Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2023

SUPPLEMENTARY MATERIAL

Synthesis of N-Oxyamide analogues of protein kinase B (Akt) targeting anionic glycoglycerolipids and their Antiproliferative Activity on Human Ovarian Carcinoma Cells.

TABLE OF CONTENTS

Page	Content	Page	Content
S1	**Figure S1**: NMR of configuration assignment of **17a**	**S25**	^{13}C spectrum of compound **11**
S2	**Figure S2:** TLC of stability studies	**S26**	^{1}H spectrum of compound **12**
S3	**Figure S3:** NMR of stability studies	**S27**	^{13}C spectrum of compound **12**
S4	**Figure S4:** NMR of serum binding study	**S28**	^{1}H spectrum of compound **13**
S5	**Figure S5:** NMR of serum binding study	**S29**	^{13}C spectrum of compound **13**
S6	^{1}H spectrum of compound **3a**	**S30**	^{1}H spectrum of compound **15**
S7	^{13}C spectrum of compound **3a**	**S31**	^{13}C spectrum of compound **15**
S8	^{1}H spectrum of compound **3b**	**S32**	^{1}H spectrum of compound **16**
S9	^{13}C spectrum of compound **3b**	**S33**	^{13}C spectrum of compound **16**
S10	^{1}H spectrum of compound **4a**	**S34**	^{1}H spectrum of compound **17a**
S11	^{13}C spectrum of compound **4a**	**S35**	^{13}C spectrum of compound **17a**
S12	^{1}H spectrum of compound **4b**	**S36**	^{1}H spectrum of compound **17b**
S13	^{13}C spectrum of compound **4b**	**S37**	^{13}C spectrum of compound **17b**
S14	^{1}H spectrum of compound **5**	**S38**	^{1}H spectrum of compound **18**
S15	^{13}C spectrum of compound **5**	**S39**	^{13}C spectrum of compound **18**
S16	^{1}H spectrum of compound **7**	**S40**	^{1}H spectrum of compound **19**
S17	^{13}C spectrum of compound **7**	**S41**	^{13}C spectrum of compound **19**
S18	^{1}H spectrum of compound **8**	**S42**	^{1}H spectrum of compound **20**
S19	^{13}C spectrum of compound **8**	**S43**	^{13}C spectrum of compound **20**
S20	^{1}H spectrum of compound **9**	**S44**	^{1}H spectrum of compound **21**
S21	^{13}C spectrum of compound **9**	**S45**	^{13}C spectrum of compound **21**
S22	^{1}H spectrum of compound **10**	**S46**	^{1}H spectrum of 1,3-di-*O*-decanoyl-2-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-*sn*-glycerol
S23	^{13}C spectrum of compound **10**	**S47**	^{13}C spectrum 1,3-di-*O*-decanoyl-2-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-*sn*-glycerol
S24	^{1}H spectrum of compound **11**		

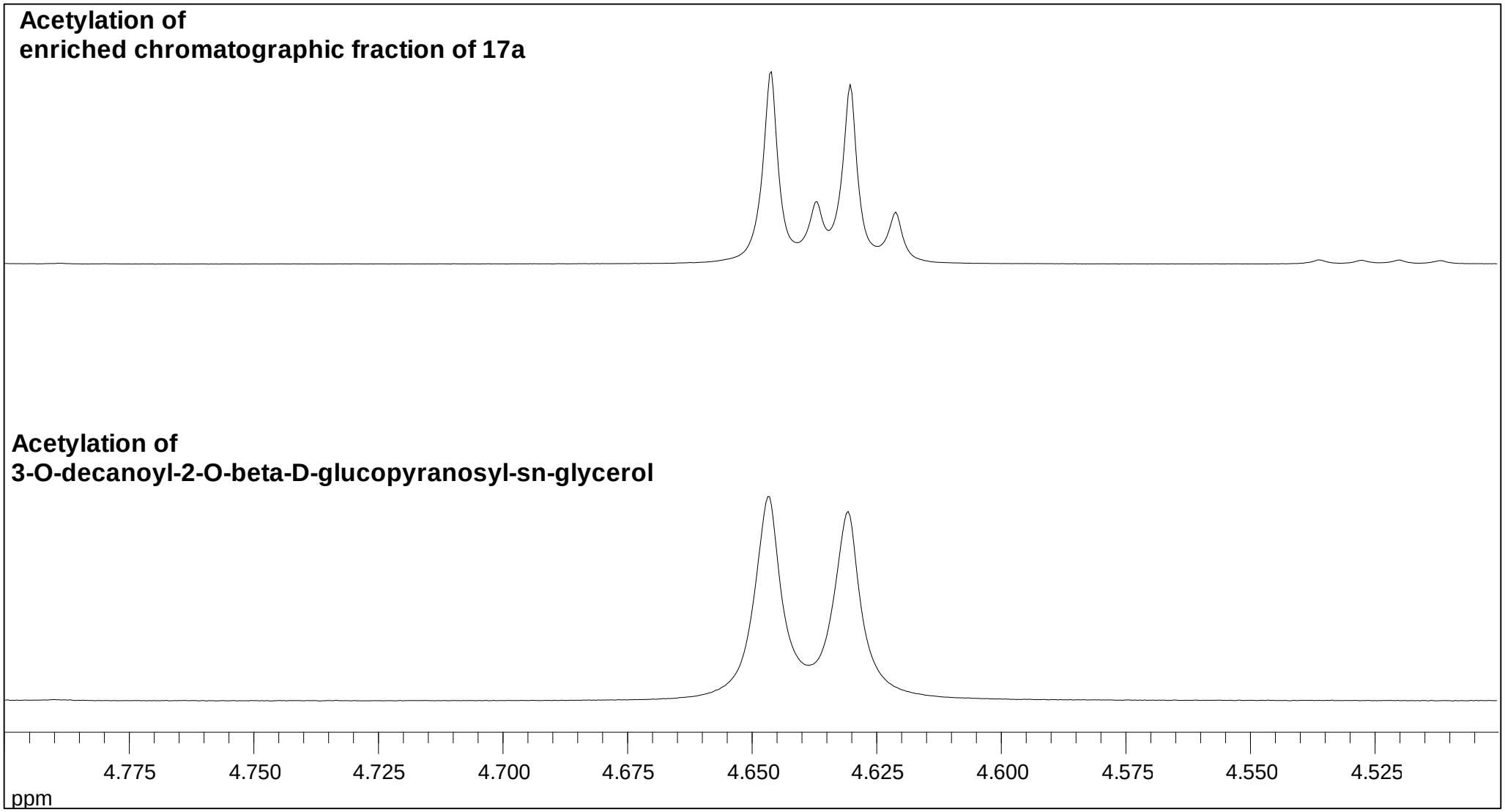
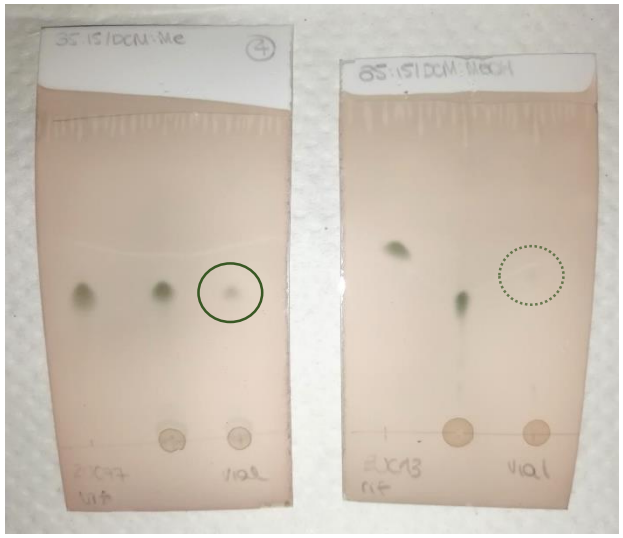
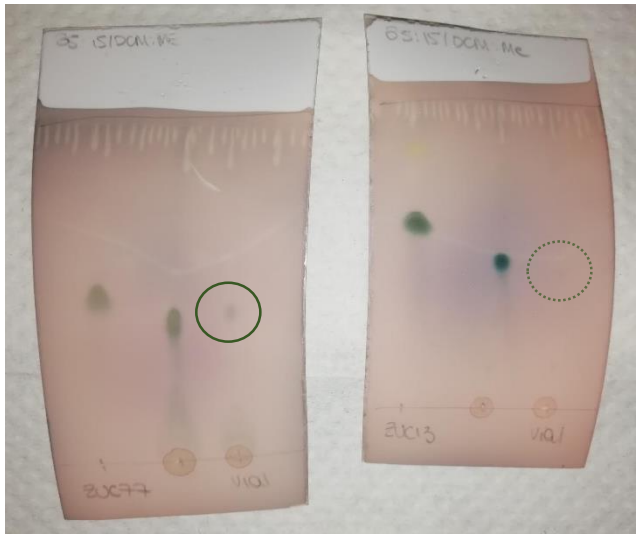


Figure S1: Configuration assignment of compound **17a** by comparison of the ^{1}H anomeric resonances.

STABILITY STUDIES



A



B

Figure S2: A. TLC at 16 h of compound **3b** (left) and **5** (right), DCM:MeOH (85:15). In each TLC the pure compound is seeded on the left while on the right after incubation with serum, in the centre the superimposition of both. **B.** TLC at 24 h of compound **3b** (left) and **5** (right), DCM:MeOH (85:15). In each TLC the pure compound is seeded on the left while on the right after incubation with serum; in the centre the superimposition of both.

STABILITY STUDIES

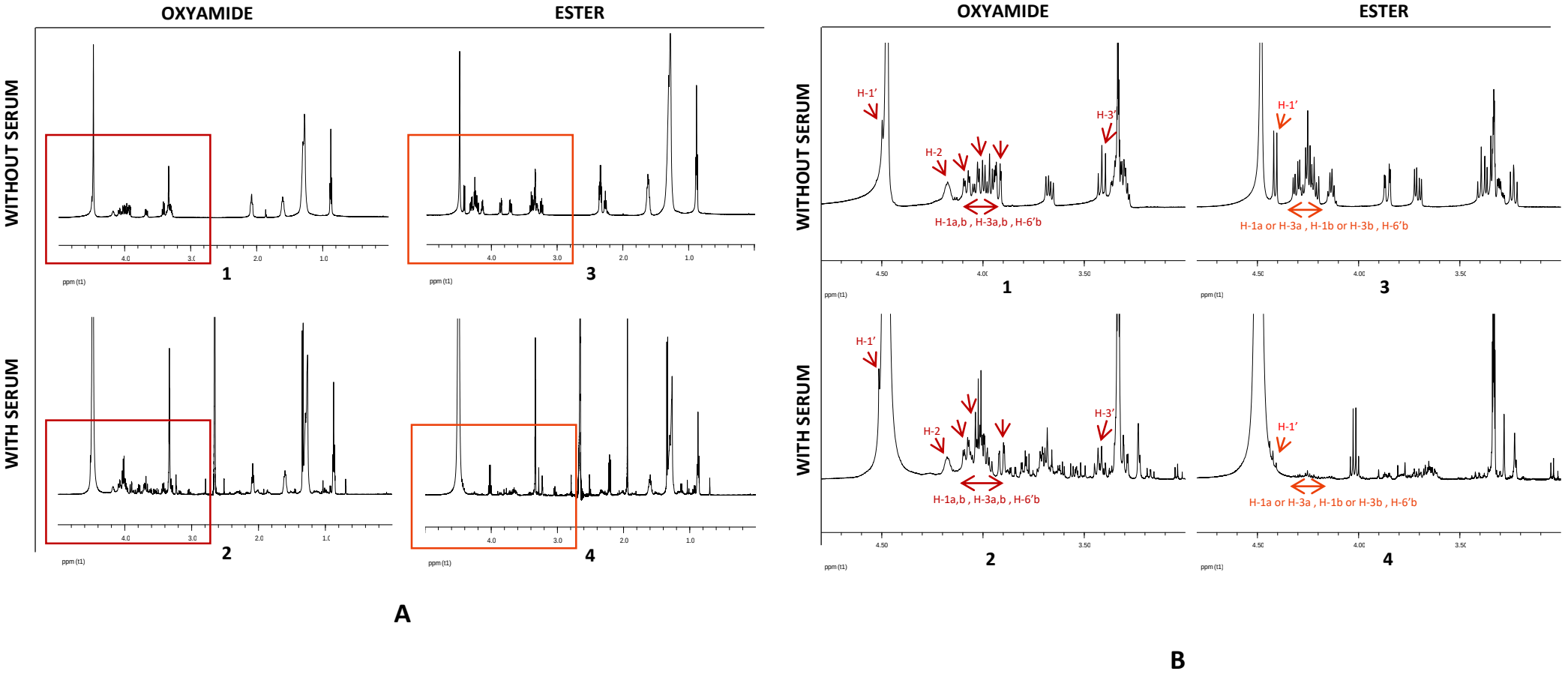


Figure S3: ^{1}H NMR spectra of compound **3b** (**A-1**), compound **3b** after incubation with serum (**A-2**), compound **5** (**A-3**), compound **5** after incubation with serum (**A-4**). **B-1/B-4**: 3.0-4.8 ppm window of the corresponding ^{1}H NMR spectra **A-1/A-4**. The arrows highlighting characteristic signals of the compounds recognisable in the NMR spectra after incubation.

SERUM BINDING STUDY on compound 3a

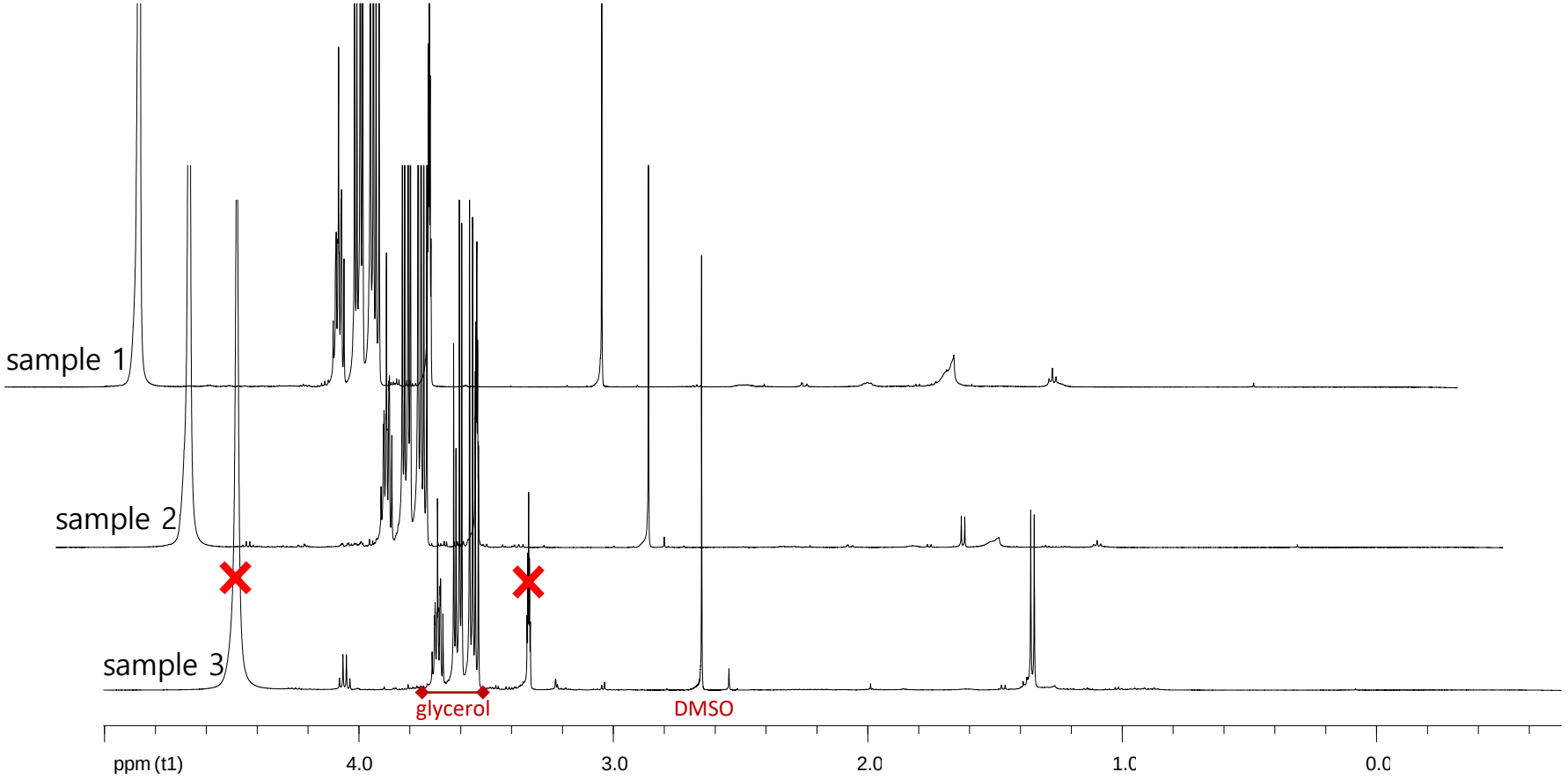


Figure S4: comparison of the ^{1}H NMR spectra of sample 1, 2 and 3 (0%, 10%, 60% serum concentration respectively). Glycerol appears as an impurity from the Amicon® Ultra-0.5 30K centrifugal filter device at 3.53-3.70 ppm. DMSO (2.65 ppm) is used as an internal standard.

SERUM BINDING STUDY on compound 3a

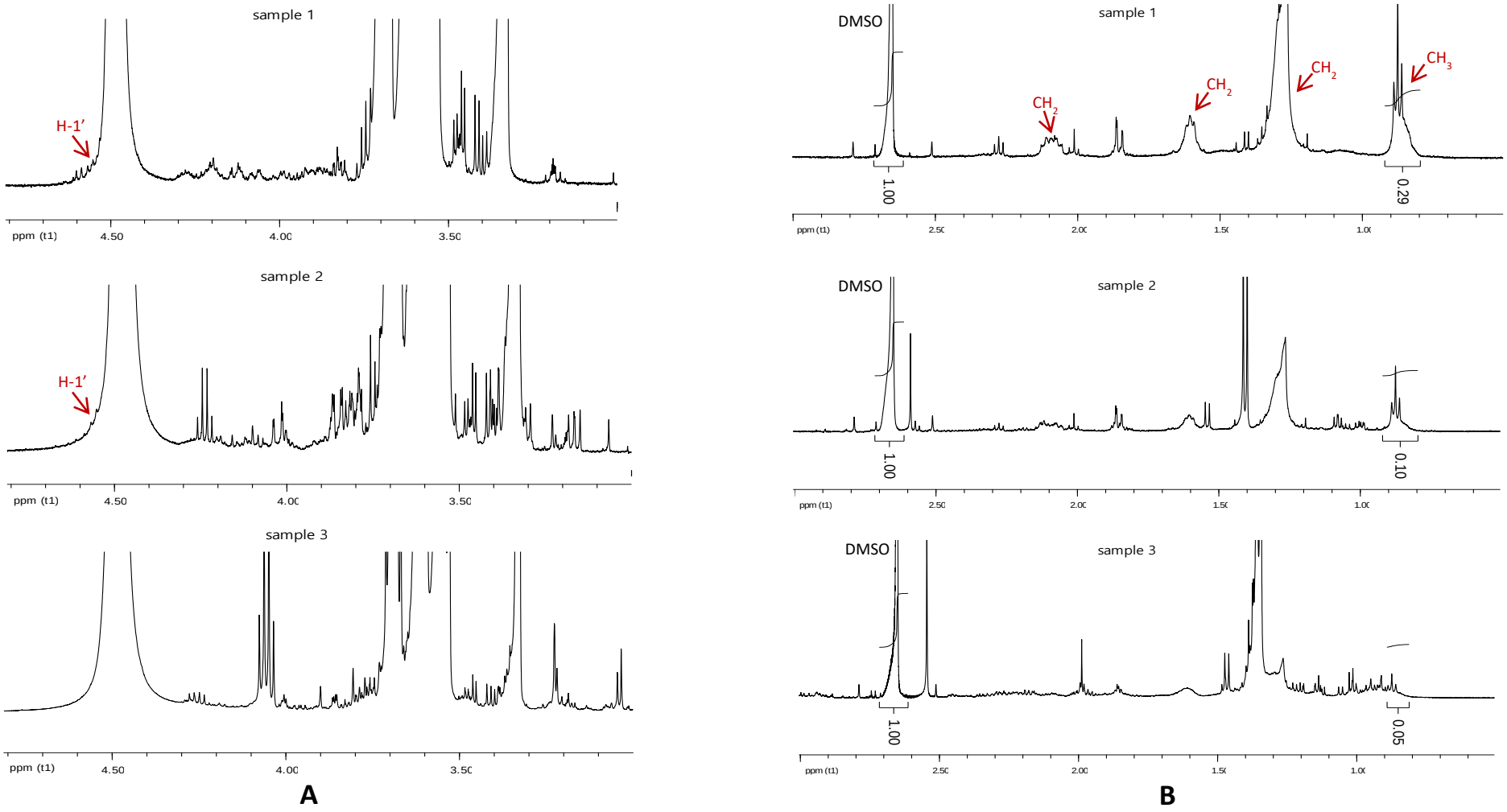
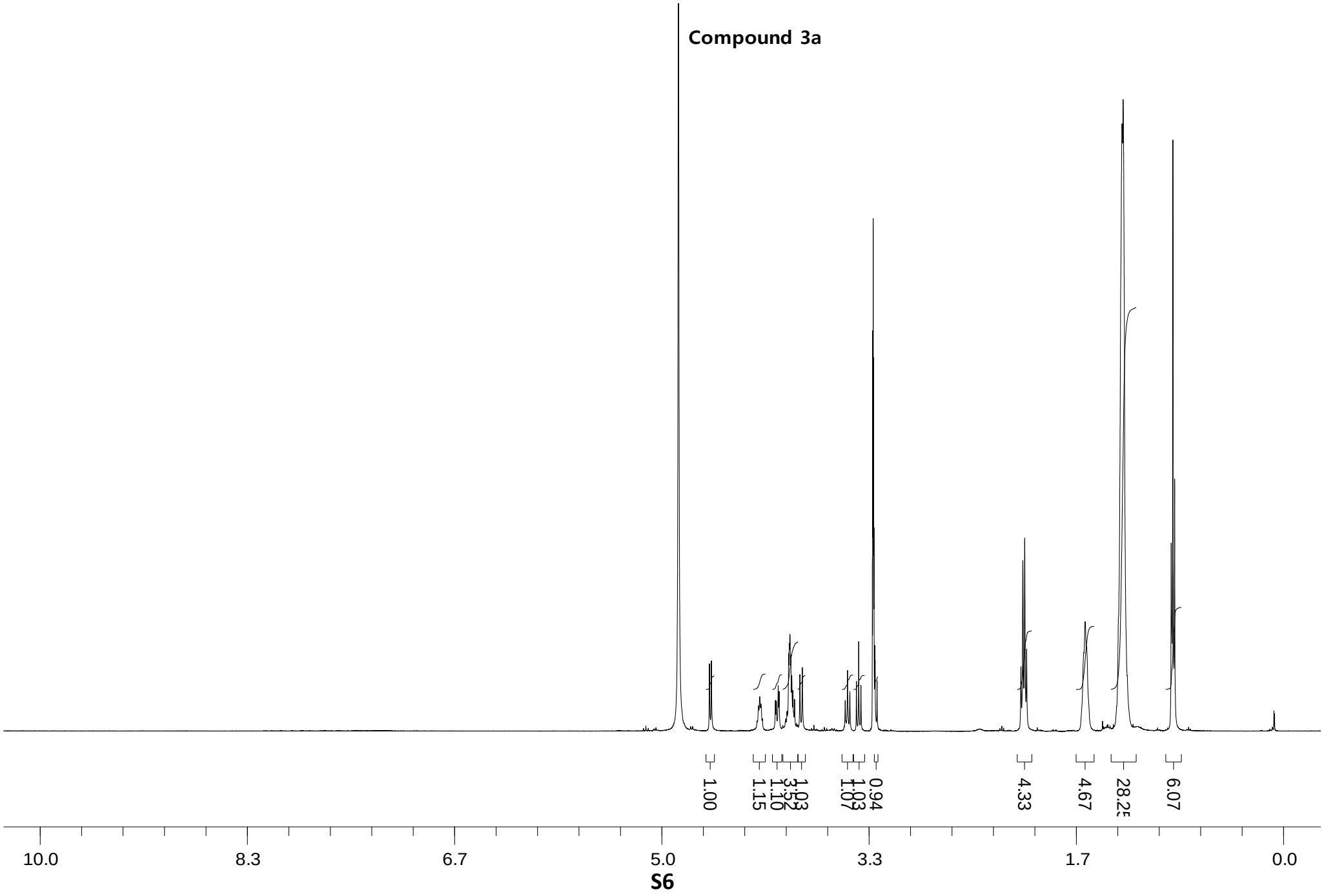
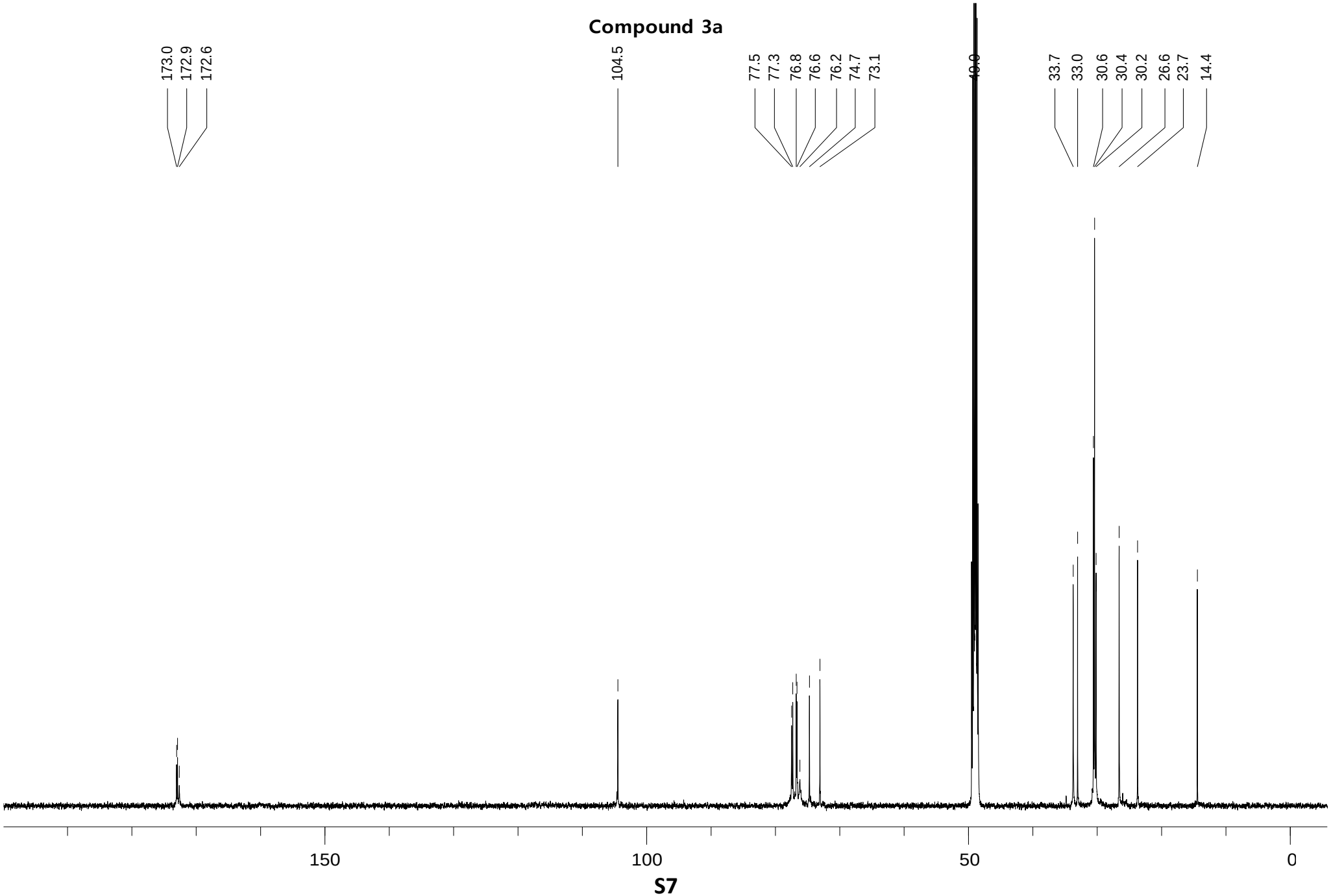


