Supporting information

Supported synthesis of oxo-apratoxin

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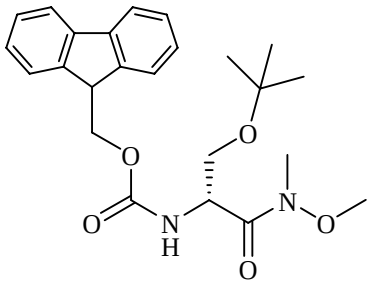
General procedures. ^{1}H NMR and ^{13}C NMR spectra were recorded at 75 MHz and 300 MHz or 100 MHz and 400 MHz respectively. Shifts are reported to the residual solvent peak. Data are reported as follows: Chemical shifts (δ), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), coupling constant and integration. Analytical TLC were performed on silica gel $60F_{254}$, and visualized by ultraviolet light and treatment with phosphomolybdic acid 20% in ethanol followed by heating. Column chromatography was performed on silica gel 60 (0.063-0.2 mm). Analytical HPLC were performed on a RP_{18}, 3.5μm (4.6x50mm) column, coupled to a UV-Vis detector. Chromatogram were obtained from a linear gradient of acetonitrile (0.1% TFA) in water (0.1% TFA), 0 to 100% within 15 minutes with a 1 mL/min flow. Preparative HPLC were performed usong a RP18 5μm (19x100mm) column coupled to a UV detector (214 nm). Chromatogram were obtained from a linear gradient of acetonitrile (0.1% TFA or TFA free) in water (0.1% TFA or TFA free), with a 20 mL/min flow. Retention time (t_R) are given in minutes. LC/ESI-MS are obtained using a C18 cartridge. Melting point were measured with a Büchi apparatus and are uncorrected. Optical rotations values were measured at 20°C, sodium ray. Dry THF was distilled from sodium with a small amount of benzophenone, dry DCM was distilled from CaH_2. All other anhydrous solvents have been used as received (on molecular sieves). All the supported reactions were performed in polypropylene syringes (10 or 20 mL) fitted with a polyethylene porous disc. For each Fmoc protected supported intermediates, an aliquot of resin was treated with DCM/TFE/AcOH (6:2:2) to give an analytical sample of the compound.

(*R*)-(9H-fluoren-9-yl)methyl 3-*tert*-butoxy-1-(methoxy(methyl)amino)-1-oxopropan-2-yl carbamate



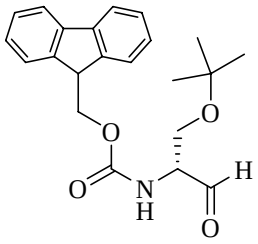
To a solution of HCl·HN(Me)-OMe (0.28 g, 2.87 mmol) in DMF (23 ml) were added Fmoc-(*D*)Ser(tBu)-OH (1 g, 2.61 mmol), BOP (1.154 g, 2.61 mmol) and N-methylmorpholine (0.66 ml, 6 mmol). After being stirred overnight at room temperature, the mixture was concentrated under reduce pressure and the residue dissolved in AcOEt. The organic layer was washed 3 times with a molar solution of $KHSO_4$, brine, saturated $NaHCO_3$, dried over $MgSO_4$ and concentrated under reduce pressure to afford the desired Weinreb amide (1.072 g, 93%) as a white foam, used for the next step without further purification.

t_R: 13.3 min

ESI+: $[M+H]^+$ = 427.3 (calculated: 427.21)

$[2M+H]^+$= 853.3 (calculated: 853.43)

(*R*)-(9H-fluoren-9-yl)methyl 1-*tert*-butoxy-3-oxopropan-2-yl carbamate (13)

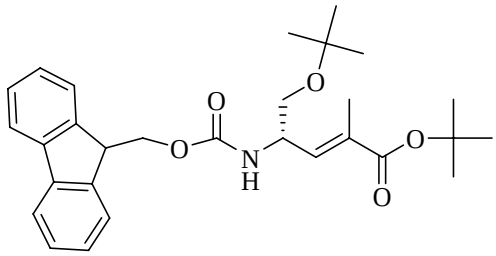


To a solution of the Weinreb amide (1.032 g, 2.42 mmol) in anhydrous THF (25 ml) at 0°C was added dropwise $LiAlH_4$ (4.6 ml, 1M/THF, 4.6 mmol). After being stirred for 45 min at the same temperature, the reaction was quenched by addition of $KHSO_4$ (1M, 100ml). Then, THF was removed under reduce pressure, the aqueous layer was extracted 3 times with AcOEt, the organic was washed with brine, dried

over $MgSO_4$ and concentrated under reduced pressure to afford the aldehyde **13** (820.7 mg, 93%). The latter was used without further purification to avoid epimerisation at its Cα position.

HRMS (FAB+) m/z: 368.1854 (calculated = 368.1784).

(*S*,*E*)-*tert*-butyl-4-(((9H-fluoren-9-yl)methoxy)carbonylamino)-5-*tert*-butoxy-2-methylpent-2-enoate (14)



To a solution of the aldehyde **13** (867 mg, 2.36 mmol) in anhydrous DCM (5 ml) was added phosphorane (1.05g, 2.83 mmol) at room temperature, the mixture was stirred for 3 hours and then concentrated under reduce pressure. Purification of the residue on silica gel (hexane/AcOEt 8:2, Rf:0.3) gave the pure protected serine vinylogue **14** (820 mg, 72%) as a white solid.

t_R: 16.0 min

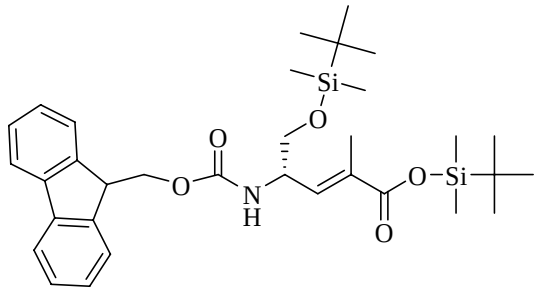
ESI+: $[M+H]^+$ = 480.20 (calculated: 480.23)

$[\alpha]^{20}_d$: + 9 (c=1, $CHCl_3$)

^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.21(s, 9H), 1.45 (s, 3H), 1.52 (s, 9H), 3.40 (m, 1H), 3.50 (m, 1H), 4.25 (t, *J*= 6.9 Hz, 1H), 4.42 (m, 2H), 4.59 (m, 1H), 5.28 (s, 1H), 6.62 (d, *J*= 8.8 Hz, 1H), 7.38 (m, 4H), 7.61 (d, *J*= 7.3, 2H), 7.79 (d, *J*= 7.5, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 12.9 (CH_3), 27.4 (CH_3), 28.1 (CH_3), 47.2 (CH), 49.7 (CH), 63.3 (CH_2), 66.8 (CH_2), 73.4 (C), 80.4 (C), 120.0 (CH), 125.1 (CH), 127.0 (CH), 127.7 (CH), 131.5 (C), 137.4 (CH), 141.3 (C), 143.9 (C), 155.9 (C), 167.1 (C).

(*S*,*E*)-*tert*-butyldimethylsilyl-4-(((9H-fluoren-9-yl)methoxy)carbonylamino)-5-(*tert*-butyldimethylsilyloxy)-2-methylpent-2-enoate



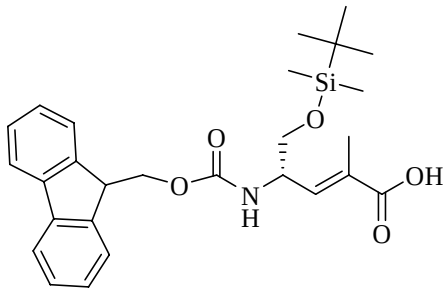
To a solution of the diprotected serine vinylogue **14** (820 mg, 1.71 mmol) in 2 ml of anhydrous DCM was added dropwise TBDMSOTf (0.894 ml, 3.89 mmol) at room temperature. After being stirred for 2 hours, the mixture was cooled down to 0°C, and 2,6 lutidine (0.453 ml, 3.89 mmol) was added. After 3 hours at 0°C, the reaction was quenched by addition of 2 ml of saturated sodium bicarbonate. After being stirred for 10 min to room temperature, the mixture was diluted with AcOEt, then the organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give a pale yellow oil, which was used for the next step without purification.

t_R: 18.5 min

ESI+: $[M+H]^+$ = 596.3 (calculated: 596.31)

$[M+NH_4]^+$ = 613.2 (calculated: 613.35)

(*S*,*E*)-4-(((9H-fluoren-9-yl)methoxy)carbonylamino)-5-(*tert*-butyldimethylsilyloxy)-2-methylpent-2-enoic acid (15)



To a solution of the crude disilylated serine vinylogue (1.4 g, 2.35 mmol) in a 2:1:1 THF/methanol/water mixture (15 ml) was added at room temperature potassium carbonate (974 mg,

7.05 mmol). After being stirred for 30 minutes at room temperature, the mixture was diluted with water and saturated sodium bicarbonate. The aqueous layer was extracted 3 times with AcOEt, the combined organic layers dried over $MgSO_4$ and concentrated under reduce pressure. Silica gel chromatography afforded the protected modified serine **15** as a white solid (660 mg, 80% over 2 steps).

t_R: 15.4 min

HRMS (FAB+) m/z: 482.2333 (calculated = 482.2284)

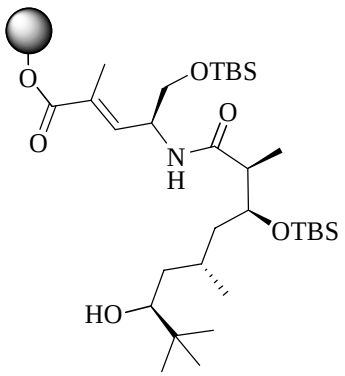
$[\alpha]^{20}_d$: +1 (c = 1.03, $CHCl_3$)

^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.00 (s, 6H), 0.81 (s, 9H), 1.86 (s, 3H), 3.57 (m, 1H), 3.64 (m, 1H), 4.12 (t, *J*= 6.8 Hz, 1H), 4.29 (m, 2H), 4.47 (m, 1H), 5.17 (d, *J*= 6.5 Hz, 1H), 6.69 (d, *J*= 8.4 Hz, 1H), 7.15-7.35 (m, 4H), 7.47 (m, 2H), 7.66 (d, *J*= 7.5, 2H)

^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): -5.47 (CH_3), 18.3(C), 20.8 (CH_3), 25.8 (CH_3), 47.2 (CH), 51.0 (CH), 64.6 (CH_2), 66.9 (CH_2), 125.0 (CH), 127.0 (CH), 127.7 (CH), 129.6 (C), 140.7 (CH), 141.3 (C), 143.8 (C), 155.9 (C), 172.6 (C), 176.9 (C)

Synthesis of the first linear precursor (22)

Anchoring of the modified serine 16 and coupling with the polyketide 12 (16)



To 1g of chlorinated chlorotrityl resin swelled in DCM (5 ml) and DIEA (310 µl, 1.78 mmol) was added the protected modified serine **15** (0.89 mmol) dissolved in DCM (5 ml) with DIEA (310 µl, 1.78 mmol). After being stirred for 3 hours, the resin was washed with DCM (3x10 ml). The remaining chlorinated active sites of the resin were then capped by swelling the resin in DCM (8 ml) with MeOH (1 ml) and DIEA (1 ml). After 1 hour stirring, the resin was washed several times with DCM and dried under reduce pressure.

Removal of the Fmoc protecting group was carried out by treatment with a solution of DMF/pyridine 4:1 (10 ml) and the mixture was stirred for 30 min. After filtration, the resin was treated again with DMF/pyridine 4:1 (10 ml) for 30 min. After filtration, the resin was washed with DCM (3x10 ml), isopropanol (3x10 ml) and DCM (3x10 ml) and dried under vacuum.

To the resin (1 equiv. of free NH_2, calculated by dosing the deprotected Fmoc by UV-Vis spectra) swelled in DMF and DIEA (2.6 equiv.) was added the polyketide **12** (1.5 equiv.), which was first pre-activated in DMF and DIEA (2.6 equiv.) with the activating agent BOP (1.65 equiv.) for 5 minutes. The mixture was stirred overnight and the resin was washed 2 times with DMF, 2 times with isopropanol and 4 times with DCM.

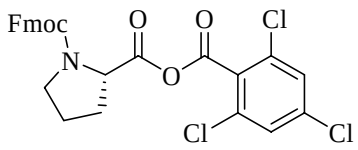
The compound **16** was used for the next step directly.

t_R: 17.14 min

ESI+ $[M+H]^+$: 602.4 (calculated: 602.4)

Fmoc-proline esterification on solid support (17)

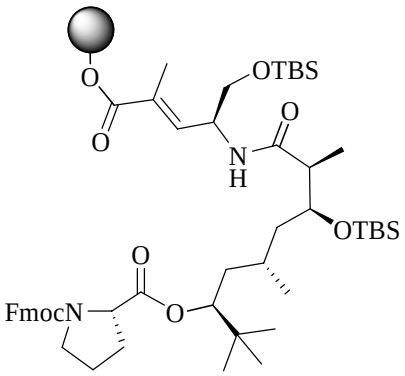
Mixed anhydride formation



To the Fmoc-Pro (710 mg, 2.1 mmol, 1 equiv.) in of THF (3 ml) was added DIEA (580 µl, 1.6 equiv.) followed by trichlorobenzoyl chloride (400 µl, 1.2 equiv.). The mixture was stirred for 3 hours at room

temperature and filtrated over a pad of silica gel. The filtrate was concentrated under reduced pressure to give the mixed anhydride as a white foam in quantitative yield. The latter was used without purification for the next step.

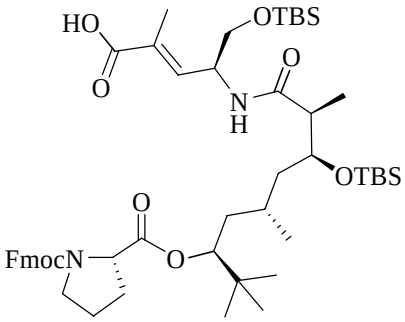
Polyketide supported acylation (17)

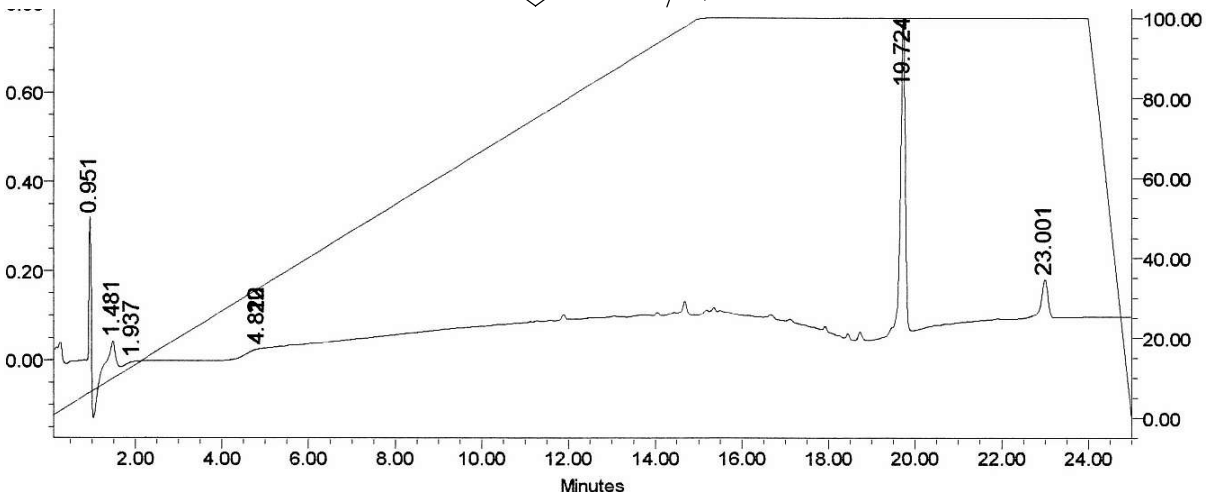


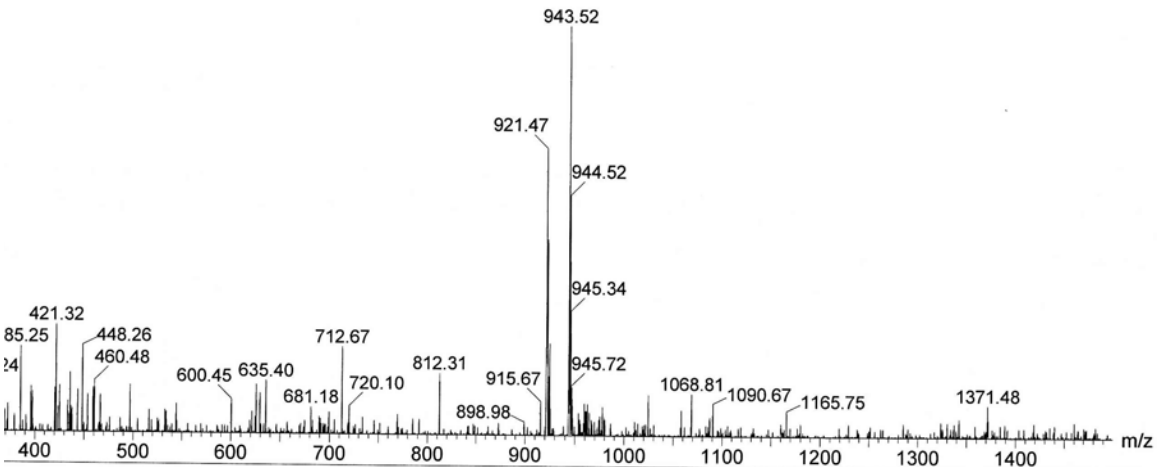
To the mixed anhydride (5 equiv.) dissolved in toluene was added the resin charged with the free alcohol (1 equiv.). DMAP (5 equiv.) dissolved in toluene was then added and the mixture was allowed to stir overnight at room temperature. The toluene was then removed by filtration, and the resin was washed 4 times with MeOH, 4 times with DCM and dried under vacuum to give the supported protected fragment **17**. An analytic sample was cleaved from the resin.

t_R: 19.72 min

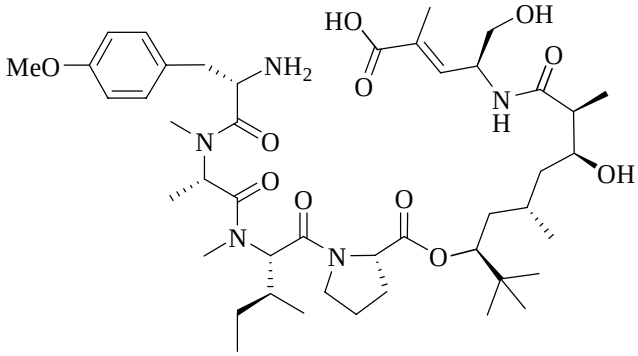
ESI+ $[M+H]^+$: 921.47 (calculated: 921.54); **$[M+Na]^+$:** 943.52 (calculated: 943.53)





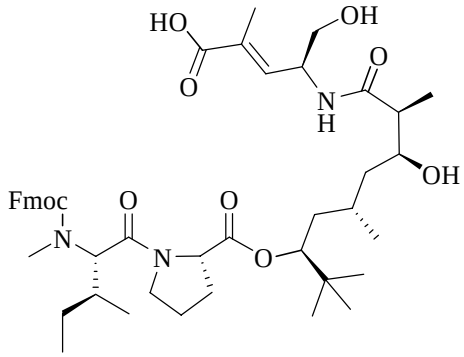


Deprotected linear precursor 22



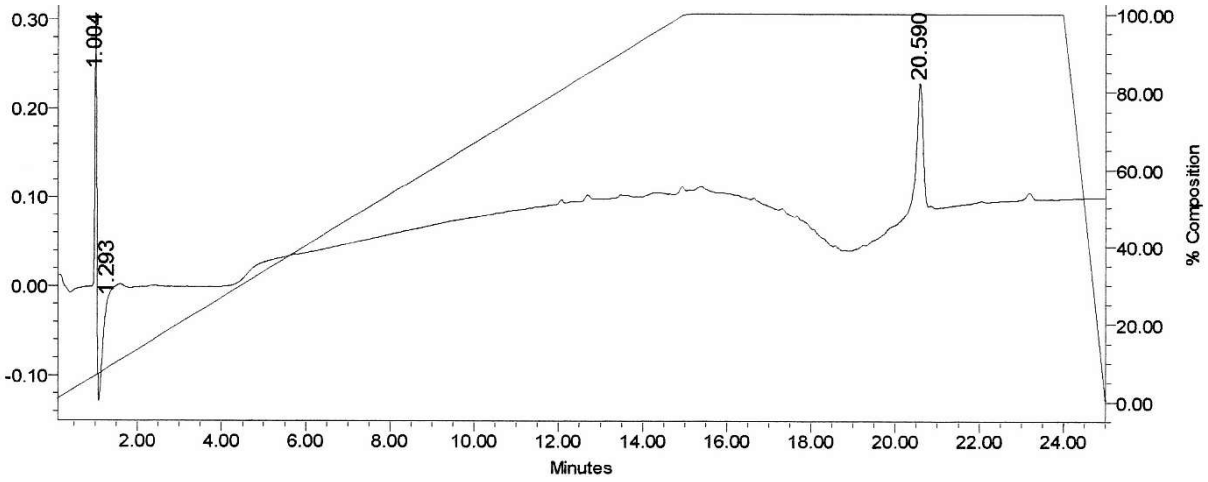
The Fmoc protecting group was removed from the fragment **17** as described previously. To the resin (1 equiv. of free NH_2, calculated by dosing the deprotected Fmoc by UV-Vis spectra) swelled in DMF and DIEA (4.4 equiv.) was added the *N*-Fmoc-*N*-Me-Ile (4 equiv.), which was first pre-activated in DMF and DIEA (4.4 equiv.) with HATU (4.4 equiv.) for 5 minutes. The mixture was stirred overnight and the resin was washed 2 times with DMF, 2 times with isopropanol and 4 times with DCM.

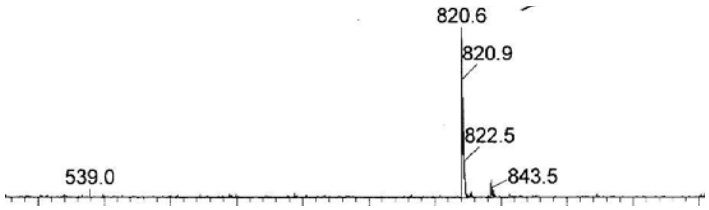
Intermediate analysis (18)



t_R: 20.59 min

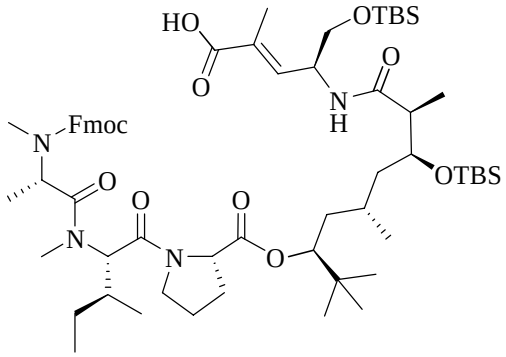
ESI+ $[M+H]^+$: 820.6 (calculated: 820.47: corresponding to the mass of the compound without the 2 TBS protecting group, which have been cleaved during the MS analysis).





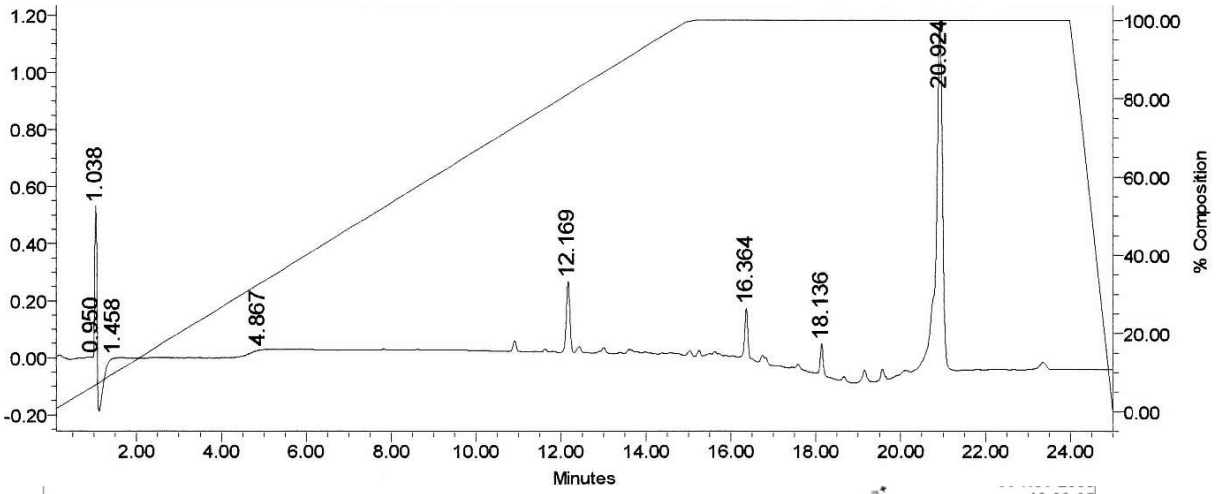
After Fmoc deprotection, *N*-Fmoc-*N*-Me-Ala (4 equiv.) was coupled under the same conditions (DIEA (8.8 equiv.) HATU (4.4 equiv.) in DMF). This coupling was carried uot twice under the same conditions.

