The synthesis of solasodine F-homo-analogues

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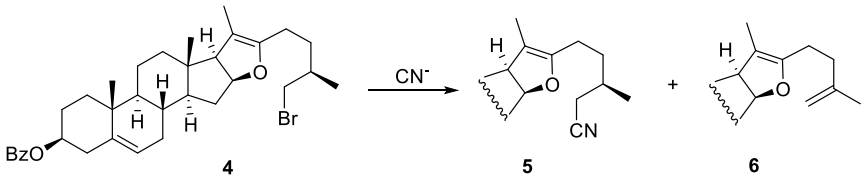
Table of Contents

1. Table S1. The optimization of 26-bromopseudodiosgenin **4** substitution reaction by cyanide S2
2. Characterization of compound **3** S3
4. X-ray diffraction analysis of compounds **3** and **10** S4
6. Spectra (^{1}H NMR, ^{13}CNMR) of compounds **1-11** S6-S28

Table S1. The optimization of 26-bromopseudodiosgenin **4** substitution reaction by cyanide



4 **5** **6**

Entry	Reagent (equiv)	Conditions	Yield of 5	Yield of 6
1	NaCN (1.1)	DMF, 80˚C, 16 h	<5%	<5%
2	NaCN (1.1), 18-Crown-6 (cat)	DMF, 80˚C, 36 h	<5%	<5%
3	KCN (1.1)	DMF, rt, 1 h	3%	6%
4	KCN (1.1)	DMF, 60˚C, 16 h	16%	4%
5	KCN (1.1), KI (cat)	DMF, 60˚C, 16 h	18%	4%
6	KCN (1.1)	DMSO, 120˚C, 5 h	<2%	<2%
7	KCN (3)	acetone, reflux, 3 h	<5%	<5%
8	KCN (3), 18-Crown-6 (cat)	acetone, reflux, 3 h	40%	-
9	KCN(2), 18-Crown-6 (cat)	MeCN, reflux, 24 h	13%	-
10	TMSCN (1.5), TBAF (1.5)	MeCN, rt, 48 h	48%	18%
11	TMSCN (1.5), TBAF (1.5)	MeCN, 40˚C, 48 h	48%	18%
12	TMSCN (1.5), TBAF (1.5)	MeCN, reflux, 4 h	65%	10%
13	TMSCN (2), TBAF (2)	THF, 40˚C, 24 h	69%	-

Characterization compound 3

*(22R,25R)-3β-benzoyloxy-22-cyanofurost-5-en-26-yl mesylate (**3**)*

To the cooled to 0ºC solution of nitrile **2** (95 mg, 0.17 mmol) and Et_3N (0.04 mL, 0.26 mmol) in dry DCM (10 mL) solution of MsCl (0.02 mL, 0.209 mmol) in DCM (5 mL) was added dropwise. After 30 min the reaction mixture was removed from the ice bath and stirred at ambient temperature for 16 h. Next the reaction mixture was poured into aq. $NaHCO_3$ and extracted with DCM (3x50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. DFC chromatography on silica gel (elution with hexane/ethyl acetate 7:3) gave **3** (83 mg, 0.133 mmol, 97%) as a white solid, mp 197-199 ºC (hexane/ethyl acetate); **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 (m, 2H), 7.55 (m, 1H), 7.44 (m, 2H), 5.42 (m, 1H), 4.86 (m, 1H), 4.63 (m, 1H), 4.10 (m, 2H), 3.03 (s, 3H), 2.48 (m, 2H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.09 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 165.8 (C), 139.6 (C), 132.7 (CH), 130.6 (C), 129.4 (2xCH), 128.2 (2xCH), 122.1 (CH), 118.3 (C), 88.7 (C), 84.1 (CH), 74.2 (CH), 73.5 (CH_2), 62.8 (CH), 56.6 (CH), 49.6 (CH), 41.9 (CH), 40.6 (C), 39.1 (CH_2), 38.0 (CH_2), 37.2 (CH_3), 36.8 (CH_2), 36.6 (C), 34.3 (CH_2), 32.7 (CH), 31.8 (CH_2), 31.4 (CH_2), 31.3 (CH), 27.8 (CH_2), 27.7 (CH_2), 20.5 (CH_2), 19.3 (CH_3), 17.0 (CH_3), 16.4 (CH_3) 16.3 (CH_3); **ESI-MS**: 597 $[M\text{-}CN]^+$, 683 $[M+AcOH]^+$, 1269 $[2M+Na]^+$; **IR ATR, ν_{max} (cm^{-1})** 2921, 2854, 1705, 1454, 1344, 1273, 1172, 1109, 969, 822, 711.

X-ray diffraction analysis of compound 3 and 10

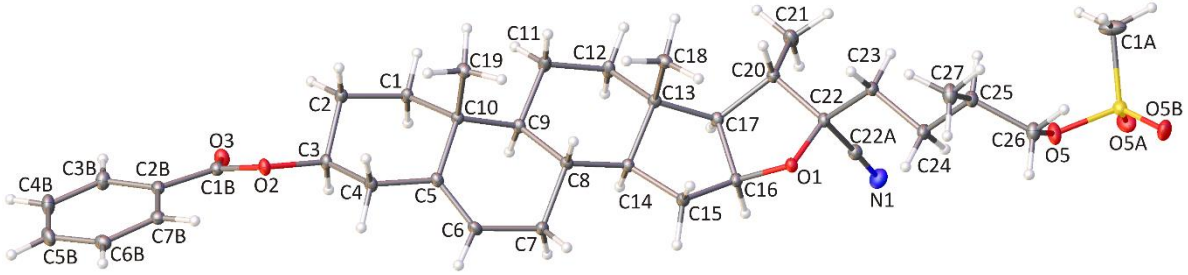


Figure 2. X-ray structure of 26-mesyloxy-22-nitrile **3**. Displacement ellipsoids are drawn at the 30% probability level [1].

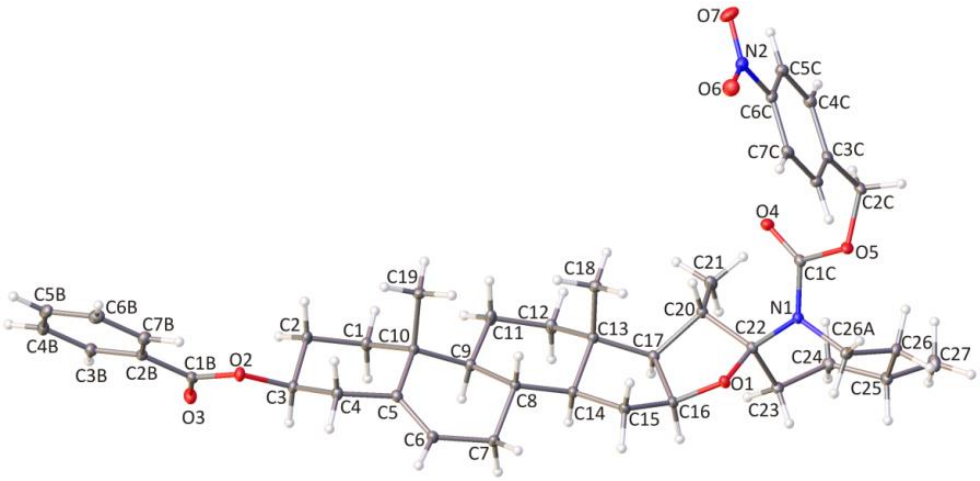


Figure 3. X-ray structures of *N*-acylated 26a-homosolasodine analogue **10**. Displacement ellipsoids are drawn at the 30% probability level [1].

X-ray diffraction analysis of 3 and 10. Crystals suitable for X-ray diffraction study were obtained at room temperature by slow evaporation from a mixture of AcOEt-DCM (**3**) and MeOH-DCM (**10**). The X-ray diffraction data were measured at 100(2) K on SuperNova diffractometer (Rigaku) with CCD detector and $Cu_{K\alpha}$ radiation. The crystal structures were solved using direct methods with *SHELXT* [2] and refined with *SHELXL* [3]. All hydrogen atoms were initially located in electron-density difference maps and were constrained to idealized positions, with C-H = 0.95-1.00 Å and with U_{iso}(H) = 1.5U_{eq}(C) for methyl hydrogen atoms and U_{iso}(H) = 1.2U_{eq}(C) for others. The *PLATON* software [4] was used to validate the crystallographic data.

Crystal data for **3**: $C_{36}H_{49}NO_6N$, M_r = 623.82, colourless prism, 0.45 × 0.22 × 0.06 mm^3, monoclinic space group $P2_1$, a = 6.4115(1) Å, b = 9.6586(1) Å, c = 26.3967(1) Å, β = 91.615(1)°, V = 1633.99(2) $Å^3$, Z = 2, ρ_{calcd} = 1.268 $g{\cdot}cm^{-3}$, μ = 1.253 mm^{-1}, $F(000)$ = 672, R_1 = 0.033, wR^2=0.091, 6829 independent reflections, θ_{max} = 76.7°, θ_{min} = 3.3°, 403 parameters. CCDC 1901930 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Crystal data for **10**: $C_{36}H_{49}NO_6N$, M_r = 623.82, colourless prism, 0.45 × 0.22 × 0.06 mm^3, monoclinic space group $P2_1$, a = 6.4115(1) Å, b = 9.6586(1) Å, c = 26.3967(1) Å, β = 91.615(1)°, V = 1633.99(2) $Å^3$, Z = 2, ρ_{calcd} = 1.268 $g{\cdot}cm^{-3}$, μ = 1.253 mm^{-1}, $F(000)$ = 672, R_1 = 0.033, wR^2=0.091, 6829 independent reflections, θ_{max} = 76.7°, θ_{min} = 3.3°, 403 parameters. CCDC 1901930 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

