Supporting information

Synthesis and Biological Evaluation of Heterocyclic Ring-substituted Betulinic Acid Derivatives as Novel Inhibitors of Osteoclast Differentiation and Bone Resorption

Jun Xu[ξ†], Zhenxi Li[ξ¶], Jian Luo[ξ¶], Fan Yang[†], Ting Liu[†], Mingyao Liu*[¶], Wen-Wei Qiu*[‡] and Jie Tang*[†]

[†]Shanghai Engineering Research Center for Molecular Theraputics and NewDrug Development, East China Normal University, Shanghai 200062, China.

[‡]Institute of Medicinal Chemistry and Department of Chemistry, East China Normal University, Shanghai 200062, China.

[¶] Shanghai Key laboratory of Regulatory Biology, Institute of Biomedical Sciences and School of Life Sciences, East China Normal University, Shanghai 200241, China.

Contents

1. HPLC Analysis of BA analogues **S2**

2. The effect of BA on osteoclast differentiation **S3**

3. Compound 20 inhibits the expression of osteoclast mark genes in a dose-dependent manner **S3**

4. Copies of Selected ^{1}H and ^{13}C NMR Spectra **S4**

1. HPLC Analysis of BA analogues

Purity of all final analogues for biological testing was confirmed to be > 95% (Table 2) as determined by HPLC analysis. HPLC analysis was conducted according to the following method with the retention time expressed in min at UV detection of 210, 230 and 254 nM. For HPLC method, an Agilent 1200 series HPLC instrument was used, with chromatography performed on a ZORBAX 150x4.6 mm, 5μm C18 column with mobile phase gradient of 0-10% H_2O in MeOH (Table 1), with a follow rate of 1.0 mL/min.

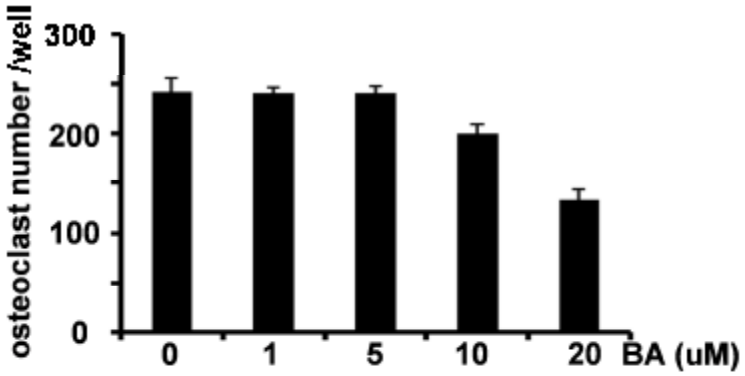
Table 1. HPLC conditions

Time (min)	H_2O (V%)	MeOH (V%)
0	10	90
5	0	100
20	0	100
21	10	90
30	10	90

Table 2. HPLC purity data for BA derivatives

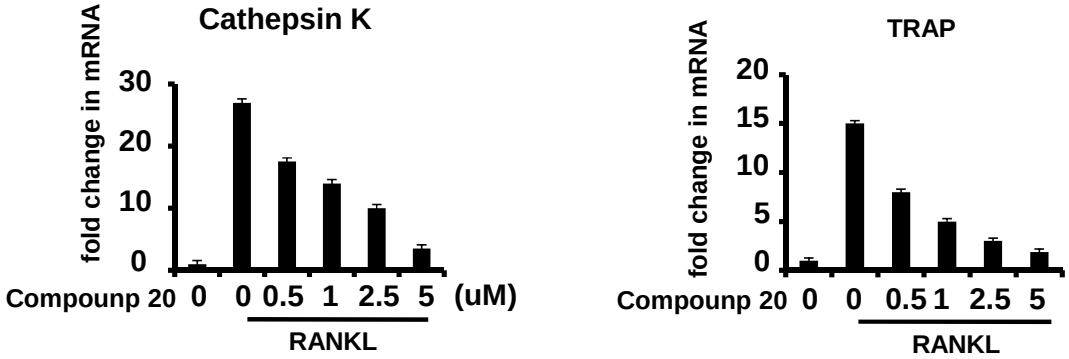
Compound	UV(nm)	RT(min)	Purity(%)	Compound	UV(nm)	RT (min)	Purity(%)
2	254	6.636	96.9	20	230	5.387	98.2
4	254	6.318	95.4	21	230	6.265	97.6
5	210	6.164	97.8	22	230	5.579	98.5
12	254	4.902	96.0	23	230	4.755	98.7
13	230	5.738	96.1	27	230	6.636	95.2
14	230	6.562	95.2	29	230	7.861	96.2
15	230	6.003	95.1	30	230	8.250	97.7
16	230	5.166	96.5	32	230	10.507	97.8
17	230	5.814	96.2	33	230	8.743	95.1
18	254	4.708	96.3	34	230	7.009	96.7
19	230	6.497	96.2	35	230	6.307	98.3

2. The effect of BA on osteoclast differentiation



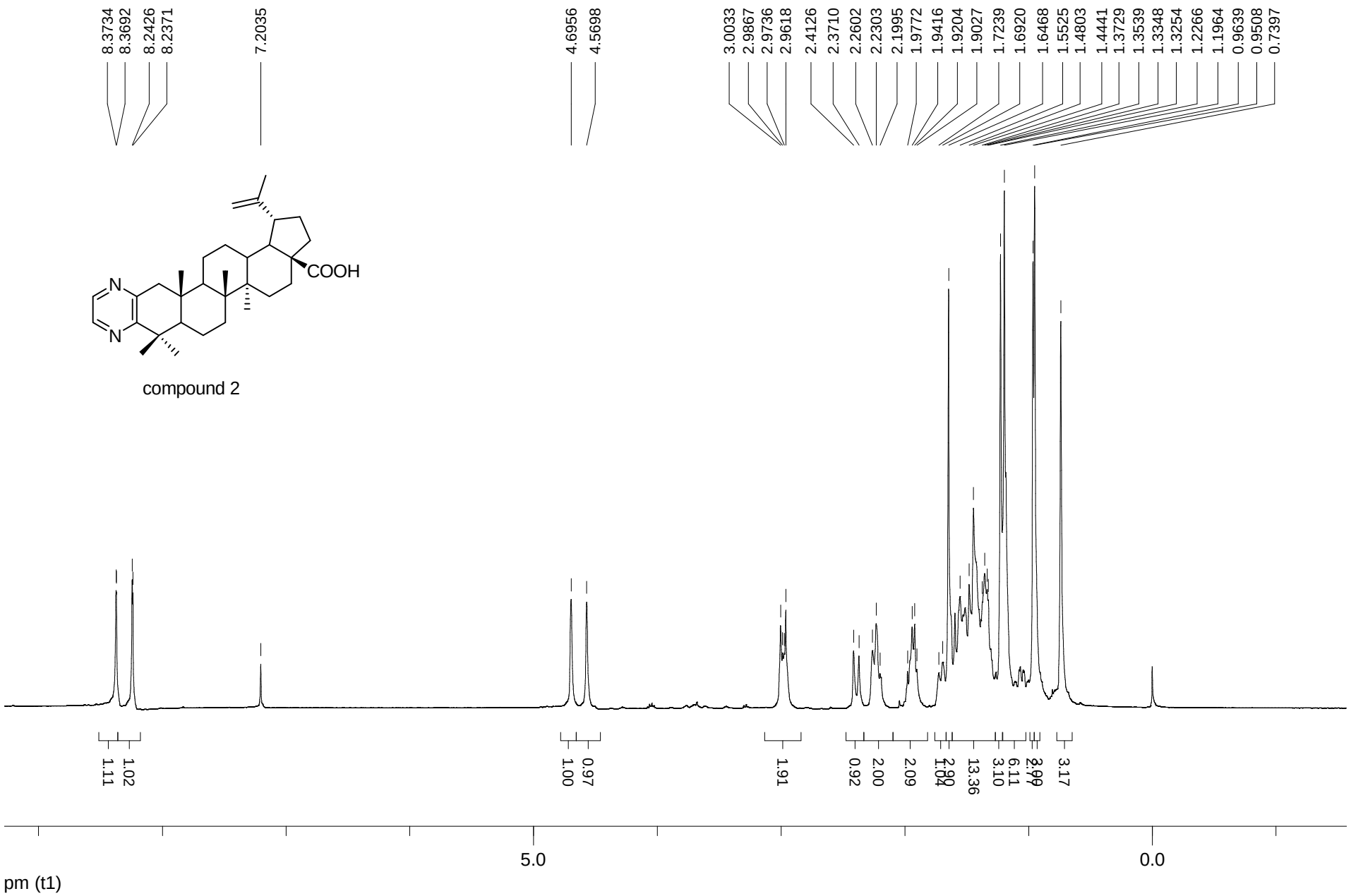
SFigure 1. The effect of BA on osteoclast differentiation. RAW 264.7 cells (3×103 cells/well) were treated with or without RANKL (50 ng/mL), followed by addition of the indicated concentrations of BA for 3-5 days and stained for TRAP expression. TRAP positive multinucleated (>3 nuclei) osteoclasts were counted. Column, means of three experiments carried out in triplicates. SD, bar.

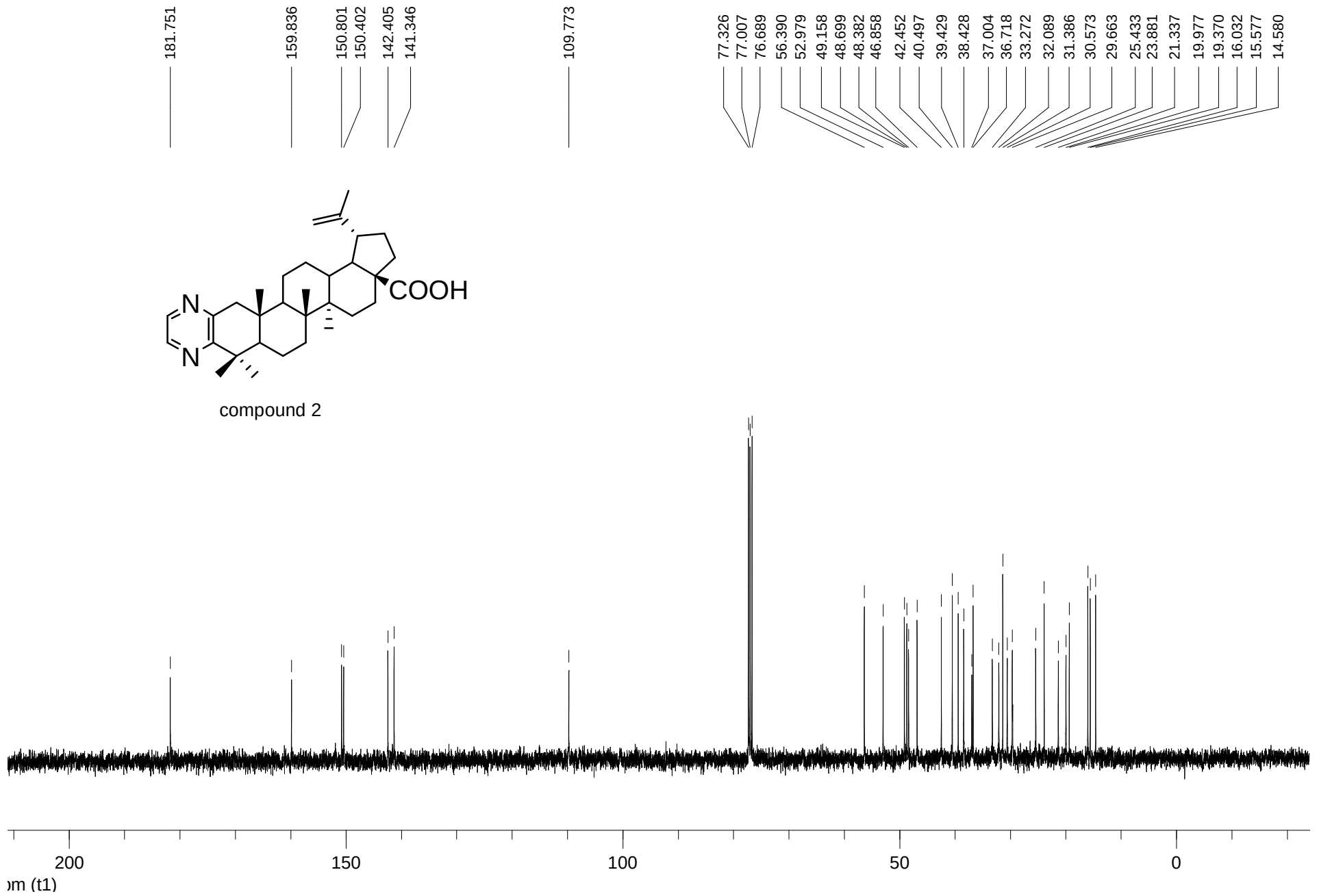
3. Compound 20 inhibits the expression of osteoclast mark genes in a dose-dependent manner



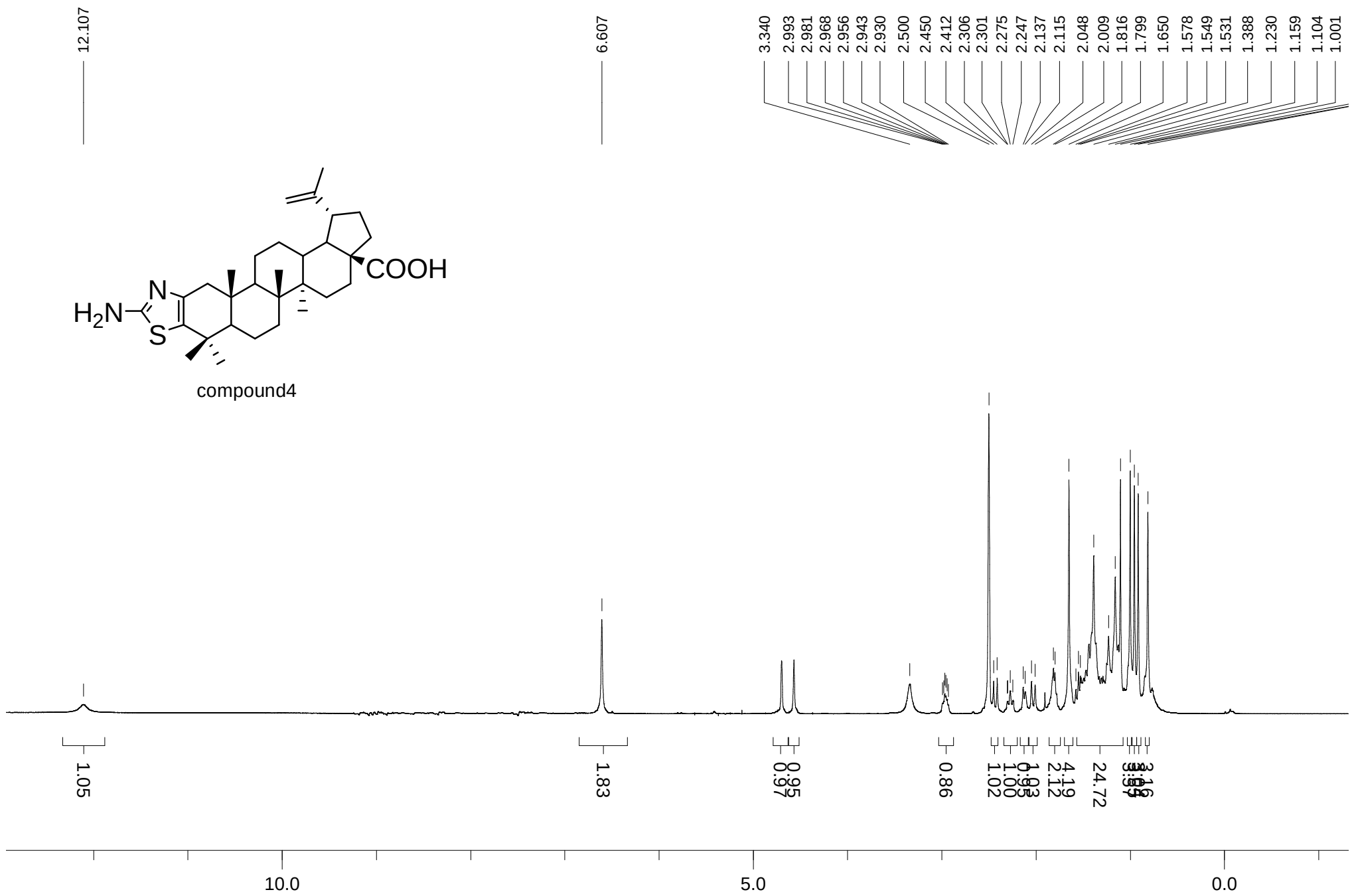
SFigure 2. Compound 20 inhibits the expression of osteoclast mark genes in a dose-dependent manner. RAW264.7 cells were pretreated with indicated concentration of 20 for 6 hours, followed by stimulation of RANKL (50ng/mL) for 3 days. Total RNA was isolated and subjected to quantitative real-time PCR for the expression levels of TRAP and cathepsin K.

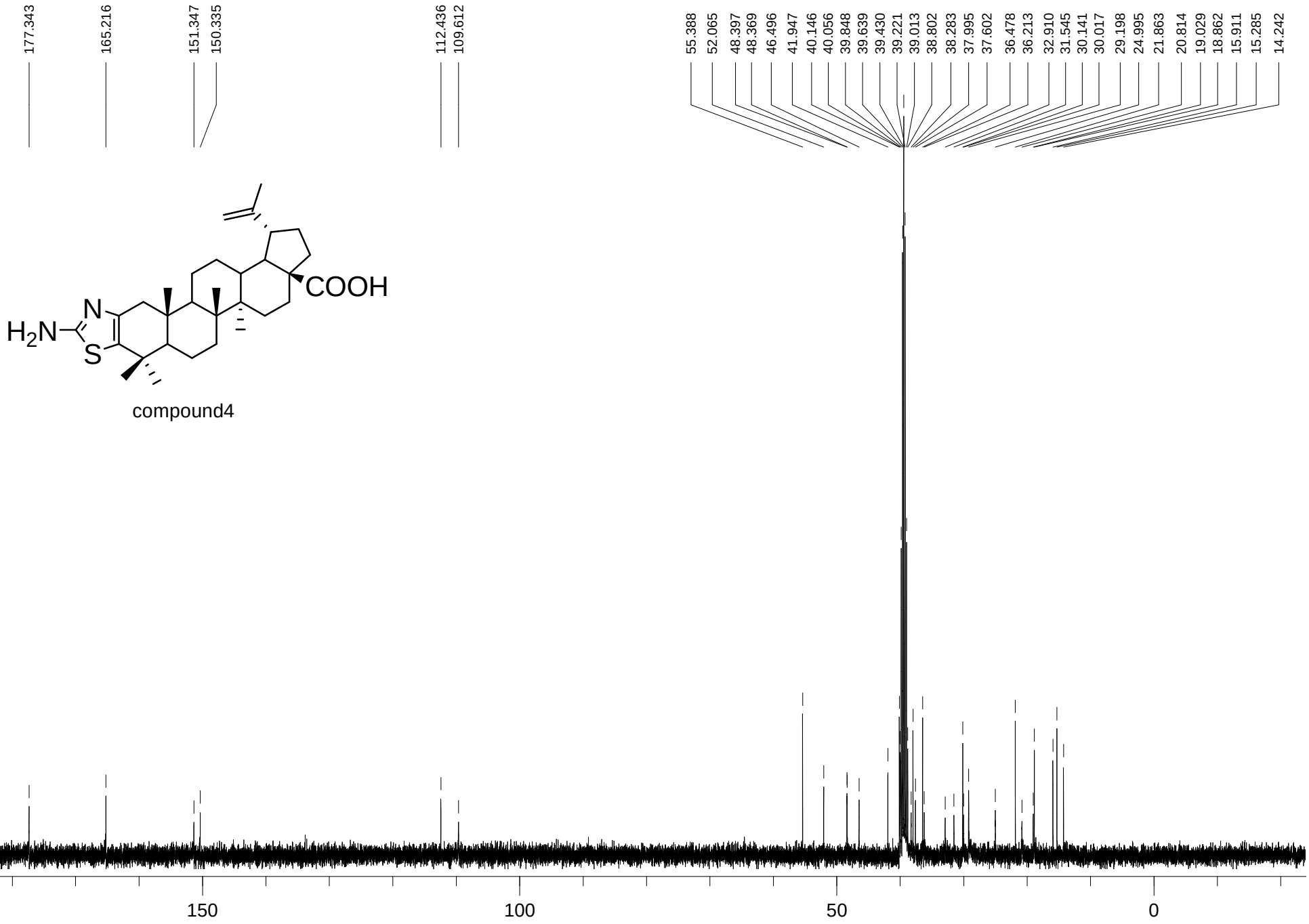
4. Copies of Selected ^{1}H and ^{13}C NMR Spectra


8.3734
8.3692
8.2426
8.2371
7.2035
4.6956
4.5698
3.0033
2.9867
2.9736
2.9618
2.4126
2.3710
2.2602
2.2303
2.1995
1.9772
1.9416
1.9204
1.9027
1.7239
1.6920
1.6468
1.5525
1.4803
1.4441
1.3729
1.3539
1.3348
1.3254
1.2266
1.1964
0.9639
0.9508
0.7397
COOH
N
N
compound 2
1.11
1.02
1.00
0.97
1.91
0.92
2.00
2.09
13.36
3.10
6.11
3.17
5.0
0.0
pm (t1)