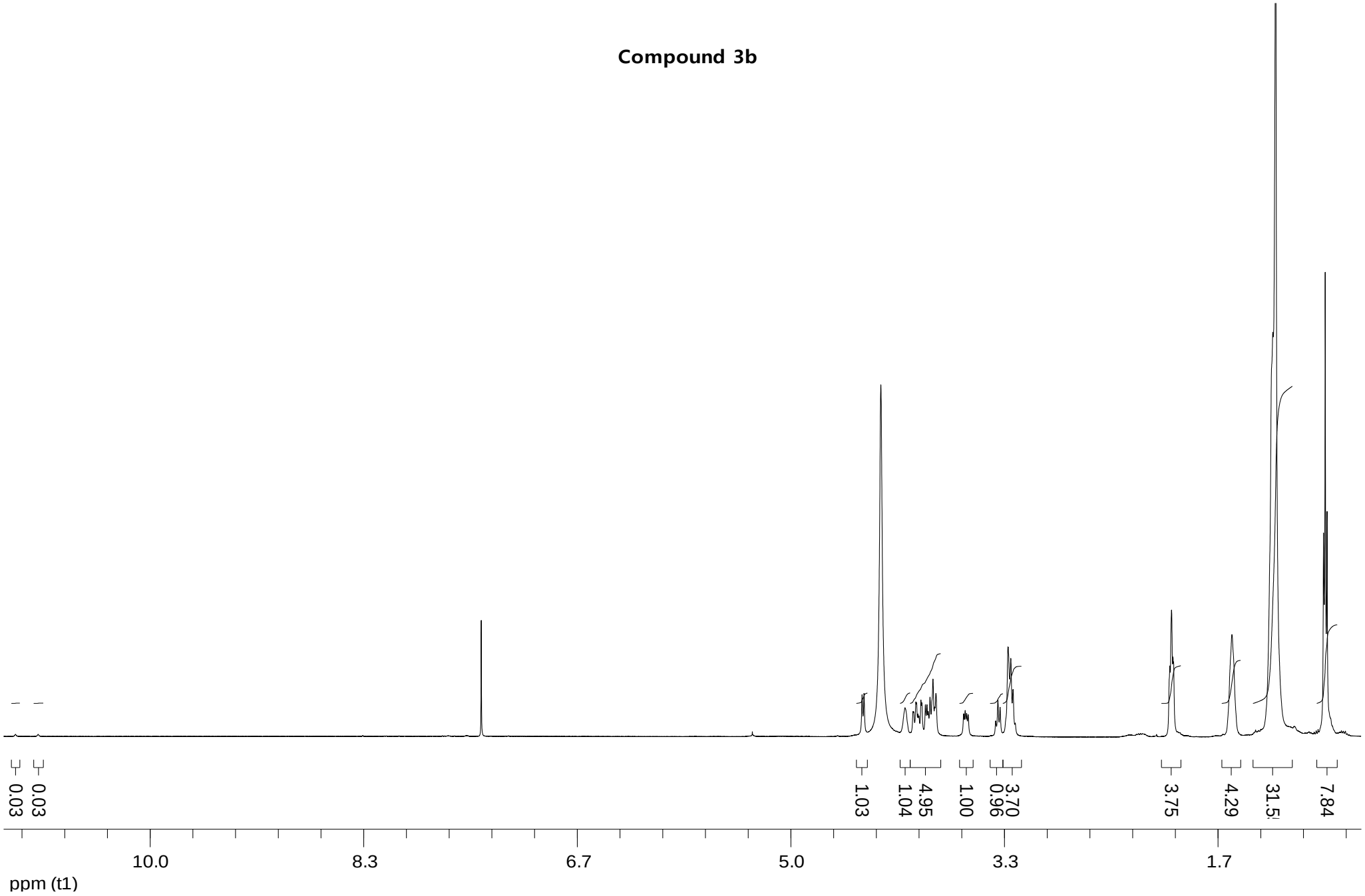
Figure S5: A. 3.0-4.8 ppm window of the ^{1}H NMR spectra of sample 1, 2, and 3 (0%, 10%, 60% serum concentration respectively): the arrows indicate the H-1′ of the glucose mojety. **B.** 0-3 ppm window of the ^{1}H NMR spectra of sample 1, 2 and 3: integrals of signals at 2.65 ppm (DMSO, internal standard) and 0.863 ppm (CH_3 of the acyl chains) are shown. Their comparison shows the diminishing of non-bound **3a** with the increase of serum amount. The arrows indicate characteristic resonances of compound **3a**.


Compound 3a
1.00
1.15
1.10
3.52
1.03
1.07
1.03
0.94
4.33
4.67
28.25
6.07
10.0
8.3
6.7
5.0
3.3
1.7
0.0

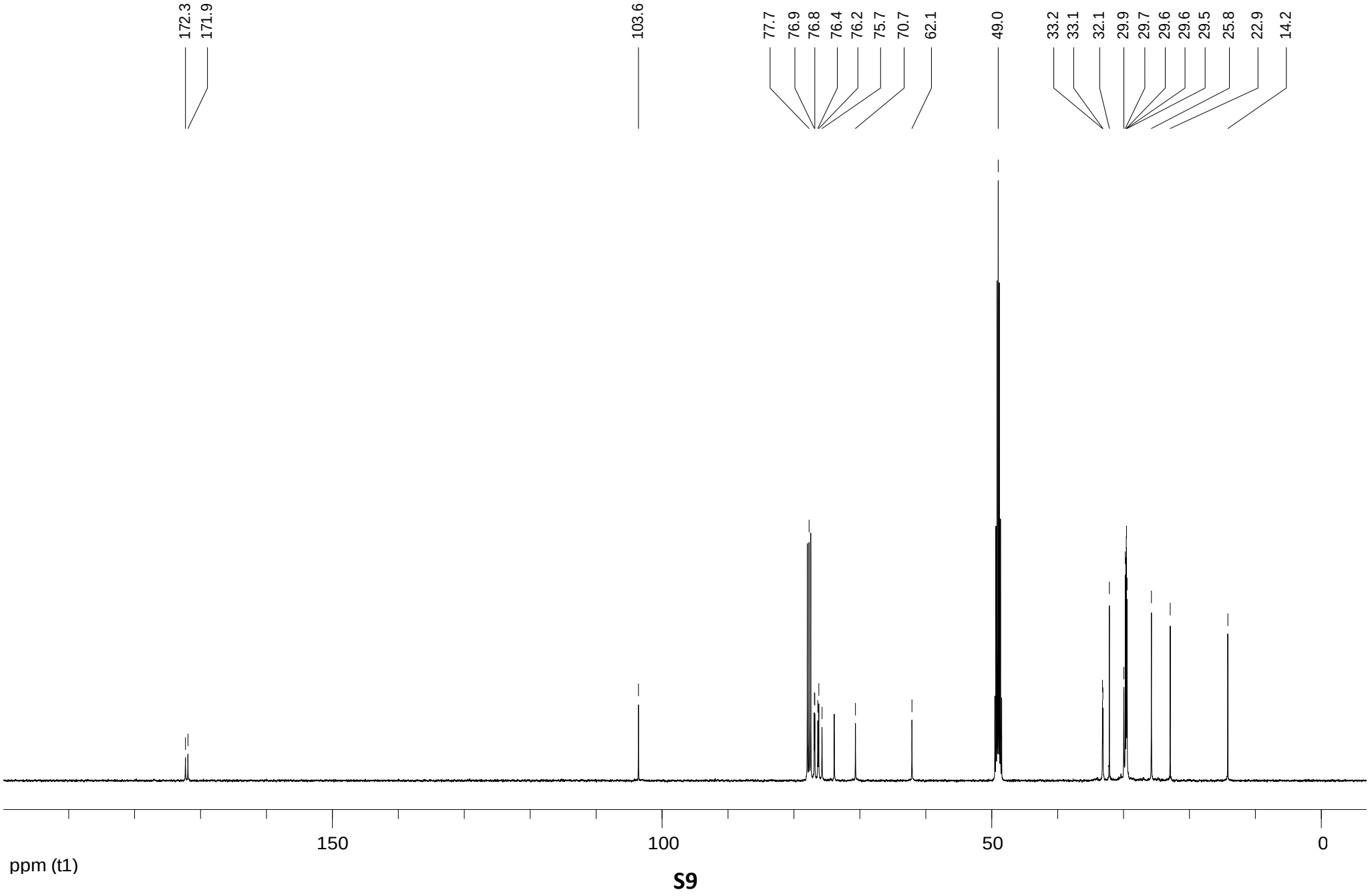
Compound 3a


173.0
172.9
172.6
104.5
77.5
77.3
76.8
76.6
76.2
74.7
73.1
49.0
33.7
33.0
30.6
30.4
30.2
26.6
23.7
14.4
150
100
50
0

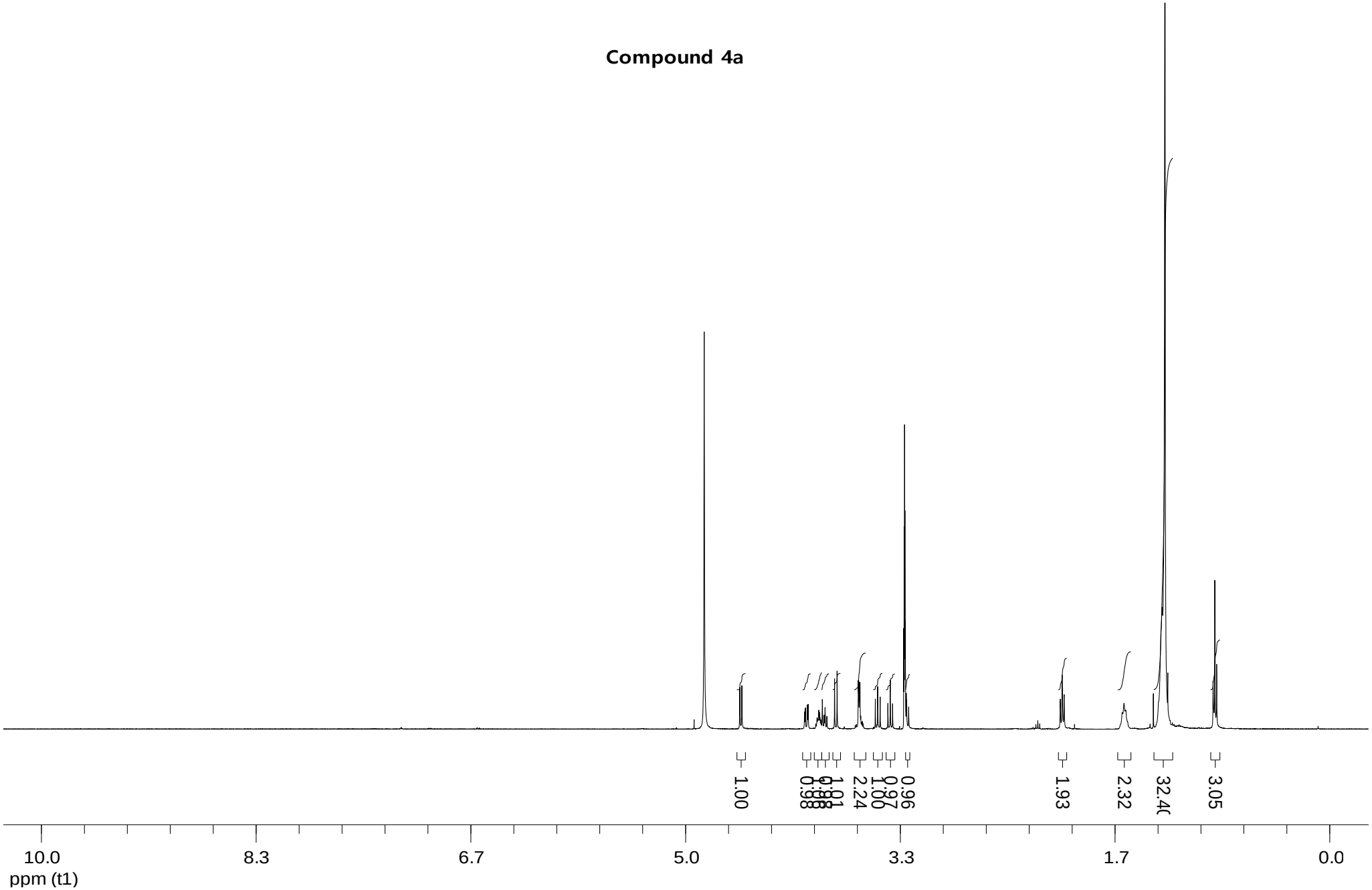
Compound 3b

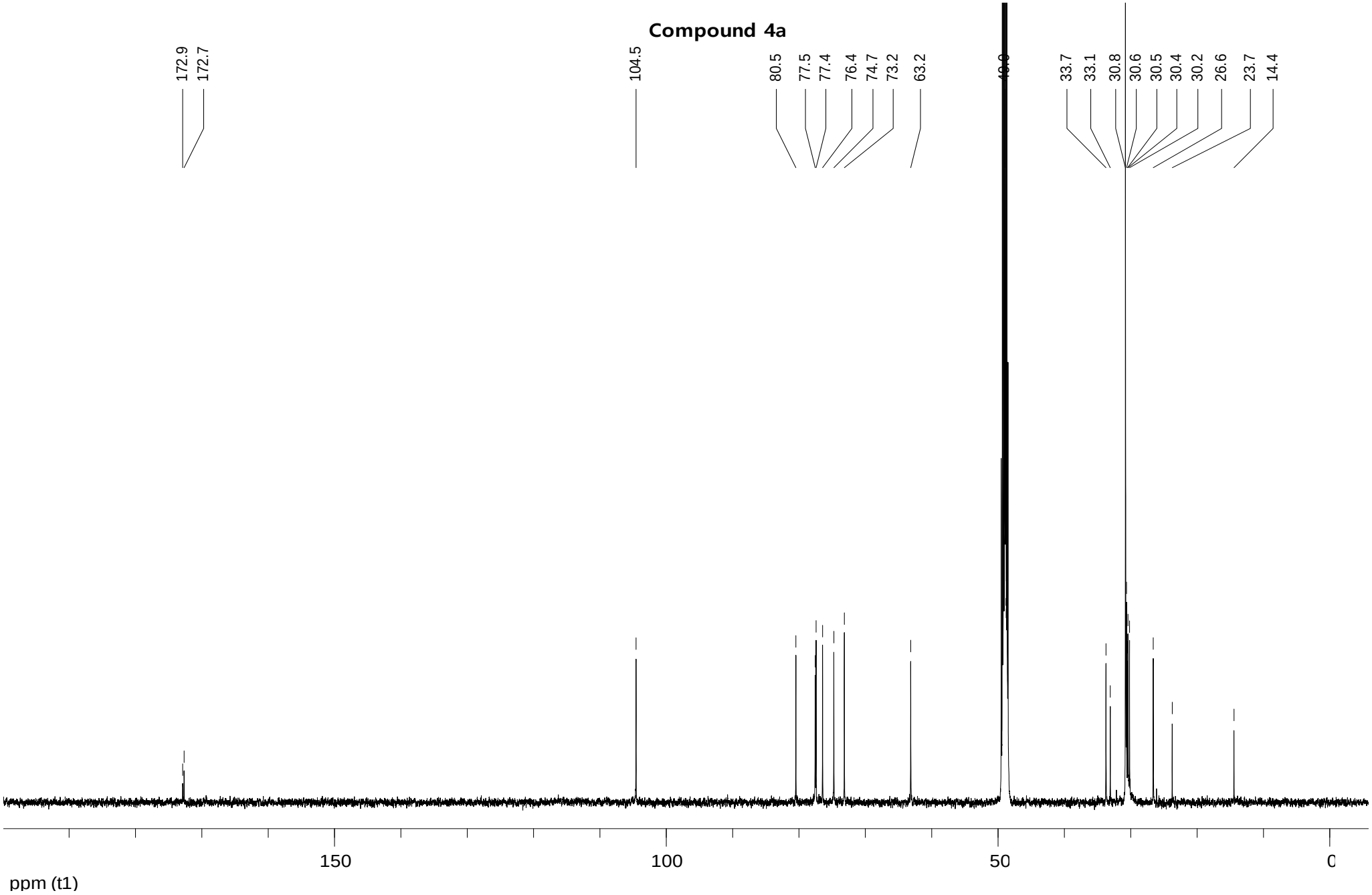

0.03
0.03
1.03
1.04
4.95
1.00
0.96
3.70
3.75
4.29
31.5
7.84
10.0
8.3
6.7
5.0
3.3
1.7
ppm (t1)

