Supplementary Material

Design, synthesis, anticonvulsant and analgesic studies of new pyrazole analogues: A Knoevenagel reaction approach

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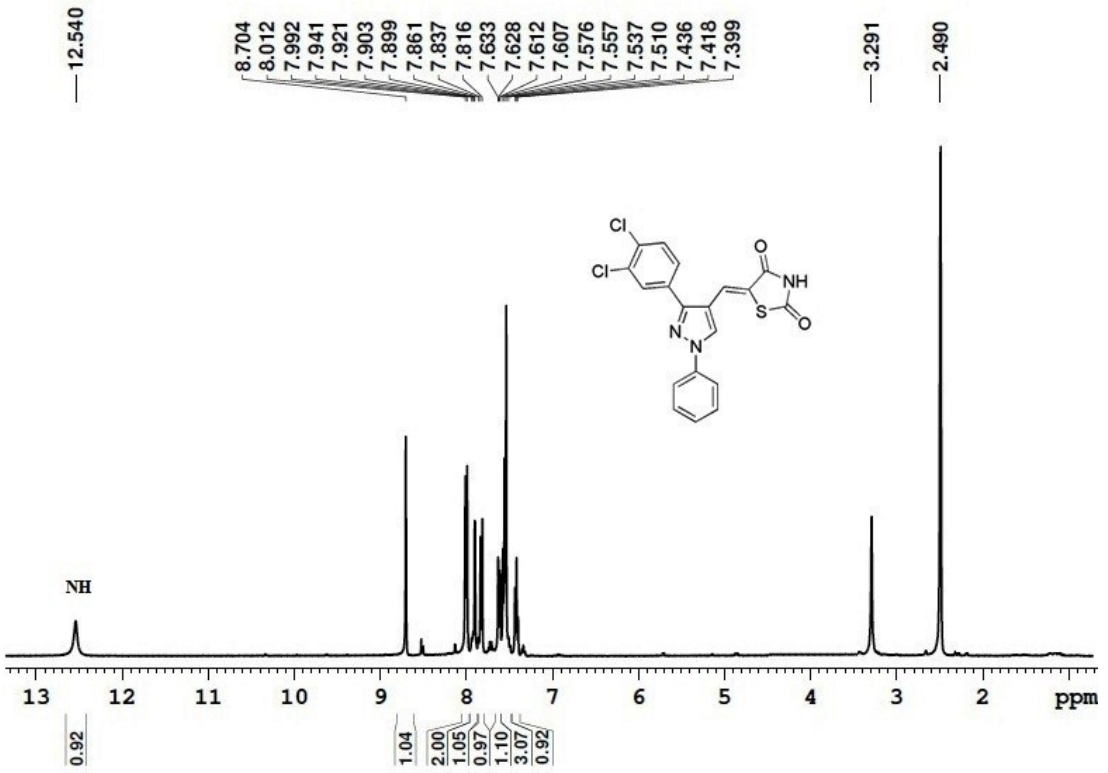
Experimental

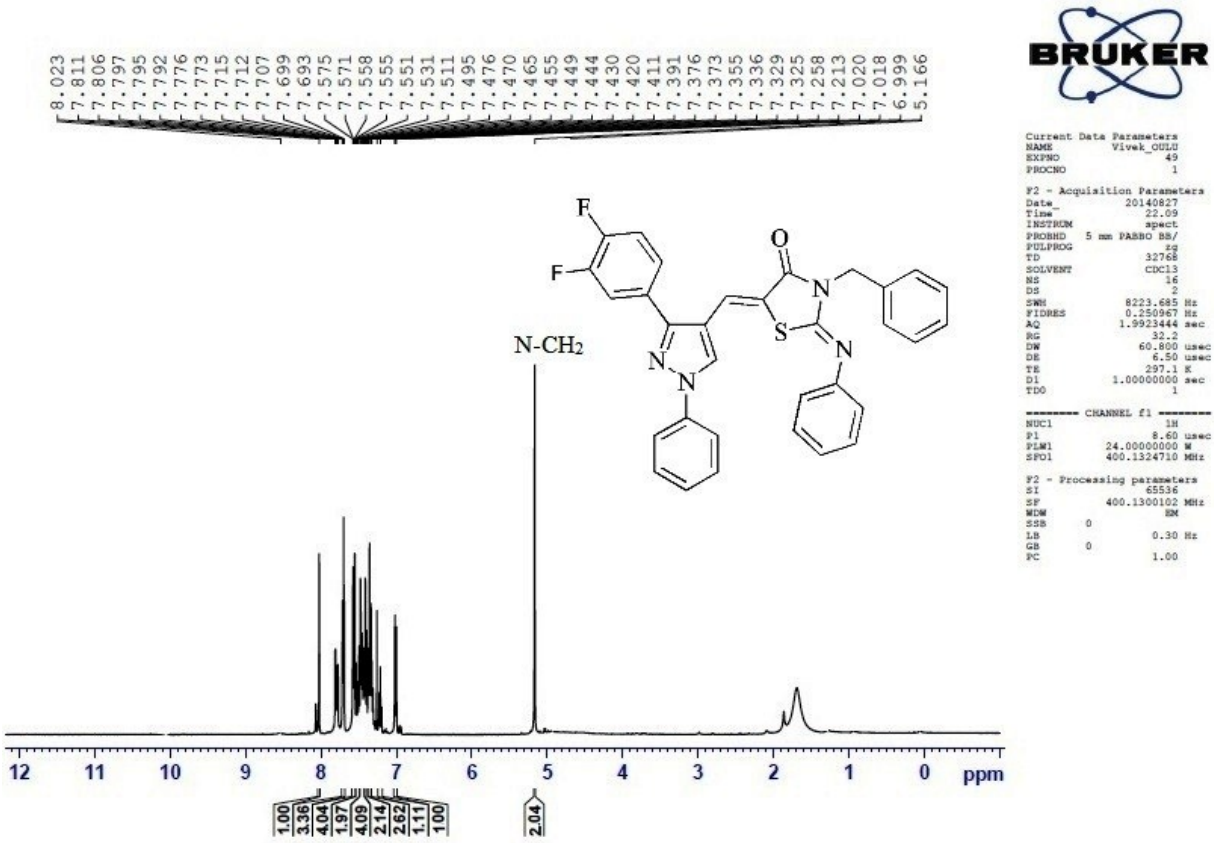
Methods and materials

All the reagents were purchased from commercial suppliers Sigma-Aldrich, Spectrochem India and used without further purification. Melting points were determined in an open capillary tube and were uncorrected. The progress of each reaction was monitored by ascending thin layer chromatography (TLC) on silica gel G (Merck 1.05570.0001), visualized by UV light. The IR spectra (in KBr pellets) were recorded on a Shimadzu-FTIR spectrometer and the wave numbers were given in cm^{-1}. The ^{1}H NMR and ^{13}C NMR spectra were recorded ($CDCl_3$/DMSO-d_6 mixture) on a Bruker AMX-400 NMR spectrometer with 5mm PABBO BB-1H TUBES with TMS as internal standard. The X-ray intensity data were collected at a temperature of 296 K on a Bruker Proteum2 CCD diffractometer equipped with an X-ray generator operating at 45 kV and 10 mA, using CuK_α radiation. Mass spectra were recorded in Agilent Technology LC-mass spectrometer. Elemental analyses were carried out using VARIO EL-III (Elementar Analysensysteme GmBH).

^{1}H NMR of compound of **1a**



^{1}H NMR of compound of **2b**



BRUKER

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EXPNO                        49
PROCNO                        1

F2 - Acquisition Parameters
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INSTRUM                spect
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PULPROG                   zg
TD                     32768
SOLVENT                CDCl3
NS                        16
DS                         2
SWH                 8223.685 Hz
FIDRES              0.250967 Hz
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RG                      32.2
DW                   60.800 usec
DE                    6.50 usec
TE                    297.1 K
D1                  1.00000000 sec
TD0                        1

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PLW1            24.00000000 W
SFO1            400.1324710 MHz

F2 - Processing parameters
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LB                     0.30 Hz
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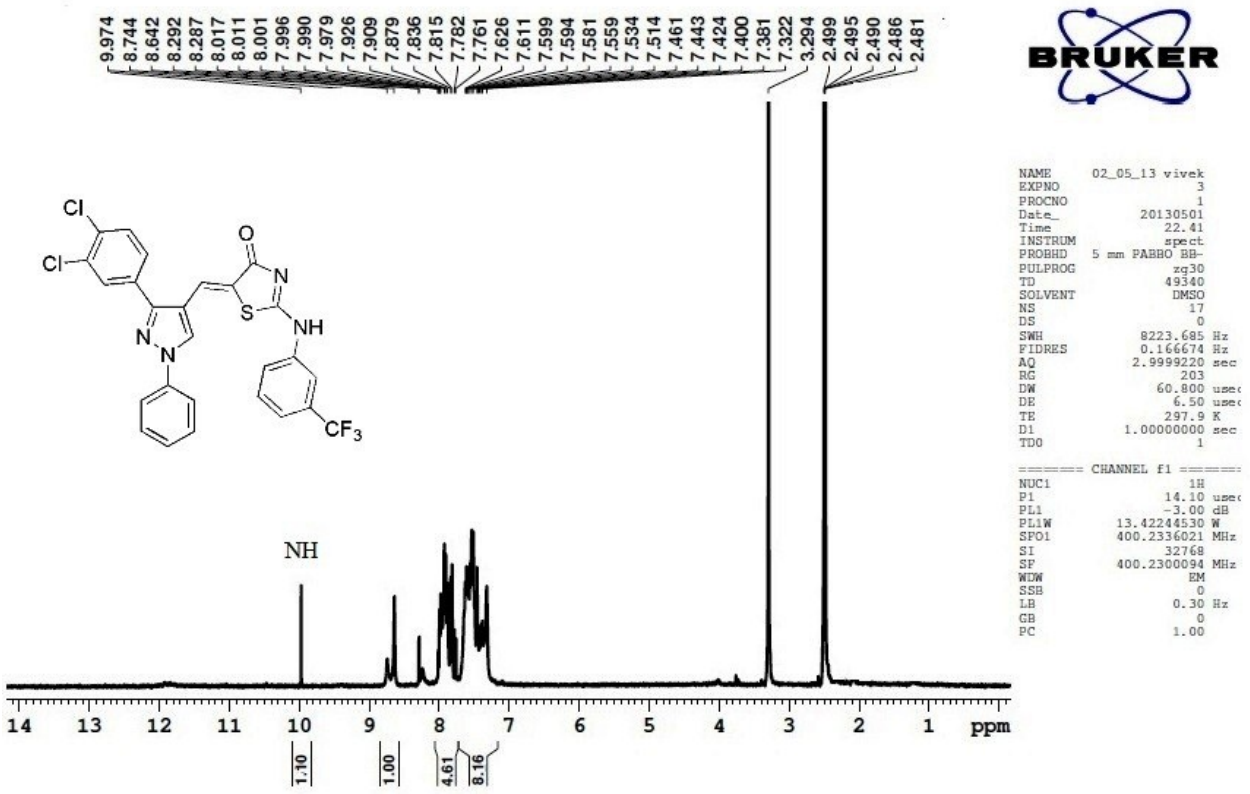
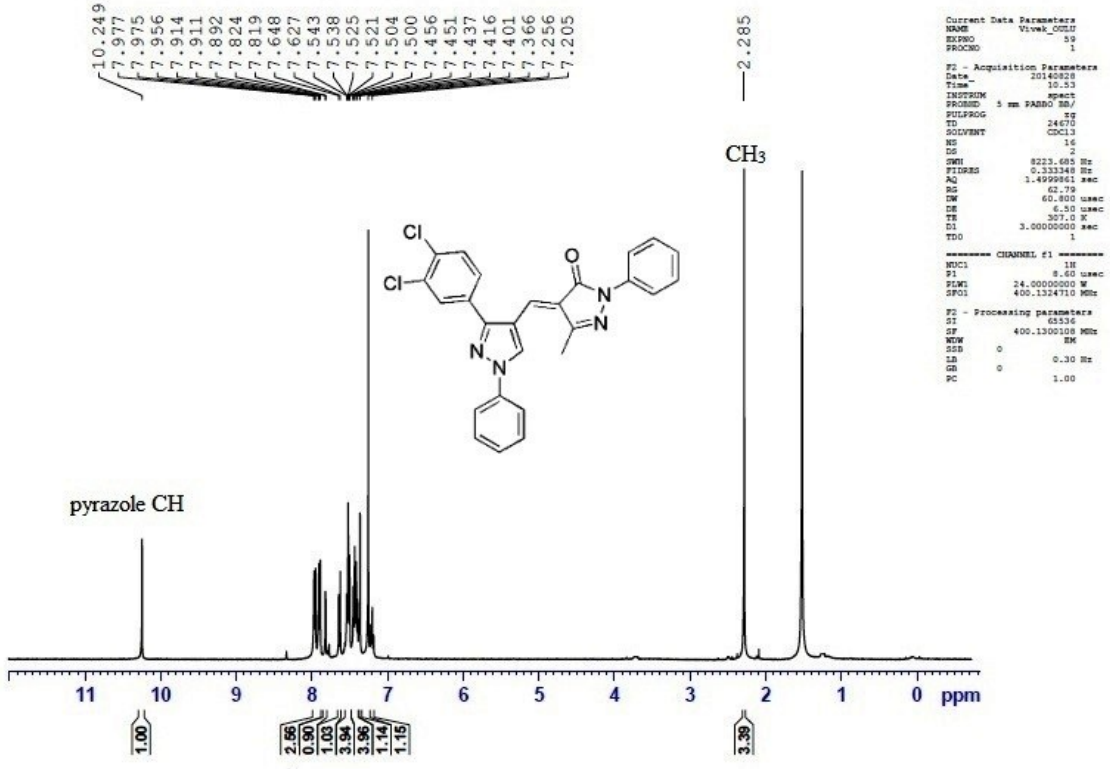
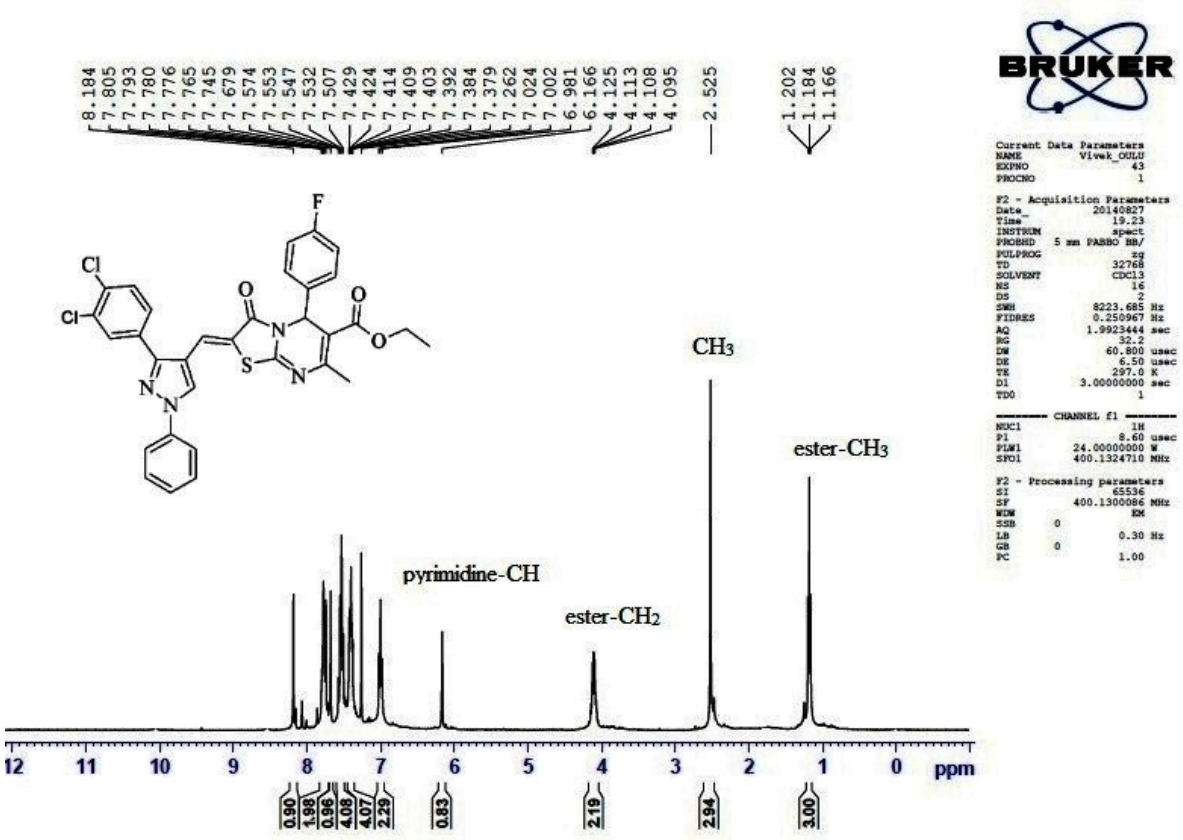
^{1}H NMR of compound of **3a**