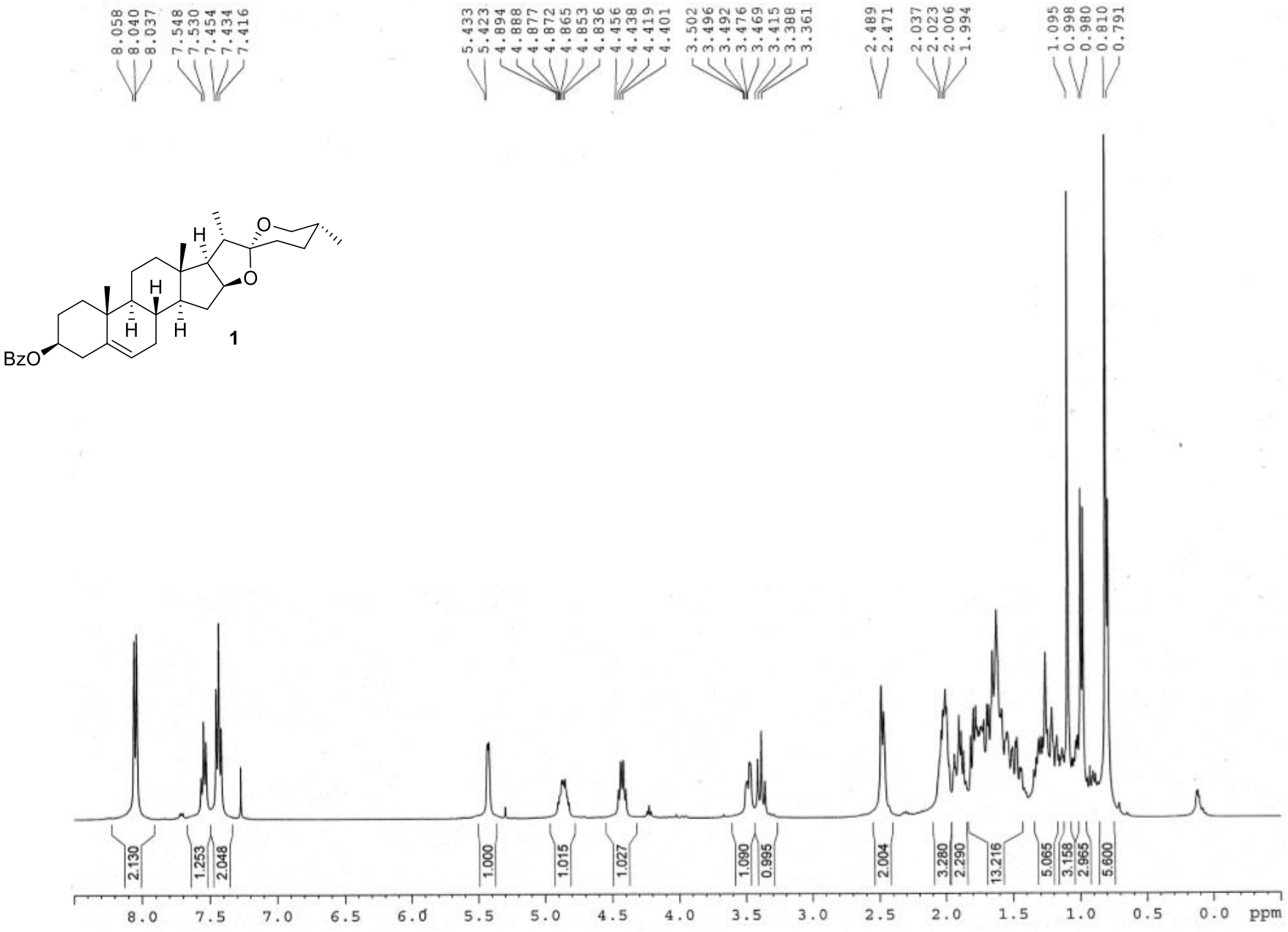
[1] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann. (2009). *J. Appl. Cryst.* **42,** 339-341.

[2] G. M. Sheldrick. (2015) *Acta Crystallogr. Sect. A* (2015) **71,** 3-8.

[3] G. M. Sheldrick. (2015) *Acta Crystallogr. Sect. C* (2015) **71,** 3-8.

[4] Spek, A. L. (2009). *Acta Crystallogr. Sect. D: Biol. Crystallogr.* **65,** 148–155.

