 246-248 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.45 (s, 1H), 9.28 (s, 1H), 8.47 (d, J = 7.9 Hz, 1H), 8.13 (d, J = 8.9 Hz, 2H), 8.06 (d, J = 7.9 Hz, 1H), 7.84 (d, J = 8.9 Hz, 2H), 7.76 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 147.7, 147.3, 144.4, 138.7, 132.7, 129.7, 129.1, 127.3, 125.4, 122.3, 122.0, 121.0,

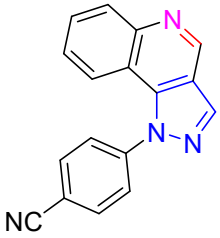
119.5, 118.0; HRMS (ESI): *m/z* calculated for $C_{16}H_{10}BrN_3$ 324.0131 $[M + H]^+$; found 324.0134.

1-(4-Methoxyphenyl)-1*H*-pyrazolo[4,3-*c*]quinoline (7c)



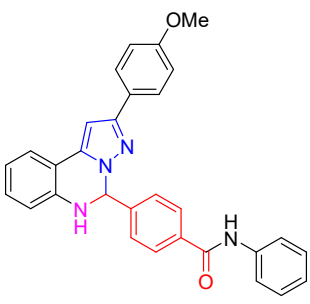
Purification: hexane: ethyl acetate (60:40) was used to synthesize compound **7c**; color: yellow solid; yield: 81% (104mg); m.p. 234-236 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.32 (s, 1H), 9.27 (s, 1H), 8.48 (d, J = 9.6 Hz, 1H), 8.06 (d, J = 9.2 Hz, 3H), 7.74 (t, J = 8.5 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.18 (d, J = 9.2 Hz, 2H), 3.86 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 159.1, 147.5, 147.0, 144.1, 133.0, 129.5, 128.8, 127.2, 124.9, 122.0, 121.9, 119.7, 116.9, 114.9, 55.6. HRMS (ESI): *m/z* calculated for $C_{17}H_{13}N_3O$ 276.1132 $[M + H]^+$; found 276.1131.

4-(1*H*-pyrazolo[4,3-*c*]quinolin-1-yl) benzonitrile (7d)



Purification: hexane: ethyl acetate (40:60) was used to synthesize compound **7d**; color: yellow solid; yield: 76% (97mg); m.p. 262-264 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.58 (s, 1H), 9.30 (s, 1H), 8.49 (dd, J = 8.0, 1.6 Hz, 1H), 8.39 (d, J = 8.2 Hz 2H), 8.14 (d, J = 8.9 Hz, 2H), 8.07 (d, J = 8.5 Hz, 1H), 7.78 (t, J = 7.7 Hz, 1H), 7.71 (t, J = 7.5 Hz, 1H); ^{13}C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 148.2, 148.2, 144.9, 142.9, 134.6, 130.1, 129.9, 127.9, 126.5, 122.5, 121.2, 119.80, 118.8, 117.7, 110.9. HRMS (ESI): *m/z* calculated for $C_{17}H_{10}N_4$ 271.0979 $[M + H]^+$; found 271.0977.

4-(2-(4-Methoxyphenyl)-5,6-dihydropyrazolo[1,5-*c*]quinazolin-5-yl)-*N*-phenyl benzamide (9)

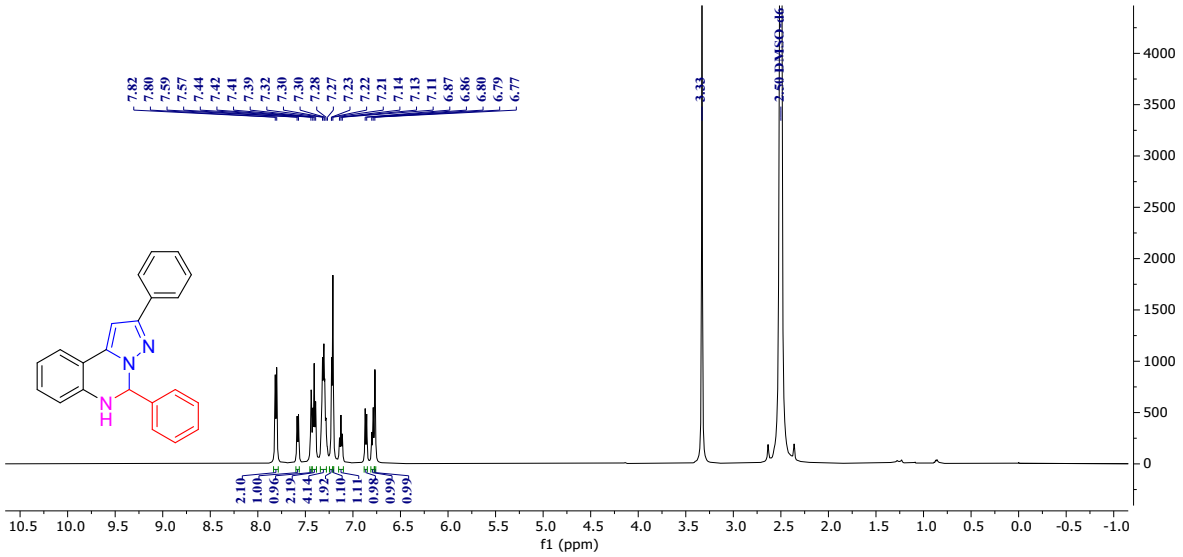


Yellow solid; yield: 92% (110mg); m.p. 285-286 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.15 (s, 1H), 7.84 (d, J = 8.1 Hz, 2H), 7.73 (dd, J = 16.6, 8.4 Hz, 4H), 7.58 (d, J = 8.0 Hz, 1H), 7.50 (s, 1H), 7.33 (d, J = 8.0 Hz, 4H), 7.13 (d, J = 13.0 Hz, 2H), 7.07 (t, J = 7.6 Hz, 1H), 6.98 (d, J = 8.5 Hz, 2H), 6.91 – 6.77 (m, 3H), 3.78 (s, 3H); 13C {^{1}H} NMR (125 MHz, DMSO-d_6) δ 166.1, 159.7, 151.6, 144.9, 140.2, 139.2, 139.1, 135.5, 130.3, 129.3, 128.4, 127.2, 126.4, 126.0, 124.7, 124.6, 121.1, 119.4, 115.6,

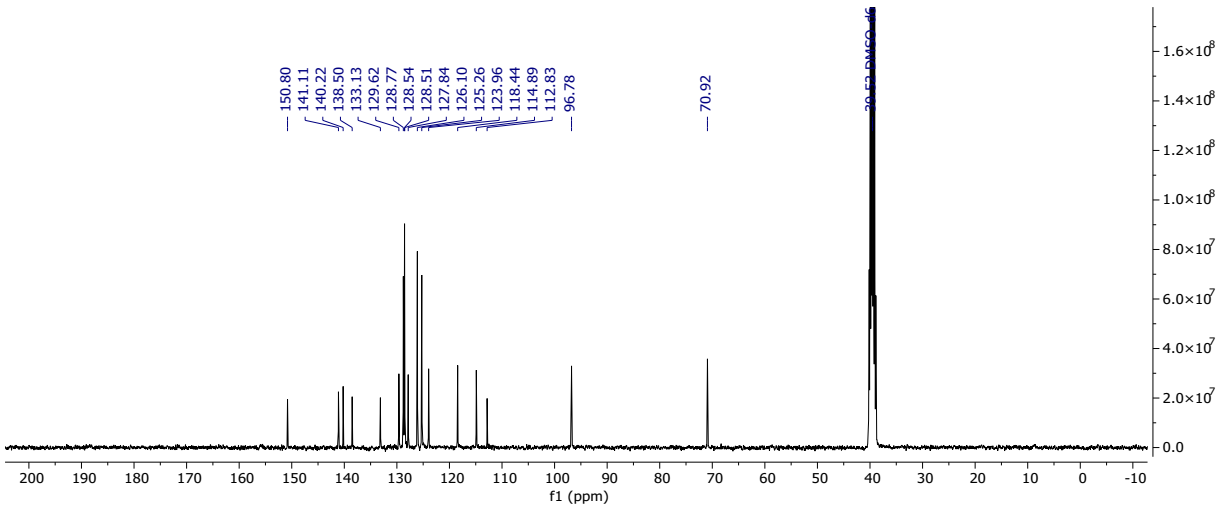
114.7, 113.4, 96.9, 70.8, 55.7.