^{1}H NMR of compound of **4a**



^{1}H NMR of compound of **5a**



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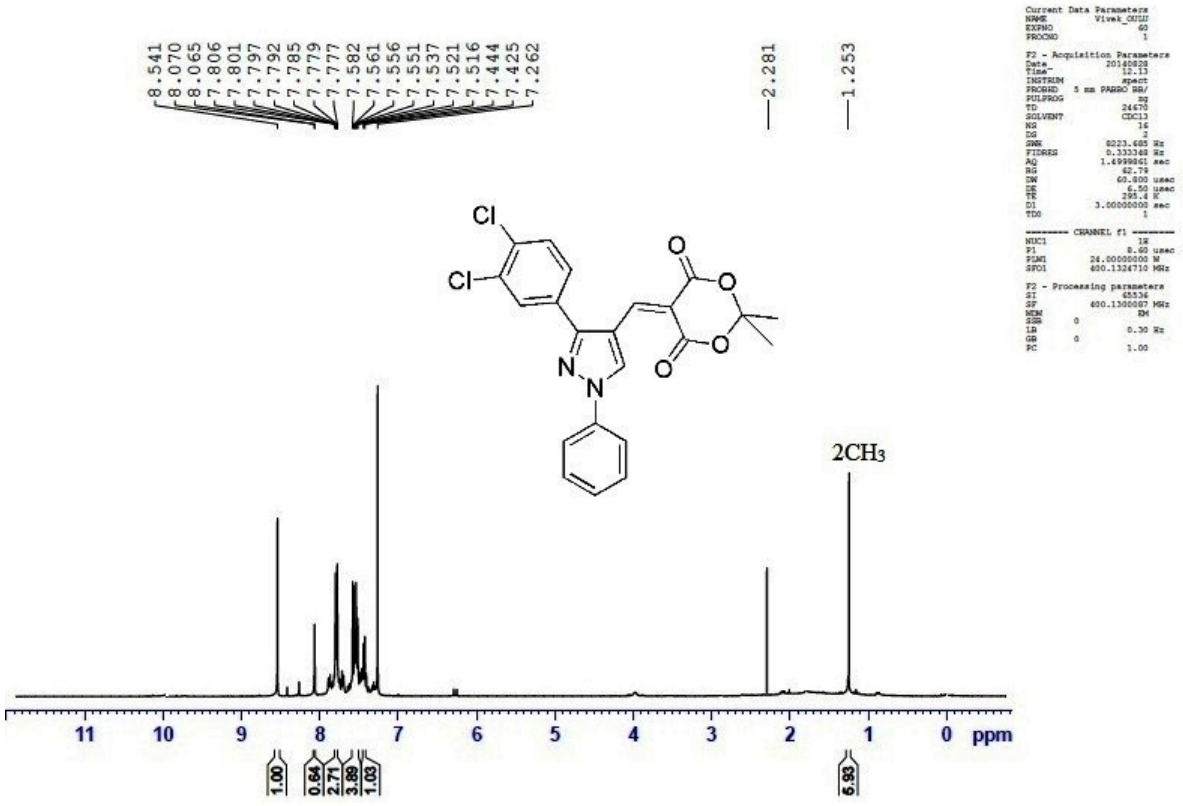
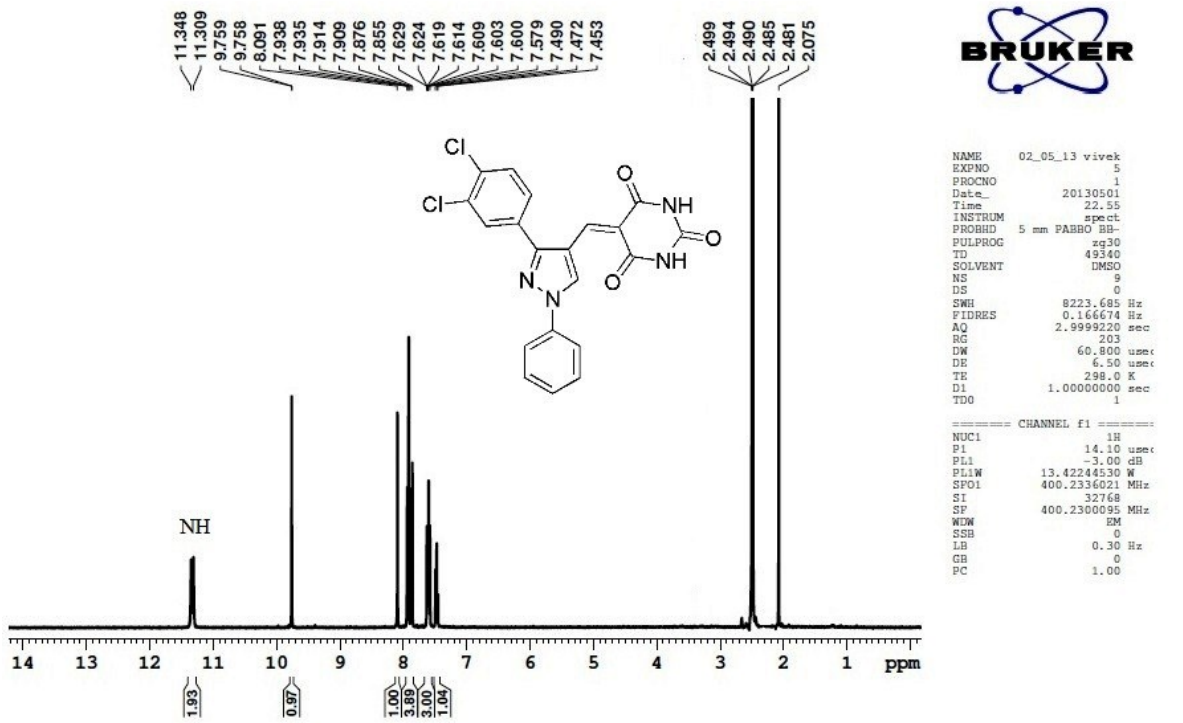
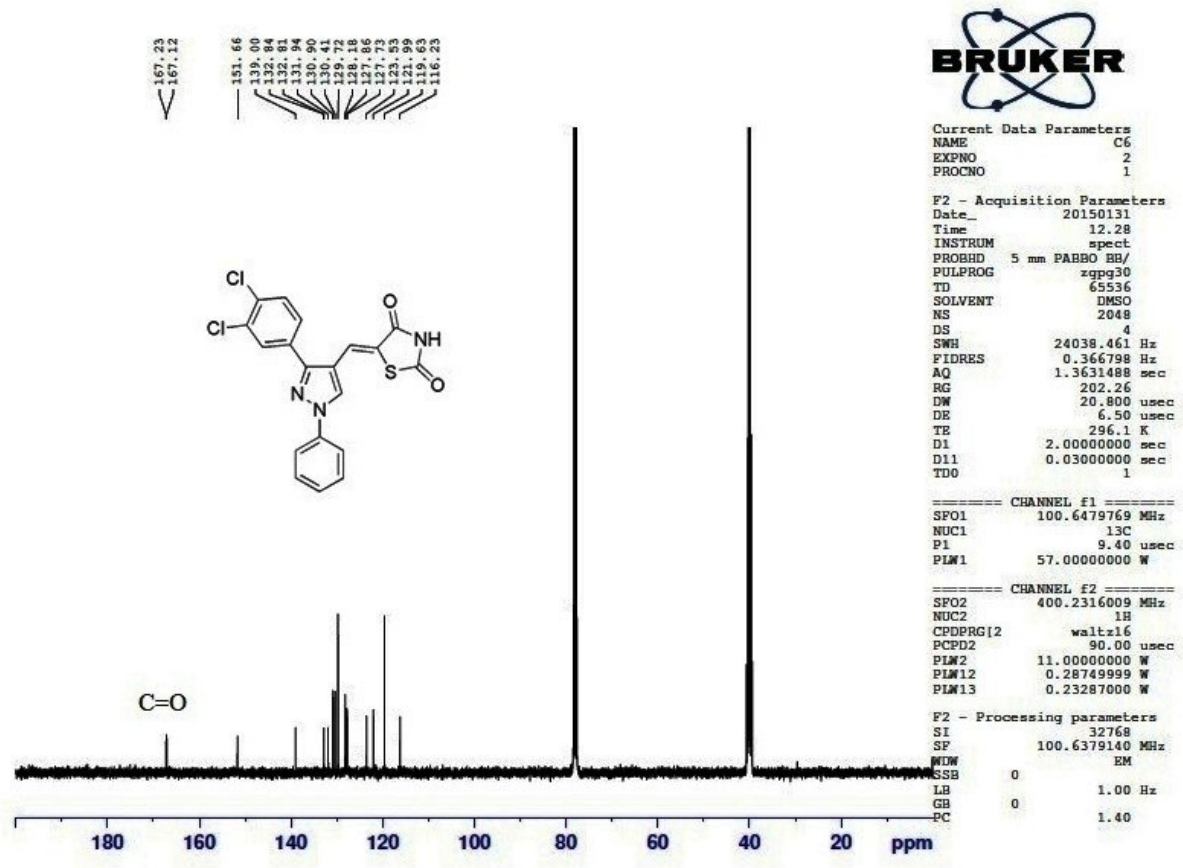


