SUPPORTING INFORMATION

New-synthesised oxime and lactone derivatives from *Dipterocarpus alatus* dipterocarpol as anti-diabetic inhibitors: experimental bioassay-based evidence and theoretical computation-based prediction

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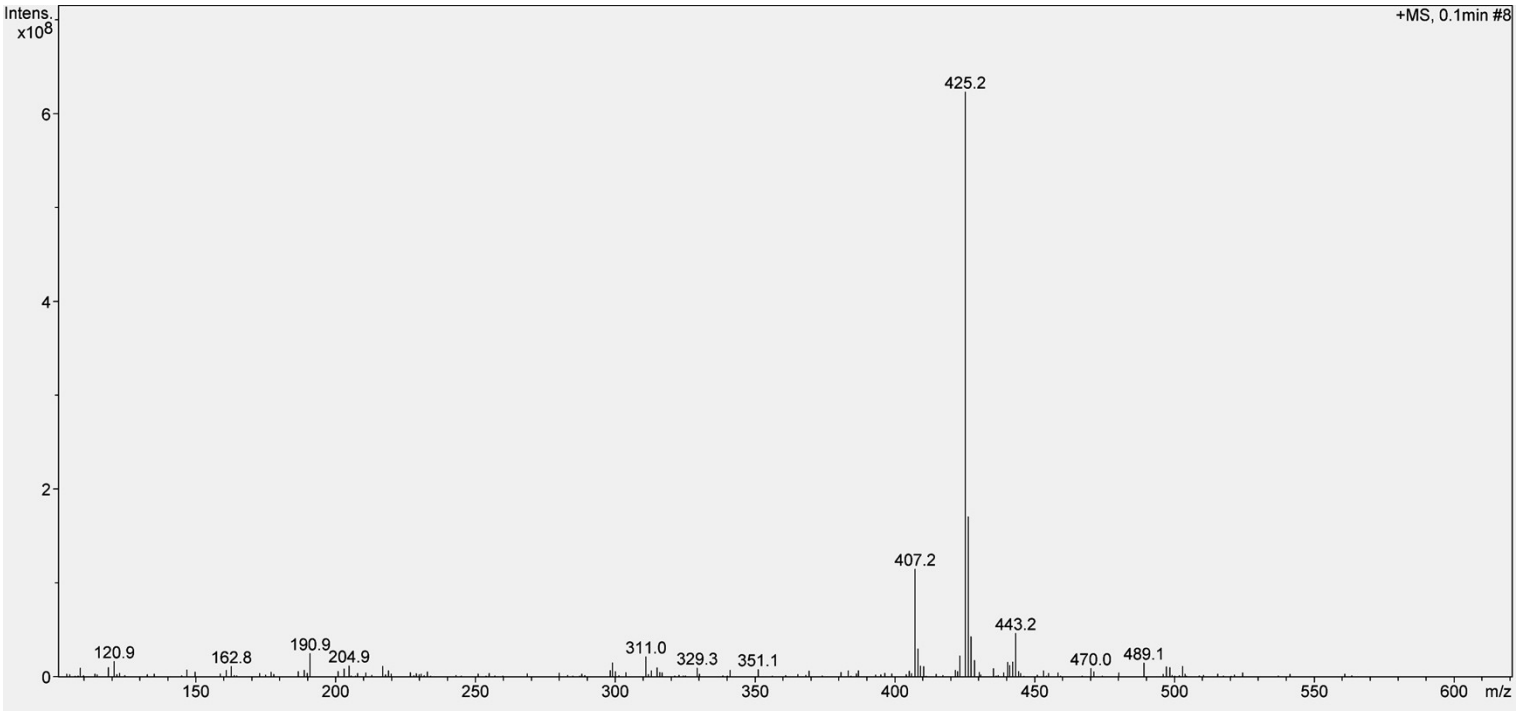
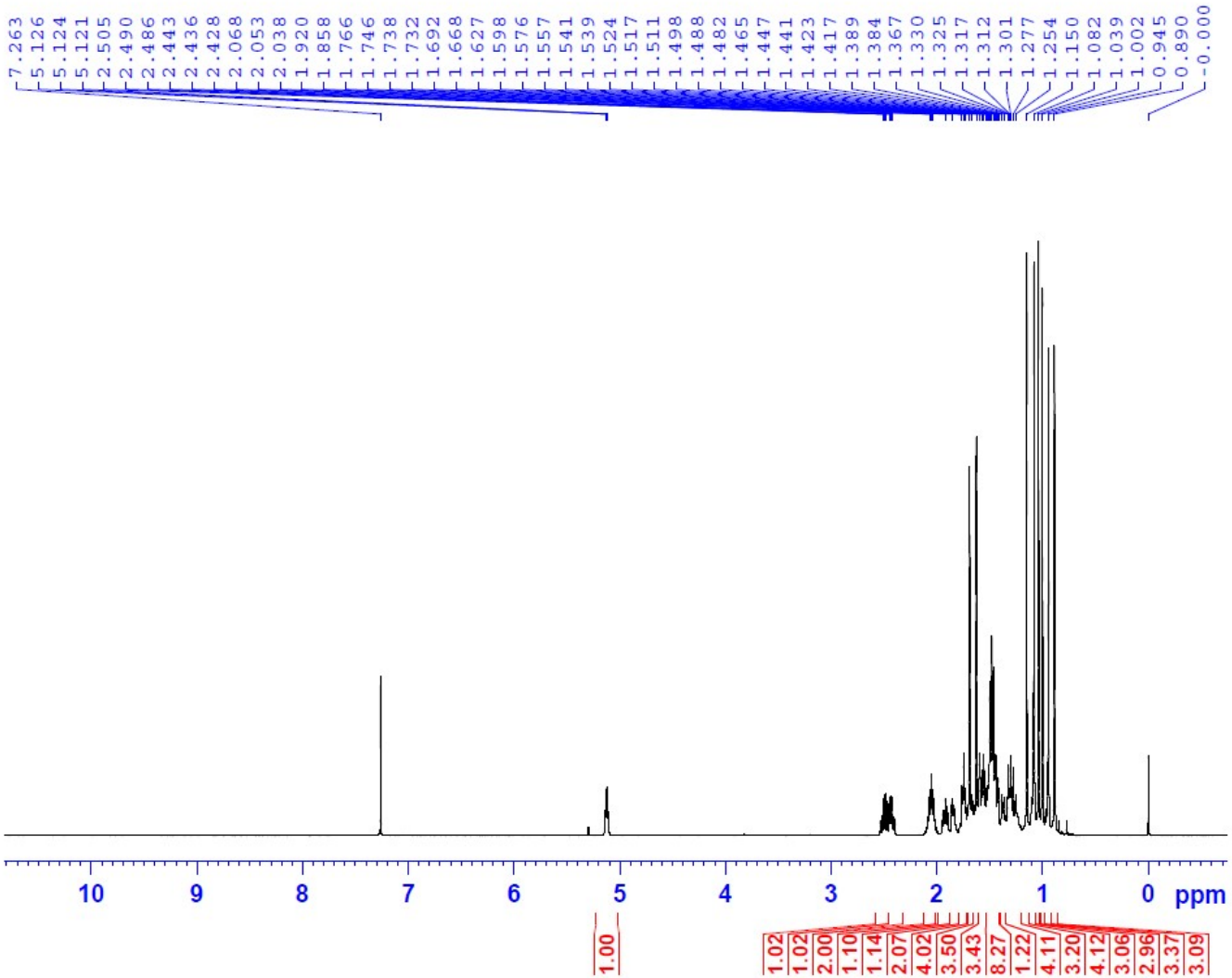
Nguyen Thi Ai Nhung (E-mail: ntanhung@hueuni.edu.vn)

1. EXPERIMENTAL CHARACTERISATION

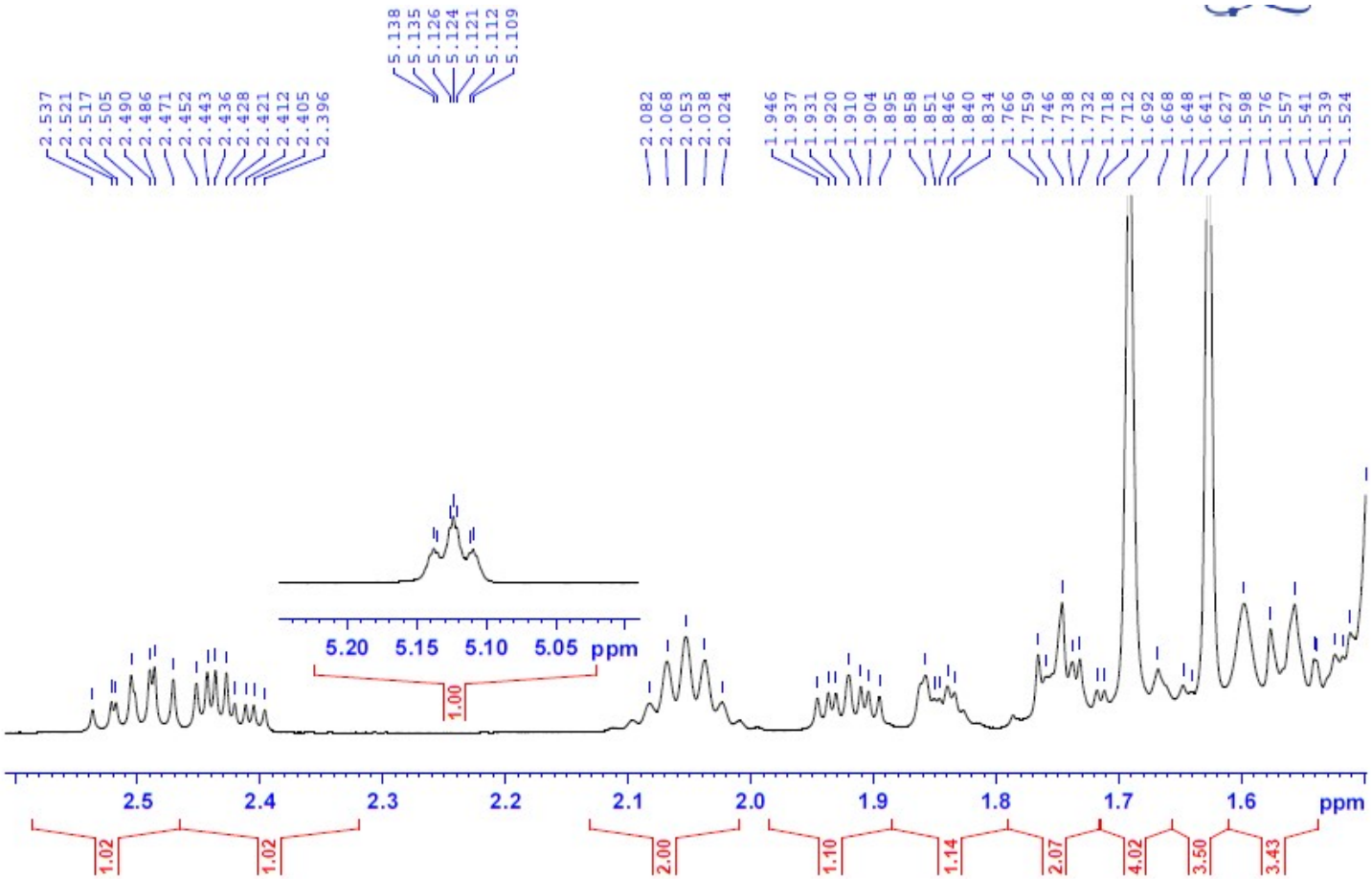
1.1. Compound 1



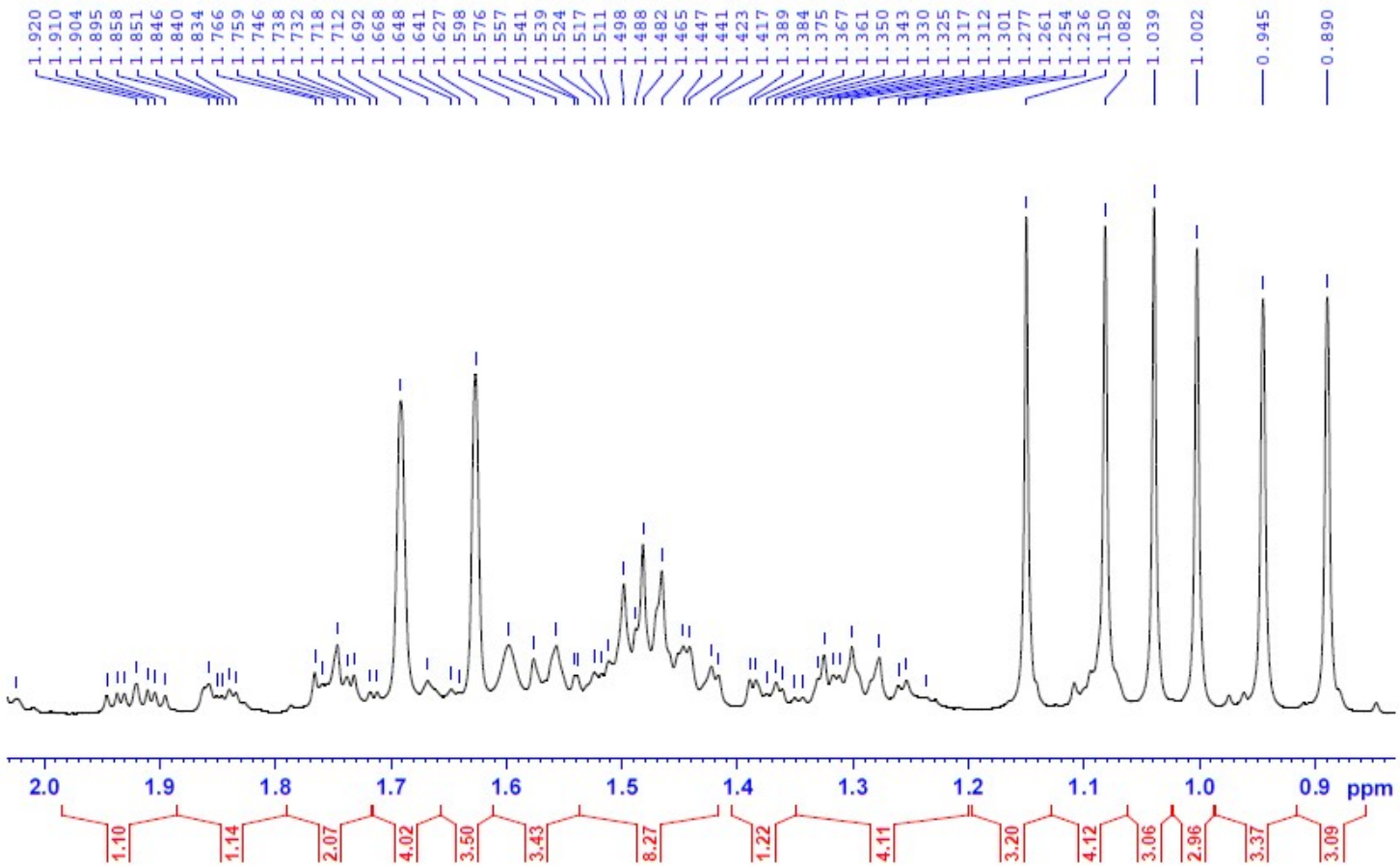
(+)-ESI–MS spectrum of compound **1**



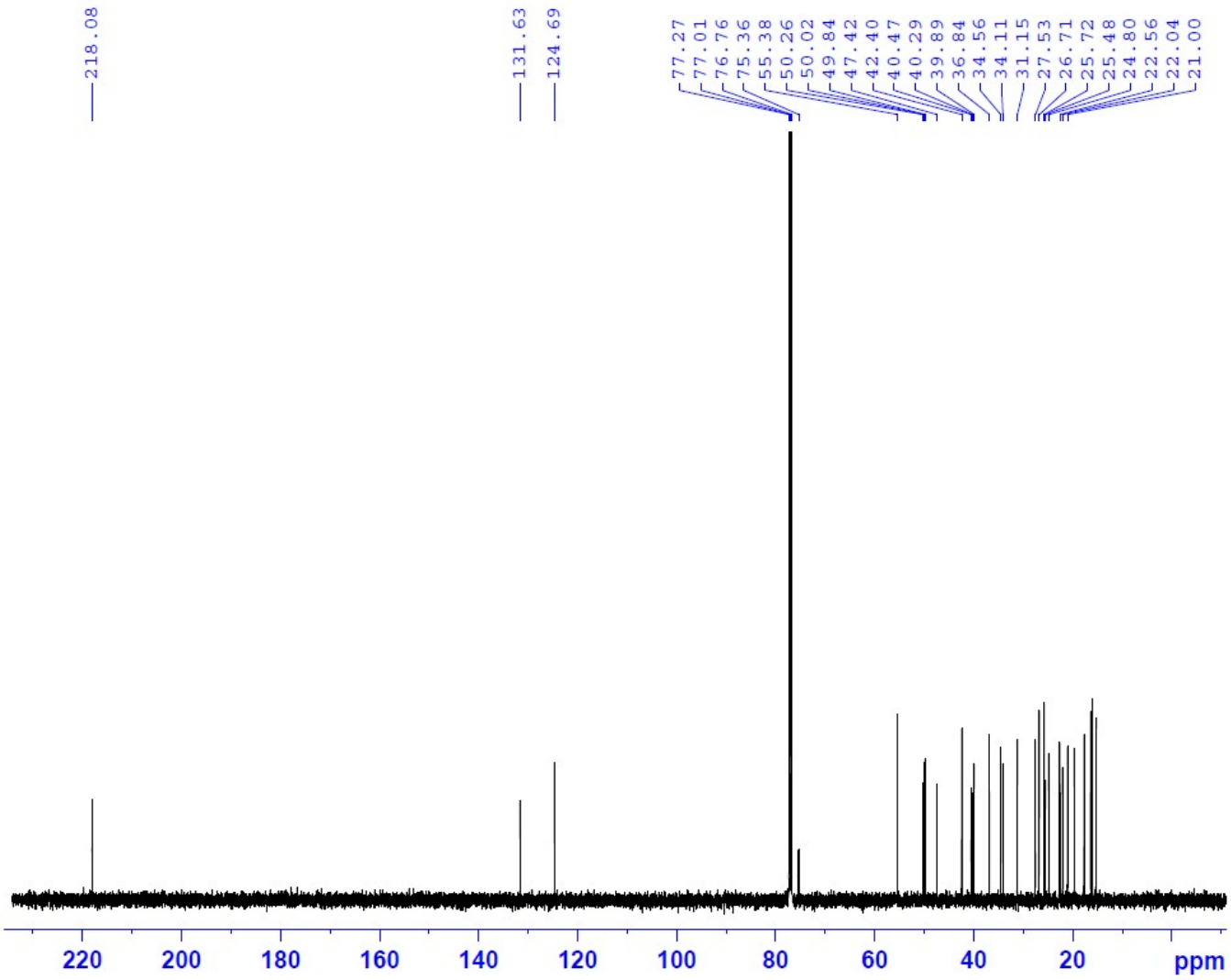
^{1}H-NMR spectrum of compound **1**


2.537
2.521
2.517
2.505
2.490
2.486
2.471
2.452
2.443
2.436
2.428
2.421
2.412
2.405
2.396
5.138
5.135
5.126
5.124
5.121
5.112
5.109
2.082
2.068
2.053
2.038
2.024
1.946
1.937
1.931
1.920
1.910
1.904
1.895
1.858
1.851
1.846
1.840
1.834
1.766
1.759
1.746
1.738
1.732
1.718
1.712
1.692
1.668
1.648
1.641
1.627
1.598
1.576
1.557
1.541
1.539
1.524
5.20
5.15
5.10
5.05
ppm
1.00
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
ppm
1.02
1.02
2.00
1.10
1.14
2.07
4.02
3.50
3.43

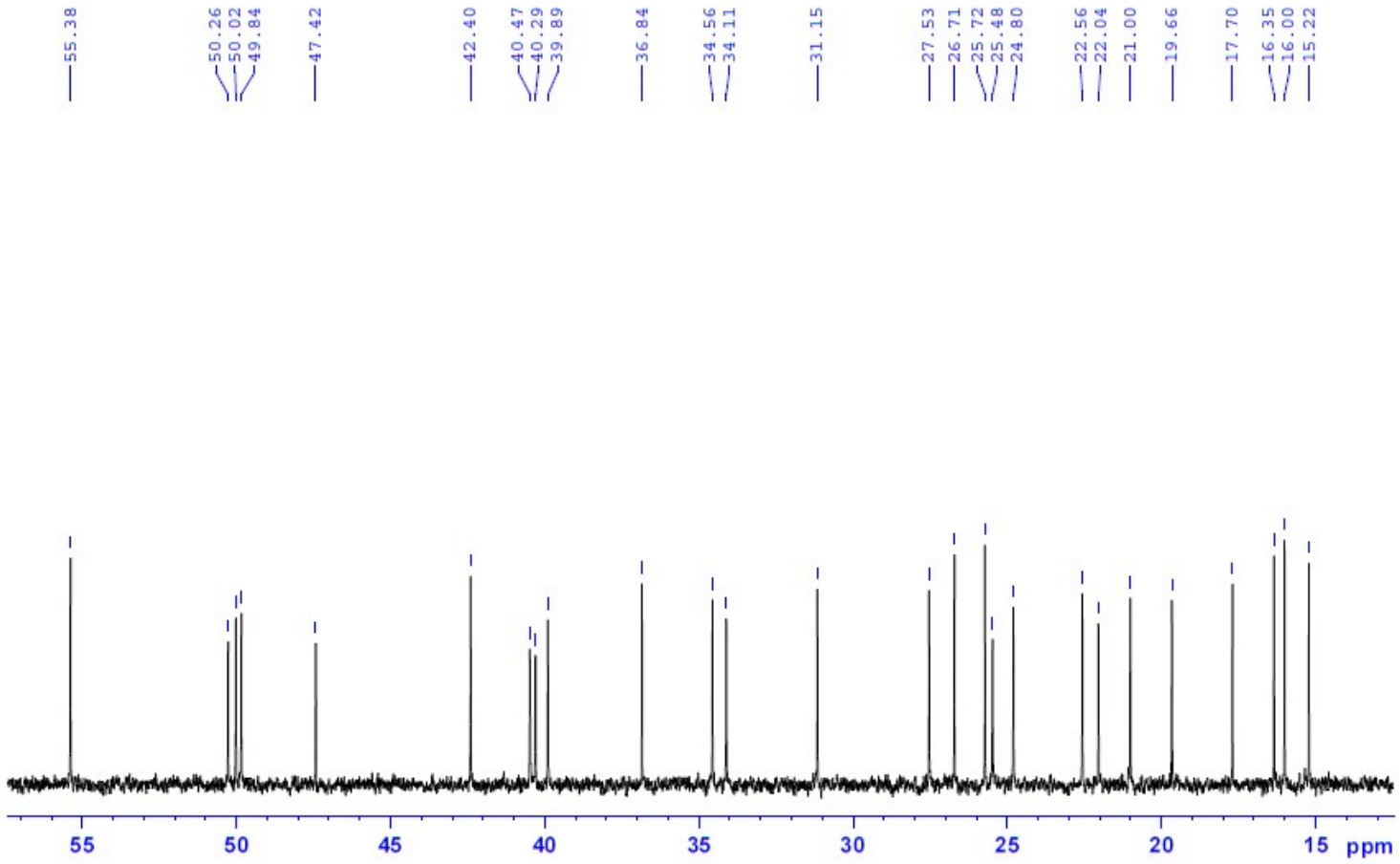
^{1}H-NMR spectrum of compound **1** (extension)


1.920
1.910
1.904
1.895
1.858
1.851
1.846
1.840
1.834
1.766
1.759
1.746
1.738
1.732
1.718
1.712
1.692
1.668
1.648
1.641
1.627
1.598
1.576
1.557
1.541
1.539
1.524
1.517
1.511
1.498
1.488
1.482
1.465
1.447
1.441
1.423
1.417
1.389
1.384
1.375
1.367
1.361
1.350
1.343
1.330
1.325
1.317
1.312
1.301
1.277
1.261
1.254
1.236
1.150
1.082
1.039
1.002
0.945
0.890
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
ppm
1.10
1.14
2.07
4.02
3.50
3.43
8.27
1.22
4.11
3.20
4.12
3.06
2.96
3.37
3.09

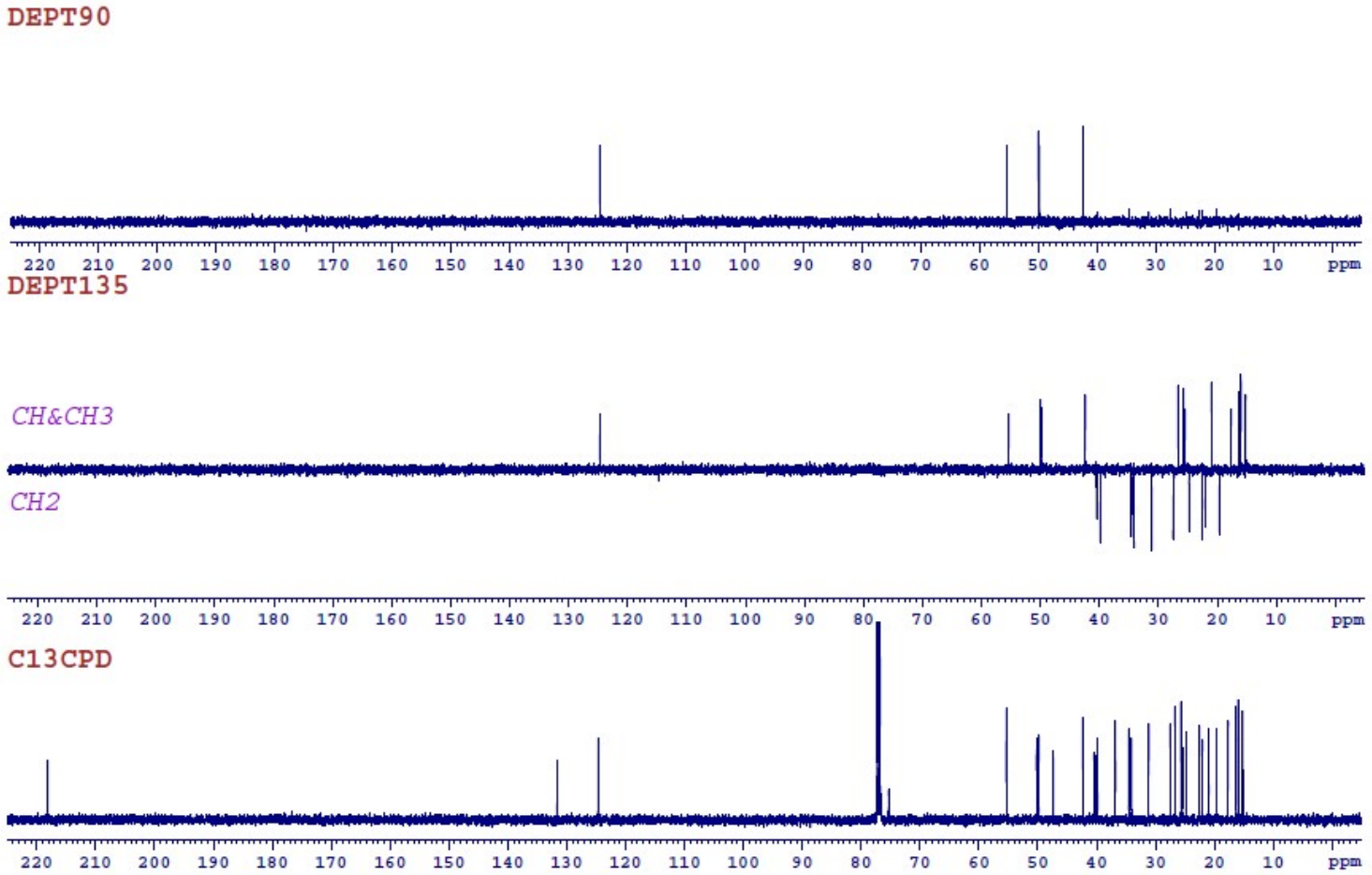
^{1}H-NMR spectrum of compound **1** (extension)



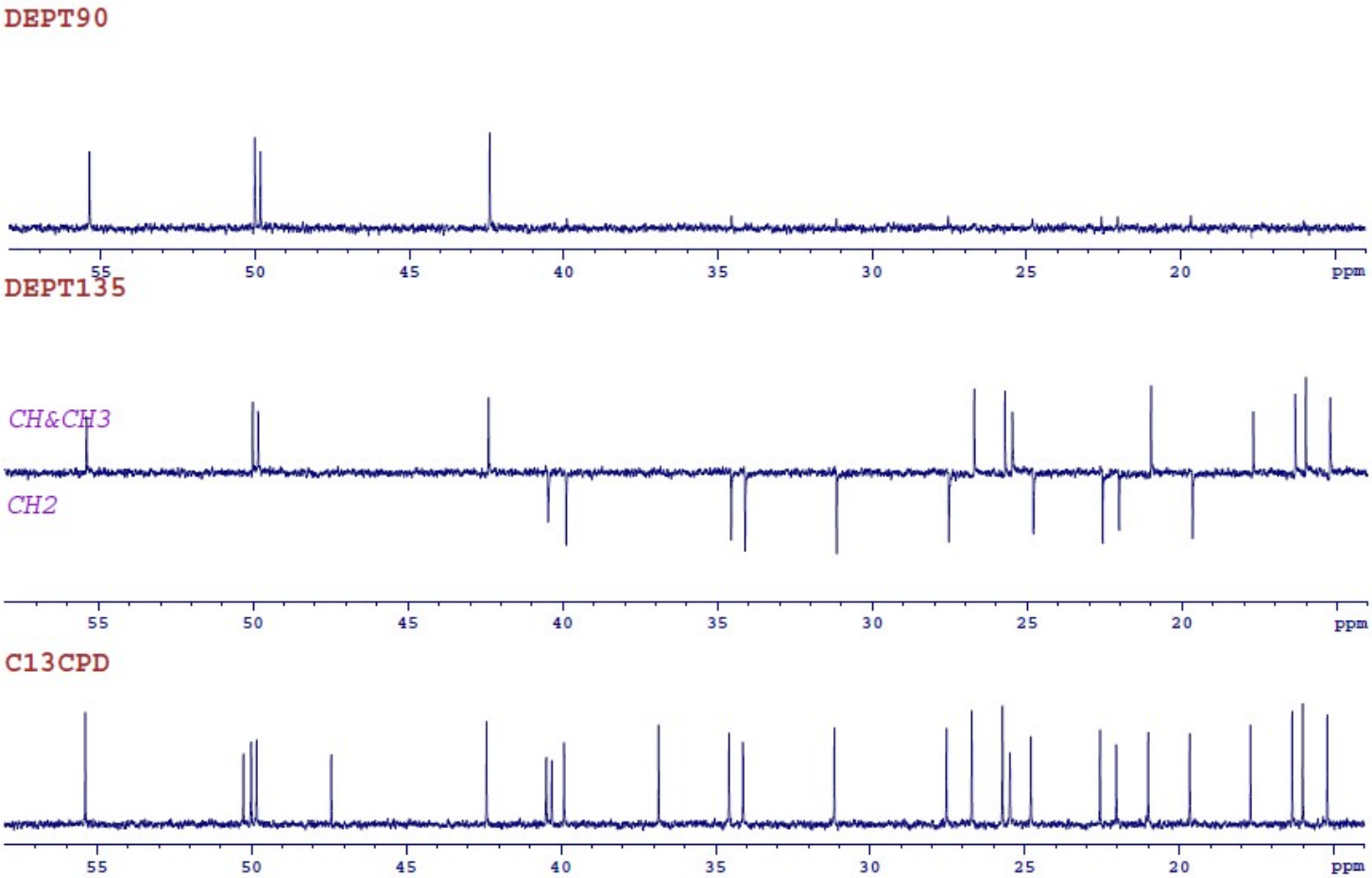
^{13}C-NMR spectrum of compound **1**


55.38
50.26
50.02
49.84
47.42
42.40
40.47
40.29
39.89
36.84
34.56
34.11
31.15
27.53
26.71
25.72
25.48
24.80
22.56
22.04
21.00
19.66
17.70
16.35
16.00
15.22
55
50
45
40
35
30
25
20
15
ppm

^{13}C-NMR spectrum of compound **1** (extension)

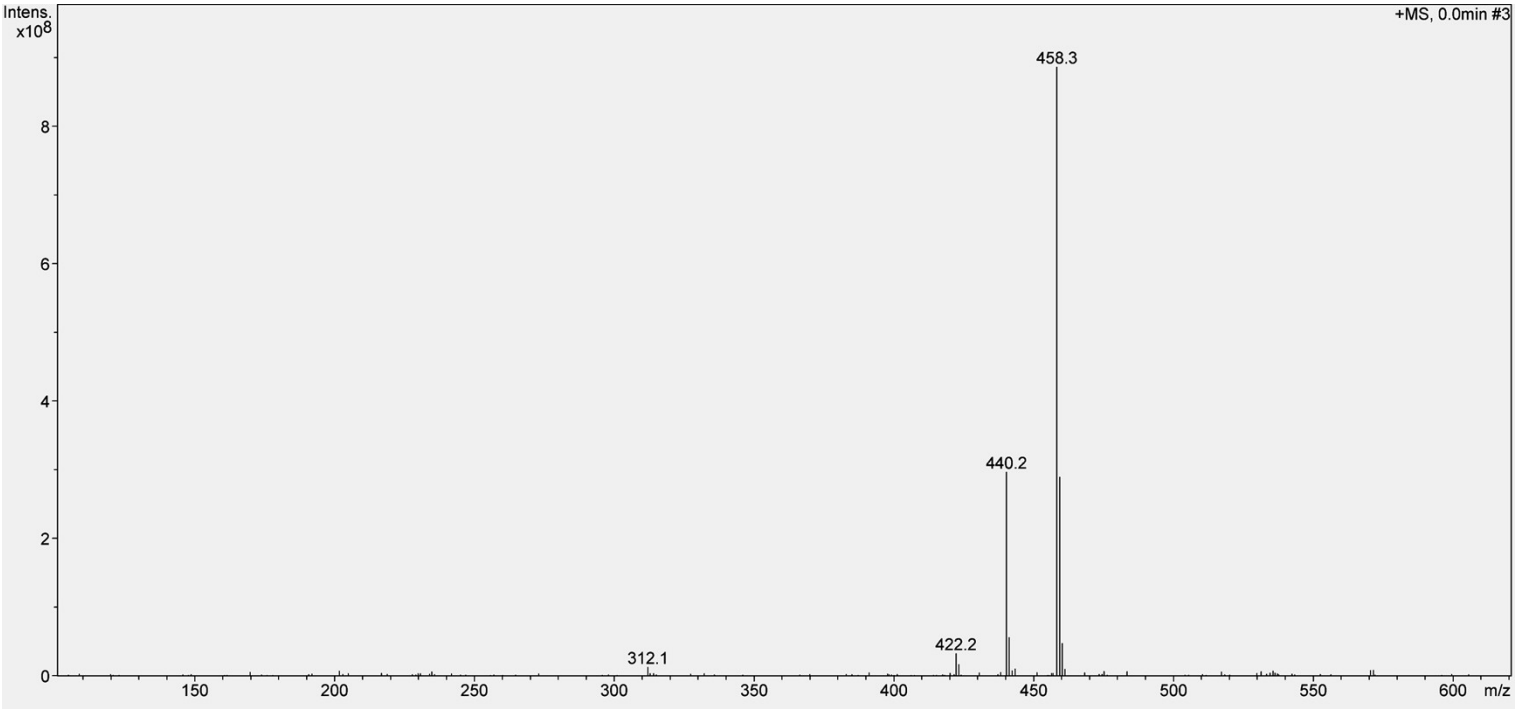


DEPT spectrum of compound **1**

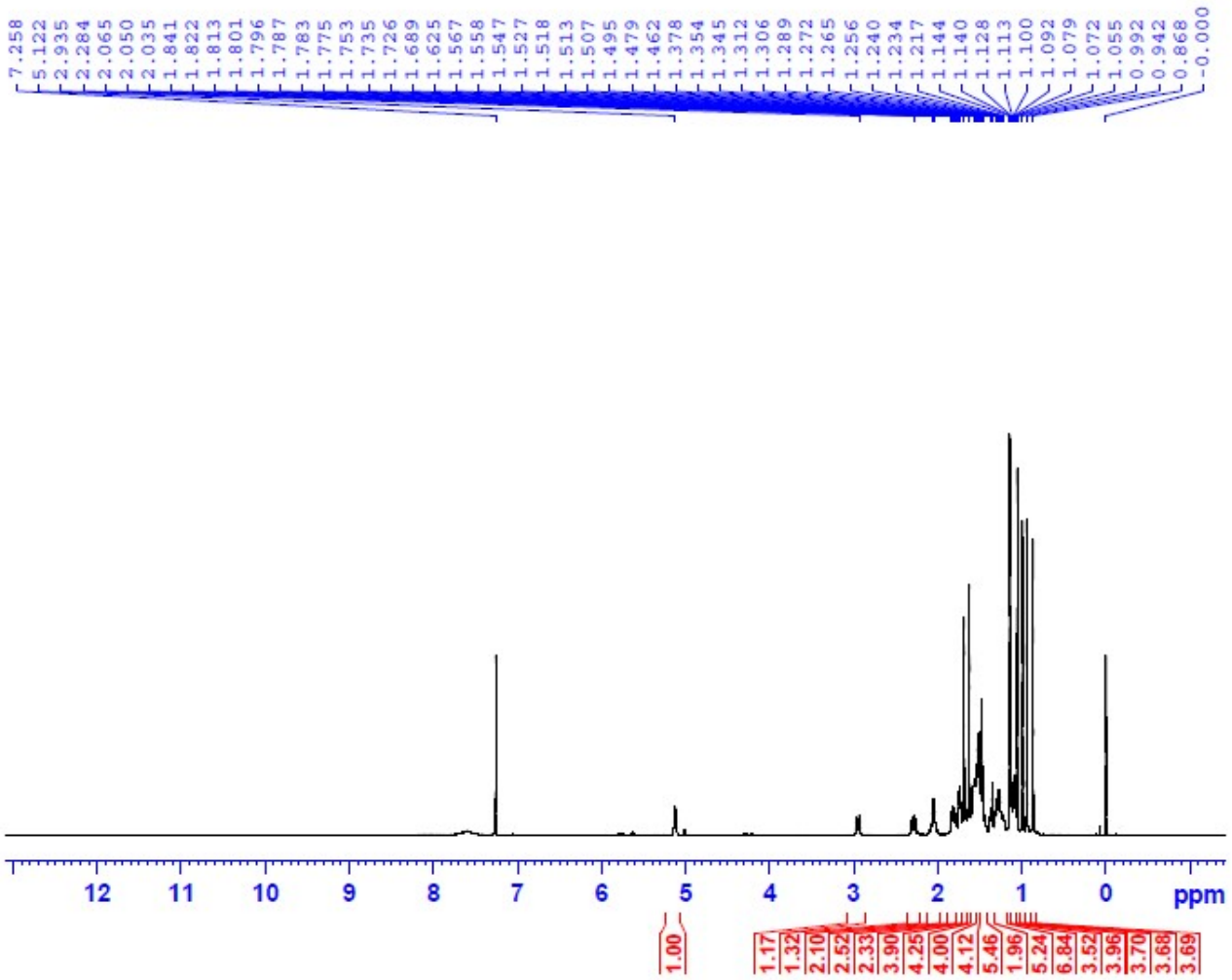


DEPT spectrum of compound **1** (extension)

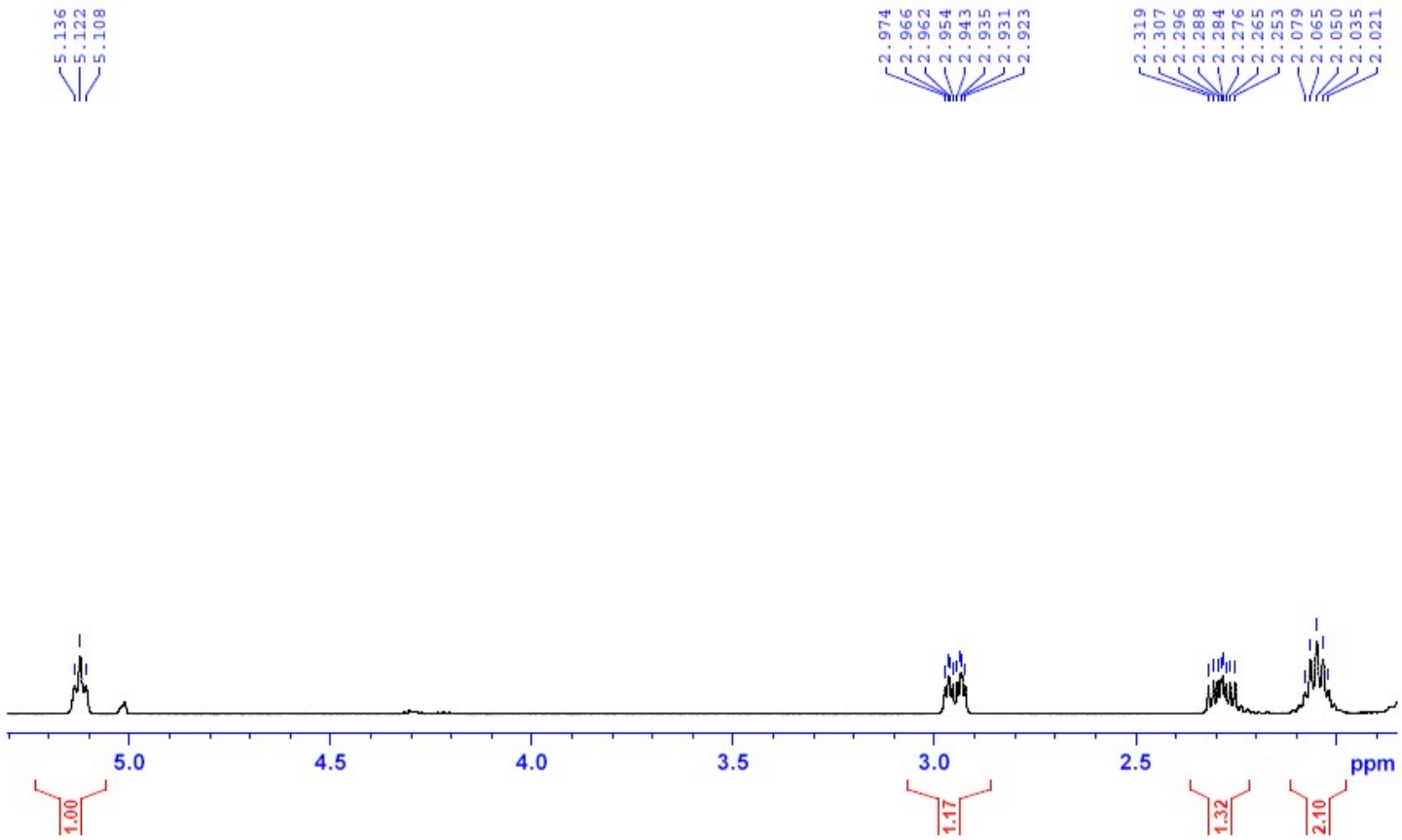
1.2. Compound 2



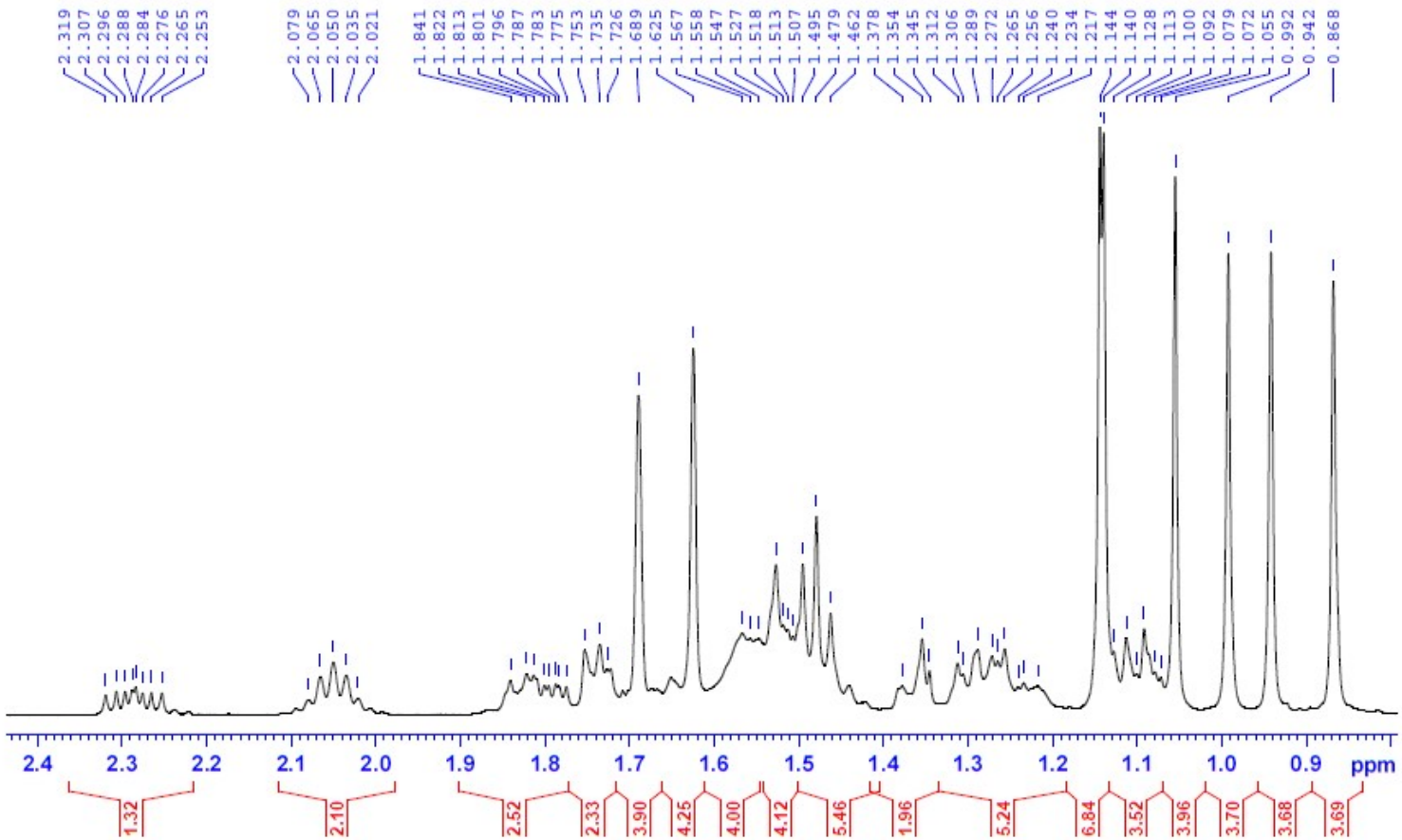
(+)-ESI–MS spectrum of compound **2**



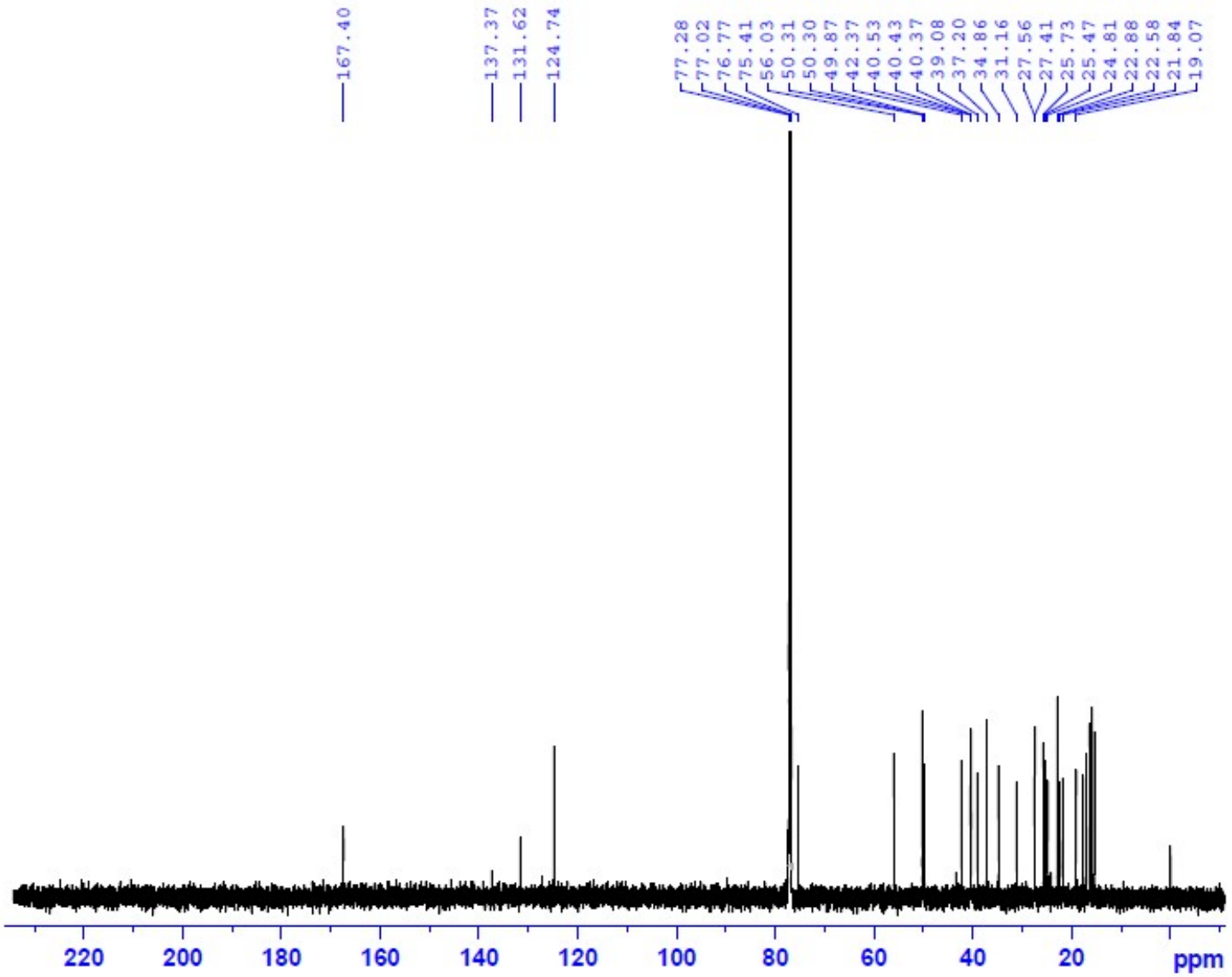
^{1}H-NMR spectrum of compound **2**


5.136
5.122
5.108
2.974
2.966
2.962
2.954
2.943
2.935
2.931
2.923
2.319
2.307
2.296
2.288
2.284
2.276
2.265
2.253
2.079
2.065
2.050
2.035
2.021
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.00
1.17
1.32
2.10

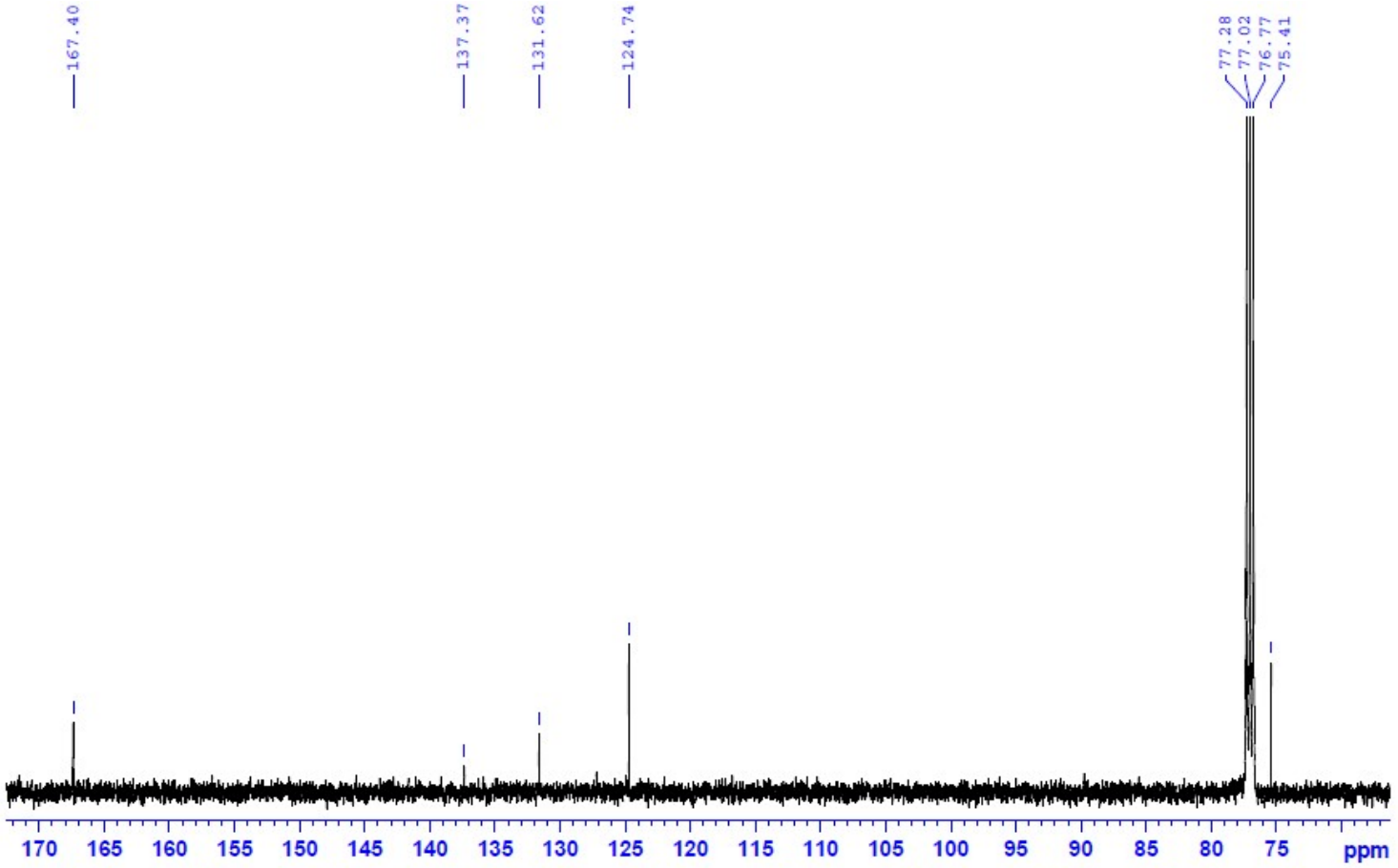
^{1}H-NMR spectrum of compound **2** (extension)


2.319
2.307
2.296
2.288
2.284
2.276
2.265
2.253
2.079
2.065
2.050
2.035
2.021
1.841
1.822
1.813
1.801
1.796
1.787
1.783
1.775
1.753
1.735
1.726
1.689
1.625
1.567
1.558
1.547
1.527
1.518
1.513
1.507
1.495
1.479
1.462
1.378
1.354
1.345
1.312
1.306
1.289
1.272
1.265
1.256
1.240
1.234
1.217
1.144
1.140
1.128
1.113
1.100
1.092
1.079
1.072
1.055
0.992
0.942
0.868
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
ppm
1.32
2.10
2.52
2.33
3.90
4.25
4.00
4.12
5.46
1.96
5.24
6.84
3.52
3.96
3.70
3.68
3.69

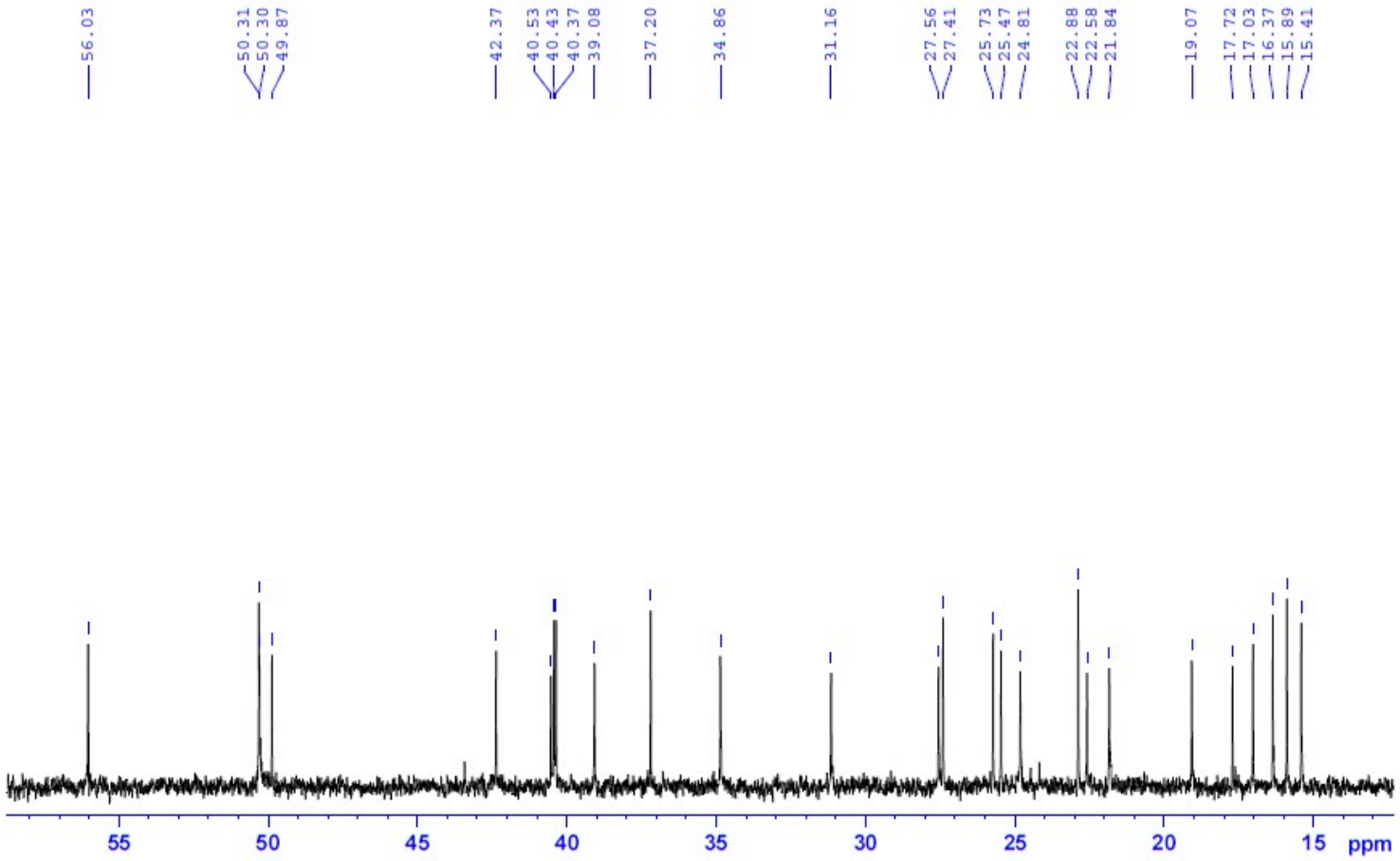
[1]H-NMR spectrum of compound **2** (extension)



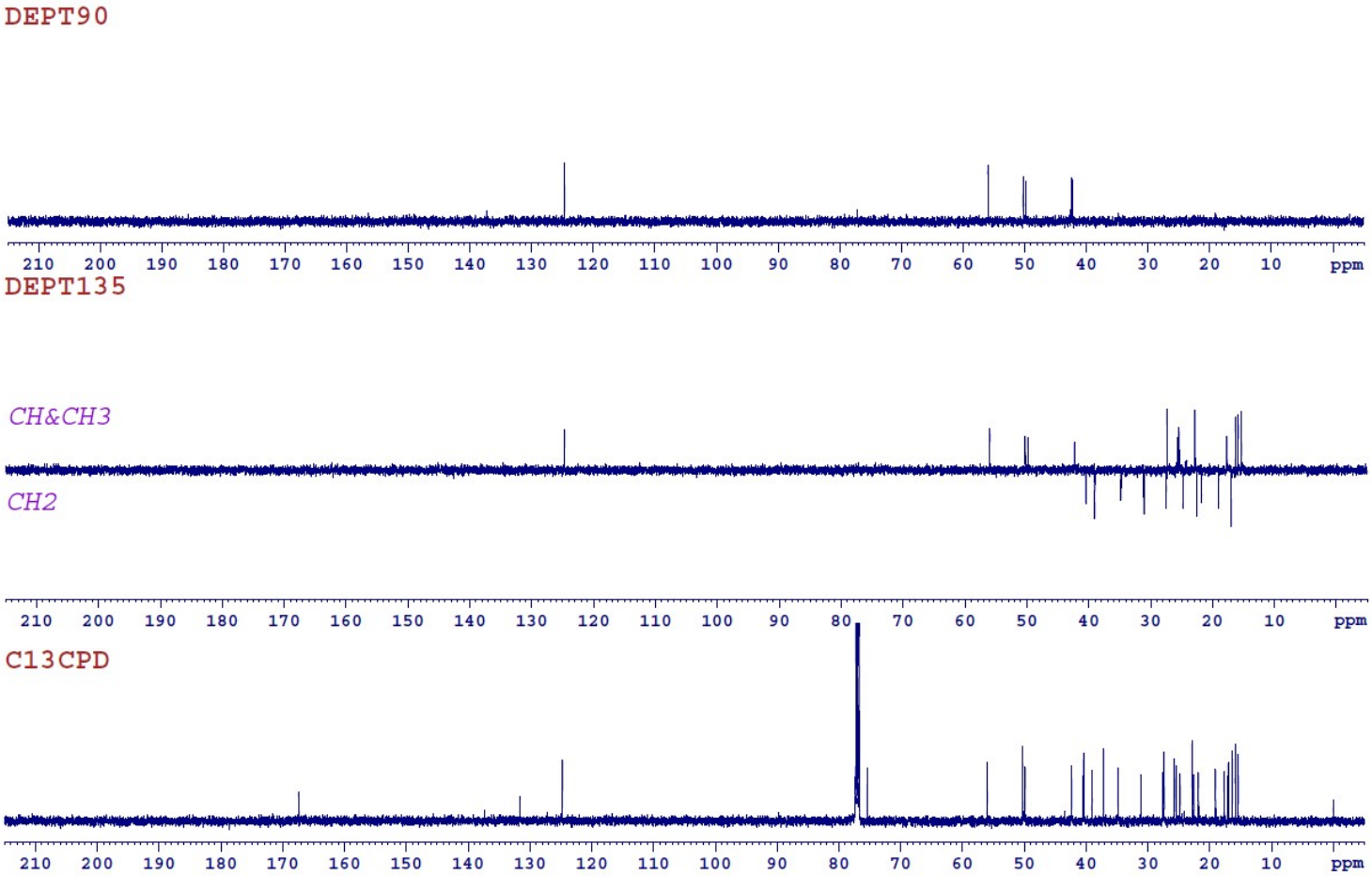
[13]C-NMR spectrum of compound **2**



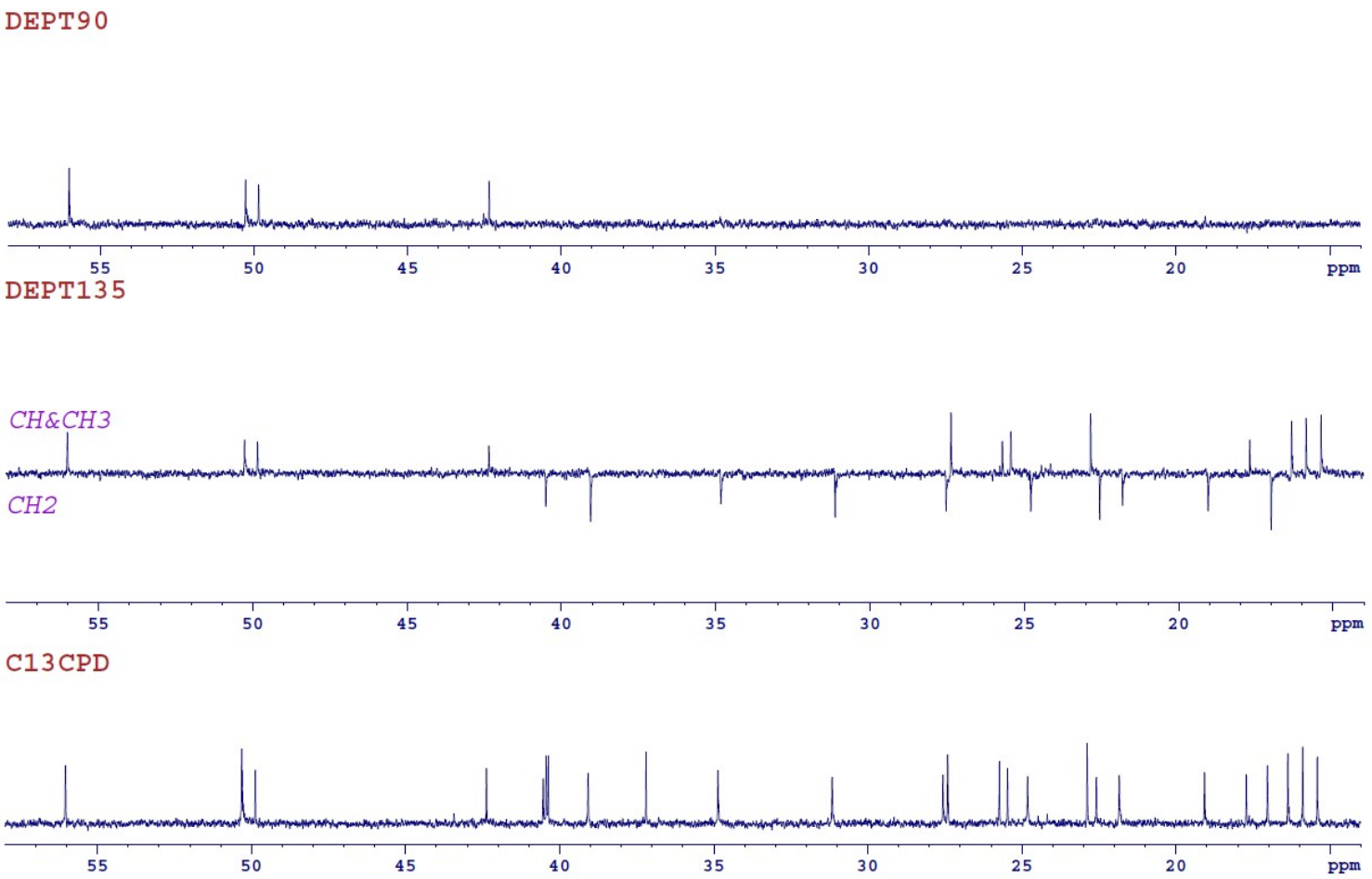
^{13}C-NMR spectrum of compound **2** (extension)


56.03
50.31
50.30
49.87
42.37
40.53
40.43
40.37
39.08
37.20
34.86
31.16
27.56
27.41
25.73
25.47
24.81
22.88
22.58
21.84
19.07
17.72
17.03
16.37
15.89
15.41
55
50
45
40
35
30
25
20
15
ppm

^{13}C-NMR spectrum of compound **2** (extension)



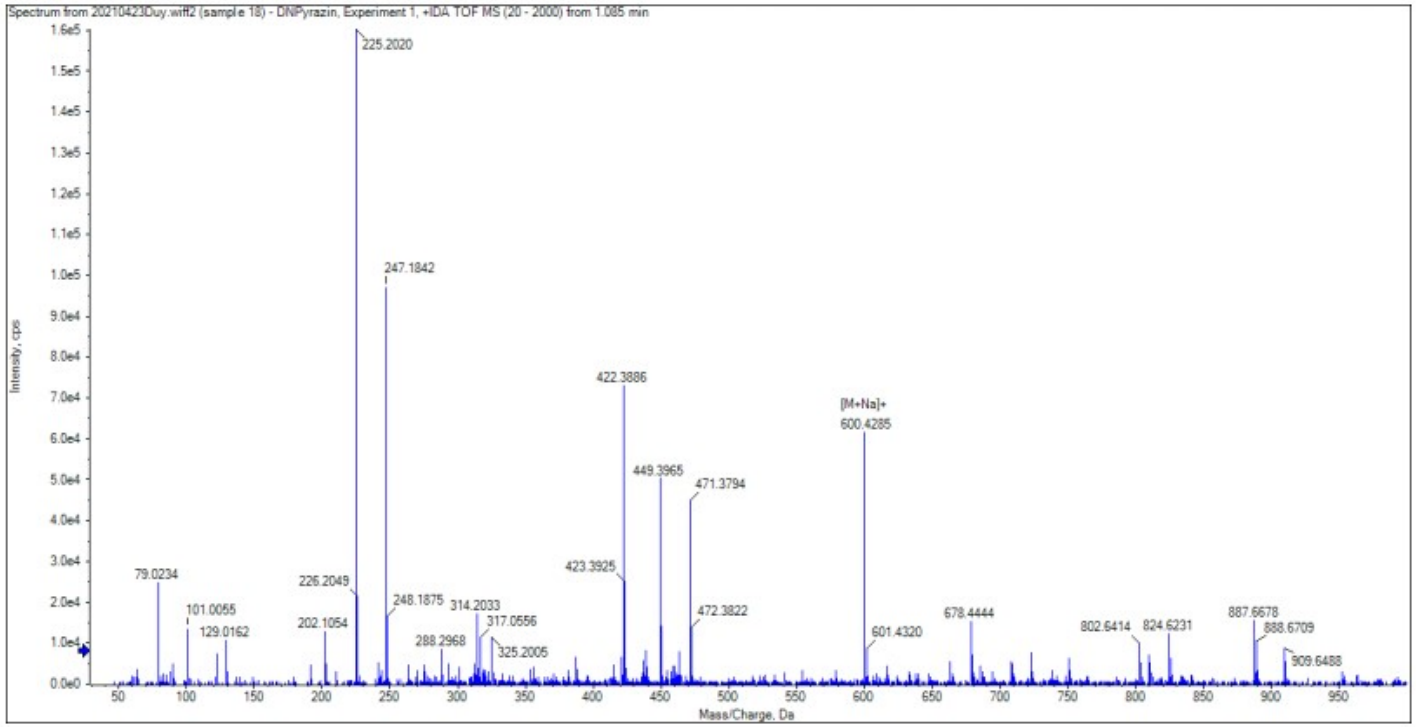
DEPT spectrum of compound **2**



DEPT spectrum of compound **2** (extension)

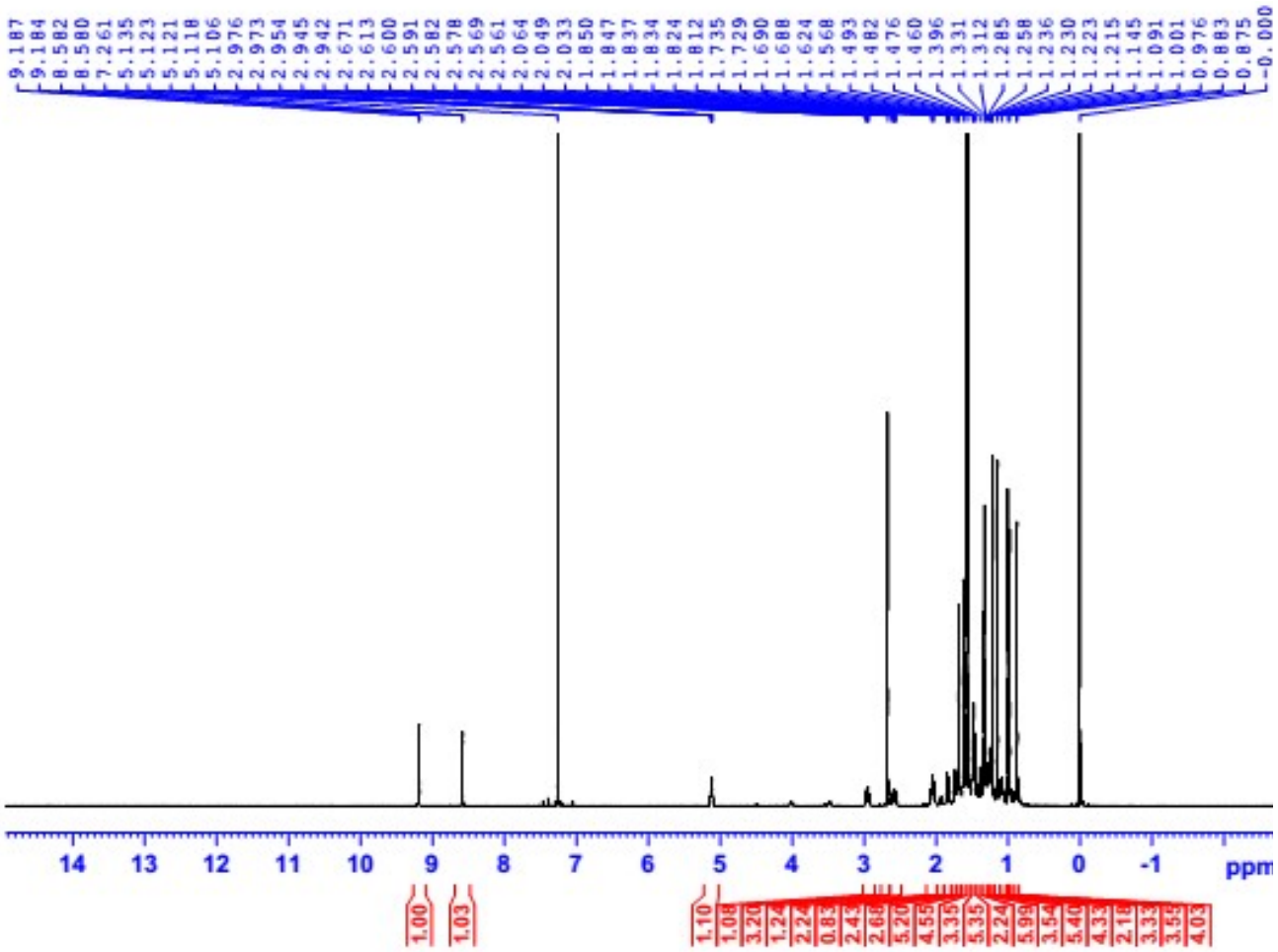
1.3. Compound 3a

Sample name: DNPyrazin
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

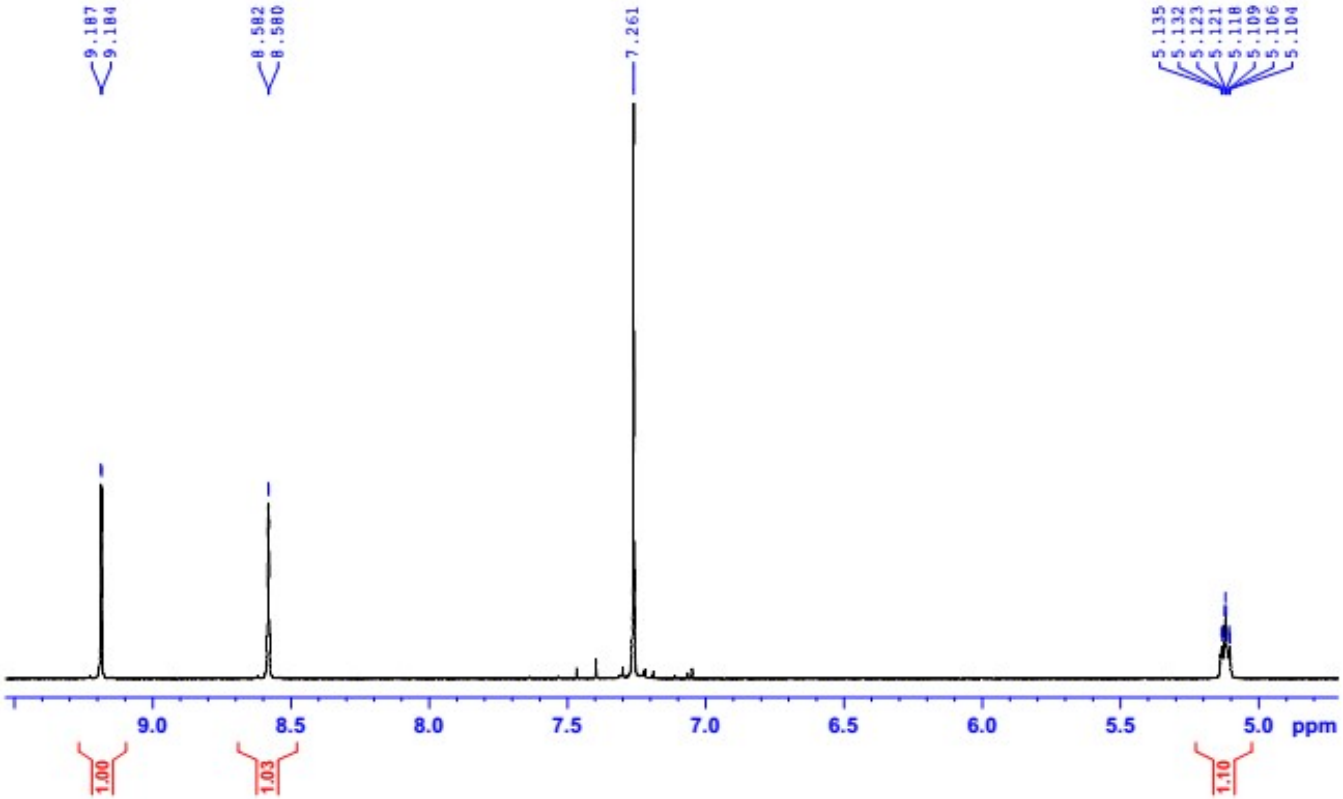


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C36H55N3O3	600.42456	11.0	4.5	1			NA/NA

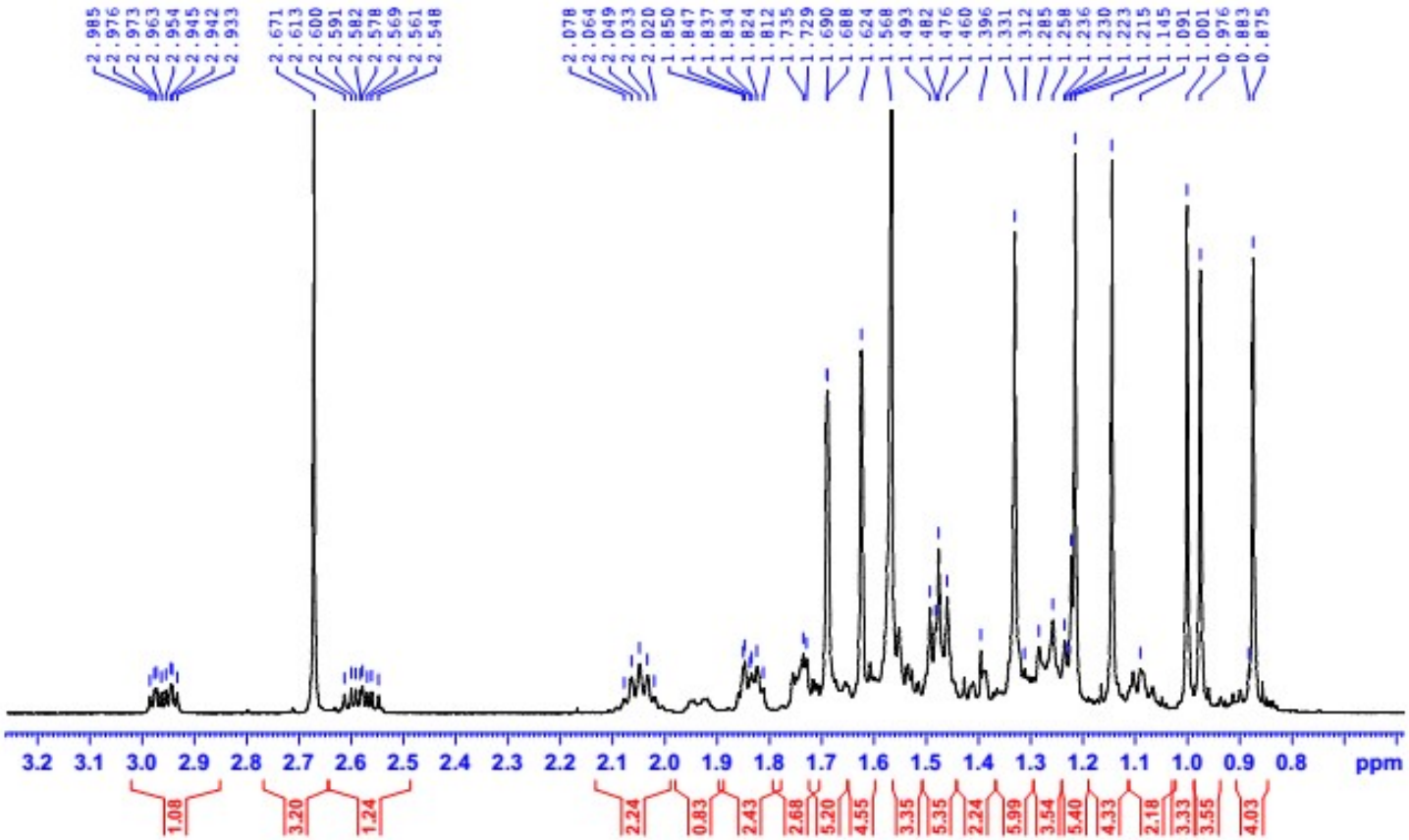
(+)-HR-ESI-MS spectrum of compound **3a**



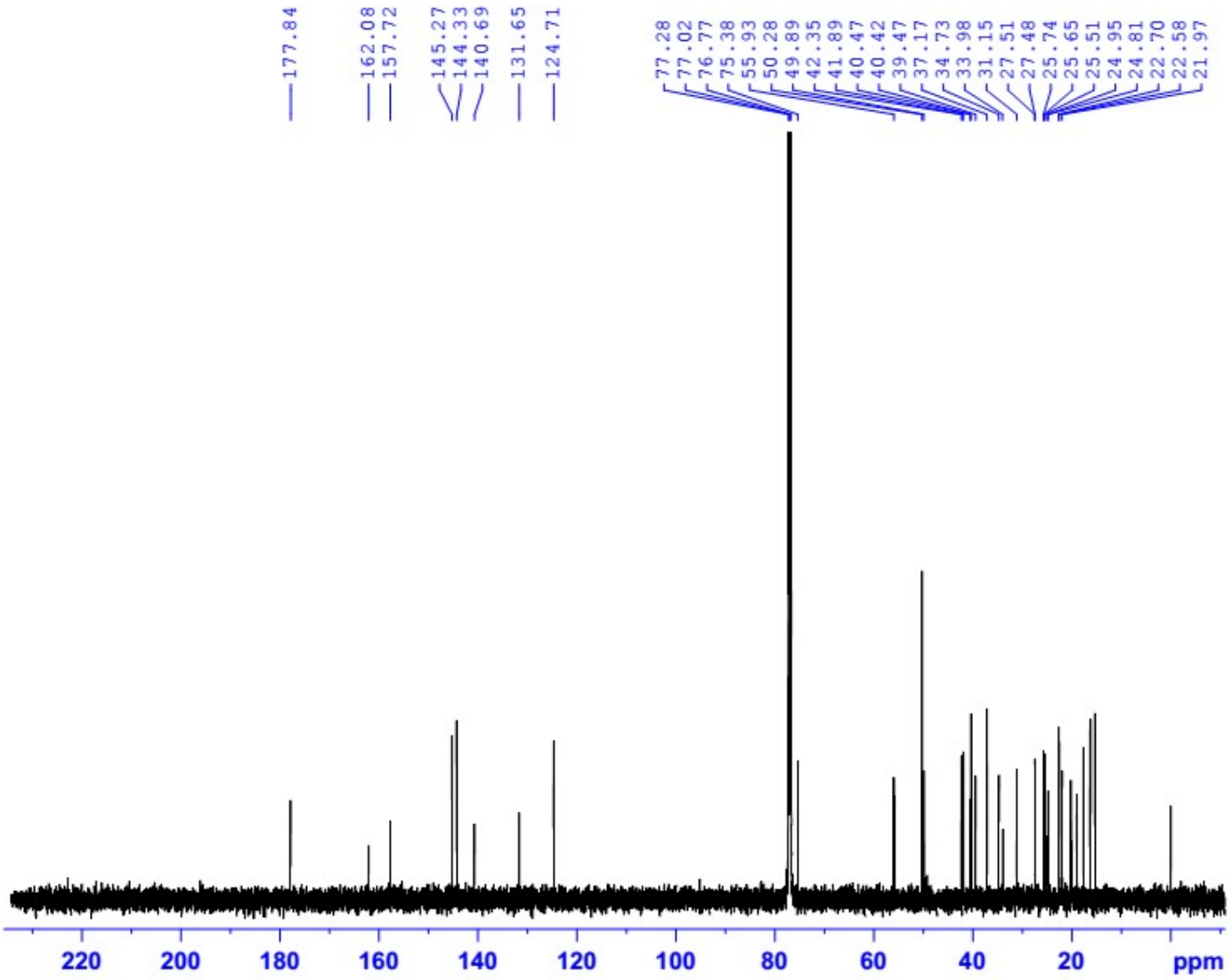
^{1}H-NMR spectrum of compound **3a**



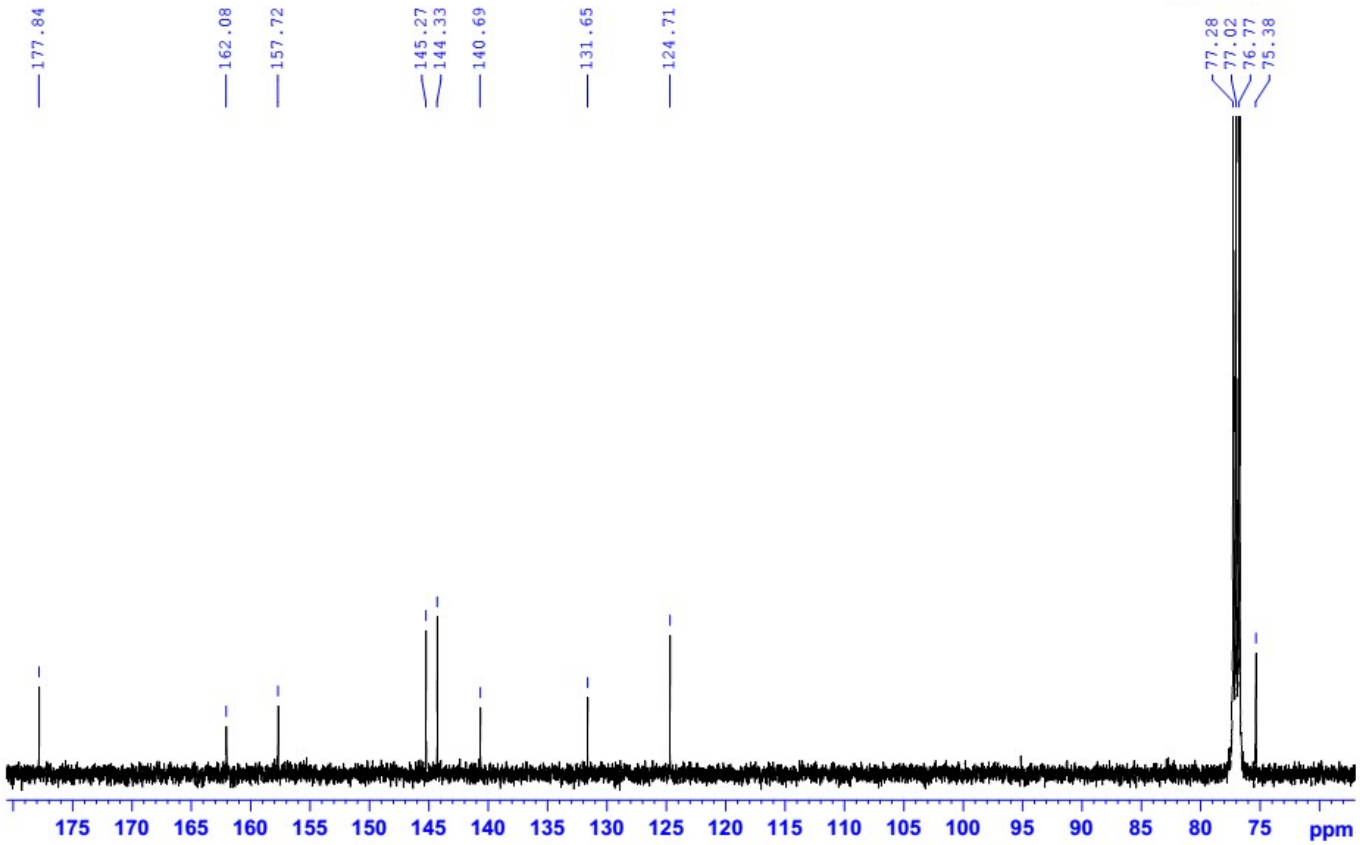
^{1}H-NMR spectrum of compound **3a** (extension)



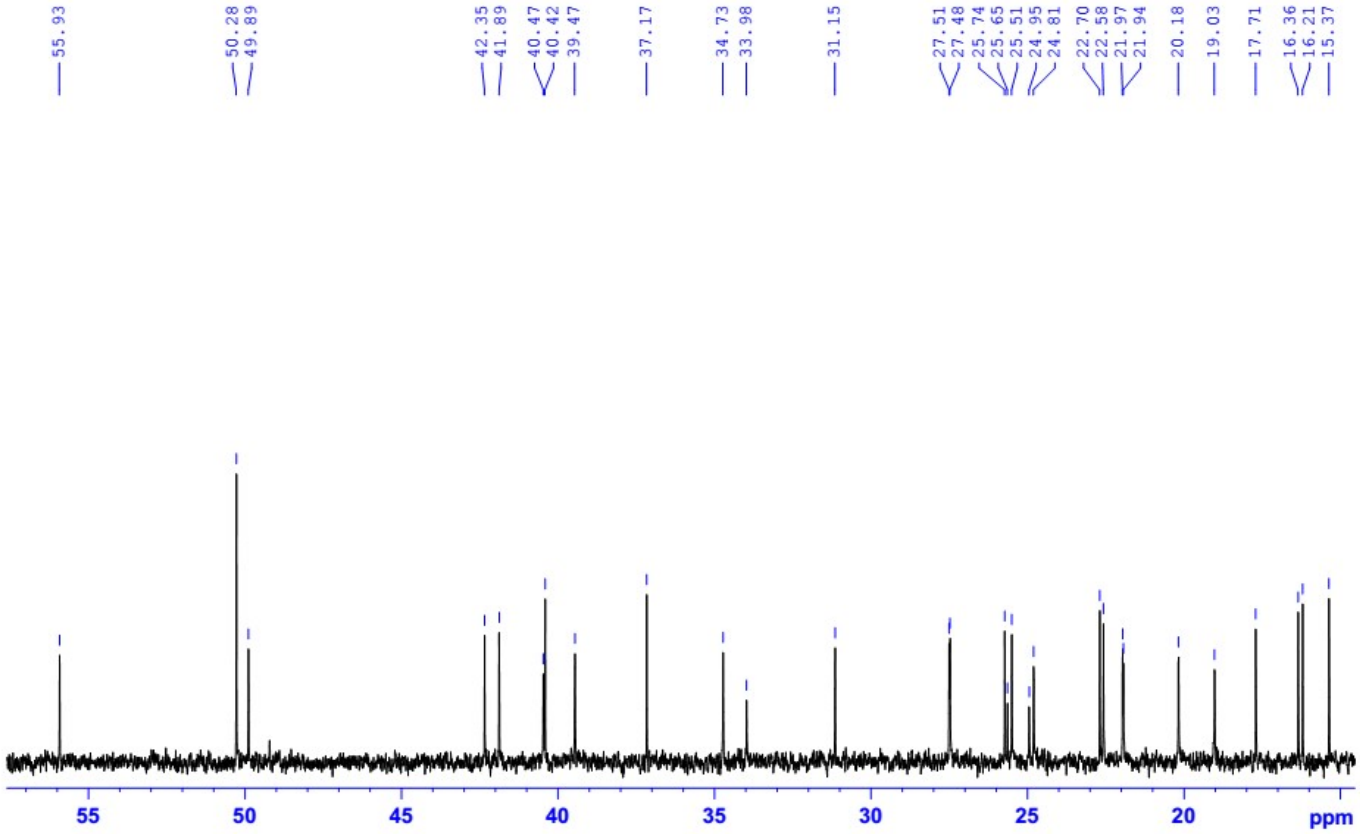
^{1}H-NMR spectrum of compound **3a** (extension)



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



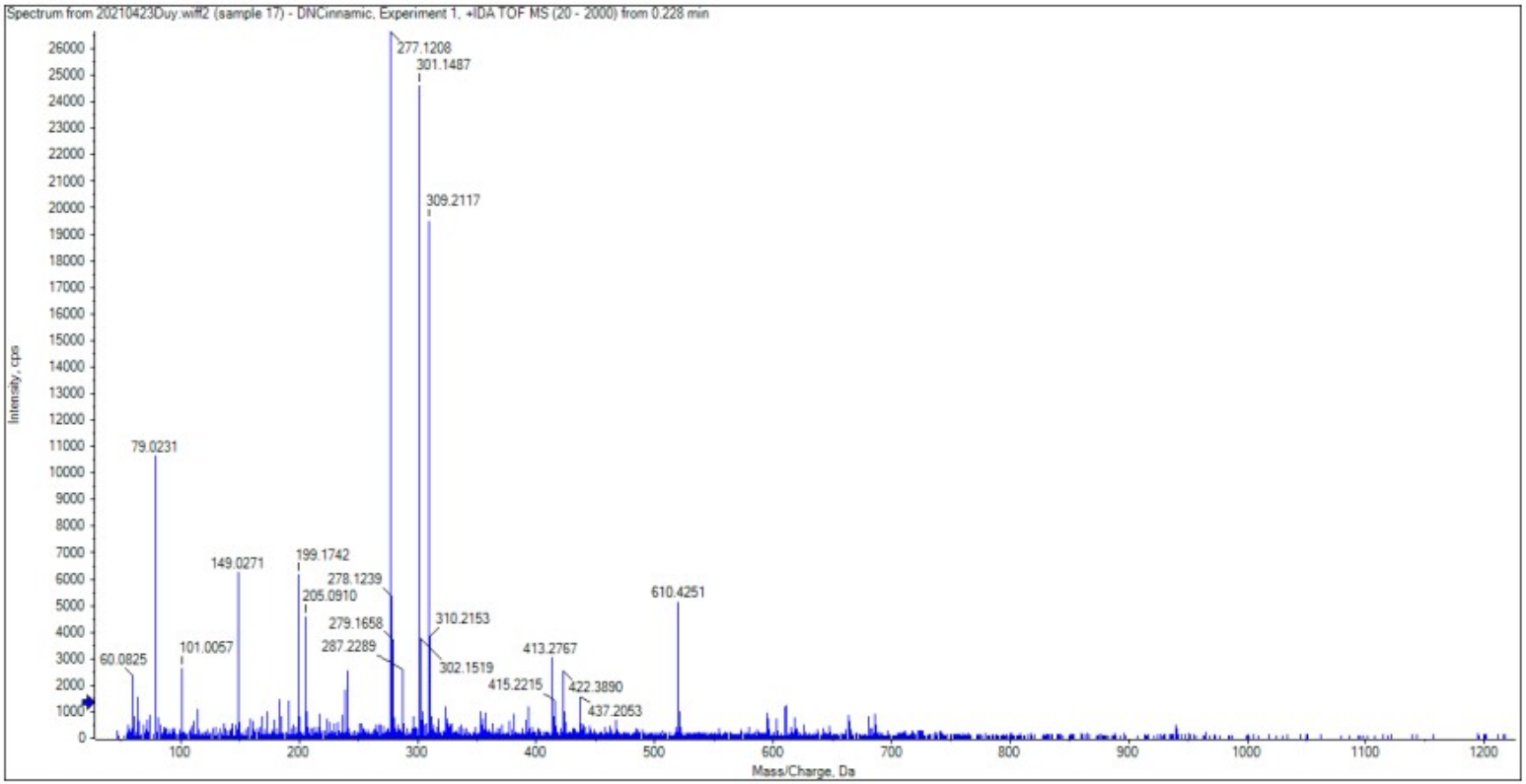
^{13}C-NMR spectrum of compound **3a** (extension)