10. Copies of ^{1}H, ^{13}C and HRMS data of pyrazolo quinazolines/quinolines (3a-z, 5a-d and 7a-d)

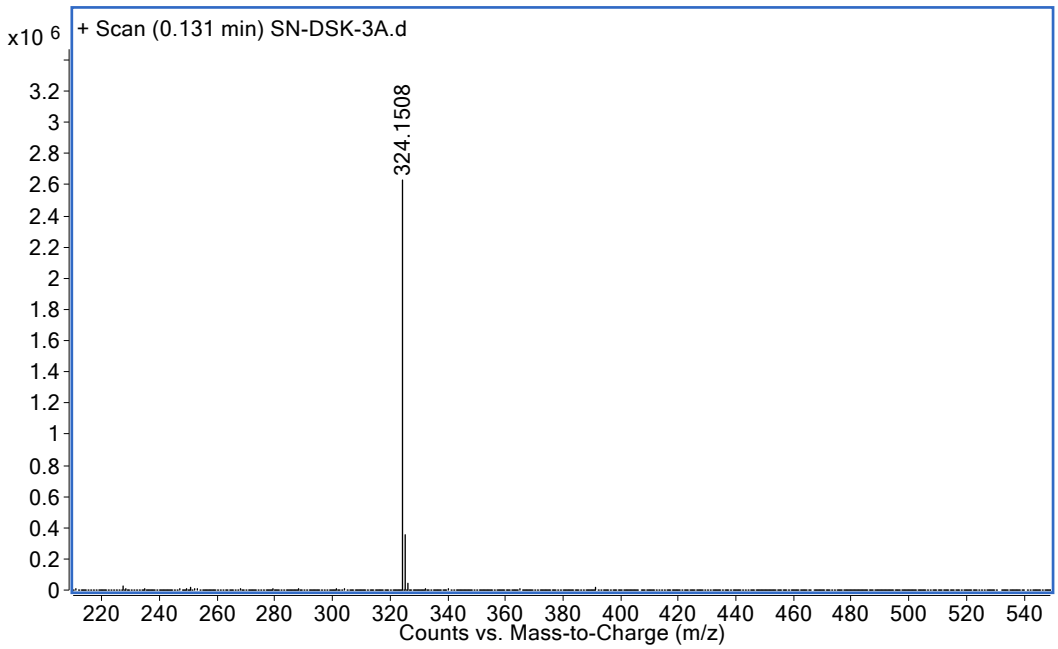
NMR spectrum of compound 3a



^{1}H-NMR spectrum of compound 3a, DMSO-d_6, 500MHz

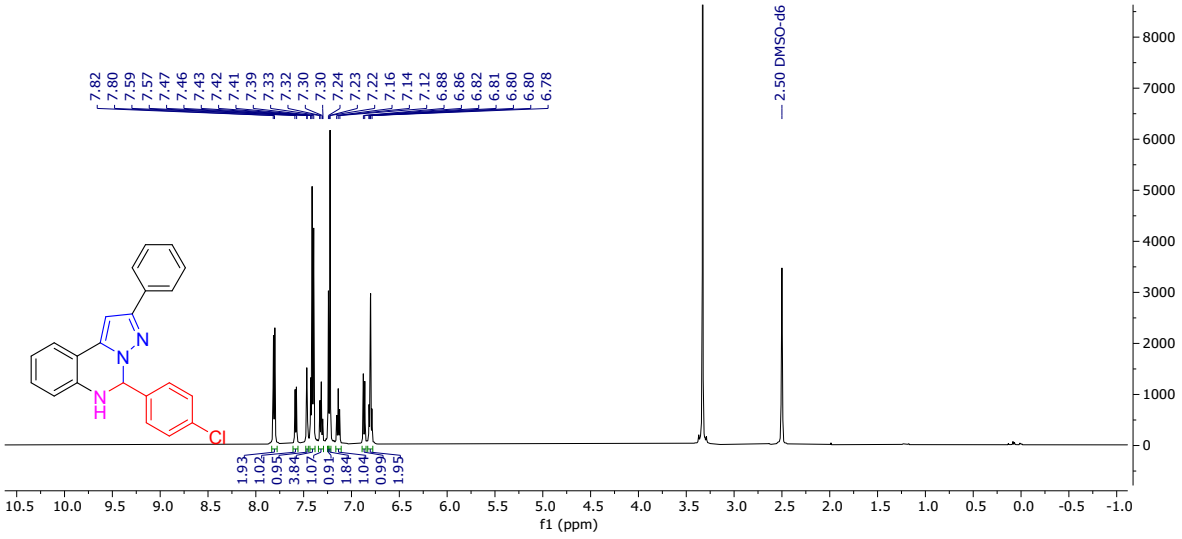


^{13}C {^{1}H} NMR of compound 3a, DMSO-d_6, 125MHz

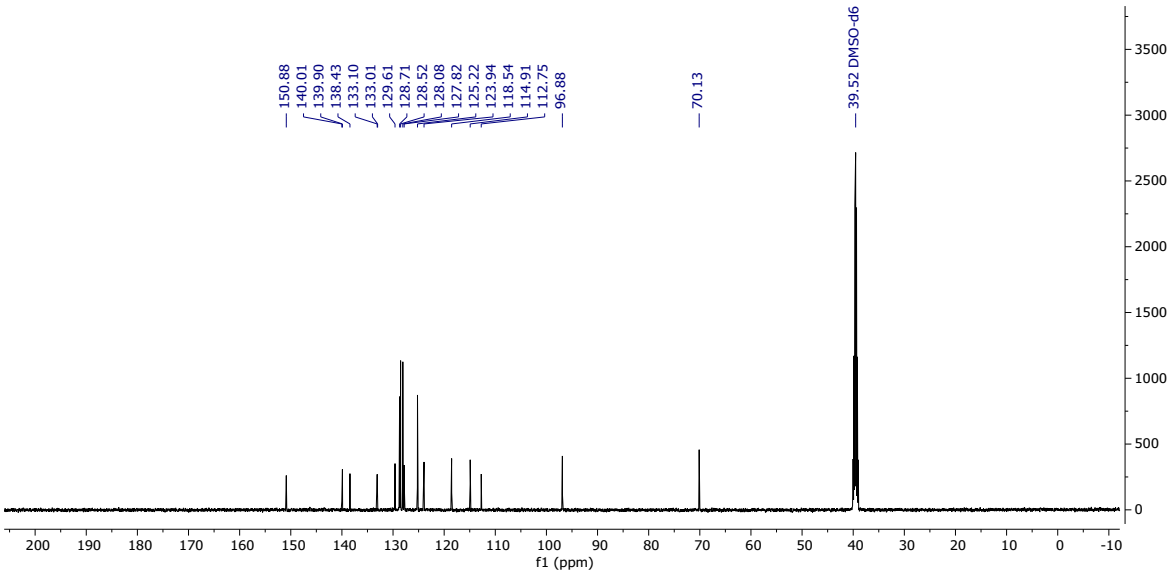


HRMS spectra of compound 3a

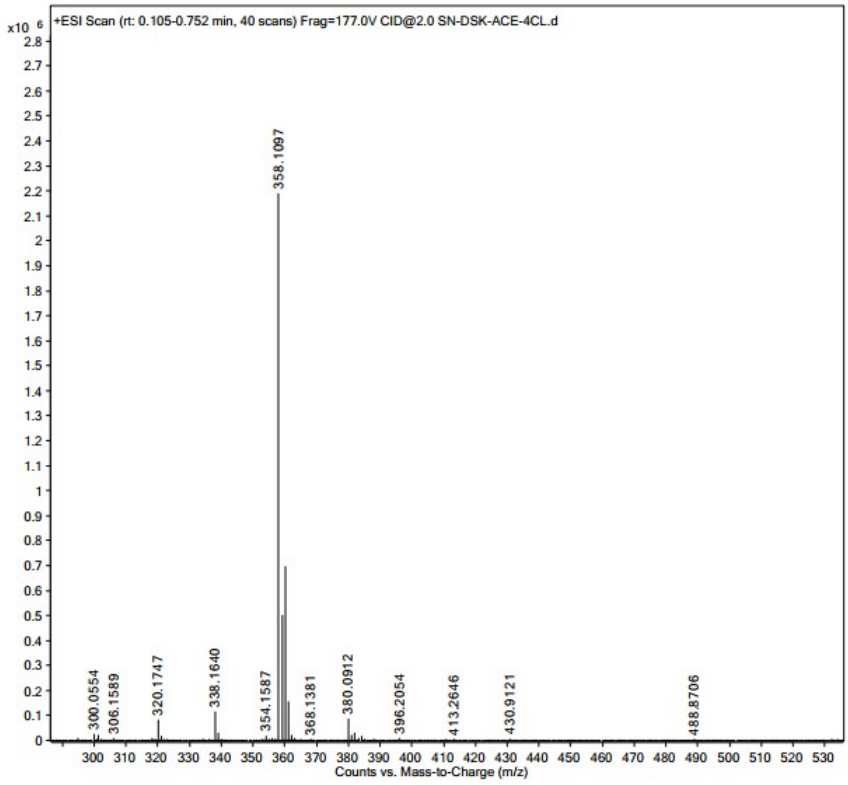
NMR spectrum of compound 3b



^{1}H-NMR spectrum of compound 3b, DMSO-d_6, 500MHz

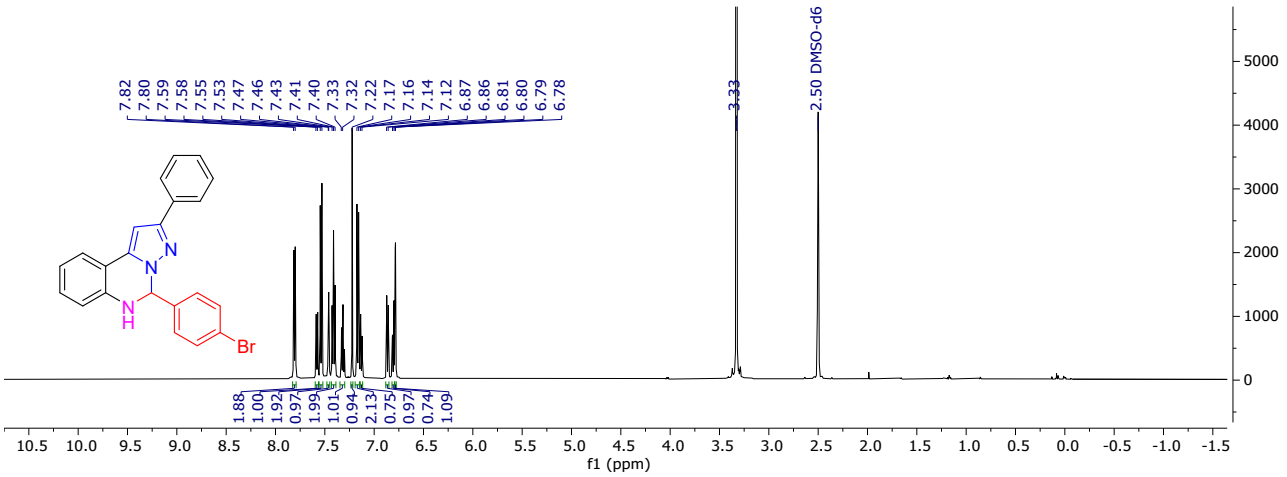


^{13}C {^{1}H} NMR of compound 3b, DMSO-d_6, 125MHz

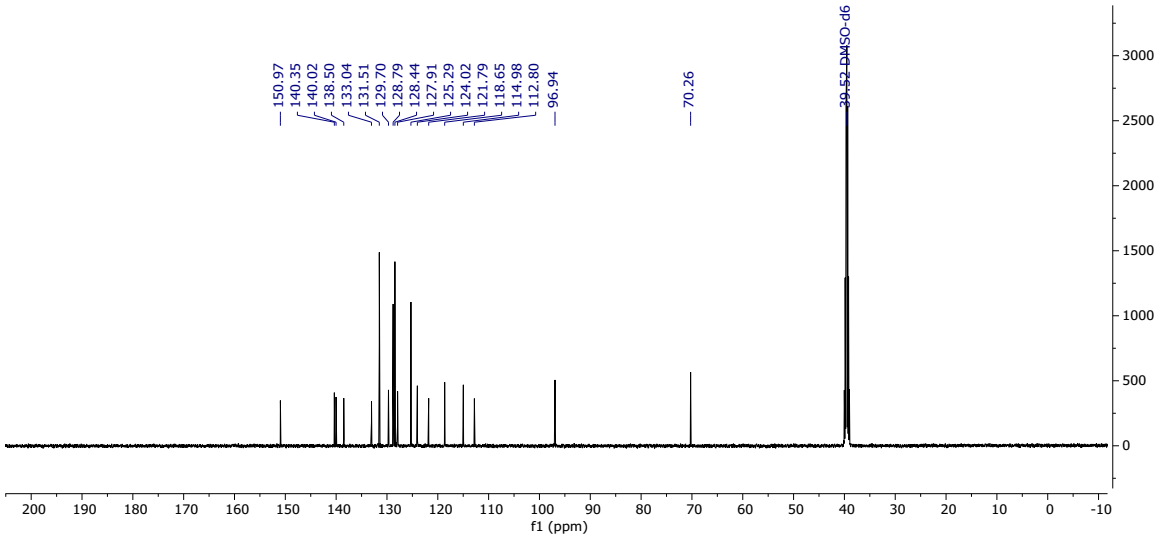


HRMS spectra of compound 3b

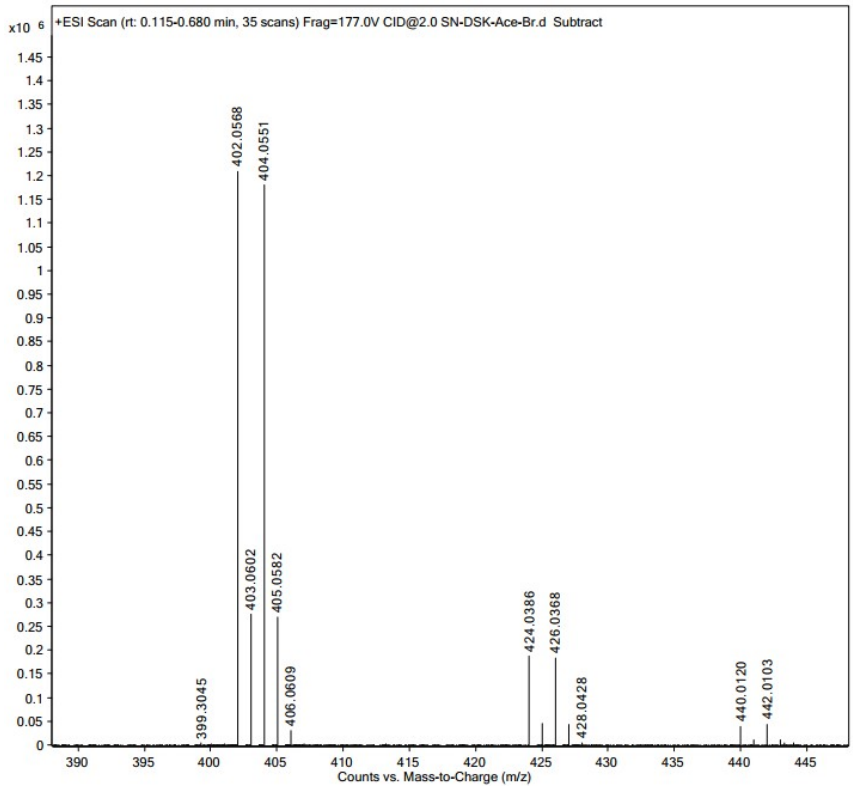
NMR spectrum of compound 3c



^{1}H-NMR spectrum of compound 3c, DMSO-d_6, 500MHz

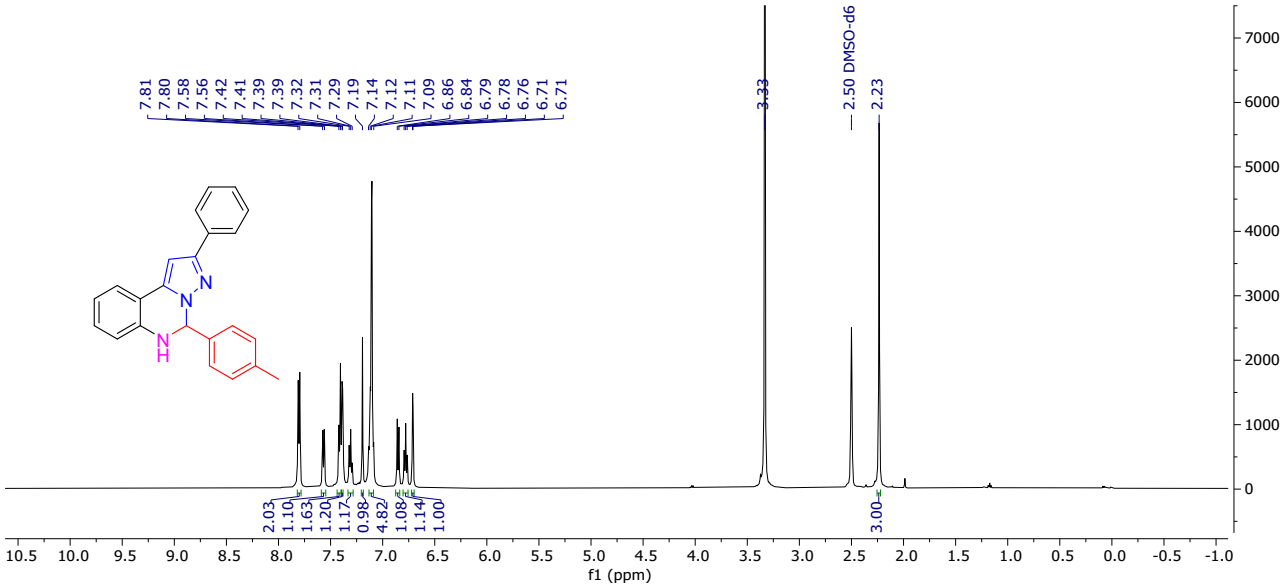


^{13}C {^{1}H} NMR of compound 3c, DMSO-d_6, 125MHz

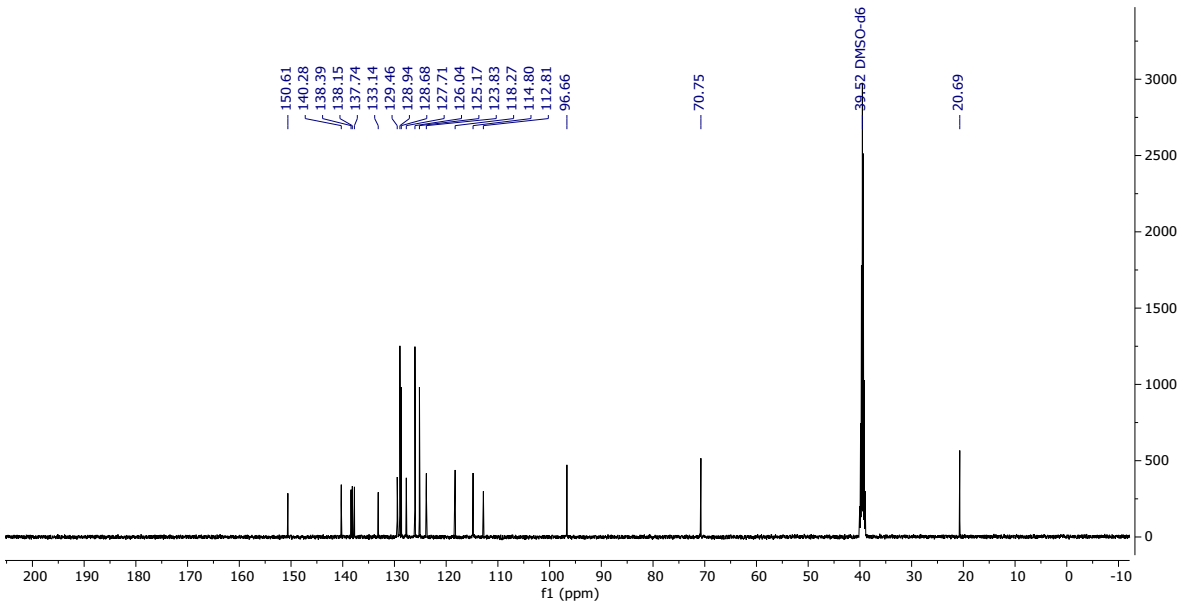


HRMS spectra of compound 3c

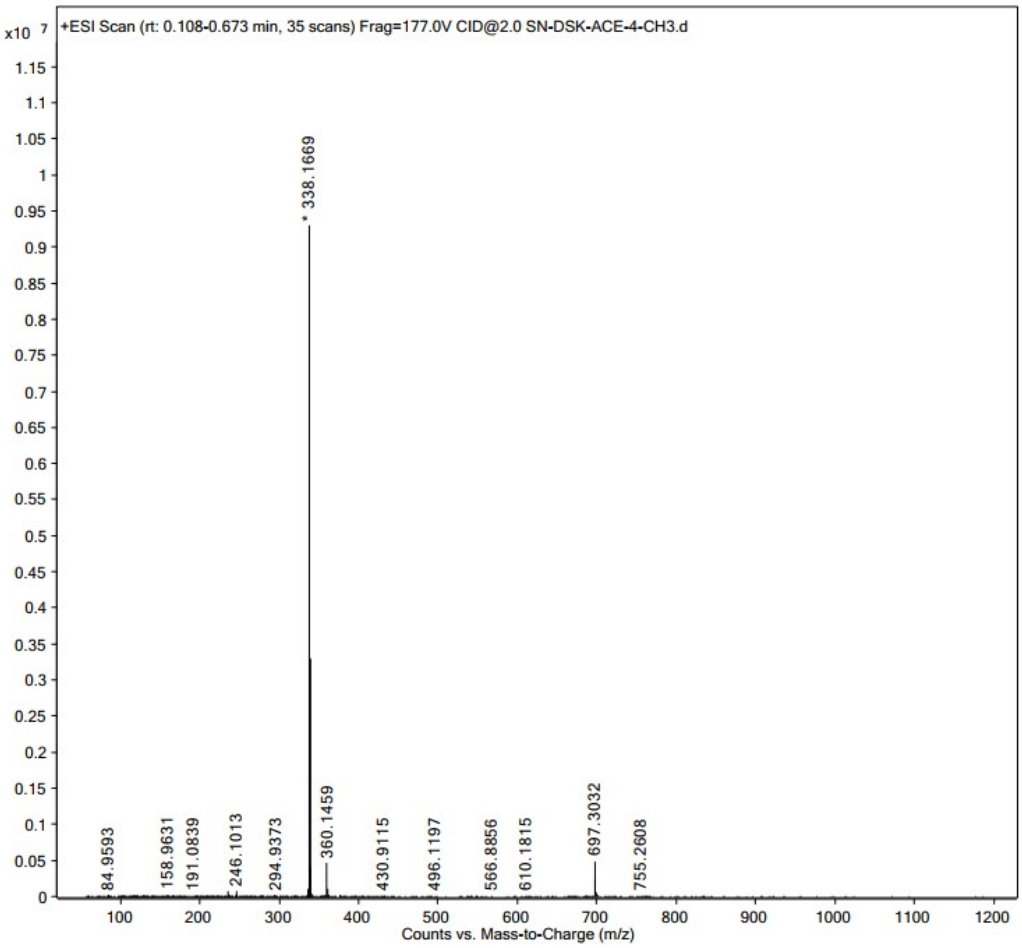
NMR spectrum of compound 3d



^{1}H-NMR spectrum of compound 3d, DMSO-d_6, 500MHz

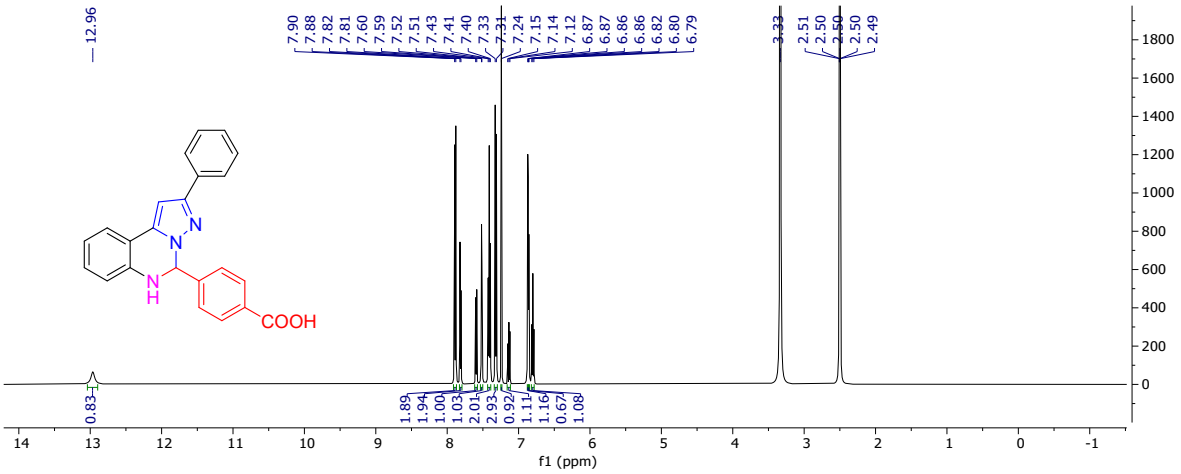


^{13}C {^{1}H} NMR of compound 3d, DMSO-d_6, 125MHz

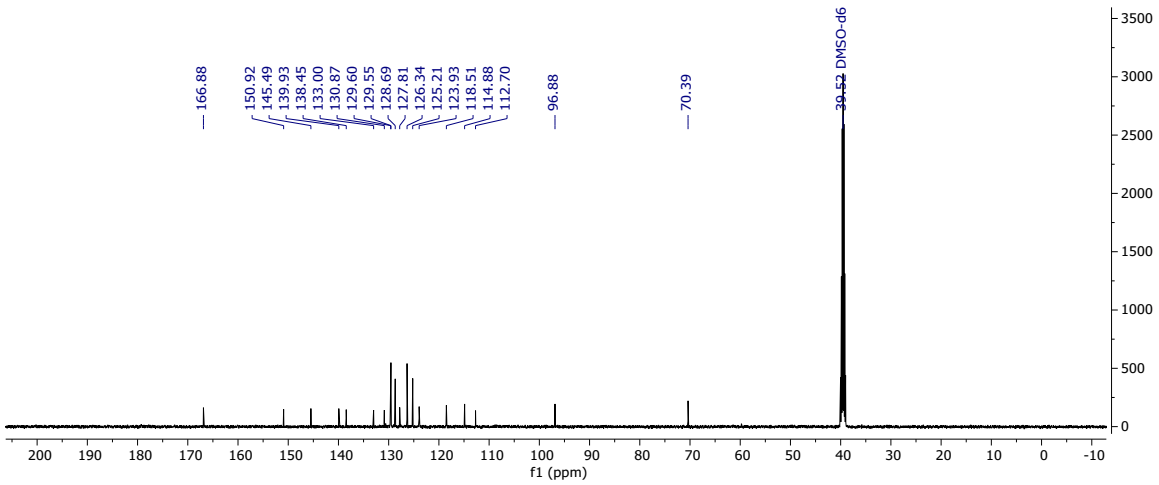


HRMS spectra of compound 3d

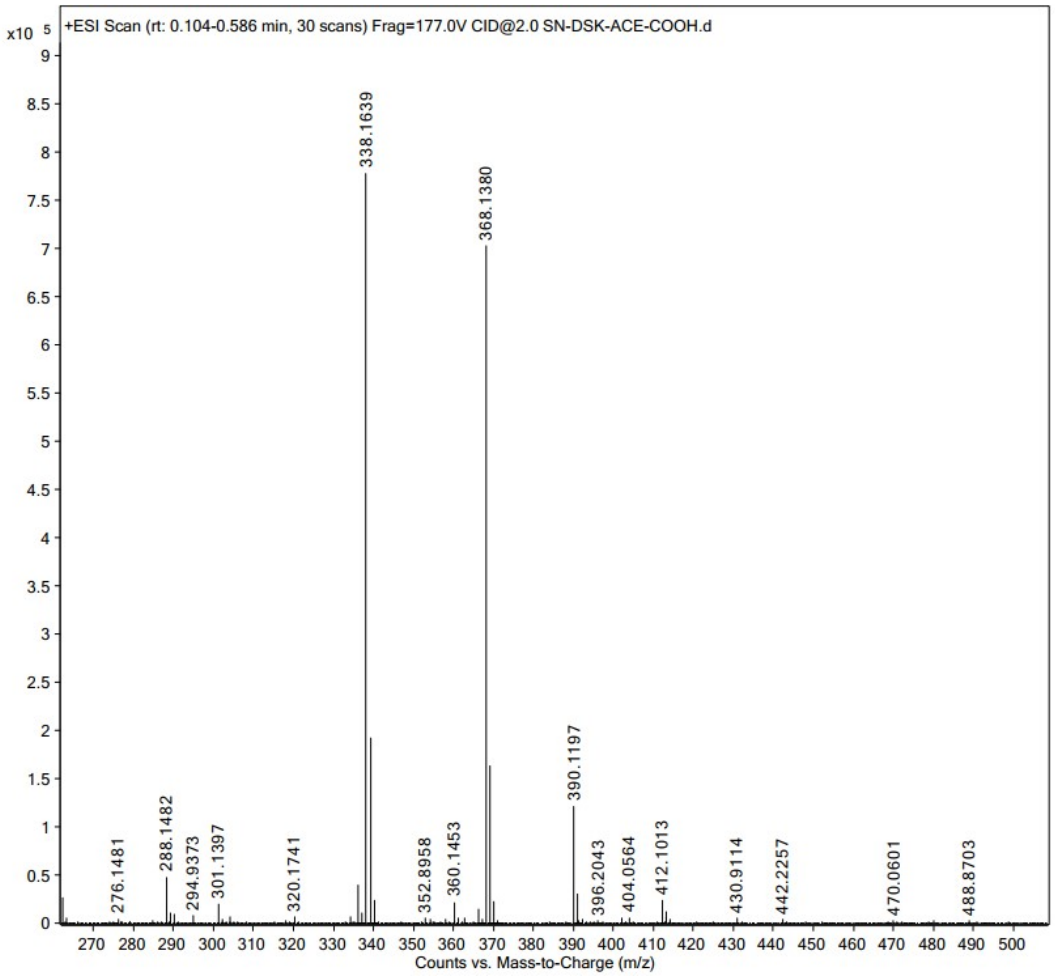
NMR spectrum of compound 3e



^{1}H-NMR spectrum of compound 3e, DMSO-d_6, 500MHz

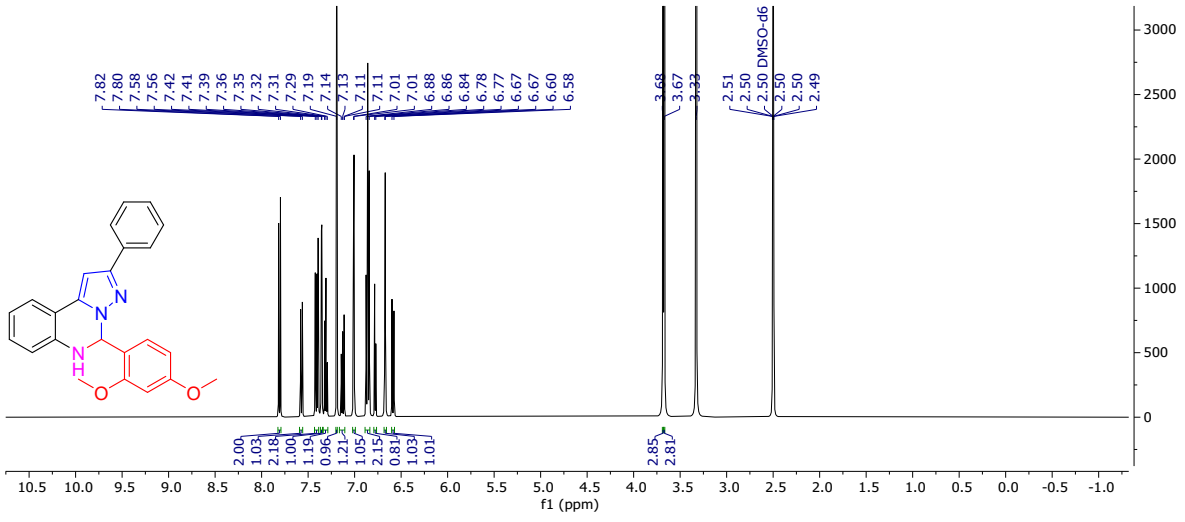


^{13}C {^{1}H} NMR of compound 3e, DMSO-d_6, 125MHz

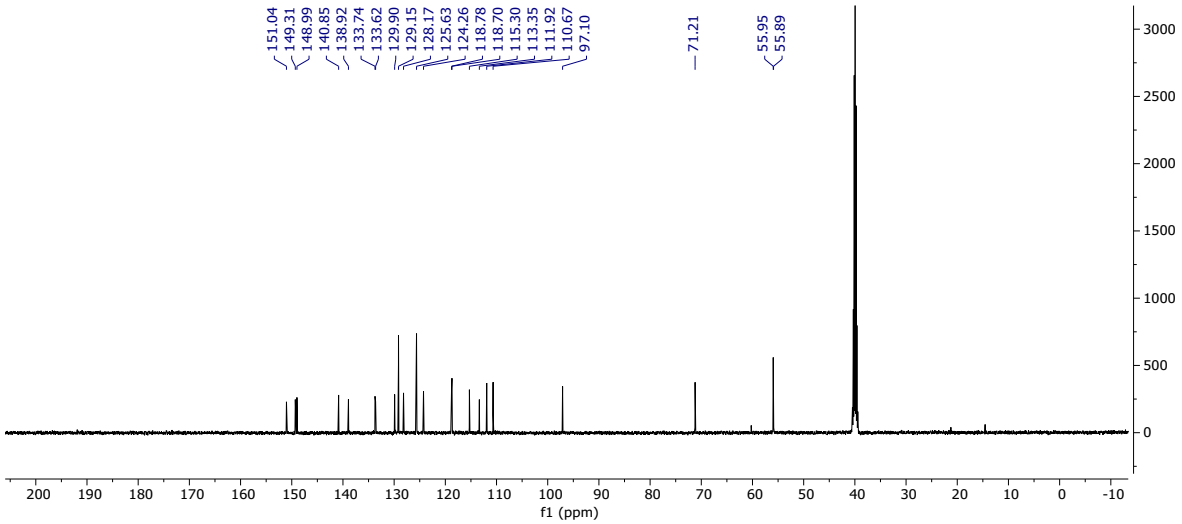


HRMS spectra of compound 3e

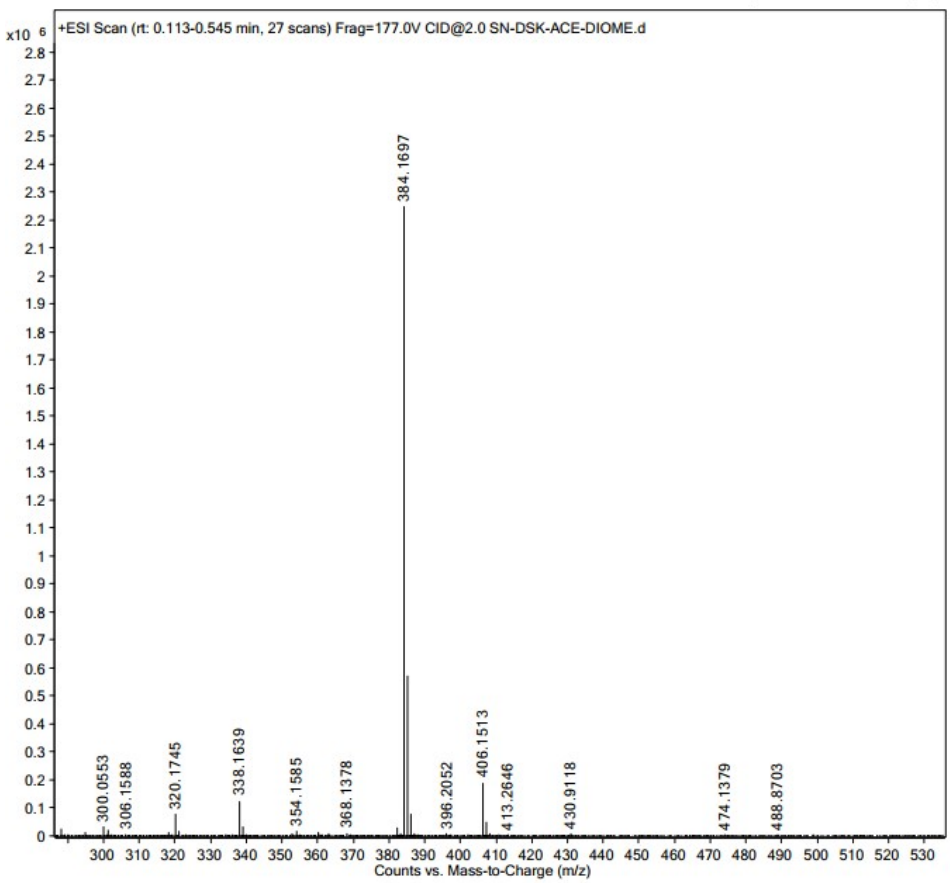
NMR spectrum of compound 3f



^{1}H-NMR spectrum of compound 3f, DMSO-d_6, 500MHz

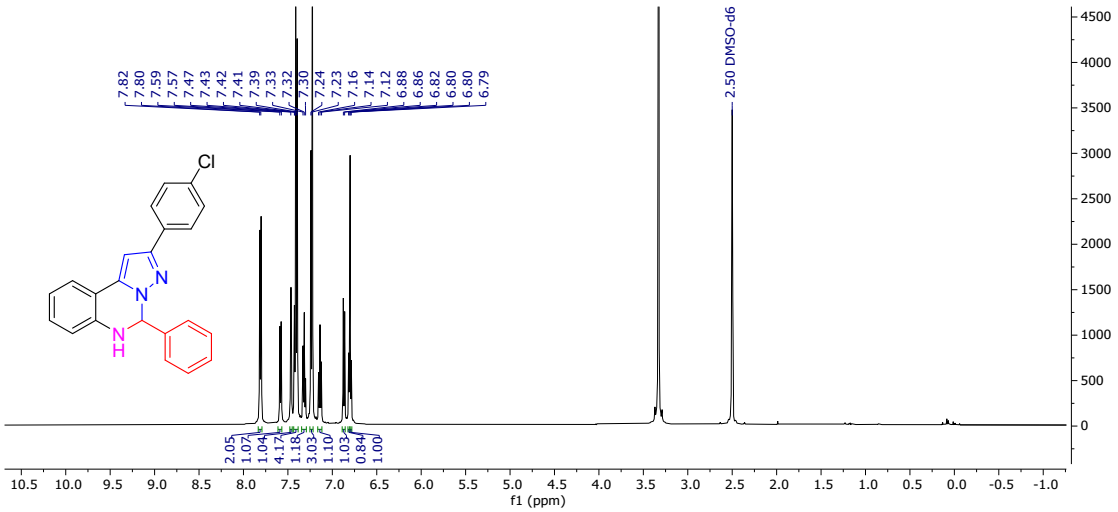


^{13}C {^{1}H} NMR of compound 3f, DMSO-d_6, 125MHz

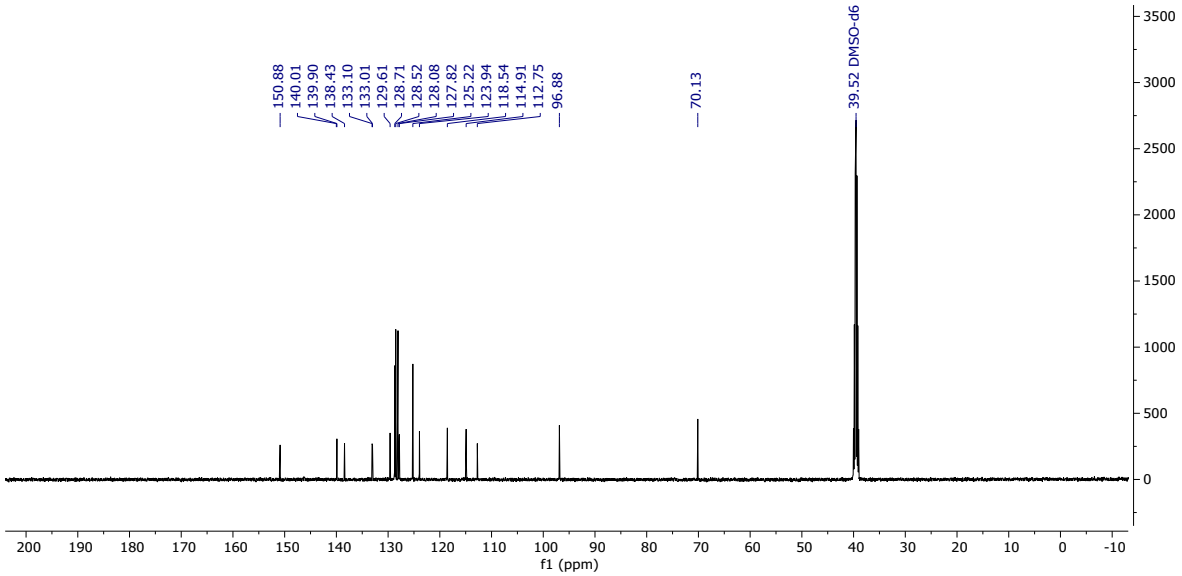


HRMS spectra of compound 3f

NMR spectrum of compound 3g



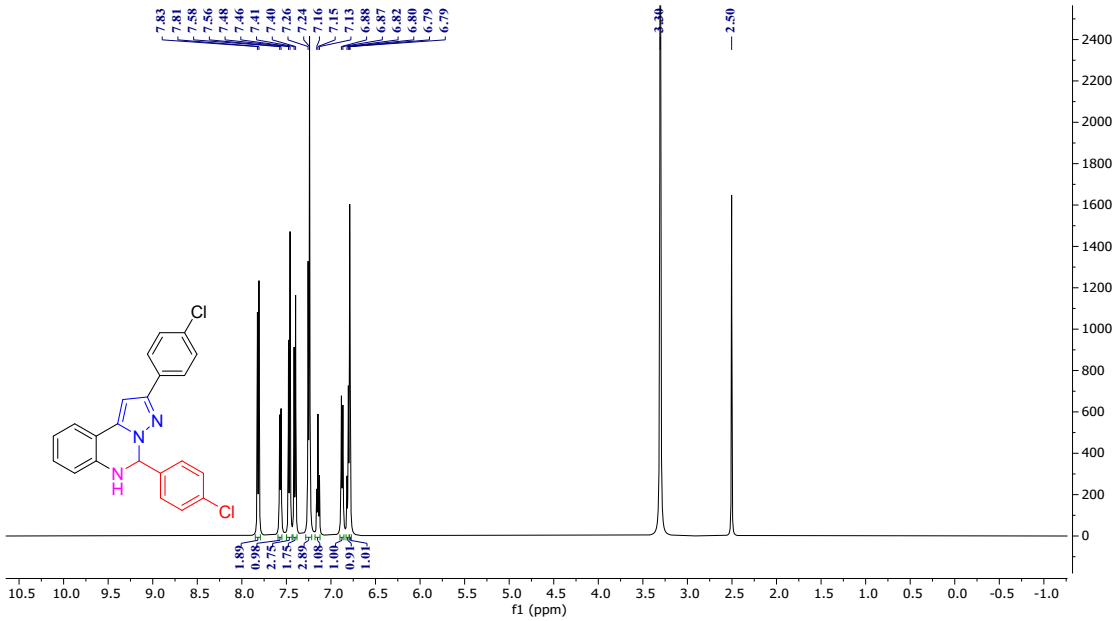
^{1}H-NMR spectrum of compound 3g, DMSO-d_6, 500MHz



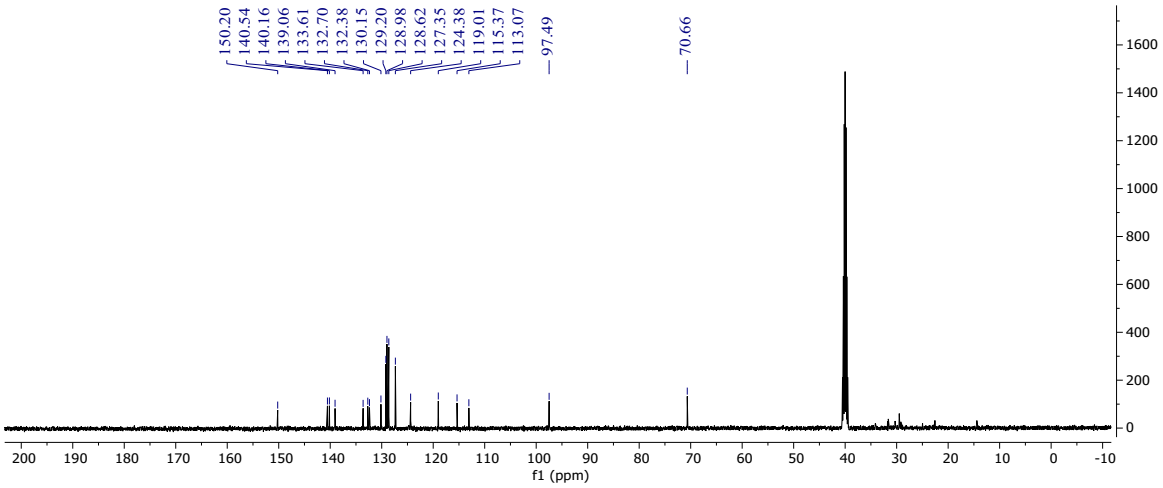
^{13}C {^{1}H} NMR of compound 3g, DMSO-d_6, 125MHz