Spectra (^{1}H NMR, ^{13}CNMR) of compounds 1-11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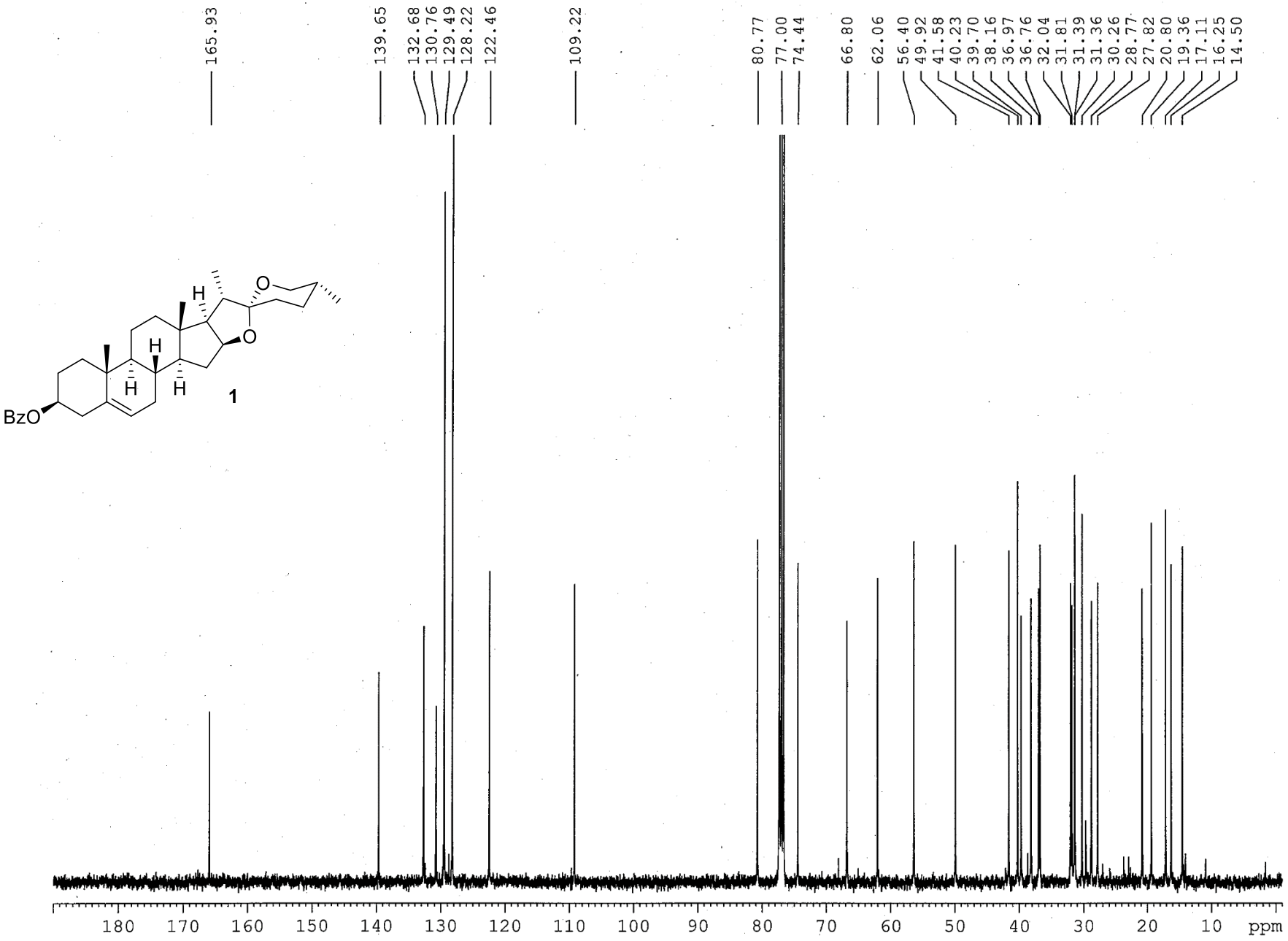
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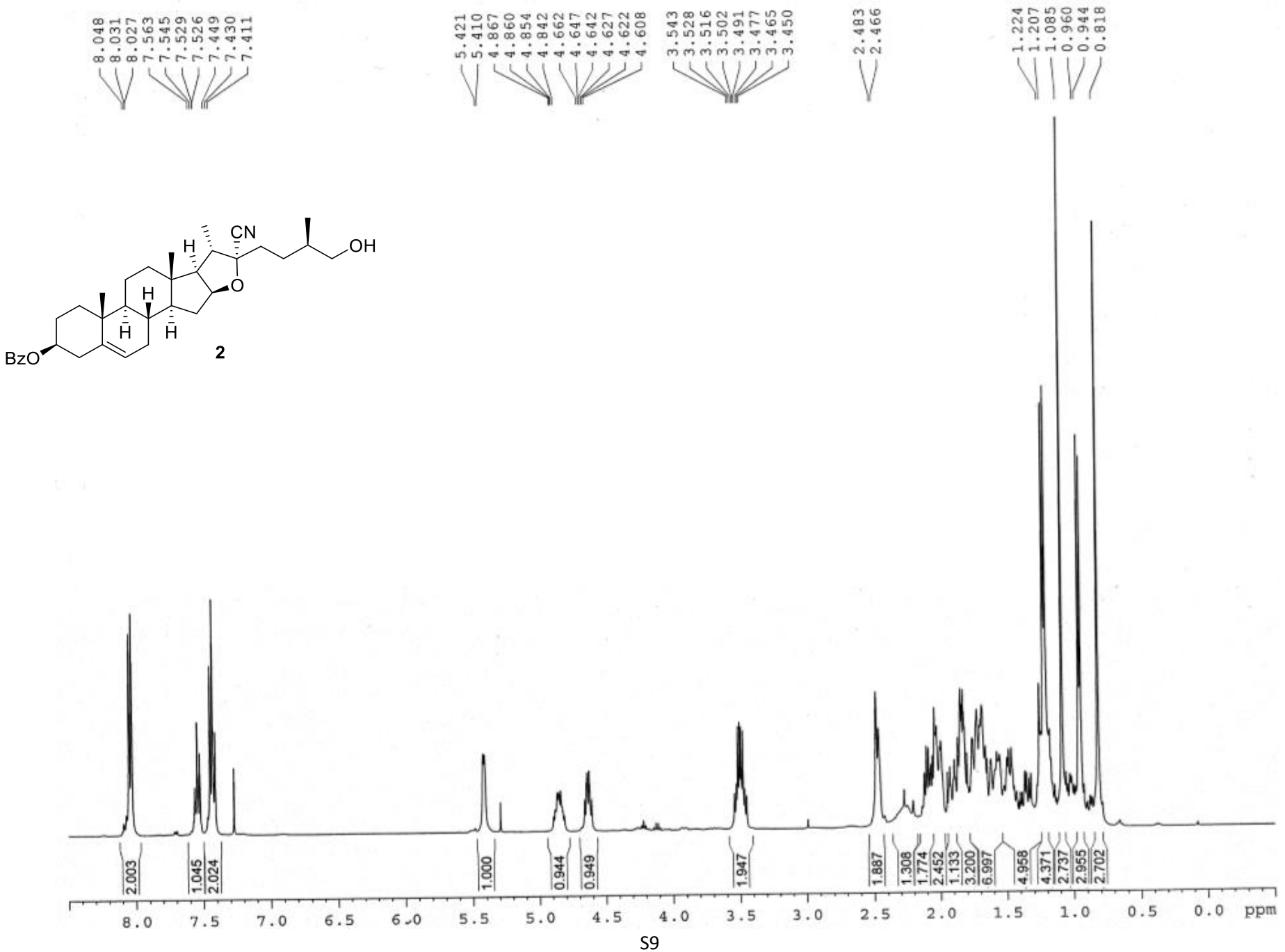
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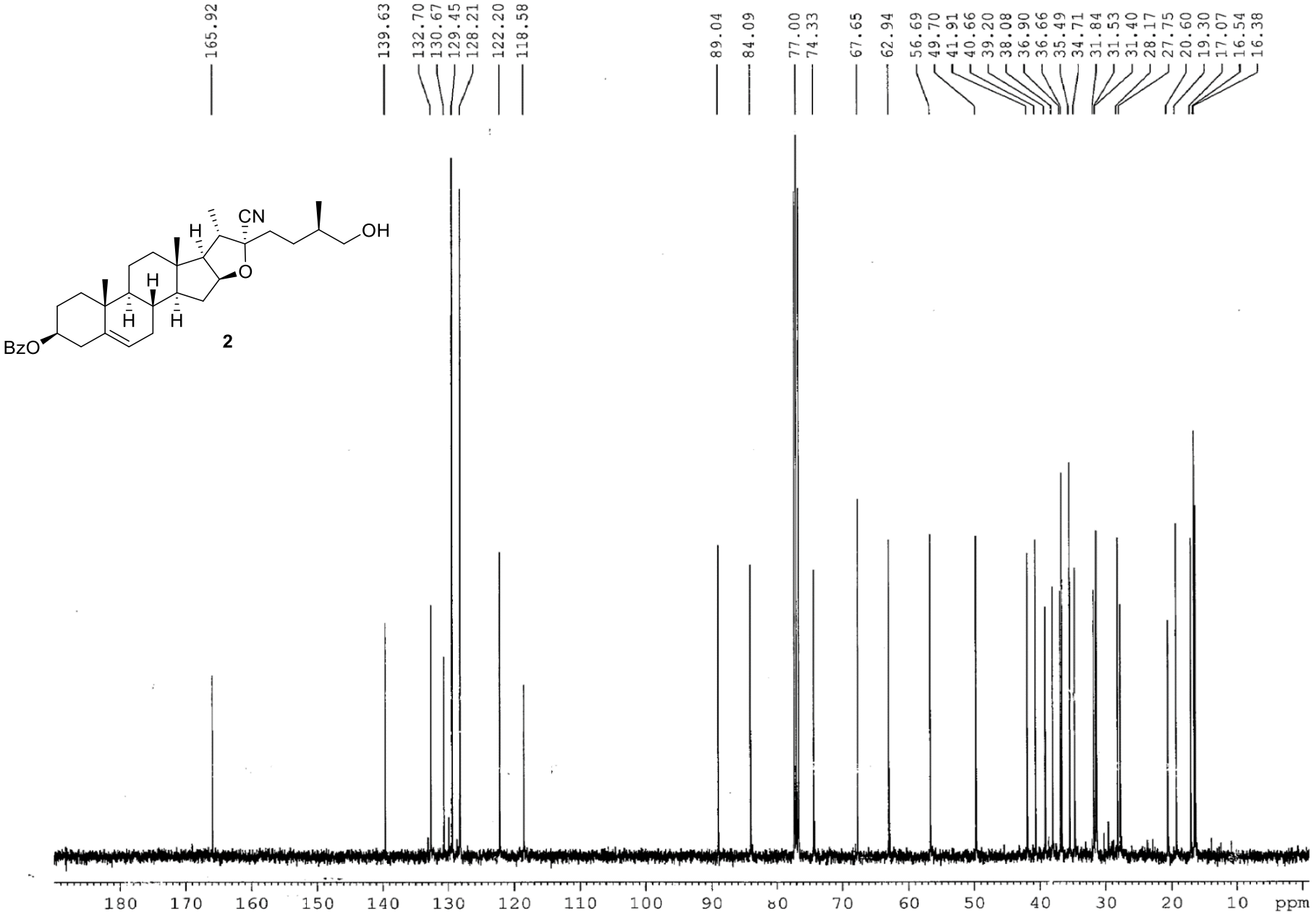
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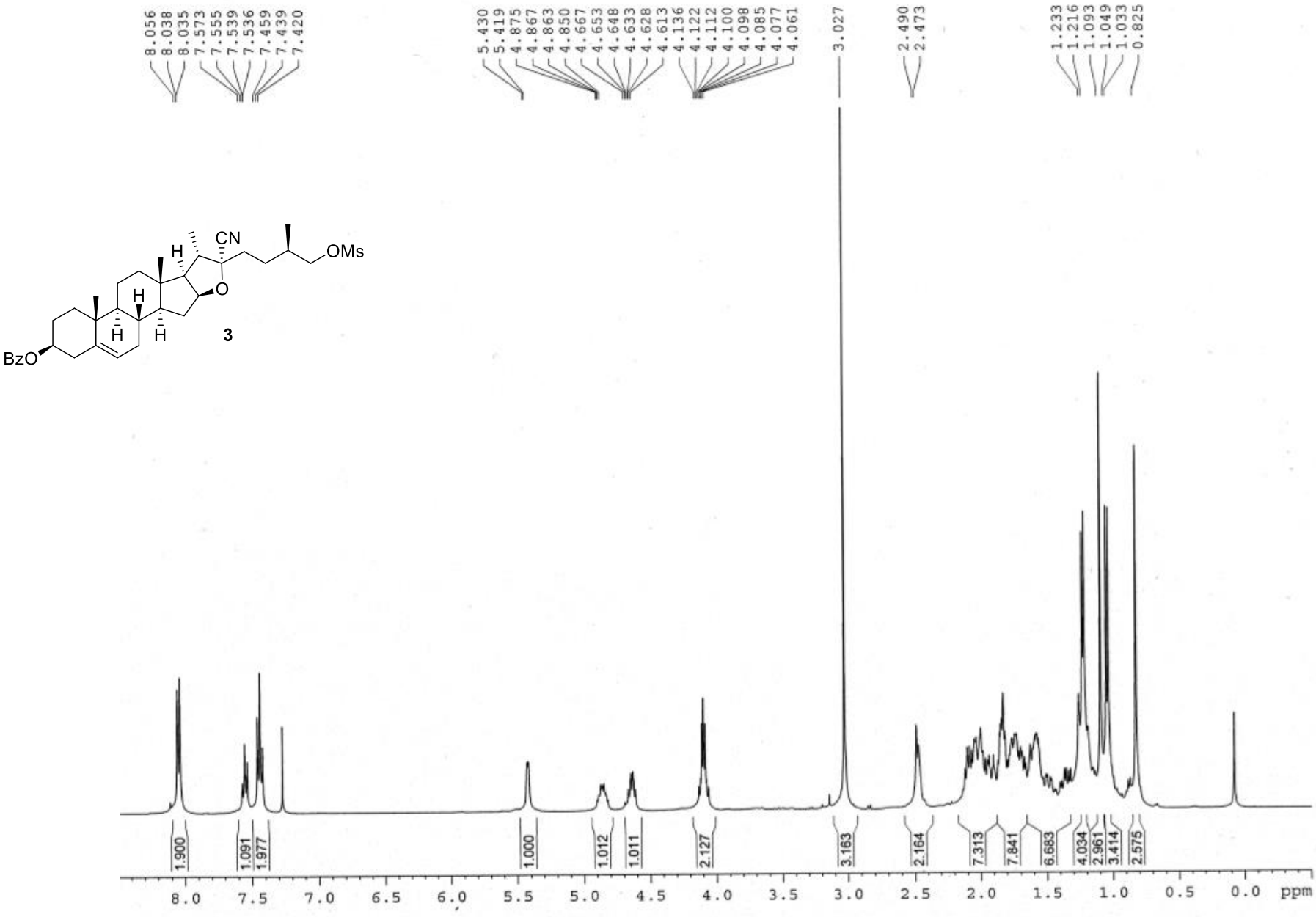