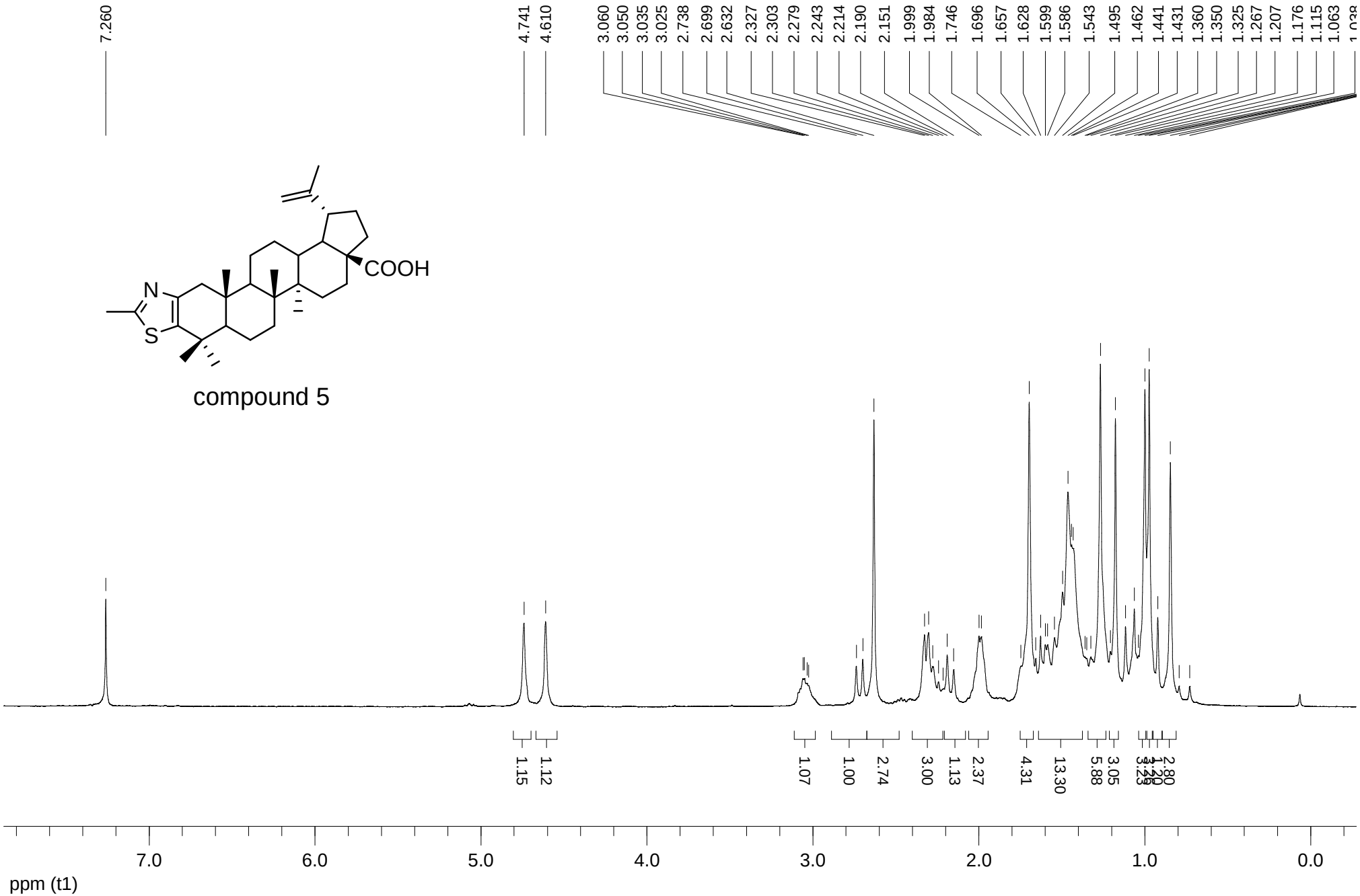

181.751
159.836
150.801
150.402
142.405
141.346
109.773
77.326
77.007
76.689
56.390
52.979
49.158
48.699
48.382
46.858
42.452
40.497
39.429
38.428
37.004
36.718
33.272
32.089
31.386
30.573
29.663
25.433
23.881
21.337
19.977
19.370
16.032
15.577
14.580
COOH
N
N
200
150
100
50
0
m (t1)

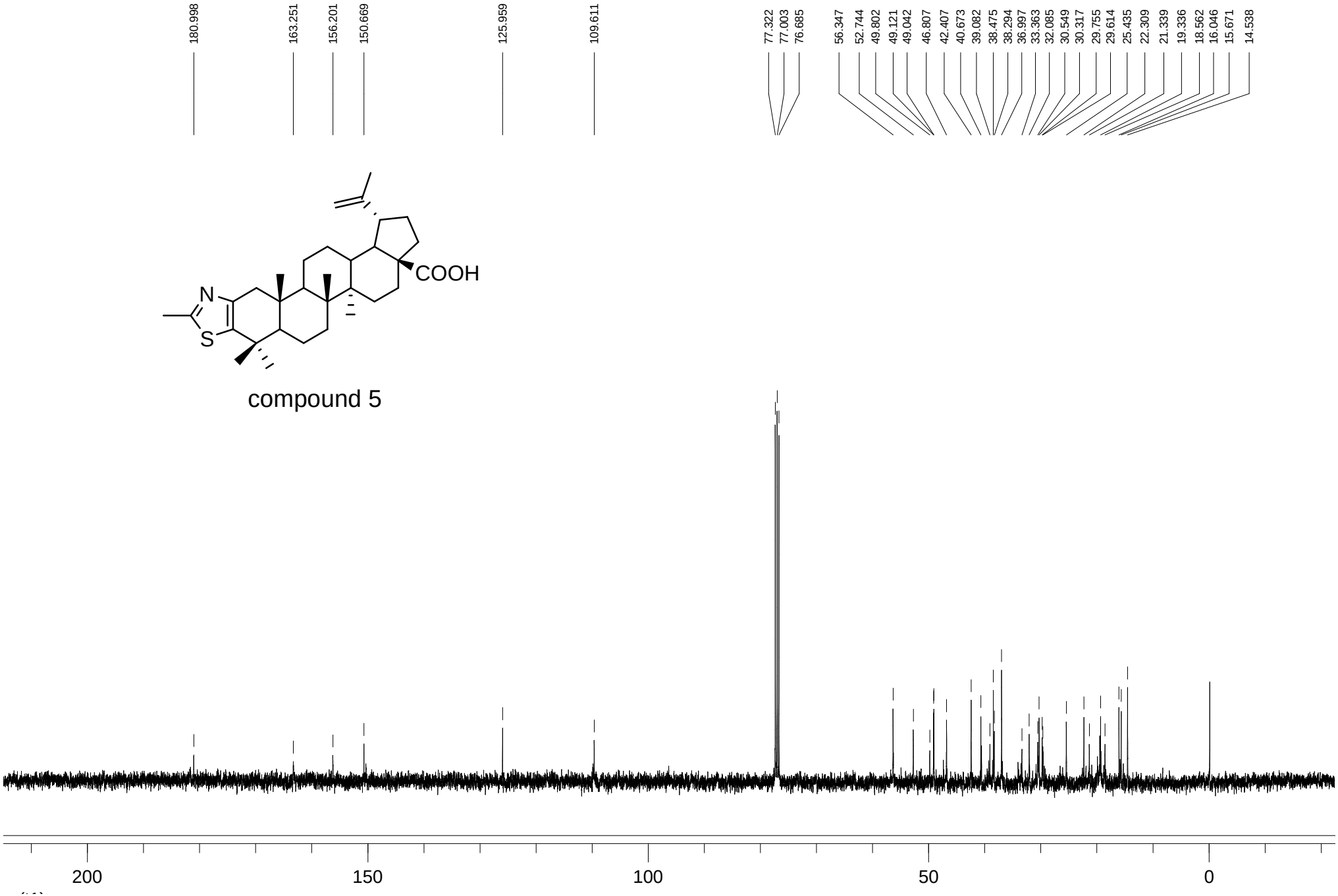
compound 2


12.107
6.607
3.340
2.993
2.981
2.968
2.956
2.943
2.930
2.500
2.450
2.412
2.306
2.301
2.275
2.247
2.137
2.115
2.048
2.009
1.816
1.799
1.650
1.578
1.549
1.531
1.388
1.230
1.159
1.104
1.001
COOH
N
H_2N
S
compound4
1.05
1.83
0.97
0.95
0.86
1.02
1.00
2.12
4.19
24.72
10.0
5.0
0.0

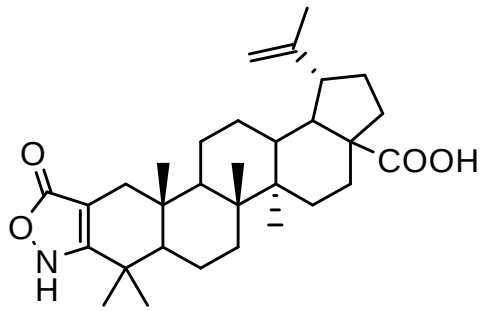

177.343
165.216
151.347
150.335
112.436
109.612
55.388
52.065
48.397
48.369
46.496
41.947
40.146
40.056
39.848
39.639
39.430
39.221
39.013
38.802
38.283
37.995
37.602
36.478
36.213
32.910
31.545
30.141
30.017
29.198
24.995
21.863
20.814
19.029
18.862
15.911
15.285
14.242
COOH
N
H_2N
S
150
100
50
0

compound4


7.260
4.741
4.610
3.060
3.050
3.035
3.025
2.738
2.699
2.632
2.327
2.303
2.279
2.243
2.214
2.190
2.151
1.999
1.984
1.746
1.696
1.657
1.628
1.599
1.586
1.543
1.495
1.462
1.441
1.431
1.360
1.350
1.325
1.267
1.207
1.176
1.115
1.063
COOH
N
S
compound 5
1.15
1.12
1.07
1.00
2.74
3.00
1.13
2.37
4.31
13.30
5.88
3.05
2.80
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

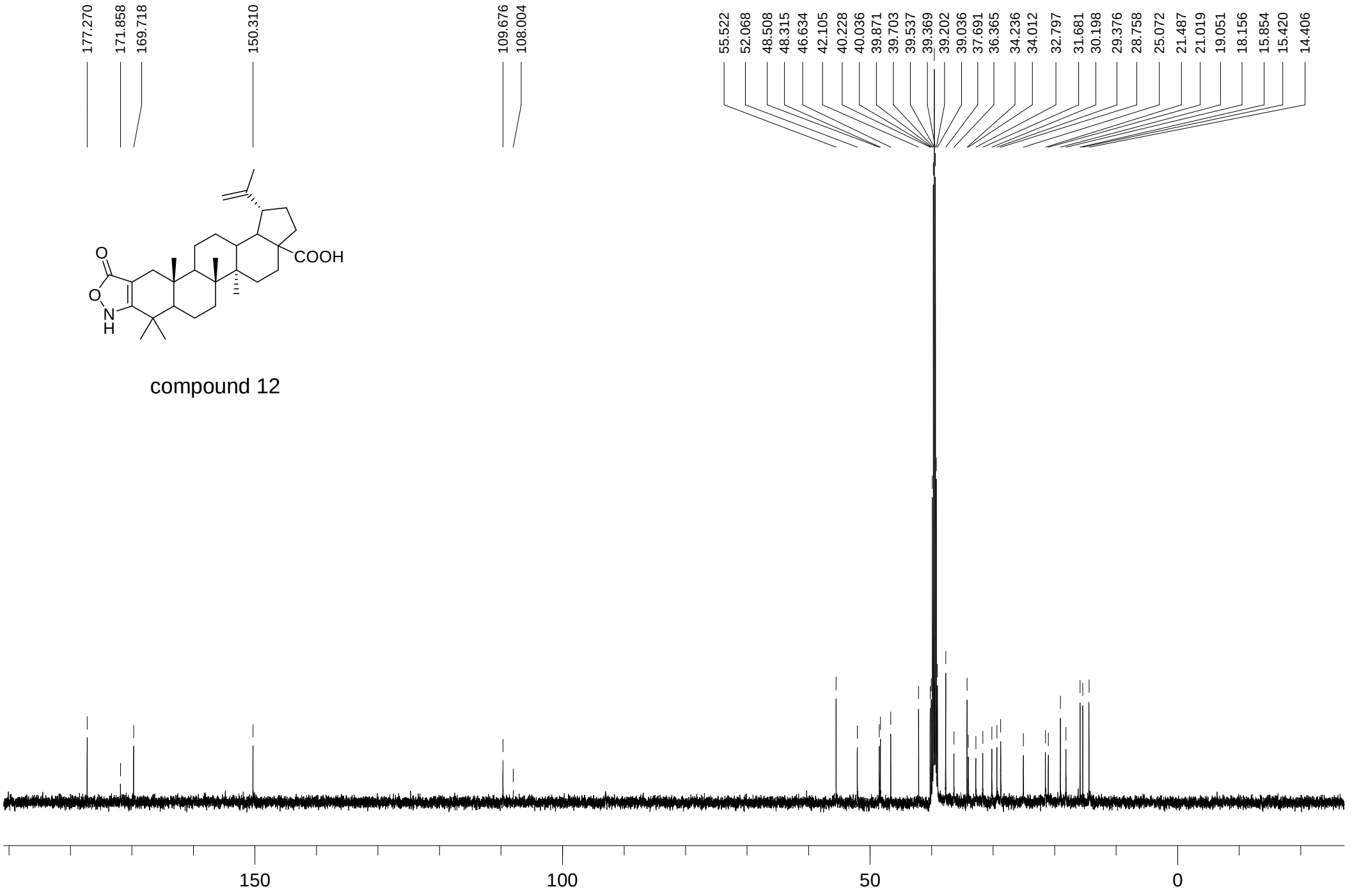

180.998
163.251
156.201
150.669
125.959
109.611
77.322
77.003
76.685
56.347
52.744
49.802
49.121
49.042
46.807
42.407
40.673
39.082
38.475
38.294
36.997
33.363
32.085
30.549
30.317
29.755
29.614
25.435
22.309
21.339
19.336
18.562
16.046
15.671
14.538
COOH
N
S
200
150
100
50
0

compound 5

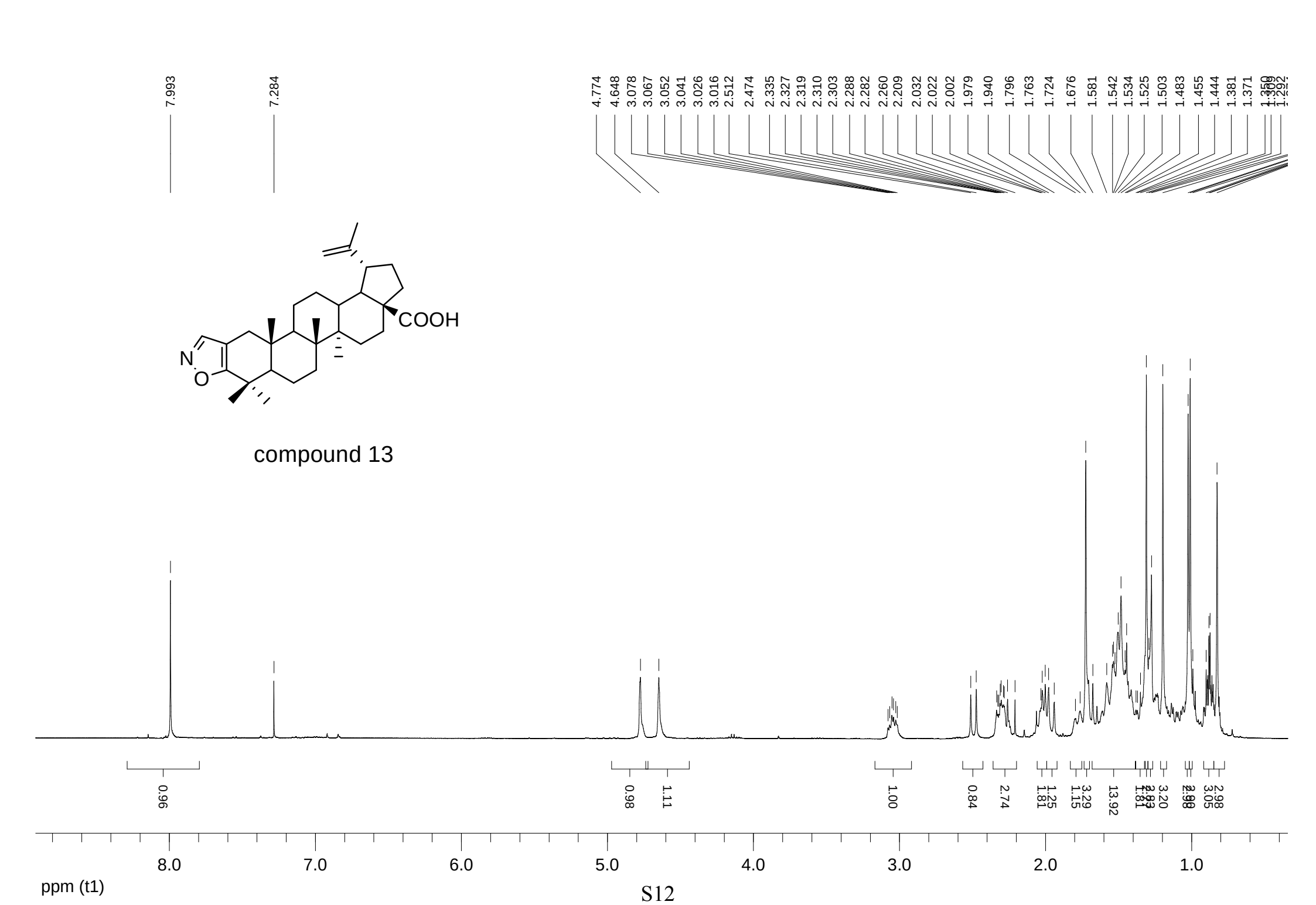

O
O
N
H
COOH

compound 12

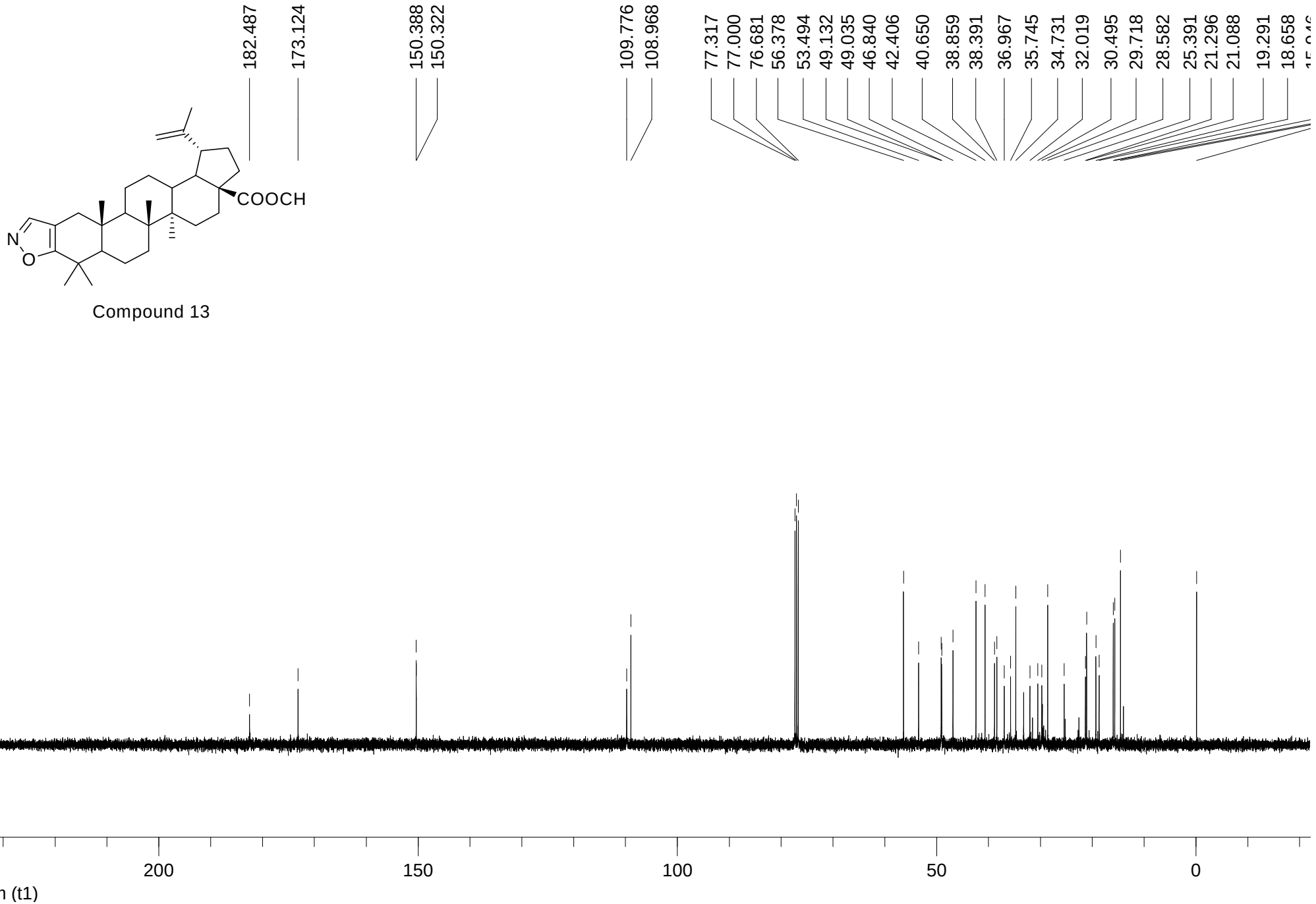
4.705
4.579
3.357
2.982
2.973
2.962
2.953
2.942
2.932
2.501
2.273
2.124
2.104
2.100
2.093
1.985
1.813
1.799
1.658
1.630
1.598
1.556
1.542
1.533
1.489
1.461
1.391
1.312
1.289
1.254
1.231
1.167
1.131
1.063
0.957
0.910
2.14
1.00
0.92
1.06
1.89
3.11
14.81
15.0
10.0
5.0
0.0
ppm (t1)


