Supporting data file:

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

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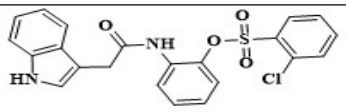
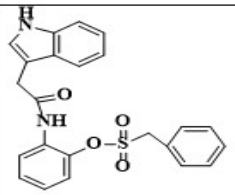
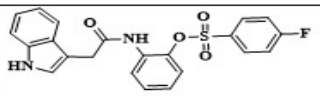
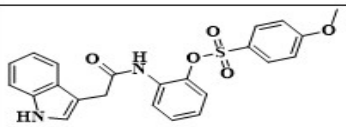
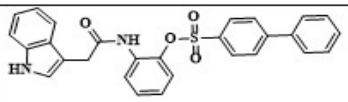
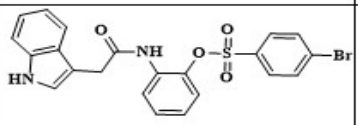
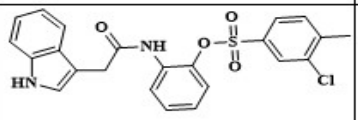
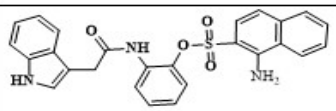
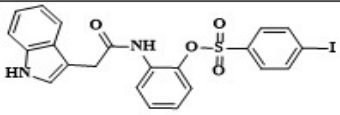
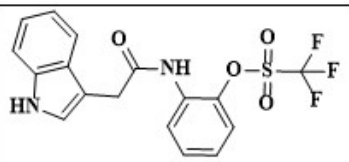
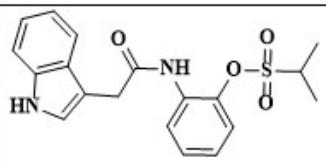
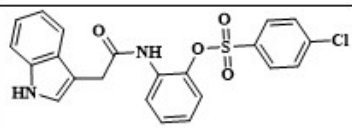
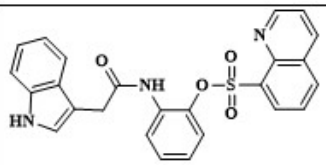
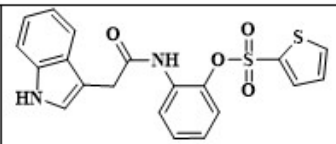
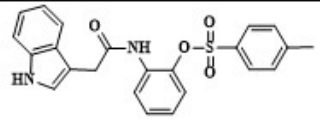
Table of Contents:

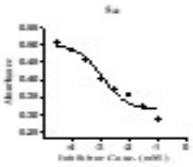
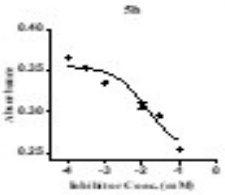
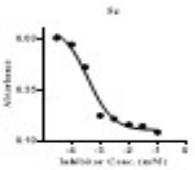
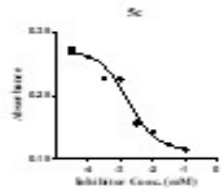
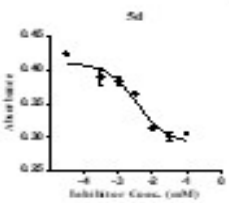
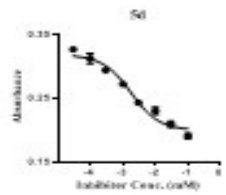
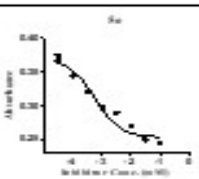
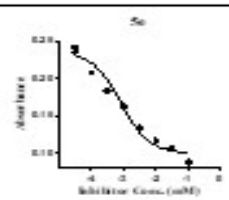
1-Table S1: Indole acetic acid sulfonate derivatives (5a-5o) description

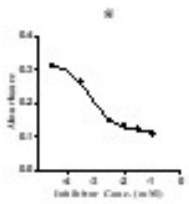
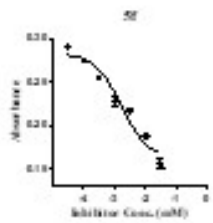
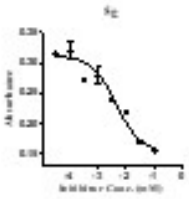
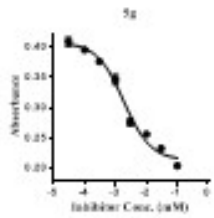
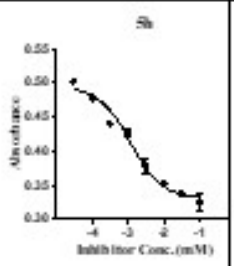
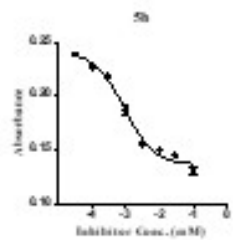
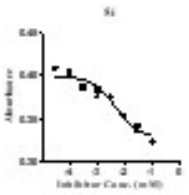
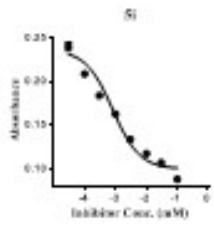
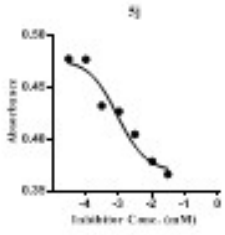
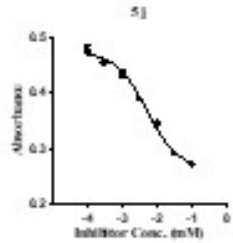
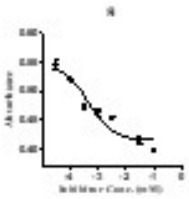
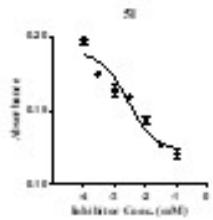
Comp #	IUPAC Name	Mol.wt	Mol. Formula	Solubility	Product structure	Appearance	Melting point
5a	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 2-chlorobenzenesulfonate	440.90	$C_{22}H_{17}ClN_2O_4S$	DMSO Acetone		Off white crystalline powder	181-183°C
5b	P2-(2-(1*H*-indol-3-yl)acetamido)phenyl phenylmethanesulfonate	420.48	$C_{23}H_{20}N_2O_4S$	DMSO Acetone		Off white crystalline powder	134-137°C
5c	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-fluorobenzenesulfonate	424.45	$C_{22}H_{17}FN_2O_4S$	DMSO Acetone		white crystalline powder	161-163°C
5d	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-Methoxy-benzenesulfonate	436.48	$C_{23}H_{20}N_2O_5S$	DMSO Acetone		Off white crystalline powder	200-203°C
5e	2-(2-(1*H*-indol-3-yl)acetamido)phenyl [1,1'-biphenyl]-4-sulfonate	482.55	$C_{28}H_{22}N_2O_4S$	DMSO Acetone		Off white crystalline powder	193-195°C
5f	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-bromobenzenesulfonate	485.35	$C_{22}H_{17}BrN_2O_4S$	DMSO Acetone		Off white crystalline powder	183-186°C
5g	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 3-chloro-4-methylbenzenesulfonate	454.93	$C_{22}H_{17}ClN_2O_4S$	DMSO Acetone		Off white crystalline powder	115-117°C
5h	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 1-aminonaphthalene-2-sulfonate	471.53	$C_{22}H_{17}ClN_2O_4S$	DMSO Acetone		Off white crystalline powder	116-118°C
5i	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-	532.35	$C_{22}H_{17}IN_2O_4S$	DMSO Acetone		Off white crystalline powder	169-172°C

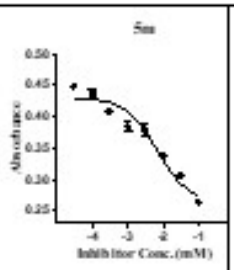
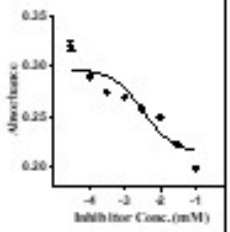
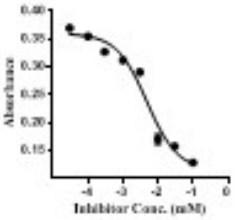
5j	2-(2-(1*H*-indol-3-yl)acetamido)phenyltrifluoromethanesulfonate	398.36	$C_{17}H_{13}F_3N_2O_4S$	DMSO Acetone		Off white crystalline powder	114-116°C
5k	2-(2-(1*H*-indol-3-yl)acetamido)phenyl propane-2-sulfonate	372.44	$C_{19}H_{20}N_2O_4S$	DMSO Acetone		Off white crystalline powder	139-141°C
5l	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-chlorobenzenesulfonate	440.90	$C_{22}H_{17}ClN_2O_4S$	DMSO Acetone		Off white crystalline powder	186-188°C
5m	2-(2-(1*H*-indol-3-yl)acetamido)phenyl quinoline-8-sulfonate	457.50	$C_{25}H_{19}N_3O_4S$	DMSO Acetone		Off white crystalline powder	178-180°C
5n	2-(2-(1*H*-indol-3-yl)acetamido)phenyl thiophene-2-sulfonate	412.48	$C_{20}H_{16}N_2O_4S_2$	DMSO Acetone		Off white crystalline powder	180-183°C
5o	2-(2-(1*H*-indol-3-yl)acetamido)phenyl 4-methylbenzene sulfonate	420.48	$C_{23}H_{20}N_2O_4S$	DMSO 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

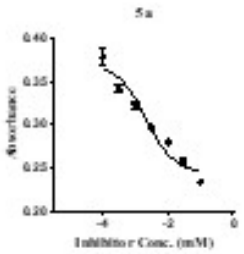
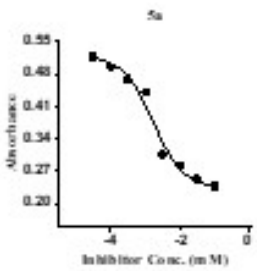
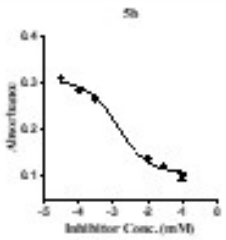
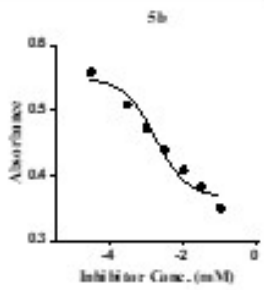
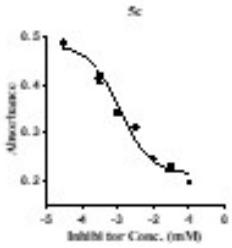
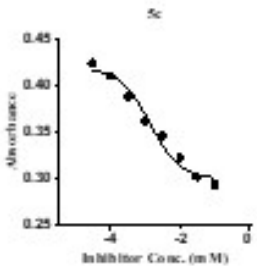
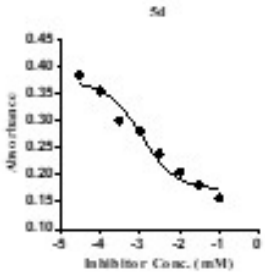
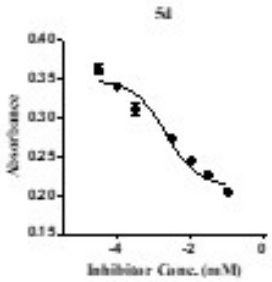
a)*h*-e5´NT and *r*-e5´NT

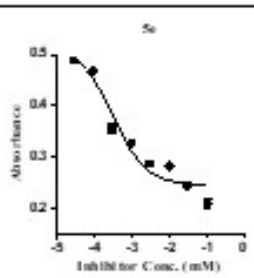
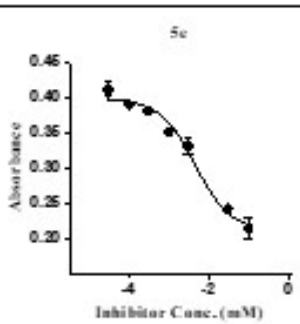
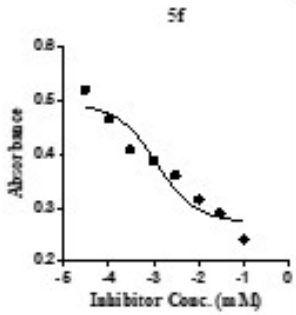
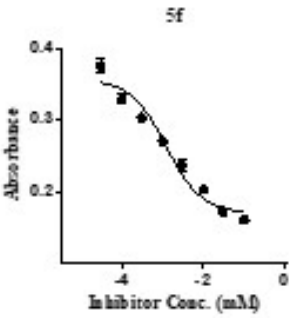
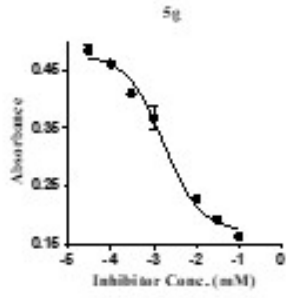
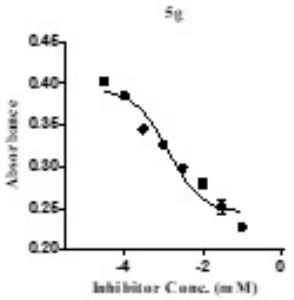
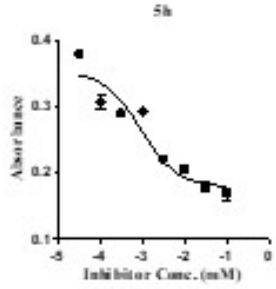
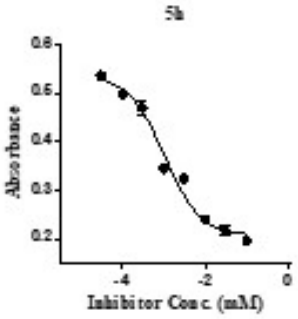
S.No	Comp. Code	*h*-e5´NT		*r*-e5´NT	
		Graph	IC_{50}±SEM (µM) / %Inhibition	Graph	IC_{50}±SEM (µM) / %Inhibition
1.	5a		1.19±0.02	-	22.72%
2.	5b		13.22±3.14	-	38.52%
3.	5c		0.37±0.03		1.66±0.04
4.	5d		3.46±0.12		1.77±0.12
5.	5e		0.56±0.016		0.98±0.02

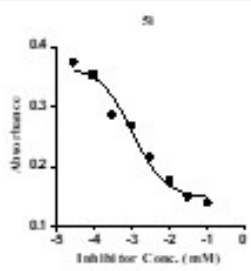
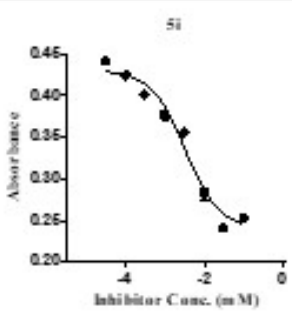
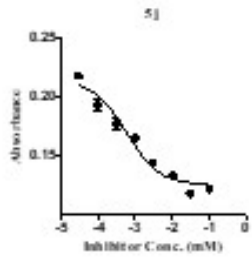
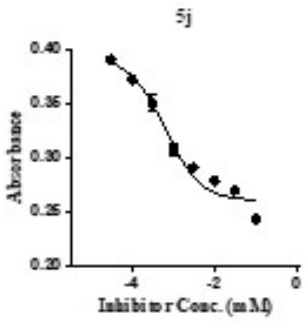
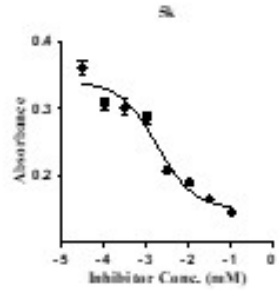
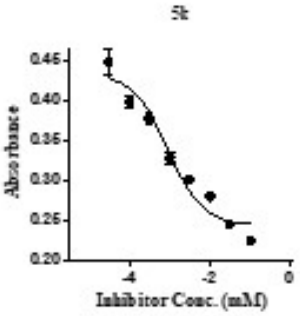
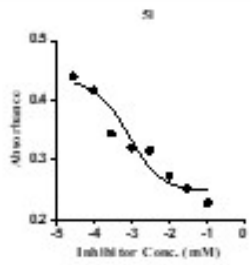
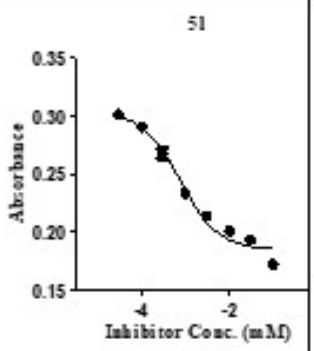
6.	**5f**		**0.69±0.001**		**1.64±0.02**
7.	**5g**		**4.4±0.19**		**1.85±0.11**
8.	**5h**		**1.17±0.13**		**0.91±0.04**
9.	**5i**		**4.85±0.55**		**0.81±0.05**
10.	**5j**		**0.89±0.04**		**5.12±0.61**
11.	**5k**	-	**37.52%**	-	**28.65%**
12.	**5l**		**0.43±0.03**		**5.67±0.11**

