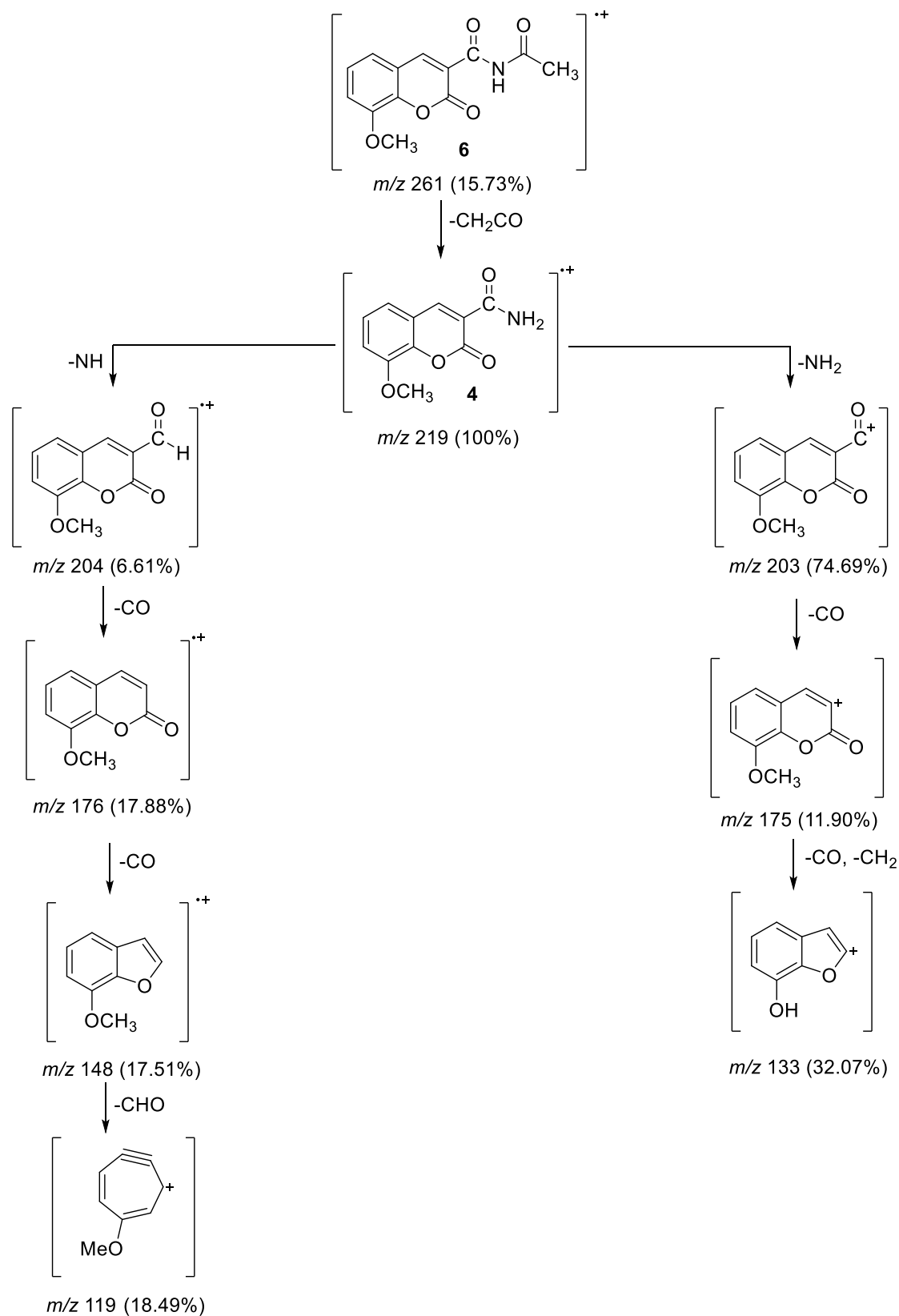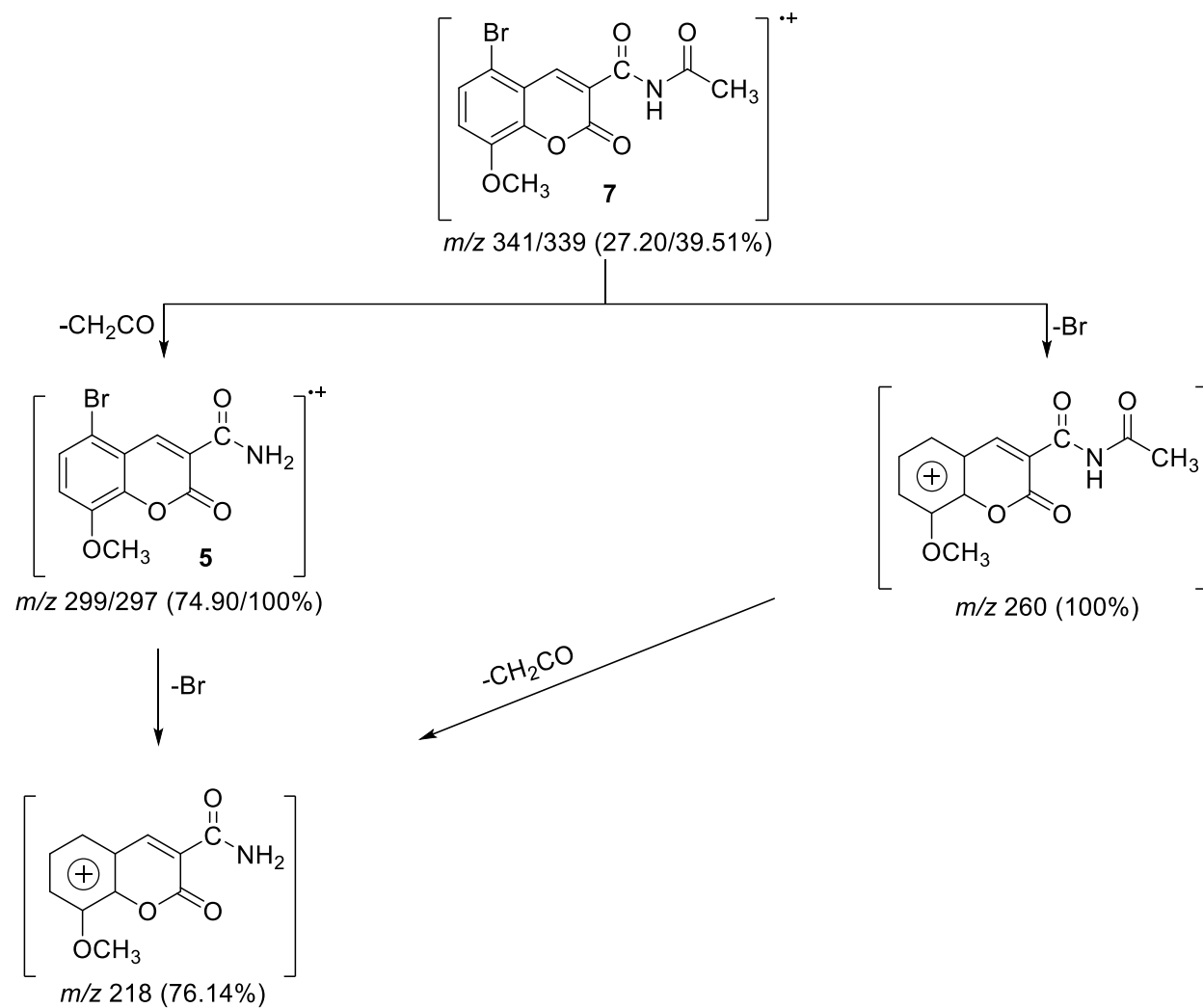# Supplementary Materials

Novel 8-Methoxycoumarin-3-Carboxamides with potent Anticancer activity against Liver Cancer *via* targeting caspase-3/7 and β-tubulin polymerization
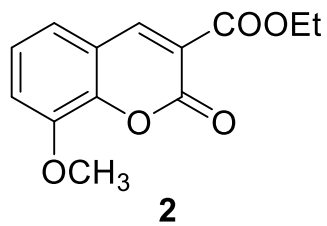
Ahmad Alzamami [1], Eman M. Radwan [2], Eman Abo-Elabass [3], Mohammed El Behery [3], Hussah Abdullah Alshwyeh [4,5], Ebtesam Al-Olayan[6], Abdulmalik S. Altamimi [7], Nashwah G M Attallah [8], Najla Altwaijry [9], Mariusz Jaremko [10,*], and Essa M. Saied [11,12,*]

m/z 261 (15.73%)

-CH$_2$CO

m/z 219 (100%)

-NH

-NH$_2$

m/z 204 (6.61%)

m/z 203 (74.69%)

-CO

-CO

m/z 176 (17.88%)

m/z 175 (11.90%)

-CO

-CO, -CH$_2$

m/z 148 (17.51%)

m/z 133 (32.07%)

-CHO

m/z 119 (18.49%)

Scheme S1: Main fragmentation pattern of compounds 4 and 6.

Scheme S1: Main fragmentation pattern of compounds 5 and 7.

