

Supporting Information

Targeting Tubulin Polymerization and DNA Binding of 4-Thiazolidinone-umbelliferone Hybrids: Synthesis and Cytotoxicity Evaluation

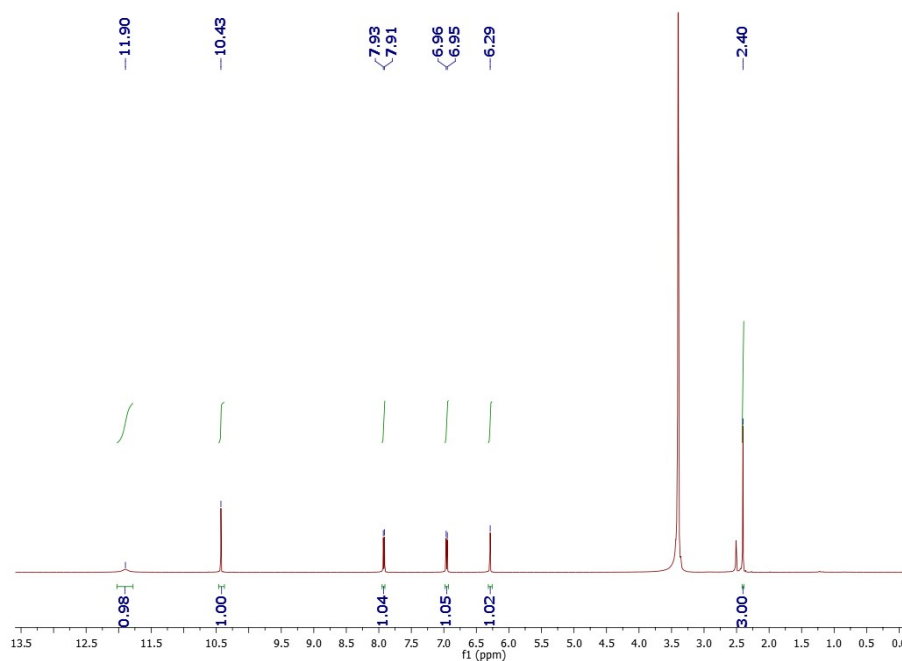
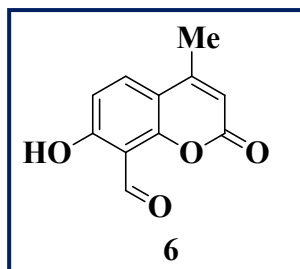
Dilep Kumar Sigalapalli^a, Gaddam Kiranmai^b, Ramya Tokala^a, Chaturvedula Tripura^b,
Ramesh Ambatwar^a, Saiprasad N. Nunewar^a, Manasa Kadagathur^a, Nagula Shankaraiah^{a*},
Narayana Nagesh^{b*}, Bathini Nagendra Babu^{c*}, Neelima D. Tangellamudi^{a*}

^a*Department of Medicinal Chemistry, National Institute of Pharmaceutical
Education and Research (NIPER), Hyderabad 500037, India*

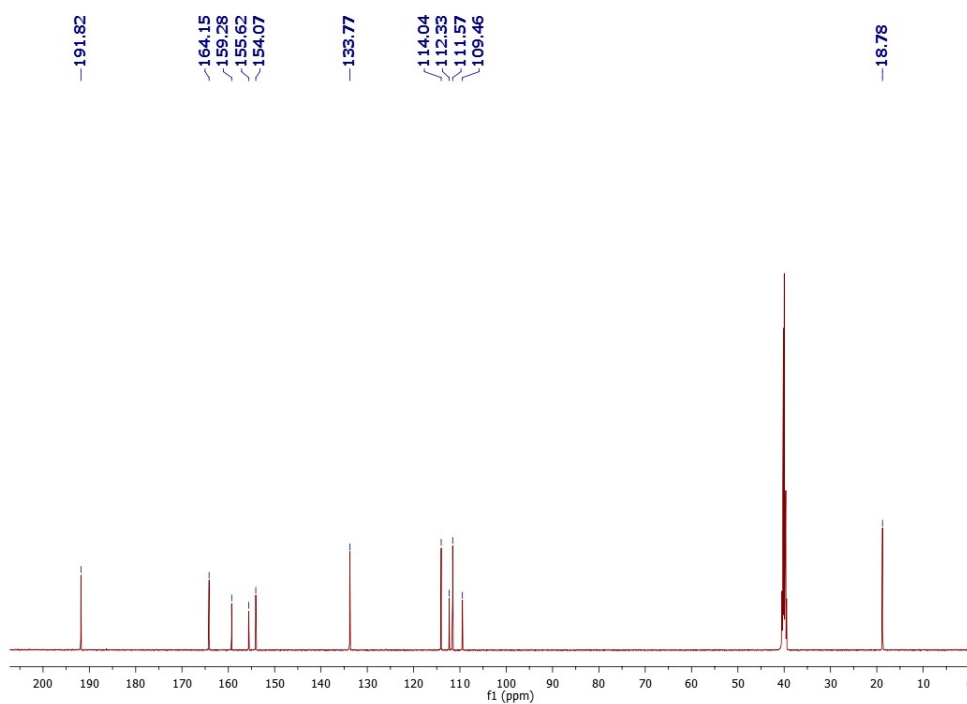
^b*CSIR-Centre for Cellular and Molecular Biology, Medical Biotechnology
Complex, ANNEXE II, Uppal Road, Hyderabad 500007, India*

^c*Department of Fluoro-Agrochemicals, CSIR-Indian Institute of Chemical
Technology, Hyderabad 500007, India*

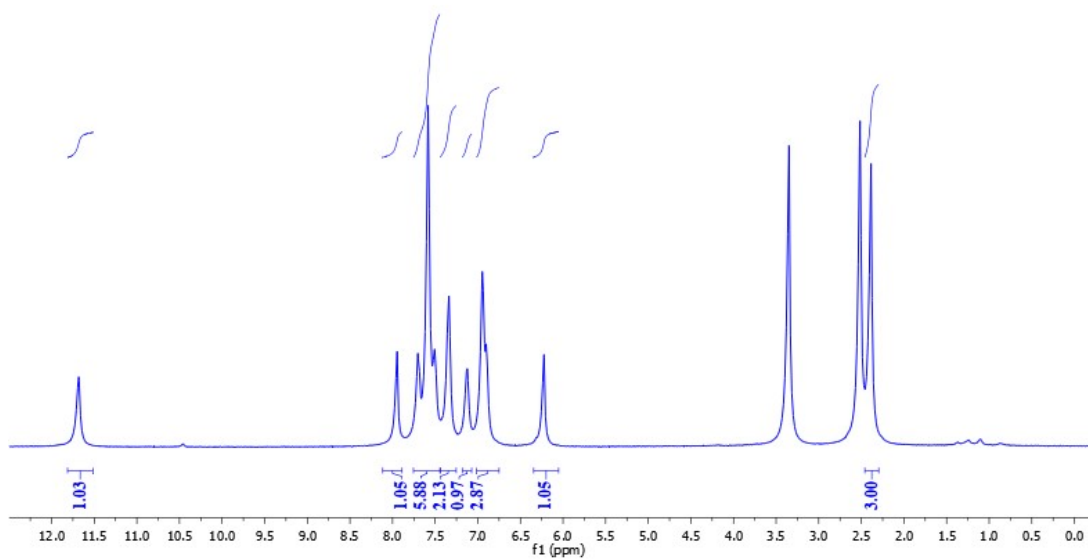
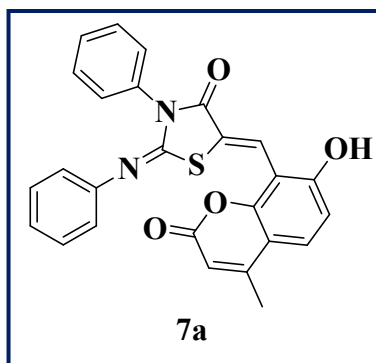
Copies of ^1H and ^{13}C NMR spectra



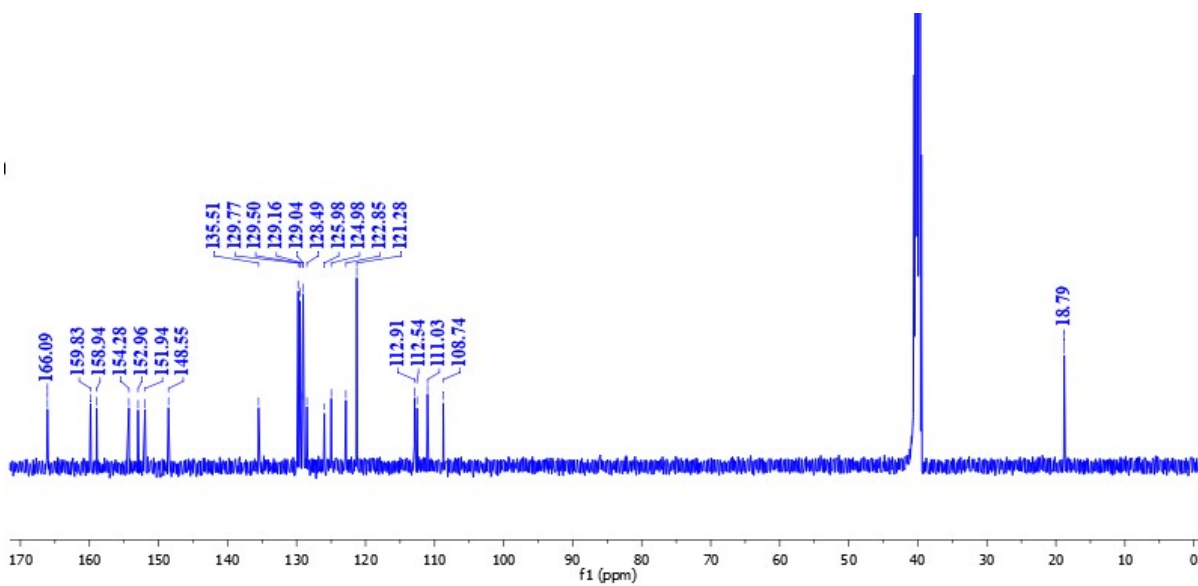
Compound (**6**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



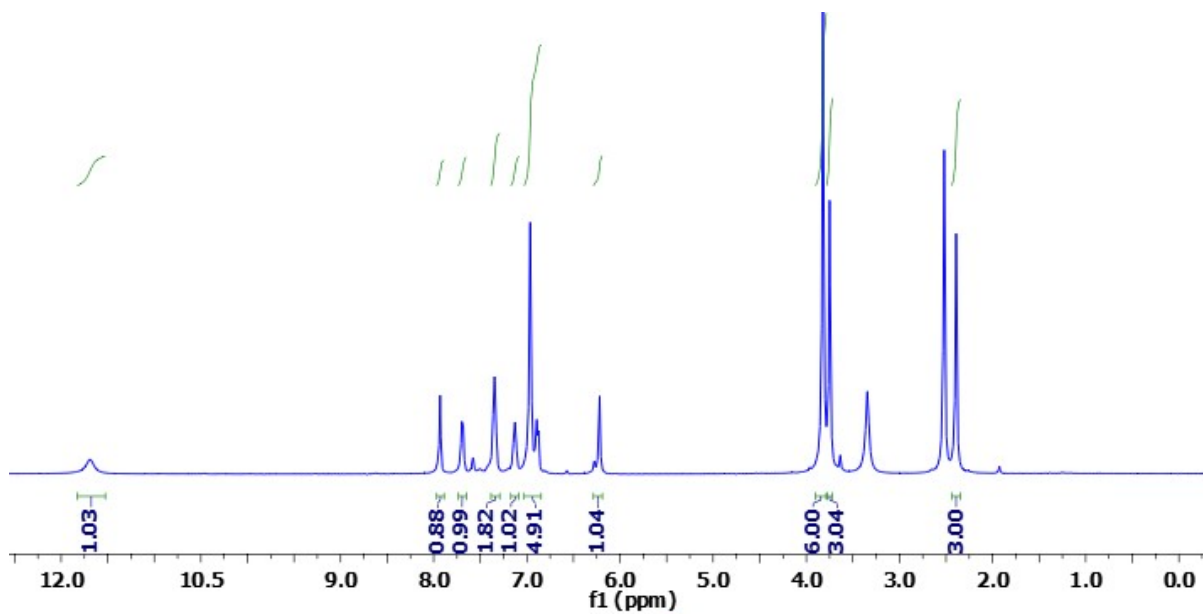
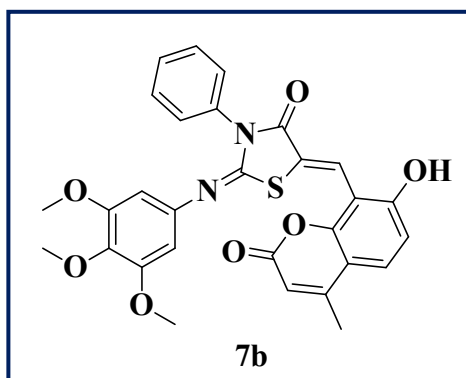
Compound (**6**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



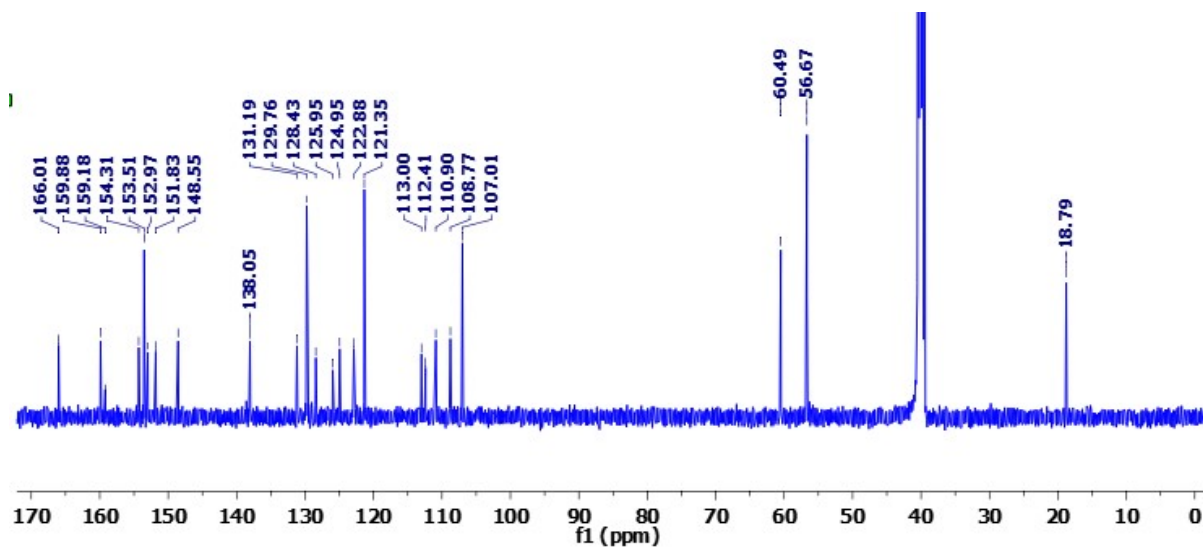
Compound (**7a**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



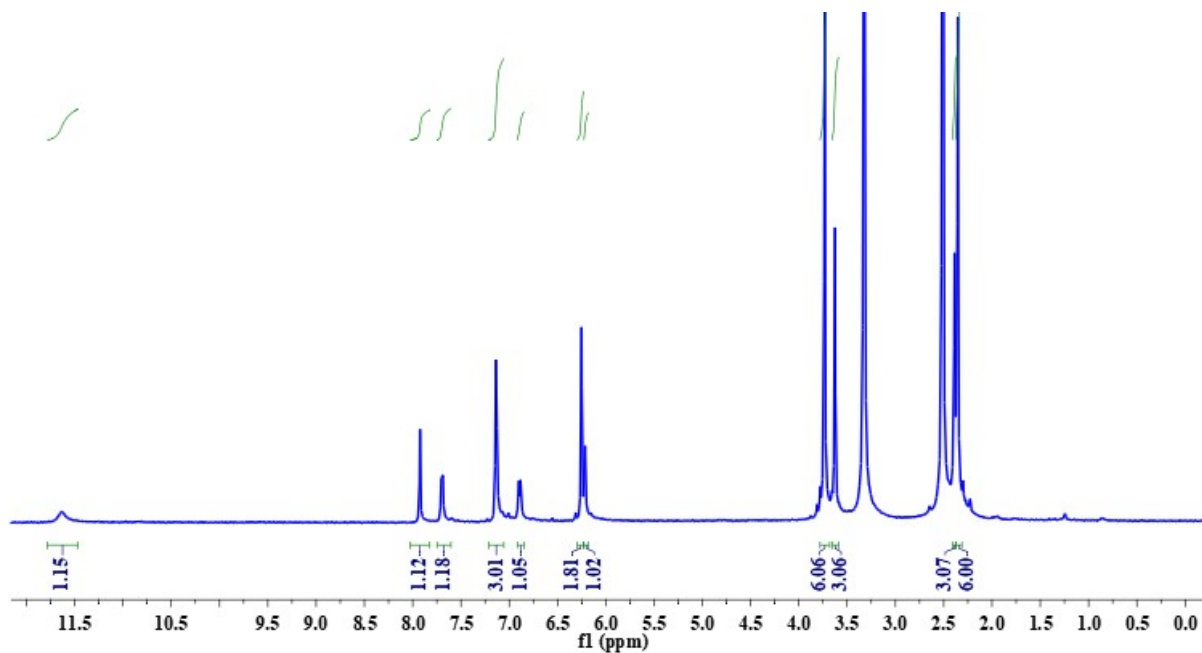
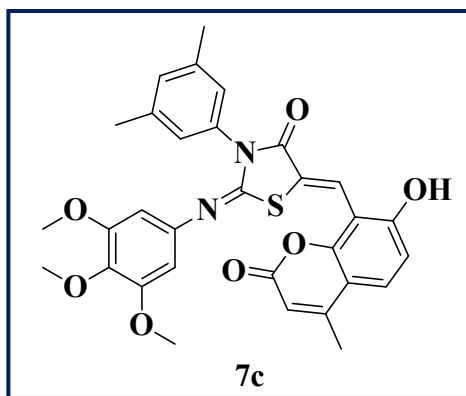
Compound (**7a**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



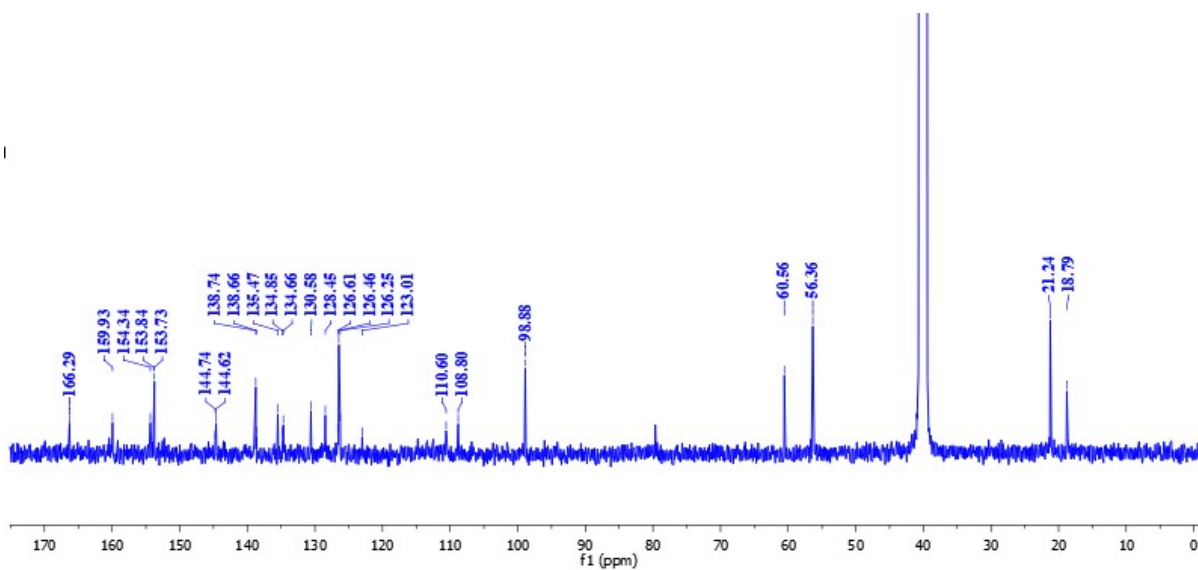
Compound (**7b**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



