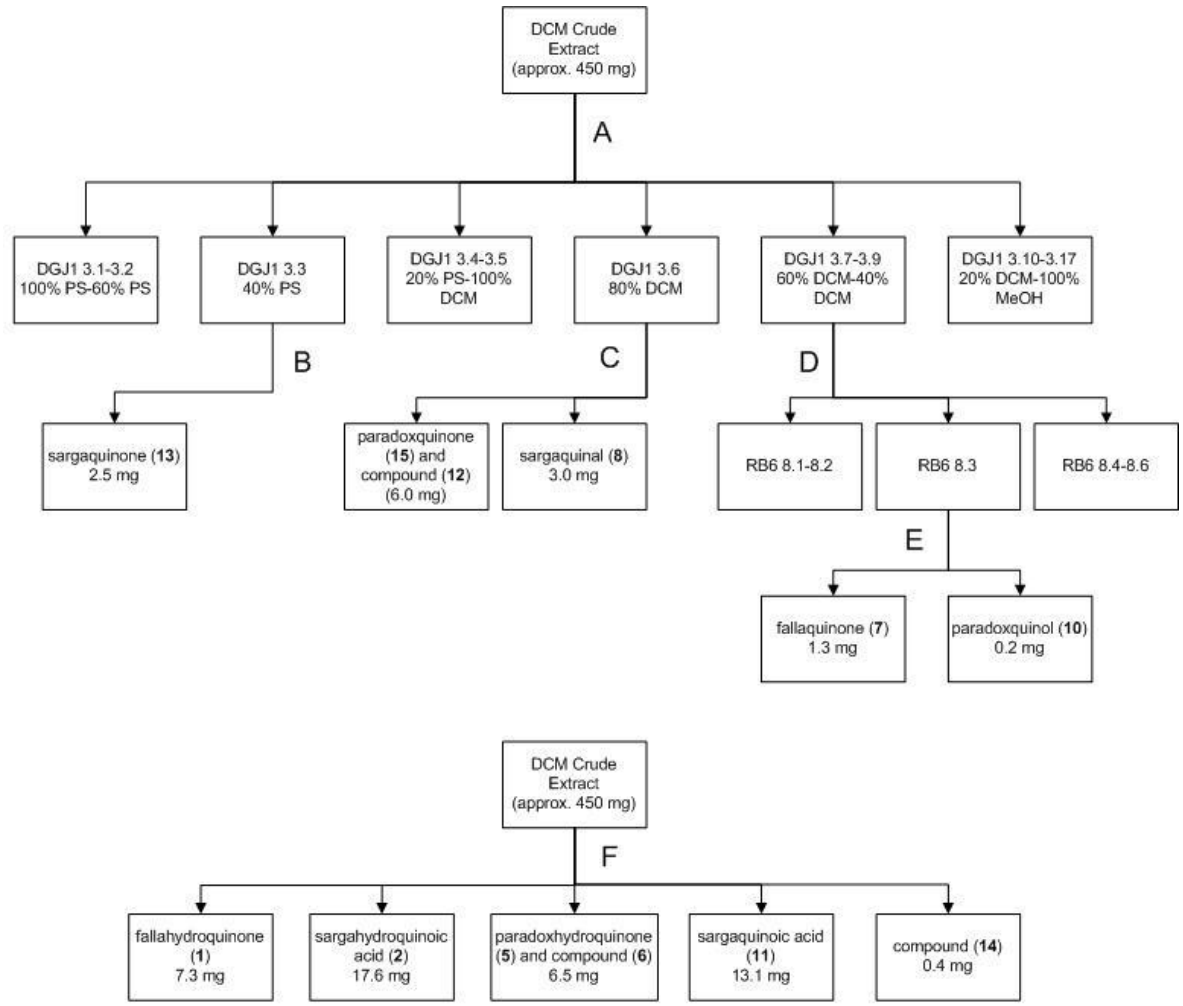
Supplementary Information



A – Flash silica gel column (20% stepwise elution from PS → DCM → EtOAc → MeOH)
B – RP-HPLC (100% CH_3CN)
C – RP-HPLC (95% CH_3CN/H_2O)
D – fractions combined, Sephadex LH-20 column (100% MeOH)
E – RP-HPLC (85% CH_3CN/H_2O)
F – RP-HPLC (90% CH_3CN/H_2O)

PS – petroleum spirits (60-80°C)
DCM – dichloromethane
EtOAc -ethyl acetate
MeOH - methanol

Figure S1. Bioassay-guided isolation scheme for *S. paradoxum*.

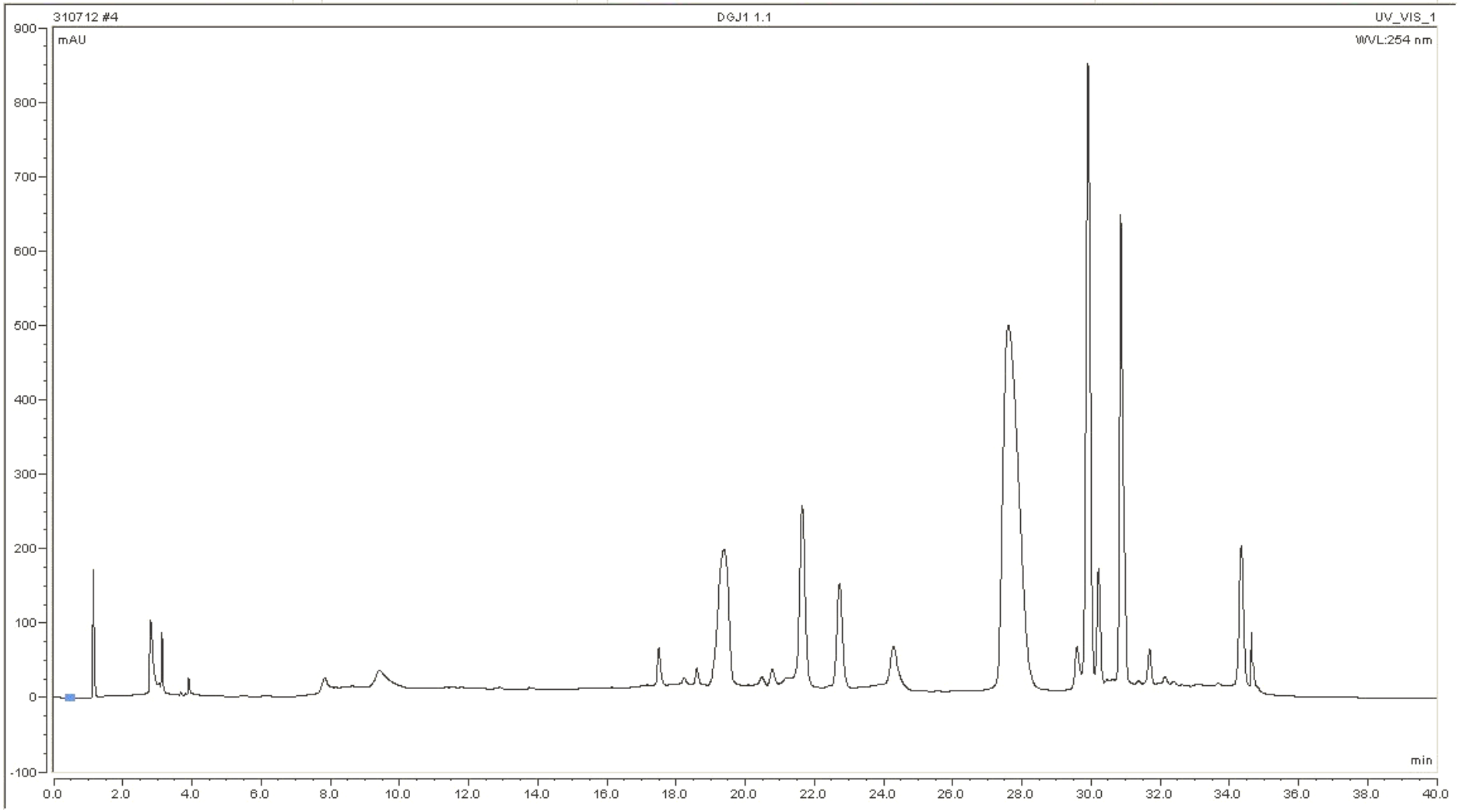


Figure S2. Analytical HPLC chromatogram of DCM crude extract of *S. paradoxum*.

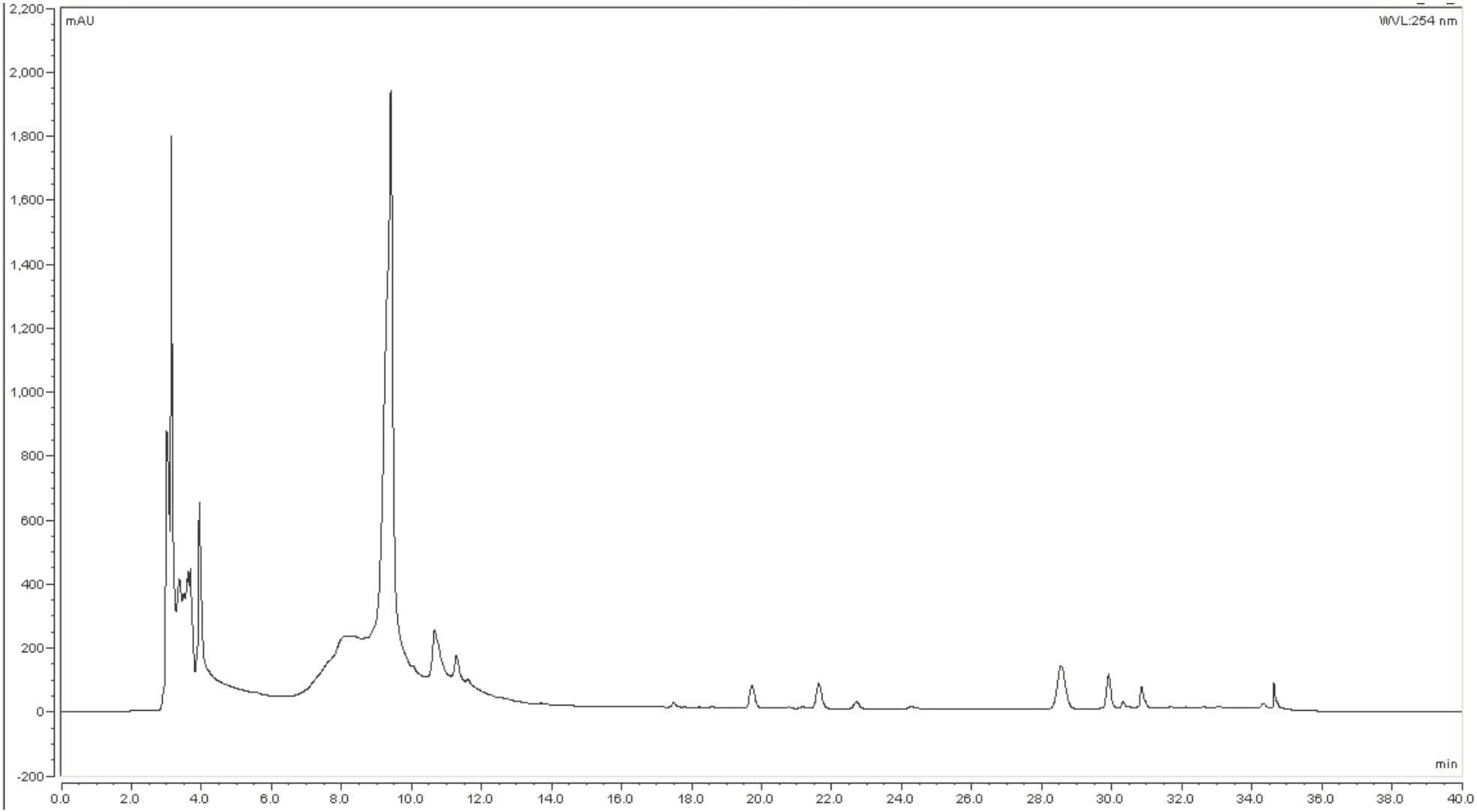


Figure S3. Analytical HPLC chromatogram of MeOH crude extract of *S. paradoxum*.

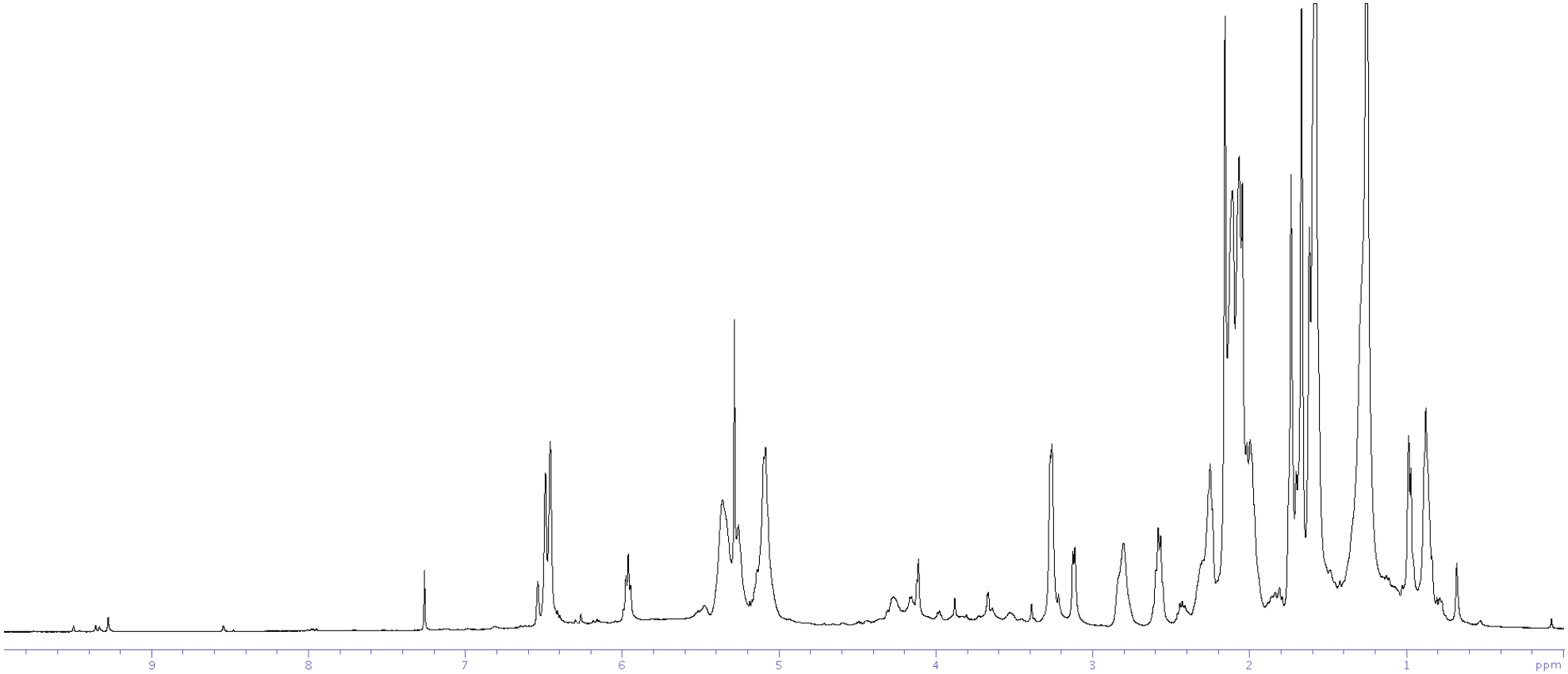


Figure S4. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of DCM crude extract of *S. paradoxum*.

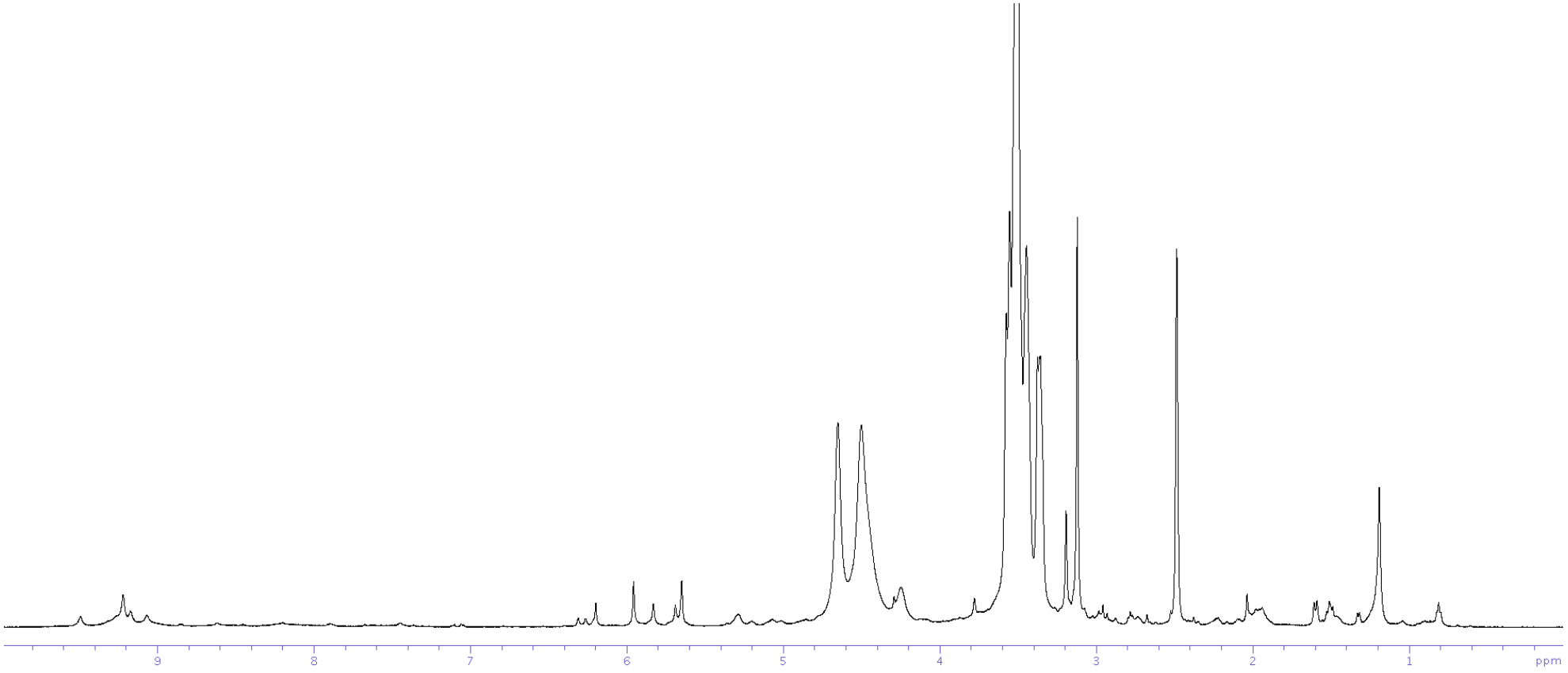


Figure S5. ^{1}H NMR spectrum (500 MHz, d_6-DMSO) of MeOH crude extract of *S. paradoxum*.

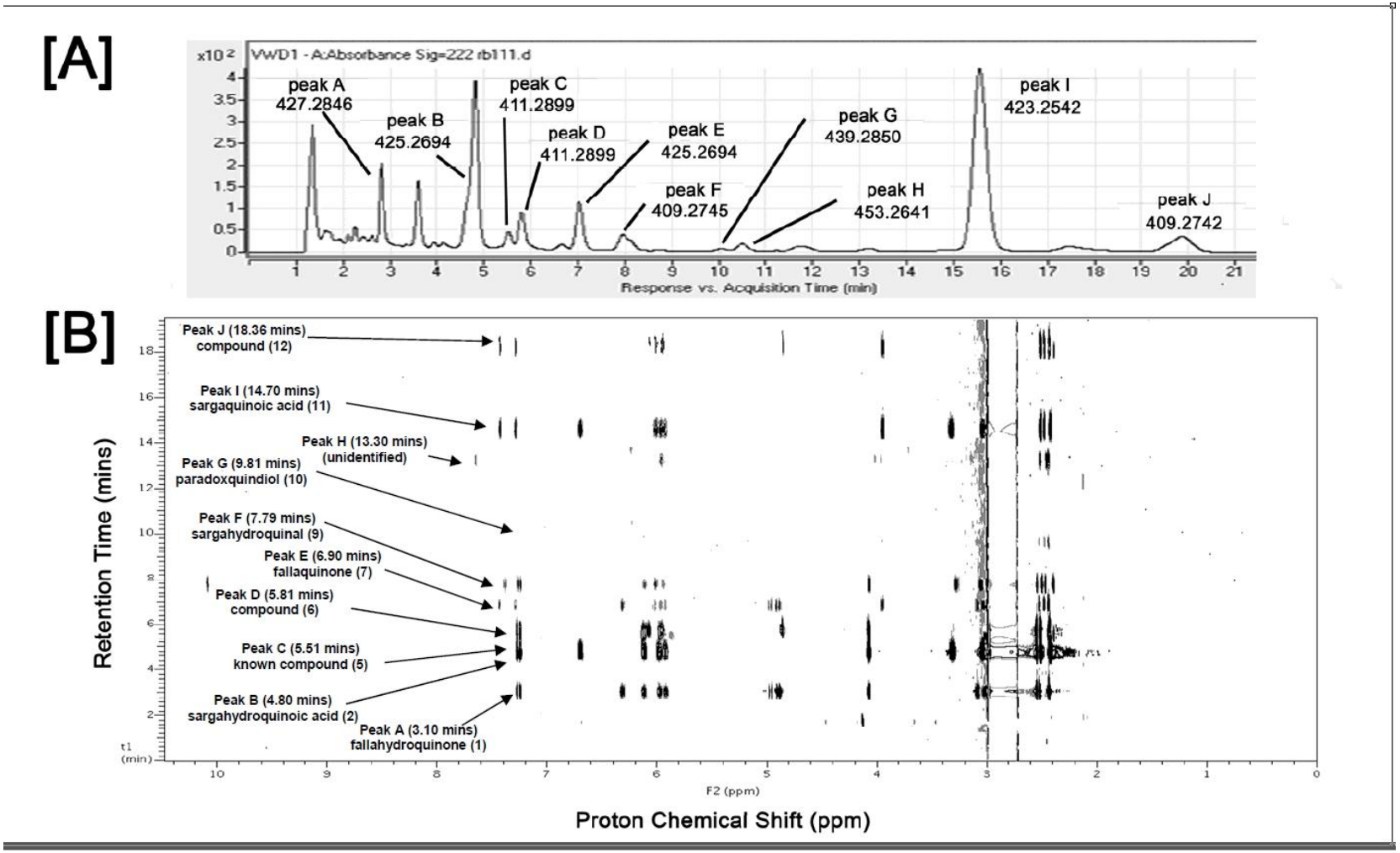


Figure S6. [**A**] HPLC-MS chromatographic trace showing the corresponding high resolution *m*/*z* ions of peaks A–J (Negative mode ESI MS with UV detection at 222 nm) and [**B**] On-flow 2D HPLC-NMR contour plot resulting from the analysis of the dichloromethane crude extract of *Sargassum paradoxum* showing the detection of peaks A–J.

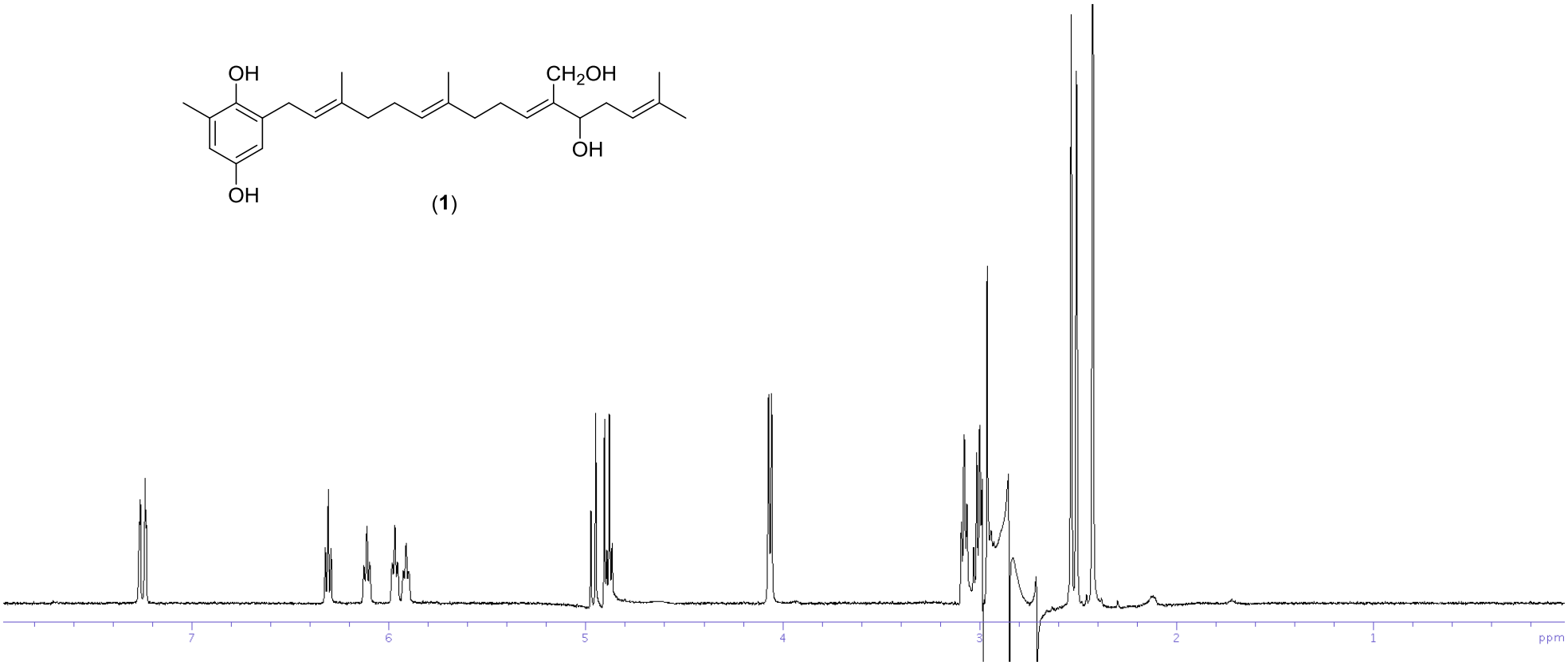


Figure S7. Stop-flow WET1D Proton NMR spectrum of peak A (3.10 min) (compound **1**).