- Compound **7**: *m/z* 341/339 (27.20/39.51%)
- -CH$_2$CO → Compound **5**: *m/z* 299/297 (74.90/100%)
- -Br → *m/z* 260 (100%)
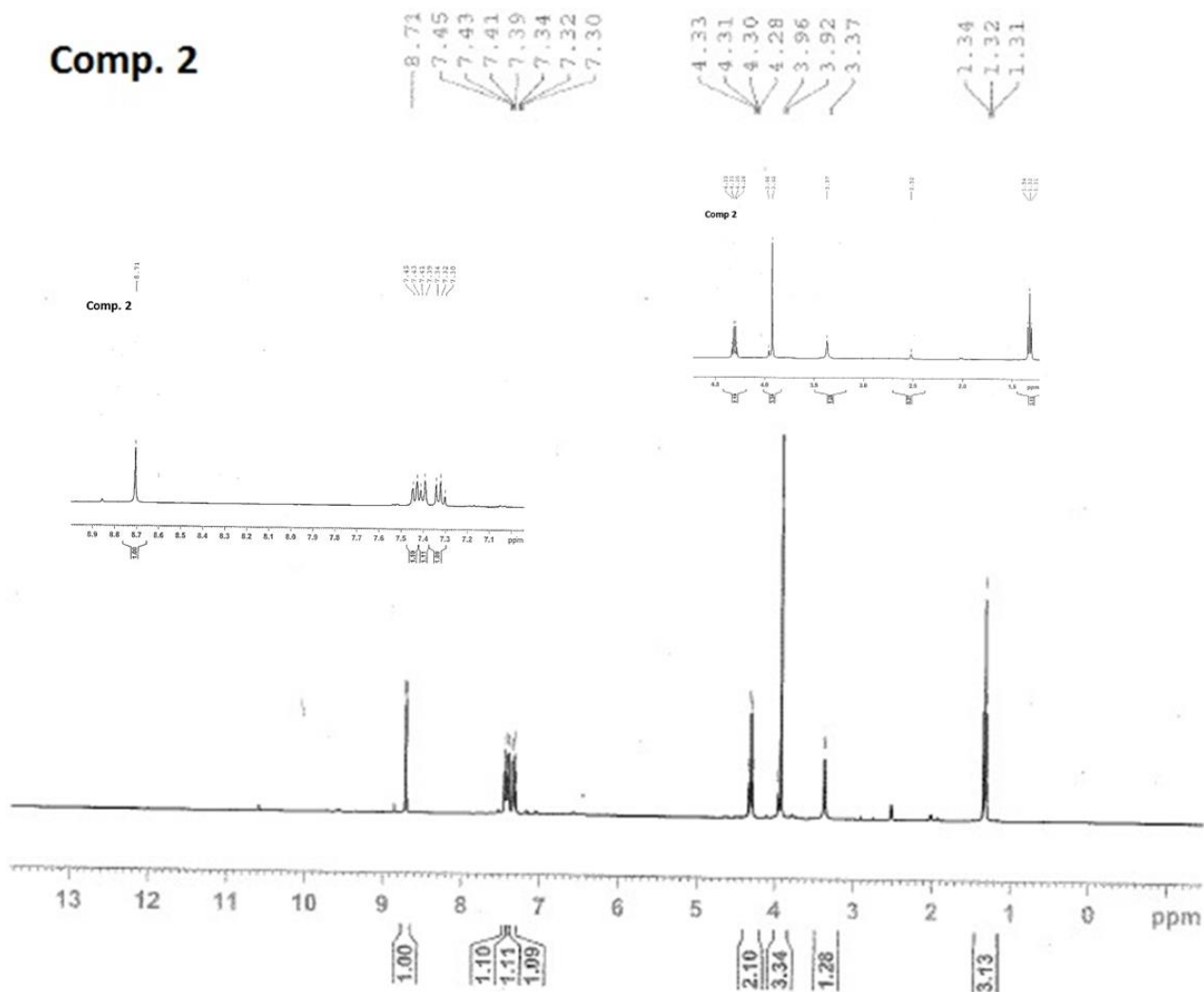- -Br and -CH$_2$CO → *m/z* 218 (76.14%)
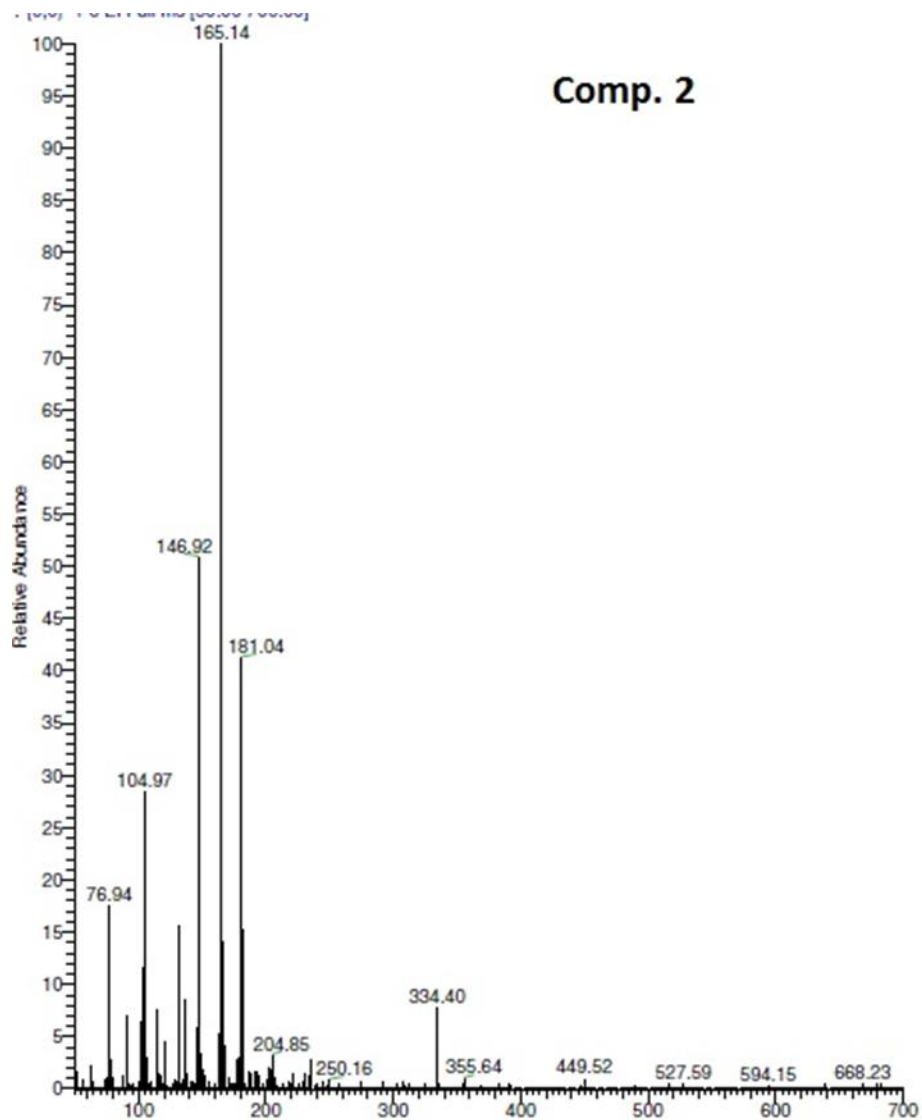
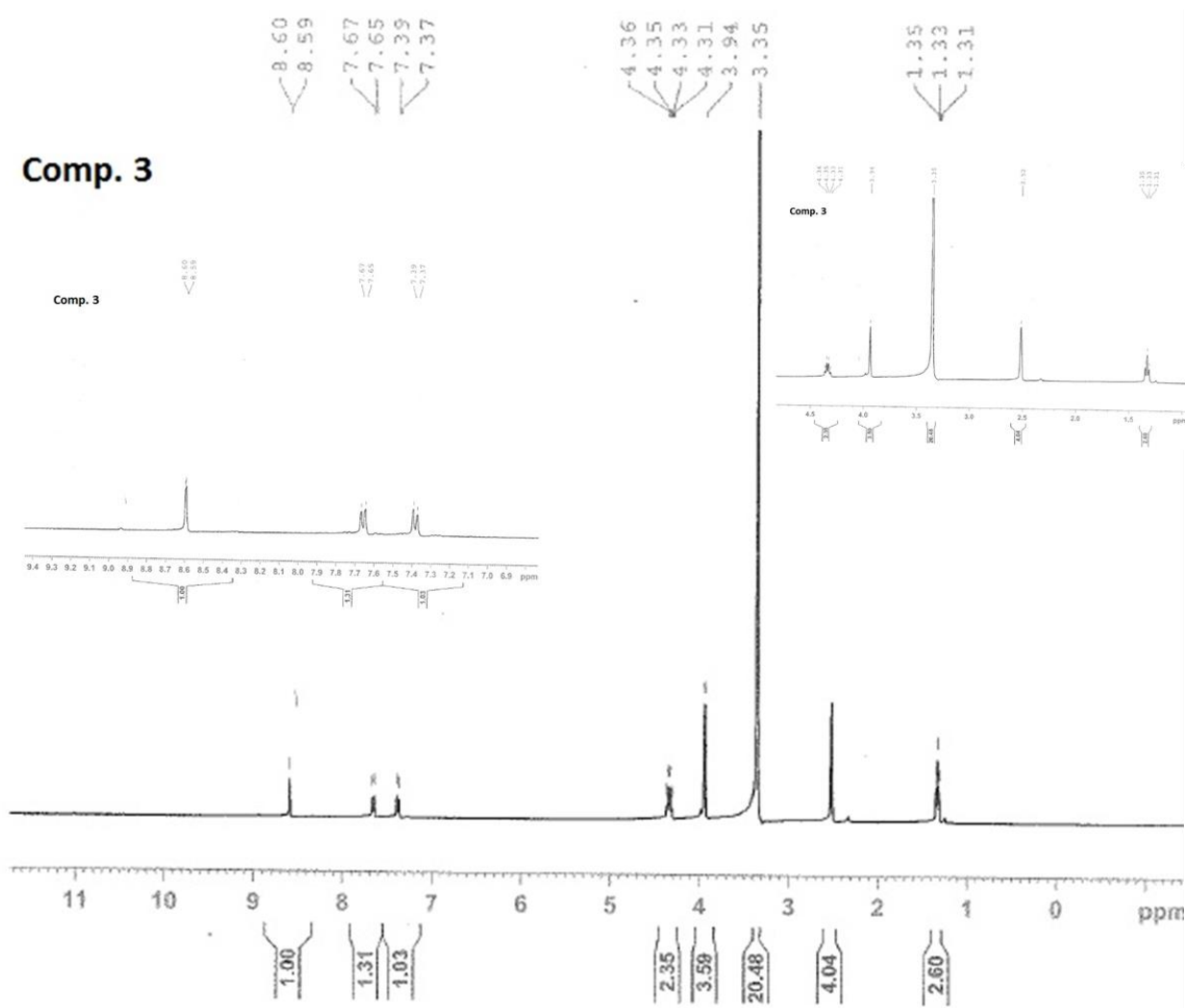**Figure S1a.** ^{1}H NMR spectra of compound 2
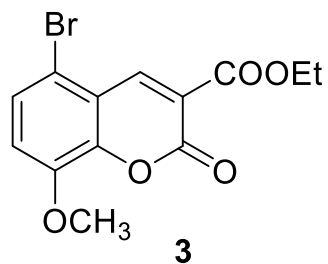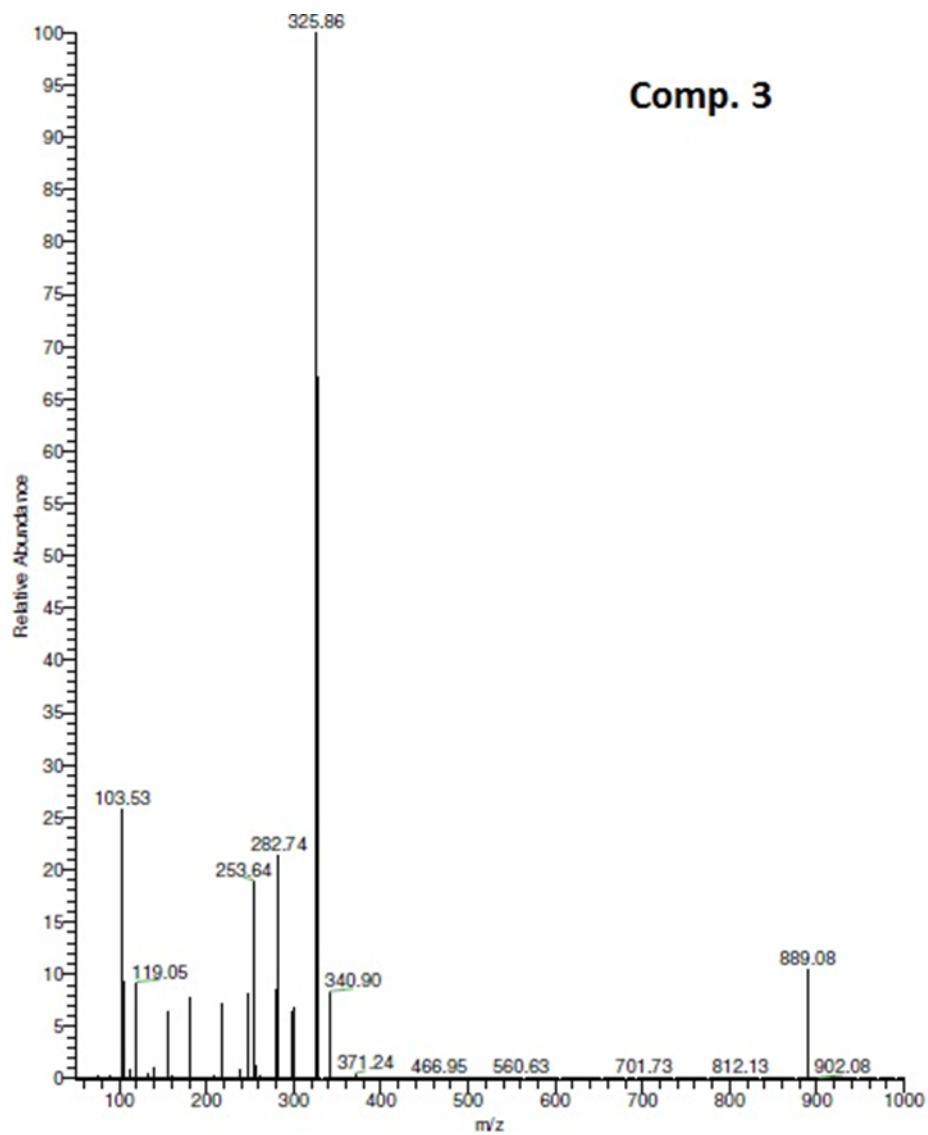
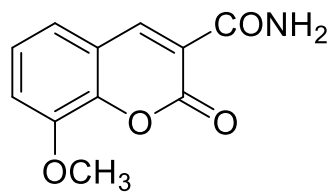**Figure S1b. Mass spectrum of compound 2.**

