

Supporting Information for:-

Discovery of monocarbonyl curcumin hybrids as a novel class of human DNA ligase I inhibitors: *In silico* design, synthesis and biology[#]

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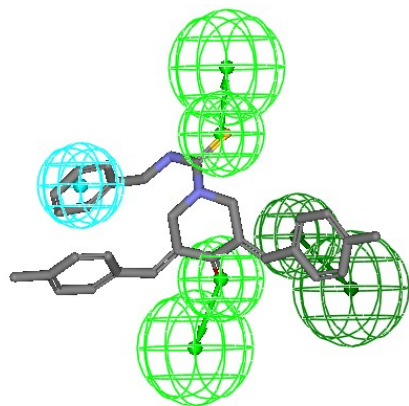
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[§]Both authors contributed equally.

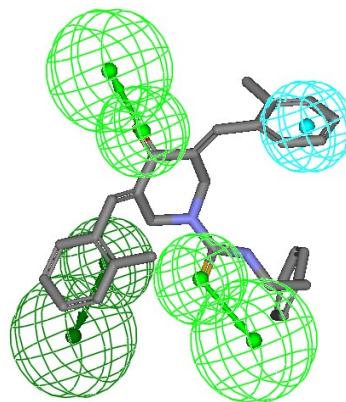
TABLE OF CONTENTS

1. Figure S1	S2
2. Table S1&Table S2	S3-S4
3. ¹H NMR spectral data (14-49) and ¹³C NMR spectral data (14-36, 38-49)	S5-S46
4. DEPT 135 spectra of compound 47	S47
5. HRMS spectra (14-28, 30-43, 45-49)	S48-S58
6. IC₅₀ calculation	S59

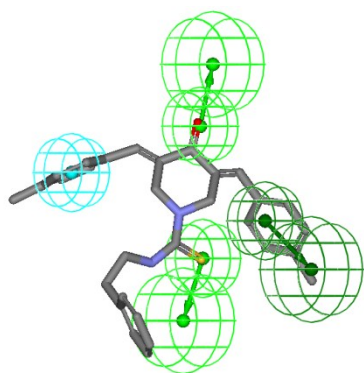
Figure S1. Ligand pharmacophore mapping of the top designed compounds on the pharmacophore model.



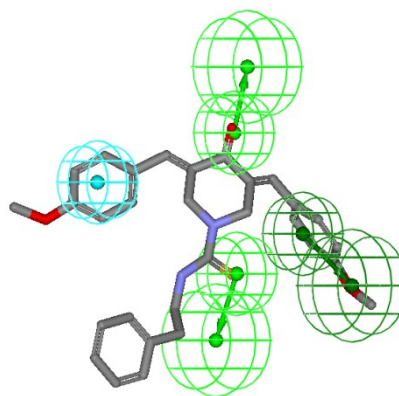
17



22



23



24

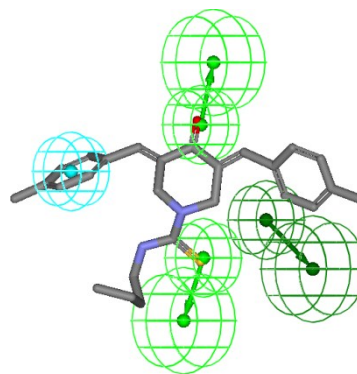
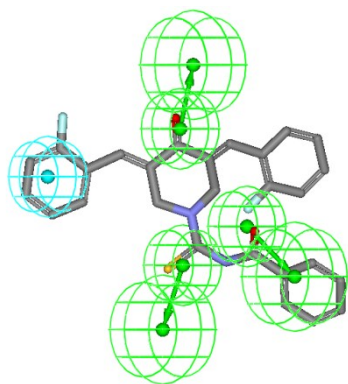


Table S1. The summaries of hypothesis run

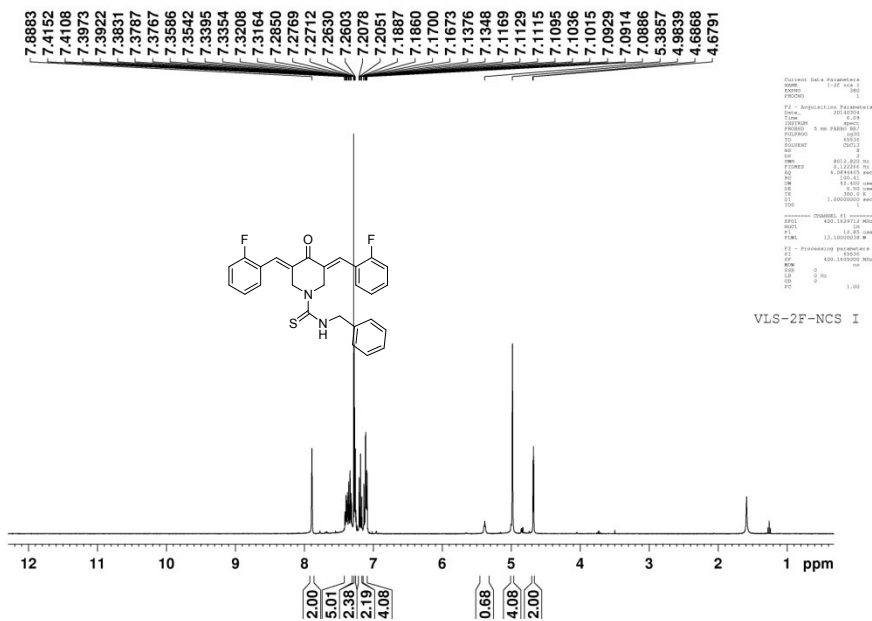
Features	Rank	Direct Hit	Partial Hit	Max Fit	Max. Fit
01	ZHHH	84.746	1111111111	0000000000	4
02	ZHHH	83.126	1111111111	0000000000	4
03	ZHHH	82.598	1111111111	0000000000	4
04	ZHHH	82.530	1111111111	0000000000	4
05	ZHHH	82.411	1111111111	0000000000	4
06	ZHHH	80.785	1111111111	0000000000	4
07	ZHHH	80.301	1111111111	0000000000	4
08	ZHHH	79.399	1111111111	0000000000	4
09	ZHHH	78.215	1111111111	0000000000	4
10	ZHHH	78.215	1111111111	0000000000	4

Direct hitmask indicates [1] or (0) not a training set molecule mapped every feature. Partial hit mask indicates whether [1] or (0) not a molecule mapped all but one feature. ^aZ; hydrophobic, A; hydrogen bond acceptor (HBA) and R; ring aromatic

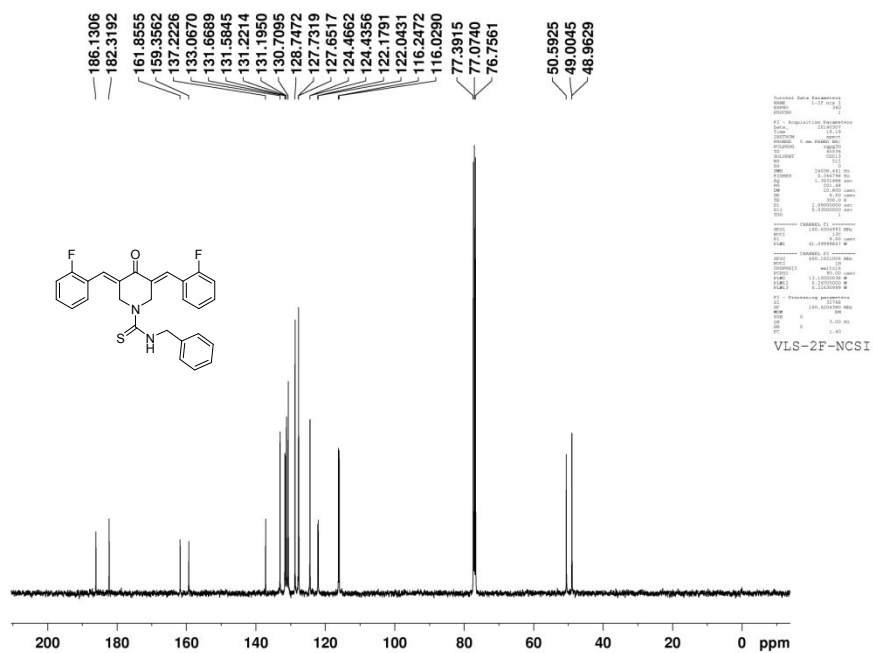
Table S2. The scoring functions from docking runs and fit values from generated pharmacophore model.

Ligand	MolDockScore	Rerank Score	FitValue
14	-131.536	-110.624	2.792
15	-148.516	-108.418	2.798
16	-137.323	-101.381	2.753
17	-148.269	-105.554	2.741
18	-147.602	-115.819	2.739
19	-156.207	-125.423	2.682
20	-145.67	-120.854	2.797
21	-144.586	-110.387	2.806
22	-148.069	-119.987	2.755
23	-165.362	-137.674	2.922
24	-149.463	-122.416	2.75
25	-154.501	-115.94	2.674

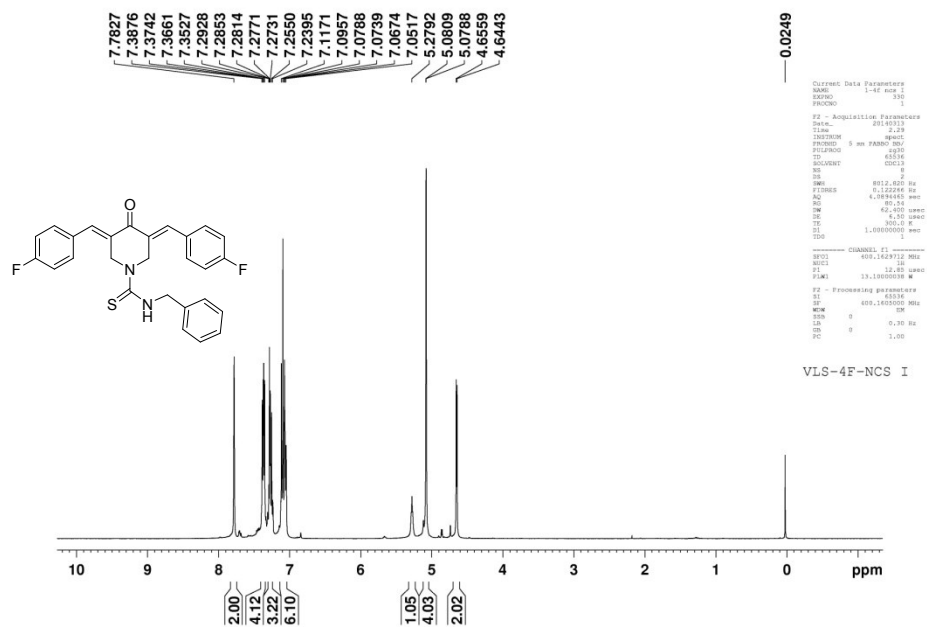
26	-144.309	-107.627	2.782
27	-137.104	-108.952	2.799
28	-137.589	-107.367	2.772
29	-139.567	-103.621	2.831
30	-146.031	-116.305	2.776
31	-148.960	-117.481	1.998
32	-145.045	-114.59	2.786
33	-137.574	-110.395	2.803
34	-143.556	-116.201	2.742
35	-137.815	-109.852	2.827
36	-160.53	-120.778	2.711
37	-161.024	-126.558	2.679
38	-127.897	-106.193	2.792
39	-128.885	-104.055	2.792
40	-137.145	-107.476	2.74
41	-135.849	-106.064	2.729
42	-140.872	-108.73	2.73
43	-159.141	-120.764	2.691
44	-145.608	-112.409	2
45	-135.752	-111.656	1.987
46	-139.066	-111.258	1.989
47	-137.595	-111.823	1.997
48	-165.078	-120.678	2.115
49	-155.153	-122.533	1.992



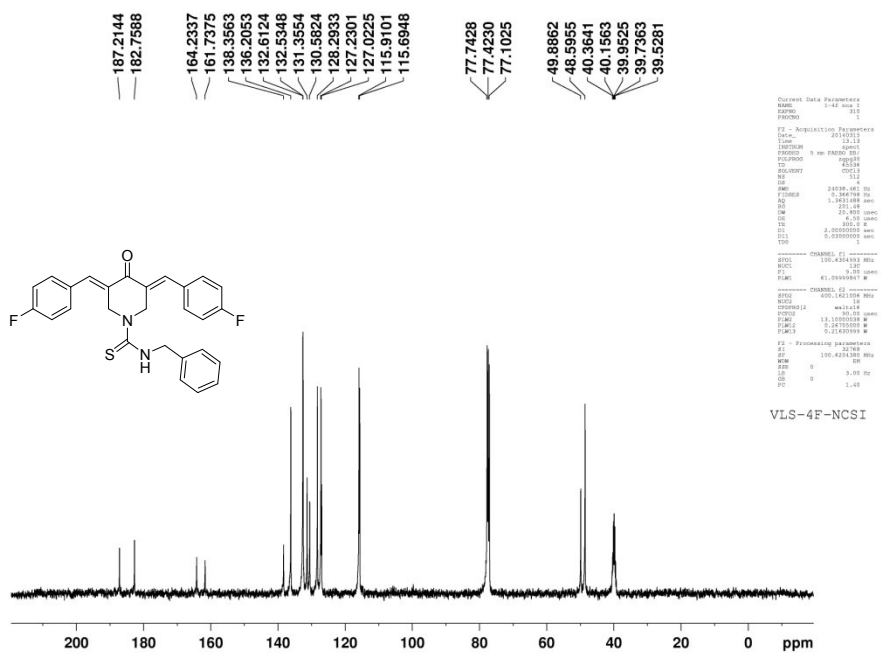
¹H NMR Spectra of compound **14**(400 MHz, CDCl₃)



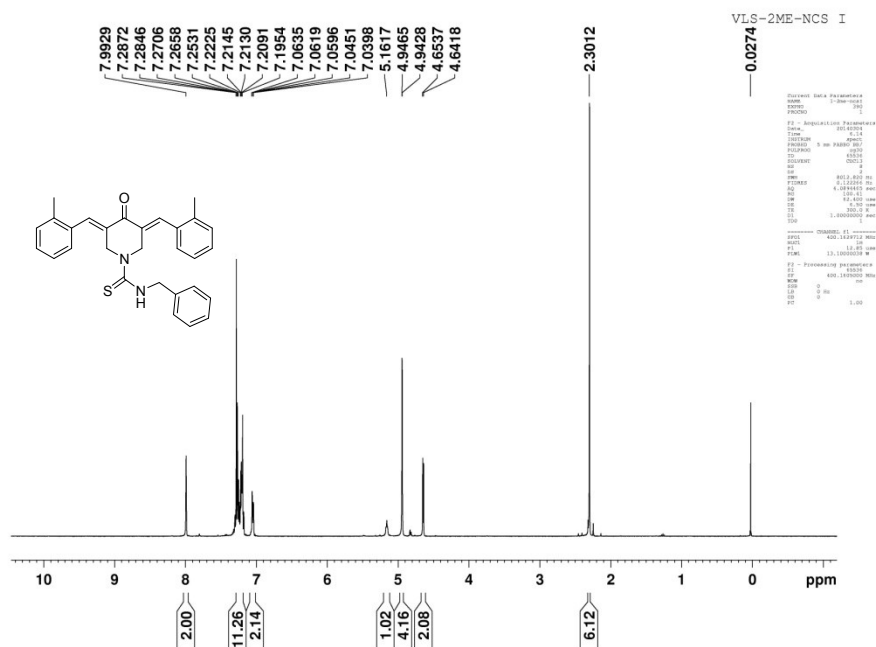
¹³C NMR Spectra of compound **14**(100 MHz, CDCl₃)



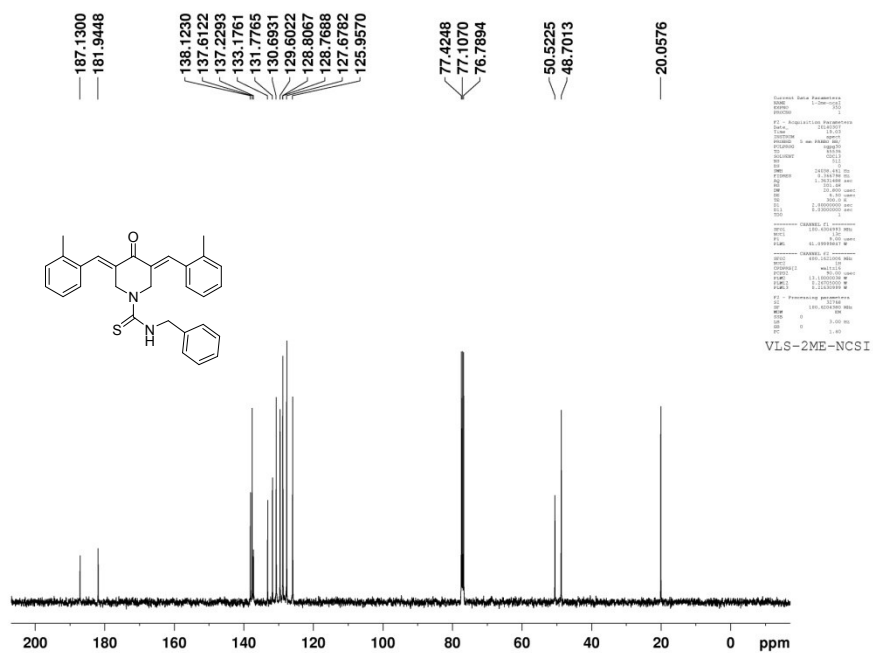
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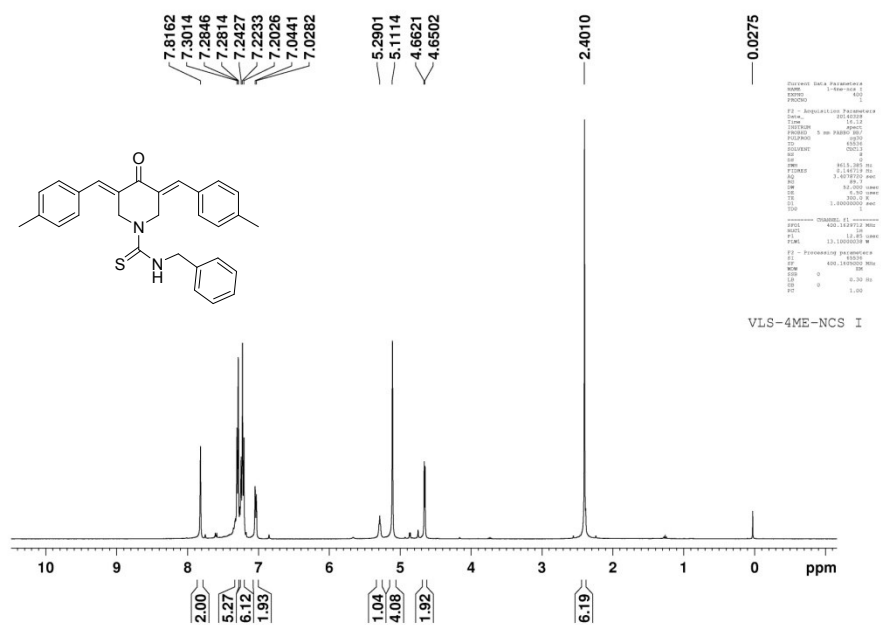
¹³C NMR Spectra of compound **15**(100 MHz, CDCl₃+DMSO-*d*₆)



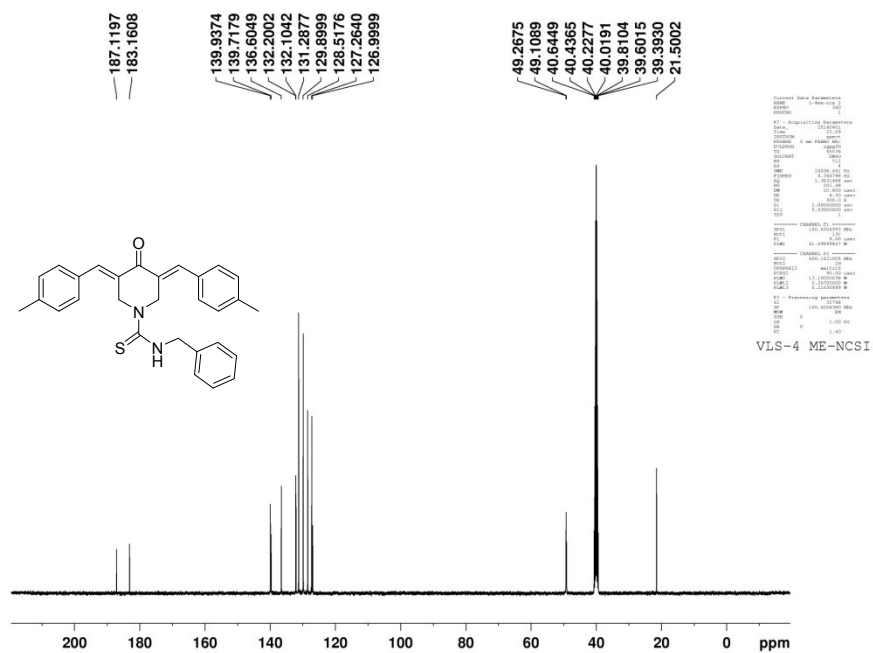
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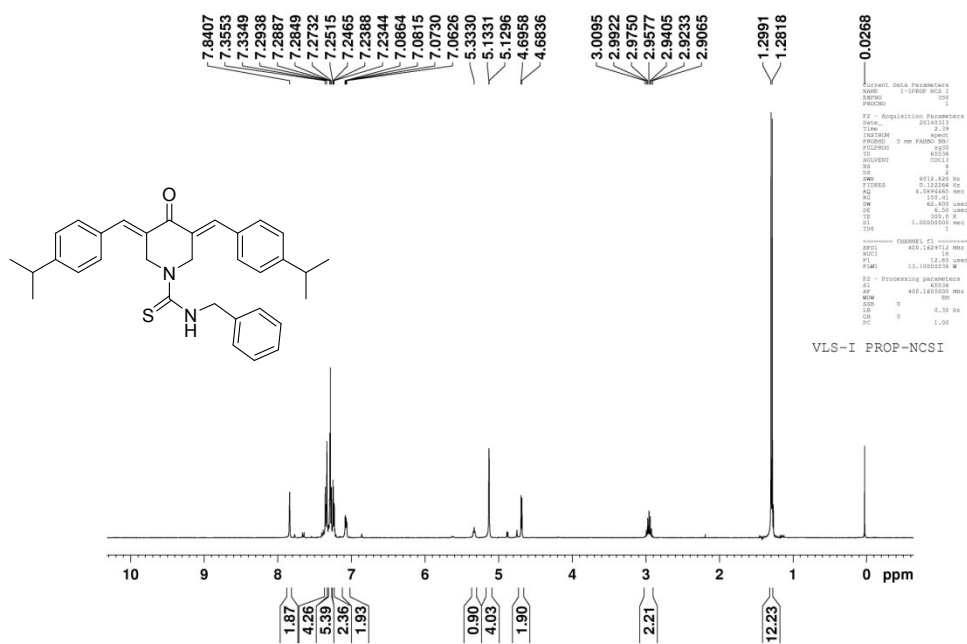
¹³C NMR Spectra of compound **16**(100 MHz, CDCl₃)



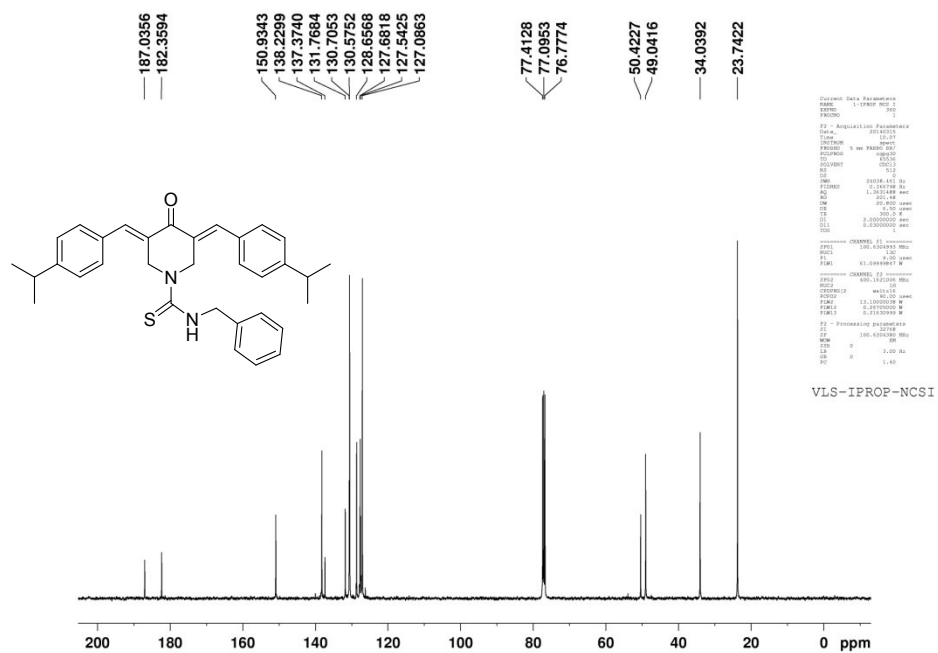
¹H NMR Spectra of compound 17(400 MHz, CDCl₃)