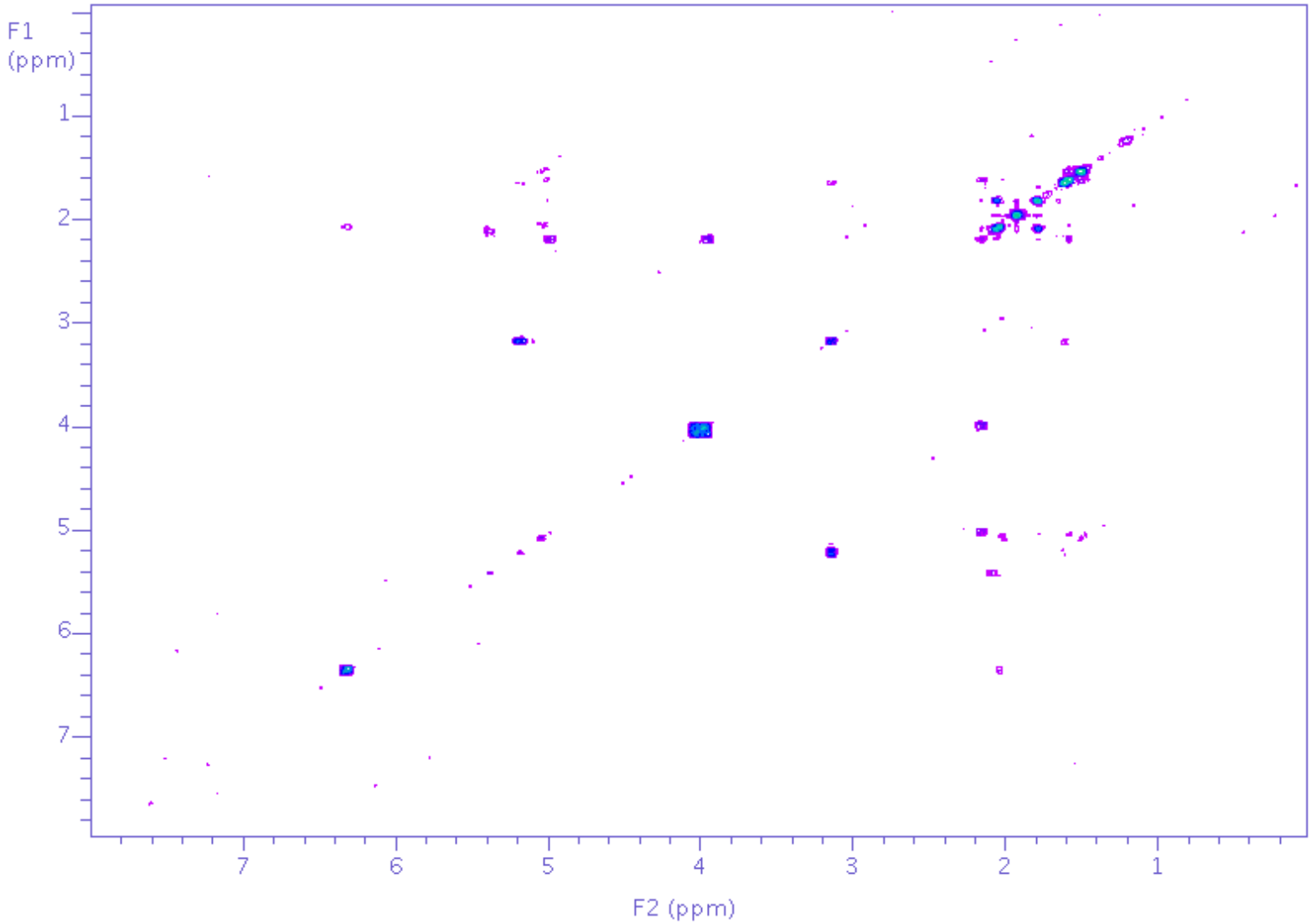


Figure S8. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak A (3.10 min) (compound **1**).

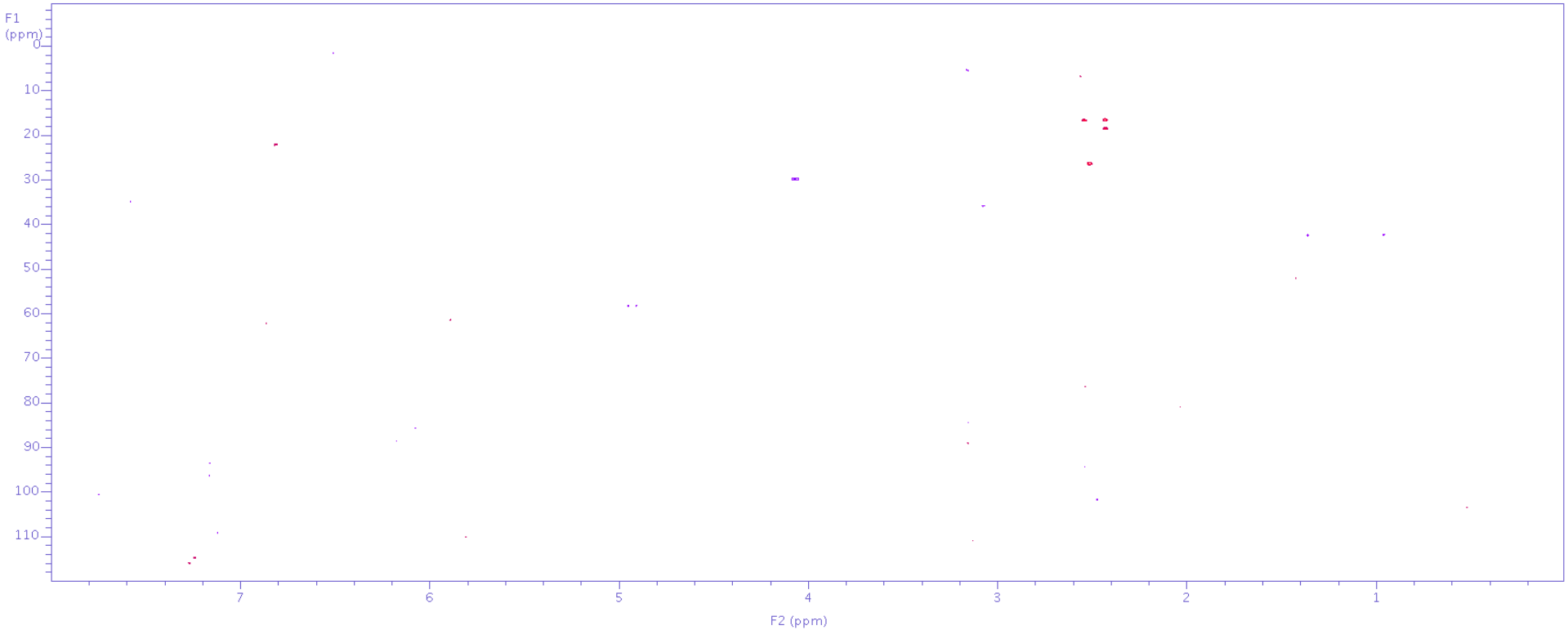


Figure S9. gHSQCAD NMR spectrum (from stop-flow HPLC-NMR) of peak A (3.10 min) (compound **1**).

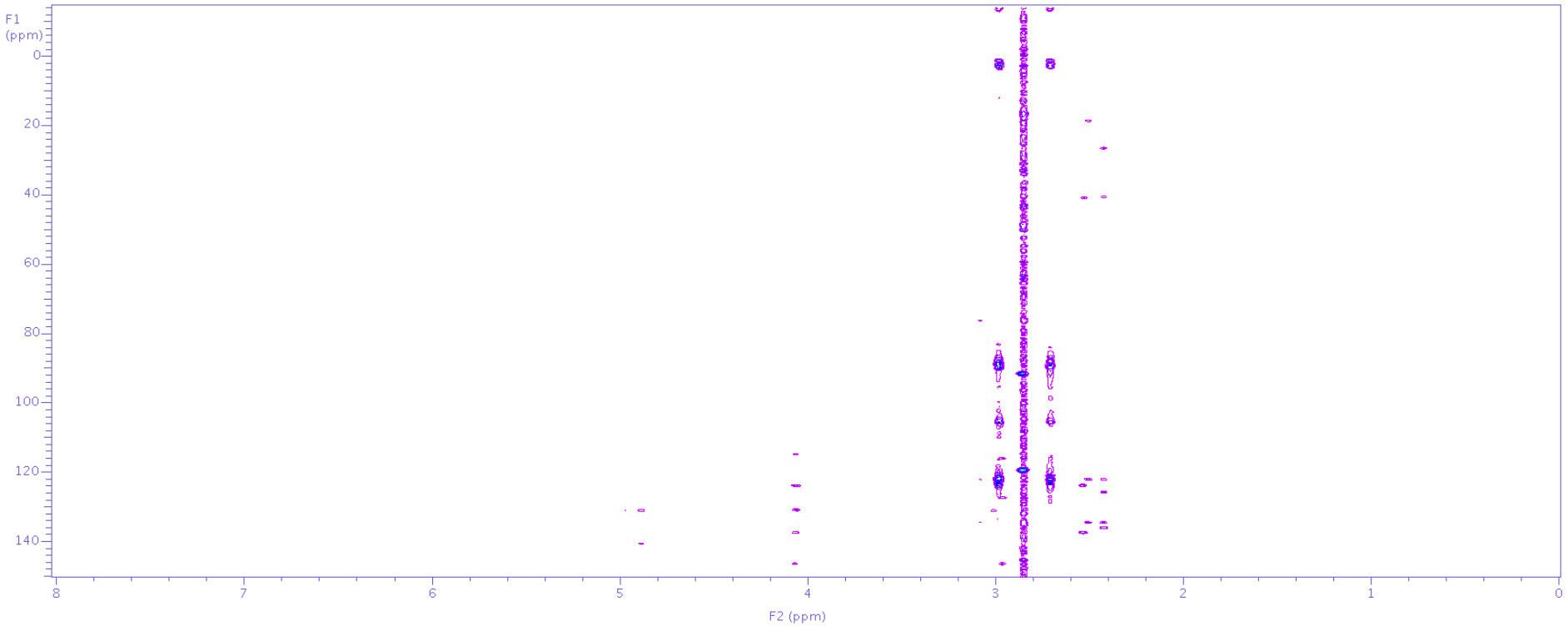


Figure S10. gHMBCAD NMR spectrum (from stop-flow HPLC-NMR) of peak A (3.10 min) (compound **1**).

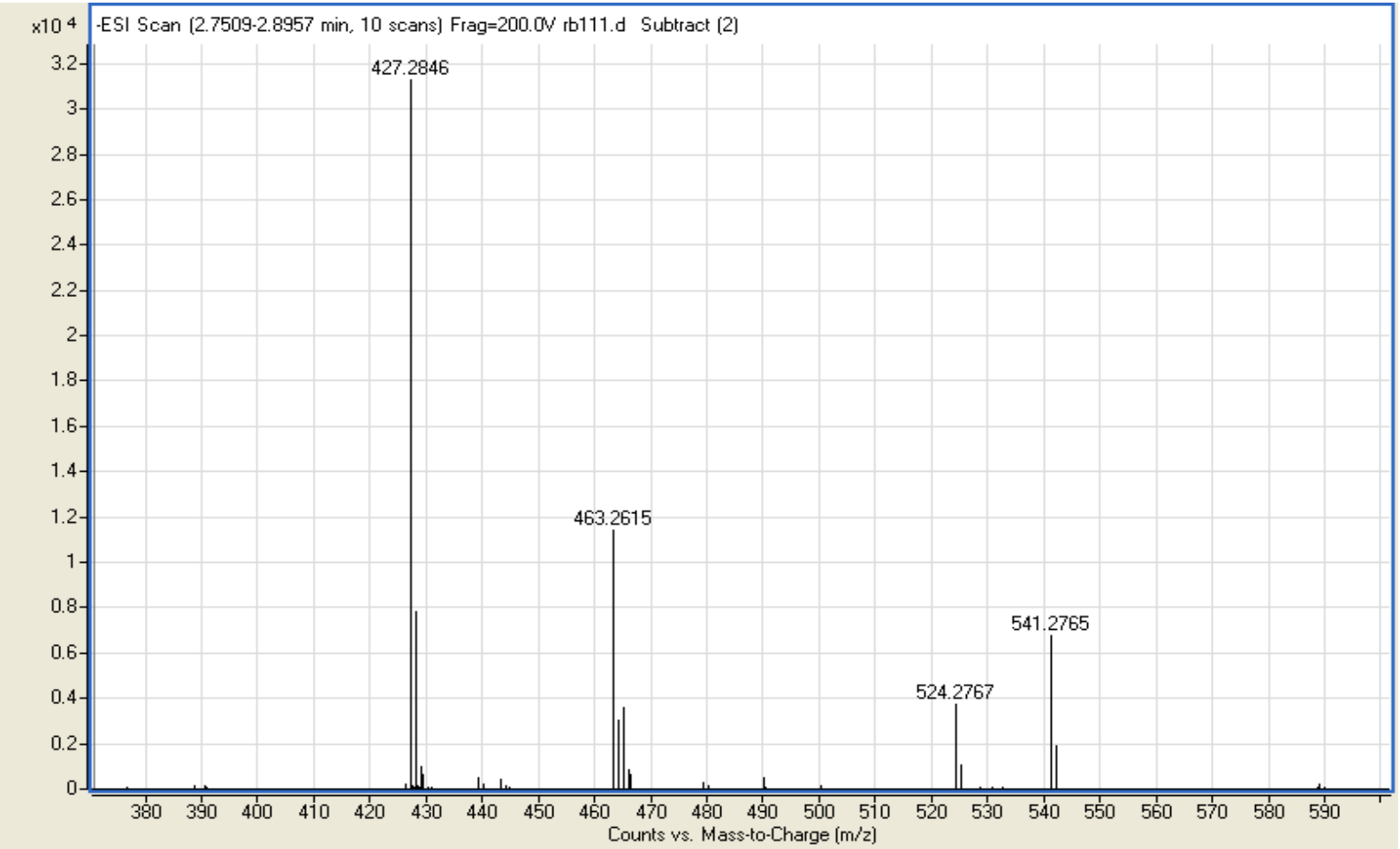


Figure S11. High resolution negative ESI-MS of peak A (3.10 min) (compound **1**) from HPLC-MS.

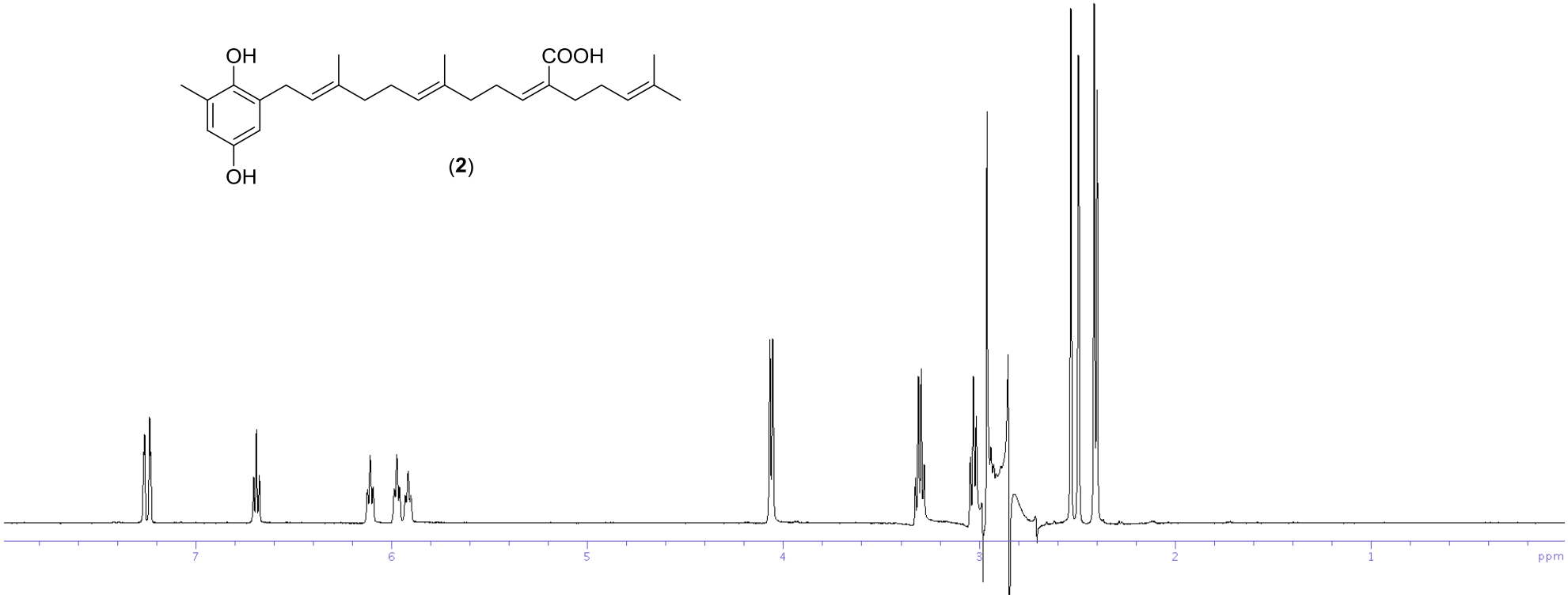


Figure S12. Stop-flow WET1D Proton NMR spectrum of peak B (4.80 min) (compound **2**).

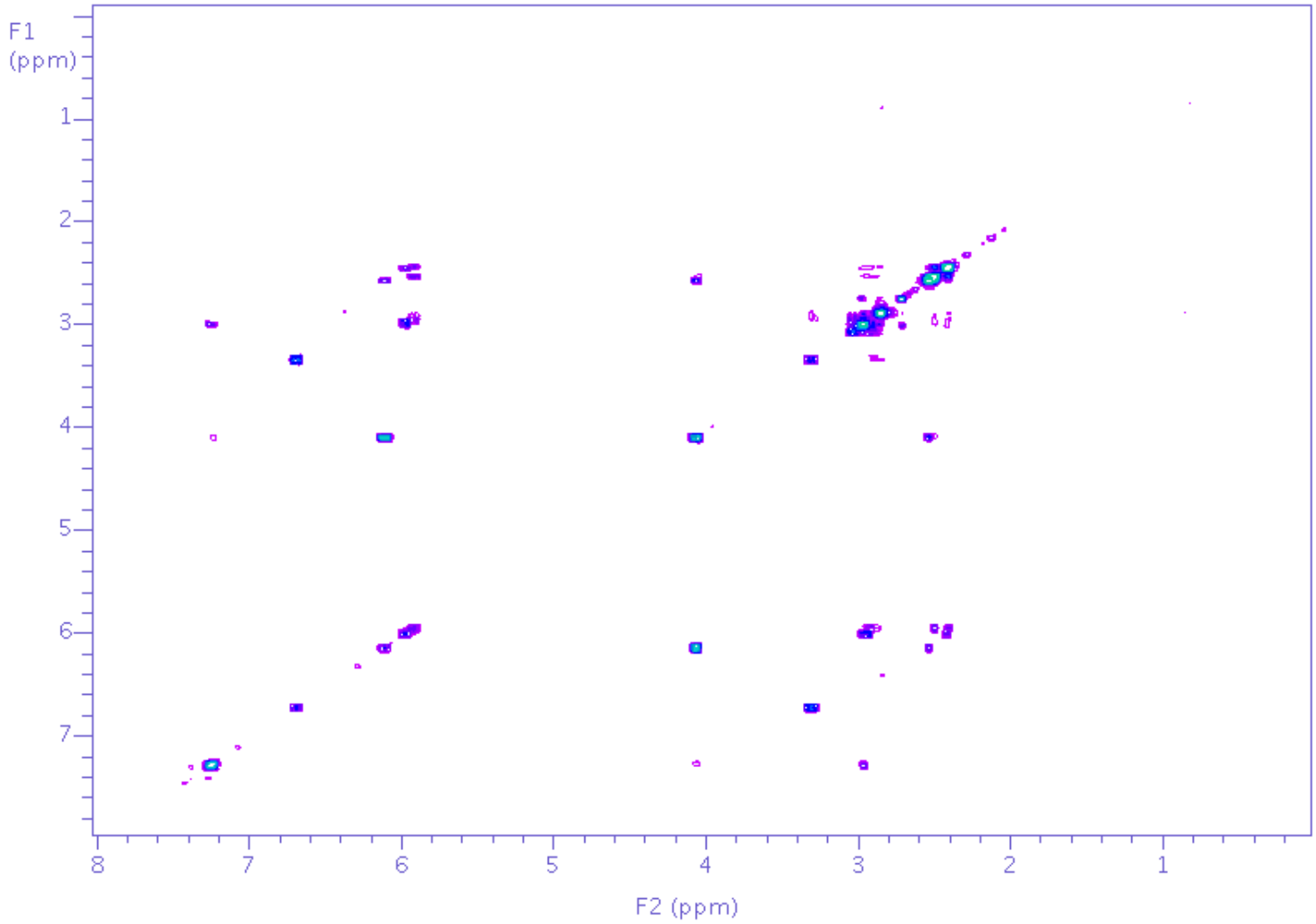


Figure S13. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak B (4.80 min) (compound **2**).

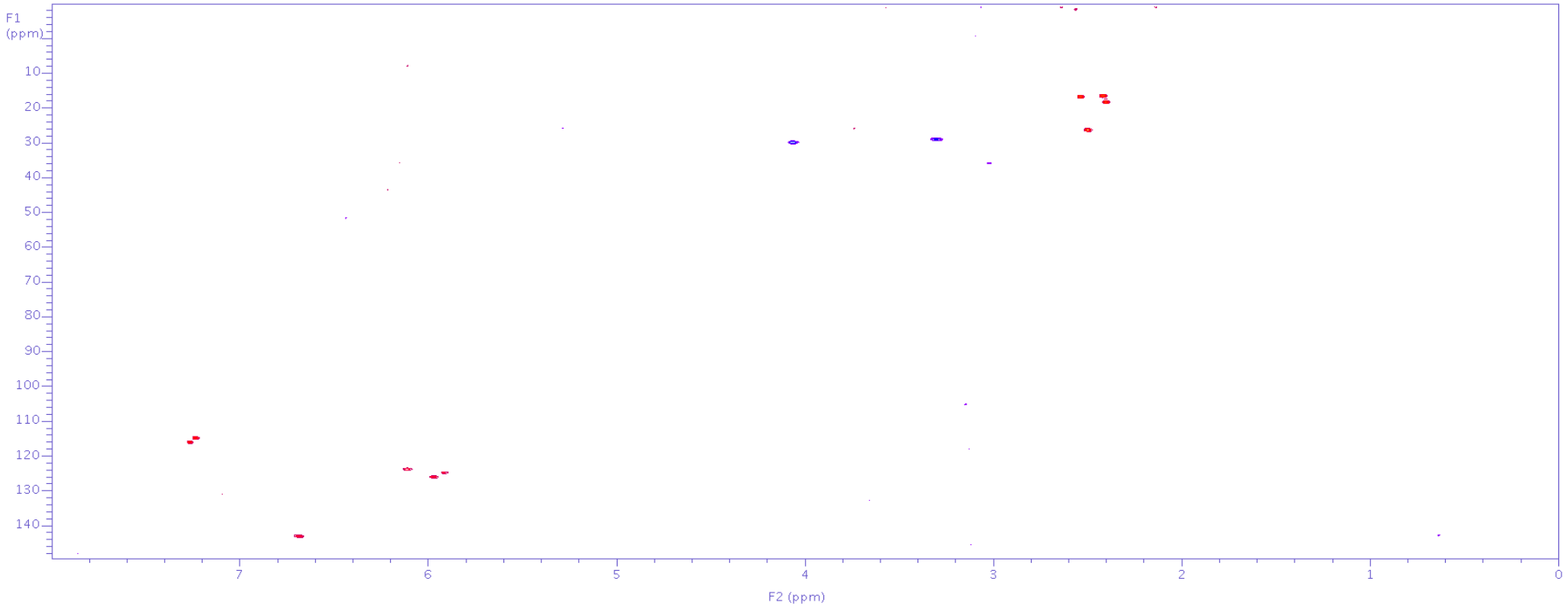


Figure S14. gHSQCAD NMR spectrum (from stop-flow HPLC-NMR) of peak B (4.80 min) (compound **2**).

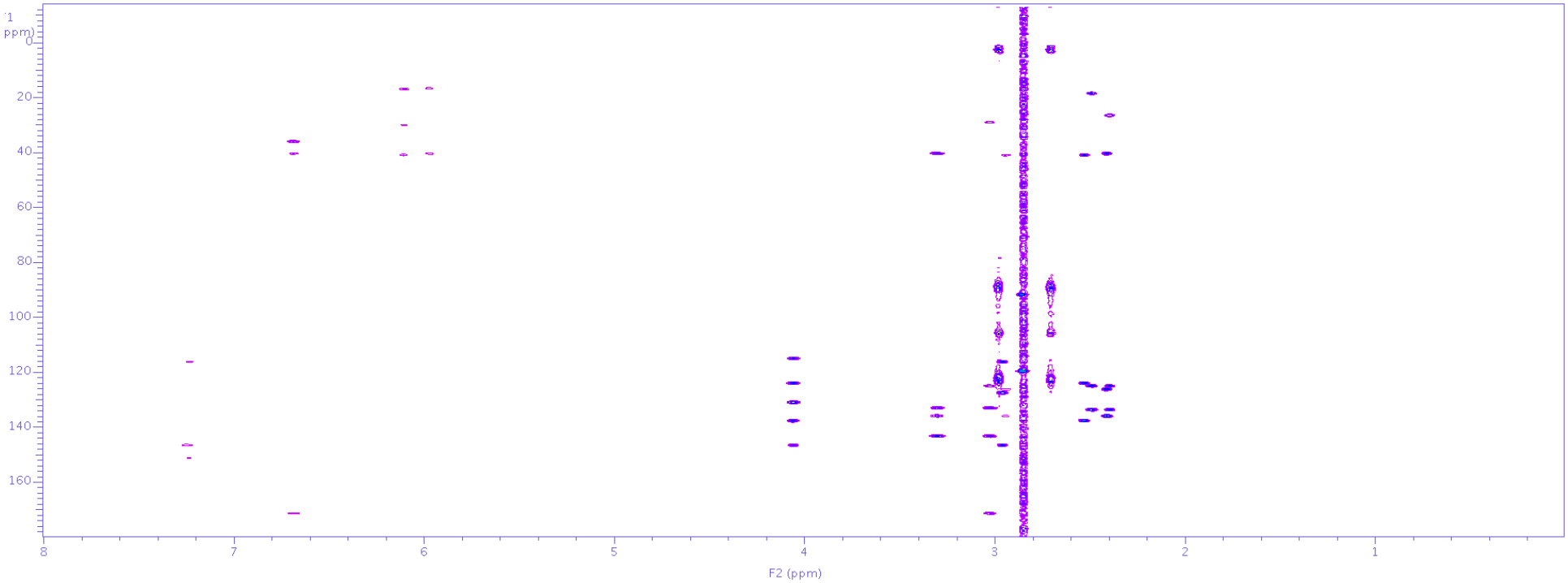


Figure S15. gHMBCAD NMR spectrum (from stop-flow HPLC-NMR) of peak B (4.80 min) (compound **2**).