HRMS spectra of compound 3g

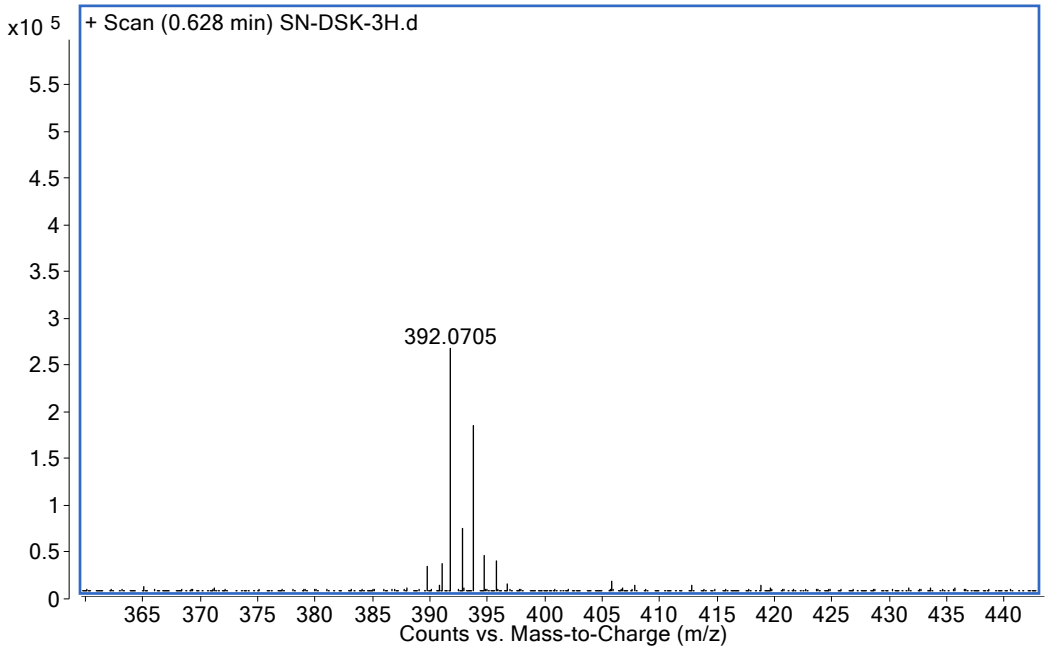
NMR spectrum of compound 3h



^{1}H-NMR spectrum of compound 3h, DMSO-d_6, 500MHz

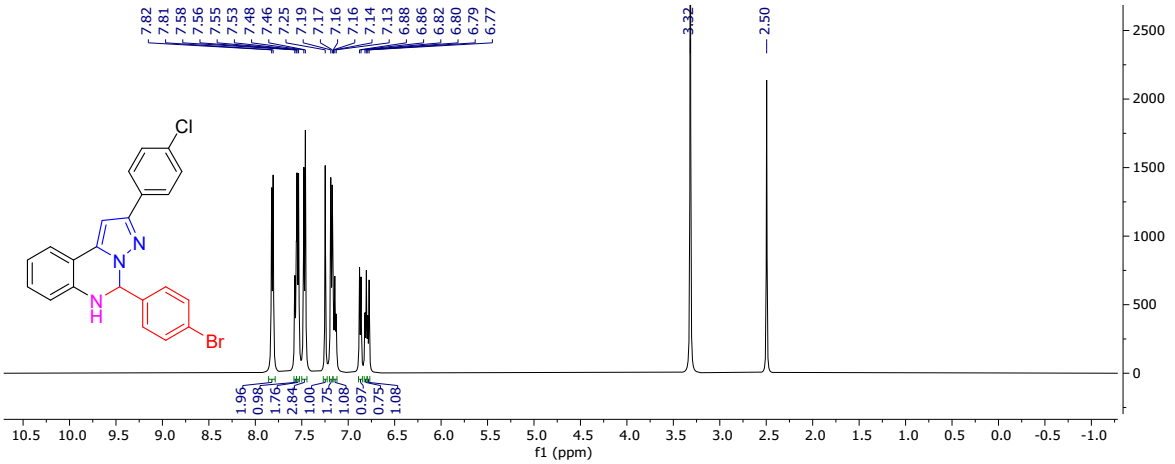


^{13}C {^{1}H} NMR of compound 3h, DMSO-d_6, 125MHz

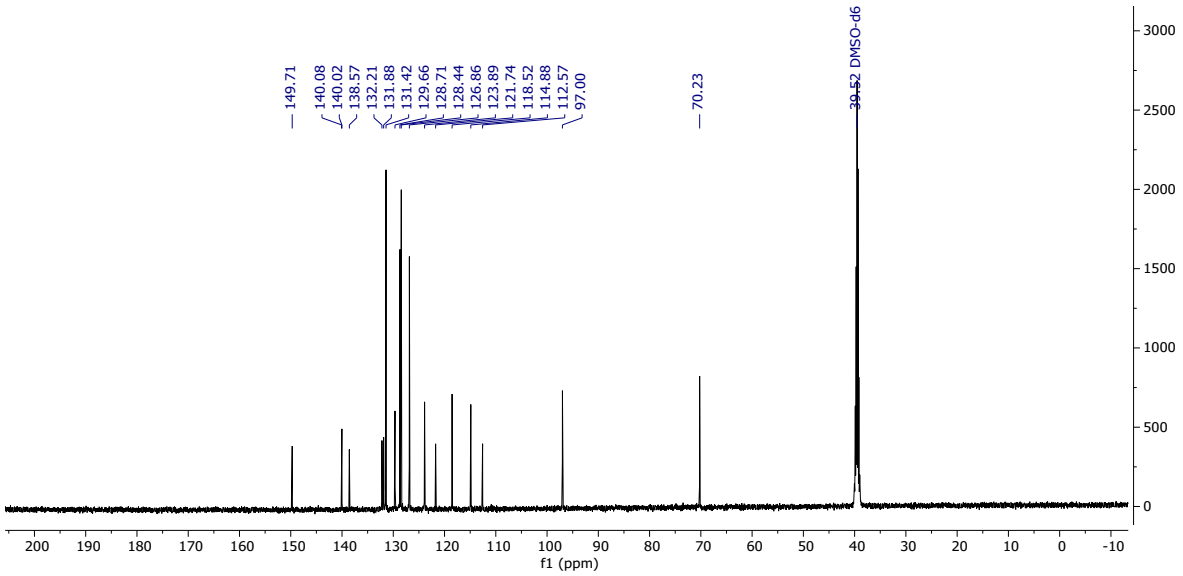


HRMS spectra of compound 3h

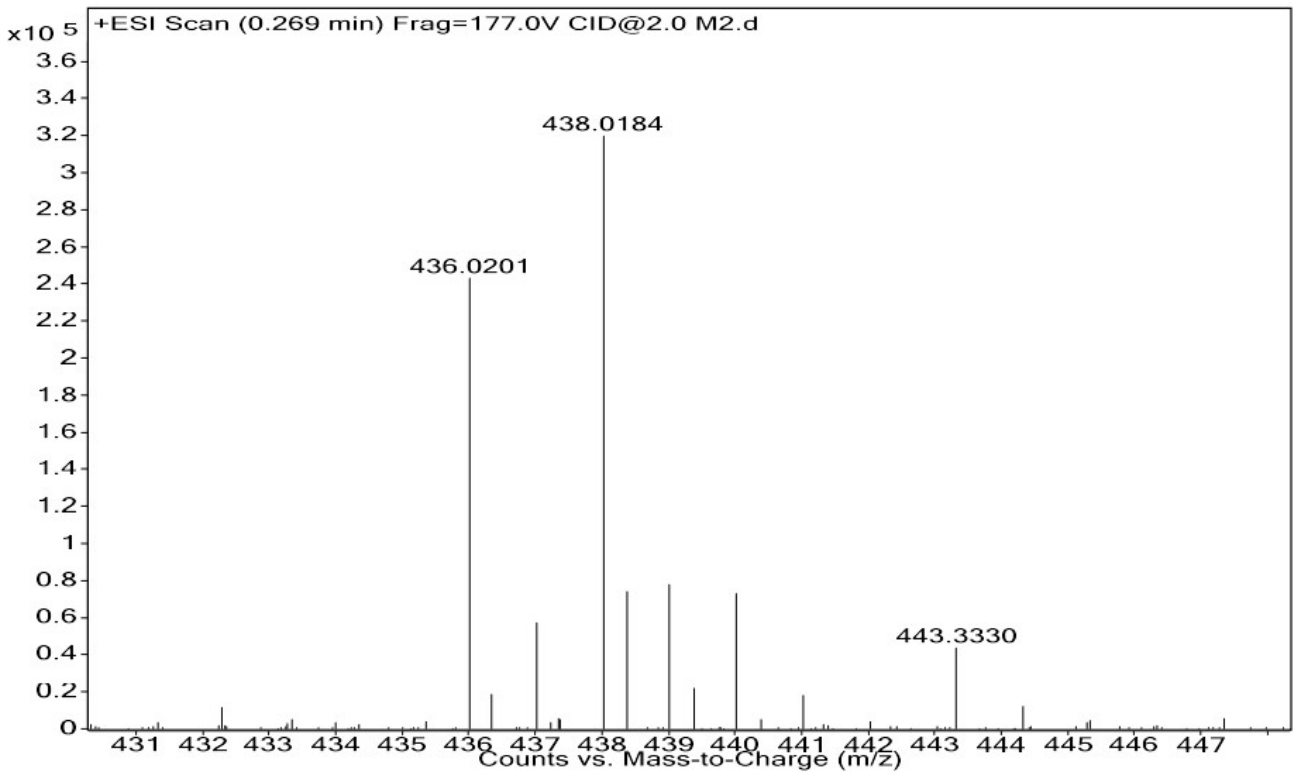
NMR spectrum of compound 3i



^{1}H-NMR spectrum of compound 3i, DMSO-d_6, 500MHz

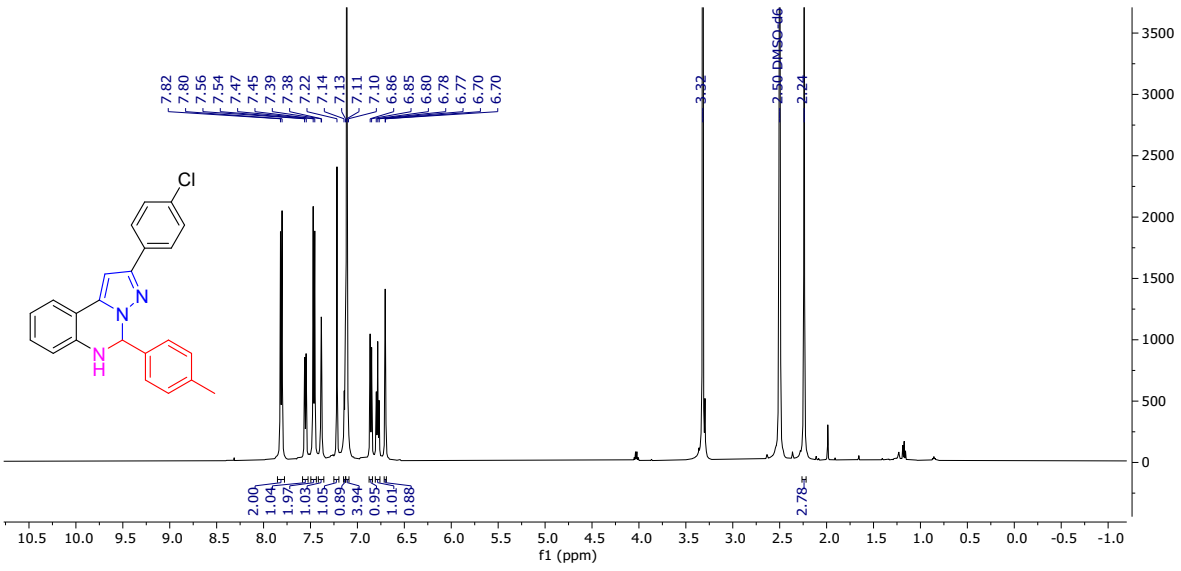


^{13}C {^{1}H} NMR of compound 3i, DMSO-d_6, 125MHz

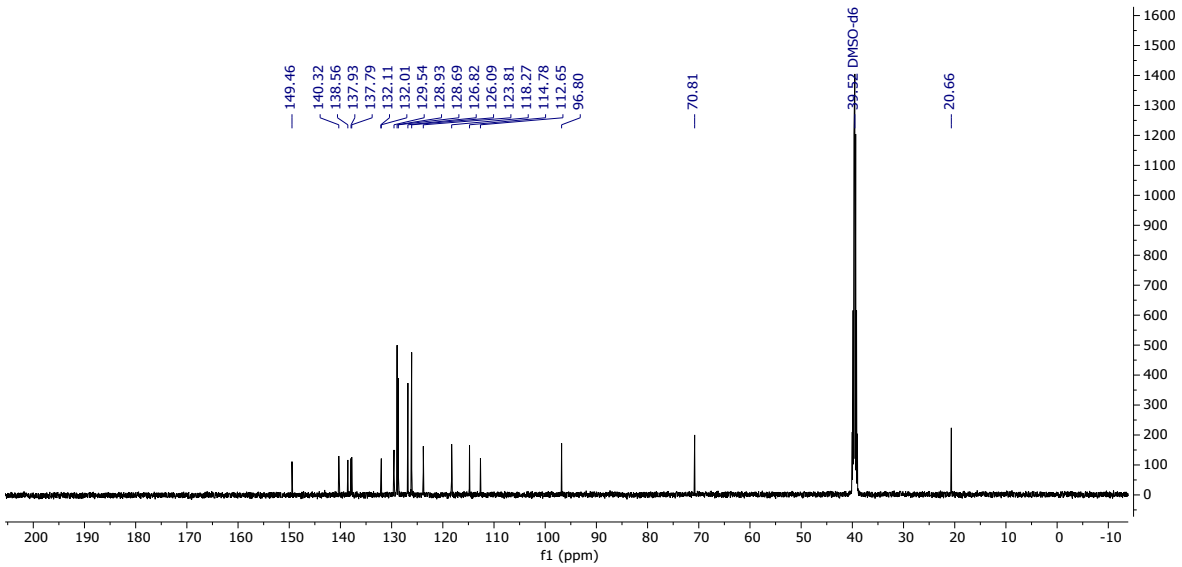


HRMS spectra of compound 3i

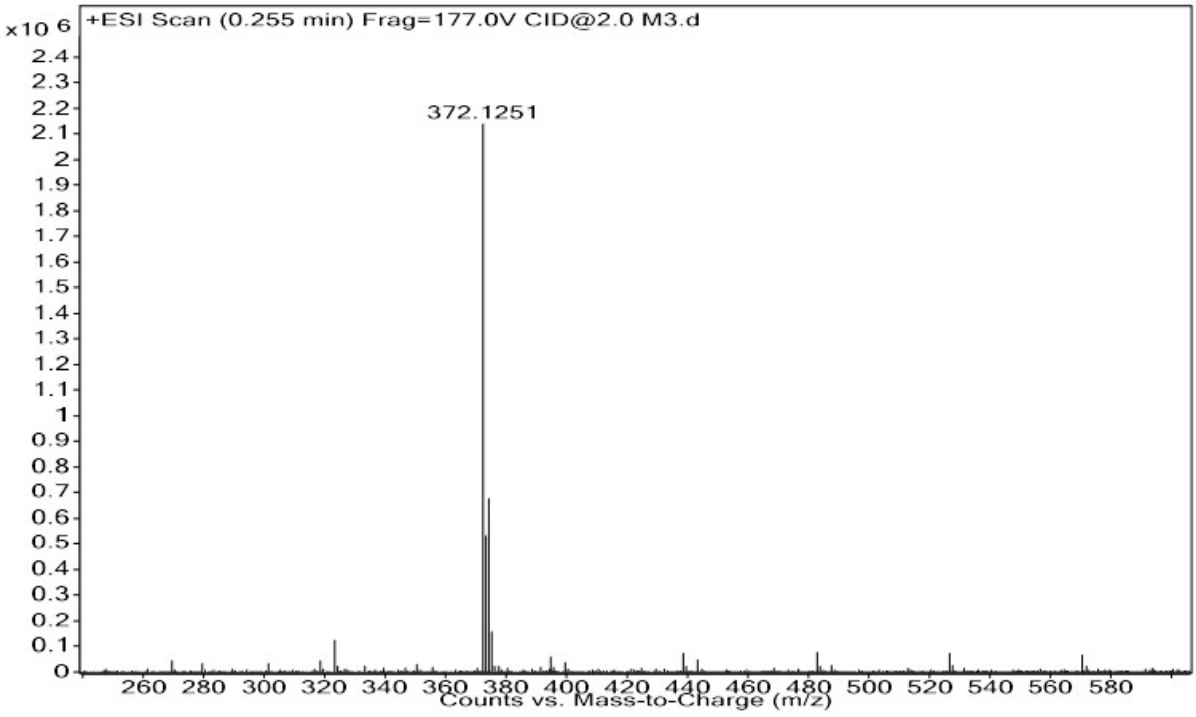
NMR spectrum of compound 3j



^{1}H-NMR spectrum of compound 3j, DMSO-d_6, 500MHz

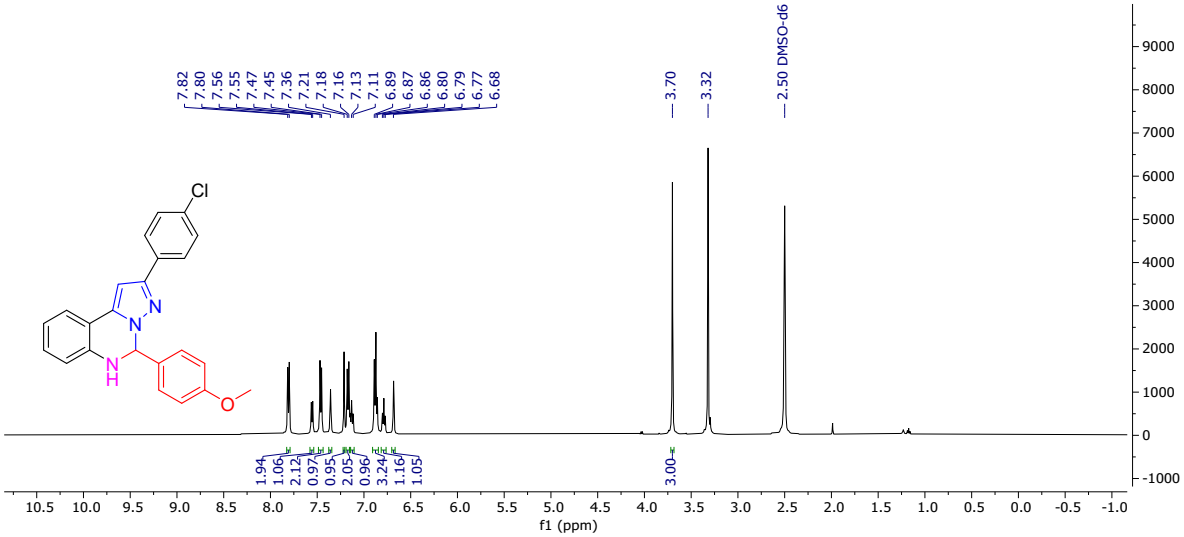


^{13}C {^{1}H} NMR of compound 3j, DMSO-d_6, 125MHz

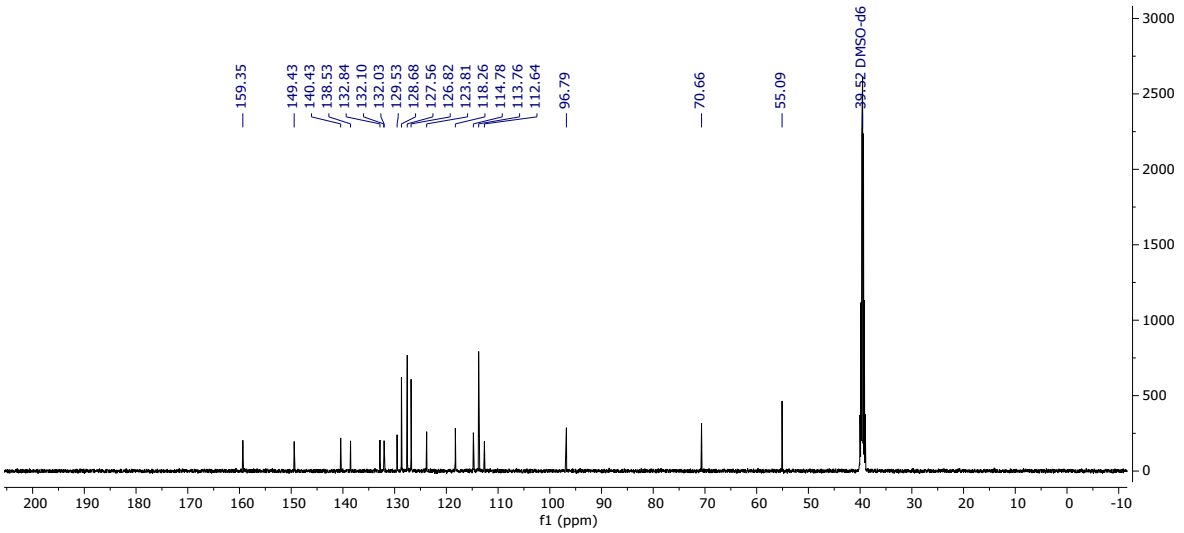


HRMS spectra of compound 3j

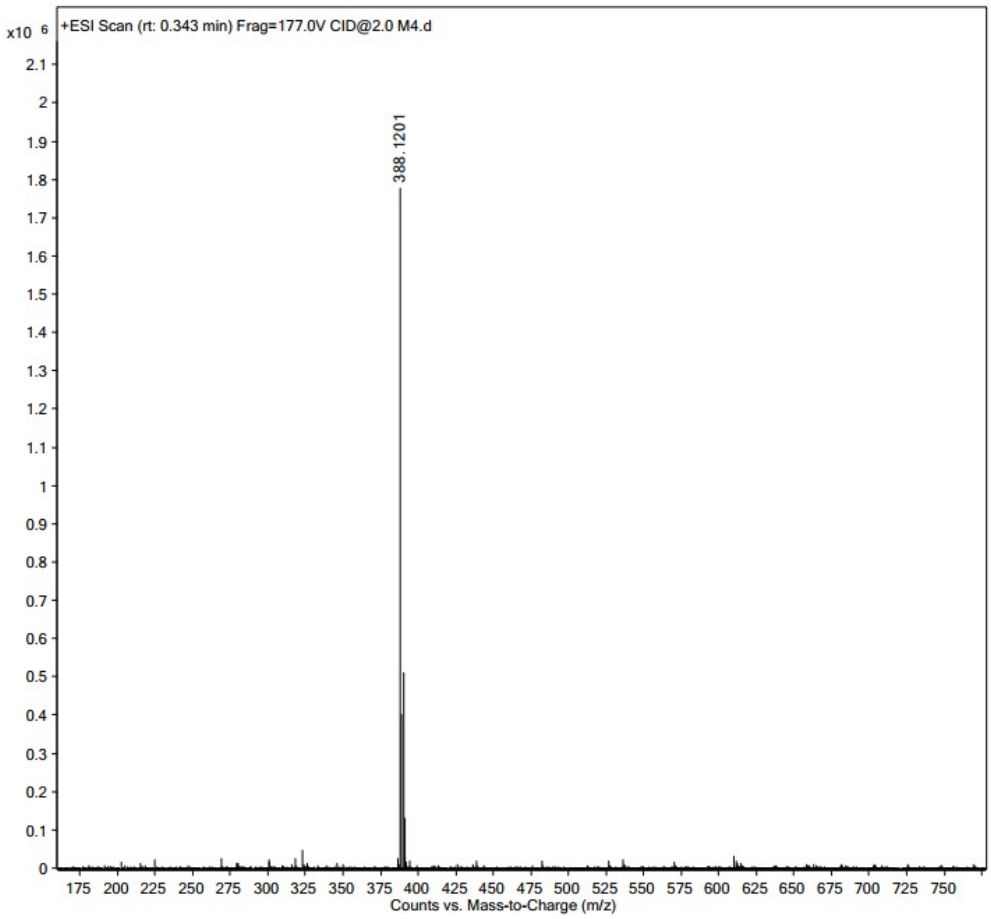
NMR spectrum of compound 3k



^{1}H-NMR spectrum of compound 3k, DMSO-*d*$_6$, 500MHz

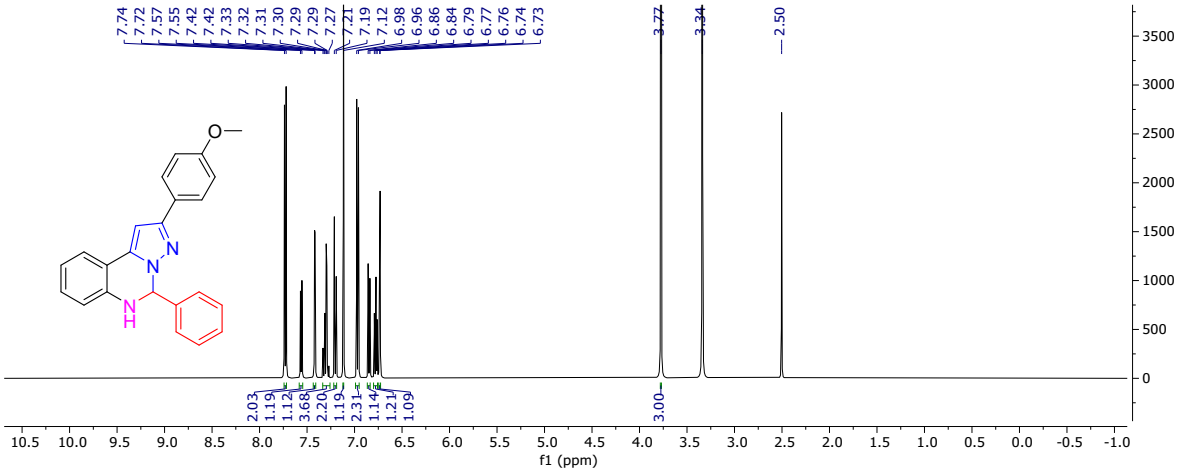


^{13}C {^{1}H} NMR of compound 3k, DMSO-*d*$_6$, 125MHz

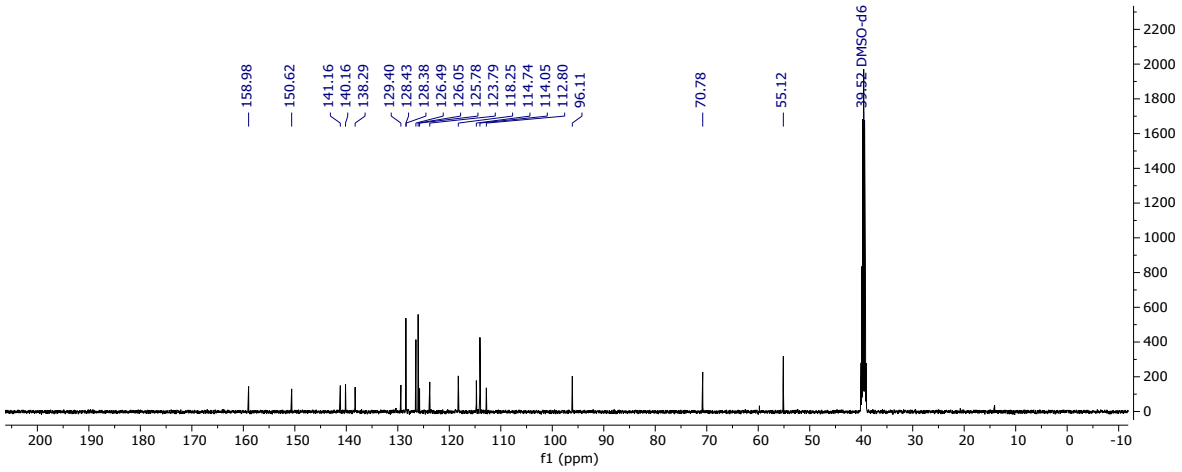


HRMS spectra of compound 3k

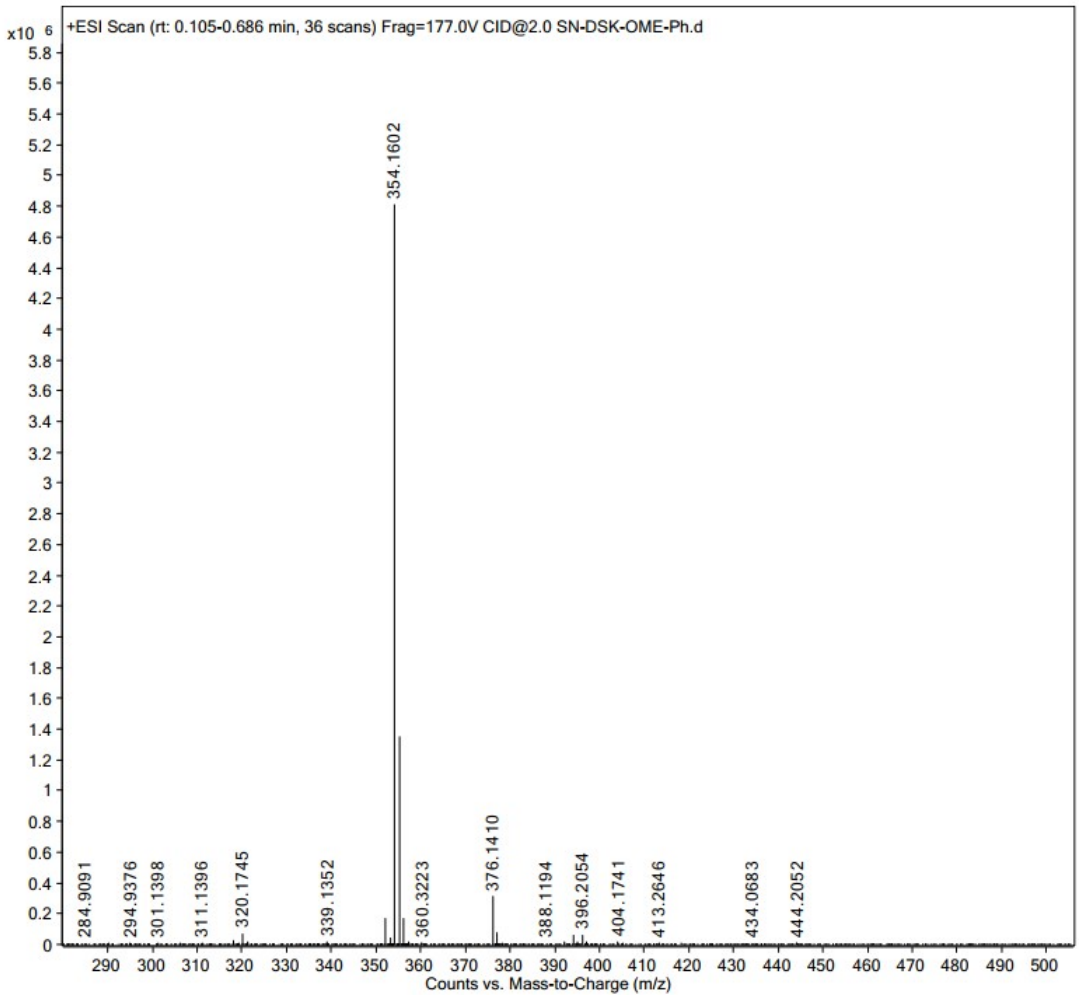
NMR spectrum of compound 3l



^{1}H-NMR spectrum of compound 3l, DMSO-d_6, 500MHz

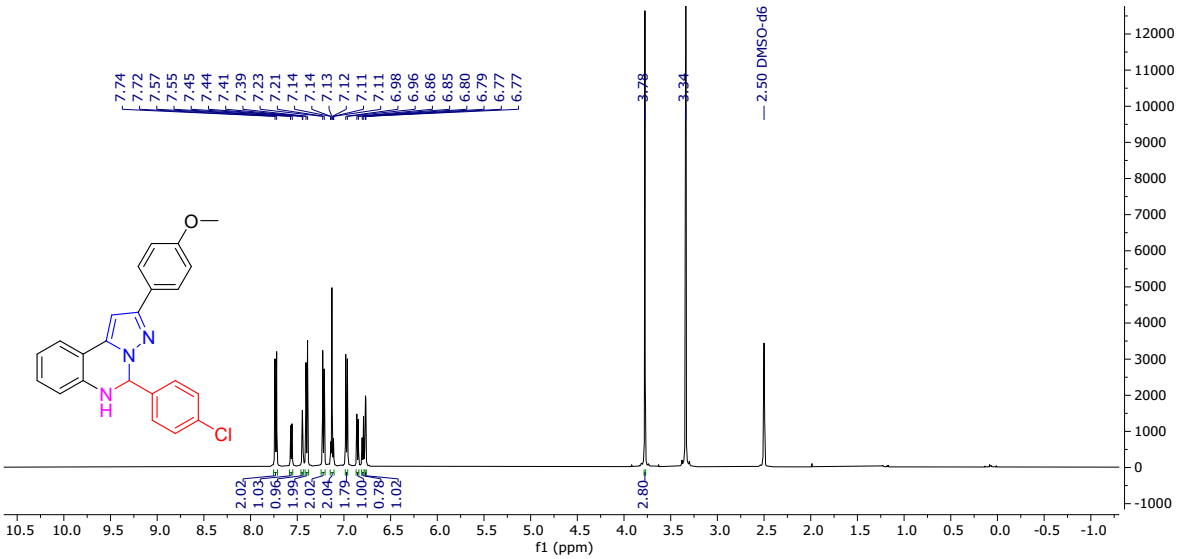


^{13}C {^{1}H} NMR of compound 3l, DMSO-d_6, 125MHz

