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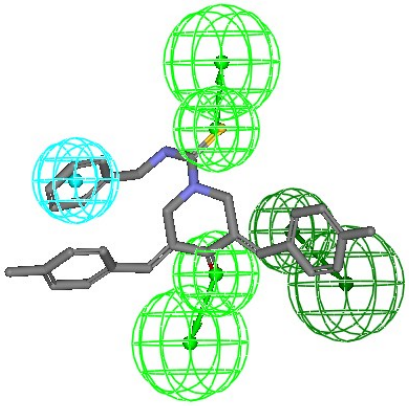
Figure S1. Ligand pharmacophore mapping of the top designed compounds on the pharmacophore model.



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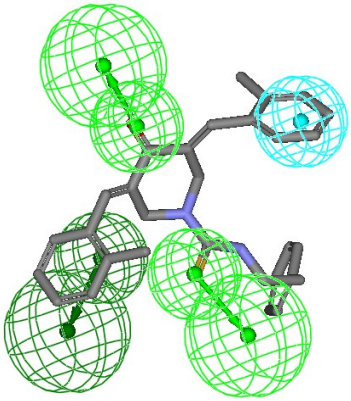

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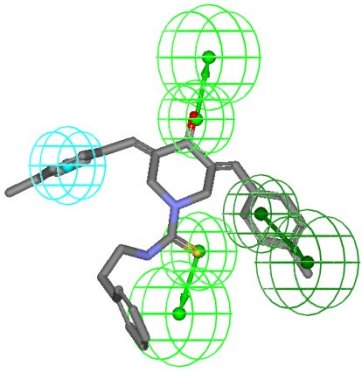

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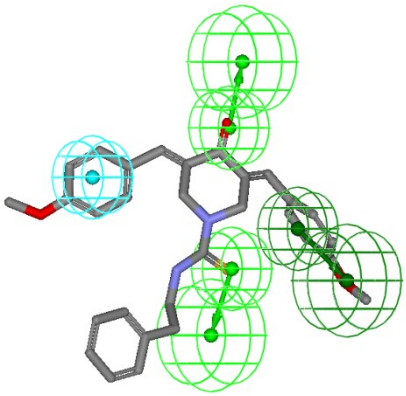

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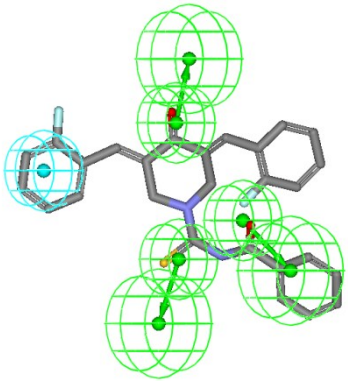

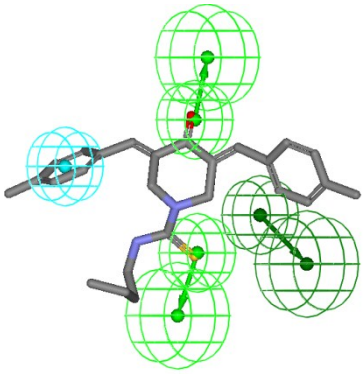

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Table S1. The summaries of hypothesis run

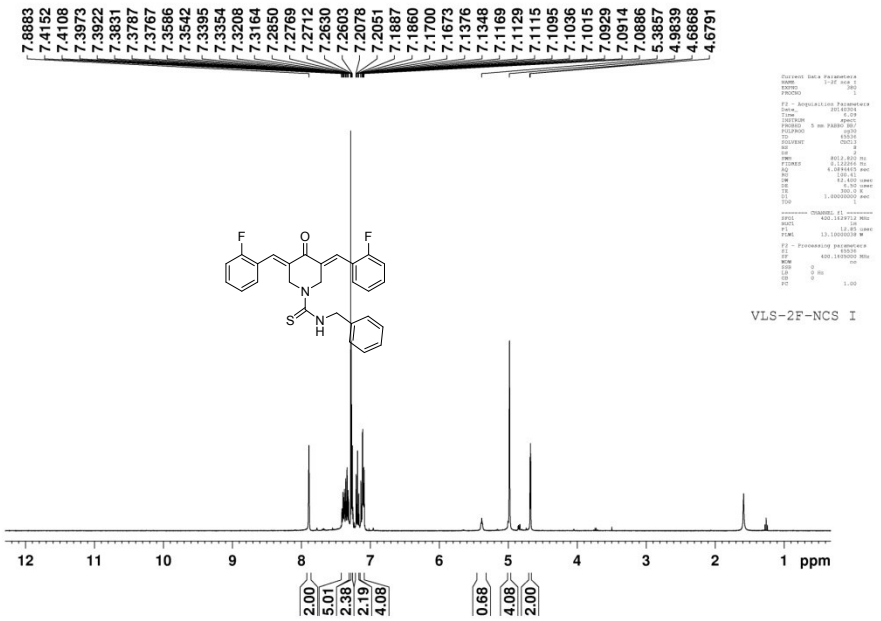
Features	Rank	Direct Hit	Partial Hit	Max Fit	Max. Fit
01	ZHHH	84.746	1111111111	0000000000	4
02	ZHHH	83.126	1111111111	0000000000	4
03	ZHHH	82.598	1111111111	0000000000	4
04	ZHHH	82.530	1111111111	0000000000	4
05	ZHHH	82.411	1111111111	0000000000	4
06	ZHHH	80.785	1111111111	0000000000	4
07	ZHHH	80.301	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. [a]Z; hydrophobic, A; hydrogen bond acceptor (HBA) and R; ring aromatic

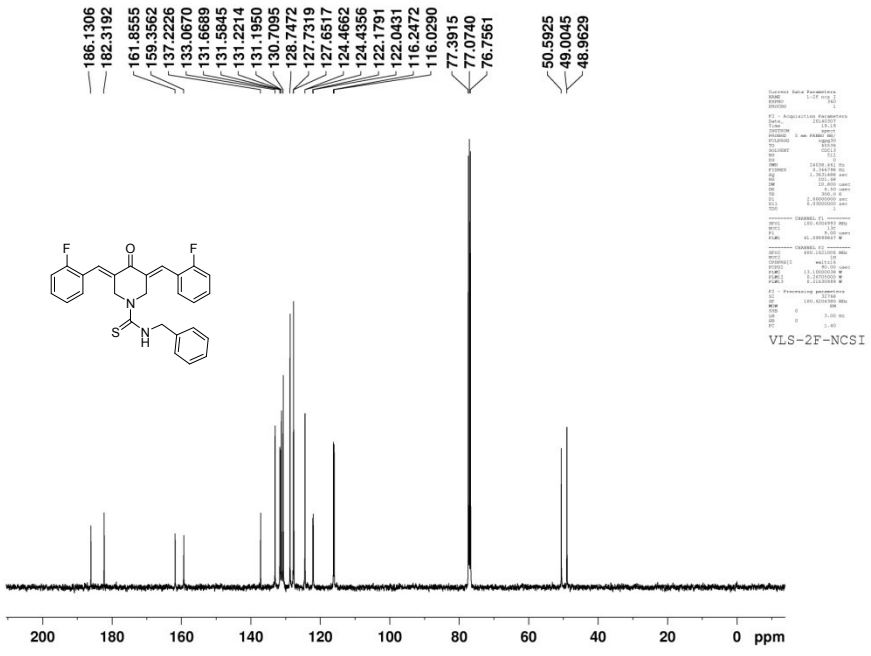
Table S2. The scoring functions from docking runs and fit values from generated pharmacophore model.

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



^{1}H NMR Spectra of compound **14**(400 MHz, $CDCl_3$)



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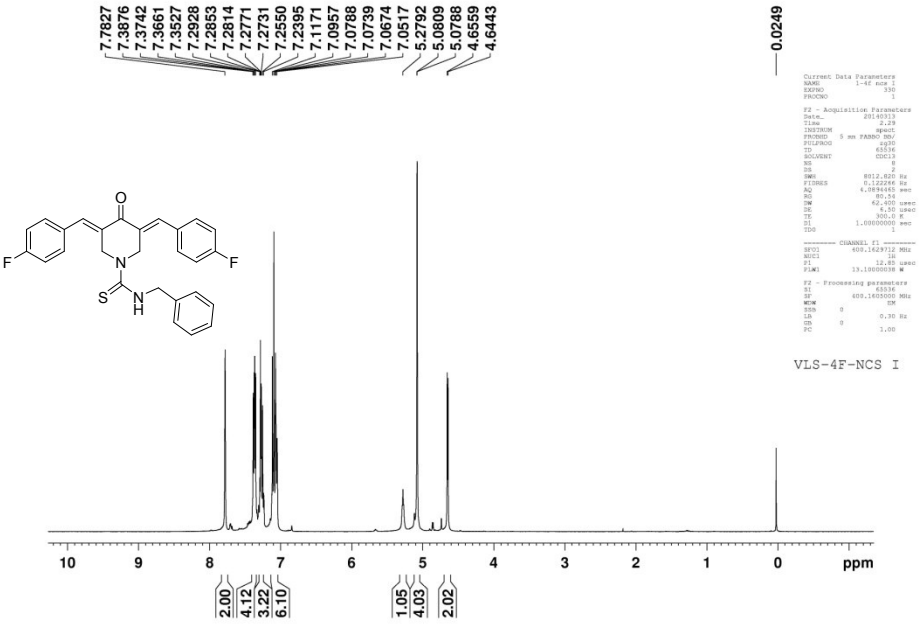

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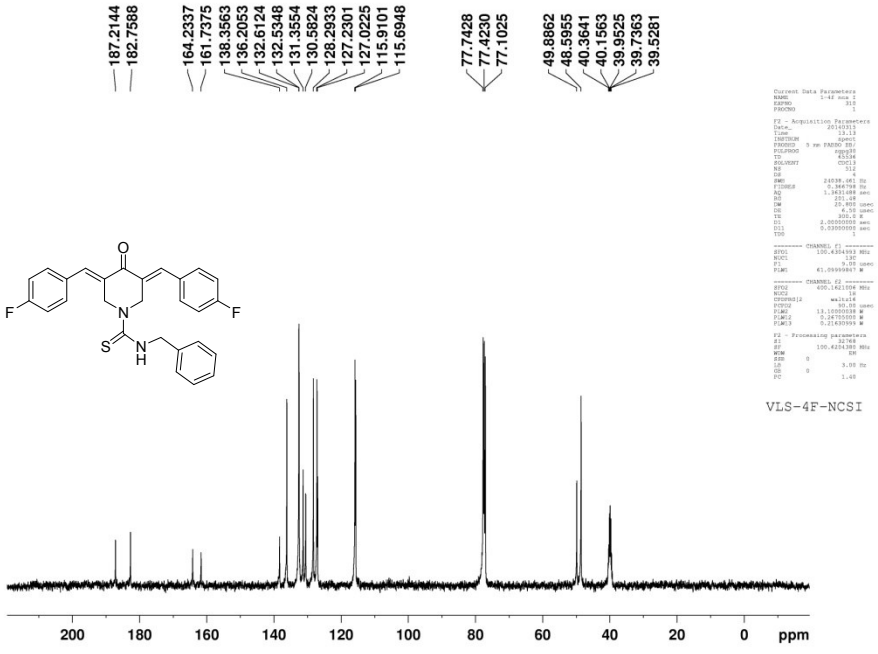

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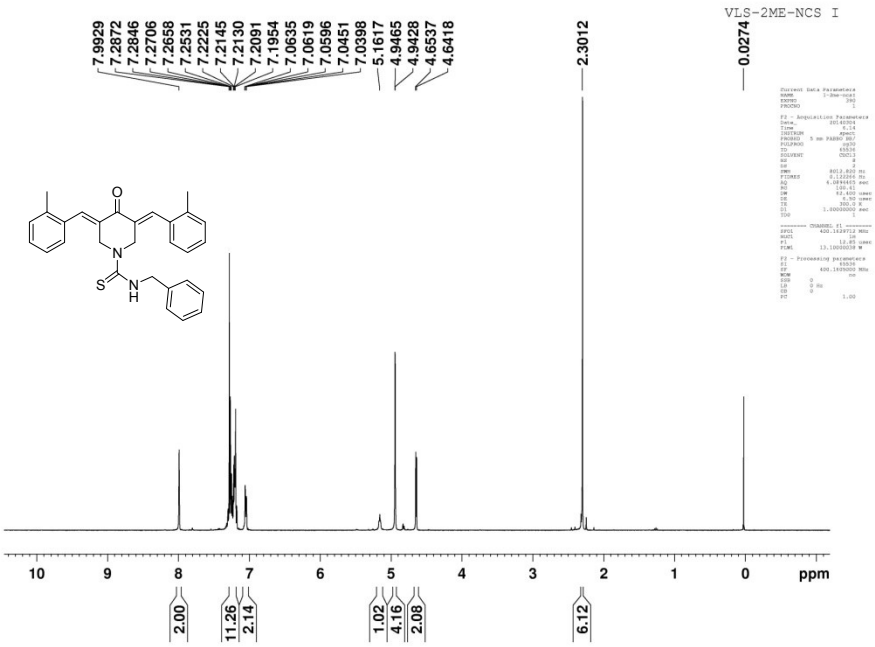

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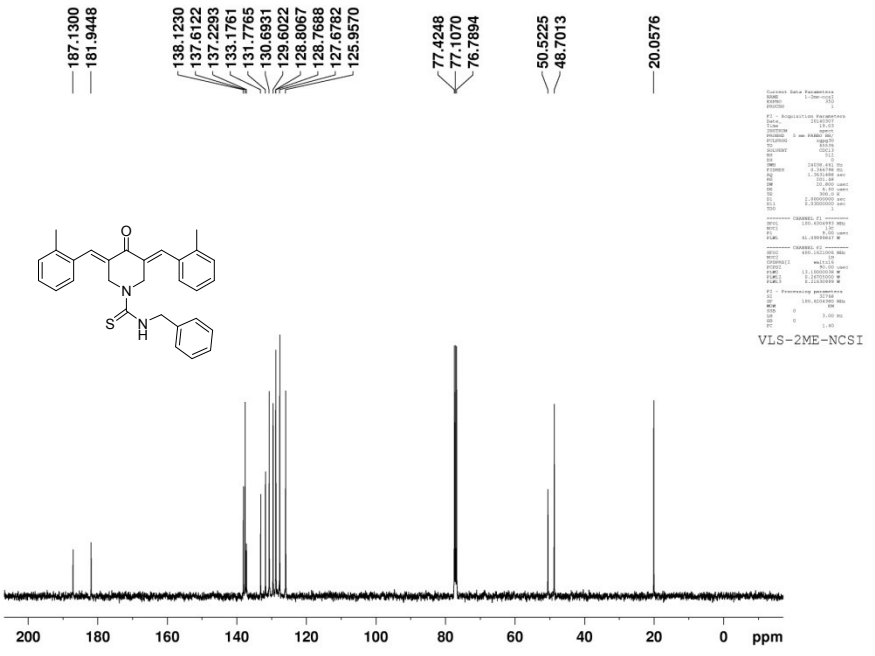

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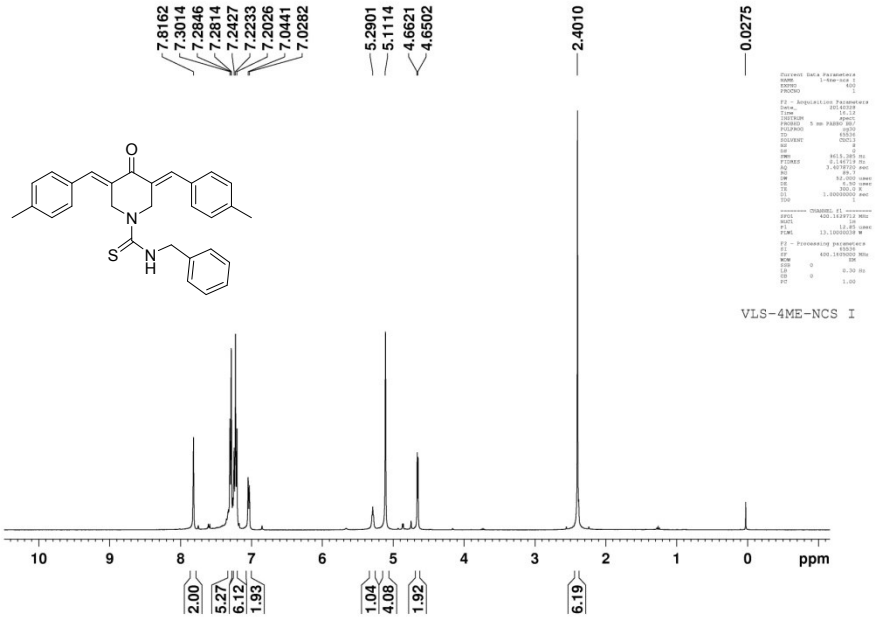

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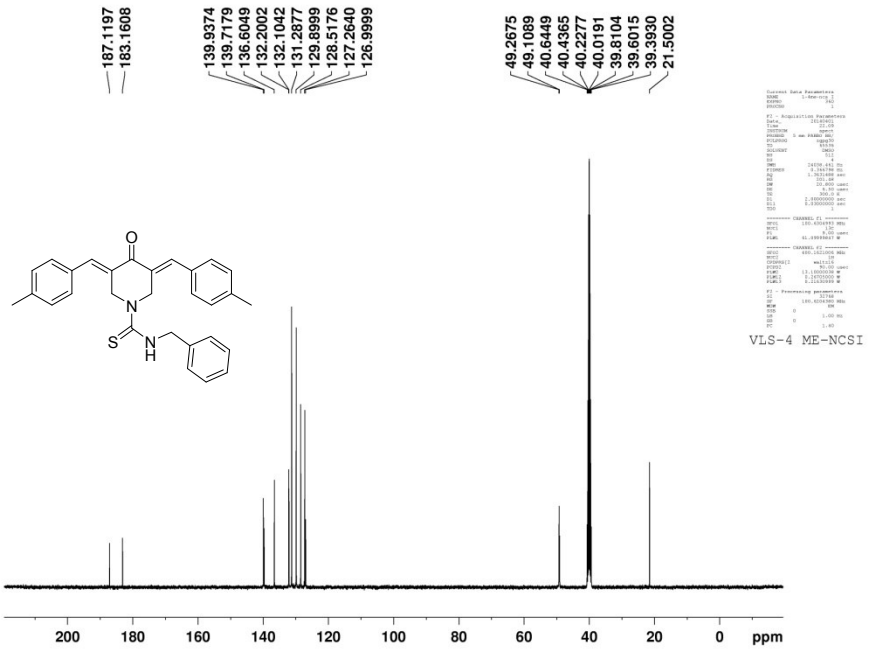

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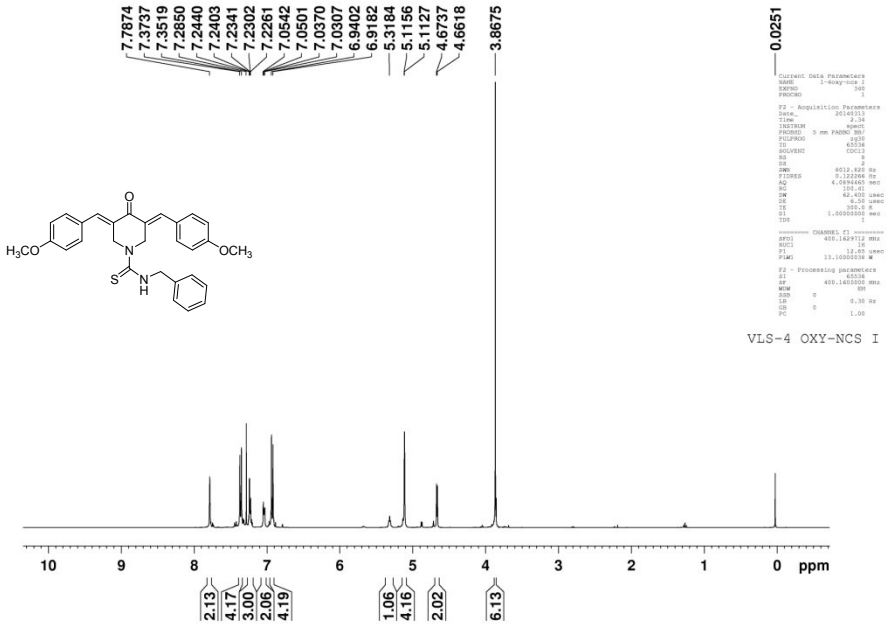

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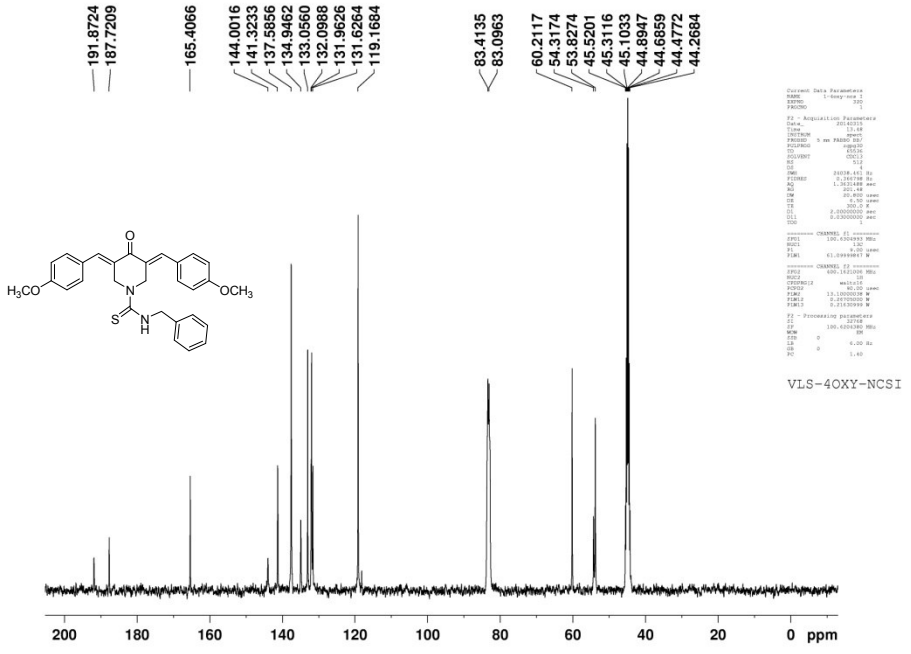

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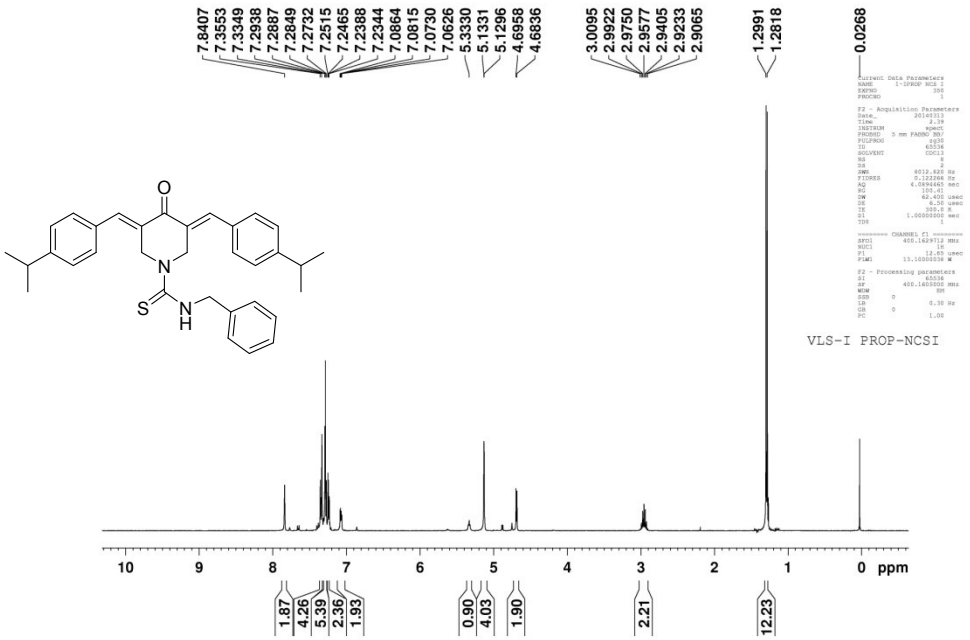

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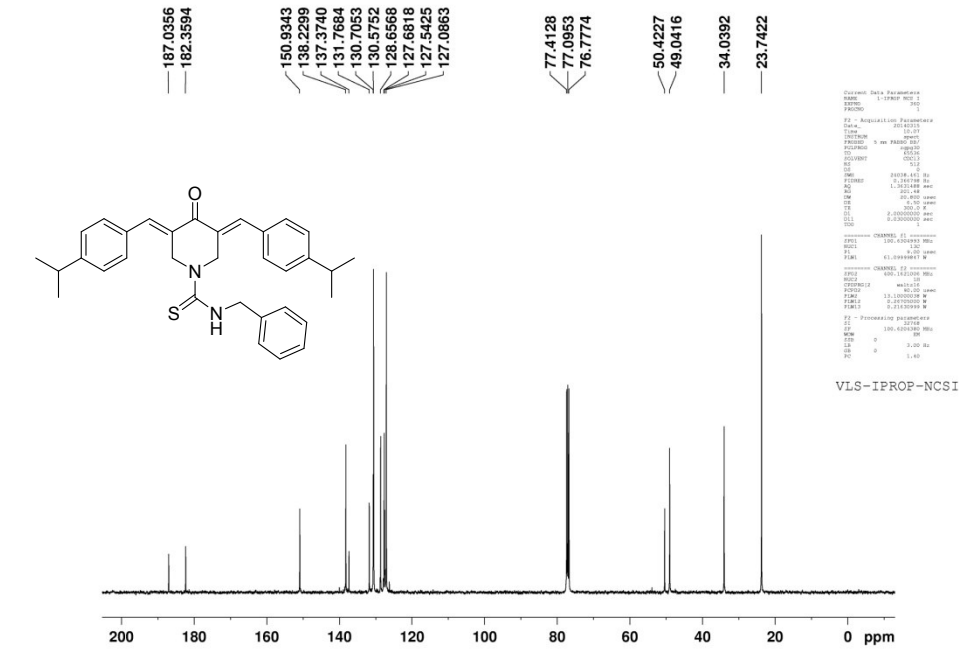

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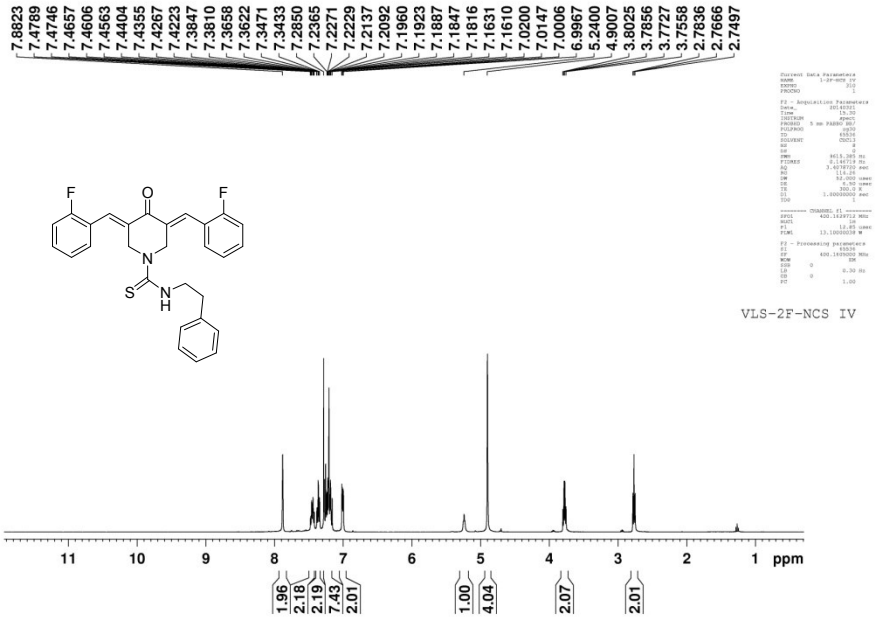

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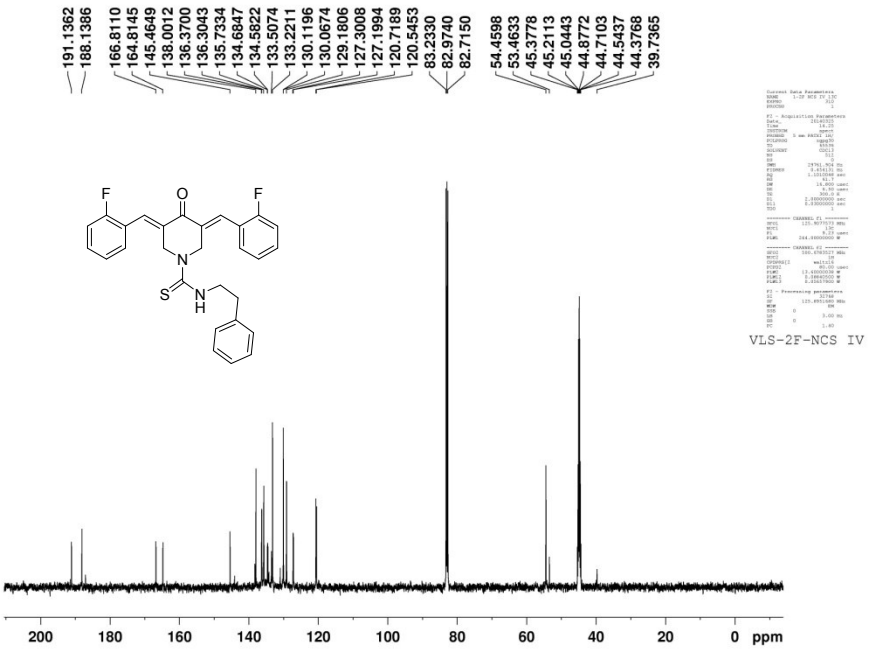

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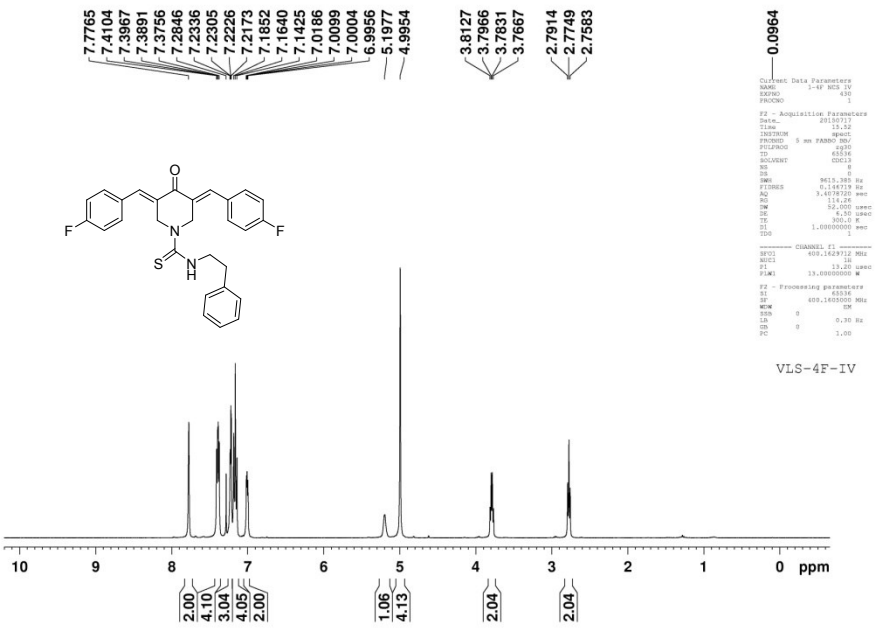