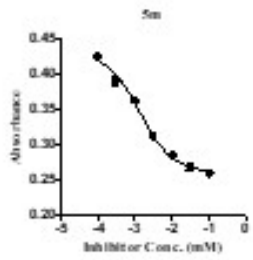
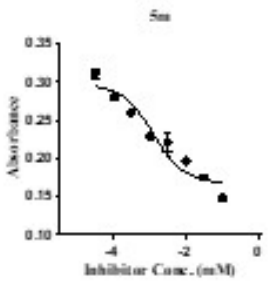
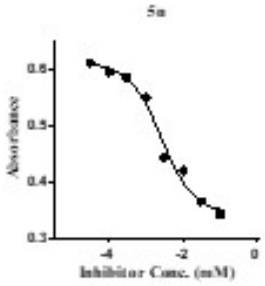
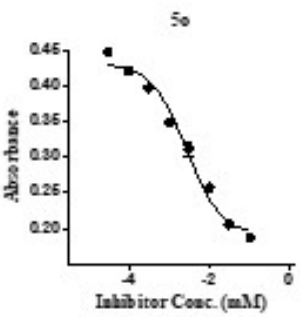
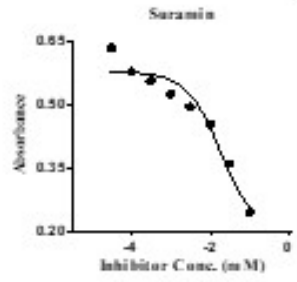
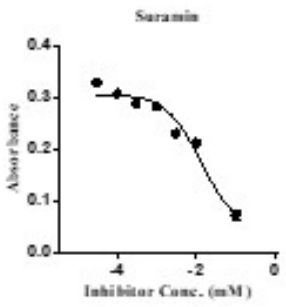
13.	**5m**		**6.53±0.67**	-	**30.03%**
14.	**5n**	-	**44.68%**	-	**46.64%**
15.	**5o**		**3.21±0.83**		**4.86±0.04**
16.	**Sulfamic acid**		**42.1 ± 7.80a**		**77.3 ± 7.0a**

b)Human ENPP1 and ENPP3

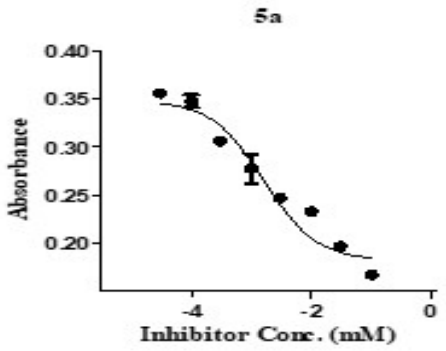
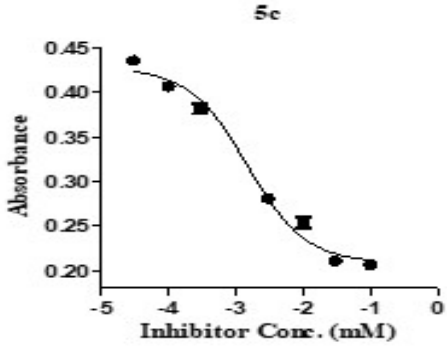
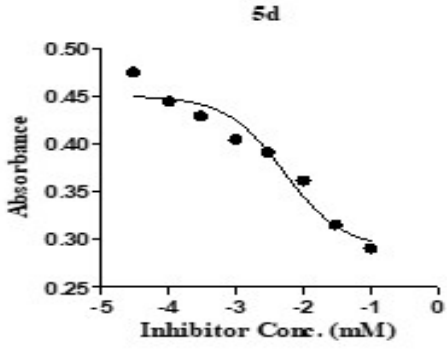
S.No	Comp .Code	NPP1		NPP3	
		Graph	IC_{50}±SEM (µM) / %Inhibition	Graph	IC_{50}±SEM (µM) / %Inhibition
1.	5a		2.07±0.22		1.66±0.007
2.	5b		1.35±0.02		1.71±0.11
3.	5c		1.12±0.12		1.37±0.05
4.	5d		1.09±0.01		2.05±0.25

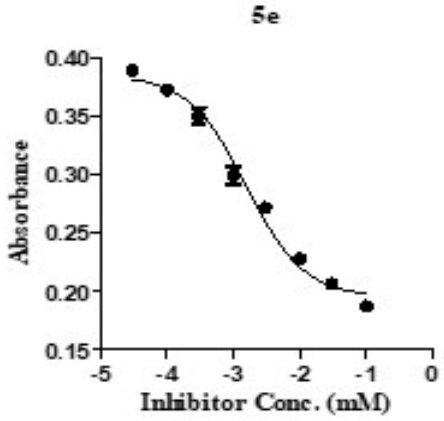
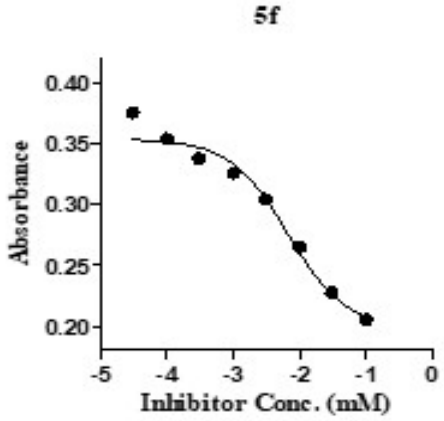
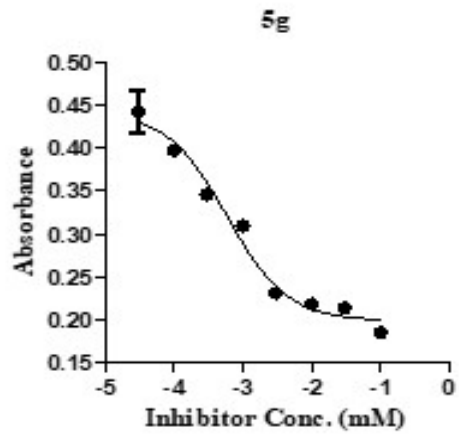
5.	**5e**		**0.32±0.01**		**4.51±0.38**
6.	**5f**		**1.14±0.002**		**1.23±0.01**
7.	**5g**		**1.69±0.05**		**1.31±0.11**
8.	**5h**		**0.91±0.02**		**1.02±0.004**

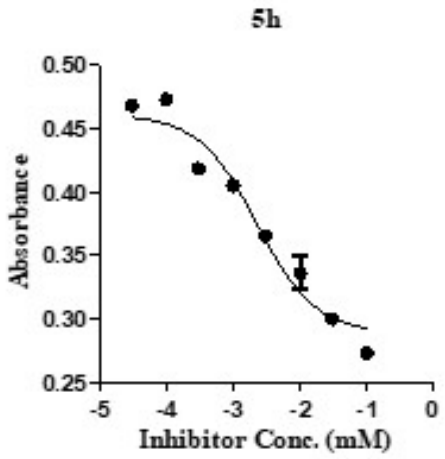
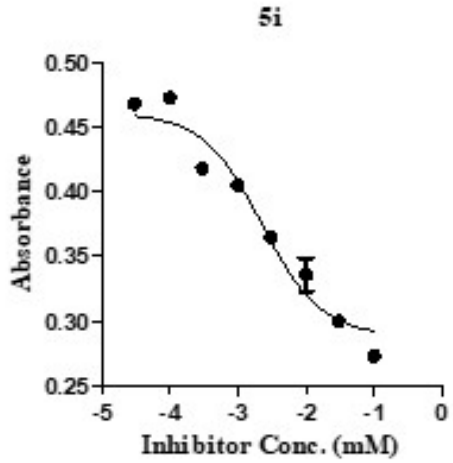
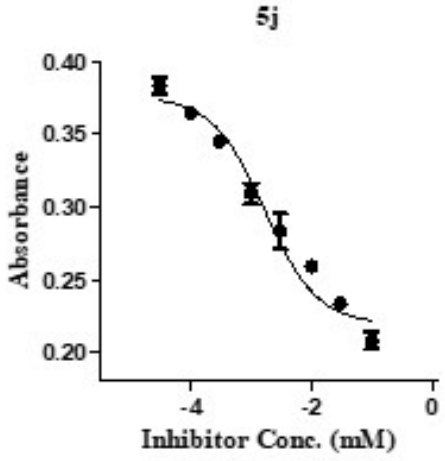
9.	**5i**		**1.07±0.06**		**3.26±0.15**
10.	**5j**		**0.59±0.003**		**0.62±0.003**
11.	**5k**		**1.74±0.05**		**0.89±0.04**
12.	**5l**		**0.85±0.03**		**0.77±0.03**

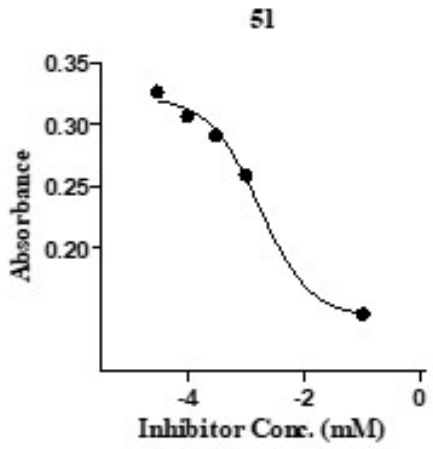
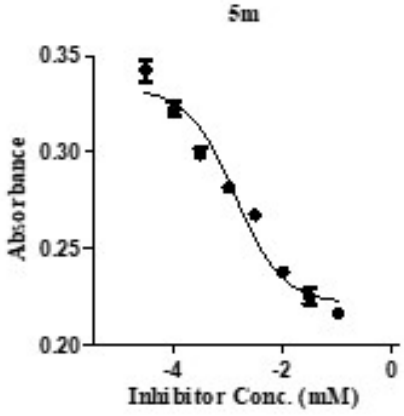
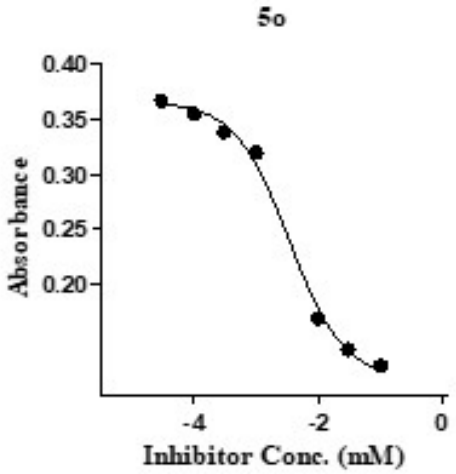
13.	**5m**		**1.36±0.09**		**1.22±0.01**
14.	**5n**	-	**38.03%**		**2.55±0.07**
15.	**5o**	-	**28.32%**		**2.67±0.46**
16	**Suramin** (as standard drug)		**18.54±1.14**		**12.83±0.23**

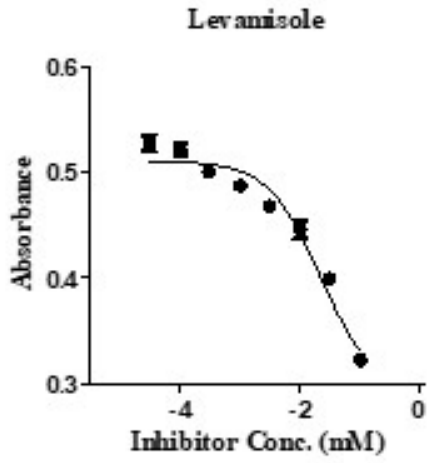
c)*h*-TNAP

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

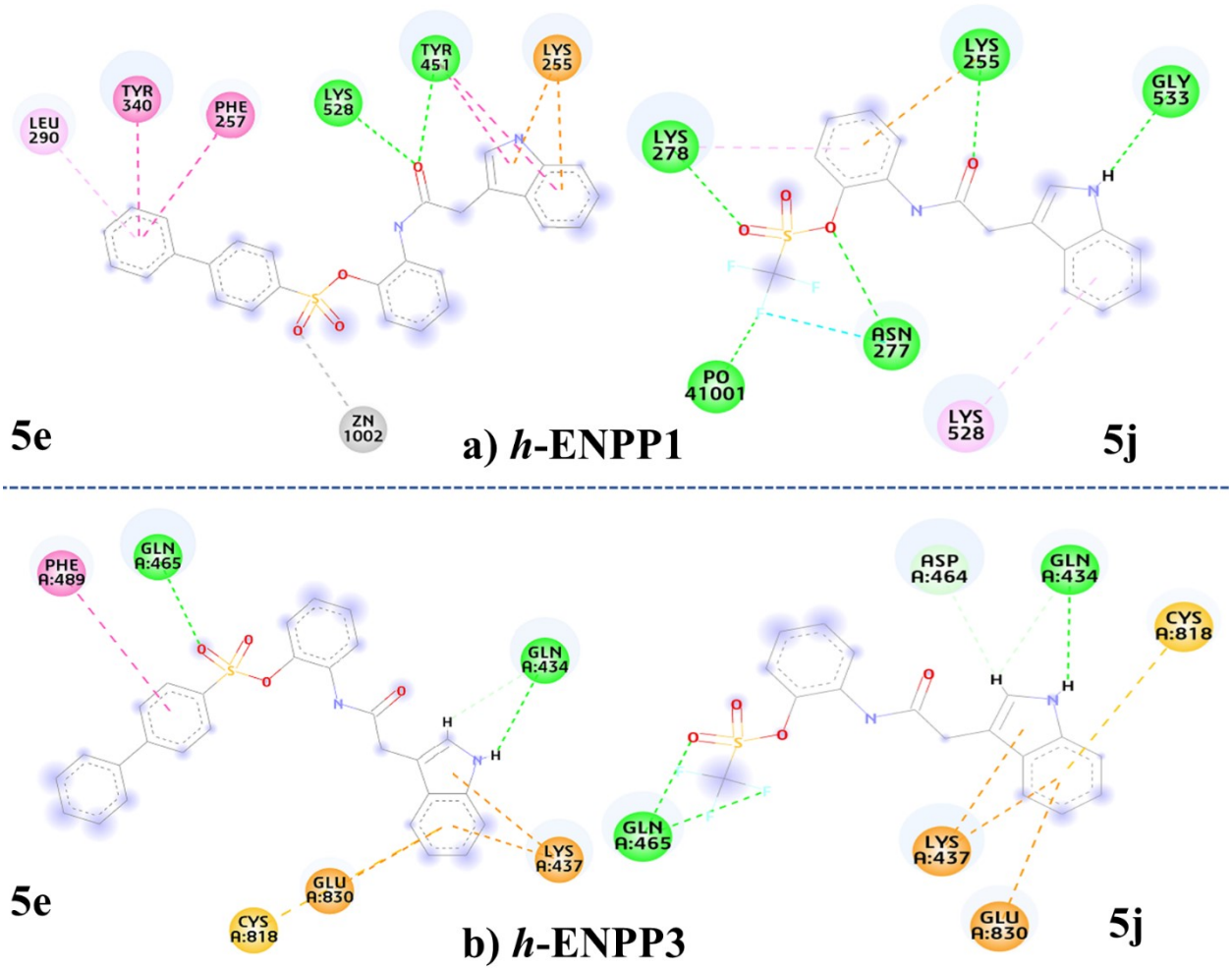
5.	**5e**		**1.56±0.03**
6.	**5f**		**6.58±0.25**
7.	**5g**		**0.59±0.08**

8.	**5h**		**2.86±0.06**
9.	**5i**		**2.27±0.24**
10	**5j**		**1.68±0.07**
11	**5k**	-	**31.75%**

