Chapter 4

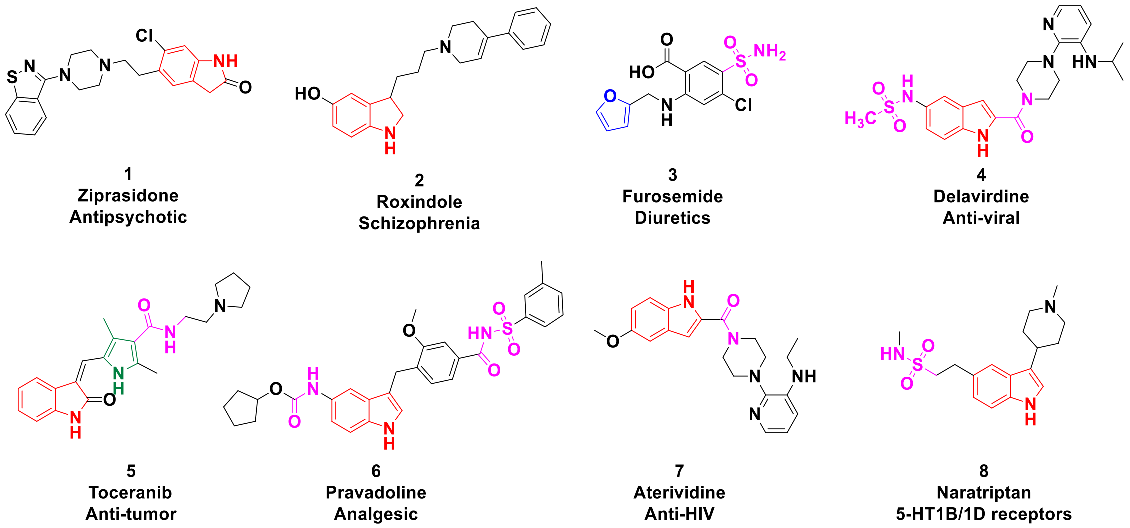
Targeted Synthesis, *In Vitro* Antimicrobial Profiling and *In Silico* Investigation of Furan- and Pyrrole-Linked Indoline Hybrids Incorporating Amide and Sulfonamide Functionalities

4.1 Introduction

Microbial pathogenic illnesses affect a substantial portion of the Earth's biomass, which accounts for approximately sixty percent of the total biomass.[164] This poses a significant risk to the health of people worldwide.[165] This problem necessitates the urgent need for new classes of pharmaceuticals that are not currently available on the market. This is because it is becoming increasingly important to address the challenges associated with antibiotic and antimicrobial resistance, which complicate both healthcare settings and agricultural practices.[166] The indoline moiety is an essential component in organic chemistry, especially because of the many uses it has in the fields of materials science and medicine.[167] This structural component, which is distinguished by its one-of-a-kind bicyclic framework, has attracted a great deal of interest due to the fact that it has the potential to be utilized in the production of a wide variety of bioactive compounds.[168] It is possible to synthesize a large variety of derivatives that have potential pharmacological effects thanks to the indoline moiety, which acts as a flexible scaffold. Its incorporation into molecular frameworks has resulted in major breakthroughs in the production of medicinal agents, therefore positioning it as a primary focus in research and innovation.[169]

Significant heterocyclic scaffolds, furan and pyrrole, are well-known for their use in synthetic and medicinal chemistry, particularly when paired with the indoline moiety. Furan and pyrrole are both examples of heterocyclic scaffolds.[170] By combining these electron-rich heterocycles with partially saturated indole, it is possible to construct frameworks that have a higher level of biological activity.[171] Amide bonds are one of the most fundamental and stable functional groups in organic and medicinal chemistry.[172] They were found prominently in drug molecules due to their powerful hydrogen-bonding capabilities and conformational stability, which contributed to improved metabolic stability and bioavailability.[173] Amide bonds are also one of the most stable functional groups. On the other hand, sulphonamide linkages are well-known pharmacophores in the field of medicinal chemistry. They are notably important in the field of antibacterial treatments, such as sulfa drugs.[174] Pyrrole-containing indoline derivatives have been found to display a wide range of pharmacological activities, including as central nervous system (CNS)-related effects,[175] anti-inflammatory effects,[176] antimicrobial effects,[177] anti-diabetic benefits,[178] anticancer effects.[179] As a result of the planarity and aromaticity of furan, as well as the structural flexibility of the indoline core, furan-indoline hybrids have garnered a lot of interest for their potential to act as enzyme inhibitors,[180] antioxidants,[181] and neuroprotective agents.[182] In a similar vein, furan-indoline hybrids have attracted attention for their potential to act as enzyme inhibitors.[183] Furthermore, it has been demonstrated that the insertion of these heterocycles into drug candidates might have an effect on the binding affinity and metabolic stability of the medication. This makes them appealing motifs for the creation of novel therapeutic treatments.[184]

Several pharmaceuticals incorporating the indoline structure have been developed and are currently marketed for their effectiveness in treating specific health conditions some are antipsychotic (Ziprasidone, **1**),[185] schizophrenia (Roxindole, **2**),[186] diuretics (Furosemide, **3**),[187] anti-viral (Delavirdine, **4**),[188] anti-tumor (Toceranib, **5**),[189] analgesic (Pravadoline, **6**),[190] anti-HIV (Aterividine,7),[191] and 5HT1B/1D receptors (Naratriptan, **8**)[192] (**Figure 1**).



1
Ziprasidone
Antipsychotic

2
Roxindole
Schizophrenia

3
Furosemide
Diuretics

4
Delavirdine
Anti-viral

5
Toceranib
Anti-tumor

6
Pravadoline
Analgesic

7
Aterividine
Anti-HIV

8
Naratriptan
5-HT1B/1D receptors

Figure 1: Marketed drugs containing furan, pyrrole and indoline antimoiety.

4.1.1 Synthetic methodologies for the substituted indoline containing framework and their biological significance

Ethyl indoline-2-carboxylate (**9**) was easily converted into its corresponding ethyl 1*H*-indole-2-carboxylate (**10**) via one step reaction with trimethylamine-*N*-oxide in toluene, and reaction was stirred at 100 °C for 20 h (**Figure 2**).[193]

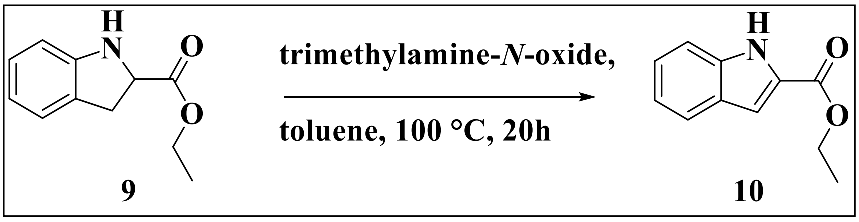


Figure 2

To stirred a solution of indoline (**11**) in MeOH and *N*,*N*-dimethylaniline, with methyl 2-(chlorosulfonyl)benzoate (**12**) was added and reaction was stirred at 25 °C for 2 h for generate the methyl 2-(indolin-1-ylsulfonyl)benzoate (**13**) (**Figure 3**).[194]

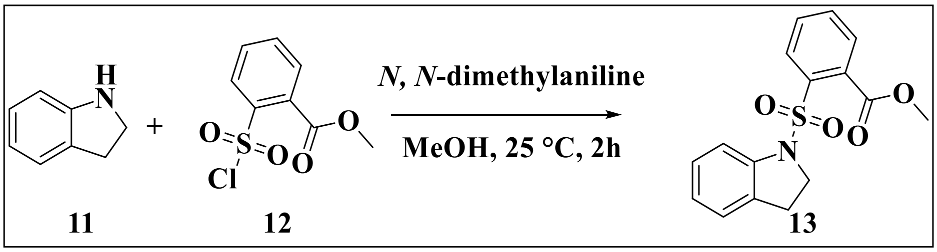


Figure 3

Reduction of 1-((2-nitrophenyl)sulphonyl)indoline(NO_2) (**14**) in presence of H_2-Pd/C in ethanol at 25 °C for 16 h under 1 atm H_2 pressure for generate the 2-(indolin-1-ylsulfonyl)aniline (**15**) (**Figure 4**).[195]

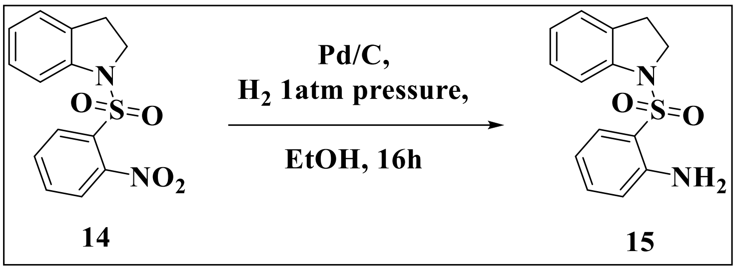


Figure 4

2-(indolin-1-ylsulfonyl)aniline (**15**) was reacted with 5-bromo-2-hydroxybenzaldehyde (**16**) in presence of acetic acid in EtOH at 25 °C for 24 h to generate the (*Z*)-4-bromo-2-(((2-(indolin-1-ylsulfonyl)phenyl)imino)methyl)phenol (imine formation) (**17**) (**Figure 5**).[196]

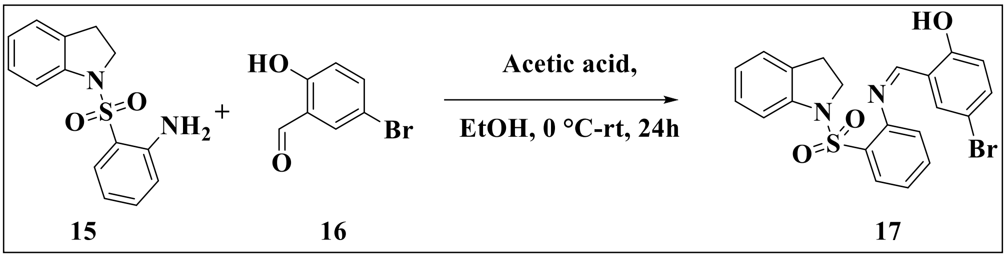


Figure 5

To a conversion of methyl 1-((4-methoxyphenyl)sulfonyl)indoline-2-carboxylate (**18**) to *N*-hydroxy-1-((4-methoxyphenyl)sulfonyl)indoline-2-carboxamide (**19**) via potassium cyanide (KCN) in THF:MeOH and stirred at 25 °C for 24 h (**Figure 6**).[197]

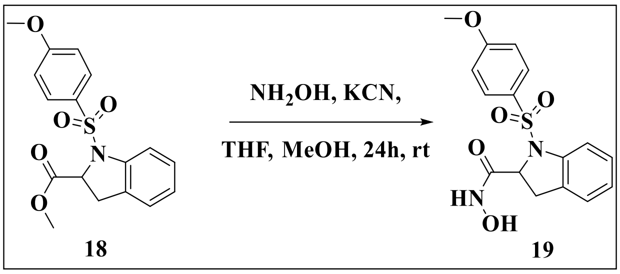


Figure 6

Nitration of methyl 1-acetylindoline-2-carboxylate (**20**) with mild condition with $Fe(NO_3)_3.9H_2O$ to generate the methyl 1-acetyl-5-nitroindoline-2-carboxylate (**21**) (**Figure 7**).[198]

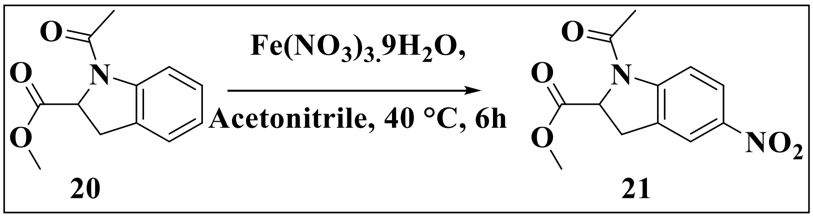


Figure 7

Ethyl 2-allyl-1-methylindoline-2-carboxylate (**24**) was prepared from ethyl 1-methylindoline-2-carboxylate (**22**) via anion generation with freshly prepared lithium diisopropylamide (LDA) and 3-bromoprop-1-ene (**23**) at -78°C under argon atmosphere (**Figure 8**).[199]

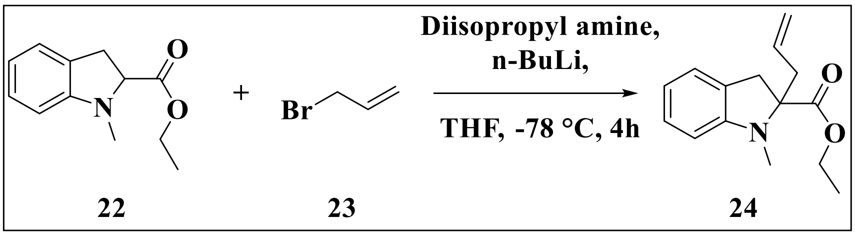


Figure 8

Double bond reduction of 1-(tert-butyl)-2-methyl indoline-1,2-dicarboxylate (**25**) with platinum (iv)oxide in acetic acid at 60 °C for 16 h under 20kg pressure of hydrogen to generate the 1-(*tert*-butyl)-2-methyloctahydro-1*H*-indole-1,2-dicarboxylate (**26**) (**Figure 9**).[200]

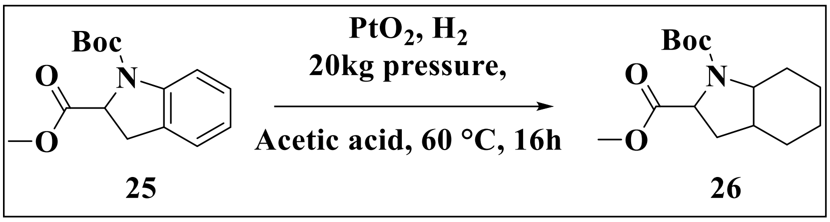


Figure 9

Some important indoline derivatives having biological activity, such as HDAC inhibitor (**26**),[201] apoptosis inducer (**27**),[202] NL-2 (**28**),[203] anticancer (**29**),[204] antimicrobial (30),[205] antiinflammatory (31),[206] antidiabetic (32),[207] antifungal (33)[208] (**Figure 10**).

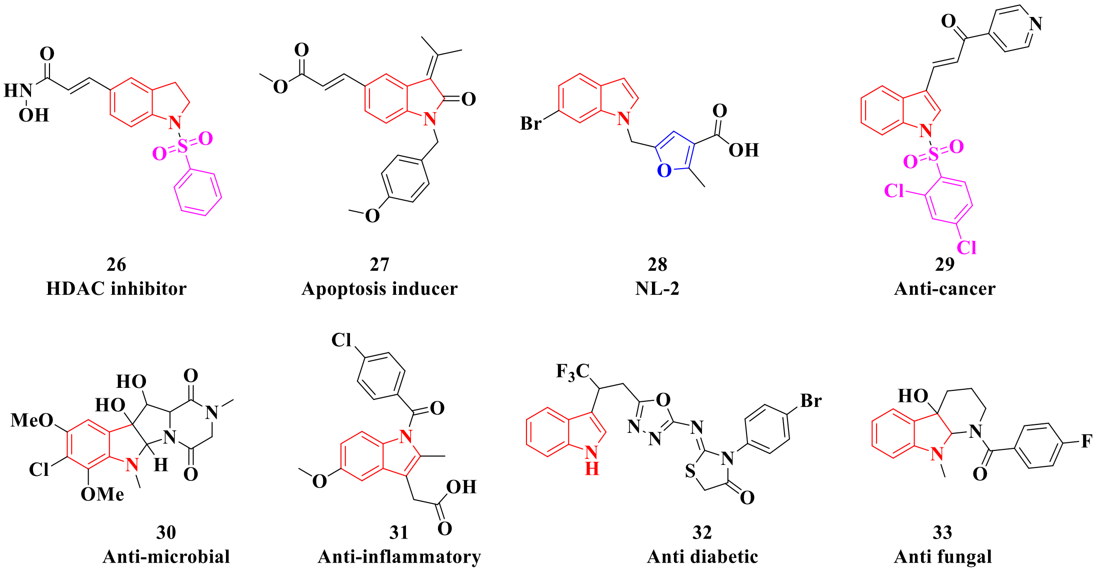

26 **HDAC inhibitor**
27 **Apoptosis inducer**
28 **NL-2**
29 **Anti-cancer**
30 **Anti-microbial**
31 **Anti-inflammatory**
32 **Anti diabetic**
33 **Anti fungal**

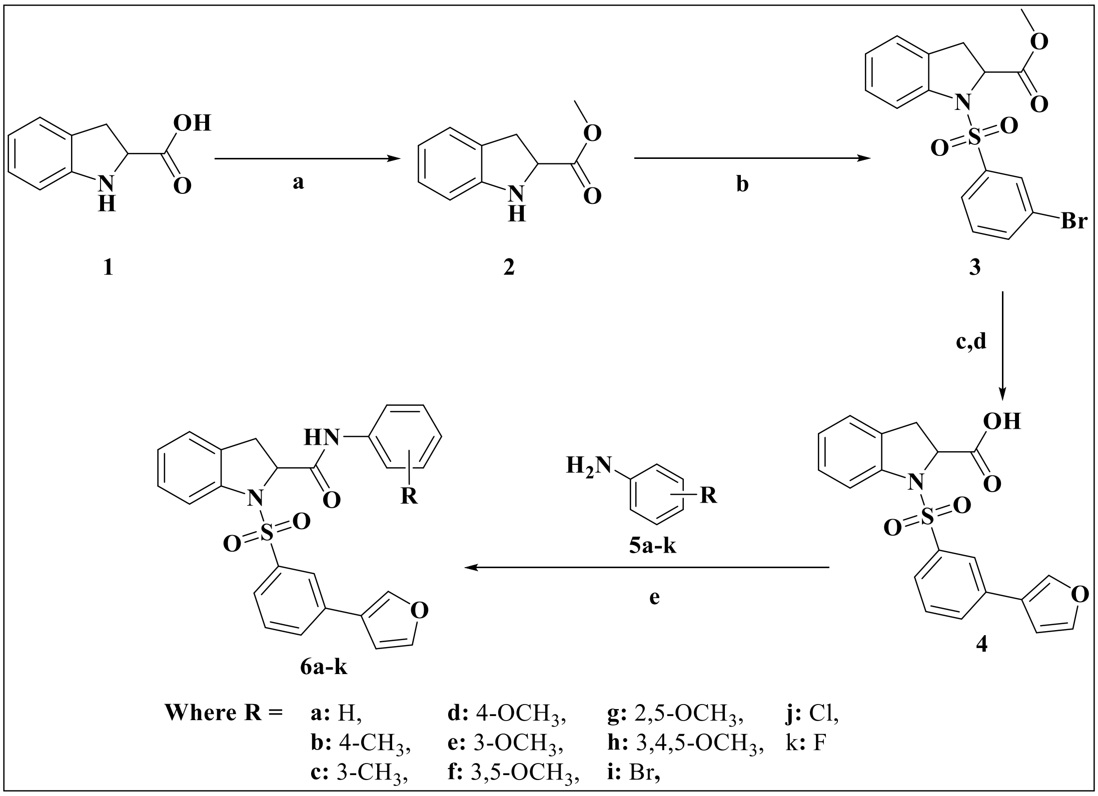
Figure 10: Important compounds containing indoline motifs.

4.2 Results and Discussion

4.2.1 Chemistry

In order to investigate a variety of chemical and possible pharmacological features a carefully designed series of compounds focused on functional group modification was used to synthesize the indoline hybrid with amide linkage containing furan ring (**6a-k**). By following a reported process, indoline-2-carboxylic acid (**1**) was easily esterified using thionyl chloride to produce methyl indoline-2-carboxylate (**2**)[209] with a 92% yield and an 82% purity by LC-MS. In a next step methyl {1-[(3-

bromophenyl)sulfonyl]}indoline-2-carboxylate (**3**)[210] with 80% yield and 91% purity was prepared from compound **2** by reacting it with 3-bromobenzenesulfonyl chloride in pyridine. By employing a suzuki reaction methodology, (furan-3-yl)boronic acid was reacted with compound **3** and the resulting crude intermediate was then hydrolysed with sodium hydroxide to produce {1-[(3-(furan-3-yl)phenyl]sulfonyl)}indoline-2-carboxylic acid (**4**)[211,212] with a 71% yield after two steps and the characteristic signal of the COOH group proton in ^1H NMR at 13.13 δppm. Acid-amine coupling of compound **4** was carried out with substituted anilins (**5a-k**) using HATU and DIPEA in DMF to obtain the final compounds (**6a-k**) with a purity above 95% (Scheme 1).

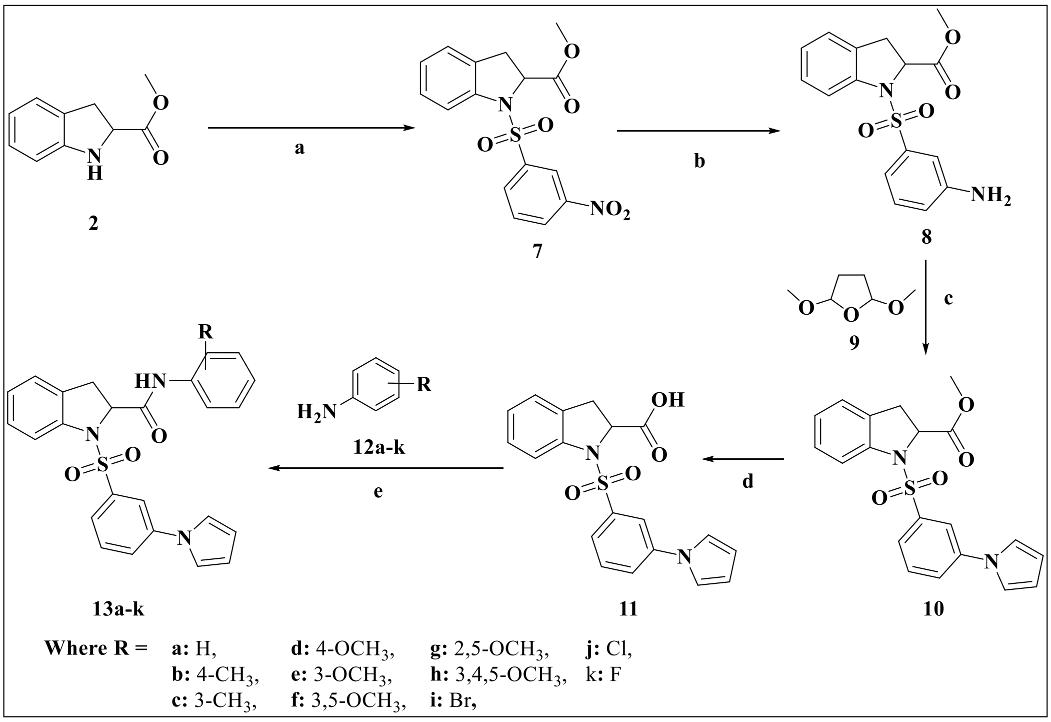


Reagents and conditions: a) $SOCl_2$ (2.0 eq), MeOH, 0 °C-rt, 3h; **b)** 3-bromobenzenesulfonyl chloride (1.2 eq), Pyridine 0 °C- rt 16h; **c)** (furan-3-yl)boronic acid (1.5 eq), $PdCl_2$ (dppf) (0.05 eq), Na_2CO_3 (3.0 eq), 1,4-dioxane:H_2O (2:1), 100 °C, 4h; **d)** NaOH (3.0 eq), MeOH:H_2O (2:1), rt, 16h; **e)** corresponding aniline (1.5 eq), HATU (1.5 eq), DIPEA (3.0 eq), DMF 0 °C-rt 3h.

Scheme 1: Synthesis of furan-indoline hybrid with amide linkage (**6a-k**).

For the synthesis of compounds **13a-k**, initially compound **2** was reacted with 3-nitrobenzenesulfonyl chloride in pyridine to obtain methyl {1-[(3-nitrophenyl)sulfonyl]}indoline-2-carboxylate (**7**) with 73% yield and 100% purity. The

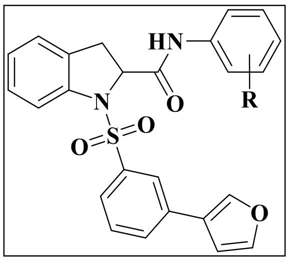
NO_2 group of compound **7** was reduced using NH_4Cl and Fe metal to produce methyl 1-[(3-aminophenyl)sulfonyl]indoline-2-carboxylate (**8**)[213] with a 92% yield and according to LC-MS the purity was 99%. Subsequently compound **8** was reacted with 2,5-dimethoxytetrahydrofuran (**9**) in acetic acid to generate pyrrole ring of compound **10** with a 71% yield and 100% purity.[214] The hydrolysed compound 1-{[3-(1*H*-pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (**11**) with 89% yield was obtained by the sodium hydroxide treatment, which has a characteristic COOH proton at 13.21 δppm in ^{1}H NMR. In a last step, HATU and DIPEA was employed to furnish acid-amine coupling of compound **11** with substituted anilins (**12a-k**) to construct the final compounds (**13a-k**) (**Scheme 2**). Using FTIR spectroscopy, ^{1}H NMR, ^{13}C NMR, elemental analysis, and LC-MS, all the newly synthesized compounds **6a-k** and **13a-k** were characterized.



Reagents and conditions: a) 3-nitrobenzenesulfonyl chloride (1.2 eq), pyridine 0 °C, rt 16h; **b)** NH_4Cl (5.0 eq), Fe (5.0 eq), EtOH:H_2O (2:1), 80 °C, 16h; **c)** Compound **9** (1.0 eq), AcOH 60 °C, 16 h; **d)** NaOH (3.0 eq), MeOH:H_2O (2:1), rt, 16h; **e)** corresponding aniline (1.5 eq), HATU (1.5 eq), DIPEA (3.0 eq), DMF 0 °C-rt 3h.

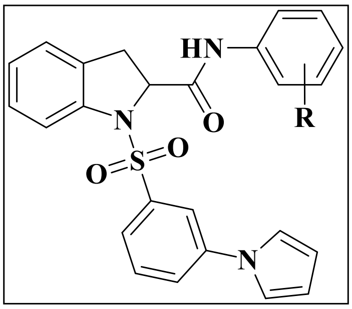
Scheme 2: Synthesis of pyrrole-indoline hybrid with amide linkage (**13a-k**).

Table 1: Physicochemical characteristics of the novel furan containing indoline derivatives **6a-k**.



Compounds	R	Molecular Weight	Molecular Formula	Yield (%)	Melting Point (°C)
6a	H	444.50	$C_{25}H_{20}N_2O_4S$	83	114-118
6b	4-CH_3	458.53	$C_{26}H_{22}N_2O_4S$	84	117-120
6c	3-CH_3	458.53	$C_{26}H_{22}N_2O_4S$	82	105-108
6d	4-OCH_3	474.53	$C_{26}H_{22}N_2O_5S$	87	102-105
6e	3-OCH_3	474.53	$C_{26}H_{22}N_2O_5S$	74	110-114
6f	3,5-OCH_3	504.55	$C_{27}H_{24}N_2O_6S$	84	98-100
6g	2,5-OCH_3	504.55	$C_{27}H_{24}N_2O_6S$	80	100-103
6h	3,4,5-OCH_3	534.58	$C_{28}H_{26}N_2O_7S$	80	99-101
6i	Br	523.40	$C_{25}H_{19}BrN_2O_4S$	83	107-110
6j	Cl	478.95	$C_{25}H_{19}ClN_2O_4S$	90	102-105
6k	F	462.49	$C_{25}H_{19}FN_2O_4S$	80	103-106

Table 2: Physicochemical characteristics of the novel pyrrole containing indoline derivatives **13a-k**.



Compounds	R	Molecular Weight	Molecular Formula	Yield (%)	Melting Point (°C)
13a	H	443.52	$C_{25}H_{21}N_3O_3S$	66	110-112

13b	4-CH_3	457.54	$C_{26}H_{23}N_3O_3S$	80	128-130
13c	3-CH_3	457.54	$C_{26}H_{23}N_3O_4S$	80	119-121
13d	4-OCH_3	473.54	$C_{26}H_{23}N_3O_4S$	78	114-116
13e	3-OCH_3	473.54	$C_{26}H_{23}N_3O_4S$	78	120-122
13f	3,5-OCH_3	503.57	$C_{27}H_{25}N_3O_5S$	73	125-130
13g	2,5-OCH_3	503.57	$C_{27}H_{25}N_3O_5S$	73	125-130
13h	3,4,5-OCH_3	533.60	$C_{28}H_{27}N_3O_6S$	76	118-122
13i	Br	522.41	$C_{25}H_{20}BrN_3O_3S$	84	112-115
13j	Cl	477.96	$C_{25}H_{20}ClN_3O_3S$	88	117-120
13k	F	461.51	$C_{25}H_{20}FN_3O_3S$	92	121-124

4.3 Antimicrobial activity

The potential towards antimicrobial activity of the newly synthesized hybrid indoline derivatives with furan (**6a-k**) and pyrrole (**13a-k**) was tested against a variety of Gram-positive (*Bacillus subtilis* ATCC6051 and *Staphylococcus aureus* ATCC12600), Gram-negative (*Pseudomonas aeruginosa* ATCC10415 and *Escherichia coli* ATCC9637), and fungal strains (*Aspergillus niger* ATCC16888 and *Candida albicans* ATCC10231). Nystatin was used as a positive control for antifungal activity, while ampicillin and gentamicin served as positive controls for antibacterial activity when measuring the inhibition zone (mm). The antimicrobial evaluation demonstrated that these compounds exhibited significant activity against most of the tested strains, and the results were recorded in Figures **11** to **13**.

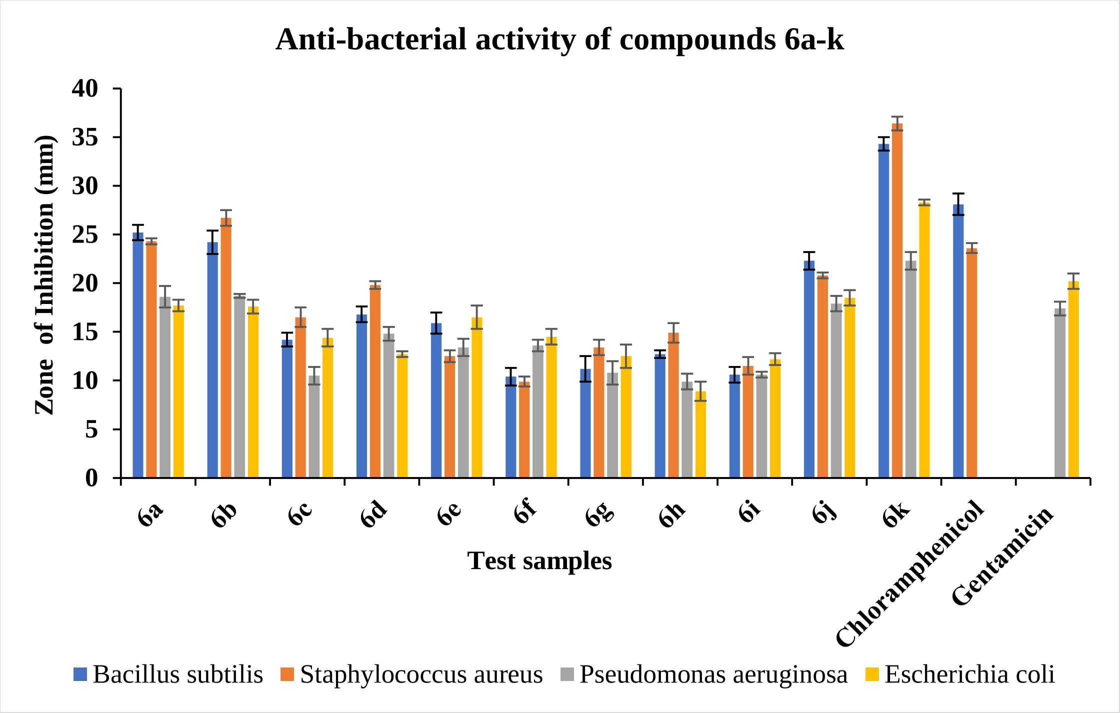


Figure 11: Graphical presentation of anti-bacterial activity of newly synthesized furan containing indoline derivatives **6a-k**.

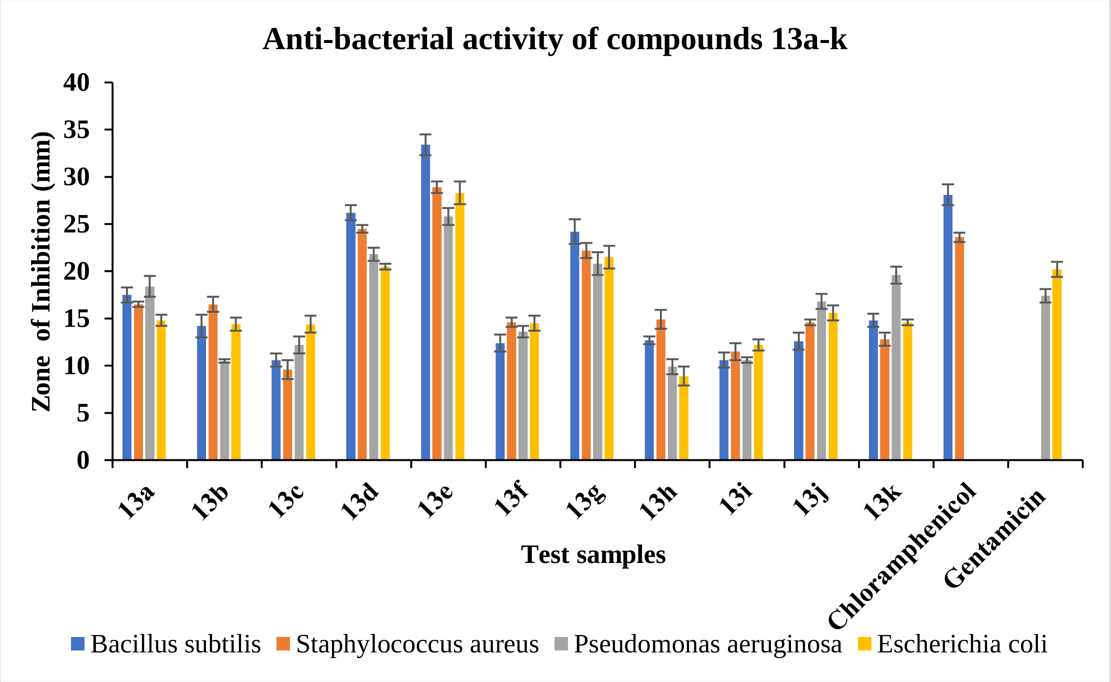


Figure 12: Graphical presentation of anti-bacterial activity of newly synthesized pyrrol containing indoline derivatives **13a-k**.

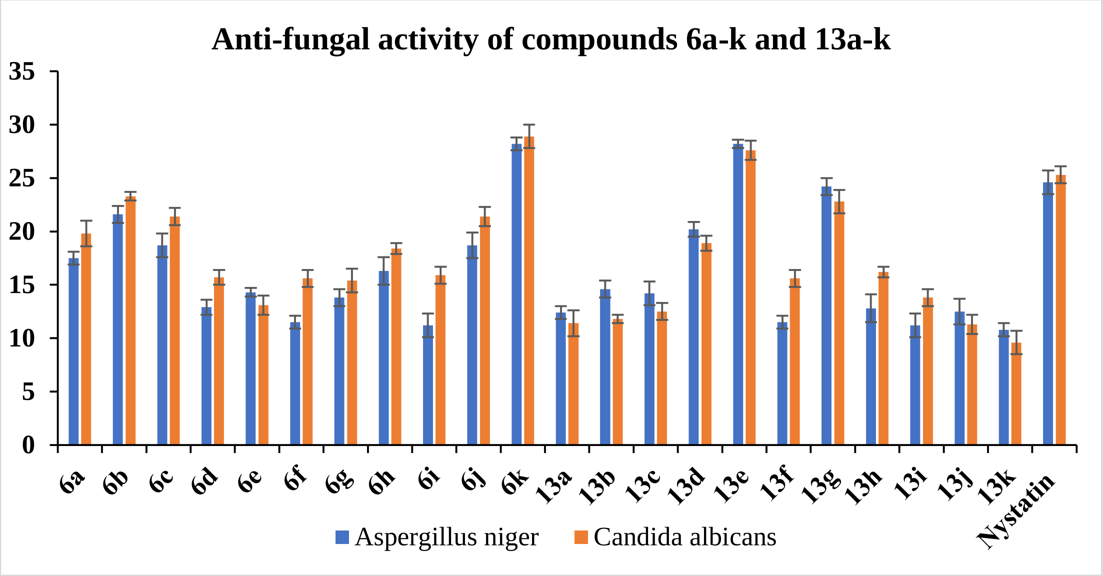


Figure 13: Graphical presentation of anti-fungal activity of newly synthesized furan containing indoline derivatives **6a-k** and pyrrole containing indoline derivatives **13a-k**.

4.4 Structure Activity Relationship (SAR)

In context of *Gram-positive* bacteria, among the furan-containing indoline derivatives (**6a-k**), the compound containing 4-fluoro substitution (**6k**) exhibited promising antibacterial activity against both *B. subtilis* (34.3 ± 0.7 mm) and *S. aureus* (36.4 ± 0.7 mm). While out of the pyrrole-containing indoline derivatives (**13a-k**), compound **13e** bearing a 3-methoxy group demonstrated encouraging antibacterial activity against the same pathogens, specifically *B. subtilis* (33.4 ± 1.1 mm) and *S. aureus* (28.9 ± 0.6 mm). In contrast, the standard drug chloramphenicol produced inhibitory zones of 28.1 ± 1.1 mm and 23.6 ± 0.5 mm against the respective bacterial strains. Against *Gram-negative* pathogens, both compounds **6k** and **13e** showed promising results compared to the standard drug tested.

Regarding antifungal activity, compound **6k** with a 4-fluoro substitution exhibited the highest activity, whereas compound **13k** with the same substitution showed the least activity among all furan- and pyrrole-containing derivatives. In the case of 3-methoxy substituted derivatives, compound **13e** demonstrated superior activity among pyrrole series, while compound **6e** showcased comparatively lower activity within the furan series. Amongst the methyl substited derivatives with the furan ring, compounds **6b** (4-CH_3) and **6c** (3-CH_3) were more potent than their pyrrole counterparts **13b** (4-CH_3) and **13c** (3-CH_3). Additionally, the halogen substituted furan-containing derivatives **6i** (4-

Br) and **6j** (4-Cl) displayed higher activity than the corresponding pyrrole-containing derivatives **13i** (4-Br) and compound **13j** (4-Cl). Overall, the hybrid derivatives containing furan ring (**6a-k**) demonstrated better and more promising activity compared to those containing pyrrole ring (**13a-k**).

4.5 Molecular Docking

The molecular docking study provided valuable insight into the potential interaction strength and stability of the compounds within the protein binding pocket.[215] Among the compounds **6a-k** and **13a-k**, compound **6k** (-8.4 kcal/mol) and **13e** (-9.8 kcal/mol) exhibited the highest binding affinities within their respective derivatives, outperforming the reference drug chloramphenicol (-6.3 kcal/mol). Other compounds, such as **6a**, **6b**, and **6j** demonstrated similarly strong binding affinities (-8.3 kcal/mol), while compounds **13a**, **13b** and **13j** showed good binding affinities of -7.9, -8.0, -8.0 kcal/mol respectively (Table 3), indicating their potential as potent inhibitors of the 4DUH protein.

Table 3. Molecular docking results of the compounds **6a-k** and **13a-k** against *E. coli* DNA gyrase B protein receptor (PDB: 4DUH).

Comp.	Binding energy (Kcal/mol)	Interacting residues (Å)	No. of H bonds	Comp.	Binding energy (Kcal/mol)	Interacting residues (Å)	No. of H bonds
6a	-8.3	Arg20 (3.80), Lys57 (3.81), Glu174 (3.90), Ser202 (2.54), Arg204 (2.72)	02	**13a**	-7.9	Arg20 (3.57), Glu58 (3.59), His147 (3.70), Glu174 (3.70)	0
6b	-8.3	Ile48 (3.57), Ala53 (3.75), Lys103 (3.73), Leu194 (3.94)	01	**13b**	-8.0	Gln72 (3.69), Asp74 (3.83), Ile140 (3.56), Glu146 (3.73), Glu46 (4.65)	0
6c	-7.6	Arg20 (3.44), Lys57 (3.60), His217 (3.92), Asp17 (3.06)	01	**13c**	-8.0	Lys57 (3.72), Glu58 (3.65), Glu174 (3.79), Ser202 (3.10), Arg204 (2.82)	02

6d	-7.9	Pro23 (3.74), Glu173 (3.85), His217 (3.81), Ser202 (3.64), Arg204 (2.38)	02	**13d**	-8.2	Glu58 (3.75), Ile60 (3.61), His147 (3.69), Glu58 (2.78), Asp73 (3.49), Gln135 (2.70), Asp17 (5.11), Glu58 (4.23)	02
6e	-8.0	Arg20 (3.96), Glu174 (3.65), Lys (2.25), Arg204 (5.43)	01	**13e**	-9.8	Asn46 (3.66), Arg76 (3.77), Ile78 (3.44), Pro79 (3.63), Ile94 (3.70), Lys103 (3.93), Phe104 (3.85), Val120 (3.35), Asn46 (4.08), Glu50 (3.22)	02
6f	-7.7	Arg20 (3.71), Lys21 (3.87), Arg204 (3.12)	01	**13f**	-8.0	Arg20 (3.90), Glu58 (3.54), Glu174 (3.77), Glu58 (2.63), Glu174 (3.07)	02
6g	-7.8	Arg20 (3.67), Lys21 (3.63), Lys57 (3.93), Lys162 (2.35), Asp17 (4.48), Glu58 (4.46)	01	**13g**	-8.2	Arg20 (3.76), Ser202 (2.99), Ser202 (2.08), Arg204 (1.96), Glu58 (4.85)	03
6h	-7.5	Arg20 (3.95), Glu58 (3.52), Glu174 (3.55), Arg20 (3.50), Ser199 (3.40), Ser202 (3.63), Asp17 (4.79), Glu58 (4.62)	03	**13h**	-8.1	Arg20 (3.96), Lys57 (3.77), His147 (3.87), Glu174 (3.95), Glu58 (2.90), Glu174 (3.08), Asp17 (5.14)	02
6i	-7.7	Arg20 (3.63), Lys21 (3.75), Glu58 (3.70), His217 (3.65), Ser202 (3.46), Arg204 (2.29)	02	**13i**	-7.8	Leu16 (3.66), Gln72 (3.55), Asp74 (3.69), His147 (3.99), Asp17 (2.50), Arg20 (3.01), Lys162 (3.29)	03

6j	-8.3	Arg20 (3.93), Lys57 (3.74), Arg20 (3.28), Arg204 (3.42)	02	**13j**	-7.9	His217 (3.98), Asp17 (2.81), Arg20 (2.55), Arg204 (2.37)	03
6k	-8.4	Lys57 (3.80), Asp74 (3.66), Ser202 (2.17), Arg204 (2.17), Asp17 (5.01), Glu58 (4.27)	02	**13k**	-7.9	Glu174 (3.61), His217 (3.83), Asp17 (3.01), Ser202 (2.66), Arg204 (2.89)	03
Chloramphenicol					-6.3	Ile78 (3.97), Arg76 (2.42), Gly77 (2.02), Thr165 (2.17)	02

The docking analysis identified the active site of the 4DUH protein as the primary binding pocket for compounds **6k** and **13e**. The interaction of the ligand within the binding pocket is stabilized through key hydrogen bonding and hydrophobic interactions. The 2D and 3D interaction maps for **6k** (Figures **6a** and **6b**), **13e** (Figures **6c** and **6d**) and chloramphenicol (Figures **6e** and **6f**) highlight the involvement of essential residues in ligand binding, which contribute to the ligand's high affinity. The 2D interaction map for **6k** (Figure **6a**) illustrates the detailed interaction profile with the 4DUH protein. Critical hydrogen bonds were observed with residues ARG-204, SER-202, and GLU-174, which help stabilize the ligand within the binding site. Hydrophobic interactions with ASP-74 and LYS-57 further reinforce binding stability, with electrostatic interactions also contribute to the enhanced affinity. Similarly, the 2D interaction map for **13e** (**Figure 6c**) shows its interaction profile with the 4DUH protein. Key hydrogen bonds were observed with GLU-150, ASP-76, and THR-165, stabilizing the ligand within the binding pocket. Hydrophobic interactions with VAL-120 and ALA-47, along with electrostatic interactions, further enhance the binding affinity.