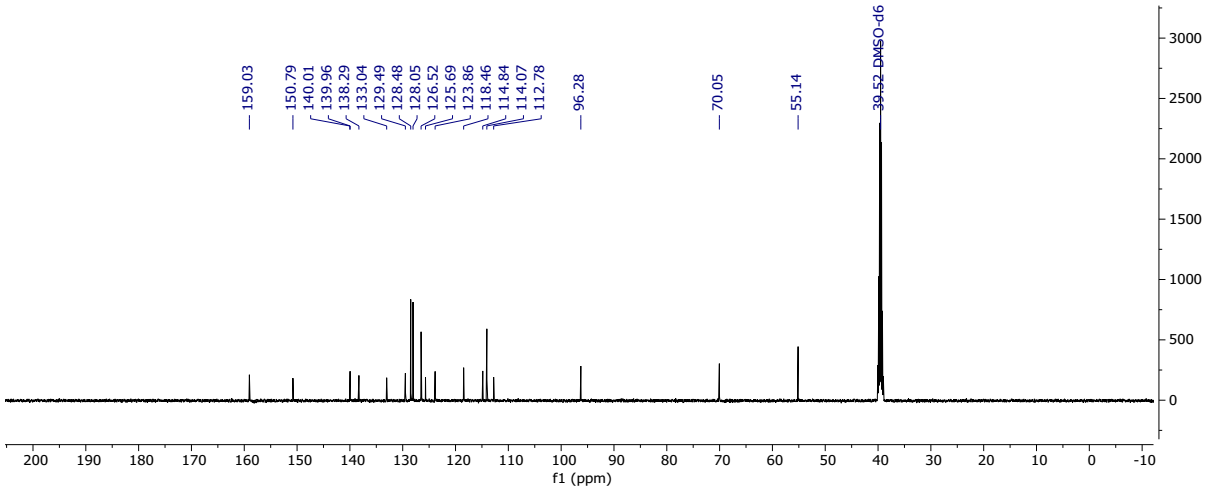


HRMS spectra of compound 3l

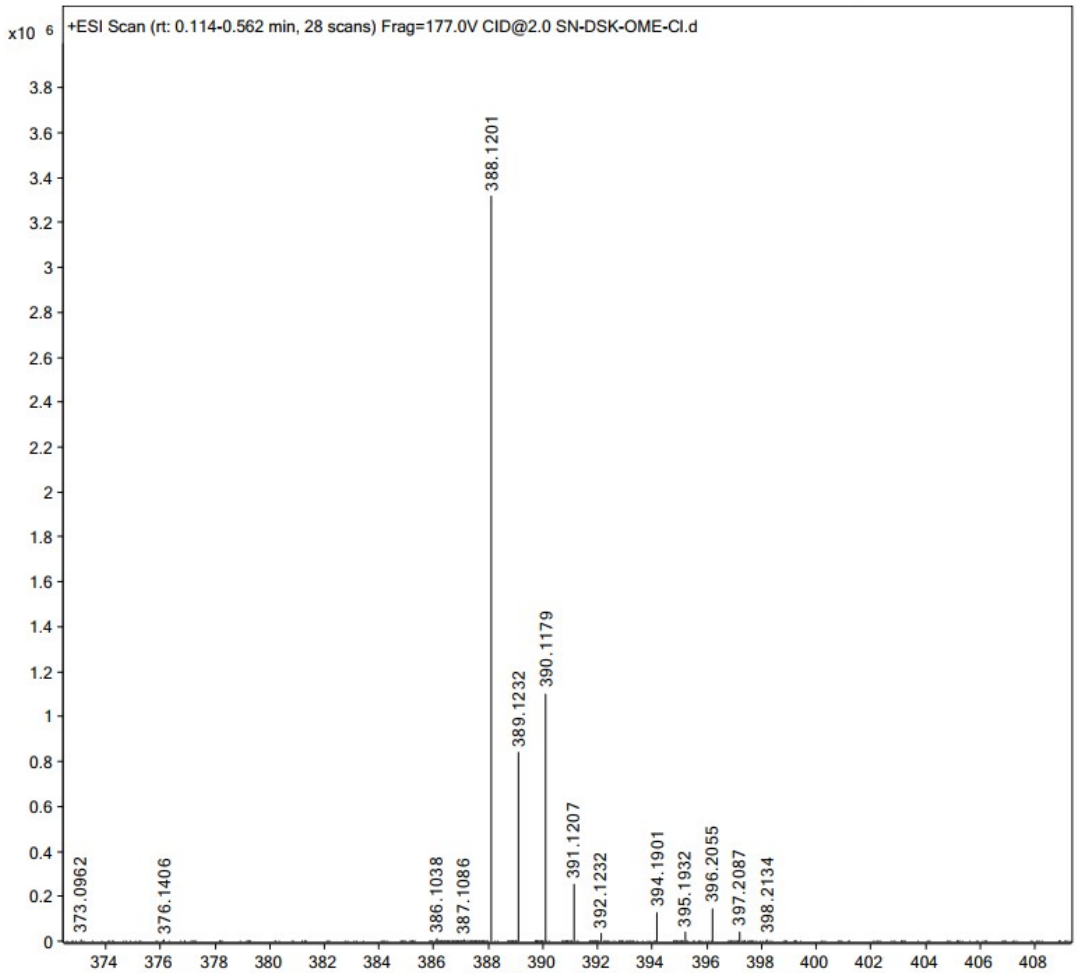
NMR spectrum of compound 3m



^{1}H-NMR spectrum of compound 3m, DMSO-d_6, 500MHz

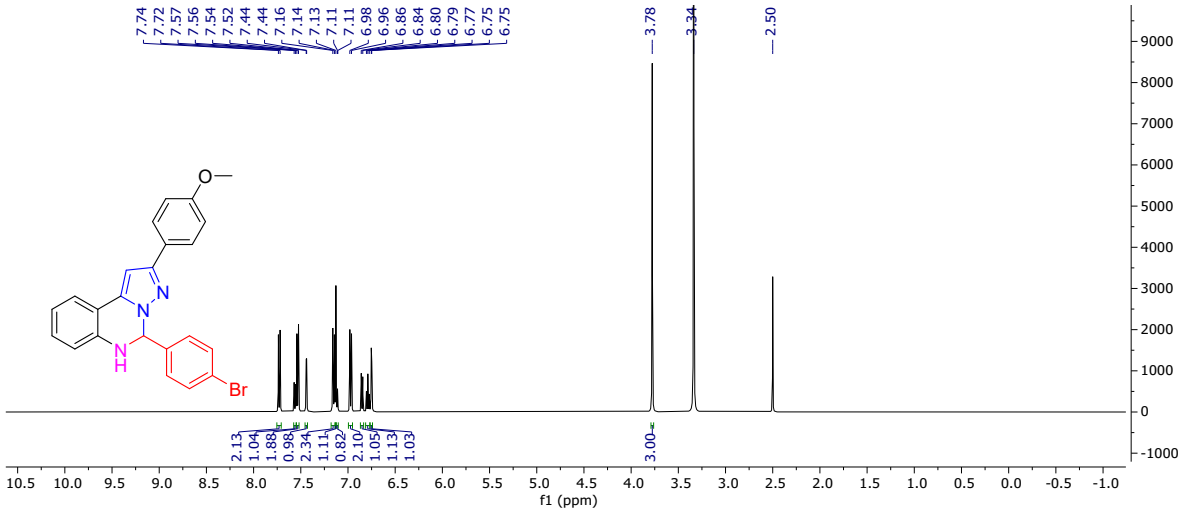


^{13}C {^{1}H} NMR of compound 3m, DMSO-d_6, 125MHz

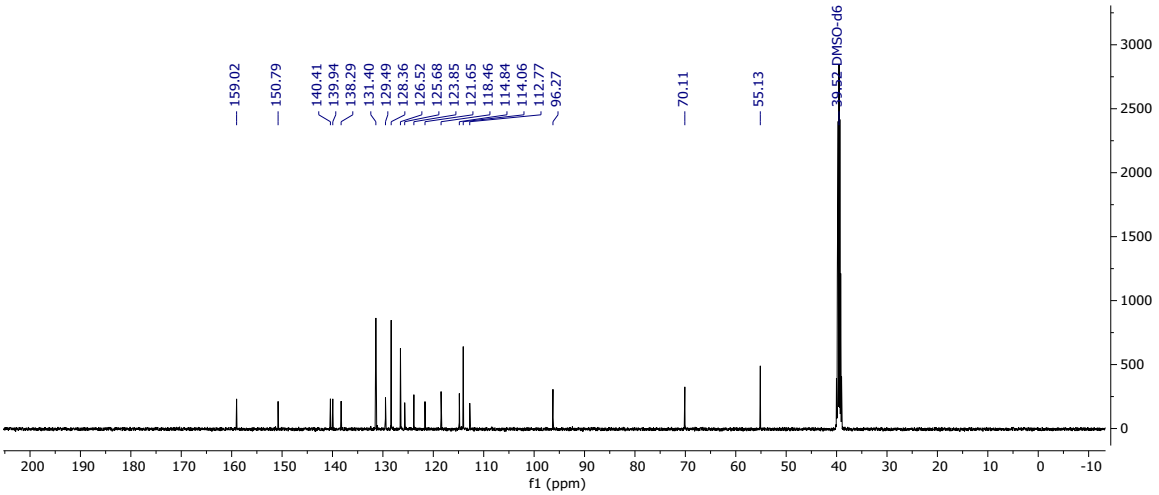


HRMS spectra of compound 3m

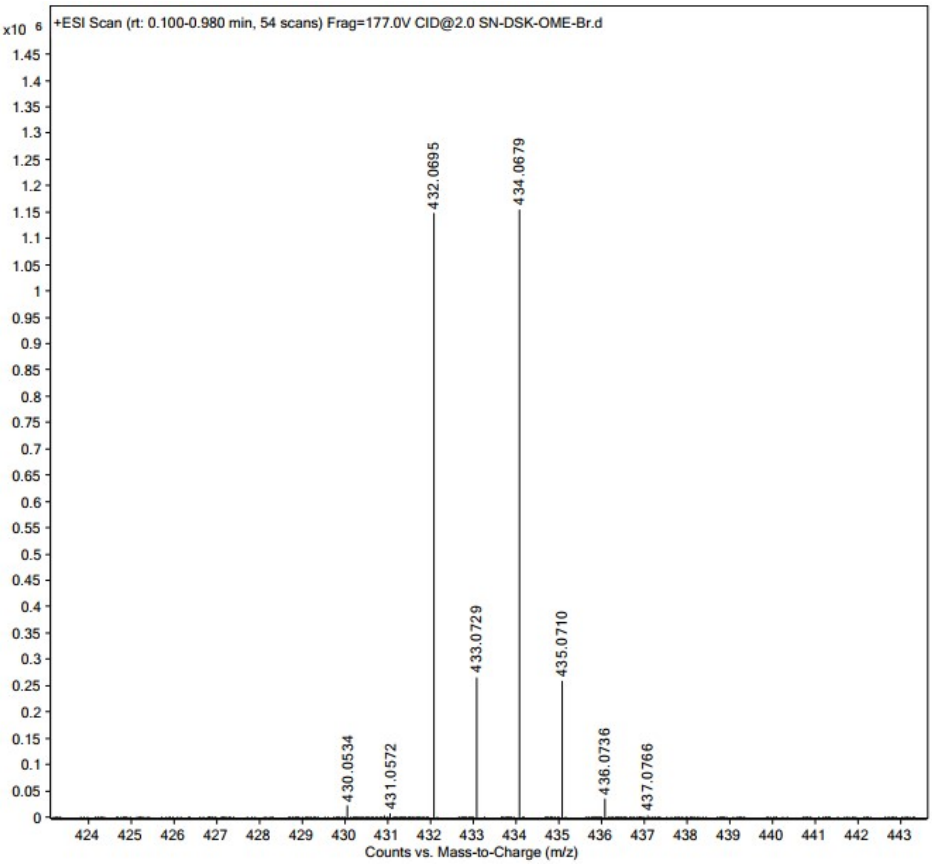
NMR spectrum of compound 3n



^{1}H-NMR spectrum of compound 3n, DMSO-d_6, 500MHz

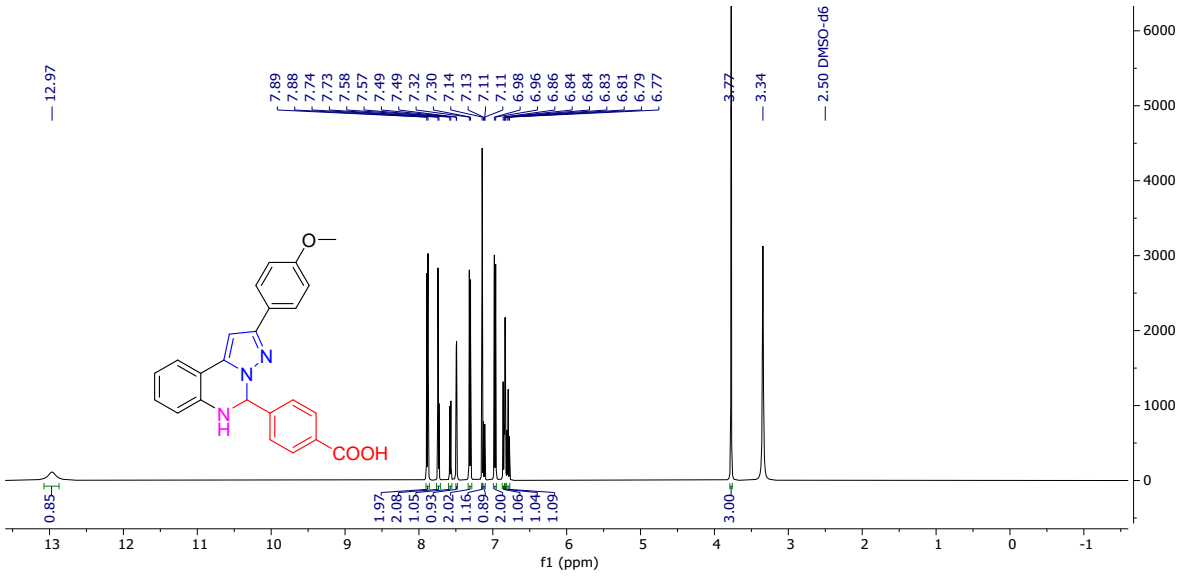


^{13}C {^{1}H} NMR of compound 3n, DMSO-d_6, 125MHz

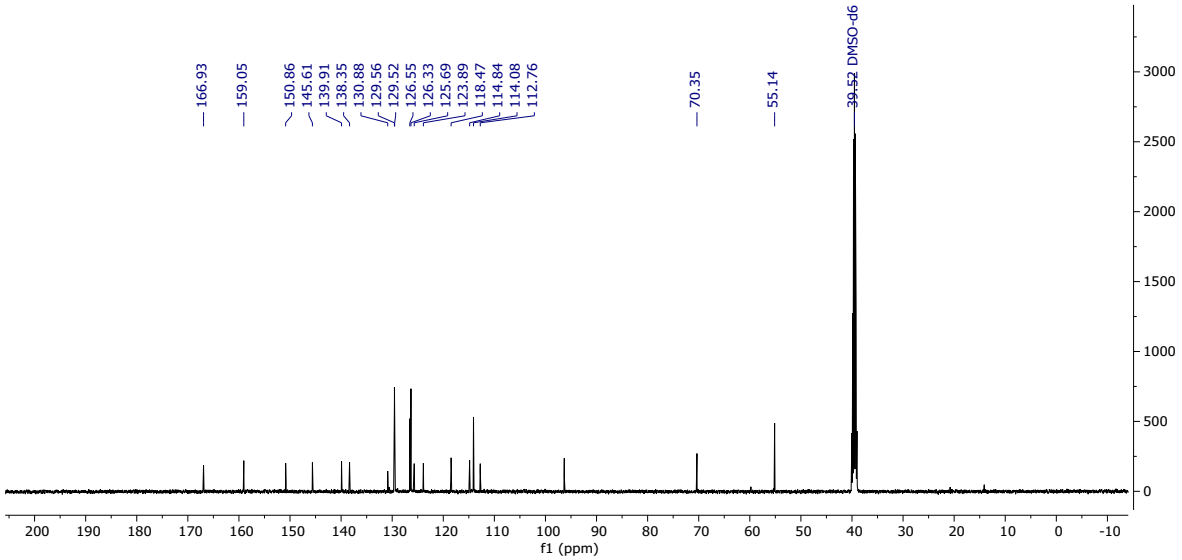


HRMS spectra of compound 3n

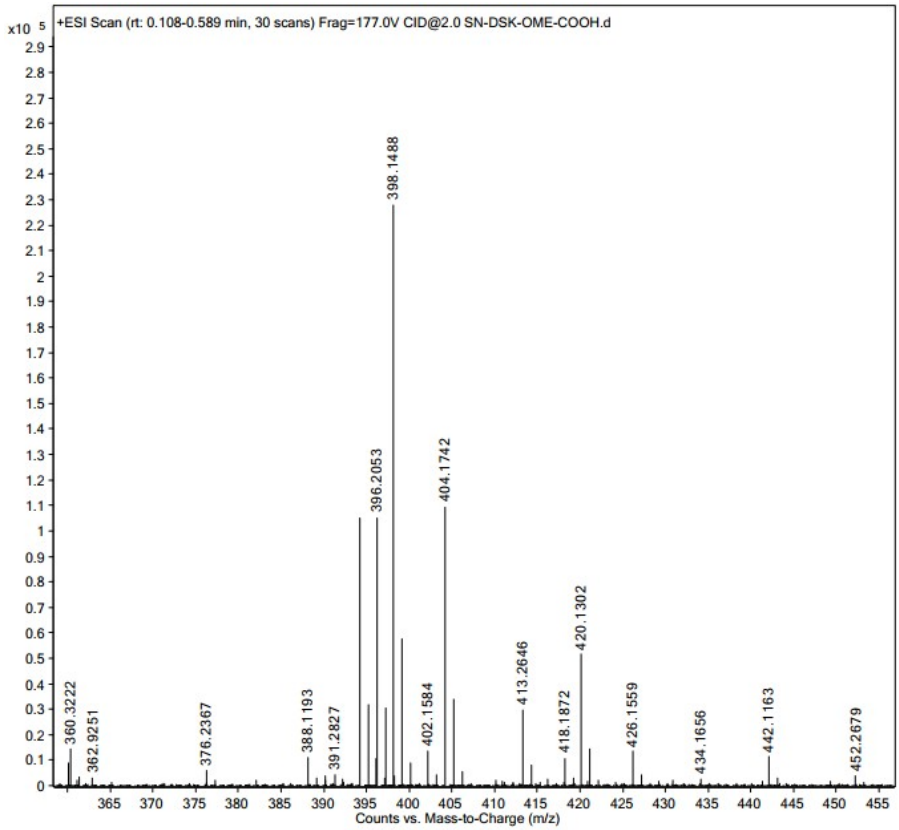
NMR spectrum of compound 3o



^{1}H-NMR spectrum of compound 3o, DMSO-d_6, 500MHz

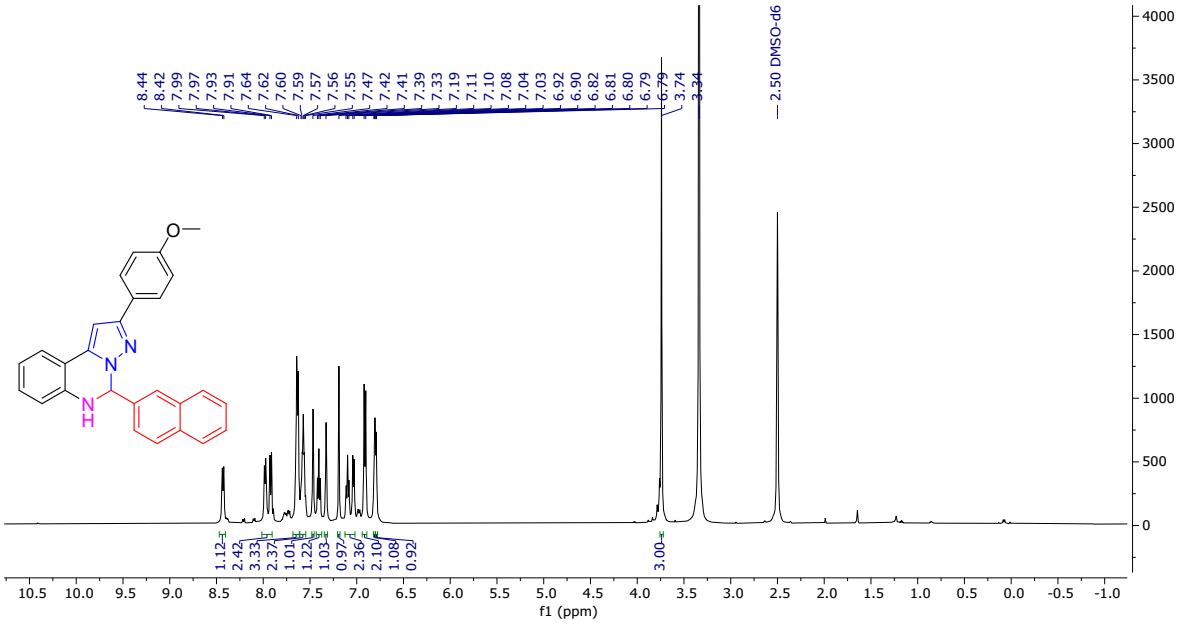


^{13}C {^{1}H} NMR of compound 3o, DMSO-d_6, 125MHz

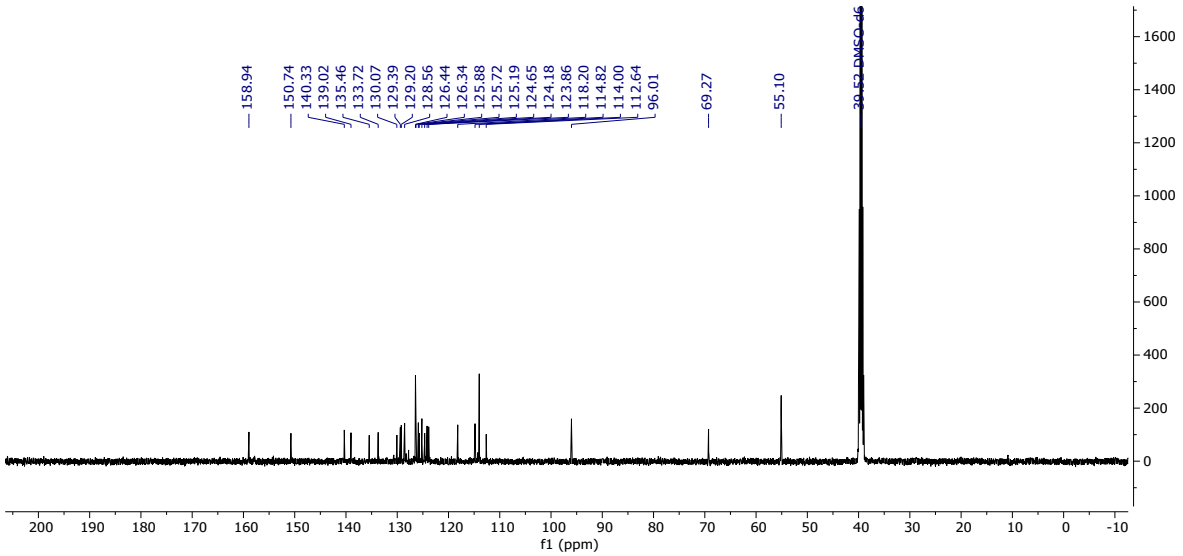


HRMS spectra of compound 3o

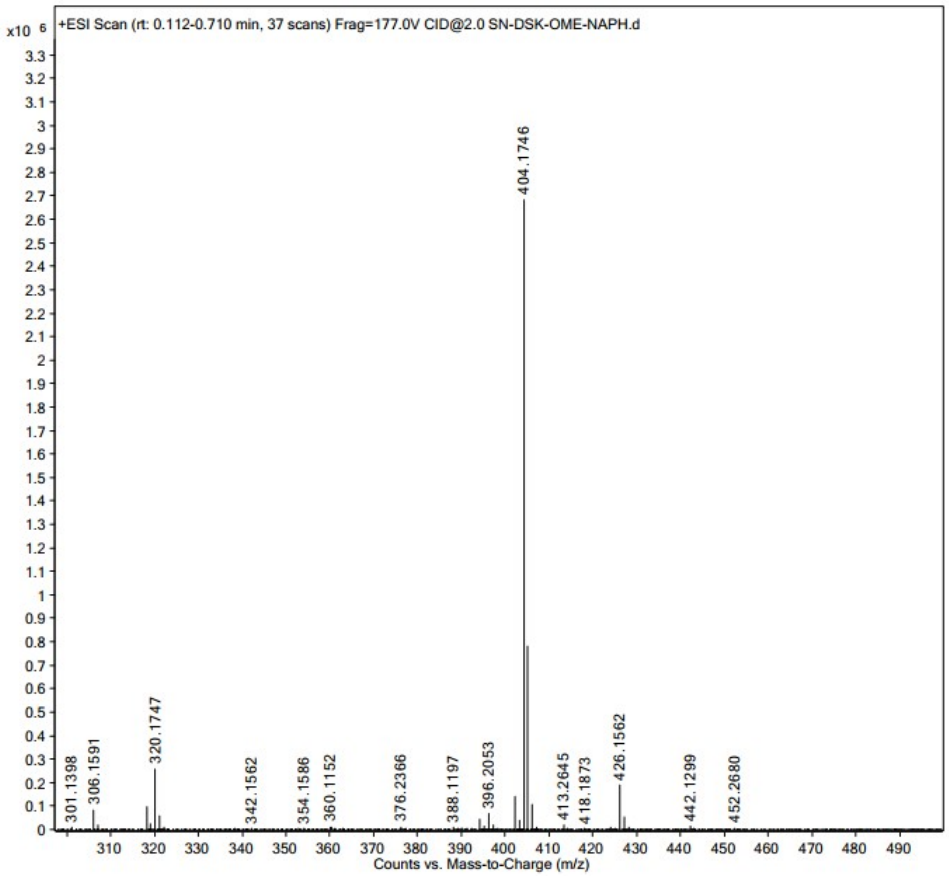
NMR spectrum of compound 3p



^{1}H-NMR spectrum of compound 3p, DMSO-d_6, 500MHz

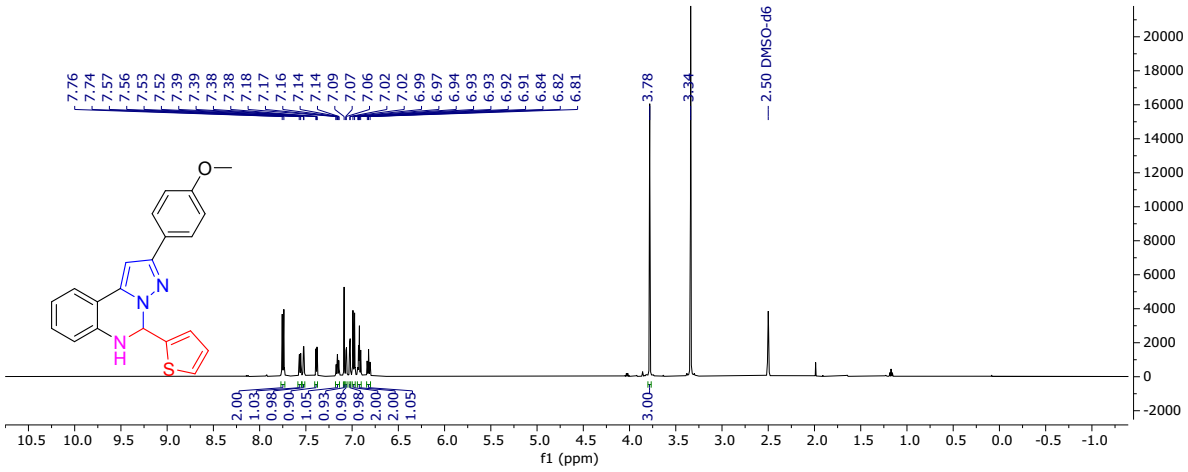


^{13}C {^{1}H} NMR of compound 3p, DMSO-d_6, 125MHz

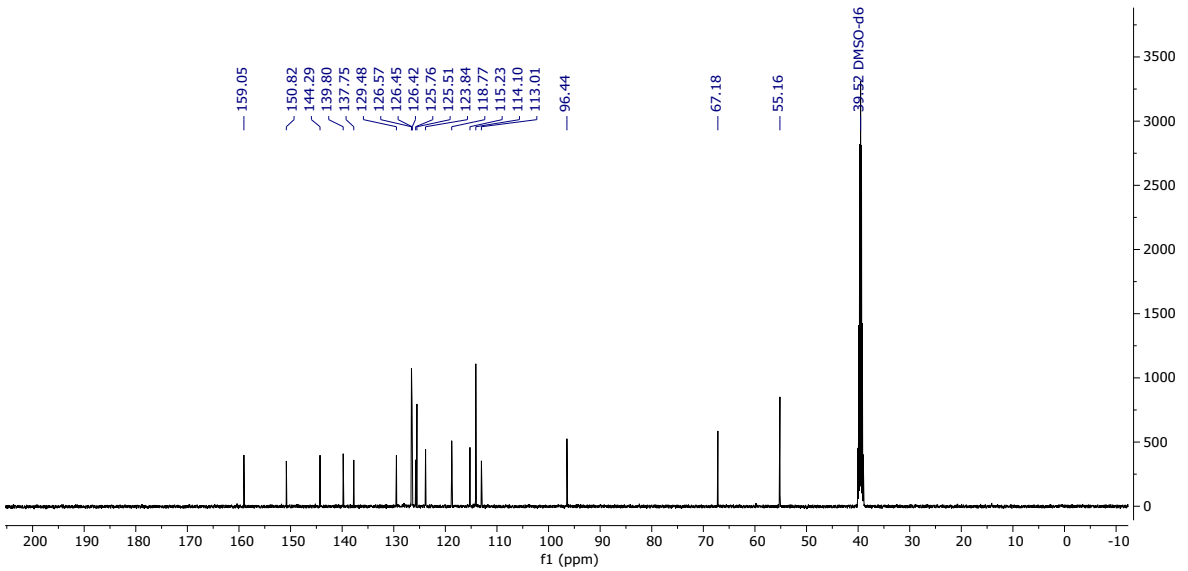


HRMS spectra of compound 3p

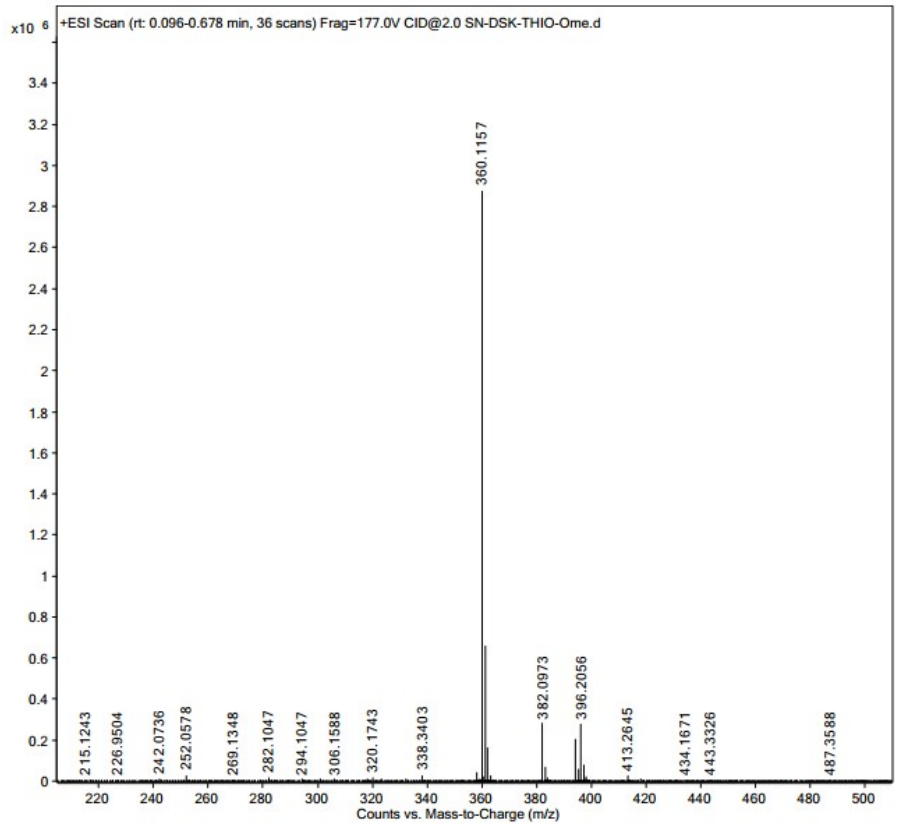
NMR spectrum of compound 3q



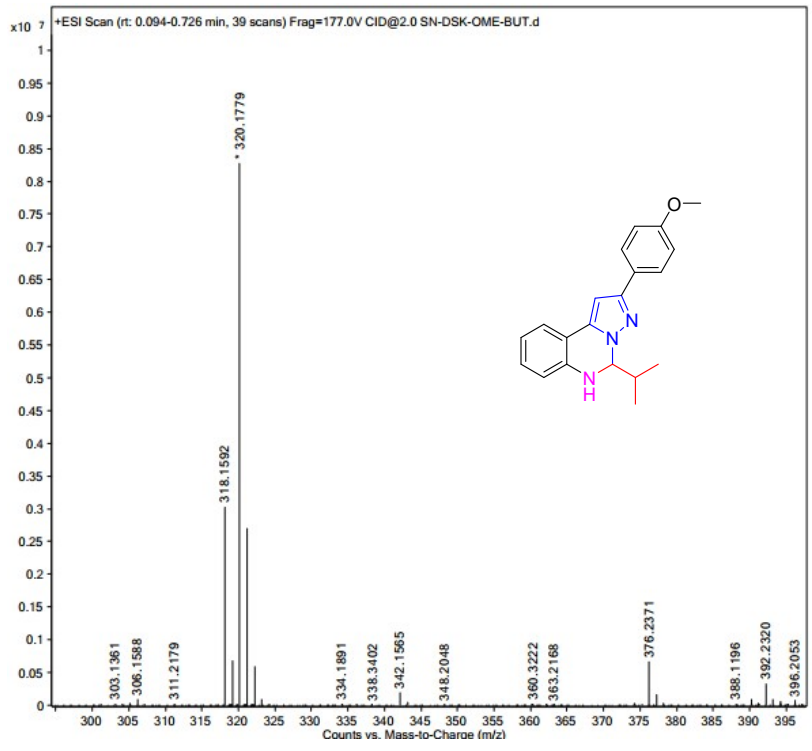
^{1}H-NMR spectrum of compound 3q, DMSO-d_6, 500MHz