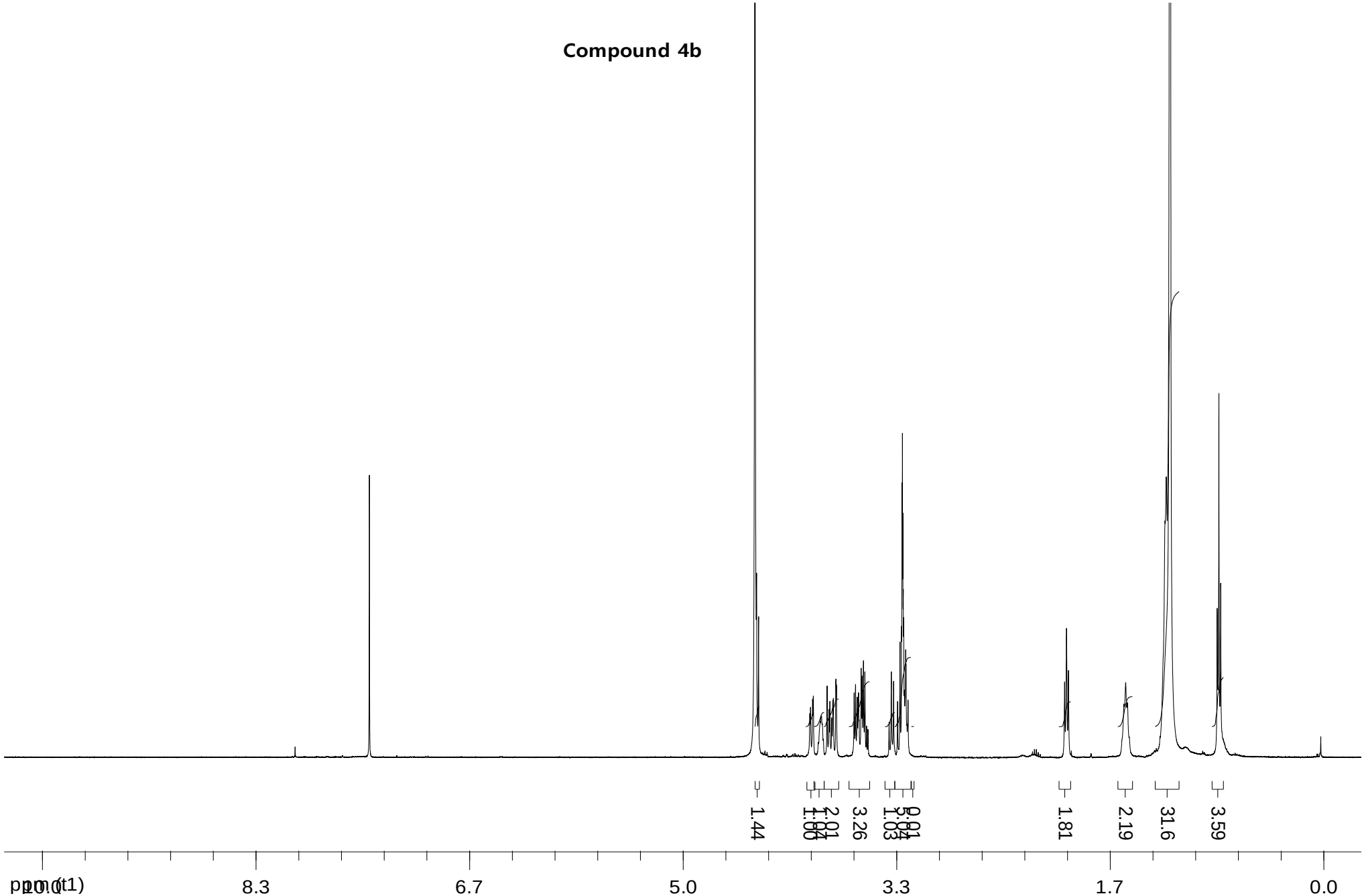
Compound 3b


172.3
171.9
103.6
77.7
76.9
76.8
76.4
76.2
75.7
70.7
62.1
49.0
33.2
33.1
32.1
29.9
29.7
29.6
29.6
29.5
25.8
22.9
14.2
150
100
50
0
ppm (t1)

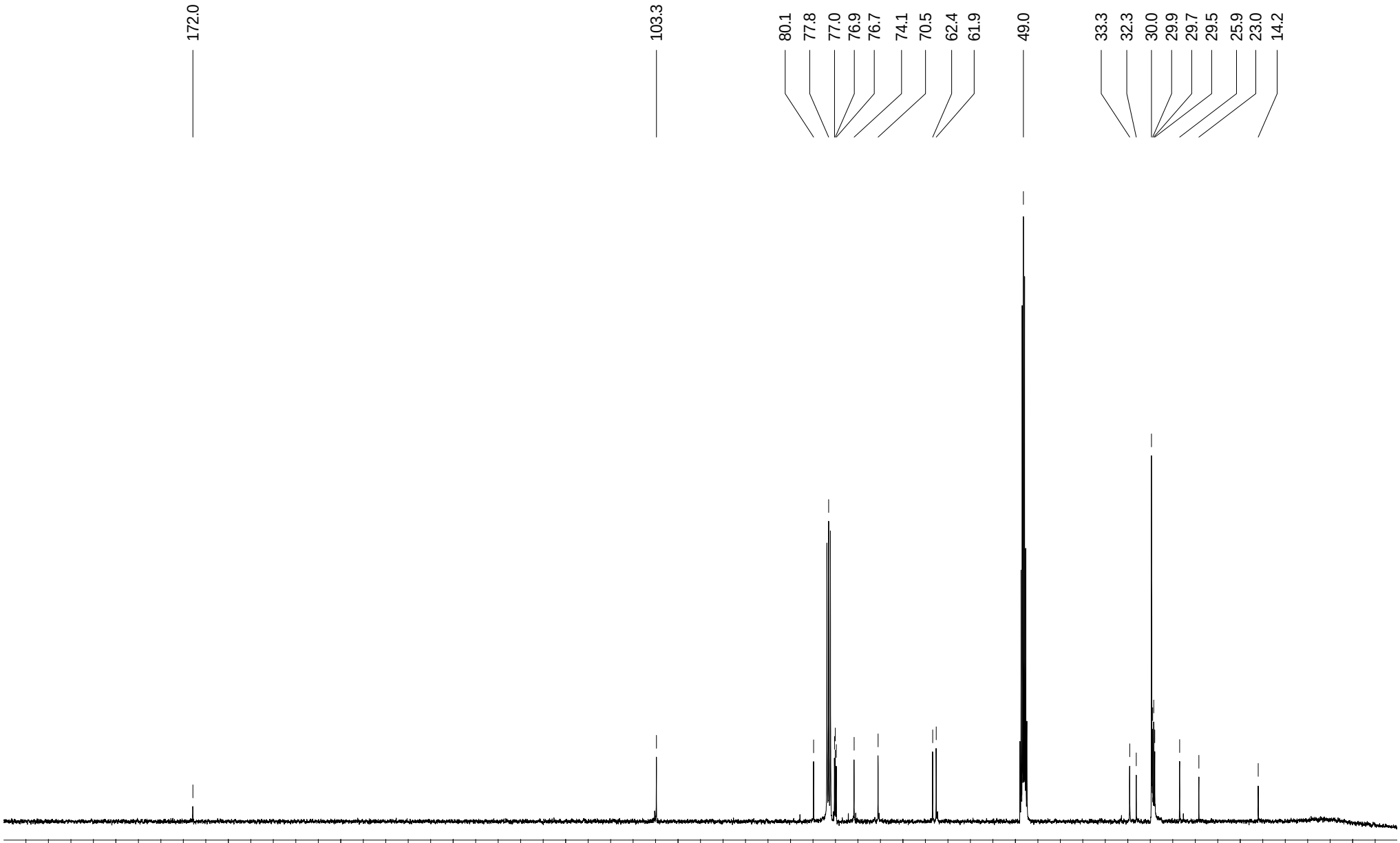
Compound 4a

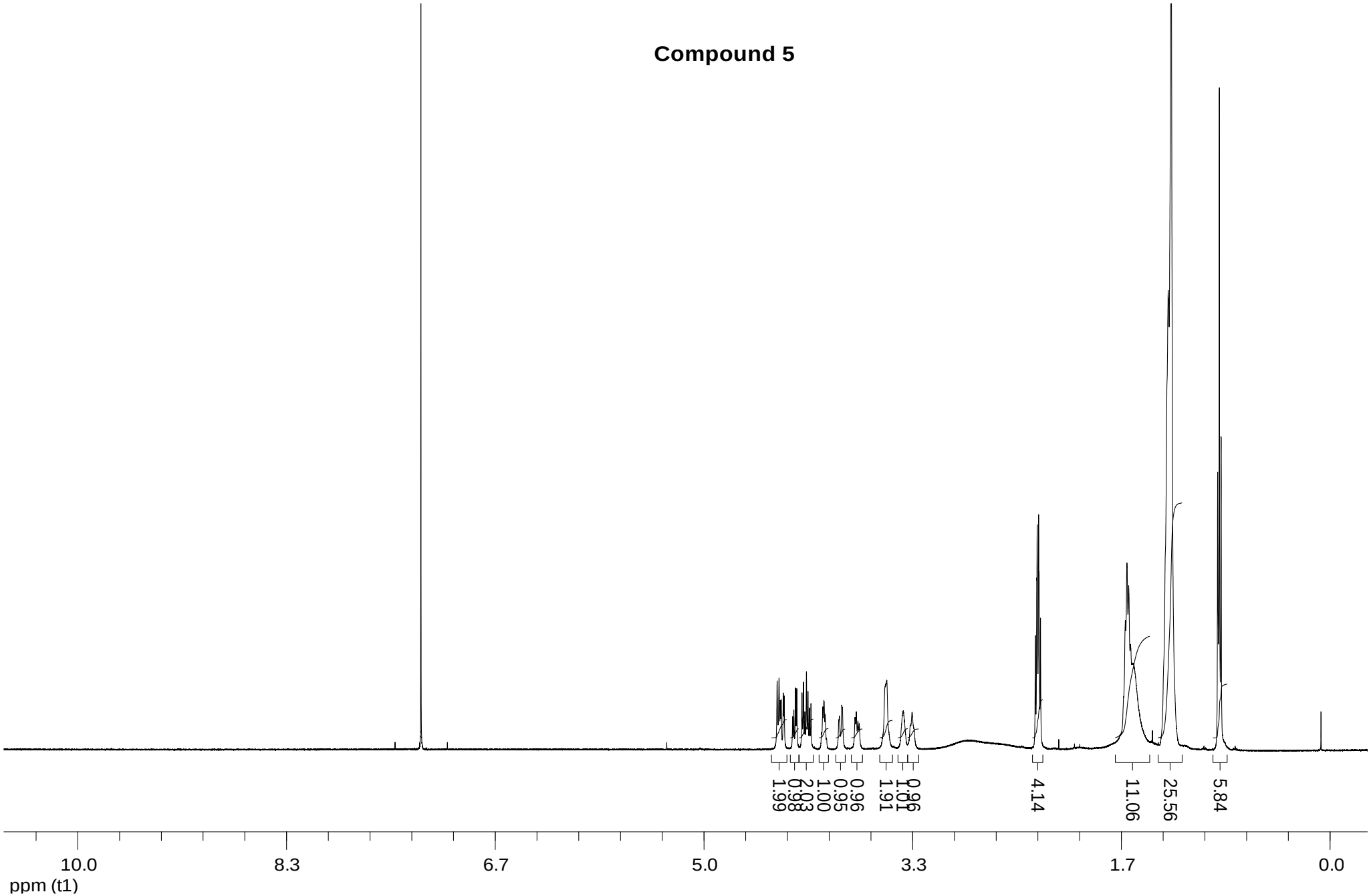

1.00
0.98
0.96
2.24
1.00
0.97
0.96
1.93
2.32
32.4(
3.05
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)


Compound 4a
172.9
172.7
104.5
80.5
77.5
77.4
76.4
74.7
73.2
63.2
40.0
33.7
33.1
30.8
30.6
30.5
30.4
30.2
26.6
23.7
14.4
150
100
50
0
ppm (t1)

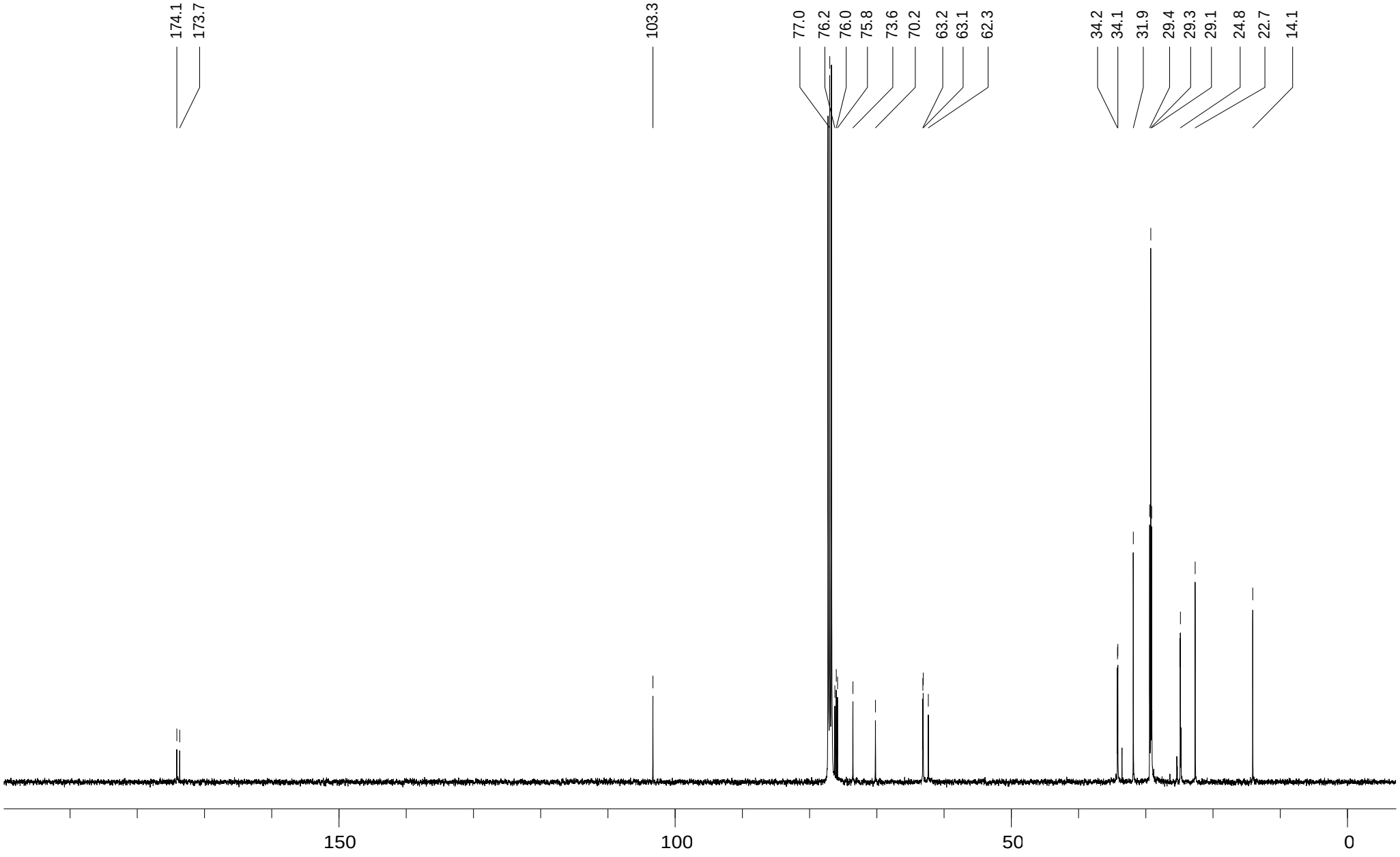

Compound 4b
1.44
1.00
2.01
1.87
3.26
1.03
5.04
0.91
1.81
2.19
31.6
3.59
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

Compound 4b

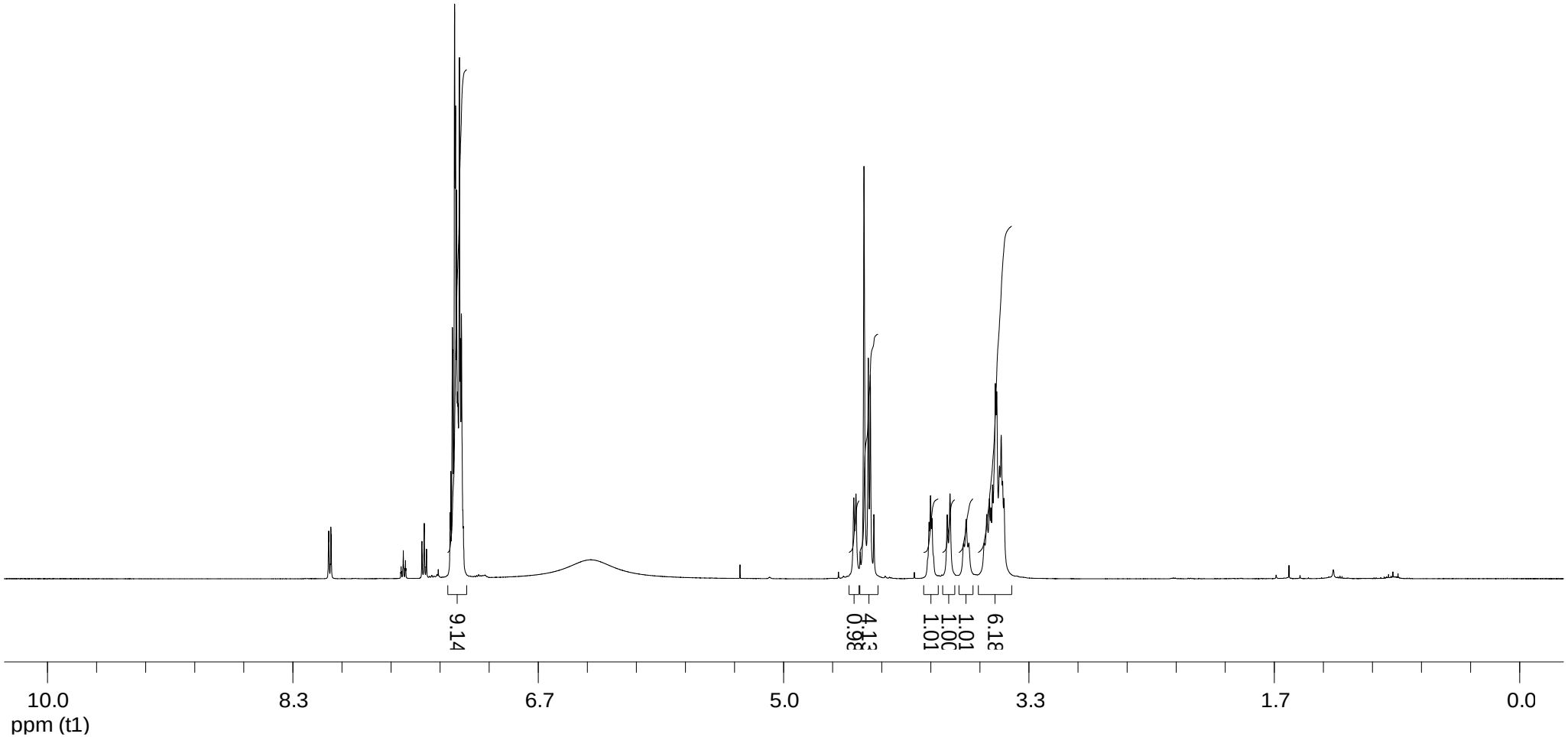

172.0
103.3
80.1
77.8
77.0
76.9
76.7
74.1
70.5
62.4
61.9
49.0
33.3
32.3
30.0
29.9
29.7
29.5
25.9
23.0
14.2
ppm (t1)
183
167
150
133
117
100
83
67
50
33
17
0


Compound 5
1.99
0.98
2.03
1.00
0.95
0.96
1.91
1.01
0.96
4.14
11.06
25.56
5.84
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

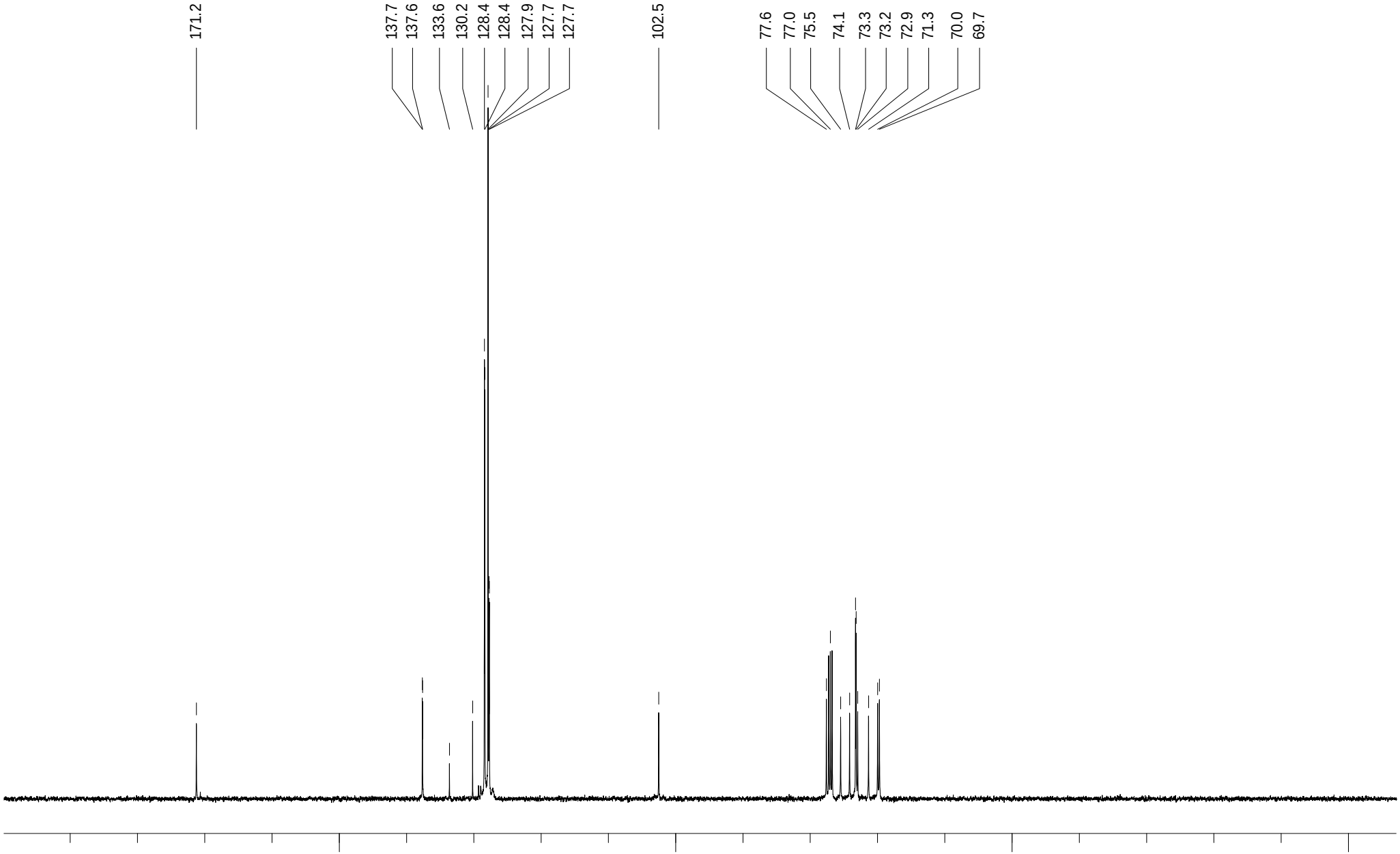
Compound 5


174.1
173.7
103.3
77.0
76.2
76.0
75.8
73.6
70.2
63.2
63.1
62.3
34.2
34.1
31.9
29.4
29.3
29.1
24.8
22.7
14.1
150
100
50
0
ppm (t1)