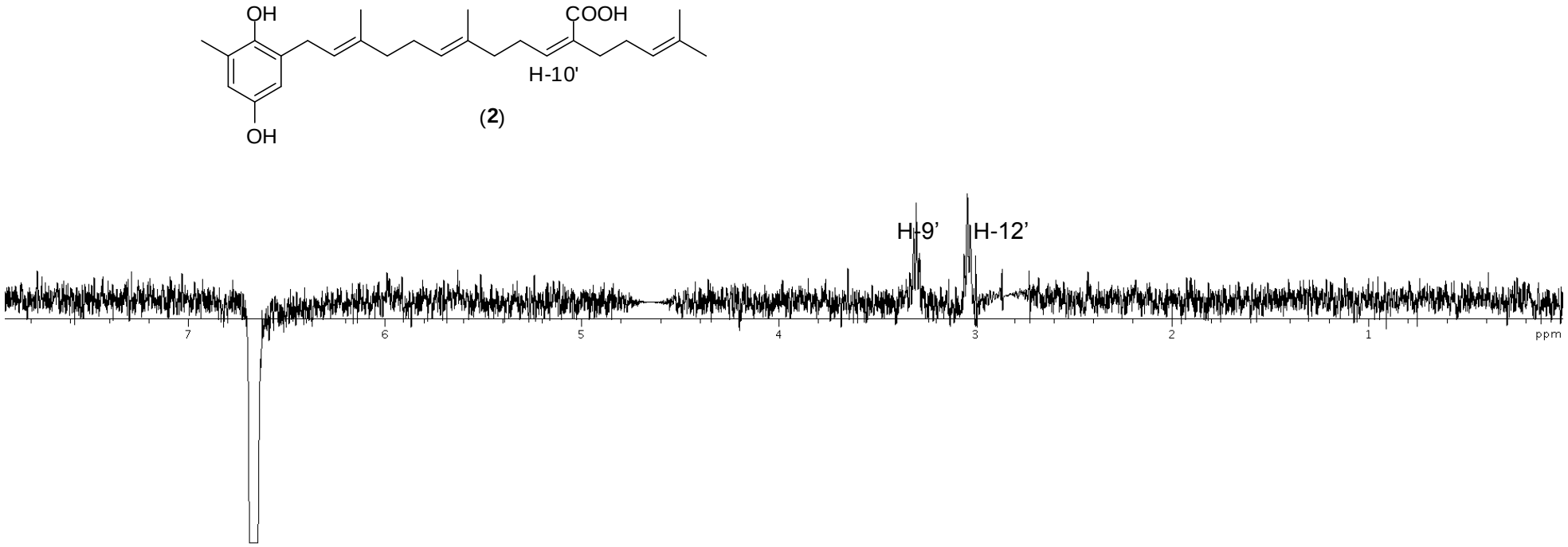


Figure S16. Single irradiation nOe NMR spectrum (from stop-flow HPLC-NMR) of peak B (compound **2**) showing the irradiation of δ_H 6.69 (H-10′).

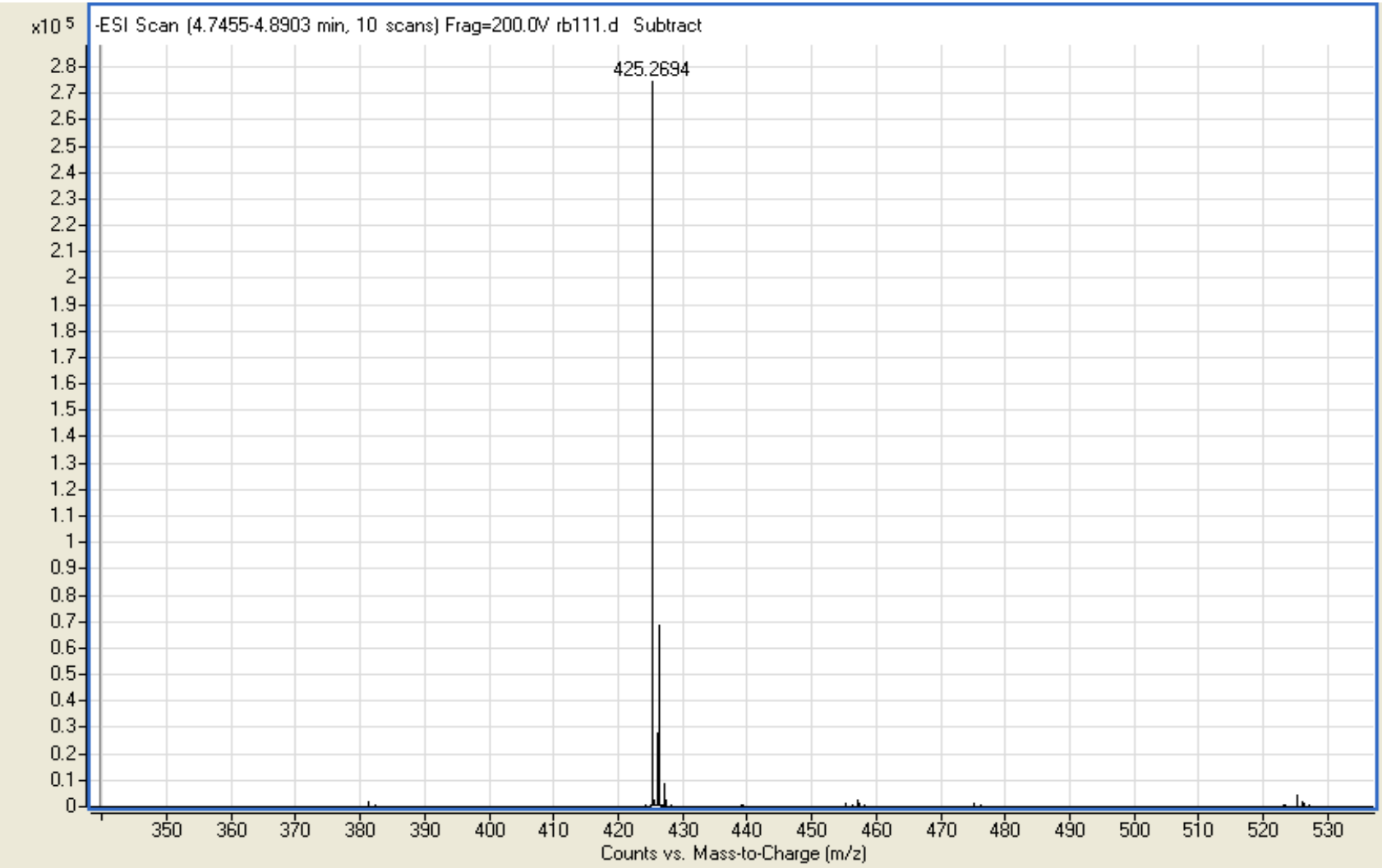


Figure S17. High resolution negative ESI-MS of peak B (4.80 min) (compound **2**) from HPLC-MS.

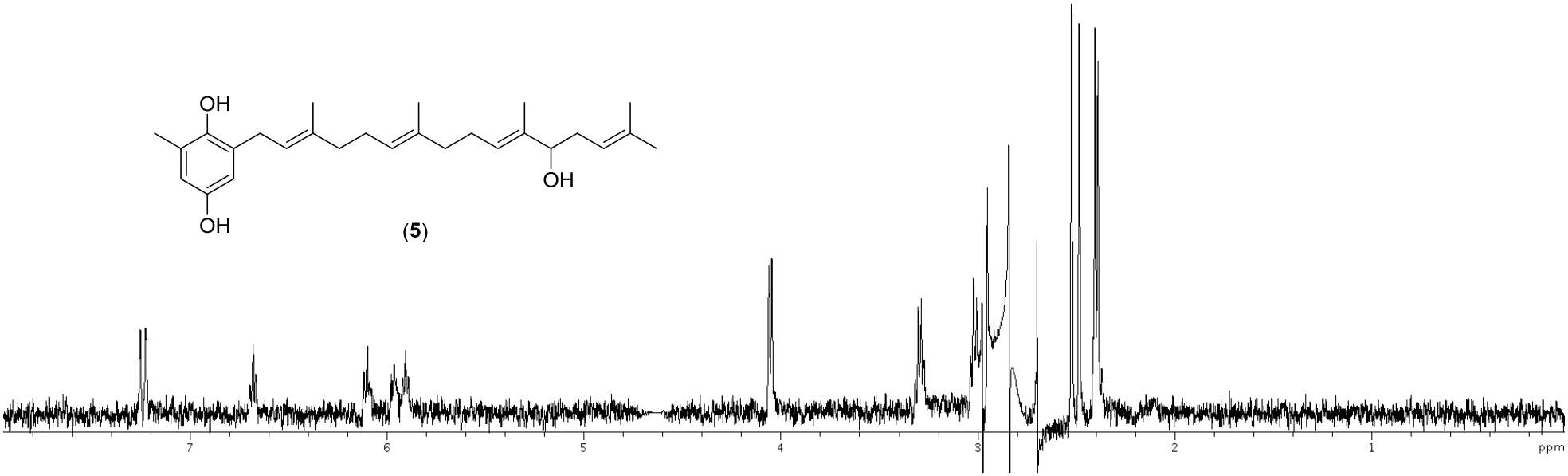


Figure S18. On-flow WET1D Proton NMR spectrum of peak C (5.51 min) (compound **5**).

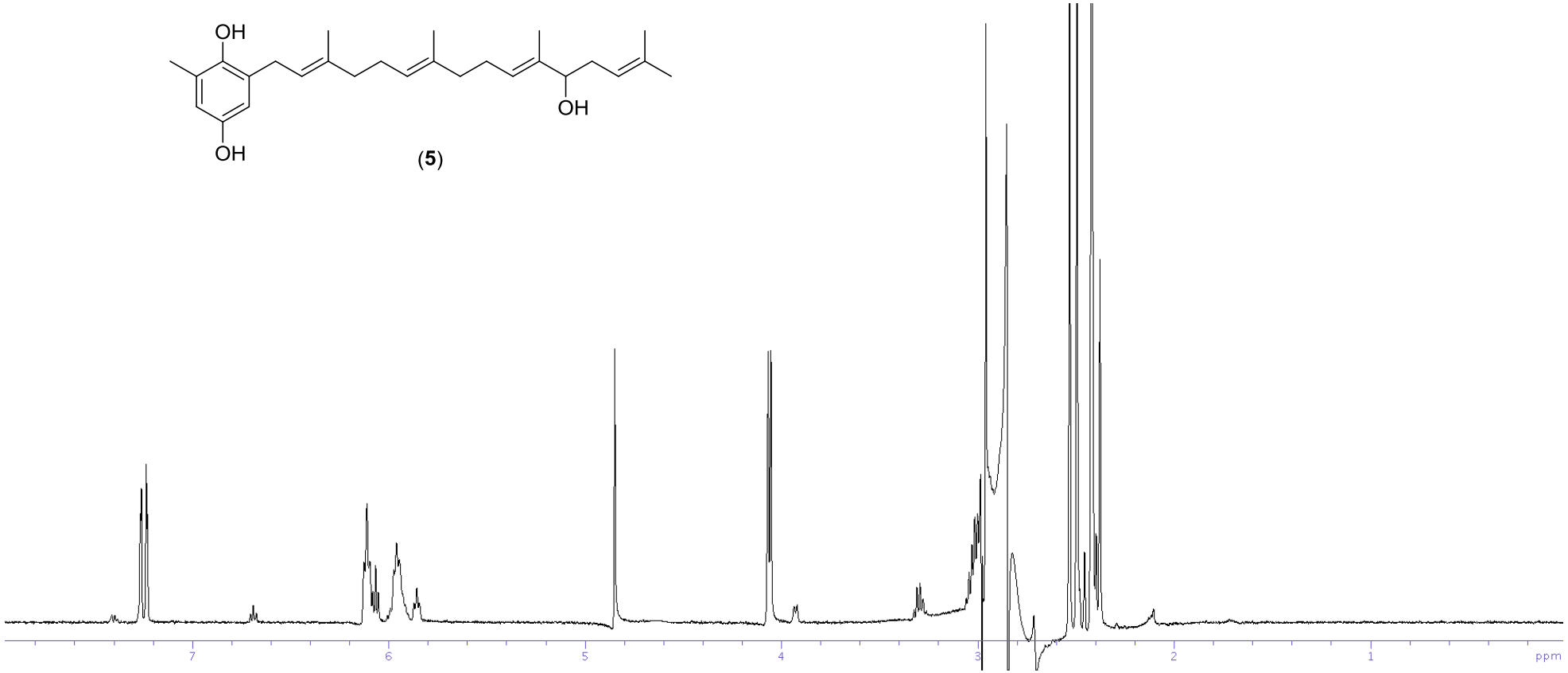


Figure S19. Stop-flow WET1D Proton NMR spectrum of peak C (5.51 min) (compound **5**).

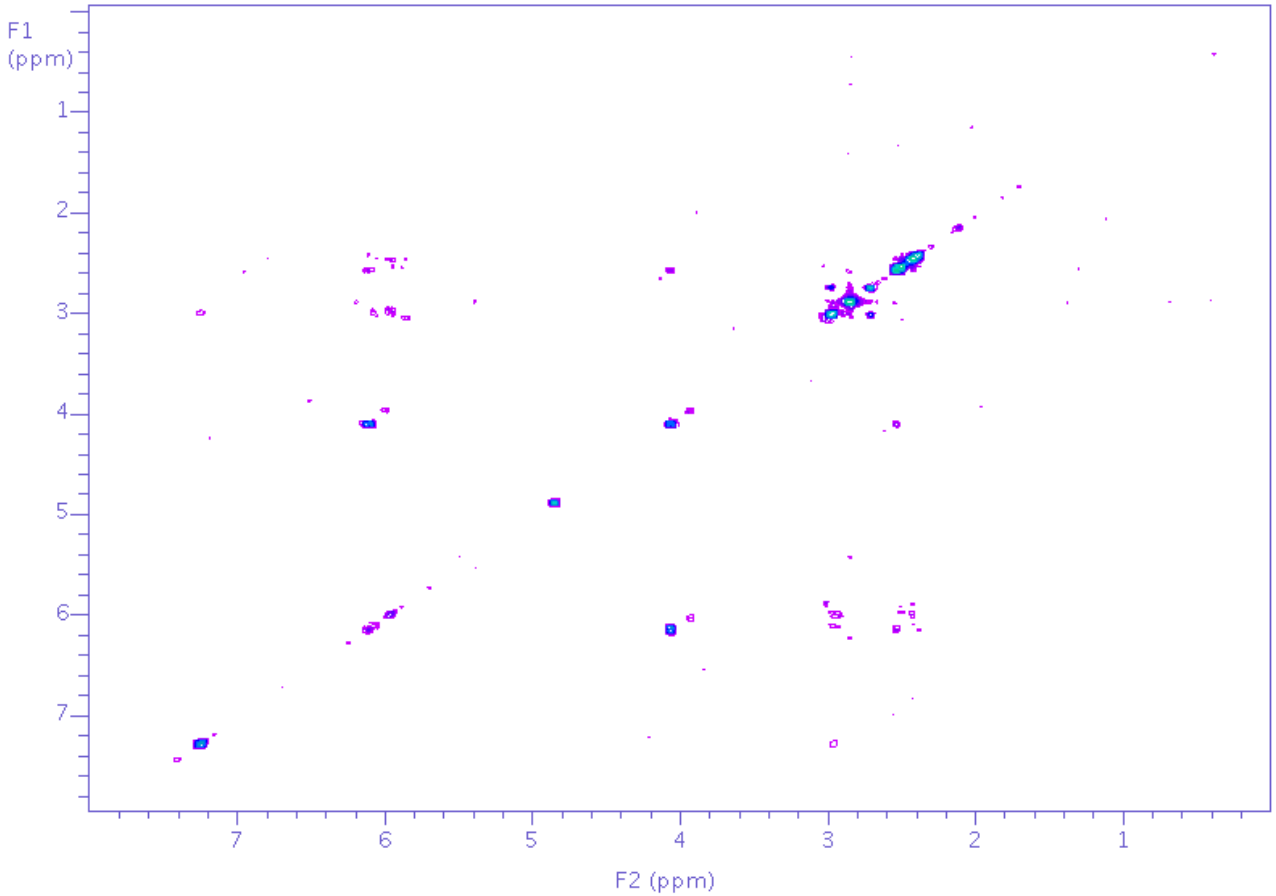


Figure S20. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak C (5.51 min) (compound 5).

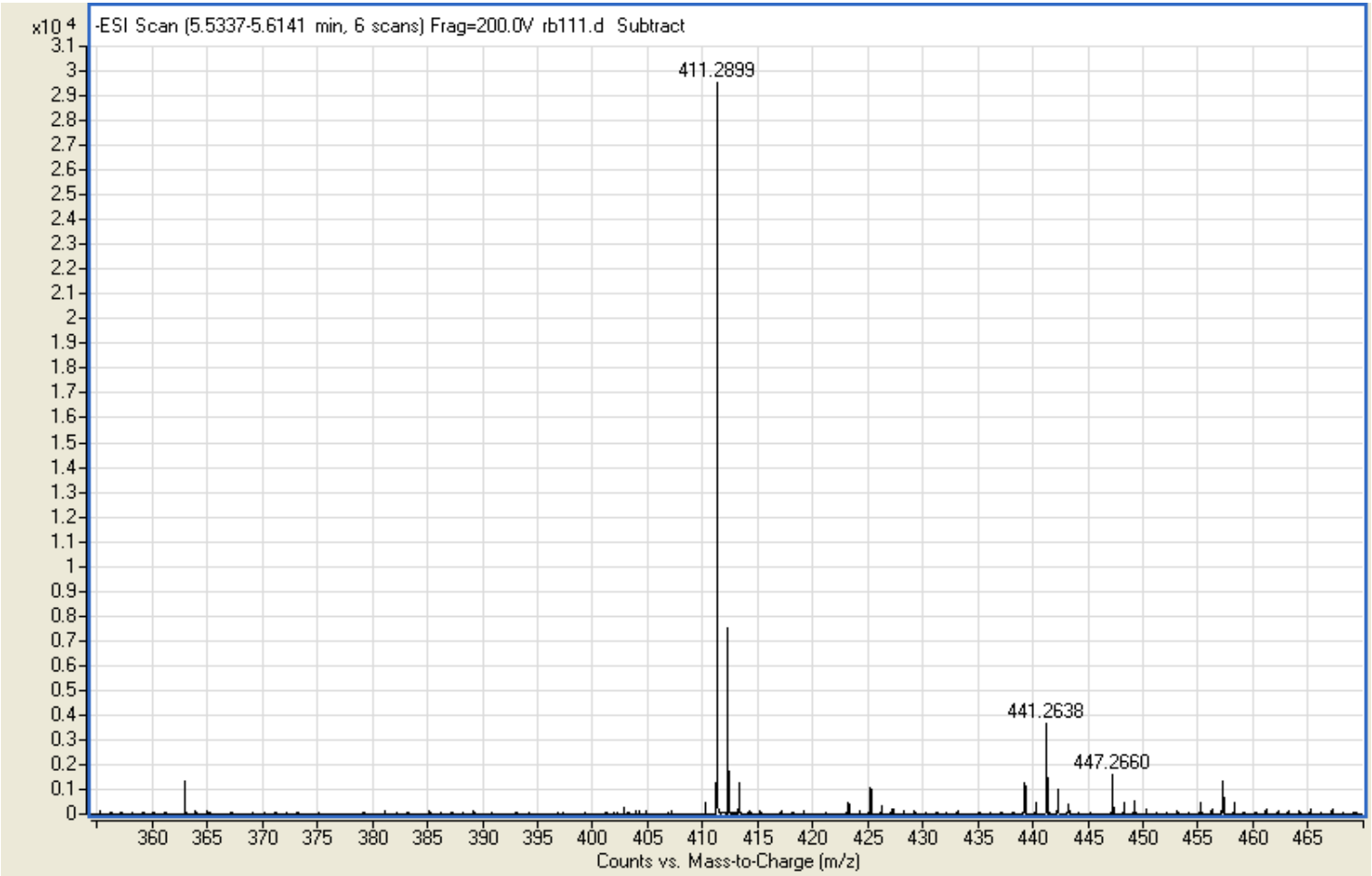


Figure S21. High resolution negative ESI-MS of peak C (5.51 min) (compound 5) from HPLC-MS.

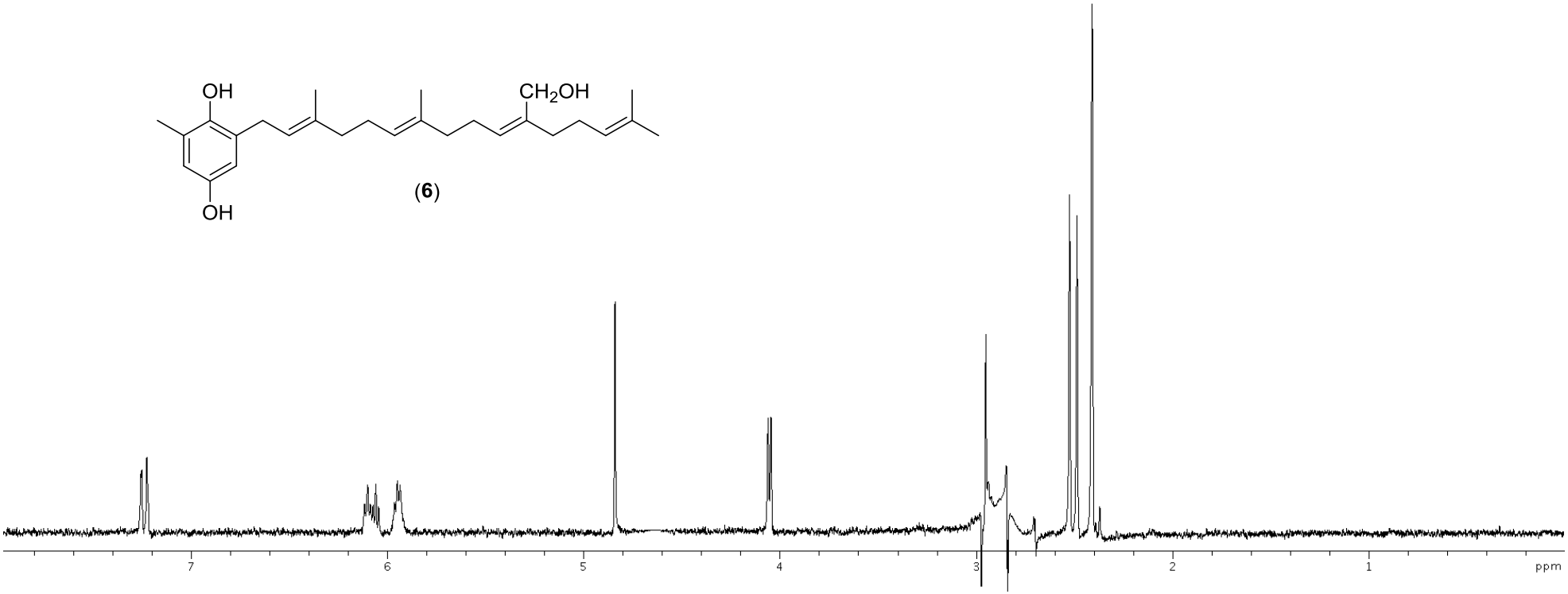


Figure S22. On-flow WET1D Proton NMR spectrum of peak D (5.81 min) (compound **6**).

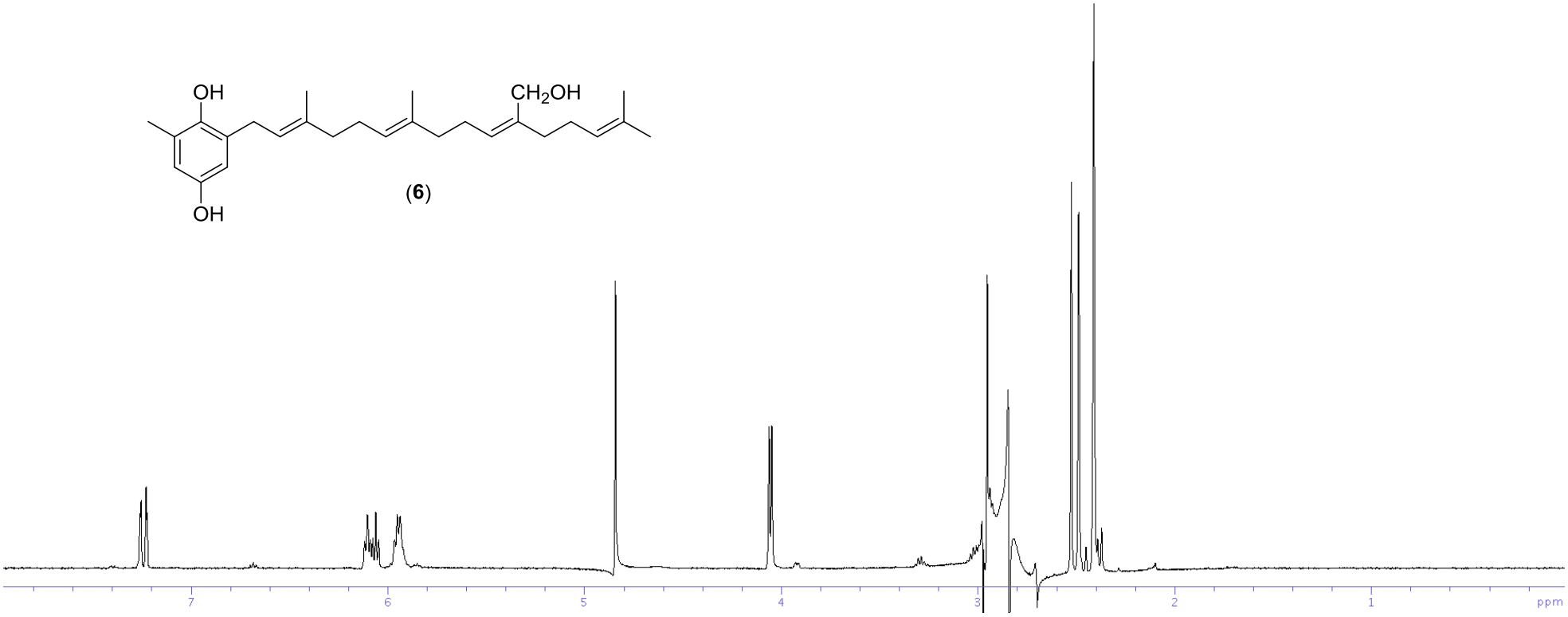


Figure S23. Stop-flow WET1D Proton NMR spectrum of peak D (5.81 min) (compound **6**).

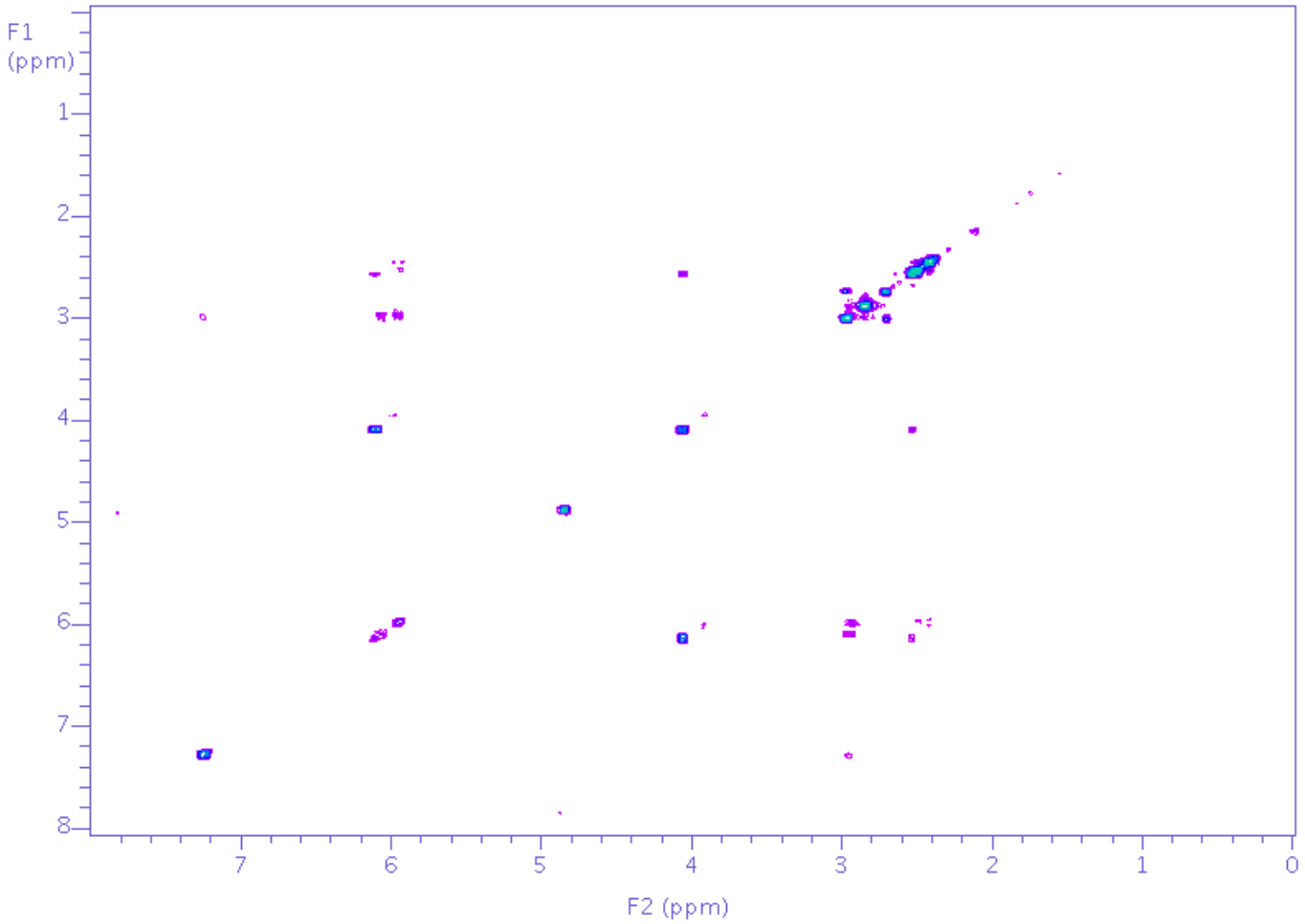


Figure S24. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak D (5.81 min) (compound **6**).

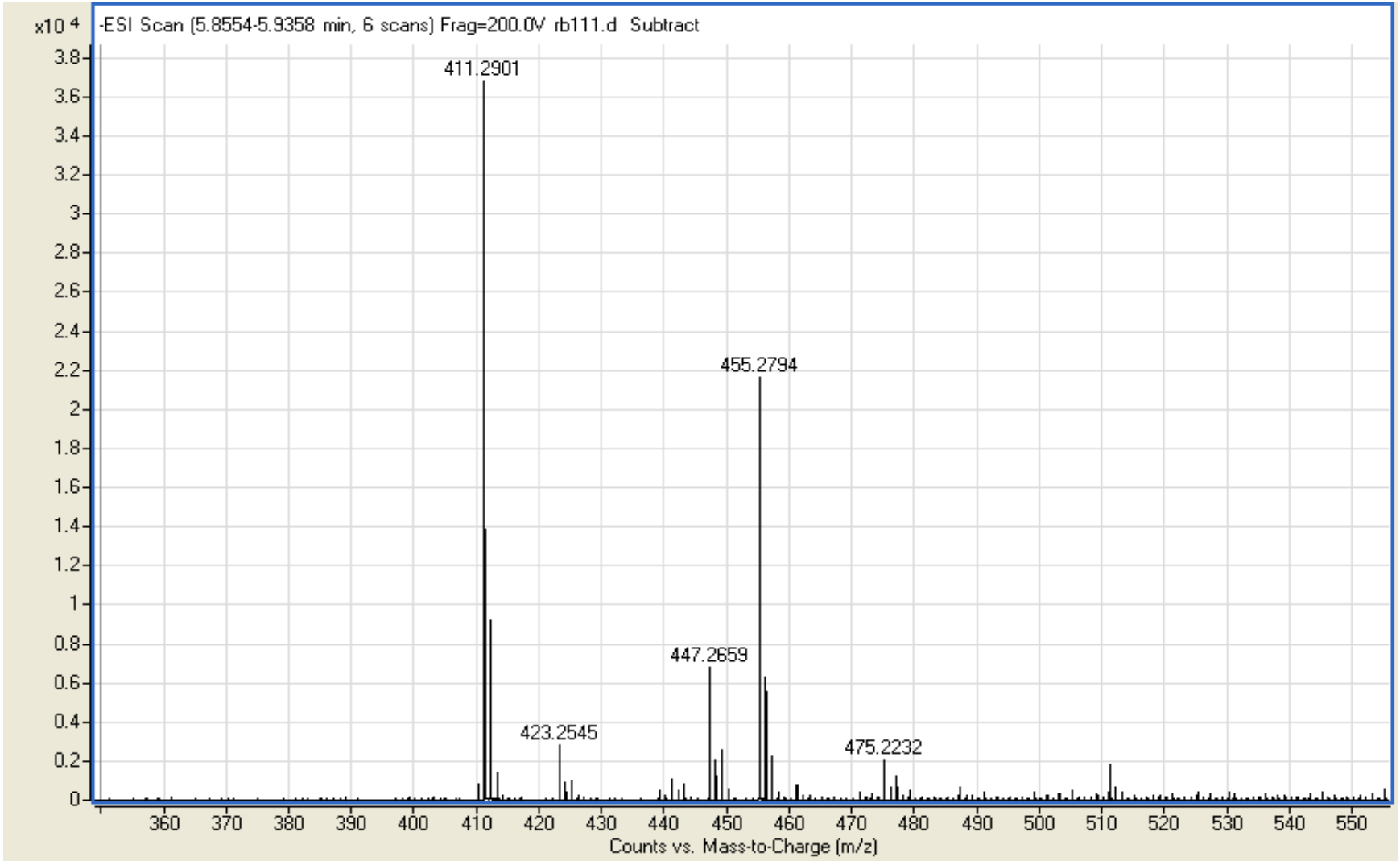


Figure S25. High resolution negative ESI-MS of peak D (5.81 mins) (compound 6) from HPLC-MS.

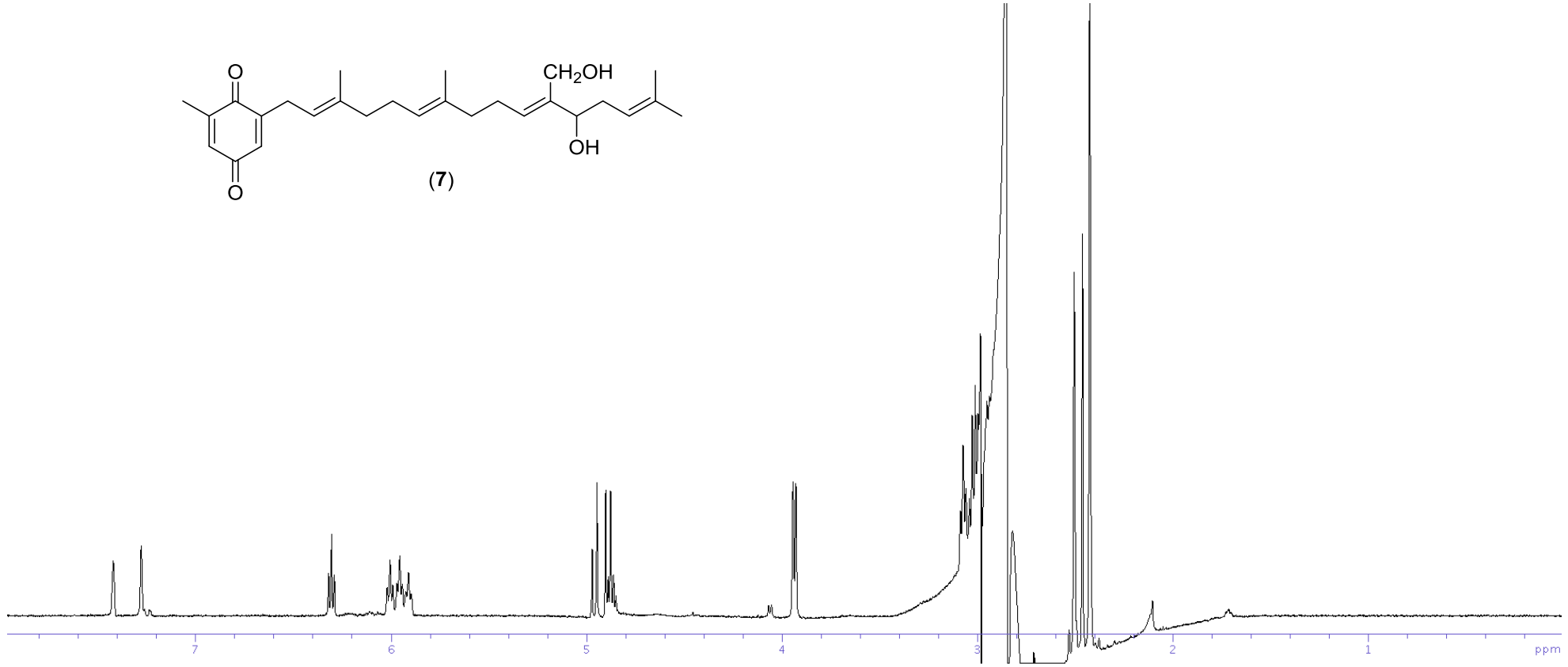


Figure S26. Stop-flow WET1D Proton NMR spectrum of peak E (6.90 mins) (compound 7).

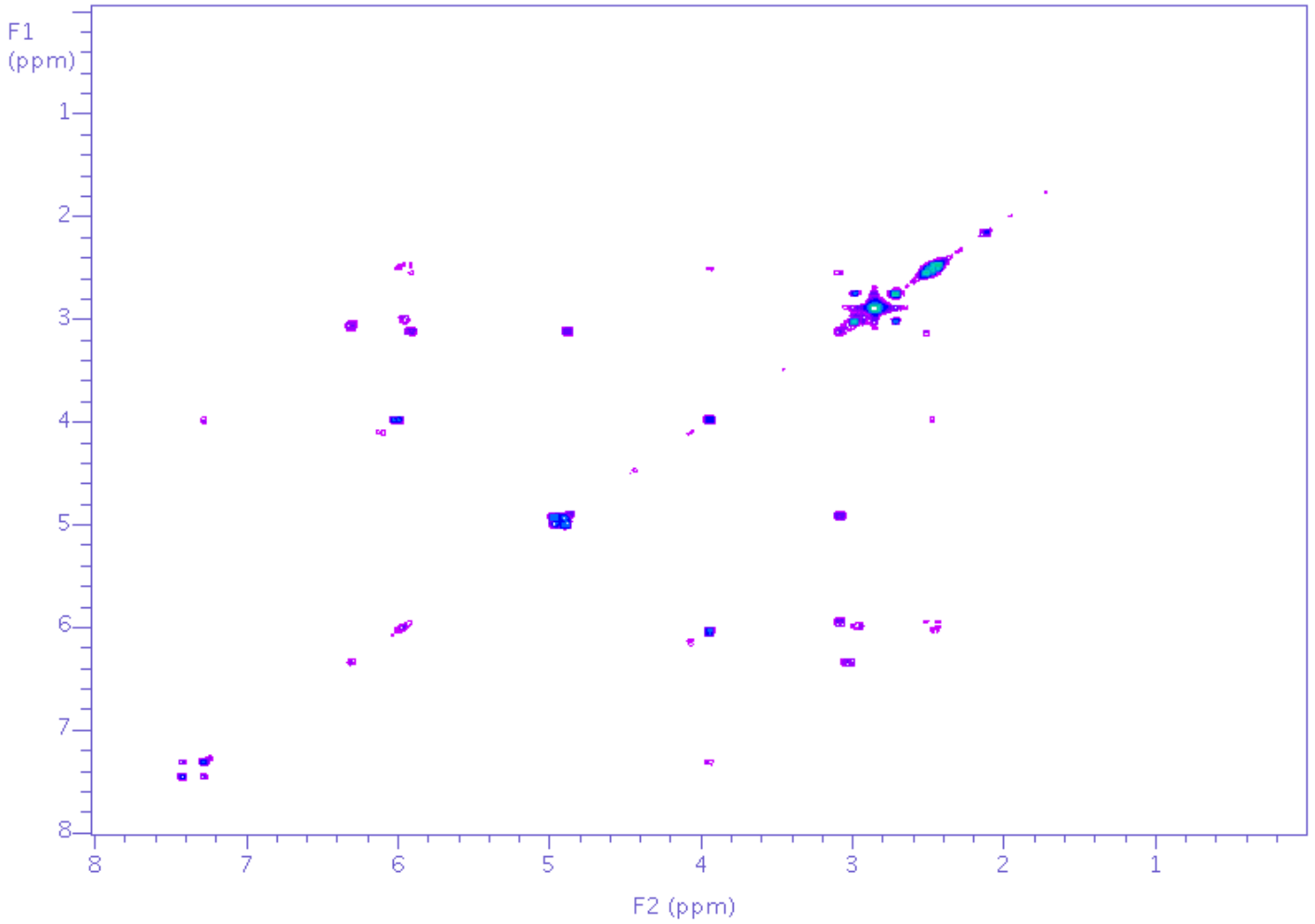


Figure S27. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak E (6.90 min) (compound **7**).

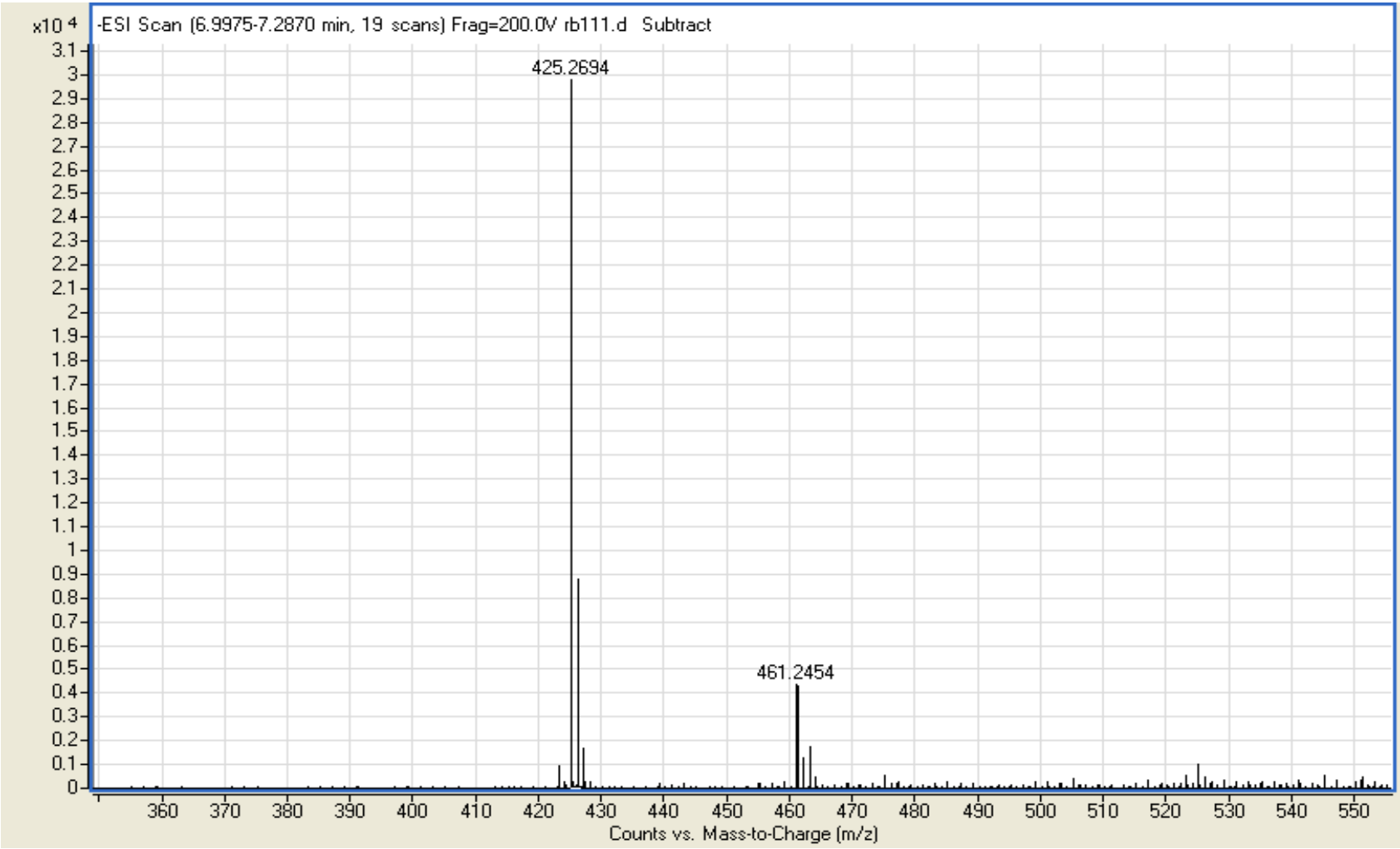


Figure S28. High resolution negative ESI-MS of peak E (6.90 min) (compound **7**) from HPLC-MS.

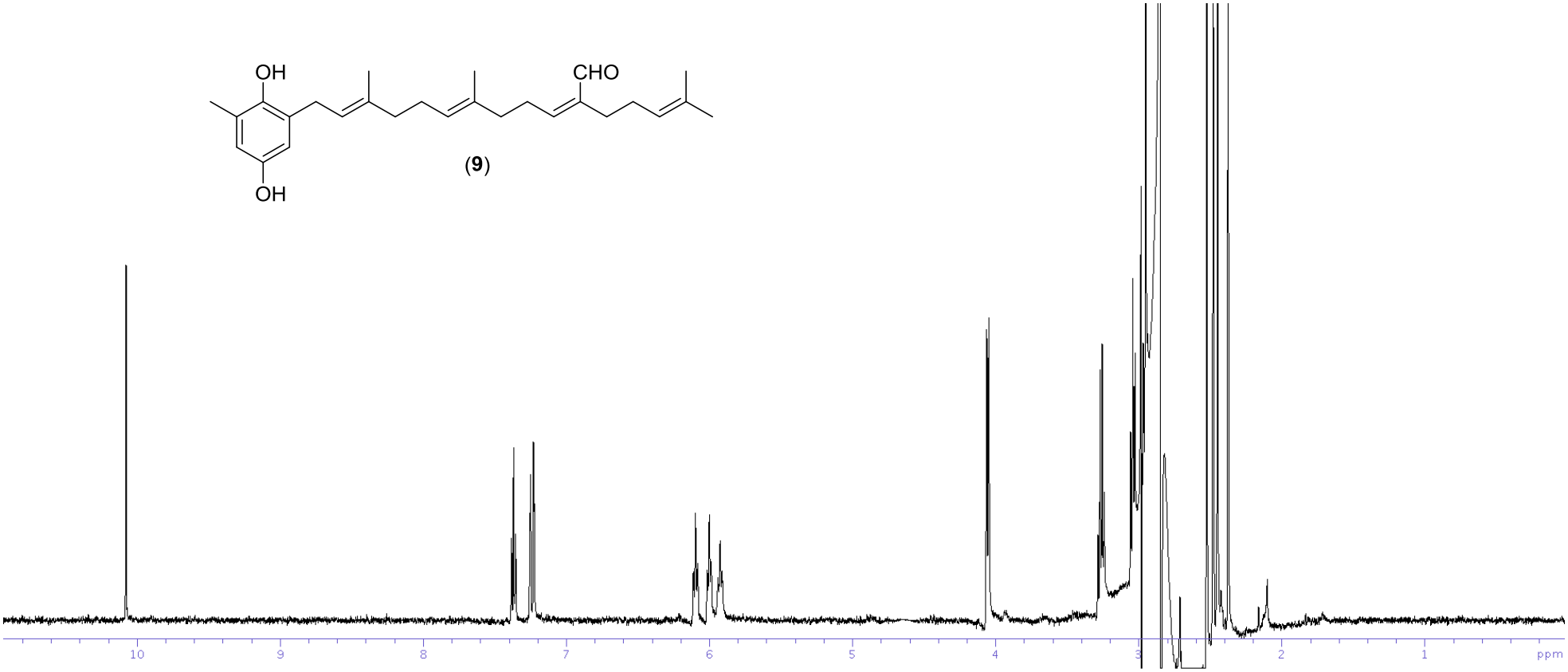


Figure S29. Stop-flow WET1D Proton NMR spectrum of peak F (7.79 min) (compound **9**).

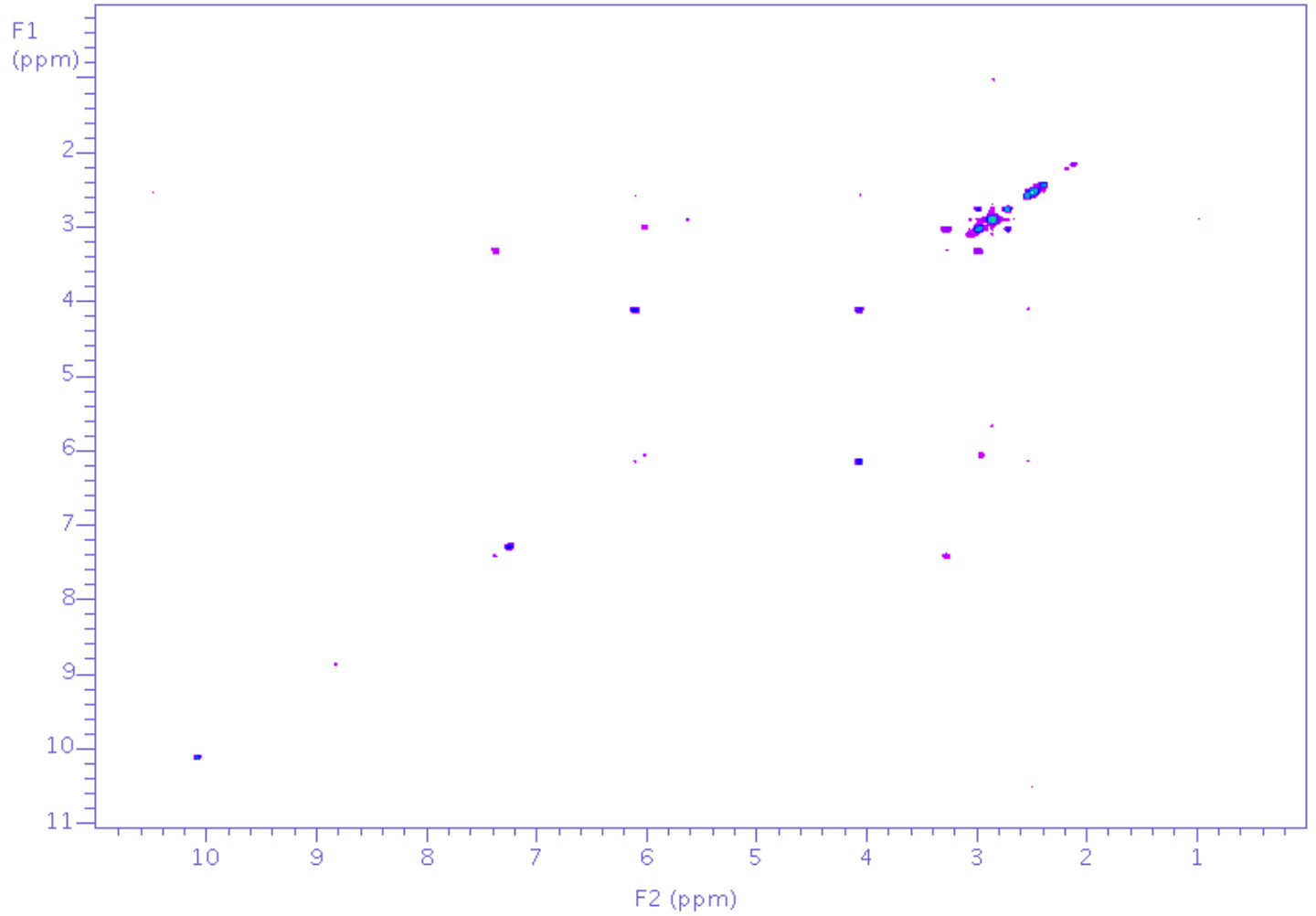


Figure S30. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak F (7.79 min) (compound **9**).

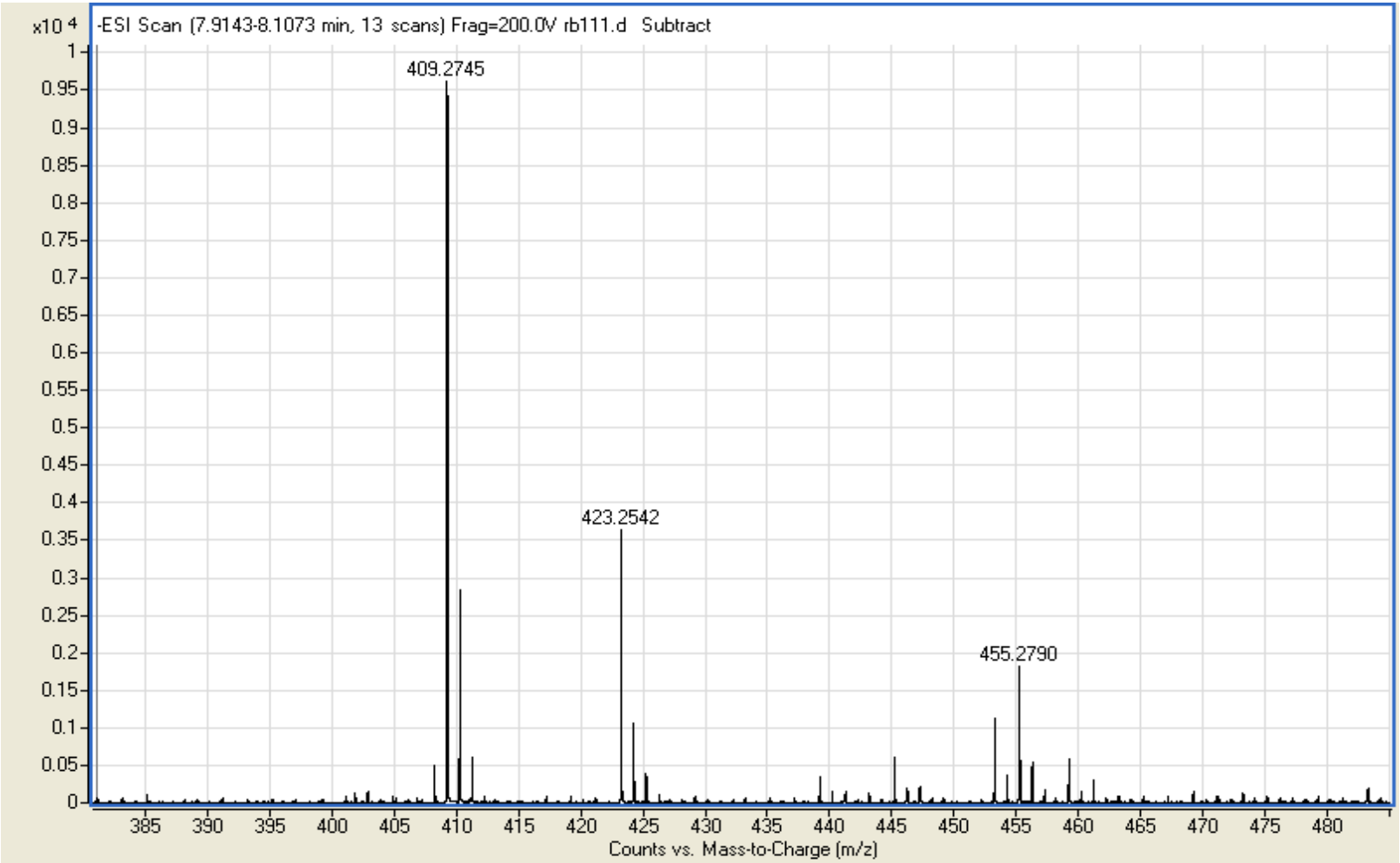


Figure S31. High resolution negative ESI-MS of peak F (7.79 min) (compound **9**) from HPLC-MS.

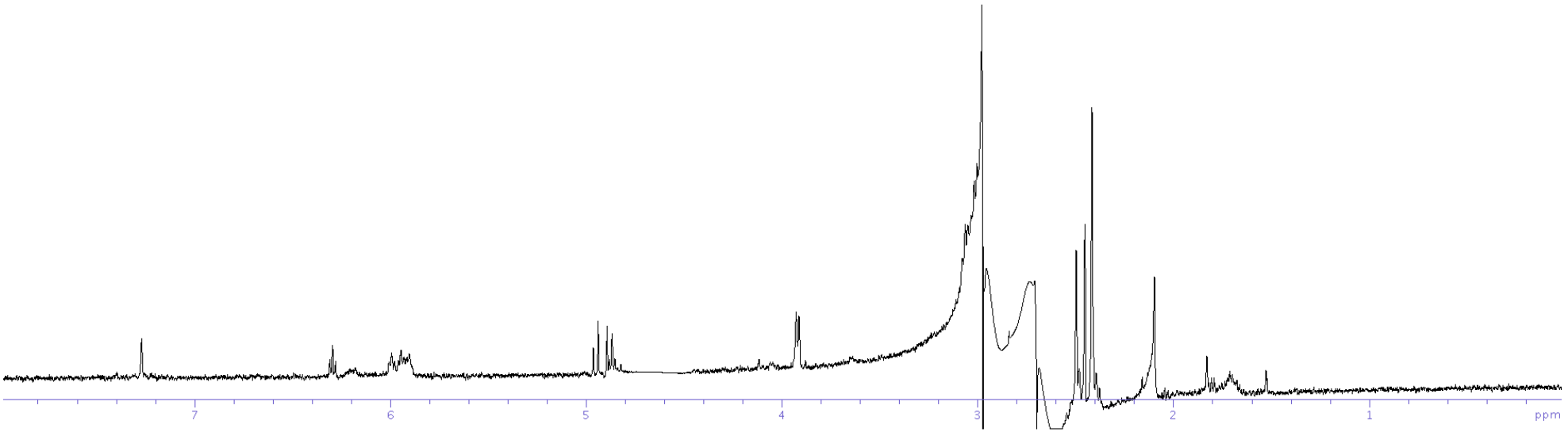


Figure S32. Stop-flow WET1D Proton NMR spectrum of peak G (9.81 min) (compound **10**).

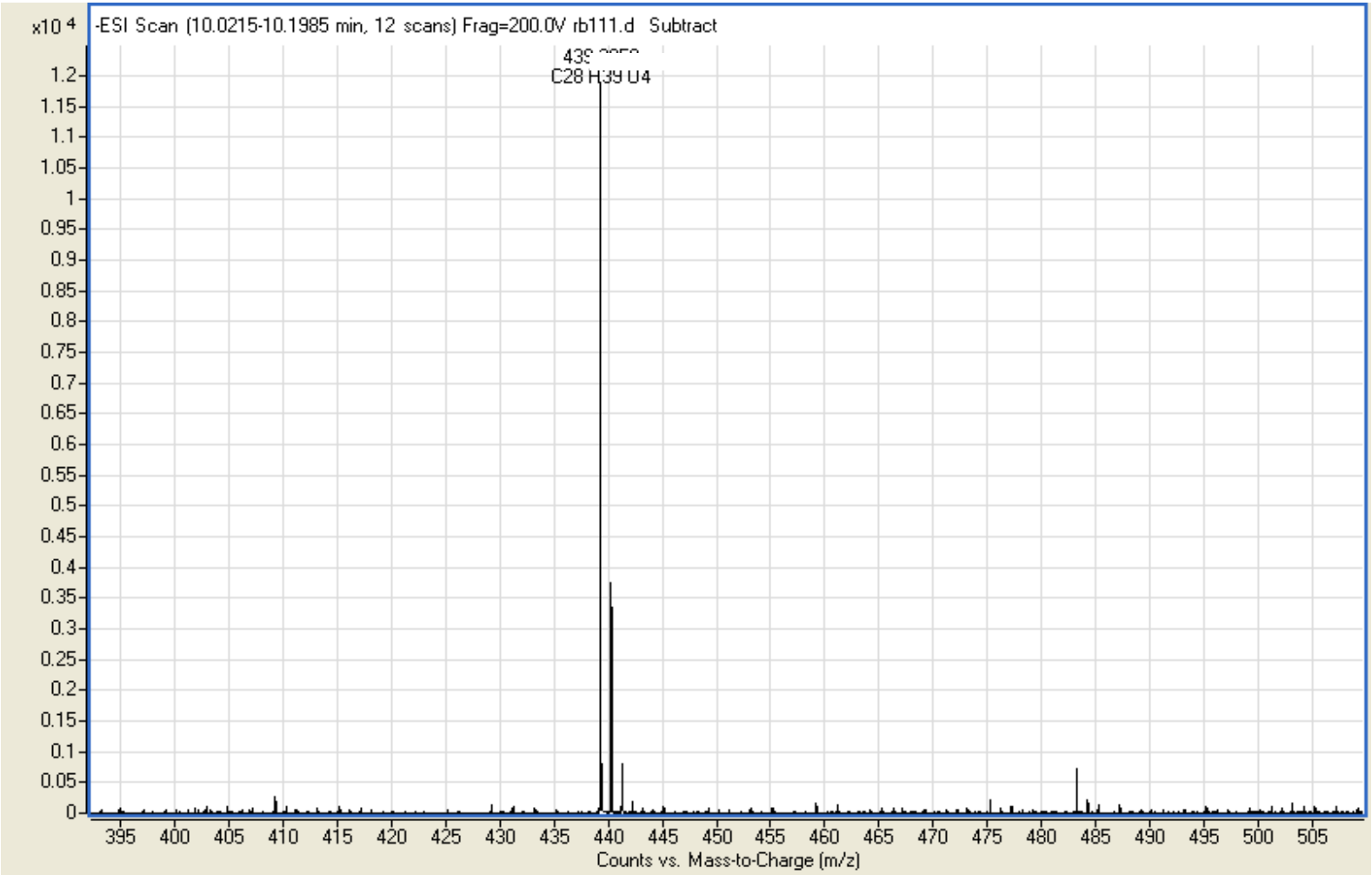
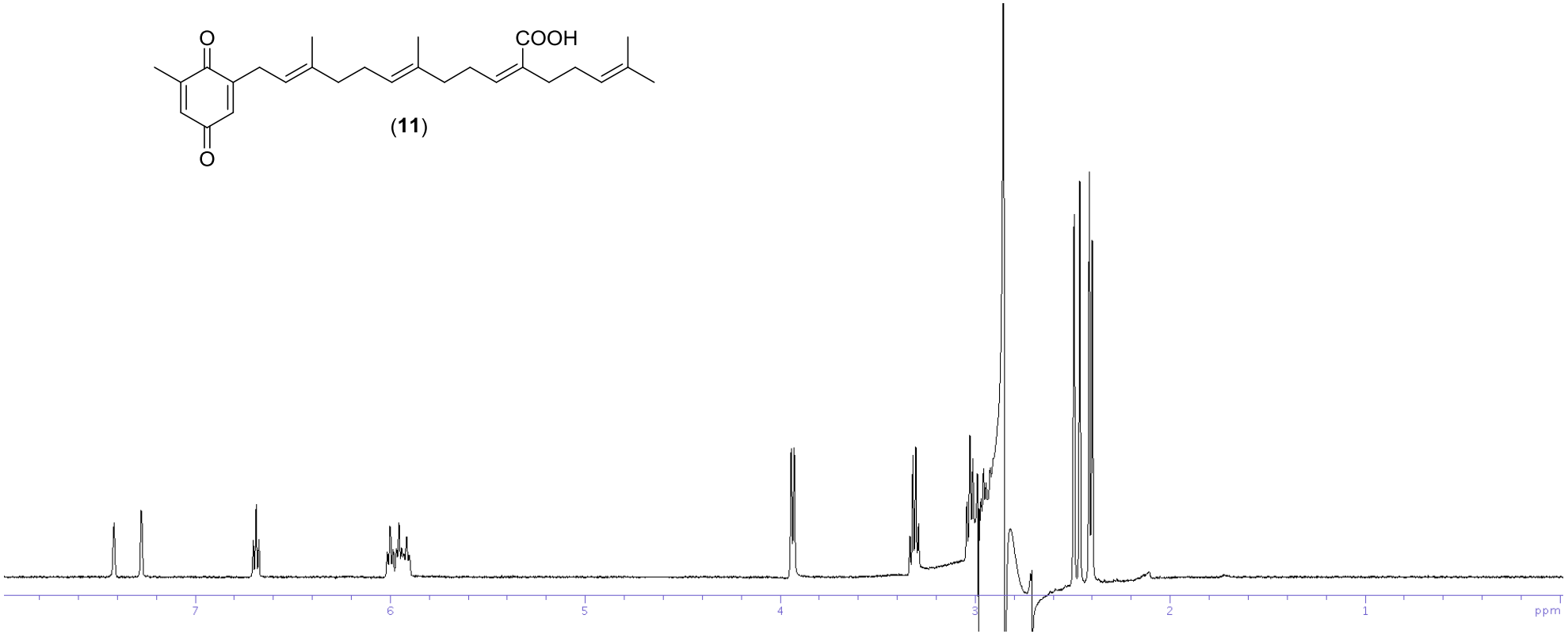


Figure S33. High resolution negative ESI-MS of peak G (9.81 min) (compound **10**) from HPLC-MS.



(**11**)

Figure S34. Stop-flow WET1D Proton NMR spectrum of peak I (14.70 min) (compound **11**).

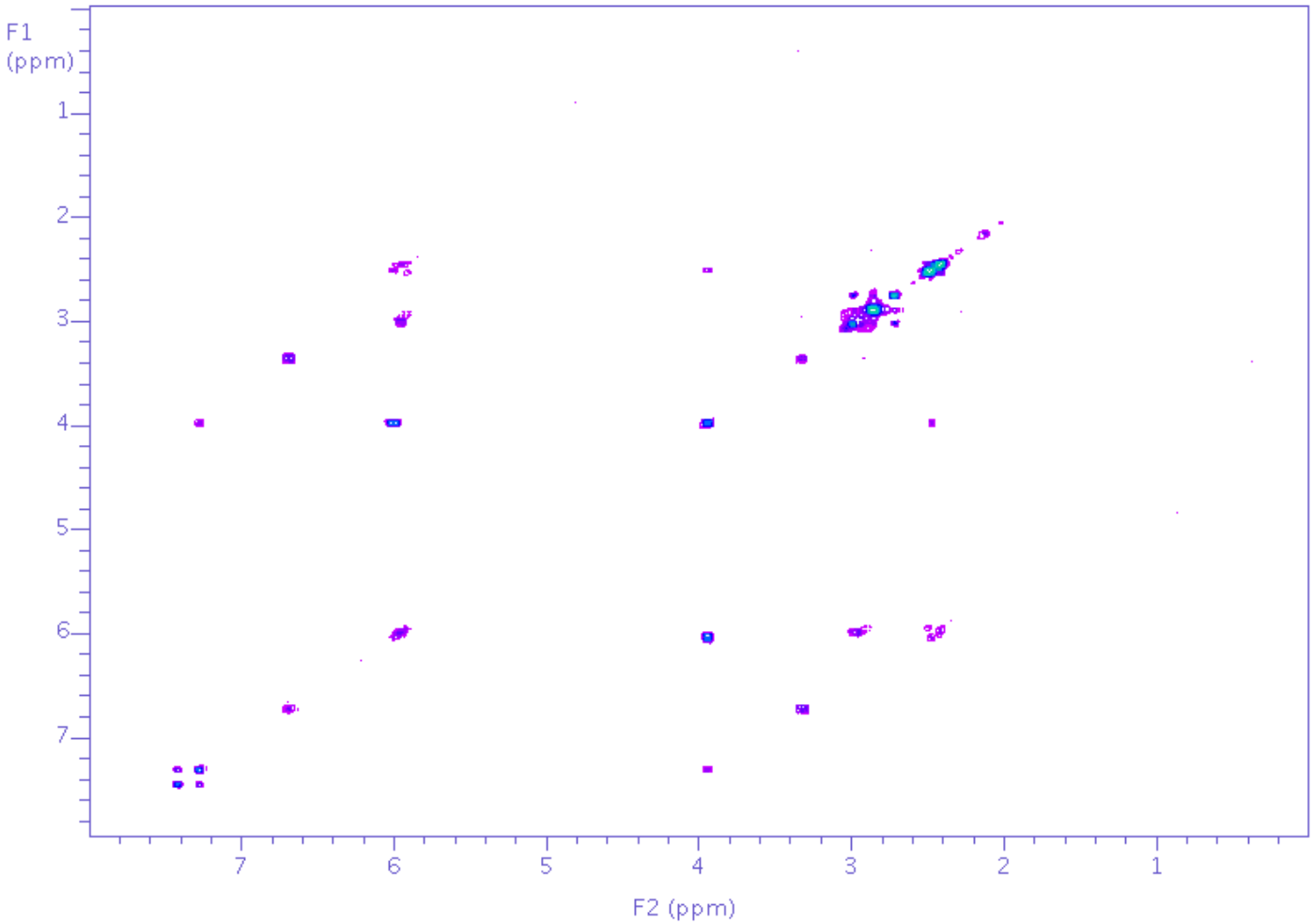


Figure S35. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak I (14.70 min) (compound **11**).

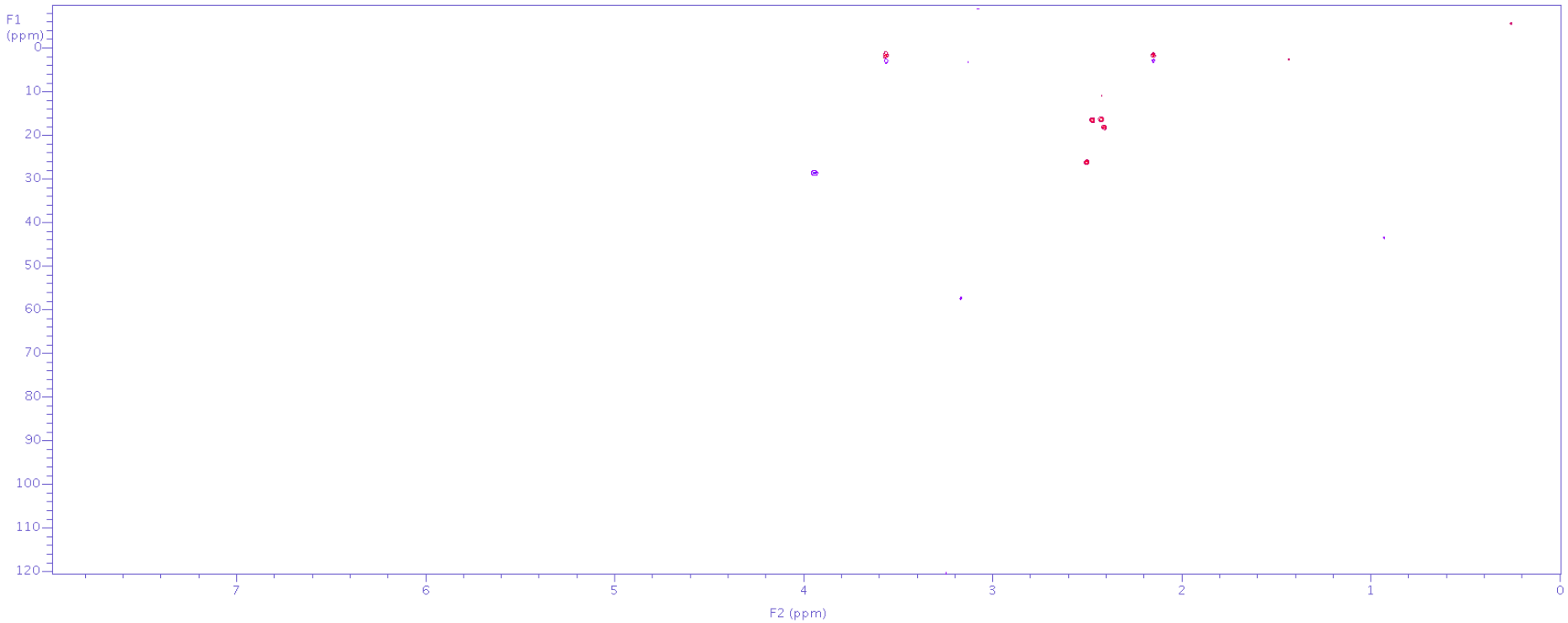


Figure S36. gHSQCAD NMR spectrum (from stop-flow HPLC-NMR) of peak I (14.70 min) (compound **11**).

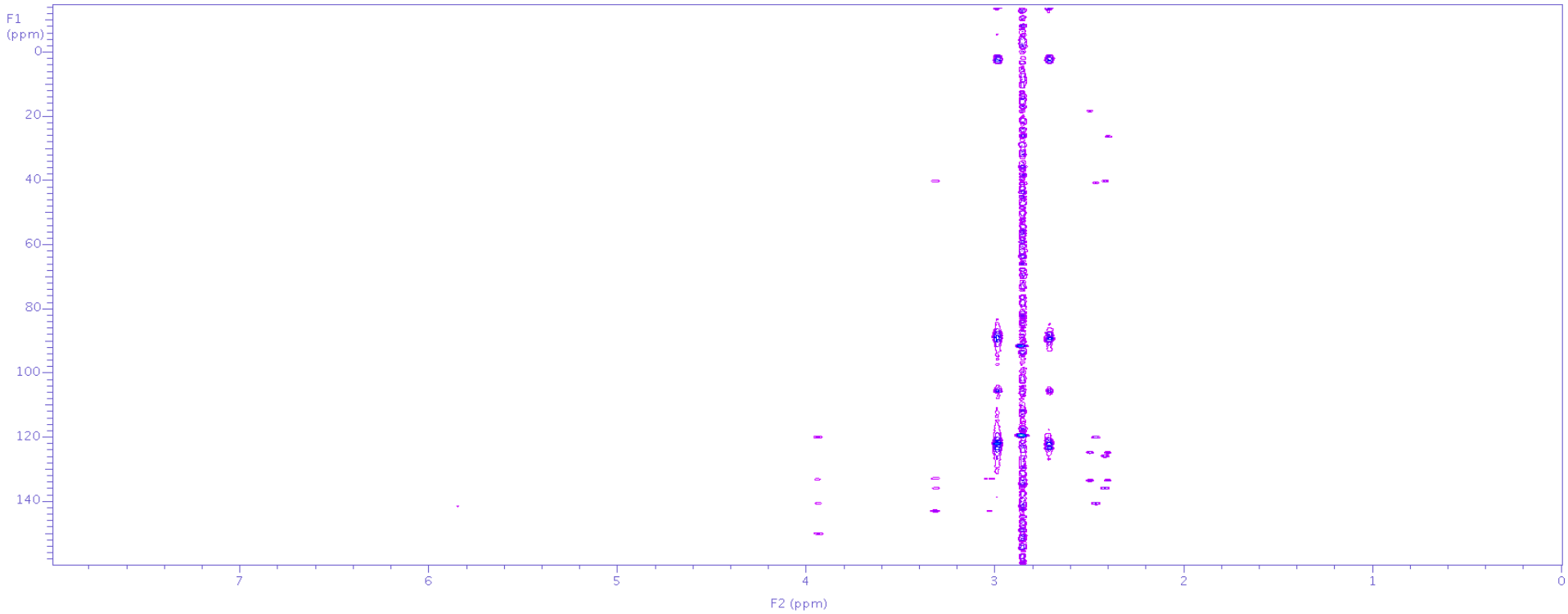


Figure S37. gHMBCAD NMR spectrum (from stop-flow HPLC-NMR) of peak I (14.70 min) (compound **11**).

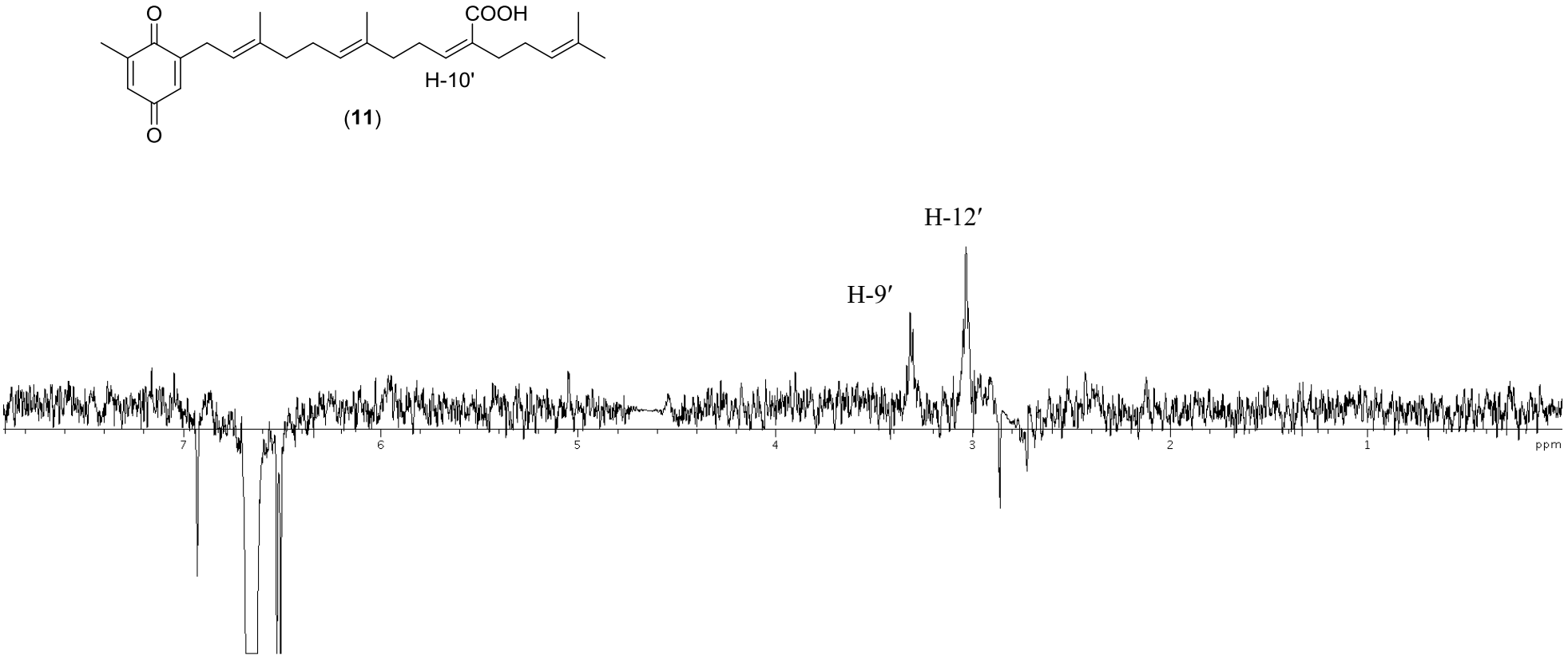


Figure S38. Single irradiation nOe NMR spectrum (from stop-flow HPLC-NMR) of peak I (compound **11**) showing the irradiation of δ_H 6.69 (H-10′).

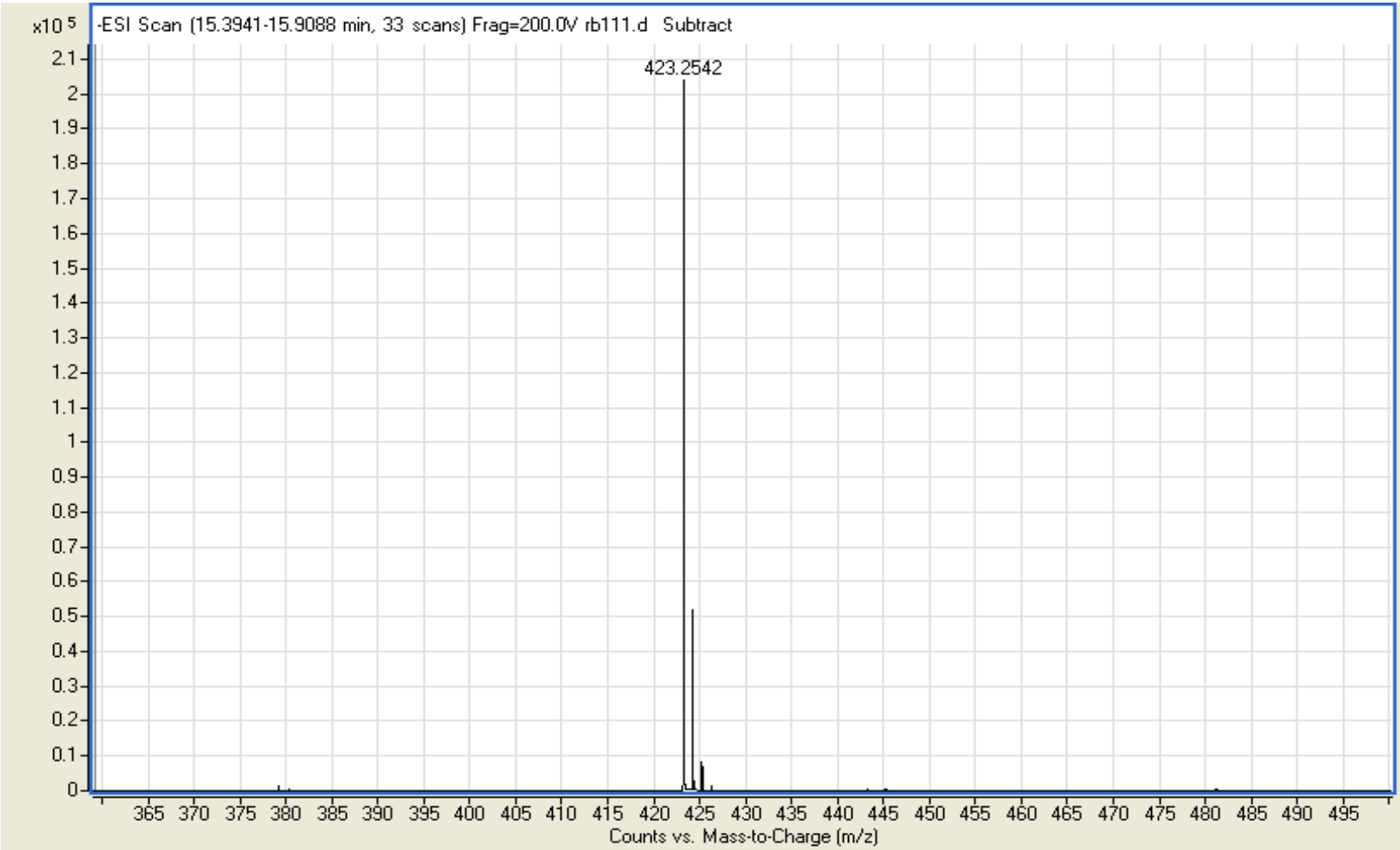


Figure S39. High resolution negative ESI-MS of peak I (14.70 min) (compound **11**) from HPLC-MS.

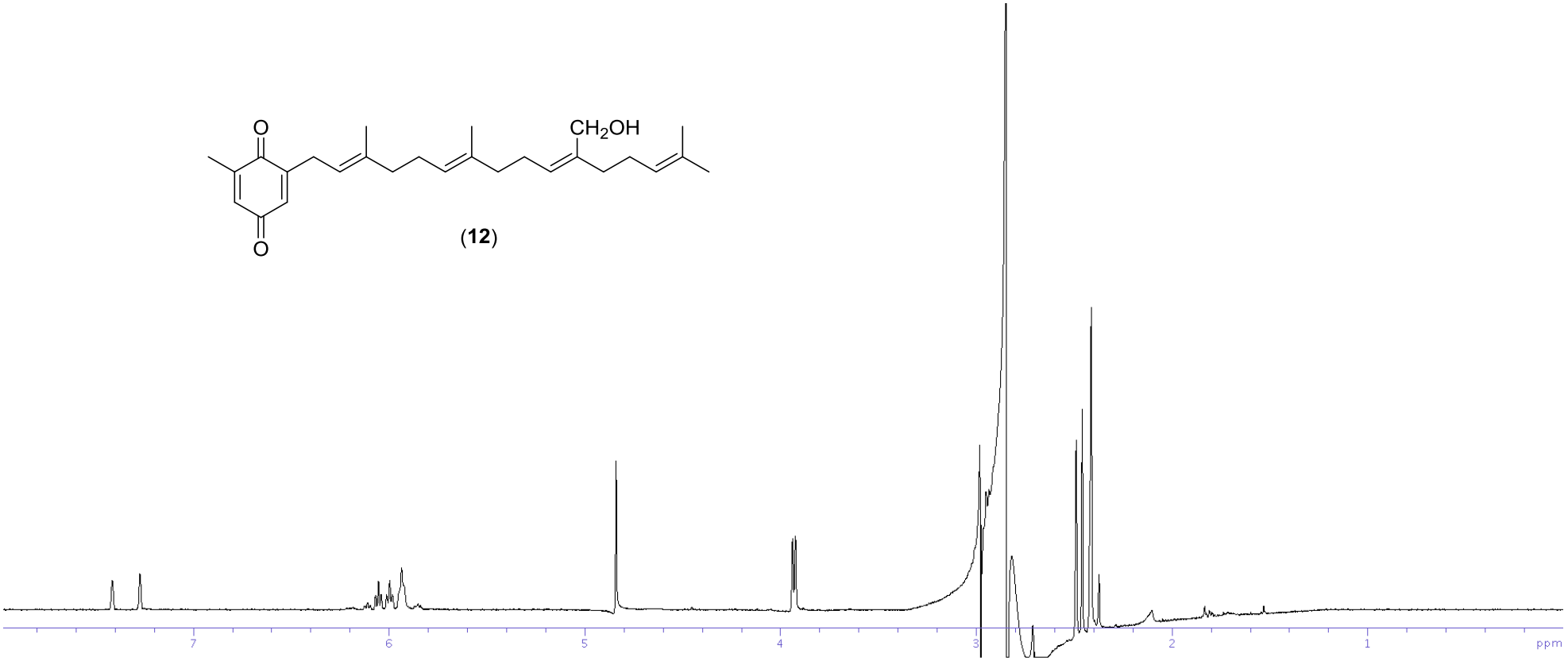


Figure S40. Stop-flow WET1D Proton NMR spectrum of peak J (18.36 min) (compound **12**).

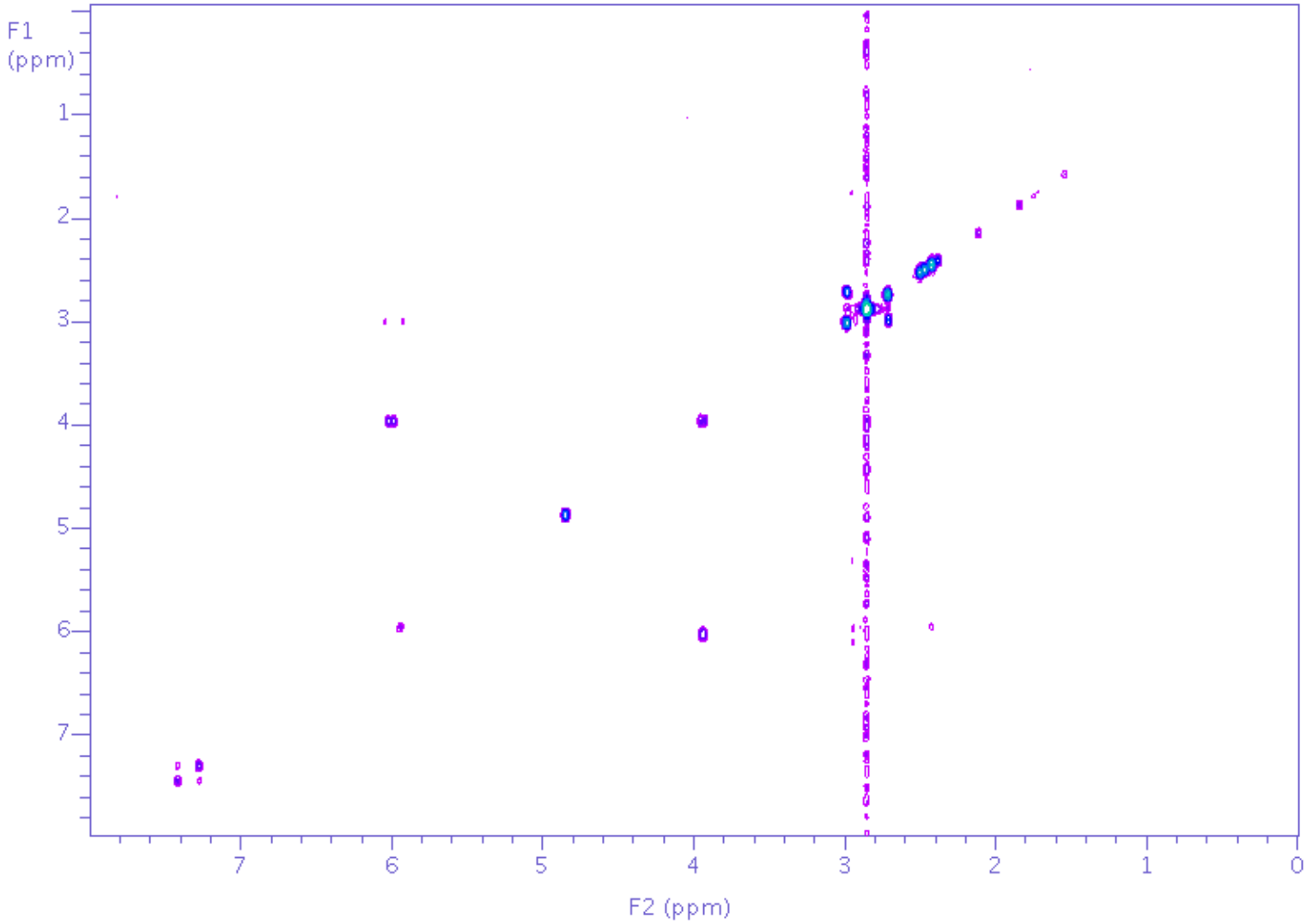


Figure S41. gCOSY NMR spectrum (from stop-flow HPLC-NMR) of peak J (18.36 min) (compound **12**).

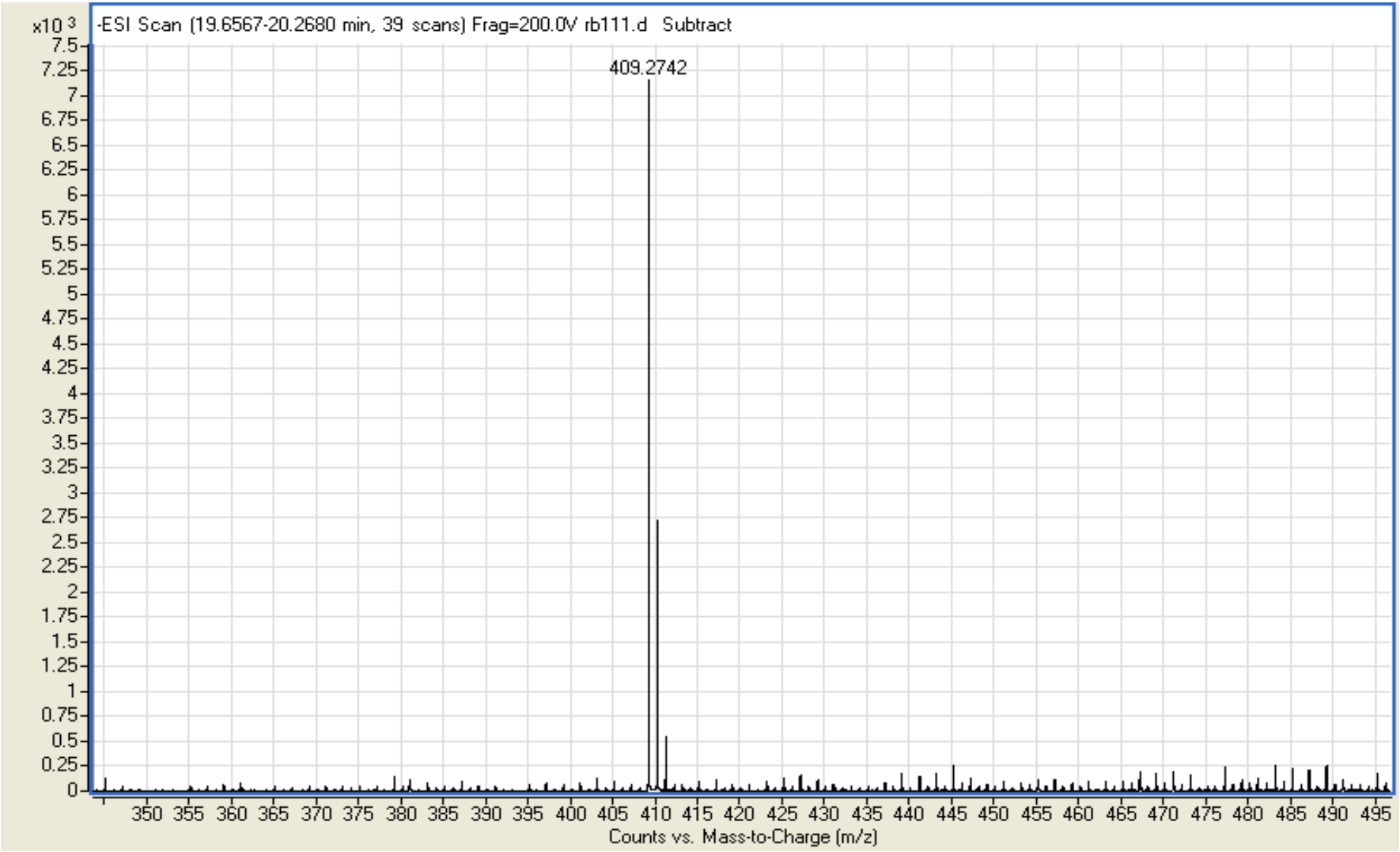


Figure S42. High resolution negative ESI-MS of peak J (18.36 min) (compound **12**) from HPLC-MS.

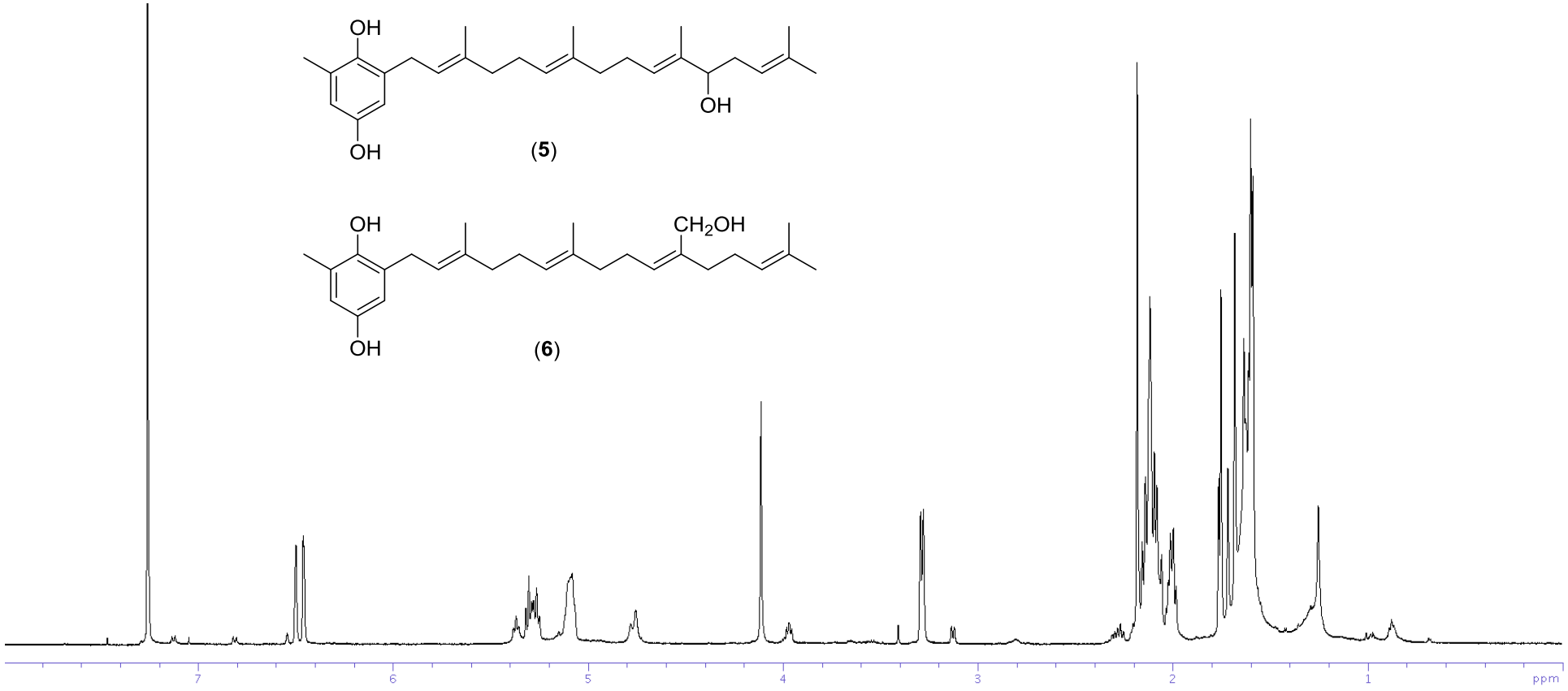


Figure S43. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of paradoxhydroquinone (**5**) and 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**) mixture.

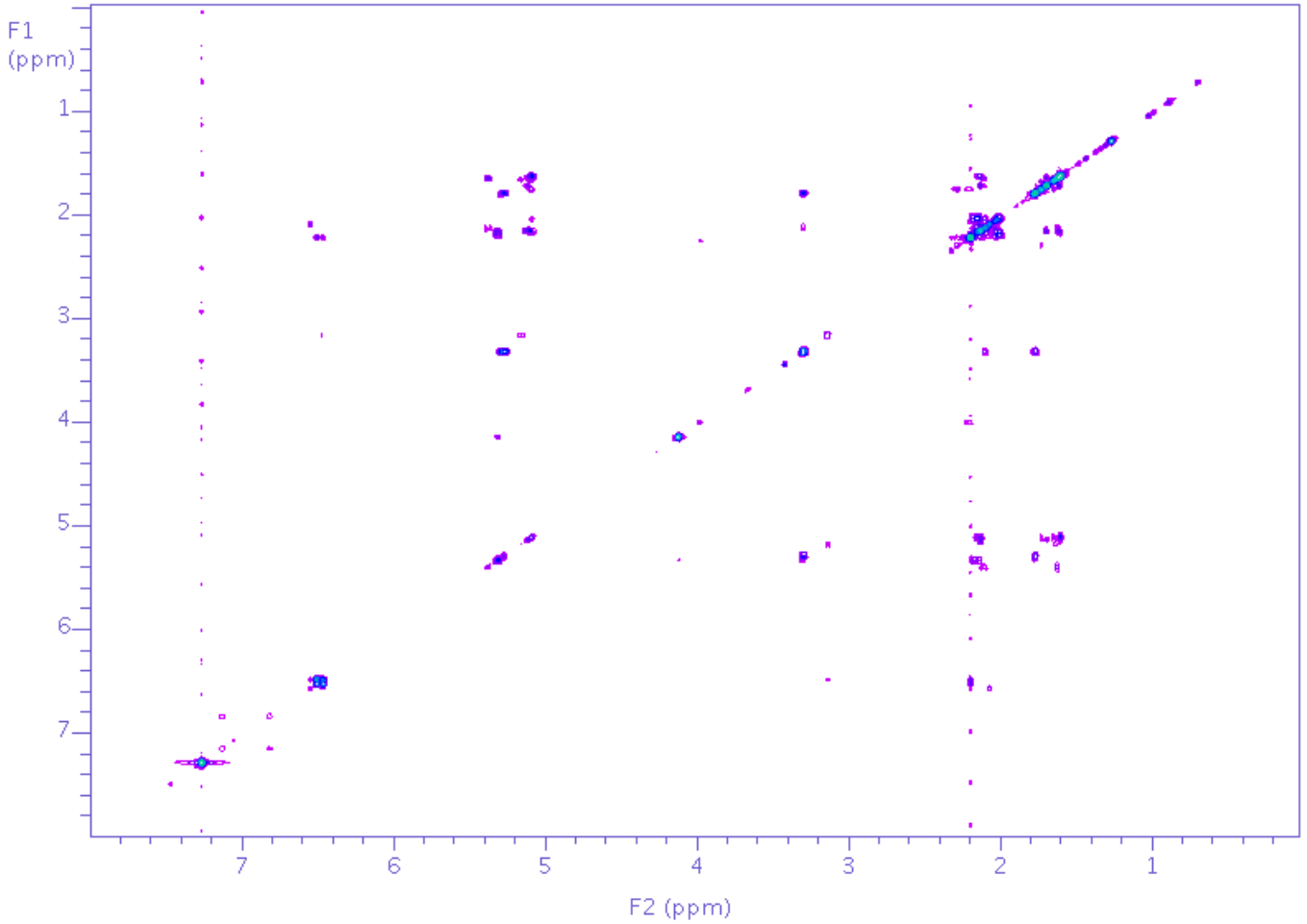


Figure S44. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of paradoxhydroquinone (**5**) and 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**) mixture.

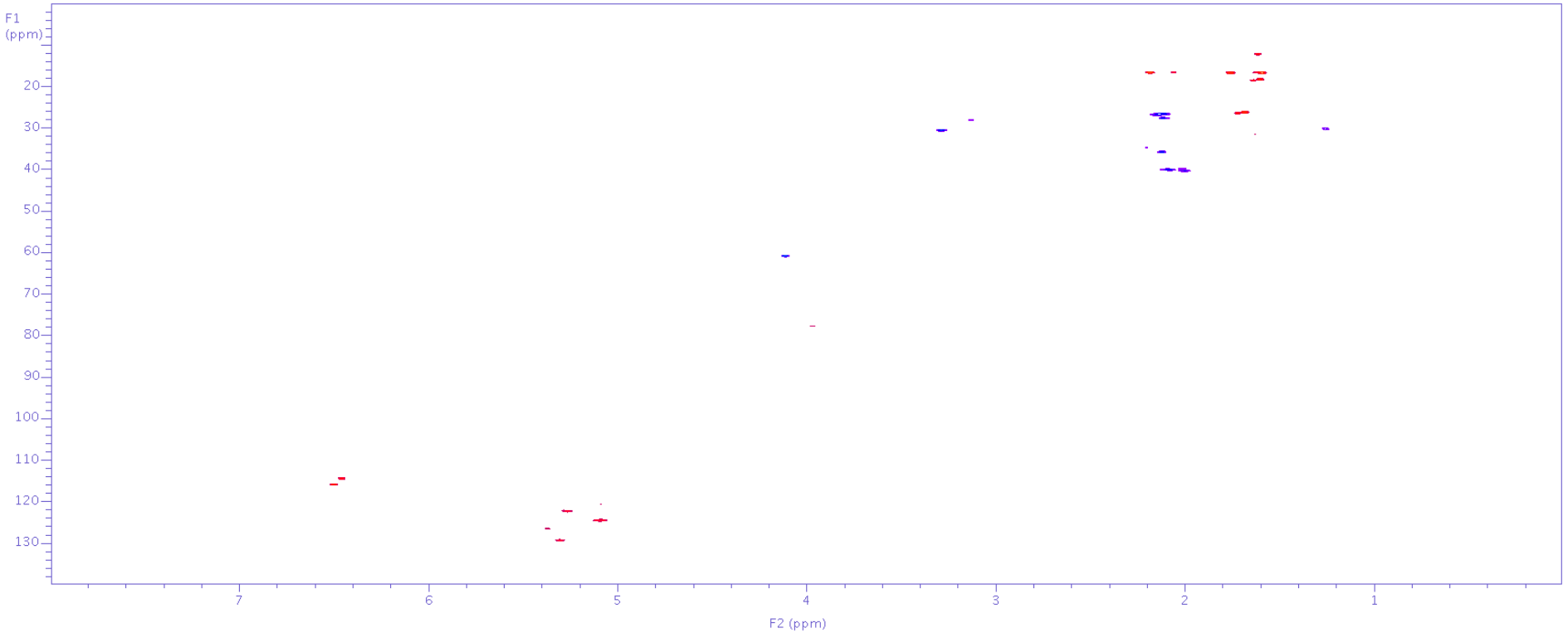


Figure S45. gHSQCAD NMR spectrum (500 MHz, $CDCl_3$) of paradoxhydroquinone (**5**) and 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**) mixture.

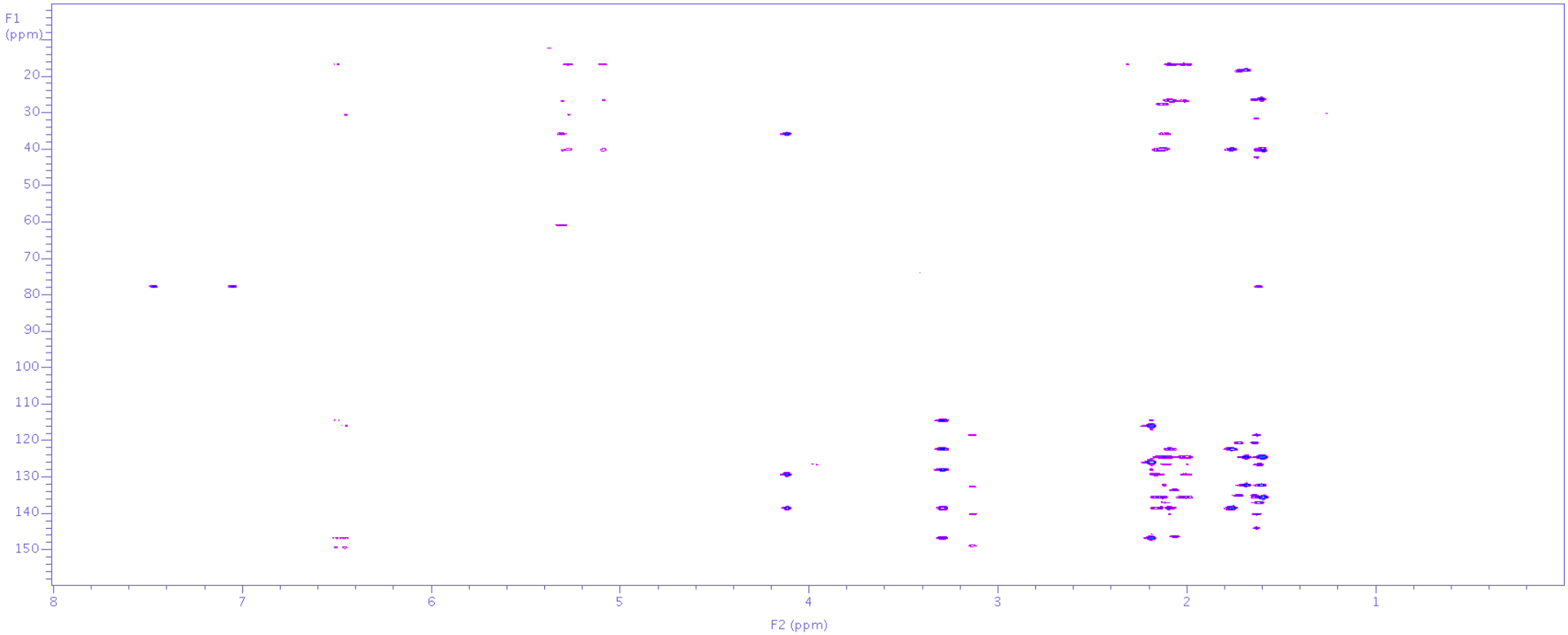


Figure S46. gHMBCAD NMR spectrum (500 MHz, $CDCl_3$) of paradoxhydroquinone (**5**) and 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**) mixture.

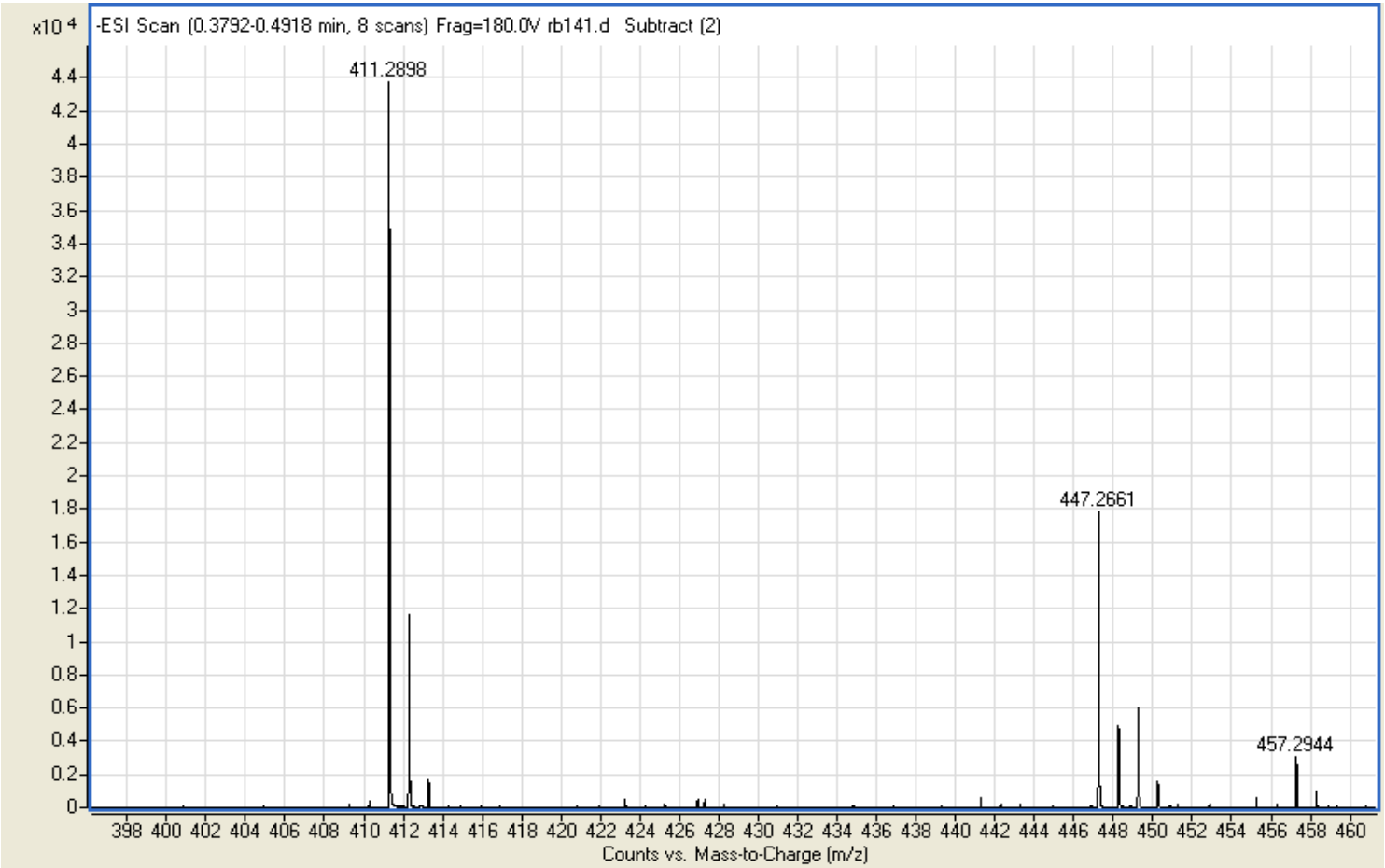


Figure S47. High resolution negative ESI-MS of paradoxhydroquinone (**5**) and 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**) mixture.

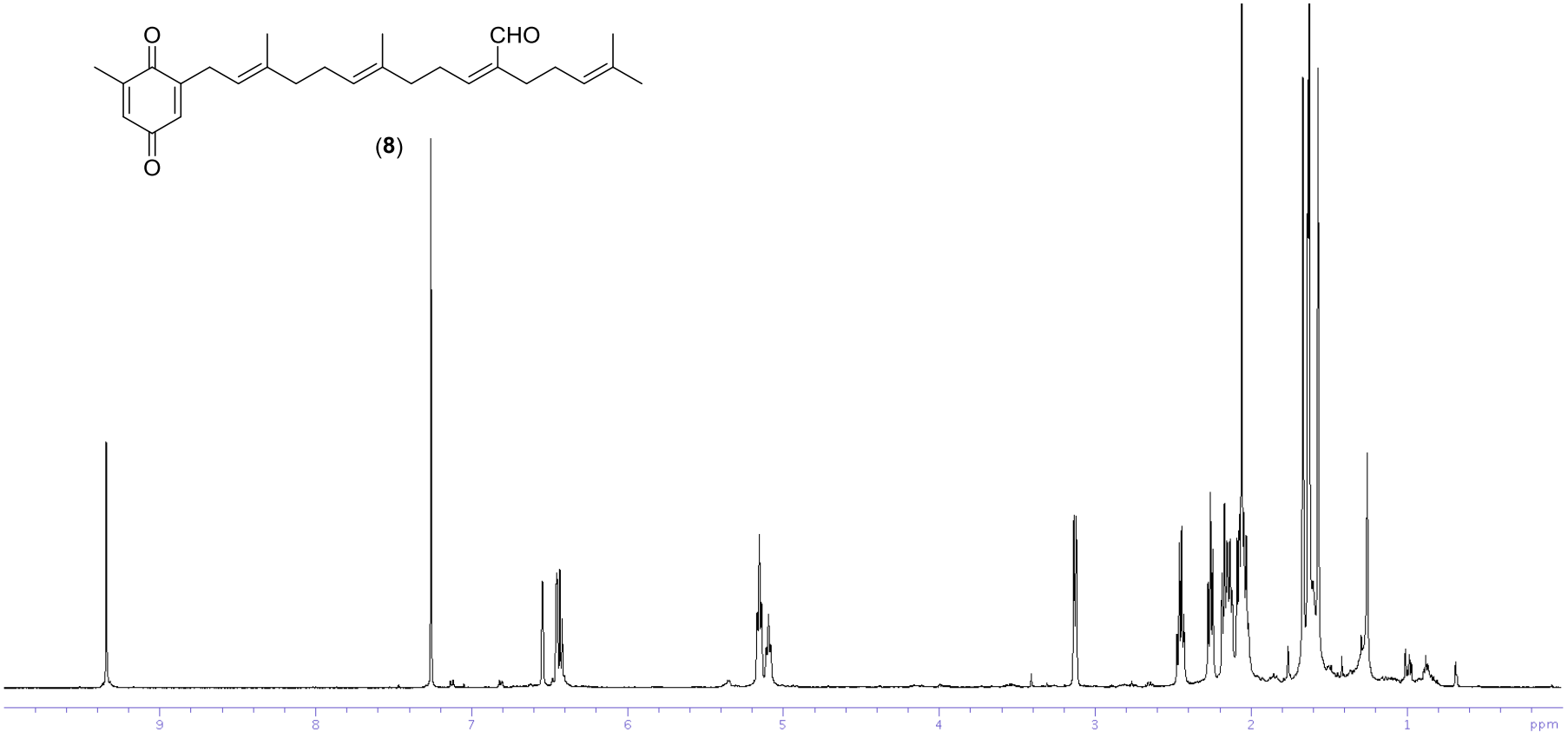


Figure S48. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of sargaquinal (**8**).

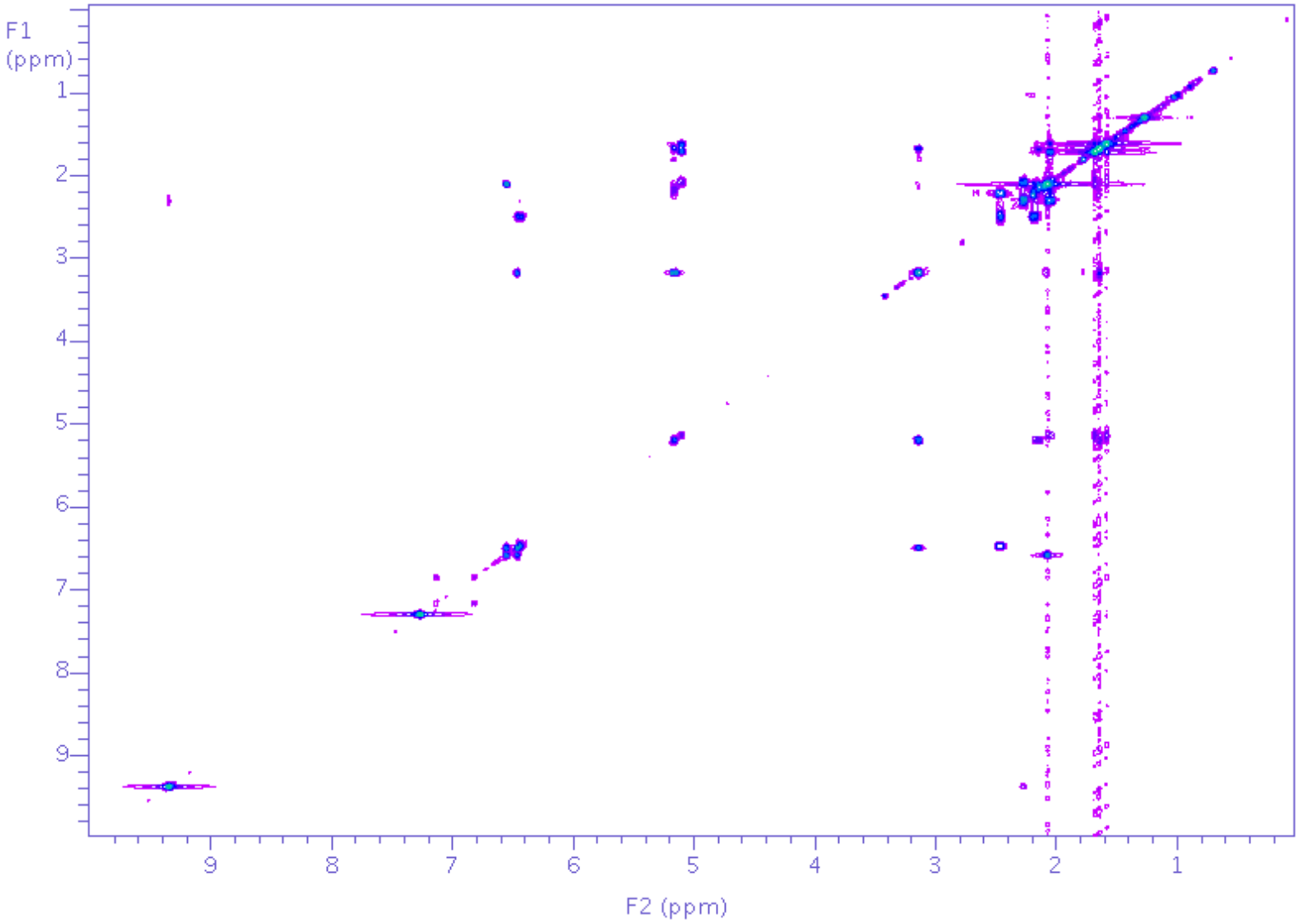


Figure S49. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of sargaquinal (**8**).

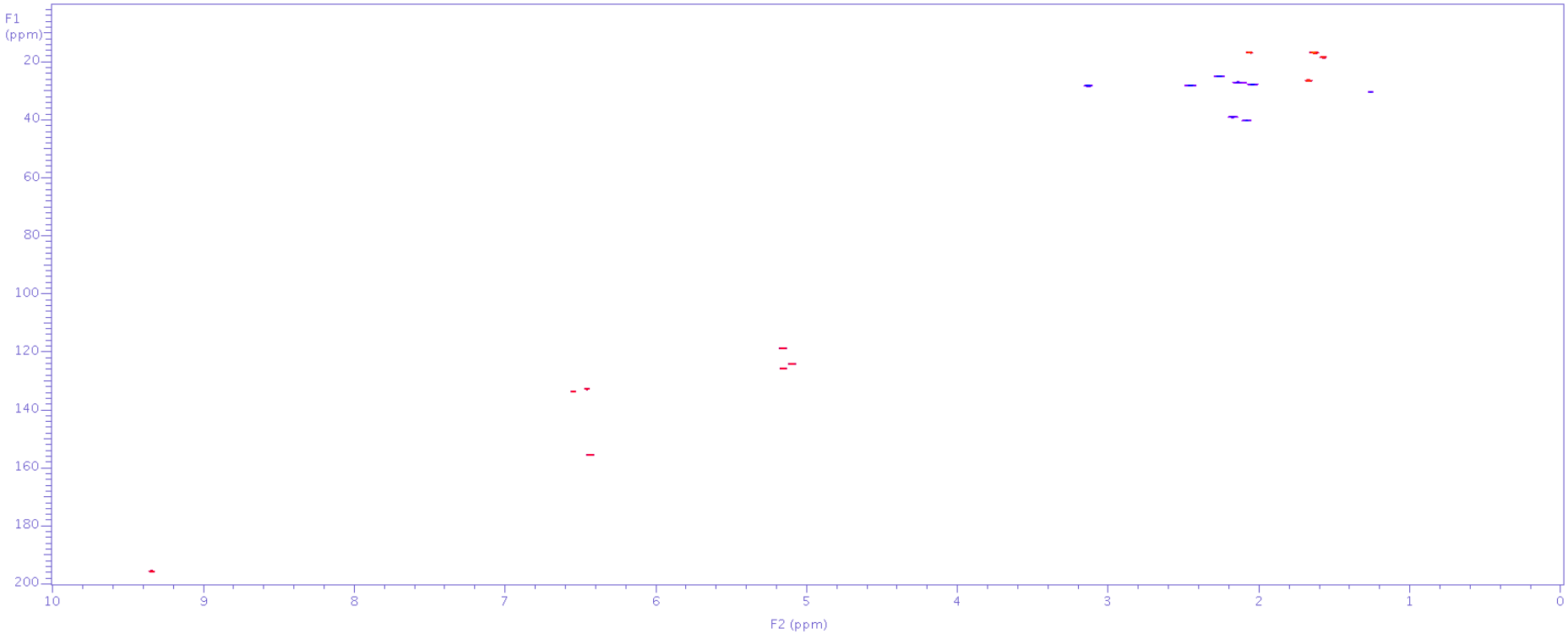


Figure S50. gHSQCAD NMR spectrum (500 MHz, $CDCl_3$) of sargaquinal (8).

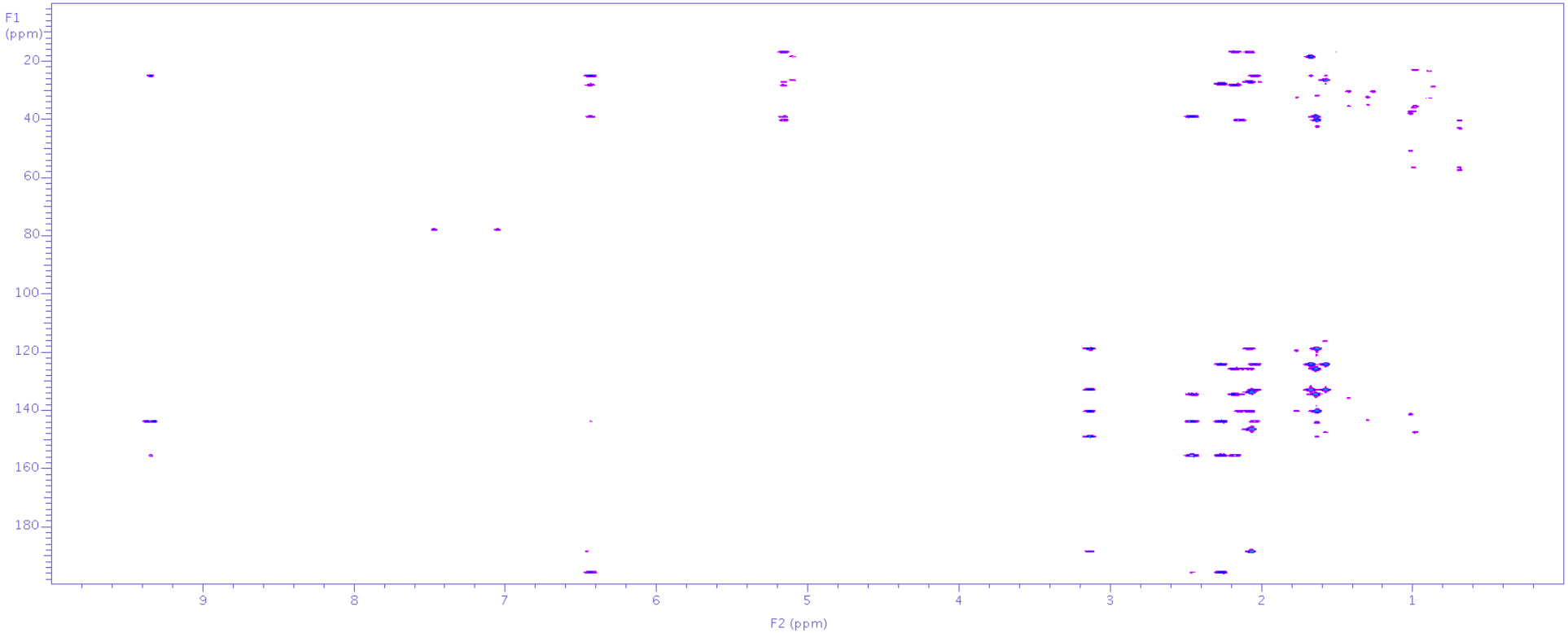


Figure S51. gHMBCAD NMR spectrum (500 MHz, $CDCl_3$) of sargaquinal (**8**).

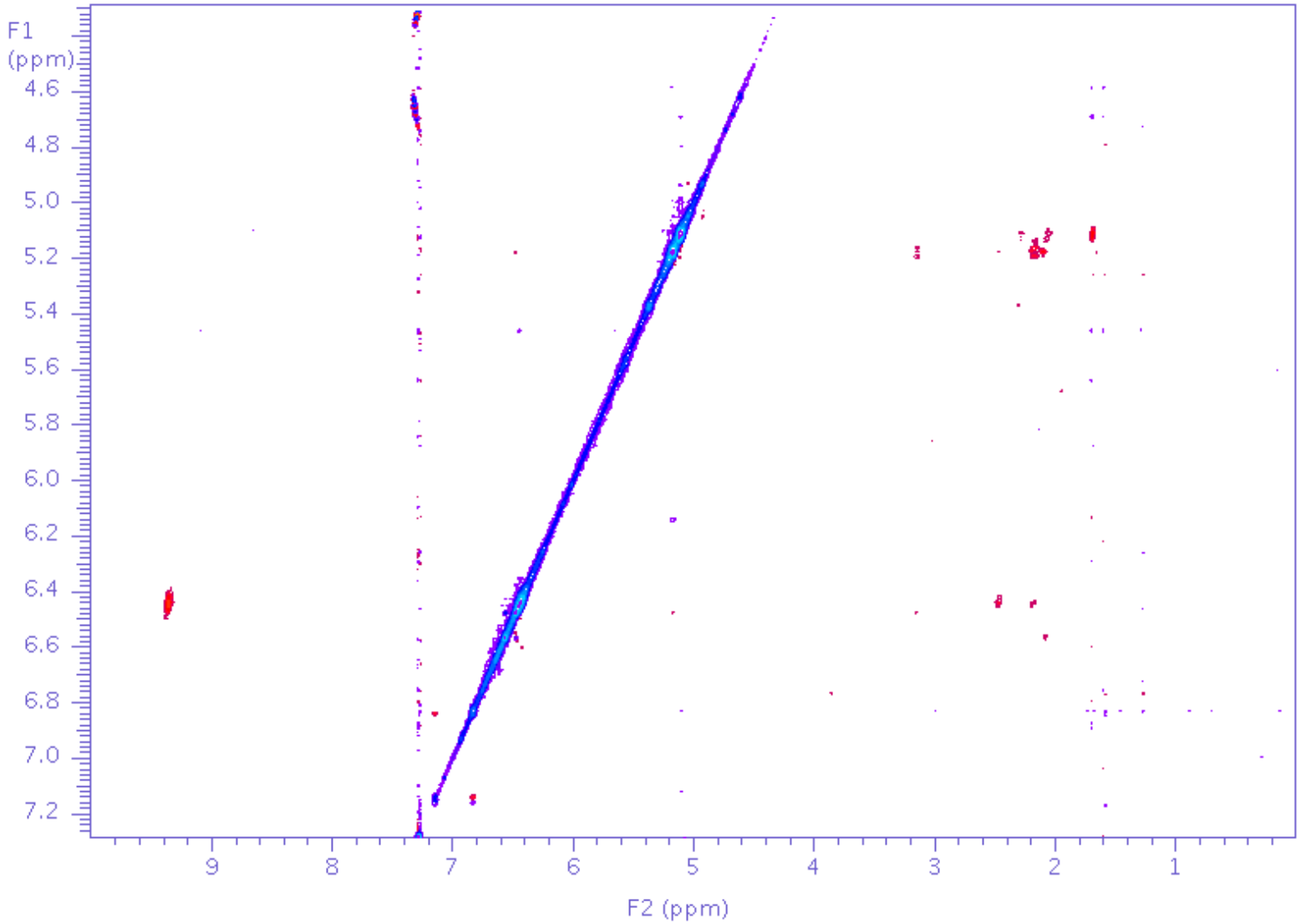


Figure S52. Band selective NOESY NMR spectrum (500 MHz, $CDCl_3$) of sargaquinal (**8**) showing the irradiation between δ_H 4.15-6.40.

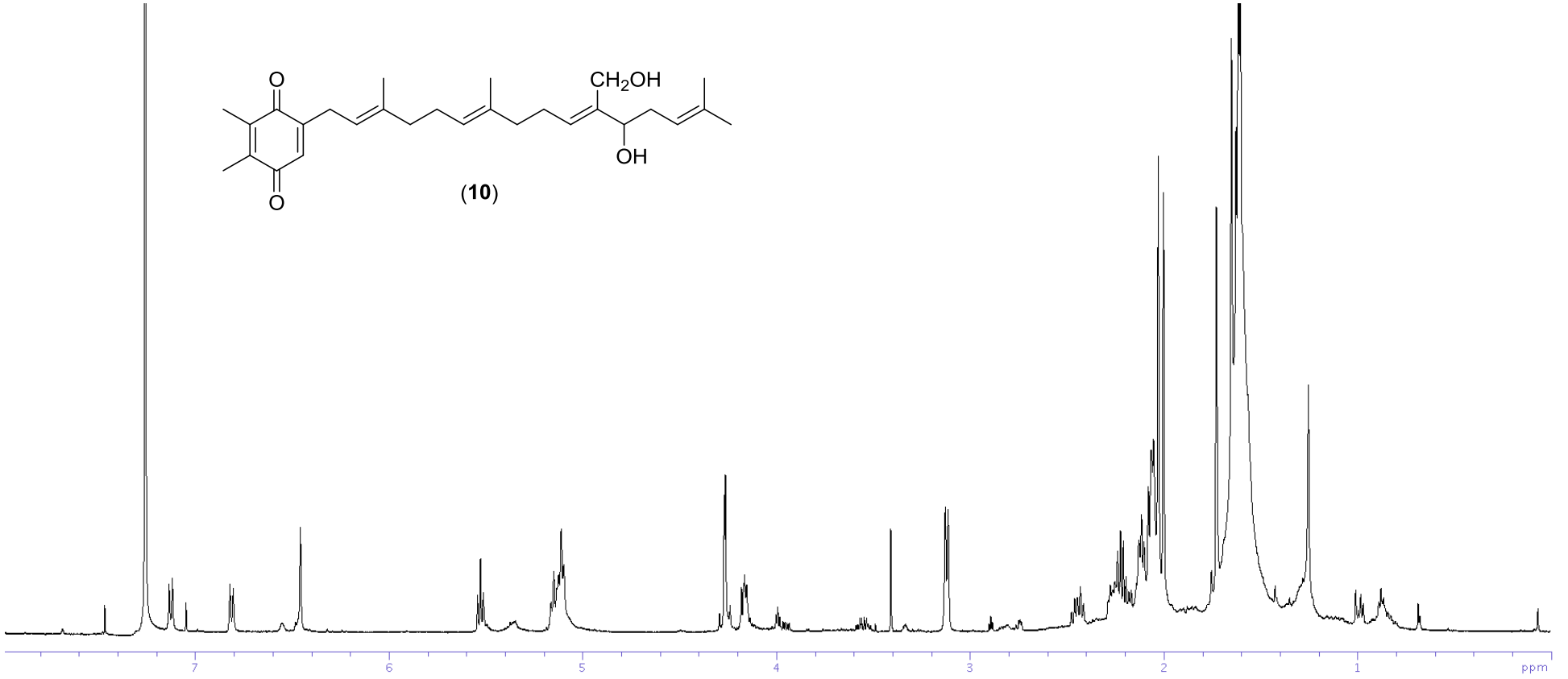


Figure S53. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of paradoxquinone (**10**).

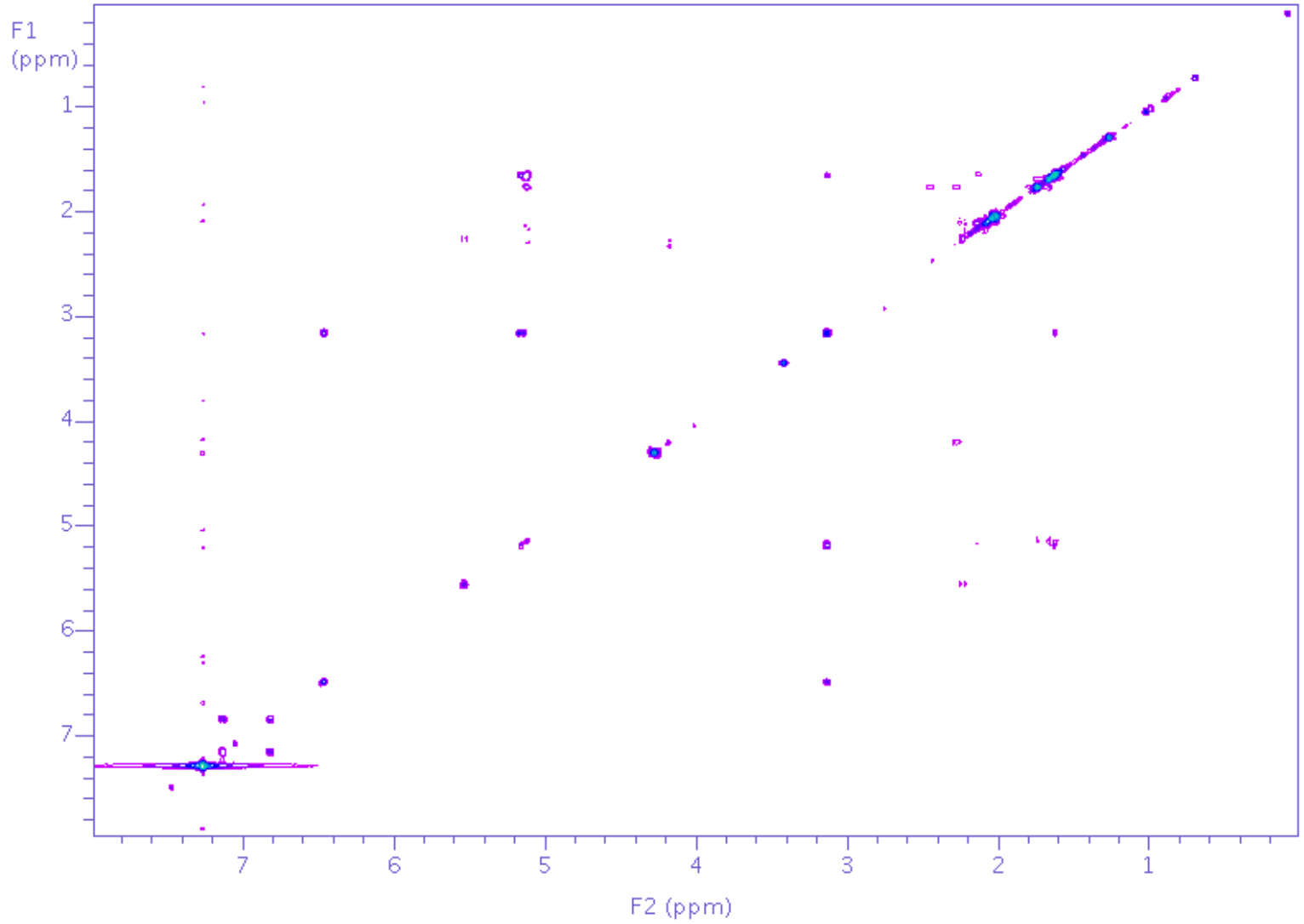


Figure S54. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of paradoxquinone (**10**).