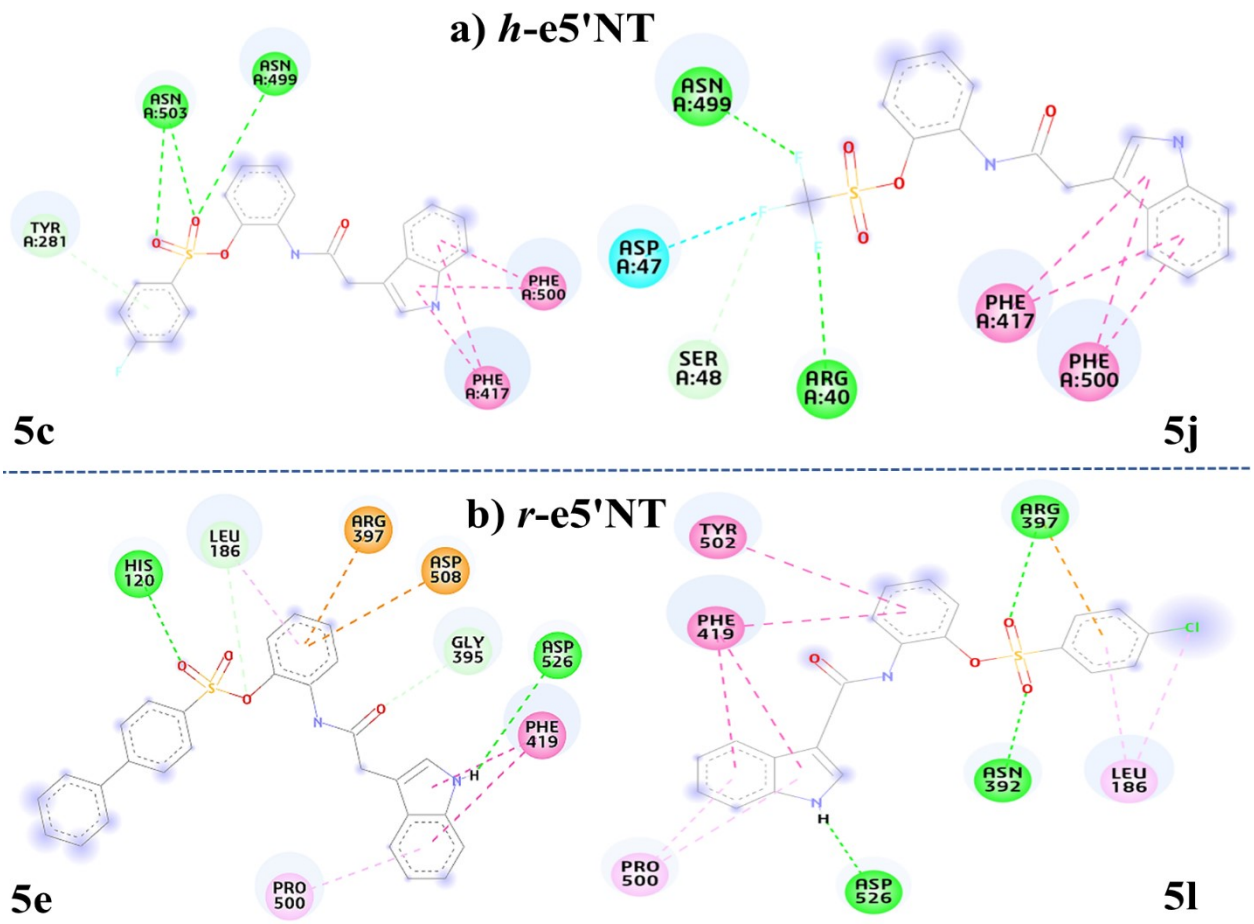
12.	**5l**		**1.69±0.18**
13.	**5m**		**1.3±0.38**
14.	**5n**	-	**28.88%**
15.	**5o**		**3.37±0.05**

16.	**Levamisole**		**21.38±4.17**

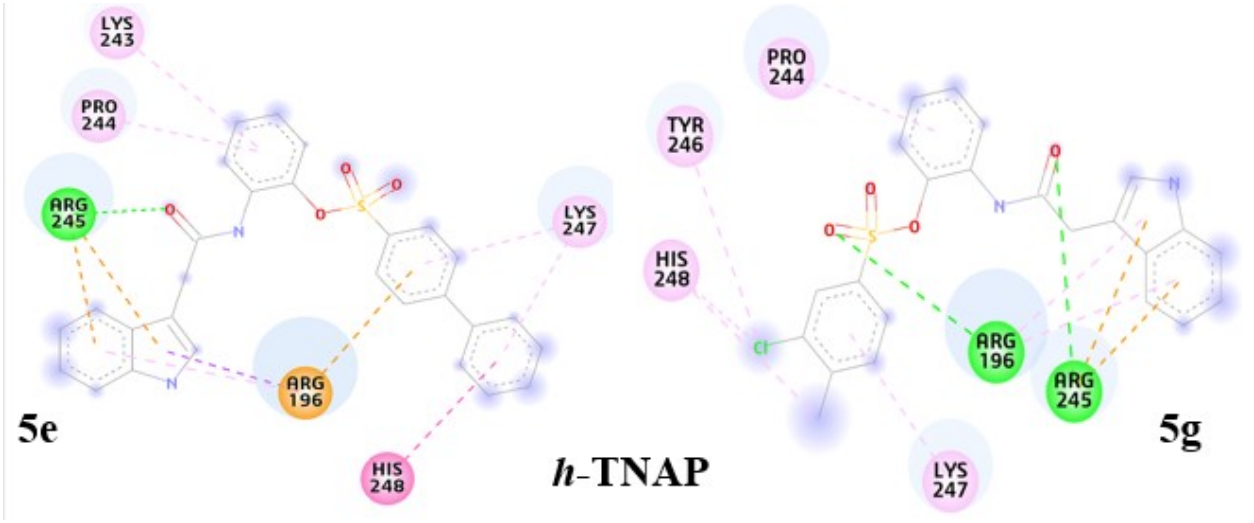
Molecular docking of Indole acetic acid sulfonate derivatives (5a-5o), 2D Images of most active compounds



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



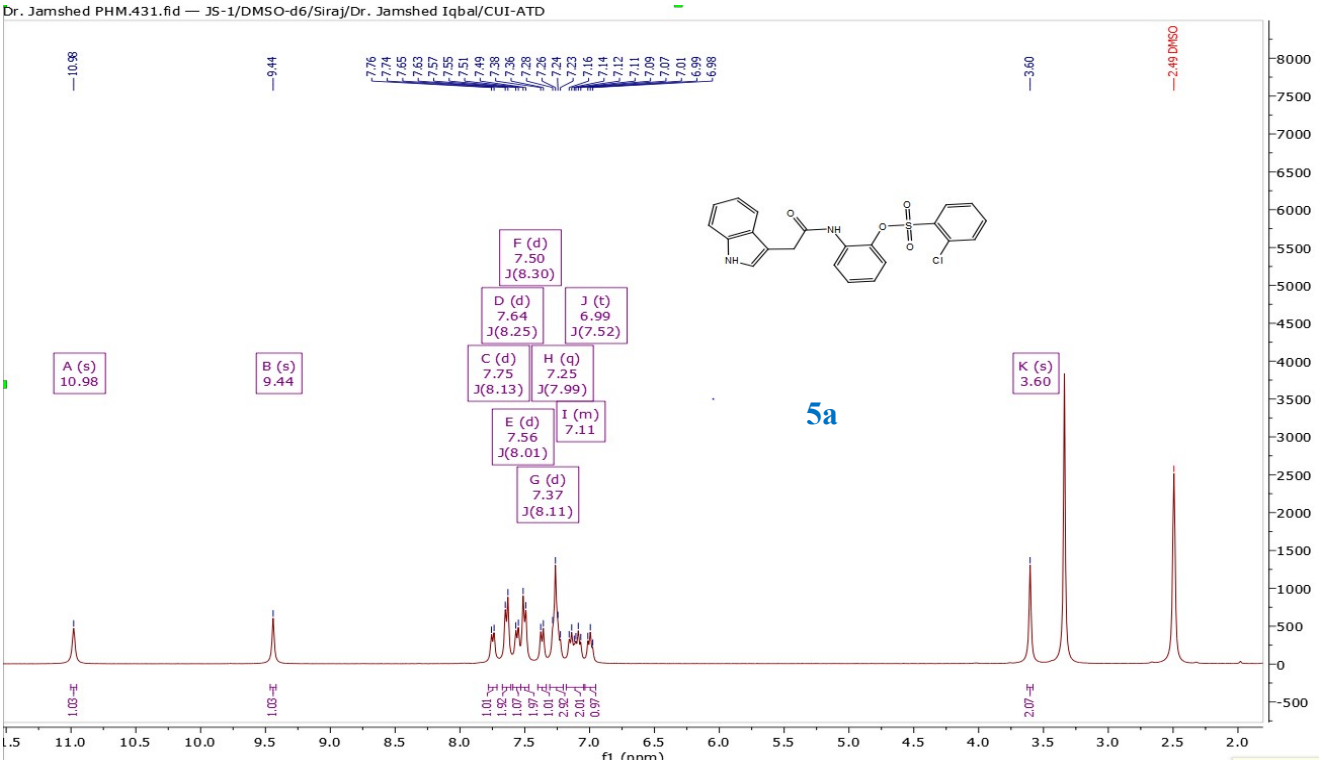
4-Figure FS2. Presentation of 2D binding modes of inhibitor **5c** and **5j** against **a)** *h*-e5′NT residues and **5e** and **5l** against **b)** *r*-e5′NT residues



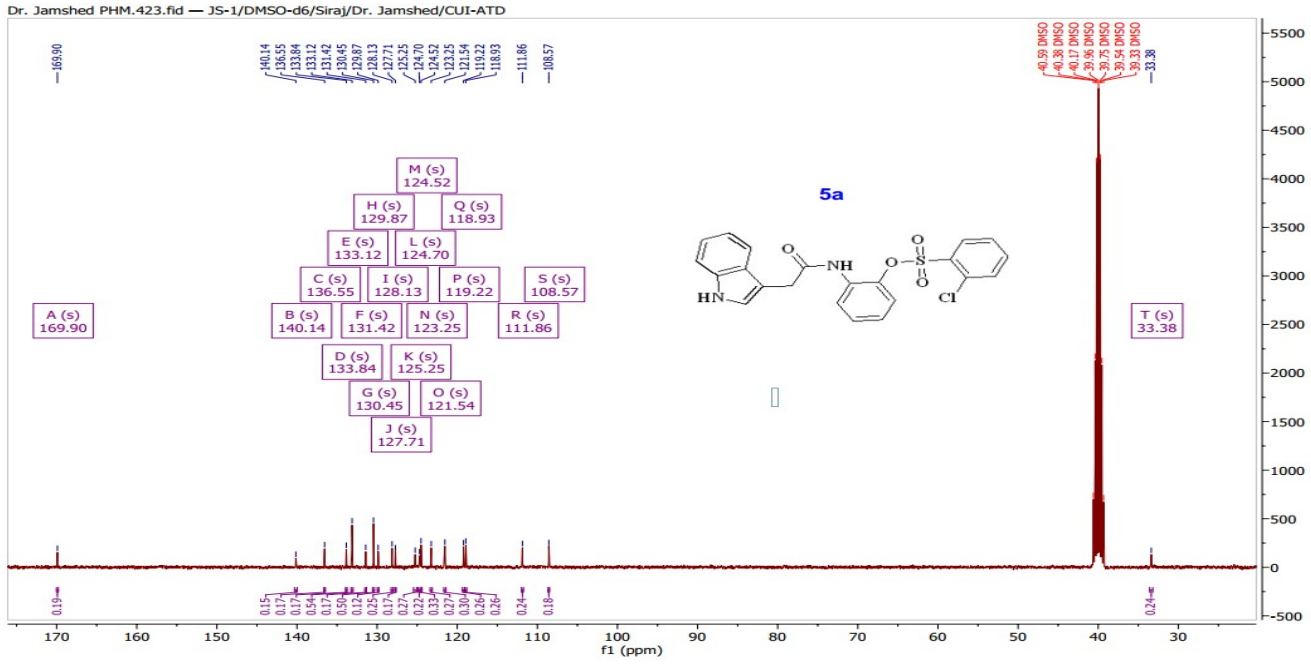
5-Figure FS3. 2D ligand-Protein Interactions docked conformations presentation for compound **5e** and **5g** against *h*-TNAP