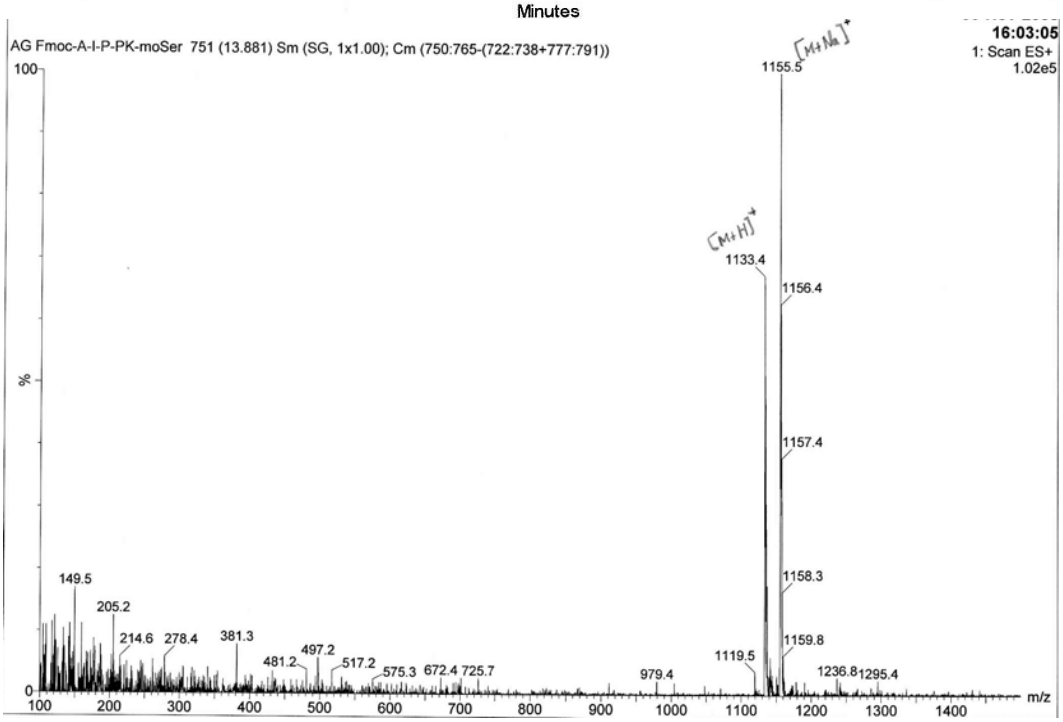
Intermediate analysis (19)



t_R: 20.92 min

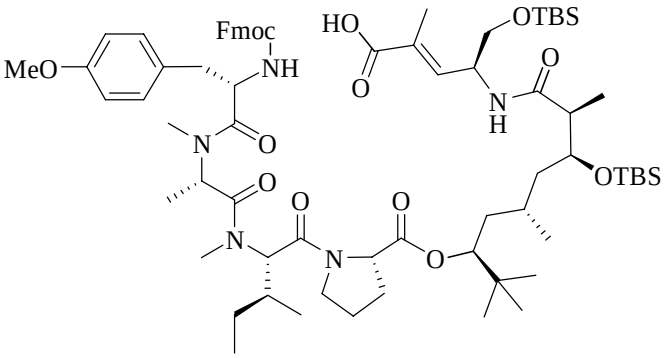
ESI+ $[M+H]^+$: 1133.4 (calculated: 1133.69); **$[M+Na]^+$:** 1155.5 (calculated: 1155.67)





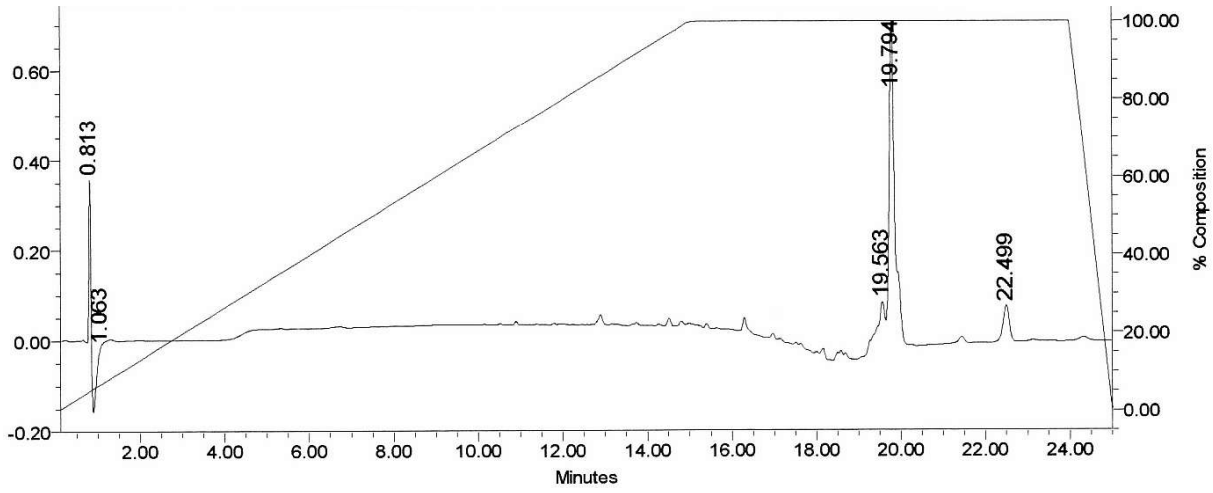
After Fmoc deprotection, *N*-Fmoc-*O*-Me-Tyr (4 equiv.) was coupled under the same conditions (DIEA (8.8 equiv.) HATU (4.4 equiv.) in DMF).

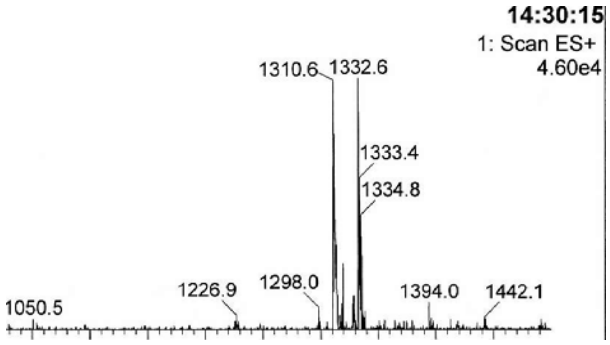
Intermediate analysis (20)



t_R: 19.79 min

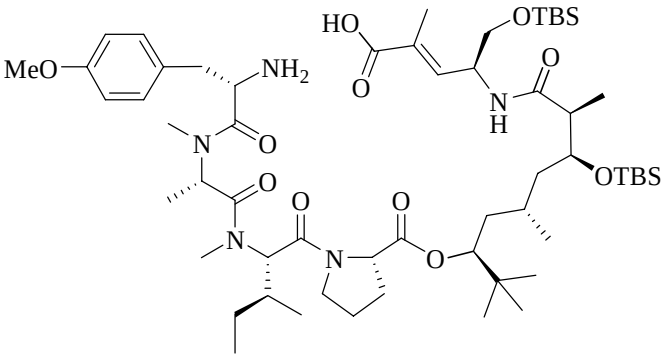
ESI+ $[M+H]^+$: 1310.6 (calculated: 1310.77); $[M+Na]^+$: 1332.6 (calculated: 1332.76)





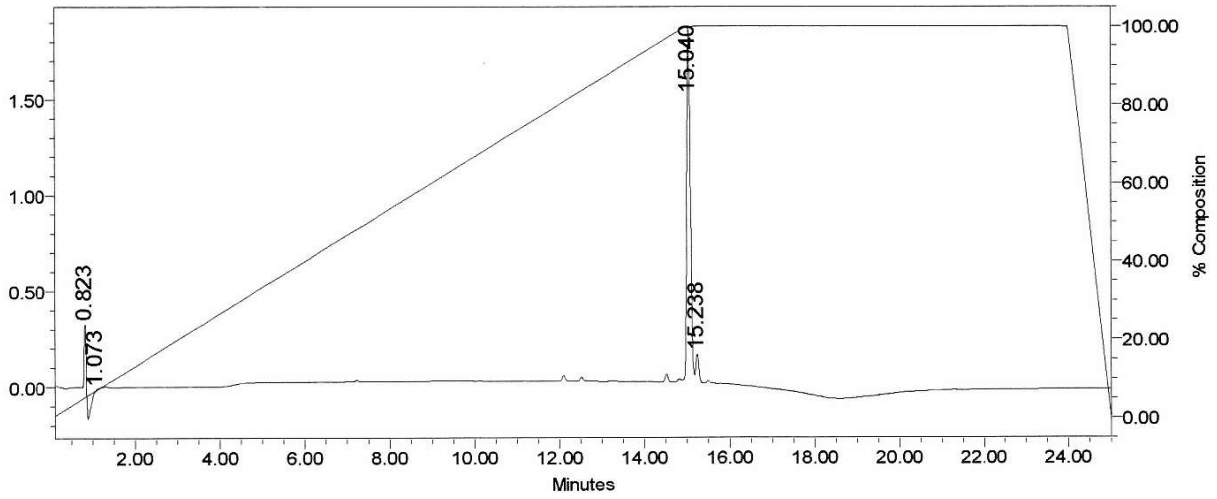
After Fmoc deprotection, the compound was cleaved from the resin by treatment with DCM/TFE/AcOH (6:2:2) during 40 min. This treatment was repeated twice and the combined filtrates were concentrated under vacuum to give the TBS-protected linear precursor.

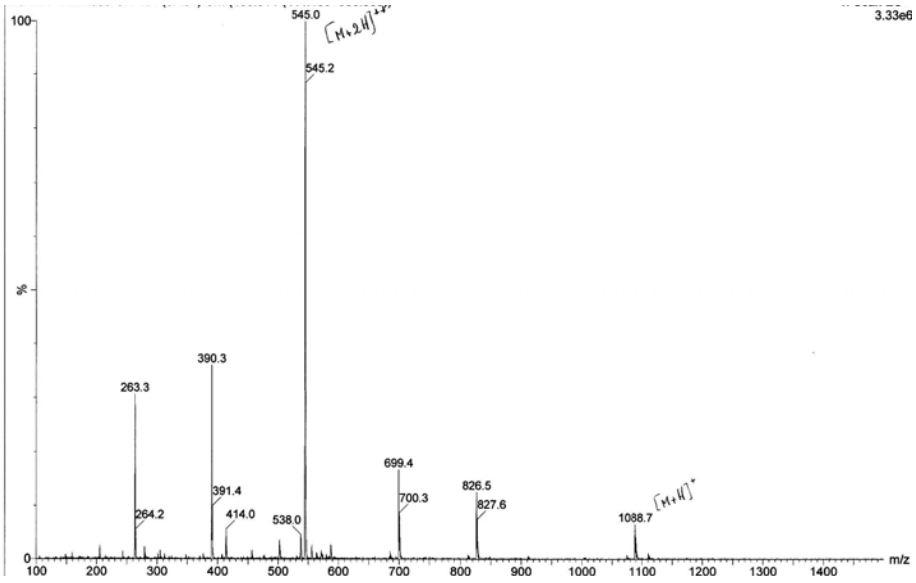
Intermediate analysis (21)



t_R: 15.04 min

ESI+ $[M+H]^+$: 1088.7 (calculated: 1088.70); **$[M+2H]^{2+}$:** 545.0 (calculated: 544.85)

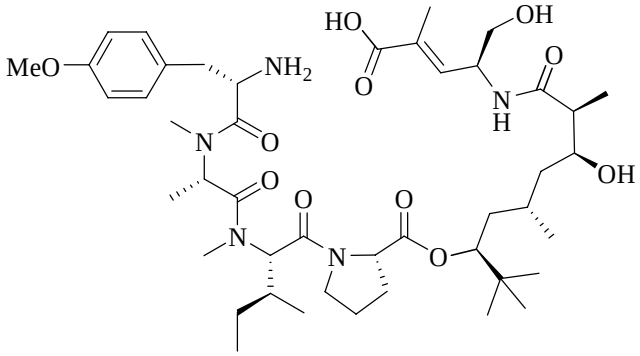


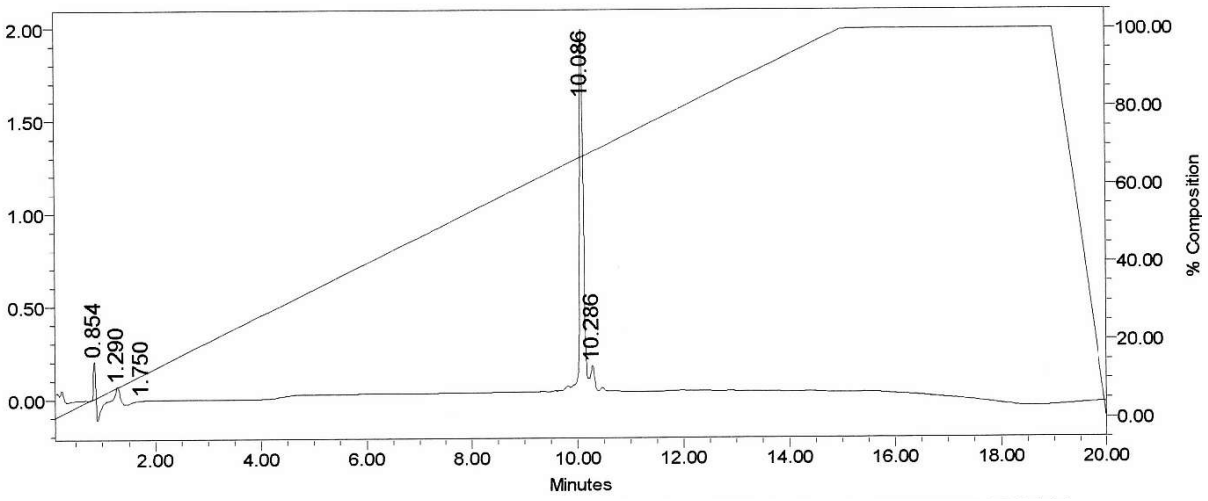


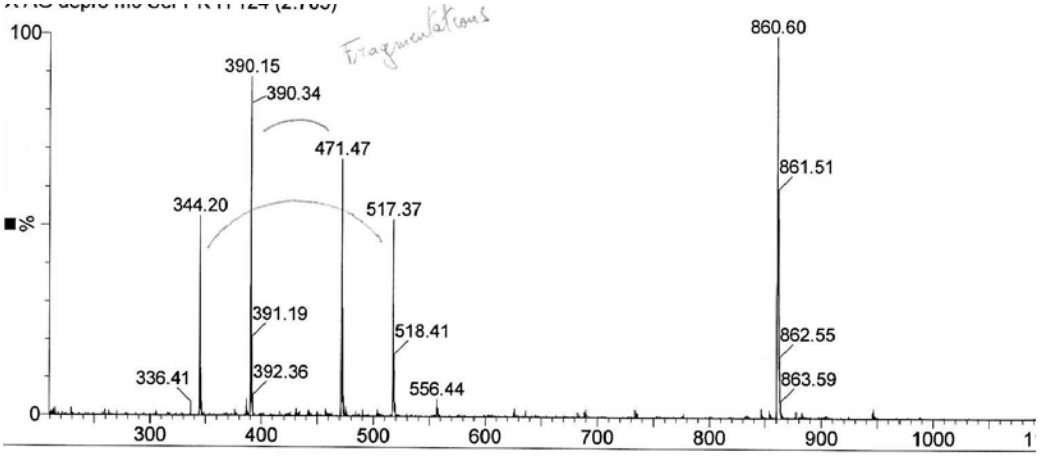
To remove the 2 TBS protecting group, the compound was subjected to several dissolution in 0.1% TFA in ACN solution followed by concentration under reduce pressure, until complete deprotection. The compound was used directly in the next lactamisation step.

The overall yield for precursor elongation and deprotection was 68%.

Deprotected linear precursor 22 analysis





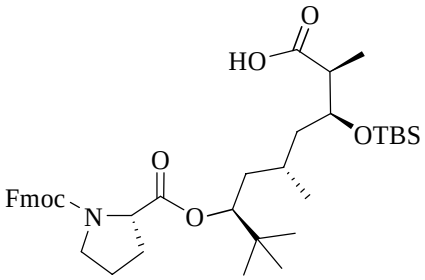


Synthesis of the second linear precursor (25)

The polyketide was anchored first, following the method reported for the serine analogue anchoring.

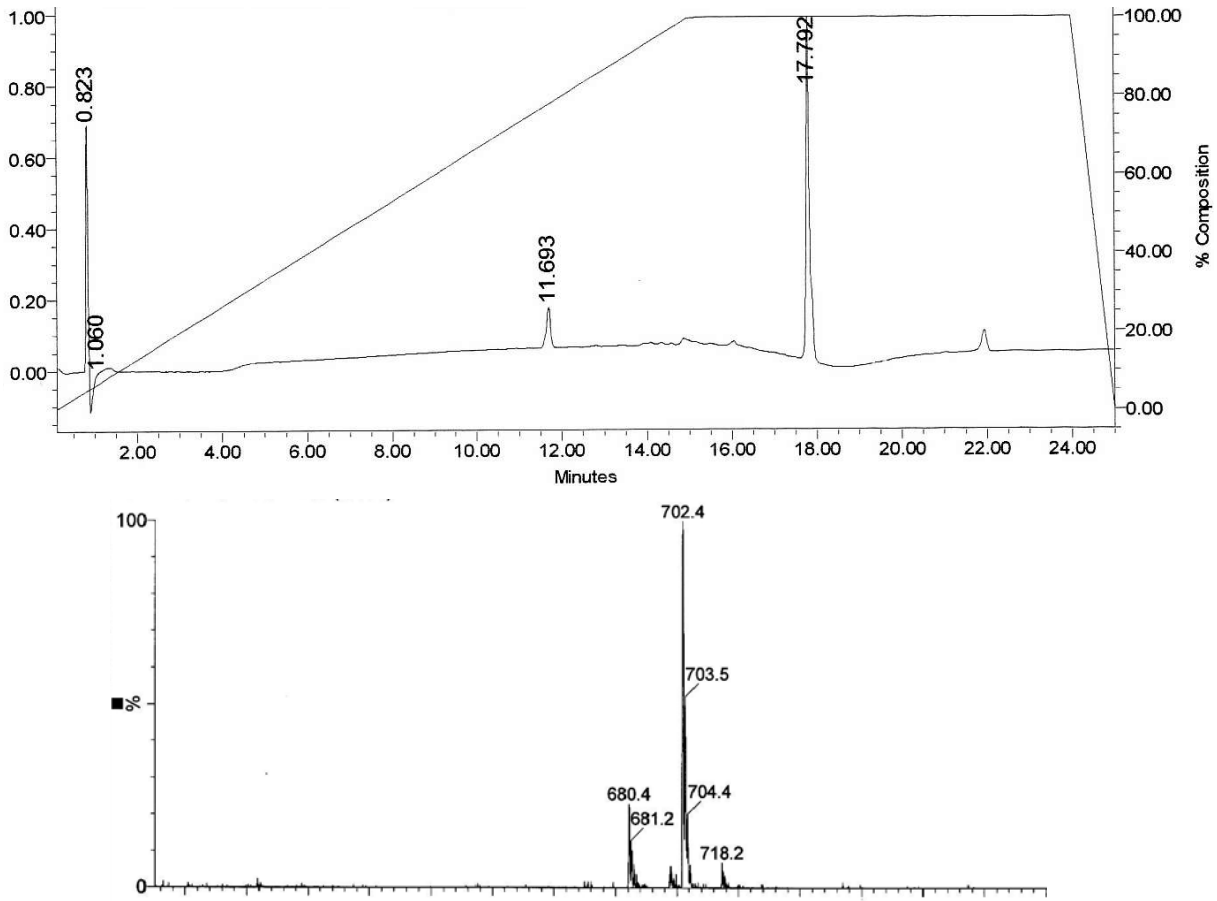
The Fmoc-Pro was then coupled using the previously reported Yamaguchi esterification.

Intermediate analysis (23)



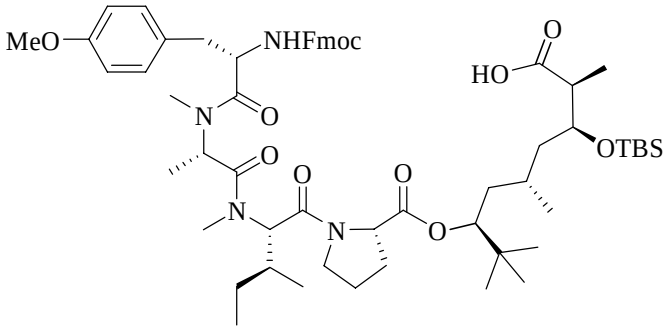
t_R: 17.79 min

ESI+ $[M+H]^+$: 680.4 (calculated: 680.39); **$[M+Na]^+$:** 702.4 (calculated: 702.38)



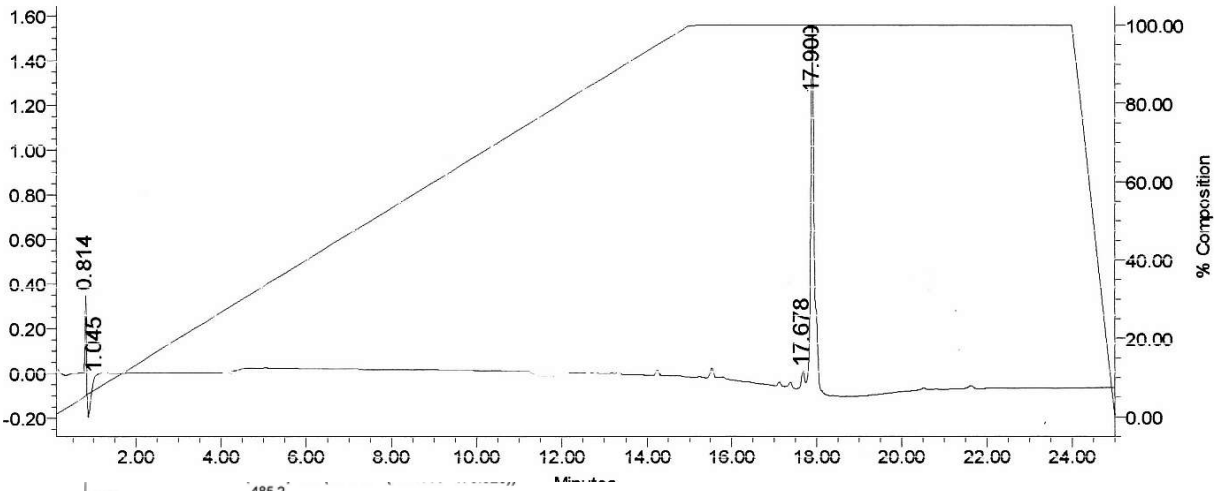
The next *N*-Fmoc-*N*-Me-Ile, *N*-Fmoc-*N*-Me-Ala and *N*-Fmoc-*O*-Me-Tyr deprotections and coupling sequence were carried out as described above.

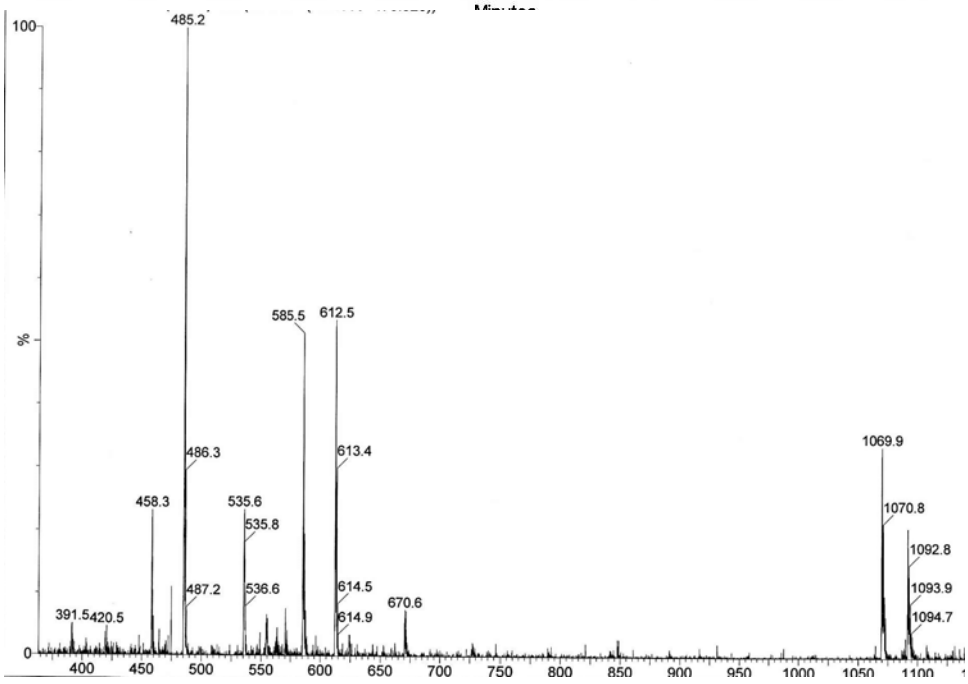
Intermediate analysis



t_R: 17.90 min

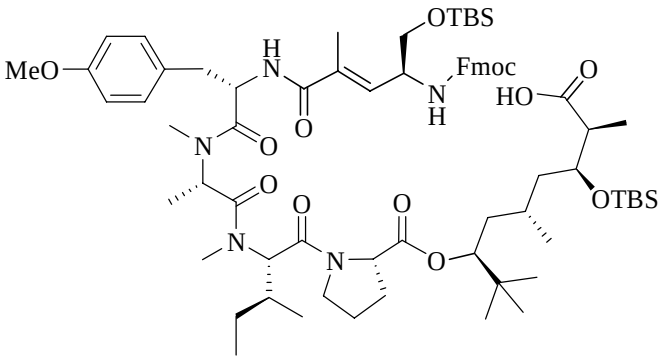
ESI+ $[M+H]^+$: 1069.9 (calculated: 1069.62); fragmentations: 485.2+585.2 and 458.3+612.5





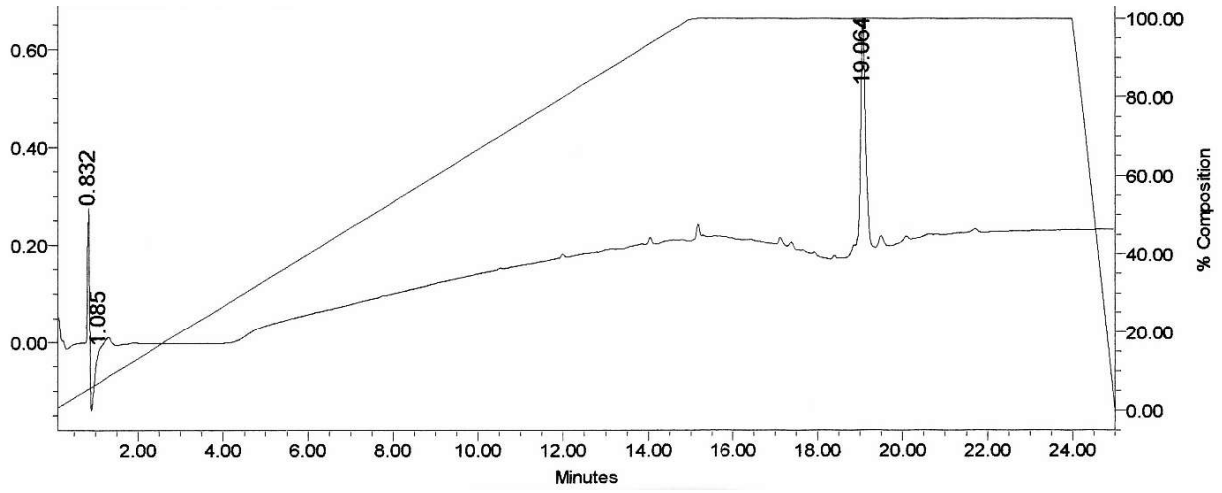
After Fmoc removal from the terminal amino group, the Fmoc protected serine analogue (4 equiv.) was coupled using HATU (4.4 equiv.) with DIEA (8.8 equiv.) as described above.