177.270
171.858
169.718
150.310
109.676
108.004
55.522
52.068
48.508
48.315
46.634
42.105
40.228
40.036
39.871
39.703
39.537
39.369
39.202
39.036
37.691
36.365
34.236
34.012
32.797
31.681
30.198
29.376
28.758
25.072
21.487
21.019
19.051
18.156
15.854
15.420
14.406
O
O
N
H
COOH
150
100
50
0
ppm (t1)

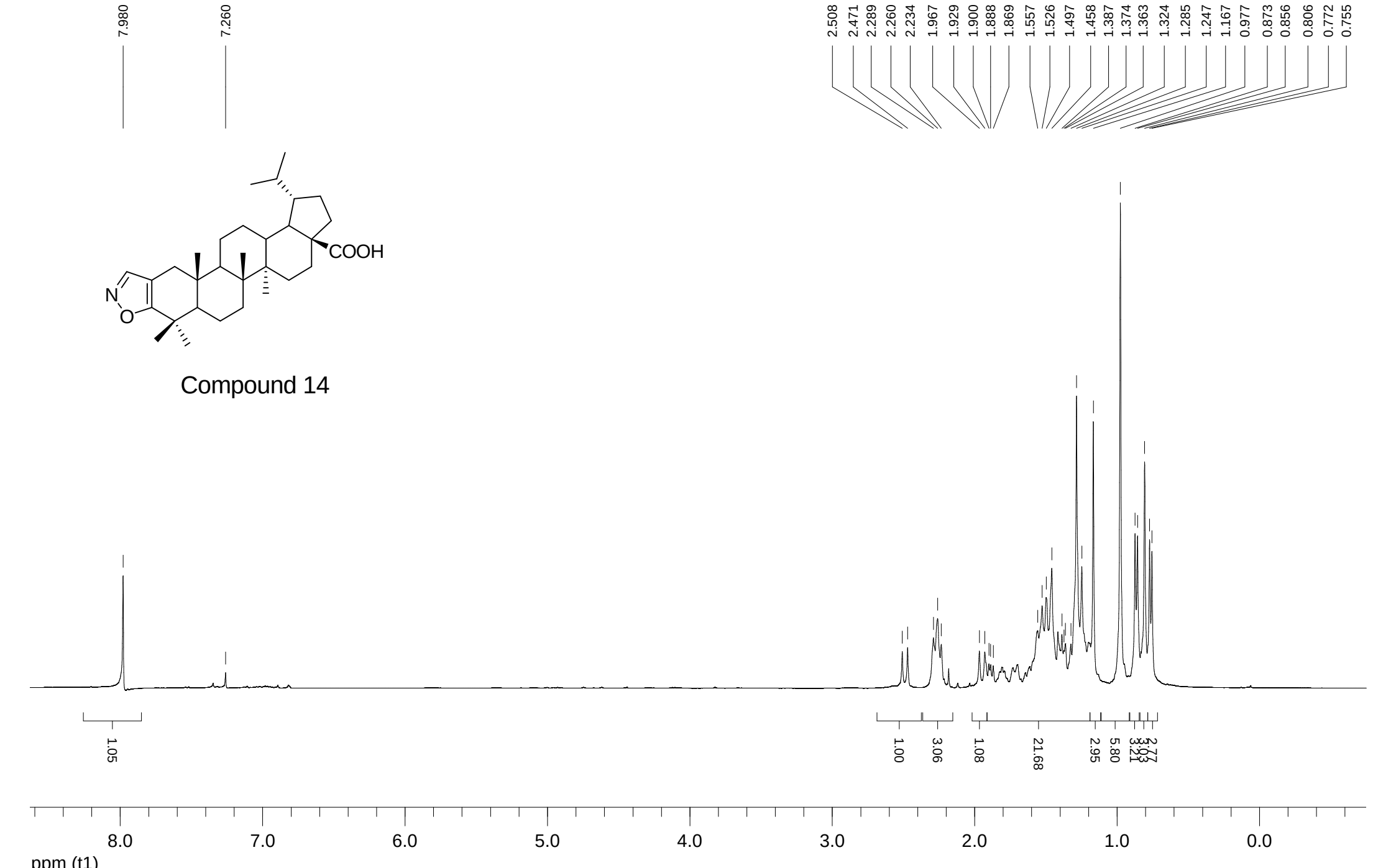
compound 12


7.993
7.284
4.774
4.648
3.078
3.067
3.052
3.041
3.026
3.016
2.512
2.474
2.335
2.327
2.319
2.310
2.303
2.288
2.282
2.260
2.209
2.032
2.022
2.002
1.979
1.940
1.796
1.763
1.724
1.676
1.581
1.542
1.534
1.525
1.503
1.483
1.455
1.444
1.381
1.371
COOH
N
O
0.96
0.98
1.11
1.00
0.84
2.74
1.25
1.81
3.29
1.15
13.92
3.20
2.98
3.05
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

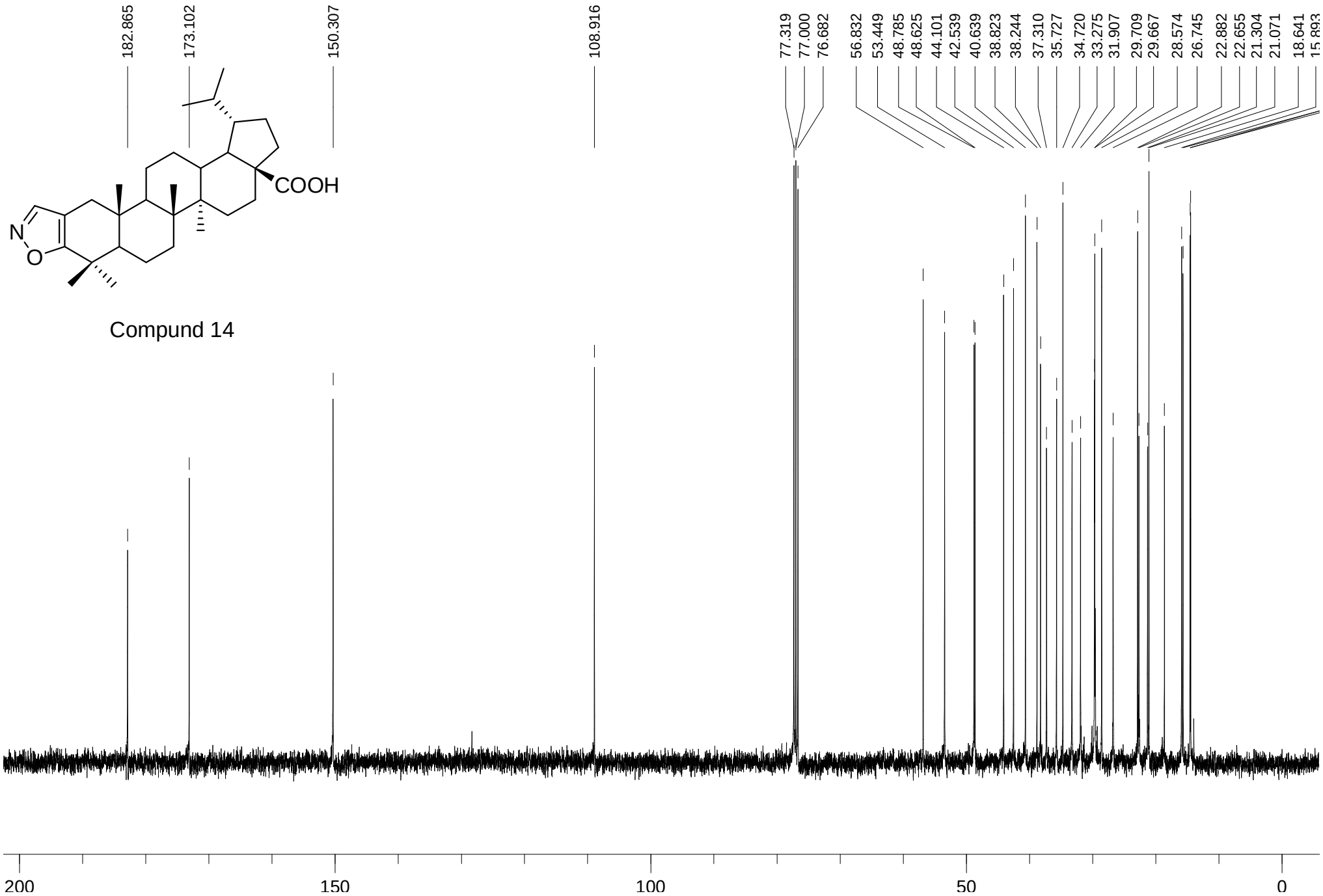
compound 13


182.487
173.124
150.388
150.322
109.776
108.968
77.317
77.000
76.681
56.378
53.494
49.132
49.035
46.840
42.406
40.650
38.859
38.391
36.967
35.745
34.731
32.019
30.495
29.718
28.582
25.391
21.296
21.088
19.291
18.658
COOCH
N
O
200
150
100
50
0
ppm (t1)

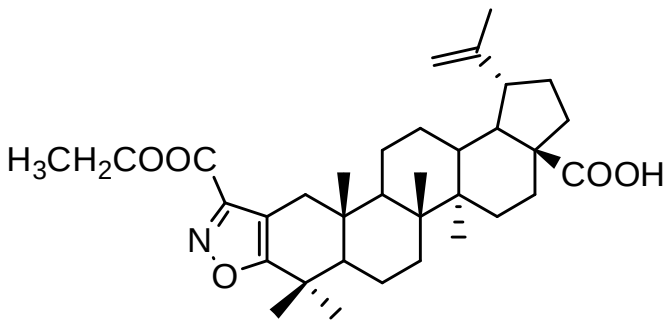
Compound 13


7.980
7.260
2.508
2.471
2.289
2.260
2.234
1.967
1.929
1.900
1.888
1.869
1.557
1.526
1.497
1.458
1.387
1.374
1.363
1.324
1.285
1.247
1.167
0.977
0.873
0.856
0.806
0.772
0.755
COOH
N
O
1.05
1.00
3.06
1.08
21.68
2.95
5.80
3.21
3.03
2.77
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

Compound 14

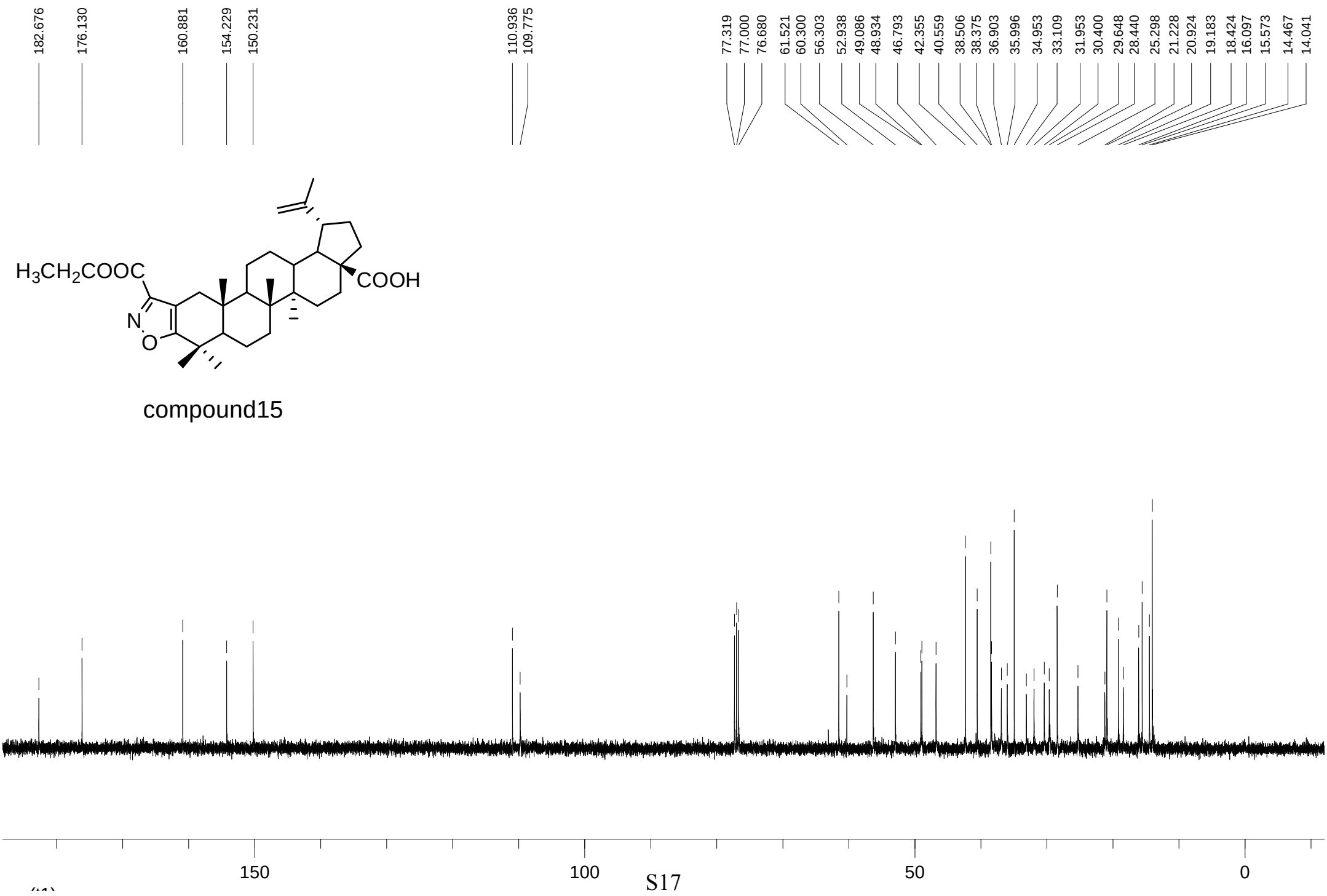

182.865
173.102
150.307
108.916
77.319
77.000
76.682
56.832
53.449
48.785
48.625
44.101
42.539
40.639
38.823
38.244
37.310
35.727
34.720
33.275
31.907
29.709
29.667
28.574
26.745
22.882
22.655
21.304
21.071
18.641
15.893
COOH
N
O
200
150
100
50
0

Compund 14

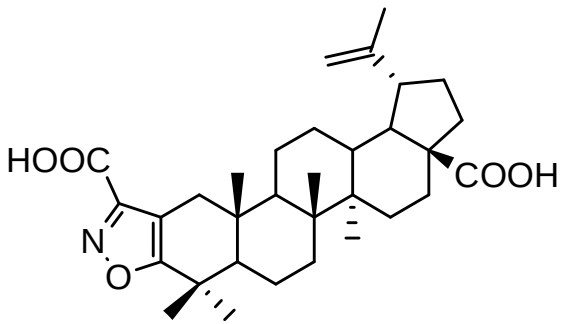

H3CH2COOC
COOH
N
O

compound15

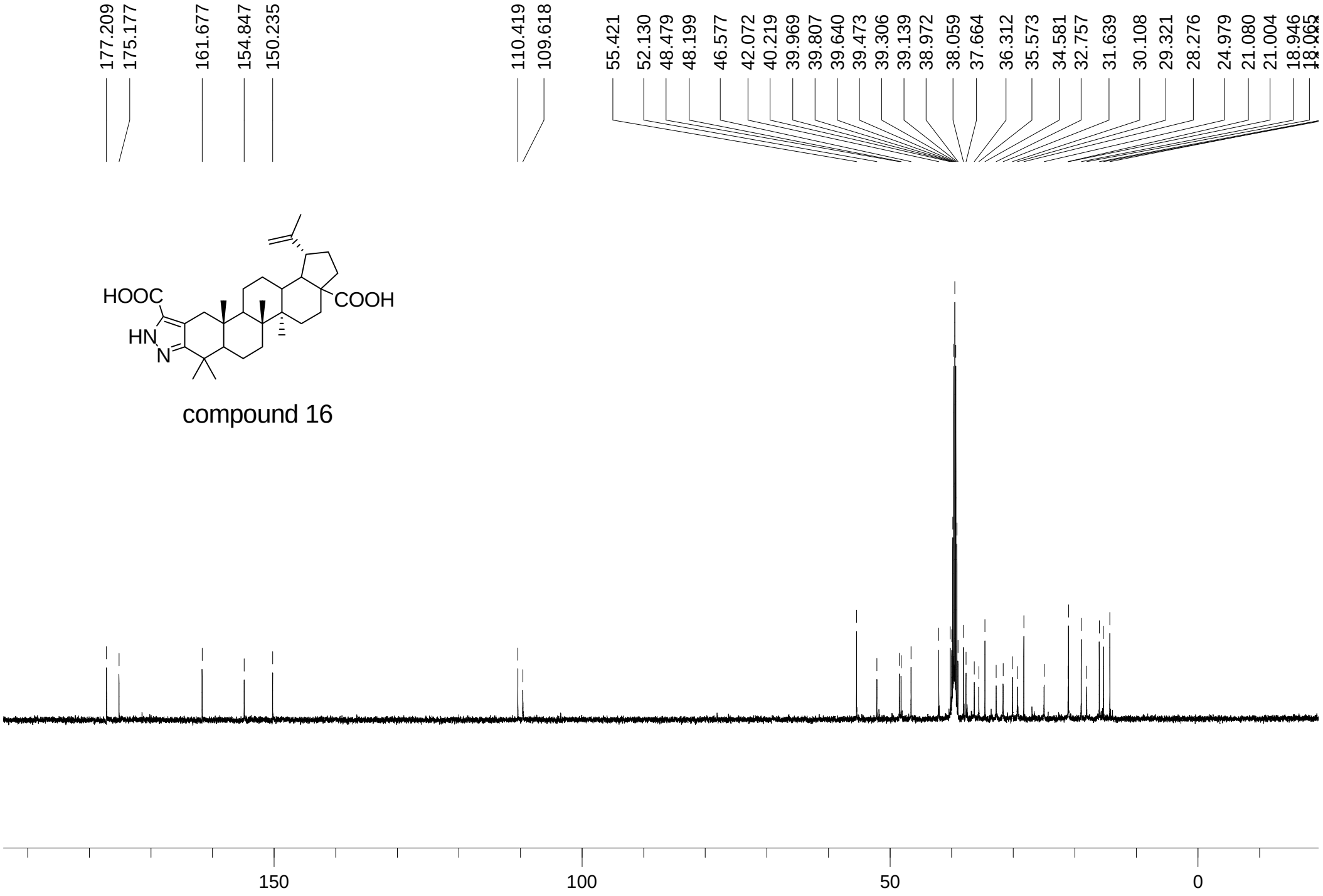
4.715
4.585
4.246
4.232
4.218
4.204
3.366
2.993
2.982
2.974
2.966
2.965
2.954
2.945
2.926
2.908
2.876
2.500
2.316
2.312
2.291
2.264
2.262
2.136
2.117
1.987
1.955
1.817
1.803
1.790
1.690
1.687
1.667
1.591
1.569
1.547
1.499
1.405
1.379
1.353
1.270
1.256
1.242
1.08
1.12
1.91
1.07
0.87
0.90
1.02
1.94
3.78
20.33
3.11
3.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


182.676
176.130
160.881
154.229
150.231
110.936
109.775
77.319
77.000
76.680
61.521
60.300
56.303
52.938
49.086
48.934
46.793
42.355
40.559
38.506
38.375
36.903
35.996
34.953
33.109
31.953
30.400
29.648
28.440
25.298
21.228
20.924
19.183
18.424
16.097
15.573
14.467
14.041
H3CH2COOC
COOH
N
O
150
100
50
0