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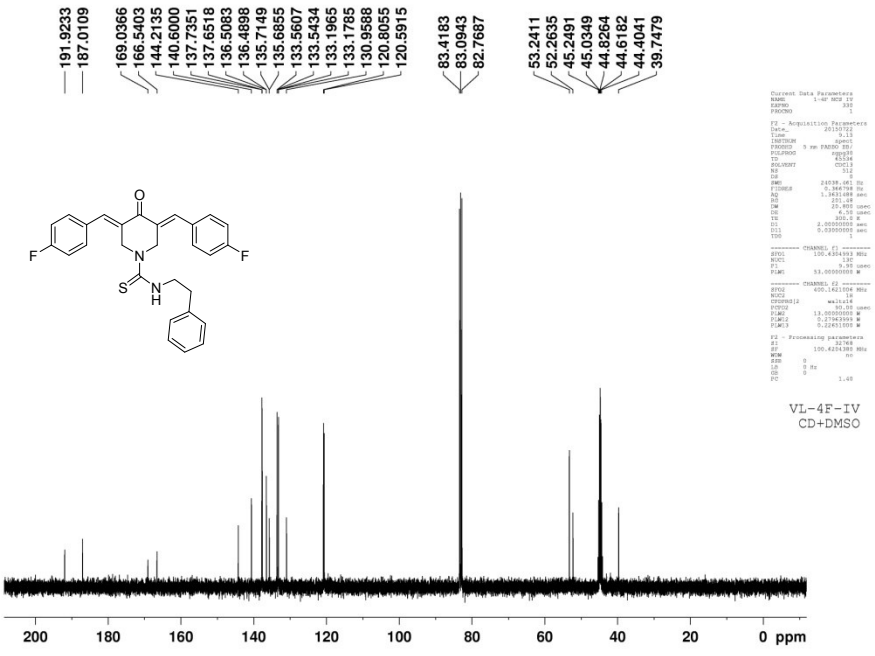

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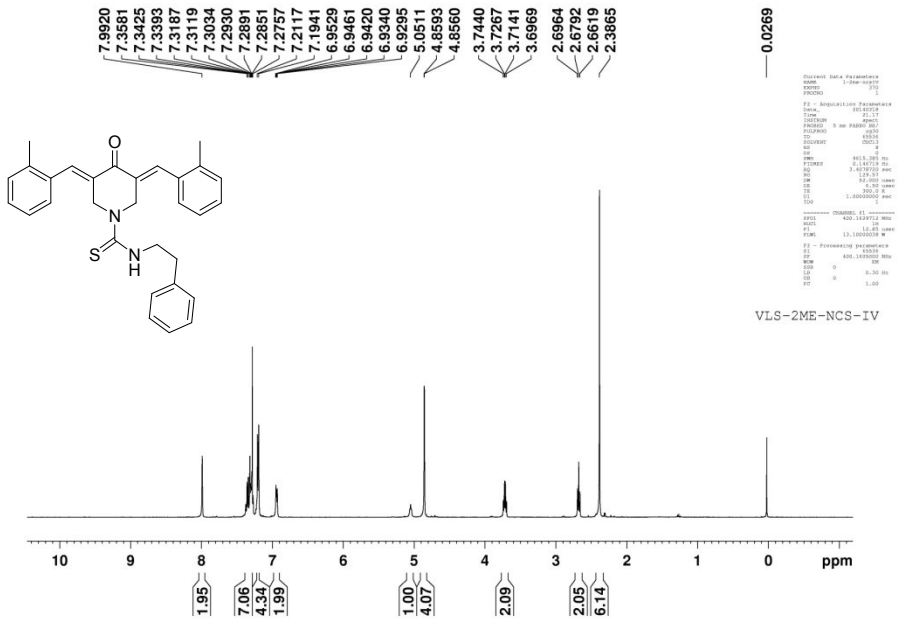
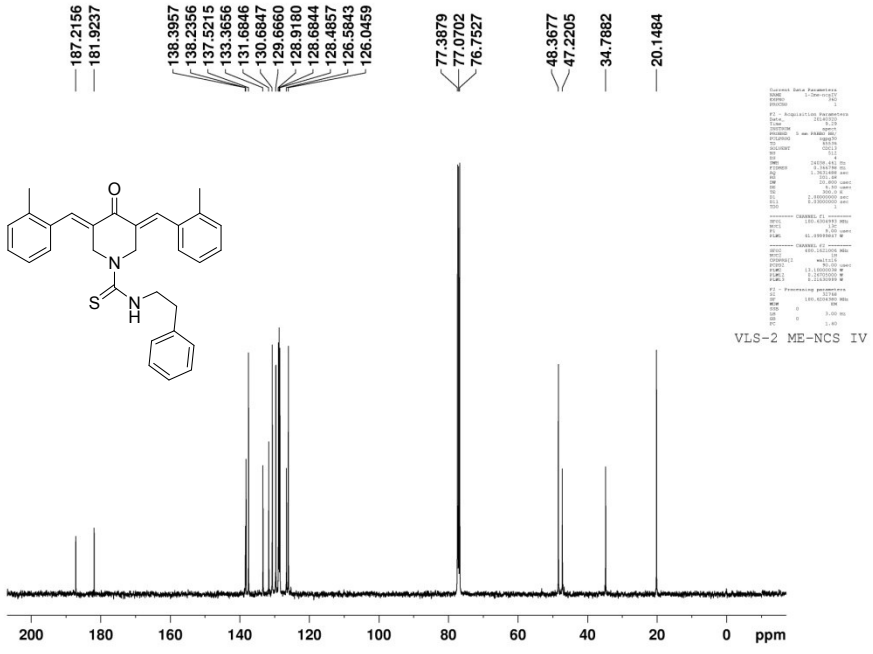


^{1}H NMR Spectra of compound **22**(400 MHz, $CDCl_3$)



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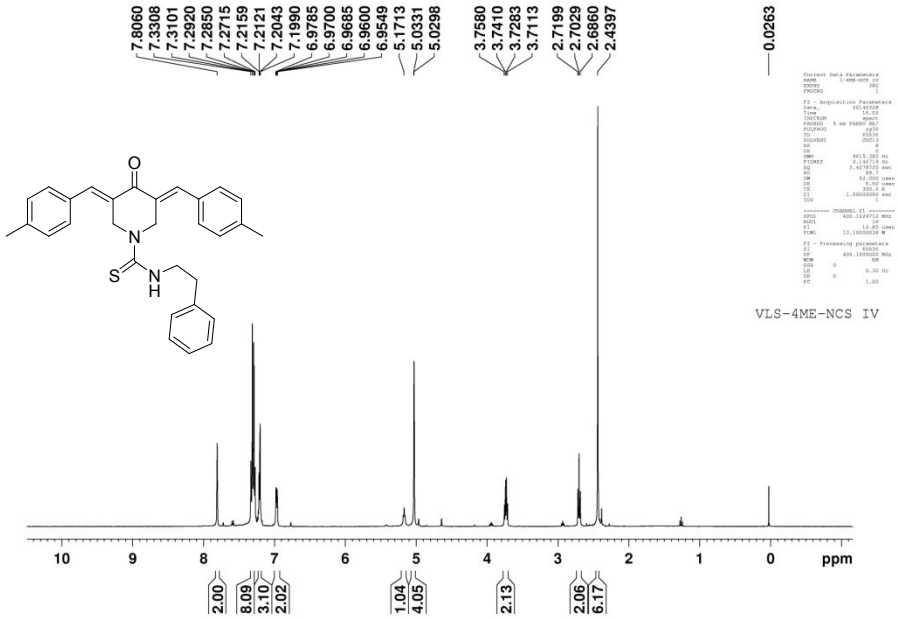

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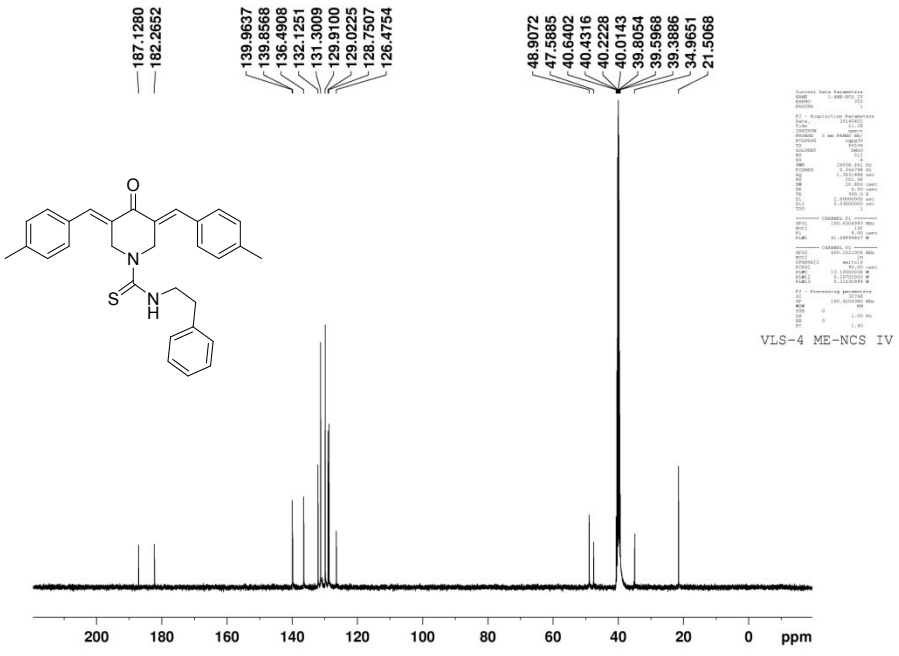

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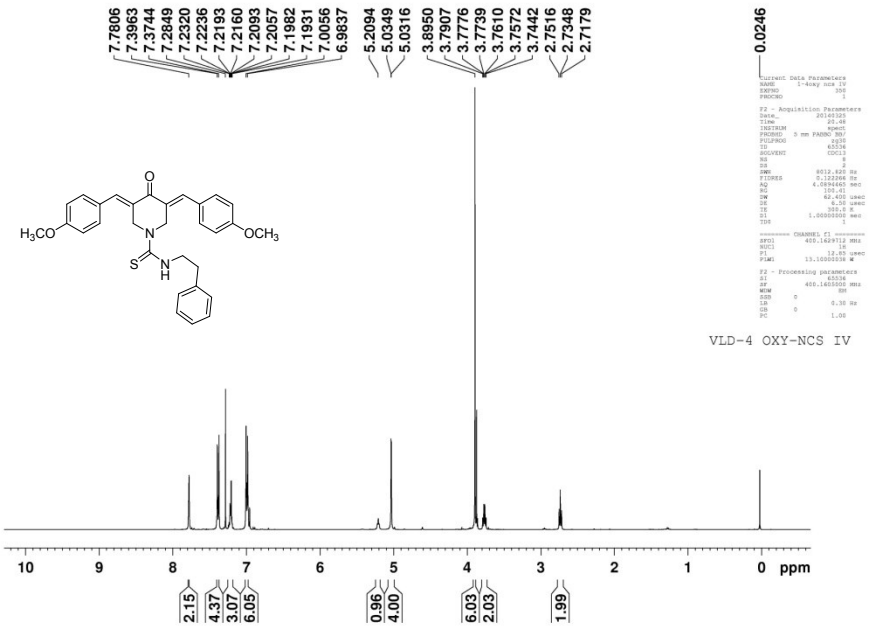

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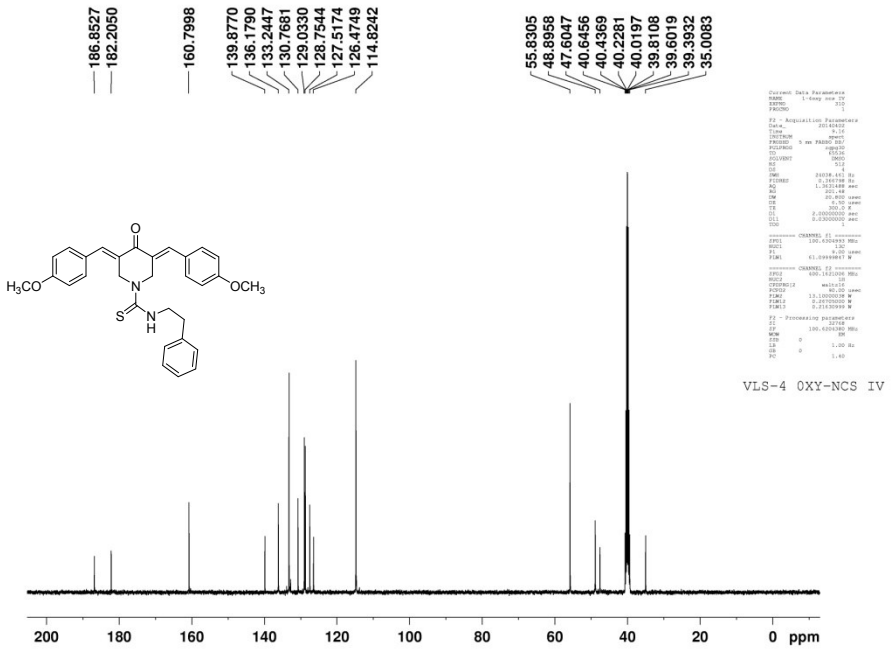

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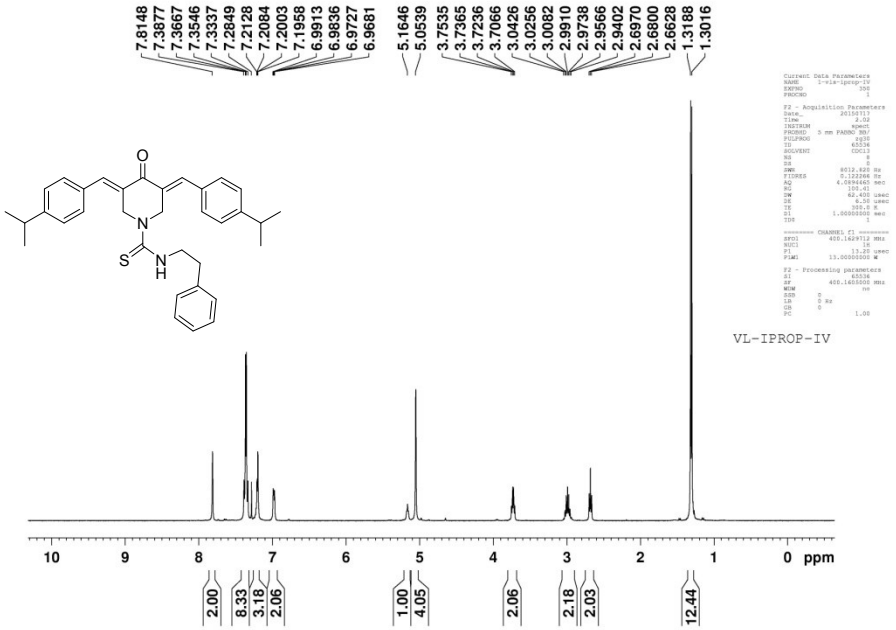

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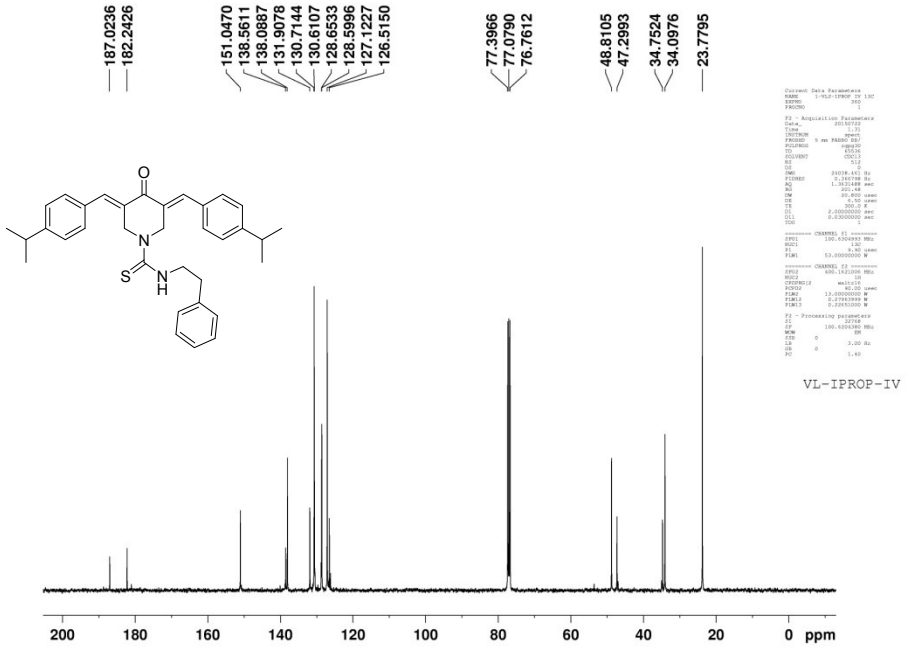

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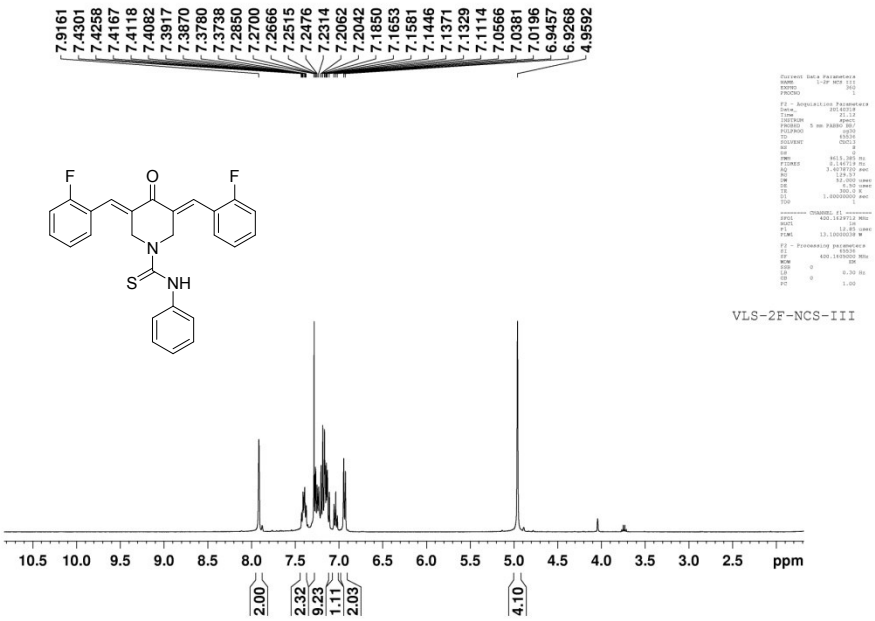

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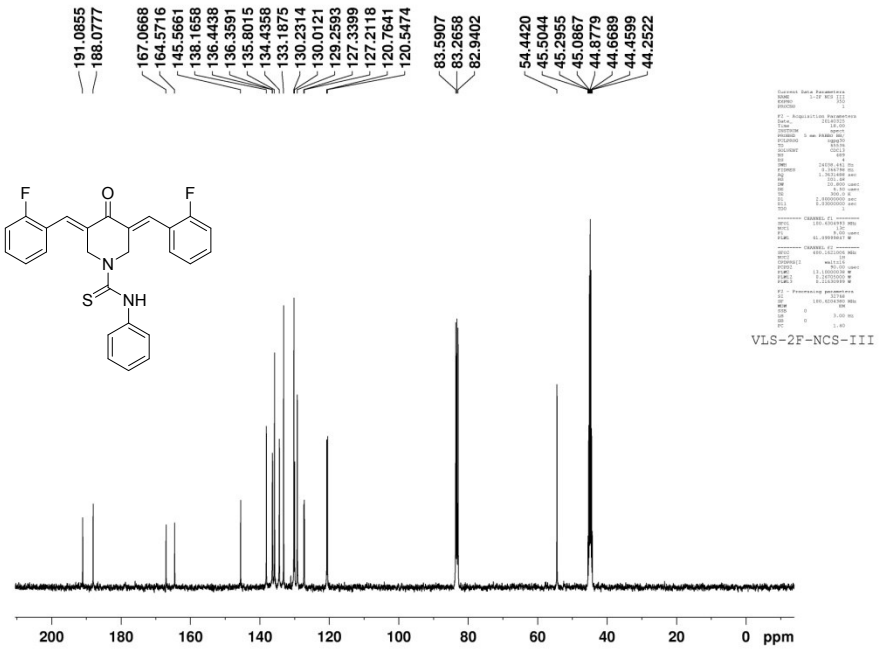
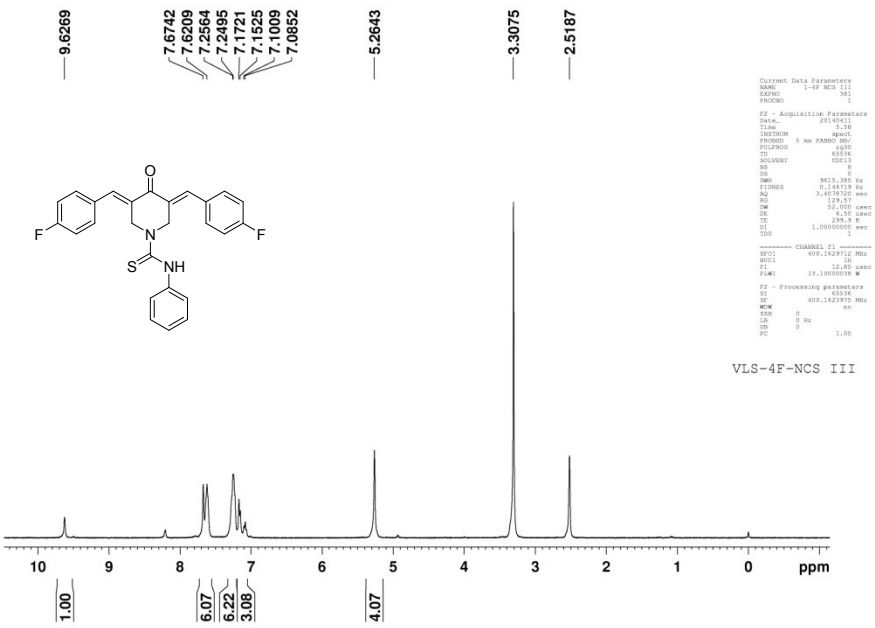


^{13}C NMR Spectra of compound **26**(100 MHz, $CDCl_3$+DMSO-d_6)



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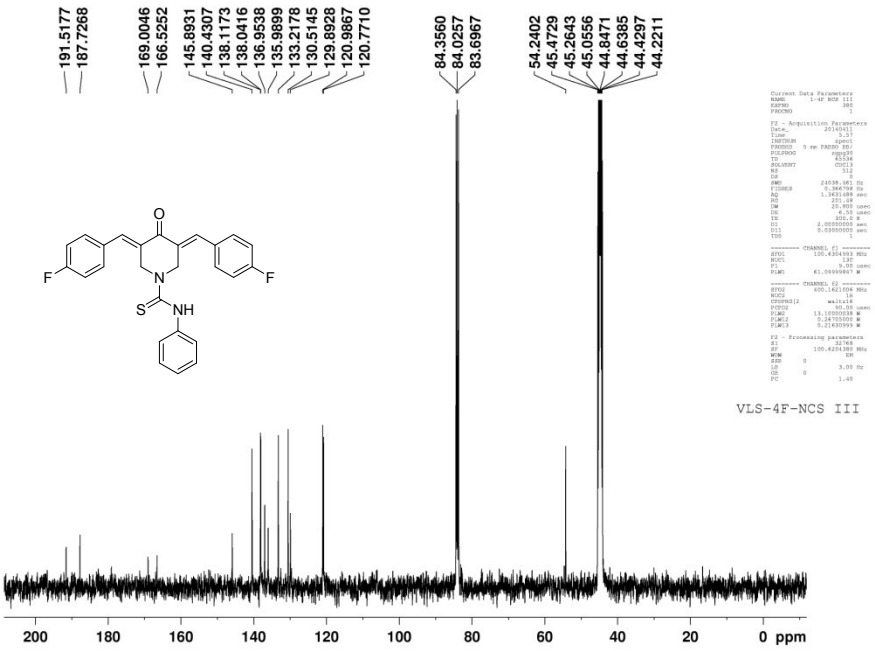

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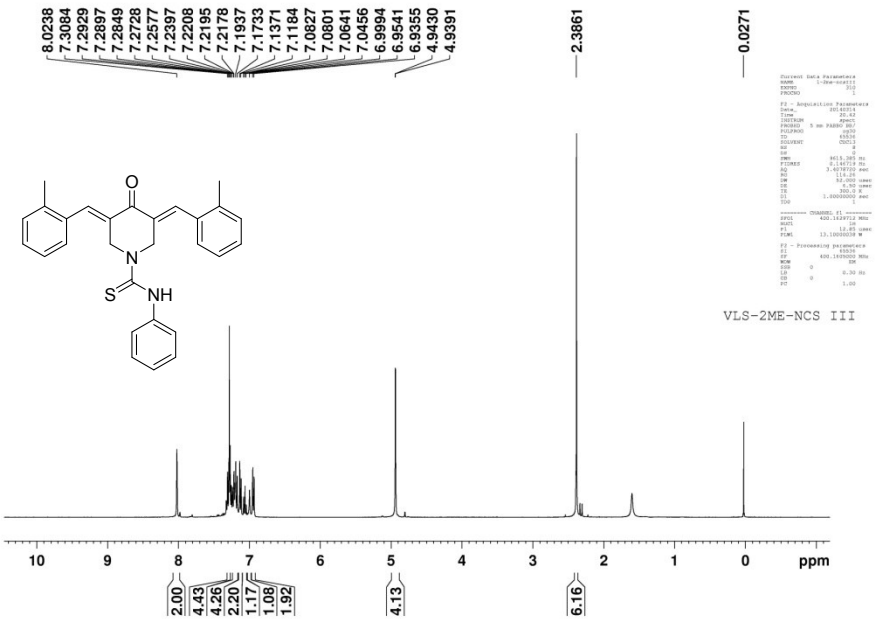

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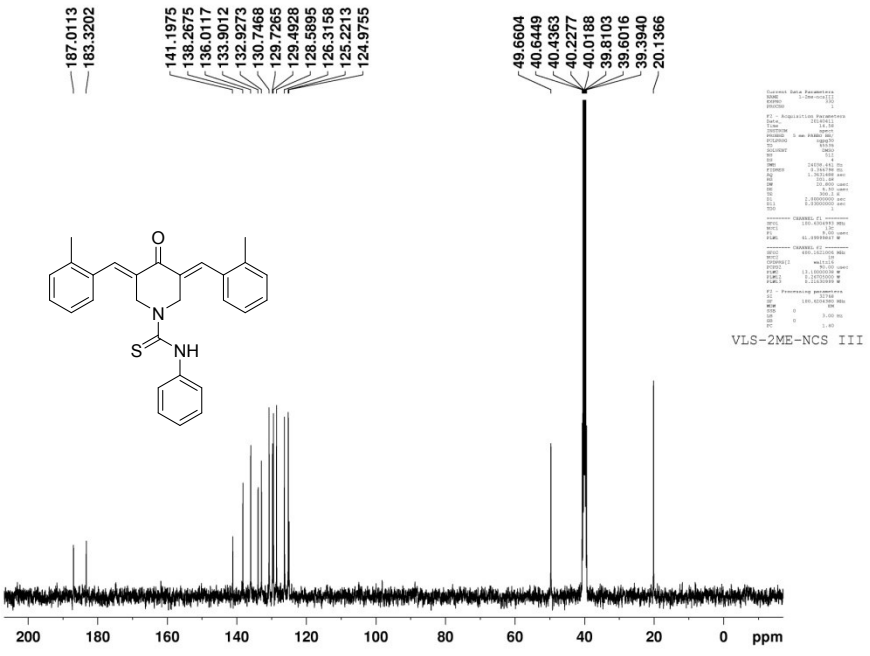

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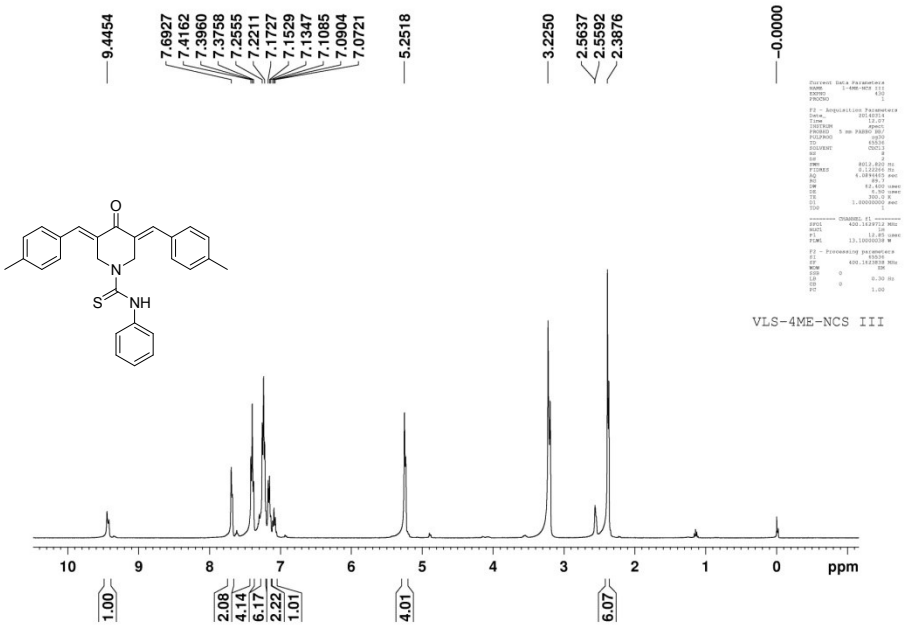