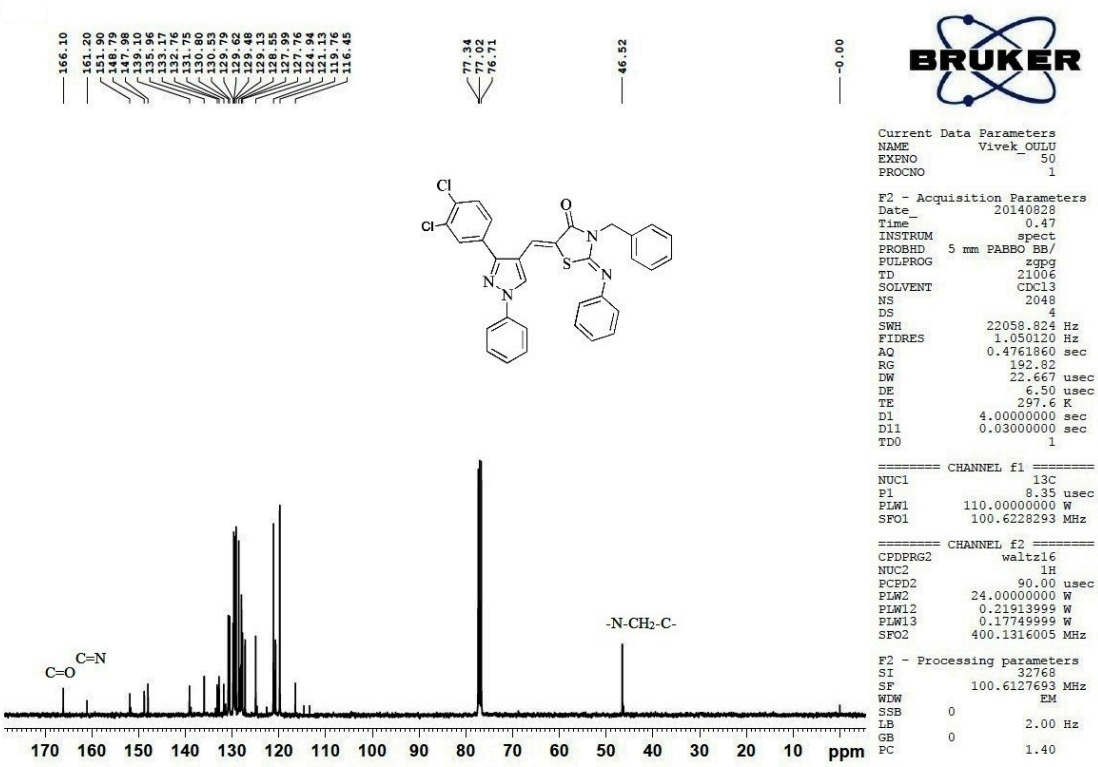
^{1}H NMR of compound of **7a**



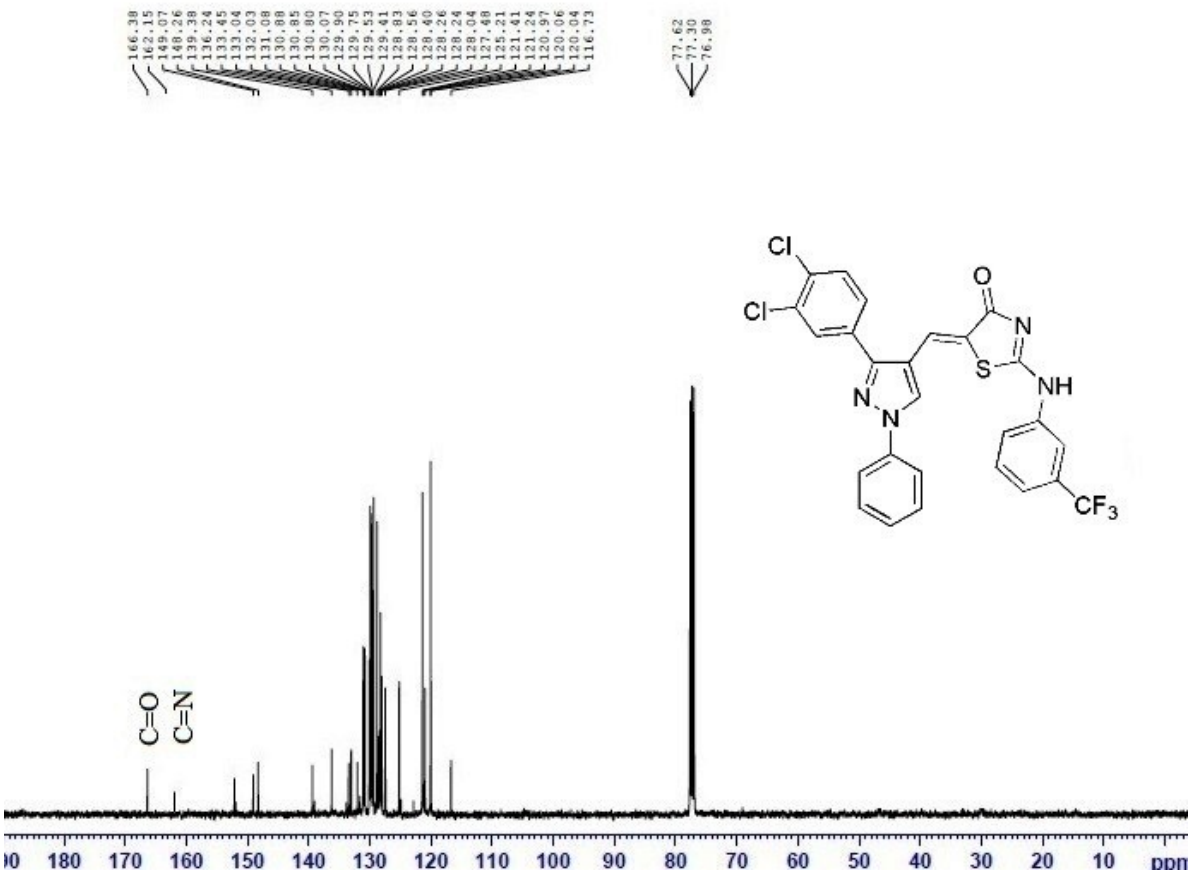
^{13}C NMR of compound of **1a**



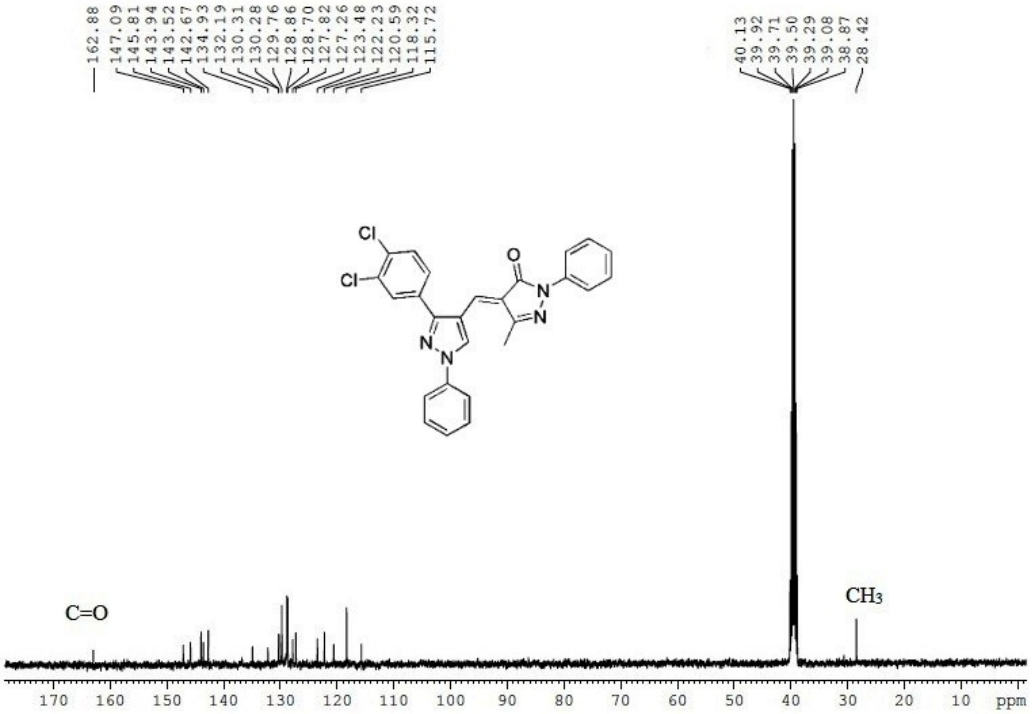
^{13}C NMR of compound of **2a**



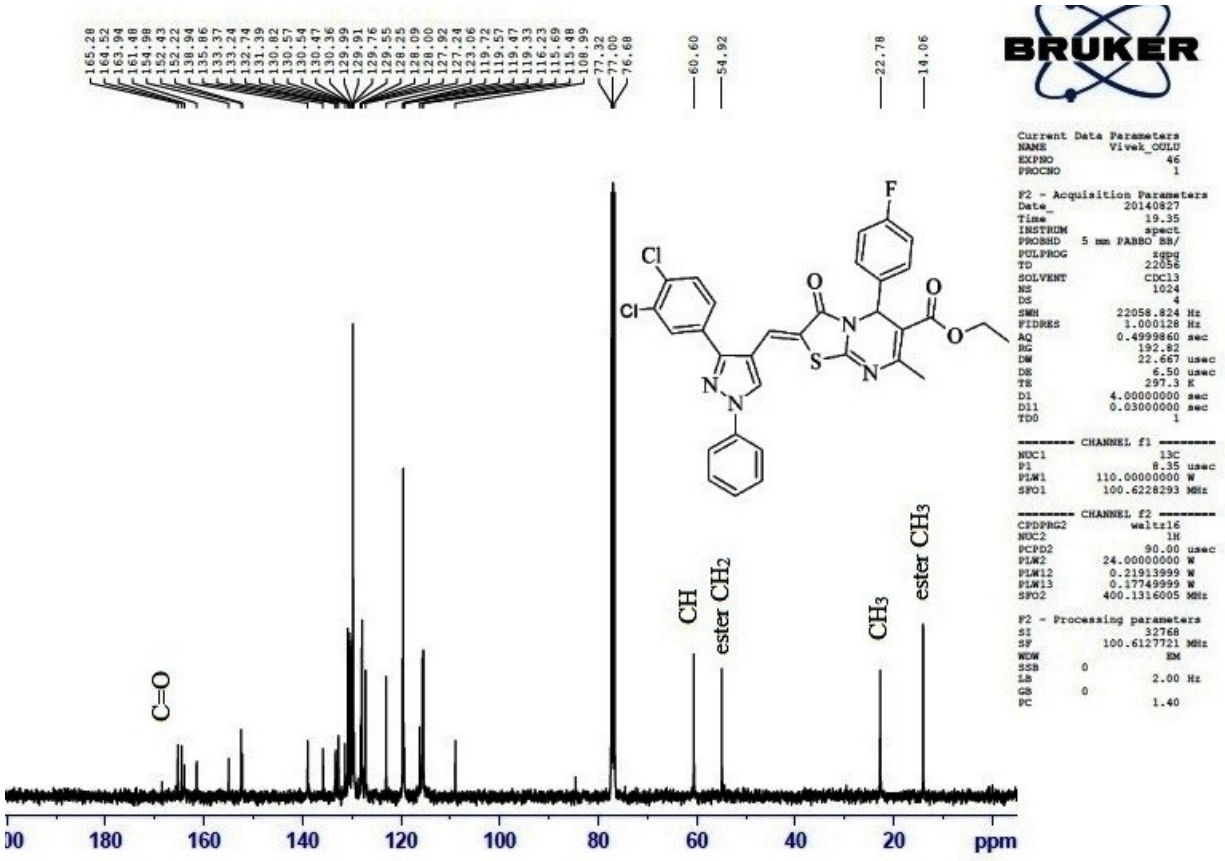
^{13}C NMR of compound of **3a**



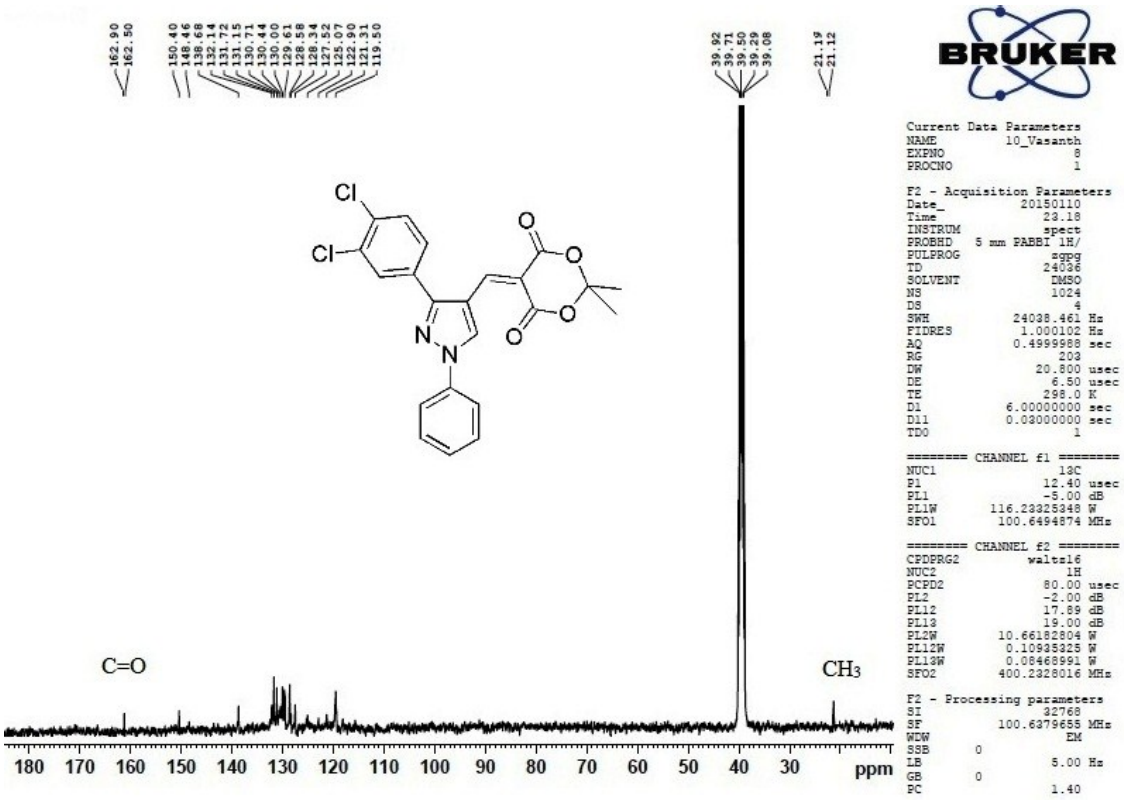
^{13}C NMR of compound of **4a**



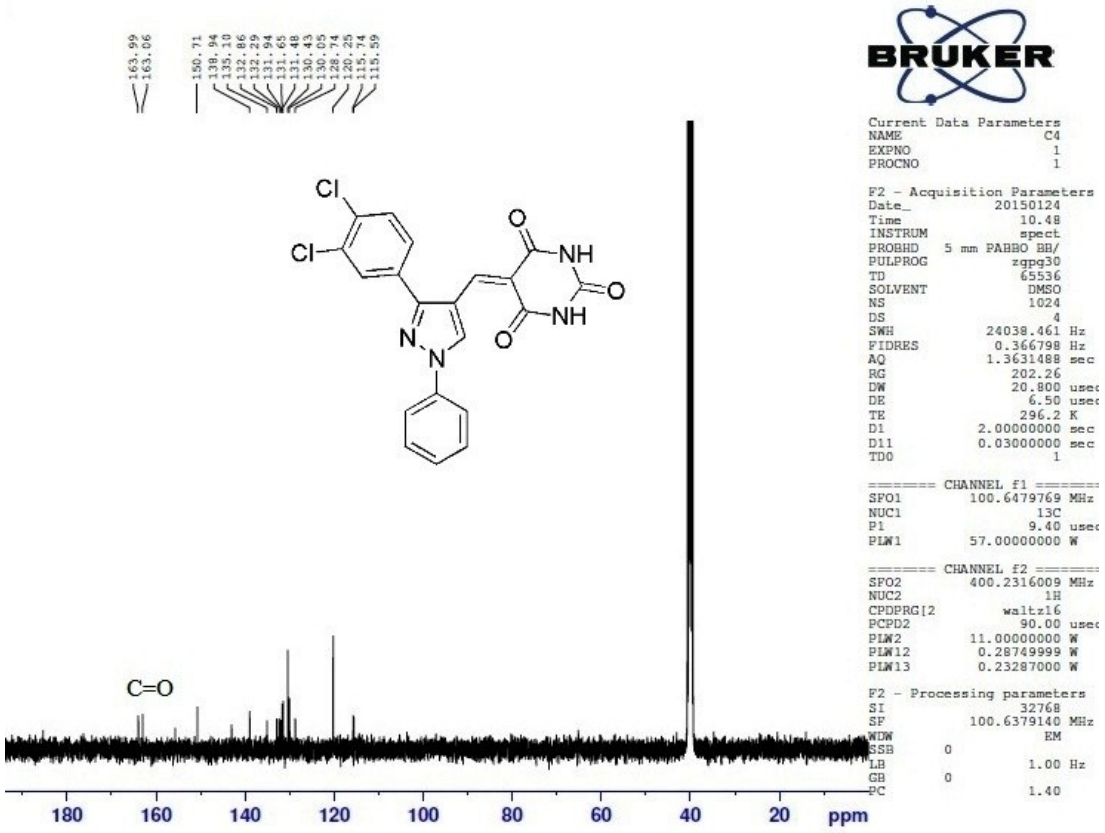
^{13}C NMR of compound of **5a**



^{13}C NMR of compound of **6a**



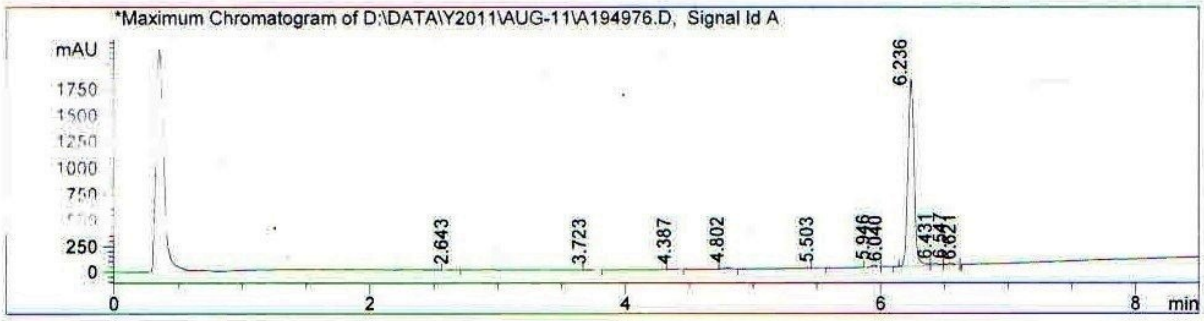
^{13}C NMR of compound of **7a**



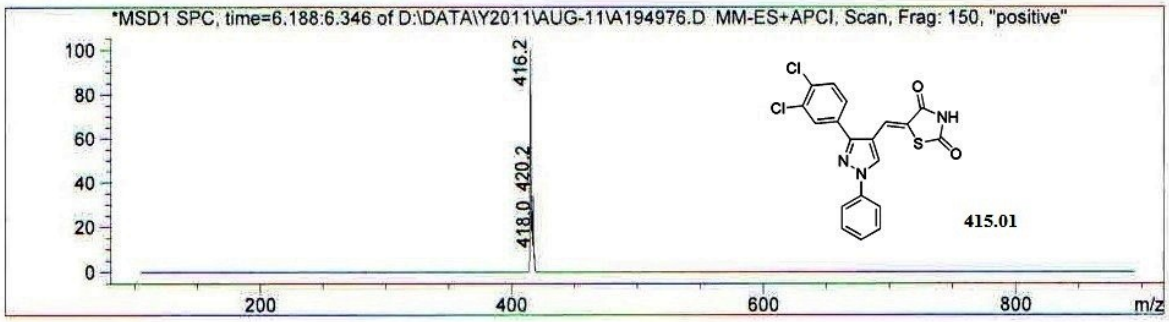
LCMS spectra of compound **1a**

Method info : A : 0.1%TFA IN H2O B: 0.1%TFA IN ACN Flow = 2.0 mL/min