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

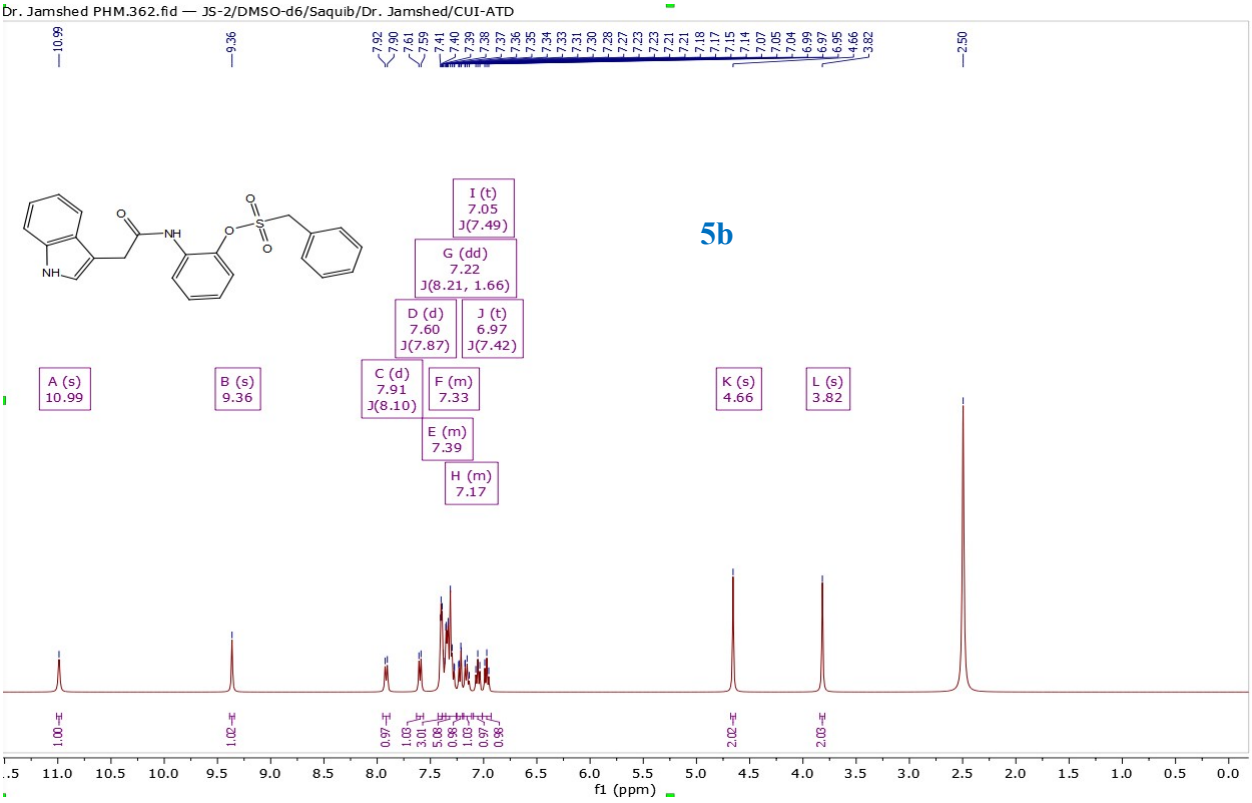
5a. ^{1}H NMR



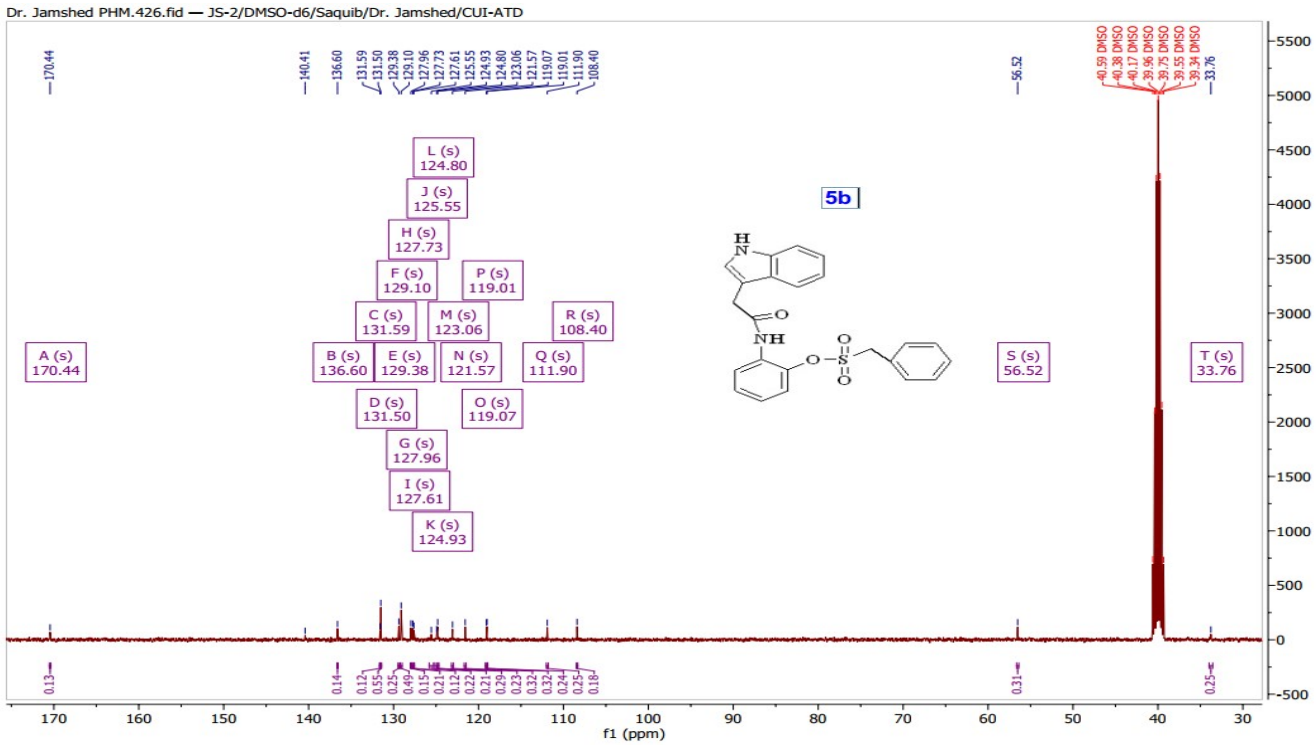
5a. ^{13}C NMR



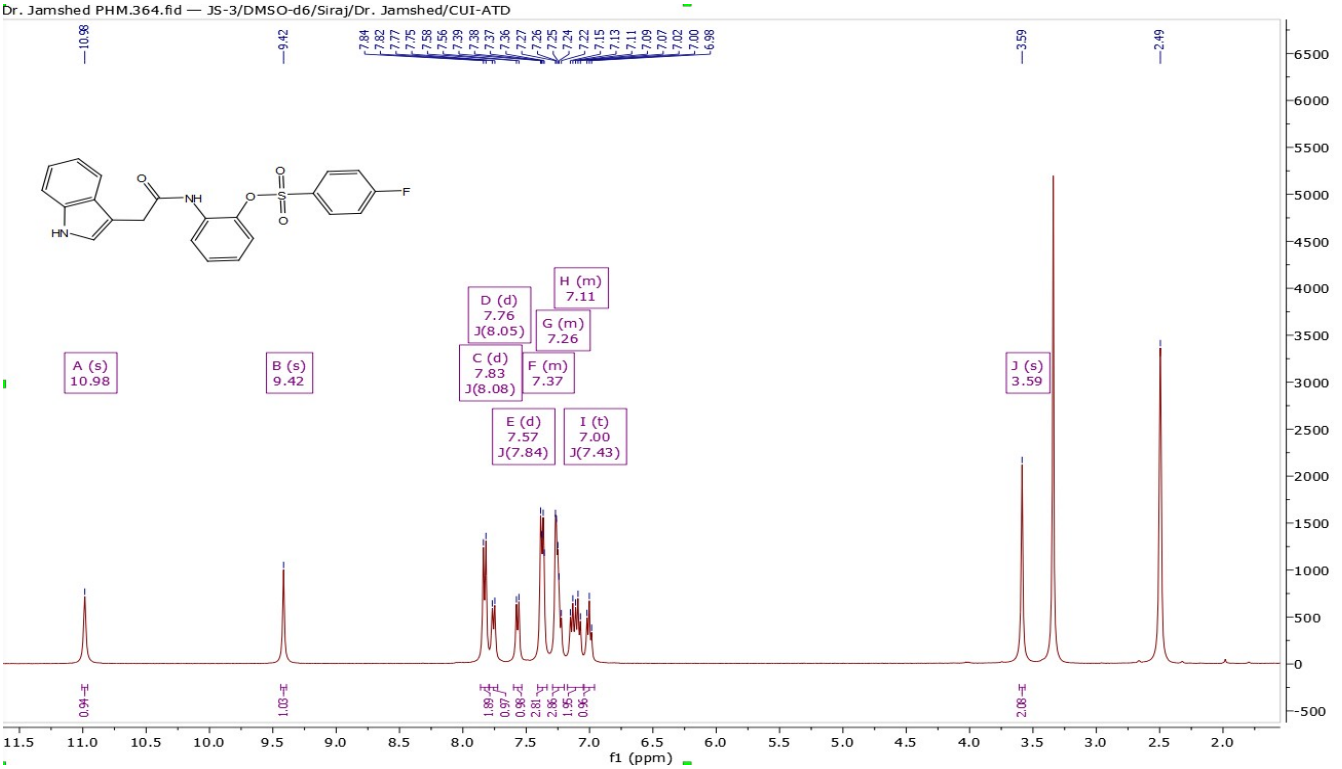
5b. ^{1}H NMR



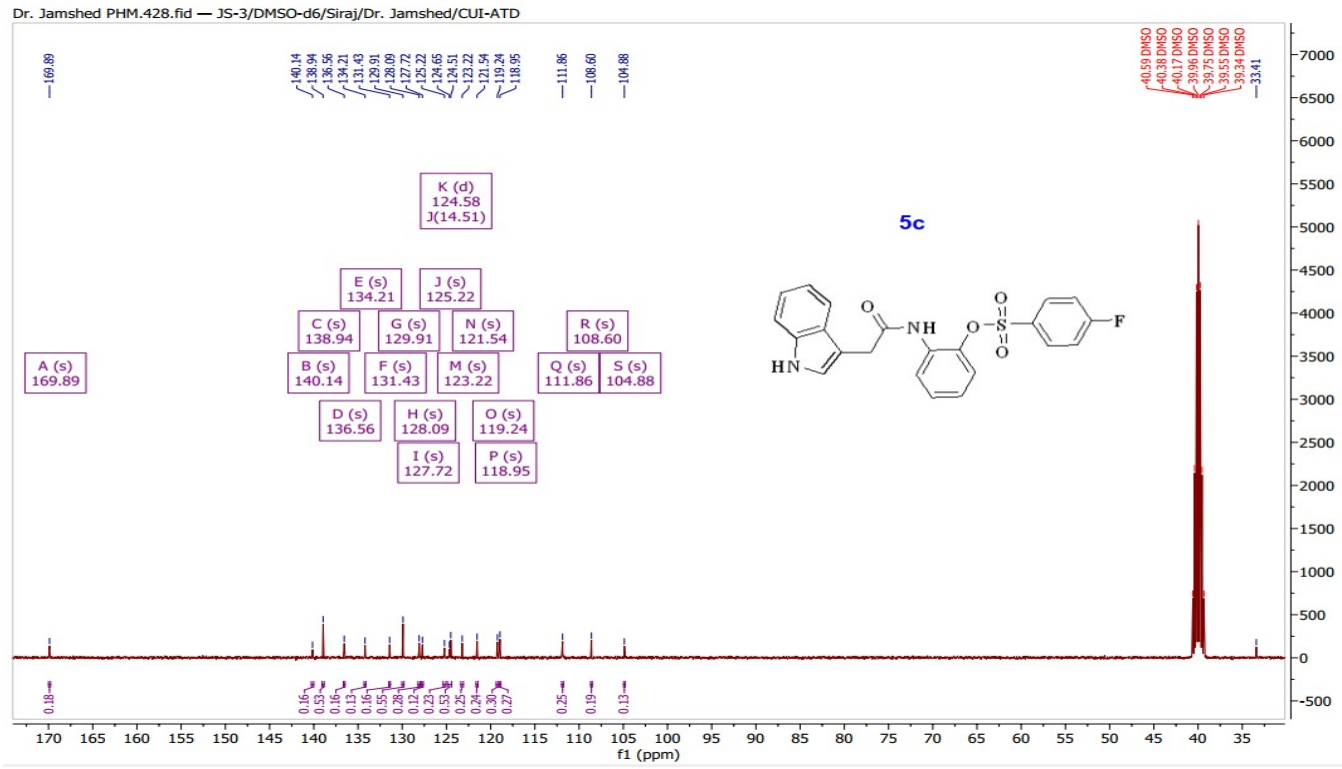
5b. ^{13}C NMR



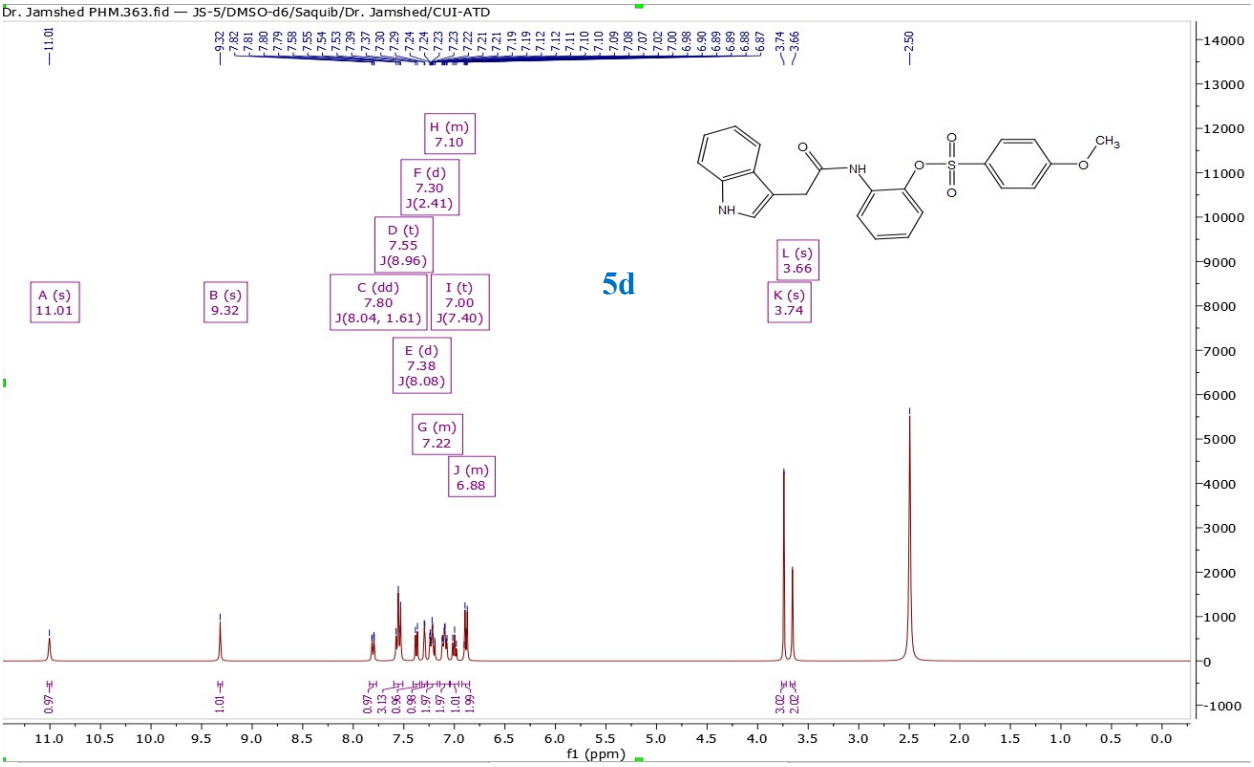
5c. ^{1}H NMR



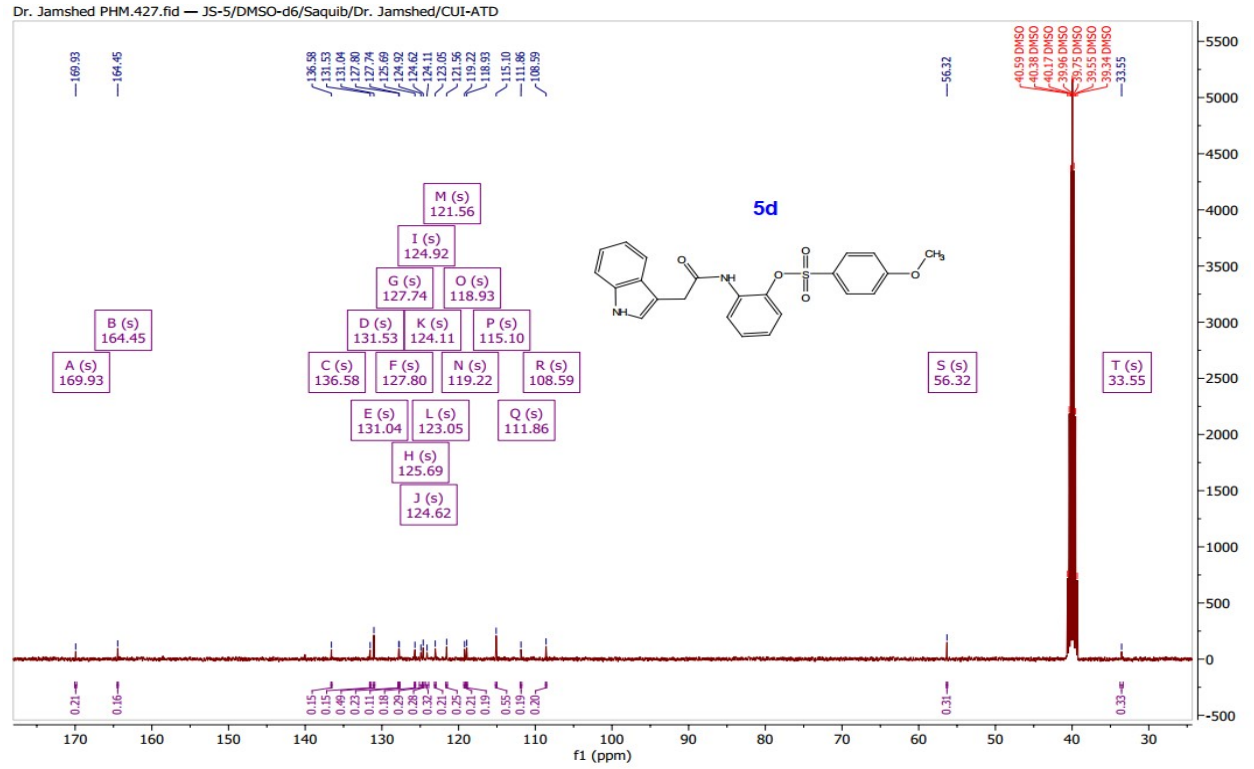