Figure S2a. ^{1}H NMR spectra of compound 3
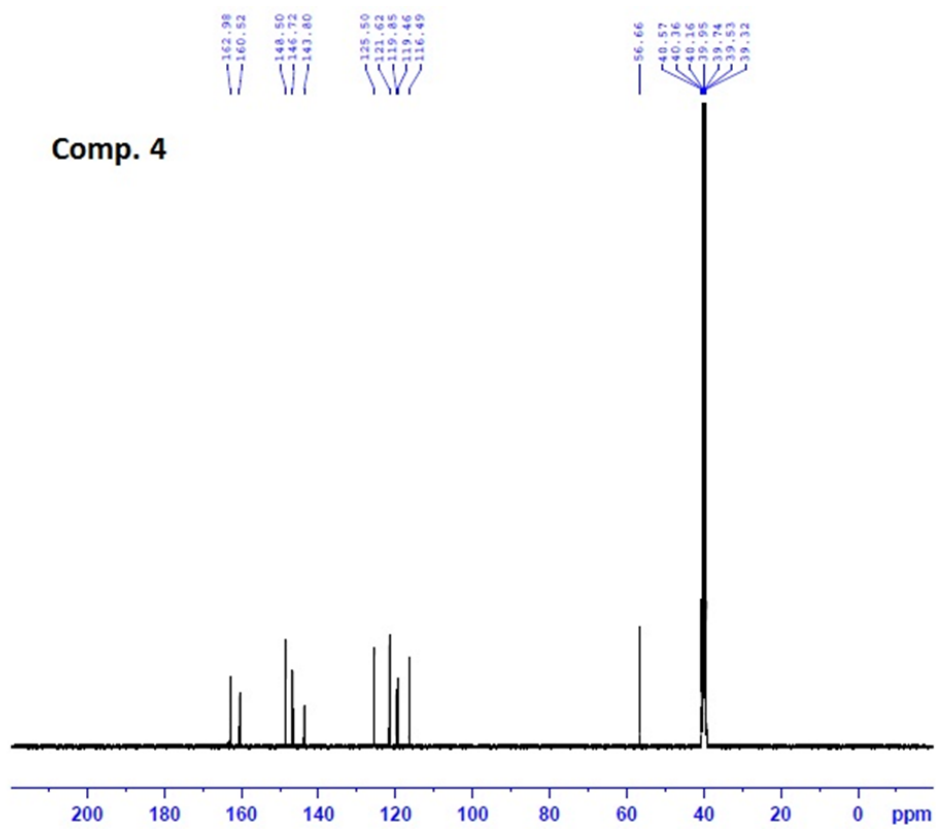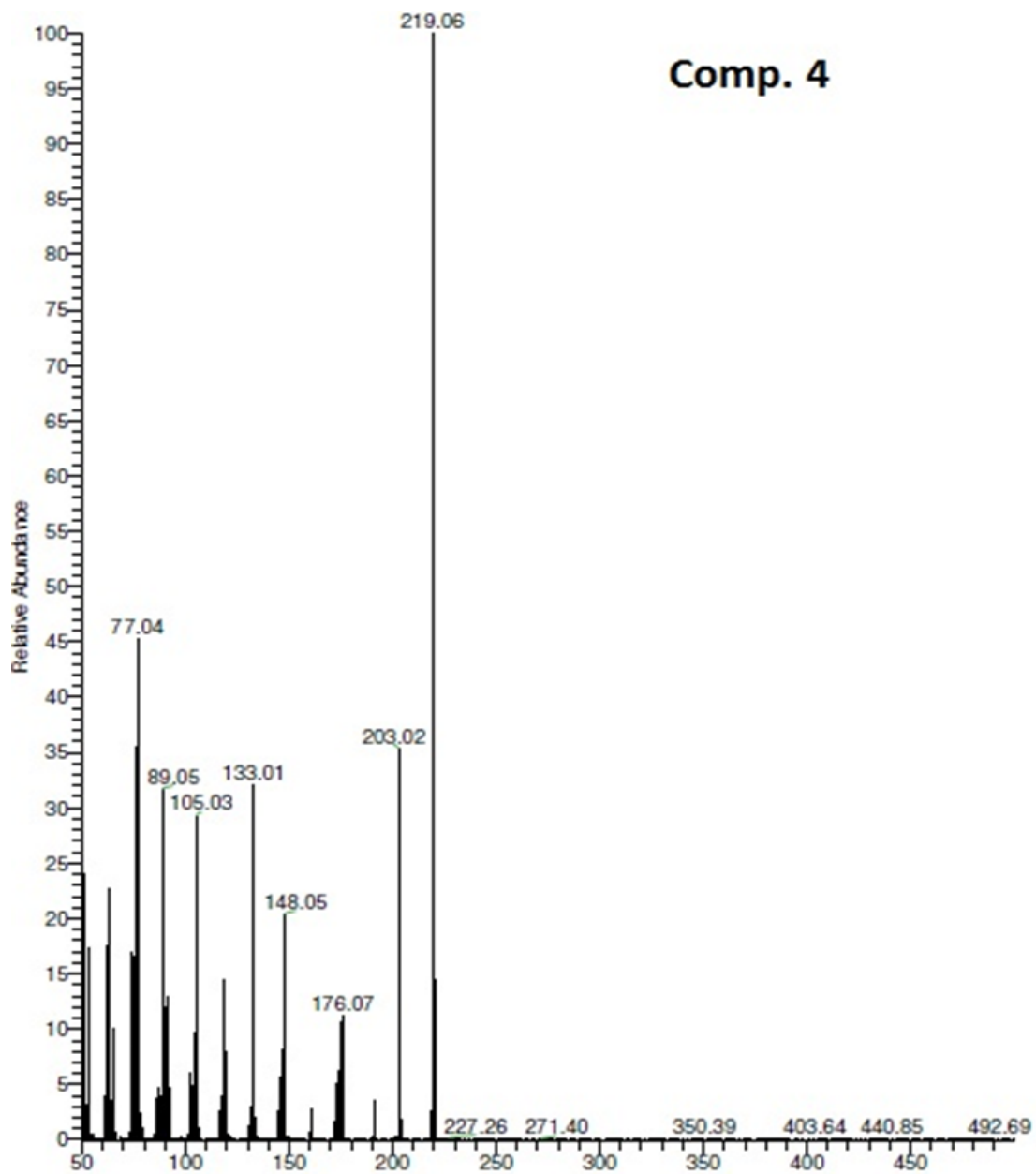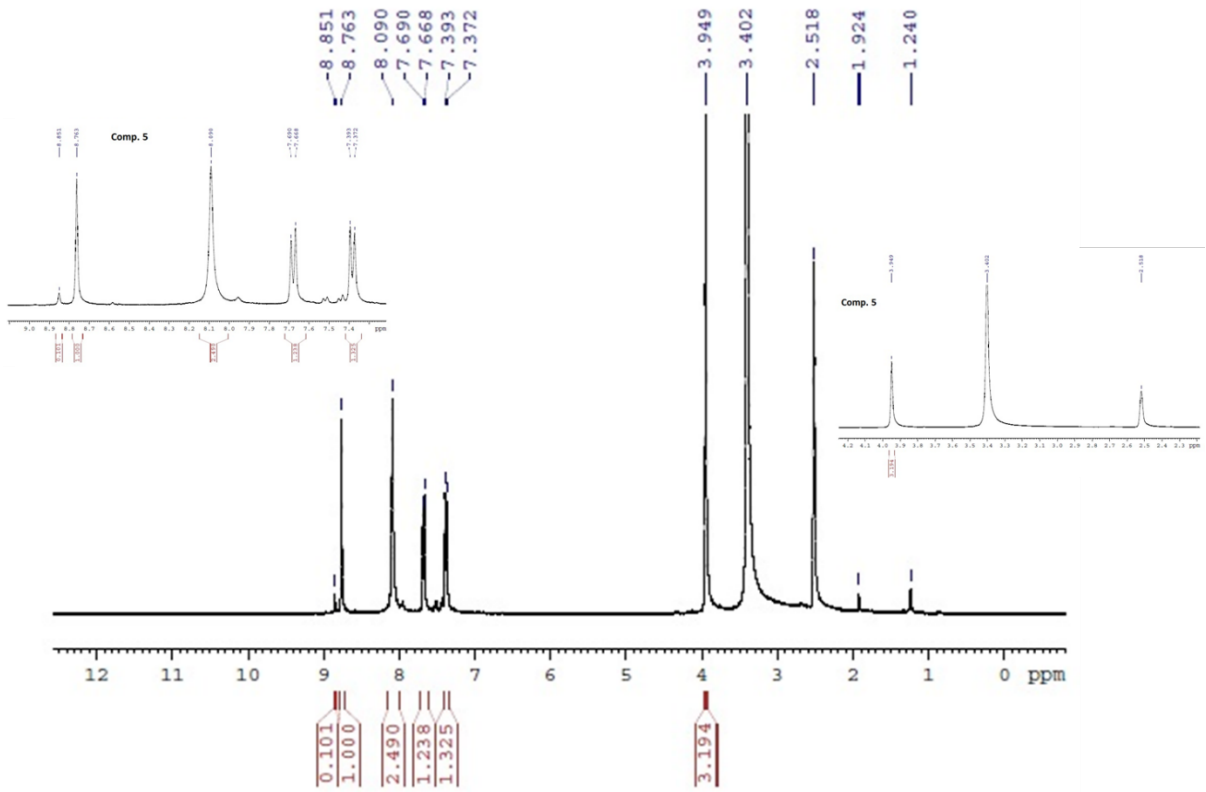
Figure S2b. Mass spectrum of compound 3.