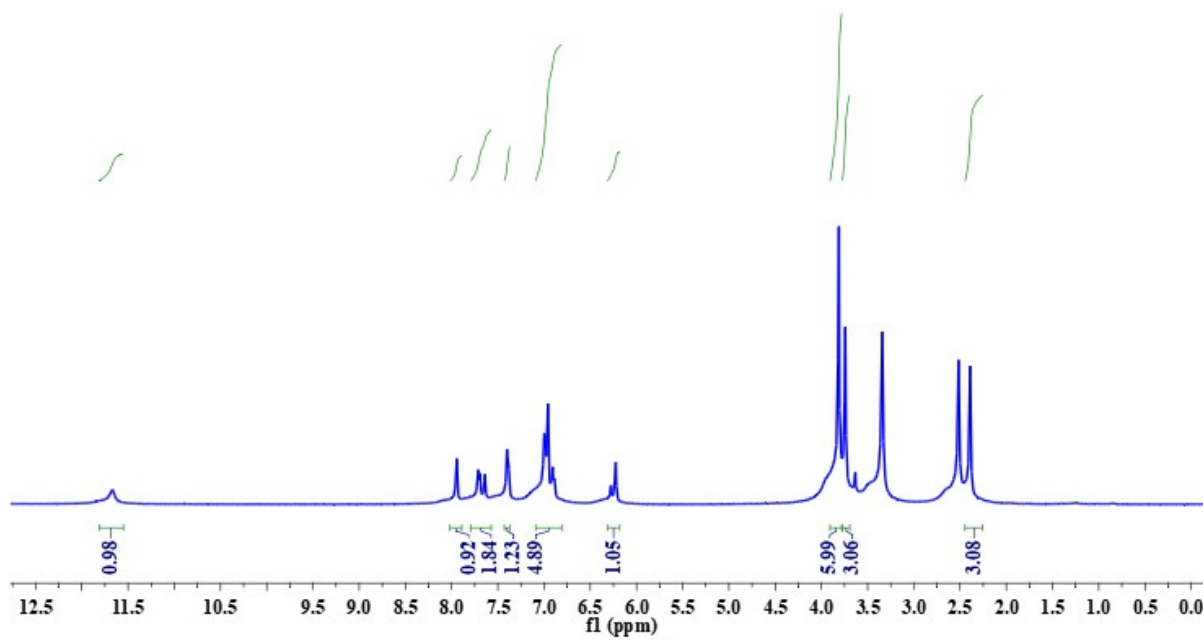
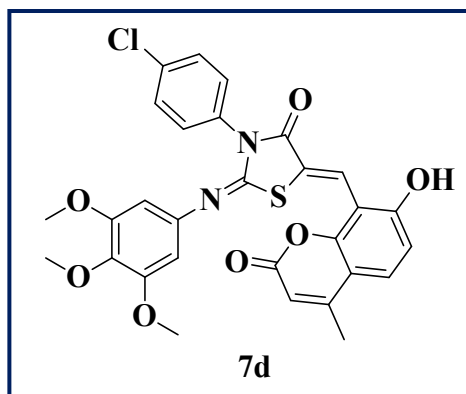
Compound (**7b**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



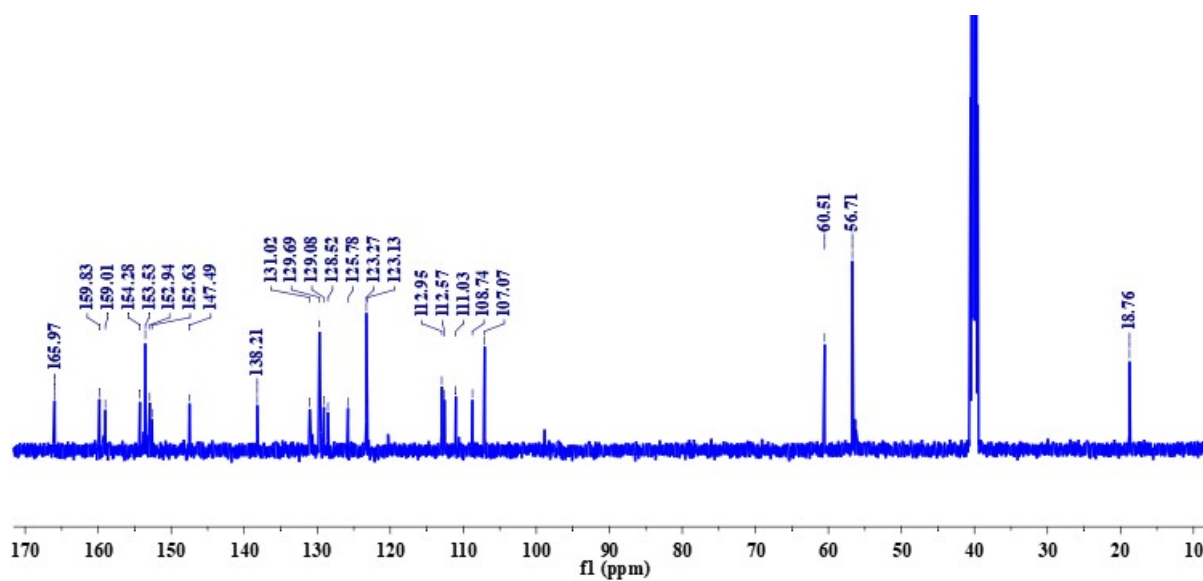
Compound (7c): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



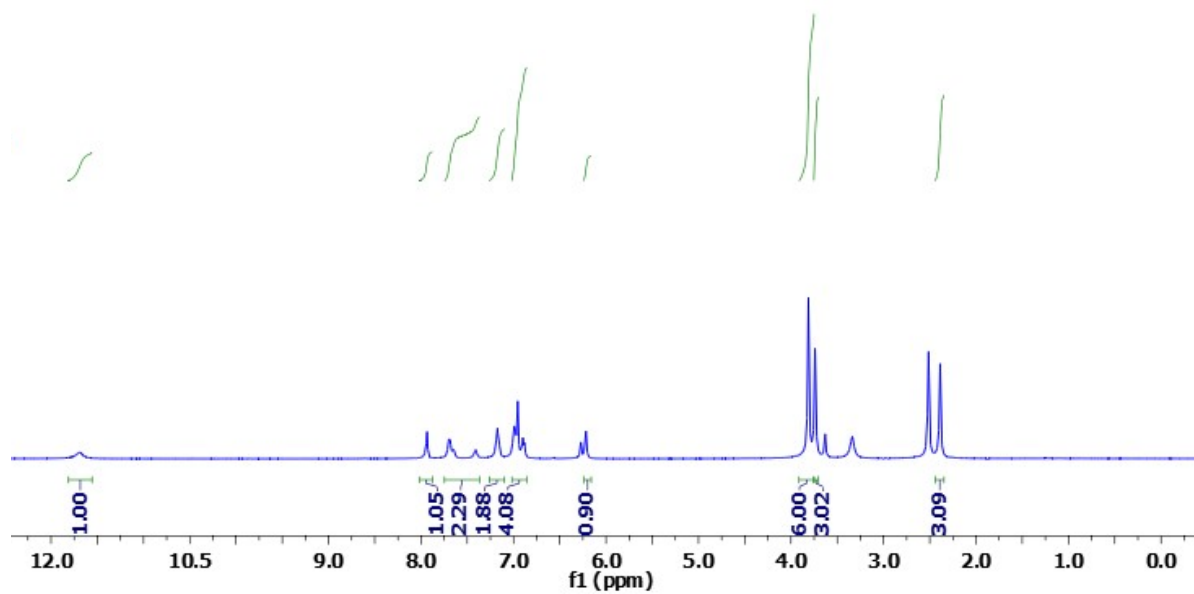
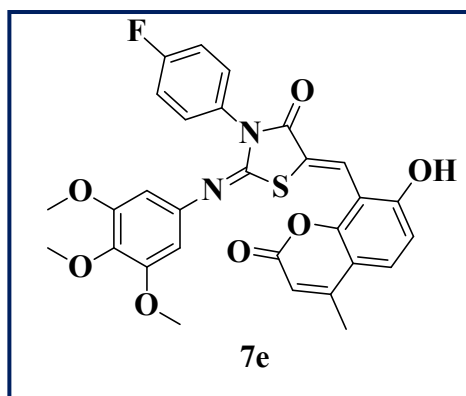
Compound (7c): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



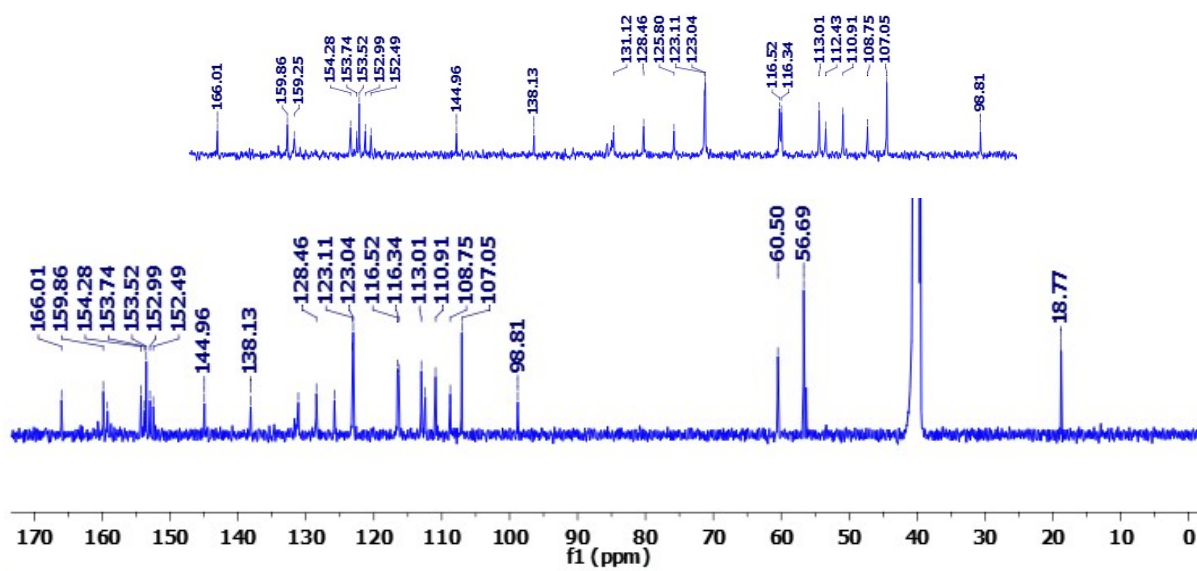
Compound (**7d**): ¹H NMR (500 MHz, DMSO-*d*₆)



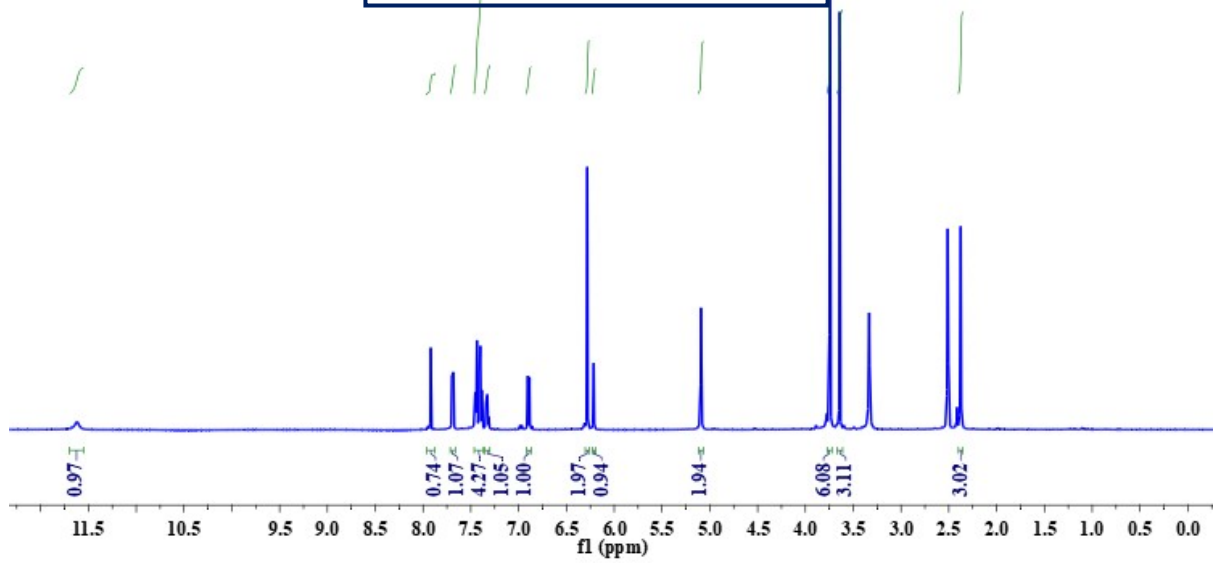
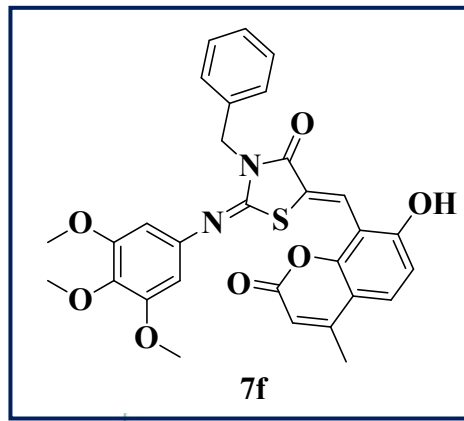
Compound (**7d**): ¹³C NMR (125 MHz, DMSO-*d*₆)



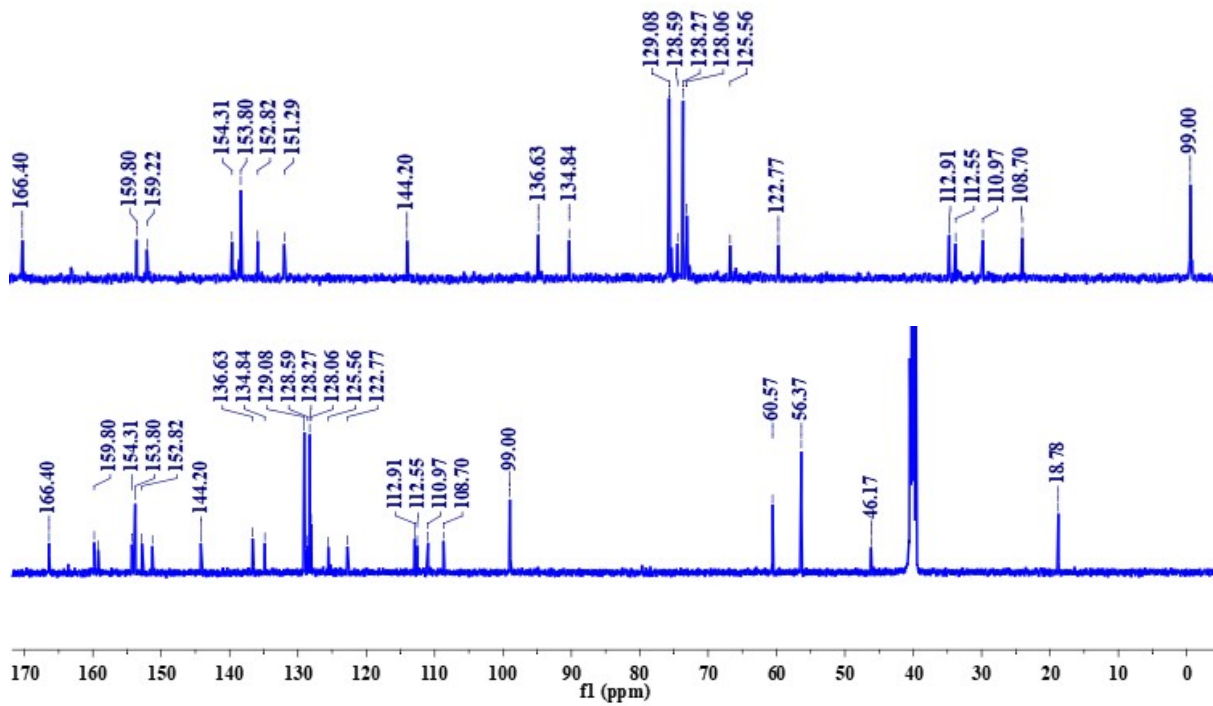
Compound (7e): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



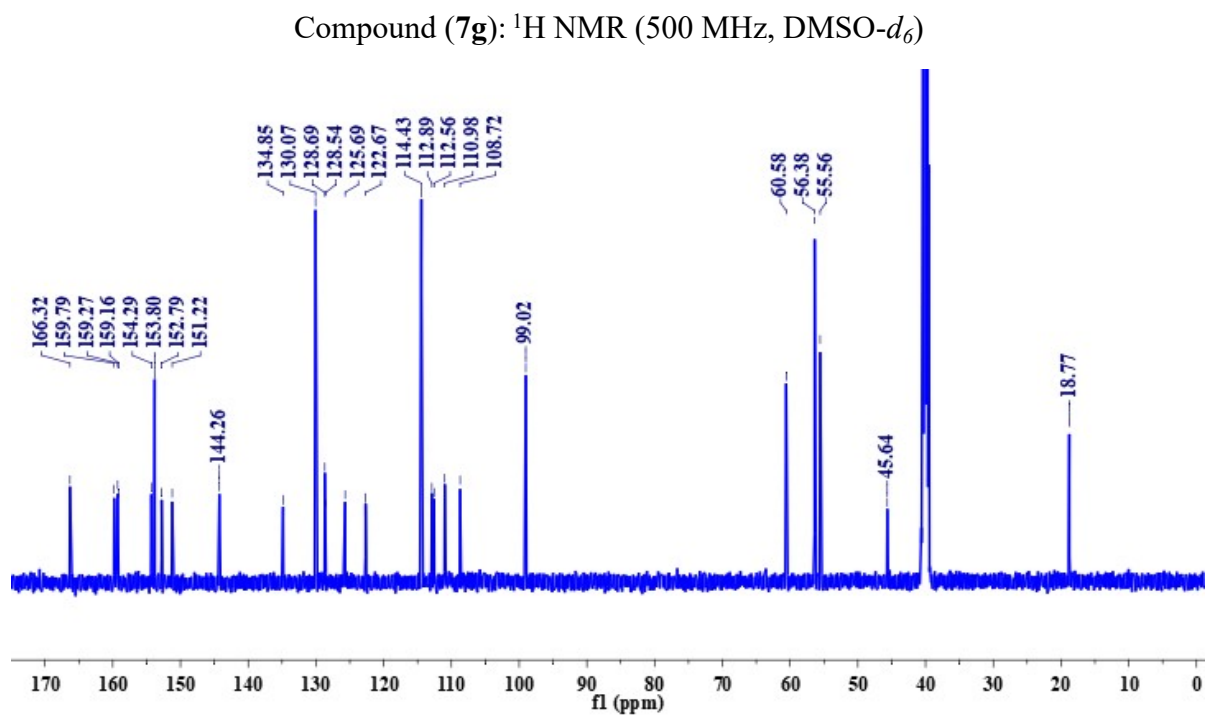
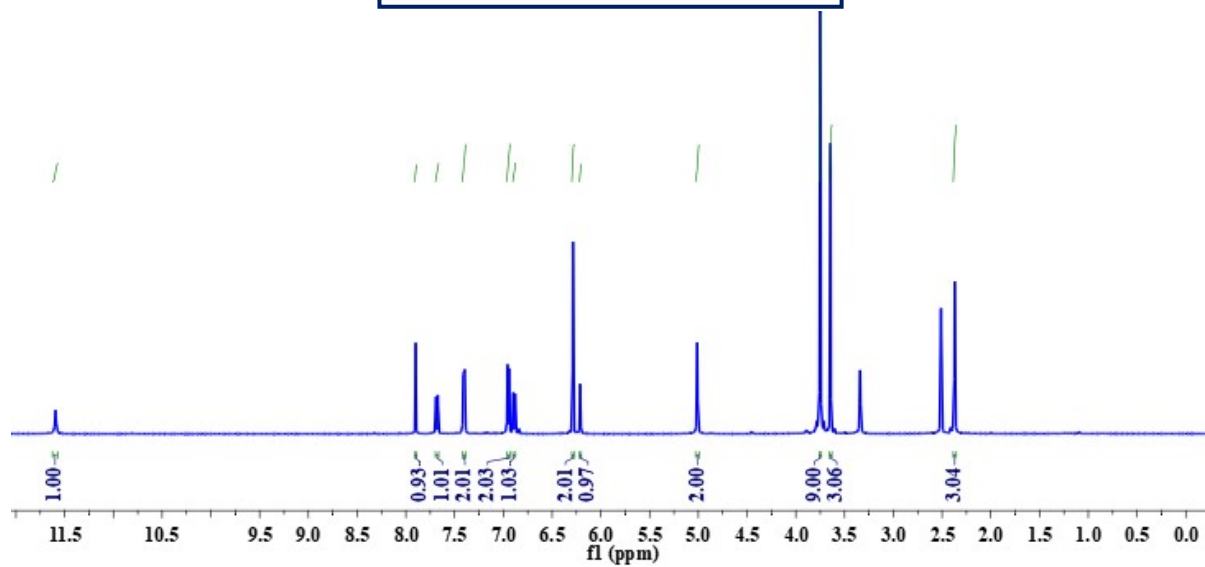
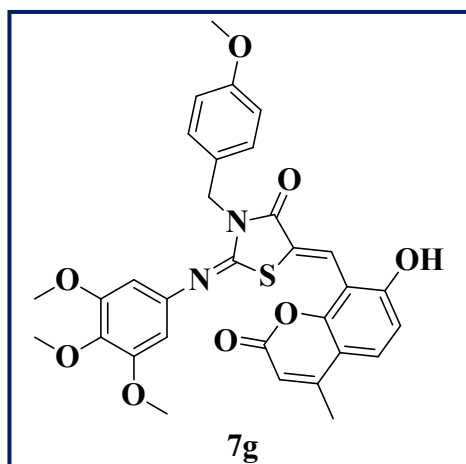
Compound (7e): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)