^{13}C {^{1}H} NMR of compound 3q, DMSO-d_6, 125MHz

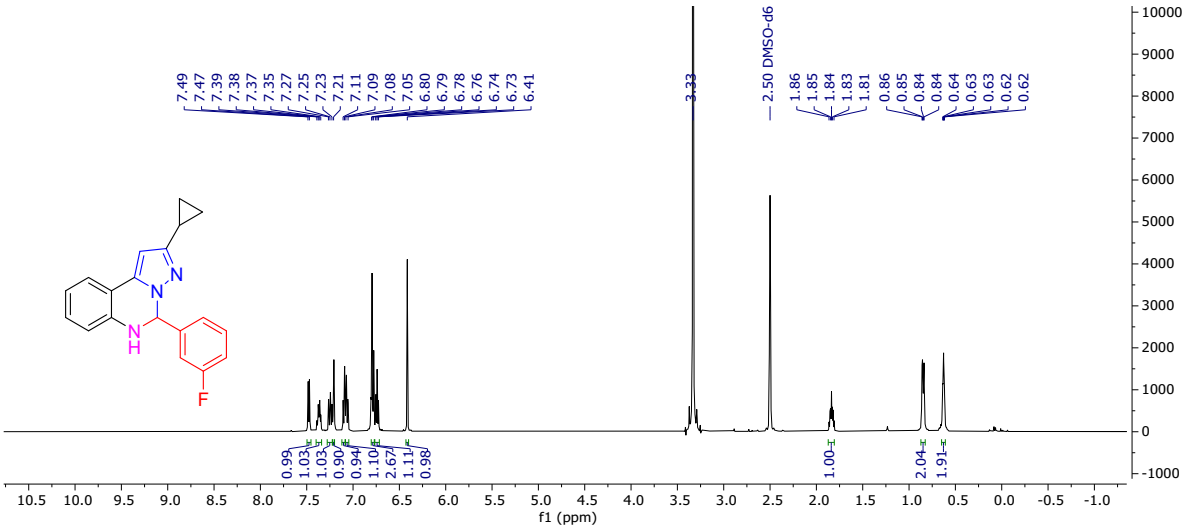


HRMS spectra of compound 3q

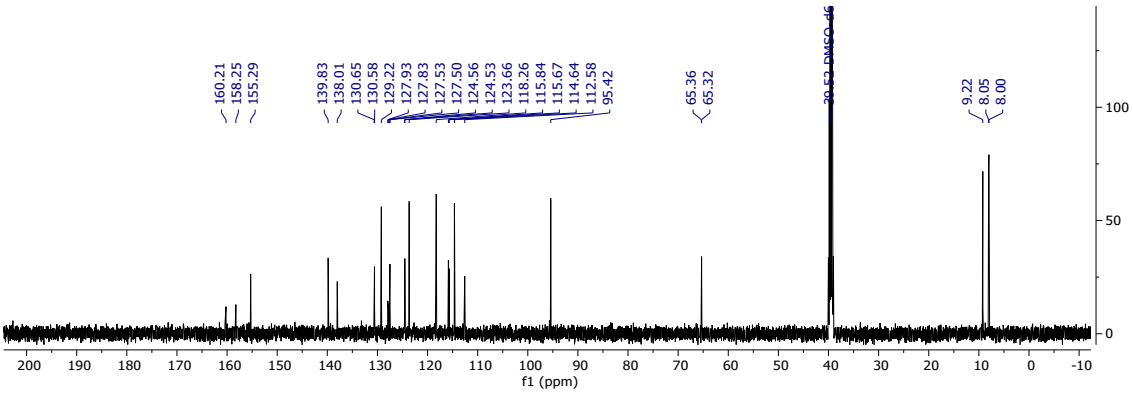


HRMS spectra of compound 3r

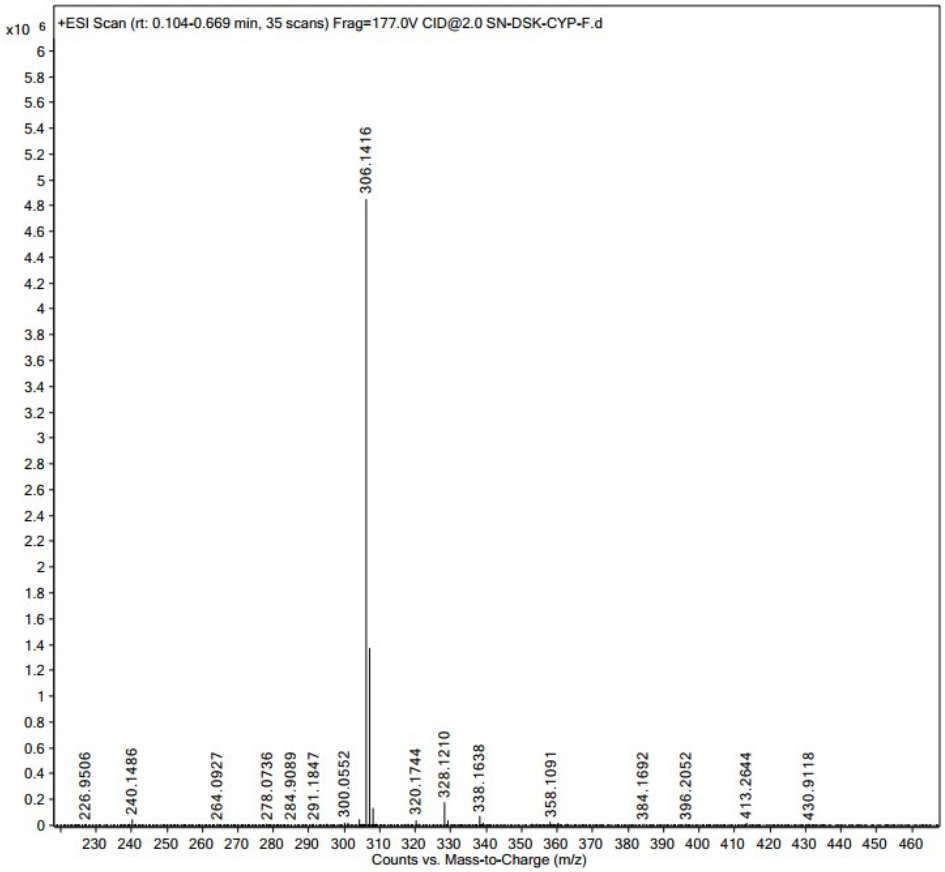
NMR spectrum of compound 3s



^{1}H-NMR spectrum of compound 3s, DMSO-d_6, 500MHz

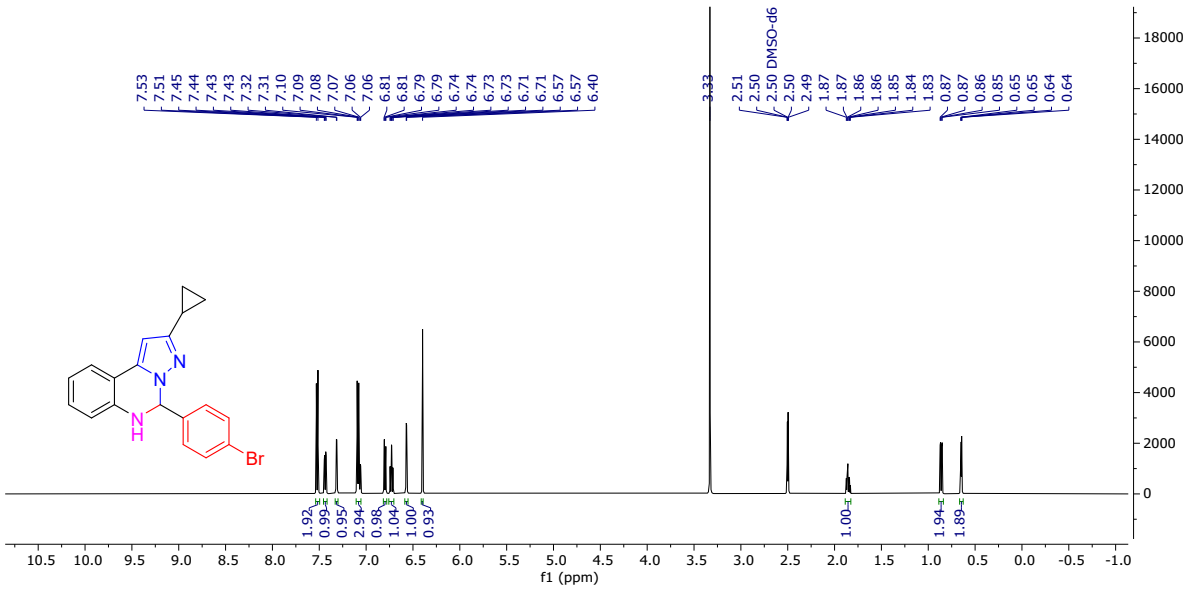


^{13}C {^{1}H} NMR of compound 3s, DMSO-d_6, 125MHz

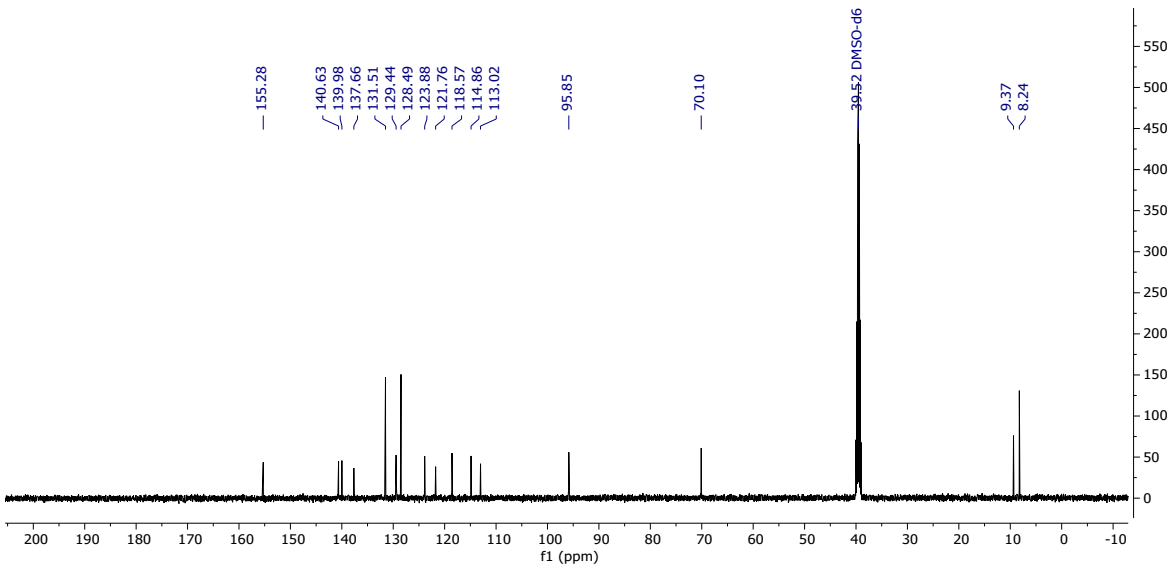


HRMS spectra of compound 3s

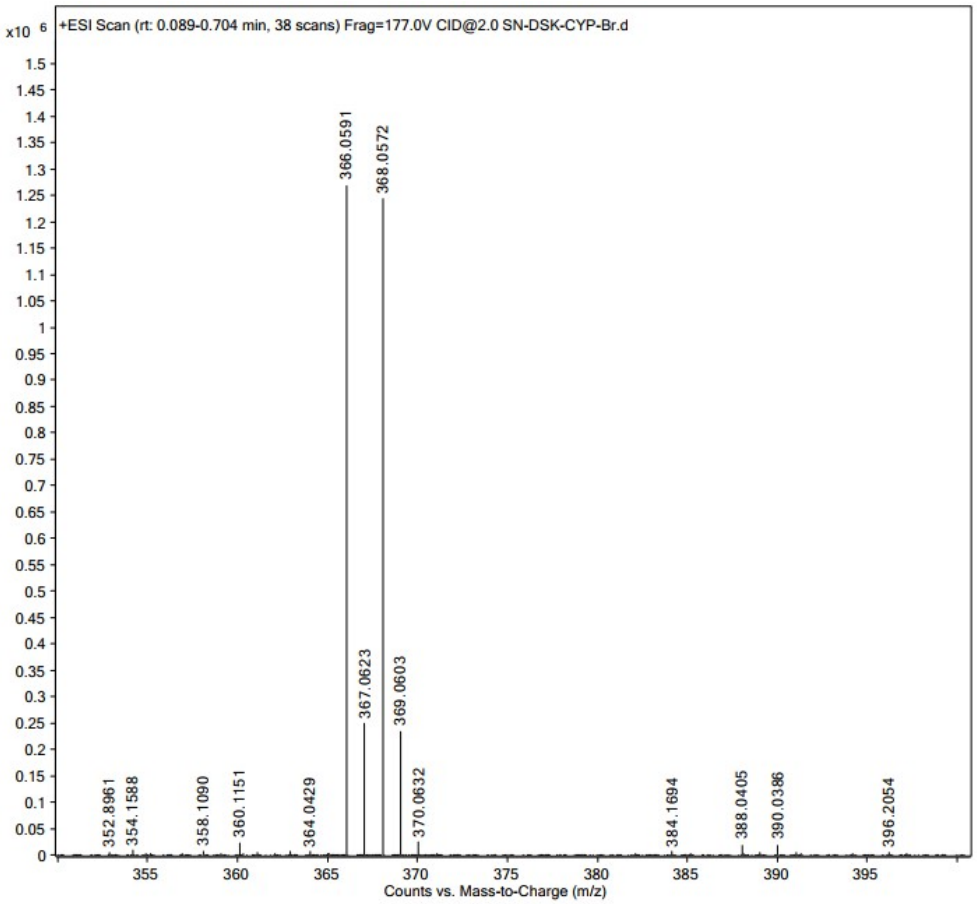
NMR spectrum of compound 3t



^{1}H-NMR spectrum of compound 3t, DMSO-*d6*, 500MHz

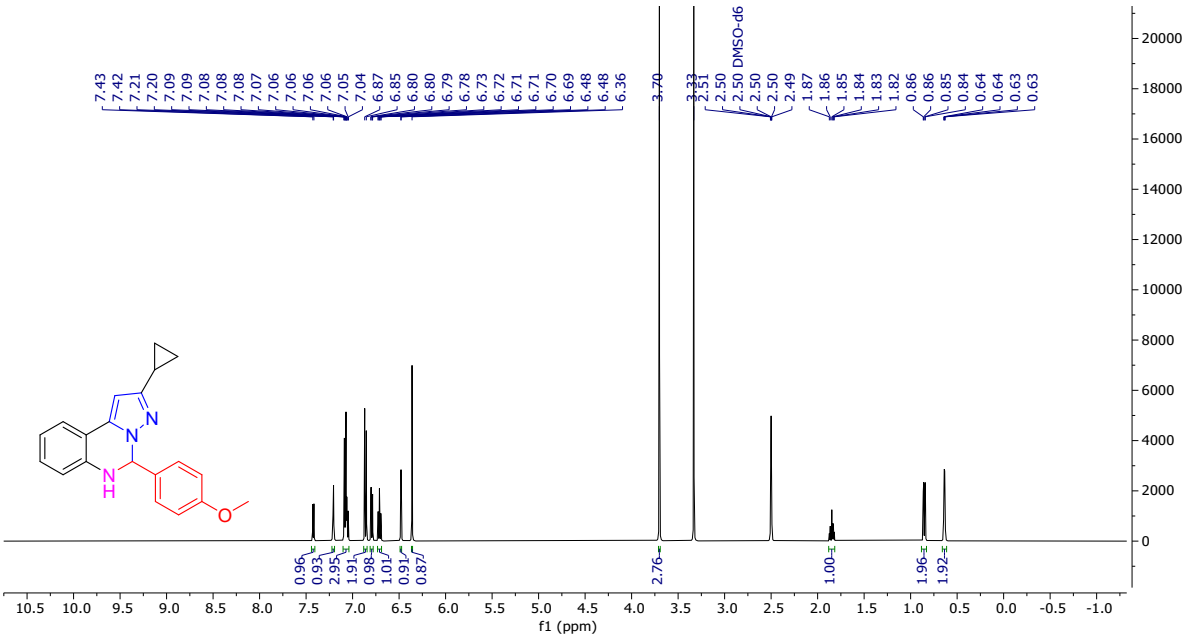


^{13}C {^{1}H} NMR of compound 3t, DMSO-d_6, 125MHz

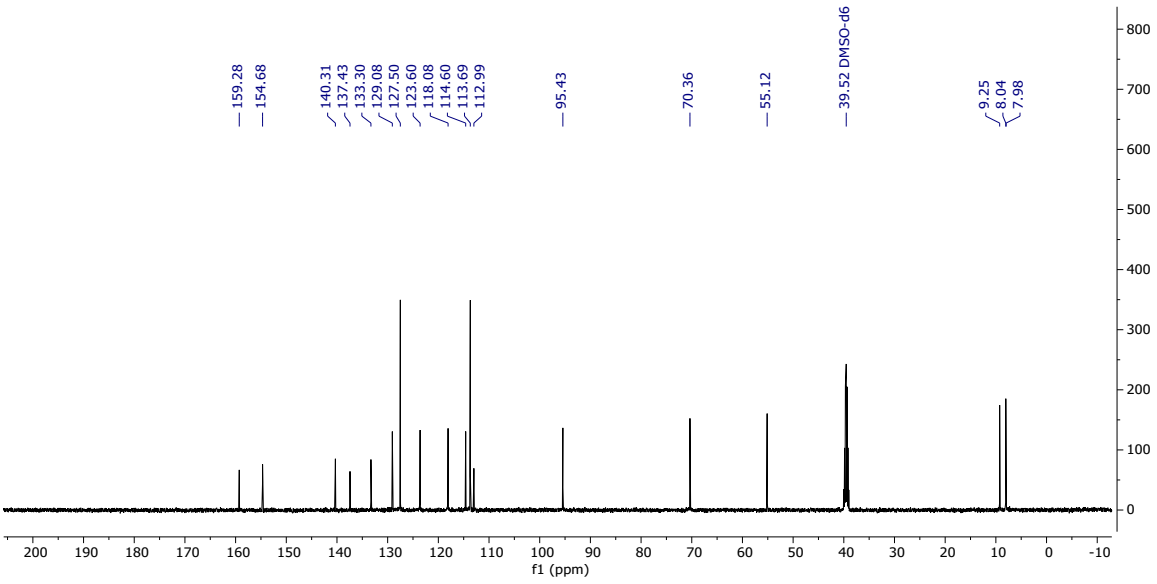


HRMS spectra of compound 3t

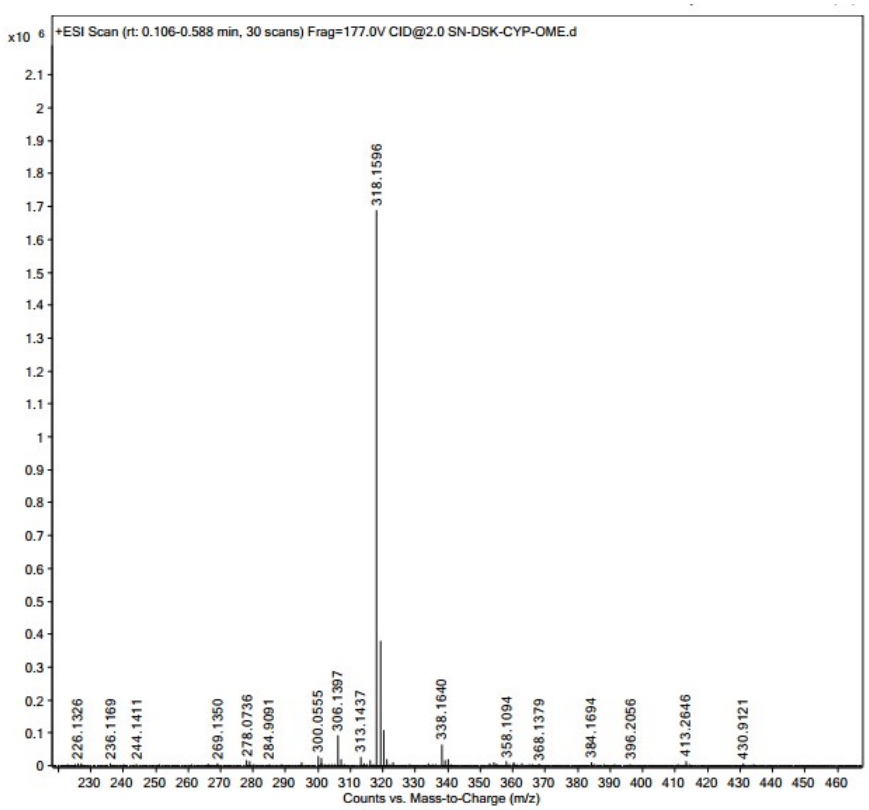
NMR spectrum of compound 3u



^{1}H-NMR spectrum of compound 3u, DMSO-d_6, 500MHz

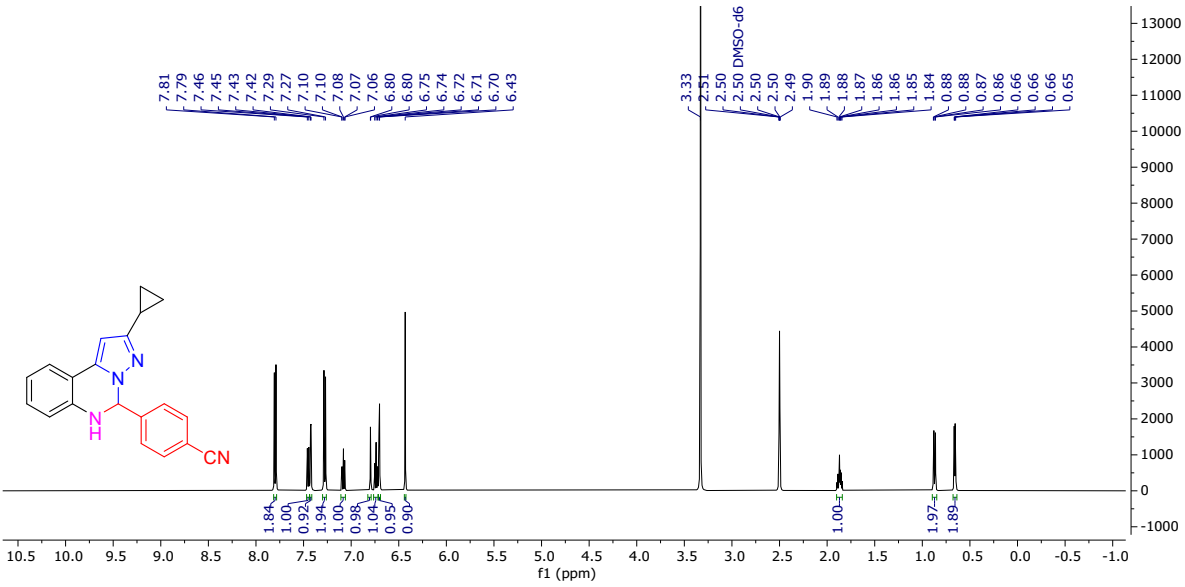


^{13}C {^{1}H} NMR of compound 3u, DMSO-d_6, 125MHz

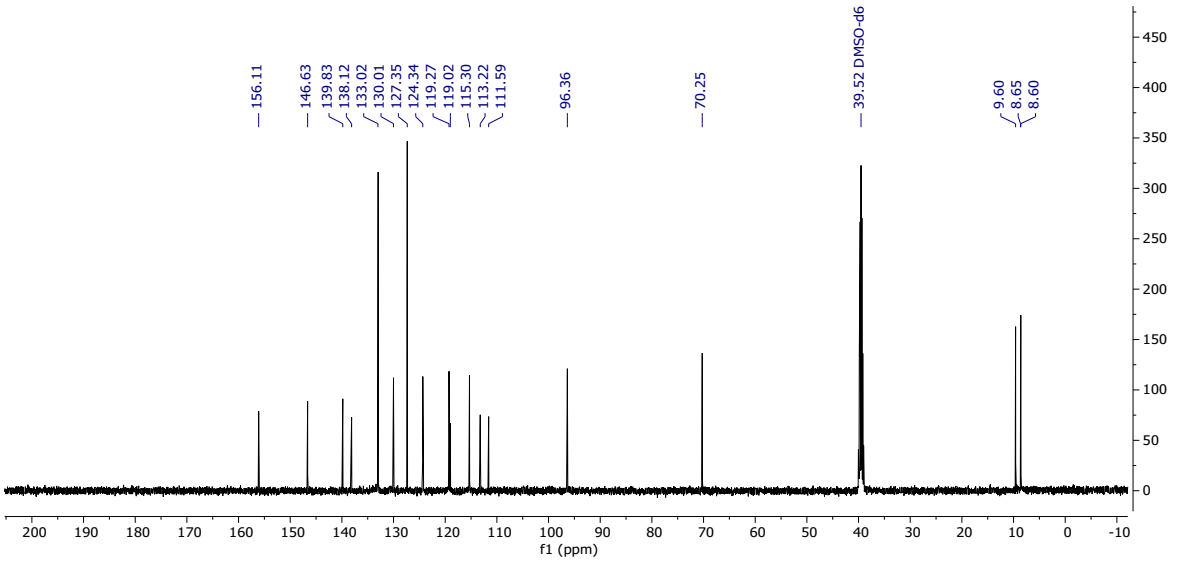


HRMS spectra of compound 3u