Comp. 4

8.846
8.098
7.953
7.521
7.502
7.444
7.425
7.391
7.371
7.351
3.944
3.383
2.517

1.000
1.003
1.074
1.115
2.577
3.008

12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

Comp. 4

162.98
160.52
148.50
146.72
143.80
125.50
121.62
119.85
119.46
116.49
56.66
40.57
40.36
40.16
39.95
39.74
39.53
39.32
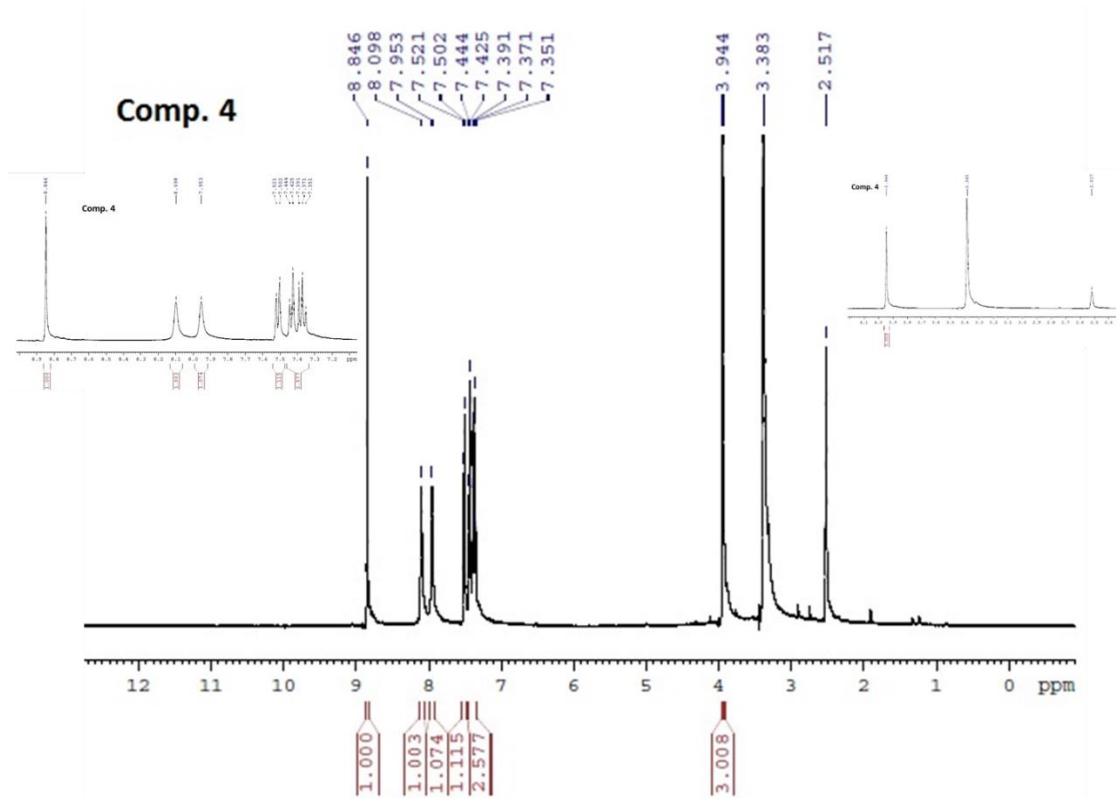
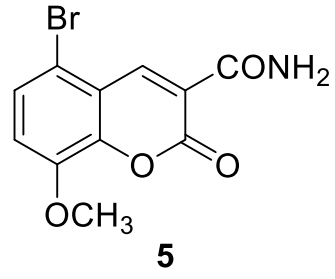**Figure S3a.** ^{1}H NMR and ^{13}C NMR spectra of compound 4
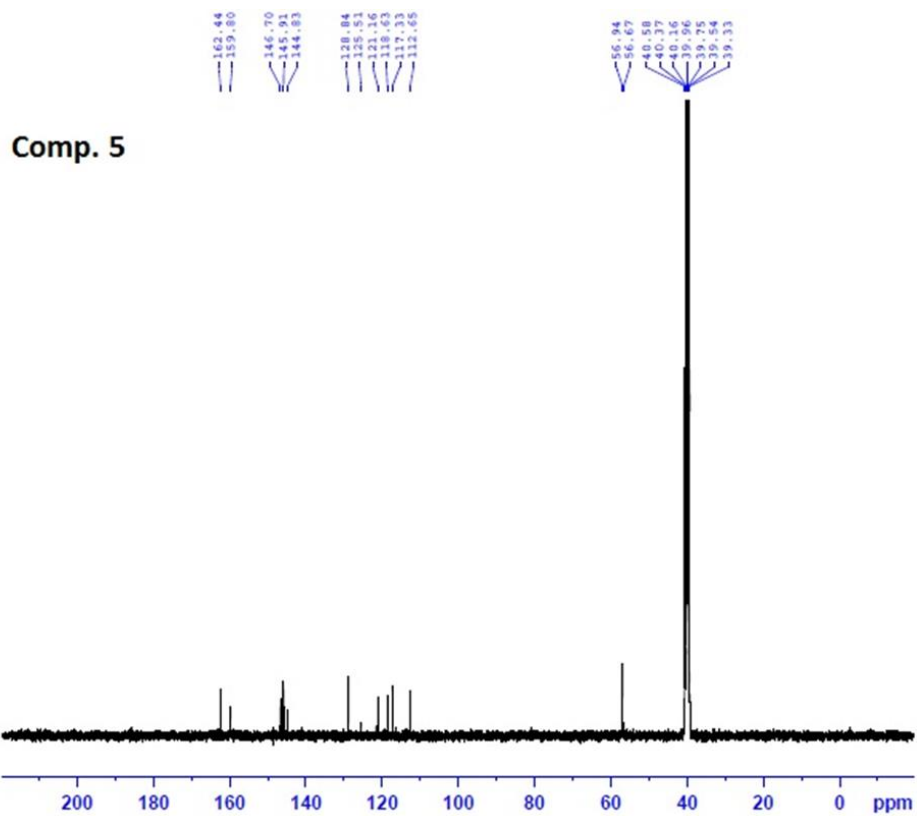
S9

Figure S3b. Mass spectrum of compound 4.