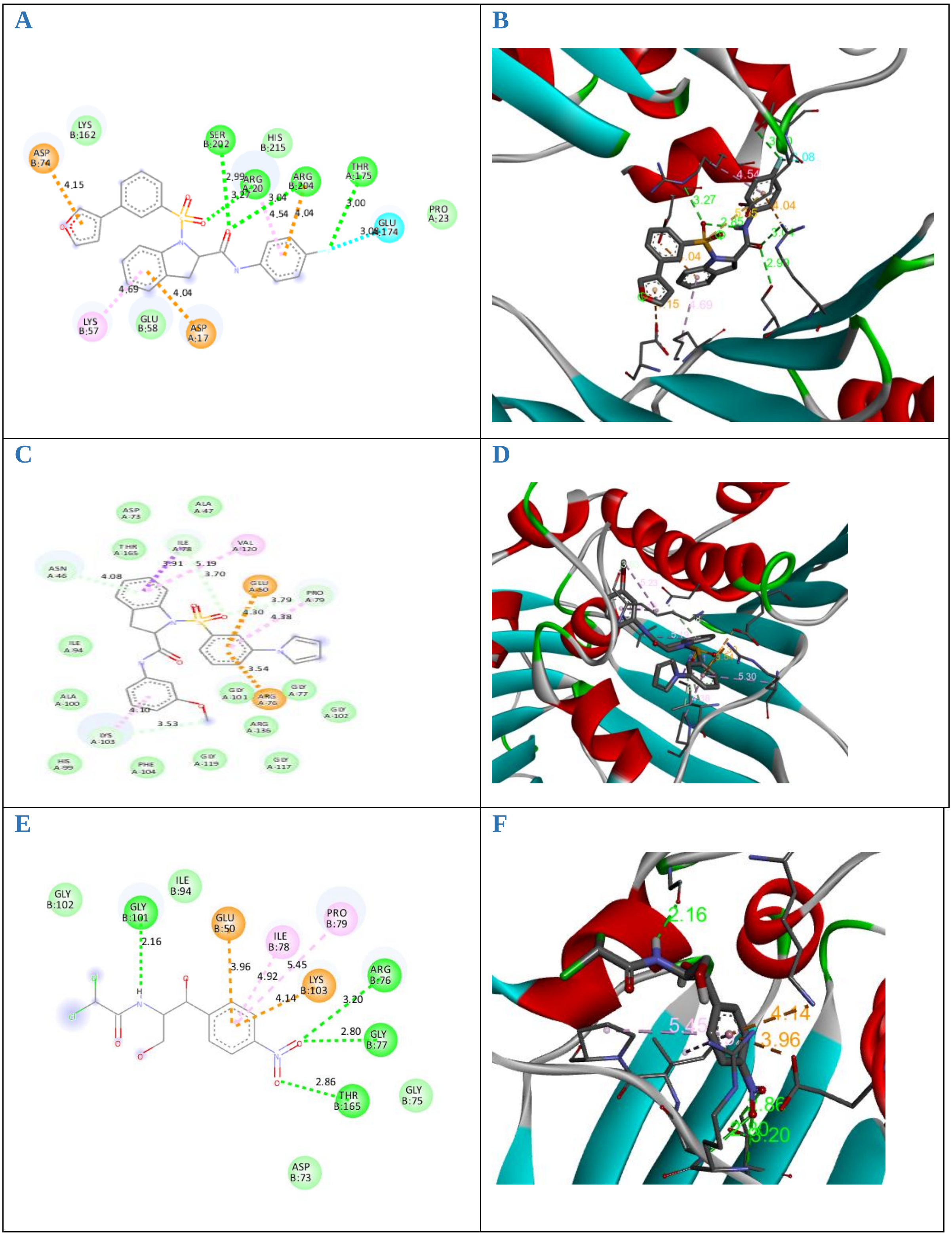


Figure 14: Receptor-ligand interaction on a 2D diagram: (**A**) compound **6k**; (**C**) compound **13e**; (**E**) chloramphenicol. Receptor-ligand interaction on a 3D diagram: (**B**) compound **6k**; (**D**) compound **13e**; **(F)** chloramphenicol.

4.6 Molecular Dynamics Simulation Analysis

After the docking analysis, compound **6k** and **13e** were selected for further investigation using molecular dynamics simulation (MDS). In MDS, the root mean square deviation (RMSD) and root mean square fluctuation (RMSF) provide valuable insights into the structural dynamics of the protein-ligand complex over the simulation period.[216]

The RMSD plot (**Figure 15**) indicates that the **6k-**4DUH complex remained stable throughout the 100 ns simulation. The protein backbone RMSD fluctuated between 3.0-6.4 Å, reaching equilibrium after approximately 40 ns. The ligand RMSD remained within 7.0-9.5 Å, suggesting minimal positional deviations and strong retention within the binding pocket. In contrast, the RMSD plot for the **13e-**4DUH complex (**Figure 16**) showed significant initial fluctuations, with RMSD values reaching as high as 80 Å during the first 30 ns. However, the system stabilized after 40 ns, with the protein backbone RMSD converging around 30 Å and the ligand RMSD stabilizing around 35 Å. This suggests that despite early instability, the ligand ultimately adopted a stable conformation within the binding pocket.

The RMSF plot (**Figures 17** and **18**) highlights the flexibility of individual residues, most residues exhibited low fluctuation. However, higher RMSF values for **6k** (**Figure 17**) was observed at residue indices around 300, suggesting flexibility in the loop region, which does not disrupt the ligand binding stability. While the RMSF values for **13e** (**Figure 18**) was observed at residue indices 50-100 and 180-220, corresponding to loop regions. The binding site residues, however, exhibited relatively low fluctuations, indicating strong ligand engagement within the active site. The binding site residues remained relatively stable throughout the simulation, confirming strong ligand engagement.

The hydrogen bond occupancy analysis (**Figures 19** and **20**) further supported stable interactions during the simulation. The analysis for **6k** (**Figure 19**) showed that key residues ASP-74, ARG-204, and GLU-174 showed high interaction fractions, consistently stabilizing the ligand within the binding pocket. The average of 3-5 hydrogen bonds was maintained throughout the simulation, reinforcing the ligand's strong binding profile. Similarly, for **13e** (**Figure 20**), residues GLU-150, ASP-76, and THR-165 demonstrated high interaction fractions, indicating their persistent role in stabilizing the ligand within the active site. The average number of hydrogen bonds during the simulation was approximately 2-4, supporting the ligand's strong binding profile.

The computed interaction energy analysis revealed that van der Waals and electrostatic forces were the primary contributors to ligand binding. The energy profile remained stable throughout the simulation, indicating that both the **6k-**4DUH and **13e-**4DUH complexes achieved thermodynamic stability. Cluster analysis of the simulation trajectory identified a dominant conformations, with the primary cluster representing over 75% of frames for **6k** and over 60% for **13e**, suggesting stable ligand binding poses. The convergence analysis of RMSD and energy plots confirmed that equilibrium was achieved after 40 ns, indicating that both systems attained a stable state.

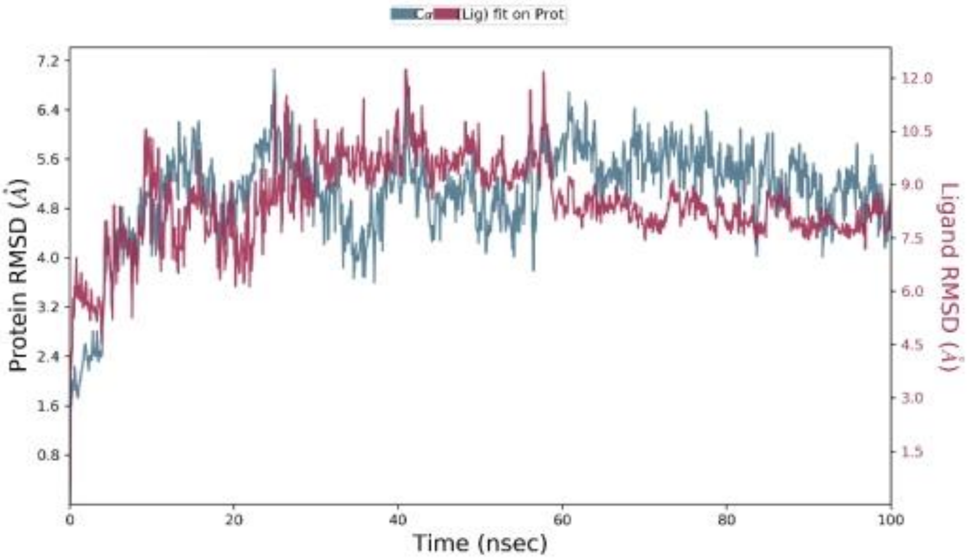


Figure 15: RMSD plot of compound **6k-**4DUH complex.

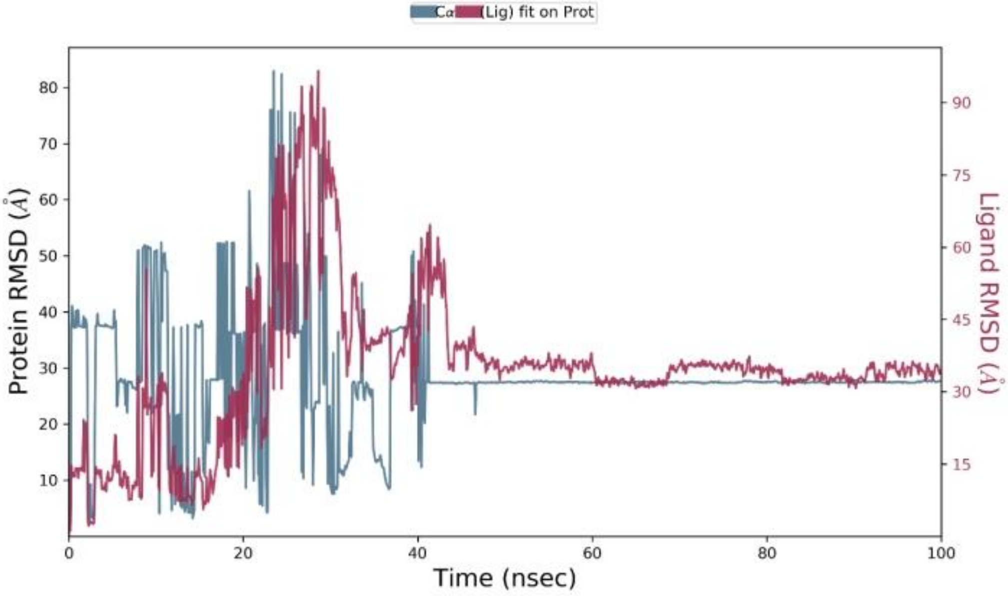


Figure 16: RMSD plot of compound **13e-**4DUH complex.

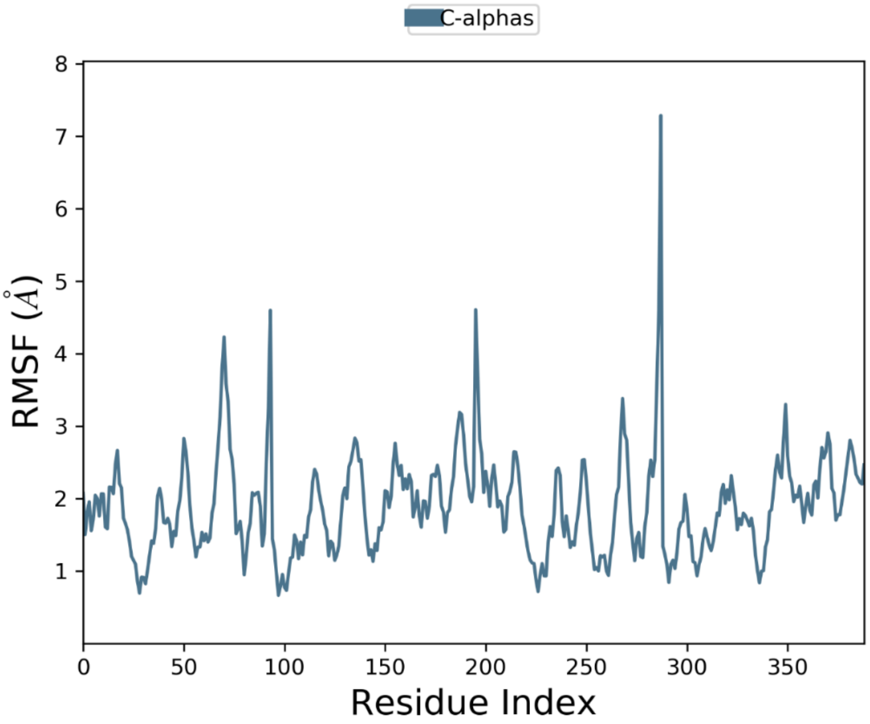


Figure 17: RMSF plot of compound **6k**-4DUH complex

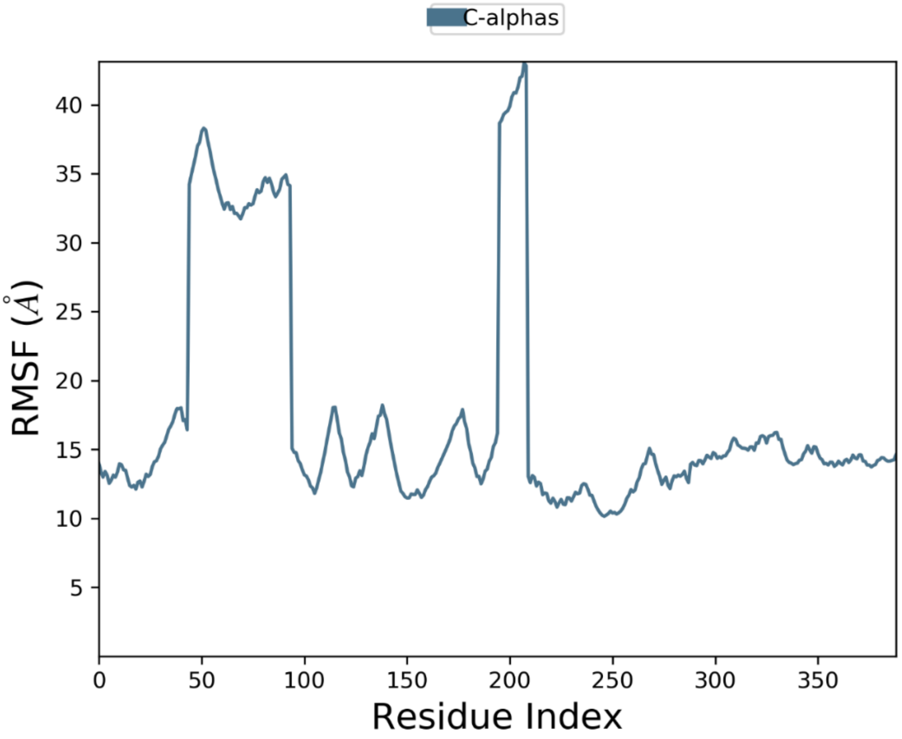


Figure 18: RMSF plot of compound **13e**-4DUH complex

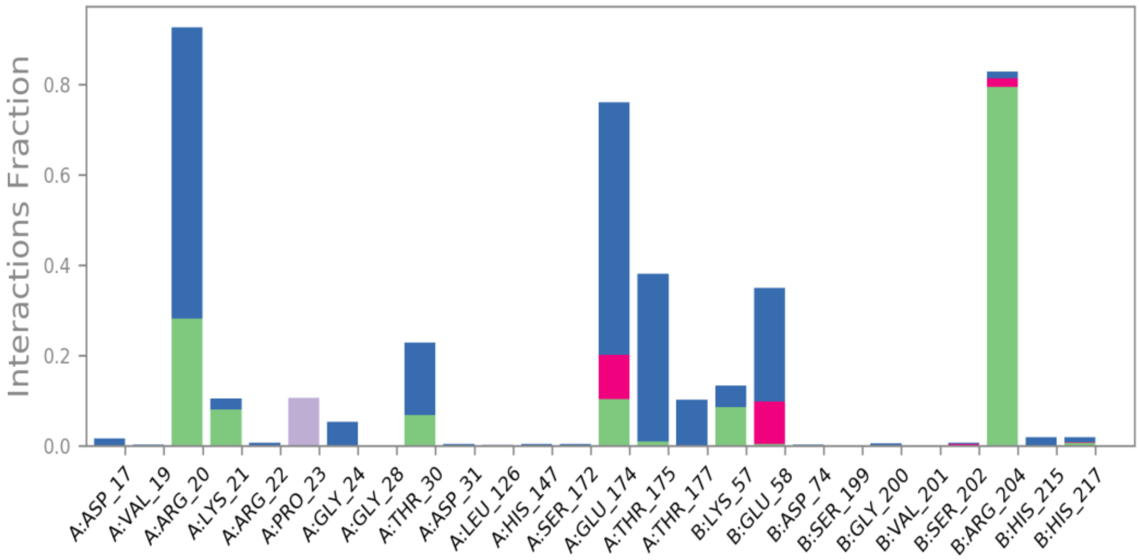


Figure 19: Interaction graph of compound **6k**-4DUH contacts.

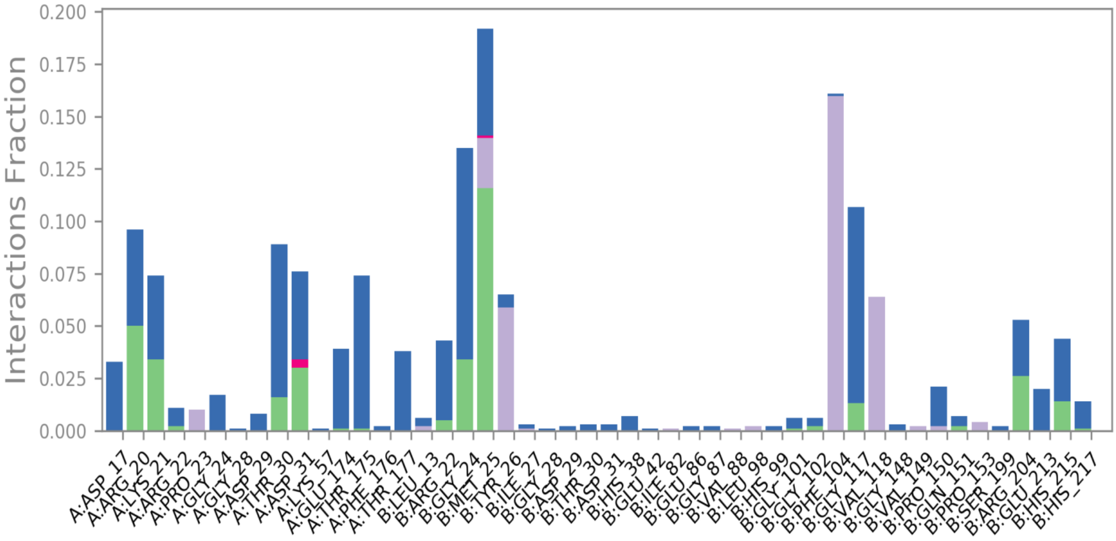


Figure 20: Interaction graph of compound **13e**-4DUH contacts.

4.7 ADMET evaluation

Many potential drug candidates fail to advance in the drug development process due to inadequate pharmacokinetic and physicochemical properties.[217] However, employing SwissADMET methods t enables early evaluation of newly synthesized compounds, allowing researchers to identify and address such limitations during the initial stages of drug discovery.[218] The ADMET assessment of the newly synthesized indoline derivatives, as summarized in Table 4, revealed that the water solubility (Log S) values ranged from -5.25 to -6.34, indicating moderate solubility and suggesting potential oral bioavailability. The lipophilicity (Log P_o/w) values ranged from 4.75 to 5.98, remaining below the threshold of 6, indicative of favorable membrane permeability. Notably, all synthesized compounds complied with Lipinski's Rule of Five, with the exception of **6f**, **6g**, **6h**, **6i**, **13f**, **13g**, **13h** and **13i**, whose molecular weights exceeded 500 Da. The central nervous system (CNS) permeability scores for the indoline derivatives were within the range of -3.37 to -1.86, suggesting limited but acceptable CNS penetration. Additionally, the hERG inhibition scores is in the range 0.64 to 0.78, which further support the drug-like nature with a relatively low risk of cardiotoxicity for these molecules. In summary, all the parameters indicate that most of the synthesized compounds possess promising pharmacokinetic and physicochemical characteristics.

Table 2. ADMET properties of newly synthesized furan containing indoline (**6a-k**) derivatives and pyrrole containing indoline (**13a-k**) derivatives.

Physicochemical properties*						**Pharmacokinetics***		**Medicinal chemistry***		**Distribution^**		**Toxicity$^{\$}$**			
Compound	**MW$^{\#}$**	**HBA**	**HBD**	**TPSA**	**Log S**	**GIA**	**Log Kp**	**ROF**	**SA**	**CNS permeability**	**BBB permeability**	**hERG Blockers**	**hERG Blockers (10um)**	**Skin Sensitization**	**Eye Irritation**
6a	444.5	4	1	88	-5.43	High	-5.97	0	3.96	-2.01	-0.57	0.68	0.58	0.32	0.81
6b	458.5	4	1	88	-5.74	High	-5.79	0	4.07	-1.92	-0.58	0.70	0.60	0.29	0.81
6c	458.5	4	1	88	-5.74	High	-5.79	0	4.08	-1.90	-0.51	0.69	0.58	0.32	0.84
6d	474.5	5	1	97.23	-5.50	High	-6.17	0	4.05	-2.19	-0.76	0.72	0.57	0.12	0.69
6e	474.5	5	1	97.23	-5.50	High	-6.17	0	4.09	-2.18	-0.69	0.71	0.58	0.12	0.75
6f	504.5	6	1	106.46	-5.58	High	-6.37	1	4.27	-2.37	-1.10	0.72	0.59	0.10	0.58
6g	504.5	6	1	106.46	-5.58	High	-6.37	1	4.30	-2.32	-0.92	0.74	0.56	0.07	0.49
6h	534.5	7	1	115.69	-5.66	Low	-6.57	1	4.43	-3.29	-1.31	0.73	0.62	0.07	0.39
6i	523.4	4	1	88	-6.34	High	-5.96	1	3.99	-1.86	-0.77	0.72	0.64	0.43	0.86
6j	478.9	4	1	88	-6.03	High	-5.73	0	3.95	-1.88	-0.76	0.80	0.70	0.35	0.61
6k	462.4	5	1	88	-5.59	High	-6.00	0	3.96	-2.01	-0.79	0.69	0.60	0.11	0.72
13a	443.5	3	1	79.79	-5.25	High	-6.17	0	3.84	-2.10	-0.56	0.64	0.61	0.83	0.52
13b	457.5	3	1	79.79	-5.54	High	-6.00	0	3.95	-2.03	-0.57	0.66	0.63	0.81	0.52
13c	457.5	3	1	79.79	-5.54	High	-6.00	0	3.96	-2.01	-0.50	0.66	0.61	0.83	0.58
13d	473.5	4	1	89.02	-5.32	High	-6.37	0	3.93	-2.29	-0.74	0.69	0.60	0.59	0.36
13e	473.5	4	1	89.02	-5.32	High	-6.37	0	3.97	-2.28	-0.67	0.68	0.61	0.60	0.43
13f	503.5	5	1	98.25	-5.39	High	-6.57	1	4.15	-2.47	-1.08	0.68	0.62	0.54	0.26
13g	503.5	5	1	98.25	-5.39	High	-6.57	1	4.19	-2.43	-0.90	0.71	0.59	0.43	0.20

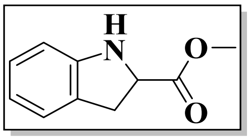
13h	533.6	6	1	107.48	-5.47	High	-6.78	1	4.32	-3.37	-1.29	0.70	0.64	0.46	0.14
13i	522.4	3	1	79.79	-6.15	High	-6.16	1	3.88	-1.97	-0.75	0.69	0.67	0.89	0.60
13j	477.9	3	1	79.79	-6.15	High	-6.16	1	3.88	-1.99	-0.74	0.78	0.73	0.85	0.29
13k	461.5	4	1	79.79	-5.40	High	-6.20	0	3.84	-2.14	-0.77	0.65	0.63	0.57	0.40
Doxycycline	444.4	9	6	181.62	-2.35	Low	-8.63	0	5.25	-4.07	-1.98	0.006	0.02	0.97	0.20

Analyzed using: *SwissADMET, ^pkCSM, and $^{\$}$ADMET3.0. $^{\#}$Molecular Weight (MW), hydrogen bond acceptors (HBA), hydrogen bond donors (HBD), topological polar surface area (TPSA), water solubility (Log S), gastrointestinal absorption (GIA), skin permeation (Log Kp), Lipinski's rule of five (RoF), encompassing synthetic accessibility (SA), central nervous system (CNS permeability), Blood–brain barrier (BBB permeability), human ether-à-go-go-related gene (hERG).

4.8 Experimental Section

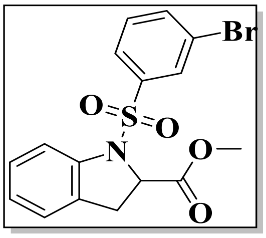
4.8.1 Chemistry

Synthesis of methyl indoline-2-carboxylate (2)



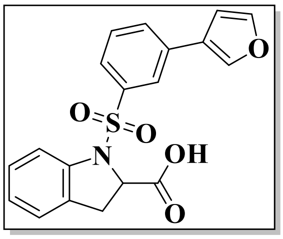
Compound methyl indoline-2-carboxylate (**2**) was synthesized using previously reported method with yield: 92%. mp: 150-152 °C (Reported mp: 151-155 °C).[209]

Procedure for the synthesis of methyl 1-[(3-bromophenyl) sulfonyl]indoline-2-carboxylate (3)



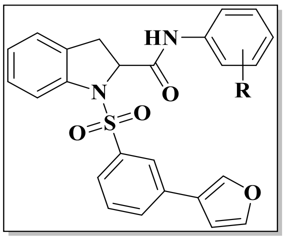
To a solution of methyl indoline-2-carboxylate (10 g, 56.43 mmol) in pyridine (200 mL) in 3-neck RBF under nitrogen atmosphere, 3-bromobenzenesulfonyl chloride (17.30 g, 67.72 mmol) at 0 °C and the reaction was stirred at 25 °C for 16h. After completion of the reaction, reaction was quenched with dilute HCl to adjust the pH in the range of 3 to 4, the resulting mass was extracted with ethyl acetate (2 times). The combined organic layer was washed with a brine and evaporated to get crude product. The obtained crude was purified using flash chromatography (0-15% EtOAc in hexane) to obtain pale white solid (18 g, 80% yield) methyl 1-[(3-bromophenyl)sulfonyl]indoline-2-carboxylate (**3**).[210] mp: 150-152 °C. IR (KBr) ν_{max}/cm^{-1}: 3035 (aromatic CH), 2950 (aliphatic CH), 1750 (COO), 1571 (C=C), 1112 (C-N), 1026 (C-O). ^{1}H NMR (400 MHz, *DMSO-d*$_6$): δppm 8.00-7.99 (t, *J* = 2Hz, 1H, Ar-CH), 7.90-7.85 (m, 2H, 2 x Ar-CH), 7.53-7.49 (t, *J* = 8Hz, 1H, Ar-CH), 7.38-7.36 (d, *J* = 8Hz, 1H, Ar-CH), 7.24-7.16 (m, 2H, 2 x Ar-CH), 7.05-7.01 (m, 1H, Ar-CH), 5.23-5.19 (m, 1H, Al-CH), 3.71 (s, 3H, OCH_3), 3.30 (s, 1H, Al-CH), 3.11-3.06 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d*$_6$): δppm 171.66, 140.62, 139.46, 137.29, 132.13, 130.52, 129.88, 128.43, 126.73, 125.97, 124.94, 122.93, 114.68, 63.32, 53.10, 32.86. LC-MS (*m/z*): 91% $[M^{79}Br^{+1}]^+$: 396, $[M^{81}Br^{+1}]^+$: 398. Anal. Calcd. $C_{16}H_{14}BrNO_4S$ (396.26): C, 48.50; H, 3.56; N, 3.53%. Found C, 48.32; H, 3.50; N, 3.58%.

Procedure for the synthesis of 1-{[3-(furan-3-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (4)



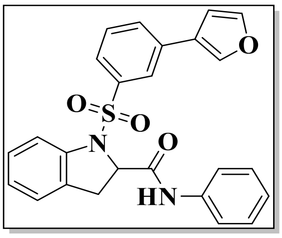
To a solution of methyl 1-[(3-bromophenyl)sulfonyl]indoline-2-carboxylate (**3**, 15 g, 37.87 mmol) in 1,4-dioxane (100 mL) and H_2O (50 mL), (furan-3-yl)boronic acid (6.36 g, 56.81 mmol) and Na_2CO_3 (12.04 g, 113.61 mmol) were added and the resulting mass was degassed with nitrogen for 15 min, after 15 min $PdCl_2$(dppf) (1.38 g, 1.89 mmol) was added and reaction was stirred at 100 °C for 4h. After the completion of the reaction, it was quenched with dilute. HCl to adjust the pH in the range of 3 to 4, the resulting mass was extracted with ethyl acetate (3 times). The combined organic layer was washed with brine (2 times) dried over sodium sulphate and evaporate it to get crude product. The obtained crude was a mixture of ester and acid. So direct used for next step without purification. Crude was stirred with water and MeOH and NaOH (4.54 g, 113.61mmol) was added and the reaction was stirred at 25 °C for 16h. After completion of the reaction, reaction was quenched with dil. HCl to adjust the pH in the range of 3 to 4, the resulting mass was extracted with ethyl acetate (3 times). The combine organic layer was washed with brine and evaporated to get the crude product. 1-{[3-(furan-3-yl)phenyl]sulfonyl}indoline-2-carboxylic acid **(4)** 10 g, 71% yield.[211-212] mp: 120-123 °C. ^{1}H NMR (400 MHz, *DMSO-d$_6$*): 13.13 (s, 1H, CONH), 8.32 (s, 1H, Ar-CH), 8.00 (s, 1H, Ar-CH), 7.91-7.89 (d, *J* = 8Hz, 1H, Ar-CH), 7.79-7.78 (m, 1H, Ar-CH), 7.72-7.70 (d, *J* = 8Hz, 1H, Ar-CH), 7.58-7.54 (t, *J* = 7.6 Hz, 1H, Ar-CH), 7.42-7.40 (d, *J* = 8Hz, 1H, Ar-CH), 7.23-7.19 (t, *J* = 8Hz, 1H, Ar-CH), 7.15-7.13 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.01-6.97 (m, 2H, 2 x Ar-CH), 5.11-5.07 (m, 1H, Al-CH), 3.30-3.27 (m, 1H, Al-CH), 3.07-3.02 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 172.36, 144.68, 140.68, 140.55, 138.14, 133.30, 130.55, 130.20, 129.93, 127.71, 125.32, 125.28, 124.27, 124.09, 123.37, 114.38, 108.50, 62.00, 32.53. IR (KBr) ν_{max}/cm^{-1}: 3391 (COOH), 3065 (aromatic CH), 2920 (aliphatic CH), 1718 (C=O), 1507 (C=C), 1159 (C-N), 1017 (C-O). LC-MS (*m/z*): 96% [M+1]$^+$: 370. Anal. Calcd. $C_{19}H_{15}NO_5S$ (369.39): C, 61.78; H, 4.09; N, 3.79%. Found C, 61.82; H, 4.15; N, 3.82%.

General procedure for the synthesis of furan containing indoline hybrid compounds with amide linkage (6*a-k*)



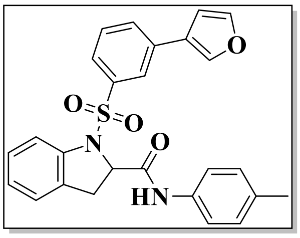
To a solution of 1-{[3-(furan-3-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (**4**,1 eq) in DMF (10 volumes), HATU (1.5 eq) was added at 0 °C under a nitrogen atmosphere. The mixture was stirred for 30 minutes at 0 °C, and the corresponding amine (**5a-k**, 1.5 eq) and DIPEA (3.0 eq) were added. The reaction was then stirred for an additional 3h at 25 °C. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was quenched with cold water and extracted with ethyl acetate the organic layer was evaporated under vacuo to get the crude product. The crude product was then purified using reverse phase chromatography (Acetonitrile: 0.1% formic acid in water). The combined fractions were concentrated and dried with lyophilization to obtain the final compounds **6a-k**.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-phenylindoline-2-carboxamide (6a)



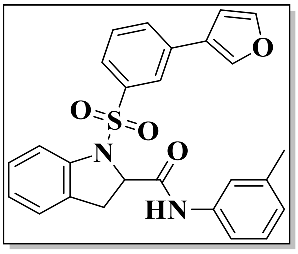
Compound **6a** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol) and **5a** (0.075 g, 0.81 mmol). White solid (0.2 g, 83% yield). mp: 114-118 °C. IR (KBr) ν_{max}/cm^{-1}: 3371 (NH), 3065 (aromatic CH), 2981 (aliphatic CH), 1684 (C=O-NH), 1521 (C=C), 1161 (C-N), 1017 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.56 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 8.00-7.99 (m, 1H, Ar-CH), 7.94-7.92 (m, 1H, Ar-CH), 7.80 (s, 1H, Ar-CH), 7.74-7.72 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.65-7.59 (m, 3H, 3 x Ar-CH), 7.52-7.50 (d, *J* = 8Hz, 1H, Ar-CH), 7.37-7.33 (t, *J* = 8Hz, 2H, 2 x Ar-CH), 7.27-7.24 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.16-7.09 (m, 2H, 2 x Ar-CH), 7.02-7.00 (m, 1H, Ar-CH), 6.96 (s, 1H, Ar-CH), 5.04-5.00 (m, 1H, Al-CH), 3.31-3.27 (m, 1H, Al-CH), 3.08-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 168.98, 144.85, 141.27, 140.56, 138.62, 137.64, 133.37, 130.80, 130.40, 128.86, 127.75, 125.31, 124.35, 124.16, 123.65, 119.59, 114.55, 108.56, 63.18, 32.25. LC-MS (*m/z*): 99% $[M+1]^+$: 445, $[M+2]^+$: 446. Anal. Calcd. $C_{25}H_{20}N_2O_4S$ (444.51): C, 67.55; H, 4.54; N, 6.30%. Found C, 67.60; H, 4.57; N, 6.35%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(p-tolyl)indoline-2-carboxamide (6b)



Compound **6b** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol) and **5b** (0.075 g, 0.81 mmol). White solid (0.2 g, 83% yield). mp: 114-118 °C. IR (KBr) ν_{max}/cm^{-1}: 3371 (NH), 3065 (aromatic CH), 2981 (aliphatic CH), 1684 (C=O-NH), 1521 (C=C), 1161 (C-N), 1017 (C-O). ^1H NMR (400MHz, *DMSO-d₆*): δppm 10.56 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 8.00-7.99 (m, 1H, Ar-CH), 7.94-7.92 (m, 1H, Ar-CH), 7.80 (s, 1H, Ar-CH), 7.74-7.72 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.65-7.59 (m, 3H, 3 x Ar-CH), 7.52-7.50 (d, *J* = 8Hz, 1H, Ar-CH), 7.37-7.33 (t, *J* = 8Hz, 2H, 2 x Ar-CH), 7.27-7.24 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.16-7.09 (m, 2H, 2 x Ar-CH), 7.02-7.00 (m, 1H, Ar-CH), 6.96 (s, 1H, Ar-CH), 5.04-5.00 (m, 1H, Al-CH), 3.31-3.27 (m, 1H, Al-CH), 3.08-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 168.98, 144.85, 141.27, 140.56, 138.62, 137.64, 133.37, 130.80, 130.40, 128.86, 127.75, 125.31, 124.35, 124.16, 123.65, 119.59, 114.55, 108.56, 63.18, 32.25. LC-MS (*m/z*): 99% $[M+1]^+$: 445, $[M+2]^+$: 446. Anal. Calcd. $C_{25}H_{20}N_2O_4S$ (444.51): C, 67.55; H, 4.54; N, 6.30%. Found C, 67.60; H, 4.57; N, 6.35%.