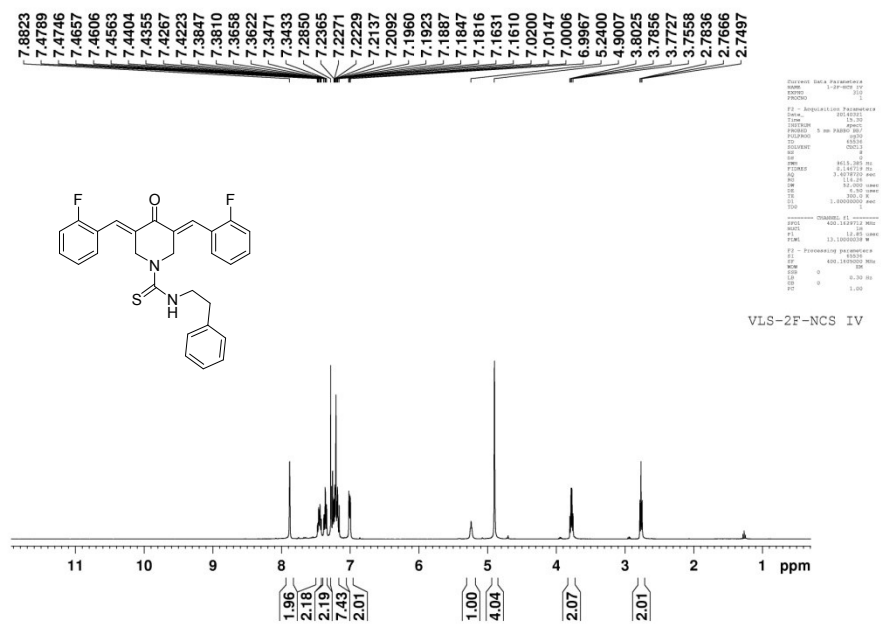
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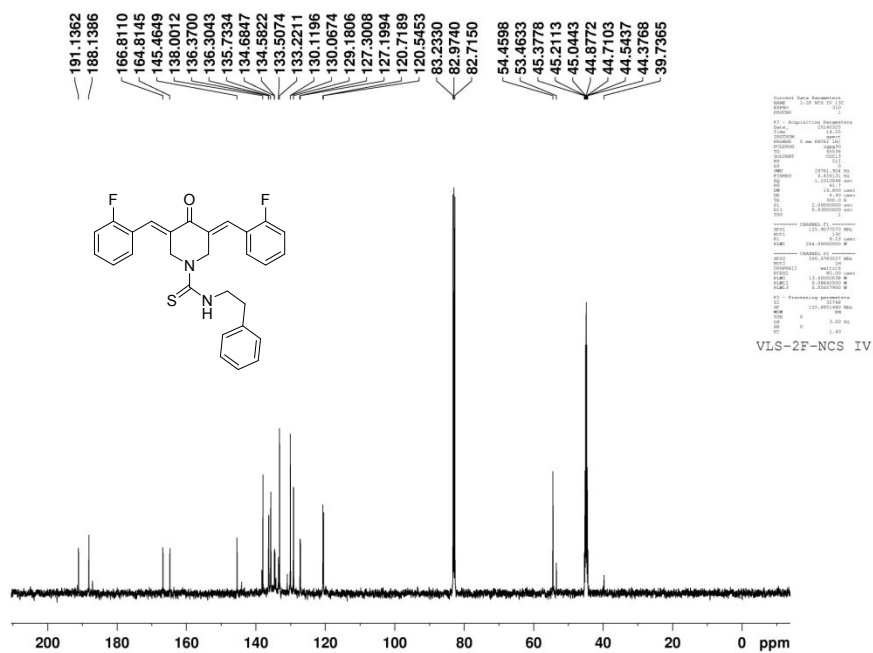
¹H NMR Spectra of compound **19**(400 MHz, CDCl₃)



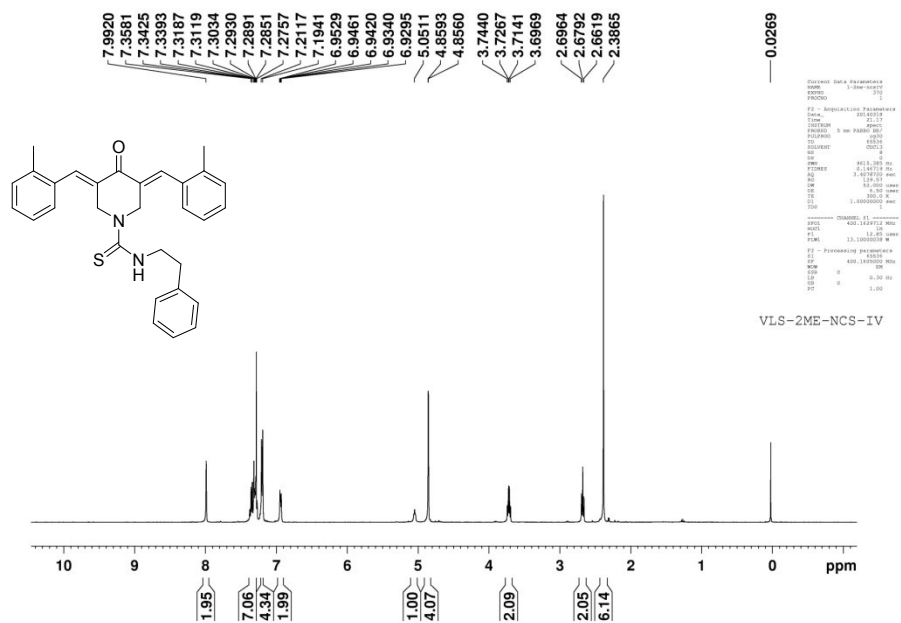
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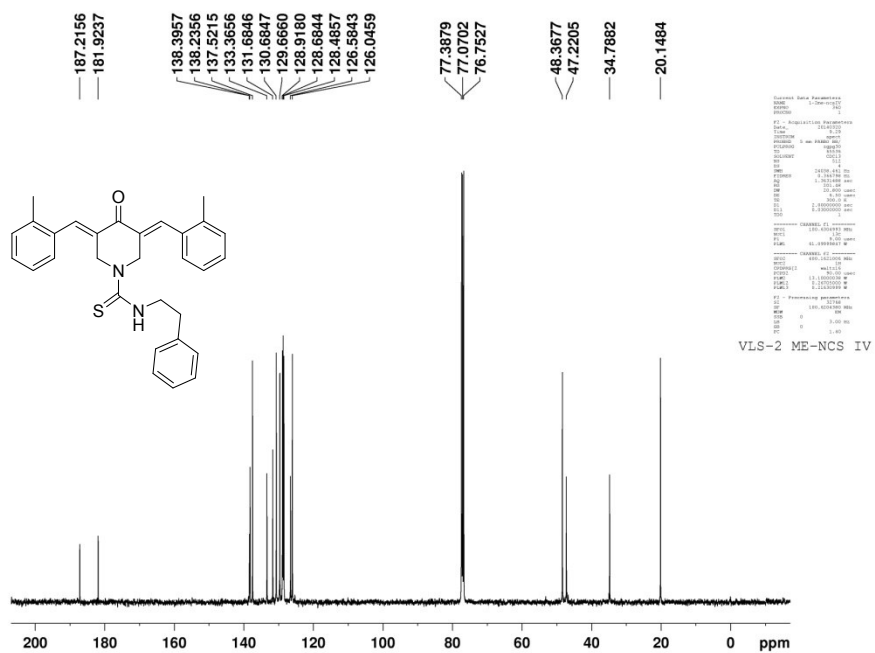
¹H NMR Spectra of compound **20**(400 MHz, CDCl₃)



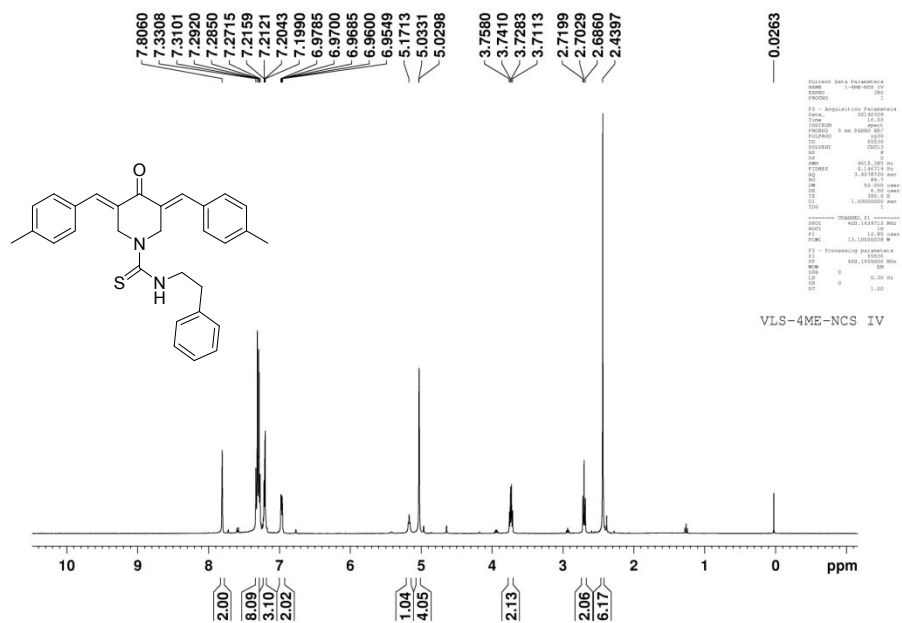
¹³C NMR Spectra of compound **20**(100 MHz, CDCl₃+DMSO-*d*₆)



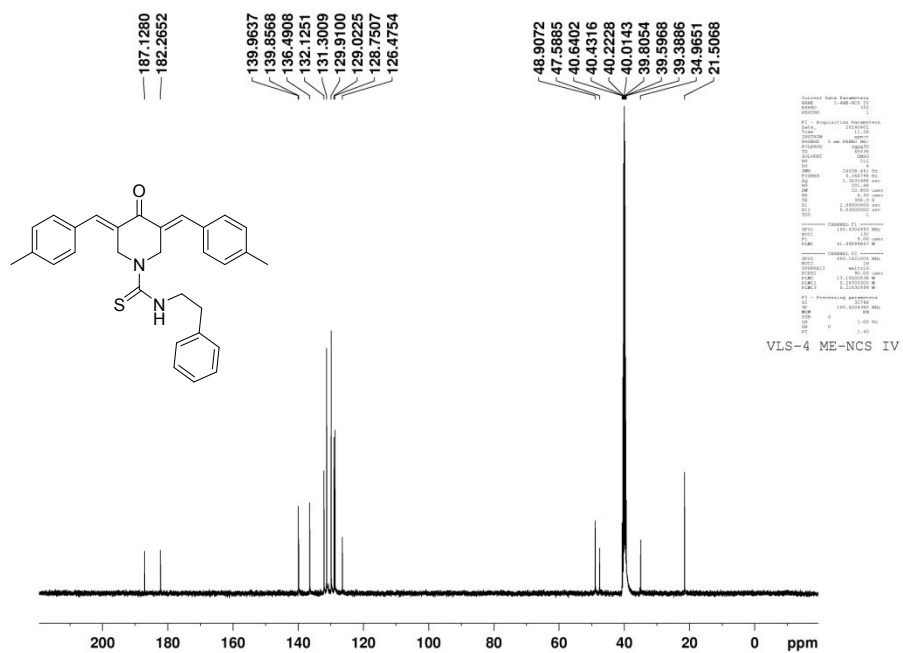
¹H NMR Spectra of compound **22**(400 MHz, CDCl₃)



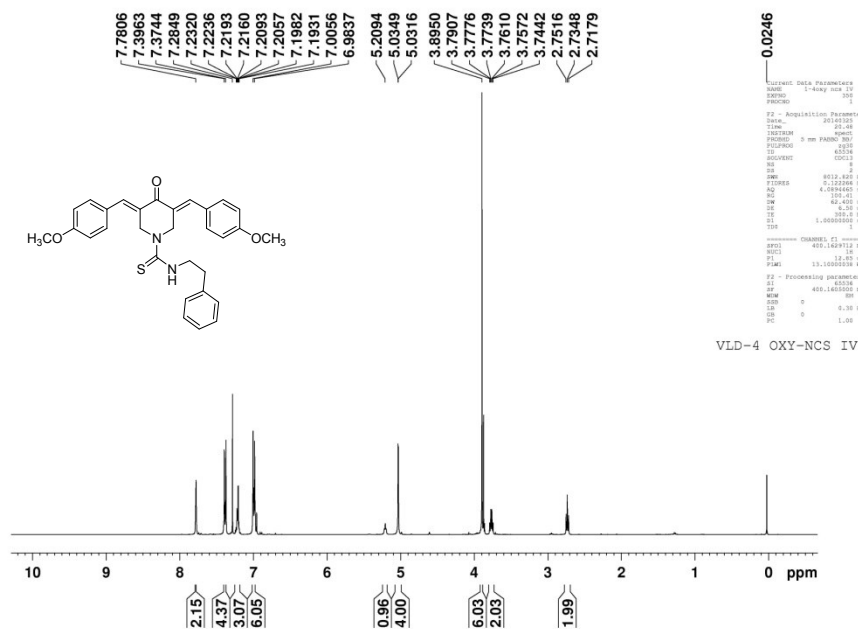
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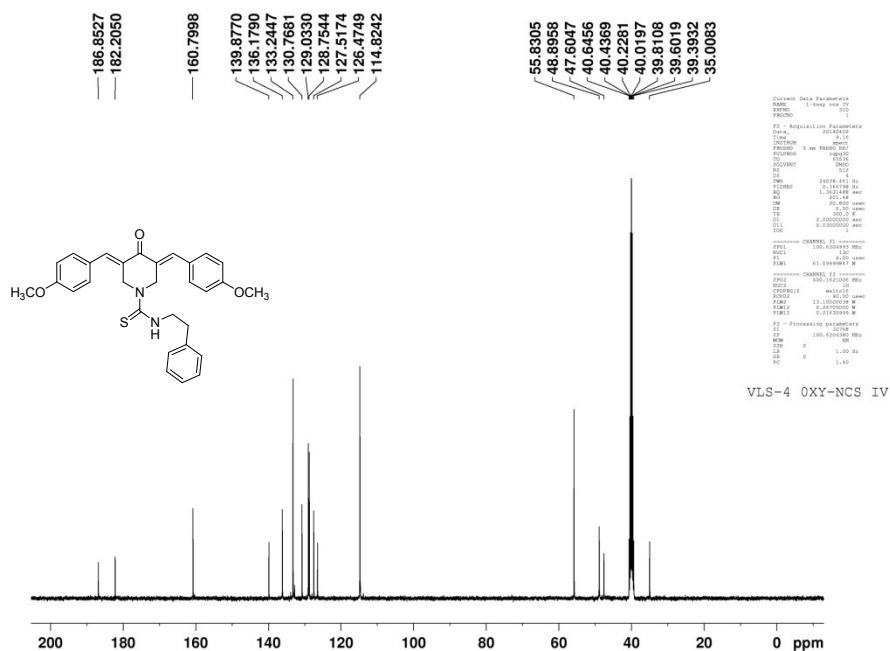
¹H NMR Spectra of compound **23**(400 MHz, CDCl₃)



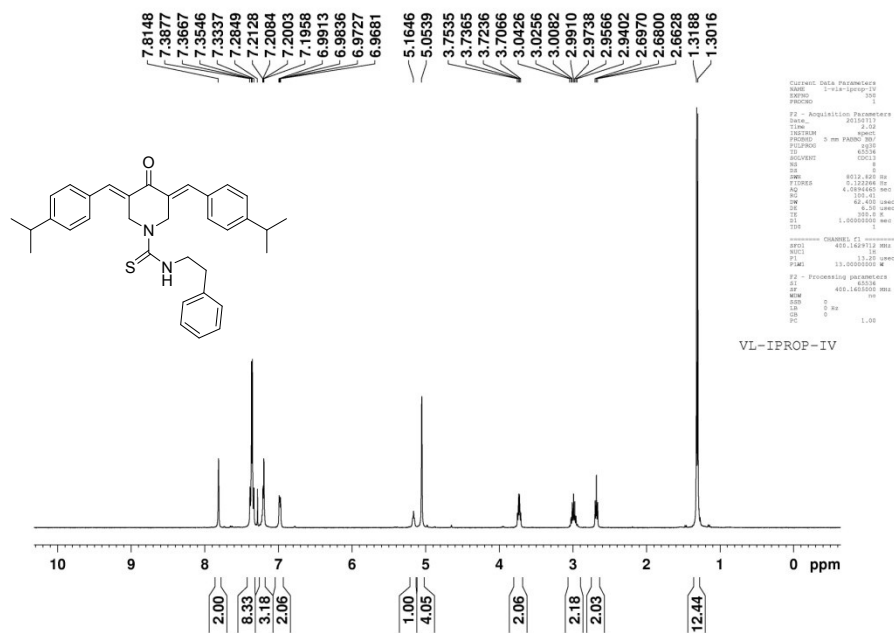
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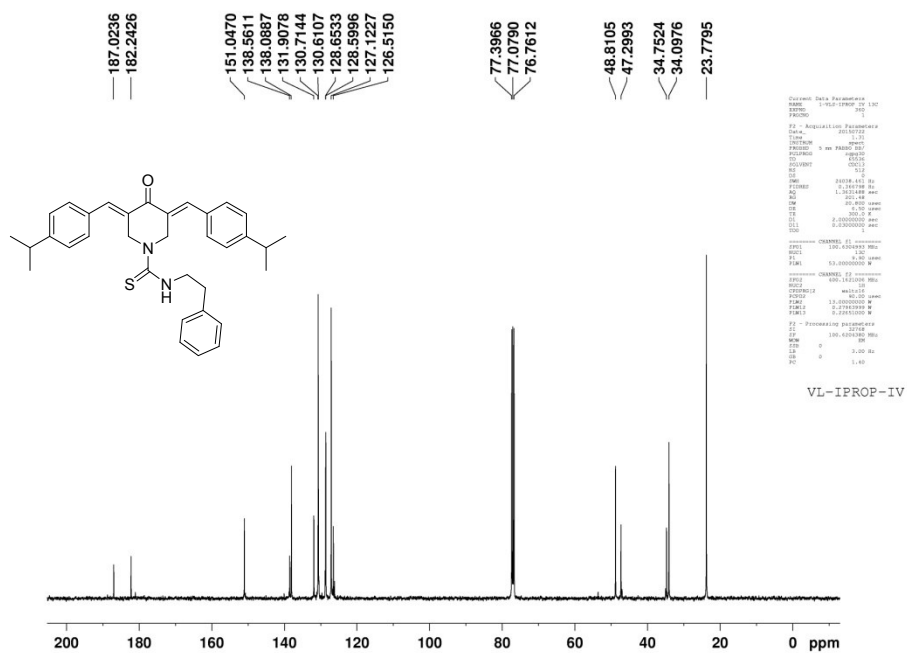
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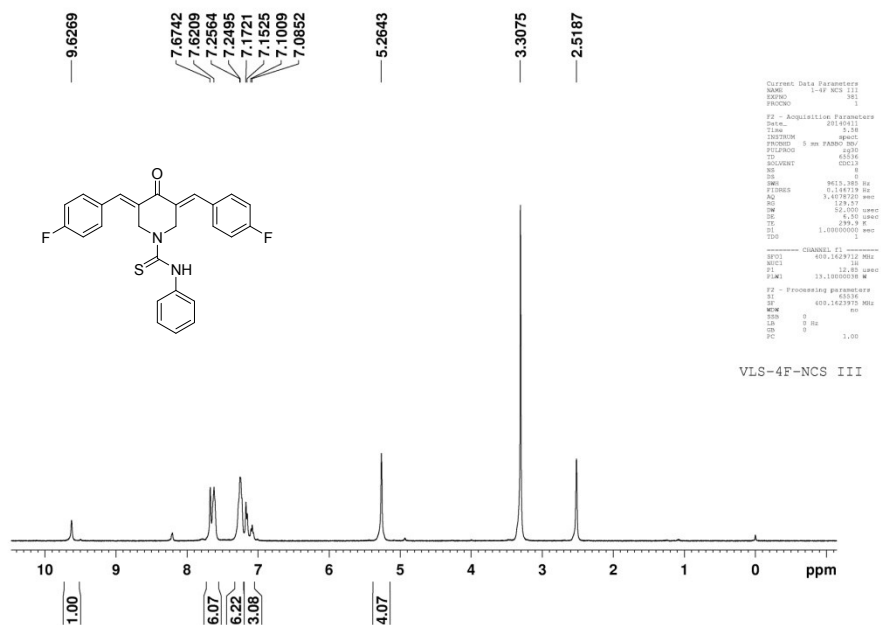
¹³C NMR Spectra of compound **24**(100 MHz, DMSO-*d*₆)



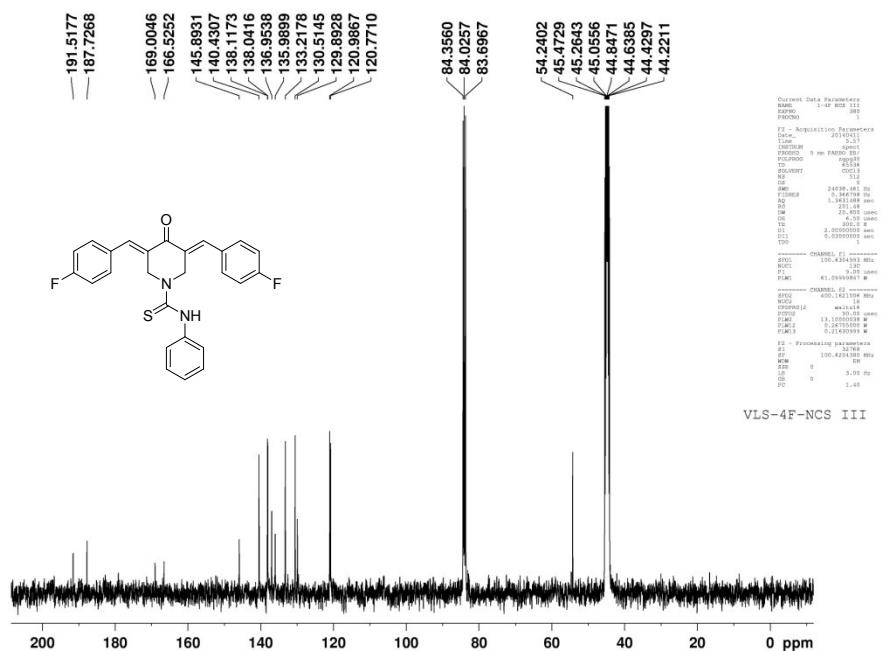
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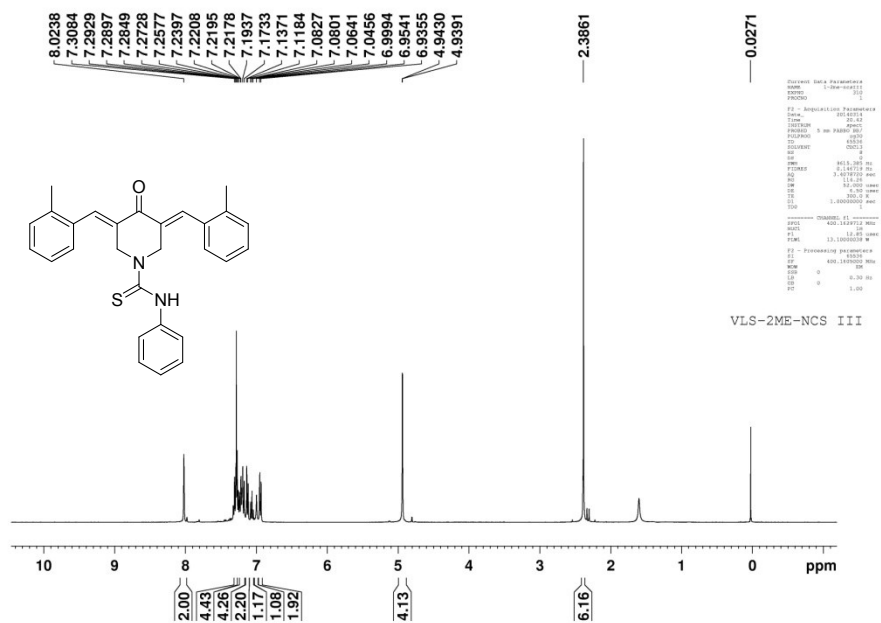
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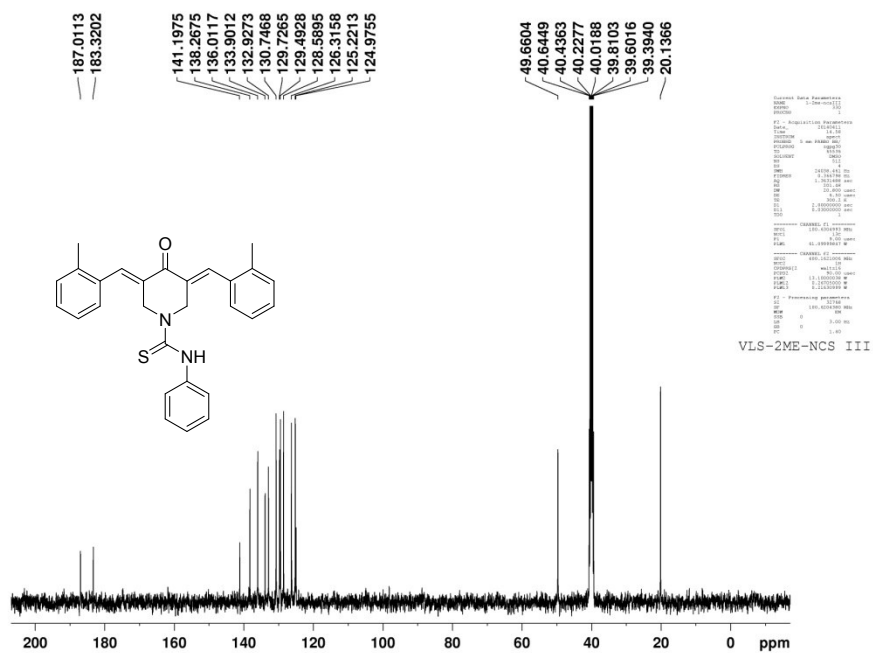
¹H NMR Spectra of compound **27**(400 MHz, CDCl₃)



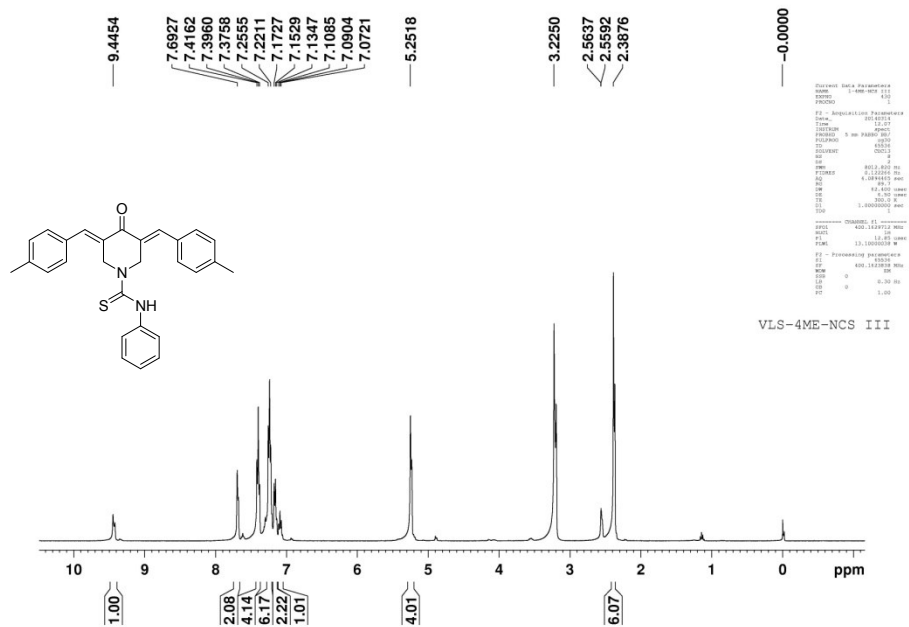
¹³C NMR Spectra of compound **27**(100 MHz, CDCl₃+DMSO-*d*₆)