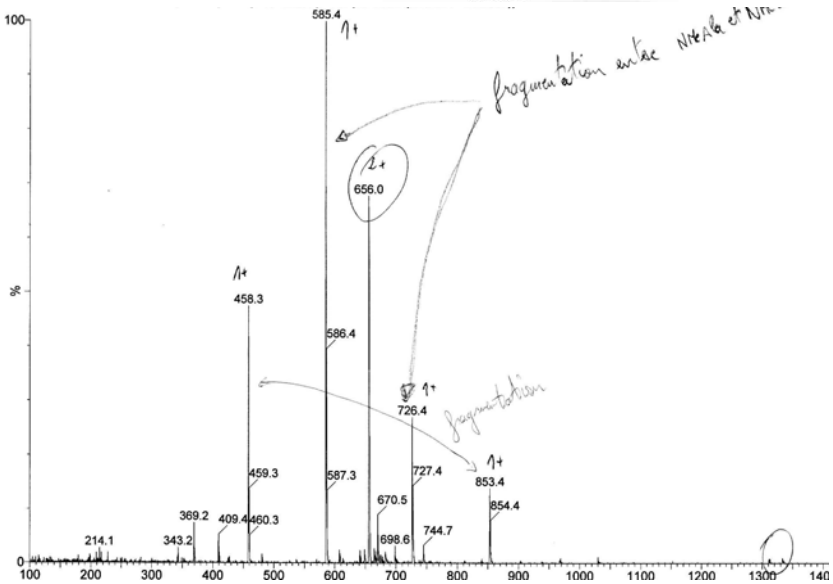
Intermediate analysis

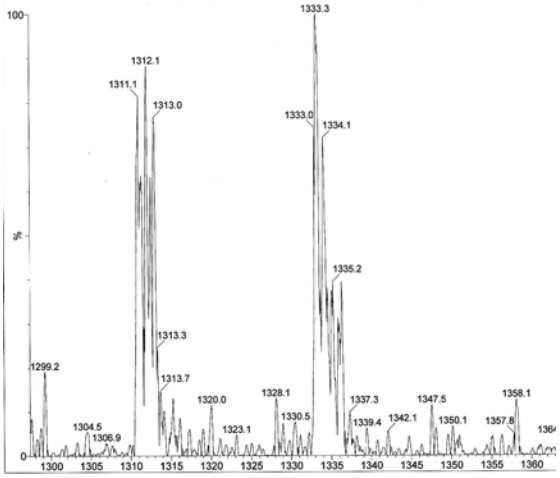


t_R: 19.06 min

ESI+ $[M+H]^+$: 1311.1 (calculated: 1310.77); **$[M+Na]^+$:** 1333.3 (calculated: 1333.76); **$[M+2H]^{2+}$:** 656.0; fragmentations: 458.3+853.4 and 585.4+726.4

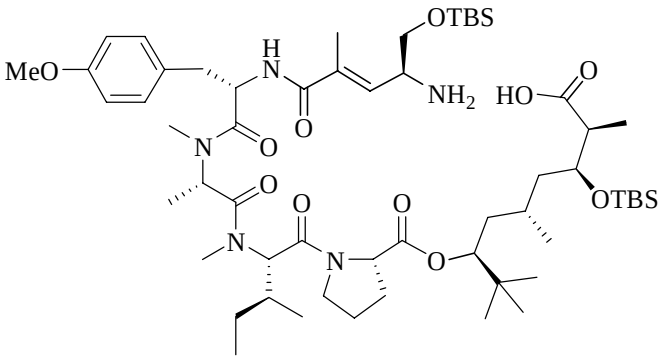






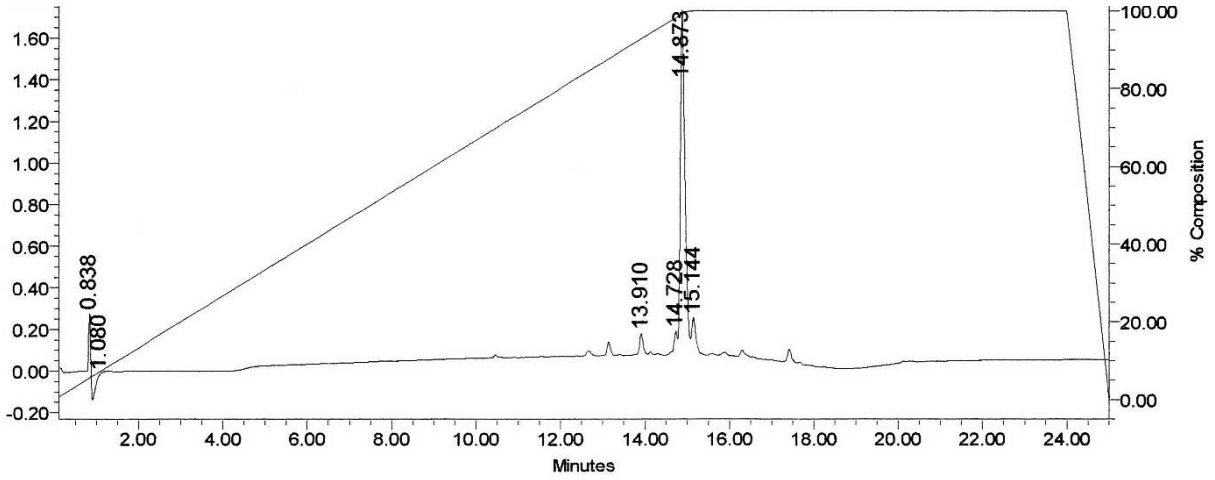
After Fmoc deprotection, the compound was cleaved from the resin by treatment with DCM/TFE/AcOH (6:2:2) during 40 min. This treatment was repeated twice and the combined filtrates were concentrated under vacuum to give the TBS protected linear precursor.

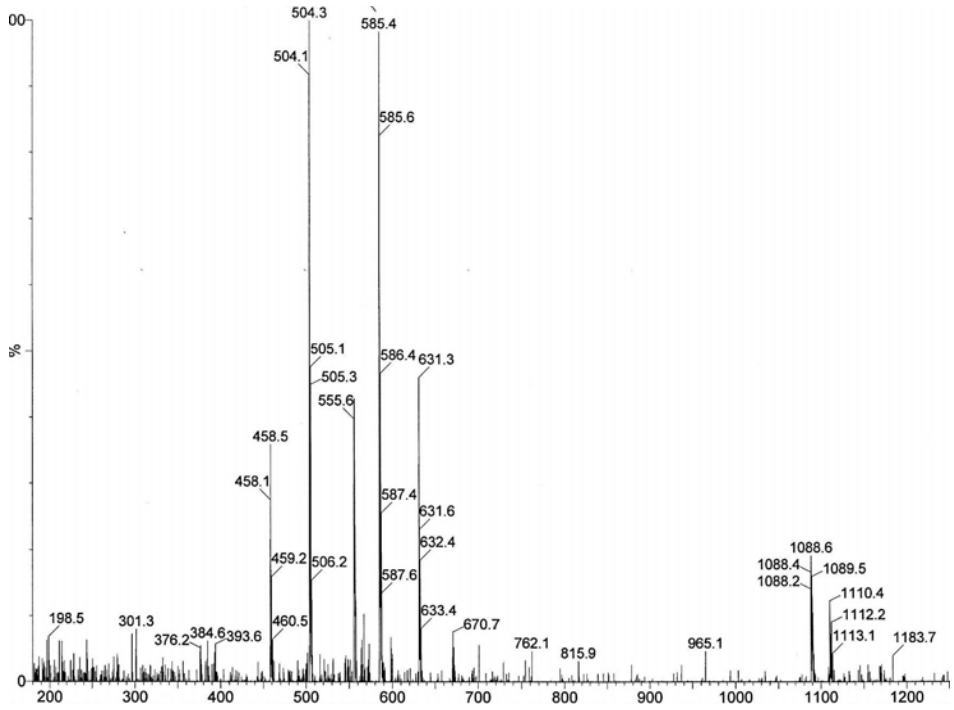
Intermediate analysis (24)



t_R: 14.87 min.

ESI+ $[M+H]^+$: 1088.6 (calculated: 1088.70); **$[M+Na]^+$:** 1110.4 (calculated: 1110.69); **$[M+H+Na]^{2+}$:** 555.6; fragmentations: 458.3+631.3 and 585.4+504.3.

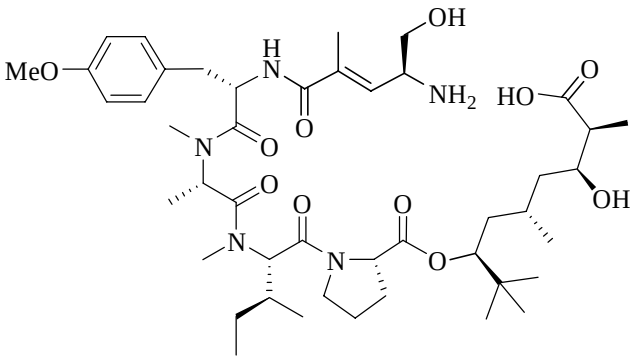




To remove the 2 TBS protecting group, the compound **24** was subjected several times to dissolution in a 0.1% TFA in ACN solution followed by concentration under reduce pressure, until complete deprotection. The compound was used as it for the next lactamisation step.

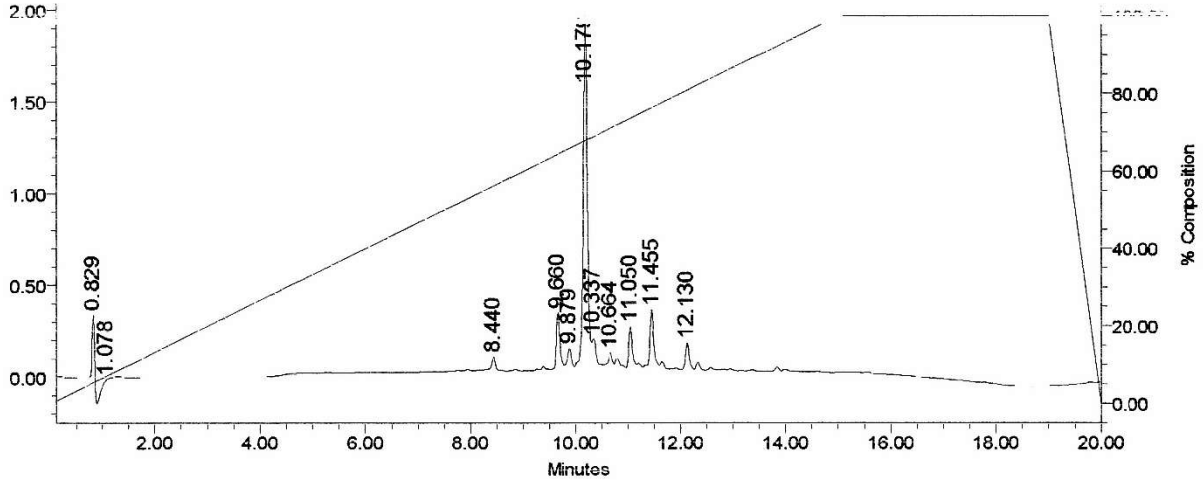
The overall yield for precursor elongation and deprotection was 70%.

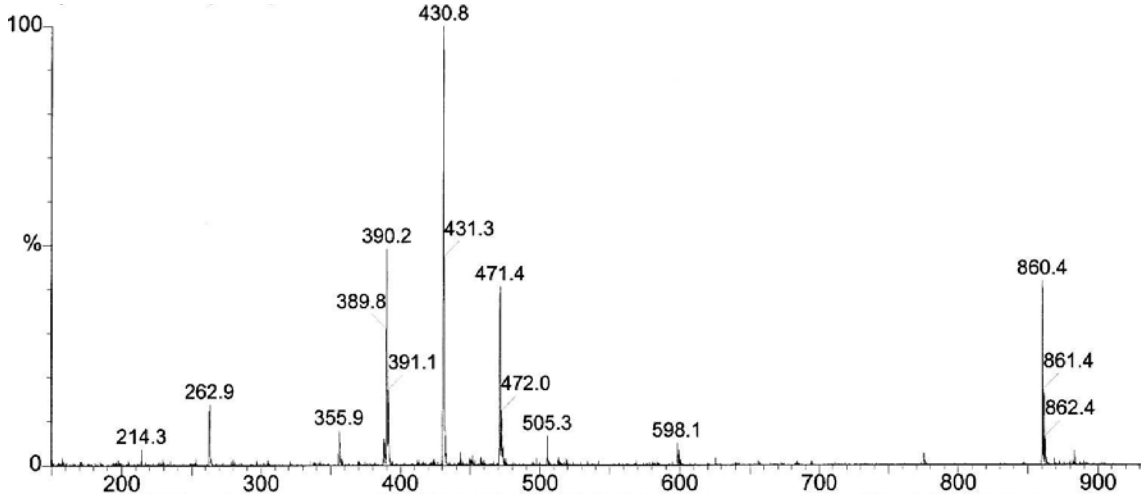
Deprotected linear precursor 25 analysis



t_R: 17.18 min.

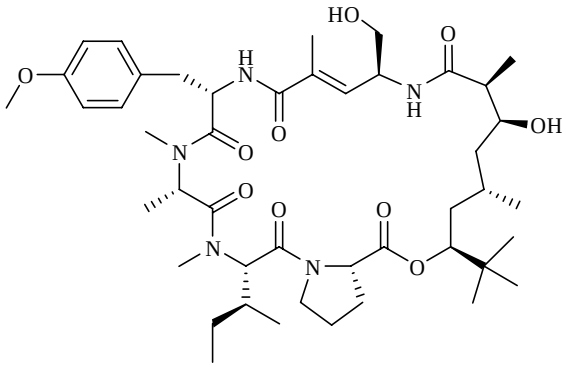
ESI+ $[M+H]^+$: 860.4 (calculated: 860.53) ; **$[M+2H]^{2+}$:** 430.8; fragmentations: 389.8+471.4.

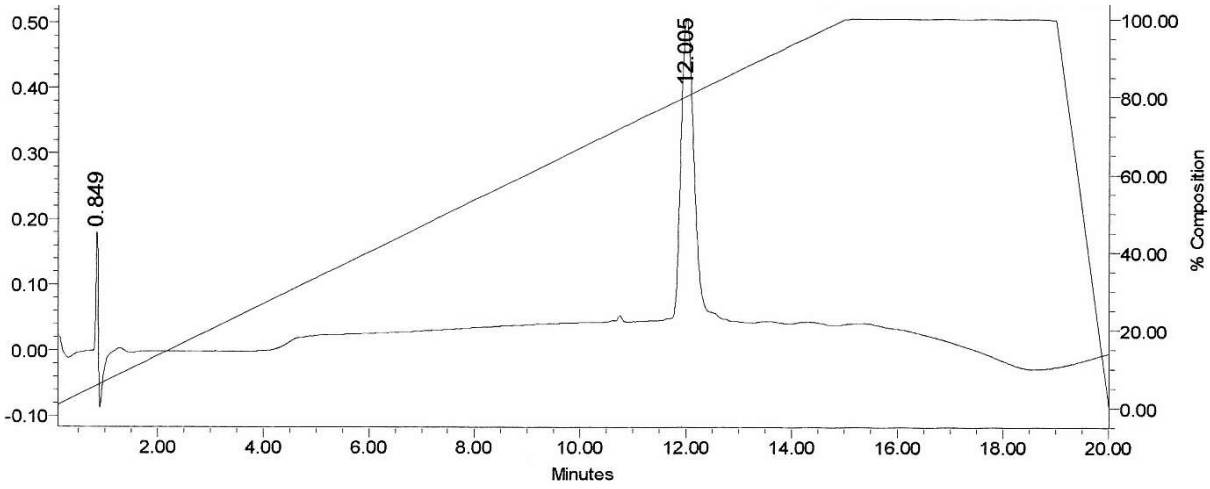


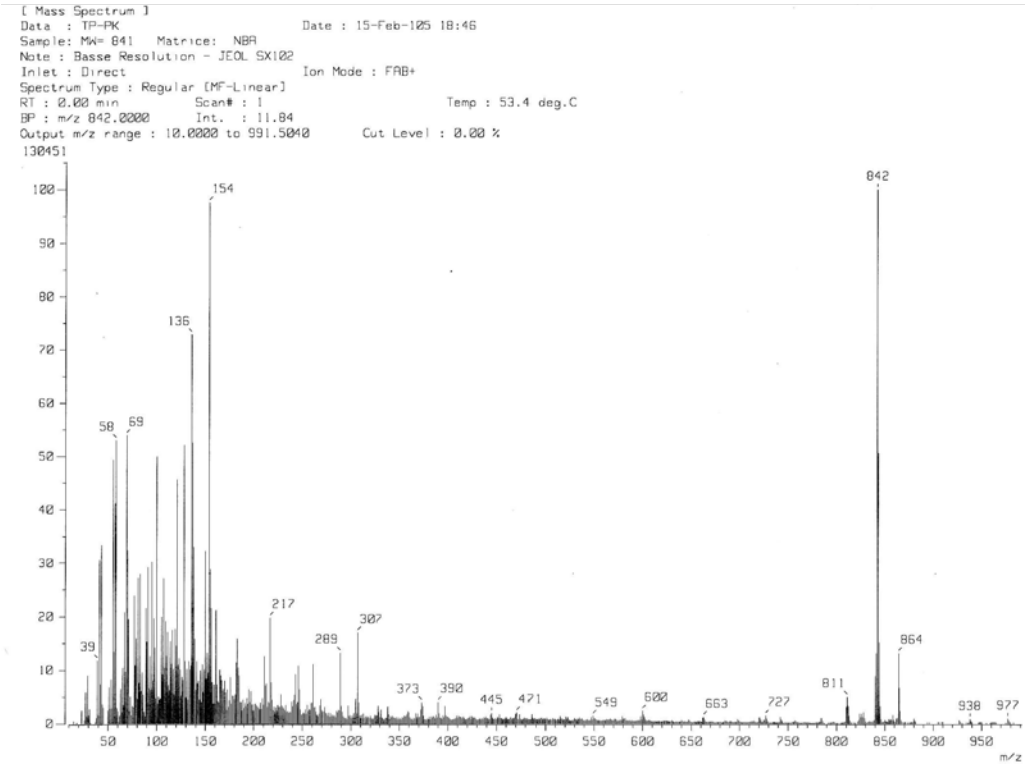


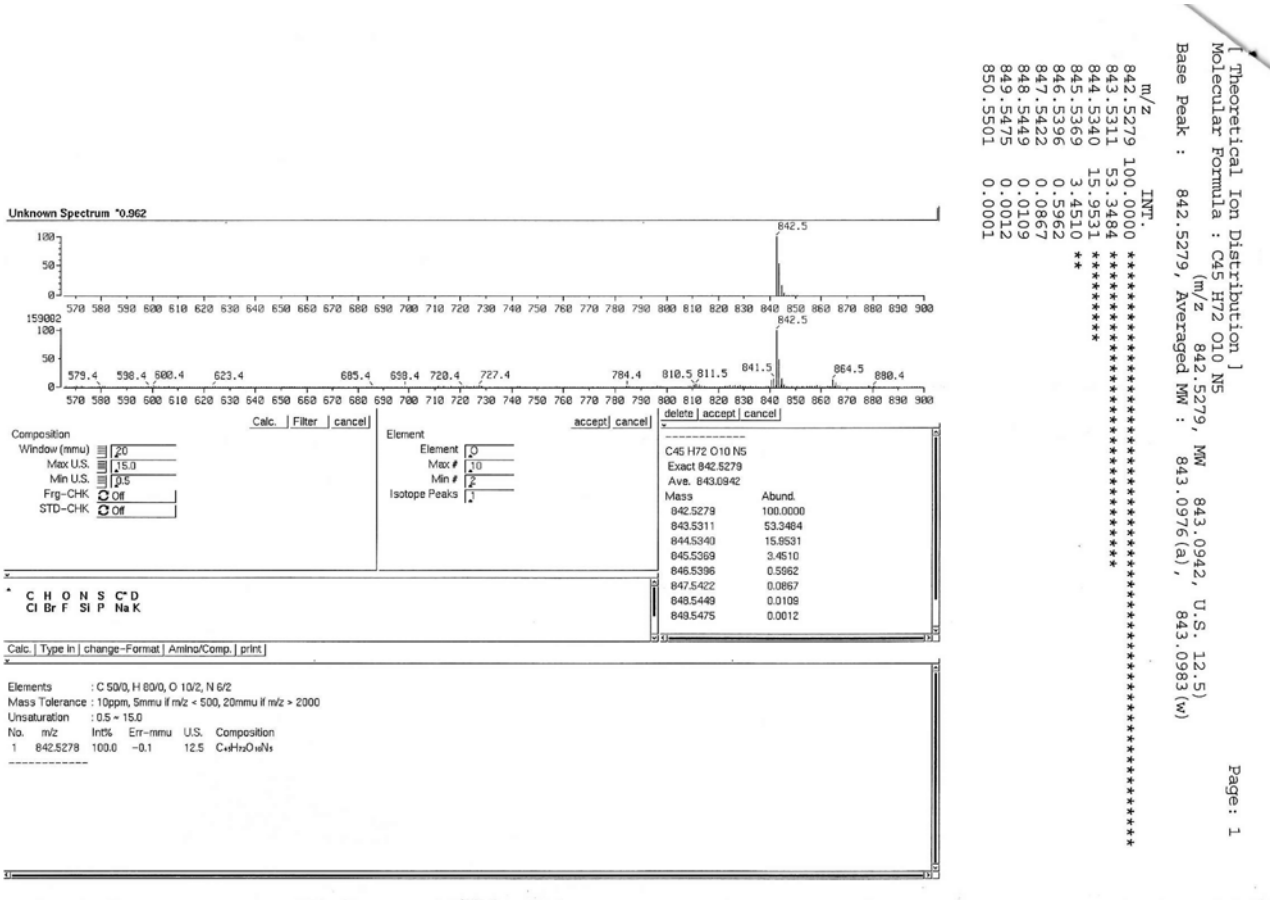
Macrolactamisation of linear precursors 22 and 25 (26):