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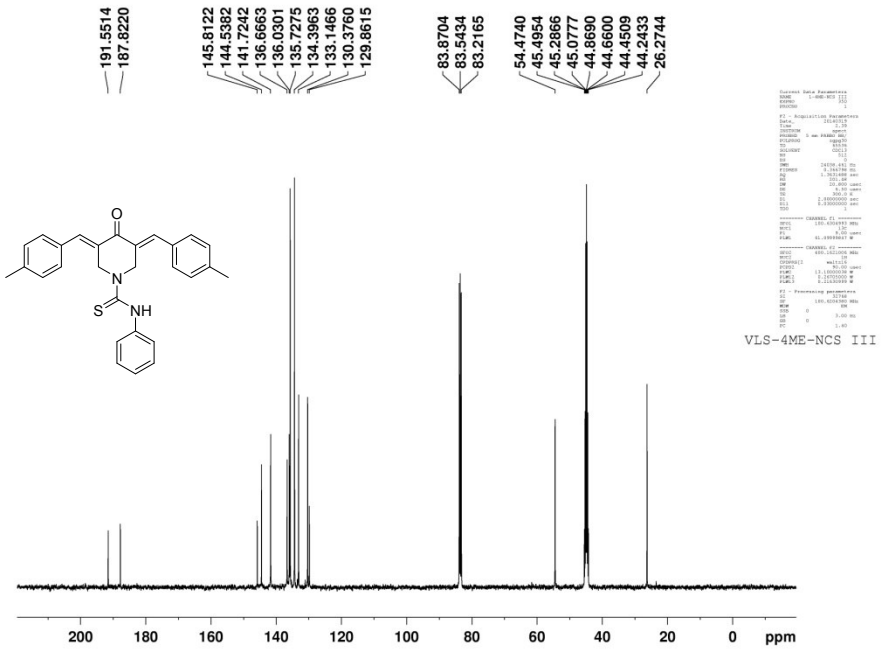

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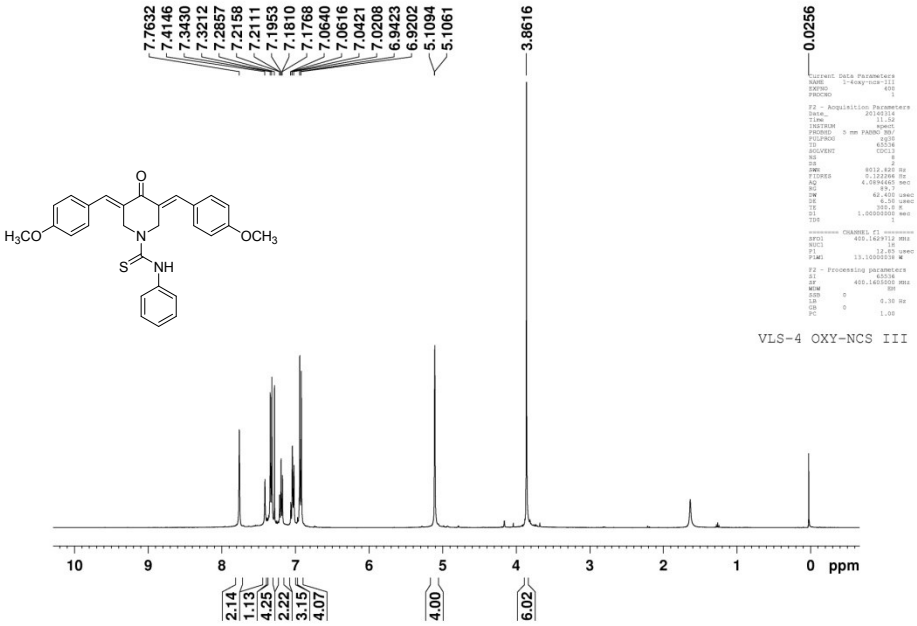
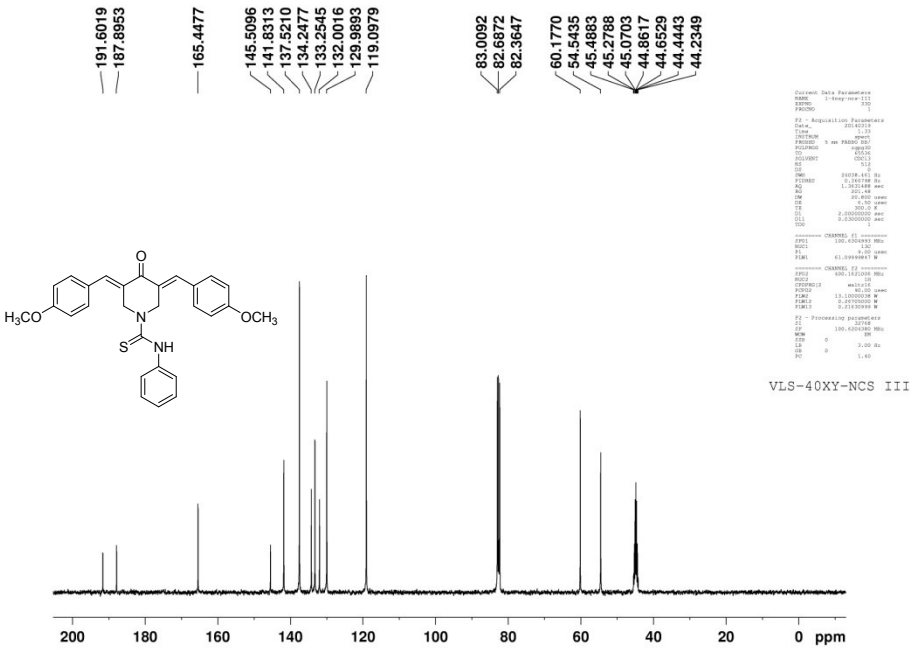


^{1}H NMR Spectra of compound **30**(400 MHz, $CDCl_3$)



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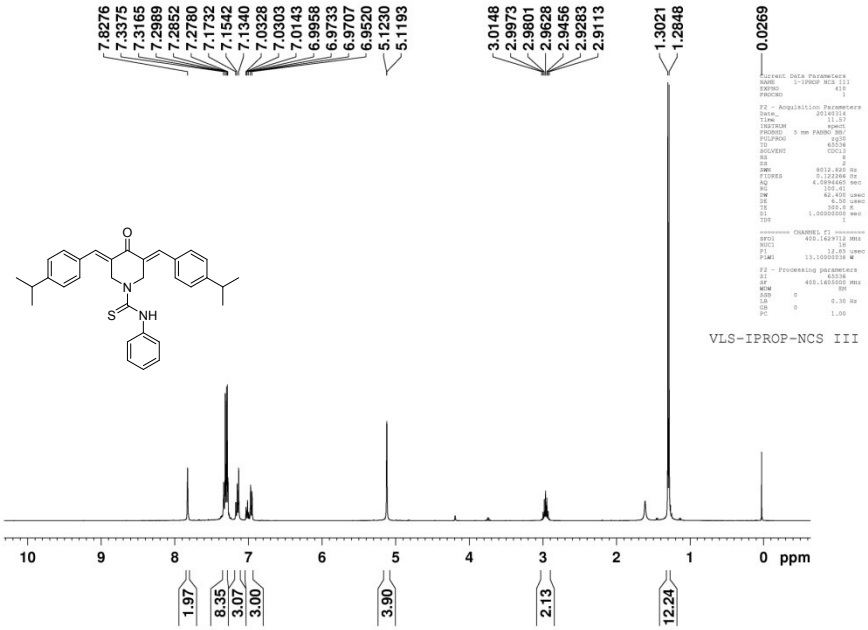

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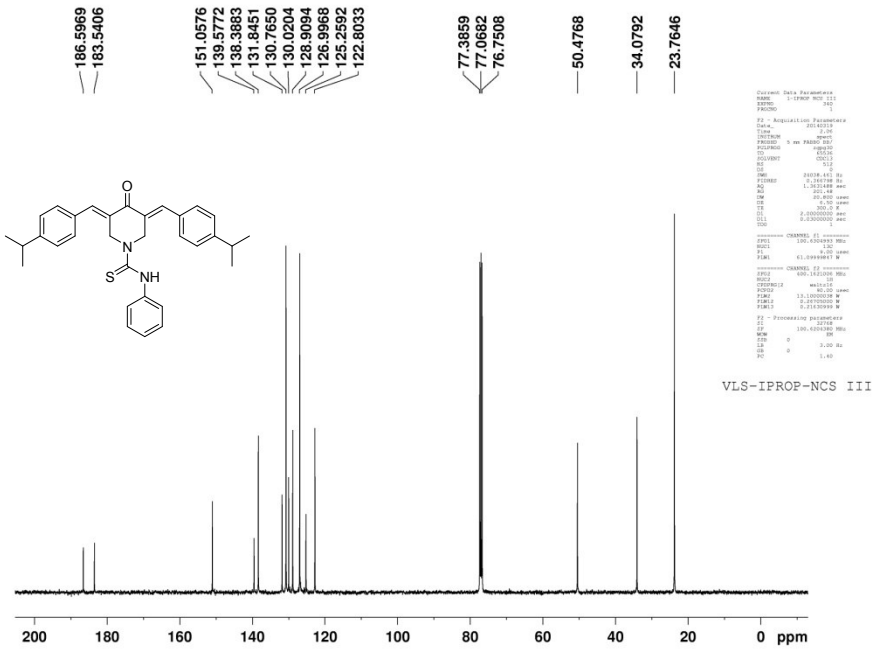

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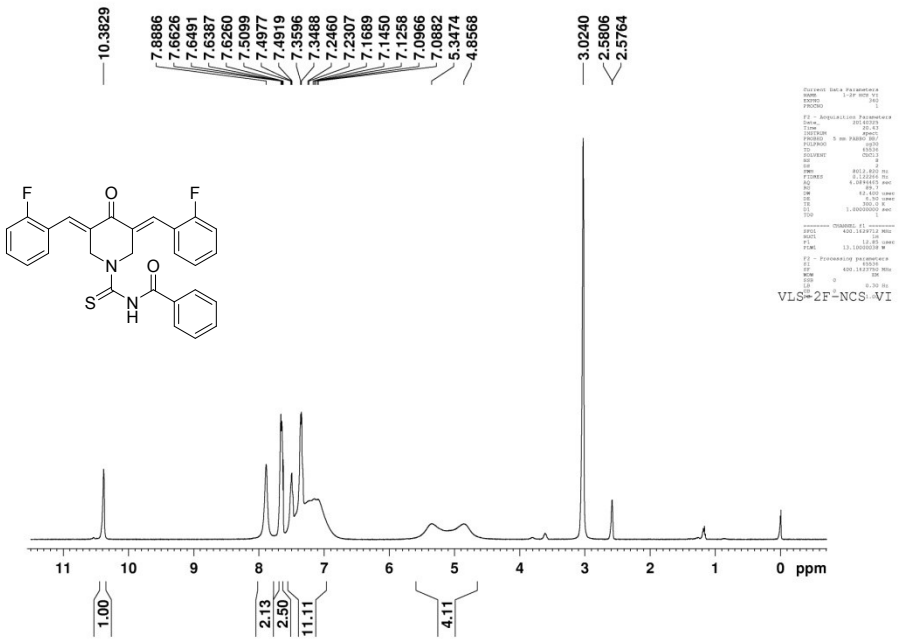

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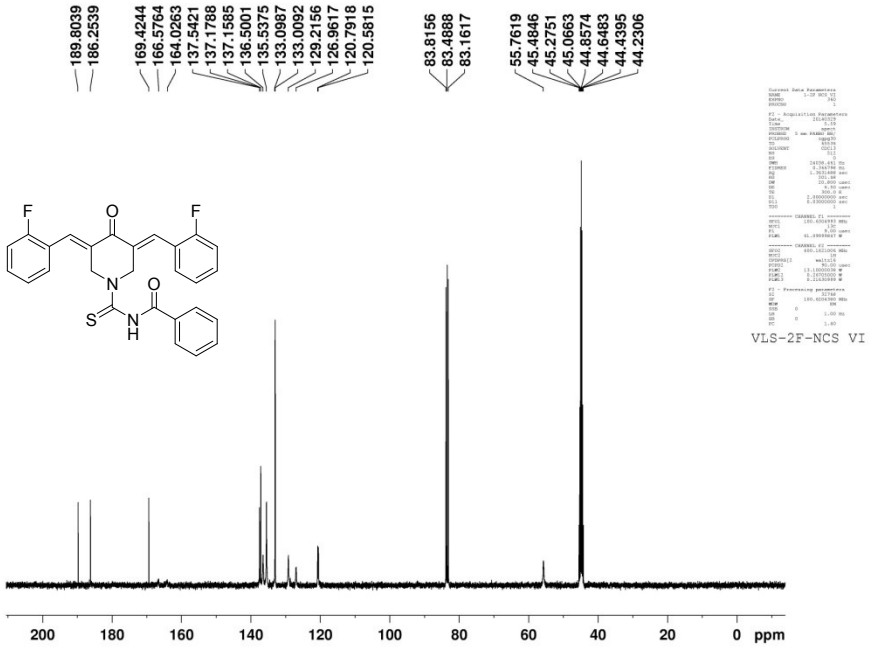
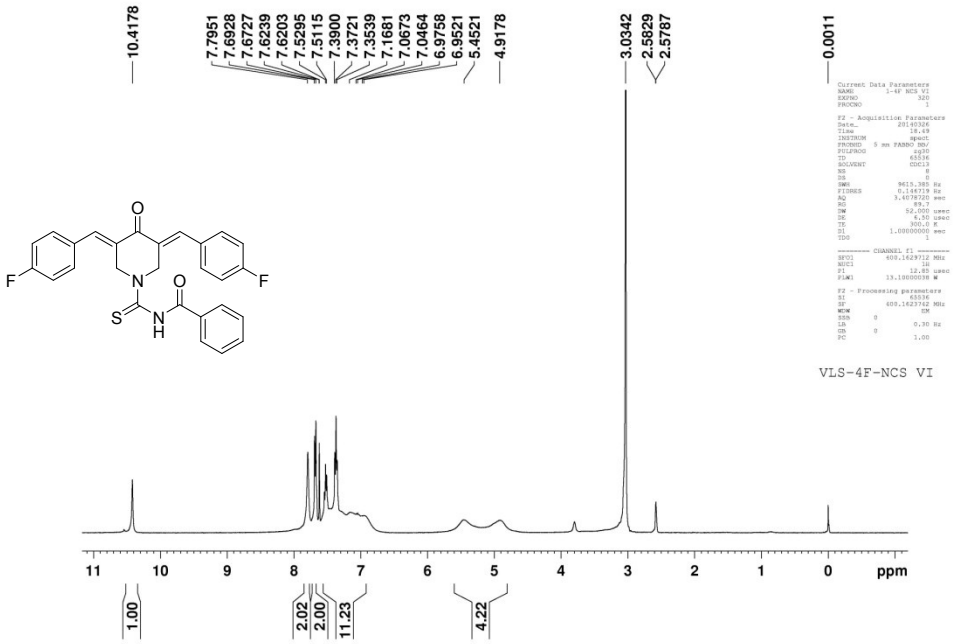
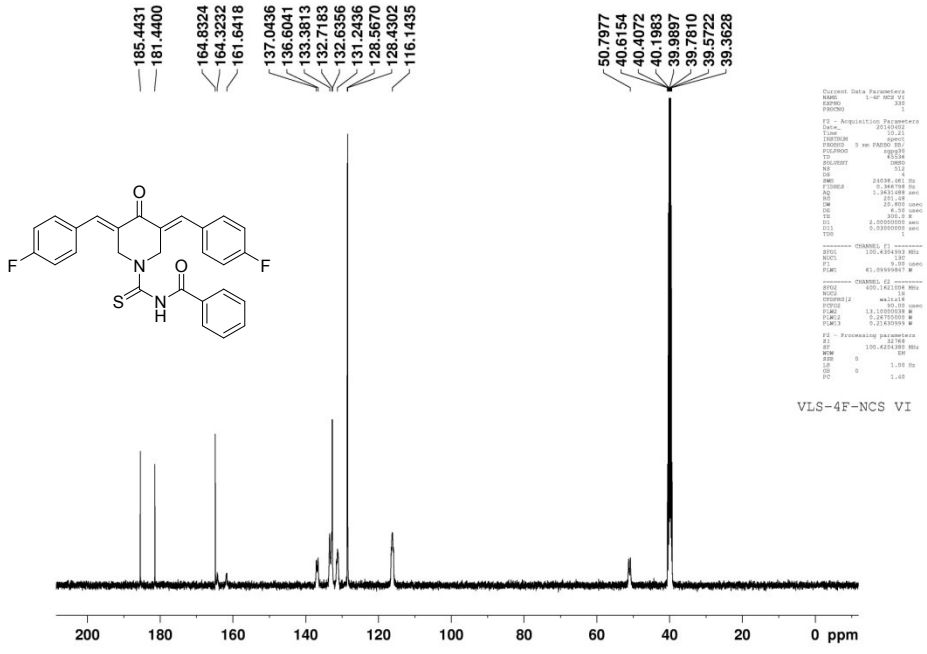


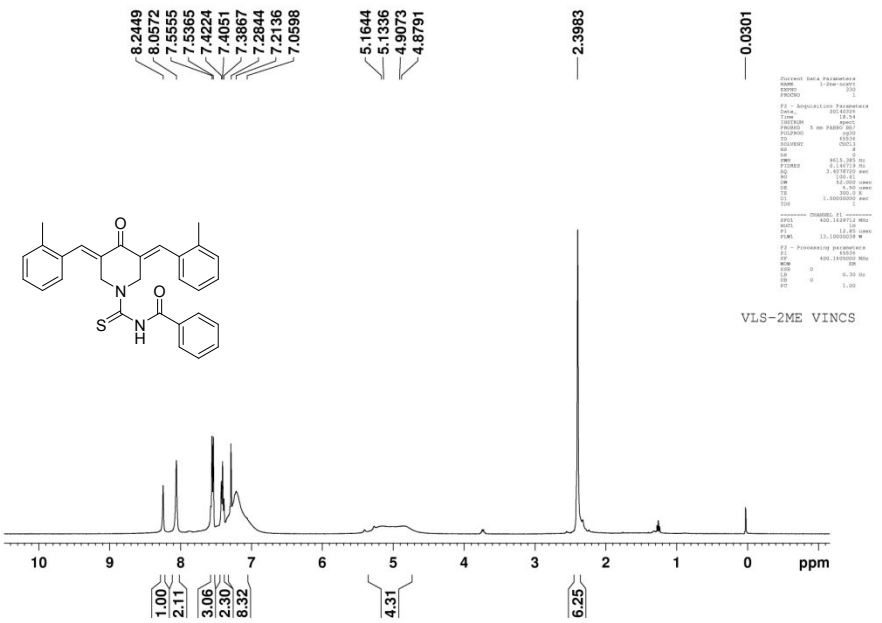
^{13}C NMR Spectra of compound **32**(100 MHz, $CDCl_3$+DMSO-d_6)



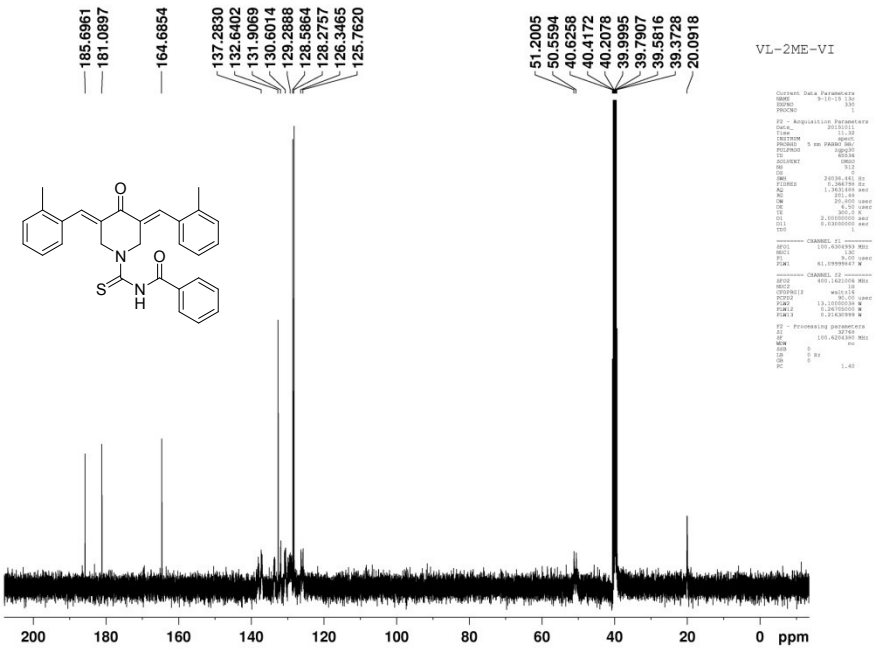
^{1}H NMR Spectra of compound **33**(400 MHz, $CDCl_3$+DMSO-d_6)



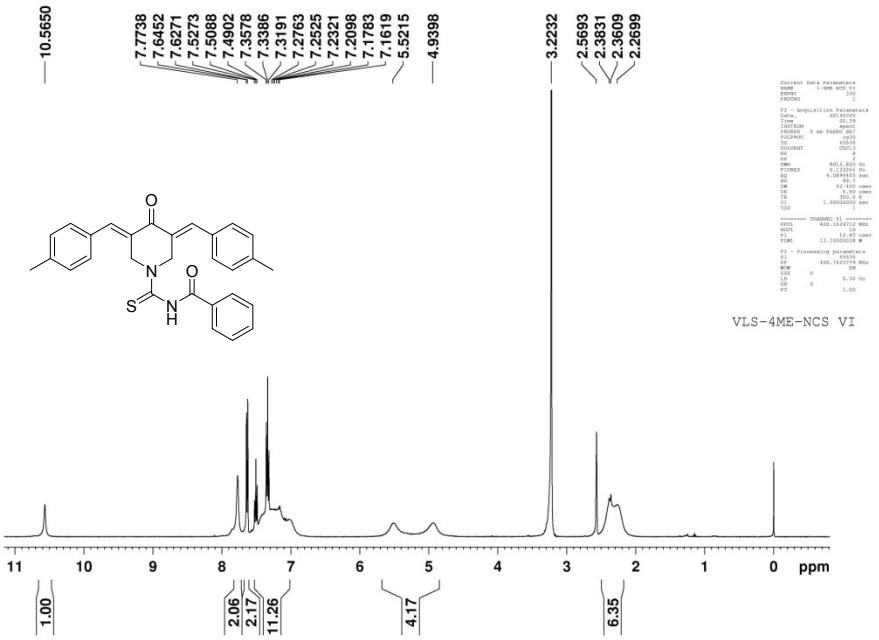
^{13}C NMR Spectra of compound **33**(100 MHz, DMSO-d_6)



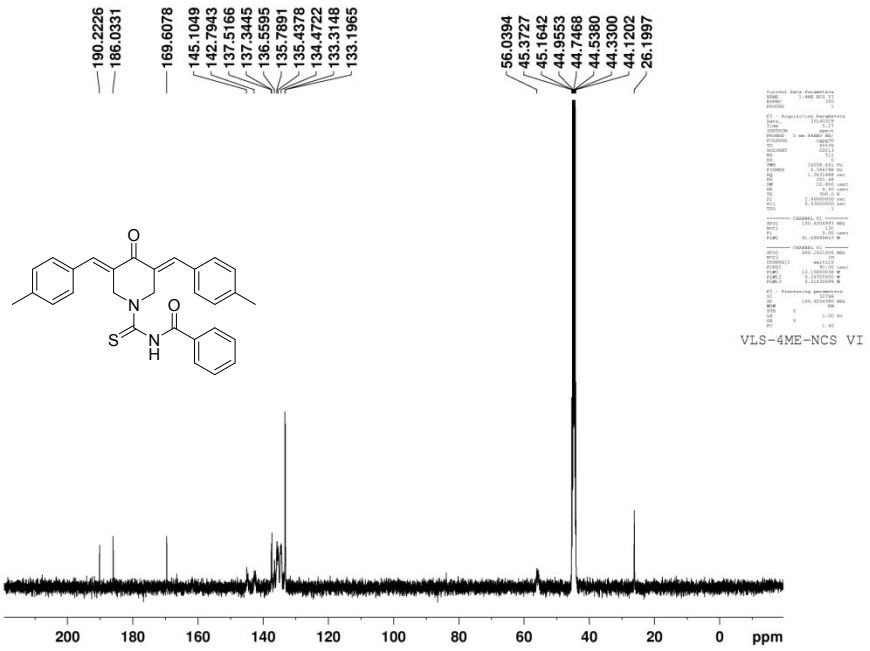
^{1}H NMR Spectra of compound **34**(400 MHz, $CDCl_3$)



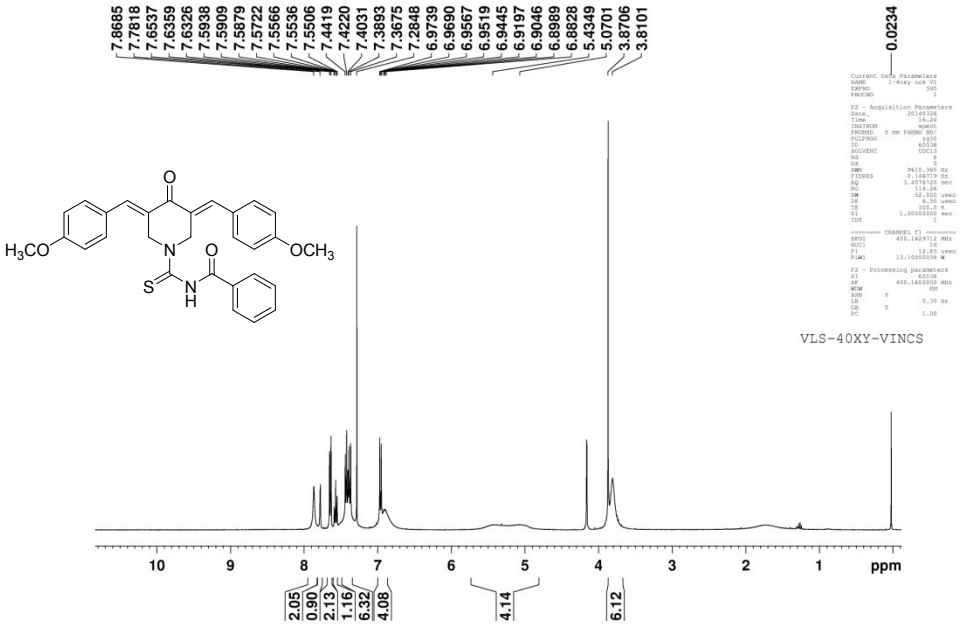
^{13}C NMR Spectra of compound **34**(100 MHz, DMSO-d_6)



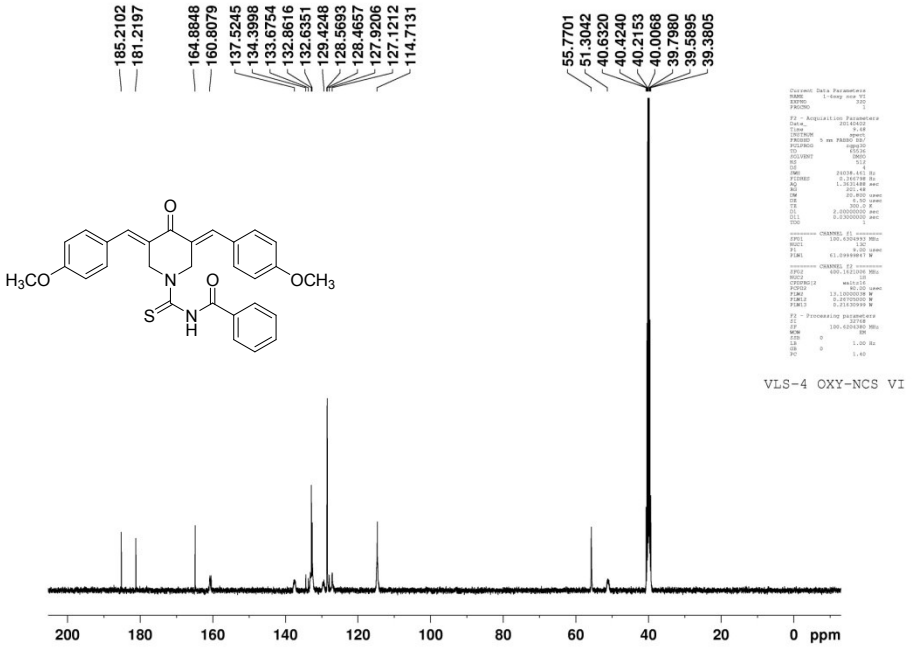
^{1}H NMR Spectra of compound **35**(400 MHz, $CDCl_3$+DMSO-d_6)



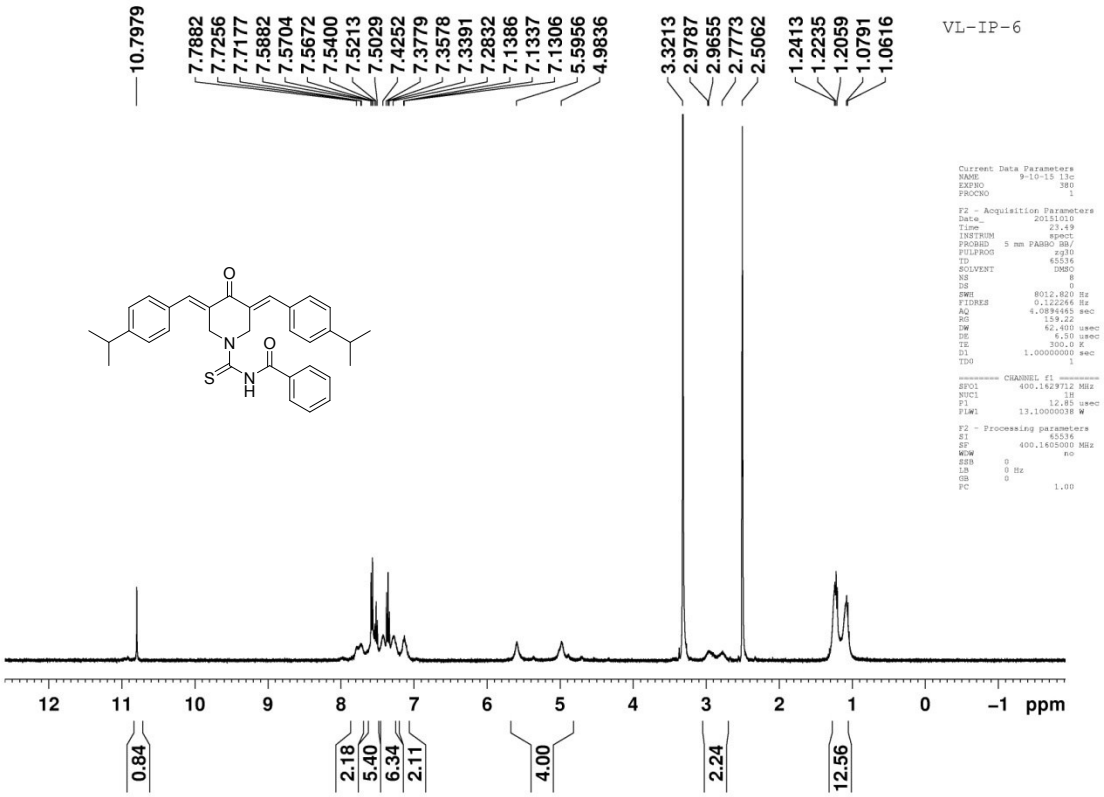
^{13}C NMR Spectra of compound **35**(100 MHz, DMSO-d_6)