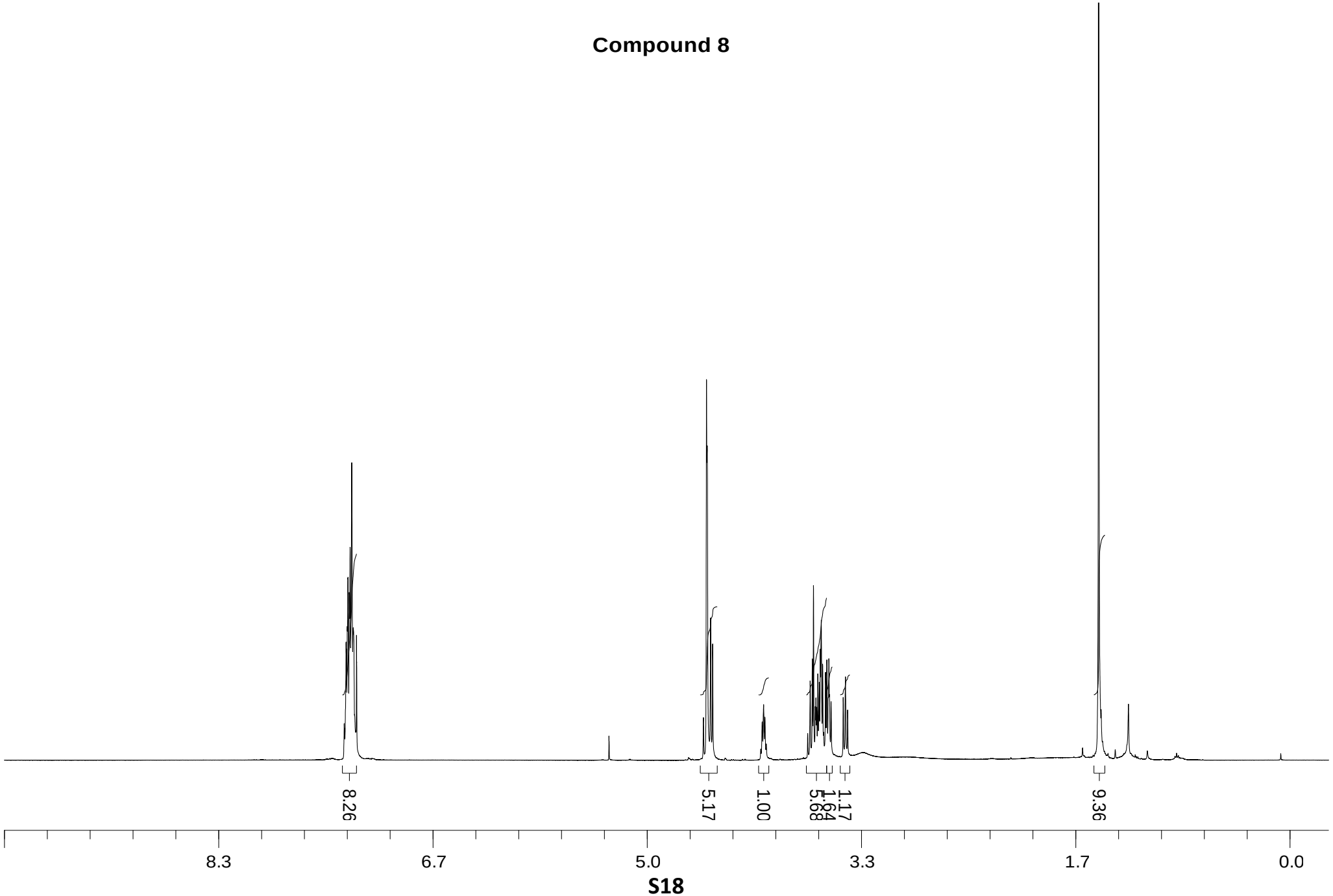
Compound 7



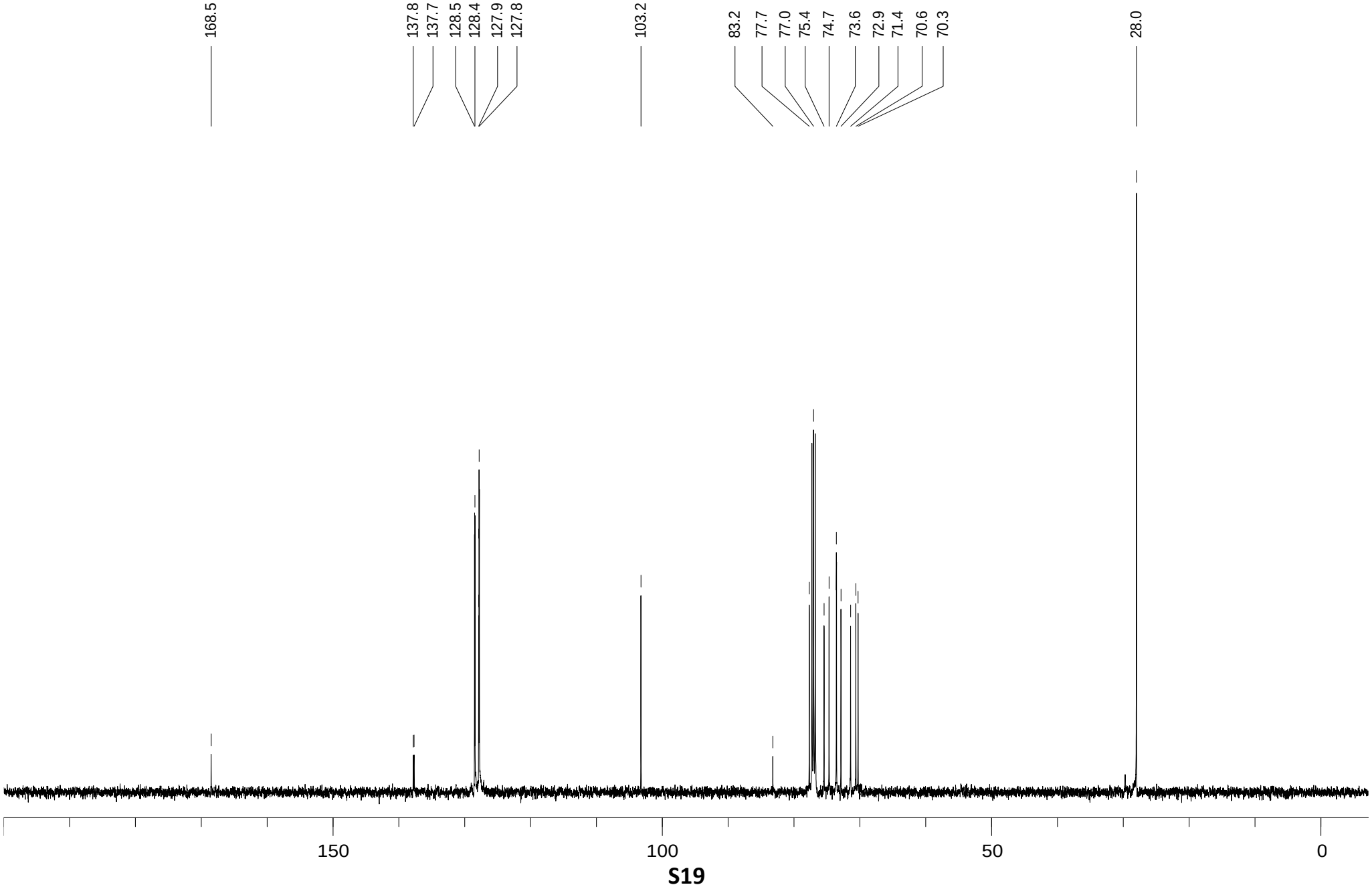
Compound 7


171.2
137.7
137.6
133.6
130.2
128.4
128.4
127.9
127.7
127.7
102.5
77.6
77.0
75.5
74.1
73.3
73.2
72.9
71.3
70.0
69.7
150
100
50
0

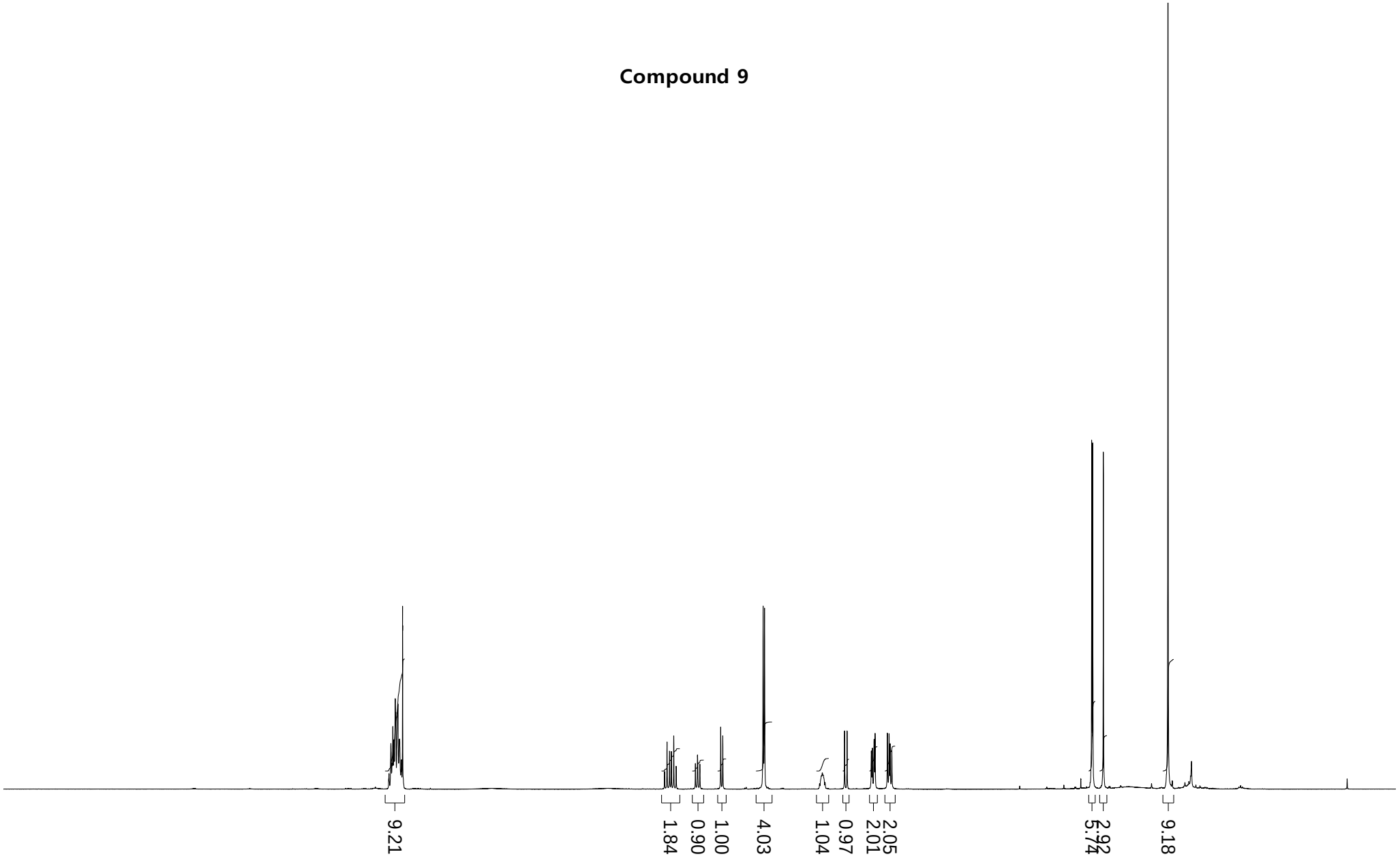
Compound 8



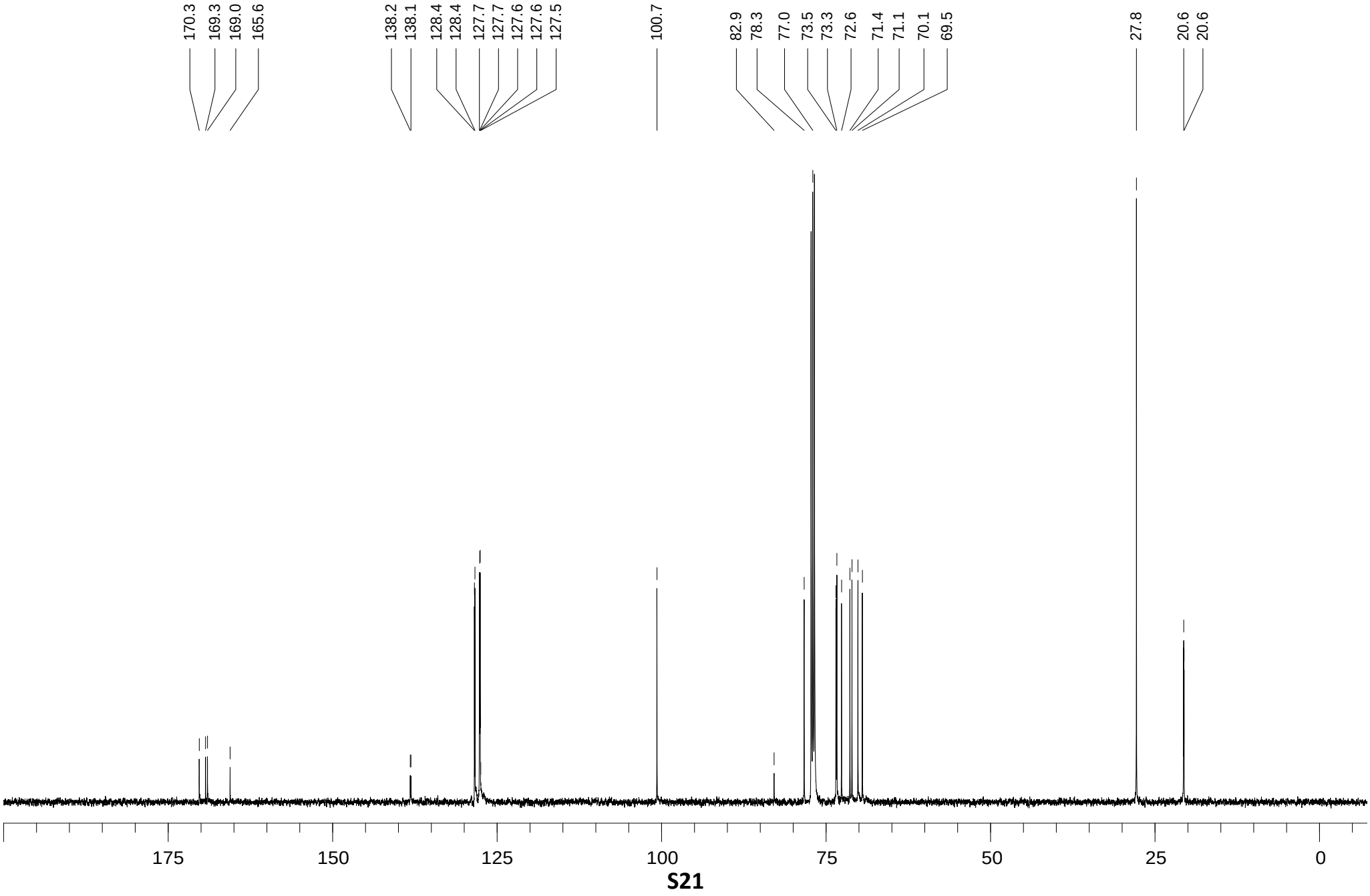
Compound 8


168.5
137.8
137.7
128.5
128.4
127.9
127.8
103.2
83.2
77.7
77.0
75.4
74.7
73.6
72.9
71.4
70.6
70.3
28.0
150
100
50
0

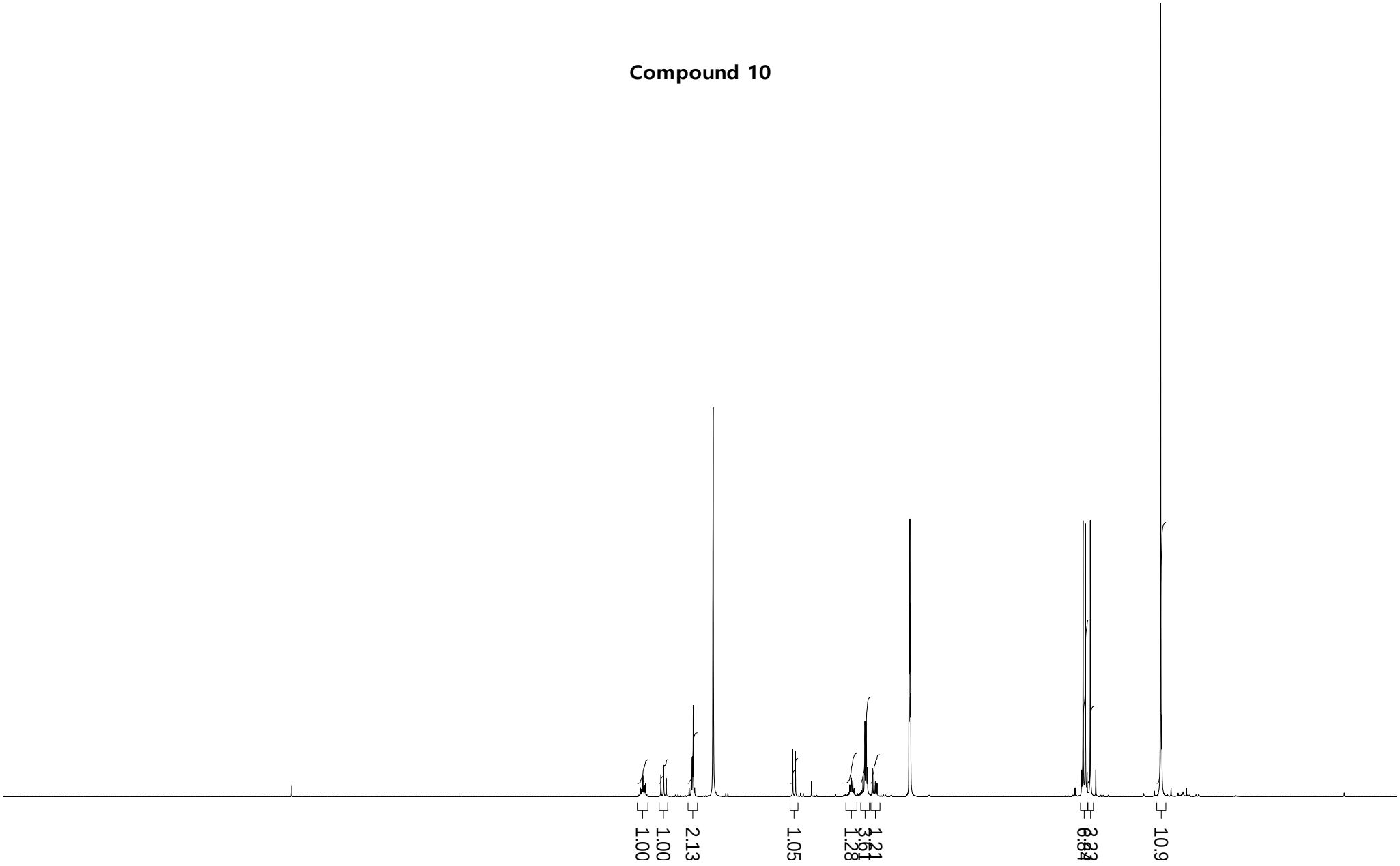
Compound 9

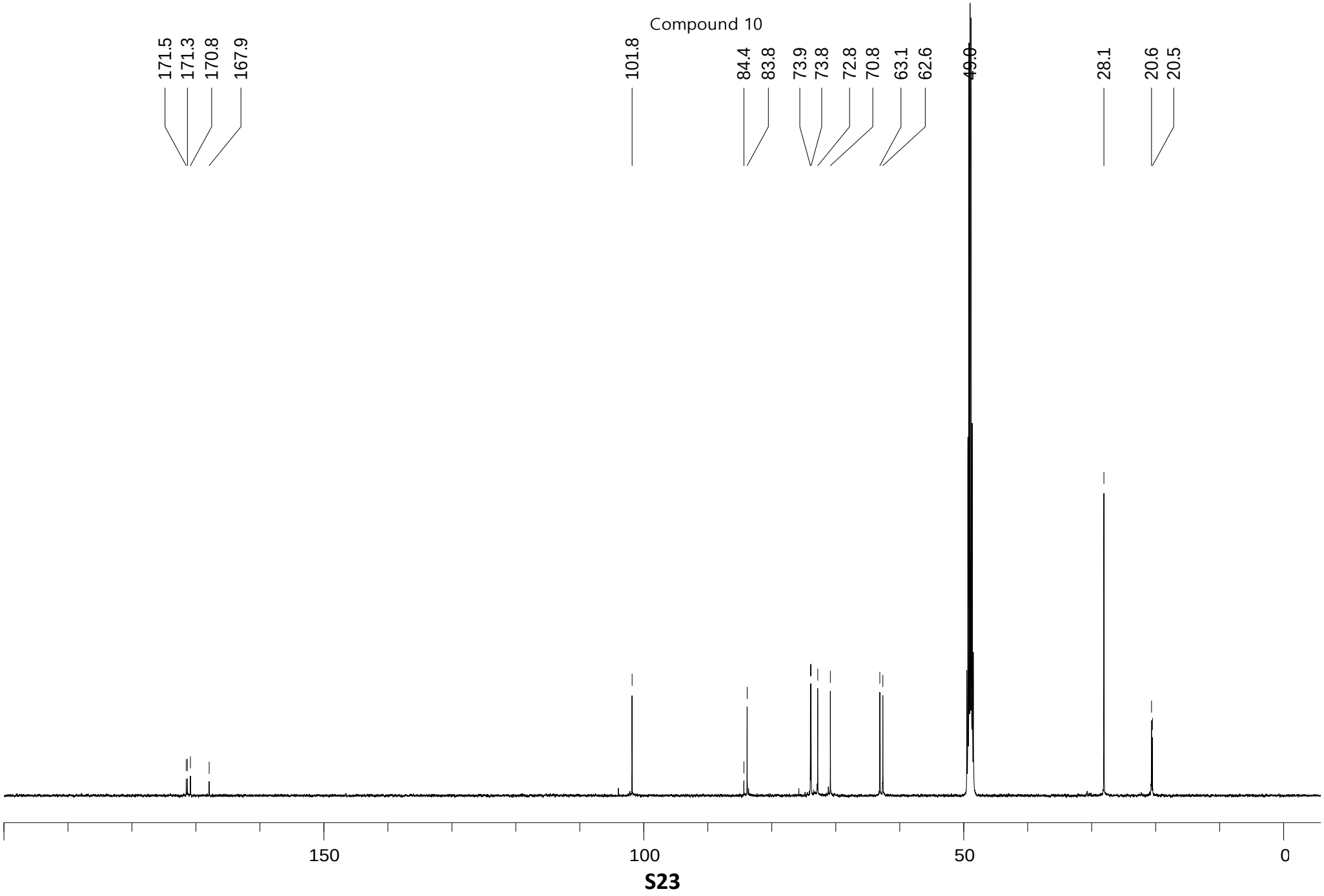

9.21
1.84
0.90
1.00
4.03
1.04
0.97
2.01
2.05
5.74
2.92
9.18
10.0
8.3
6.7
5.0
3.3
1.7
0.0