5

Comp. 5

162.44
159.80
146.70
145.91
144.83
128.84
125.51
121.16
118.63
117.33
112.45
56.94
56.67
40.58
40.37
40.16
39.96
39.75
39.54
39.33

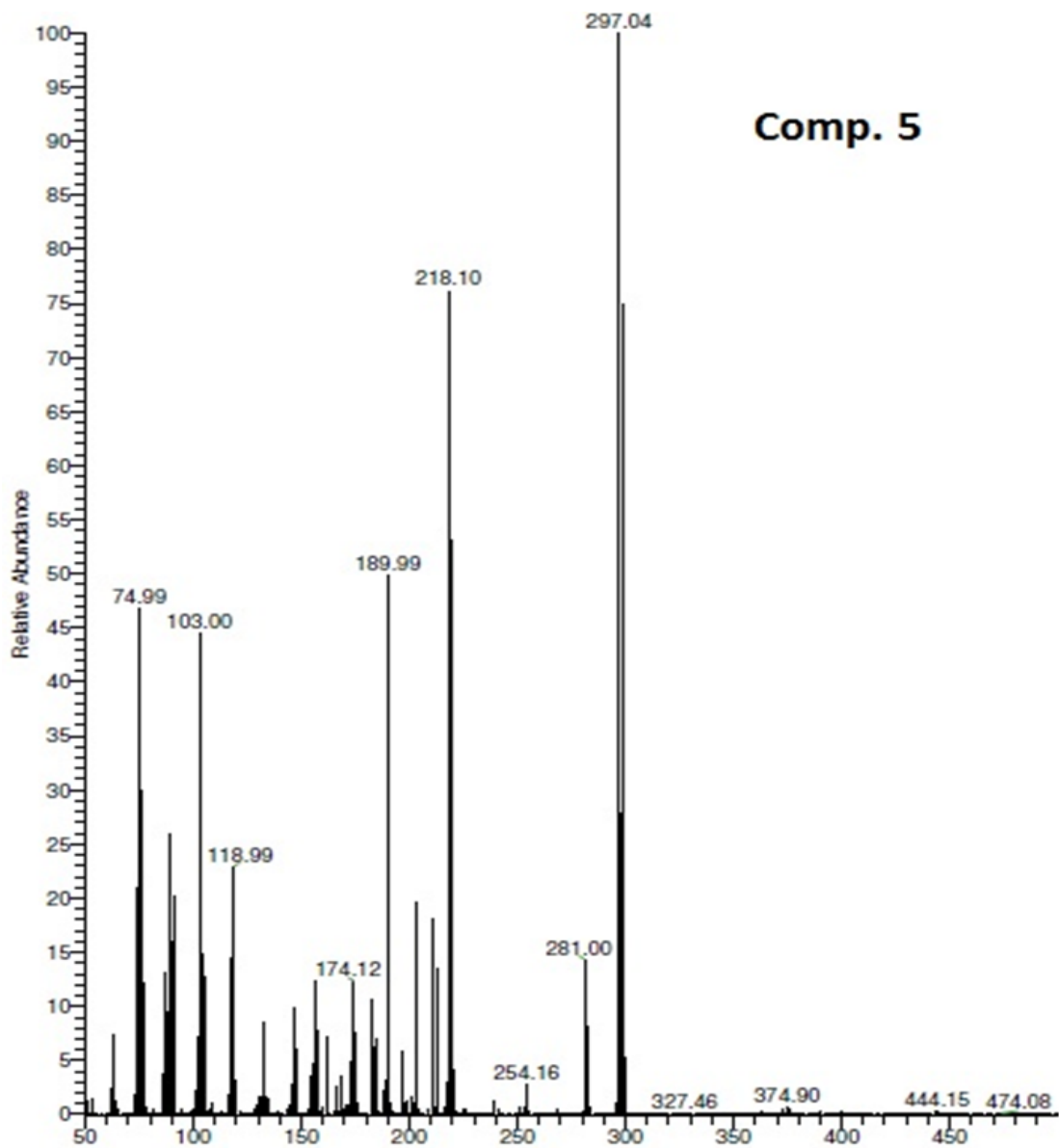200 180 160 140 120 100 80 60 40 20 0 ppm

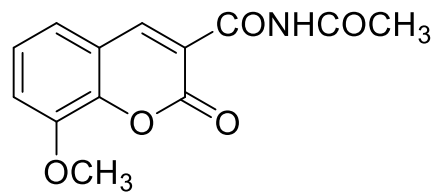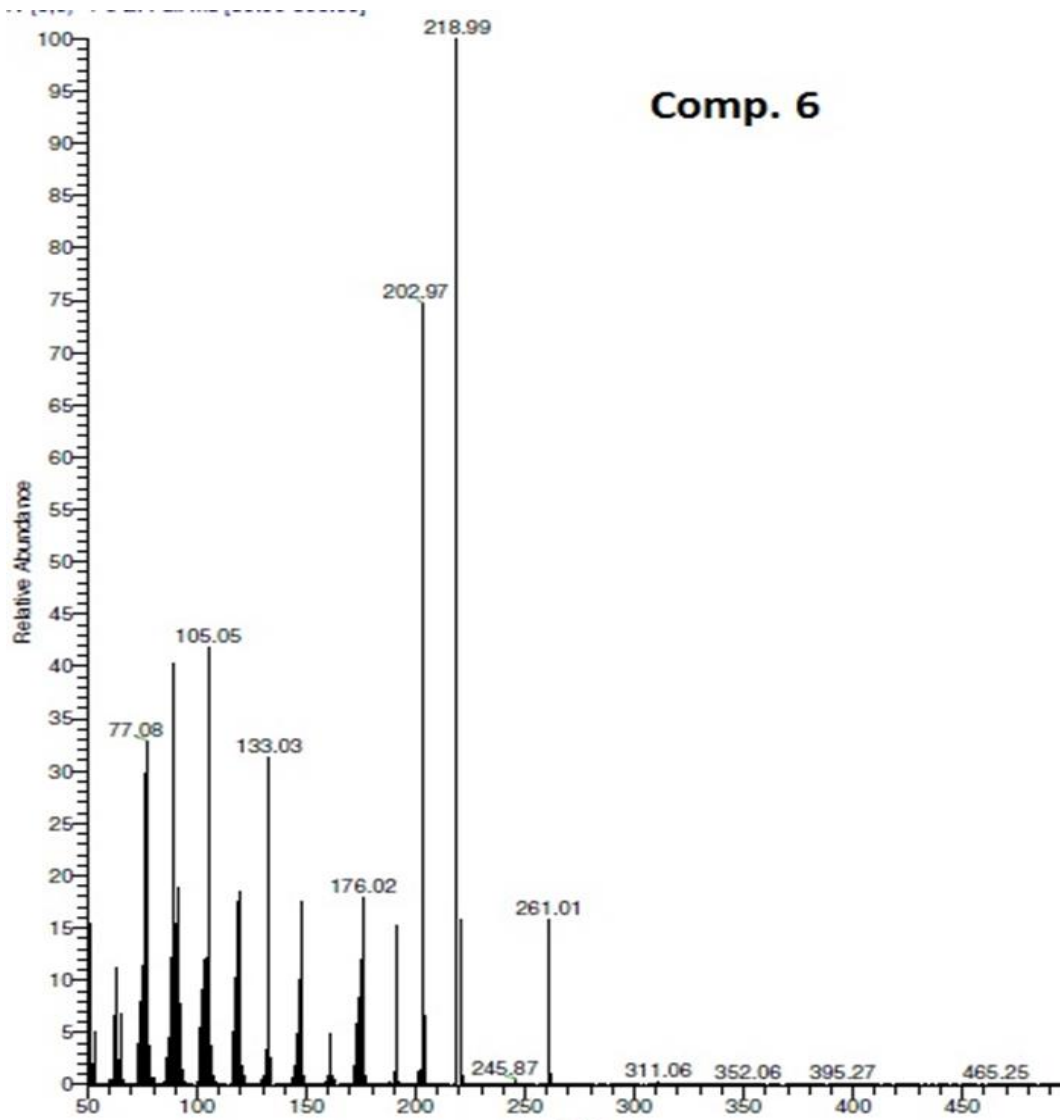**Figure S4a. ¹H NMR and ¹³C NMR spectra of compound 5**
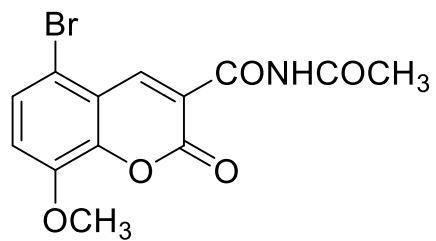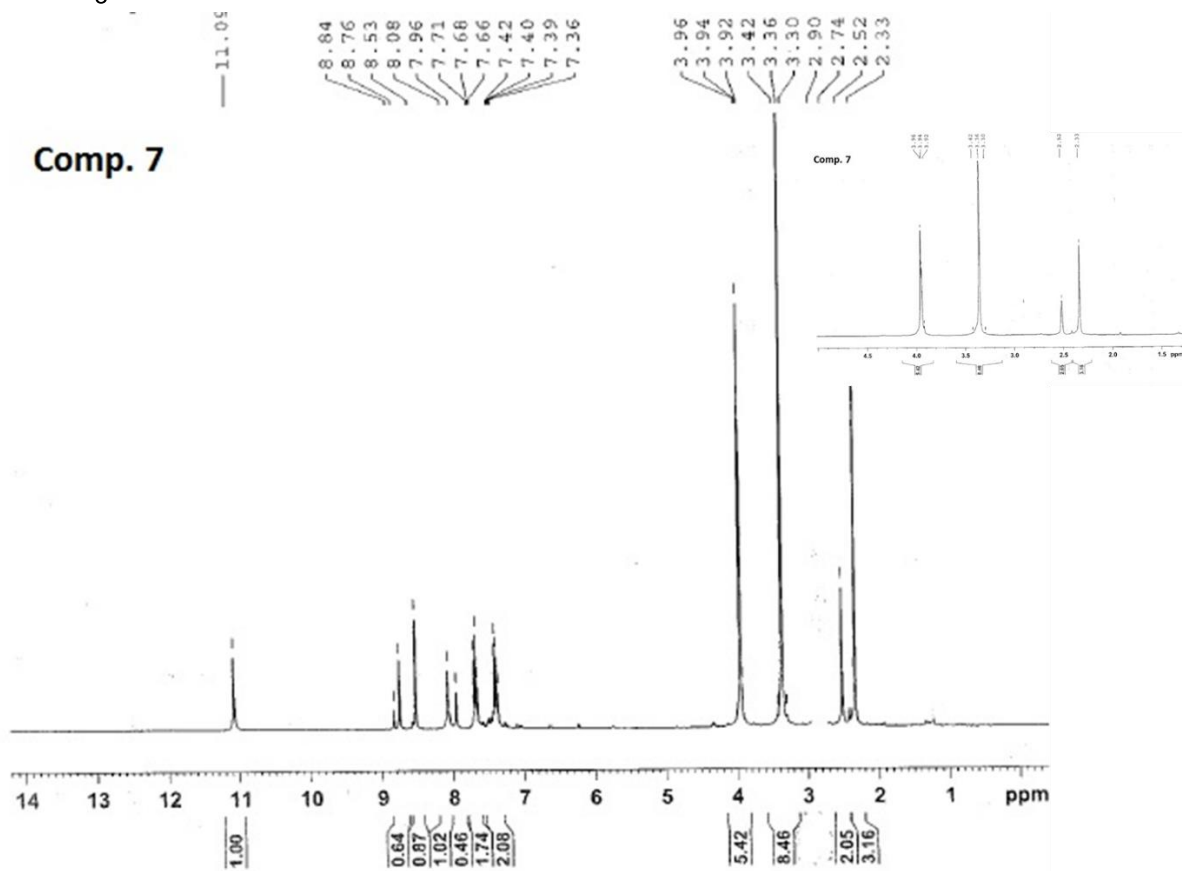
Figure S4b. Mass spectrum of compound 5.
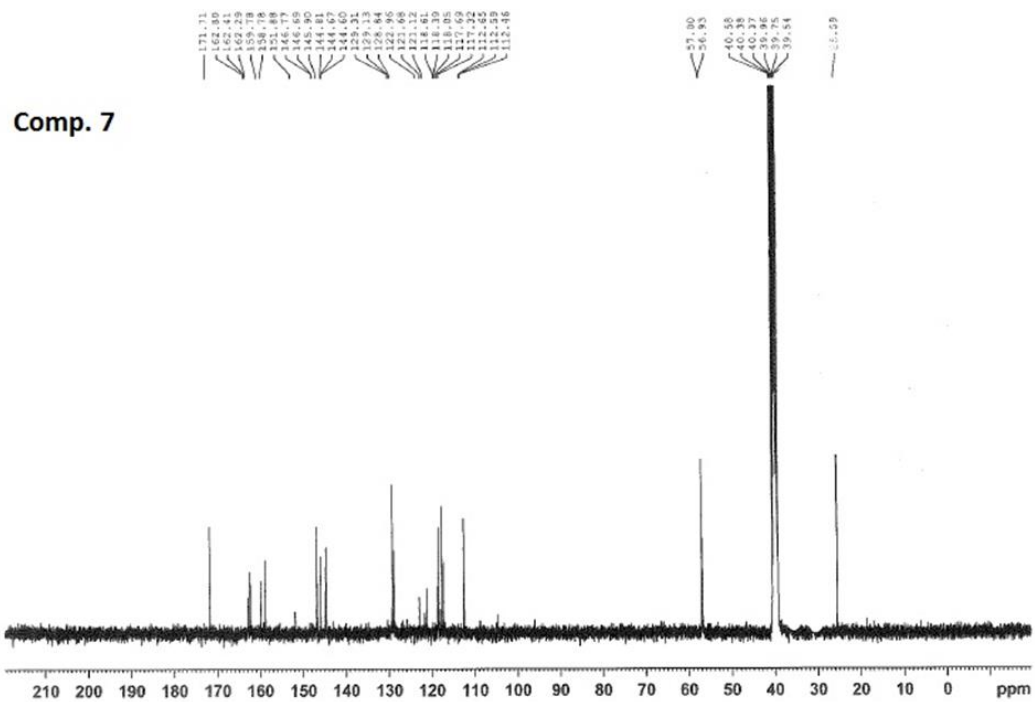
Figure S5. Mass spectrum of compound 6.