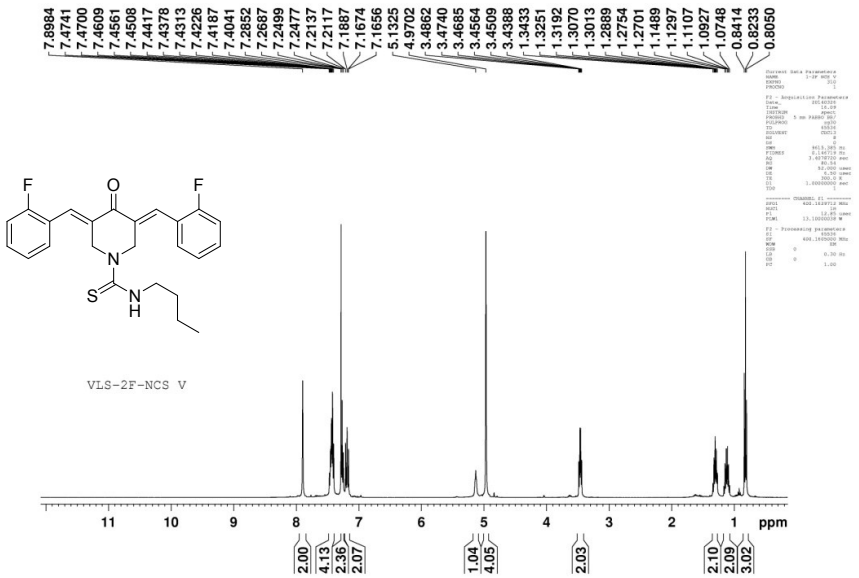
^{1}H NMR Spectra of compound **36**(400 MHz, $CDCl_3$+DMSO-d_6)



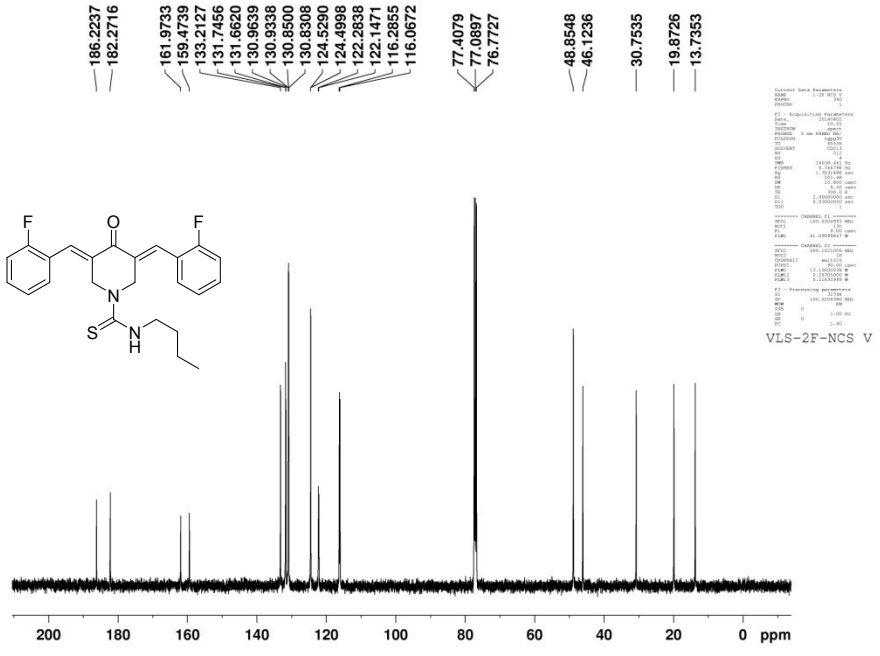
^{13}C NMR Spectra of compound **36**(100 MHz, DMSO-d_6)



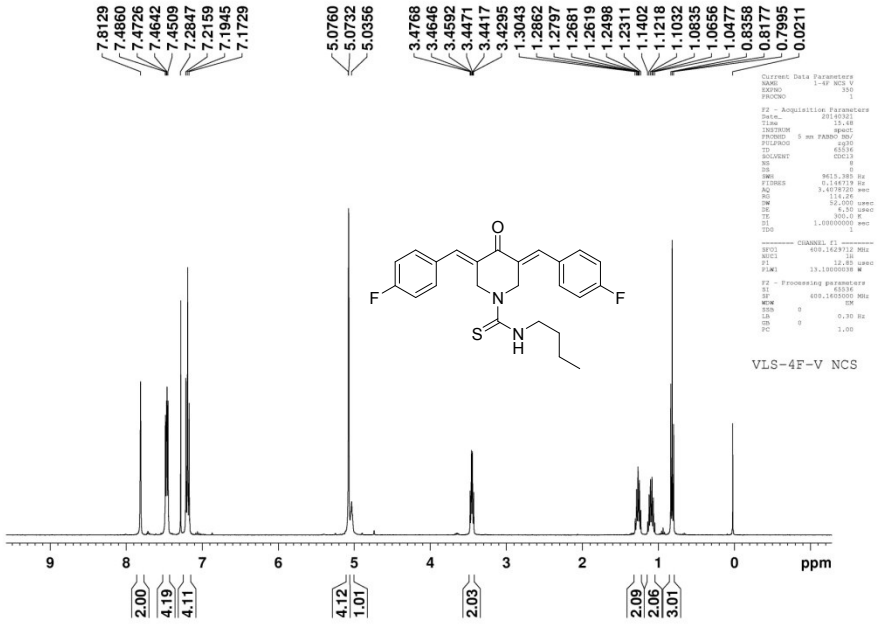
^{1}H NMR Spectra of compound **37**(400 MHz, DMSO-d_6)



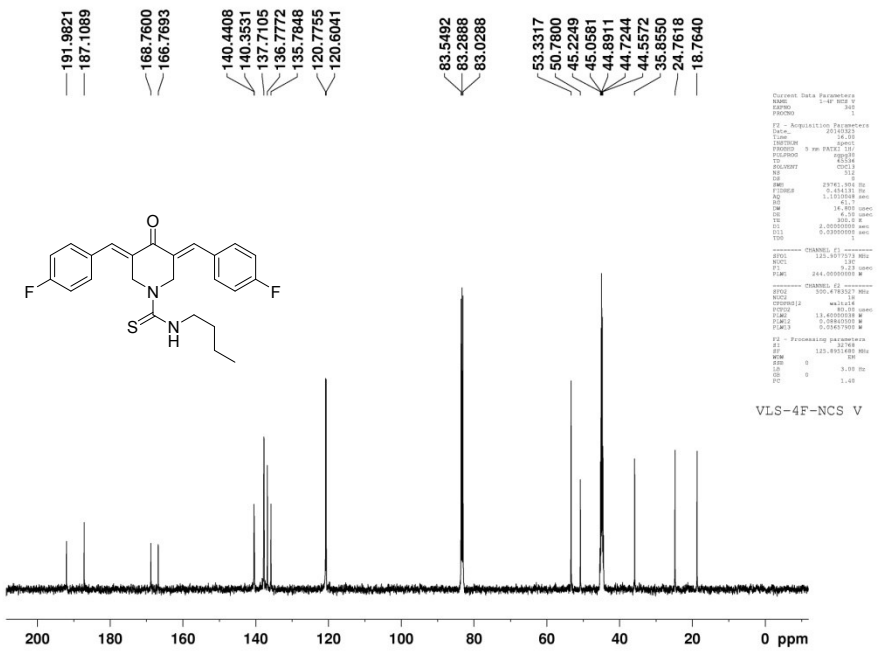
^{1}H NMR Spectra of compound **38**(400 MHz, $CDCl_3$)



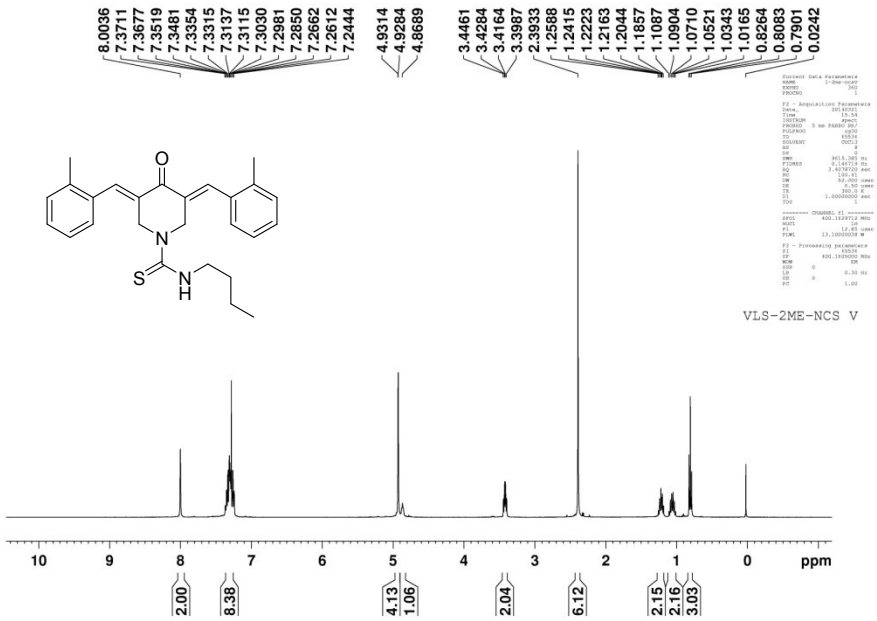
^{13}C NMR Spectra of compound **38**(100 MHz, $CDCl_3$)



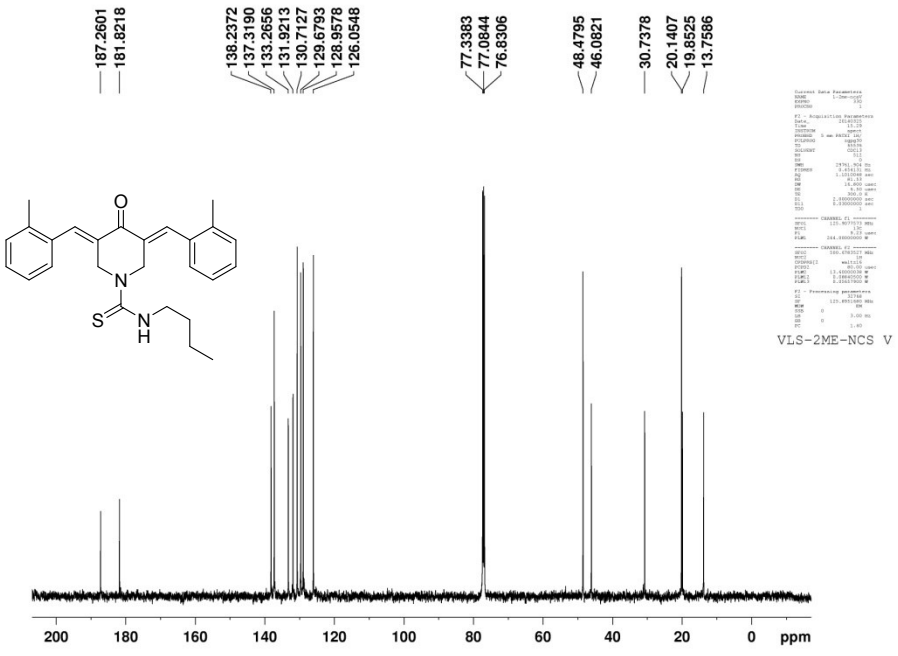
^{1}H NMR Spectra of compound **39**(400 MHz, $CDCl_3$)



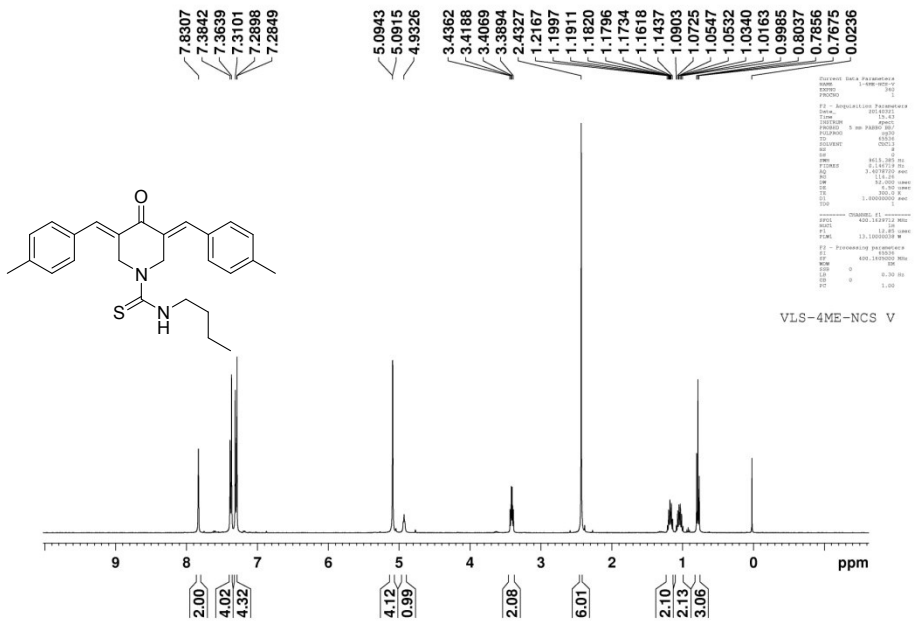
^{13}C NMR Spectra of compound **39**(100 MHz, $CDCl_3$+DMSO-d_6)



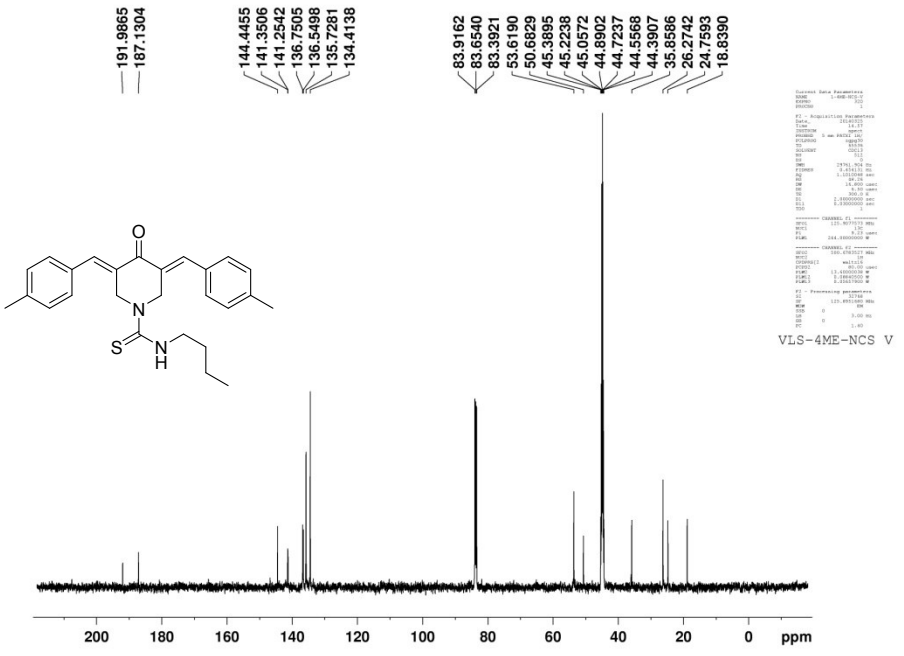
^{1}H NMR Spectra of compound **40**(400 MHz, $CDCl_3$)



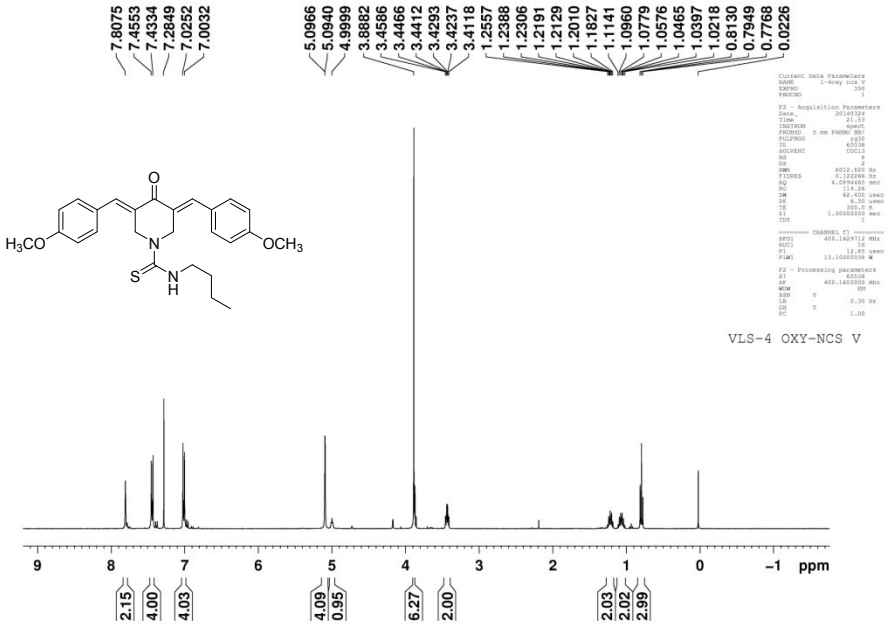
^{13}C NMR Spectra of compound **40**(100 MHz, $CDCl_3$)



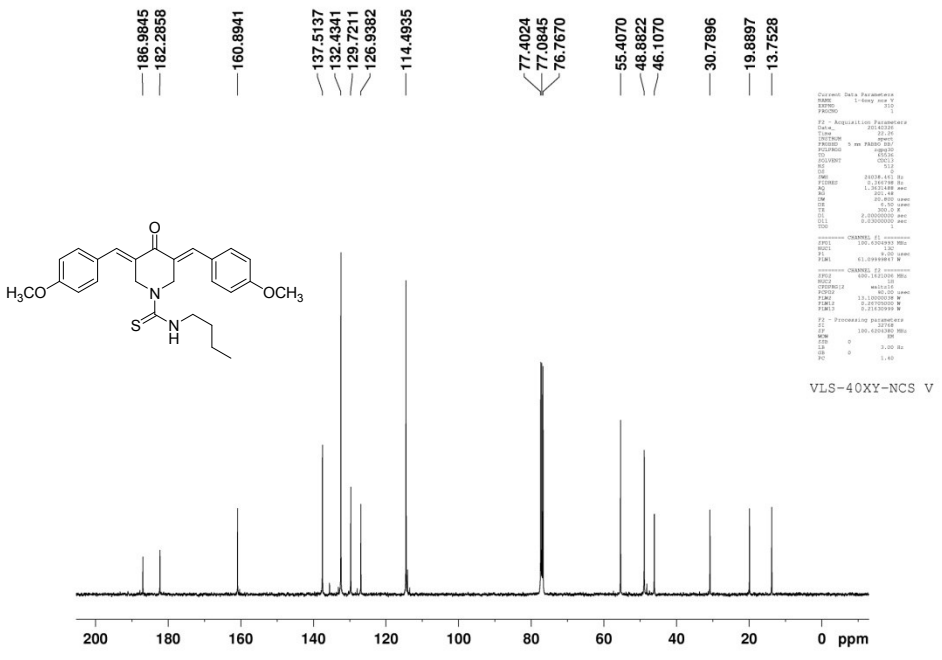
^{1}H NMR Spectra of compound **41**(400 MHz, $CDCl_3$)



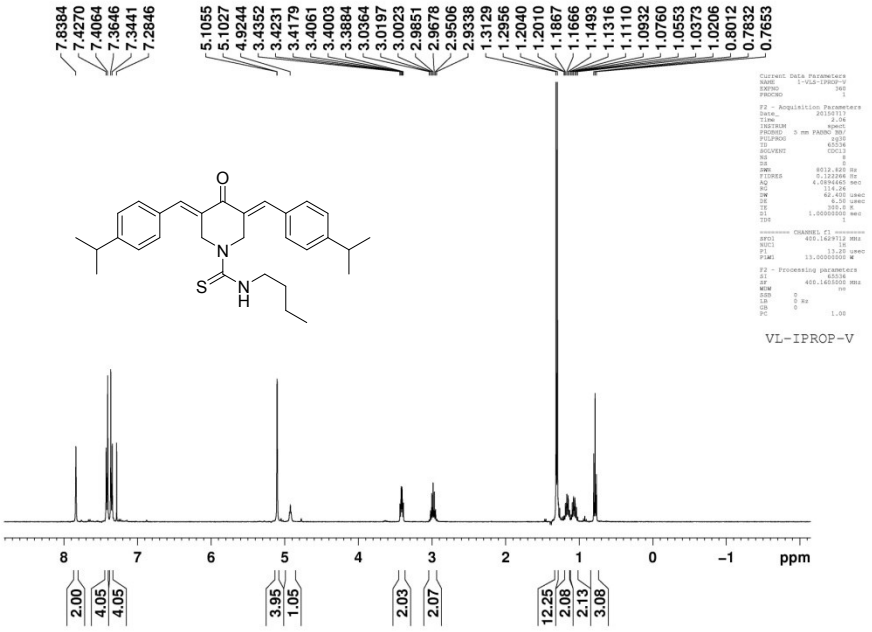
^{13}C NMR Spectra of compound **41**(100 MHz, $CDCl_3$+DMSO-d_6)



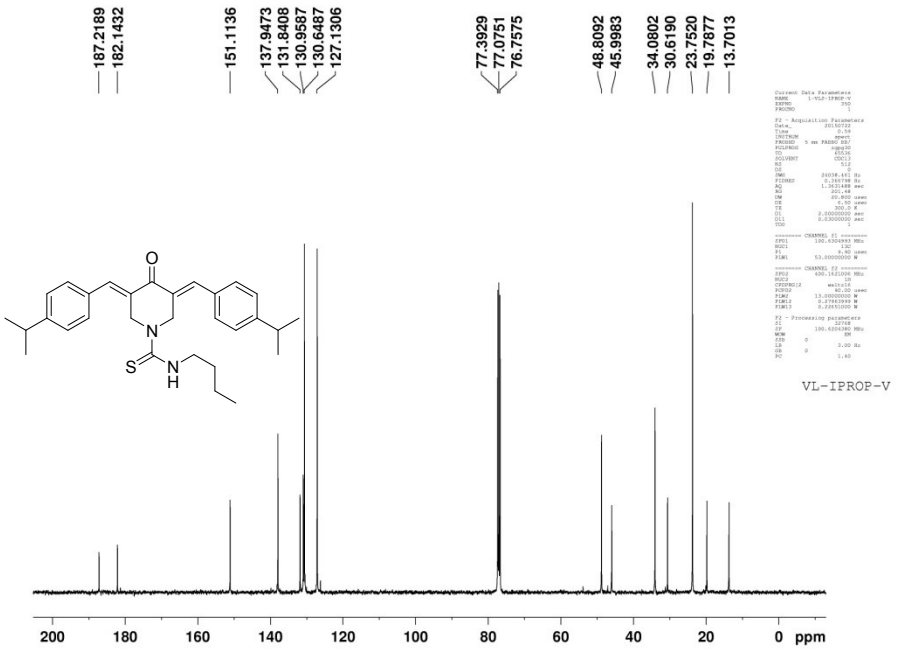
^{1}H NMR Spectra of compound **42**(400 MHz, $CDCl_3$)



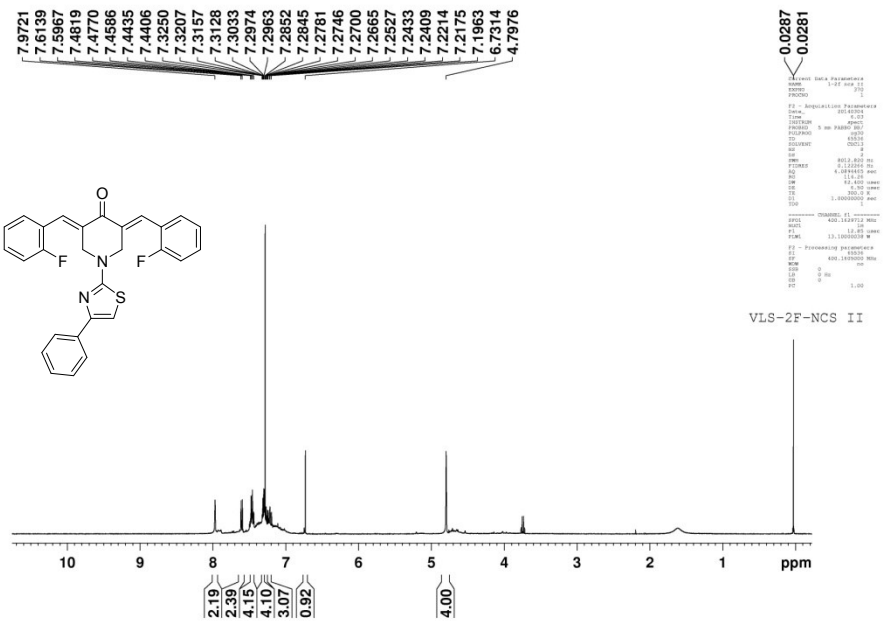
^{13}C NMR Spectra of compound **42**(100 MHz, $CDCl_3$)



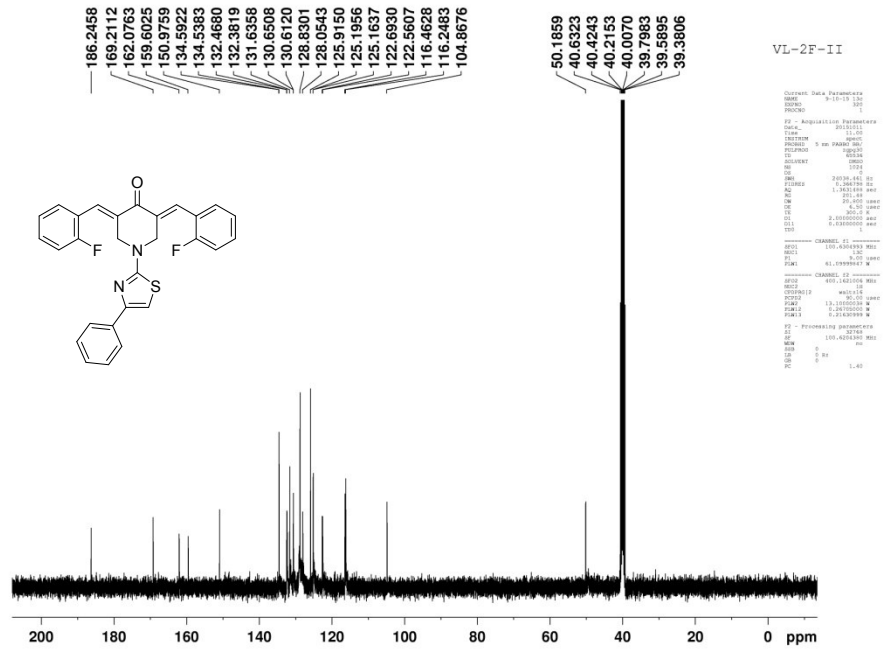
^{1}H NMR Spectra of compound **43**(400 MHz, $CDCl_3$)



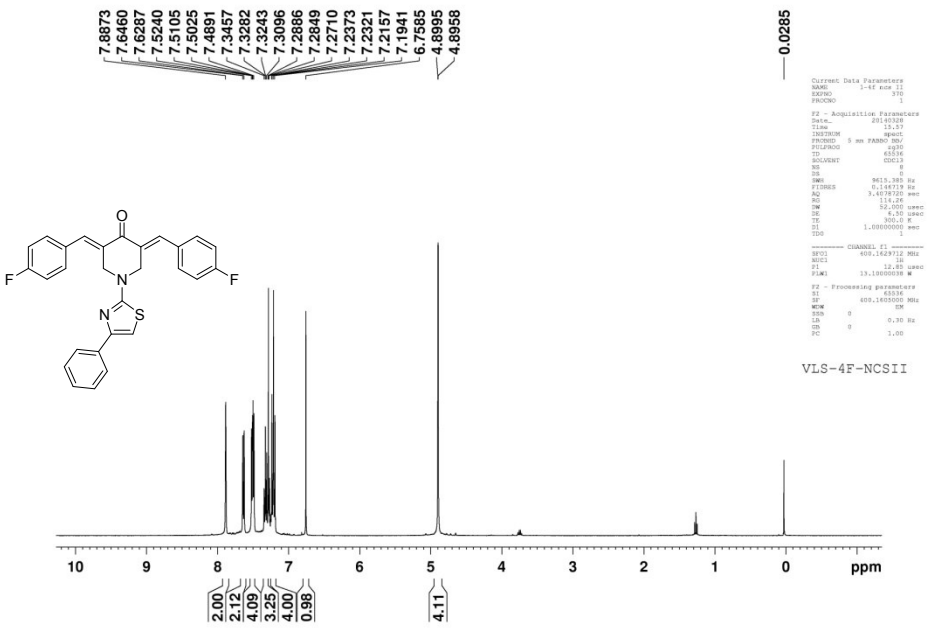
^{13}C NMR Spectra of compound **43**(100 MHz, $CDCl_3$)



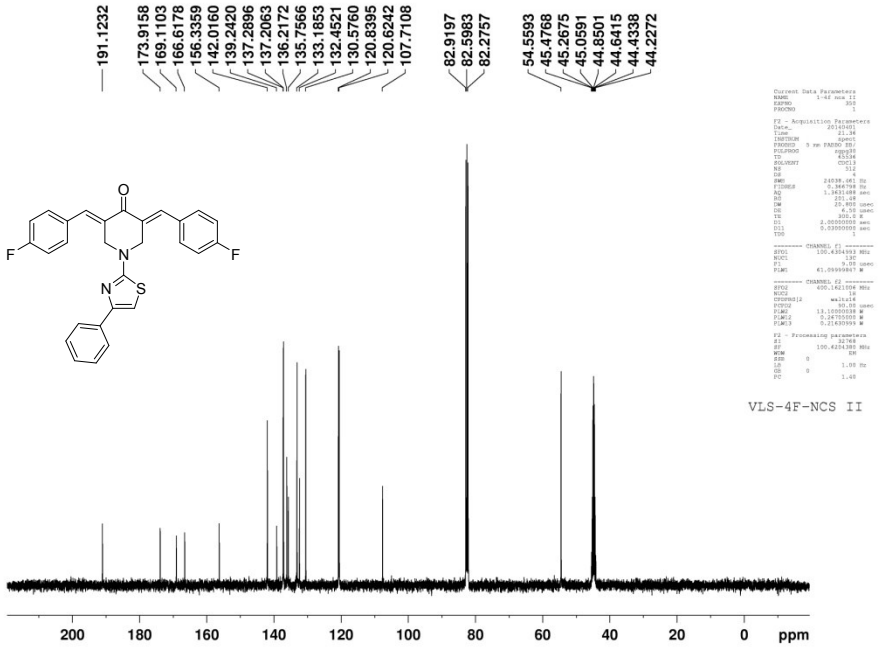
^{1}H NMR Spectra of compound **44**(400 MHz, $CDCl_3$)