HPLC and HRMS

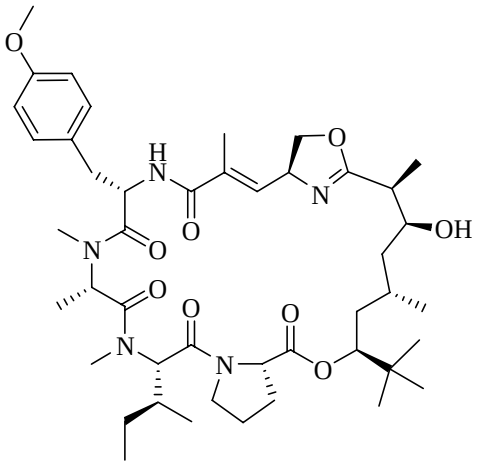


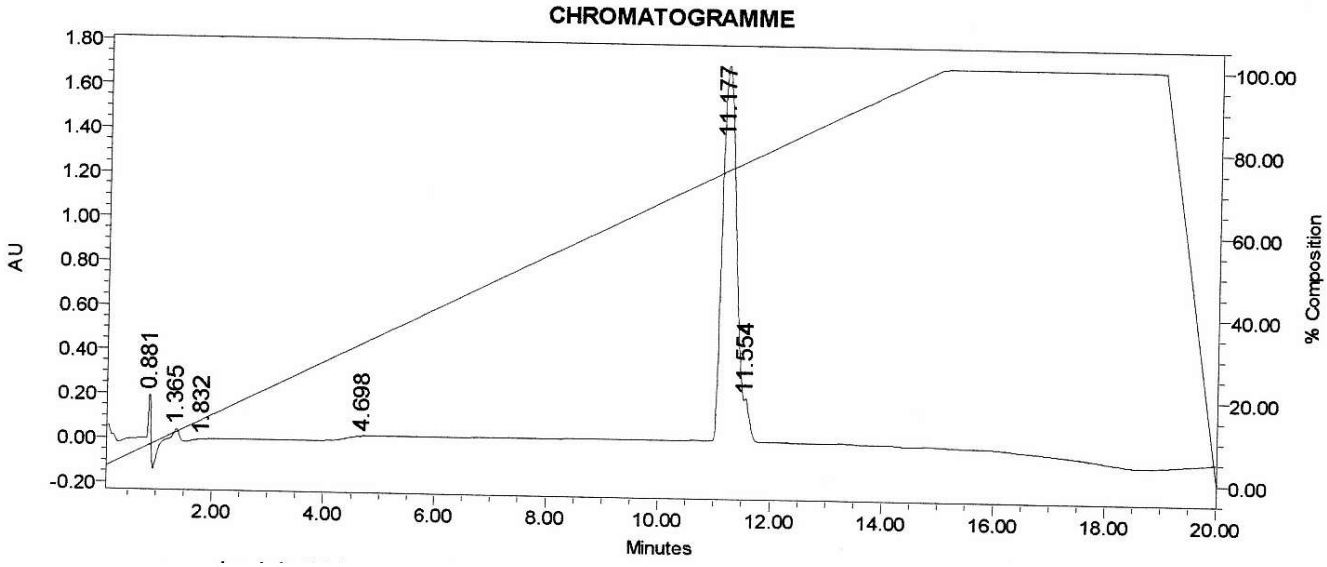






Oxazoline analogue of apratoxin A (oxo-apratoxin): HPLC and HRMS



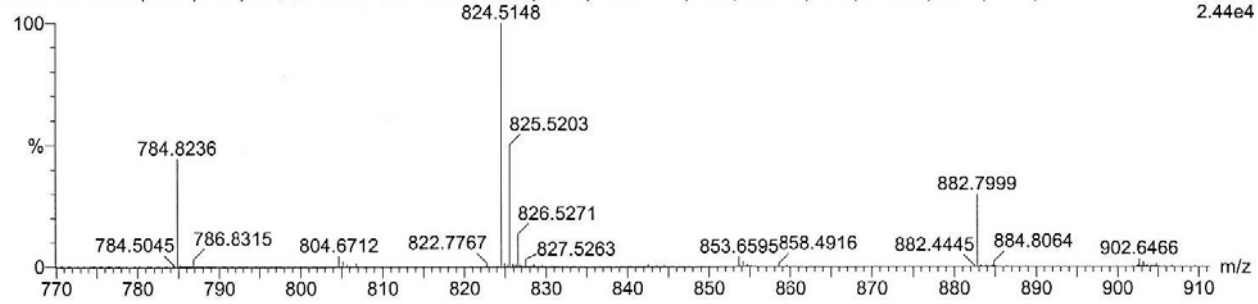


Elemental Composition Report **Page 1**

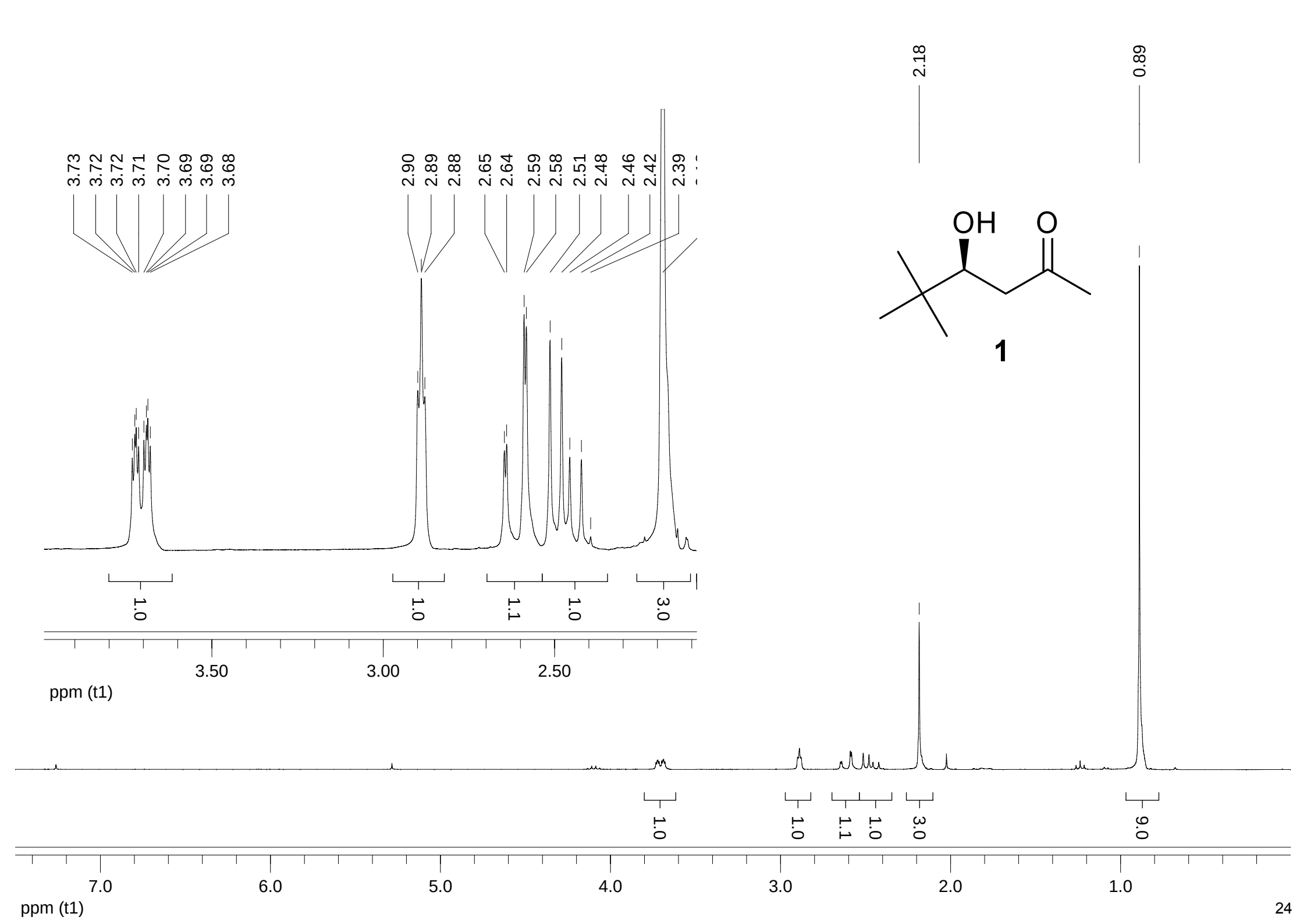
Single Mass Analysis (displaying only valid results)
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 30.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Even Electron Ions
508 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)

Q-TOF AG analogue Oxazoline 21-JUL-2006
L210706 02 52 (1.024) AM (Cen,4, 80.00, Ar,5000.0,0.00,1.00); Sm (SG, 2x1.00); Sb (1,40.00); Sb (1,40.00); Cm (47:55) TOF MS ES+
2.44e4



Minimum:				-1.5		
Maximum:		5.0	5.0	30.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
824.5148	824.5133	1.5	1.8	9.5	1	C40 H70 N7 O11
	824.5174	-2.6	-3.1	13.5	3	C45 H70 N5 O9
	824.5120	2.8	3.4	4.5	2	C39 H74 N3 O15
	824.5187	-3.9	-4.7	18.5	4	C46 H66 N9 O5
	824.5192	-4.4	-5.3	0.5	5	C33 H74 N7 O16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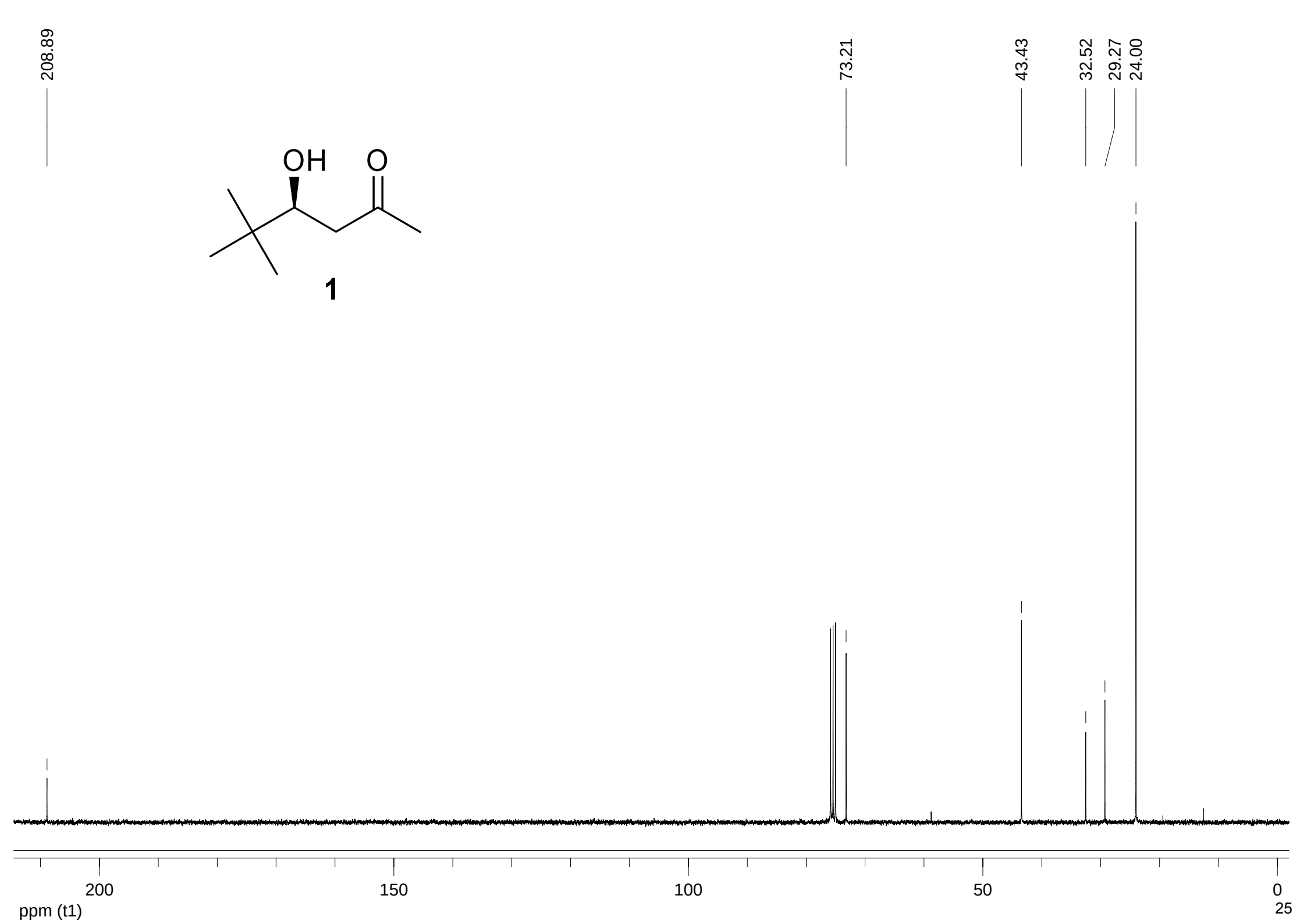
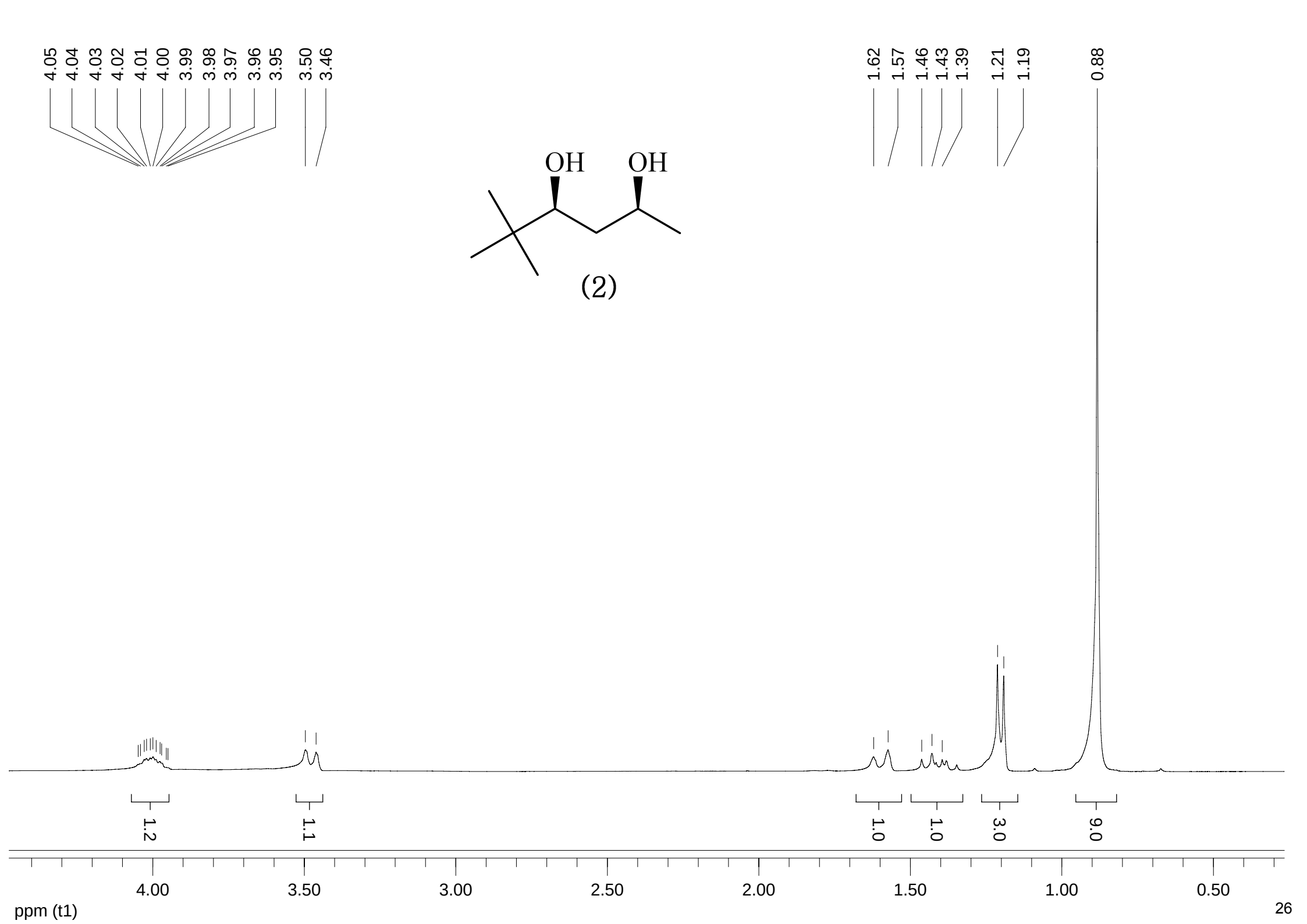
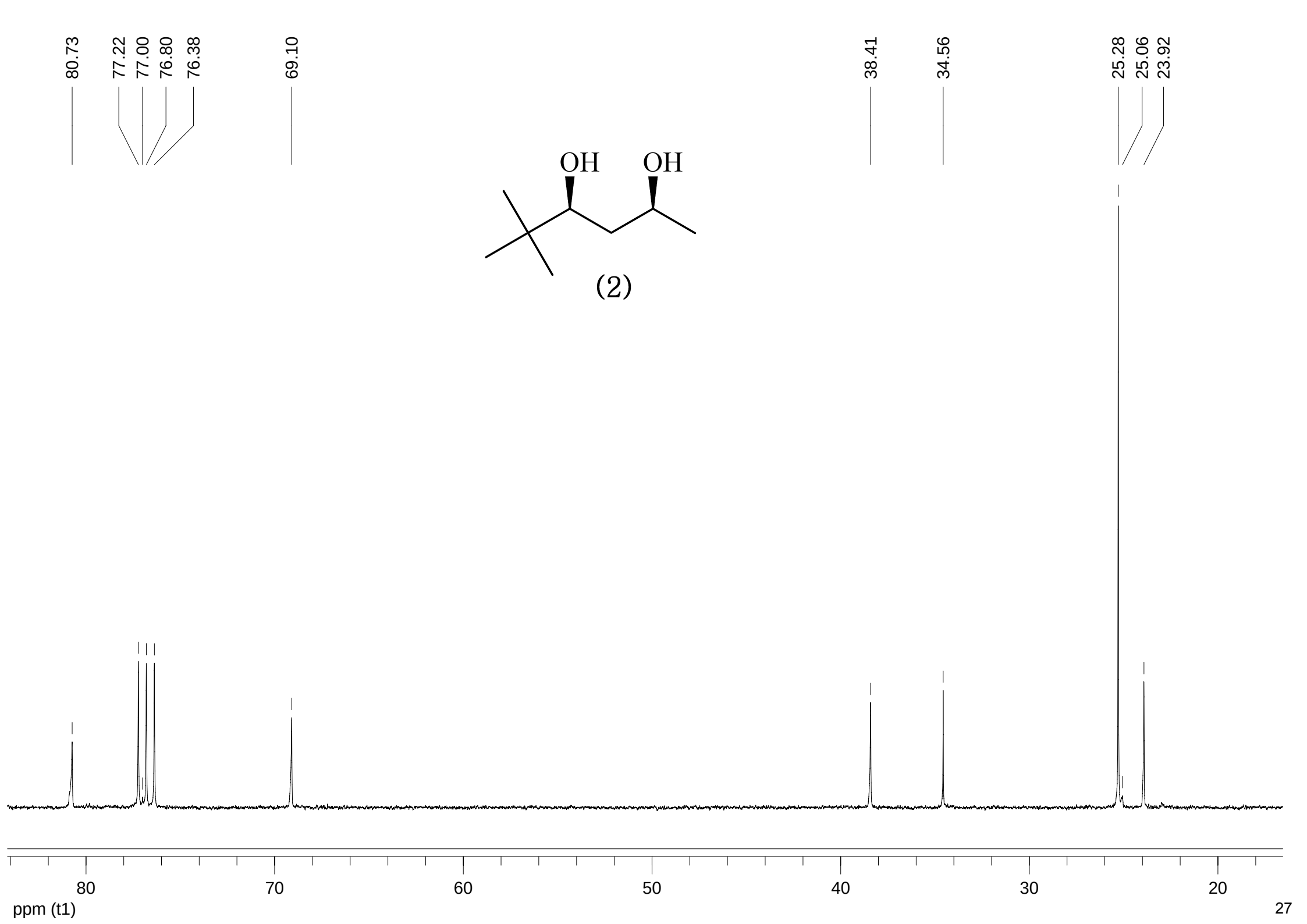
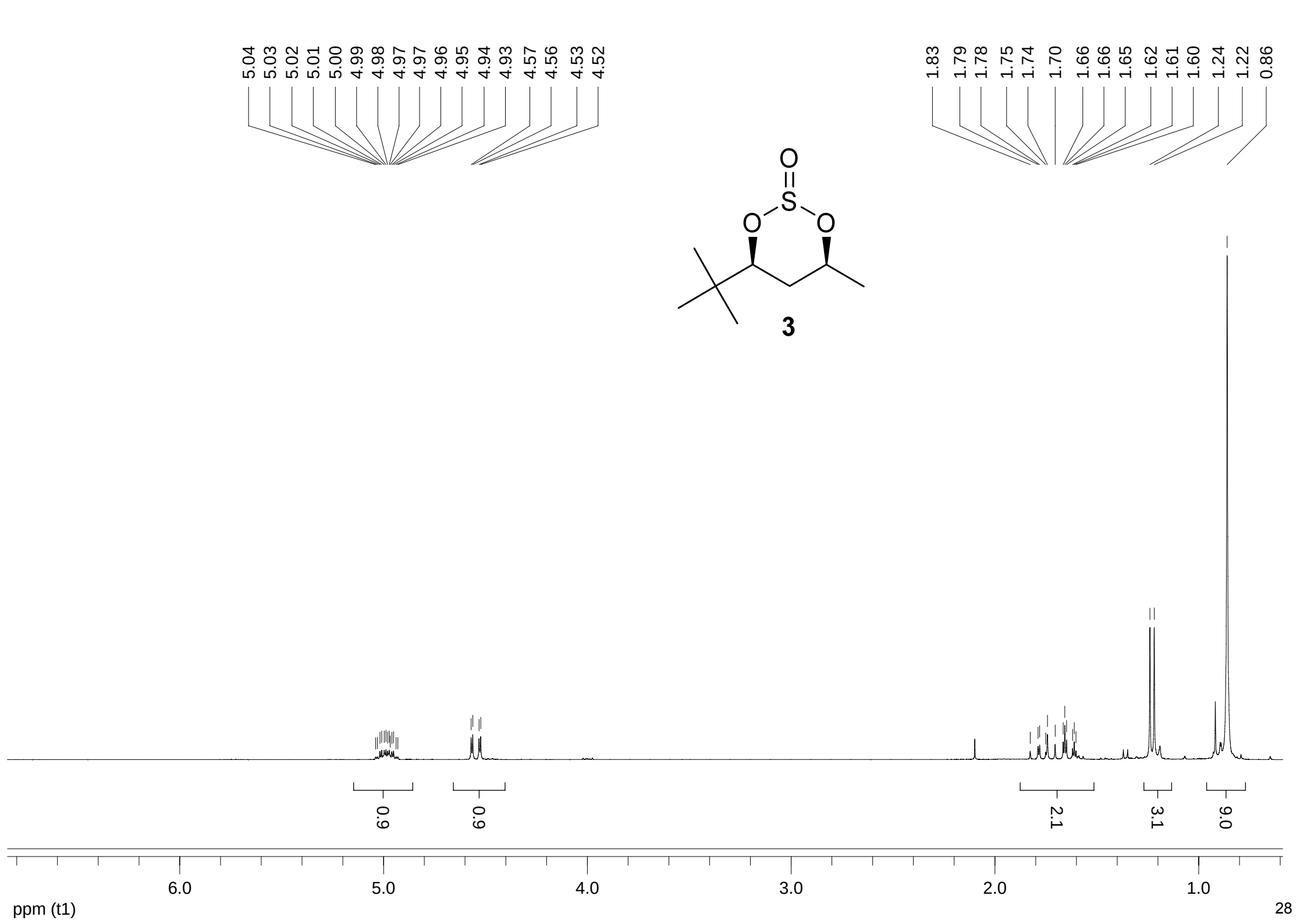
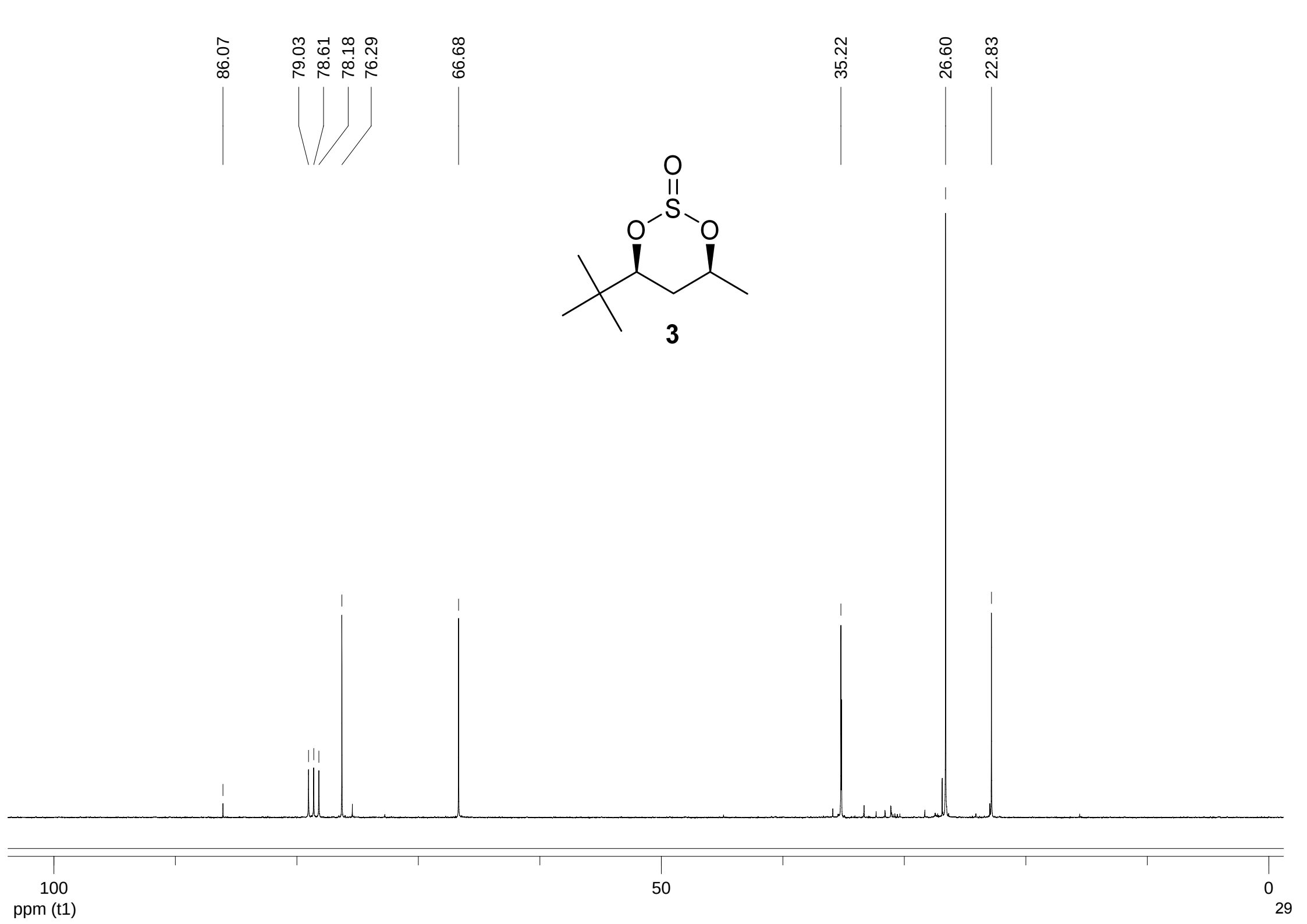
3.72
3.72
3.71
3.70
3.69
3.69
3.68
2.90
2.89
2.88
2.65
2.64
2.59
2.58
2.51
2.48
2.46
2.42
2.39
2.18
0.89
OH
O
1
1.0
1.0
1.1
1.0
3.0
3.50
3.00
2.50
ppm (t1)
1.0
1.0
1.1
1.0
3.0
9.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