5c. ^{13}C NMR



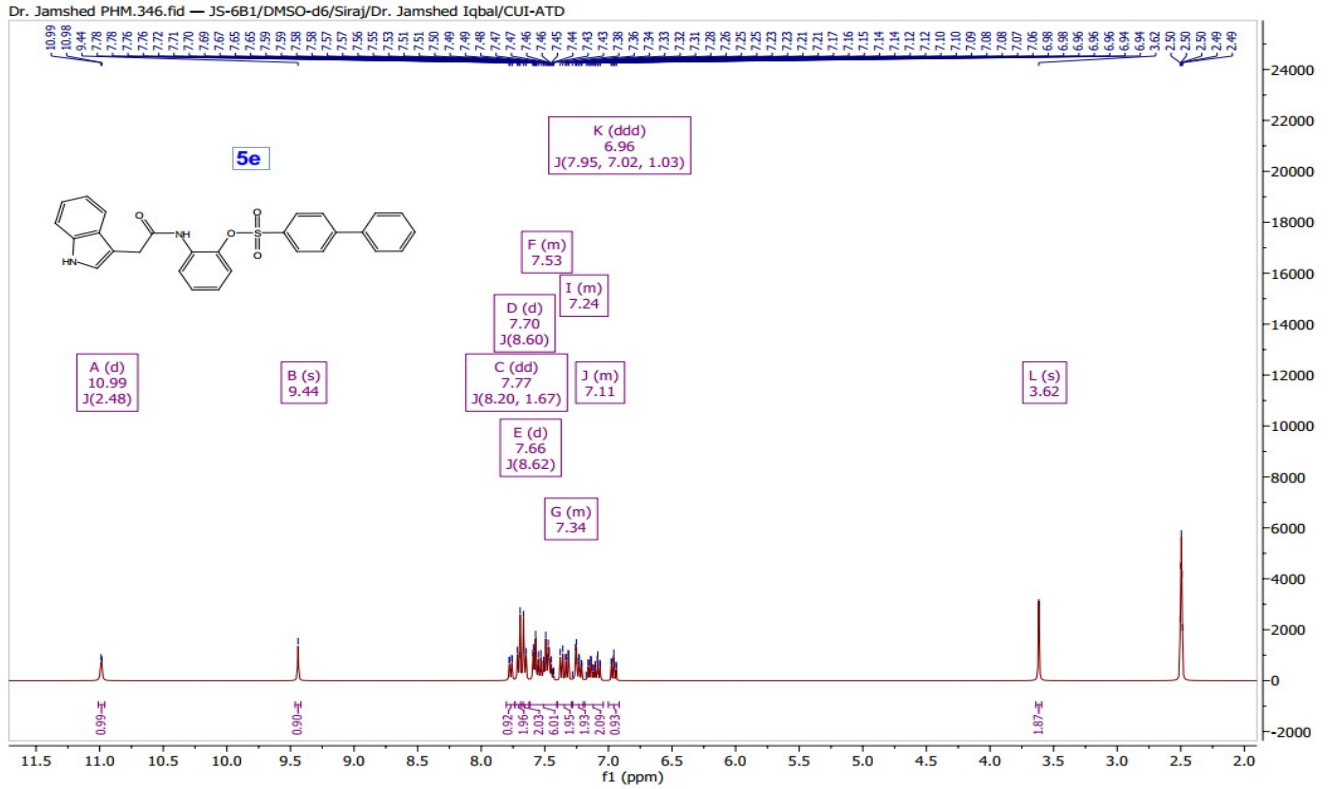
5d. ^{1}HNMR



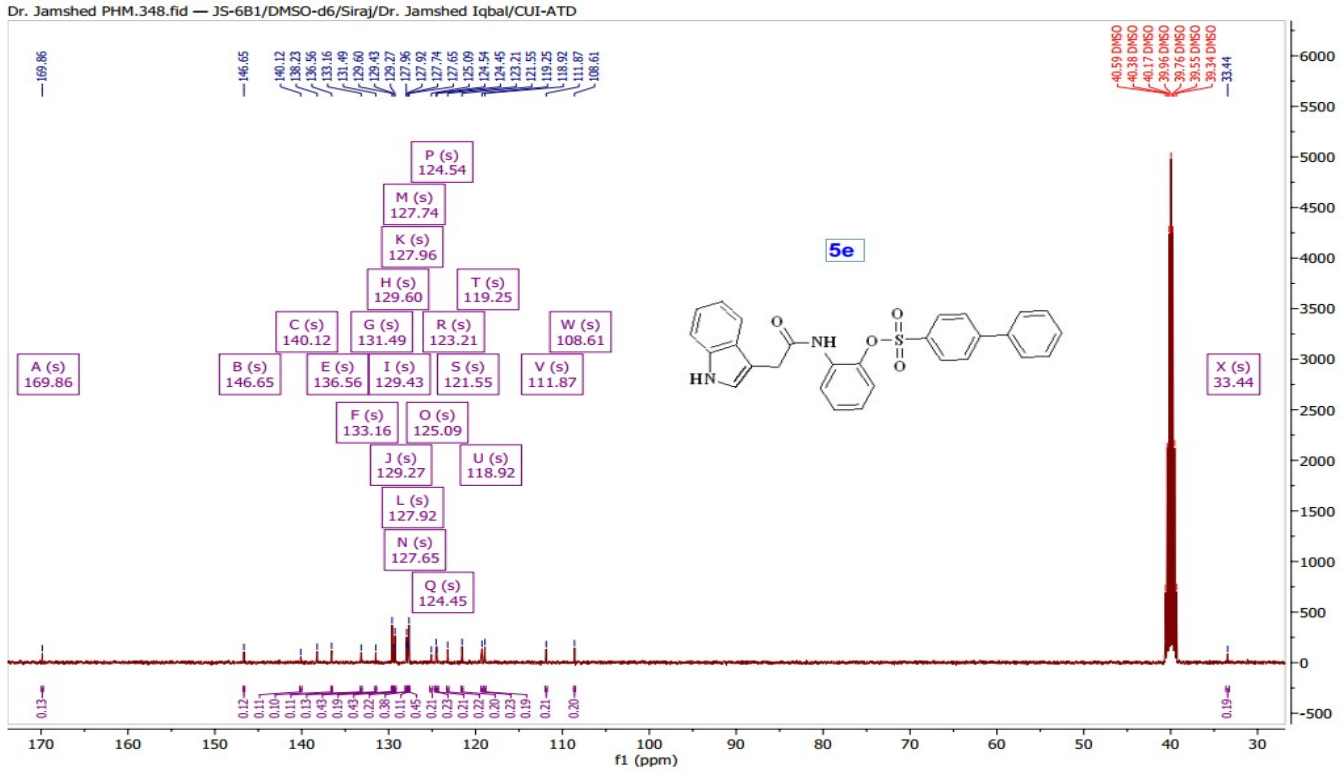
5d. ^{13}C NMR



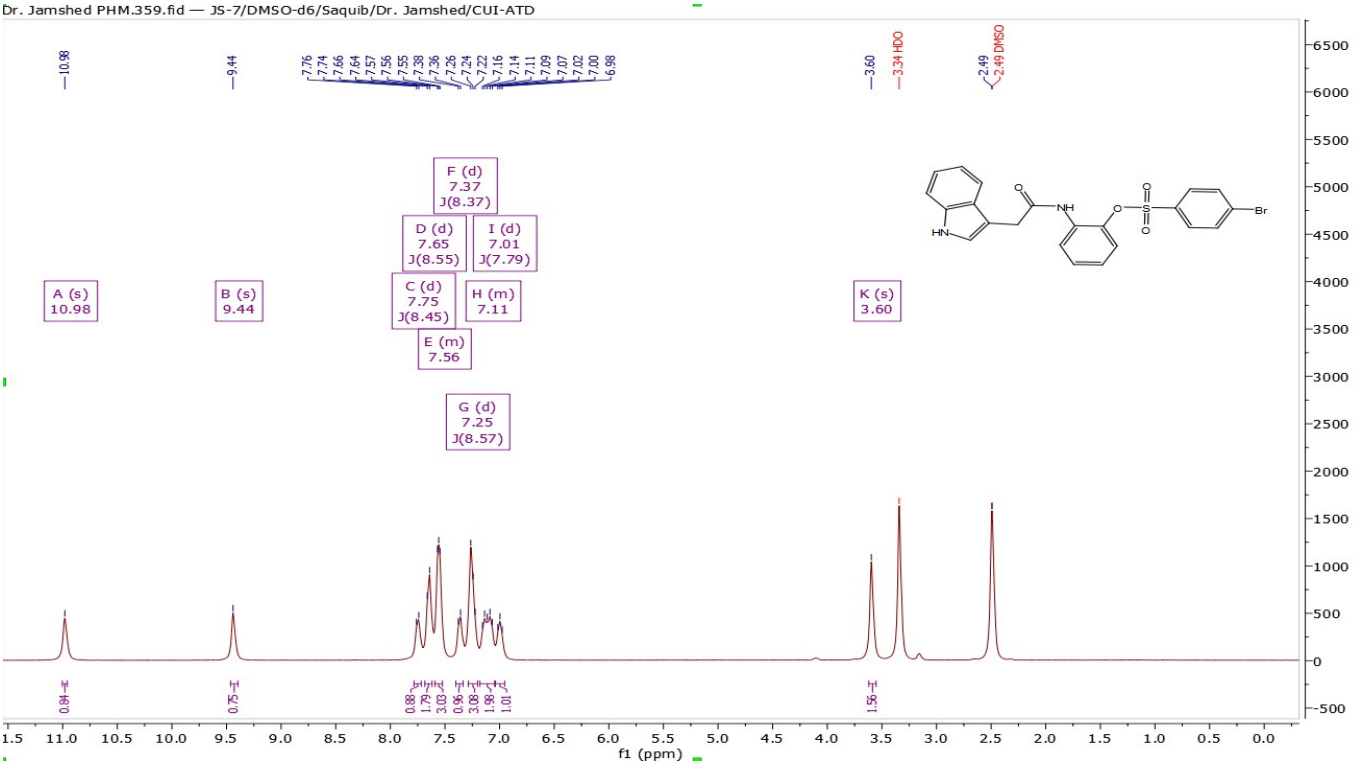
5e. ^{1}H NMR



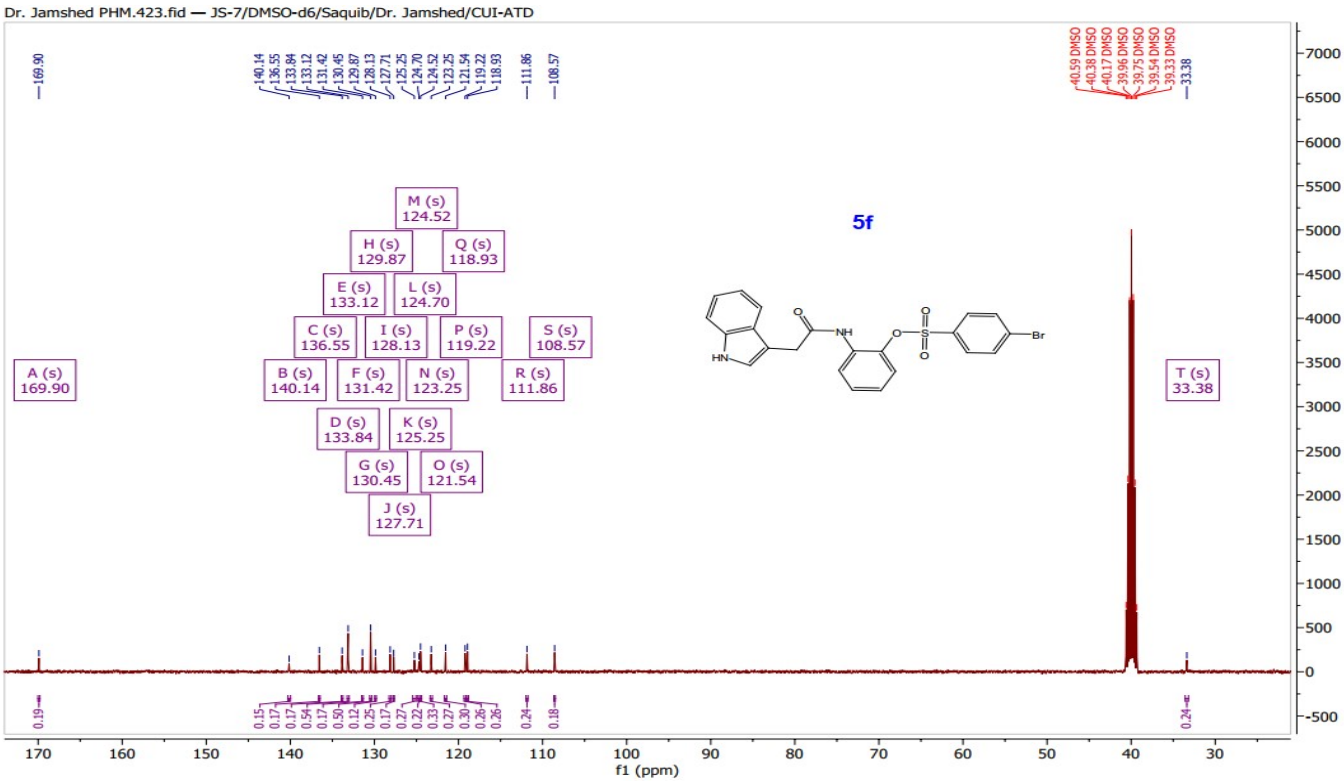
5e. ^{13}C NMR



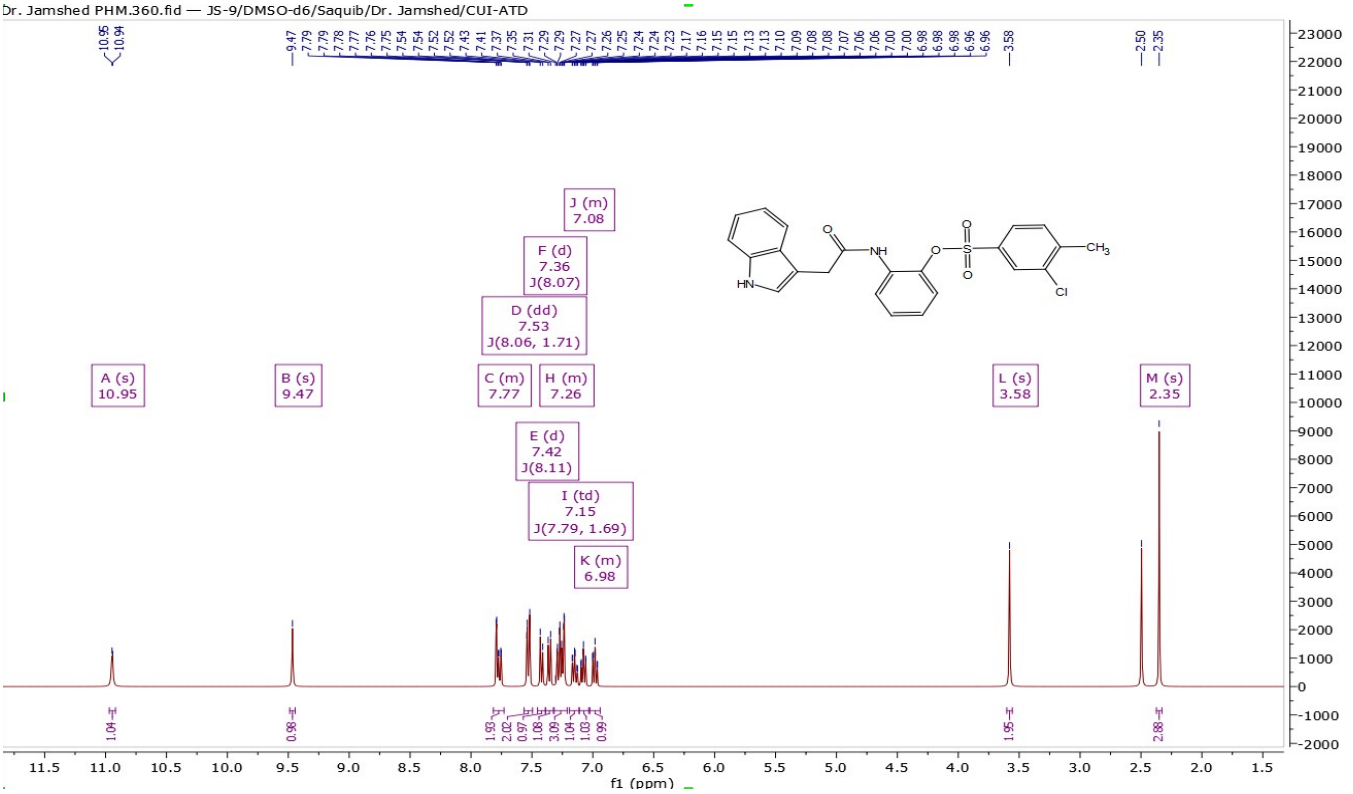
5f. ^{1}H NMR



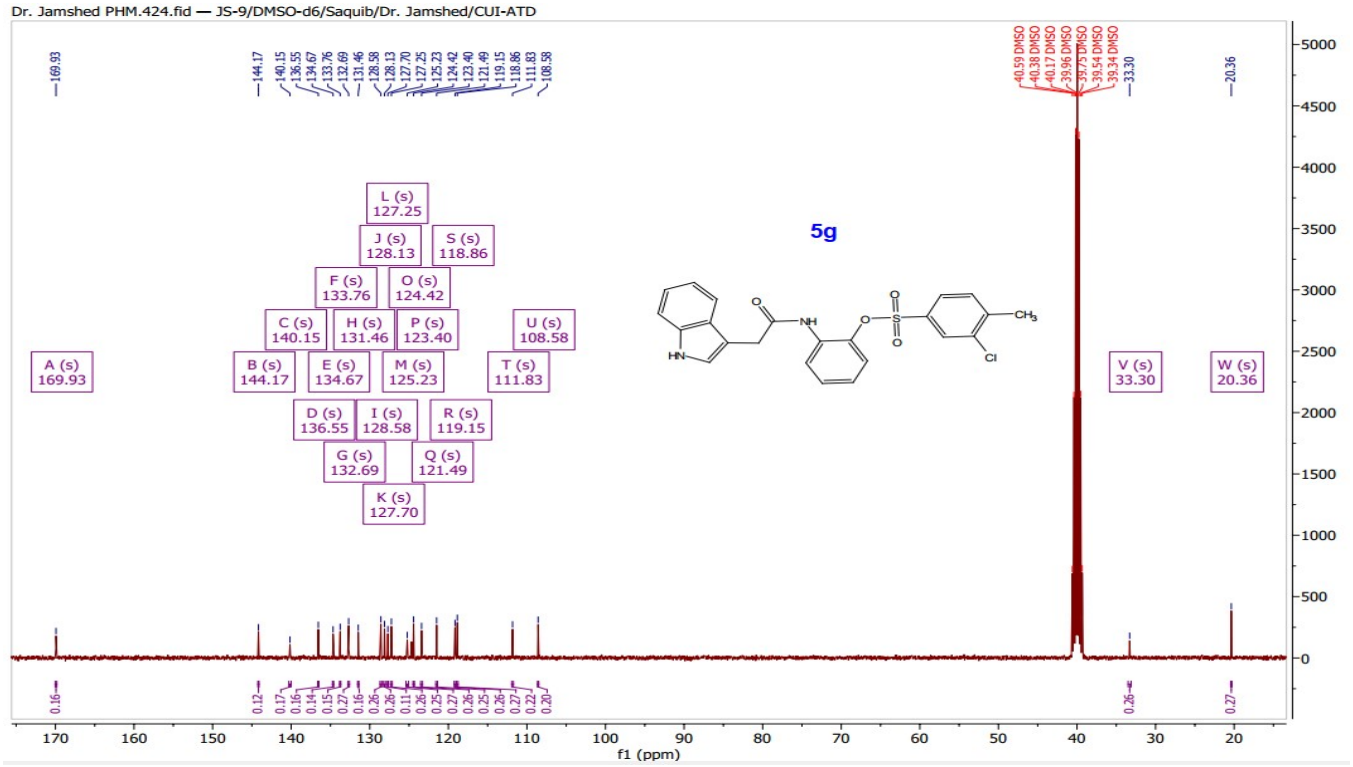
5f. ^{13}C NMR



