SUPPLEMENTARY MATERIAL

Neuroprotective Metabolites from Vietnamese Marine Derived Fungi of Aspergillus and Penicillium Genera

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Abstract: Low molecular weight secondary metabolites of marine fungi *Aspergillus flocculosus*, *Aspergillus terreus* and *Penicillium* sp. from Van Phong and Nha Trang Bays (Vietnam) were studied and a number of polyketides, bis-indole quinones and terpenoids were isolated. The structures of the isolated compounds were determined by 1D and 2D NMR and HRESIMS techniques. Stereochemistry of some compounds was established based on ECD data. A chemical structure of asterriquinone F (**6**) was thoroughly described for the first time. Anthraquinone (**13**) was firstly obtained from natural source. Neuroprotective influences of the isolated compounds against 6-OHDA, paraquat and rotenone toxicity were investigated. 4-Hydroxyscytalone (**1**), 4-hydroxy-6-dehydroxyscytalone (**2**) and demethylcitreoviranol (**3**) have shown significant increasing of paraquat- and rotenone-treated Neuro-2a cell viability and anti-ROS activity.

Keywords: *Aspergillus terreus*; *Aspergillus flocculosus*; *Penicillium* sp.; marine-derived fungi; South China Sea; secondary metabolites; asterriquinones; polyketides; neuroprotective activity; reactive oxygen species

Content

Table S1. ^{13}C NMR (δ in ppm) data for asterriquinones A3 (**7**), B4 (**8**), C1 (**9**), C2 (**10**) and D (**11**)

Atom	**7***	**8***	**9***	**10***	**11****
1	184.0, C	183.70, C	184.0, C	183.8, C	185.2, C
2	120.7, C	120.7, C	120.7, C	120.7, C	130.2, C
3	156.2, C	156.7, C	156.2, C	153.9, C	155.4, C
4	183.8, C	183.68, C	183.8, C	183.8, C	185.2, C
5	122.2, C	120.66, C	126.7, C	120.66, C	130.2, C
6	153.9, C	156.8, C	154.4, C	153.9, C	155.4, C
2′	142.1, C	142.1, C	142.1, C	127.4, CH	130.1, CH
3′	101.8, C	101.84, C	101.7, C	105.7, C	106.7, C
3a′	129.9, C	129.9, C	129.9, C	126.7, C	128.7, C
4′	122.1, CH	118.7, CH	118.7, CH	119.4, CH	123.0, CH
5′	120.3, CH	120.2, CH	120.3, CH	120.7, CH	121.2, CH
6′	118.7, CH	122.1, CH	122.1, CH	122.21, CH	123.2, CH
7′	110.6, CH	110.6, CH	110.6, CH	124.1, C	113.1, CH
7a′	134.5, C	134.5, C	134.5, C	135.0, C	137.8, C
8′	39.3, C	39.3, C	39.3, C	30.8, CH_2	
9′	27.0, CH_3	27.1, CH_3	27.1, CH_3	122.21, CH	
10′	26.8, CH_3	27.0, CH_3	26.8, CH_3	133.6, C	
11′	145.5, CH	145.50, CH	145.4, CH	18.0, CH_3	
12′	112.3, CH_2	112.2, CH_2	112.3, CH_2	25.7, CH_3	
2″	129.2, CH	141.9, C	127.8, CH	121.5, CH	130.1, CH
3″	103.4, C	101.78, C	105.5, C	105.9, C	106.7, C
3a″	128.7, C	129.7, C	126.7, C	126.6, C	128.7, C
4″	121.1, CH	118.4, CH	121.4, CH	127.8, CH	123.0, CH
5″	119.9, CH	120.3, CH	120.5, CH	120.6, CH	121.2, CH
6″	121.7, CH	122.06, CH	122.4, CH	122.5, CH	123.2, CH
7″	114.0, CH	110.7, CH	111.3, CH	111.3, CH	113.1, CH
7a″	135.3, C	134.51, C	135.6, C	135.7, C	137.8, C
8″	39.3, C	39.3, C			
9″	28.03, CH_3	26.8, CH_3			
10″	28.01, CH_3	26.8, CH_3			
11″	143.8, CH	145.52, CH			
12″	113.9, CH_2	112.4, CH_2			
3-OMe	60.1, CH_3	60.1, CH_3	60.0, CH_3	60.65, CH_3	61.5, CH_3
6-OMe	60.6, CH_3	61.2, CH_3	60.7, CH_3	60.68, CH_3	61.5, CH_3

* - data were obtained in $CDCl_3$, 125 MHz; ** - data were obtained in acetone-d_6, 176 MHz

Table S2. ^{1}H NMR data (δ in ppm, J in Hz) for asterriquinones A3(**7**), B4 (**8**), C1 (**9**), C2 (**10**) and D (**11**)

Atom	**7***	**8***	**9***	**10***	**11****
1′(NH)	8.11, brs	8.13, brs	8.14, brs	8.53, brs	
2′				7.59, d (2.8)	7.69, s
4′	7.164, m	7.32, d (7.5)	7.29, d (7.9)	7.44, d (4.2)	7.54, d (8.0)
5′	7.09, t (7.45)	7.12, t (7.4)	7.09, t (7.5)	7.12, t (7.5)	7.09, t (7.5)
6′	7.29, d (7.9)	7.17, td (7.4, 3.8)	7.33, d (8.1)	7.05, d (7.2)	7.16, t (7.5)
7′	7.33, d (8.1)	7.33, d (7.6)	7.33, d (8.1)		7.49, d (8.1)
8′				3.62, brs 3.61, brs	
9′	1.51, s	1.50, brs	1.51, s	5.46, t (7.3)	
10′	1.50, s	1.50, brs	1.50, s		
11′	6.11, dd (17.4, 10.5)	6.11, t (10.7)	6.11, dd (10.5, 6.9)	1.85, s	
12′	5.15, d (10.5) 5.20, d (17.4)	5.18, d (10.5) 5.24, d (10.7)	5.15, d (10.5) 5.20, d (6.9)	1.81, s	
1″		NH, 8.11, brs	NH, 8.56, brs	NH, 8.51, brs	
2″	7.74, s		7.60, s	7.60, brs	7.69, s
4″		7.22, d (7.9)	7.58, d (8.0)	7.62, d (2.7)	7.54, d (8.0)
5″	7.155, m	7.09, t (7.5)	7.19, m	7.19, t (7.5)	7.09, t (7.5)
6″	7.56, dd (6.9, 1.9)	7.17, td (7.4, 3.8)	7.24, d (7.6)	7.25, d (7.7)	7.16, t (7.5)
7″	7.57, dd 7.4, 1.5)	7.33, d (7.6)	7.43, d (8.1)	7.43, d (4.2)	7.49, d (8.1)
9″	1.84, s	1.53, s			
10″	1.84, s	1.53, s			
11″	6.22, dd (17.4, 10.5)	6.14, t (10.7)			
12″	5.27, d (10.7) 5.24, d (17.4)	5.13, d (10.5) 5.21, t (16.7)			
3-OMe	3.80, s	3.70, brs	3.70, s	3.786, brs	3.82, s
6-OMe	3.69, s	3.70, brs	3.81, s	3.793, brs	3.82, s

* - data were obtained in $CDCl_3$, 500 MHz; ** - data were obtained in acetone-d_6, 700 MHz

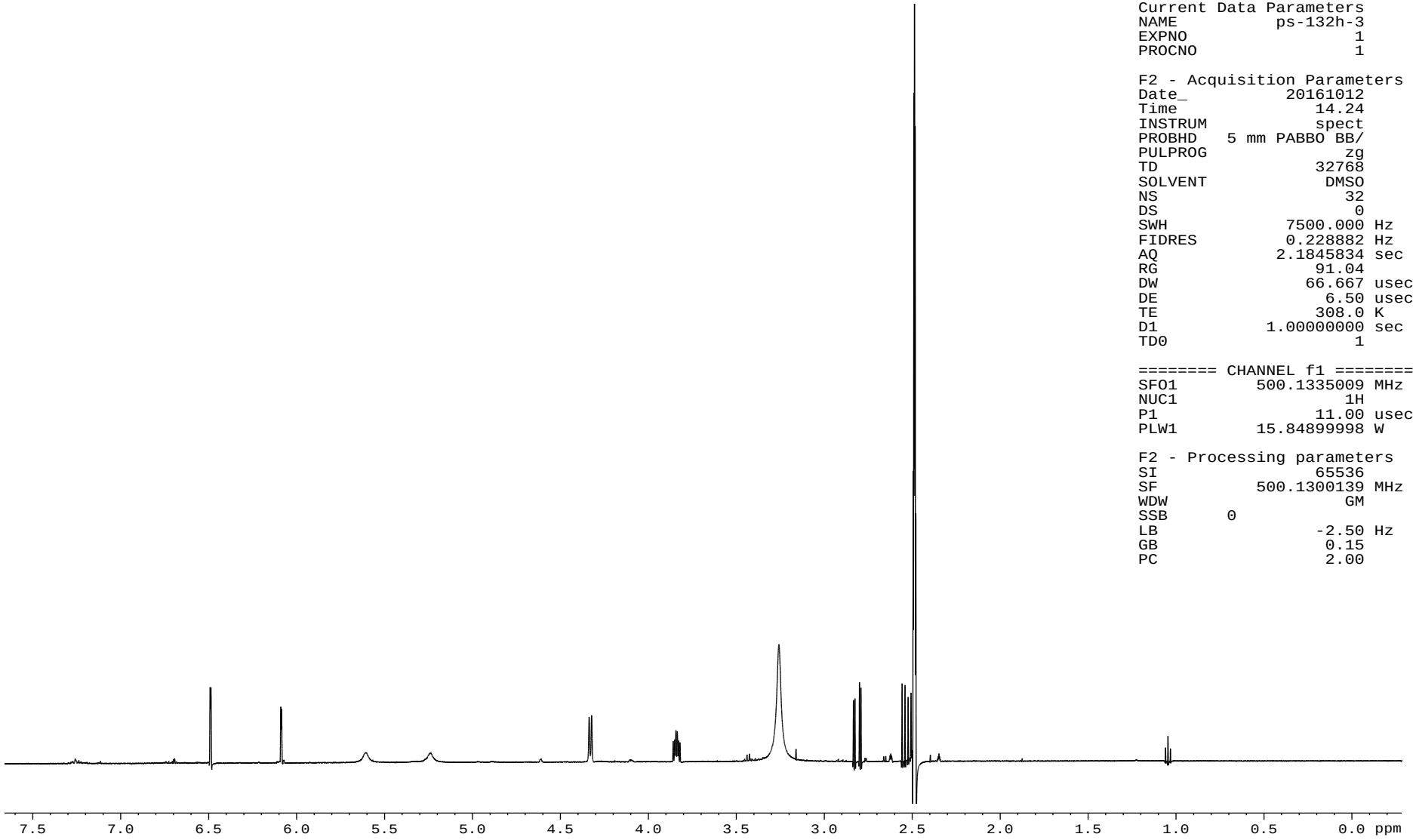
Table S3. ^{1}H and ^{13}C NMR data (700 MHz, DMSO-d_6, δ in ppm) for 1,2,5-trihydroxy-7-methyl-9,10-antraquinone (**13**)

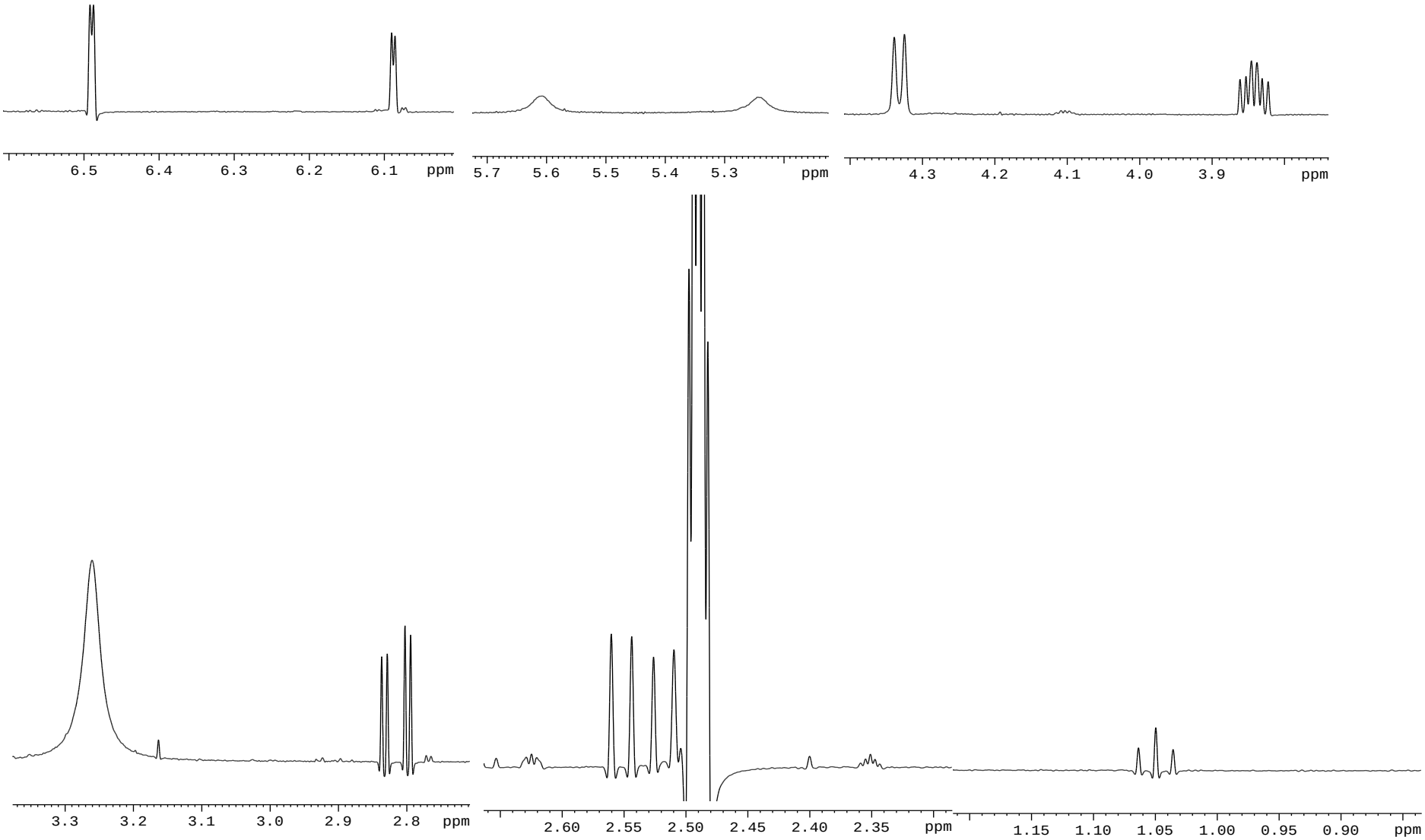
Atom	^{13}C, mult	^{1}H, *J* in Hz
1	164.4, C	
2	165.5, C	
3	107.9, CH	6.60, d (2.5)
4	108.9, CH	7.14, d (2.5)
4a	108.7, C	
5	161.3, C	
6	124.1, CH	7.18, brs
7	148.2, C	
8	120.4, CH	7.52, brs
8a	135.1, C	
9	189.7, C	
9a	132.8, C	
10	181.4, C	
10a	113.4, C	
7-Me	21.4, CH_3	2.42, s
1-OH		12.09, brs
2-OH		11.33, brs
5-OH		12.02, brs

Table S4. ^{1}H and ^{13}C NMR data (700 MHz, $CDCl_3$, δ in ppm) for 4-hydroxy-3-(3-methylbut-2-enyl)benzaldehyde (**14**)

Atom	^{13}C, mult	^{1}H, *J* in Hz
1	130.1, C	
2	131.8, CH	7.67, s
3	127.6, C	
4	160.0, C	
5	116.2, CH	6.91, d (7.9)
6	130.5, CH	7.66, d (2.2)
1′	29.5, CH_2	3.42, s 3.41, s
2′	120.6, CH	5.33, t (7.4)
3′	136.1, C	
4′	25.8, CH_3	1.80, s
5′	179, CH_3	1.79, s
1″	191.1, CH	9.85, s
4-OH		5.83, brs

Figure S1. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of 4-hydroxyscytalone (1)

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4.3 4.2 4.1 4.0 3.9 ppm
3.3 3.2 3.1 3.0 2.9 2.8 ppm
2.60 2.55 2.50 2.45 2.40 2.35 ppm
1.15 1.10 1.05 1.00 0.95 0.90 ppm

Figure S2. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of 4-hydroxyscytalone (1)

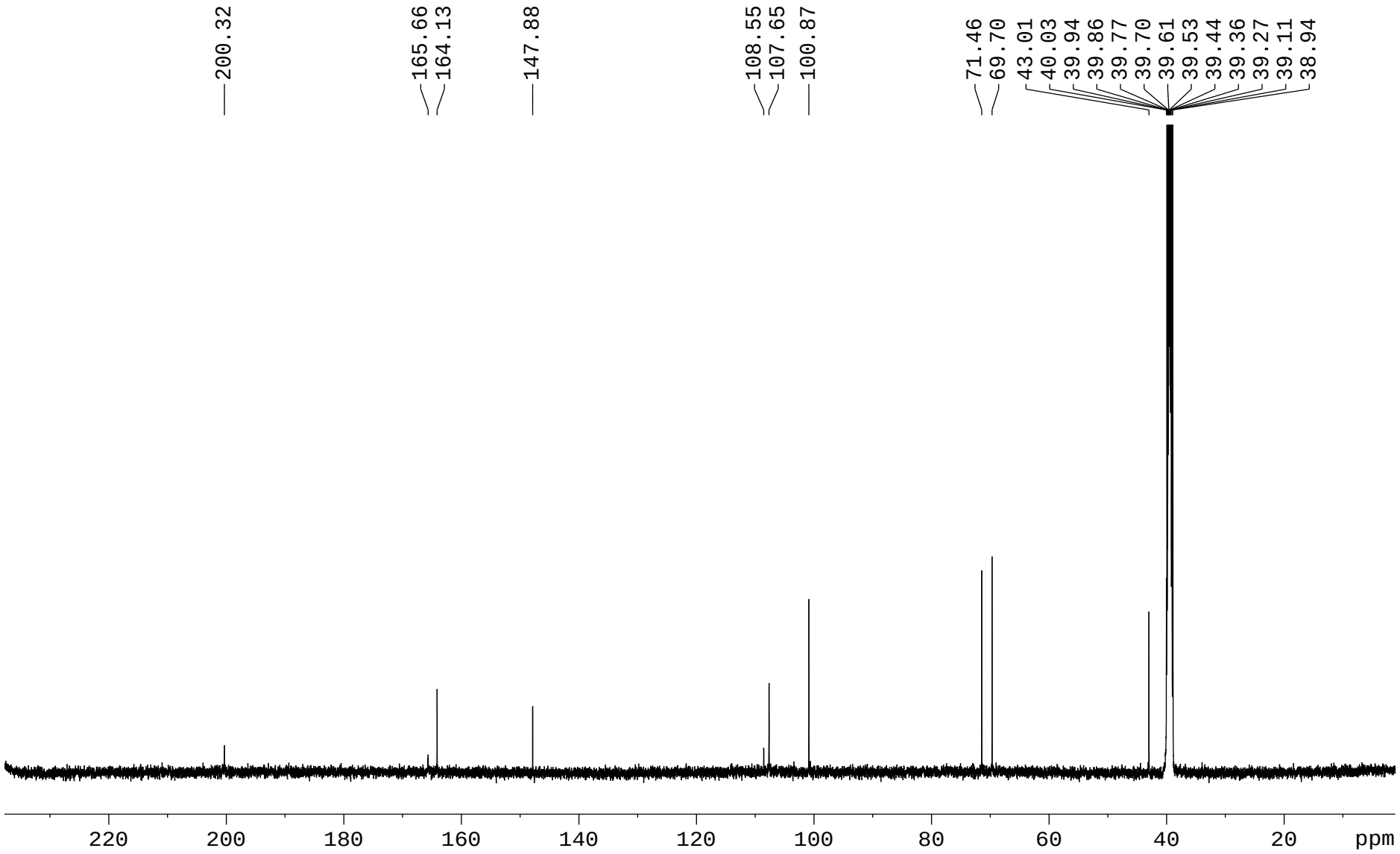


Figure S3. CD spectrum of 4-hydroxyscytalone (1)