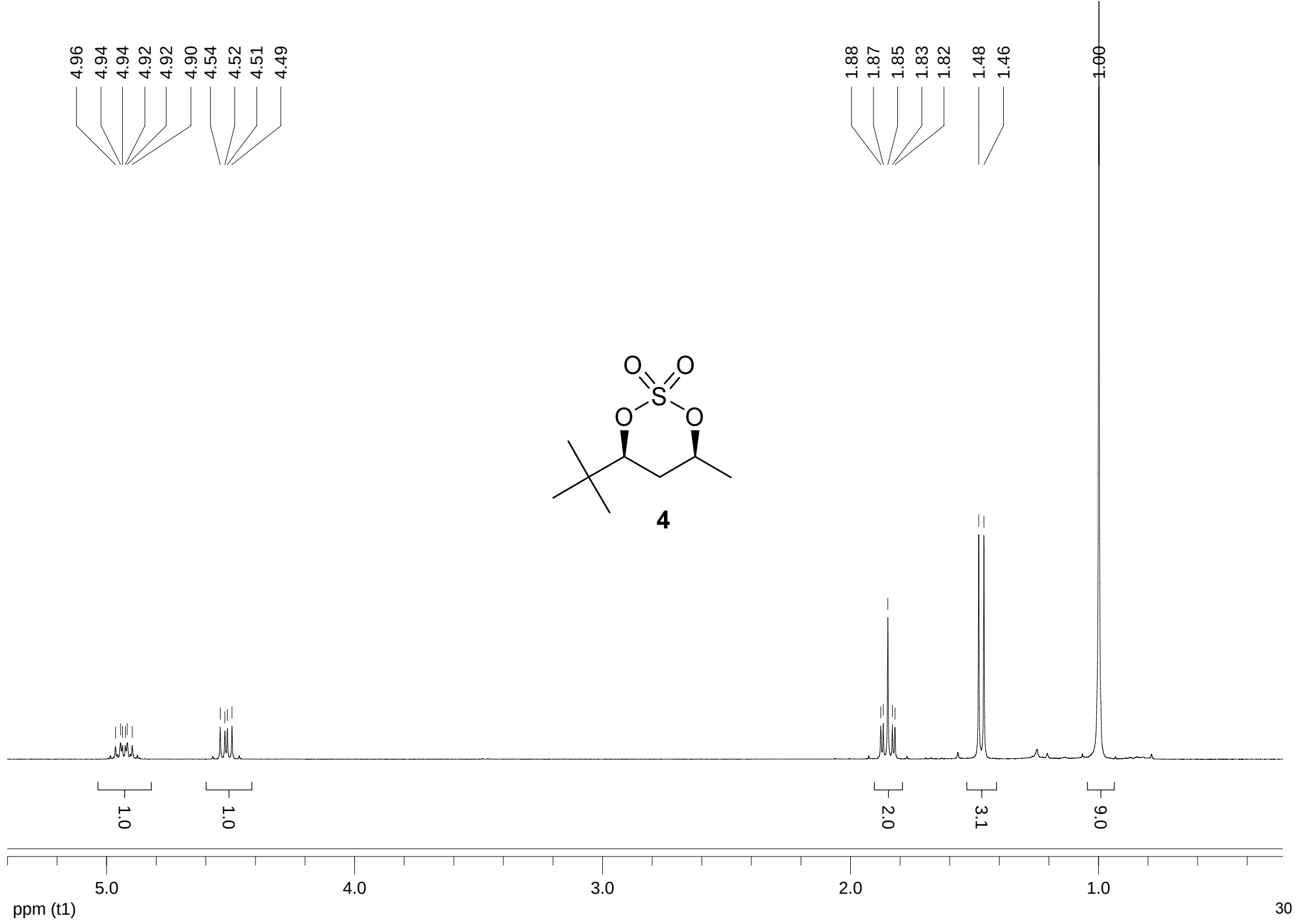

208.89
73.21
43.43
32.52
29.27
24.00
OH
O
1
200
150
100
50
0
ppm (t1)
25

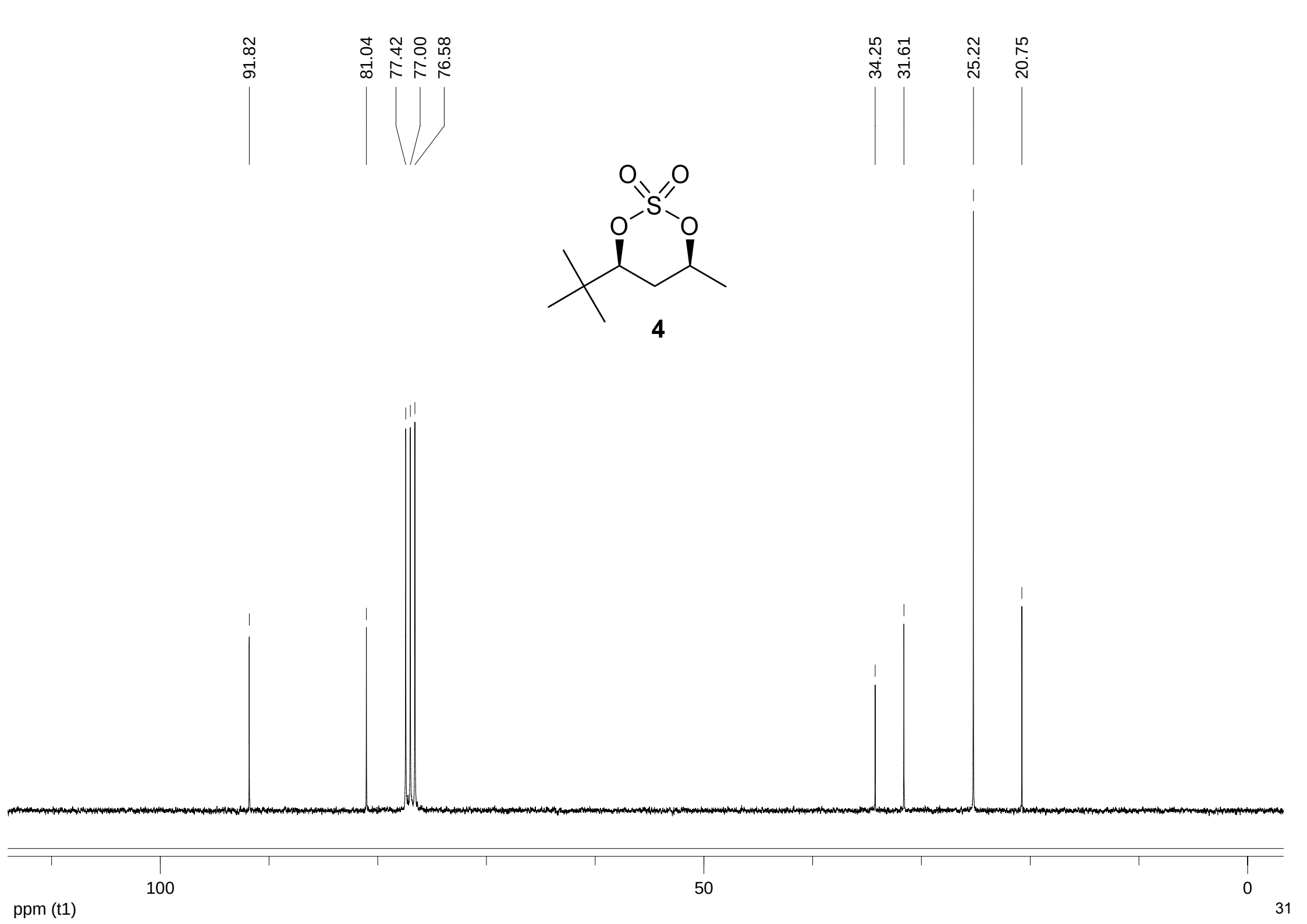

4.05
4.04
4.03
4.02
4.01
4.00
3.99
3.98
3.97
3.96
3.95
3.50
3.46
1.62
1.57
1.46
1.43
1.39
1.21
1.19
0.88
OH
OH
(2)
1.2
1.1
1.0
1.0
3.0
9.0
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)

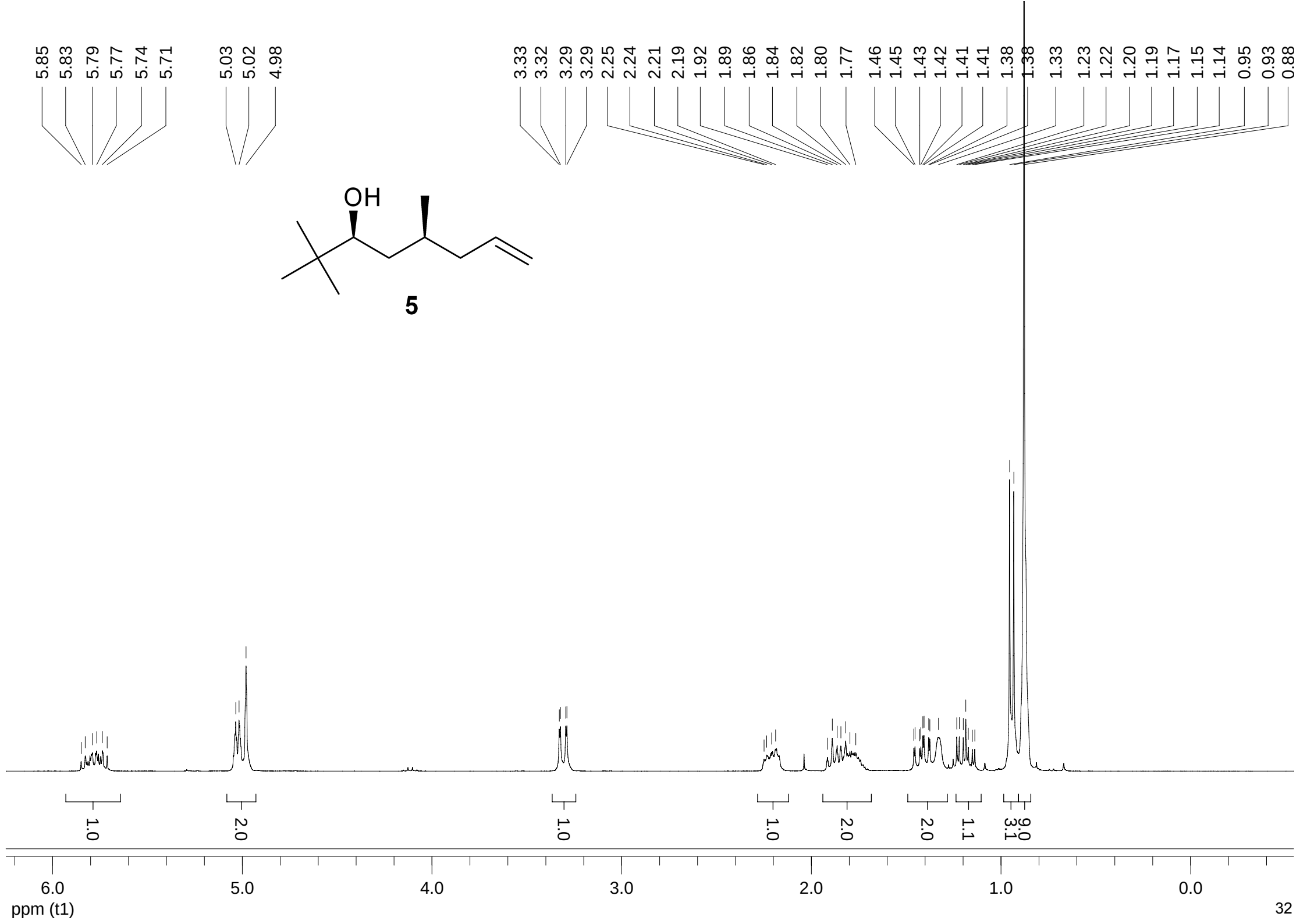

80.73
77.22
77.00
76.80
76.38
69.10
38.41
34.56
25.28
25.06
23.92
OH
OH
(2)
80
70
60
50
40
30
20
ppm (t1)

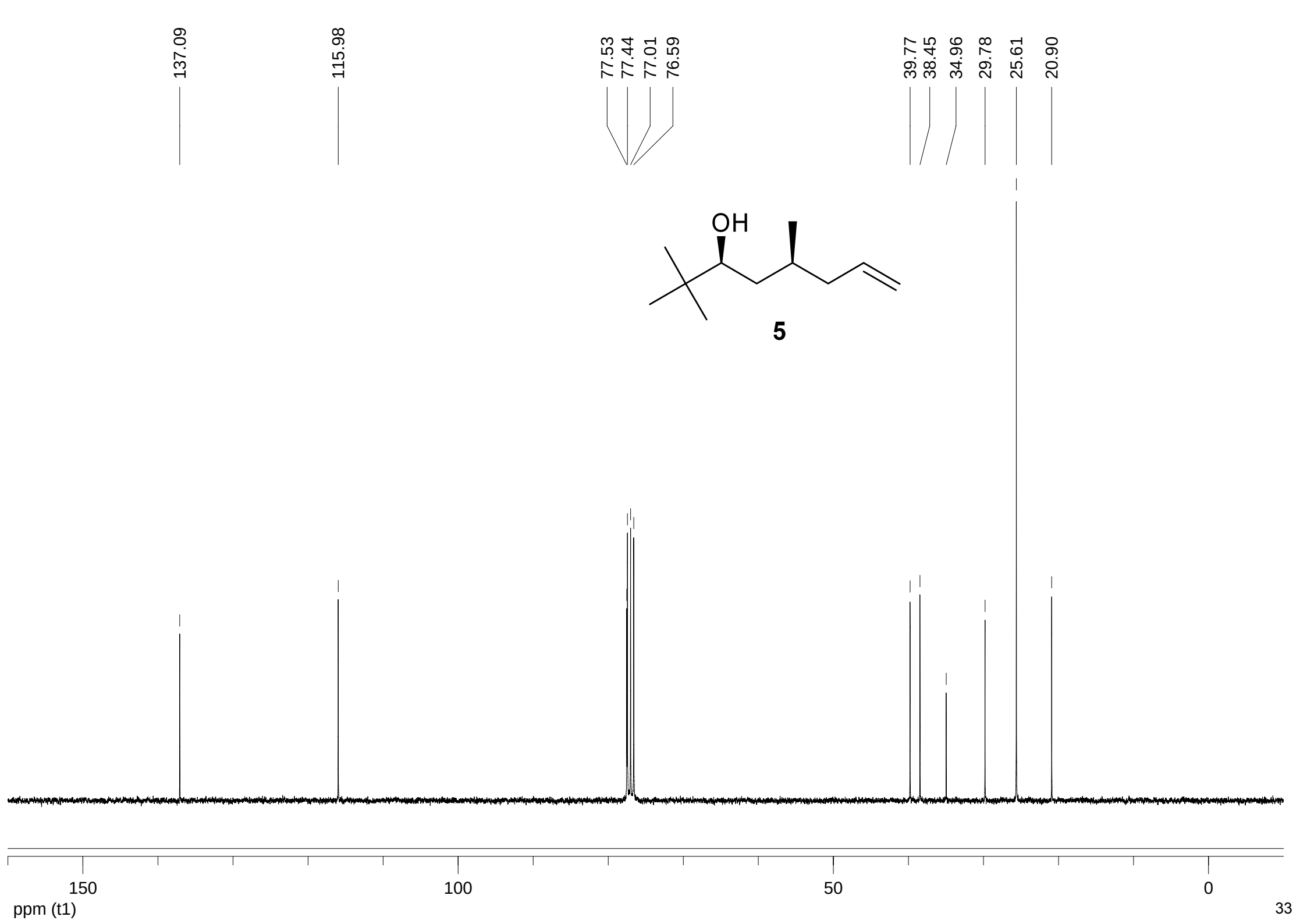

5.04
5.03
5.02
5.01
5.00
4.99
4.98
4.97
4.97
4.96
4.95
4.94
4.93
4.57
4.56
4.53
4.52
1.83
1.79
1.78
1.75
1.74
1.70
1.66
1.66
1.65
1.62
1.61
1.60
1.24
1.22
0.86
O
S
O
O
3
0.9
0.9
2.1
3.1
9.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

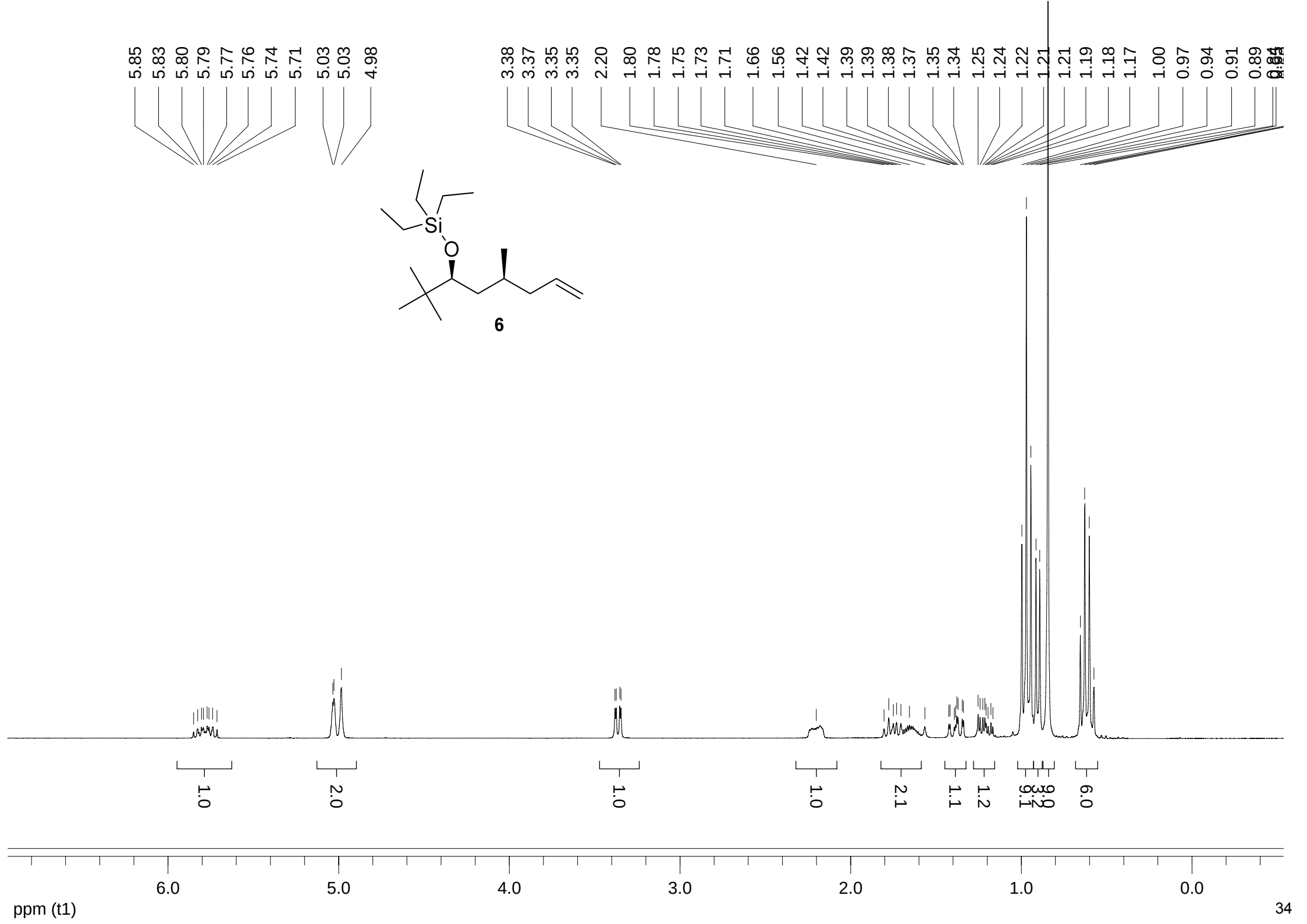

86.07
79.03
78.61
78.18
76.29
66.68
35.22
26.60
22.83
O
S
O
O
3
100
50
0
ppm (t1)

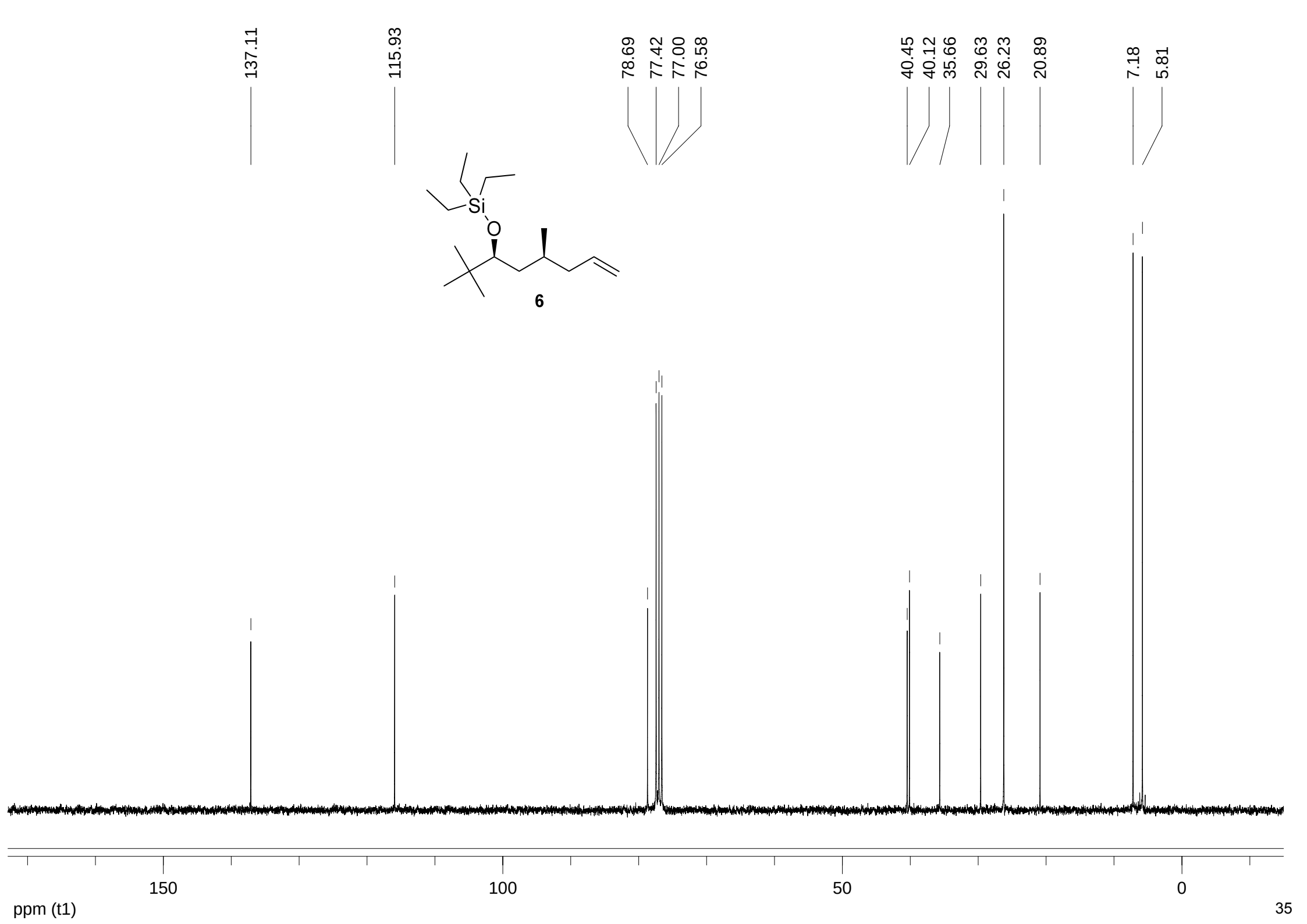

4.96
4.94
4.94
4.92
4.92
4.90
4.54
4.52
4.51
4.49
1.88
1.87
1.85
1.83
1.82
1.48
1.46
1.00
O
O
S
O
O
4
1.0
1.0
2.0
3.1
9.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