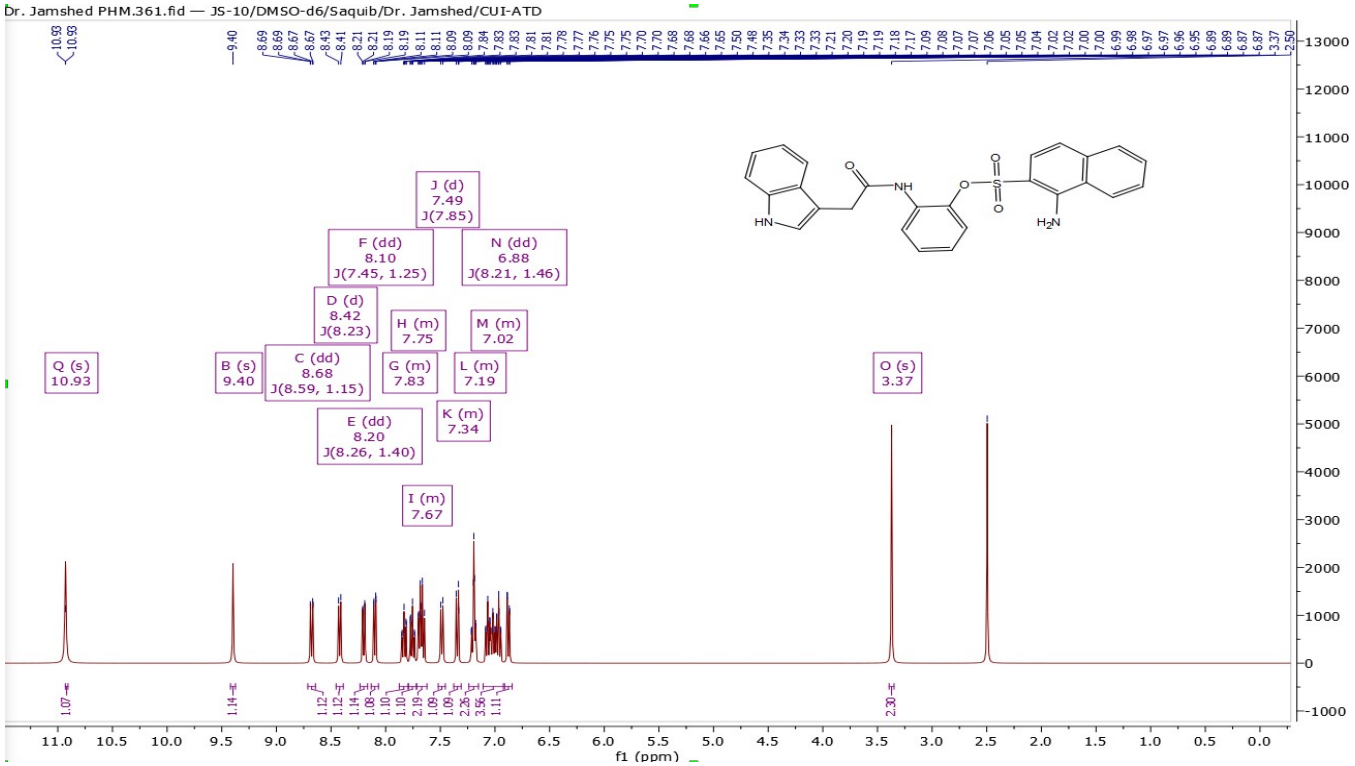
5g. ^{1}H NMR



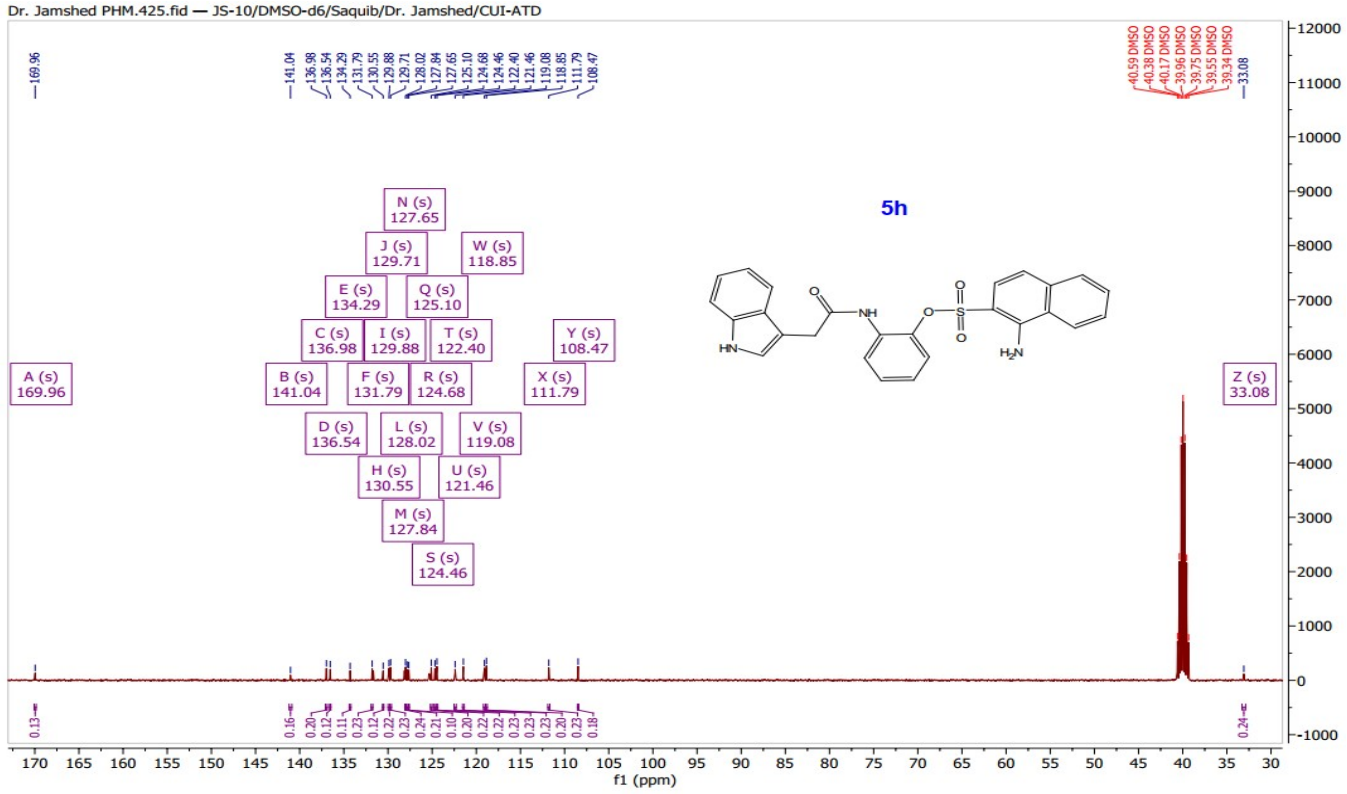
5g. ^{13}C NMR



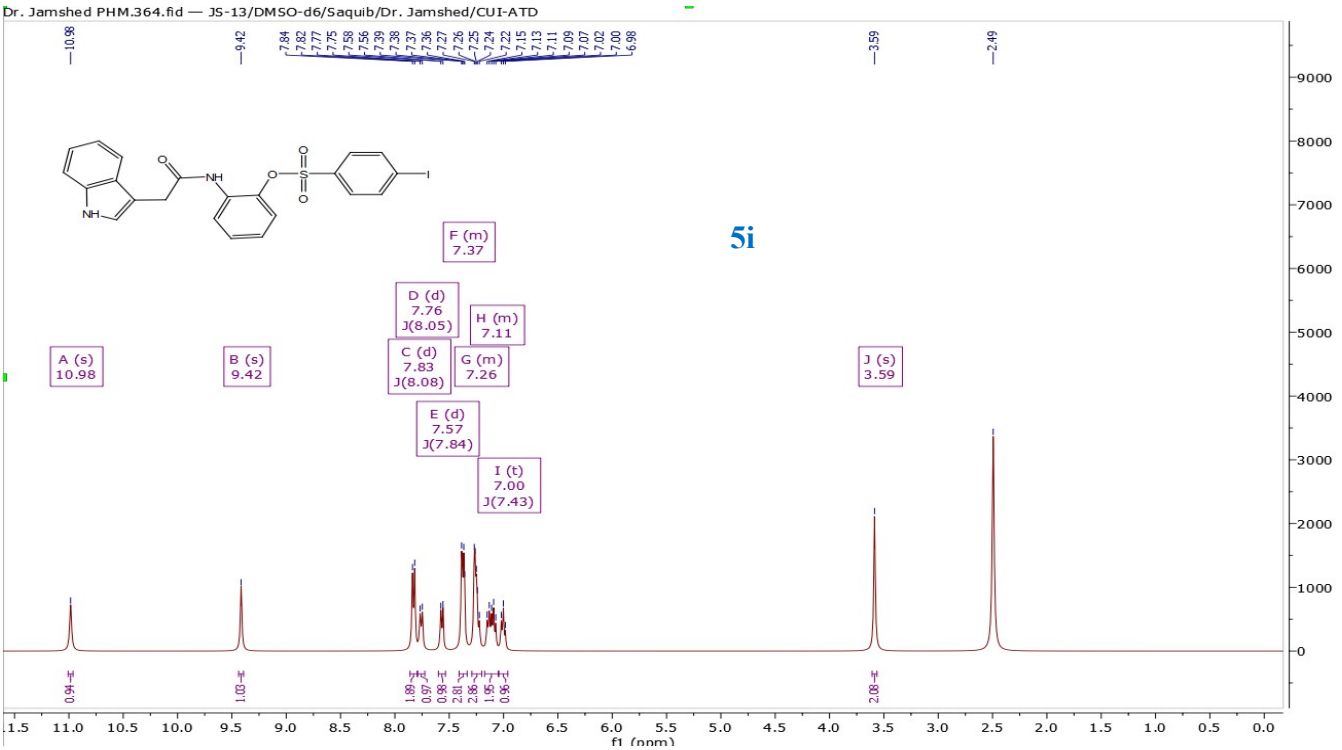
5h. ^{1}H NMR



5h. ^{13}C NMR



5i. ^{1}H NMR



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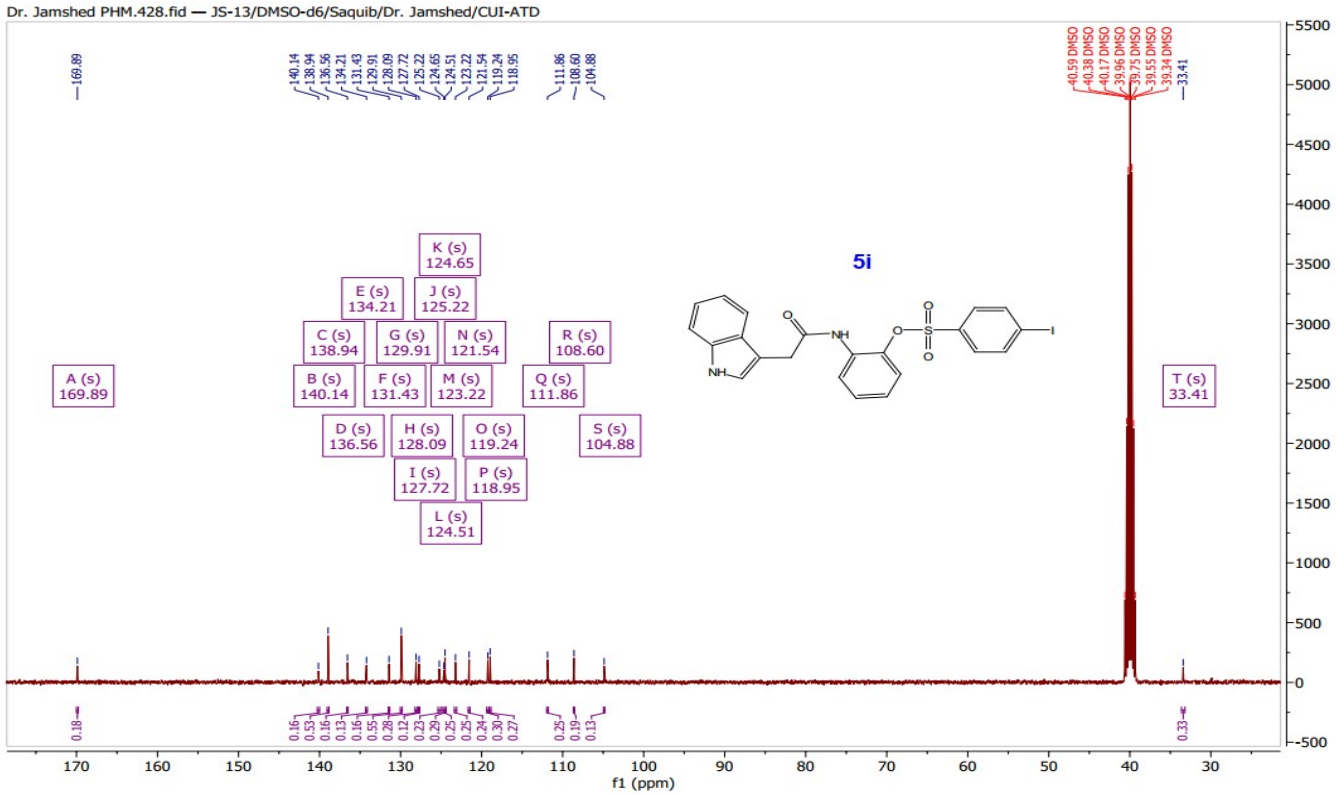
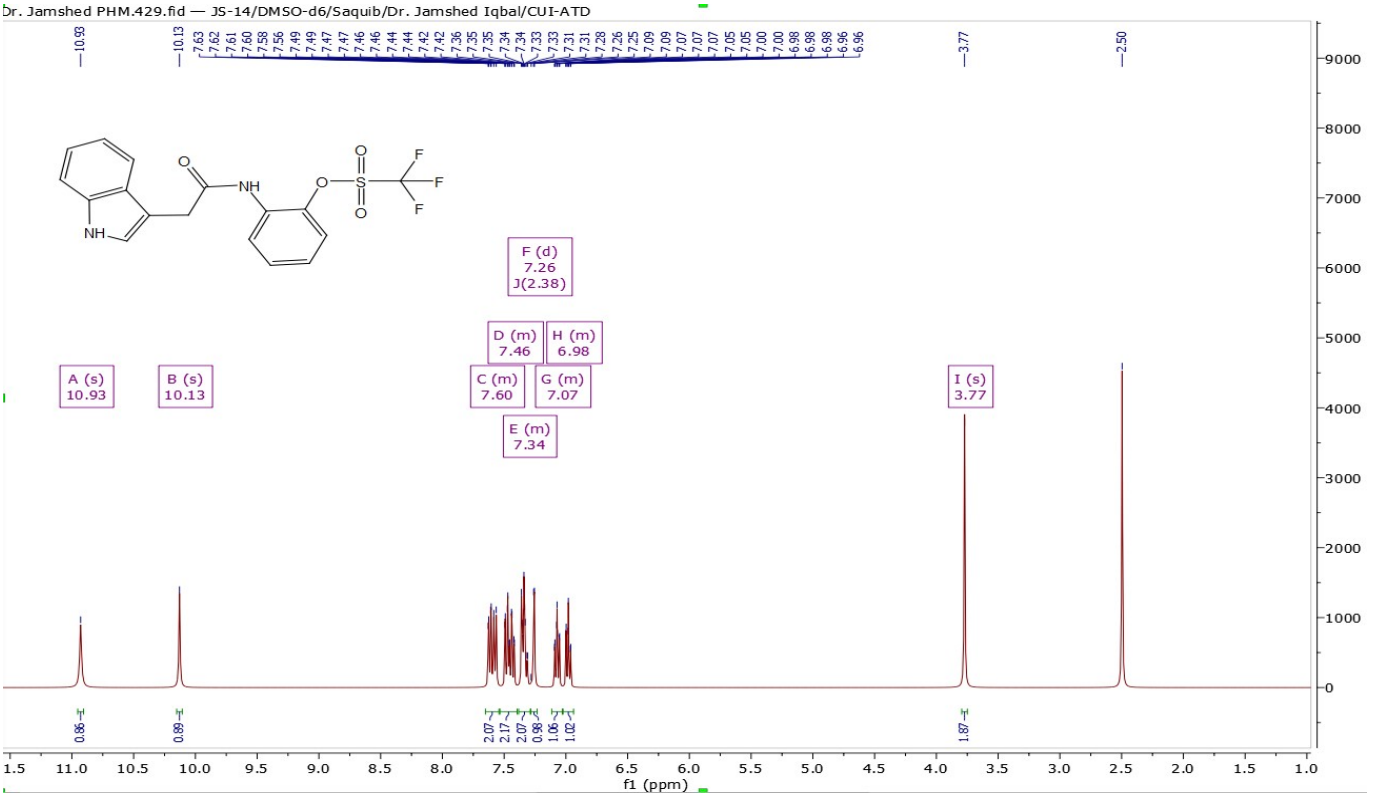
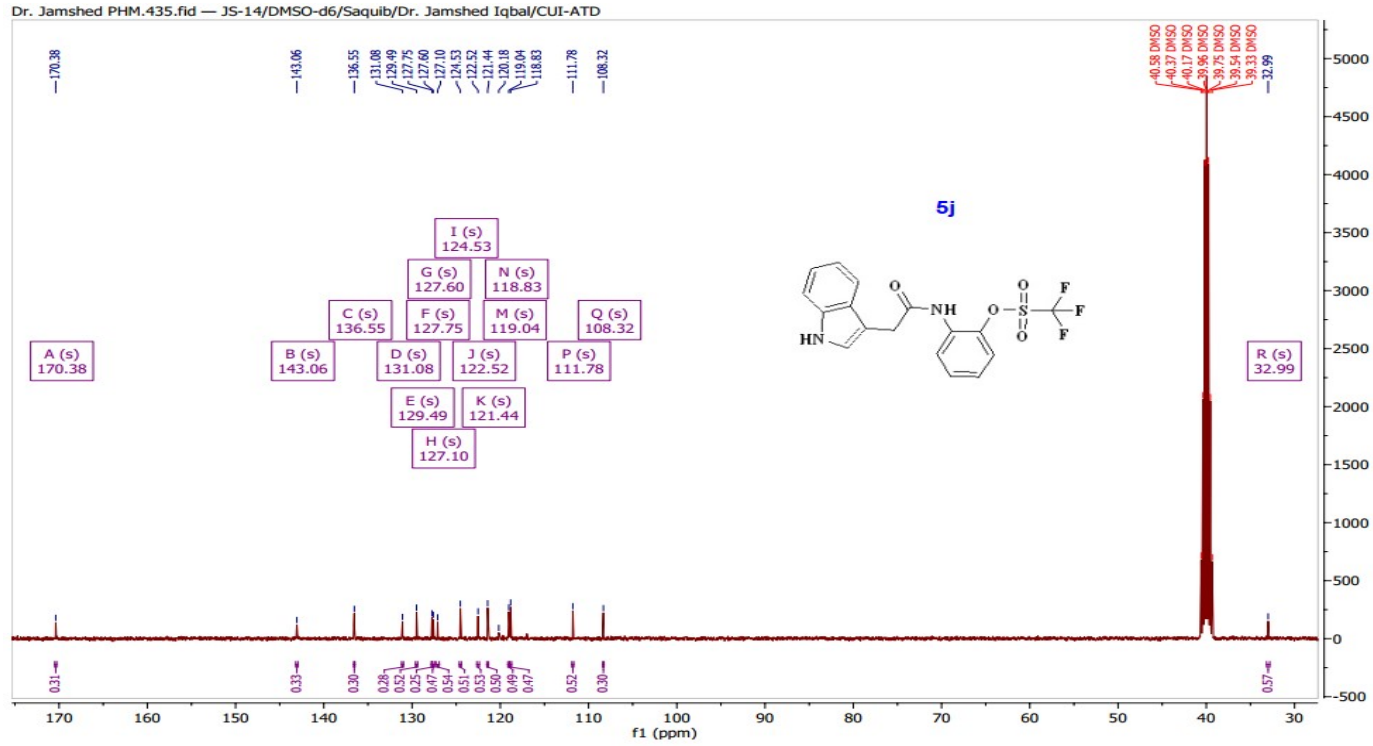