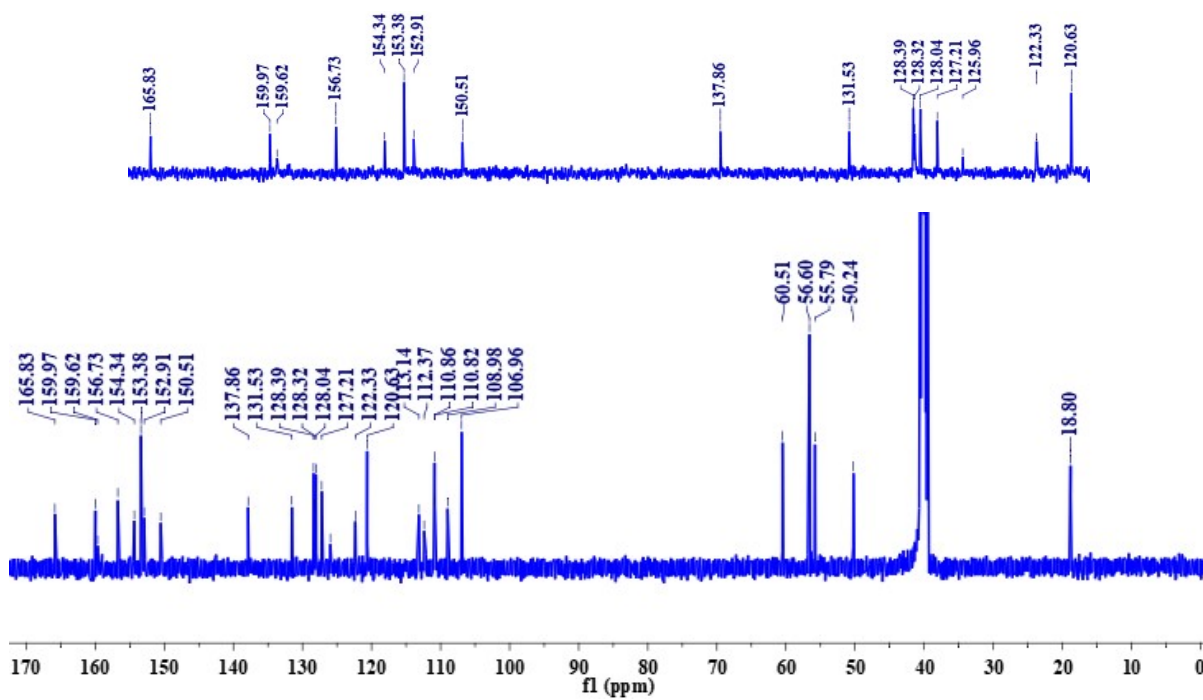
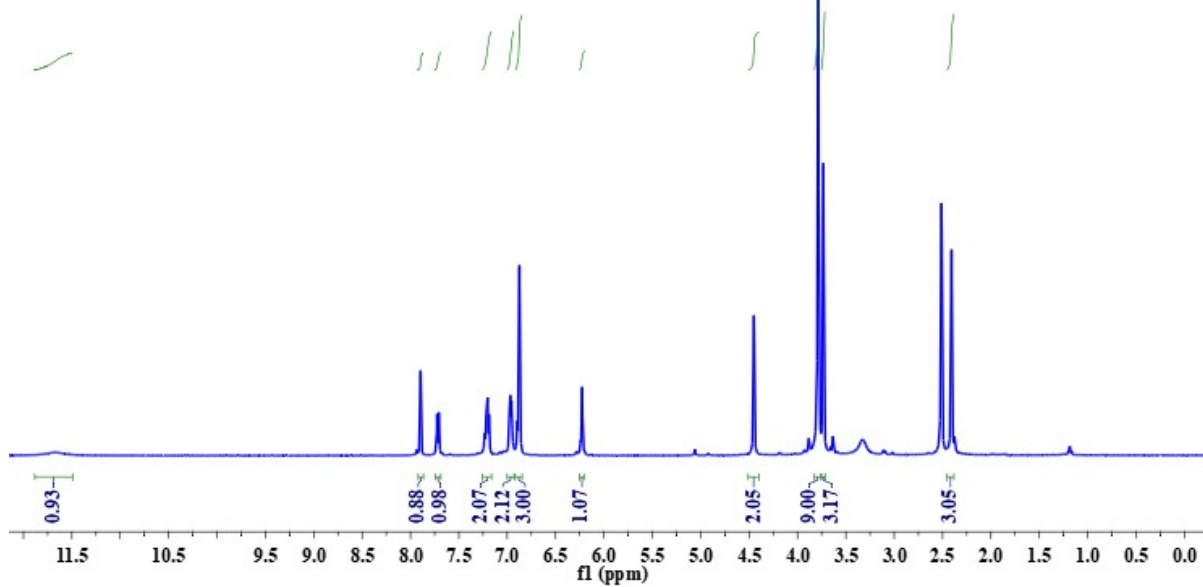
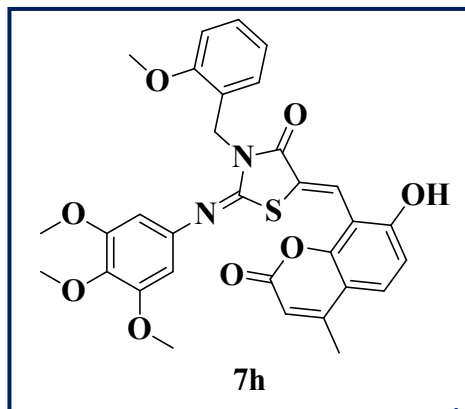


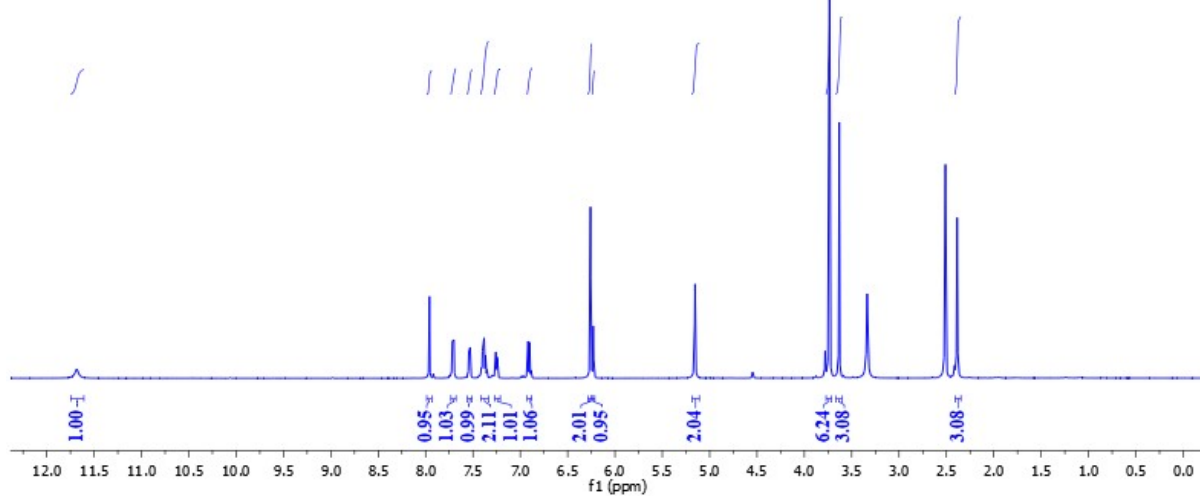
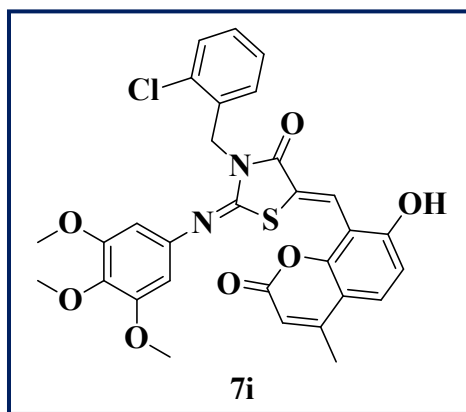
Compound (7f): ¹H NMR (500 MHz, DMSO-*d*₆)



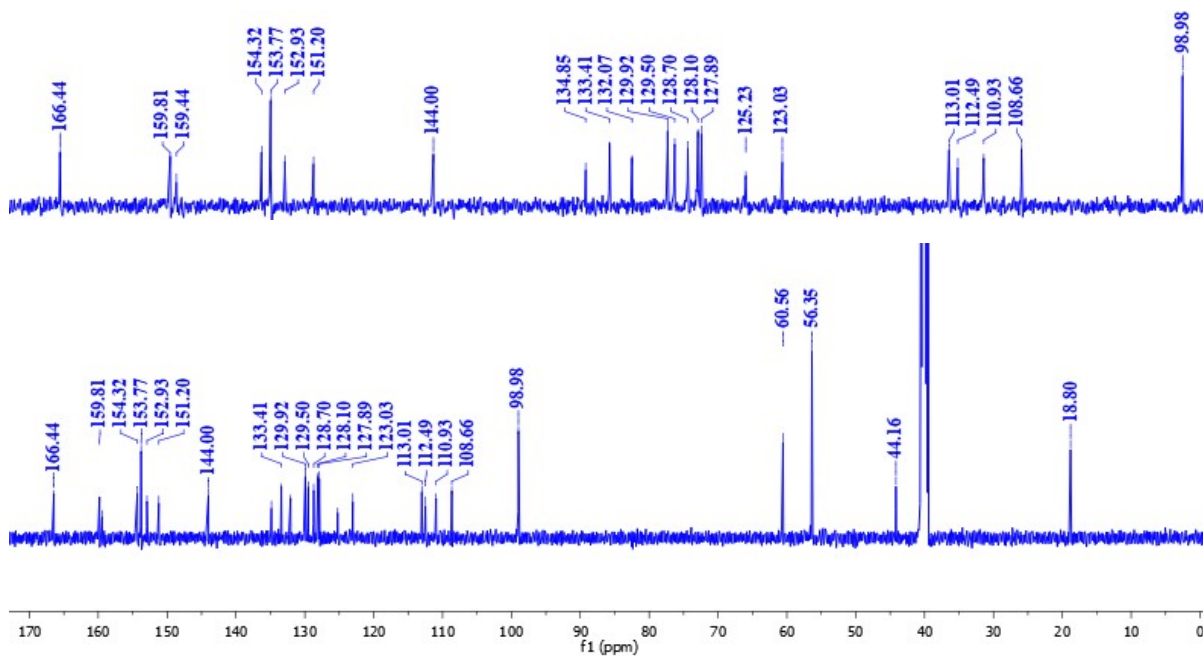
Compound (7f): ¹³C NMR (125 MHz, DMSO-*d*₆)



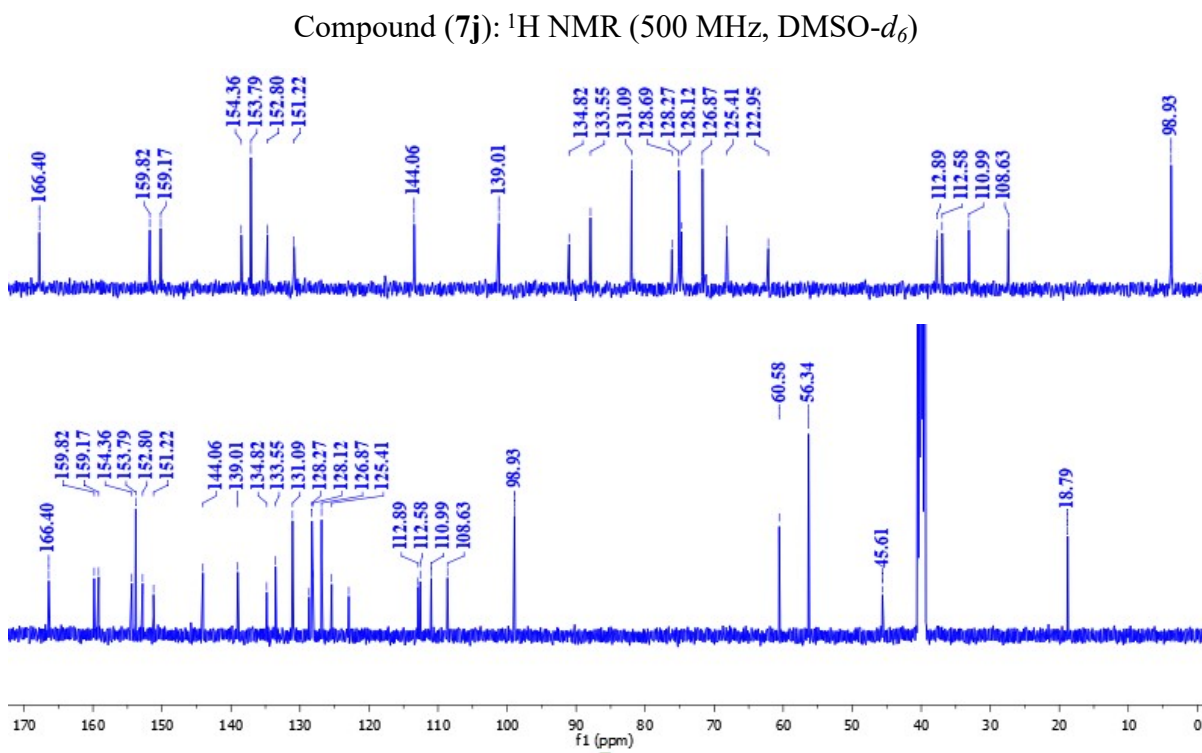
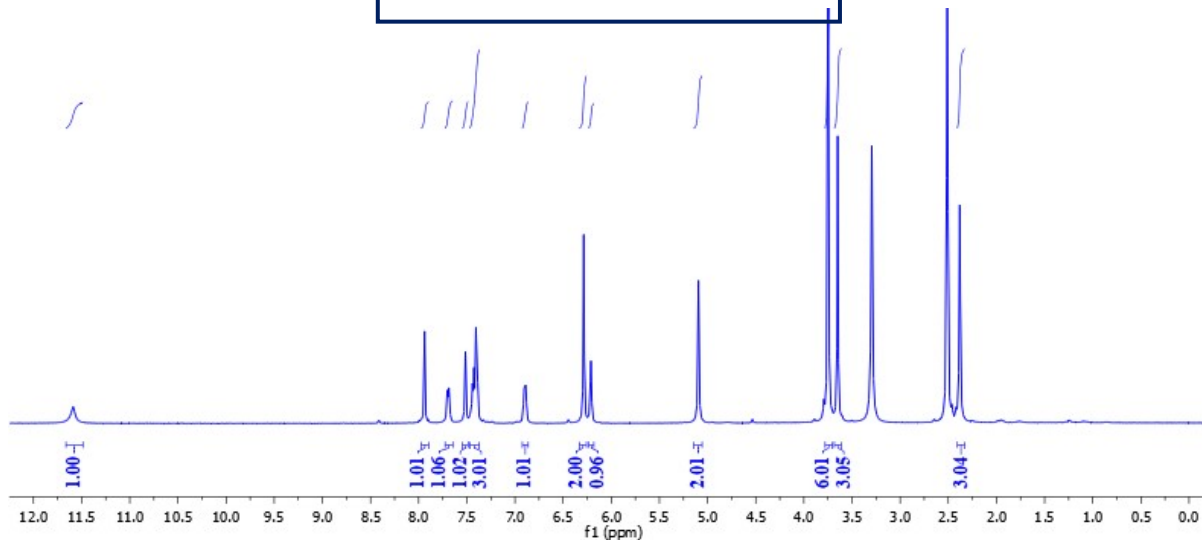
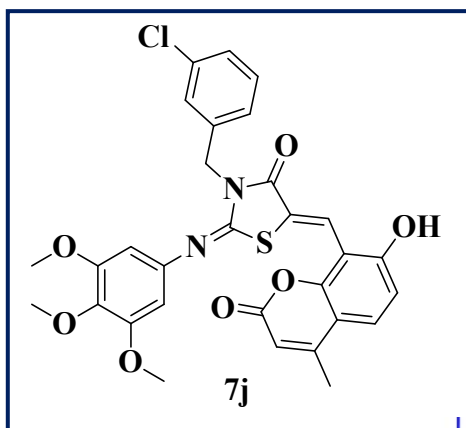


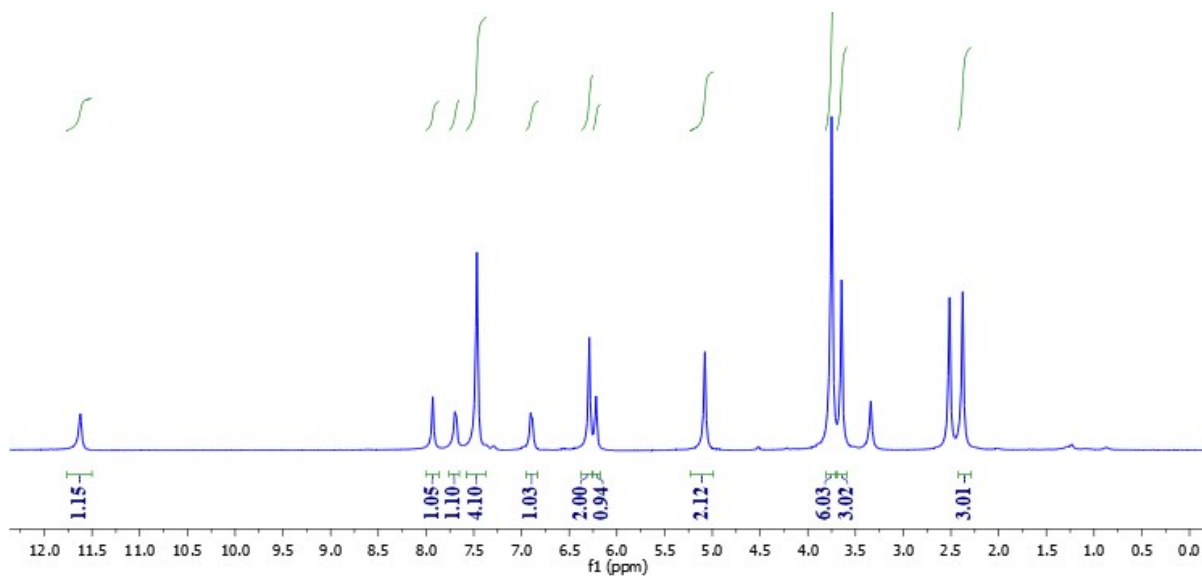
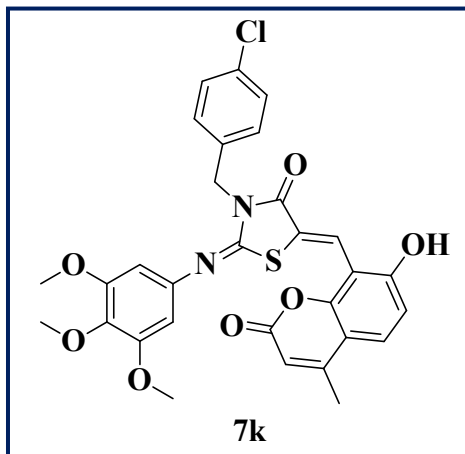


Compound (**7i**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)

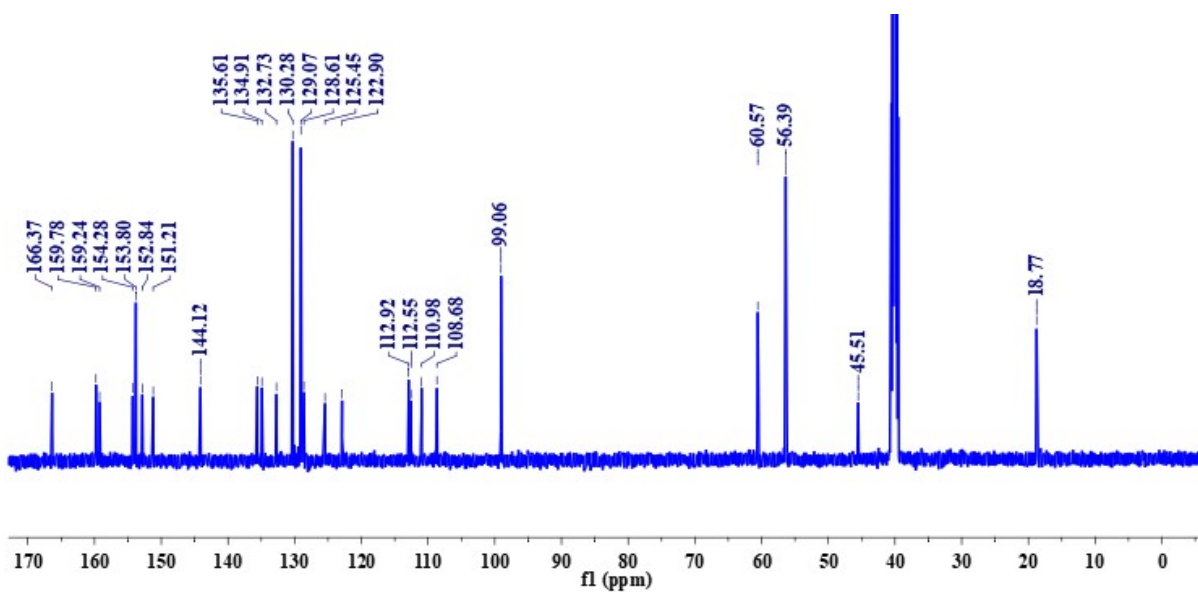


Compound (**7i**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)

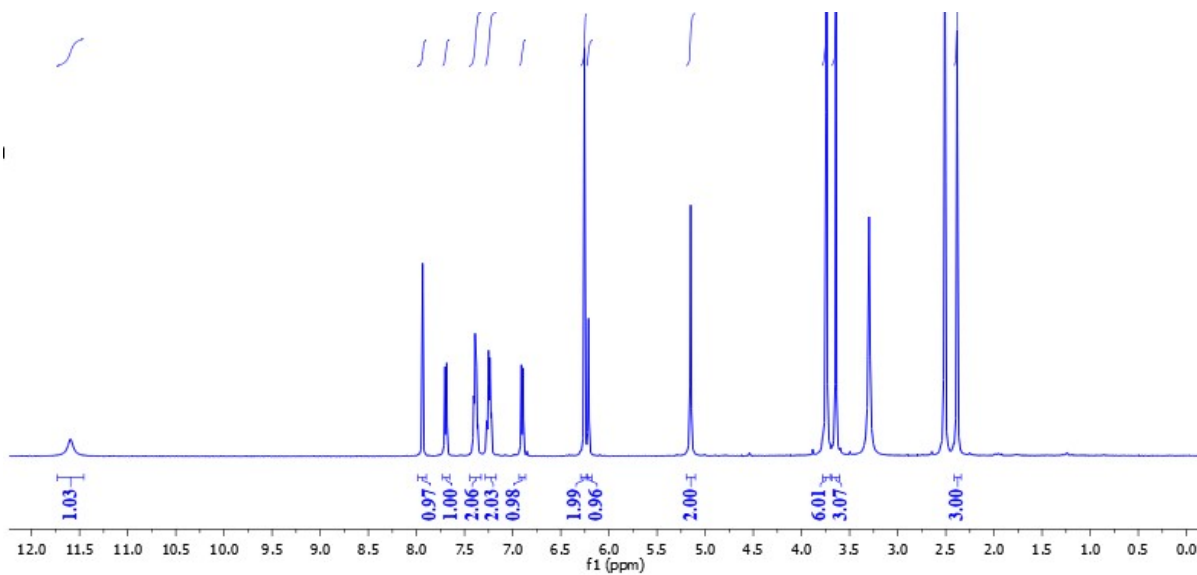
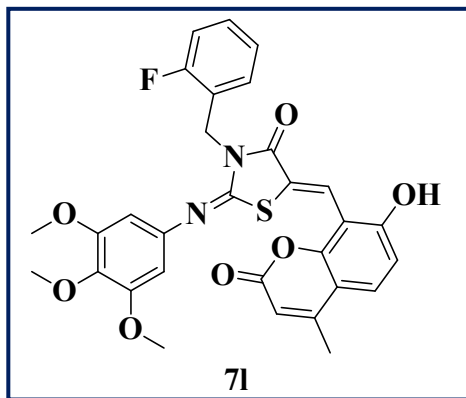




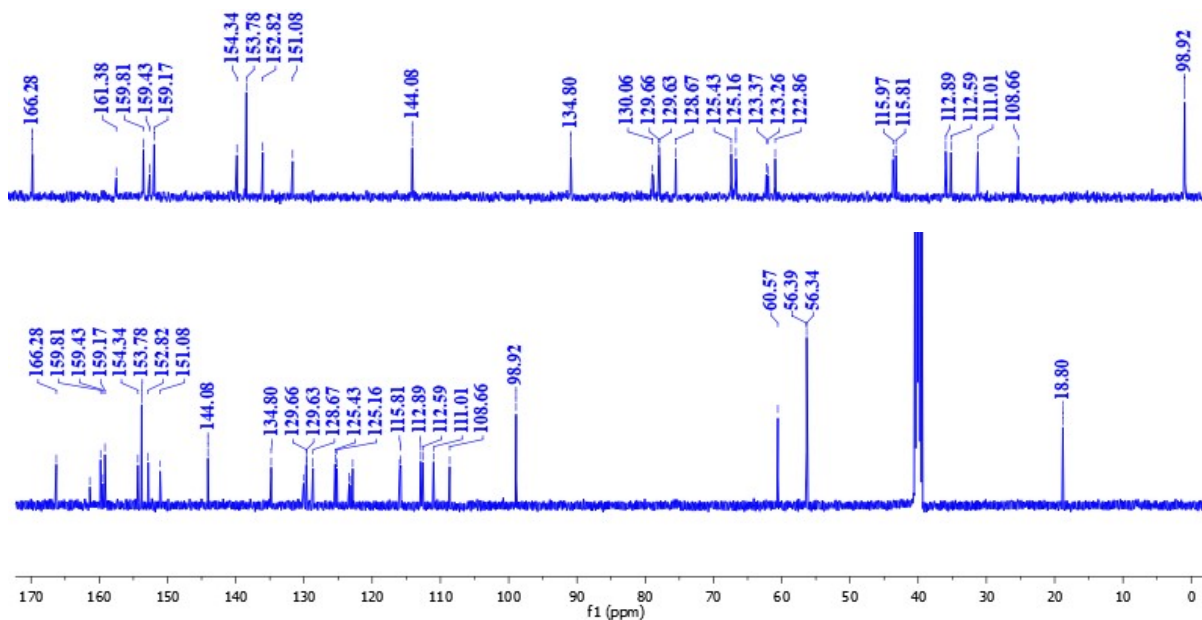
Compound (**7k**): ¹H NMR (500 MHz, DMSO-*d*₆)



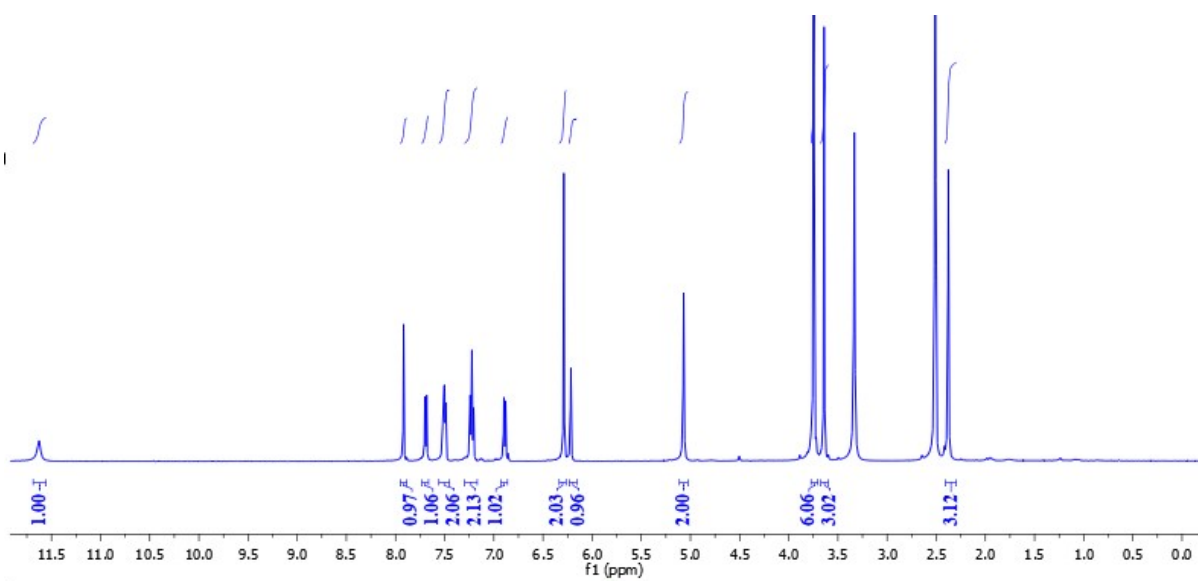
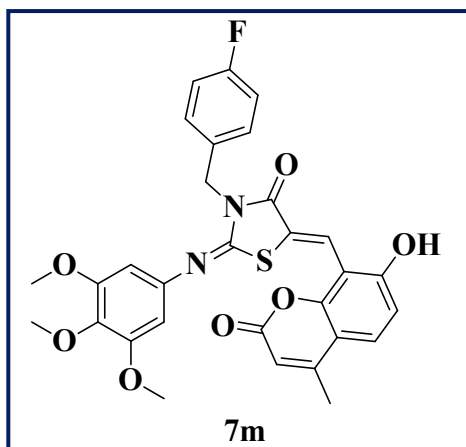
Compound (**7k**): ¹³C NMR (125 MHz, DMSO-*d*₆)



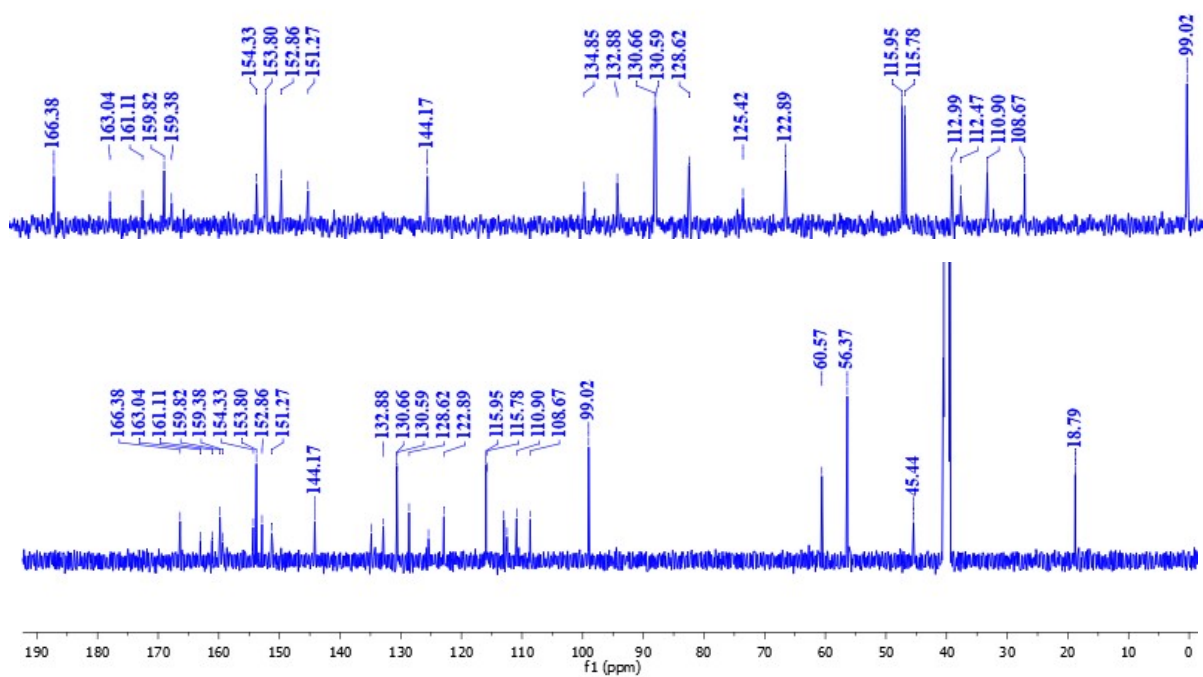
Compound (**7I**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



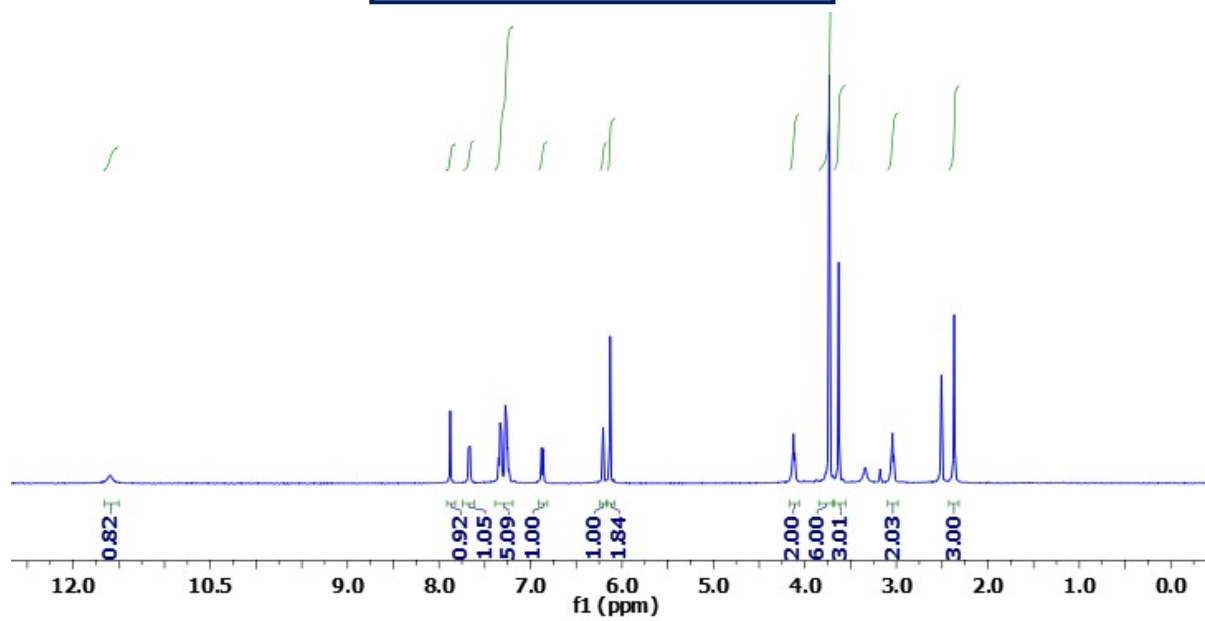
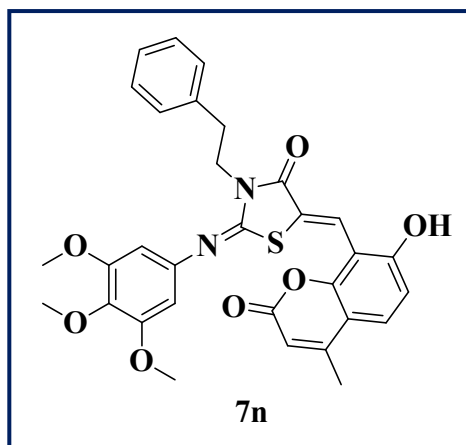
Compound (**7I**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



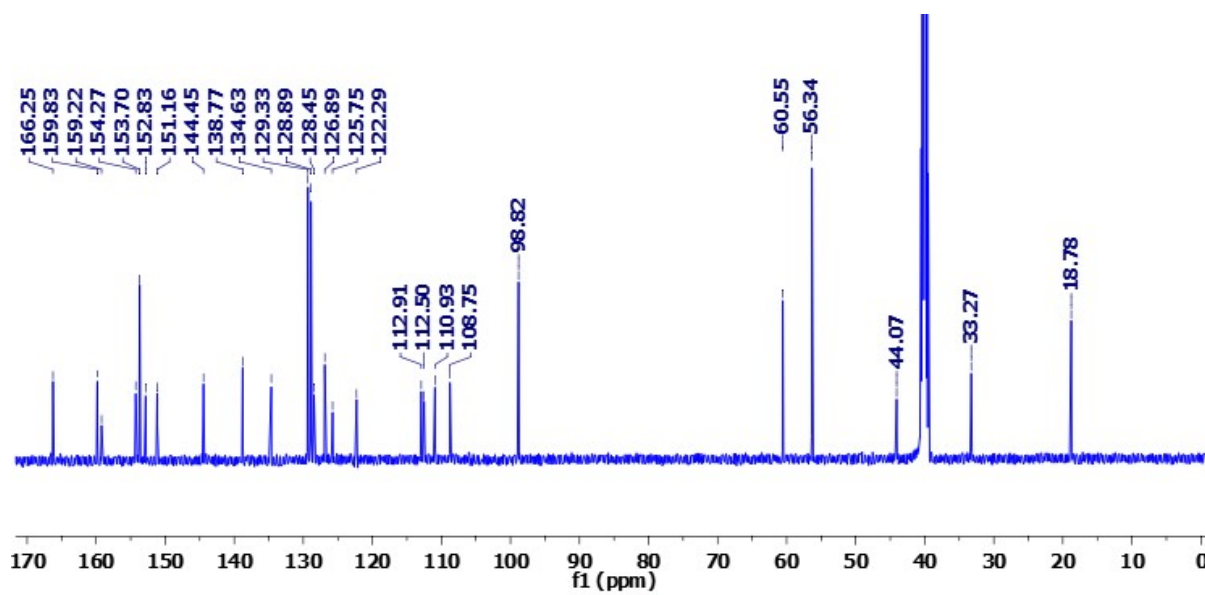
Compound (**7m**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



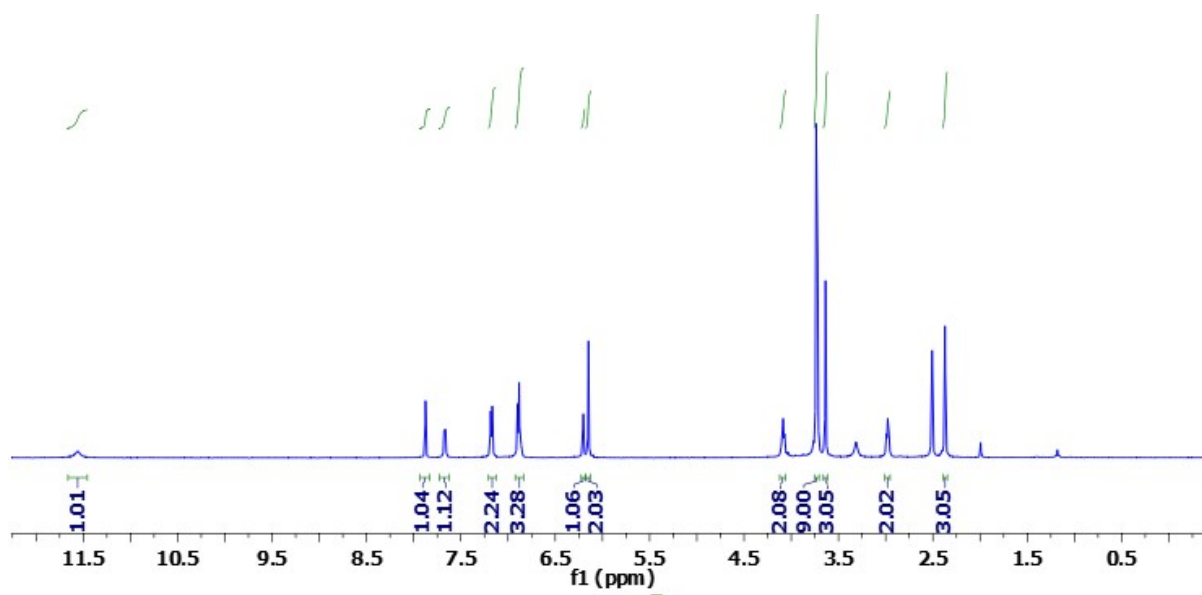
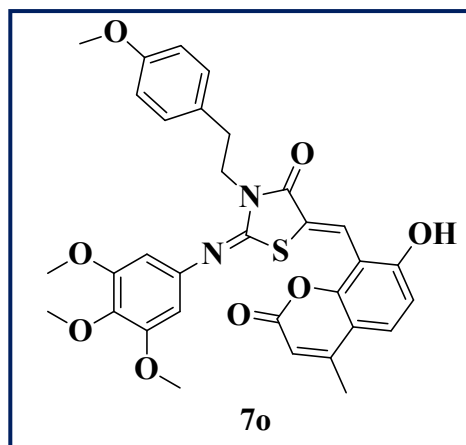
Compound (**7m**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



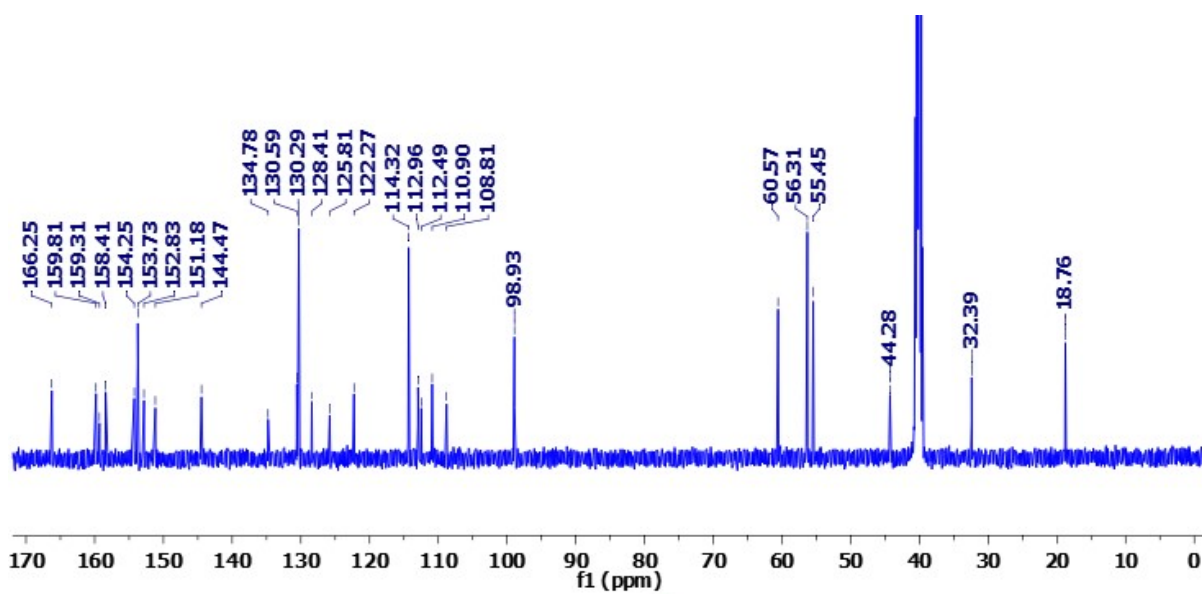
Compound (7n): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



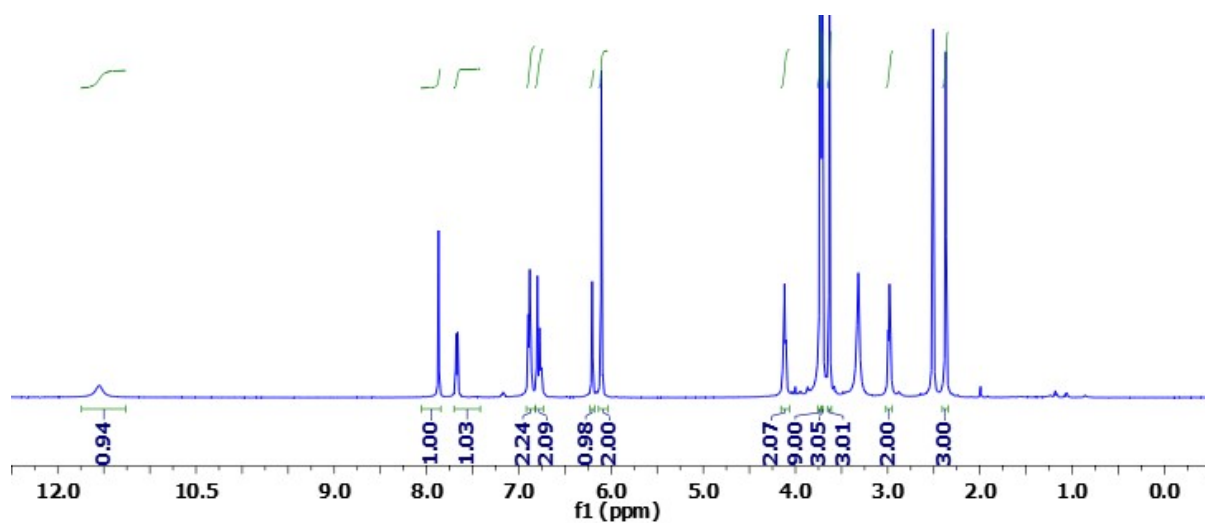
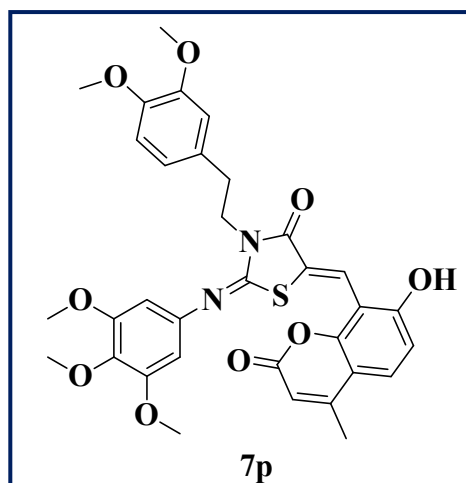
Compound (7n): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



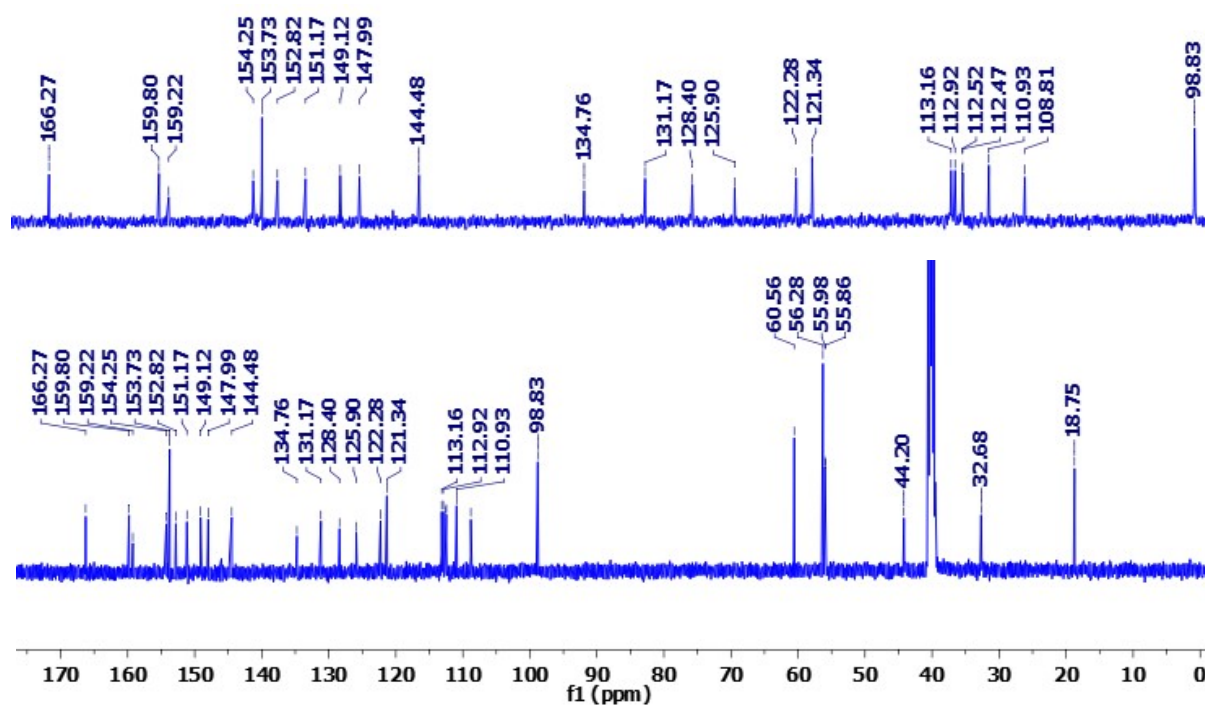
Compound (**7o**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



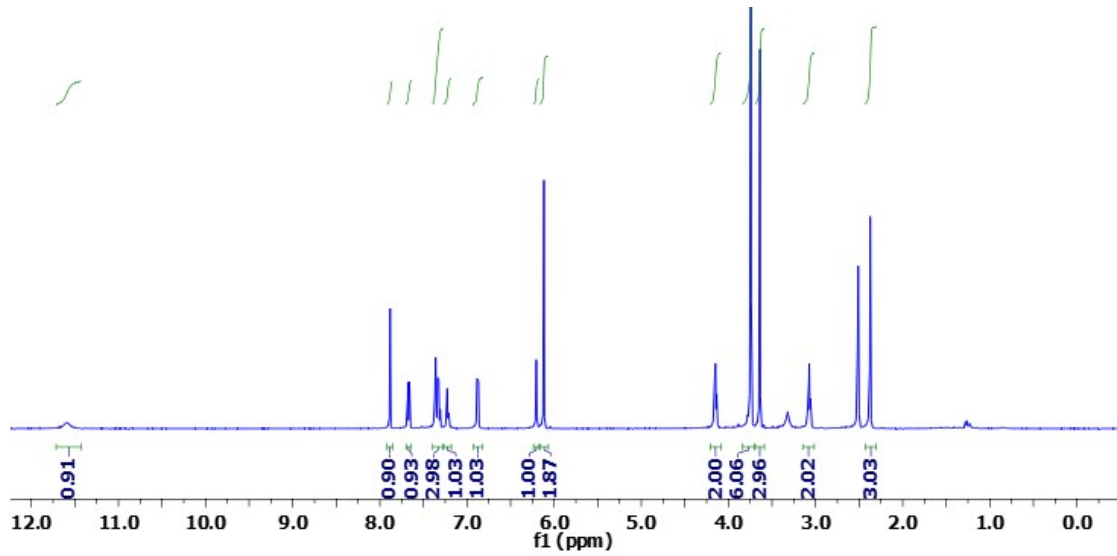
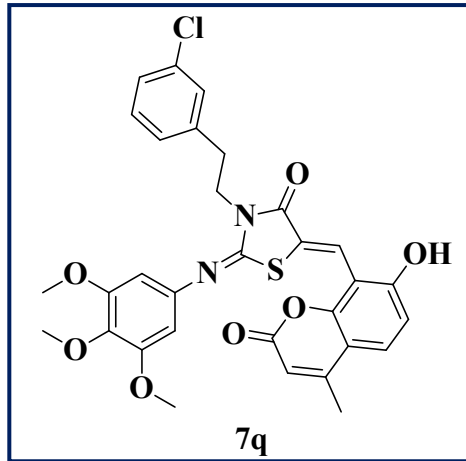
Compound (**7o**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



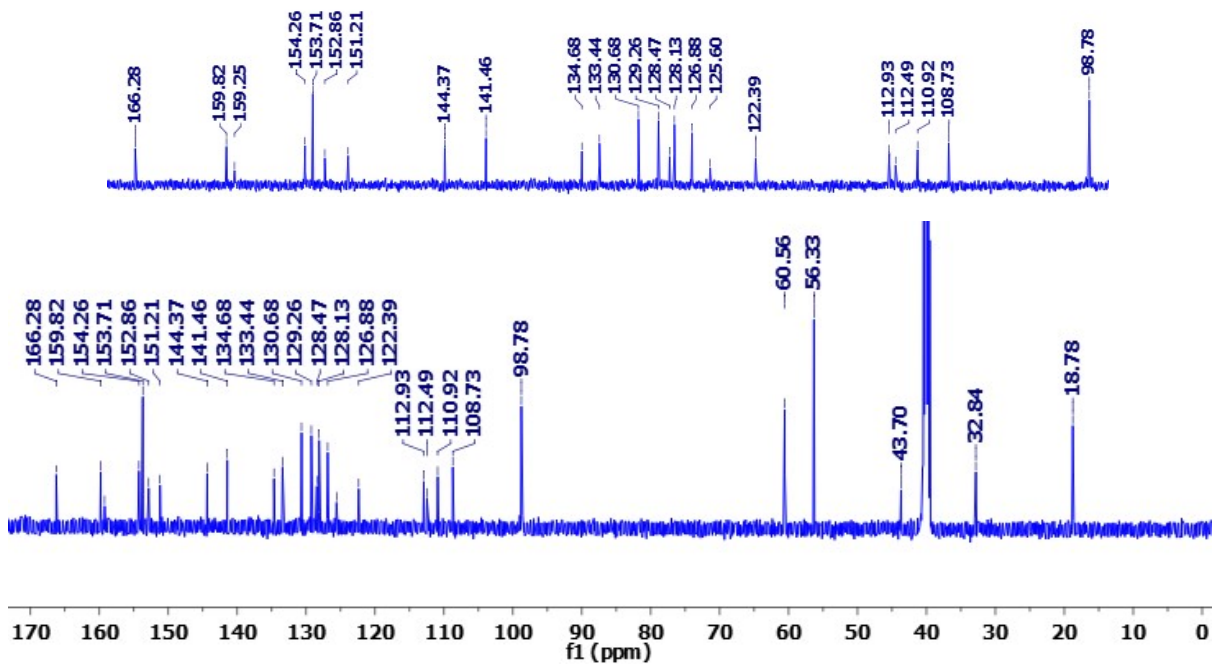
Compound (**7p**): ^1H NMR (500 MHz, $\text{DMSO-}d_6$)



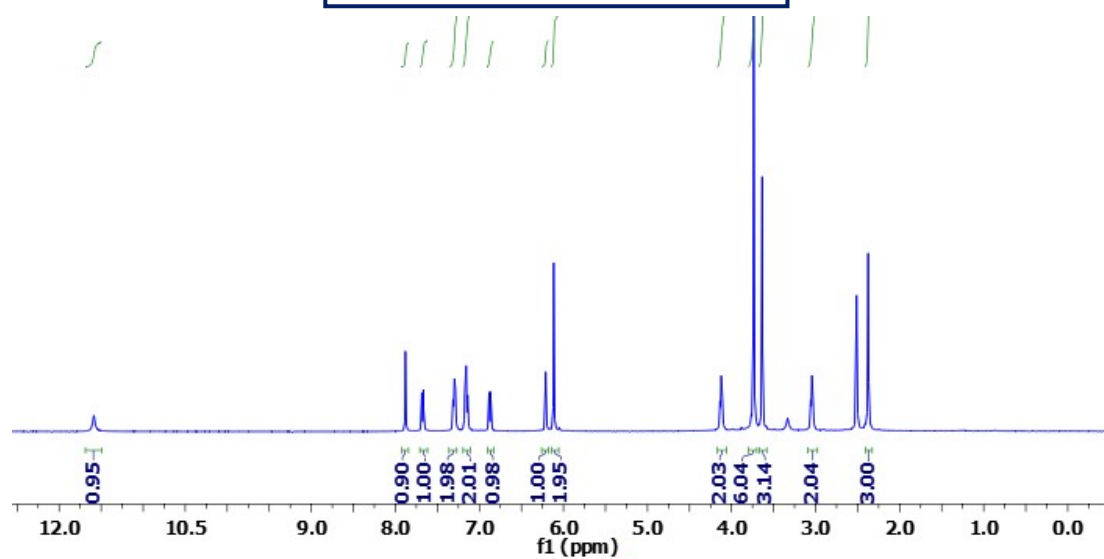
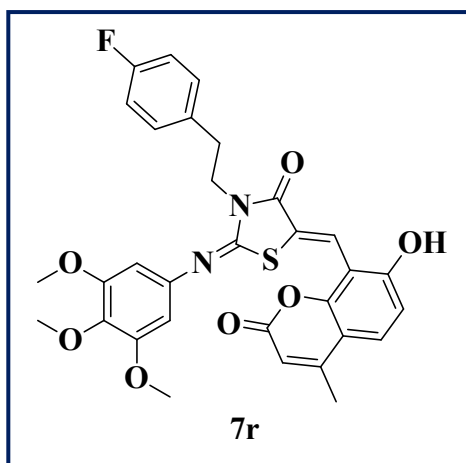
Compound (**7p**): ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$)



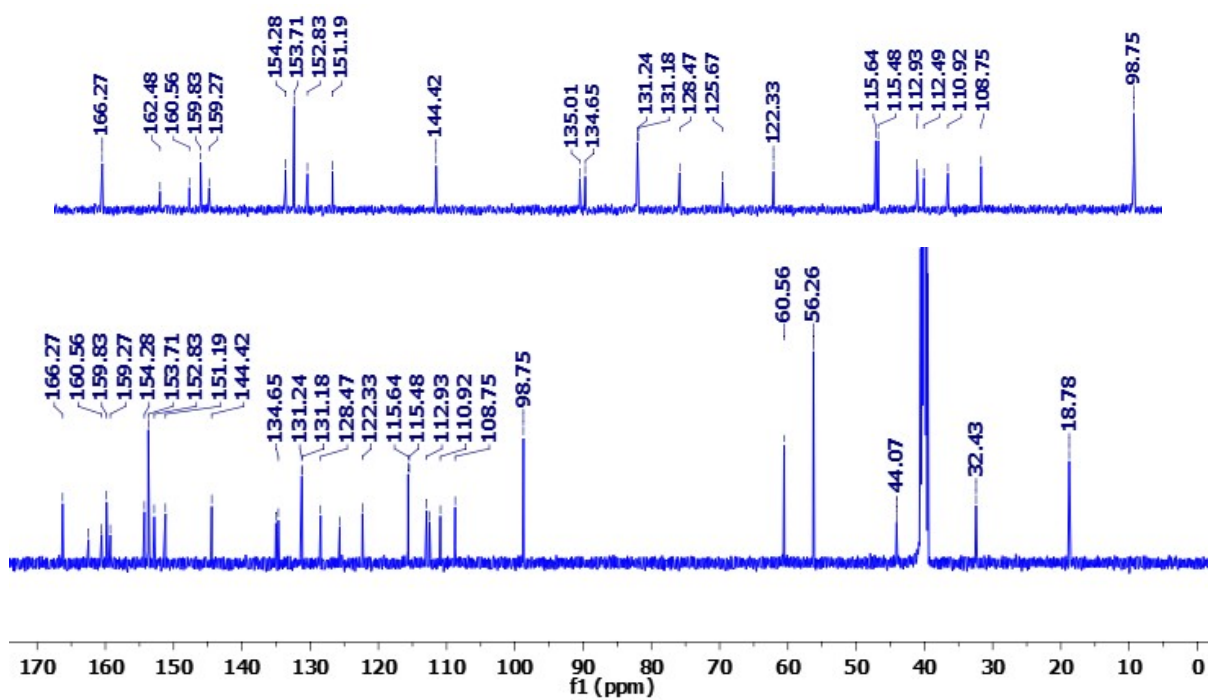
Compound (7q): ¹H NMR (500 MHz, DMSO-*d*₆)



Compound (7q): ¹³C NMR (125 MHz, DMSO-*d*₆)

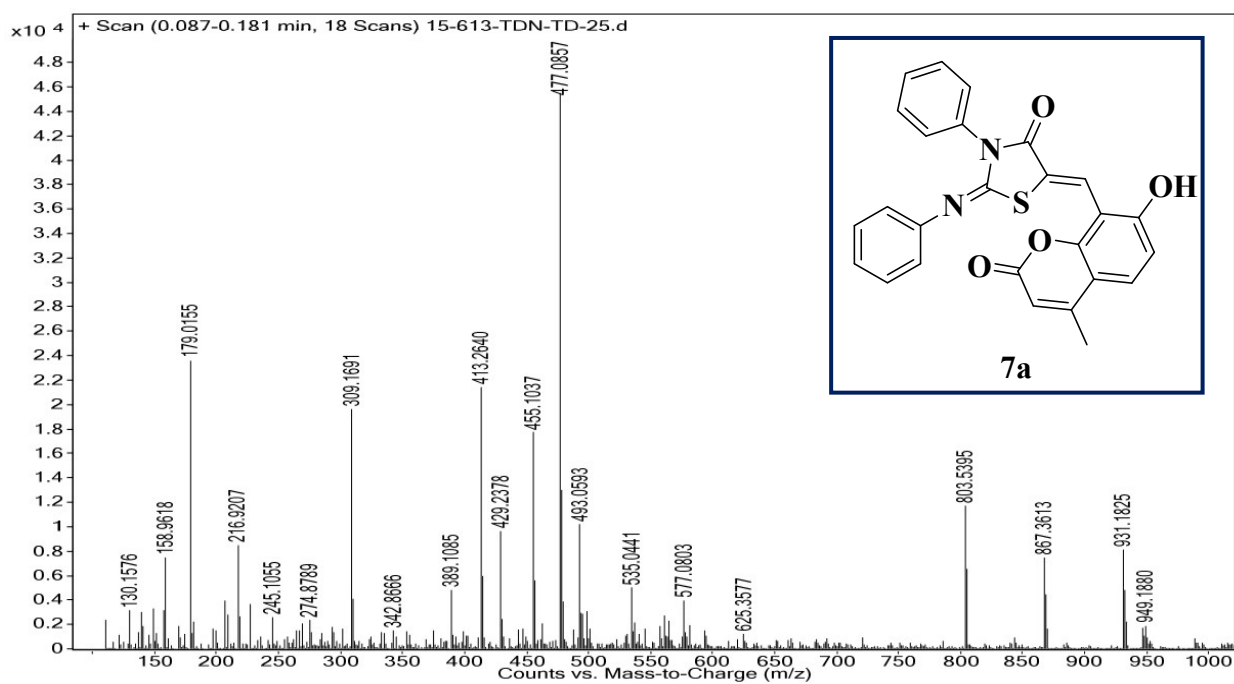


Compound (7r): ¹H NMR (500 MHz, DMSO-*d*₆)

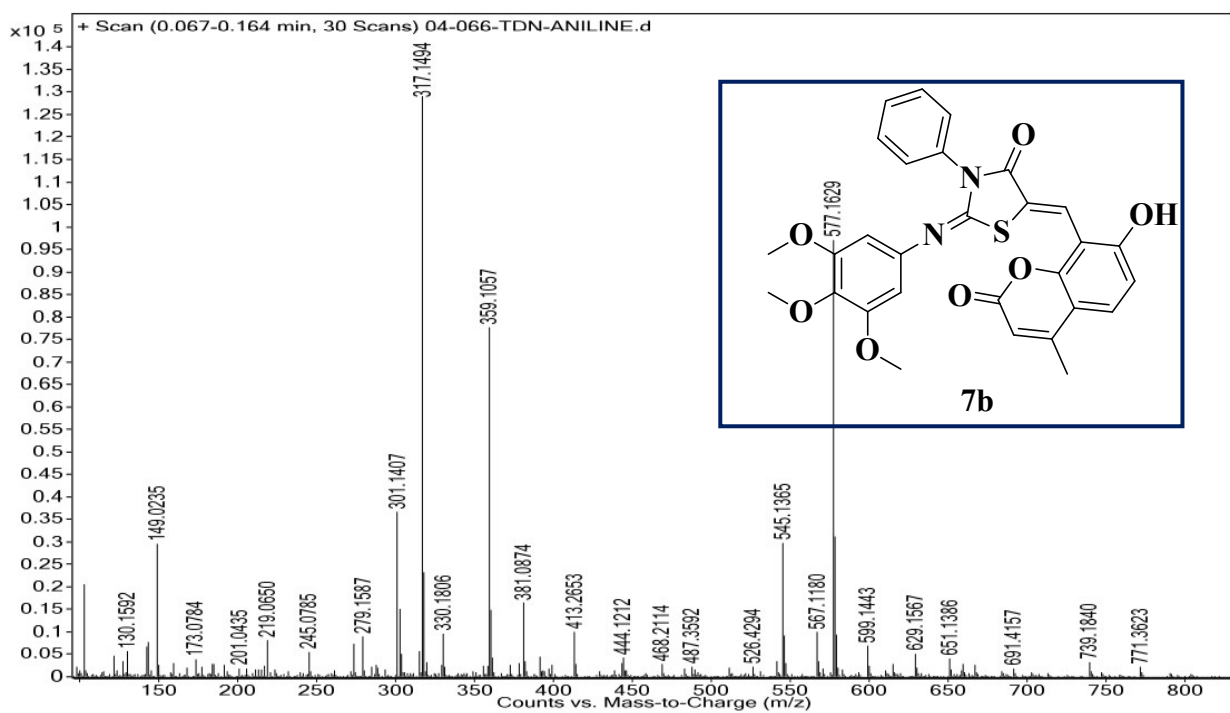


Compound (7r): ¹³C NMR (125 MHz, DMSO-*d*₆)

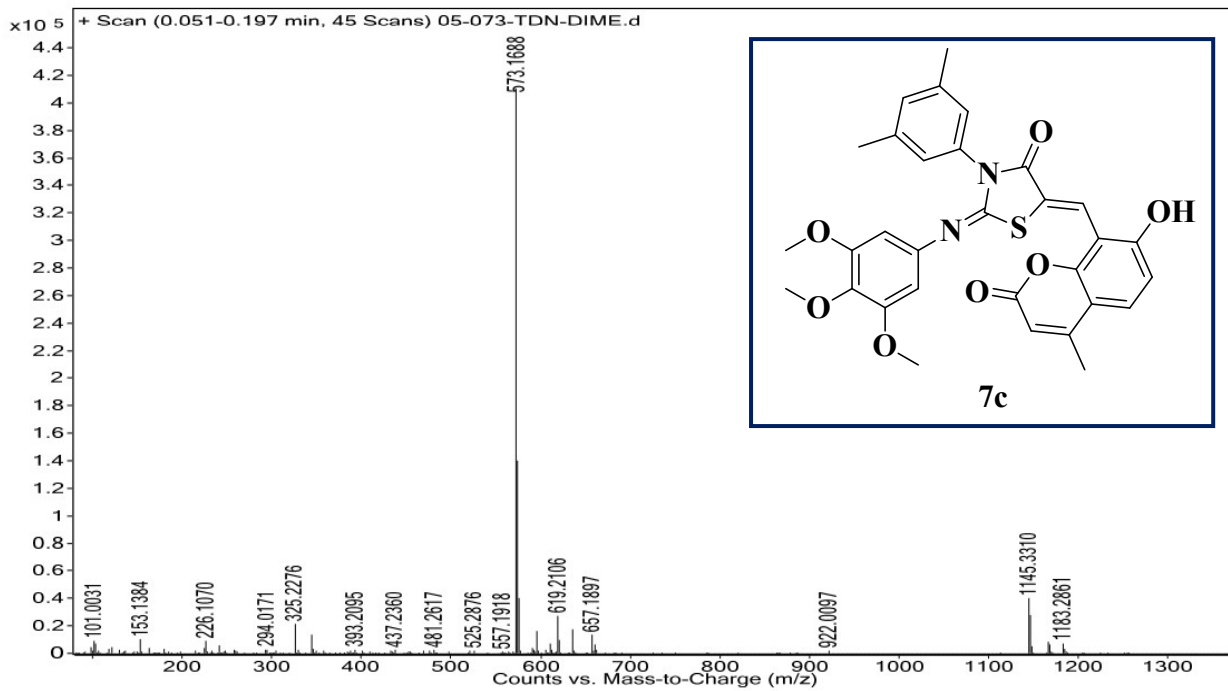
Copies of Mass spectra



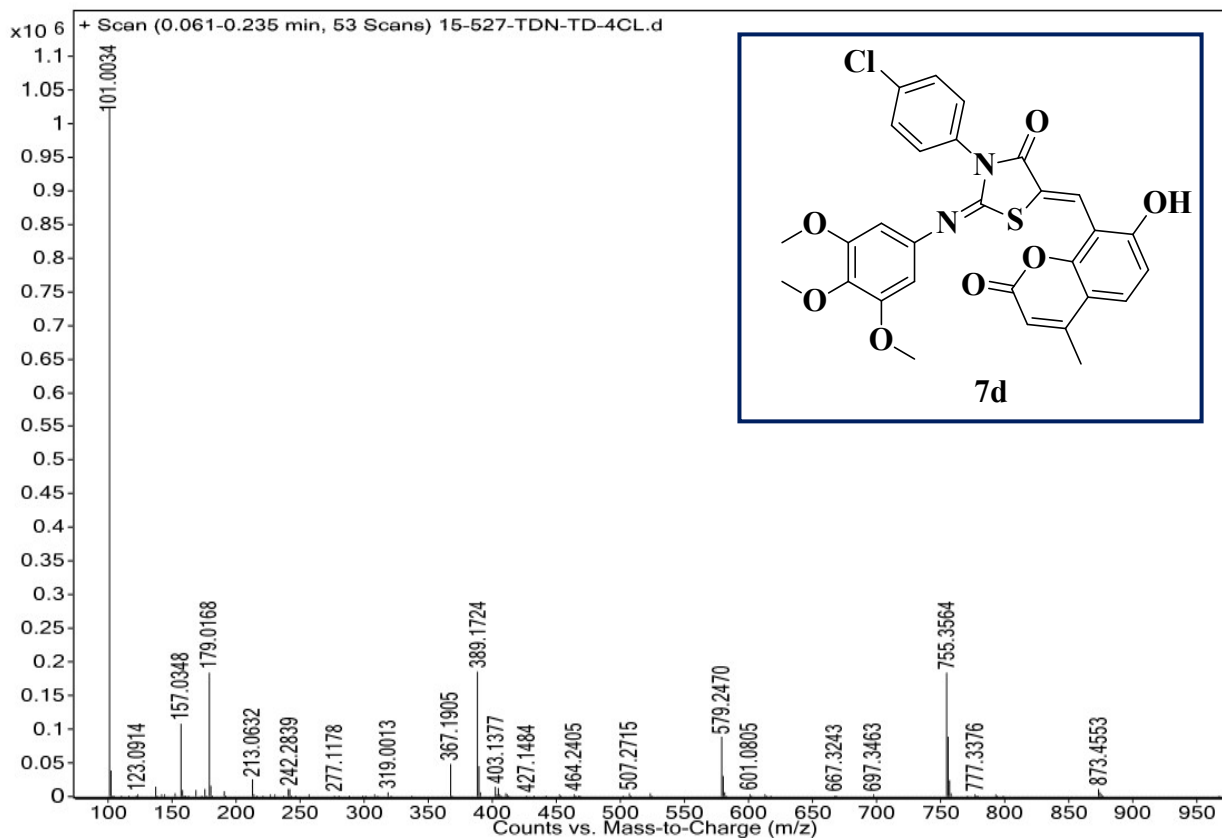
Compound (7a)



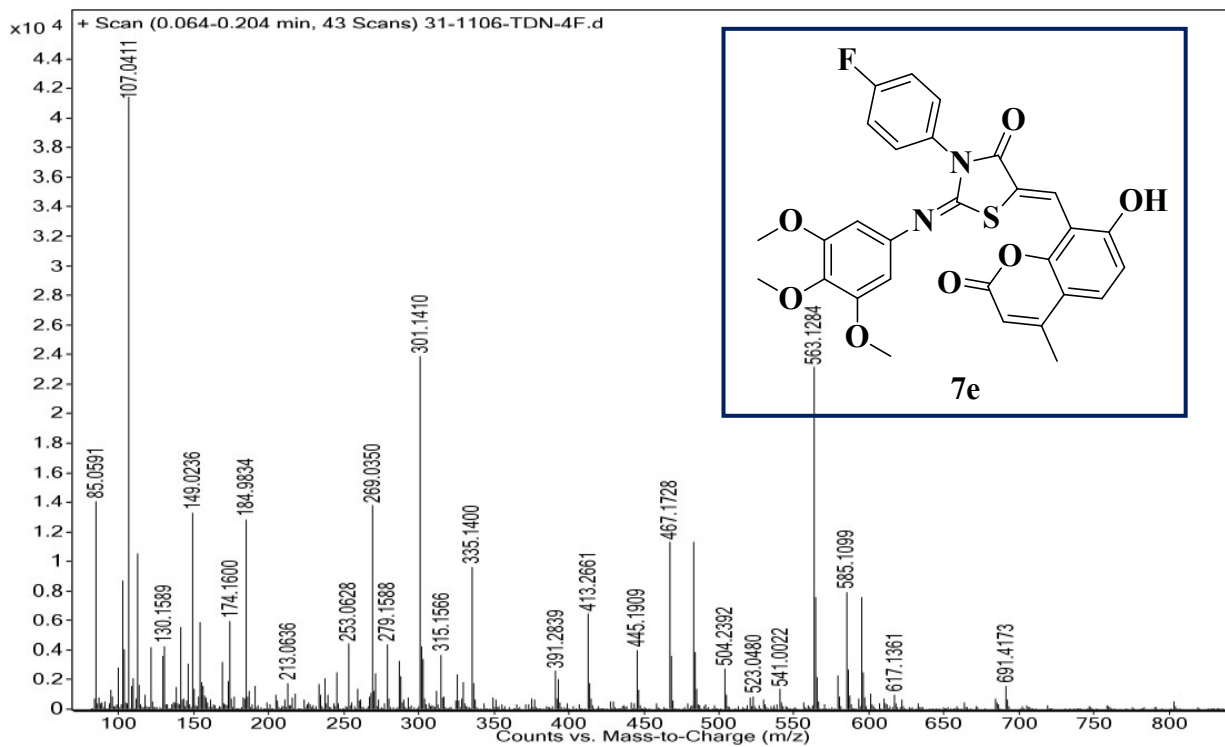
Compound (7b)



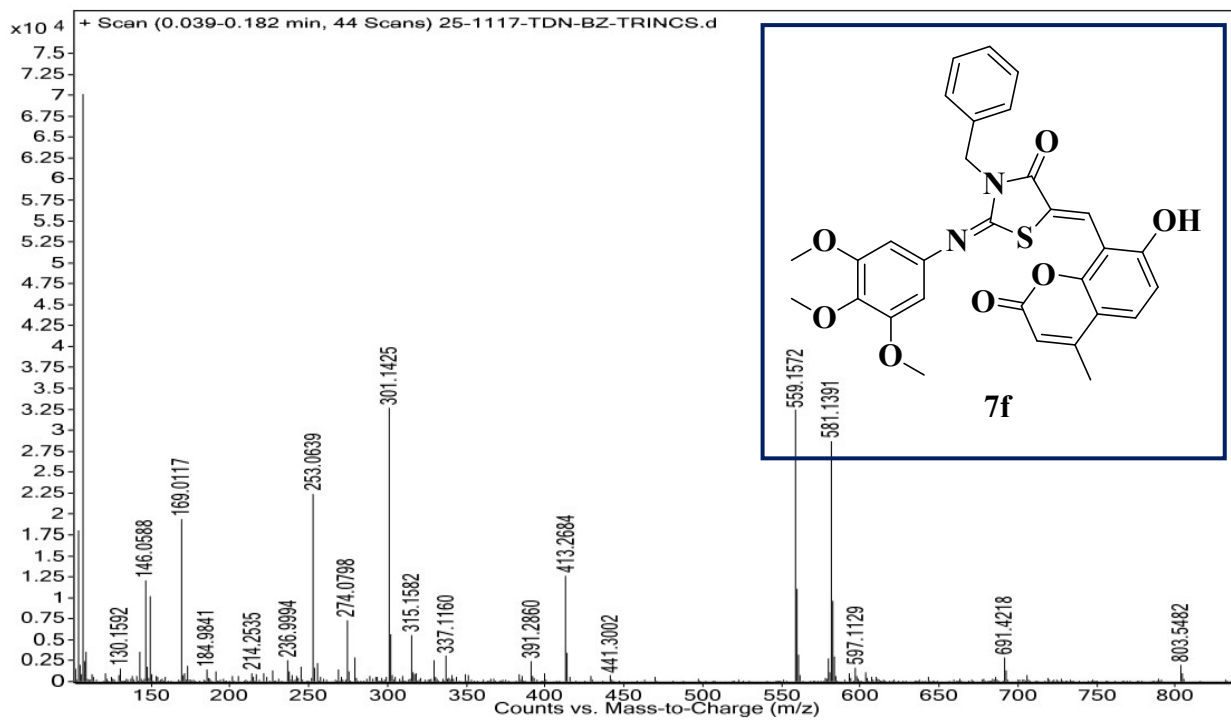
Compound (7c)



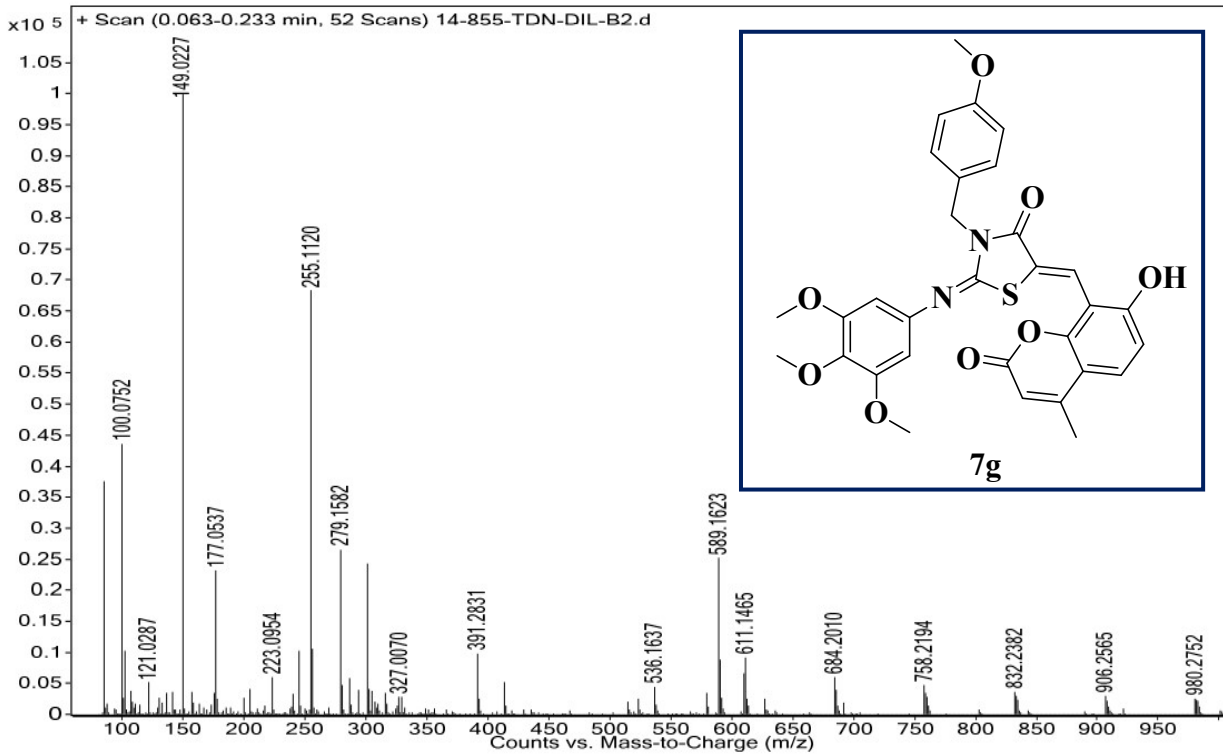
Compound (7d)



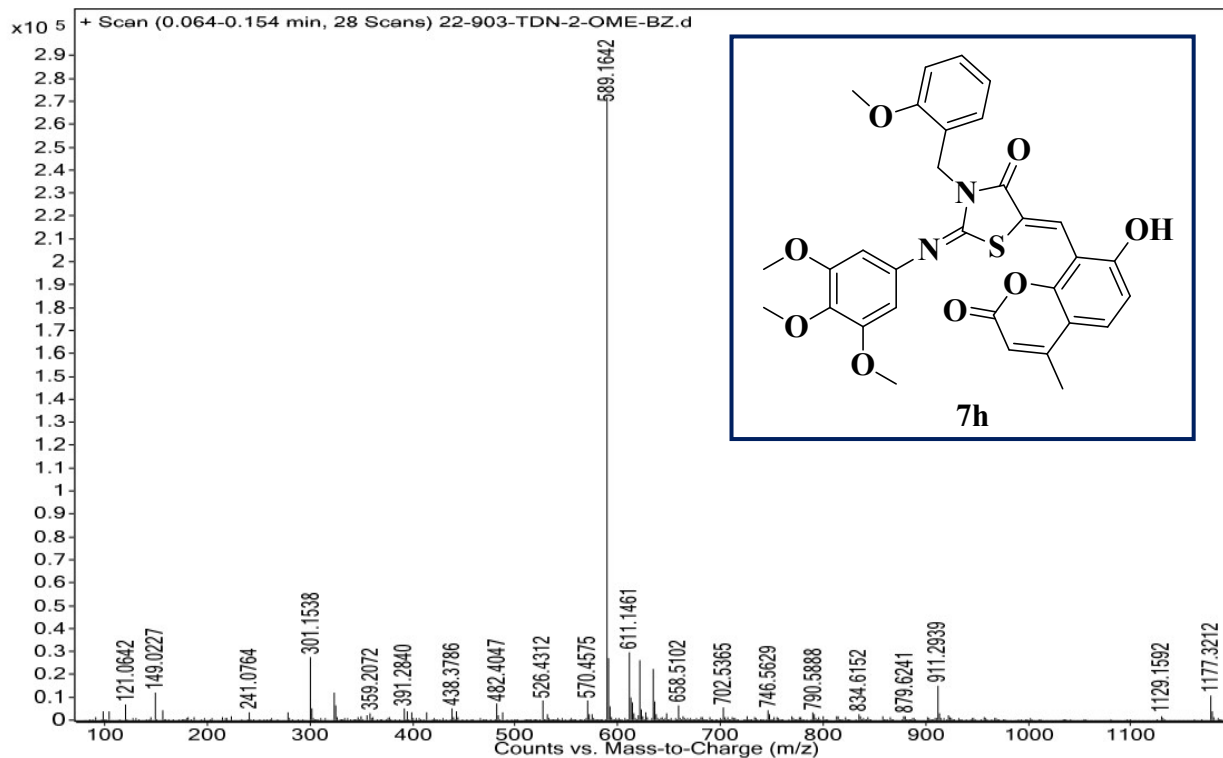
Compound (7e)



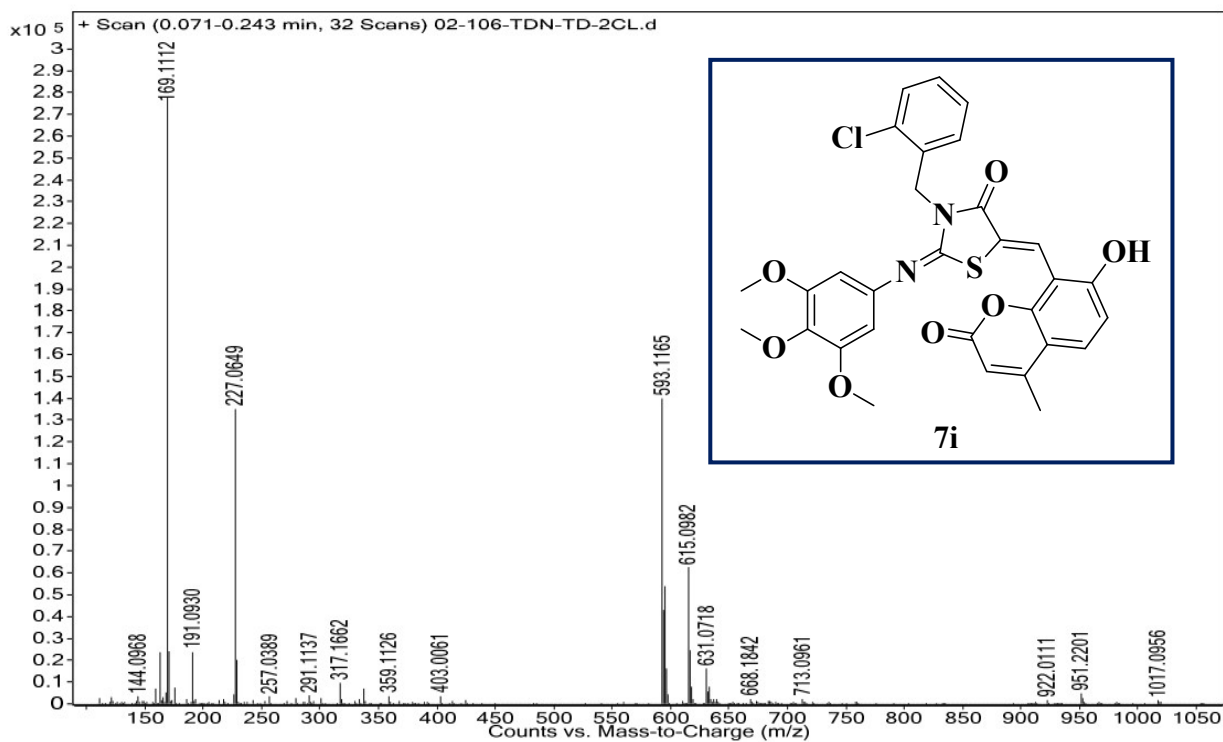
Compound (7f)



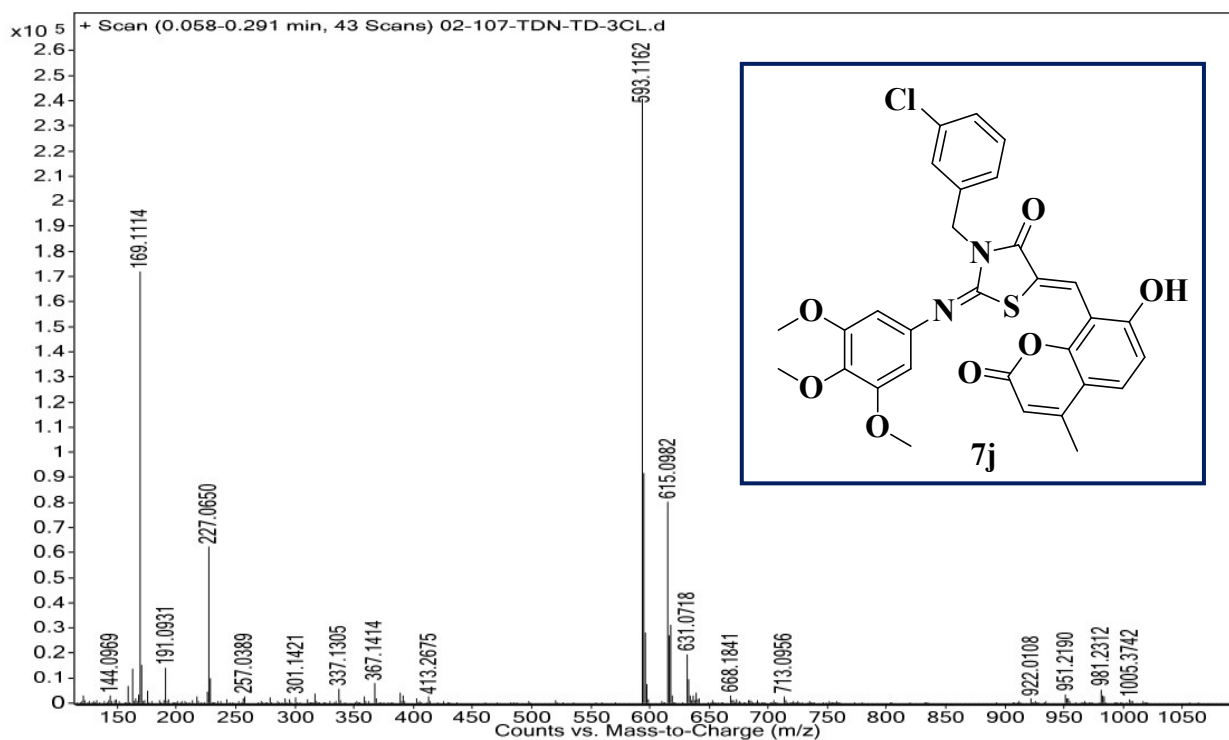
Compound (7g)



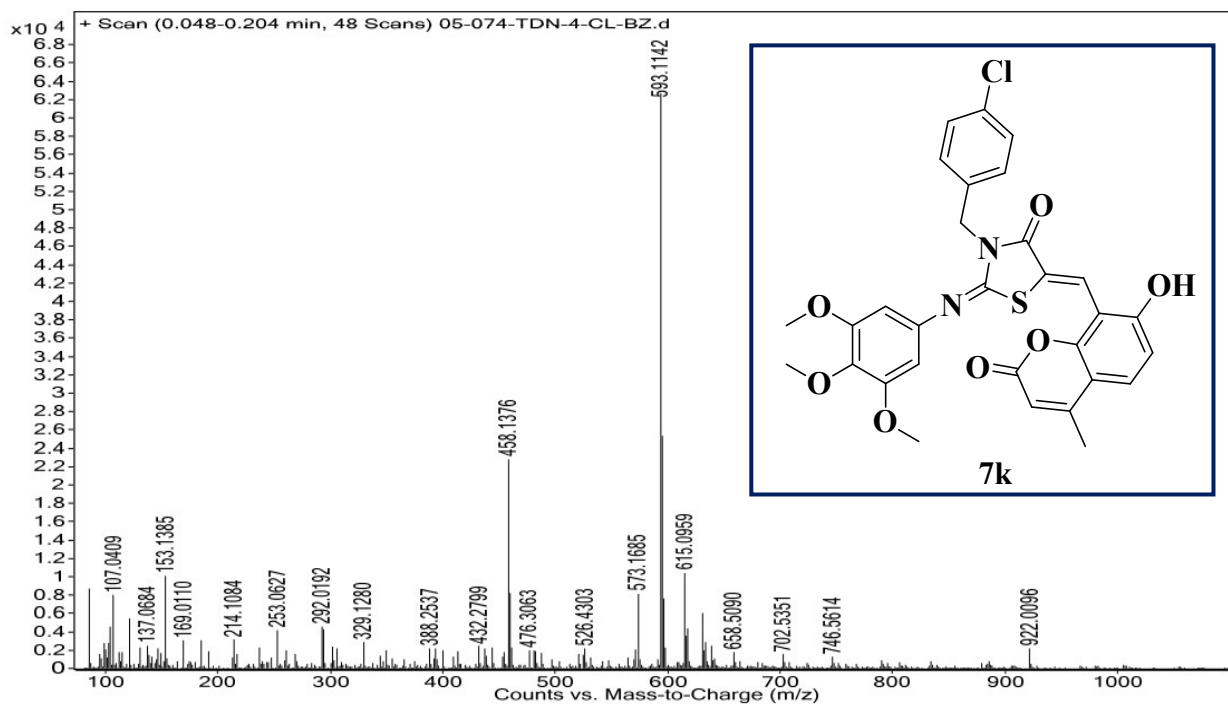
Compound (7h)



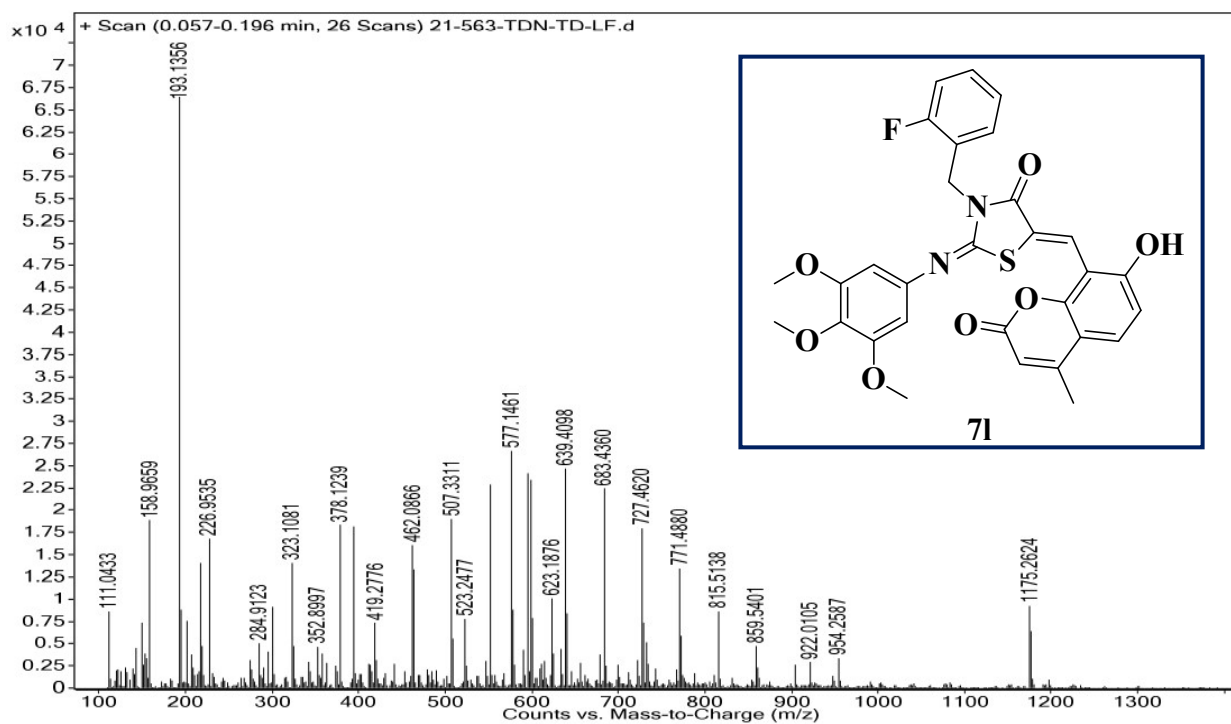
Compound (7i)



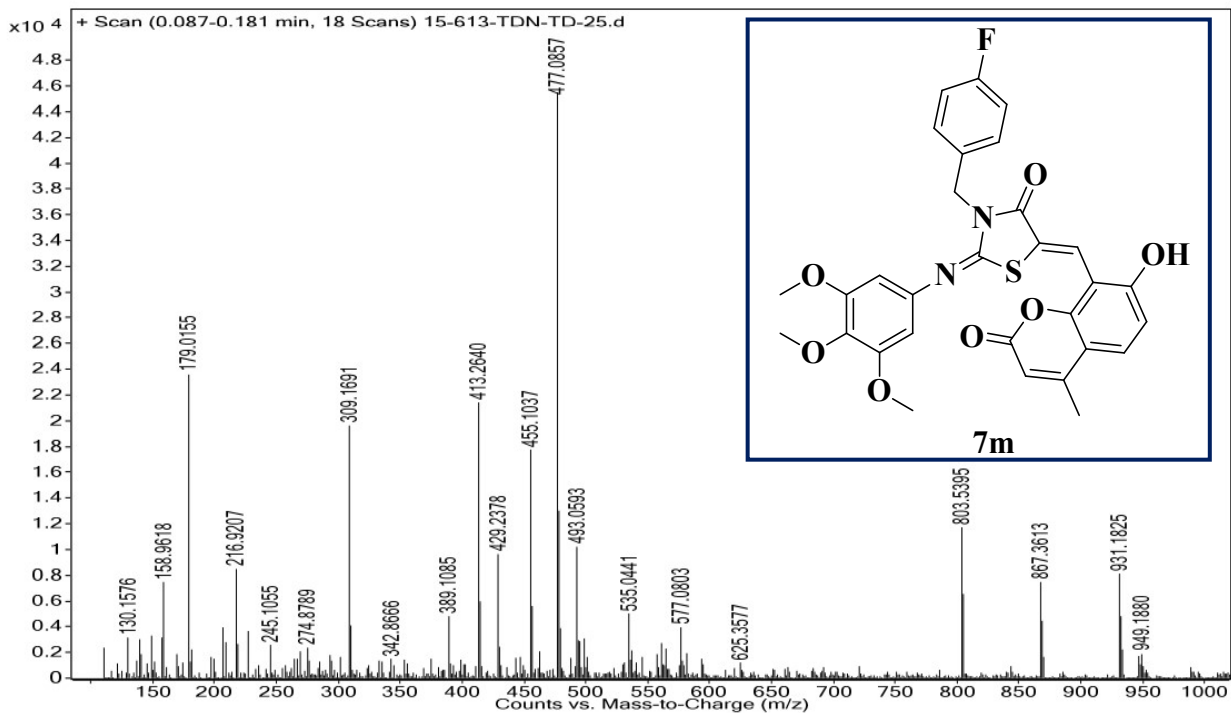
Compound (7j)



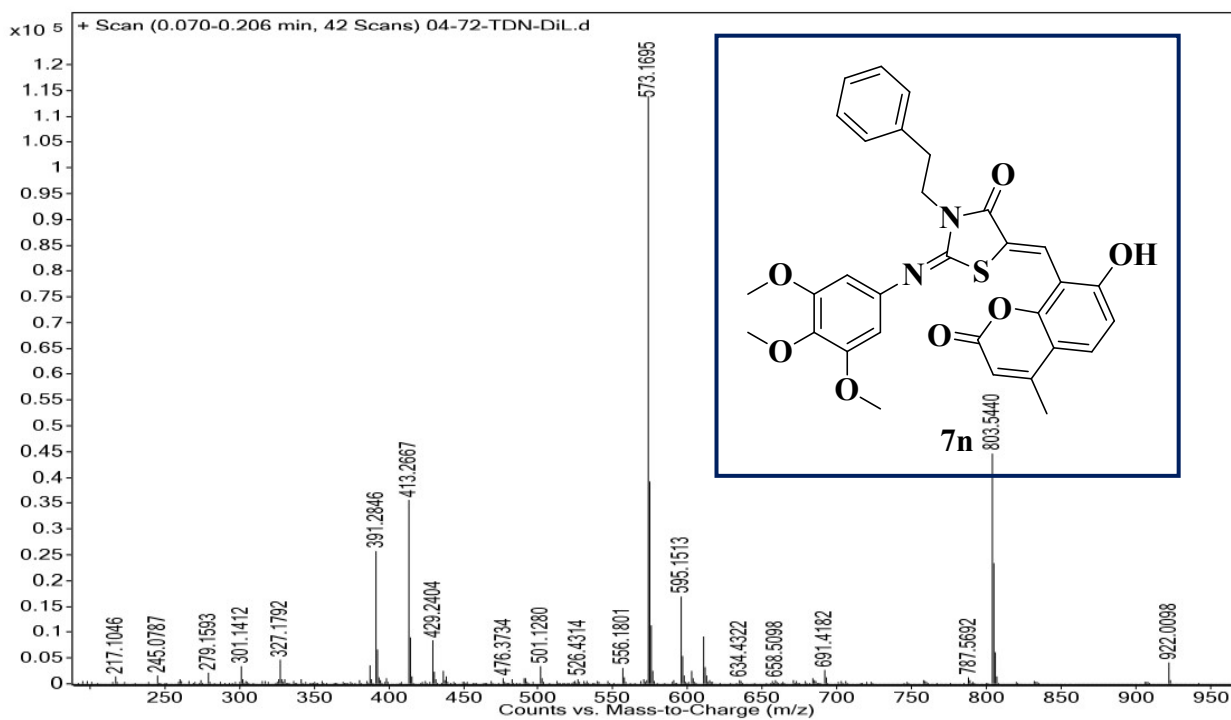
Compound (7k)



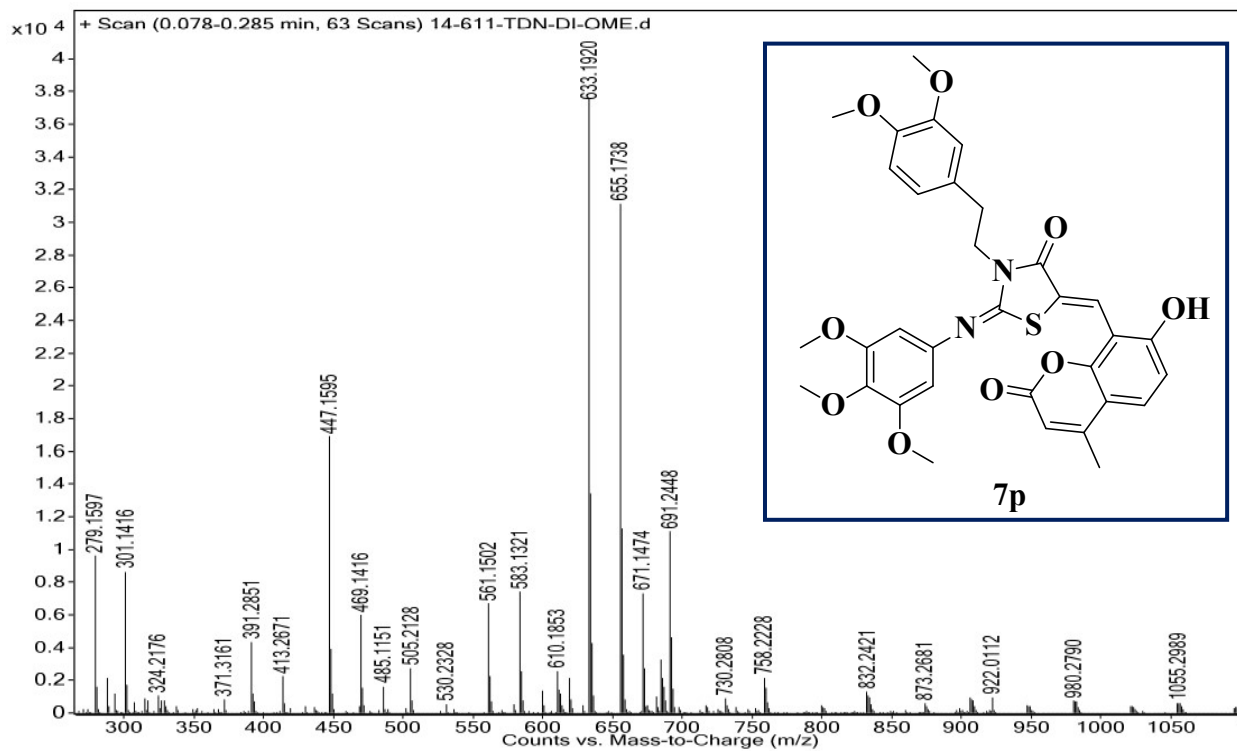
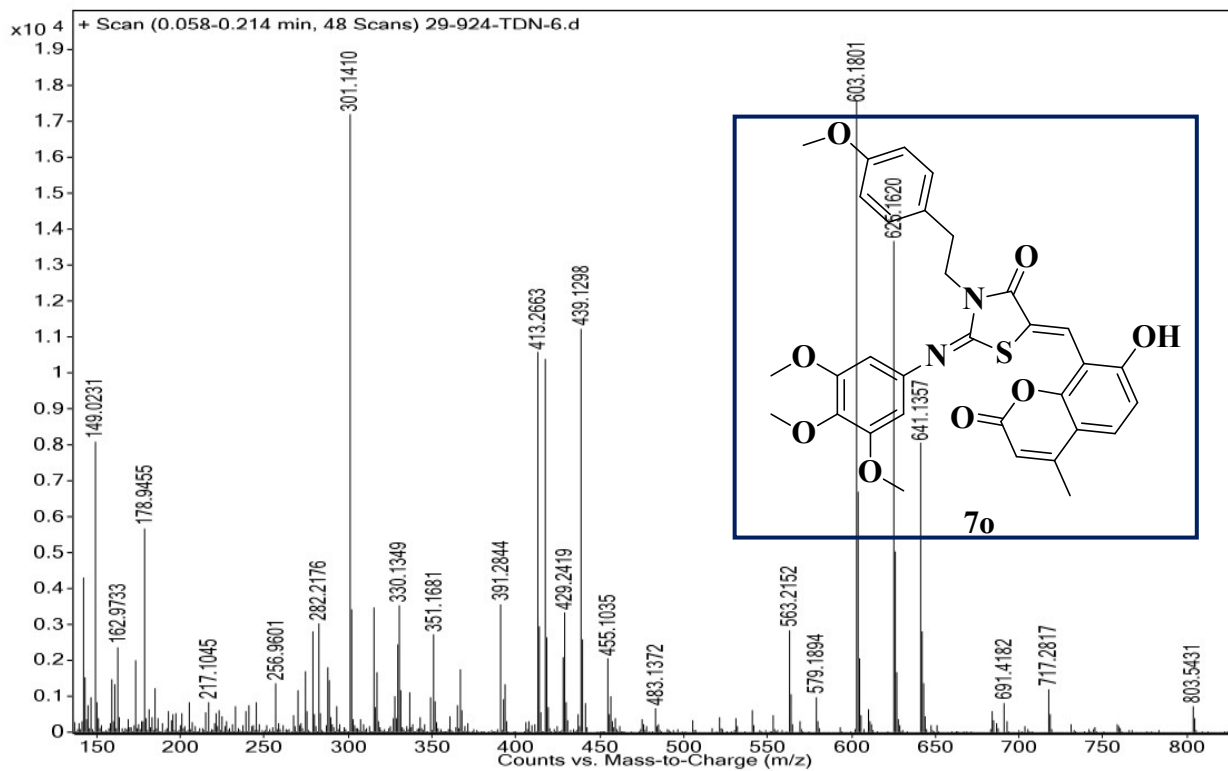
Compound (7l)