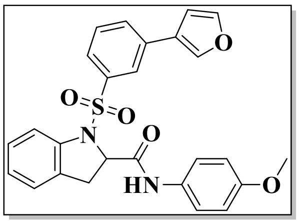
1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(m-tolyl)indoline-2-carboxamide (6c)



Compound **6c** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5c** (0.087 g, 0.81 mmol). Off cream solid (0.205 g, 82% yield). mp: 105-108 °C. IR (KBr) ν_{max}/cm^{-1}: 3371 (NH), 3017 (aromatic

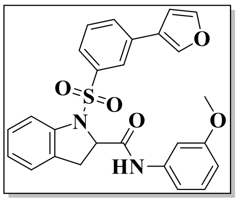
CH), 2916 (aliphatic CH), 1684 (C=O-NH), 1533 (C=C), 1161 (C-N), 1017 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.17 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 7.99 (s, 1H, Ar-CH), 7.94-7.92 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.80-7.72 (m, 1H, Ar-CH), 7.63-7.59 (m, 1H, Ar-CH), 7.51-7.48 (m, 2H, 2 x Ar-CH), 7.43-7.41 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.27-7.21 (m, 2H, 2 x Ar-CH), 7.16-7.14 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.04-6.92 (m, 2H, 2 x Ar-CH), 5.03-4.99 (m, 1H, Al-CH), 3.30-3.26 (m, 1H, Al-CH), 3.07-3.01 (m, 1H, Al-CH), 2.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.34, 145.28, 141.72, 140.99, 138.95, 138.51, 138.14, 133.81, 132.23, 130.87, 130.54, 129.12, 128.17, 125.76, 125.73, 124.93, 124.80, 124.59, 124.10, 120.63, 117.24, 115.01, 108.99, 63.65, 33.68, 21.60. LC-MS (*m/z*): 100% $[M+1]^+$: 459, $[M+2]^+$: 460. Anal. Calcd. $C_{26}H_{22}N_2O_4S$ (458.53): C, 68.15; H, 4.84; N, 6.11%. Found C, 68.17; H, 4.80; N, 6.15%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(4-methoxyphenyl)indoline-2-carboxamide (6d)



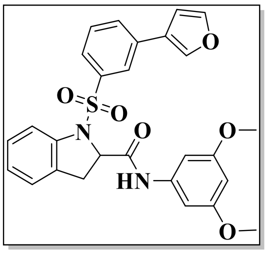
Compound **6d** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5d** (0.1 g, 0.81 mmol). Off cream solid (0.225 g, 87% yield). mp: 102-105 °C. IR (KBr) ν_{max}/cm^{-1}: 3308 (NH), 3015 (aromatic CH), 2953 (aliphatic CH), 1666 (C=O-NH), 1556 (C=C), 1168 (C-N), 1026 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.11 (s, 1H, CONH), 8.27 (s, 1H, Ar-CH), 7.99 (s, 1H, Ar-CH), 7.94-7.92 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.80-7.79 (m, 1H, Ar-CH), 7.62-7.60 (d, *J* = 8Hz, 1H, Ar-CH), 7.58-7.48 (m, 4H, 4 x Ar-CH), 7.27-7.23 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.16-7.14 (d, *J* = 7.2 Hz, 1H, Ar-CH), 7.04-6.90 (m, 4H, 4 x Ar-CH), 5.00-4.96 (m, 1H, Al-CH), 3.74 (s, 3H, OCH_3), 3.28-3.24 (m, 1H, Al-CH), 3.07-3.01 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 168.96, 156.05, 145.27, 141.72, 140.99, 138.09, 133.79, 132.12, 131.21, 130.98, 130.53, 128.15, 125.72, 124.79, 124.62, 124.09, 121.65, 115.12, 114.39, 109.00, 63.60, 55.65, 33.68. LC-MS (*m/z*): 100% $[M+1]^+$: 475, $[M+2]^+$: 476**.** Anal. Calcd. $C_{26}H_{22}N_2O_5S$ (474.53): C, 65.81; H, 4.67; N, 5.90%. Found C, 65.95; H, 4.70; N, 5.92%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(3-methoxyphenyl)indoline-2-carboxamide (6e)



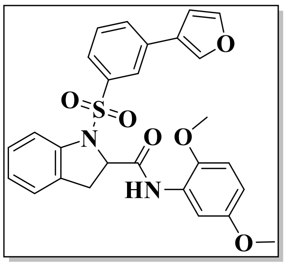
Compound **6e** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5e** (0.1 g, 0.81 mmol). Orange solid (0.190 g, 74% yield). mp: 110-114 °C. IR (KBr) ν_{max}/cm^{-1}: 3371 (NH), 3065 (aromatic CH), 2927 (aliphatic CH), 1684 (C=O-NH), 1536 (C=C), 1157 (C-N), 1038 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.24 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 8.02 (s, 1H, Ar-CH), 7.94-7.92 (d, *J* = 8Hz, 1H, Ar-CH), 7.80-7.79 (m, 1H, Ar-CH), 7.74-7.72 (d, *J* = 7.6 Hz, 1H, Ar-CH), 7.63-7.59 (t, *J* = 8Hz, 1H, Ar-CH), 7.51-7.49 (d, *J* = 8Hz, 1H, Ar-CH), 7.36-7.35 (m, 1H, Ar-CH), 7.27-7.23 (t, *J* = 8Hz, 1H, Ar-CH), 7.18-7.11 (m, 1H, Ar-CH), 7.04-7.02 (t, *J* = 7.6 Hz, 1H, Ar-CH), 7.96 (s, 1H, Ar-CH), 6.70-6.67 (m, 1H, Ar-CH), 5.03-4.99 (m, 1H, CH, Al-CH), 3.74 (s, 3H, OCH_3), 3.32-3.27 (m, 1H, CH, Al-CH), 3.07-3.02 (m, 1H, CH, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 168.99, 159.55, 144.81, 141.23, 140.52, 139.78, 137.63, 133.33, 130.76, 130.35, 130.08, 129.63, 127.72, 125.27, 124.31, 124.11, 123.60, 114.48, 111.71, 109.41, 108.51, 105.11, 63.16, 54.99, 33.23. LC-MS (*m/z*): 99% [M+1]$^+$: 475 , [M+2]$^+$: 476. Anal. Calcd. $C_{26}H_{22}N_2O_5S$ (474.53): C, 65.81; H, 4.67; N, 5.90%. Found C, 65.97; H, 4.68; N, 5.91%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(3,5-dimethoxyphenyl)indoline-2-carboxamide (6f)



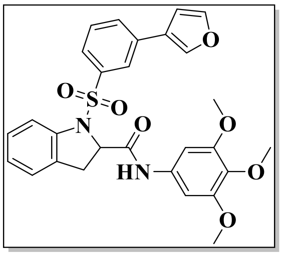
Compound **6f** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5f** (0.124 g, 0.81 mmol). Brown solid (0.230 g, 84% yield). mp: 98-100 °C. IR (KBr) ν_{max}/cm^{-1}: 3393 (NH), 3015 (aromatic CH), 2939 (aliphatic CH), 1686 (C=O-NH), 1541 (C=C), 1151 (C-N), 1056 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 9.48 (s, 1H, CONH), 7.97 (s, 1H, Ar-CH), 8.28 (s, 1H, Ar-CH), 7.93-7.91 (d, *J* = 8Hz, 1H, Ar-CH), 7.85-7.79 (m, 2H, 2 x Ar-CH), 7.68-7.66 (d, *J* = 8.4Hz, 1H, Ar-CH), 7.59-7.54 (m, 2H, 2 x Ar-CH), 7.29-7.25 (t, *J* = 7.6 Hz, 1H, Ar-CH), 7.17-7.15 (d, *J* = 6.8Hz, 1H, Ar-CH), 7.07-6.96 (m, 3H, 3 x Ar-CH), 6.68-6.65 (m, 1H, Ar-CH), 5.43-5.40 (m, 1H, Al-CH), 3.85 (s, 3H, OCH_3), 3.11-3.04 (m, 2H, 2 x Al-CH). ^{13}C NMR (100 MHz, *DMSO-d*$_6$): δppm 169.01, 160.52, 144.80, 141.22, 140.51, 140.26, 137.66, 133.33, 130.75, 130.34, 130.07, 127.71, 125.24, 124.11, 123.58, 114.46, 108.50, 97.66, 95.95, 63.19, 55.11, 33.23. LC-MS (*m/z*): 99% $[M+1]^+$: 505, $[M+2]^+$: 506**.** Anal. Calcd. $C_{27}H_{24}N_2O_6S$ (504.56): C, 64.27; H, 4.79; N, 5.55%. Found C, 64.20; H, 4.80; N, 5.57%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(2,5-dimethoxyphenyl)indoline-2-carboxamide (6g)



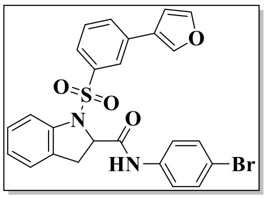
Compound **6g** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5g** (0.124 g, 0.81 mmol). Grey solid (0.220 g, 80% yield). mp: 100-103 °C. IR (KBr) ν_{max}/cm^{-1}: 3117 (NH), 3019 (aromatic CH), 2944 (aliphatic CH), 1675 (C=O-NH), 1530 (C=C), 1105 (C-N), 1047 (C-O). ^1H NMR (400MHz, *DMSO-d*$_6$): δppm 9.48 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 7.97 (s, 1H, Ar-CH), 7.93-7.91 (d, *J* = 8Hz, 1H, Ar-CH), 7.85-7.79 (m, 2H, 2 x Ar-CH), 7.68-7.66 (d, *J* = 8.4Hz, 1H, Ar-CH), 7.59-7.54 (m, 2H, 2 x Ar-CH), 7.29-7.25 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.17-7.15 (d, *J* = 6.8Hz, 1H, Ar-CH), 7.07-6.96 (m, 3H, 3 x Ar-CH), 6.68-6.65 (m, 1H, Ar-CH), 5.43-5.40 (m, 1H, Al-CH), 3.85 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.17-3.04 (m, 2H, 2 x Al-CH). ^{13}C NMR (100 MHz, *DMSO-d*$_6$): δppm 169.30, 153.52, 145.25, 143.33, 141.13, 141.06, 137.74, 133.83, 131.71, 131.30, 130.49, 128.30, 128.12, 125.87, 125.42, 124.74, 124.06, 116.13, 112.52, 109.01, 108.81, 107.18, 63.79, 57.02, 55.80, 32.89. LC-MS (*m/z*): 99% $[M+1]^+$: 505, $[M+2]^+$: 506. Anal. Calcd. $C_{27}H_{24}N_2O_6S$ (504.56): C, 64.27; H, 4.79; N, 5.55%. Found C, 64.35; H, 4.80; N, 5.57%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(3,4,5-trimethoxyphenyl)indoline-2-carboxamide (6h)



Compound **6h** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5h** (0.148 g, 0.81 mmol). Off white solid (0.220 g, 80% yield). mp: 99-101 °C. IR (KBr) ν_{max}/cm^{-1}: 3367 (NH), 3069 (aromatic CH), 2937 (aliphatic CH), 1686 (C=O-NH), 1504 (C=C), 1123 (C-N), 1056 (C-O). ^1H NMR (400MHz, *DMSO-d6*): δppm 10.21 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 8.01 (s, 1H, Ar-CH), 7.95-7.93 (d, *J* = 8Hz, 1H, Ar-CH), 7.81-7.80 (m, 1H, Ar-CH), 7.74-7.72 (d, J = 7.6Hz, 1H, Ar-CH), 7.64-7.60 (t, *J* = 8Hz, 1H, Ar-CH), 7.51-7.49 (d, *J* = 8Hz, 1H, Ar-CH), 7.28-7.24 (t, *J* = 7.6 Hz, 1H, Ar-CH), 7.17-7.15 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.05-7.01 (m, 3H, 3 x Ar-CH), 6.96 (s, 1H, Ar-CH), 5.03-4.99 (m, 1H, Al-CH), 3.77 (s, 6H, 2 x OCH_3), 3.64 (s, 3H, OCH_3), 3.32-3.24 (m, 1H, Al-CH), 3.07-3.01 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d6*): δppm 169.27, 153.25, 145.28, 143.33, 141.75, 140.96, 138.23, 135.19, 134.24, 133.82, 131.22, 130.93, 130.54, 128.17, 125.84, 125.72, 124.80, 124.60, 124.08, 123.88, 114.99, 108.97, 97.66, 63.70, 60.60, 56.17, 33.73. LC-MS (*m/z*): 100% $[M+1]^+$: 535, $[M+2]^+$: 536**.** Anal. Calcd. $C_{28}H_{26}N_2O_7S$ (534.58): C, 62.91; H, 4.90; N, 5.24%. Found C, 62.98; H, 4.89; N, 5.26%.

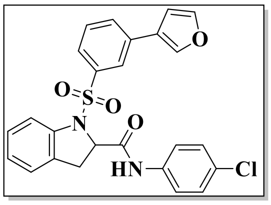
1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(4-bromophenyl)indoline-2-carboxamide (6i)



Compound **6i** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5i** (0.139 g, 0.81 mmol). Off white solid (0.235 g, 83% yield). mp: 107-110 °C. IR (KBr) ν_{max}/cm^{-1}: 3367 (NH), 3067 (aromatic CH), 2953 (aliphatic CH), 1684 (C=O-NH), 1507 (C=C), 1162 (C-N), 1008 (C-O). ^1H NMR (400MHz, *DMSO-d6*): δppm 10.40 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 7.98 (s, 1H, Ar-CH), 7.94-7.92 (d, *J* = 8Hz, 1H, Ar-CH), 7.80 (s, 1H, Ar-CH), 7.74-7.72 (d, *J* =

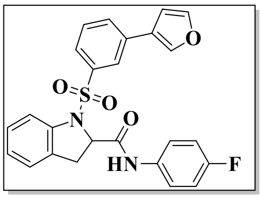
8Hz, 1H, Ar-H), 7.64-7.59 (m, 3H, 3 x Ar-CH), 7.56-7.51 (m, 3H, 3 x Ar-CH), 7.28-7.24 (t, *J* = 8Hz, 1H, Ar-CH), 7.14-7.16 (d, *J* = 8Hz, 1H, Ar-CH), 7.01-7.05 (t, *J* = 8Hz, 1H, Ar-CH), 6.96 (s, 1H, Ar-CH), 4.97-5.01 (m, 1H, Al-CH), 3.28-3.31 (m, 1H, Al-CH), 3.03-3.09 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.58, 145.28, 141.67, 141.01, 138.41, 138.01, 133.83, 132.12, 131.27, 130.75, 130.57, 128.22, 125.75, 124.78, 124.63, 124.09, 122.05, 115.91, 115.00, 109.00, 63.67, 33.66. LC-MS (*m/z*): 99% $[M^{79}Br^{+1}]^+$: 523, $[M^{81}Br^{+1}]^+$: 525. Anal. Calcd. $C_{25}H_{19}BrN_2O_4S$ (523.40): C, 57.37; H, 3.66; N, 5.35%. Found C, 57.42; H, 3.67; N, 5.36%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(4-chlorophenyl)indoline-2-carboxamide (6j)



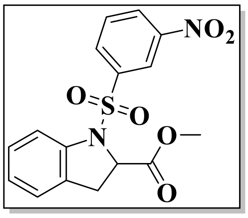
Compound **6j** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5j** (0.103 g, 0.81 mmol). Off orange solid (0.235 g, 90% yield). mp: 102-105 °C. IR (KBr) ν_{max}/cm^{-1}: 3352 (NH), 3062 (aromatic CH), 2950 (aliphatic CH), 1684 (C=O-NH), 1507 (C=C), 1162 (C-N), 1013 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.41 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 7.99 (s, 1H, Ar-CH), 7.94-7.92 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.80 (s, 1H, Ar-CH), 7.74-7.59 (m, 4H, 4 x Ar-CH), 7.53-7.51 (d, *J* = 8Hz, 1H, Ar-CH), 7.42-7.40 (d, *J* = 8.8Hz, 2H, 2 x Ar-CH), 7.27-7.24 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.16-7.14 (d, *J* = 7.2Hz, 1H, Ar-CH), 7.04-6.95 (m, 2H, 2 x Ar-CH), 5.01-4.97 (m, 1H, Al-CH), 3.28-3.24 (m, 1H, Al-CH), 3.08-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.58, 145.28, 141.65, 141.02, 137.98, 133.82, 131.27, 130.57, 129.21, 128.22, 127.84, 124.77, 124.62, 124.08, 114.98, 108.99, 125.75, 63.64, 33.66. LC-MS (*m/z*): 100% $[M^{35}Cl^{+1}]^+$: 479, $[M^{37}Cl^{+1}]^+$: 481**.** Anal. Calcd. $C_{25}H_{19}ClN_2O_4S$ (478.95): C, 62.69; H, 4.00; N, 5.85%. Found C, 62.75; H, 4.02; N, 5.87%.

1-{[3-(Furan-3-yl)phenyl]sulfonyl}-*N*-(4-fluorophenyl)indoline-2-carboxamide (6k)



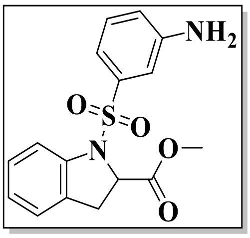
Compound **6k** was prepared from **4** (0.2 g, 0.54 mmol) and HATU (0.308 g, 0.81 mmol) in DMF (4 mL), DIPEA (0.209 g, 1.62 mmol), **5k** (0.09 g, 0.81 mmol). Off orange solid (0.2 g, 80% yield). mp: 103-106 °C. IR (KBr) ν_{max}/cm^{-1}: 3367 (NH), 3078 (aromatic CH), 2920 (aliphatic CH), 1669 (C=O-NH), 1505 (C=C), 1161 (C-N), 1015 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.32 (s, 1H, CONH), 8.28 (s, 1H, Ar-CH), 7.99 (s, 1H, Ar-H), 7.95-7.93 (d, *J* = 8Hz, 1H, Ar-CH), 7.75 (s, 1H, Ar-CH), 7.74-7.72 (d, *J* = 8Hz, 1H, Ar-CH), 7.69-7.59 (m, 3H, 3 x Ar-CH), 7.53-7.51 (d, *J* = 8Hz, 1H, Ar-CH), 7.26-7.22 (t, *J* = 8Hz, 1H, Ar-CH), 7.21-7.15 (m, 3H, 3 x Ar-CH), 7.05-7.01 (t, *J* = 8Hz, 1H, Ar-CH), 6.96 (s, 1H, Ar-CH), 5.01-4.97 (m, 1H, Al-CH), 3.32-3.27 (m, 1H, Al-CH), 3.09-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.36, 159.96, 157.57, 145.28, 141.69, 140.99, 138.05, 135.42, 133.82, 131.25, 130.83, 130.55, 128.19, 125.75, 124.78, 124.62, 124.10, 121.97, 121.89, 115.98, 115.76, 115.04, 108.99, 63.63, 33.67. LC-MS (*m/z*): 97% [M+1]$^+$: 463, [M+2]$^+$: 464. Anal. Calcd. $C_{25}H_{19}FN_2O_4S$ (462.50): C, 64.92; H, 4.14; N, 6.06%. Found C, 64.96; H, 4.16; N, 6.07%.

Procedure for the synthesis of methyl 1-[(3-nitrophenyl)sulfonyl]indoline-2-carboxylate (7)



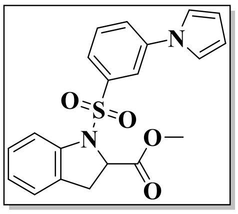
To a solution of methyl indoline-2-carboxylate (**2**, 10 g, 56.43 mmol) in pyridine (200 mL) under nitrogen atmosphere, 3-nitrobenzenesulfonyl chloride (15 g, 67.72 mmol) at 0 °C was added and the reaction was stirred at 25 °C for 16 h. After completion of the reaction, reaction was quenched with diluted HCl and pH was adjusted upto 3 to 4, and reaction mixture was extracted with ethyl acetate (2 times). Combine organic and washed with a saturated brine solution to get crude product. Crude was purified by using flash chromatography (0-15% EtOAc in hexane) to gives pale white solid (15 g, 73% yield) as methyl 1-((3-nitrophenyl)sulfonyl)indoline-2-carboxylate (**7**). mp: 110-112 °C. IR (KBr) ν_{max}/cm^{-1}: 3106 (aromatic CH), 2953 (aliphatic CH), 1712 (COO), 1604 (C=N), 1526 (C=C), 1114 (C-N), 1023 (C-O). ^{1}H NMR (400 MHz, *DMSO-d$_6$*): δppm 8.51-8.48 (m, 2H, 2 x Ar-CH), 8.29-8.26 (m, 1H, Ar-CH), 7.88-7.84 (t, *J* = 8Hz, 1H, Ar-CH), 7.44-7.42 (d, *J* = 8Hz, 1H, Ar-CH), 7.27-7.23 (t, *J* = 8Hz, 1H, Ar-CH), 7.19-7.17 (d, *J* = 7.2Hz, 1H, Ar-CH), 7.07-7.03 (t, *J* = 8Hz, 1H, Ar-CH), 5.25-5.21 (m, 1H, Al-CH), 3.74 (s, 3H, OCH_3), 3.37-3.34 (m, 1H, Al-CH), 3.31-3.08 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 171.56, 148.48, 140.42, 138.86, 133.33, 132.06, 130.59, 128.97, 128.53, 126.06, 125.15, 122.54, 114.69, 62.33, 53.16, 32.86. LC-MS (*m/z*): 100% $[M+1]^+$: 363. Anal. Calcd. $C_{16}H_{14}N_2O_6S$ (362.36): C, 53.04; H, 3.89; N, 7.73%. Found C, 53.18; H, 3.90; N, 7.74%.

Synthesis of methyl 1-[(3-aminophenyl)sulfonyl]indoline-2-carboxylate (8)



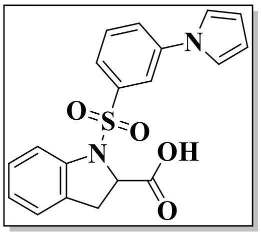
To a solution of **7** (10 g, 27.59 mmol) in EtOH (100 mL) and H_2O (50 mL) in 3-Neck RBF, NH_4Cl (7.38 g, 137.98 mmol) and Fe-Powder (7.7 g, 137.98 mmol) and the reaction was stirred at 80 °C for 16 h. After completion of the reaction, the reaction mixture was filtered through a celite bed and washed with MeOH. The collected filtrate was dried over sodium sulfate and evaporated to give a brown solid (8.5 g, 92% yield) methyl 1-[(3-aminophenyl)sulfonyl]indoline-2-carboxylate (**8**).[213] mp: 112-115 °C. IR (KBr) ν_{max}/cm^{-1}: 3375 (NH), 3069 (aromatic CH), 2950 (aliphatic CH), 1735 (COO), 1623 (C=N), 1508 (C=C), 1146 (C-N), 1025 (C-O). ^{1}H NMR (400 MHz, *DMSO-d₆*): δppm 7.37-7.35 (d, *J* = 8Hz, 1H, Ar-CH), 7.23-7.19 (t, *J* = 7.2Hz, 1H, Ar-CH), 7.16-7.12 (m, 2H, 2 x Ar-CH), 7.02-6.99 (m, 2H, 2 x Ar-CH), 6.87-6.85 (d, *J* = 7.6Hz, 1H, Ar-CH), 6.78-6.75 (m, 1H, Ar-CH), 5.63 (s, 2H, CH, NH_2), 4.92-4.88 (m, 1H, CH, Al-CH), 3.73 (s, 3H, OCH_3), 3.42-3.33 (m, 1H, Al-CH), 3.09-3.04 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 171.56, 148.48, 140.42, 138.86, 133.33, 132.06, 130.59, 128.97, 128.53, 126.06, 125.15, 122.54, 114.69, 62.33, 53.16, 32.86. LC-MS (*m/z*): 99% $[M+1]^+$: 333. Anal. Calcd. $C_{16}H_{16}N_2O_4S$ (332.37): C, 57.82; H, 4.85; N, 8.43%. Found C, 57.94; H, 4.87; N, 8.45%.

Synthesis of methyl 1-{[3-(pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylate (10)



To a solution of **8** (8.5 g, 25.60 mmol) in acetic acid (200 mL) in RBF under nitrogen atmosphere, 2,5-dimethoxytetrahydrofuran (**9**, 3.38 g, 25.60 mmol) at 0 °C and the reaction was stirred at 60 °C for 3 h. After completion of the reaction, Reaction was quenched with saturated $NaHCO_3$ and extracted with ethyl acetate (2 times). Combine organic and washed with a saturated brine solution to get crude product. Crude was purified by using flash chromatography (0-20% EtOAc in hexane) to give a brown solid (7 g, 71% yield) as methyl 1-{[3-pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylate (**10**).^{214} mp: 108-110 °C. IR (KBr) ν_{max}/cm^{-1}: 3037 (aromatic CH), 2951 (aliphatic CH), 1751 (COO), 1591 (C=C), 1023 (C-O). ^1H NMR (400 MHz, *DMSO-d₆*): δppm 7.91-7.90 (m, 2H, 2 x Ar-CH), 7.69-7.60 (m, 2H, 2 x Ar-CH), 7.47-7.42 (m, 3H, 3 x Ar-CH), 7.26-7.22 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.17-7.15 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.04-7.01 (m, 1H, Ar-CH), 6.31-6.30 (m, 2H, 2 x Ar-CH), 5.32-5.29 (m, 1H, Al-CH), 3.74 (s, 3H, OCH_3), 3.30-3.28 (m, 1H, Al-CH), 3.12-3.07 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 171.75, 140.90, 139.03, 131.46, 130.66, 128.35, 125.88, 124.89, 124.80, 124.09, 119.68, 117.37, 115.04, 111.81, 62.39, 53.04, 32.91. LC-MS (*m/z*): 100% $[M+1]^+$: 383, $[M+2]^+$: 384. Anal. Calcd. $C_{20}H_{18}N_2O_4S$ (382.43): C, 62.81; H, 4.74; N, 7.33%. Found C, 62.90; H, 4.75; N, 7.35%.

Synthesis of 1-{[3-(pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (11)

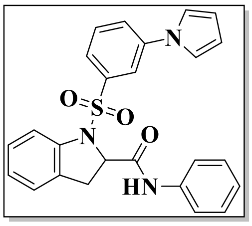


To a solution of **10** (7 g, 18.30 mmol) in MeOH (70 mL) and H_2O (35 mL) in 3 neck RBF, NaOH (2.19 g, 54.91 mmol) was added and the reaction was stirred at rt for 16h. After completion of ester solvent was evaporated under reduced pressure after that water was added into the reaction mixture and 2-3 pH was adjusted with diluted HCl and extracted with 10% MeOH in DCM to gives brown solid (6g, 89% yield) as 1-{[3-(pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (**11**). mp: 117-120 °C. ^1H NMR (400 MHz, *DMSO-d₆*): 13.21 (s, 1H, COOH), 7.92-7.89 (m, 2H, 2 x Ar-CH), 7.70-7.60 (m, 2H, 2 x Ar-CH), 7.43 (m, 3H, 3 x Ar-CH), 7.24-7.21 (t, *J* = 7.6 Hz, 1H, Ar-CH), 7.17-7.15 (d, *J* = 7.2Hz, 1H, Ar-CH), 3.08-3.03 (m, 1H, Al-CH), 7.03-6.99 (t, *J* = 6.8Hz, 1H, Ar-CH), 6.31-6.30 (m, 2H, 2 x Ar-CH), 5.17-5.14 (m, 1H, Al-CH), 3.32-3.29 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 172.89, 141.07, 140.84, 139.33, 131.43, 130.81, 128.27, 125.86, 124.71, 124.66, 124.01, 119.66, 117.34, 114.91, 111.81, 62.49, 33.06. IR (KBr) ν_{max}/cm^{-1}: 3332 (COOH), 3071 (aromatic CH), 2924 (aliphatic CH), 1720 (C=O), 1597 (C=C), 1162 (C-N), 1025 (C-O). LC-MS (*m/z*): 95% $[M-1]^+$: 367. Anal. Calcd. $C_{19}H_{16}N_2O_4S$ (368.41): C, 61.94; H, 4.38; N, 7.60%. Found C, 61.98; H, 4.39; N, 7.63%.

General procedure for the synthesis of compounds 13a-k

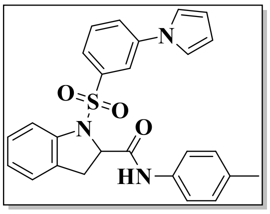
To a solution of methyl 1-{[3-(1*H*-pyrrol-1-yl)phenyl]sulfonyl}indoline-2-carboxylic acid (**11**, 1 eq) in DMF (10 vol), HATU (1.5 eq) was added at 0 °C under nitrogen atmosphere. The mixture was stirred for 30 min at 0 °C and corresponding amine (**12-k**, 1.5 eq) and DIPEA (3.0 eq) were added, the reaction was then stirred at another 3 h at 25 °C. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was quenched with cold water and extracted with ethyl acetate the organic layer was evaporated under vacuo to get the crude product. The crude product was then purified using reverse phase chromatography (Acetonitrile: 0.1% formic acid in water). The combined fractions were concentrated and dried with lyophilization to obtain the final compounds **13a-k.**

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-phenylindoline-2-carboxamide (13a)



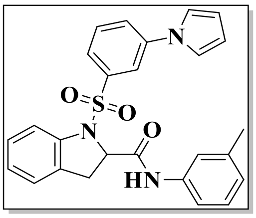
Compound **13a** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), with DIPEA (0.105 g, 0.81 mmol), **12a** (0.037 g, 0.40 mmol). Off-white solid (0.08 g, 66% yield). mp: 110-112 °C. IR (KBr) ν_{max}/cm^{-1}: 3367 (NH), 3067 (aromatic CH), 2920 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1524 (C=C), 1164 (C-N), 1020 (C-O). ^1H NMR (400MHz, *DMSO-d₆*): δppm 10.28 (s, 1H, CONH), 7.93 (s, 2H, 2 x Ar-CH), 7.72-7.63 (m, 4H, 4 x Ar-CH), 7.52-7.50 (d, *J* = 8Hz, 1H, Ar-CH), 7.39-7.34 (m, 4H, 4 x Ar-CH), 7.29-7.25 (t, *J* = 8Hz, 1H, Ar-CH), 7.18-7.03 (m, 3H, 3 x Ar-CH), 6.33 (s, 2H, 2 x Ar-CH), 5.08-5.04 (m, 1H, Al-CH), 4.06-4.01 (m, 1H, Al-CH), 3.09-3.04 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 169.39, 141.62, 140.88, 139.02, 138.81, 131.53, 130.97, 129.31, 128.23, 125.81, 124.94, 124.71, 124.28, 123.95, 111.89, 119.66, 117.63, 115.00, 120.07, 63.62, 33.69. LC-MS (*m/z*): 99% $[M+1]^+$: 444, $[M+2]^+$: 445. Anal. Calcd. $C_{25}H_{21}N_3O_3S$ (443.52): C, 67.70; H, 4.77; N, 9.47%. Found C, 67.75; H, 4.80; N, 9.49%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(p-tolyl)indoline-2-carboxamide (13b)



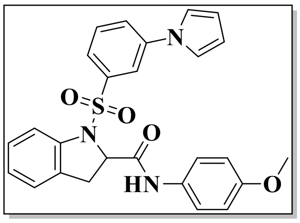
Compound **13b** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), and **12b** (0.043 g, 0.40 mmol). Off white solid (0.1 g, 80% yield). mp: 128-130 °C. IR (KBr) ν_{max}/cm^{-1}: 3254 (NH), 3045 (aromatic CH), 2945 (aliphatic CH), 1686 (C=O), 1599 (C=N), 1552 (C=C), 1172 (C-N), 1038 (C-O). ^1H NMR (400MHz, *DMSO-d₆*): δppm 10.20 (s, 1H, CONH), 7.94-7.93 (m, 2H, 2 x Ar-CH), 7.69-7.65 (m, 2H, 2 x Ar-CH), 7.54-7.50 (t, *J* = 8.4Hz, 3H, 3 x Ar-CH), 7.39-7.38 (m, 2H, 2 x Ar-CH), 7.29-7.25 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.17-7.15 (m, 3H, 3 x Ar-CH), 7.06-7.03 (t, *J* = 7.6Hz, 1H, Ar-CH), 6.33 (s, 2H, 2 x Ar-CH), 5.06-5.02 (m, 1H, CH), 3.33-3.28 (m, 1H, CH), 3.08-3.03 (m, 1H, CH), 2.28 (s, 3H, CH_3). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 169.16, 141.59, 140.86, 138.76, 136.49, 133.25, 131.52, 131.02, 129.67, 128.21, 125.80, 124.90, 124.71, 123.94, 120.07, 119.65, 117.59, 115.03, 111.89, 63.57, 33.67, 20.94. LC-MS (*m/z*): 99% $[M+1]^+$: 458, $[M+2]^+$: 459. Anal. Calcd. $C_{26}H_{23}N_3O_3S$ (457.55): C, 68.25; H, 5.07; N, 9.18%. Found C, 68.35; H, 5.09; N, 9.20%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(m-tolyl)indoline-2-carboxamide (13c)



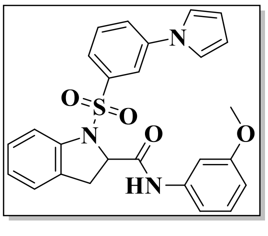
Compound **13c** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12c** (0.043 g, 0.40 mmol). Yellow solid (0.1 g, 80% yield). mp: 119-121 °C. IR (KBr) ν_{max}/cm^{-1}: 3363 (NH), 3073 (aromatic CH), 2920 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1533 (C=C), 1164 (C-N), 1023 (C-O). ^1H NMR (400MHz, *DMSO-d₆*): δppm 10.18 (s, 1H, CONH), 7.94-7.92 (m, 2H, 2 x Ar-CH), 7.71-7.65 (m, 2H, 2 x Ar-CH), 7.51-7.49 (m, 2H, 2 x Ar-CH), 7.43-7.37 (m, 3H, 3 x Ar-CH), 7.18-7.16 (d, *J* = 7.2Hz, 1H, Ar-CH), 7.06-7.02 (t, *J* = 7.2Hz, 1H, Ar-CH), 6.94-6.92 (d, *J* = 7.2Hz, 1H, Ar-CH), 6.33-6.32 (m, 2H, 2 x Ar-CH), 5.07-5.03 (m, 1H, Al-CH), 3.30 (m, 1H, Al-CH(merge in moisture peak)), 3.08-3.03 (m, 1H, Al-CH), 2.30 (s, 3H, CH_3). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.34, 141.61, 140.88, 138.93, 138.83, 138.54, 131.52, 130.98, 129.14, 128.22, 125.80, 124.96, 124.92, 124.69, 123.96, 120.63, 119.65, 117.62, 117.24, 114.98, 111.89, 63.64, 33.67, 21.61. LC-MS (*m/z*): 100% $[M+1]^+$: 458 , $[M+2]^+$: 459. Anal. Calcd. $C_{26}H_{23}N_3O_4S$ (457.55): C, 68.25; H, 5.07; N, 9.18%. Found C, 68.35; H, 5.09; N, 9.19%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(4-methoxyphenyl)indoline-2-carboxamide (13d)



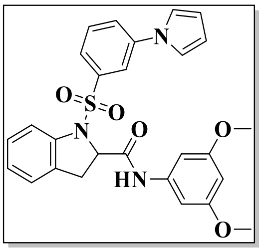
Compound **13d** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12d** (0.049 g, 0.40 mmol). Off white solid (0.100 g, 78% yield). mp: 114-116 °C. IR (KBr) ν_{max}/cm^{-1}: 3308 (NH), 3013 (aromatic CH), 2920 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1559 (C=C), 1164 (C-N), 1026 (C-O).^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.16 (s, 1H, CONH), 7.93 (s, 1H, Ar-CH), 7.71-7.65 (m, 2H, 2 x Ar-CH), 7.57-7.46 (m, 3H, 3 x Ar-CH), 7.39 (s, 2H, 2 x Ar-CH), 7.29-7.25 (t, *J* = 8Hz, 1H, Ar-CH), 7.18-7.16 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.06-7.03 (t, *J* = 7.6Hz, 1H, Ar-CH), 6.94-6.92 (d, *J* = 8.8Hz, 2H, 2 x Ar-CH), 6.33 (s, 2H, 2 x Ar-H), 5.31-5.01 (m, 1H, Al-CH), 3.75 (s, 3H, OCH_3), 3.32-3.27 (m, 1H, Al-CH), 3.08-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 168.94, 156.09, 141.63, 140.87, 138.81, 132.09, 131.51, 131.10, 128.20, 125.79, 124.90, 124.72, 123.95, 121.67, 119.65, 117.62, 115.10, 114.43, 111.89, 63.59, 55.68, 33.68. LC-MS (*m/z*): 100% $[M+1]^+$: 474 , $[M+2]^+$: 475. Anal. Calcd. $C_{26}H_{23}N_3O_4S$ (473.55): C, 65.95; H, 4.90; N, 8.87%. Found C, 65.99; H, 4.95; N, 8.90%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(3-methoxyphenyl)indoline-2-carboxamide (13e)



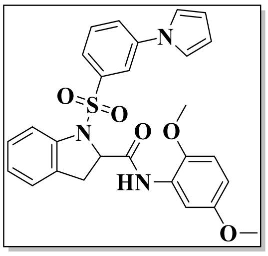
Compound **13e** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (4 mL), DIPEA (0.105 g, 0.81 mmol), **12e** (0.049 g, 0.40 mmol). Off white solid (0.100 g, 78% yield). mp: 120-122 °C. IR (KBr) ν_{max}/cm^{-1}: 3356 (NH), 3069 (aromatic CH), 2920 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1530 (C=C), 1155 (C-N), 1026 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.27 (s, 1H, CONH), 7.93 (s, 2H, 2 x Ar-CH), 7.69-7.65 (m, 2H, 2 x Ar-CH), 7.50-7.48 (d, *J* = 8.4Hz, 1H, Ar-CH), 7.38-7.36 (m, 3H, 3 x Ar-CH), 7.28-7.26 (t, *J* = 6.8Hz, 2H, 2 x Ar-CH), 7.18-7.16 (d, *J* = 7.6Hz, 2H, 2 x Ar-CH), 7.06-7.02 (t, *J* = 7.6Hz, 1H, Ar-CH), 6.70-6.68 (m, 1H, Ar-CH), 6.32-6.31 (m, 2H, 2 x Ar-CH), 5.07-5.03 (m, 1H, Al-CH), 3.74 (s, 3H, OCH_3), 3.30 (m, 1H, Al-CH(merge in moisture peak)), 3.08-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 160.04, 141.60, 140.88, 140.23, 138.81, 131.53, 130.94, 130.12, 128.24, 125.81, 124.92, 124.69, 123.93, 119.64, 117.59, 114.94, 112.20, 111.89, 109.95, 169.45, 105.60, 63.62, 55.47, 33.70. LC-MS (*m/z*): 96% $[M+1]^+$: 474, $[M+2]^+$: 475. Anal. Calcd. $C_{26}H_{23}N_3O_4S$ (473.55): C, 65.95; H, 4.90; N, 8.87%. Found C, 65.98; H, 4.91; N, 8.88%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(3,5-dimethoxyphenyl)indoline-2-carboxamide (13f)



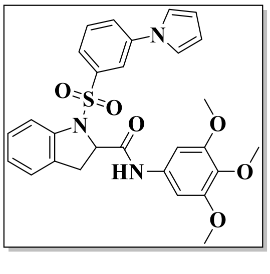
Compound **13f** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12f** (0.061 g, 0.40 mmol). Black solid (0.1 g, 73% yield). mp: 125-130 °C. IR (KBr) ν_{max}/cm^{-1}: 3360 (NH), 3103 (aromatic CH), 2933 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1541 (C=C), 1151 (C-N), 1023 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.24 (s, 1H, CONH), 7.91 (s, 2H, 2 x Ar-CH), 7.67-7.65 (m, 2H, 2 x Ar-CH), 7.47-7.45 (d, *J* = 8Hz, 2H, 2 x Ar-CH), 7.47-7.45 (d, *J* = 8Hz, 2H, 2 x Ar-CH), 7.37-7.36 (m, 2H, 2 x Ar-CH), 7.26-7.22 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.15-7.13 (t, *J* = 7.2Hz, 1H, Ar-CH), 7.03-7.00 (t, *J* = 7.2Hz, 1H, Ar-CH), 6.88-6.87 (m, 2H, 2 x Ar-CH), 6.30-6.29 (m, 2H, 2 x Ar-CH), 6.24 (s, 1H, Ar-CH), 5.03-4.99 (m, 1H, Al-CH), 3.71 (s, 6H, 2 x OCH_3), 3.04-2.99 (m, 2H, 2 x Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): 169.50, 161.01, 141.59, 140.88, 140.73, 138.83, 131.54, 130.92, 128.24, 125.82, 124.91, 124.68, 123.93, 119.64, 117.57, 114.90, 111.90, 98.13, 96.48, 63.64, 55.59, 33.71. LC-MS (*m/z*): 100% $[M+1]^+$: 504.5 , $[M+2]^+$: 505.5. Anal. Calcd. $C_{27}H_{25}N_3O_5S$ (503.57): C, 64.40; H, 5.00; N, 8.34%. Found C, 64.46; H, 5.10; N, 8.45%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(2,5-dimethoxyphenyl)indoline-2-carboxamide (13g)



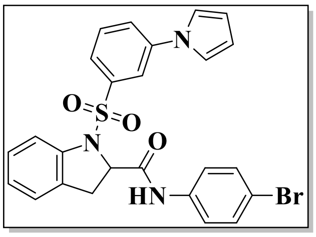
Compound **13g** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12g** (0.061 g, 0.40 mmol). Black solid (0.1 g, 73% yield). mp: 125-130 °C. IR (KBr) ν_{max}/cm^{-1}: 3373 (NH), 3069 (aromatic CH), 2920 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1530 (C=C), 1131 (C-N), 1023 (C-O). ^1H NMR (400MHz, *DMSO-d₆*): δppm 9.51 (s, 1H, CONH), 7.91 (s, 2H, 2 x Ar-CH), 7.85 (s, 1H, Ar-CH), 7.63 (s, 2H, 2 x Ar-CH), 7.56-7.47 (m, 1H, Ar-CH), 7.40 (s, 2H, 2 x Ar-CH), 7.31-7.27 (t, *J* = 7.6Hz, 1H, Ar-CH), 7.19-7.17 (d, *J* = 7.2Hz, 1H, Ar-CH), 7.09-7.01 (m, 2H, 2 x Ar-CH), 6.68-6.66 (d, *J* = 8.4Hz, 1H, Ar-CH), 6.32 (s, 2H, 2 x Ar-CH), 5.49-5.45 (t, *J* =7.6Hz, 1H, Al-CH), 3.85 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.13-3.12 (m, 2H, 2 x Al-CH). ^{13}C NMR (100 MHz, *DMSO-d₆*): δppm 169.30, 153.52, 143.37, 141.09, 140.85, 138.41, 131.77, 131.48, 128.34, 128.12, 125.93, 125.46, 124.93, 124.02, 119.67, 117.54, 116.07, 112.53, 111.86, 108.88, 107.26, 63.69, 57.01, 55.80, 32.94. LC-MS (*m/z*): 99% $[M+1]^+$: 504, $[M+2]^+$: 505. Anal. Calcd. $C_{27}H_{25}N_3O_5S$ (503.57): C, 64.40; H, 5.00; N, 8.34%. Found C, 64.46; H, 5.02; N, 8.35%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(3,4,5-trimethoxyphenyl)indoline-2-carboxamide (13h)



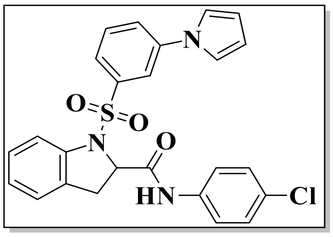
Compound **13h** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12h** (0.073 g, 0.40 mmol). Off white solid (0.110 g, 76% yield). mp: 118-122 °C. IR (KBr) ν_{max}/cm^{-1}: 3352 (NH), 3062 (aromatic CH), 2929 (aliphatic CH), 1684 (C=O), 1599 (C=N), 1541 (C=C), 1123 (C-N), 1003 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.24 (s, 1H, CONH), 7.95-7.89 (m, 2H, 2 x Ar-CH), 7.69-7.62 (m, 2H, 2 x Ar-CH), 7.49-7.47 (d, *J* = 8Hz, 1H, Ar-CH), 7.42-7.37 (m, 2H, 2 x Ar-CH), 7.28-7.24 (m, 1H, Aromatic CH), 7.24-7.16 (m, 1H, Ar-CH), 7.06-7.02 (m, 3H, 3 x Ar-CH), 6.32-6.31 (m, 2H, 2 x Ar-CH), 5.06-5.02 (m, 1H, Al-CH), 3.76-3.74 (m, 6H, 2 x OCH_3), 3.66 (s, 1H, Al-CH), 3.63 (s, 3H, OCH_3), 3.07-3.02 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 168.81, 152.77, 141.14, 140.40, 138.43, 134.70, 133.70, 131.05, 130.53, 127.75, 125.32, 124.41, 124.20, 123.58, 119.14, 117.10, 114.43, 111.41, 97.08, 63.17, 60.11, 55.67, 33.24. LC-MS (*m/z*): 100% [M+1]$^+$: 534, [M+2]$^+$: 535. Anal. Calcd. $C_{28}H_{27}N_3O_6S$ (533.60): C, 63.03; H, 5.10; N, 7.88%. Found C, 63.12; H, 5.18; N, 8.02%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(4-bromophenyl)indoline-2-carboxamide (13i)



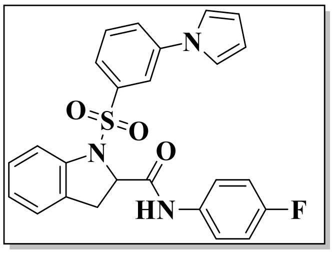
Compound **13i** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12i** (0.069 g, 0.40 mmol). Off orange solid (0.120 g, 84% yield). mp: 112-115 °C. IR (KBr) ν_{max}/cm^{-1}: 3356 (NH), 3073 (aromatic CH), 2953 (aliphatic CH), 1684 (C=O), 1597 (C=N), 1517 (C=C), 1164 (C-N), 1008 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.44 (s, 1H, CONH), 7.94-7.92 (d, *J* = 8Hz, 2H, 2 x Ar-CH), 7.70-7.68 (m, 2H, 2 x Ar-CH), 7.66-7.63 (m, 2H, 2 x Ar-CH), 7.62-7.52 (m, 3H, 3 x Ar-CH), 7.39 (s, 2H, 2 x Ar-CH), 7.30-7.26 (t, *J* = 8Hz, 1H, Ar-CH), 7.19-7.17 (d, *J* = 8Hz, 1H, Aromatic CH), 7.07-7.03 (t, *J* = 8Hz, 1H, Ar-CH), 6.33 (s, 2H, 2 x Ar-CH), 5.04-5.00 (m, 1H, Al-CH), 3.35-3.28 (m, 1H, Al-CH), 3.07-3.03 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.57, 141.54, 140.87, 141.54, 169.57, 138.65, 138.38, 132.14, 131.55, 130.85, 130.85, 128.26, 125.83, 124.96, 124.73, 123.94, 122.04, 119.65, 117.59, 115.94, 114.97, 111.90, 63.63, 33.64. LC-MS (*m/z*): 99% [M^{79}Br^{+1}]$^+$: 522, [M^{81}Br^{+1}]$^+$: 524. Anal. Calcd. $C_{25}H_{20}BrN_3O_3S$ (522.42): C, 57.48; H, 3.86; N, 8.04%. Found C, 57.54; H, 3.87; N, 8.06%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(4-chlorophenyl)indoline-2-carboxamide (13j)



Compound **13j** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12j** (0.051 g, 0.40 mmol). Off yellow solid (0.115 g, 88% yield). mp: 117-120 °C. IR (KBr) ν_{max}/cm^{-1}: 3263 (NH), 3073 (aromatic CH), 2953 (aliphatic CH), 1671 (C=O), 1597 (C=N), 1550 (C=C), 1170 (C-N), 1004 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.36 (s, 1H, CONH), 7.70 (s, 2H, 2 x Ar-CH), 7.53-7.51 (m, 1H,Ar- CH), 7.67-7.65 (s, 4H, 4 x Ar-CH), 7.43 (s, 2H, 2 x Ar-CH), 7.39-7.18 (m, 4H, 4 x Ar-CH), 7.07-7.03 (m, 1H, Ar-CH), 6.33 (s, 2H, 2 x Ar-CH), 5.05-5.01 (m, 1H, Al-CH), 3.30-3.25 (m, 1H, Al-CH), 3.10-3.05 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.07, 141.07, 140.40, 138.18, 137.48, 131.08, 130.39, 128.75, 128.47, 127.79, 127.41, 125.35, 124.48, 124.26, 123.46, 121.19, 119.17, 117.12, 115.14, 114.50, 111.42, 63.14, 33.18. LC-MS (*m/z*): 100% $[M^{35}Cl^{+1}]^+$: 478, $[M^{37}Cl^{+1}]^+$: 480. Anal. Calcd. $C_{25}H_{20}ClN_3O_3S$ (477.96): C, 62.82; H, 4.22; N, 8.49%. Found C, 63.02; H, 4.23; N, 8.51%.

1-{[3-(Pyrrol-1-yl)phenyl]sulfonyl}-*N*-(4-fluorophenyl)indoline-2-carboxamide (13k)



Compound **13k** was prepared from **11** (0.1 g, 0.27 mmol) and HATU (0.154 g, 0.40 mmol) in DMF (2 mL), DIPEA (0.105 g, 0.81 mmol), **12k** (0.045 g, 0.40 mmol). Off orange solid (0.115 g, 92% yield). mp: 121-124 °C. IR (KBr) ν_{max}/cm^{-1}: 3272 (NH), 3095 (aromatic CH), 2957 (aliphatic CH), 1690 (C=O), 1565 (C=N), 1496 (C=C), 1108 (C-N), 1028 (C-O). ^{1}H NMR (400MHz, *DMSO-d$_6$*): δppm 10.36 (s, 1H, CONH), 7.94-7.92 (m, 2H, 2 x Ar-CH), 7.69-7.66 (m, 4H, 4 x Ar-CH), 7.53-7.51 (d, *J* = 7.6Hz, 1H, Ar-CH), 7.42-7.38 (m, 2H, 2 x Ar-CH), 7.29-7.25 (t, *J* = 8Hz, 1H, Ar-CH), 7.22-7.17

(m, 3H, 3 x Ar-CH), 7.06-7.03 (t, *J* =7.2Hz, 1H, Ar-CH), 6.86-6.82 (m, 0.5H, F), 6.55-6.54 (m, 0.5H, F), 6.33 (s, 2H, 2 x Ar-CH), 5.04-5.01 (m, 1H, Al-CH), 3.30 (s, 1H, Al-CH), 3.09-3.05 (m, 1H, Al-CH). ^{13}C NMR (100 MHz, *DMSO-d$_6$*): δppm 169.34, 141.56, 140.86, 138.68, 135.39, 131.54, 130.93, 128.24, 125.81, 124.94, 124.72, 123.94, 121.95, 121.88, 119.65, 117.60, 116.01, 115.79, 115.66, 115.44, 115.01, 111.89, 63.58, 33.66. LC-MS (*m/z*): 96% $[M+1]^+$: 462, $[M+2]^+$: 463. Anal. Calcd. $C_{25}H_{20}FN_3O_3S$ (461.51): C, 65.06; H, 4.37; N, 9.11%. Found C, 65.20; H, 4.38; N, 9.12%.

4.8.2 Protocol of antimicrobial activity

keThe antibacterial and antifungal properties were assessed against prevalessnt fungal pathogens Aspergillus niger and Candida albicans, in addition to bacterial strains including two gram-positive bacteria (*B. subtilis* and *S. aureus*) and two gram-negative bacteria (*P. aeruginosa* and *E. coli*). The inhibition zones (mm) were evaluated against antibacterial and antifungal standards: chloramphenicol (30 µg/disc), gentamicin (10 µg/disc), and nystatin (10 µg/disc), respectively. The nutritional agar utilized for the experiments comprised the following components (g/L): sodium chloride, 5.0; beef extract, 10.0; peptone, 10.0, with the medium calibrated to a pH of 7.2 prior to sterilization.[220]

4.8.3 Protocol of molecular docking study

High-resolution crystal structures of *E. coli* DNA gyrase B (PDB: 4DUH) were obtained from the PDB database (https://www.rcsb.org/). Discovery Studio Visualizer (v21.1.0) was employed to exclude any bound ligands and water molecules from the protein receptors, so guaranteeing that the molecular docking investigation remained unaffected by extraneous factors. Subsequently, energy reduction was executed with empirical force fields to provide lower-energy conformations for the proteins.[221] Molecular docking study was performed with AutoDock (v4.2) virtual screening software, with the 4DUH protein designated as the macromolecule and the drugs as ligand molecules. A cubic grid box of 72.77 × 47.35 × 62.99 was established for 4DUH. Each chemical was subjected to eight separate docking simulations, and the conformations were grouped according to an RMSD of less than 2.0 Å.[222] The binding conformation exhibiting the lowest free binding energy (in kcal/mol) was chosen for each chemical. Molecular interactions were examined with Discovery Studio Visualizer (v21.1.0) to get comprehensive insights into the binding profiles.

4.8.4 Protocol of molecular dynamic simulation

A 100-nanosecond molecular dynamics simulation was conducted with desmond software from schrodinger LLC.[223] Before commencing the MDS, protein-ligand docking was performed to ascertain the binding orientation of the molecule within the protein's active site. MDS, utilizing Newton's classical equations of motion, models atomic motions over time, providing comprehensive insights into ligand-binding dynamics within a physiological context.[224]
The ligand-receptor complex was pre-processed with Maestro's protein preparation wizard, including optimization, energy reduction, and the incorporation of any requisite missing residues. The system was subsequently configured via the system builder tool. Before executing the simulation, the models underwent a relaxation phase, and trajectories were documented at 100 ps intervals for further comprehensive examination.

4.8.5 Protocol of ADMET study

To assess the pharmacokinetic characteristics of the novel drug candidates, *in silico* ADME experiments were carried out using the SwissADME server, which is a component of the Swiss Institute of Bioinformatics' Advanced Model for Drug Evaluation. Among other things, this procedure involved evaluating a number of physicochemical properties, including molecular weight, polar surface area, water solubility, pharmacokinetics, drug-likeness, and the existence of hydrogen bond donors and acceptors.[225-227] Additionally, Central Nervous System (CNS) and blood-brain barrier (BBB) permeability predictions were obtained using the pkCSM server[228] while hERG inhibition potential, skin sensitization, and eye irritation risks were evaluated using the ADMET 3.0 platform.[229]

4.9 Conclusion

The biological assessment results indicated that all examined bacterial strains were markedly inhibited by the produced compounds, with inhibition zones of between 10 and 36 mm. The inhibition zones for fungal species varied from 11 to 30 mm. The synthesized compounds had moderate to high antibacterial efficacy, frequently exceeding that of the reference medications. The antimicrobial activity was evaluated at a concentration of 10 µg per disk for each drug dissolved in DMSO. The integrated findings from molecular docking and MD simulation reveal that compound **6k** possesses the greatest binding affinity (-8.4 kcal/mol) in the **6a-k** series. In contrast, compound **13e** shows the highest binding affinity (-9.8 kcal/mol) in the **13a-k** series. Both compounds retain persistent contacts inside the 4DUH active site. The MD simulation confirms the structural stability of the **6a-k** and **13a-k** compounds, with RMSD, RMSF, and hydrogen bond investigations further substantiating the ligand's binding stability and effectiveness. These results designate compounds **6k** and **13e** as good candidates for subsequent experimental validation and possible pharmaceutical development.

4.10 Representative spectral data

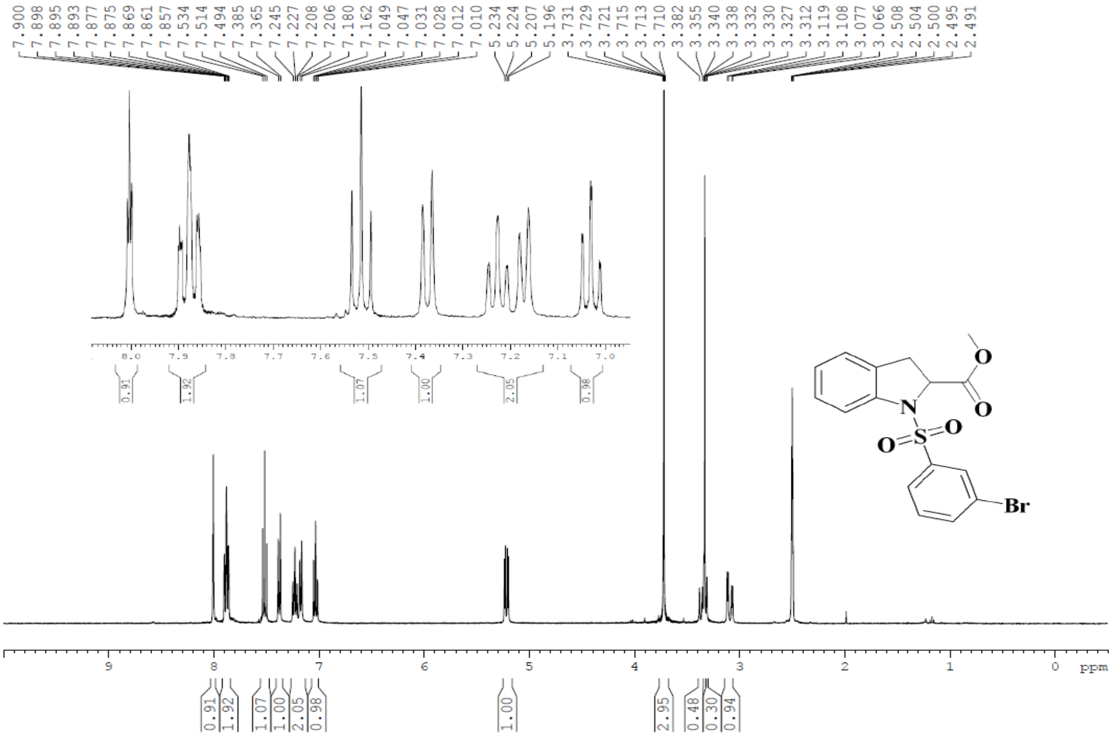


Figure 21: ^{1}H NMR of compound **3.**

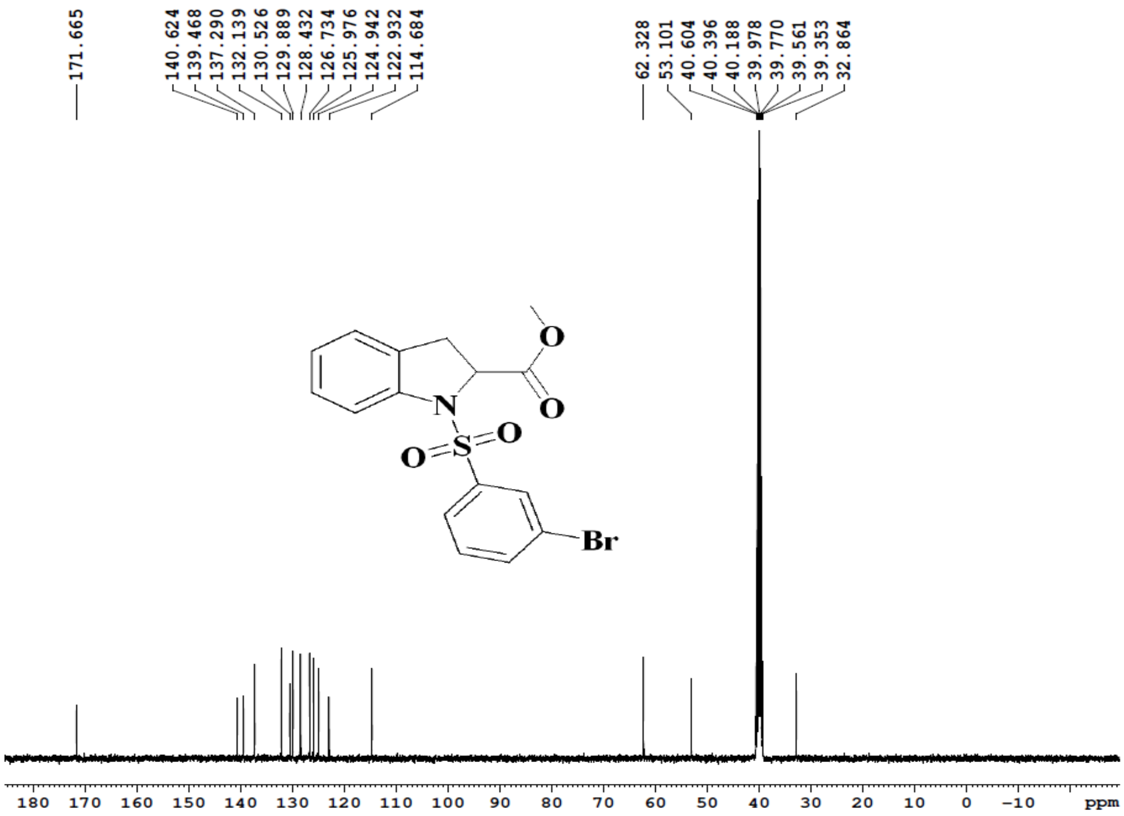
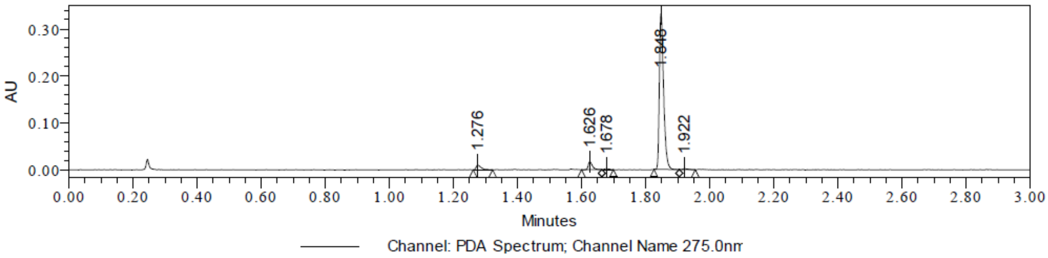
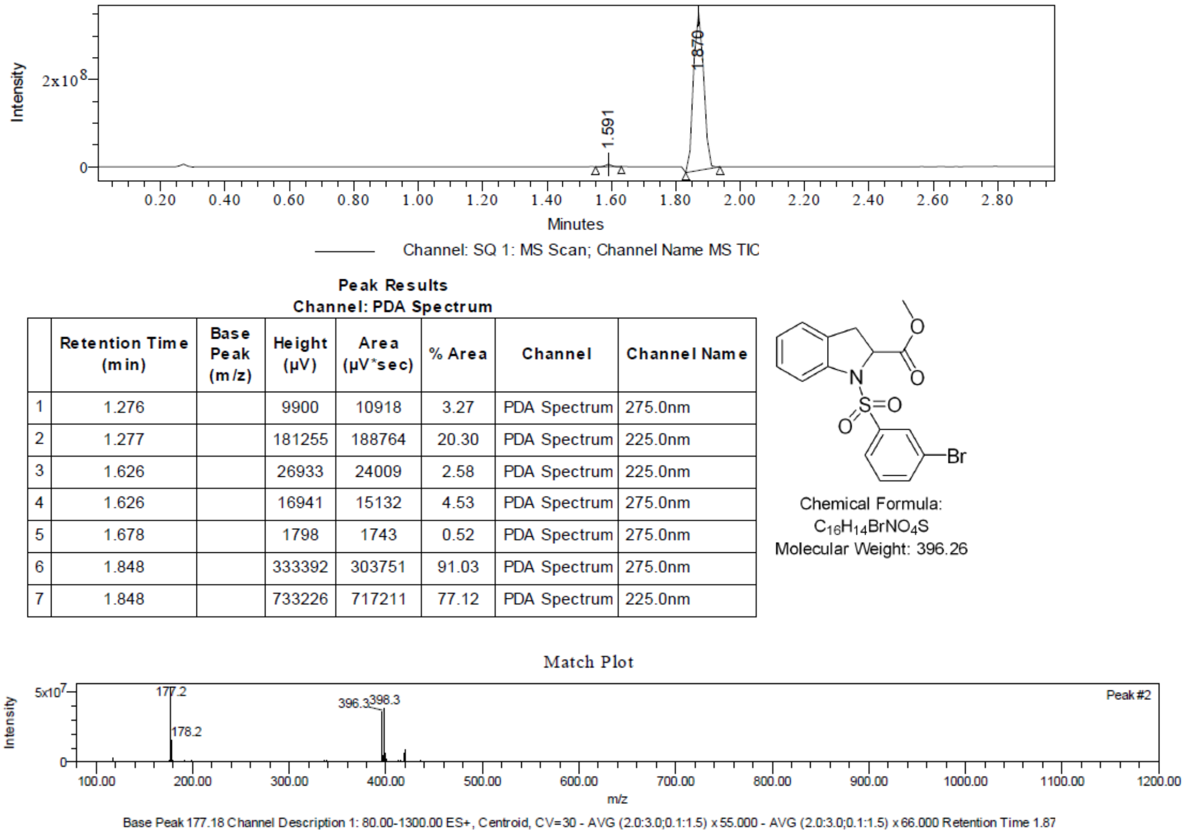


Figure 22: ^{13}C NMR of compound **3.**

Sample Name: 3
Sample Type: Unknown
Vial: 2:B,3
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-02_JULY-2023_21072023
Date Acquired: 21-07-2023 14:20:47 IST
Date Processed: 21-07-2023 14:30:23 IST, 21-07-2023 14:30:49 IST, 21-07-2023 14:31:12 IST

Acquired By: LCMS-02
Sample Set Name: 21072023 UCH 185 1ST
Acq. Method Set: METHOD C3
Processing Method: METHOD_C3, METHOD_C3_03
Channel Name: 275.0nm, 225.0nm, MS TIC
Proc. Chnl. Descr.: PDA 275.0 nm Blank Subtracted





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.276		9900	10918	3.27	PDA Spectrum	275.0nm
2	1.277		181255	188764	20.30	PDA Spectrum	225.0nm
3	1.626		26933	24009	2.58	PDA Spectrum	225.0nm
4	1.626		16941	15132	4.53	PDA Spectrum	275.0nm
5	1.678		1798	1743	0.52	PDA Spectrum	275.0nm
6	1.848		333392	303751	91.03	PDA Spectrum	275.0nm
7	1.848		733226	717211	77.12	PDA Spectrum	225.0nm

Chemical Formula: $C_{16}H_{14}BrNO_4S$
Molecular Weight: 396.26

Base Peak 177.18 Channel Description 1: 80.00-1300.00 ES+, Centroid, CV=30 - AVG (2.0:3.0;0.1:1.5) x 55.000 - AVG (2.0:3.0;0.1:1.5) x 66.000 Retention Time 1.87

Figure 23: LC-MS of compound **3.**

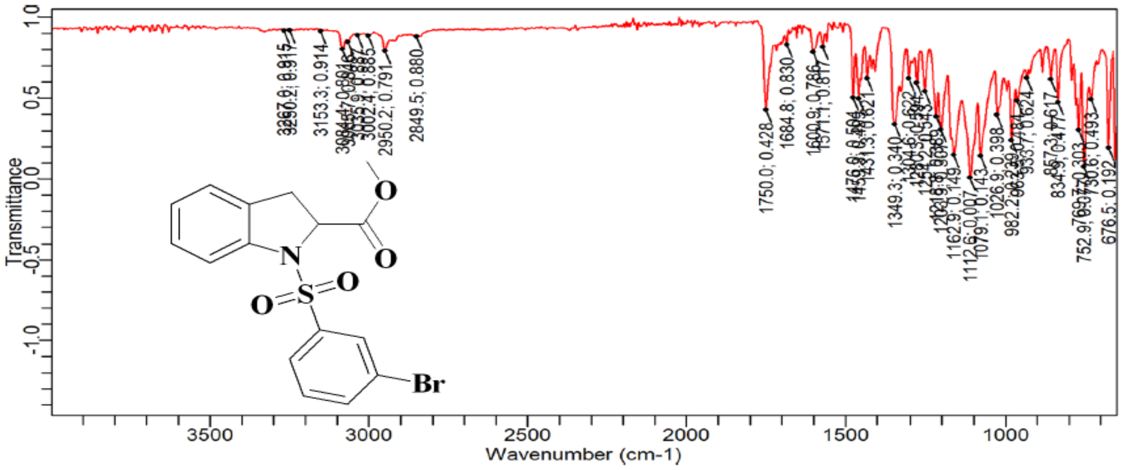
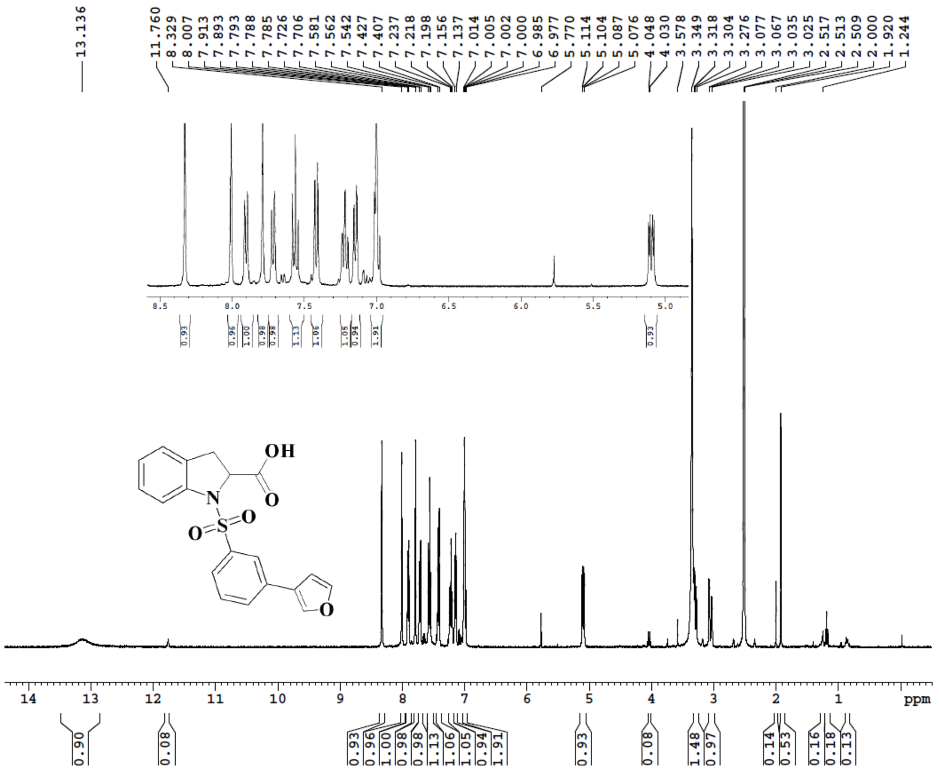


Figure 24: IR of compound **3.**



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EXPNO                 1
PROCNO                1

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INSTRUM           spect
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PULPROG            zg30
TD                16384
SOLVENT            DMSO
NS                   16
DS                    0
SWH            8012.820 Hz
FIDRES         0.978127 Hz
AQ            1.0223616 sec
RG               201.52
DW               62.400 usec
DE                 6.50 usec
TE                429.7 K
D1           1.00000000 sec
TD0                   1
SFO1        400.3024720 MHz
NUC1                 1H
P0                 5.00 usec
P1                15.00 usec
PLW1        14.00000000 W

F2 - Processing parameters
SI                65536
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WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
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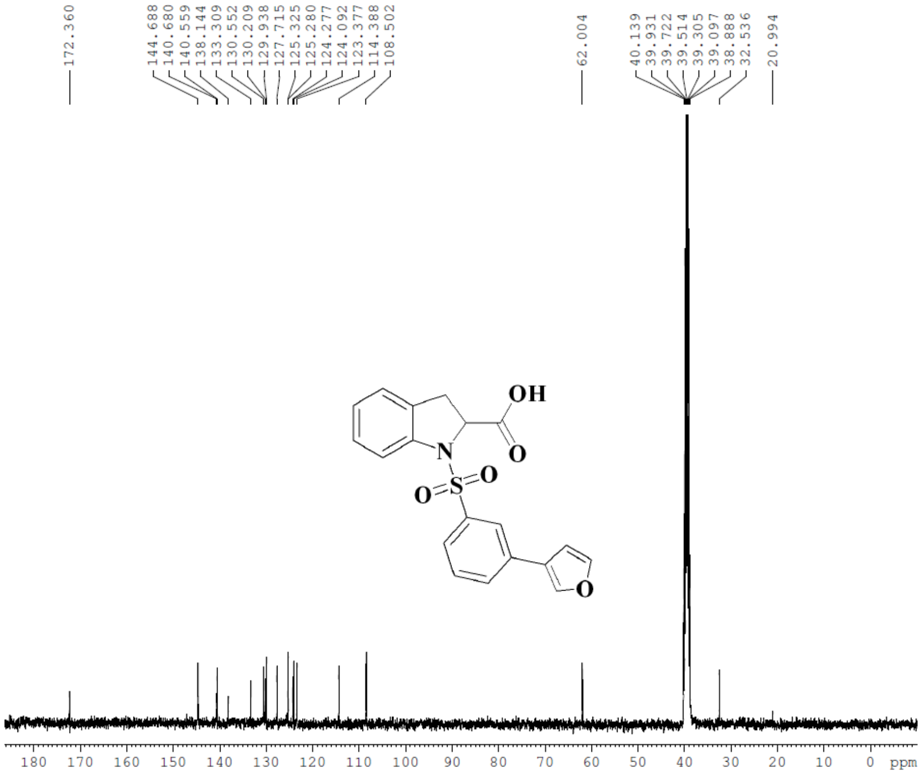
Figure 25: ^{1}H NMR of compound **4.**



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Current Data Parameters
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PROCNO                1

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NS                 1024
DS                    4
SWH           32051.281 Hz
FIDRES         0.489064 Hz
AQ            1.0223616 sec
RG                  203
DW               15.600 usec
DE                 6.50 usec
TE                304.9 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1        53.95100021 W

======== CHANNEL f2 ========
SFO2        400.1316005 MHz
NUC2                 1H
CPDPRG[2        waltz16
PCPD2             90.00 usec
PLW2        16.00000000 W
PLW12        0.38716000 W
PLW13        0.31360000 W

F2 - Processing parameters
SI                32768
SF          100.6128196 MHz
WDW                  EM
SSB      0
LB                 2.00 Hz
GB       0
PC                 1.40
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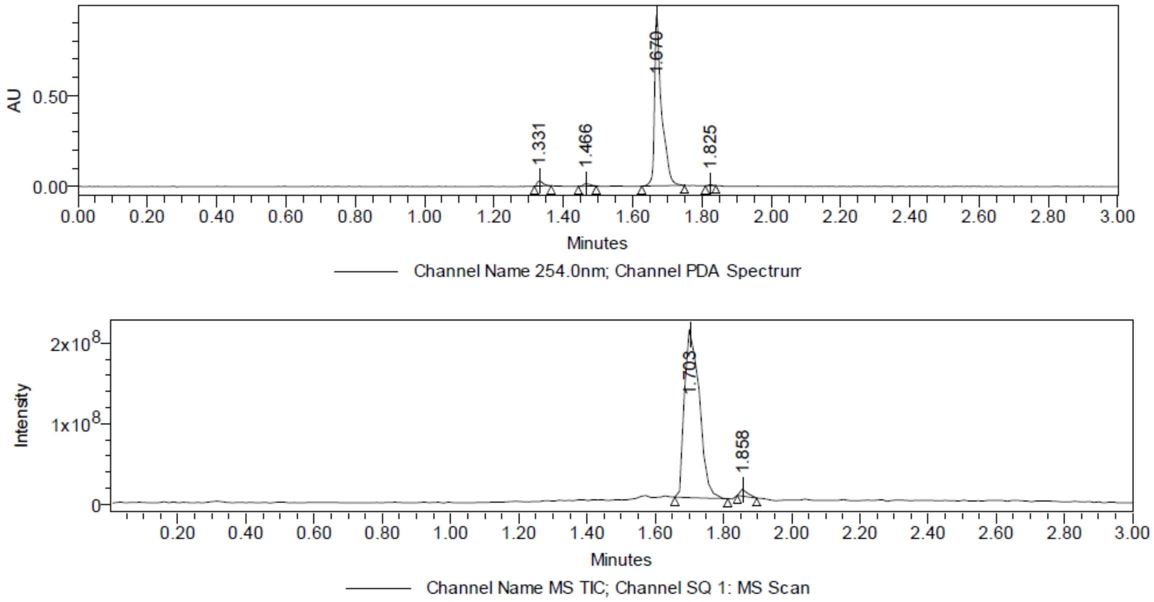
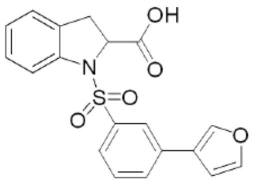
Figure 26: ^{13}C NMR of compound **4.**



Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.331		28190	33442	2.42	PDA Spectrum	254.0nm
2	1.331		48498	60524	2.80	PDA Spectrum	225.0nm
3	1.464		150896	201290	9.31	PDA Spectrum	225.0nm
4	1.466		12680	17953	1.30	PDA Spectrum	254.0nm
5	1.670		941224	1326748	95.93	PDA Spectrum	254.0nm
6	1.670		1316662	1899168	87.88	PDA Spectrum	225.0nm
7	1.825		5922	4838	0.35	PDA Spectrum	254.0nm



Chemical Formula:
$C_{19}H_{15}NO_5S$
Molecular Weight: 369.39

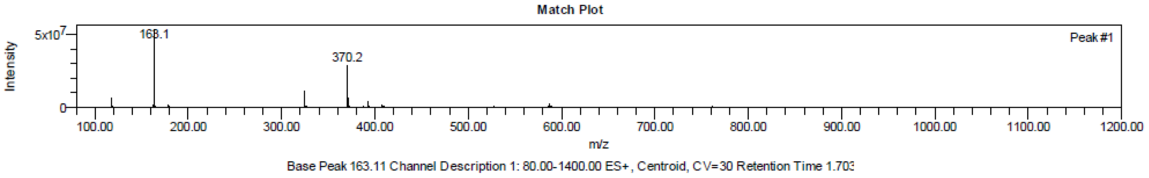


Figure 27: LC-MS of compound **4.**

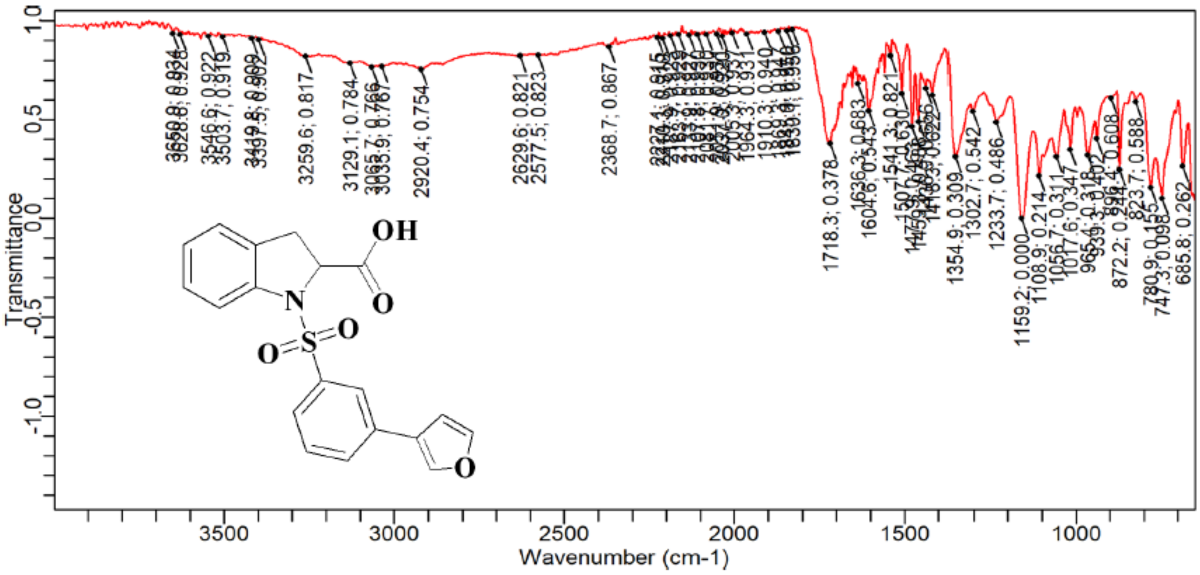
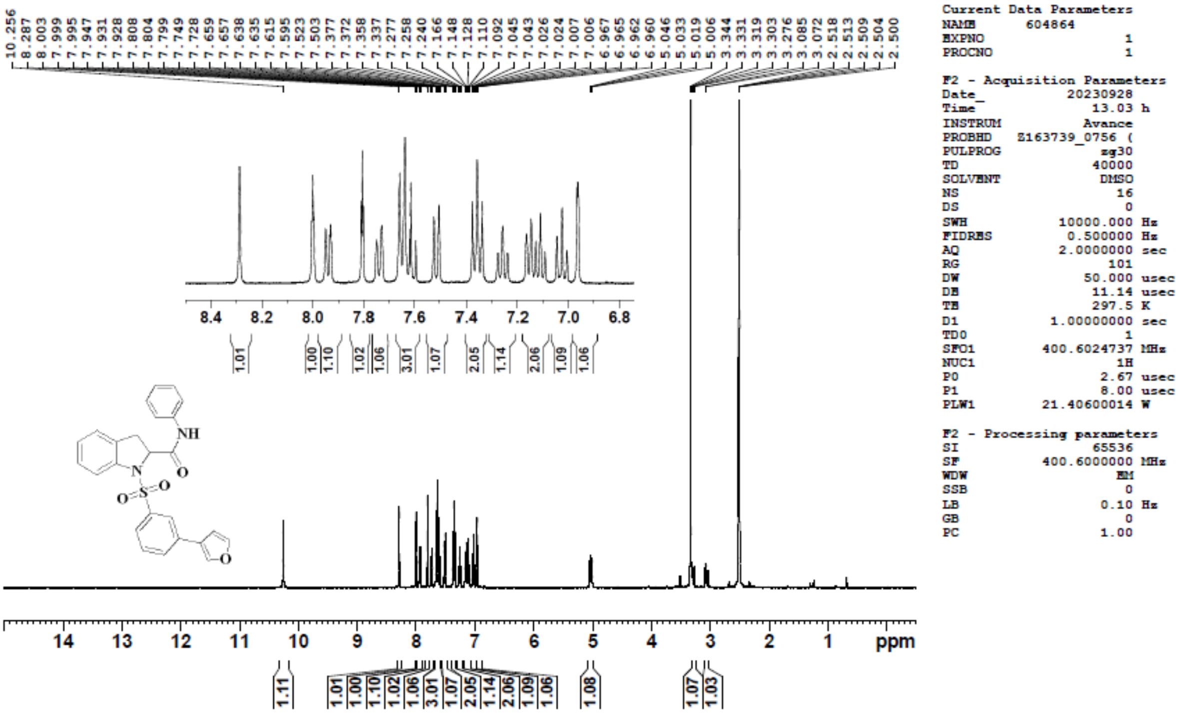


Figure 28: IR of compound **4.**

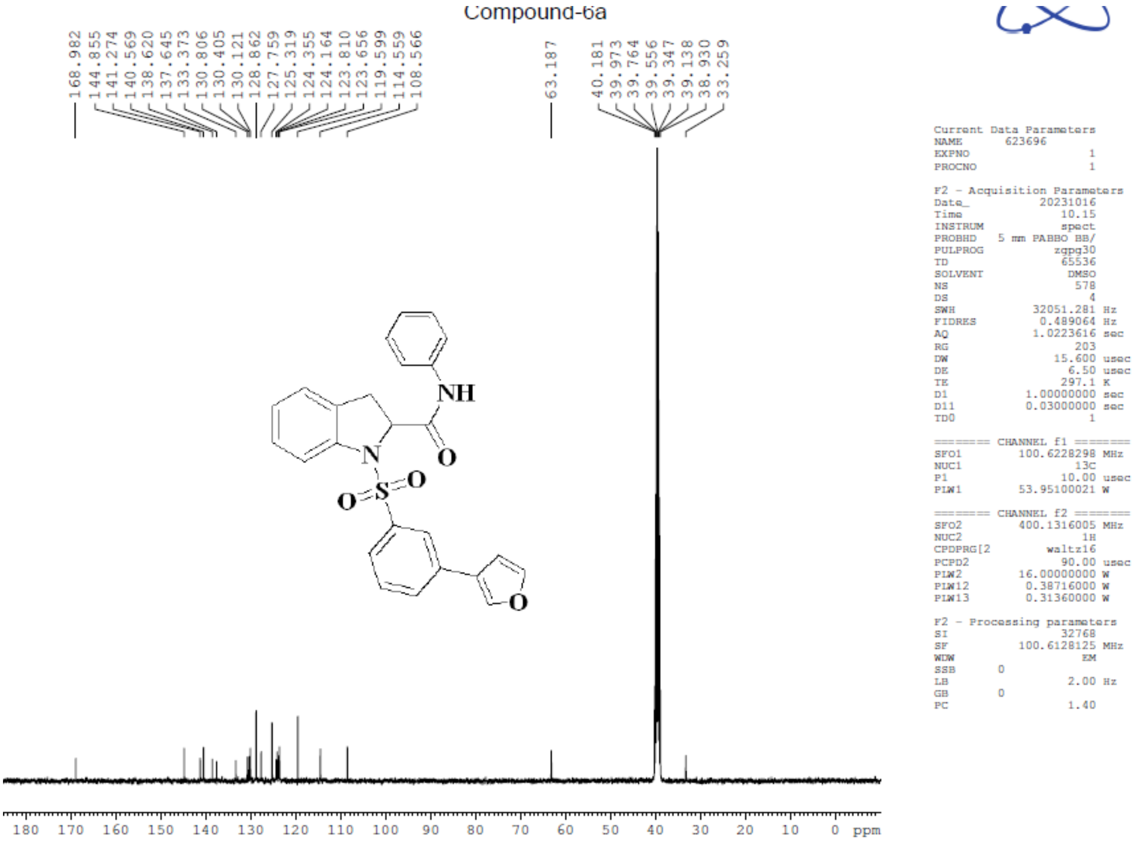


Current Data Parameters
NAME 604864
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20230928
Time 13.03 h
INSTRUM Avance
PROBHD Z163739_0756 (
PULPROG zg30
TD 40000
SOLVENT DMSO
NS 16
DS 0
SWH 10000.000 Hz
FIDRES 0.500000 Hz
AQ 2.0000000 sec
RG 101
DW 50.000 usec
DE 11.14 usec
TE 297.5 K
D1 1.00000000 sec
TD0 1
SFO1 400.6024737 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 21.40600014 W

F2 - Processing parameters
SI 65536
SF 400.6000000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

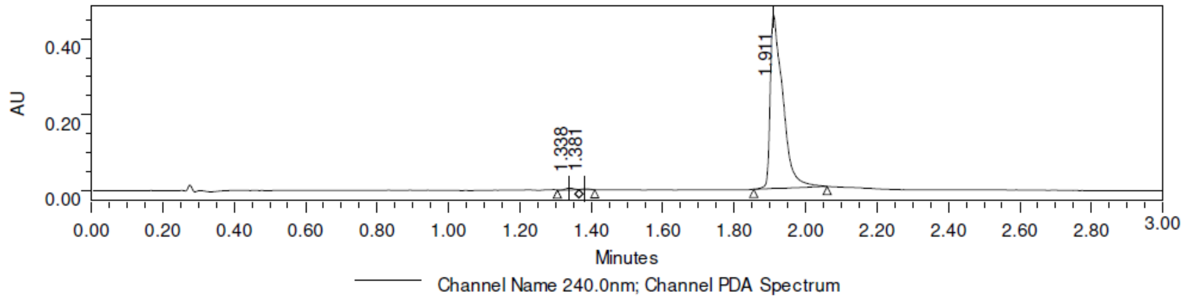
Figure 29: ^{1}H NMR of compound **6a.**

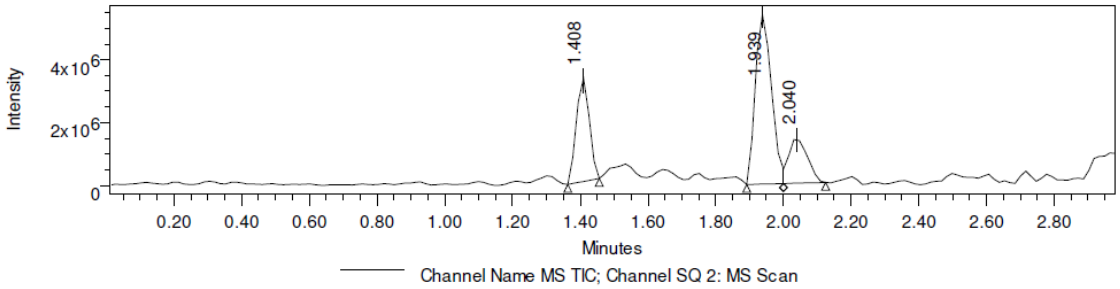


```
Current Data Parameters
NAME        623696
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20231016
Time                 10.15
INSTRUM              spect
PROBHD   5 mm PABBO BB/
PULPROG            zgpg30
TD                   65536
SOLVENT               DMSO
NS                     578
DS                       4
SWH              32051.281 Hz
FIDRES            0.489064 Hz
AQ               1.0223616 sec
RG                     203
DW                  15.600 usec
DE                    6.50 usec
TE                   297.1 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                      1

======= CHANNEL f1 =======
SFO1           100.6228298 MHz
NUC1                   13C
P1                   10.00 usec
PLW1           53.95100021 W

======= CHANNEL f2 =======
SFO2           400.1316005 MHz
NUC2                    1H
CPDPRG[2           waltz16
PCPD2                90.00 usec
PLW2           16.00000000 W
PLW12           0.38716000 W
PLW13           0.31360000 W

F2 - Processing parameters
SI                   32768
SF             100.6128125 MHz
WDW                     EM
SSB      0
LB                    2.00 Hz
GB       0
PC                    1.40
```

Figure 30: ^{13}C NMR of compound **6a.**

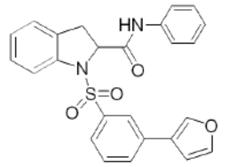
Sample Name:	Compound-6a		
Sample Type:	Unknown	Acquired By:	LCMS_03
Vial:	2:C,5	Sample Set Name:	20092023_UCH 159_1ST JM
Injection #:	1	Acq. Method Set:	PDS_METHOD_C
Injection Volume:	1.00 ul	Processing Method:	PDS_METHOD_C_3,
Run Time:	3.0 Minutes	Channel Name:	240.0nm, 225.0nm, MS TIC
Project Name	LCMS-03_SEP-2023_20092023	Proc. Chnl. Descr.:	SQ 2: MS Scan MS TIC,
Date Acquired:	20-09-2023 15:39:41 IST		
Date Processed:	20-09-2023 15:49:09 IST, 20-09-2023 15:50:00 IST, 20-09-2023 15:50:24 IST		



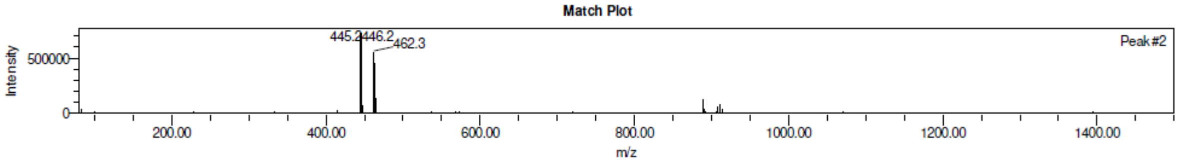


Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.294		3436	1678	0.17	PDA Spectrum	225.0nm
2	1.338		4446	7785	0.69	PDA Spectrum	240.0nm
3	1.381		2593	4137	0.36	PDA Spectrum	240.0nm
4	1.911		406657	957903	99.83	PDA Spectrum	225.0nm
5	1.911		459567	1124072	98.95	PDA Spectrum	240.0nm



Chemical Formula: $C_{25}H_{20}N_2O_4S$
Molecular Weight: 444.51



Base Peak 445.24 Channel Description 2: 80.00-1500.00 ES+, Centroid, CV=10 - AVG (2.1:2.9) x 44.000 Retention Time 1.93

Figure 31: LC-MS of compound **6a.**

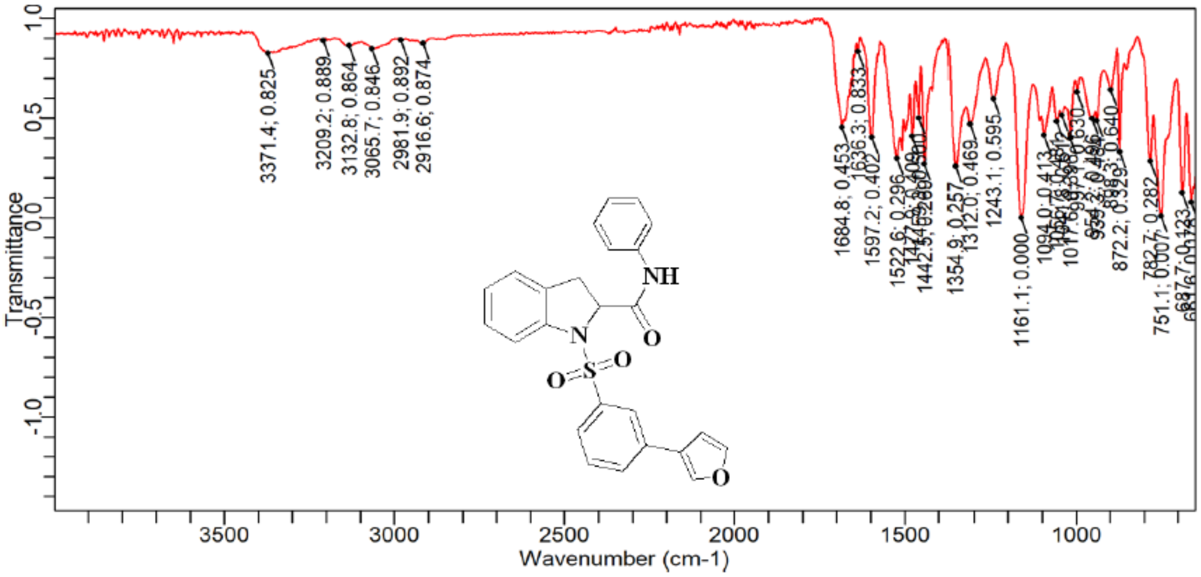


Figure 32: IR of compound **6a.**

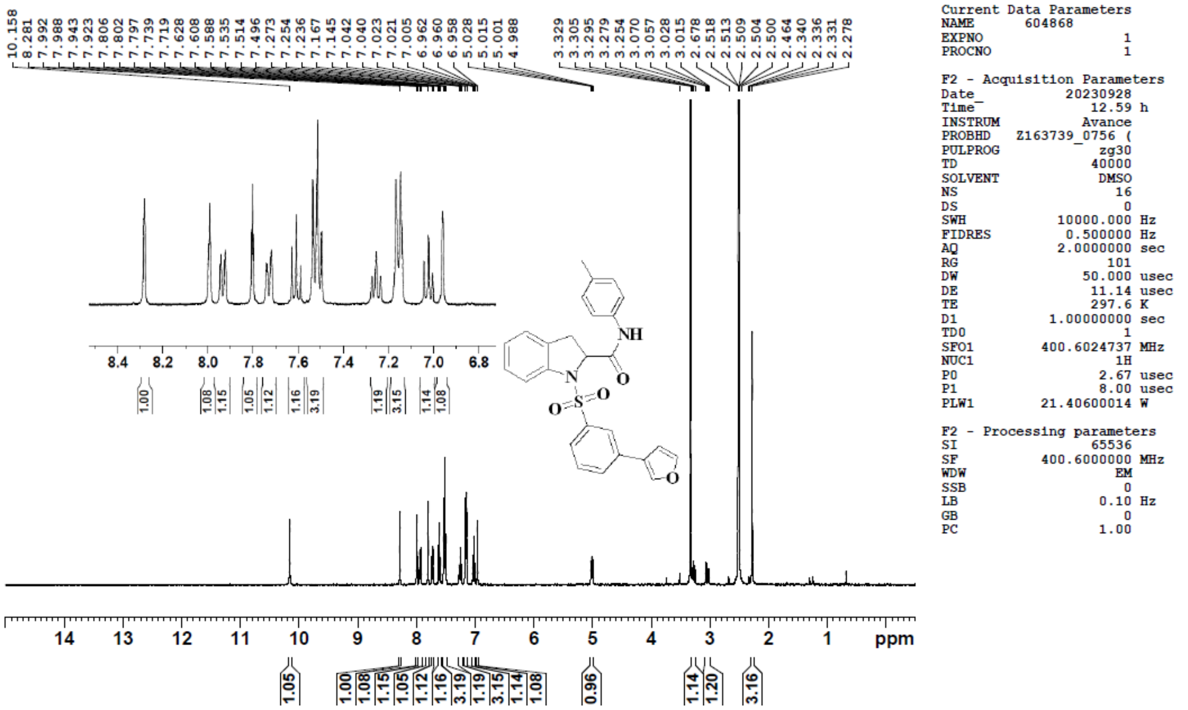


Figure 33: ^{1}H NMR of compound **6b.**

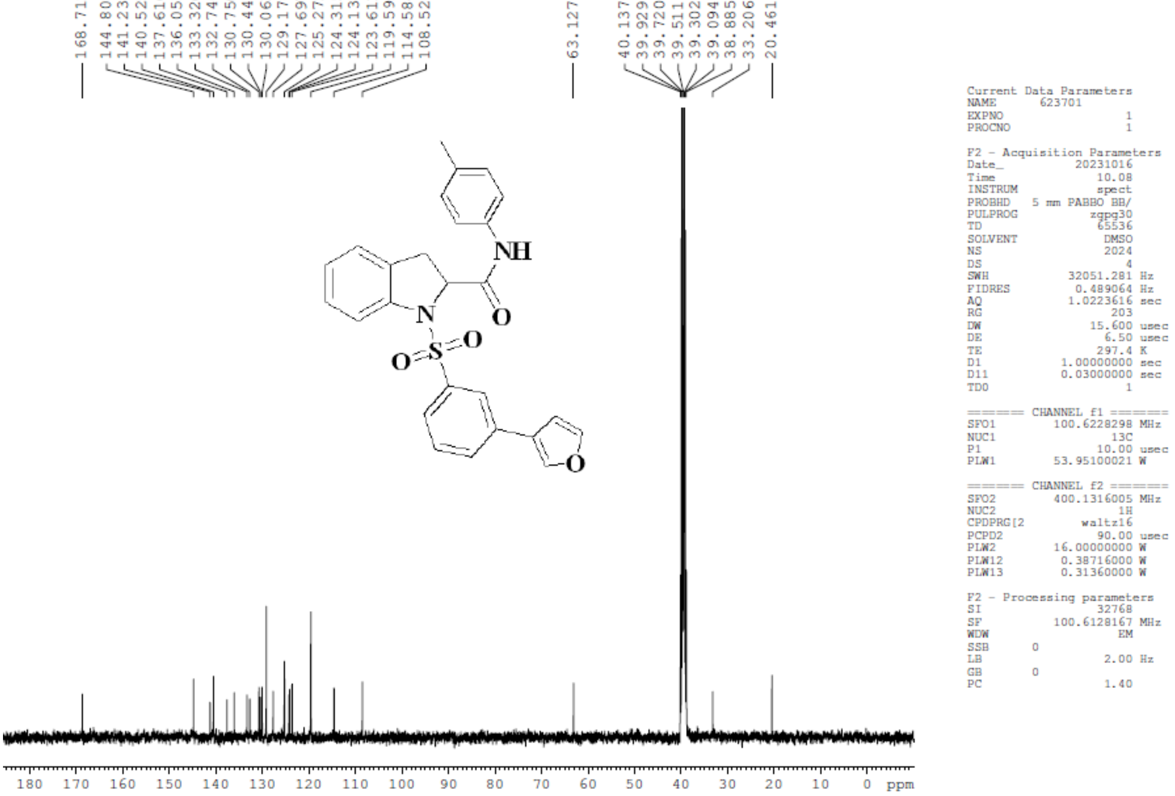
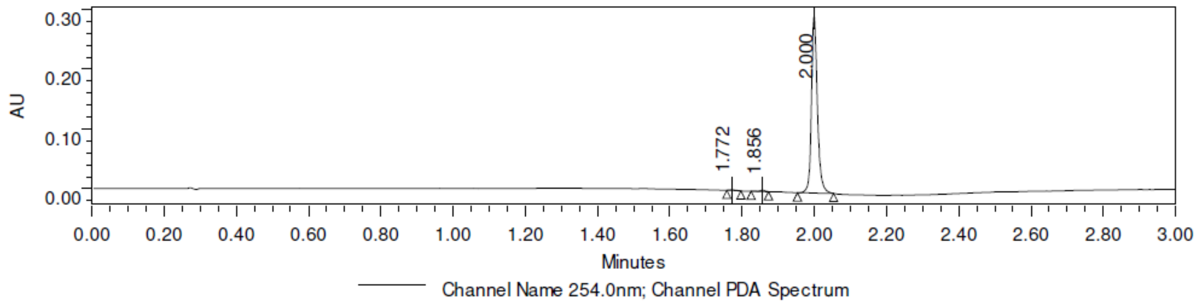
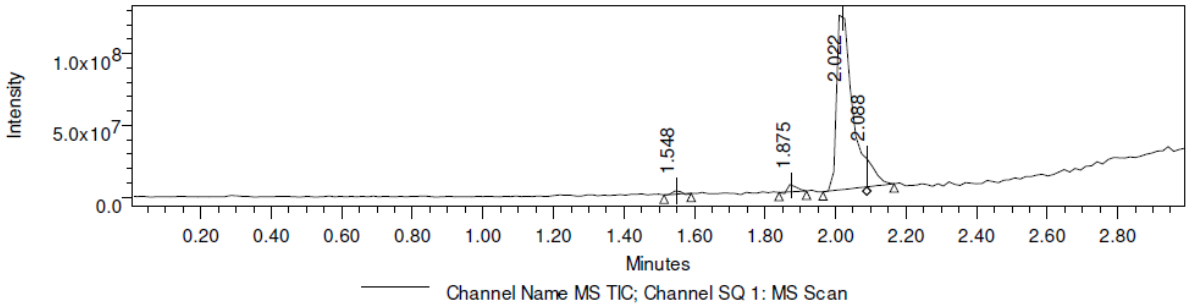


Figure 34: ^{13}C NMR of compound **6b.**

Sample Name: Compound-6b
Sample Type: Unknown
Vial: 2:A,5
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-03_SEP-2023_18092023
Date Acquired: 18-09-2023 22:38:24 IST
Date Processed: 19-09-2023 04:09:56 IST, 19-09-2023 04:10:07 IST, 19-09-2023 04:10:25 IST

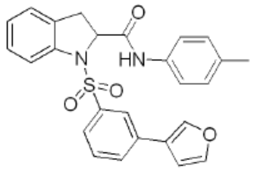
Acquired By: LCMS_03
Sample Set Name: 18092023_UCH 125_NIGHT
Acq. Method Set: PDS_METHOD_C
Processing Method: PDS_METHOD_C_302,
Channel Name: 202.0nm, MS TIC, 254.0nm
Proc. Chnl. Descr.: PDA 254.0 nm Blank Subtracted





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.772		979	1115	0.33	PDA Spectrum	254.0nm
2	1.855		7984	7054	0.76	PDA Spectrum	202.0nm
3	1.856		1915	1905	0.56	PDA Spectrum	254.0nm
4	1.903		872	551	0.06	PDA Spectrum	202.0nm
5	2.000		297201	339209	99.12	PDA Spectrum	254.0nm
6	2.000		776523	923596	99.18	PDA Spectrum	202.0nm



Chemical Formula: $C_{26}H_{22}N_2O_4S$
Molecular Weight: 458.53

Figure 35: LC-MS of compound **6b.**

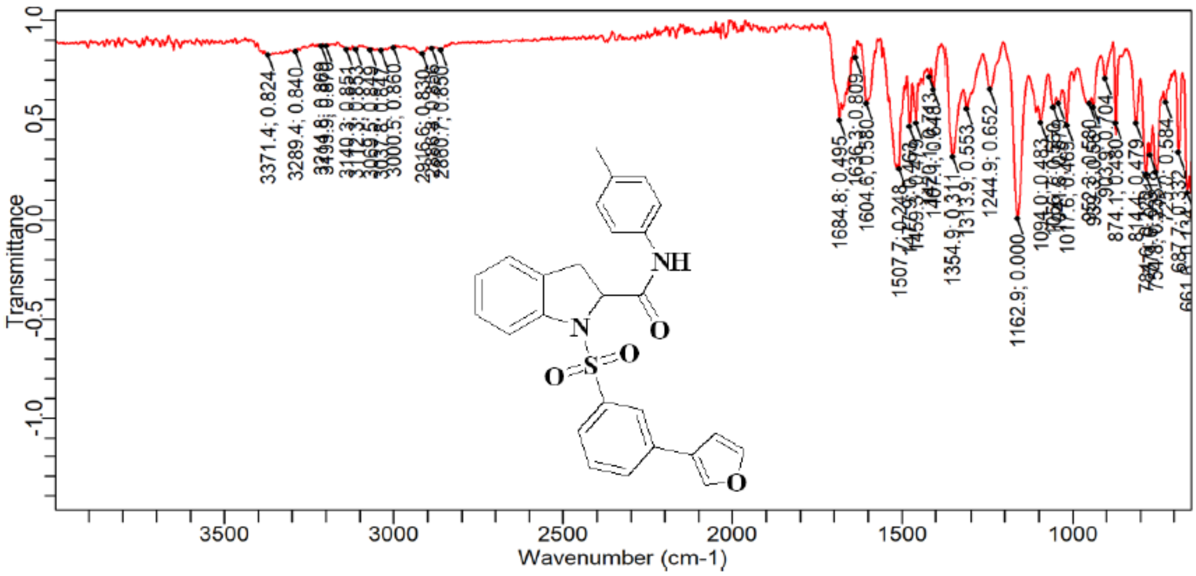
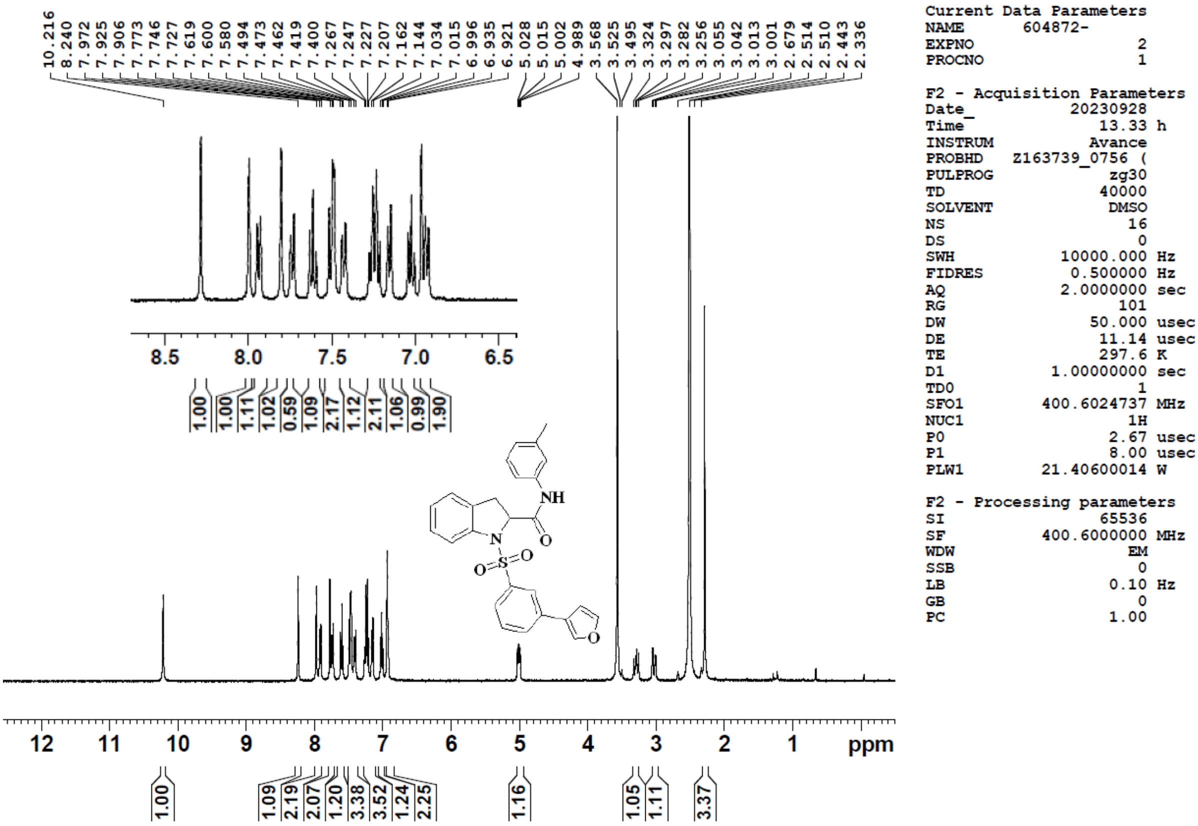
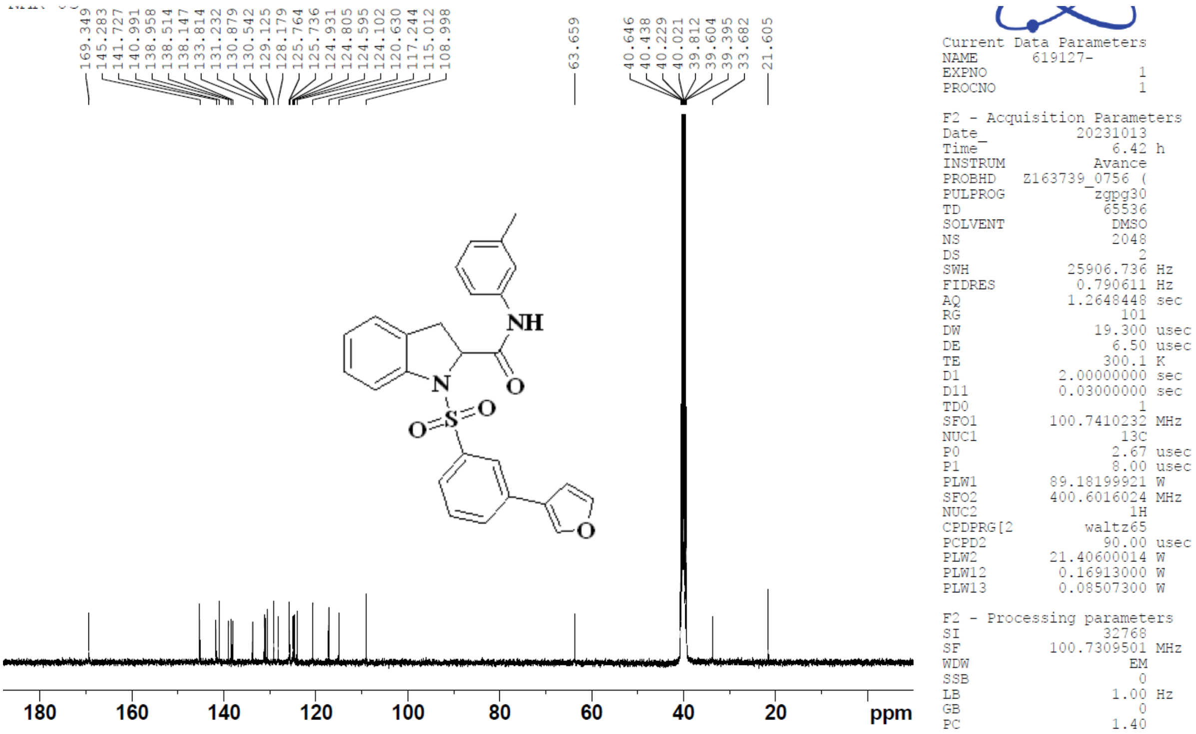


Figure 36: IR of compound **6b.**



```
Current Data Parameters
NAME       604872-
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20230928
Time              13.33 h
INSTRUM           Avance
PROBHD   Z163739_0756 (
PULPROG            zg30
TD                40000
SOLVENT            DMSO
NS                   16
DS                    0
SWH           10000.000 Hz
FIDRES         0.500000 Hz
AQ            2.0000000 sec
RG                  101
DW               50.000 usec
DE                11.14 usec
TE                297.6 K
D1           1.00000000 sec
TD0                   1
SFO1        400.6024737 MHz
NUC1                 1H
P0                 2.67 usec
P1                 8.00 usec
PLW1        21.40600014 W

F2 - Processing parameters
SI                65536
SF          400.6000000 MHz
WDW                  EM
SSB                   0
LB                 0.10 Hz
GB                    0
PC                 1.00
```

Figure 37: ^{1}H NMR of compound **6c.**

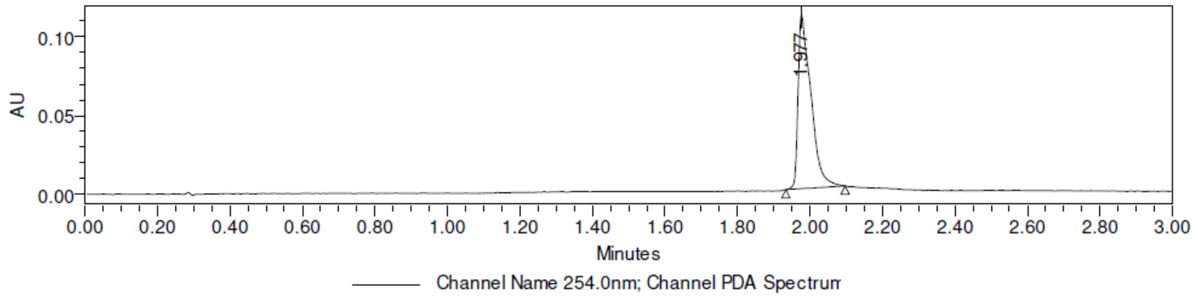


```
Current Data Parameters
NAME       619127-
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20231013
Time                  6.42 h
INSTRUM             Avance
PROBHD    Z163739_0756 (
PULPROG             zgpg30
TD                   65536
SOLVENT               DMSO
NS                    2048
DS                       2
SWH              25906.736 Hz
FIDRES            0.790611 Hz
AQ               1.2648448 sec
RG                     101
DW                  19.300 usec
DE                    6.50 usec
TE                   300.1 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1
SFO1           100.7410232 MHz
NUC1                   13C
P0                    2.67 usec
P1                    8.00 usec
PLW1           89.18199921 W
SFO2           400.6016024 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2                90.00 usec
PLW2           21.40600014 W
PLW12           0.16913000 W
PLW13           0.08507300 W

F2 - Processing parameters
SI                   32768
SF             100.7309501 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Figure 38: ^{13}C NMR of compound **6c.**

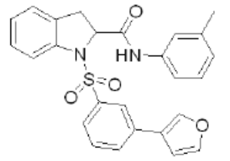
Sample Name: Compound-6c
Sample Type: Unknown
Vial: 2:C,3
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-03_SEP-2023_20092023
Date Acquired: 20-09-2023 15:31:35 IST
Date Processed: 20-09-2023 15:35:12 IST, 20-09-2023 15:35:27 IST, 20-09-2023 15:35:35 IST

Acquired By: LCMS_03
Sample Set Name: 20092023_UCH 159_1ST JM
Acq. Method Set: PDS_METHOD_C
Processing Method: PDS_METHOD_C_3,
Channel Name: 220.0nm, 254.0nm, MS TIC
Proc. Chnl. Descr.: PDA 254.0 nm Blank Subtracted

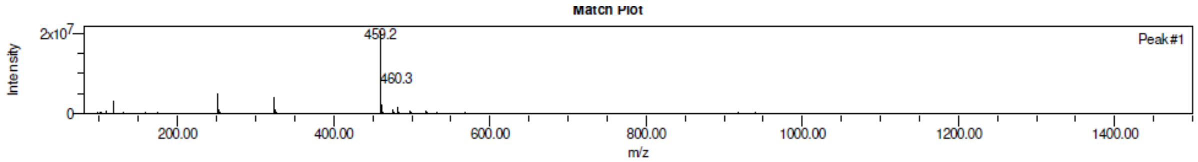


Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.977		110380	271242	100.00	PDA Spectrum	254.0nm
2	1.977		120336	285386	100.00	PDA Spectrum	220.0nm



Chemical Formula: $C_{26}H_{22}N_2O_4S$
Molecular Weight: 458.53



Base Peak 459.24 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 Retention Time 2.001

Figure 39: LC-MS of compound **6c.**

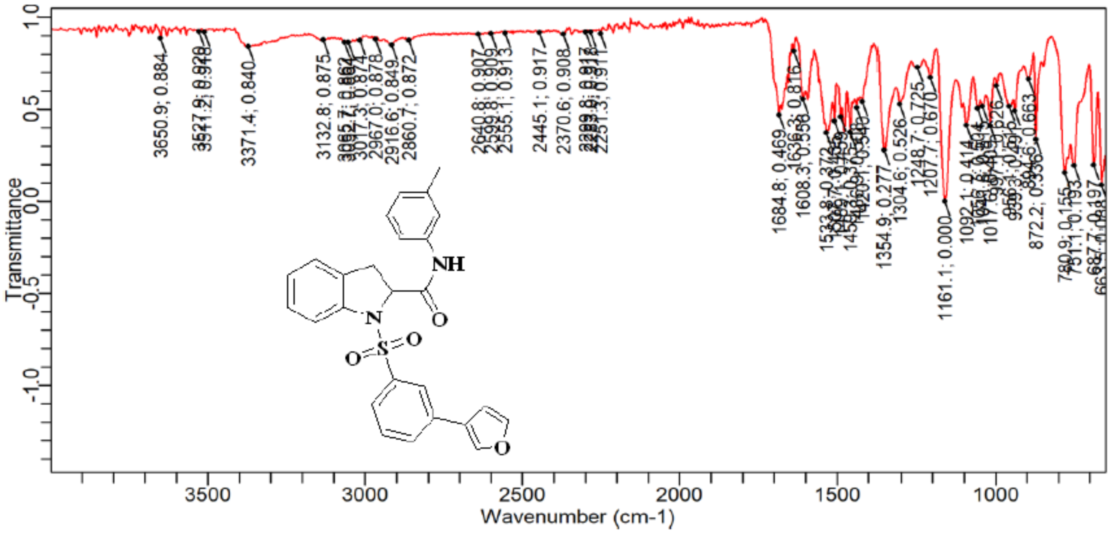
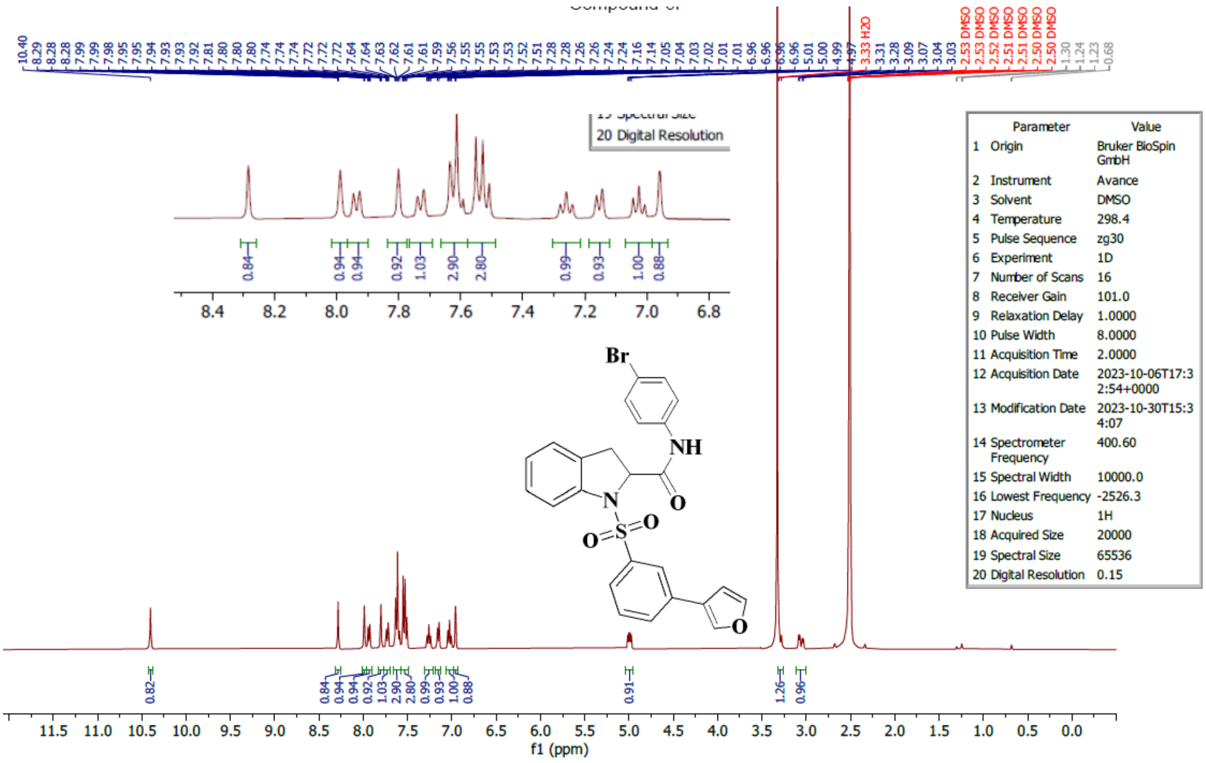
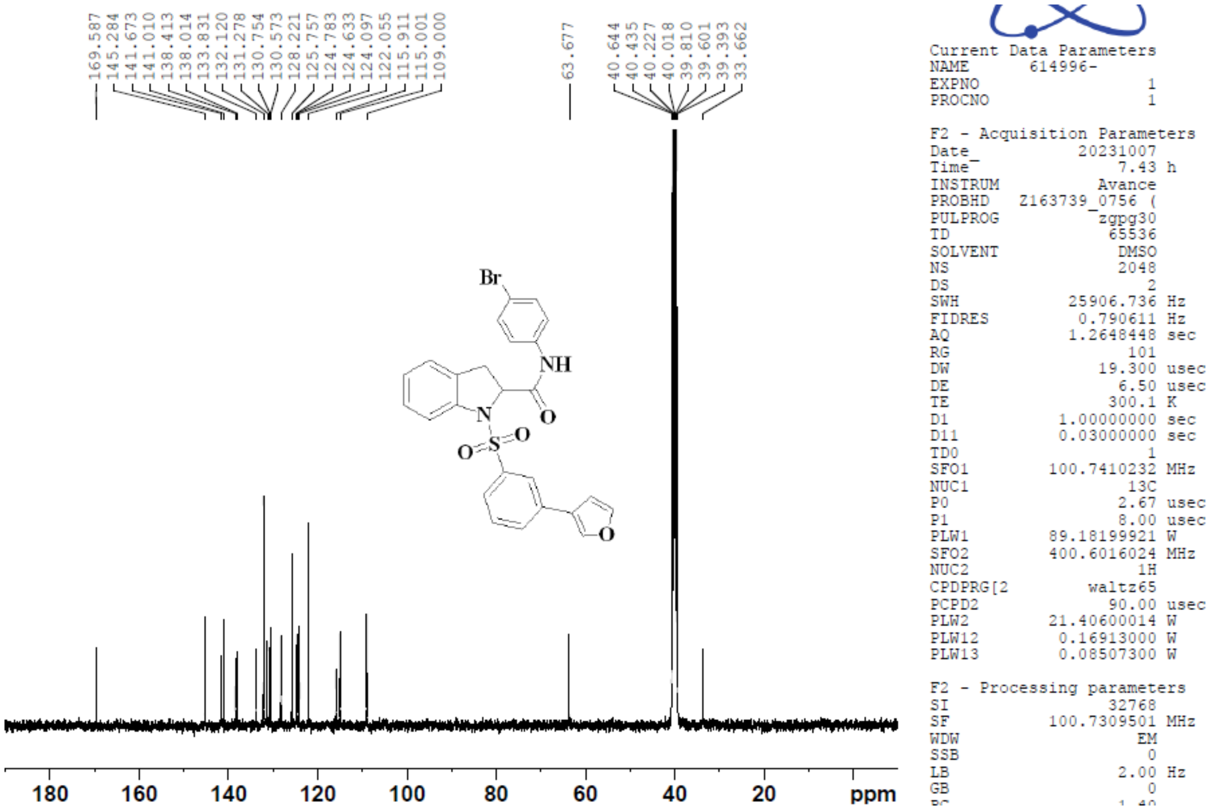


Figure 40: IR of compound **6c.**



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	DMSO
4	Temperature	298.4
5	Pulse Sequence	zg30
6	Experiment	1D
7	Number of Scans	16
8	Receiver Gain	101.0
9	Relaxation Delay	1.0000
10	Pulse Width	8.0000
11	Acquisition Time	2.0000
12	Acquisition Date	2023-10-06T17:32:54+0000
13	Modification Date	2023-10-30T15:34:07
14	Spectrometer Frequency	400.60
15	Spectral Width	10000.0
16	Lowest Frequency	-2526.3
17	Nucleus	1H
18	Acquired Size	20000
19	Spectral Size	65536
20	Digital Resolution	0.15

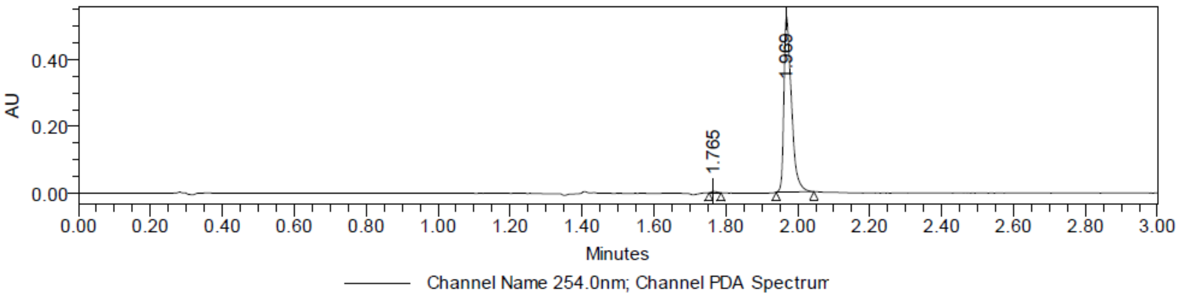
Figure 41: ^{1}H NMR of compound **6i.**

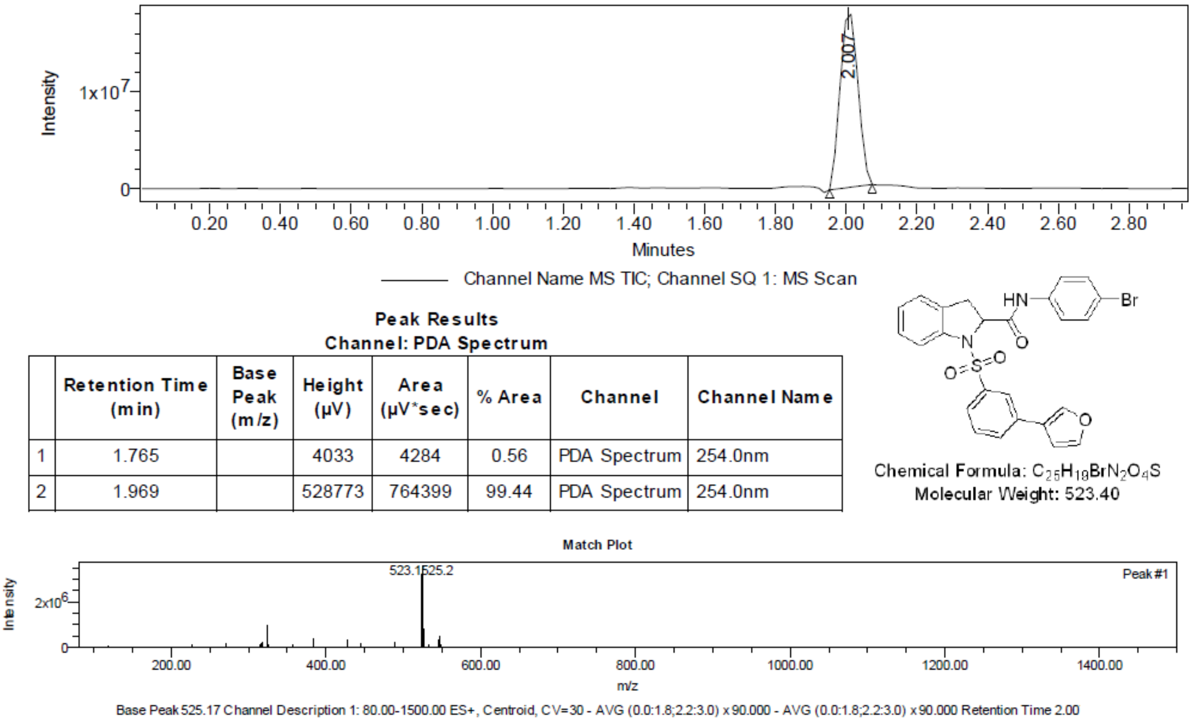


```
Current Data Parameters
NAME       614996-
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20231007
Time               7.43 h
INSTRUM          Avance
PROBHD   Z163739_0756 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 2048
DS                    2
SWH           25906.736 Hz
FIDRES         0.790611 Hz
AQ            1.2648448 sec
RG                  101
DW               19.300 usec
DE                 6.50 usec
TE                300.1 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.7410232 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        89.18199921 W
SFO2        400.6016024 MHz
NUC2                 1H
CPDPRG[2        waltz65
PCPD2             90.00 usec
PLW2        21.40600014 W
PLW12        0.16913000 W
PLW13        0.08507300 W

F2 - Processing parameters
SI                32768
SF          100.7309501 MHz
WDW                  EM
SSB                   0
LB                 2.00 Hz
GB                    0
```

Figure 42: ^{13}C NMR of compound **6i.**

Sample Name:	Compound-6i		
Sample Type:	Unknown	Acquired By:	LCMS_06
Vial:	1:B,5	Sample Set Name:	27092023_UCH125_2nd_
Injection #:	1	Acq. Method Set:	PDS_METHOD_C3
Injection Volume:	1.00 ul	Processing Method:	PDS_METHOD_C3 4,
Run Time:	3.0 Minutes	Channel Name:	MS TIC, 254.0nm
Project Name:	LCMS-06_SEP-2023_27092023	Proc. Chnl. Descr.:	PDA 254.0 nm Blank Subtracted
Date Acquired:	28-09-2023 00:36:19 IST		
Date Processed:	28-09-2023 00:53:08 IST, 28-09-2023 00:53:31 IST		





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.765		4033	4284	0.56	PDA Spectrum	254.0nm
2	1.969		528773	764399	99.44	PDA Spectrum	254.0nm

Chemical Formula: $C_{25}H_{18}BrN_2O_4S$
Molecular Weight: 523.40

Base Peak 525.17 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 - AVG (0.0:1.8;2.2:3.0) x 90.000 - AVG (0.0:1.8;2.2:3.0) x 90.000 Retention Time 2.00

Figure 43: LC-MS of compound **6i.**

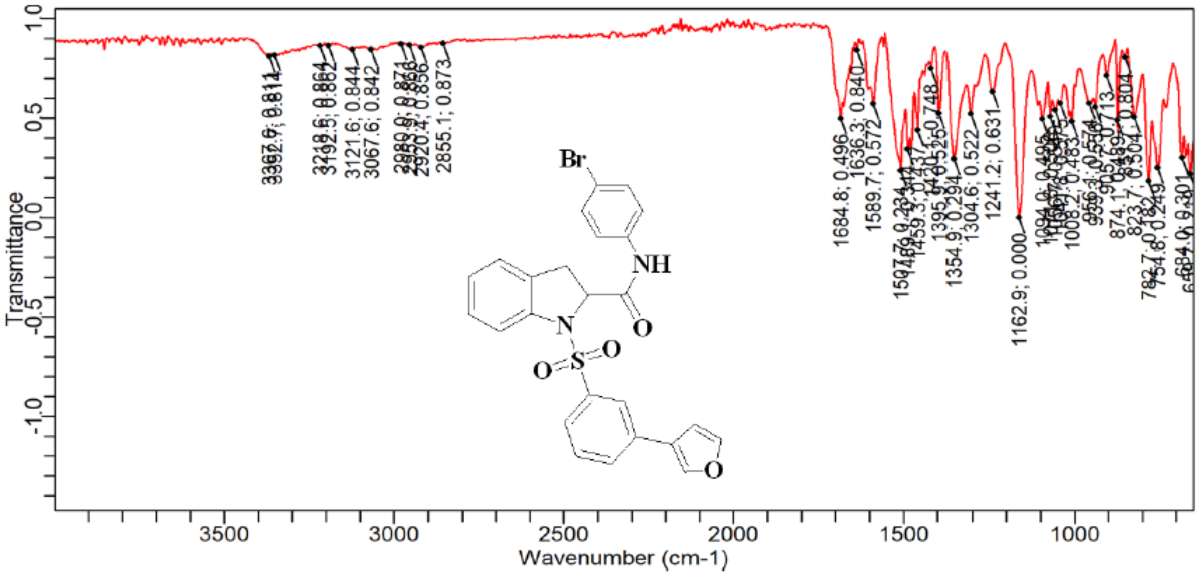
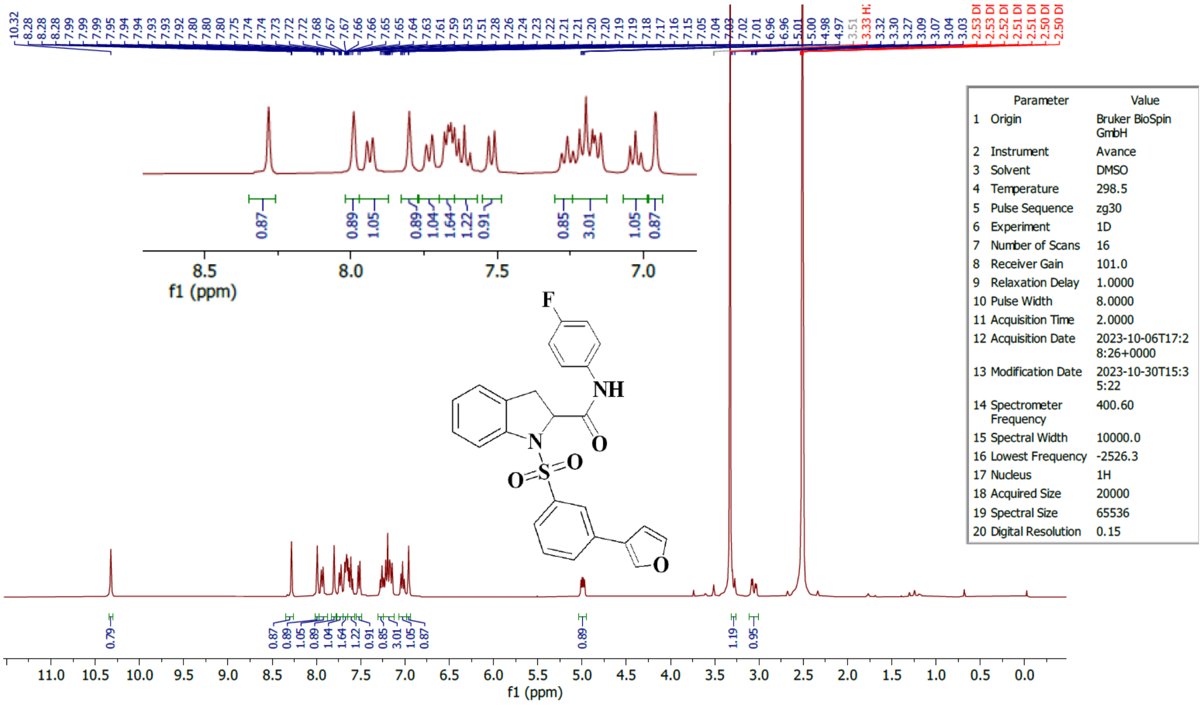
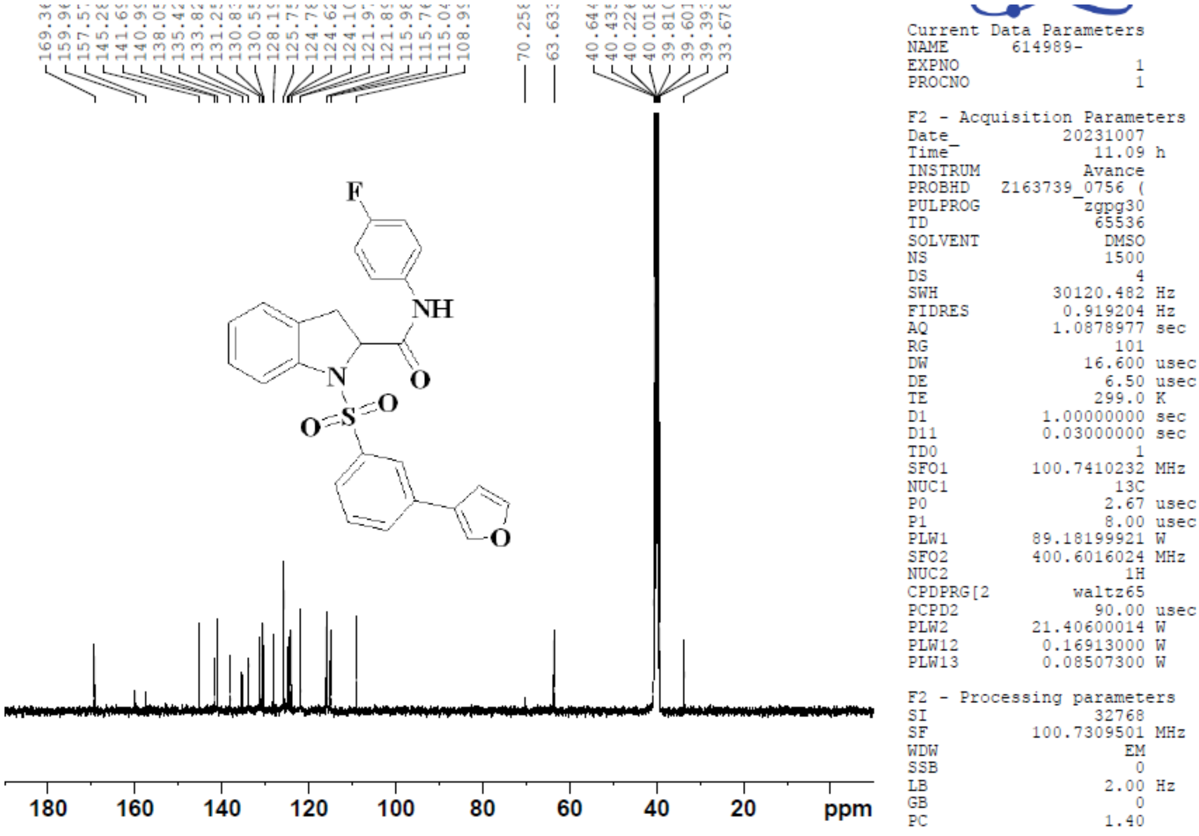


Figure 44: IR of compound **6i.**



	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	DMSO
4	Temperature	298.5
5	Pulse Sequence	zg30
6	Experiment	1D
7	Number of Scans	16
8	Receiver Gain	101.0
9	Relaxation Delay	1.0000
10	Pulse Width	8.0000
11	Acquisition Time	2.0000
12	Acquisition Date	2023-10-06T17:28:26+0000
13	Modification Date	2023-10-30T15:35:22
14	Spectrometer Frequency	400.60
15	Spectral Width	10000.0
16	Lowest Frequency	-2526.3
17	Nucleus	1H
18	Acquired Size	20000
19	Spectral Size	65536
20	Digital Resolution	0.15

Figure 45: ^{1}H NMR of compound **6k.**

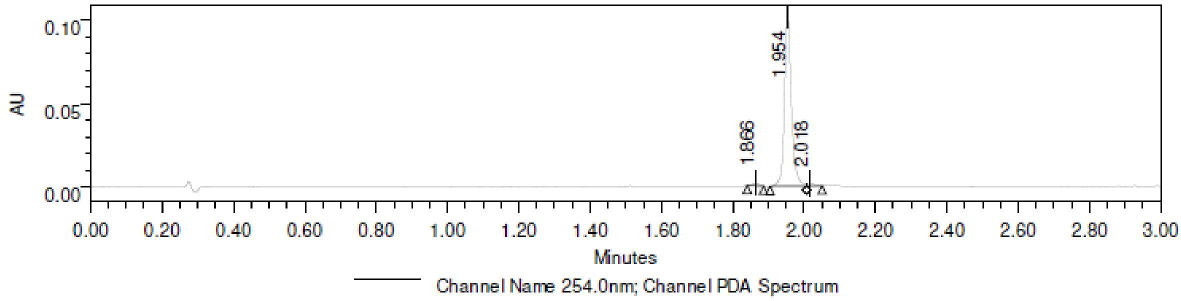


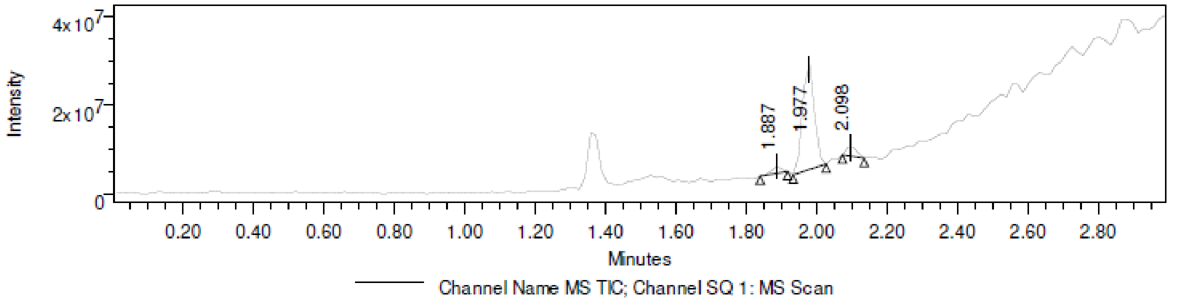
```
Current Data Parameters
NAME         614989-
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_          20231007
Time              11.09 h
INSTRUM          Avance
PROBHD   Z163739_0756 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 1500
DS                    4
SWH           30120.482 Hz
FIDRES         0.919204 Hz
AQ            1.0878977 sec
RG                  101
DW               16.600 usec
DE                 6.50 usec
TE                299.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.7410232 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        89.18199921 W
SFO2        400.6016024 MHz
NUC2                 1H
CPDPRG[2        waltz65
PCPD2             90.00 usec
PLW2        21.40600014 W
PLW12        0.16913000 W
PLW13        0.08507300 W

F2 - Processing parameters
SI                32768
SF          100.7309501 MHz
WDW                  EM
SSB                   0
LB                 2.00 Hz
GB                    0
PC                 1.40
```

Figure 46: ^{13}C NMR of compound **6k.**

Sample Name: Compound-6k
Sample Type: Unknown
Vial: 1:C,7
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-03_SEP-2023_25092023
Date Acquired: 26-09-2023 00:42:07 IST
Date Processed: 26-09-2023 02:45:24 IST, 26-09-2023 02:45:47 IST

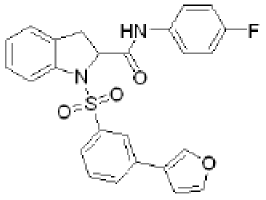
Acquired By: LCMS_03
Sample Set Name: 25092023_UCH 125_NIGHT
Acq. Method Set: PDS_METHOD_C
Processing Method: PDS_METHOD_C_2,
Channel Name: MS TIC, 254.0nm
Proc. Chnl. Descr.: PDA 254.0 nm Blank Subtracted





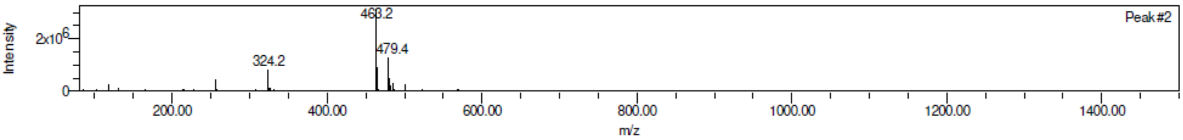
Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.866		1553	2081	1.47	PDA Spectrum	254.0nm
2	1.954		102916	136934	96.96	PDA Spectrum	254.0nm
3	2.018		1523	2210	1.56	PDA Spectrum	254.0nm



Chemical Formula: $C_{25}H_{19}FN_2O_4S$
Molecular Weight: 462.50

Match Plot



Base Peak 463.23 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 Retention Time 1.977

Figure 47: LC-MS of compound **6k.**

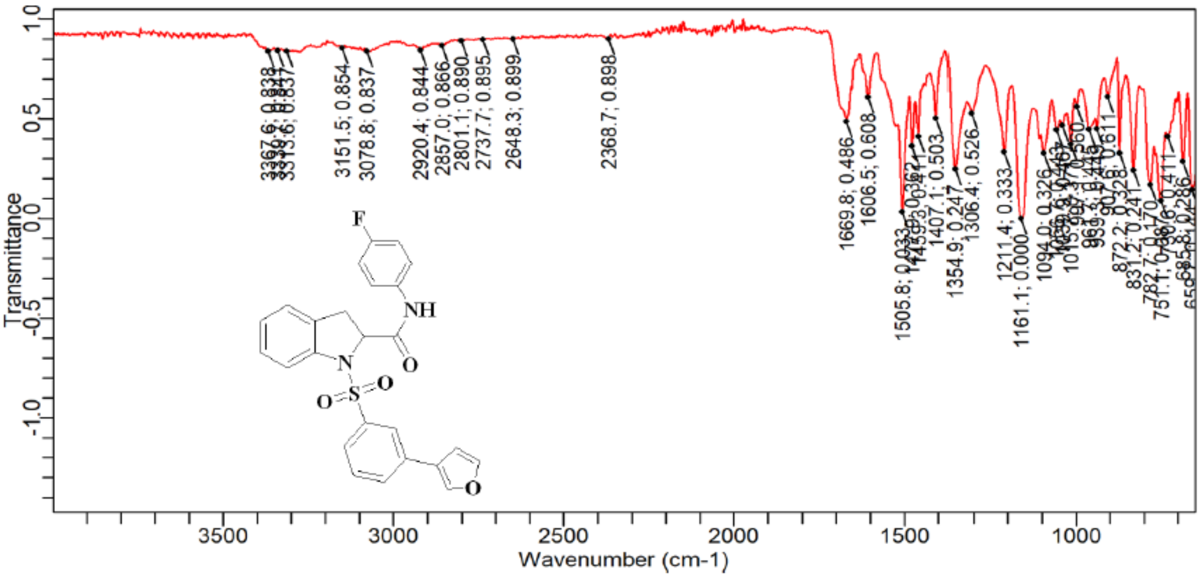


Figure 48: IR of compound **6k.**

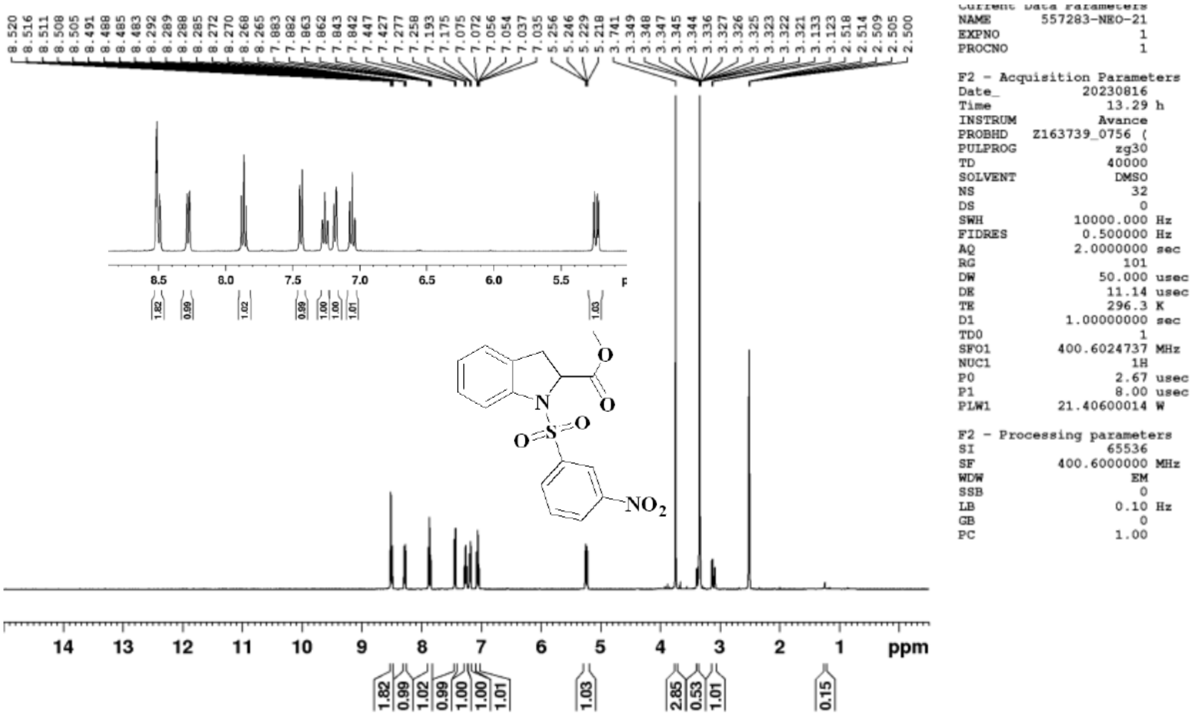


Figure 49: ^{1}H NMR of compound **7.**

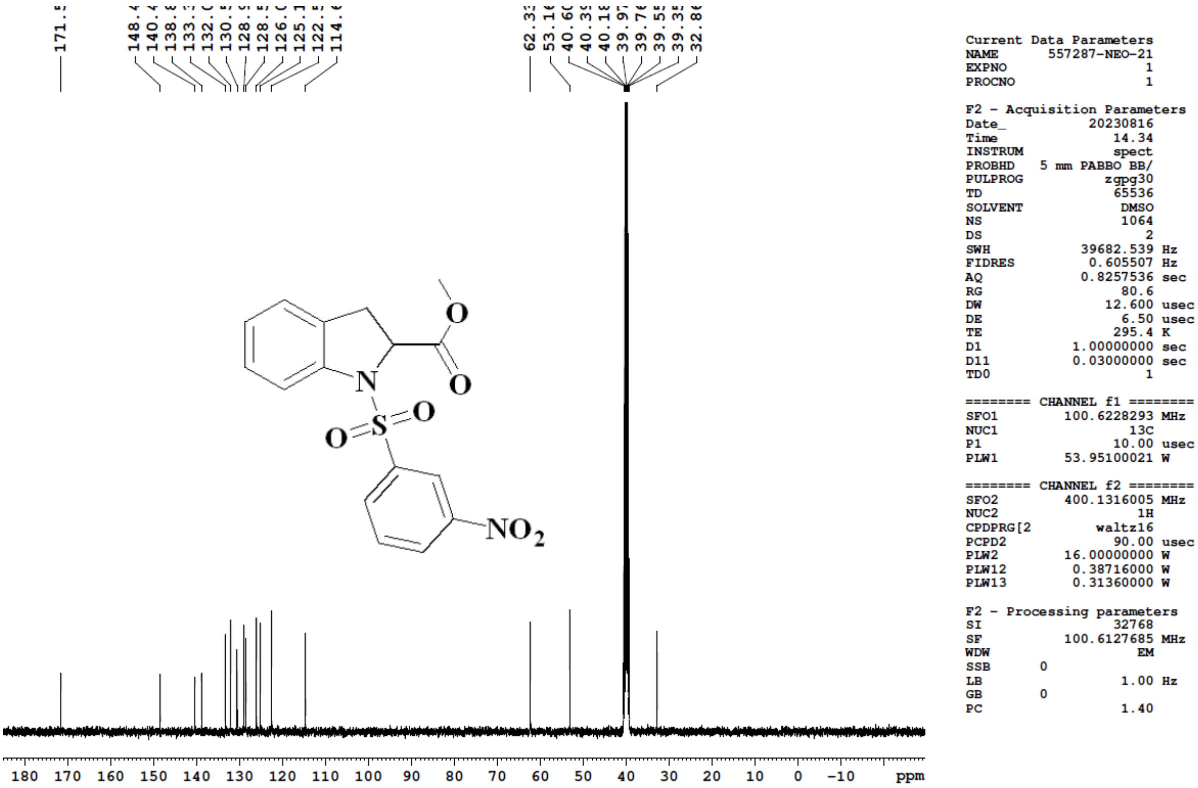
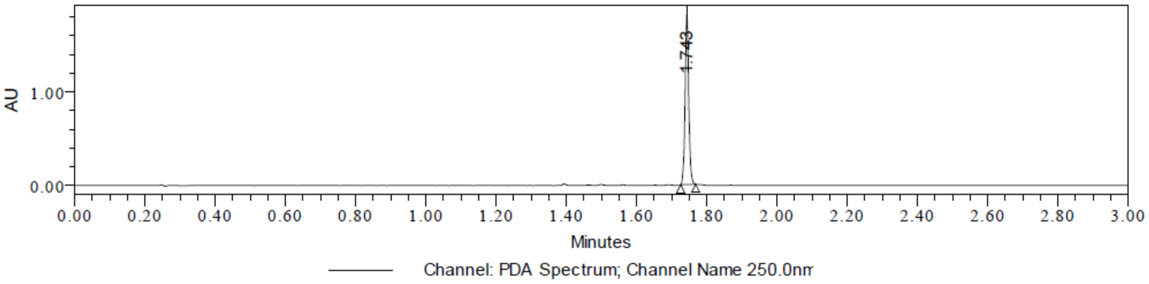
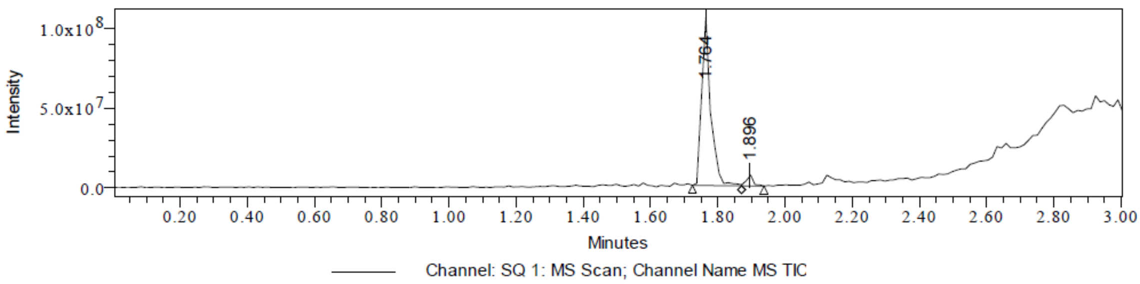


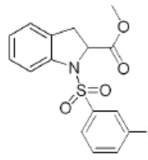
Figure 50: ^{13}C NMR of compound **7.**



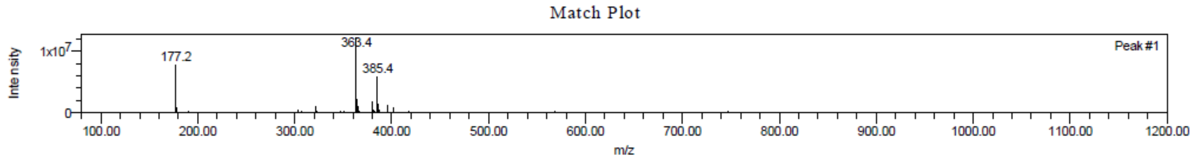


Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.743		1819328	1300945	100.00	PDA Spectrum	250.0nm
2	1.744		1286748	1249425	100.00	PDA Spectrum	220.0nm



Chemical Formula: $C_{16}H_{14}N_2O_6S$
Molecular Weight: 362.36



Base Peak 363.43 Channel Description 1: 80.00-1300.00 ES+, Centroid, CV=30 Retention Time 1.764

Figure 51: LC-MS of compound **7.**

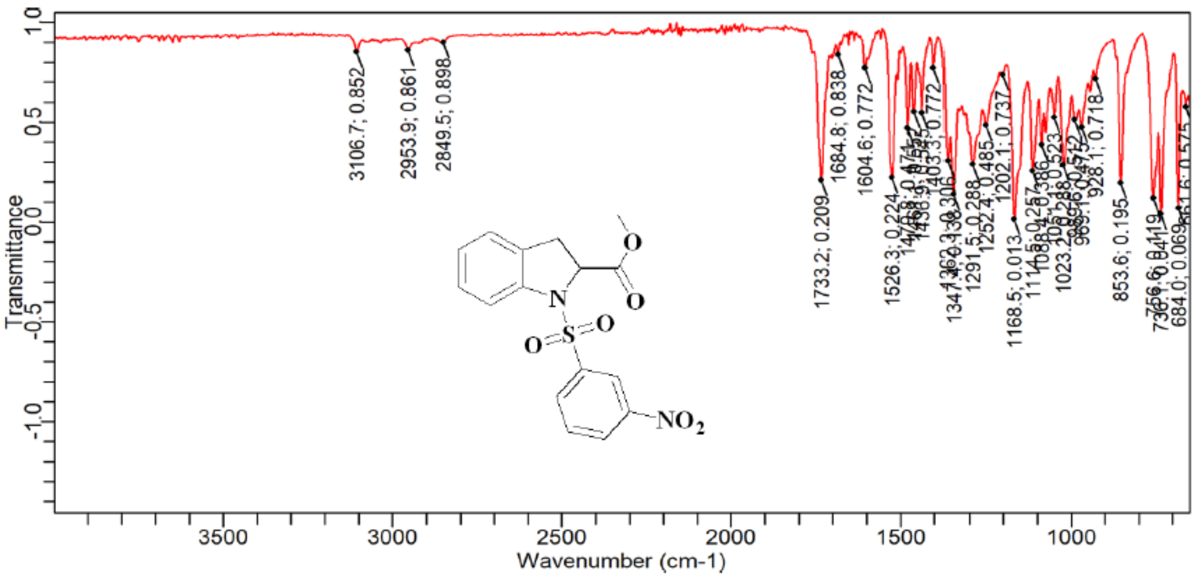
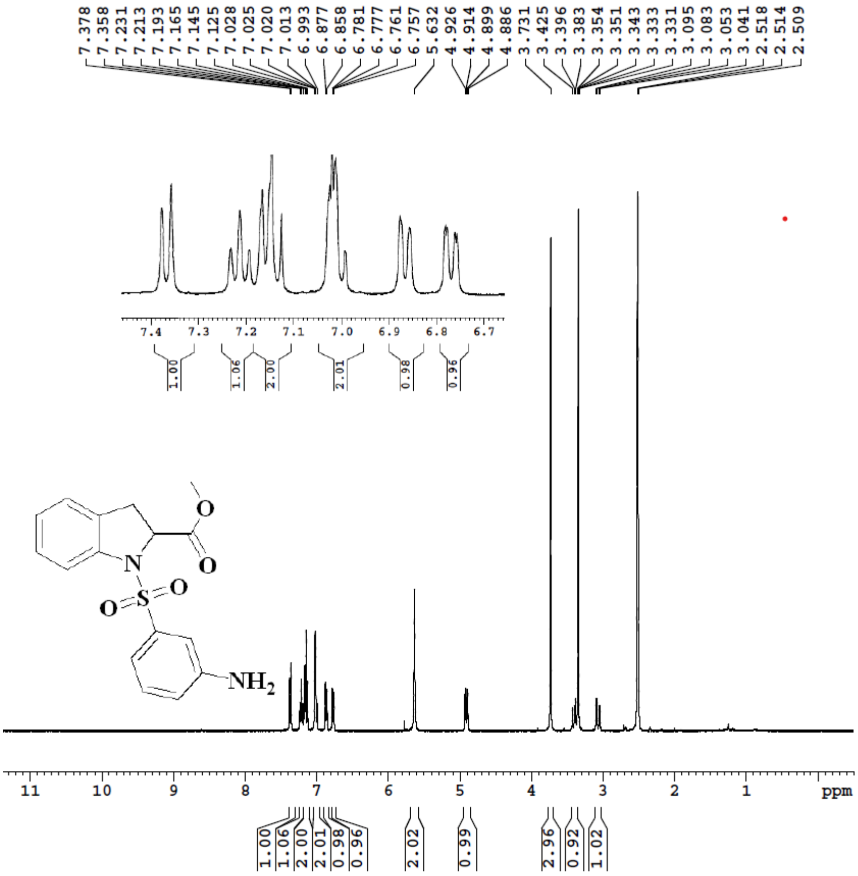
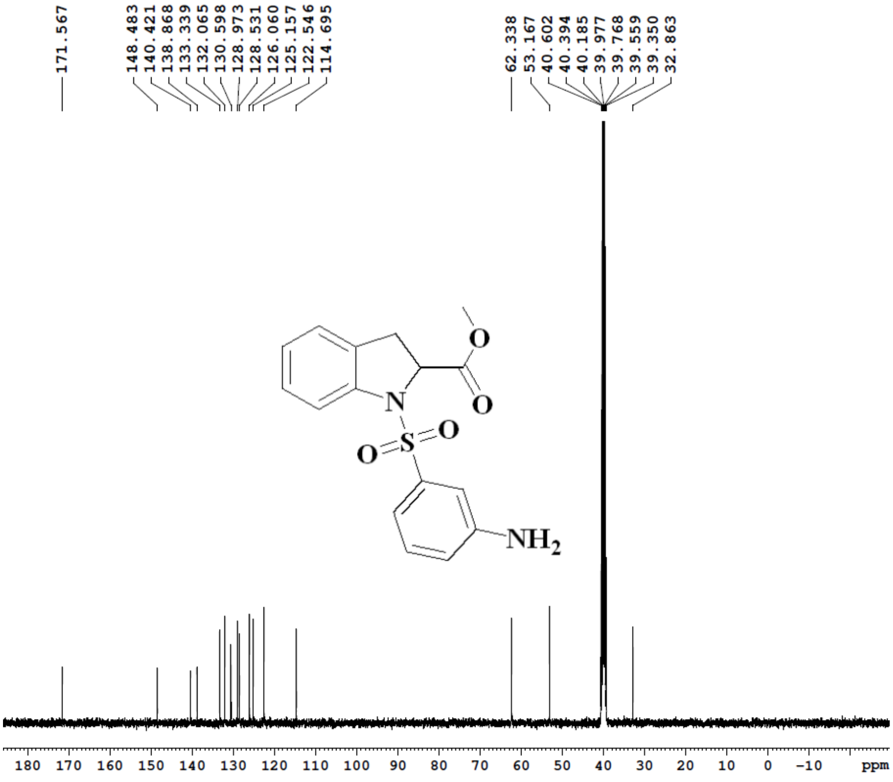


Figure 52: IR of compound **7.**



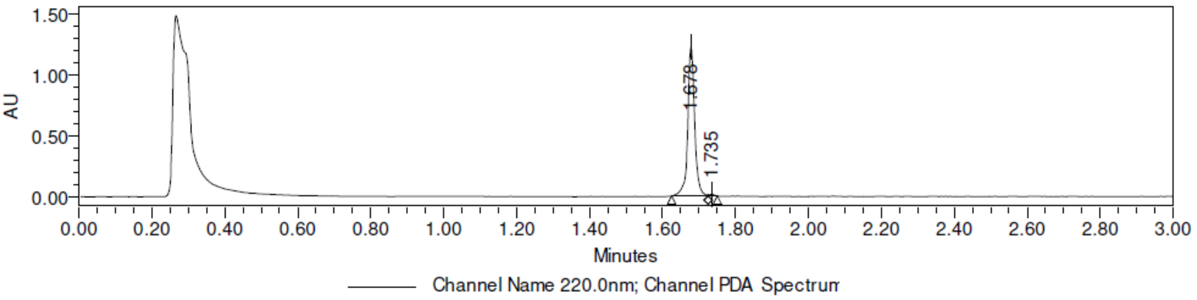
```
Current Data Parameters
NAME       566815-Neo 21
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230823
Time               22.35 h
INSTRUM            spect
PROBHD    Z108618_0769 (
PULPROG             zg30
TD                 16384
SOLVENT             DMSO
NS                    16
DS                     0
SWH             8012.820 Hz
FIDRES          0.978127 Hz
AQ             1.0223616 sec
RG                201.52
DW                62.400 usec
DE                  6.50 usec
TE                 295.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.3024720 MHz
NUC1                  1H
P0                  5.00 usec
P1                 15.00 usec
PLW1         14.00000000 W

F2 - Processing parameters
SI                 65536
SF           400.2999993 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

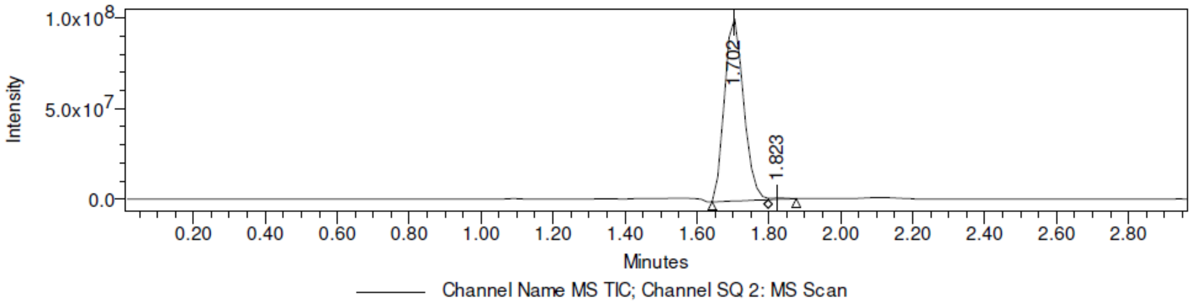
Figure 53: ^{1}H NMR of compound **8.**



```
Current Data Parameters
NAME       557287-NEO-21
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230816
Time               14.34
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 65536
SOLVENT             DMSO
NS                  1064
DS                     2
SWH            39682.539 Hz
FIDRES          0.605507 Hz
AQ             0.8257536 sec
RG                  80.6
DW                12.600 usec
DE                  6.50 usec
TE                 295.4 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.6228293 MHz
NUC1                 13C
P1                 10.00 usec
PLW1         53.95100021 W

======== CHANNEL f2 ========
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2         waltz16
PCPD2              90.00 usec
PLW2         16.00000000 W
PLW12         0.38716000 W
PLW13         0.31360000 W

F2 - Processing parameters
SI                 32768
SF           100.6127685 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

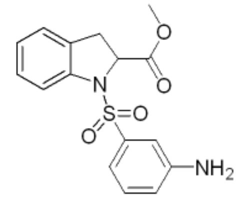
Figure 54: ^{13}C NMR of compound **8.**





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.678		312555	365072	99.11	PDA Spectrum	280.0nm
2	1.678		1225219	1606342	99.26	PDA Spectrum	220.0nm
3	1.734		2926	3291	0.89	PDA Spectrum	280.0nm
4	1.735		12897	12018	0.74	PDA Spectrum	220.0nm



Chemical Formula: $C_{16}H_{16}N_2O_4S$
Molecular Weight: 332.37

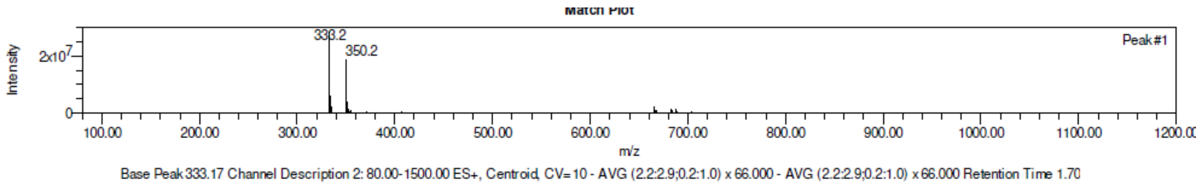


Figure 55: LC-MS of compound **8.**

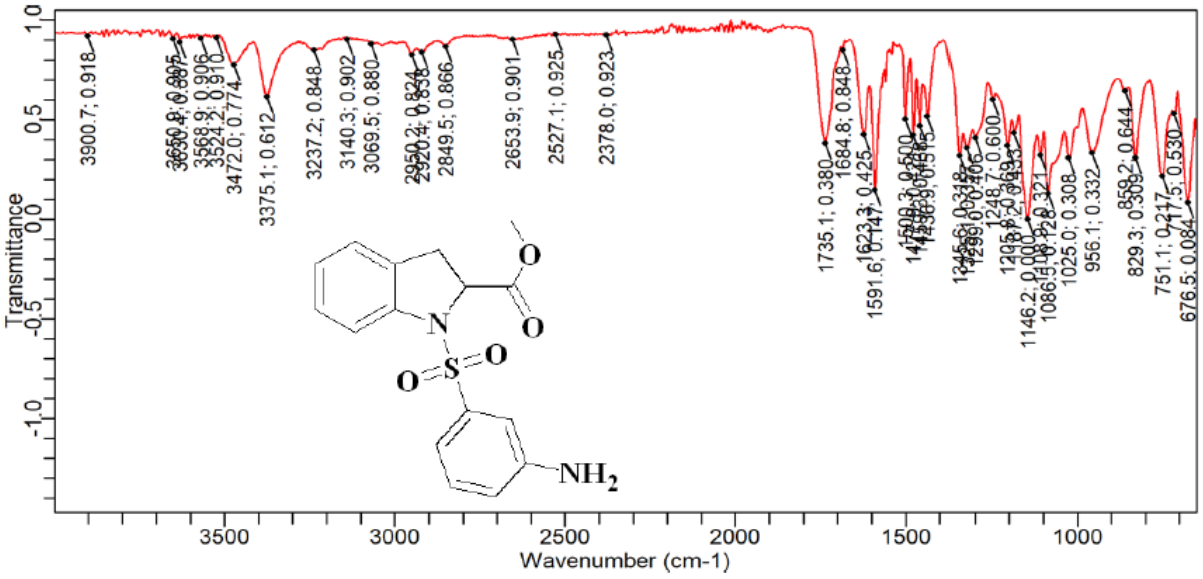
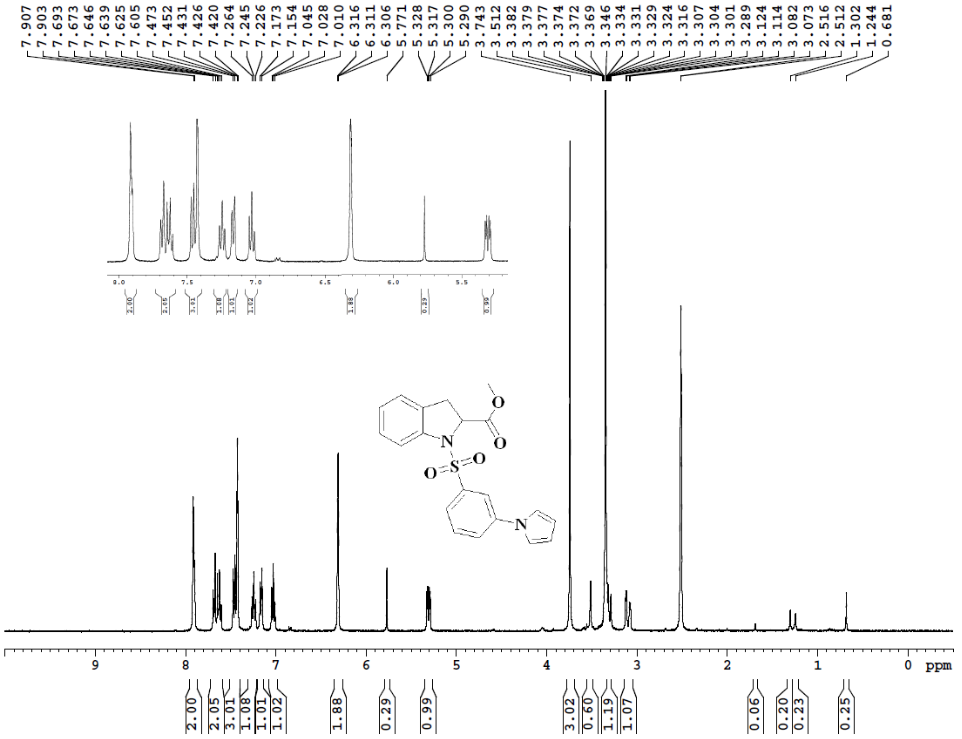


Figure 56: IR of compound **8.**



```
Current Data Parameters
NAME       559584-Neo 21
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20230817
Time               18.35 h
INSTRUM            spect
PROBHD    Z108618_0769 (
PULPROG             zg30
TD                 16384
SOLVENT             DMSO
NS                    16
DS                     0
SWH             8012.820 Hz
FIDRES          0.978127 Hz
AQ             1.0223616 sec
RG                201.52
DW                62.400 usec
DE                  6.50 usec
TE                 321.9 K
D1            1.00000000 sec
TD0                    1
SFO1         400.3024720 MHz
NUC1                  1H
P0                  5.00 usec
P1                 15.00 usec
PLW1         14.00000000 W

F2 - Processing parameters
SI                 65536
SF           400.2999993 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

Figure 57: ^{1}H NMR of compound **10.**

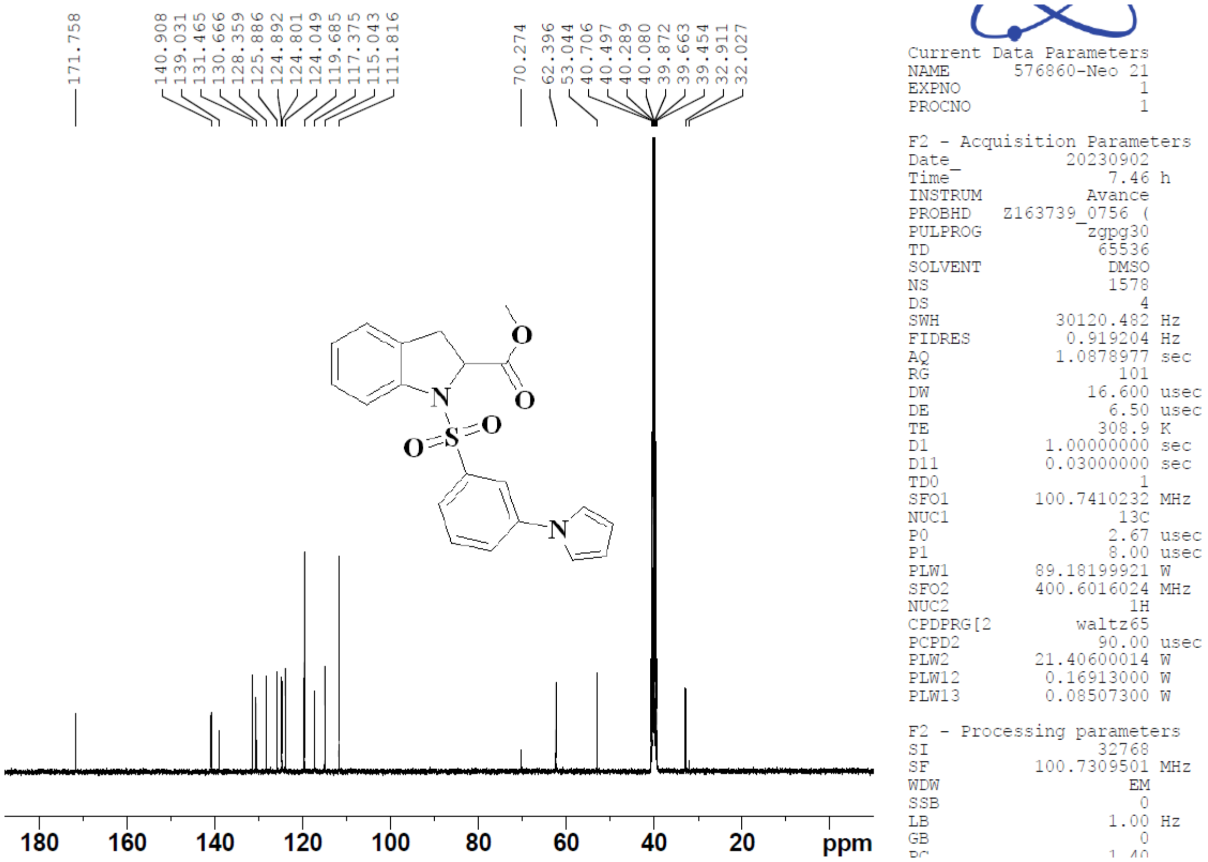
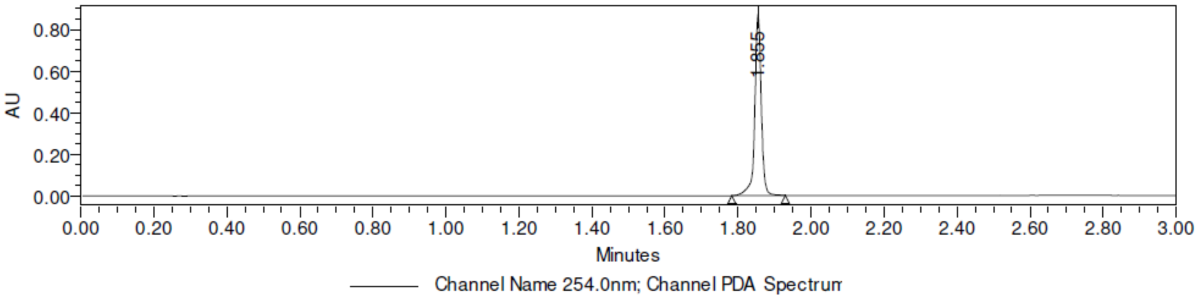
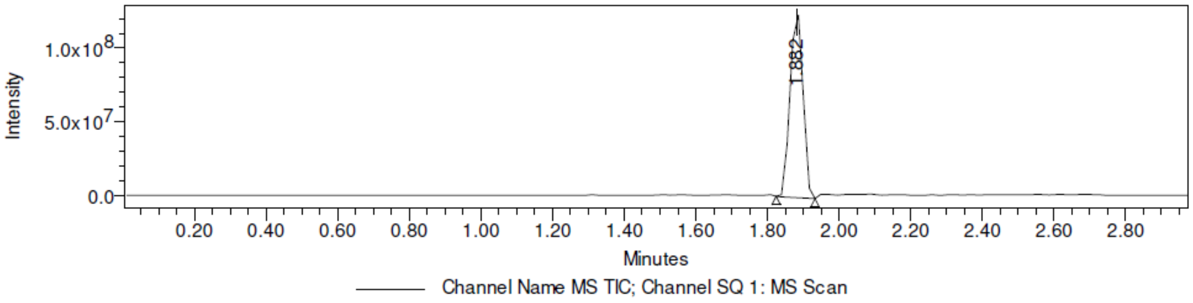


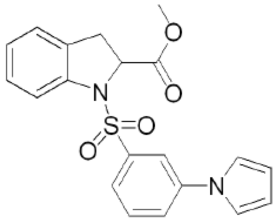
Figure 58: ^{13}C NMR of compound **10.**



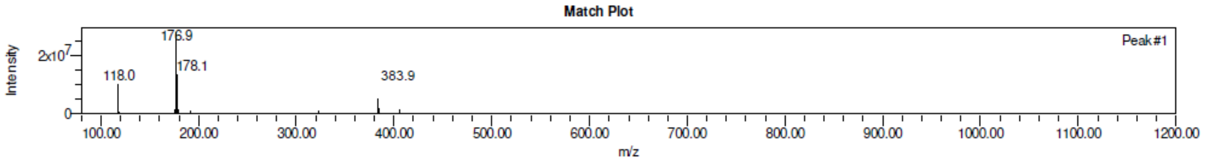


Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.818		20181	13494	1.46	PDA Spectrum	220.0nm
2	1.855		867358	1075826	100.00	PDA Spectrum	254.0nm
3	1.855		736811	912374	98.54	PDA Spectrum	220.0nm



Chemical Formula: $C_{20}H_{18}N_2O_4S$
Molecular Weight: 382.43



Base Peak 176.92 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 - AVG (2.0:3.0) x 66.000 Retention Time 1.88

Figure 59: LC-MS of compound **10.**

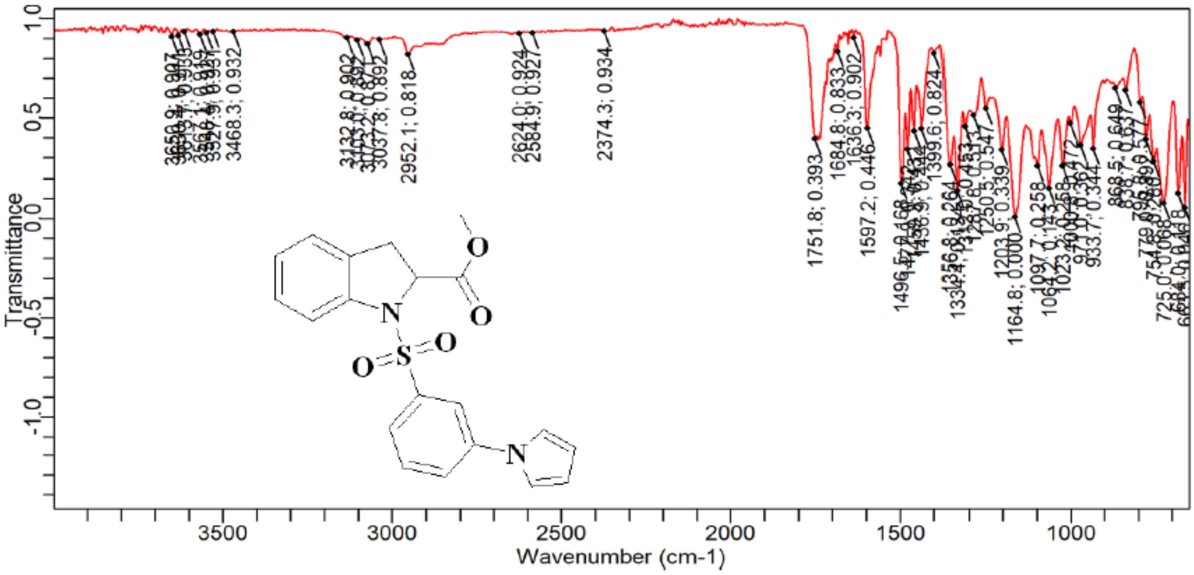
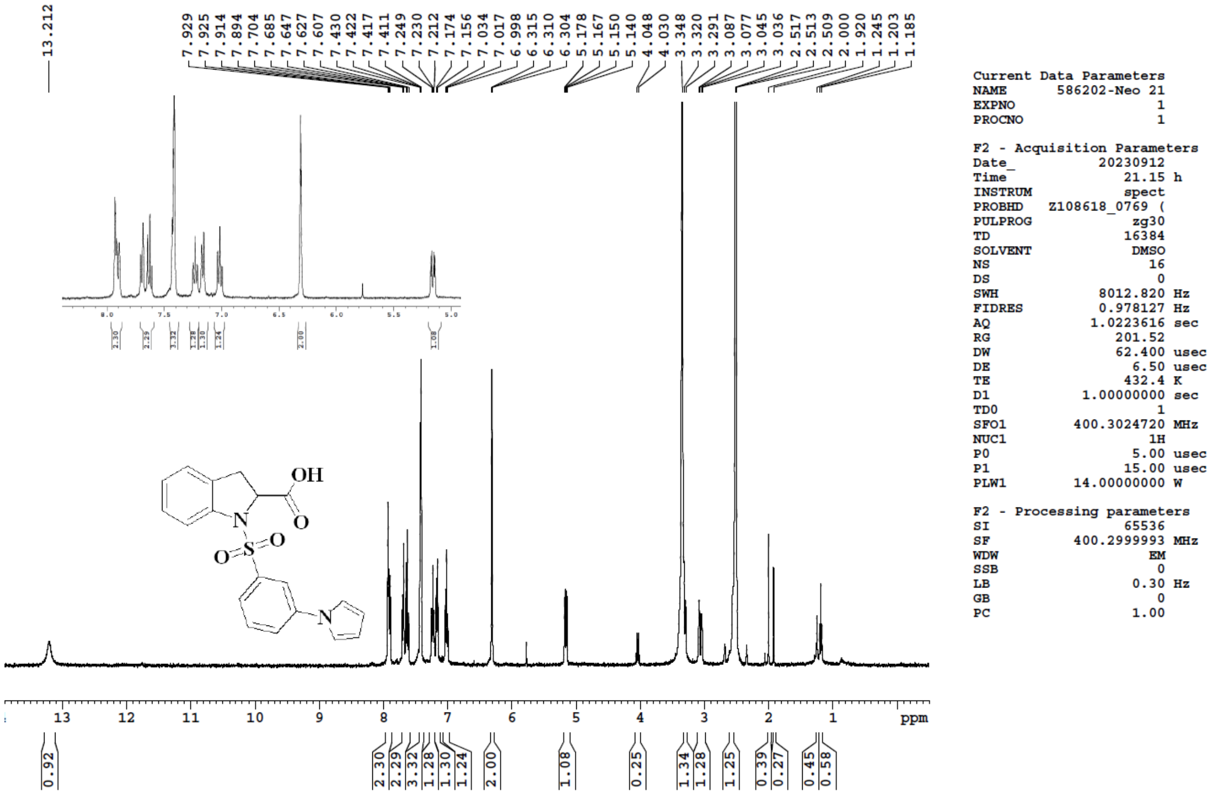
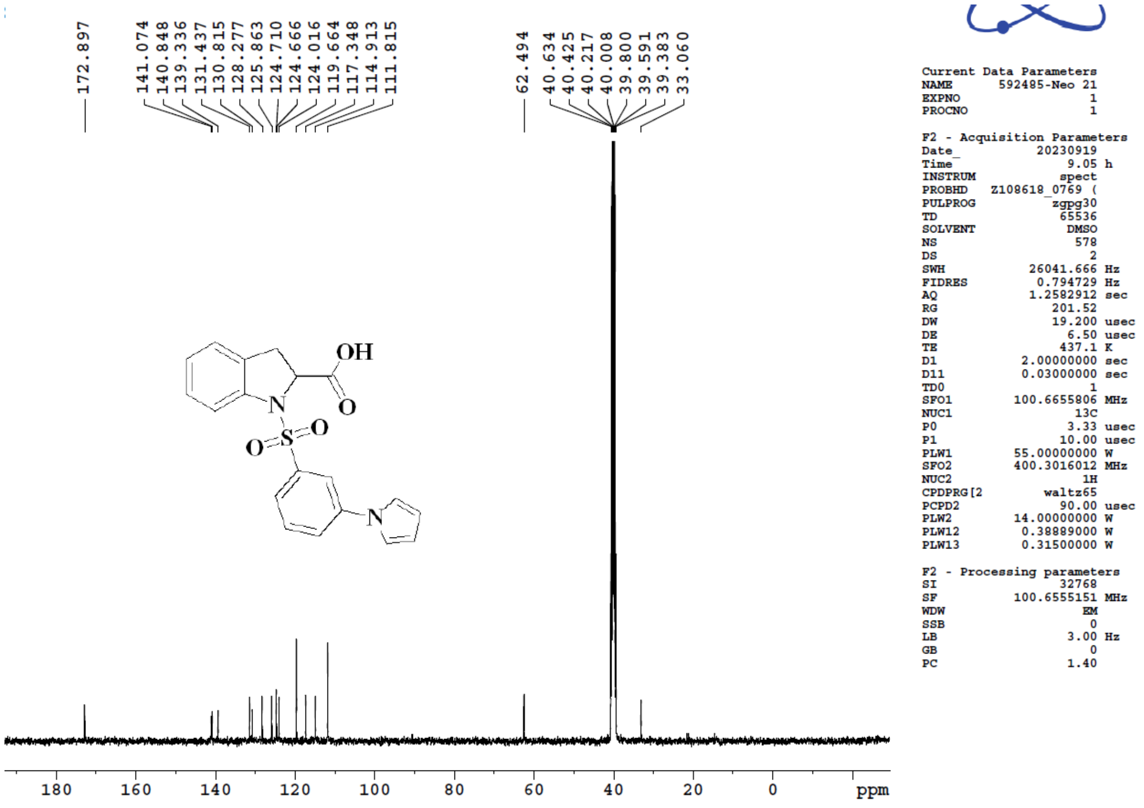


Figure 60: IR of compound **10.**



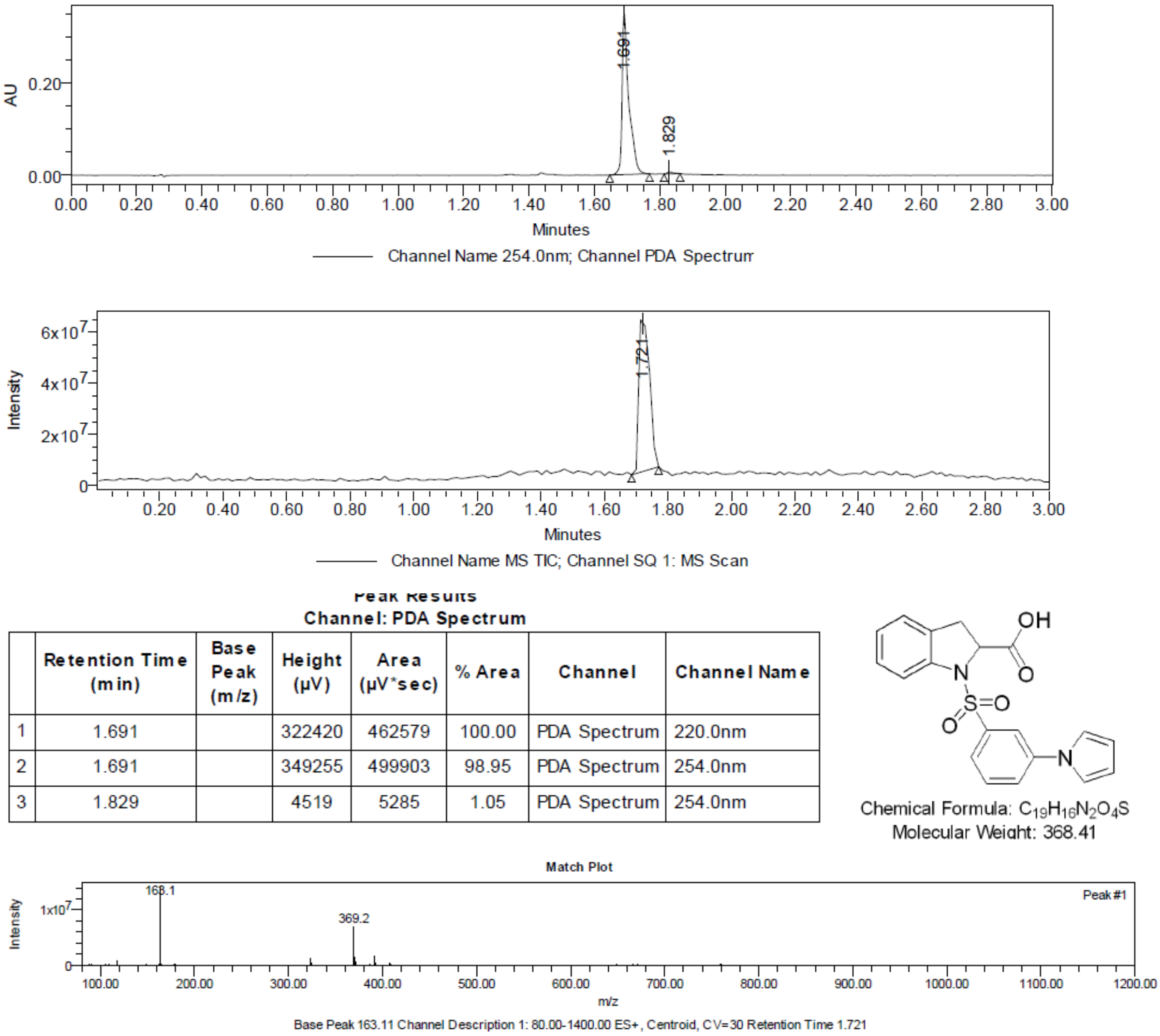
```
Current Data Parameters
NAME      586202-Neo 21
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20230912
Time              21.15 h
INSTRUM           spect
PROBHD   Z108618_0769 (
PULPROG            zg30
TD                16384
SOLVENT            DMSO
NS                   16
DS                    0
SWH            8012.820 Hz
FIDRES         0.978127 Hz
AQ            1.0223616 sec
RG               201.52
DW               62.400 usec
DE                 6.50 usec
TE                432.4 K
D1           1.00000000 sec
TD0                   1
SFO1        400.3024720 MHz
NUC1                 1H
P0                 5.00 usec
P1                15.00 usec
PLW1        14.00000000 W

F2 - Processing parameters
SI                65536
SF          400.2999993 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

Figure 61: ^{1}H NMR of compound **11.**



```
Current Data Parameters
NAME      592485-Neo 21
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20230919
Time               9.05 h
INSTRUM           spect
PROBHD   Z108618_0769 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                  578
DS                    2
SWH           26041.666 Hz
FIDRES         0.794729 Hz
AQ            1.2582912 sec
RG               201.52
DW               19.200 usec
DE                 6.50 usec
TE                437.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6655806 MHz
NUC1                13C
P0                 3.33 usec
P1                10.00 usec
PLW1        55.00000000 W
SFO2        400.3016012 MHz
NUC2                 1H
CPDPRG[2        waltz65
PCPD2             90.00 usec
PLW2        14.00000000 W
PLW12        0.38889000 W
PLW13        0.31500000 W

F2 - Processing parameters
SI                32768
SF          100.6555151 MHz
WDW                  EM
SSB                   0
LB                 3.00 Hz
GB                    0
PC                 1.40
```

Figure 62: ^{13}C NMR of compound **11.**



Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.691		322420	462579	100.00	PDA Spectrum	220.0nm
2	1.691		349255	499903	98.95	PDA Spectrum	254.0nm
3	1.829		4519	5285	1.05	PDA Spectrum	254.0nm

Chemical Formula: $C_{19}H_{16}N_2O_4S$
Molecular Weight: 368.41

Base Peak 163.11 Channel Description 1: 80.00-1400.00 ES+, Centroid, CV=30 Retention Time 1.721

Figure 63: LC-MS of compound **11.**

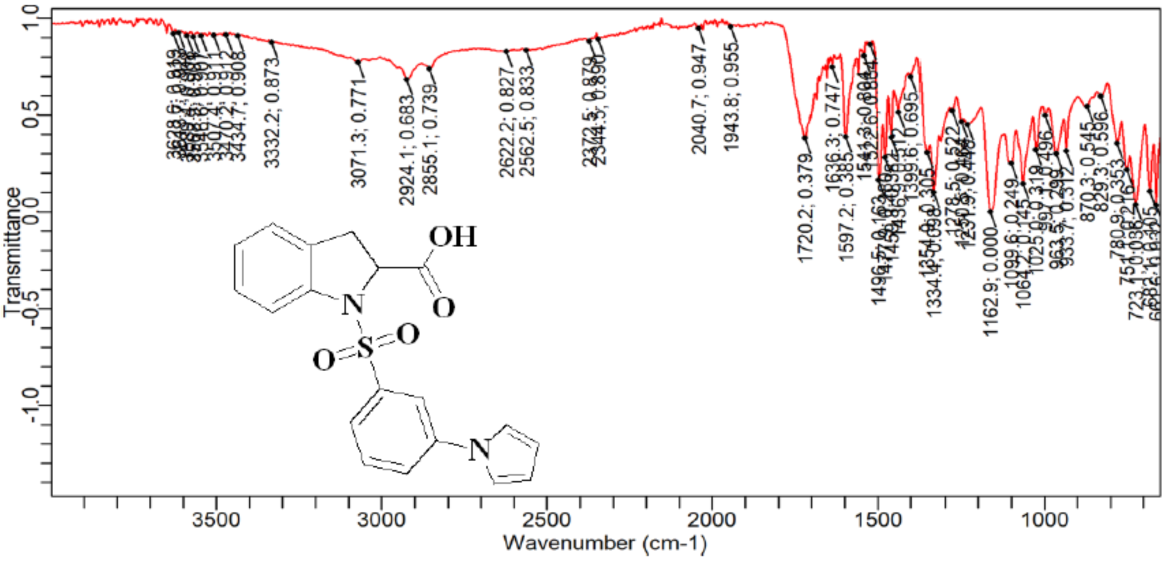
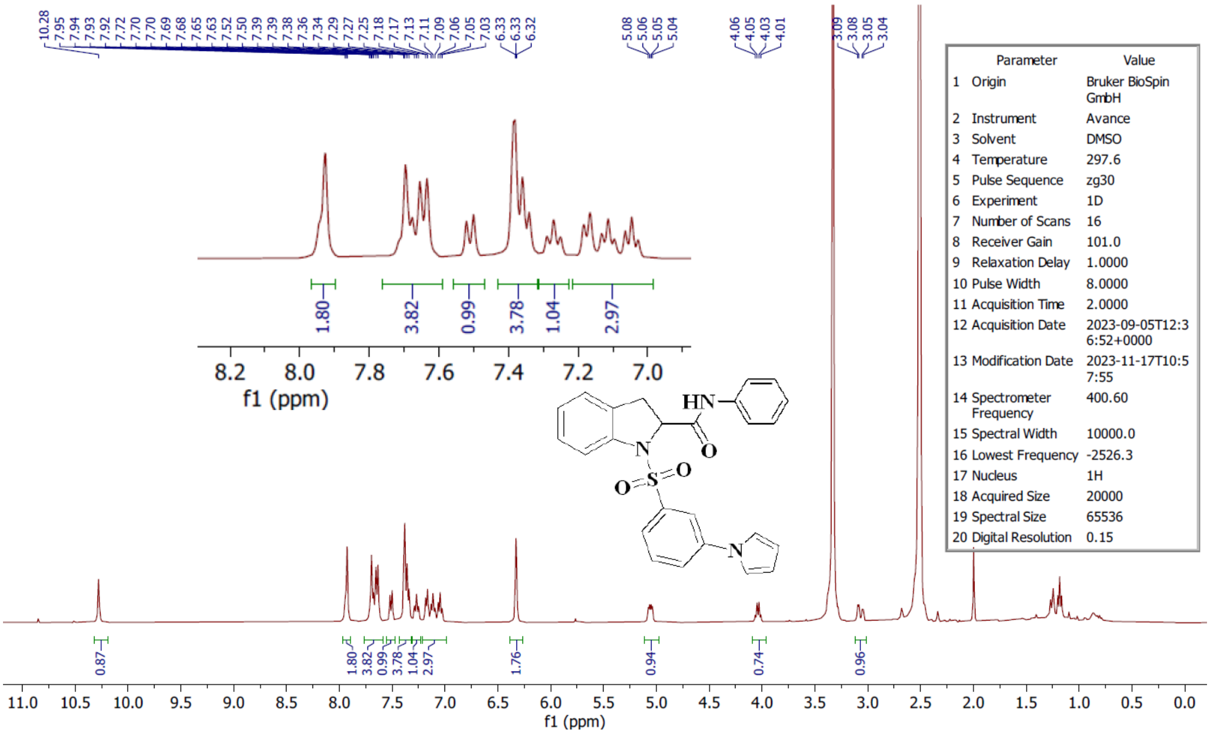
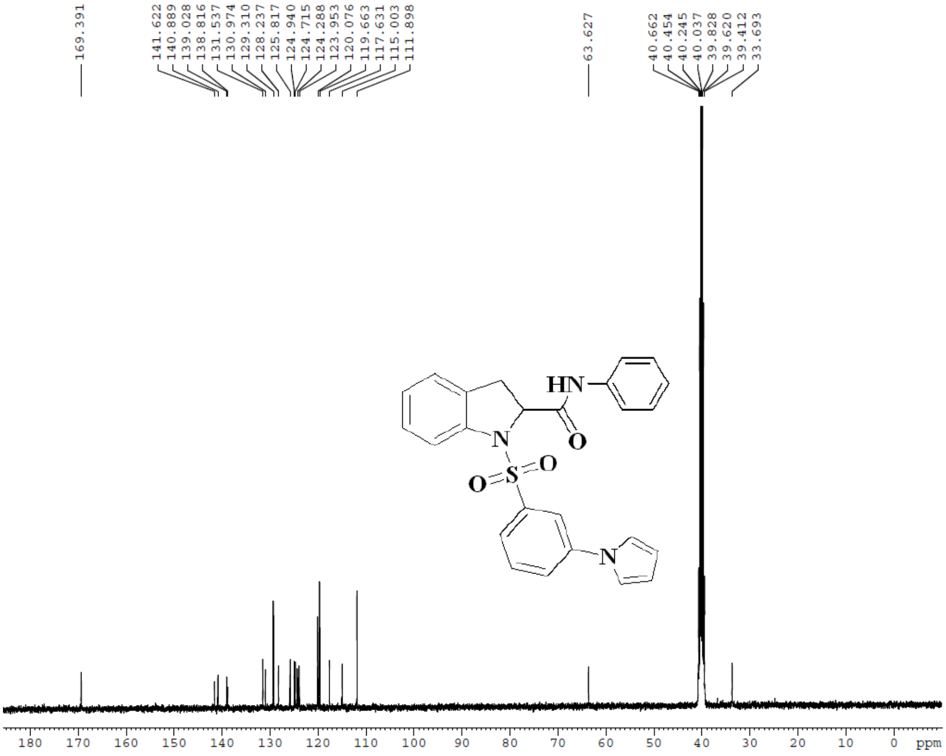


Figure 64: IR of compound **11.**



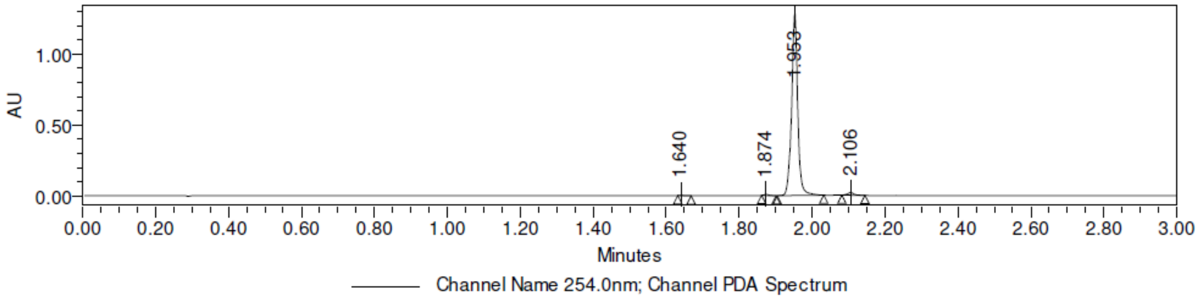
	Parameter	Value
1	Origin	Bruker BioSpin GmbH
2	Instrument	Avance
3	Solvent	DMSO
4	Temperature	297.6
5	Pulse Sequence	zg30
6	Experiment	1D
7	Number of Scans	16
8	Receiver Gain	101.0
9	Relaxation Delay	1.0000
10	Pulse Width	8.0000
11	Acquisition Time	2.0000
12	Acquisition Date	2023-09-05T12:36:52+0000
13	Modification Date	2023-11-17T10:57:55
14	Spectrometer Frequency	400.60
15	Spectral Width	10000.0
16	Lowest Frequency	-2526.3
17	Nucleus	1H
18	Acquired Size	20000
19	Spectral Size	65536
20	Digital Resolution	0.15

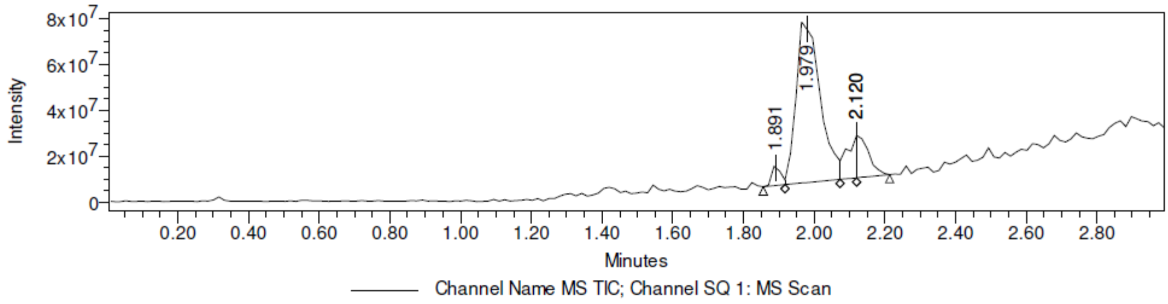
Figure 65: ^{1}H NMR of compound **13a.**



```
Current Data Parameters
NAME          630697-
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20231021
Time                 2.04 h
INSTRUM               spect
PROBHD   Z108618_0769 (
PULPROG             zgpg30
TD                   65536
SOLVENT               DMSO
NS                    1500
DS                       4
SWH             32051.281 Hz
FIDRES           0.978127 Hz
AQ              1.0223616 sec
RG                 201.52
DW                 15.600 usec
DE                   6.50 usec
TE                  299.3 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                      1
SFO1          100.6655806 MHz
NUC1                   13C
P0                   3.33 usec
P1                  10.00 usec
PLW1          55.00000000 W
SFO2          400.3016012 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2               90.00 usec
PLW2          14.00000000 W
PLW12          0.38889000 W
PLW13          0.31500000 W

F2 - Processing parameters
SI                   32768
SF            100.6555151 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

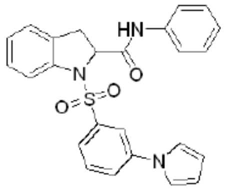
Figure 66: ^{13}C NMR of compound **13a.**





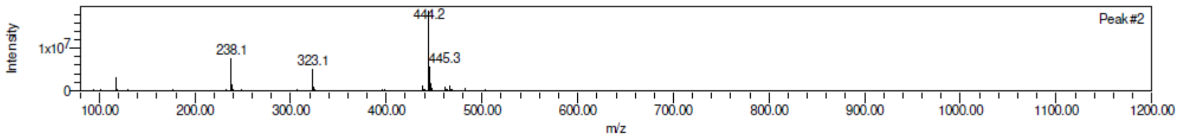
Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.640		1759	1234	0.08	PDA Spectrum	254.0nm
2	1.874		6888	6352	0.42	PDA Spectrum	254.0nm
3	1.892		32931	40079	3.78	PDA Spectrum	220.0nm
4	1.953		806790	998924	94.12	PDA Spectrum	220.0nm
5	1.953		1284657	1494491	98.15	PDA Spectrum	254.0nm
6	2.105		21093	22334	2.10	PDA Spectrum	220.0nm



Chemical Formula: $C_{25}H_{21}N_3O_3S$
Molecular Weight: 443.52

Match Plot



Base Peak 444.24 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 Retention Time 1.979

Figure 67: LC-MS of compound **13a.**

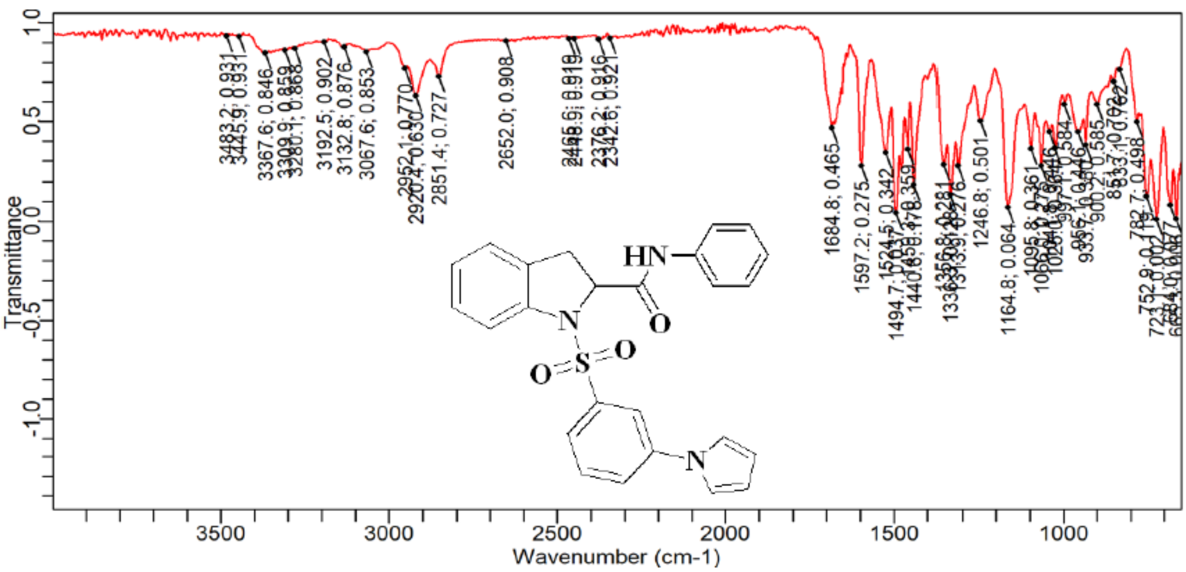
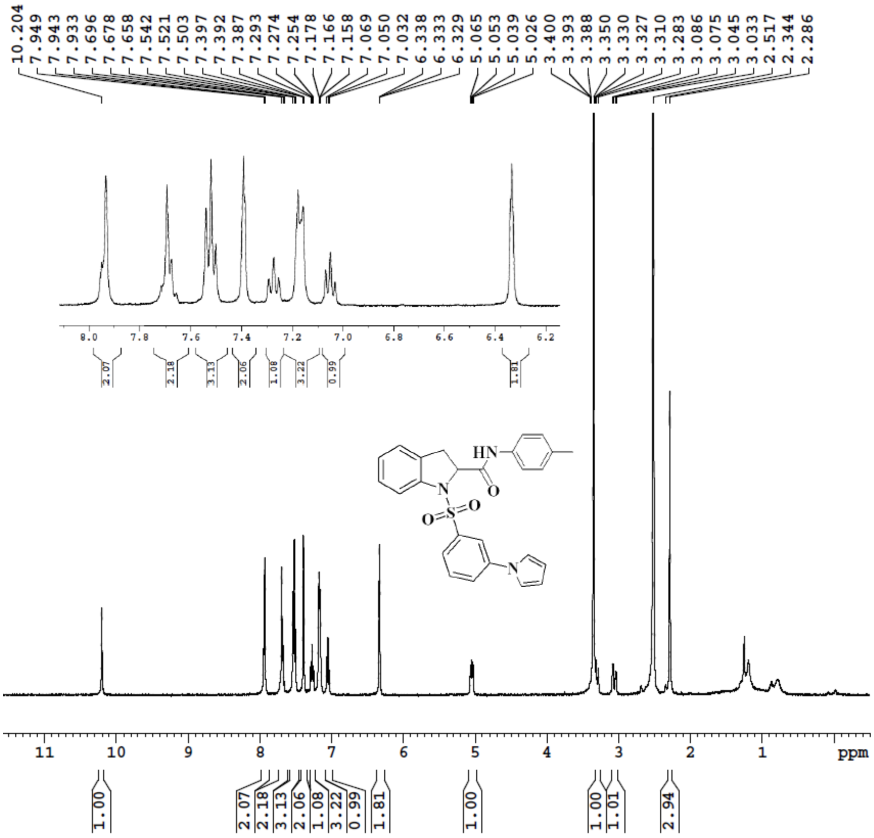
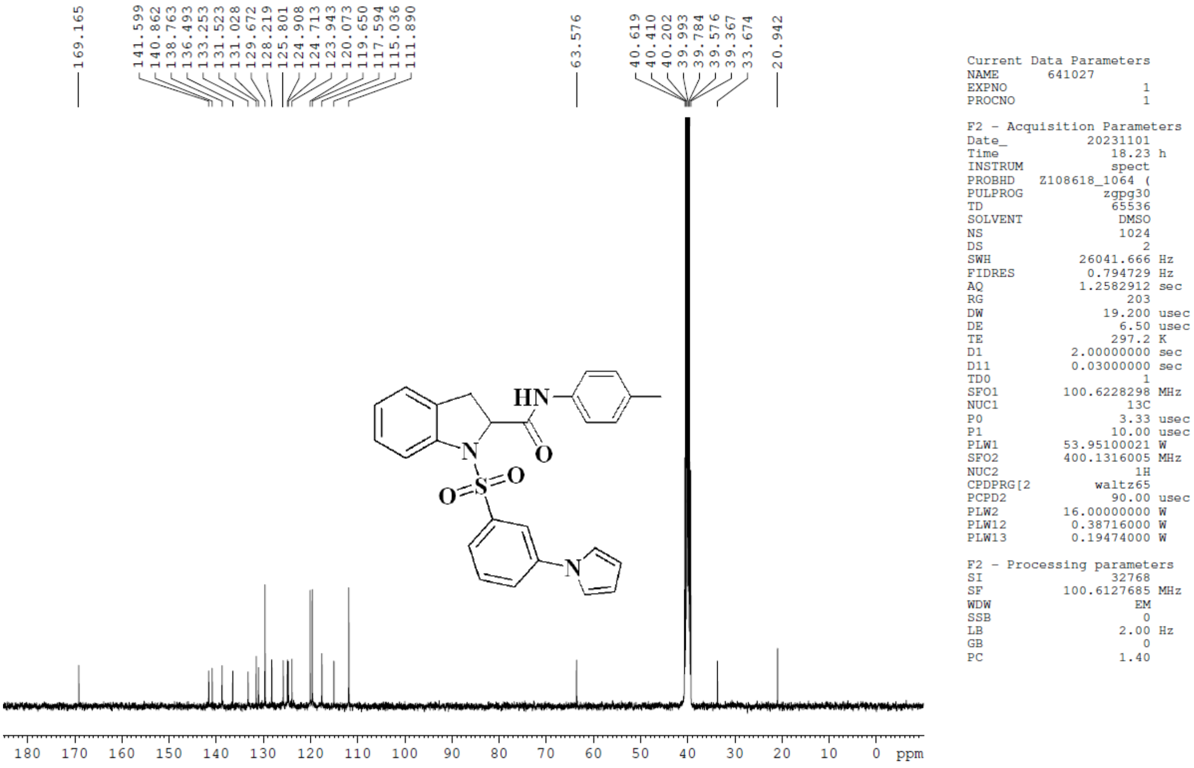


Figure 68: IR of compound **13a.**



```
Current Data Parameters
NAME        650717
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20231116
Time                 11.08 h
INSTRUM              spect
PROBHD    Z108618_0769 (
PULPROG               zg30
TD                   16384
SOLVENT               DMSO
NS                      16
DS                       0
SWH               8012.820 Hz
FIDRES            0.978127 Hz
AQ               1.0223616 sec
RG                  201.52
DW                  62.400 usec
DE                    6.50 usec
TE                   311.7 K
D1              1.00000000 sec
TD0                      1
SFO1           400.3024720 MHz
NUC1                    1H
P0                    5.00 usec
P1                   15.00 usec
PLW1           14.00000000 W

F2 - Processing parameters
SI                   65536
SF             400.2999993 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

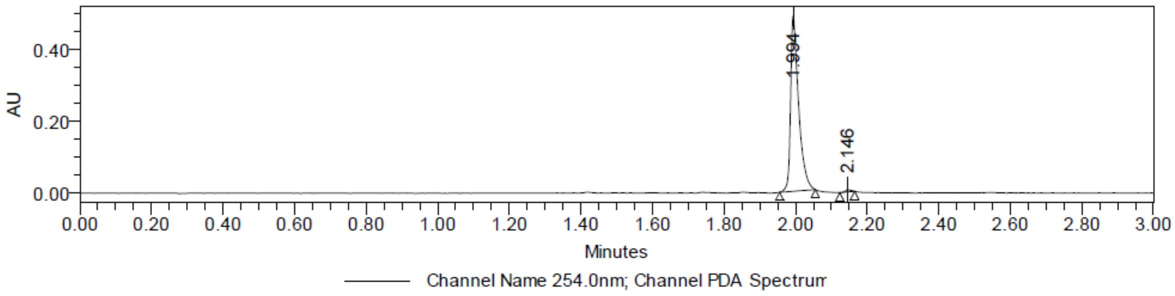
Figure 69: ^{1}H NMR of compound **13b.**

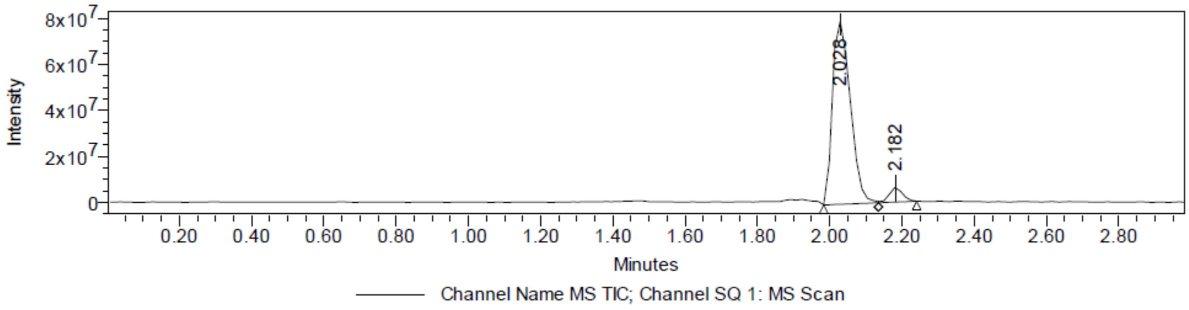


```
Current Data Parameters
NAME       641027
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20231101
Time                 18.23 h
INSTRUM              spect
PROBHD   Z108618_1064 (
PULPROG            zgpg30
TD                   65536
SOLVENT               DMSO
NS                    1024
DS                       2
SWH              26041.666 Hz
FIDRES            0.794729 Hz
AQ               1.2582912 sec
RG                     203
DW                  19.200 usec
DE                    6.50 usec
TE                   297.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1
SFO1           100.6228298 MHz
NUC1                   13C
P0                    3.33 usec
P1                   10.00 usec
PLW1           53.95100021 W
SFO2           400.1316005 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2                90.00 usec
PLW2           16.00000000 W
PLW12           0.38716000 W
PLW13           0.19474000 W