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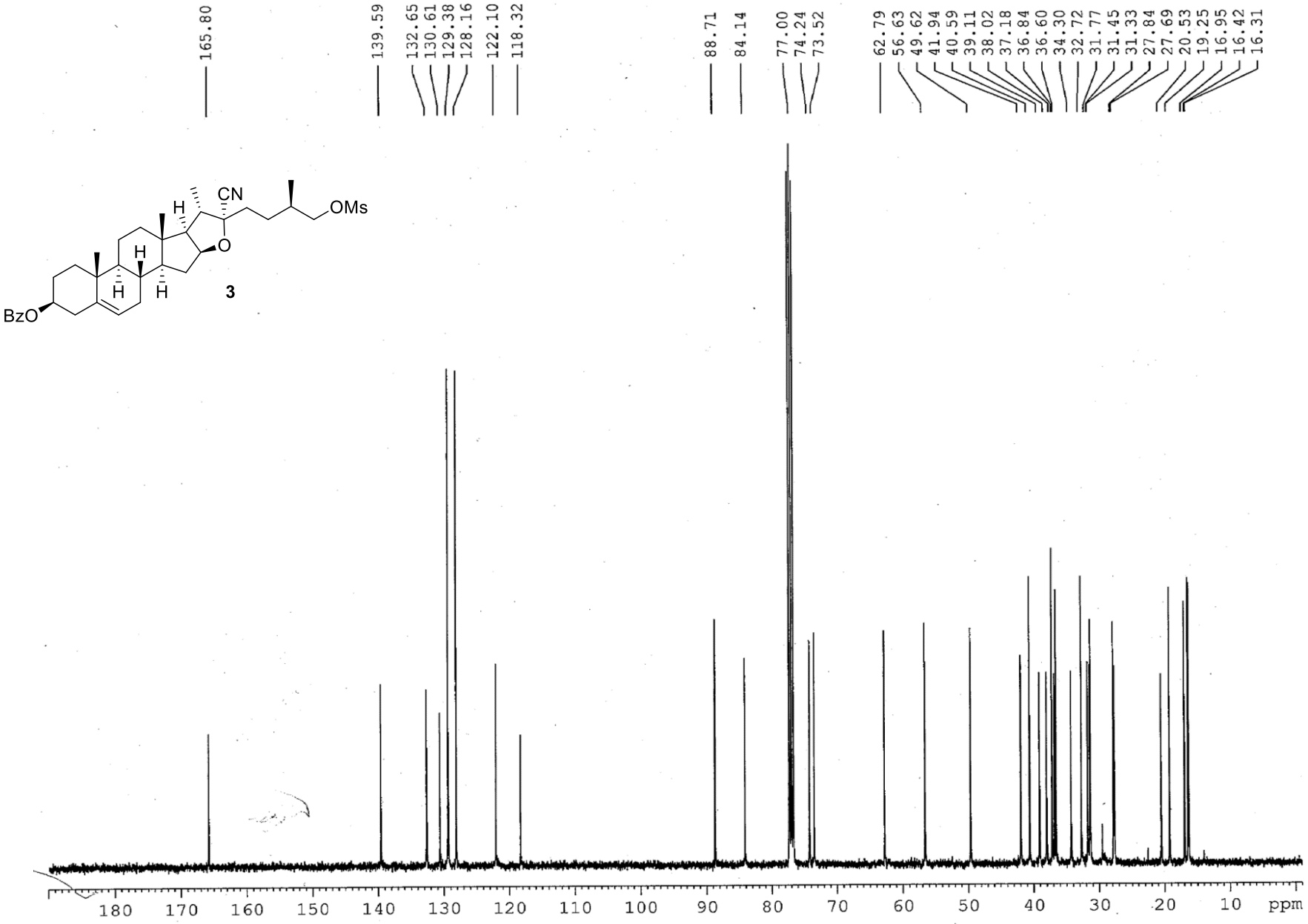
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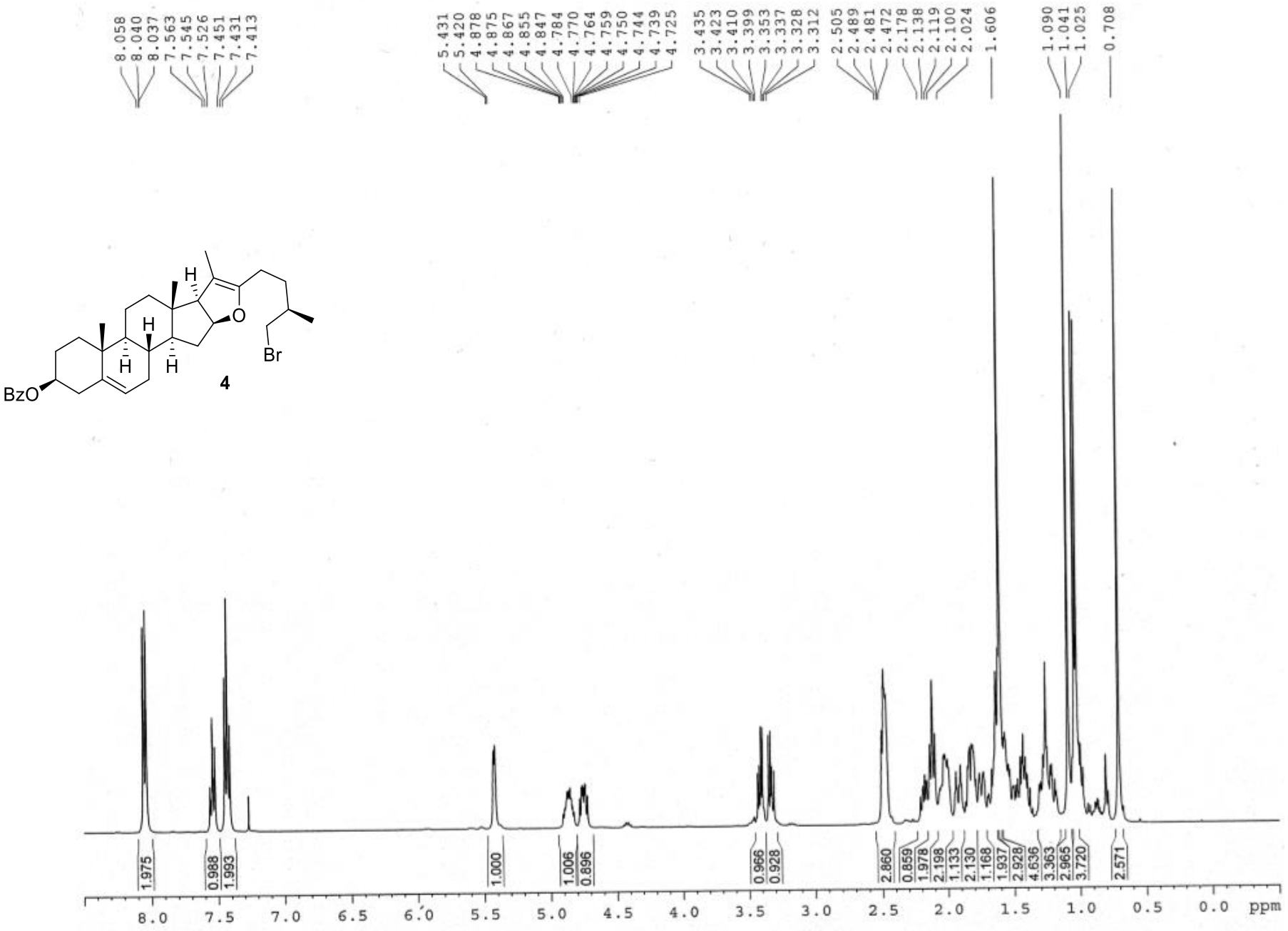
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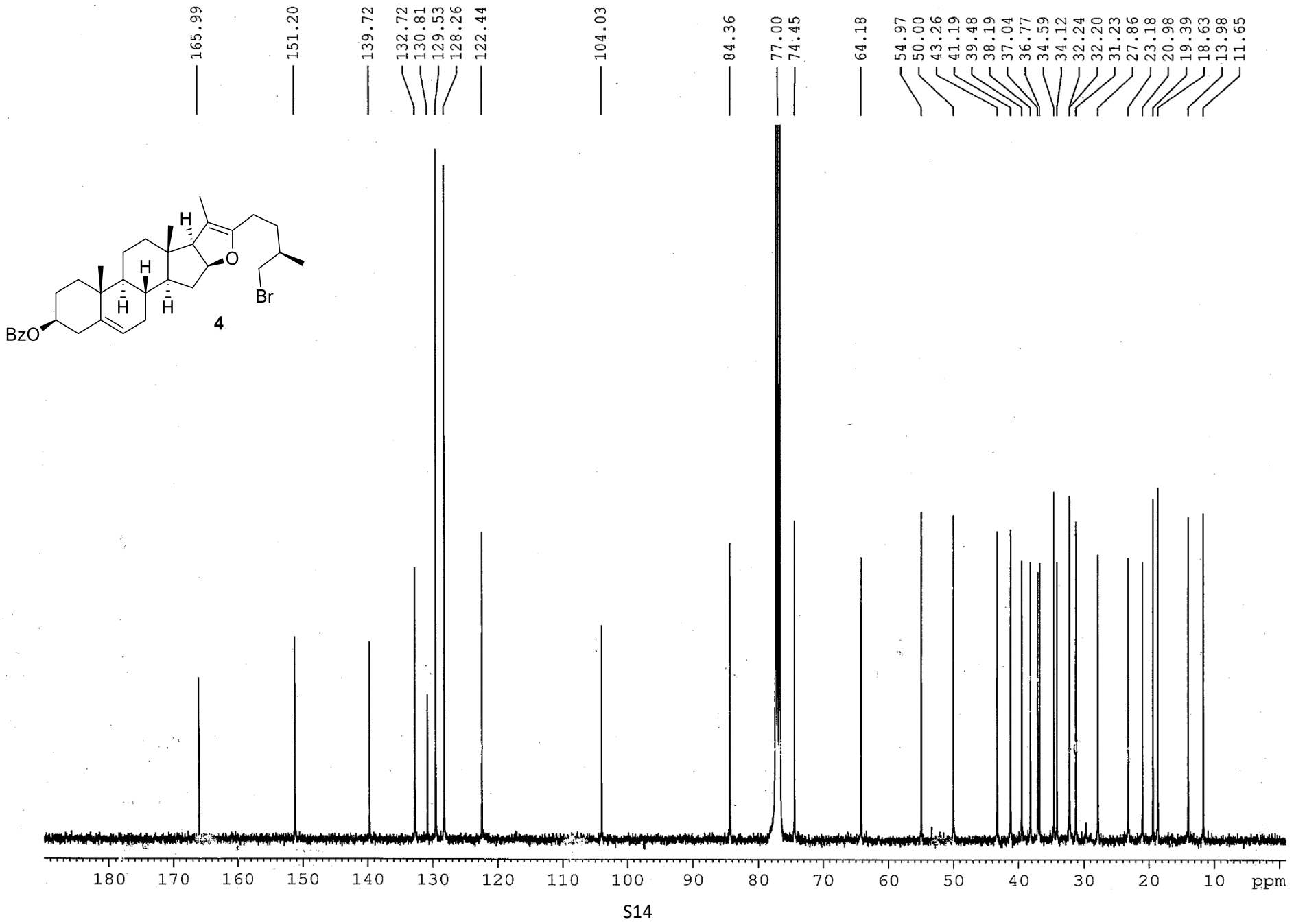
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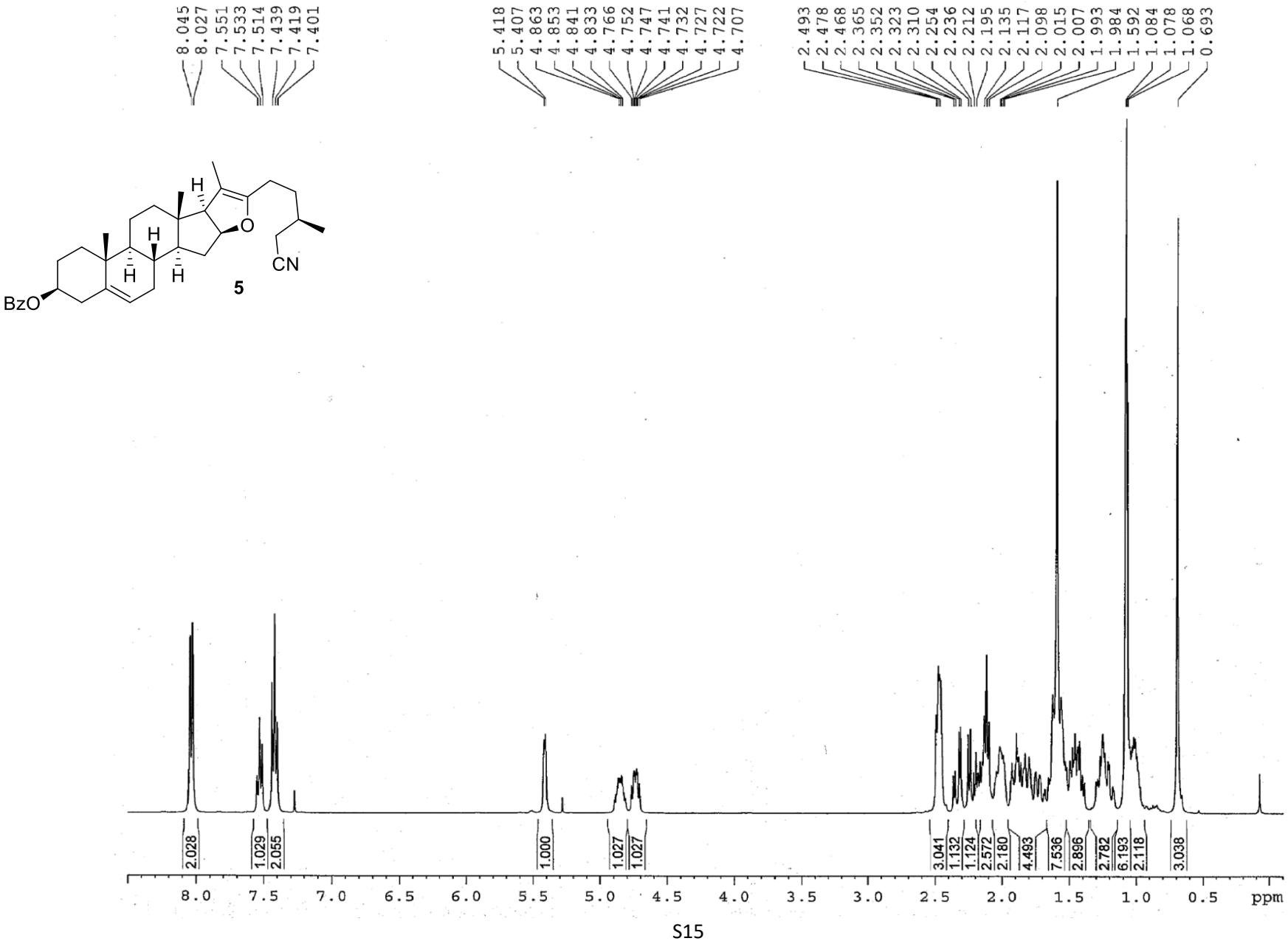