COLUMN:XBridge C8 (50X4.6)mm,3.5µm , +ve mode

Time	% of B
0	5
8.0	100
8.1	100
8.5	5
10.0	5



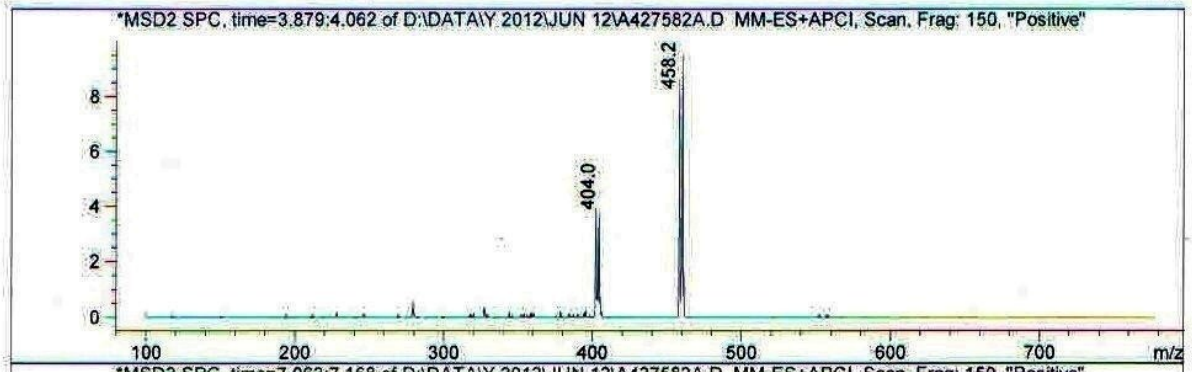
Peak No	RT min	Area	Area %
1	2.643	9.585e+000	0.153
2	3.723	2.066e+001	0.329
3	4.387	2.394e+001	0.382
4	4.802	4.906e+001	0.782
5	5.503	1.950e+001	0.311
6	5.946	4.539e+001	0.723
7	6.040	1.146e+001	0.183
8	6.236	5.969e+003	95.124
9	6.431	6.862e+001	1.094
10	6.547	5.590e+001	0.891
11	6.621	1.829e+000	0.029

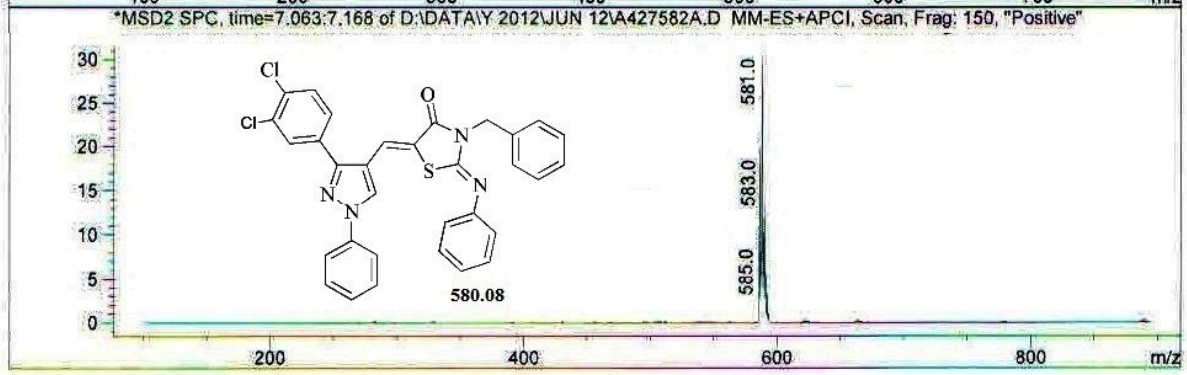


LCMS spectra of compound **2a**

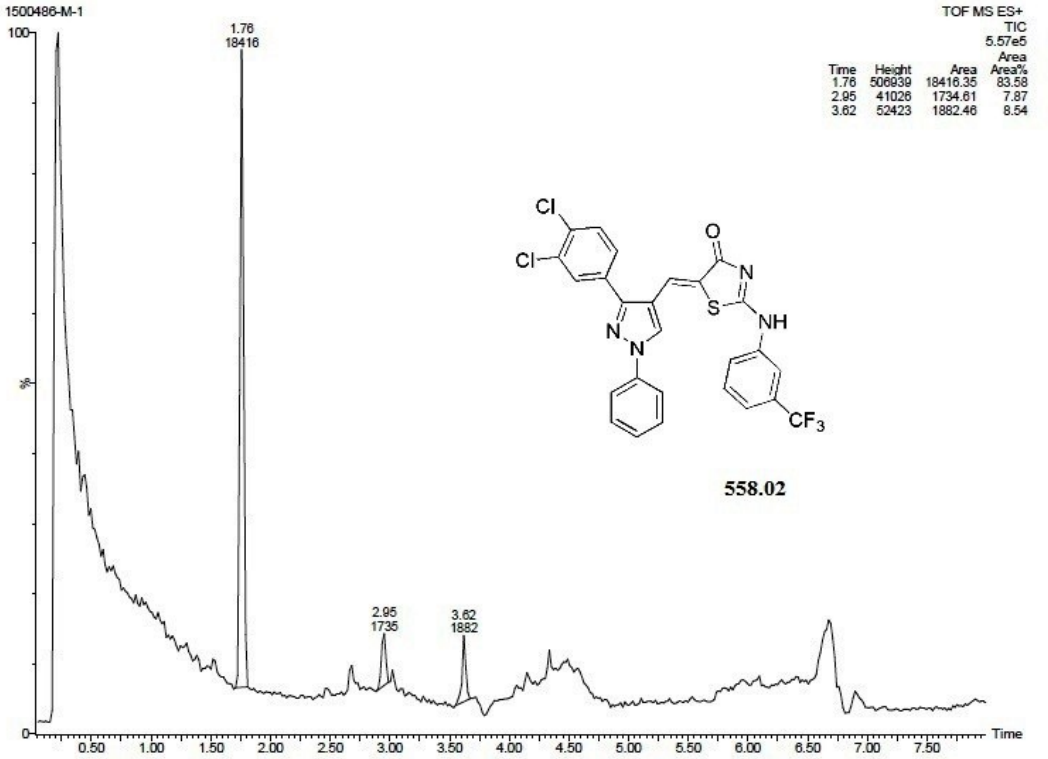
Method info : A : 0.1%TFA IN H2O B: 0.1%TFA IN ACN Flow = 2.0 mL/min
COLUMN:XBridge C8 (50X4.6)mm,3.5µm , +ve mode