Comp. 7

Comp. 7

Figure S6a. ¹H NMR and ¹³C NMR spectra of compound 7.
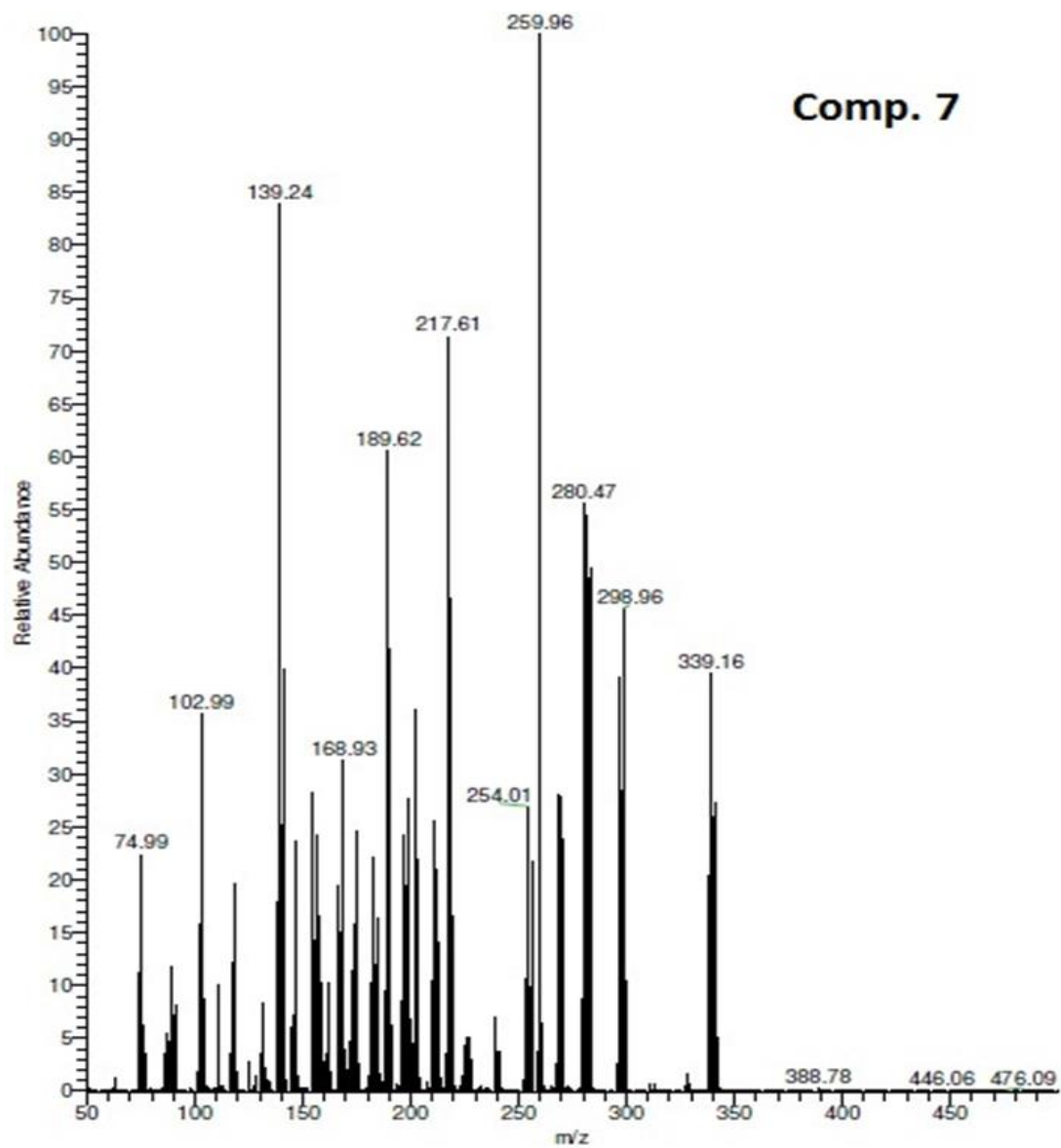
Figure S6b. Mass spectrum of compound 7.