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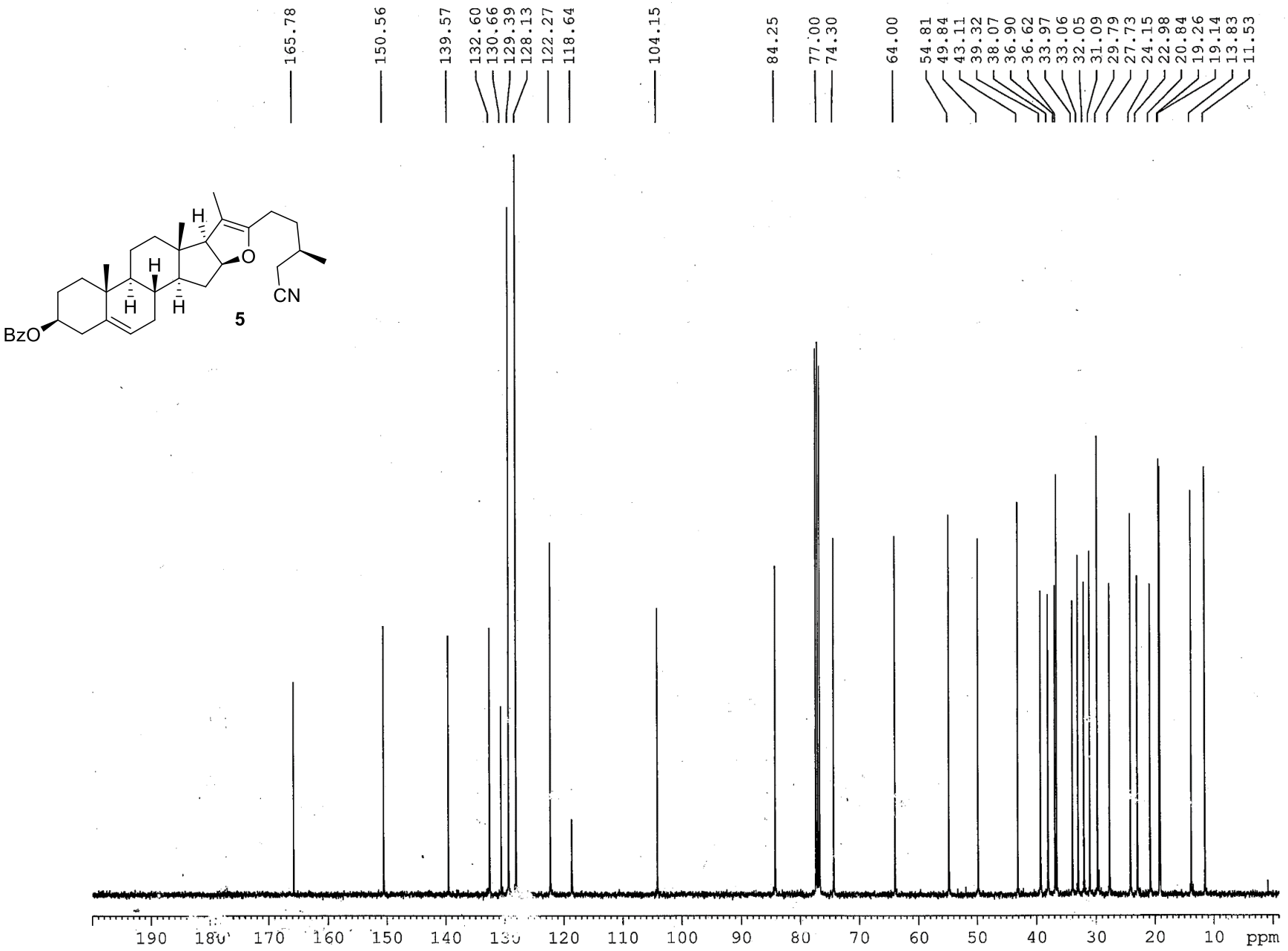
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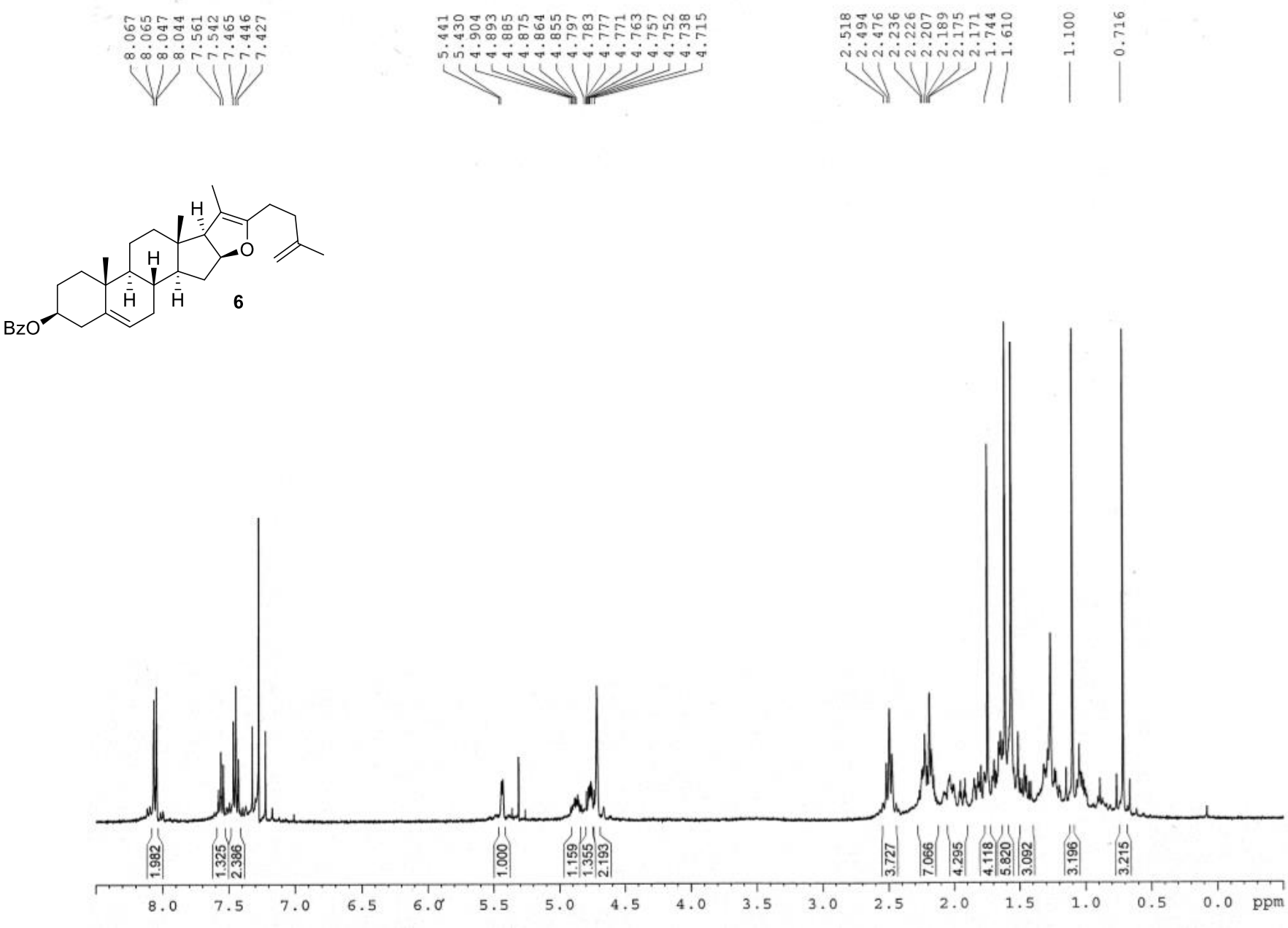
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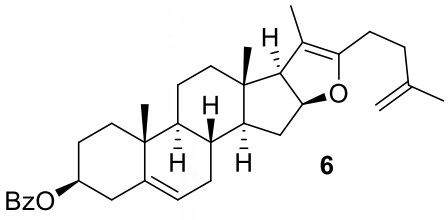
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H
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H
O
BzO