^{13}C-NMR spectrum of compound **3a** (extension)

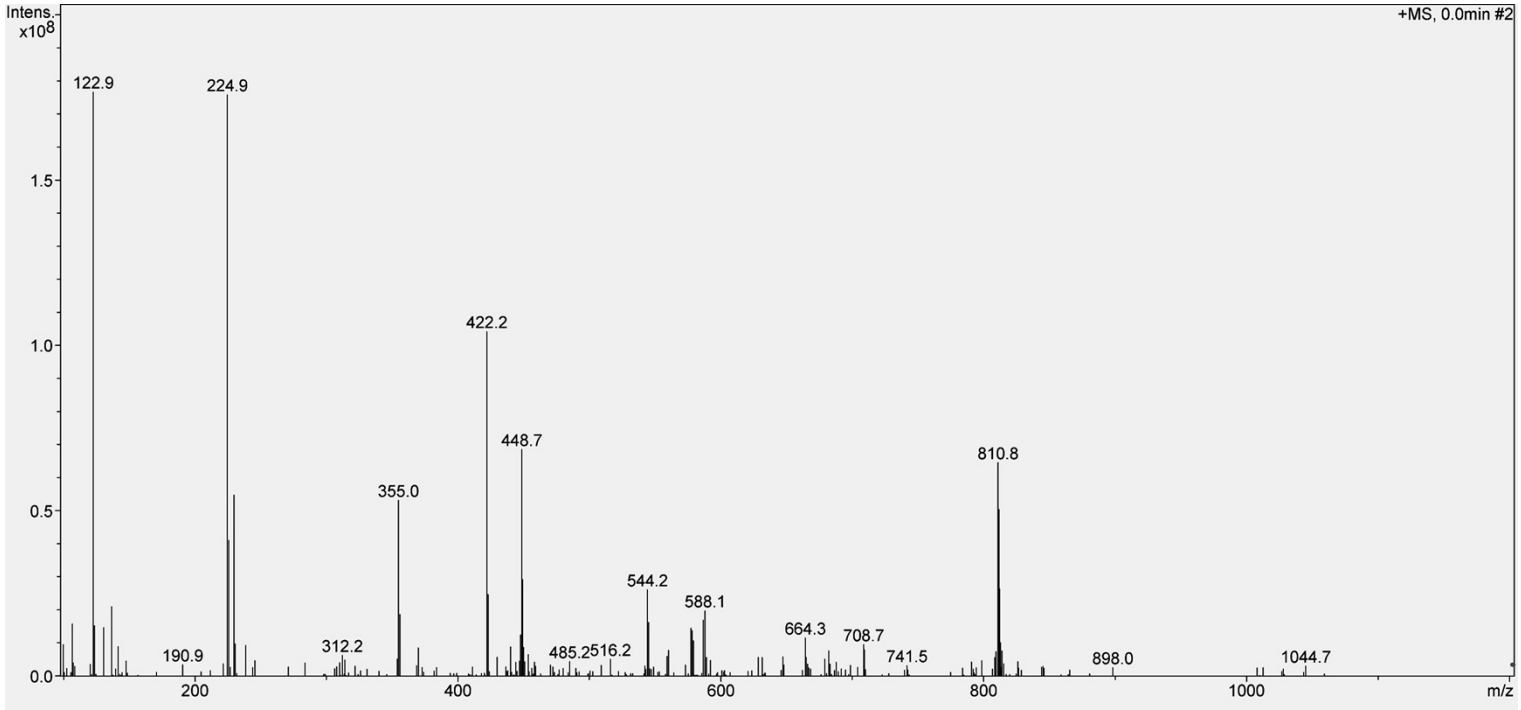
1.4. Compound 3b

Sample name: DNcinnamic
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

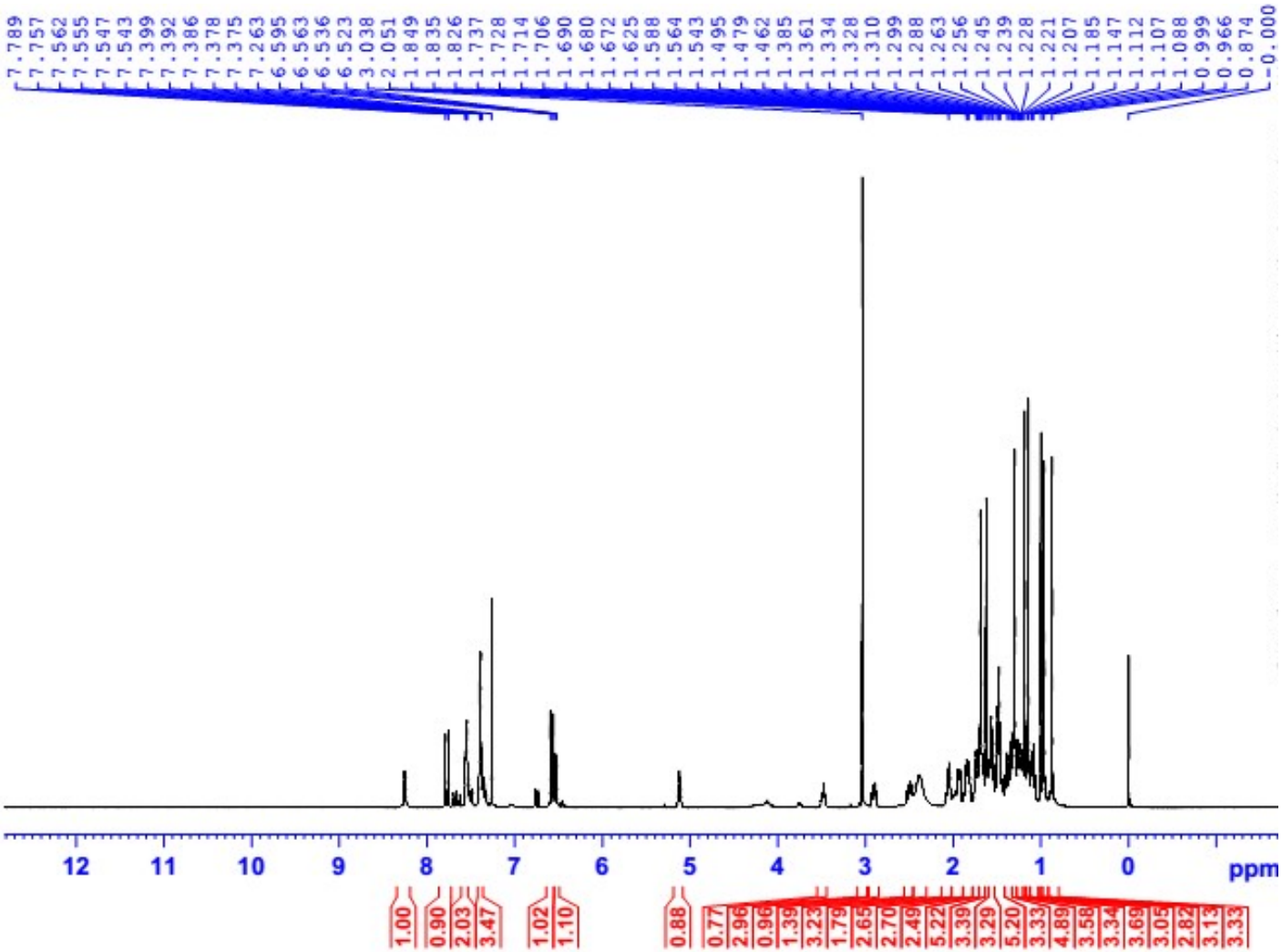


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C39H57NO3	610.42361	12	2.4	1			NA/NA

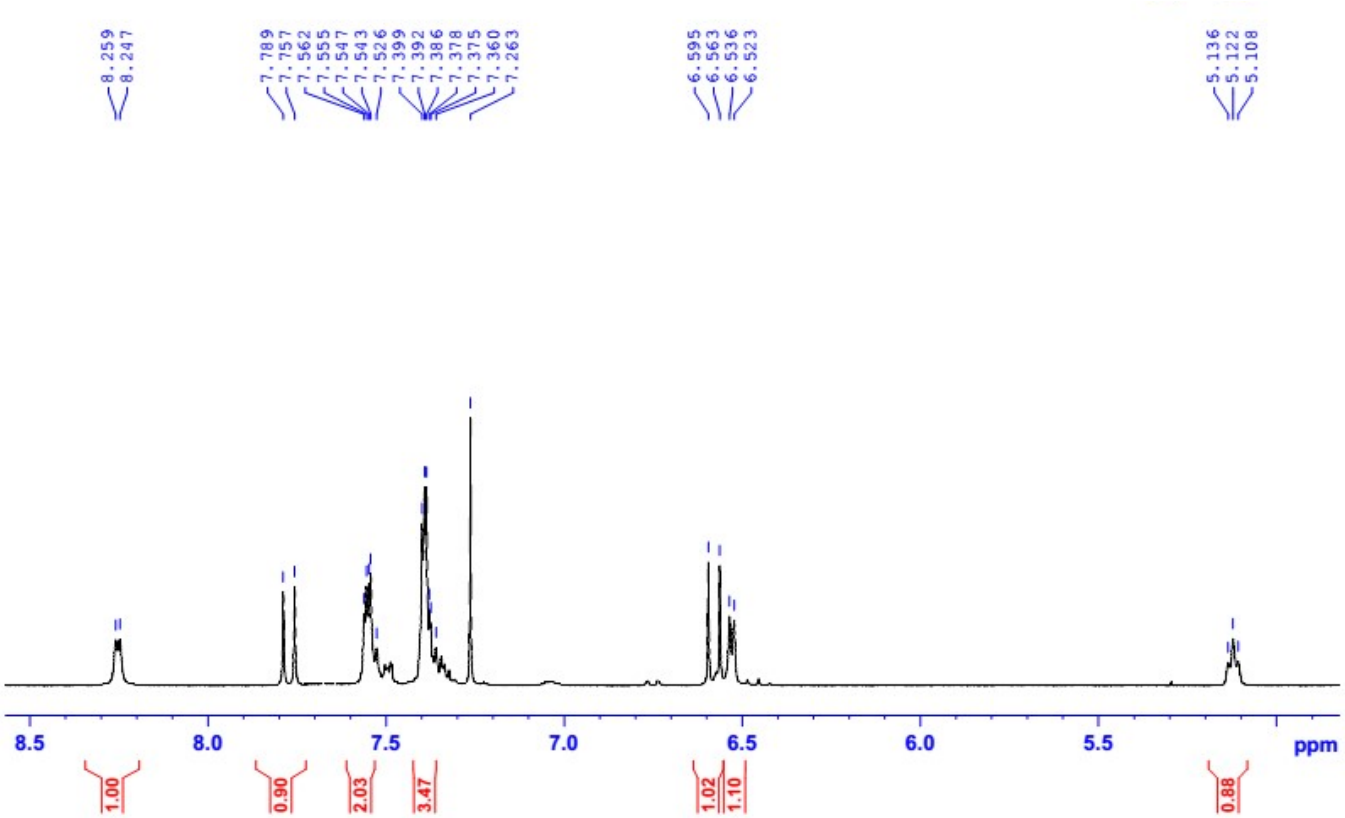
(+)-HR-ESI-MS spectrum of compound **3b**



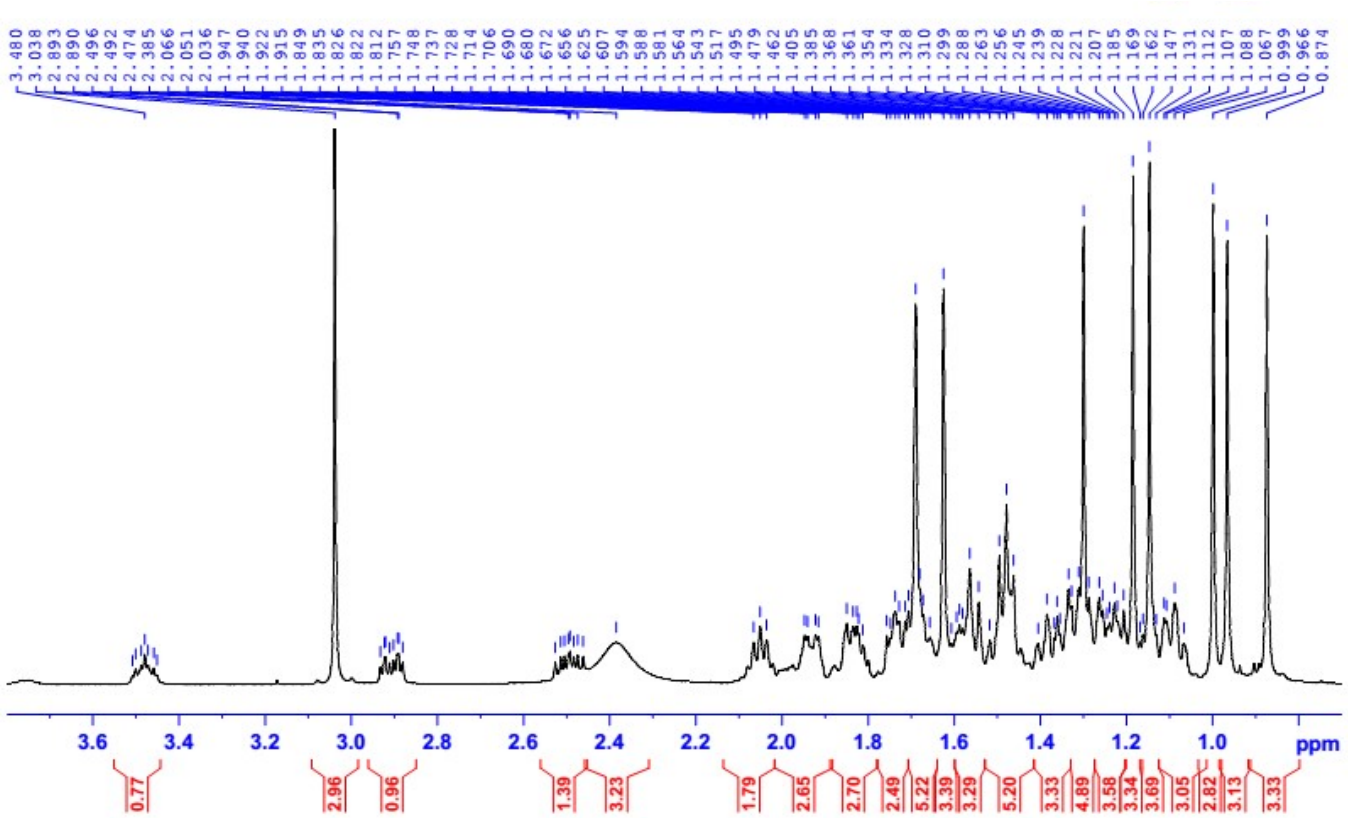
(+)-ESI–MS spectrum of compound **3b**



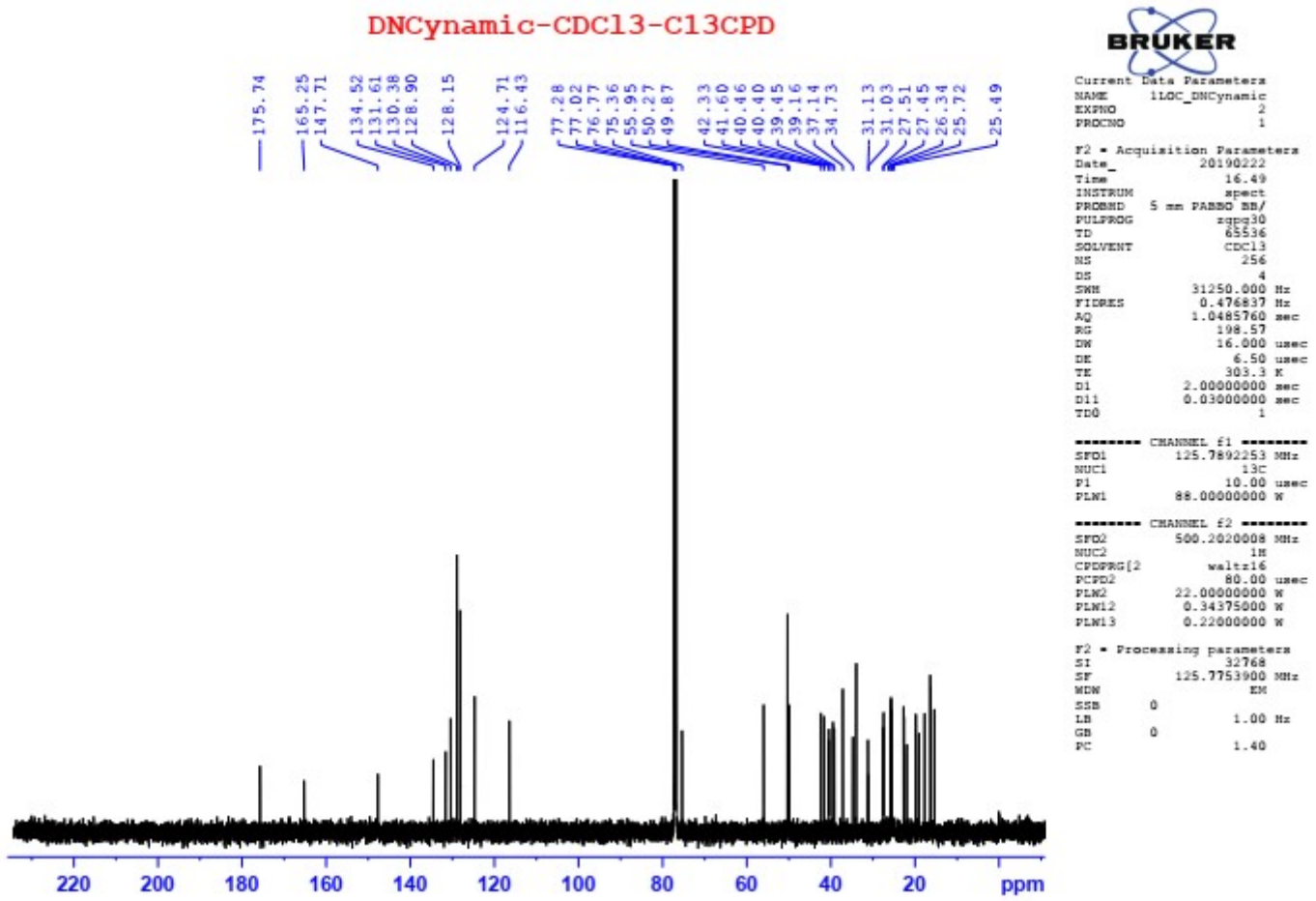
^{1}H-NMR spectrum of compound **3b**



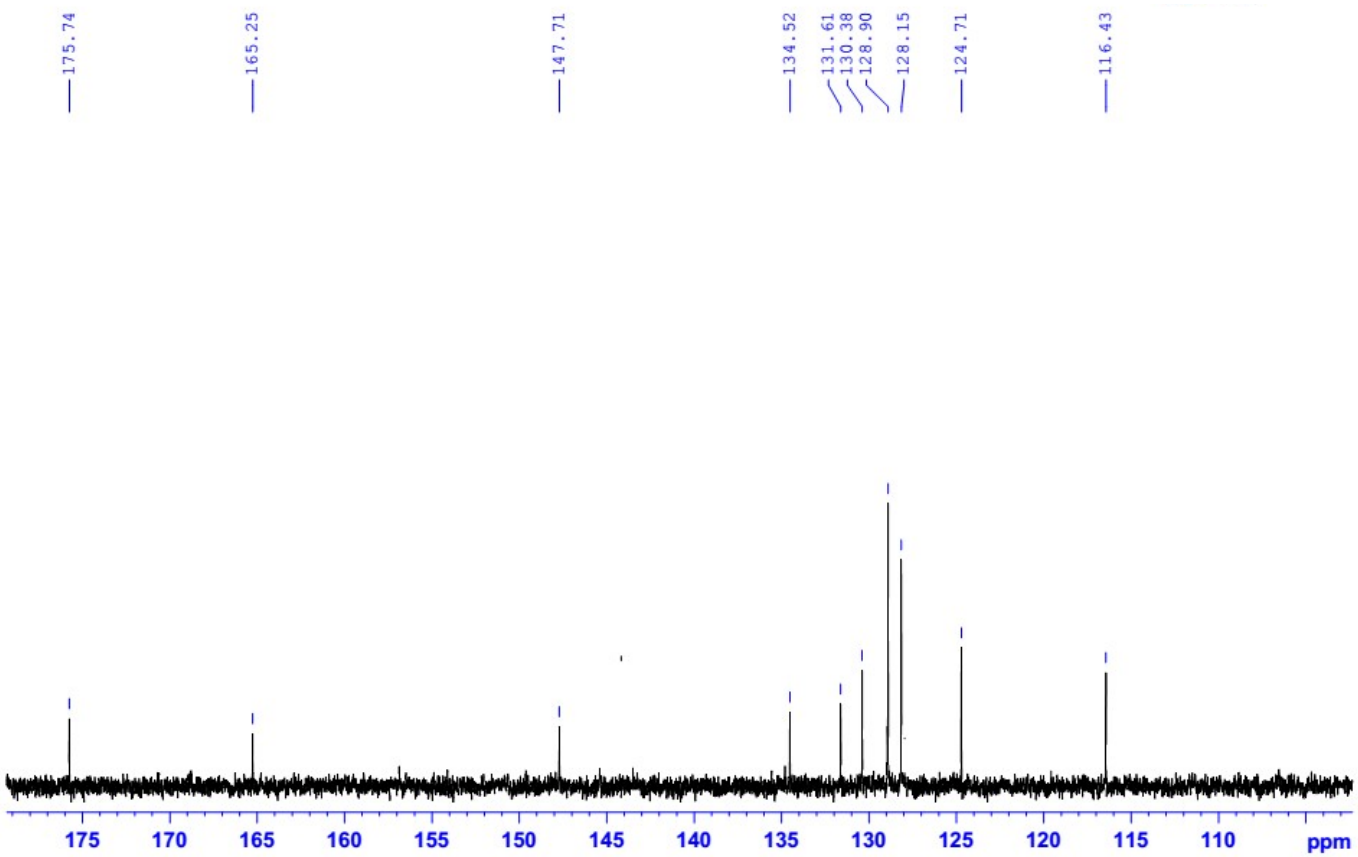
^{1}H-NMR spectrum of compound **3b** (extension)



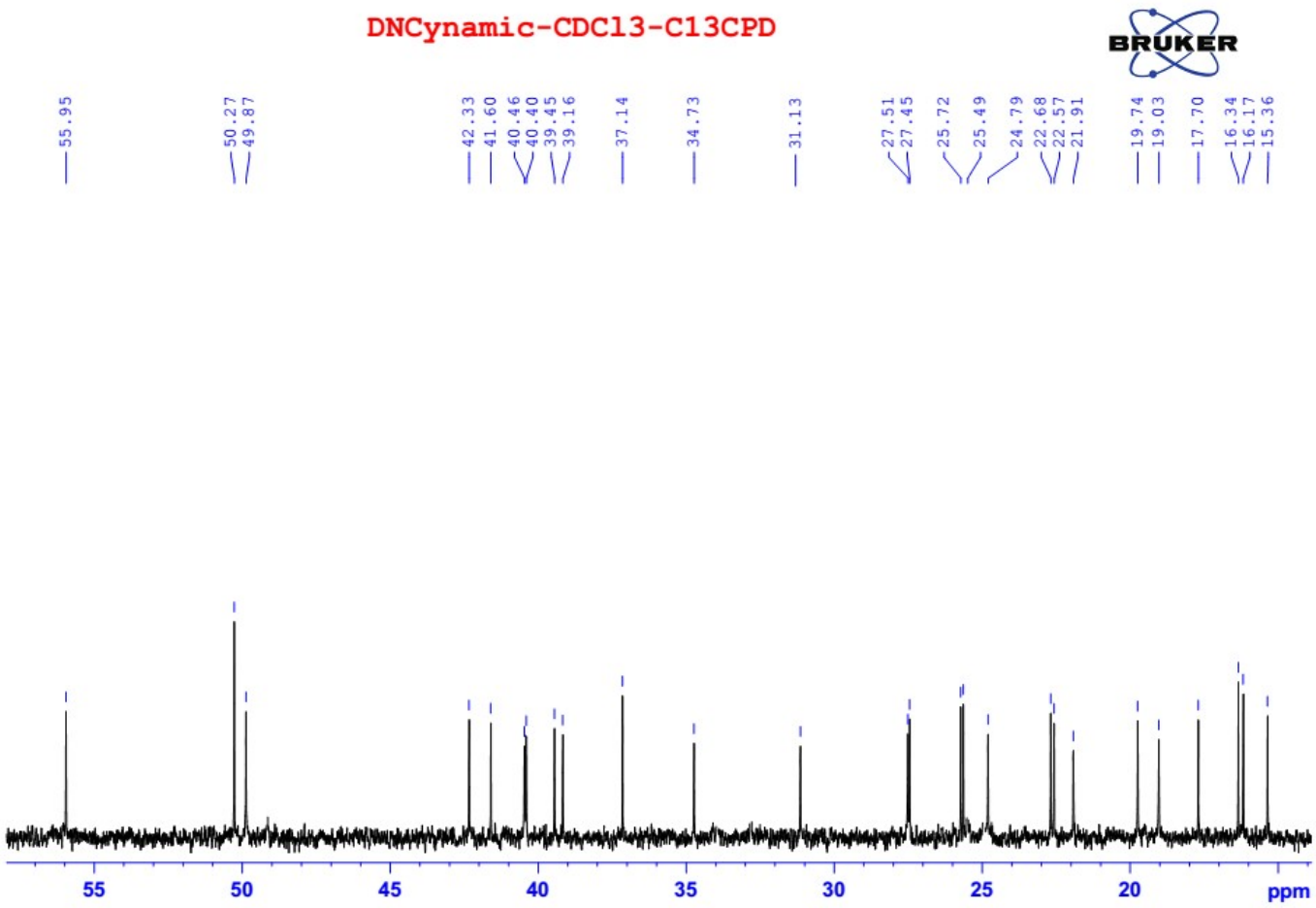
^{1}H-NMR spectrum of compound **3b** (extension)



^{13}C-NMR spectrum of compound **3b**



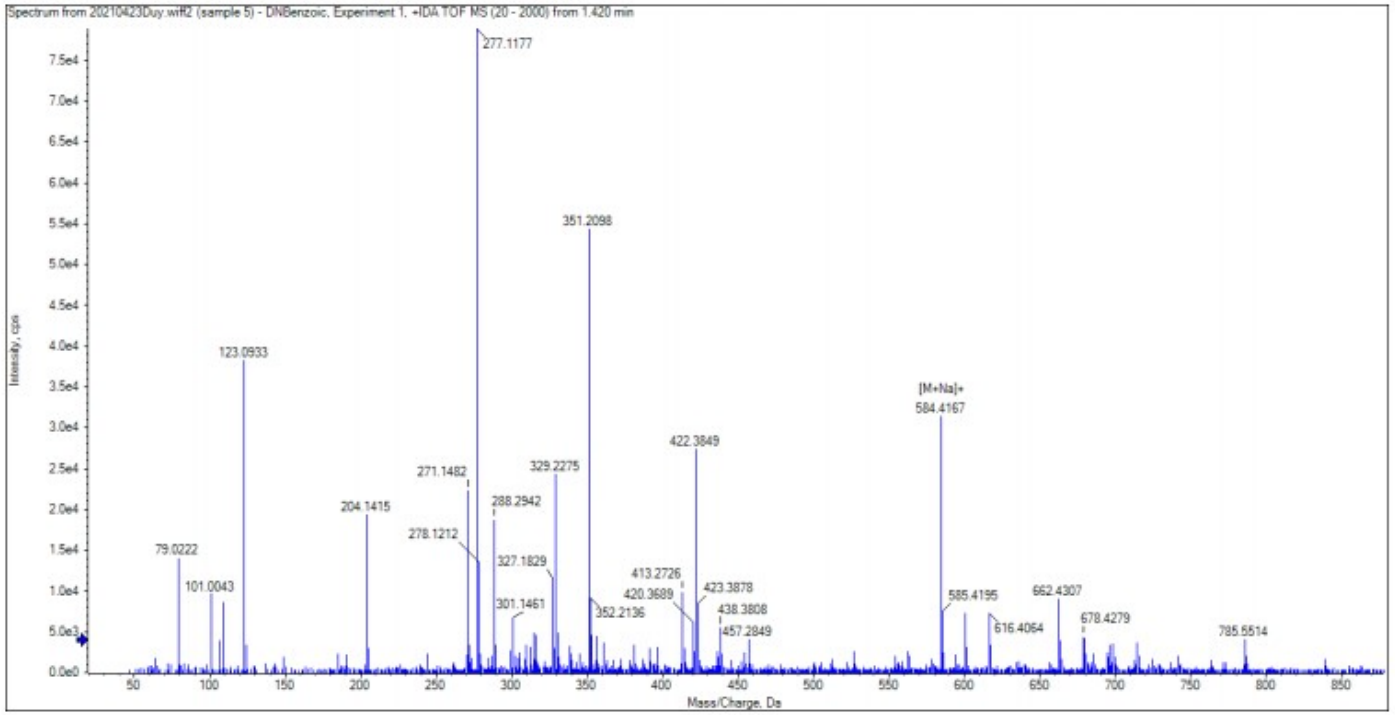
^{13}C-NMR spectrum of compound **3b** (extension)



^{13}C-NMR spectrum of compound **3b** (extension)

1.5. Compound 3c

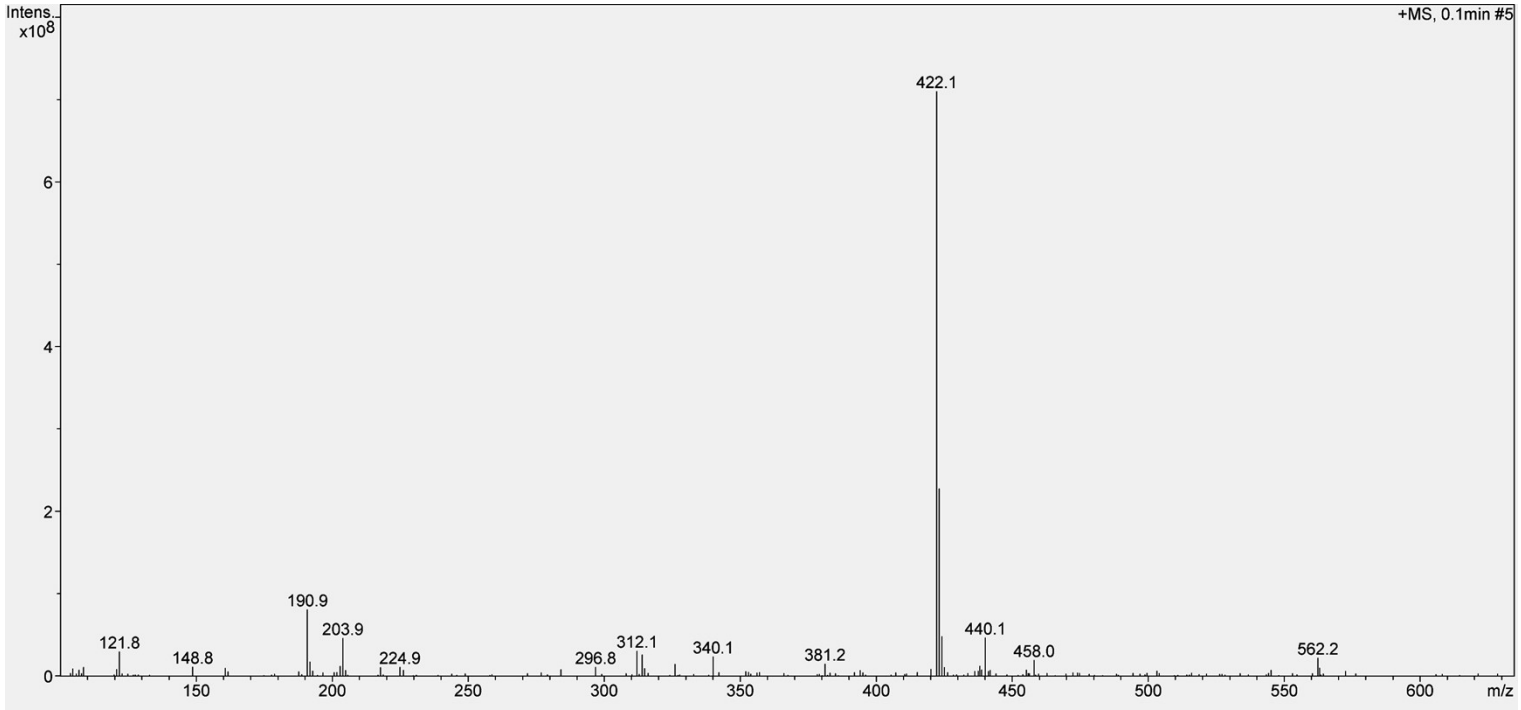
Sample name: DNBenzoic
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23



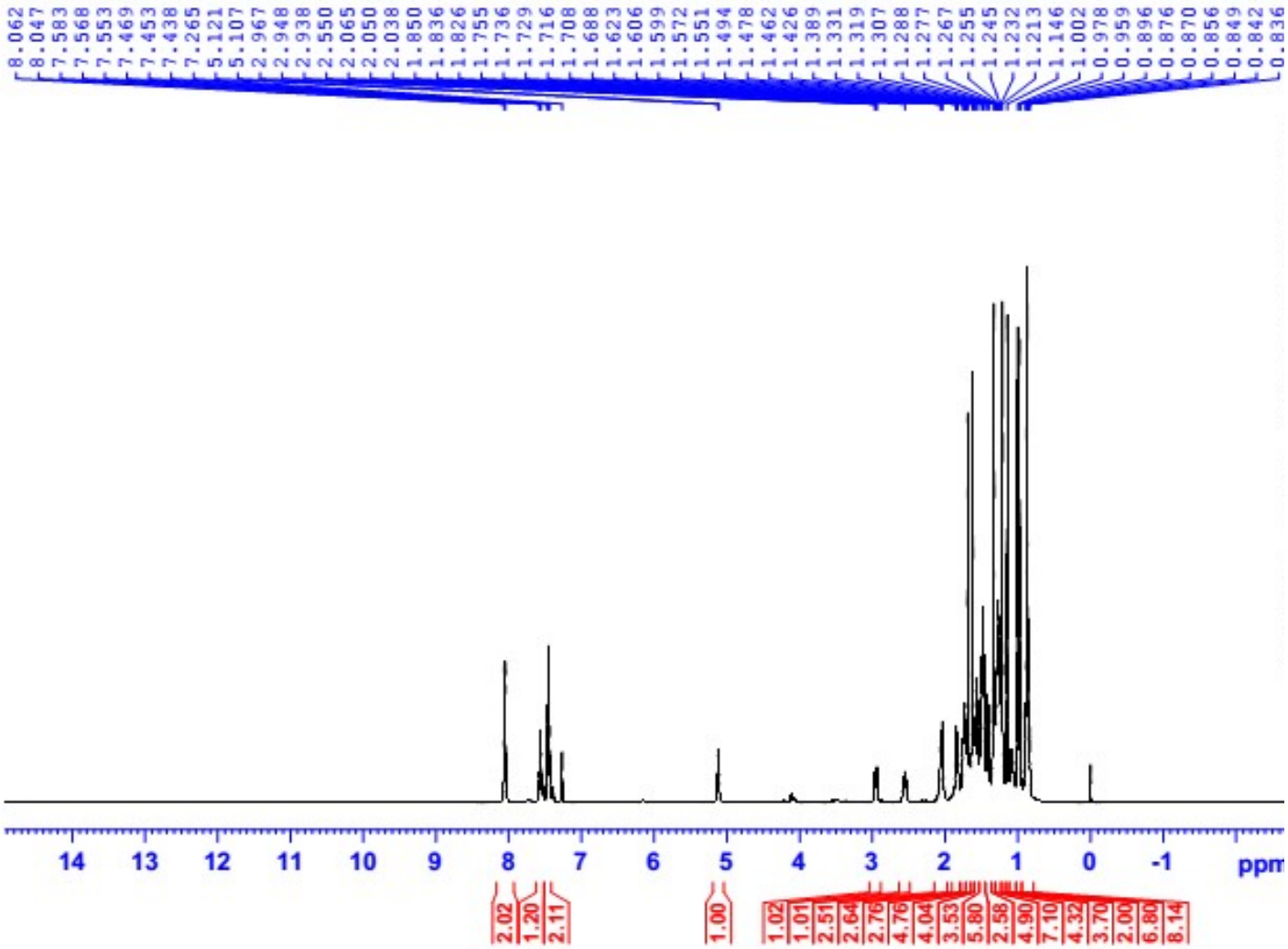
Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C37H55NO3	584.4142	11.0	3.0	1			NA/NA

Device Model: SCIEX X500 QTOF

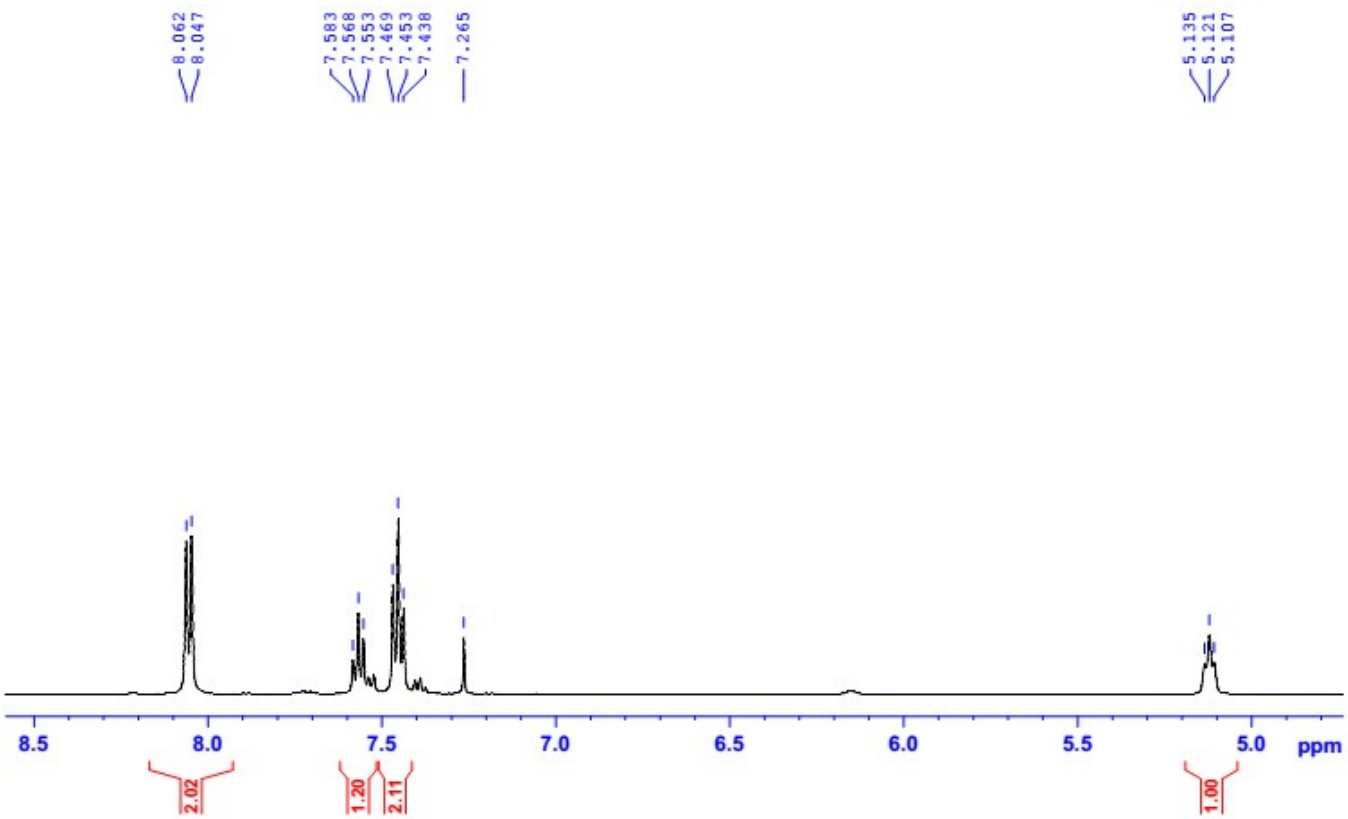
(+)-HR-ESI-MS spectrum of compound **3c**



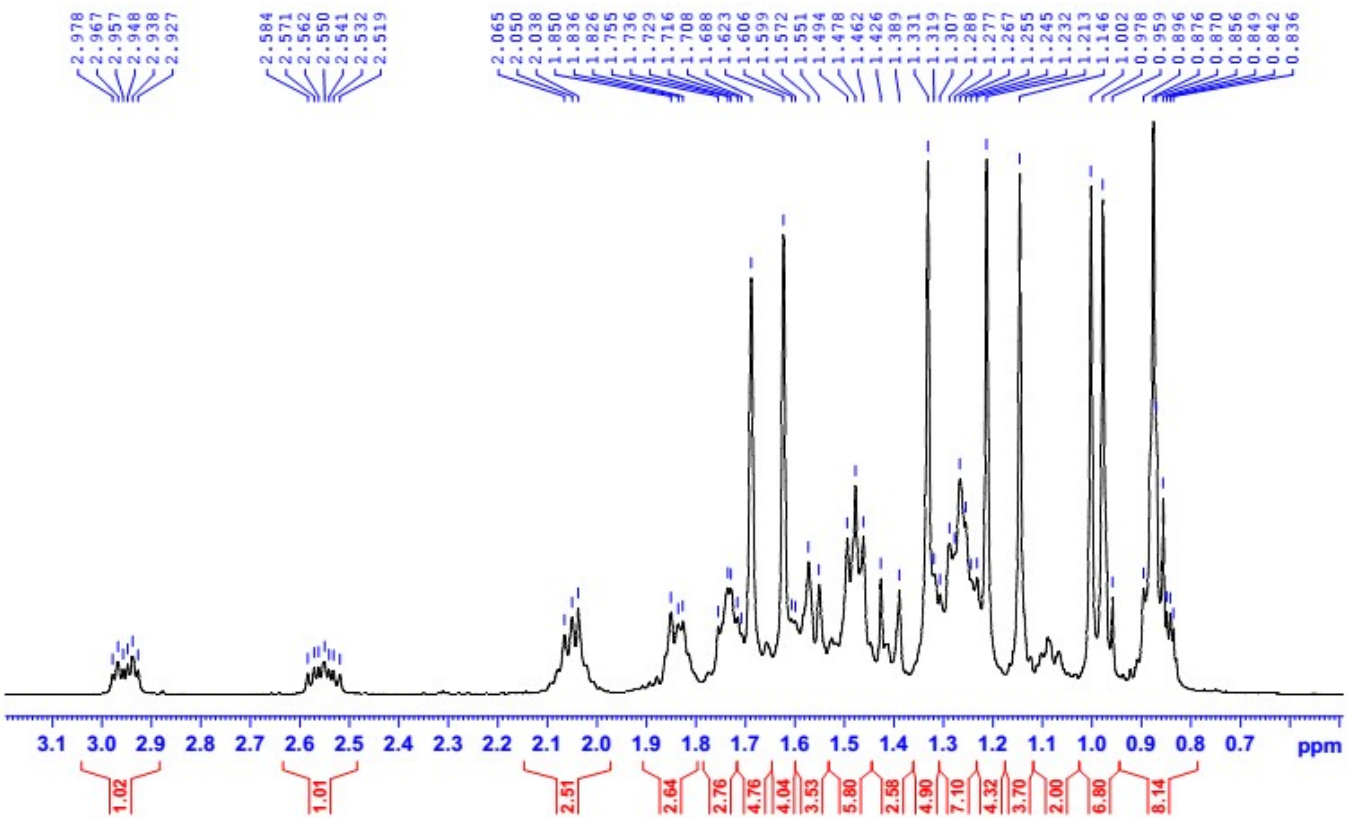
(+)-ESI-MS spectrum of compound **3c**



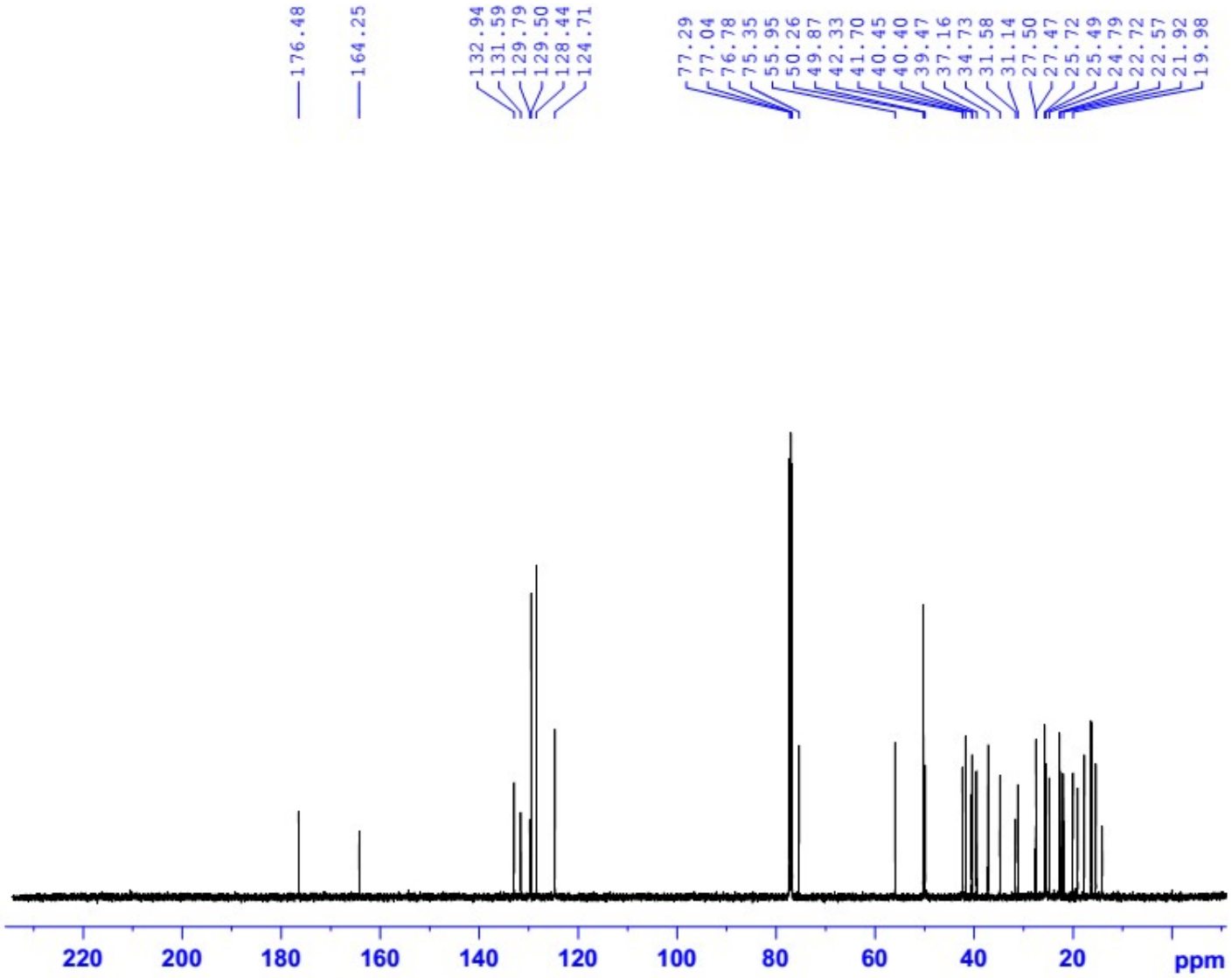
^{1}H-NMR spectrum of compound **3c**



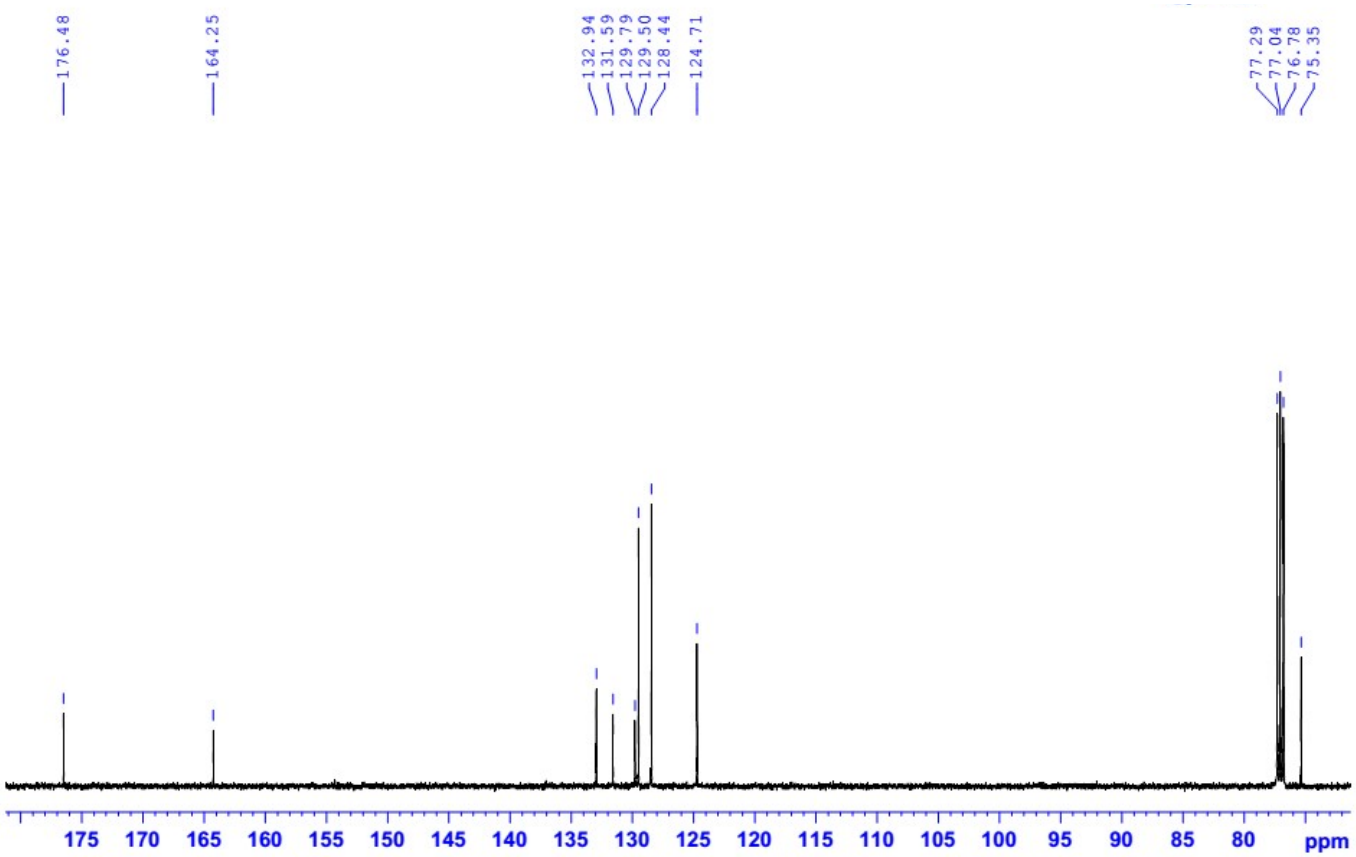
^{1}H-NMR spectrum of compound **3c** (extension)



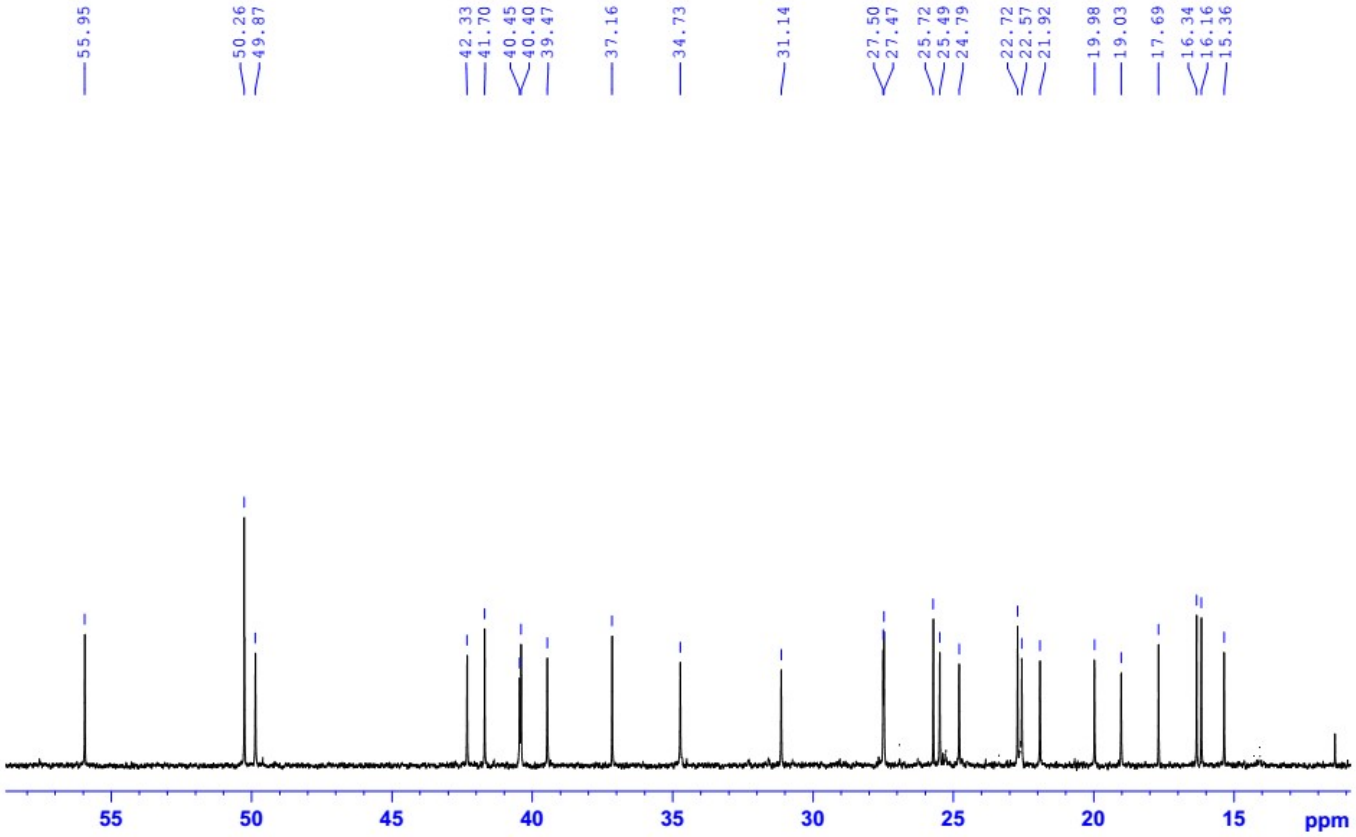
^{1}H-NMR spectrum of compound **3c** (extension)



^{13}C-NMR spectrum of compound **3c**



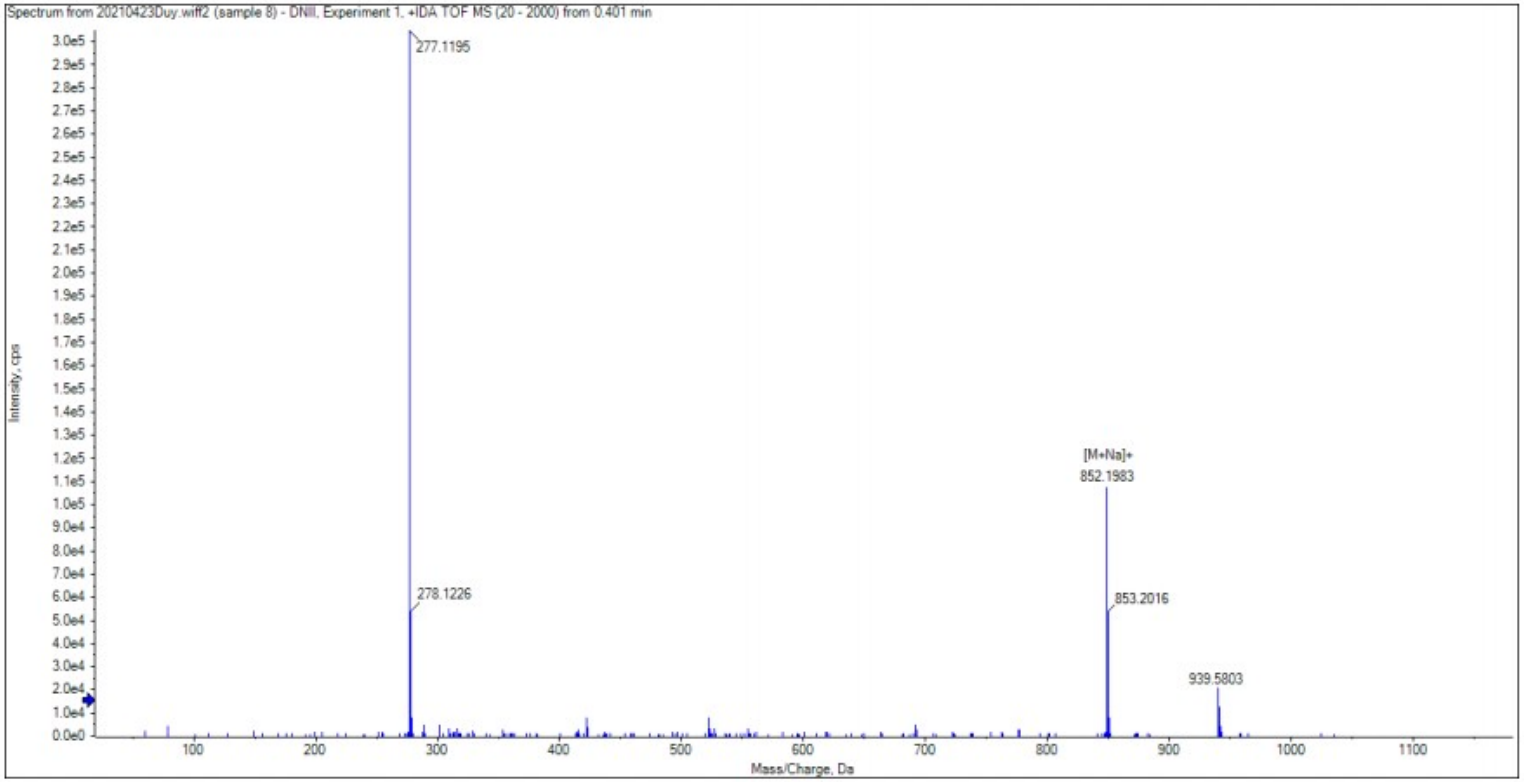
^{13}C-NMR spectrum of compound **3c** (extension)



^{13}C-NMR spectrum of compound **3c** (extension)

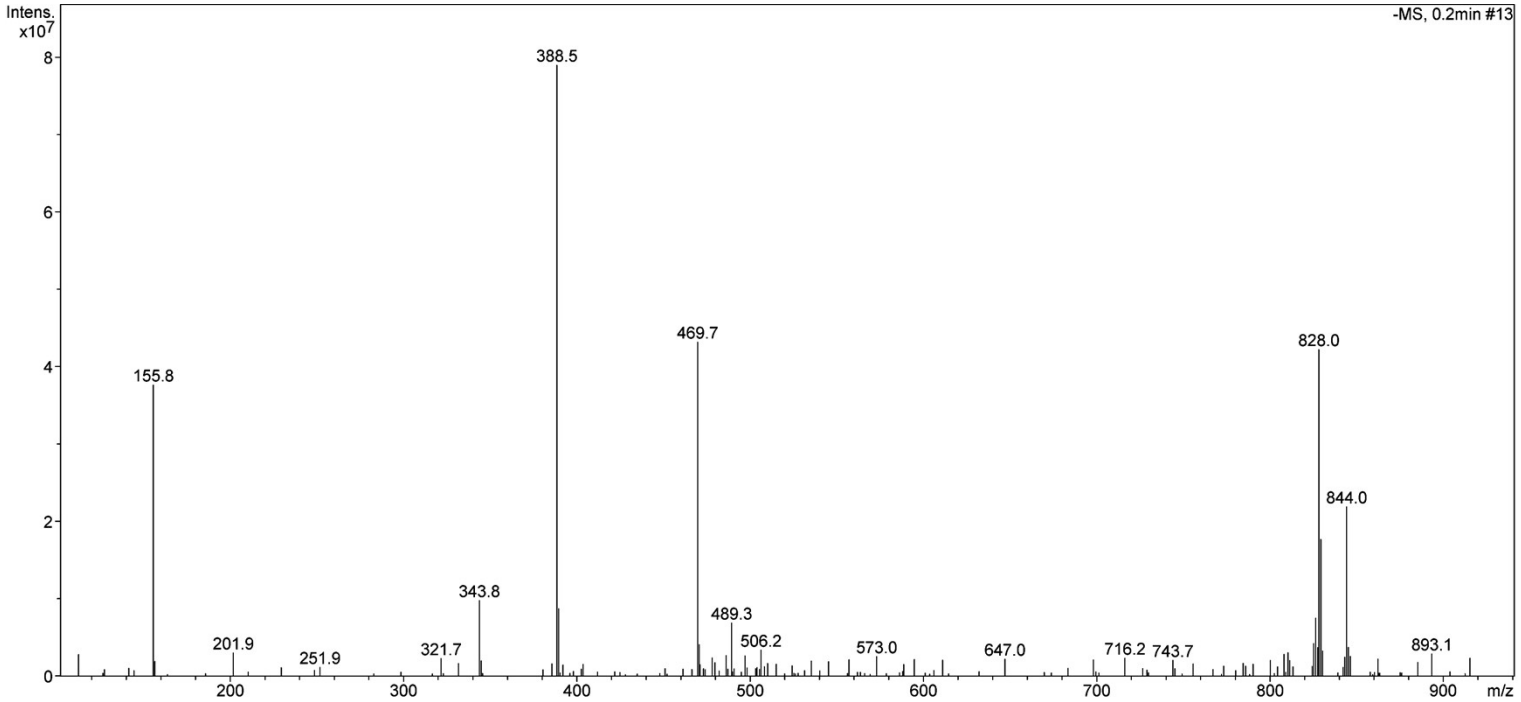
1.6. Compound 3d

Sample name: DNII
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

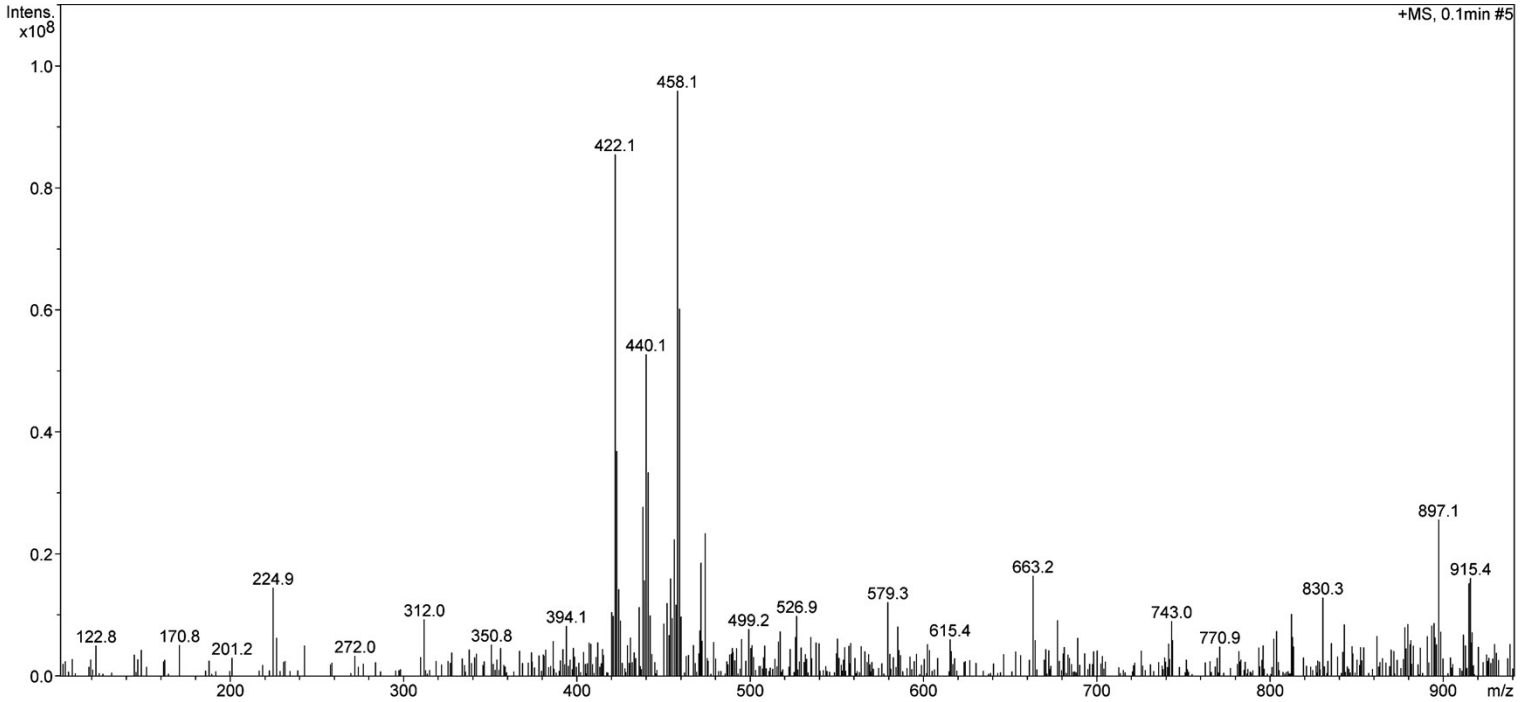


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C37H53I2NO4	852.19617	11.0	2.6	1			NA/NA

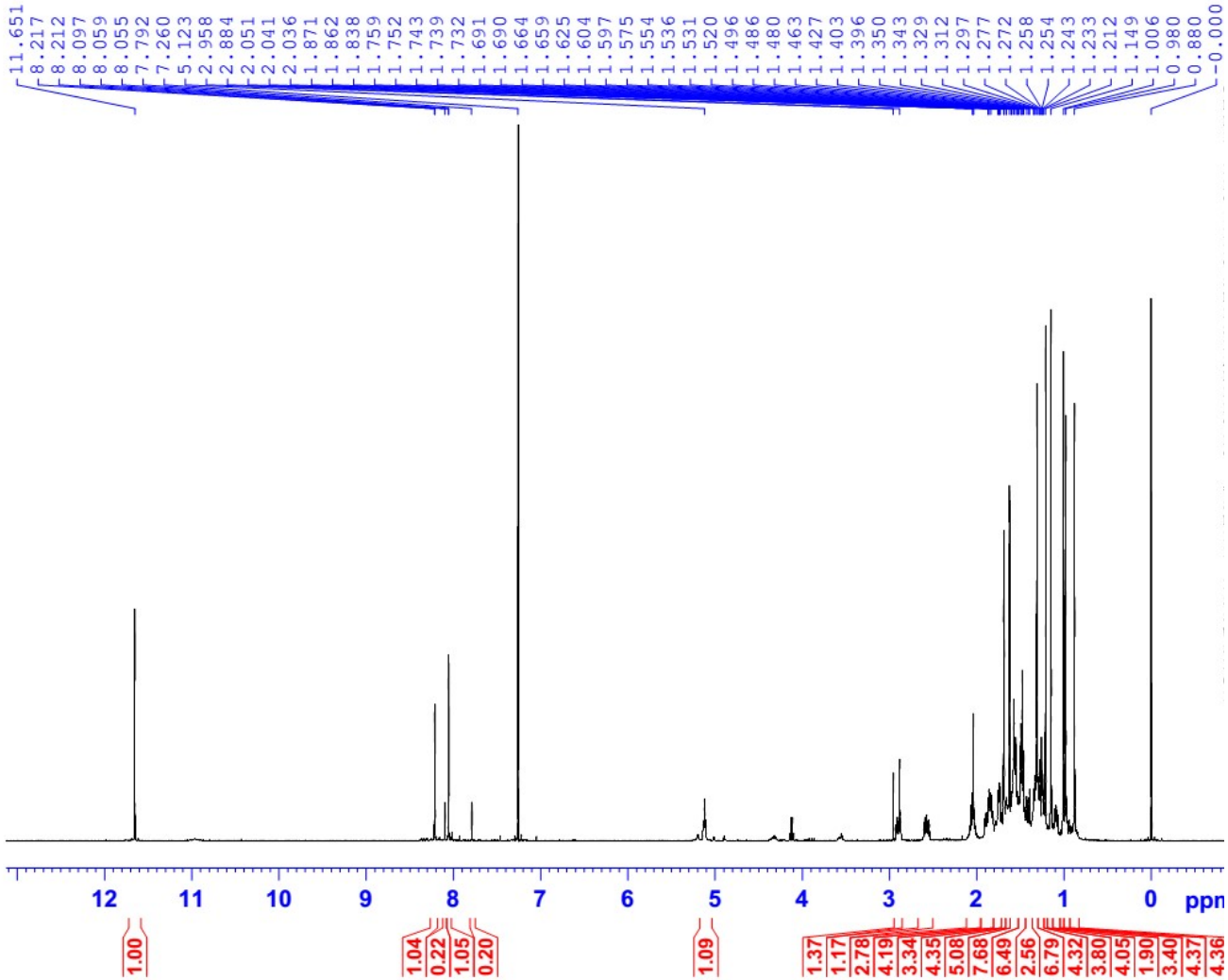
(+)-HR-ESI-MS spectrum of compound **3d**



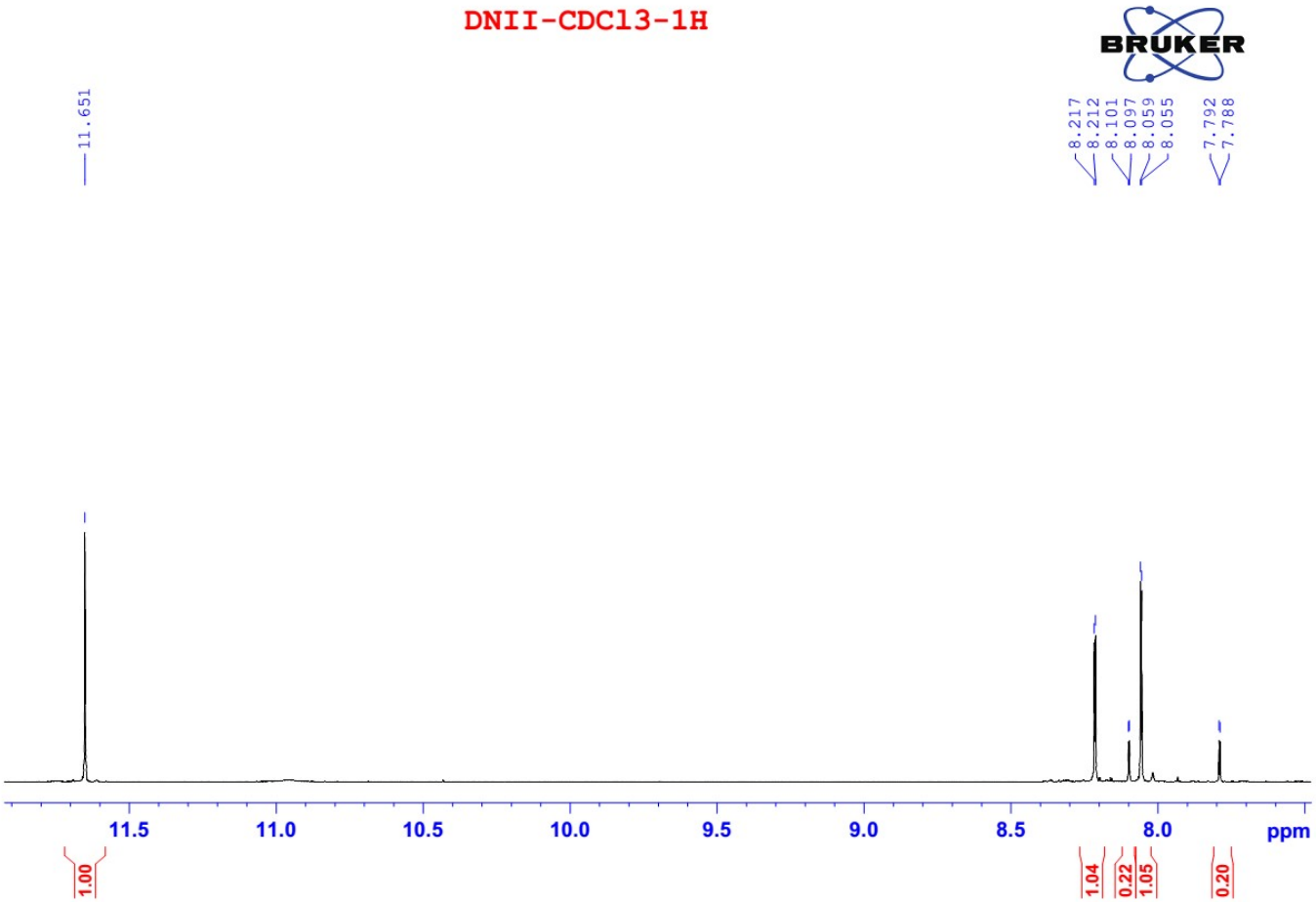
(–)-ESI–MS spectrum of compound **3d**



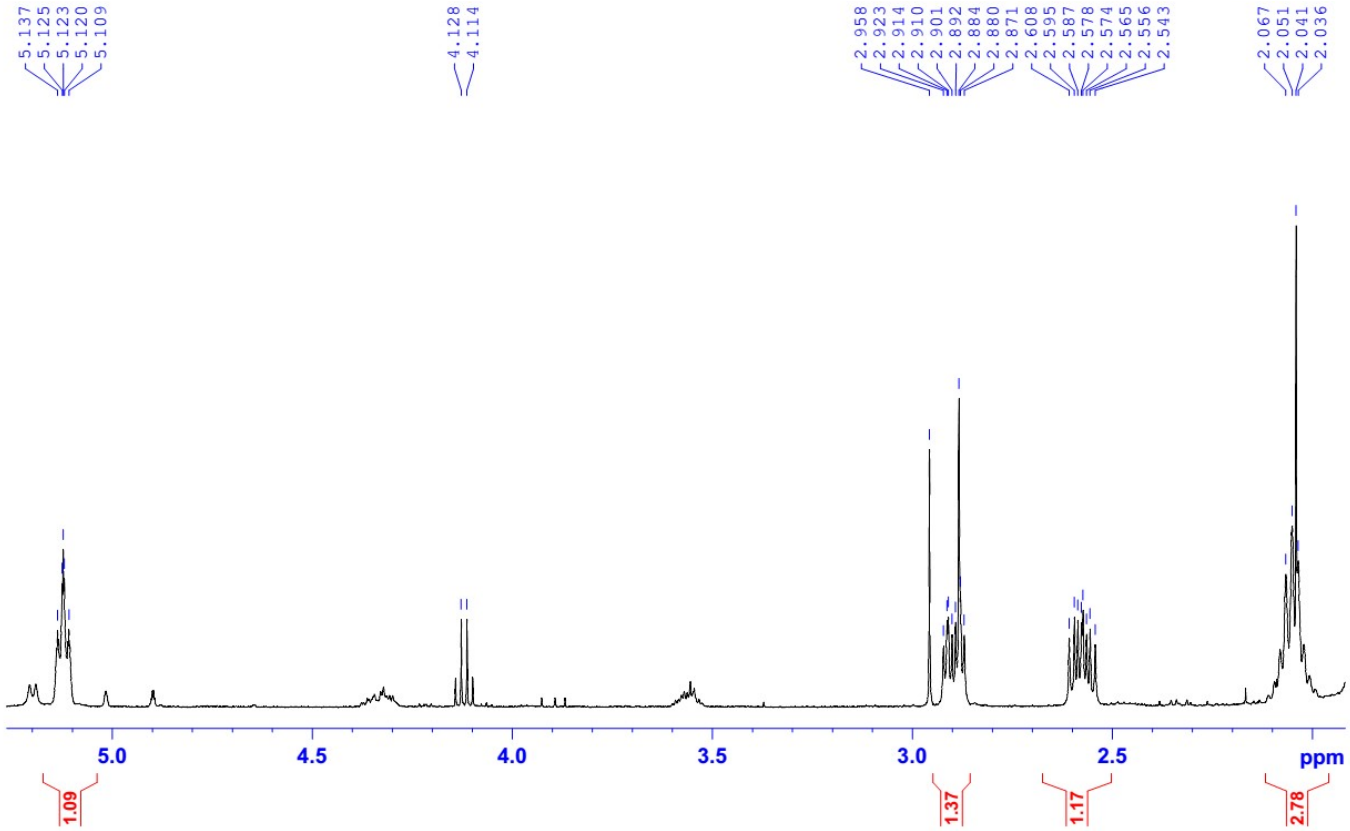
(+)-ESI–MS spectrum of compound **3d**



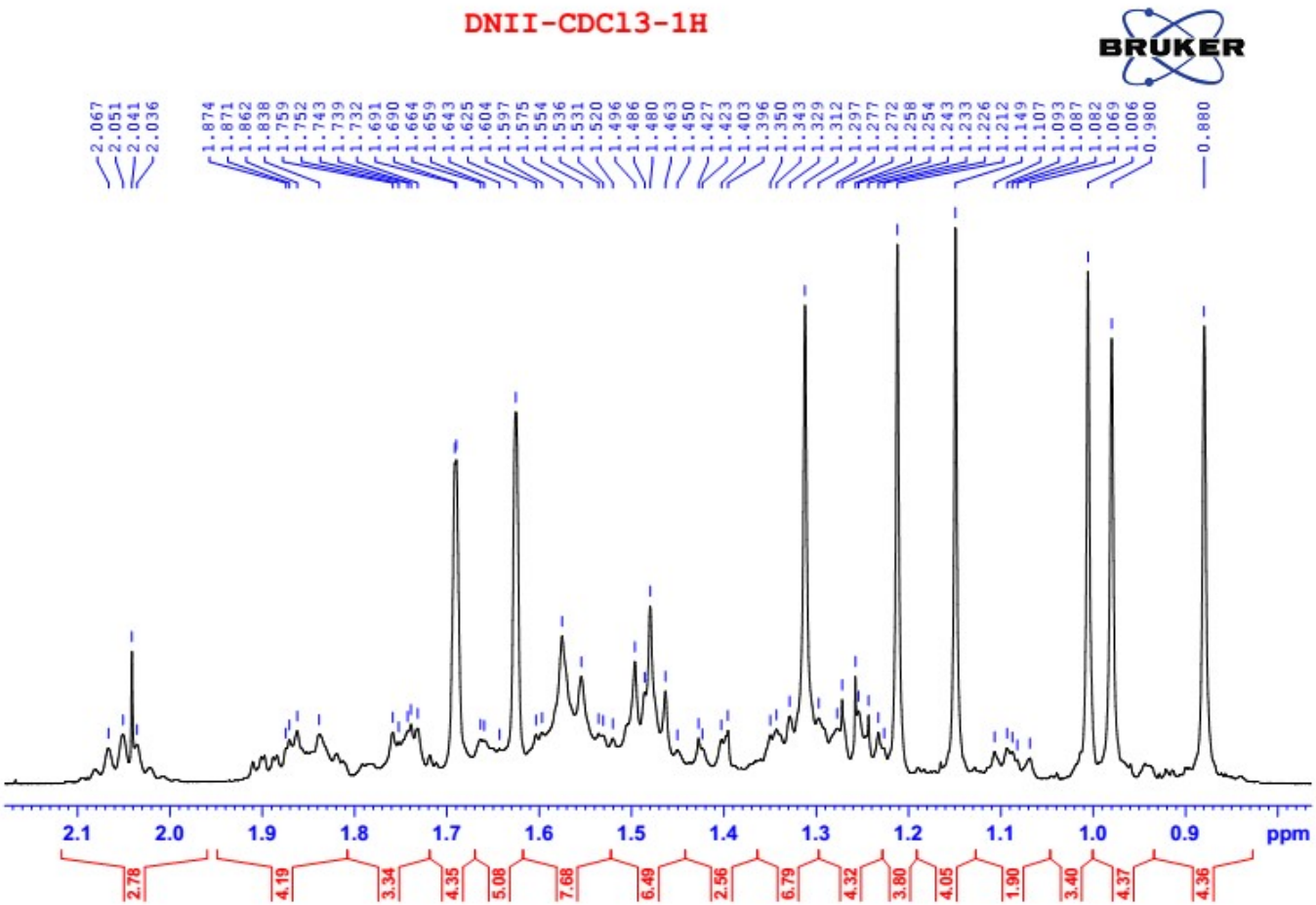
[1]H-NMR spectrum of compound **3d**



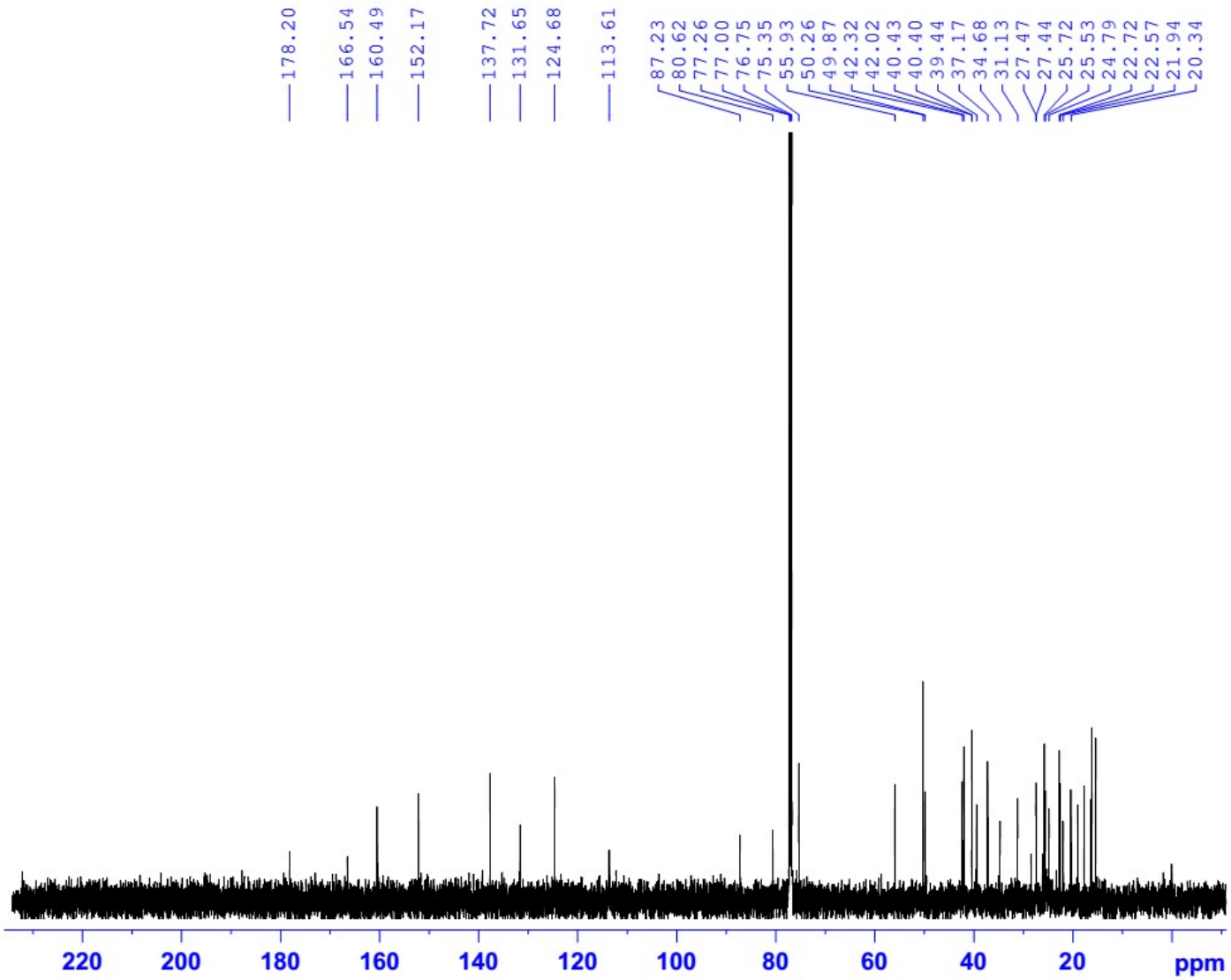
^{1}H-NMR spectrum of compound **3d** (extension)



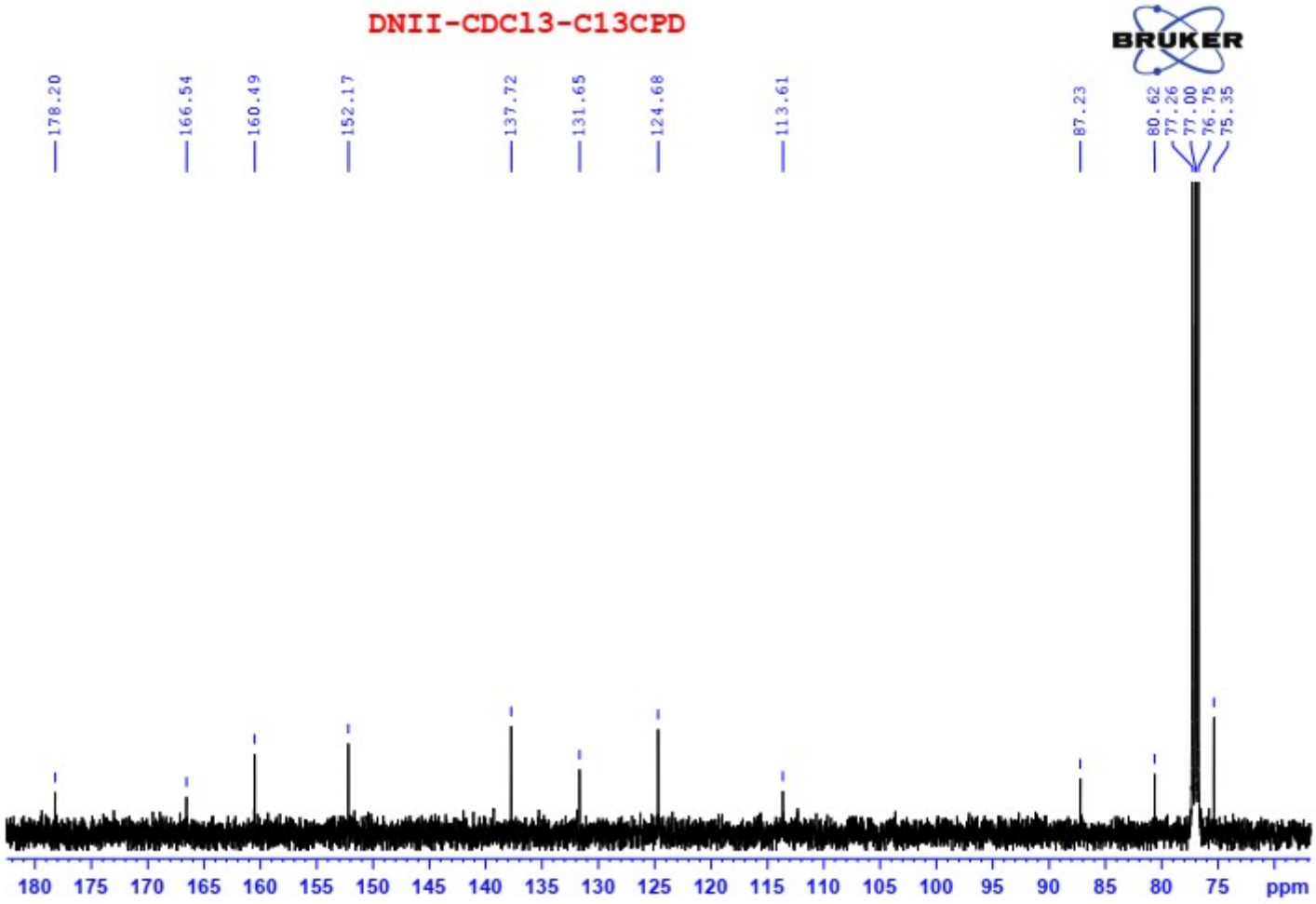
^{1}H-NMR spectrum of compound **3d** (extension)



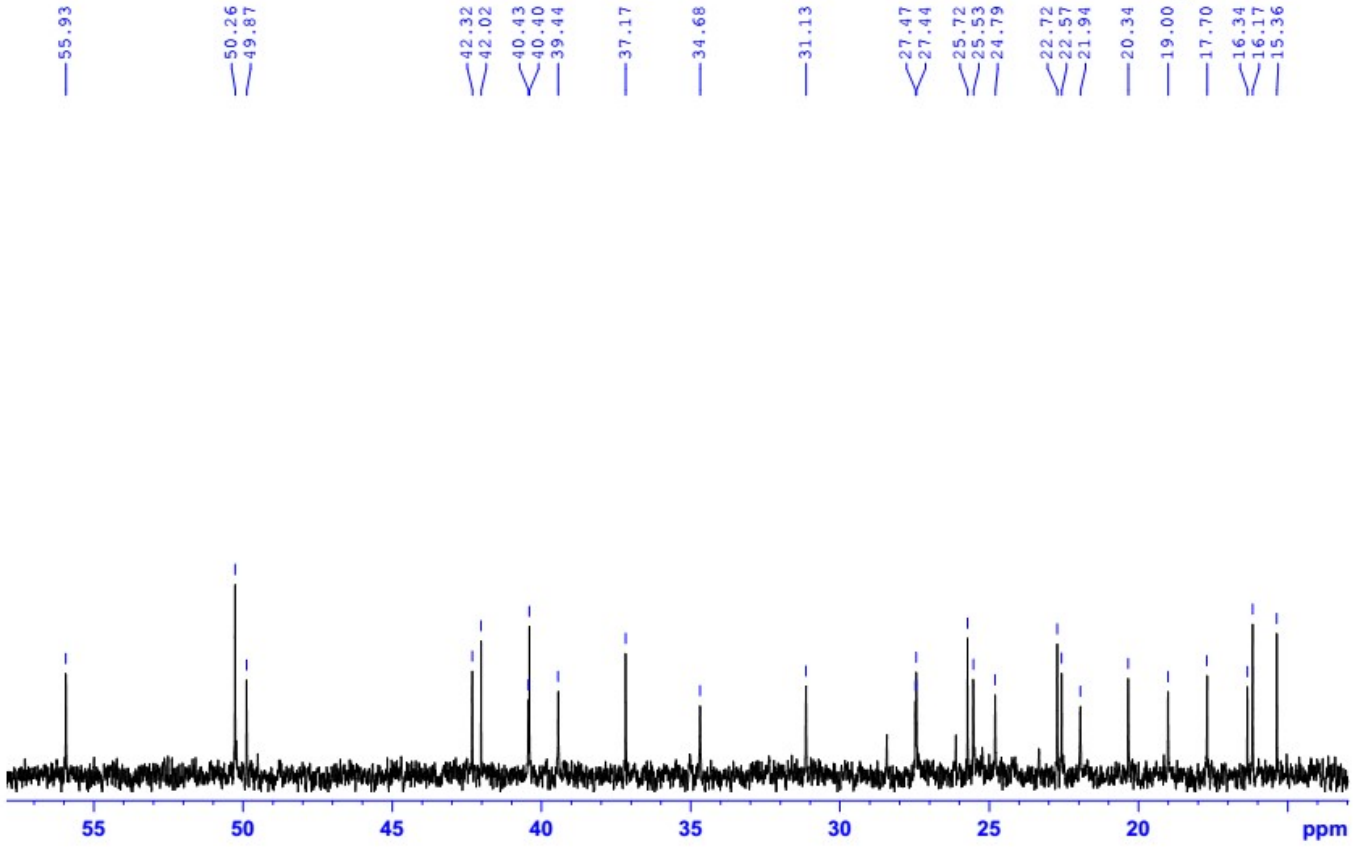
^{1}H-NMR spectrum of compound **3d** (extension)