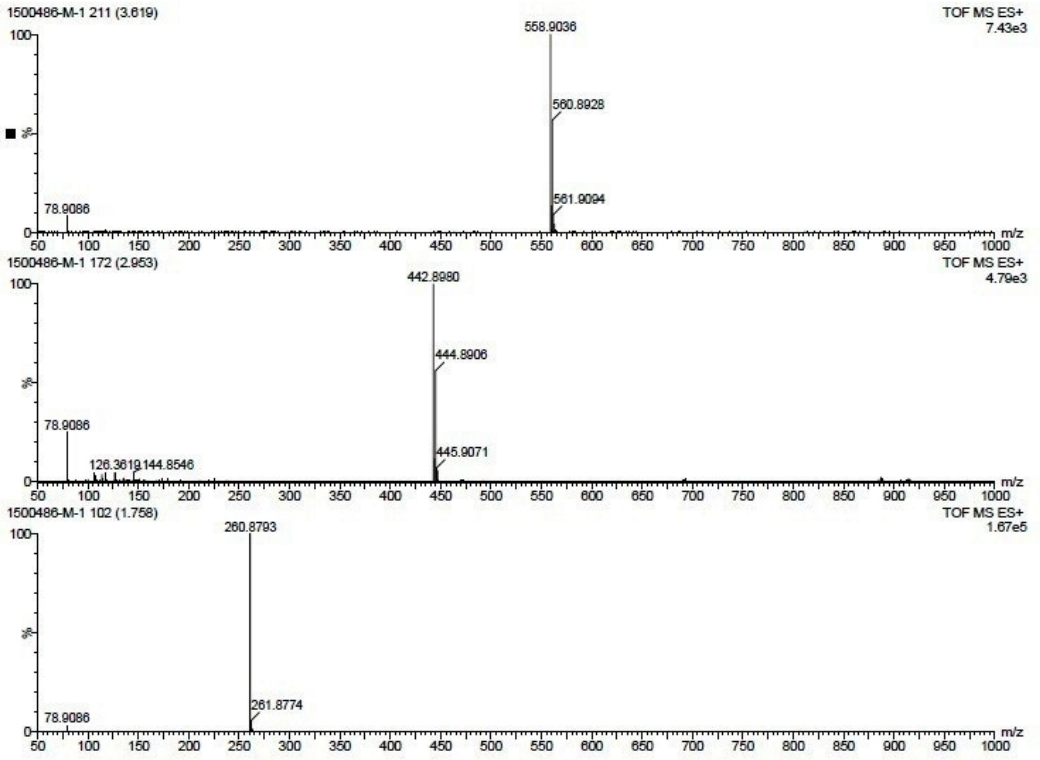
Time	% of B
0	5
8.0	100
8.1	100
8.5	5
10.0	5





LCMS spectra of compound **3a**

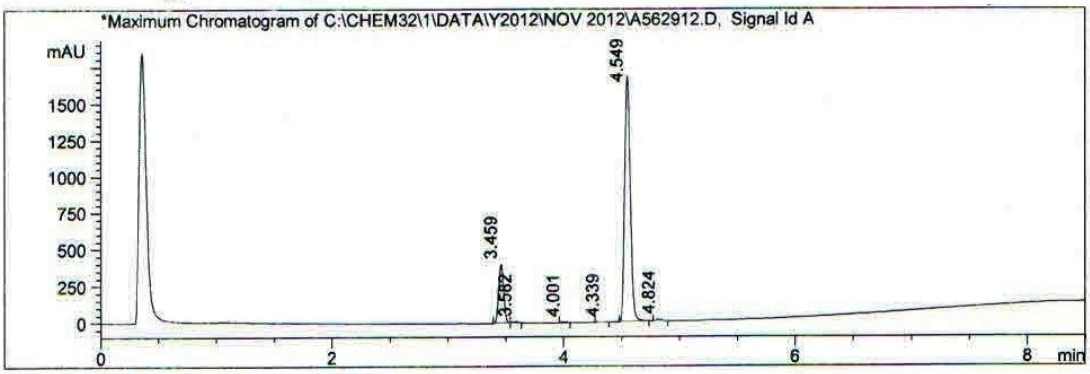




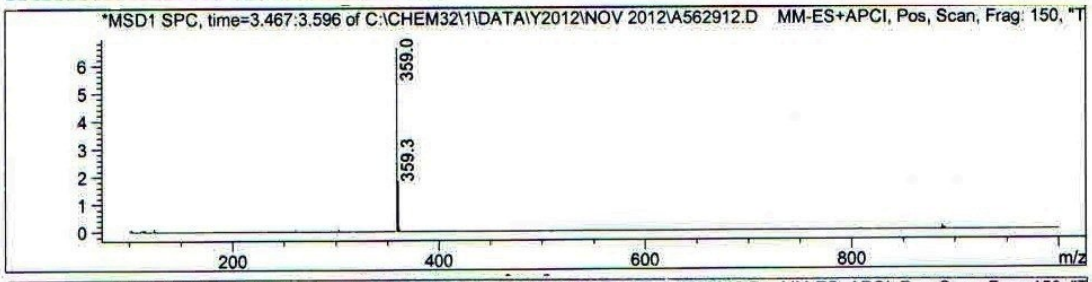
LCMS spectra of compound **4a**

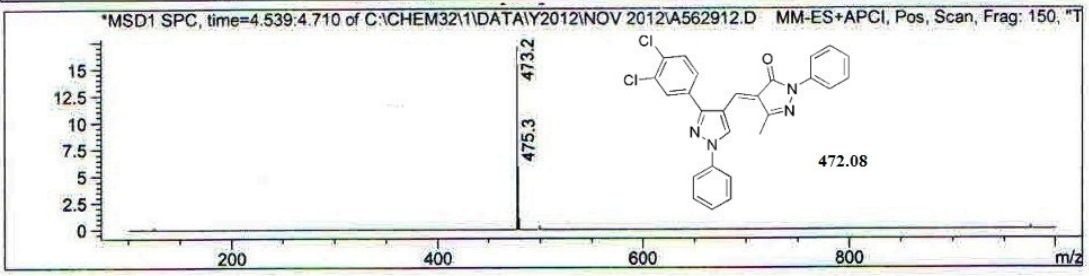
Method info : A: 0.1% TFA IN H2O , B:0.1% TFA IN ACN ; Flow Rate:2.0 ml/min
COLUMN:XBridge C8 (50x4.6mm, 3.5µm), +ve mode

TIME	%B
0	05
8.0	100
8.1	100
8.5	05
10	05



Peak No	RT min	Area	Area %
1	3.459	1.198e+003	17.207
2	3.582	3.089e+001	0.444
3	4.001	1.827e+001	0.262
4	4.339	1.084e+001	0.156
5	4.549	5.671e+003	81.475
6	4.824	3.175e+001	0.456

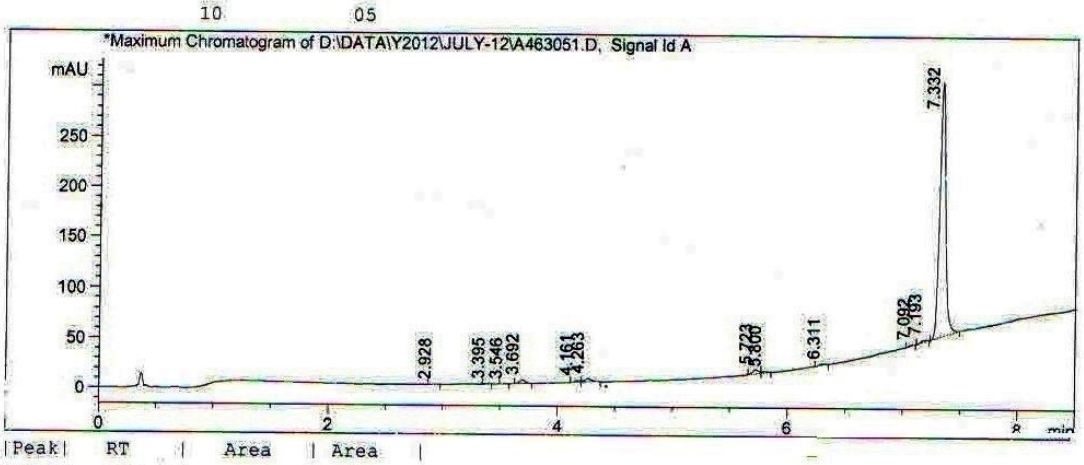




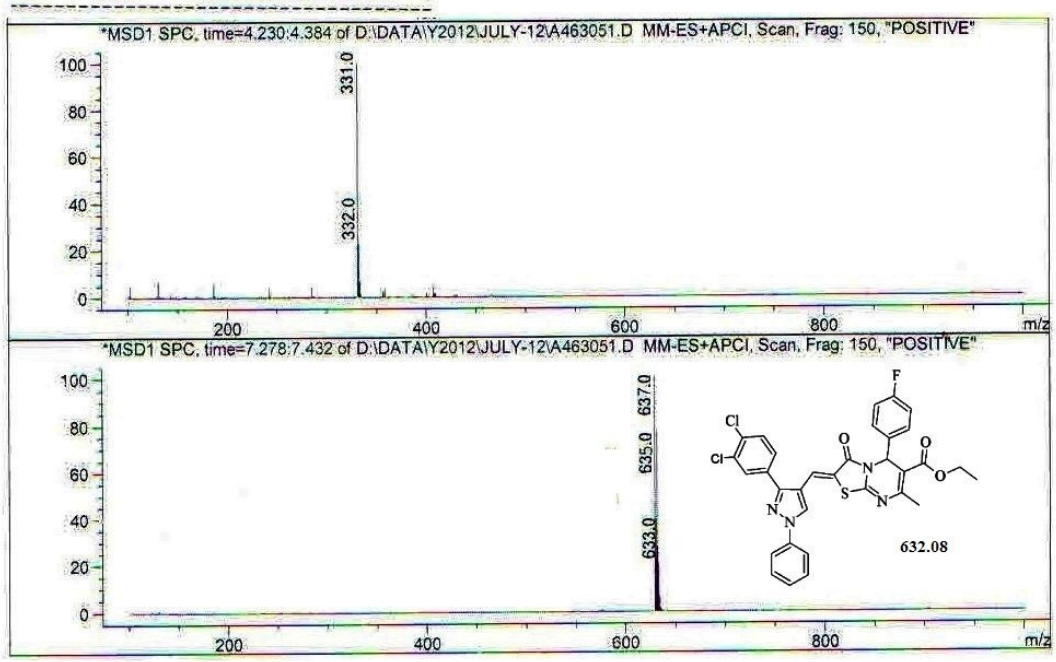
LCMS spectra of compound **5a**

Method info : A-0.1% TFA IN H2O , B-0.1% TFA IN ACN Flow: 2.0 ml/min
COLUMN: XBridge C8 (50X4.6mm, 3.5µm), +ve mode

TIME	%B
0	05
8.0	100
8.1	100
8.5	05
10	05



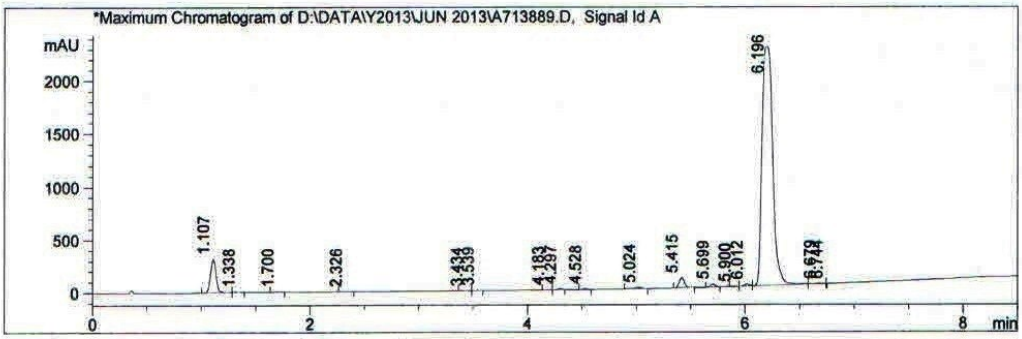
Peak No	RT min	Area	Area %
1	2.928	1.938e+000	0.195
2	3.395	7.781e-001	0.078
3	3.546	1.482e+000	0.149
4	3.692	1.261e+001	1.270
5	4.161	5.517e+000	0.556
6	4.263	1.508e+001	1.519
7	5.723	1.728e+001	1.741
8	5.800	6.842e+000	0.689
9	6.311	5.229e+000	0.527
10	7.092	3.415e+000	0.344
11	7.193	8.189e+000	0.825
12	7.332	9.144e+002	92.107