6

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74.47
64.20
54.95
53.41
50.00
43.20
39.52
38.19
37.04
36.77
35.20
34.12
32.21
31.22
27.86
24.42
22.39
20.98
19.40
13.94
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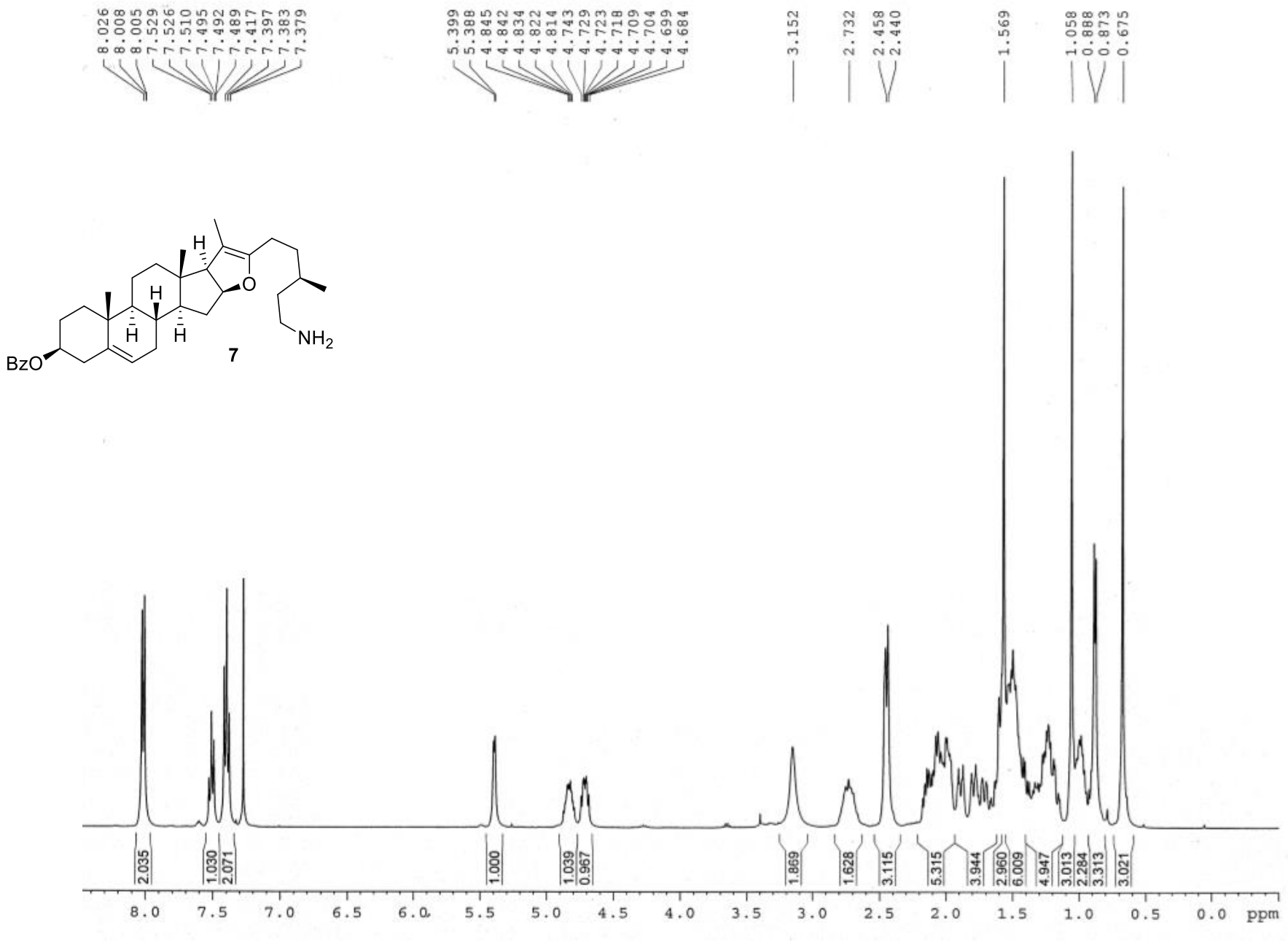
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4.822
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H
H
H
O
NH2
7
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2.071
1.000
1.039
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1.869
1.628
3.115
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3.944
2.960
6.009
4.947
3.013
2.284
3.313
3.021
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7.0
6.5
6.0
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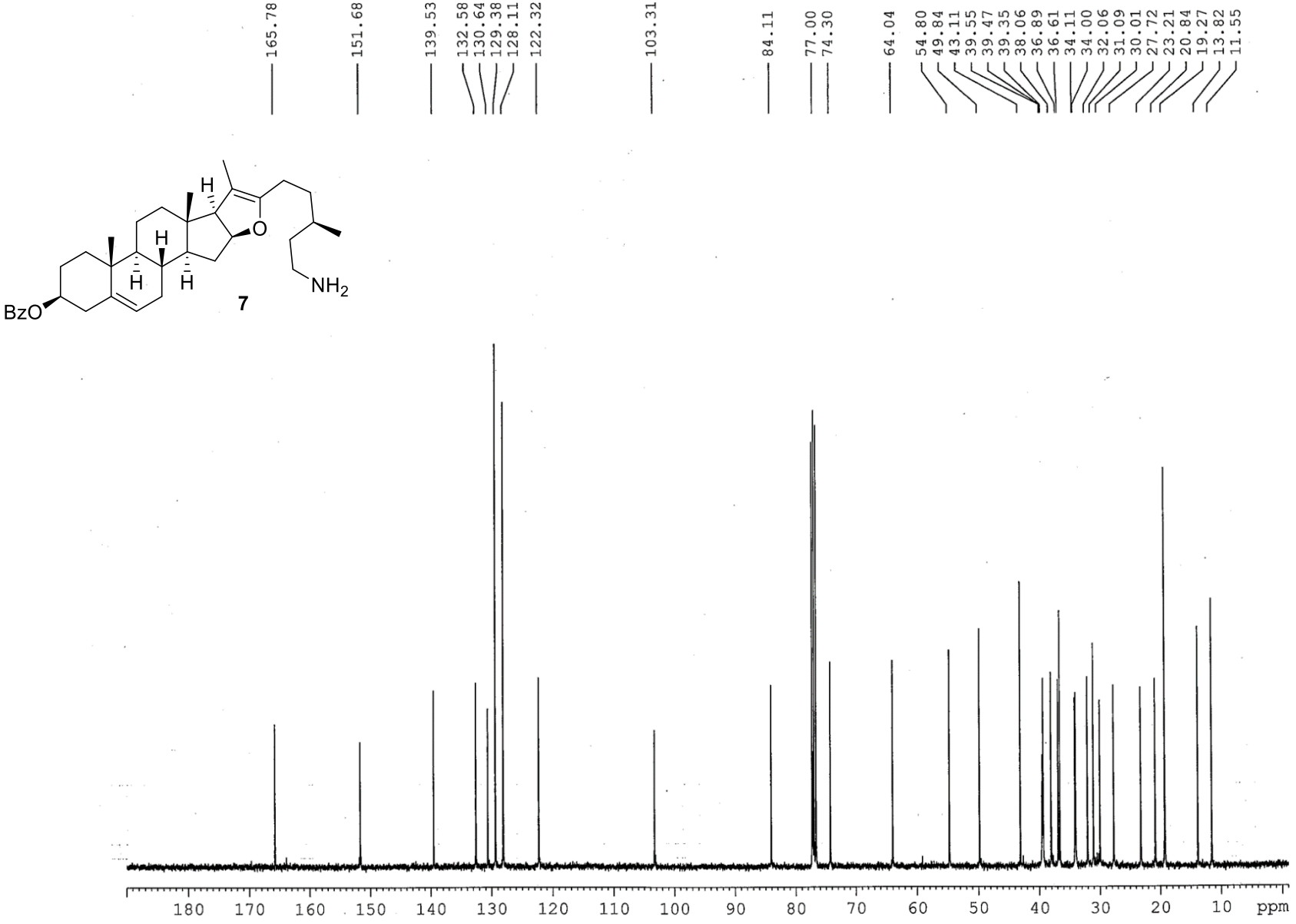
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54.80
49.84
43.11
39.55
39.47
39.35
38.06
36.89
36.61
34.11
34.00
32.06
31.09
30.01
27.72
23.21
20.84
19.27
13.82
11.55
BzO
H
H
H
H
O
NH2
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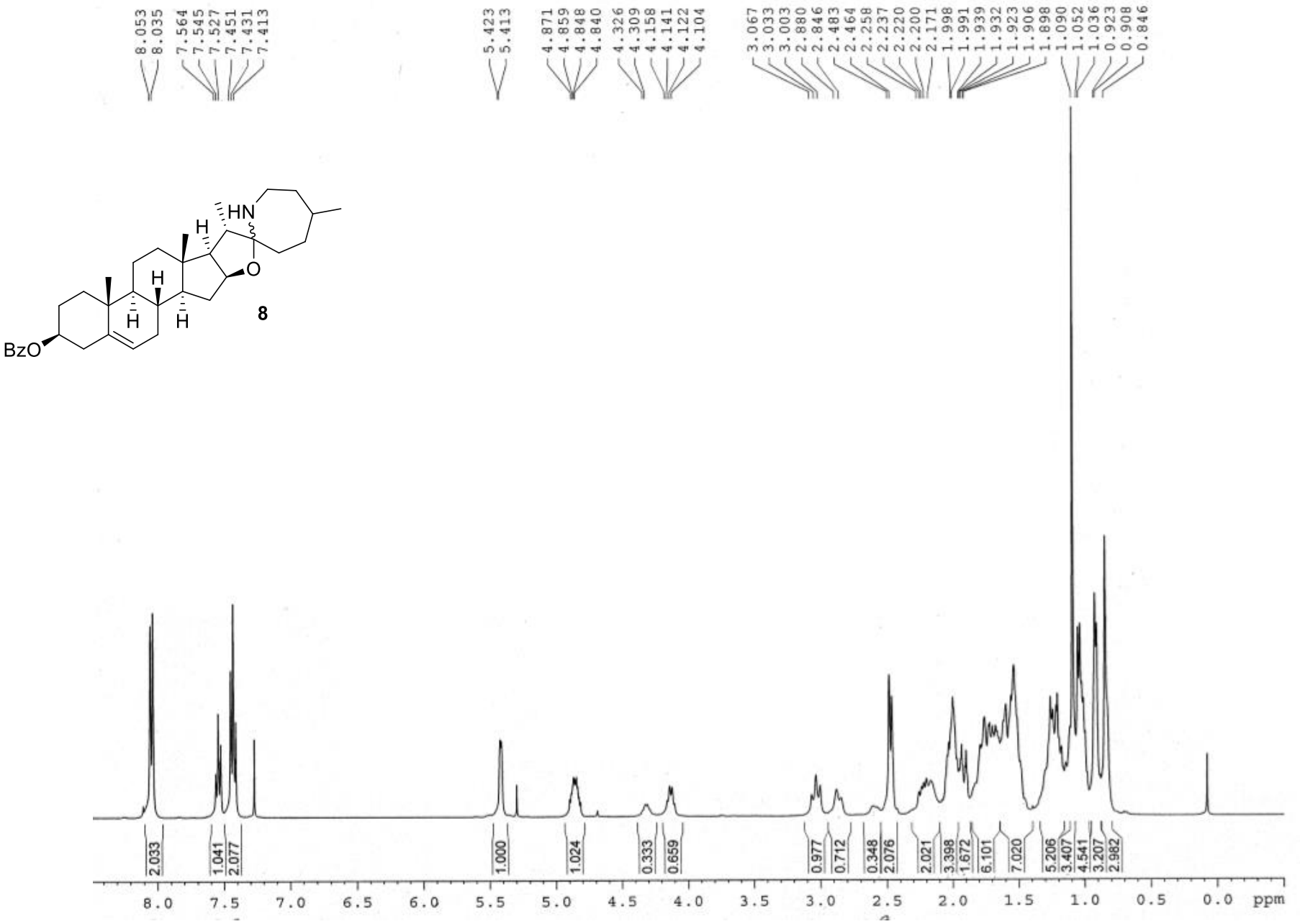
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4.840
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4.309
4.158
4.141
4.122
4.104
3.067
3.033
3.003
2.880
2.846
2.483
2.464
2.258
2.237
2.220
2.200
2.171
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1.991
1.939
1.932
1.923
1.906
1.898
1.090
1.052
1.036
0.923
0.908
0.846
HN
H
O
H
H
H
BzO
8
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2.077
1.000
1.024
0.333
0.659
0.977
0.712
0.348
2.076
2.021
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1.672
6.101
7.020
5.206
3.407
4.541
3.207
2.982
8.0
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7.0
6.5
6.0
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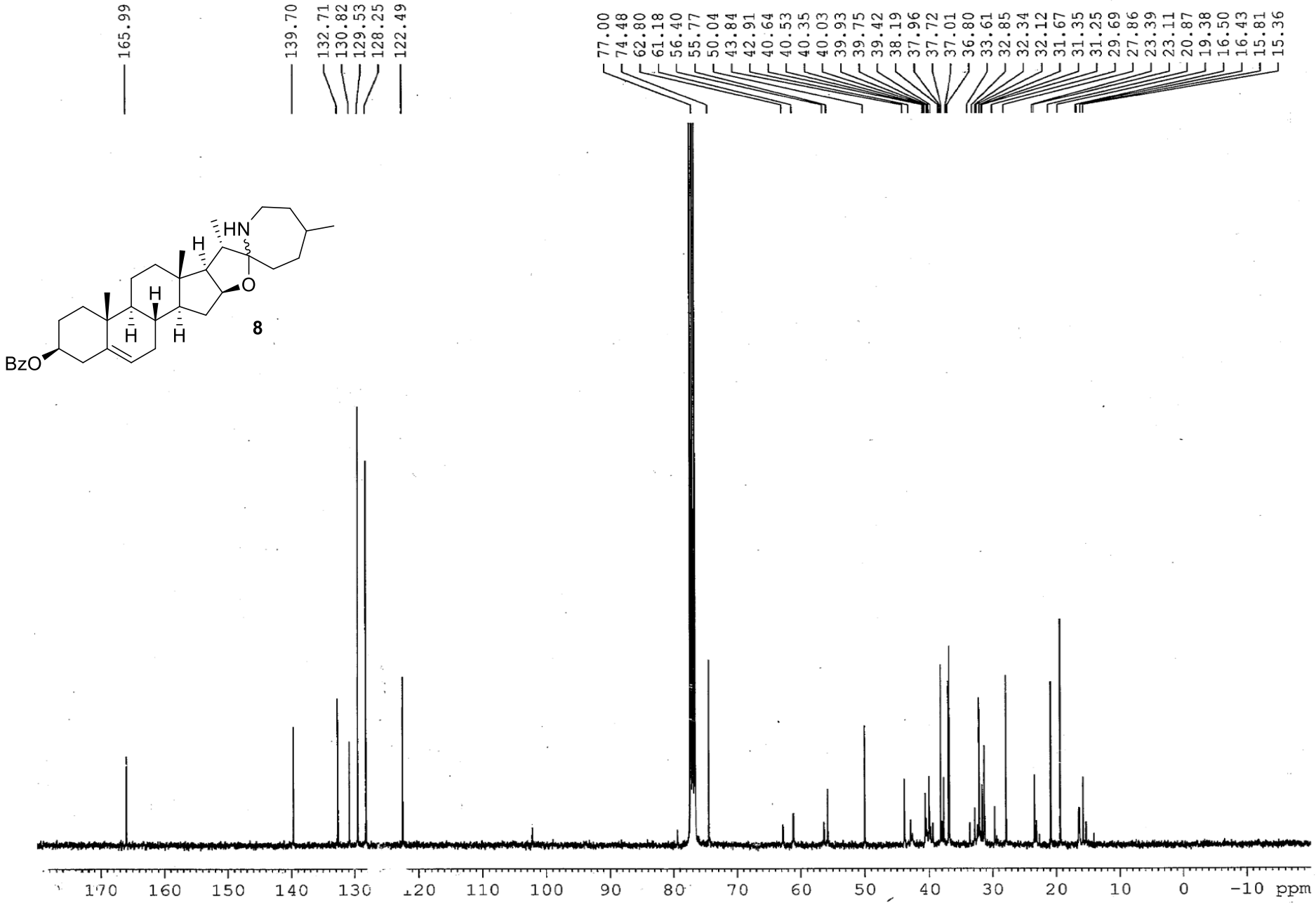
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43.84
42.91
40.64
40.53
40.35
40.03
39.93
39.75
39.42
38.19
37.96
37.72
37.01
36.80
33.61
32.85
32.34
32.12
31.67
31.35
31.25
29.69
27.86
23.39
23.11
20.87
19.38
16.50
16.43
15.81
15.36
HN
H
O
H
H
H
BzO
8
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130
120
110
100
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80
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60
50
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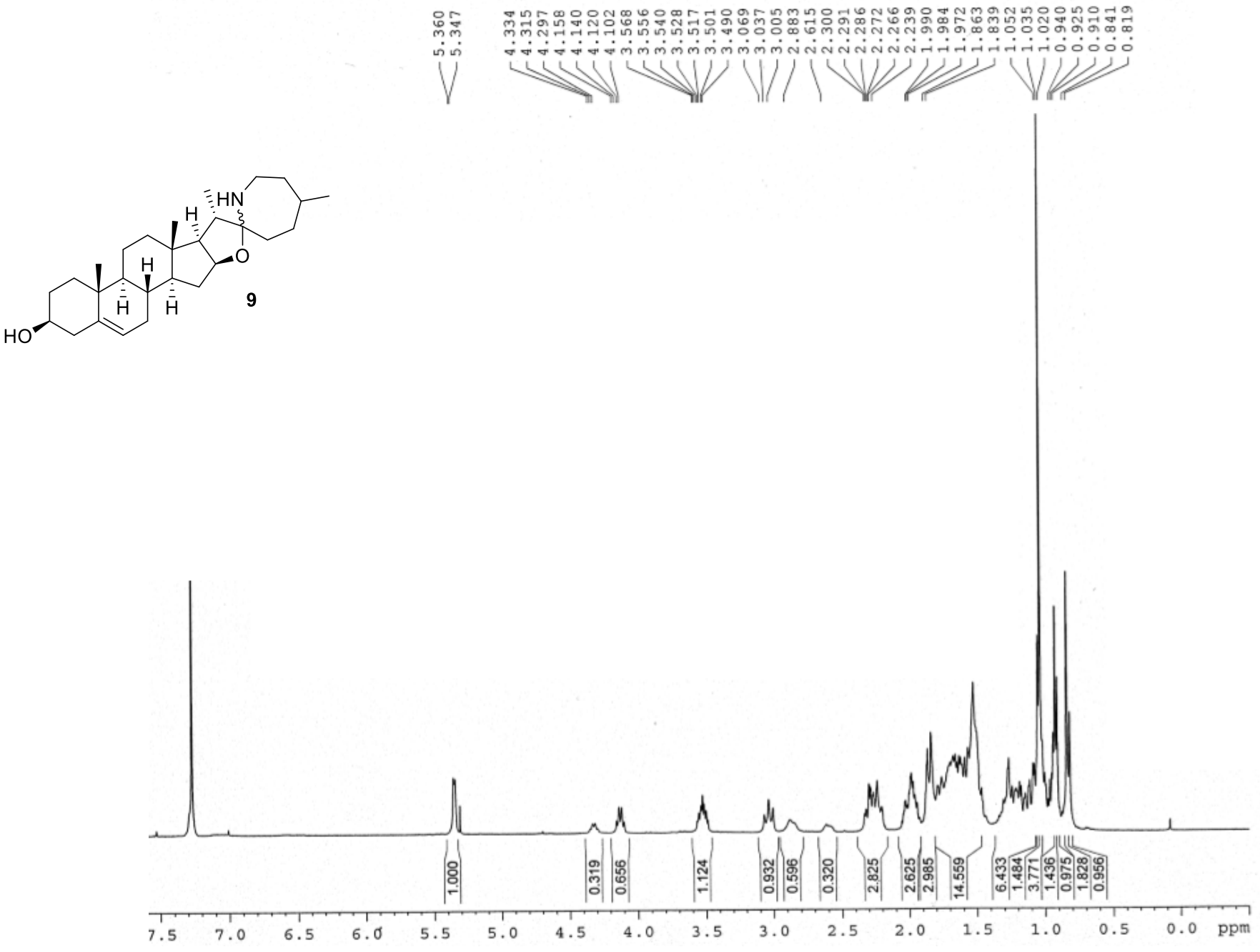
-10 ppm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3.517
3.501
3.490
3.069
3.037
3.005
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2.300
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2.286