F2 - Processing parameters
SI                   32768
SF             100.6127685 MHz
WDW                     EM
SSB                      0
LB                    2.00 Hz
GB                       0
PC                    1.40
```

Figure 70: ^{13}C NMR of compound **13b.**

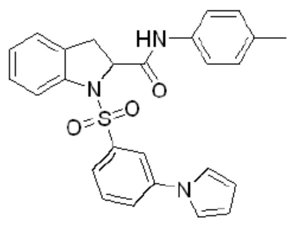
Sample Name:	Compound-13b		
Sample Type:	Unknown	Acquired By:	LCMS_06
Vial:	1:E,3	Sample Set Name:	04102023_UCH_125_1ST
Injection #:	1	Acq. Method Set:	PDS_METHOD_C3
Injection Volume:	1.00 ul	Processing Method:	PDS_METHOD_C3 R,
Run Time:	3.0 Minutes	Channel Name:	MS TIC, 254.0nm, 210.0nm
Project Name:	LCMS-06_OCT-2023_04102023	Proc. Chnl. Descr.:	PDA 254.0 nm Blank Subtracted
Date Acquired:	04-10-2023 10:27:12 IST		
Date Processed:	04-10-2023 11:15:23 IST, 04-10-2023 11:15:49 IST, 04-10-2023 11:16:32 IST		





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.994		488552	758914	99.19	PDA Spectrum	254.0nm
2	1.994		472492	761252	99.22	PDA Spectrum	210.0nm
3	2.142		10247	5947	0.78	PDA Spectrum	210.0nm
4	2.146		5861	6193	0.81	PDA Spectrum	254.0nm



Chemical Formula: $C_{26}H_{23}N_3O_3S$
Molecular Weight: 457.55

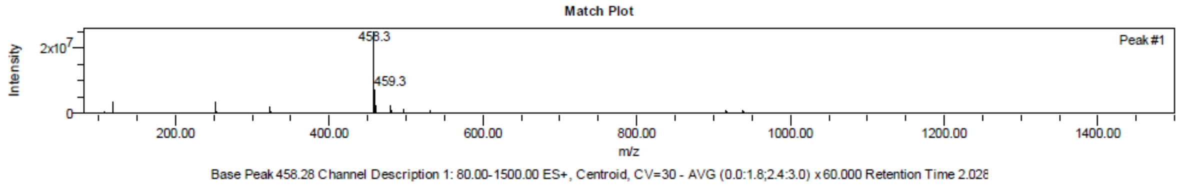


Figure 71: LC-MS of compound **13b.**

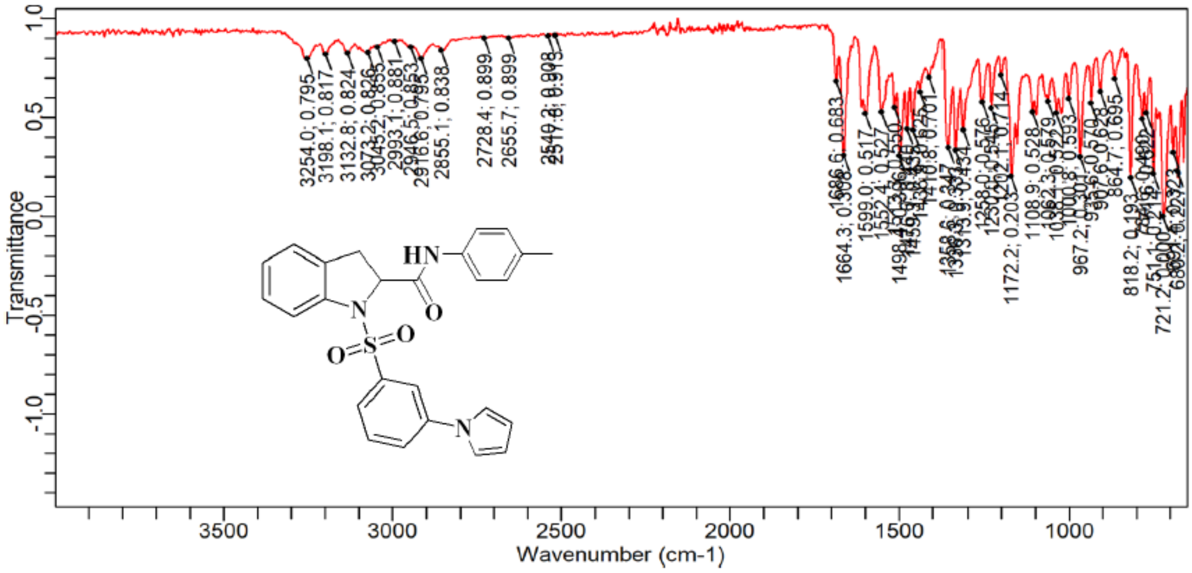
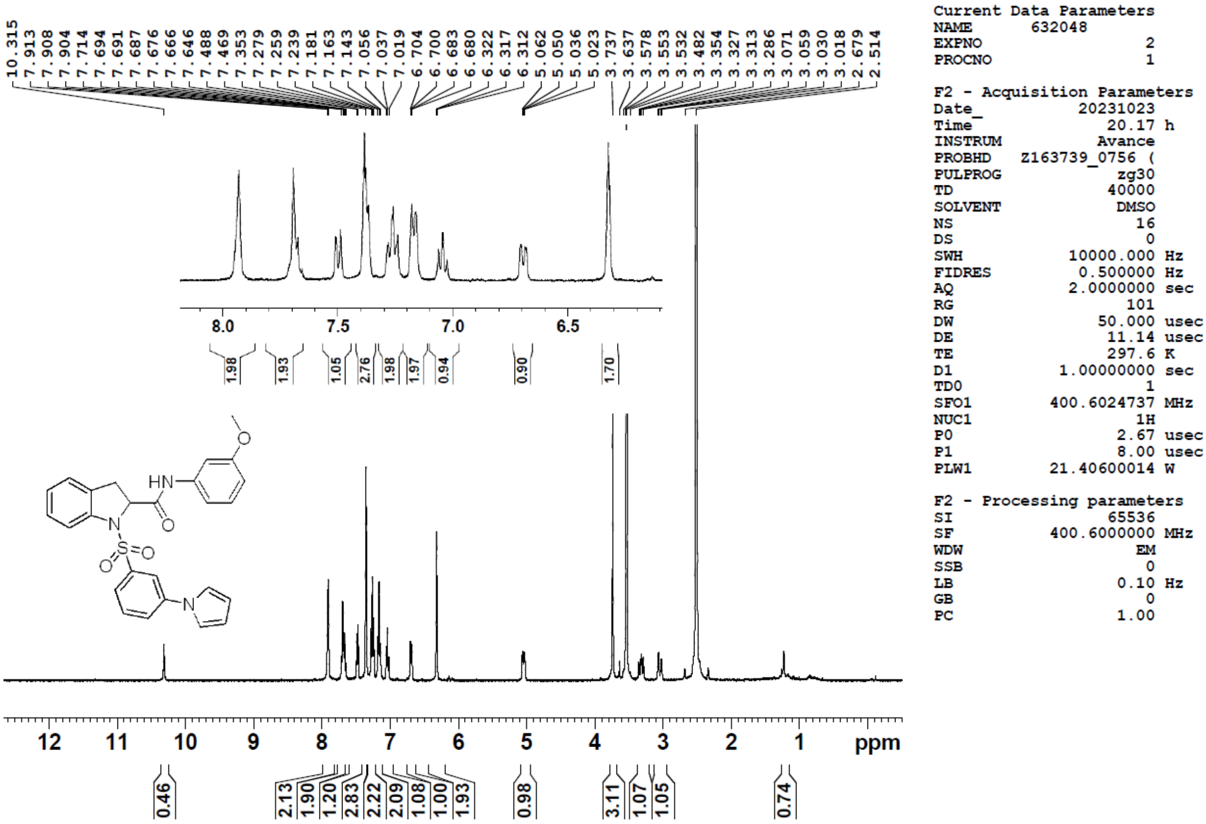
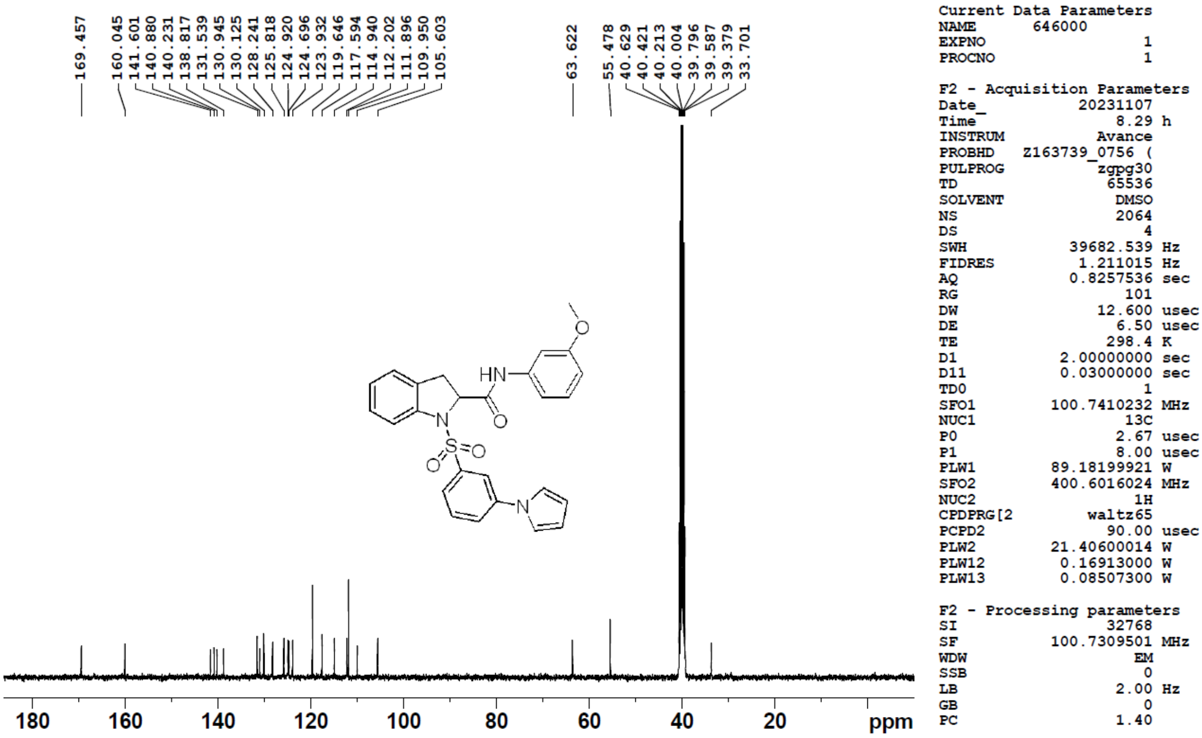


Figure 72: IR of compound **13b.**



```
Current Data Parameters
NAME        632048
EXPNO            2
PROCNO           1

F2 - Acquisition Parameters
Date_          20231023
Time              20.17 h
INSTRUM          Avance
PROBHD   Z163739_0756 (
PULPROG            zg30
TD                40000
SOLVENT            DMSO
NS                   16
DS                    0
SWH           10000.000 Hz
FIDRES         0.500000 Hz
AQ            2.0000000 sec
RG                  101
DW               50.000 usec
DE                11.14 usec
TE                297.6 K
D1           1.00000000 sec
TD0                   1
SFO1        400.6024737 MHz
NUC1                 1H
P0                 2.67 usec
P1                 8.00 usec
PLW1        21.40600014 W

F2 - Processing parameters
SI                65536
SF          400.6000000 MHz
WDW                  EM
SSB                   0
LB                 0.10 Hz
GB                    0
PC                 1.00
```

Figure 73: ^{1}H NMR of compound **13e.**

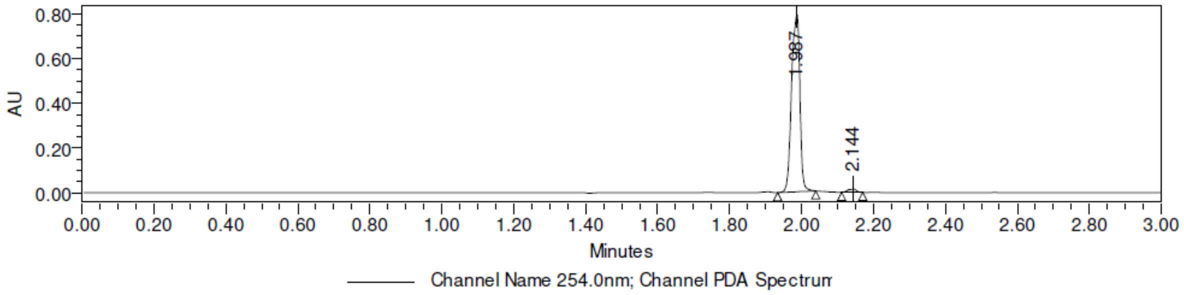


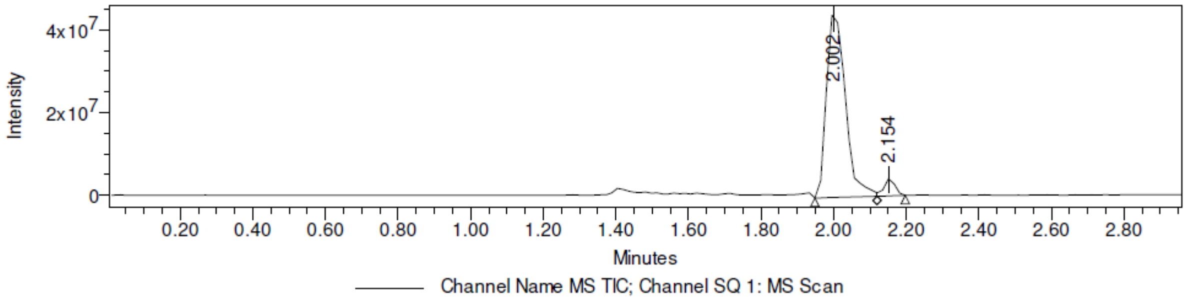
```
Current Data Parameters
NAME        646000
EXPNO            1
PROCNO           1

F2 - Acquisition Parameters
Date_          20231107
Time               8.29 h
INSTRUM          Avance
PROBHD   Z163739_0756 (
PULPROG          zgpg30
TD                65536
SOLVENT            DMSO
NS                 2064
DS                    4
SWH           39682.539 Hz
FIDRES         1.211015 Hz
AQ            0.8257536 sec
RG                  101
DW               12.600 usec
DE                 6.50 usec
TE                298.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.7410232 MHz
NUC1                13C
P0                 2.67 usec
P1                 8.00 usec
PLW1        89.18199921 W
SFO2        400.6016024 MHz
NUC2                 1H
CPDPRG[2         waltz65
PCPD2             90.00 usec
PLW2        21.40600014 W
PLW12        0.16913000 W
PLW13        0.08507300 W

F2 - Processing parameters
SI                32768
SF          100.7309501 MHz
WDW                  EM
SSB                   0
LB                 2.00 Hz
GB                    0
PC                 1.40
```

Figure 74: ^{13}C NMR of compound **13e.**

Sample Name: Compound-13e
Sample Type: Unknown
Vial: 1:A,7
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-03_OCT-2023_03102023
Date Acquired: 03-10-2023 18:54:32 IST
Date Processed: 03-10-2023 18:59:02 IST, 03-10-2023 18:59:30 IST, 03-10-2023 18:59:42 IST

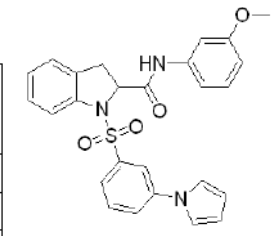
Acquired By: LCMS_03
Sample Set Name: 03102023_UCH_191_2ND
Acq. Method Set: PDS_METHOD_C_C D LINE
Processing Method: PDS_METHOD_C_C D LINE,
Channel Name: 220.0nm, MS TIC, 254.0nm
Proc. Chnl. Descr.: PDA 220.0 nm Blank Subtracted





Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.987		809189	1380173	96.77	PDA Spectrum	220.0nm
2	1.987		792502	1272065	98.18	PDA Spectrum	254.0nm
3	2.144		14314	23569	1.82	PDA Spectrum	254.0nm
4	2.145		30027	46020	3.23	PDA Spectrum	220.0nm



Chemical Formula: $C_{26}H_{23}N_3O_4S$
Molecular Weight: 473.55

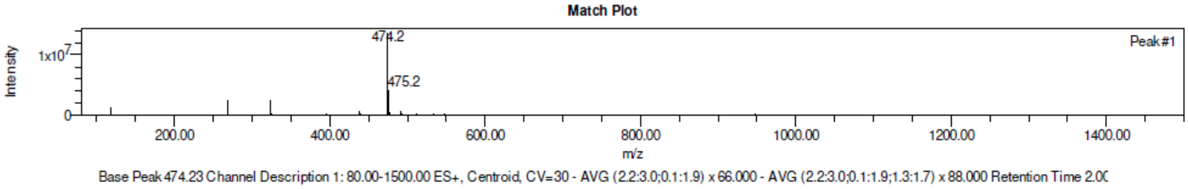


Figure 75: LC-MS of compound **13e.**

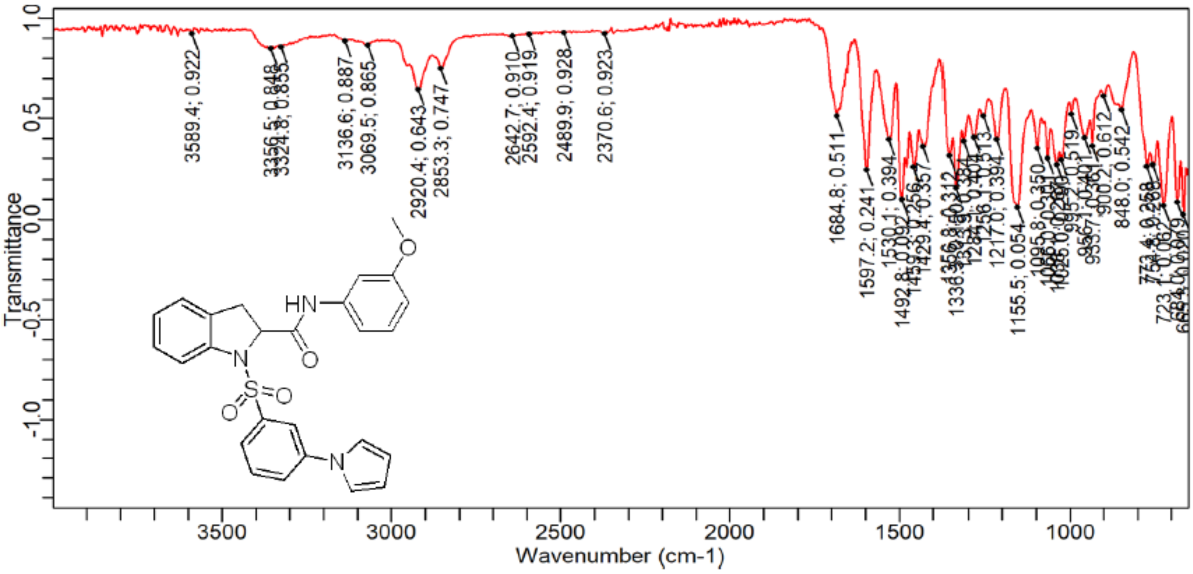
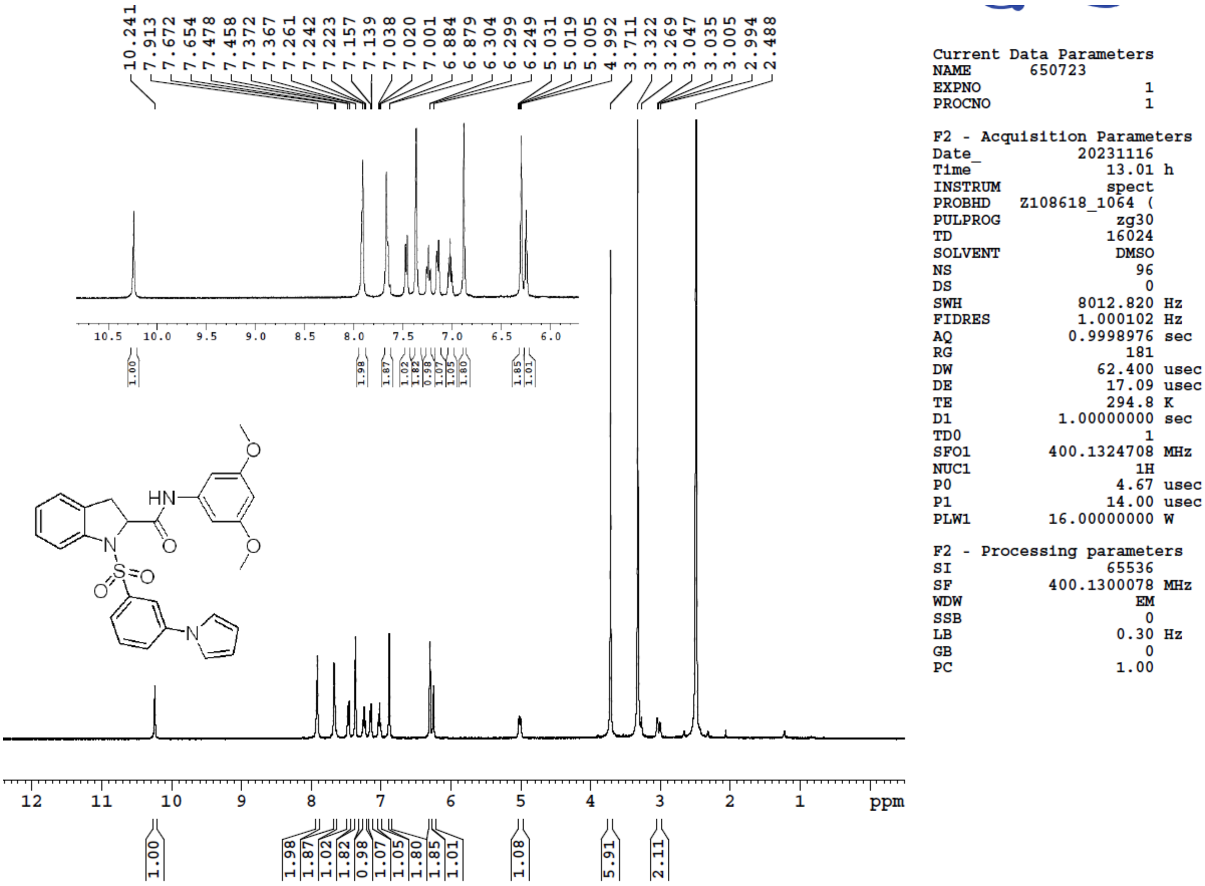
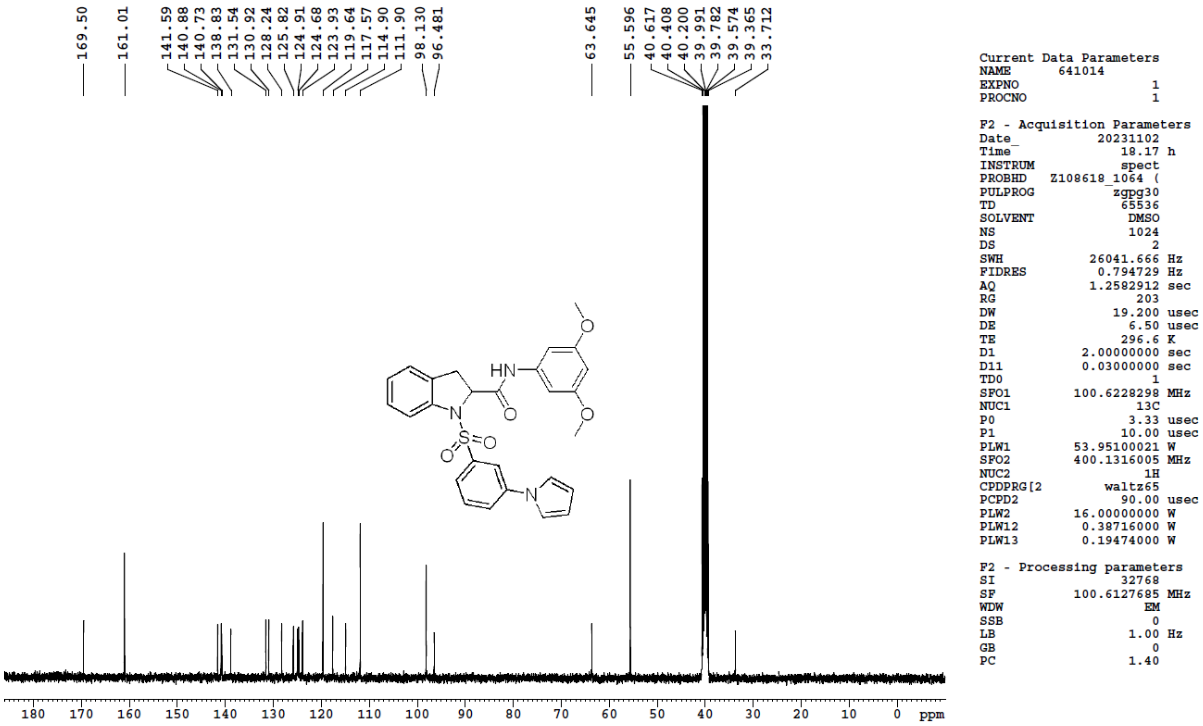


Figure 76: IR of compound **13e.**



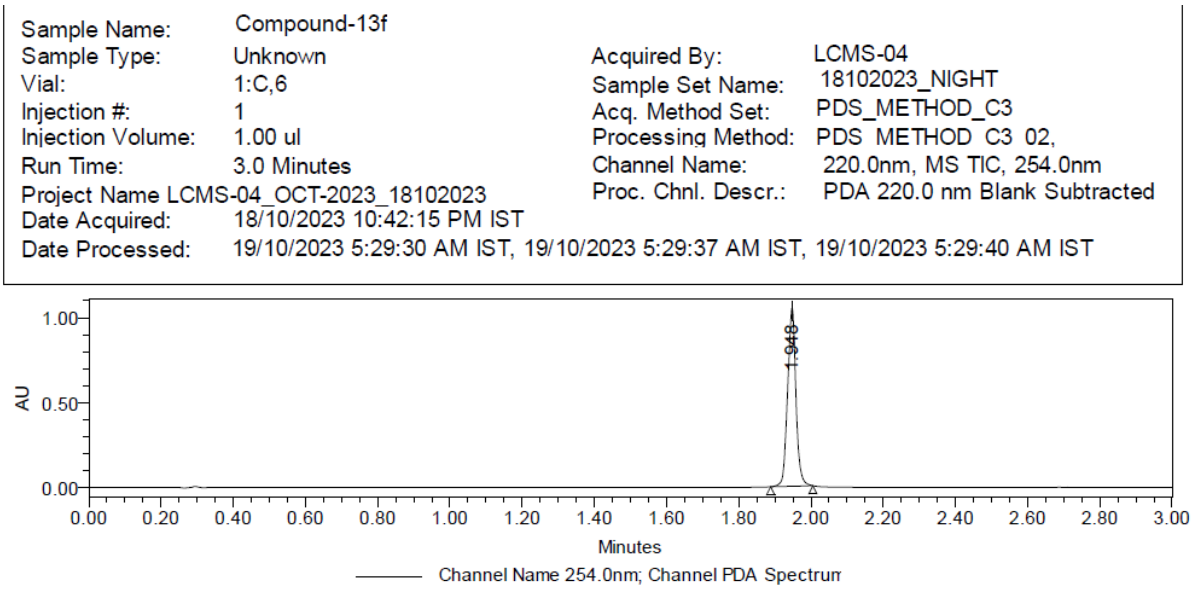
```
Current Data Parameters
NAME        650723
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_          20231116
Time              13.01 h
INSTRUM           spect
PROBHD    Z108618_1064 (
PULPROG            zg30
TD                16024
SOLVENT            DMSO
NS                   96
DS                    0
SWH            8012.820 Hz
FIDRES         1.000102 Hz
AQ            0.9998976 sec
RG                  181
DW               62.400 usec
DE                17.09 usec
TE                294.8 K
D1           1.00000000 sec
TD0                   1
SFO1        400.1324708 MHz
NUC1                 1H
P0                 4.67 usec
P1                14.00 usec
PLW1        16.00000000 W

F2 - Processing parameters
SI                65536
SF          400.1300078 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

Figure 77: ^{1}H NMR of compound **13f.**



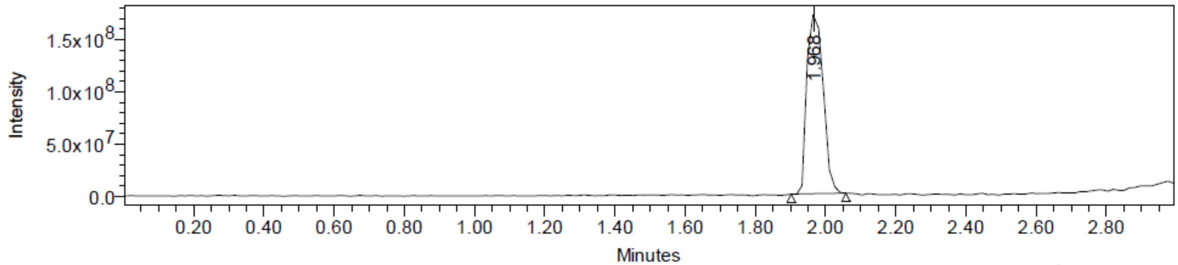
```
Current Data Parameters
NAME       641014
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20231102
Time                 18.17 h
INSTRUM              spect
PROBHD   Z108618_1064 (
PULPROG             zgpg30
TD                   65536
SOLVENT               DMSO
NS                    1024
DS                       2
SWH              26041.666 Hz
FIDRES            0.794729 Hz
AQ               1.2582912 sec
RG                     203
DW                  19.200 usec
DE                    6.50 usec
TE                   296.6 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1
SFO1           100.6228298 MHz
NUC1                   13C
P0                    3.33 usec
P1                   10.00 usec
PLW1           53.95100021 W
SFO2           400.1316005 MHz
NUC2                    1H
CPDPRG[2           waltz65
PCPD2                90.00 usec
PLW2           16.00000000 W
PLW12           0.38716000 W
PLW13           0.19474000 W

F2 - Processing parameters
SI                   32768
SF             100.6127685 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

Figure 78: ^{13}C NMR of compound **13f.**



Sample Name: Compound-13f
Sample Type: Unknown
Vial: 1:C,6
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-04_OCT-2023_18102023
Date Acquired: 18/10/2023 10:42:15 PM IST
Date Processed: 19/10/2023 5:29:30 AM IST, 19/10/2023 5:29:37 AM IST, 19/10/2023 5:29:40 AM IST

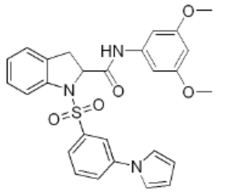
Acquired By: LCMS-04
Sample Set Name: 18102023_NIGHT
Acq. Method Set: PDS_METHOD_C3
Processing Method: PDS METHOD C3 02,
Channel Name: 220.0nm, MS TIC, 254.0nm
Proc. Chnl. Descr.: PDA 220.0 nm Blank Subtracted



Channel Name MS TIC; Channel SQ 1: MS Scan

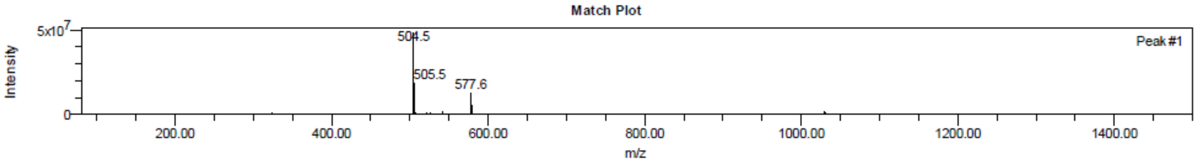
Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.947		1376768	2303029	100.00	PDA Spectrum	220.0nm
2	1.948		1051744	1669270	100.00	PDA Spectrum	254.0nm



Chemical Formula: $C_{27}H_{25}N_3O_5S$
Molecular Weight: 503.57

13f



Base Peak 504.50 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 Retention Time 1.968

Figure 79: LC-MS of compound **13f.**

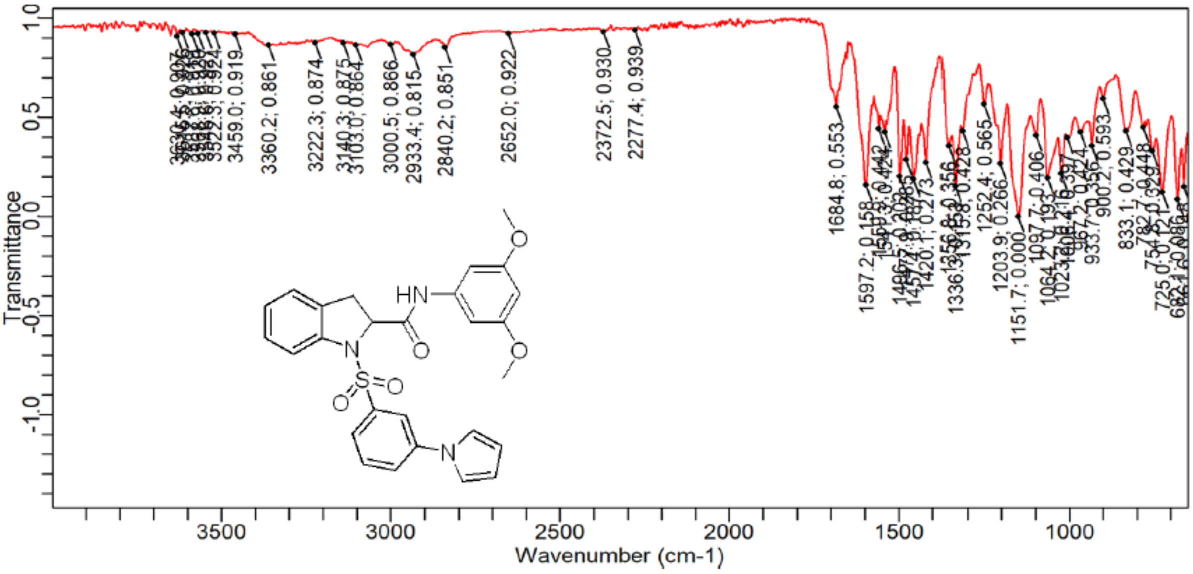
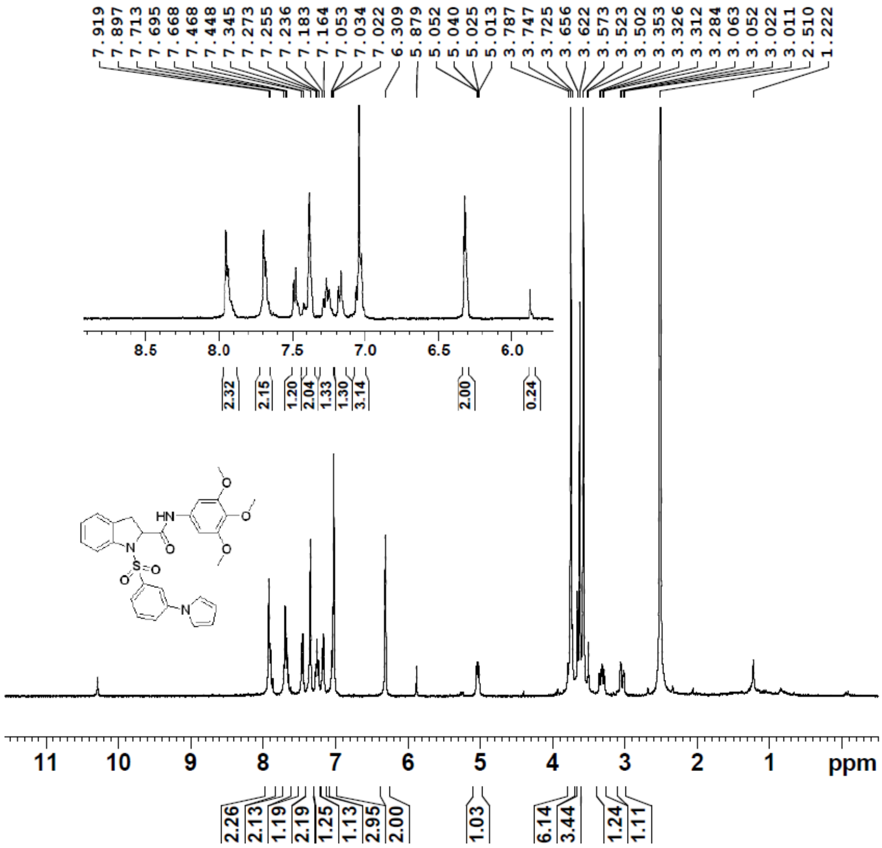
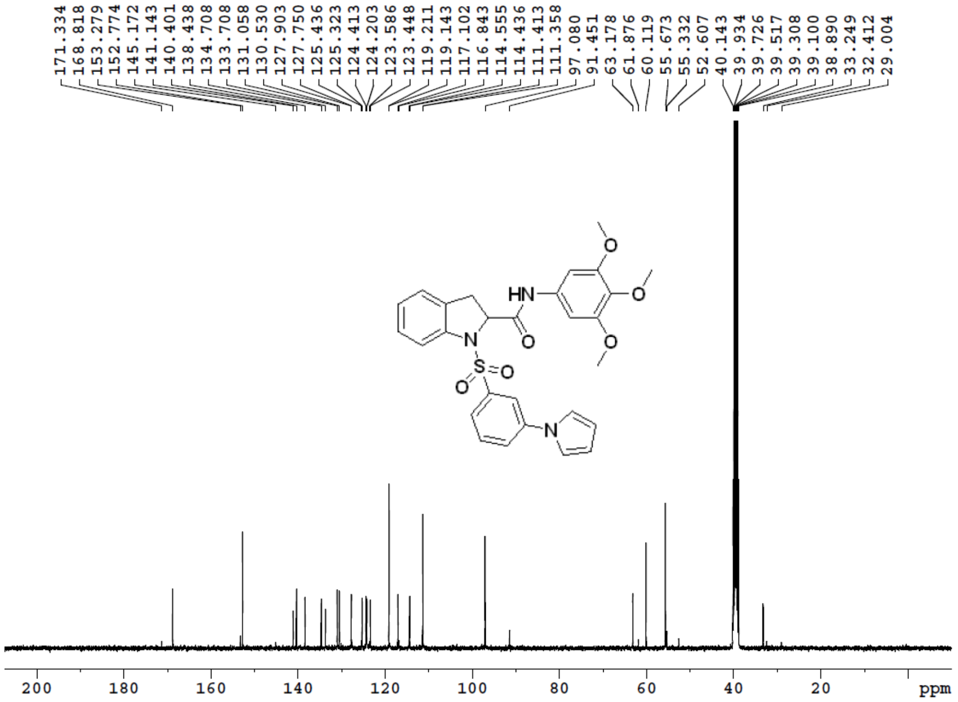


Figure 80: IR of compound **13f.**



```
Current Data Parameters
NAME       630681
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_            20231021
Time                 0.06 h
INSTRUM            Avance
PROBHD    Z163739_0756 (
PULPROG              zg30
TD                  40000
SOLVENT              DMSO
NS                     16
DS                      0
SWH             10000.000 Hz
FIDRES           0.500000 Hz
AQ              2.0000000 sec
RG                    101
DW                 50.000 usec
DE                  11.14 usec
TE                  297.8 K
D1             1.00000000 sec
TD0                     1
SFO1          400.6024737 MHz
NUC1                   1H
P0                   2.67 usec
P1                   8.00 usec
PLW1          21.40600014 W

F2 - Processing parameters
SI                  65536
SF            400.6000000 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
PC                   1.00
```

Figure 81: ^{1}H NMR of compound **13h.**

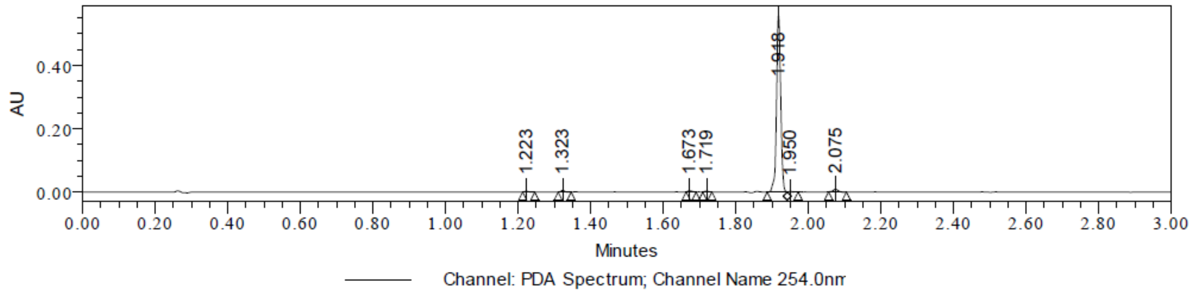


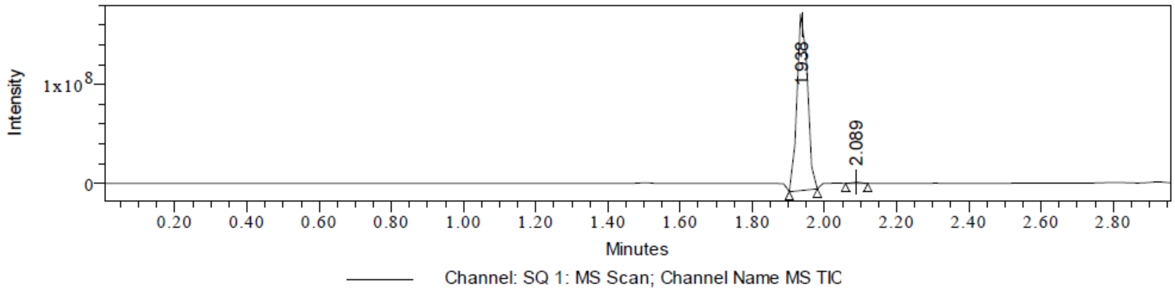
```
Current Data Parameters
NAME       644559
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_            20231104
Time                 3.18 h
INSTRUM             spect
PROBHD    Z108618_1064 (
PULPROG            zgpg30
TD                  65536
SOLVENT              DMSO
NS                   5000
DS                      4
SWH             39682.539 Hz
FIDRES           1.211015 Hz
AQ              0.8257536 sec
RG                    203
DW                 12.600 usec
DE                   6.50 usec
TE                  297.1 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                     1
SFO1          100.6228298 MHz
NUC1                  13C
P0                   3.33 usec
P1                  10.00 usec
PLW1          53.95100021 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz65
PCPD2               90.00 usec
PLW2          16.00000000 W
PLW12          0.38716000 W
PLW13          0.19474000 W

F2 - Processing parameters
SI                  32768
SF            100.6128157 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```

Figure 82: ^{13}C NMR of compound **13h.**

Sample Name: 13h
Sample Type: Unknown
Vial: 1:E,4
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 3.0 Minutes
Project Name LCMS-02_OCT-2023_11102023
Date Acquired: 11-10-2023 11:41:00 IST
Date Processed: 11-10-2023 11:45:23 IST, 11-10-2023 11:45:39 IST, 11-10-2023 11:46:05 IST

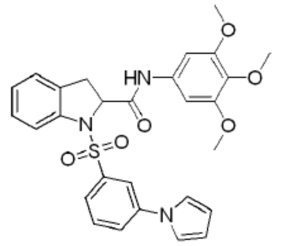
Acquired By: LCMS-02
Sample Set Name: 11102023 UCH 197 1ST
Acq. Method Set: METHOD C3
Processing Method: METHOD_C3, METHOD_C3_03
Channel Name: 220.0nm, MS TIC, 254.0nm
Proc. Chnl. Descr.: PDA 220.0 nm Blank Subtracted





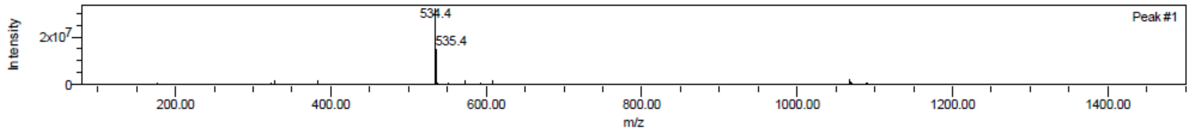
Peak Results
Channel: PDA Spectrum

	Retention Time (min)	Base Peak (m/z)	Height (µV)	Area (µV*sec)	% Area	Channel	Channel Name
1	1.223		2589	1908	0.41	PDA Spectrum	254.0nm
2	1.223		24247	18811	3.24	PDA Spectrum	220.0nm
3	1.247		3332	2069	0.36	PDA Spectrum	220.0nm
4	1.323		5230	3559	0.76	PDA Spectrum	254.0nm
5	1.671		13903	10743	1.85	PDA Spectrum	220.0nm
6	1.673		3687	3030	0.65	PDA Spectrum	254.0nm
7	1.719		3155	2190	0.47	PDA Spectrum	254.0nm



Chemical Formula: $C_{28}H_{27}N_3O_6S$
Molecular Weight: 533.60
13h

Match Plot



Base Peak 534.40 Channel Description 1: 80.00-1500.00 ES+, Centroid, CV=30 - AVG (2.2:3.0;2.1:3.0;0.0:1.9) x 55.000 - AVG (2.2:3.0;2.1:3.0;0.0:1.9) x 66.000 Retention Time 1.93

Figure 83: LC-MS of compound **13h.**

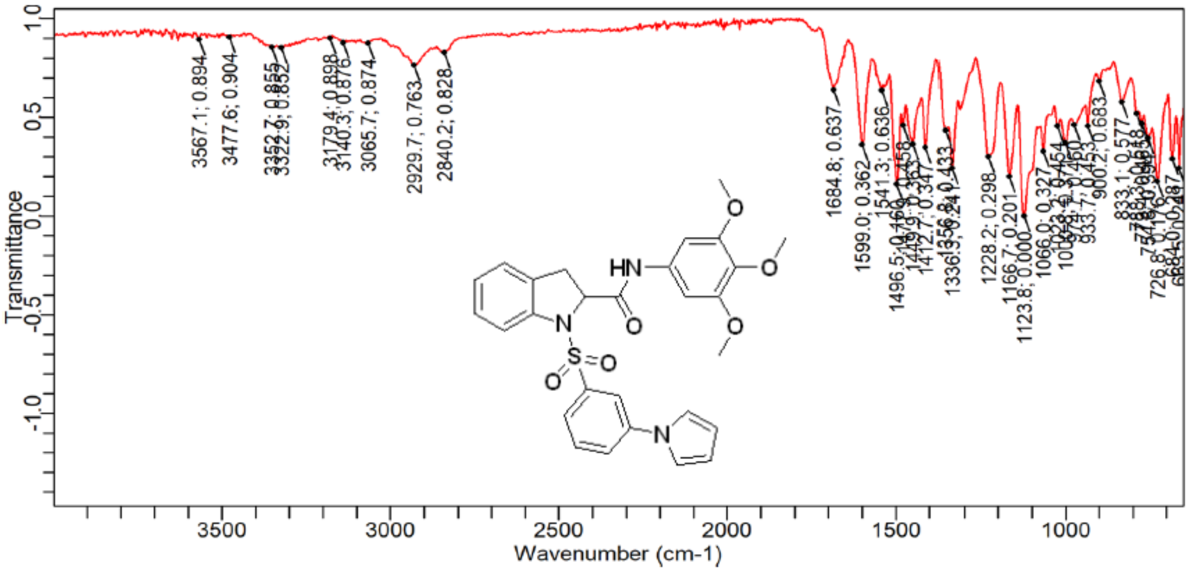


Figure 84: IR of compound **13h.**