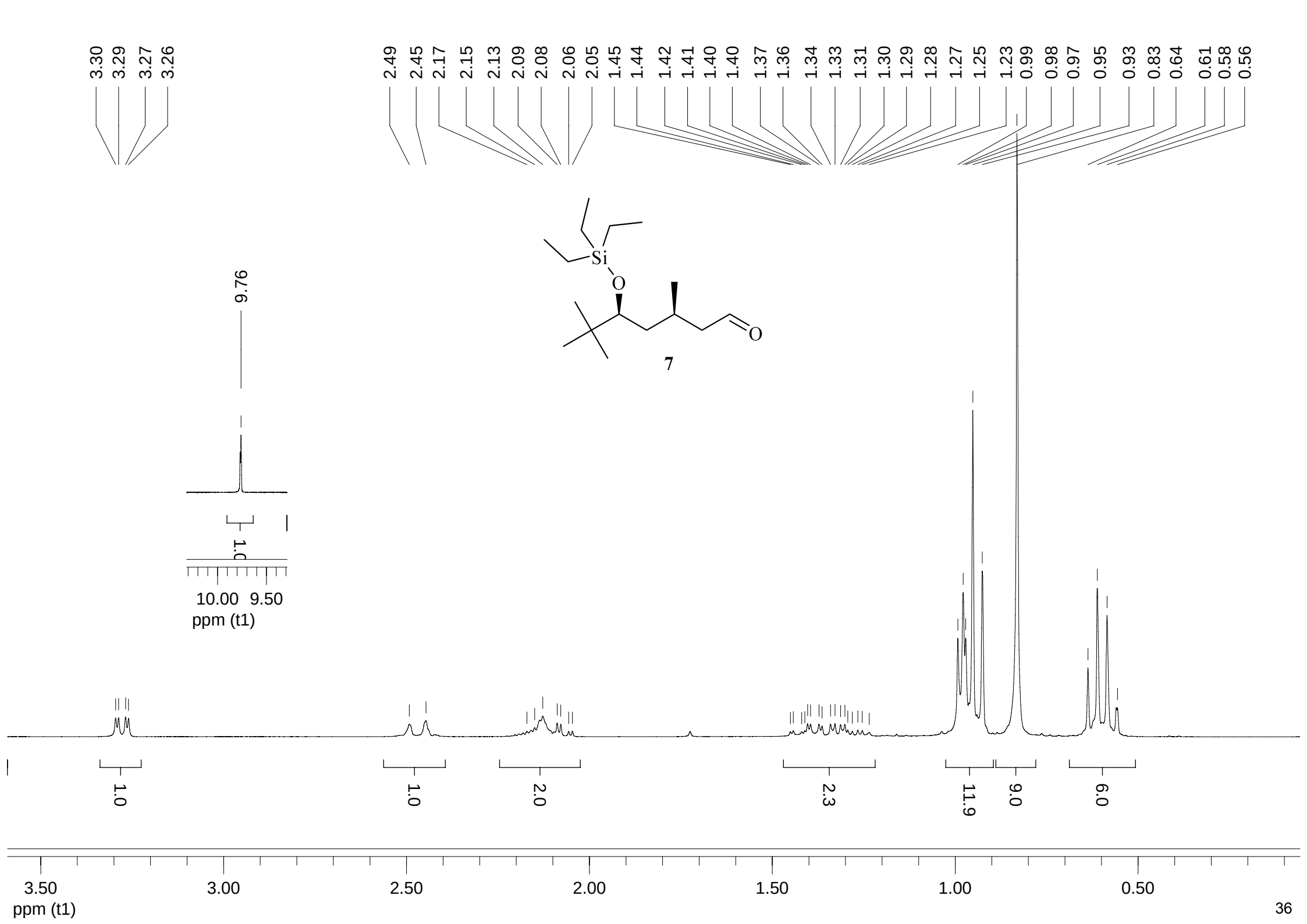

91.82
81.04
77.42
77.00
76.58
34.25
31.61
25.22
20.75
O
O
S
O
O
4
100
50
0
ppm (t1)

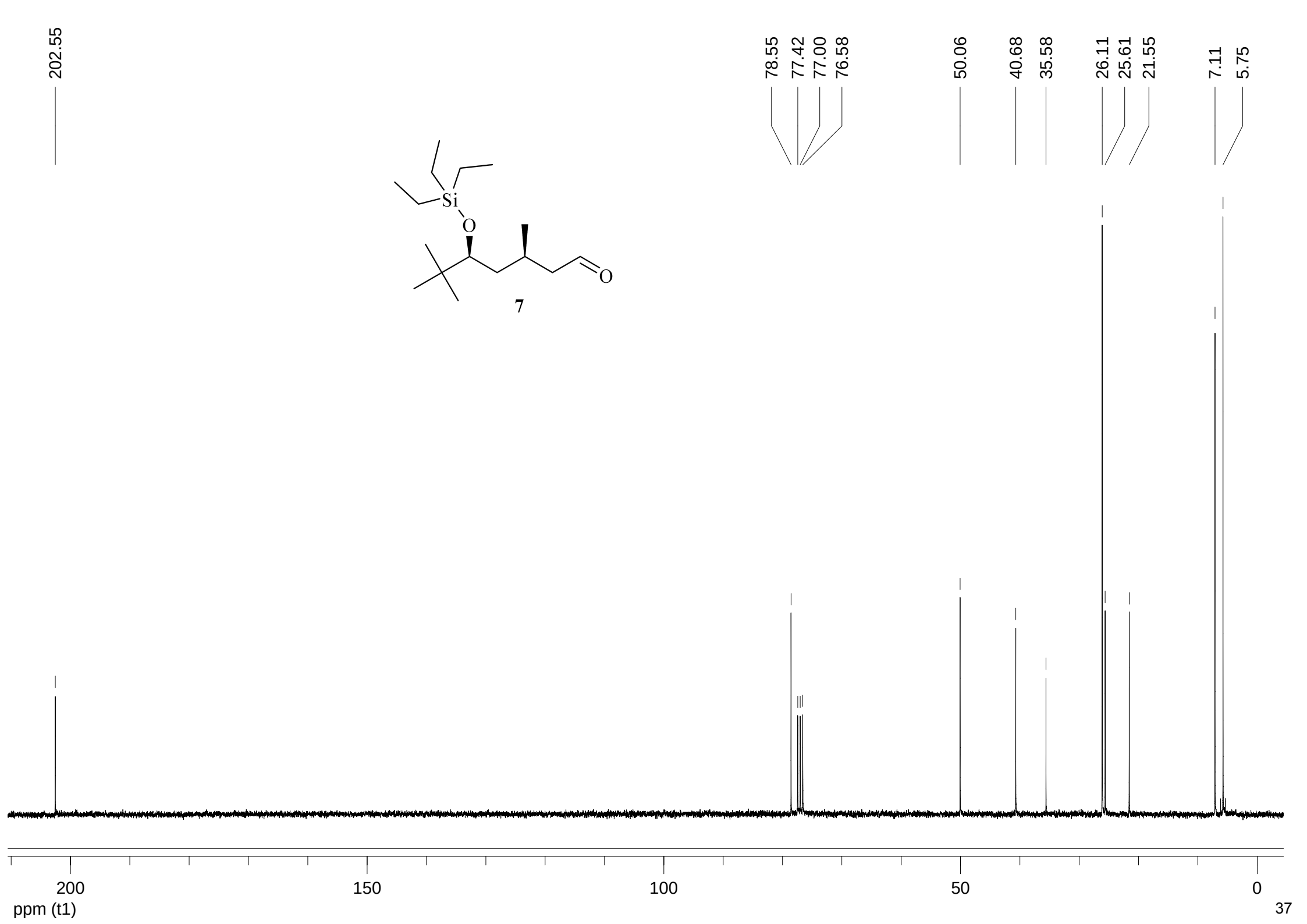

5.85
5.83
5.79
5.77
5.74
5.71
5.03
5.02
4.98
3.33
3.32
3.29
3.29
2.25
2.24
2.21
2.19
1.92
1.89
1.86
1.84
1.82
1.80
1.77
1.46
1.45
1.43
1.42
1.41
1.41
1.38
1.38
1.33
1.23
1.22
1.20
1.19
1.17
1.15
1.14
0.95
0.93
0.88
OH
5
1.0
2.0
1.0
1.0
2.0
2.0
1.1
3.1
9.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

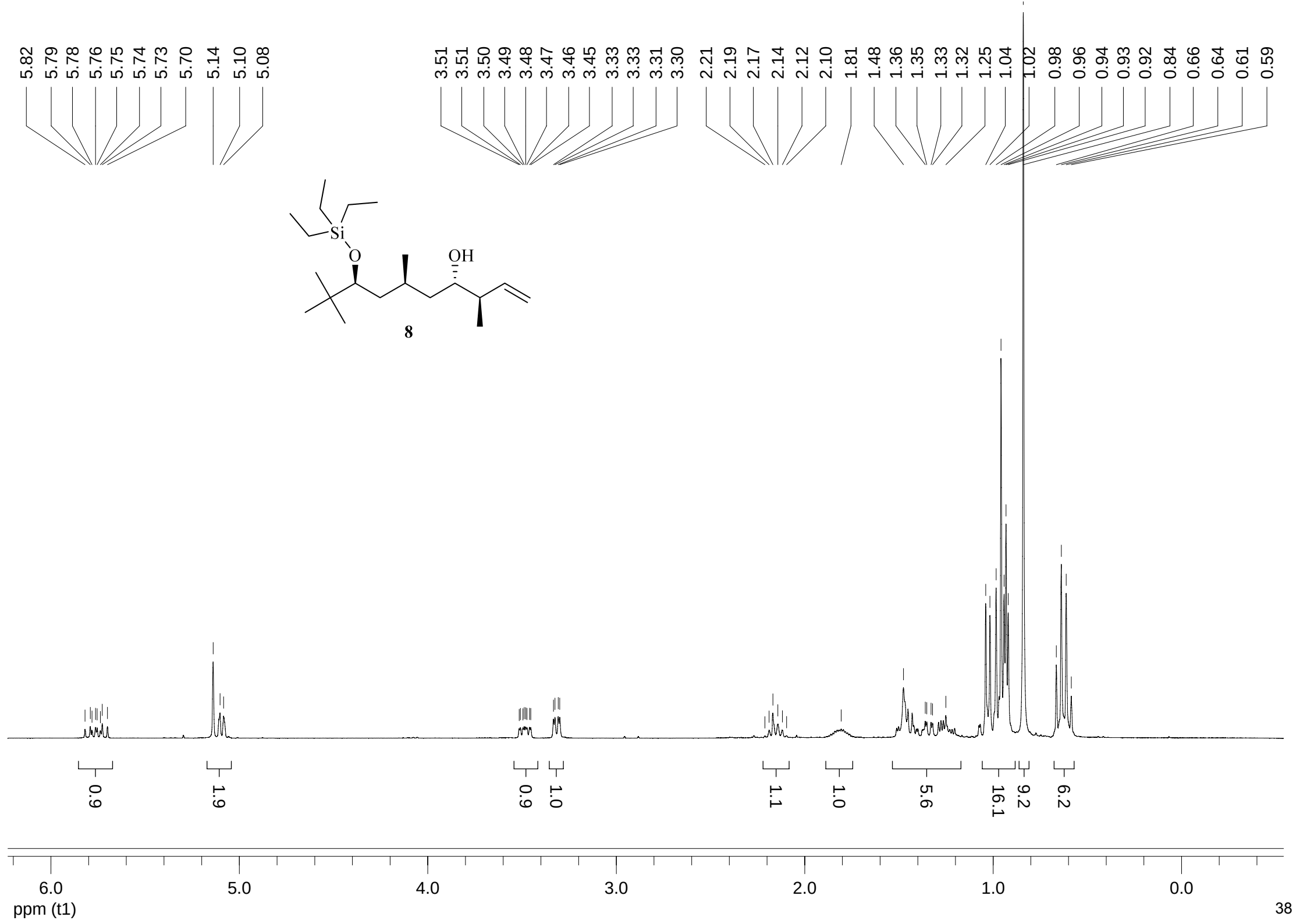

137.09
115.98
77.53
77.44
77.01
76.59
39.77
38.45
34.96
29.78
25.61
20.90
OH
5
150
100
50
0
ppm (t1)

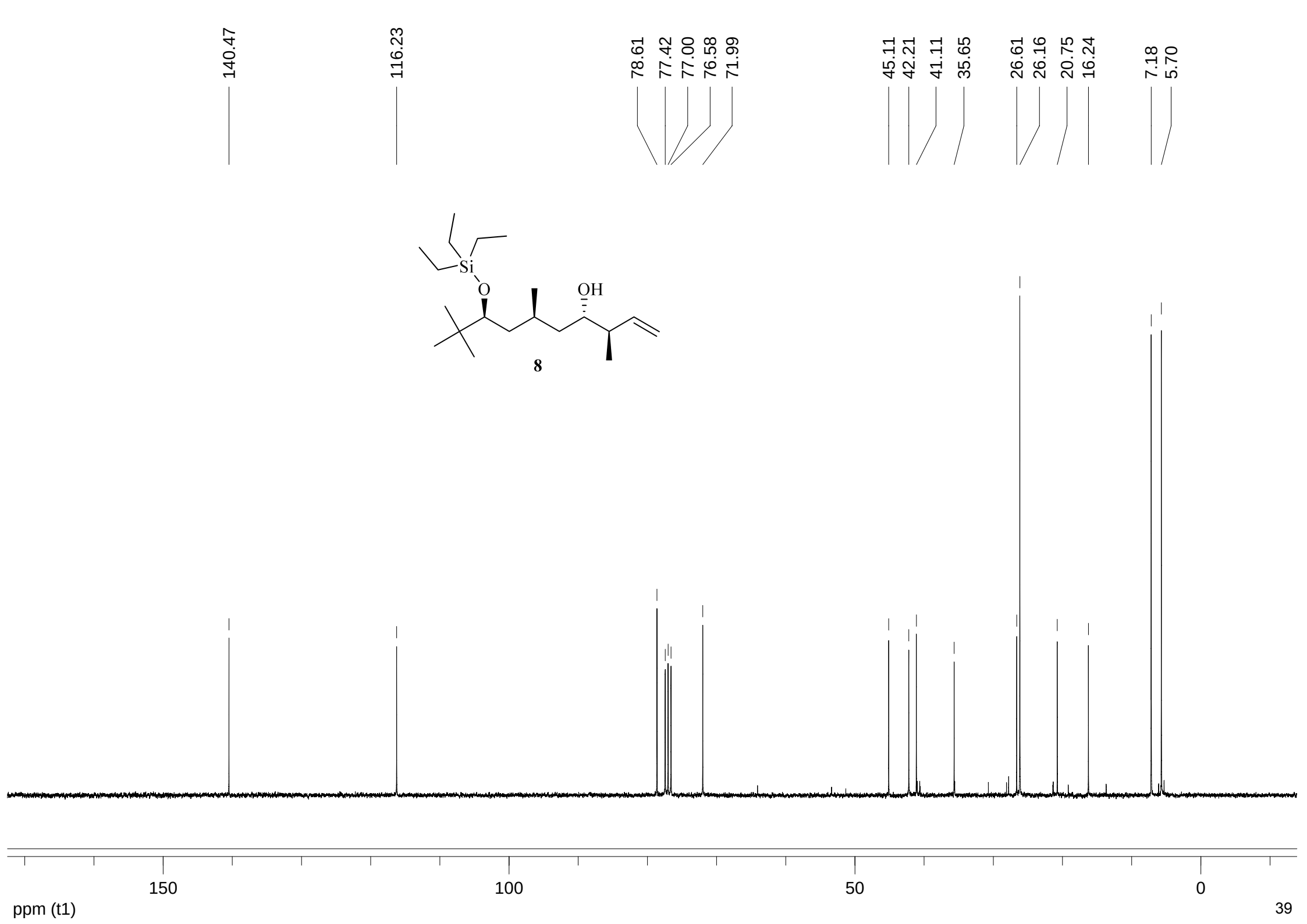

5.85
5.83
5.80
5.79
5.77
5.76
5.74
5.71
5.03
5.03
4.98
3.38
3.37
3.35
3.35
2.20
1.80
1.78
1.75
1.73
1.71
1.66
1.56
1.42
1.42
1.39
1.39
1.38
1.37
1.35
1.34
1.25
1.24
1.22
1.21
1.21
1.19
1.18
1.17
1.00
0.97
0.94
0.91
0.89
Si
O
6
1.0
2.0
1.0
1.0
2.1
1.1
1.2
6.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

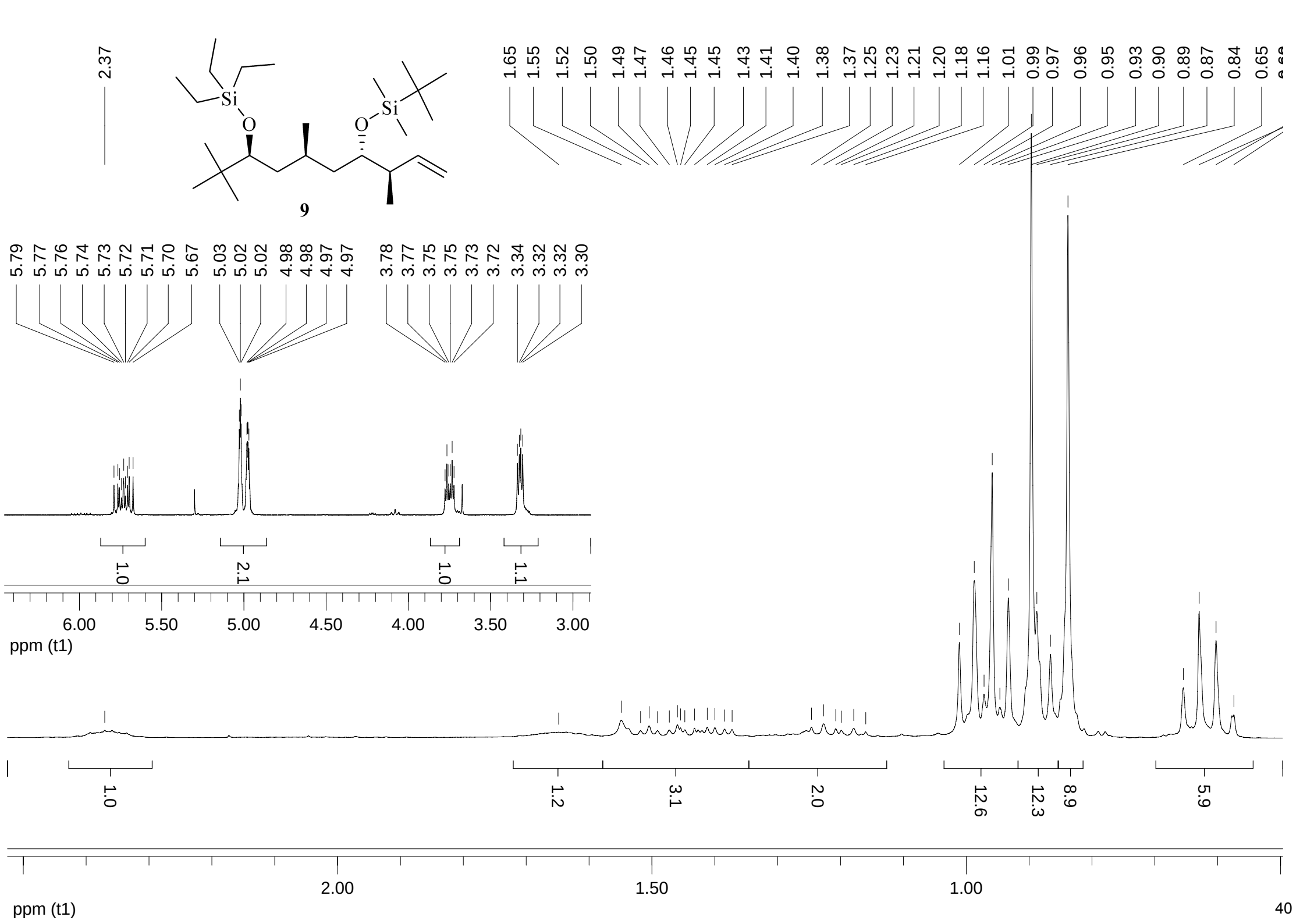

137.11
115.93
78.69
77.42
77.00
76.58
40.45
40.12
35.66
29.63
26.23
20.89
7.18
5.81
Si
O
6
150
100
50
0
ppm (t1)

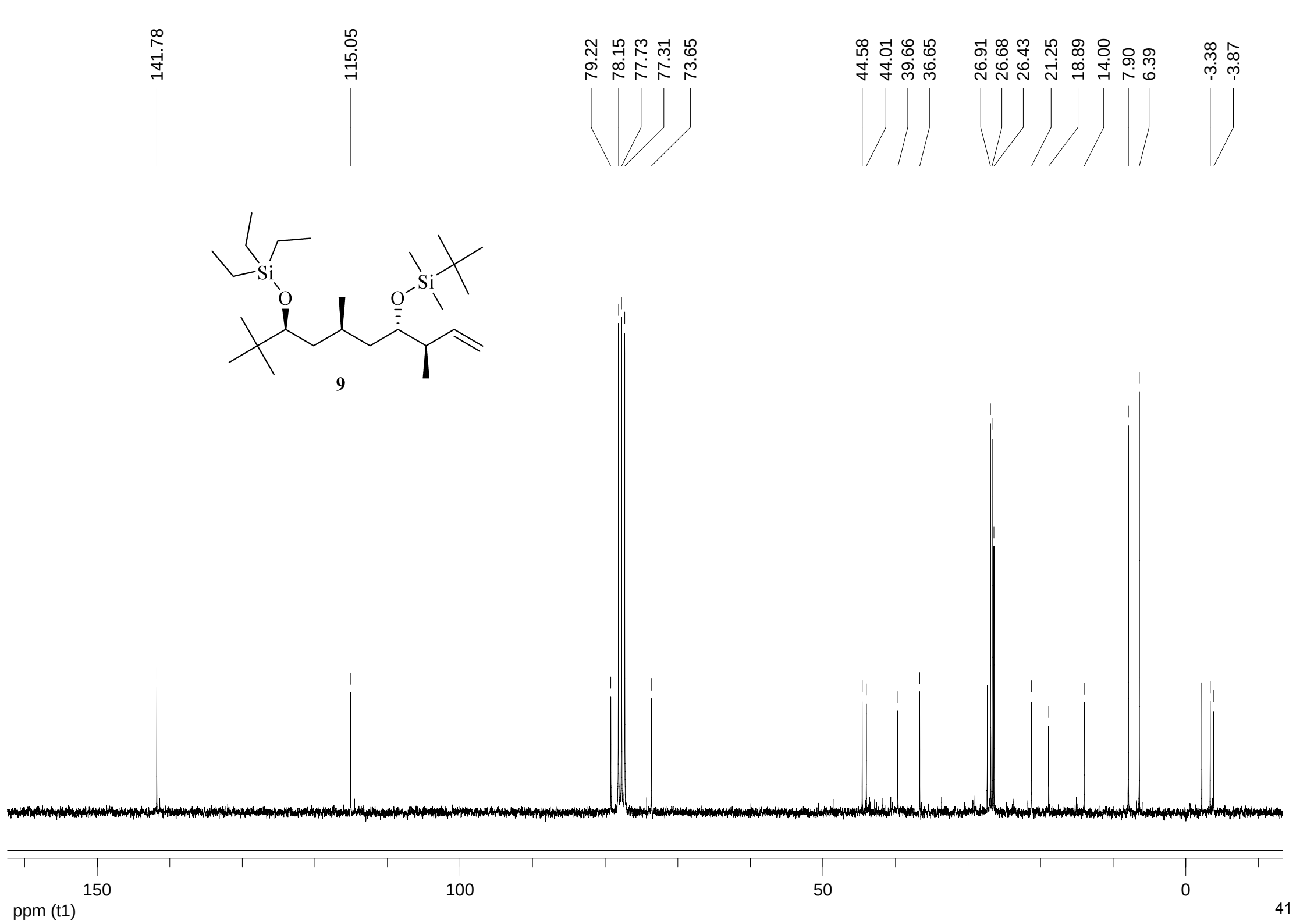

3.30
3.29
3.27
3.26
2.49
2.45
2.17
2.15
2.13
2.09
2.08
2.06
2.05
1.45
1.44
1.42
1.41
1.40
1.40
1.37
1.36
1.34
1.33
1.31
1.30
1.29
1.28
1.27
1.25
1.23
0.99
0.98
0.97
0.95
0.93
0.83
0.64
0.61
0.58
0.56
Si
O
O
7
9.76
1.0
10.00 9.50
ppm (t1)
1.0
1.0
2.0
2.3
11.9
9.0
6.0
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)