Comp. 8

8.71
7.45
7.43
7.42
7.41
7.39
7.39
7.35
7.33
7.31

3.93

2.52
2.52

1.00
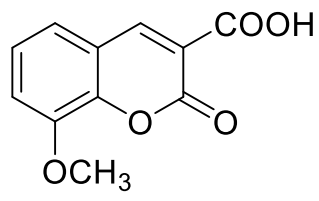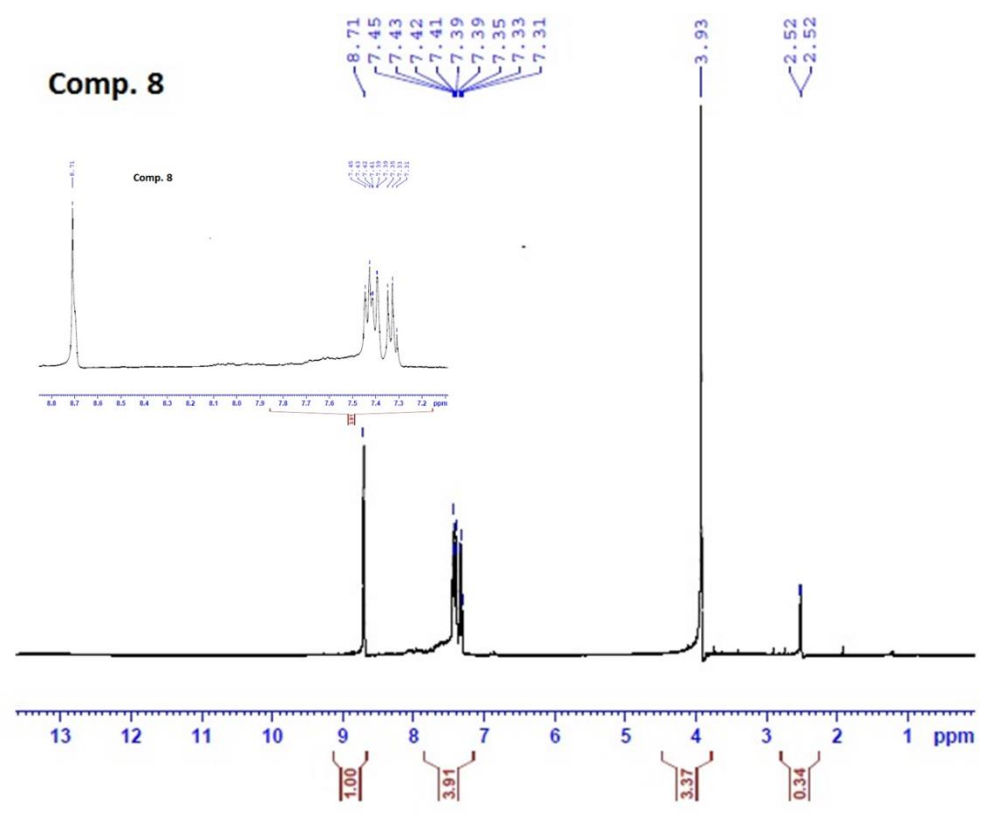3.91
3.37
0.34

Comp. 8

Figure S7a. ¹H NMR and ¹³C NMR spectra of compound 8.

Figure S7b. Mass spectrum of compound 8.

Comp. 9
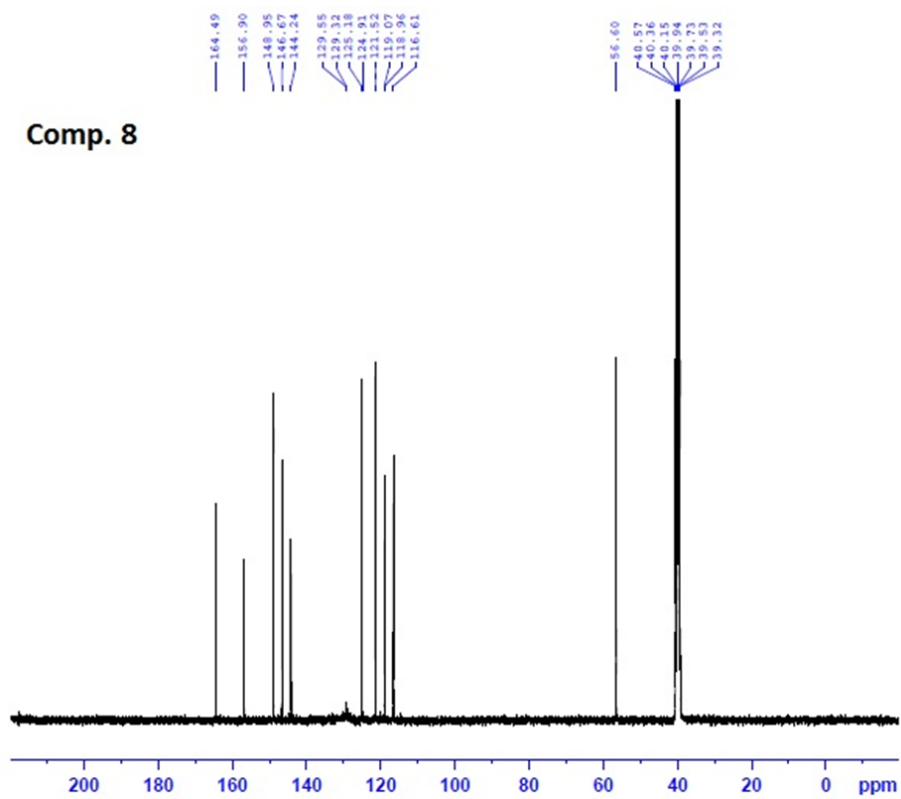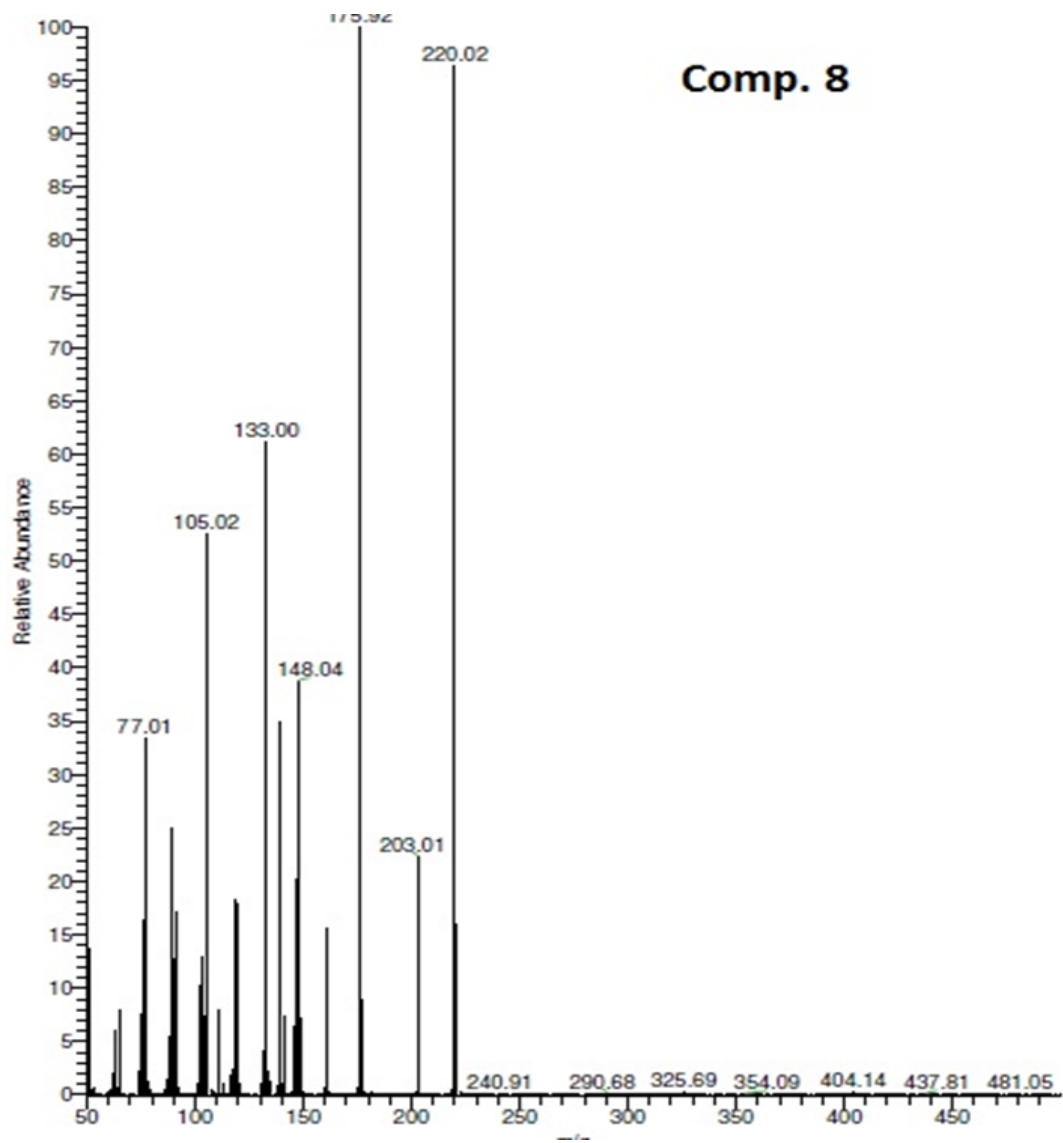
8.45