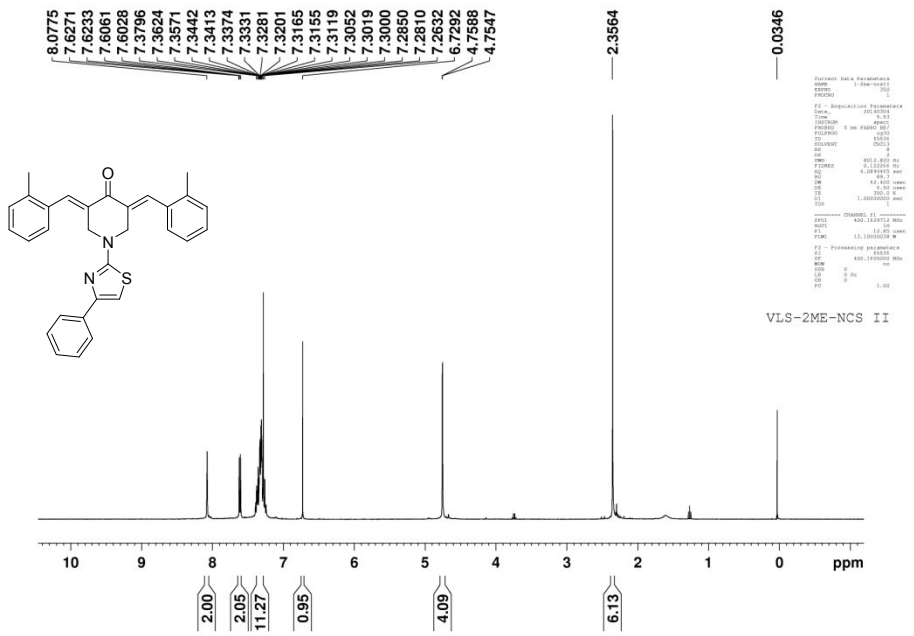
^{13}C NMR Spectra of compound **44**(100 MHz, DMSO-d_6)



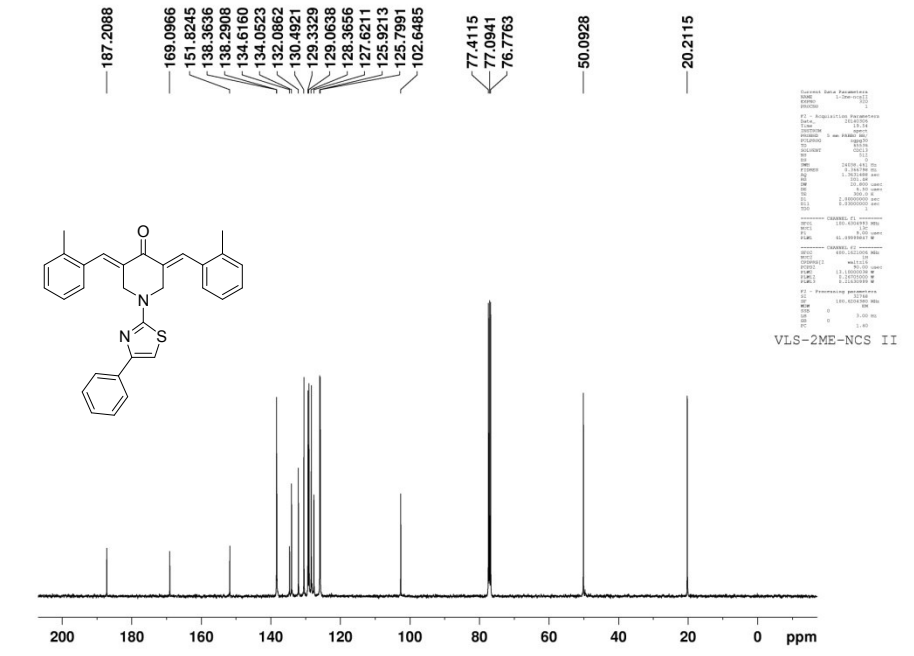
^{1}H NMR Spectra of compound **45**(400 MHz, $CDCl_3$)



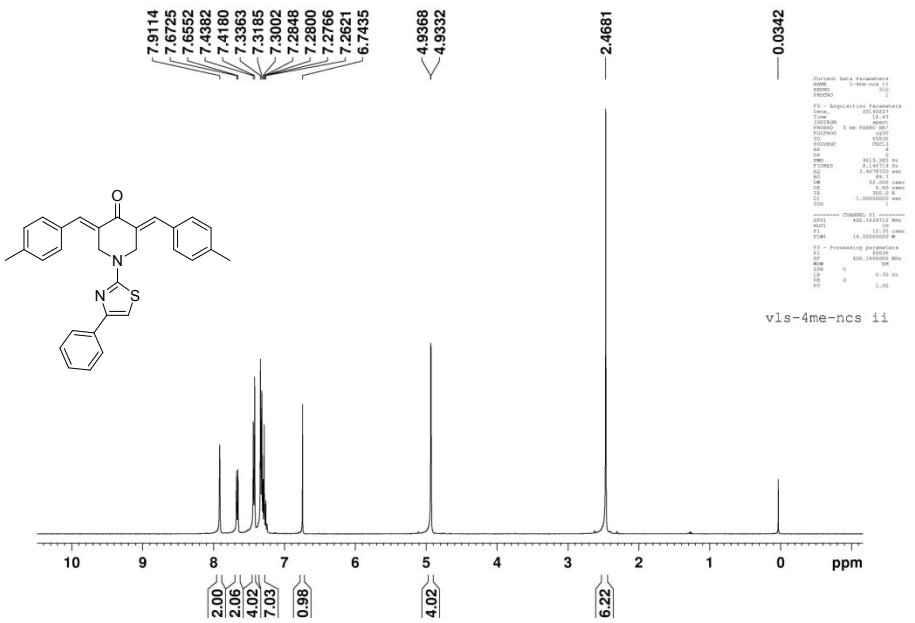
^{13}C NMR Spectra of compound **45**(100 MHz, CDCl3+DMSO-d_6)



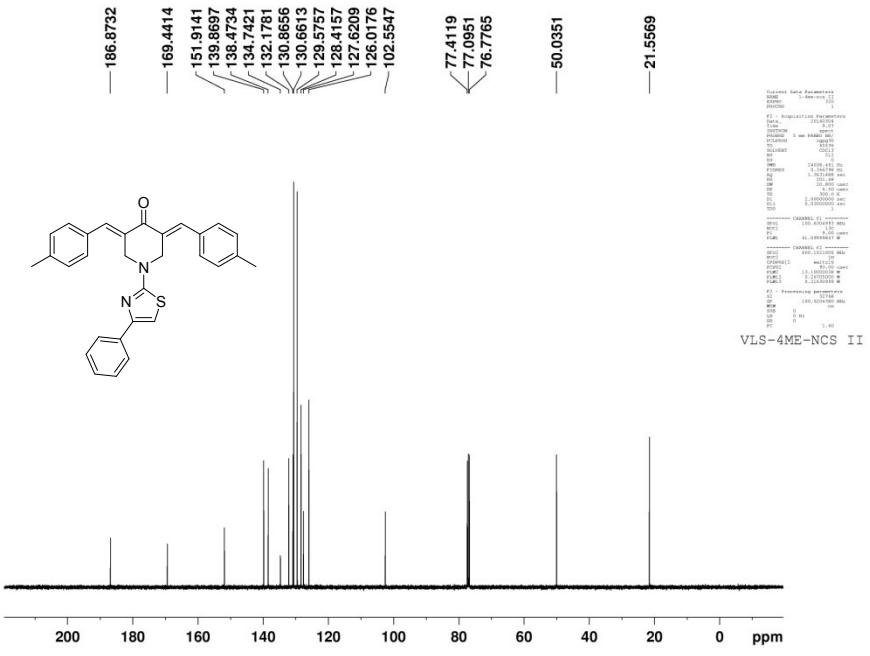
^{1}H NMR Spectra of compound **46**(400 MHz, $CDCl_3$)



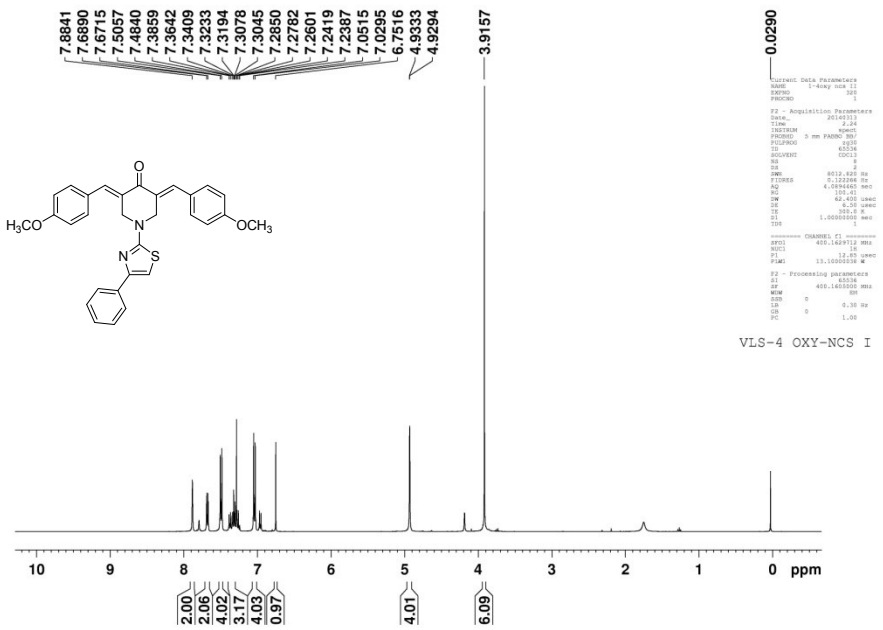
^{13}C NMR Spectra of compound **46**(100 MHz, $CDCl_3$)



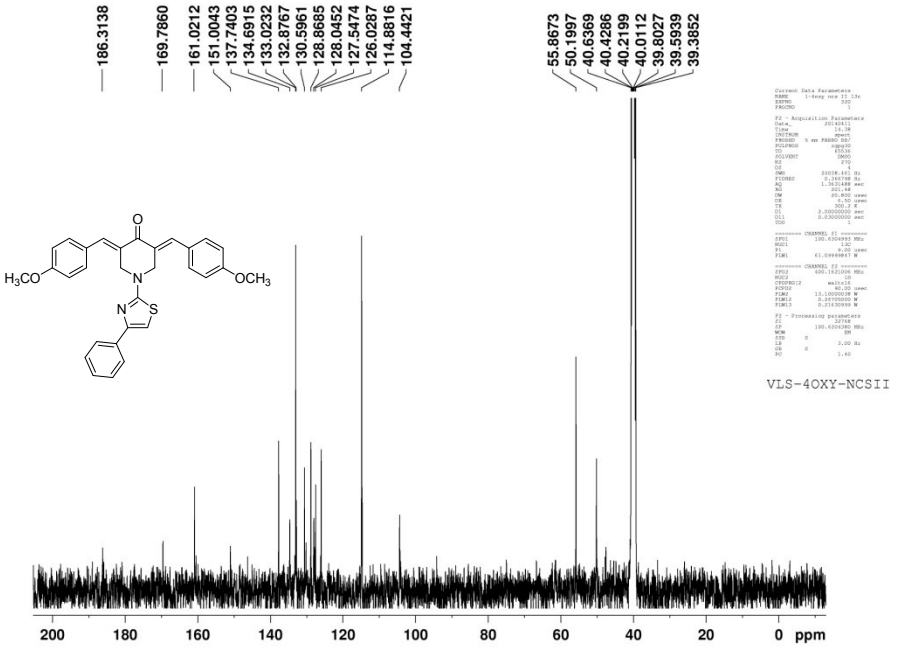
^{1}H NMR Spectra of compound **47**(400 MHz, $CDCl_3$)



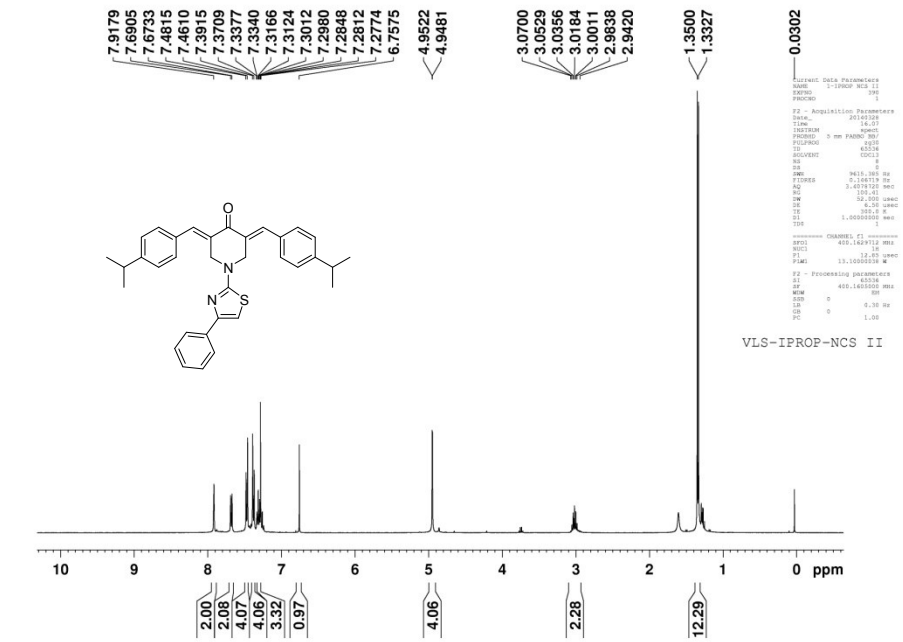
^{13}C NMR Spectra of compound **47**(100 MHz, $CDCl_3$)



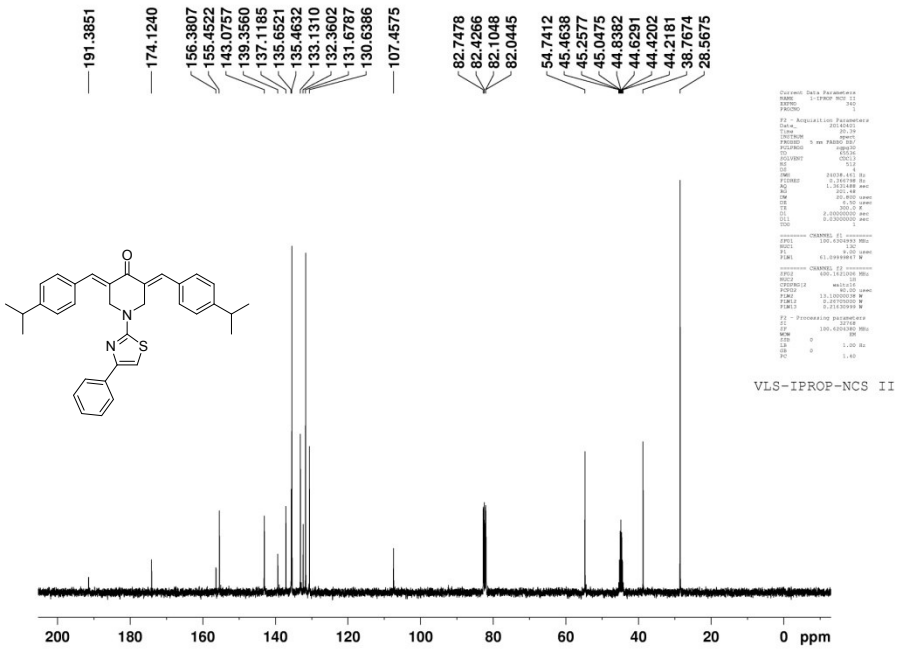
^{1}H NMR Spectra of compound **48**(400 MHz, $CDCl_3$)



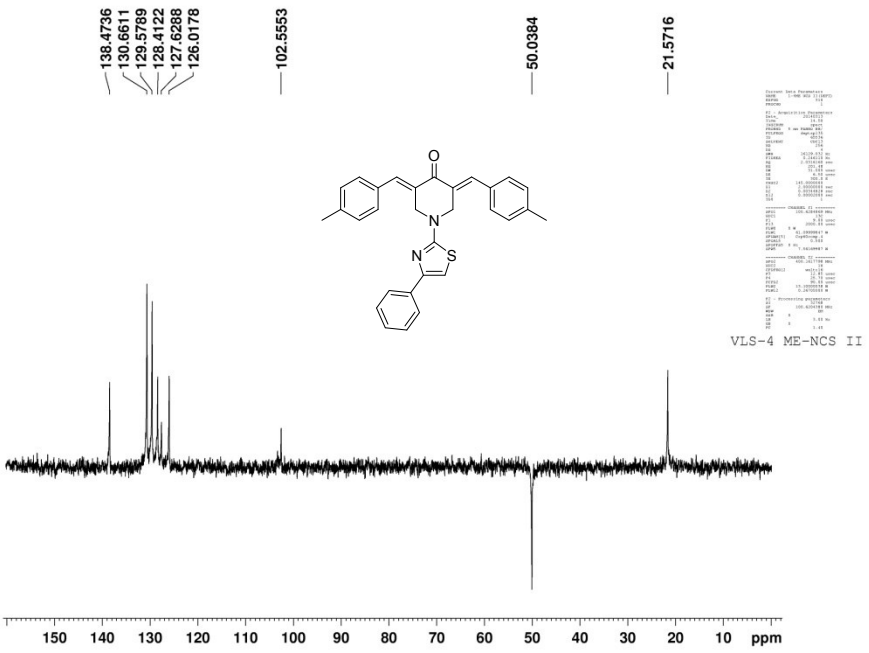
^{13}C NMR Spectra of compound **48**(100 MHz, DMSO-d_6)



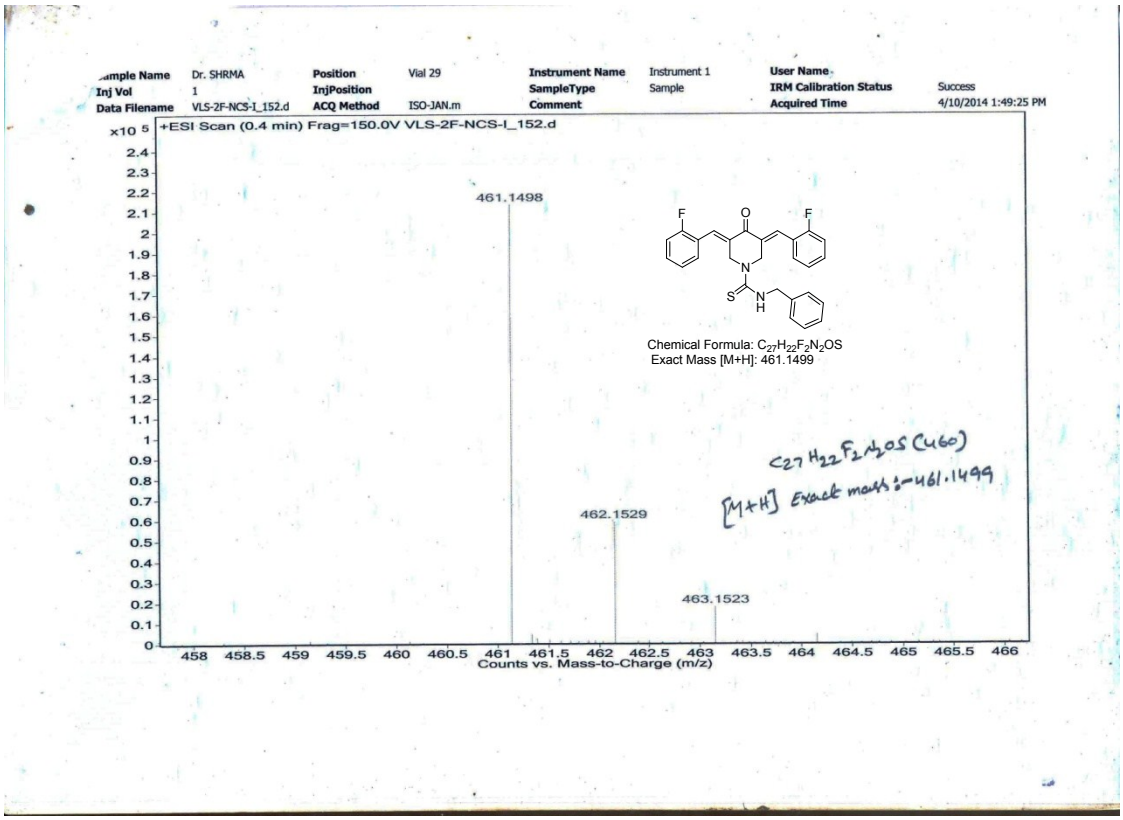
^{1}H NMR Spectra of compound **49**(400 MHz, $CDCl_3$)



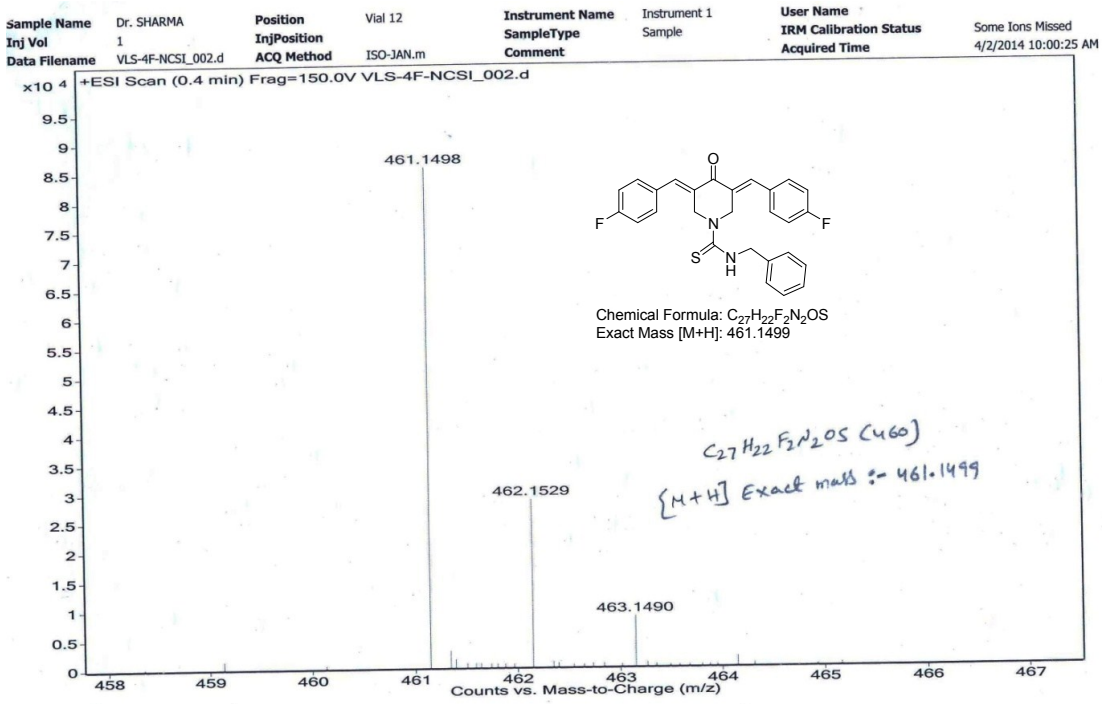
^{13}C NMR Spectra of compound **49**(100 MHz, $CDCl_3$+DMSO-d_6)



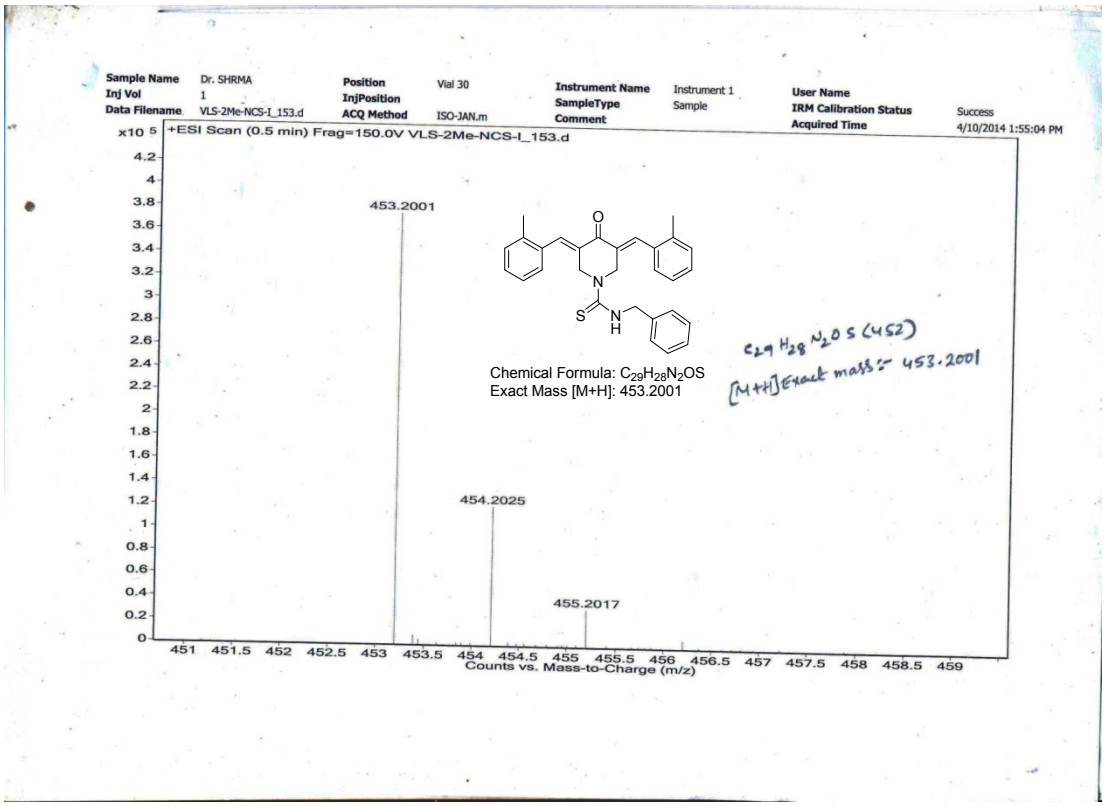
DEPT-135 Spectra of compound **47**(100 MHz, $CDCl_3$)