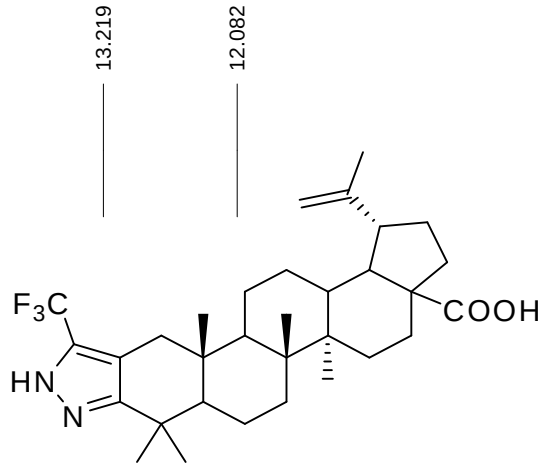
compound15



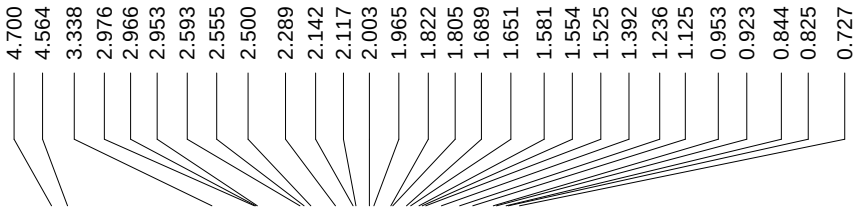
compound16

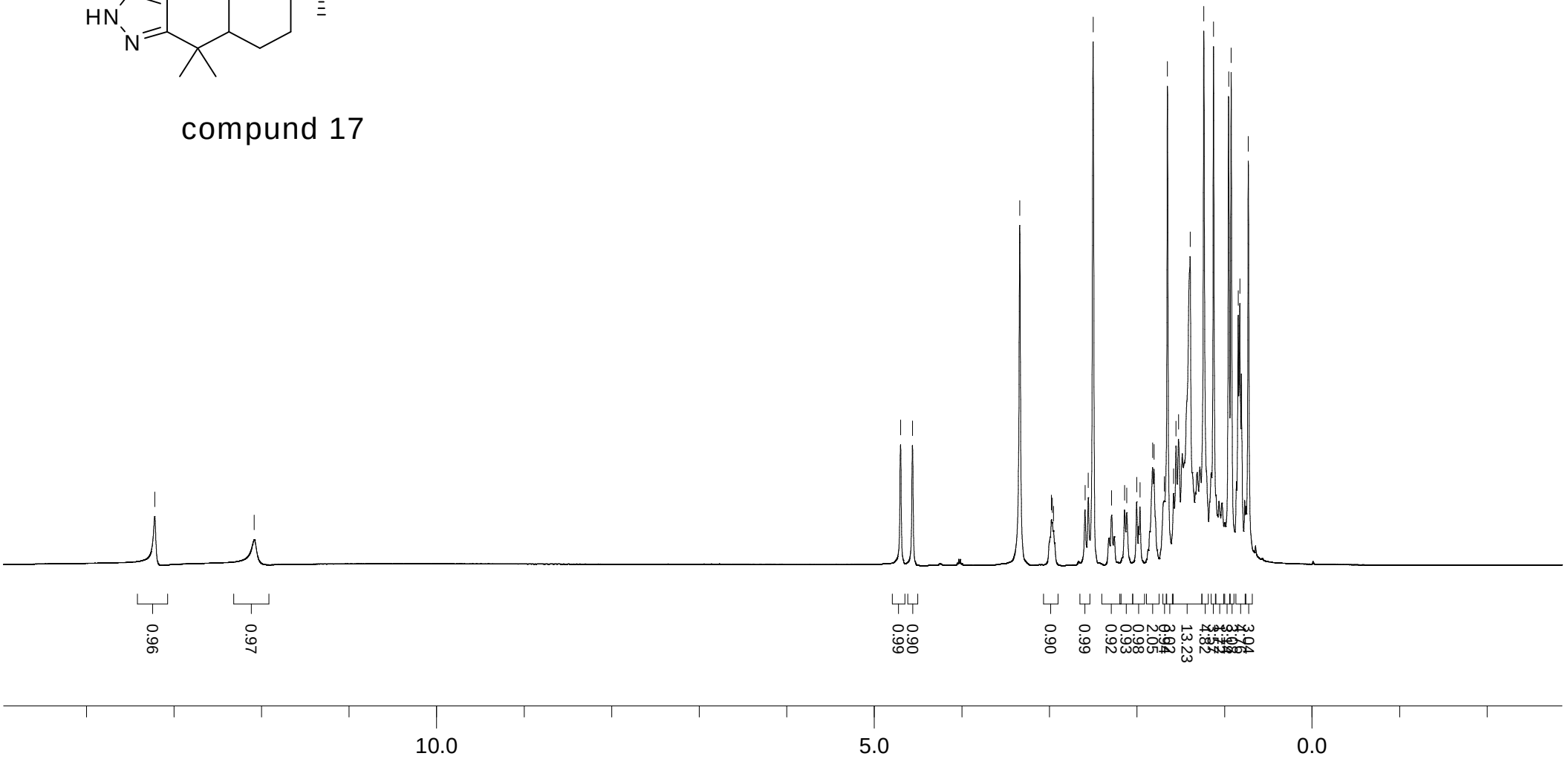

177.209
175.177
161.677
154.847
150.235
110.419
109.618
55.421
52.130
48.479
48.199
46.577
42.072
40.219
39.969
39.807
39.640
39.473
39.306
39.139
38.972
38.059
37.664
36.312
35.573
34.581
32.757
31.639
30.108
29.321
28.276
24.979
21.080
21.004
18.946
HOOC
COOH
HN
N
150
100
50
0
ppm (t1)

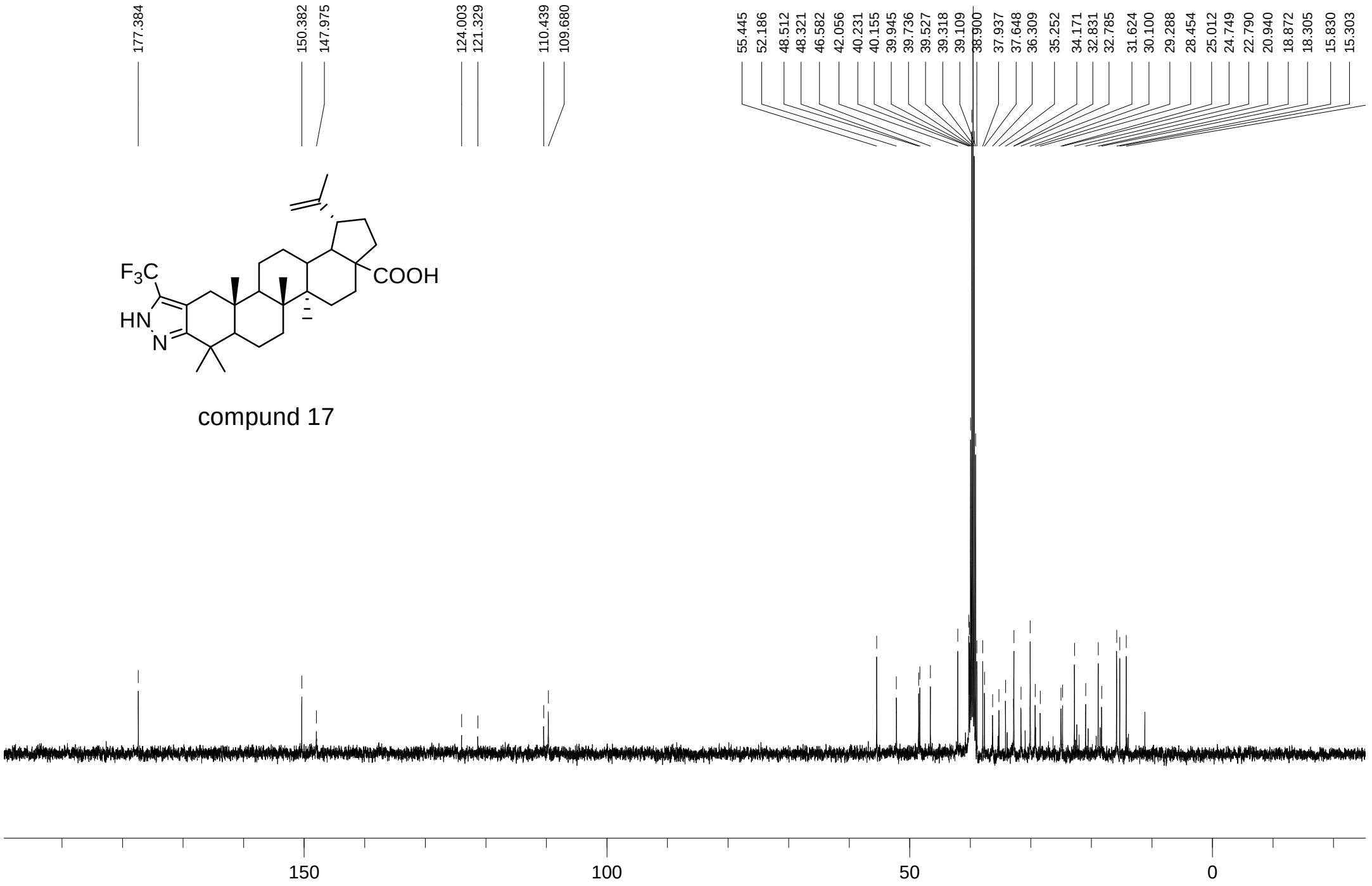
compound 16


13.219
12.082
F3C
HN
N
COOH

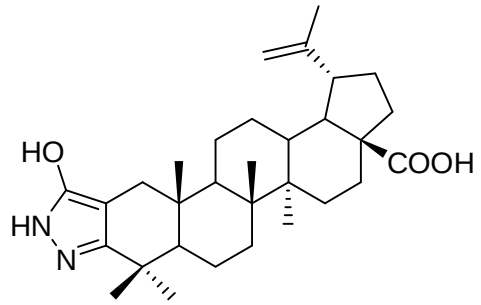
compund 17


4.700
4.564
3.338
2.976
2.966
2.953
2.593
2.555
2.500
2.289
2.142
2.117
2.003
1.965
1.822
1.805
1.689
1.651
1.581
1.554
1.525
1.392
1.236
1.125
0.953
0.923
0.844
0.825
0.727


0.96
0.97
0.99
0.90
0.90
0.99
0.92
0.93
0.98
2.05
13.23
3.04
10.0
5.0
0.0
ppm (t1)

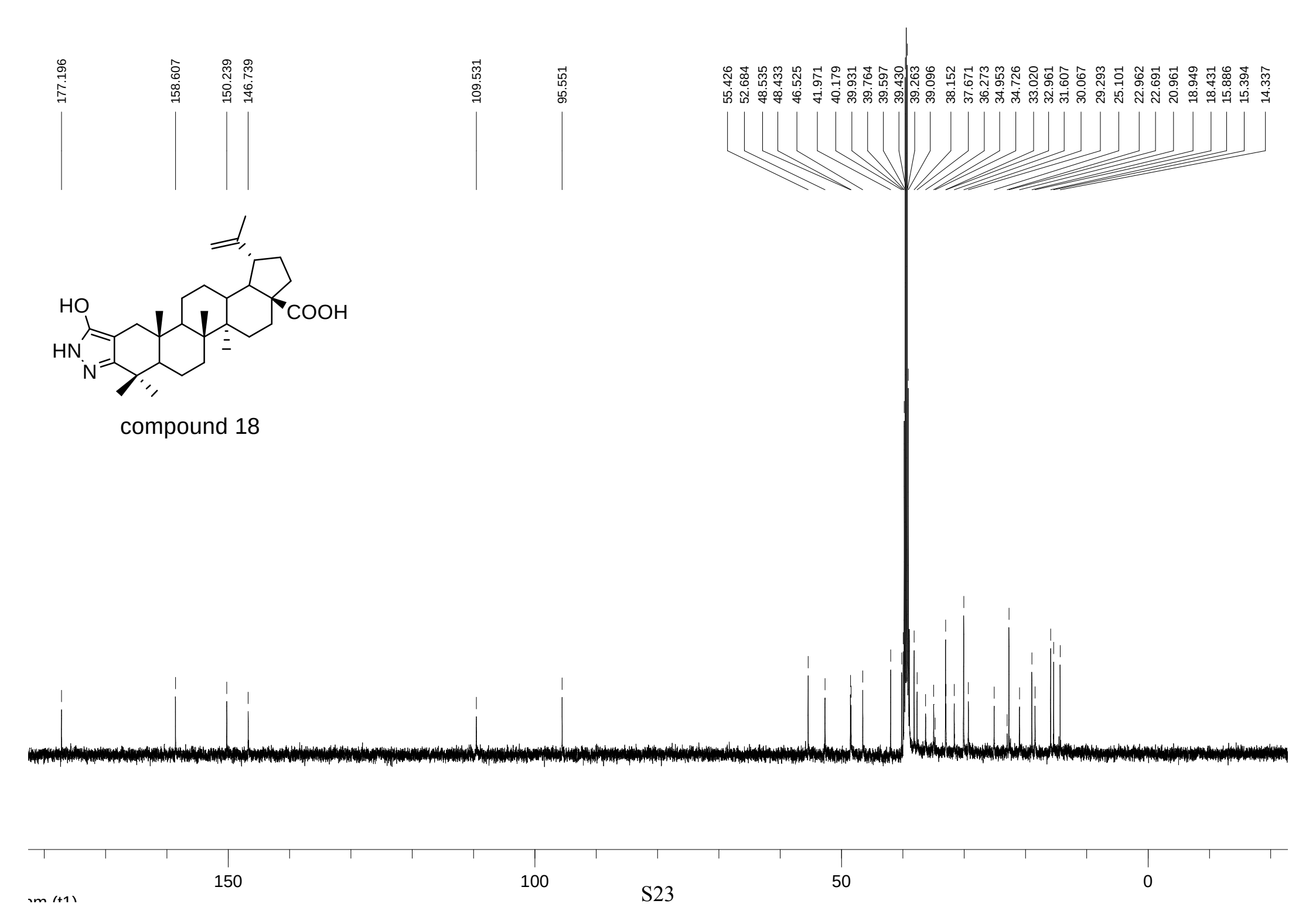

177.384
150.382
147.975
124.003
121.329
110.439
109.680
55.445
52.186
48.512
48.321
46.582
42.056
40.231
40.155
39.945
39.736
39.527
39.318
39.109
38.900
37.937
37.648
36.309
35.252
34.171
32.831
32.785
31.624
30.100
29.288
28.454
25.012
24.749
22.790
20.940
18.872
18.305
15.830
15.303
F3C
HN
N
COOH
150
100
50
0
ppm (t1)

compund 17

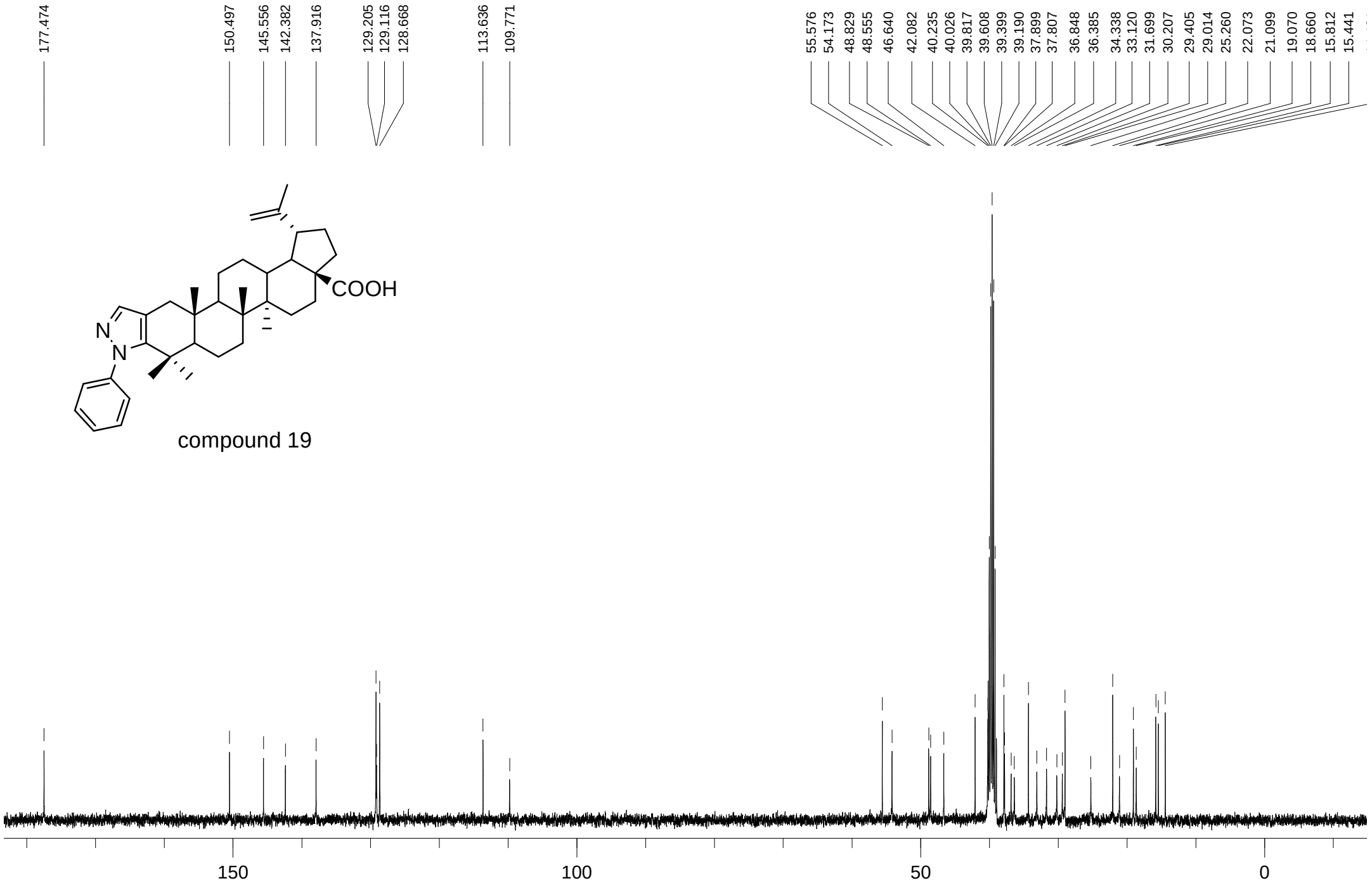

HO
HN
N
COOH

compound 18

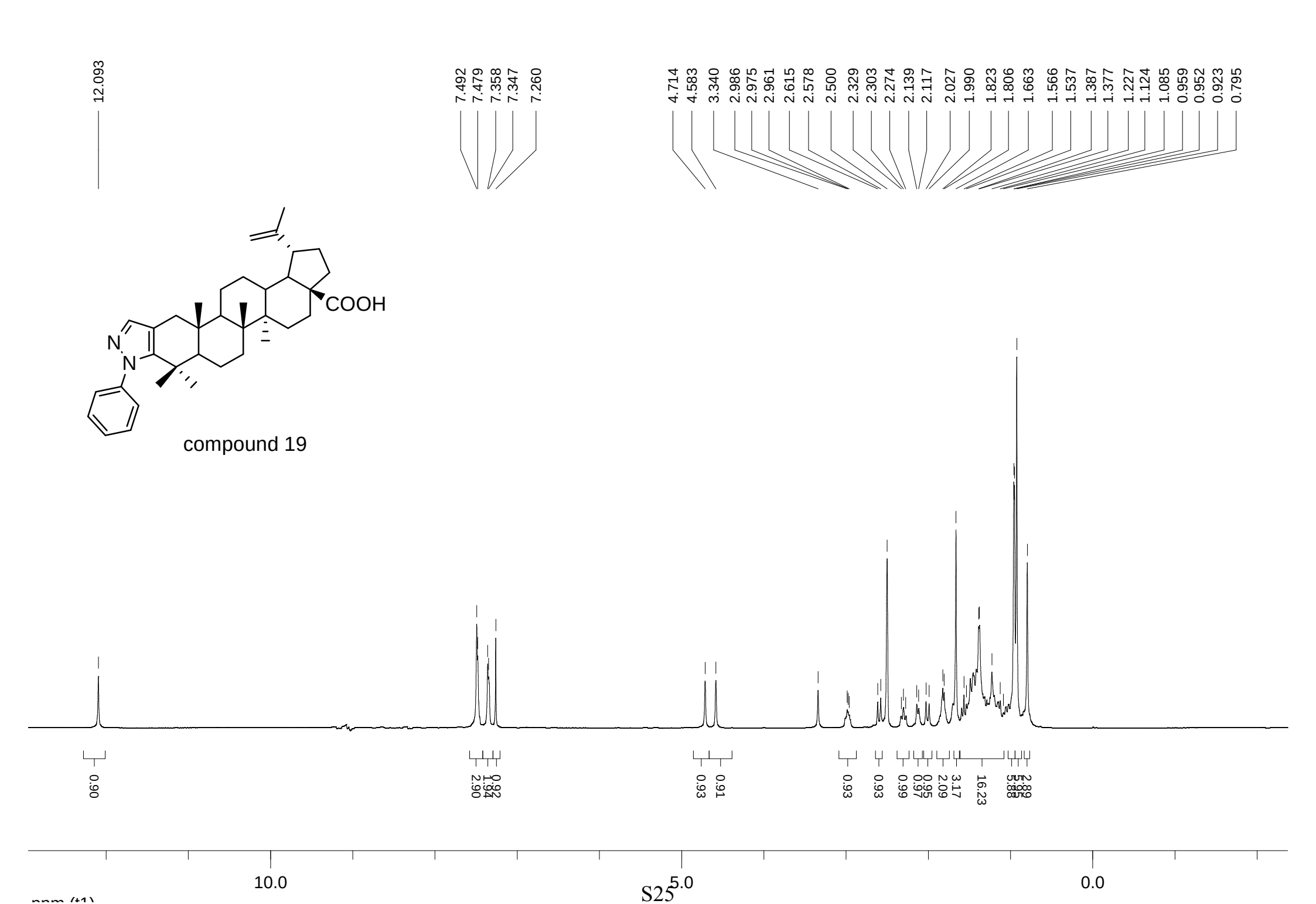
4.705
4.578
3.389
2.990
2.979
2.969
2.960
2.949
2.940
2.939
2.501
2.366
2.343
2.313
2.278
2.258
2.133
2.112
1.814
1.800
1.658
1.439
1.385
1.229
1.148
1.036
0.958
0.939
0.914
0.729
0.717
0.94
0.89
0.91
1.77
0.92
1.79
13.92
6.36
1.16
3.28
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


177.196
158.607
150.239
146.739
109.531
95.551
55.426
52.684
48.535
48.433
46.525
41.971
40.179
39.931
39.764
39.597
39.430
39.263
39.096
38.152
37.671
36.273
34.953
34.726
33.020
32.961
31.607
30.067
29.293
25.101
22.962
22.691
20.961
18.949
18.431
15.886
15.394
14.337
HO
HN
N
COOH
150
100
50
0