7.60
7.58
7.31
7.29

3.94
3.92

2.52

13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

0.76   1.39 1.00   3.77   0.54
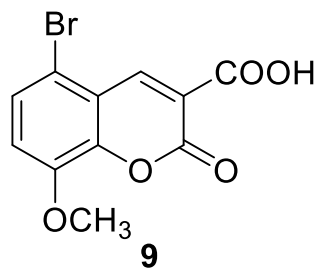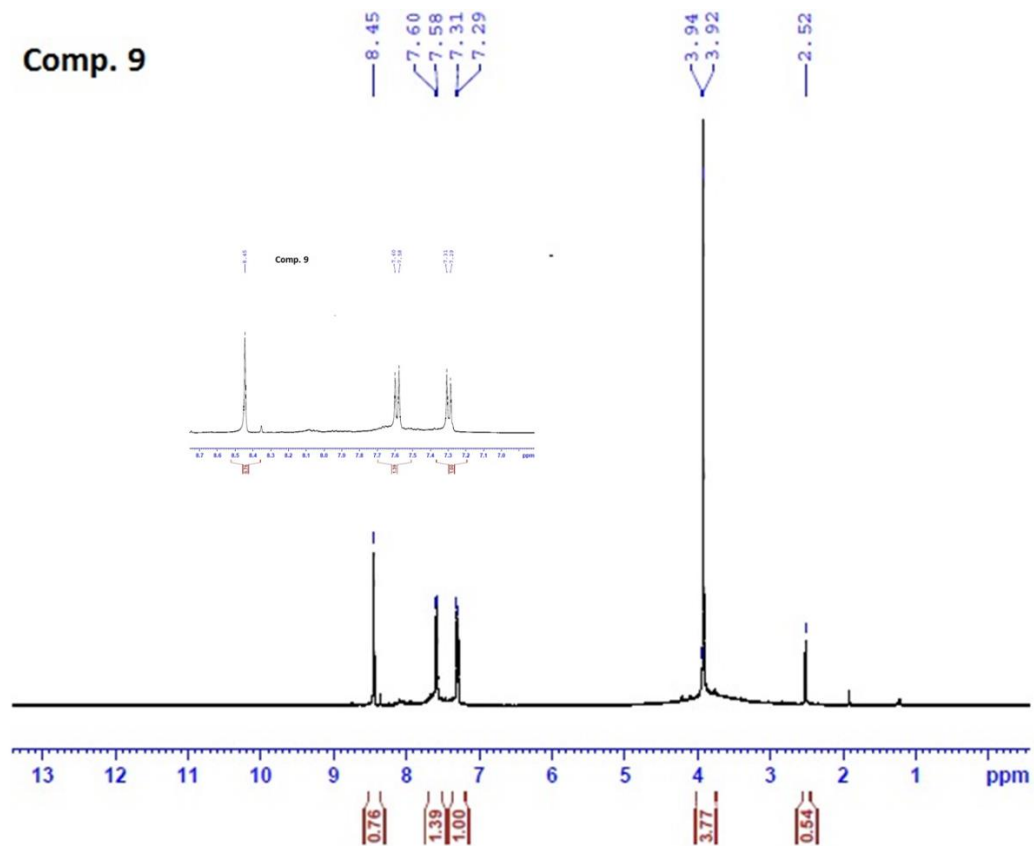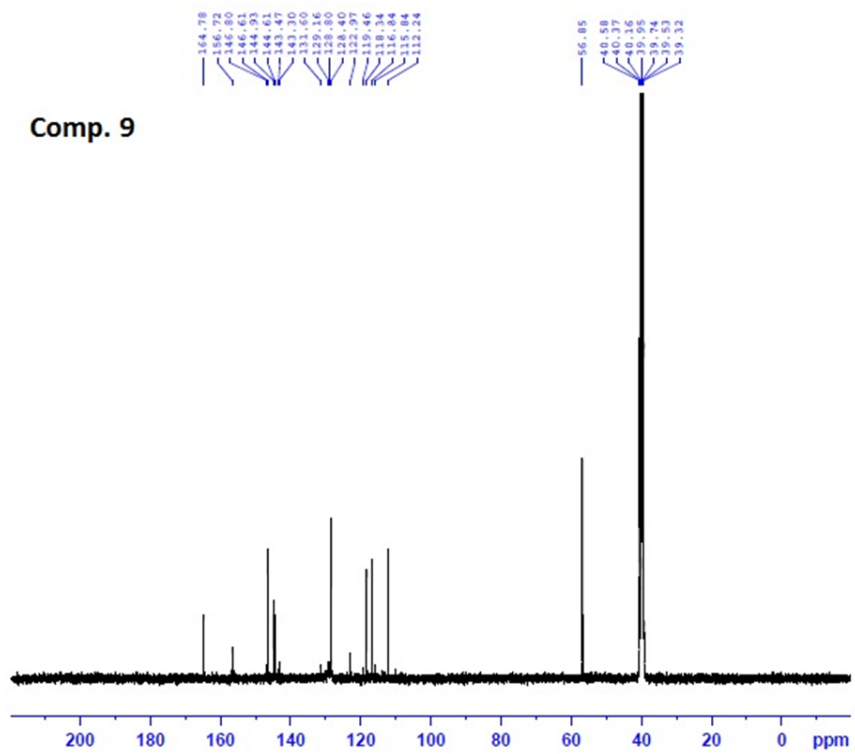
Comp. 9

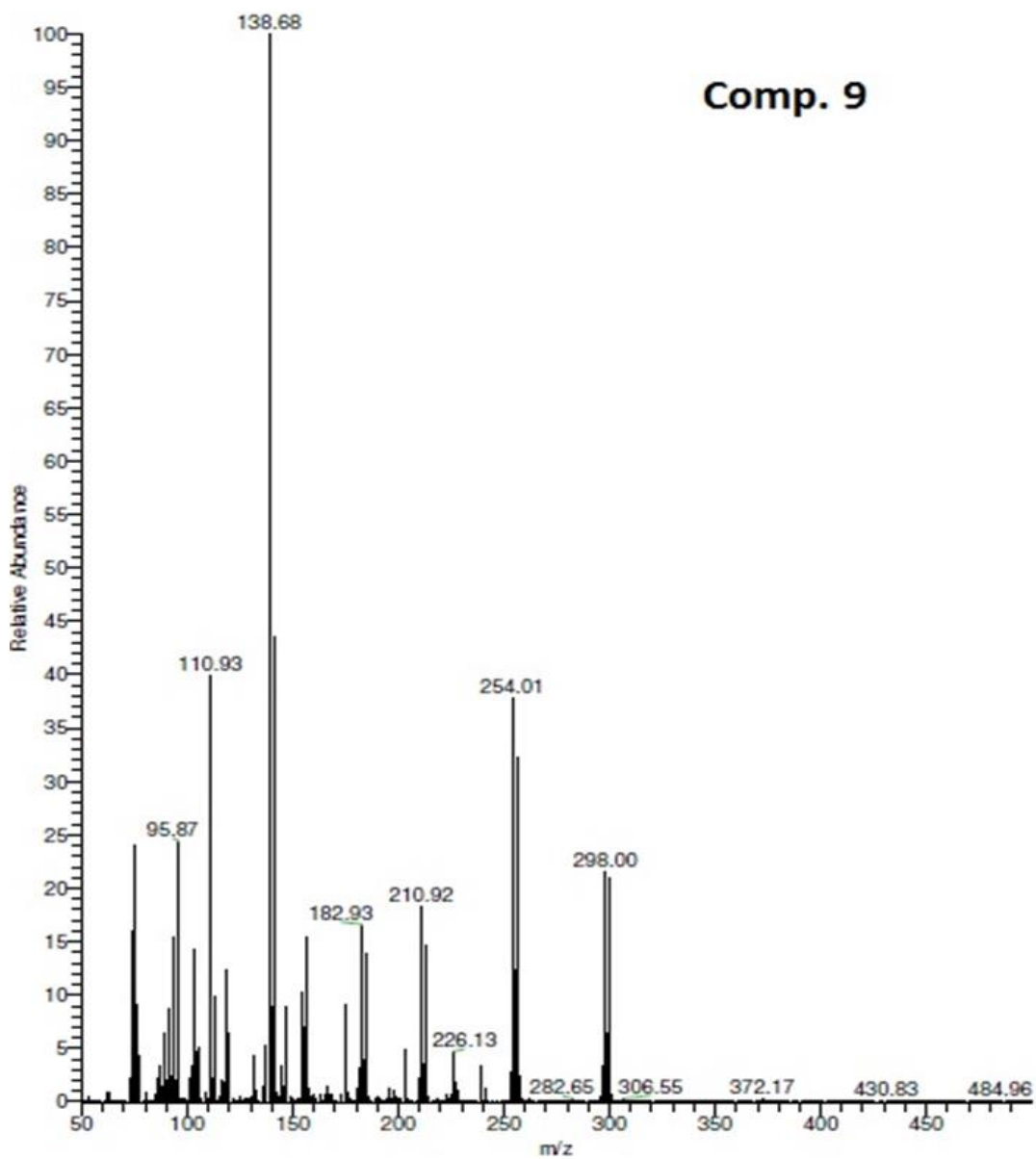Figure S8a. ¹H NMR and ¹³C NMR spectra of compound 9.

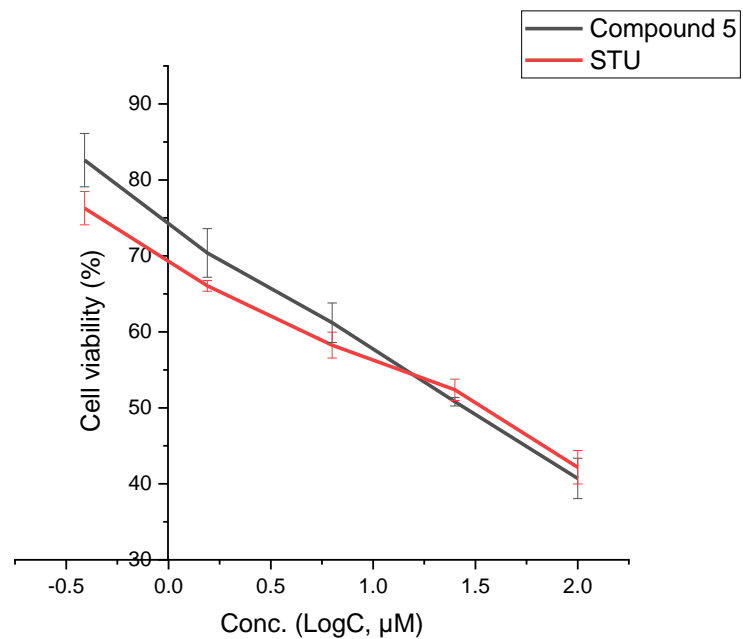**Figure S8b. Mass spectrum of compound 9.**

Figure S9. The dose-dependent cytotoxic activity of synthesized compound **5** toward WI 38 cells, as compared to STU. The presented data shows the mean ± standard deviation of the mean obtained from at least three independent experiments.

Table S1: Cytotoxic evaluation of compounds **4-9**, as compared to STU, against human liver carcinoma HepG2.

Concentration	HepG2-Cell Viability (%)						
LogC, μM	Compound 4	Compound 5	Compound 6	Compound 7	Compound 8	Compound 9	STU
2	37.94±2.75	34.02±3.21	27.04±2.87	45.03±3.1	24.59±1.84	42.17±2.94	29.43±3.14
1.4	47.29±3.09	43.91±2.73	37.53±2.14	53.19±2.87	35.26±1.93	50.19±3.07	39.57±2.71
0.8	57.78±2.46	52.05±2.11	44.64±1.98	60.52±2.64	40.63±1.66	55.34±2.24	55.04±1.96
0.19	65.8±1.73	60.49±1.84	54.47±1.72	68.52±2.36	46.68±1.21	66.86±1.86	62.49±1.62
-0.41	75.81±1.48	68.4±1.52	59.86±1.33	77.18±1.73	53.85±1.34	73.23±1.47	75.85±1.26