^{13}C-NMR spectrum of compound **3d**



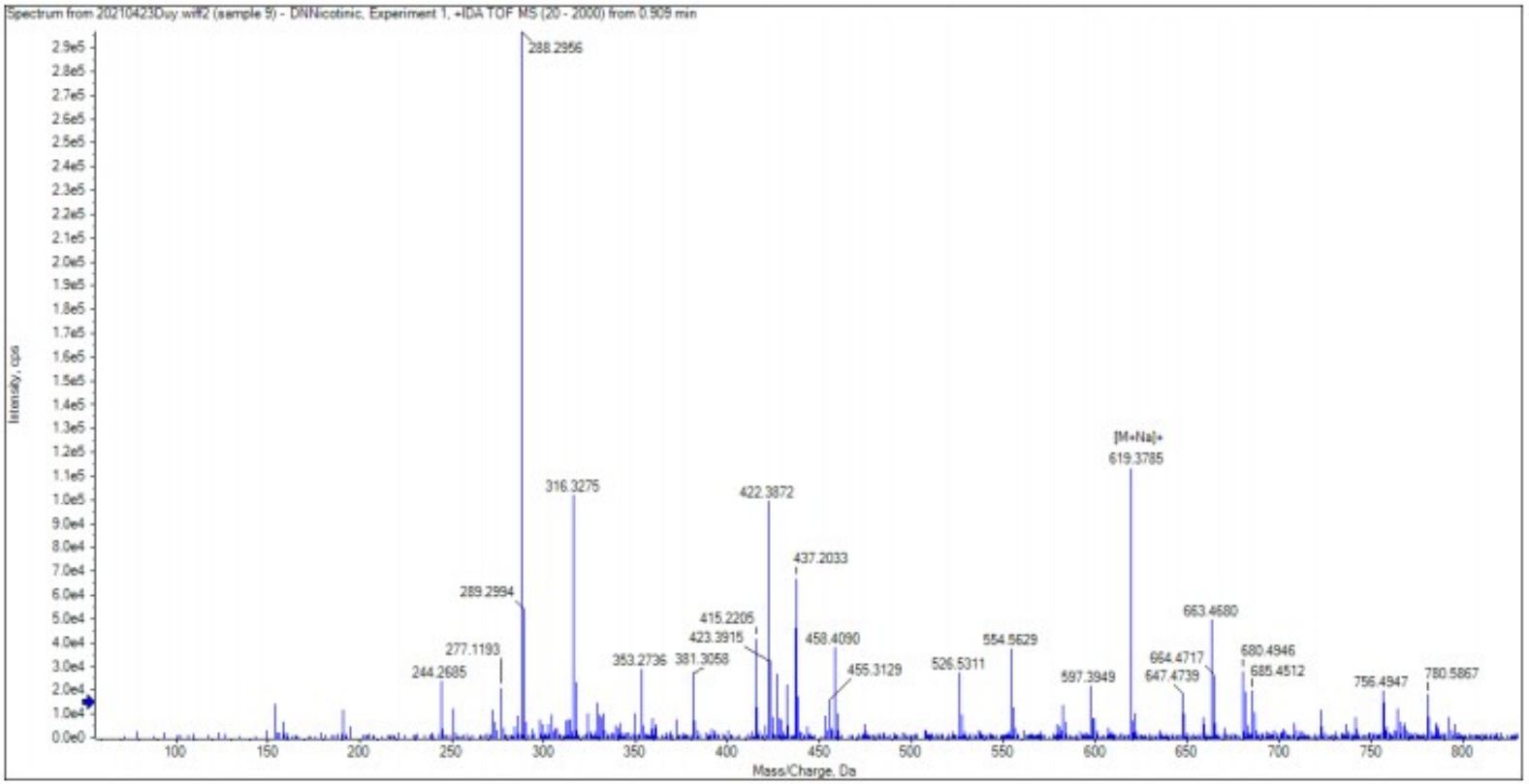
^{13}C-NMR spectrum of compound **3d** (extension)



^{13}C-NMR spectrum of compound **3d** (extension)

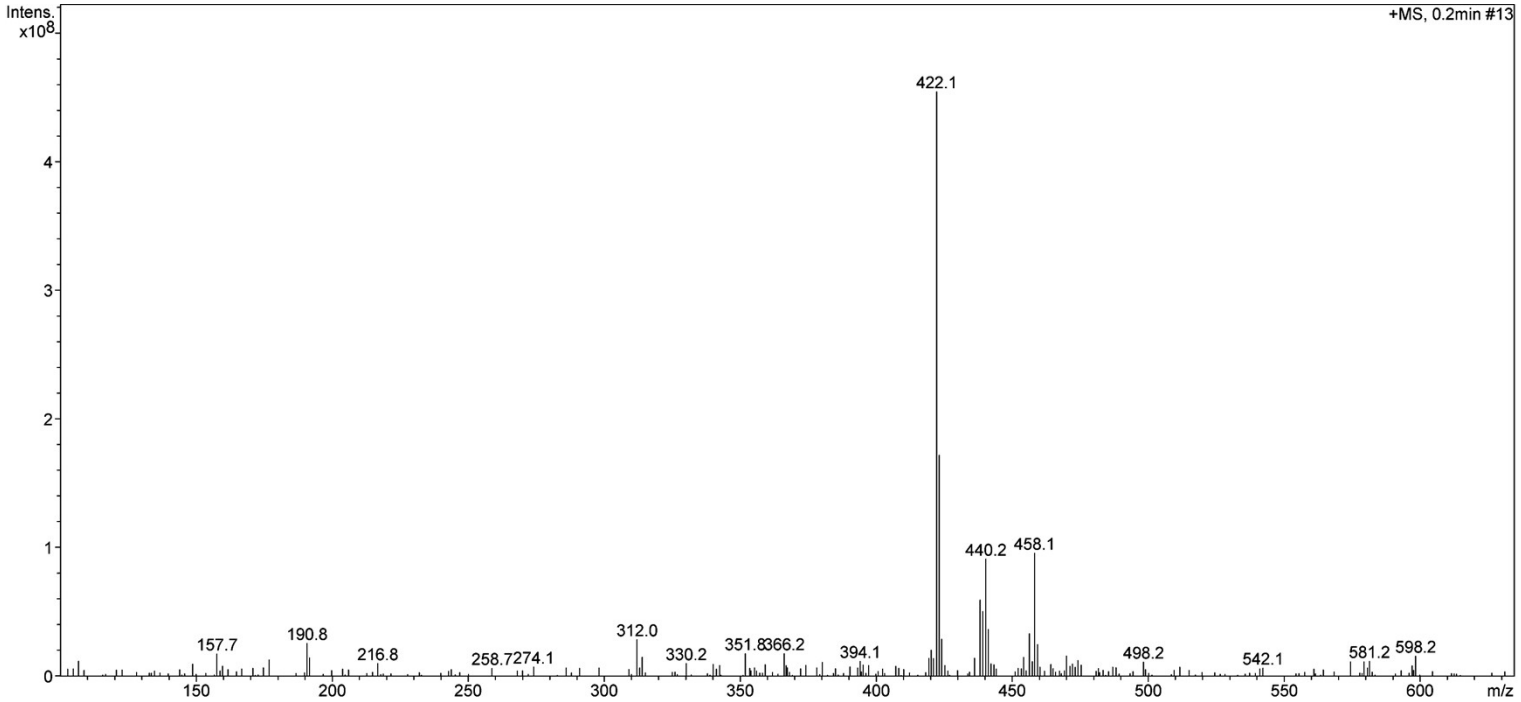
1.7. Compound 3e

Sample name: DNNicotinic
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

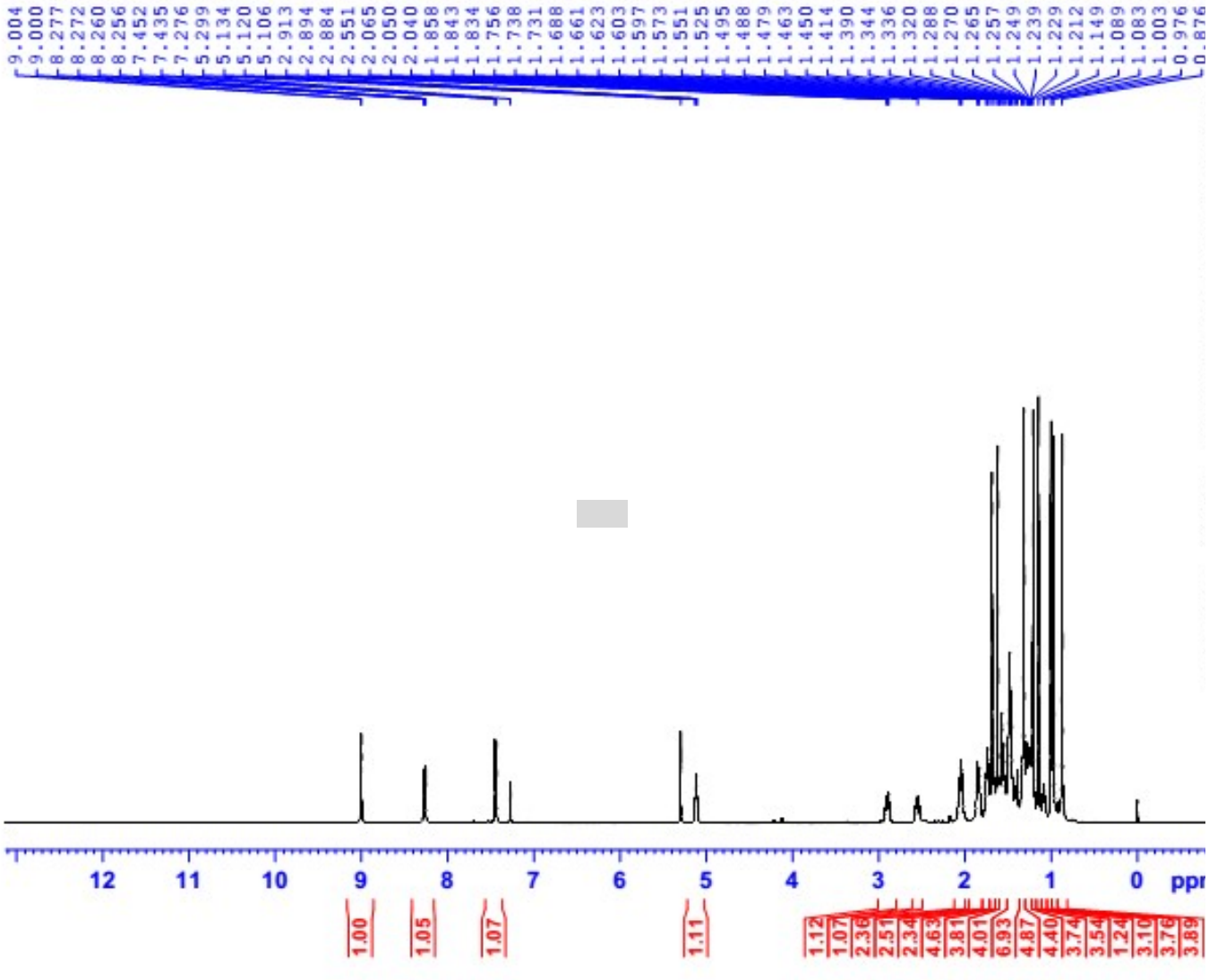


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C36H53ClN2O3	619.3759	11.0	3.9	1			NA/NA

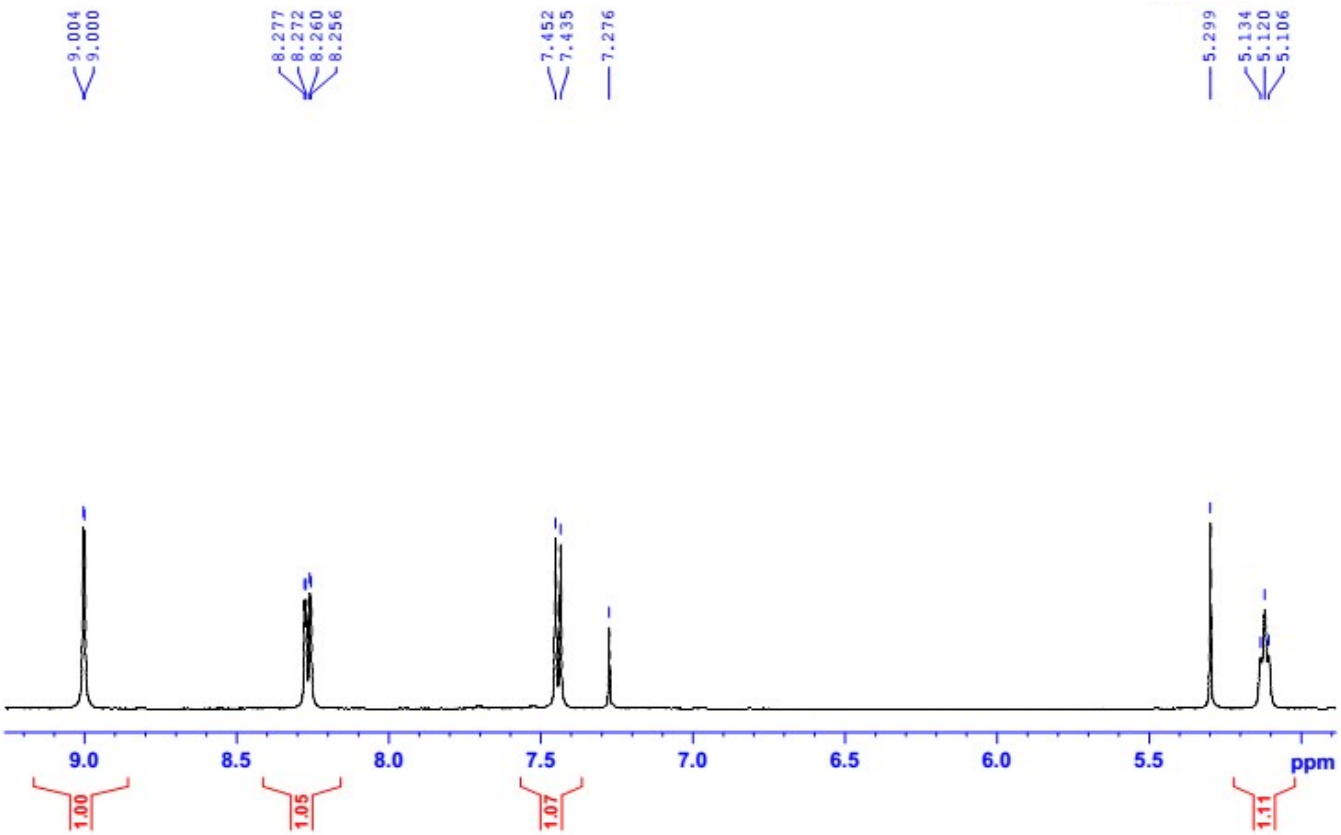
(+)-HR-ESI-MS spectrum of compound **3e**



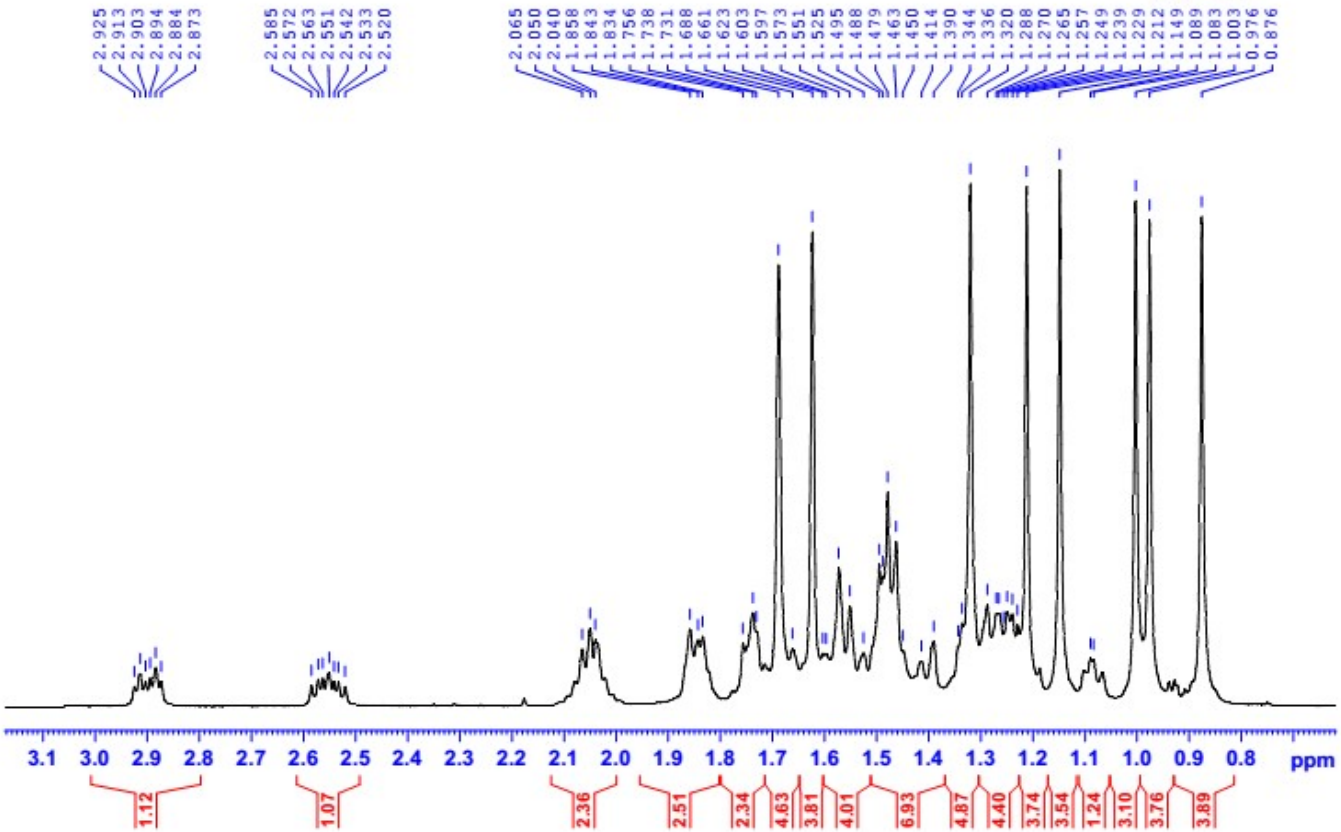
(+)-ESI–MS spectrum of compound **3e**



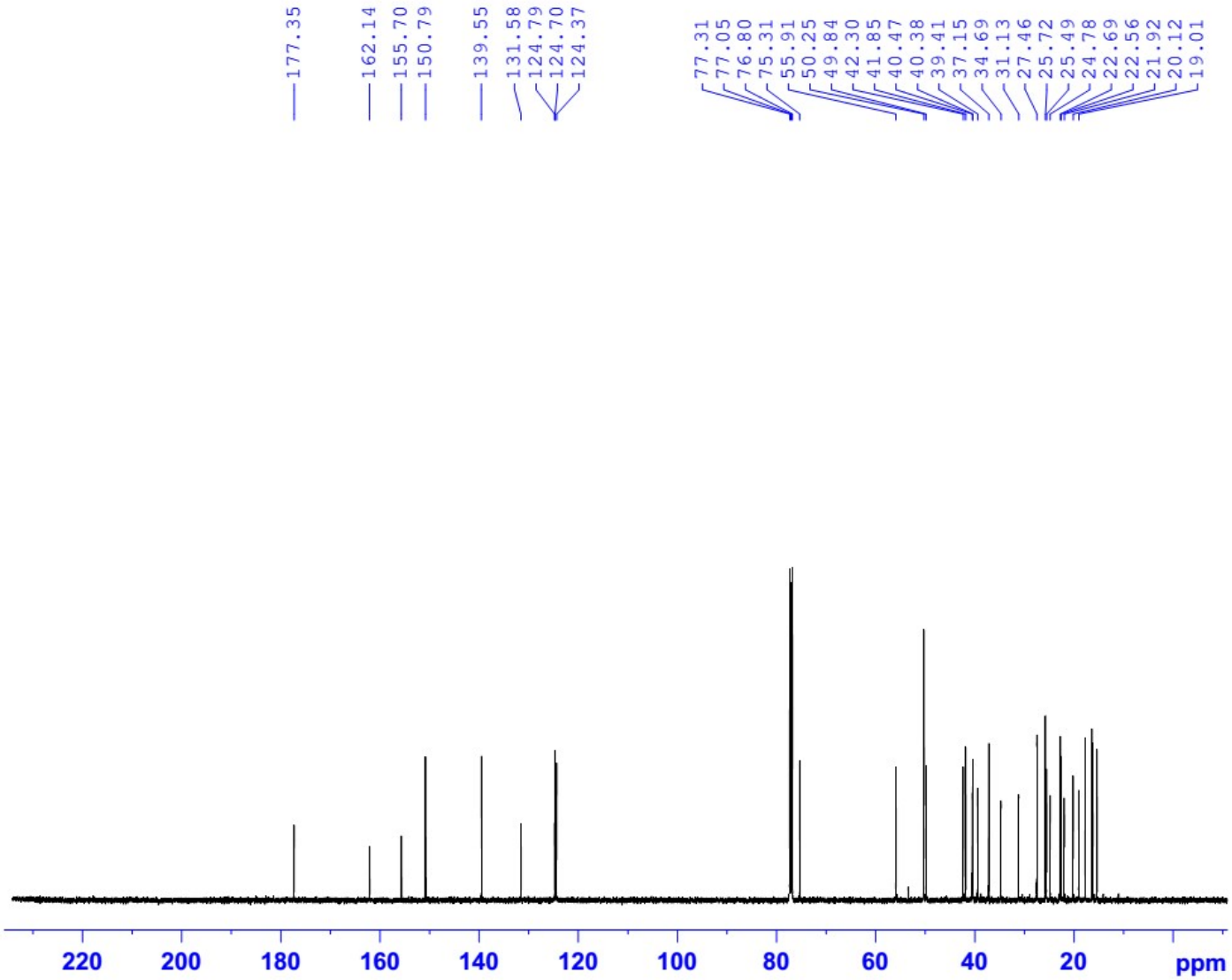
^{1}H-NMR spectrum of compound **3e**



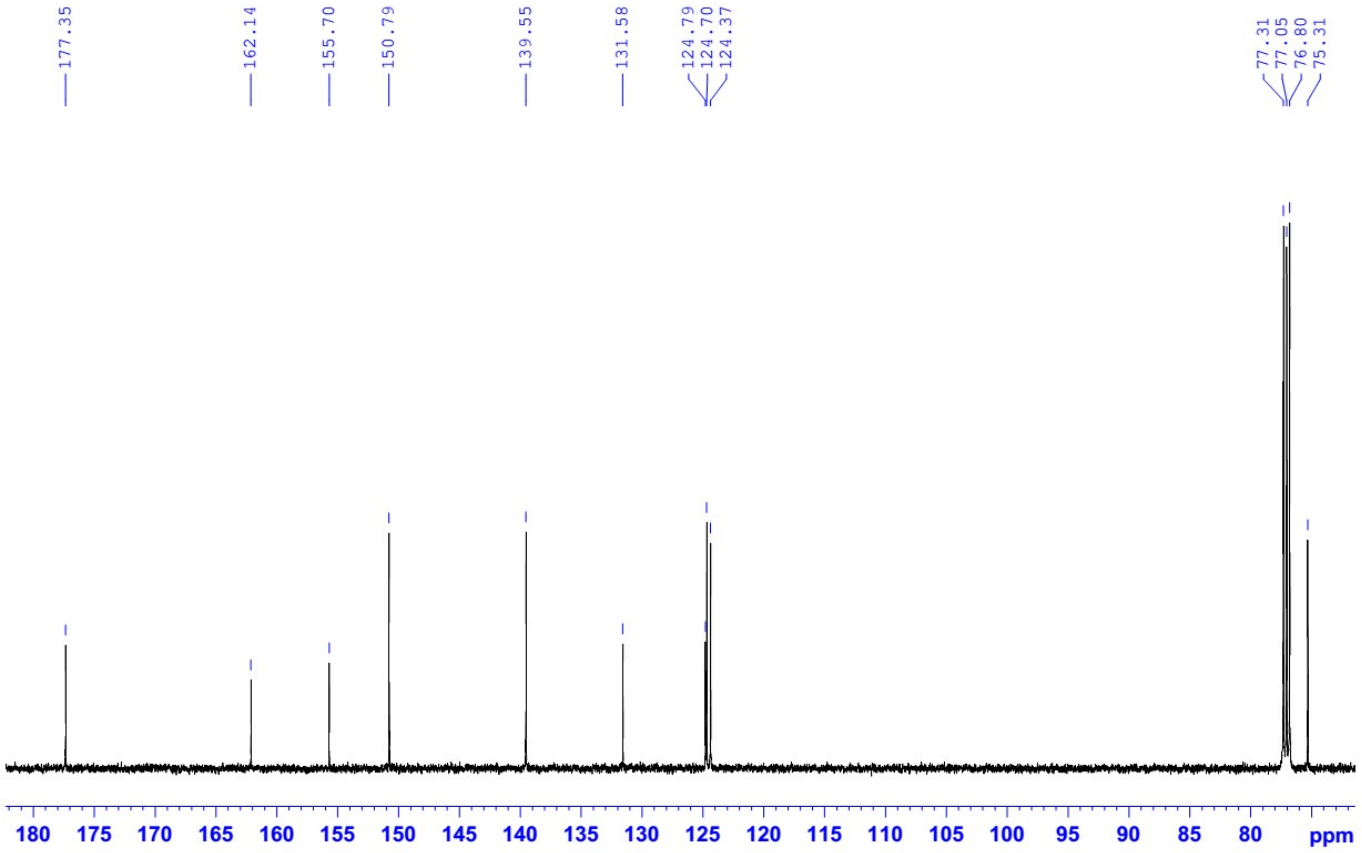
^{1}H-NMR spectrum of compound **3e** (extension)



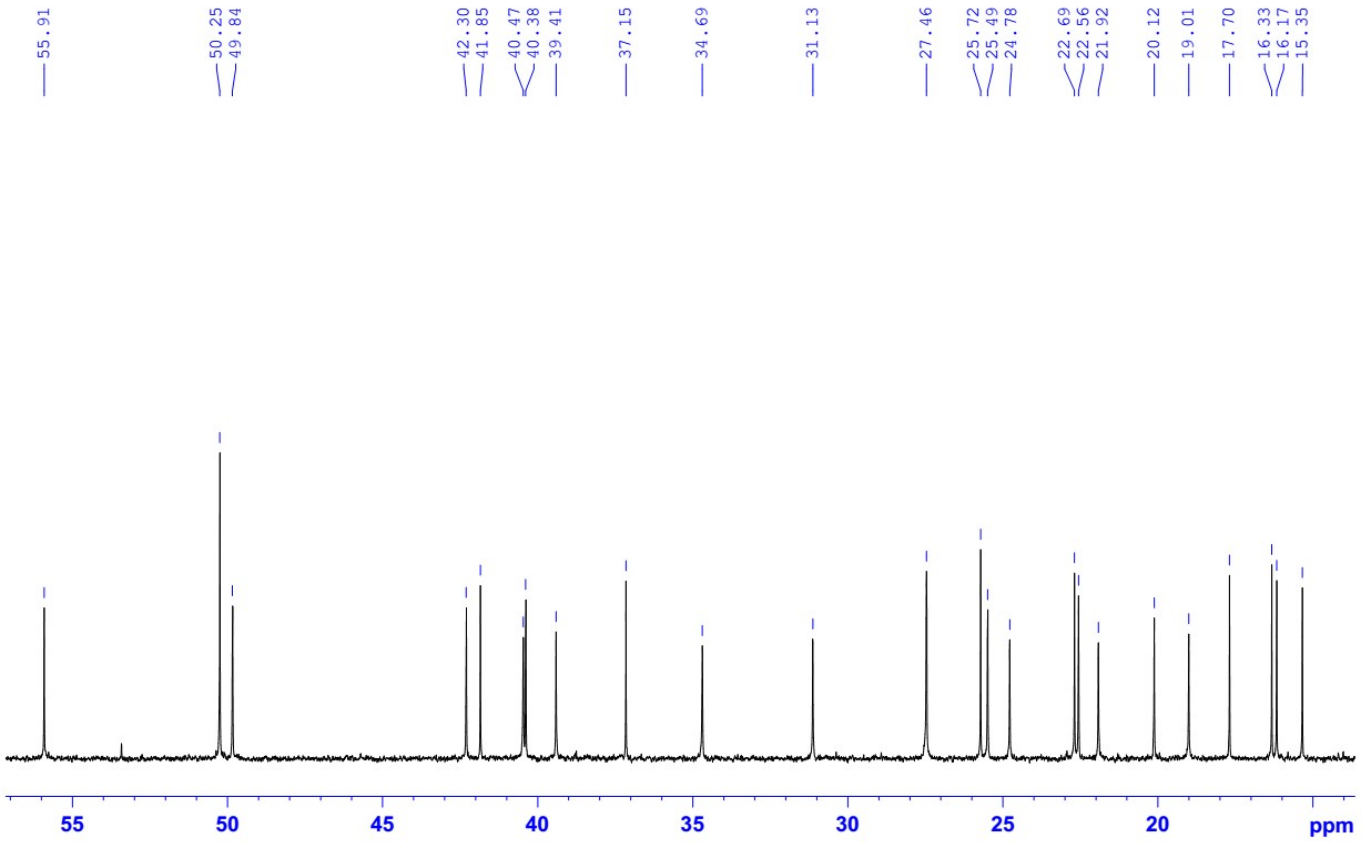
^{1}H-NMR spectrum of compound **3e** (extension)



^{13}C-NMR spectrum of compound **3e**



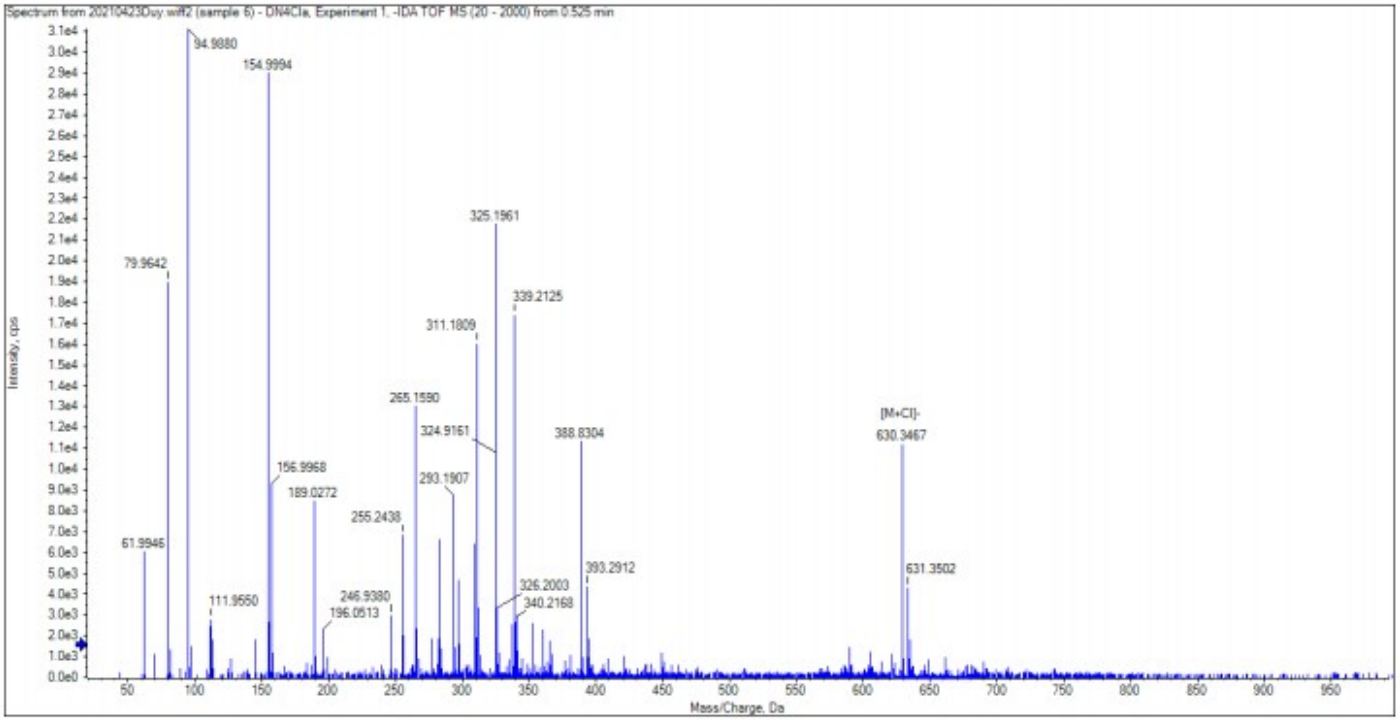
^{13}C-NMR spectrum of compound **3e** (extension)



^{13}C-NMR spectrum of compound **3e** (extension)

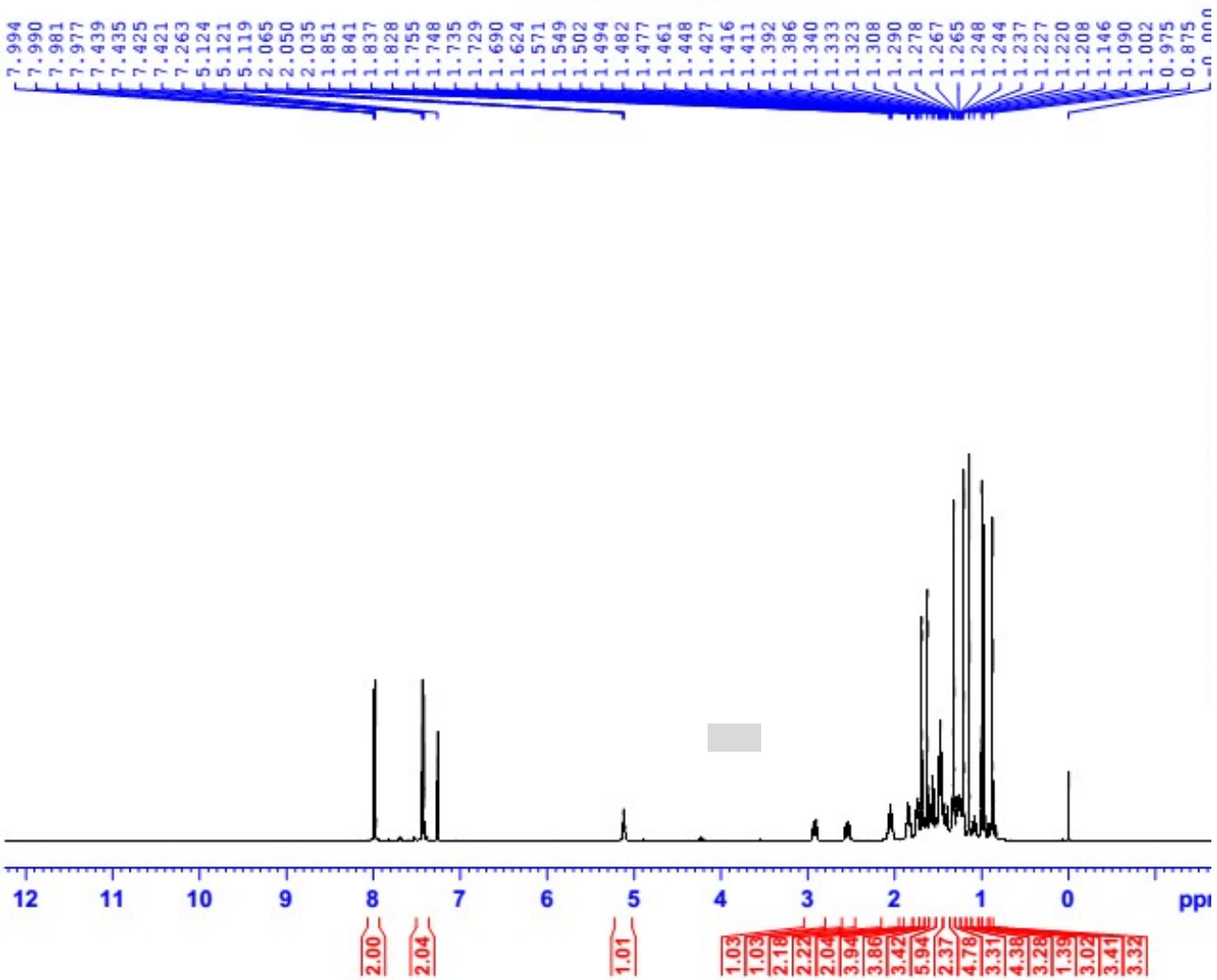
1.8. Compound 3f

Sample name: DN4Cla
Operator: Le Anh VHH
Method: -IDA TOF MS/MS
Date: 2021.04.23

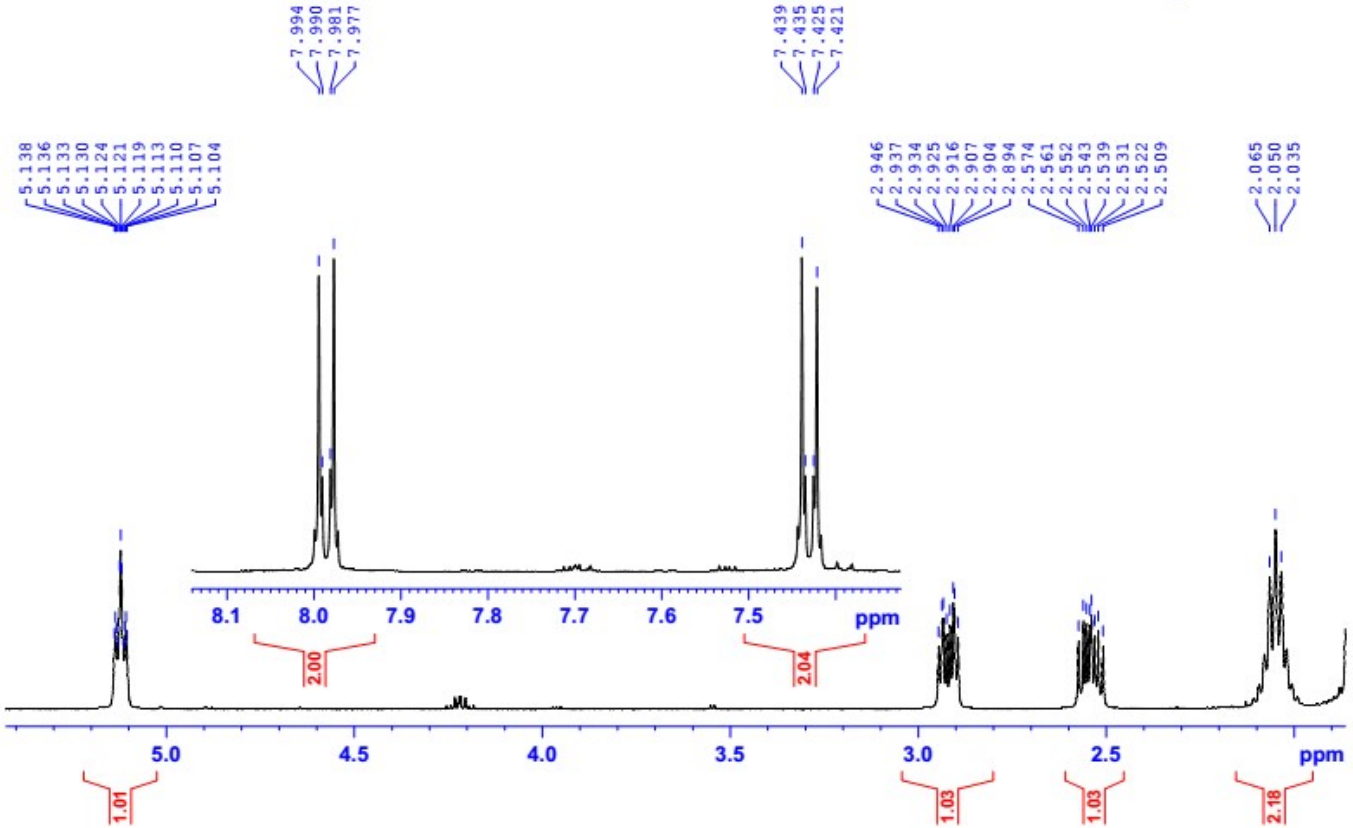


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C37H54ClNO3	630.34862	10.0	-1.2	1			NA/NA

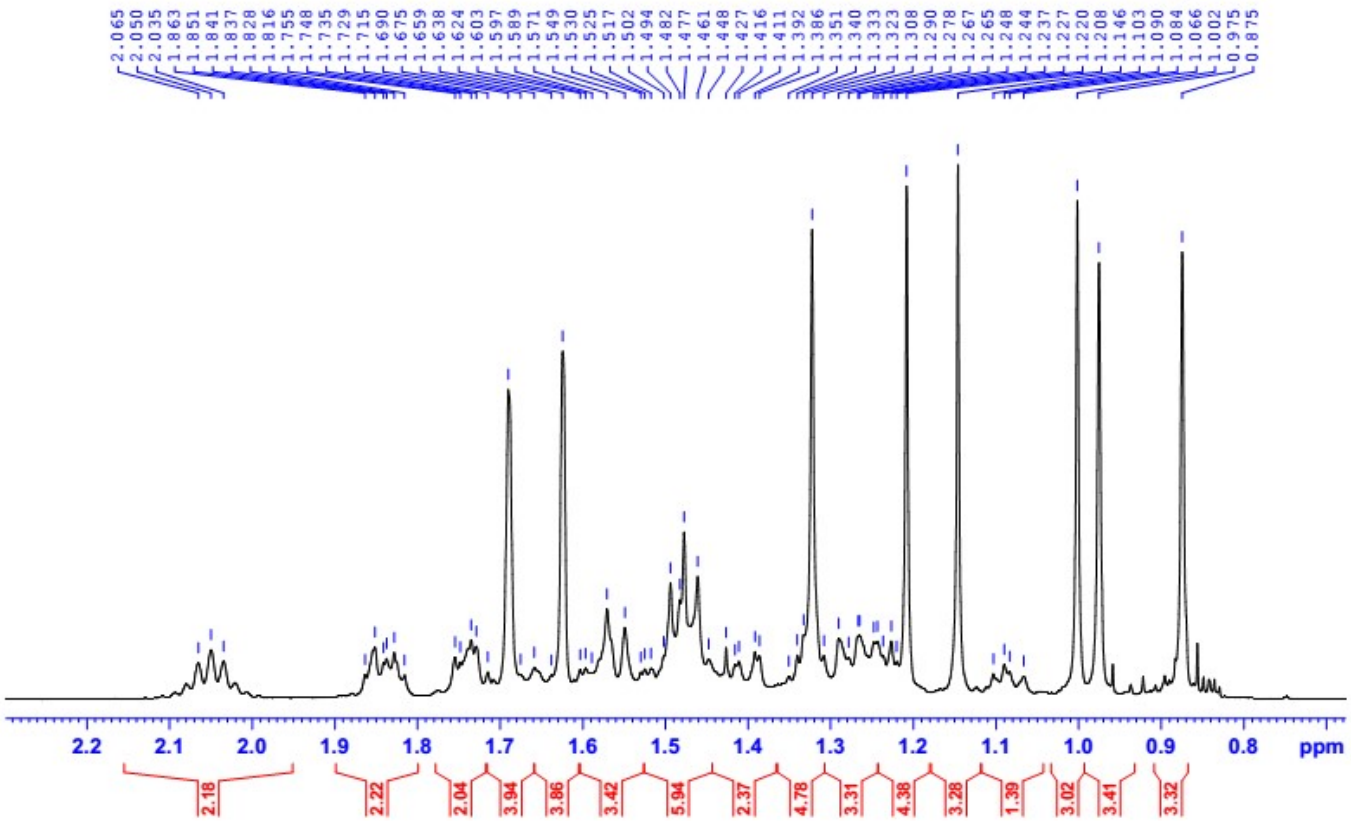
(-)-HR-ESI-MS spectrum of compound **3f**



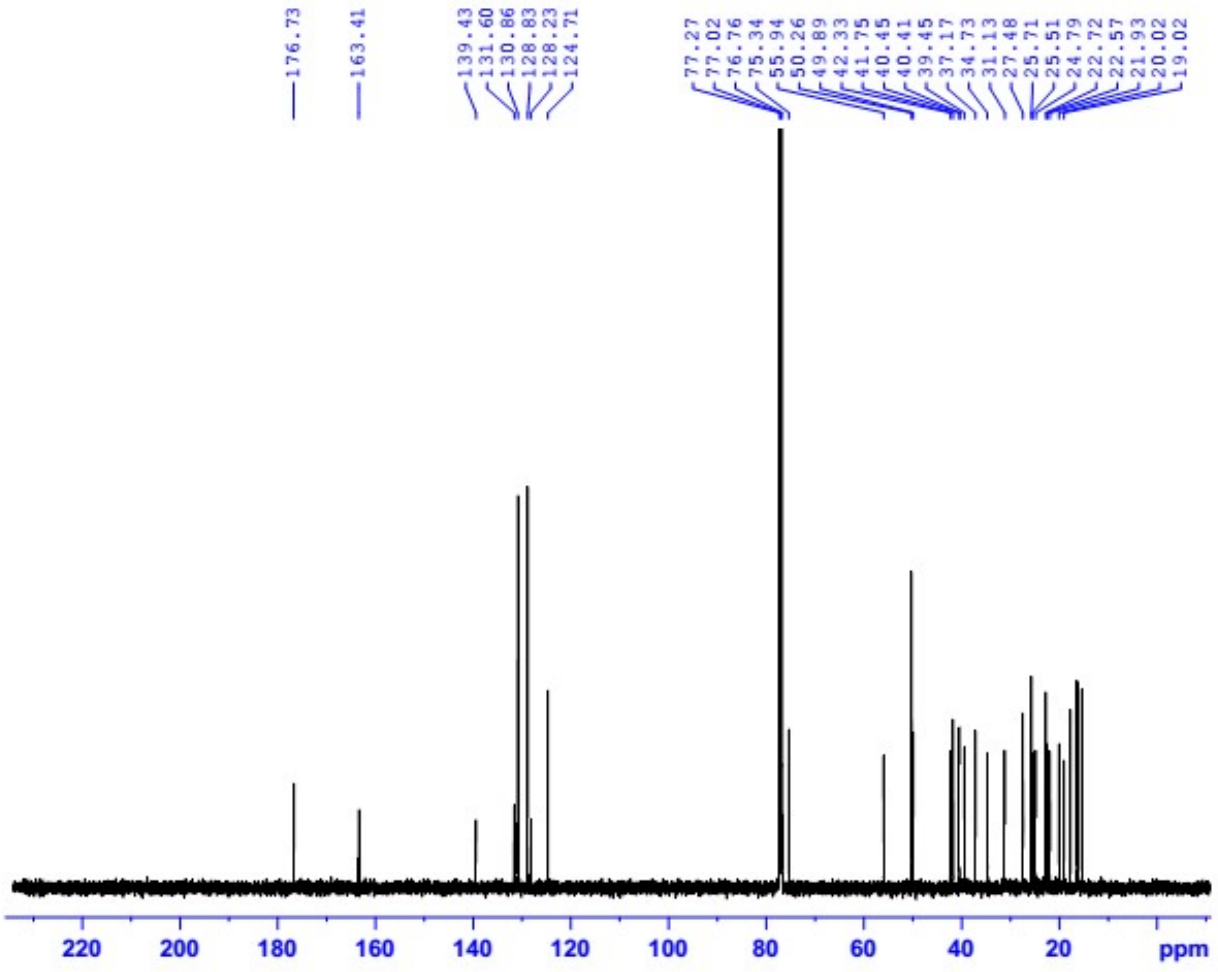
^{1}H-NMR spectrum of compound **3f**



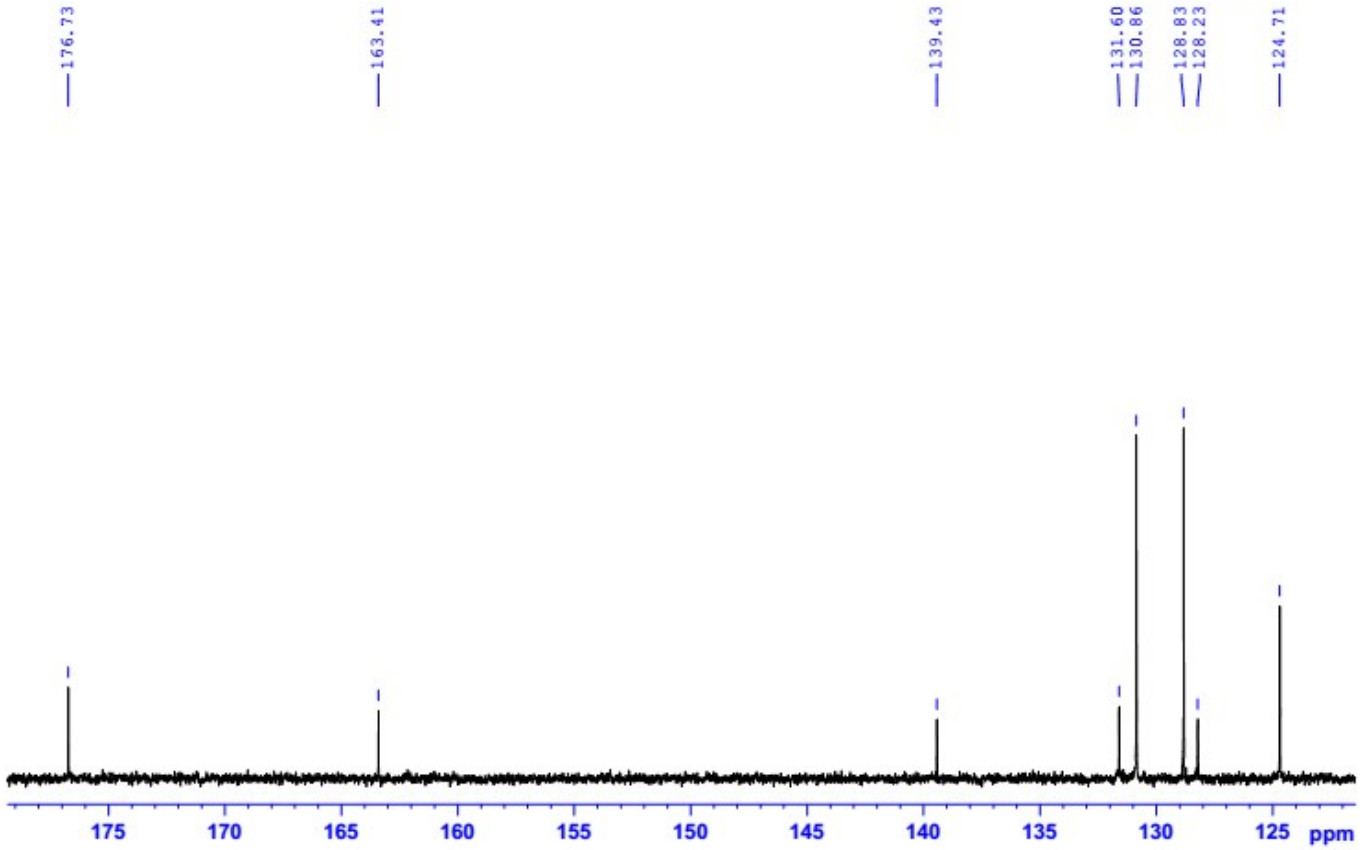
^{1}H-NMR spectrum of compound **3f** (extension)



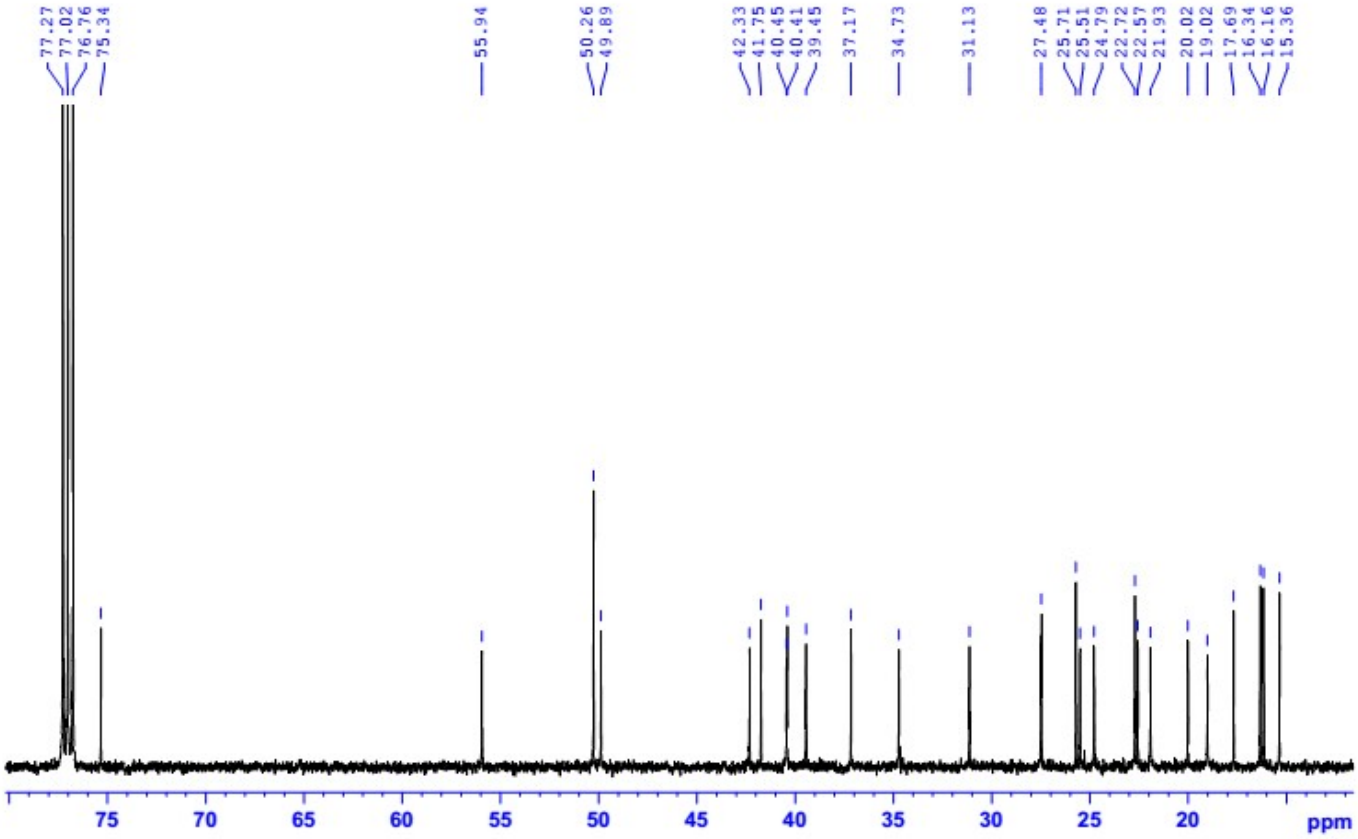
^{1}H-NMR spectrum of compound **3f** (extension)



^{13}C-NMR spectrum of compound **3f**



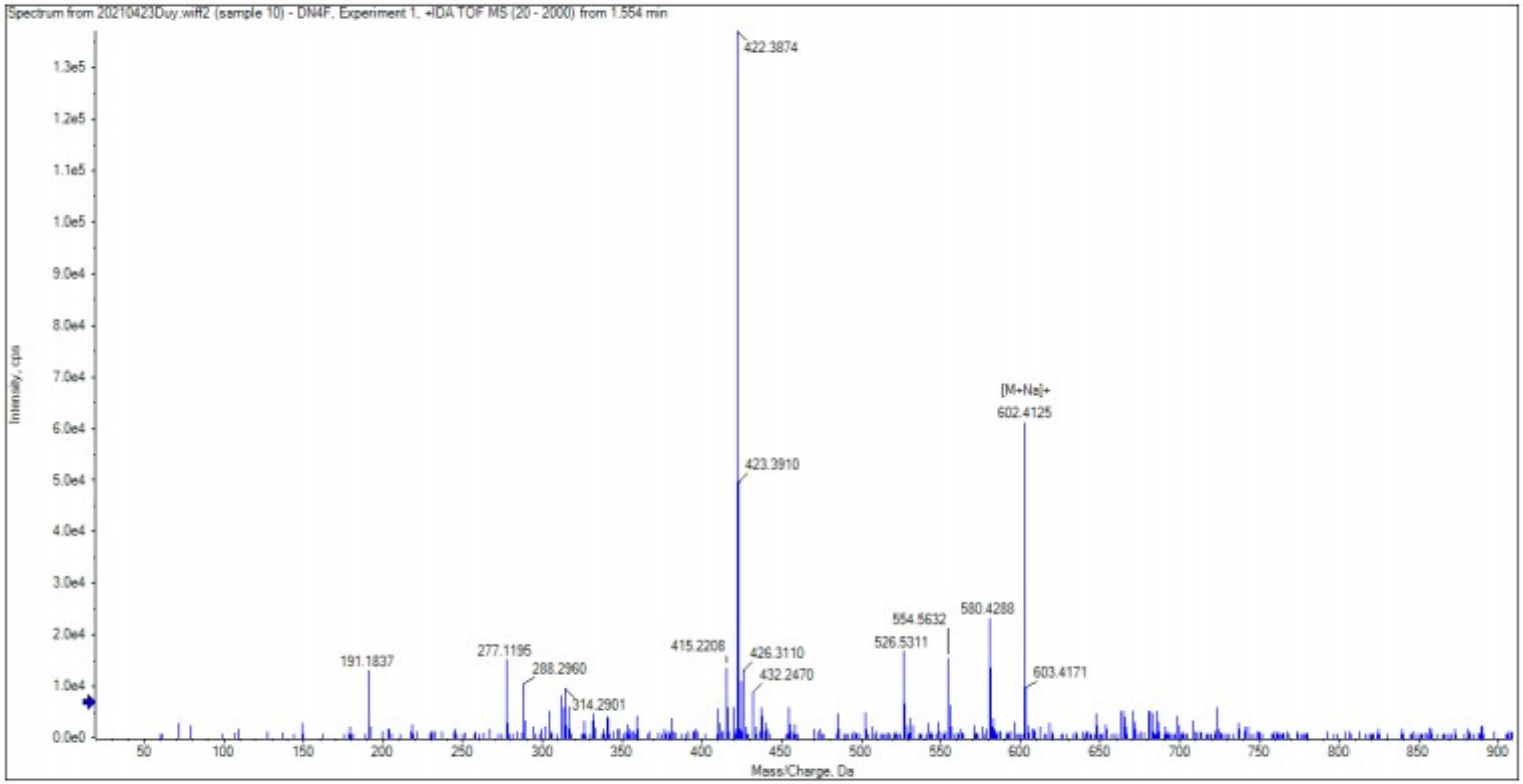
^{13}C-NMR spectrum of compound **3f** (extension)



^{13}C-NMR spectrum of compound **3f** (extension)

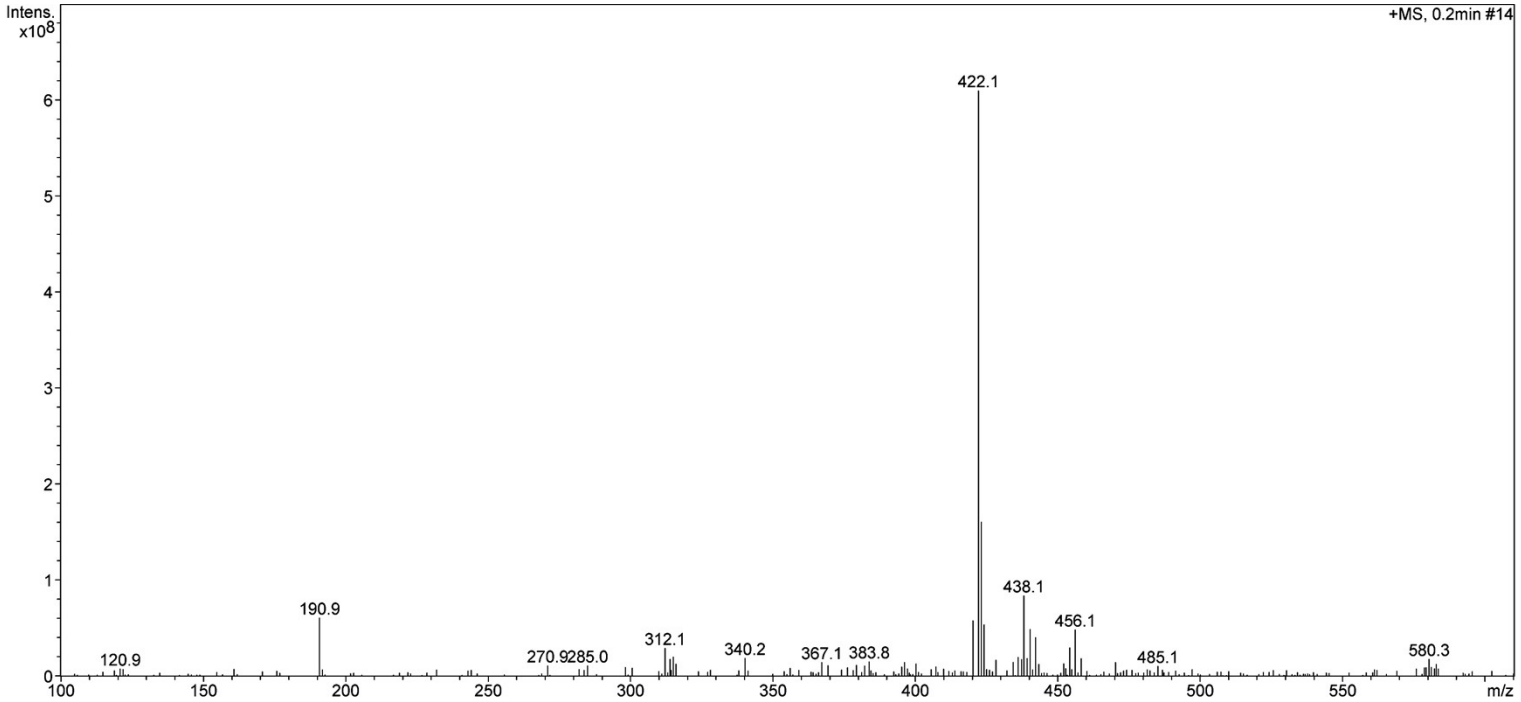
1.9. Compound 3g

Sample name: DN4F
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

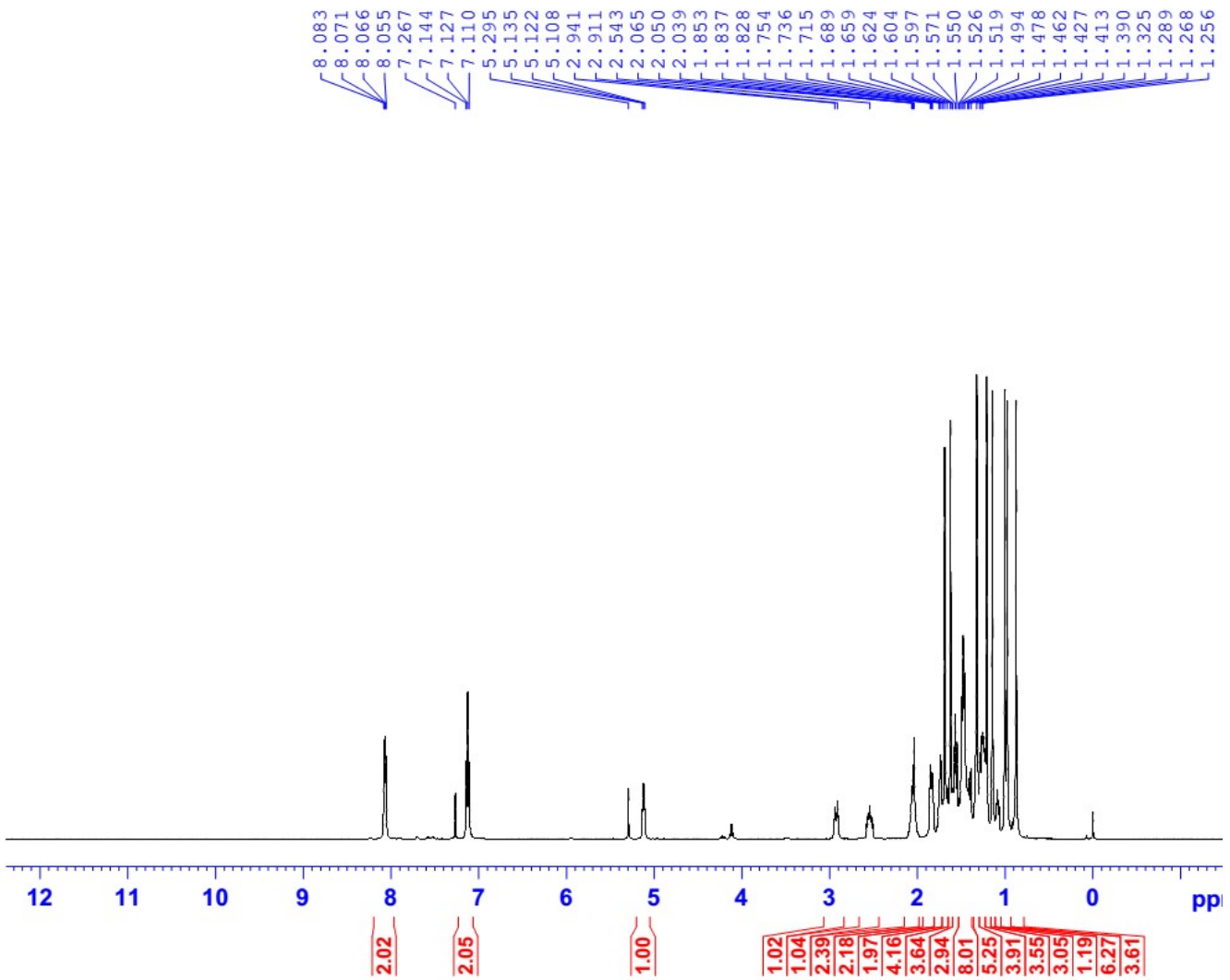


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C37H54FNO3	602.40979	11.0	4.0	1			NA/NA

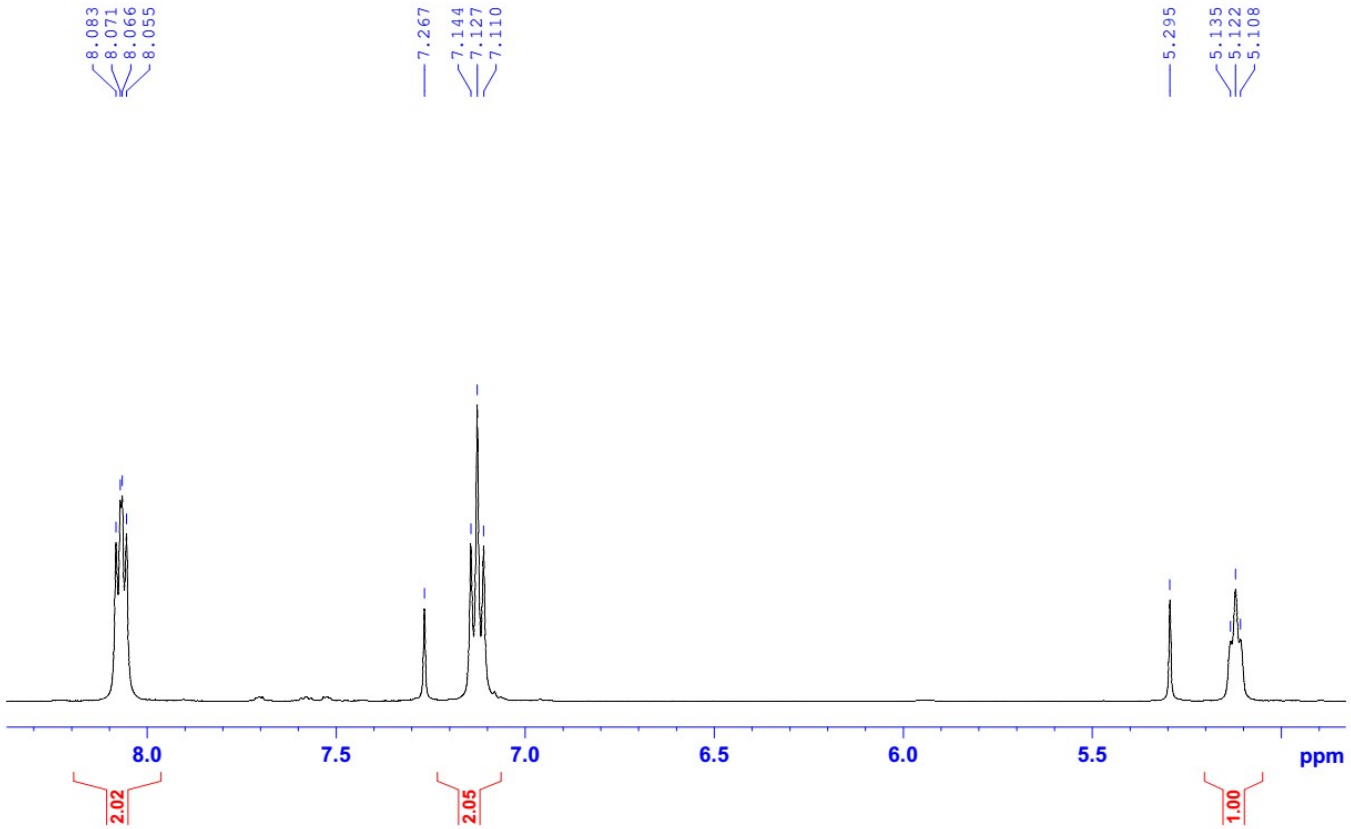
(+)-HR-ESI-MS spectrum of compound **3g**



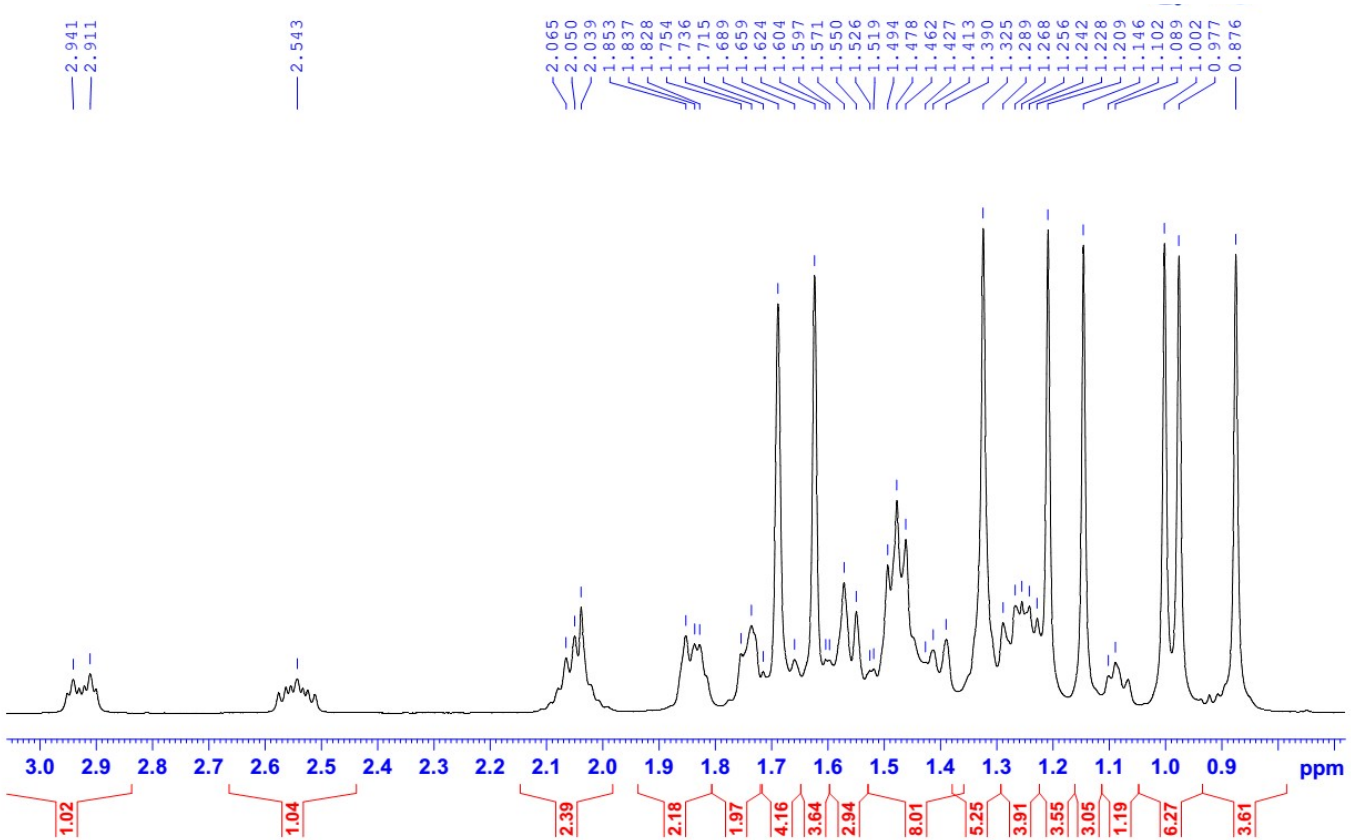
(+)-ESI–MS spectrum of compound **3g**



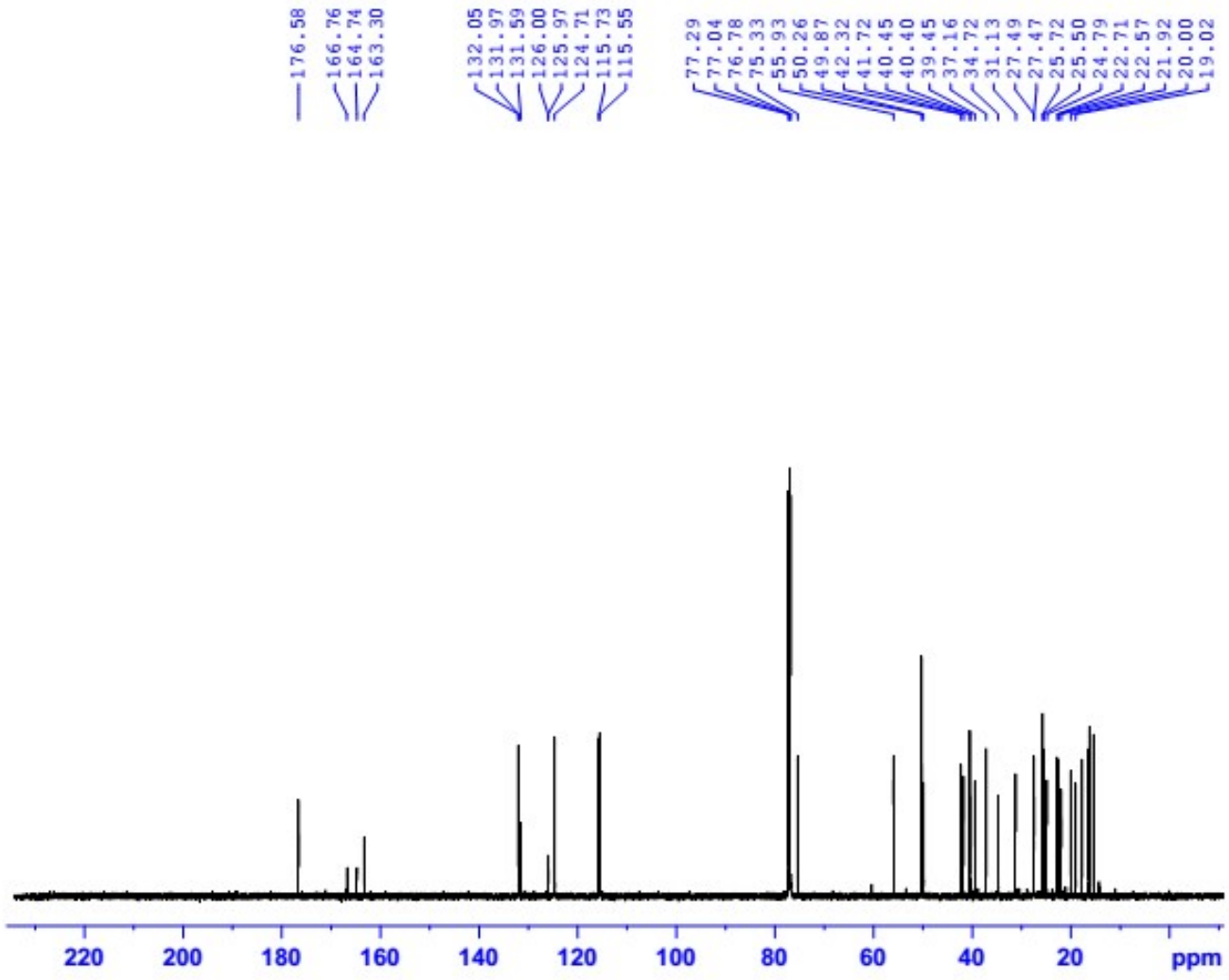
^{1}H-NMR spectrum of compound **3g**



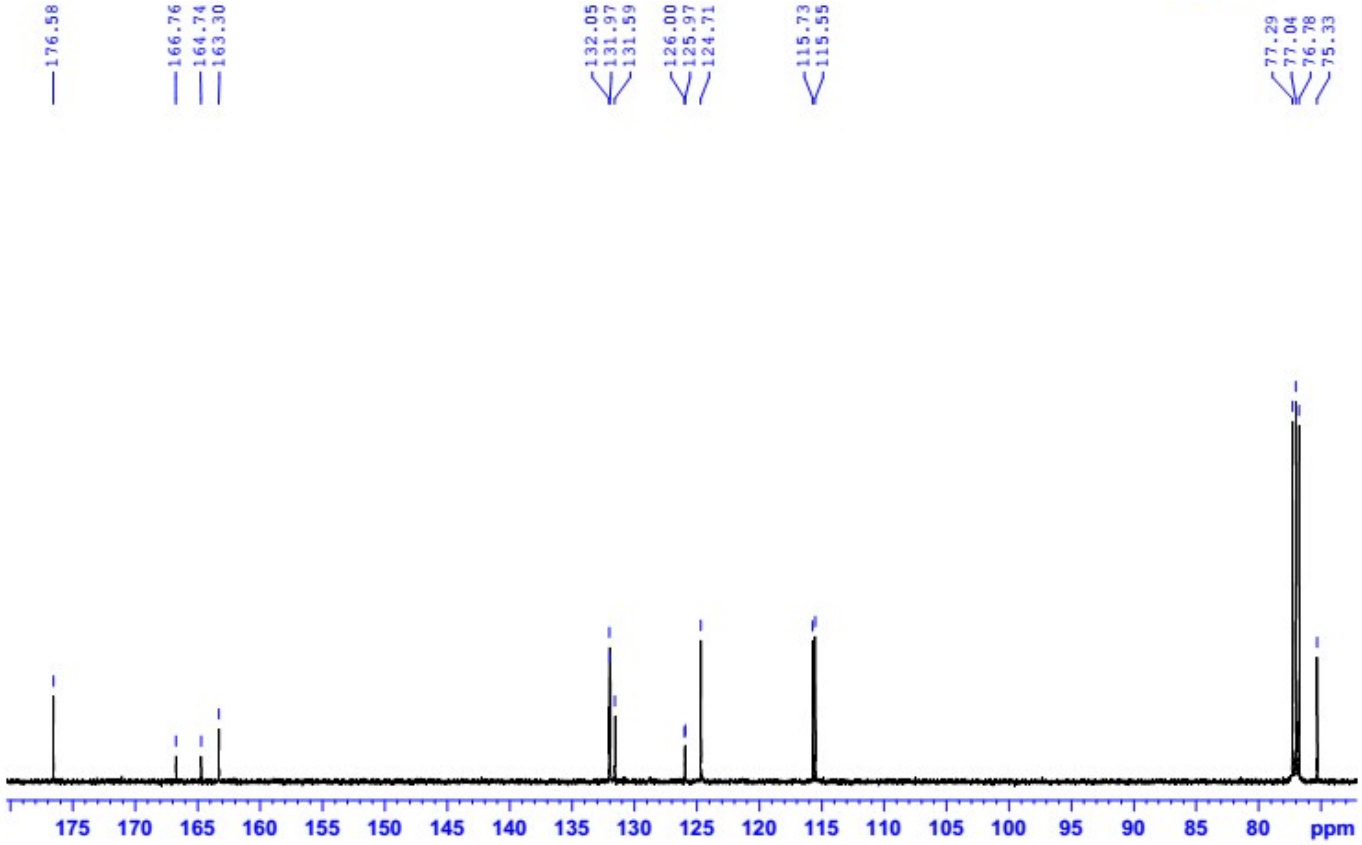
^{1}H-NMR spectrum of compound **3g** (extension)



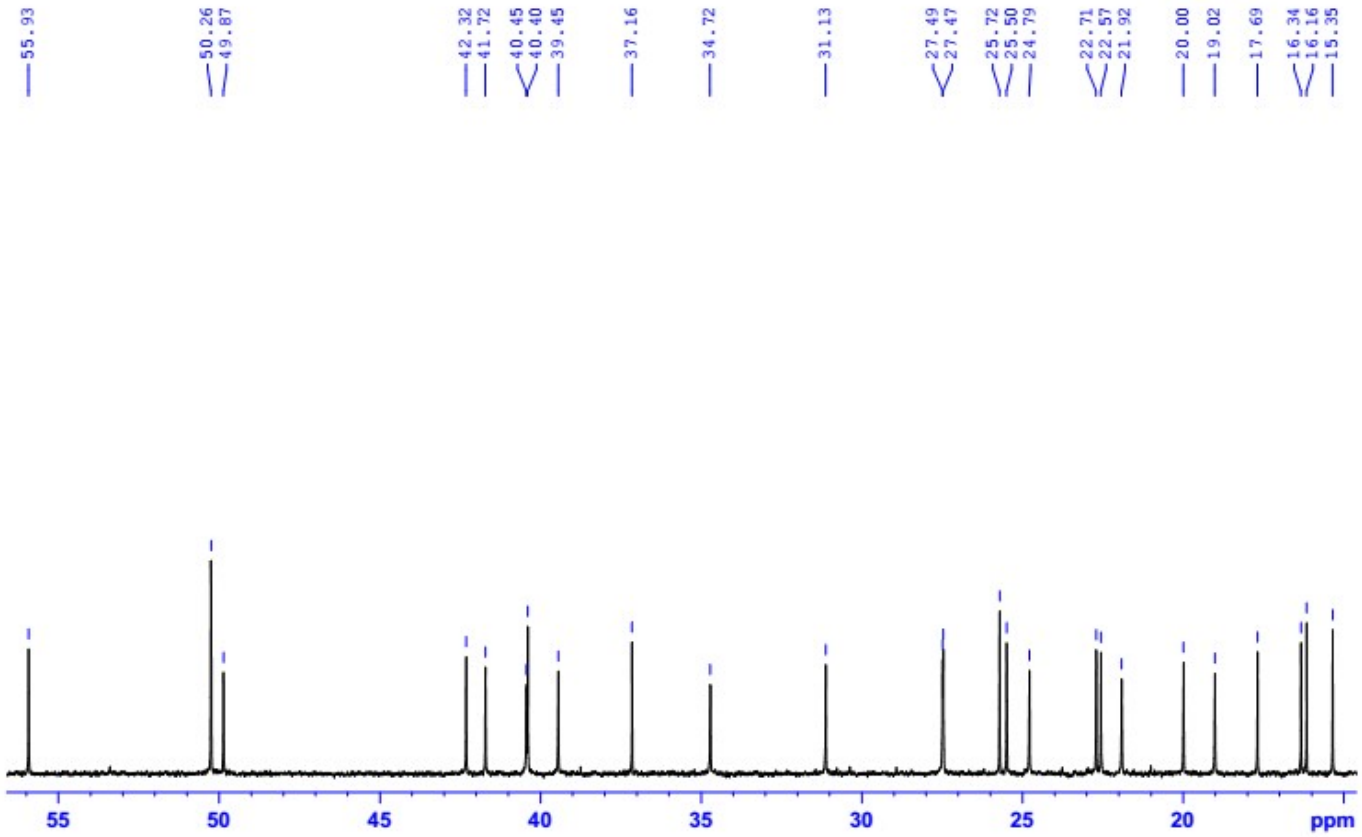
^{1}H-NMR spectrum of compound **3g** (extension)



^{13}C-NMR spectrum of compound **3g**



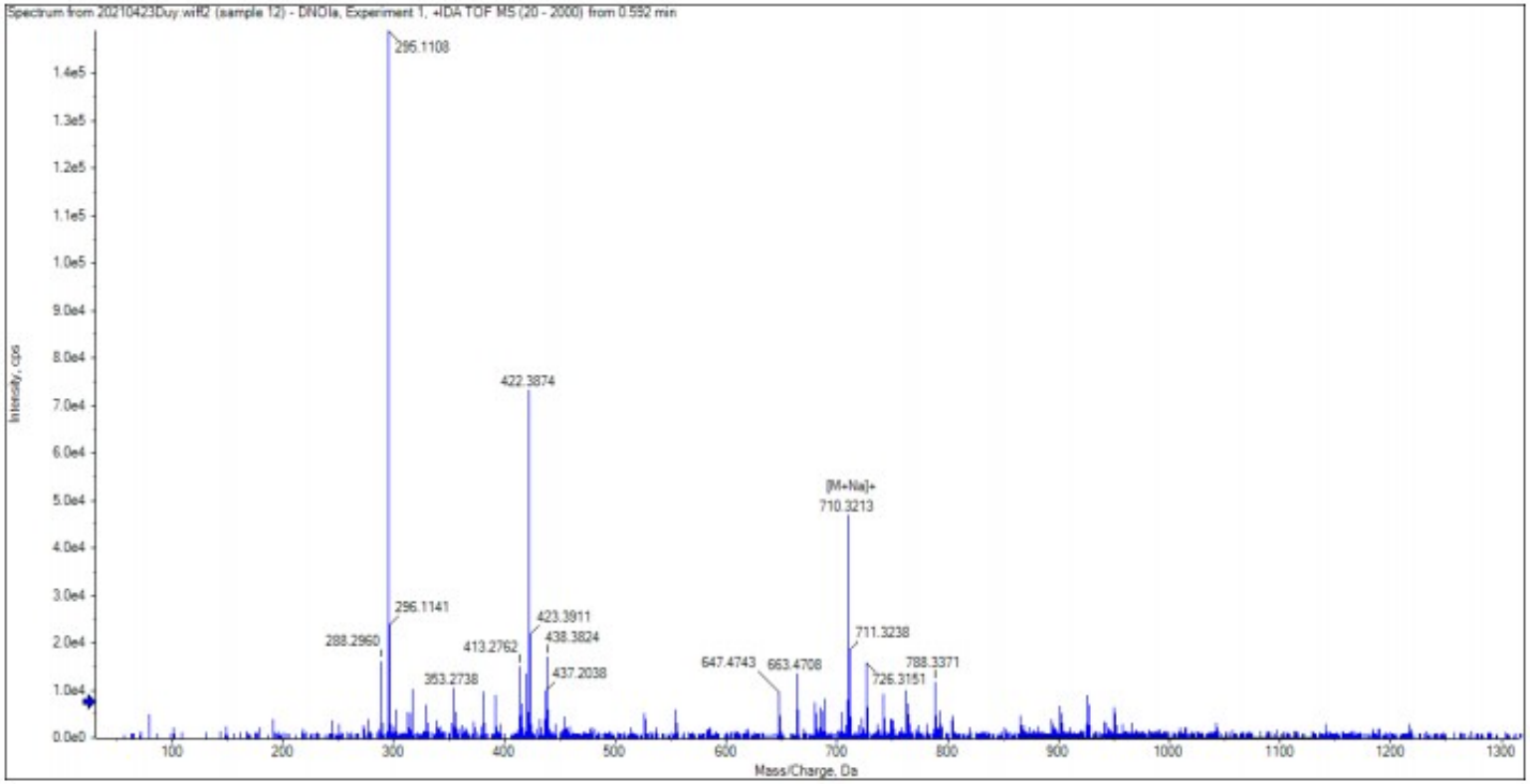
^{13}C-NMR spectrum of compound **3g** (extension)



^{13}C-NMR spectrum of compound **3g** (extension)

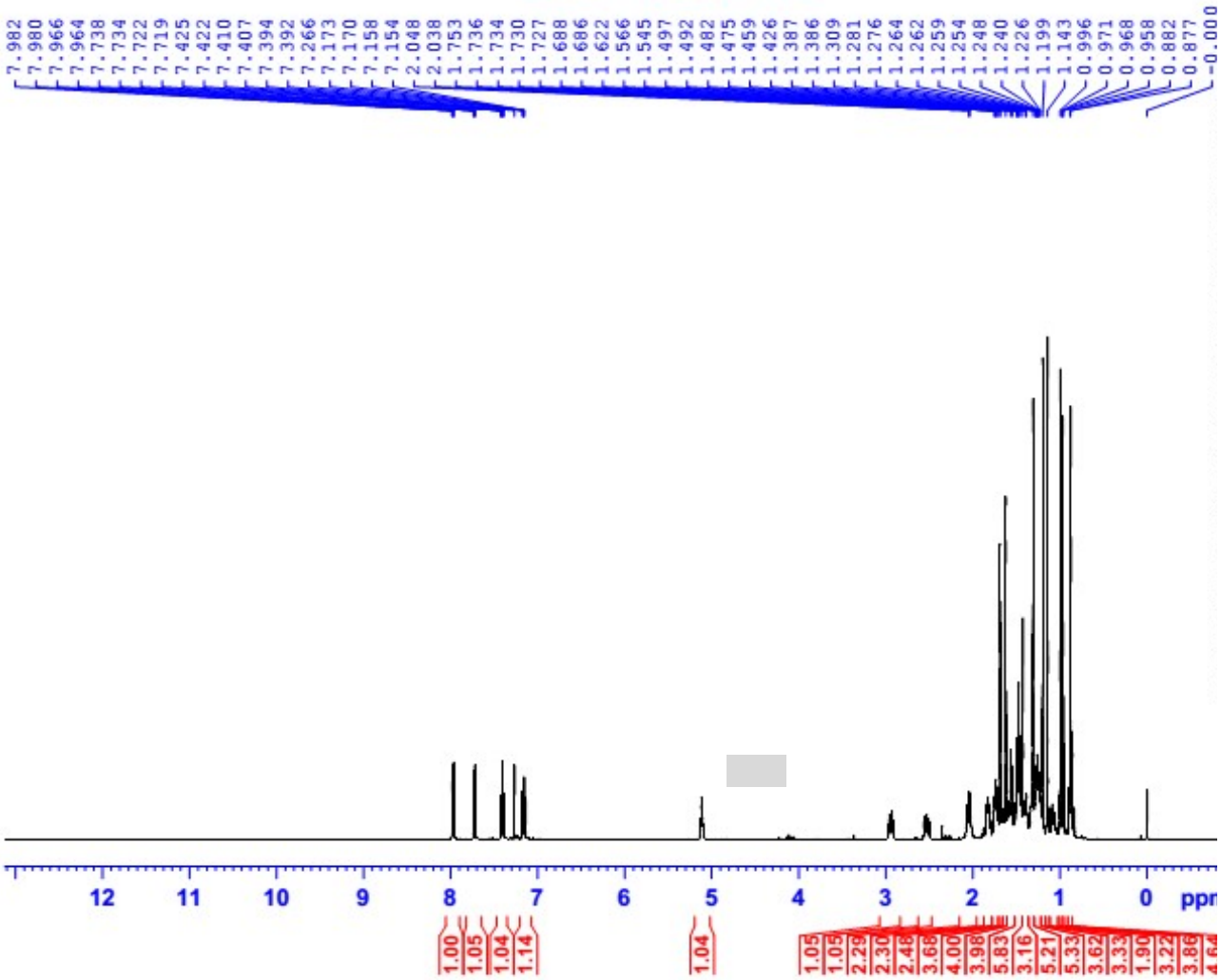
1.10. Compound 3h

Sample name: DNOIa
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

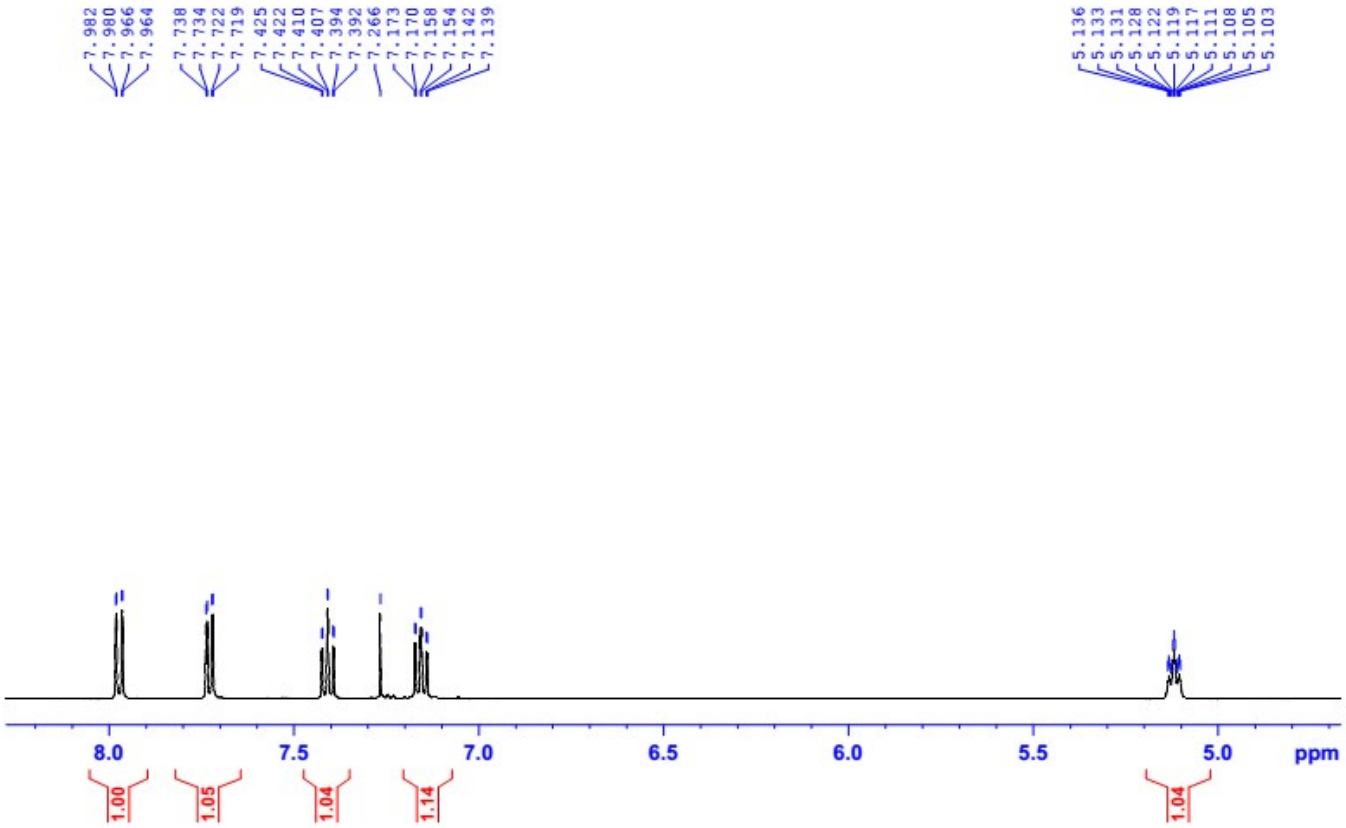


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C37H54INO3	710.31706	11.0	4.3	1			NA/NA

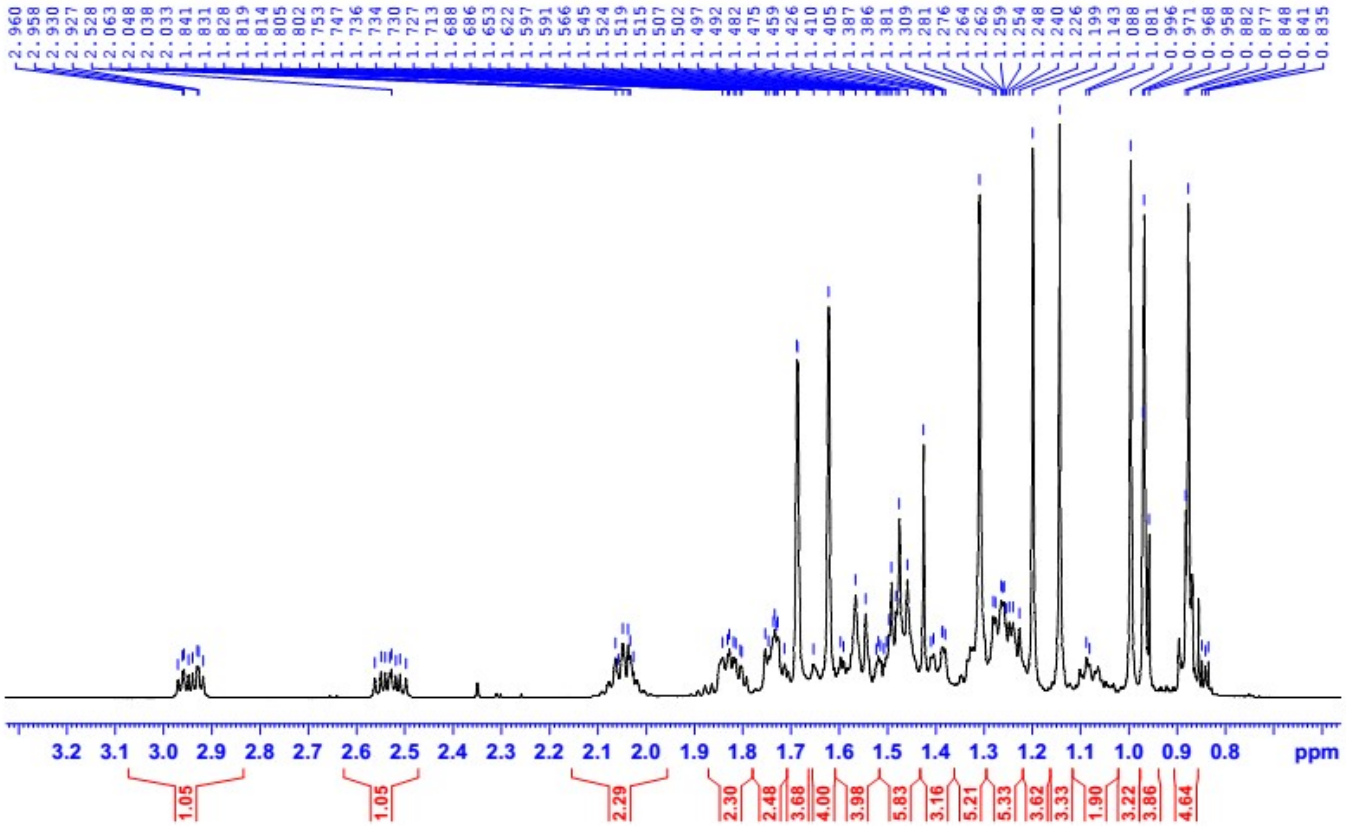
(+)-HR-ESI-MS spectrum of compound **3h**



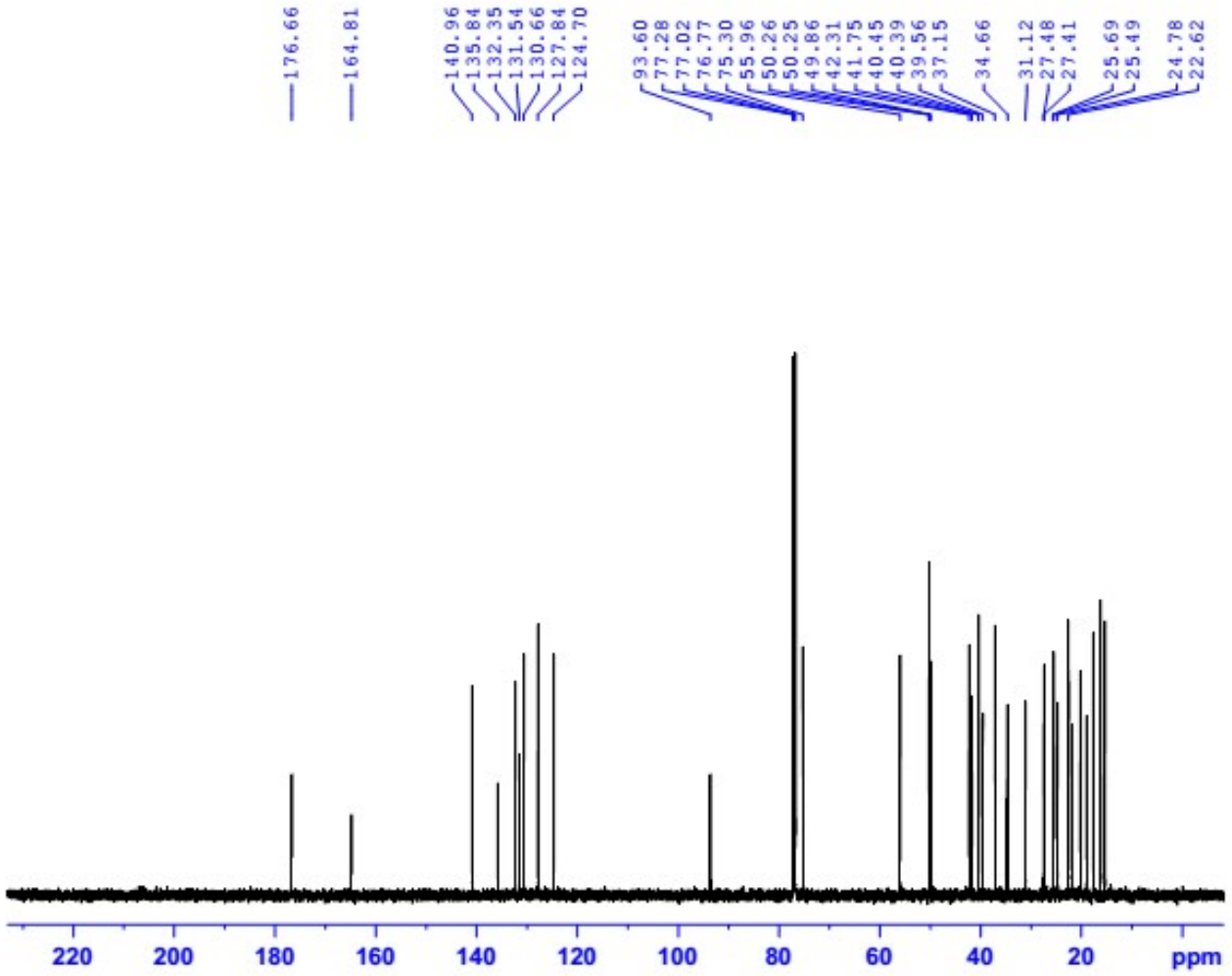
^{1}H-NMR spectrum of compound **3h**



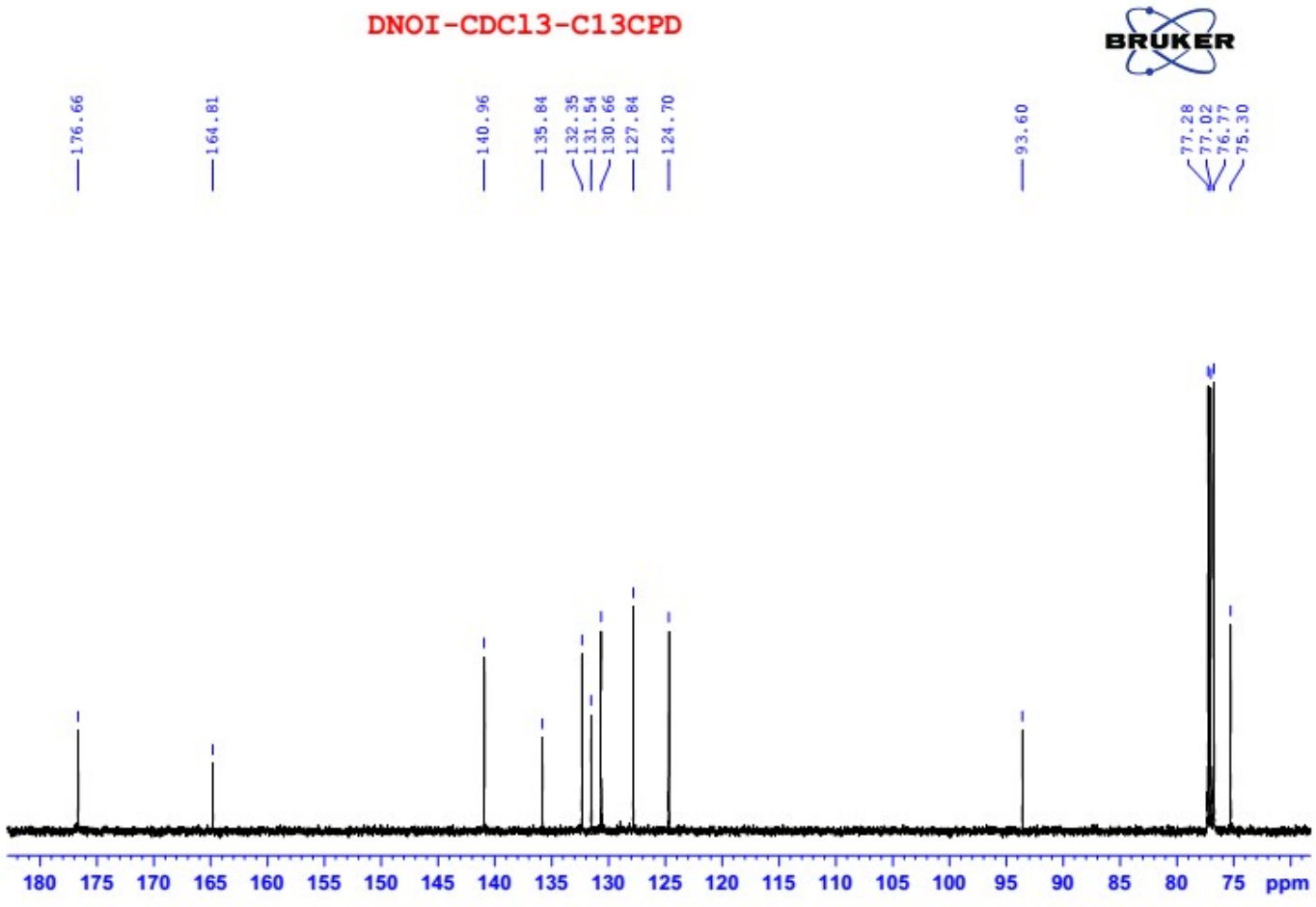
^{1}H-NMR spectrum of compound **3h** (extension)



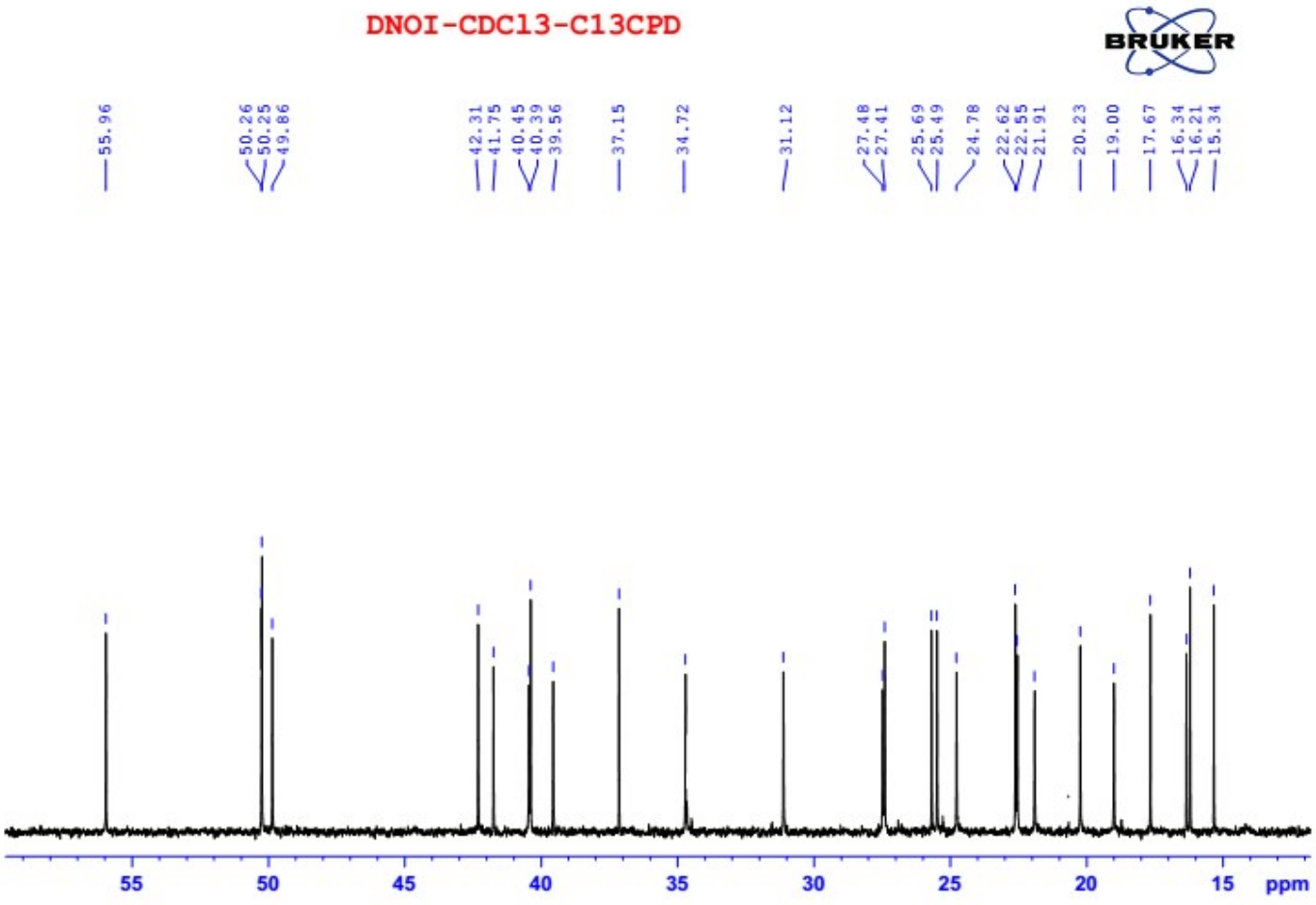
^{1}H-NMR spectrum of compound **3h** (extension)



^{13}C-NMR spectrum of compound **3h**

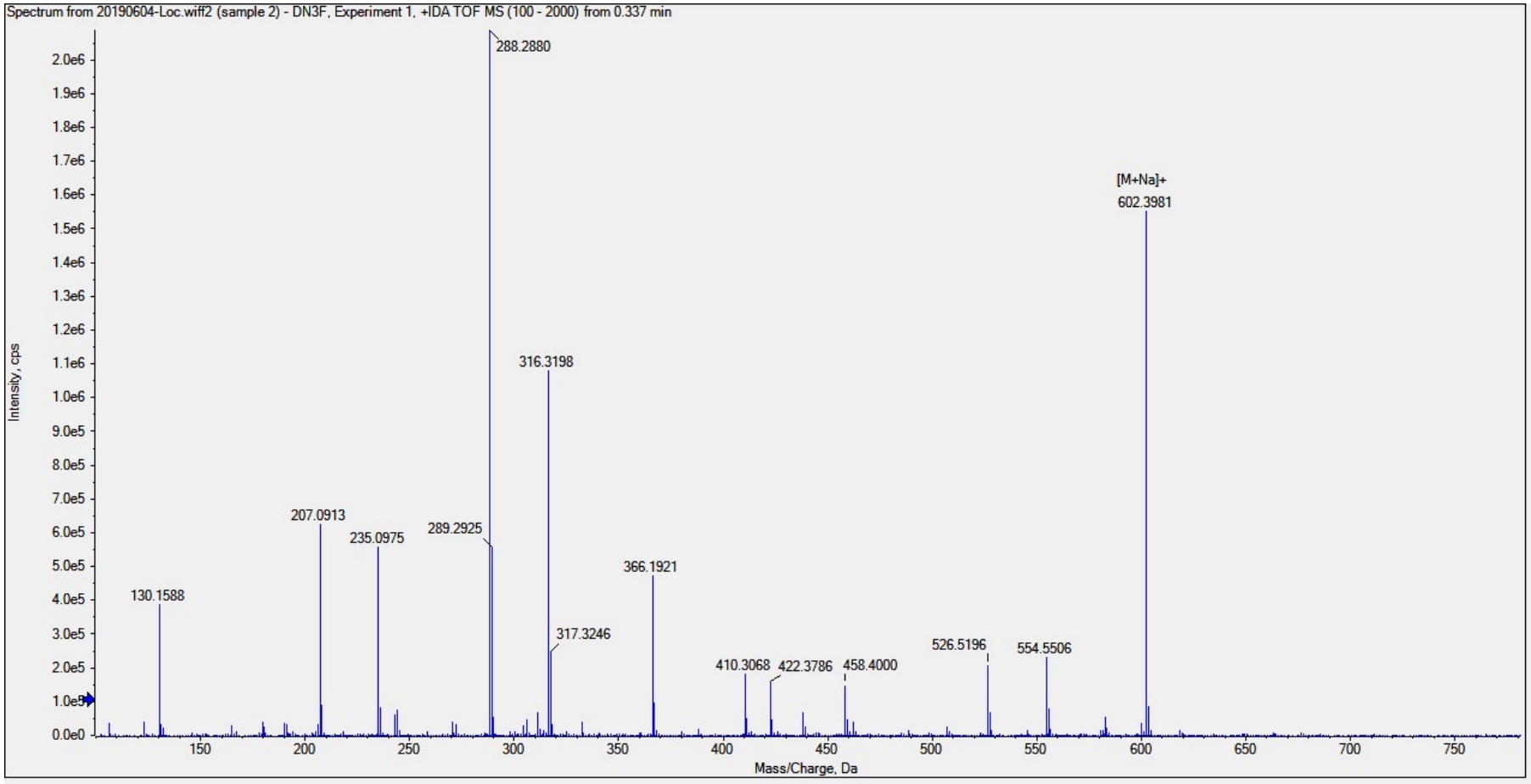


^{13}C-NMR spectrum of compound **3h** (extension)

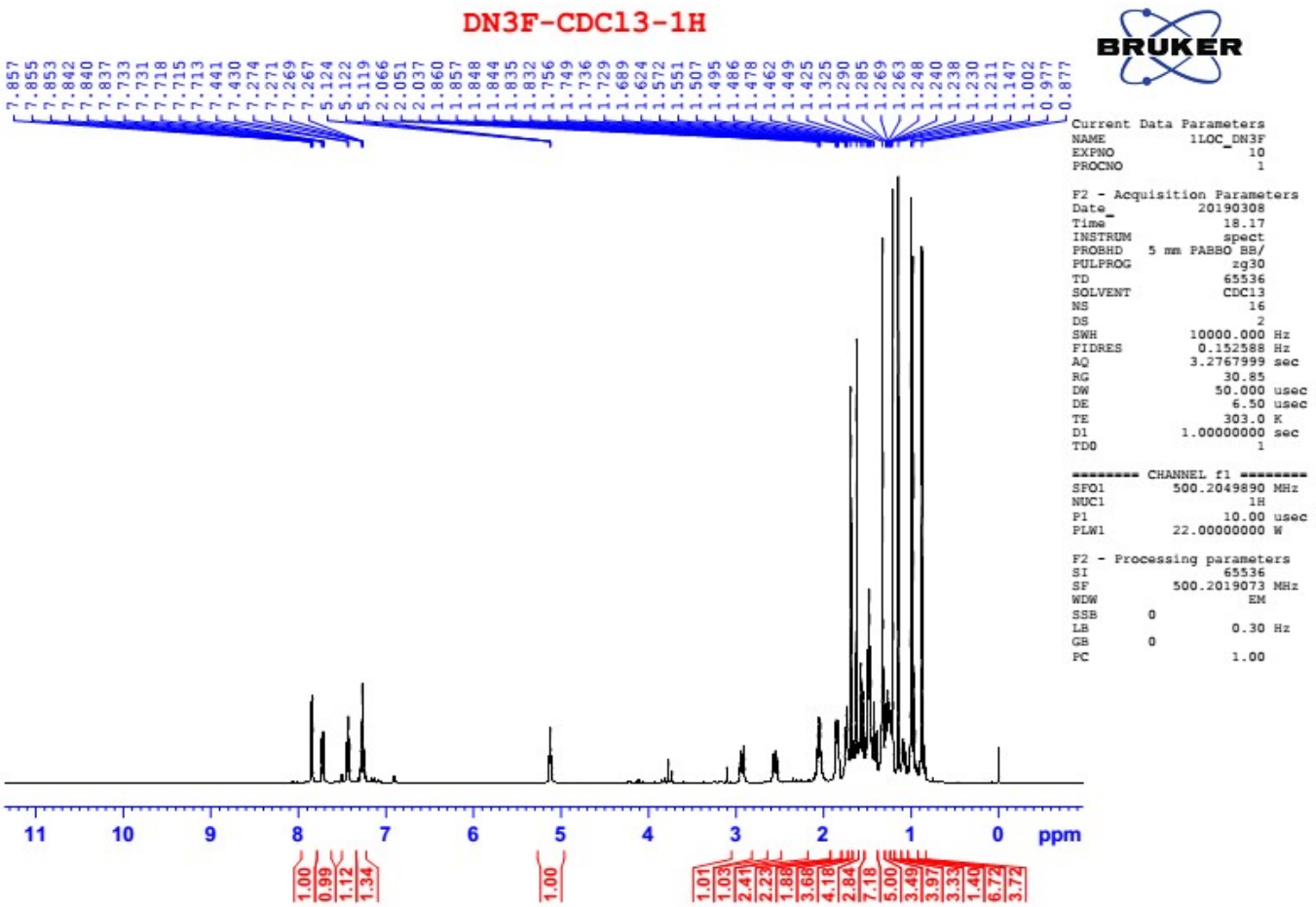


^{13}C-NMR spectrum of compound **3h** (extension)

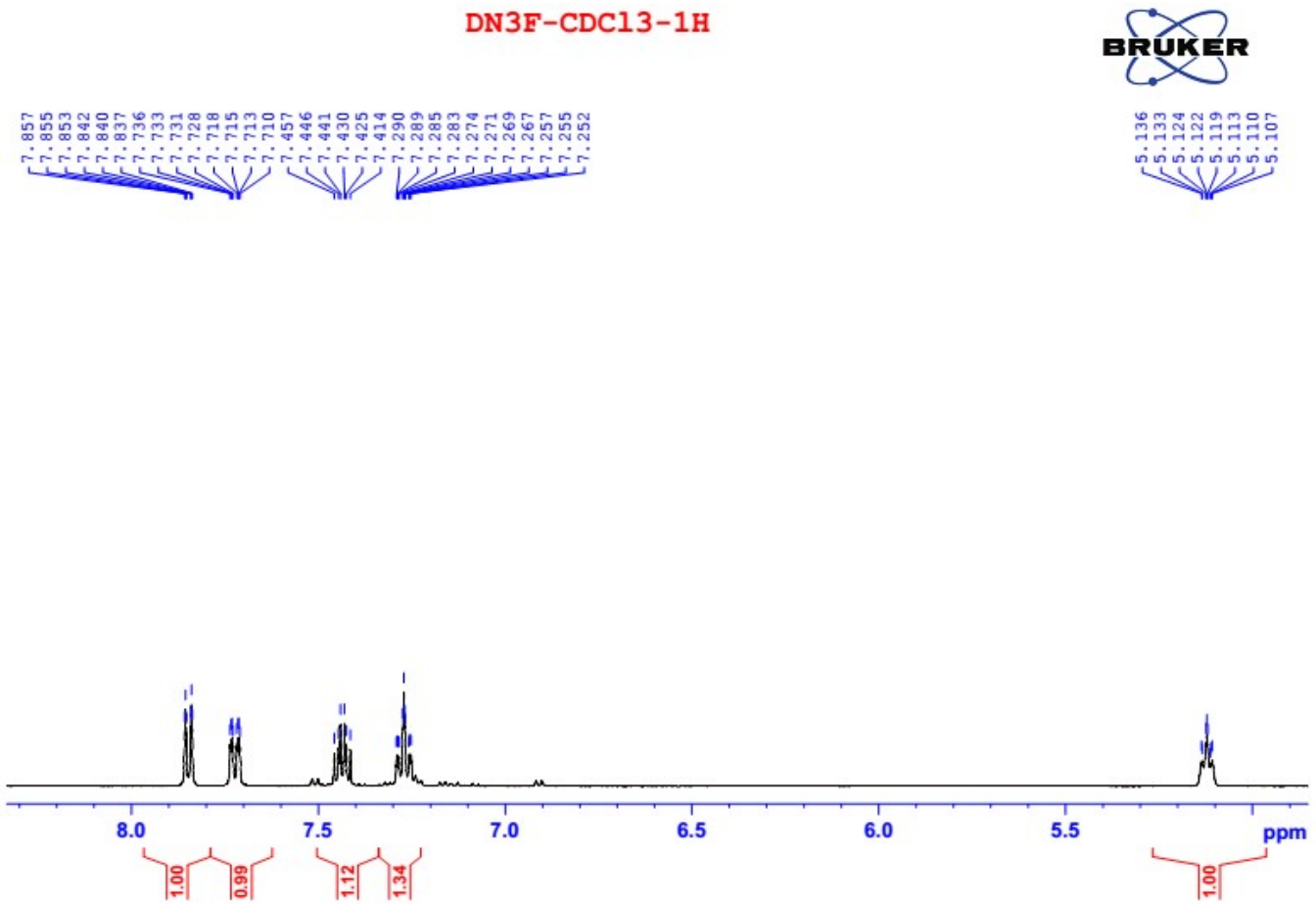
1.11. Compound 3i



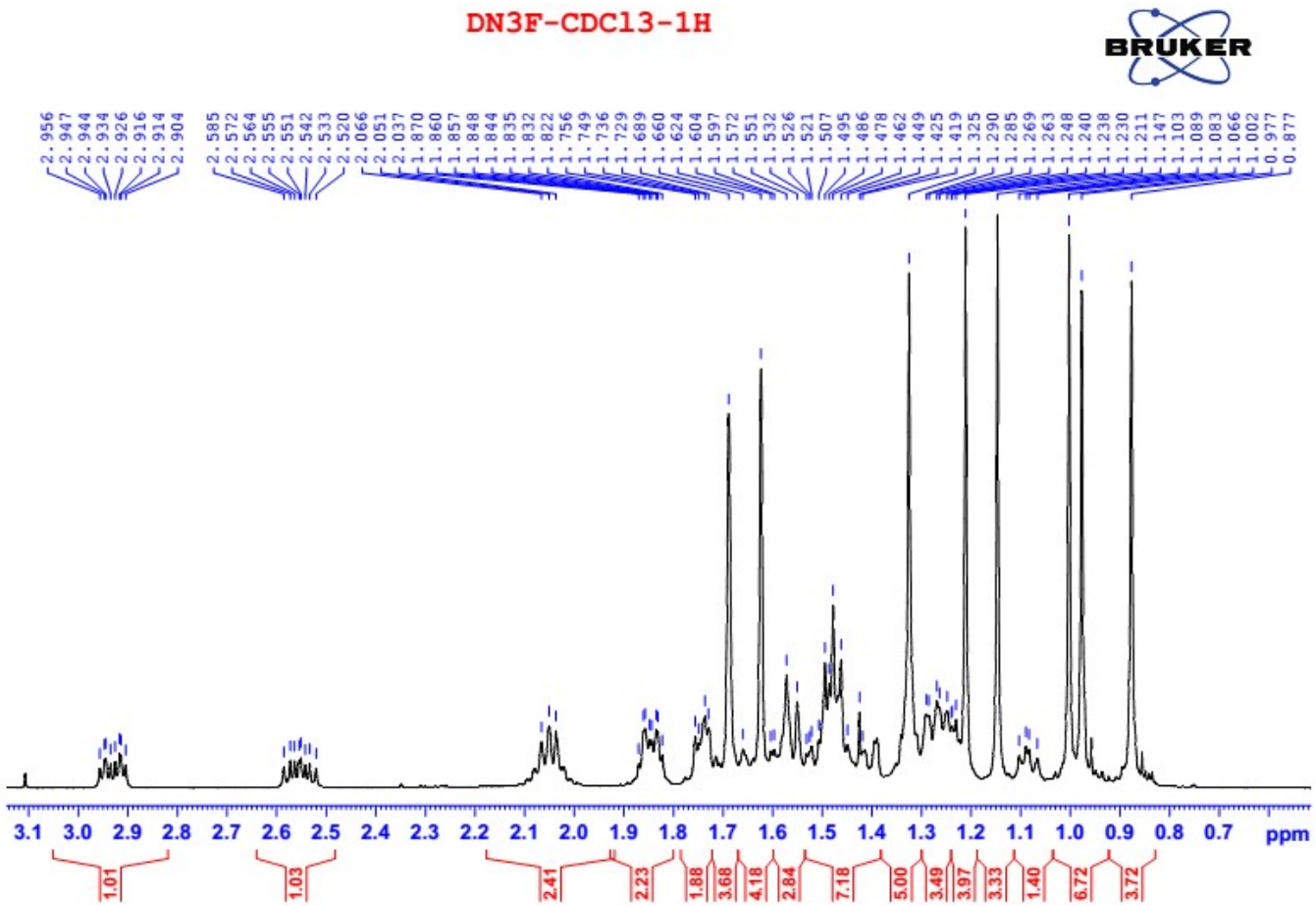
(+)-HR-ESI-MS spectrum of compound **3i**



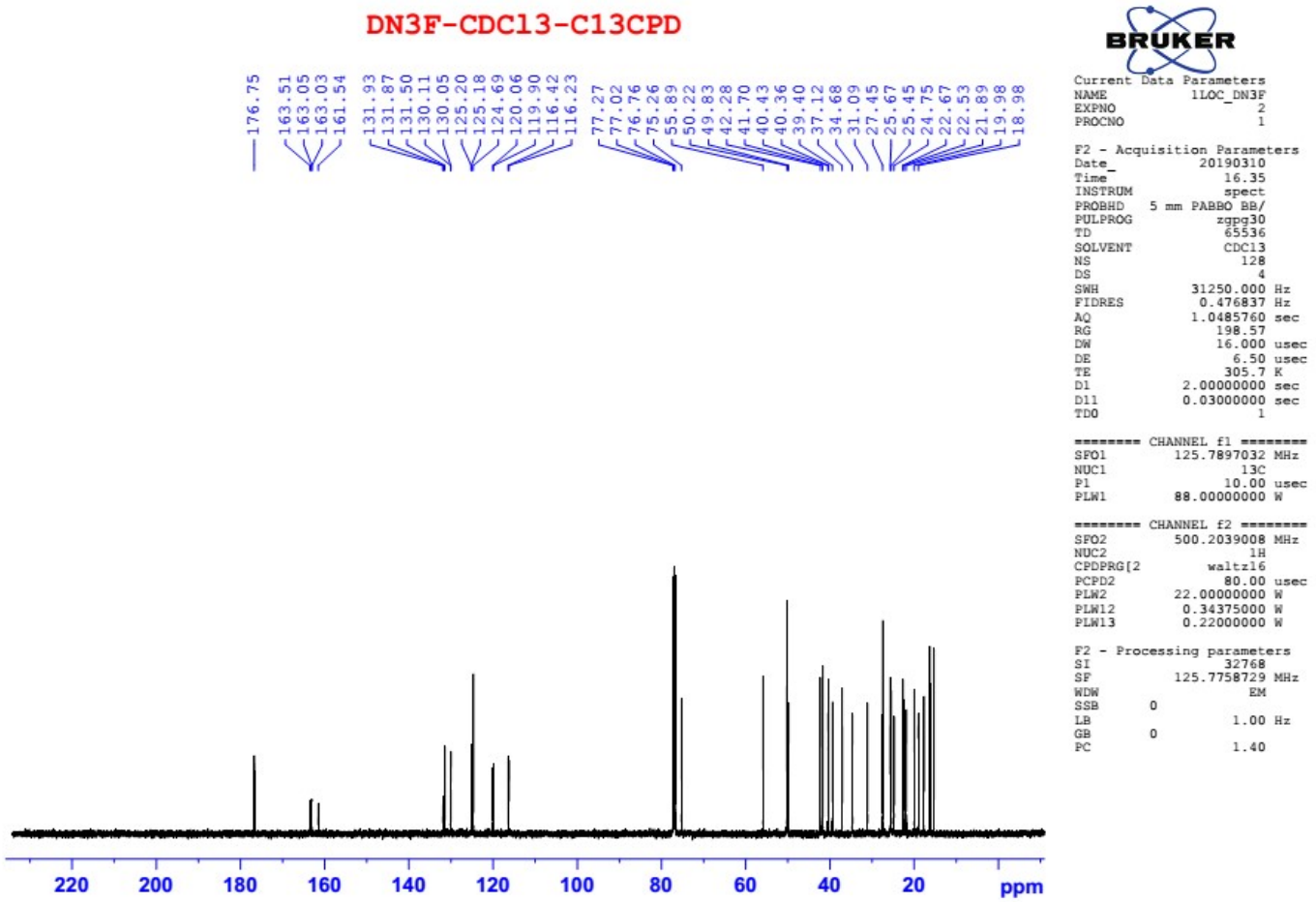
[1]H-NMR spectrum of compound **3i**



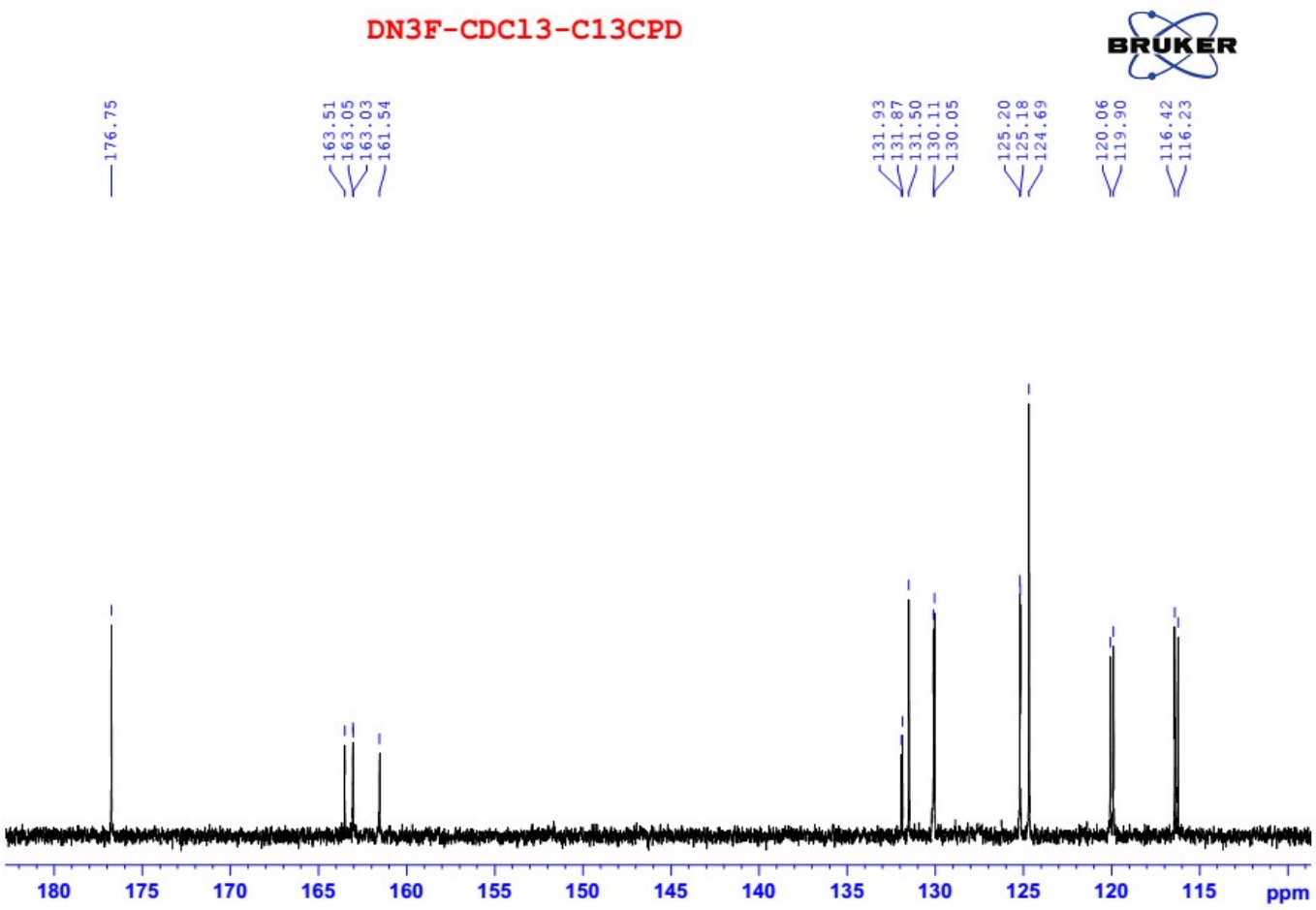
^{1}H-NMR spectrum of compound **3i** (extension)



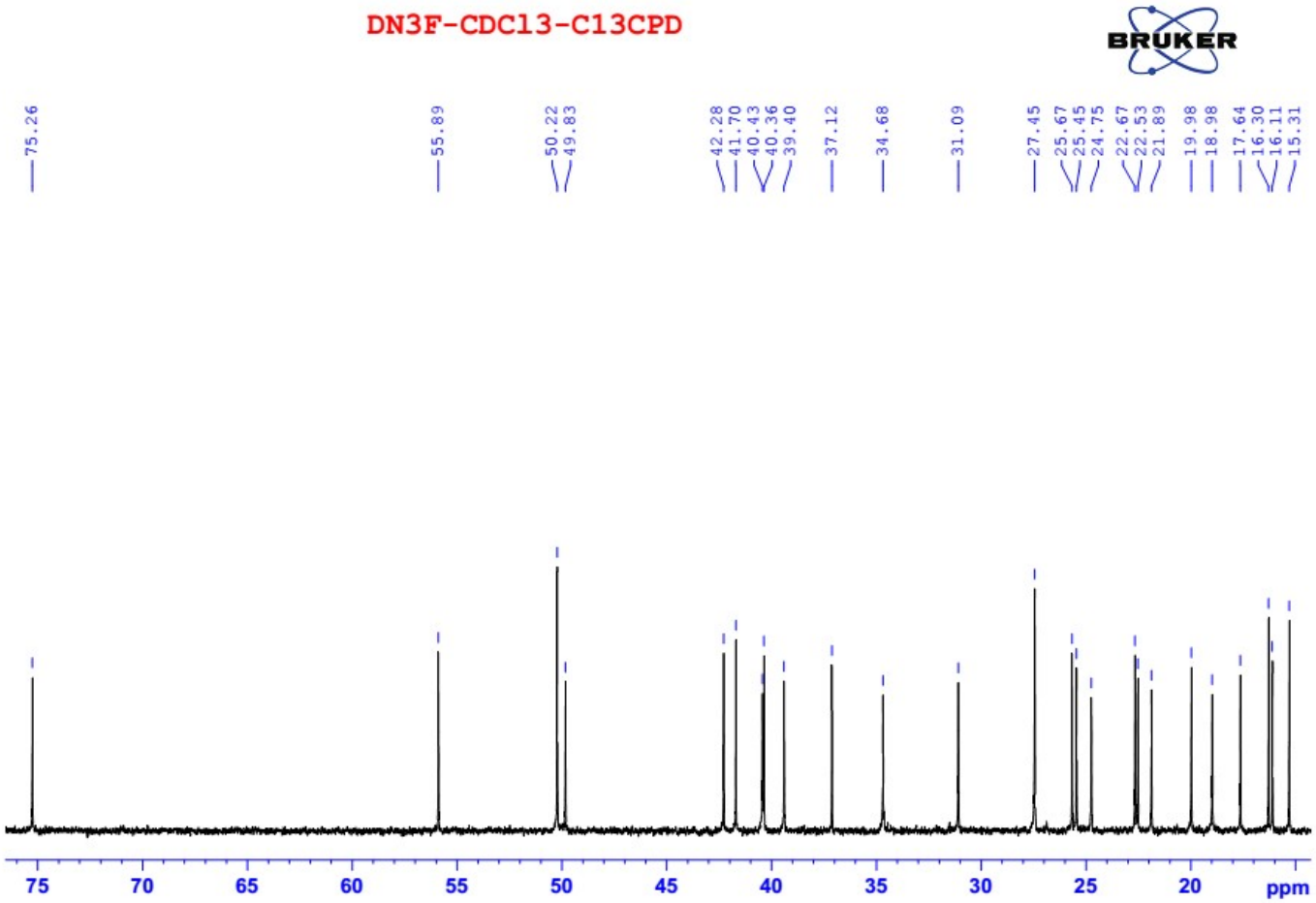
^{1}H-NMR spectrum of compound **3i** (extension)



^{13}C-NMR spectrum of compound **3i**



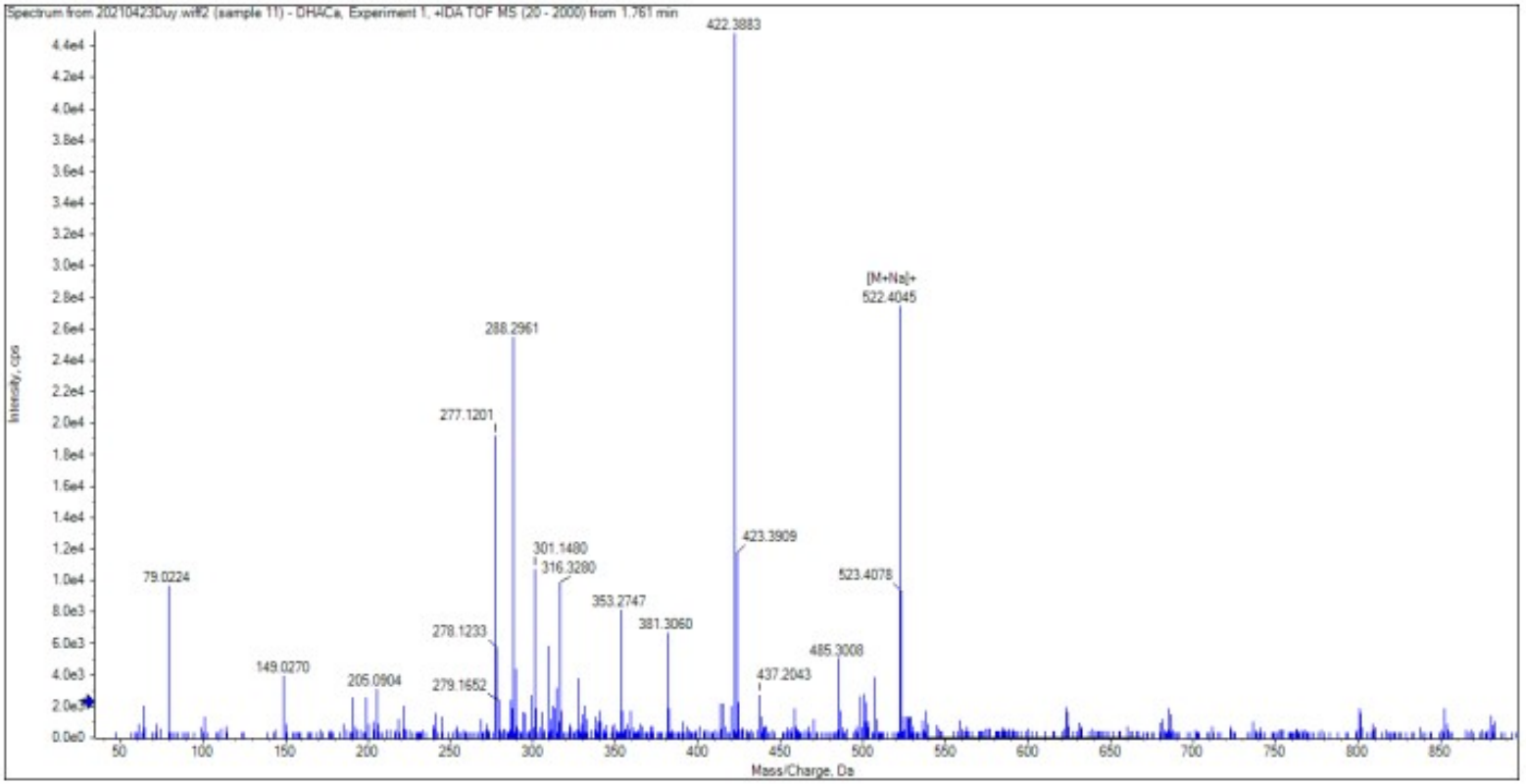
^{13}C-NMR spectrum of compound **3i** (extension)



^{13}C-NMR spectrum of compound **3i** (extension)

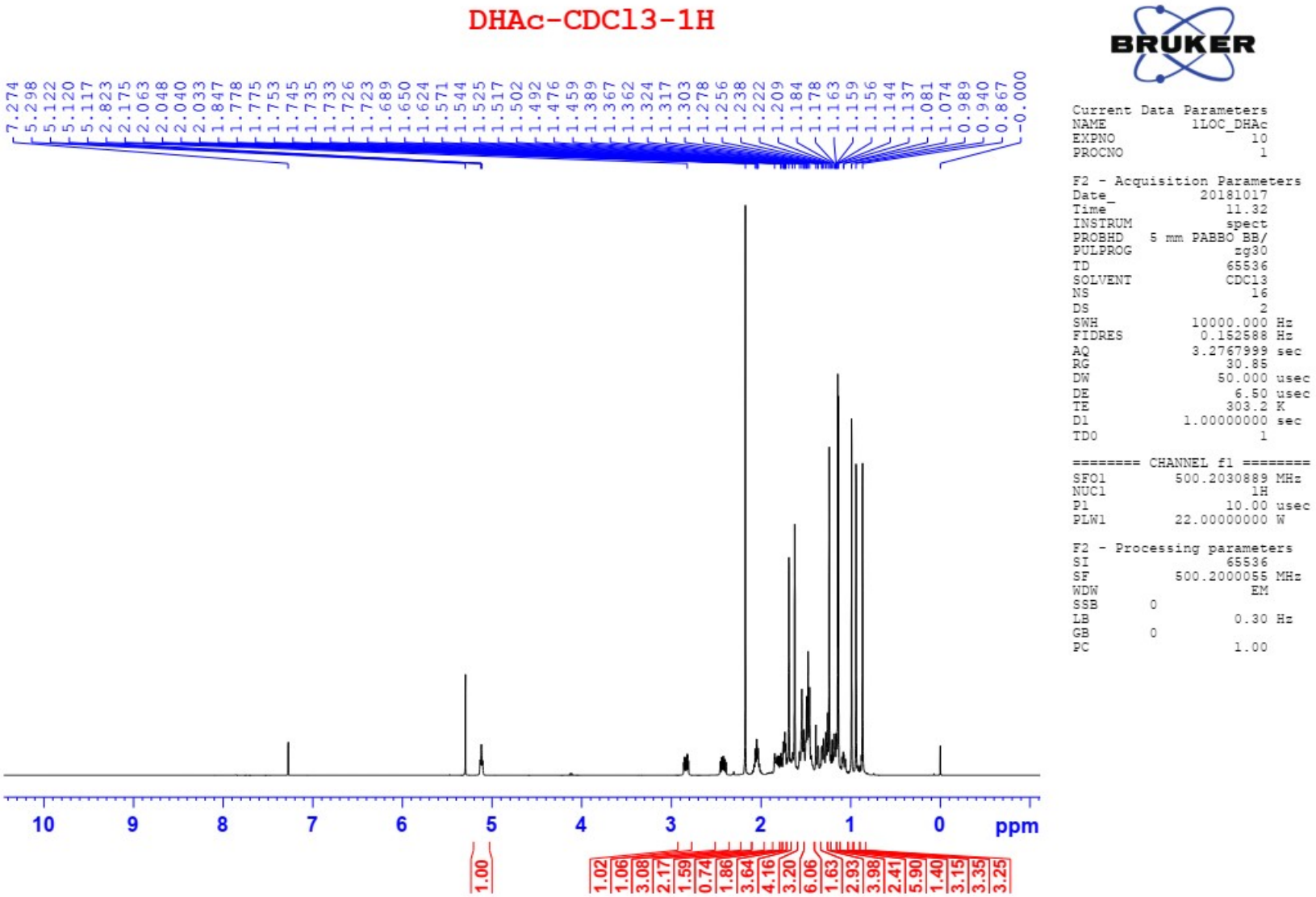
1.12. Compound 3k

Sample name: DNAca
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

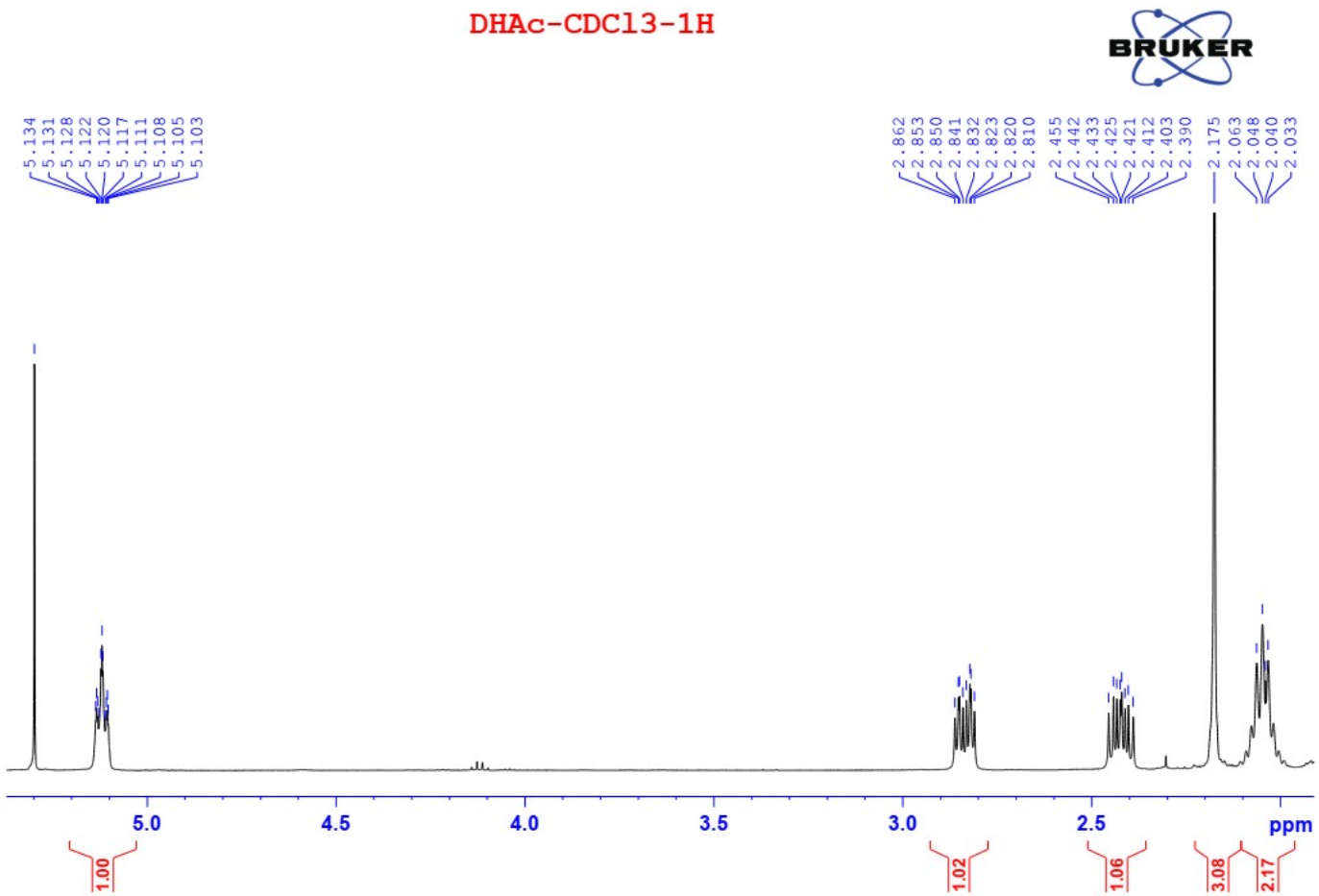


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C32H53NO3	522.39977	7.0	4.4	1			NA/NA

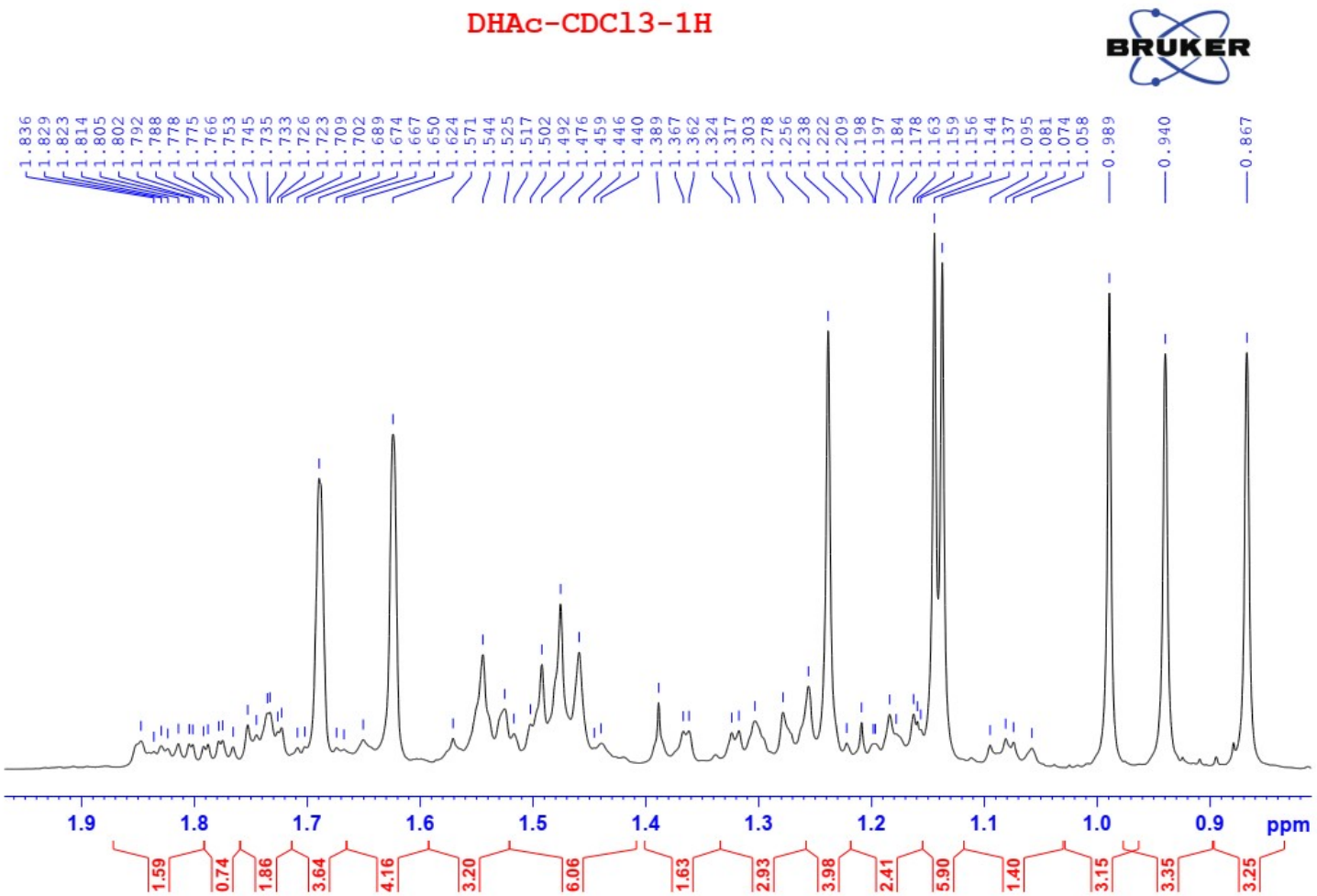
(+)-HR-ESI-MS spectrum of compound **3k**



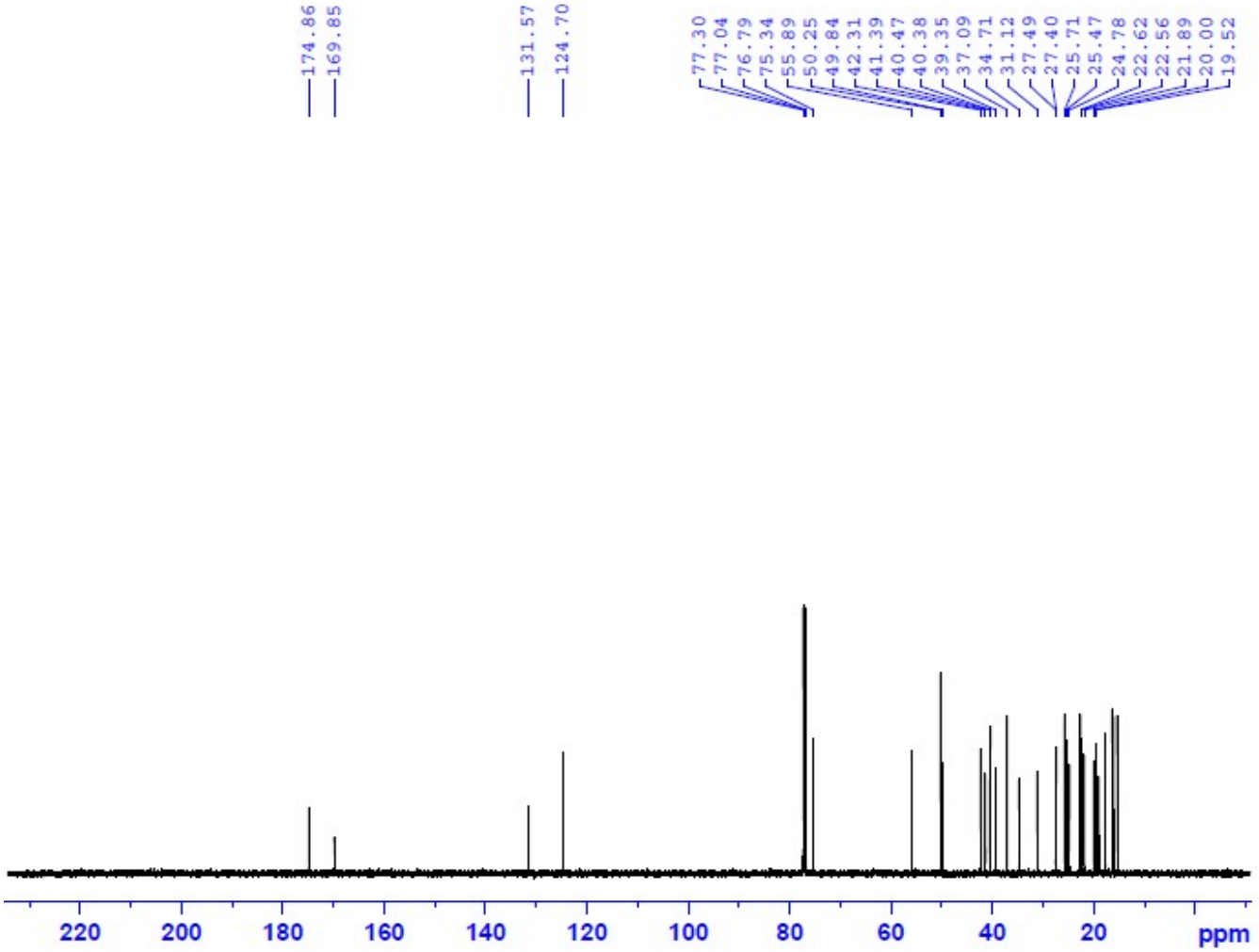
[1]H-NMR spectrum of compound **3k**



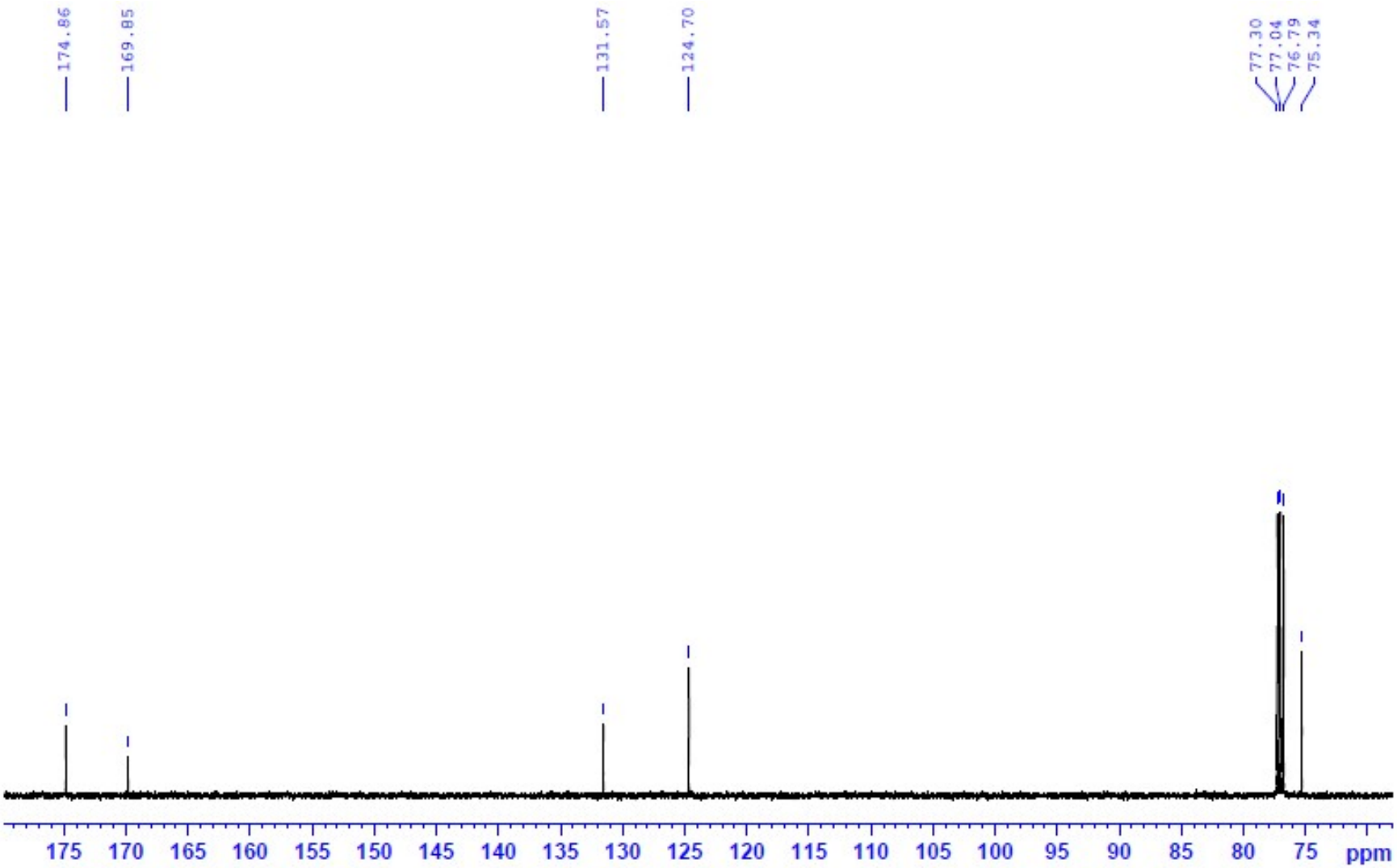
[1]H-NMR spectrum of compound **3k** (extension)



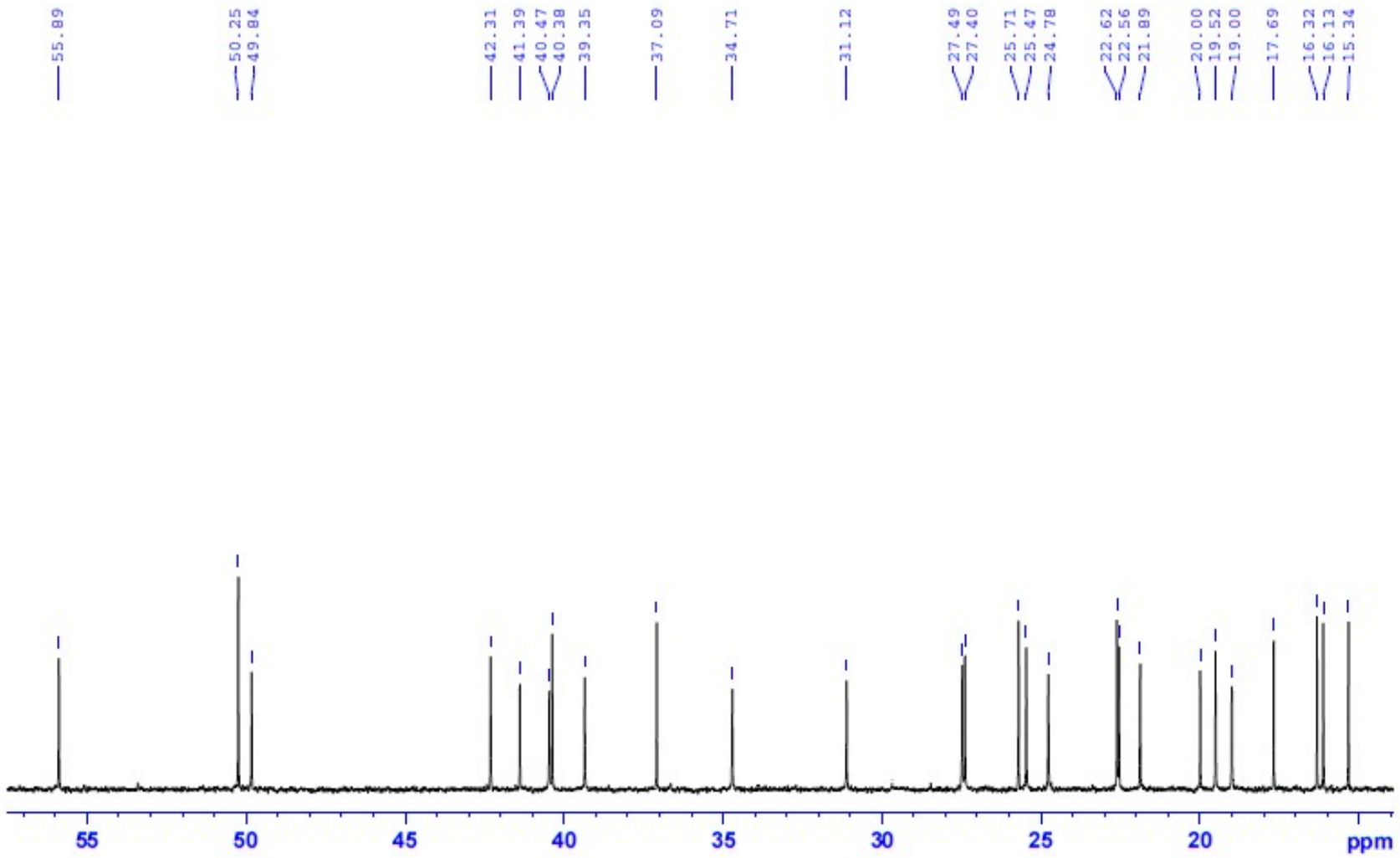
^{1}H-NMR spectrum of compound **3k** (extension)



^{13}C-NMR spectrum of compound **3k**



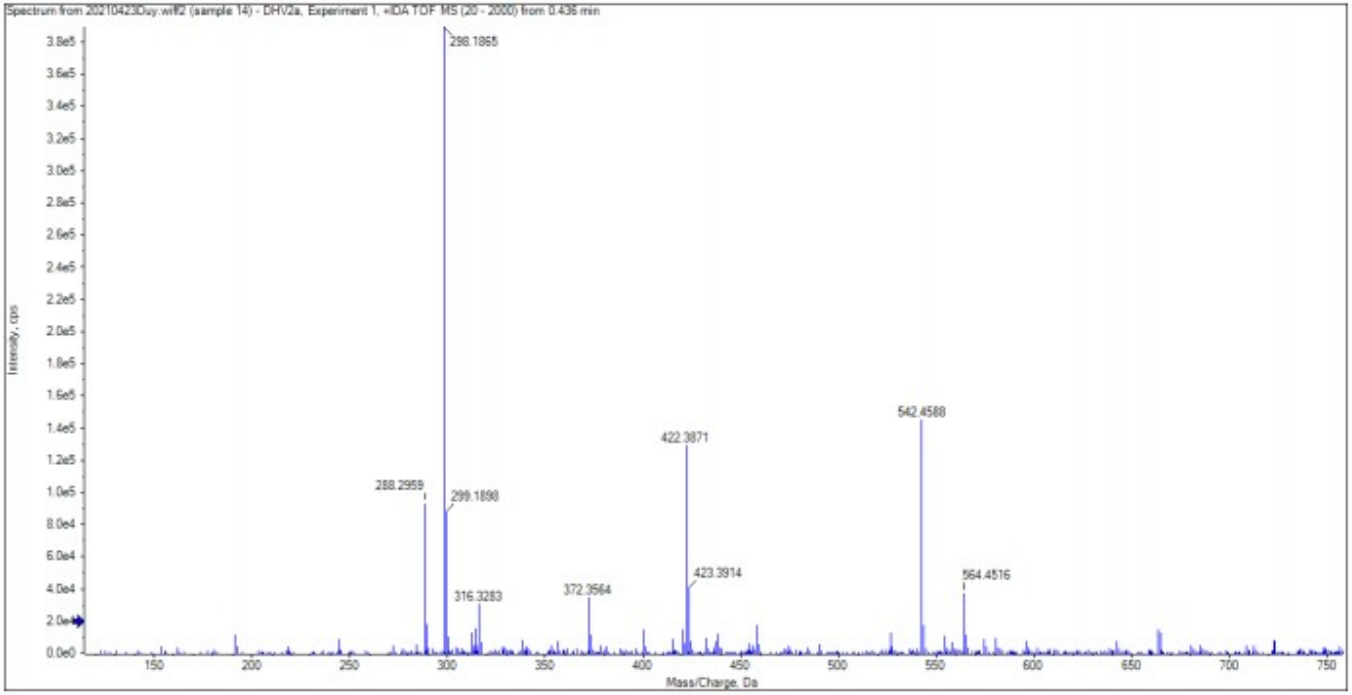
^{13}C-NMR spectrum of compound **3k** (extension)


55.89
50.25
49.84
42.31
41.39
40.47
40.38
39.35
37.09
34.71
31.12
27.49
27.40
25.71
25.47
24.78
22.62
22.56
21.89
20.00
19.52
19.00
17.69
16.32
16.13
15.34
55
50
45
40
35
30
25
20
ppm

^{13}C-NMR spectrum of compound **3k** (extension)

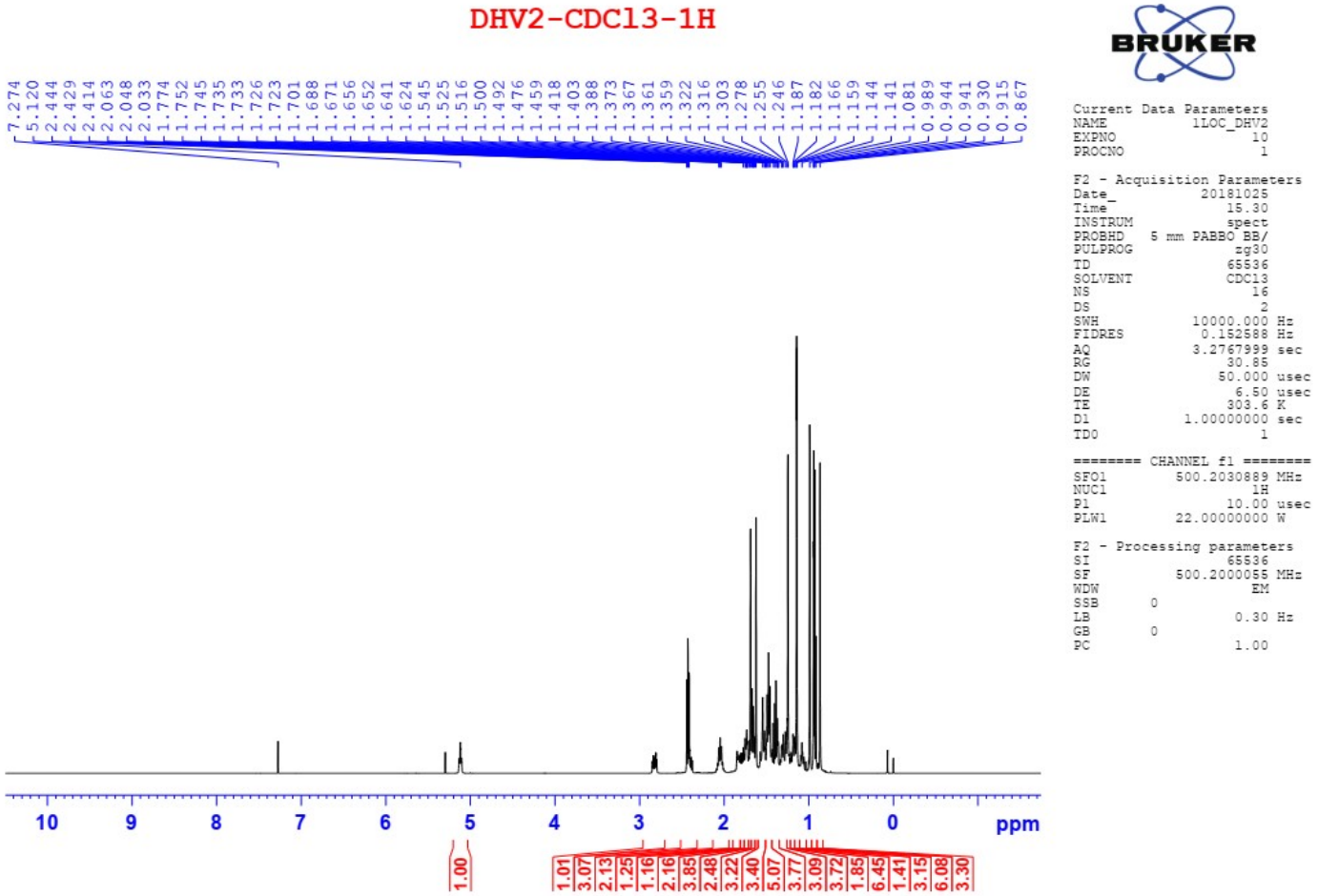
1.13. Compound 3l

Sample name: DHV2a
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

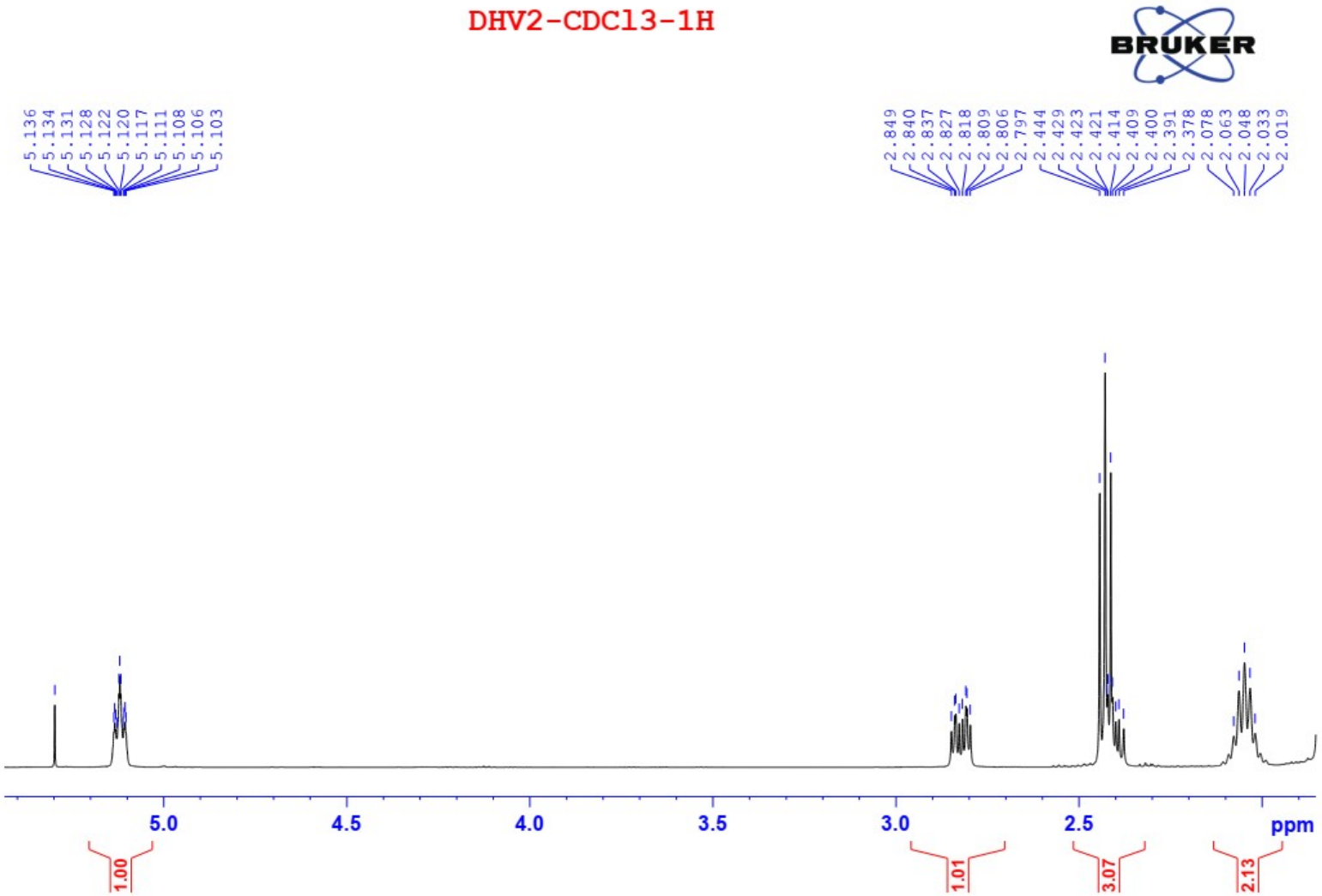


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C35H59NO3	542.45677	7.0	3.7	1			NA/NA

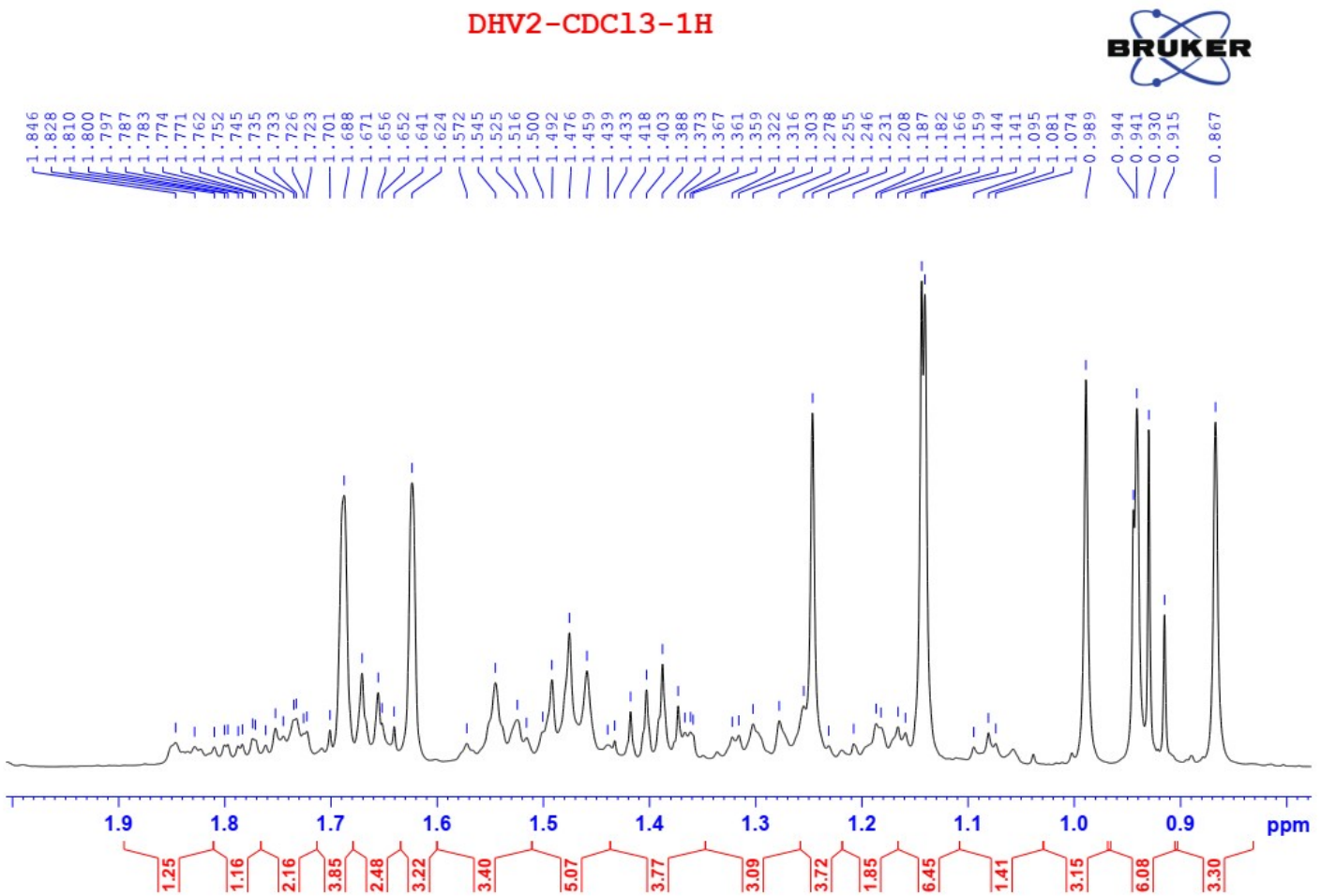
(+)-HR-ESI-MS spectrum of compound **3l**



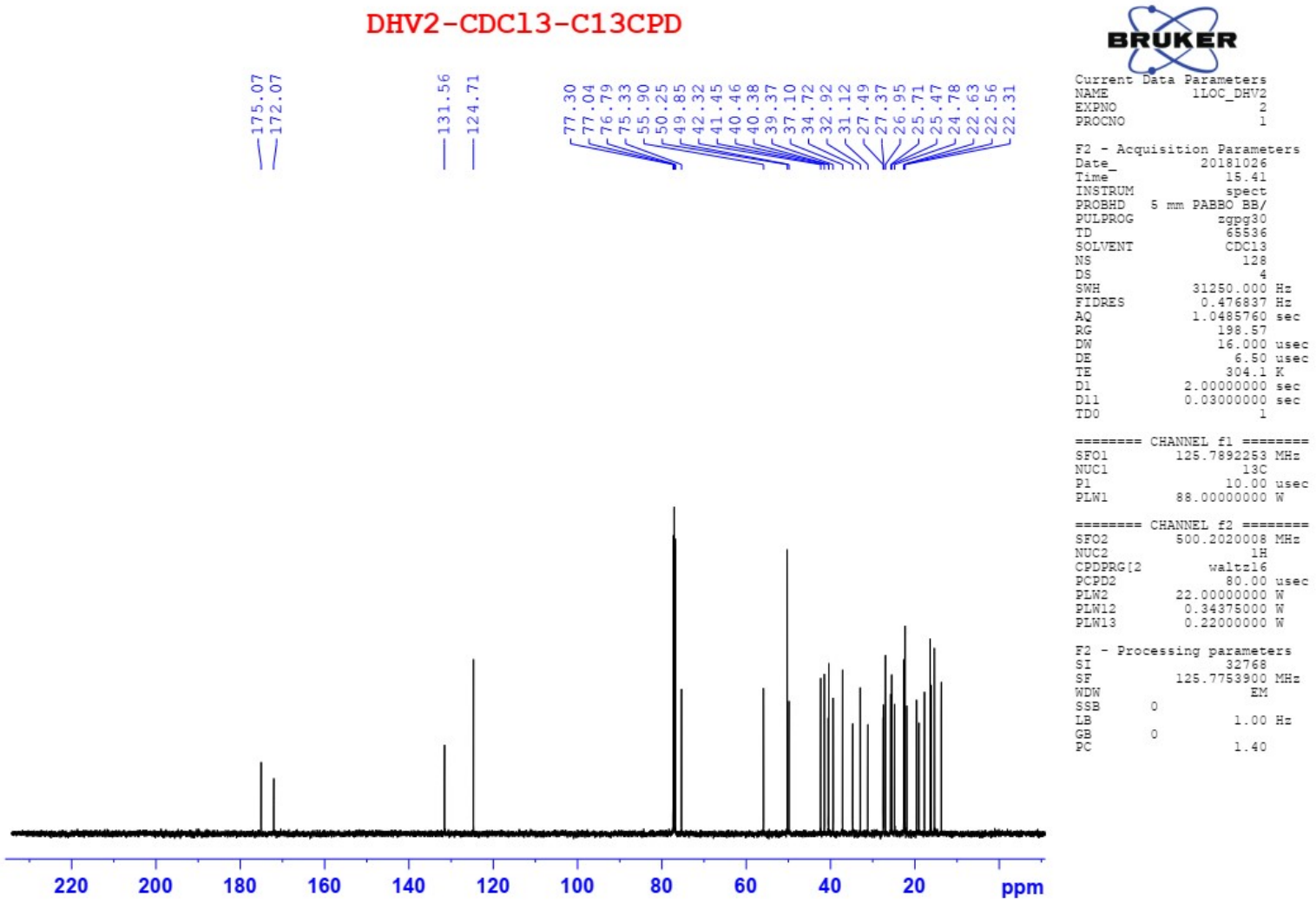
^{1}H-NMR spectrum of compound **3l**



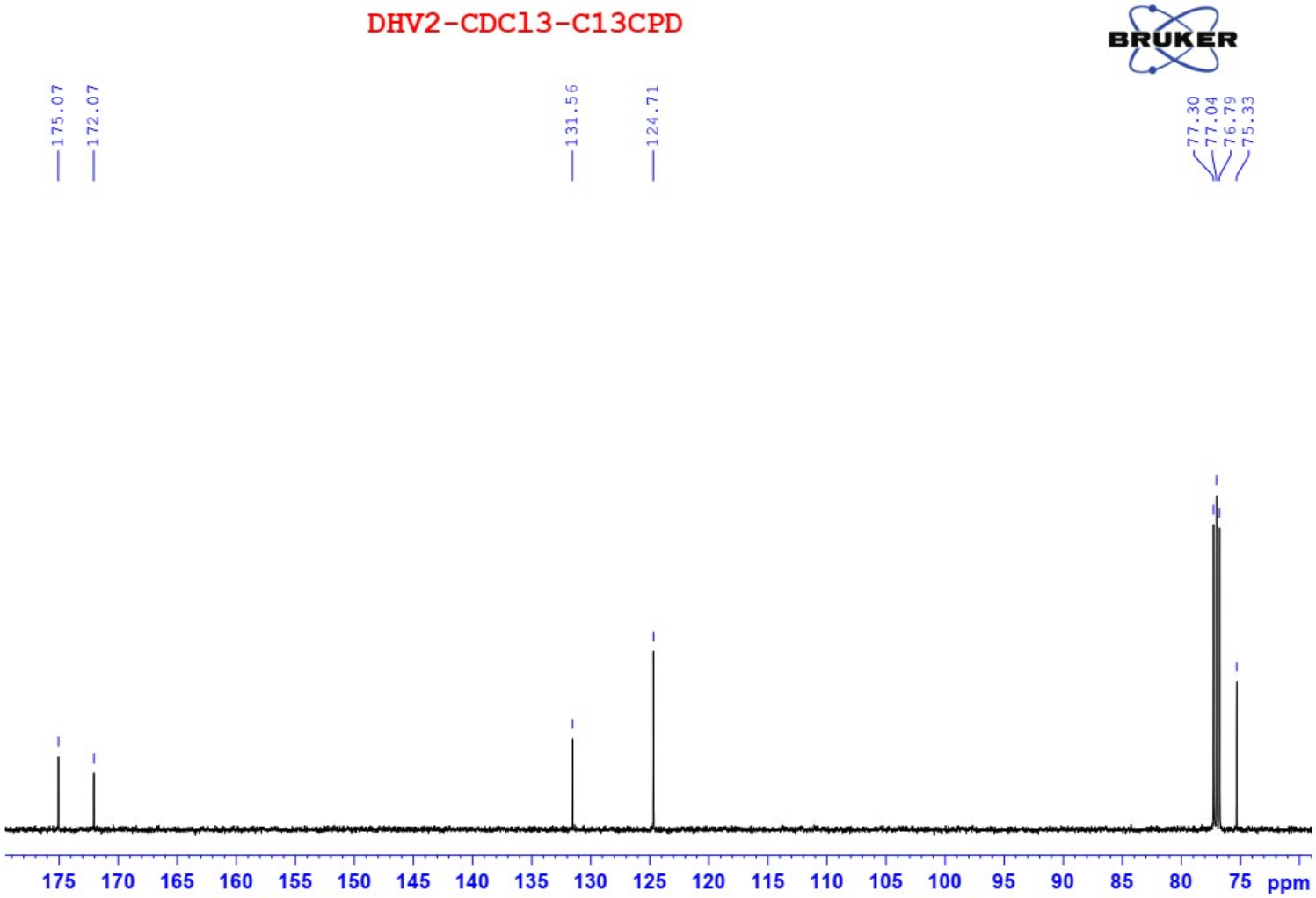
^{1}H-NMR spectrum of compound **3l** (extension)



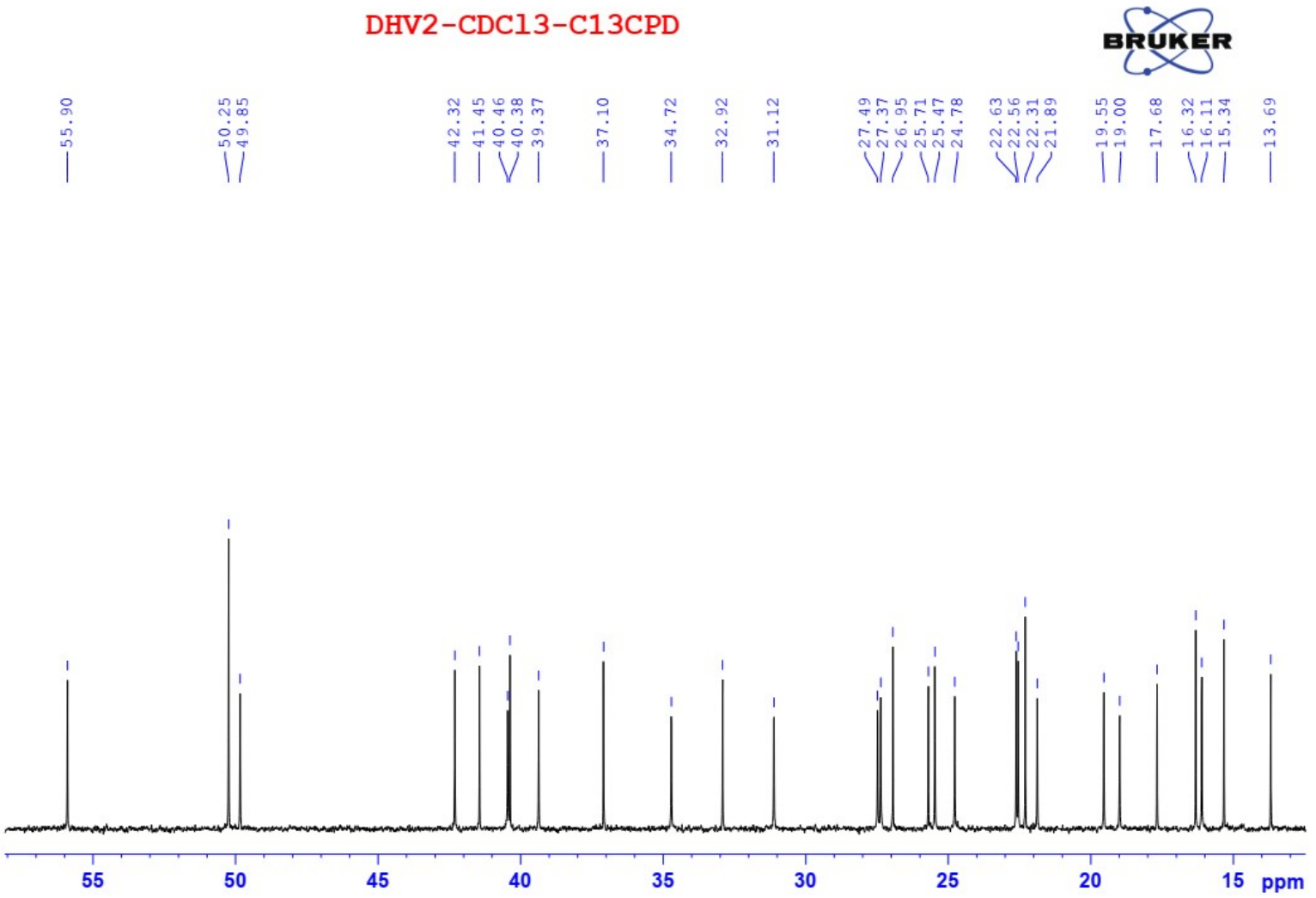
^{1}H-NMR spectrum of compound **3l** (extension)



^{13}C-NMR spectrum of compound **3l**



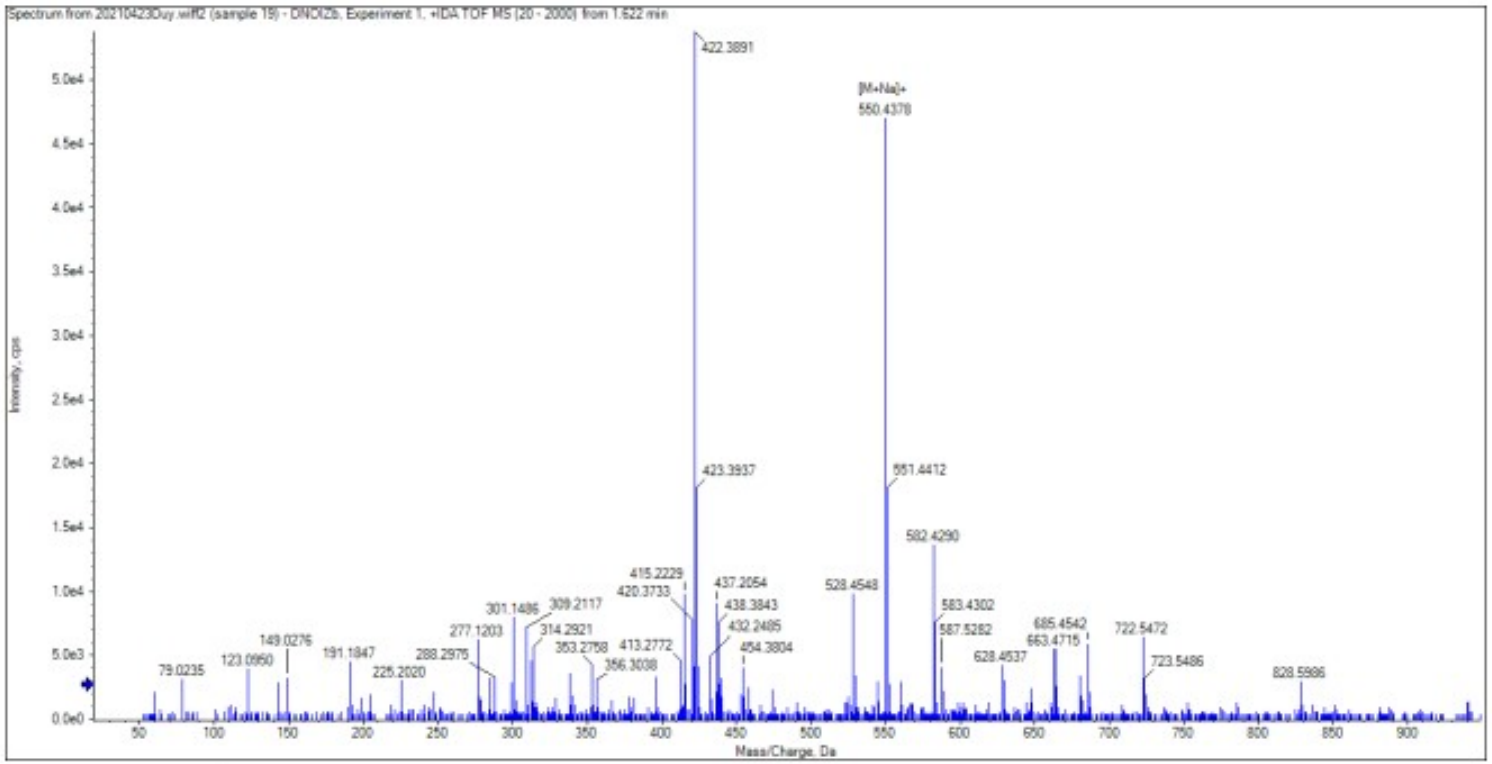
^{13}C-NMR spectrum of compound **3l** (extension)



^{13}C-NMR spectrum of compound **3l** (extension)

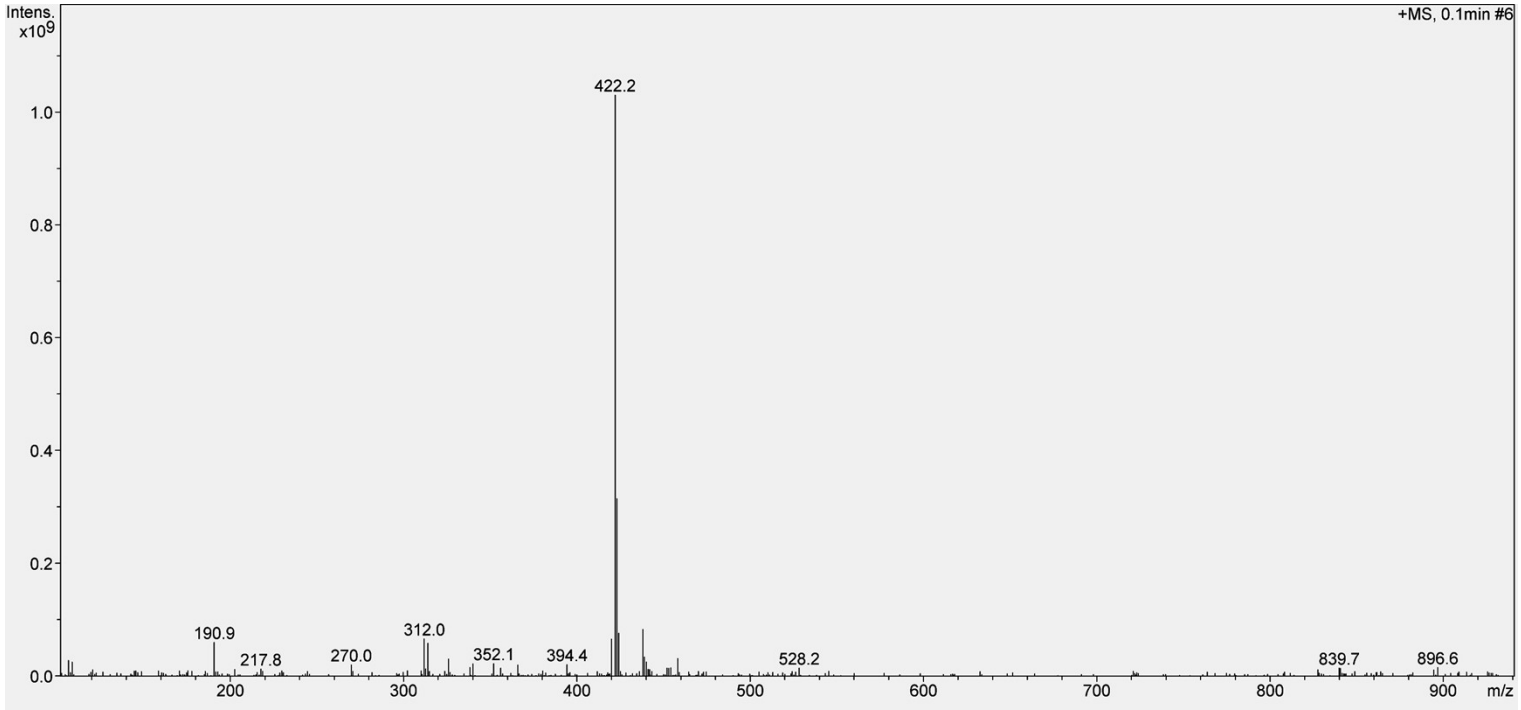
1.14. Compound 3m

Sample name: DNOIZb
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

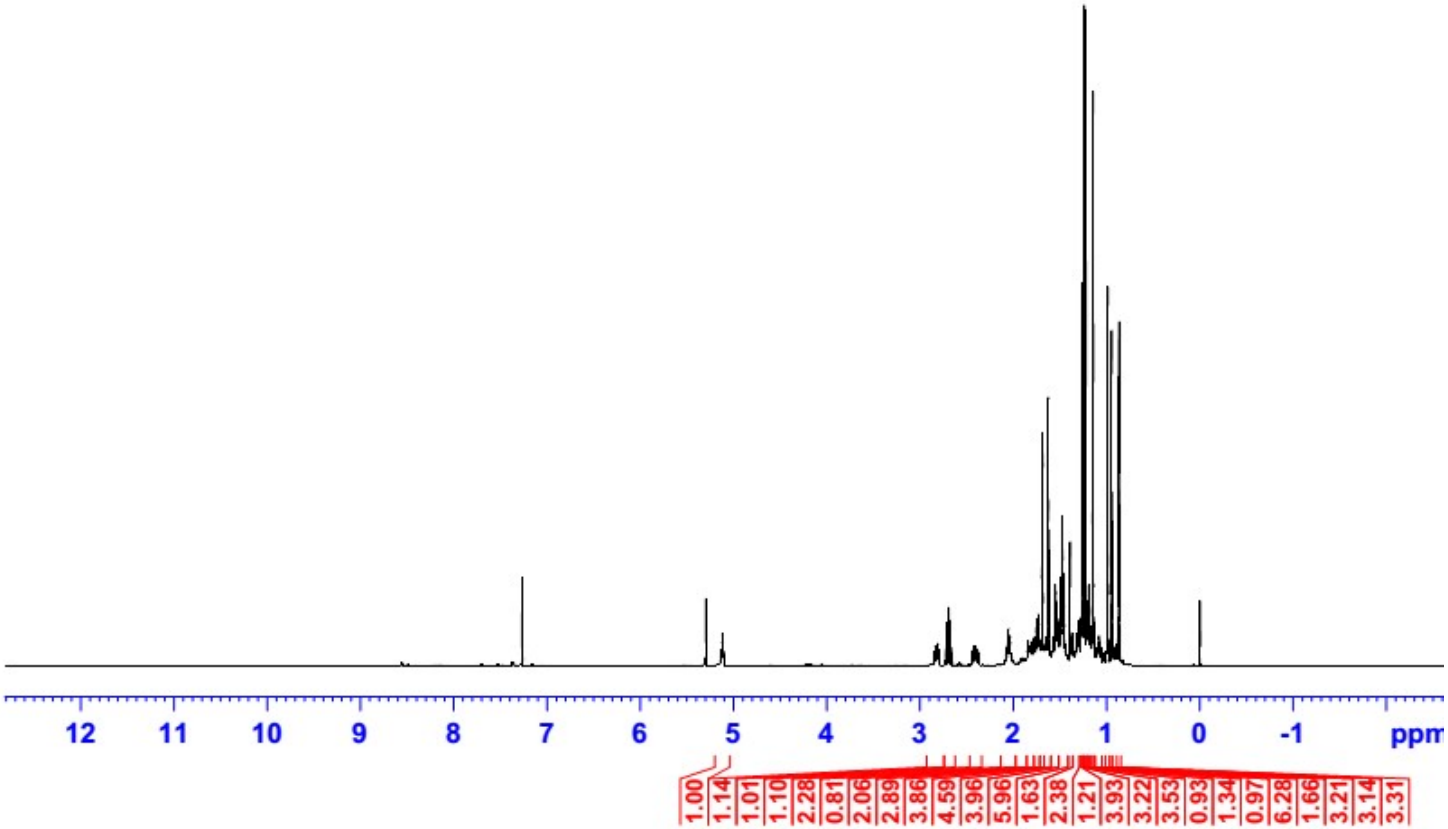


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C34H57NO3	550.43307	7.0	4.8	1			NA/NA

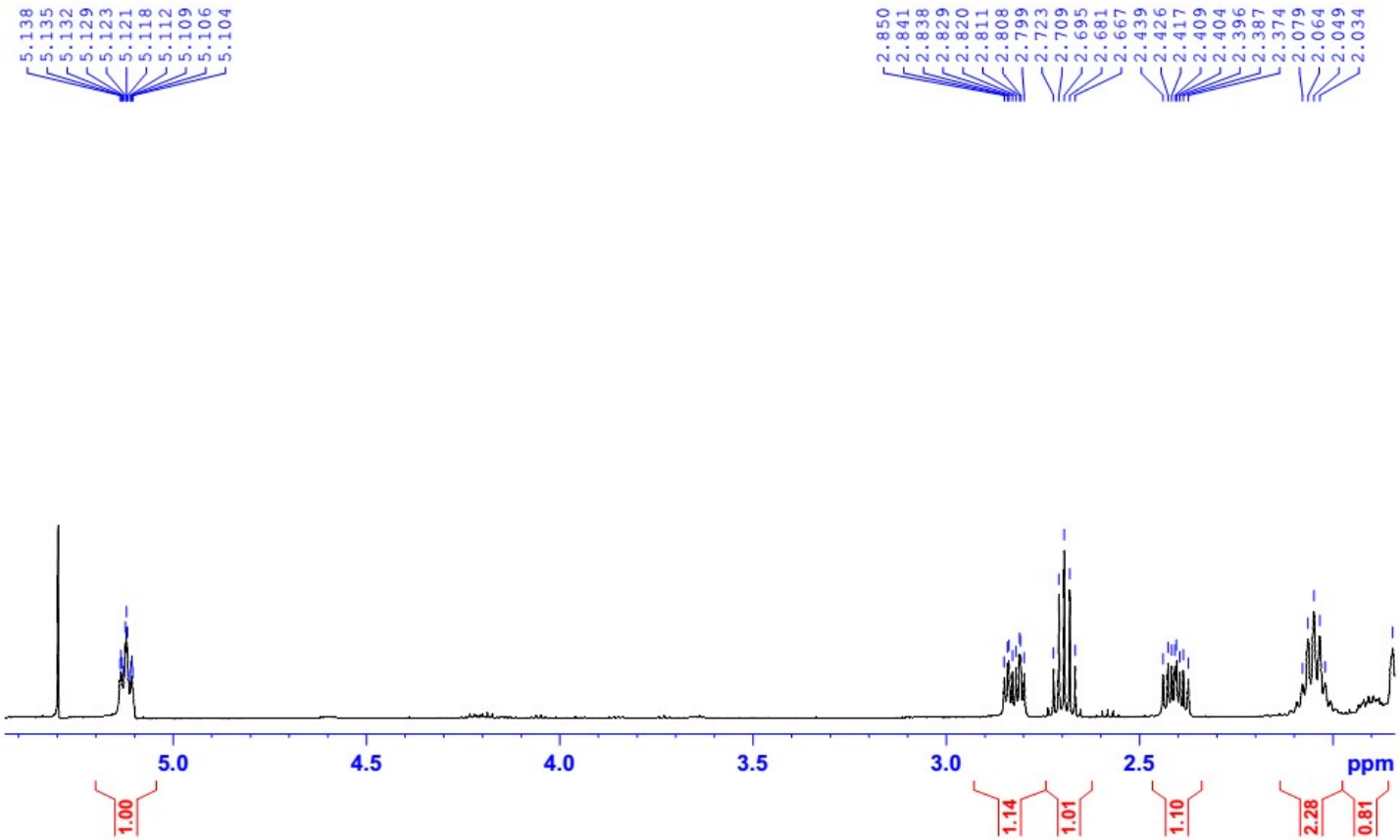
(+)-HR-ESI-MS spectrum of compound **3m**



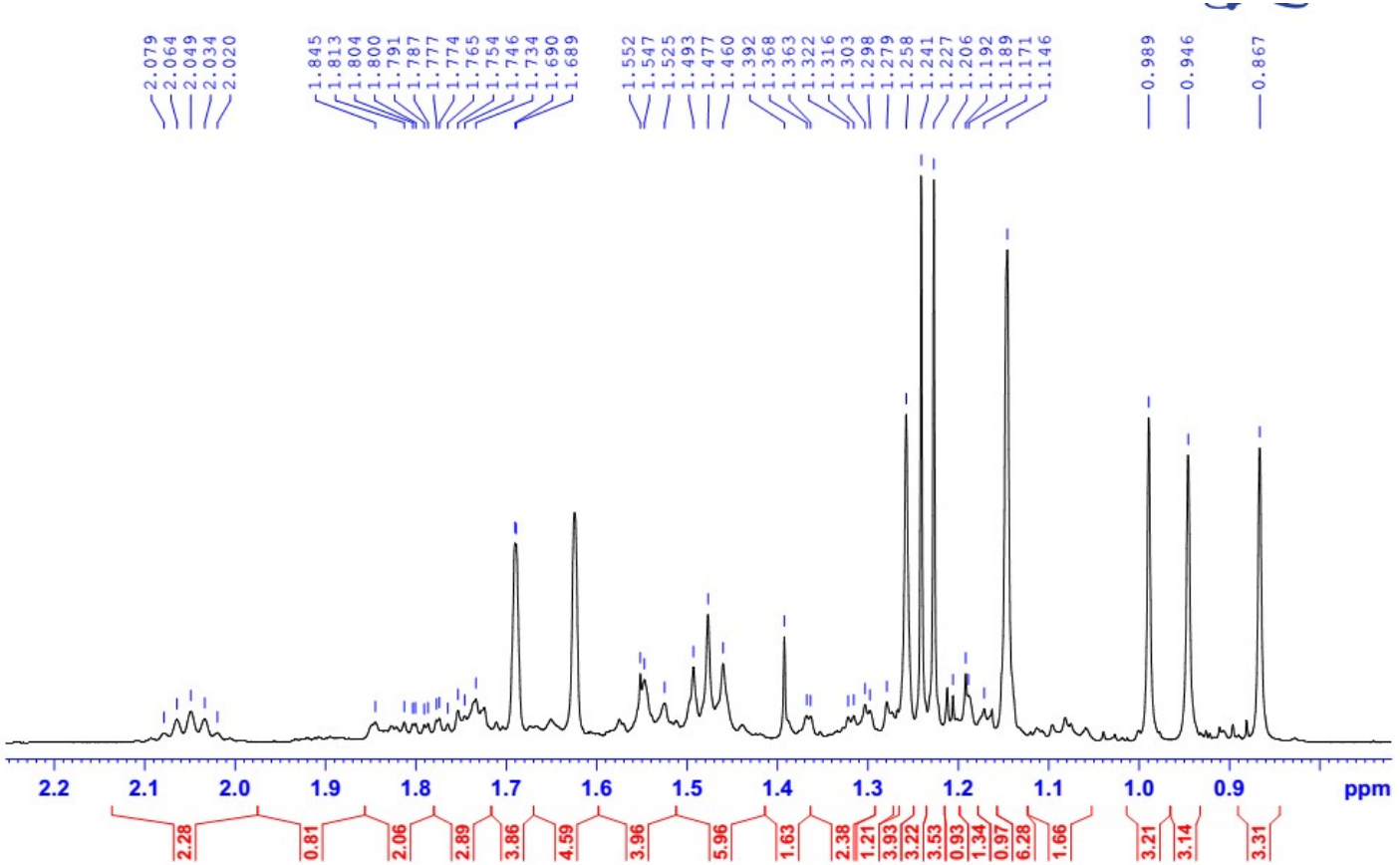
(+)-ESI–MS spectrum of compound **3m**



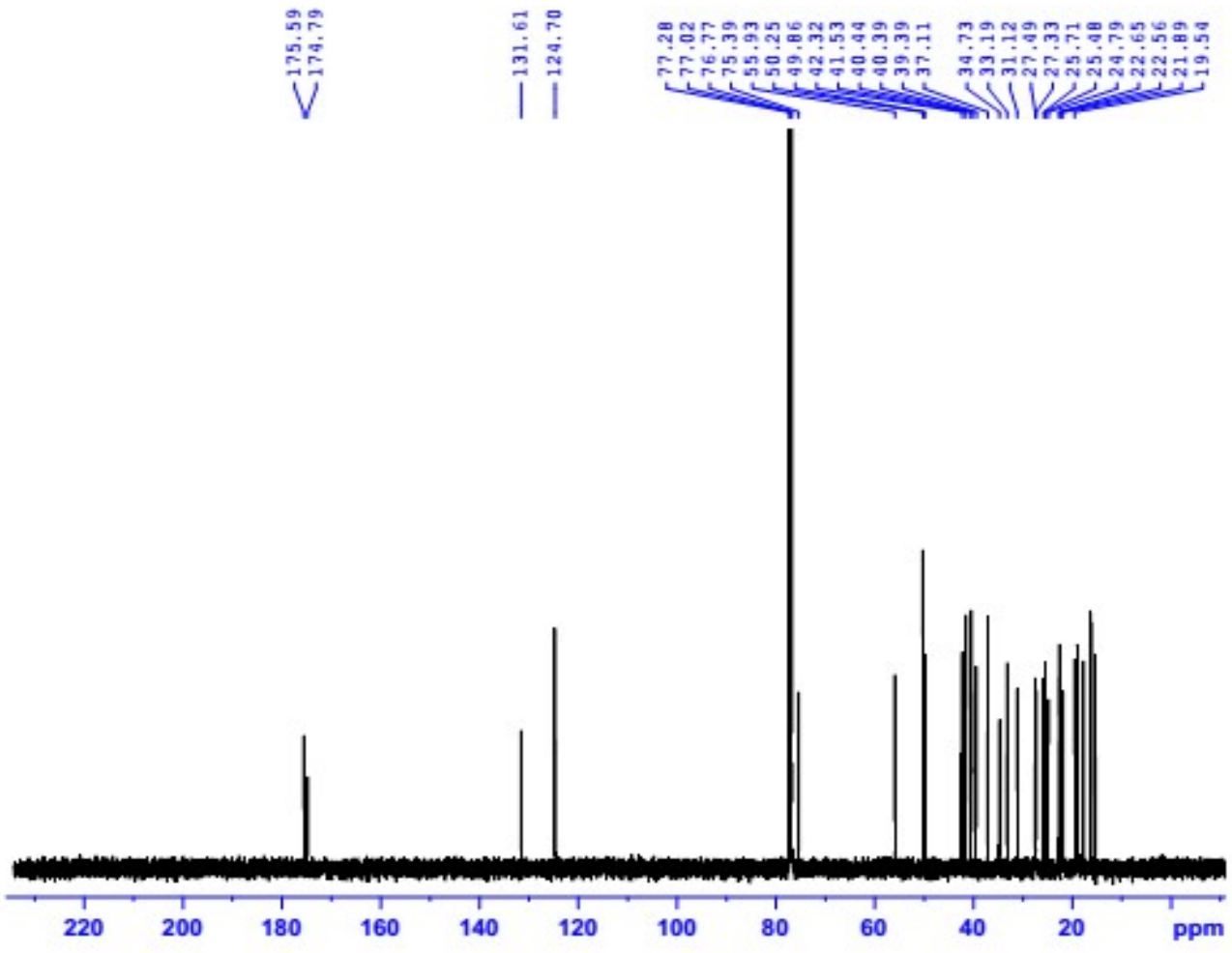
^{1}H NMR spectrum of compound **3m**



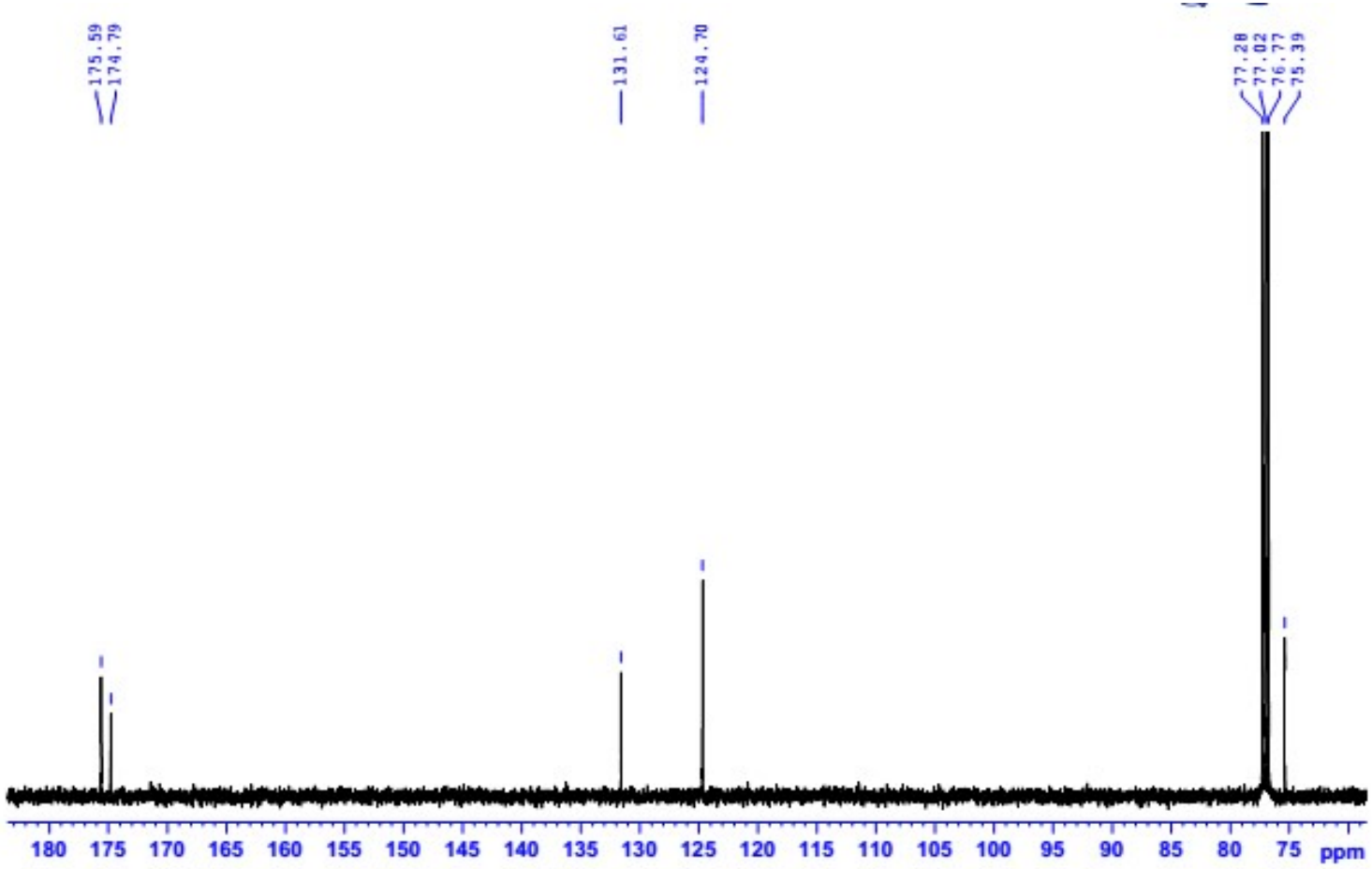
^{1}H NMR spectrum of compound **3m** (extension)



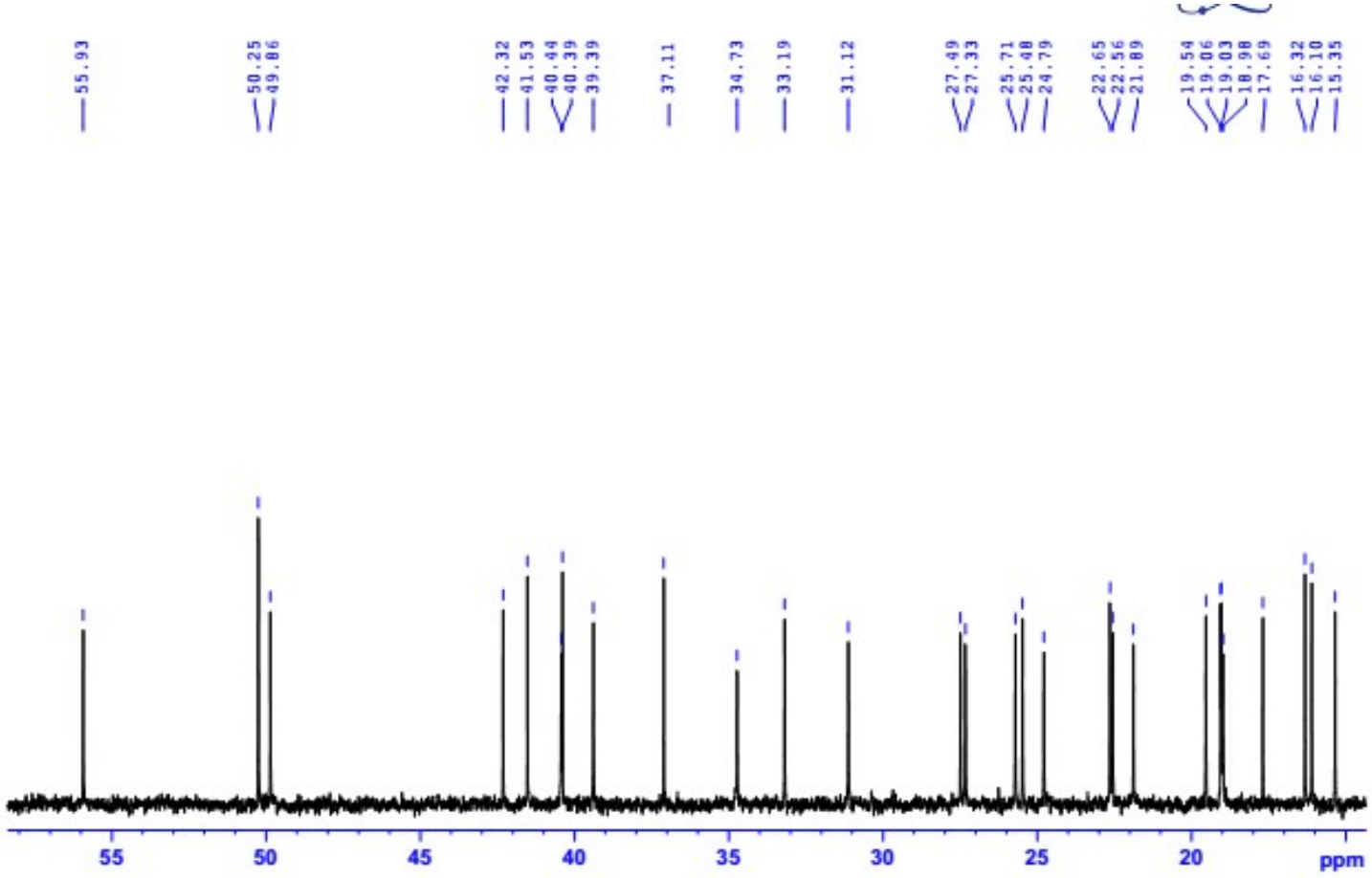
^{1}H NMR spectrum of compound **3m** (extension)



^{13}C-NMR spectrum of compound **3m**



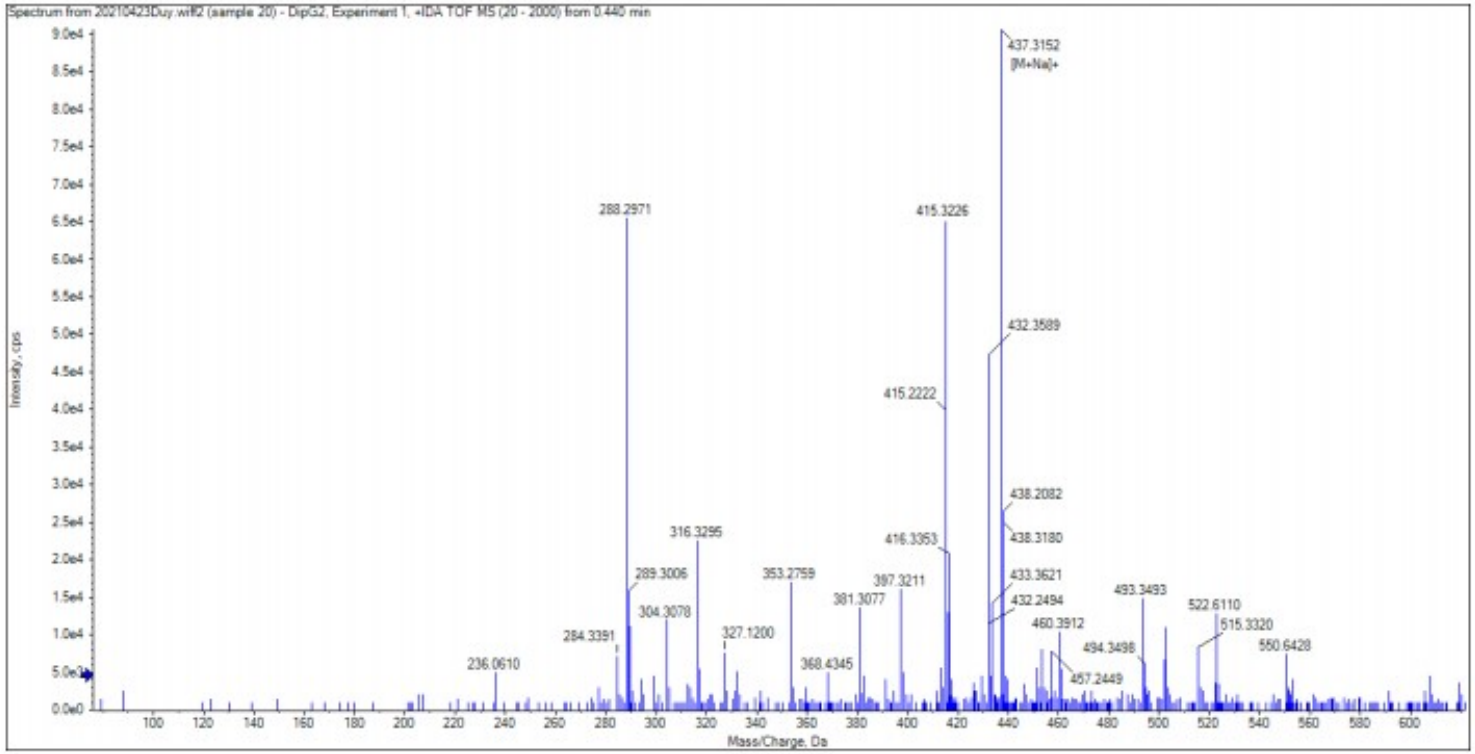
^{13}C-NMR spectrum of compound **3m** (extension)



^{13}C-NMR spectrum of compound **3m** (extention)

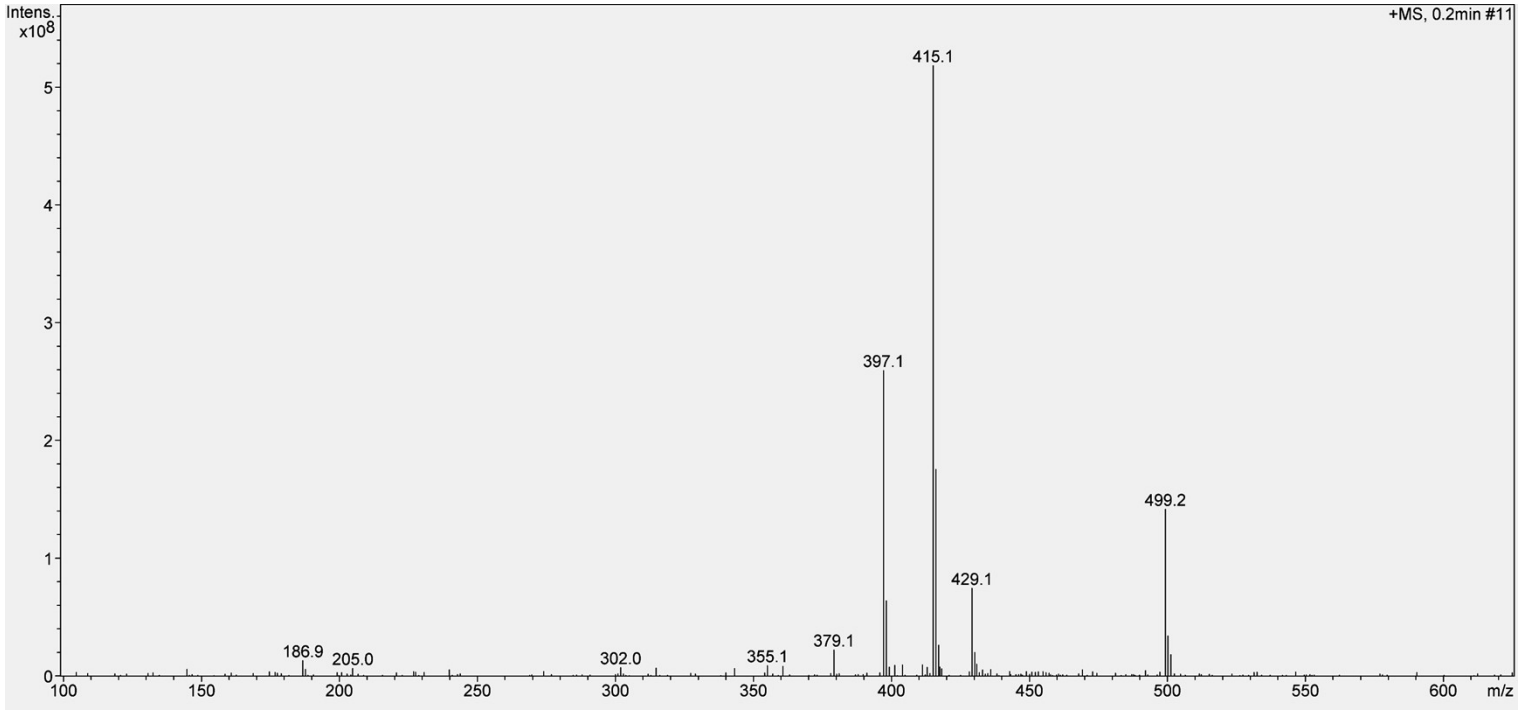
1.15. Compound 4

Sample name: DipG2
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

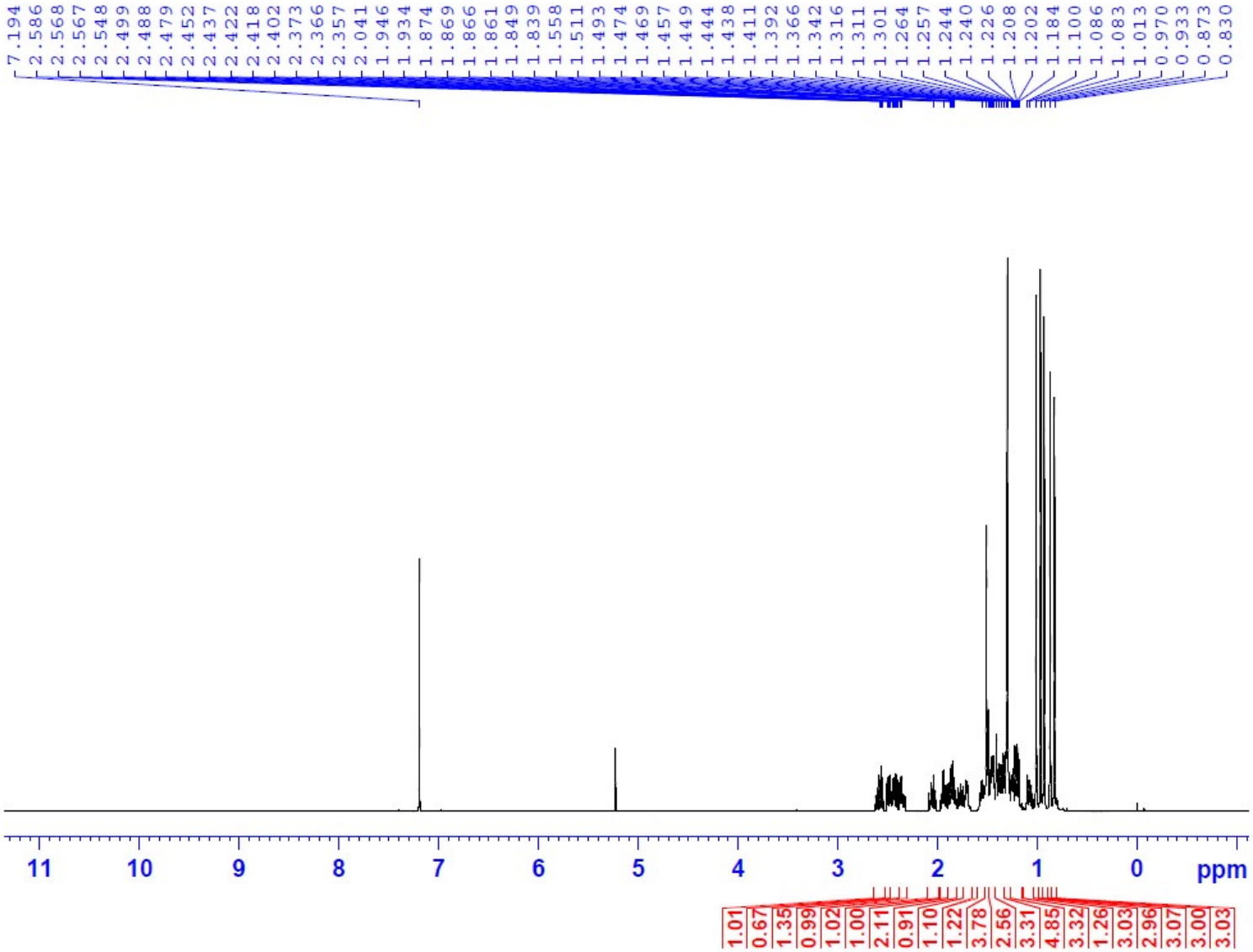


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C27H42O3	415.32067	7.0	2.3	1			NA/NA

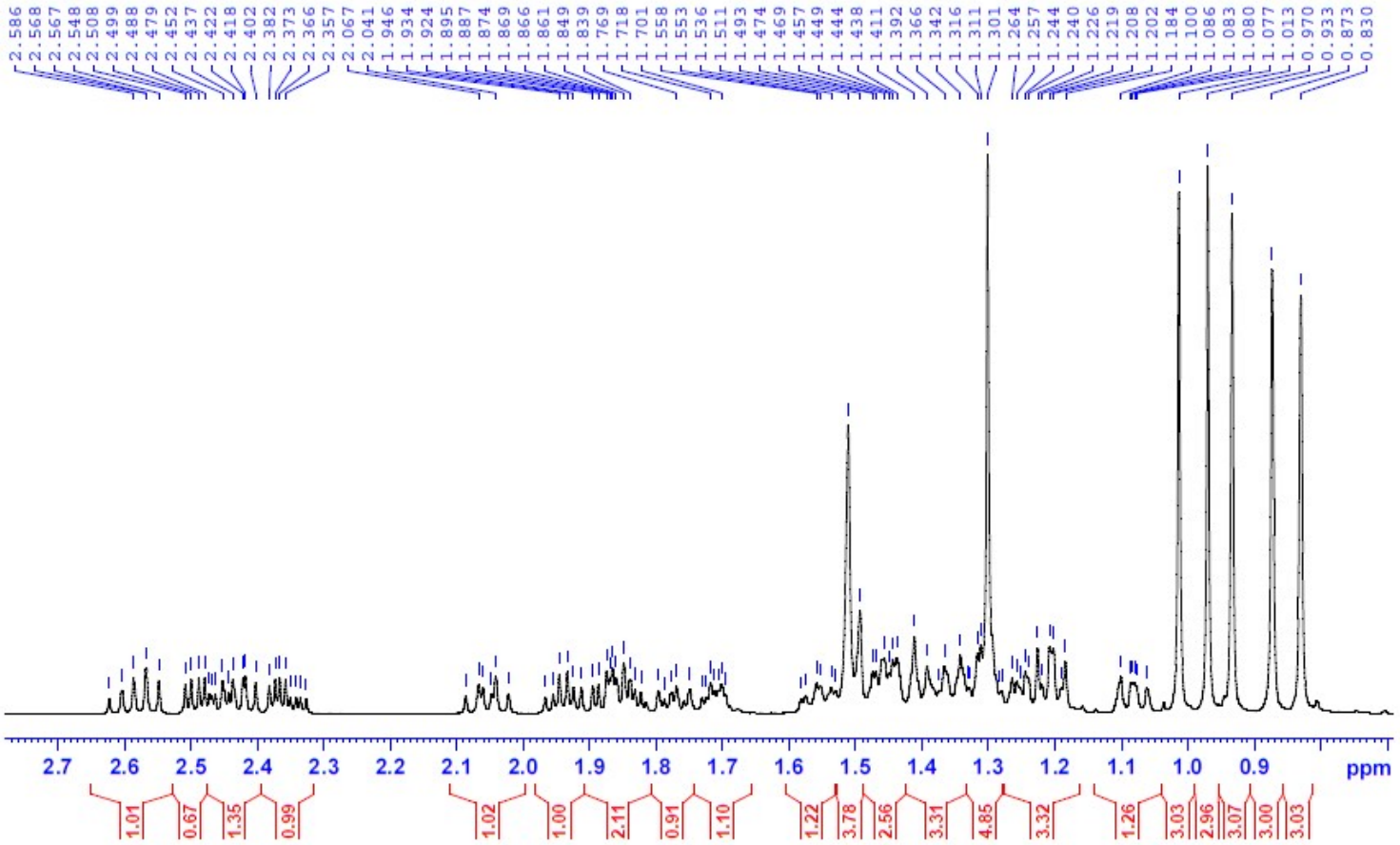
(+)-HR-ESI-MS spectrum of compound **4**



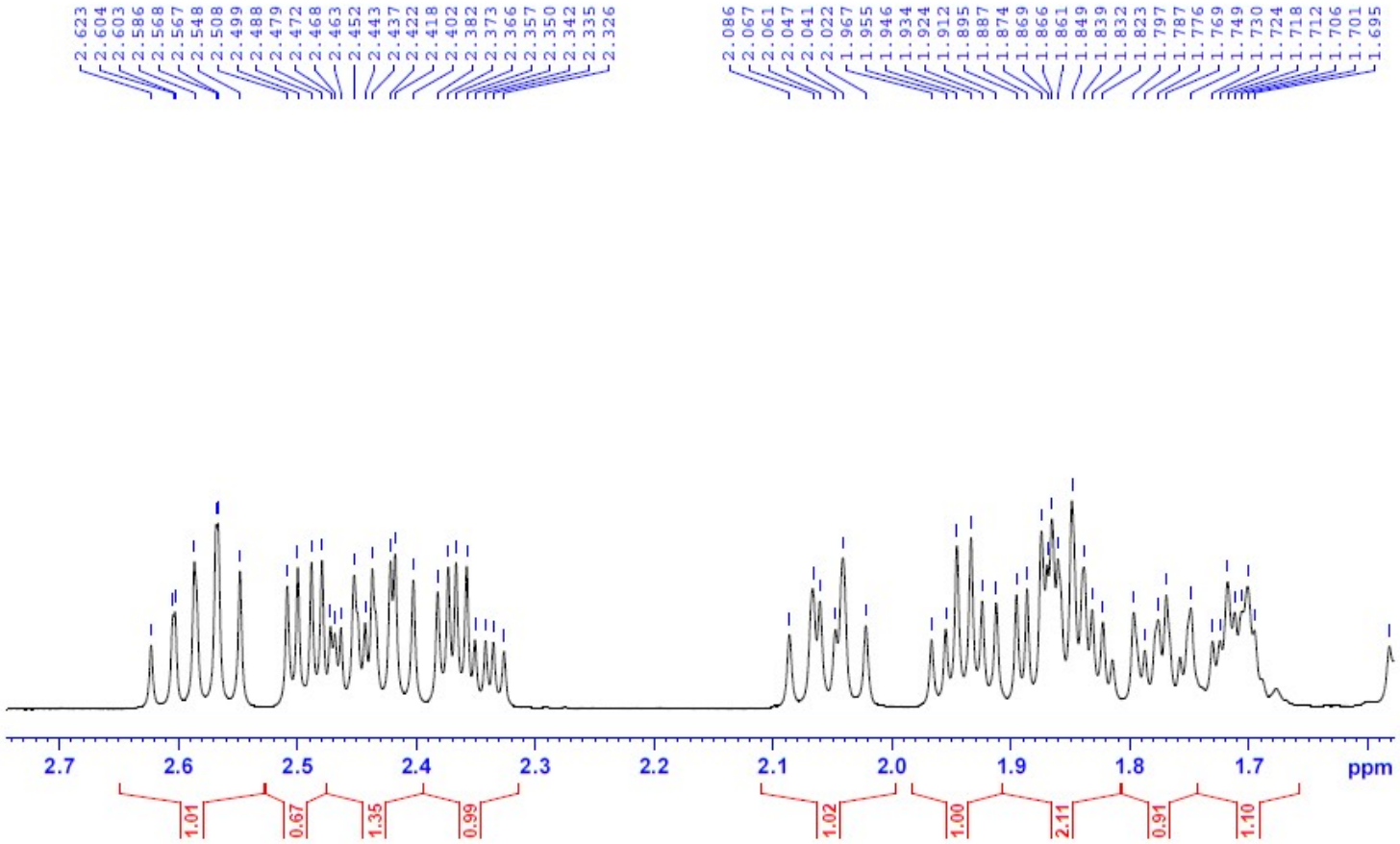
(+)-ESI-MS spectrum of compound **4**



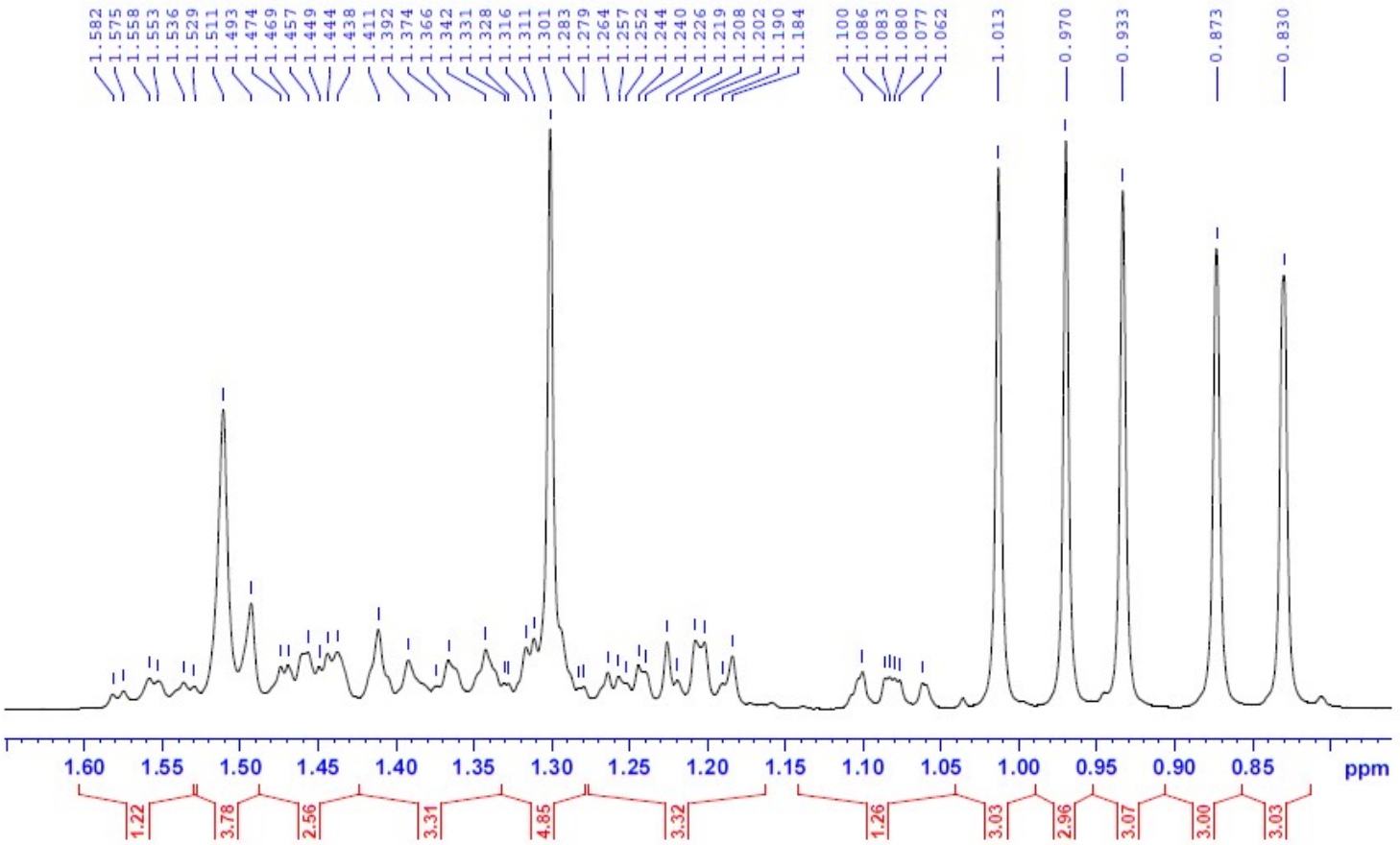
^{1}H-NMR spectrum of compound **4**


2.586
2.568
2.567
2.548
2.508
2.499
2.488
2.479
2.452
2.437
2.422
2.418
2.402
2.382
2.373
2.366
2.357
2.067
2.041
1.946
1.934
1.924
1.895
1.887
1.874
1.869
1.866
1.861
1.849
1.839
1.769
1.718
1.701
1.558
1.553
1.536
1.511
1.493
1.474
1.469
1.457
1.449
1.444
1.438
1.411
1.392
1.366
1.342
1.316
1.311
1.301
1.264
1.257
1.244
1.240
1.226
1.219
1.208
1.202
1.184
1.100
1.086
1.083
1.080
1.077
1.013
0.970
0.933
0.873
0.830
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
ppm
1.01
0.67
1.35
0.99
1.02
1.00
2.11
0.91
1.10
1.22
3.78
2.56
3.31
4.85
3.32
1.26
3.03
2.96
3.07
3.00
3.03

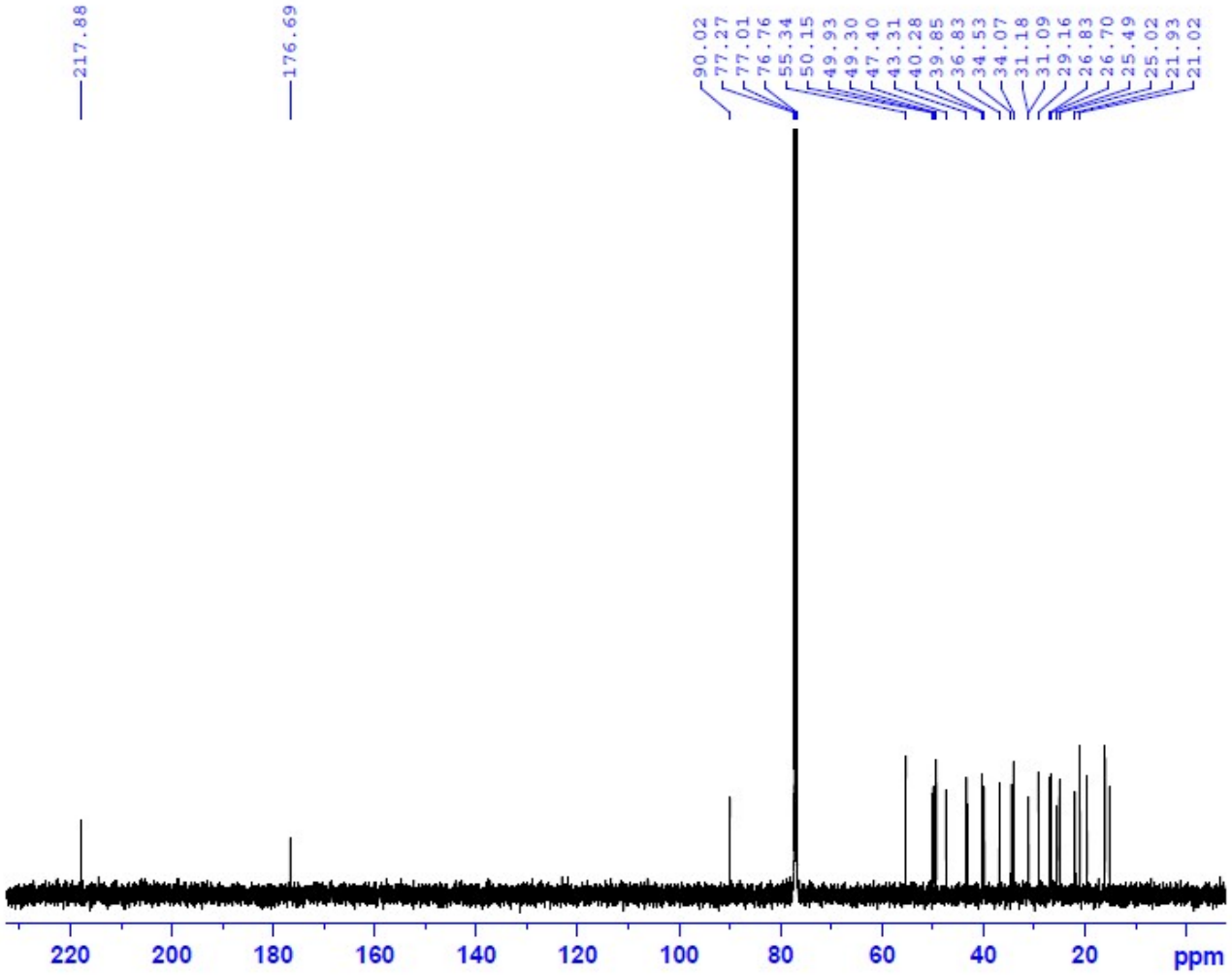
^{1}H-NMR spectrum of compound **4** (extension)


2.623
2.604
2.603
2.586
2.568
2.567
2.548
2.508
2.499
2.488
2.479
2.472
2.468
2.463
2.452
2.443
2.437
2.422
2.418
2.402
2.382
2.373
2.366
2.357
2.350
2.342
2.335
2.326
2.086
2.067
2.061
2.047
2.041
2.022
1.967
1.955
1.946
1.934
1.924
1.912
1.895
1.887
1.874
1.869
1.866
1.861
1.849
1.839
1.832
1.823
1.797
1.787
1.776
1.769
1.749
1.730
1.724
1.718
1.712
1.706
1.701
1.695
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
ppm
1.01
0.67
1.35
0.99
1.02
1.00
2.11
0.91
1.10

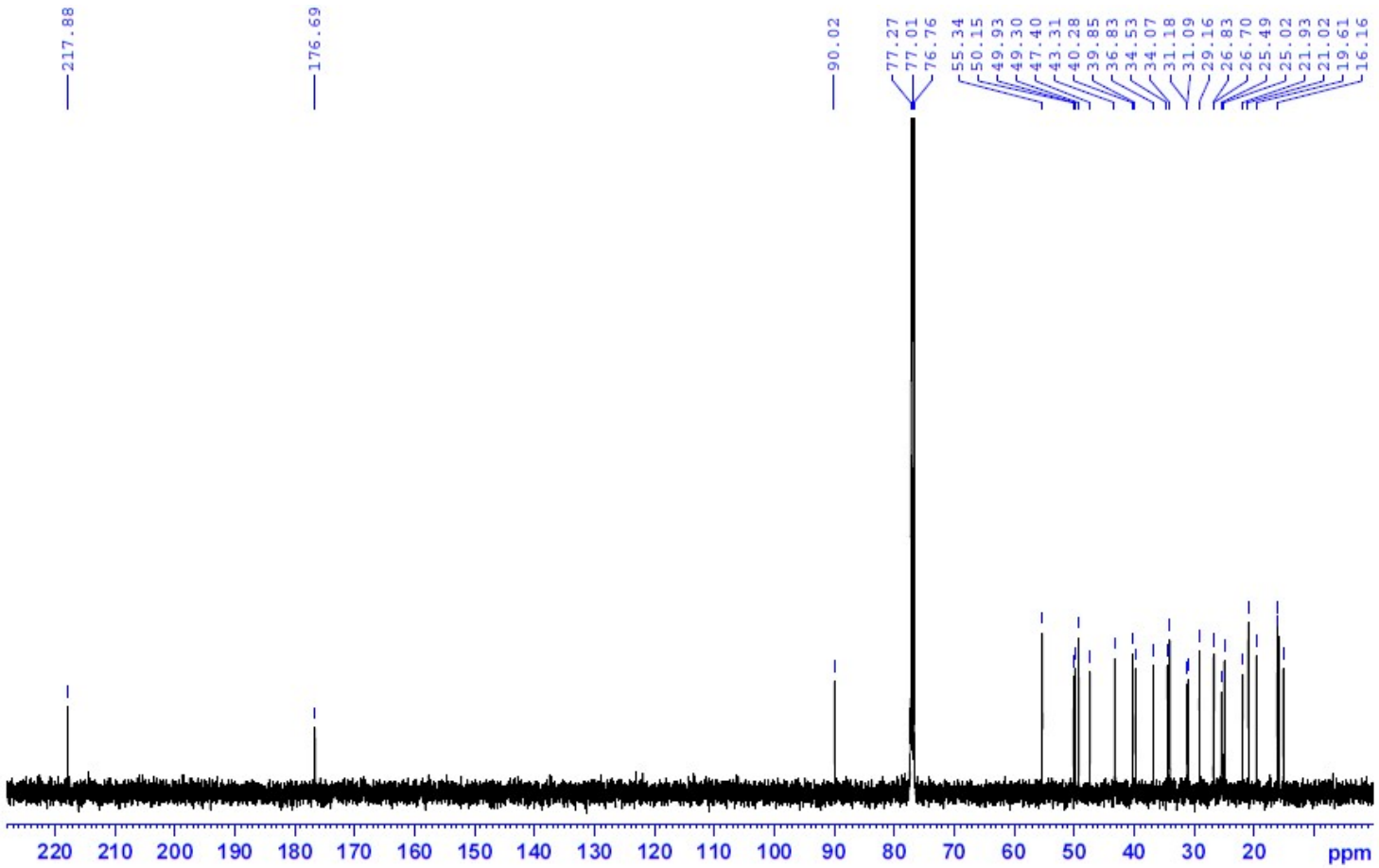
^{1}H-NMR spectrum of compound **4** (extension)


1.582
1.575
1.558
1.553
1.536
1.529
1.511
1.493
1.474
1.469
1.457
1.449
1.444
1.438
1.411
1.392
1.374
1.366
1.342
1.331
1.328
1.316
1.311
1.301
1.283
1.279
1.264
1.257
1.252
1.244
1.240
1.226
1.219
1.208
1.202
1.190
1.184
1.100
1.086
1.083
1.080
1.077
1.062
1.013
0.970
0.933
0.873
0.830
1.60
1.55
1.50
1.45
1.40
1.35
1.30
1.25
1.20
1.15
1.10
1.05
1.00
0.95
0.90
0.85
ppm
1.22
3.78
2.56
3.31
4.85
3.32
1.26
3.03
2.96
3.07
3.00
3.03

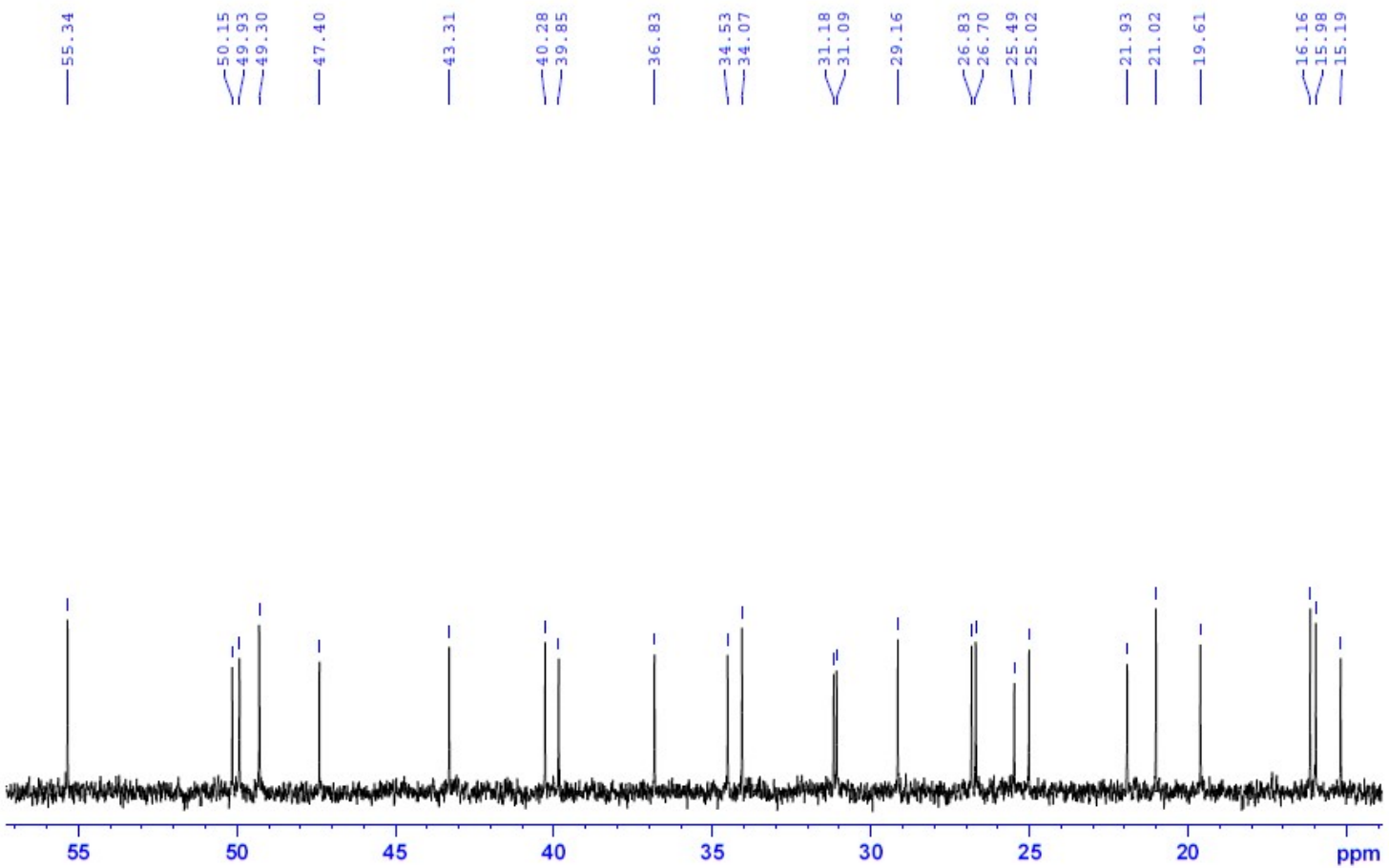
^{1}H-NMR spectrum of compound **4** (extension)



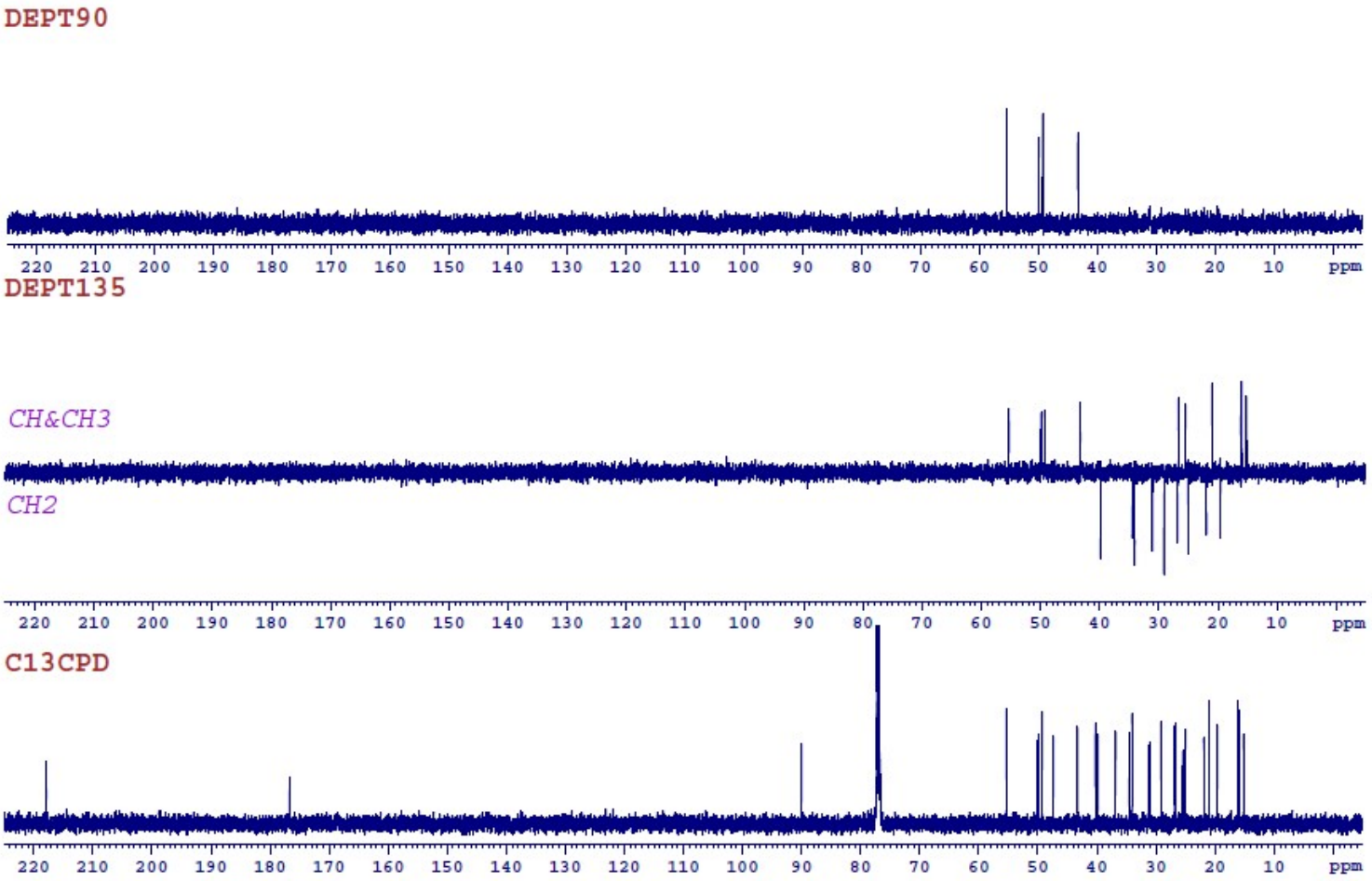
^{13}C-NMR spectrum of compound **4**


217.88
176.69
90.02
77.27
77.01
76.76
55.34
50.15
49.93
49.30
47.40
43.31
40.28
39.85
36.83
34.53
34.07
31.18
31.09
29.16
26.83
26.70
25.49
25.02
21.93
21.02
19.61
16.16
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

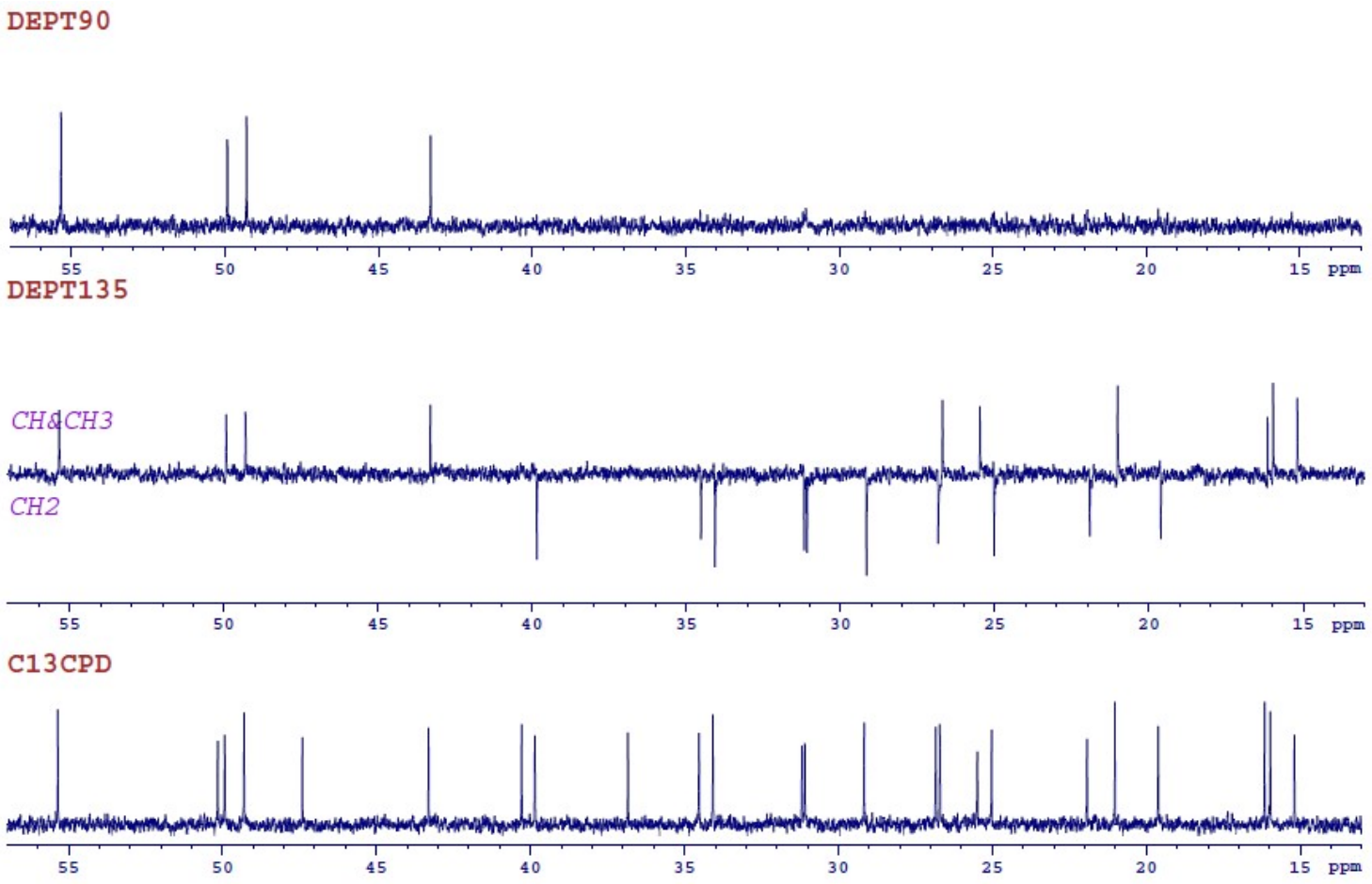
^{13}C-NMR spectrum of compound **4** (extension)


55.34
50.15
49.93
49.30
47.40
43.31
40.28
39.85
36.83
34.53
34.07
31.18
31.09
29.16
26.83
26.70
25.49
25.02
21.93
21.02
19.61
16.16
15.98
15.19
55
50
45
40
35
30
25
20
ppm

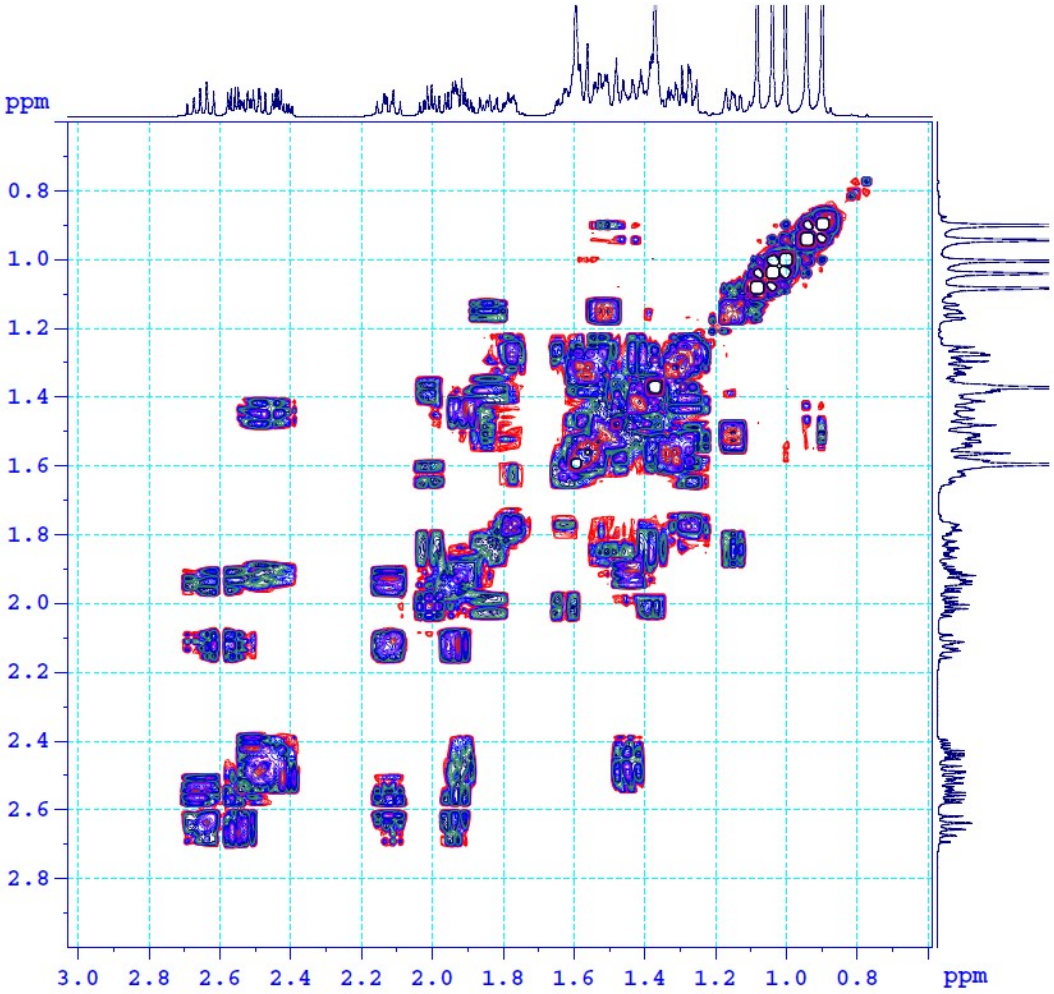
^{13}C-NMR spectrum of compound **4** (extension)



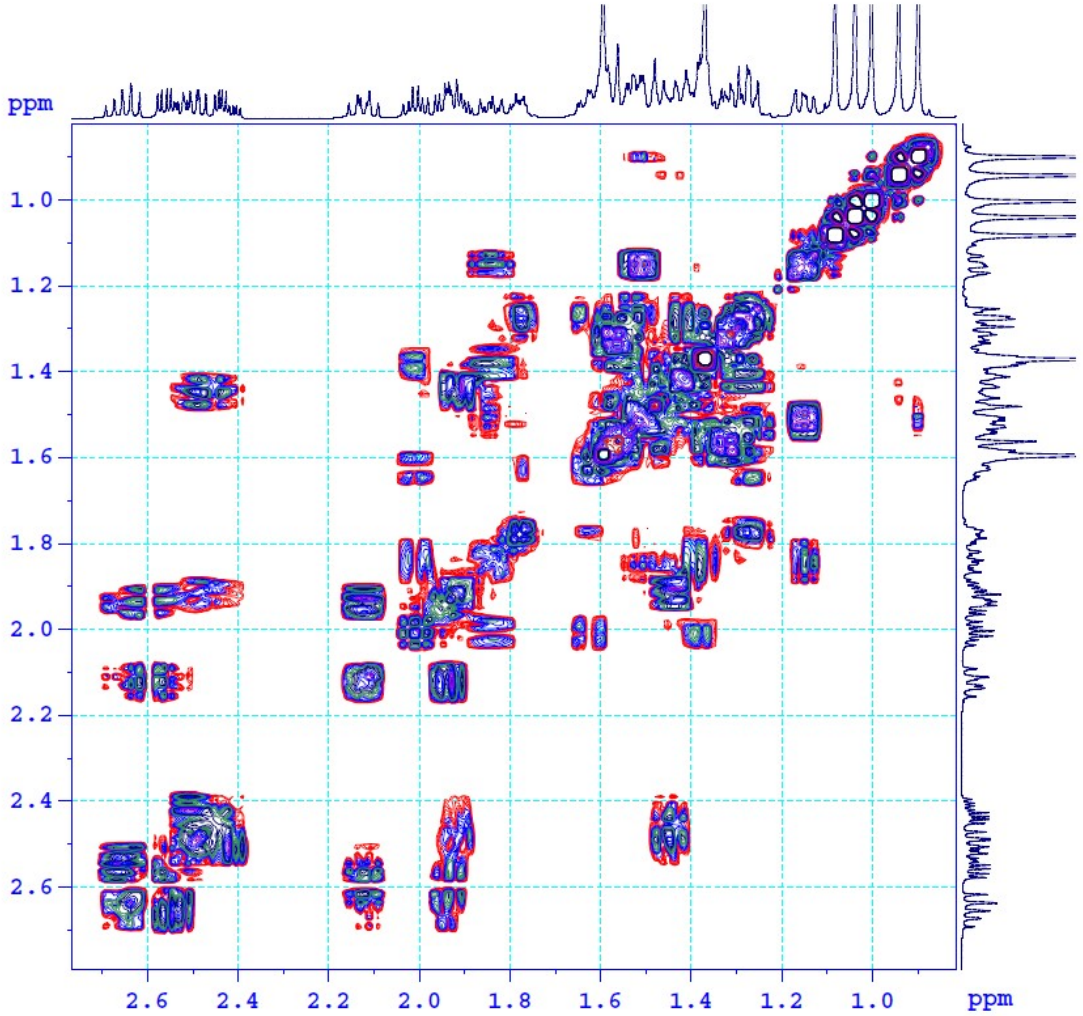
DEPT spectrum of compound **4**



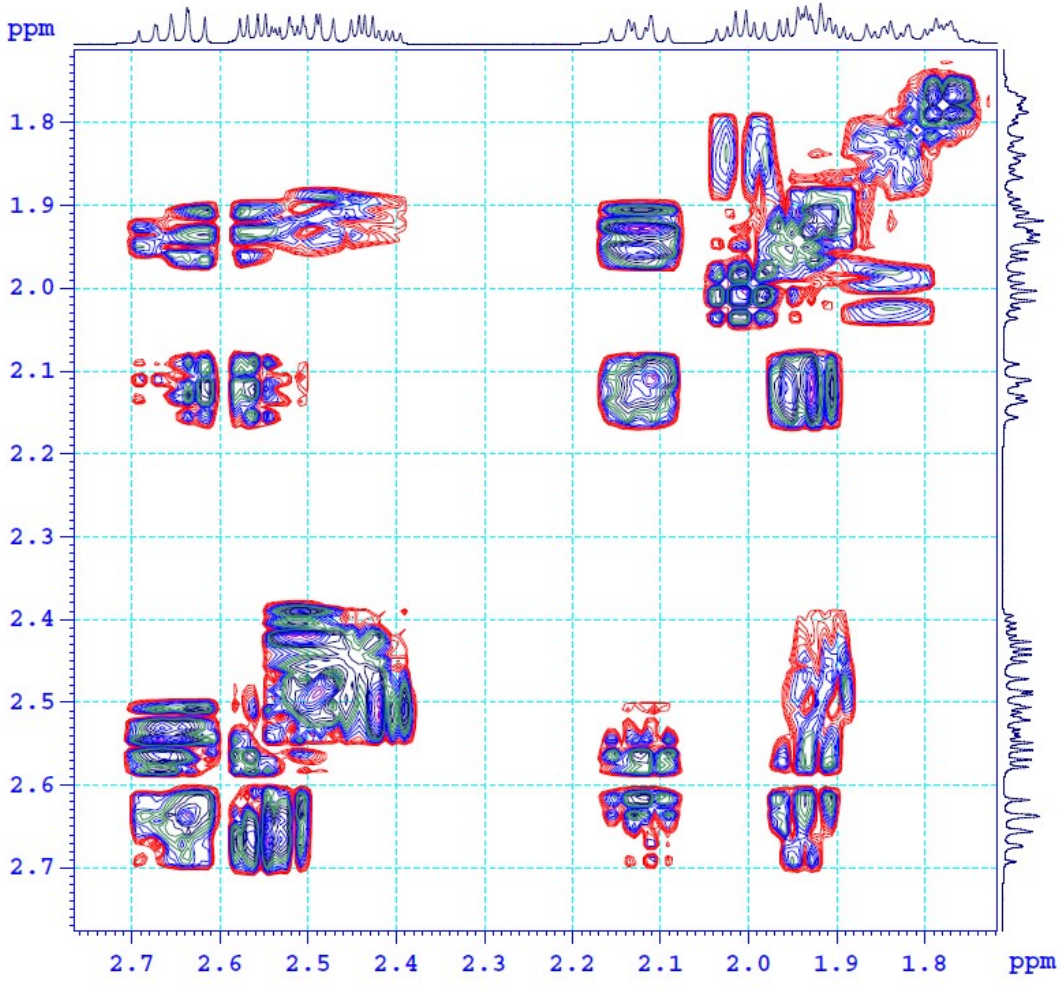
DEPT spectrum of compound **4** (extension)



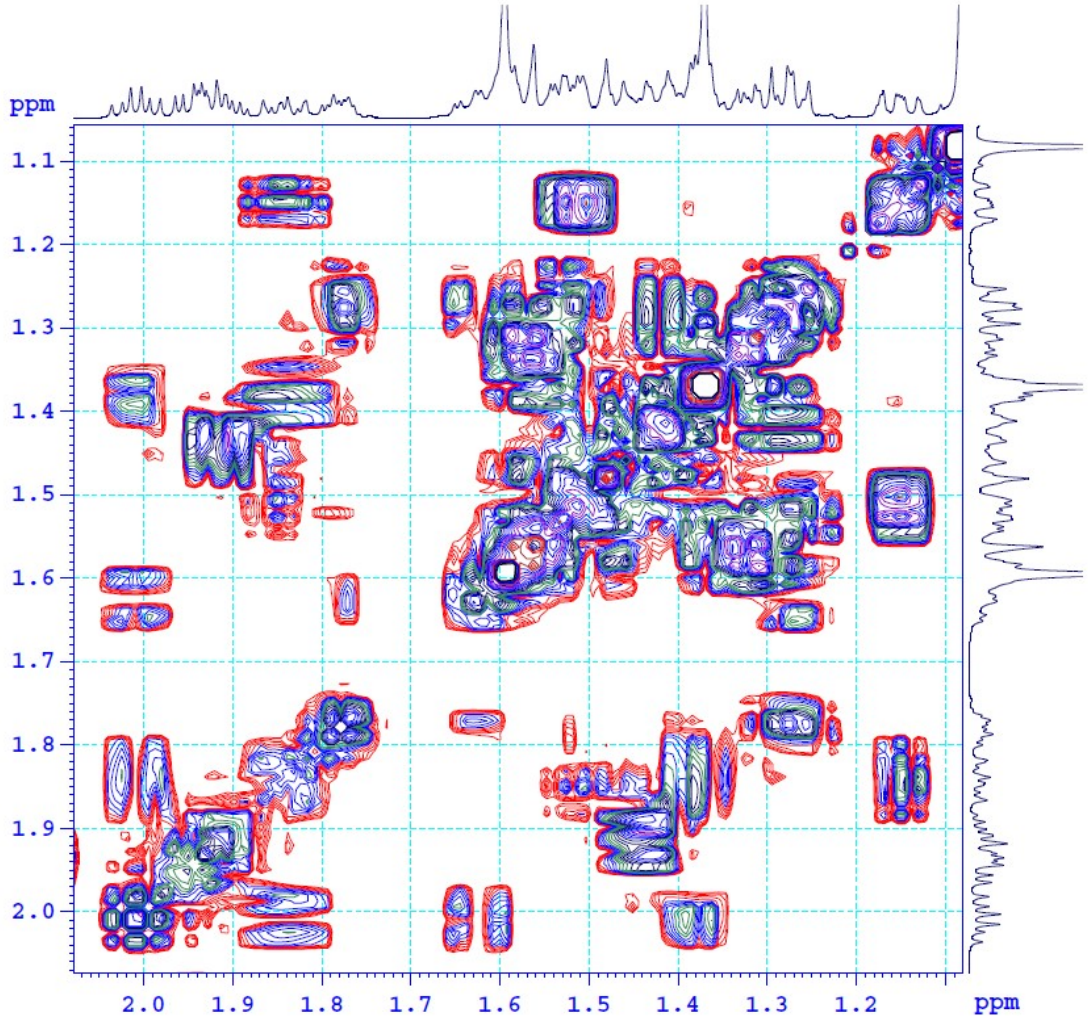
COSY spectrum of compound **4**



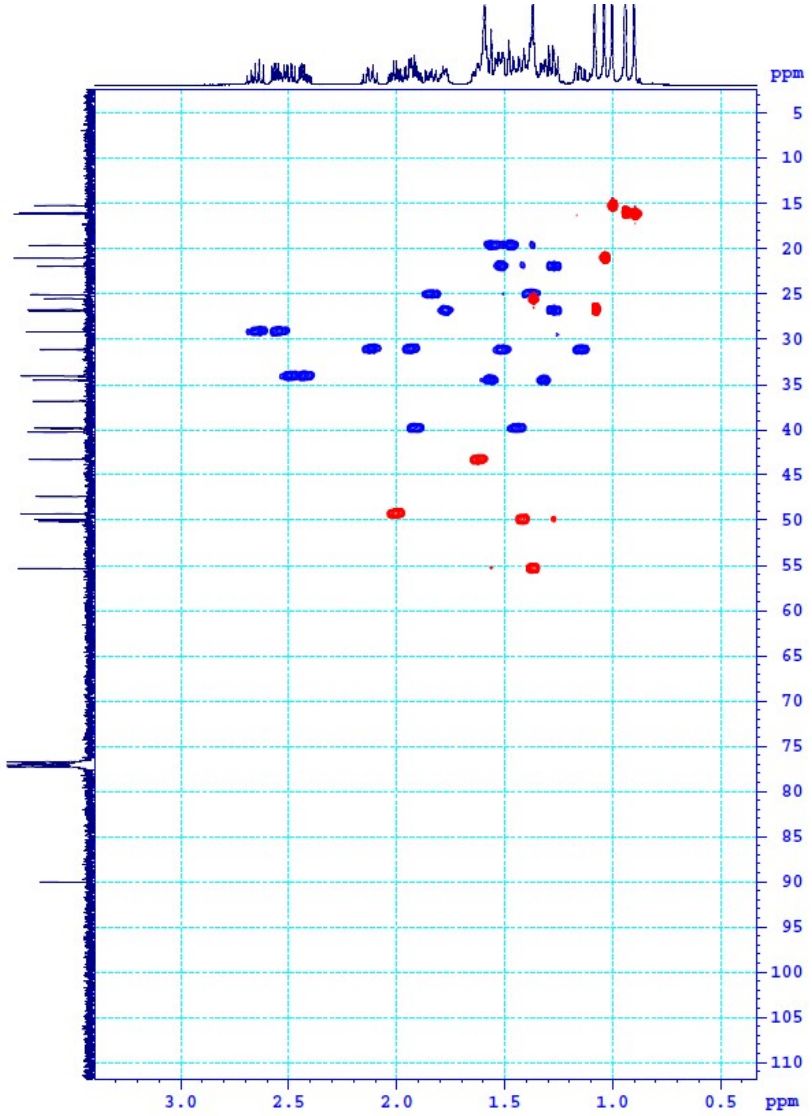
COSY spectrum of compound **4** (extension)



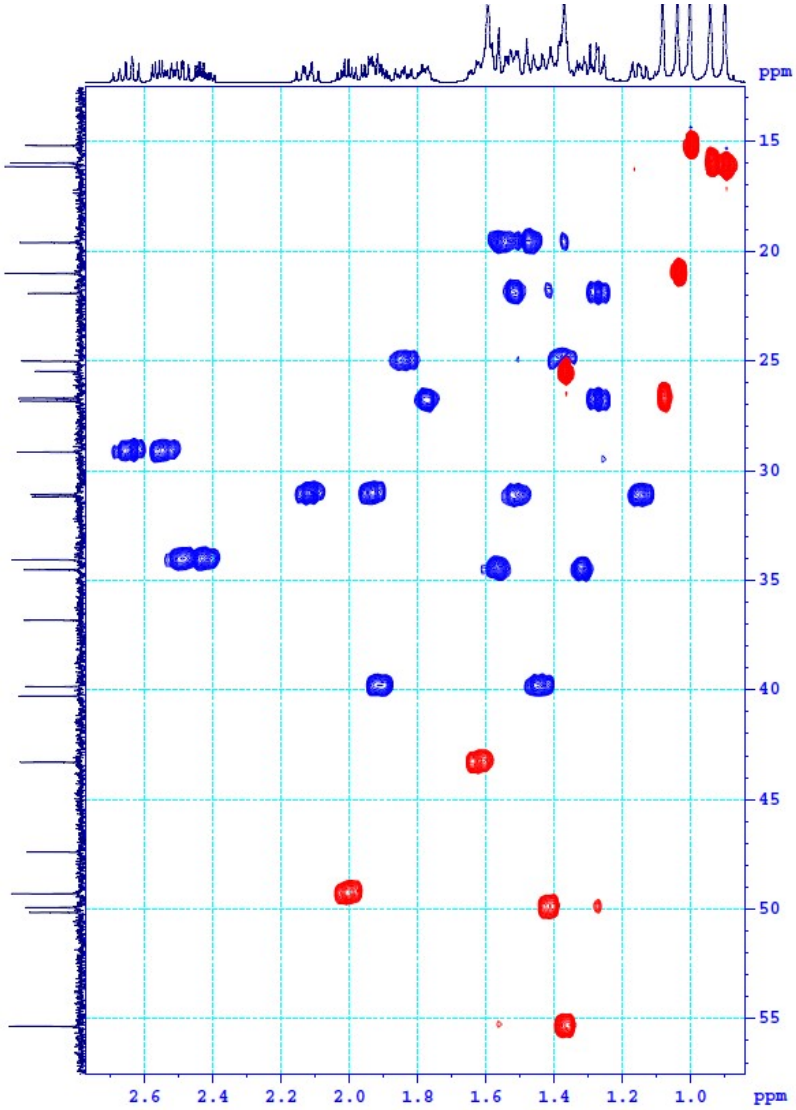
COSY spectrum of compound **4** (extension)



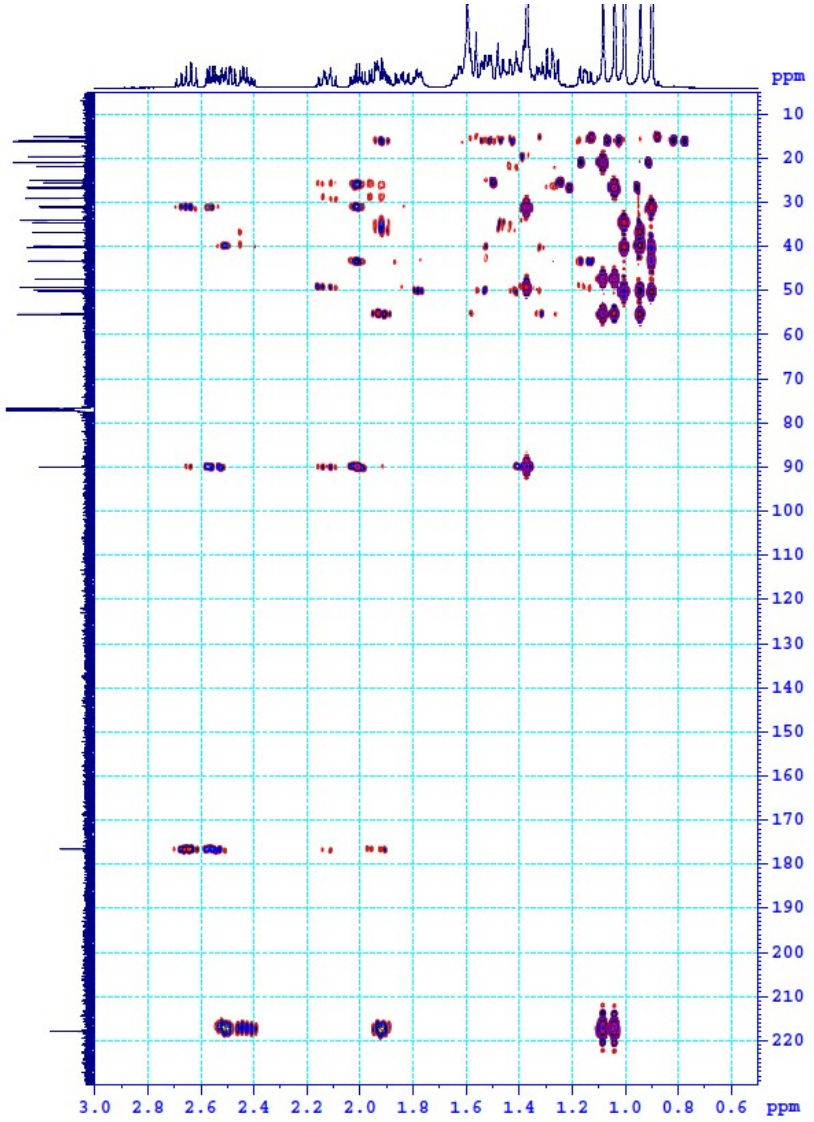
COSY spectrum of compound **4** (extension)



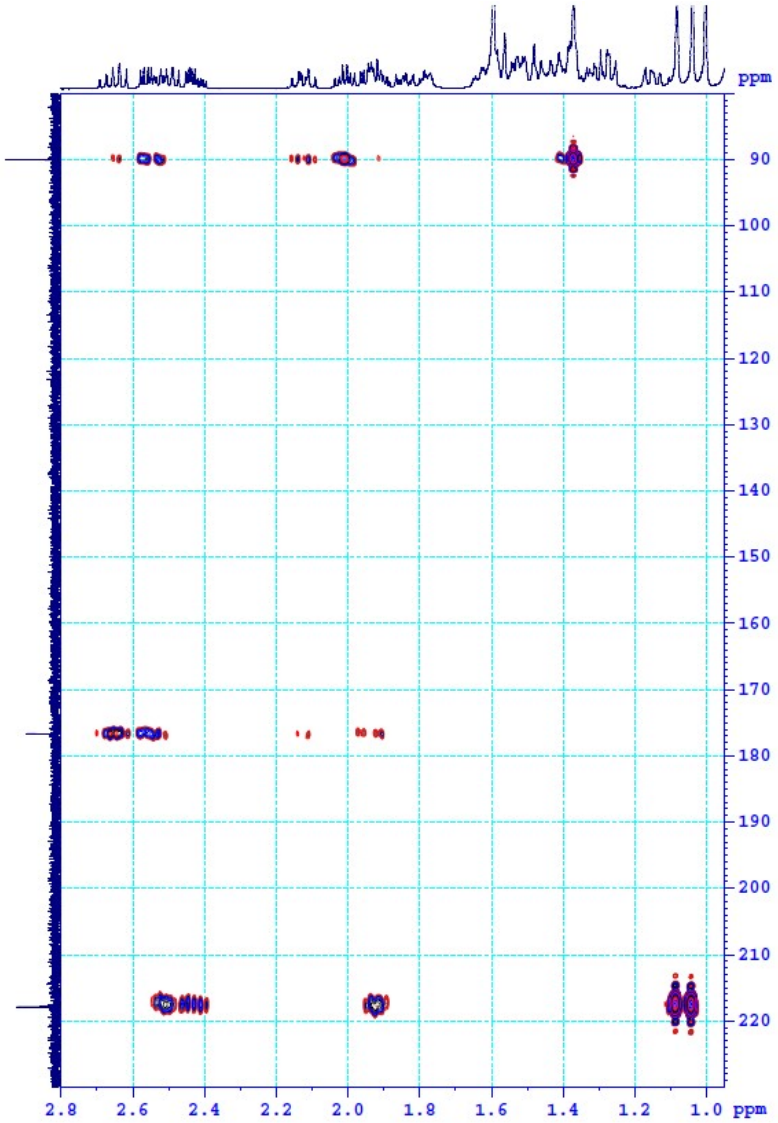
HSQC spectrum of compound **4**



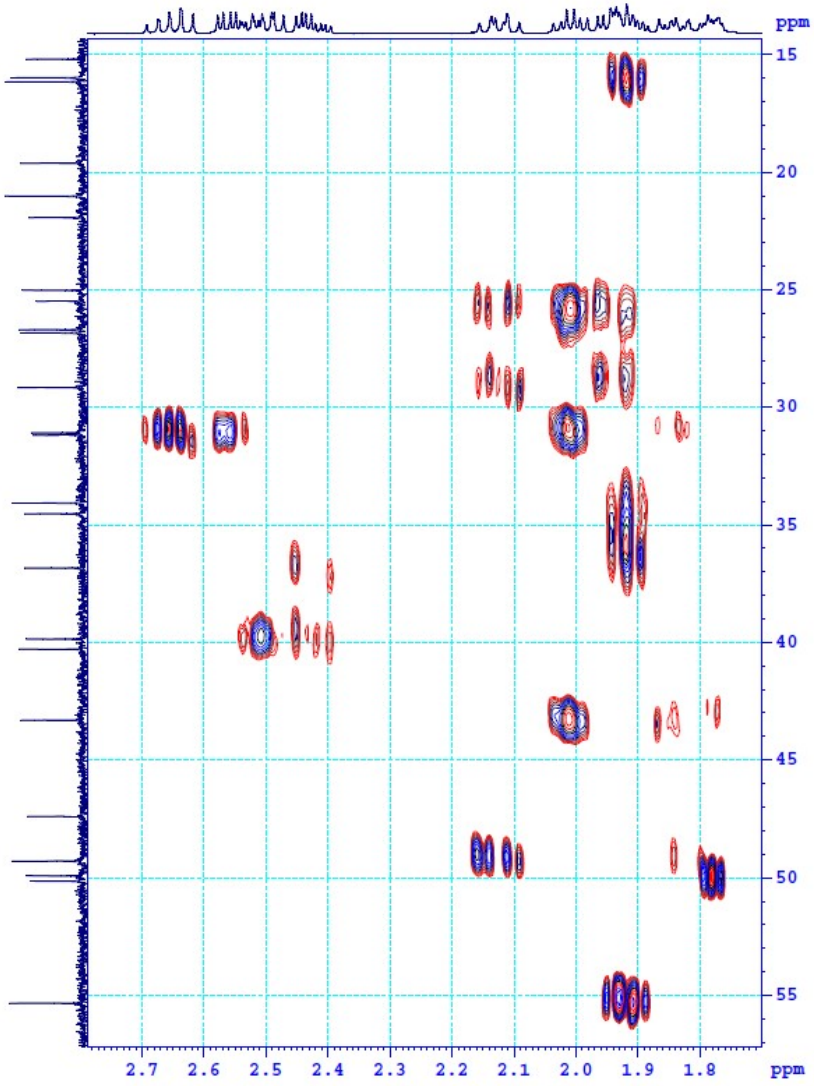
HSQC spectrum of compound **4** (extension)



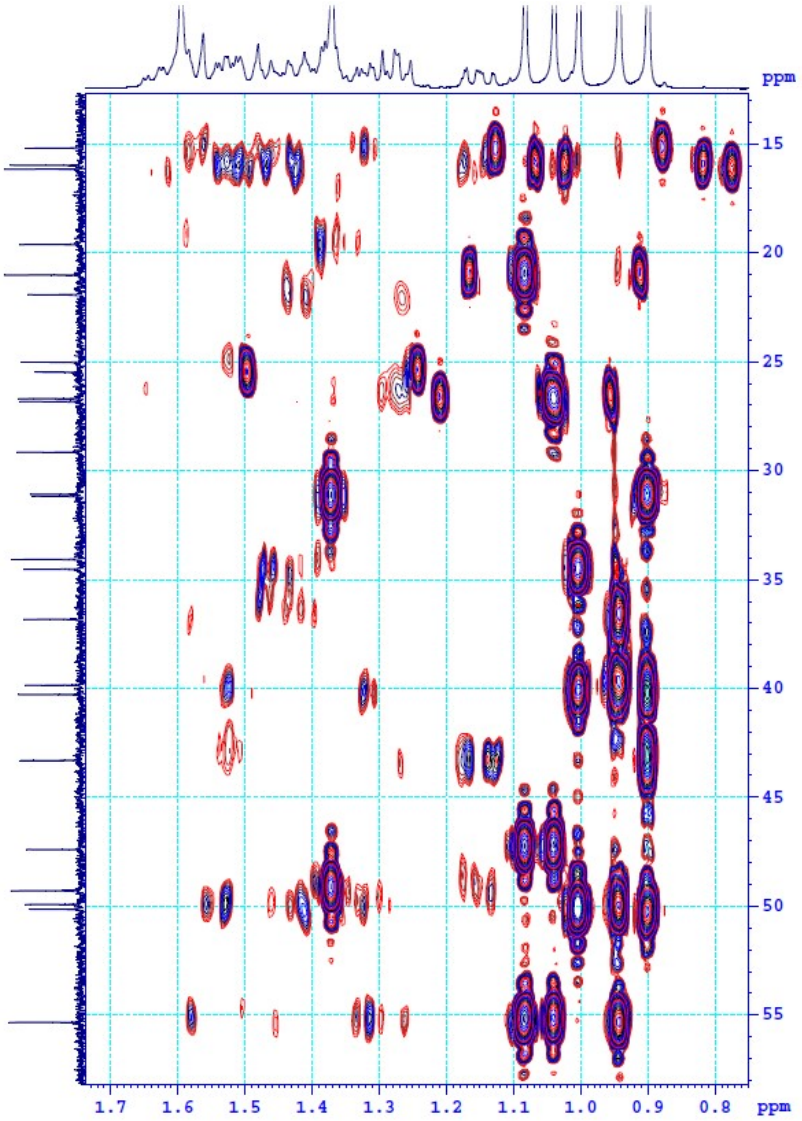
HMBC spectrum of compound 4



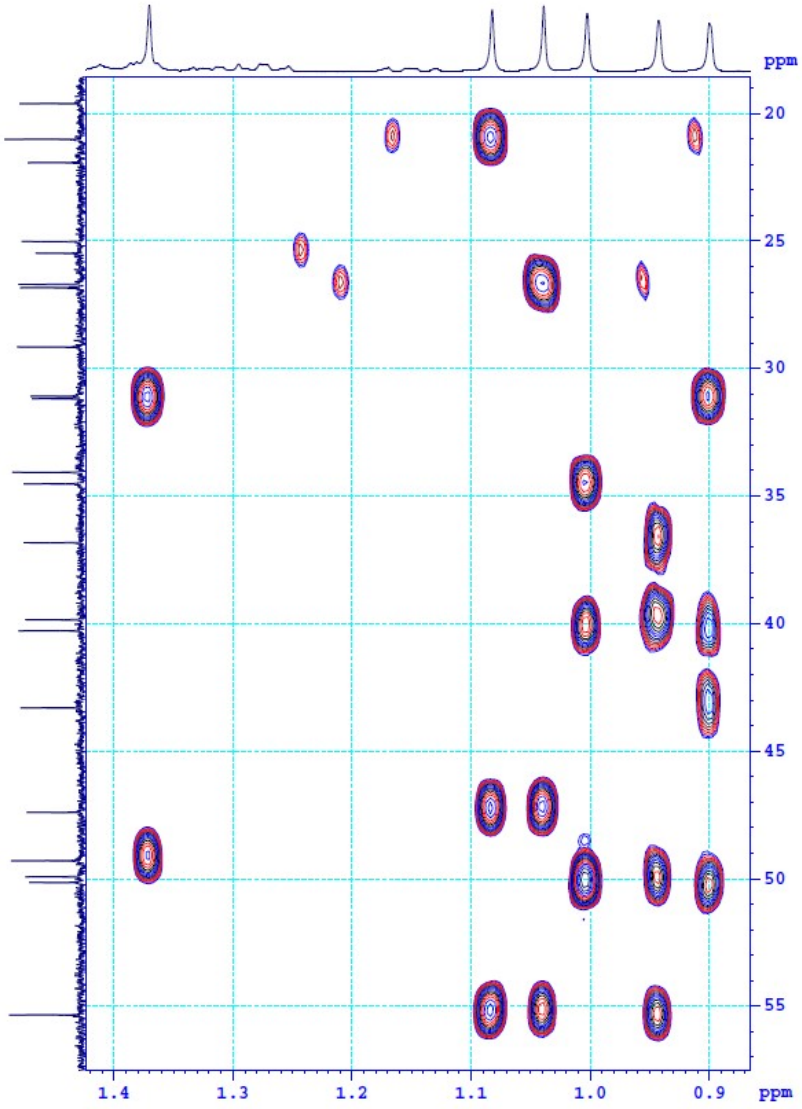
HMBC spectrum of compound **4** (extension)



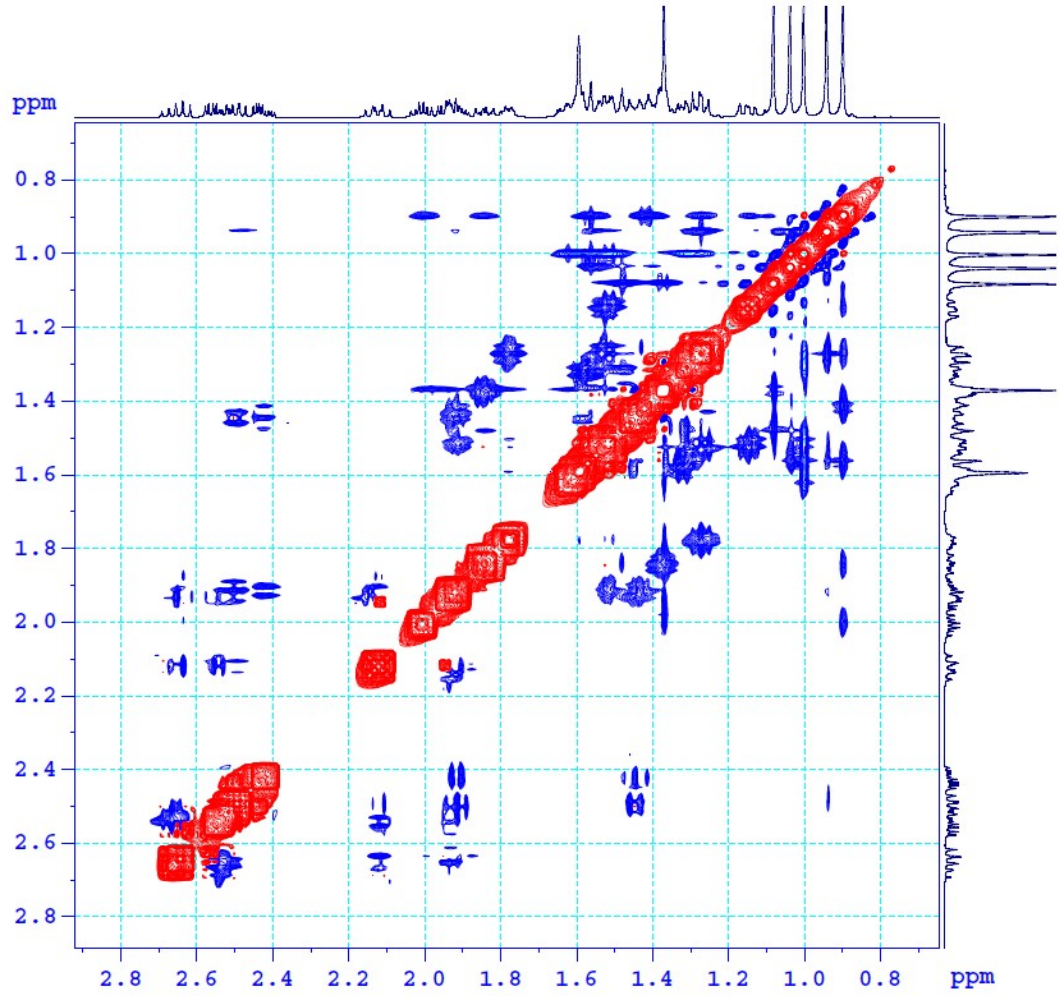
HMBC spectrum of compound **4** (extension)



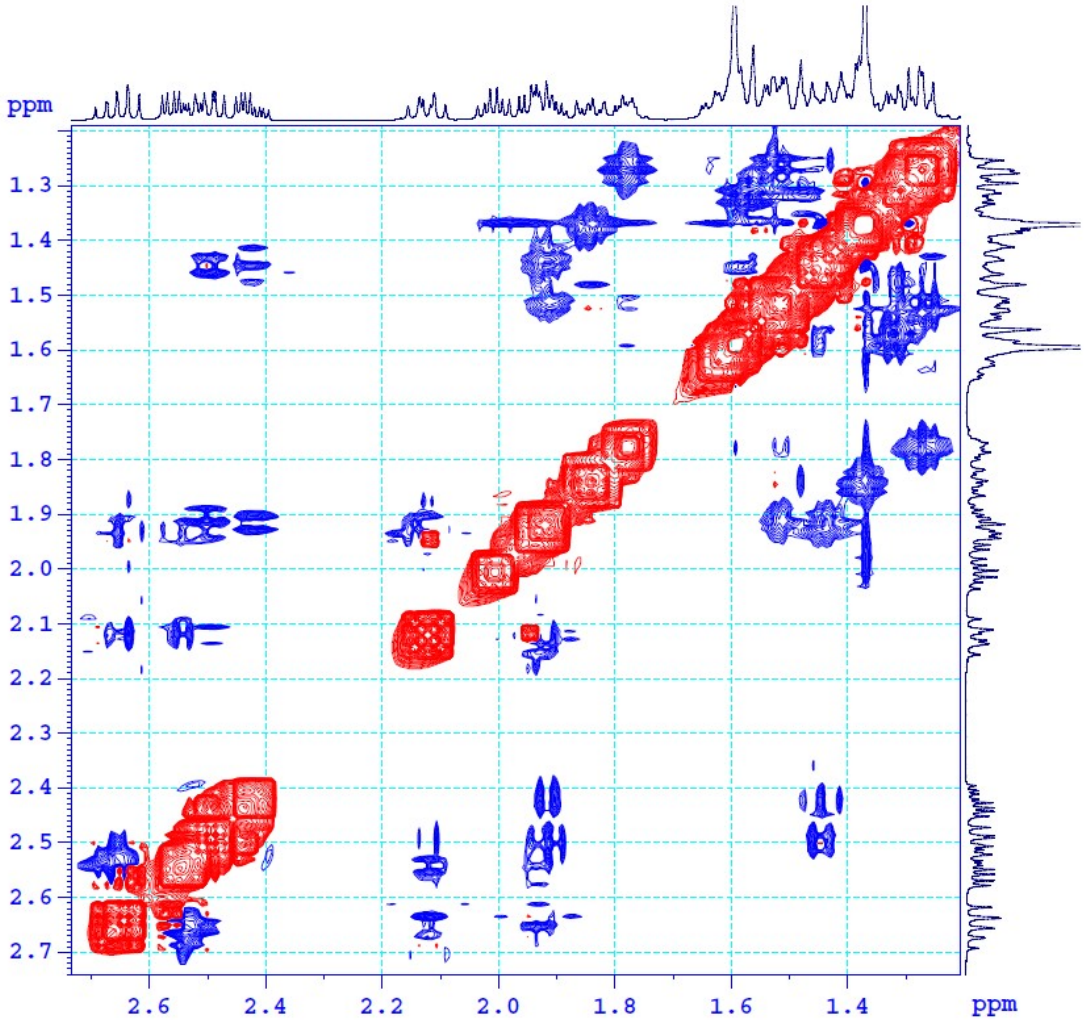
HMBC spectrum of compound **4** (extension)



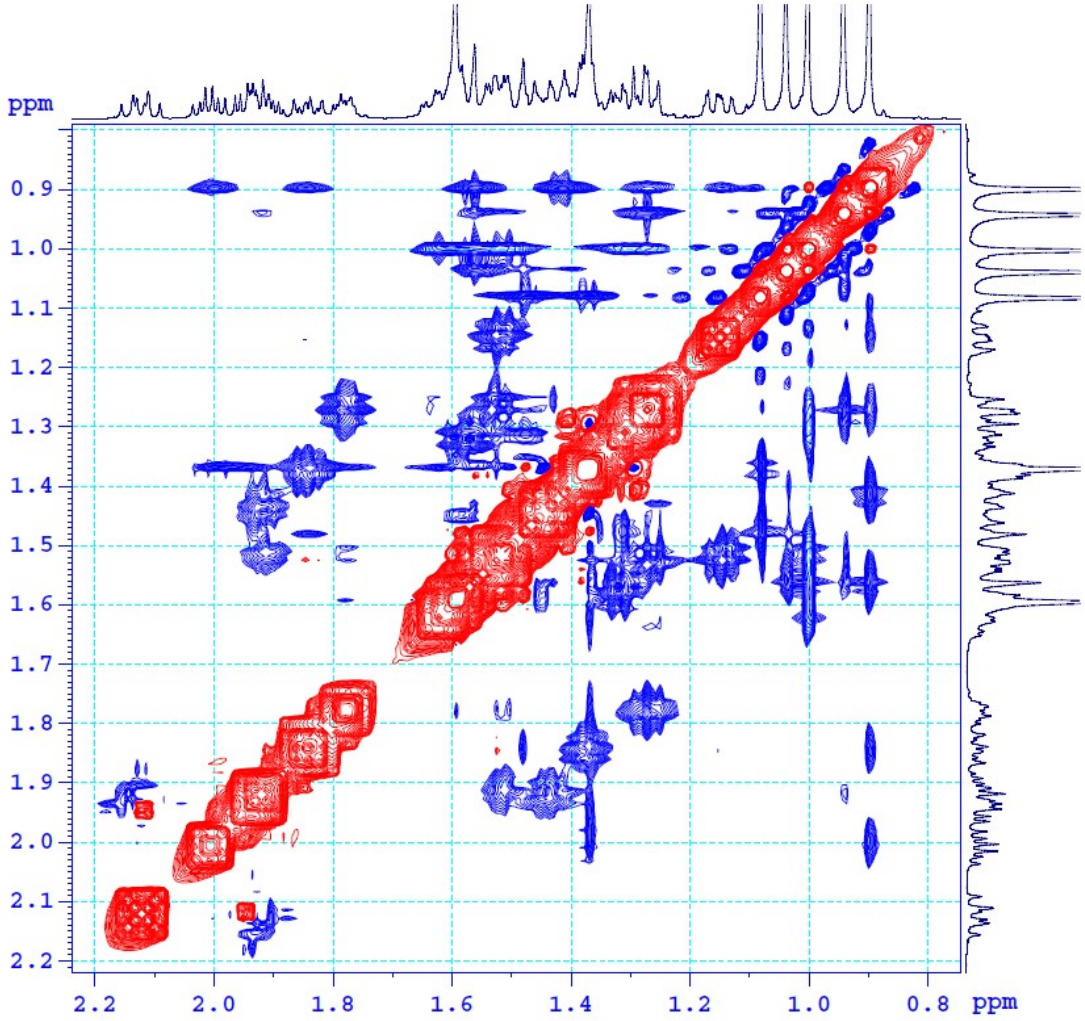
HMBC spectrum of compound **4** (extension)



NOESY spectrum of compound **4**



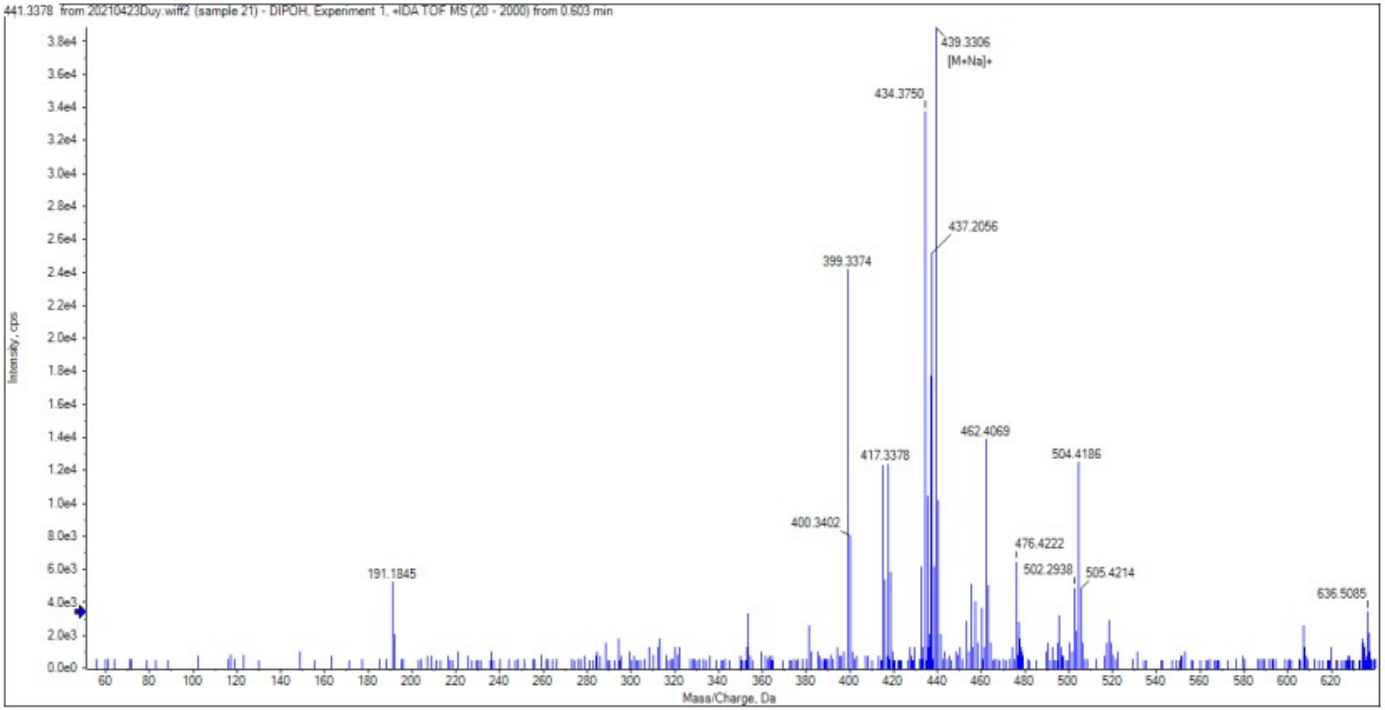
NOESY spectrum of compound **4** (extension)



NOESY spectrum of compound **4** (extension)

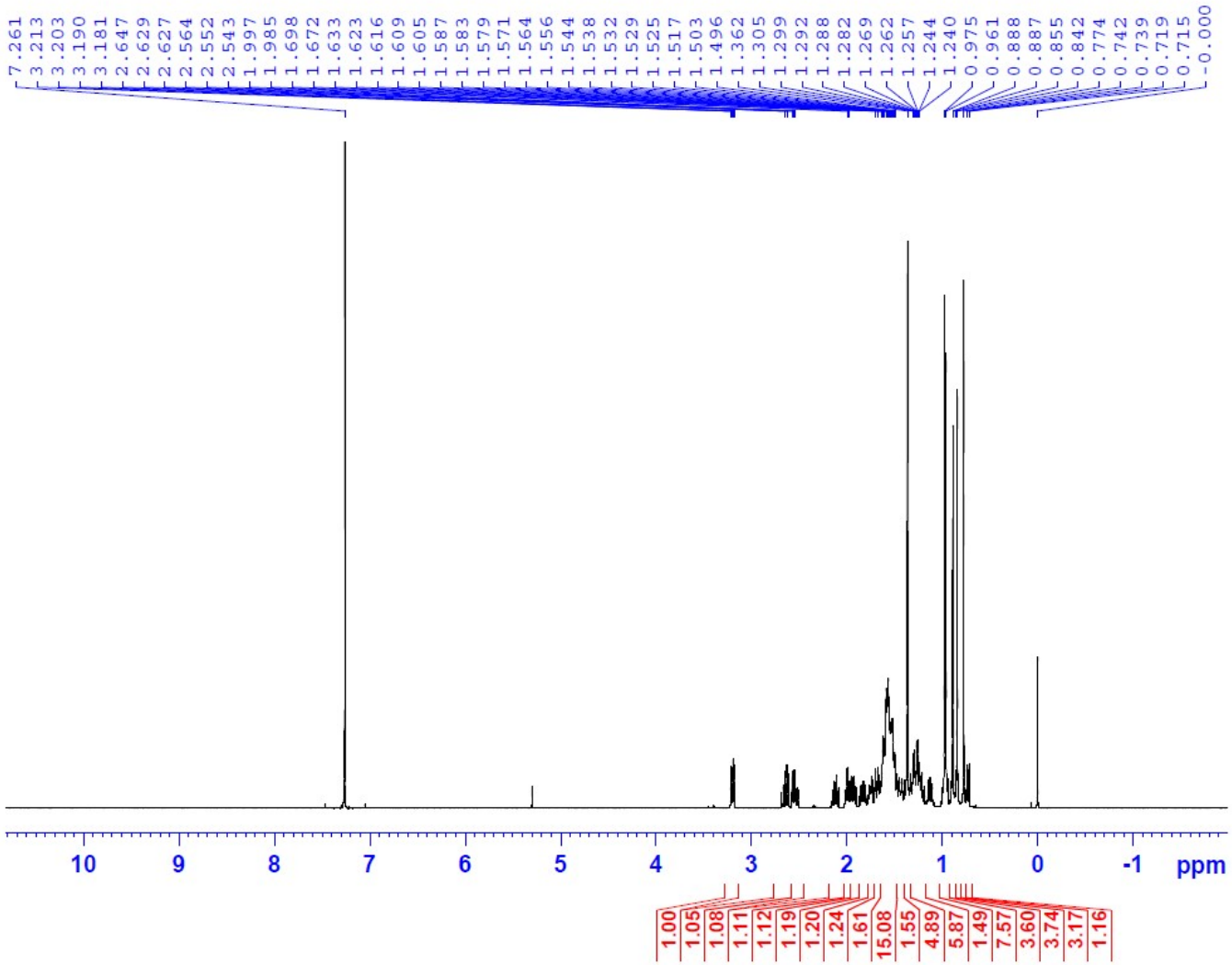
1.16. Compound 5

Sample name: DipOH
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

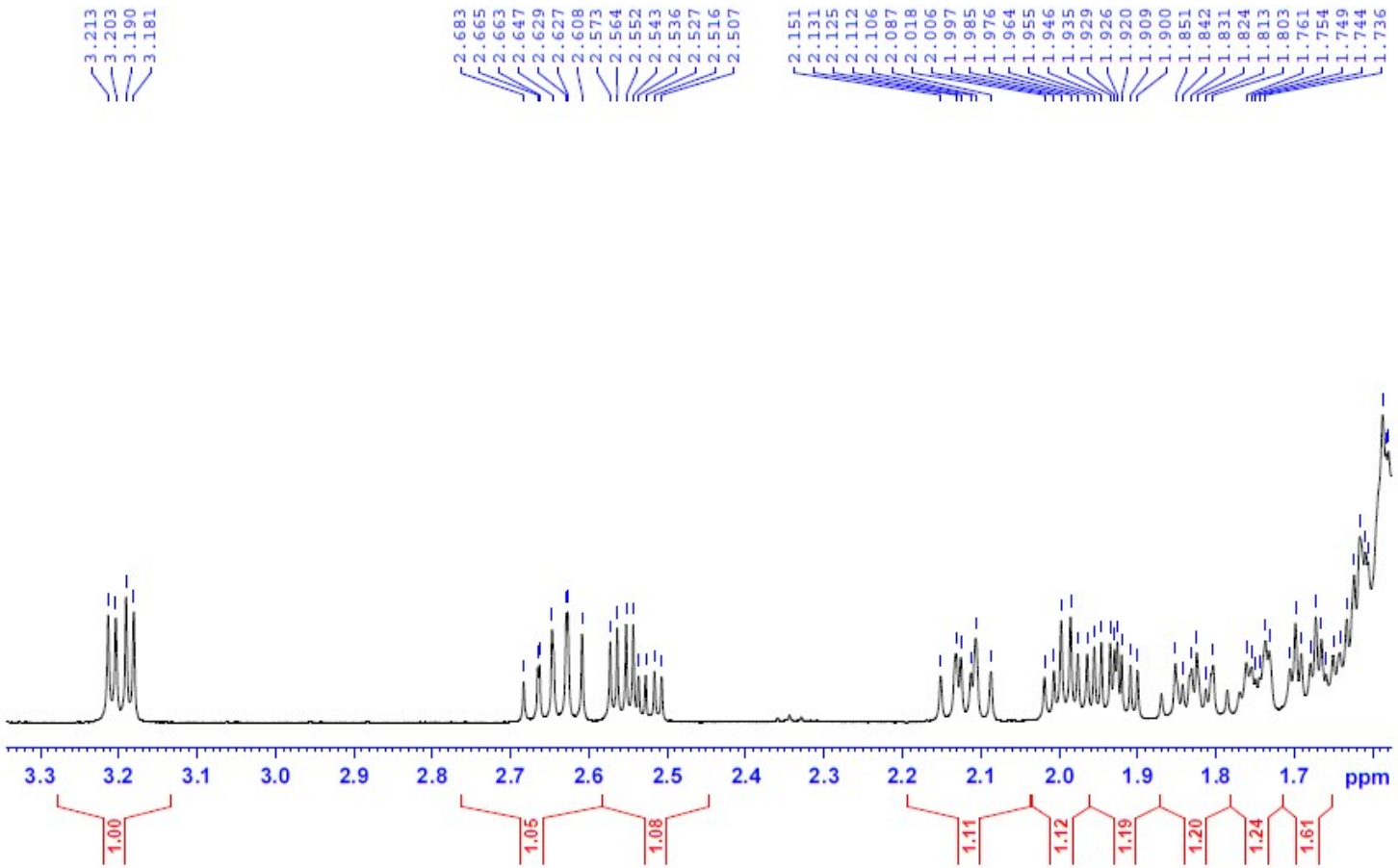


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C27H44O3	417.33632	6.0	1.9	1			NA/NA

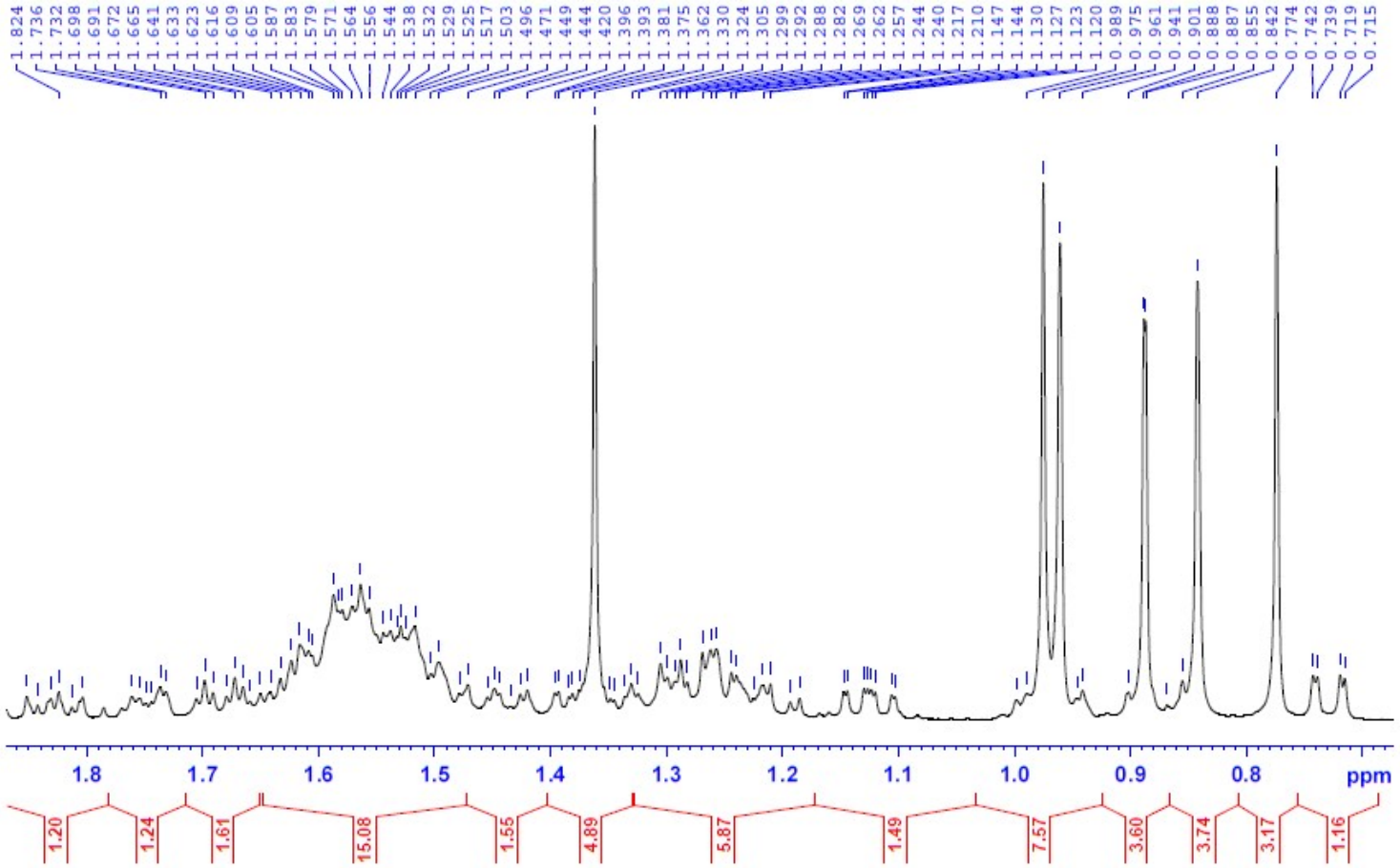
(+)-HR-ESI-MS spectrum of compound **5**



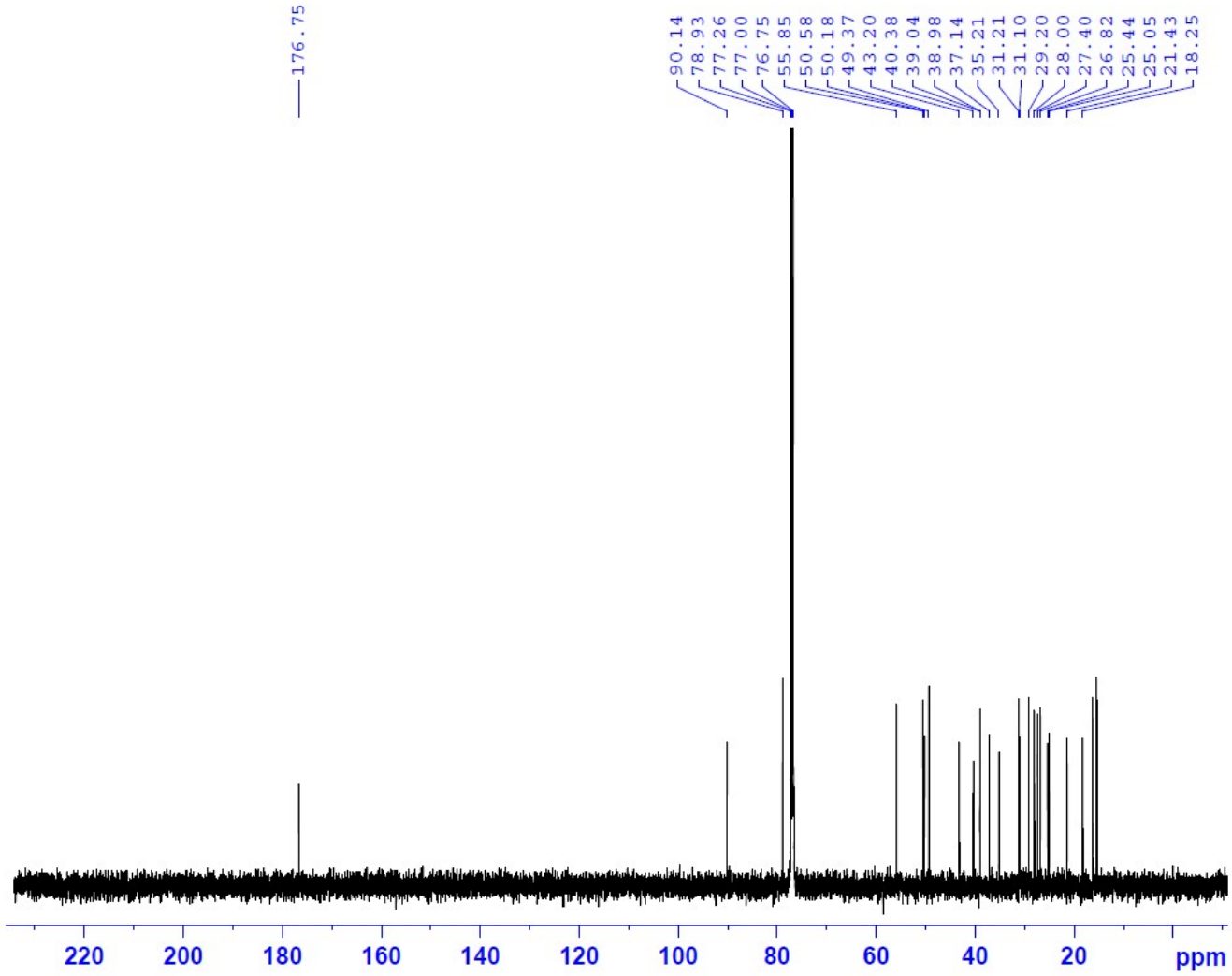
^{1}H-NMR spectrum of compound **5**


3.213
3.203
3.190
3.181
2.683
2.665
2.663
2.647
2.629
2.627
2.608
2.573
2.564
2.552
2.543
2.536
2.527
2.516
2.507
2.151
2.131
2.125
2.112
2.106
2.087
2.018
2.006
1.997
1.985
1.976
1.964
1.955
1.946
1.935
1.929
1.926
1.920
1.909
1.900
1.851
1.842
1.831
1.824
1.813
1.803
1.761
1.754
1.749
1.744
1.736
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
ppm
1.00
1.05
1.08
1.11
1.12
1.19
1.20
1.24
1.61

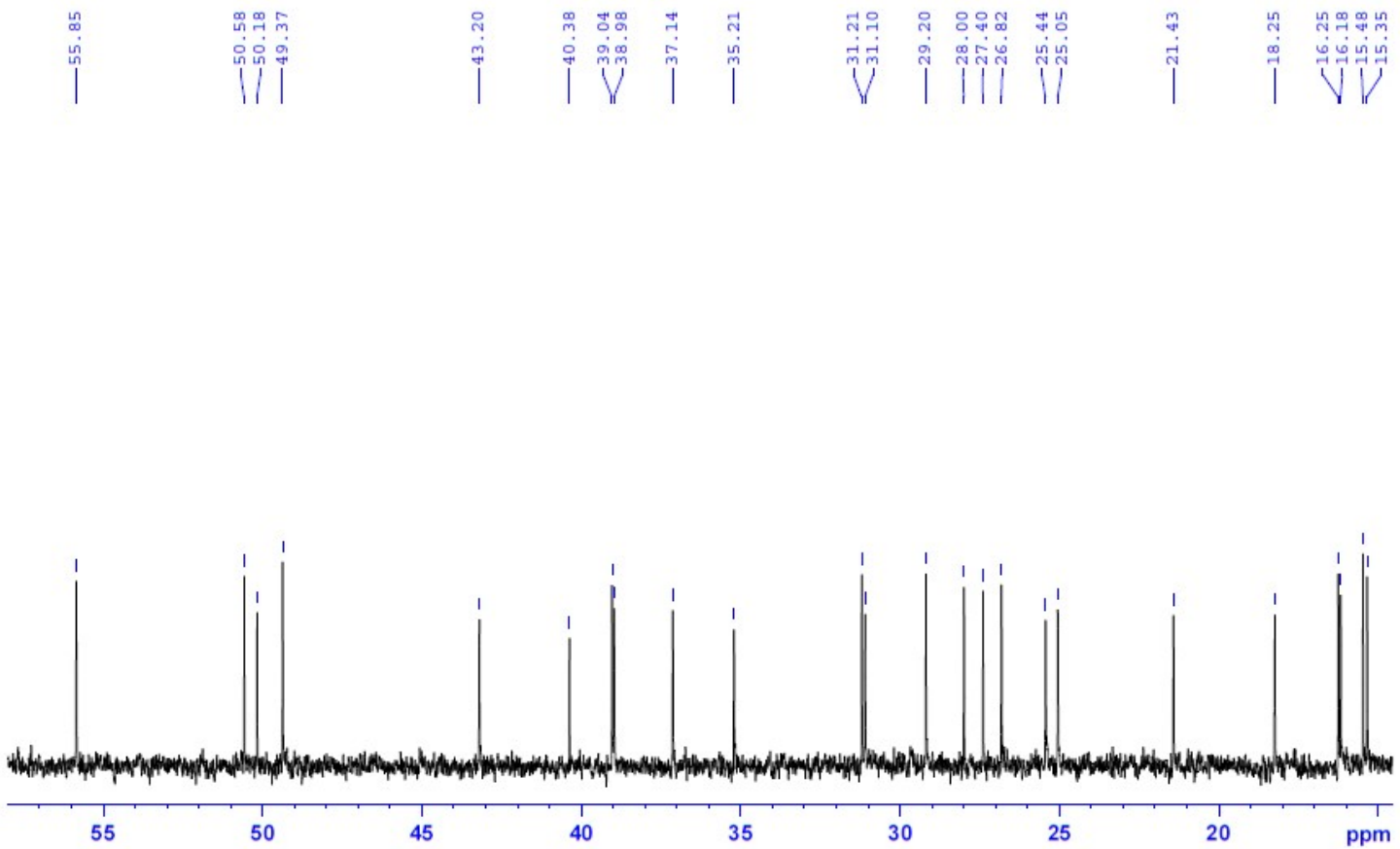
^{1}H-NMR spectrum of compound **5** (extension)


1.824
1.736
1.732
1.698
1.691
1.672
1.665
1.641
1.633
1.623
1.616
1.609
1.605
1.587
1.583
1.579
1.571
1.564
1.556
1.544
1.538
1.532
1.529
1.525
1.517
1.503
1.496
1.471
1.449
1.444
1.420
1.396
1.393
1.381
1.375
1.362
1.330
1.324
1.305
1.299
1.292
1.288
1.282
1.269
1.262
1.257
1.244
1.240
1.217
1.210
1.147
1.144
1.130
1.127
1.123
1.120
0.989
0.975
0.961
0.941
0.901
0.888
0.887
0.855
0.842
0.774
0.742
0.739
0.719
0.715
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm
1.20
1.24
1.61
15.08
1.55
4.89
5.87
1.49
7.57
3.60
3.74
3.17
1.16

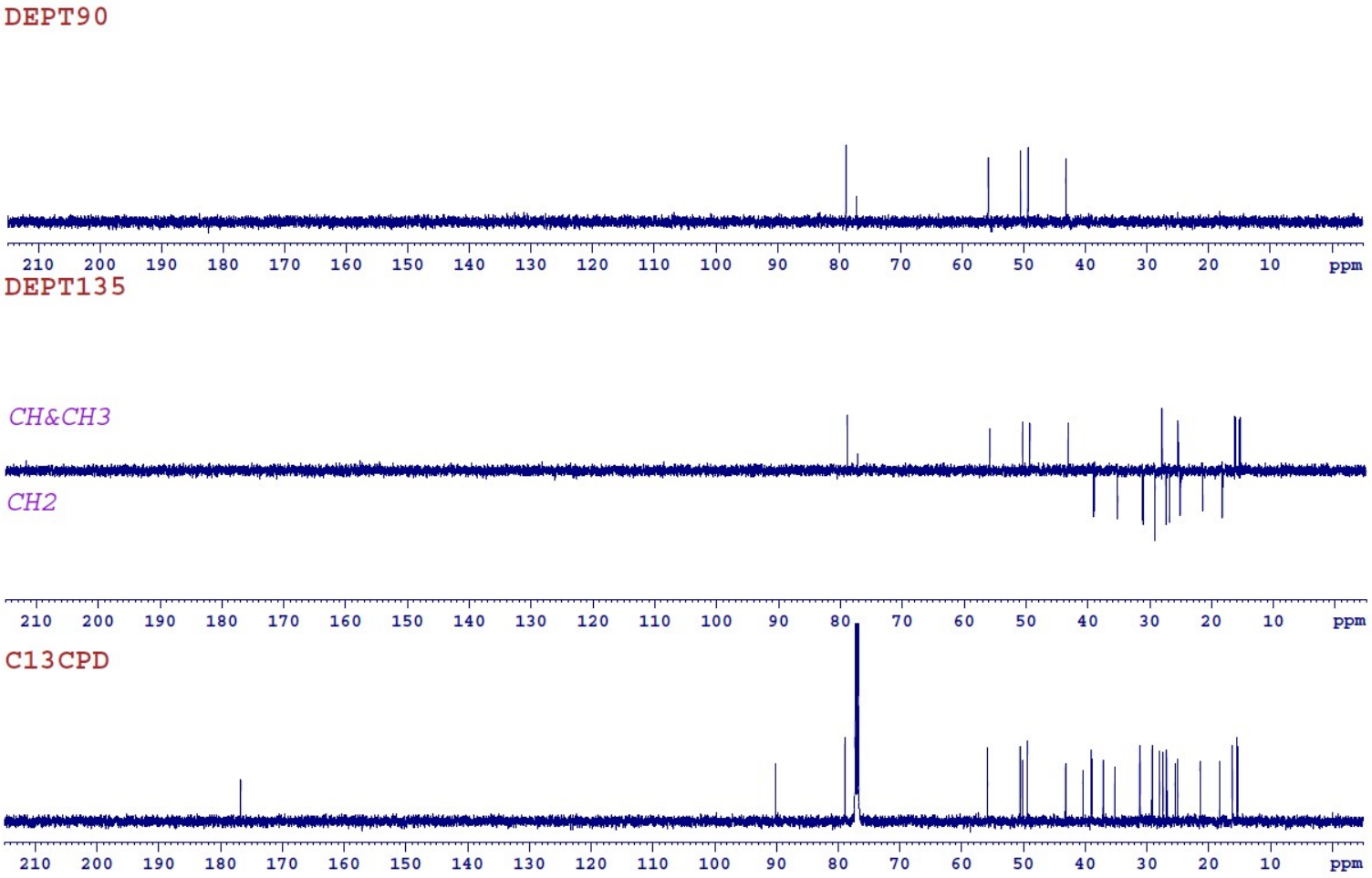
^{1}H-NMR spectrum of compound **5** (extension)



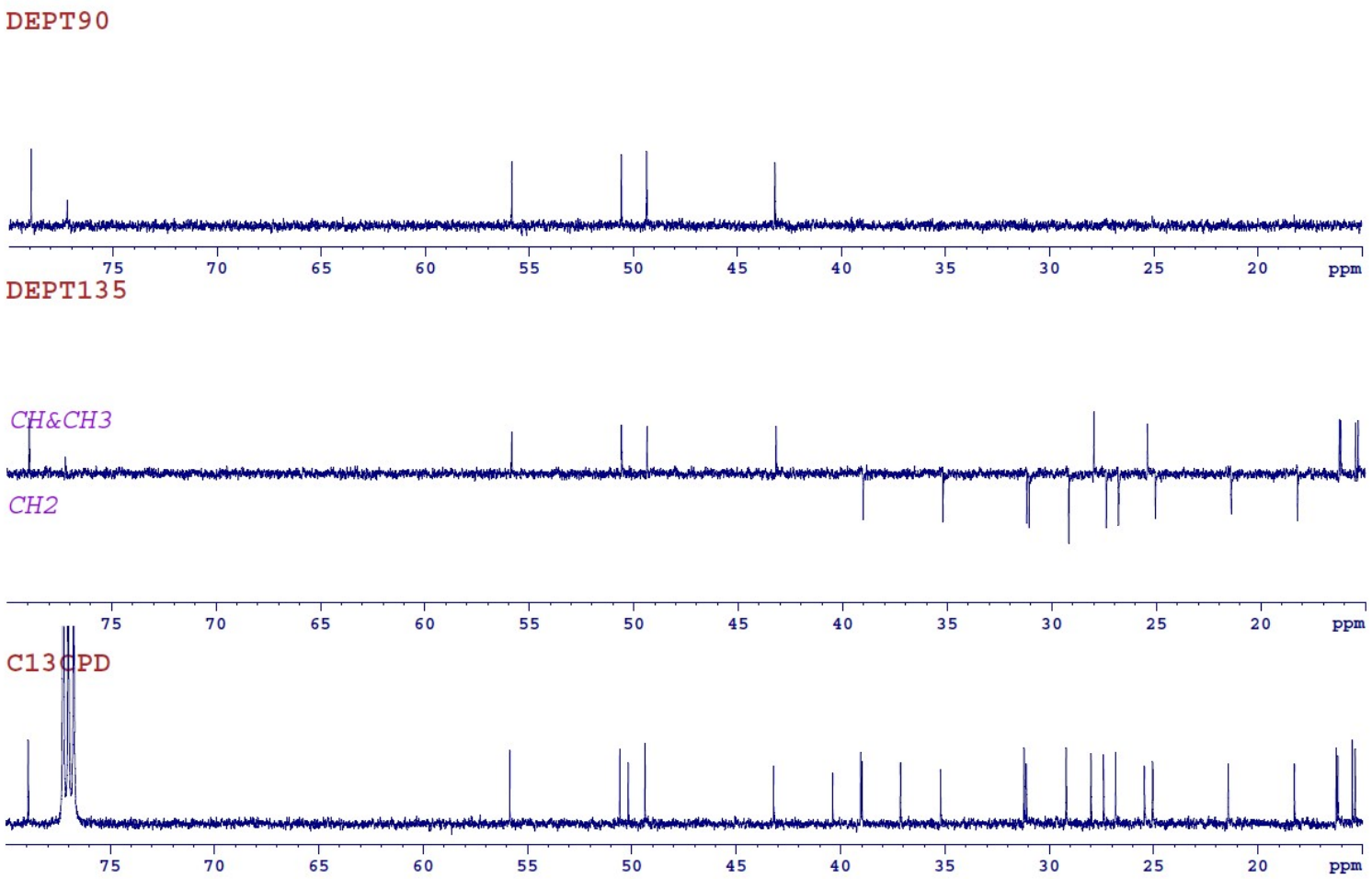
^{13}C-NMR spectrum of compound **5**


55.85
50.58
50.18
49.37
43.20
40.38
39.04
38.98
37.14
35.21
31.21
31.10
29.20
28.00
27.40
26.82
25.44
25.05
21.43
18.25
16.25
16.18
15.48
15.35
55
50
45
40
35
30
25
20
ppm

^{13}C-NMR spectrum of compound **5** (extension)



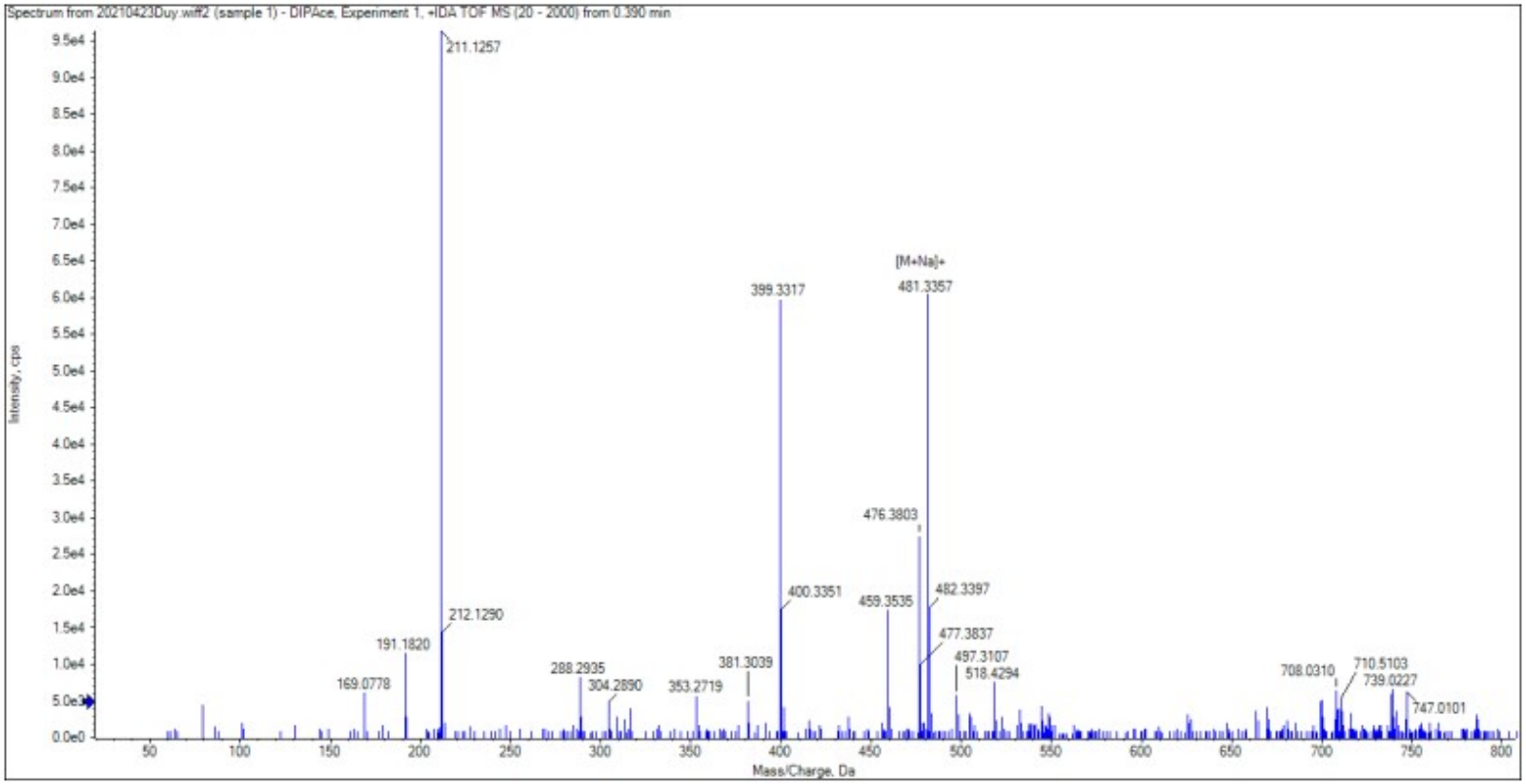
DEPT spectrum of compound **5**



DEPT spectrum of compound **5** (extension)

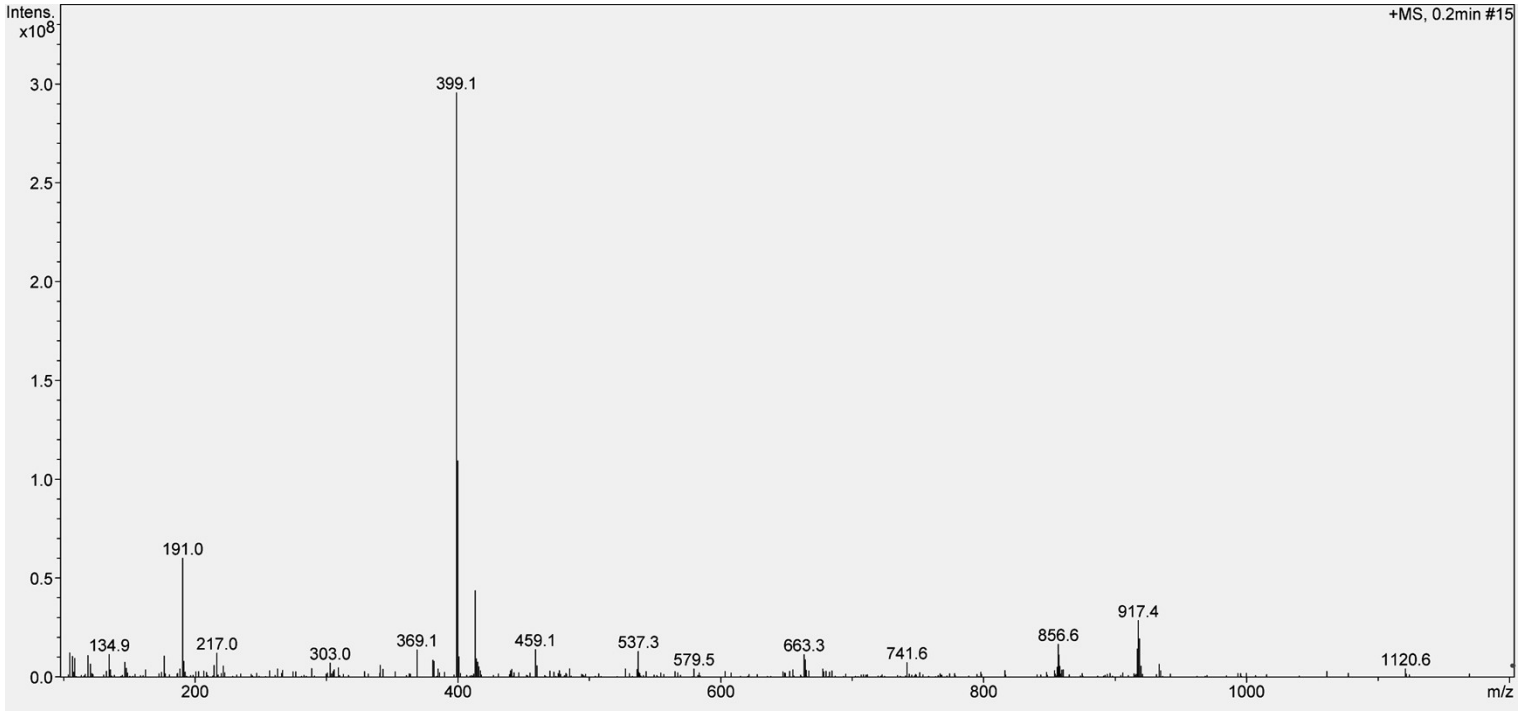
1.17. Compound 6a

Sample name: DIPAcE
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

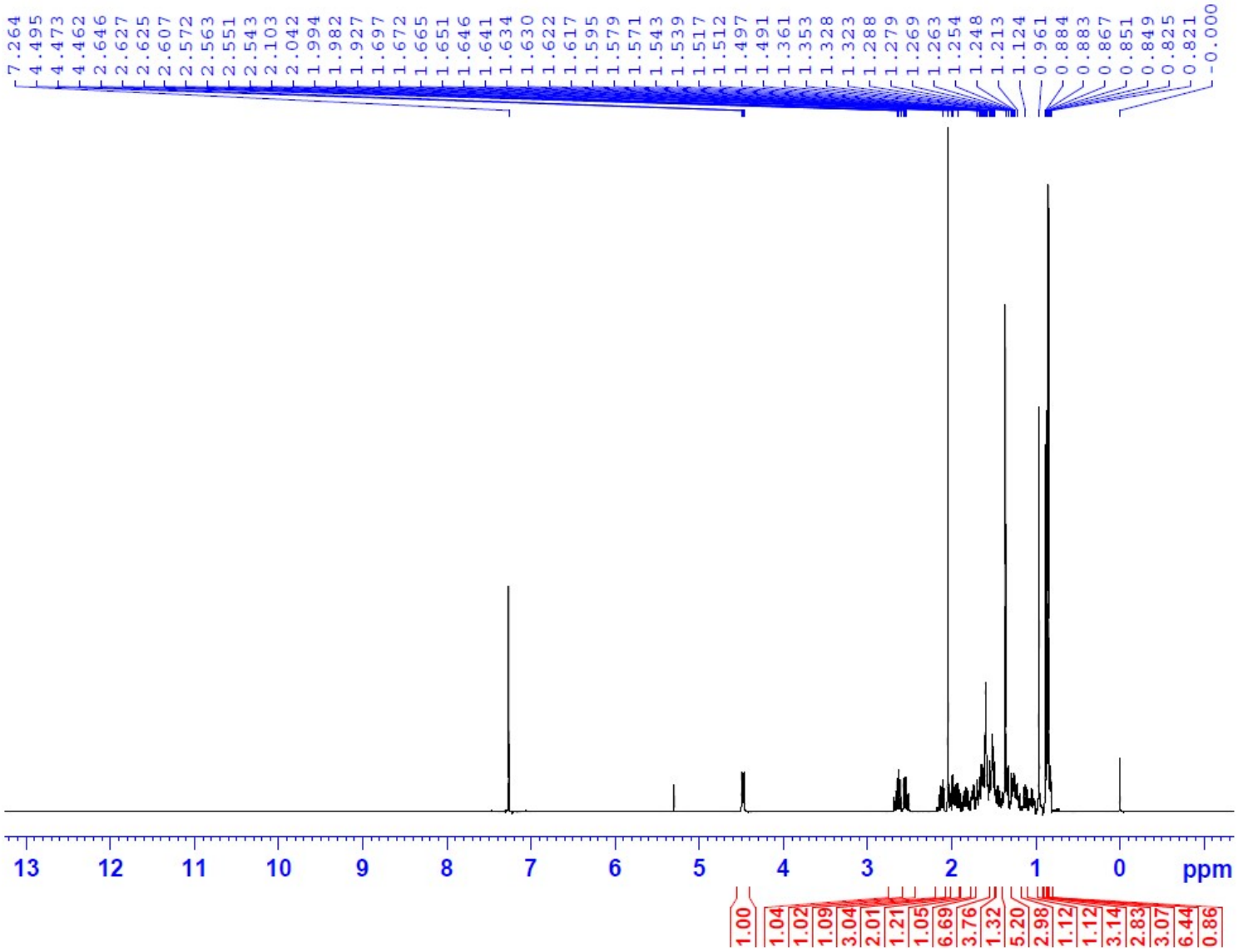


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C29H46O4	481.32883	7.0	4.3	1			NA/NA

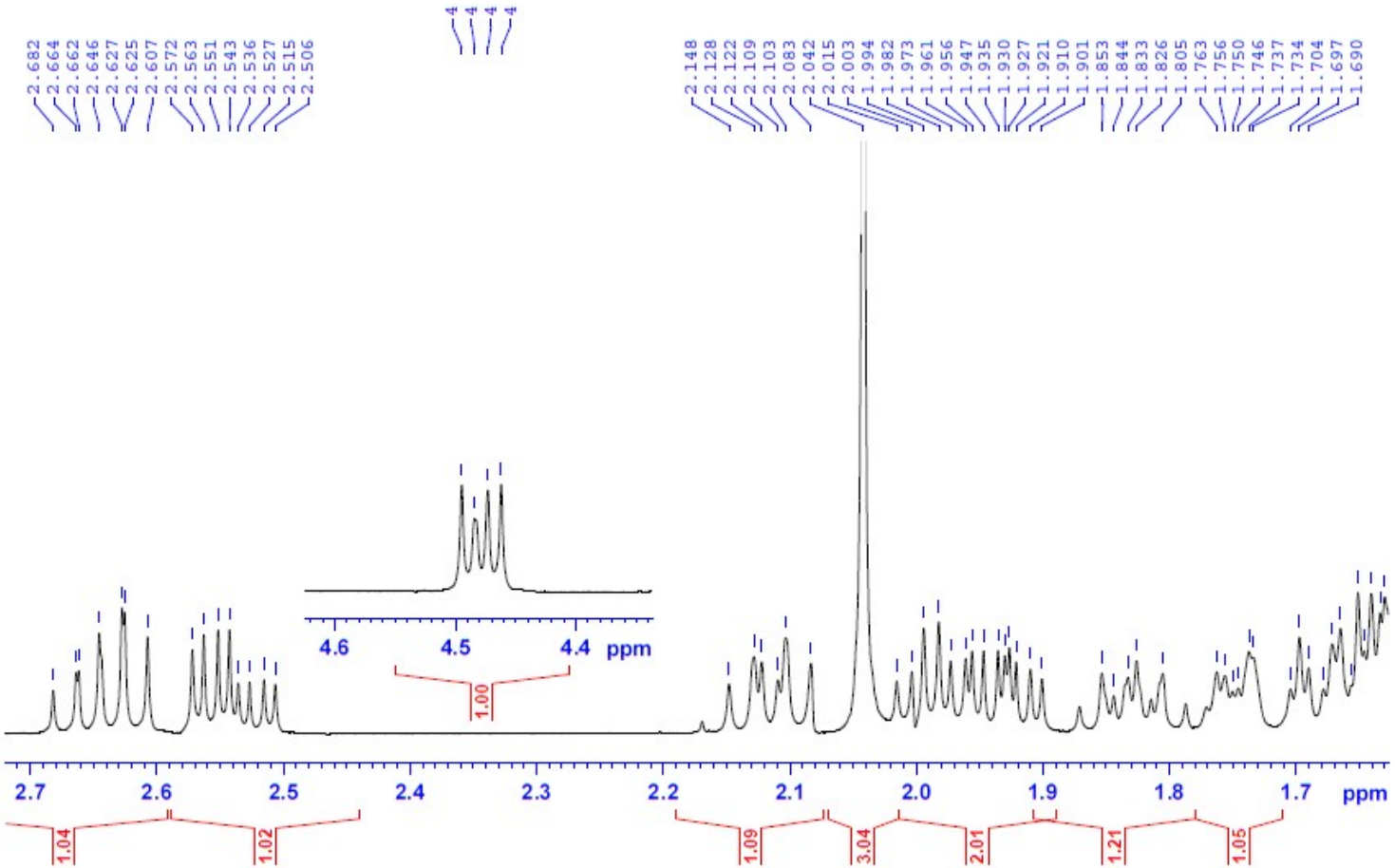
(+)-HR-ESI-MS spectrum of compound **6a**



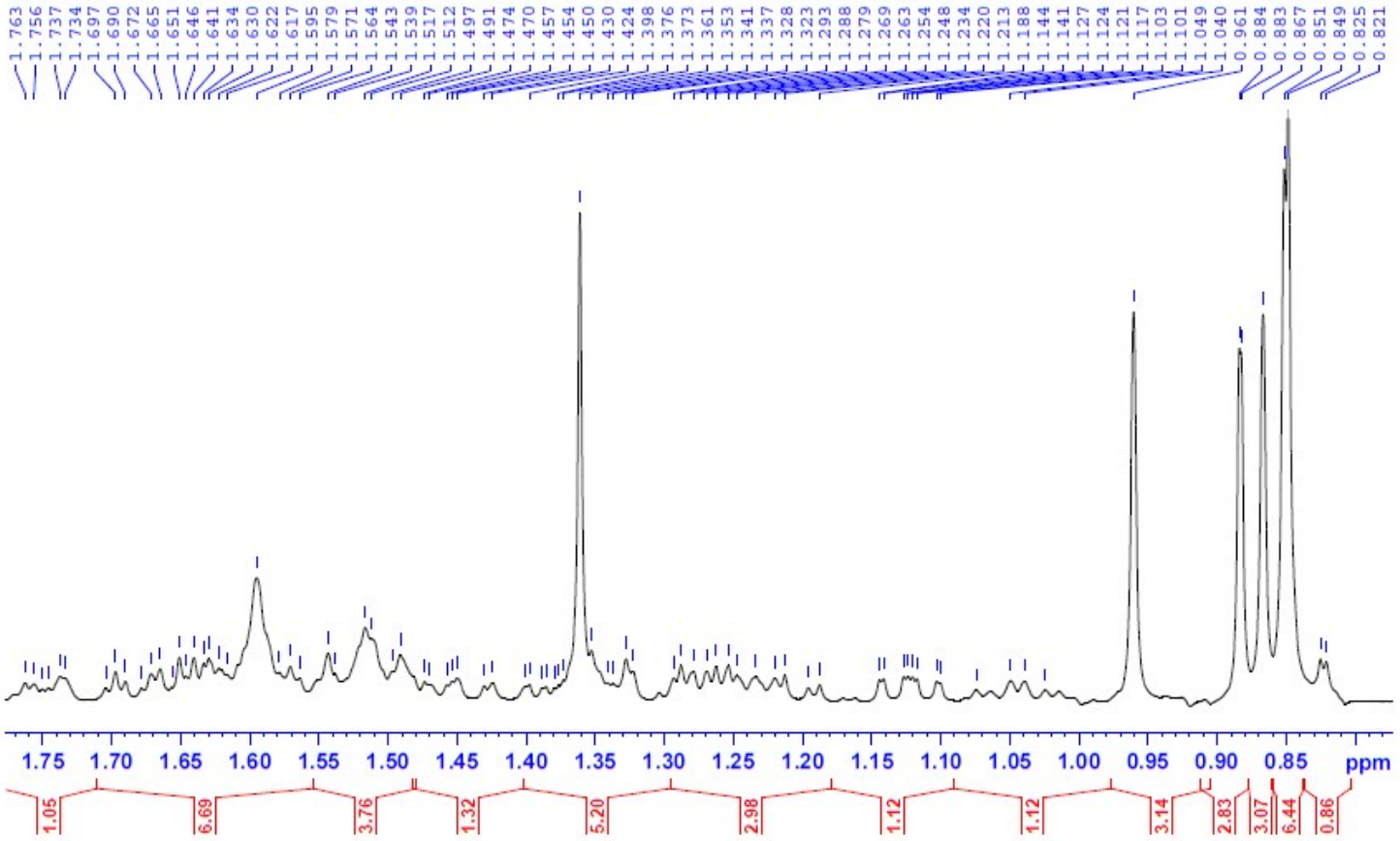
(+)-ESI–MS spectrum of compound **6a**



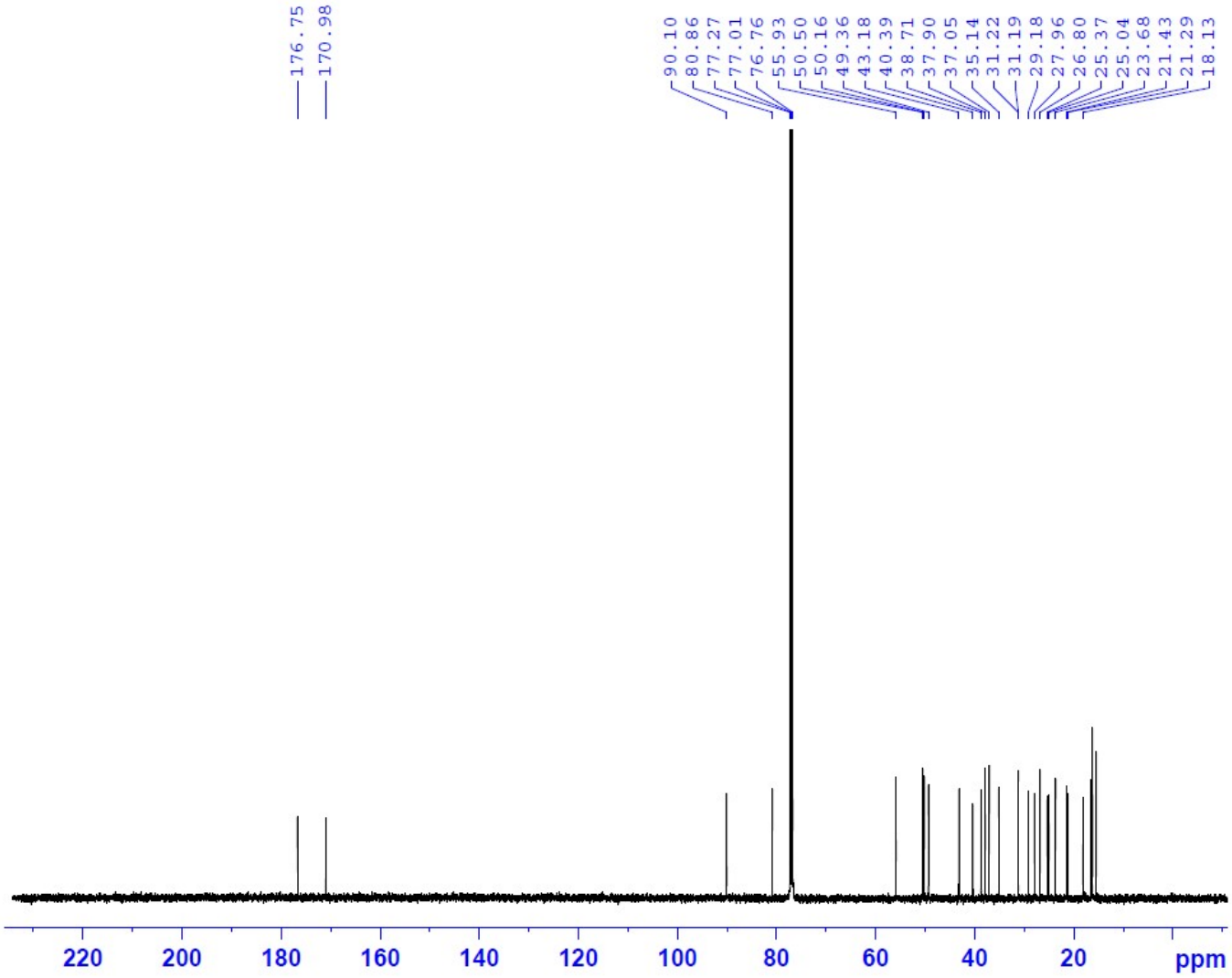
^{1}H-NMR spectrum of compound **6a**


2.682
2.664
2.662
2.646
2.627
2.625
2.607
2.572
2.563
2.551
2.543
2.536
2.527
2.515
2.506
4
4
4
4
2.148
2.128
2.122
2.109
2.103
2.083
2.042
2.015
2.003
1.994
1.982
1.973
1.961
1.956
1.947
1.935
1.930
1.927
1.921
1.910
1.901
1.853
1.844
1.833
1.826
1.805
1.763
1.756
1.750
1.746
1.737
1.734
1.704
1.697
1.690
4.6
4.5
4.4 ppm
1.00
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7 ppm
1.04
1.02
1.09
3.04
2.01
1.21
1.05

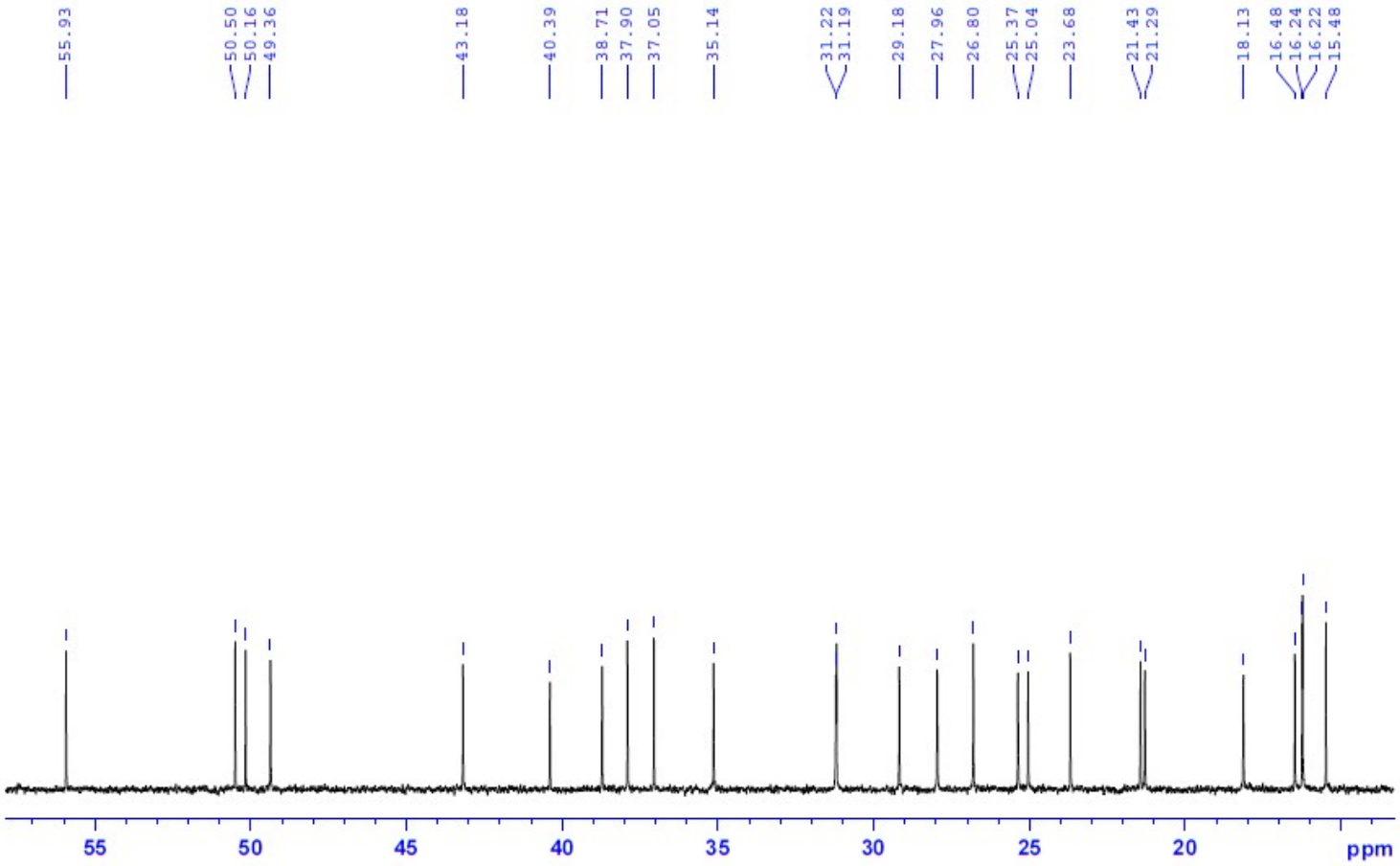
^{1}H-NMR spectrum of compound **6a** (extension)


1.763
1.756
1.737
1.734
1.697
1.690
1.672
1.665
1.651
1.646
1.641
1.634
1.630
1.622
1.617
1.595
1.579
1.571
1.564
1.543
1.539
1.517
1.512
1.497
1.491
1.474
1.470
1.457
1.454
1.450
1.430
1.424
1.398
1.376
1.373
1.361
1.353
1.341
1.337
1.328
1.323
1.293
1.288
1.279
1.269
1.263
1.254
1.248
1.234
1.220
1.213
1.188
1.144
1.141
1.127
1.124
1.121
1.117
1.103
1.101
1.049
1.040
0.961
0.884
0.883
0.867
0.851
0.849
0.825
0.821
1.75 1.70 1.65 1.60 1.55 1.50 1.45 1.40 1.35 1.30 1.25 1.20 1.15 1.10 1.05 1.00 0.95 0.90 0.85 ppm
1.05
6.69
3.76
1.32
5.20
2.98
1.12
1.12
3.14
2.83
3.07
6.44
0.86

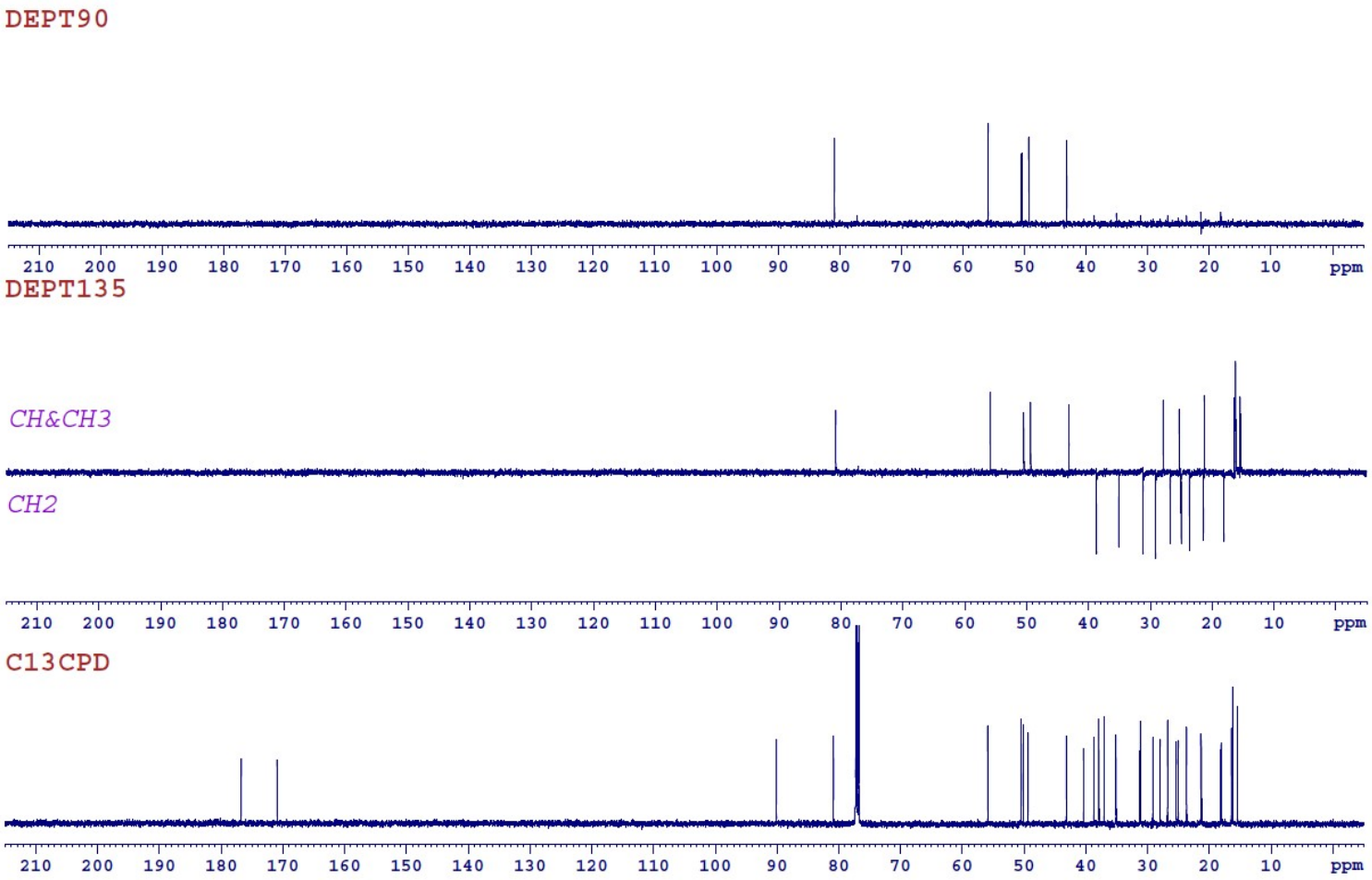
^{1}H-NMR spectrum of compound **6a** (extension)



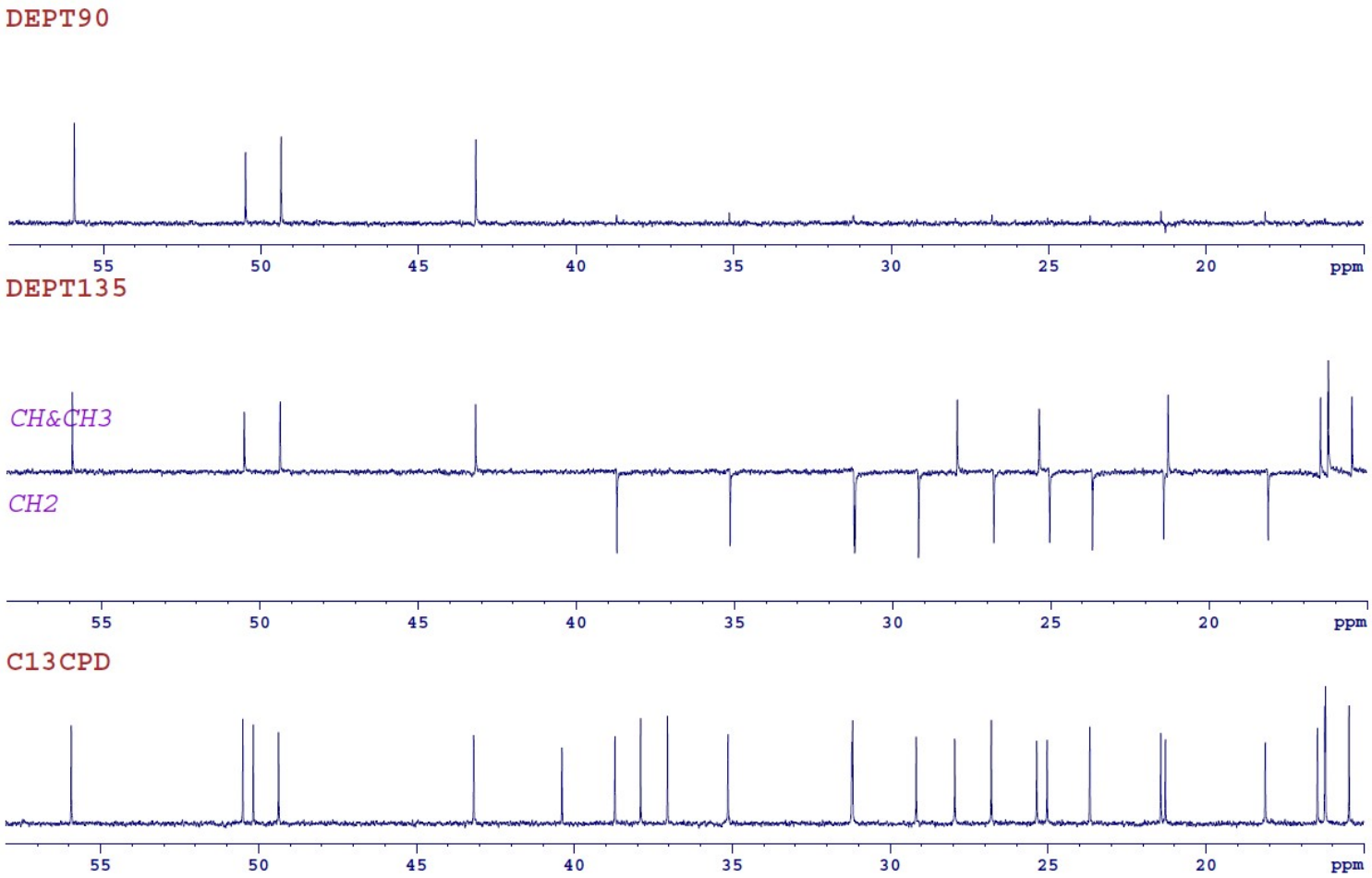
^{13}C-NMR spectrum of compound **6a**


55.93
50.50
50.16
49.36
43.18
40.39
38.71
37.90
37.05
35.14
31.22
31.19
29.18
27.96
26.80
25.37
25.04
23.68
21.43
21.29
18.13
16.48
16.24
16.22
15.48
55
50
45
40
35
30
25
20
ppm

^{13}C-NMR spectrum of compound **6a** (extension)



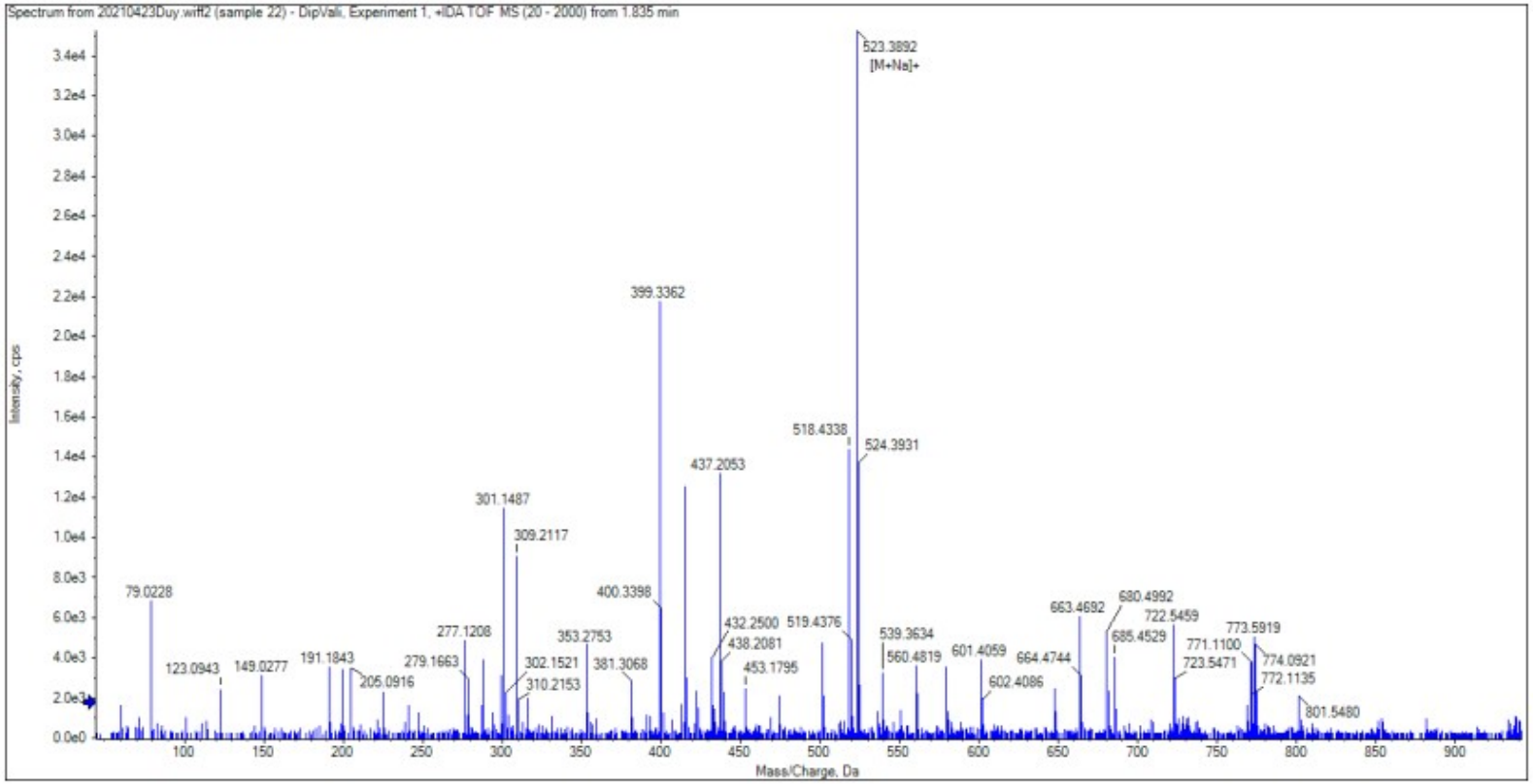
DEPT spectrum of compound **6a**



DEPT spectrum of compound **6a** (extension)

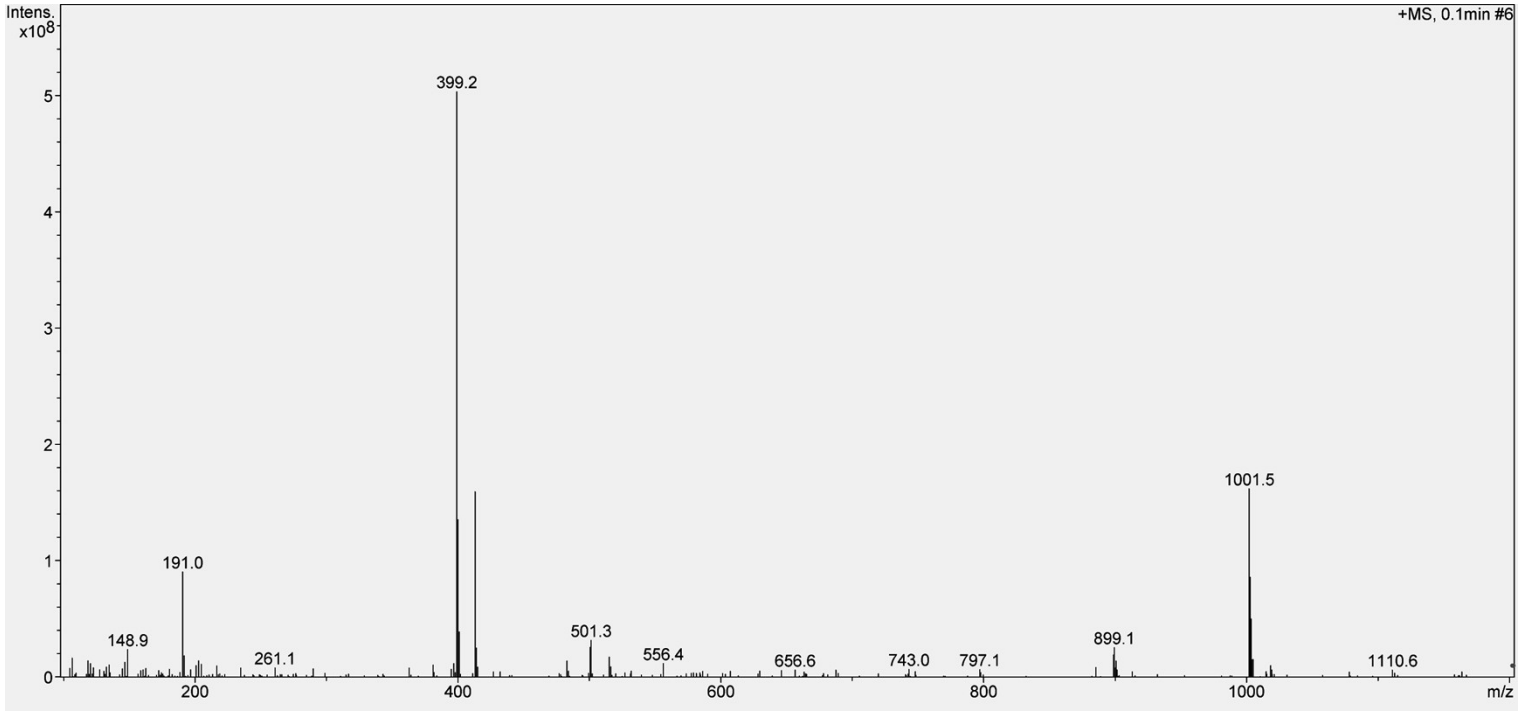
1.18. Compound 6b

Sample name: DipVali
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

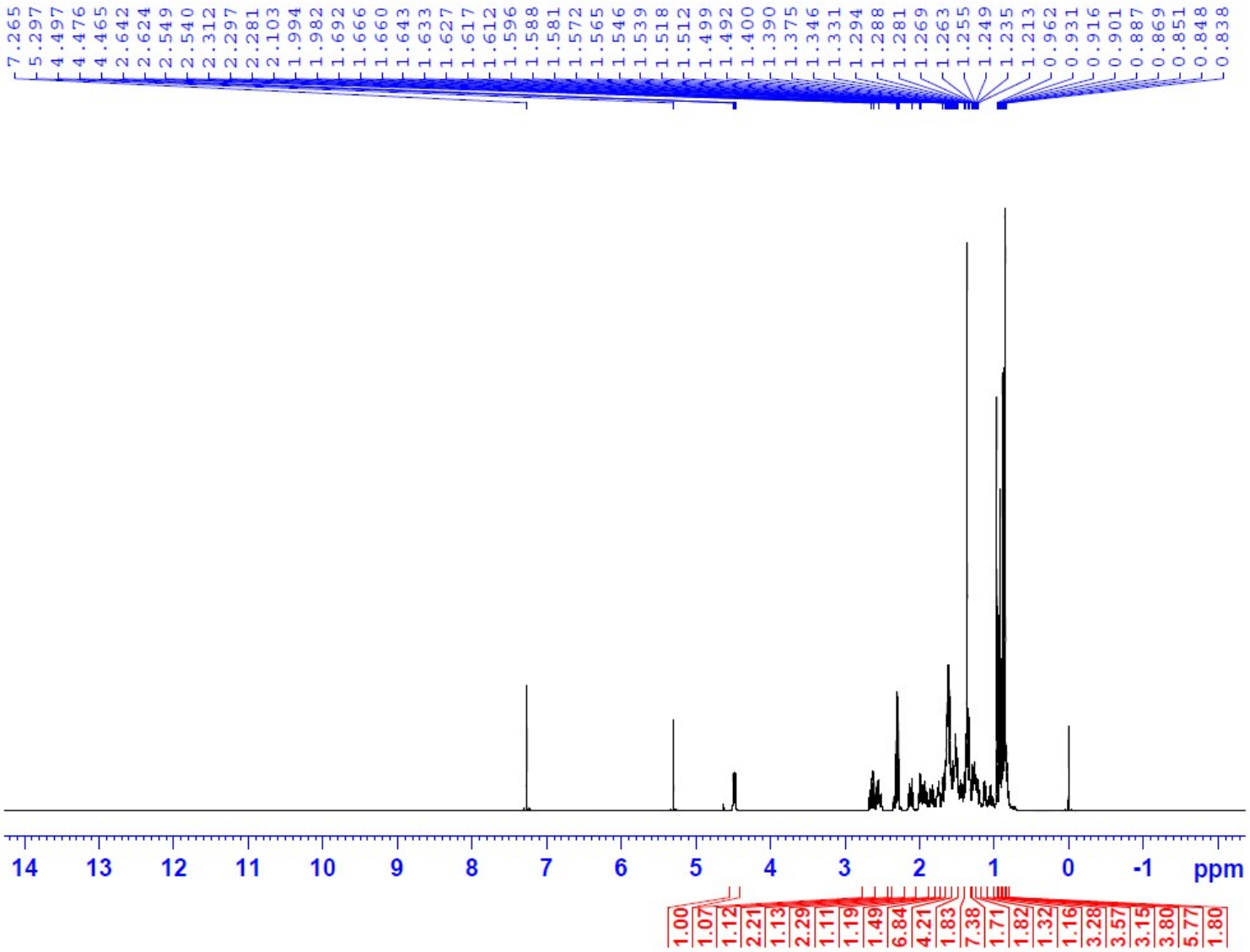


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C32H52O4	523.3858	7.0	3.6	1			NA/NA

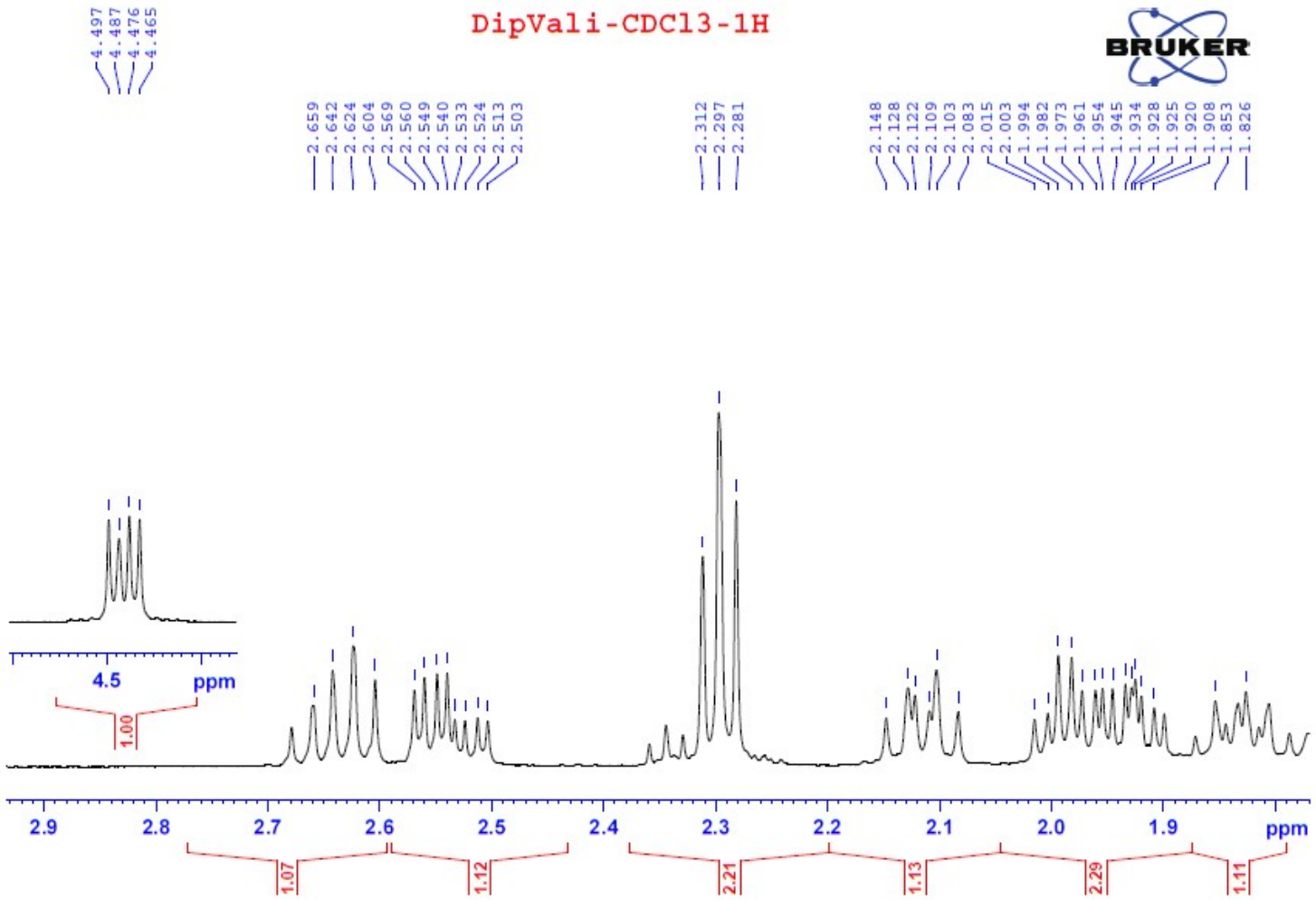
(+)-HR-ESI-MS spectrum of compound **6b**



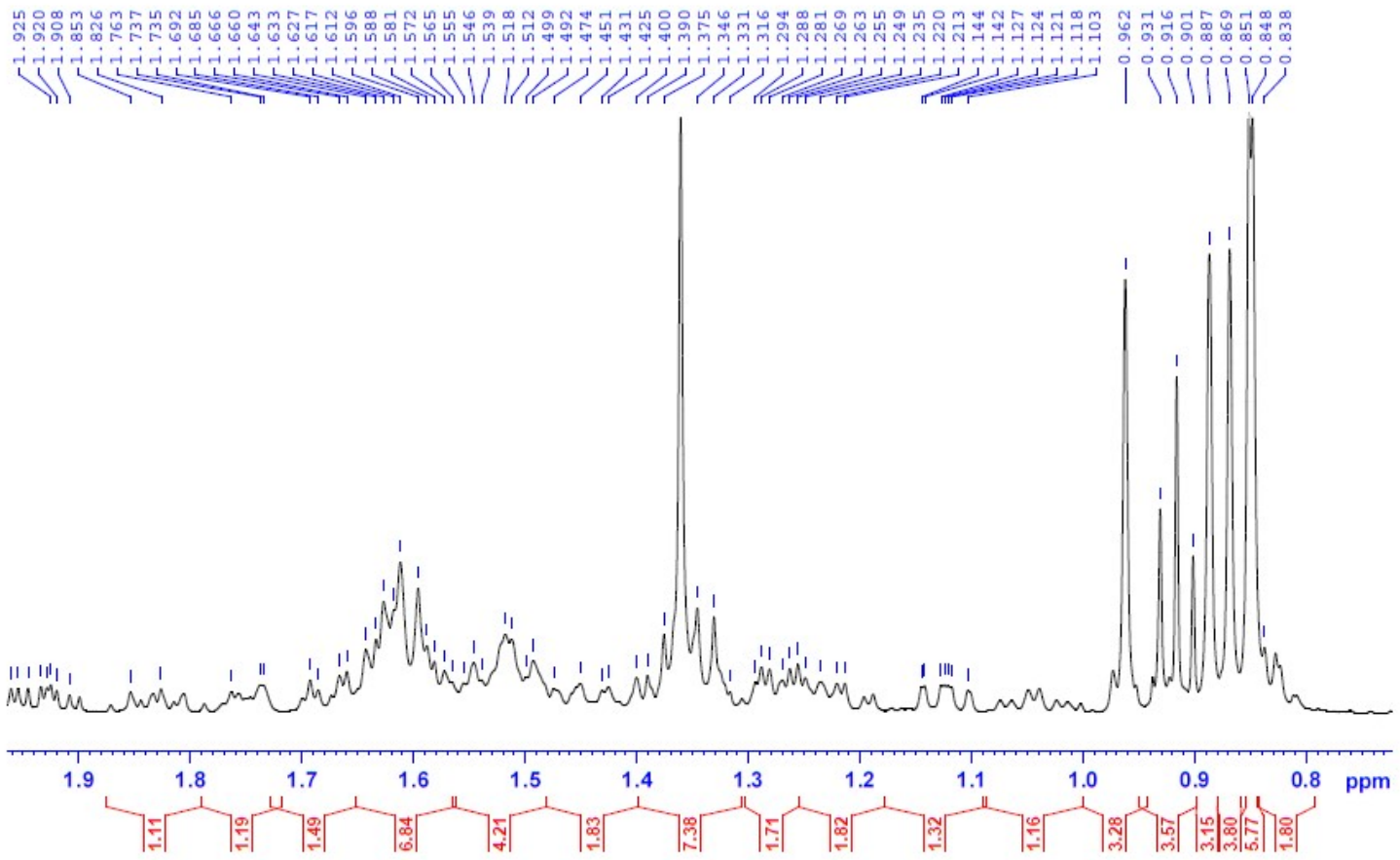
(+)-ESI–MS spectrum of compound **6b**



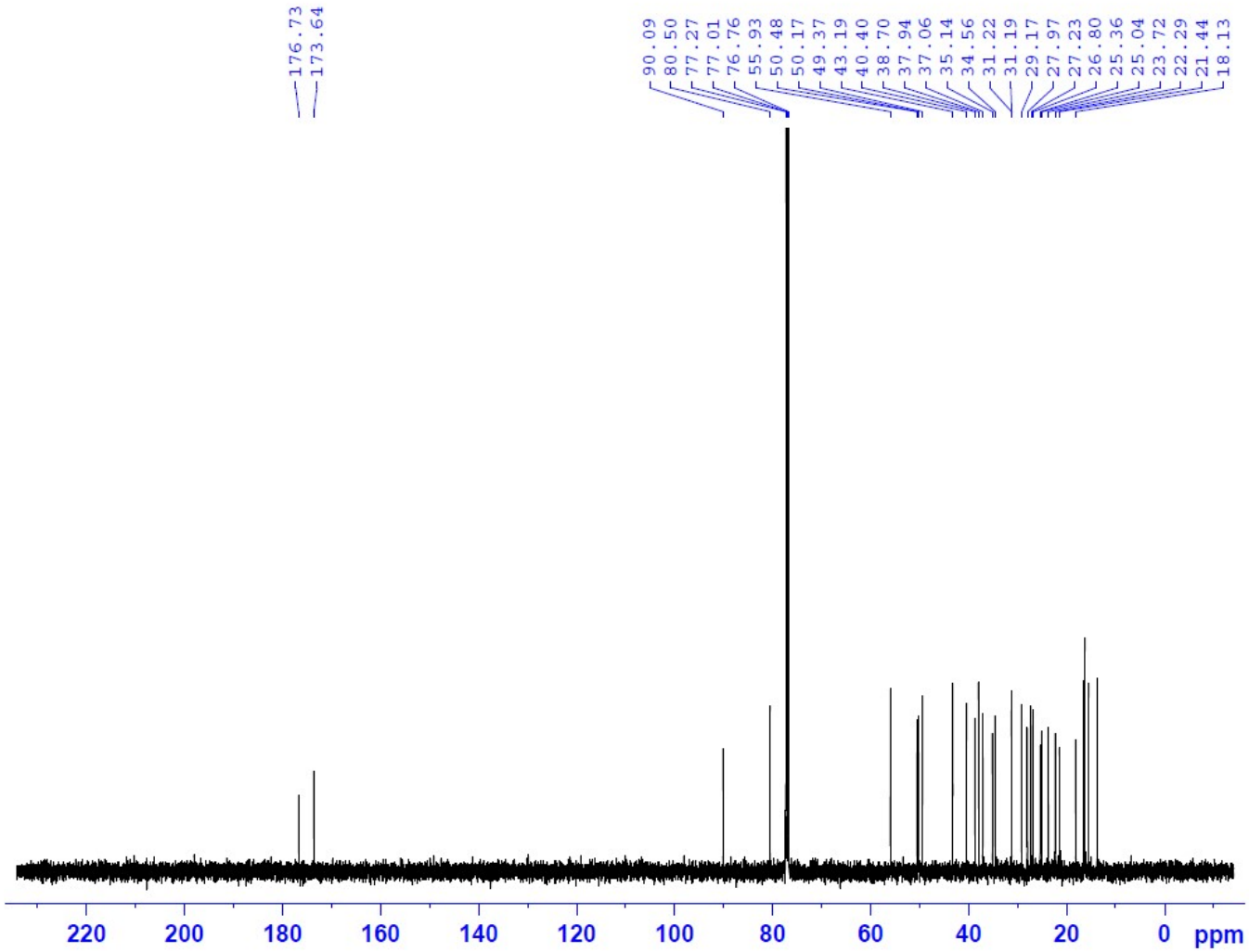
^{1}H-NMR spectrum of compund **6b**


DipVali-CDCl3-1H
BRUKER
4.497
4.487
4.476
4.465
2.659
2.642
2.624
2.604
2.569
2.560
2.549
2.540
2.533
2.524
2.513
2.503
2.312
2.297
2.281
2.148
2.128
2.122
2.109
2.103
2.083
2.015
2.003
1.994
1.982
1.973
1.961
1.954
1.945
1.934
1.928
1.925
1.920
1.908
1.853
1.826
4.5
ppm
1.00
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
ppm
1.07
1.12
2.21
1.13
2.29
1.11

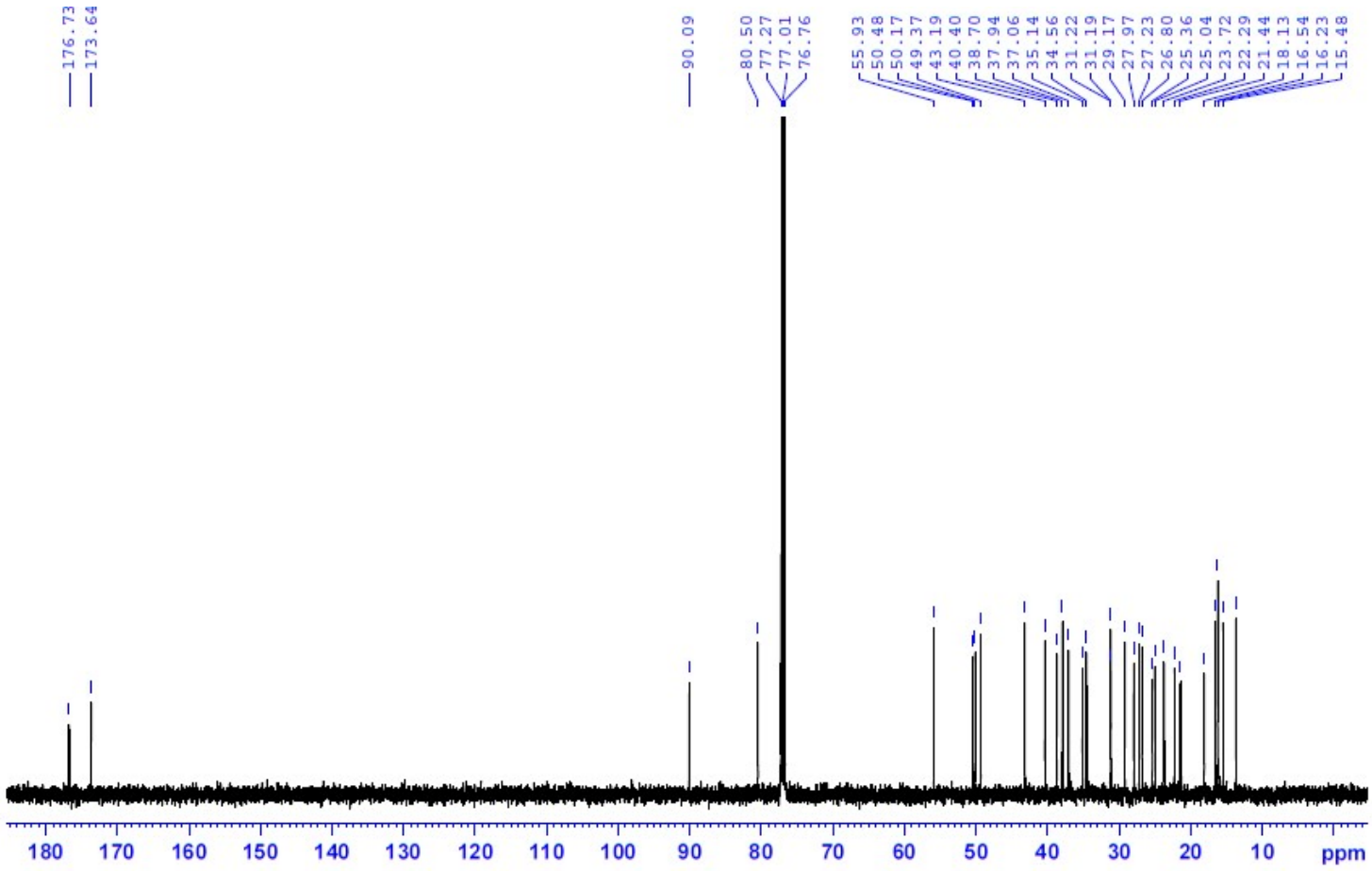
^{1}H-NMR spectrum of compound **6b** (extension)


1.925
1.920
1.908
1.853
1.826
1.763
1.737
1.735
1.692
1.685
1.666
1.660
1.643
1.633
1.627
1.617
1.612
1.596
1.588
1.581
1.572
1.565
1.555
1.546
1.539
1.518
1.512
1.499
1.492
1.474
1.451
1.431
1.425
1.400
1.390
1.375
1.346
1.331
1.316
1.294
1.288
1.281
1.269
1.263
1.255
1.249
1.235
1.220
1.213
1.144
1.142
1.127
1.124
1.121
1.118
1.103
0.962
0.931
0.916
0.901
0.887
0.869
0.851
0.848
0.838
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm
1.11
1.19
1.49
6.84
4.21
1.83
7.38
1.71
1.82
1.32
1.16
3.28
3.57
3.15
3.80
5.77
1.80

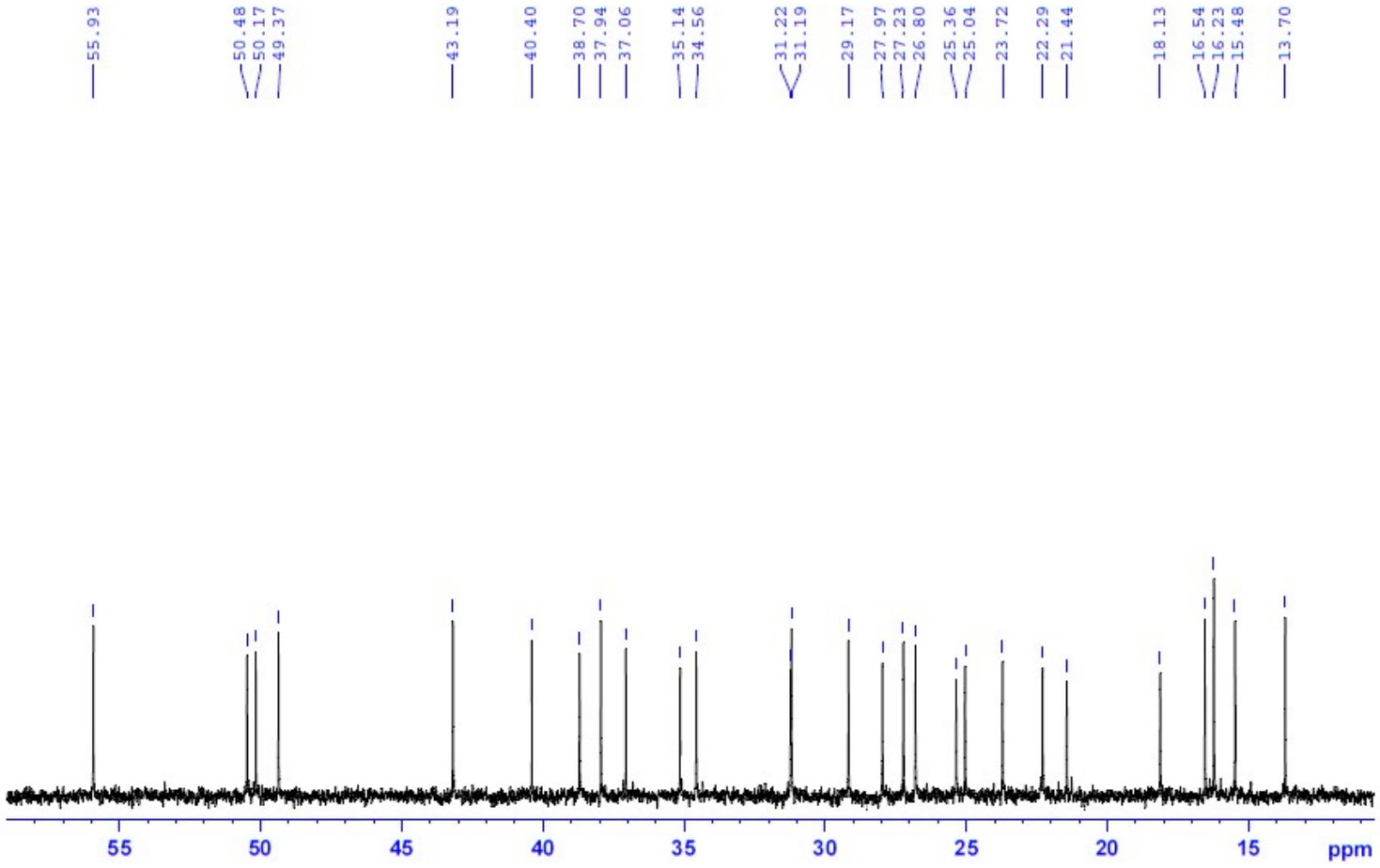
^{1}H-NMR spectrum of compound **6b** (extension)



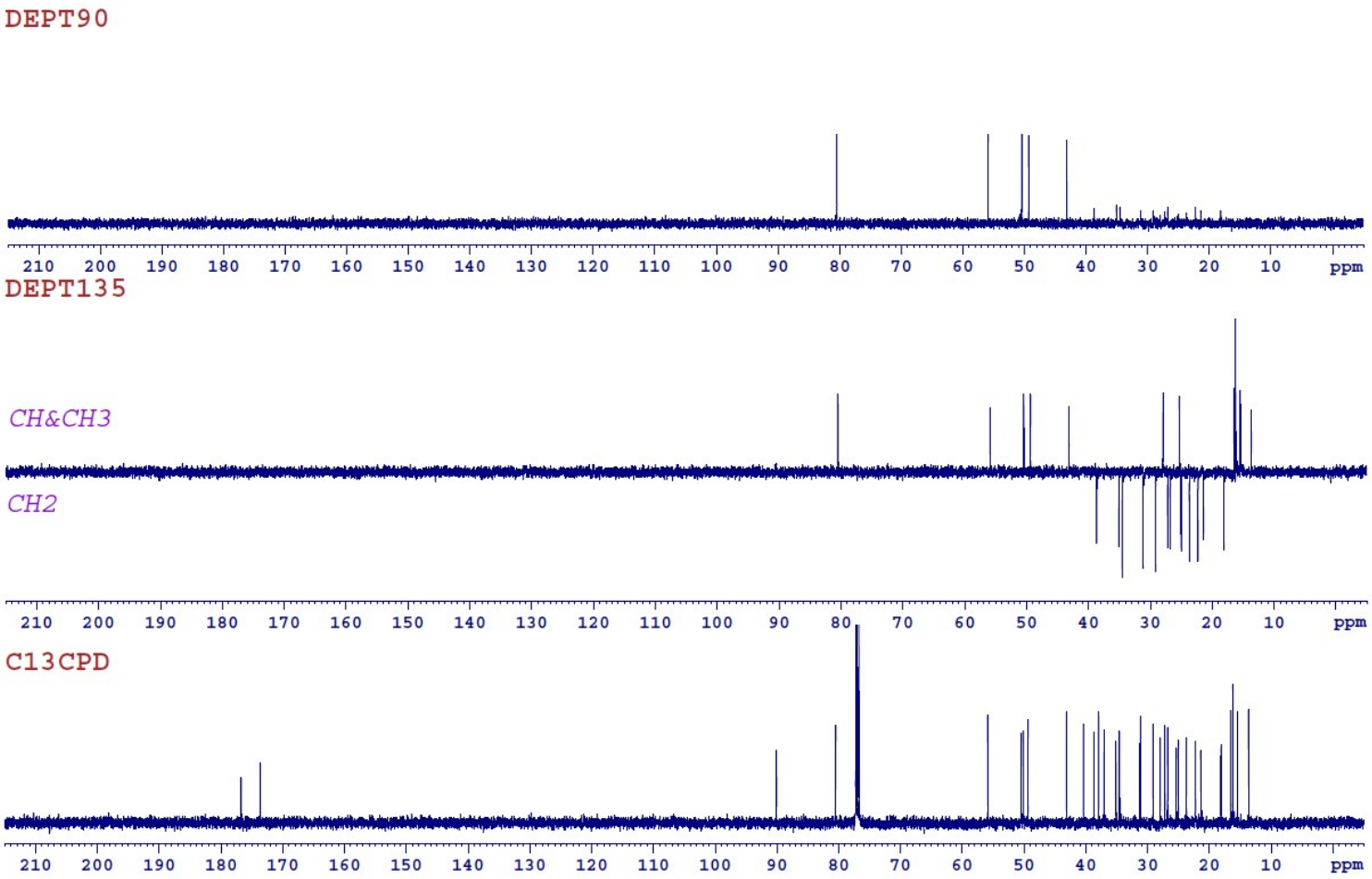
^{13}C-NMR spectrum of compound **6b**


176.73
173.64
90.09
80.50
77.27
77.01
76.76
55.93
50.48
50.17
49.37
43.19
40.40
38.70
37.94
37.06
35.14
34.56
31.22
31.19
29.17
27.97
27.23
26.80
25.36
25.04
23.72
22.29
21.44
18.13
16.54
16.23
15.48
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

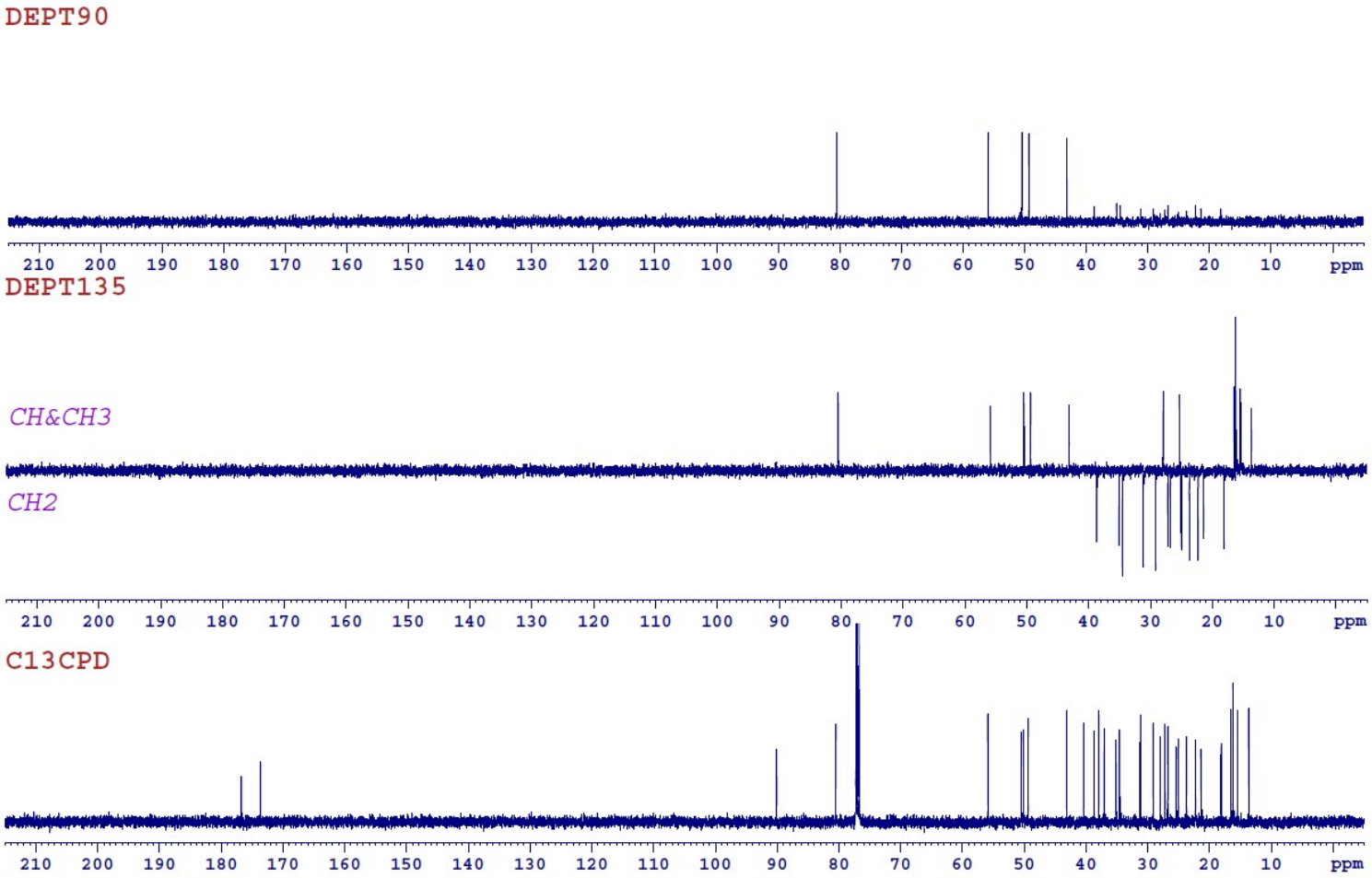
^{13}C-NMR spectrum of compound **6b** (extension)


55.93
50.48
50.17
49.37
43.19
40.40
38.70
37.94
37.06
35.14
34.56
31.22
31.19
29.17
27.97
27.23
26.80
25.36
25.04
23.72
22.29
21.44
18.13
16.54
16.23
15.48
13.70
55
50
45
40
35
30
25
20
15
ppm

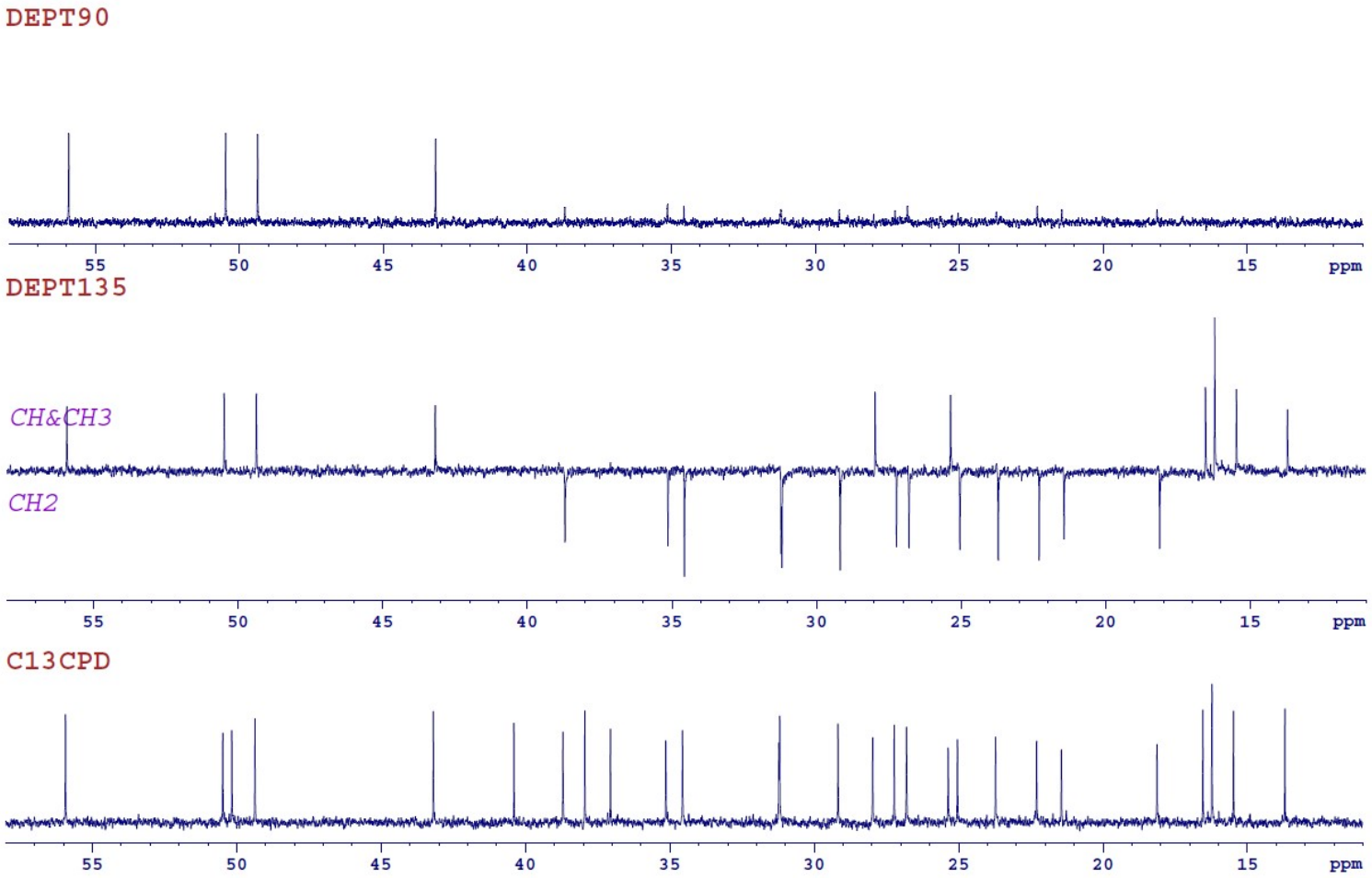
^{13}C-NMR spectrum of compound **6b** (extension)



DEPT spectrum of compound **6b**



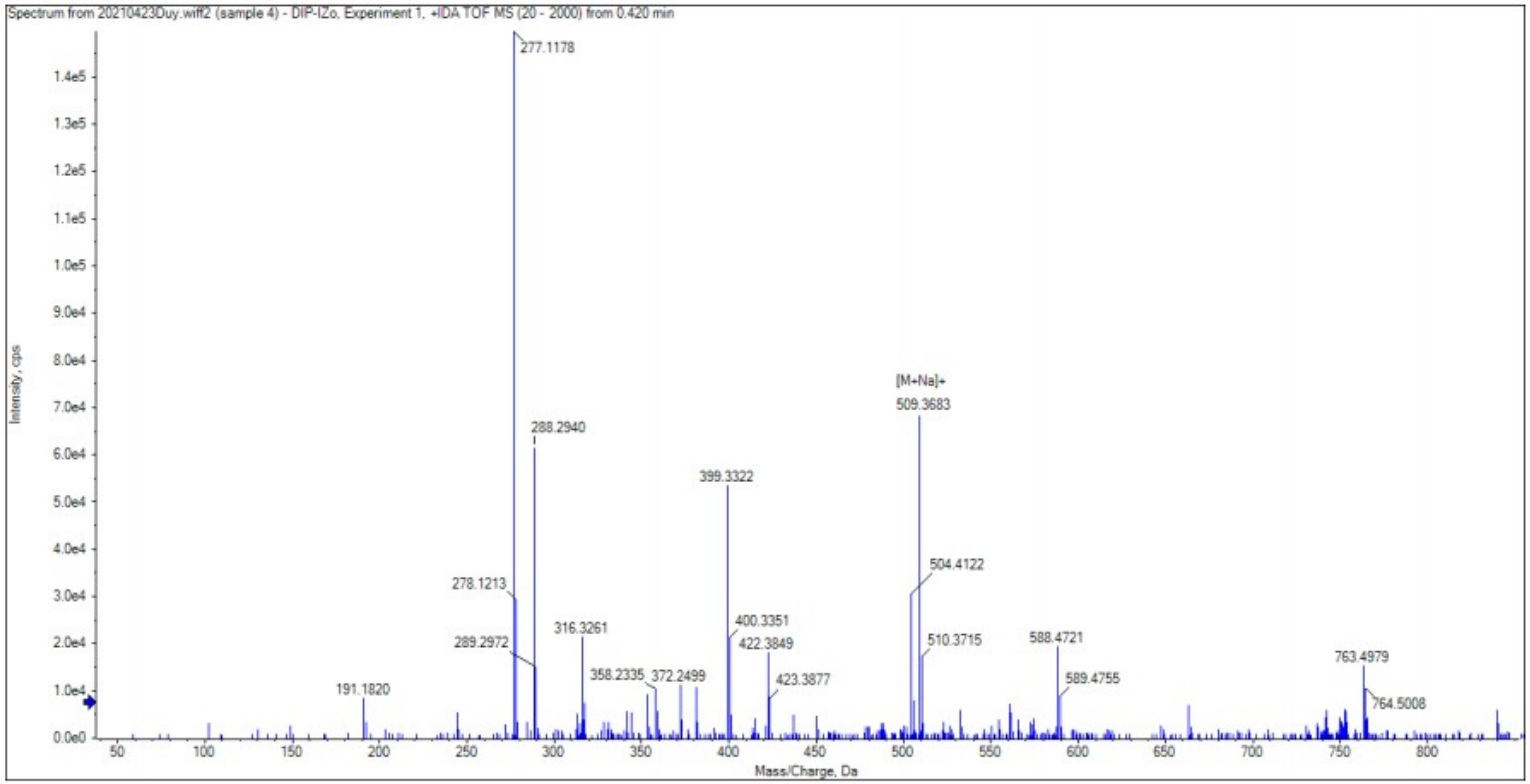
DEPT spectrum of compound **6b** (extension)



DEPT spectrum of compound **6b** (extension)

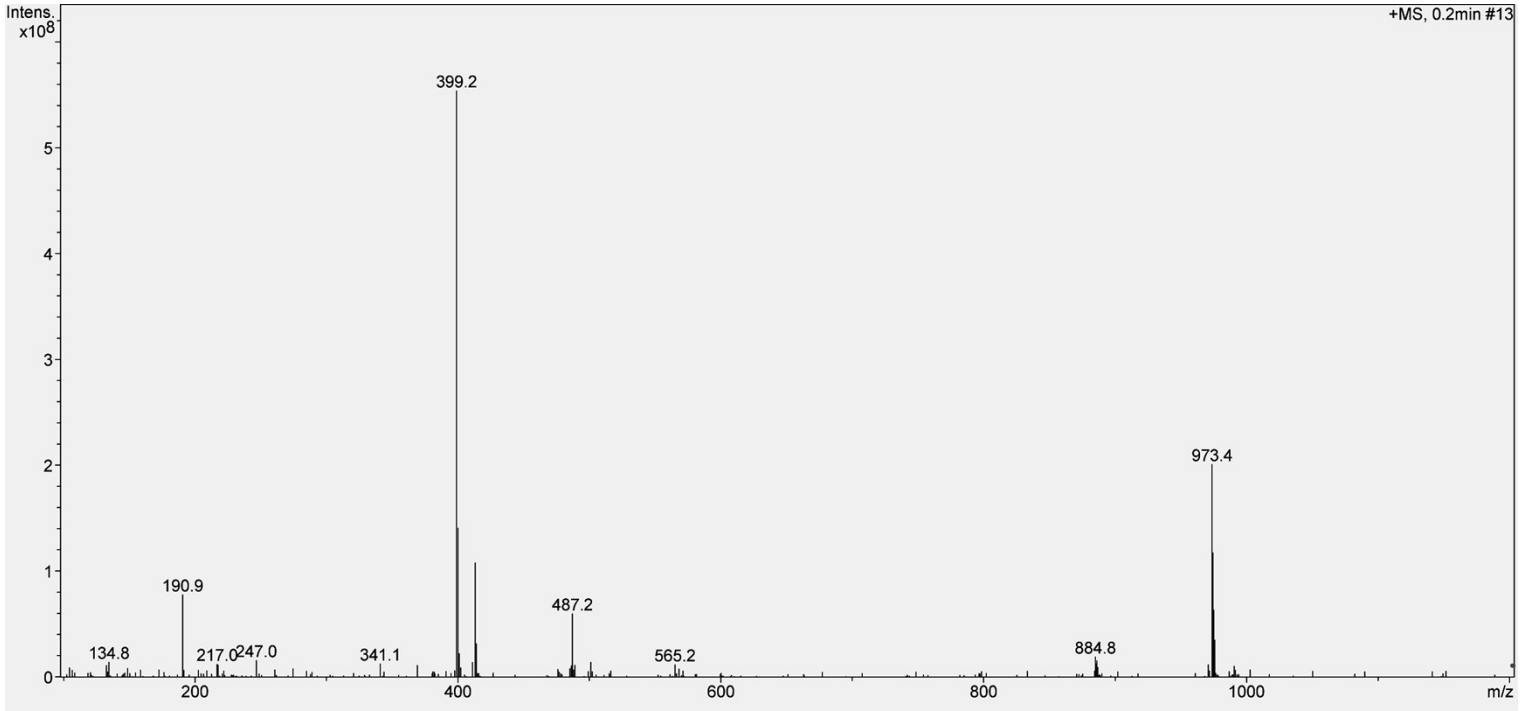
1.19. Compound 6c

Sample name: DipIzo
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

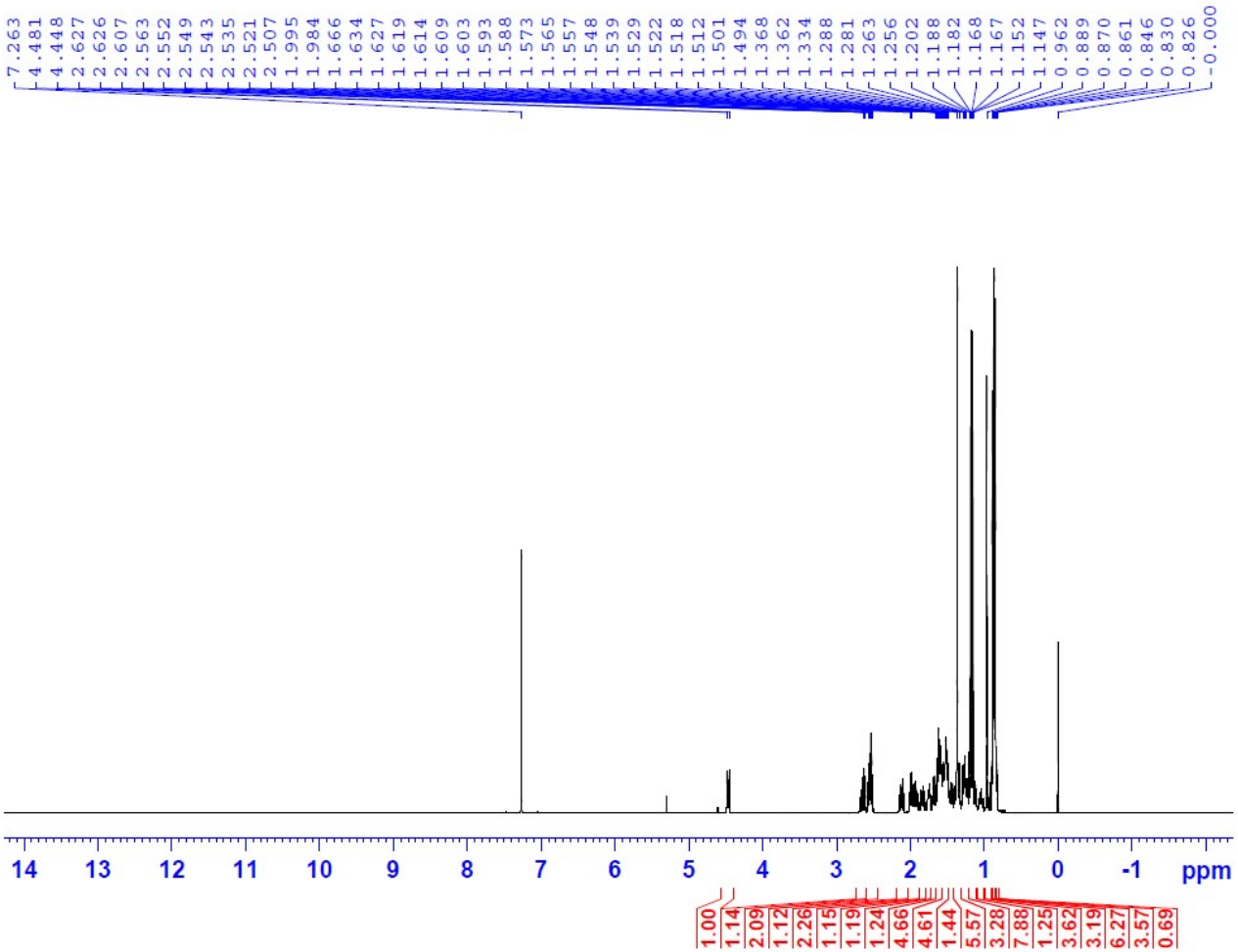


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C31H50O4	509.36713	7.0	3.1	1			NA/NA

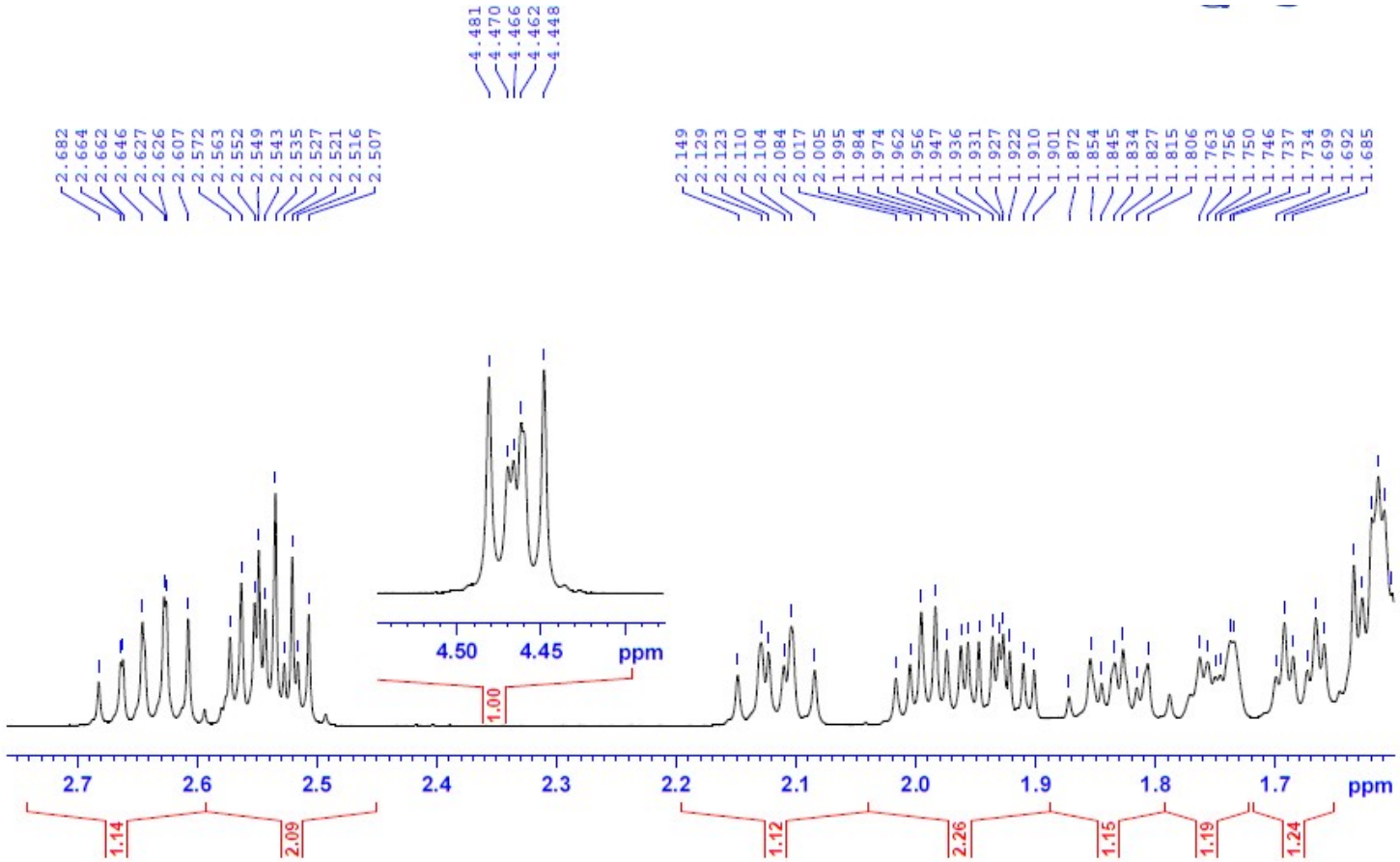
(+)-HR-ESI-MS spectrum of compound **6c**



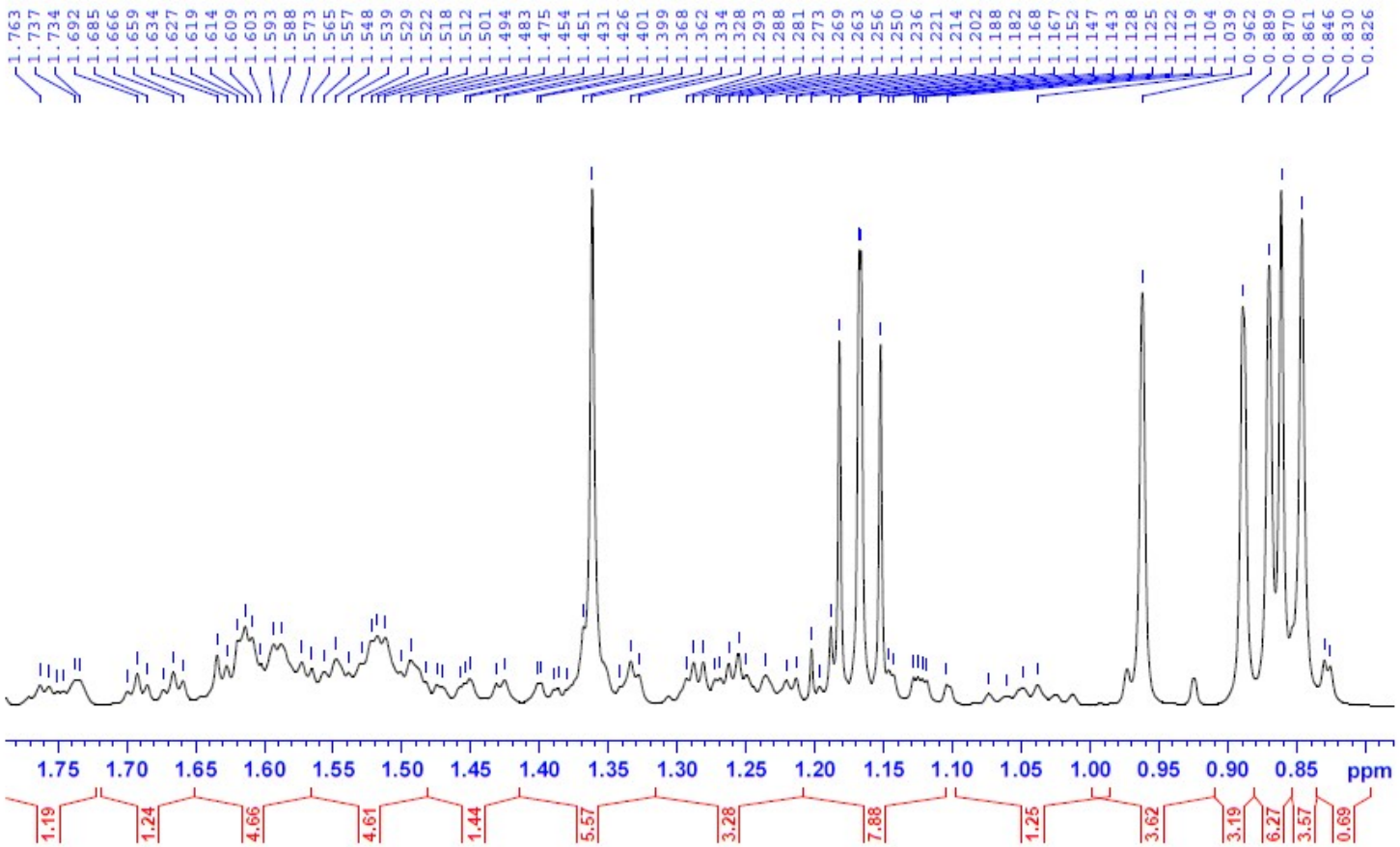
(+)-ESI–MS spectrum of compound **6c**



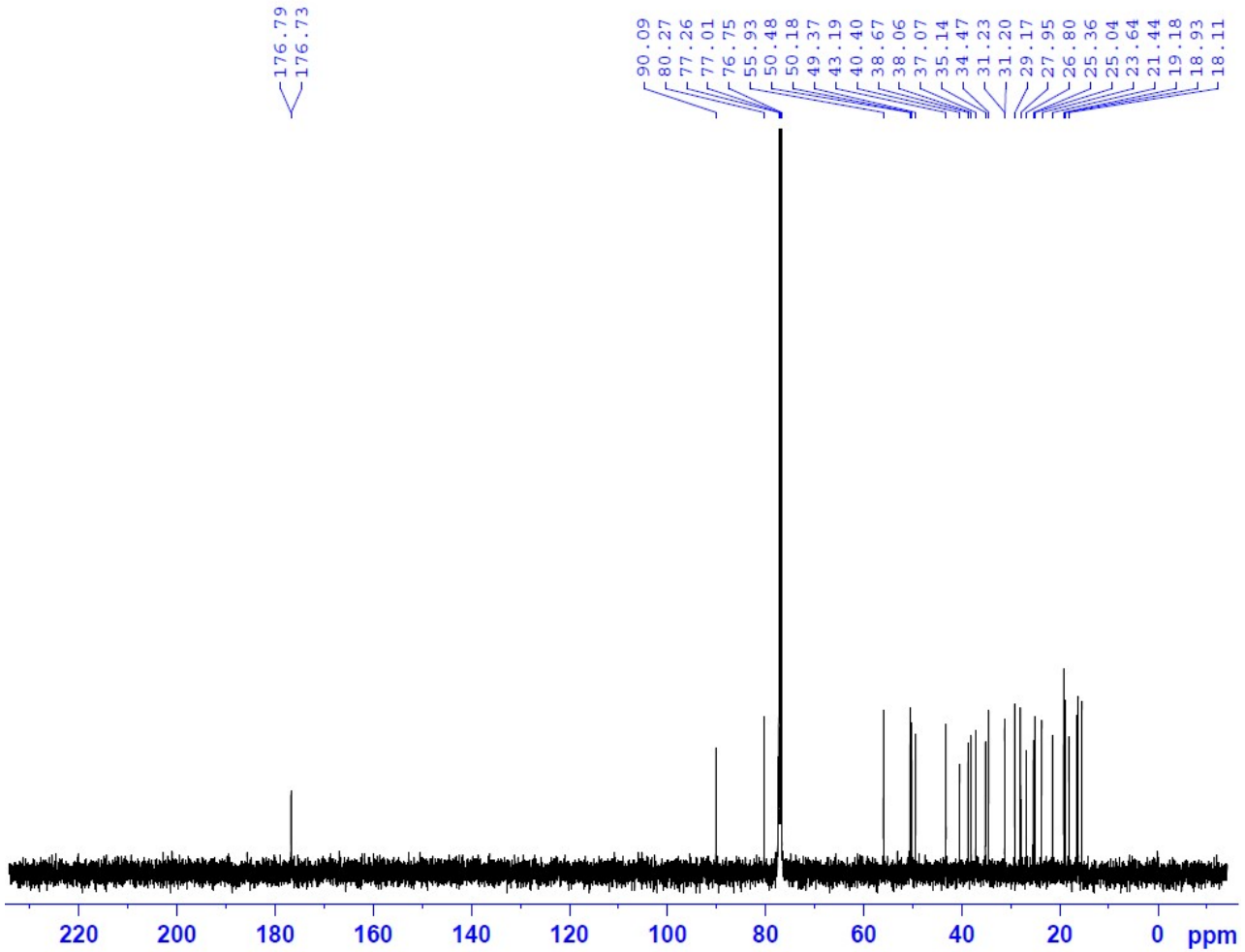
^{1}H-NMR spectrum of compound **6c**


4.481
4.470
4.466
4.462
4.448
2.682
2.664
2.662
2.646
2.627
2.626
2.607
2.572
2.563
2.552
2.549
2.543
2.535
2.527
2.521
2.516
2.507
2.149
2.129
2.123
2.110
2.104
2.084
2.017
2.005
1.995
1.984
1.974
1.962
1.956
1.947
1.936
1.931
1.927
1.922
1.910
1.901
1.872
1.854
1.845
1.834
1.827
1.815
1.806
1.763
1.756
1.750
1.746
1.737
1.734
1.699
1.692
1.685
4.50
4.45
ppm
1.00
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
ppm
1.14
2.09
1.12
2.26
1.15
1.19
1.24

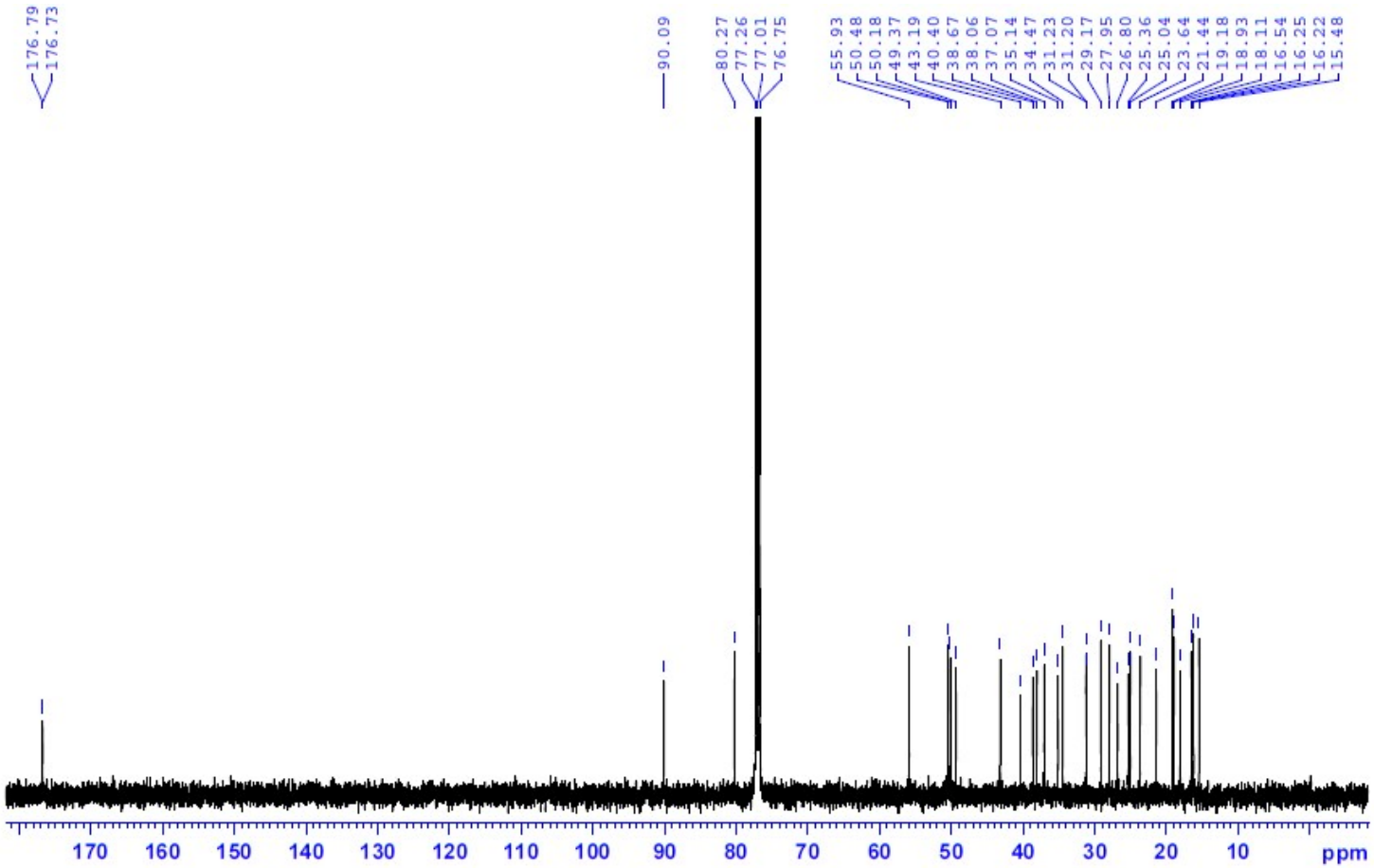
^{1}H-NMR spectrum of compound **6c** (extension)


1.763 1.737 1.734 1.692 1.685 1.666 1.659 1.634 1.627 1.619 1.614 1.609 1.603 1.593 1.588 1.573 1.565 1.557 1.548 1.539 1.529 1.522 1.518 1.512 1.501 1.494 1.483 1.475 1.454 1.451 1.431 1.426 1.401 1.399 1.368 1.362 1.334 1.328 1.293 1.288 1.281 1.273 1.269 1.263 1.256 1.250 1.236 1.221 1.214 1.202 1.188 1.182 1.168 1.167 1.152 1.147 1.143 1.128 1.125 1.122 1.119 1.104 1.039 0.962 0.889 0.870 0.861 0.846 0.830 0.826
1.75 1.70 1.65 1.60 1.55 1.50 1.45 1.40 1.35 1.30 1.25 1.20 1.15 1.10 1.05 1.00 0.95 0.90 0.85 ppm
1.19 1.24 4.66 4.61 1.44 5.57 3.28 7.88 1.25 3.62 3.19 6.27 3.57 0.69

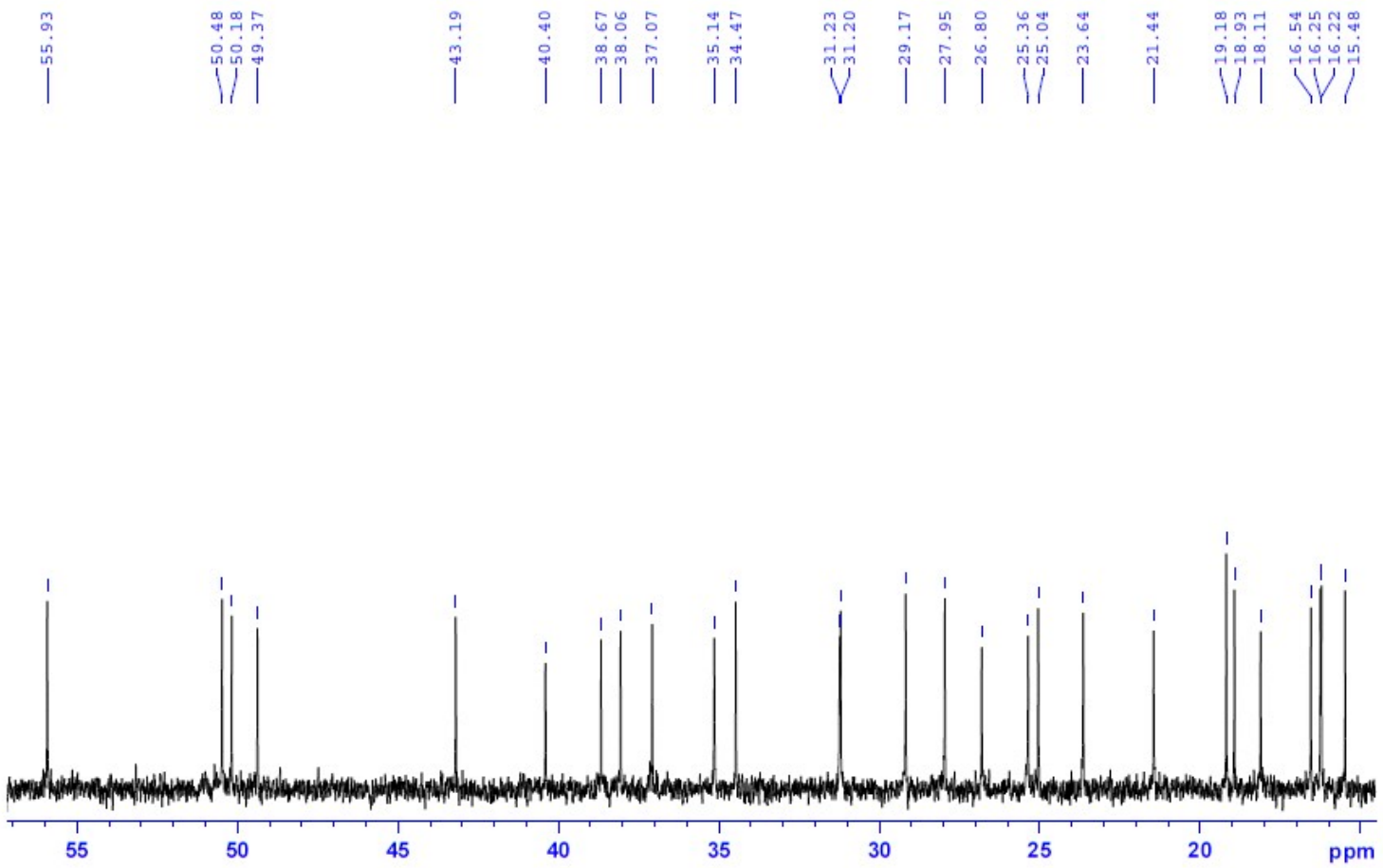
^{1}H-NMR spectrum of compound **6c** (extension)



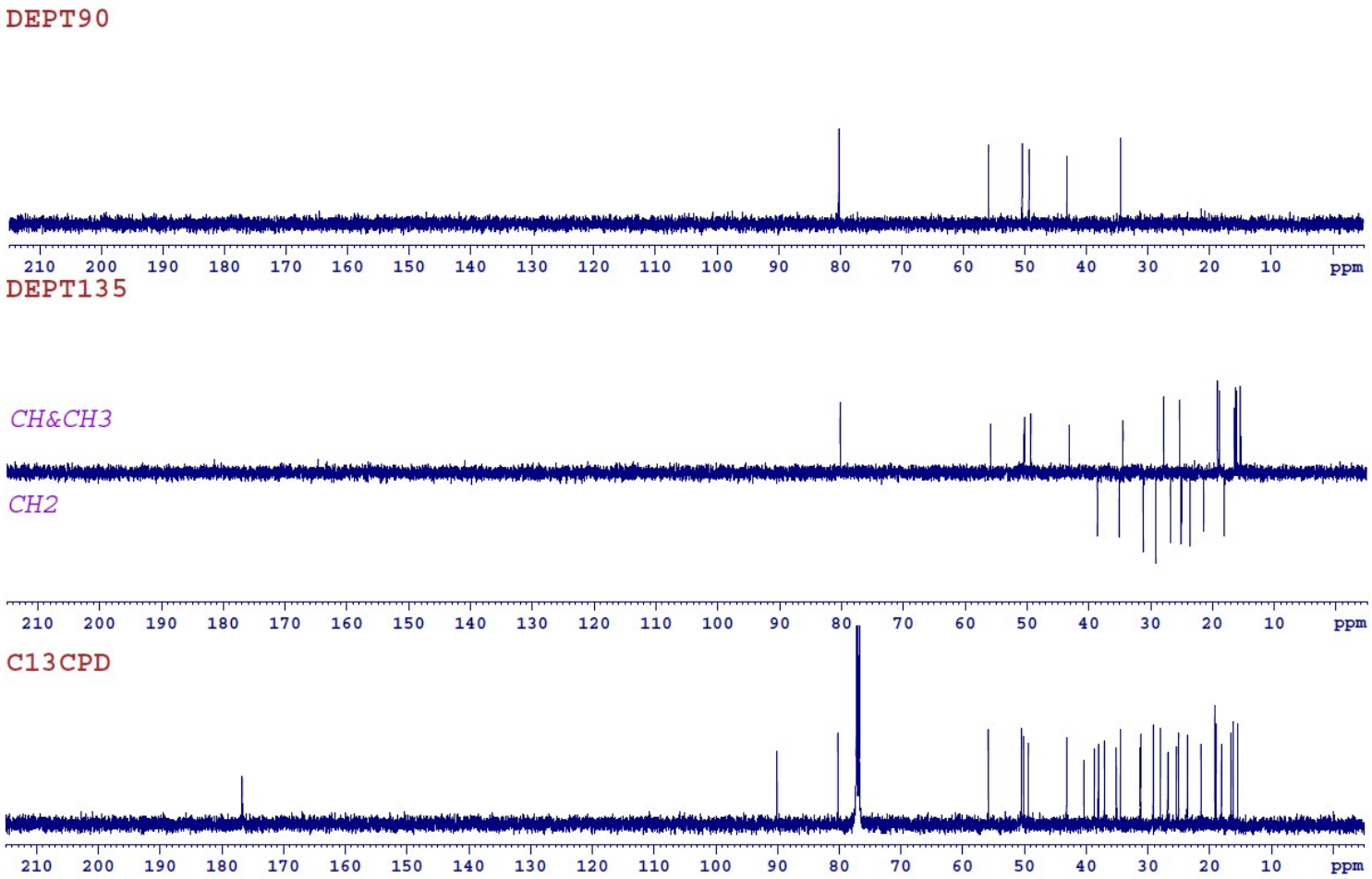
^{13}C-NMR spectrum of compound **6c**


176.79
176.73
90.09
80.27
77.26
77.01
76.75
55.93
50.48
50.18
49.37
43.19
40.40
38.67
38.06
37.07
35.14
34.47
31.23
31.20
29.17
27.95
26.80
25.36
25.04
23.64
21.44
19.18
18.93
18.11
16.54
16.25
16.22
15.48
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

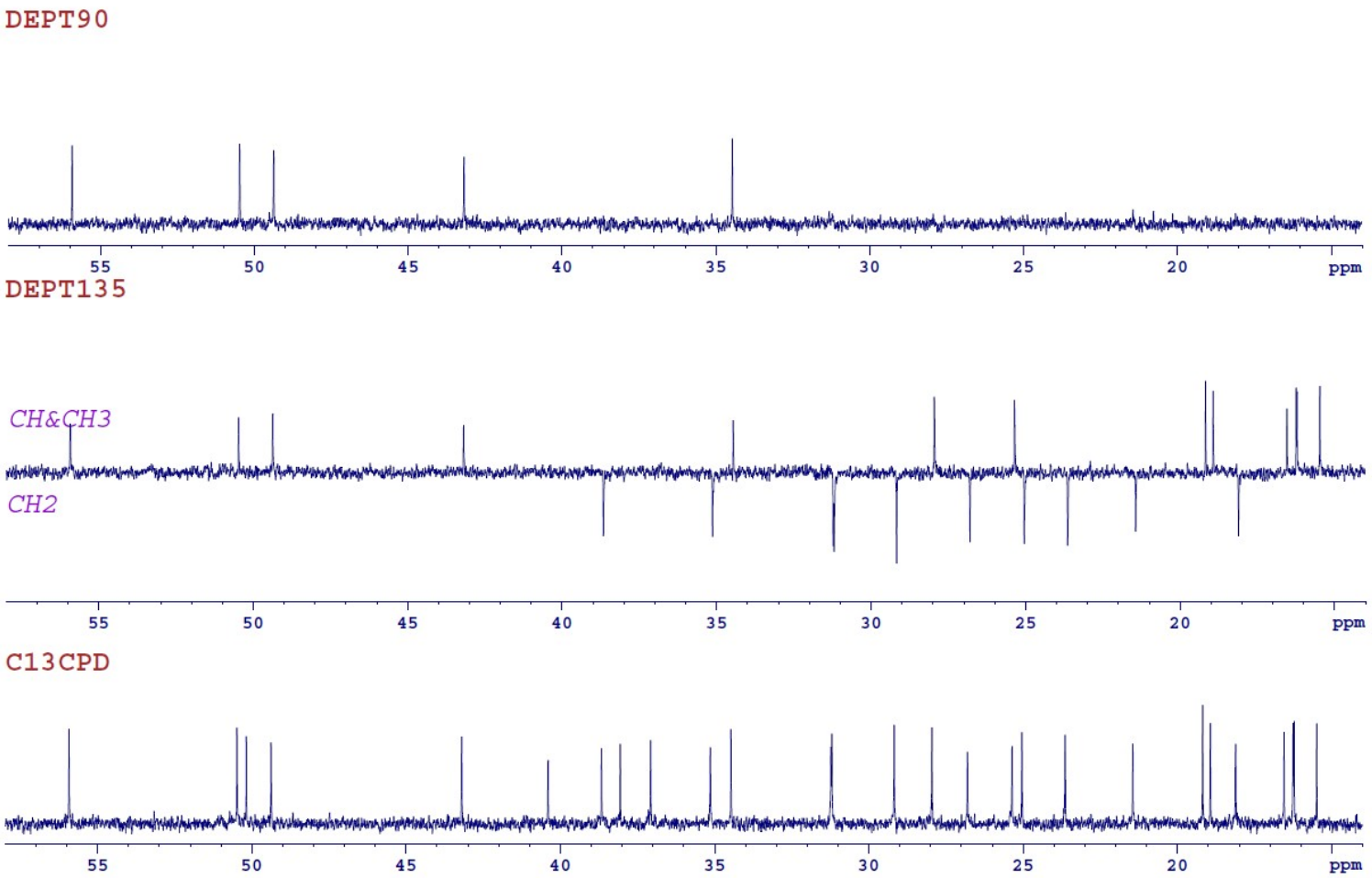
^{13}C-NMR spectrum of compound **6c** (extension)


55.93
50.48
50.18
49.37
43.19
40.40
38.67
38.06
37.07
35.14
34.47
31.23
31.20
29.17
27.95
26.80
25.36
25.04
23.64
21.44
19.18
18.93
18.11
16.54
16.25
16.22
15.48
55
50
45
40
35
30
25
20
ppm

^{13}C-NMR spectrum of compound **6c** (extension)



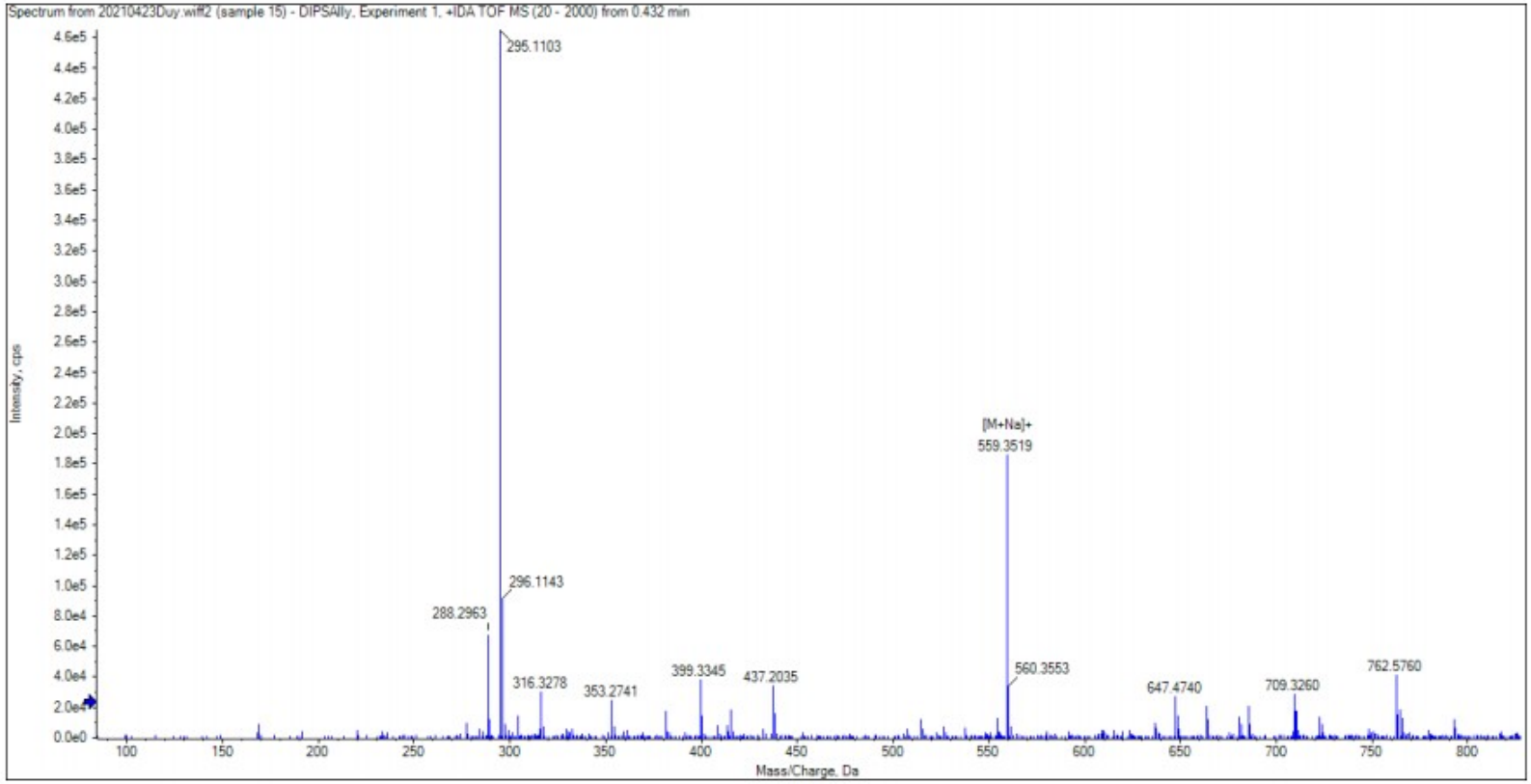
DEPT spectrum of compound **6c**



DEPT spectrum of compound **6c** (extension)

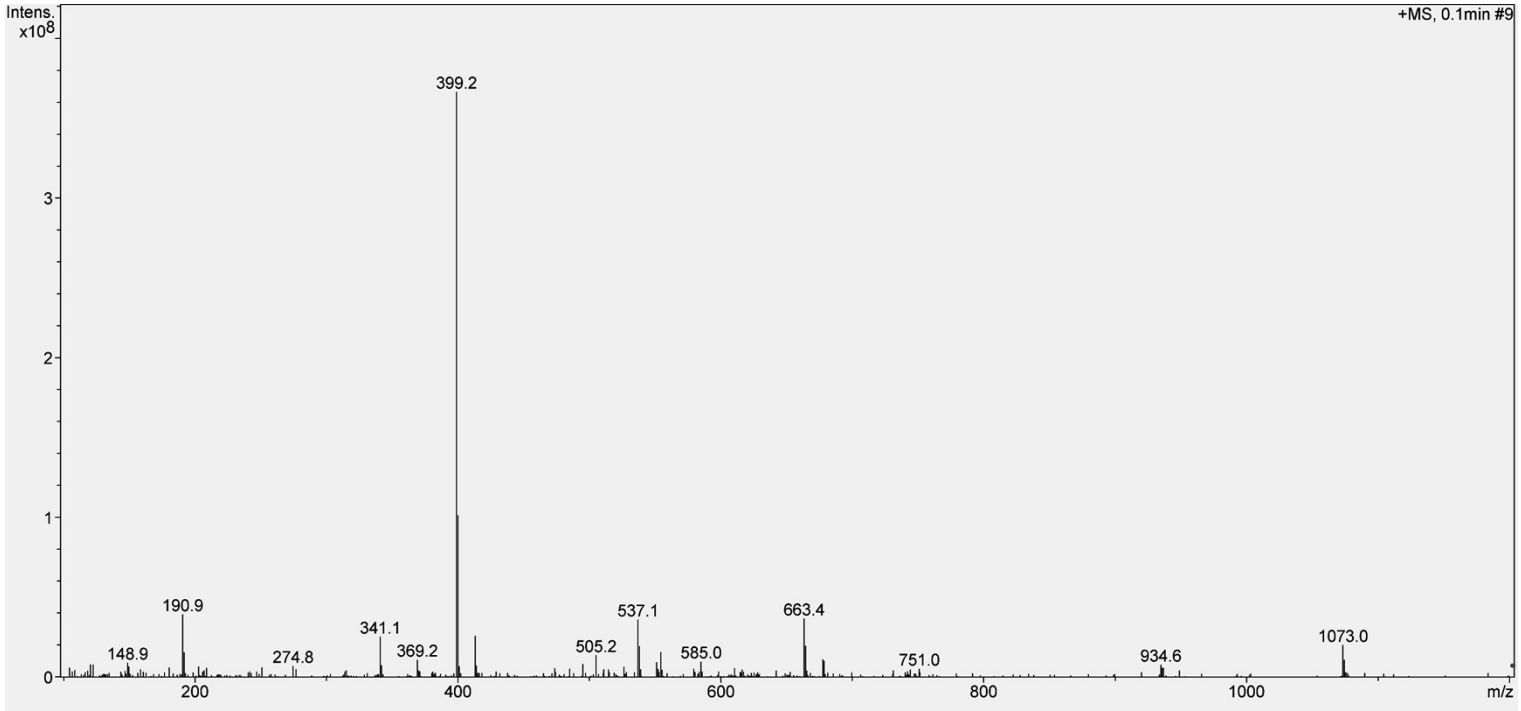
1.20. Compound 6d

Sample name: DipSali
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23

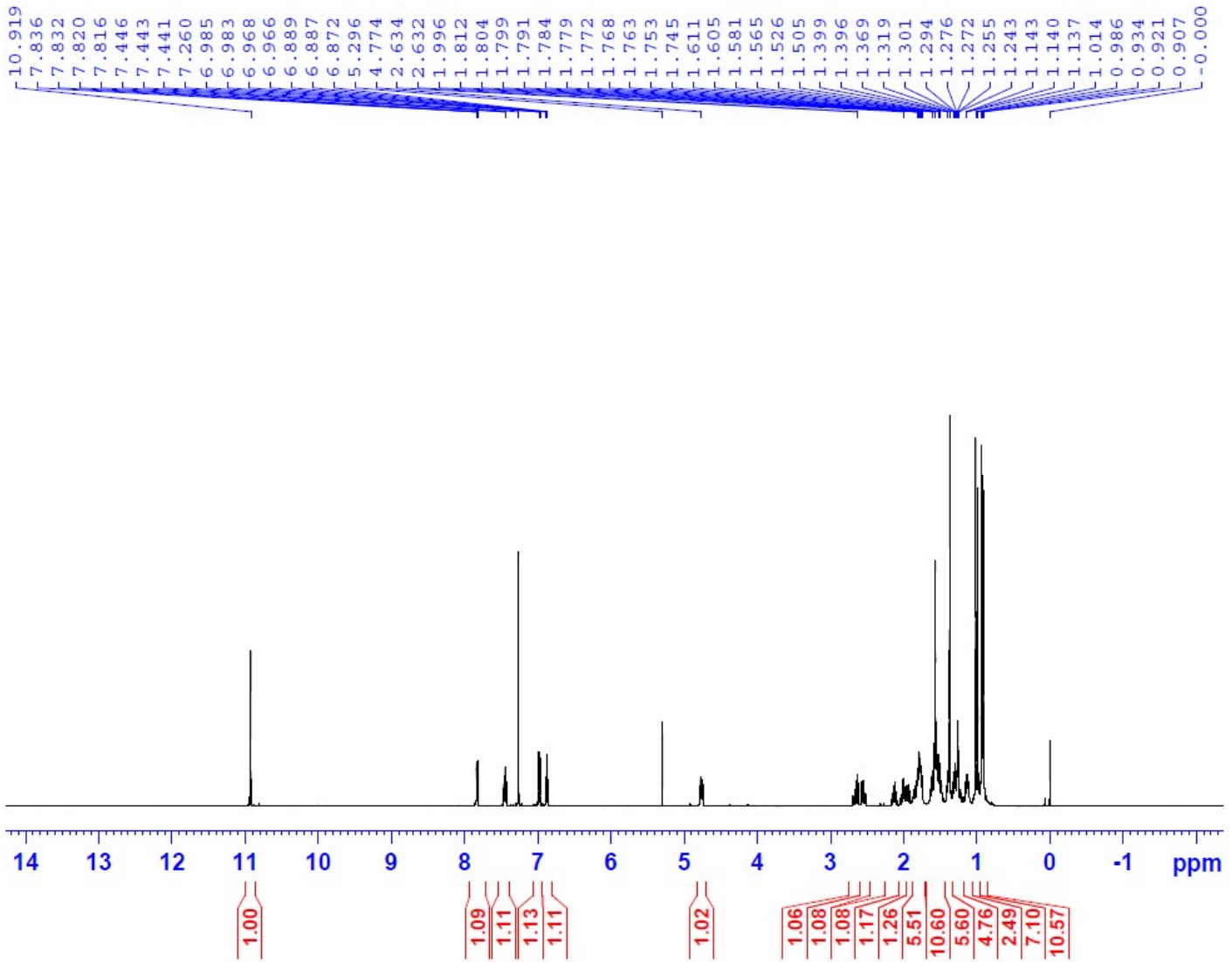


Hit	Formula	m/z	RDB	ppm	MS Rank	MSMS ppm	MSMS Rank	Found
1	C34H48O5	559.34940	11.0	2.4	1			NA/NA

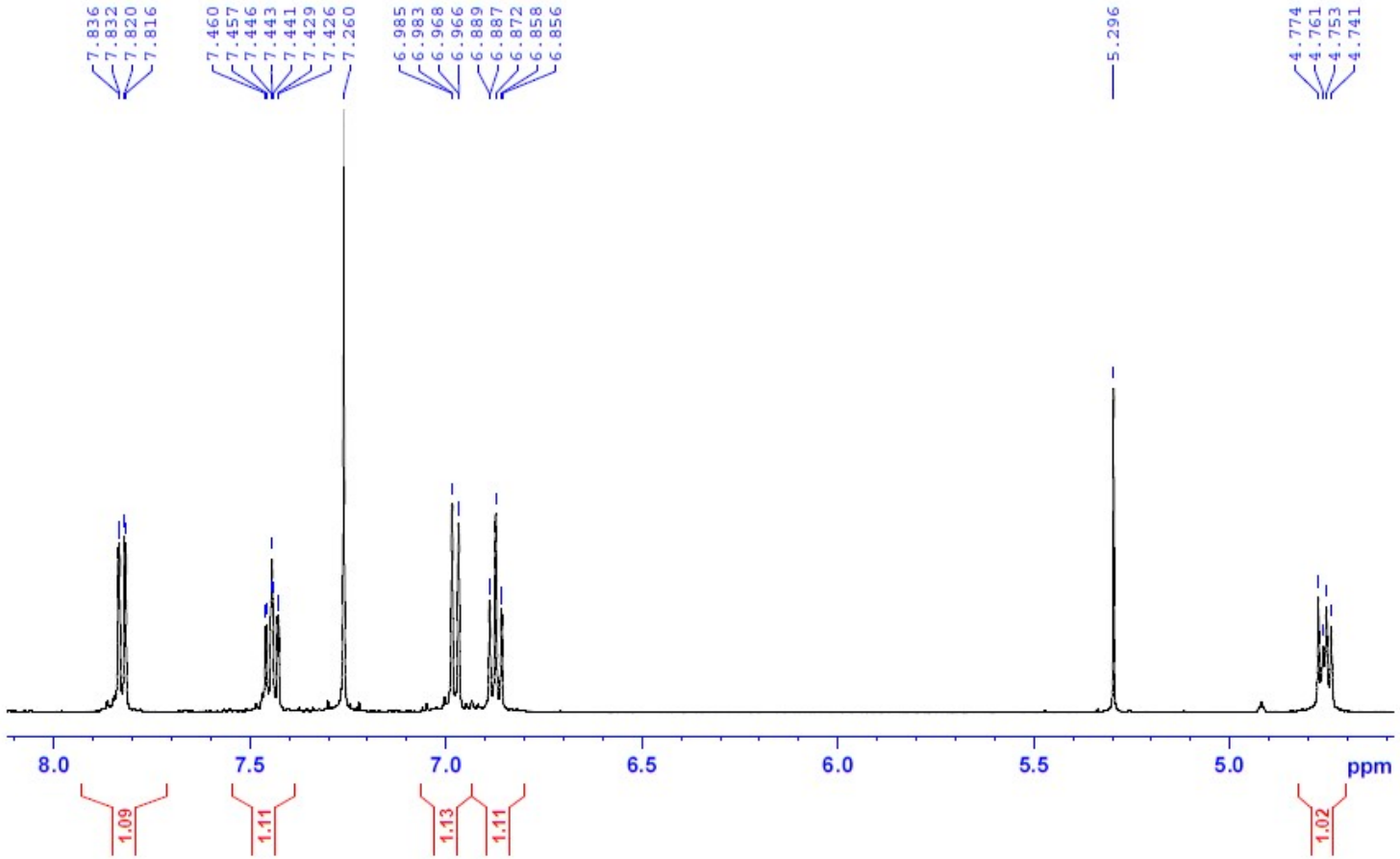
(+)-HR-ESI-MS spectrum of compound **6d**



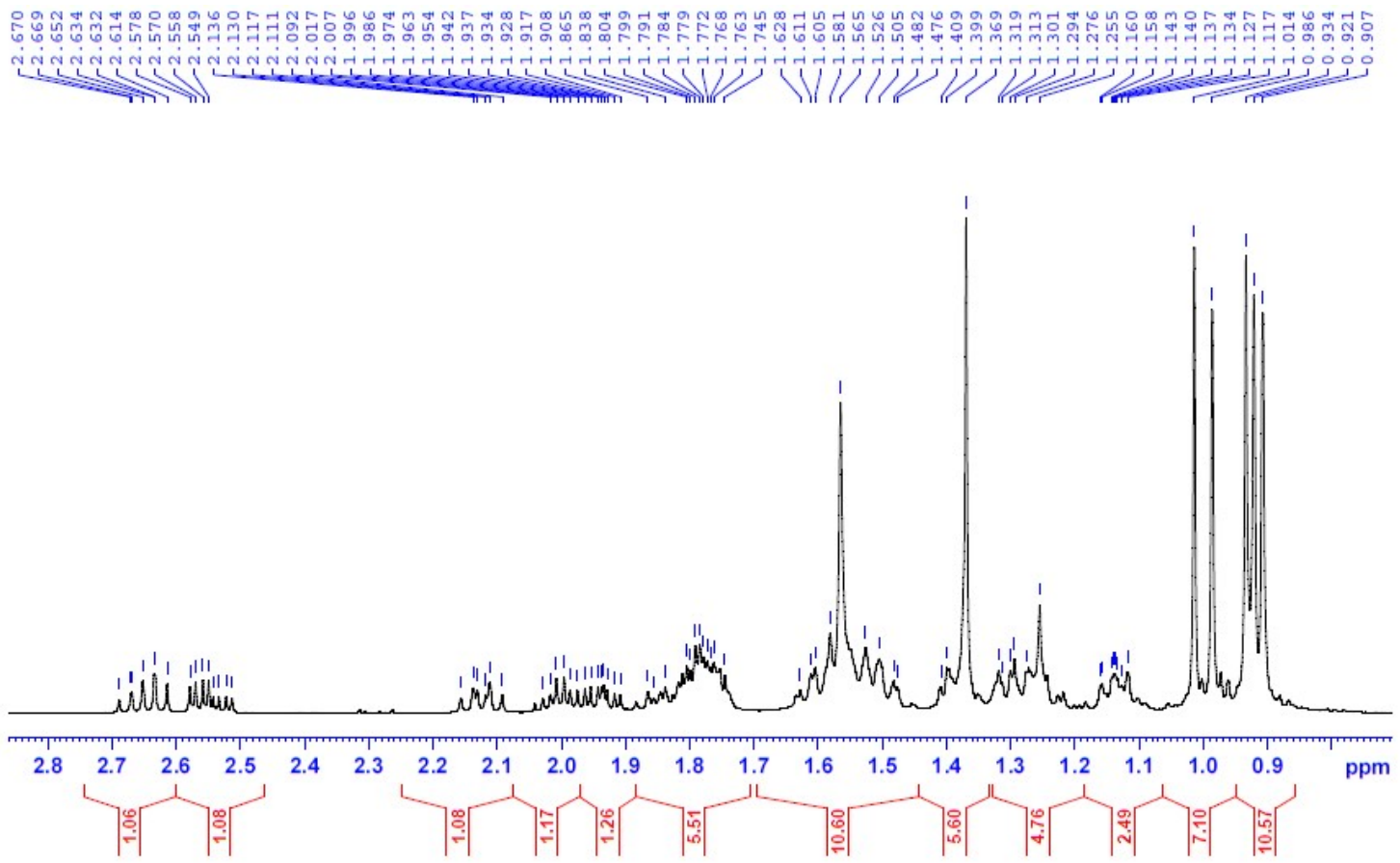
(+)-ESI–MS spectrum of compound **6d**



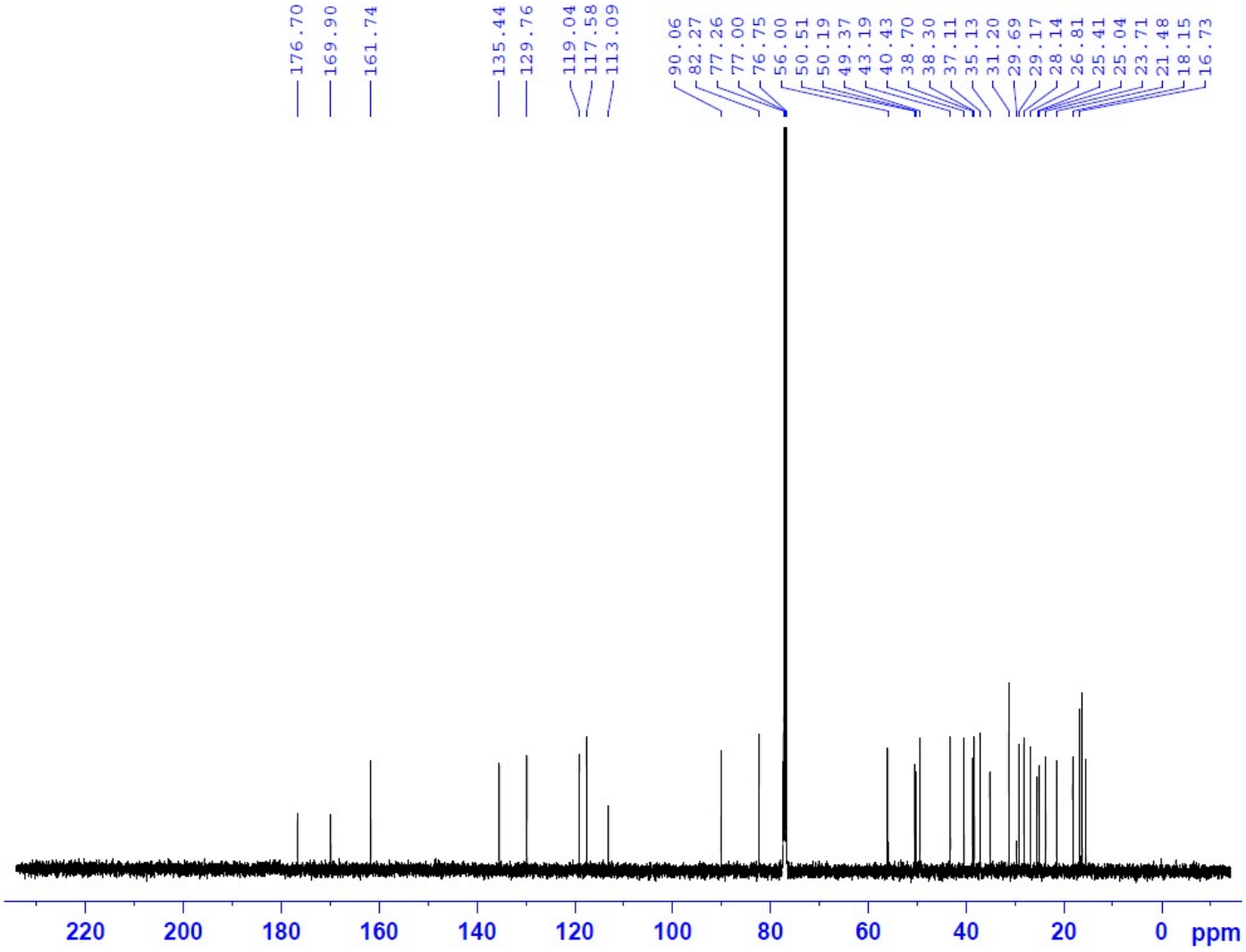
^{1}H-NMR spectrum of compound **6d**


7.836
7.832
7.820
7.816
7.460
7.457
7.446
7.443
7.441
7.429
7.426
7.260
6.985
6.983
6.968
6.966
6.889
6.887
6.872
6.858
6.856
5.296
4.774
4.761
4.753
4.741
8.0
7.5
7.0
6.5
6.0
5.5
5.0
ppm
1.09
1.11
1.13
1.11
1.02

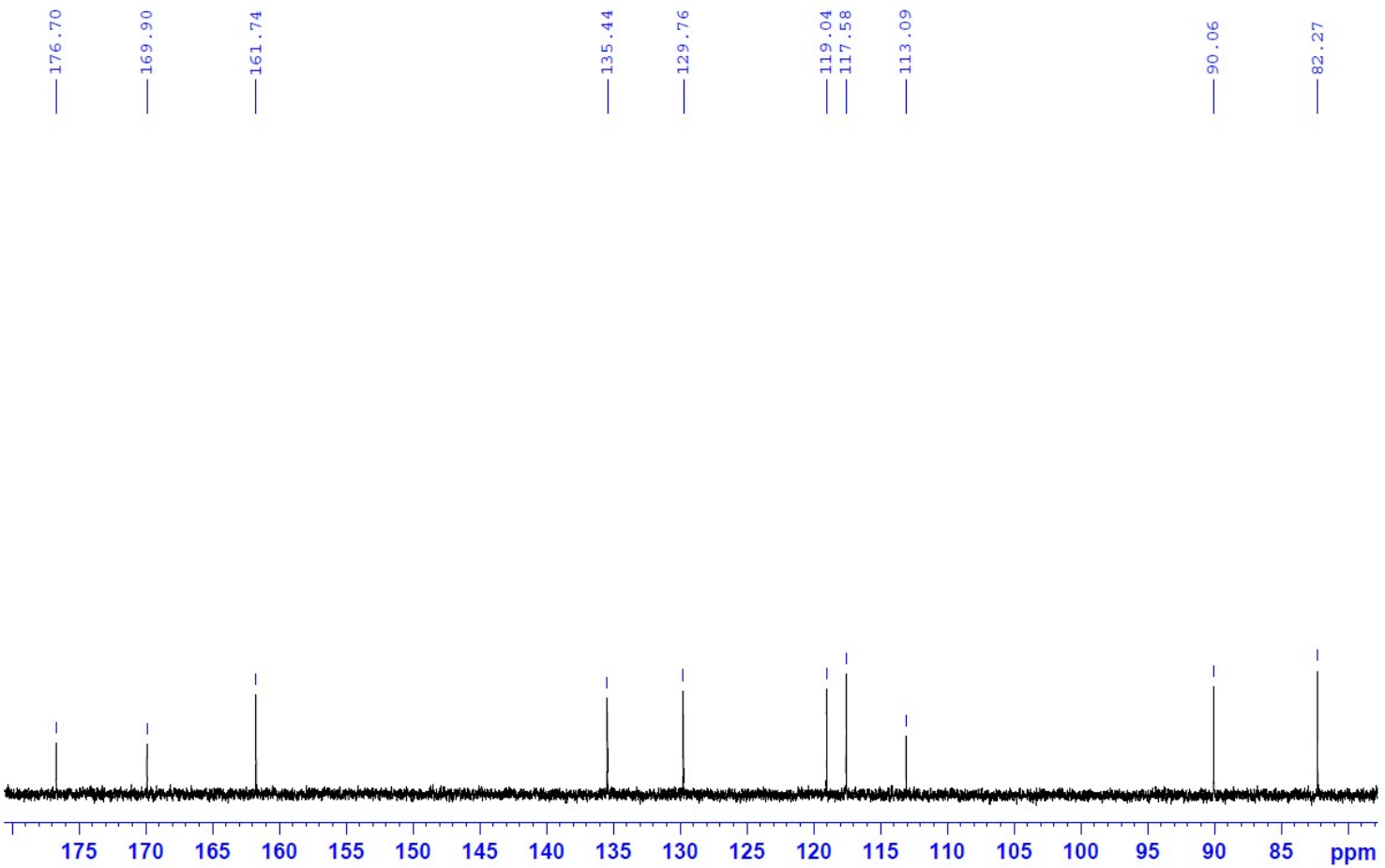
^{1}H-NMR spectrum of compound **6d** (extension)


2.670
2.669
2.652
2.634
2.632
2.614
2.578
2.570
2.558
2.549
2.136
2.130
2.117
2.111
2.092
2.017
2.007
1.996
1.986
1.974
1.963
1.954
1.942
1.937
1.934
1.928
1.917
1.908
1.865
1.838
1.804
1.799
1.791
1.784
1.779
1.772
1.768
1.763
1.745
1.628
1.611
1.605
1.581
1.565
1.526
1.505
1.482
1.476
1.409
1.399
1.369
1.319
1.313
1.301
1.294
1.276
1.255
1.160
1.158
1.143
1.140
1.137
1.134
1.127
1.117
1.014
0.986
0.934
0.921
0.907
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
ppm
1.06
1.08
1.08
1.17
1.26
5.51
10.60
5.60
4.76
2.49
7.10
10.57

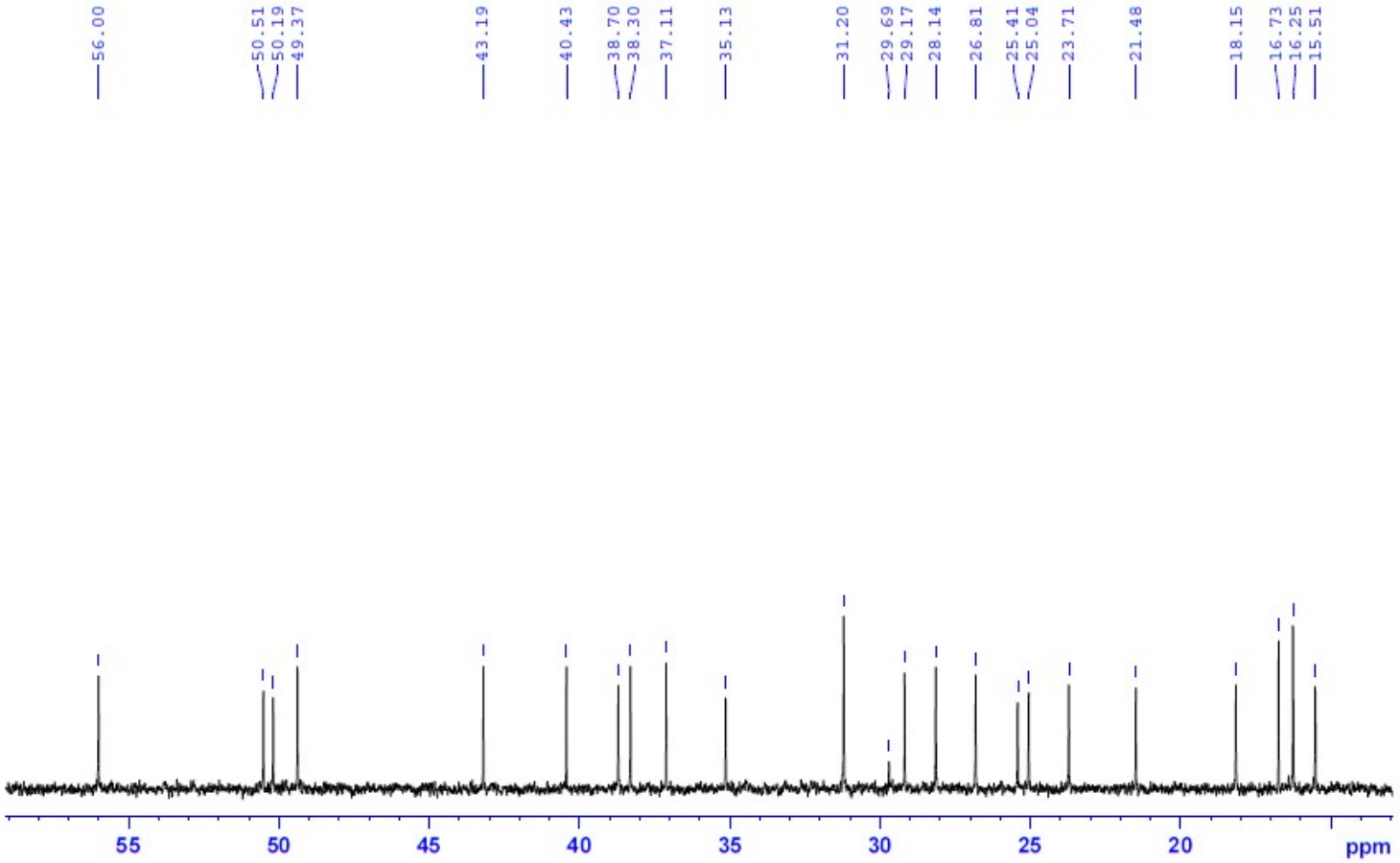
^{1}H-NMR spectrum of compound **6d** (extension)



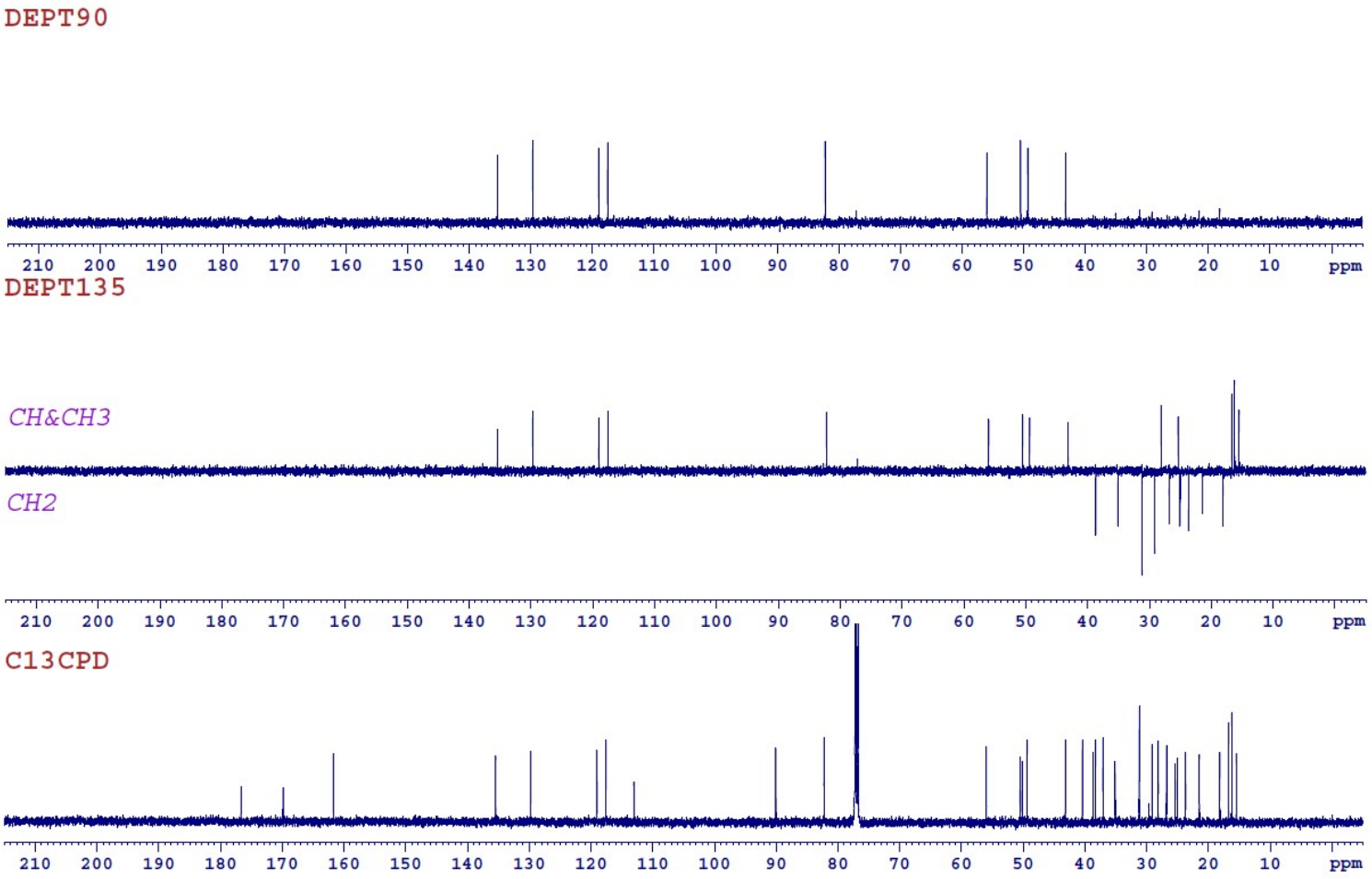
^{13}C-NMR spectrum of compound **6d**



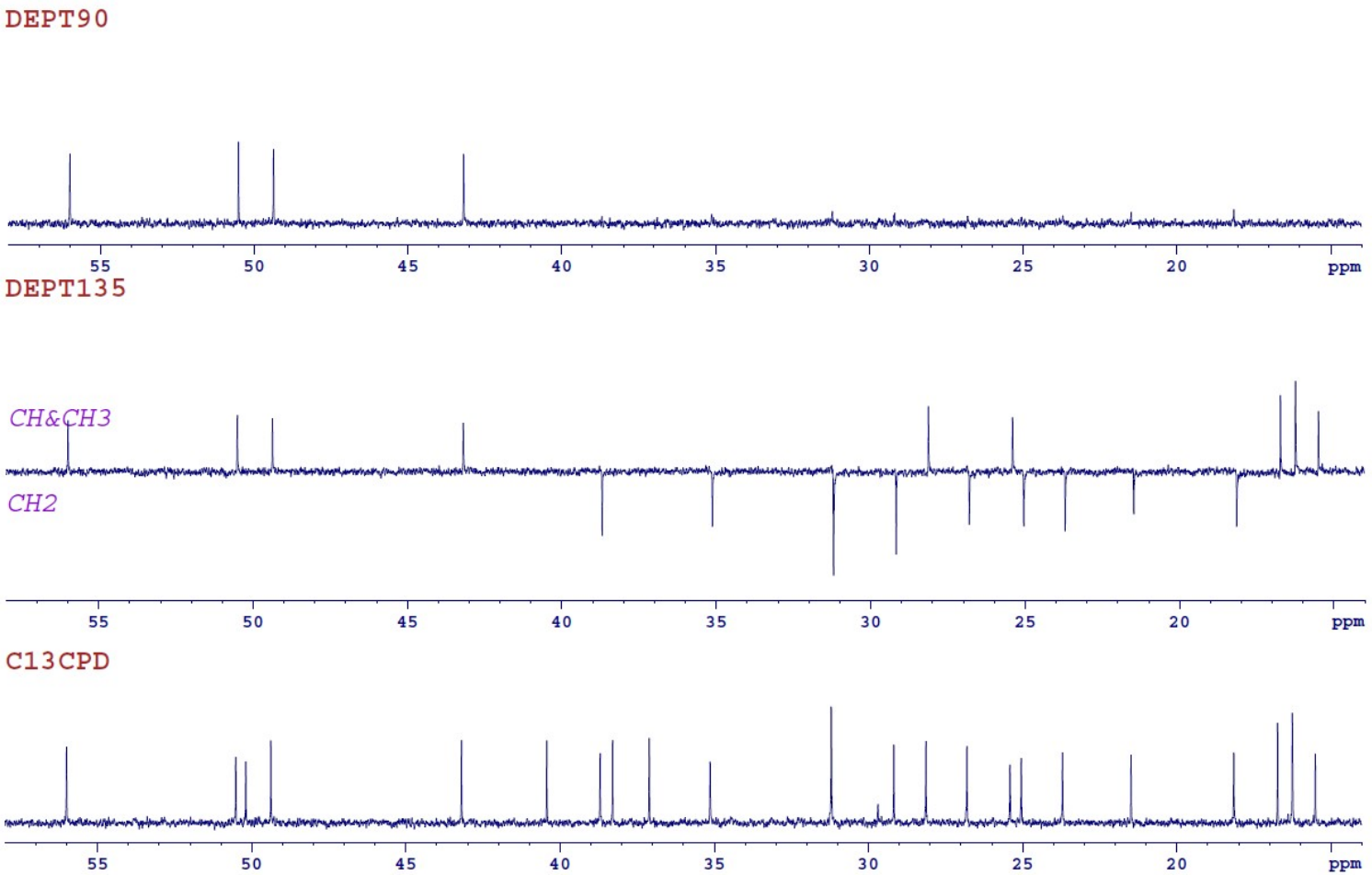
^{13}C-NMR spectrum of compound **6d** (extension)


56.00
50.51
50.19
49.37
43.19
40.43
38.70
38.30
37.11
35.13
31.20
29.69
29.17
28.14
26.81
25.41
25.04
23.71
21.48
18.15
16.73
16.25
15.51
55
50
45
40
35
30
25
20
ppm

^{13}C-NMR spectrum of compound **6d** (extension)



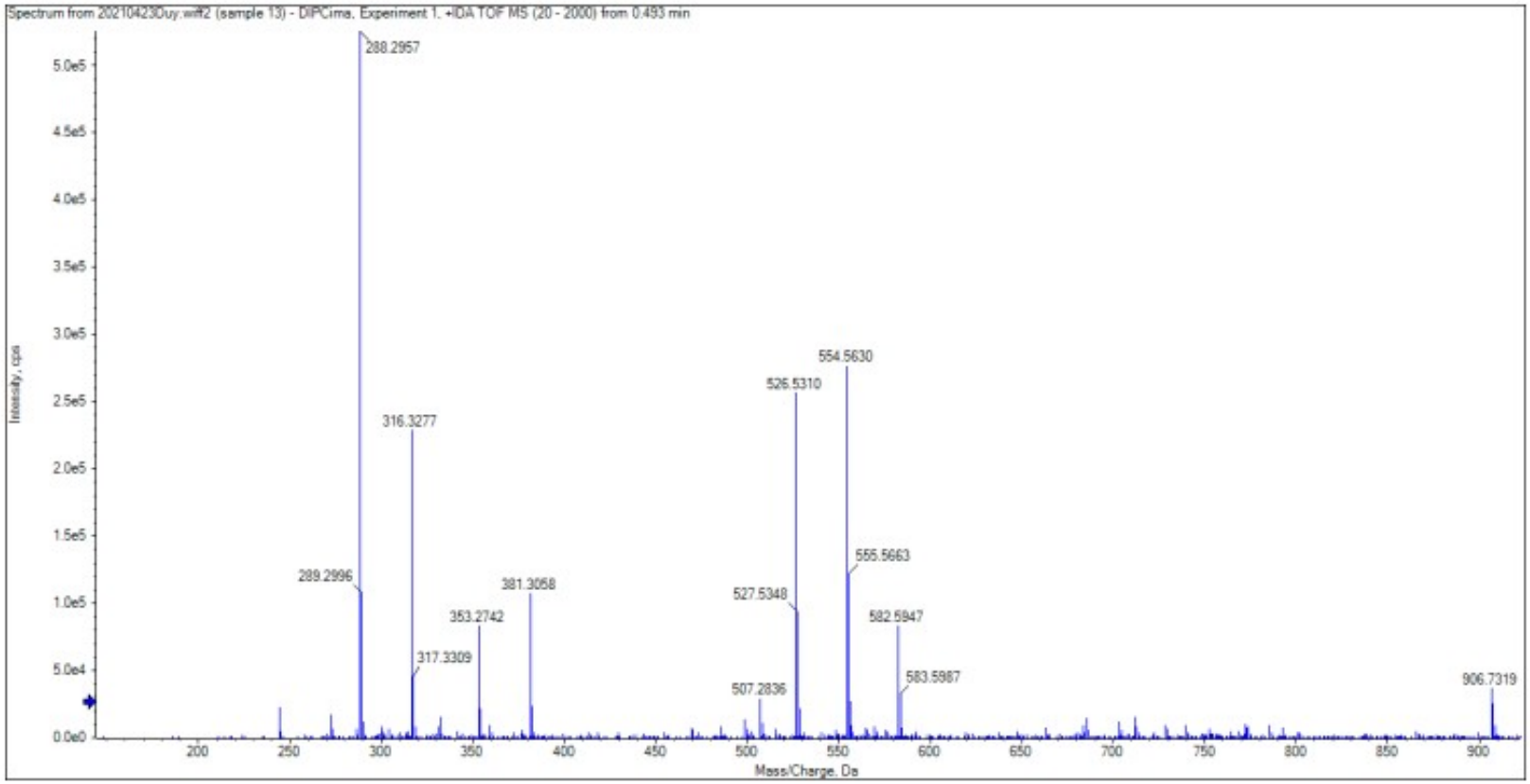
DEPT spectrum of compound **6d**



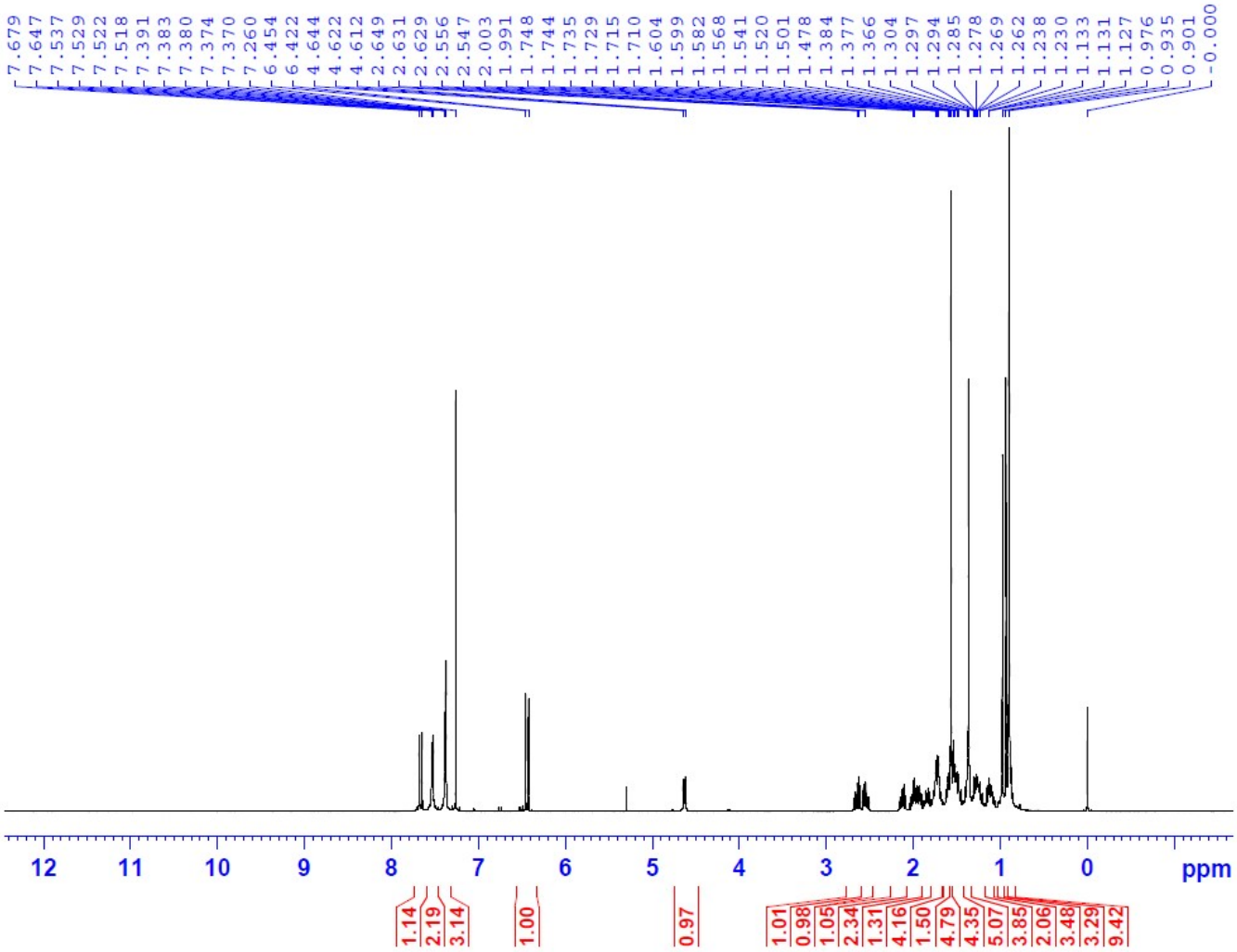
DEPT spectrum of compound **6d** (extension)

1.21. Compound 6e

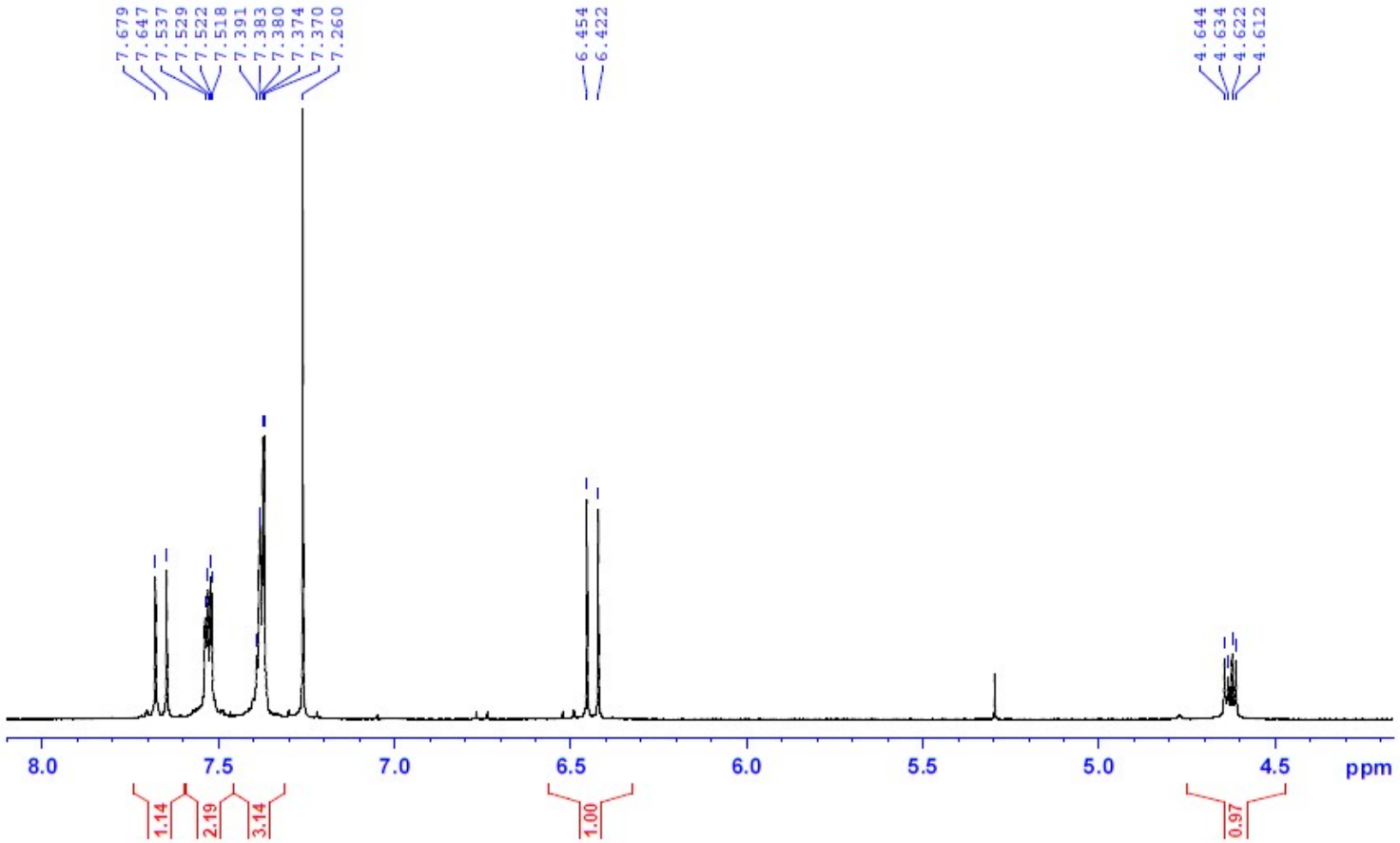
Sample name: DipCima
Operator: Le Anh VHH
Method: +IDA TOF MS/MS
Date: 2021.04.23



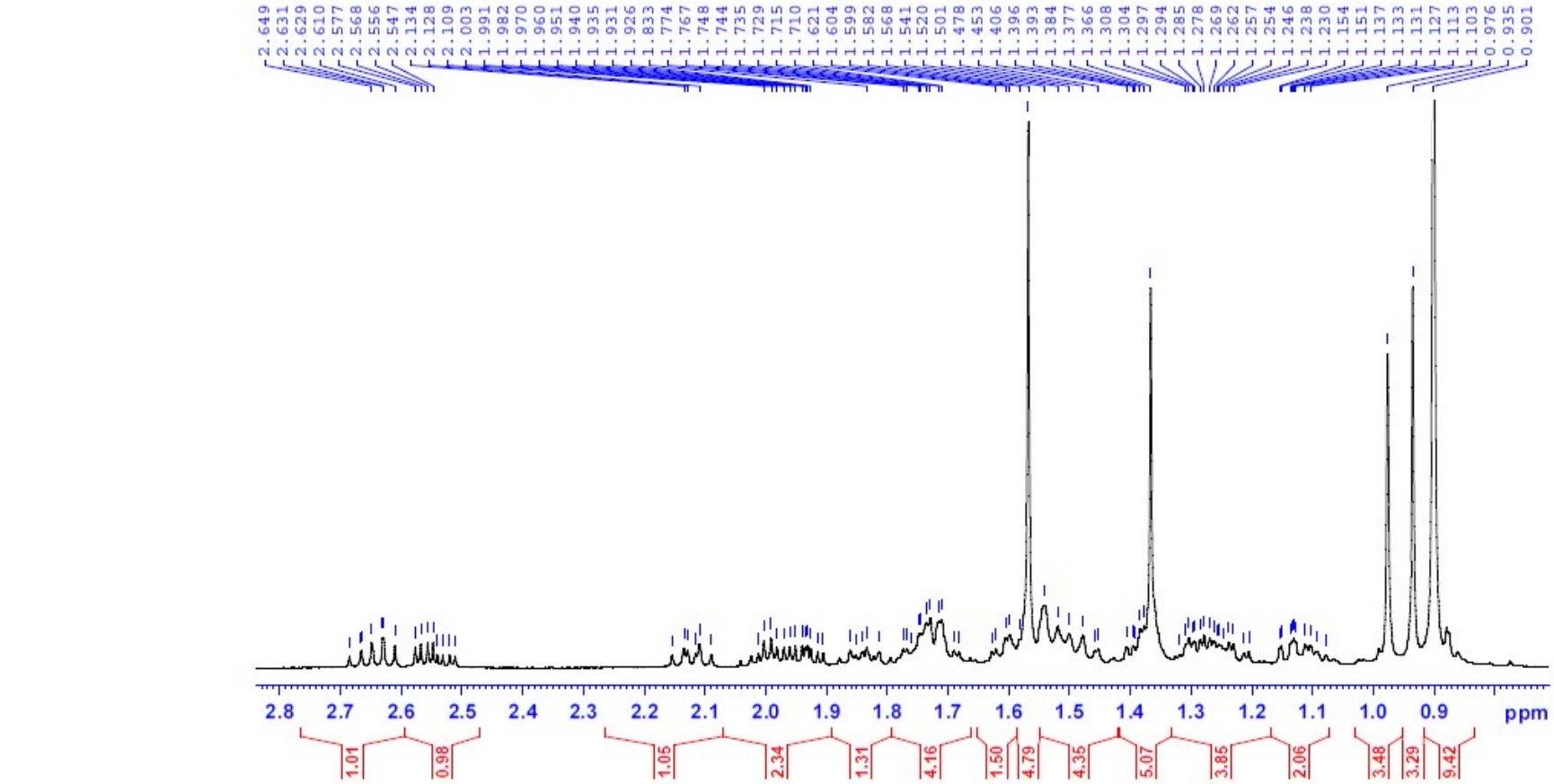
(+)-HR-ESI-MS spectrum of compound **6e**



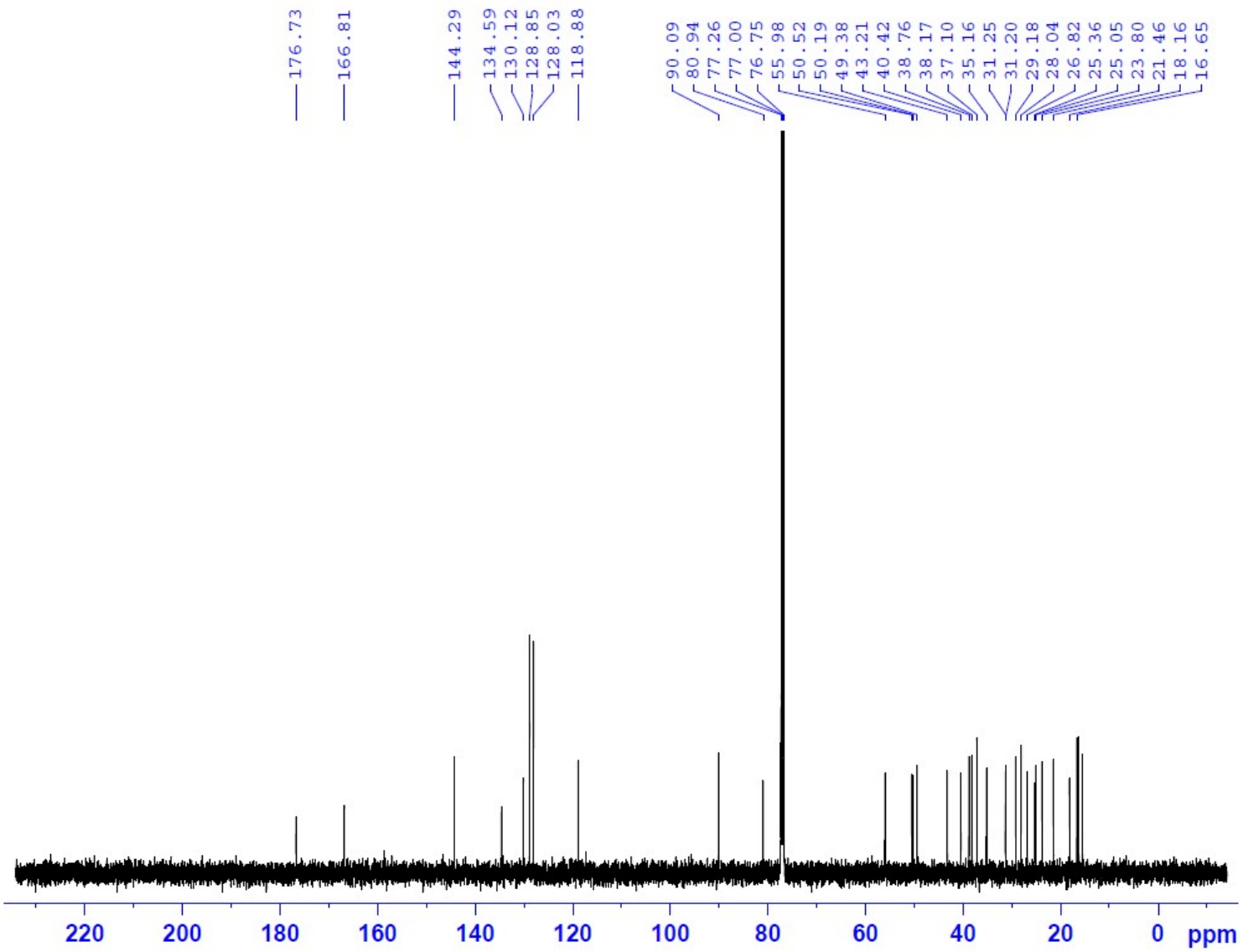
[1]H-NMR spectrum of compound **6e**


7.679
7.647
7.537
7.529
7.522
7.518
7.391
7.383
7.380
7.374
7.370
7.260
6.454
6.422
4.644
4.634
4.622
4.612
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm
1.14
2.19
3.14
1.00
0.97

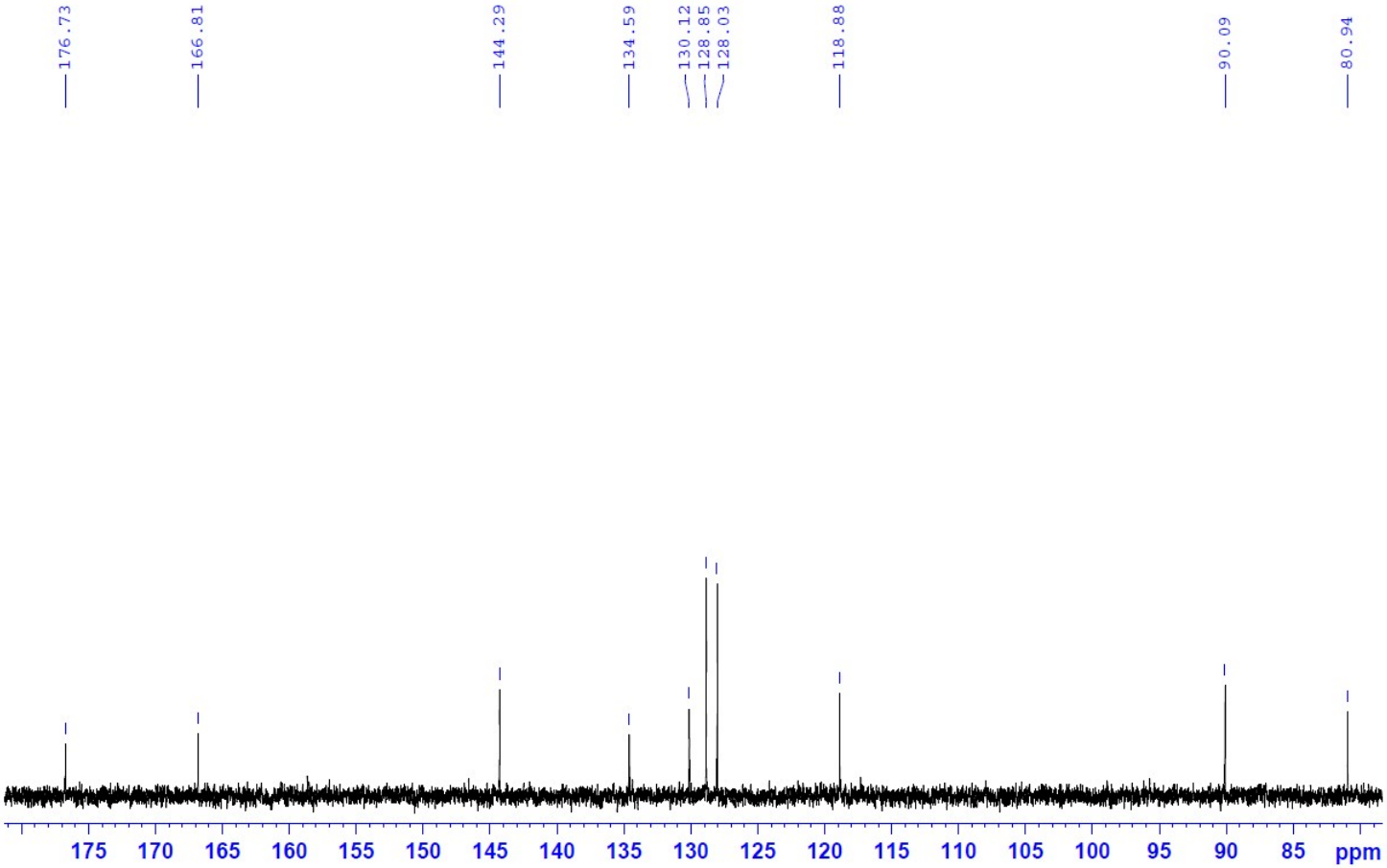
^{1}H-NMR spectrum of compound **6e** (extension)


2.649
2.631
2.629
2.610
2.577
2.568
2.556
2.547
2.134
2.128
2.109
2.003
1.991
1.982
1.970
1.960
1.951
1.940
1.935
1.931
1.926
1.833
1.774
1.767
1.748
1.744
1.735
1.729
1.715
1.710
1.621
1.604
1.599
1.582
1.568
1.541
1.520
1.501
1.478
1.453
1.406
1.396
1.393
1.384
1.377
1.366
1.308
1.304
1.297
1.294
1.285
1.278
1.269
1.262
1.257
1.254
1.246
1.238
1.230
1.154
1.151
1.137
1.133
1.131
1.127
1.113
1.103
0.976
0.935
0.901
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
ppm
1.01
0.98
1.05
2.34
1.31
4.16
1.50
4.79
4.35
5.07
3.85
2.06
3.48
3.29
9.42

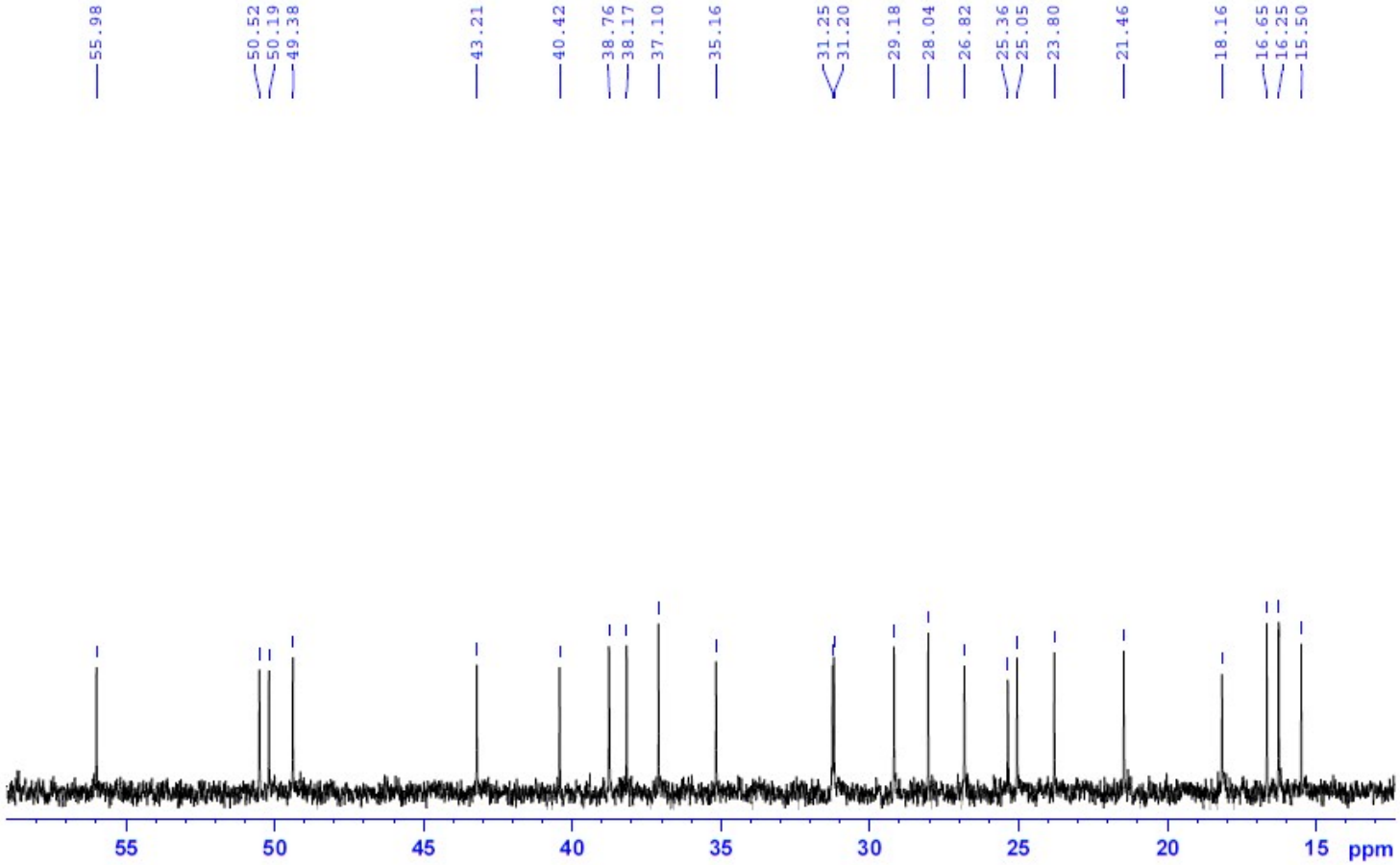
^{1}H-NMR spectrum of compound **6e** (extension)



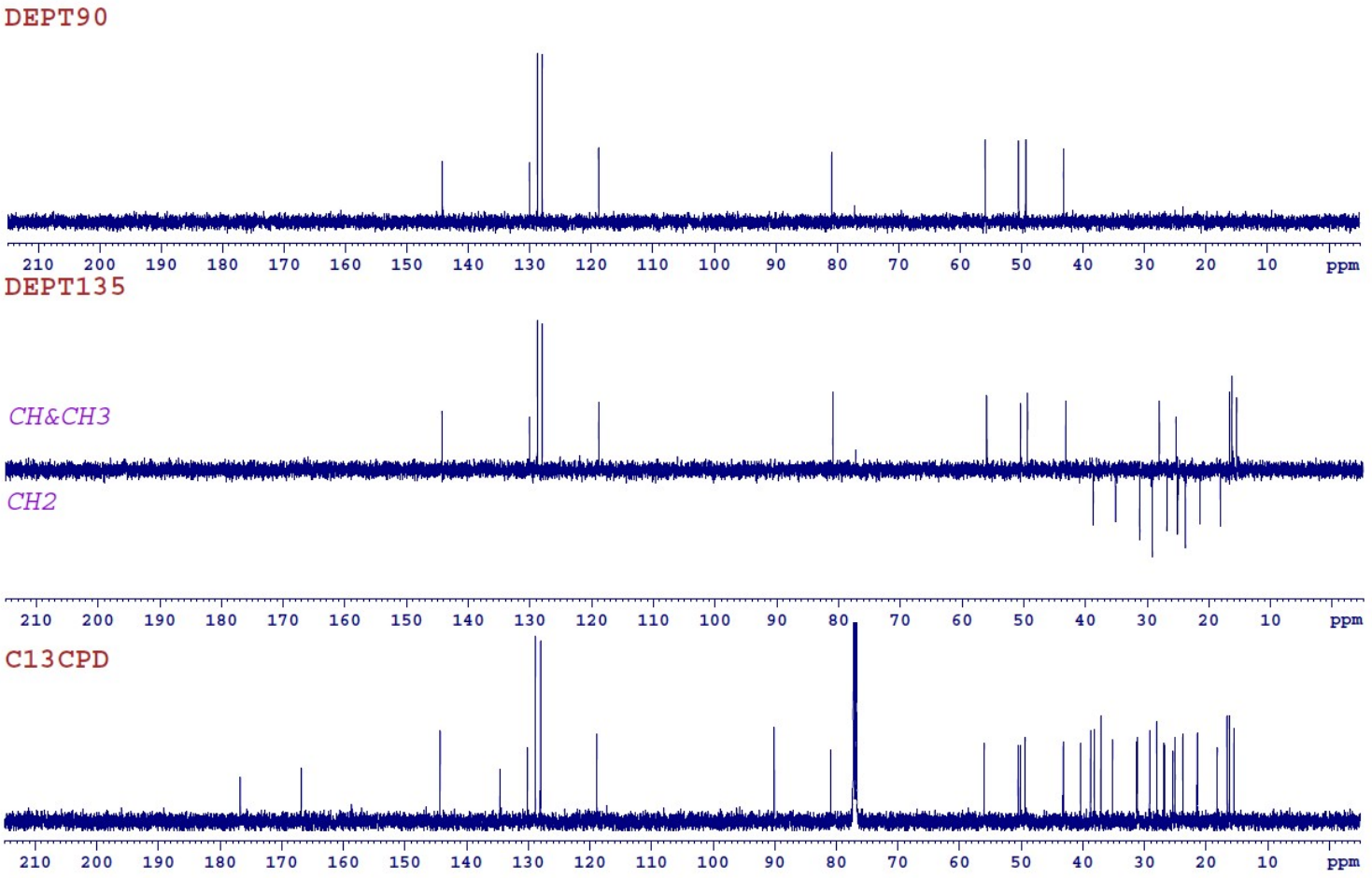
^{13}C-NMR spectrum of compound **6e**



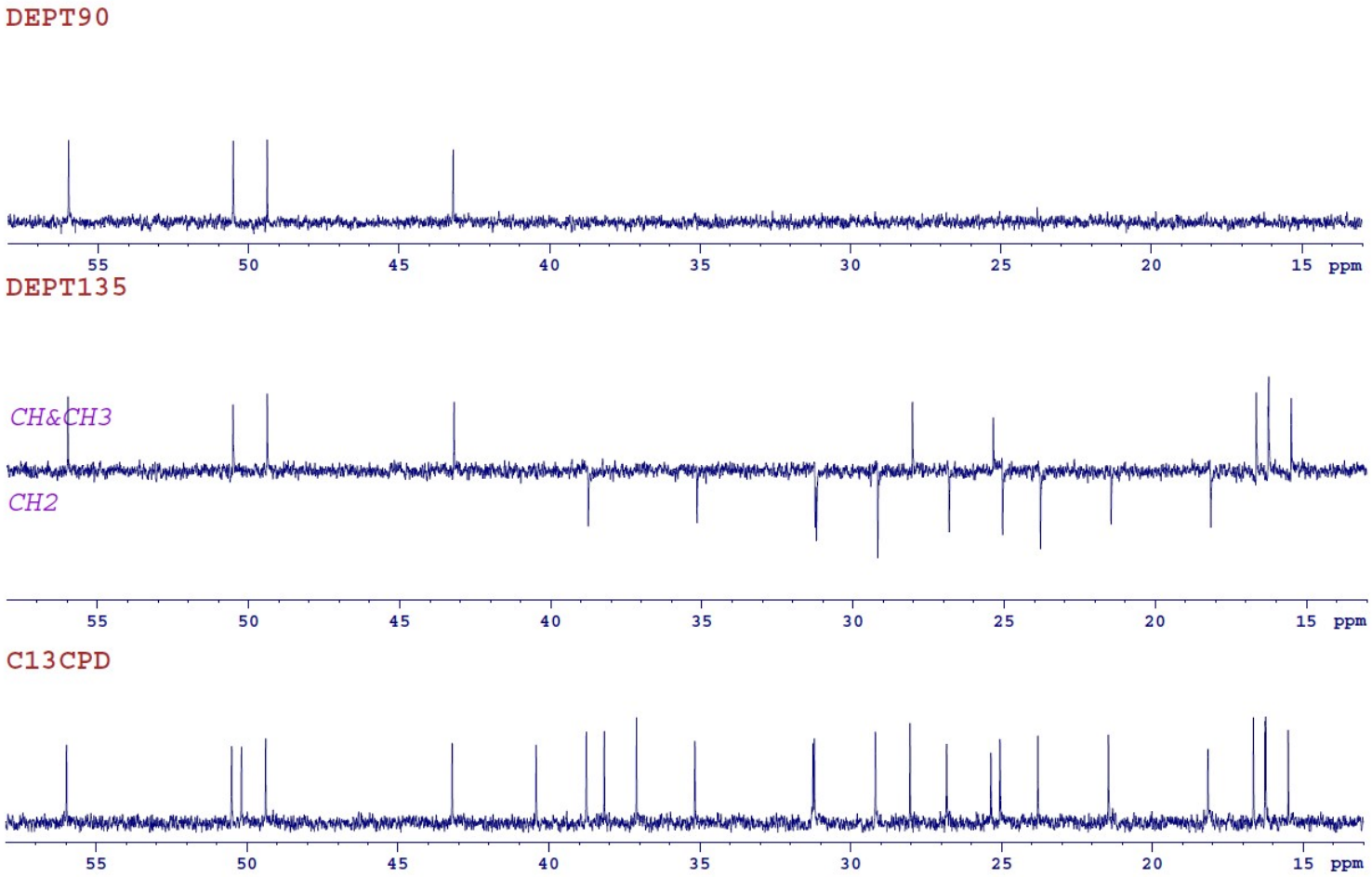
^{13}C-NMR spectrum of compound **6e** (extension)


55.98
50.52
50.19
49.38
43.21
40.42
38.76
38.17
37.10
35.16
31.25
31.20
29.18
28.04
26.82
25.36
25.05
23.80
21.46
18.16
16.65
16.25
15.50
55
50
45
40
35
30
25
20
15
ppm

^{13}C-NMR spectrum of compound **6e** (extension)



DEPT spectrum of compound **6e**



DEPT spectrum of compound **6e** (extension)

2. COMPUTATIONAL SIMULATION

2.1. In-detail data of ligand-3W37 inhibitory complexes

Table S1. Molecular docking simulation results for inhibitory complexes between the compounds and the protein 3W37 with amino acids: **1-3W37**, **2-3W37**, **3a-3W37**, **3b-3W37**, **3c-3W37**, **3d-3W37**, **3e-3W37**, **3f-3W37**, **3g-3W37**, **3h-3W37**, **3i-3W37**, **3k-3W37**, **3l-3W37**, **3m-3W37**, **4-3W37**, **5-3W37**, **6a-3W37**, **6b-3W37**, **6c-3W37**, **6d-3W37**, **6e-3W37**

Ligand-protein complex			Hydrogen bond						van de Waals interaction
Name	DS	RMSD	L	P		T	D	E	
1-3W37	-10.9	1.24	O	O	Asp666	H-donor	2.93	-0.8	Arg670, Arg699, Glu792, Ile759. Gly791, Tyr659, Thr790, Val760, Leu663, Asn758, Arg676, Ilr672, Glu302, Met302
			O	O	Thr299	H-acceptor	2.94	-1.4	
2-3W37	-12.9	1.67	O	O	Thr681	H-donor	3.04	-0.7	Thr299, Arg670, Arg699, Phe680, Glu301
			N	O	Glu792	H-donor	2.89	-7.1	
			O	N	Arg814	H-acceptor	2.94	-3.2	
			O	N	Arg814	H-acceptor	3.22	-2.2	
3a-3W37	-9.7	1.89	C	O	Ile759	H-donor	3.00	-1.0	Glu301, Ile672, Arg676, Gly791, Thr790, Val760, Pro658, Leu663, Tyr659, Glu792, Thr662, Leu663, Arg699, Asp666, Arg670, Thr681, Phe680
			N	N	Ala761	H-acceptor	2.94	-3.5	
3b-3W37	-13.4	1.78	N	N	Arg670	H-acceptor	3.10	-0.9	Glu301, Ile672, Tyr659, Ile759, Leu663, Gly791, Thr662, Arp676, Asp666, Arg699, Asp684, Phe682, Thr681
			O	N	Arg670	H-acceptor	3.02	-2.2	
			6-ring	C	Glu792	π-H	4.16	-0.9	
3c-3W37	-10.6	1.29	C	O	Asp666	H-donor	3.16	-0.7	Leu663, Arg670, Gly791, Glu792, Tyr659, Thr662, Thr790, Thr681, Phe680, Arg814, Glu301
			O	N	Arg699	H-acceptor	2.94	-1.2	
3d-3W37	-12.3	1.29	N	N	Arg670	H-acceptor	3.10	-0.8	Thr790, Gly791, Thr681, Glu301, Phe680, Pro683, Asp684, Asp666, Leu663, Ile672, Thr662, Tyr659, Glu792
			O	N	Arg670	H-acceptor	3.13	-1.2	
			O	N	Arg676	H-acceptor	3.52	-0.7	
			O	N	Arg699	ionic	3.41	-2.3	
3e-3W37	-13.8	1.12	O	S	Met302	H-donor	3.86	-1.1	Asp305, Glu792, Thr790, Arg670, Asn758, Gly700, Tyr659, Leu663, Asp666, Arg814. Glu301
			O	C	Gly791	H-acceptor	3.19	-0.7	
			N	C	Arg699	H-acceptor	3.65	-0.6	
			O	N	Arg699	ionic	3.41	-2.3	

			N	N	Arg699	ionic	3.21	-3.2	
			N	N	Arg699	ionic	3.13	-3.7	
3f-3W37	-10.5	1.94	N	N	Arg699	H-acceptor	2.91	-2.4	Pro683, Arg670, Glu301, Phe680, Asp666, Thr790, Val760, Ile754, Gly791, Ile701, Ile759, Gly700, Gly698, Thr681, Glu792, Arg814, Met302, Thr299
			6-ring	C	Tyr659	π-H	3.69	-0.6	
3g-3W37	-9.8	2.05	C	O	Asp666	H-donor	3.10	-1.0	Pro683, Leu663, Thr790, Glu792, Arg670, Tyr659, Thr662, Gly791, Thr681, Phe680, Glu301, Thr299, Arg298
			O	N	Arg699	H-acceptor	2.99	-1.2	
3h-3W37	-9.9	1.92	O	O	Asp666	H-donor	2.91	-1.2	Asp684, Glu301, Arg676, Arg699, Tyr659, Gly698, Leu663, Ile759, Val760, Thr790, Gly791, Glu792, Arg670, Thr299, Pro683
			O	N	Arg298	H-acceptor	2.98	-1.5	
3i-3W37	-11.3	1.81	N	N	Arg699	H-acceptor	3.28	-1.6	Met302, Phe680, Thr299, Glu301, Thr681, Gly791, Glu792, Tyr659, Leu663, Asp666, Ile672, Pro683, Arg298
			O	N	Arg670	H-acceptor	3.25	-0.7	
			O	N	Arg676	H-acceptor	3.21	-1.0	
			O	N	Arg676	H-acceptor	3.35	-1.2	
3k-3W37	-11.6	1.03	O	O	Thr681	H-donor	3.04	-0.8	Asp684, Pro683, Phe680, Ile672, Glu301, Arg676, Asp666, Thr790, Arg814, Gly791, Arg670, Glu792
			N	N	Arg699	H-acceptor	2.86	-1.0	
			O	N	Arg699	H-acceptor	3.64	-0.5	
3l-3W37	-10.9	1.70	O	O	Asp666	H-donor	2.96	-1.2	Arg298, Gly700, Asn758, Val760, Thr790, Tyr659, Arg699, Ile759, Gly791, Arg676, Glu792, Ile672, Glu301, Pro683, Thr299
			O	N	Arg670	H-acceptor	2.73	-0.7	
3m-3W37	-9.1	1.95	O	N	Arg699	H-acceptor	3.19	-2.3	Val760, Leu663, Gly698, Tyr659, Glu792, Thr790, Arg670, Arg676, Asp666, Pro683, Thr299, Ile759, Gly791, Asn758
4-3W37	-8.5	1.87	O	N	Arg699	H-acceptor	3.11	-1.6	Thr790, Arg670, Thr299, Met302, Arg814, Glu792, Gly791
5-3W37	-14.9	1.30	O	N	Arg670	H-acceptor	2.96	-0.9	Met302, Thr299, Gly698, Glu792, Asp666, Leu663, Arg699, Ile672, Glu301
			O	N	Arg676	H-acceptor	2.86	-4.4	
			O	N	Arg676	H-acceptor	3.22	-0.8	
6a-3W37	-9.7	1.19	O	N	Arg676	H-acceptor	2.83	-4.6	Glu792, Gly791, Asp666, Leu663, Ile759, Asn758, Thr662, Val760, Gly700, Gly698, Tyr659, Thr790, Arg670, Arg676.
6b-3W37	-10.1	1.22	O	N	Arg699	H-acceptor	2.99	-0.8	Arg670, Arg676, Glu792, Leu663, Asn758, Gly698, Val760, Gly791, Tyr659, Ile701, Ile759, Thr790, Asp666, Arg814
			O	N	Gly700	H-acceptor	2.82	-2.8	
6c-3W37	-13.2	1.12	O	O	Asn758	H-donor	2.60	-1.2	Ile759, Glu792, Tyr659, Thr662, Asp666, Leu663, Arg676, Ile672, Arg670, Val760, Gly698, Gly791, Thr790, Gly700
			O	N	Arg699	H-acceptor	2.96	-1.6	
6d-3W37	-13.7	1.31	C	O	Asp666	H-donor	3.33	-0.8	Gly698, Ile759, Leu663, Asn758, Gly791, Thr662, Tyr659, Thr790, Arg670

			O	N	Arg676	H-acceptor	3.25	-1.7	
			O	N	Arg676	H-acceptor	3.35	-0.7	
			6-ring	C	Glu792	π-H	4.34	-0.7	
6e-3W37	-15.2	0.31	O	N	Lý309	H-acceptor	3.42	-1.5	Arg699, Ile759, Tyr659, Thr662, Gly791, Leu663, Ile672, Asp666, Glu301, Asp305, Met302
			O	N	Arg670	H-acceptor	3.12	-2.1	
			O	N	Arg676	H-acceptor	3.37	-0.6	
			6-ring	C	Glu792	π-H	4.36	-0.6	
DS: Docking score energy (kcal.mol^{-1}); **RMSD**: Root-mean-square deviation (Å); **L**: Ligand; **P**: Protein; **T**: Type; **D**: Distance (Å); **E**: Energy (kcal.mol^{-1})									

2.2. In-detail data of ligand-3AJ7 inhibitory complexes

Table S2. Molecular docking simulation results for inhibitory complexes between the compounds and the protein 3AJ7 with amino acids: **1-3AJ7**, **2-3AJ7**, **3a-3AJ7**, **3b-3AJ7**, **3c-3AJ7**, **3d-3AJ7**, **3e-3AJ7**, **3f-3AJ7**, **3g-3AJ7**, **3h-3AJ7**, **3i-3AJ7**, **3k-3AJ7**, **3l-3AJ7**, **3m-3AJ7**, **4-3AJ7**, **5-3AJ7**, **6a-3AJ7**, **6b-3AJ7**, **6c-3AJ7**, **6d-3AJ7**, **6e-3AJ7**

Ligand-protein complex			Hydrogen bond						van der Waals interaction
Name	DS	RMSD	L	P		T	D	E	
1-3AJ7	-10.2	1.59	O	O	Pro312	H-donor	2.77	-2.3	Phe178, Glu411, Phe159, Gln279, Arg315, Asp242, His280, Leu313, Phe303, Ser311, Phe314, Asp307, Tyr158, Glu277, Asp252
			O	N	Arg442	H-acceptor	3.29	-2.0	
2-3AJ7	-11.9	1.46	O	O	Asp242	H-donor	2.76	-3.3	Asp69, Asp307, Glu277, His280, Phe303, Ser240, Phe178, Val216, Tyr158, Ser241, Gln279, Lys156, Pro312, Ser157, Arg315, Phe159, Glu411, Asp242
			O	N	Arg442	H-acceptor	2.75	-1.3	
3a-3AJ7	-9.5	1.77	O	O	Asp242	H-donor	2.63	-1.2	His280, Leu246, Tyr158, Asp69, Asp352, Asp215, Tyr72, Arg442, Phe178, Glu411, Phe303, Arg315, Phe159, Gln279, Pro312, Leu313, Asp307, Ph314
			C	O	Glu277	H-donor	3.05	-0.9	
			O	O	Ser240	H-acceptor	2.79	-1.5	
3b-3AJ7	-12.2	0.99	C	O	Glu277	H-donor	3.42	-0.7	Leu313, Pro312, Gln279, Tyr316, Phe314, His280, Phe303, Glu411, Arg315, Phe178, Tyr158, Asp307, Phe159, Asp215, Asp69, Asp352, Gln353, Arg442, Asp242, Val232
			C	O	Ser240	H-acceptor	2.68	-1.5	
			C	6-ring	Tyr72	H-π	4.09	-0.6	
3c-3AJ7	-11.8	1.45	O	O	Pro312	H-donor	2.64	-1.9	Asp242, Tyr158, Ser240, Lys156, Phe303, Ser241, Tyr72, Ser157, His112, Arg442, Glu277, Asp215, Asp352, Gln182, Arg446, Val216, Gln352, Asp69, Asp307, Glu411, Gln279, Arg315, His280, Leu313, Phe314
			O	N	His351	H-acceptor	3.14	-1.1	
			6-ring	6-ring	Phe178	π-π	3.96	-0.0	
3d-3AJ7	-10.9	1.43	O	O	Asp352	H-donor	3.03	-0.8	Tyr72, His112, Asp215, Tyr158, Glu277, Phe303, Phe178, Gln279, Asp307, Val216, Asp242, Pro312, Val232, Leu313, Phe314, Arg315, Glu411, Gln353, Arg442, Asp69
			N	O	Ser240	H-acceptor	3.07	-1.1	
			O	O	Ser240	H-acceptor	2.77	-1.8	
3e-3AJ7	-15.3	1.79	O	O	Asp242	H-donor	2.61	-1.0	Phe314, Pro312, Ser311, Asp307, Leu313, Phe303, His280, Arg315, Gln279, Phe178, Glu411, Asp215, Phe159, Arg446, Asp69, His351, Asp352. Tyr72, Glu277, Val215, Tyr158, Val 232
			O	O	Ser240	H-acceptor	2.88	-0.6	
			O	N	Arg442	ionic	3.21	-3.2	
			N	N	Arg442	Ionic	2.79	-6.0	
			N	N	Arg442	ionic	4.00	-0.5	
3f-3AJ7	-12.2	1.37	O	O	Asp242	H-donor	2.62	-1.3	Leu246, Ser240, Asp69, Tyr72, His112, Phe159, Gln182, Arg442, Phe178,

			C	O	Glu277	H-donor	3.08	-1.0	Asp352, Phe303, Tyr158, Arg315, Glu411, Asp307, Gln279, Ser311, Phe314, Pro312, Leu313, His280.
			C	O	Asp215	H-donor	3.30	-0.8	
3g-3AJ7	-9.9	1.14	O	O	Asp242	H-donor	2.81	-2.6	Tyr72, His112, Val109, Val216, Tyr158, Phe178, Asp215, Phe303, Phe159, Glu277, Glu411, Gln279, Asp307, His280, Pro312, Arg315, Arg442, Gln182, Gln352, Asp352, Arg446, Asp69
			O	N	His351	H-acceptor	3.12	-1.1	
3h-3AJ7	-10.4	1.43	I	O	Glu277	H-donor	3.48	-0.2	Pro312, Ser311, Arg315, Glu411, Asp353, Arg442, Val216, Tyr158, Phe303, Asp242, Gln279, Ser304, Asp307.
			C	5-ring	His280	H-π	3.55	-0.9	
3i-3AJ7	-11.7	1.26	C	O	Glu277	H-donor	3.48	-0.8	Asp242, Leu313, Ser241, Lys166, Ser240, Ser157, Leu177, His280, Tyr158, Glu411, Phe178, Phe159, Gln279, Arg442, Tyr72, His112. Asp352, Asp215, Val216, Phe303, Arg315, Phe314, Pro312
			C	O	Asp69	H-donor	3.58	-0.6	
3k-3AJ7	-12.7	1.78	O	O	Asp242	H-donor	2.78	-3.1	Ser311, Thr310, Gln279, Pro312, Thr306, Asp307, Phe303, Arg315, Tyr347, Arg213, Glu277, Glu411, His280, Ser240
			C	O	Asp352	H-donor	3.20	-0.7	
			O	N	Asn350	H-acceptor	2.98	-3.1	
			O	N	Gln353	H-acceptor	2.91	-2.2	
			C	6-ring	Tyr158	H-π	4.54	-0.8	
3l-3AJ7	-9.6	1.83	C	6-ring	Tyr158	H-π	4.49	-0.7	Ser304, Asp307, Gly309, His280, Thr310, val308, Ser241, Asp242, Ser157, Lys156, Ser240, Leu313, Pro312, Phe314
3m-3AJ7	-10.3	1.79	C	O	Glu277	H-donor	3.15	-0.8	Asp242, Pro312, Gln279, Arg315, Asp307, Phe159, Phe178, Thr306, Phe303, Phe301, Arg213, Tyr347, His351, Asp352, Tyr158, Arg442, Glu411, His280, Val232, Ser240, Leu313.
			O	N	Asn350	H-acceptor	2.78	-2.2	
			O	N	Gln353	H-acceptor	3.03	-2.3	
4-3AJ7	-10.2	1.15	O	N	Arg442	H-acceptor	3.50		Gln353, Glu277, Arg315, Phe303, Thr245, Asp242, Ser240, Lys156, Ser157, Asp307, Gln279, Glu411, Asp352, His280
			O	N	Ser241	H-acceptor	2.87		
			C	6-ring	Tyr158	H-π			
5-3AJ7	-15.9	1.02	O	N	Gln353	H-acceptor	2.96	-1.2	Ser240, Asp352, Thr306, Asp307, Phe303, Glu411, Arg442, Arg315, Pro312, Ser157, tyr316, Lys156, Asp242.
			O	N	Ser241	H-acceptor	3.04	-0.9	
			C	6-ring	Tyr158	H-π	3.96	-0.7	
			C	6-ring	Tyr158	H-π	4.35	-0.7	
6a-3AJ7	-11.6	1.67	O	N	Ser241	H-acceptor	2.99	-2.7	Val216, Asp352, Arg442, Phe314, glu411, Arg315, Ser240, Gln239, Asp242, Lys156, Asp307, Ser157, Phe159, Phe303, Gln279, His280, Phe178, Glu277, Asp216, Val216
			C	6-ring	Tyr158	H-π	4.16	-0.6	
			C	6-ring	Tyr158	H-π	4.22	-0.6	

6b-3AJ7	-10.6	1.22	C	O	Glu277	H-donor	3.39	-0.7	Tyr72, Asp352, Gln253, Arg442, Asp242, Pro312, Ser240, Val232, leu313, Asp233, His280, Gln279, Phe303, Glu411, Arg315, Tyr158, Asp215, Phe178, Val216, Arg213,
			O	N	His351	H-acceptor	3.25	-2.1	
6c-3AJ7	-13.7	0.97	O	C	Phe314	H-acceptor	3.30	-0.7	Gln353, Asp69, Asp352, Gln182, His351, tyr72, His112, Glu277, Gln279, Asp215, Phe178, Phe159, His280, Val216, Glu411, Phe303, Tyr158, Leu313, Pro312, Asp307, Ser311
			O	N	Arg315	H-acceptor	3.14	-1.6	
			O	N	Arg442	H-acceptor	2.91	-1.9	
6d-3AJ7	-12.5	0.95	O	O	Glu277	H-donor	2.70	-6.1	Asp242, Leu313, Pro312, Asp352, Asp69, Val216, Tyr72, Asp215, Phe178, Tyr158, Glu411, Phe303, His280, Arg315, Gln279, Gln239, Asp233, Val232, Phe159, Trp238.
			O	N	Lys156	H-donor	3.16	-5.0	
			O	N	Ser240	H-acceptor	3.16	-0.8	
			O	N	Arg442	H-acceptor	3.07	-1.2	
6e-3AJ7	-14.4	1.79	O	N	Ser241	H-acceptor	3.33	-1.0	Ser240, Lys156, Phe314, Pro312, His280, Leu313, Asp325, Ala329, Ile329, Ile328, Glu332, Asp307, Ser311, Thr310, Ser157, Asp242
			C	6-ring	Tyr158	H-π	4.65	-0.6	
			6-ring	C	Ser304	π-H	3.68	-0.7	
DS: Docking score energy (kcal.mol^{-1}); **RMSD**: Root-mean-square deviation (Å); **L**: Ligand; **P**: Protein; **T**: Type; **D**: Distance (Å); **E**: Energy (kcal.mol^{-1})									

2.3. In-detail data of ligand-PTP1B inhibitory complexes

Table S3. Molecular docking simulation results for inhibitory complexes between the compounds and the protein PTP1B with amino acids: **1-PTP1B**, **2-PTP1B**, **3a-PTP1B**, **3b-PTP1B**, **3c-PTP1B**, **3d-PTP1B**, **3e-PTP1B**, **3f-PTP1B**, **3g-PTP1B**, **3h-PTP1B**, **3i-PTP1B**, **3k-PTP1B**, **3l-PTP1B**, **3m-PTP1B**, **4-PTP1B**, **5-PTP1B**, **6a-PTP1B**, **6b-PTP1B**, **6c-PTP1B**, **6d-PTP1B**, **6e-PTP1B**

Ligand-protein complex			Hydrogen bond						van der Waals interaction
Name	DS	RMSD	L	P		T	D	E	
1-PTP1B	-10.5	1.19	O	N	Gly259	H-acceptor	2.87	-1.8	Arg47, Asp29, Ser28, Met258, Gly259, Ala27, Arg254, Ser50, Arg24, Lys36
2-PTP1B	-13.8	1.17	O	N	Arg24	H-acceptor	3.41	-0.7	Lys36, Asp29, Arg254, Gly259, Met258, Asp48, Cys32
			O	N	Arg24	H-acceptor	2.98	-2.5	
			O	N	Gln262	H-acceptor	3.24	-1.6	
3a-PTP1B	-9.3	1.25	C	O	Phe30	H-acceptor	3.50	-0.7	Tyr46, Asp48, Arg24, Met258, Asp29, Pro31, Phe52, Lys36, Asp181, Lys120, Phe182
			N	N	Cys32	H-acceptor	3.22	-0.8	
3b-PTP1B	-11.5	1.98	O	O	Gln262	H-donor	3.16	-0.7	Tyr46, Asp48, Val49, Cys32, Phe30, Asp29, Arg24. Phe182, Ala217, Ile219
			6-ring	C	Pro31	π-H	4.74	-0.6	
3c-PTP1B	-9.6	1.92	N	N	Arg24	H-acceptor	3.11	-2.0	Asp29, Met258, Tyr20, Gly259, Phe182, Arg254
			N	N	Gln262	H-acceptor	3.03	-1.4	
3d-PTP1B	-13.7	1.89	O	N	Arg24	H-acceptor	3.33	-0.9	Lys120, Tyr46. Val49, Asp48, Gly259, Lys116, Ser118
			O	N	Arg24	H-acceptor	2.88	-1.7	
			O	N	Gln262	H-acceptor	2.87	-1.5	
			O	N	Arg24	H-acceptor	3.31	-0.7	
			O	N	Arg254	H-acceptor	3.05	-7.2	
			O	N	Arg24	ionic	3.31	-1.3	
			O	N	Arg254	ionic	3.05	-2.5	
			6-ring	C	Met258	π-H	4.74	-0.6	
3e-PTP1B	-12.9	1.43	O	N	Arg24	H-acceptor	3.29	-1.8	Met258, Gln262, Ile219, Gly250, Cys32, Asp29, Asp48, Val49
			O	N	Lys36	H-acceptor	3.12	-2.8	
			O	N	Lys36	ionic	3.12	-2.1	
			6-ring	C	Lys36	π-H	3.55	-0.7	

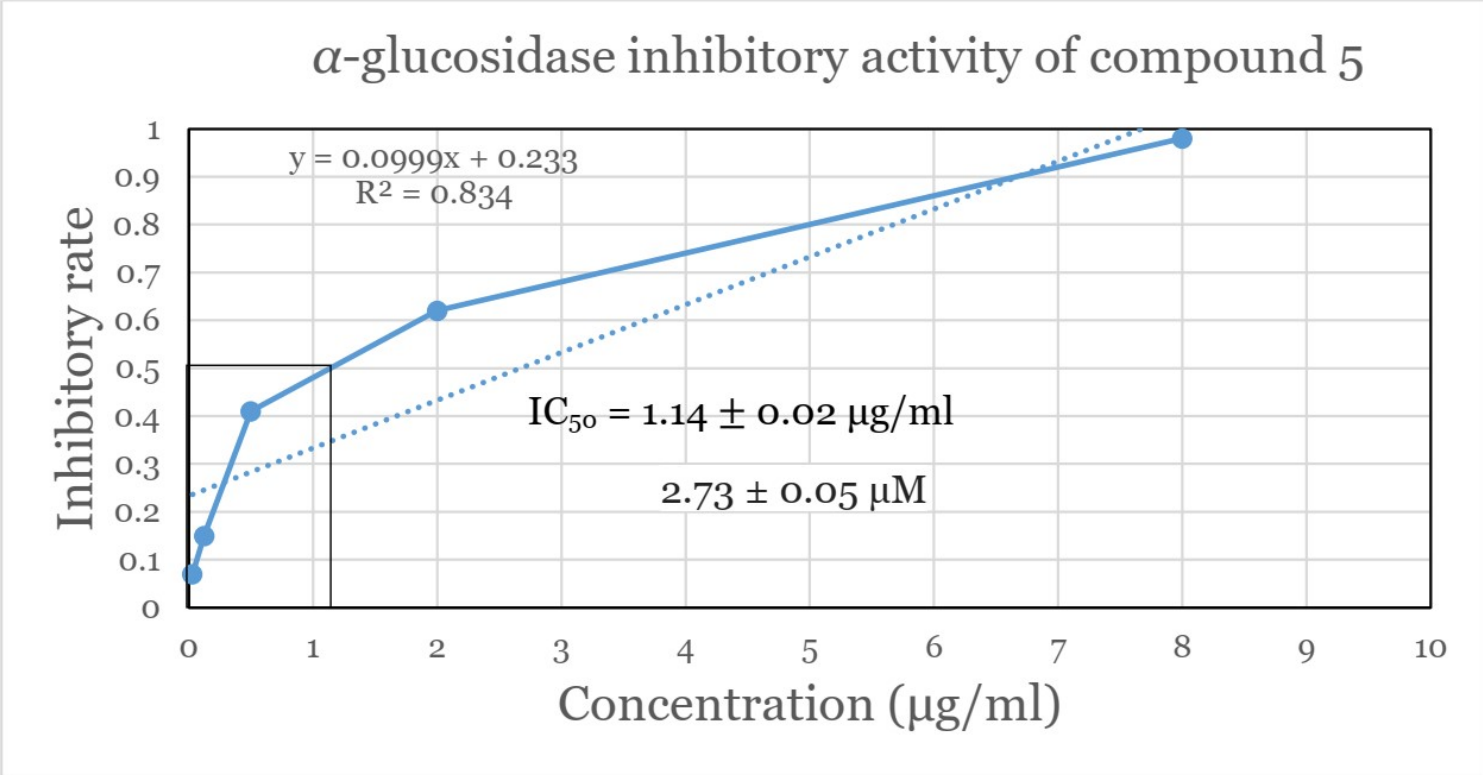
3f-PTP1B	-10.1	1.75	O	N	Cys32	H-acceptor	3.14	-1.8	Pro31, Arg33, Lys36, Met258, Asp48, Val49, Ile219, Asp29
			O	N	Arg24	H-acceptor	3.11	-2.4	
			O	N	Gln262	H-acceptor	3.57	-0.6	
3g-PTP1B	-9.0	1.90	O	N	Lys36	H-acceptor	3.23	-3.9	Cys32, Asp29, Asp48, Ile219, Val49, Phe182, Met258, Gly259
			O	N	Arg24	H-acceptor	3.32	-0.9	
			O	N	Gln262	H-acceptor	3.20	-2.0	
3h-PTP1B	-9.4	1.36	I	S	Met258	H-donor	3.66	-0.7	Val49. Ile219, Asp48, Lys36, Asp29
			O	N	Arg24	H-acceptor	2.91	-2.8	
			O	N	Gln262	H-acceptor	3.07	-2,9	
3i-PTP1B	-10.3	1.14	N	N	Gln262	H-acceptor	3.41	-0.9	Phe30, Arg33, Pro31, Asp29, Lys36, Met258, Tyr20, Asp48, Cys32
			O	N	Arg24	H-acceptor	2.87	-2.0	
			O	N	Gln262	H-acceptor	2.85	-0.7	
3k-PTP1B	-9.7	1.35	O	O	Arg24	H-donor	3.26	-0.8	Asp29, Ser28, Arg254, His25, Ala27, Gln21, Met258,
			O	N	Lys36	H-acceptor	3.06	-3.8	
3l-PTP1B	-9.9	1.60	O	N	Lys36	H-acceptor	3.36	-0.9	Val49, Asp48, Gly259, Met258, Arg33, Cys32, Asp29, Ser28, Arg24, Ille219, Gln262
			O	N	Arg254	H-acceptor	3.37	-1.2	
3m-PTP1B	-9.3	1.34	C	6-ring	Tyr46	H-π	4.42	-0.6	Met258. Asp48, Gly259, Gln262, Val49, Phe182, Arg24, Ser28, Asp29
4-PTP1B	-11.2	1.23	C	S	Met258	H-donor	3.89	-0.8	Phe30, Lys36, Asp29, Gly259, Asp48, Pro31
			O	N	Cys32	H-acceptor	3.04	-3.3	
			O	N	Arg24	H-acceptor	3.13	-1.8	
			O	N	Gln262	H-acceptor	3.08	-1.5	
5-PTP1B	-13.4	1.37	O	N	Arg24	H-acceptor	2.87	-1.9	Asp29, Ser28, Gly259, ZGln262, Tyr20. Met258, Asp48
			O	N	Arg254	H-acceptor	3.27	-1.1	
			O	N	Arg254	H-acceptor	3.05	-3.1	
			O	N	Lys36	H-acceptor	3.25	-1.0	
6a-PTP1B	-9.8	1.40	O	N	Arg254	H-acceptor	2.85	-2.0	Pro31, Arg33, Phe30, Lys36, Asp29, Met258, Gly259, Arg24
			O	N	Cys32	H-acceptor	3.13	-1.0	
6b-PTP1B	-11.5	1.85	C	S	Met258	H-donor	4.16	-0.7	Pro31, cys32, Lys36, Gly259, Arg254, tyr20, Asp48, Asp29, Phe30
			O	N	Arg24	H-acceptor	3.38	-0.9	
			O	N	Arg24	H-acceptor	3.18	-0.9	

			O	N	Gln262	H-acceptor	3.13	-1.0	
6c-PTP1B	-15.8	1.99	O	N	His25	H-acceptor	3.03	-2.0	Asp46, Ile219, Val49, Met258, Gly259, Asp29, Ala27, Arg254, Ser28
			O	N	Arg24	H-acceptor	2.96	-3.7	
			O	N	Gln62	H-acceptor	3.49	-0.7	
			C	5-ring	His25	H-π	4.30	-0.7	
6d-PTP1B	-10.7	1.70	O	O	Gln262	H-donor	3.08	-0.9	Asp29, Met258, Asp48, Phe182, Tyr20
			O	N	Arg24	H-acceptor	2.87	-1.8	
			O	N	Gln262	H-acceptor	3.07	-1.6	
6e-PTP1B	-12.2	1.54	C	O	Ser80	H-donor	3.29	-0.8	Val211, Gly209, Pro206, His208, Pro206, Leu204, Glu75, Lys73, Arg79, Ser203, Ser205
			O	N	Gln78	H-acceptor	2.83	-0.8	
			6-ring	C	Glu76	π-H	3.85	-1.2	
DS: Docking score energy (kcal.mol^{-1}); **RMSD**: Root-mean-square deviation (Å); **L**: Ligand; **P**: Protein; **T**: Type; **D**: Distance (Å); **E**: Energy (kcal.mol^{-1})									

3. DOSE RESPONSE CURVE OF THE MOST POTENT COMPOUNDS

3.1. Dose response curve of compound 5

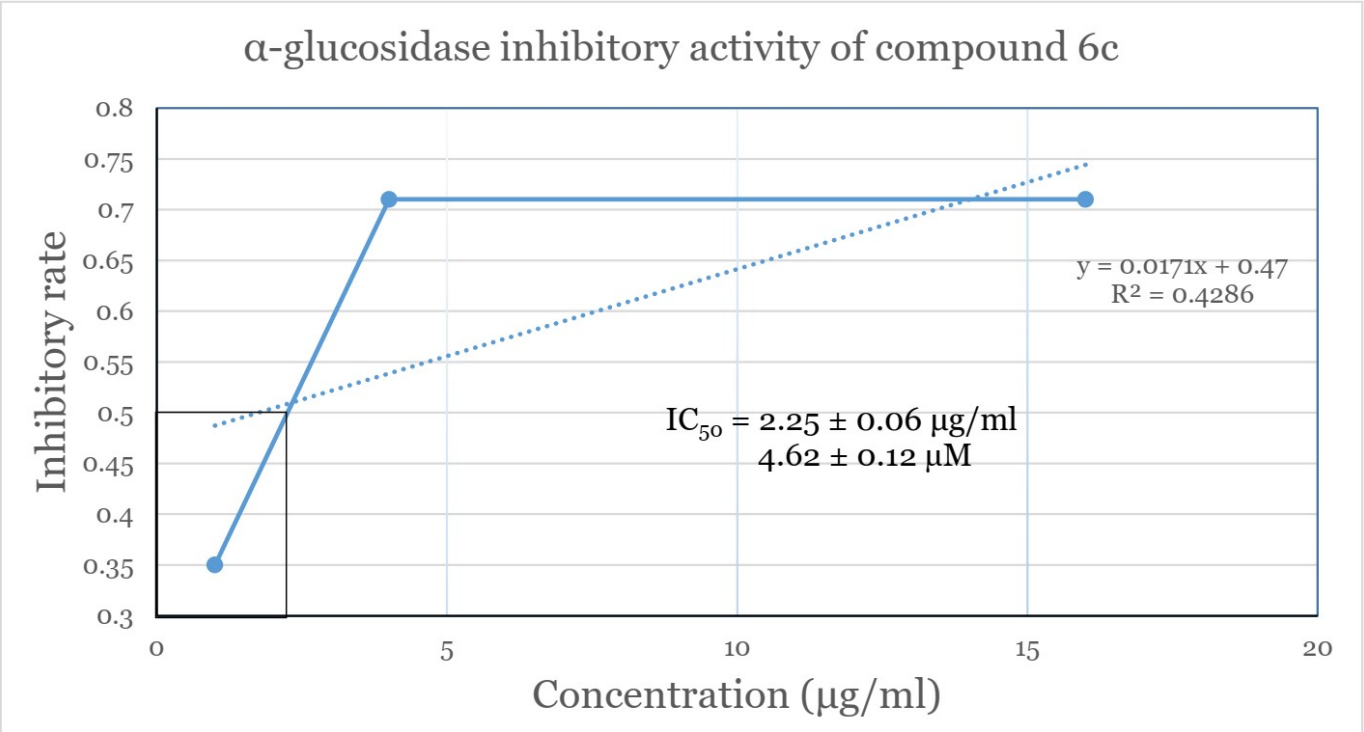
Compound 5	Concentration (µg/ml)	128	32	8	2	0.5	0.125	0.03
	Inhibitory rate (0-1)	1	0.99	0.98	0.62	0.41	0.15	0.07



Dose response curve of compound **5**.

3.2. Dose response curve of compound 6c

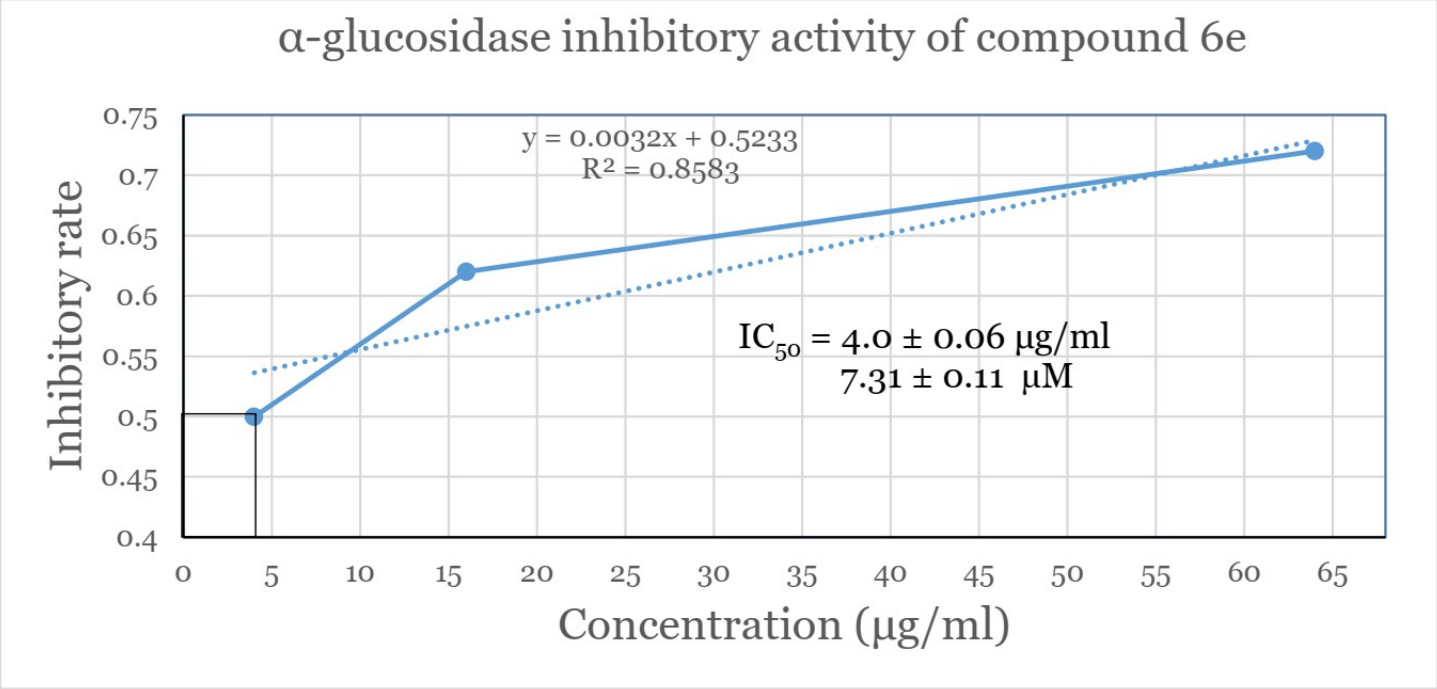
Compound 6c	Concentration (µg/ml)	256	64	16	4	1
	Inhibitory rate (0-1)	0.77	0.75	0.71	0.71	0.35



Dose response curve of compound **6c**.

3.3. Dose response curve of compound 6e

Compound 6e	Concentration (µg/ml)	256	64	16	4
	Inhibitory rate (0-1)	0.93	0.72	0.62	0.5



Dose response curve of compound **6e**.