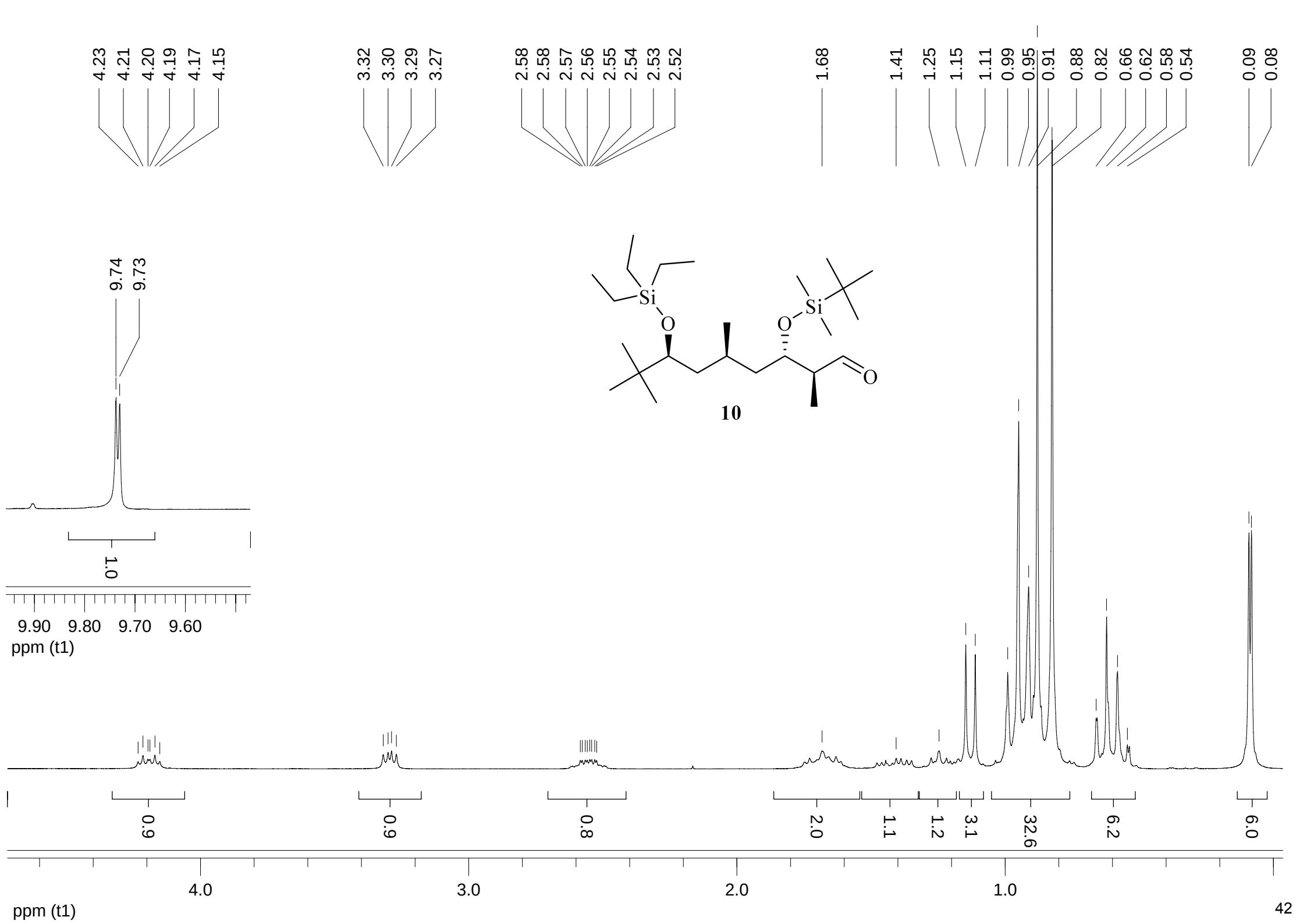

202.55
78.55
77.42
77.00
76.58
50.06
40.68
35.58
26.11
25.61
21.55
7.11
5.75
Si
O
O
7
200
150
100
50
0
ppm (t1)

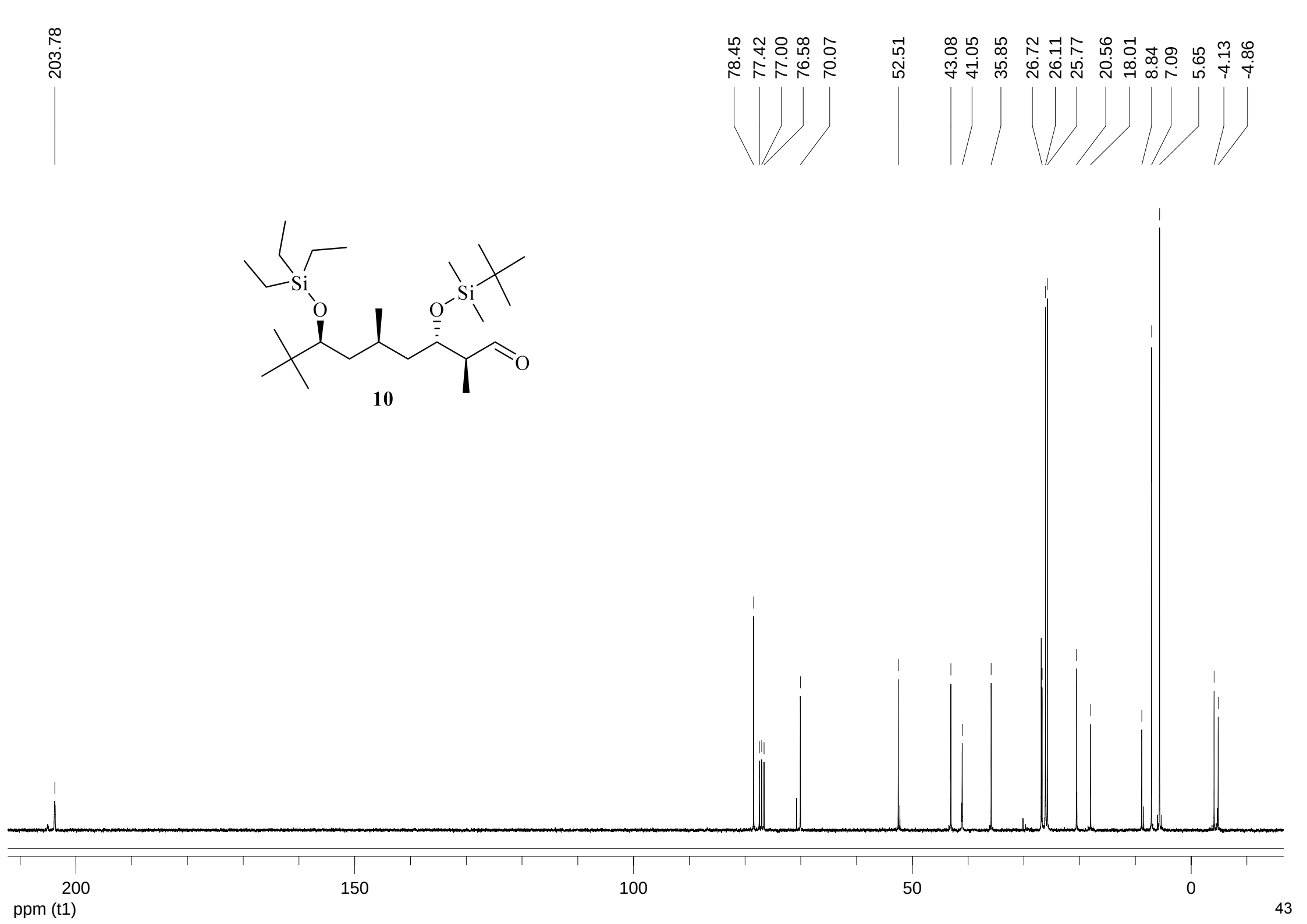

5.82
5.79
5.78
5.76
5.75
5.74
5.73
5.70
5.14
5.10
5.08
3.51
3.51
3.50
3.49
3.48
3.47
3.46
3.45
3.33
3.33
3.31
3.30
2.21
2.19
2.17
2.14
2.12
2.10
1.81
1.48
1.36
1.35
1.33
1.32
1.25
1.04
1.02
0.98
0.96
0.94
0.93
0.92
0.84
0.66
0.64
0.61
0.59
Si
O
OH
8
0.9
1.9
0.9
1.0
1.1
1.0
5.6
16.1
9.2
6.2
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

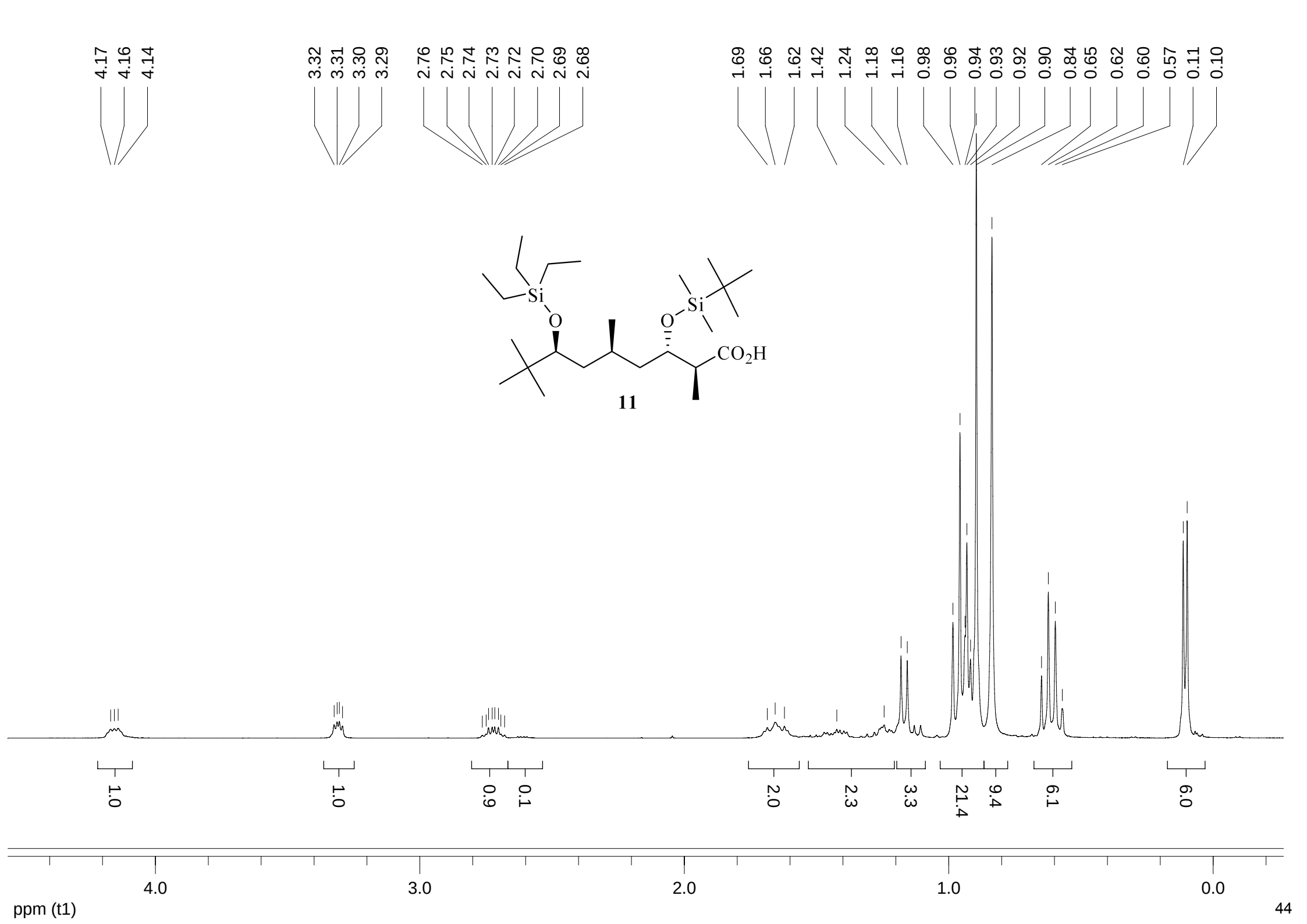

140.47
116.23
78.61
77.42
77.00
76.58
71.99
45.11
42.21
41.11
35.65
26.61
26.16
20.75
16.24
7.18
5.70
Si
O
OH
8
150
100
50
0
ppm (t1)

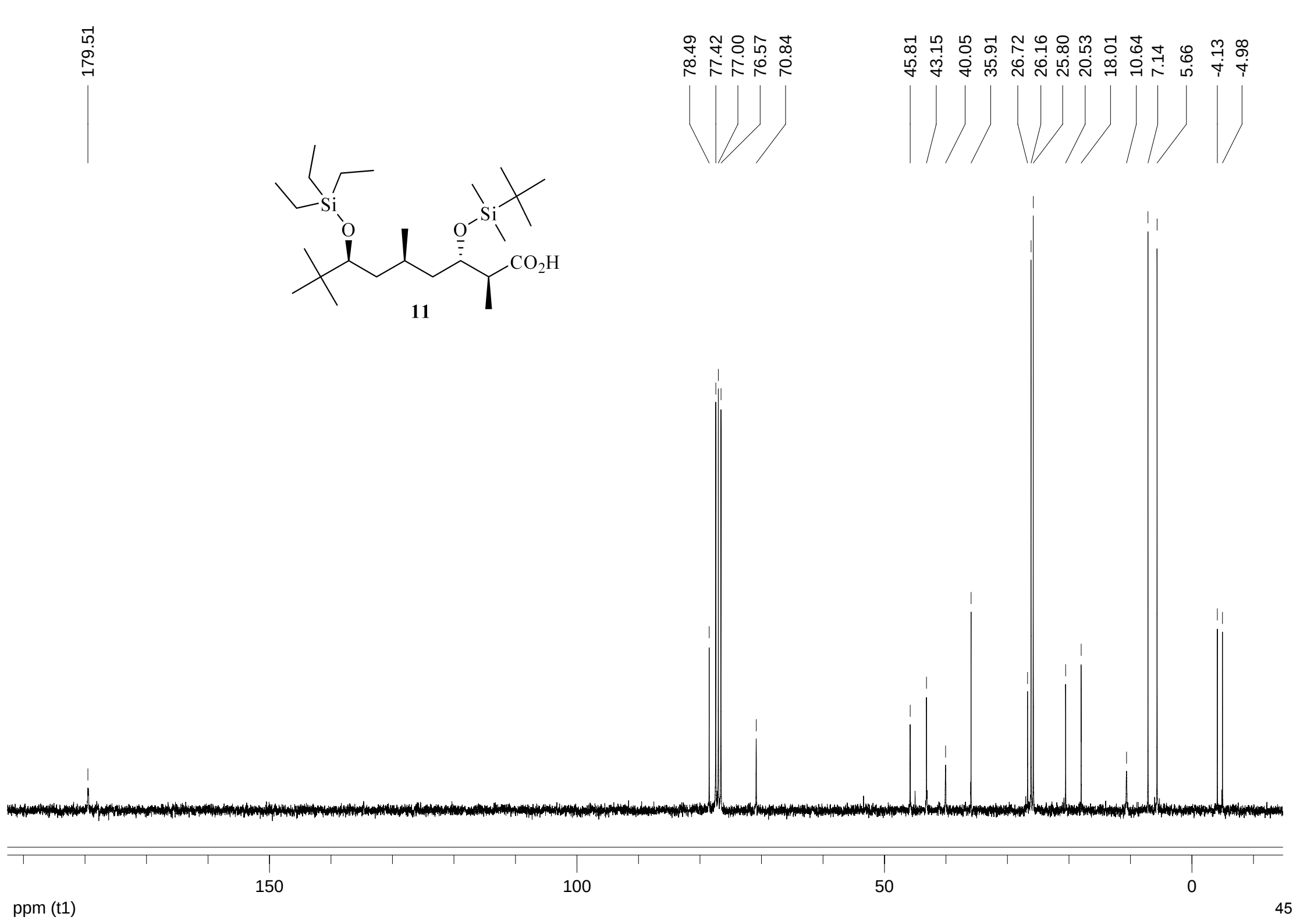

2.37
Si
O
O
Si
9
1.65 1.55 1.52 1.50 1.49 1.47 1.46 1.45 1.45 1.43 1.41 1.40 1.38 1.37 1.25 1.23 1.21 1.20 1.18 1.16 1.01 0.99 0.97 0.96 0.95 0.93 0.90 0.89 0.87 0.84 0.65
5.79 5.77 5.76 5.74 5.73 5.72 5.71 5.70 5.67 5.03 5.02 5.02 4.98 4.98 4.97 4.97 3.78 3.77 3.75 3.75 3.73 3.72 3.34 3.32 3.32 3.30
1.0 2.1 1.0 1.1
6.00 5.50 5.00 4.50 4.00 3.50 3.00
ppm (t1)
1.0 1.2 3.1 2.0 12.6 12.3 8.9 5.9
2.00 1.50 1.00
ppm (t1)

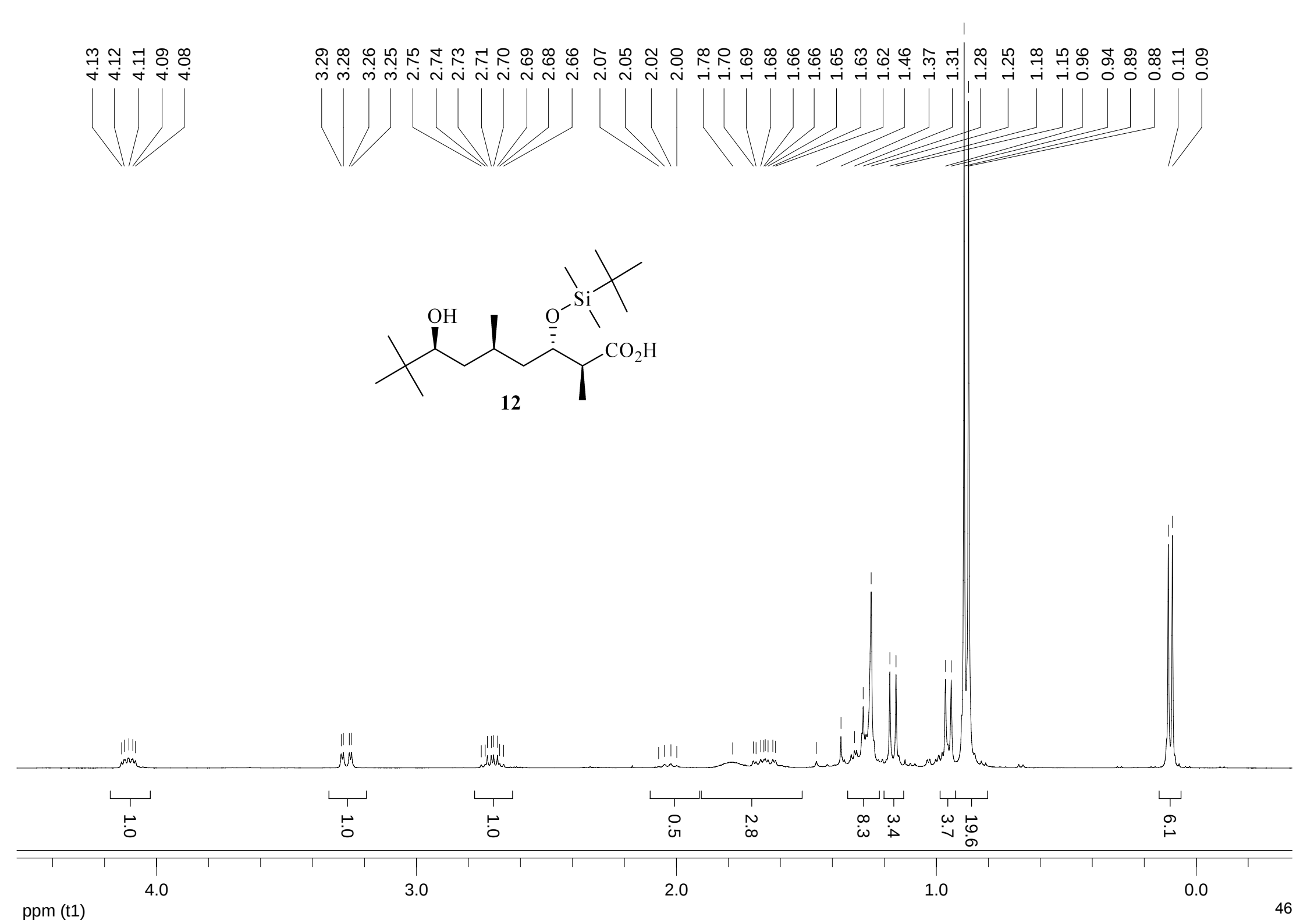

141.78
115.05
79.22
78.15
77.73
77.31
73.65
44.58
44.01
39.66
36.65
26.91
26.68
26.43
21.25
18.89
14.00
7.90
6.39
-3.38
-3.87
Si
O
O
Si
9
150
100
50
0
ppm (t1)

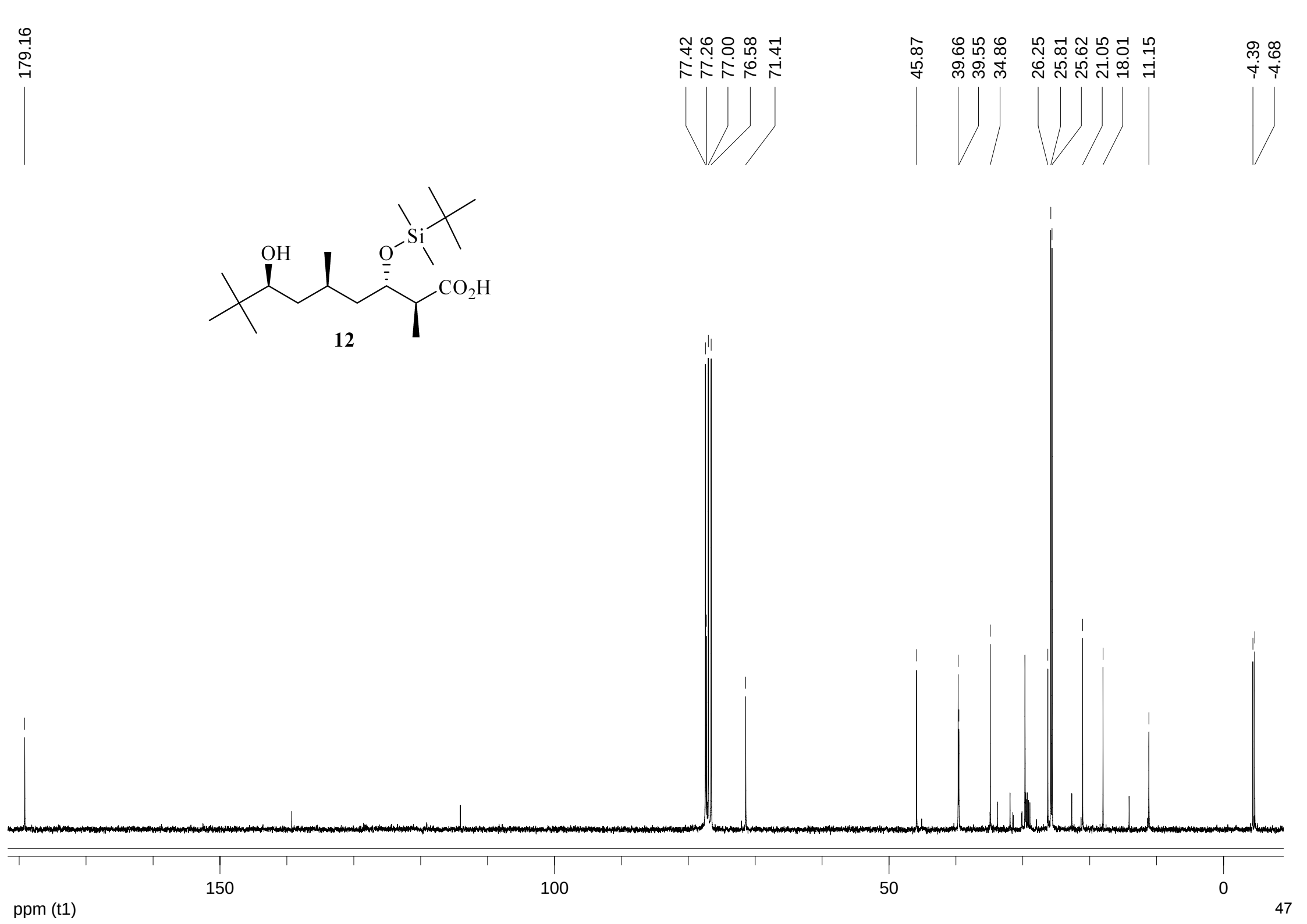

4.23
4.21
4.20
4.19
4.17
4.15
3.32
3.30
3.29
3.27
2.58
2.58
2.57
2.56
2.55
2.54
2.53
2.52
1.68
1.41
1.25
1.15
1.11
0.99
0.95
0.91
0.88
0.82
0.66
0.62
0.58
0.54
0.09
0.08
9.74
9.73
1.0
9.90
9.80
9.70
9.60
ppm (t1)
Si
O
O
Si
O
10
6.9
6.9
0.8
2.0
1.1
1.2
3.1
32.6
6.2
6.0
4.0
3.0
2.0
1.0
ppm (t1)