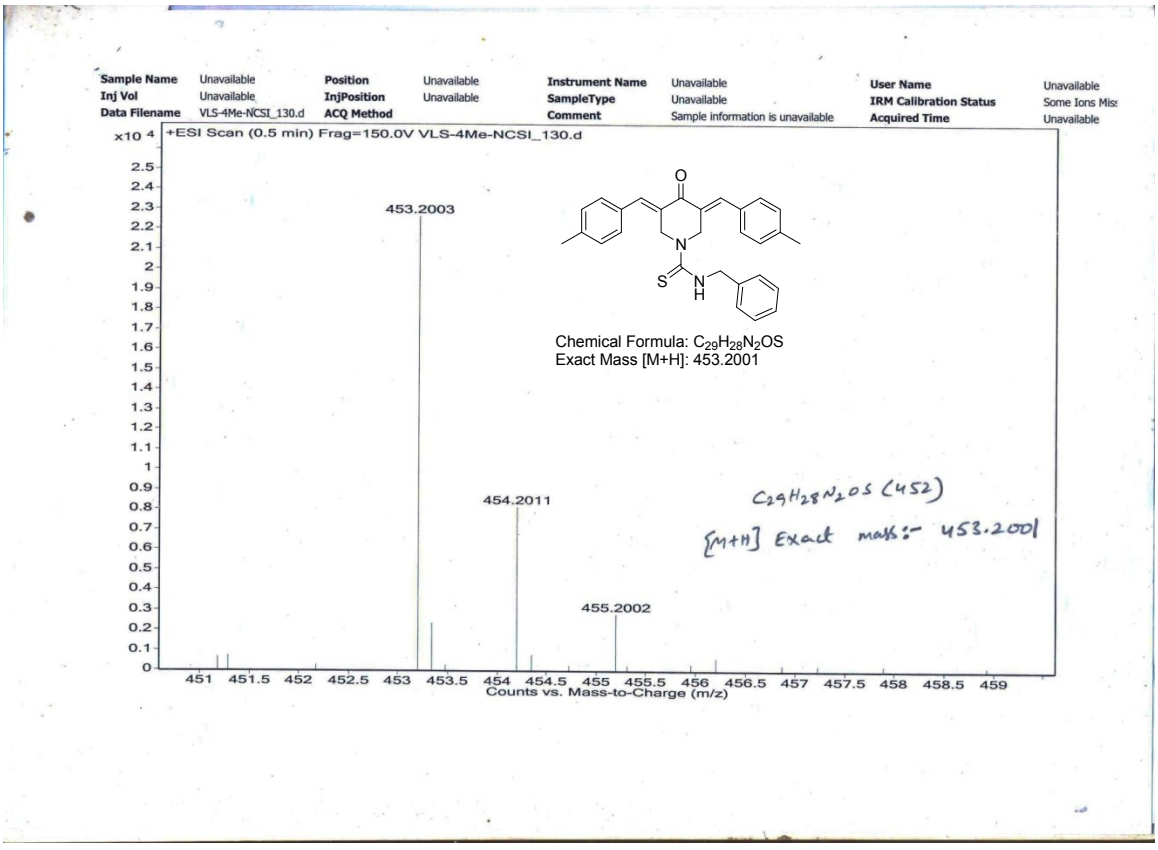
HRMS of compound **14**



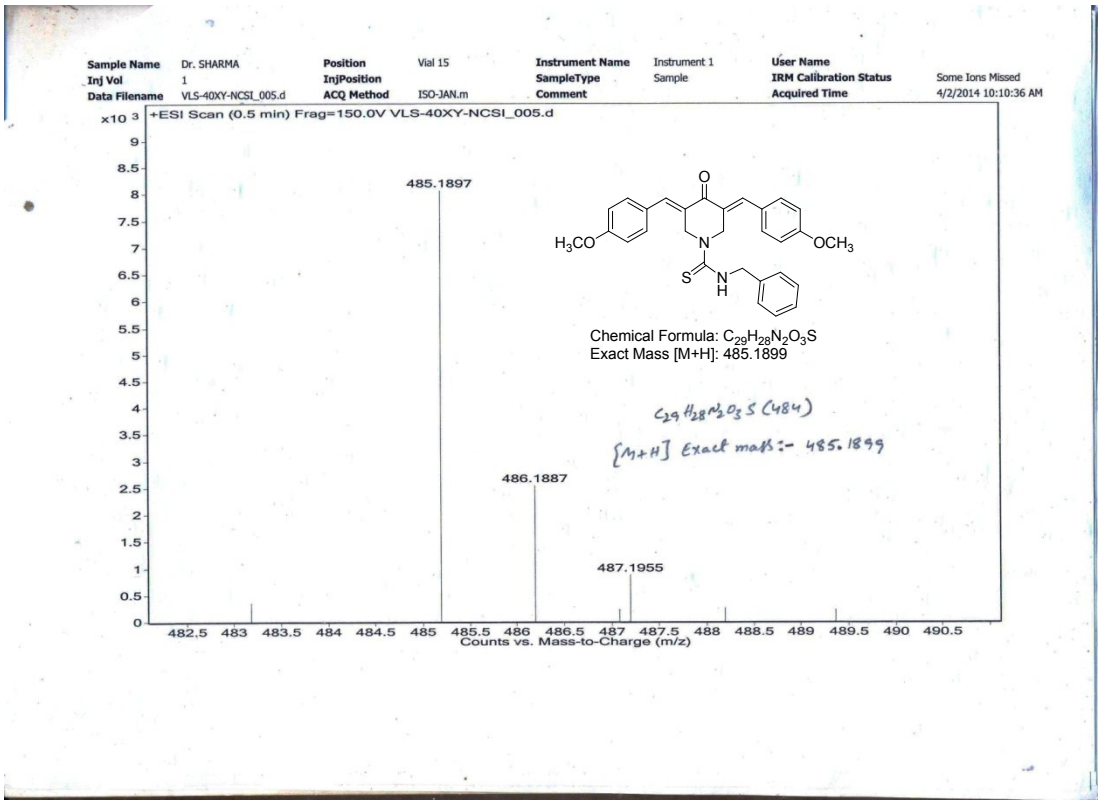
HRMS of compound **15**



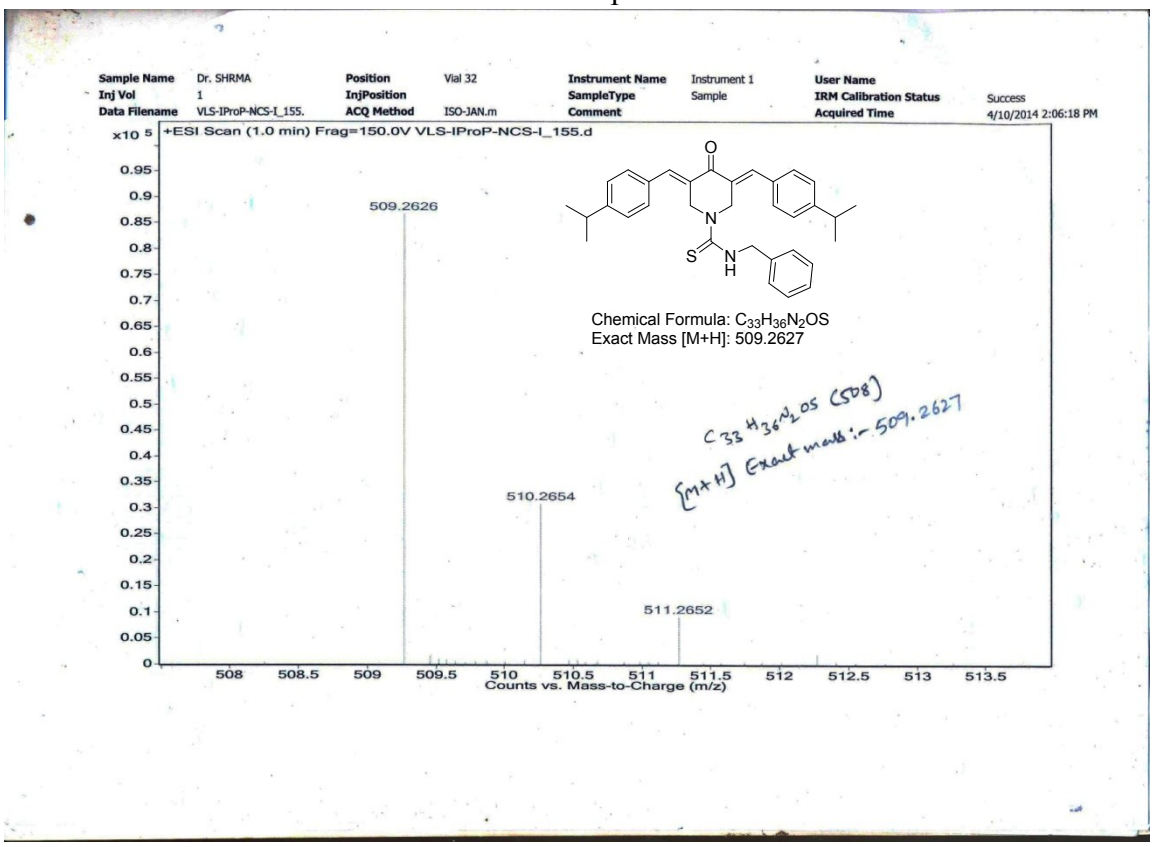
HRMS of compound **16**



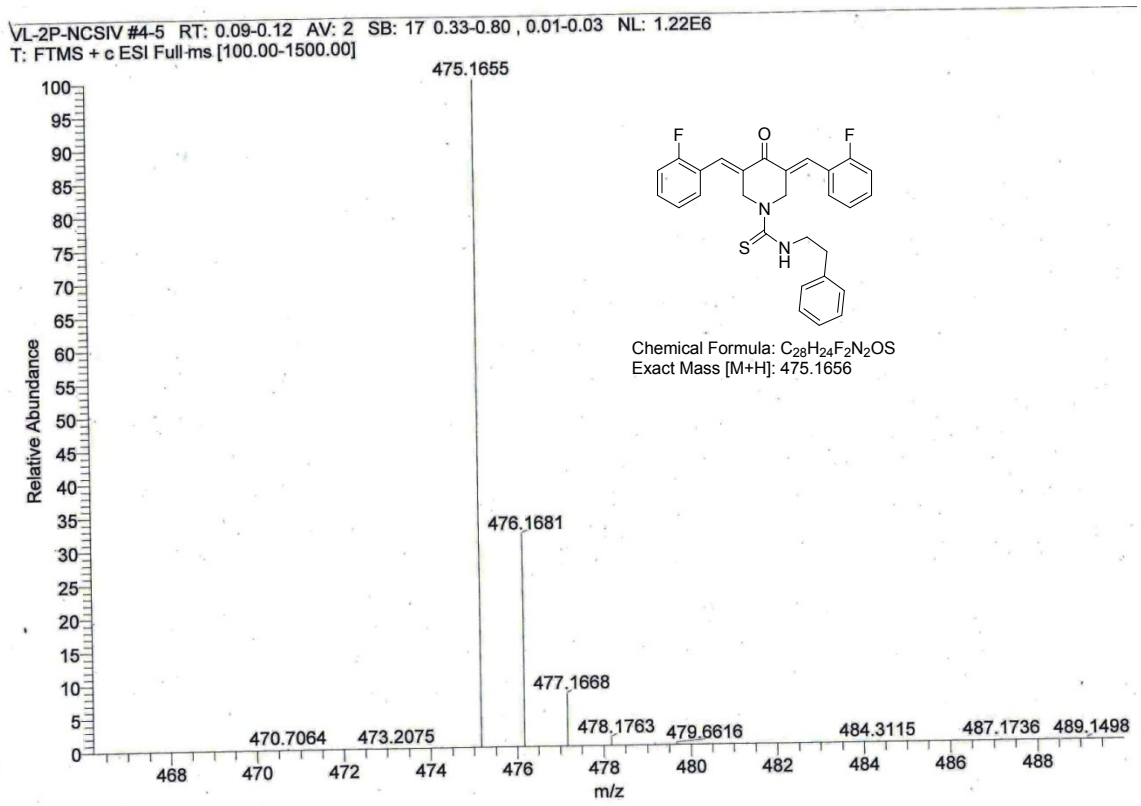
HRMS of compound **17**



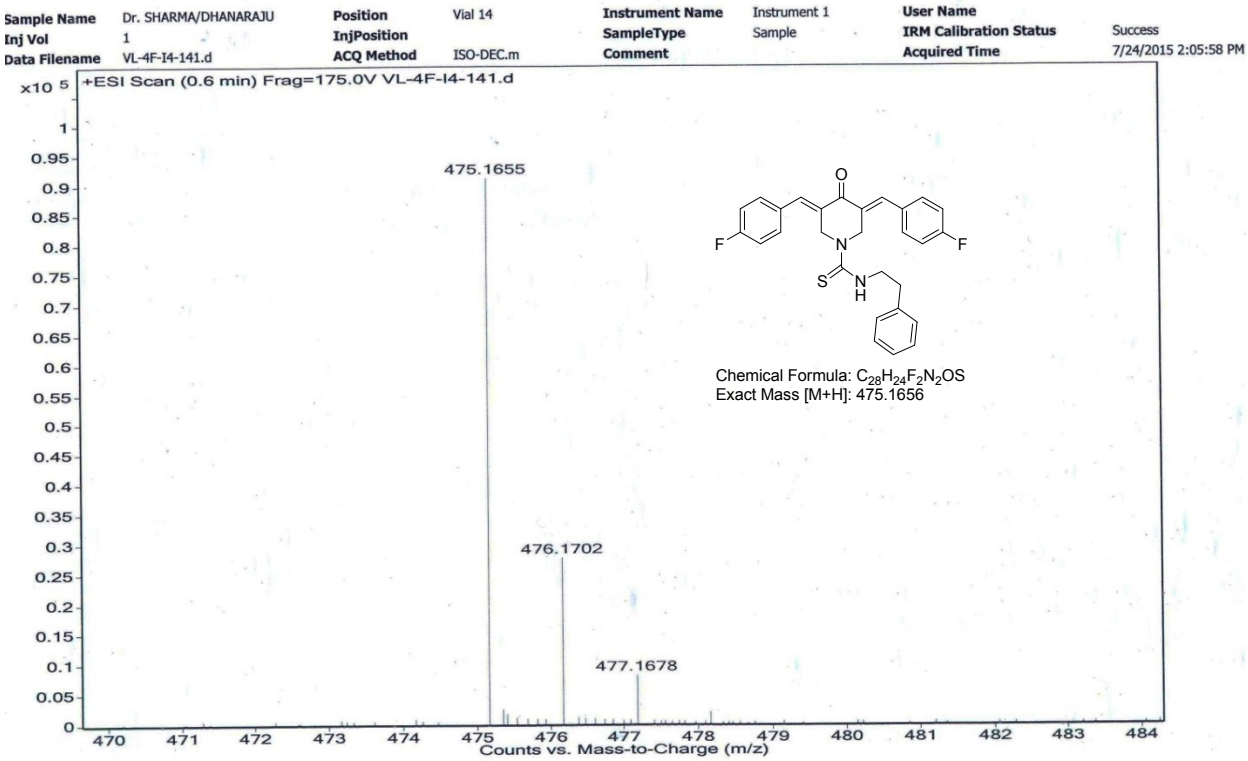
HRMS of compound **18**



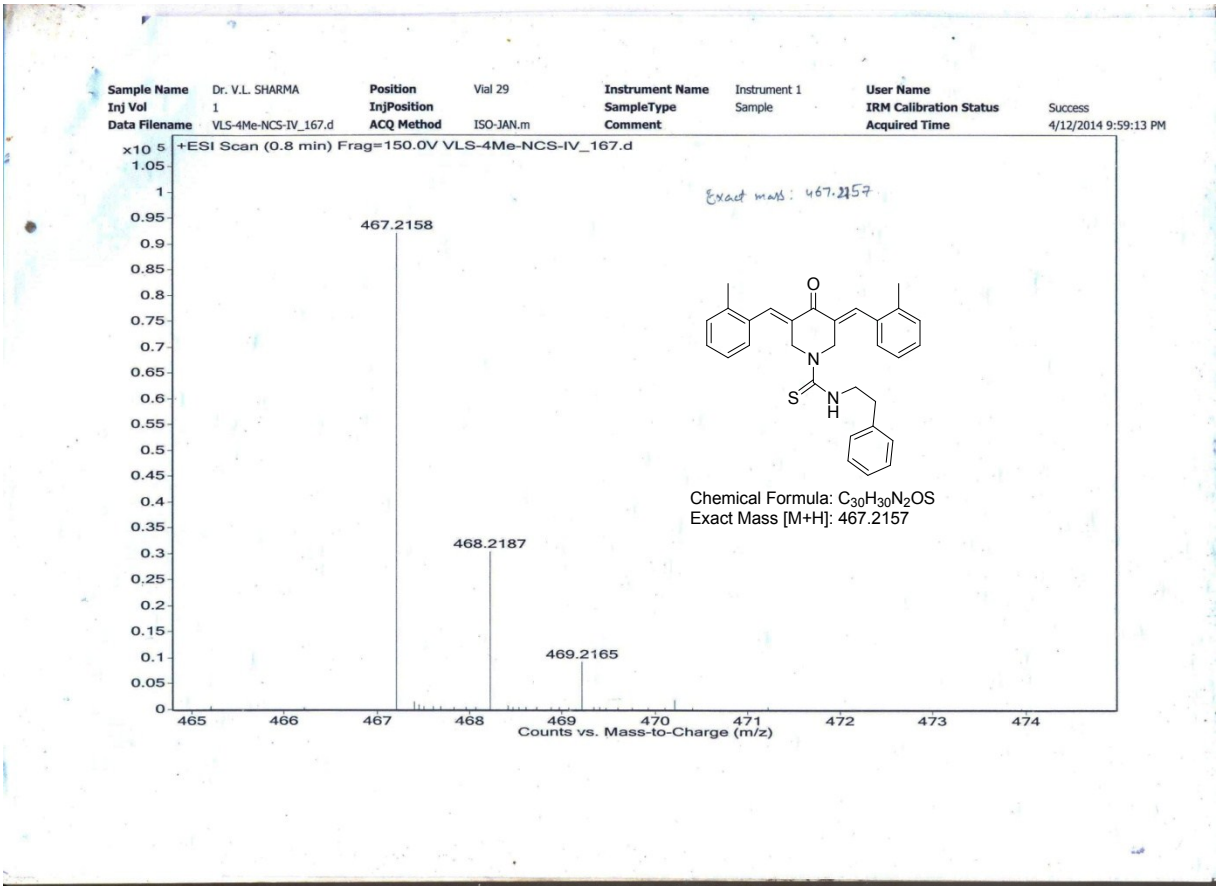
HRMS of compound **19**



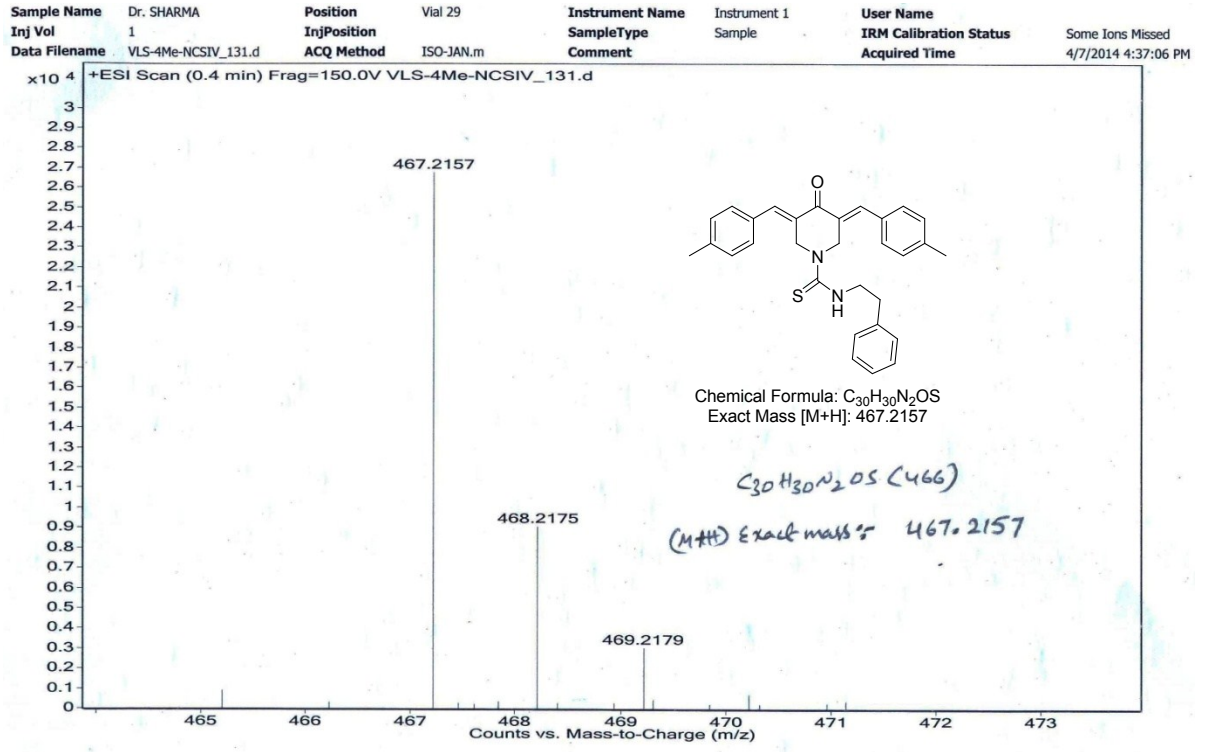
HRMS of compound **20**



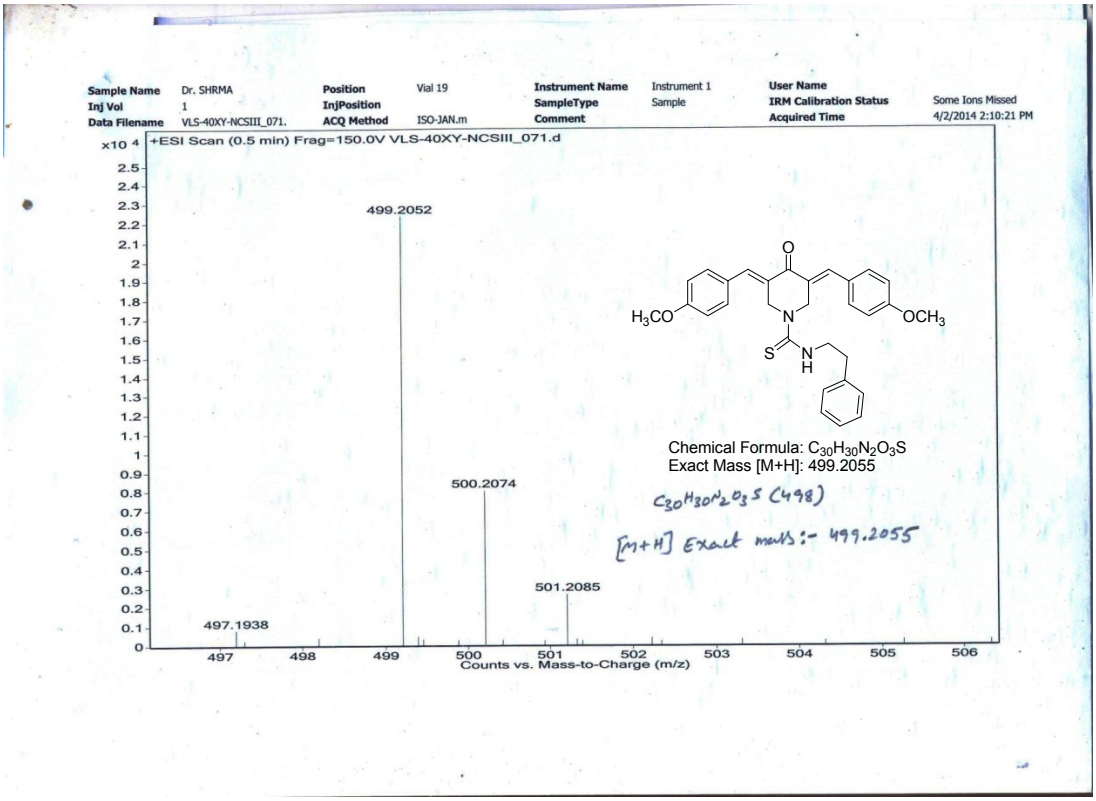
HRMS of compound **21**



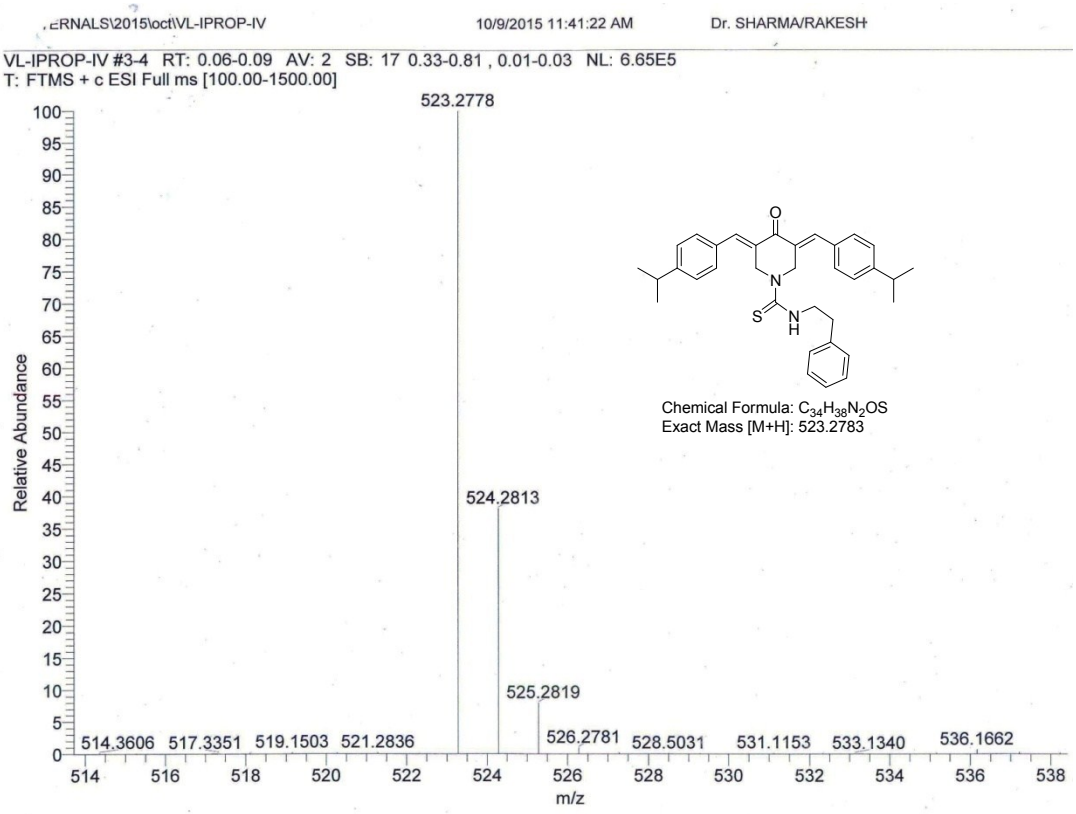
HRMS of compound **22**



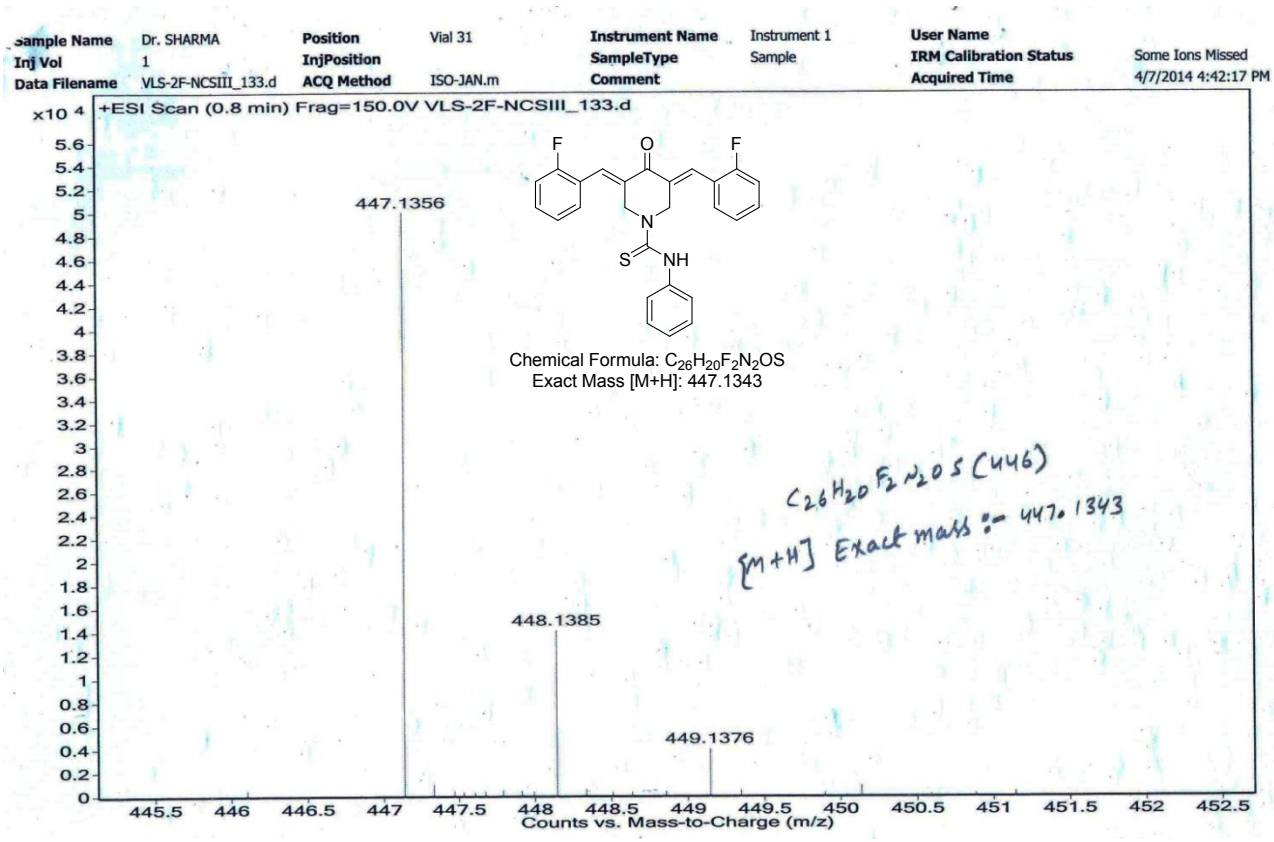
HRMS of compound **23**



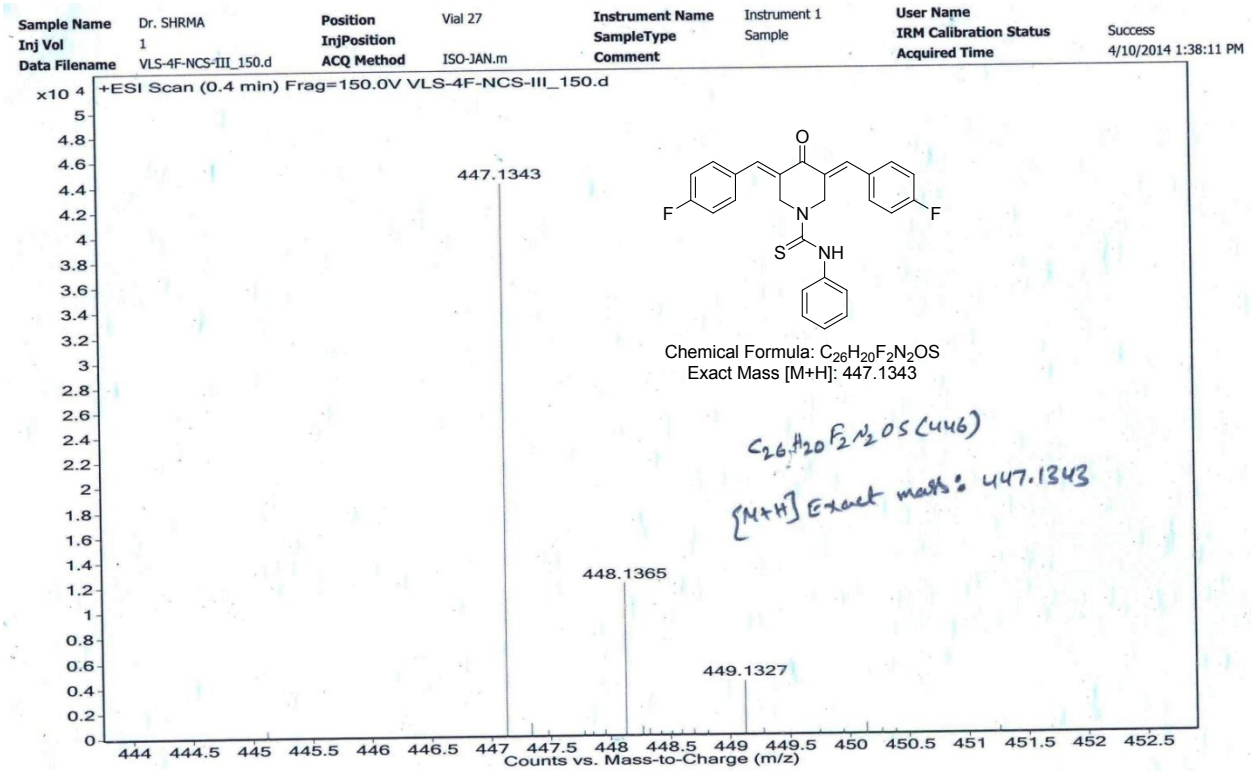
HRMS of compound **24**



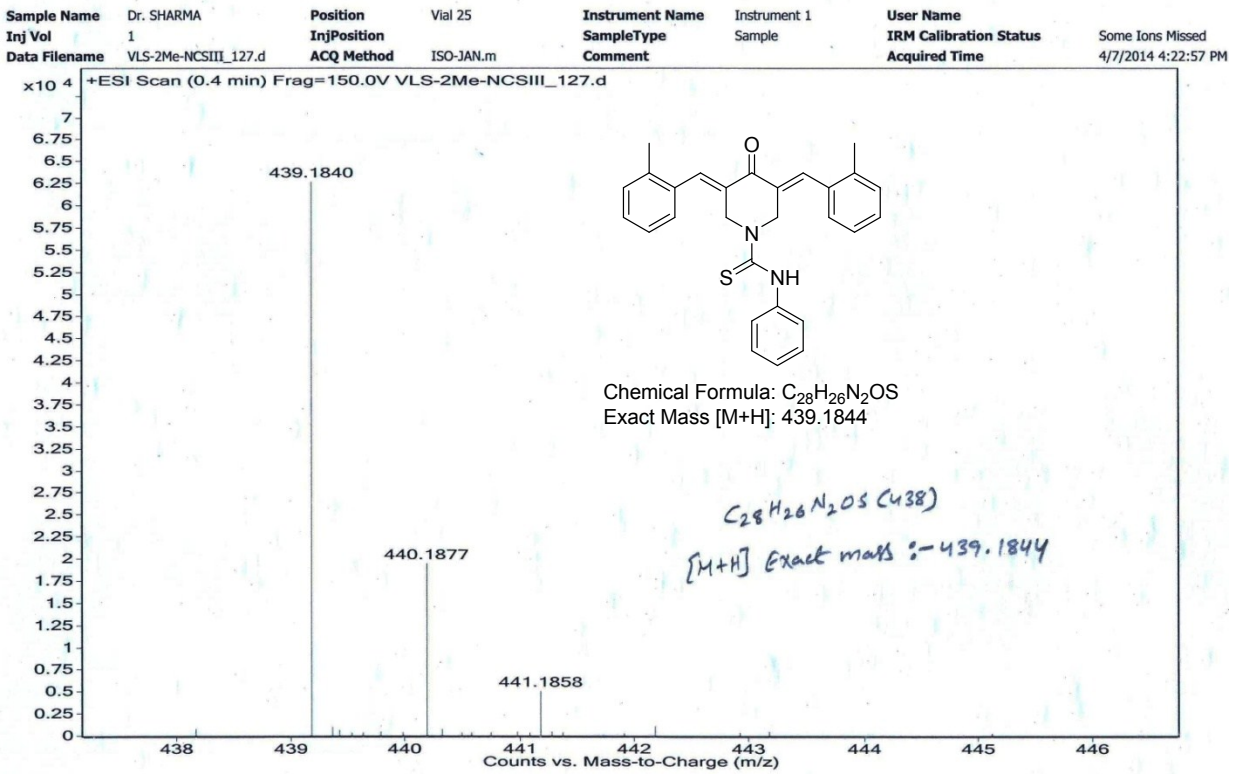
HRMS of compound **25**



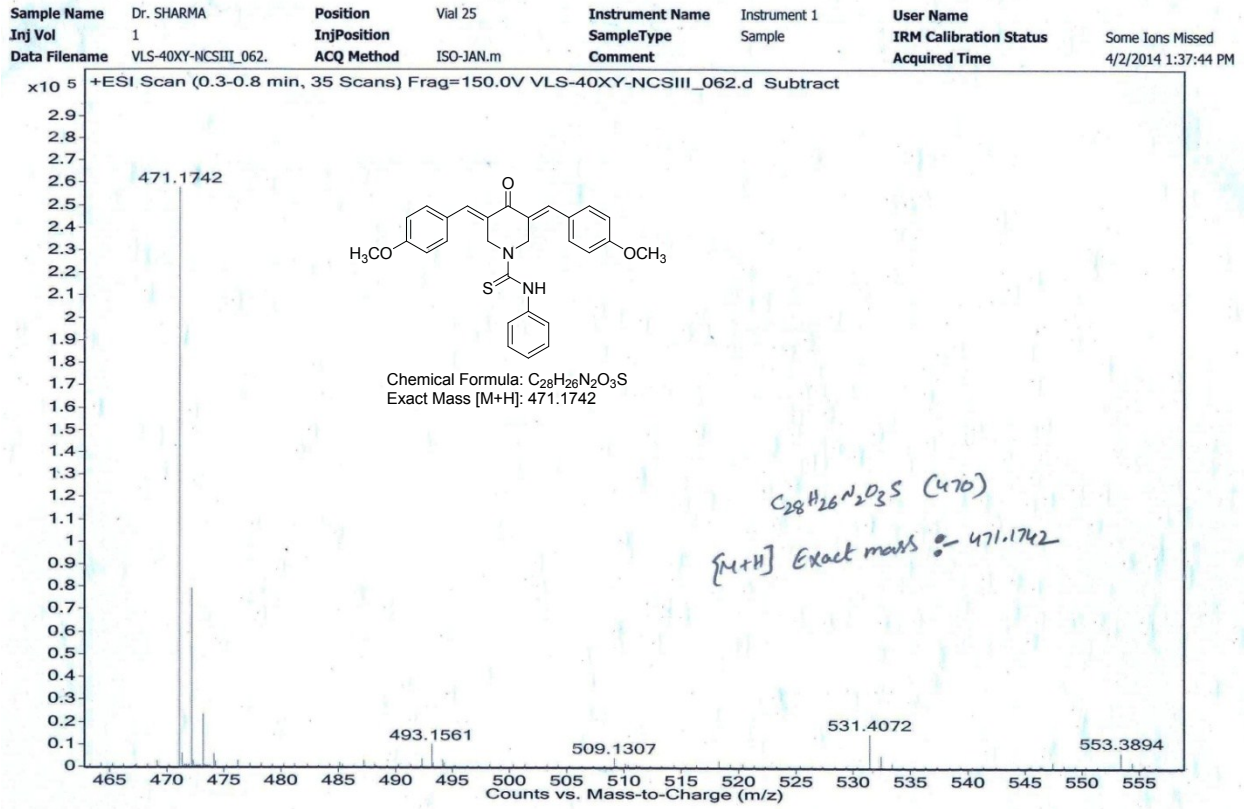
HRMS of compound **26**



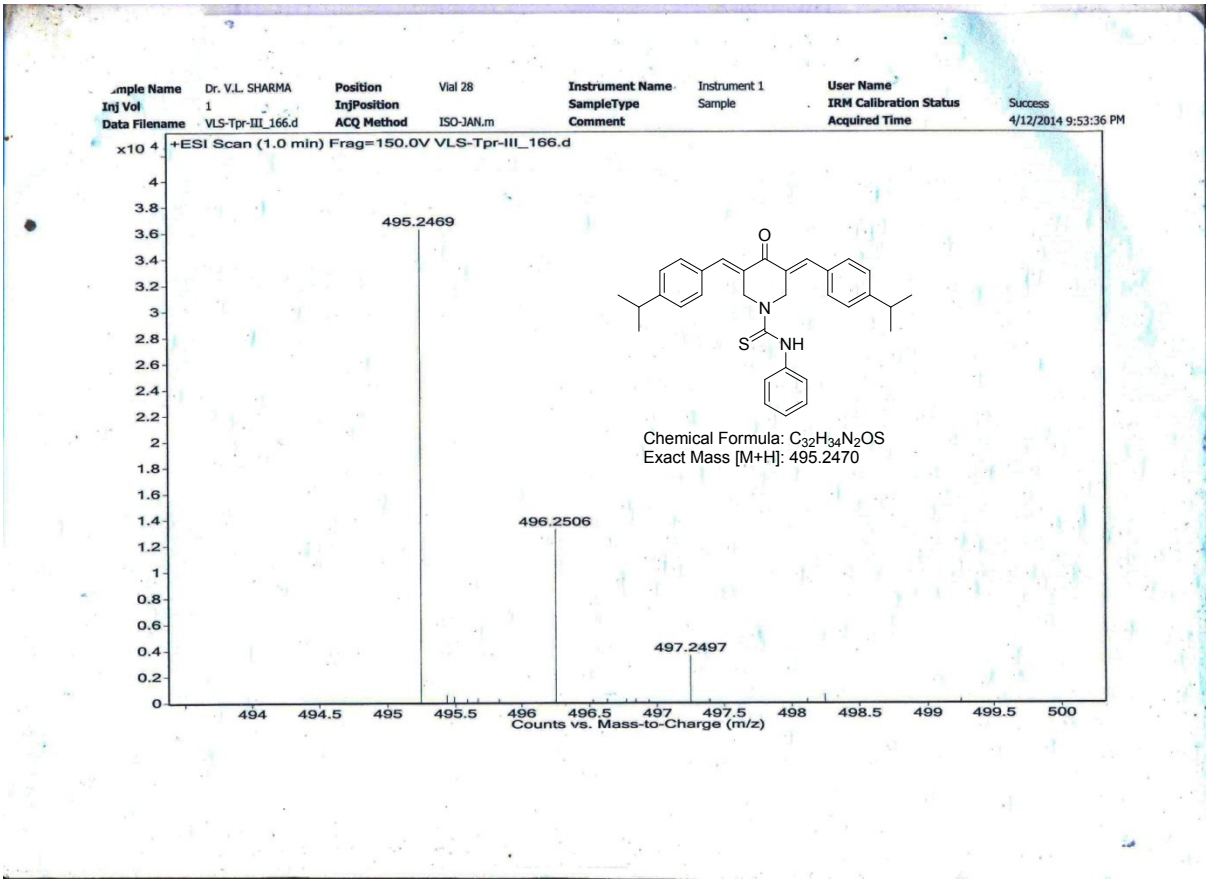
HRMS of compound **27**



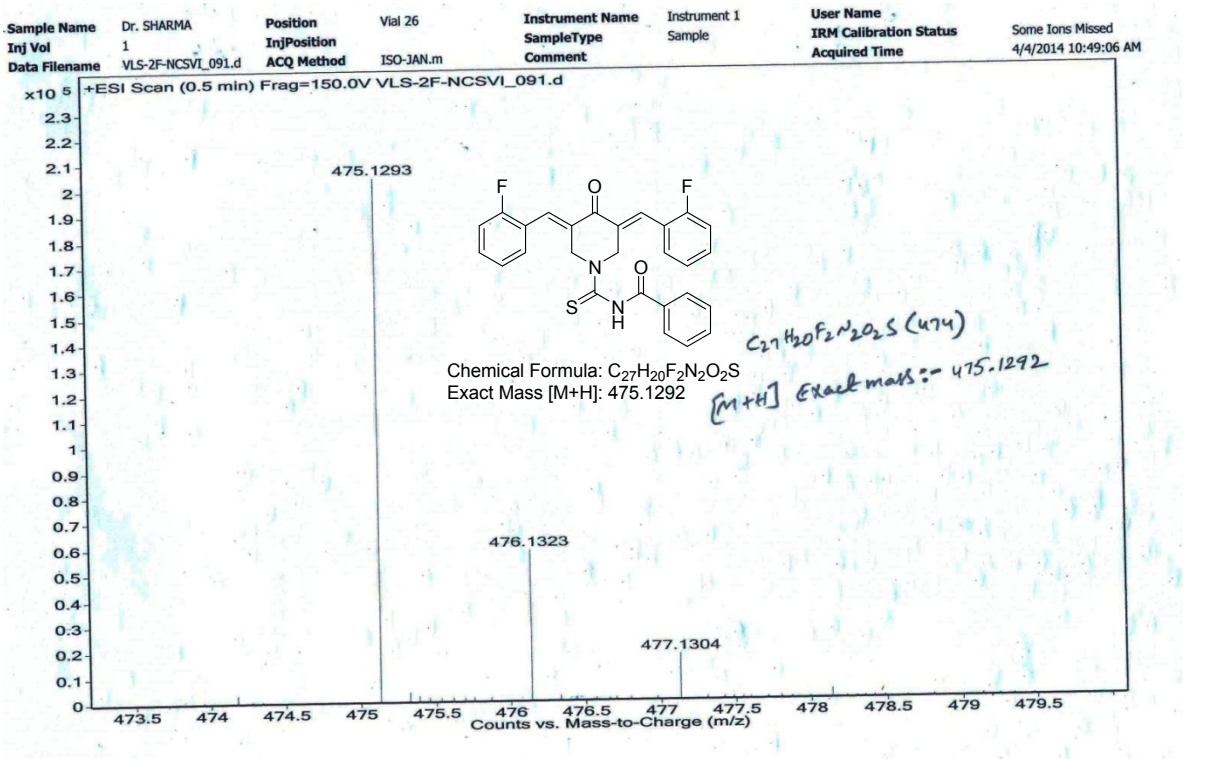
HRMS of compound **28**



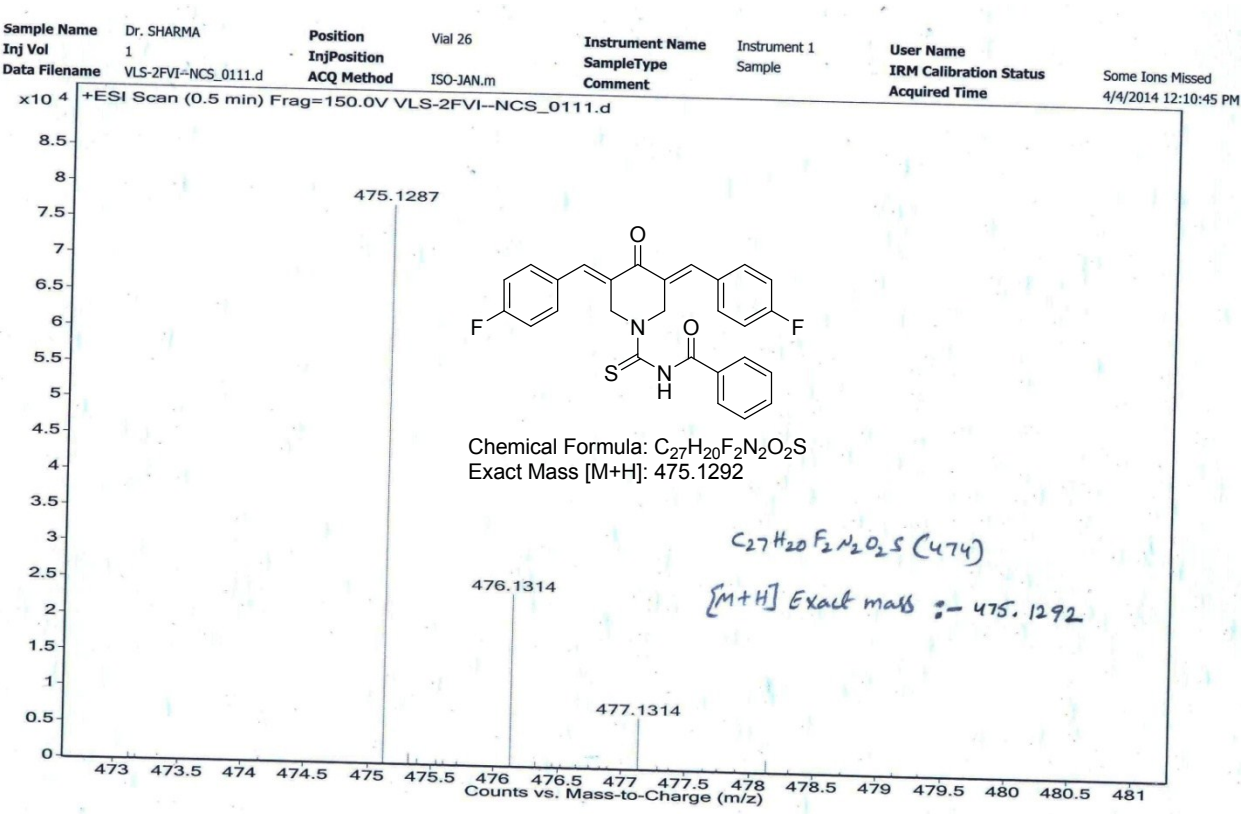
HRMS of compound **30**



HRMS of compound **31**



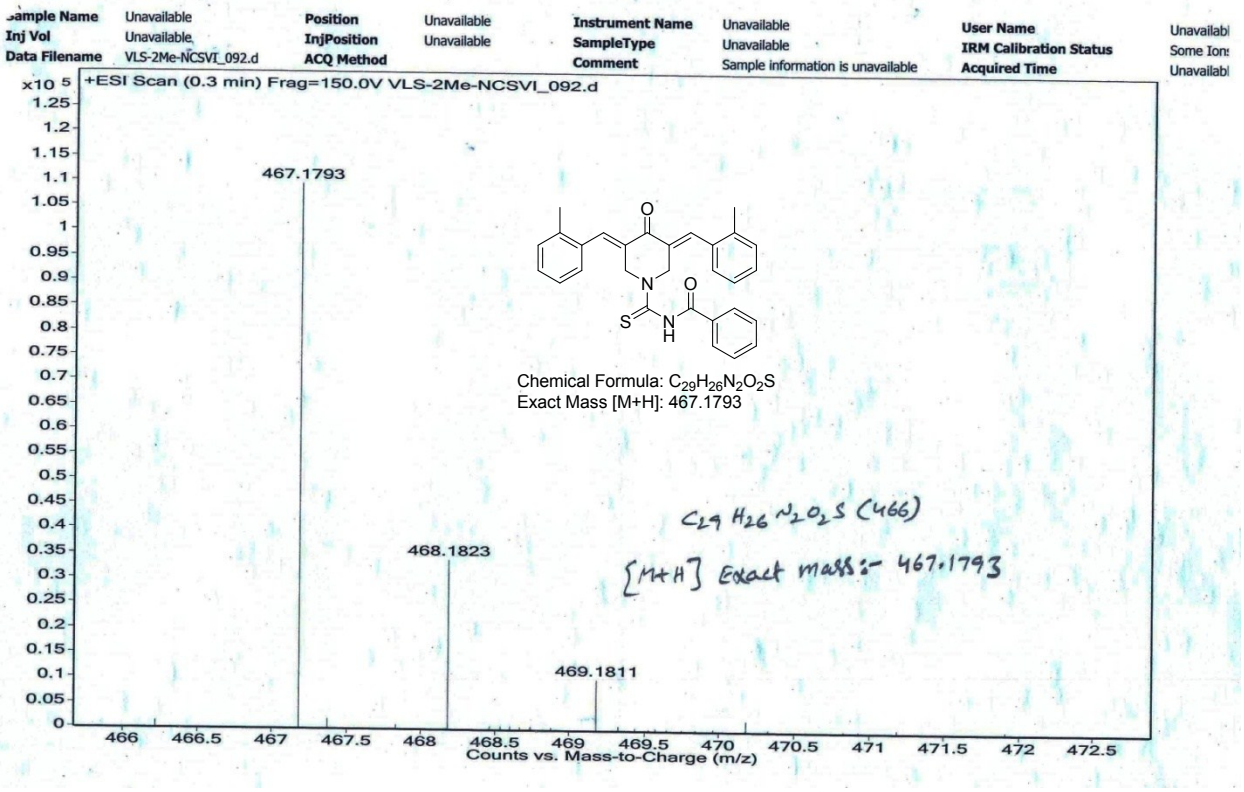
HRMS of compound **32**



Chemical Formula: $C_{27}H_{20}F_2N_2O_2S$
Exact Mass [M+H]: 475.1292

$C_{27}H_{20}F_2N_2O_2S$ (474)
[M+H] Exact mass :- 475.1292

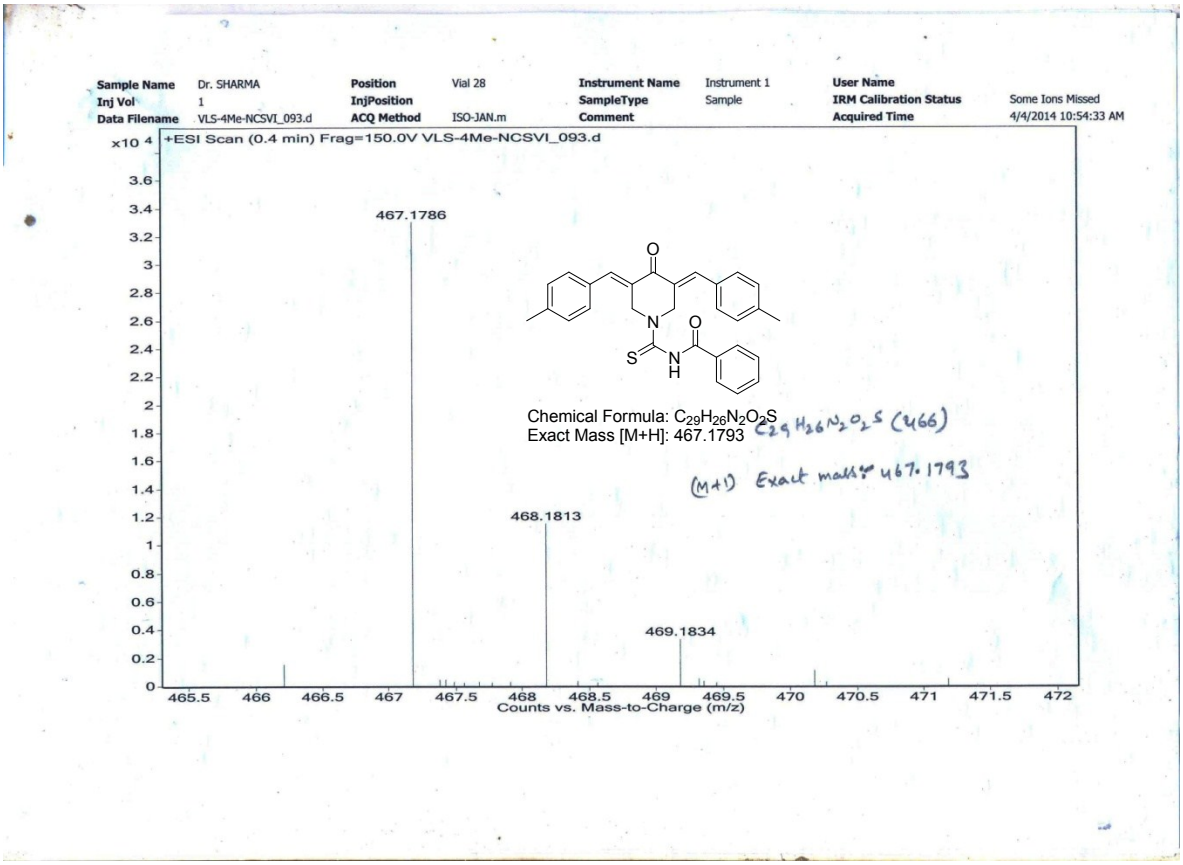
HRMS of compound **33**



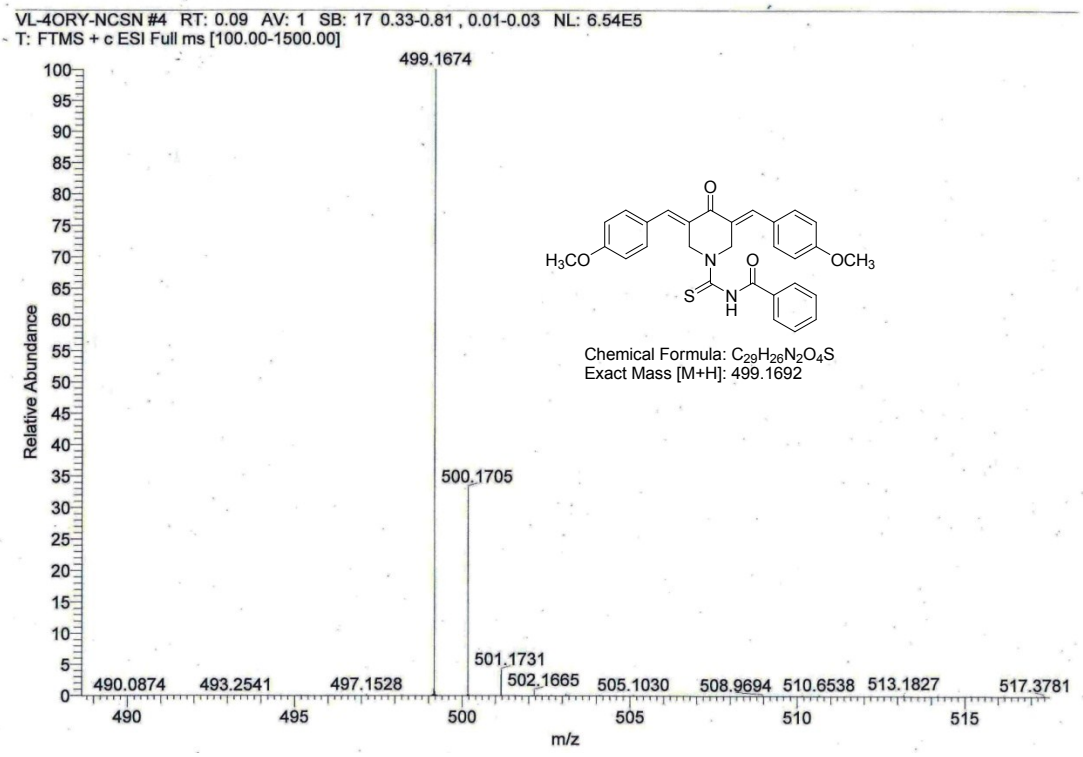
Chemical Formula: $C_{29}H_{26}N_2O_2S$
Exact Mass [M+H]: 467.1793