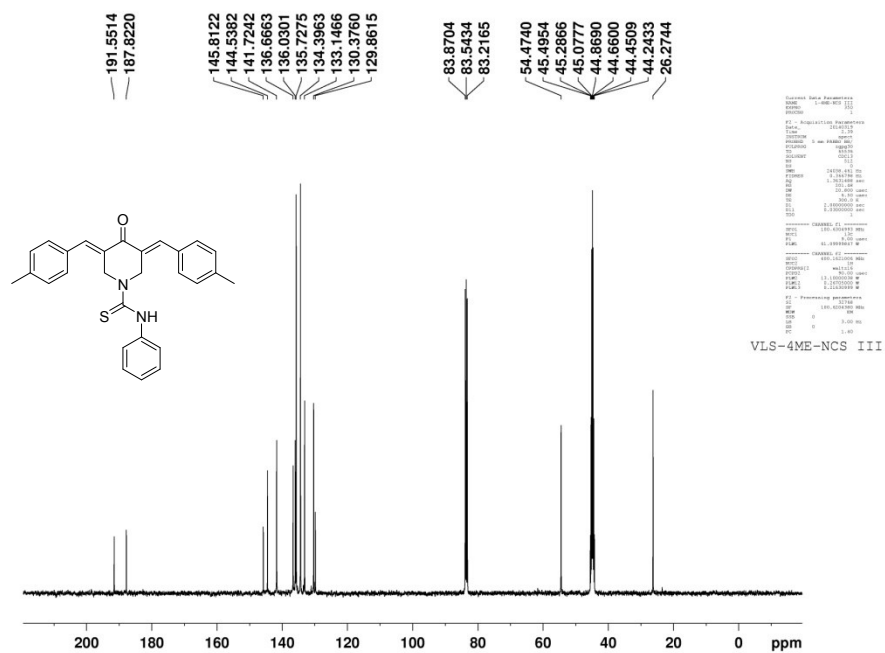
¹H NMR Spectra of compound **28**(400 MHz, CDCl₃)



¹³C NMR Spectra of compound **28**(100 MHz, DMSO-*d*₆)



¹H NMR Spectra of compound **29**(400 MHz, CDCl₃)



¹³C NMR Spectra of compound **29**(100 MHz, CDCl₃+DMSO-*d*₆)



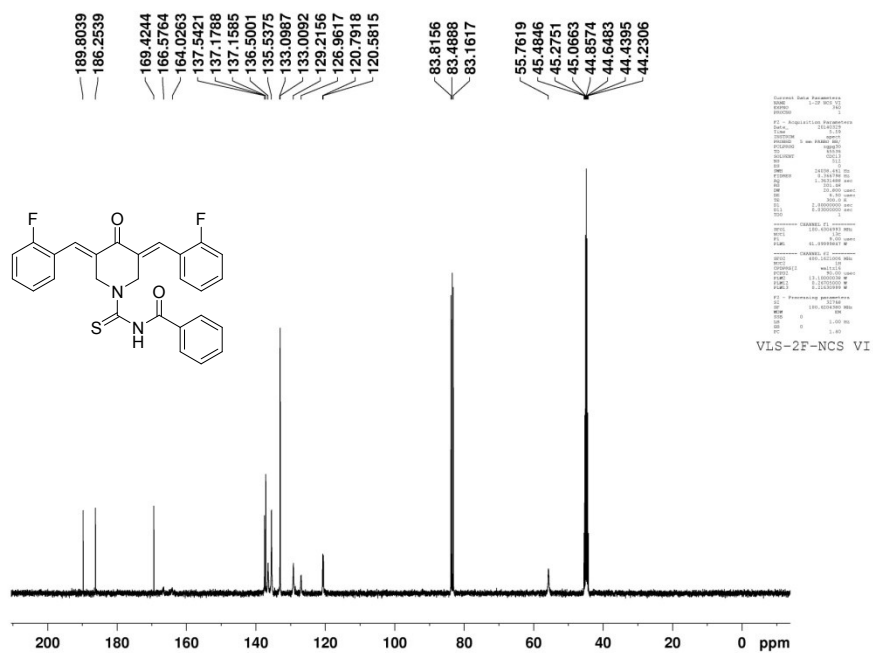
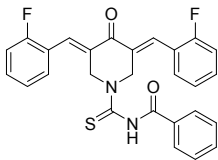
Chemical structure of VLS-40XY-NCS III:

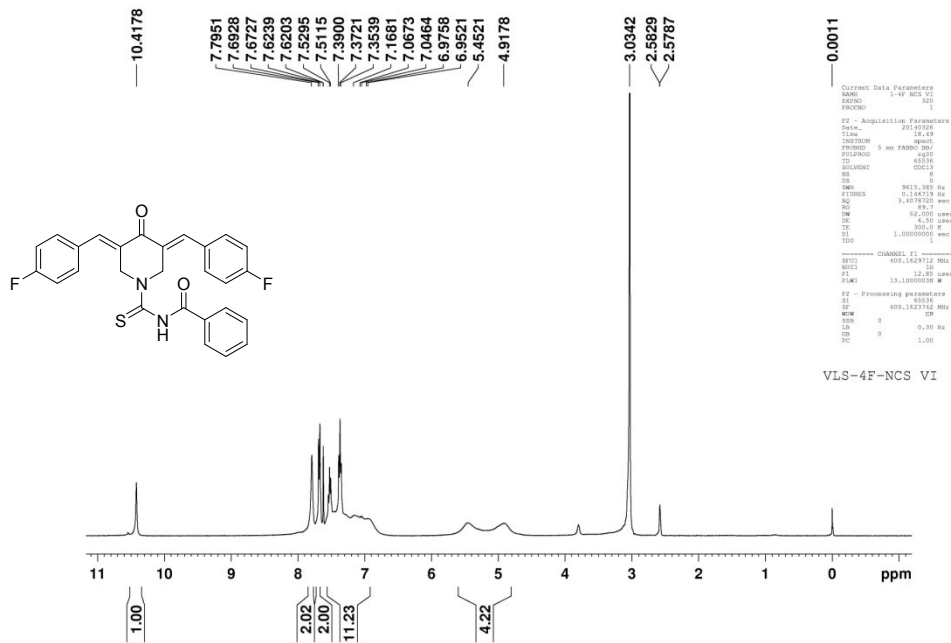
COc1ccc(cc1)/C=C2/C(=O)N(C(=S2)Nc3ccccc3)C=C4C(=O)N(C(=O)4)C5=CC(OC)=CC=C5

¹³C NMR spectrum (CDCl₃) of VLS-40XY-NCS III. The spectrum shows peaks at the following chemical shifts (ppm):

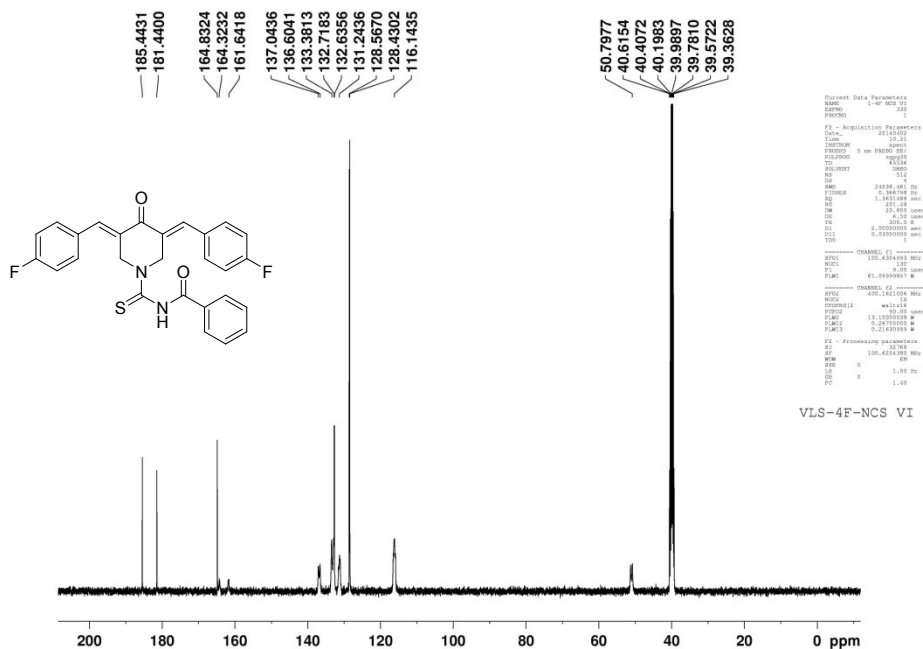
Peak Number	Chemical Shift (ppm)
191.6019	191.6019
187.8953	187.8953
165.4477	165.4477
145.5096	145.5096
141.8313	141.8313
137.5210	137.5210
134.2477	134.2477
133.2545	133.2545
132.0016	132.0016
129.9893	129.9893
119.0979	119.0979
83.0092	83.0092
82.5872	82.5872
82.3647	82.3647
60.1770	60.1770
54.5435	54.5435
45.4863	45.4863
45.2788	45.2788
45.0703	45.0703
44.8617	44.8617
44.6529	44.6529
44.4443	44.4443
44.2349	44.2349

S21

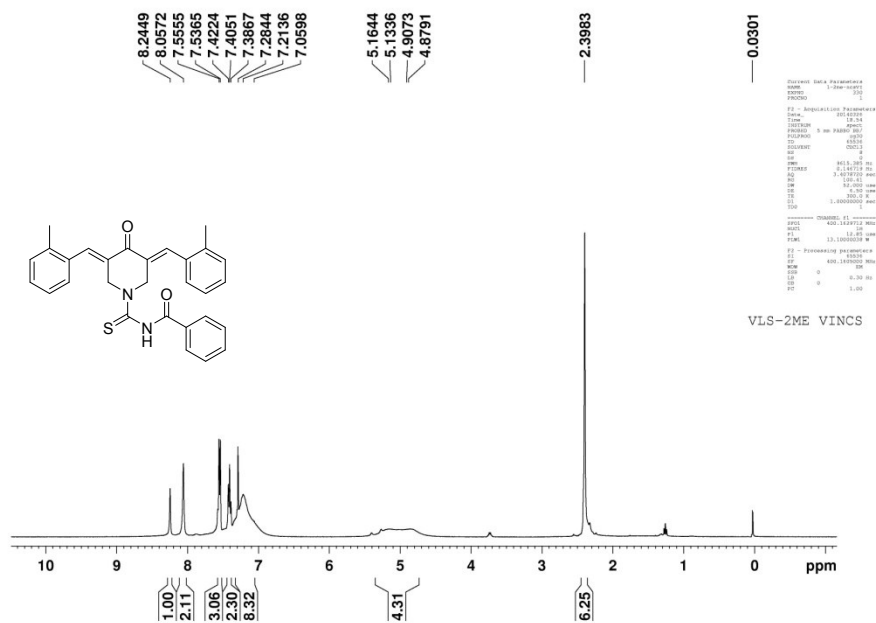




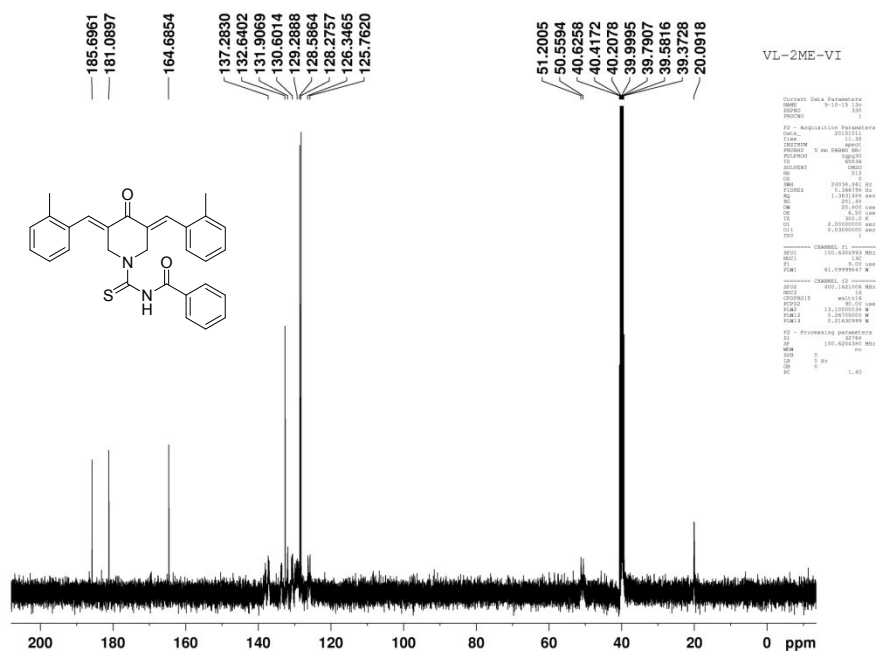
¹H NMR Spectra of compound **33**(400 MHz, CDCl₃+DMSO-*d*₆)



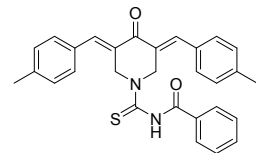
¹³C NMR Spectra of compound **33**(100 MHz, DMSO-*d*₆)



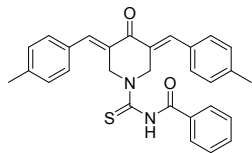
¹H NMR Spectra of compound **34**(400 MHz, CDCl₃)



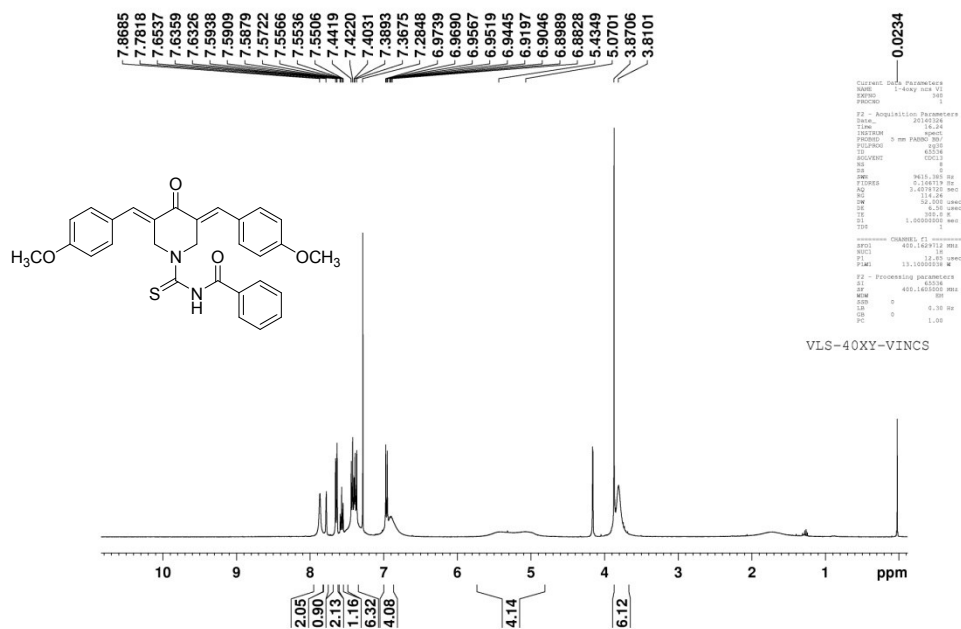
¹³C NMR Spectra of compound **34**(100 MHz, DMSO-*d*₆)



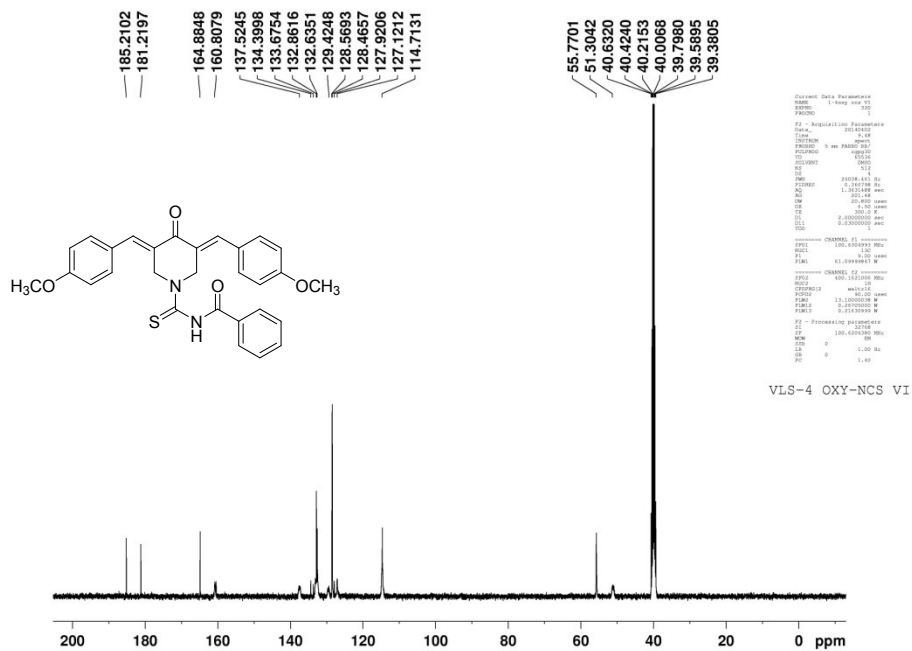
¹H NMR Spectra of compound **35**(400 MHz, CDCl₃+DMSO-*d*₆)



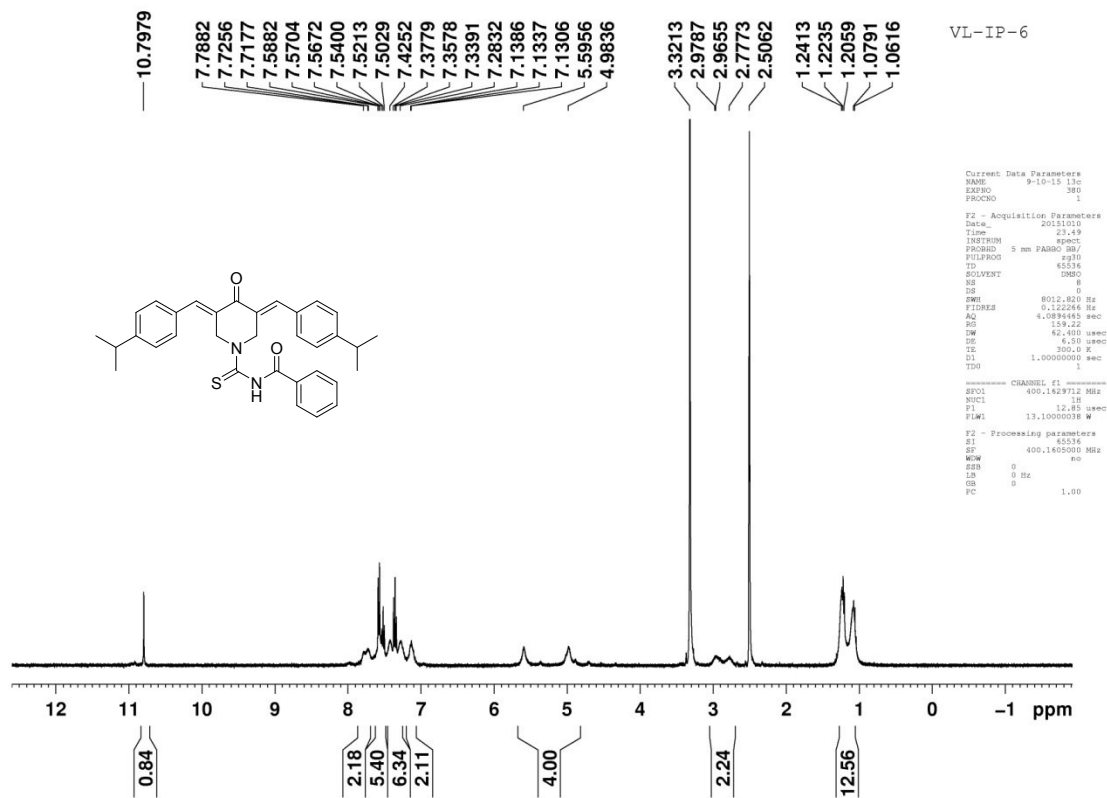
¹³C NMR Spectra of compound **35**(100 MHz, DMSO-*d*₆)



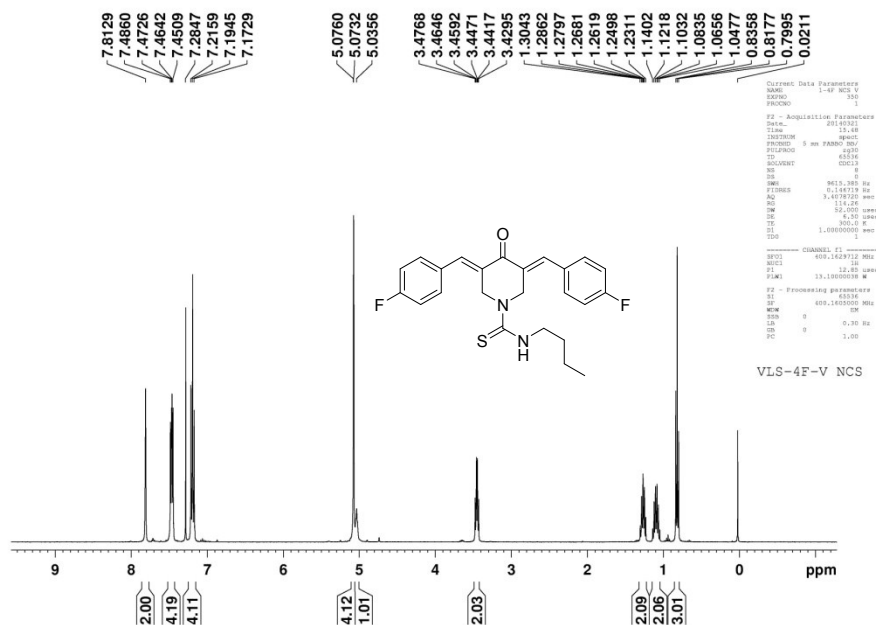
¹H NMR Spectra of compound **36**(400 MHz, CDCl₃+DMSO-*d*₆)



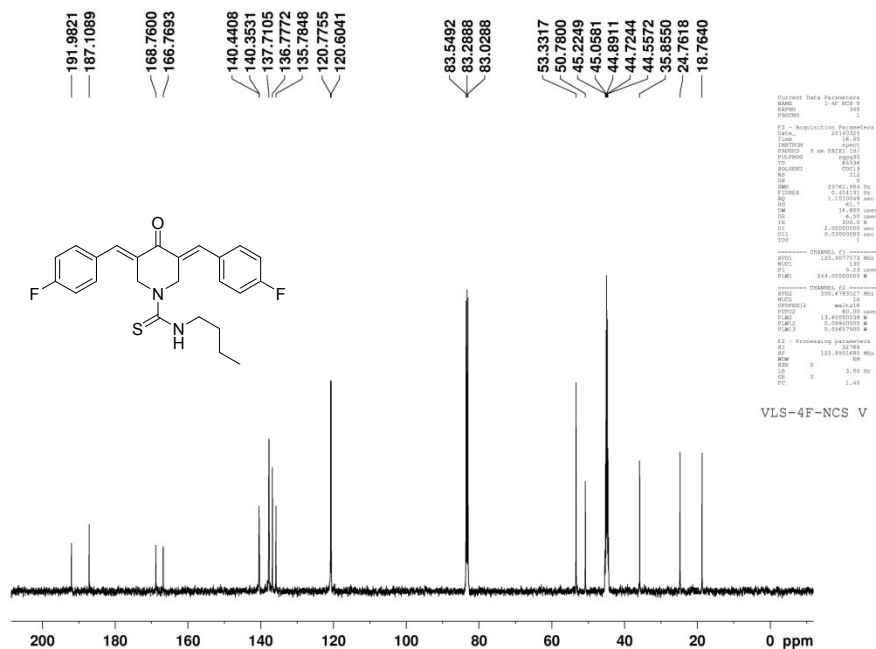
¹³C NMR Spectra of compound **36**(100 MHz, DMSO-*d*₆)



¹H NMR Spectra of compound **37**(400 MHz, DMSO-*d*₆)

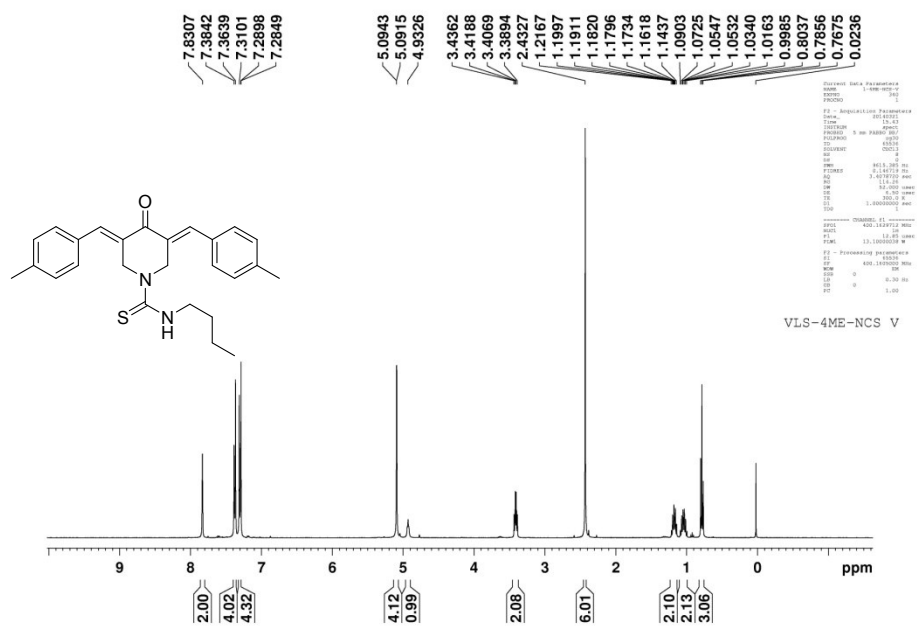


¹H NMR Spectra of compound **39**(400 MHz, CDCl₃)

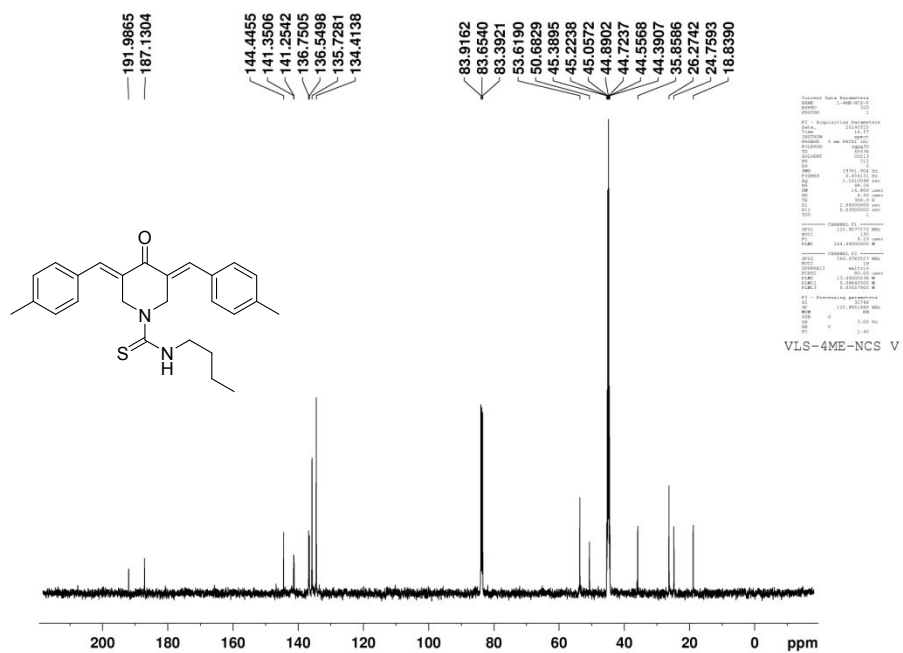


¹³C NMR Spectra of compound **39**(100 MHz, CDCl₃+DMSO-*d*₆)

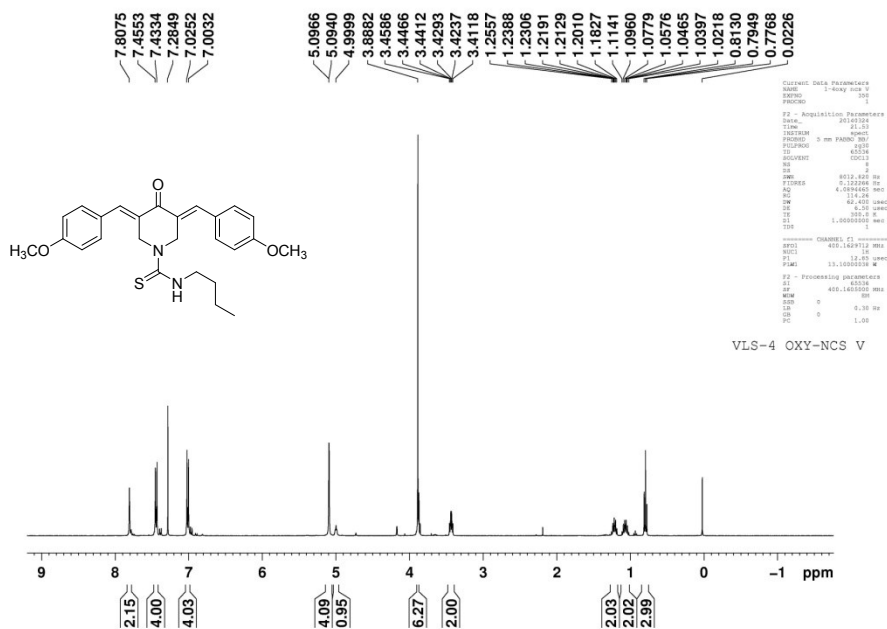




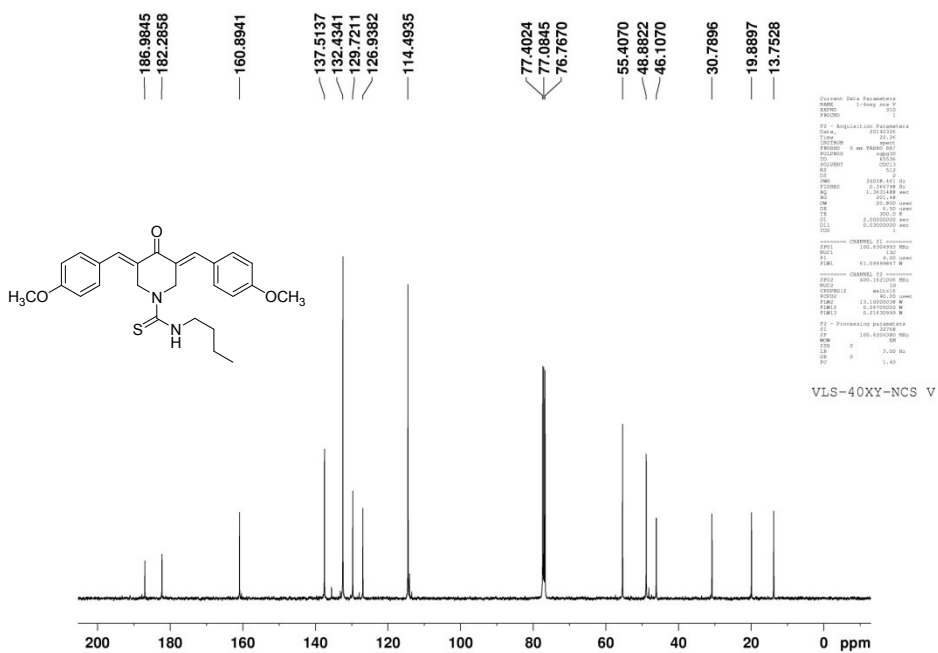
¹H NMR Spectra of compound **41**(400 MHz, CDCl₃)



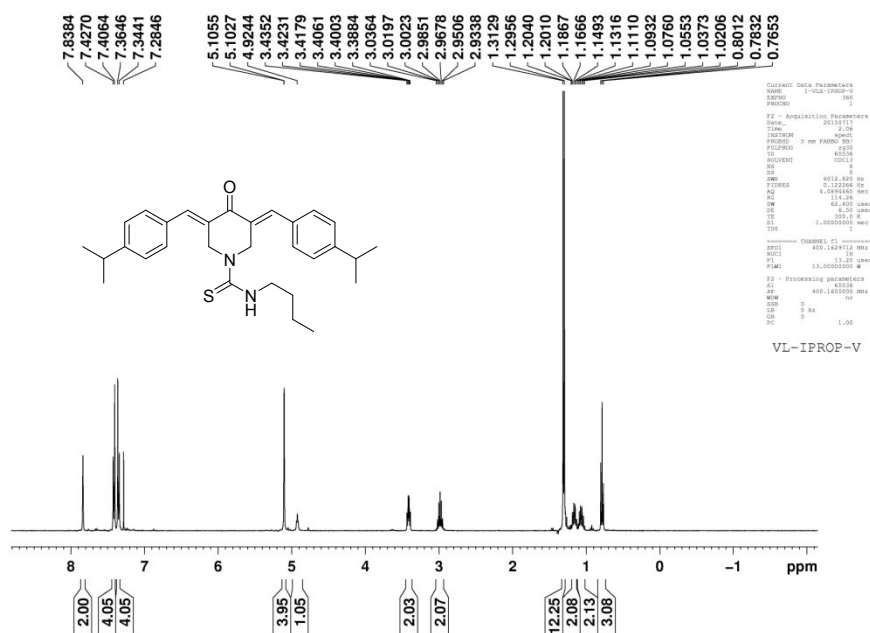
¹³C NMR Spectra of compound **41**(100 MHz, CDCl₃+DMSO-*d*₆)



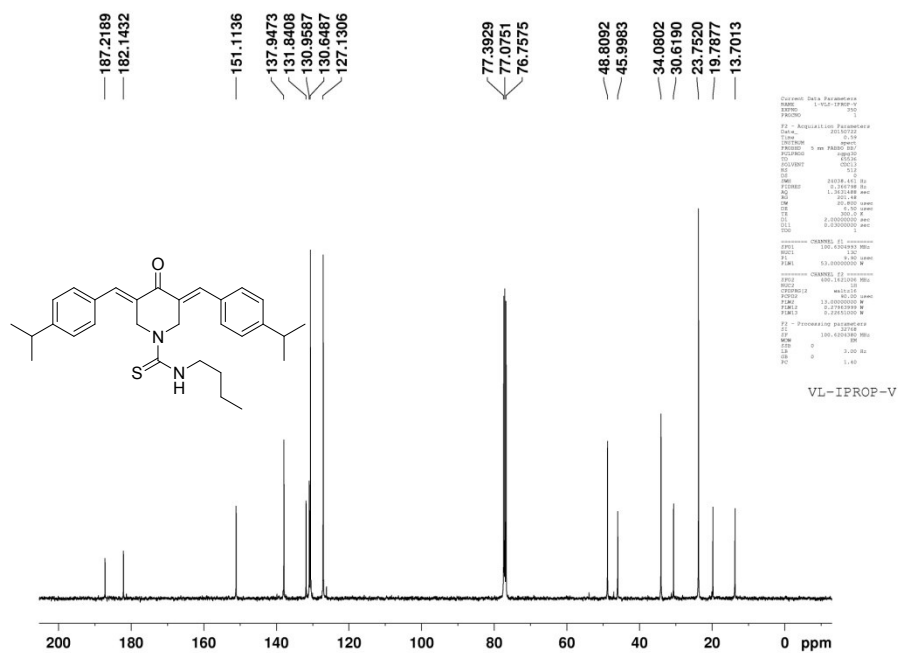
¹H NMR Spectra of compound **42**(400 MHz, CDCl₃)



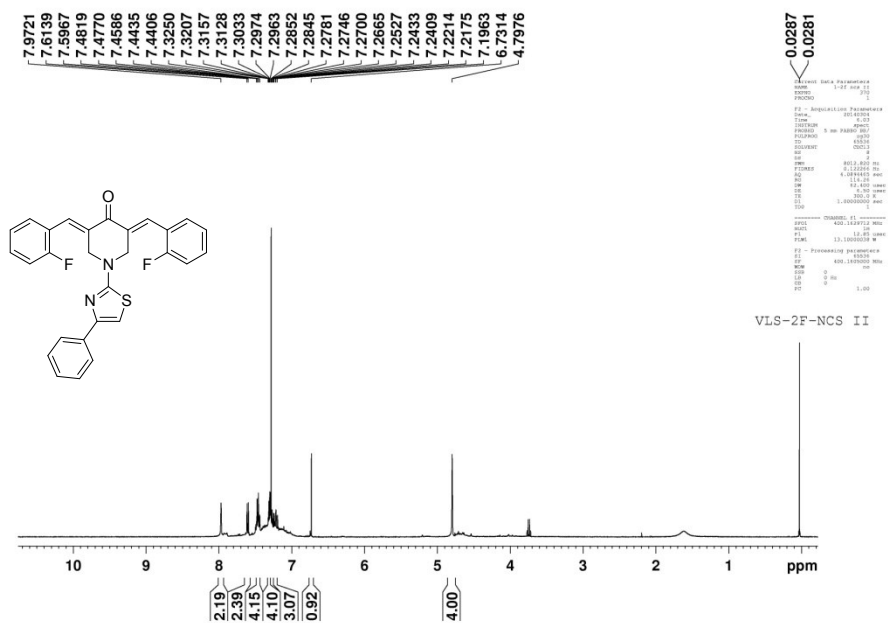
¹³C NMR Spectra of compound **42**(100 MHz, CDCl₃)



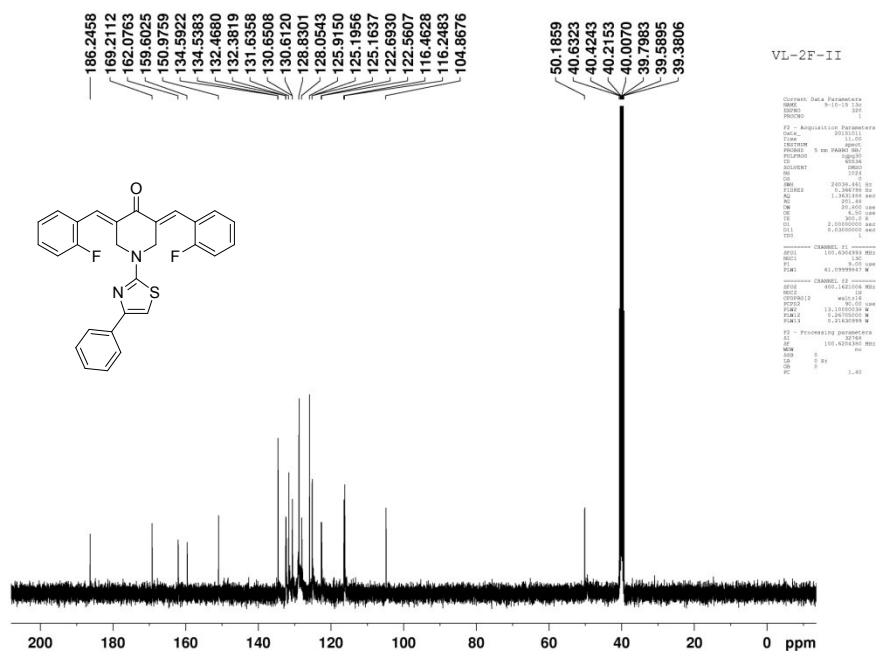
¹H NMR Spectra of compound **43**(400 MHz, CDCl₃)



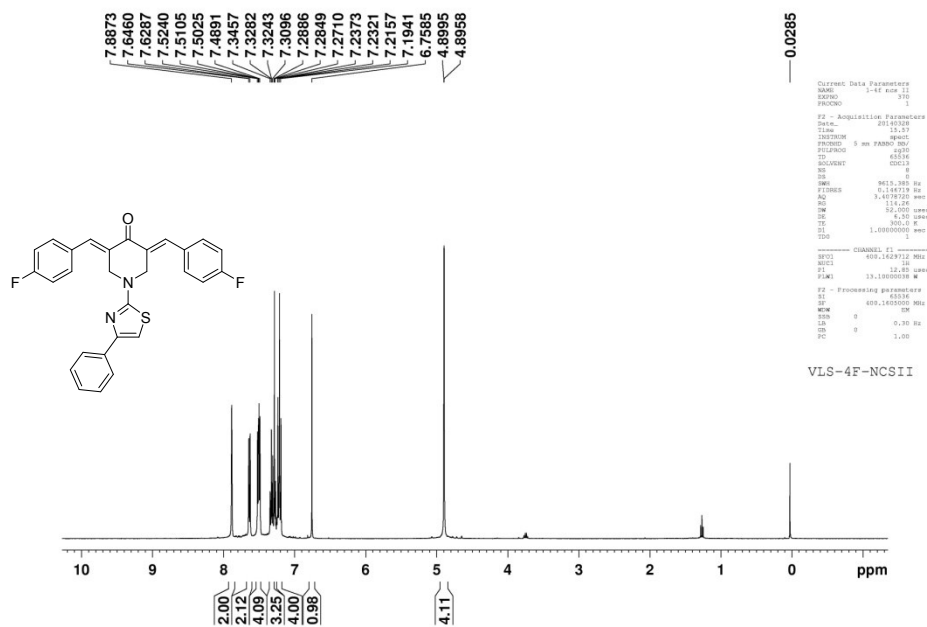
¹³C NMR Spectra of compound **43**(100 MHz, CDCl₃)



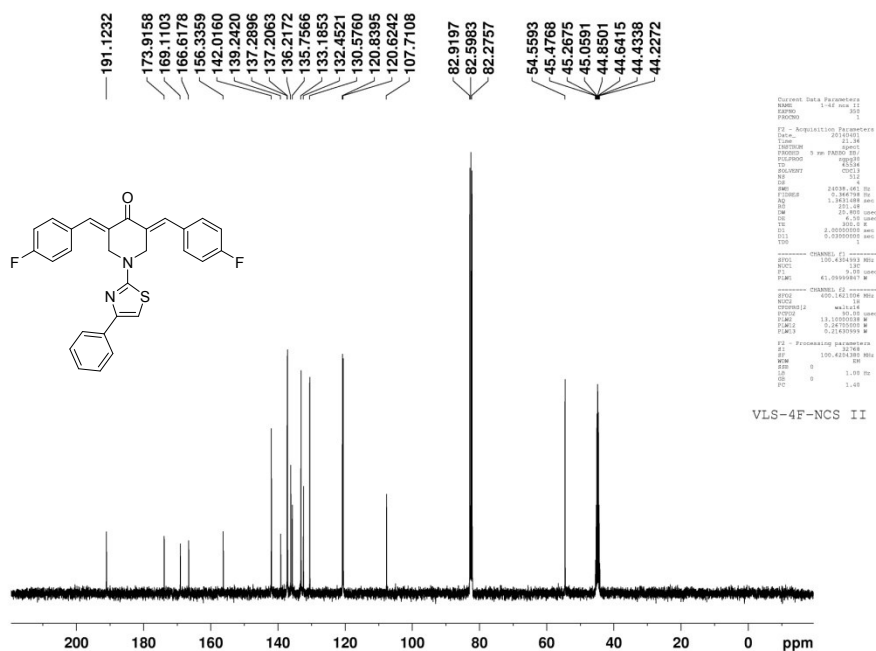
¹H NMR Spectra of compound **44**(400 MHz, CDCl₃)



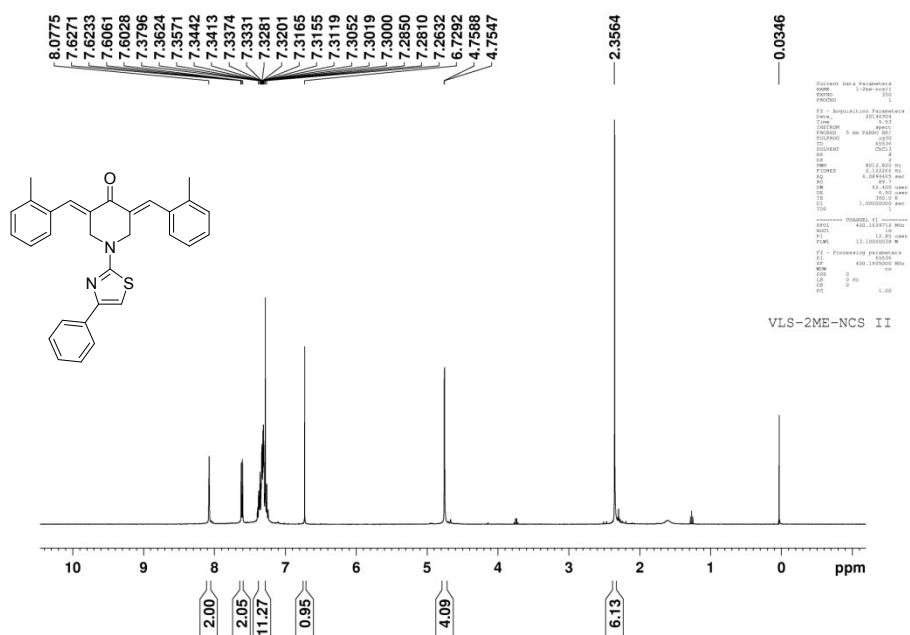
¹³C NMR Spectra of compound **44**(100 MHz, DMSO-*d*₆)



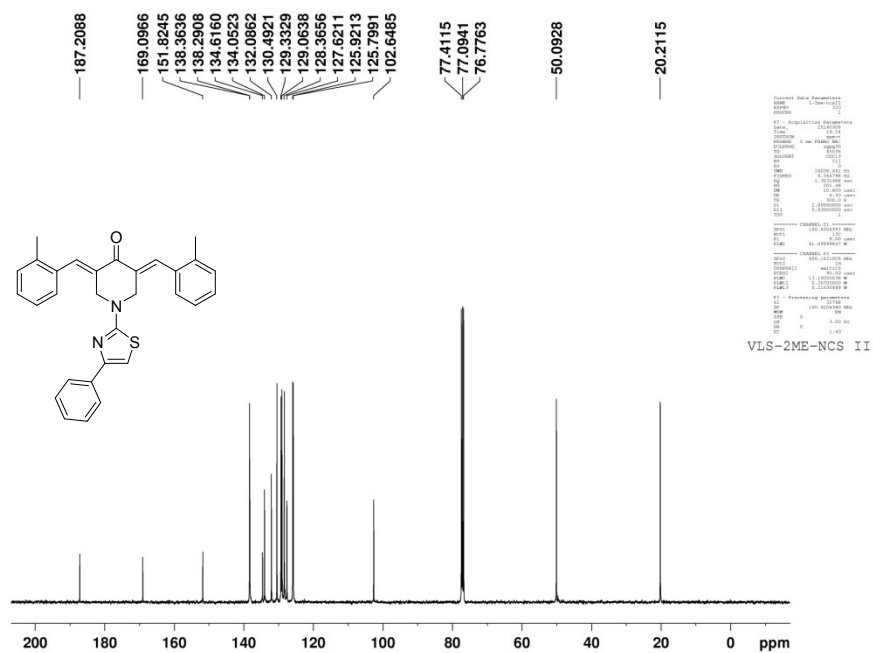
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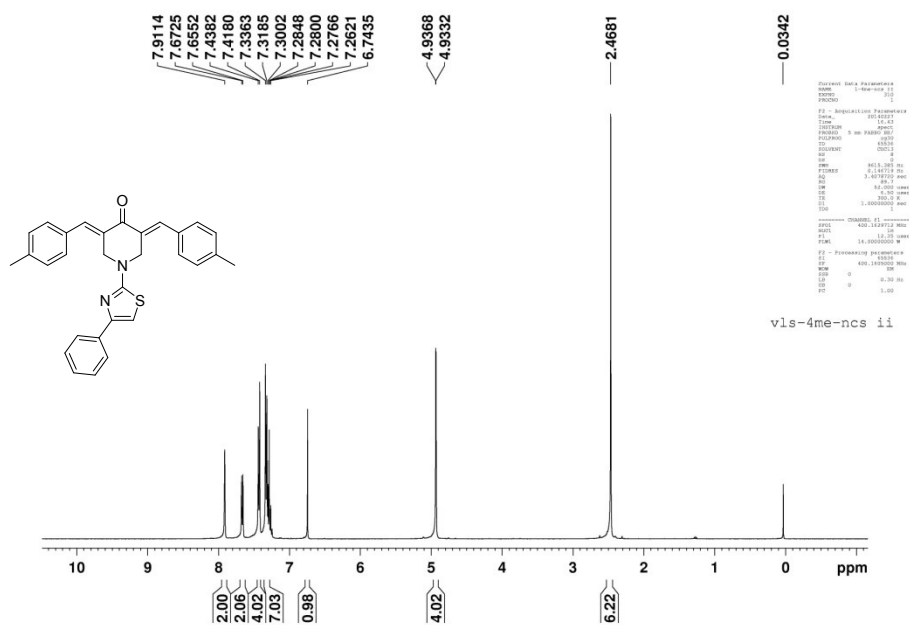
¹³C NMR Spectra of compound **45**(100 MHz, CDCl₃+DMSO-*d*₆)



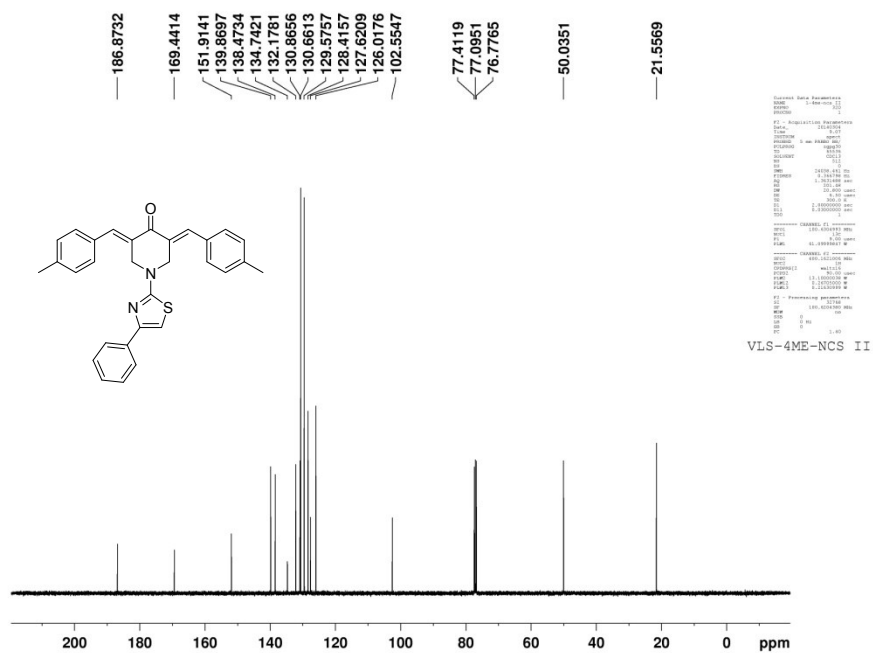
¹H NMR Spectra of compound **46**(400 MHz, CDCl₃)



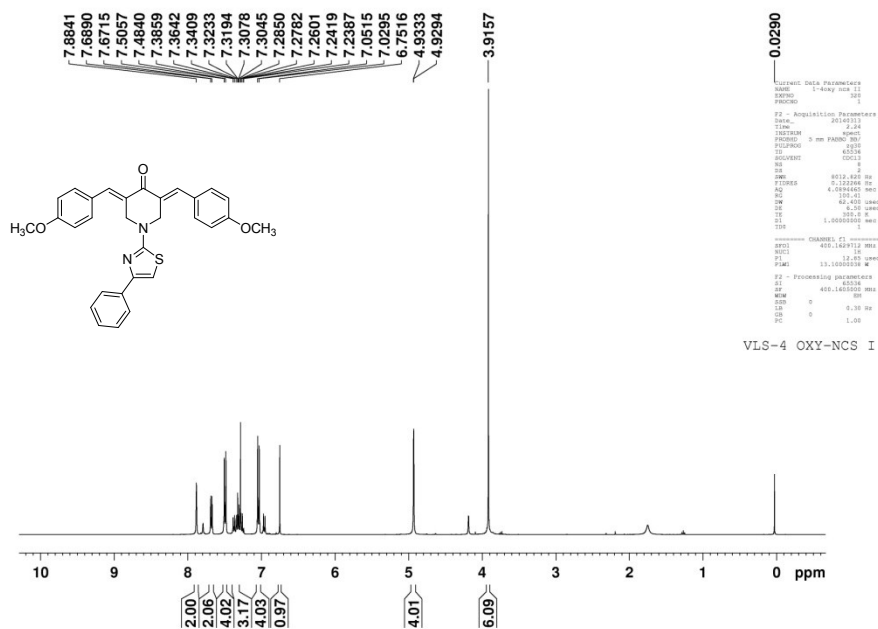
¹³C NMR Spectra of compound **46**(100 MHz, CDCl₃)



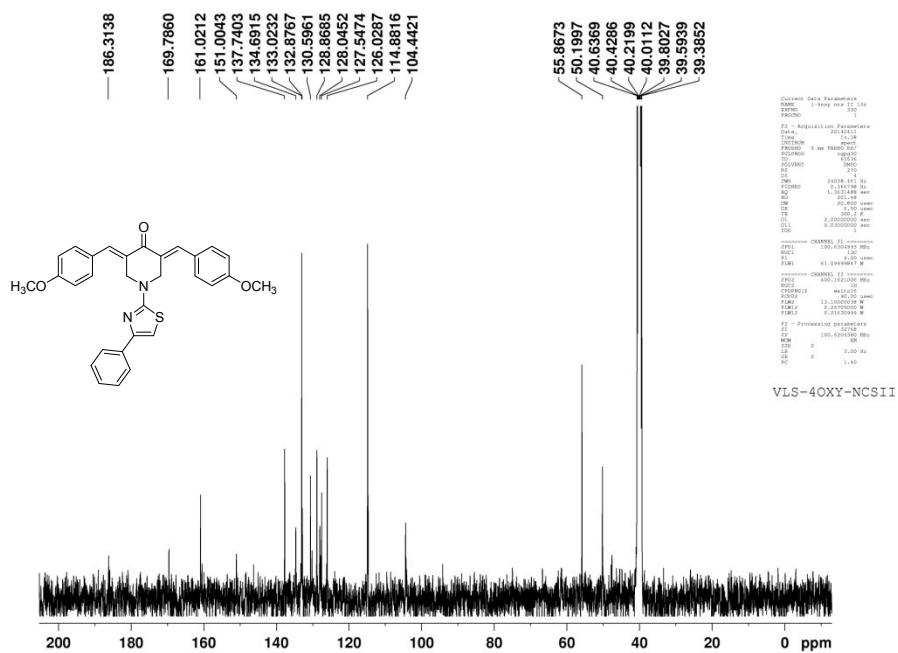
¹H NMR Spectra of compound 47(400 MHz, CDCl₃)



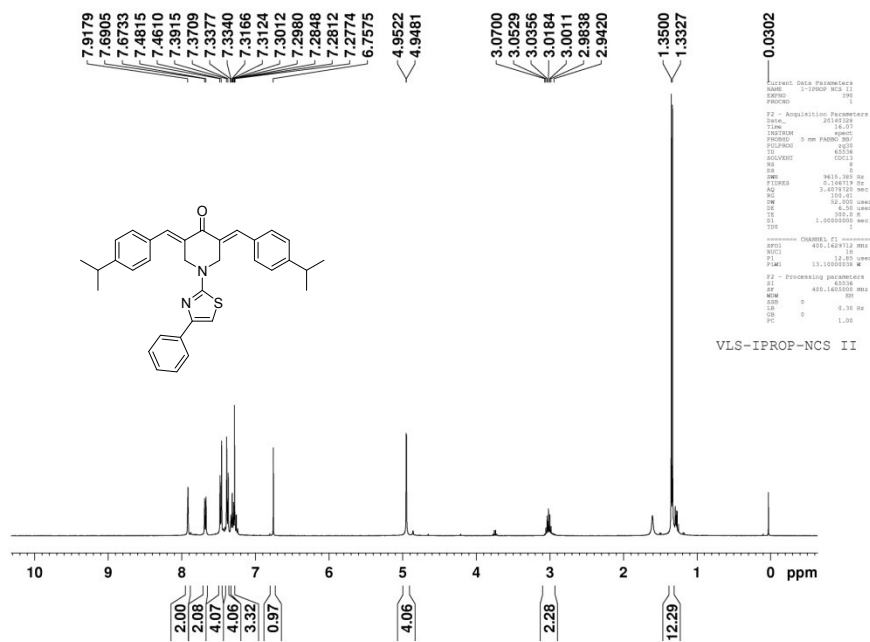
¹³C NMR Spectra of compound 47(100 MHz, CDCl₃)



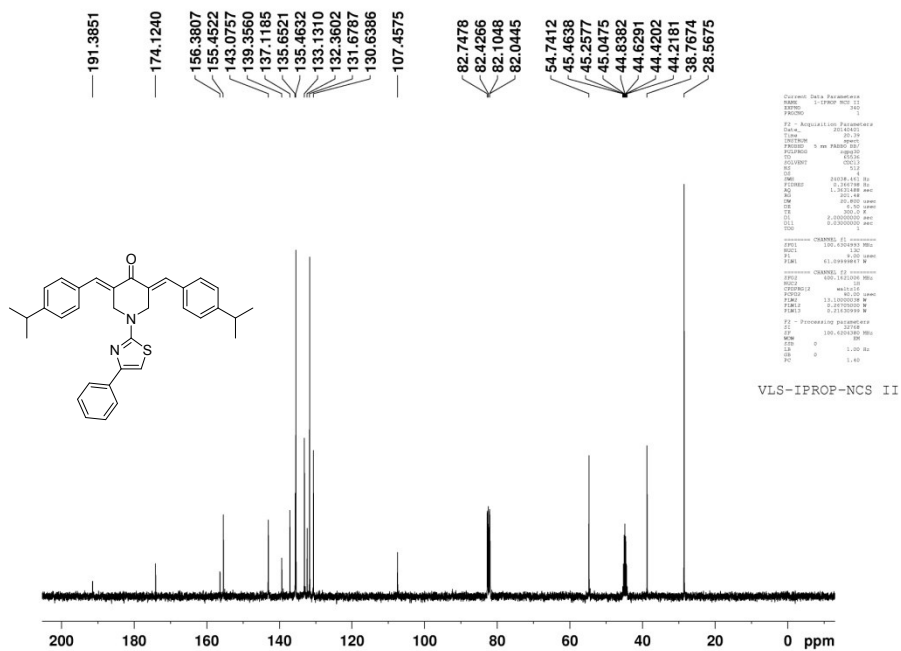
¹H NMR Spectra of compound **48**(400 MHz, CDCl₃)



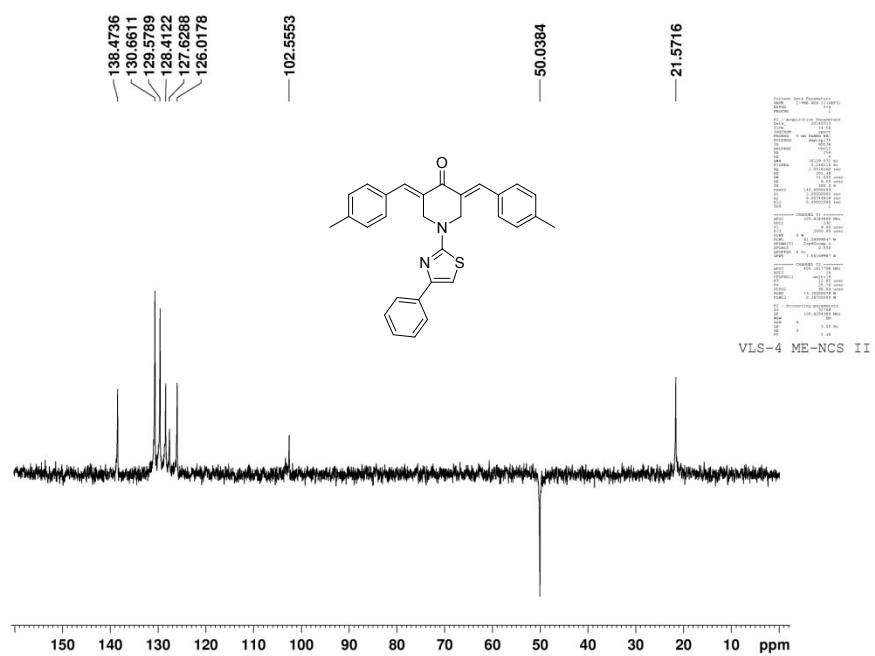
¹³C NMR Spectra of compound **48**(100 MHz, DMSO-*d*₆)



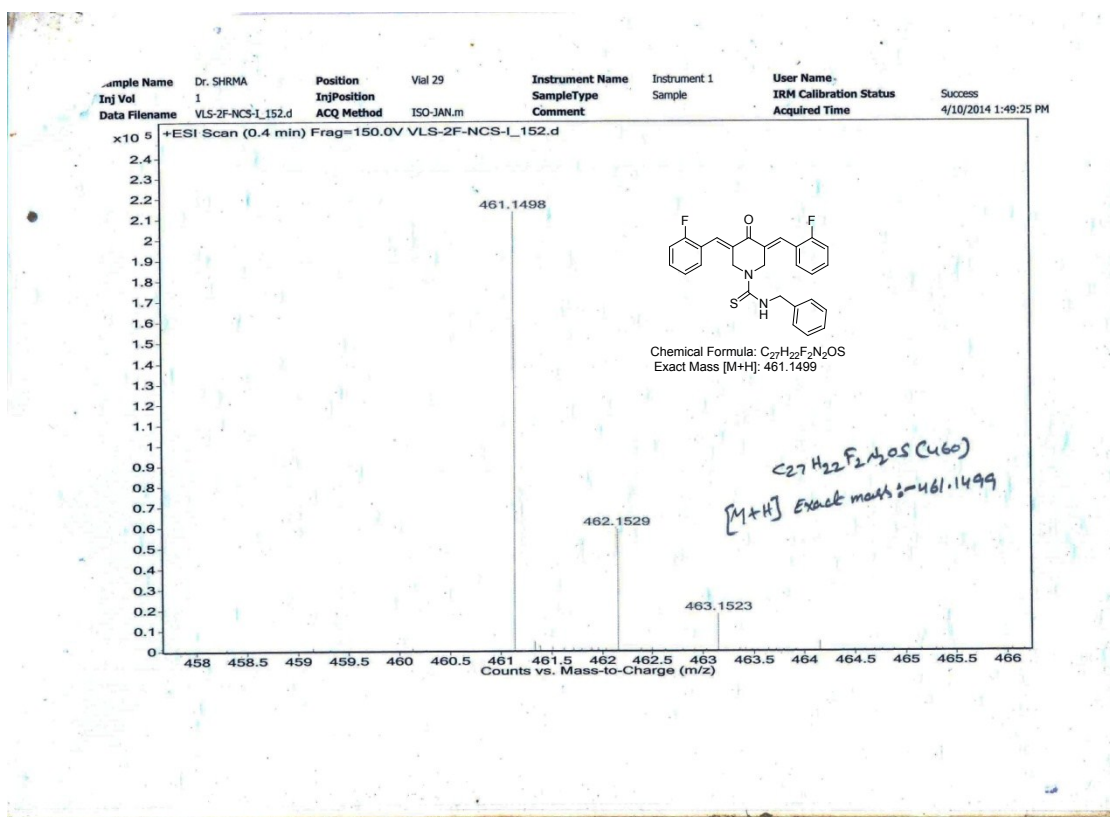
¹H NMR Spectra of compound **49**(400 MHz, CDCl₃)



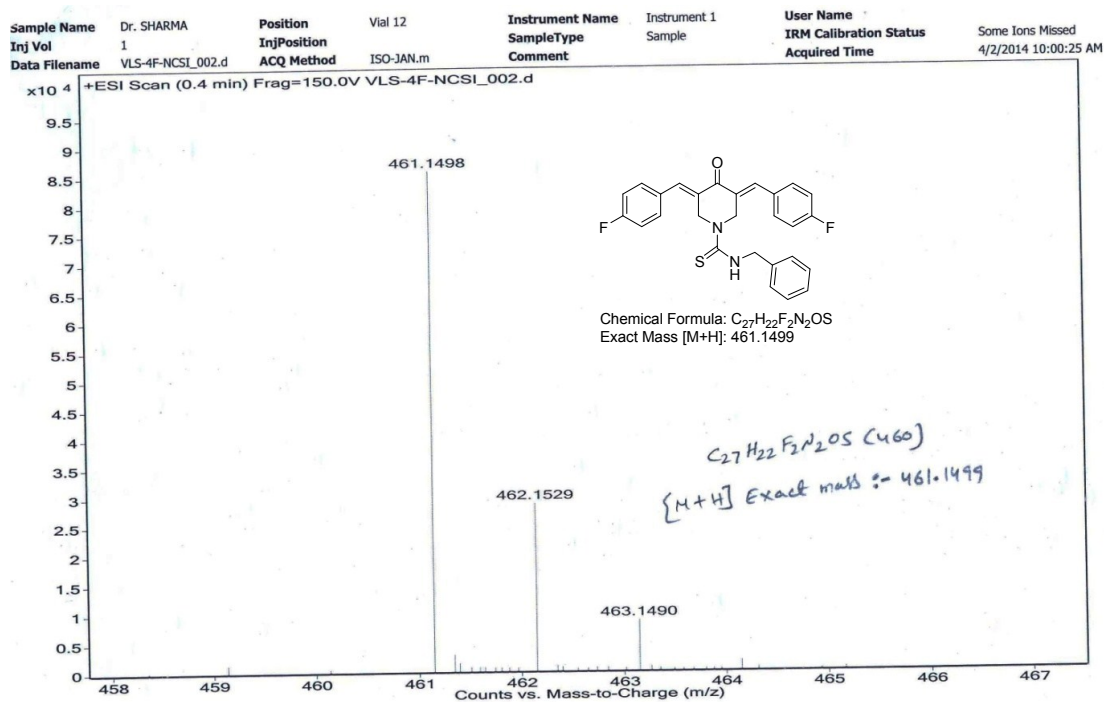
¹³C NMR Spectra of compound **49**(100 MHz, CDCl₃+DMSO-*d*₆)



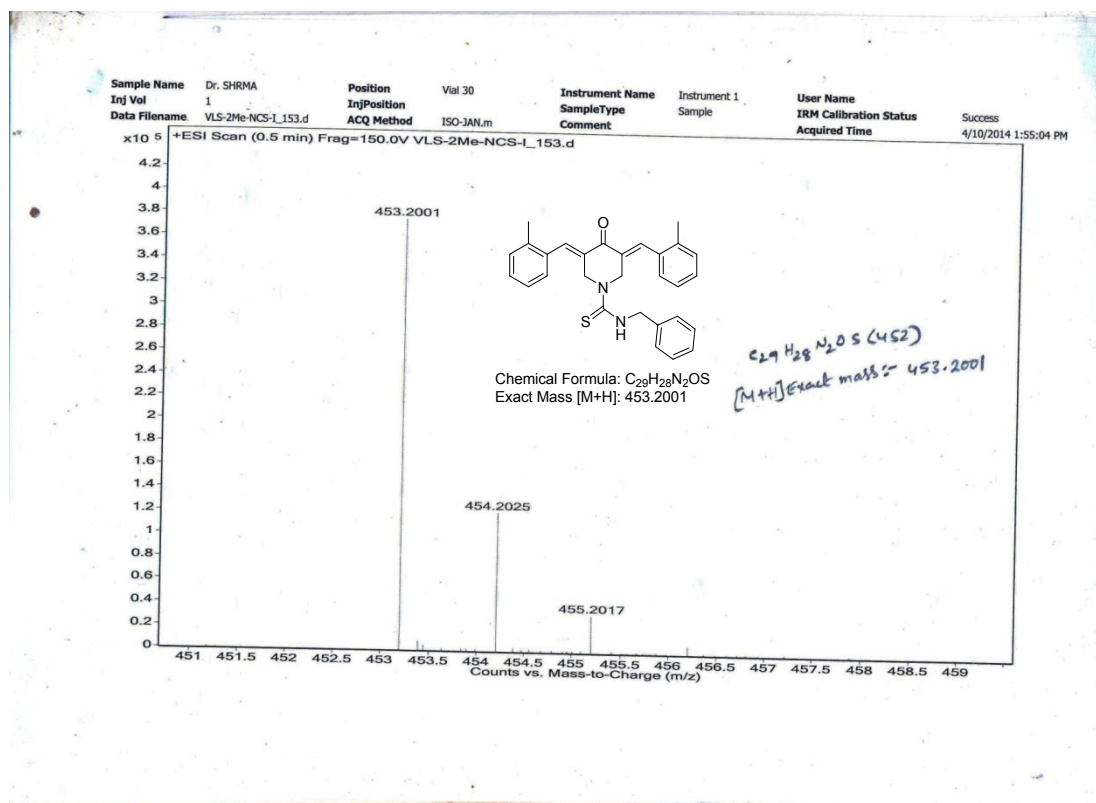
DEPT-135 Spectra of compound **47**(100 MHz, CDCl₃)



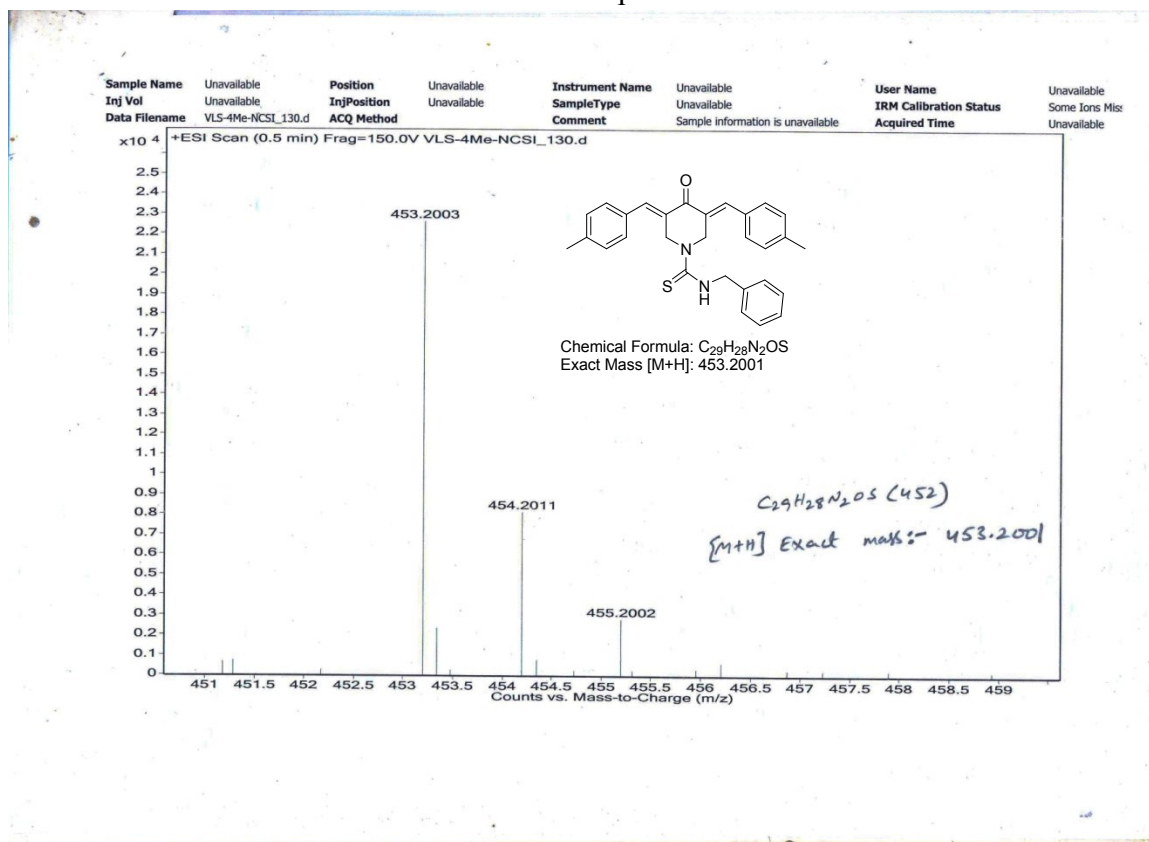
HRMS of compound 14



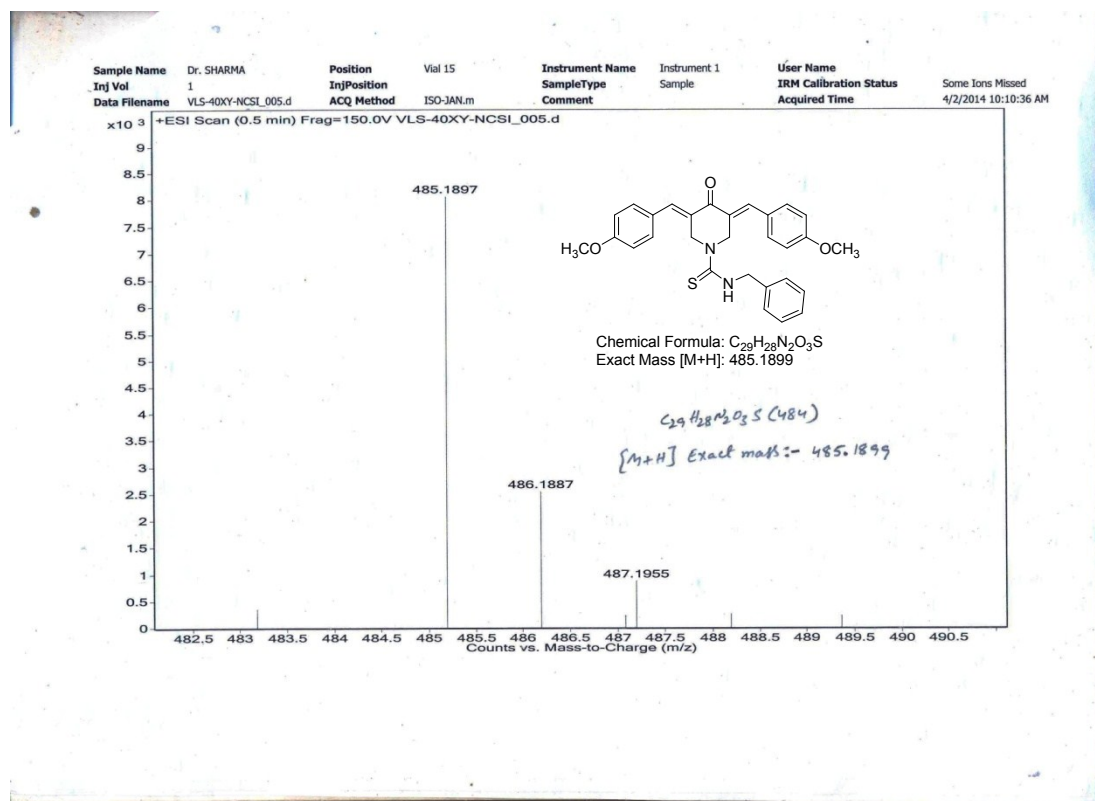
HRMS of compound 15



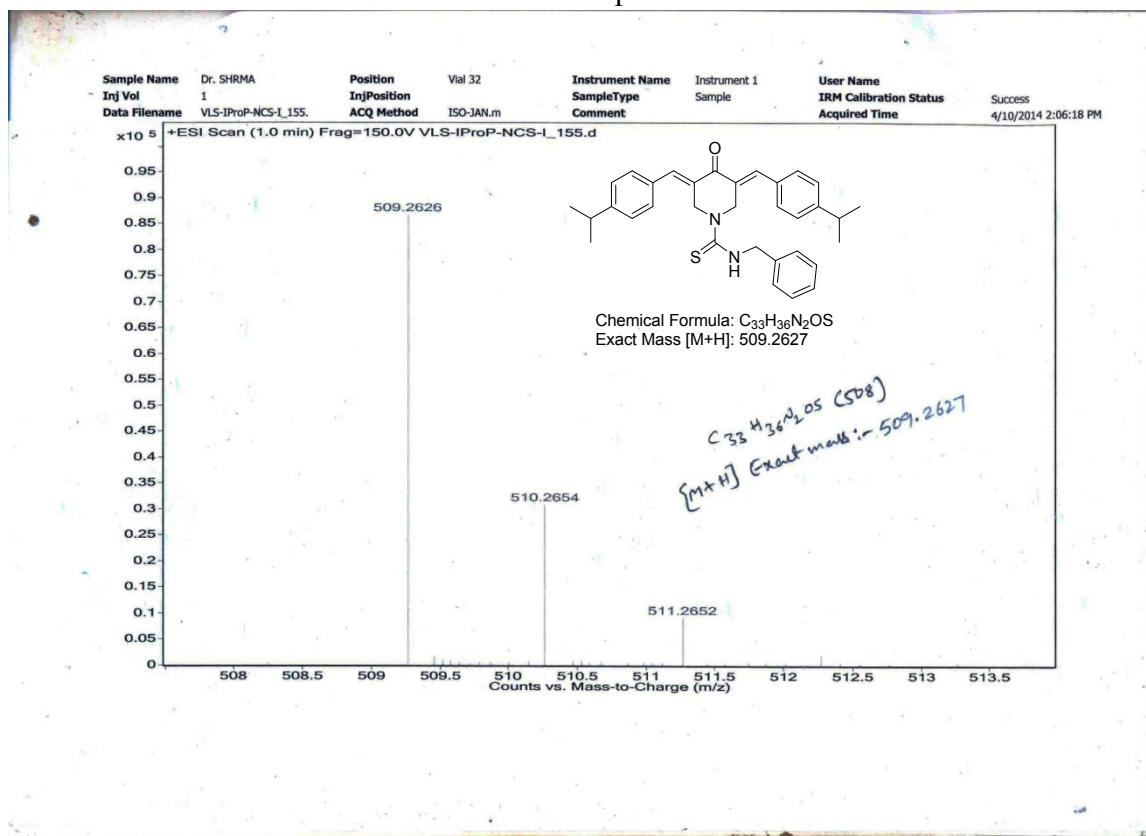
HRMS of compound 16



HRMS of compound 17

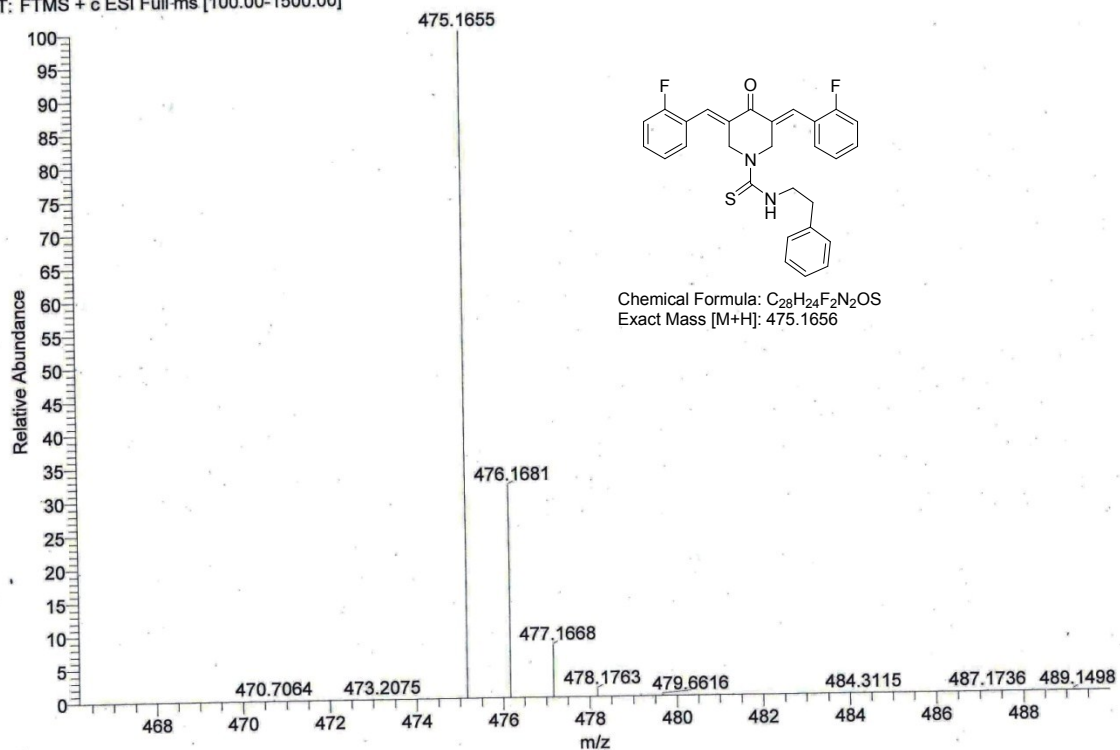


HRMS of compound 18



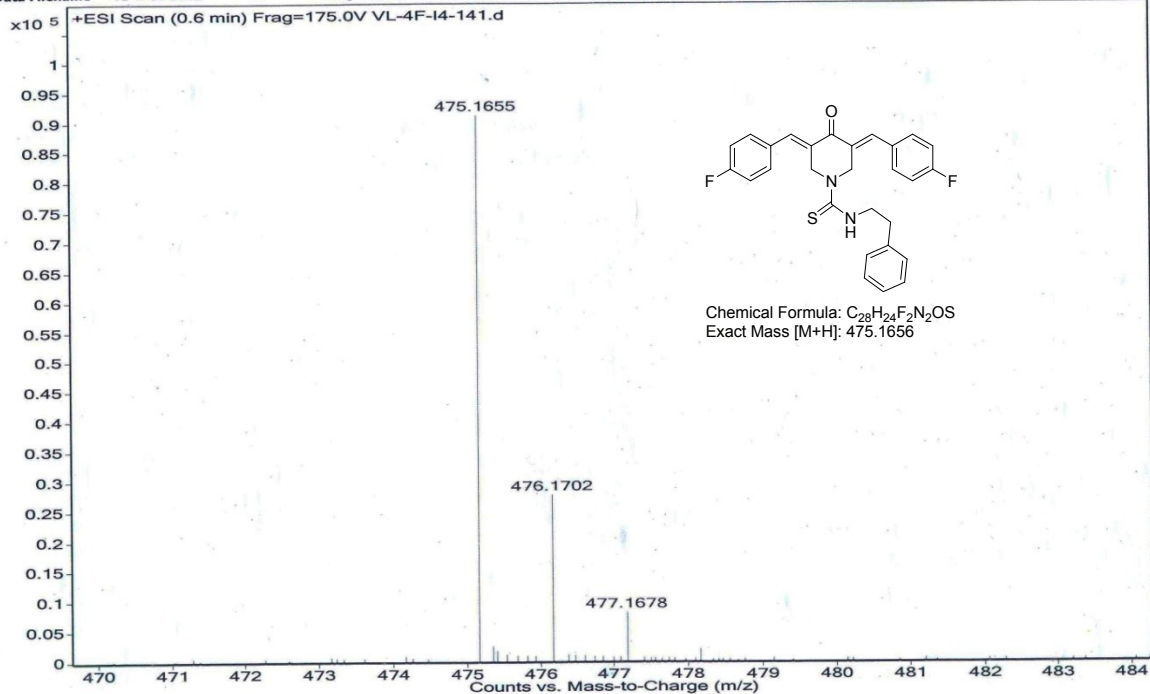
HRMS of compound 19

VL-2P-NCSIV #4-5 RT: 0.09-0.12 AV: 2 SB: 17 0.33-0.80, 0.01-0.03 NL: 1.22E6
T: FTMS + c ESI Full-ms [100.00-1500.00]

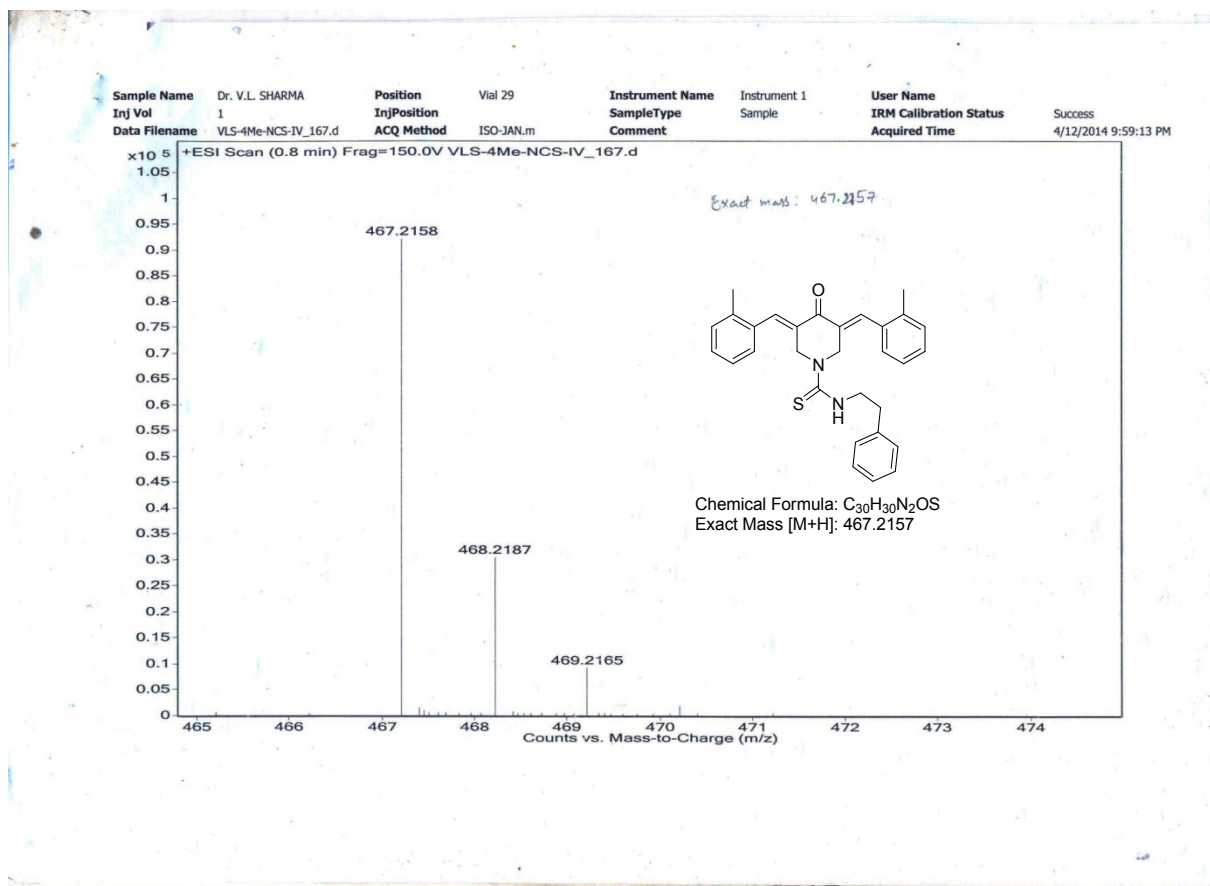


HRMS of compound 20

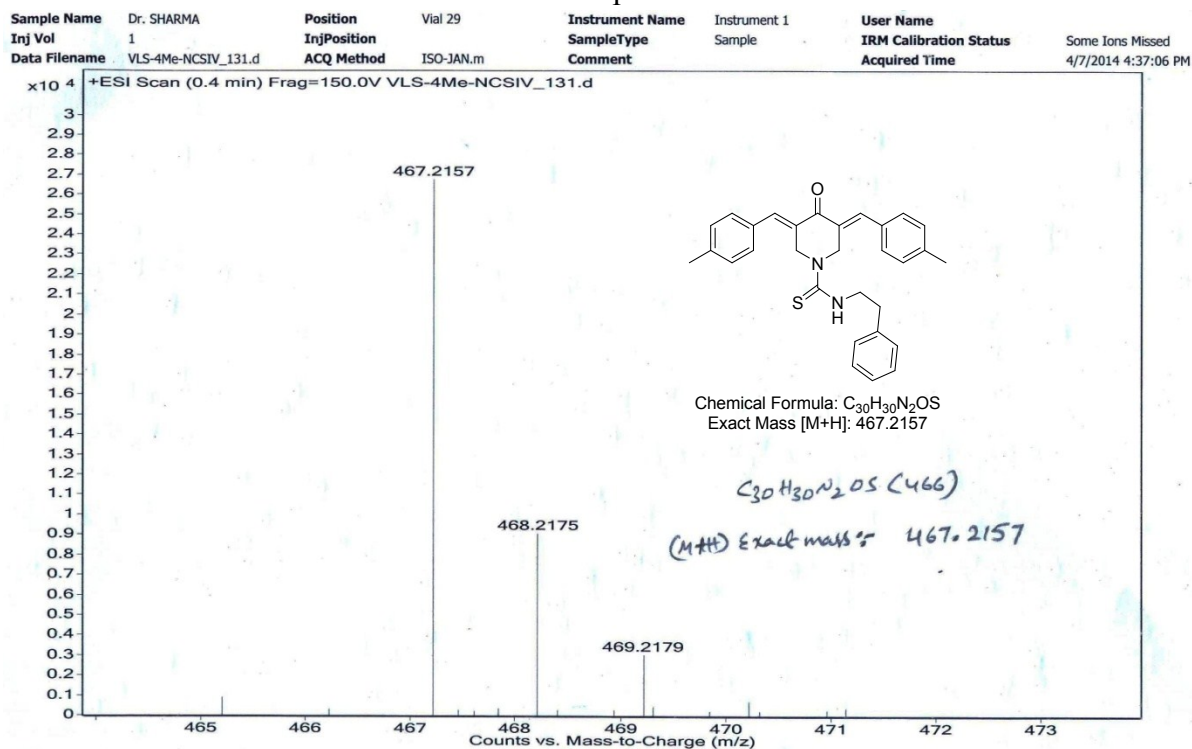
Sample Name	Dr. SHARMA/DHANARAJU	Position	Vial 14	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	VL-4F-I4-141.d	ACQ Method	ISO-DEC.m	Comment		Acquired Time	7/24/2015 2:05:58 PM



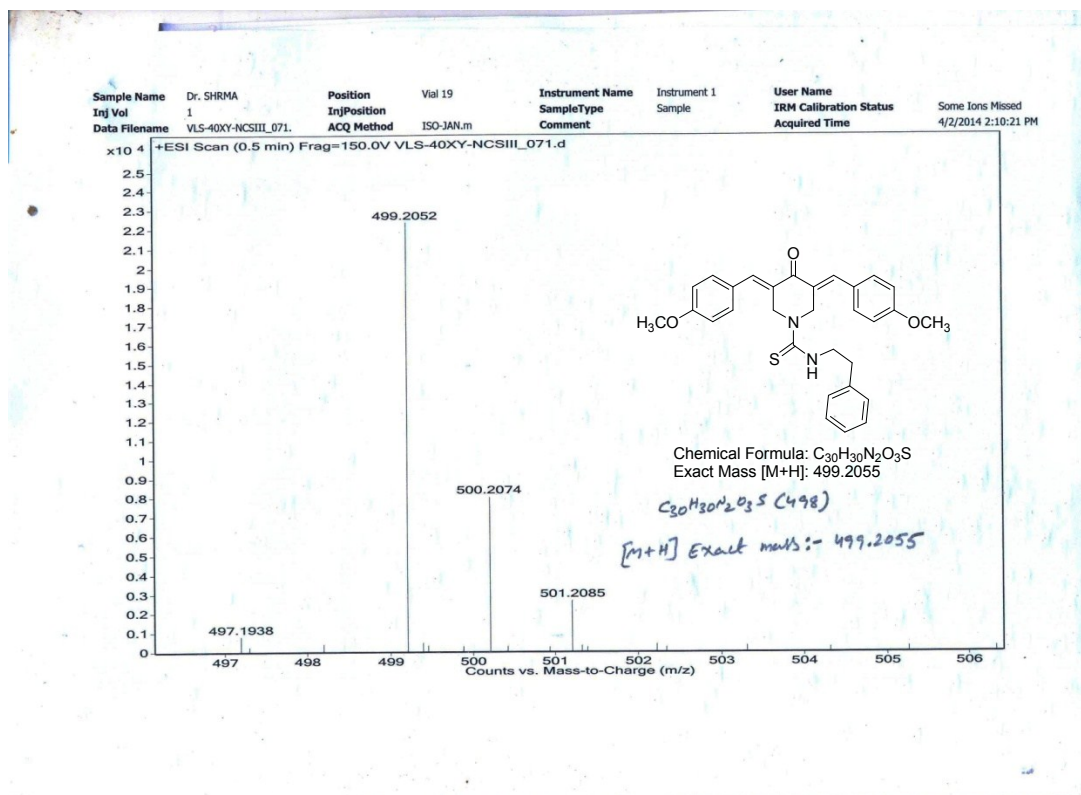
HRMS of compound 21



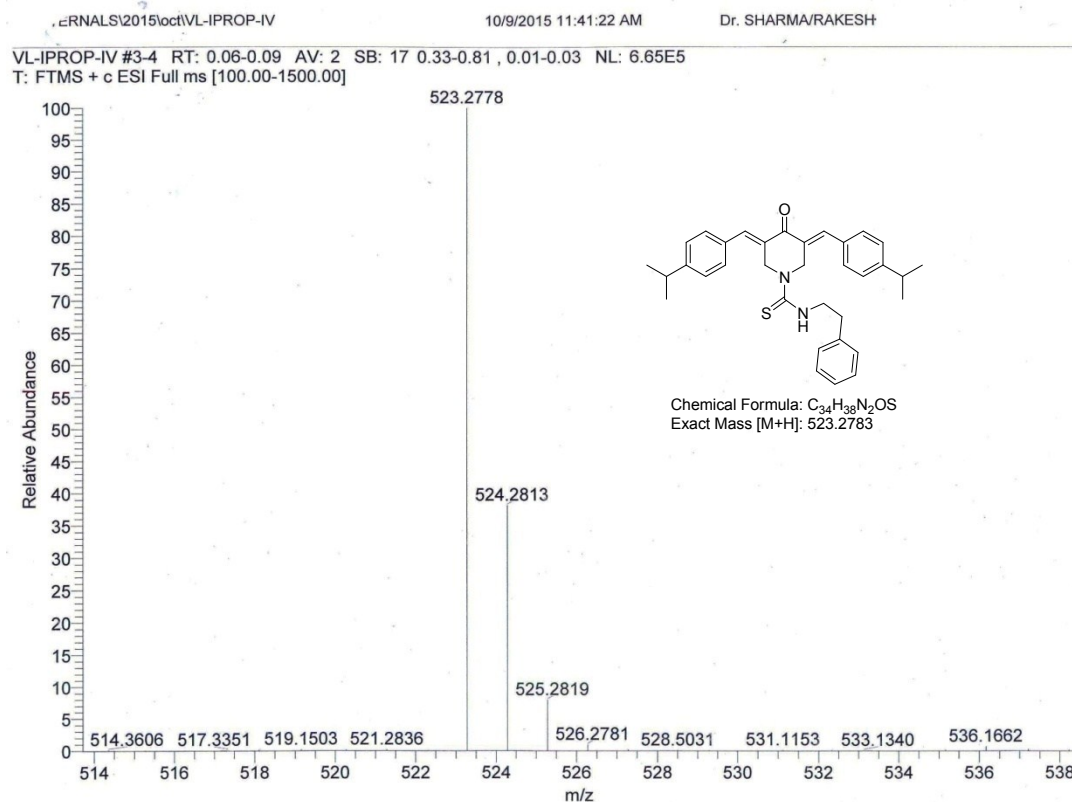
HRMS of compound 22



HRMS of compound 23

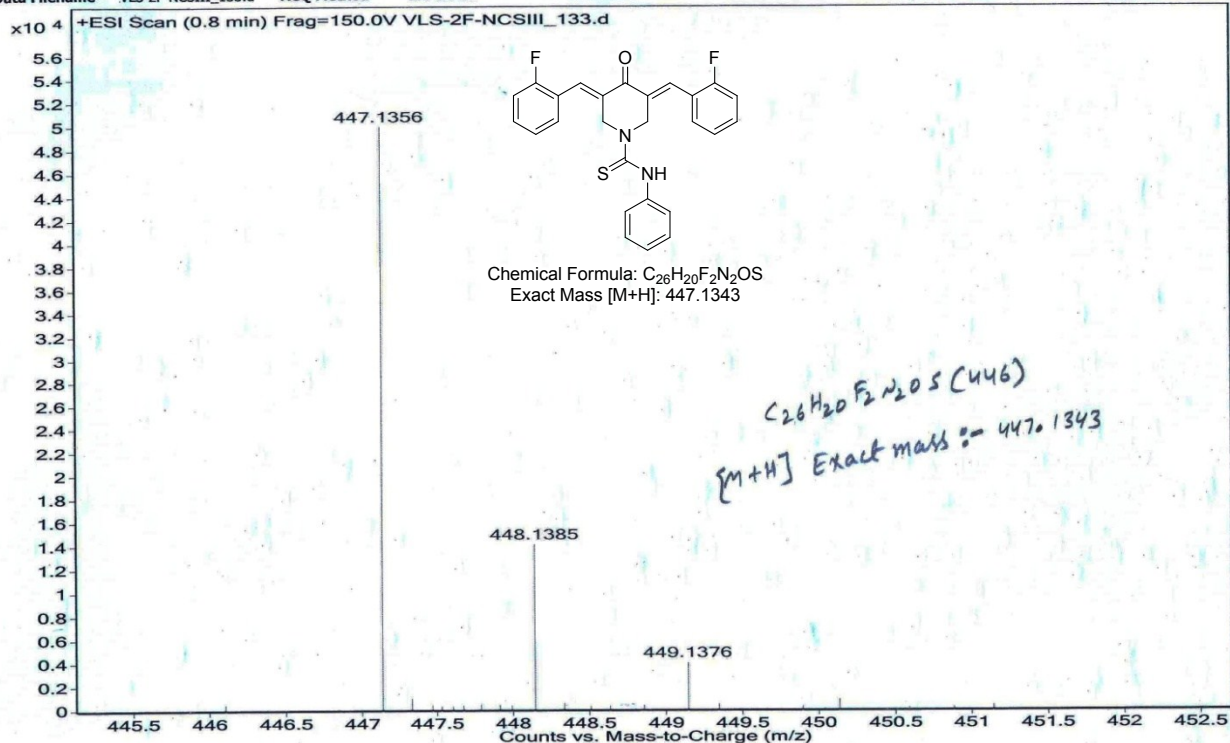


HRMS of compound 24



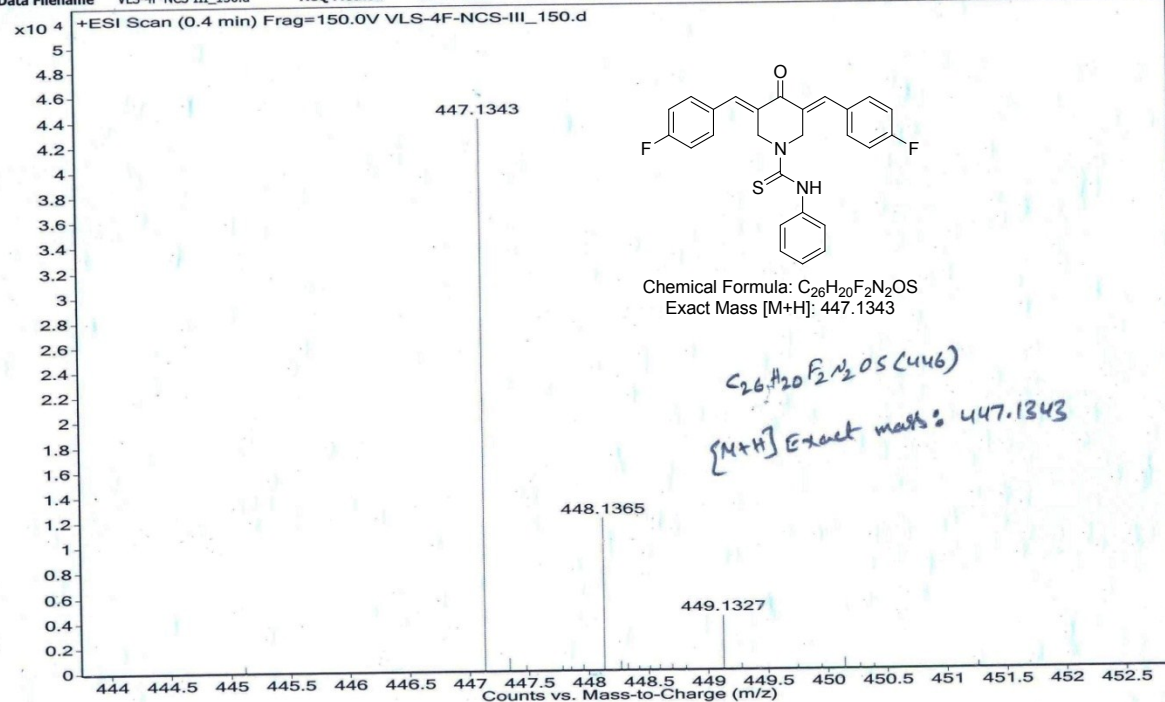
HRMS of compound 25

Sample Name	Dr. SHARMA	Position	Vial 31	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	VLS-2F-NCSIII_133.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/7/2014 4:42:17 PM



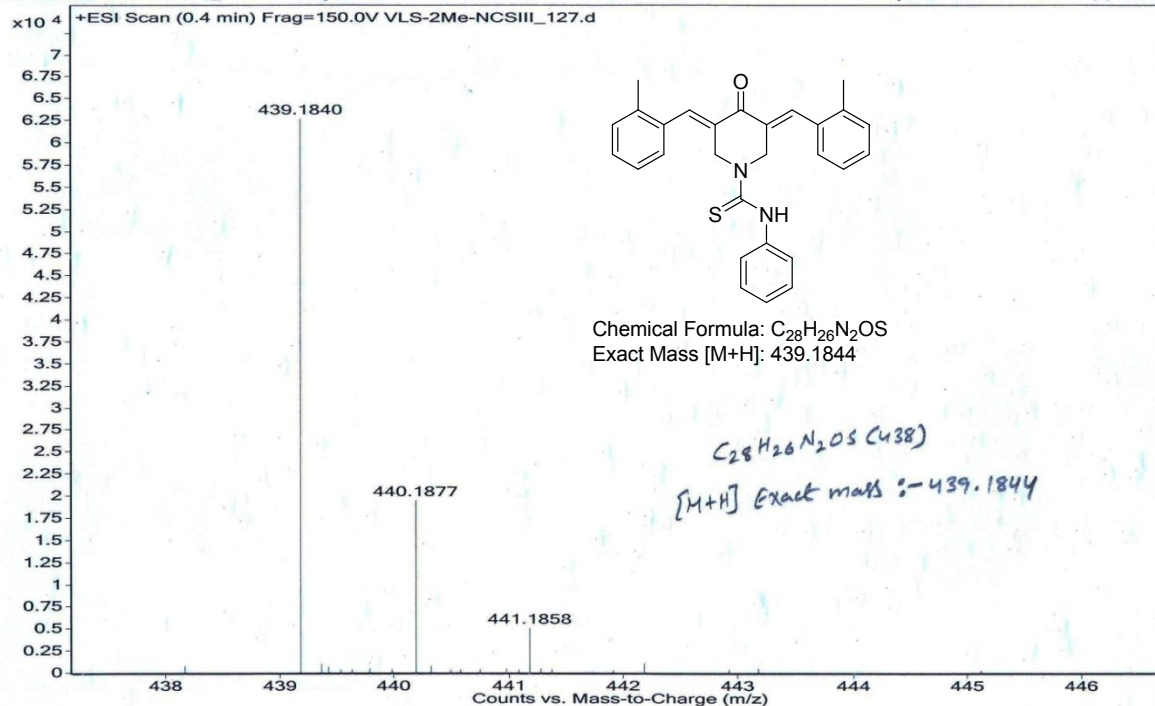
HRMS of compound 26

Sample Name	Dr. SHARMA	Position	Vial 27	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	VLS-4F-NCS-III_150.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/10/2014 1:38:11 PM



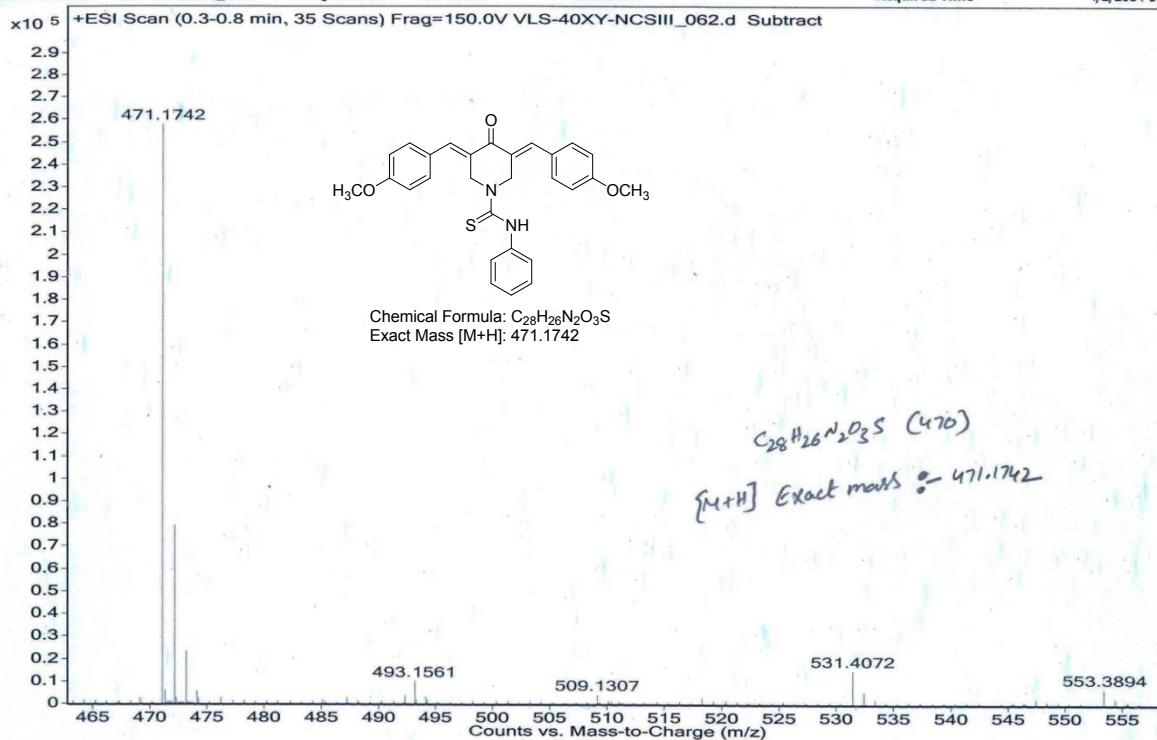
HRMS of compound 27

Sample Name	Dr. SHARMA	Position	Vial 25	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	VLS-2Me-NCSIII_127.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/7/2014 4:22:57 PM

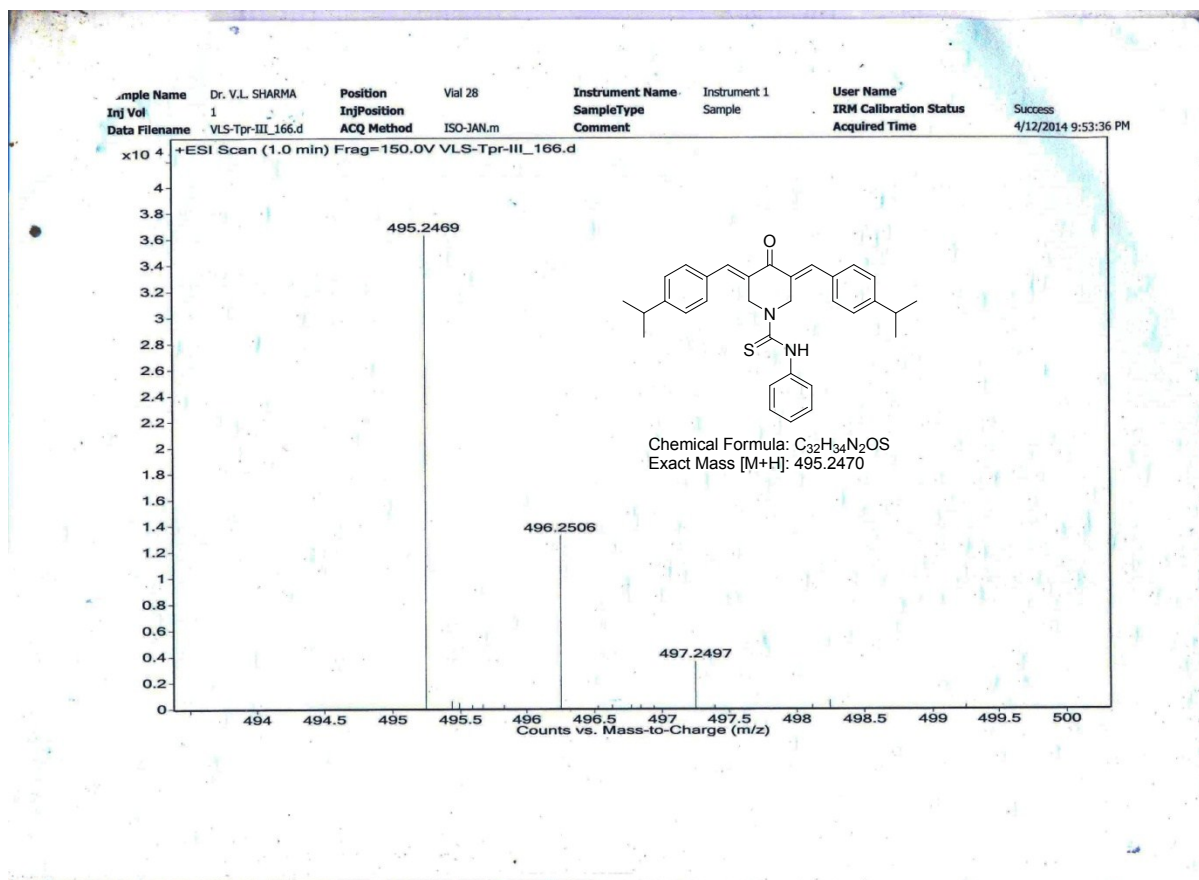


HRMS of compound 28

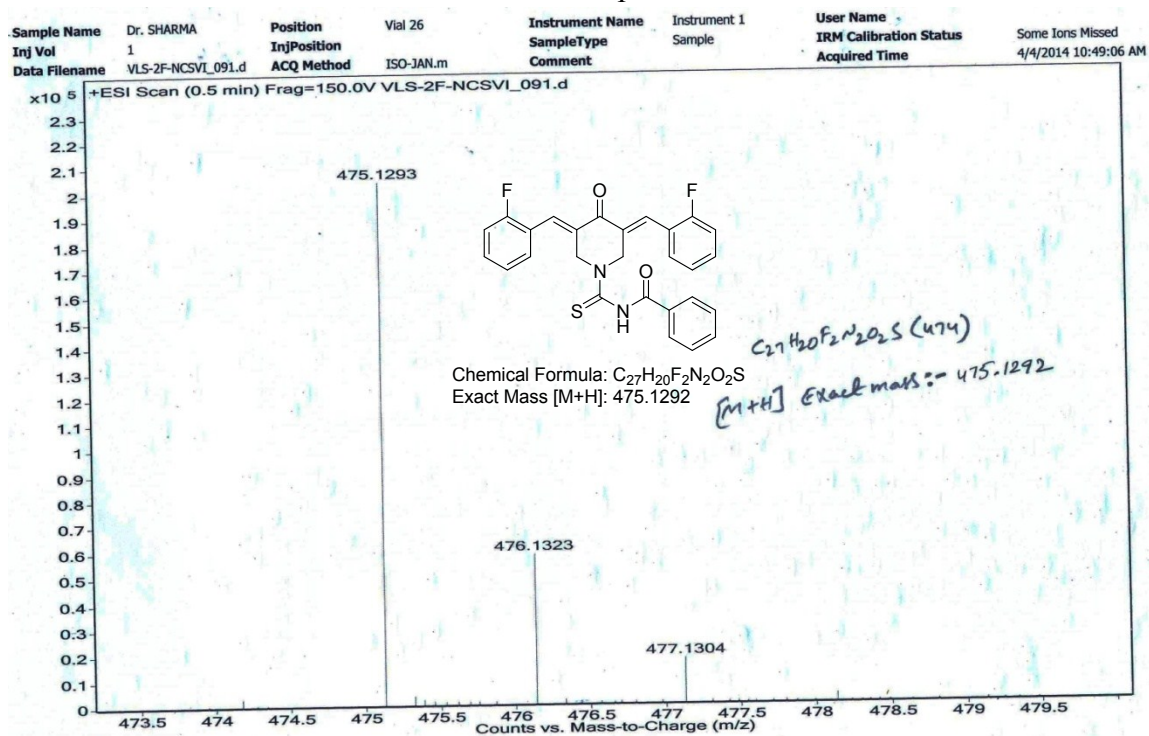
Sample Name	Dr. SHARMA	Position	Vial 25	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	VLS-40XY-NCSIII_062.	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/2/2014 1:37:44 PM



HRMS of compound 30

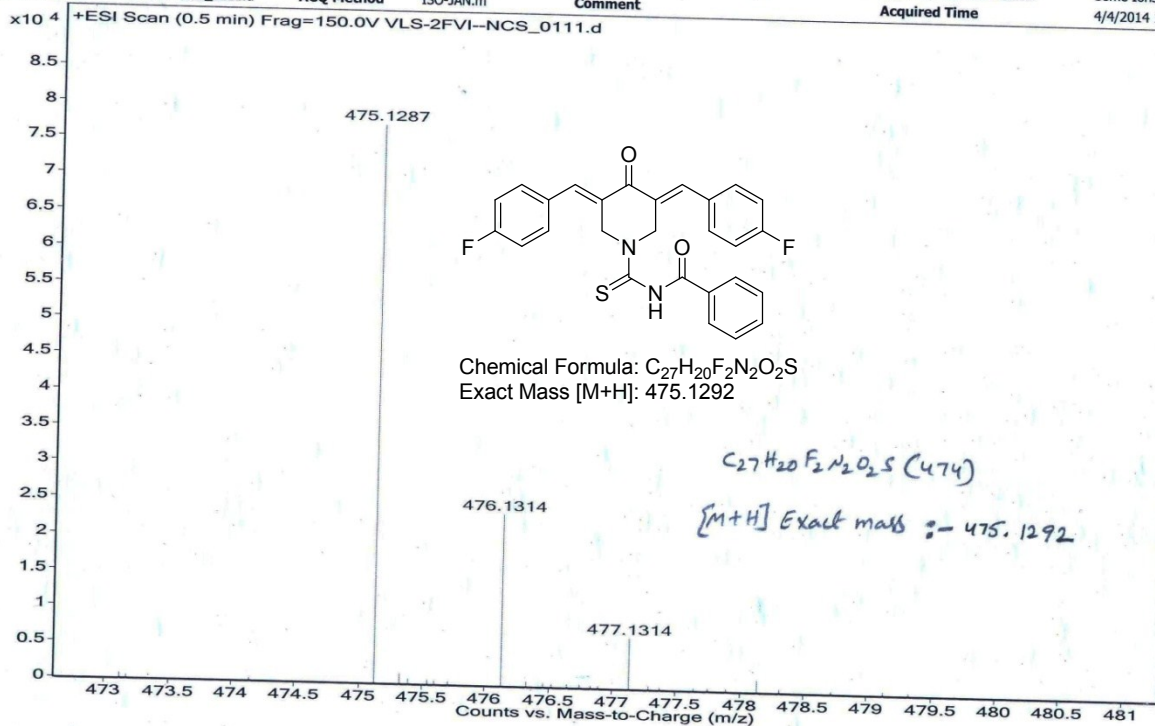


HRMS of compound 31



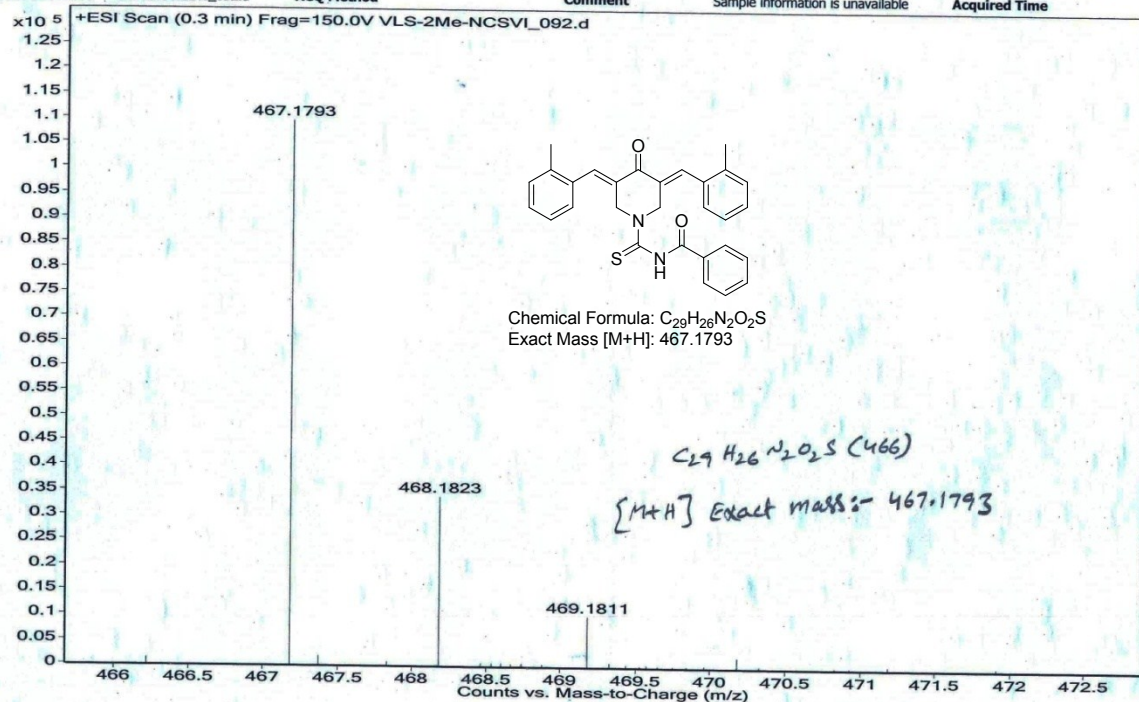
HRMS of compound 32

Sample Name	Dr. SHARMA	Position	Vial 26	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	VLS-2FVI-NCS_0111.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/4/2014 12:10:45 PM

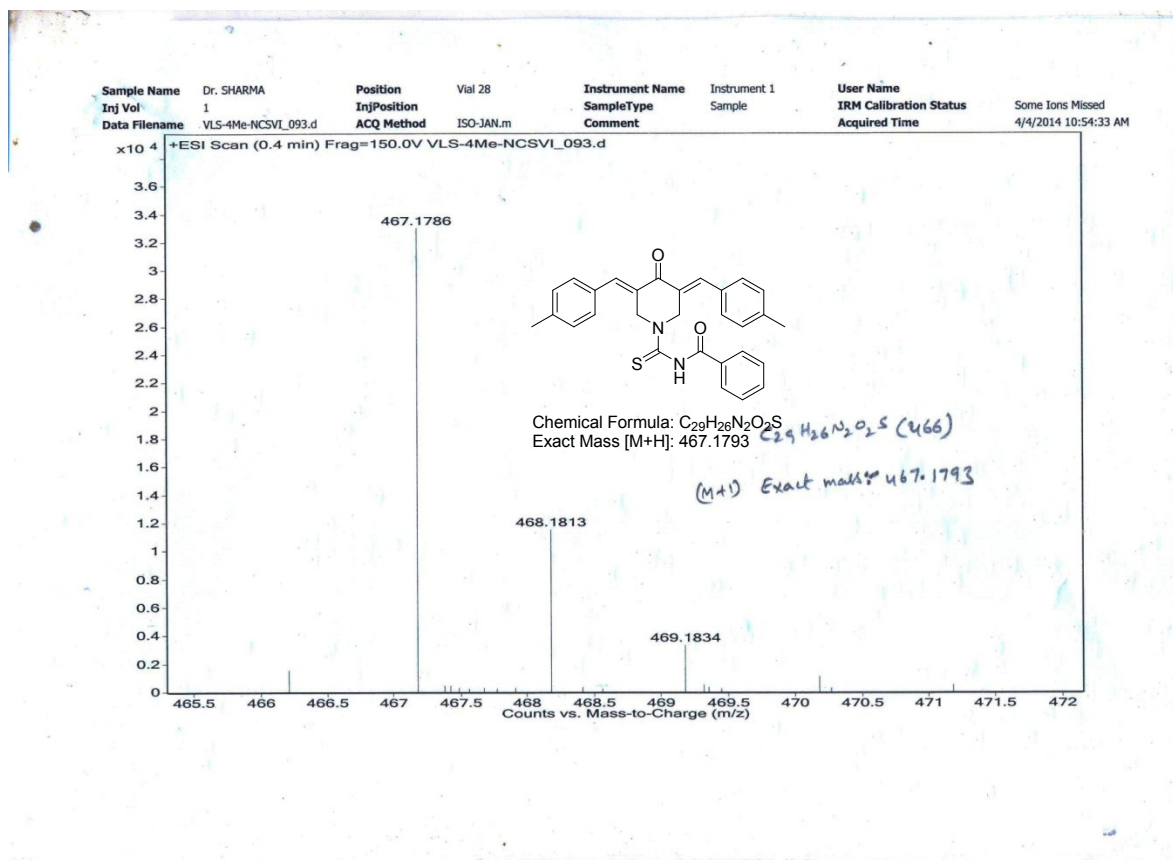


HRMS of compound 33

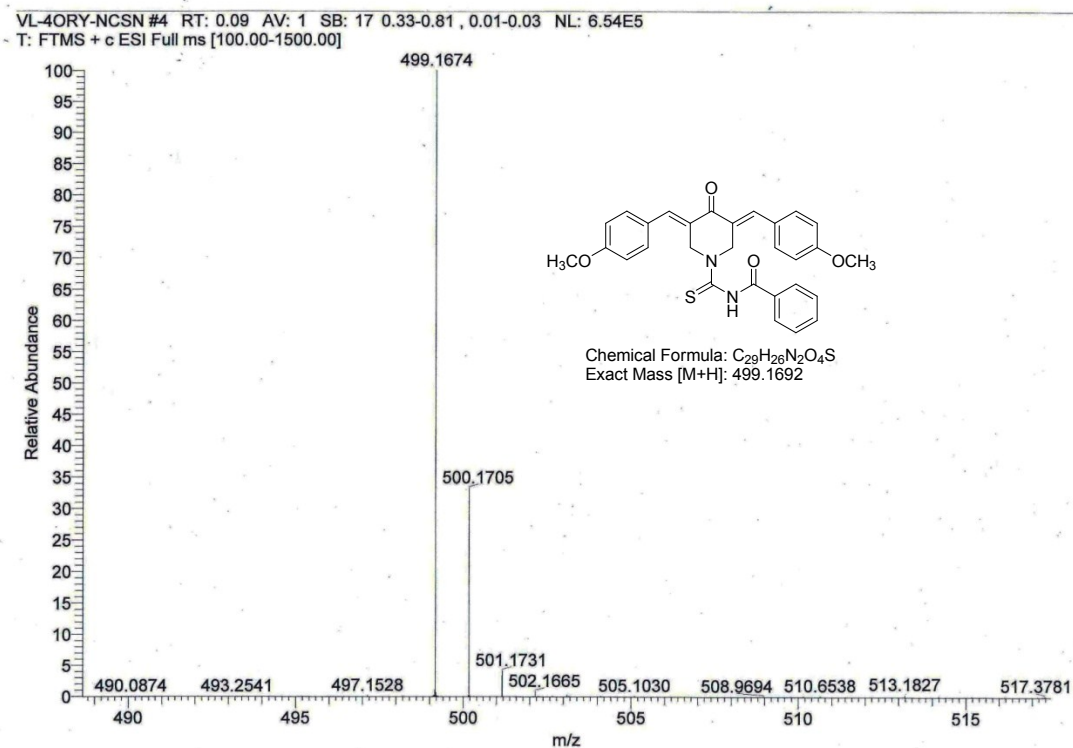
Sample Name	Unavailable	Position	Unavailable	Instrument Name	Unavailable	User Name	Unavailable
Inj Vol	Unavailable	InjPosition	Unavailable	SampleType	Unavailable	IRM Calibration Status	Some Ions
Data Filename	VLS-2Me-NCSVI_092.d	ACQ Method		Comment	Sample information is unavailable	Acquired Time	Unavailable



HRMS of compound 34

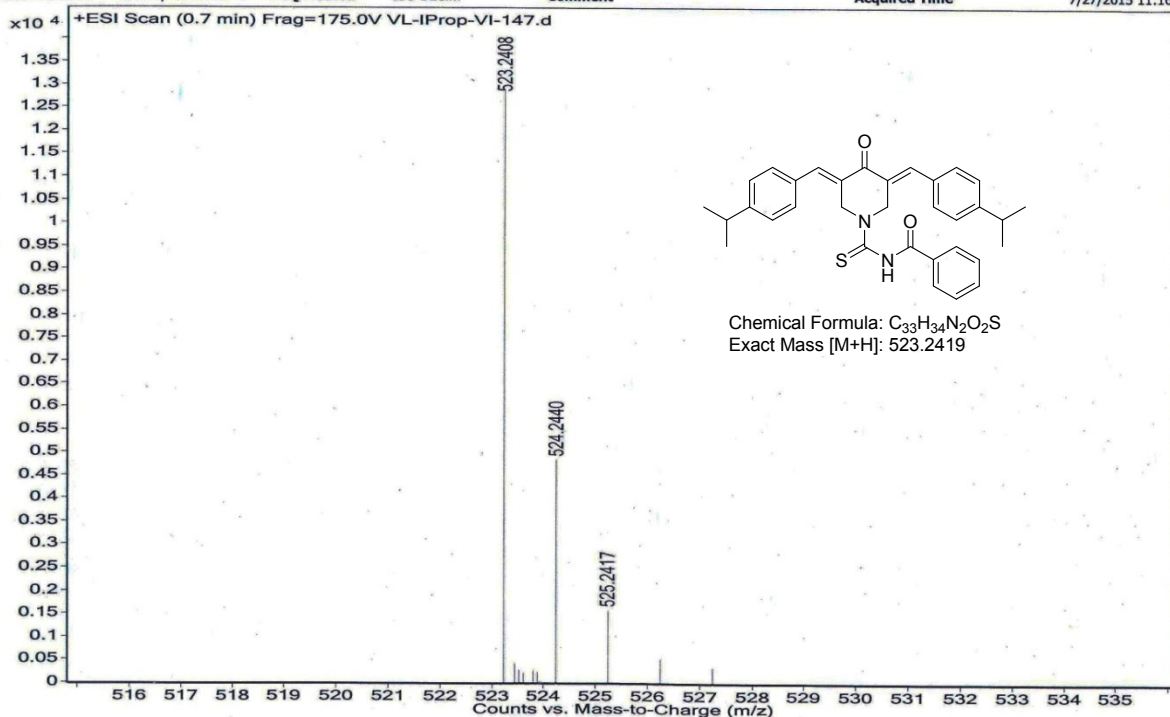


HRMS of compound 35

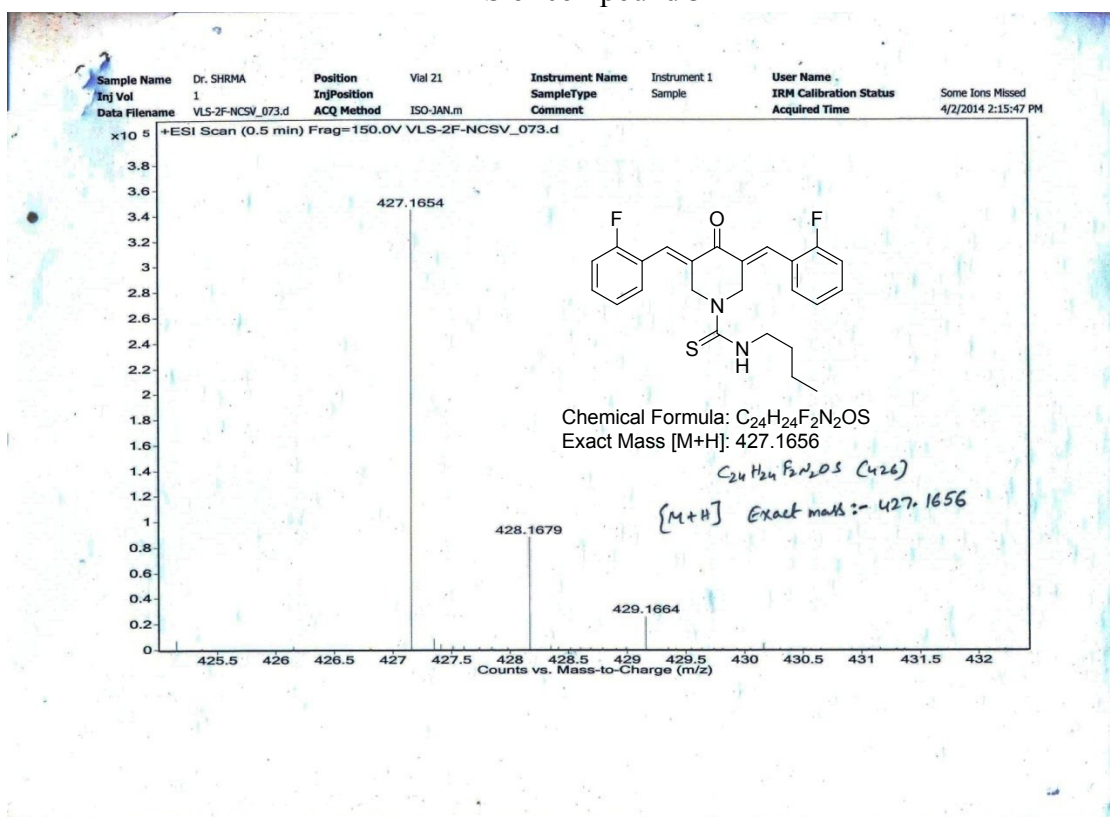


HRMS of compound 36

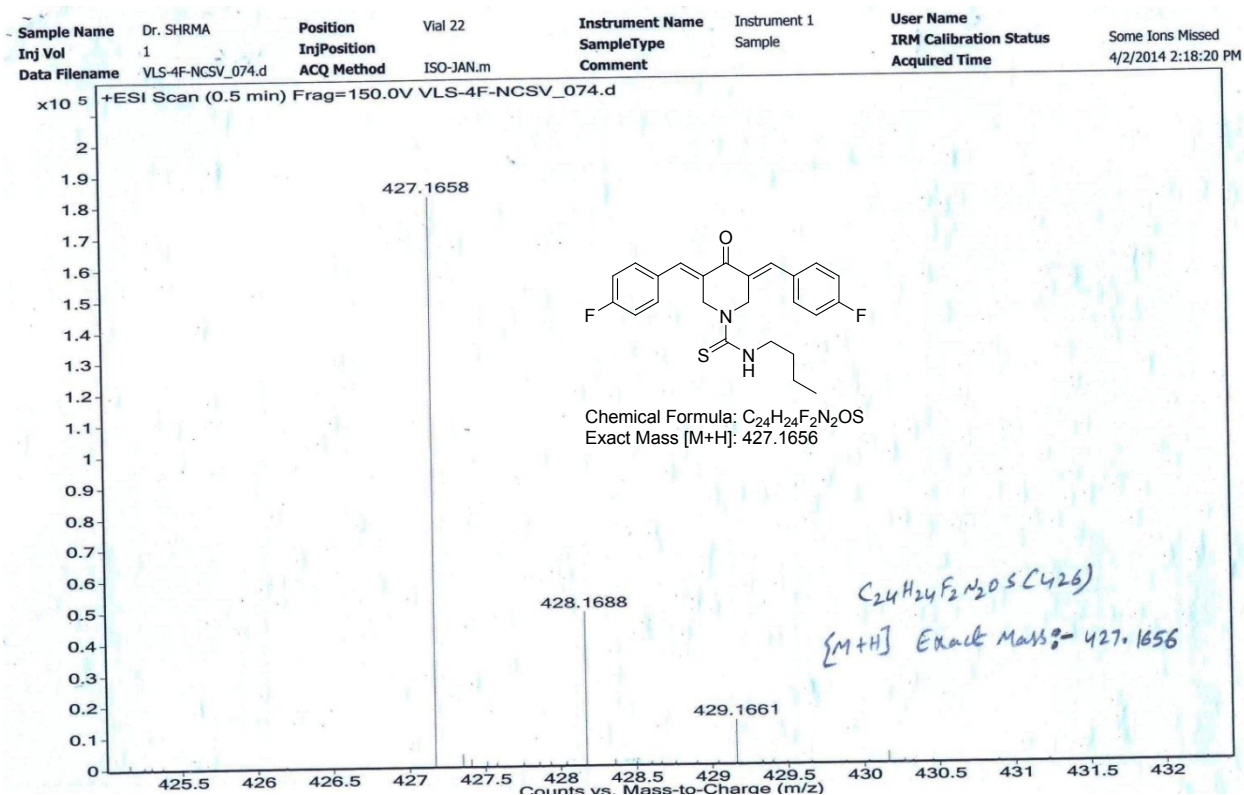
Sample Name	Dr. SHARMA/SONAL	Position	Vial 4	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	VL-IProp-VI-147.d	ACQ Method	ISO-DEC.m	Comment		Acquired Time	7/27/2015 11:16:53 AM



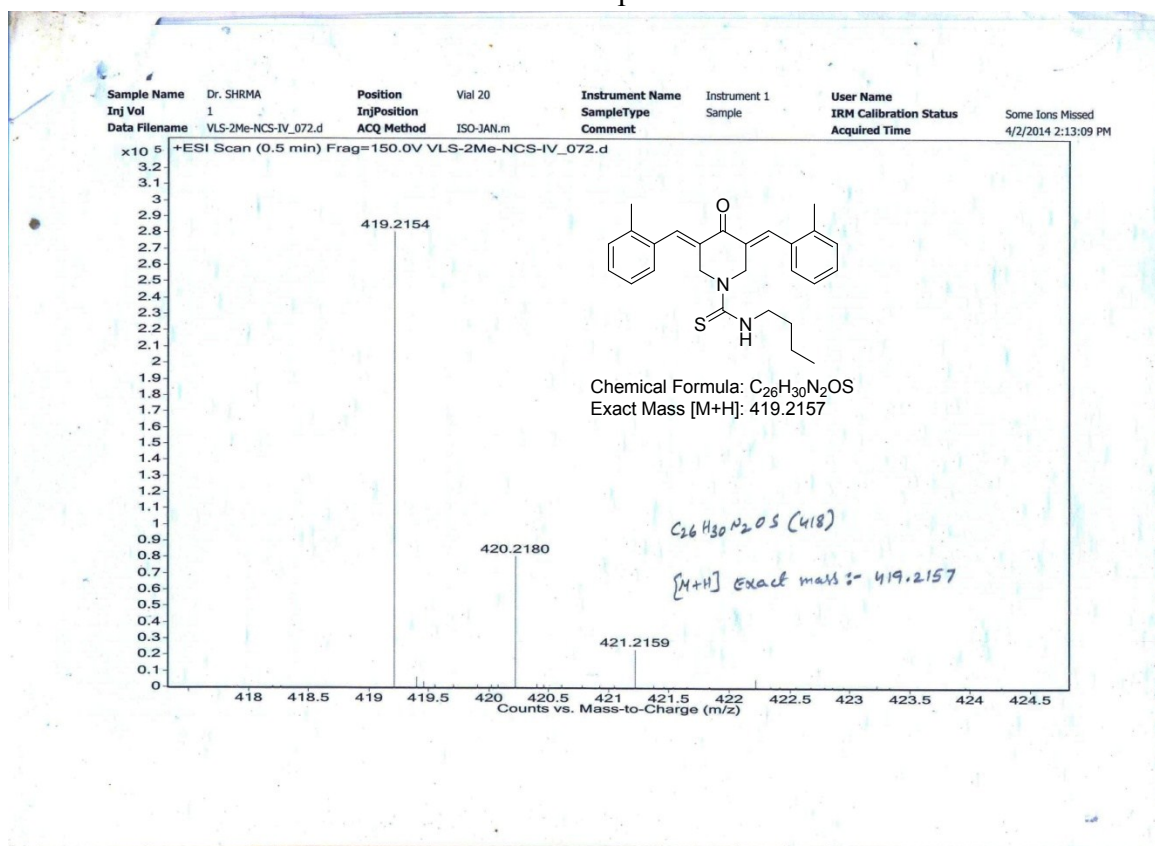
HRMS of compound **37**



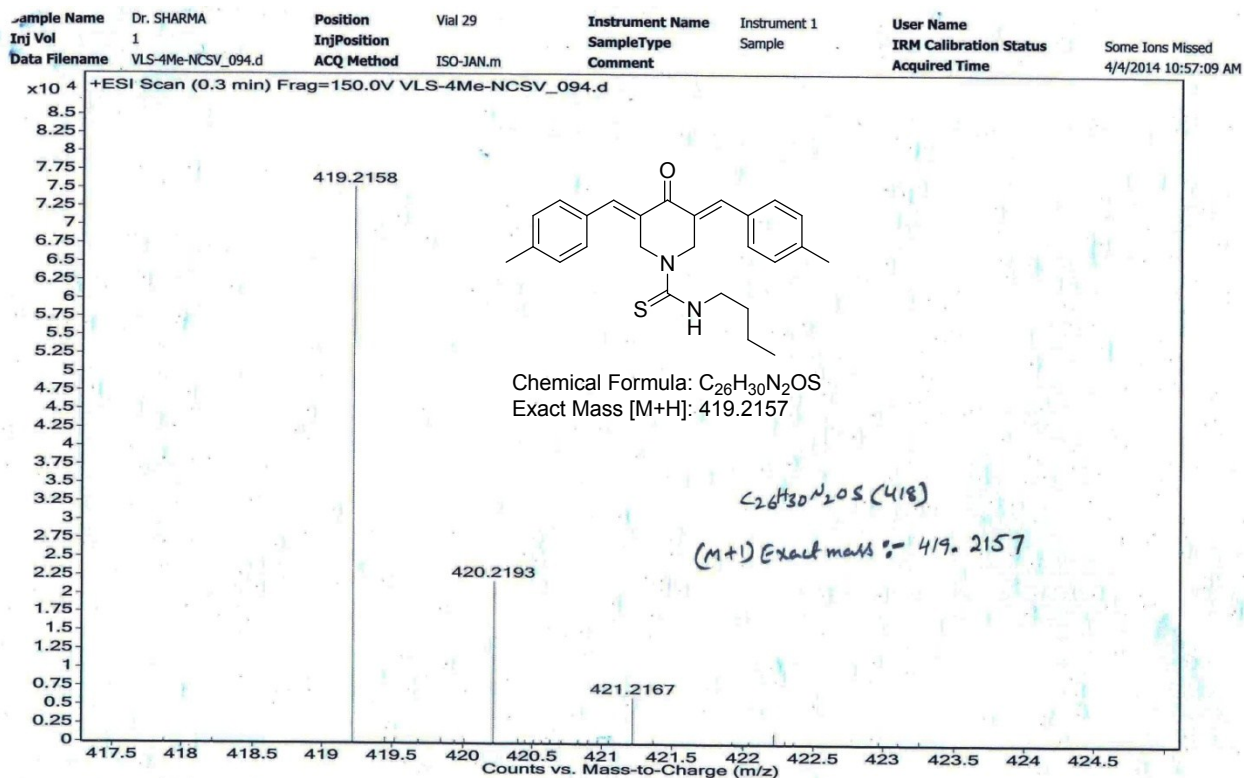
HRMS of compound **38**



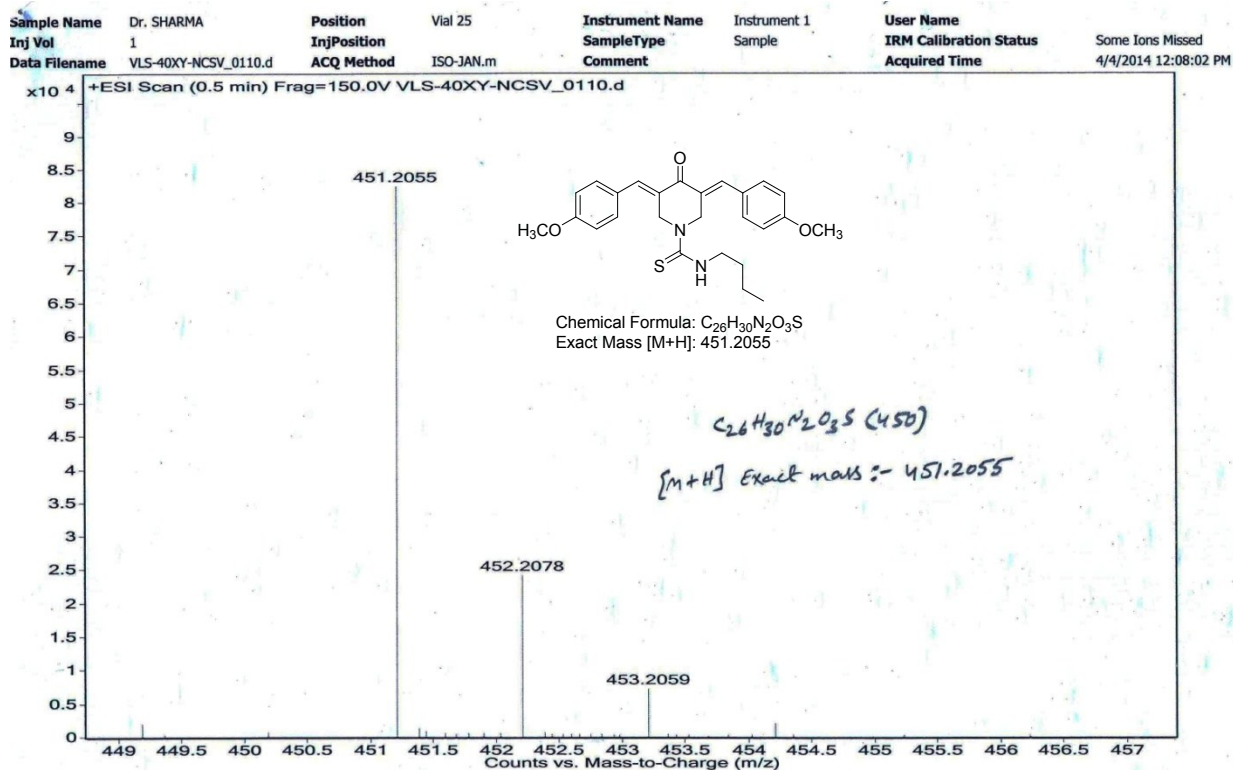
HRMS of compound 39



HRMS of compound 40

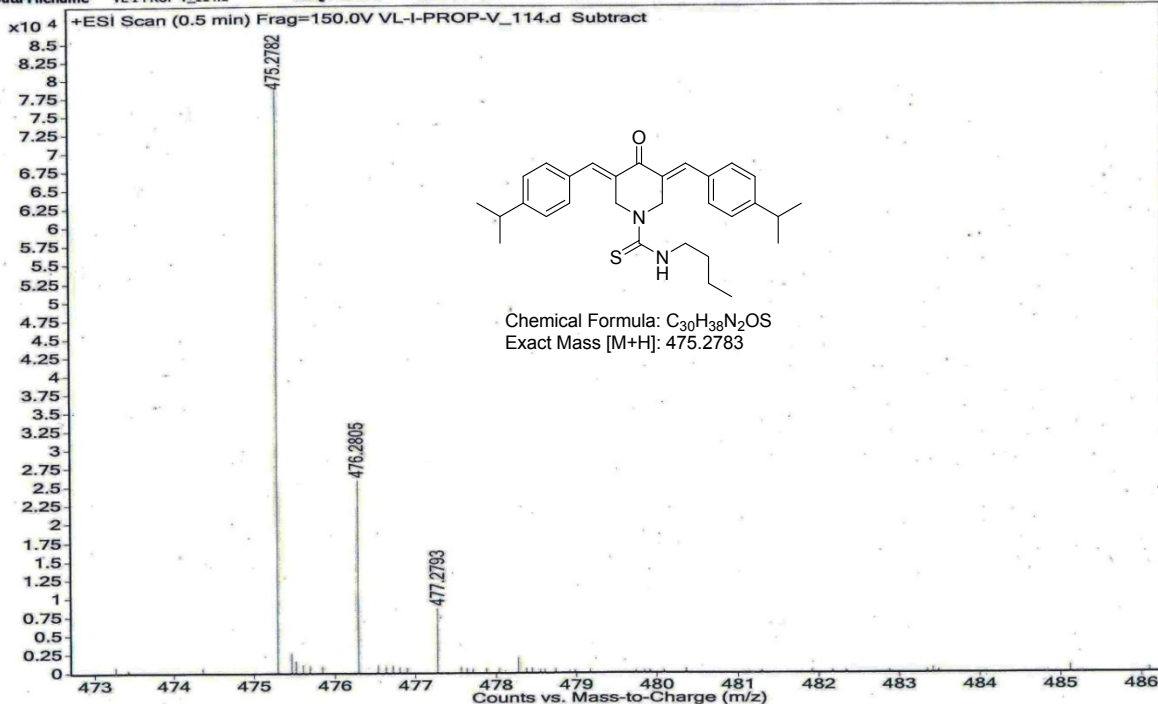


HRMS of compound 41



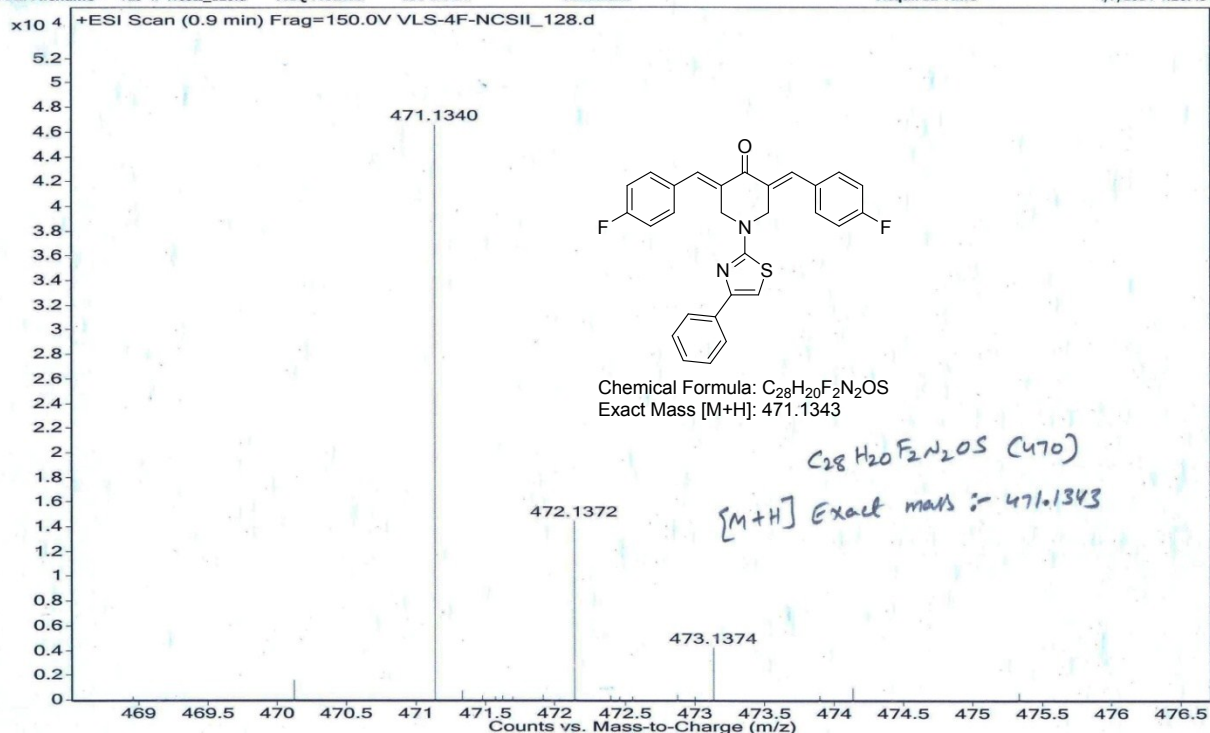
HRMS of compound 42

Sample Name	Dr.SHARMA/DHANRAJU	Position	Vial 1	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	VL-I-PROP-V_114.d	ACQ Method	ISOCRATIC.m	Comment		Acquired Time	10/14/2015 10:55:46 AM



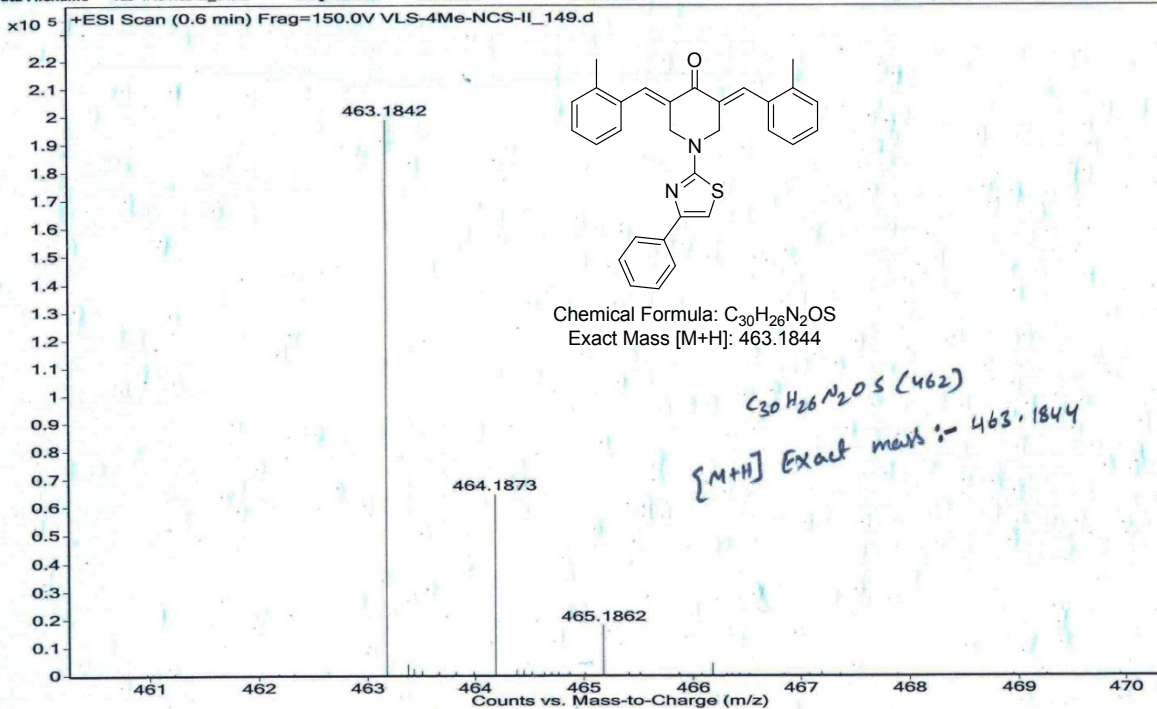
HRMS of compound 43

Sample Name	Dr. SHARMA	Position	Vial 26	Instrument Name	Instrument 1	User Name	
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	Some Ions Missed
Data Filename	VLS-4F-NCSII_128.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time	4/7/2014 4:26:45 PM



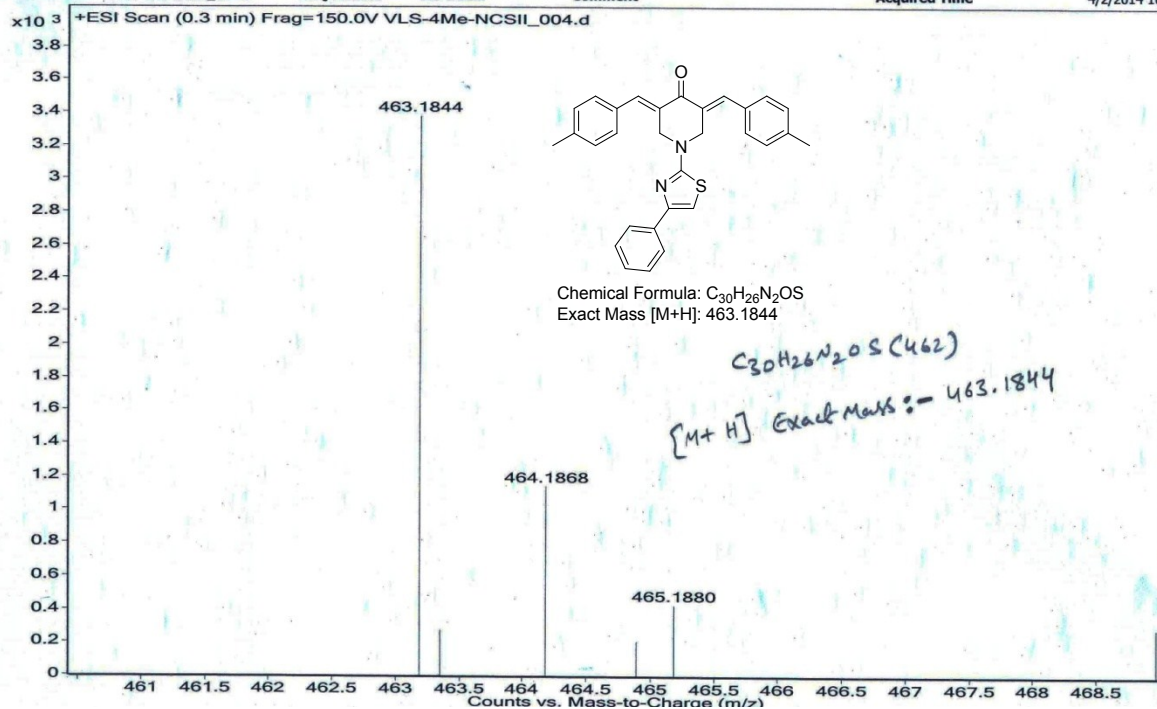
HRMS of compound 45

Sample Name	Dr. SHARMA	Position	Vial 26	Instrument Name	Instrument 1	User Name	IRM Calibration Status	Success
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status		4/10/2014 1:32:33 PM
Data Filename	VLS-4Me-NCS-II_149.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time		



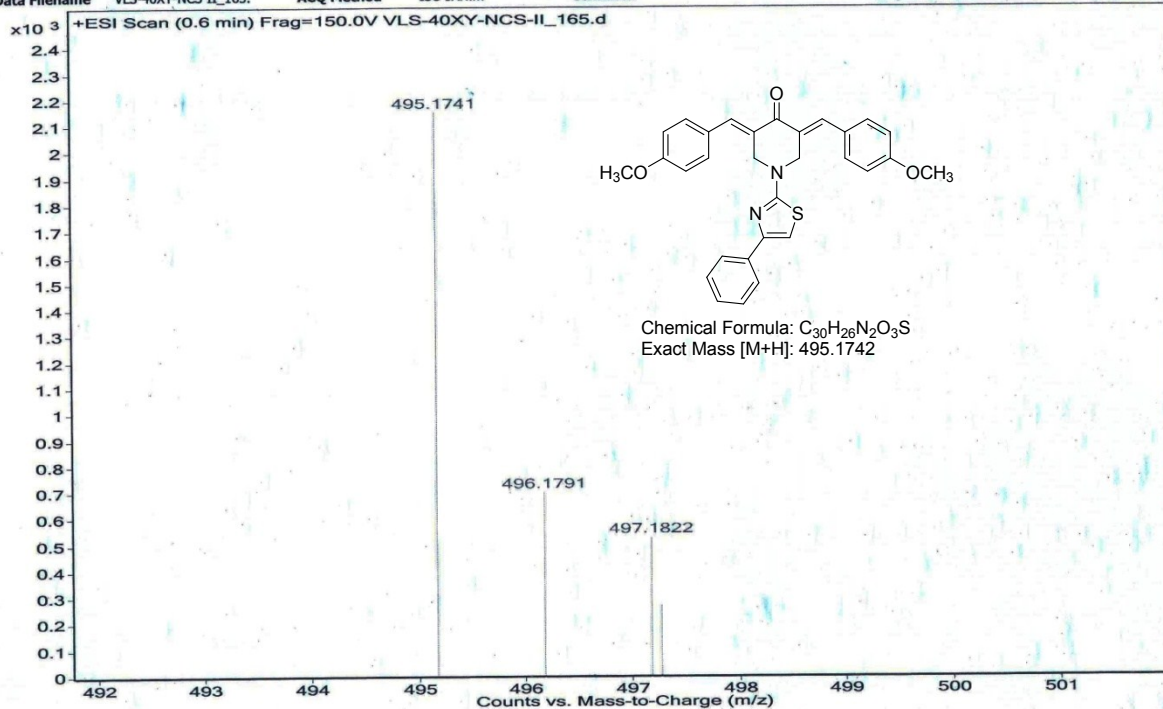
HRMS of compound 46

Sample Name	Dr. SHARMA	Position	Vial 14	Instrument Name	Instrument 1	User Name	IRM Calibration Status	Some Ions Missed
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status		4/2/2014 10:07:54 AM
Data Filename	VLS-4Me-NCSII_004.d	ACQ Method	ISO-JAN.m	Comment		Acquired Time		

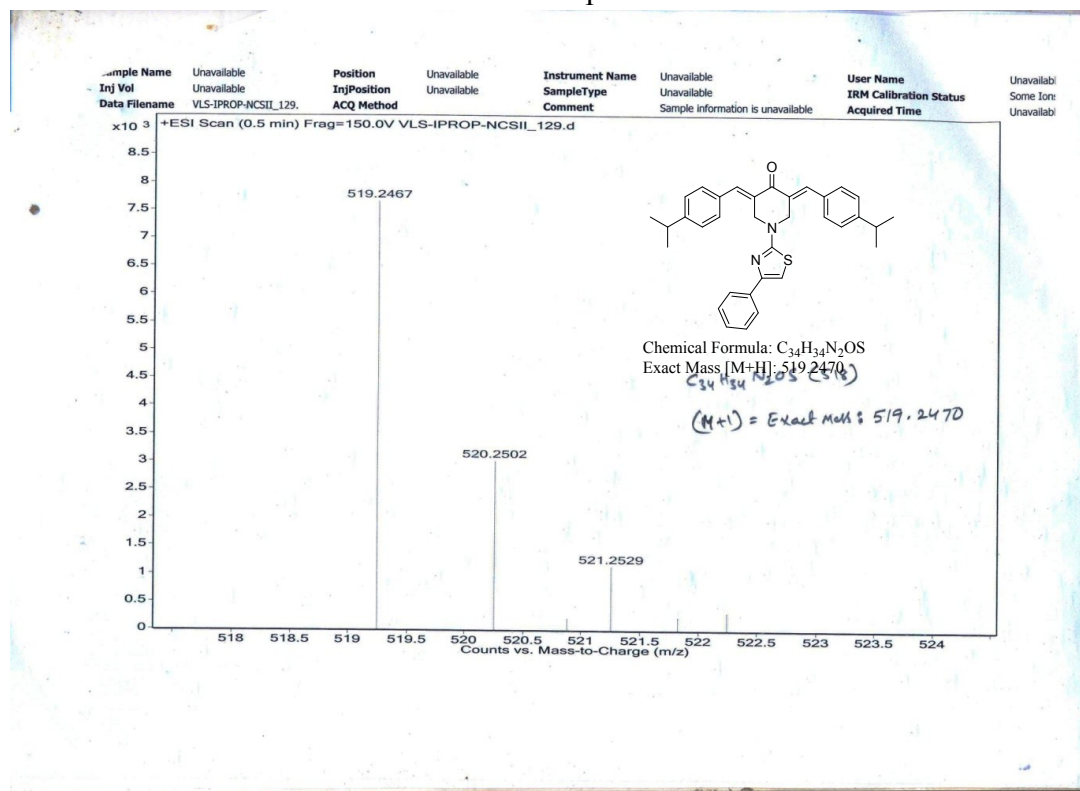


HRMS of compound 47

Sample Name	Dr. V.L. SHARMA	Position	Vial 27	Instrument Name	Instrument 1	User Name	Success
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status	4/12/2014 9:48:00 PM
Data Filename	VLS-40XY-NCS-II_165.	ACQ Method	ISO-JAN.m	Comment		Acquired Time	



HRMS of compound 48



HRMS of compound 49

IC₅₀ calculation- We have calculated the IC₅₀ value by the Graph Pad Prism software version 5.01. For the calculation of IC₅₀ values we have performed antiligase activity of compound **23** at 100, 50, 25, 12.5, and 6.25 μ M concentrations whereas antiproliferative activity was performed at 50, 25, 12.5, 6.25 and 3.12 μ M concentrations. At the different concentration of compound **23**, percent of antiligase and antiproliferative activities were determined and IC₅₀ values were calculated by plotting the data log inhibitor vs. normalised response using Graph Pad Prism. The graphs have been shown in figure S2. We have found 24.9 $\pm$ 1.8 μ M (Figure S2A) and 8.7 $\pm$ 1.9 μ M (Figure S2B) IC₅₀ values for antiligase and antiproliferative activities of compound **23** respectively.

Figure S2. Graphs for IC₅₀ calculation (A) for antiligase activity (B) for antiproliferative activity.