Compound 9

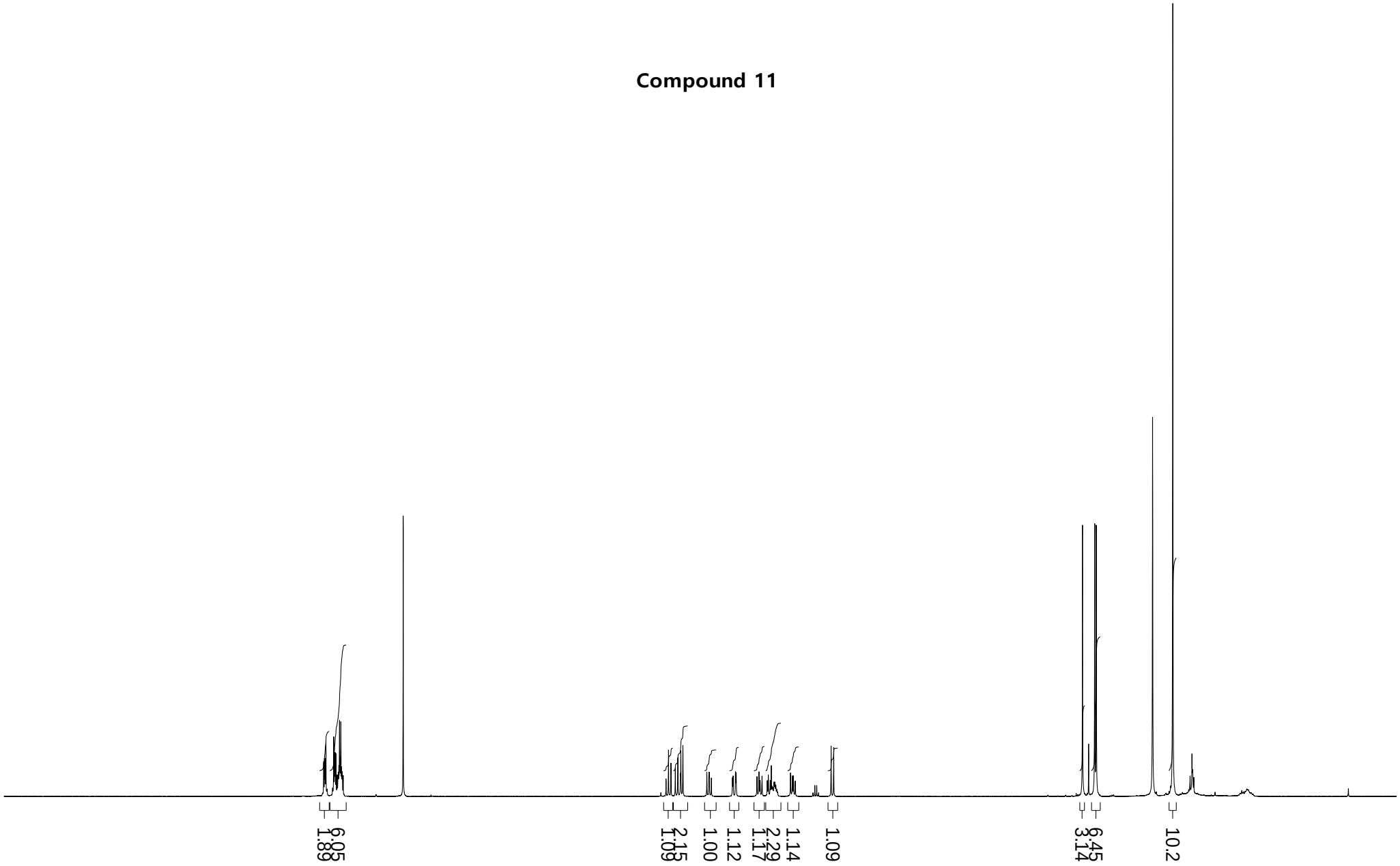

170.3
169.3
169.0
165.6
138.2
138.1
128.4
128.4
127.7
127.7
127.6
127.6
127.5
100.7
82.9
78.3
77.0
73.5
73.3
72.6
71.4
71.1
70.1
69.5
27.8
20.6
20.6
175
150
125
100
75
50
25
0

Compound 10

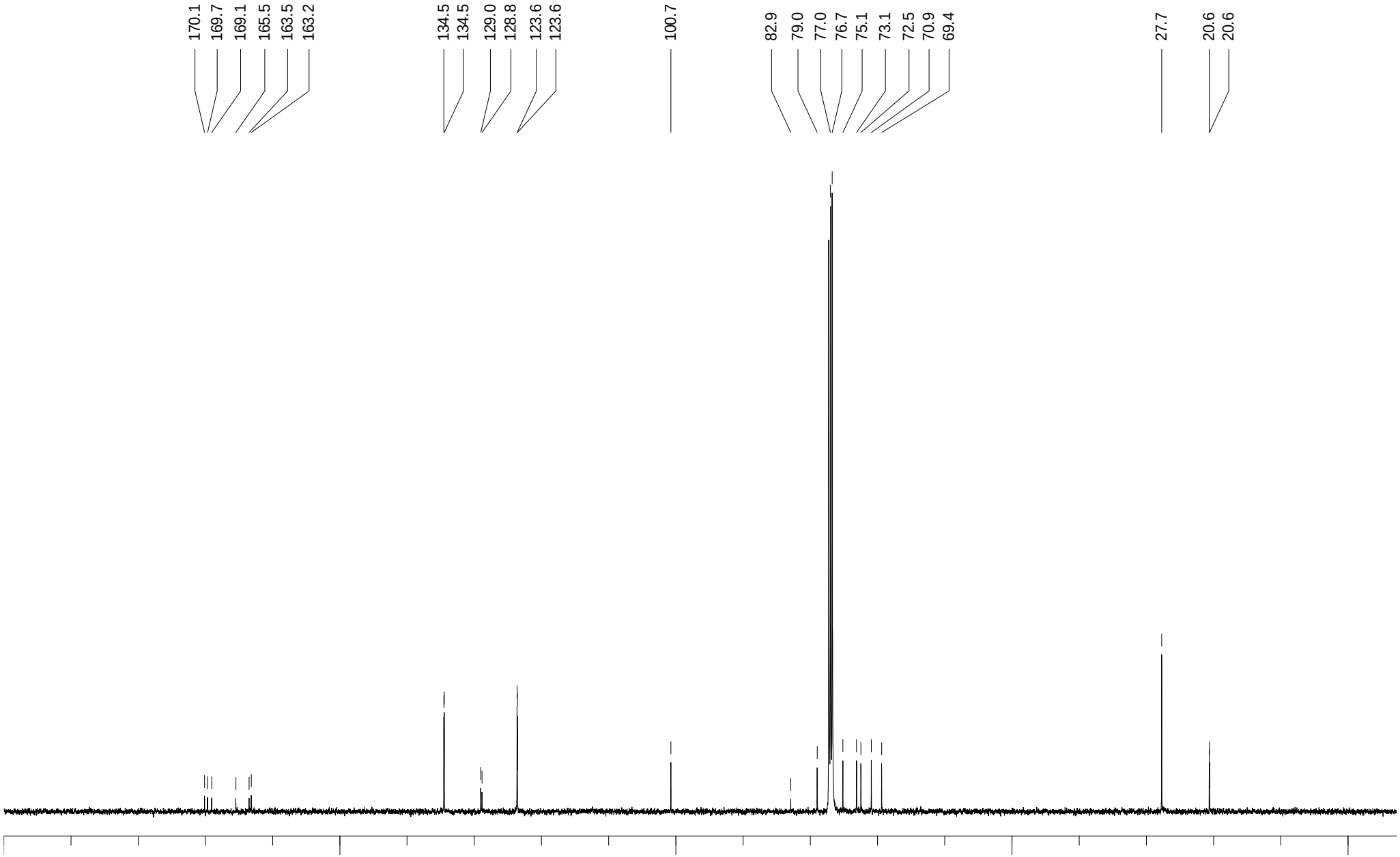



Compound 10
171.5
171.3
170.8
167.9
101.8
84.4
83.8
73.9
73.8
72.8
70.8
63.1
62.6
49.0
28.1
20.6
20.5
150
100
50
0

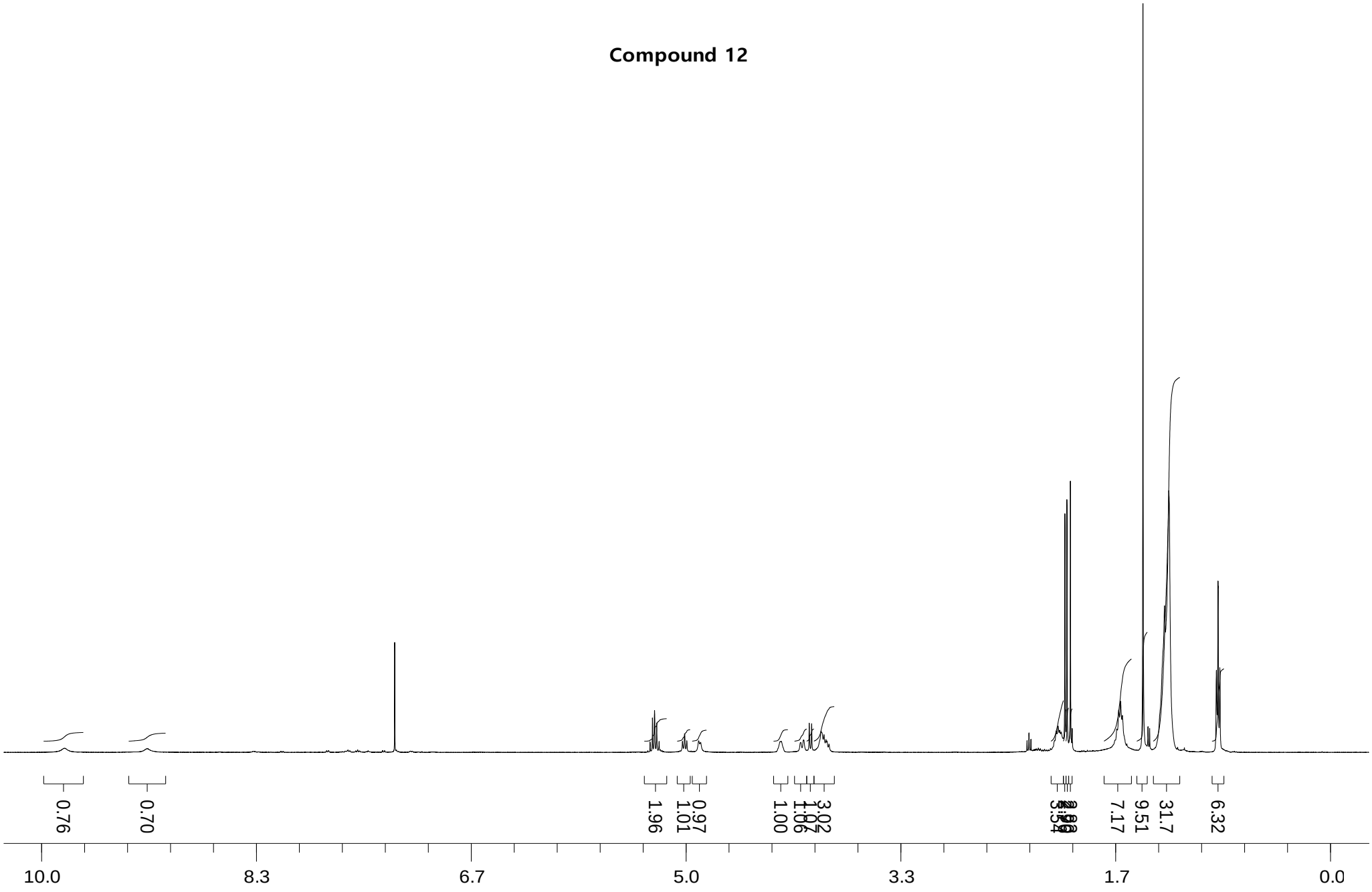
Compound 11


1.89
6.05
1.09
2.15
1.00
1.12
1.17
2.29
1.14
1.09
3.14
6.45
10.2
10.0
8.3
6.7
5.0
3.3
1.7
0.0

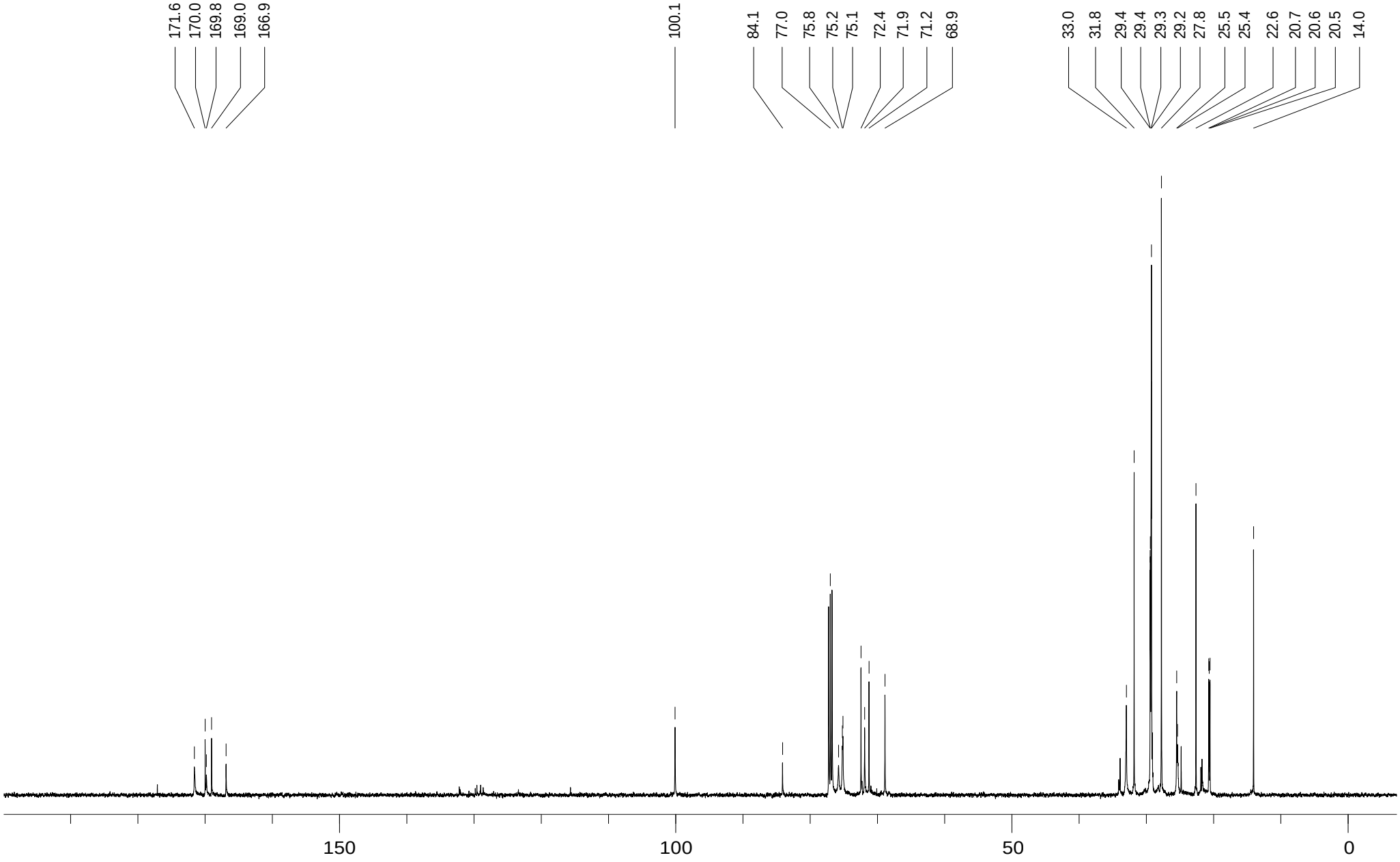
Compound 11

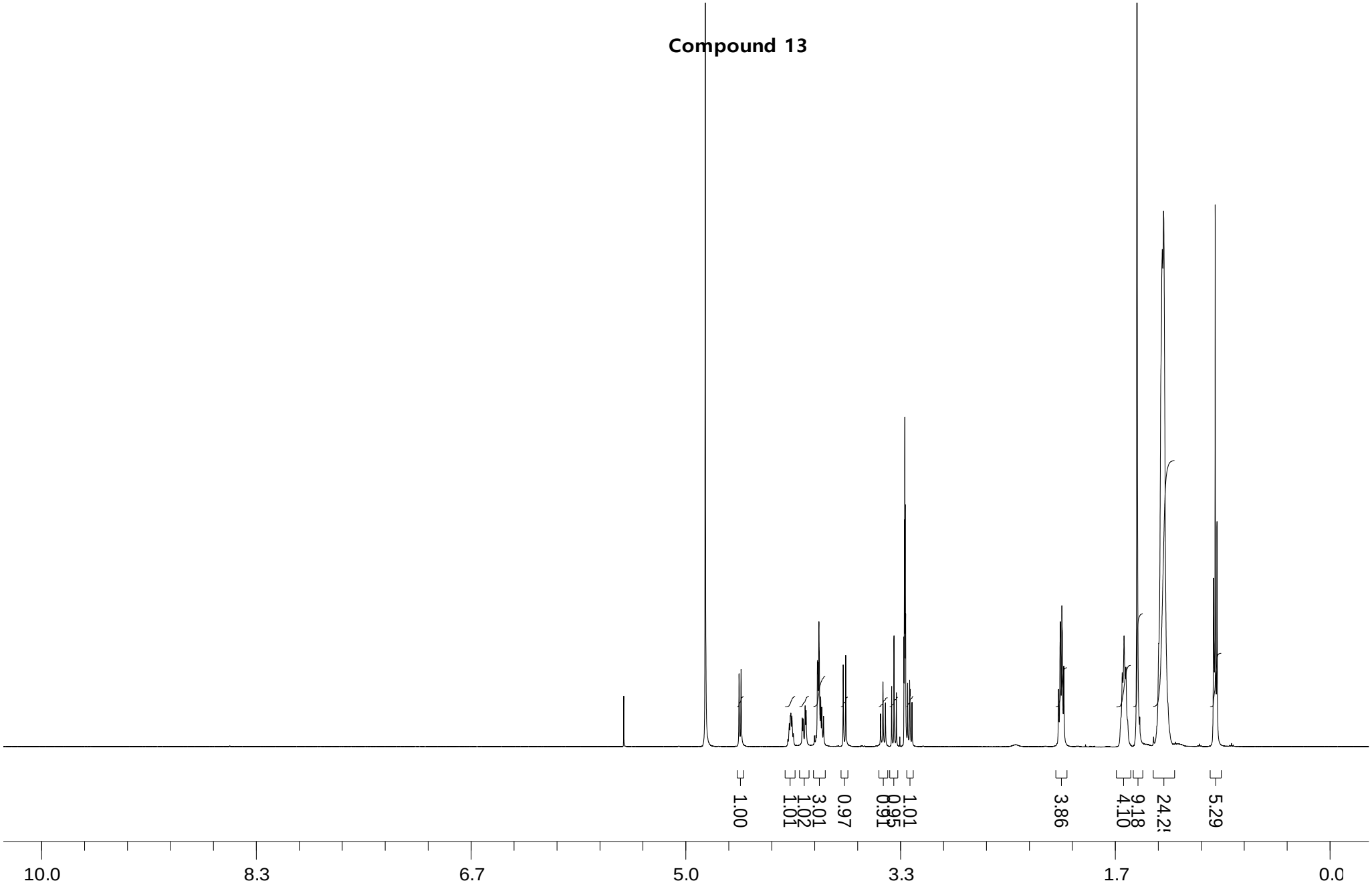

170.1
169.7
169.1
165.5
163.5
163.2
134.5
134.5
129.0
128.8
123.6
123.6
100.7
82.9
79.0
77.0
76.7
75.1
73.1
72.5
70.9
69.4
27.7
20.6
20.6
150
100
50
0

Compound 12

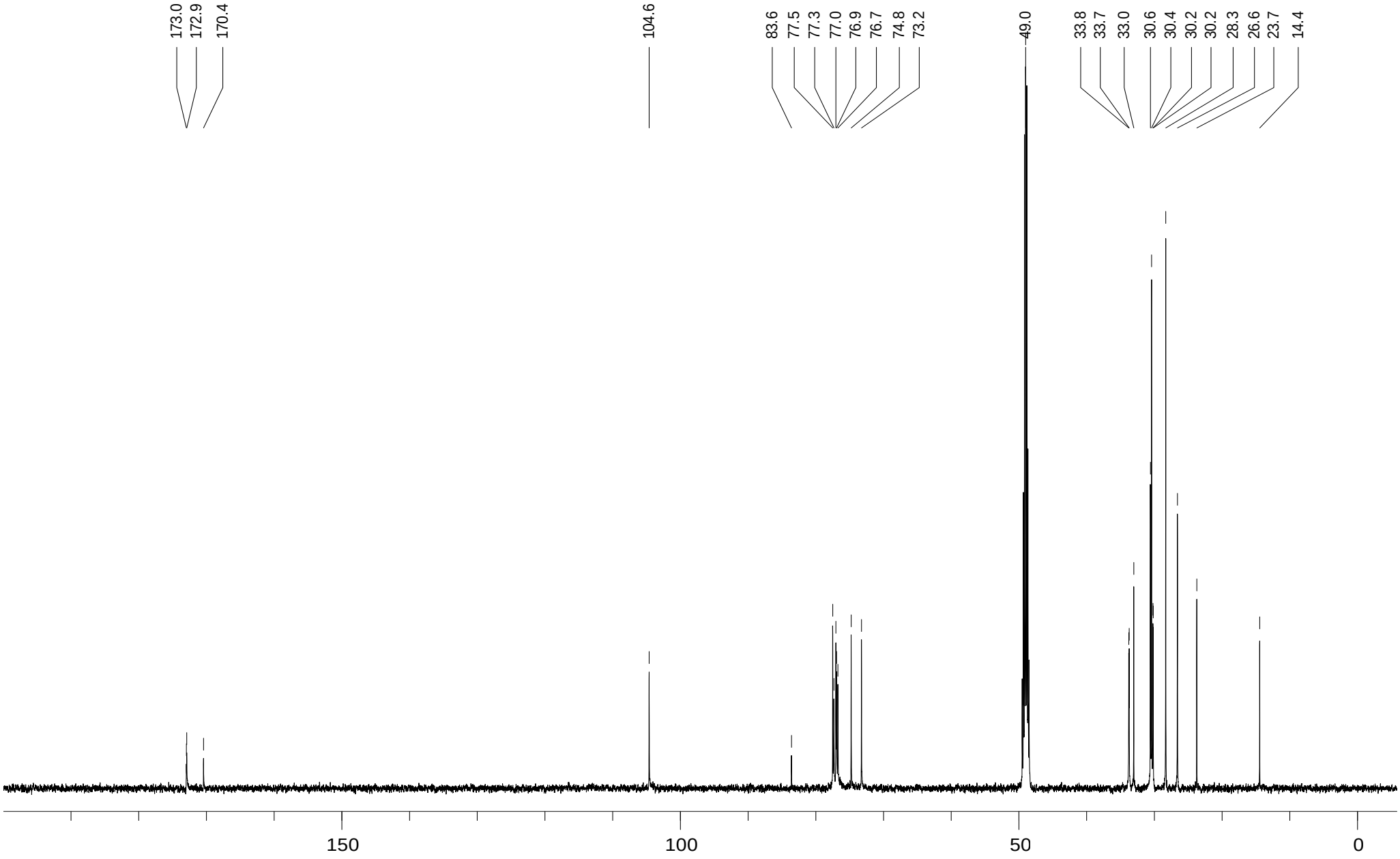

0.76
0.70
1.96
1.01
0.97
1.00
1.06
3.02
7.17
9.51
31.7
6.32
10.0
8.3
6.7
5.0
3.3
1.7
0.0