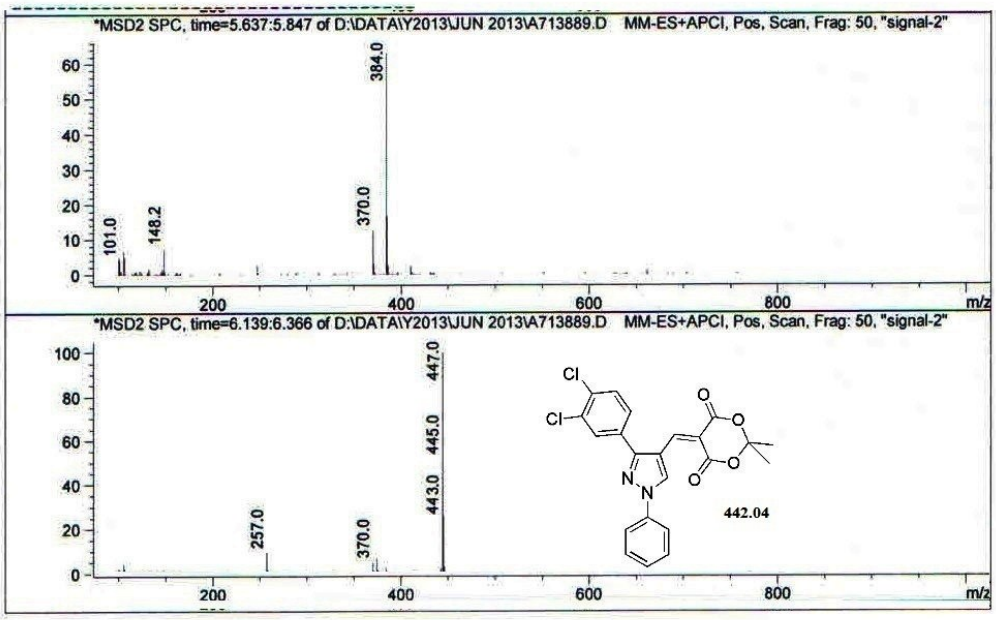
LCMS spectra of compound **6a**

Method info : A: 0.1% TFA IN H2O , B:0.1% TFA IN ACN ; Flow Rate:2.0 ml/min
COLUMN:XBridge C8 (50x4.6mm, 3.5µ), +ve mode

TIME	%B
0	05
8.0	100
8.1	100
8.5	05
10.0	05



Peak No	RT min	Area	Area %
1	1.107	1.111e+003	6.296
2	1.338	1.934e+001	0.110
3	1.700	2.205e+001	0.125
4	2.326	7.594e+000	0.043
5	3.434	6.061e+000	0.034
6	3.539	1.099e+001	0.062
7	4.183	1.292e+001	0.073
8	4.297	3.330e+001	0.189
9	4.528	4.966e+001	0.281
10	5.024	8.780e+001	0.498
11	5.415	3.351e+002	1.899
12	5.699	1.102e+002	0.625
13	5.900	1.930e+001	0.109
14	6.012	8.632e+001	0.489
15	6.196	1.568e+004	88.866
16	6.679	5.087e+001	0.288
17	6.744	2.154e+000	0.012