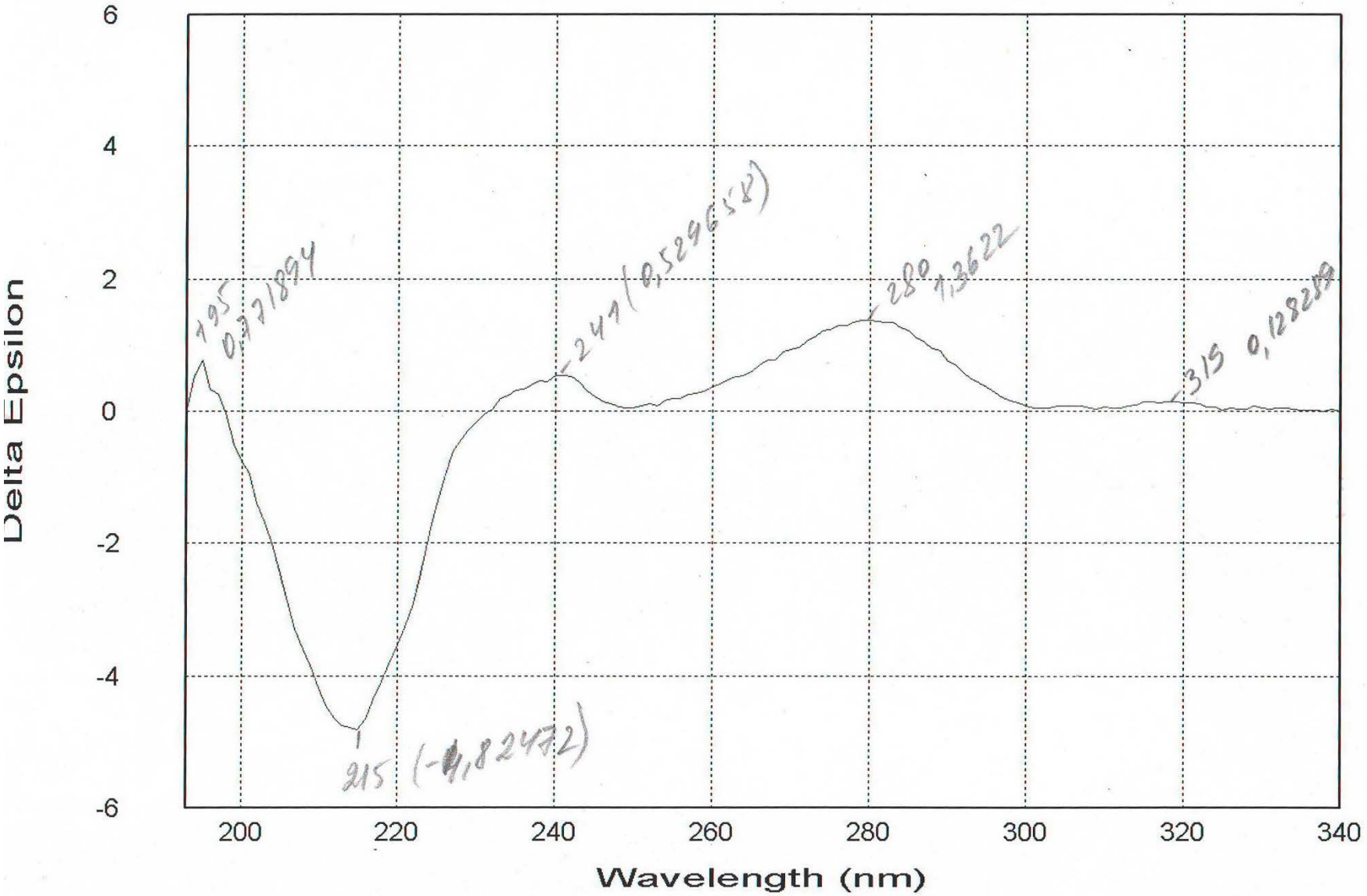
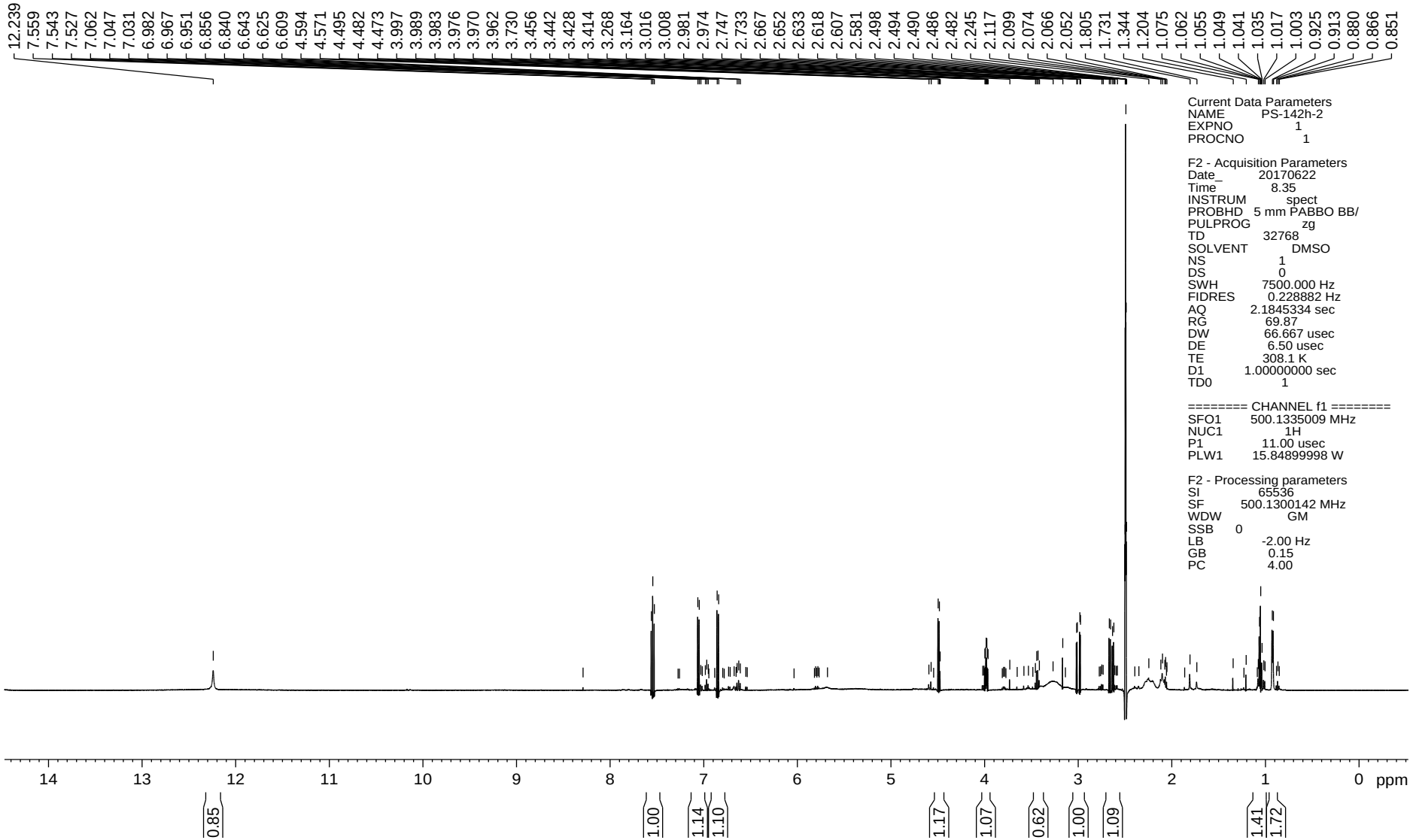
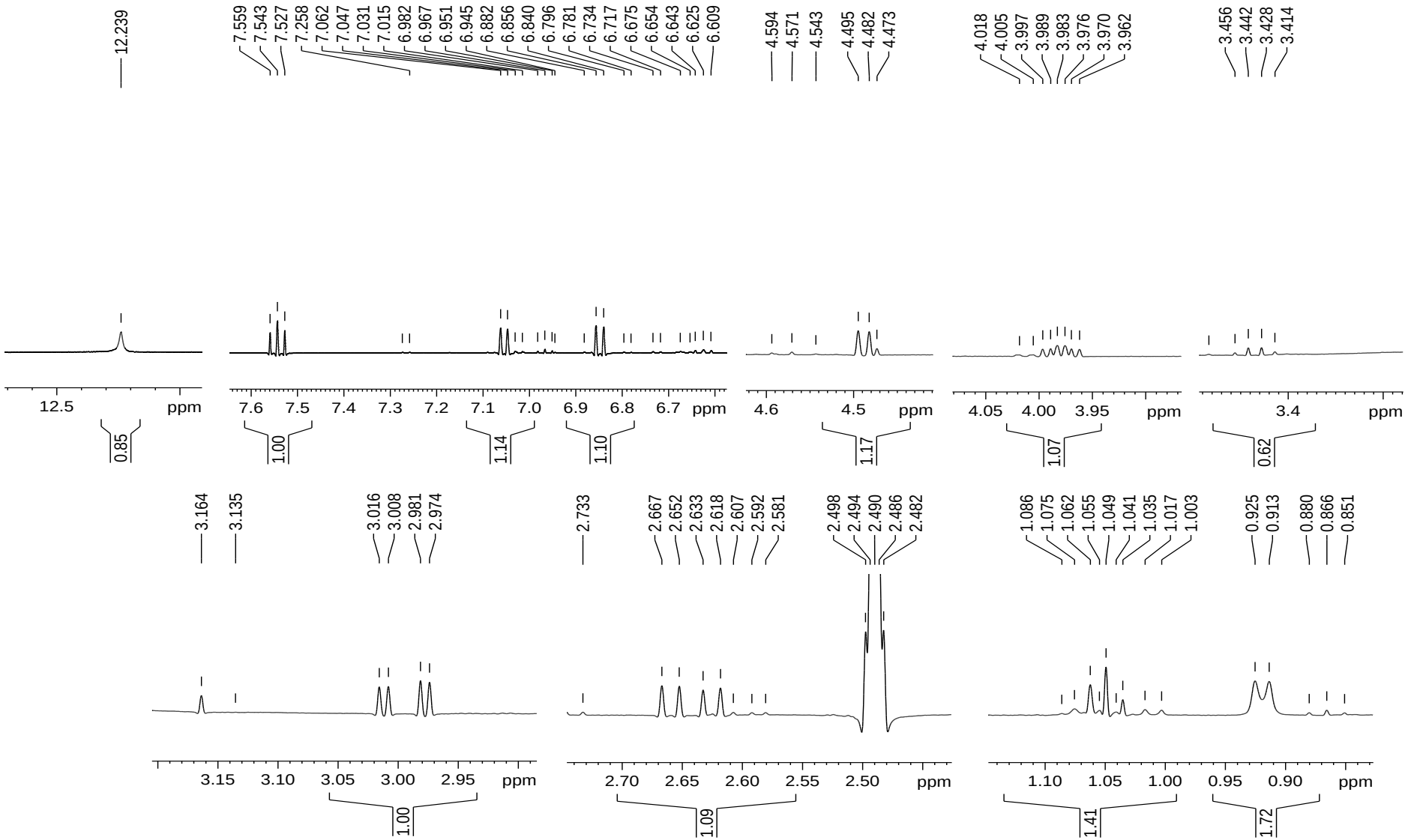


Figure S4. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of 4-hydroxy-6-dehydroxyscytalone (2)

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2.482
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1.062
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2.70
2.65
2.60
2.55
2.50
ppm
1.09
1.10
1.05
1.00
0.95
0.90
ppm
1.41
1.72

Figure S5. ^{13}C NMR (500 MHz, DMSO-d_6) spectrum of 4-hydroxy-6-dehydroxyscytalone (2)

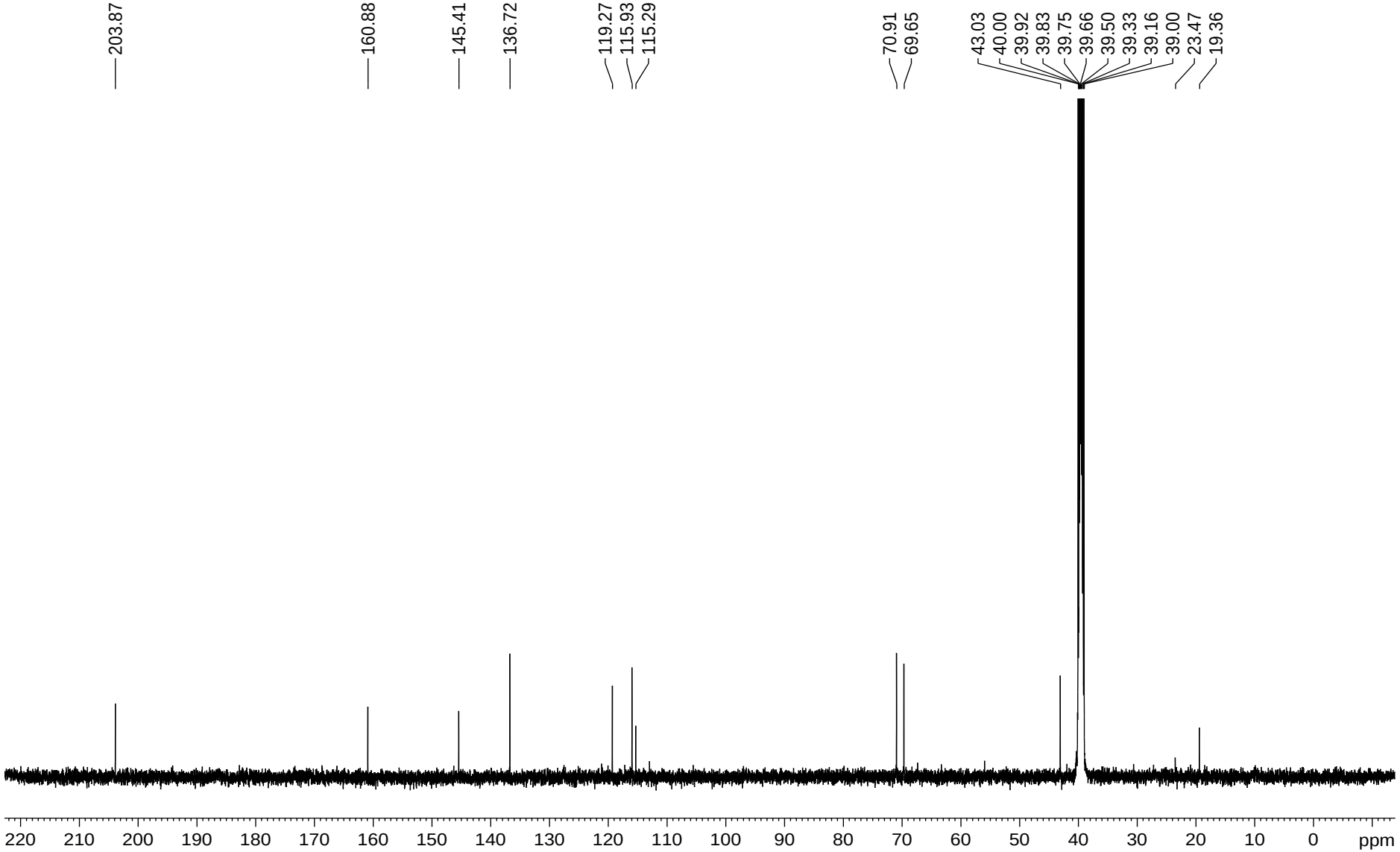
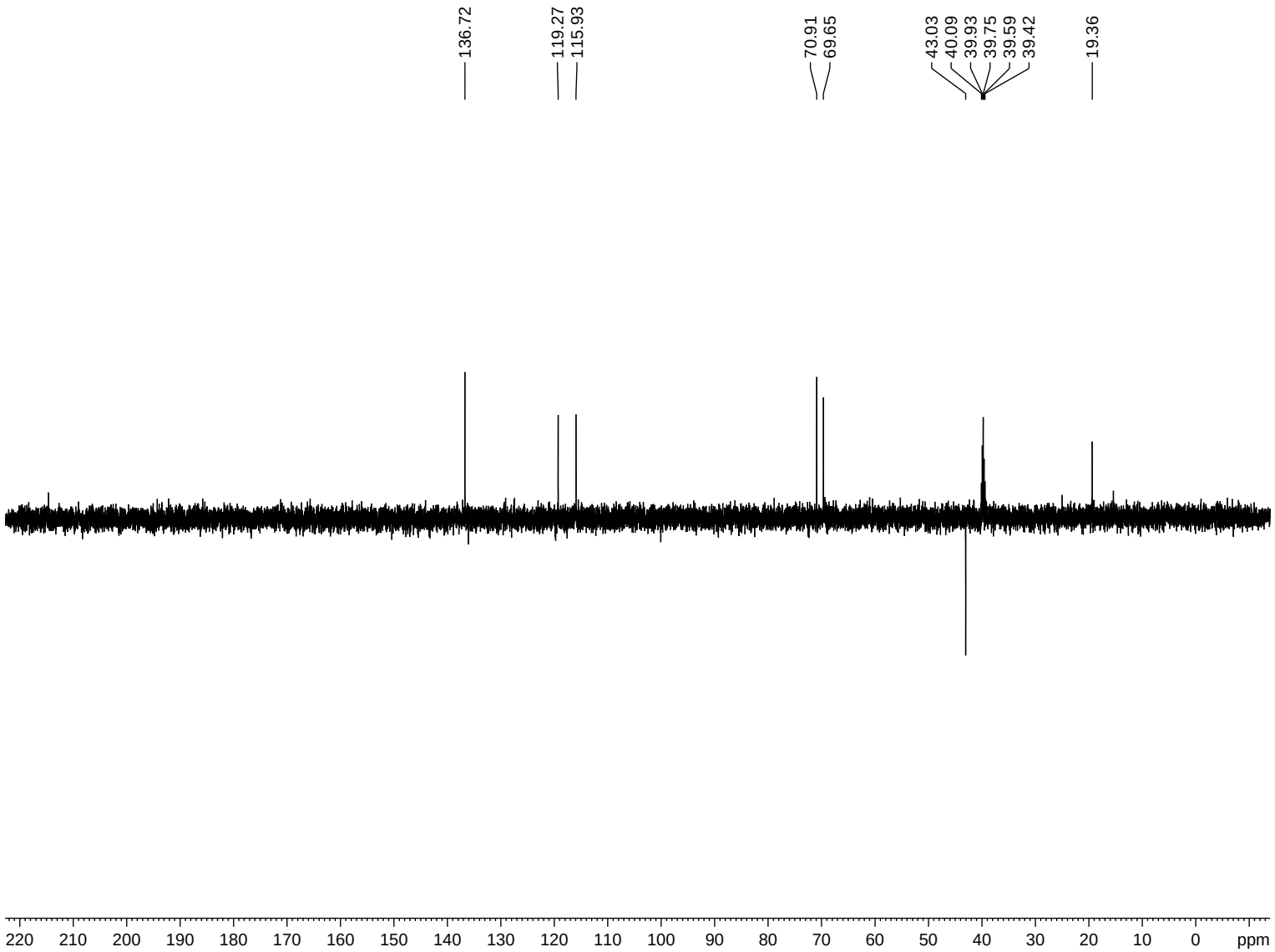


Figure S6. DEPT NMR (125 MHz, DMSO-d_6) spectrum of 4-hydroxy-6-dehydroxyscytalone (2)

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D12           0.00002000 sec
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NUC1                13C
P1                12.00 usec
P2                24.00 usec
PLW1         79.43299866 W

======== CHANNEL f2 ========
SFO2         500.1315004 MHz
NUC2                1H
CPDPRG[2         waltz16
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P4                22.00 usec
PCPD2             78.00 usec
PLW2         15.84899998 W
PLW12         0.31623000 W

F2 - Processing parameters
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Figure S7. CD spectrum of 4-hydroxy-6-dehydroxyscytalone (2)

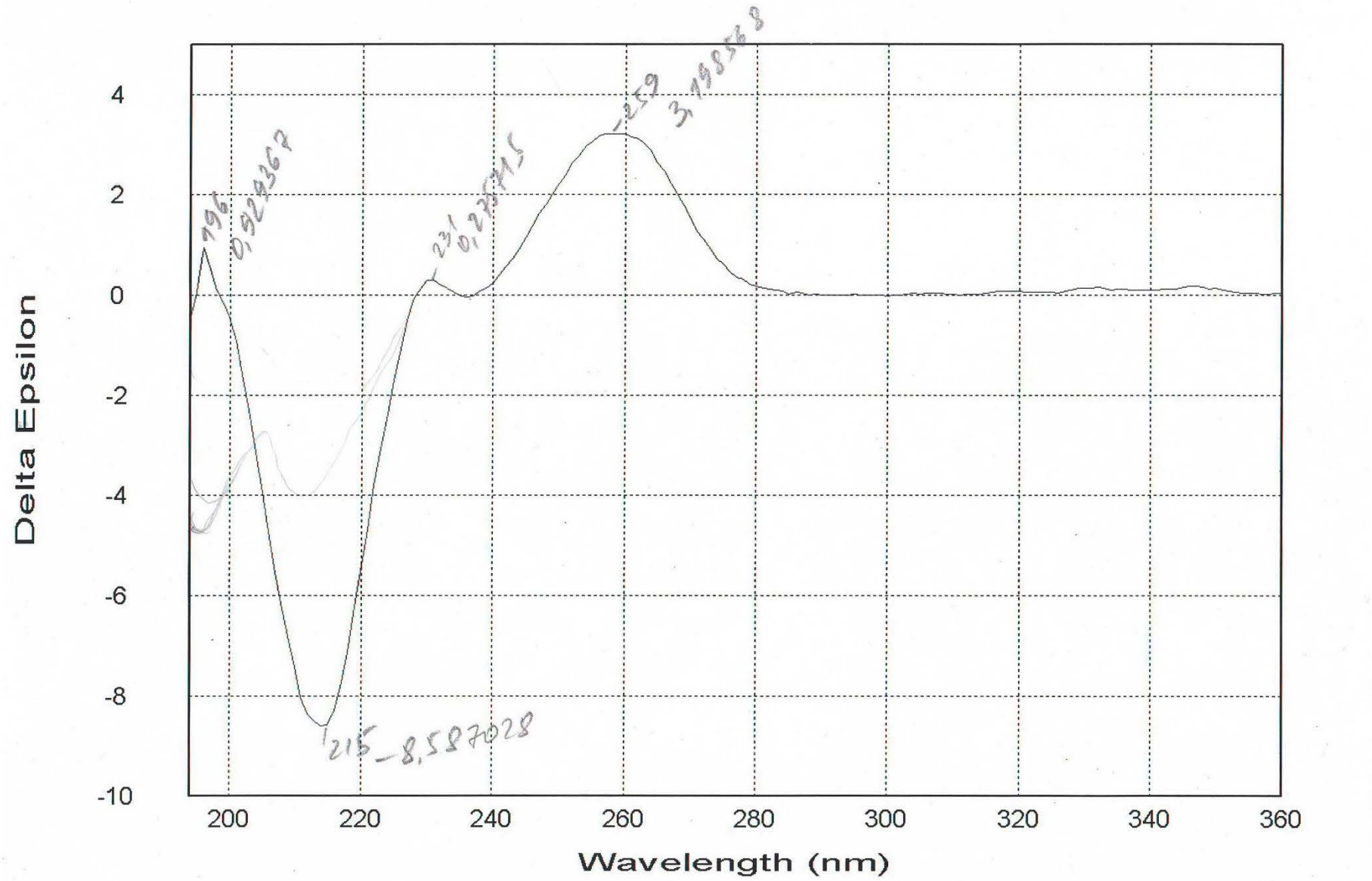
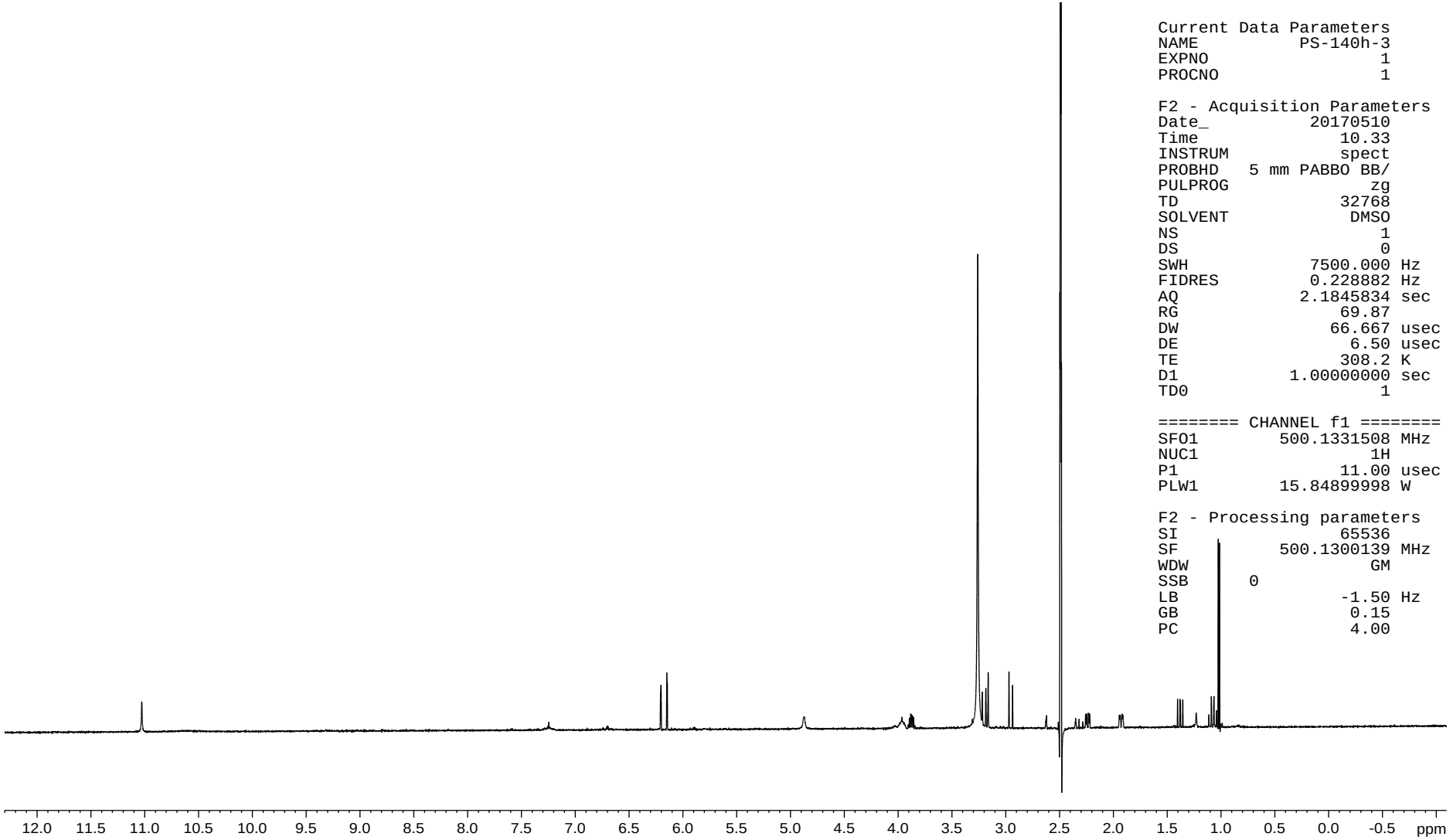


Figure S8. ^{1}H NMR (500 MHz, DMSO-d_6) spectrum of demethylcitreoviranol (3)



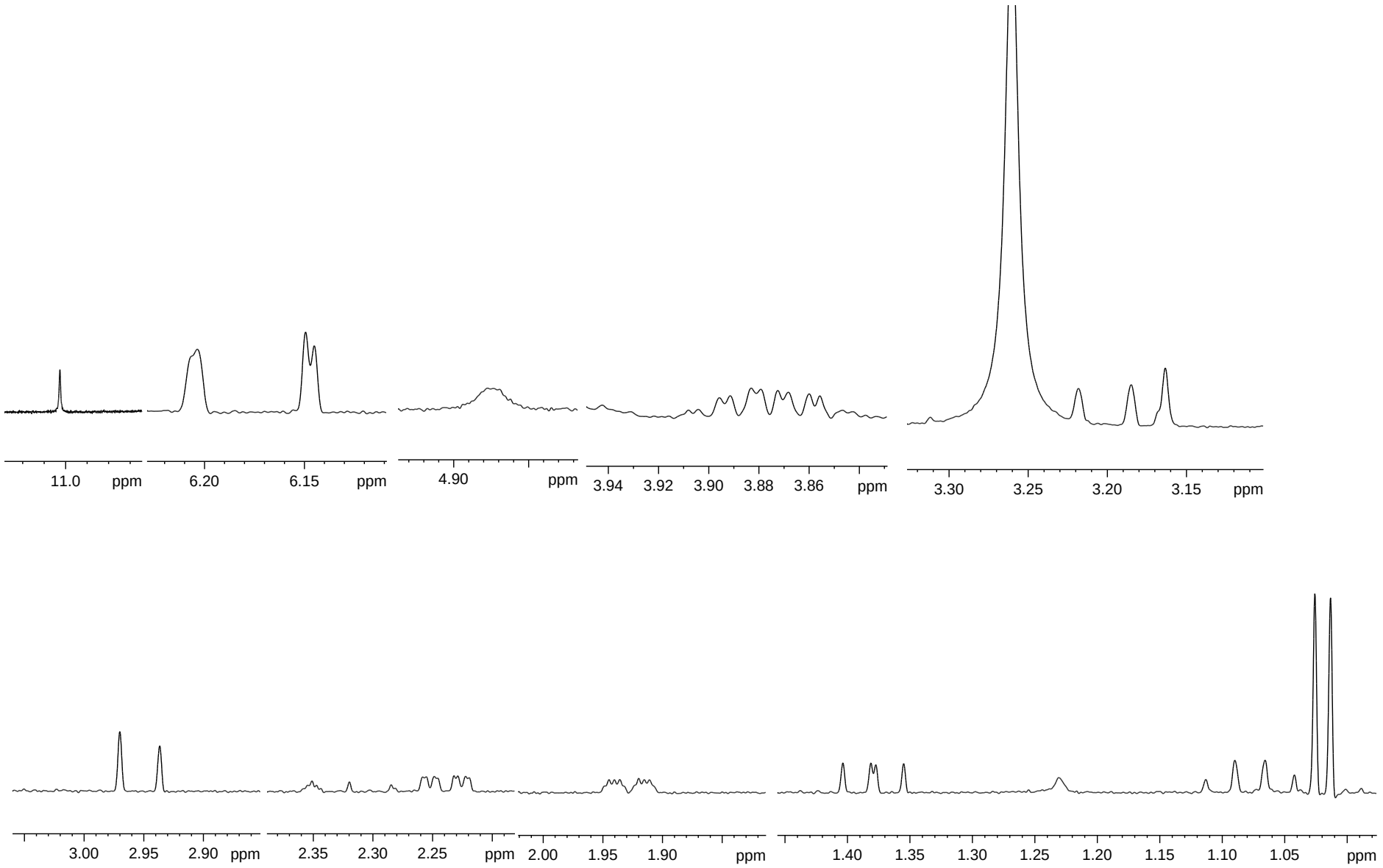
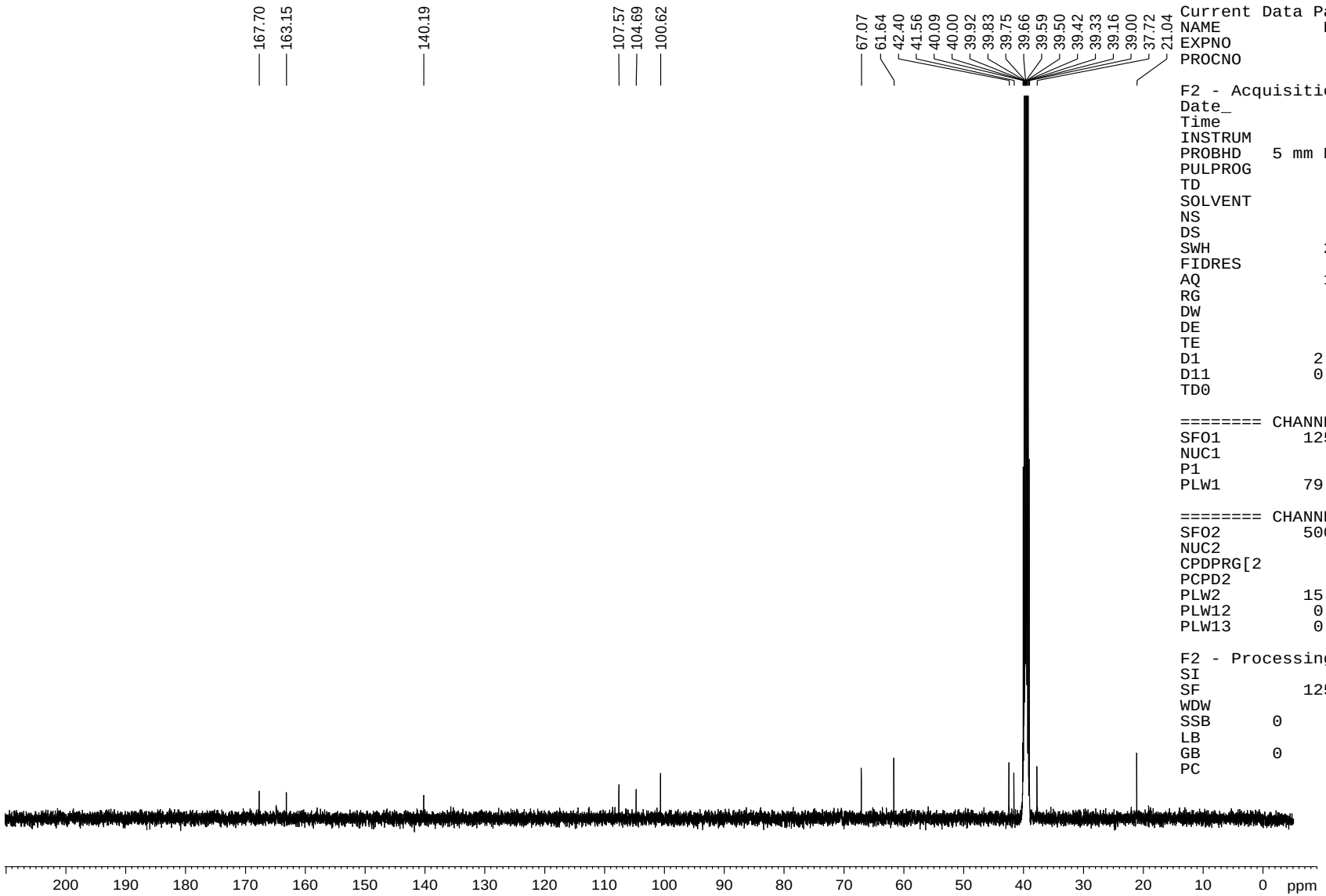


Figure S9. ^{13}C NMR (125 MHz, DMSO-d_6) spectrum of demethylcitreoviranol (3)

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TE               308.1 K
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TD0               4096

======== CHANNEL f1 ========
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P1               12.00 usec
PLW1        79.43299866 W

======== CHANNEL f2 ========
SFO2        500.1320005 MHz
NUC2               1H
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PLW13        0.15849000 W

F2 - Processing parameters
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WDW                  EM
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Figure S10. DEPT NMR (125 MHz, DMSO-d_6) spectrum of demethylcitreoviranol (3)

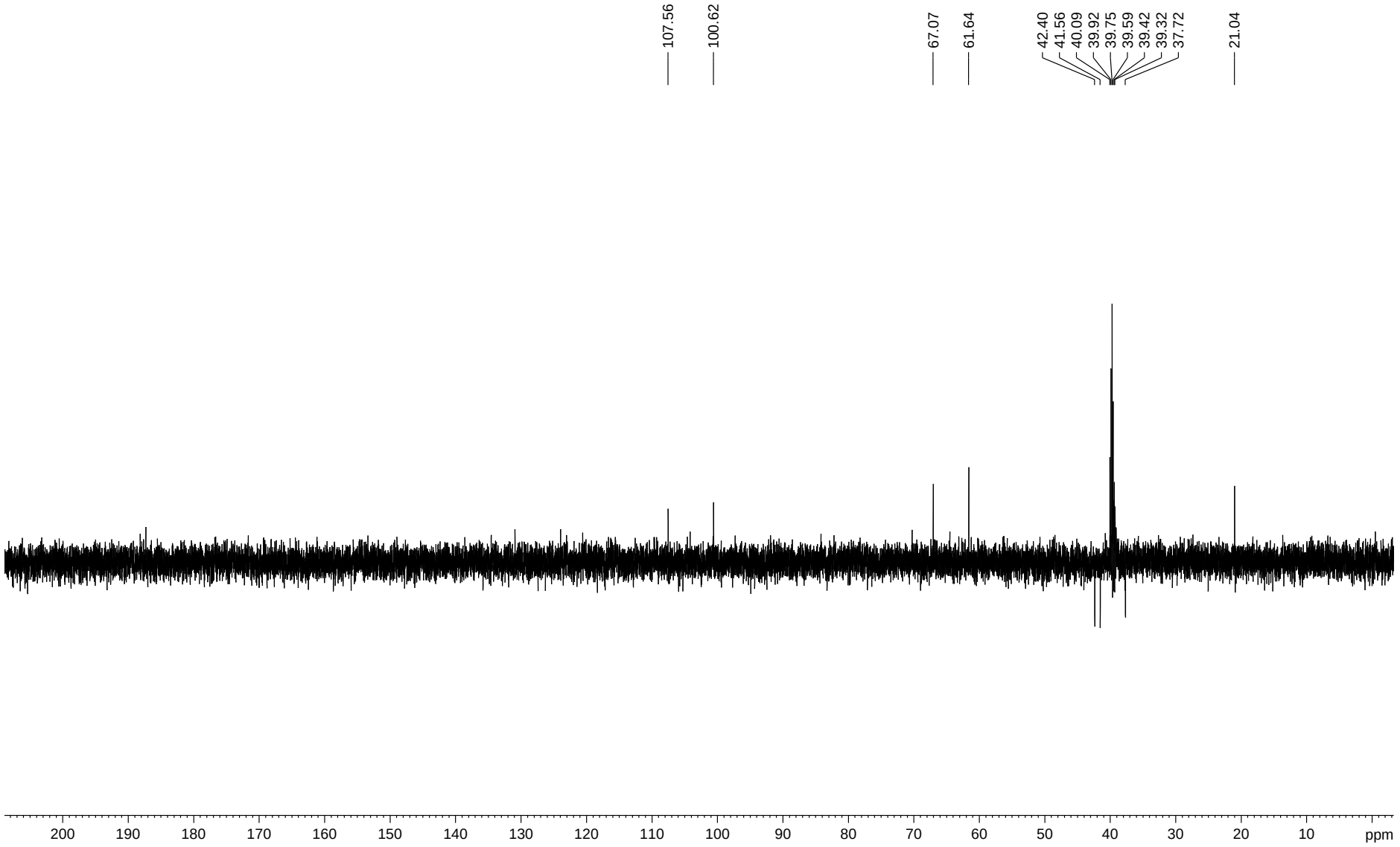


Figure S11. CD spectrum of demethylcitreoviranol (3)

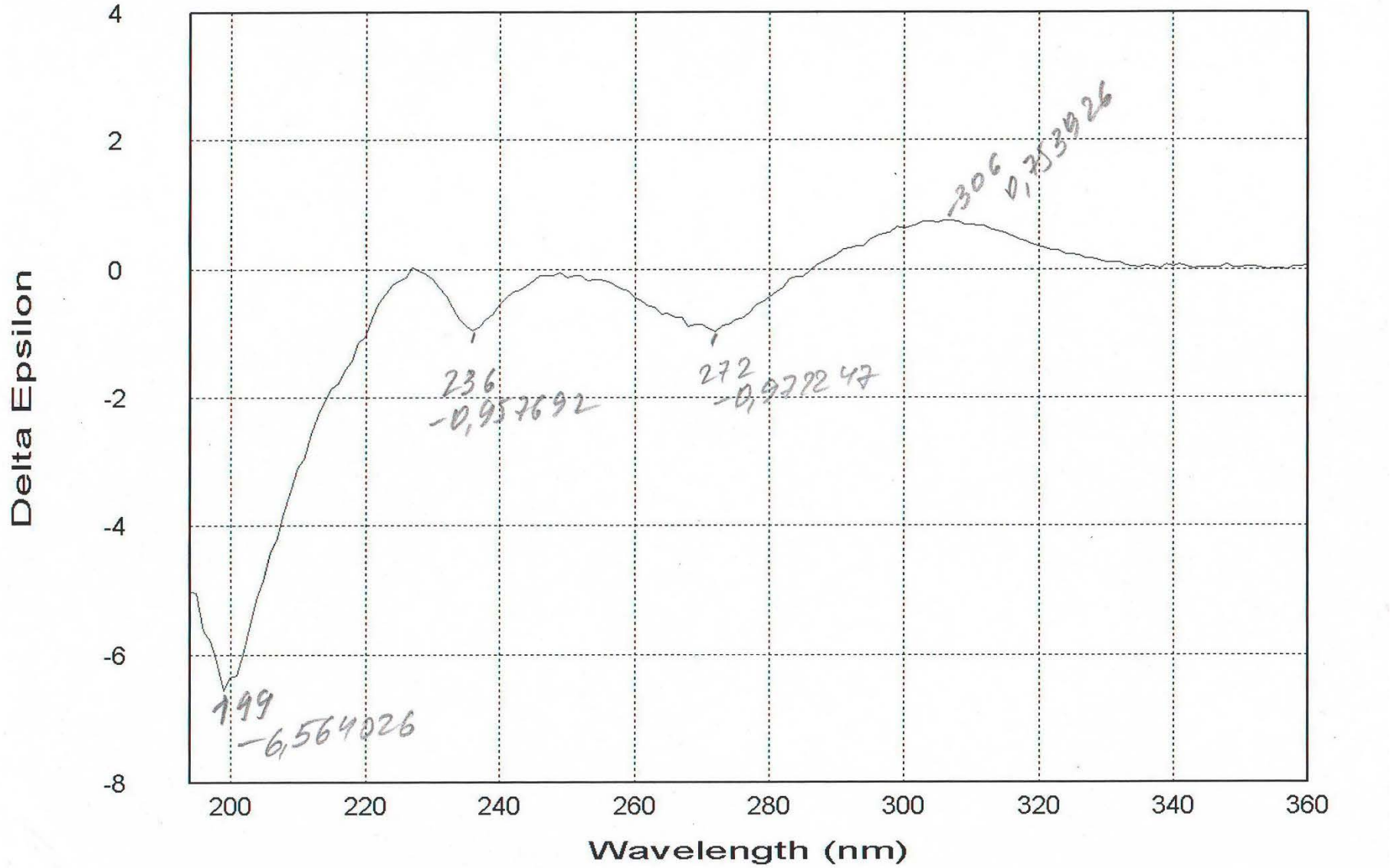
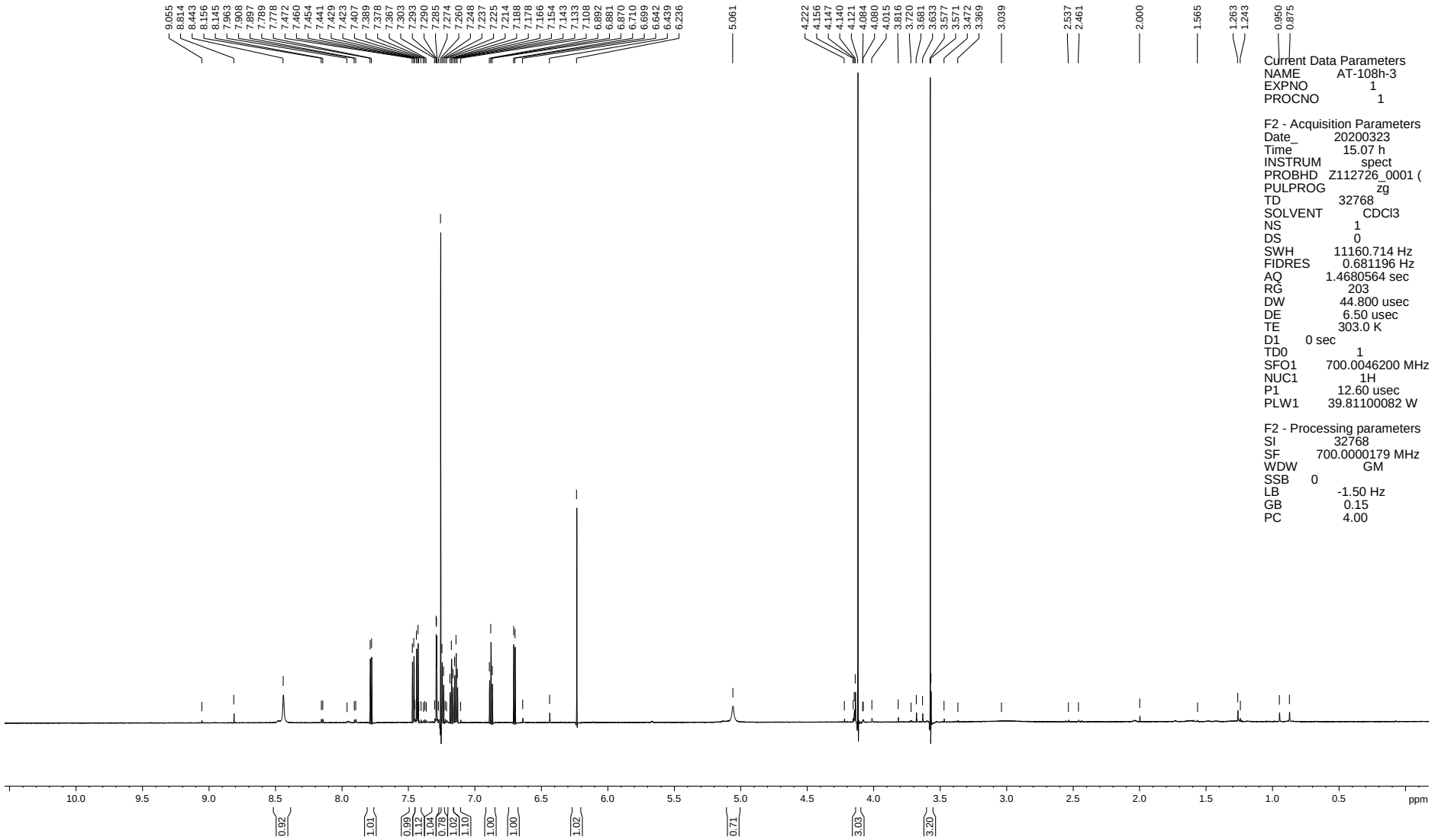
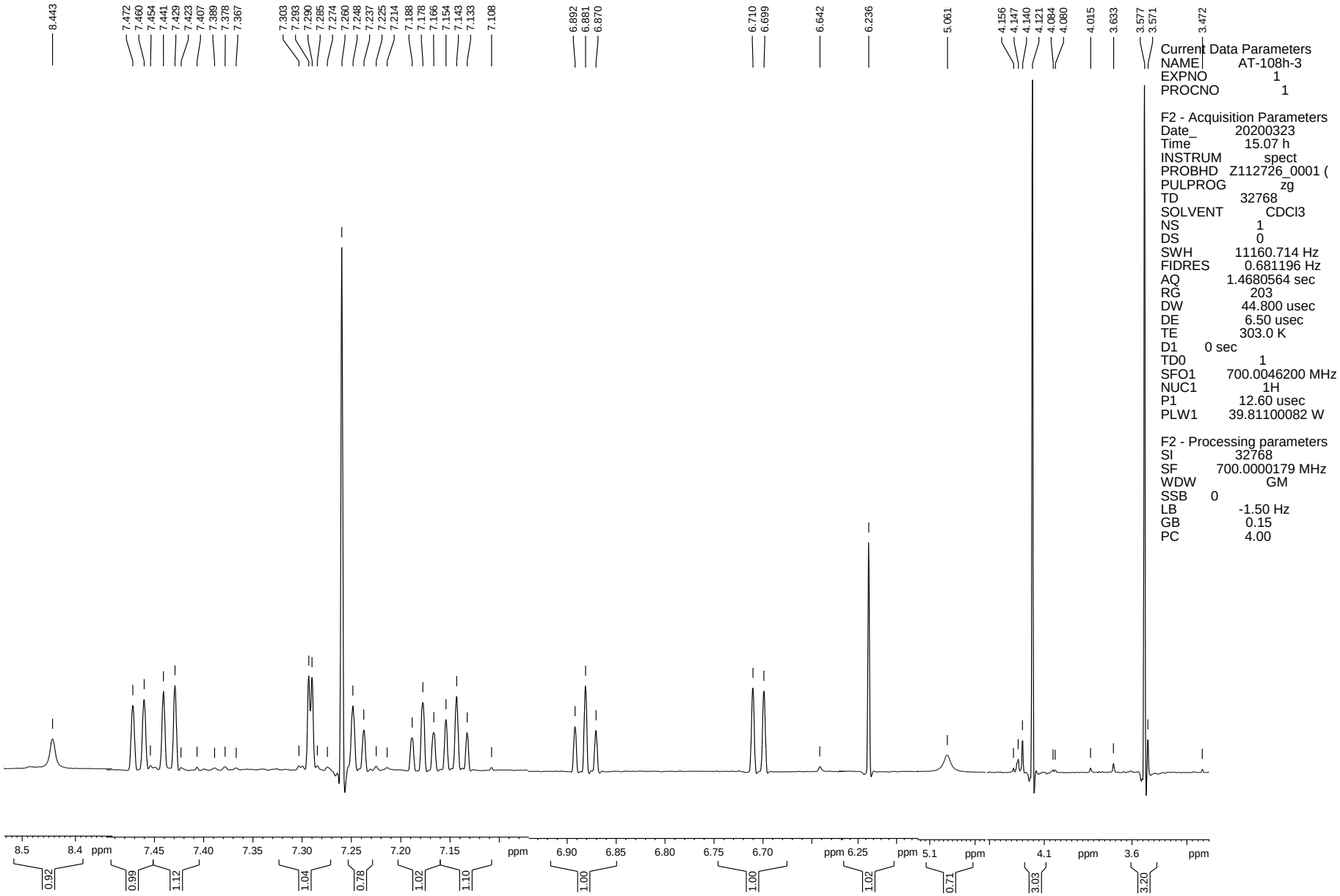


Figure S12. ^{1}H NMR (700 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

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6.710
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ppm
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6.80
6.75
6.70
ppm
6.25
ppm
5.1
ppm
4.1
ppm
3.6
ppm
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1.04
0.78
1.02
1.10
1.00
1.00
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0.71
3.03
3.20

Figure S13. ^{13}C NMR (176 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

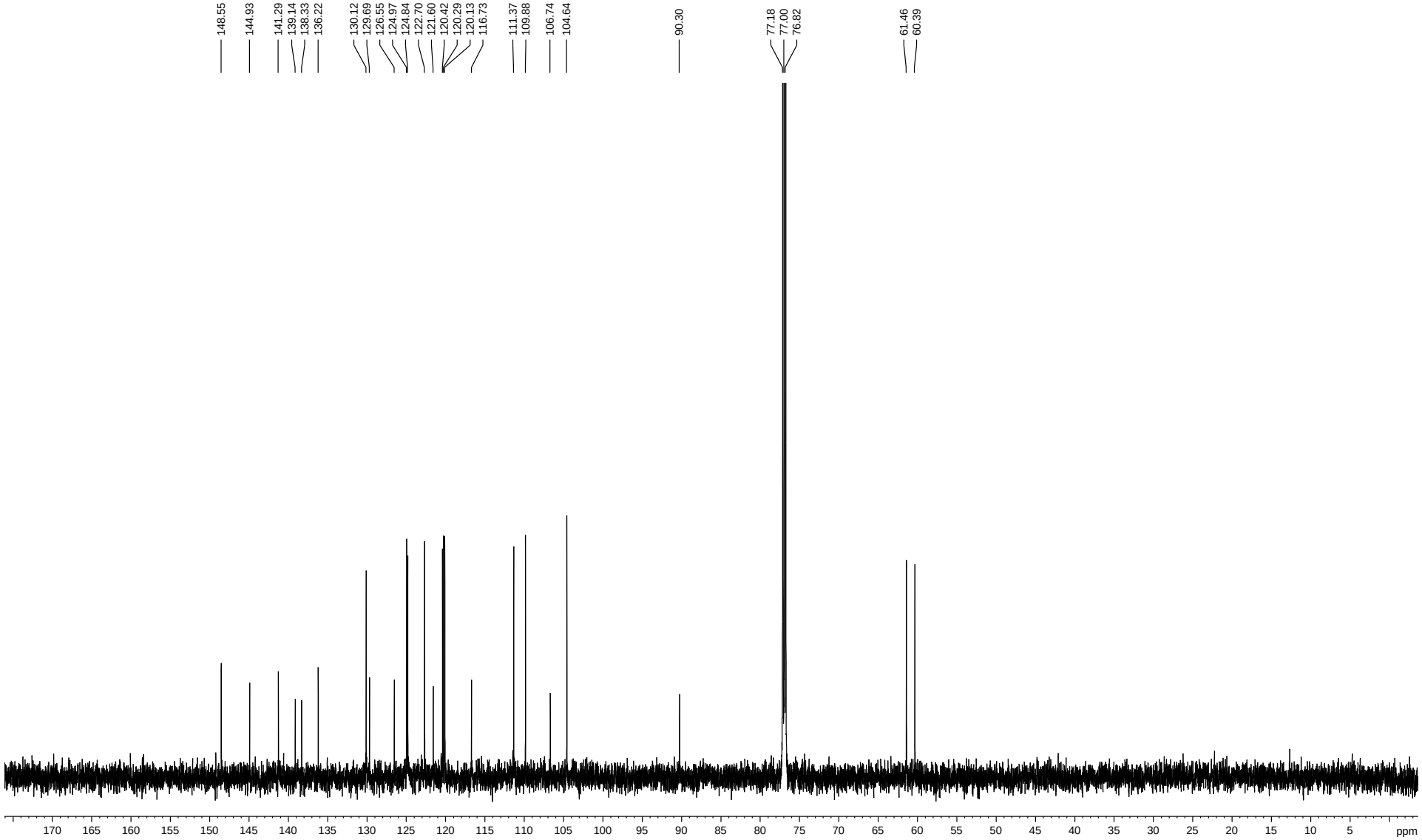

Figure S14. DEPT (176 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

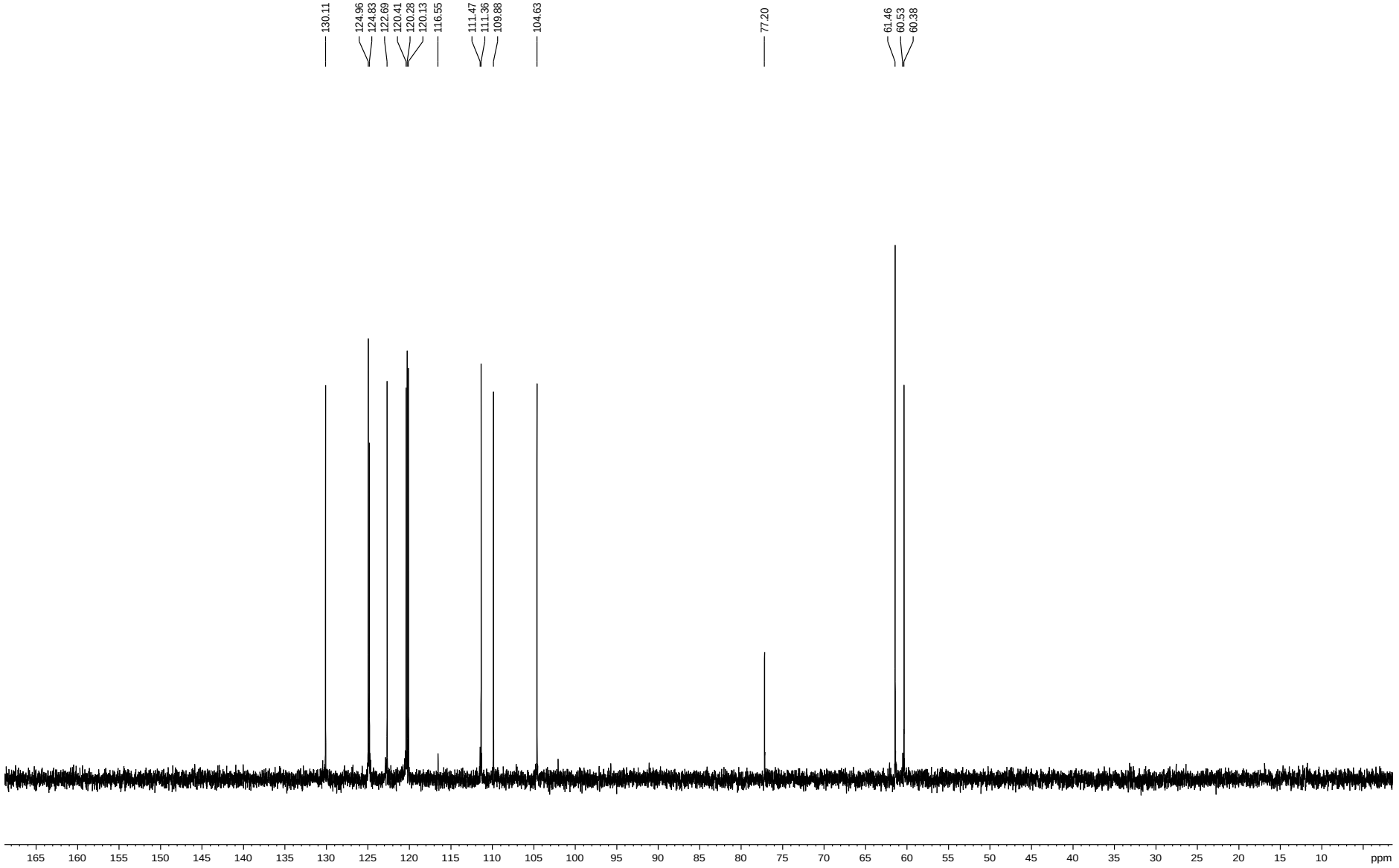

Figure S15. HSQC (176 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

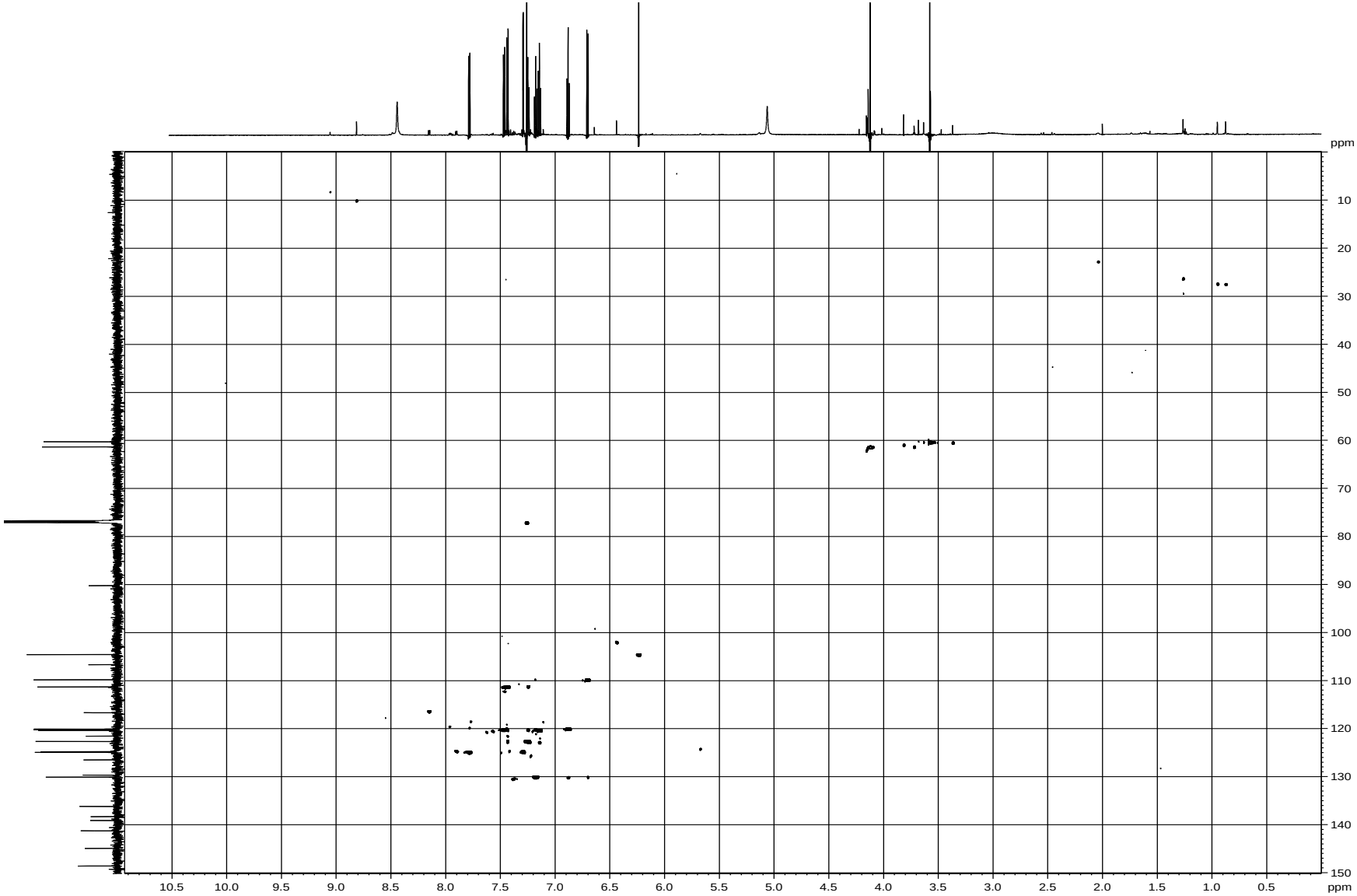

Figure S16. HMBC (176 MHz, $CDCl_3$) spectrum of Asterriquinone F (6)

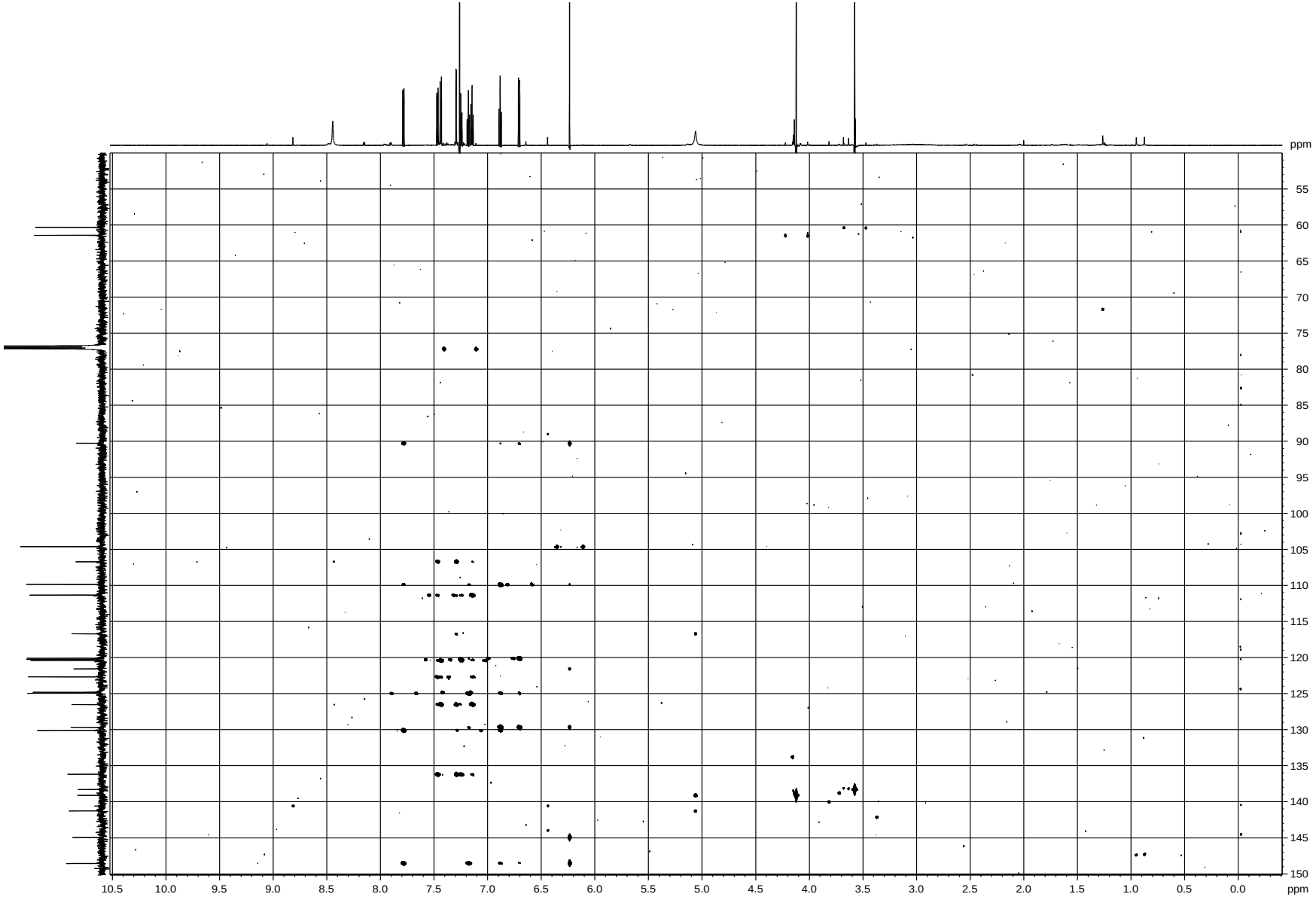

Figure S17. COSY (176 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

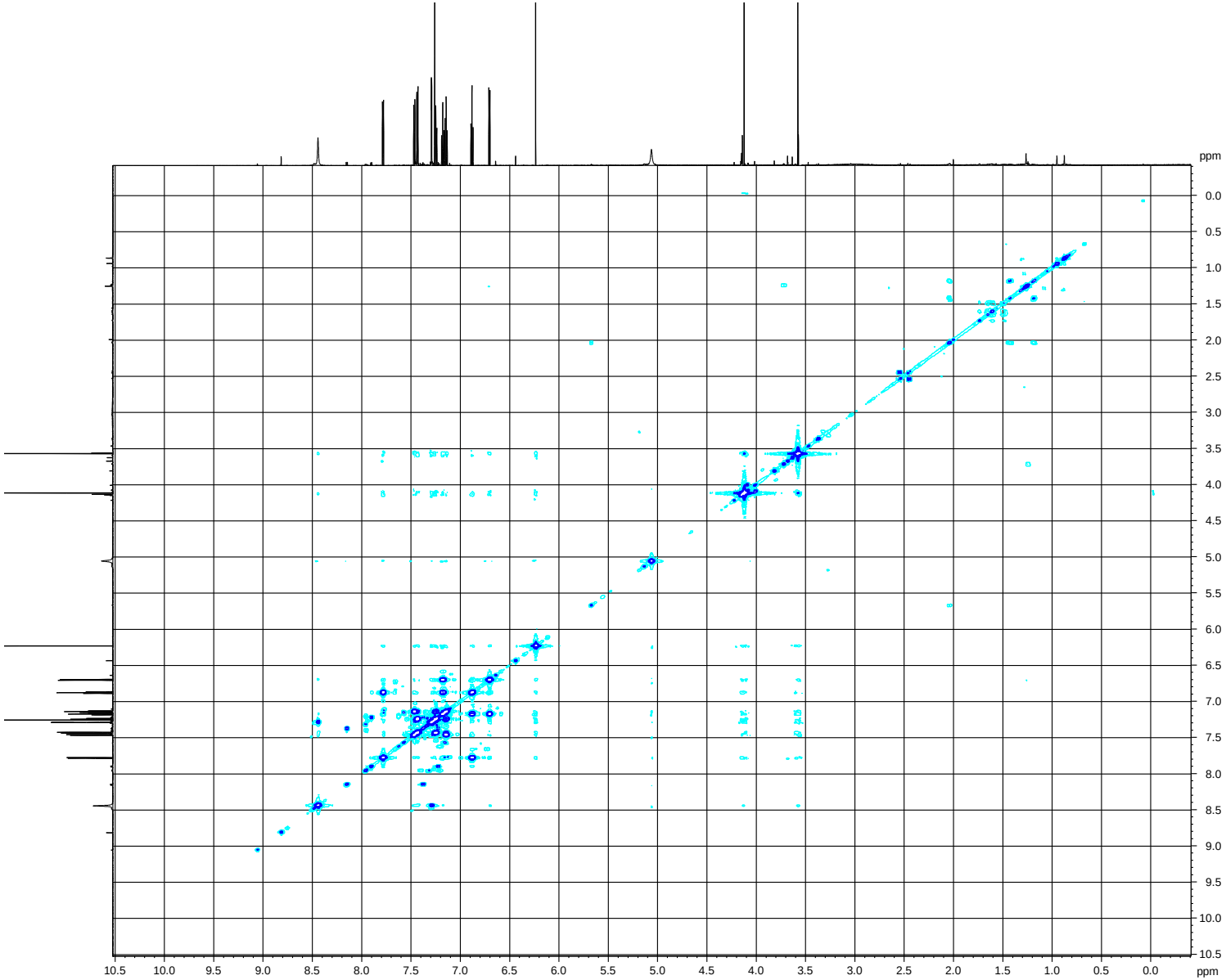

Figure S18. ROESY (176 MHz, $CDCl_3$) spectrum of asterriquinone F (6)

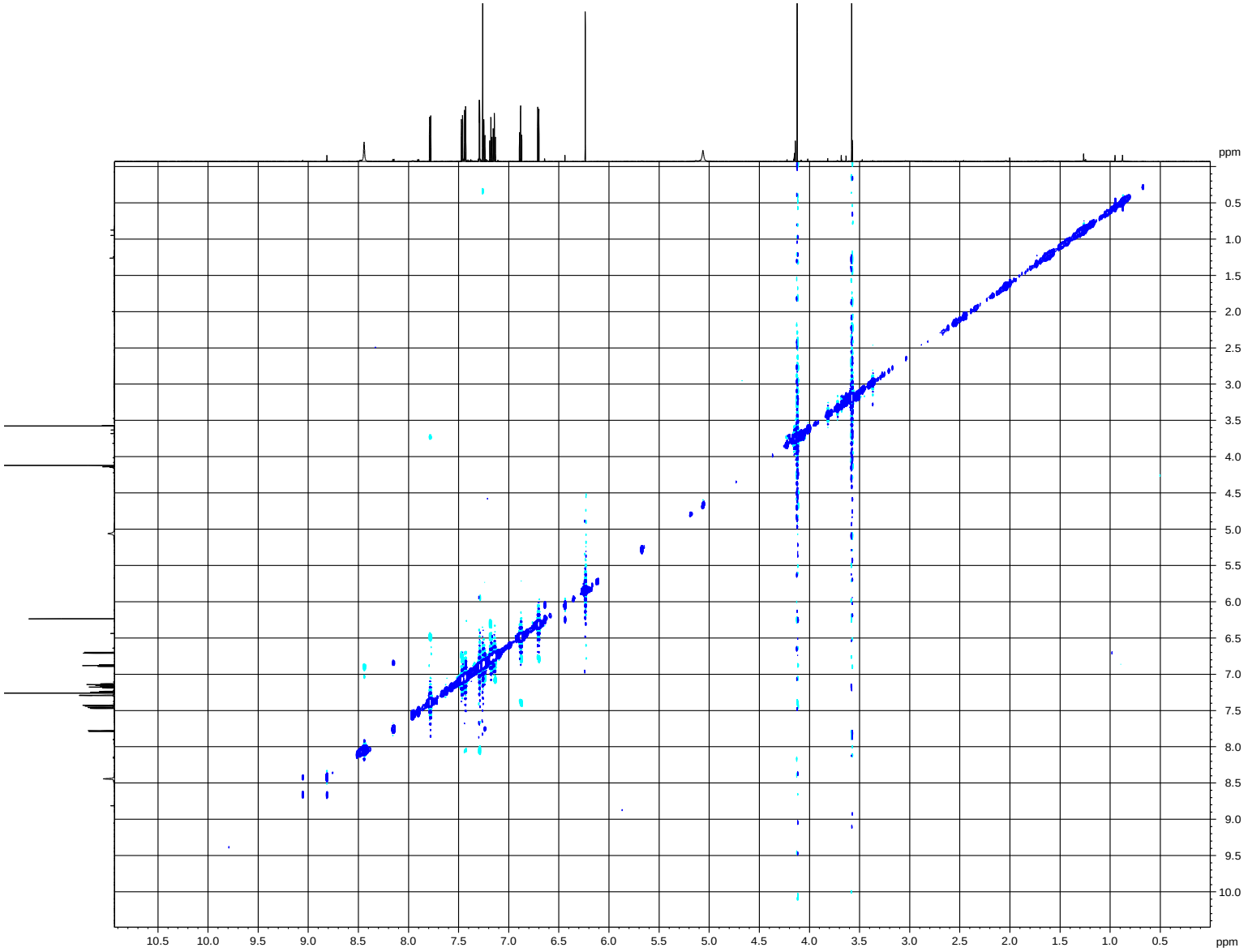

Figure S19. CD spectrum of asterriquinone F (6)

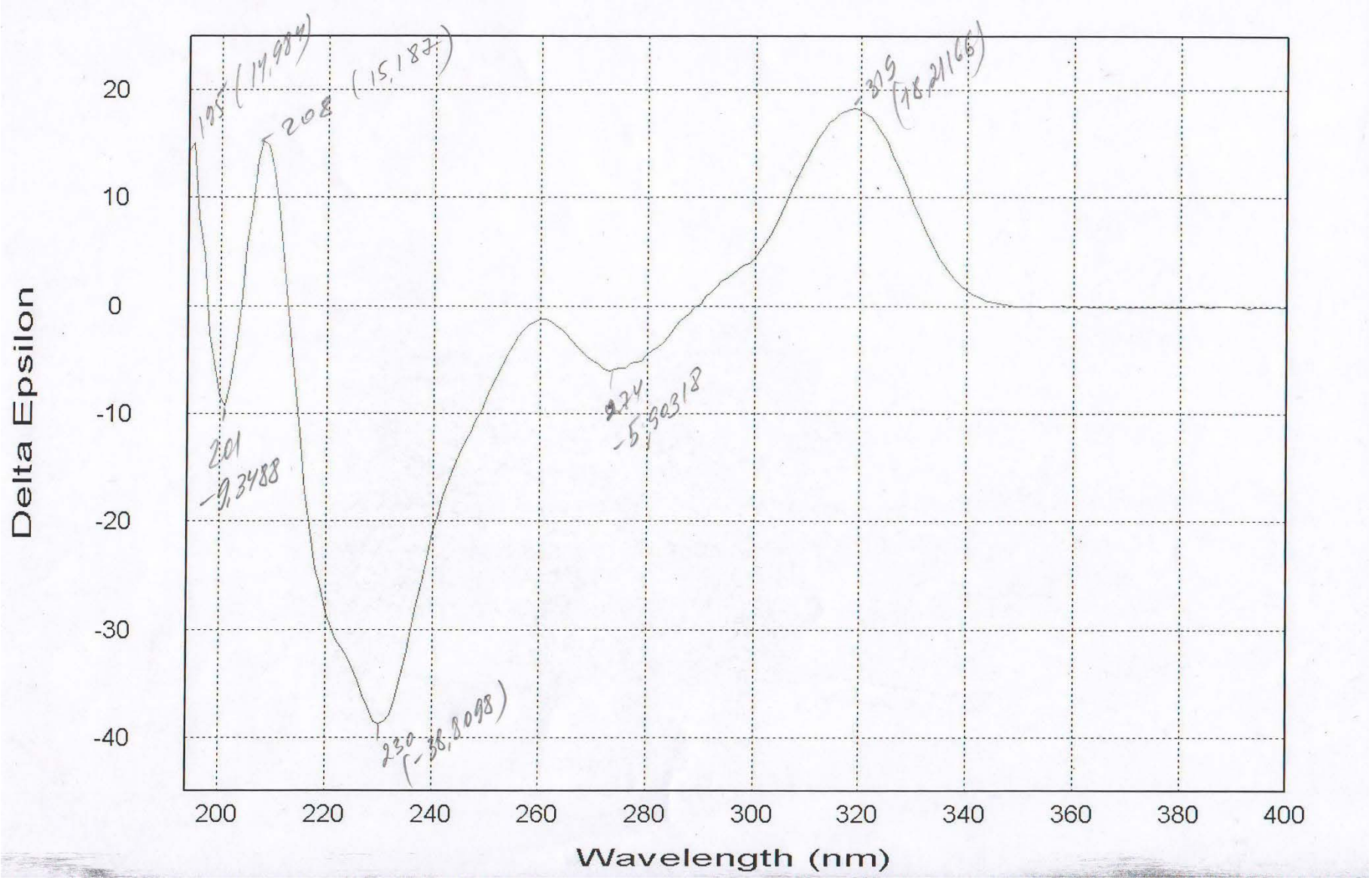

Figure S20. ^{1}H NMR (700 MHz, $CDCl_3$) spectrum of asterriquinone A3 (7)

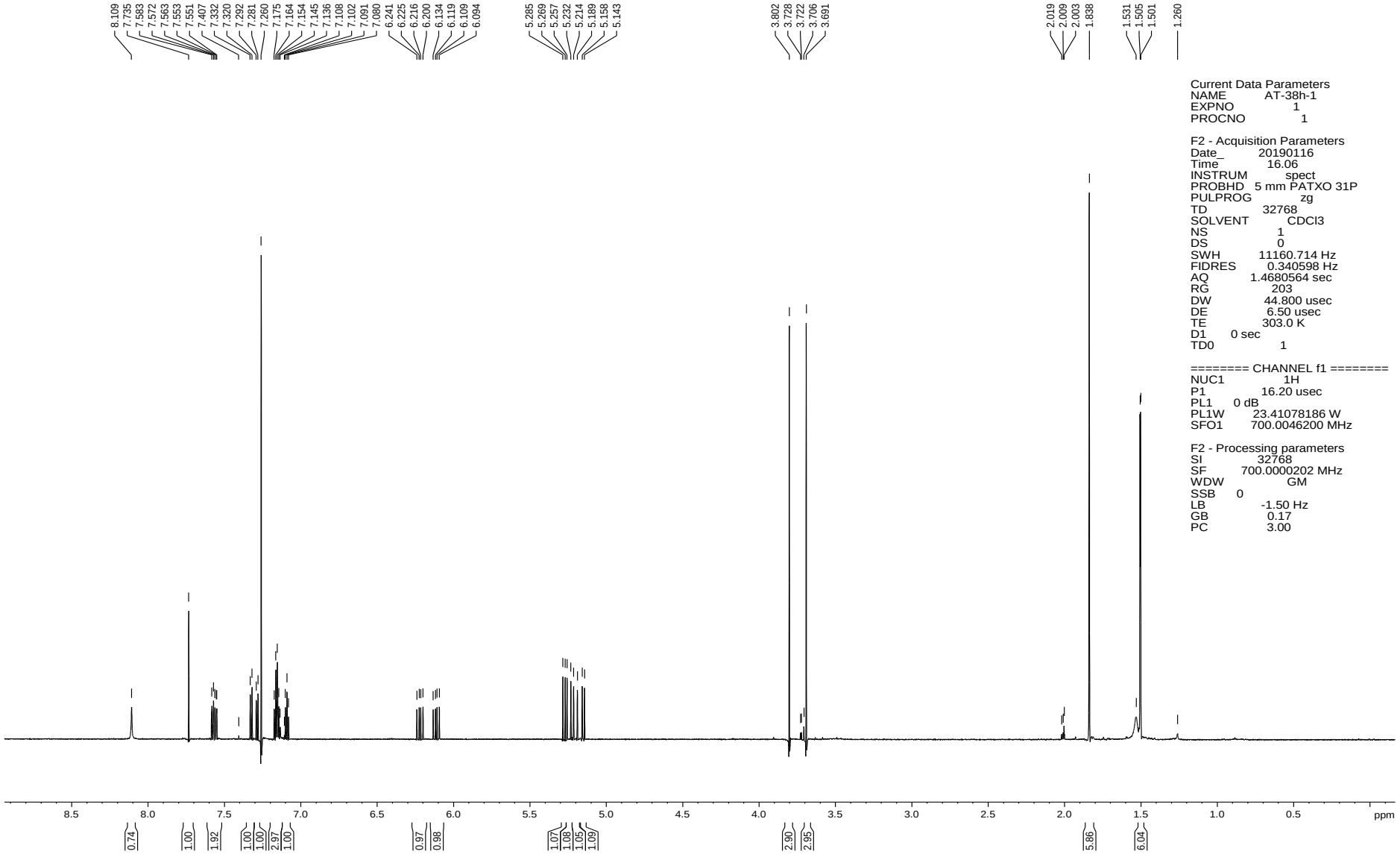

Figure S21. ^{13}C NMR (176 MHz, $CDCl_3$) spectrum of asterriquinone A3 (7)

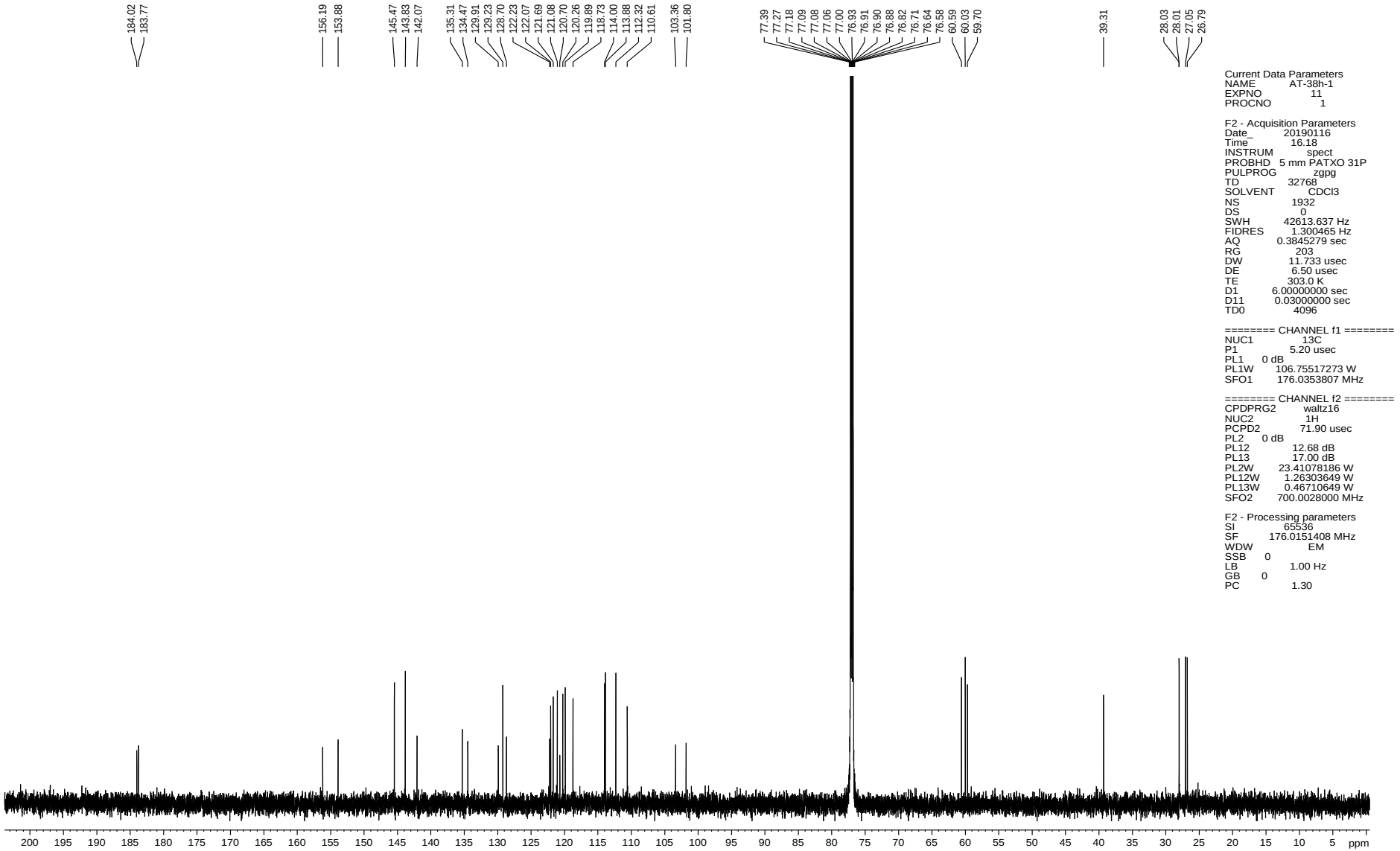

Figure S22. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of asterriquinone B4 (8)

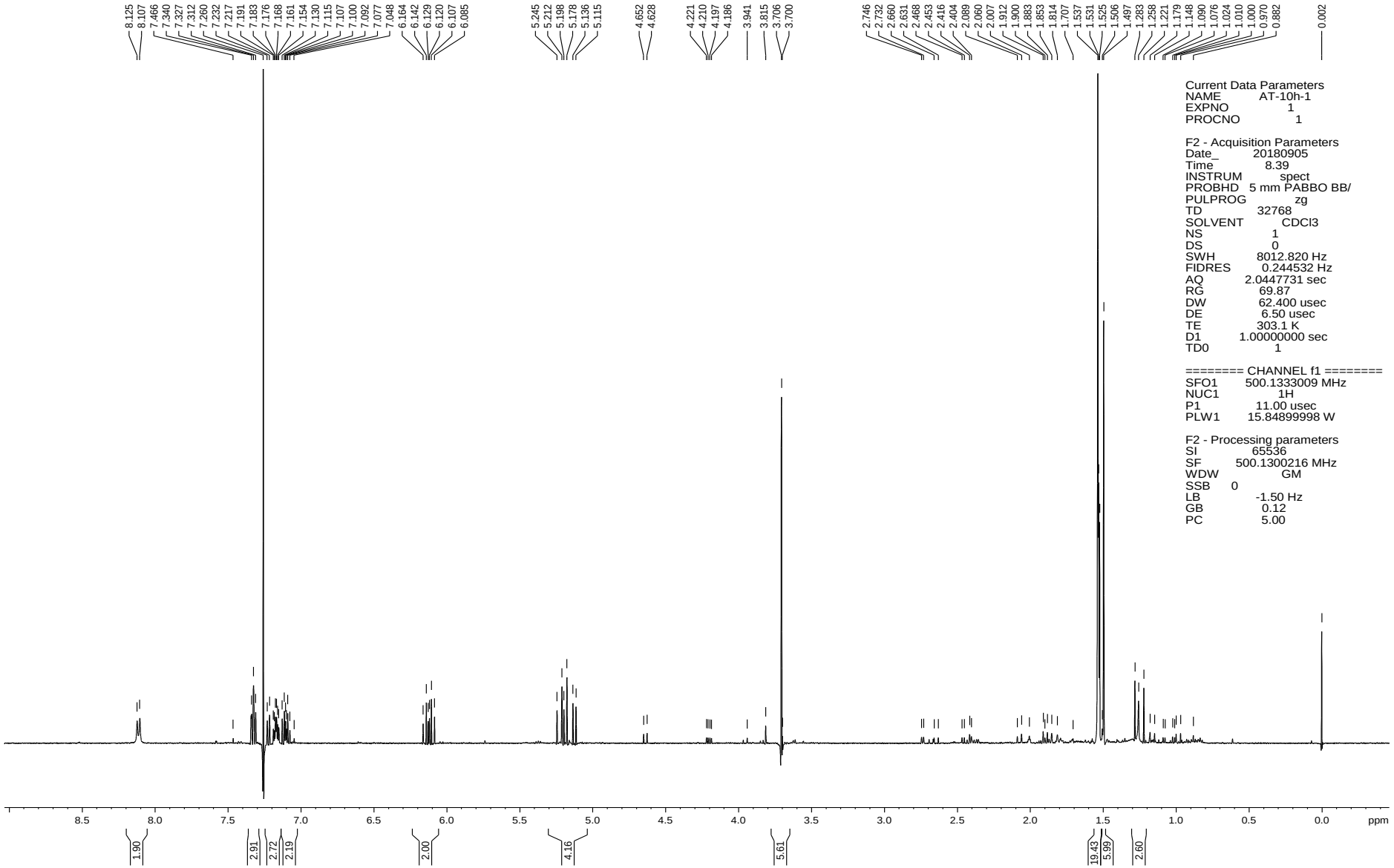

Figure S23. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of asterriquinone B4 (8)

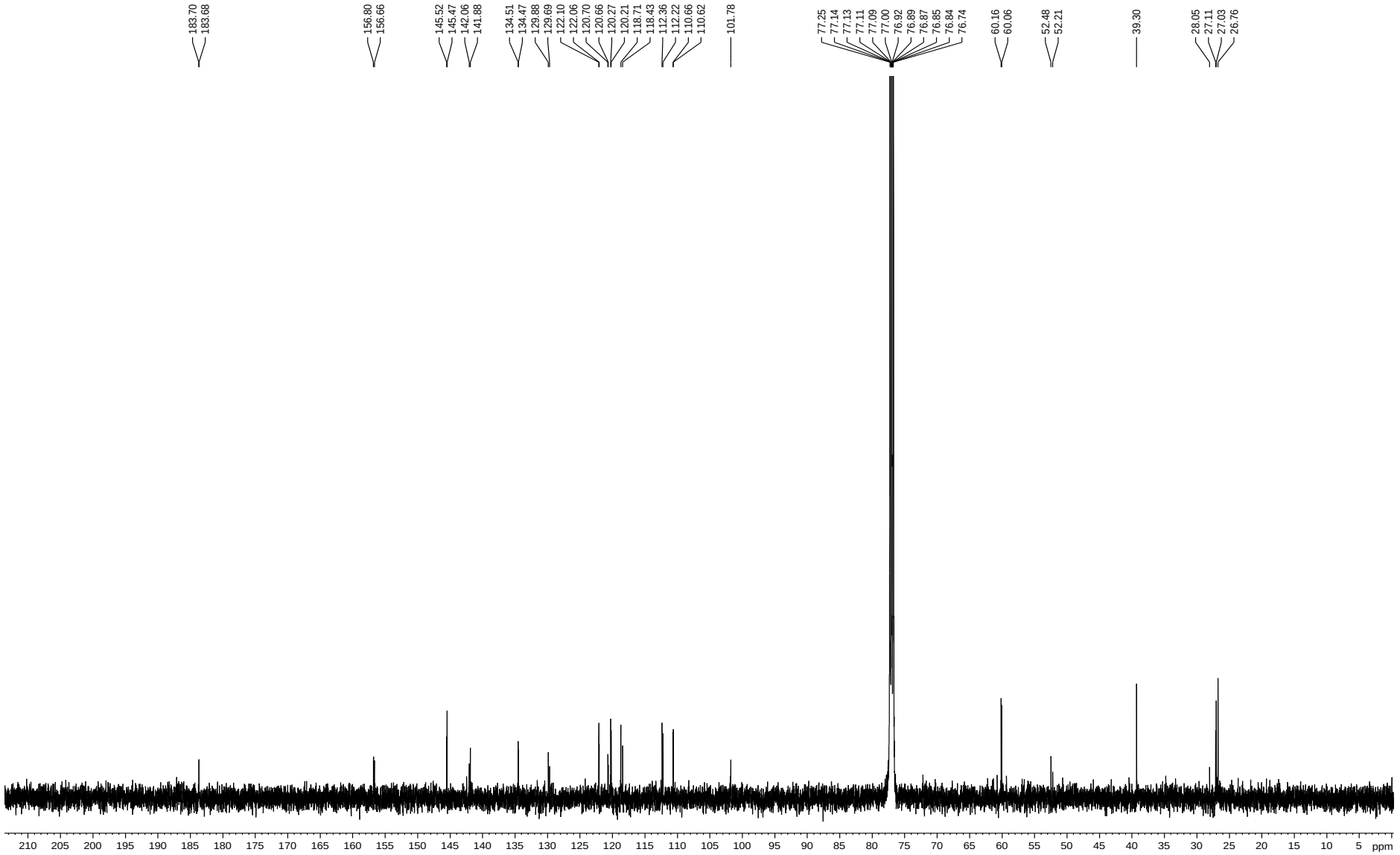

Figure S24. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of asterriquinone C1 (9)

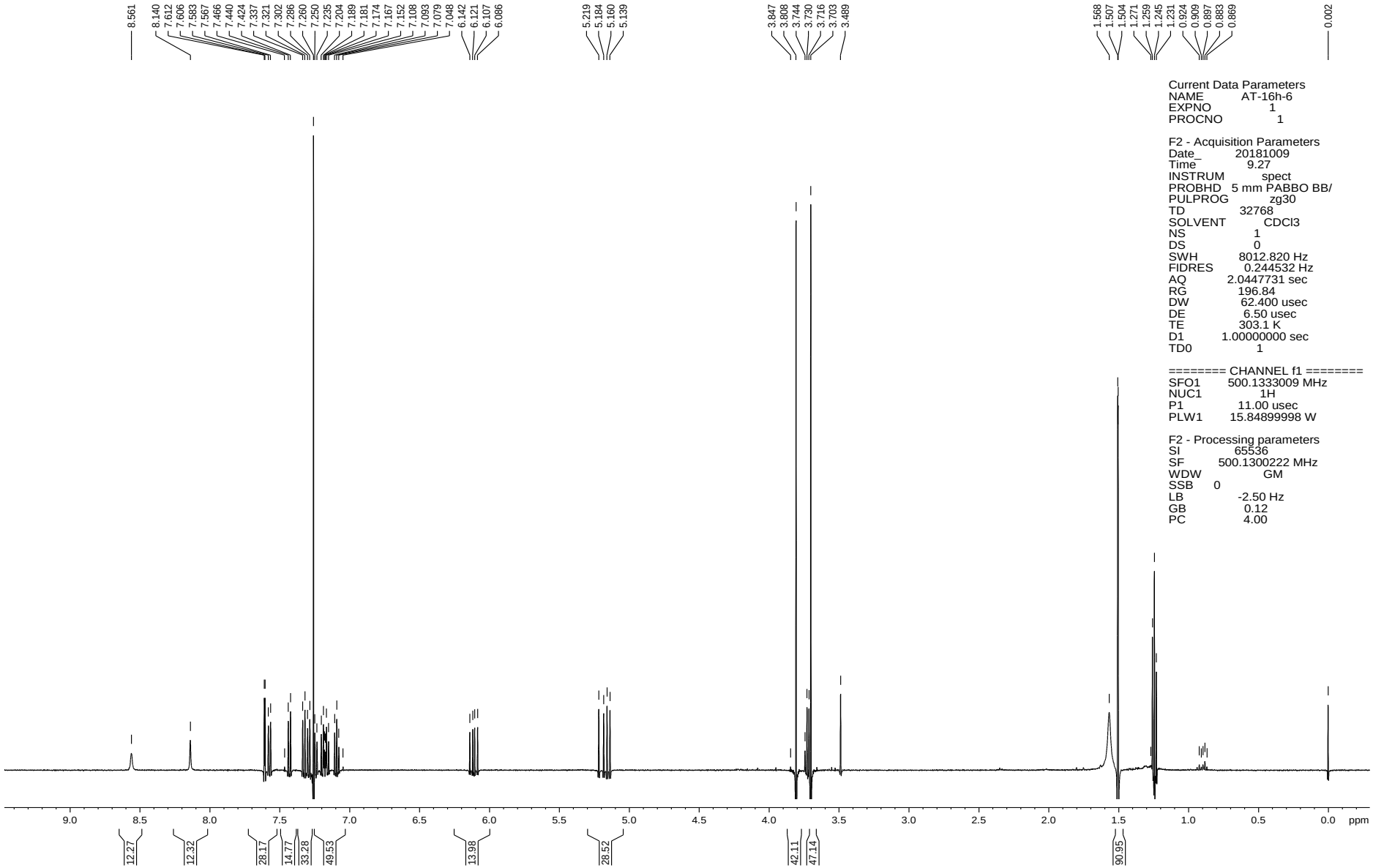

Figure S25. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of asterriquinone C1 (9)

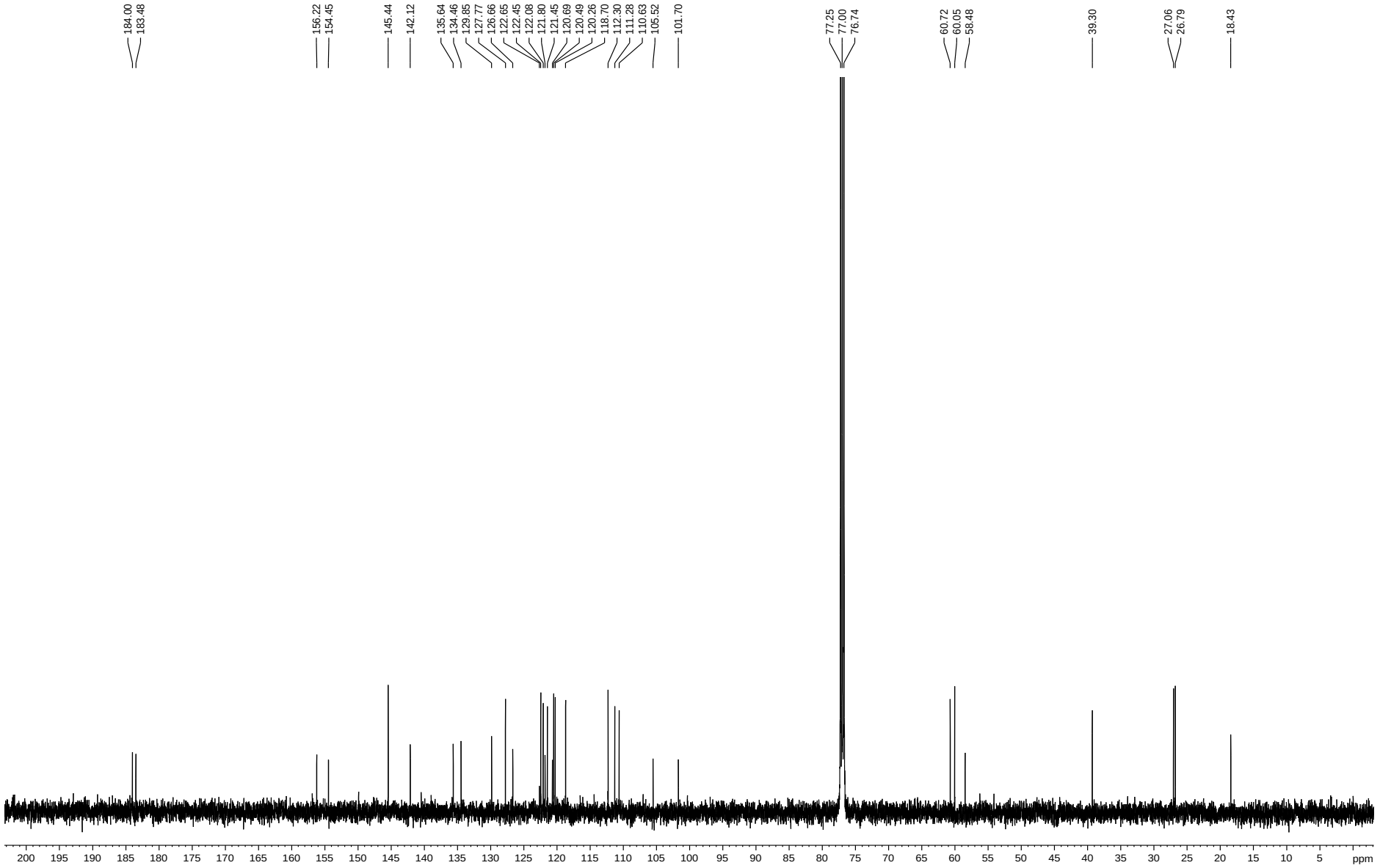

Figure S26. ^{1}H NMR (700 MHz, $CDCl_3$) spectrum of asterriquinone C2 (10)

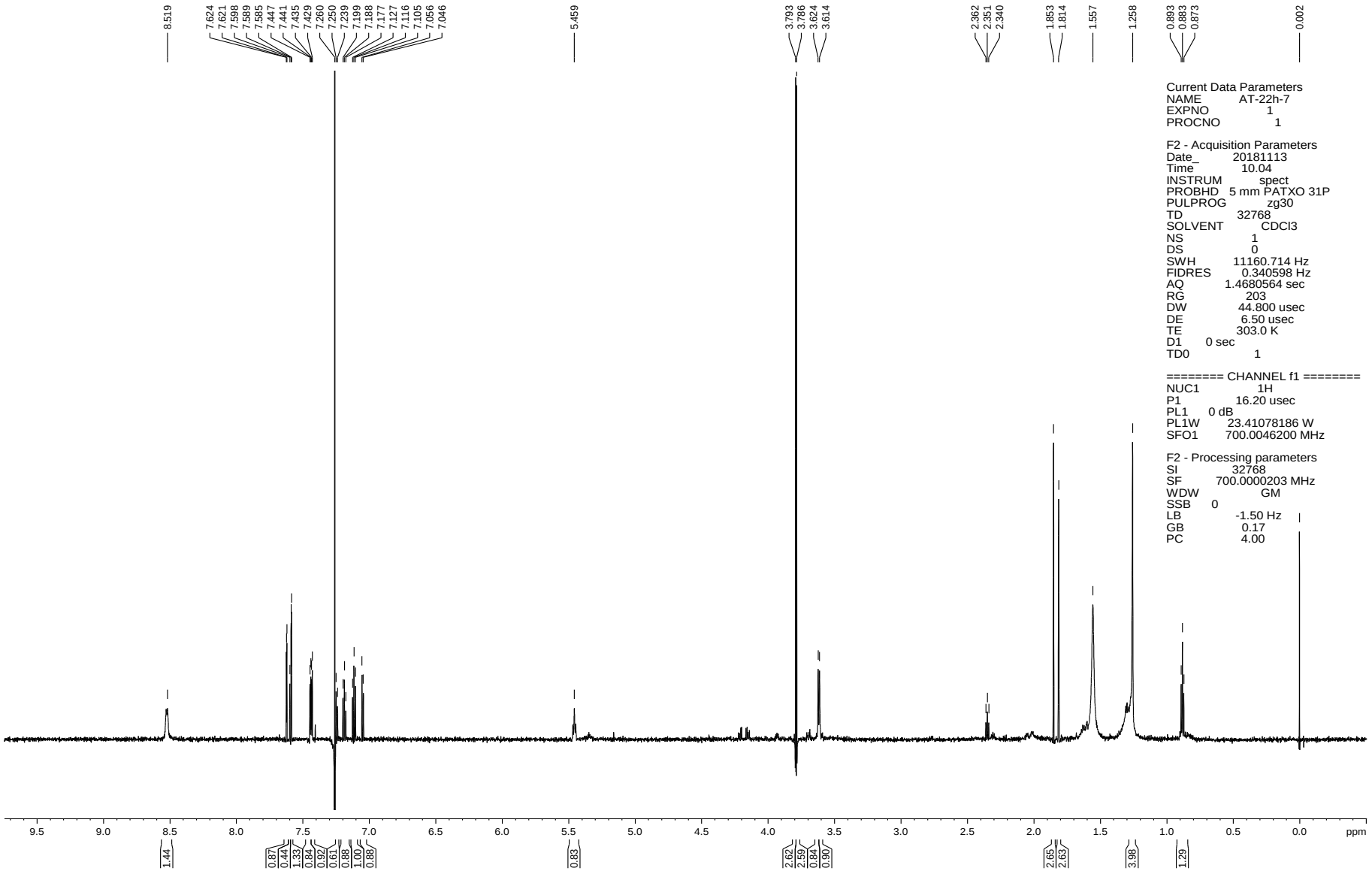

Figure S27. ^{13}C NMR (176 MHz, $CDCl_3$) spectrum of asterriquinone C2 (10)

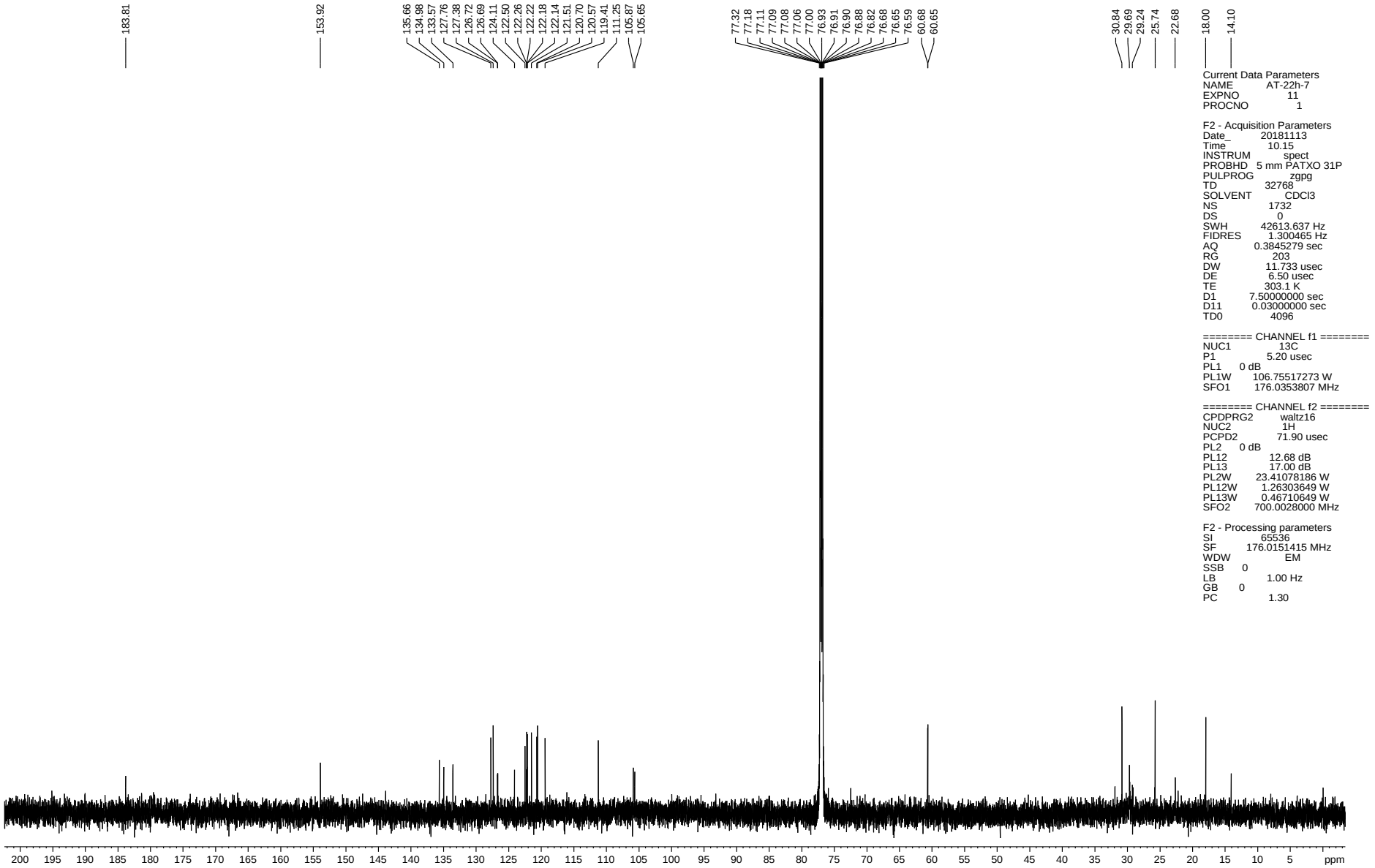

Figure S28. ^{1}H NMR (700 MHz, Acetone-d_6) spectrum of asterriquinone D (11)

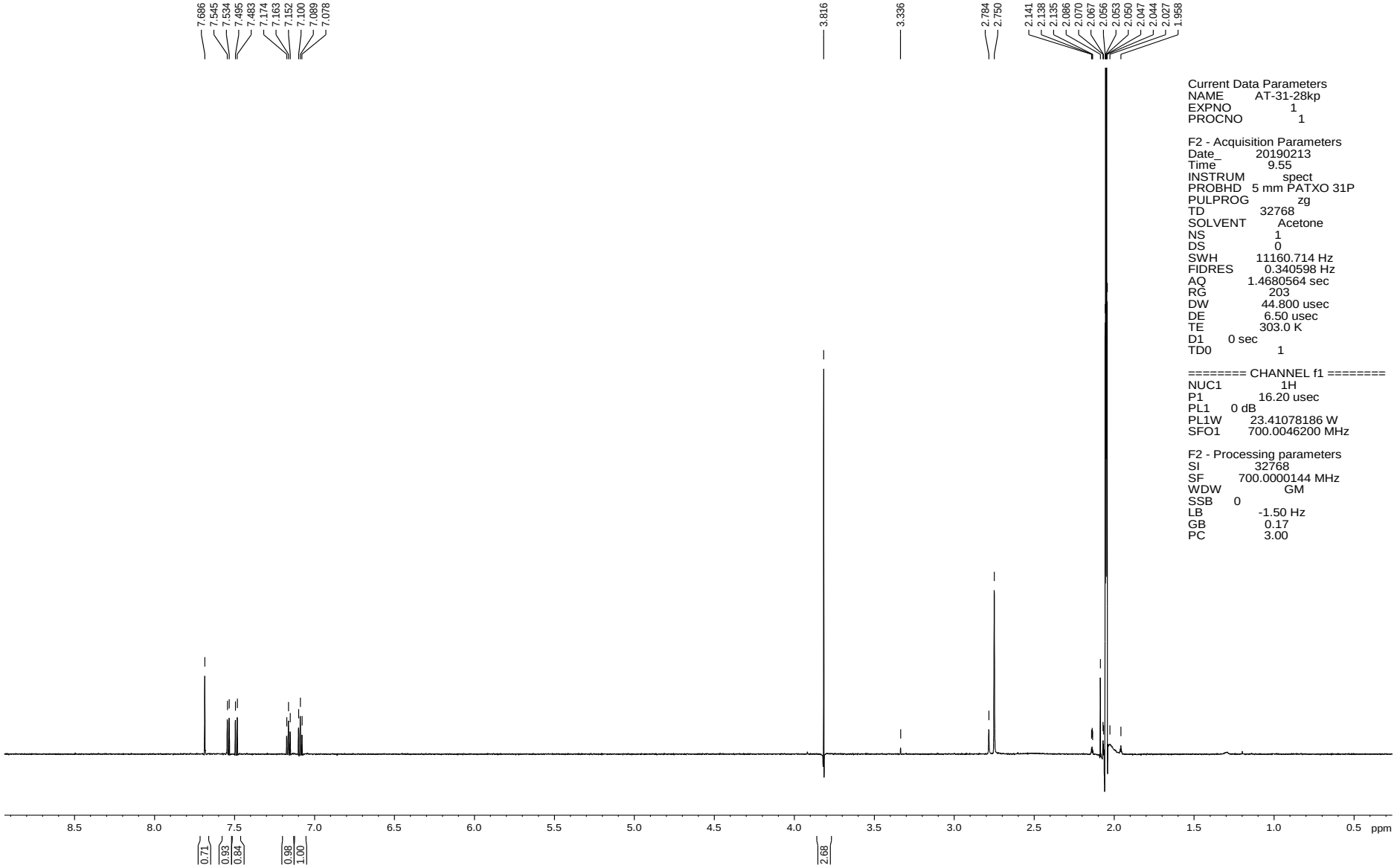

Figure S29. ^{13}C NMR (176 MHz, Acetone-d_6) spectrum of asterriquinone D (11)

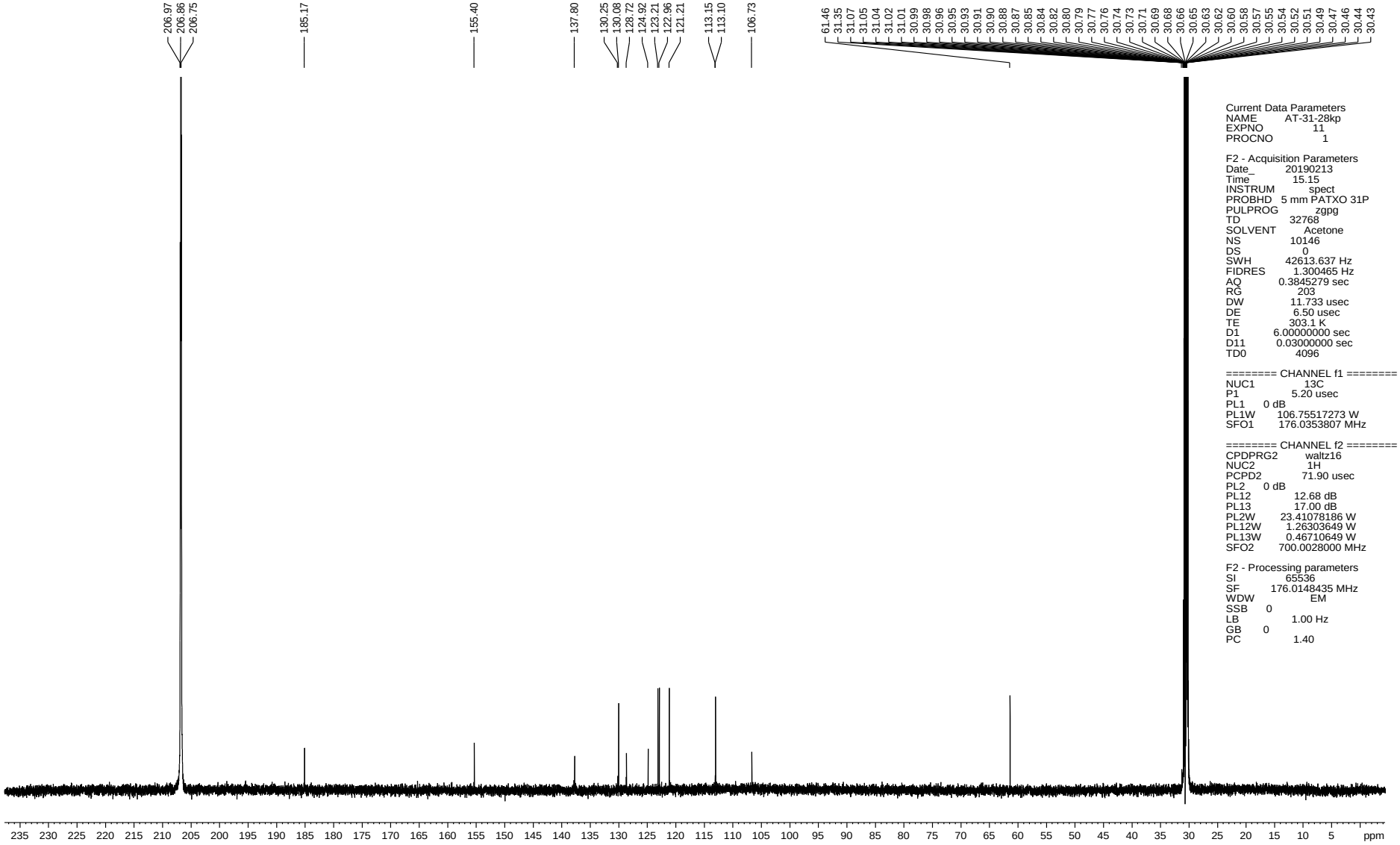

Figure S30. ^{1}H NMR (700 MHz, DMSO-d_6) spectrum of 1,2,5-trihydroxy-7-methyl-9,10-anthraquinone (13)

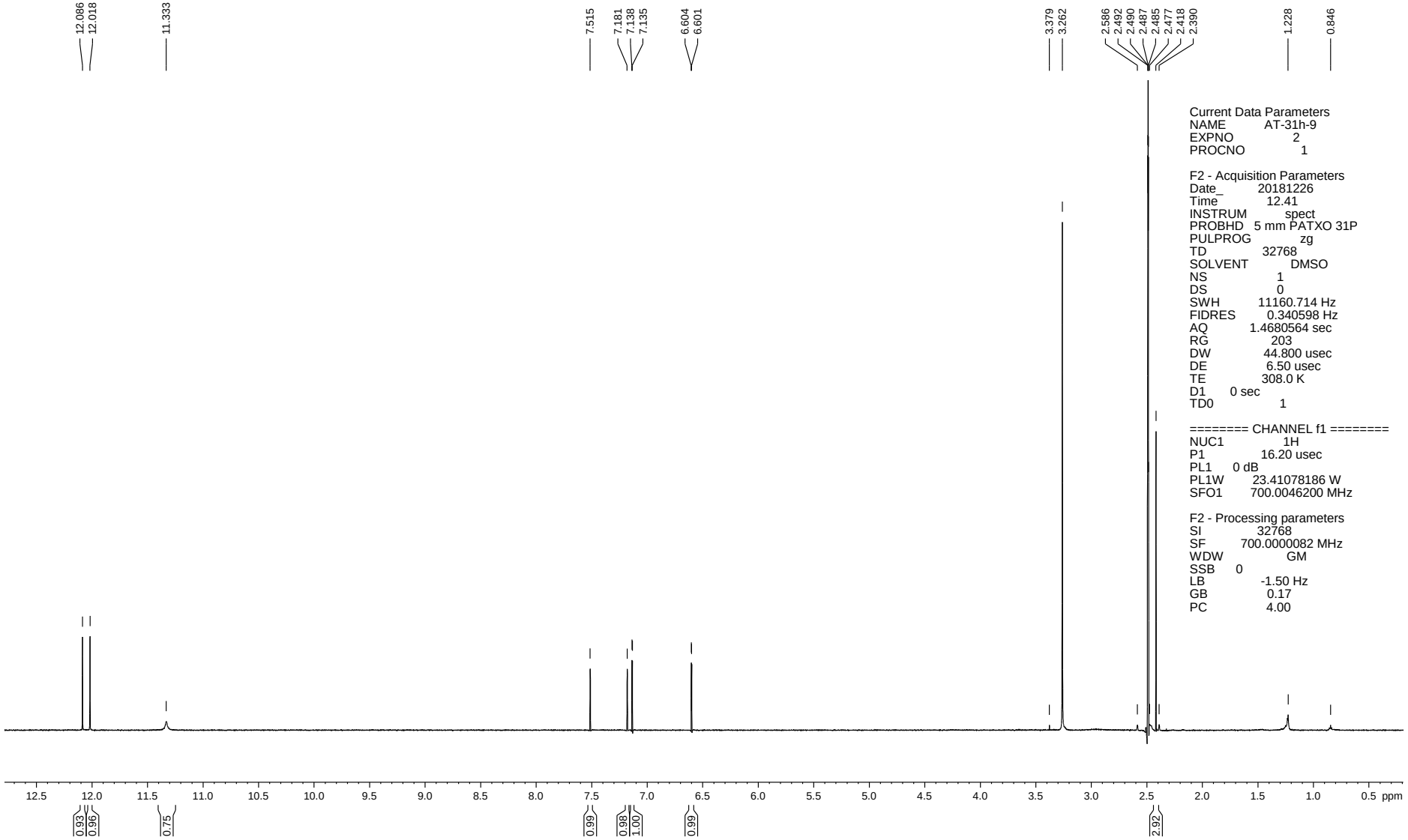

Figure S31. ^{13}C NMR (176 MHz, DMSO-d_6) spectrum of 1,2,5-trihydroxy-7-methyl-9,10-anthraquinone (13)

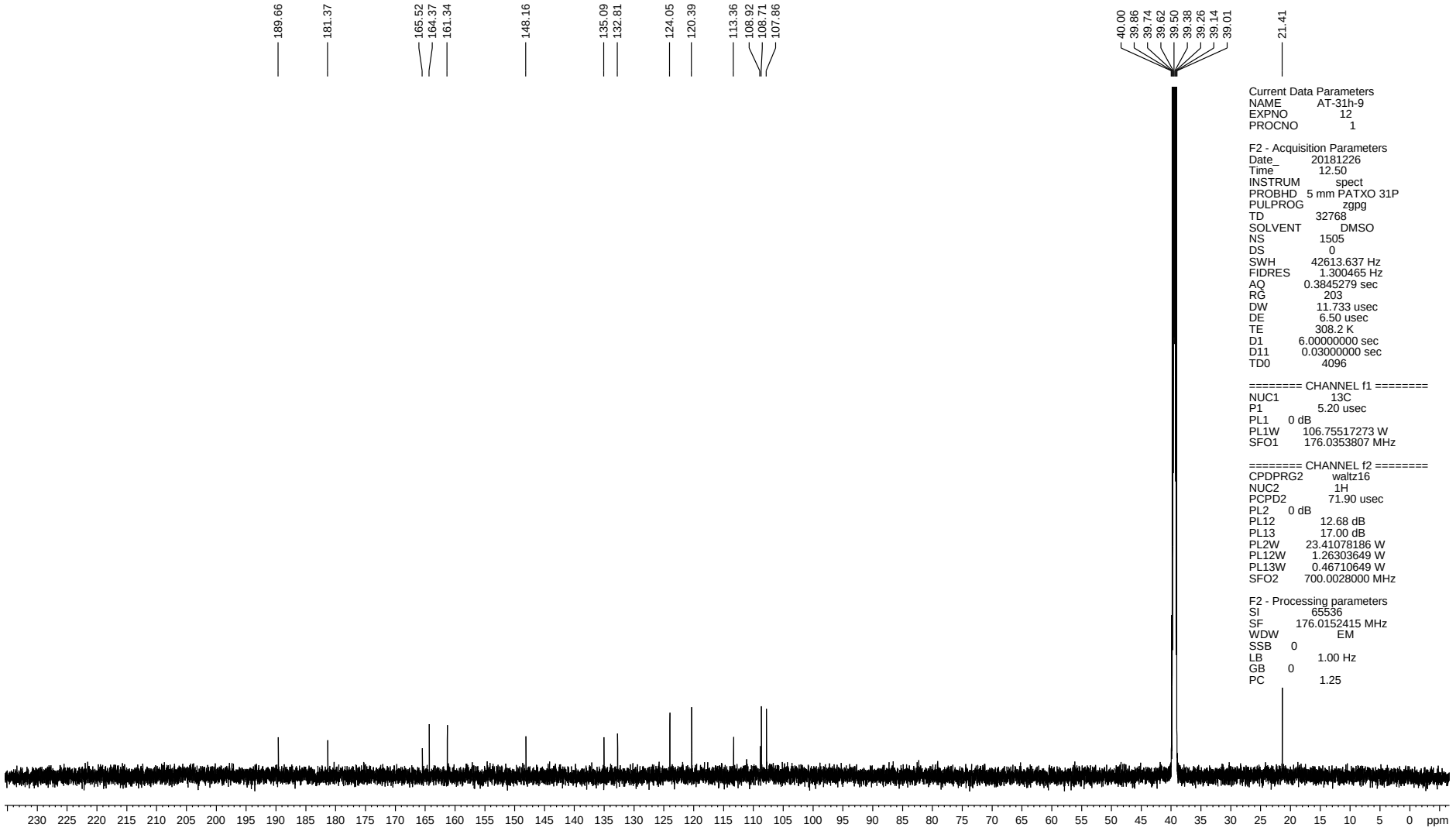

Figure S32. ^{1}H NMR (700 MHz, $CDCl_3$) spectrum of 4-hydroxy-3-(3-methylbut-2-enyl)benzaldehyde (14)

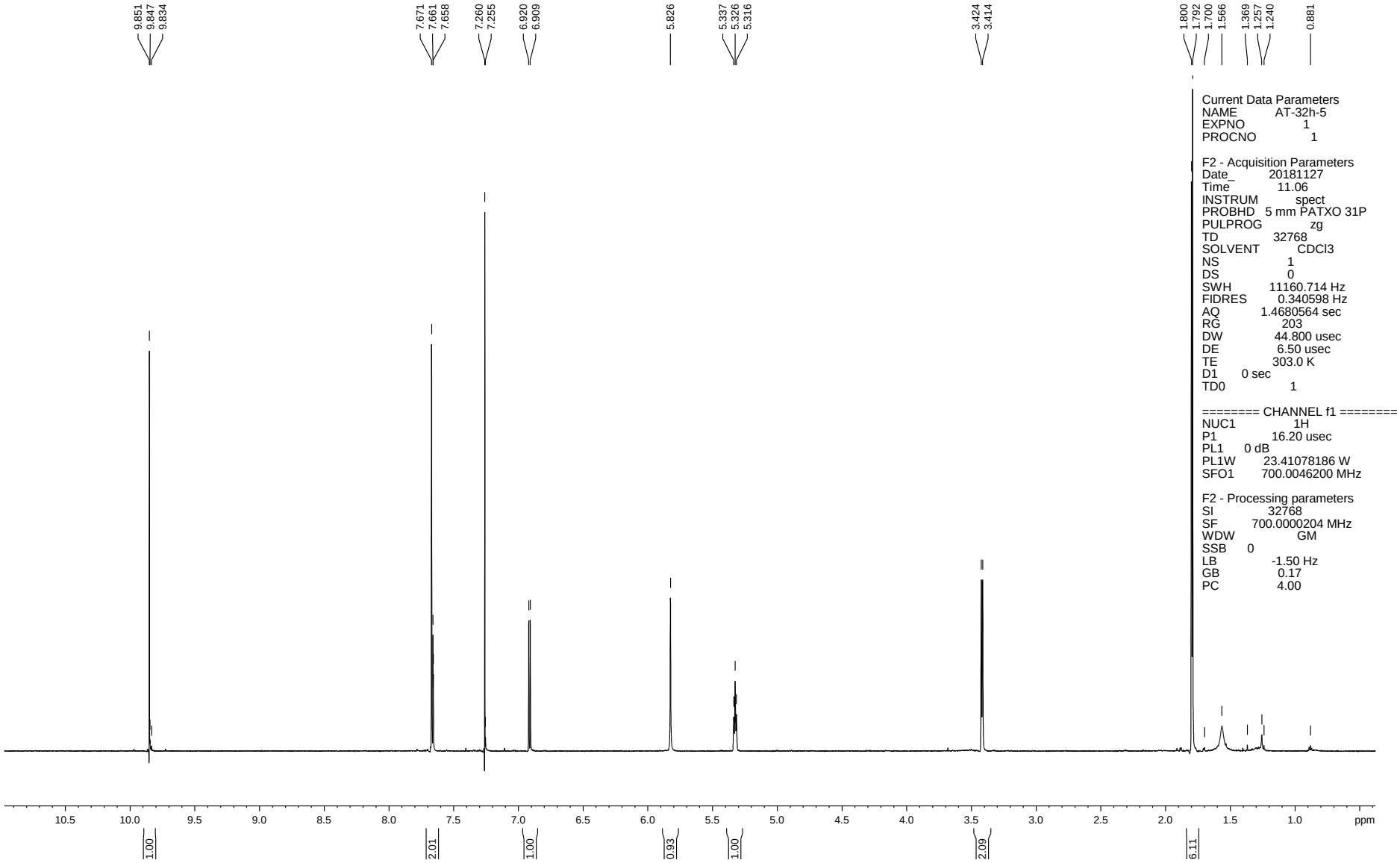

Figure S33. ^{13}C NMR (176 MHz, $CDCl_3$) spectrum of 4-hydroxy-3-(3-methylbut-2-enyl)benzaldehyde (14)

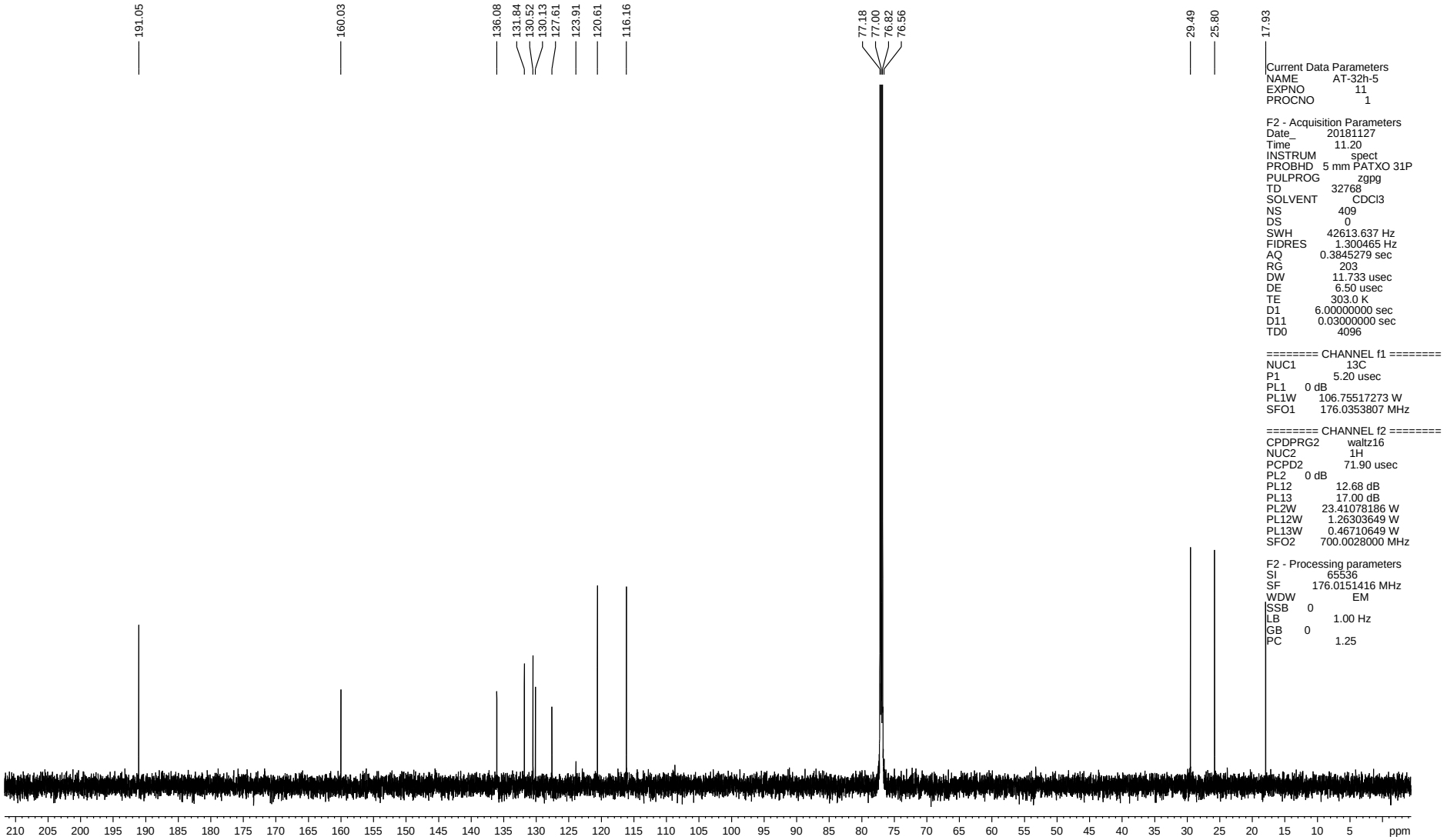

Figure S34. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of questin (12)

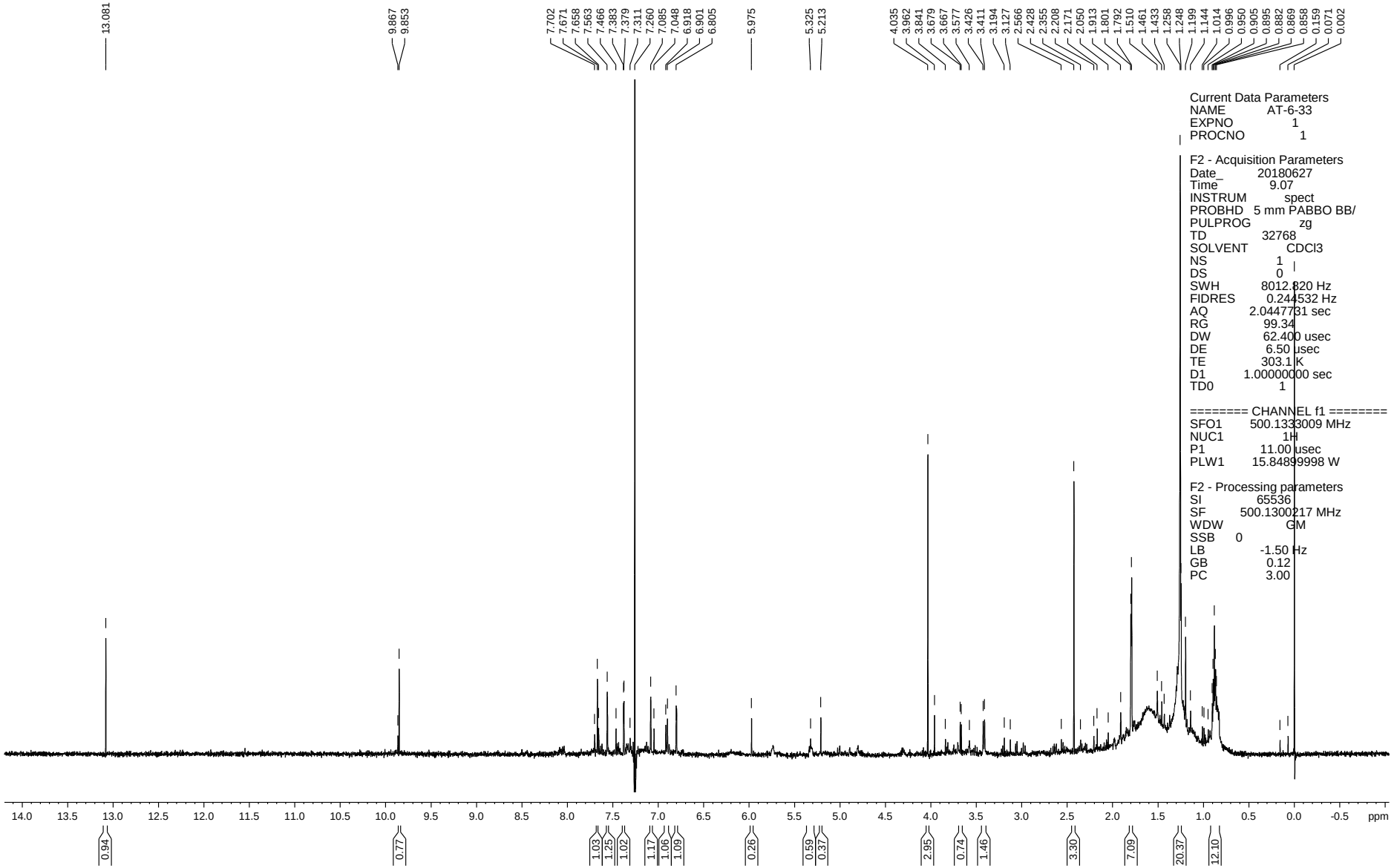

Figure S35. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of questin (12)

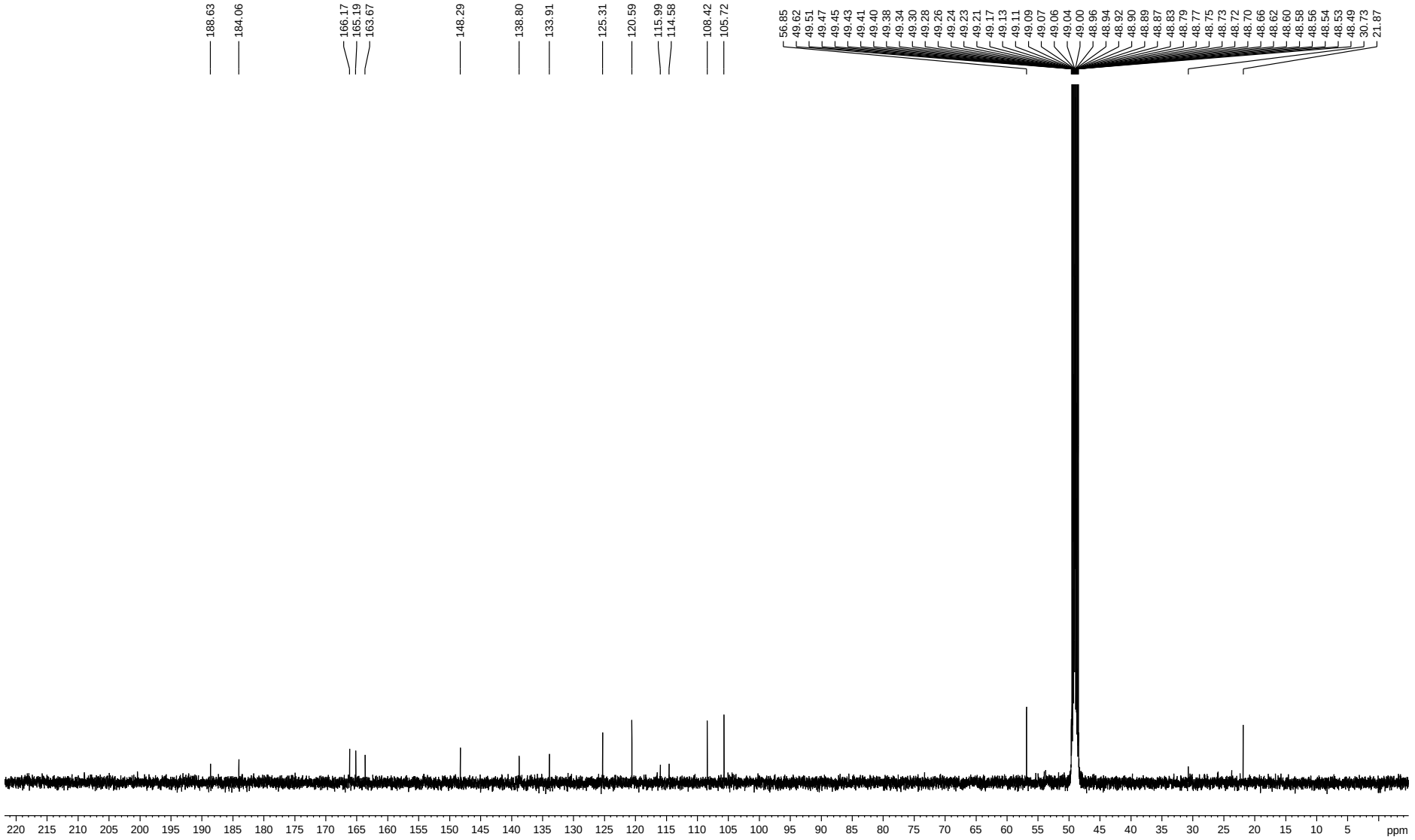

Figure S36. ^{1}H NMR (500 MHz, MeOD-d_3) spectrum of quadrone (15)

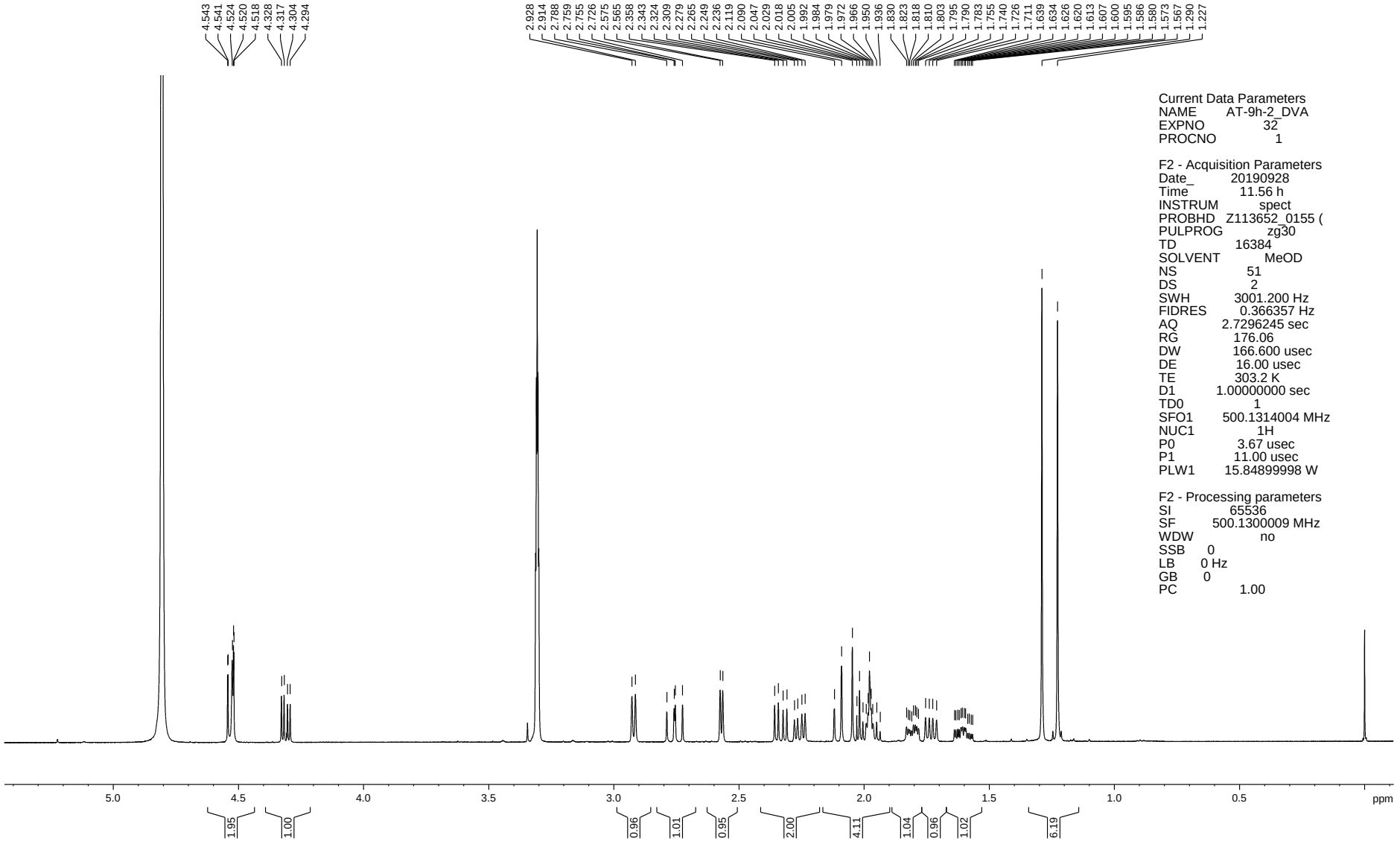

Figure S37. ^{13}C NMR (125 MHz, MeOD-d_3) spectrum of quadrone (15)

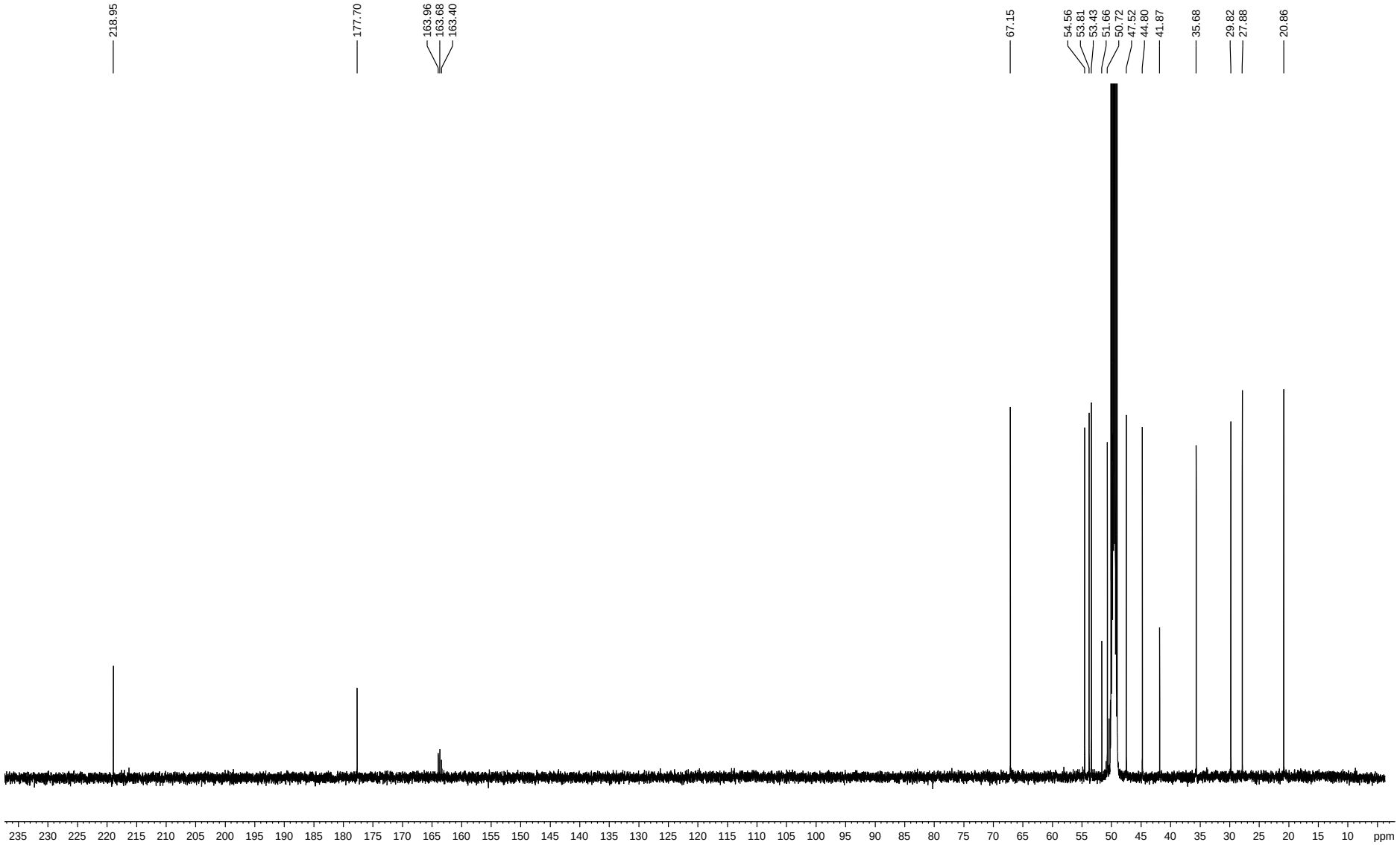

Figure S38. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of 6β-hydroxyergosta-4,7,22-trien-3-on (16)

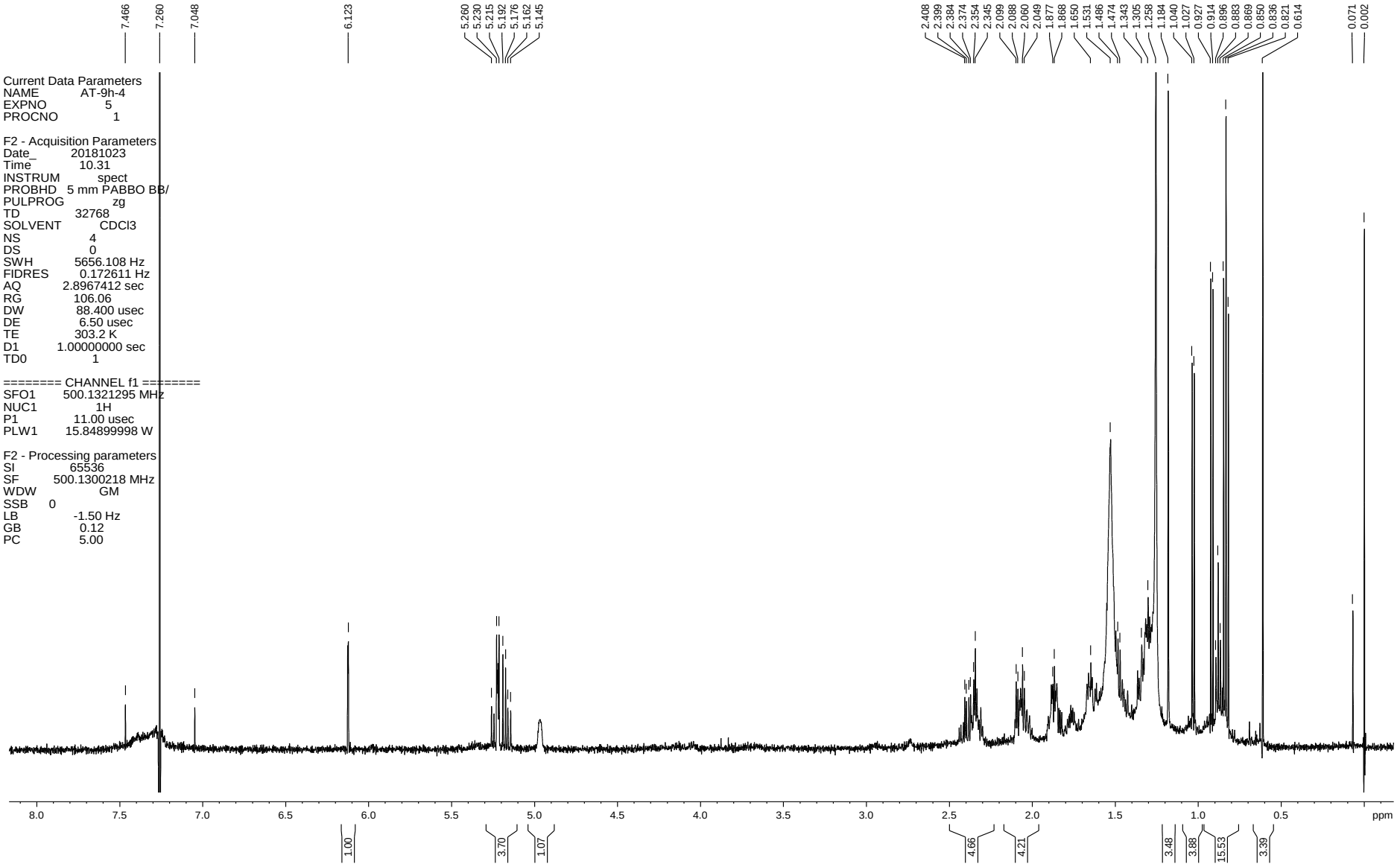

Figure S39. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of 6β-hydroxyergosta-4,7,22-trien-3-on (16)