Compound 12

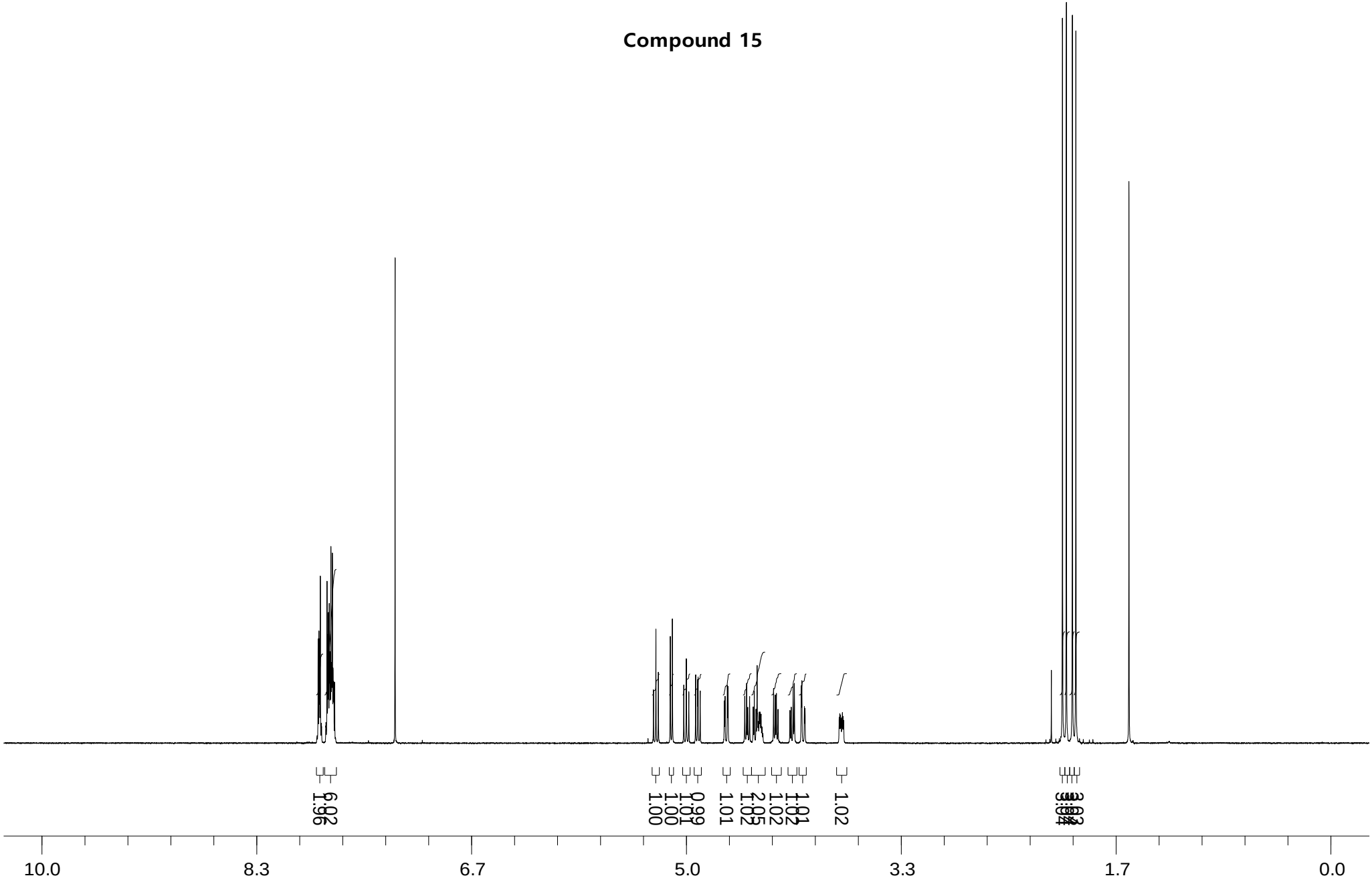

171.6
170.0
169.8
169.0
166.9
100.1
84.1
77.0
75.8
75.2
75.1
72.4
71.9
71.2
68.9
33.0
31.8
29.4
29.4
29.3
29.2
27.8
25.5
25.4
22.6
20.7
20.6
20.5
14.0
150
100
50
0


Compound 13
1.00
1.01
1.02
3.01
0.97
0.91
0.95
1.01
3.86
4.10
9.18
24.2
5.29
10.0
8.3
6.7
5.0
3.3
1.7
0.0

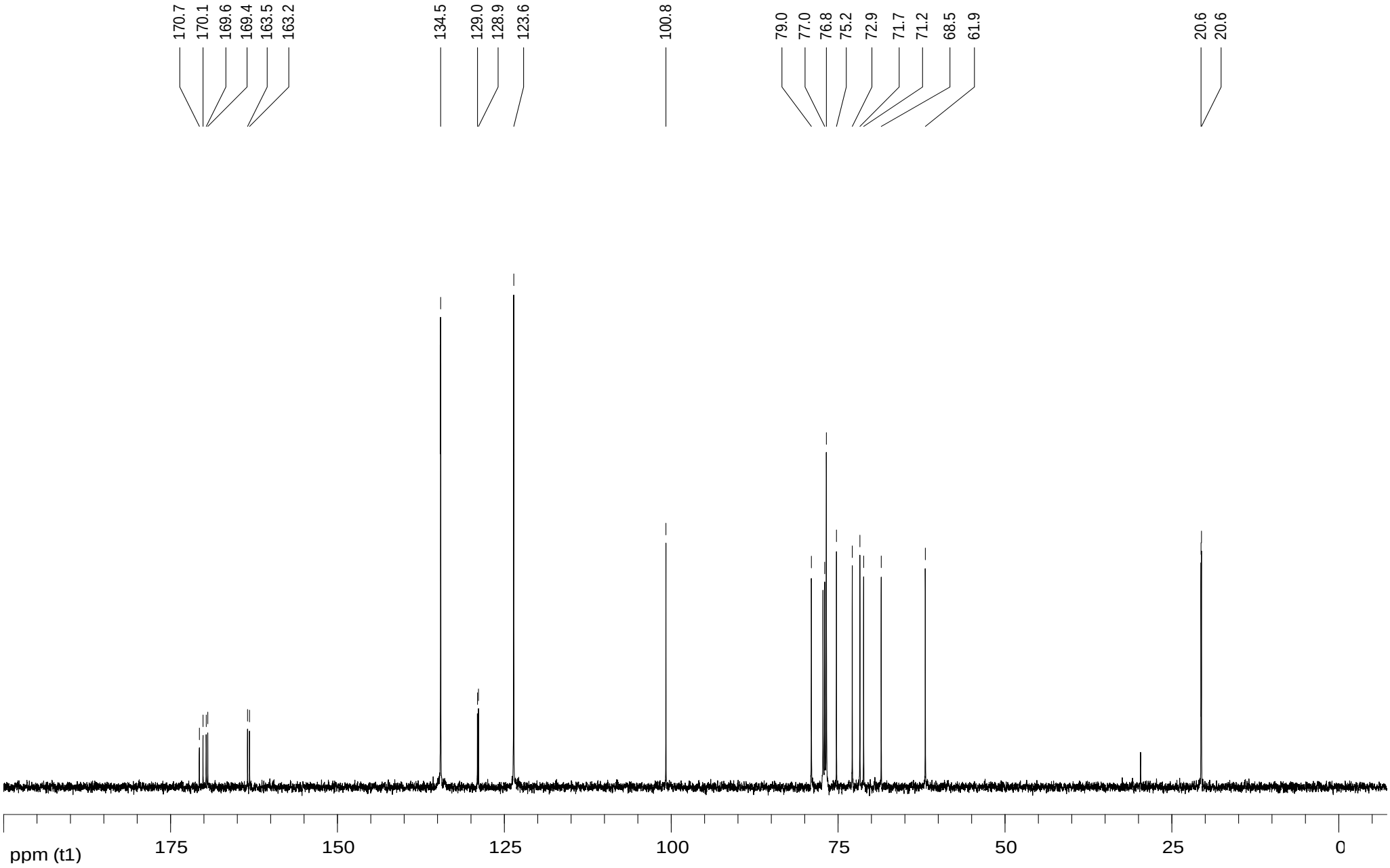
Compound 13


173.0
172.9
170.4
104.6
83.6
77.5
77.3
77.0
76.9
76.7
74.8
73.2
49.0
33.8
33.7
33.0
30.6
30.4
30.2
30.2
28.3
26.6
23.7
14.4
150
100
50
0

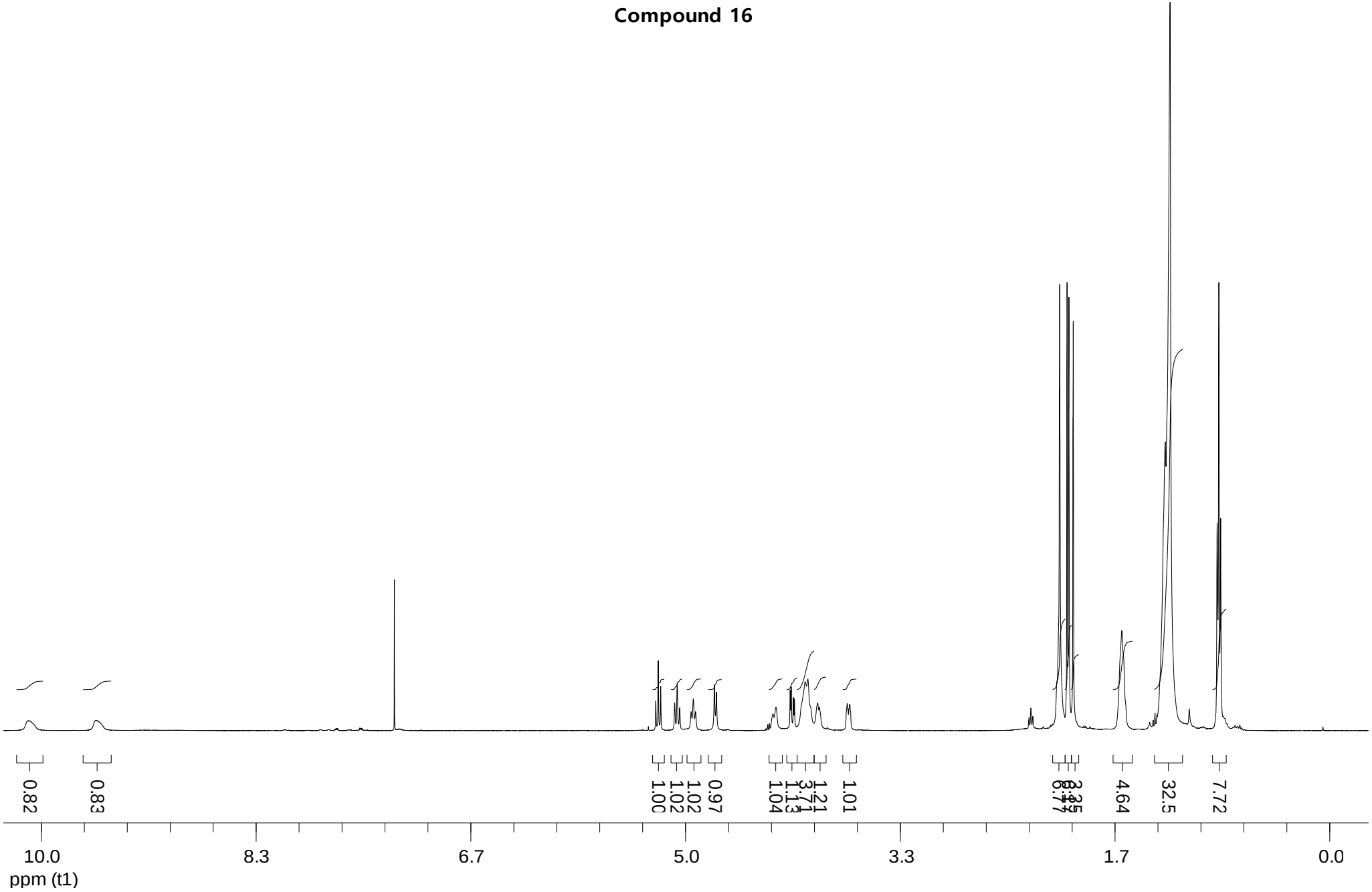
Compound 15


1.96
6.02
1.00
1.00
1.01
0.99
1.01
2.02
2.05
1.02
1.01
1.01
1.02
10.0
8.3
6.7
5.0
3.3
1.7
0.0

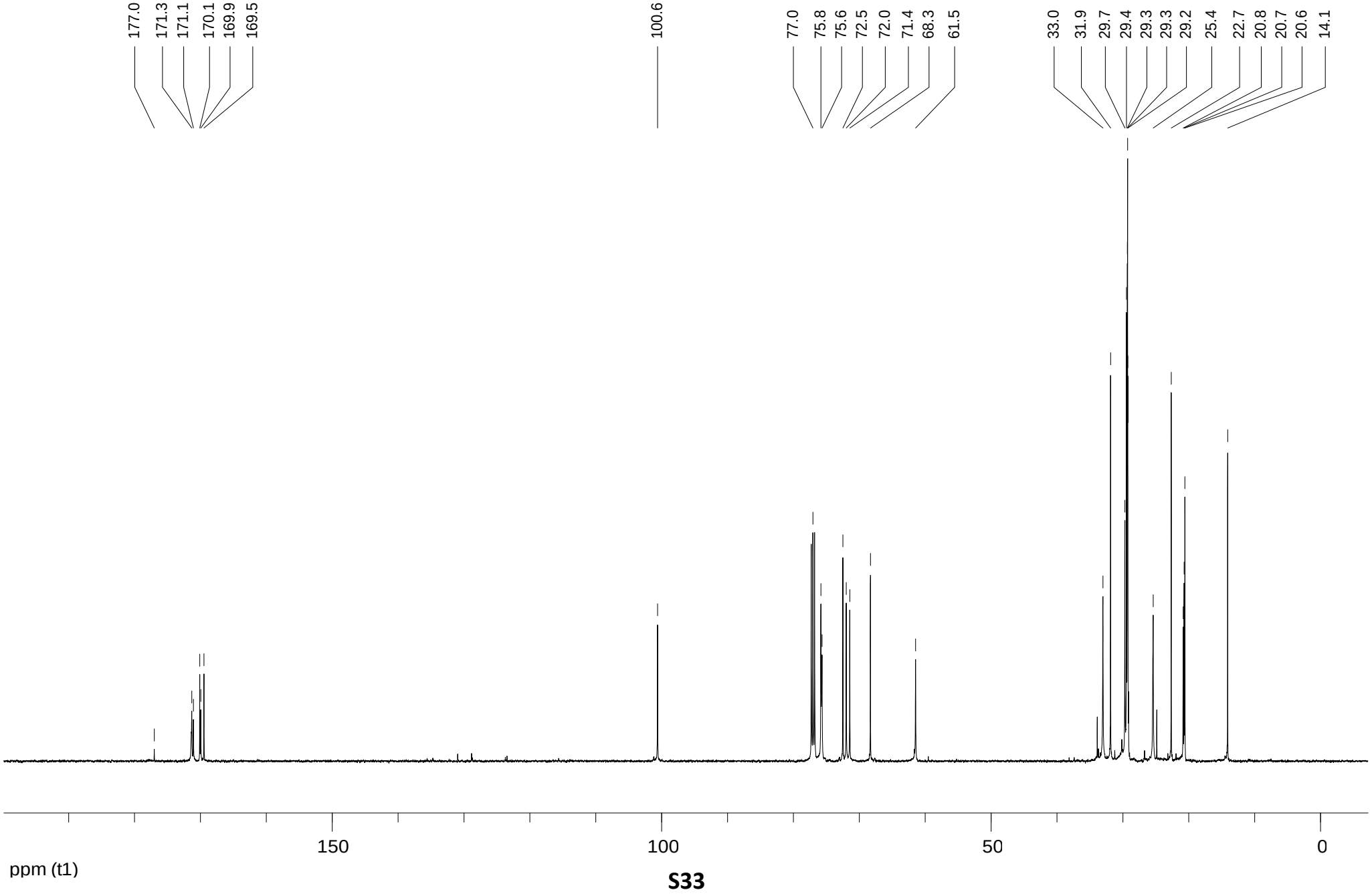
Compound 15


170.7
170.1
169.6
169.4
163.5
163.2
134.5
129.0
128.9
123.6
100.8
79.0
77.0
76.8
75.2
72.9
71.7
71.2
68.5
61.9
20.6
20.6
ppm (t1)
175
150
125
100
75
50
25
0

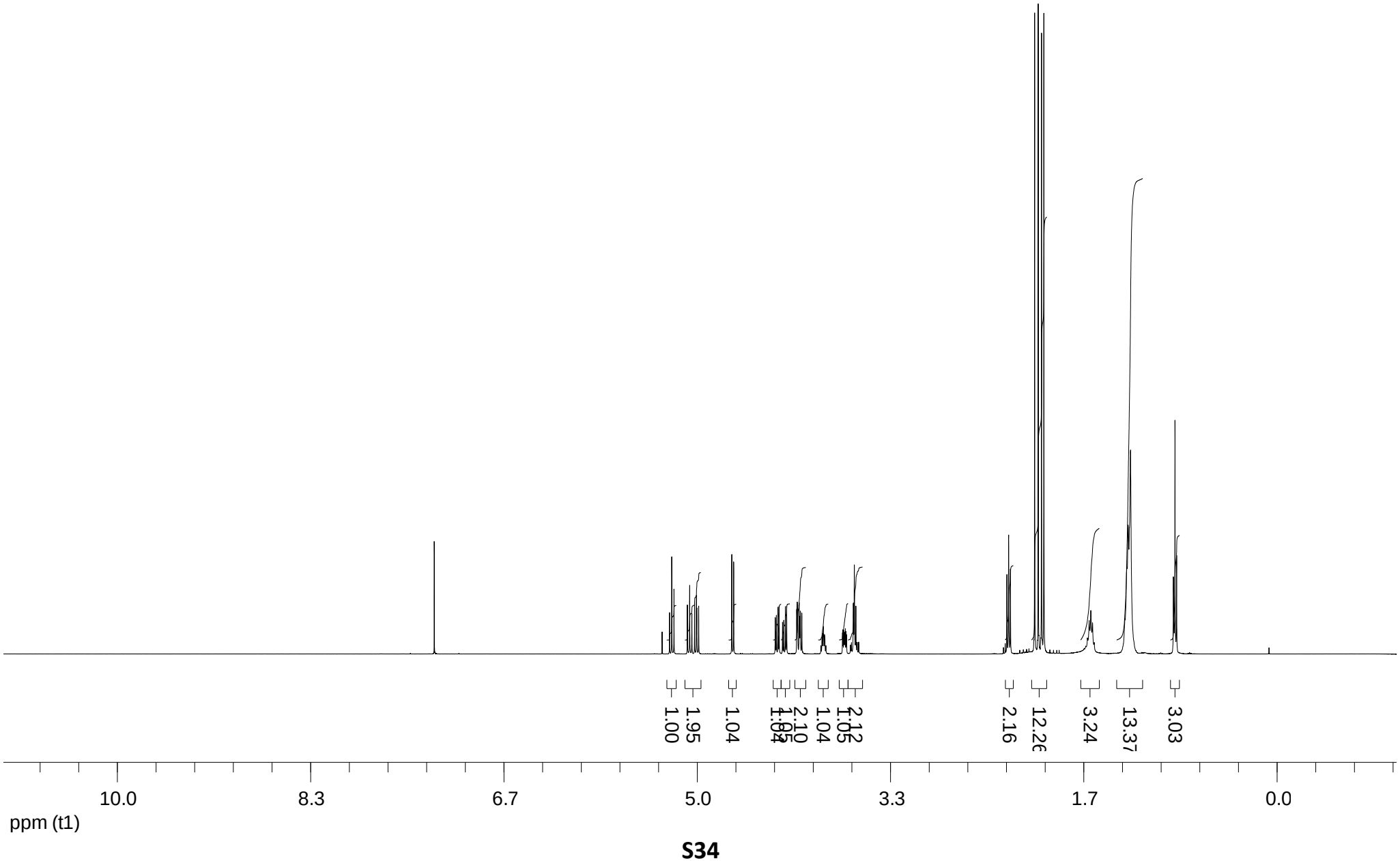
Compound 16


0.82
0.83
1.00
1.02
1.02
0.97
1.04
1.13
1.01
4.64
32.5
7.72
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

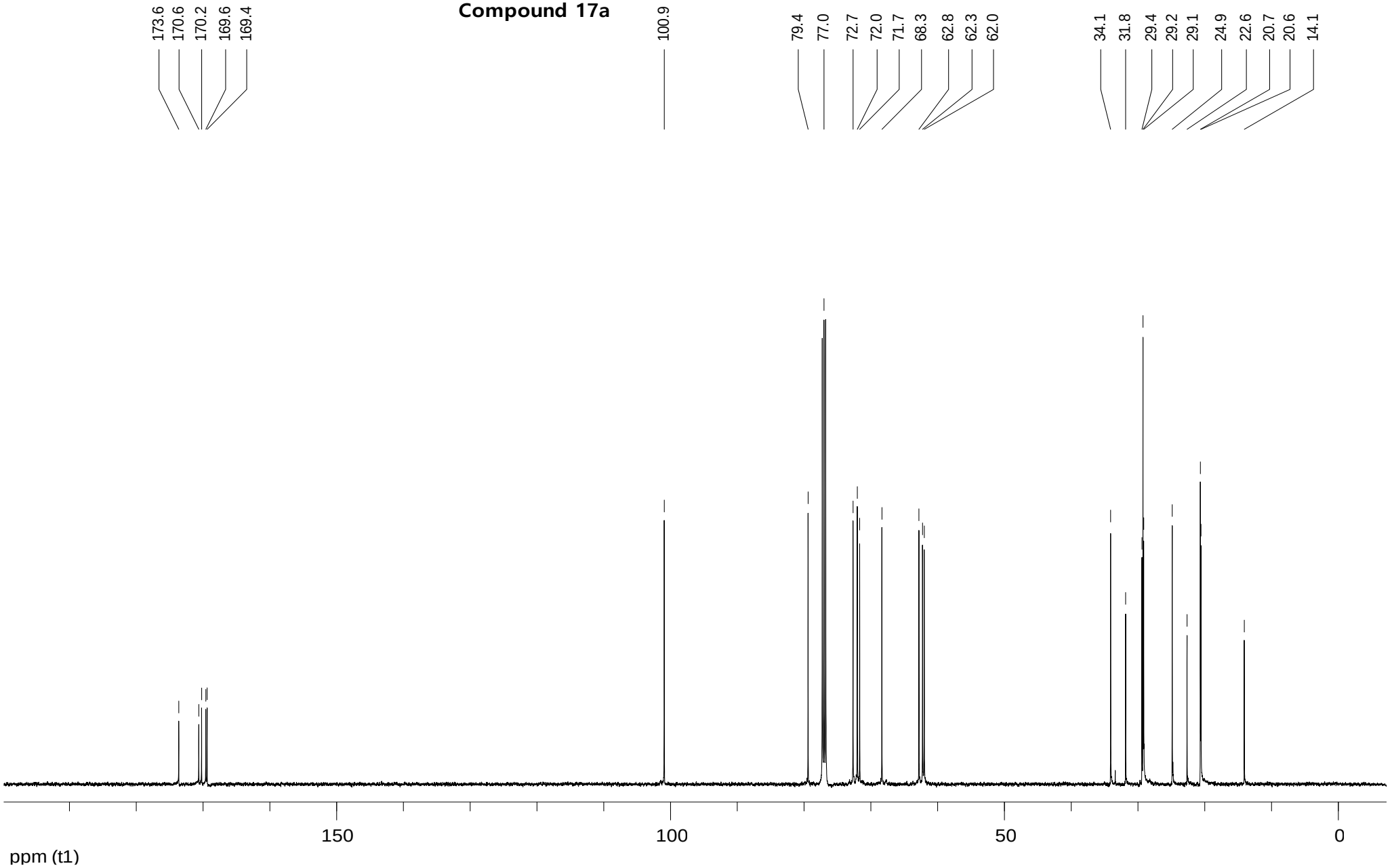
Compound 16


177.0
171.3
171.1
170.1
169.9
169.5
100.6
77.0
75.8
75.6
72.5
72.0
71.4
68.3
61.5
33.0
31.9
29.7
29.4
29.3
29.3
29.2
25.4
22.7
20.8
20.7
20.6
14.1
150
100
50
0
ppm (t1)