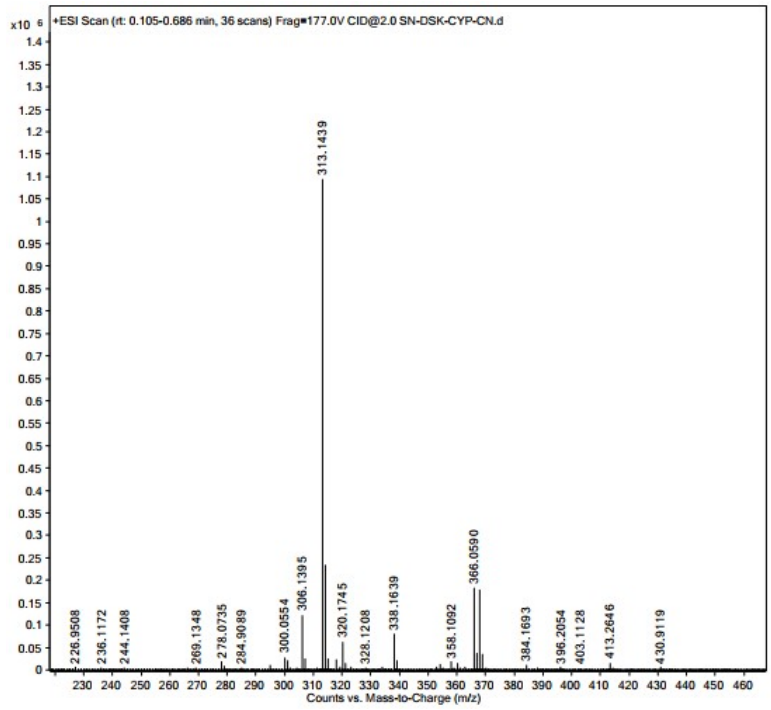
NMR spectrum of compound 3v



^{1}H-NMR spectrum of compound 3v, DMSO-d_6, 500MHz

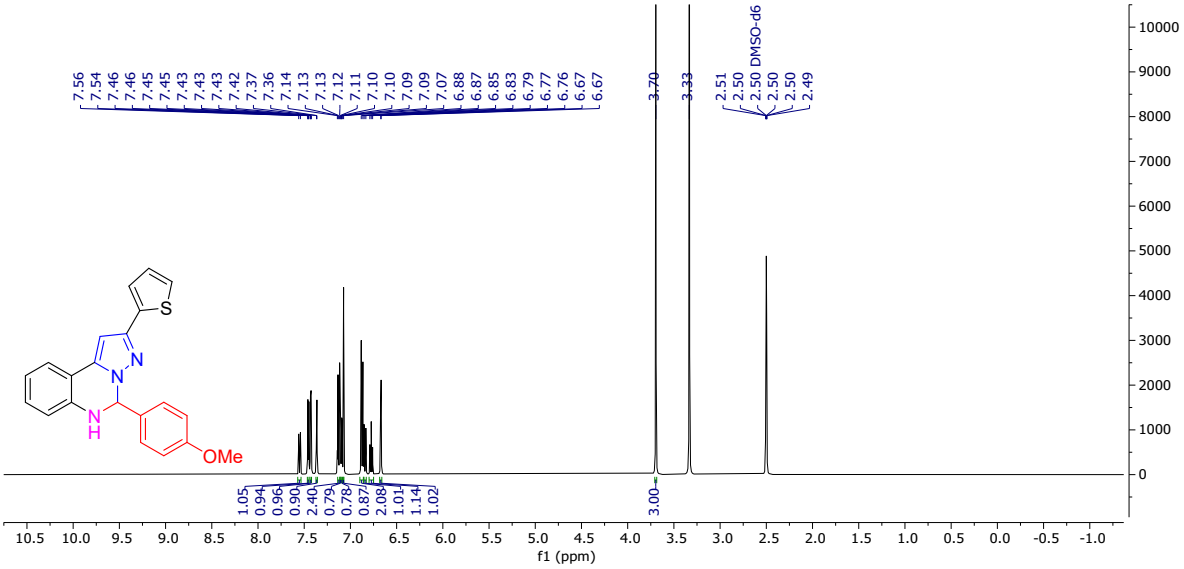


^{13}C {^{1}H} NMR of compound 3v, DMSO-d_6, 125MHz

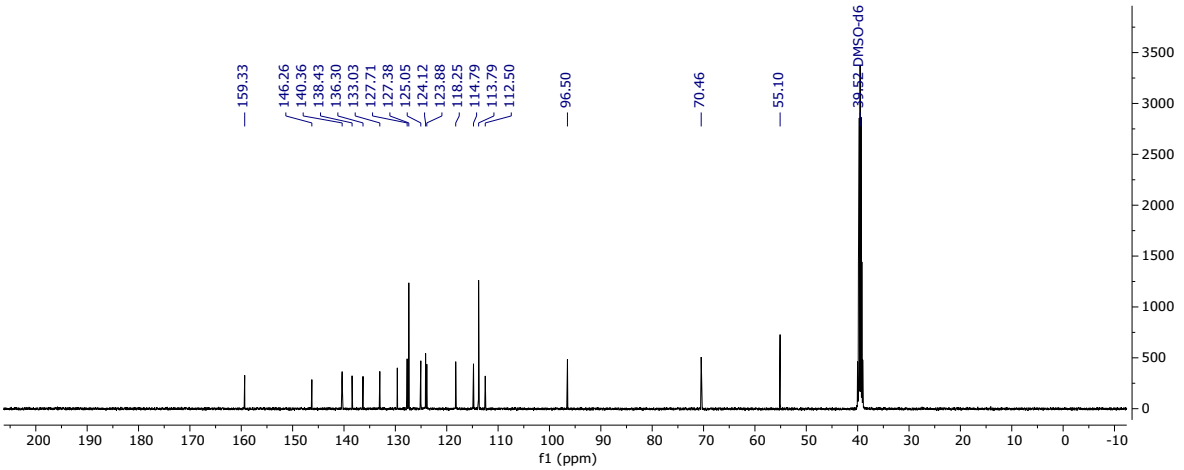


HRMS spectra of compound 3v

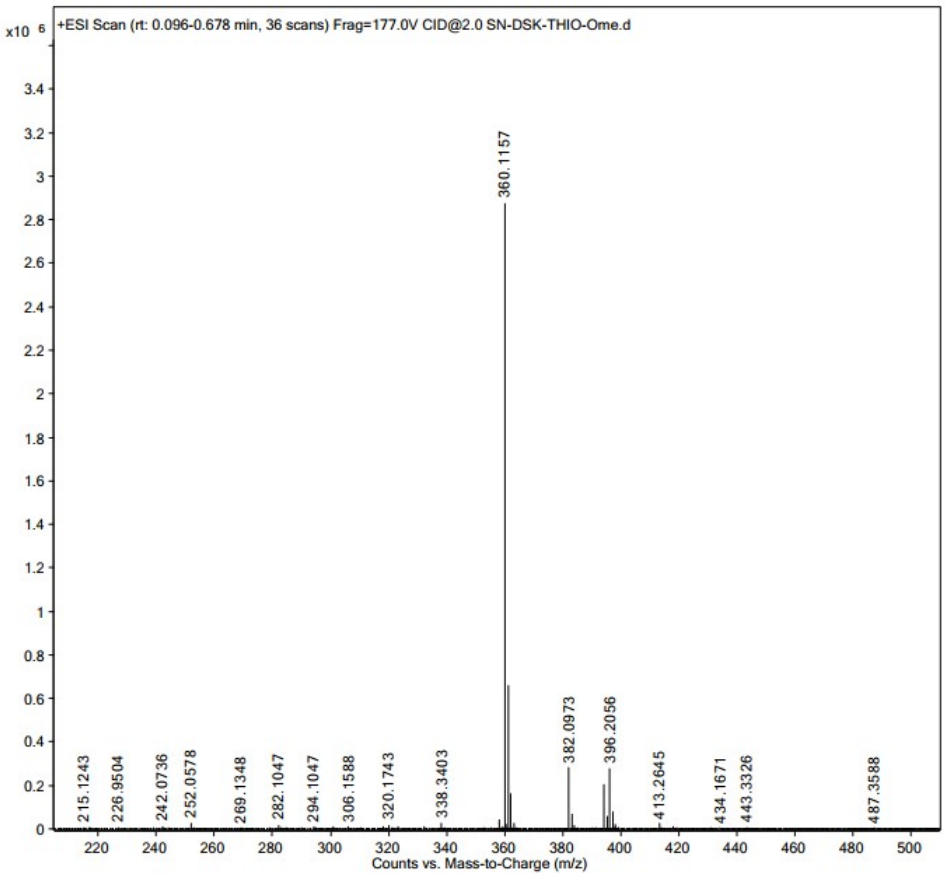
NMR spectrum of compound 3w



^{1}H-NMR spectrum of compound 3w, DMSO-*d6*, 500MHz

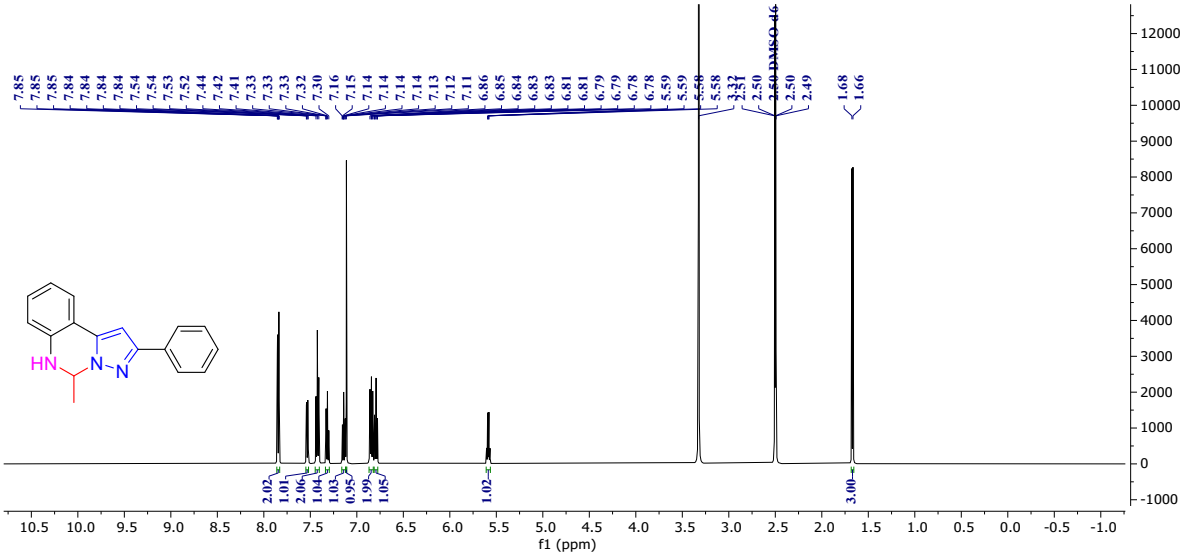


^{13}C {^{1}H} NMR of compound 3w, DMSO-d_6, 125MHz

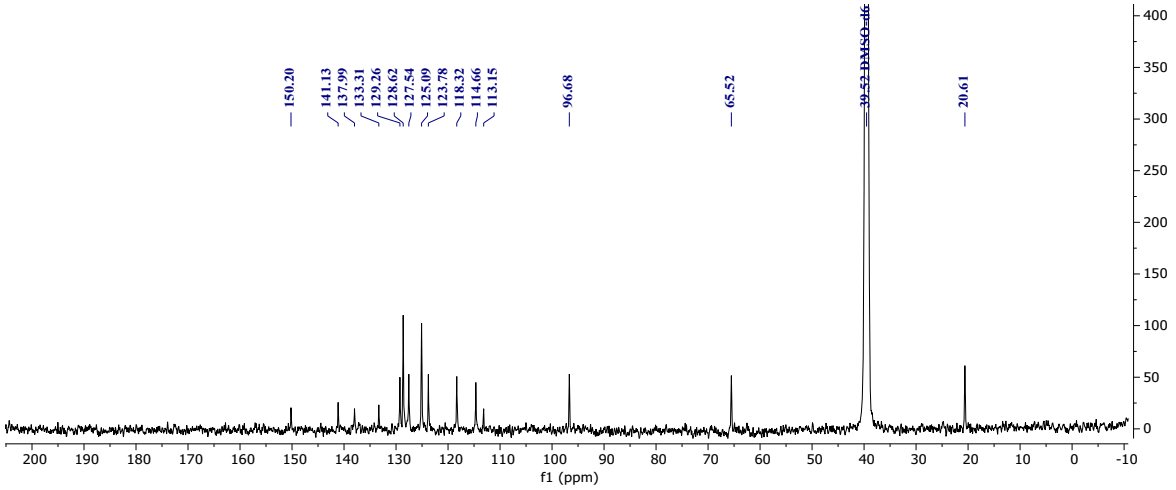


HRMS spectra of compound 3w

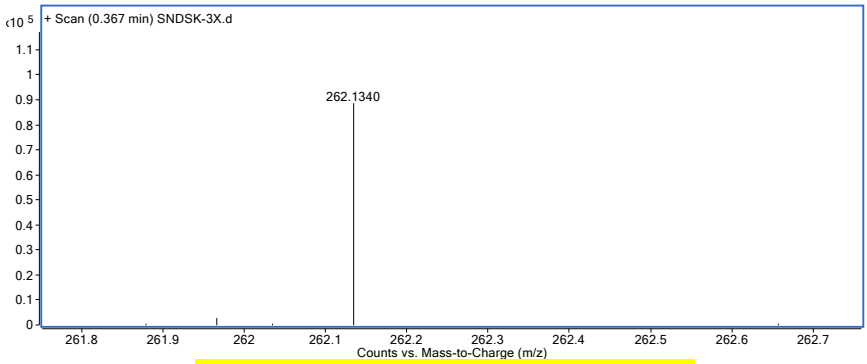
NMR spectrum of compound 3x



^{1}H-NMR spectrum of compound 3x, DMSO-*d6*, 500MHz

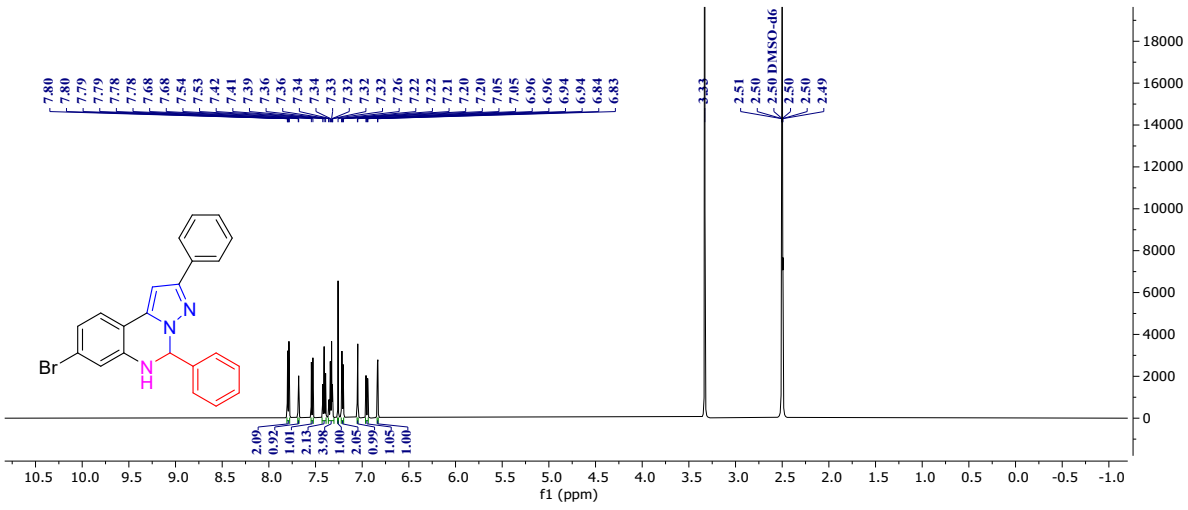


^{13}C {^{1}H} NMR of compound 3x, DMSO-d_6, 125MHz

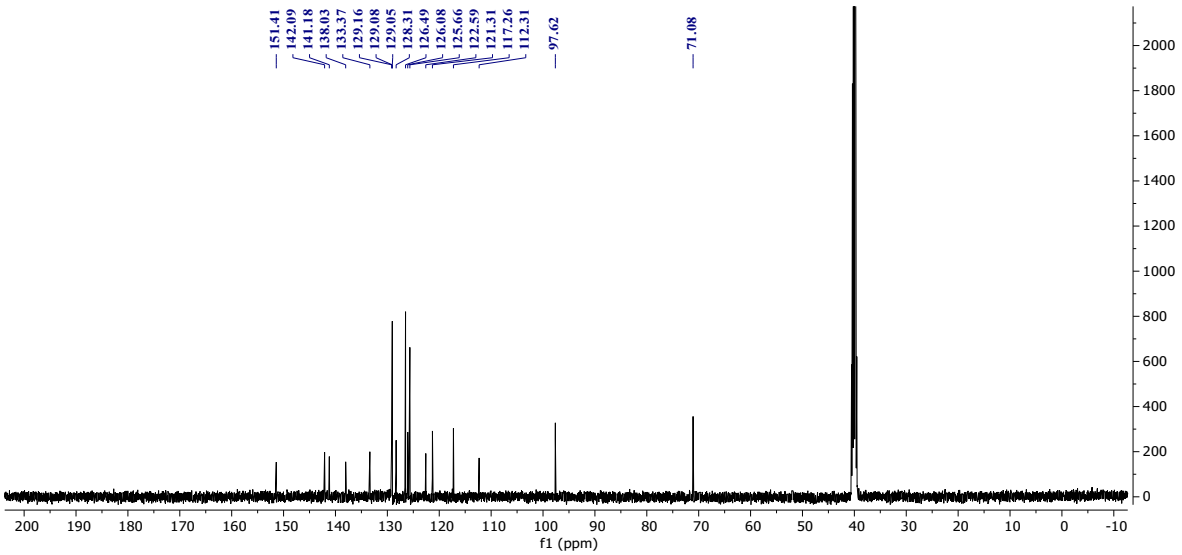


HRMS spectra of compound 3x

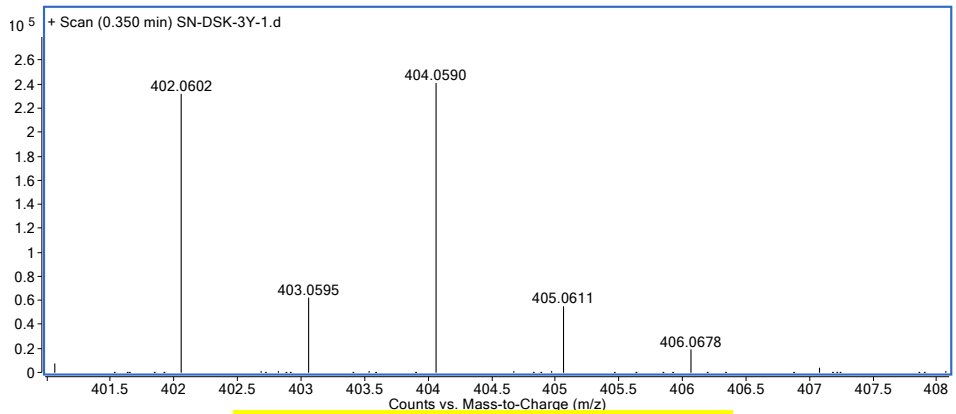
NMR spectrum of compound 3y



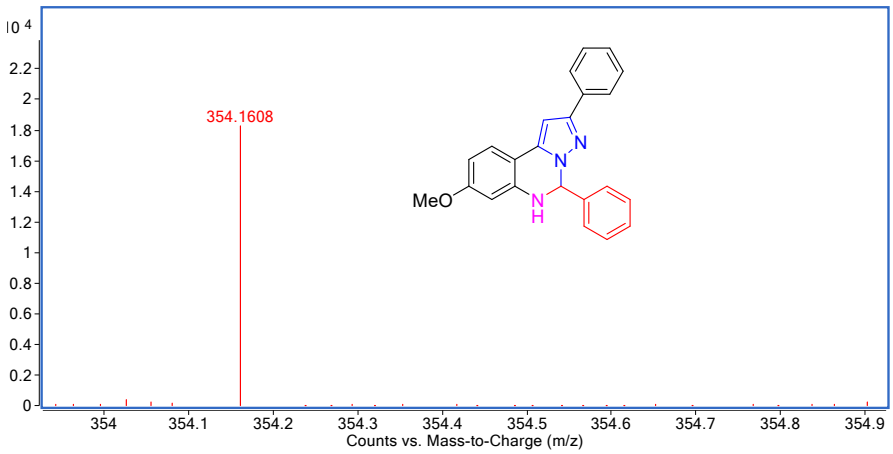
^{1}H-NMR spectrum of compound 3y, DMSO-*d6*, 500MHz