2.272
2.266
2.239
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1.972
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1.839
1.052
1.035
1.020
0.940
0.925
0.910
0.841
0.819
HO
H
HN
O
H
H
H
9
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0.656
1.124
0.932
0.596
0.320
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2.625
2.985
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6.433
1.484
3.771
1.436
0.975
1.828
0.956
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6.5
6.0
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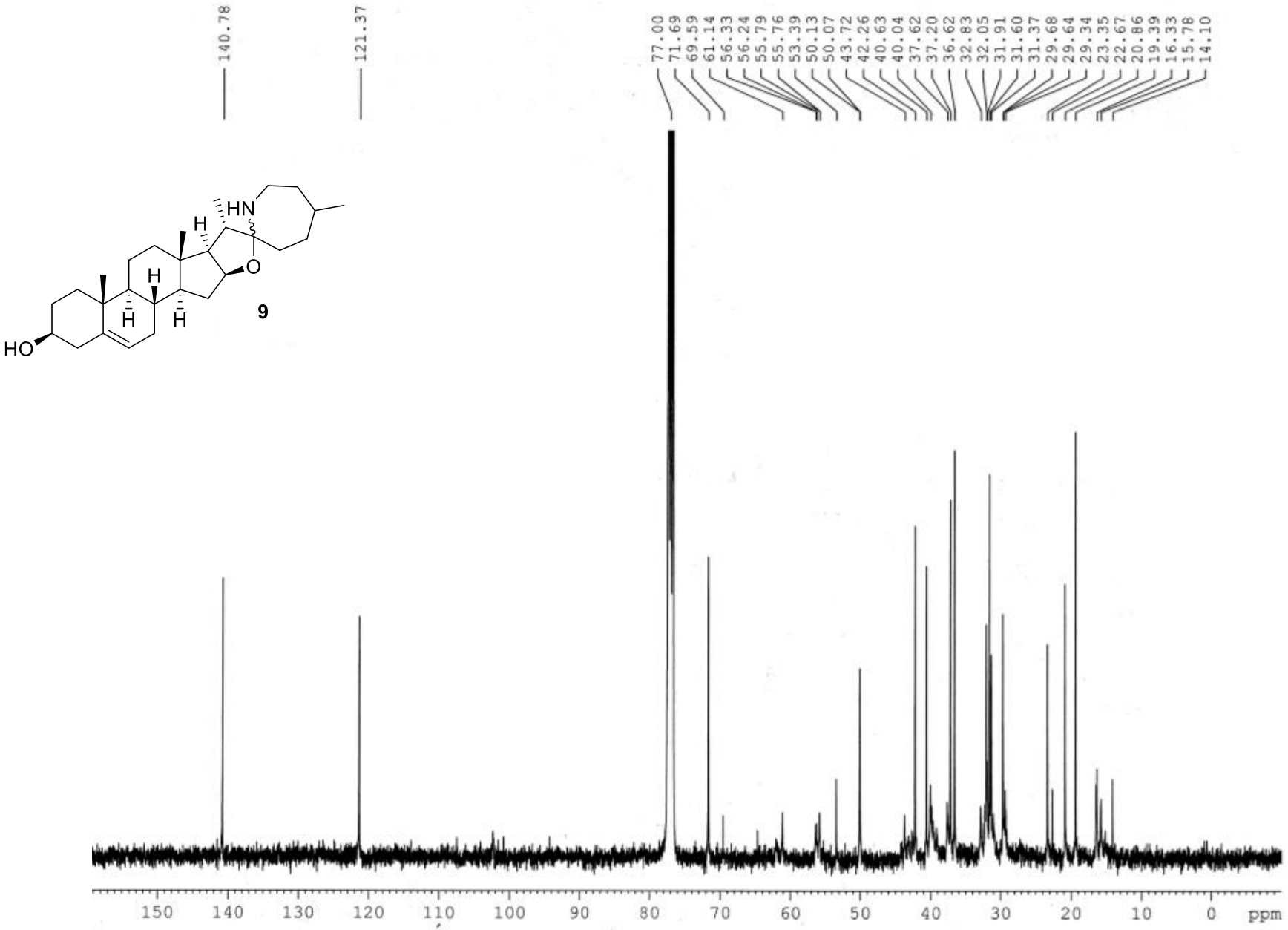
ppm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43.72
42.26
40.63
40.04
37.62
37.20
36.62
32.83
32.05
31.91
31.60
31.37
29.68
29.64
29.34
23.35
22.67
20.86
19.39
16.33
15.78
14.10
HO
H
HN
O
H
H
H
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130
120
110
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20
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0
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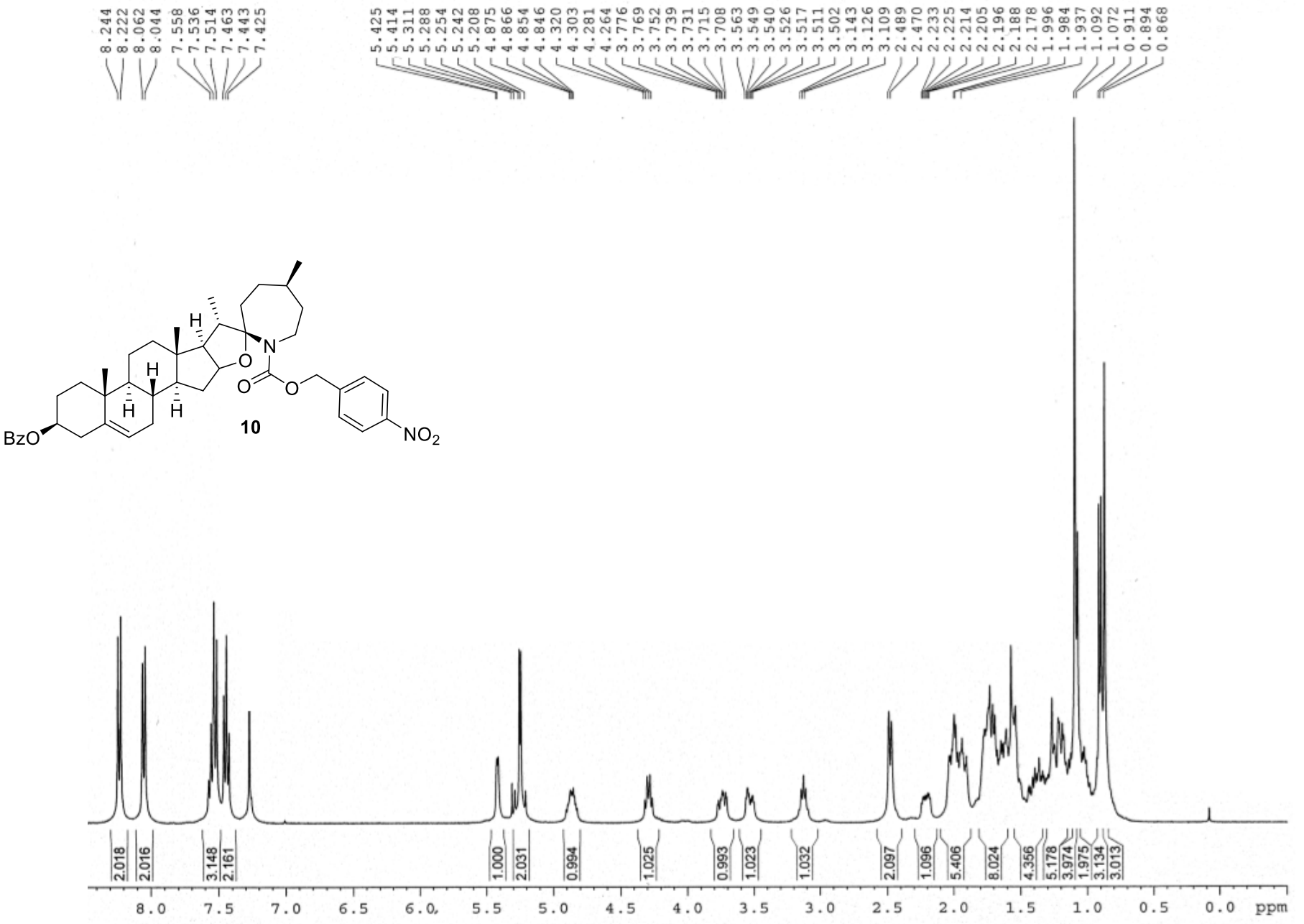
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5.288
5.254
5.242
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4.866
4.854
4.846
4.320
4.303
4.281
4.264
3.776
3.769
3.752
3.739
3.731
3.715
3.708
3.563
3.549
3.540
3.526
3.517
3.511
3.502
3.143
3.126
3.109
2.489
2.470
2.233
2.225
2.214
2.205
2.196
2.188
2.178
1.996
1.984
1.937
1.092
1.072
0.911
0.894
0.868
BzO
O
O
O
N
H
H
H
H
NO2
10
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3.148
2.161
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0.993
1.023
1.032
2.097
1.096
5.406
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4.356
5.178
3.974
1.975
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3.013
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7.0
6.5
6.0
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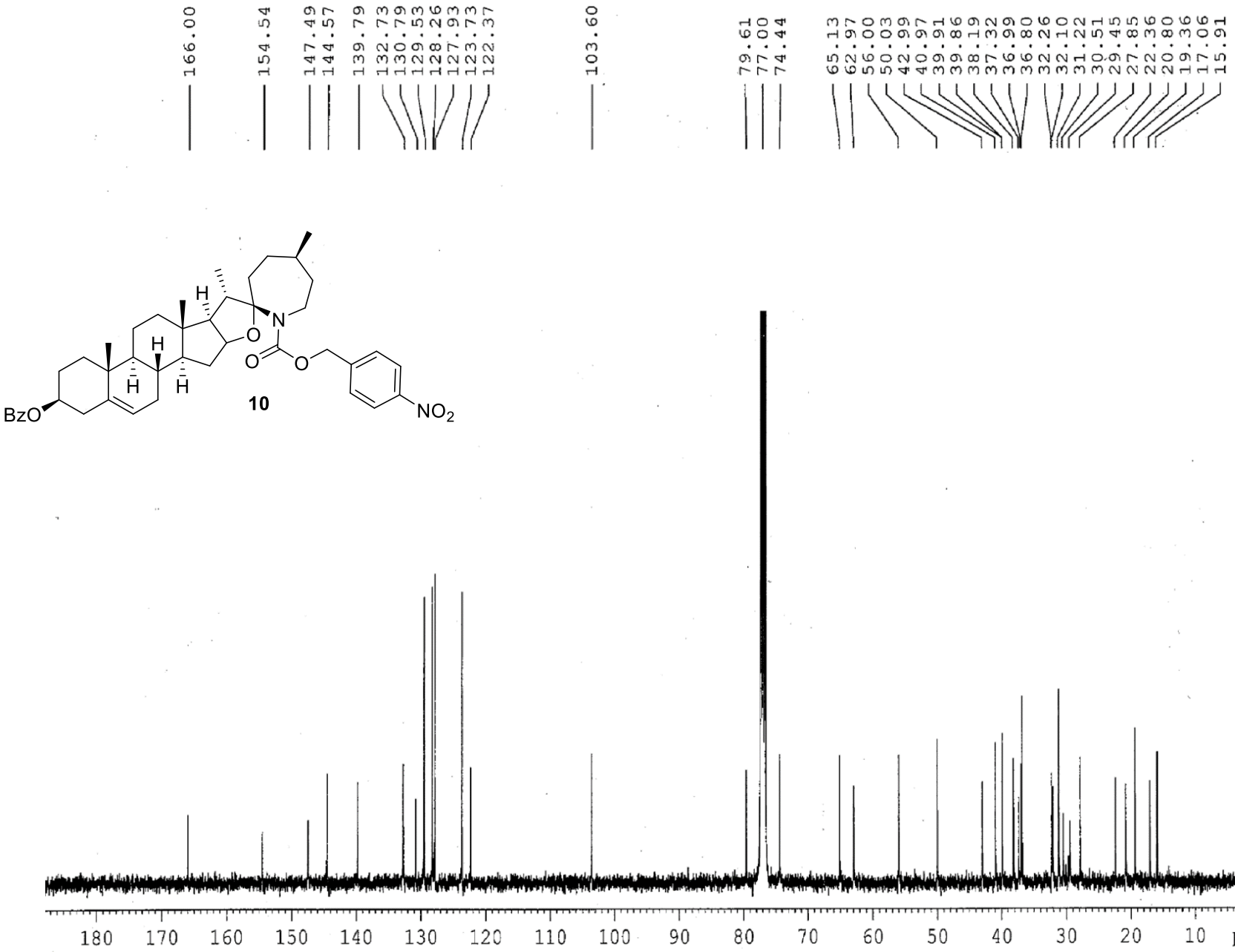
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144.57
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132.73
130.79
129.53
128.26
127.93
123.73
122.37
103.60
79.61
77.00
74.44
65.13
62.97
56.00
50.03
42.99
40.97
39.91
39.86
38.19
37.32
36.99
36.80
32.26
32.10
31.22
30.51
29.45
27.85
22.36
20.80
19.36
17.06
15.91
BzO
O
N
O
O
H
H
H
H
NO2
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150
140
130
120
110
100
90
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70
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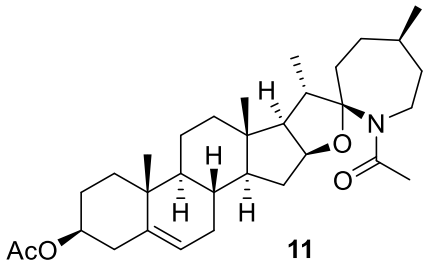
30
20
10
ppm