LCMS spectra of compound **6b**

```
Method info  :
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              COLUMN:XBridge C8 (50x4.6mm, 3.5µ), +ve mode
              TIME       %B
               0          05
               8.0       100
               8.1       100
               8.5        05
              10.0        05
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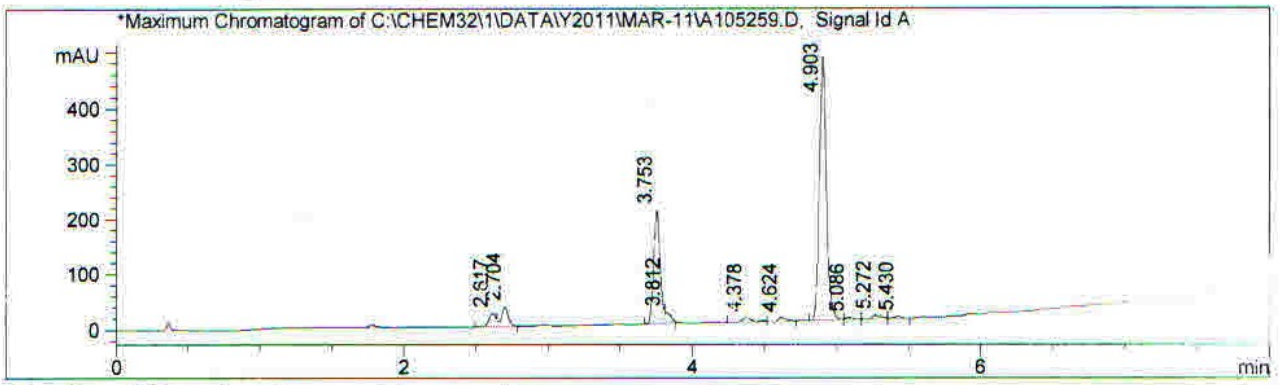
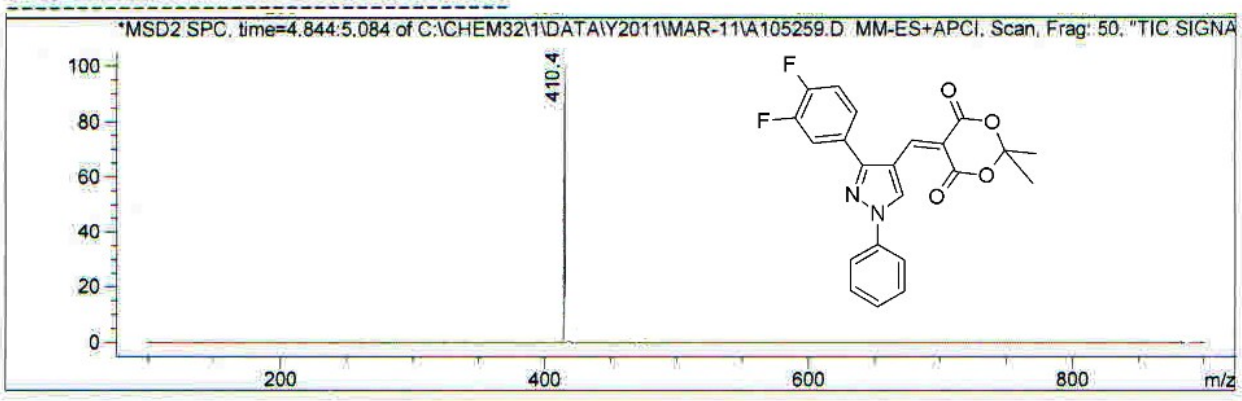
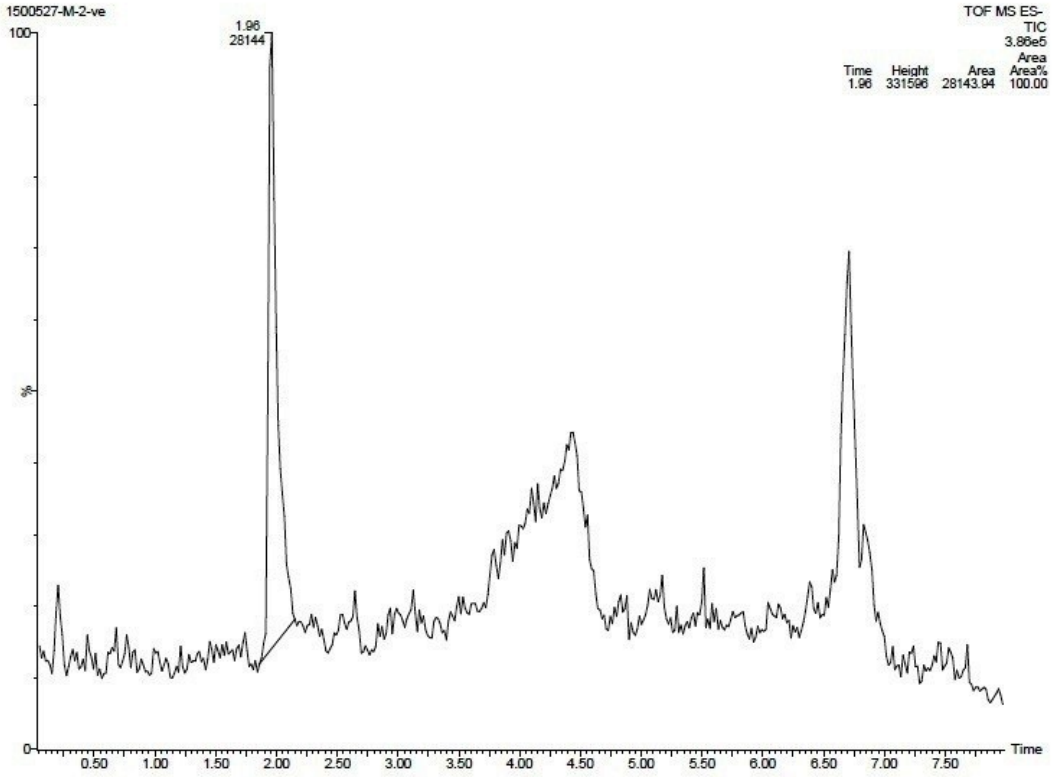
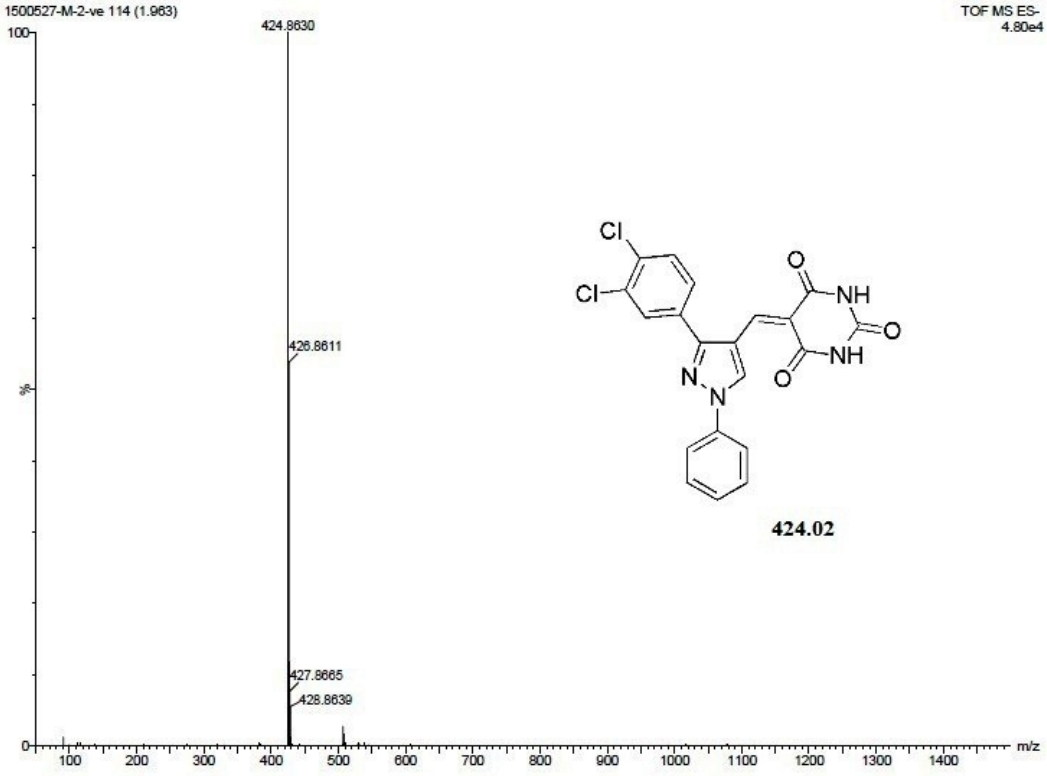


Peak No	RT min	Area	Area %
1	2.617	7.257e+001	2.772
2	2.704	1.178e+002	4.498
3	3.753	6.381e+002	24.374
4	3.812	5.511e+001	2.105
5	4.378	4.717e+001	1.802
6	4.624	3.432e+001	1.311
7	4.903	1.587e+003	60.604
8	5.086	1.225e+001	0.468
9	5.272	3.363e+001	1.285
10	5.430	2.047e+001	0.782



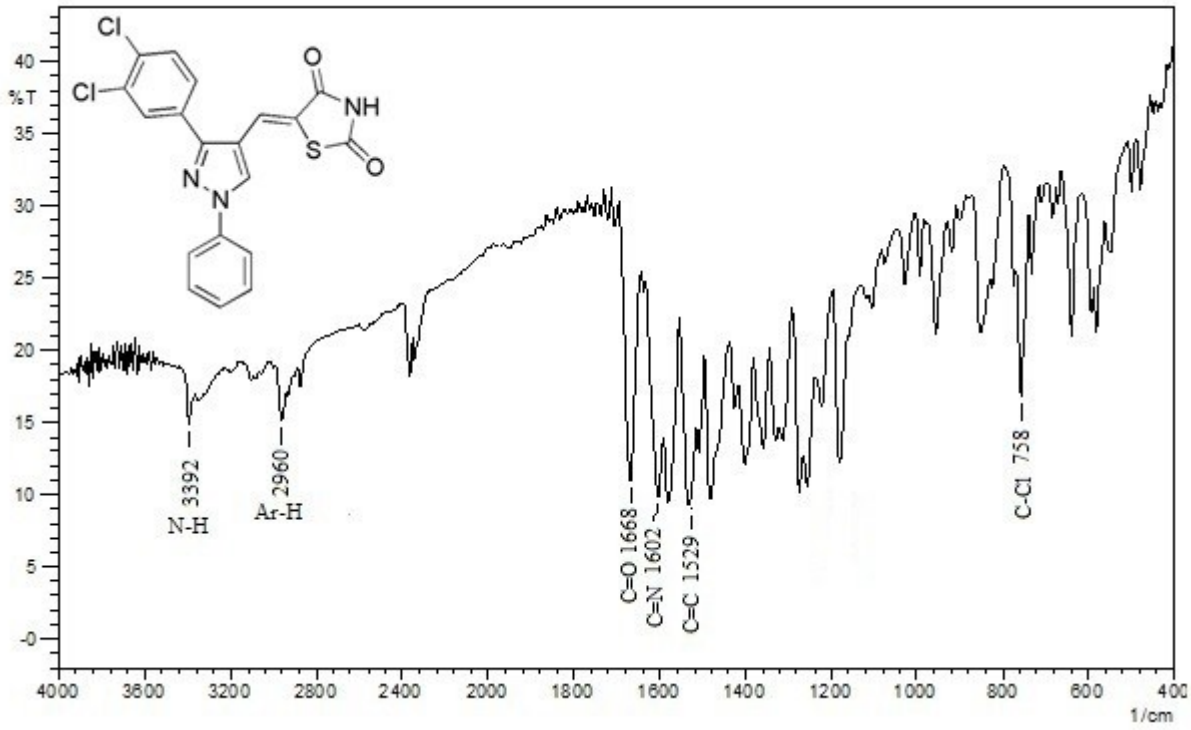
LCMS spectra of compound **7a**



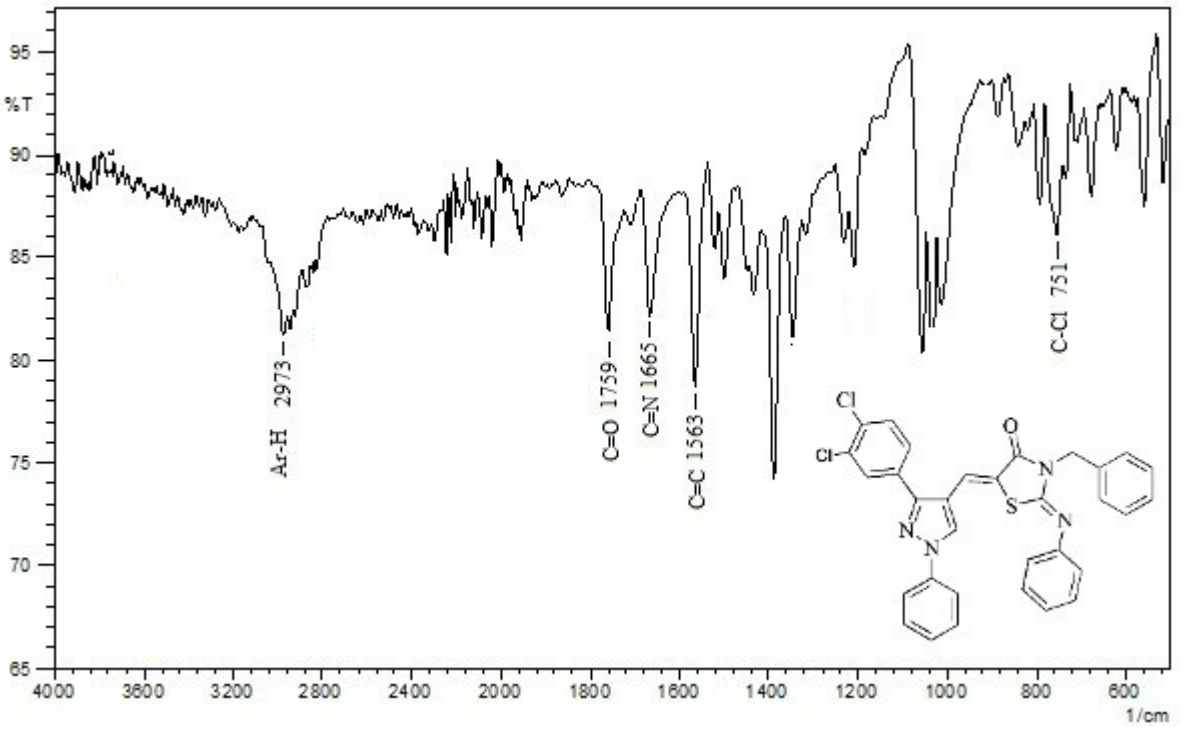


424.02

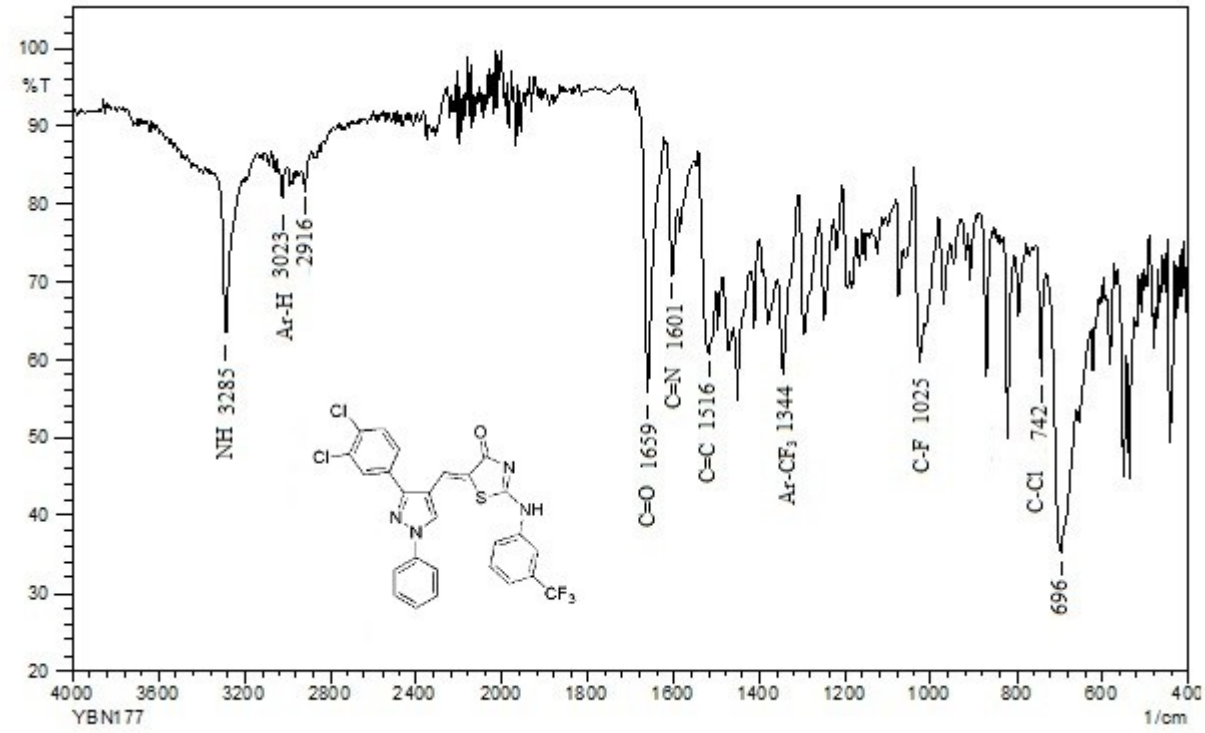
IR spectrum of compound **1a**



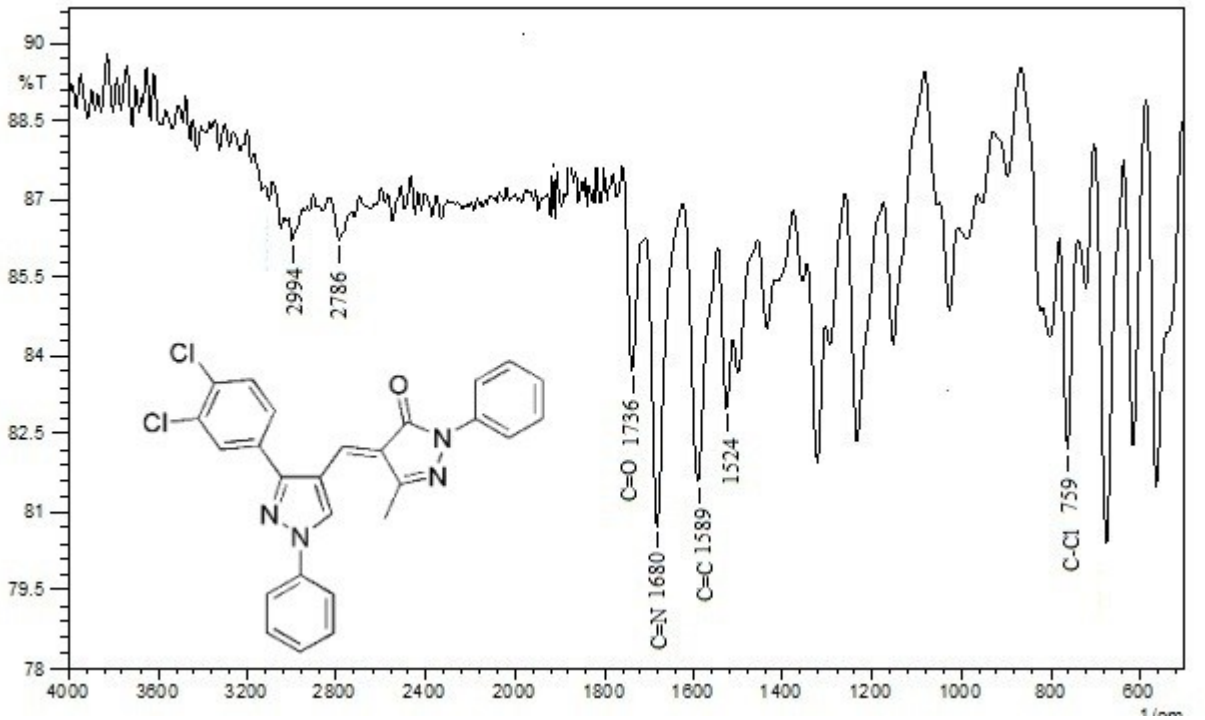
IR spectrum of compound **2a**



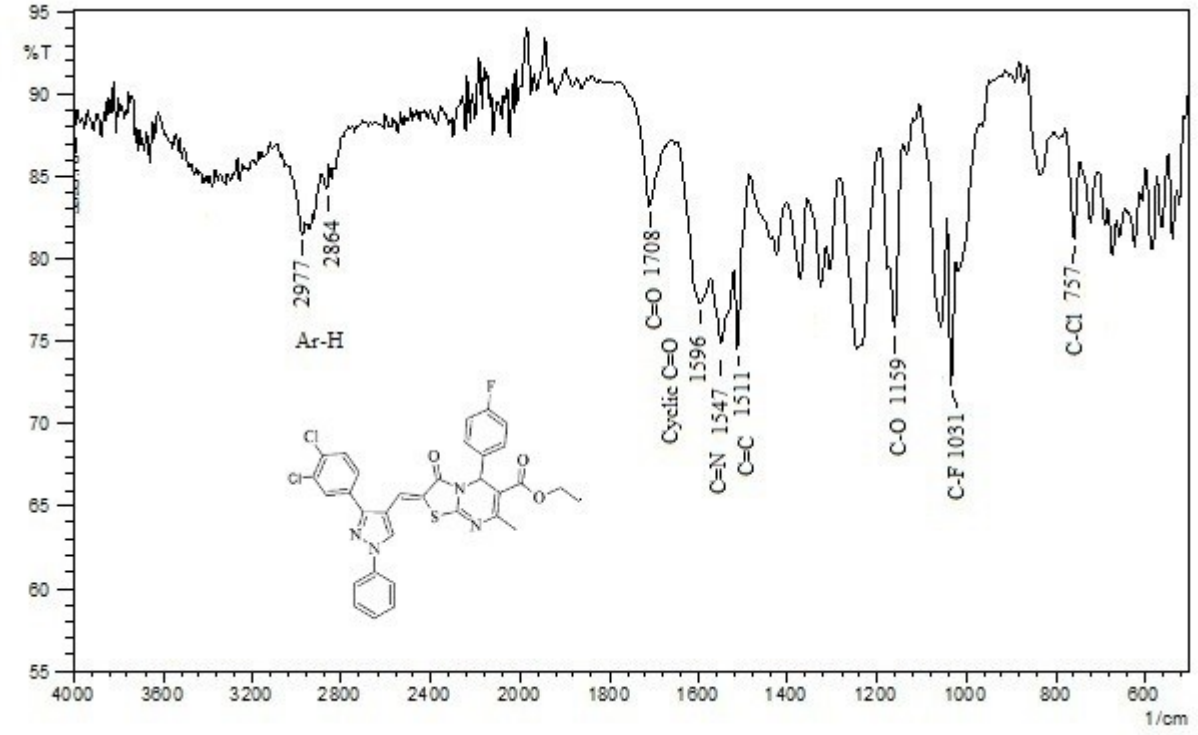
IR spectrum of compound **3a**



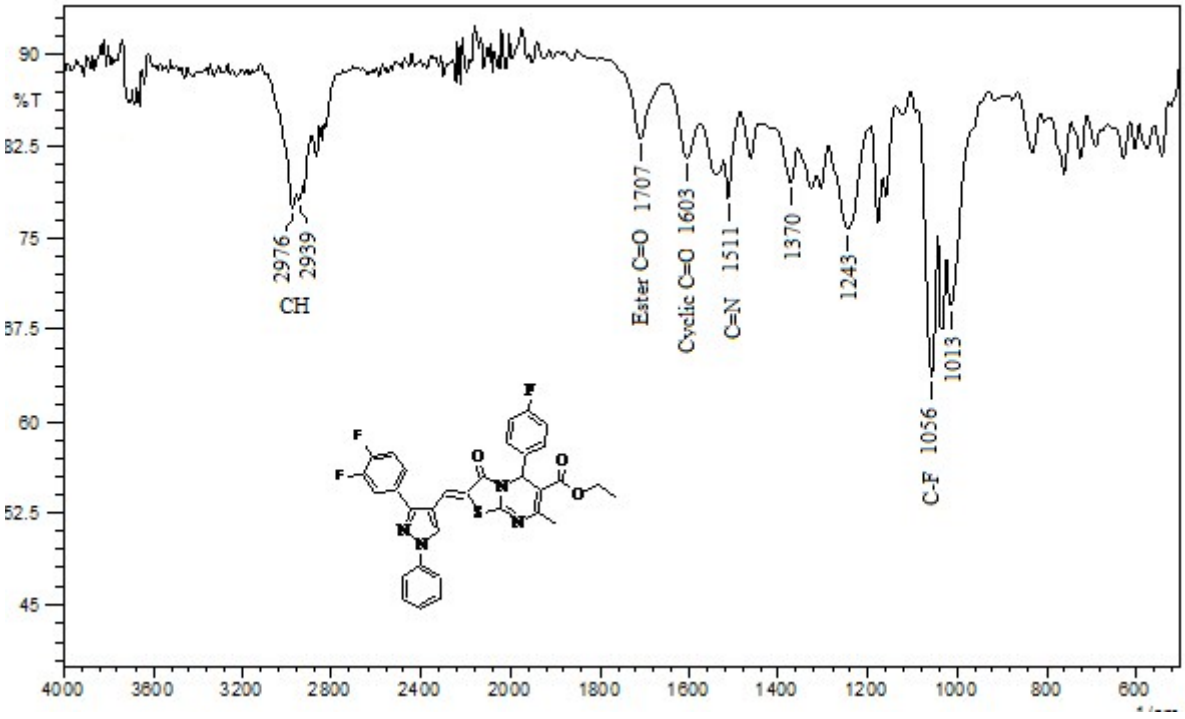
IR spectrum of compound **4a**



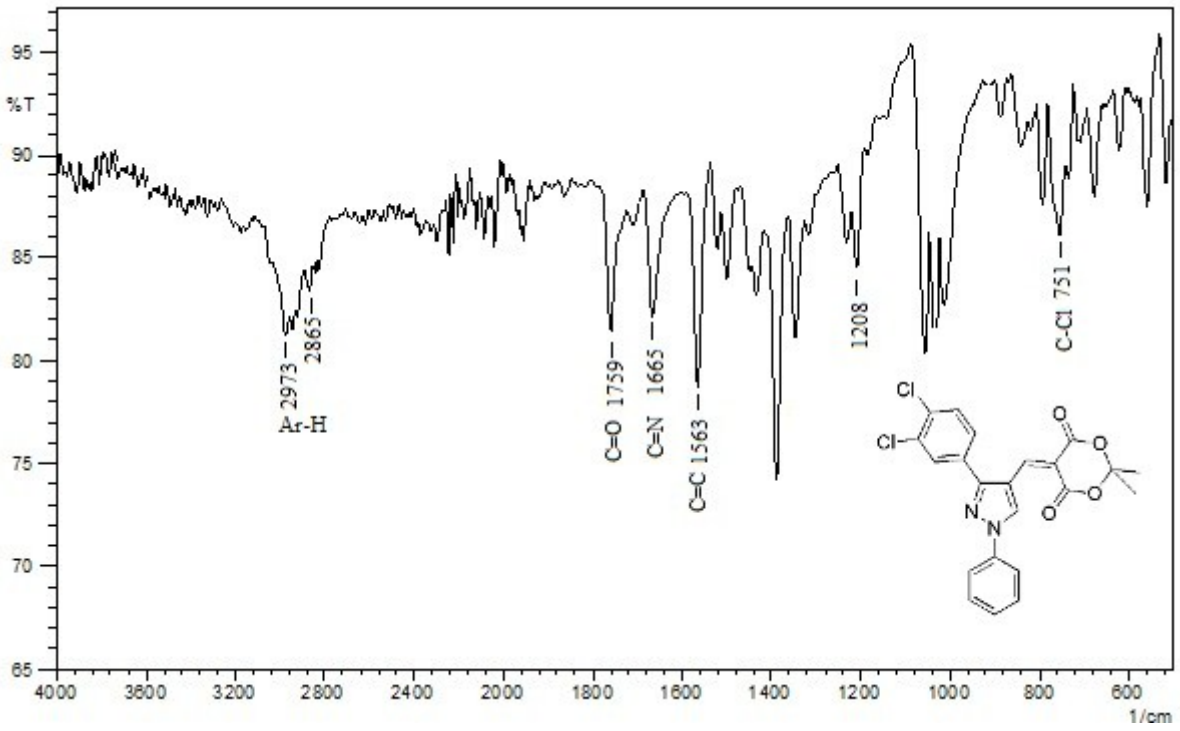
IR spectrum of compound **5a**



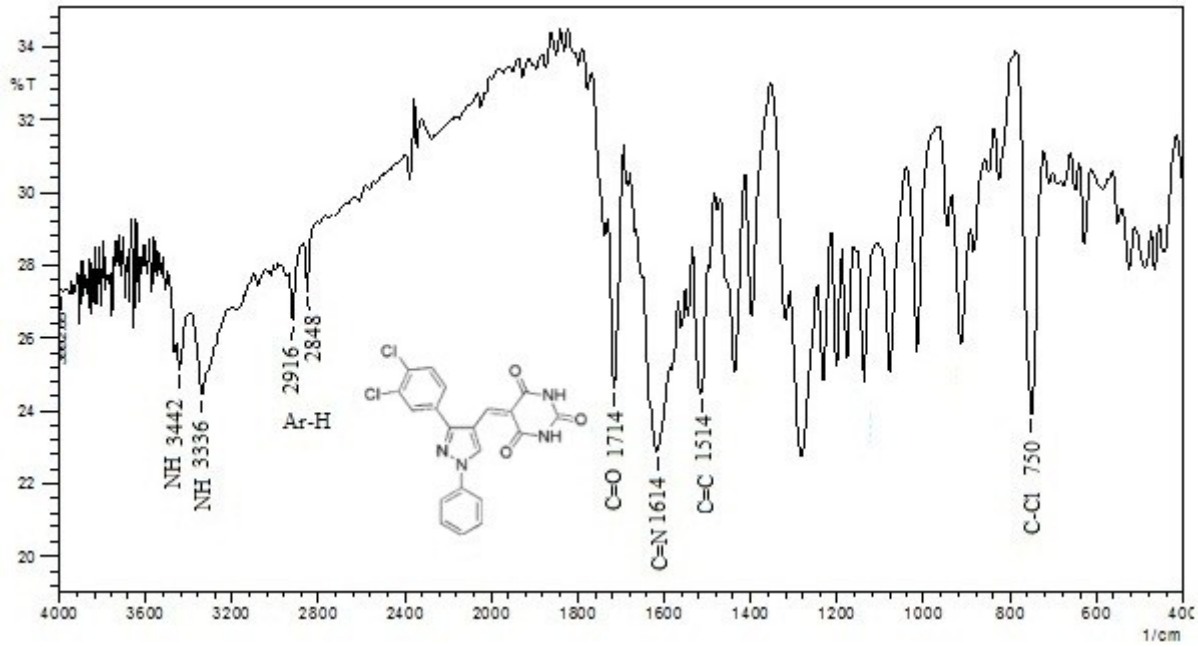
IR spectrum of compound **5b**



IR spectrum of compound **6a**



IR spectrum of compound **7a**



CHNS analysis of all the synthesised compounds

Sample Name V-1a to V-7b in the CHNS analyser data represents compounds 1a to 7a in the Manuscript.

Mangalore University
Department of Chemistry - CHNS Analyser
Elementar Vario EL III - SI. No. 11054048

17.05.15 13:22

No.	Name	Wght. [mg]	Date Time	Info	O2	C/N Ratio	Content [%]	Blank Value
~~24~~	~~PZ-1~~	~~4.3660~~	~~17.05.15 08:09~~	~~Su~~	~~Index 1~~	~~4.293~~	~~N: 13.07~~	~~0~~
							~~C: 56.14~~	~~0~~
							~~S: 0.000~~	~~0~~
							~~H: 5.928~~	~~0~~