^{13}C {^{1}H} NMR of compound 3y, DMSO-d_6, 125MHz

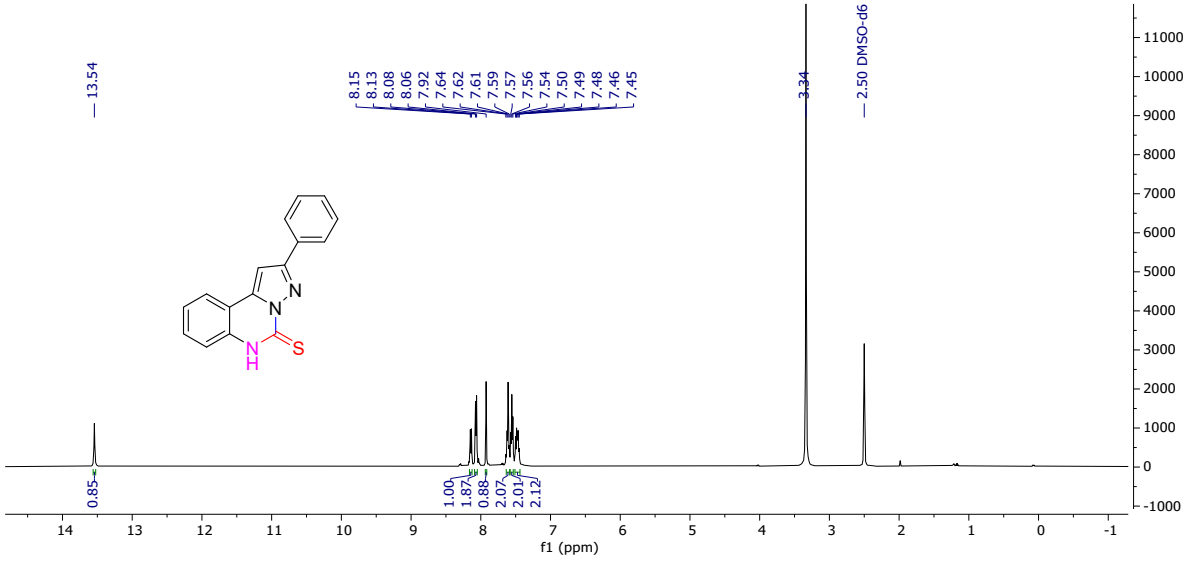


HRMS spectra of compound 3y

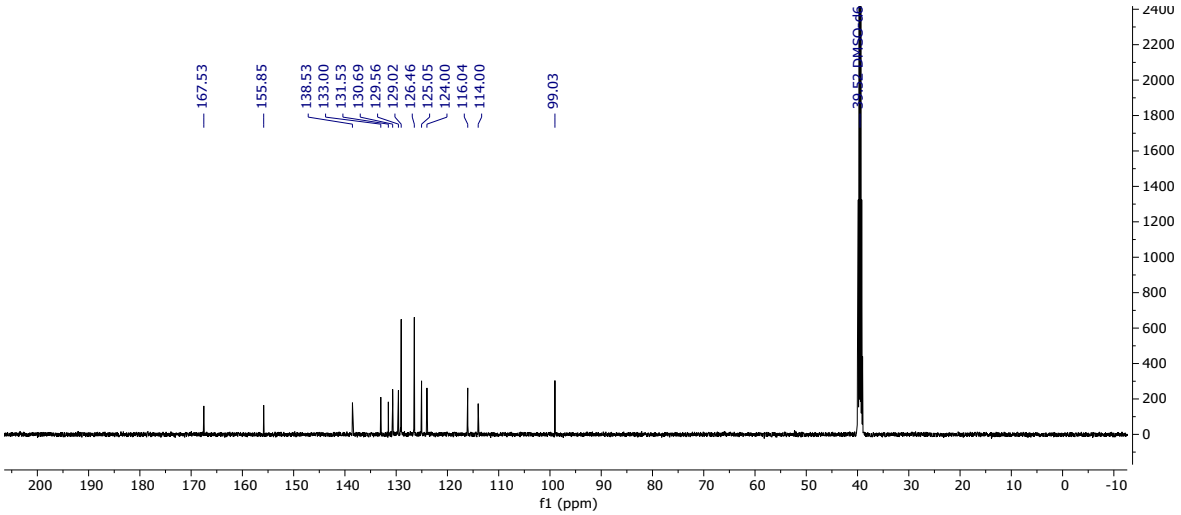


HRMS spectra of compound 3z

NMR spectrum of compound 5a



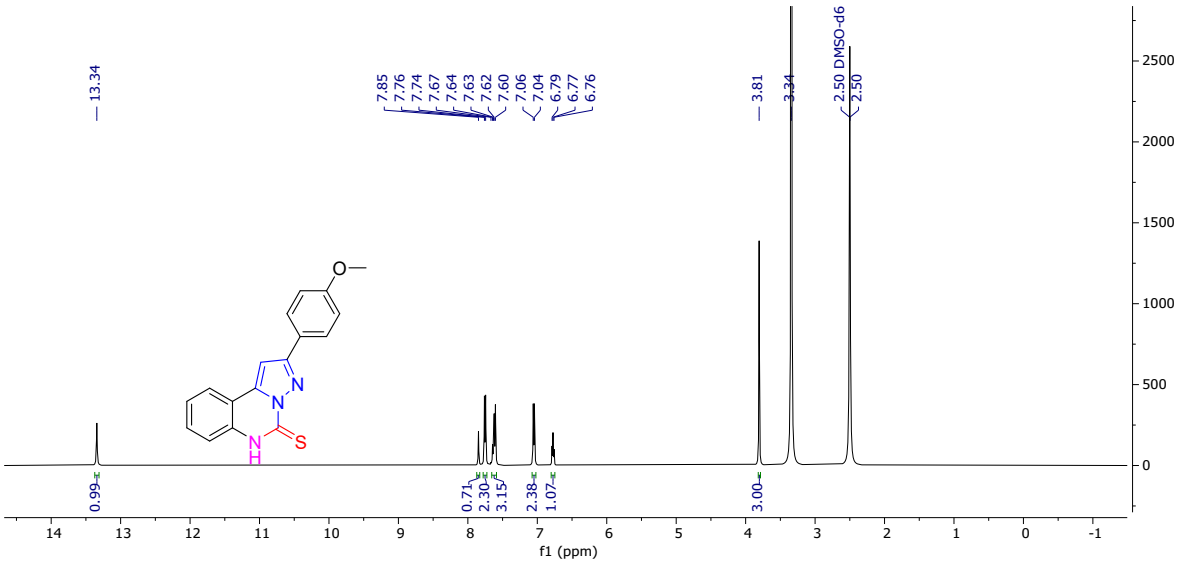
^{1}H-NMR spectrum of compound 5a, DMSO-d_6, 500MHz



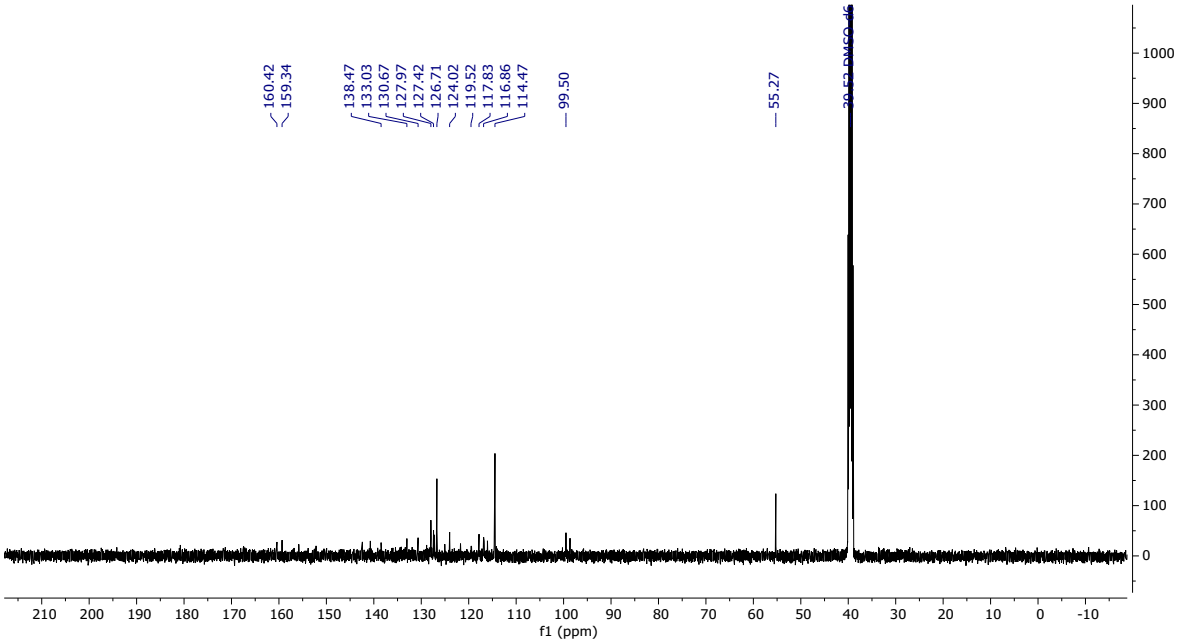
^{13}C {^{1}H} NMR of compound 5a, DMSO-d_6, 125MHz

