

## Supporting Information

for

### **CSA-Catalyzed Strategy for Constructing 1*H*-Pyrazolo[4,3-*f*]quinoline-8-carboxamide Scaffolds as antimicrobial agents**

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## 1. General Methods

### 1.1 Experimental techniques

The nomenclature of the synthesized molecules are done according to IUPAC. Also, the numbering in the carbon chain is based on the position of the carbon atom.

All the reactions are performed in an reflux atmosphere. The used glass devices (round bottomed flask) were heated with a temperature of 100 °C. All the solid and liquid reagents and needle are added to the RBF under the reflux atmosphere.

Percentages (%) refers to mass percentage.

The calculated yields refer to the limiting reagent component.

Silicone oil bath is used to record the melting points. The temperature is set and controlled by using an adjustable contact thermometer.

#### **Reagents**

All the reagents were purchased from TCI, Sigma-Aldrich, and Sisco Research Pvt. Ltd. and used without further purification. The reaction was performed using the conventional heating method.

#### **Solvents**

Solvents from the given companies were used with the corresponding quality grades and used without further purification. The following solvents were used in thin layer chromatography (TLC) and chiral High-performance liquid chromatography: ethyl acetate, n-hexane, methanol, ethanol, diethylamine, dichloromethane.

### 1.2 Analytical

#### **Thin Layer Chromatography (TLC)**

The progress of all chemical reactions was monitored by Thin-layer chromatography. For this purpose, TLC, on aluminium plates pre-coated with F252 silica gel 60 by Merck were used as the stationary phase. TLC plates were analyzed under Visible light ( $\lambda = 400$  nm to 750 nm).

#### **Nuclear Magnetic Resonance (NMR) Spectroscopy**

NMR Spectra  $^1\text{H}$  NMR &  $^{13}\text{C}$  NMR were recorded on the instruments *Bruker BioSpin GmbH* spectrometer having proton noise decoupling mode with a standard 5 mm probe. The chemical shift values are given in  $\delta$  (ppm) and the coupling constant ( $J$ ) is provided in 400MHertz. For the solvent, deuterated DMSO- $\text{d}_6$ , the signal of solvents was used in the  $^1\text{H}$  NMR spectra ( $\delta = 2.52$  ppm) and  $^{13}\text{C}$  NMR spectra ( $\delta = 39$  ppm) as an internal standard for calibration. The spectra were viewed by utilizing the MestReNova software. The following abbreviations were used for the clear assignment of the signals and for the spin multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, dd = double of doublet, td = triplet of doublet, m = multiplet.

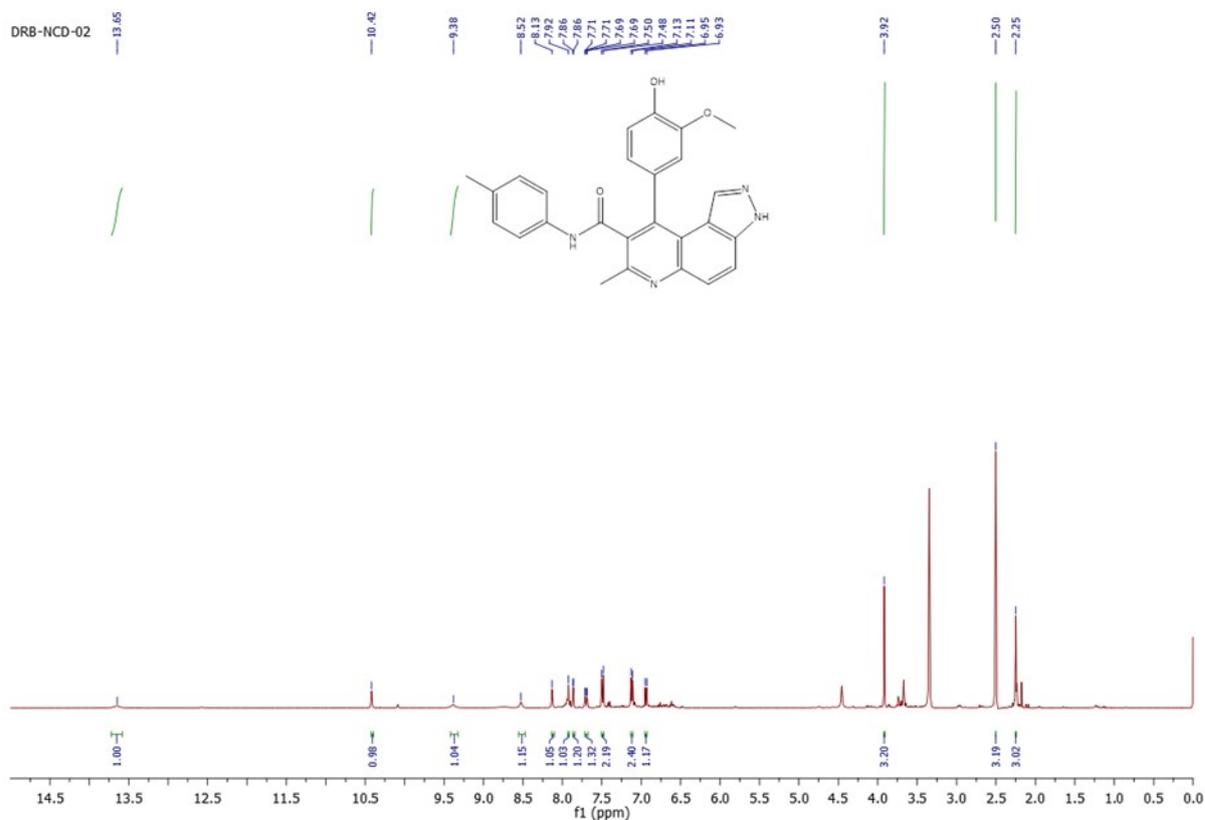
#### **Mass Spectrometry**

Mass spectra were recorded using HRMS analysis.

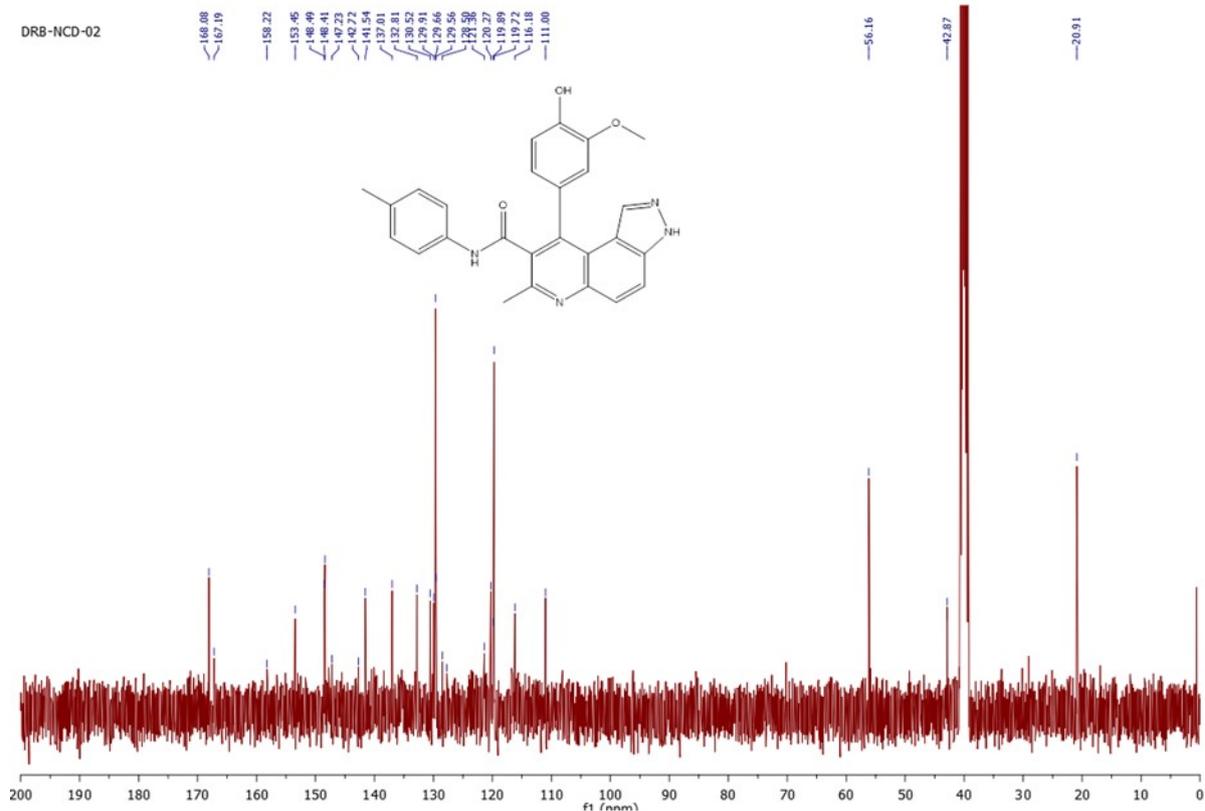
#### **Melting Points**

Melting points of the synthesized solid products **4(a-n)** were recorded using open capillary method and are uncorrected.

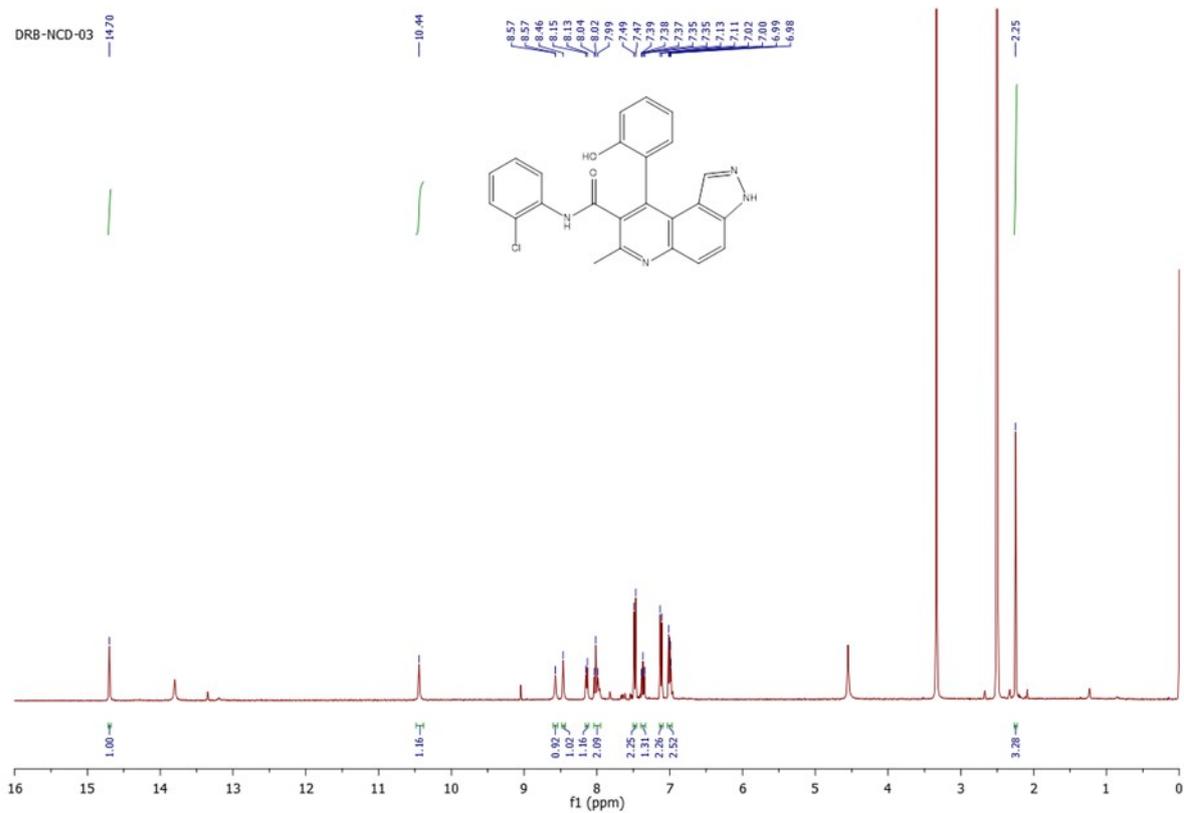
## 2. S, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR, Spectra of all representative compounds



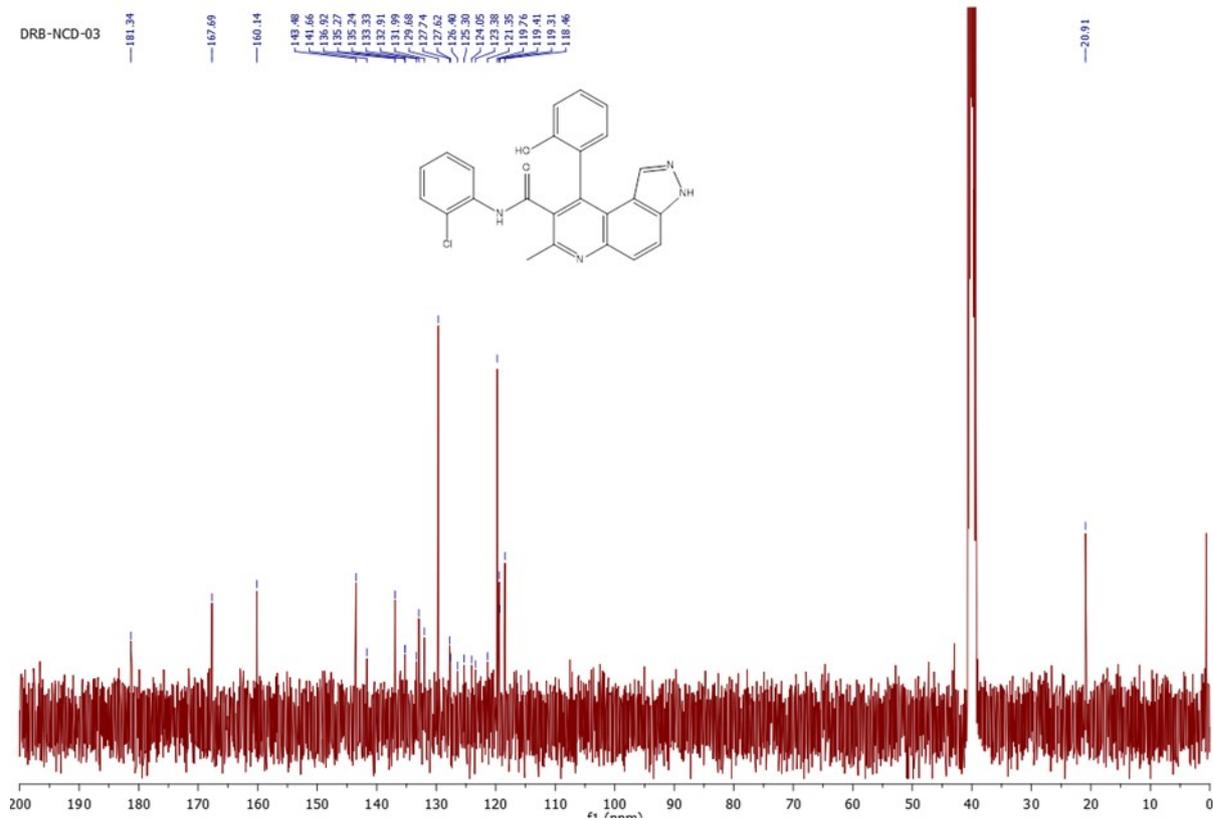
**Figure S1:** <sup>1</sup>H NMR spectra of **4a** (400MHz, DMSO-d<sub>6</sub>)



**Figure S2:**  $^{13}\text{C}$  NMR spectra of 4a (101MHz,  $\text{DMSO-d}_6$ )



**Figure S3:**  $^1\text{H}$  NMR spectra of 4b (400MHz,  $\text{DMSO-d}_6$ )



**Figure S4:**  $^{13}\text{C}$  NMR spectra of 4b (101MHz,  $\text{DMSO-d}_6$ )

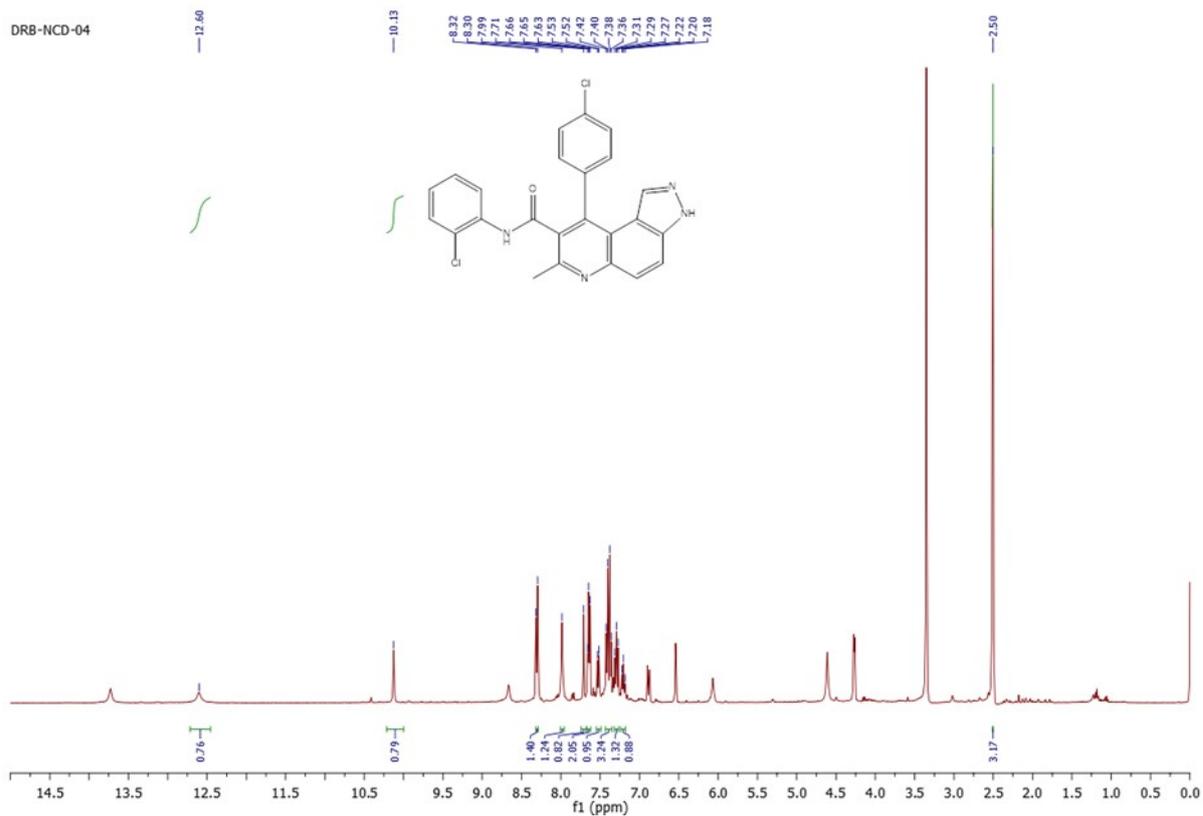


Figure S5:  $^1\text{H}$  NMR spectra of 4c (400MHz,  $\text{DMSO-d}_6$ )

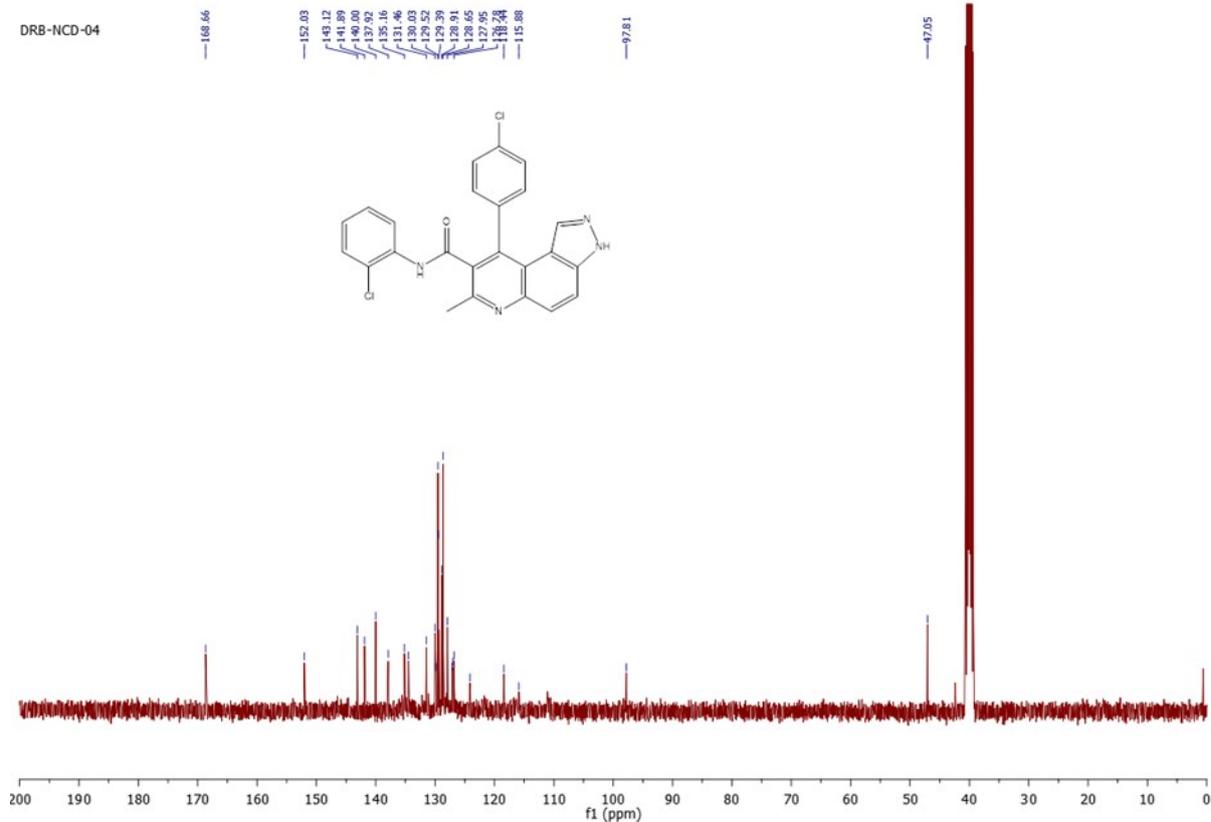
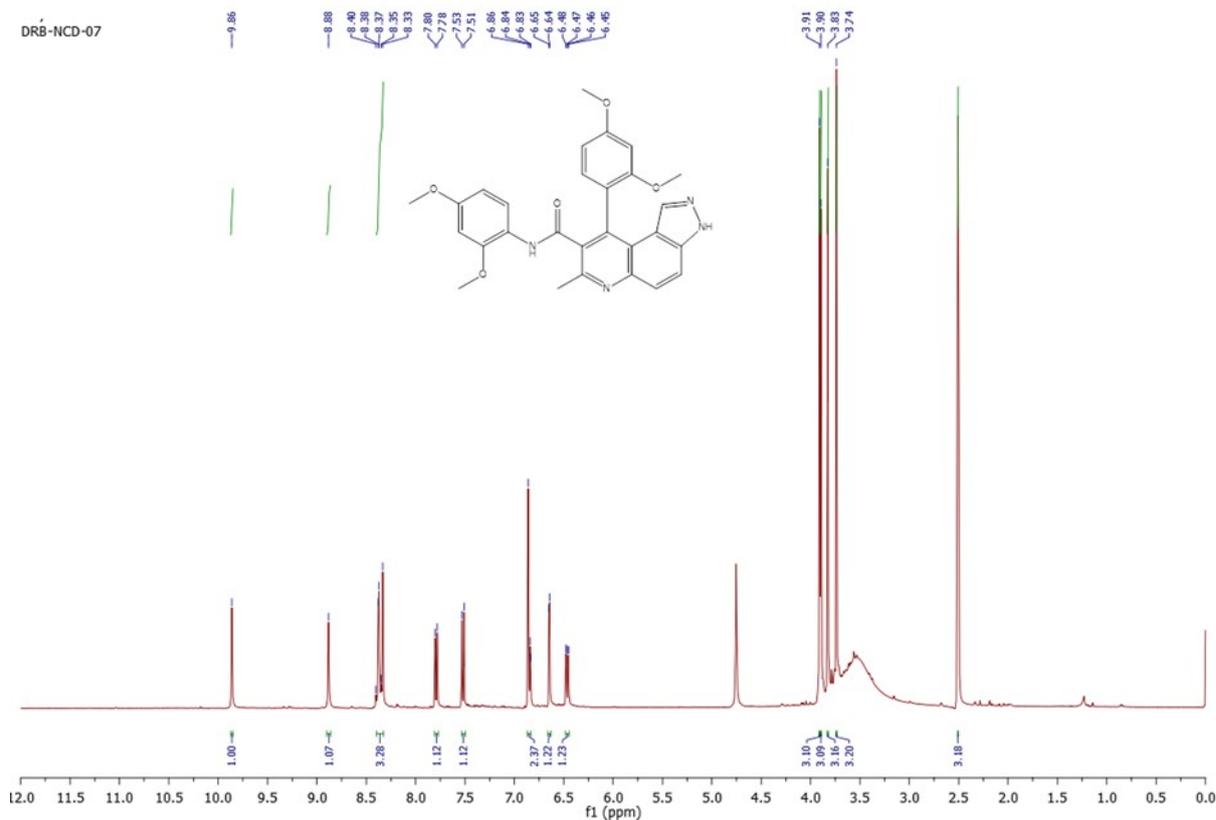
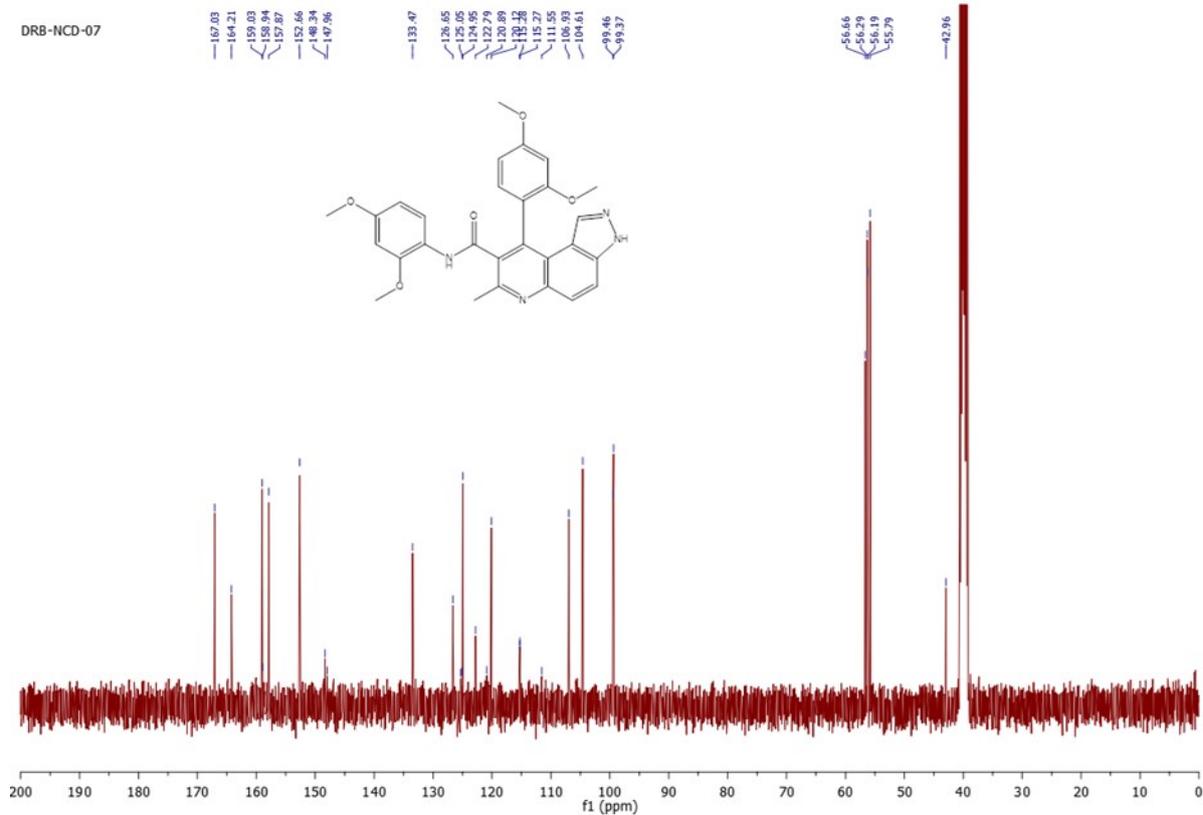


Figure S6:  $^{13}\text{C}$  NMR spectra of 4c (101MHz,  $\text{DMSO-d}_6$ )



**Figure S7:**  $^1\text{H}$  NMR spectra of 4d (400MHz,  $\text{DMSO-d}_6$ )



**Figure S8:**  $^{13}\text{C}$  NMR spectra of 4d (101MHz,  $\text{DMSO-d}_6$ )

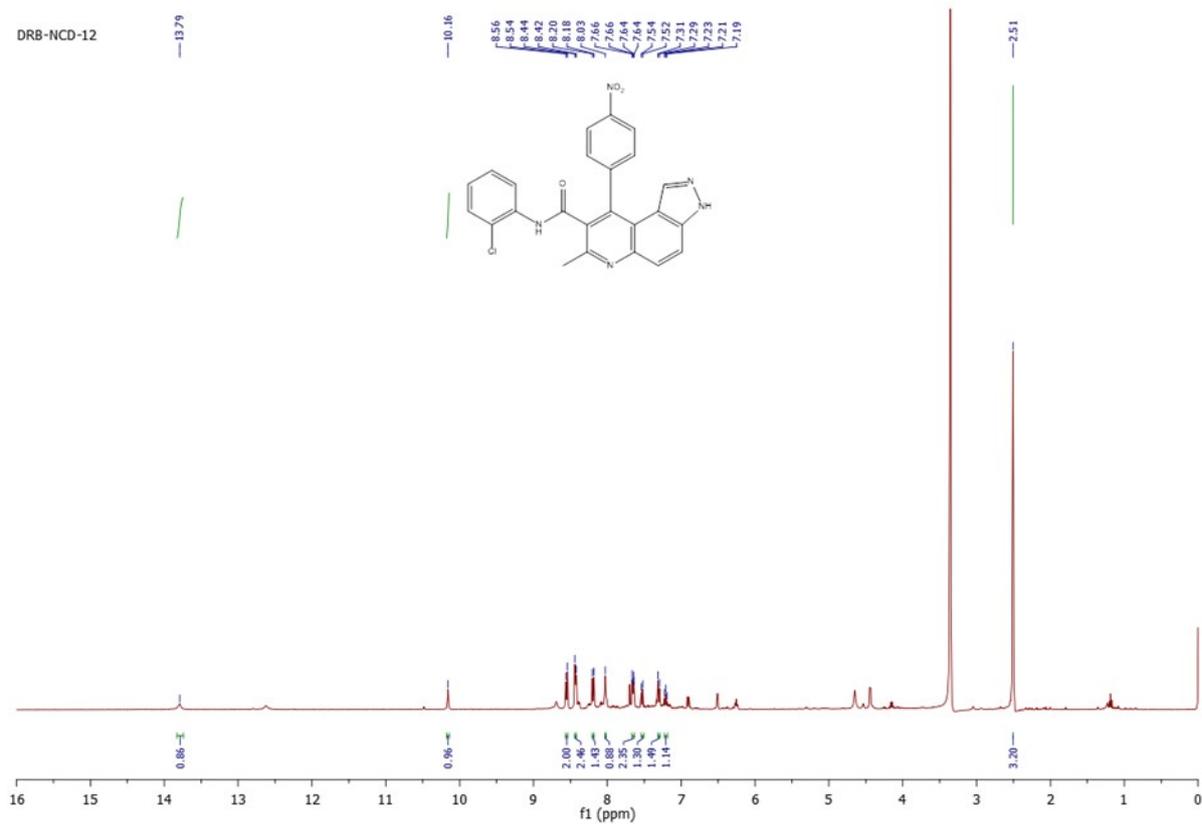


Figure S9:  $^1\text{H}$  NMR spectra of 4e (400MHz,  $\text{DMSO-d}_6$ )

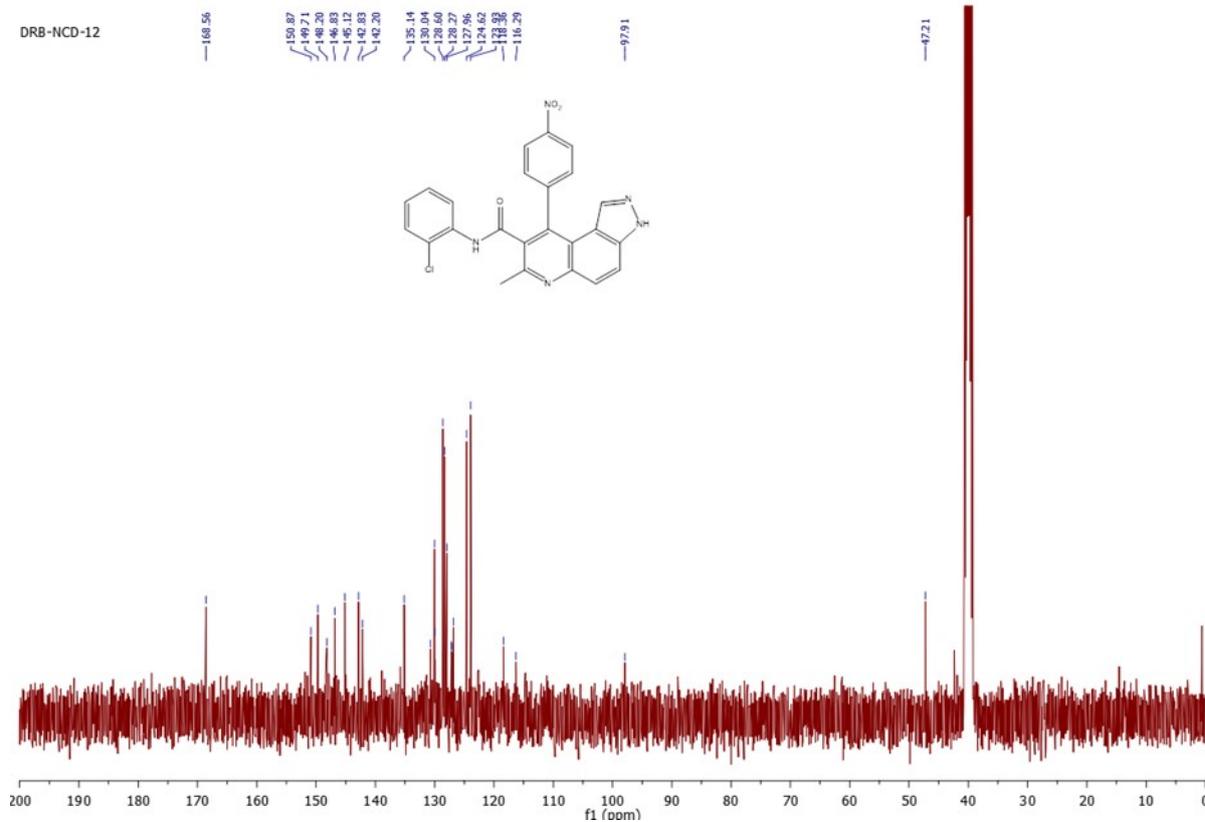


Figure S10:  $^{13}\text{C}$  NMR spectra of 4e (101MHz,  $\text{DMSO-d}_6$ )

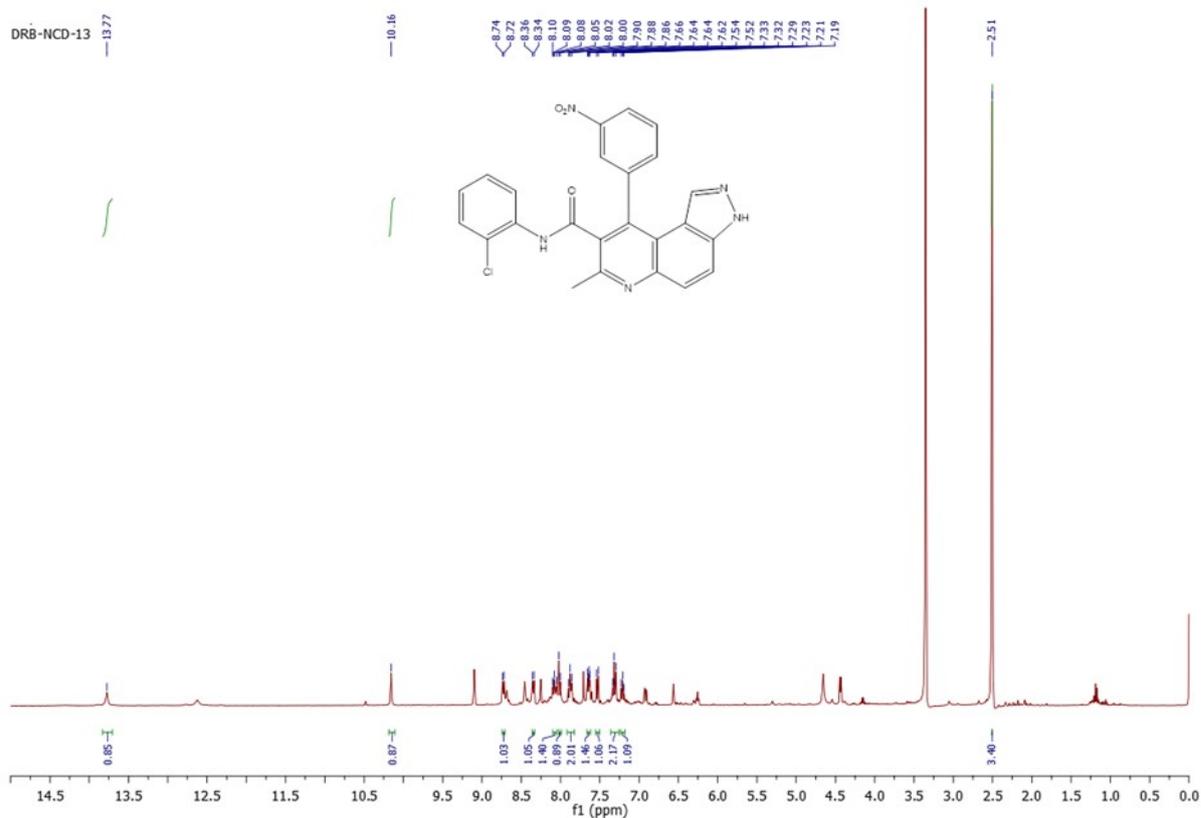


Figure S11:  $^1\text{H}$  NMR spectra of 4f (400MHz,  $\text{DMSO-d}_6$ )

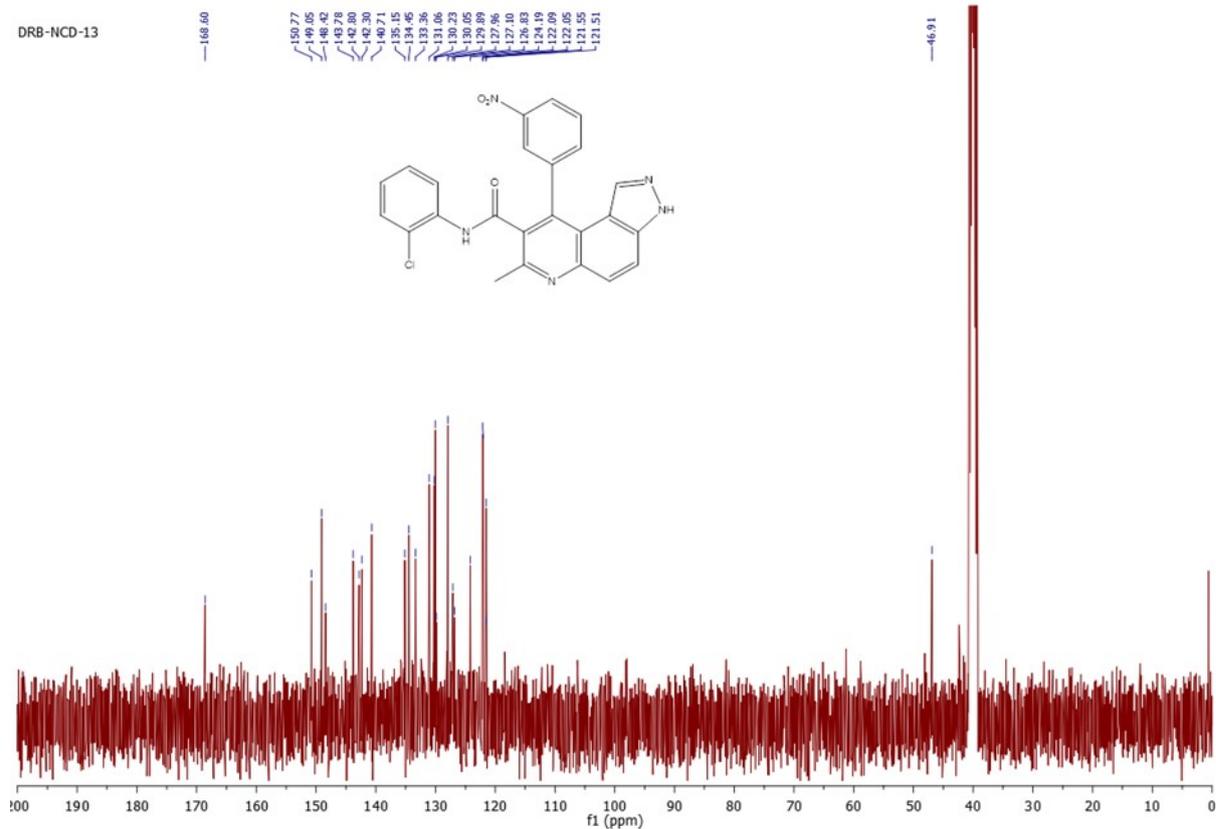


Figure S12:  $^{13}\text{C}$  NMR spectra of 4f (101MHz,  $\text{DMSO-d}_6$ )

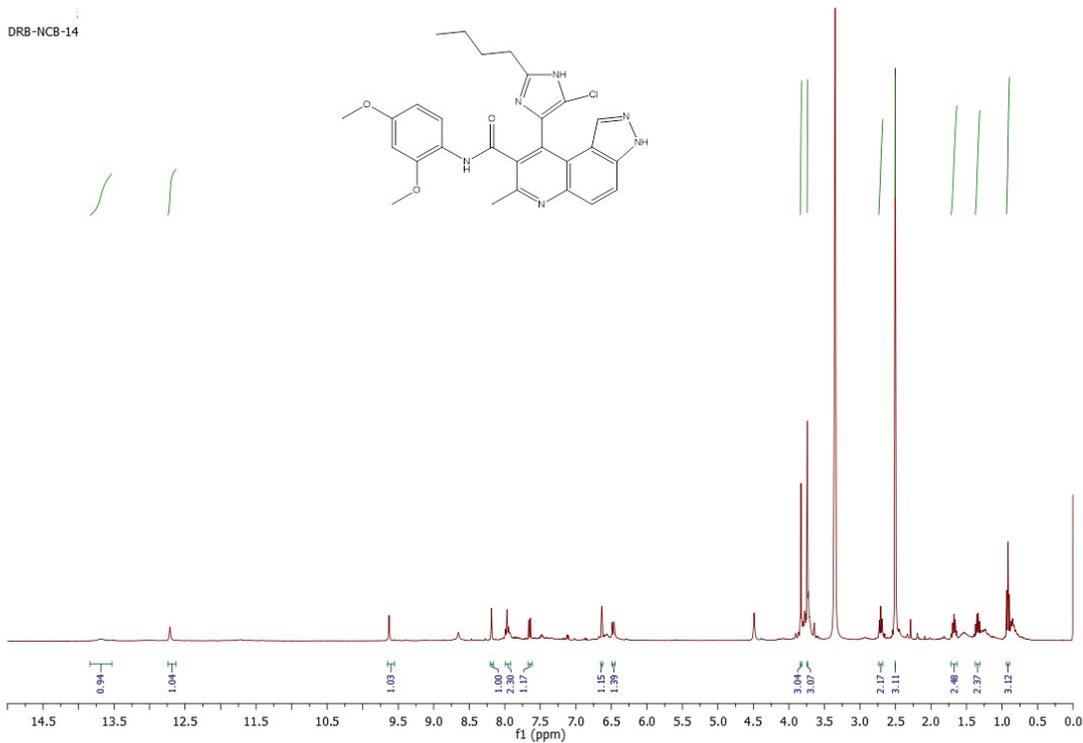


Figure S13:  $^1\text{H}$  NMR spectra of 4g (400MHz, DMSO- $\text{d}_6$ )

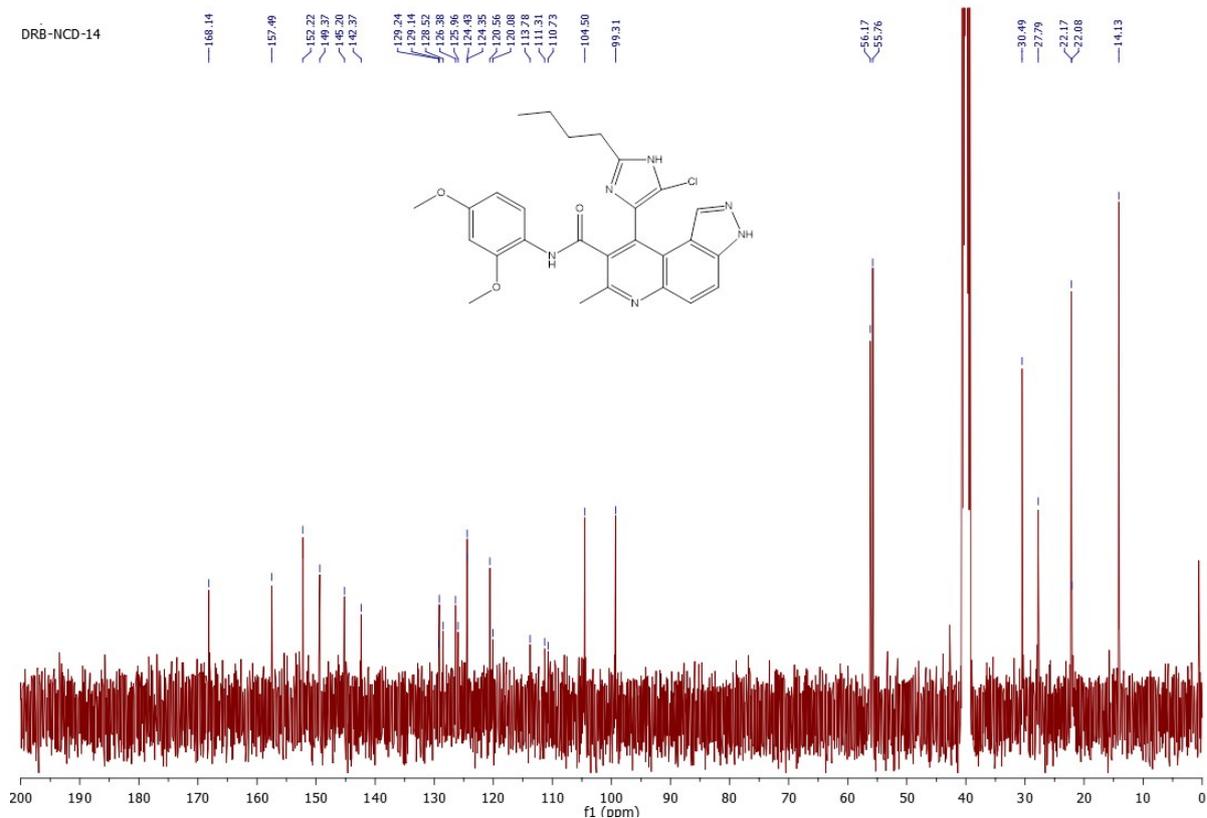
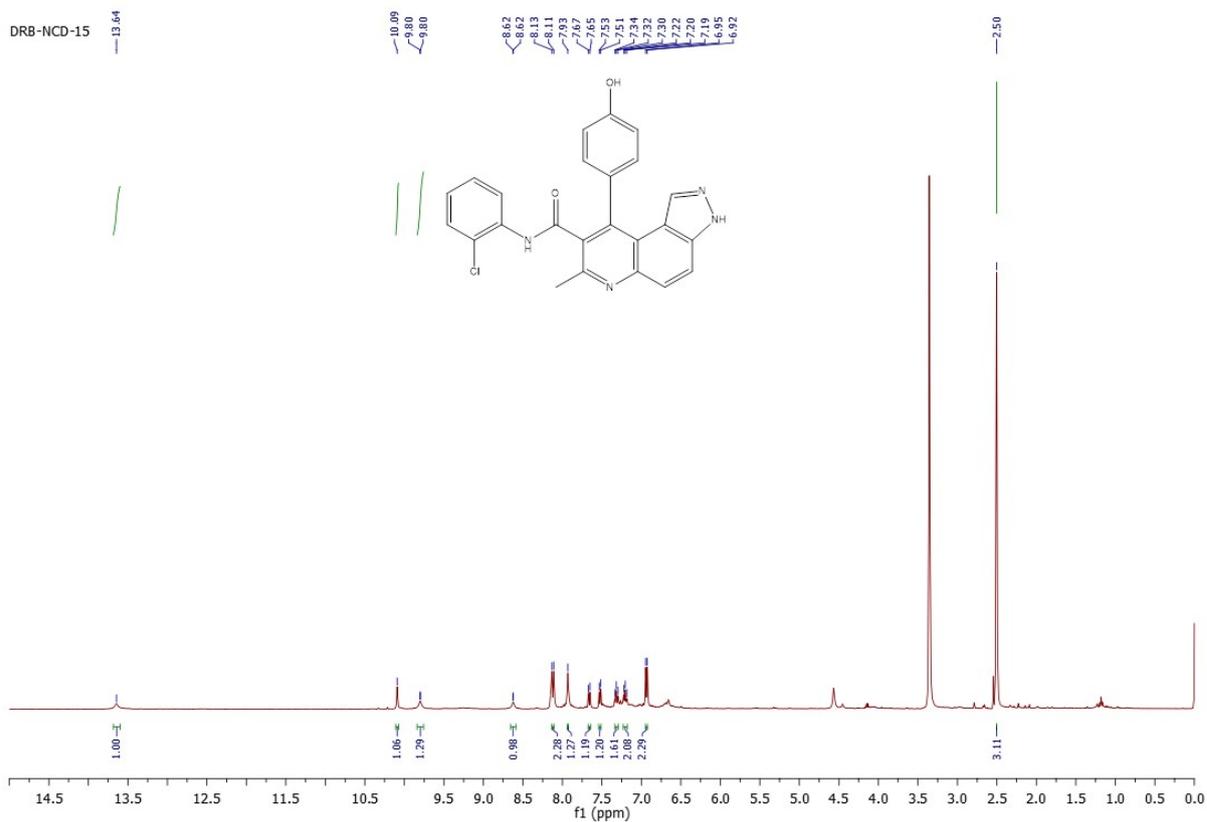
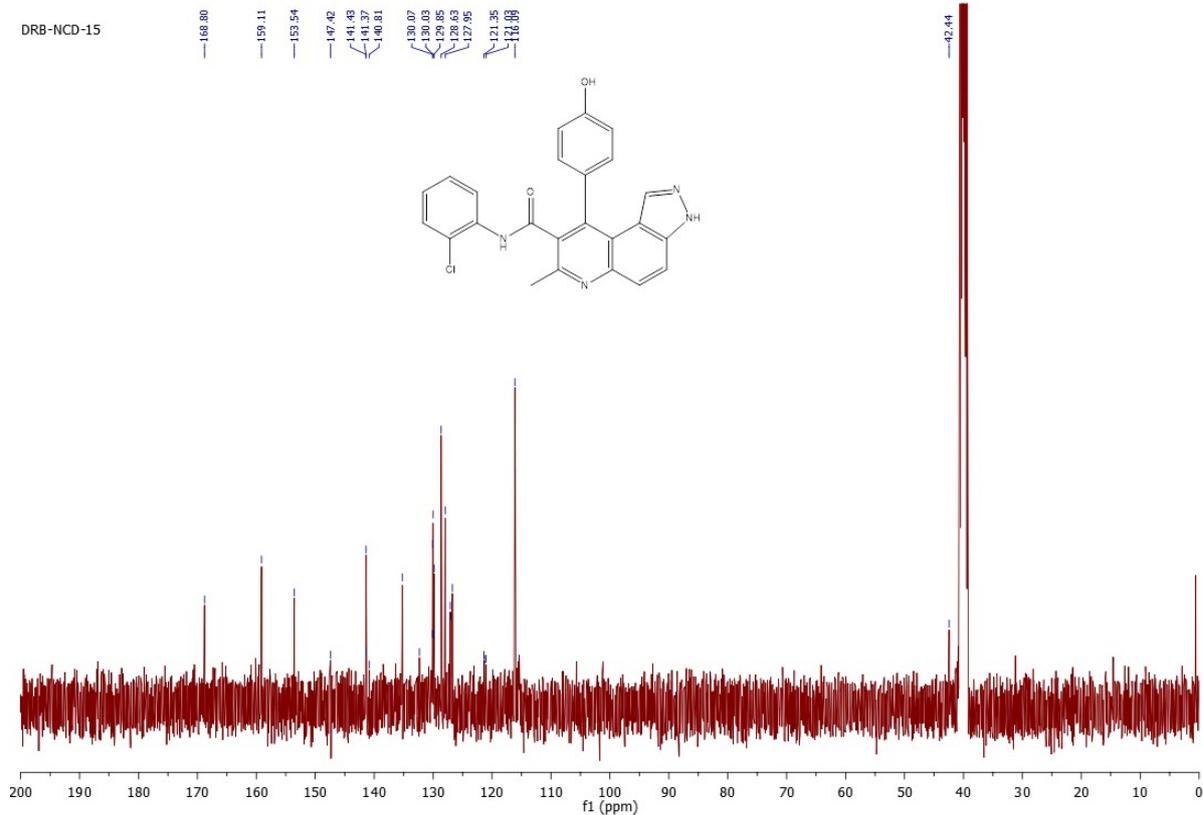


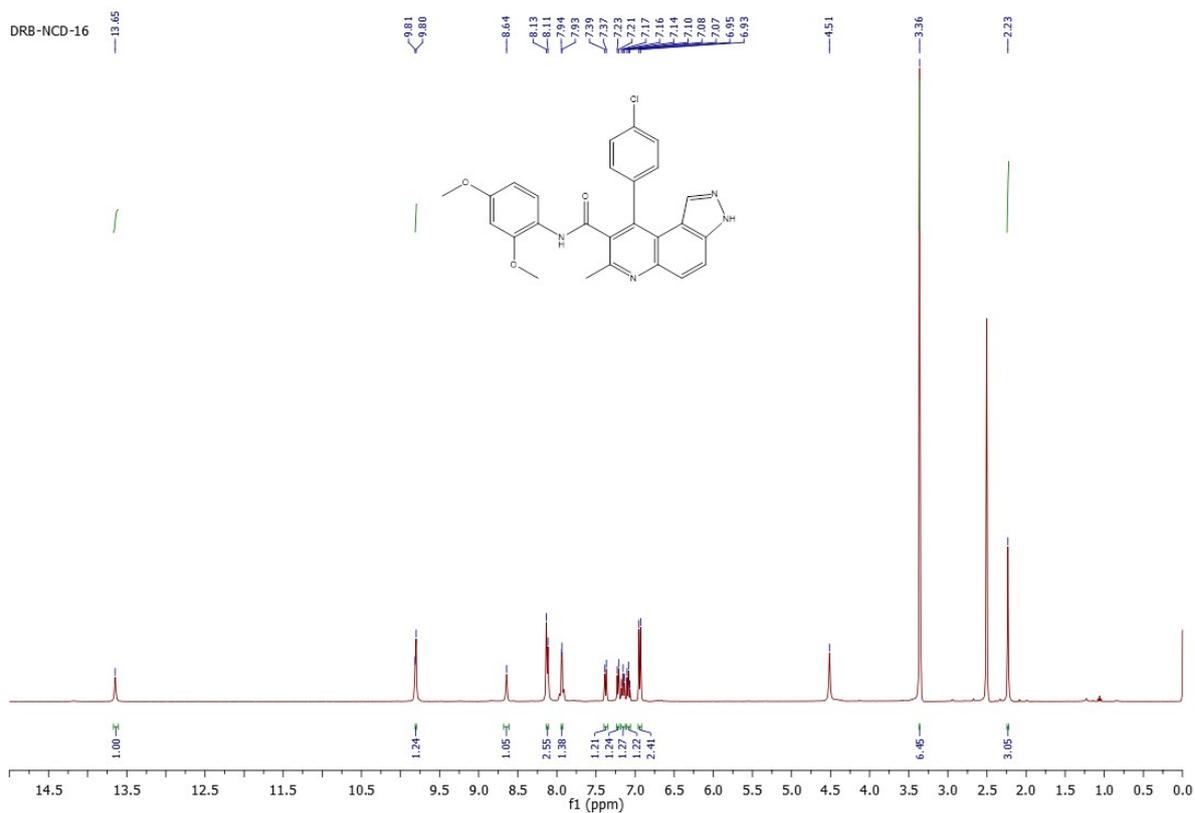
Figure S14:  $^{13}\text{C}$  NMR spectra of 4g (101MHz, DMSO- $\text{d}_6$ )



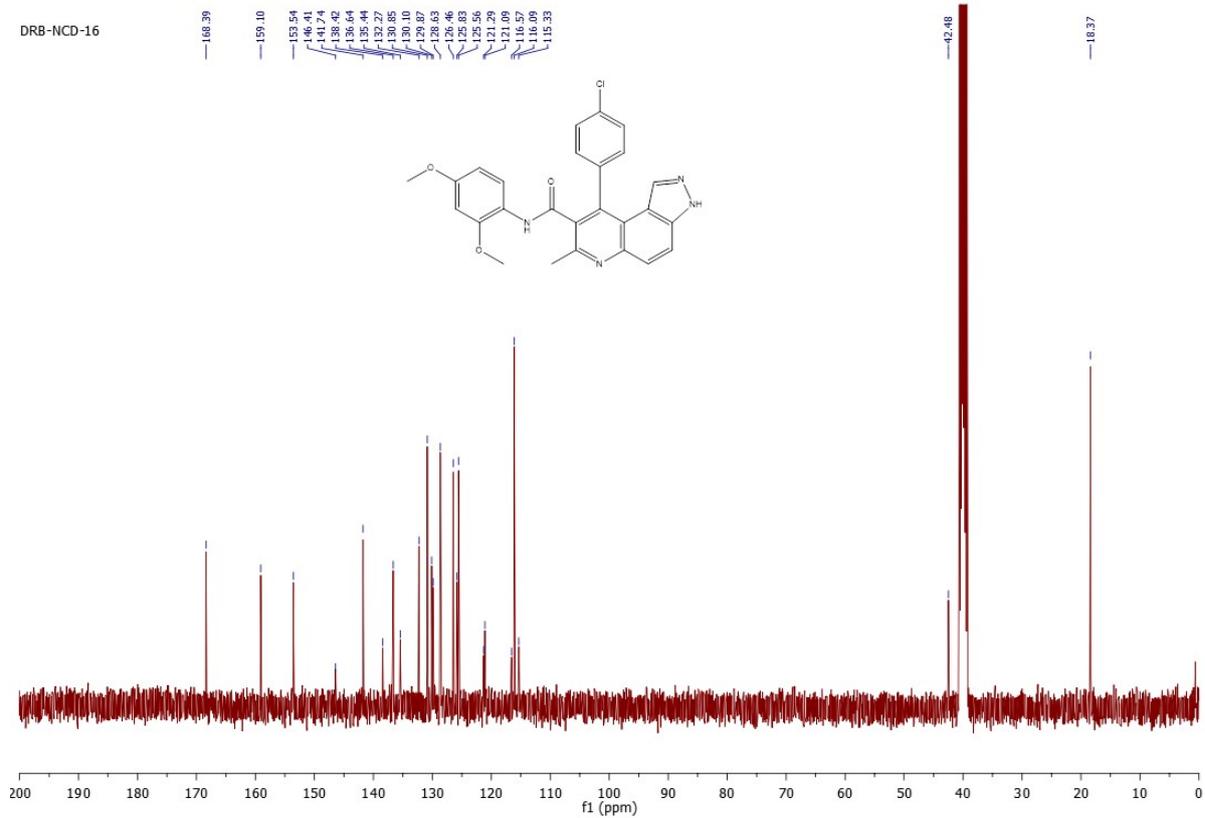
**Figure S15:**  $^1\text{H}$  NMR spectra of 4h (400MHz,  $\text{DMSO-d}_6$ )



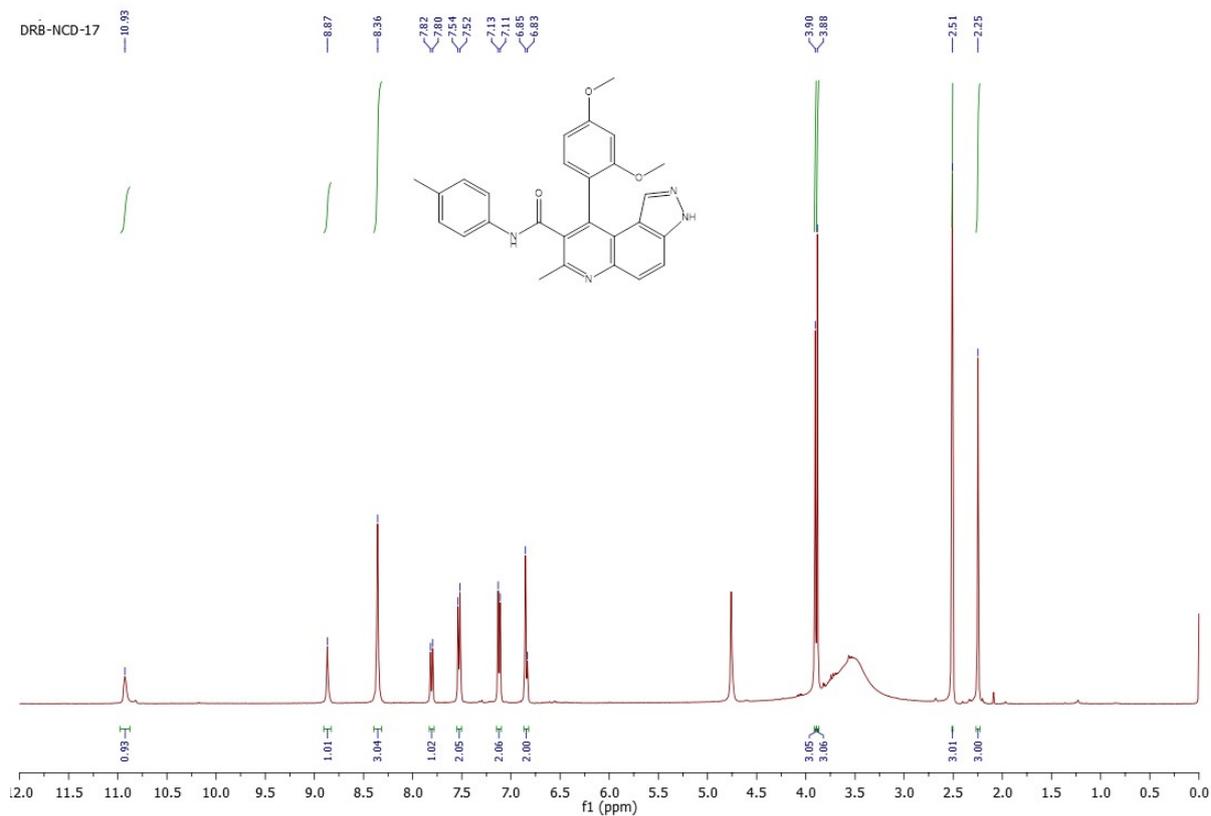
**Figure S16:**  $^{13}\text{C}$  NMR spectra of 4h (101MHz,  $\text{DMSO-d}_6$ )



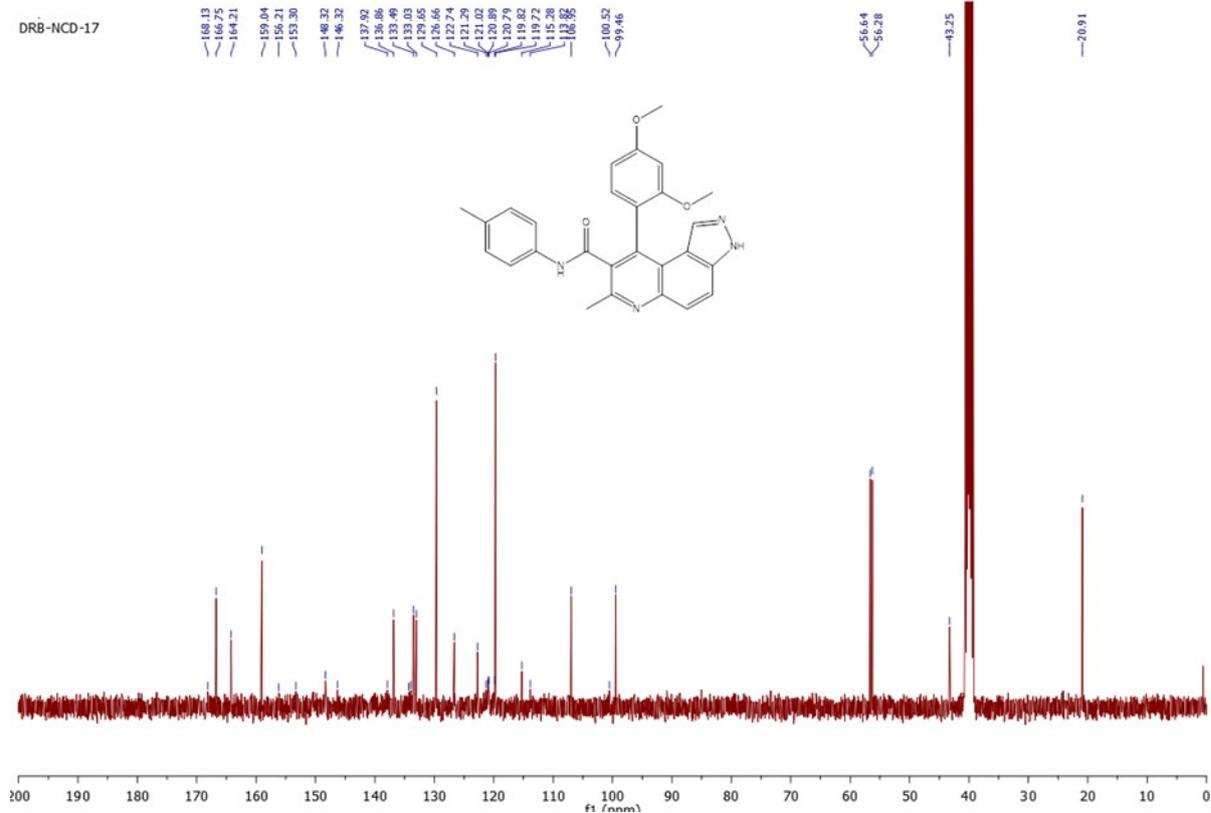
**Figure S17:**  $^1\text{H}$  NMR spectra of 4i (400MHz,  $\text{DMSO-d}_6$ )



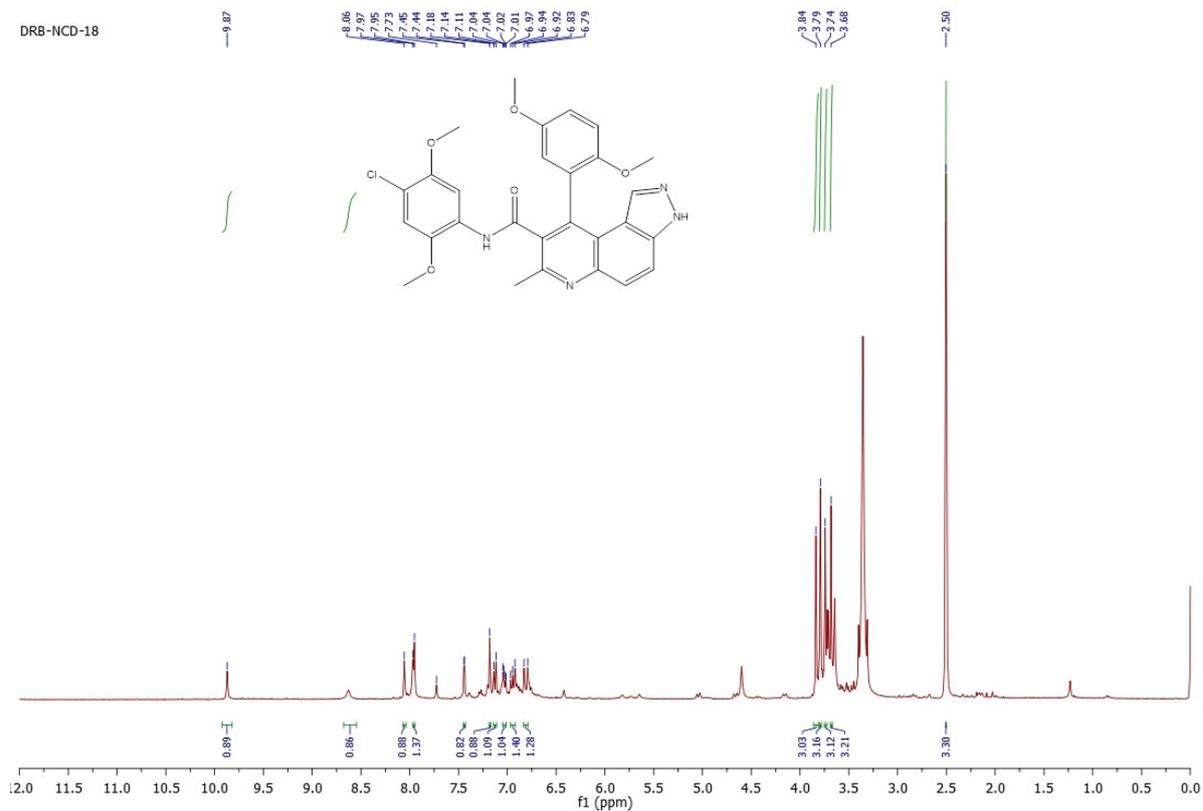
**Figure S18:**  $^{13}\text{C}$  NMR spectra of 4i (101MHz,  $\text{DMSO-d}_6$ )



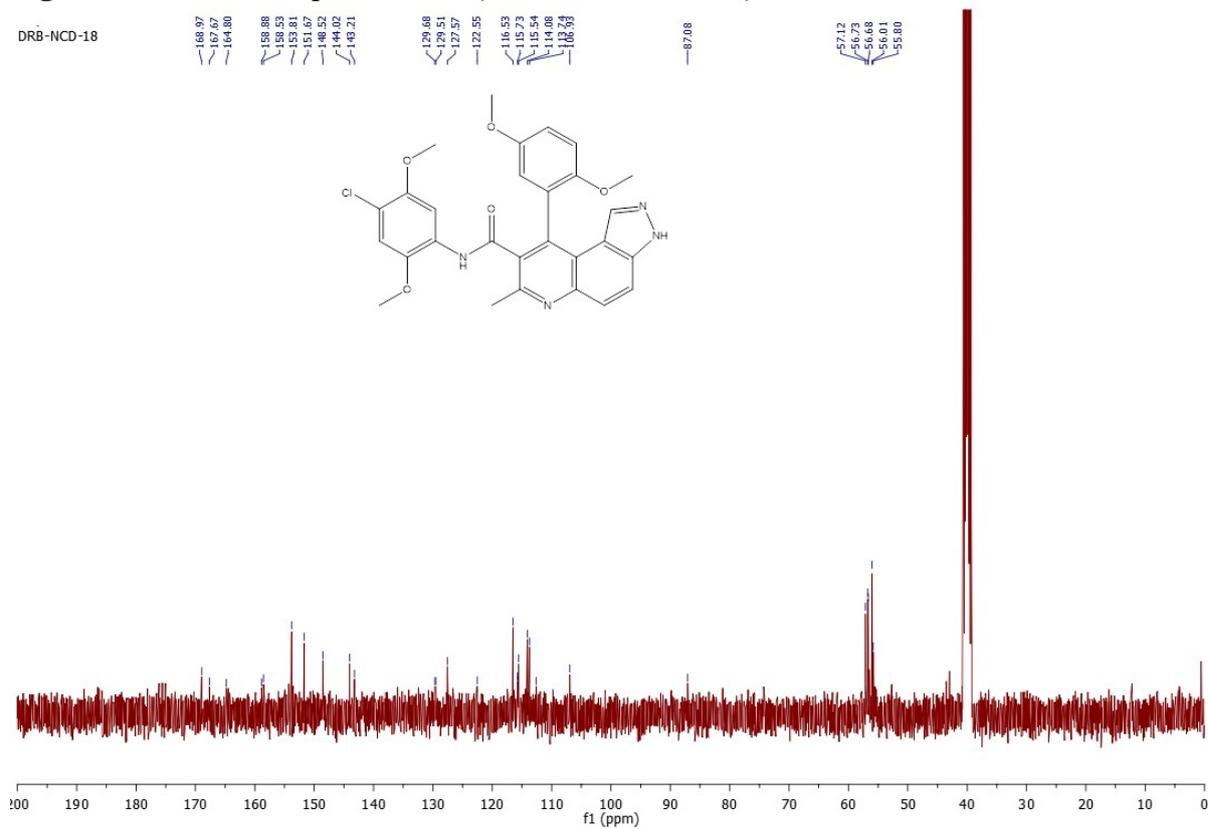
**Figure S19:**  $^1\text{H}$  NMR spectra of 4j (400MHz,  $\text{DMSO-d}_6$ )



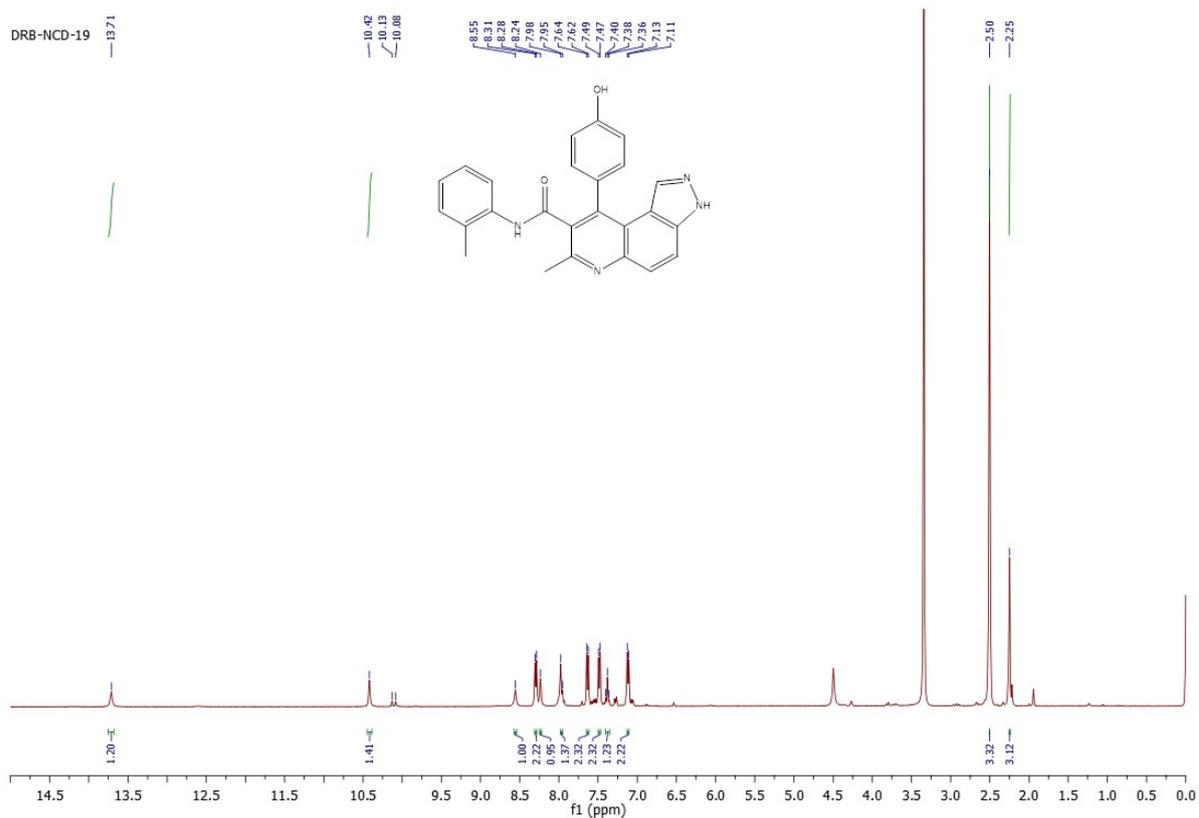
**Figure S20:**  $^{13}\text{C}$  NMR spectra of 4j (101MHz,  $\text{DMSO-d}_6$ )



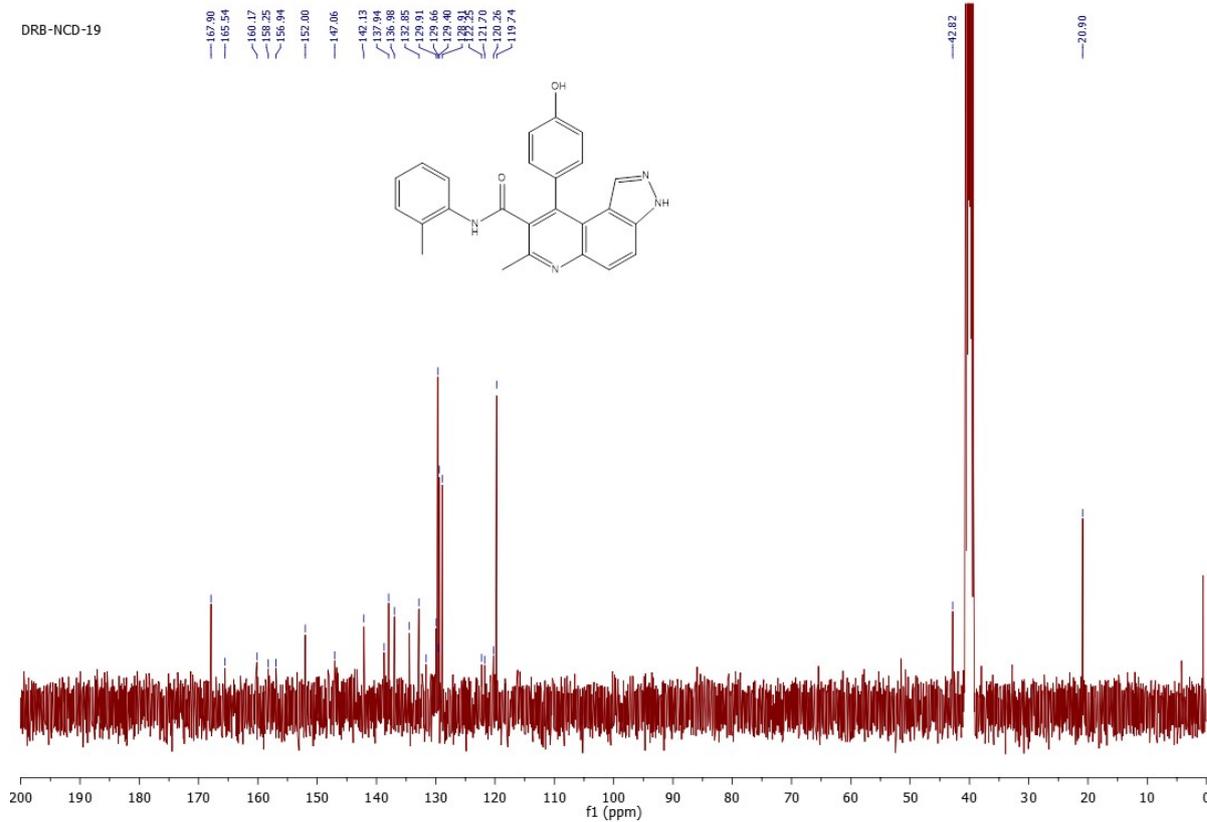
**Figure S21:**  $^1\text{H}$  NMR spectra of 4k (400MHz,  $\text{DMSO-d}_6$ )



**Figure S22:**  $^{13}\text{C}$  NMR spectra of 4k (101MHz,  $\text{DMSO-d}_6$ )



**Figure S23:**  $^1\text{H}$  NMR spectra of 4l (400MHz,  $\text{DMSO-d}_6$ )



**Figure S24:**  $^{13}\text{C}$  NMR spectra of 4l (101MHz,  $\text{DMSO-d}_6$ )

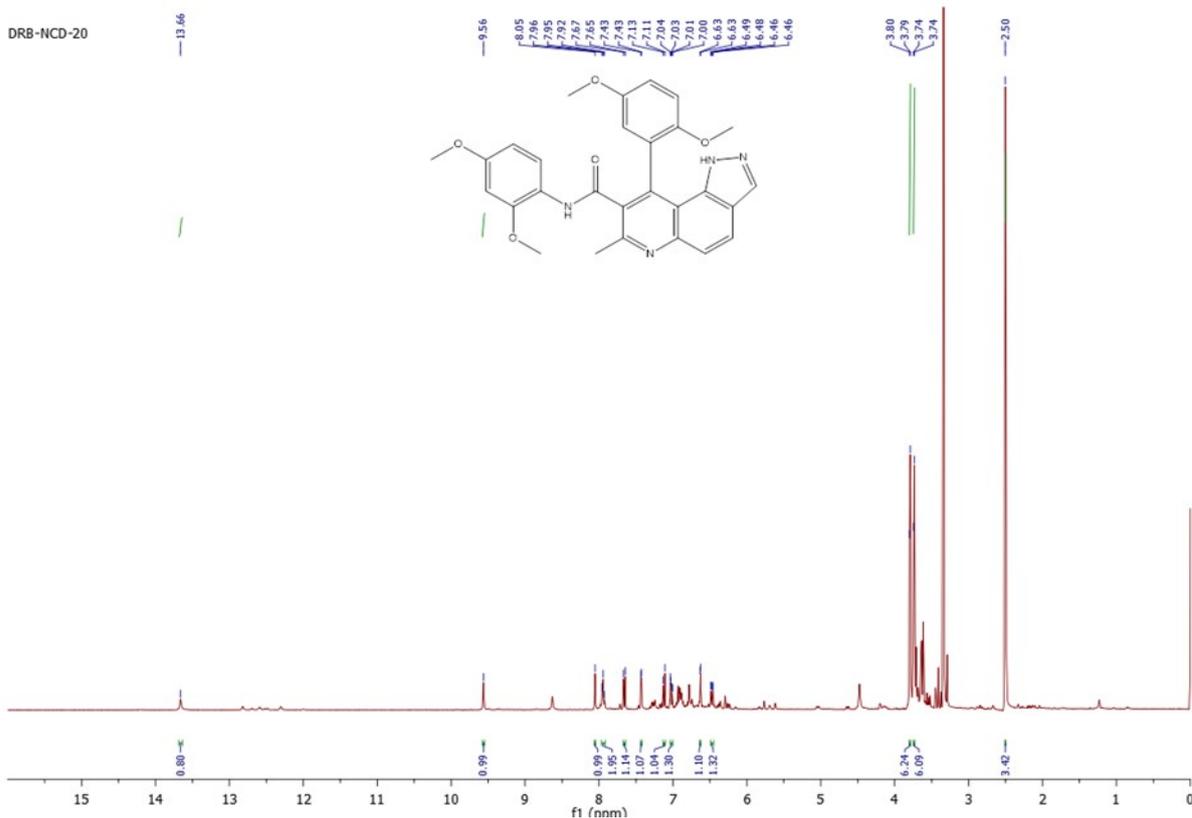


Figure S25:  $^1\text{H}$  NMR spectra of 4m (400MHz,  $\text{DMSO-d}_6$ )

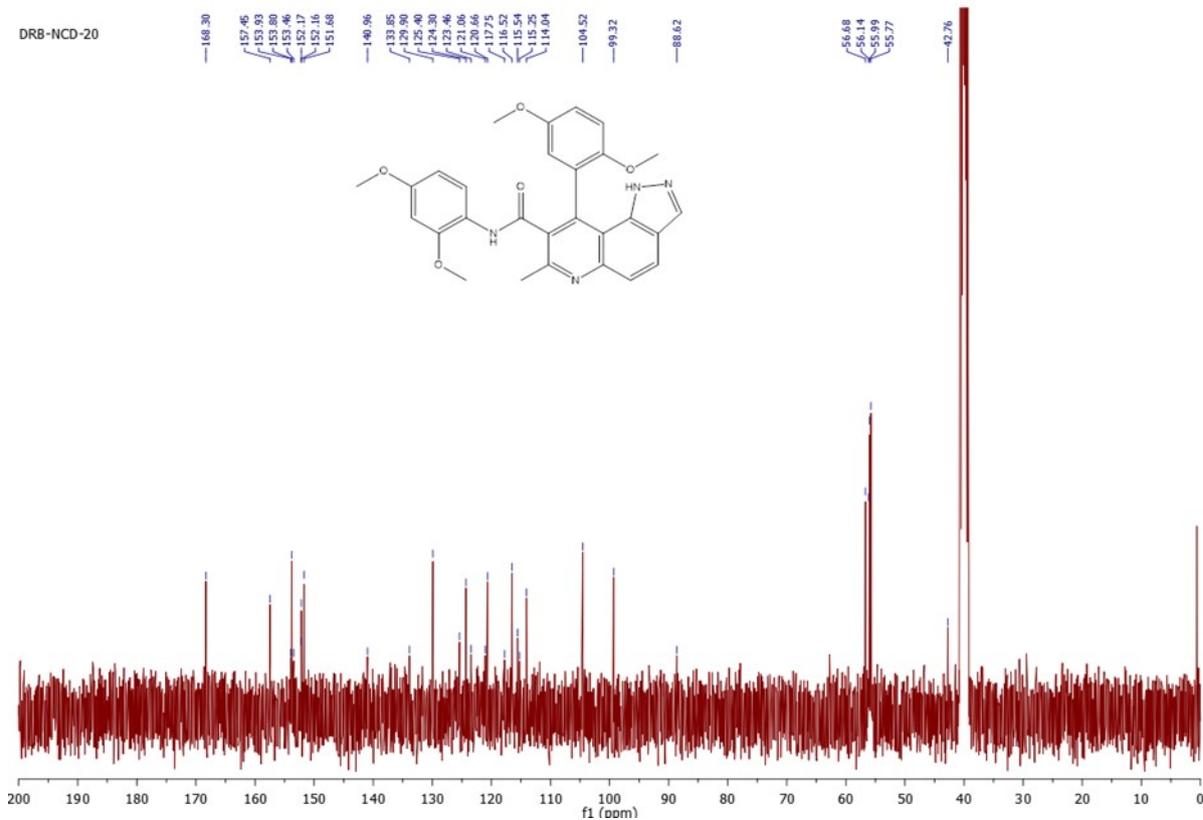
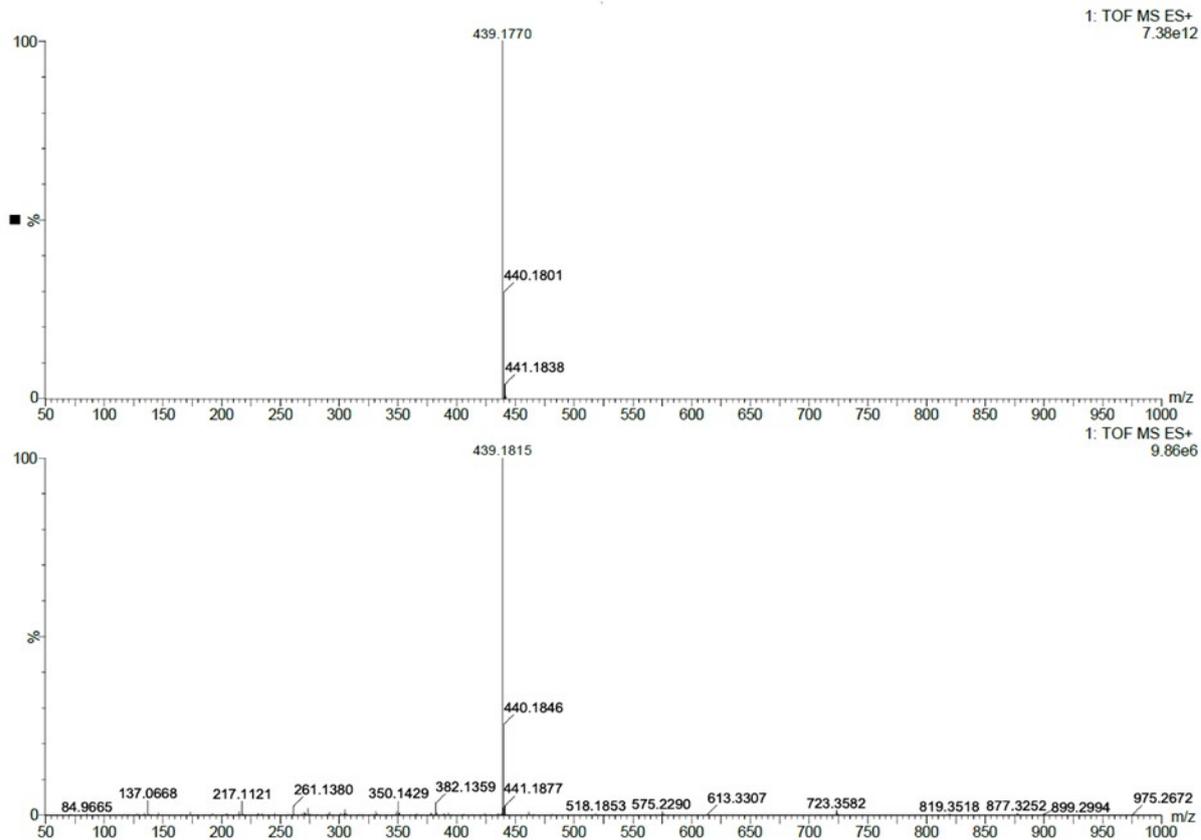
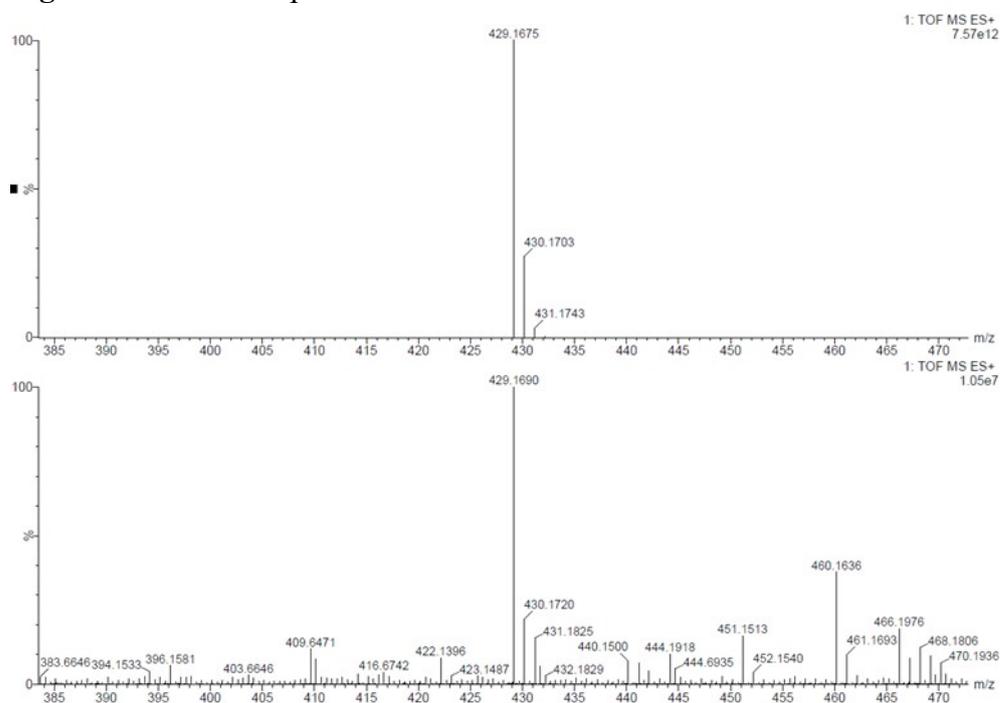


Figure S26:  $^{13}\text{C}$  NMR spectra of 4m (101MHz,  $\text{DMSO-d}_6$ )

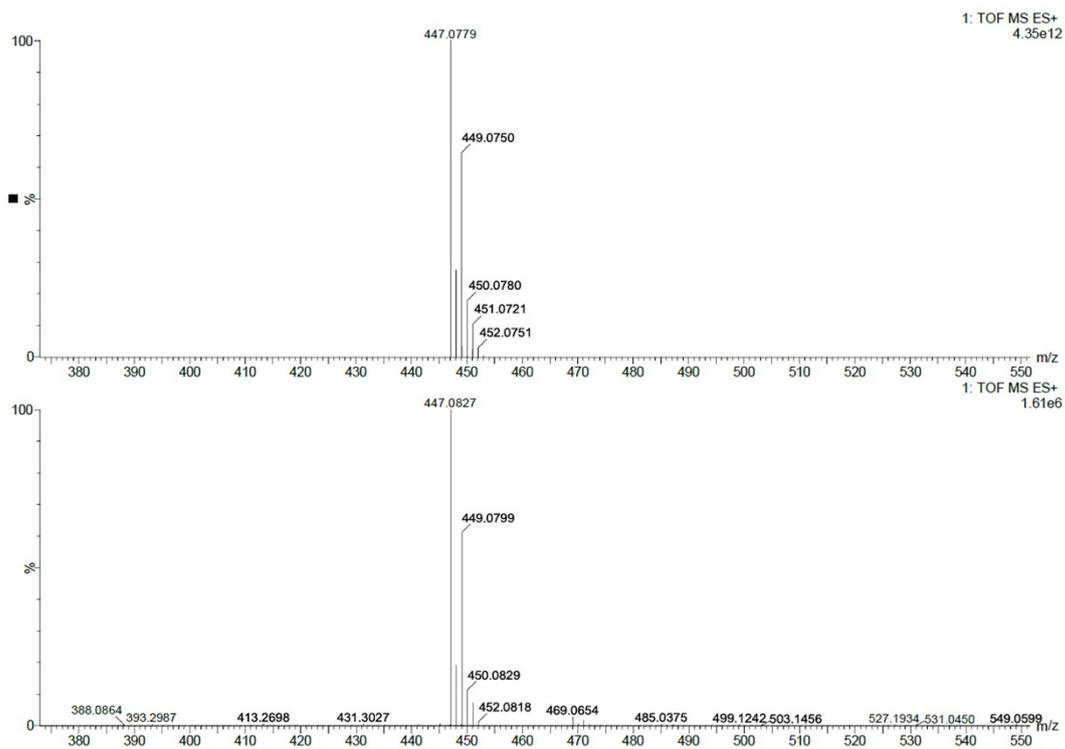




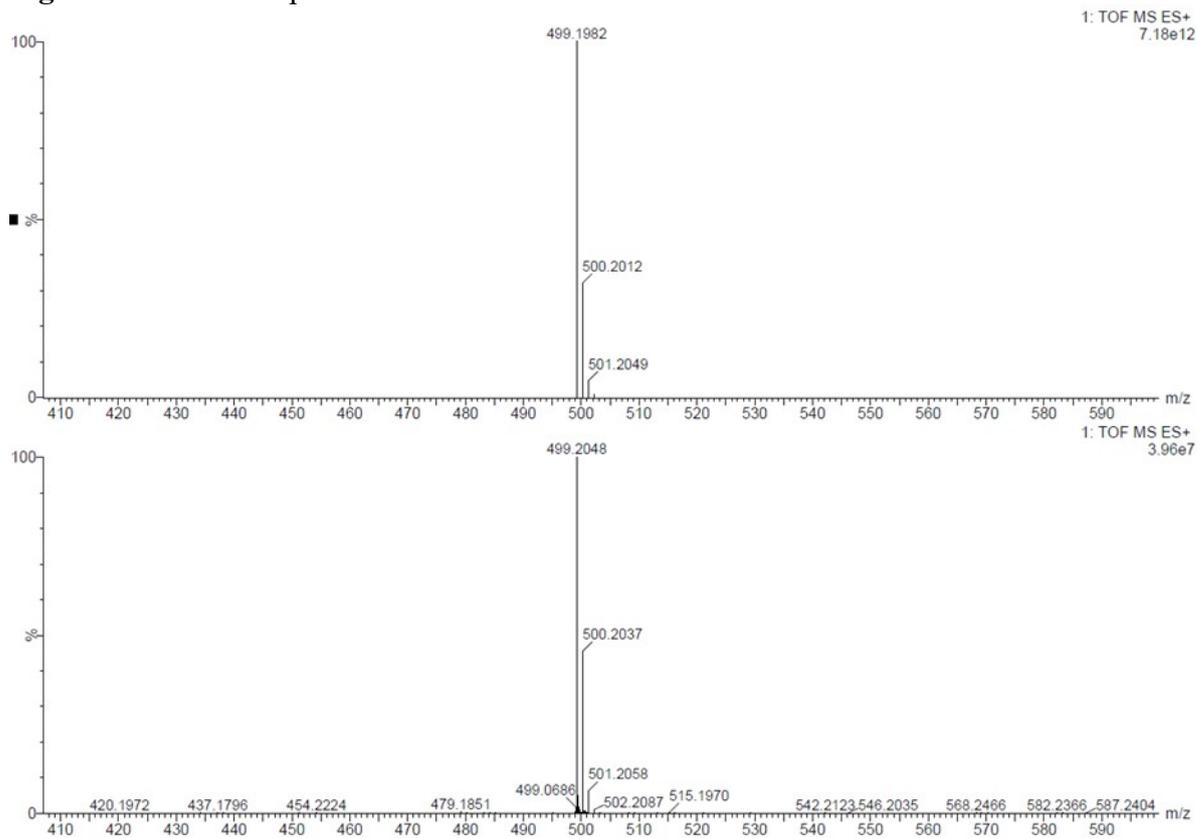
**Figure S29:** HRMS spectra of 4a



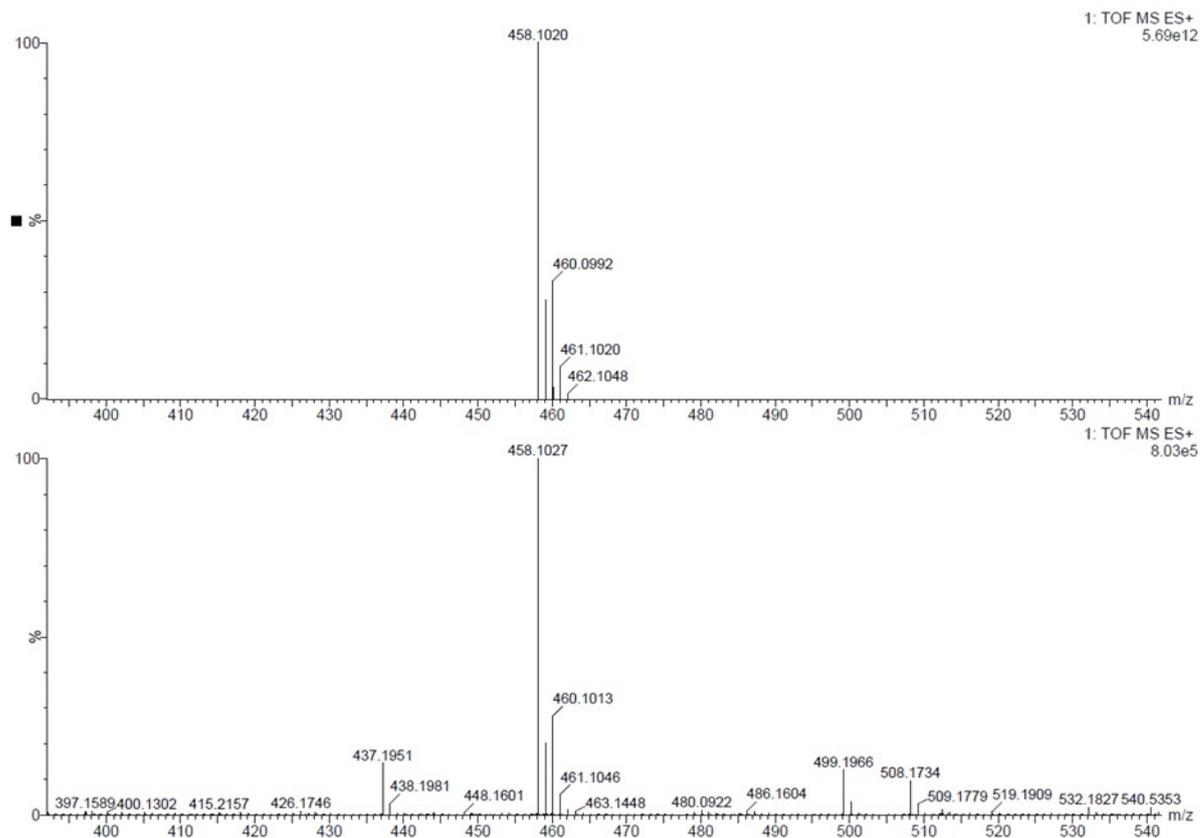
**Figure S30:** HRMS spectra of 4b



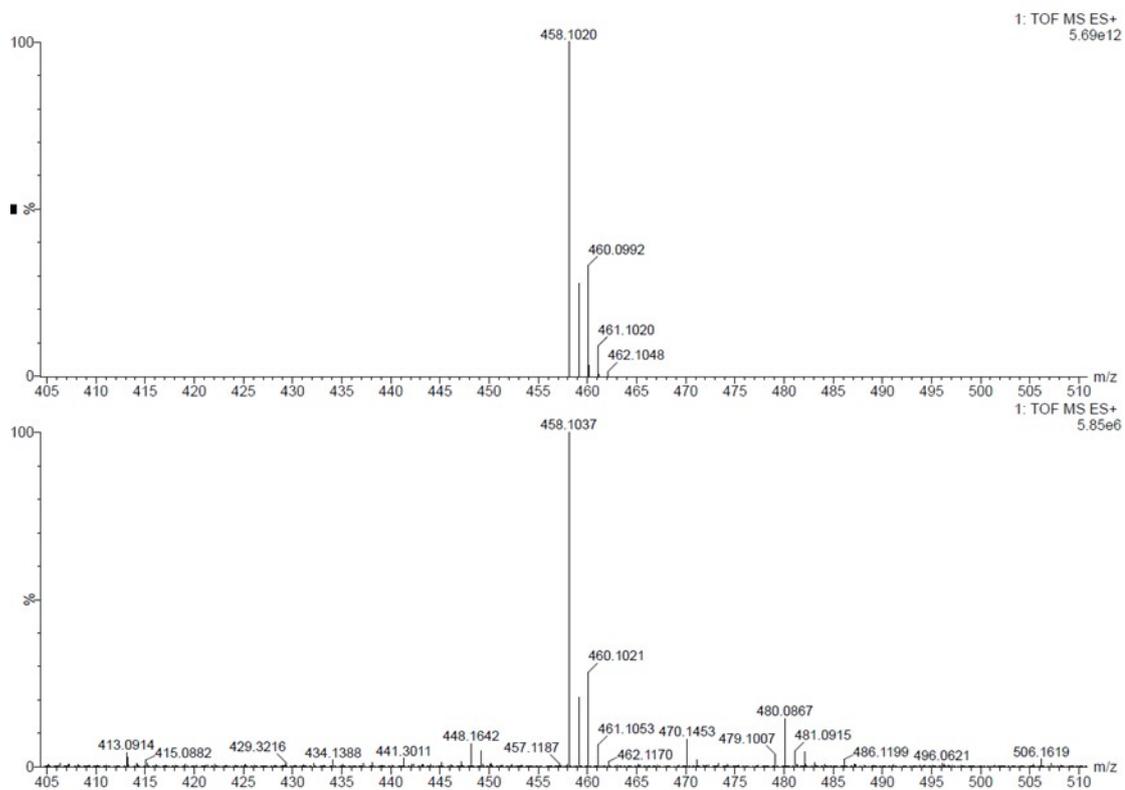
**Figure S31:** HRMS spectra of 4c



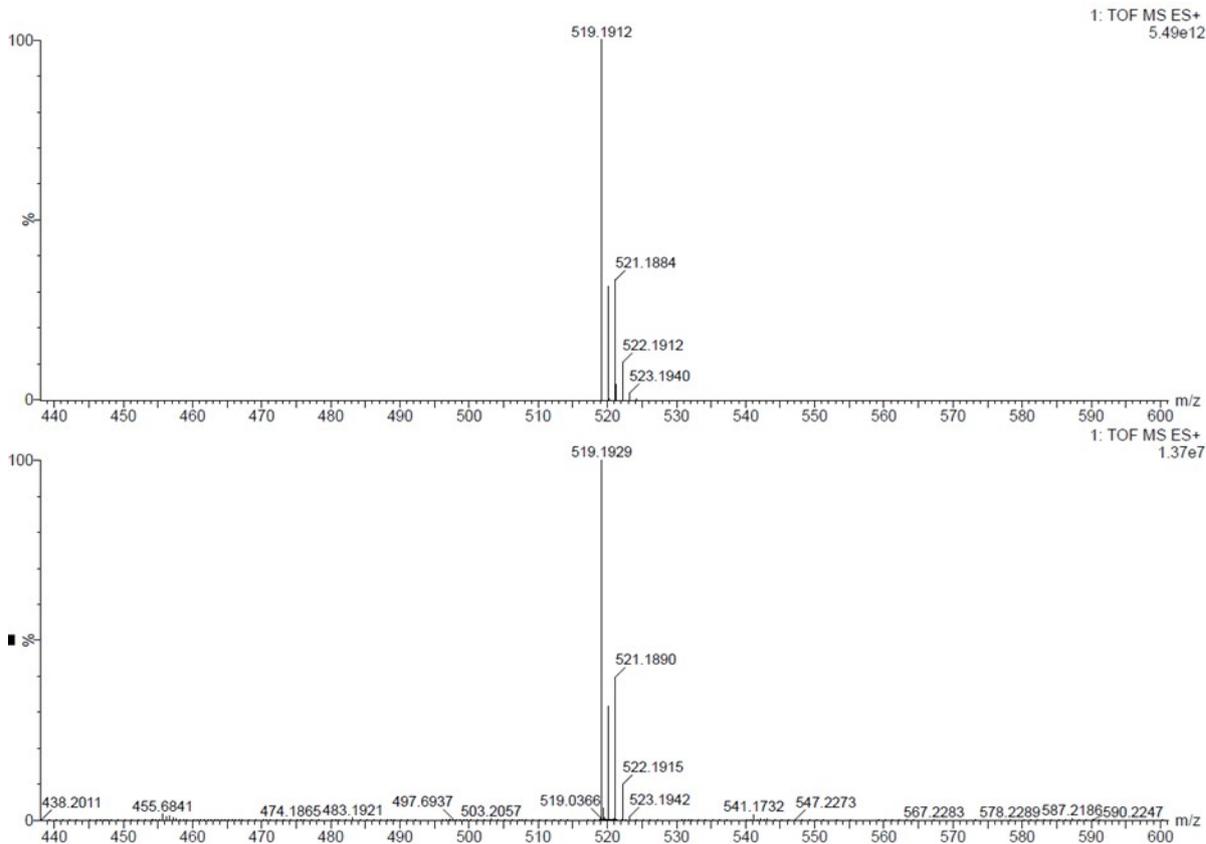
**Figure S32:** HRMS spectra of 4d



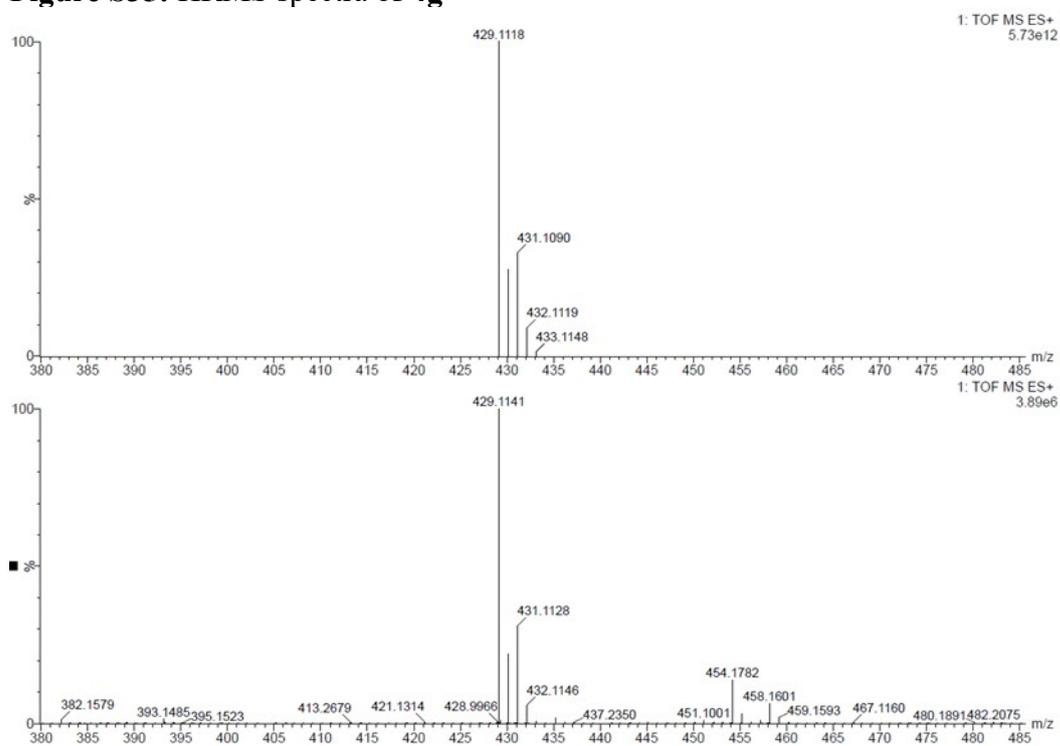
**Figure S33: HRMS spectra of 4e**



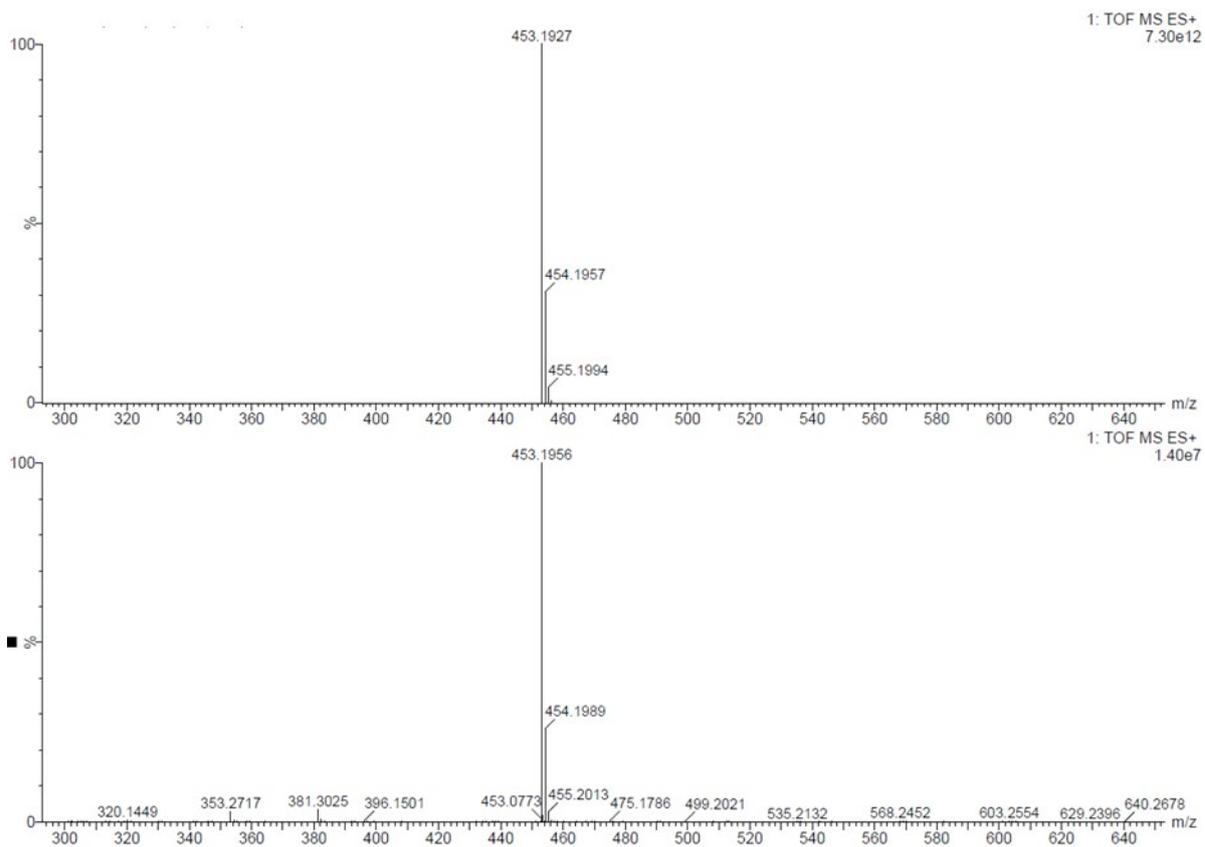
**Figure S34: HRMS spectra of 4f**



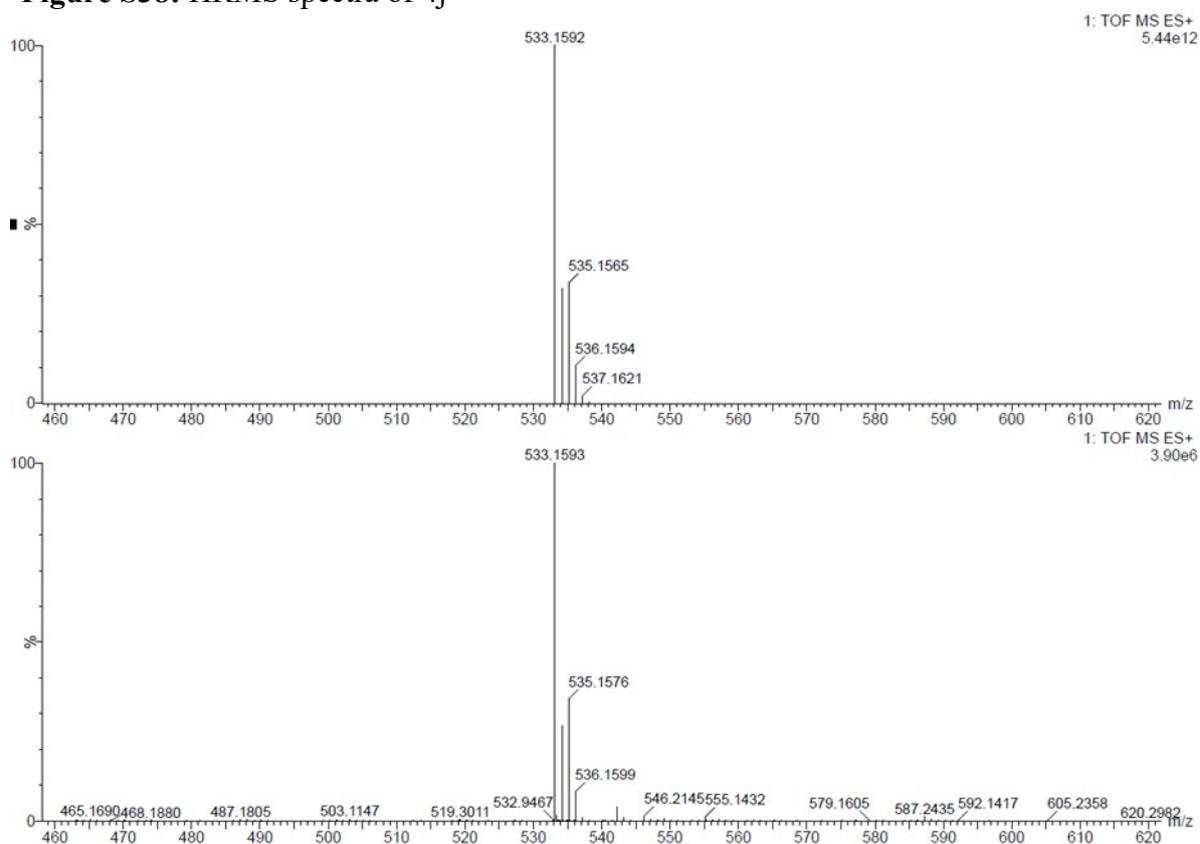
**Figure S35:** HRMS spectra of 4g



**Figure S36:** HRMS spectra of 4h



**Figure S38:** HRMS spectra of 4j



**Figure S39:** HRMS spectra of 4k

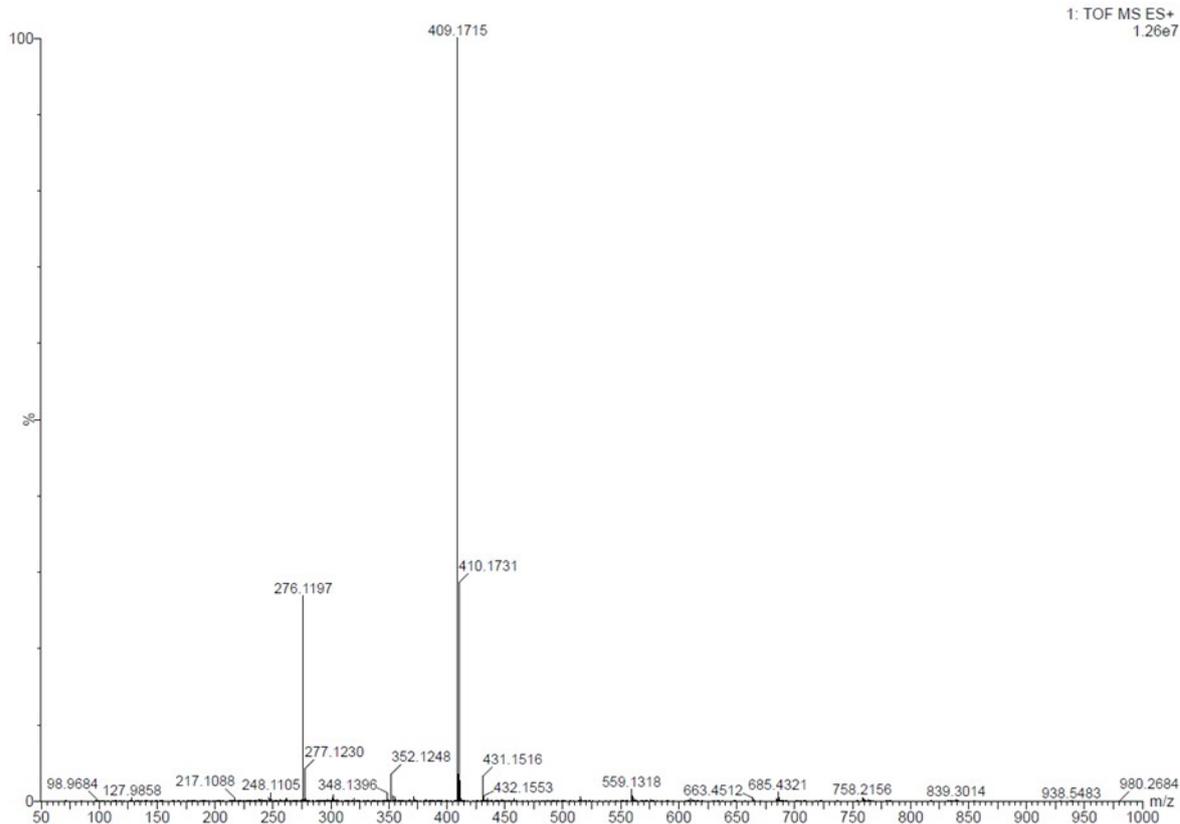


Figure S40: HRMS spectra of 4l

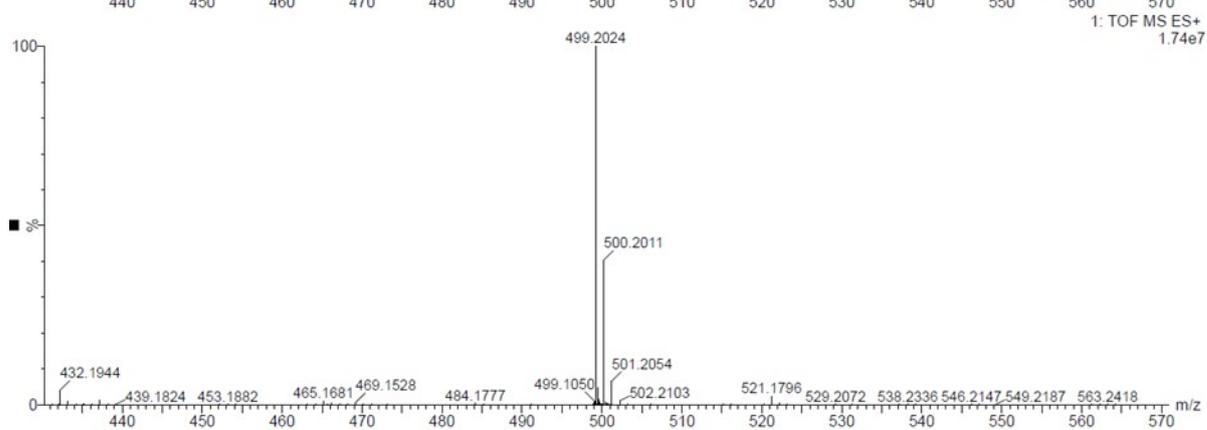
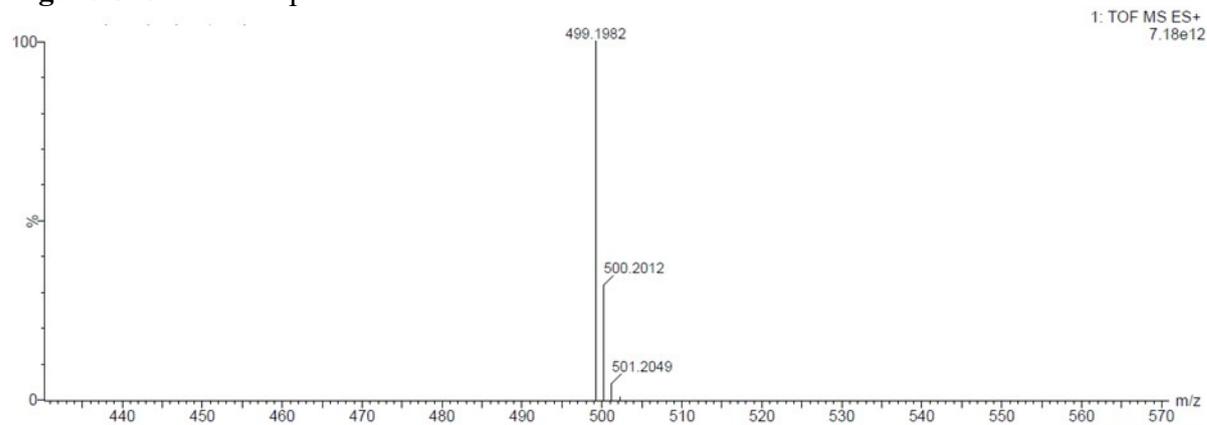
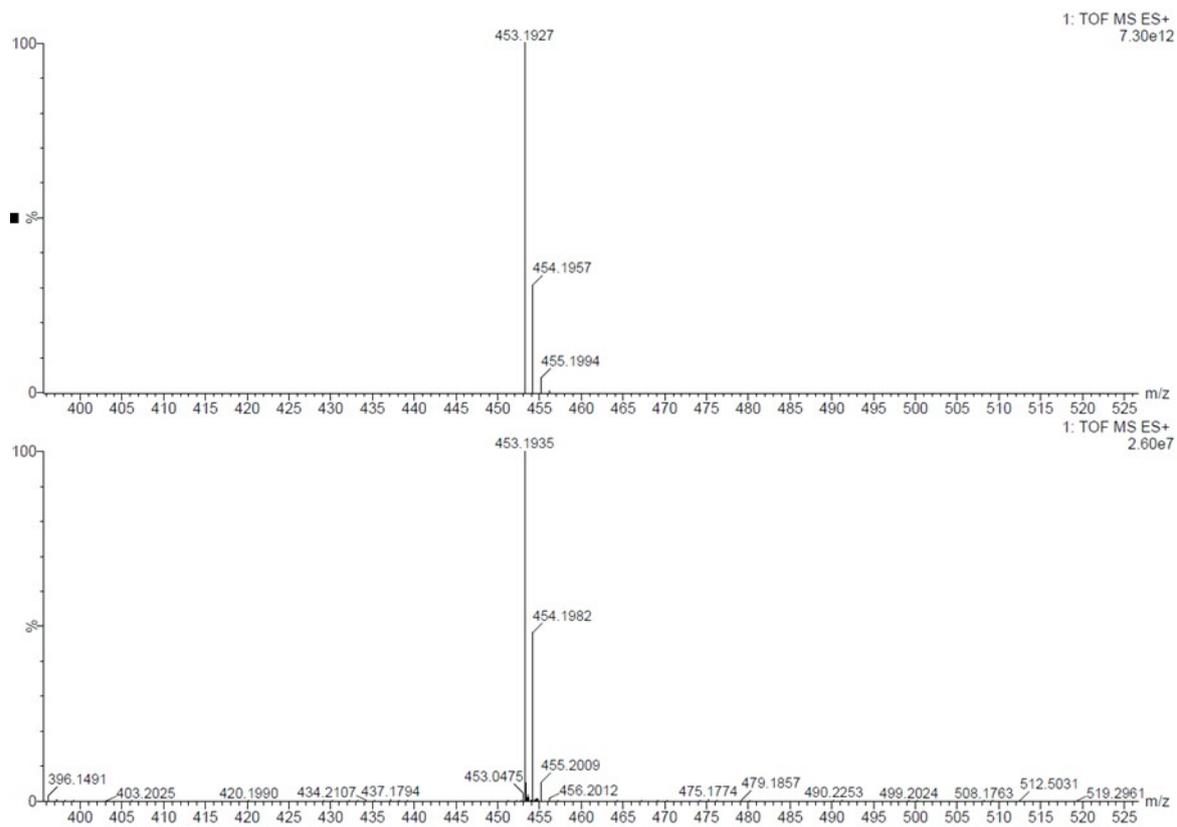


Figure S41: HRMS spectra of 4m



**Figure S42:** HRMS spectra of 4n

## 5. Green Metrics Calculation

### Validation of Green metrics for all synthesized compounds 4(a-n)

#### Materials used for green metrics calculation:

2-aminobenzimidazole **2** (1.0 mmol) with aryl aldehydes **1(a-j)** (1.0 mmol) and Acetoacetanilide **3(a-e)** (1.0 mmol).

#### Respective number of reagents:

**4a**: 0.152 gm (MW = 152.15), 2-methoxy,4-hydroxy benzaldehyde **1a**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 4-methylAcetoacetanilide **3a**: 0.191 gm (MW = 191.23);

**4b**: 0.122 gm (MW = 122.12), 2-hydroxy benzaldehyde **1b**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-choloroAcetoacetanilide **3b**: 0.211 gm (MW = 211.65);

**4c**: 0.140 gm (MW = 140.57), 4-choloro benzaldehyde **1c**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-choloro Acetoacetanilide **3b**: 0.211 gm (MW = 211.65)

**4d**: 0.166 gm (MW = 166.18), 2,4-dimethoxybenzaldehyde **1e**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2,4-dimethoxyAcetoacetanilide **3d**: 0.237 gm (MW = 237.26);

**4e**: 0.151 gm (MW = 151.12), 4-nitrobenzaldehyde **1d**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-choloroAcetoacetanilide **3b**: 0.211 gm (MW = 211.65)

**4f**: 0.151 gm (MW = 151.12), 3-nitrobenzaldehyde **1f**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-choloroAcetoacetanilide **3b**: 0.211 gm (MW = 211.65)

**4g**: 0.186 gm (MW = 186.64), 2-butyl,5-chloro imidazole carboxldehyde **1g**: 0.133 gm (MW = 133.15) 5amino indazole **2**, and 2,4-dimethoxyAcetoacetanilide **3d**: 0.237 gm (MW = 237.26);

**4h**: 0.122 gm (MW = 122.12), 4-hydroxybenzaldehyde **1h**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-choloroAcetoacetanilide **3b**: 0.211 gm (MW = 211.65)

**4i**: 0.140 gm (MW = 140.57), 4-cholorobenzaldehyde **1c**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2,4-dimethoxyAcetoacetanilide **3d**: 0.237 gm (MW = 237.26);

**4j**: 0.166 gm (MW = 166.18), 2,4-dimethoxybenzaldehyde **1d**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 4-methylAcetoacetanilide **3a**: 0.191 gm (MW = 191.23);

**4k**: 0.180 gm (MW = 180.18), 2,5-dimethoxybenzaldehyde **1i**:0.133 gm (MW = 133.15) 5-amino indazole **2**, and 4-choloro,2,5-dimethoxy,4-chloro Acetoacetanilide **3c**: 0.271 gm (MW = 271.70);

**4l** : 0.122 gm (MW = 122.12), 4-hydroxybenzaldehyde **1h**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-methyl Acetoacetanilide **3e**: 0.191 gm (MW = 191.23);

**4m**: 0.180 gm (MW = 166.18), 2,5-dimethoxybenzaldehyde **1i**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2,4-dimethoxyAcetoacetanilide **3d**: 0.237 gm (MW = 237.26);

**4n** : 0.180 gm (MW = 180.18), 3,4-dimethoxybenzaldehyde **1i**: 0.133 gm (MW = 133.15) 5-amino indazole **2**, and 2-methyl Acetoacetanilide **3e**: 0.191 gm (MW = 191.23);

#### Solvents:

Ethanol as a reaction media (5 mL): 3.945

#### Products:

**4a**: 0.438 gm (MW = 438.17 g/mol); **4b**: 0.428 gm (MW = 428.10 g/mol); **4c**: 0.446 gm (MW = 446.07 g/mol); **4d**: 0.498 gm (MW = 498.19 g/mol); **4e**: 0.457 gm (MW = 457.09 g/mol); **4f**: 0.457 gm (MW = 457.09 g/mol);

= 457.09 g/mol); **4g**: 0.518 gm (MW = 518.18 g/mol); **4h**: 0.428 gm (MW = 428.10 g/mol); **4i**: 0.452 gm (MW = 452.18 g/mol); **4j**: 0.452 gm (MW = 452.18 g/mol); **4k**: 0.532 gm (MW = 532.15 g/mol); **4l**: 0.408 gm (MW = 408.16 g/mol); **4m**: 0.498 gm (MW = 498.19 g/mol); **4n**: 0.452 gm (MW = 452.18 g/mol);

**Analysis of Green metrics:**

The following formulae were utilized for the calculation of E-factor, Atom economy (AE), Reaction mass efficiency (RME), Effective mass yield (EMY), and Optimum efficiency (OE). The calculated green metrics data for compounds **4(a-n)** are represented in **Table S1**.

$$E - factor = \frac{(Total\ mass\ of\ wastes)}{(Mass\ of\ product)}$$

OR

$$E - factor = \frac{(Mass\ of\ raw\ materials - Mass\ of\ product)}{(Mass\ of\ product)}$$

$$AE\ (\%) = \frac{(Molecular\ weight\ of\ product)}{(Total\ molecular\ weight\ of\ reactants)} \times 100$$

$$AEf = AE \times \%yield$$

$$CE = \frac{Amount\ of\ carbon\ in\ the\ product}{Total\ carbon\ present\ in\ the\ reactant} \times 100$$

$$RME\ (\%) = \frac{(Mass\ of\ isolated\ product)}{(Total\ mass\ of\ reactant)} \times 100$$

$$EMY\ (\%) = \frac{(Mass\ of\ product)}{(Mass\ of\ non - benign\ reagents)} \times 100$$

$$OE\ (\%) = \frac{RME}{AE} \times 100$$

\*Note: Solvents used in the reaction as well as in the reaction work-up process were distilled out and reused.

Sr. No.	Product	Yield (%)	E-factor	AE (%)	AEf (%)	CE (%)	RME (%)	EMY (%)	OE (%)
1	<b>4a</b>	83	0.313	91.95	76.32	221.925	76.18	76.18	82.845
2	<b>4b</b>	79	0.381	91.69	72.43	207.819	72.39	72.39	78.954
3	<b>4c</b>	88	0.238	91.9	80.87	233.302	80.76	80.76	87.879
4	<b>4d</b>	90	0.198	92.85	83.56	237.814	83.49	83.49	89.926
5	<b>4e</b>	88	0.234	92.17	81.11	234.951	81.06	81.06	87.948
6	<b>4f</b>	89	0.221	92.17	82.03	237.289	81.87	81.87	88.823
7	<b>4g</b>	88	0.224	93.02	81.86	233.011	81.68	81.68	87.807
8	<b>4h</b>	75	0.455	91.69	68.76	197.367	68.75	68.75	74.982
9	<b>4i</b>	87	0.3	92.4	80.39	214.521	76.91	76.91	83.24
10	<b>4j</b>	85	0.277	92.18	78.35	228.818	78.28	78.28	84.922
11	<b>4k</b>	87	0.236	93.19	81.08	227.427	80.91	80.91	86.818
12	<b>4l</b>	87	0.258	91.41	79.53	228.116	79.5	79.5	86.976
13	<b>4m</b>	87	0.239	92.84	80.77	229.848	80.69	80.69	86.915
14	<b>4n</b>	86	0.264	92.18	79.27	231.197	79.09	79.09	85.807