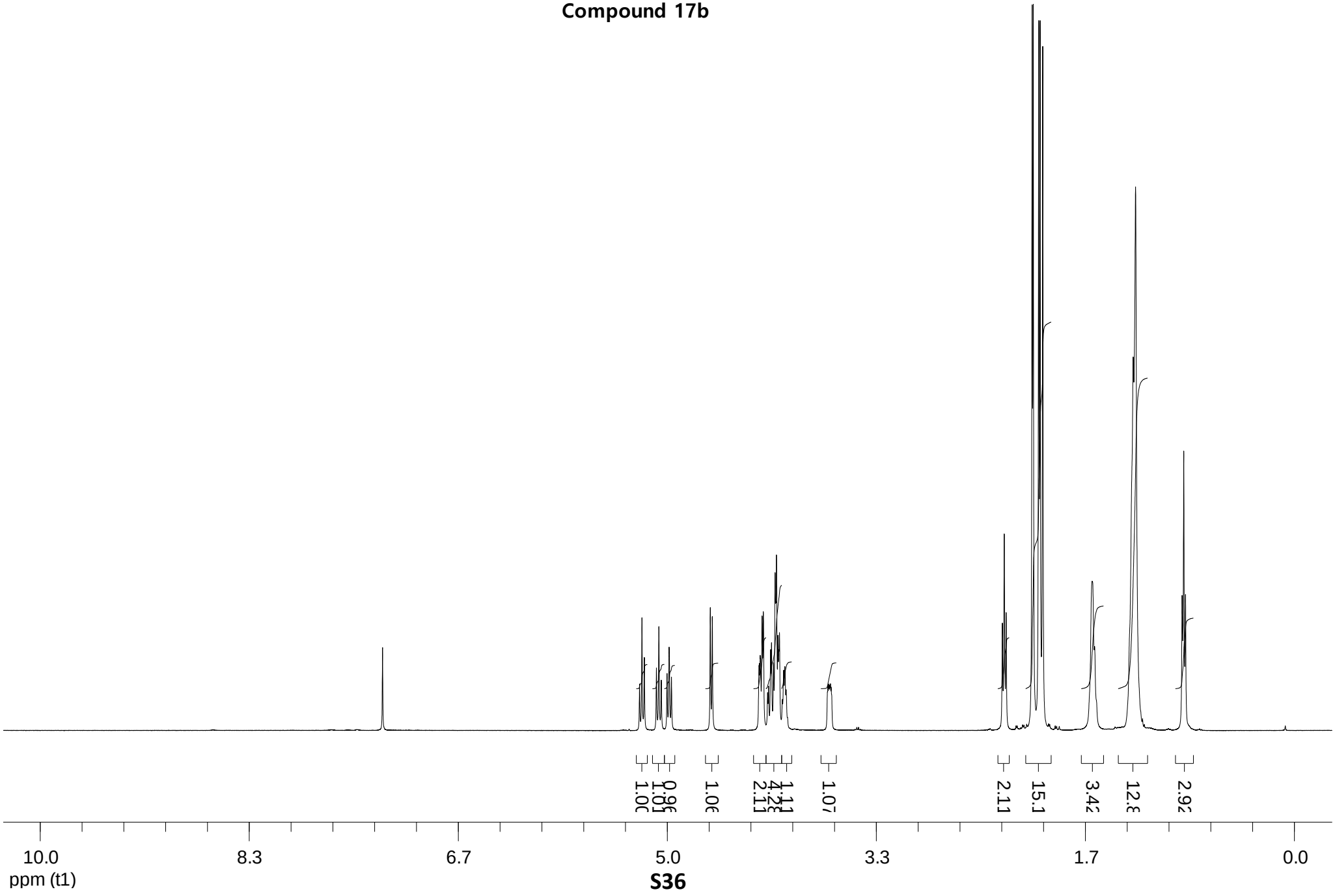
Compound 17a



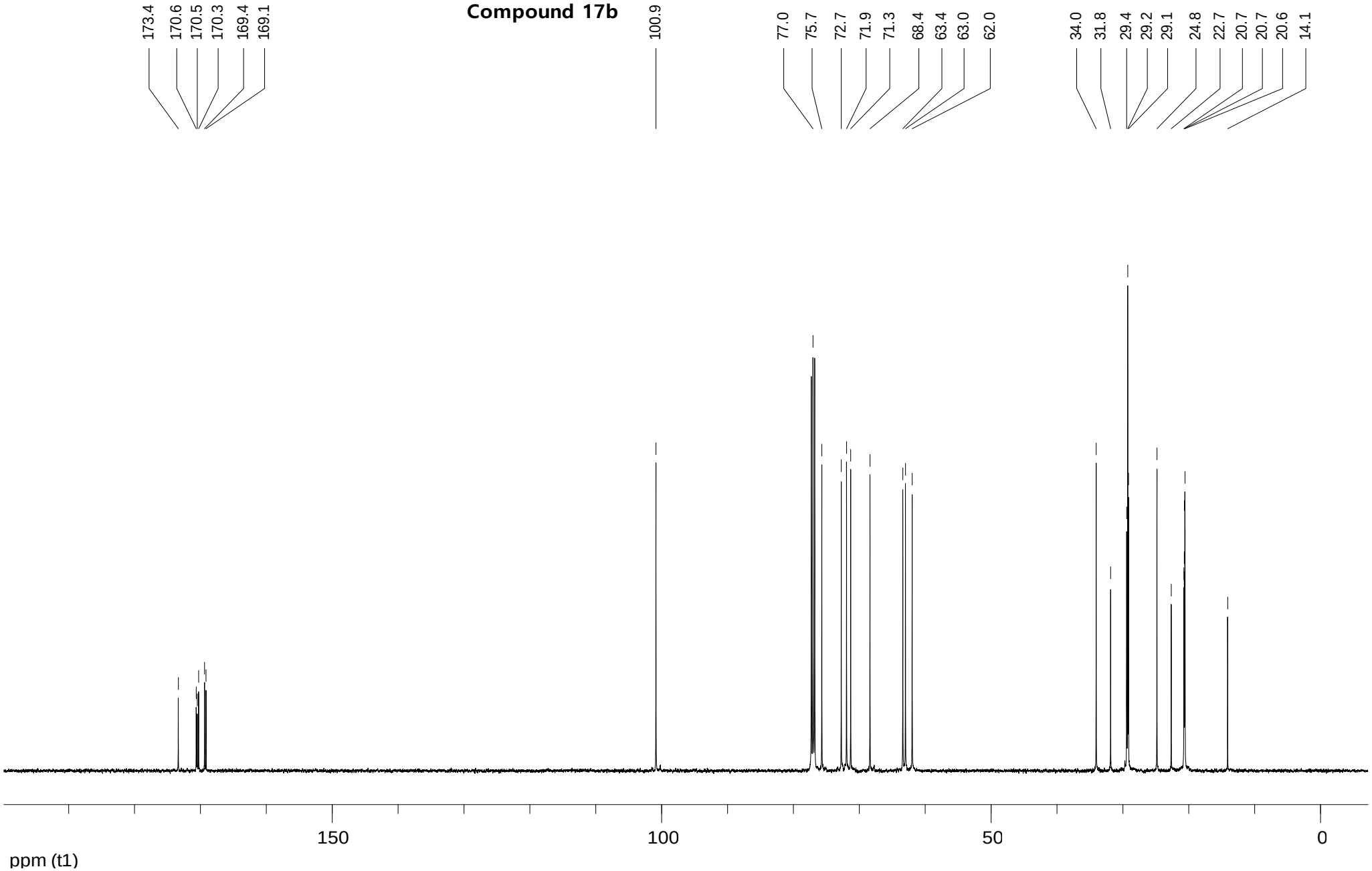
Compound 17a



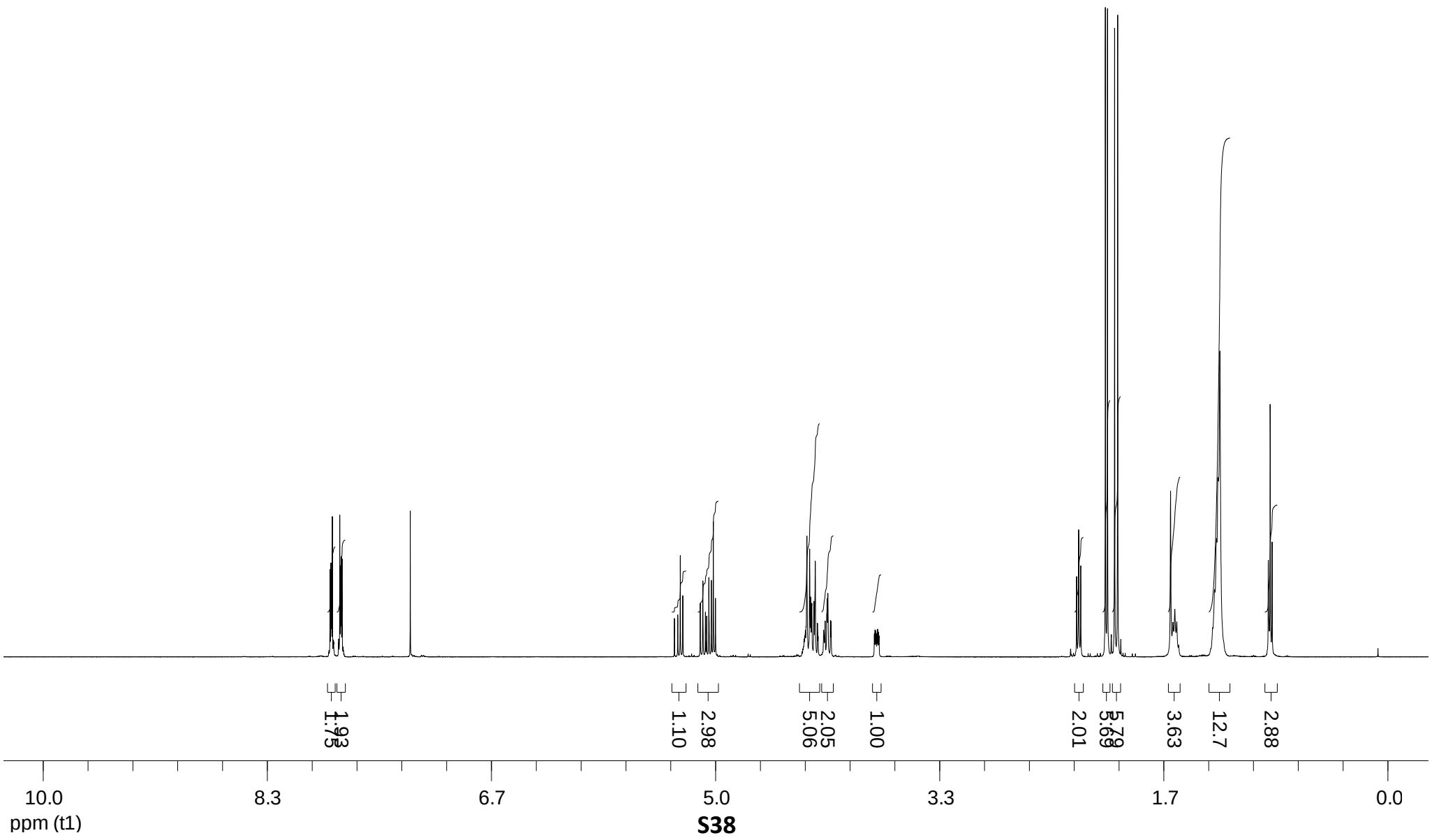
Compound 17b



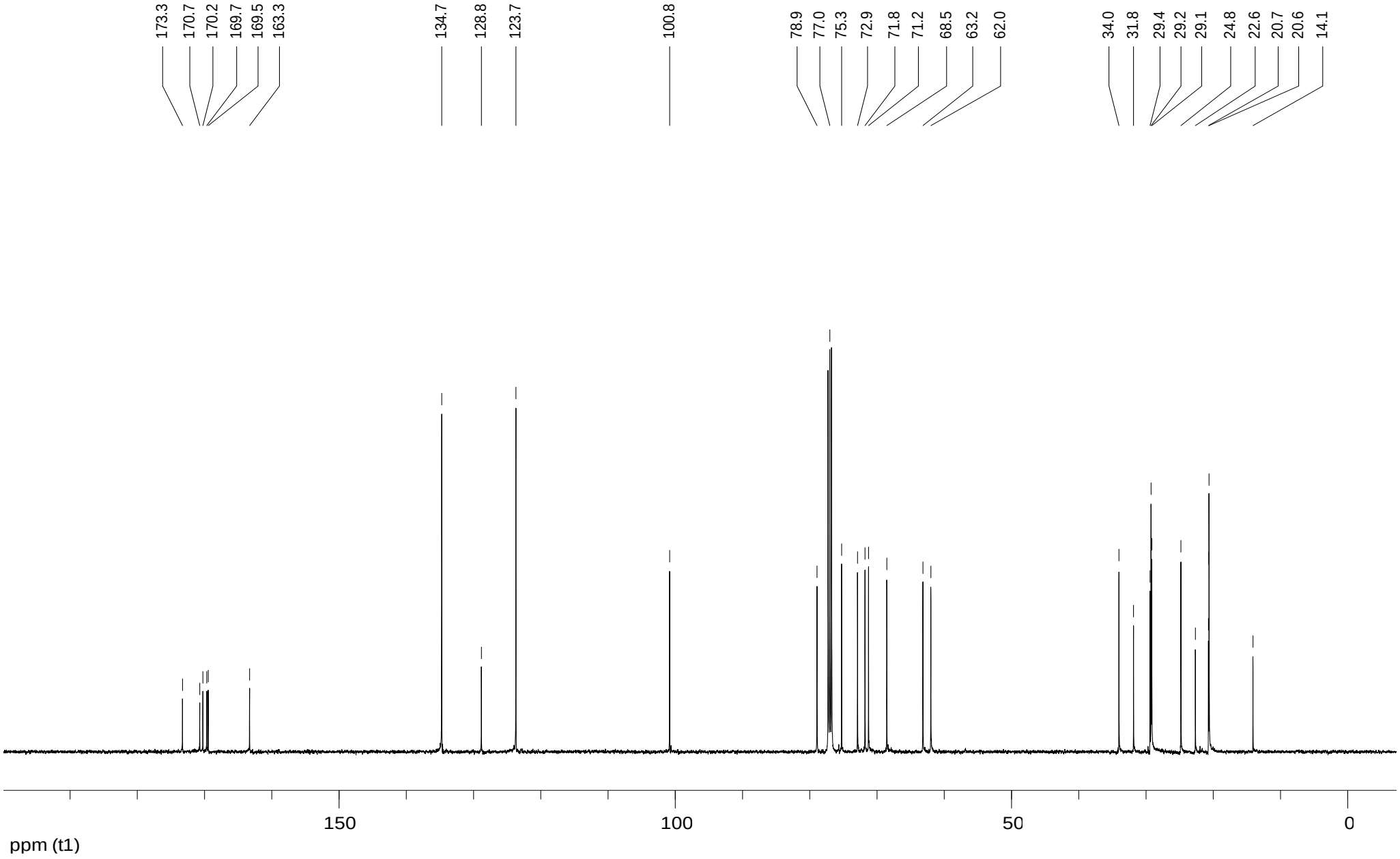
Compound 17b



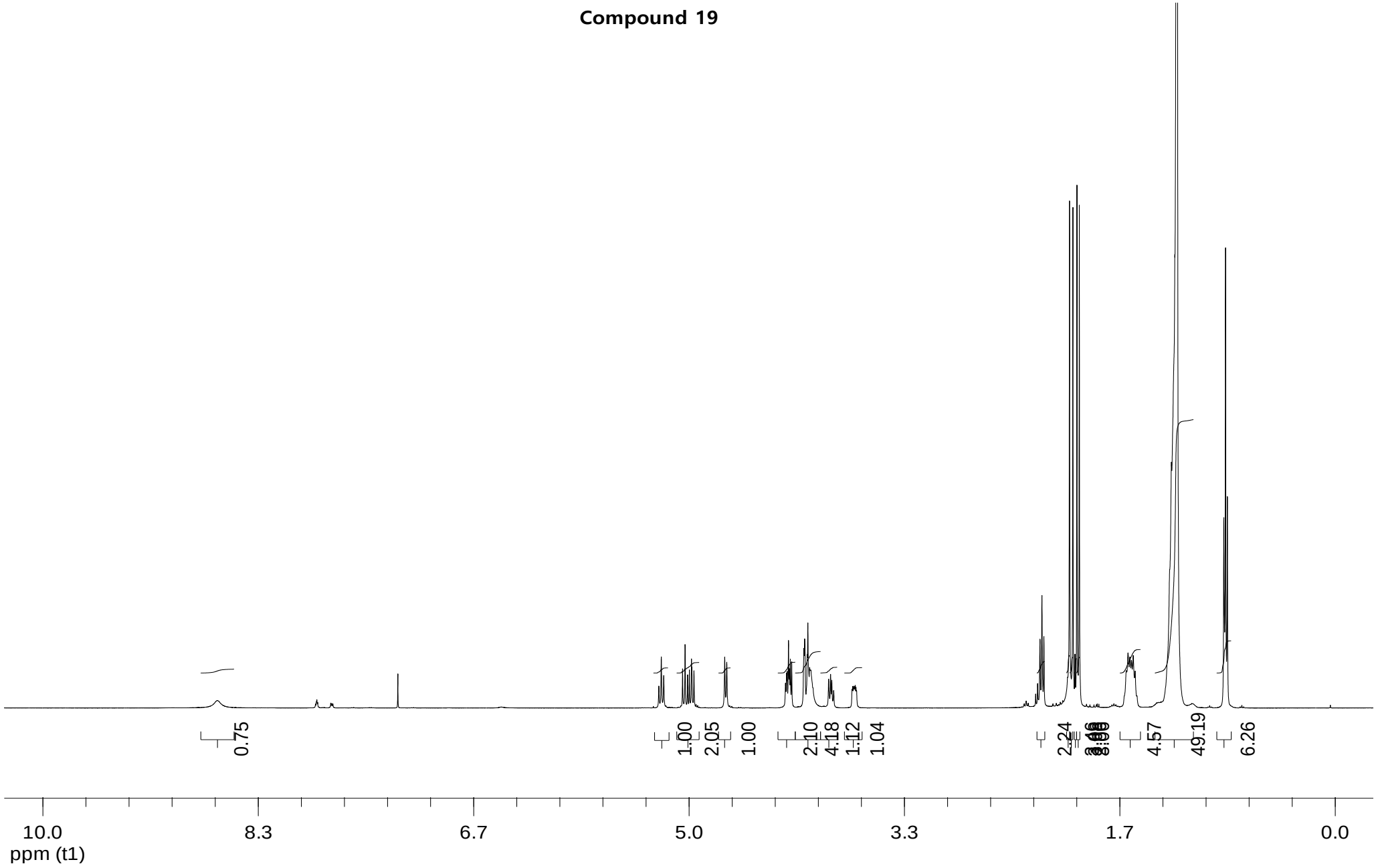
Compound 18


1.93
1.10
2.98
5.06
2.05
1.00
2.01
3.63
12.7
2.88
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

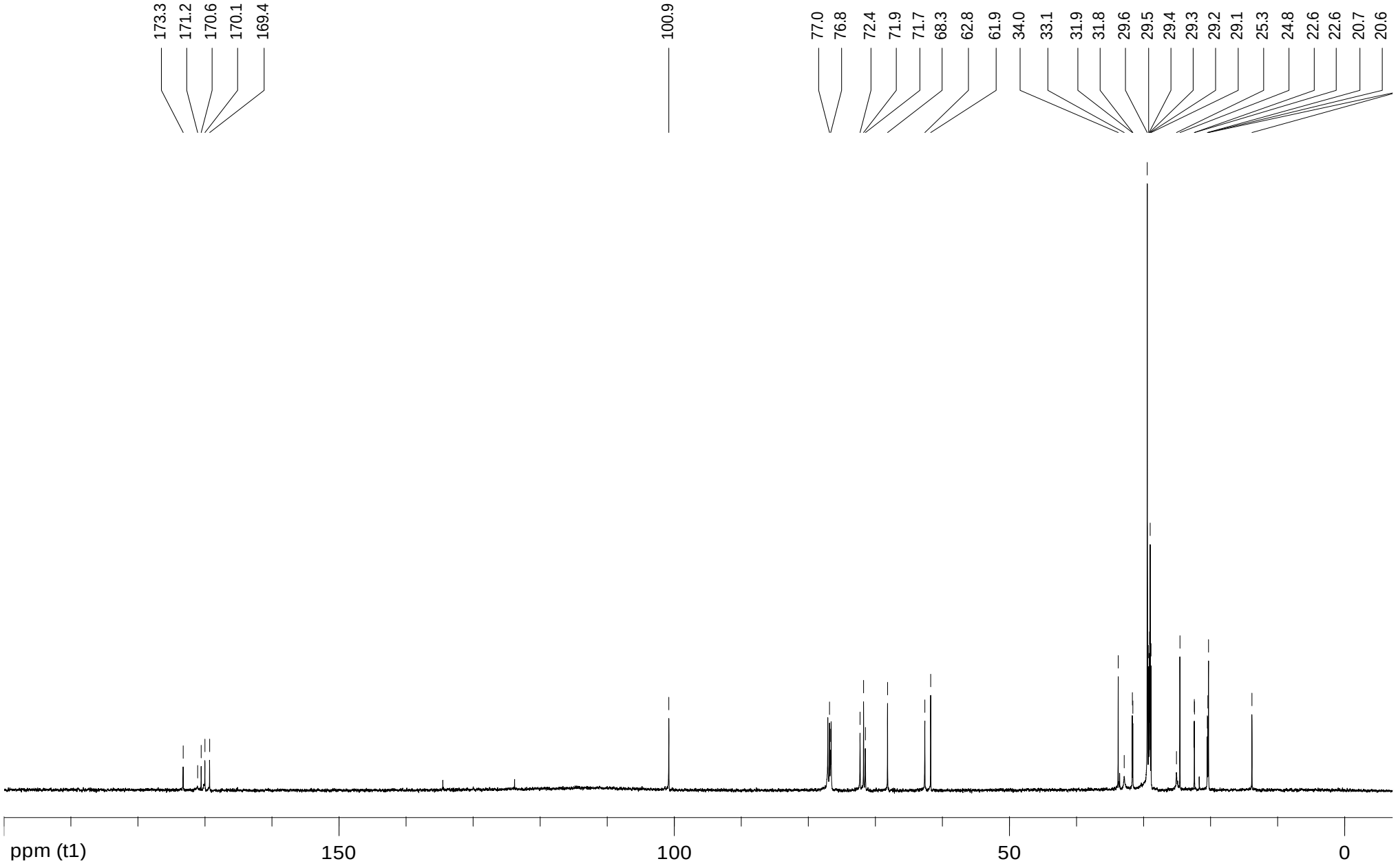
Compound 18

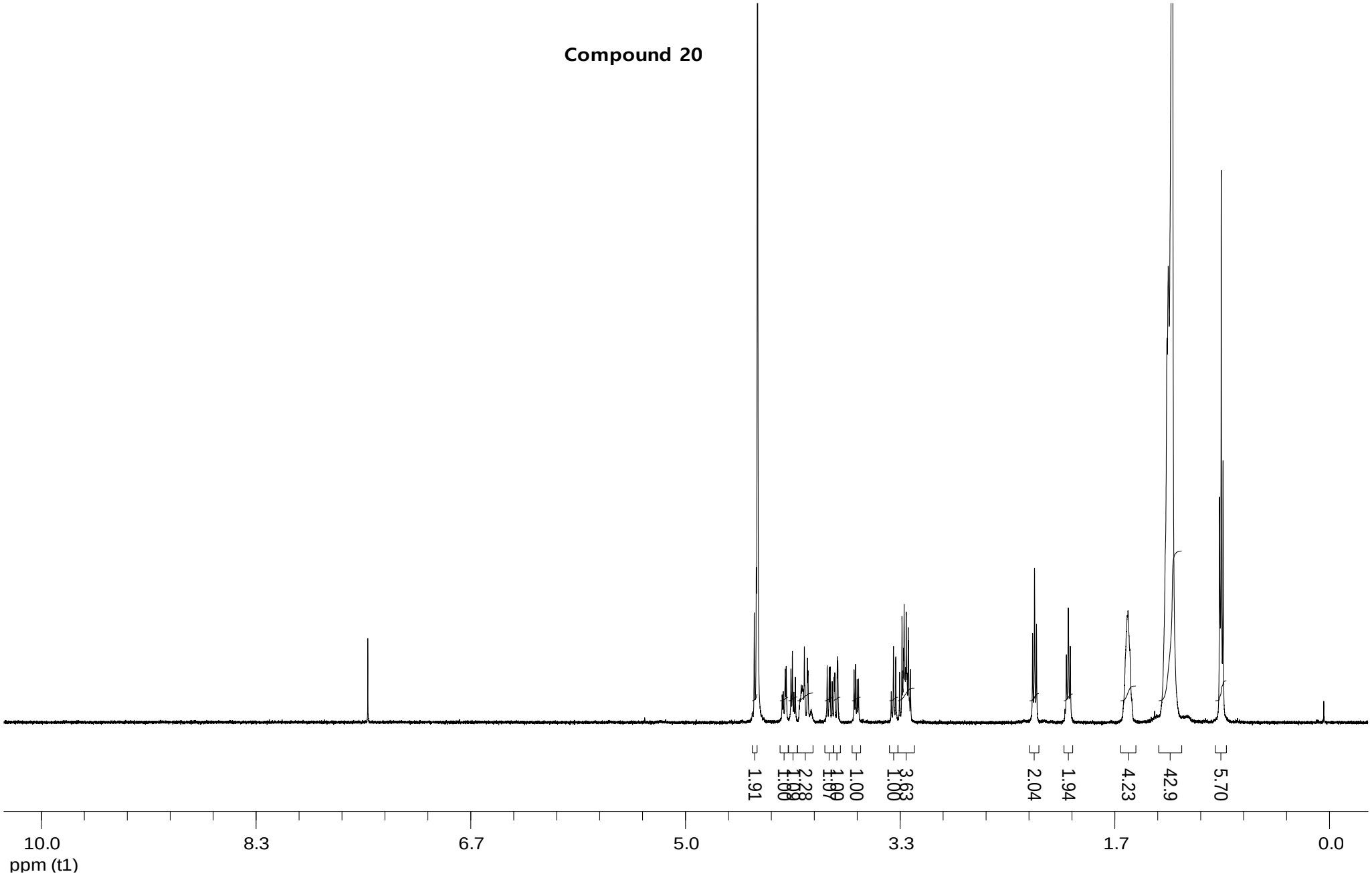

173.3
170.7
170.2
169.7
169.5
163.3
134.7
128.8
123.7
100.8
78.9
77.0
75.3
72.9
71.8
71.2
68.5
63.2
62.0
34.0
31.8
29.4
29.2
29.1
24.8
22.6
20.7
20.6
14.1
150
100
50
0
ppm (t1)