AcO
H
H
H
H
O
N
O

11

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4.619
4.607
4.592
4.583
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4.394
4.376
4.361
4.343
3.969
3.500
3.260
3.225
2.705
2.339
2.326
2.308
2.193
2.042
2.016
2.003
1.985
1.874
1.848
1.181
1.164
1.039
0.897
0.880
0.804
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0.895
0.876
0.240
0.921
0.981
3.563
3.007
3.435
3.009
2.350
8.843
6.632
3.828
3.010
3.773
2.743
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6.5
6.0
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4.0
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3.0
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1.5
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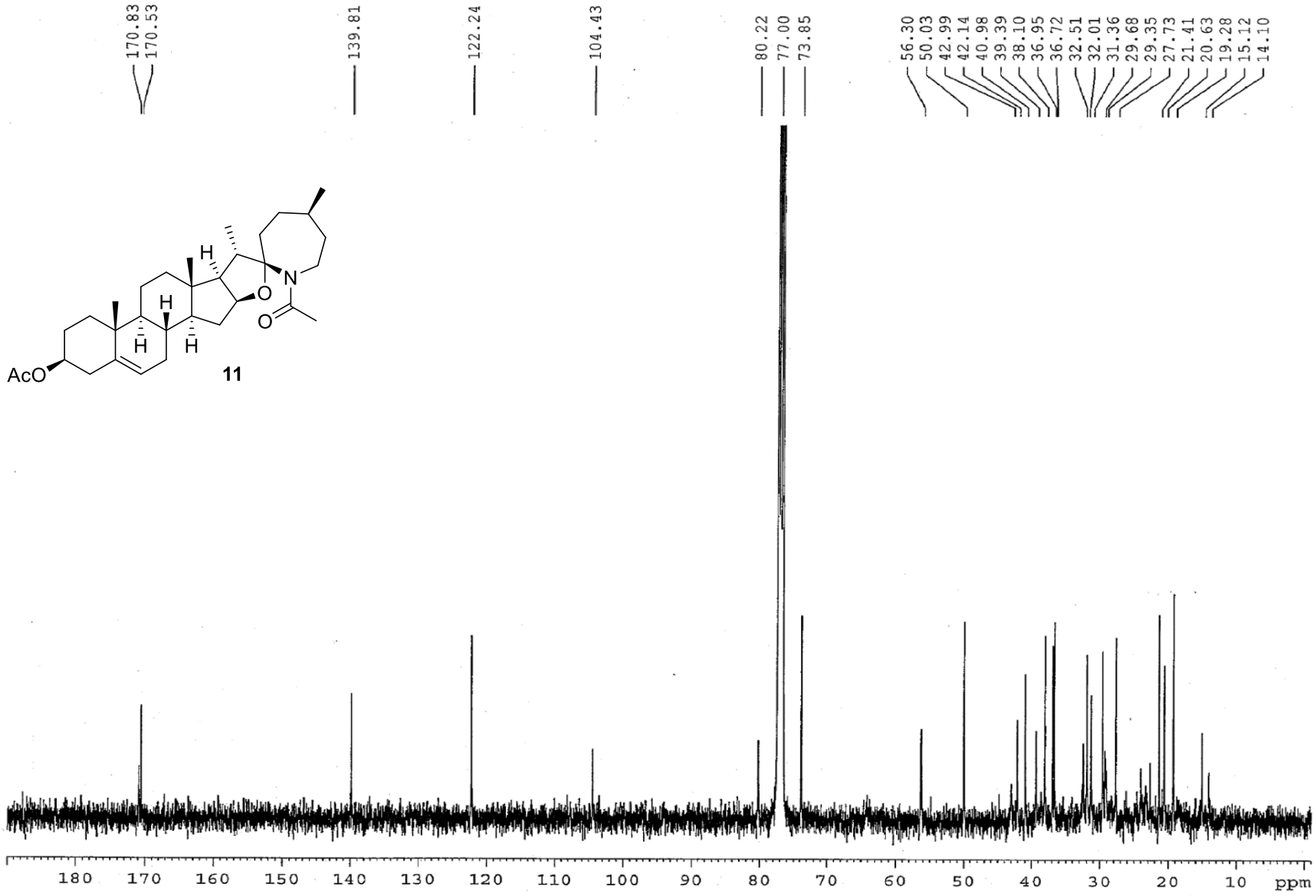
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42.14
40.98
39.39
38.10
36.95
36.72
32.51
32.01
31.36
29.68
29.35
27.73
21.41
20.63
19.28
15.12
14.10
AcO
H
H
H
H
O
N
O
11
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm