

Supporting data file:

Synthesis of New Class of Indole Acetic Acid Sulfonate Derivatives as Ectonucleotidases Inhibitors

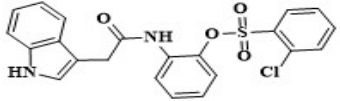
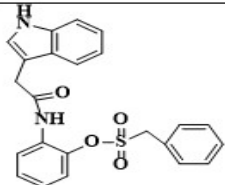
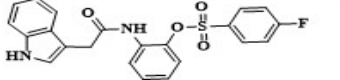
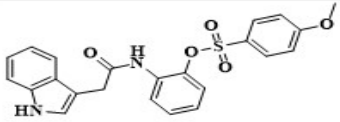
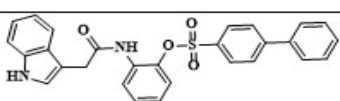
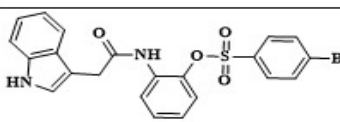
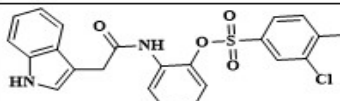
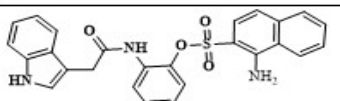
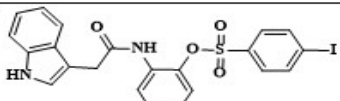
Muhammad Siraj Khan Jadoon^{a, b}, Julie Pelletier^c, Jean Sévigny^{c, d}, Jamshed Iqbal^{a, b, e *}

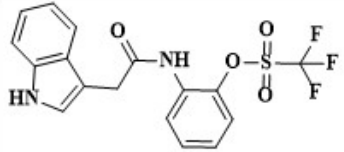
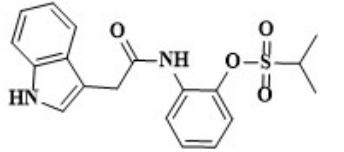
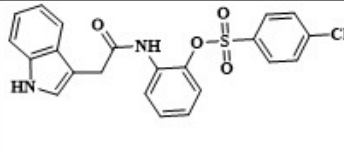
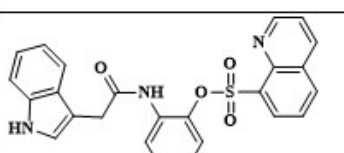
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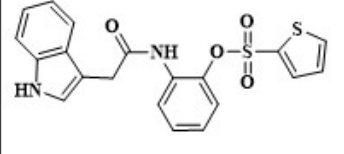
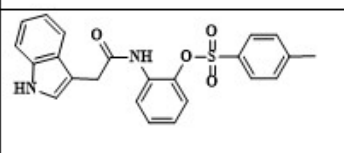
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1-Table S1: Indole acetic acid sulfonate derivatives (5a-5o) description

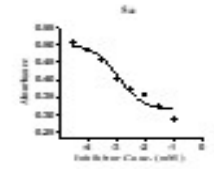
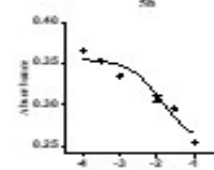
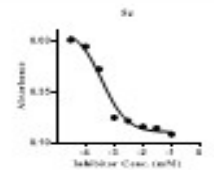
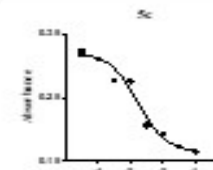
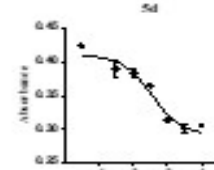
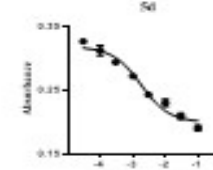
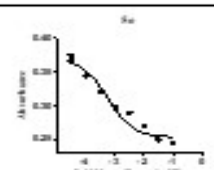
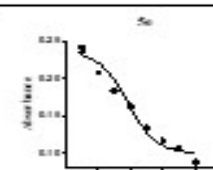
Comp #	IUPAC Name	Mol.wt.	Mol. Formula	Solubility	Product structure	Appearance	Melting point
5a	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 2-chlorobenzenesulfonate	440.90	C ₂₂ H ₁₇ ClN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	181-183°C
5b	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl phenylmethane sulfonate	420.48	C ₂₃ H ₂₀ N ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	134-137°C
5c	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-fluorobenzenesulfonate	424.45	C ₂₂ H ₁₇ FN ₂ O ₄ S	DMS O Acetone		white crystalline powder	161-163°C
5d	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-Methoxybenzenesulfonate	436.48	C ₂₃ H ₂₀ N ₂ O ₅ S	DMS O Acetone		Off white crystalline powder	200-203°C
5e	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl [1,1'-biphenyl]-4-sulfonate	482.55	C ₂₈ H ₂₂ N ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	193-195°C
5f	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-bromobenzenesulfonate	485.35	C ₂₂ H ₁₇ BrN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	183-186°C
5g	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 3-chloro-4-methylbenzenesulfonate	454.93	C ₂₂ H ₁₇ ClN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	115-117°C
5h	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 1-aminonaphthalene-2-sulfonate	471.53	C ₂₂ H ₁₇ ClN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	116-118°C
5i	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-iodobenzenesulfonate	532.35	C ₂₂ H ₁₇ IN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	169-172°C

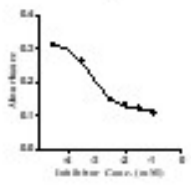
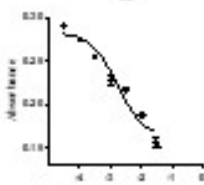
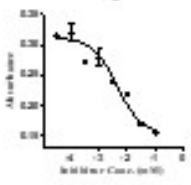
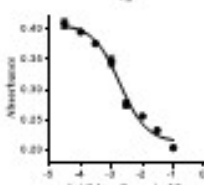
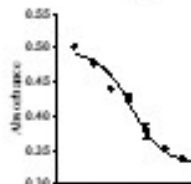
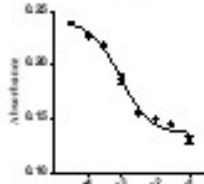
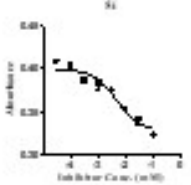
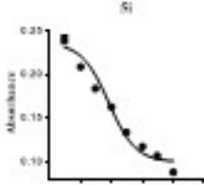
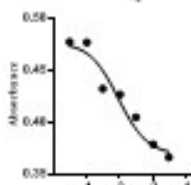
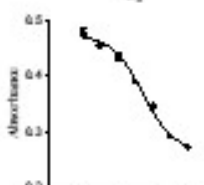
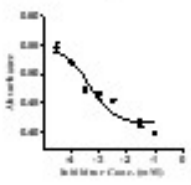
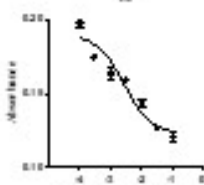
5j	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyltrifluoromethanesulfonate	398.36	C ₁₇ H ₁₃ F ₃ N ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	114-116°C
5k	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenylpropane-2-sulfonate	372.44	C ₁₉ H ₂₀ N ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	139-141°C
5l	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-chlorobenzenesulfonate	440.90	C ₂₂ H ₁₇ ClN ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	186-188°C
5m	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenylquinoline-8-sulfonate	457.50	C ₂₅ H ₁₉ N ₃ O ₄ S	DMS O Acetone		Off white crystalline powder	178-180°C

5n	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenylthiophene-2-sulfonate	412.48	C ₂₀ H ₁₆ N ₂ O ₄ S ₂	DMS O Acetone		Off white crystalline powder	180-183°C
5o	2-(2-(1 <i>H</i> -indol-3-yl)acetamido)phenyl 4-methylbenzenesulfonate	420.48	C ₂₃ H ₂₀ N ₂ O ₄ S	DMS O Acetone		Off white crystalline powder	160-162°C

2-Table S2: Biological activities results for Indole acetic acid sulfonate derivatives (5a-5o),
a) *h*-e5'NT and *r*-e5'NT, b) Human NPP1 and NPP3, c) *h*-TNAP

a) *h*-e5'NT and *r*-e5'NT

S.No	Comp. Code	<i>h</i> -e5'NT		<i>r</i> -e5'NT	
		Graph	IC ₅₀ ±SEM (μM) / %Inhibition	Graph	IC ₅₀ ±SEM (μM) / %Inhibition
1.	5a		1.19±0.02	-	22.72%
2.	5b		13.22±3.14	-	38.52%
3.	5c		0.37±0.03		1.66±0.04
4.	5d		3.46±0.12		1.77±0.12
5.	5e		0.56±0.016		0.98±0.02

6.	5f		0.69±0.001		1.64±0.02
7.	5g		4.4±0.19		1.85±0.11
8.	5h		1.17±0.13		0.91±0.04
9.	5i		4.85±0.55		0.81±0.05
10.	5j		0.89±0.04		5.12±0.61
11.	5k	-	37.52%	-	28.65%
12.	5l		0.43±0.03		5.67±0.11

13.	5m		6.53±0.67	-	30.03%
14.	5n	-	44.68%	-	46.64%
15.	5o		3.21±0.83		4.86±0.04
16.	Sulfamic acid		42.1 ± 7.80a		77.3 ± 7.0a

b)Human ENPP1 and ENPP3

S.No	Comp Code	NPP1		NPP3	
		Graph	IC ₅₀ ±SEM (μM) / %Inhibition	Graph	IC ₅₀ ±SEM (μM) / %Inhibition
1.	5a		2.07±0.22		1.66±0.007
2.	5b		1.35±0.02		1.71±0.11
3.	5c		1.12±0.12		1.37±0.05
4.	5d		1.09±0.01		2.05±0.25

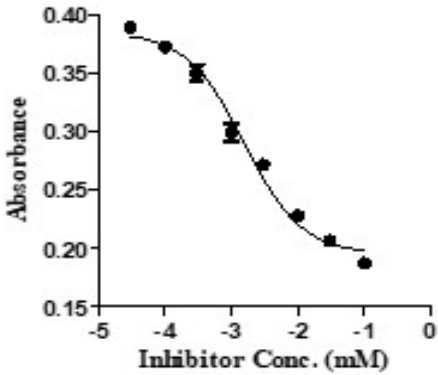
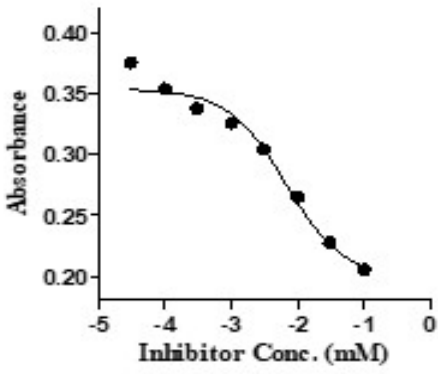
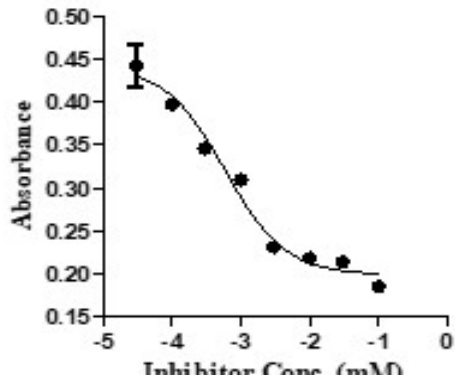
5.	5e		0.32±0.01		4.51±0.38
6.	5f		1.14±0.002		1.23±0.01
7.	5g		1.69±0.05		1.31±0.11
8.	5h		0.91±0.02		1.02±0.004

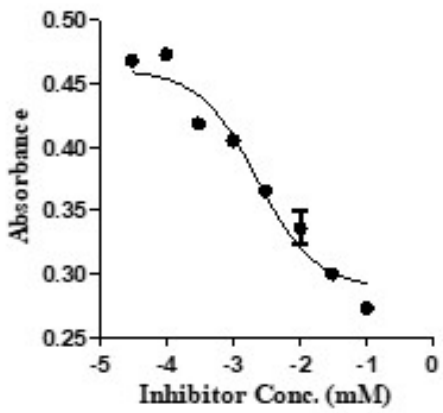
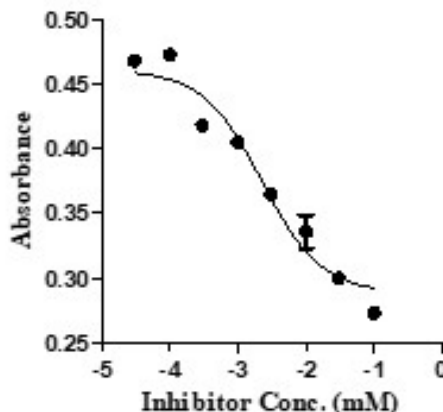
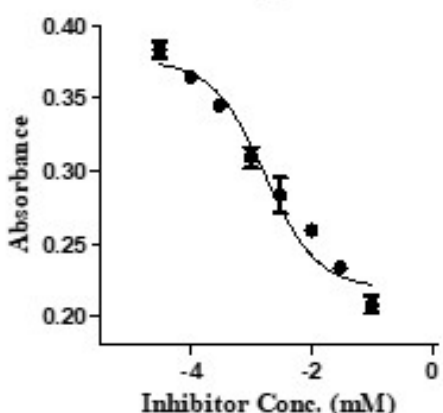
9.	5i		1.07±0.06		3.26±0.15
10.	5j		0.59±0.003		0.62±0.003
11.	5k		1.74±0.05		0.89±0.04
12.	5l		0.85±0.03		0.77±0.03

13	5m		1.36±0.09		1.22±0.01
14	5n	-	38.03%		2.55±0.07
15	5o	-	28.32%		2.67±0.46
16	Suramin (as standard drug)		18.54±1.14		12.83±0.23

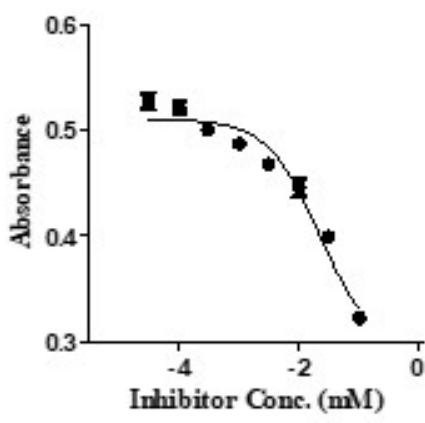
c)h-TNAP

S.No	Comp. Code	h-TNAP	
		Graph	IC ₅₀ ±SEM (μM) / %Inhibition
1.	5a	<p>5a</p>	1.6±0.11
2.	5b	-	42.39%
3.	5c	<p>5c</p>	1.48±0.02
4.	5d	<p>5d</p>	5.18±0.46

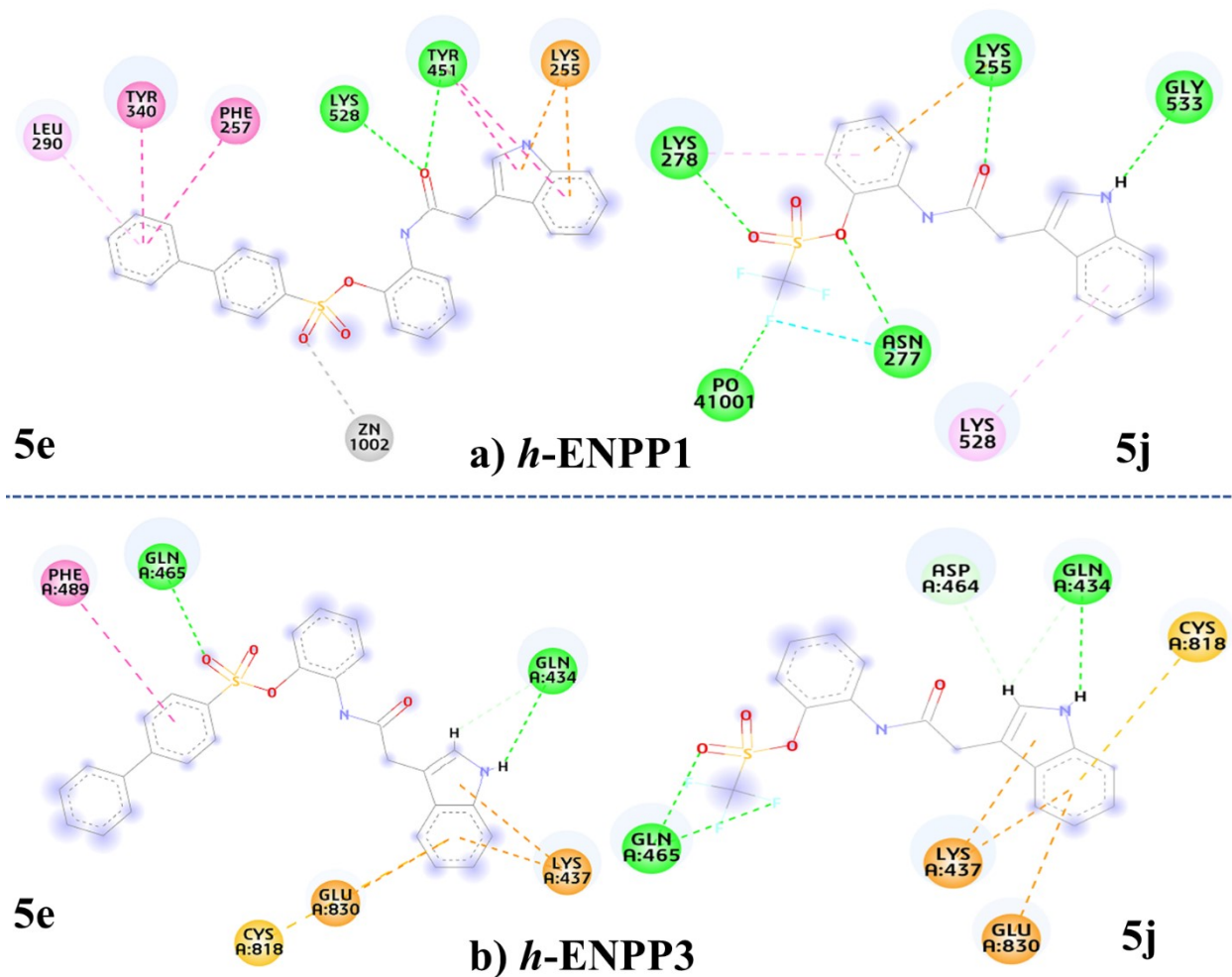
5.	5e	<p style="text-align: center;">5e</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	1.56±0.03
6.	5f	<p style="text-align: center;">5f</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	6.58±0.25
7.	5g	<p style="text-align: center;">5g</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	0.59±0.08

8.	5h	<p style="text-align: center;">5h</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	2.86±0.06
9.	5i	<p style="text-align: center;">5i</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	2.27±0.24
10	5j	<p style="text-align: center;">5j</p>  <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	1.68±0.07
11	5k	-	31.75%

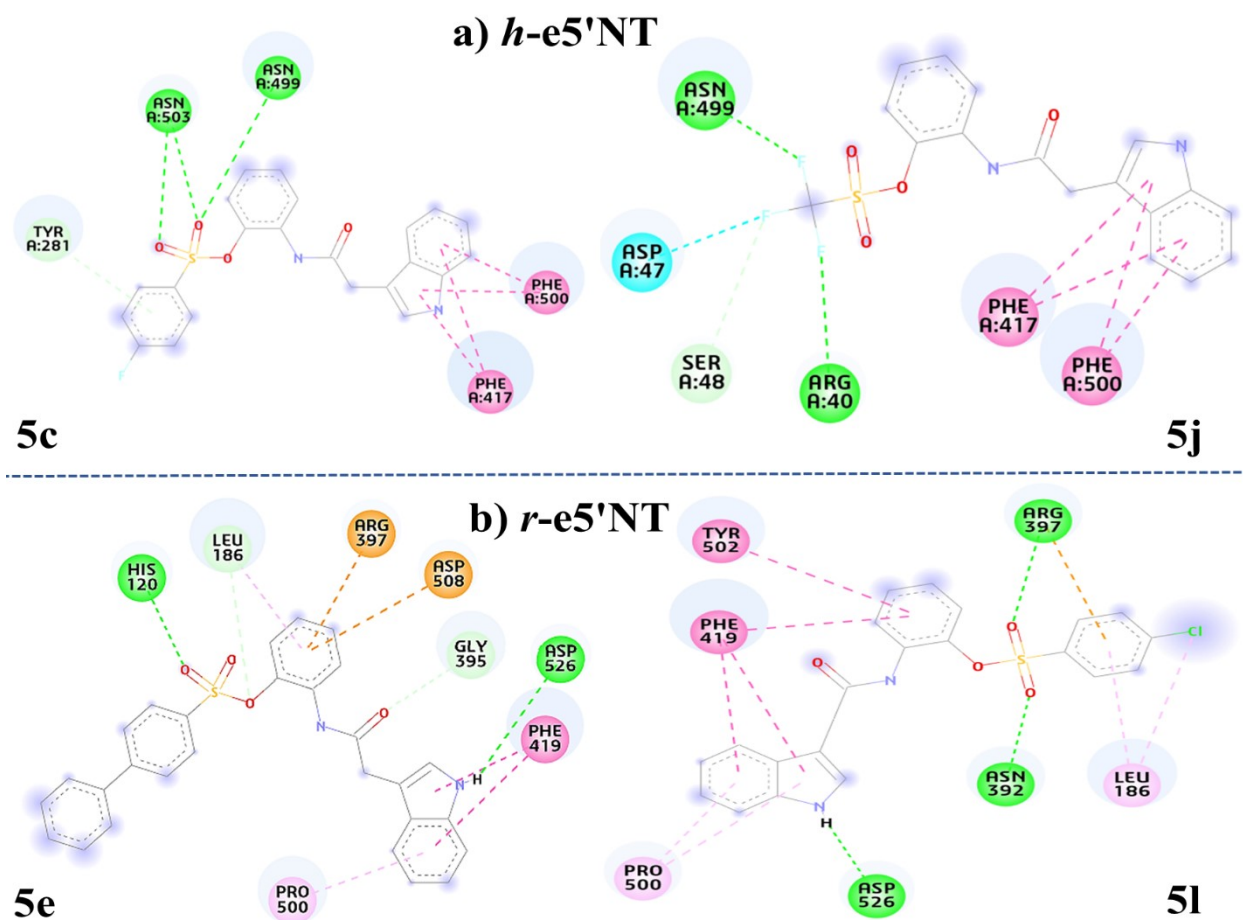
12.	5l	<p style="text-align: center;">5l</p> <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	1.69±0.18
13.	5m	<p style="text-align: center;">5m</p> <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	1.3±0.38
14.	5n	-	28.88%
15.	5o	<p style="text-align: center;">5o</p> <p style="text-align: center;">Absorbance</p> <p style="text-align: center;">Inhibitor Conc. (mM)</p>	3.37±0.05

16.	Levamisole	<p style="text-align: center;">Levamisole</p>  <table border="1" data-bbox="544 262 966 682"><caption>Estimated data points from the graph</caption><thead><tr><th>Inhibitor Conc. (nM)</th><th>Absorbance</th></tr></thead><tbody><tr><td>-4.5</td><td>0.53</td></tr><tr><td>-4.0</td><td>0.52</td></tr><tr><td>-3.5</td><td>0.50</td></tr><tr><td>-3.0</td><td>0.48</td></tr><tr><td>-2.5</td><td>0.46</td></tr><tr><td>-2.0</td><td>0.44</td></tr><tr><td>-1.5</td><td>0.40</td></tr><tr><td>-1.0</td><td>0.32</td></tr></tbody></table>	Inhibitor Conc. (nM)	Absorbance	-4.5	0.53	-4.0	0.52	-3.5	0.50	-3.0	0.48	-2.5	0.46	-2.0	0.44	-1.5	0.40	-1.0	0.32	21.38±4.17
Inhibitor Conc. (nM)	Absorbance																				
-4.5	0.53																				
-4.0	0.52																				
-3.5	0.50																				
-3.0	0.48																				
-2.5	0.46																				
-2.0	0.44																				
-1.5	0.40																				
-1.0	0.32																				

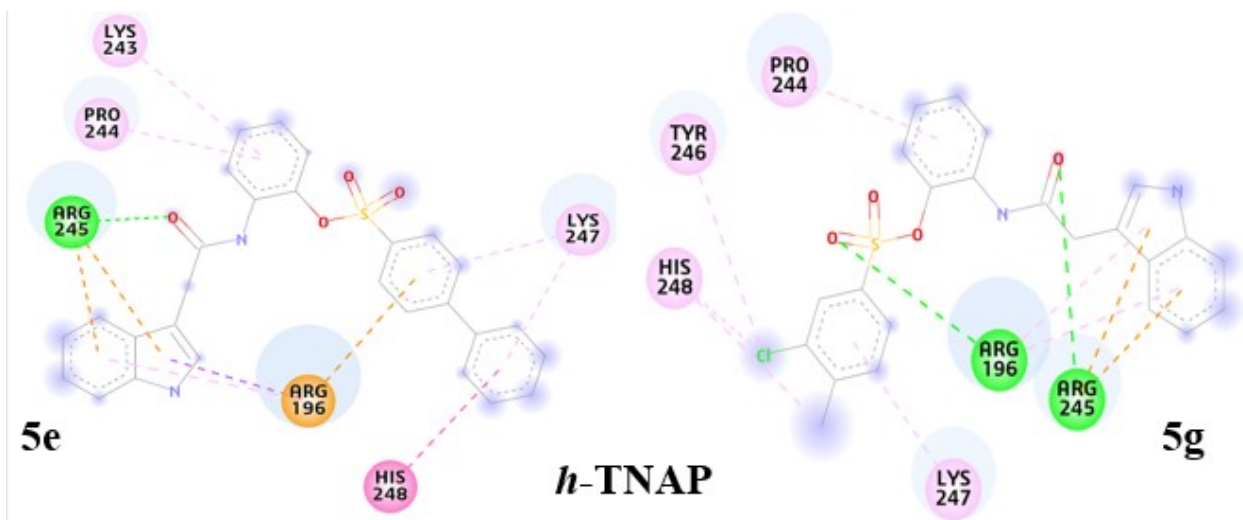
Molecular docking of Indole acetic acid sulfonate derivatives (5a-5o), 2D Images of most active compounds



3-Figure FS1: Illustration of 2D ligand-Protein interactions conformations of **5j** and **5e** against **a) *h*-ENPP1**, **b) *h*-ENPP3**



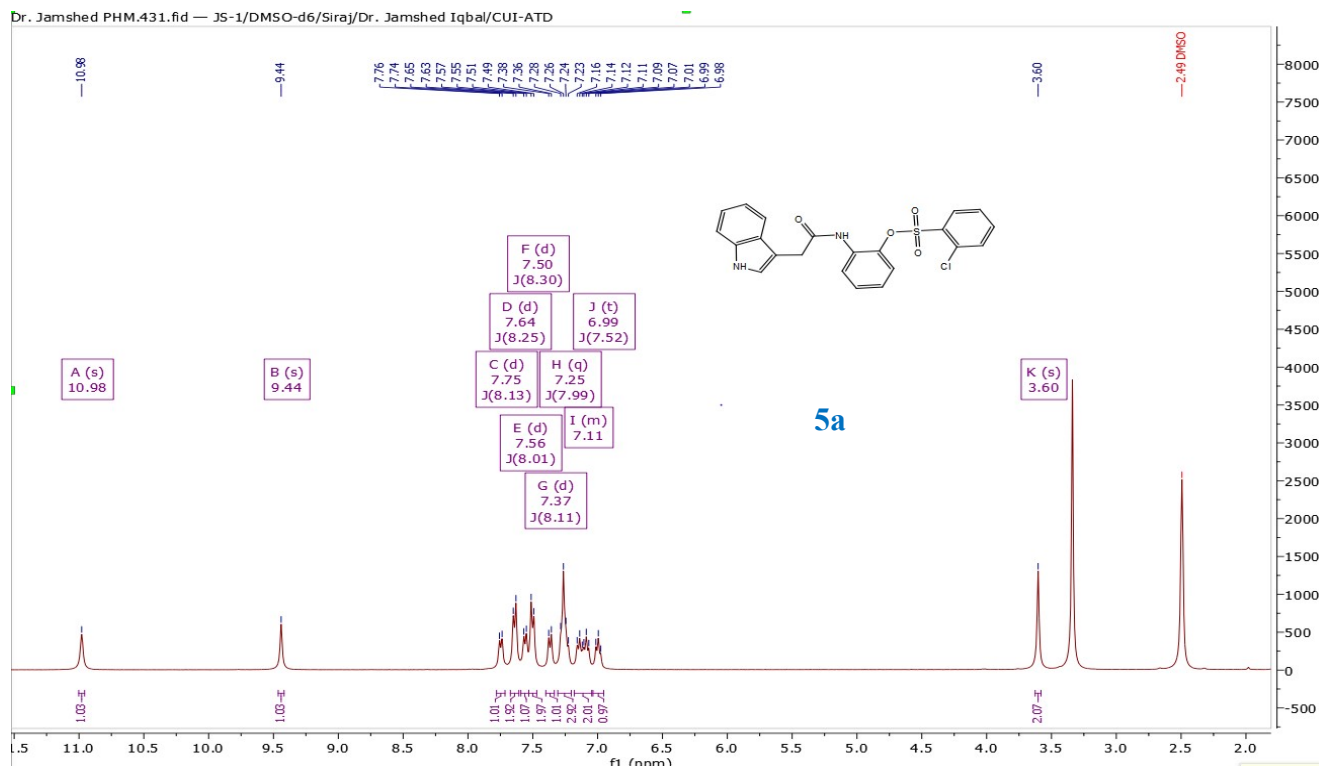
4-Figure FS2. Presentation of 2D binding modes of inhibitor **5c** and **5j** against **a) *h*-e5'NT** residues and **5e** and **5l** against **b) *r*-e5'NT** residues



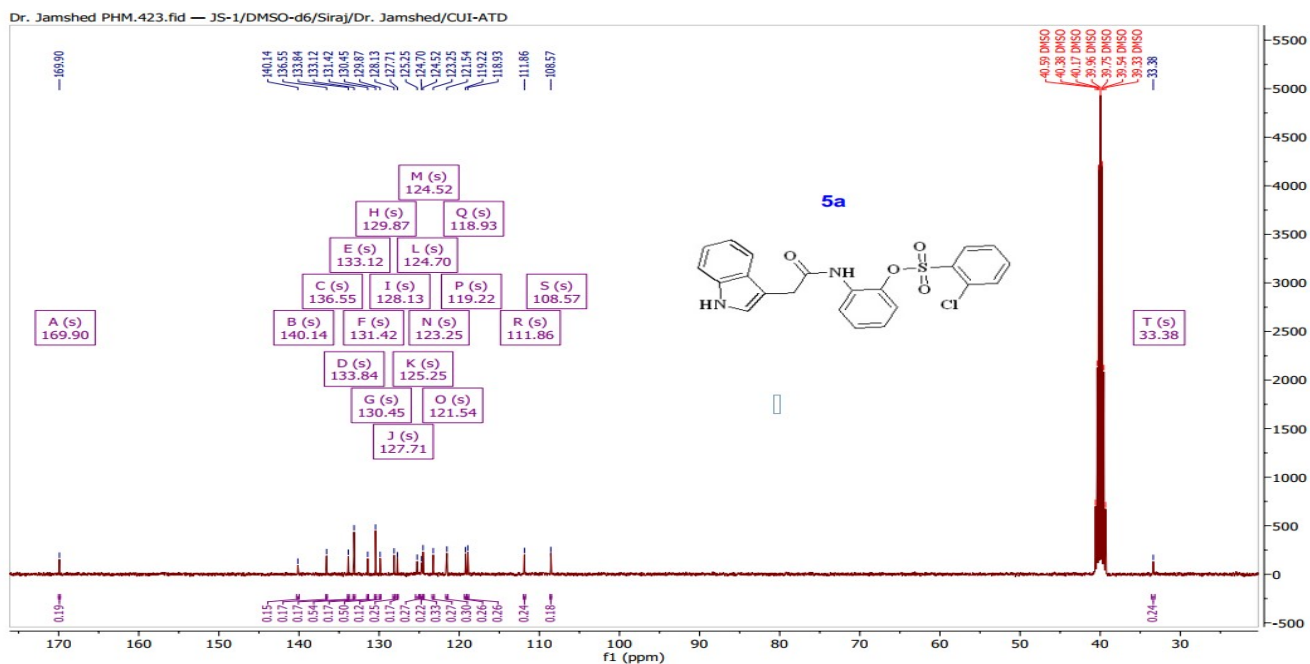
5-Figure FS3. 2D ligand-Protein Interactions docked conformations presentation for compound **5e** and **5g** against *h*-TNAP

6-Figure FS5: NMR Spectra's (presenting ¹H NMR and ¹³C NMR) of Indole Acetic Acid Sulfonate Derivatives (5a-5o)

5a. ¹H NMR

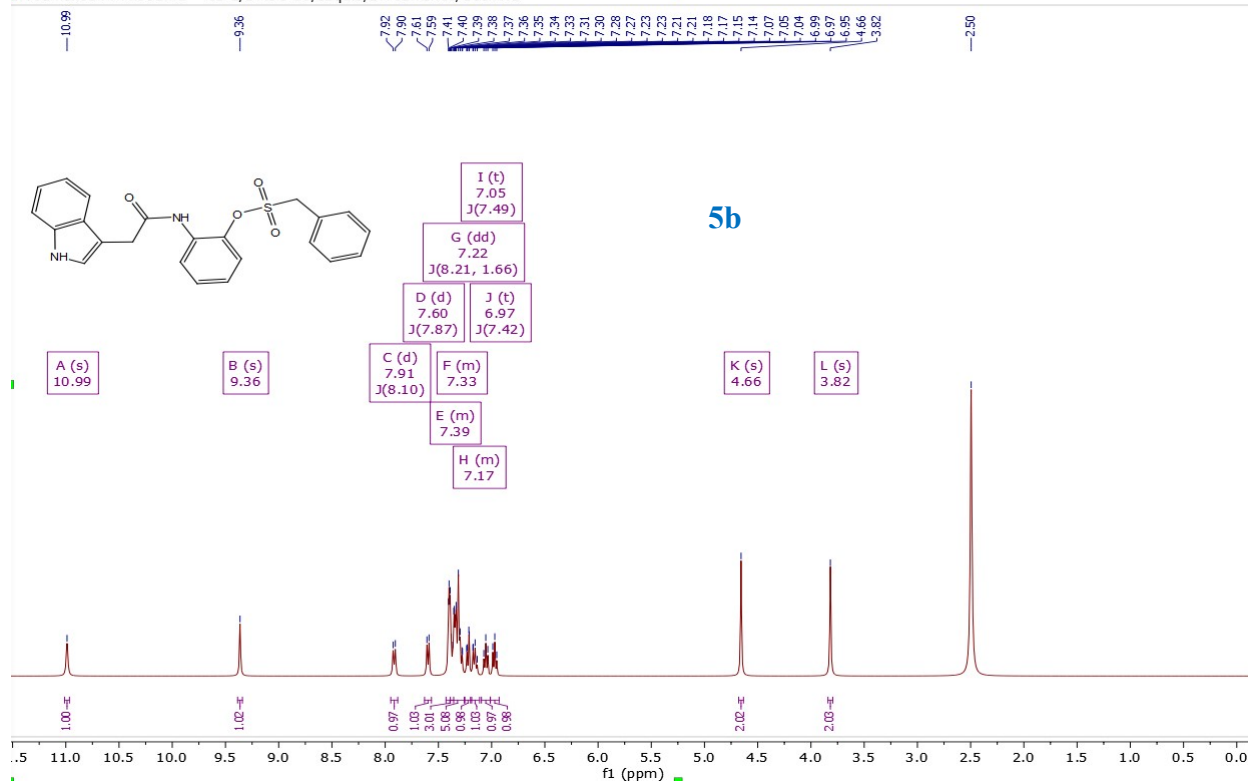


5a. ¹³C NMR



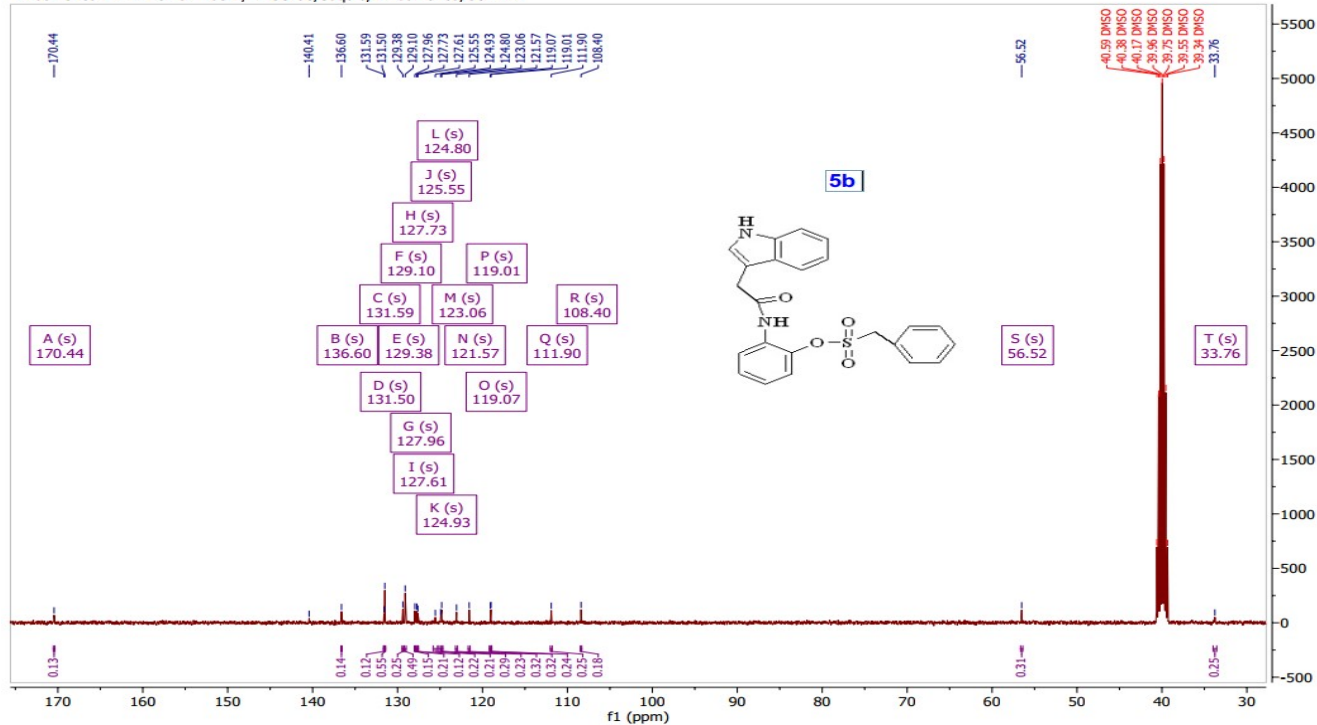
5b. ¹H NMR

Dr. Jamshed PHM.362.fid — JS-2/DMSO-d6/Sauqib/Dr. Jamshed/CUI-ATD



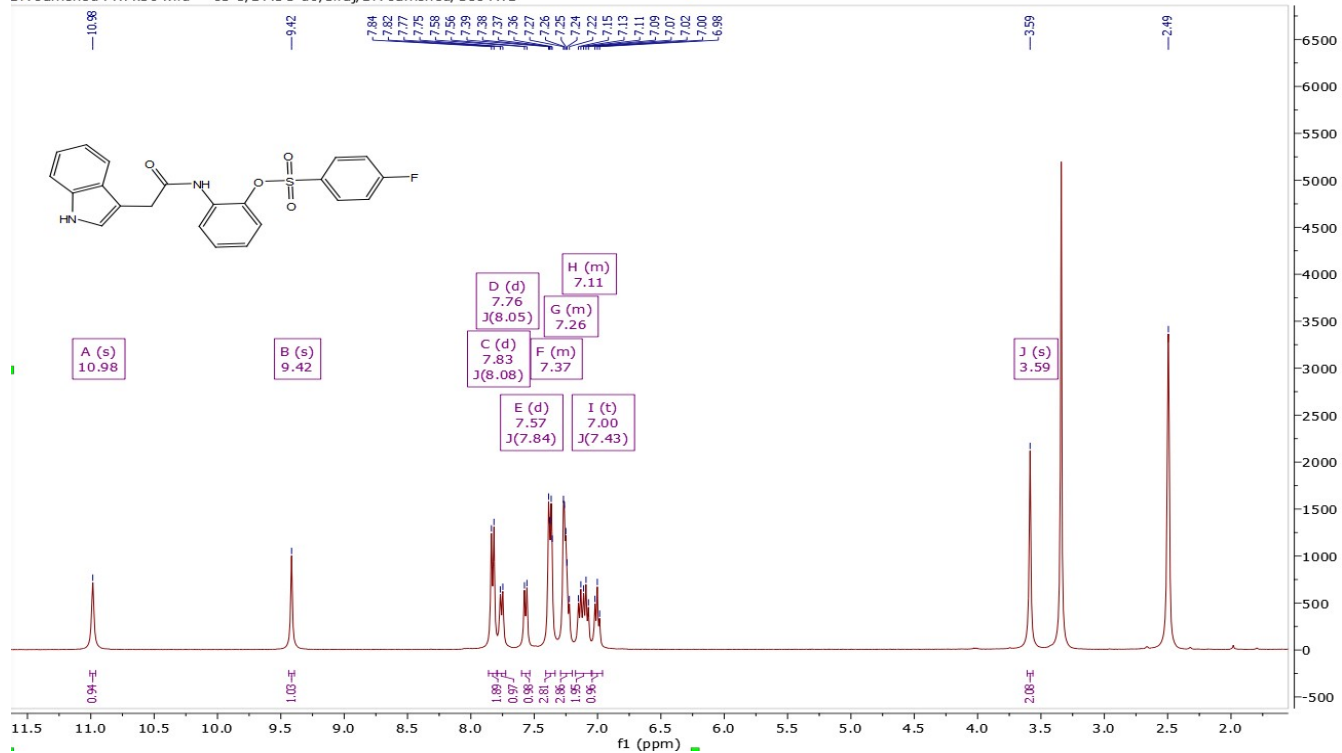
5b. ¹³C NMR

Dr. Jamshed PHM.426.fid — JS-2/DMSO-d6/Sauqib/Dr. Jamshed/CUI-ATD



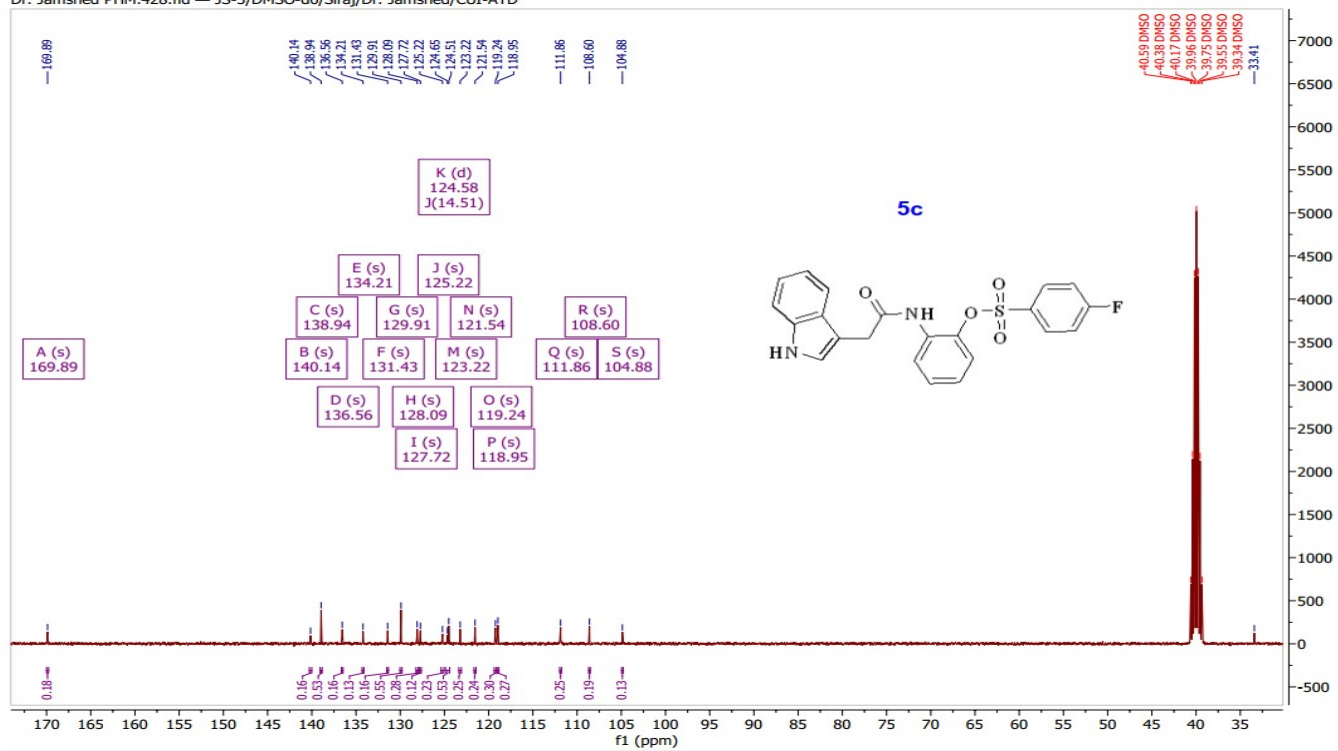
5c. ¹H NMR

Dr. Jamshed PHM.364.fid — JS-3/DMSO-d6/Siraj/Dr. Jamshed/CUI-ATD

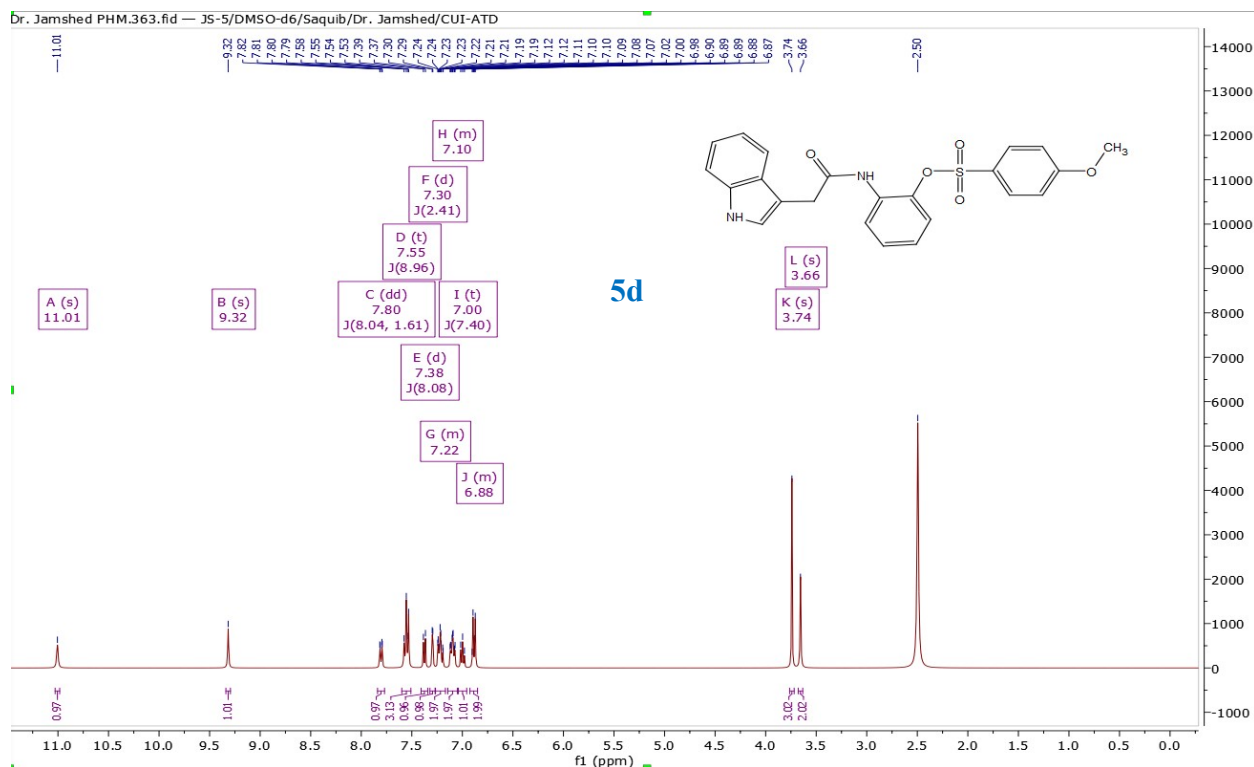


5c. ¹³C NMR

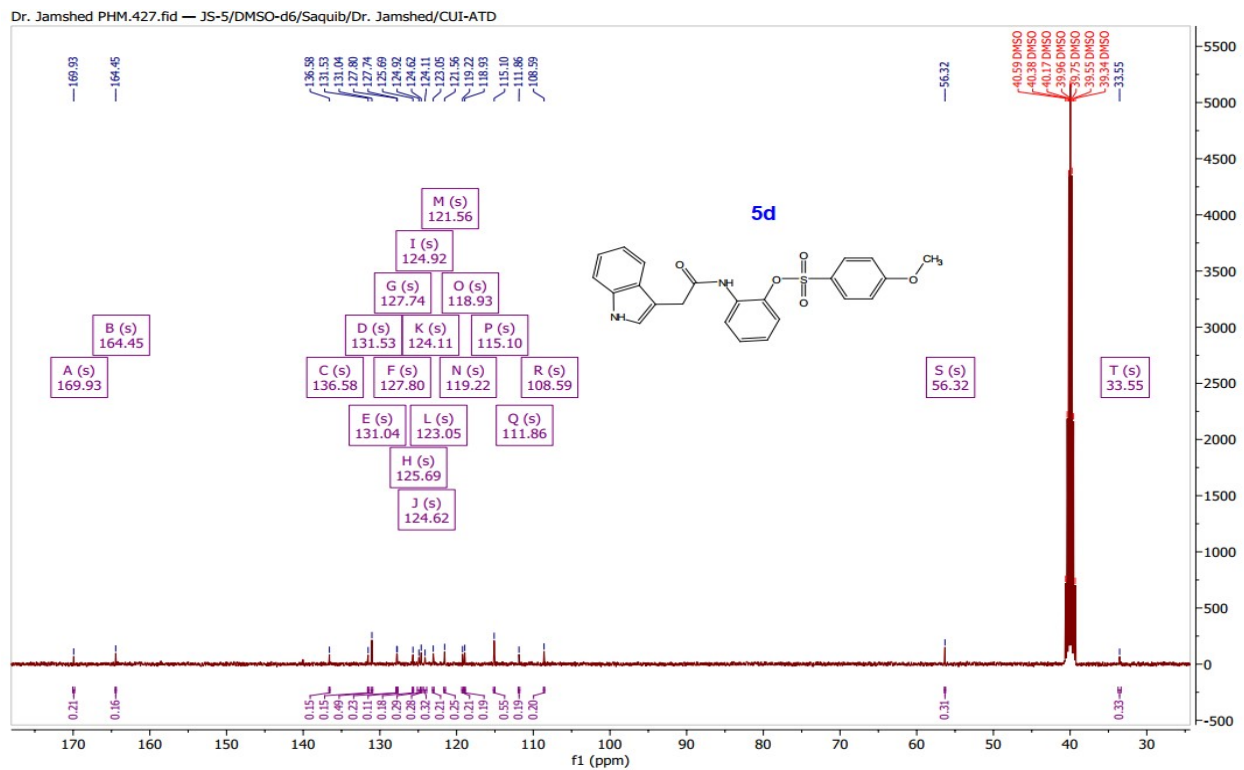
Dr. Jamshed PHM.428.fid — JS-3/DMSO-d6/Siraj/Dr. Jamshed/CUI-ATD



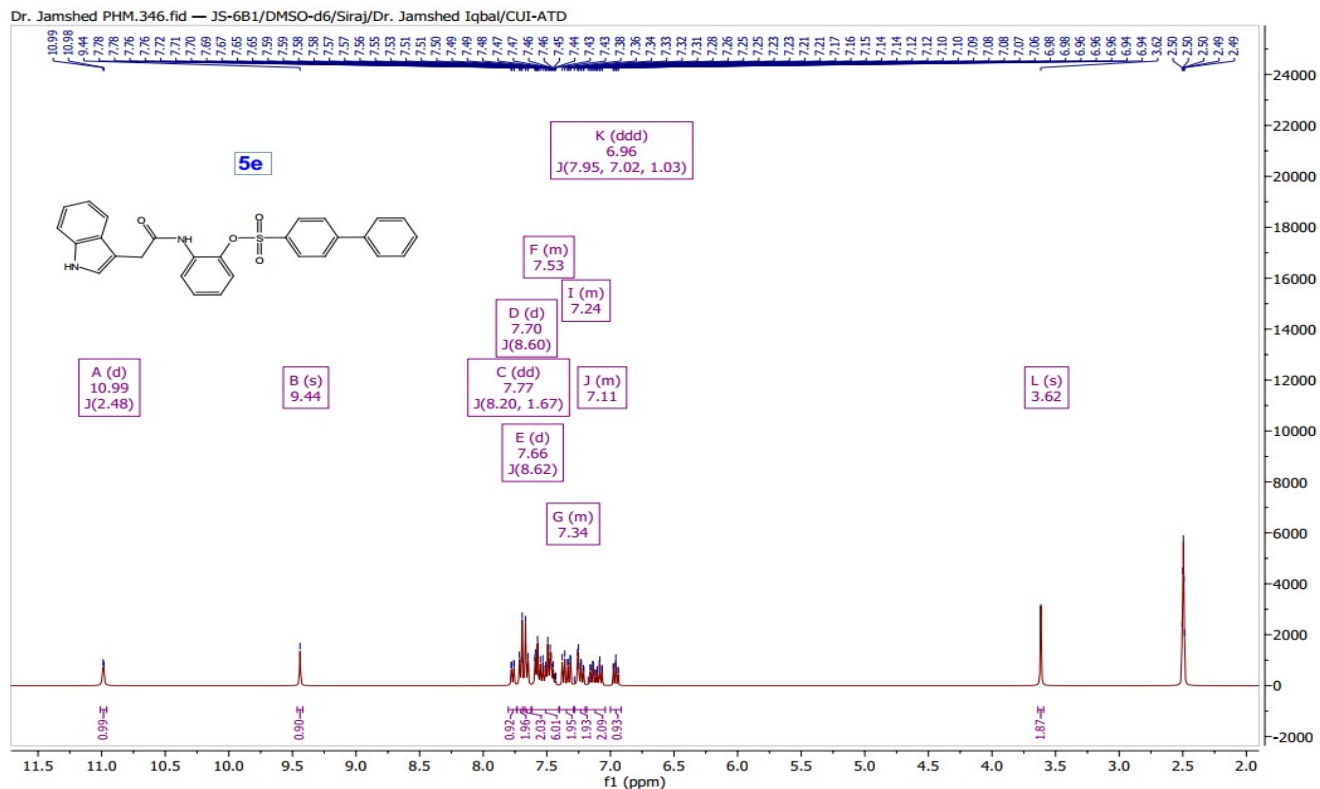
5d. ¹H NMR



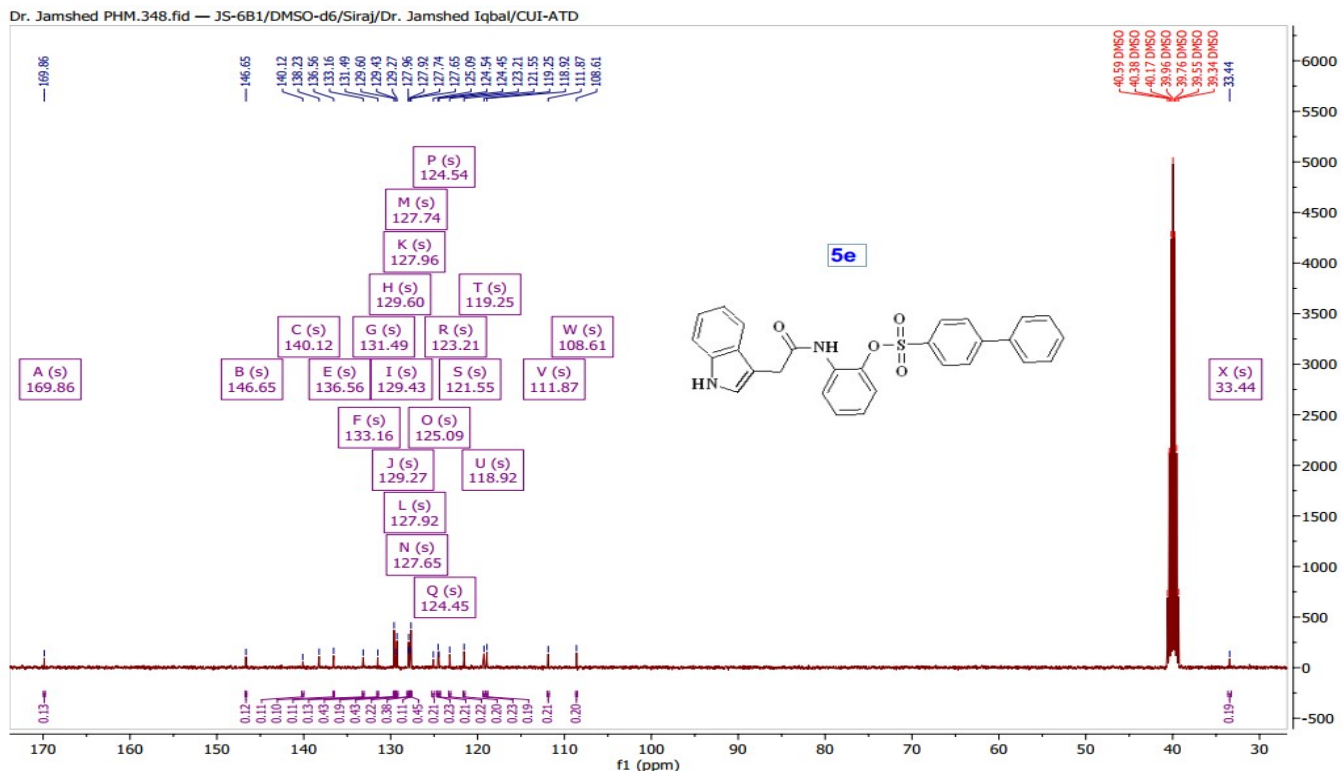
5d. ¹³C NMR



5e. ¹H NMR

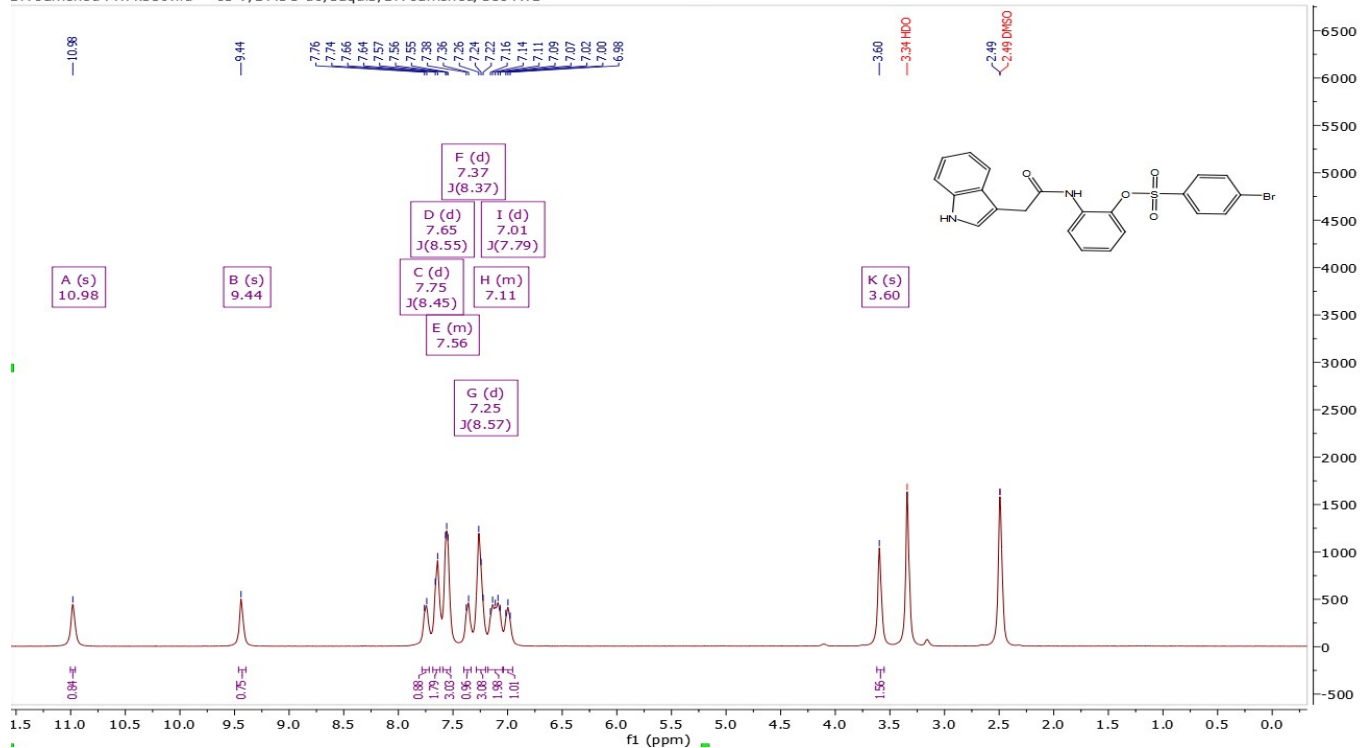


5e. ¹³C NMR



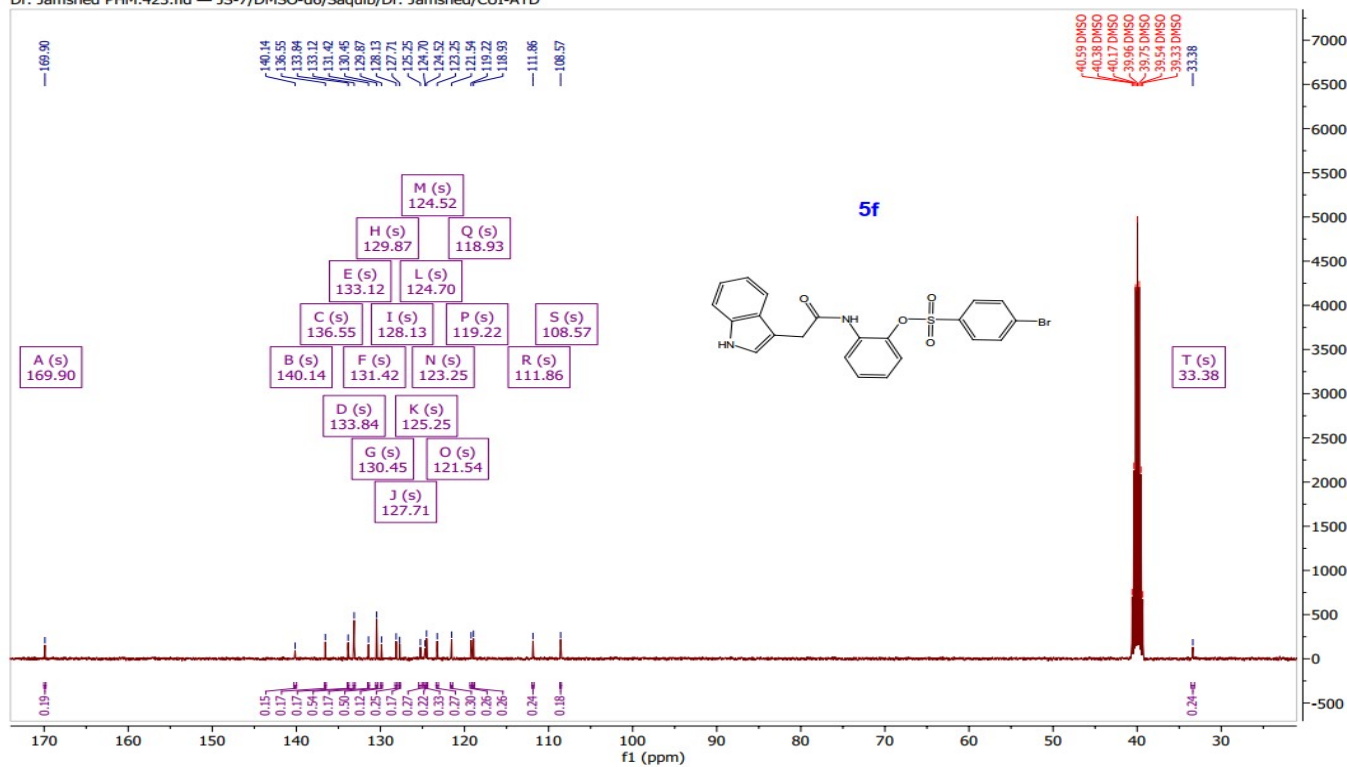
5f. ¹H NMR

Dr. Jamshed PHM.359.fid — JS-7/DMSO-d6/Saqib/Dr. Jamshed/CUI-ATD



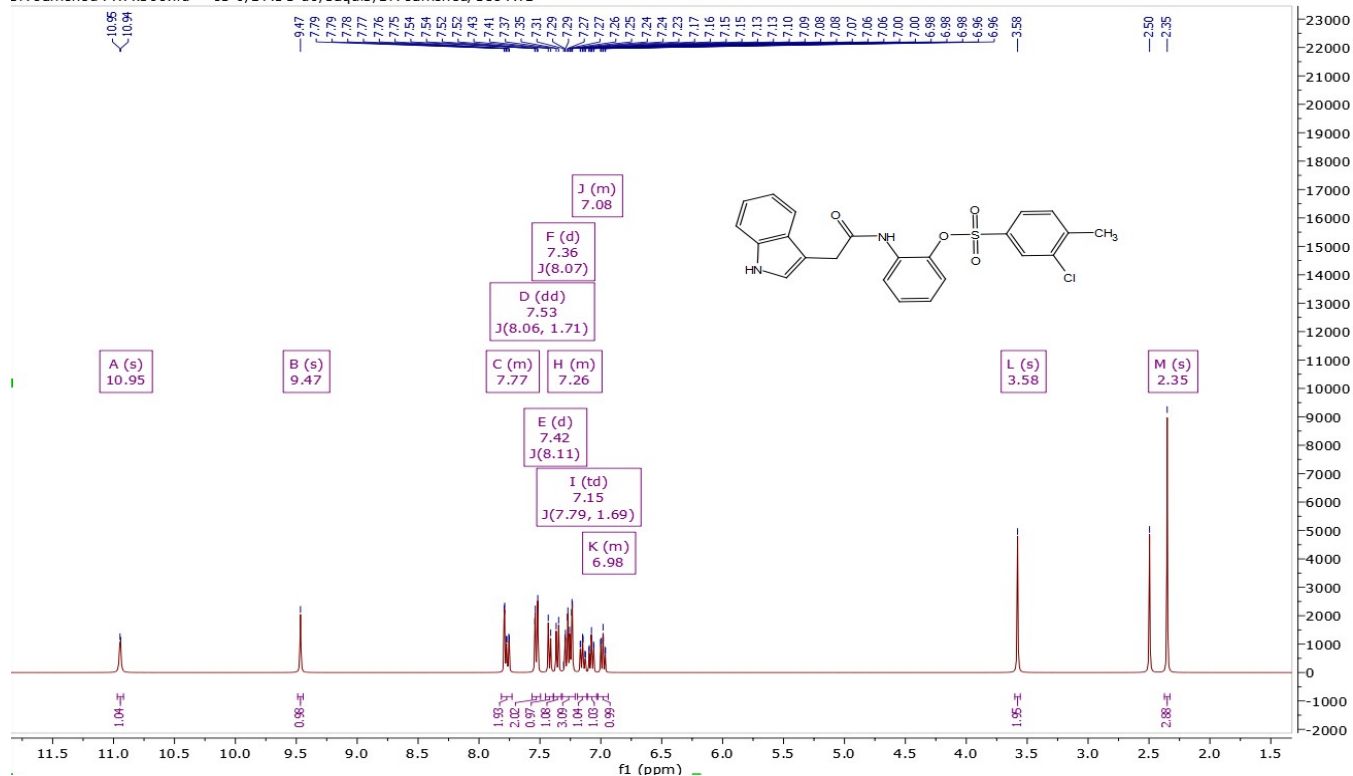
5f. ¹³C NMR

Dr. Jamshed PHM.423.fid — JS-7/DMSO-d6/Saqib/Dr. Jamshed/CUI-ATD



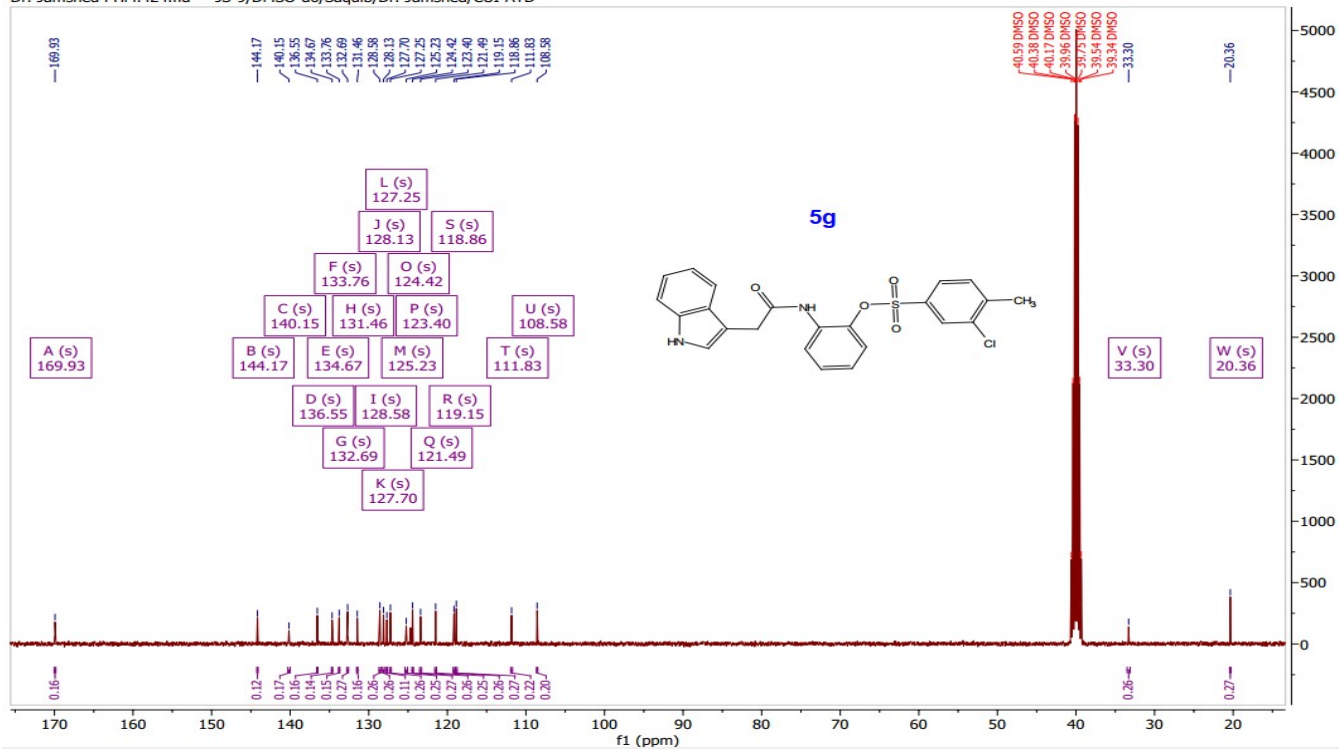
5g. ¹H NMR

Dr. Jamshed PHM.360.fid — JS-9/DMSO-d6/Saqib/Dr. Jamshed/CUI-ATD

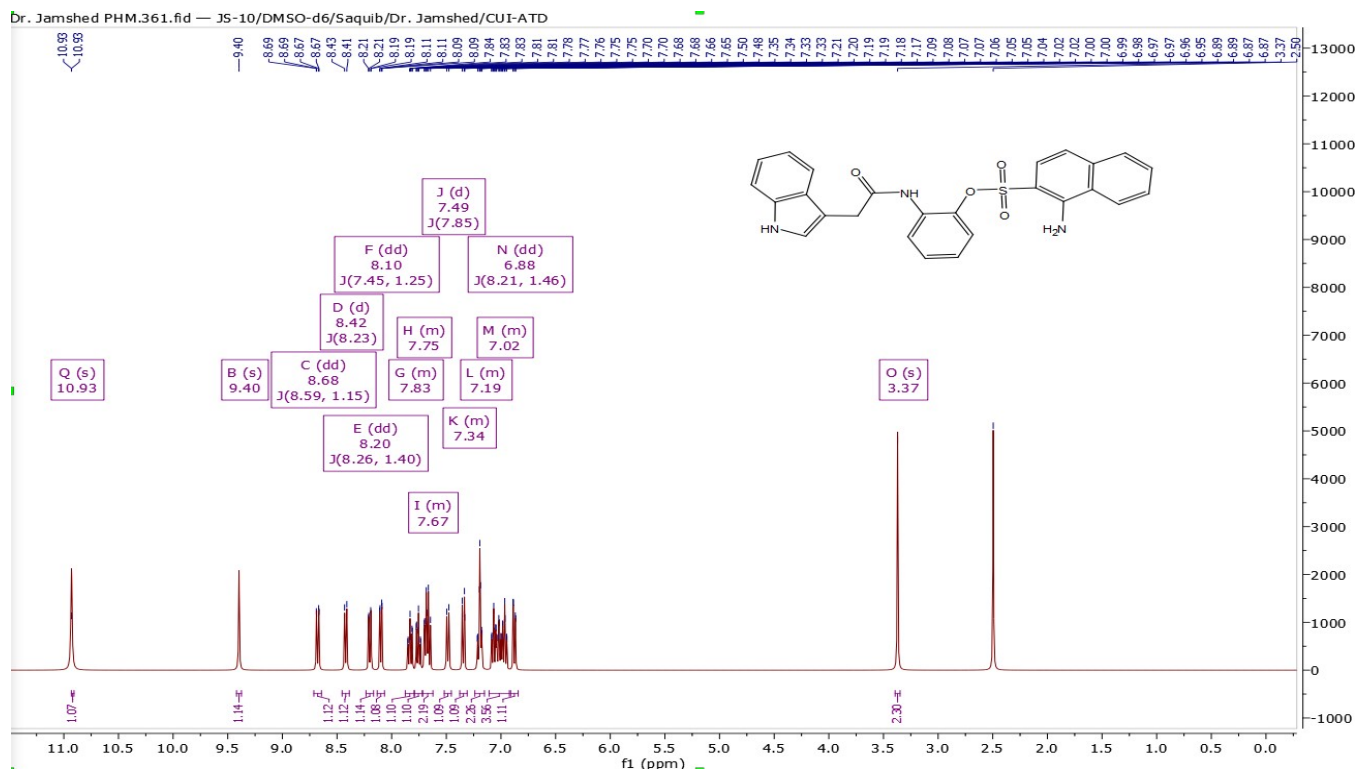


5g. ¹³C NMR

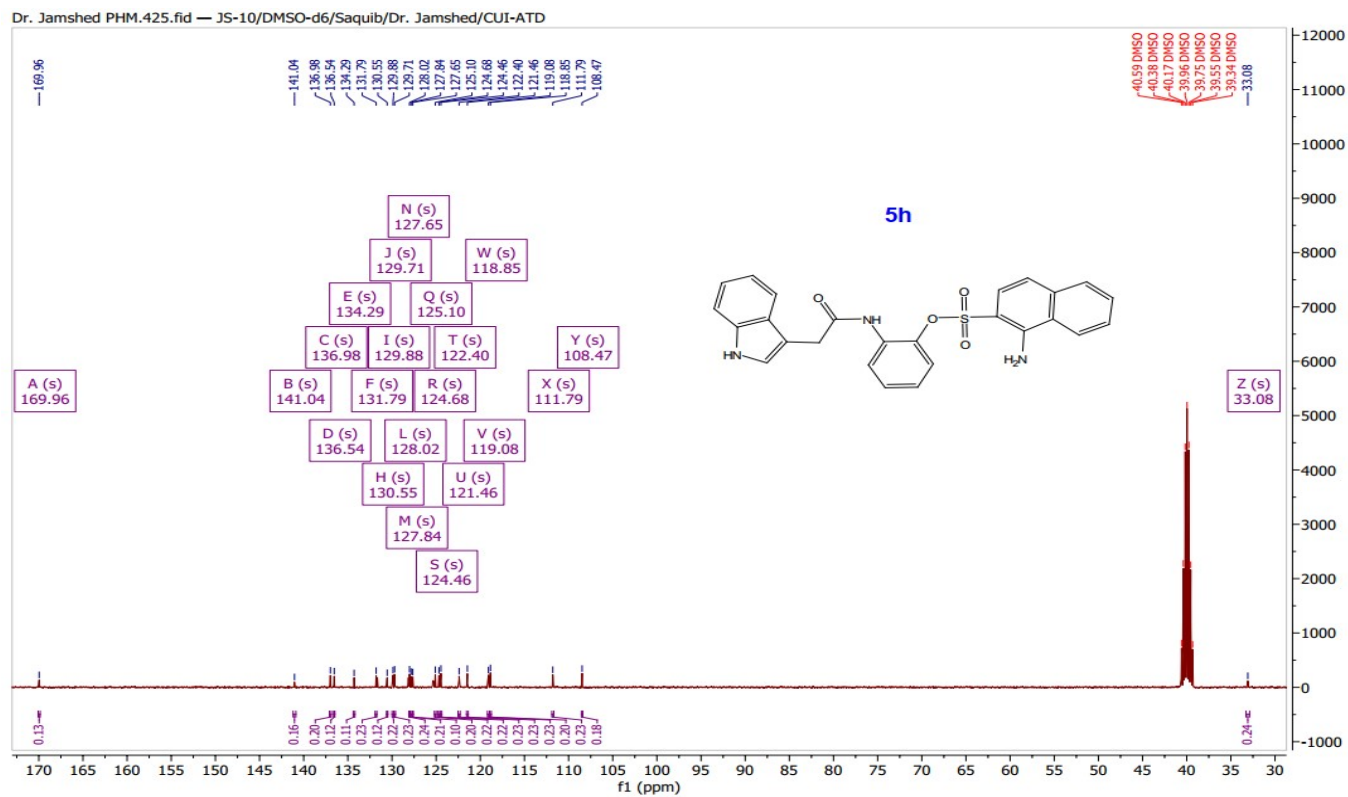
Dr. Jamshed PHM.424.fid — JS-9/DMSO-d6/Saqib/Dr. Jamshed/CUI-ATD



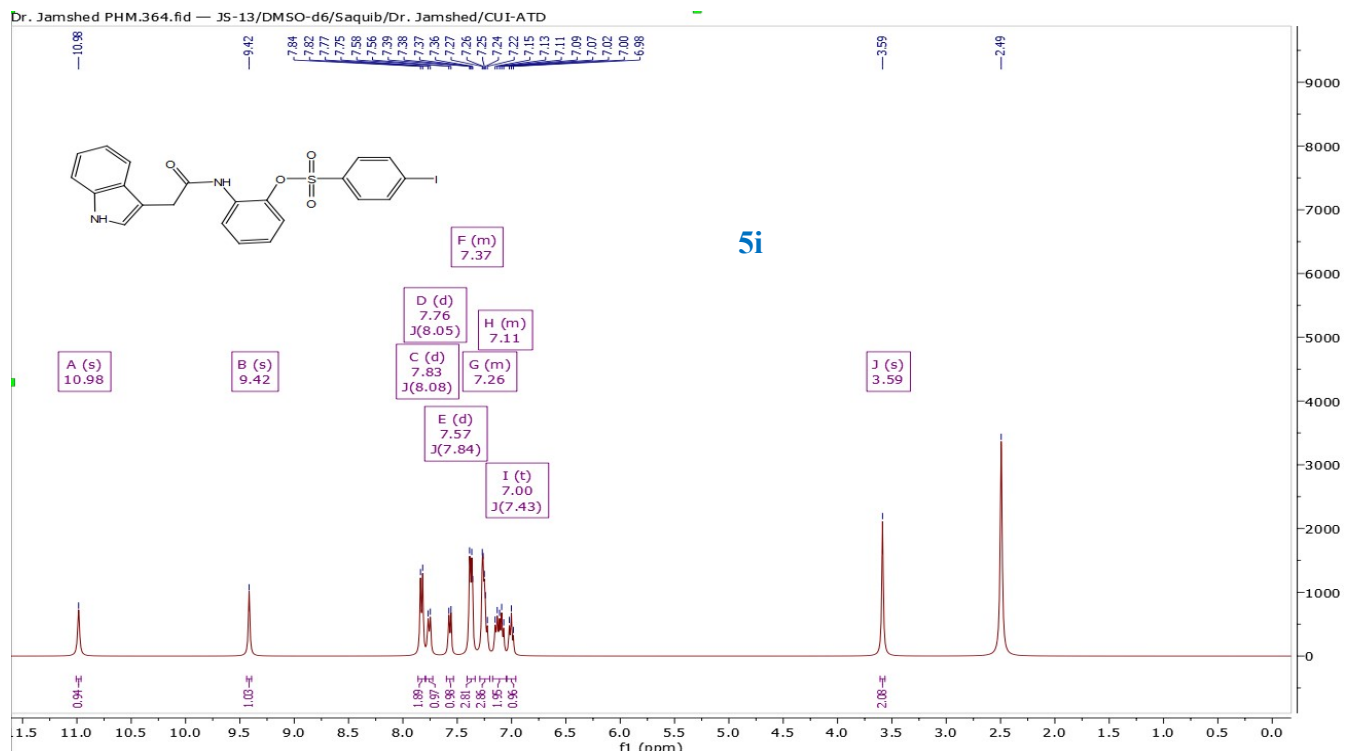
5h. ¹H NMR



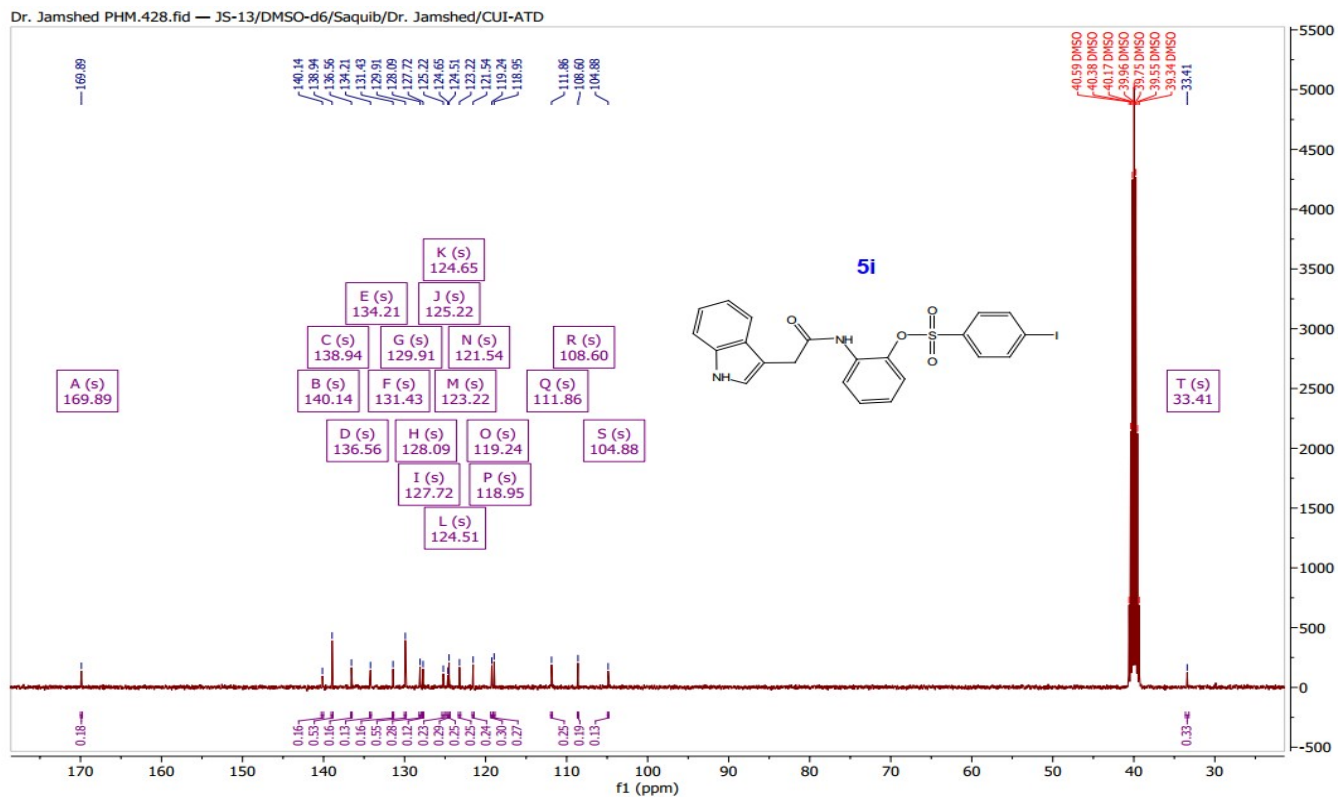
5h. ¹³C NMR



5i. ¹H NMR

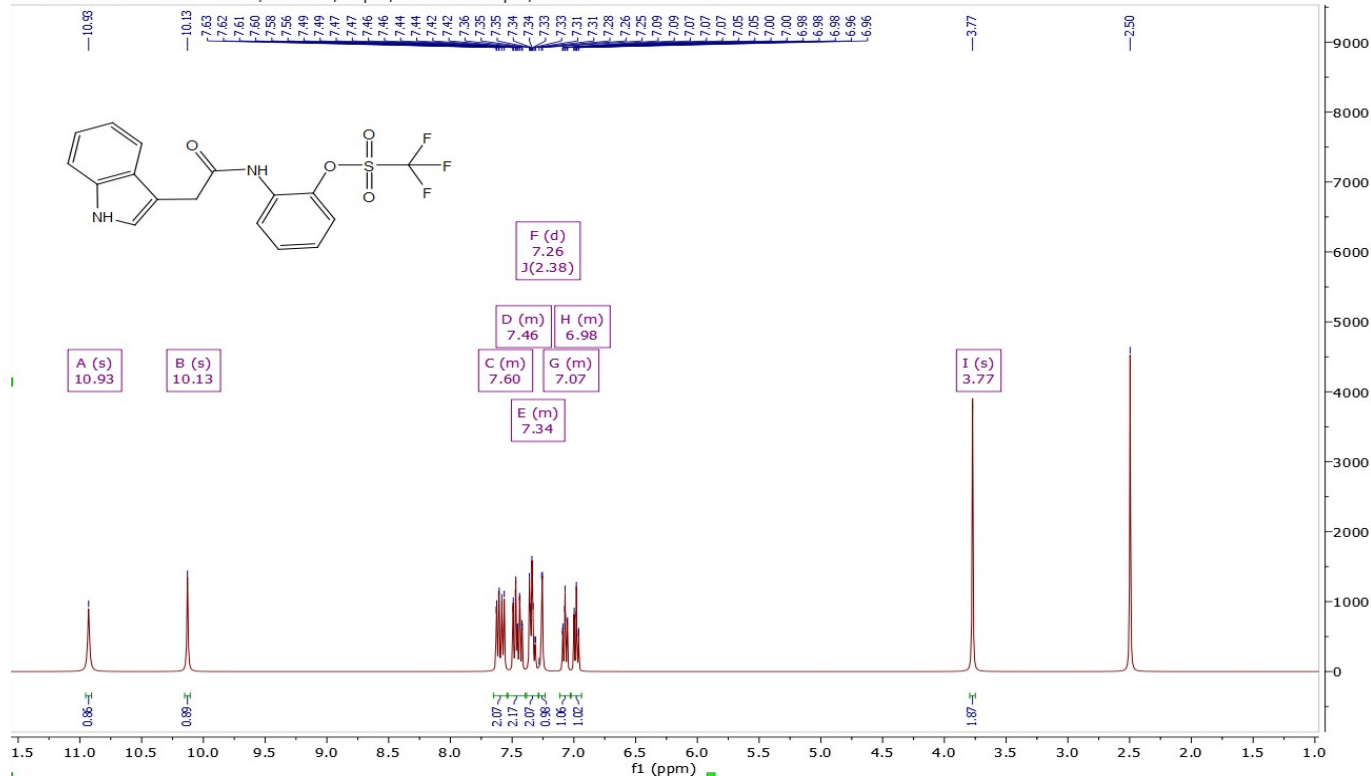


5i. ¹³C NMR



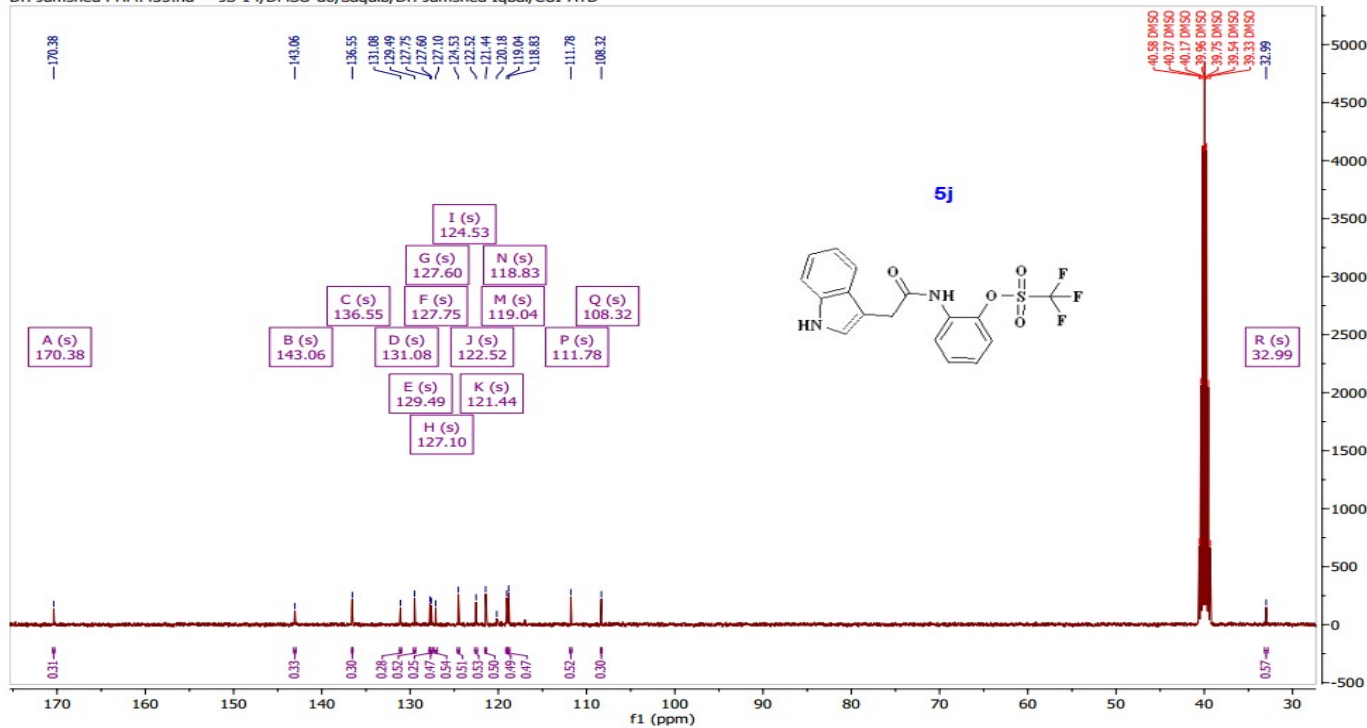
5j. ¹H NMR

Dr. Jamshed PHM.429.fid — JS-14/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