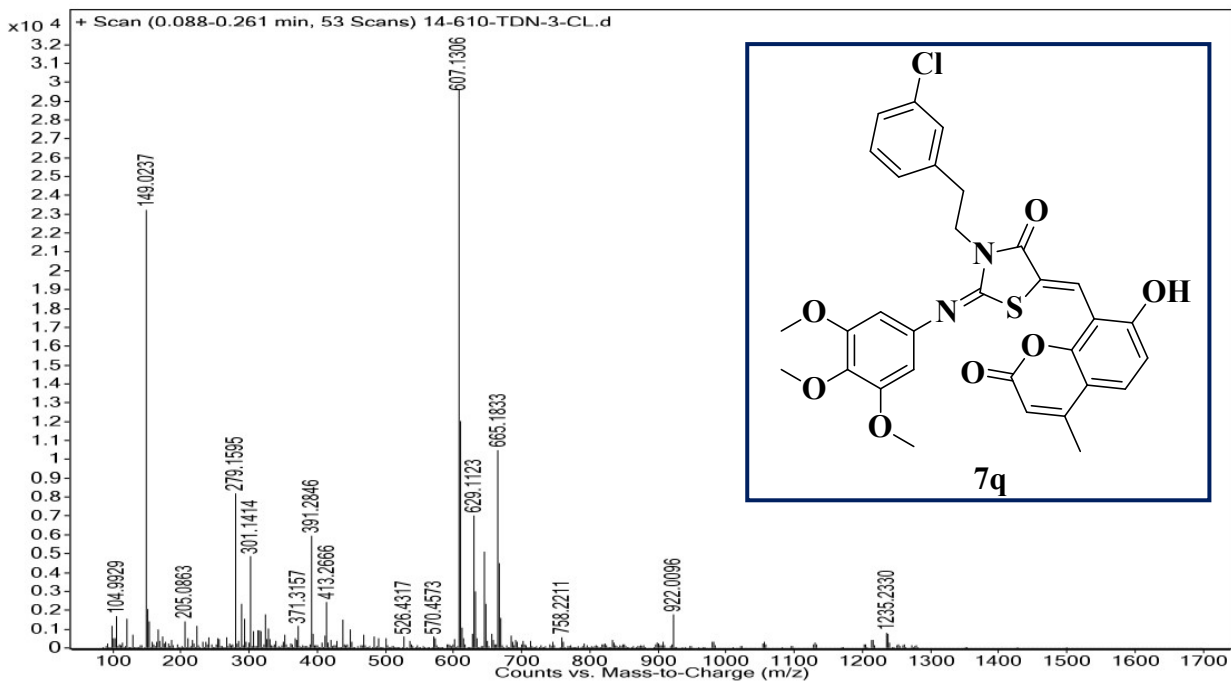


Compound (7m)

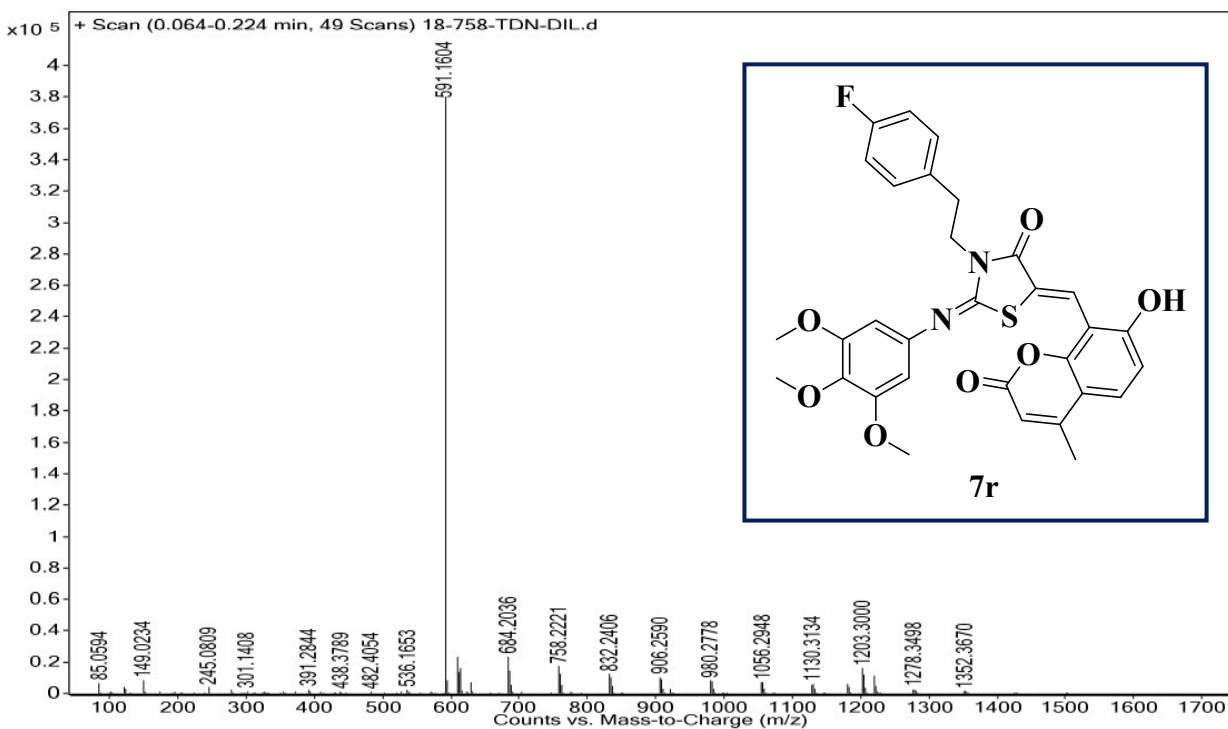


Compound (7n)



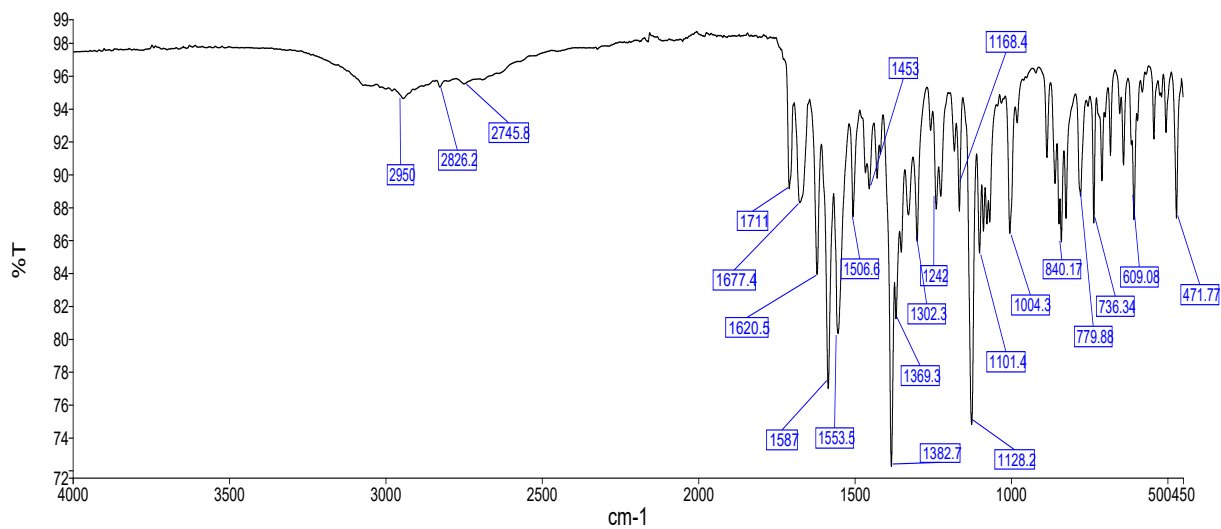
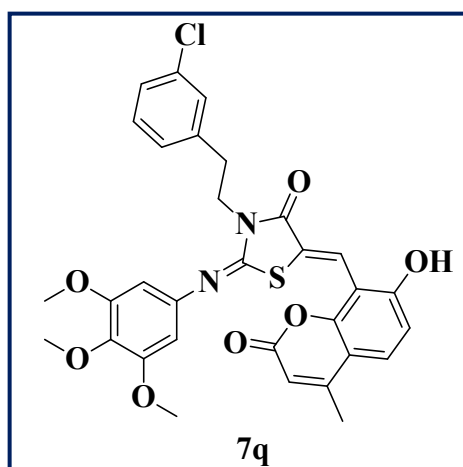


Compound (7q)



Compound (7r)

IR spectra of compound 7q



Compound (7q)

FT-IR (cm⁻¹): 2950, 2826, 2745, 1711, 1677, 1620, 1587, 1553, 1382, 1302, 1242, 1128, 1004, 840, 779, 736, 609, 471;

HPLC data of compound 7q

To check the purity of the most active compound (**7q**), HPLC analysis was performed and the results indicated >98% of purity for **7q**.

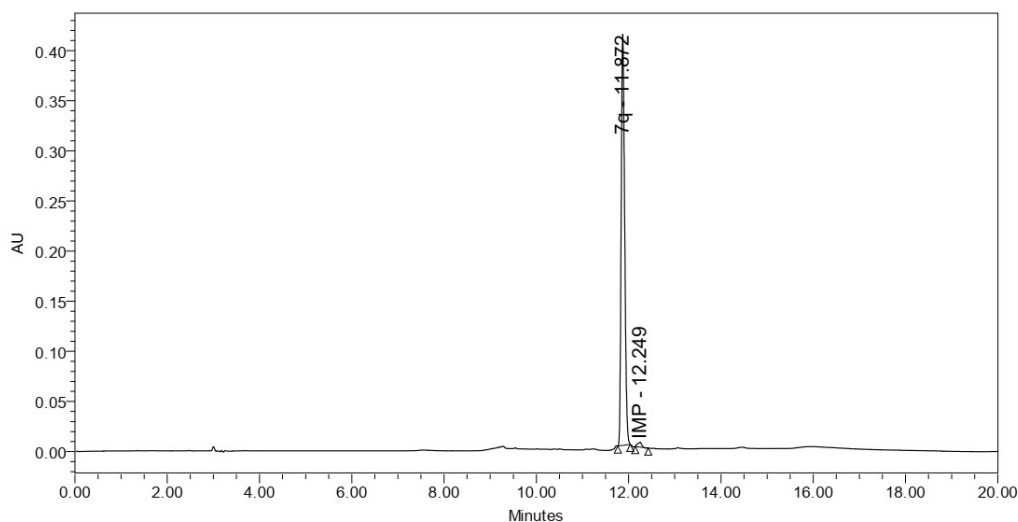
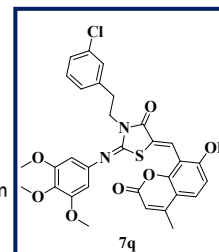


NIPER

NIPER HYDERABAD

Sample Name: std mc
Sample Type: Unknown
Vial: 25
Injection #: 1
Injection Volume: 10.00 ul
Run Time: 20.0 Minutes
Date Acquired: 8/10/2021 8:33:10 PMIST
Date Processed: 8/12/2021 6:48:03 PMIST

Acquired By: System
Sample Set Name: nagesh mc
Acq. Method Set: nagesh mc
Processing Method: MC02
Channel Name: 250.0nm
Proc. Chnl. Descr.: PDA 250.0 nm



Peak Name	RT	Area	% Area	Height
1 7q	11.872	2152898	98.62	410211
2 IMP	12.249	30063	1.38	4821

Reported by User: System
Report Method: NIPER
Report Method ID: 2721
Page: 1 of 1

Project Name: BhoopendraNAGESH
Date Printed: 8/12/2021
6:58:44 PM Asia/Calcutta

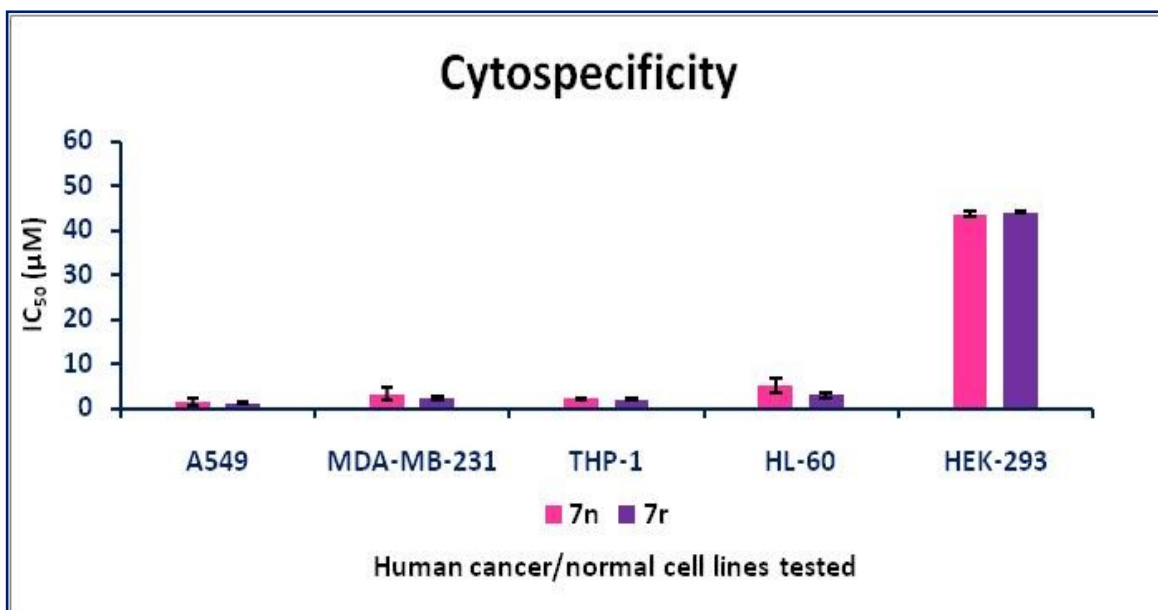


Figure S1. Cytospecificity comparison of compounds **7n** and **7r** towards human cancer cell lines tested in comparison to normal human embryonic kidney cells.

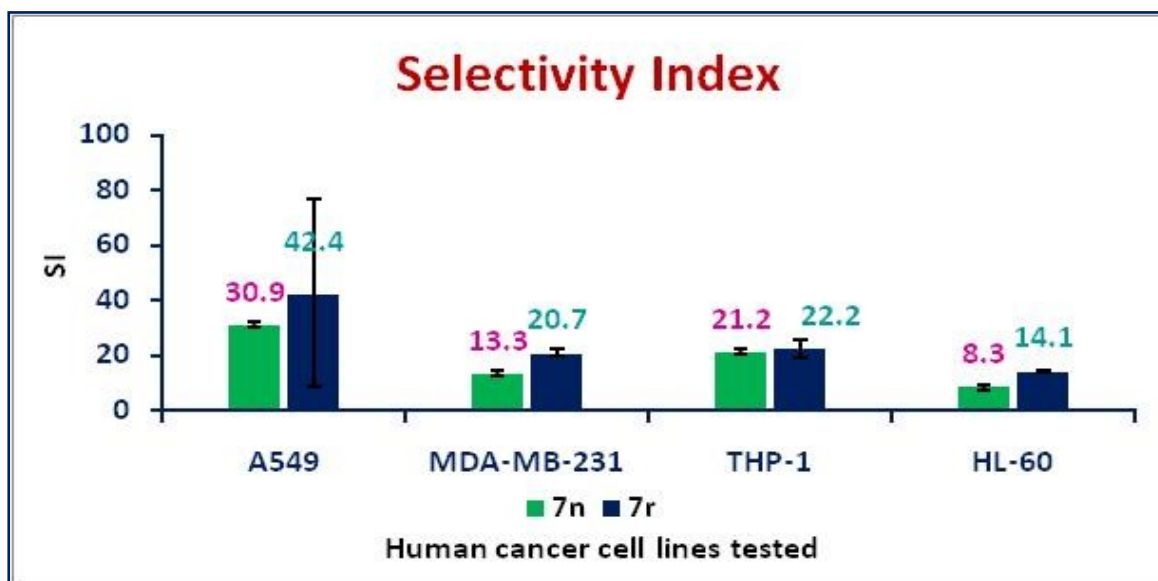


Figure S2. Selectivity Index (SI) comparison of compounds **7n** and **7r** and the order of selectivity is A549 > THP-1 > MDA-MB-231 > HL-60.

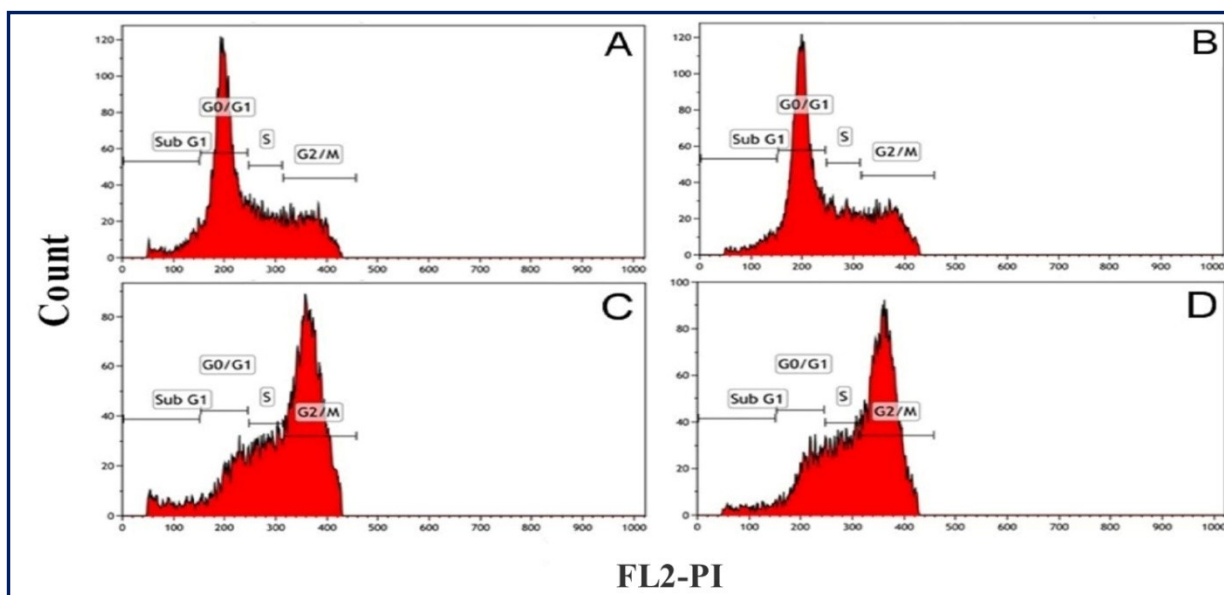


Figure S3. Flow cytometric analysis of cell cycle distribution. Dot plots obtained on treatment of HEK-293 and A549 cells with compound **7q**. Images **A** and **B** depicts the control HEK-293 and A549 cells respectively. Images **C** and **D** represents the **7q** treated HEK-293 and A549 cells respectively.