Compound 19

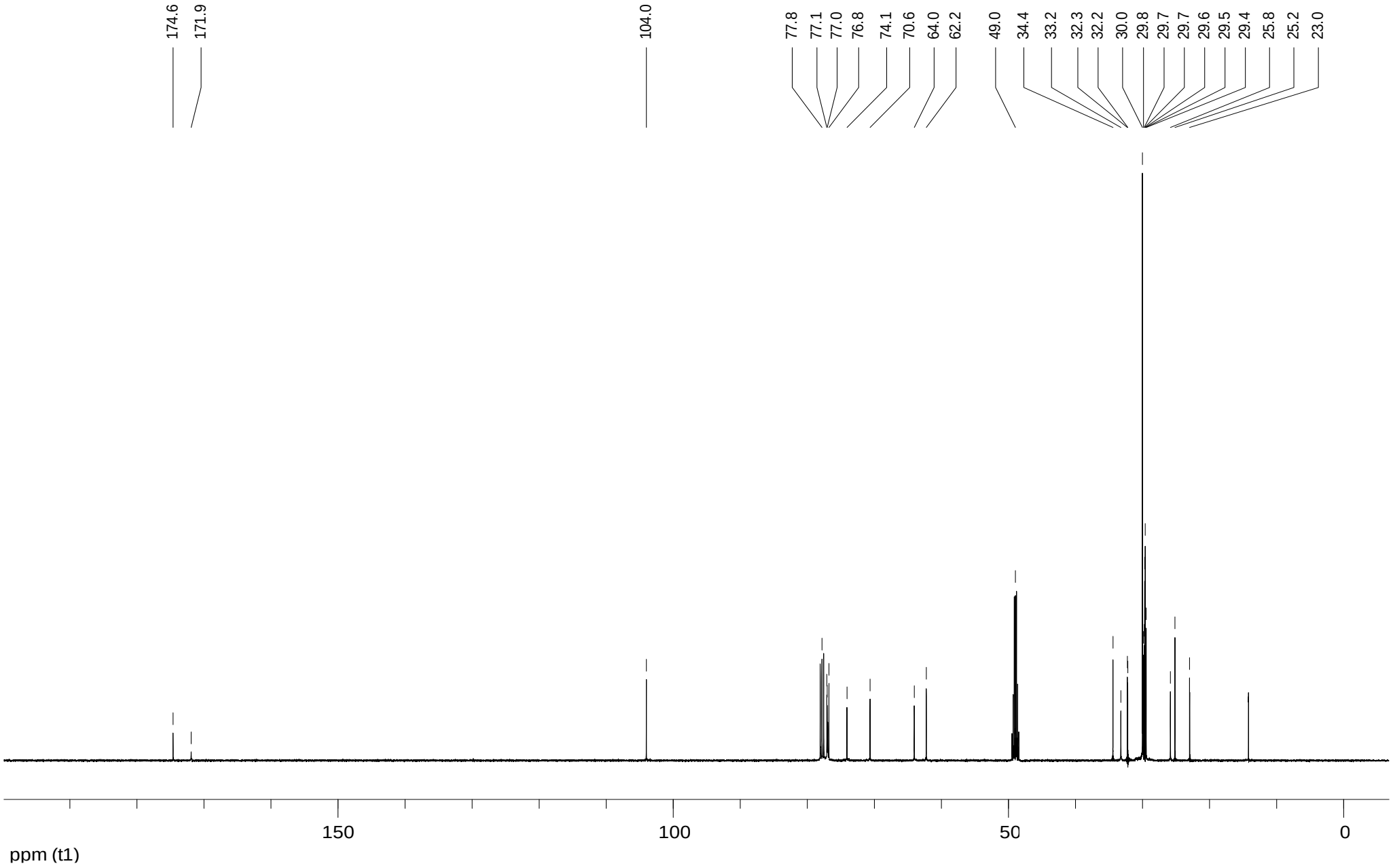

0.75
1.00
2.05
1.00
2.10
4.18
1.12
1.04
2.24
4.57
49.19
6.26
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

Compound 19

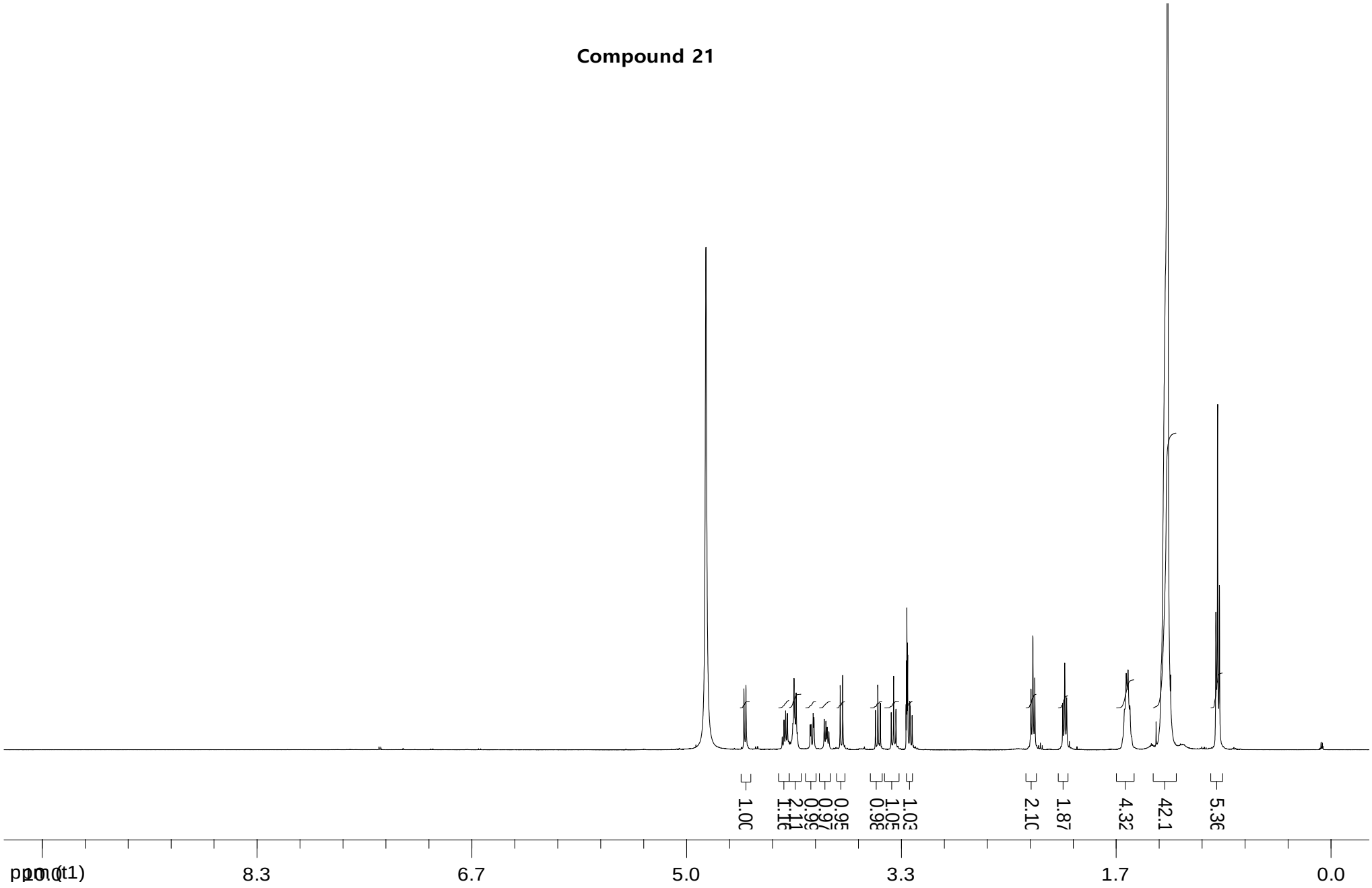

173.3
171.2
170.6
170.1
169.4
100.9
77.0
76.8
72.4
71.9
71.7
68.3
62.8
61.9
34.0
33.1
31.9
31.8
29.6
29.5
29.4
29.3
29.2
29.1
25.3
24.8
22.6
22.6
20.7
20.6
ppm (t1)
150
100
50
0


Compound 20
1.91
1.00
1.08
1.68
2.28
1.07
1.09
1.00
1.00
3.63
3.83
2.04
1.94
4.23
42.9
5.70
10.0
8.3
6.7
5.0
3.3
1.7
0.0
ppm (t1)

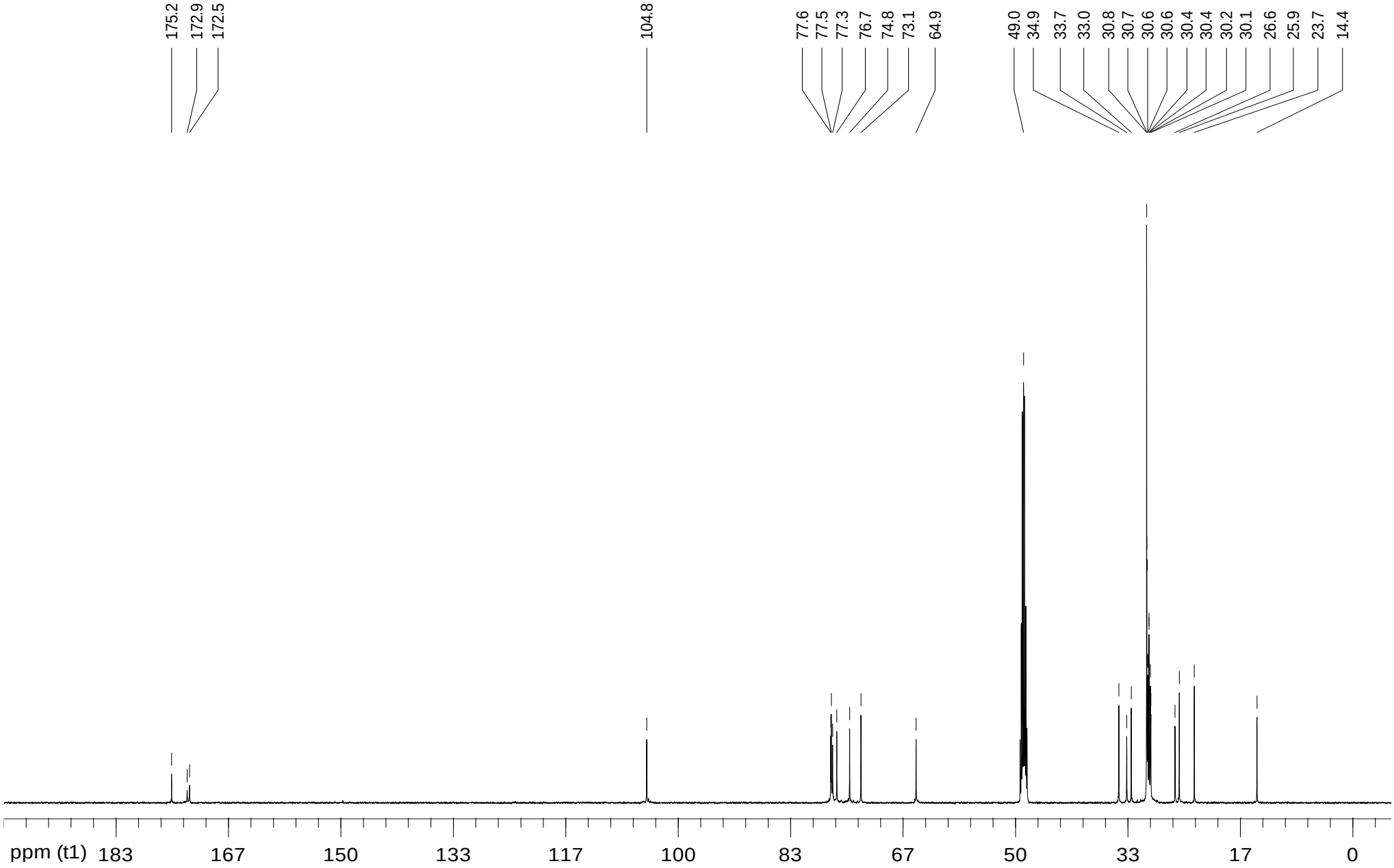
Compound 20


174.6
171.9
104.0
77.8
77.1
77.0
76.8
74.1
70.6
64.0
62.2
49.0
34.4
33.2
32.3
32.2
30.0
29.8
29.7
29.7
29.6
29.5
29.4
25.8
25.2
23.0
150
100
50
0
ppm (t1)

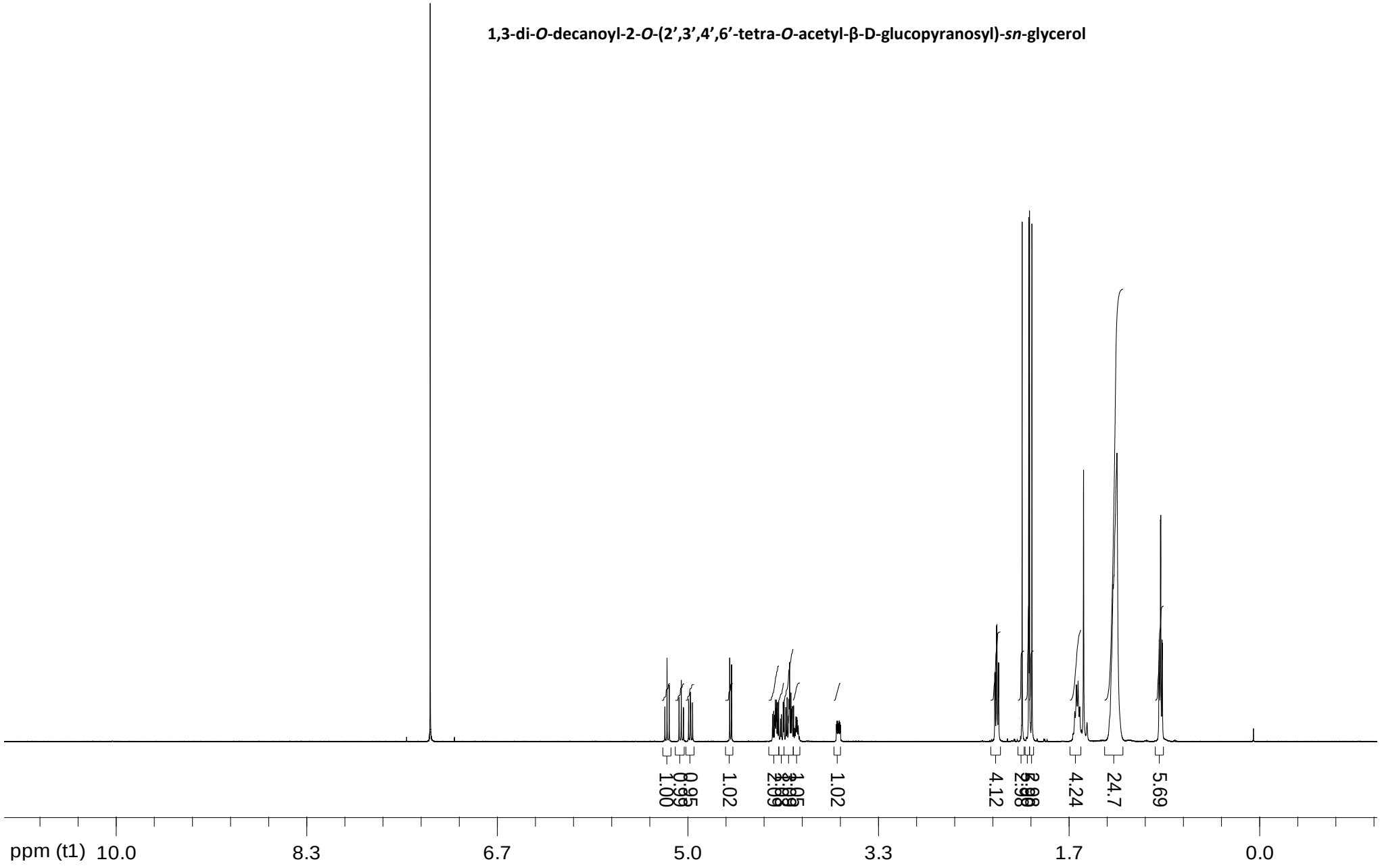
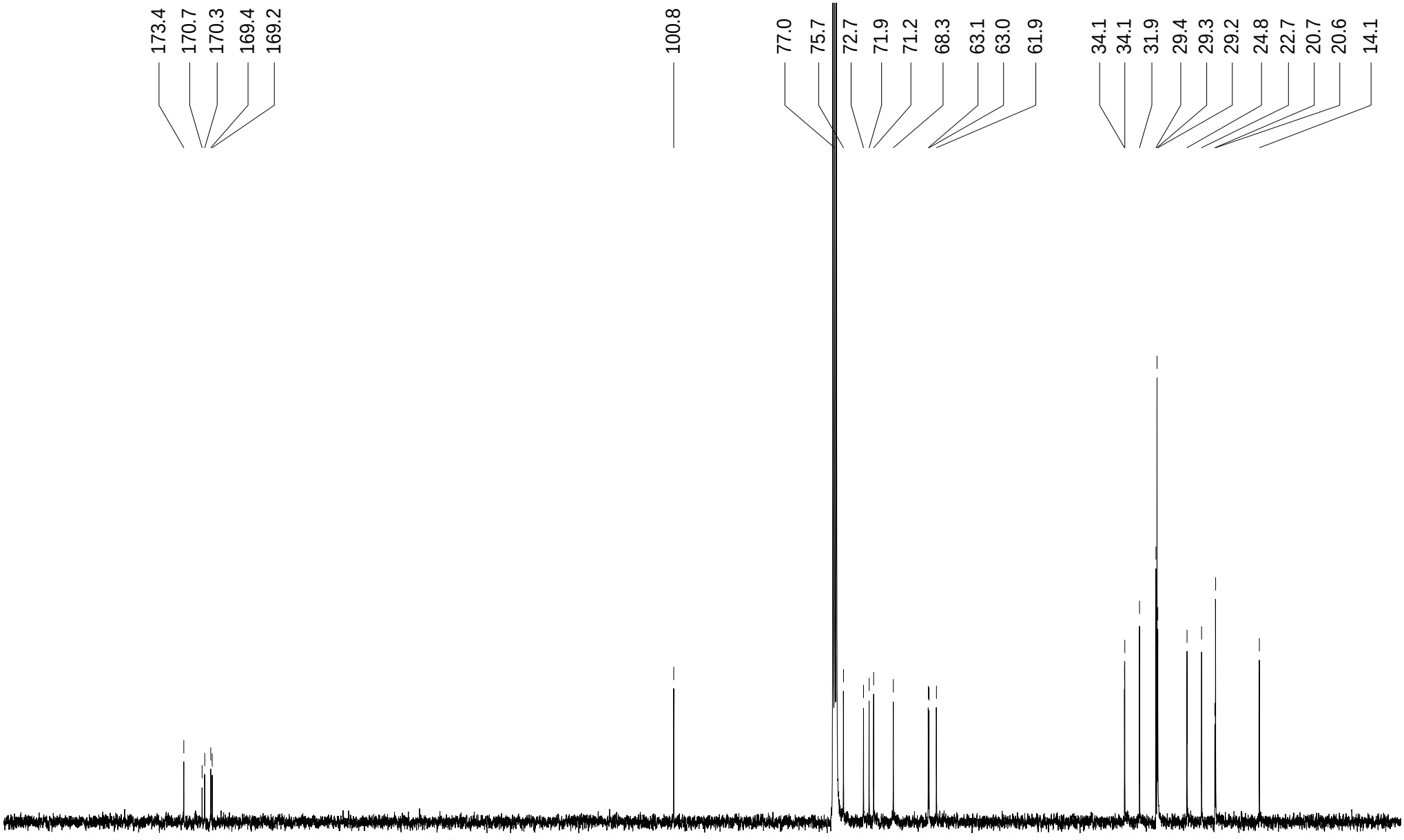
Compound 21


1.00
1.16
2.11
0.96
0.87
0.95
0.98
1.05
1.03
2.10
1.87
4.32
42.1
5.36
ppm (t1)
10.0
8.3
6.7
5.0
3.3
1.7
0.0

Compound 21


175.2
172.9
172.5
104.8
77.6
77.5
77.3
76.7
74.8
73.1
64.9
49.0
34.9
33.7
33.0
30.8
30.7
30.6
30.6
30.4
30.4
30.2
30.1
26.6
25.9
23.7
14.4
ppm (t1)
183
167
150
133
117
100
83
67
50
33
17
0

1,3-di-*O*-decanoyl-2-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-*sn*-glycerol



1,3-di-*O*-decanoyl-2-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-glucopyranosyl)-*sn*-glycerol