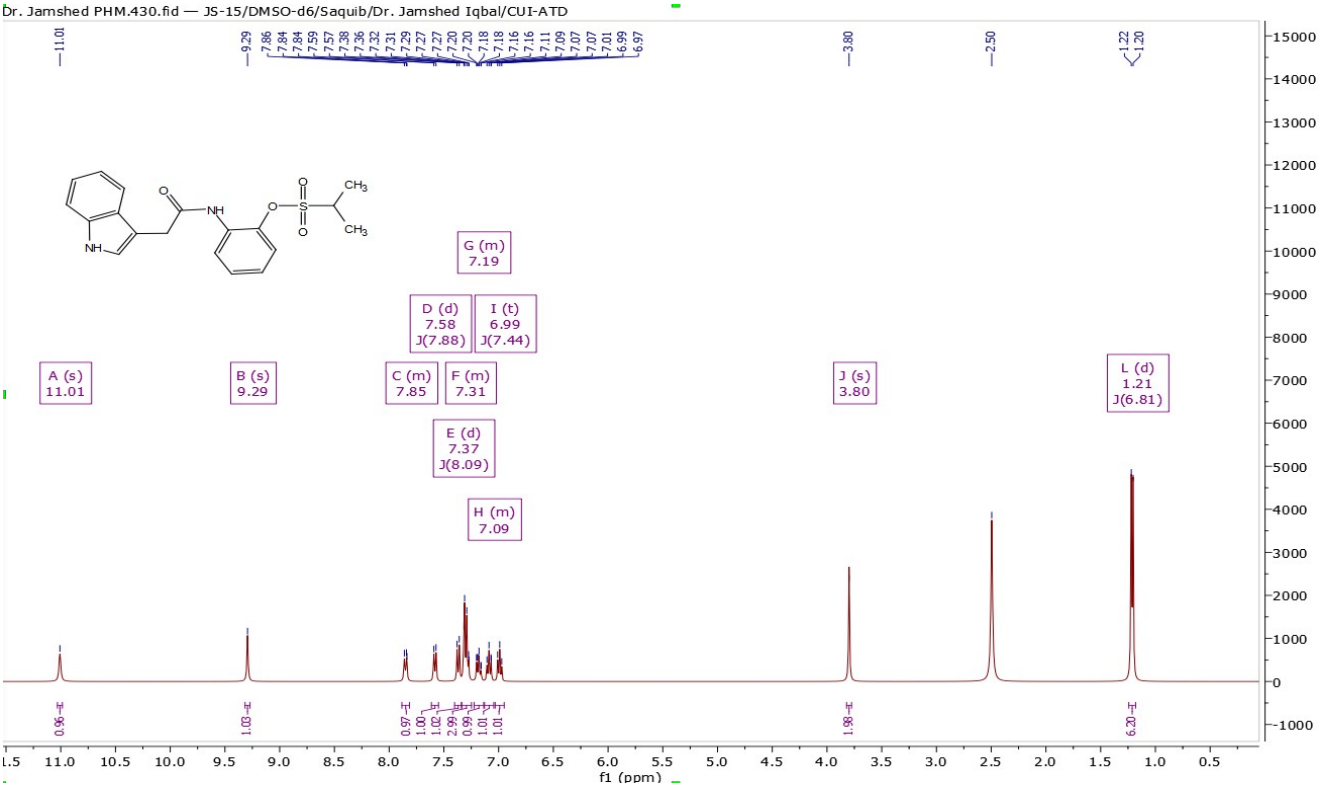
5j. ^{1}H NMR



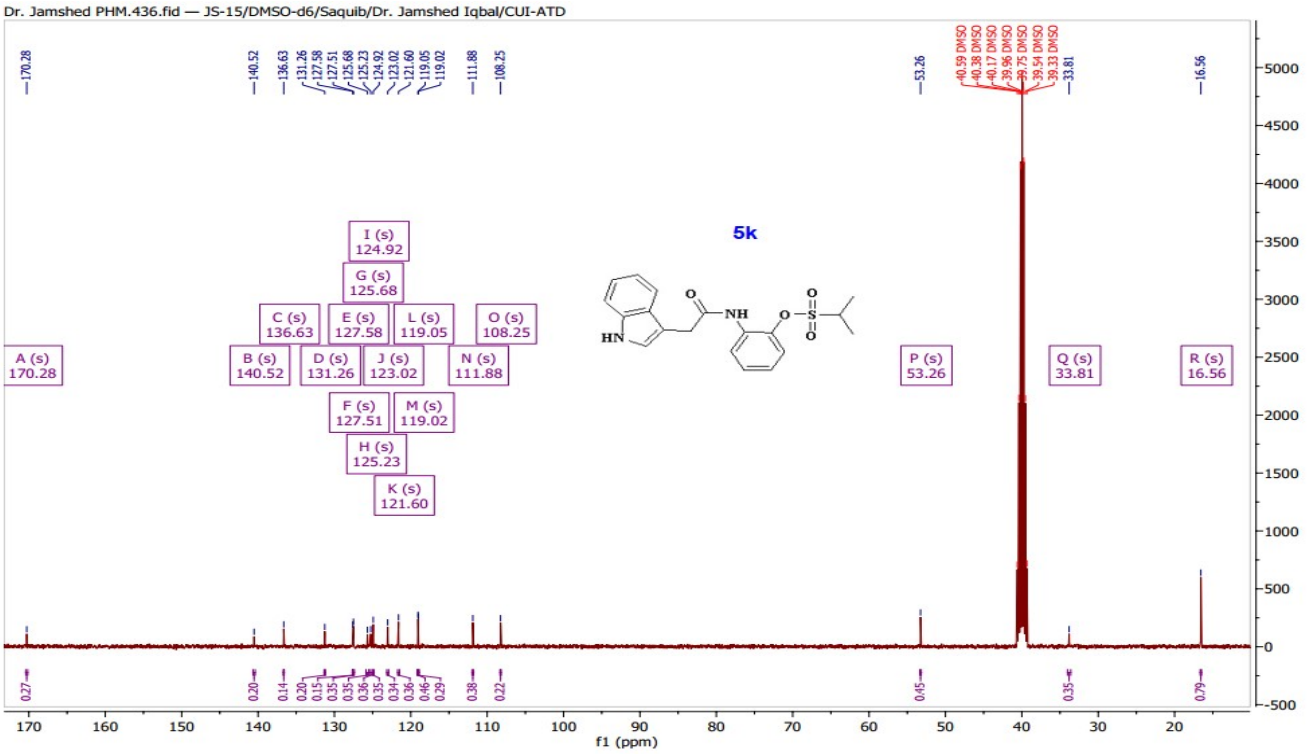
5j. ^{13}C NMR



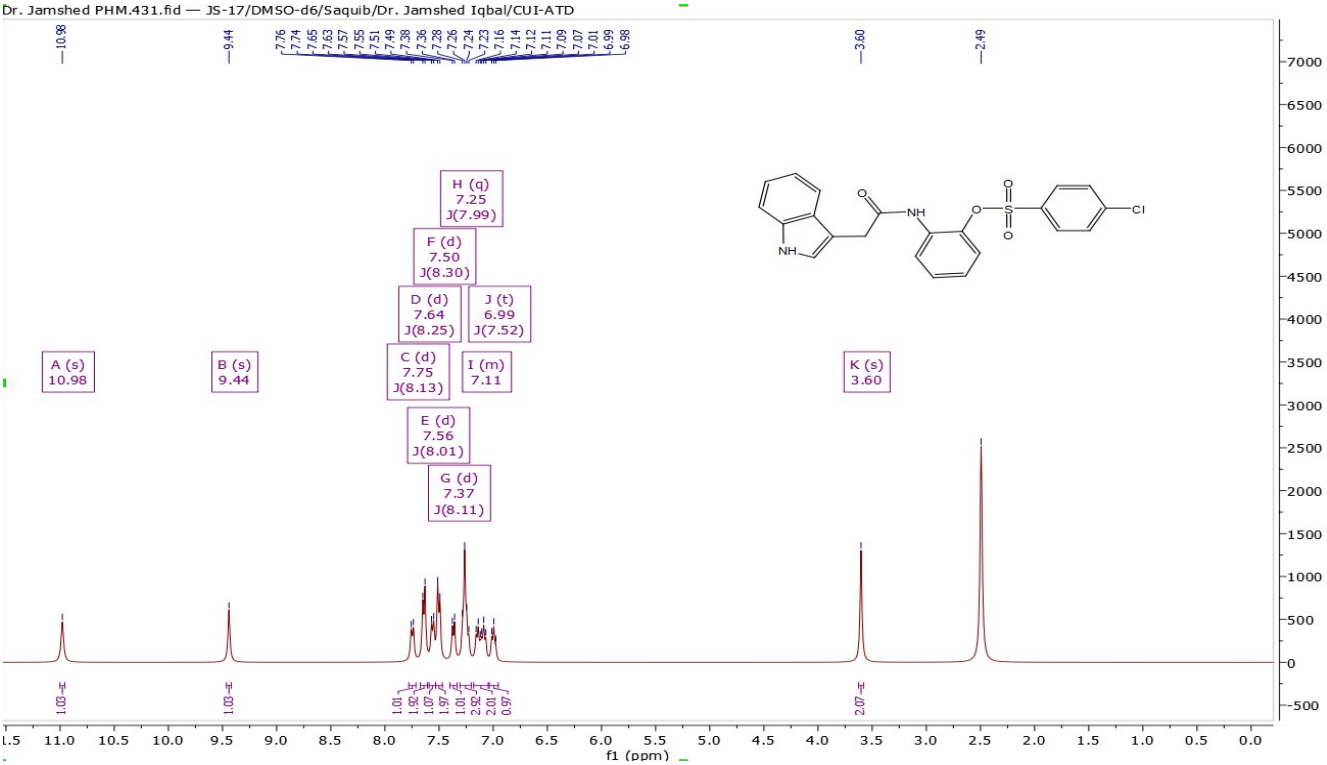
5k. ^{1}H NMR



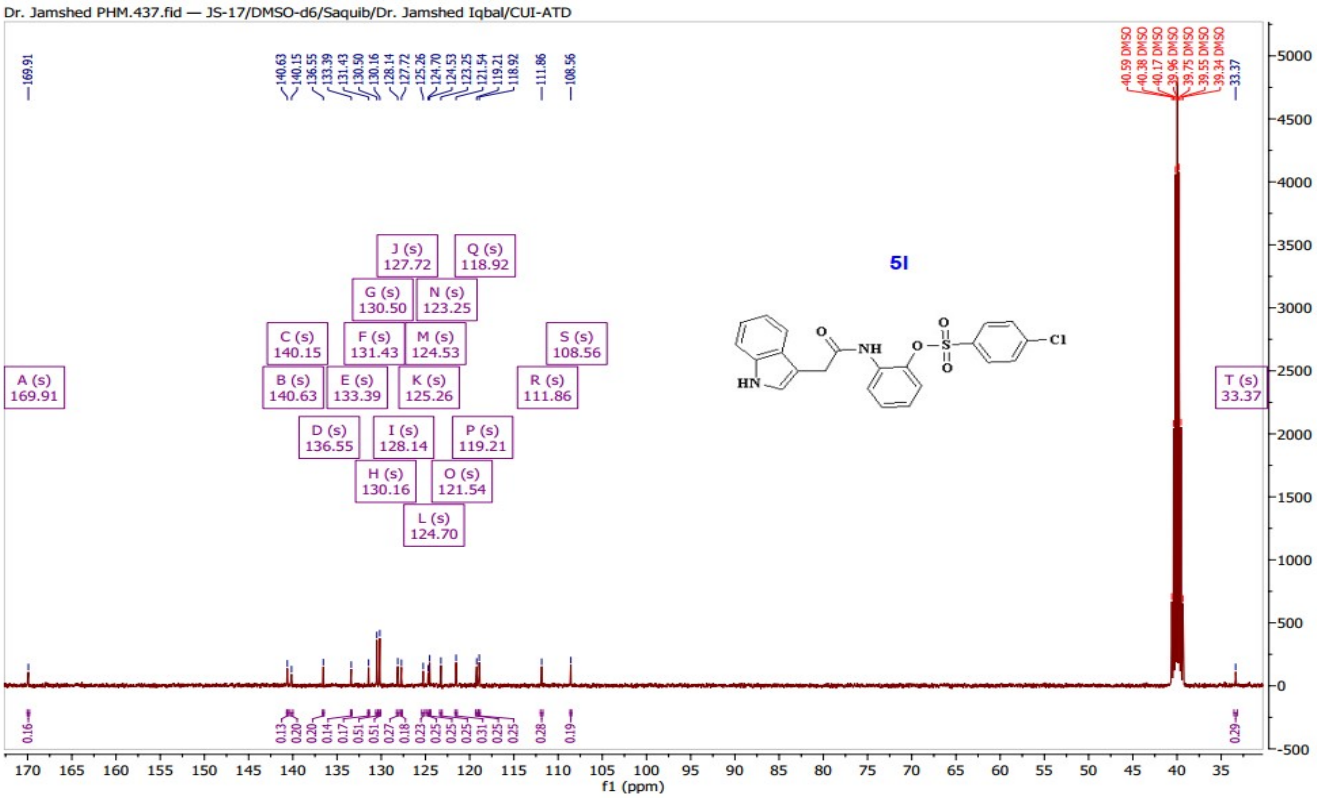
5k. ^{13}C NMR



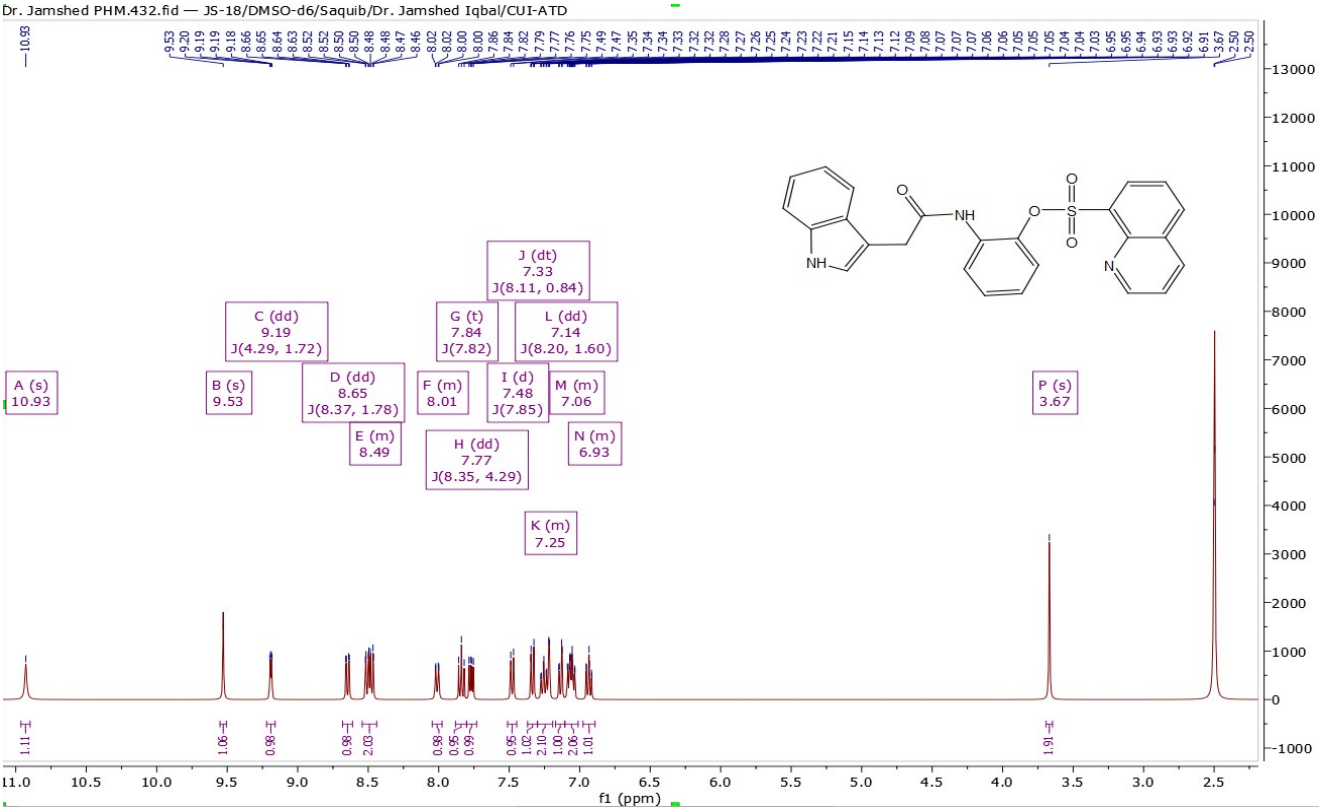
5l. ^{1}H NMR



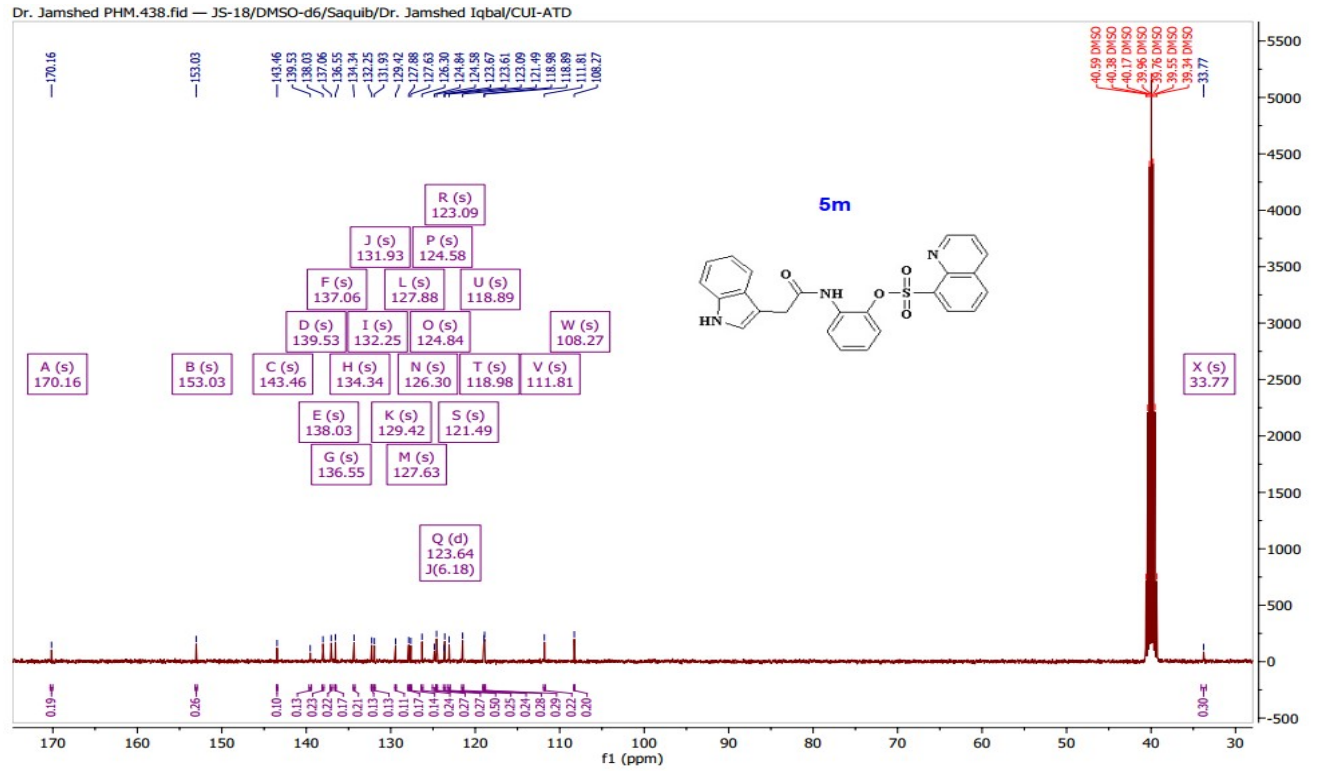
5l. ^{13}C NMR



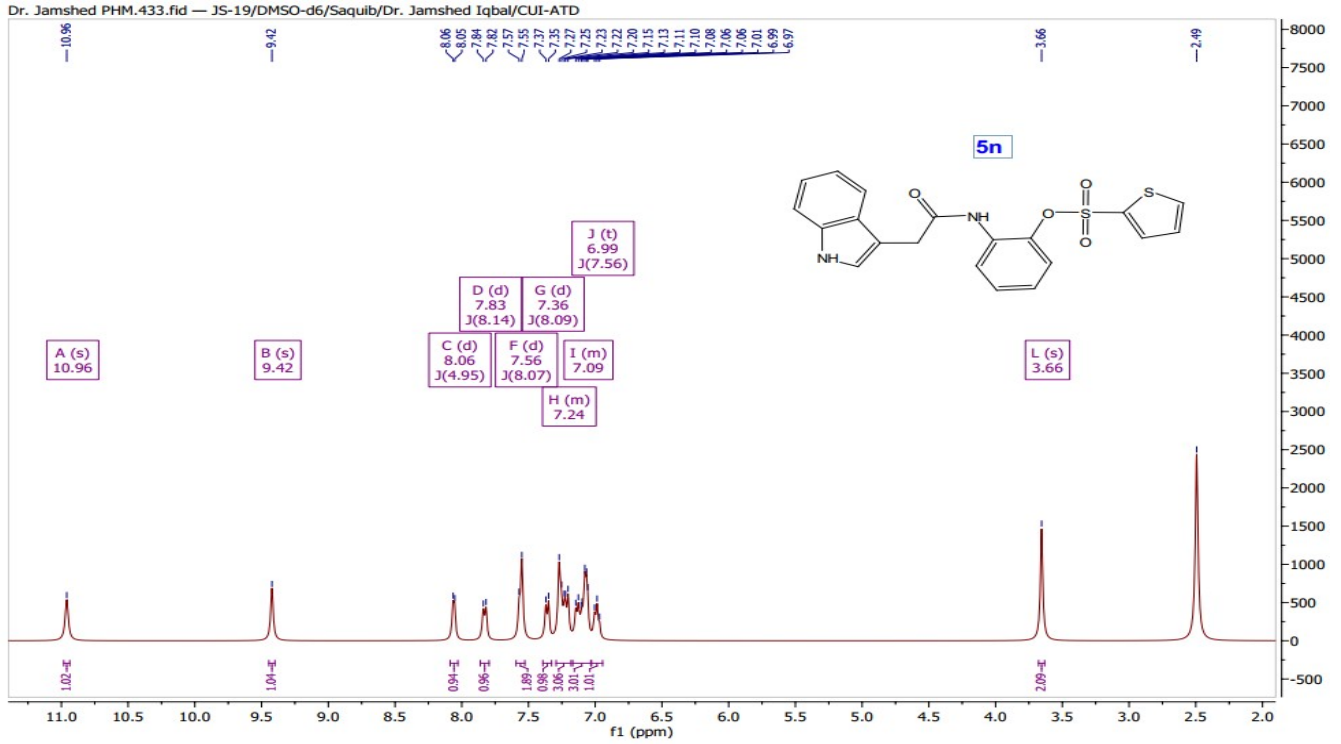
5m. ^{1}H NMR



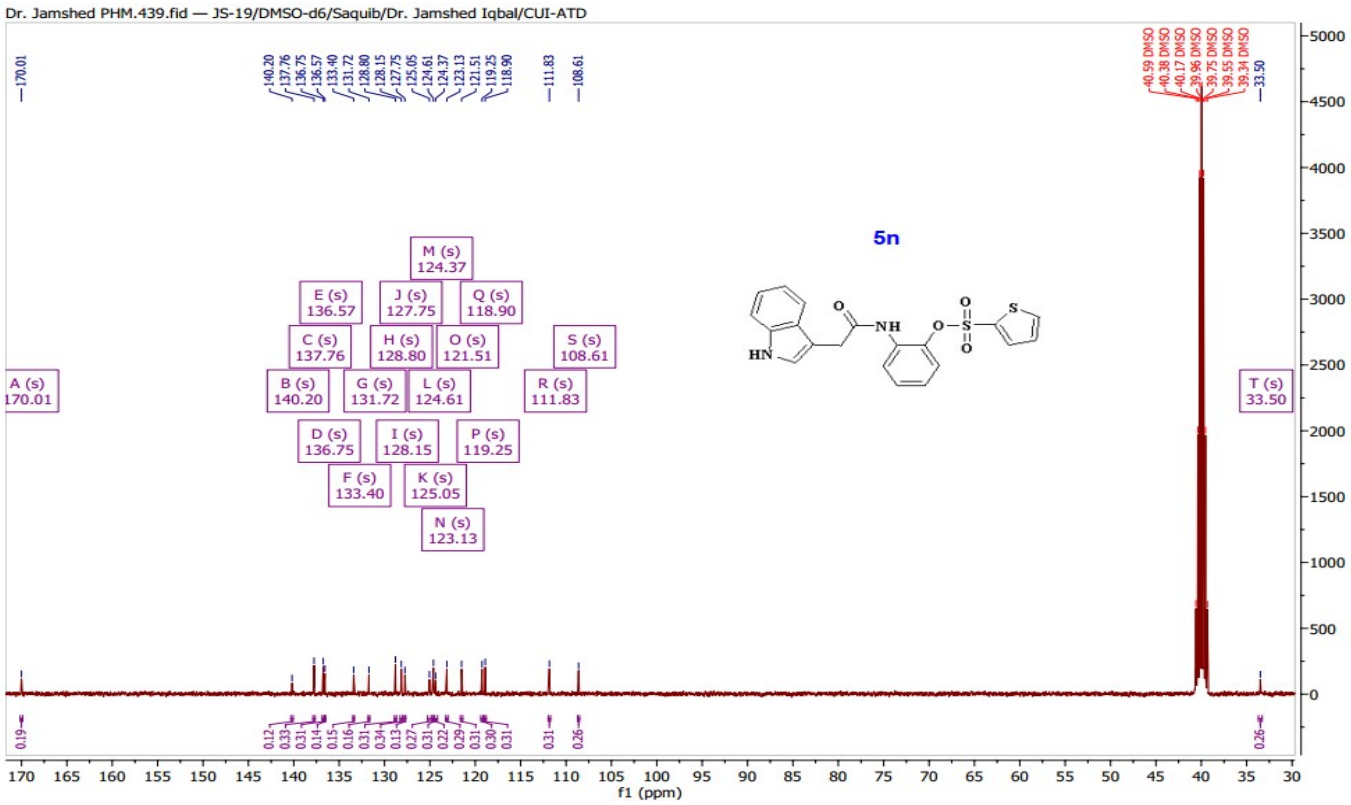
5m. ^{13}C NMR



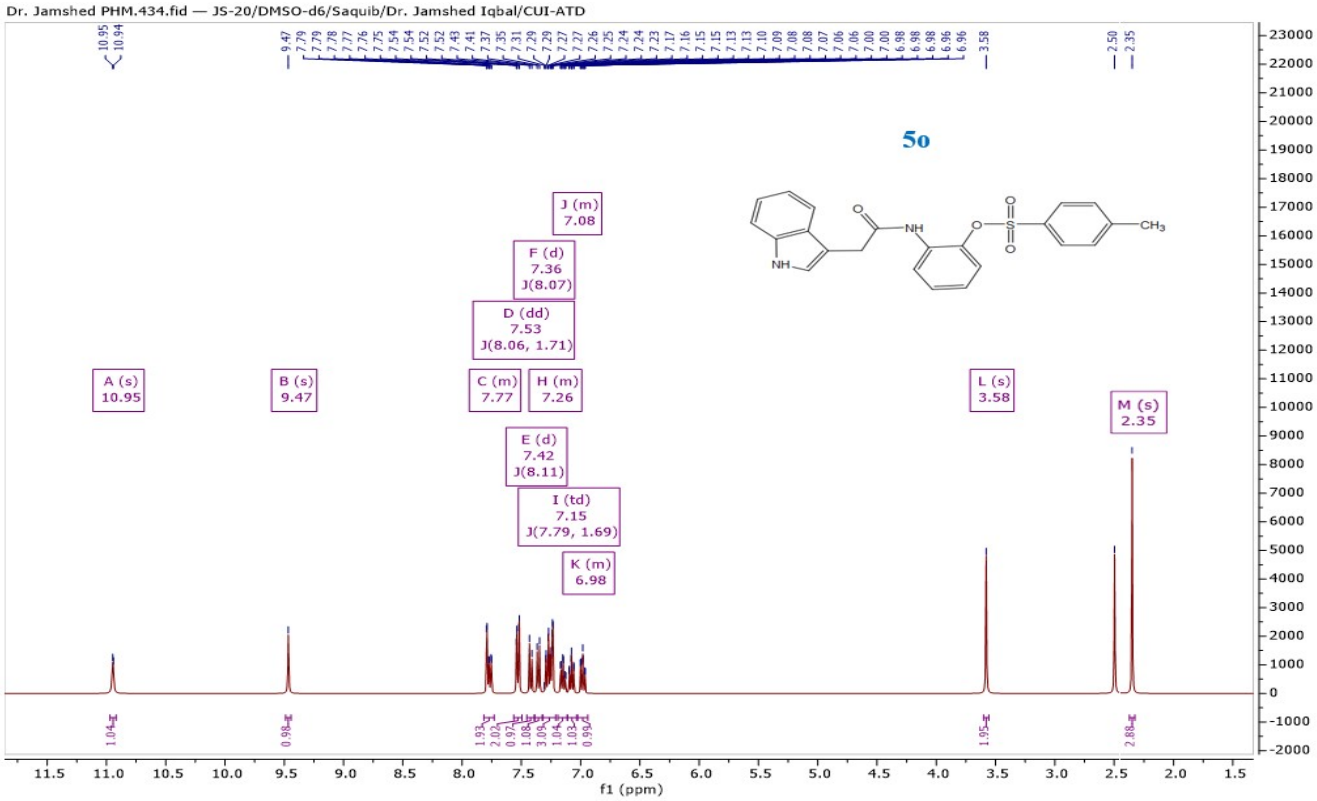
5n. ^{1}H NMR



5n. ^{13}C NMR



5o. ^{1}H NMR



5o. ^{13}C NMR