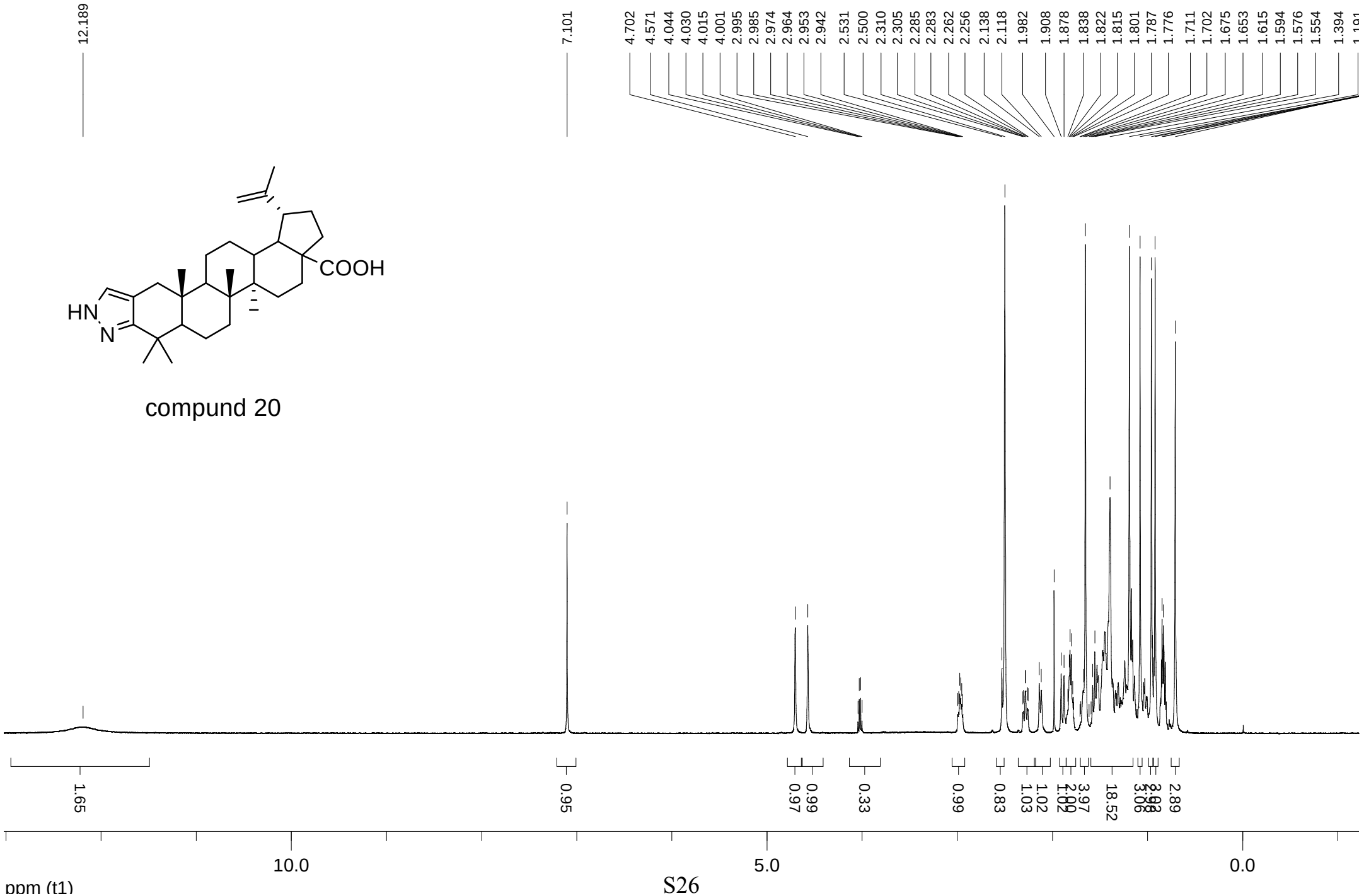
compound 18


177.474
150.497
145.556
142.382
137.916
129.205
129.116
128.668
113.636
109.771
55.576
54.173
48.829
48.555
46.640
42.082
40.235
40.026
39.817
39.608
39.399
39.190
37.899
37.807
36.848
36.385
34.338
33.120
31.699
30.207
29.405
29.014
25.260
22.073
21.099
19.070
18.660
15.812
15.441
COOH
N
N
150
100
50
0
pm (t1)

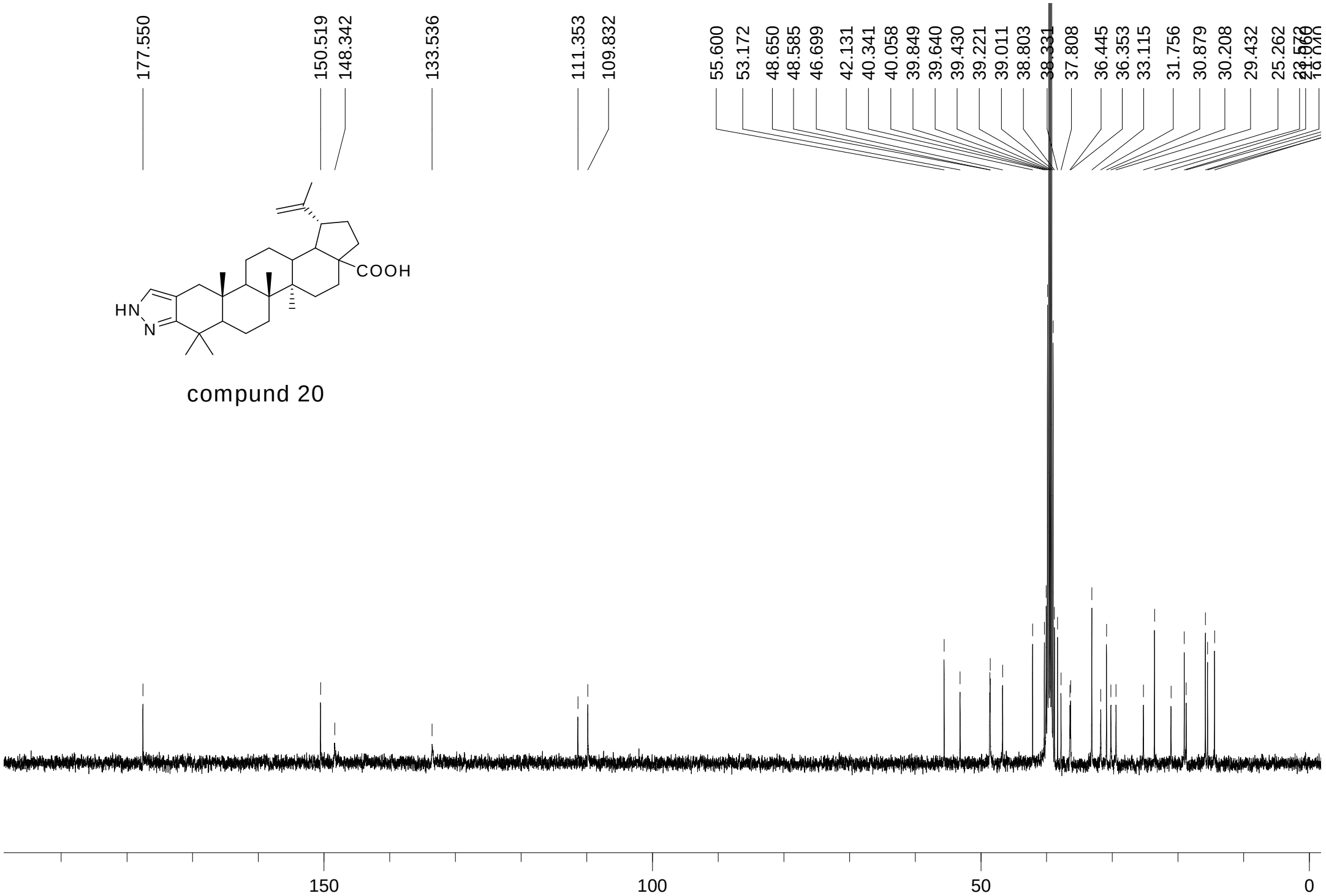
compound 19


12.093
7.492
7.479
7.358
7.347
7.260
4.714
4.583
3.340
2.986
2.975
2.961
2.615
2.578
2.500
2.329
2.303
2.274
2.139
2.117
2.027
1.990
1.823
1.806
1.663
1.566
1.537
1.387
1.377
1.227
1.124
1.085
0.959
0.952
0.923
0.795
COOH
N
N
0.90
2.90
1.94
0.92
0.93
0.91
0.93
0.93
0.99
0.97
0.95
2.09
3.17
16.23
10.0
5.0
0.0

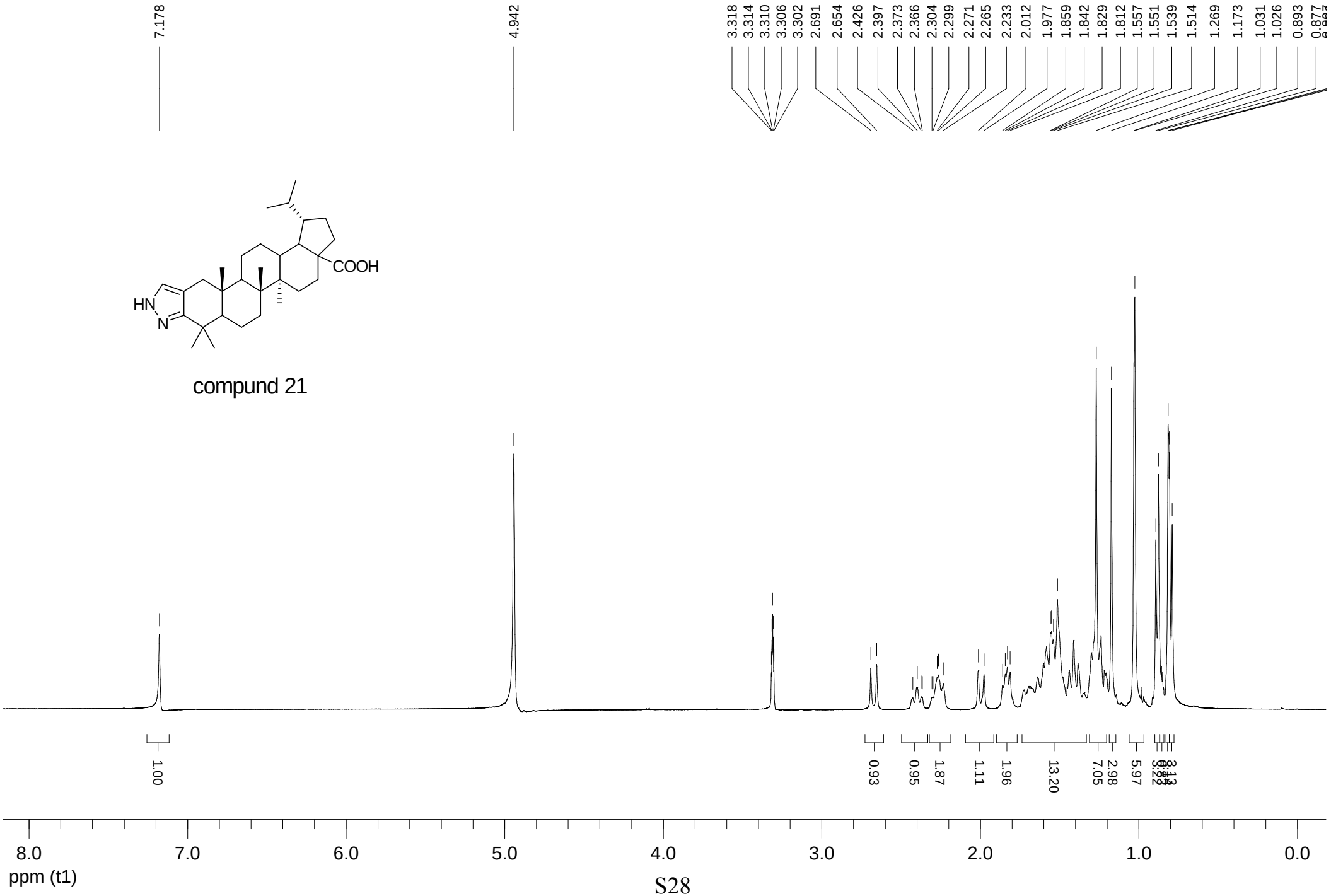
compound 19

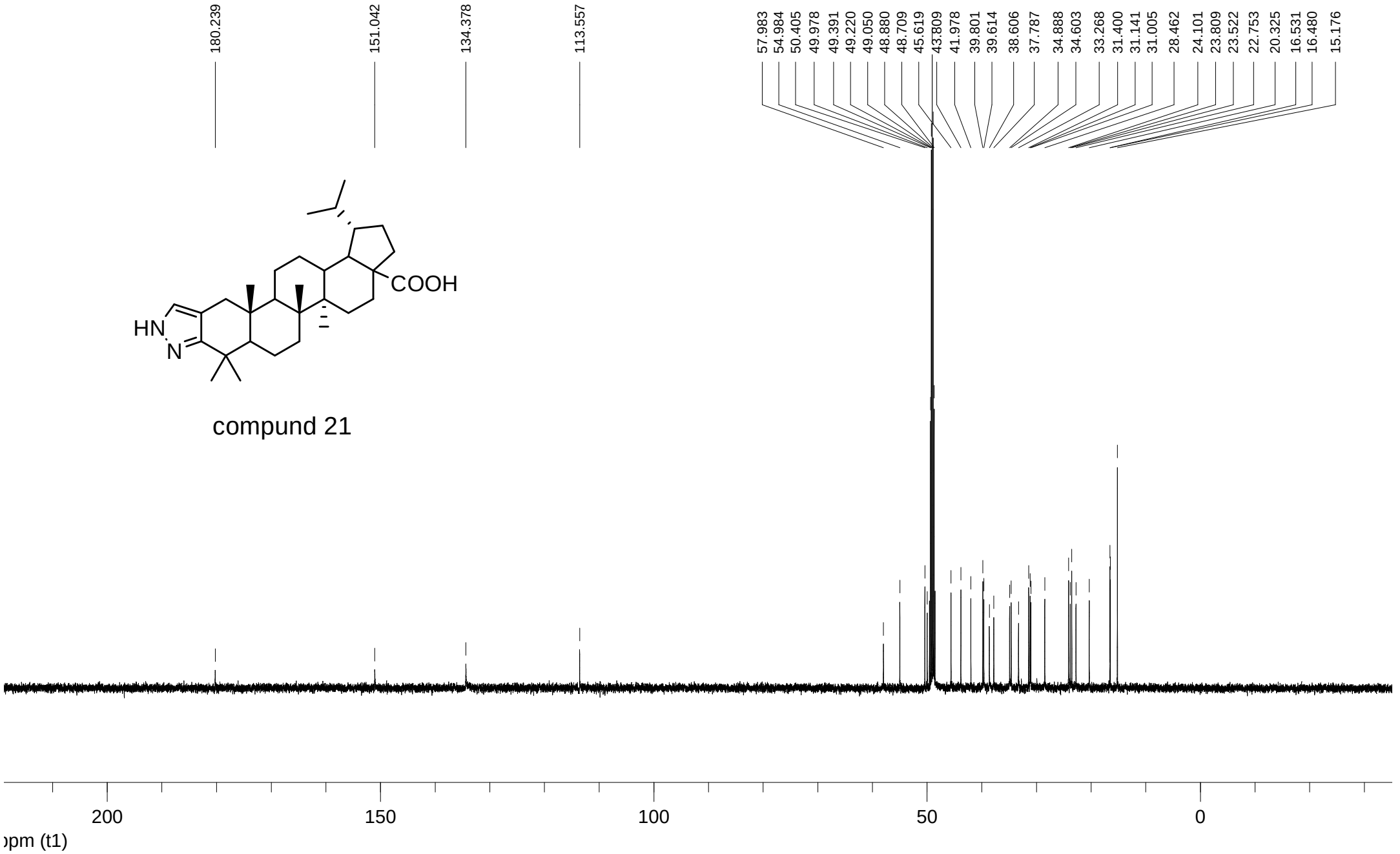

12.189
7.101
4.702
4.571
4.044
4.030
4.015
4.001
2.995
2.985
2.974
2.964
2.953
2.942
2.531
2.500
2.310
2.305
2.285
2.283
2.262
2.256
2.138
2.118
1.982
1.908
1.878
1.838
1.822
1.815
1.801
1.787
1.776
1.711
1.702
1.675
1.653
1.615
1.594
1.576
1.554
1.394
HN
N
COOH
1.65
0.95
0.97
0.99
0.33
0.99
0.83
1.03
1.02
3.97
18.52
2.89
10.0
5.0
0.0
ppm (t1)

compund 20

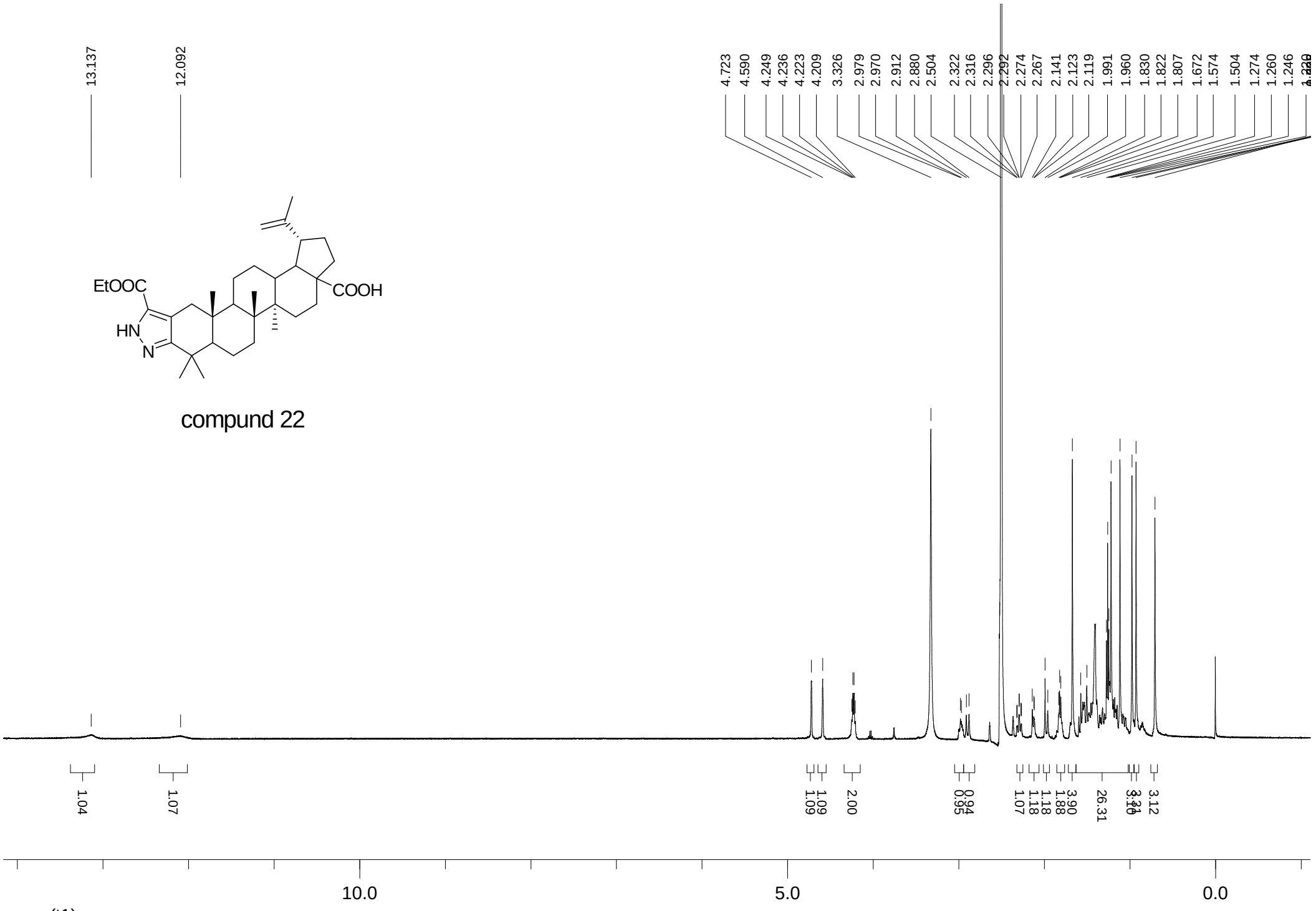

177.550
150.519
148.342
133.536
111.353
109.832
55.600
53.172
48.650
48.585
46.699
42.131
40.341
40.058
39.849
39.640
39.430
39.221
39.011
38.803
38.331
37.808
36.445
36.353
33.115
31.756
30.879
30.208
29.432
25.262
HN
N
COOH
150
100
50
0
pm (t1)

compund 20

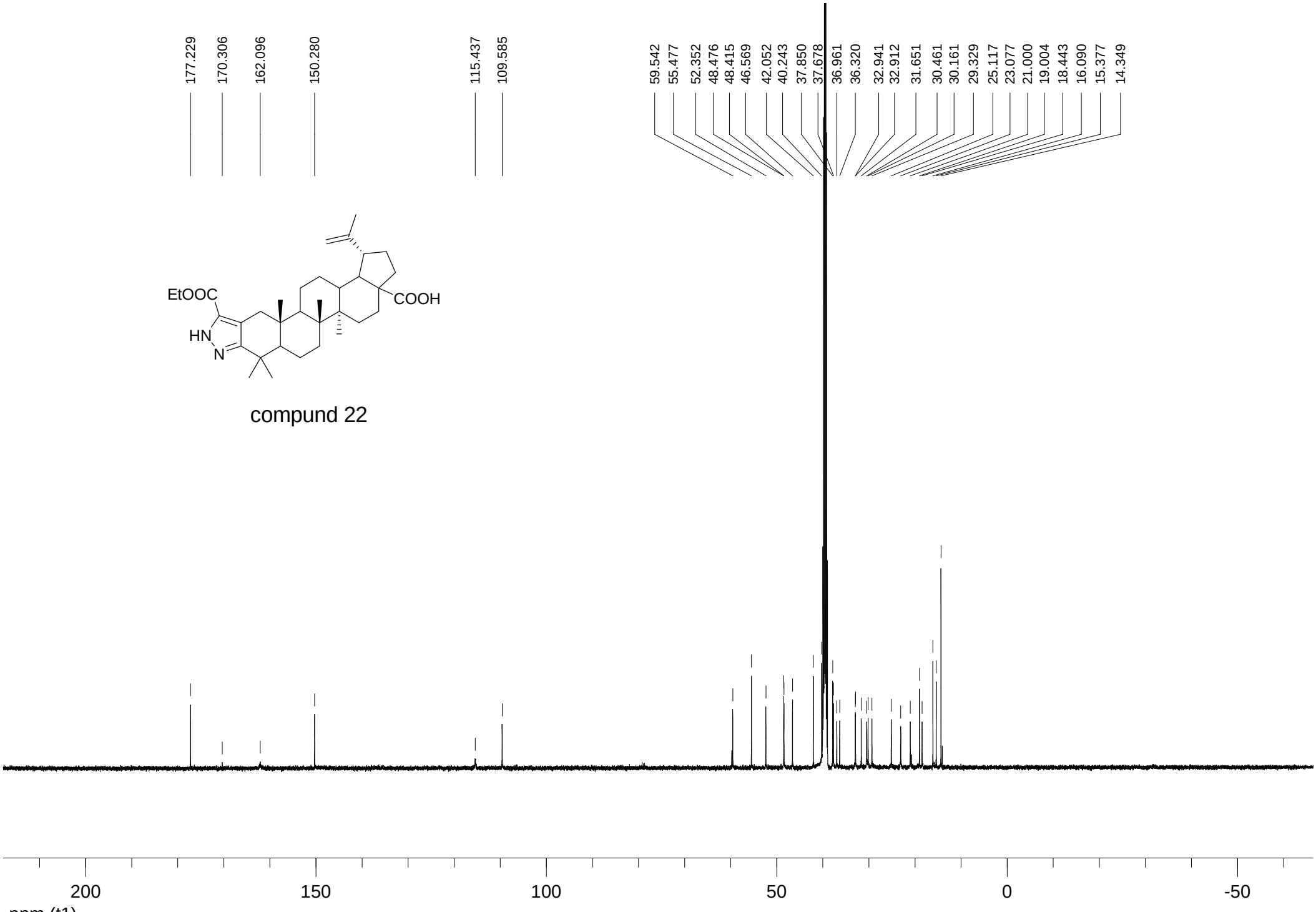

7.178
4.942
3.318
3.314
3.310
3.306
3.302
2.691
2.654
2.426
2.397
2.373
2.366
2.304
2.299
2.271
2.265
2.233
2.012
1.977
1.859
1.842
1.829
1.812
1.557
1.551
1.539
1.514
1.269
1.173
1.031
1.026
0.893
COOH
HN
N
compund 21
1.00
0.93
0.95
1.87
1.11
1.96
13.20
7.05
2.98
5.97
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


180.239
151.042
134.378
113.557
57.983
54.984
50.405
49.978
49.391
49.220
49.050
48.880
48.709
45.619
43.809
41.978
39.801
39.614
38.606
37.787
34.888
34.603
33.268
31.400
31.141
31.005
28.462
24.101
23.809
23.522
22.753
20.325
16.531
16.480
15.176
HN
N
COOH
200
150
100
50
0
ppm (t1)

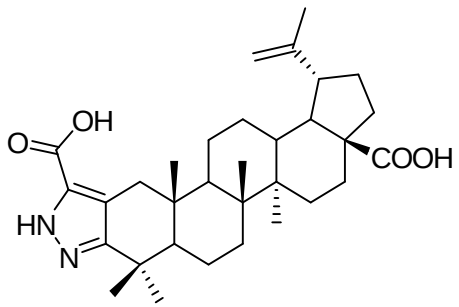
compund 21


13.137
12.092
4.723
4.590
4.249
4.236
4.223
4.209
3.326
2.979
2.970
2.912
2.880
2.504
2.322
2.316
2.296
2.292
2.274
2.267
2.141
2.123
2.119
1.991
1.960
1.830
1.822
1.807
1.672
1.574
1.504
1.274
1.260
1.246
EtOOC
COOH
HN
N
1.04
1.07
1.09
2.00
0.95
1.07
1.18
1.88
3.90
26.31
3.12
10.0
5.0
0.0
ppm (t1)

compund 22

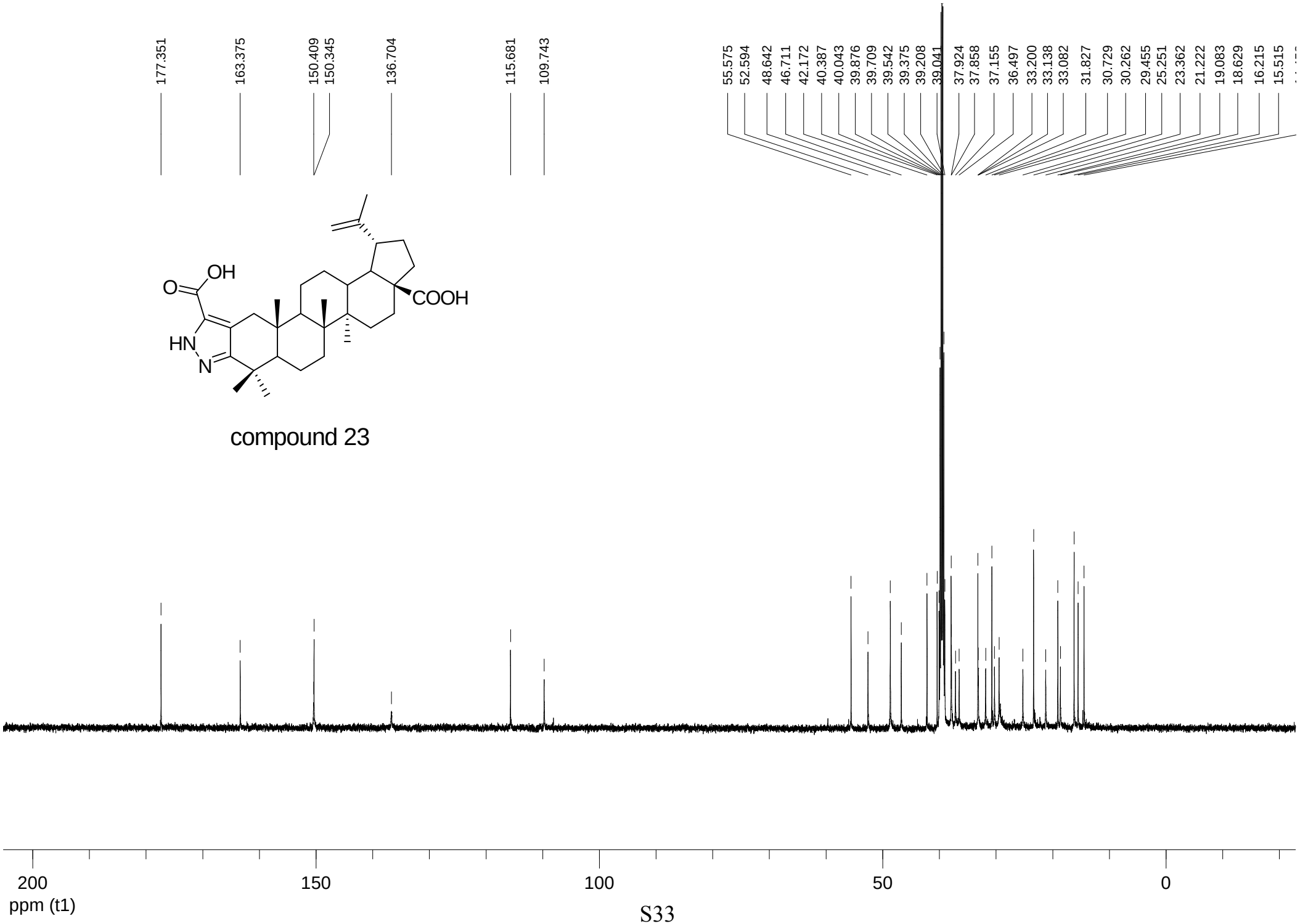

177.229
170.306
162.096
150.280
115.437
109.585
59.542
55.477
52.352
48.476
48.415
46.569
42.052
40.243
37.850
37.678
36.961
36.320
32.941
32.912
31.651
30.461
30.161
29.329
25.117
23.077
21.000
19.004
18.443
16.090
15.377
14.349
EtOOC
HN
N
COOH
200
150
100
50
0
-50
ppm (t1)

compund 22

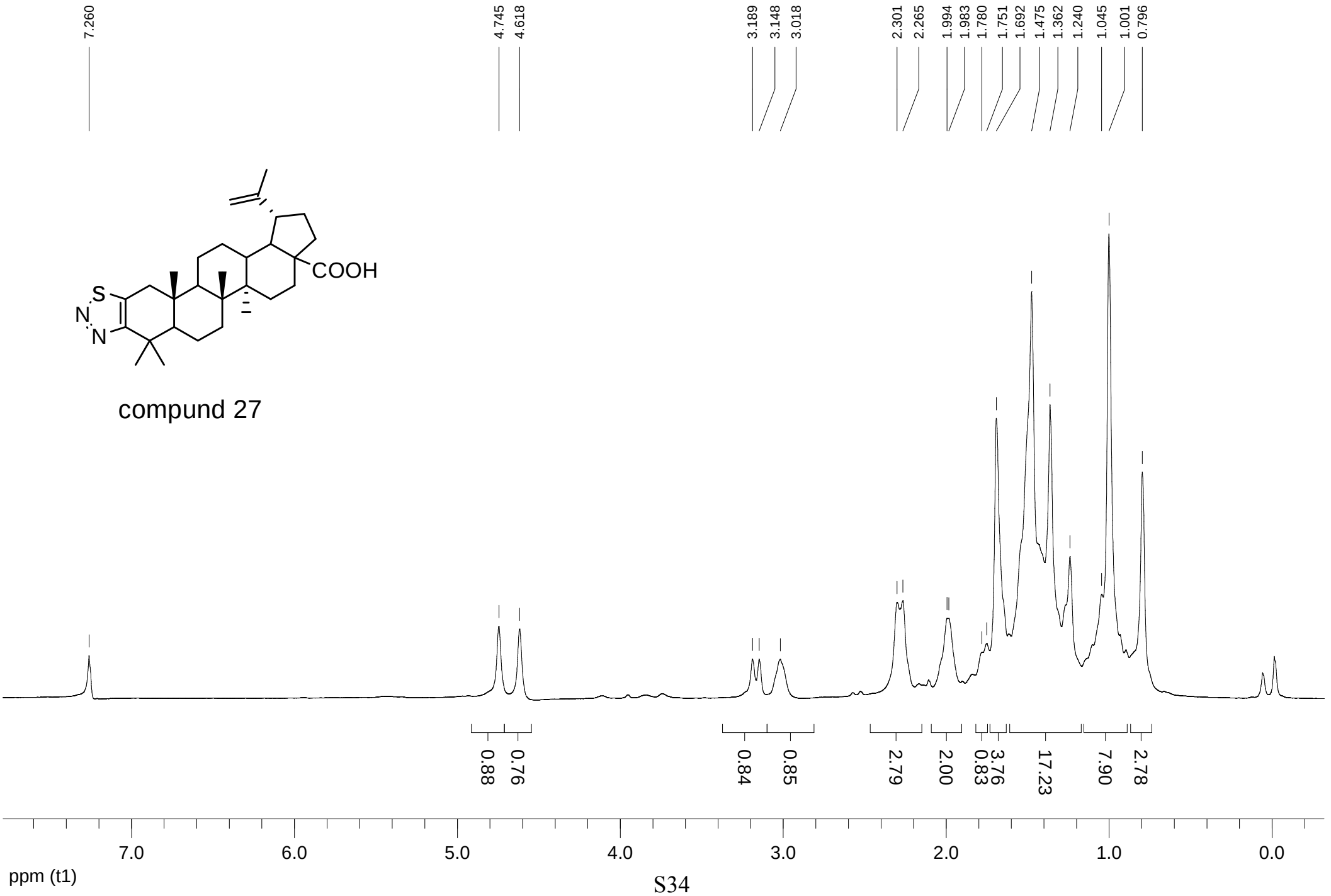

OH
O
COOH
HN
N

compound 23

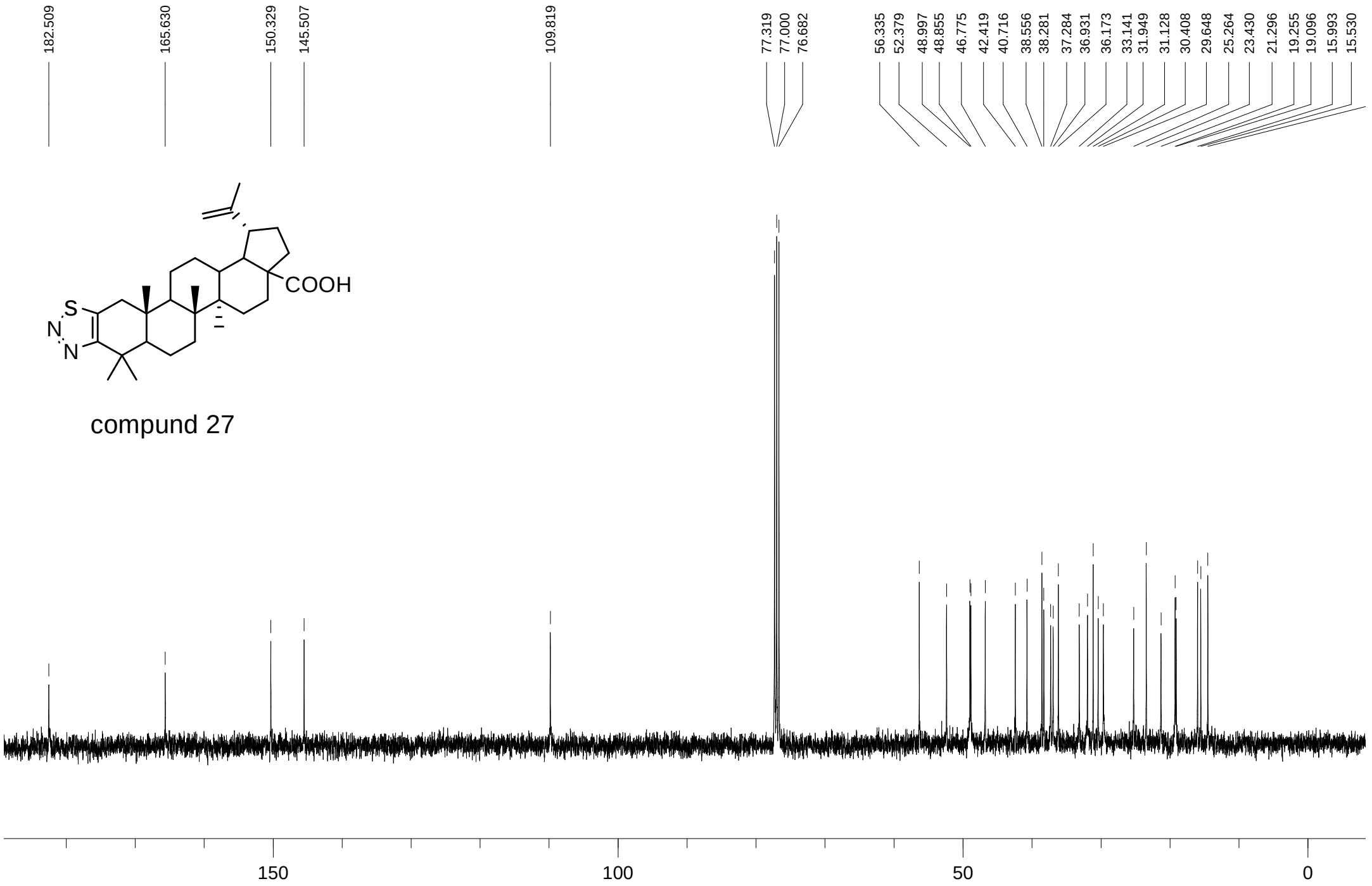
4.716
4.580
2.986
2.980
2.953
2.921
2.524
2.326
2.304
2.282
2.150
2.131
1.985
1.953
1.831
1.819
1.665
1.567
1.543
1.514
1.407
1.224
1.121
1.076
1.052
0.967
0.936
0.841
0.720
0.99
0.96
1.72
0.90
0.91
0.84
1.82
3.14
23.77
2.81
3.21
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


177.351
163.375
150.409
150.345
136.704
115.681
109.743
55.575
52.594
48.642
46.711
42.172
40.387
40.043
39.876
39.709
39.542
39.375
39.208
39.041
37.924
37.858
37.155
36.497
33.200
33.138
33.082
31.827
30.729
30.262
29.455
25.251
23.362
21.222
19.083
18.629
16.215
15.515
OH
O
COOH
HN
N
200
150
100
50
0
ppm (t1)

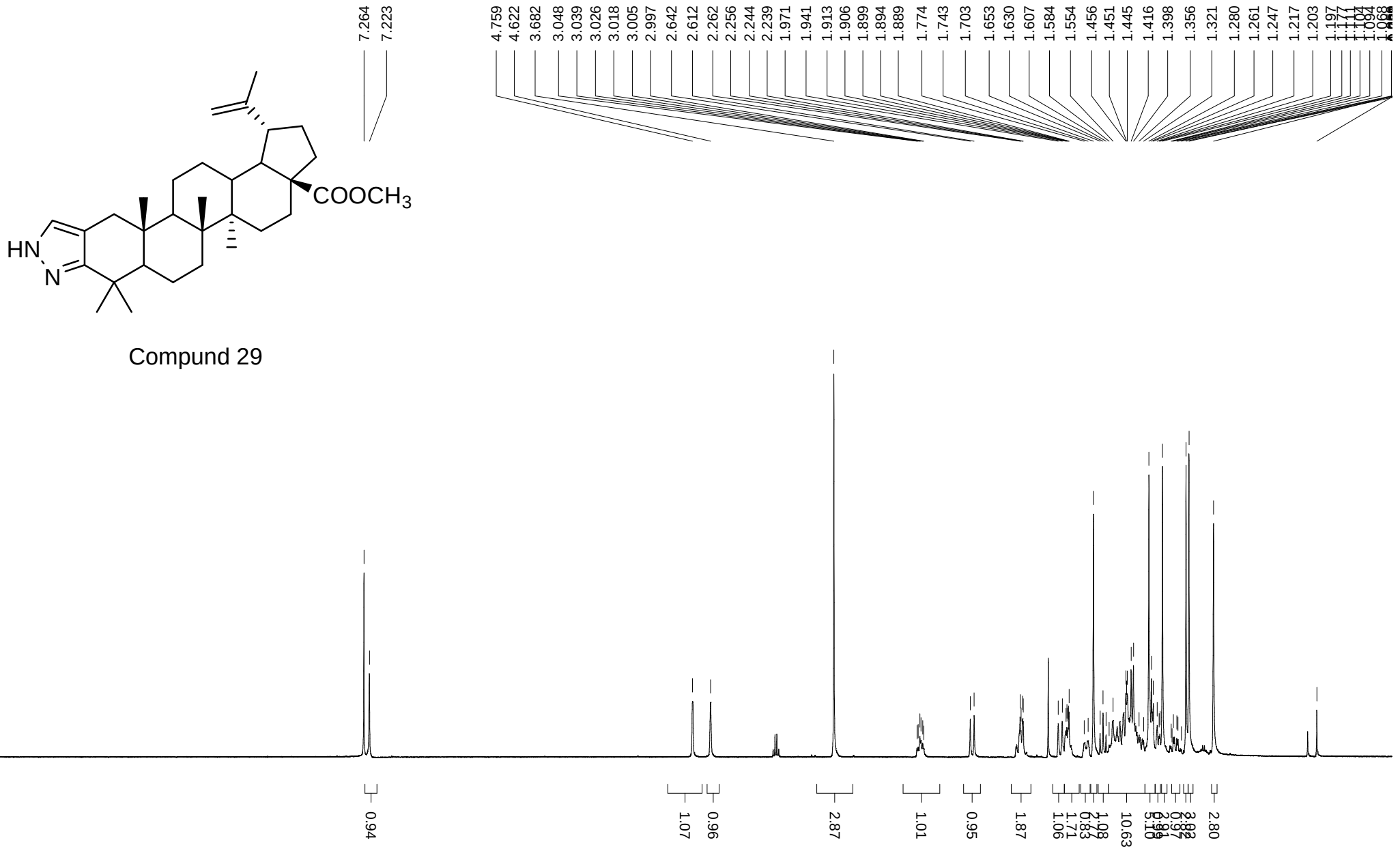
compound 23


7.260
4.745
4.618
3.189
3.148
3.018
2.301
2.265
1.994
1.983
1.780
1.751
1.692
1.475
1.362
1.240
1.045
1.001
0.796
COOH
S
N
N
0.88
0.76
0.84
0.85
2.79
2.00
0.83
3.76
17.23
7.90
2.78
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

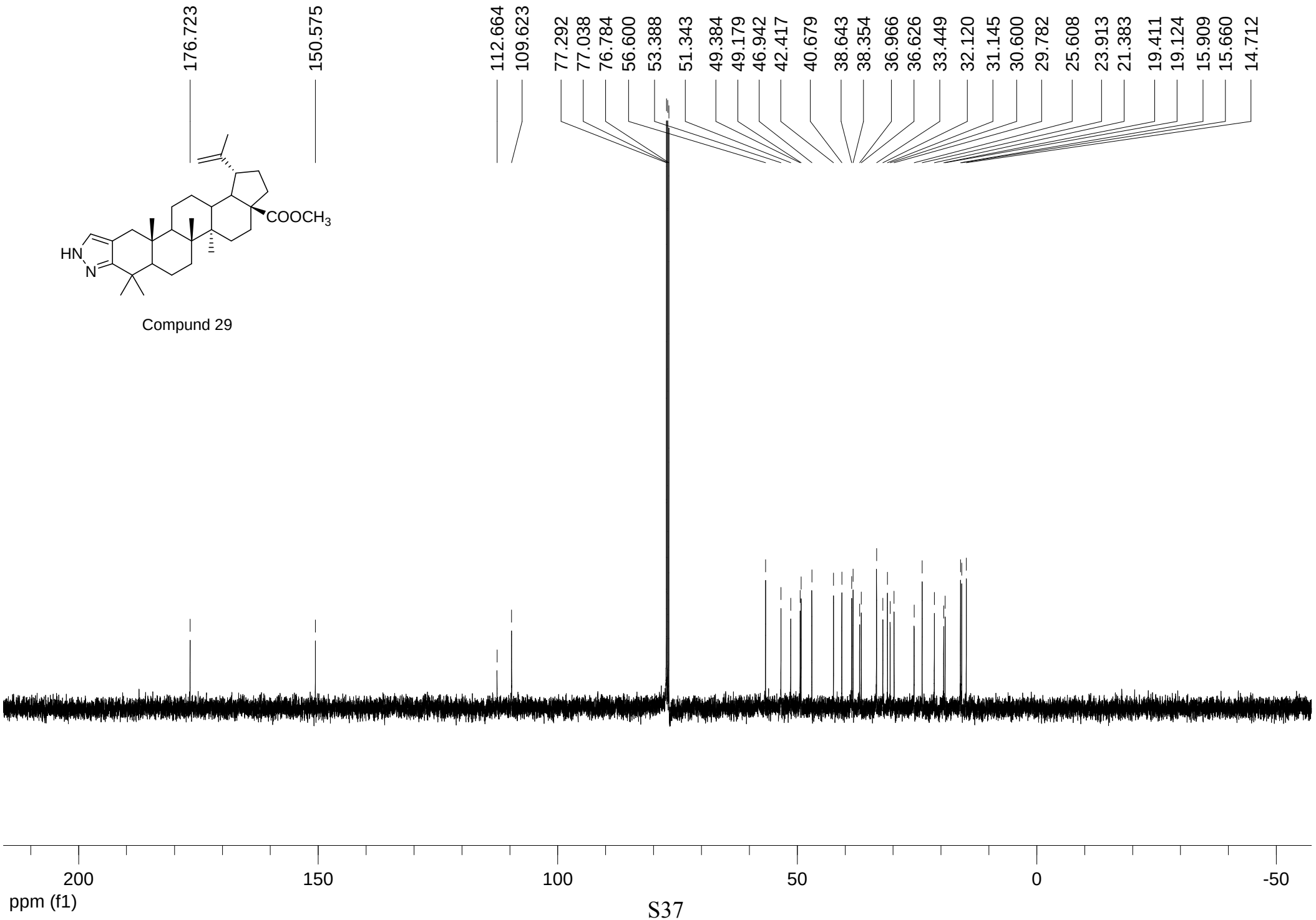
compund 27


182.509
165.630
150.329
145.507
109.819
77.319
77.000
76.682
56.335
52.379
48.997
48.855
46.775
42.419
40.716
38.556
38.281
37.284
36.931
36.173
33.141
31.949
31.128
30.408
29.648
25.264
23.430
21.296
19.255
19.096
15.993
15.530
COOH
S
N
N
150
100
50
0
ppm (t1)

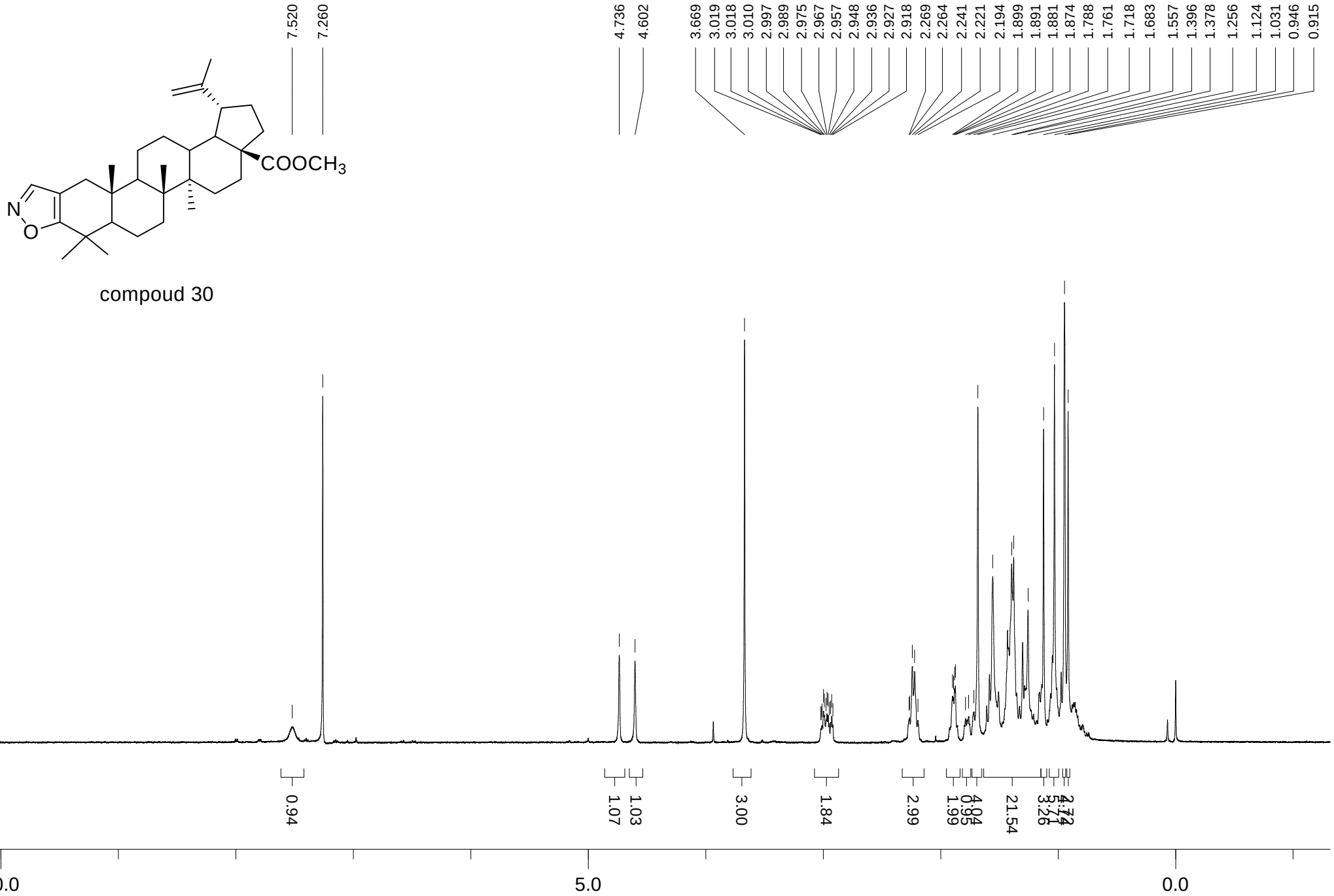
compund 27


7.264
7.223
4.759
4.622
3.682
3.048
3.039
3.026
3.018
3.005
2.997
2.642
2.612
2.262
2.256
2.244
2.239
1.971
1.941
1.913
1.906
1.899
1.894
1.889
1.774
1.743
1.703
1.653
1.630
1.607
1.584
1.554
1.456
1.451
1.445
1.416
1.398
1.356
1.321
1.280
1.261
1.247
1.217
1.203
1.197
COOCH3
HN
N
0.94
1.07
0.96
2.87
1.01
0.95
1.87
1.06
10.93
2.80
10.0
5.0
0.0
ppm (t1)

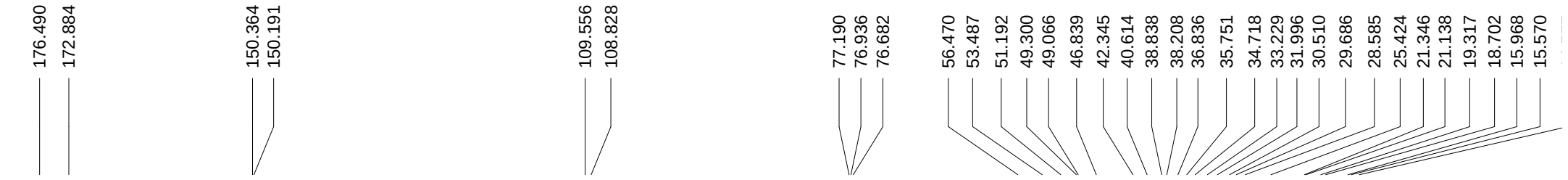
Compund 29

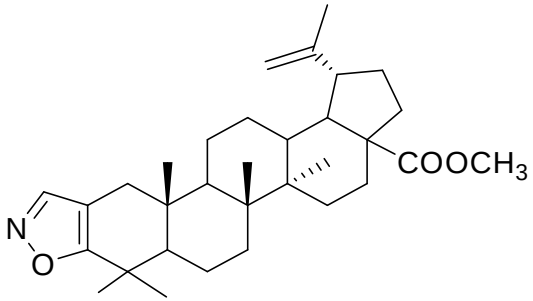

176.723
150.575
112.664
109.623
77.292
77.038
76.784
56.600
53.388
51.343
49.384
49.179
46.942
42.417
40.679
38.643
38.354
36.966
36.626
33.449
32.120
31.145
30.600
29.782
25.608
23.913
21.383
19.411
19.124
15.909
15.660
14.712
COOCH3
HN
N
200
150
100
50
0
-50
ppm (f1)

Compund 29

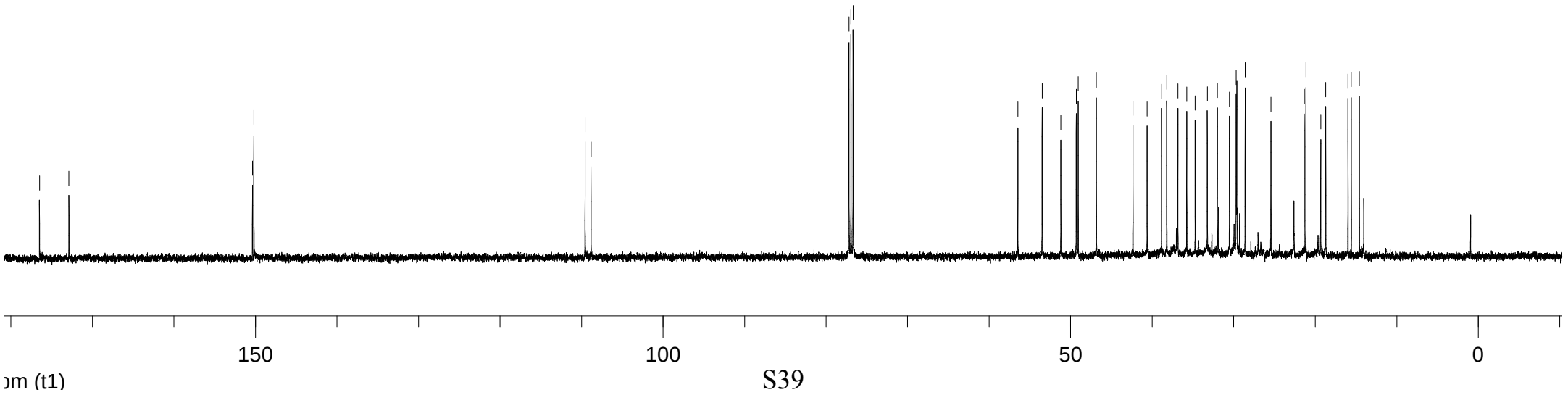

7.520
7.260
4.736
4.602
3.669
3.019
3.018
3.010
2.997
2.989
2.975
2.967
2.957
2.948
2.936
2.927
2.918
2.269
2.264
2.241
2.221
2.194
1.899
1.891
1.881
1.874
1.788
1.761
1.718
1.683
1.557
1.396
1.378
1.256
1.124
1.031
0.946
0.915
COOCH3
N
O
0.94
1.07
1.03
3.00
1.84
2.99
1.99
21.54
3.26
10.0
5.0
0.0
ppm (t1)

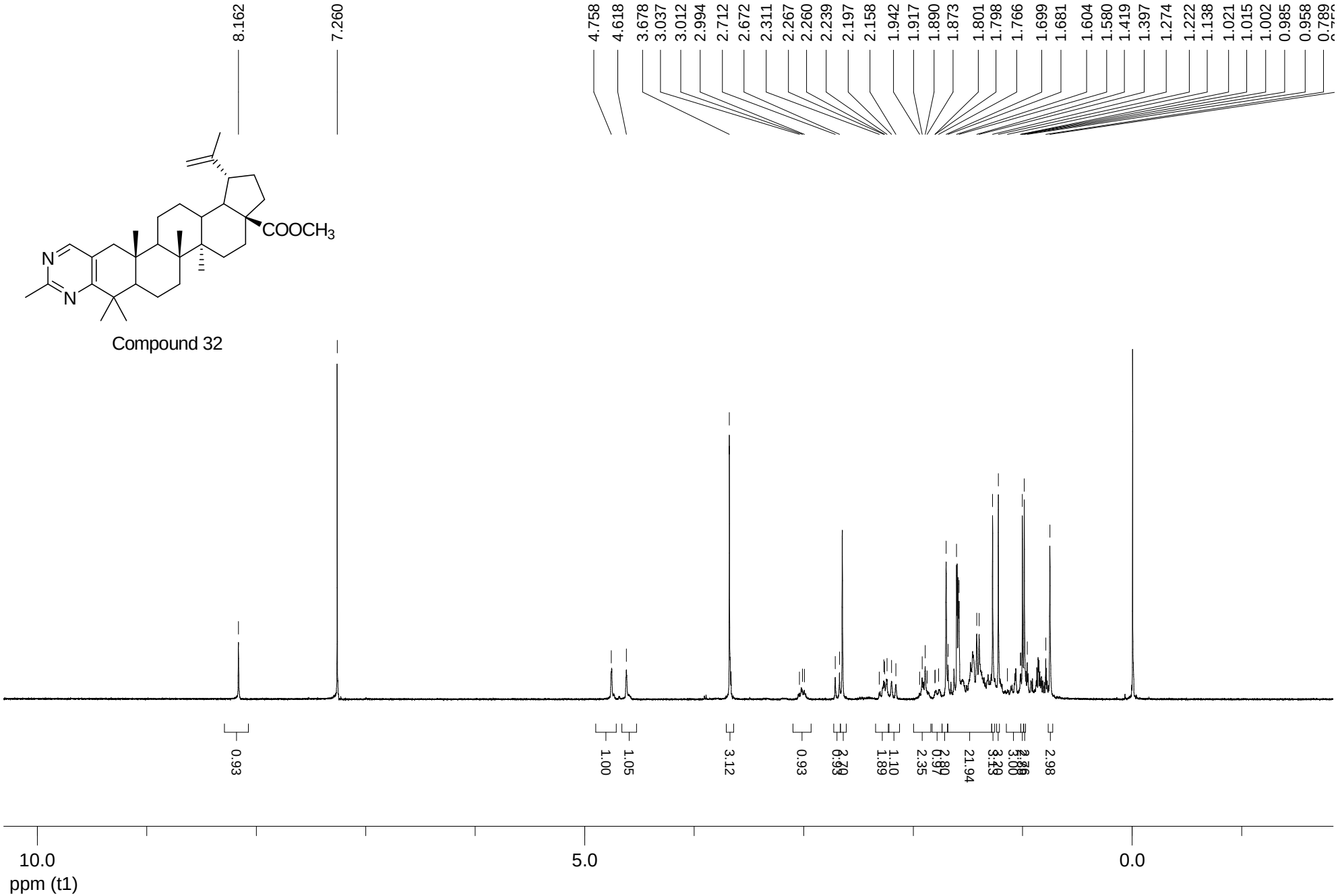
compoud 30

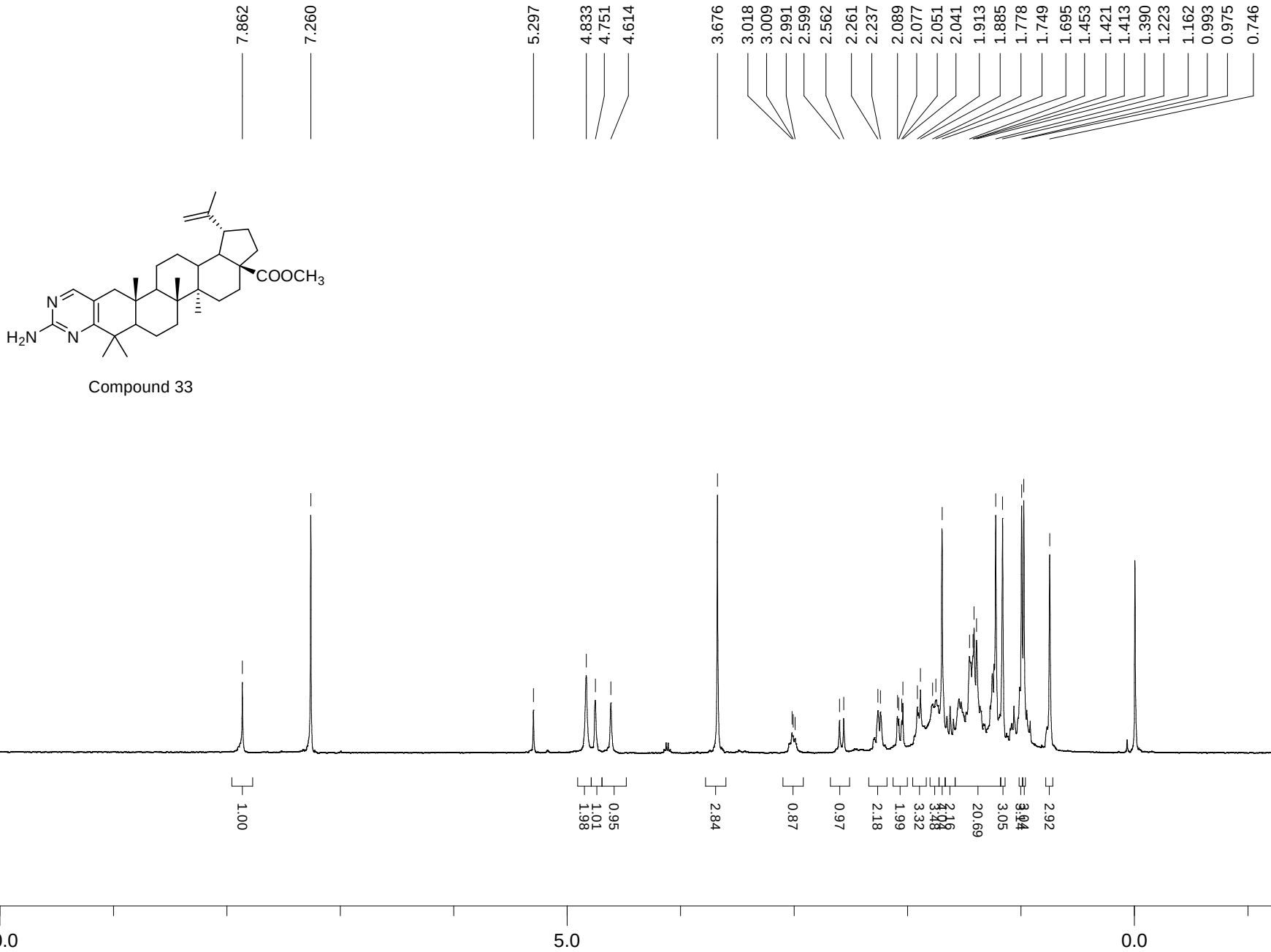

176.490
172.884
150.364
150.191
109.556
108.828
77.190
76.936
76.682
56.470
53.487
51.192
49.300
49.066
46.839
42.345
40.614
38.838
38.208
38.836
35.751
34.718
33.229
31.996
30.510
29.686
28.585
25.424
21.346
21.138
19.317
18.702
15.968
15.570


COOCH3
N
O

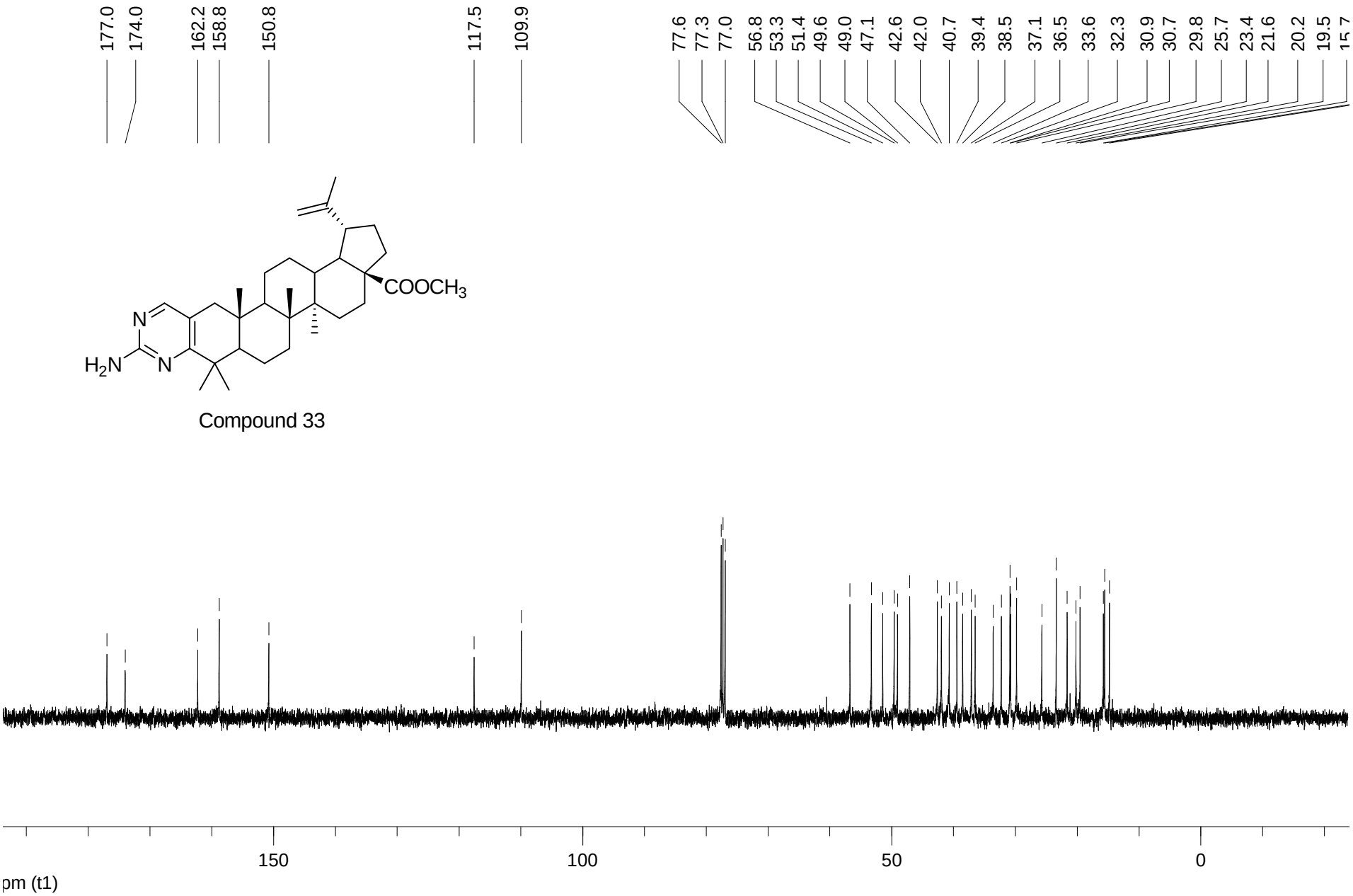
compoud30


150
100
50
0
ɔm (t1)

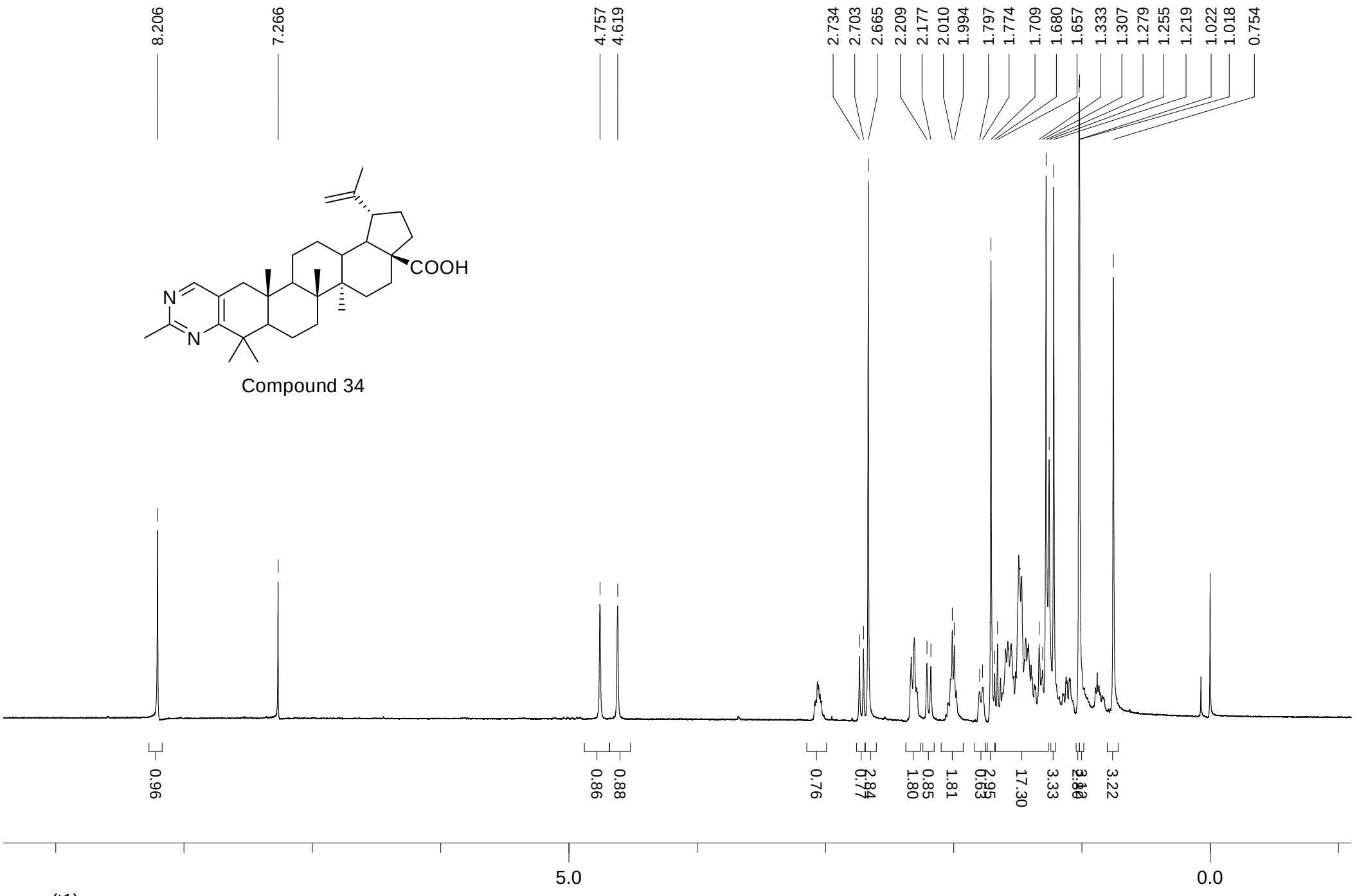

8.162
7.260
4.758
4.618
3.678
3.037
3.012
2.994
2.712
2.672
2.311
2.267
2.260
2.239
2.197
2.158
1.942
1.917
1.890
1.873
1.801
1.798
1.766
1.699
1.681
1.604
1.580
1.419
1.397
1.274
1.222
1.138
1.021
1.015
1.002
0.985
0.958
COOCH3
N
N
Compound 32
0.93
1.00
1.05
3.12
0.93
1.89
1.10
2.35
21.94
2.98
10.0
5.0
0.0
ppm (t1)


7.862
7.260
5.297
4.833
4.751
4.614
3.676
3.018
3.009
2.991
2.599
2.562
2.261
2.237
2.089
2.077
2.051
2.041
1.913
1.885
1.778
1.749
1.695
1.453
1.421
1.413
1.390
1.223
1.162
0.993
0.975
0.746
COOCH3
H2N
N
N
1.00
1.86
1.01
0.95
2.84
0.87
0.97
2.18
1.99
3.32
20.69
3.05
2.92
10.0
5.0
0.0

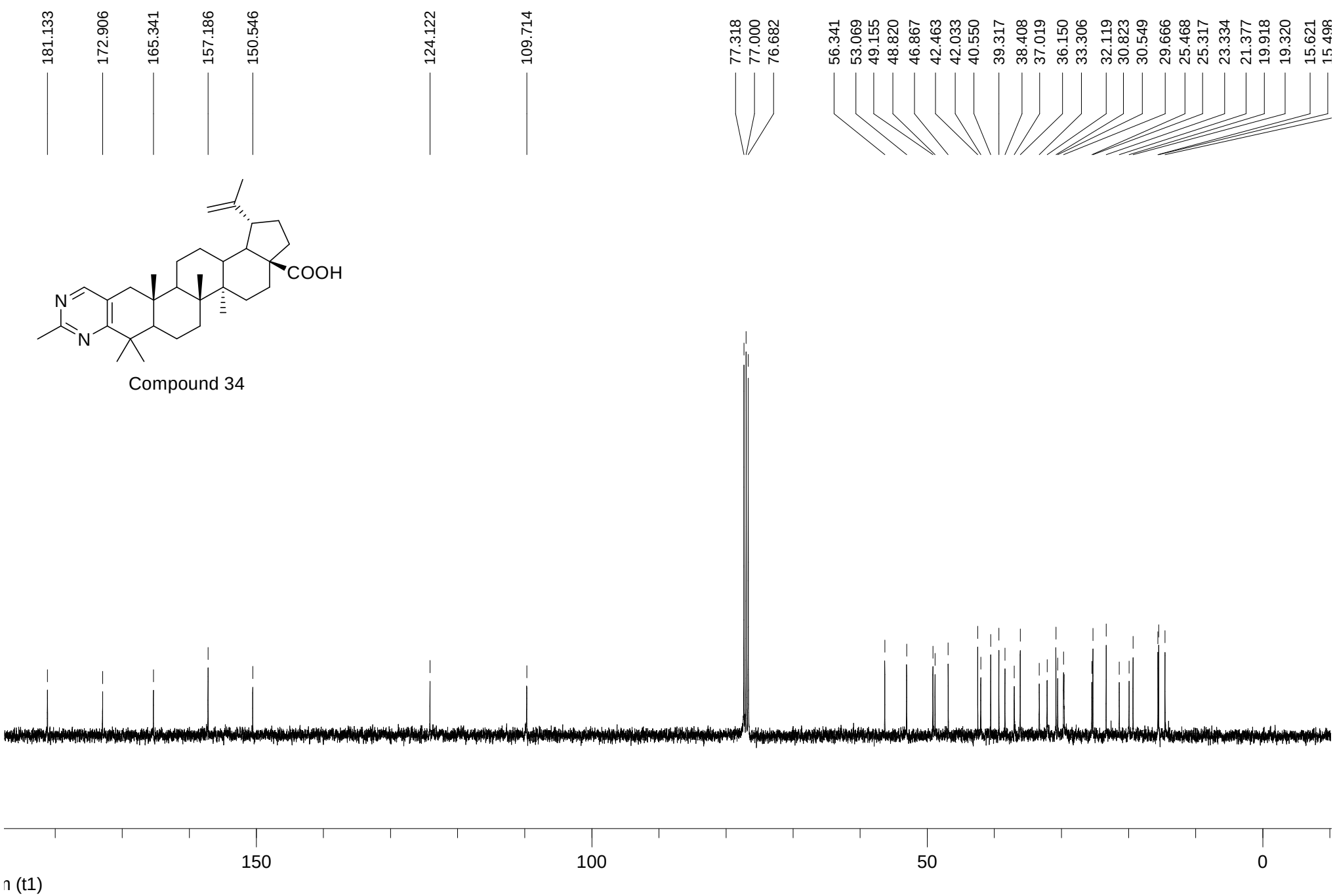
Compound 33


177.0
174.0
162.2
158.8
150.8
117.5
109.9
77.6
77.3
77.0
56.8
53.3
51.4
49.6
49.0
47.1
42.6
42.0
40.7
39.4
38.5
37.1
36.5
33.6
32.3
30.9
30.7
29.8
25.7
23.4
21.6
20.2
19.5
COOCH3
N
H2N
N
150
100
50
0
pm (t1)

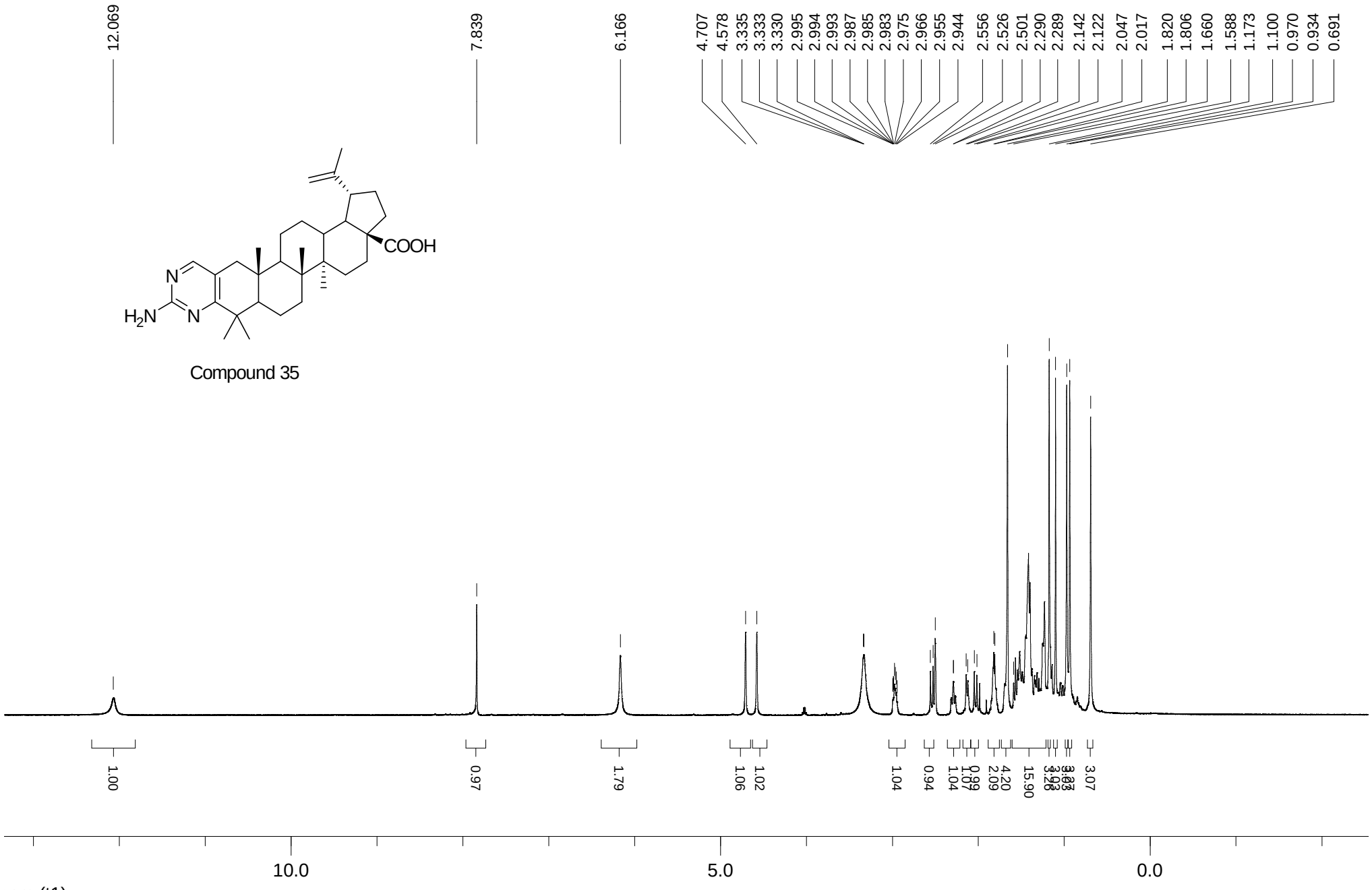
Compound 33

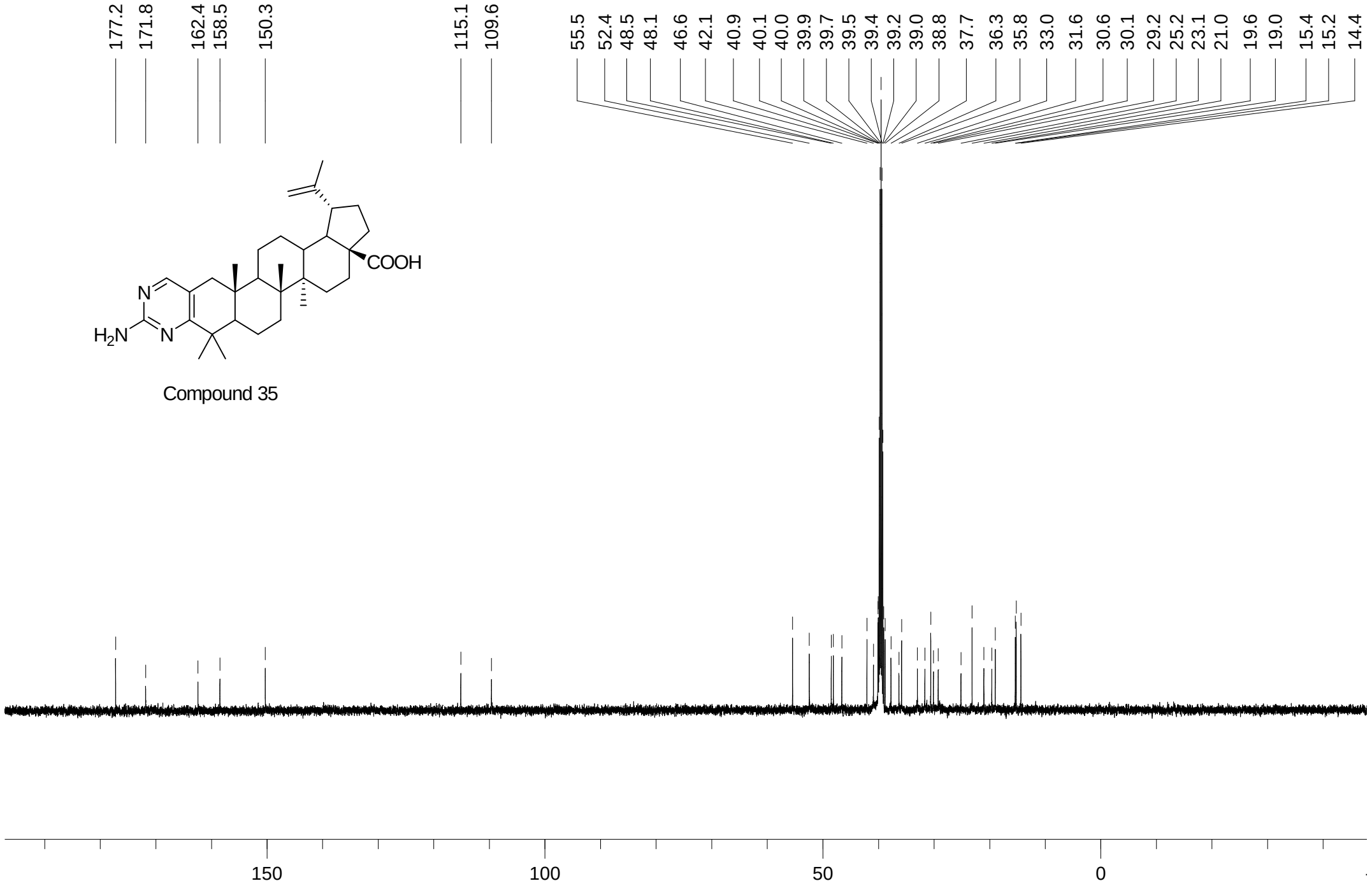

8.206
7.266
4.757
4.619
2.734
2.703
2.665
2.209
2.177
2.010
1.994
1.797
1.774
1.709
1.680
1.657
1.333
1.307
1.279
1.255
1.219
1.022
1.018
0.754
COOH
N
N
0.96
0.86
0.88
0.76
2.84
0.85
1.80
1.81
17.30
3.33
3.22
5.0
0.0
ppm (t1)

Compound 34


181.133
172.906
165.341
157.186
150.546
124.122
109.714
77.318
77.000
76.682
56.341
53.069
49.155
48.820
46.867
42.463
42.033
40.550
39.317
38.408
37.019
36.150
33.306
32.119
30.823
30.549
29.666
25.468
25.317
23.334
21.377
19.918
19.320
15.621
15.498
COOH
N
N
150
100
50
0
n (t1)

Compound 34


12.069
7.839
6.166
4.707
4.578
3.335
3.333
3.330
2.995
2.994
2.993
2.987
2.985
2.983
2.975
2.966
2.955
2.944
2.556
2.526
2.501
2.290
2.289
2.142
2.122
2.047
2.017
1.820
1.806
1.660
1.588
1.173
1.100
0.970
0.934
0.691
COOH
N
H_2N
N
Compound 35
1.00
0.97
1.79
1.06
1.02
1.04
0.94
1.04
2.09
15.90
3.07
10.0
5.0
0.0
ppm (t1)


177.2
171.8
162.4
158.5
150.3
115.1
109.6
55.5
52.4
48.5
48.1
46.6
42.1
40.9
40.1
40.0
39.9
39.7
39.5
39.4
39.2
39.0
38.8
37.7
36.3
35.8
33.0
31.6
30.6
30.1
29.2
25.2
23.1
21.0
19.6
19.0
15.4
15.2
14.4
COOH
N
H_2N
N
150
100
50
0
ppm (t1)

Compound 35