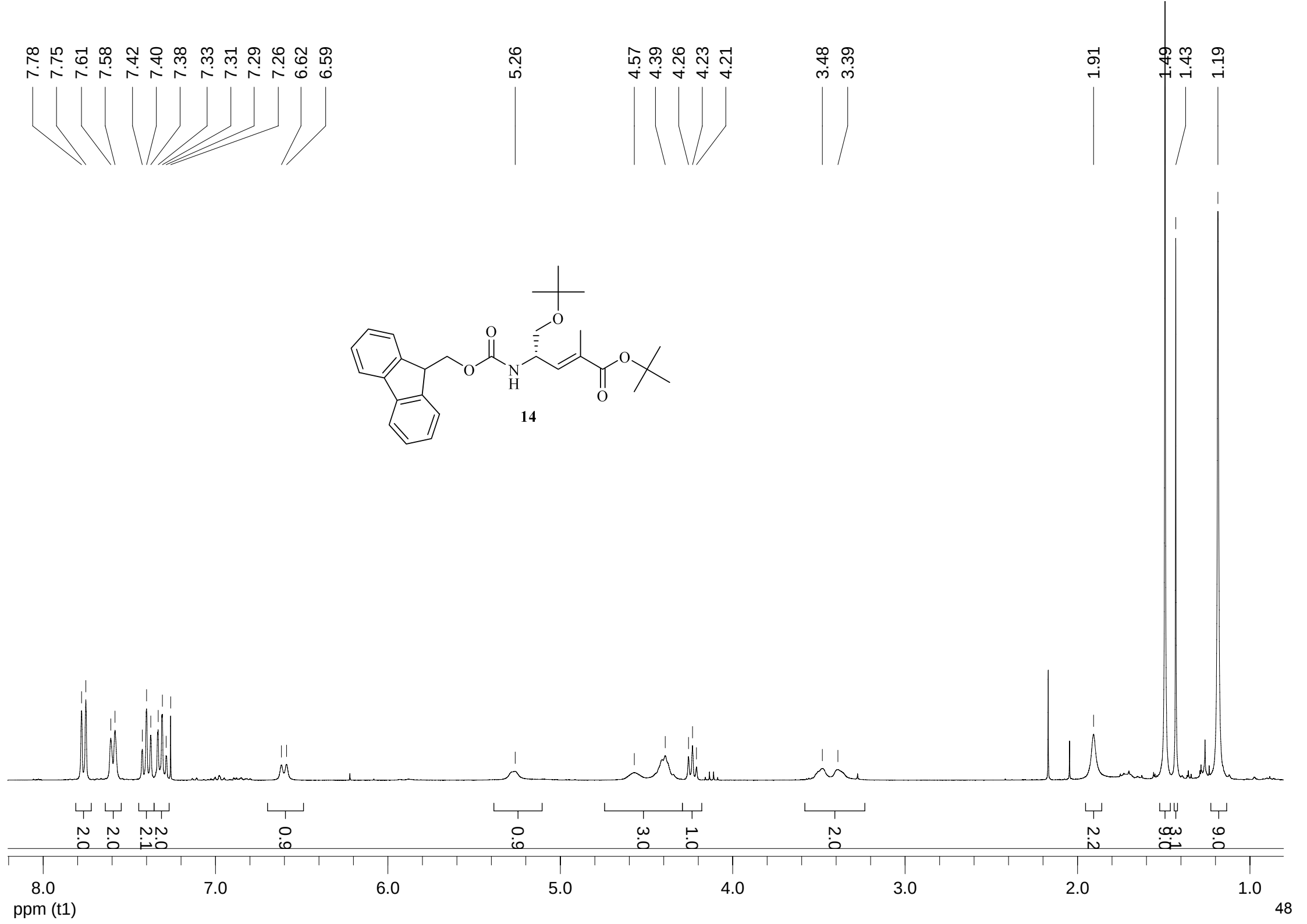

203.78
78.45
77.42
77.00
76.58
70.07
52.51
43.08
41.05
35.85
26.72
26.11
25.77
20.56
18.01
8.84
7.09
5.65
-4.13
-4.86
Si
O
O
Si
O
10
200
150
100
50
0
ppm (t1)

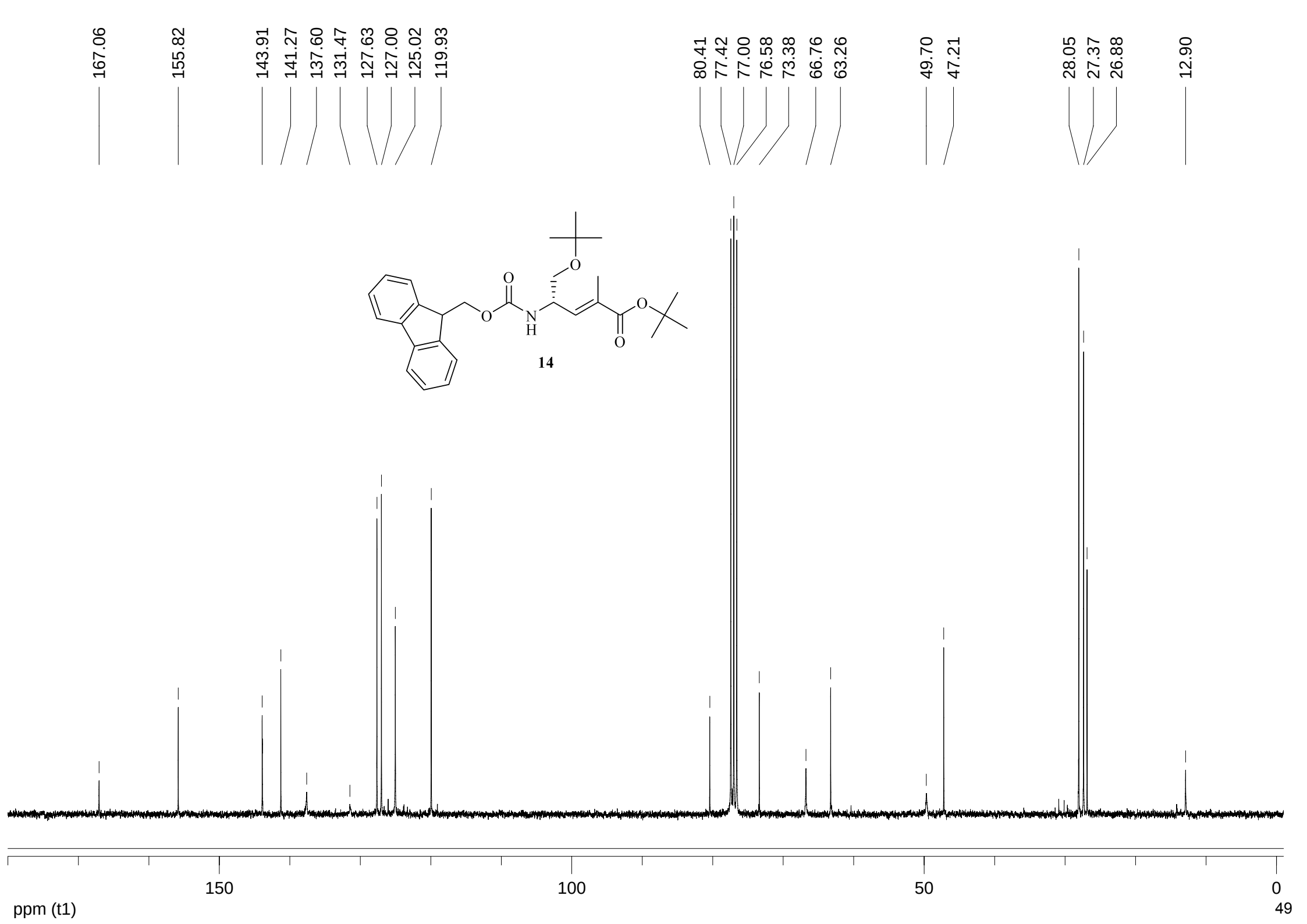

4.17
4.16
4.14
3.32
3.31
3.30
3.29
2.76
2.75
2.74
2.73
2.72
2.70
2.69
2.68
1.69
1.66
1.62
1.42
1.24
1.18
1.16
0.98
0.96
0.94
0.93
0.92
0.90
0.84
0.65
0.62
0.60
0.57
0.11
0.10
Si
O
O
Si
CO2H
11
1.0
1.0
0.9
0.1
2.0
2.3
3.3
21.4
9.4
6.1
6.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

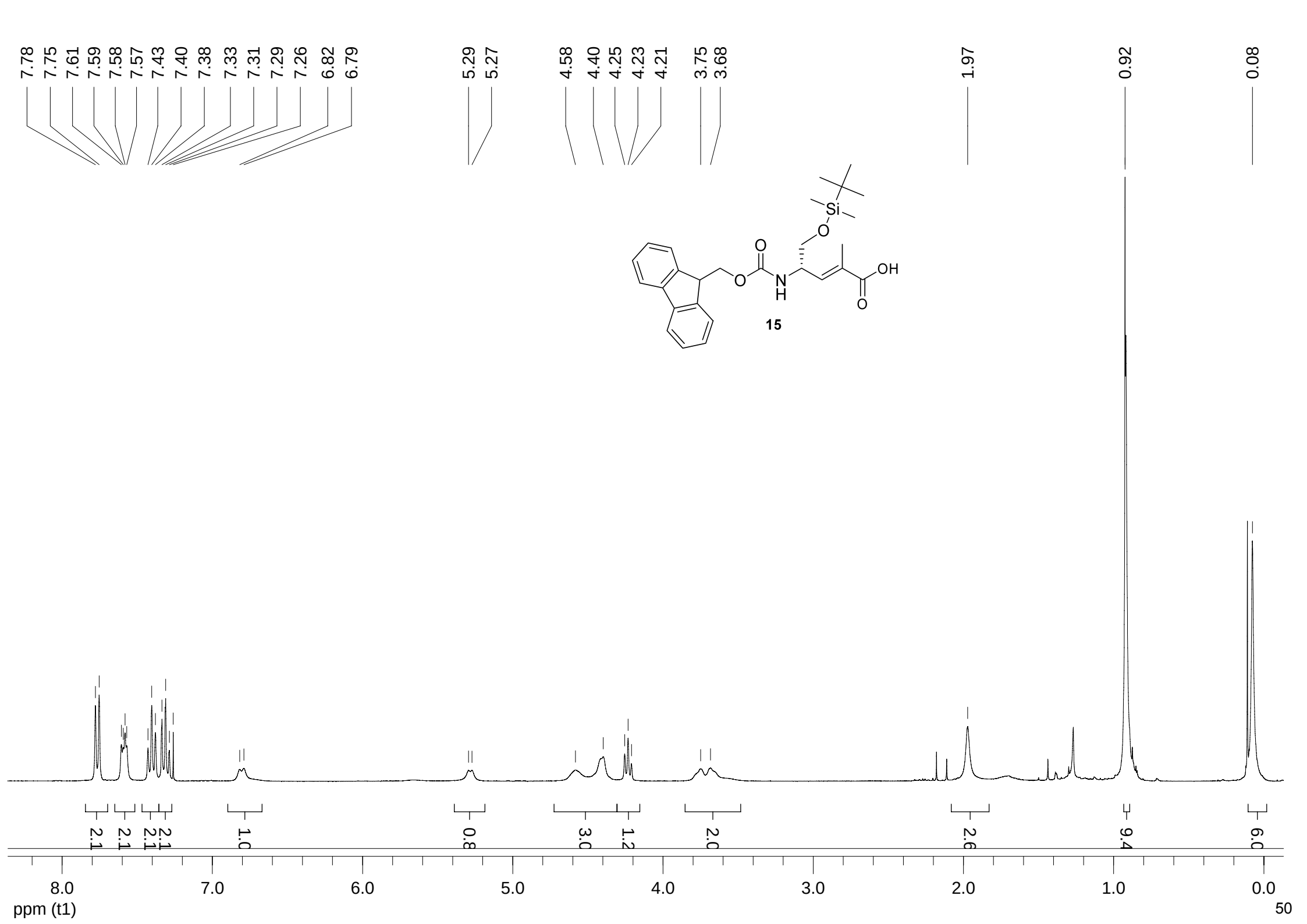

179.51
78.49
77.42
77.00
76.57
70.84
45.81
43.15
40.05
35.91
26.72
26.16
25.80
20.53
18.01
10.64
7.14
5.66
-4.13
-4.98
Si
O
O
Si
CO2H
11
150
100
50
0
ppm (t1)

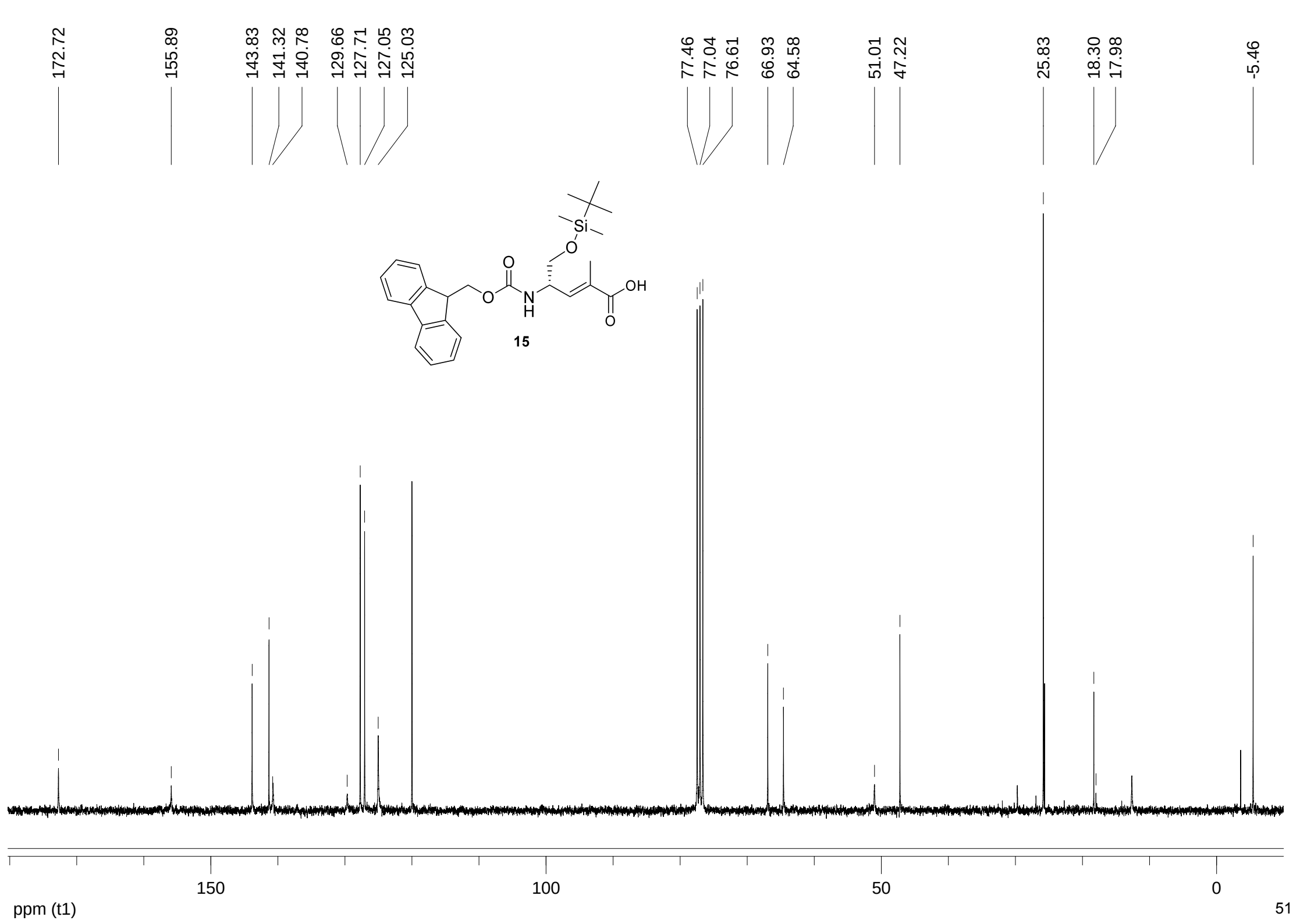

4.13
4.12
4.11
4.09
4.08
3.29
3.28
3.26
3.25
2.75
2.74
2.73
2.71
2.70
2.69
2.68
2.66
2.07
2.05
2.02
2.00
1.78
1.70
1.69
1.68
1.66
1.66
1.65
1.63
1.62
1.46
1.37
1.31
1.28
1.25
1.18
1.15
0.96
0.94
0.89
0.88
0.11
0.09
OH
O
Si
CO2H
12
1.0
1.0
1.0
0.5
2.8
8.3
3.4
3.7
19.6
6.1
4.0
3.0
2.0
1.0
0.0
ppm (t1)

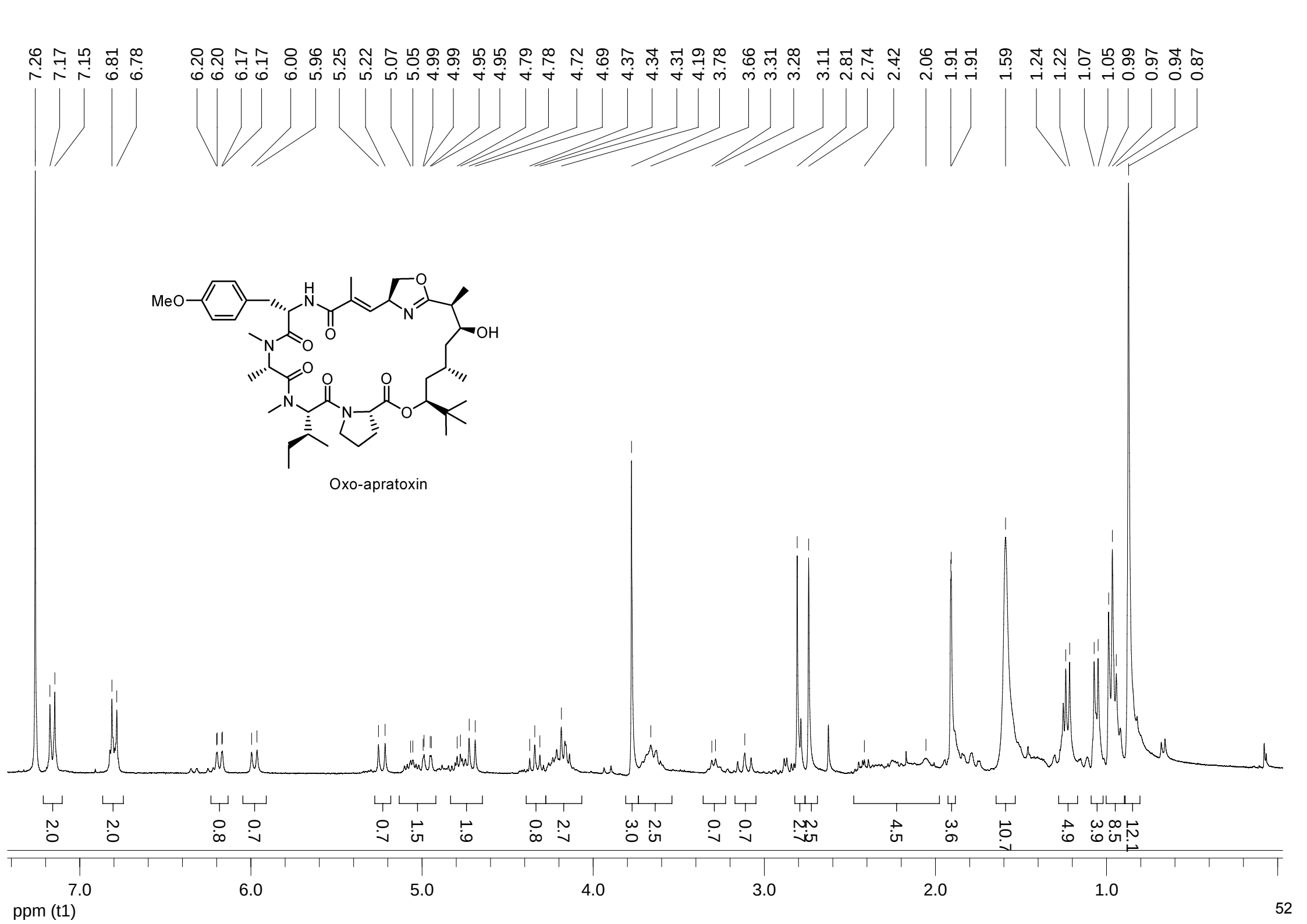

179.16
77.42
77.26
77.00
76.58
71.41
45.87
39.66
39.55
34.86
26.25
25.81
25.62
21.05
18.01
11.15
-4.39
-4.68
OH
O
Si
CO2H
12
150
100
50
0
ppm (t1)

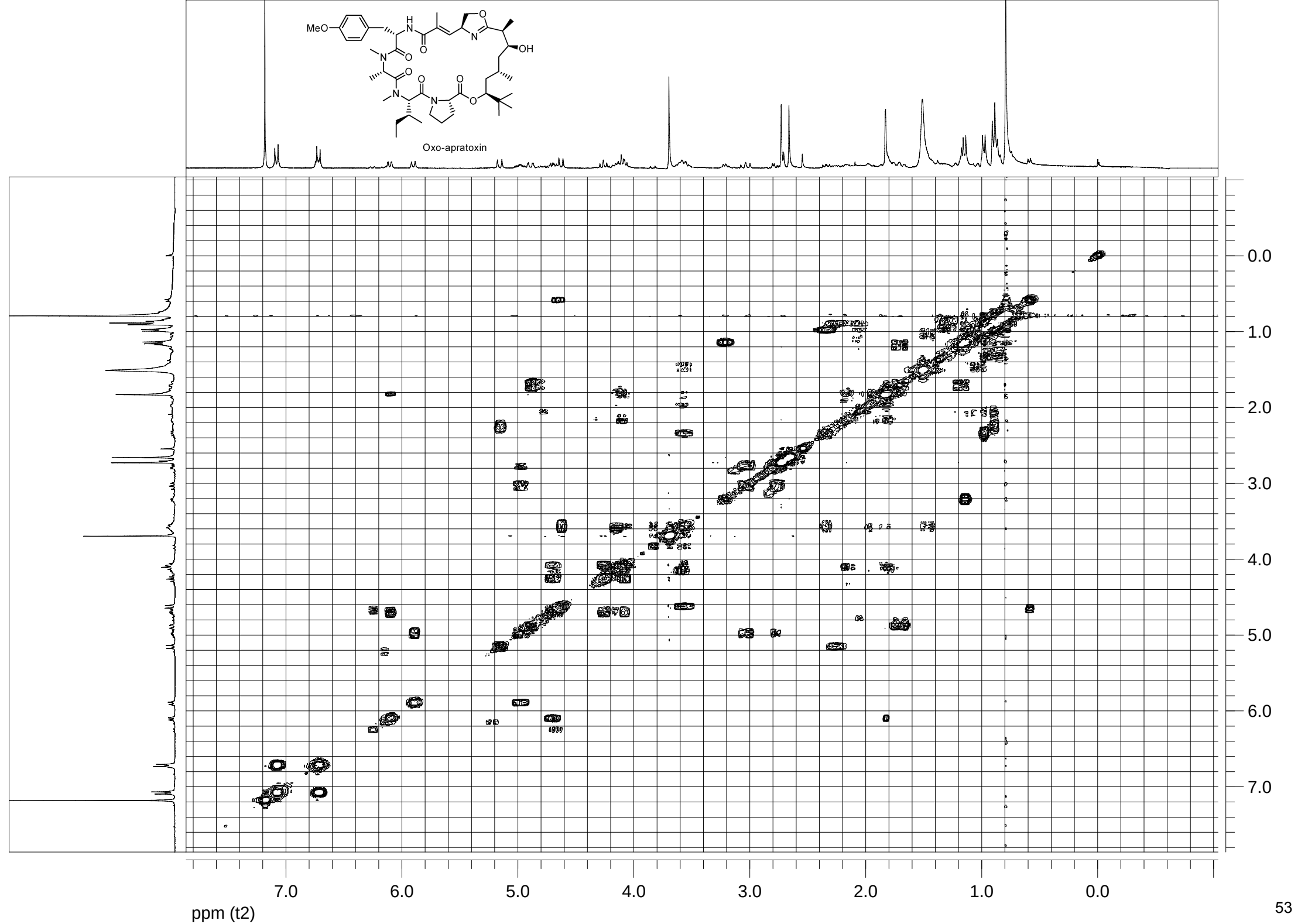

7.78
7.75
7.61
7.58
7.42
7.40
7.38
7.33
7.31
7.29
7.26
6.62
6.59
5.26
4.57
4.39
4.26
4.23
4.21
3.48
3.39
1.91
1.49
1.43
1.19
14
2.0
2.0
2.1
2.0
0.9
0.9
3.0
1.0
2.0
2.2
8.0
3.1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


167.06
155.82
143.91
141.27
137.60
131.47
127.63
127.00
125.02
119.93
80.41
77.42
77.00
76.58
73.38
66.76
63.26
49.70
47.21
28.05
27.37
26.88
12.90
O
O
O
N
H
O
O
14
150
100
50
0
ppm (t1)


7.78
7.75
7.61
7.59
7.58
7.57
7.43
7.40
7.38
7.33
7.31
7.29
7.26
6.82
6.79
5.29
5.27
4.58
4.40
4.25
4.23
4.21
3.75
3.68
1.97
0.92
0.08
Si
O
O
N
H
O
OH
O
15
2.1
2.1
2.1
2.1
1.0
0.8
3.0
1.2
2.0
2.6
9.4
6.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


172.72
155.89
143.83
141.32
140.78
129.66
127.71
127.05
125.03
77.46
77.04
76.61
66.93
64.58
51.01
47.22
25.83
18.30
17.98
-5.46
Si
O
O
N
H
O
OH
O
15
150
100
50
0
ppm (t1)


7.26
7.17
7.15
6.81
6.78
6.20
6.20
6.17
6.17
6.00
5.96
5.25
5.22
5.07
5.05
4.99
4.99
4.95
4.95
4.79
4.78
4.72
4.69
4.37
4.34
4.31
4.19
3.78
3.66
3.31
3.28
3.11
2.81
2.74
2.42
2.06
1.91
1.91
1.59
1.24
1.22
1.07
1.05
0.99
0.97
0.94
0.87
MeO
H
N
O
N
O
OH
O
N
O
O
N
O
O
Oxo-apratoxin
2.0
2.0
0.8
0.7
0.7
1.5
1.9
0.8
2.7
3.0
2.5
0.7
0.7
2.7
2.5
4.5
3.6
10.7
4.9
3.9
8.5
12.1
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


MeO
H
N
O
N
O
OH
O
N
O
O
O
N
O
Oxo-apratoxin
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t2)