$C_{29}H_{26}N_2O_2S$ (466)
[M+H] Exact mass:- 467.1793

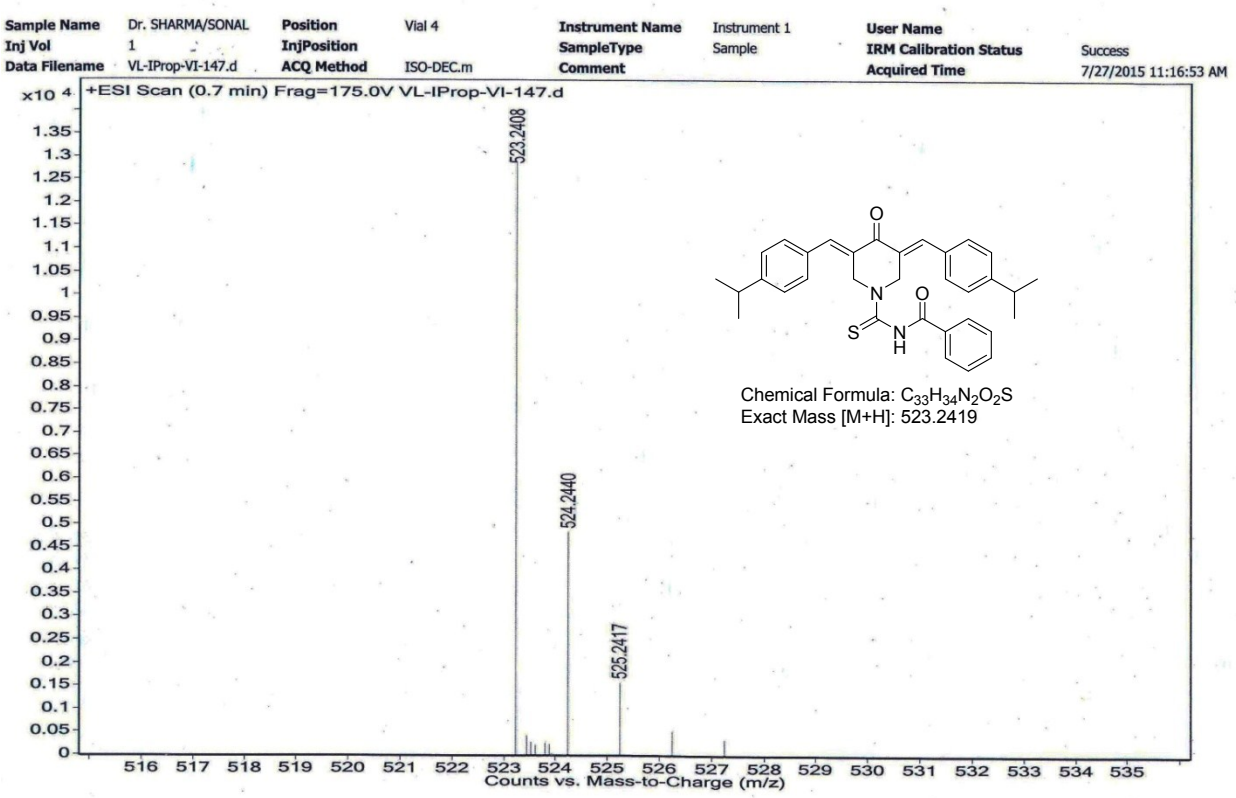
HRMS of compound **34**



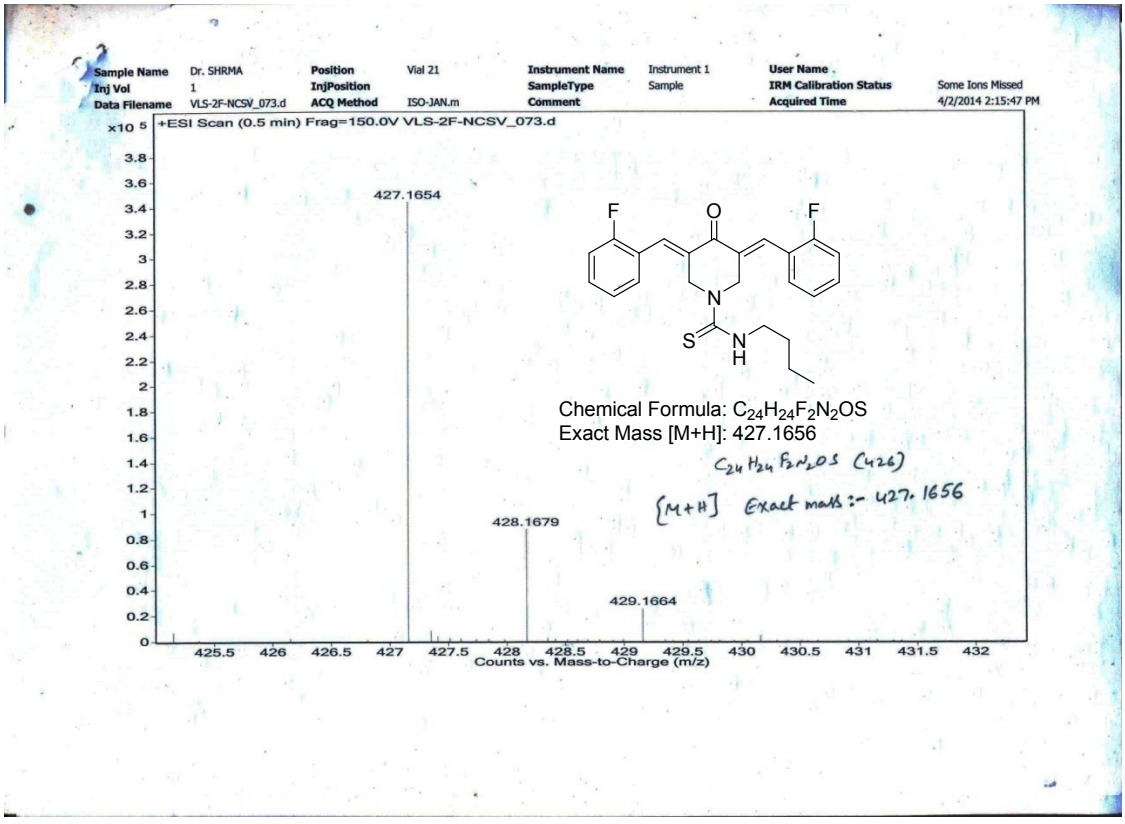
HRMS of compound **35**



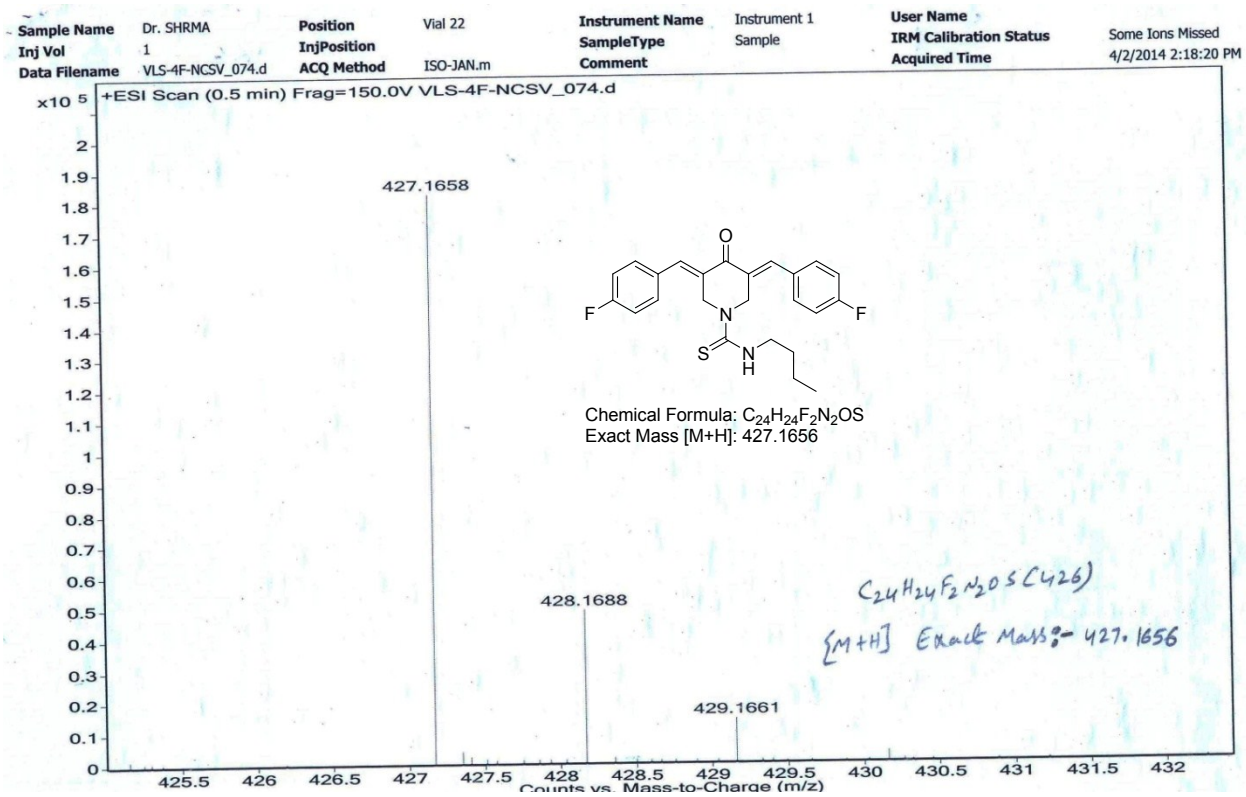
HRMS of compound **36**



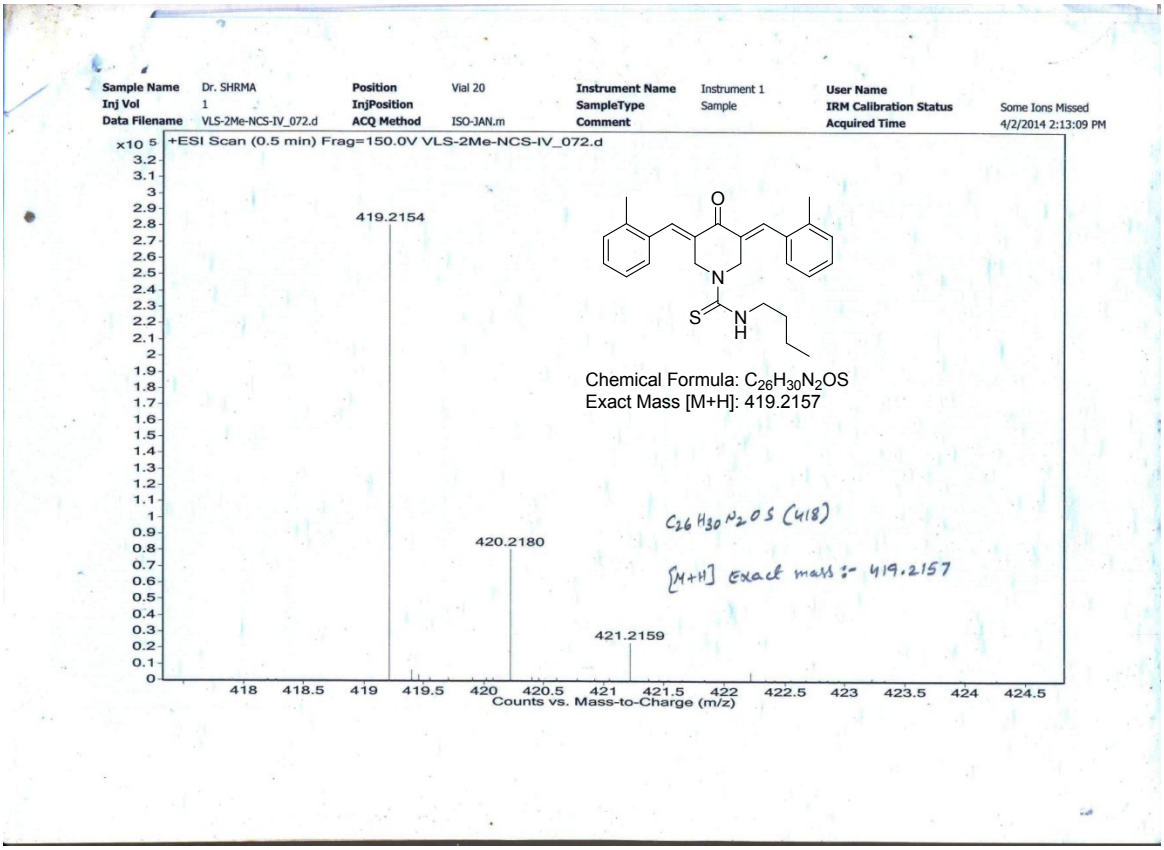
HRMS of compound **37**



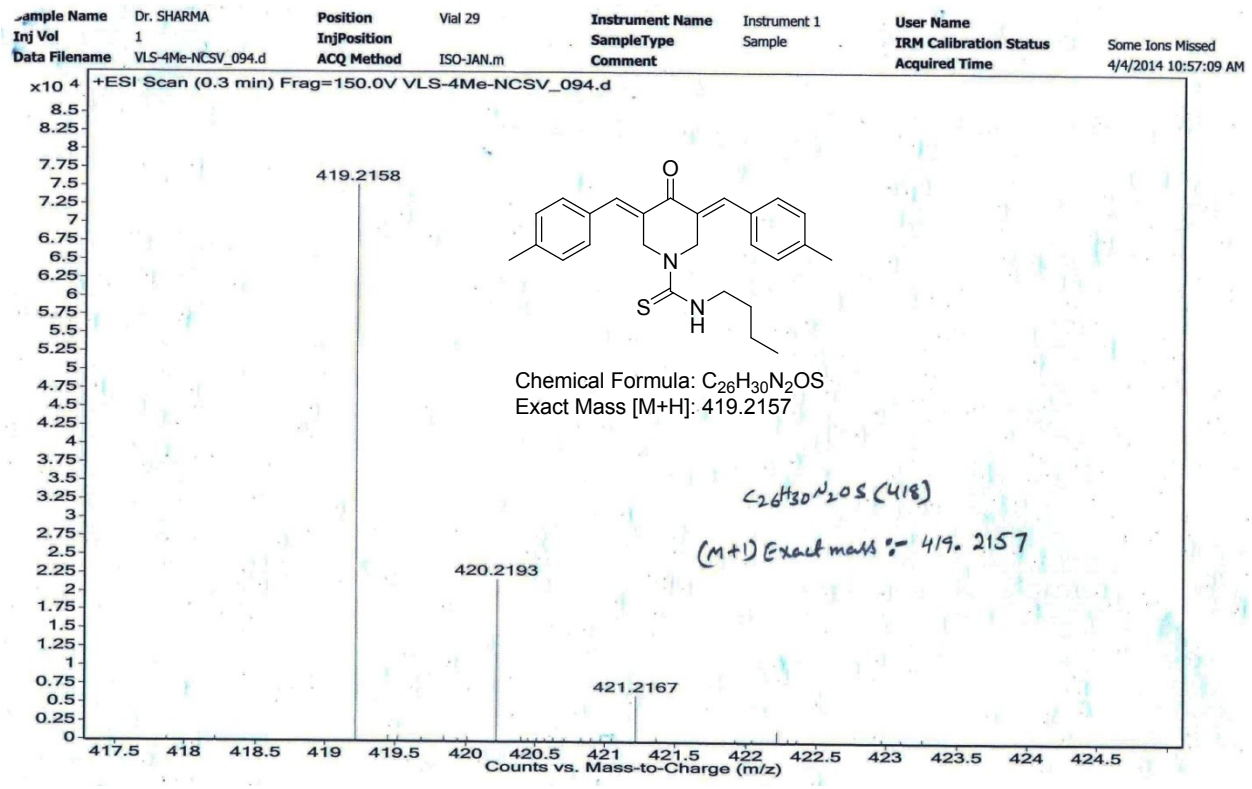
HRMS of compound **38**



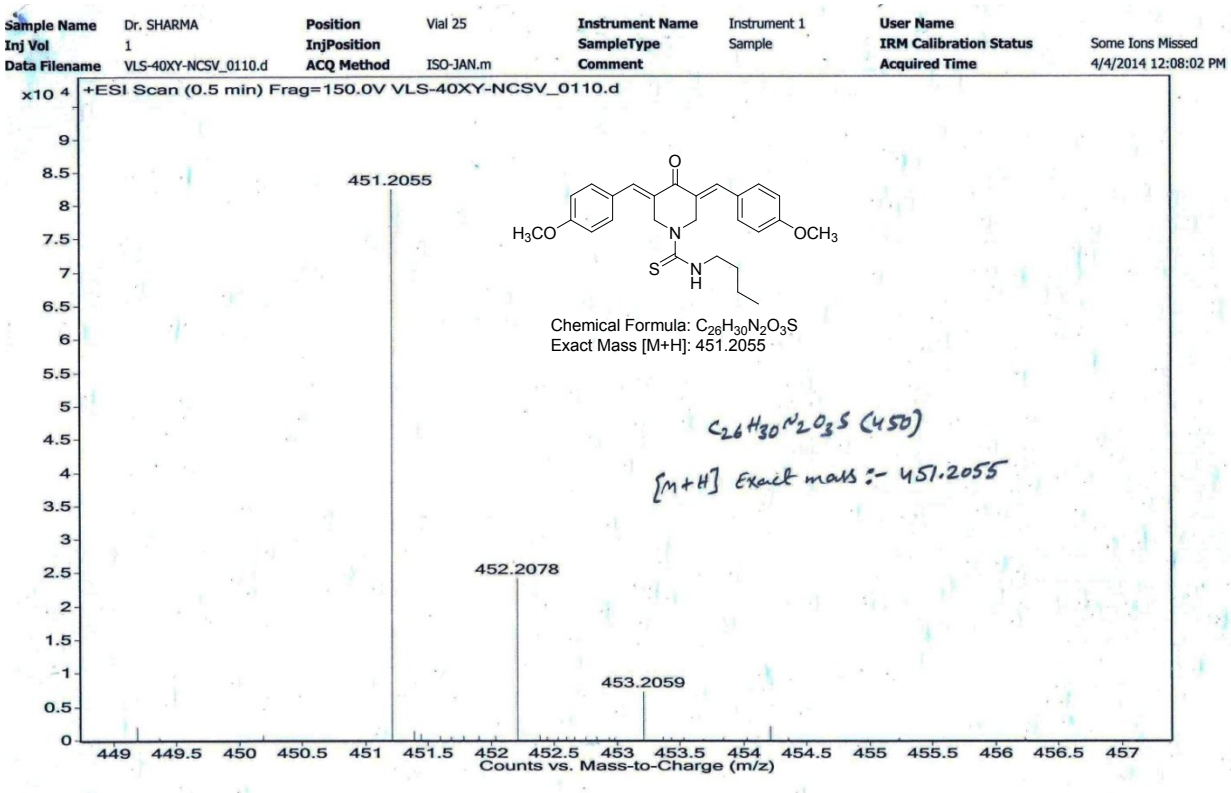
HRMS of compound **39**



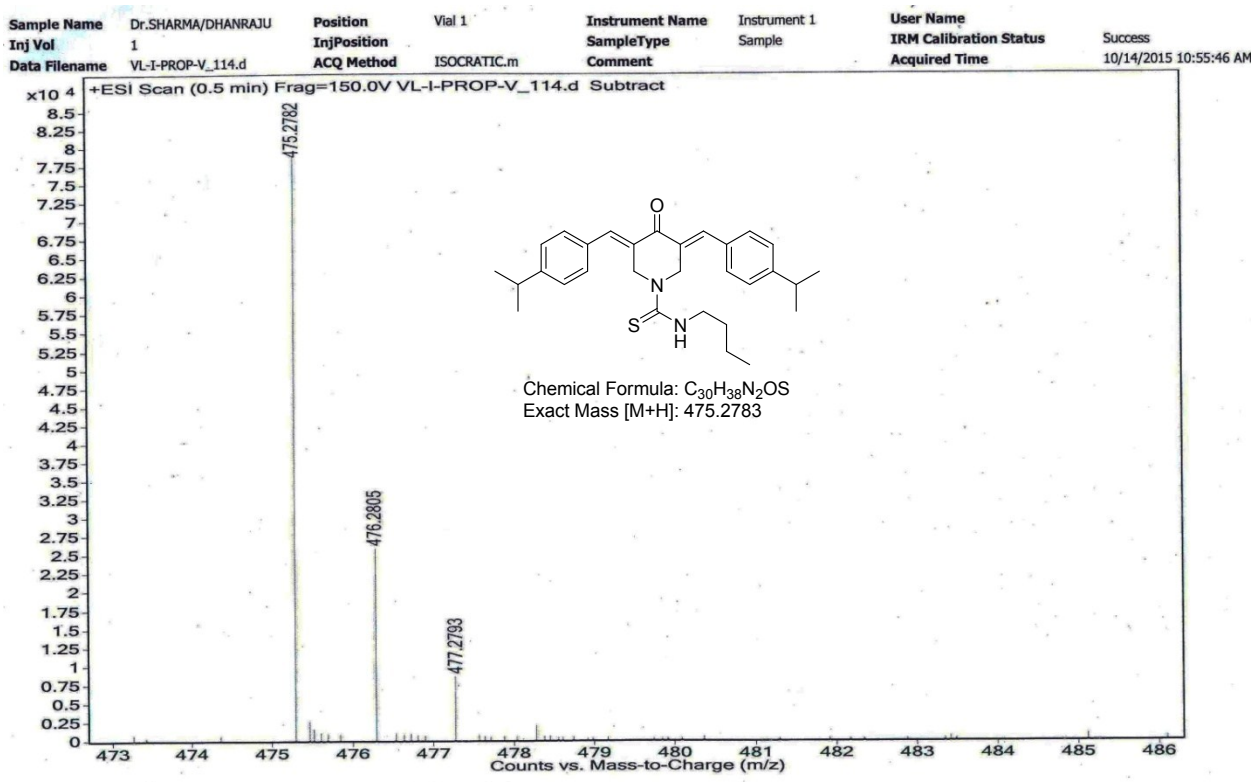
HRMS of compound **40**



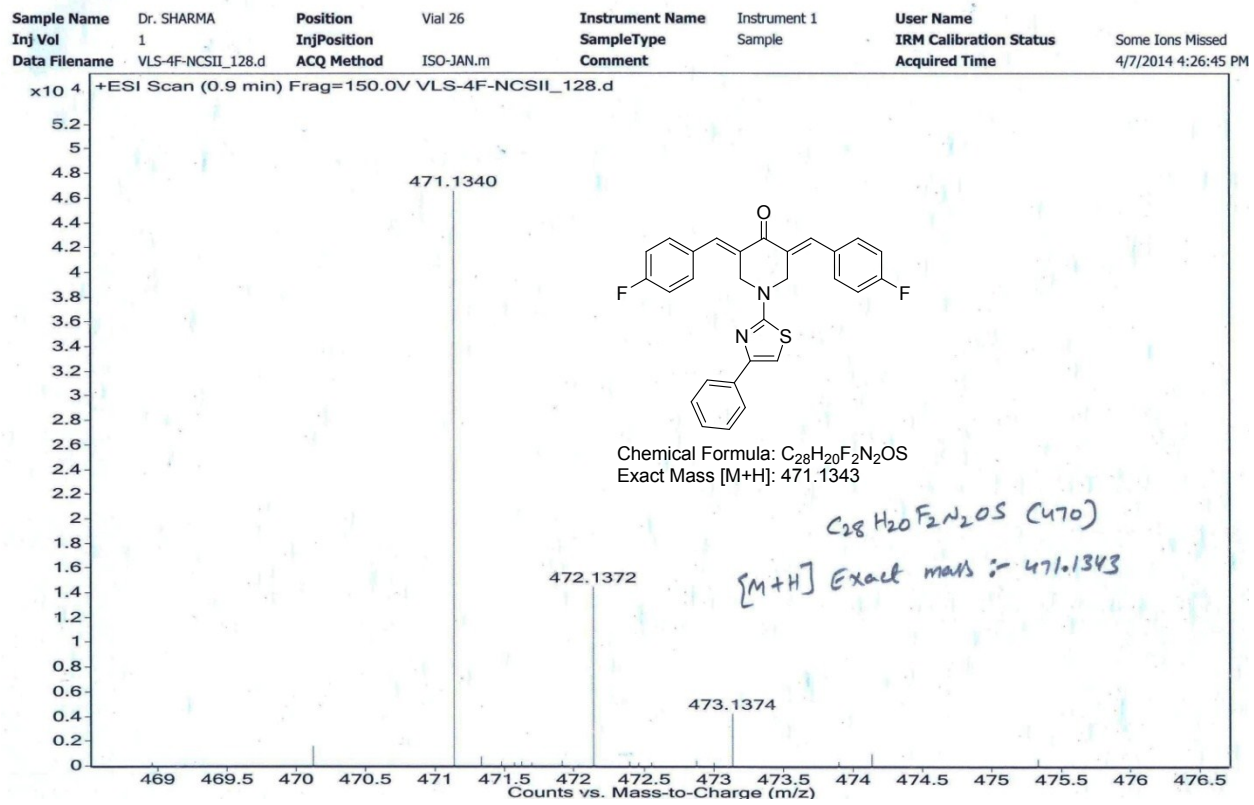
HRMS of compound **41**



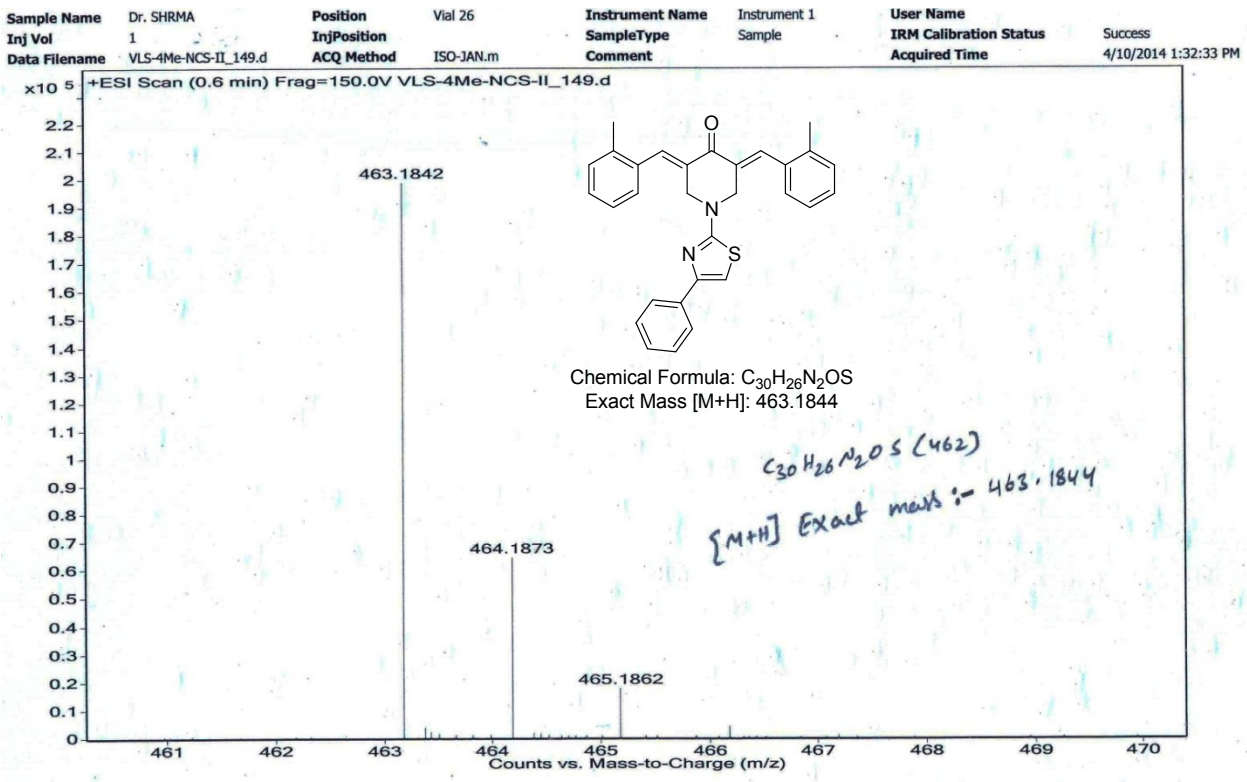
HRMS of compound **42**



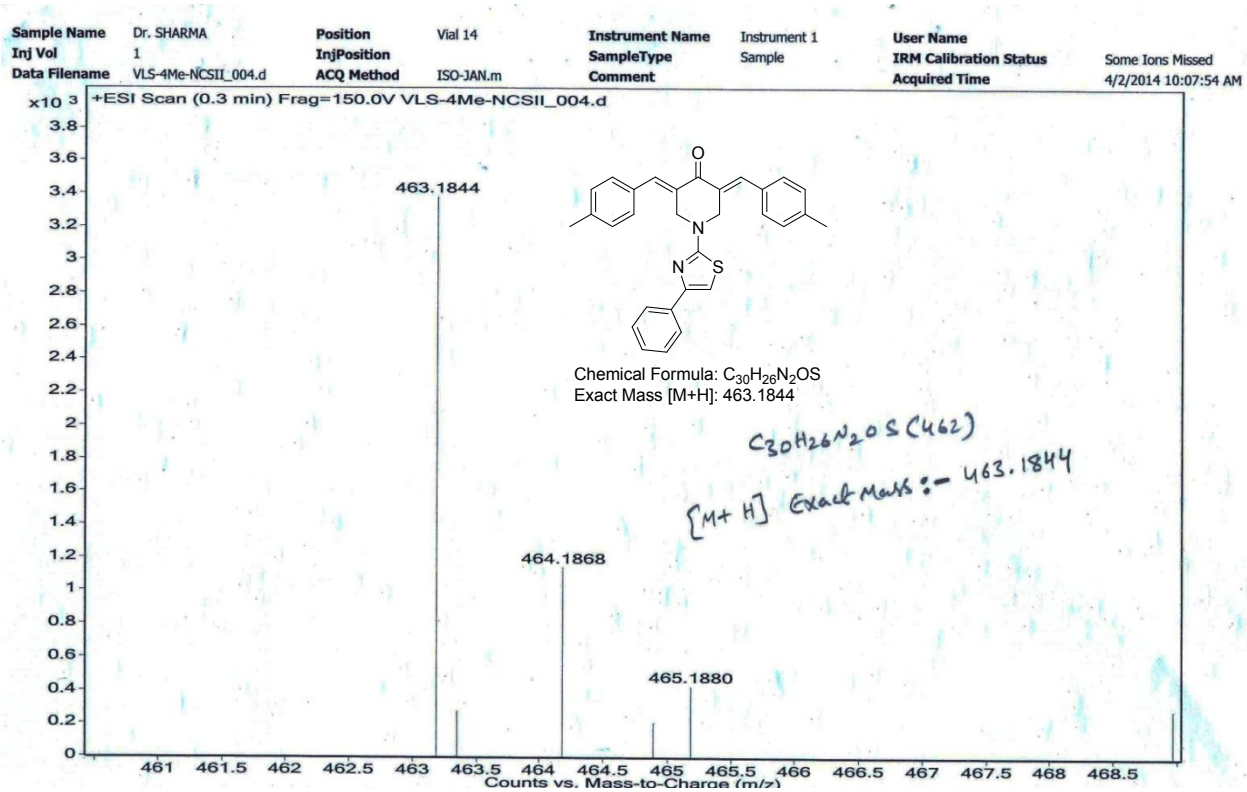
HRMS of compound **43**



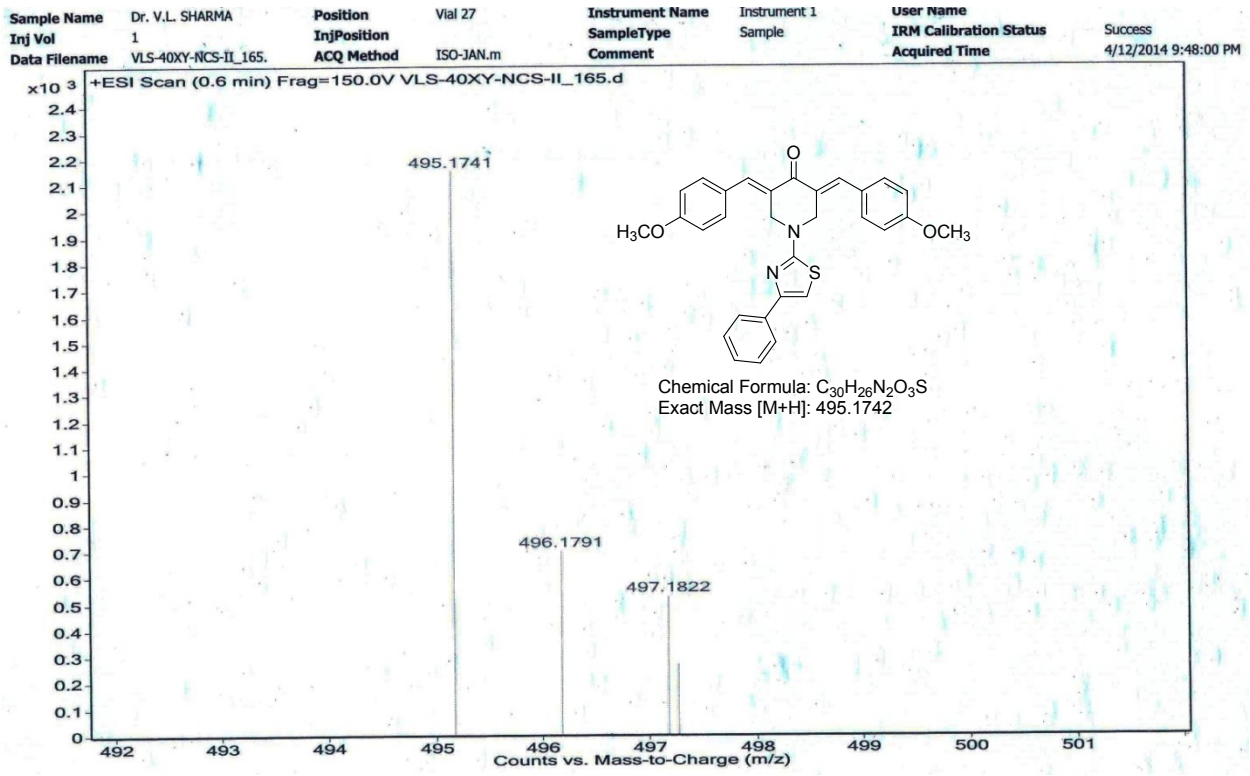
HRMS of compound **45**



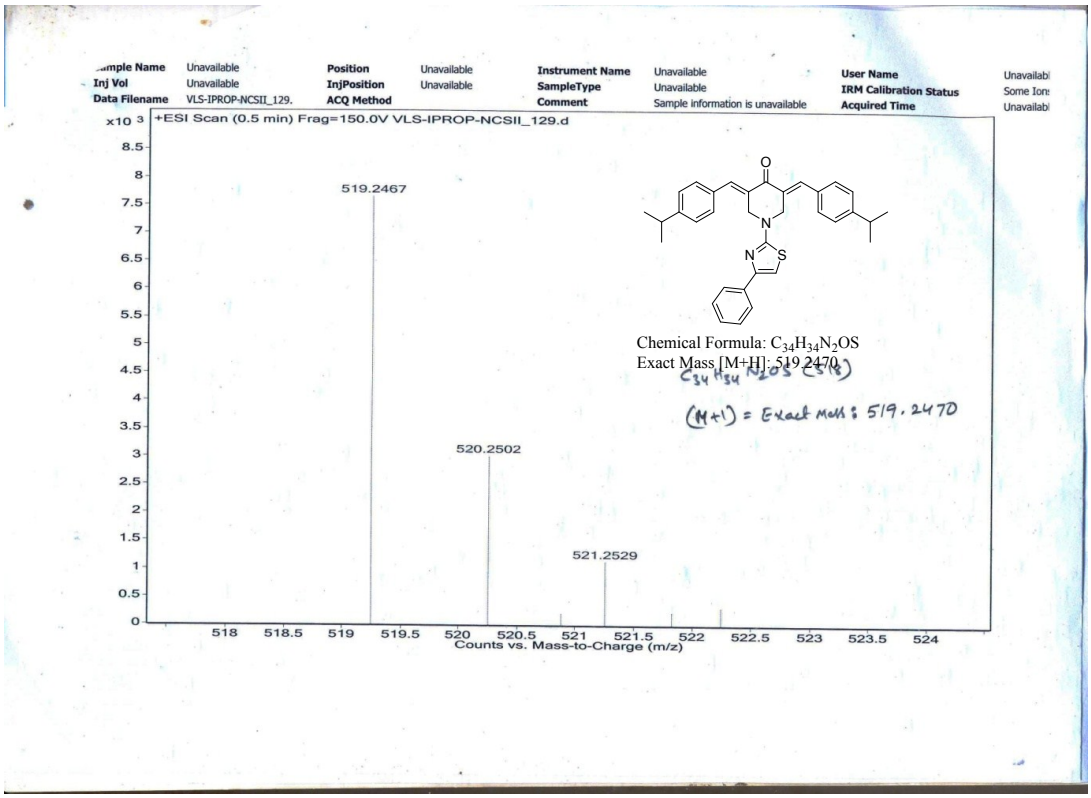
HRMS of compound **46**



HRMS of compound **47**



HRMS of compound **48**



HRMS of compound **49**

IC_{50} calculation- We have calculated the IC_{50} value by the Graph Pad Prism software version 5.01. For the calculation of IC_{50} values we have performed antiligase activity of compound **23** at 100, 50, 25, 12.5, and 6.25 µM concentrations whereas antiproliferative activity was performed at 50, 25, 12.5, 6.25 and 3.12 µM concentrations. At the different concentration of compound **23**, percent of antiligase and antiproliferative activities were determined and IC_{50} 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±1.8 µM (Figure S2A) and 8.7±1.9 µM (Figure S2B) IC_{50} values for antiligase and antiproliferative activities of compound **23** respectively.

Figure S2. Graphs for IC_{50} calculation (A) for antiligase activity (B) for antiproliferative activity.