~~22~~	~~PZ-2~~	~~4.1070~~	~~17.05.15 03:19~~	~~Su~~	~~Index 1~~	~~1.604~~	~~N: 30.09~~	~~0~~
							~~C: 48.27~~	~~0~~
							~~S: 0.007~~	~~0~~
							~~H: 4.138~~	~~0~~
23	V-1a	4.2500	17.05.15 08:39	viv	Index 1	5.448	N: 10.07	0
							C: 54.86	0
							S: 7.675	0
							H: 2.602	0
24	V-1b	3.5190	17.05.15 08:51	viv	Index 1	5.420	N: 10.98	0
							C: 59.51	0
							S: 8.388	0
							H: 2.889	0
25	V-2a	3.1990	17.05.15 09:02	viv	Index 1	6.832	N: 9.671	0
							C: 66.07	0
							S: 5.484	0
							H: 3.848	0
26	V-2b	3.5030	17.05.15 09:12	viv	Index 1	6.888	N: 10.17	0
							C: 70.05	0
							S: 5.851	0
							H: 4.068	0
27	V-3a	3.5930	17.05.15 09:24	viv	Index 1	5.580	N: 10.00	0
							C: 55.80	0
							S: 5.707	0
							H: 2.728	0
28	V-3b	3.5740	17.05.15 09:35	viv	Index 1	5.558	N: 10.67	0
							C: 59.30	0
							S: 6.078	0
							H: 2.884	0
29	V-3c	3.8890	17.05.15 09:46	viv	Index 1	5.330	N: 11.47	0
							C: 61.14	0
							S: 6.582	0
							H: 3.277	0

No.	Name	Wght. [mg]	Date Time	Info	O2	C/N Ratio	Content [%]	Blank Value
30	V-3d	3.0970	17.05.15 09:56	viv	Index 1	5.382	N: 12.17	0
							C: 65.50	0
							S: 6.970	0
							H: 3.480	0
31	V-4a	3.5600	17.05.15 10:08	viv	Index 1	5.560	N: 11.86	0
							C: 65.94	0
							S: 0.001	0
							H: 3.819	0
32	V-4b	4.4850	17.05.15 10:20	viv	Index 1	5.589	N: 12.69	0
							C: 70.93	0
							S: 0.000	0
							H: 4.103	0
33	V-5a	3.9040	17.05.15 10:38	viv	Index 1	6.818	N: 8.902	0
							C: 60.69	0
							S: 5.033	0
							H: 3.679	0
34	V-5b	4.2420	17.05.15 10:49	viv	Index 1	6.858	N: 9.327	0
							C: 63.96	0
							S: 5.327	0
							H: 3.842	0
35	V-6a	3.9570	17.05.15 11:01	viv	Index 1	9.450	N: 6.312	0
							C: 59.65	0
							S: 0.004	0
							H: 3.670	0
36	V-6b	4.7990	17.05.15 11:21	viv	Index 1	9.396	N: 6.849	0
							C: 64.35	0
							S: 0.002	0
							H: 3.943	0
37	V-7a	3.7970	17.05.15 11:32	viv	Index 1	4.288	N: 13.11	0
							C: 56.22	0
							S: 0.002	0
							H: 2.832	0
38	V-7b	3.1700	17.05.15 11:45	viv	Index 1	4.274	N: 14.25	0
							C: 60.91	0
							S: 0.001	0
							H: 3.070	0