HRMS spectra of compound 5a

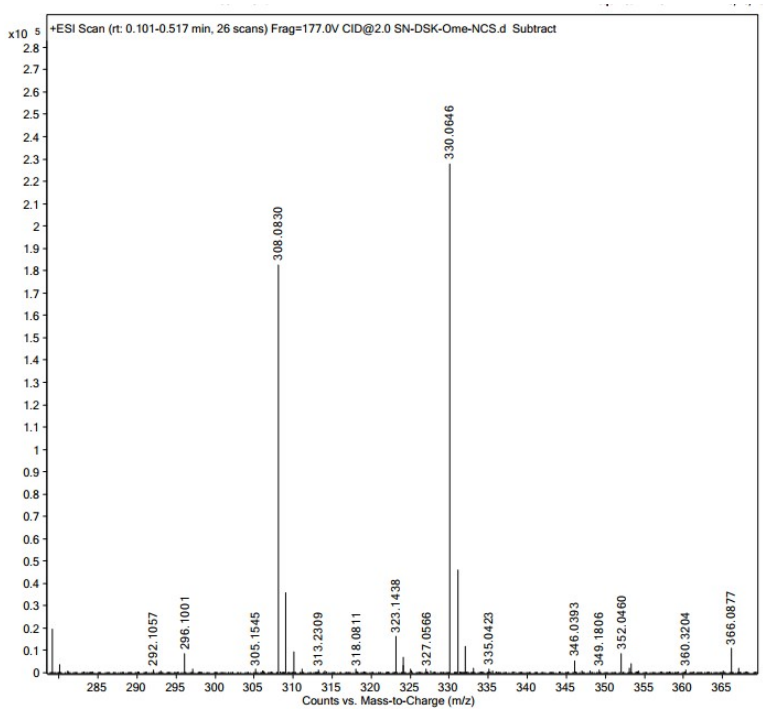
NMR spectrum of compound 5b



^{1}H-NMR spectrum of compound 5b, DMSO-d_6, 500MHz

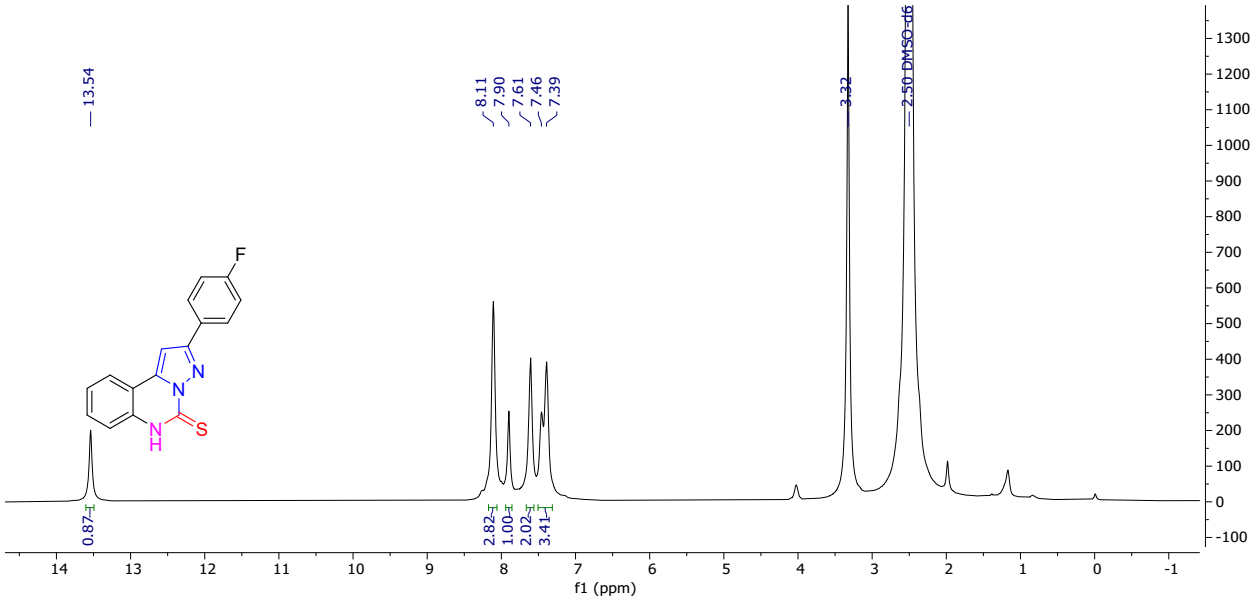


^{13}C {^{1}H} NMR of compound 5b, DMSO-d_6, 125MHz

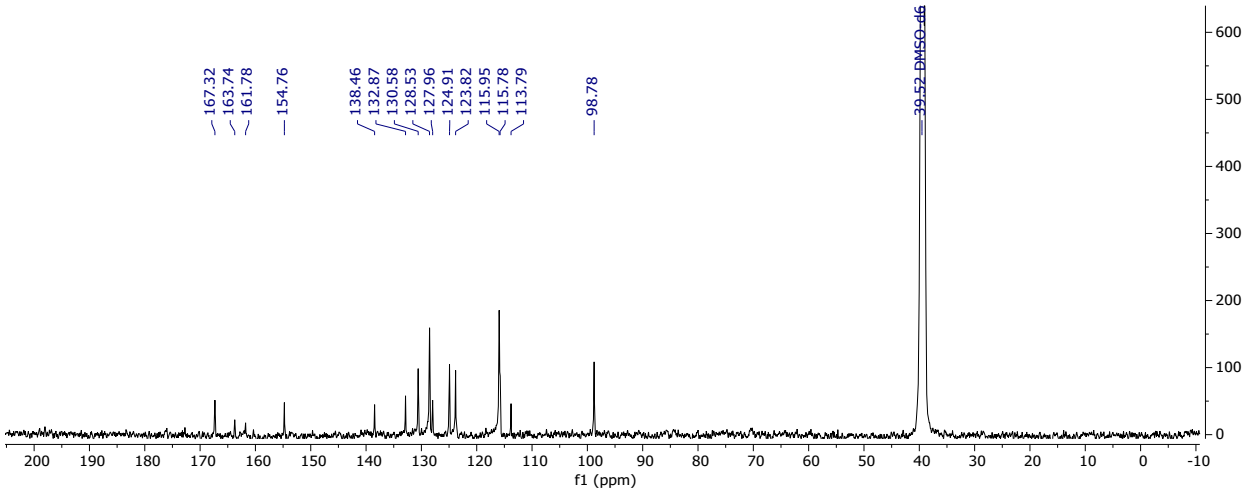


HRMS spectra of compound 5b

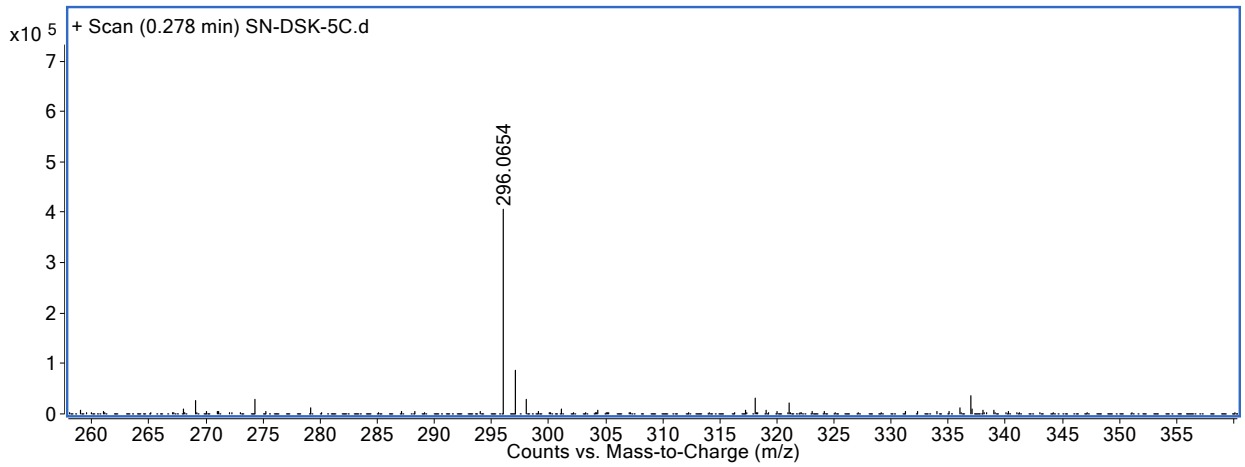
NMR spectrum of compound 5c



^{1}H-NMR spectrum of compound 5c, DMSO-d_6, 500MHz

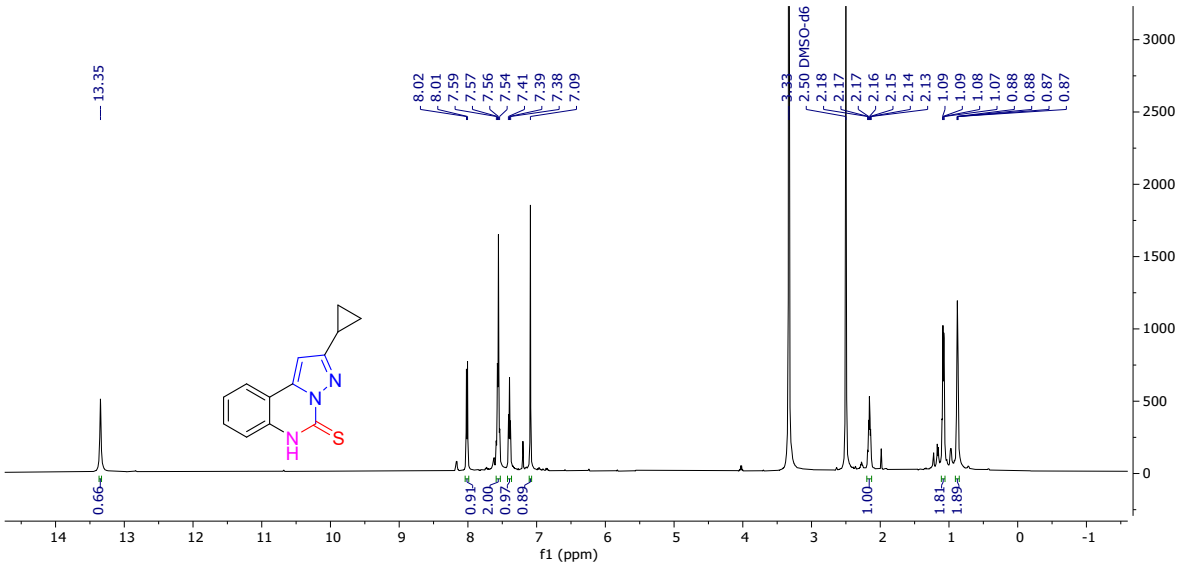


^{13}C {^{1}H} NMR of compound 5c, DMSO-d_6, 125MHz

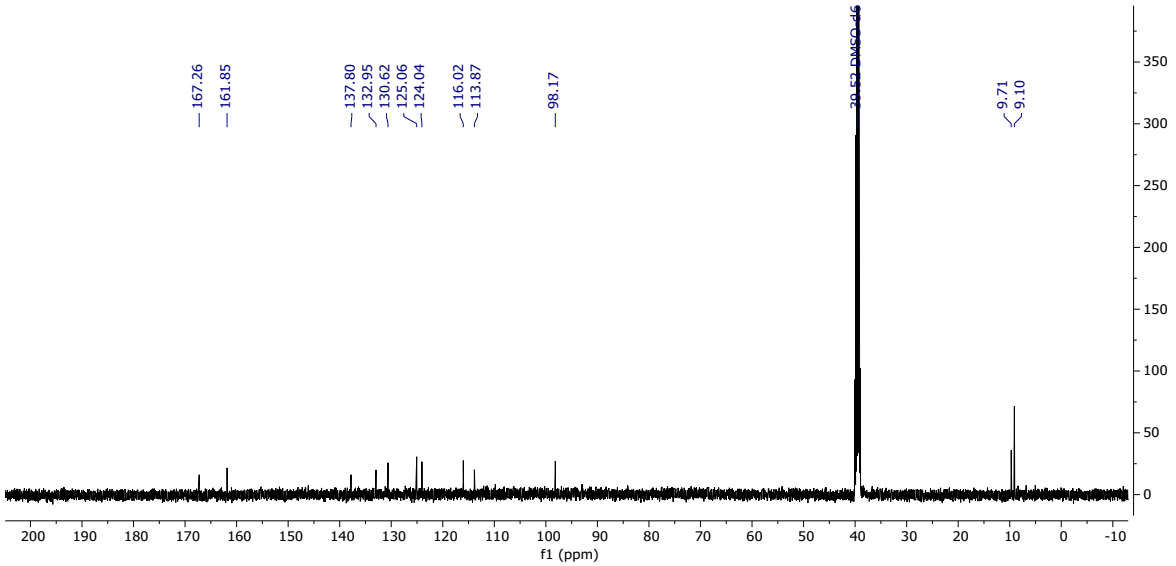


HRMS spectra of compound 5c

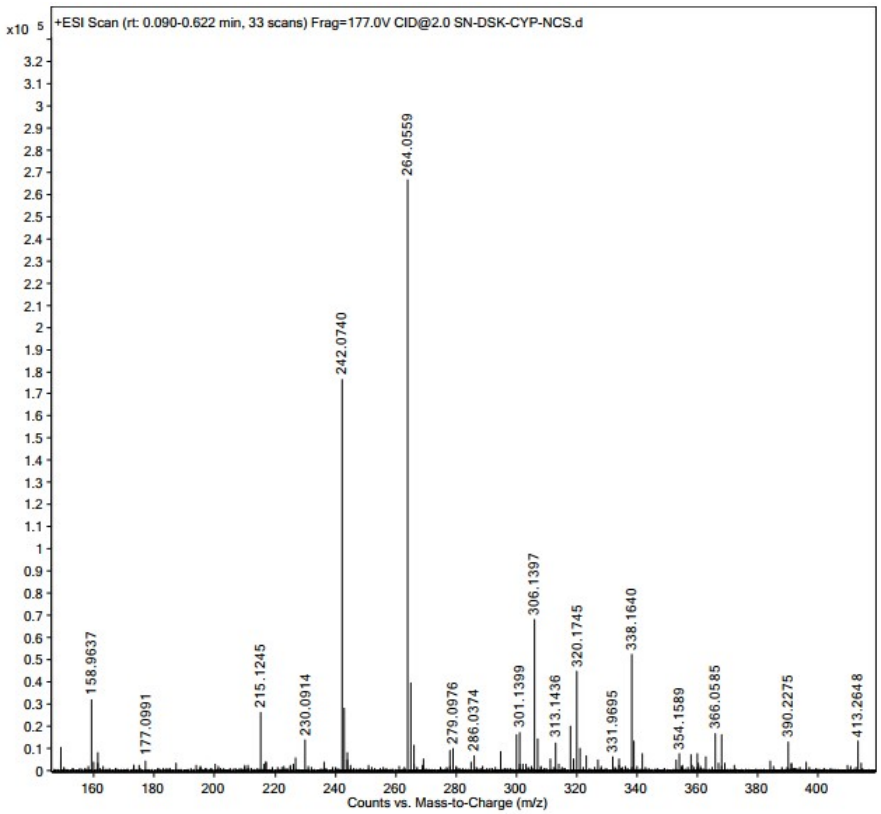
NMR spectrum of compound 5d



^{1}H-NMR spectrum of compound 5d, DMSO-d_6, 500MHz

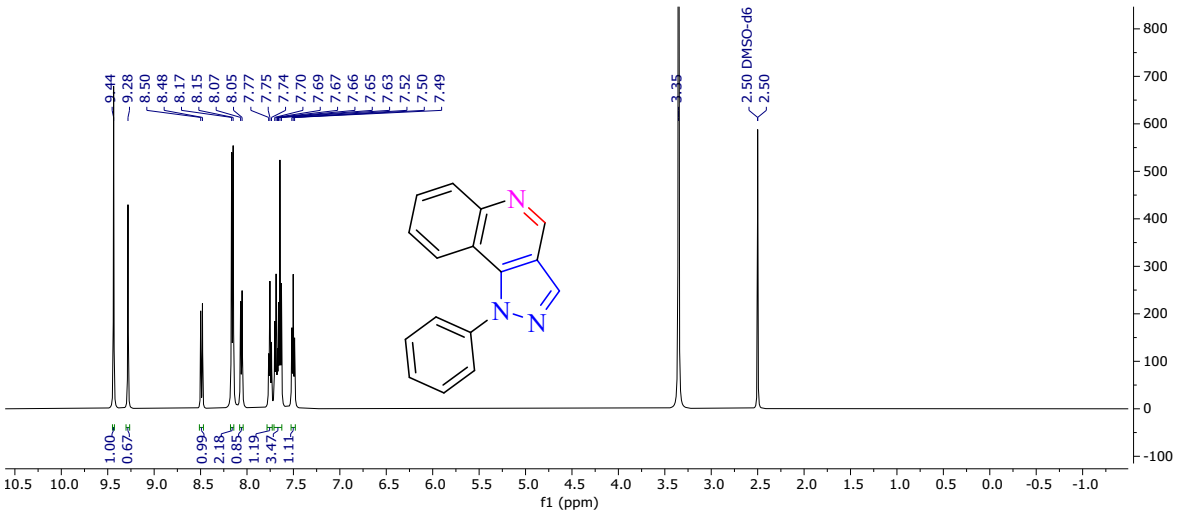


^{13}C {^{1}H} NMR of compound 5d, DMSO-d_6, 125MHz

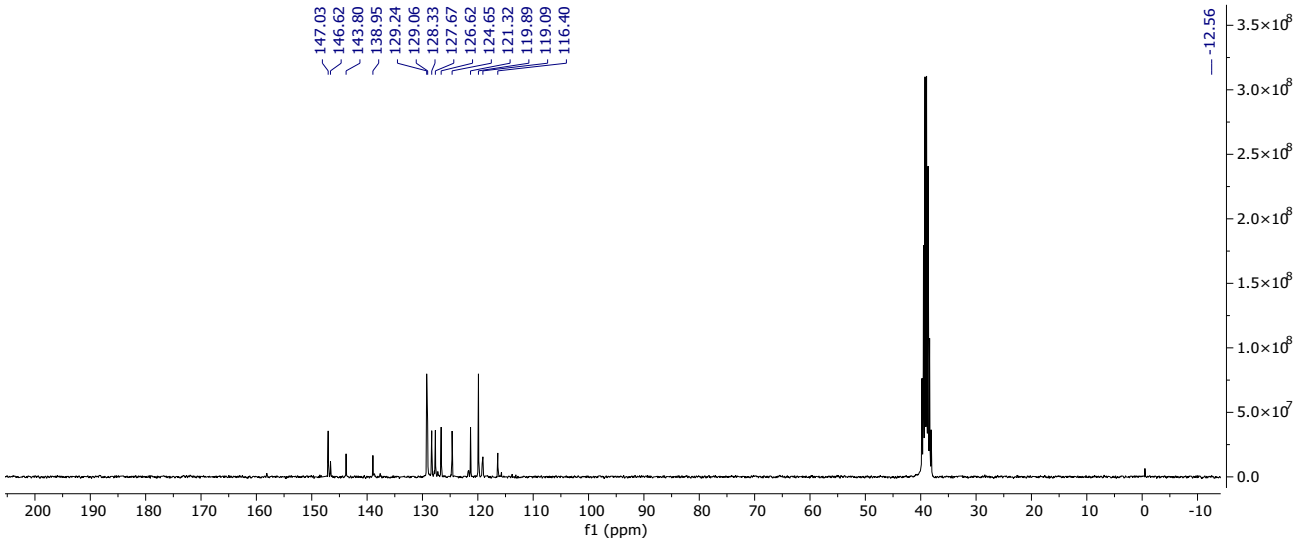


HRMS spectra of compound 5d

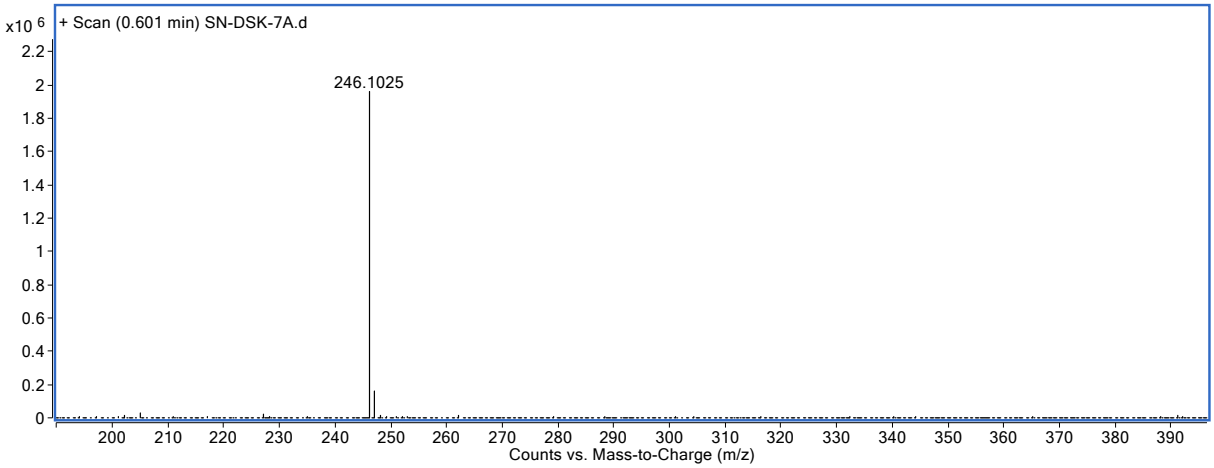
NMR spectrum of compound 7a



^{1}H-NMR spectrum of compound 7a, DMSO-d_6, 500MHz

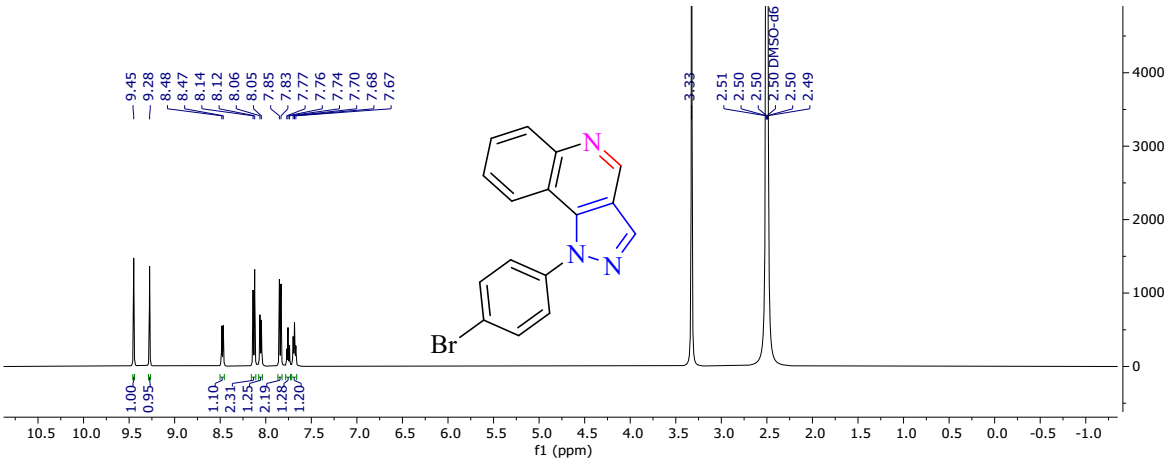


^{13}C {^{1}H} NMR of compound 7a, DMSO-d_6, 125MHz

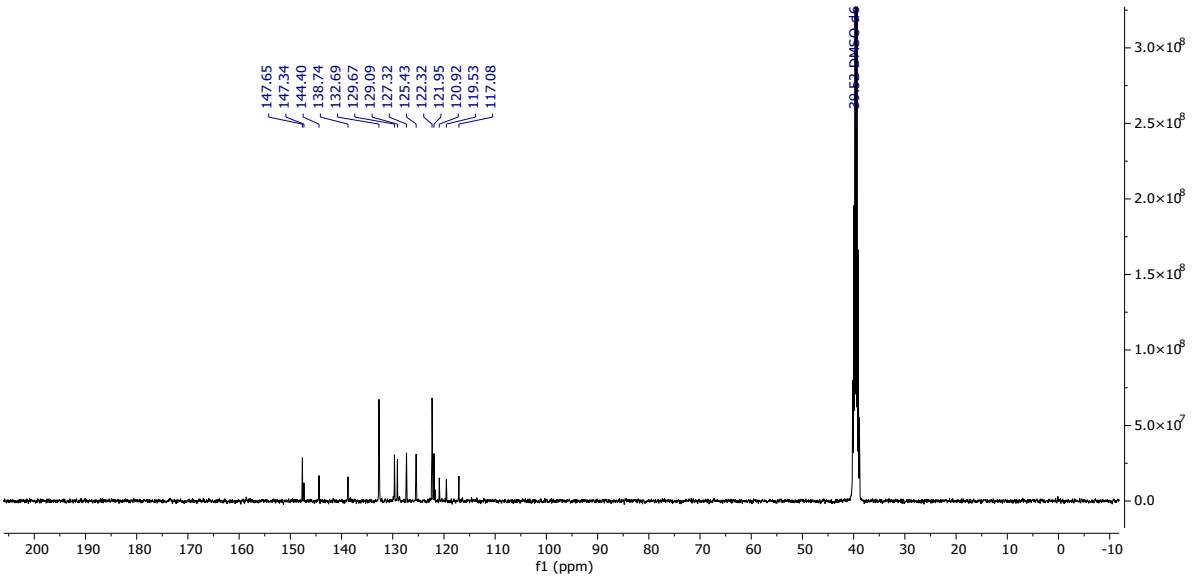


HRMS spectra of compound 7a

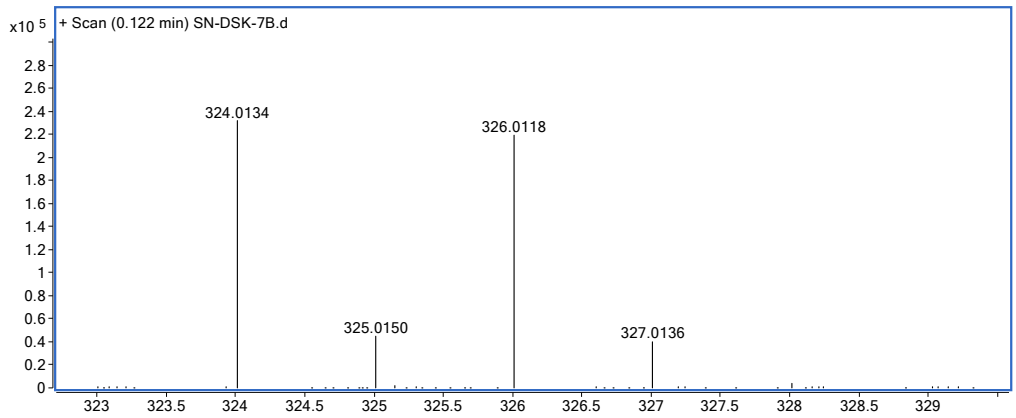
NMR spectrum of compound 7b



^{1}H-NMR spectrum of compound 7b, DMSO-d_6, 500MHz

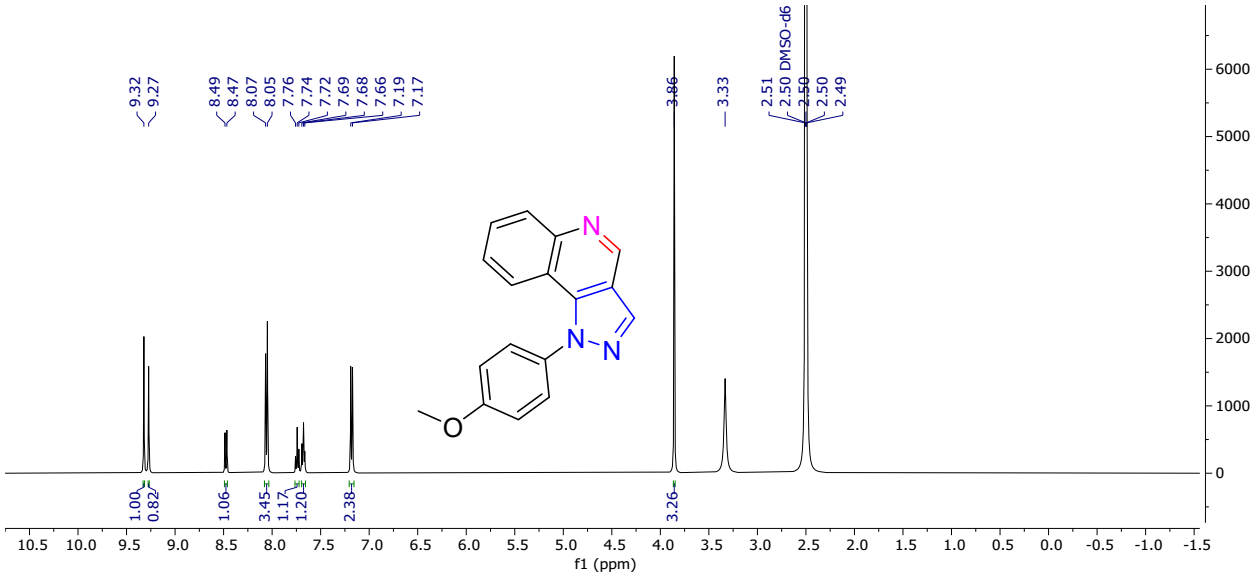


^{13}C {^{1}H} NMR of compound 7b, DMSO-d_6, 125MHz

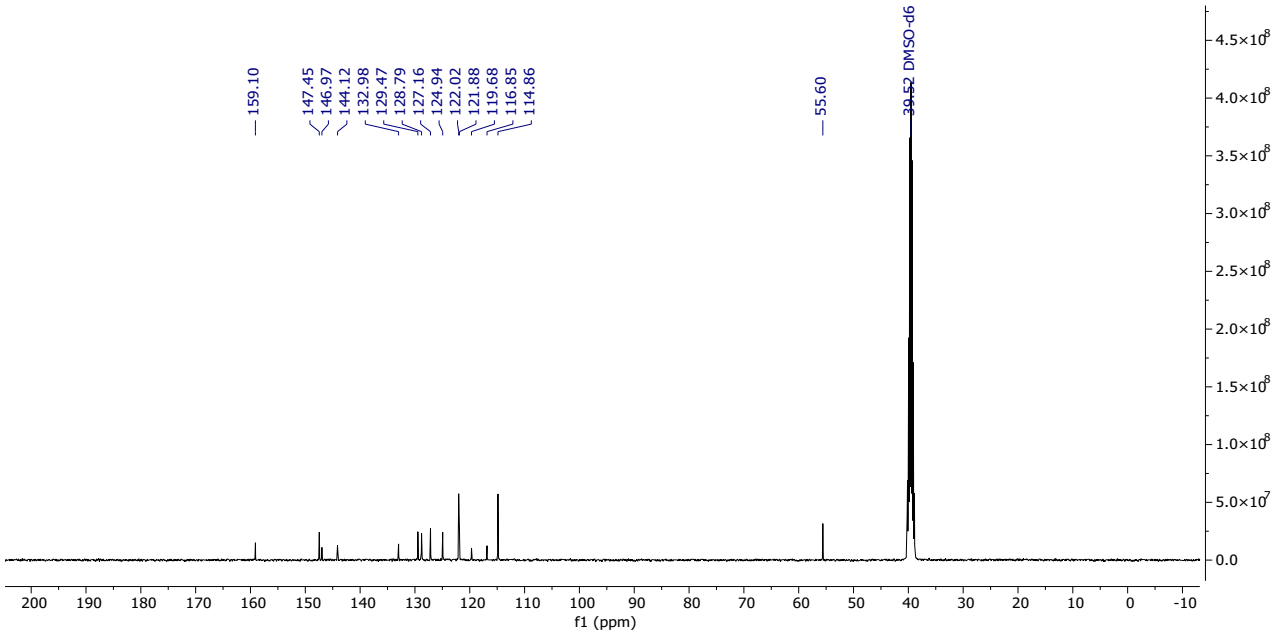


HRMS spectra of compound 7b

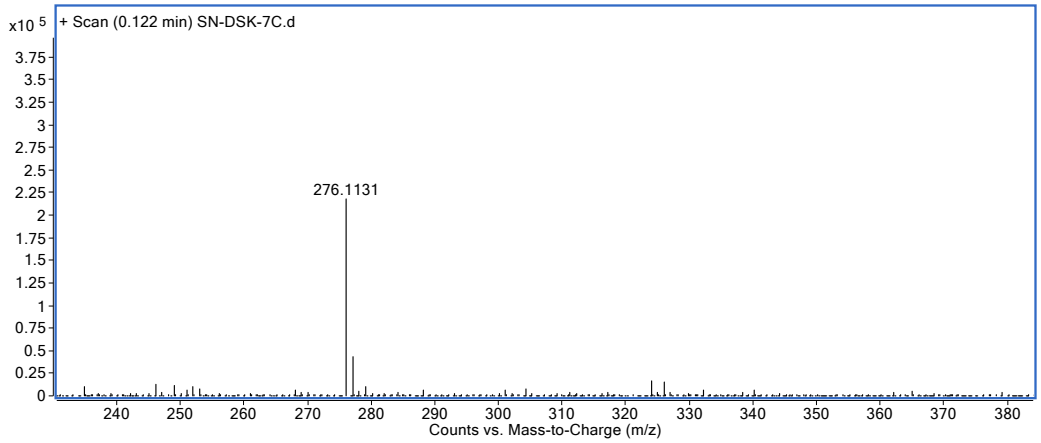
NMR spectrum of compound 7c



^{1}H-NMR spectrum of compound 7c, DMSO-d_6, 500MHz

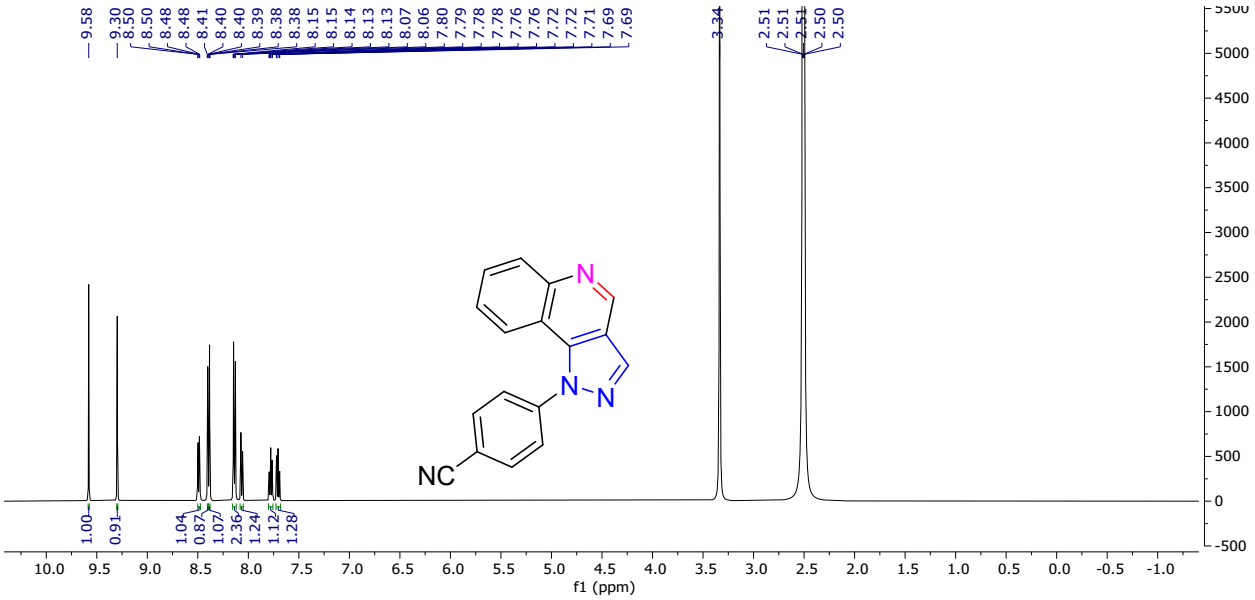


^{13}C {^{1}H} NMR of compound 7c, DMSO-d_6, 125MHz

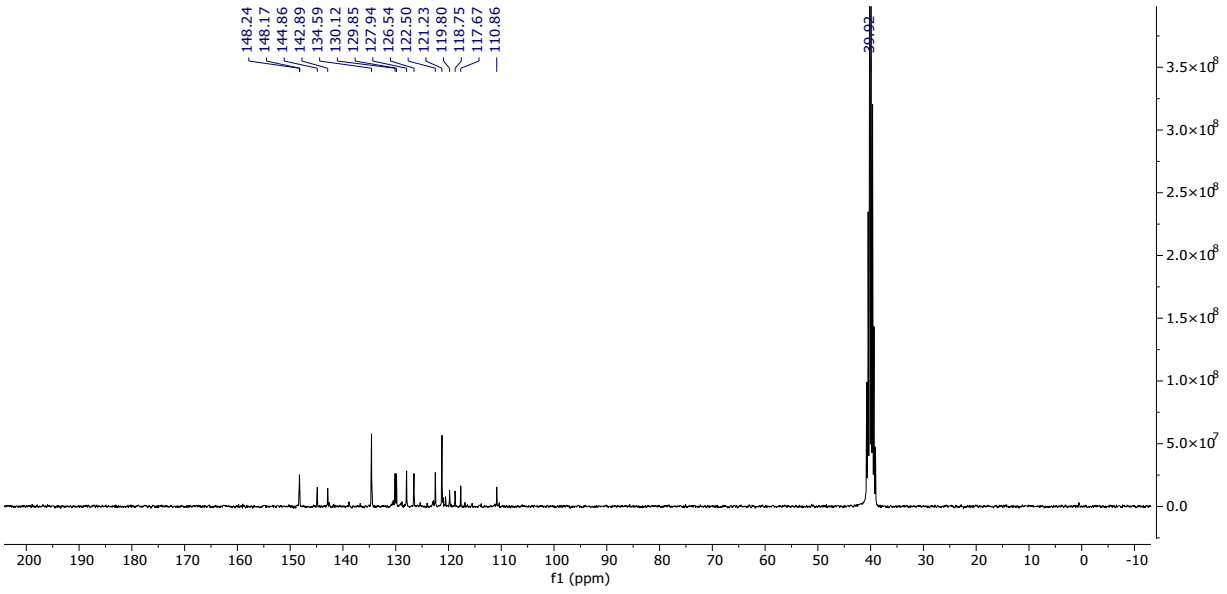


HRMS spectra of compound 7c

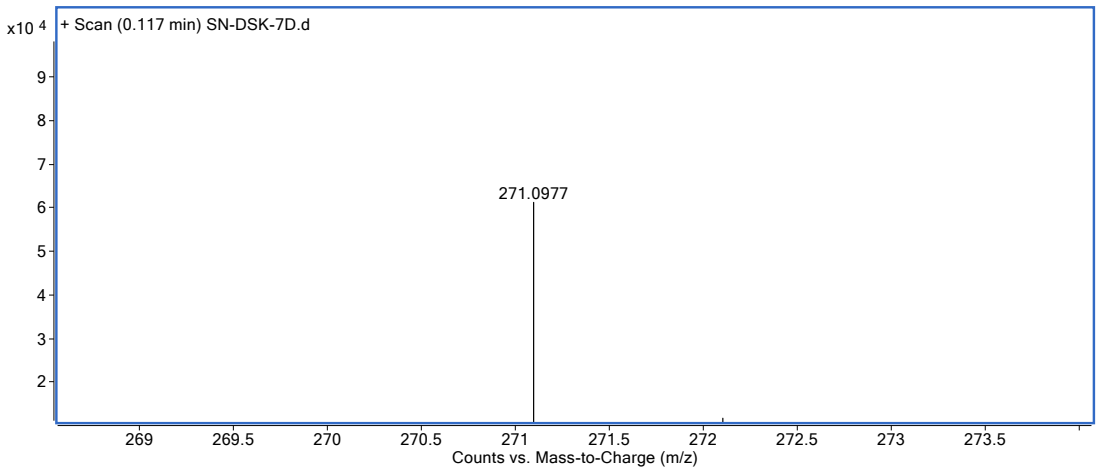
NMR spectrum of compound 7d



^{1}H-NMR spectrum of compound 7d, DMSO-d_6, 500MHz

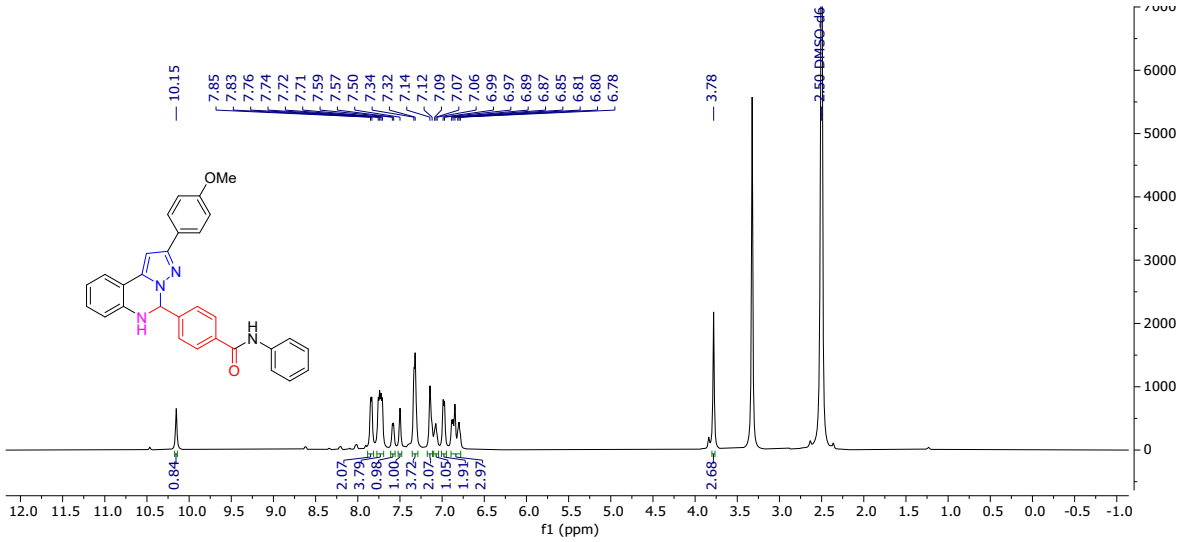


^{13}C {^{1}H} NMR of compound 7d, DMSO-d_6, 125MHz

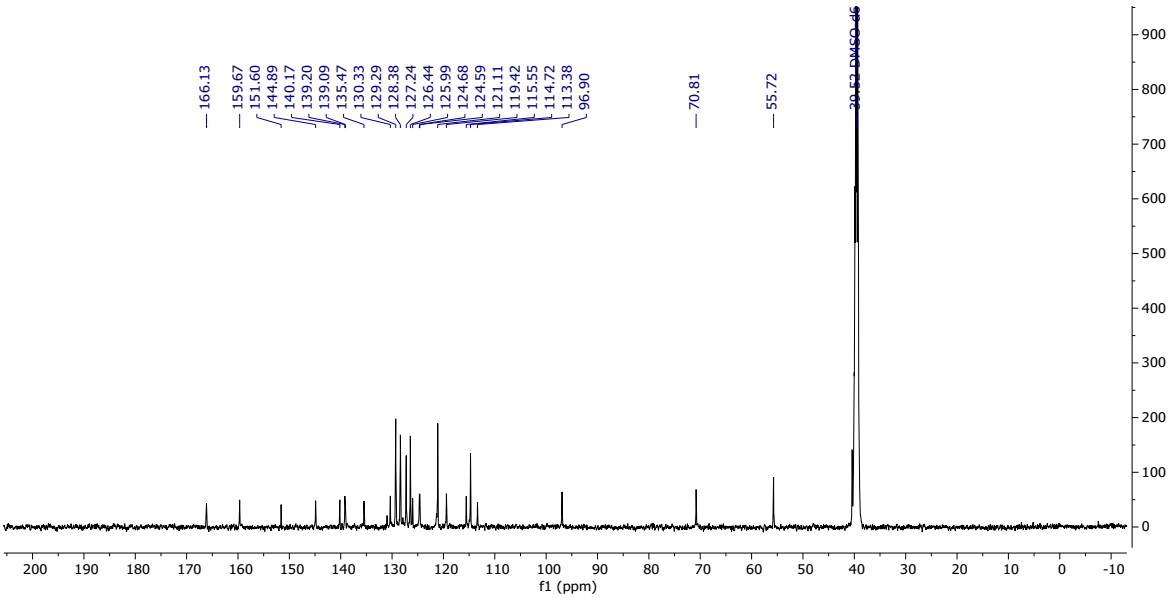


HRMS spectra of compound 7d

NMR spectrum of compound 9



^{1}H-NMR spectrum of compound 9, DMSO-d_6, 500MHz



^{13}C {^{1}H} NMR of compound 9, DMSO-d_6, 125MHz

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