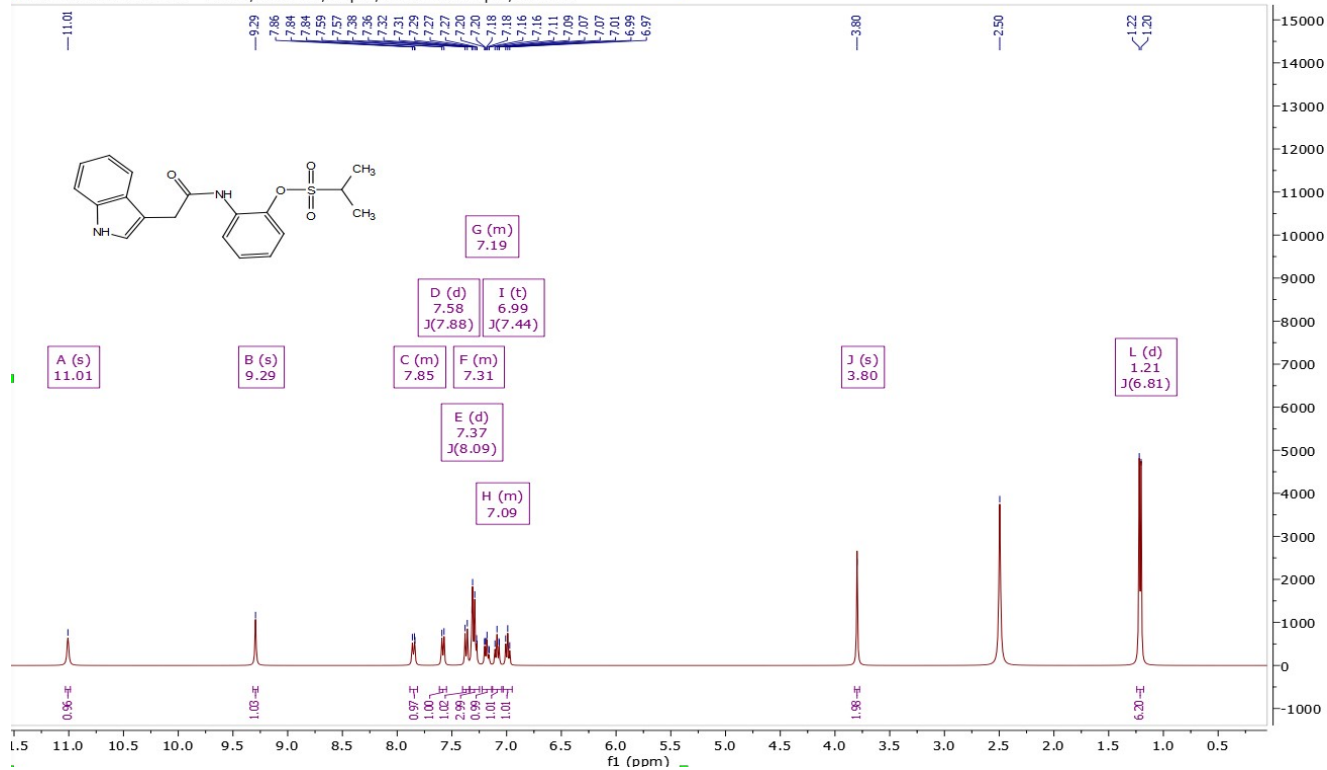
5j. ¹³C NMR

Dr. Jamshed PHM.435.fid — JS-14/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



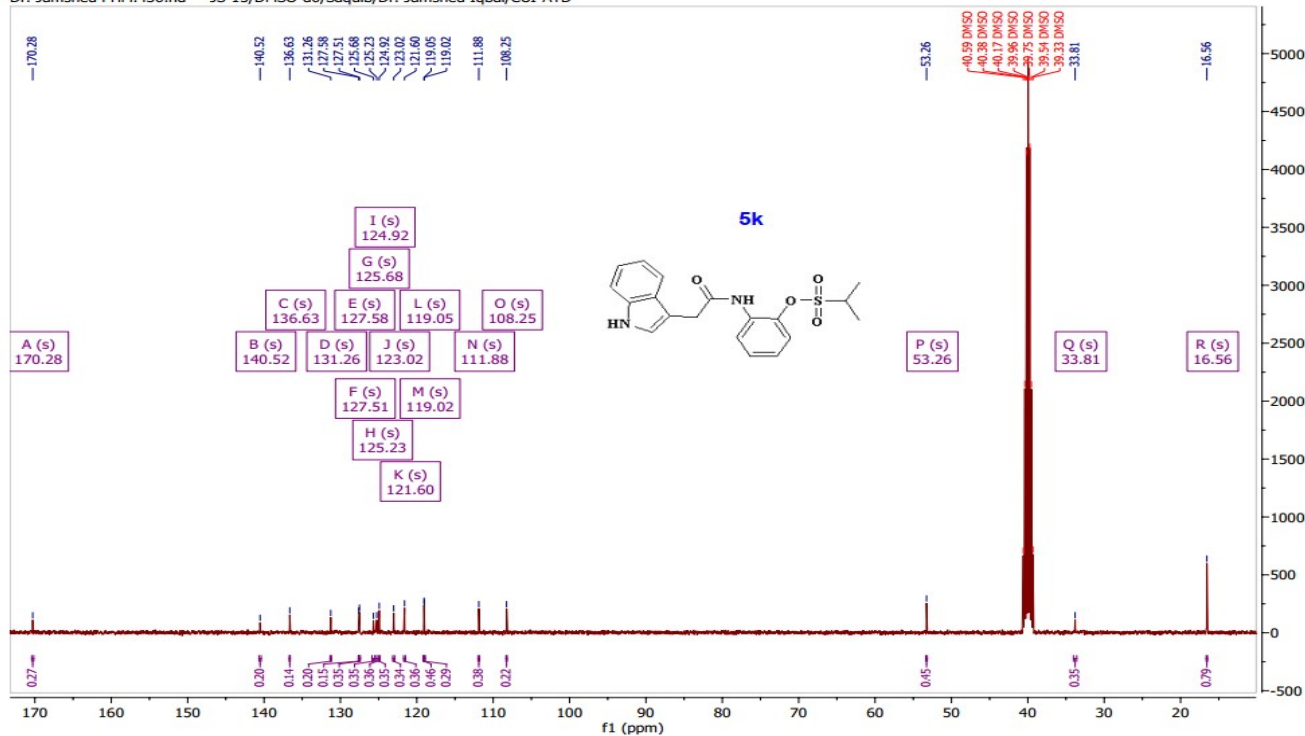
5k. ¹H NMR

Dr. Jamshed PHM.430.fid — J5-15/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



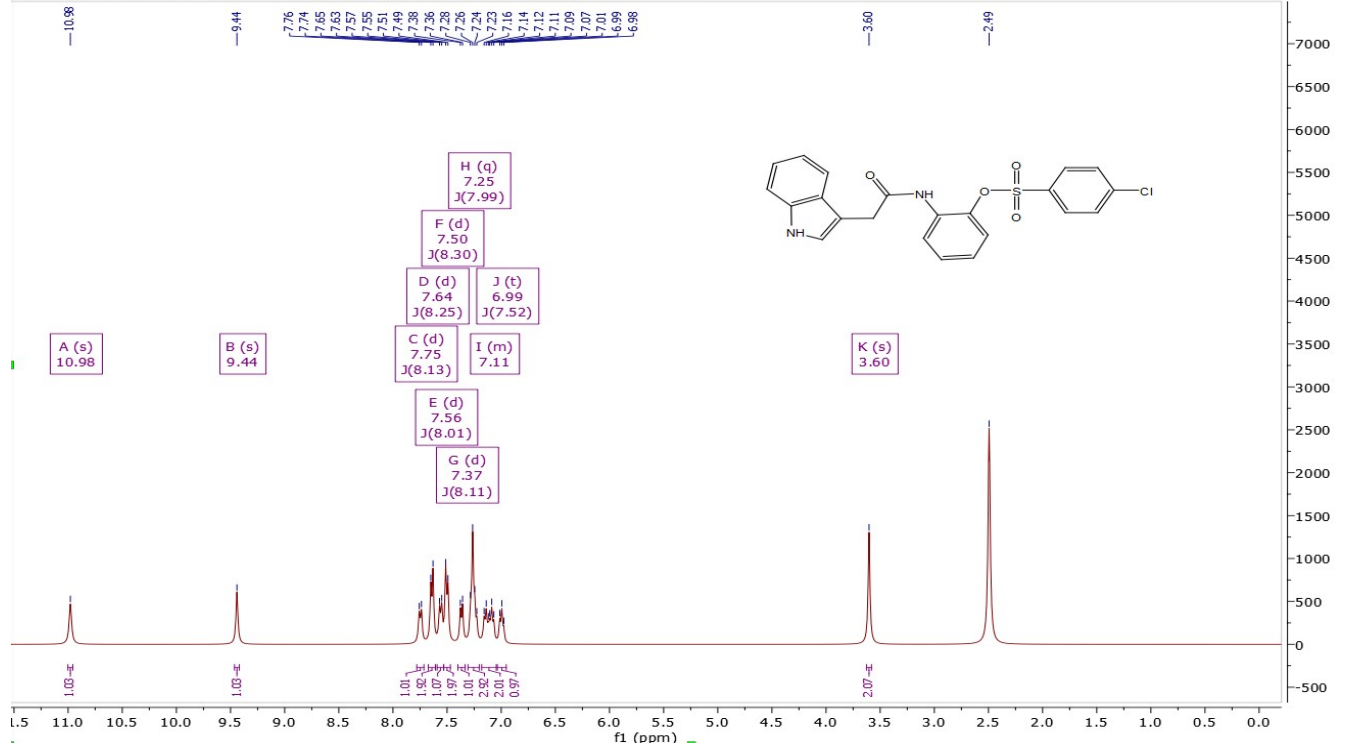
5k. ¹³C NMR

Dr. Jamshed PHM.436.fid — J5-15/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



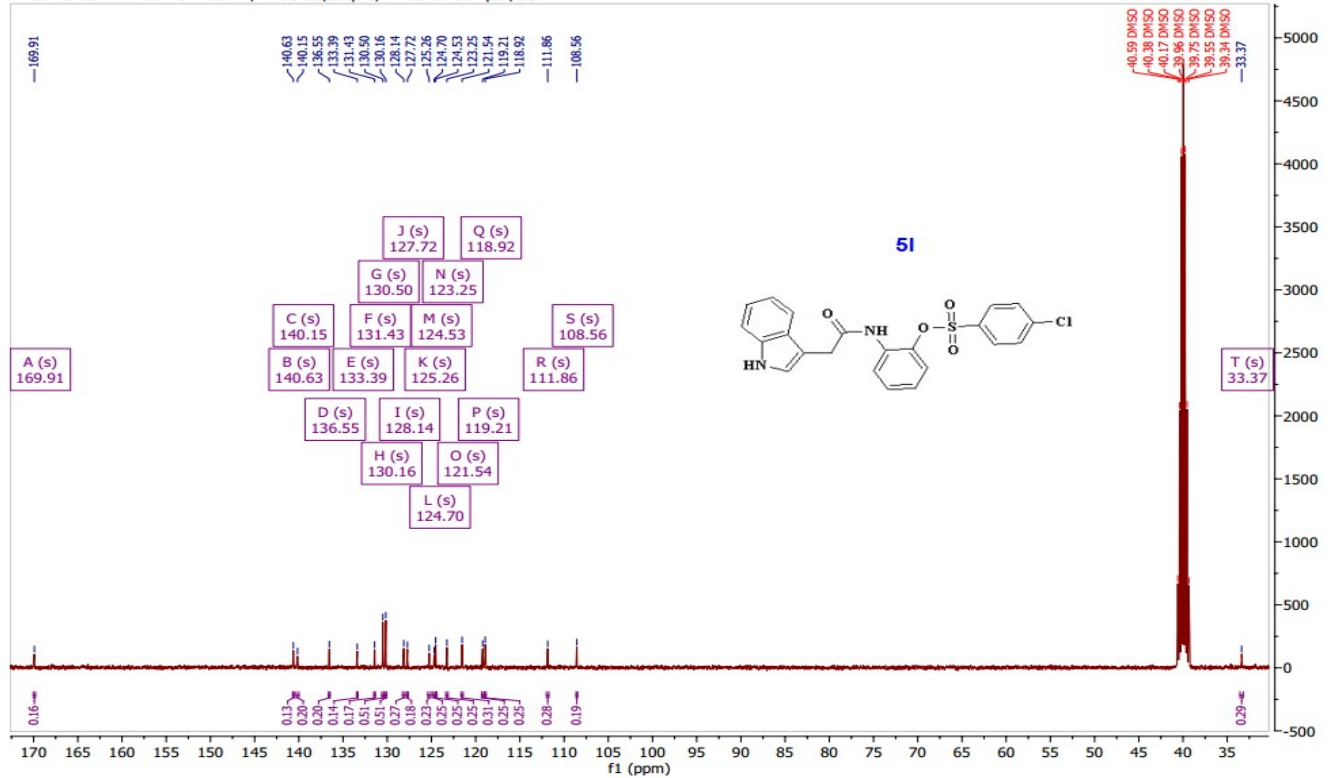
5I. ¹H NMR

Dr. Jamshed PHM.431.fid — JS-17/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



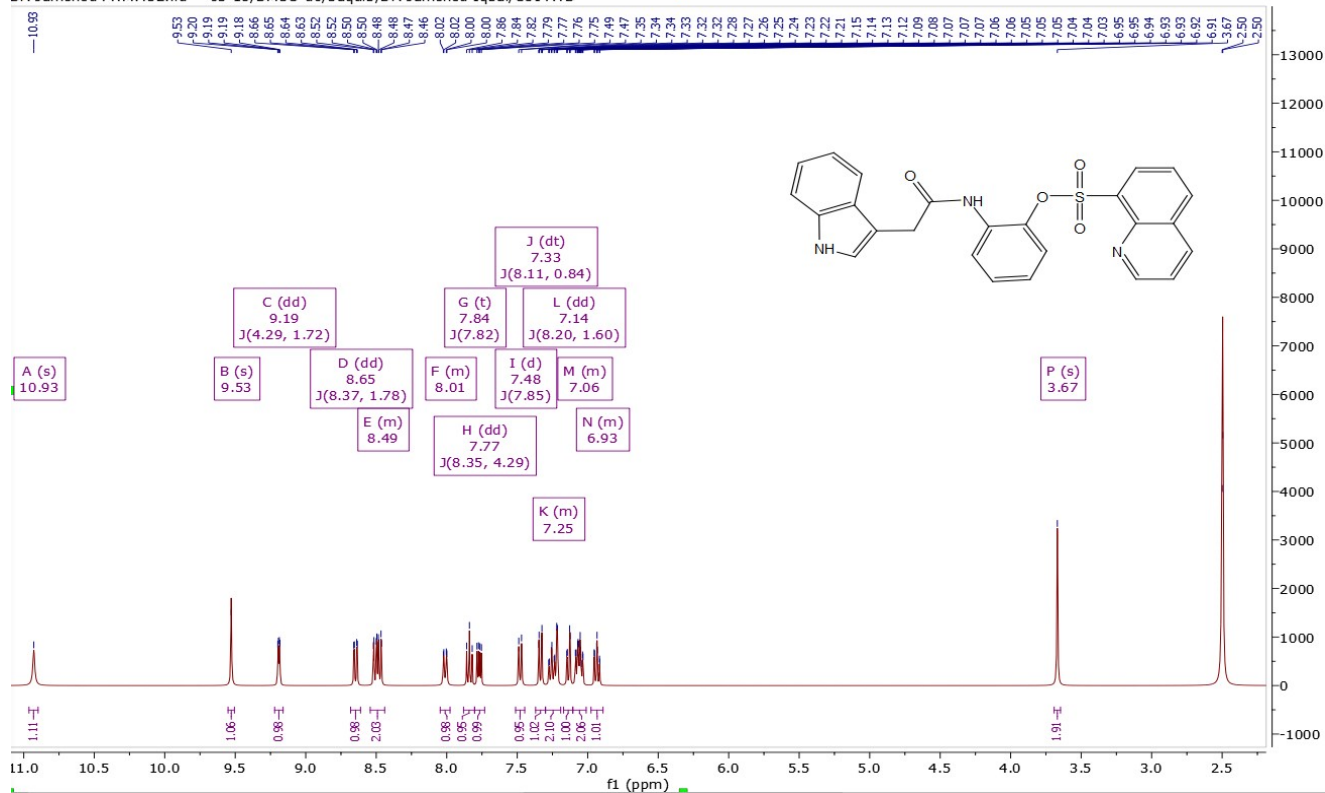
5I. ¹³C NMR

Dr. Jamshed PHM.437.fid — JS-17/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



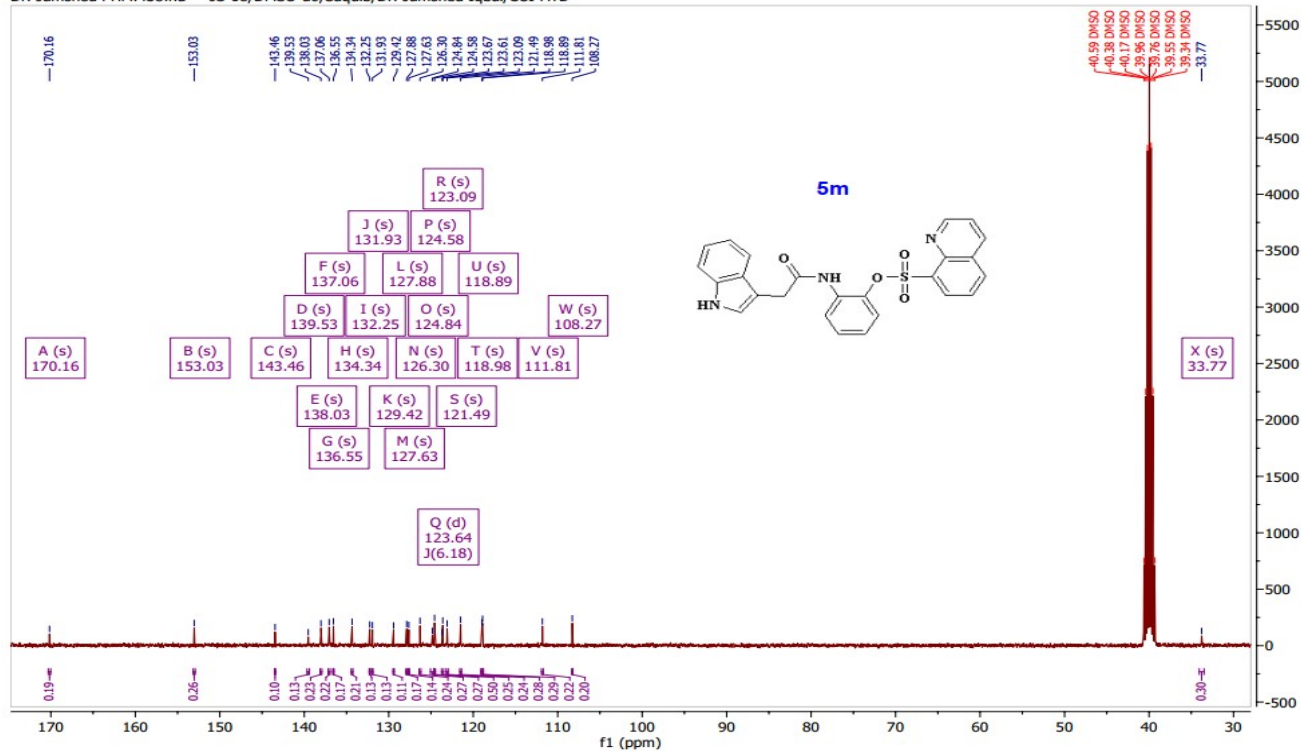
5m. ¹H NMR

Dr. Jamshed PHM.432.fid — JS-18/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD

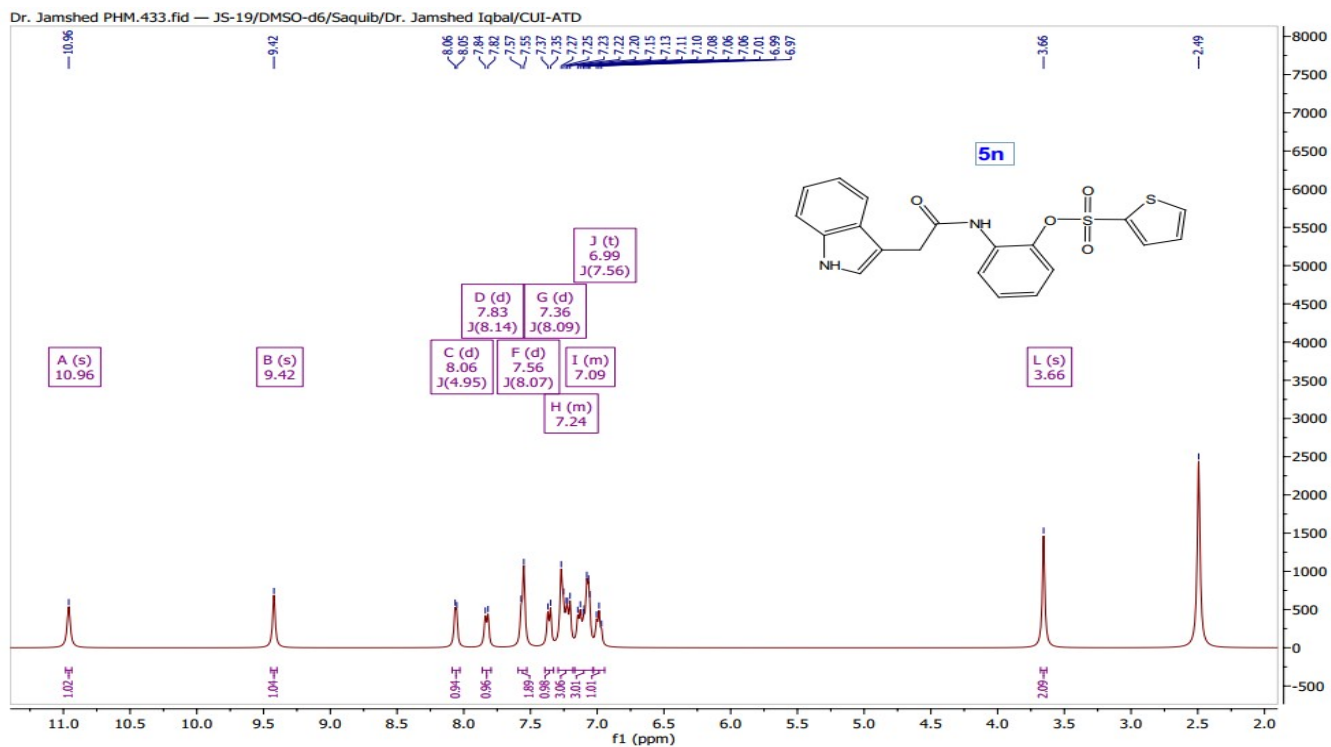


5m. ¹³C NMR

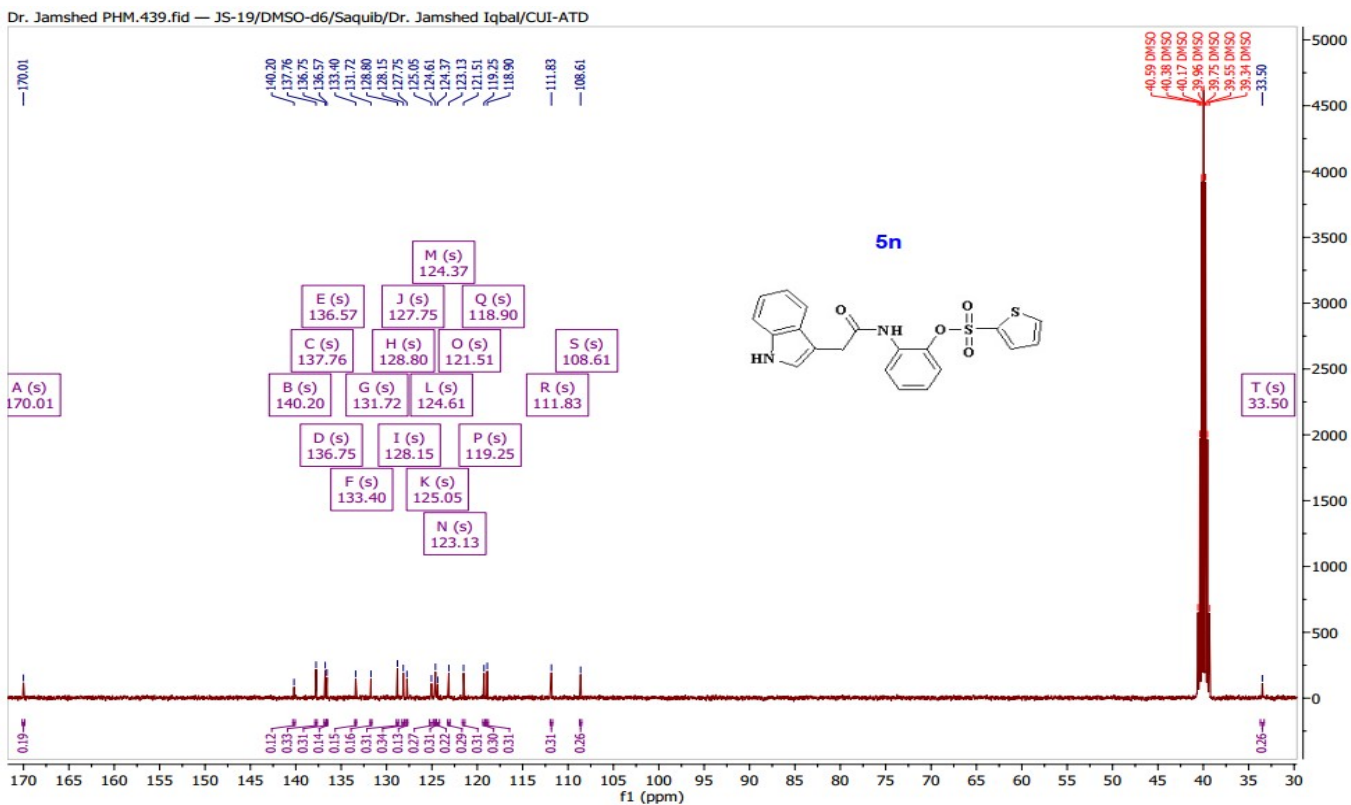
Dr. Jamshed PHM.438.fid — JS-18/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



5n. ¹H NMR

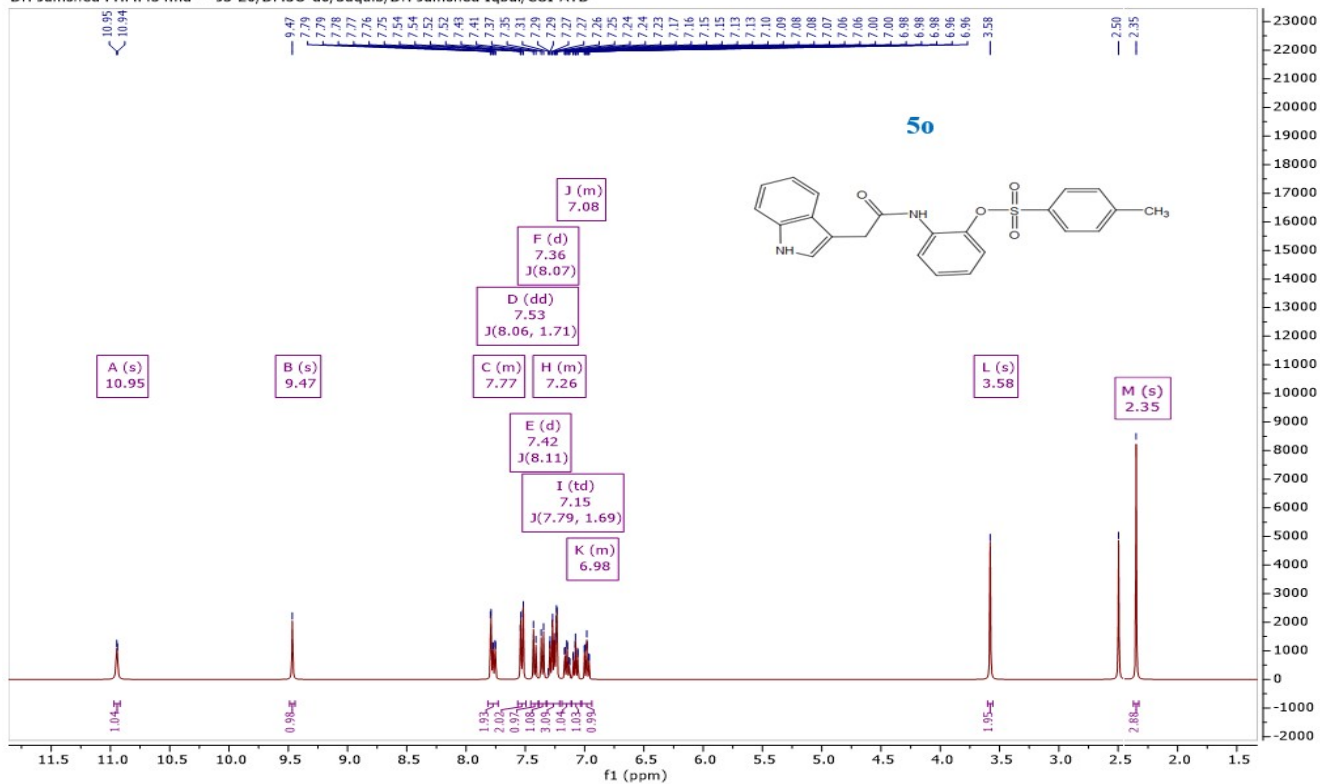


5n. ¹³C NMR



50. ¹H NMR

Dr. Jamshed PHM.434.fid — JS-20/DMSO-d6/Saqib/Dr. Jamshed Iqbal/CUI-ATD



50. ¹³C NMR

Dr. Jamshed PHM.437.fid — JS-20/DMSO-d6/Siraj/Dr. Jamshed Iqbal/CUI-ATD