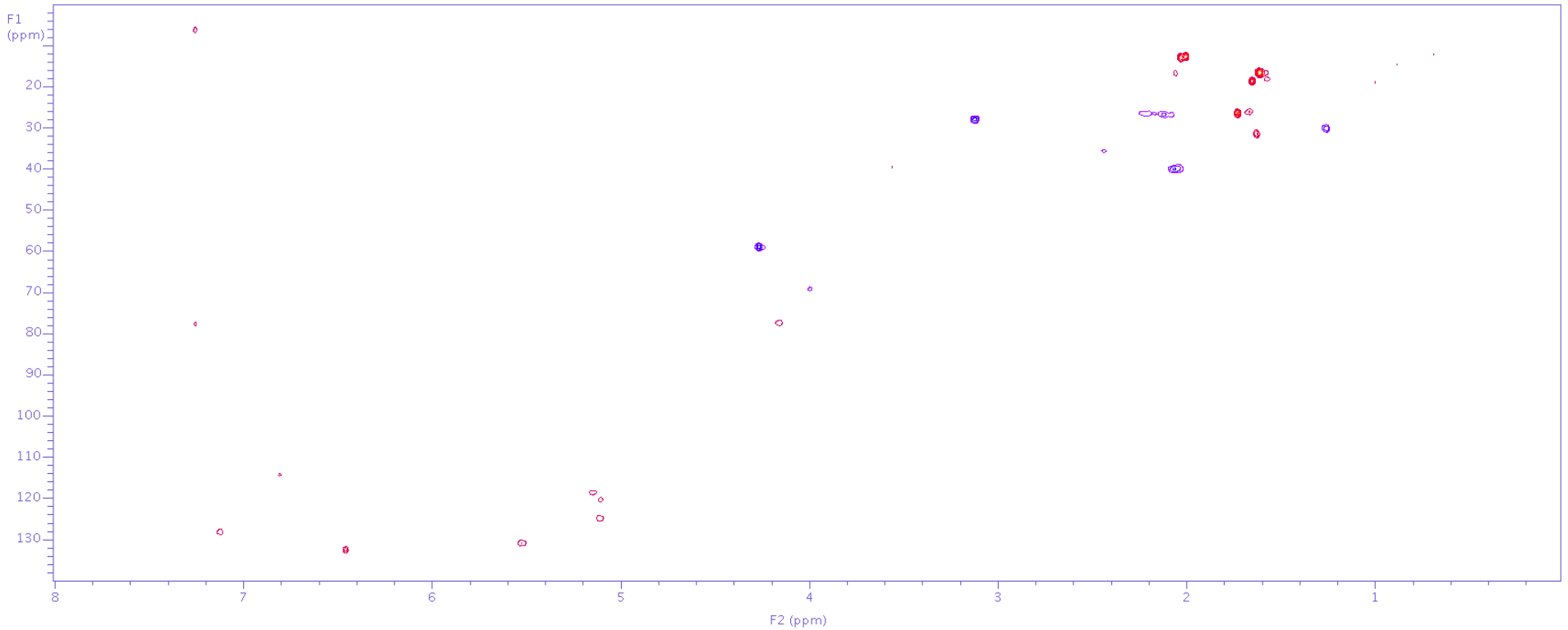


Figure S55. gHSQCAD NMR spectrum (500 MHz, $CDCl_3$) of paradoxquinone (**10**).

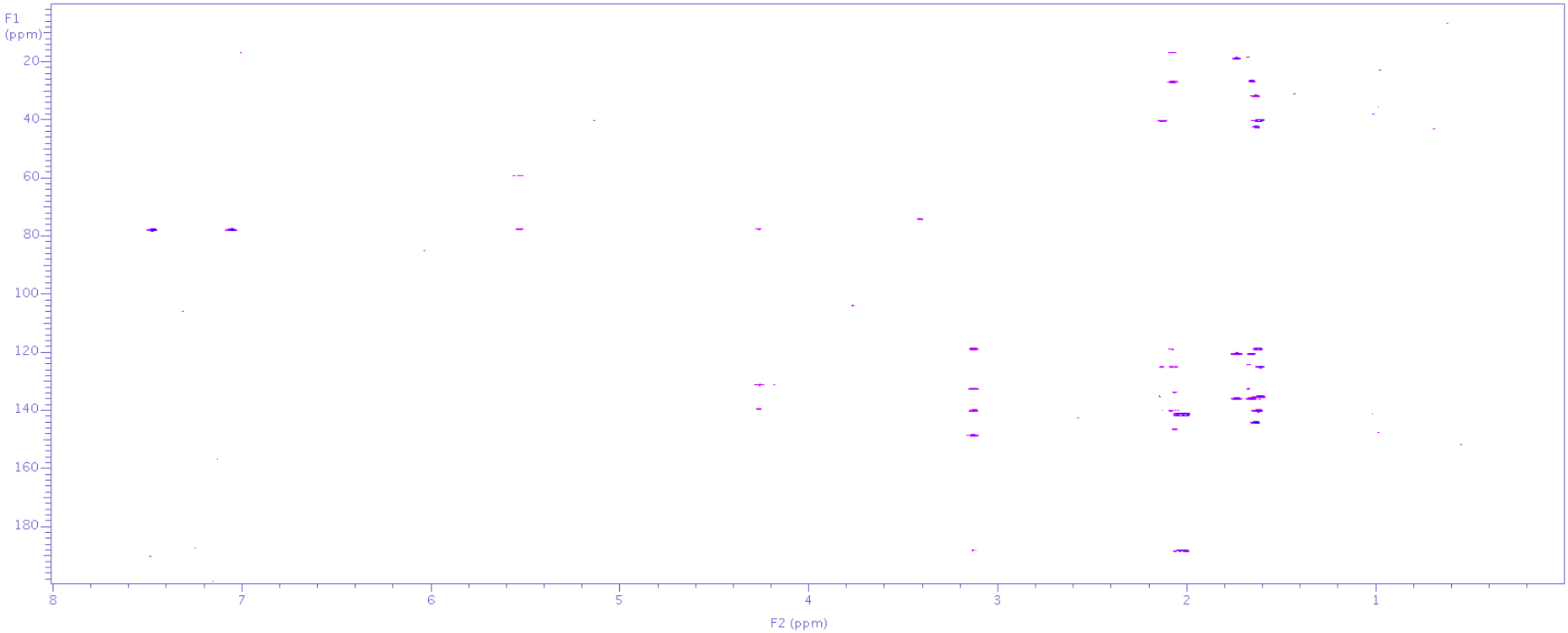


Figure S56. gHMBCAD NMR spectrum (500 MHz, $CDCl_3$) of paradoxquinone (**10**).

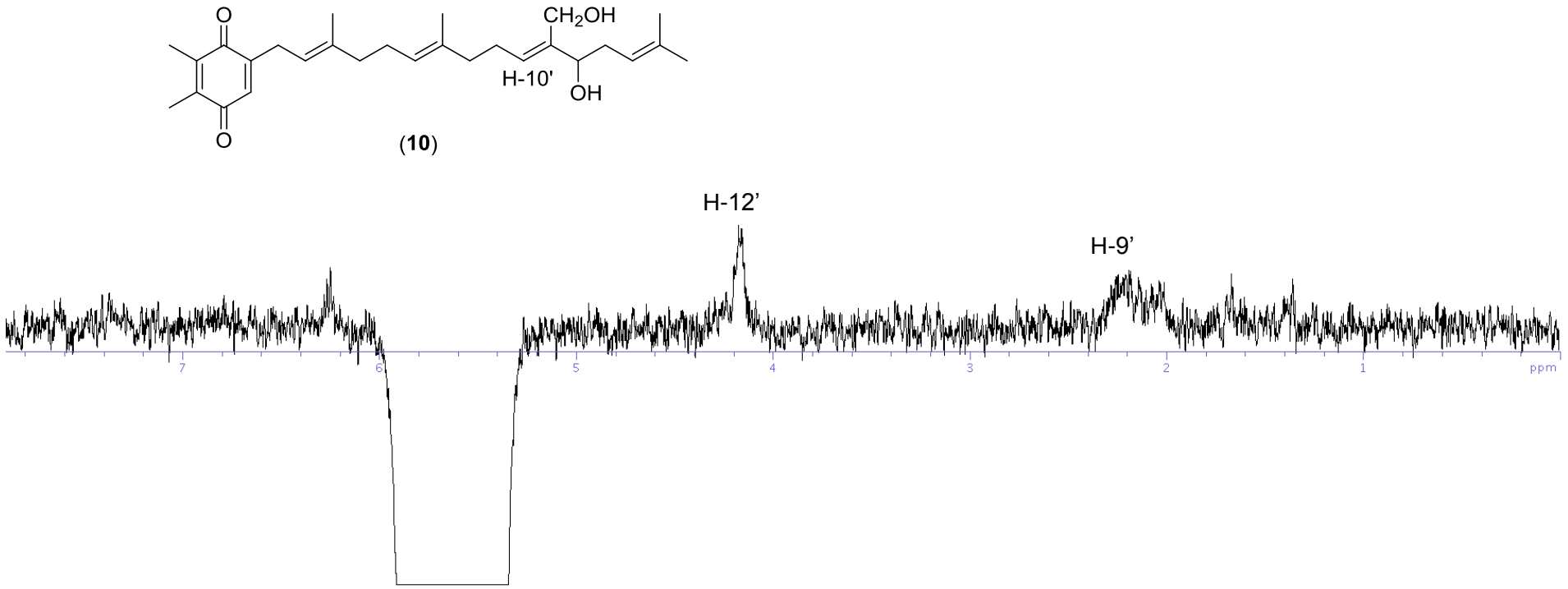


Figure S57. Single irradiation nOe NMR spectrum (500 MHz, $CDCl_3$) of paradoxquinone (**10**) showing the irradiation of δ_H 5.53 (H-10′).

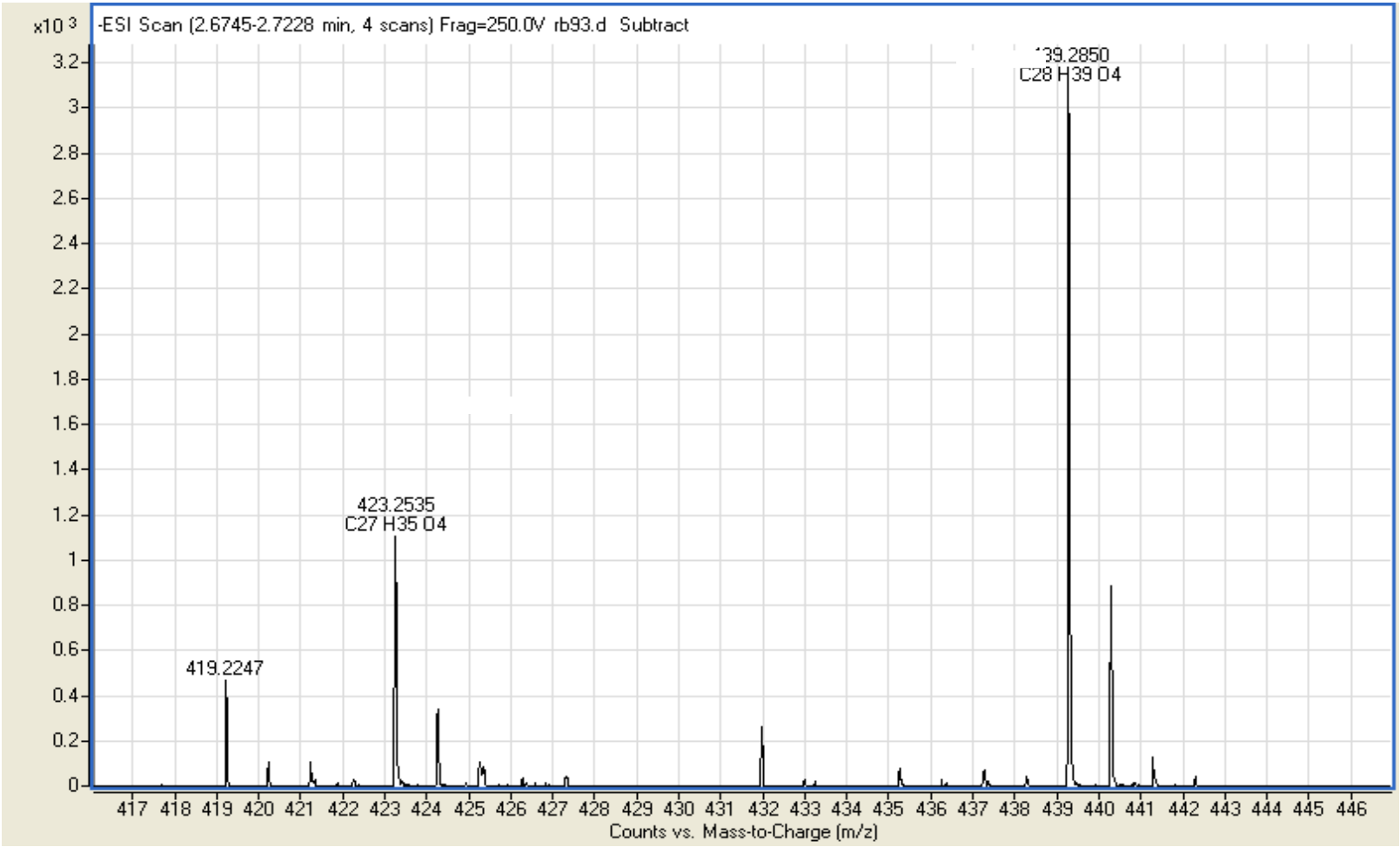


Figure S58. High resolution negative ESI-MS of paradoxquinone (**10**).

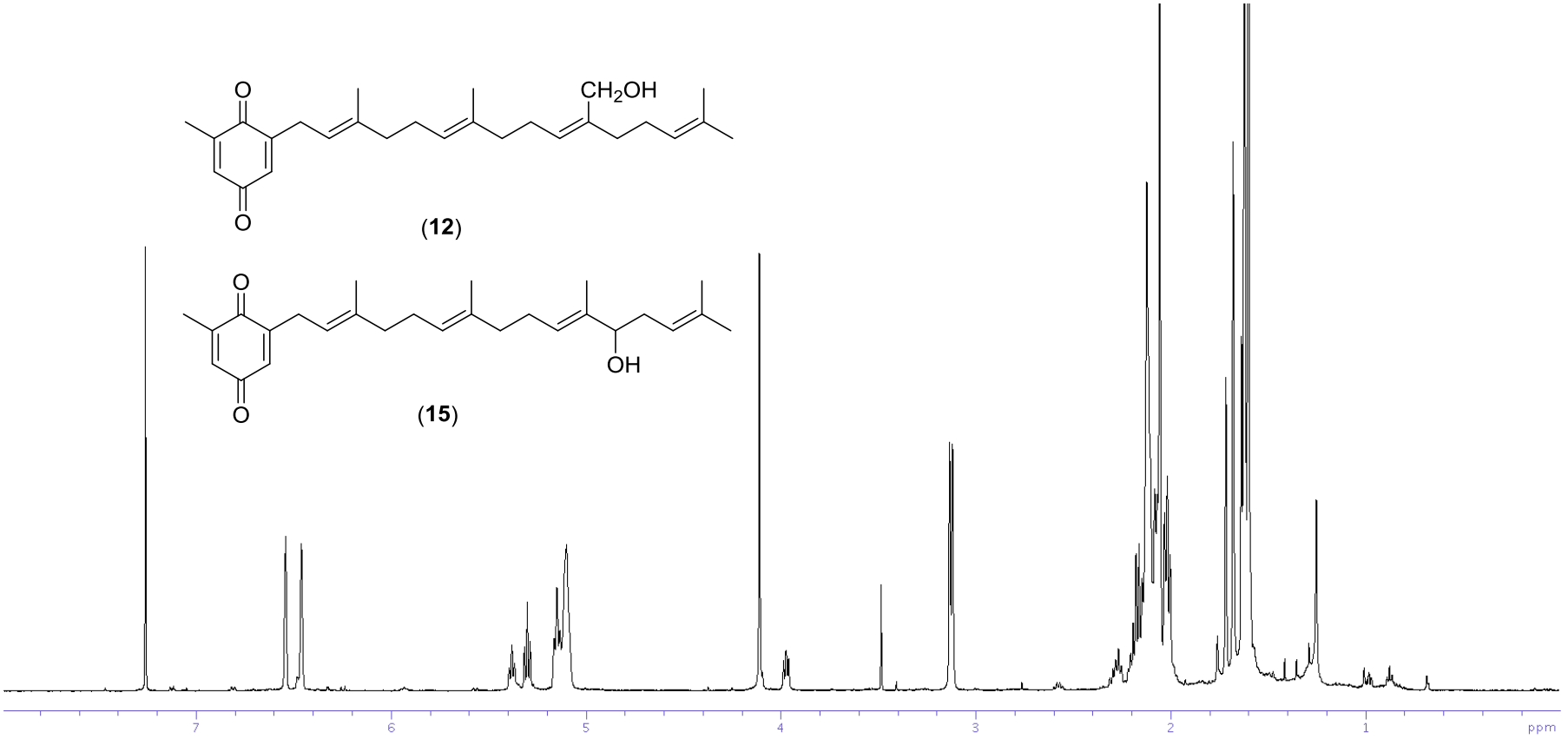


Figure S59. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture.

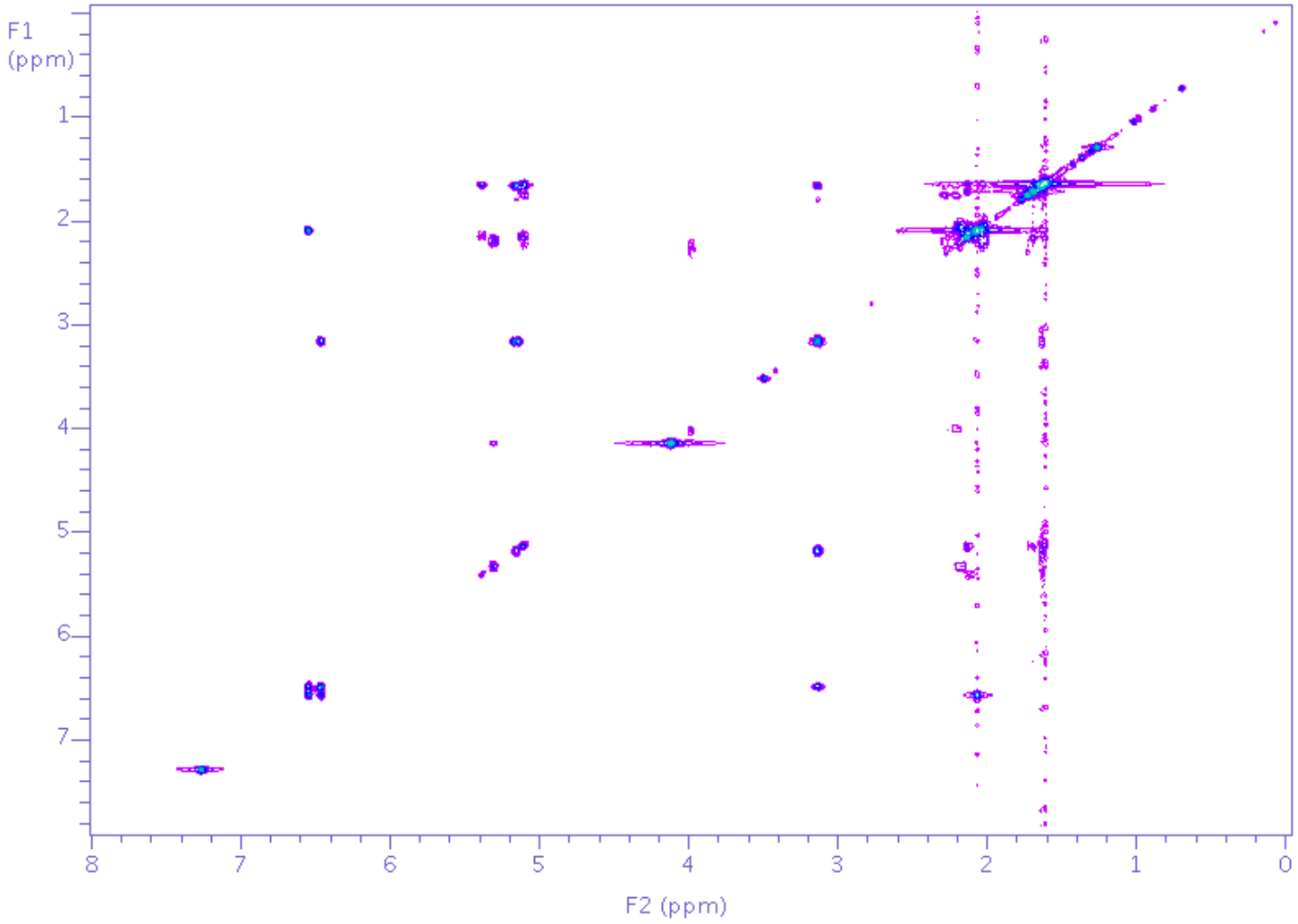


Figure S60. gCOSY NMR spectrum (500 MHz, $CDCl_3$) of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture.

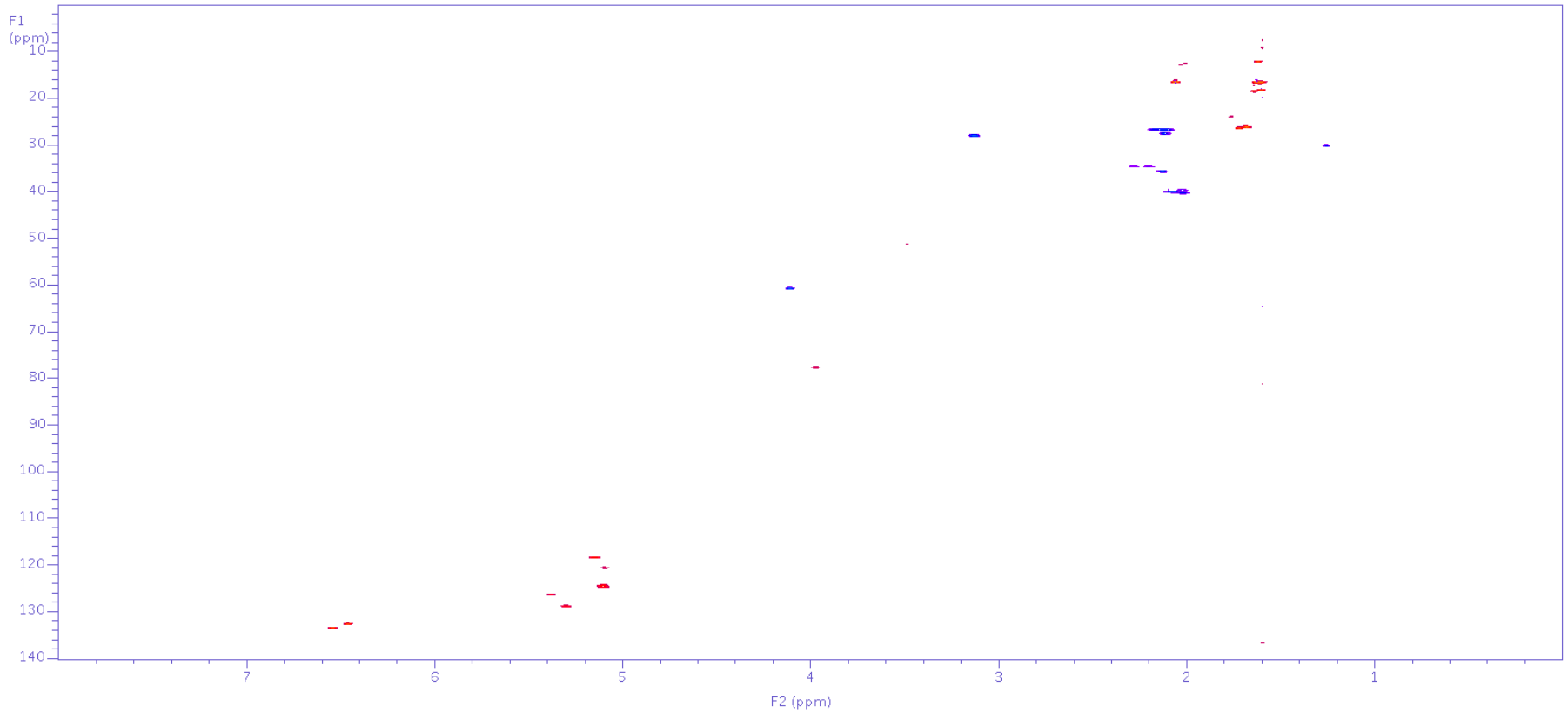


Figure S61. gHSQCAD NMR spectrum (500 MHz, $CDCl_3$) of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture.

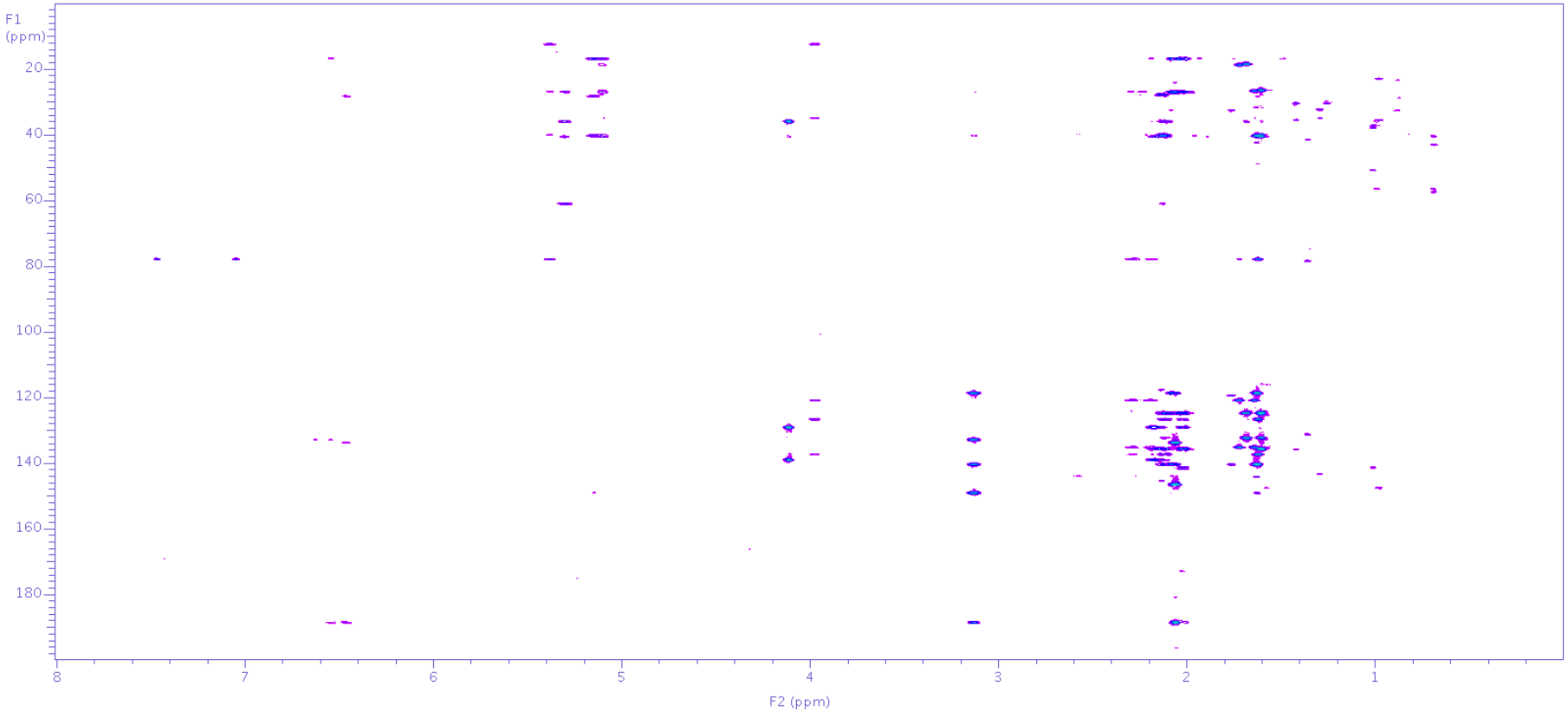


Figure S62. gHMBCAD NMR spectrum (500 MHz, $CDCl_3$) of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture.

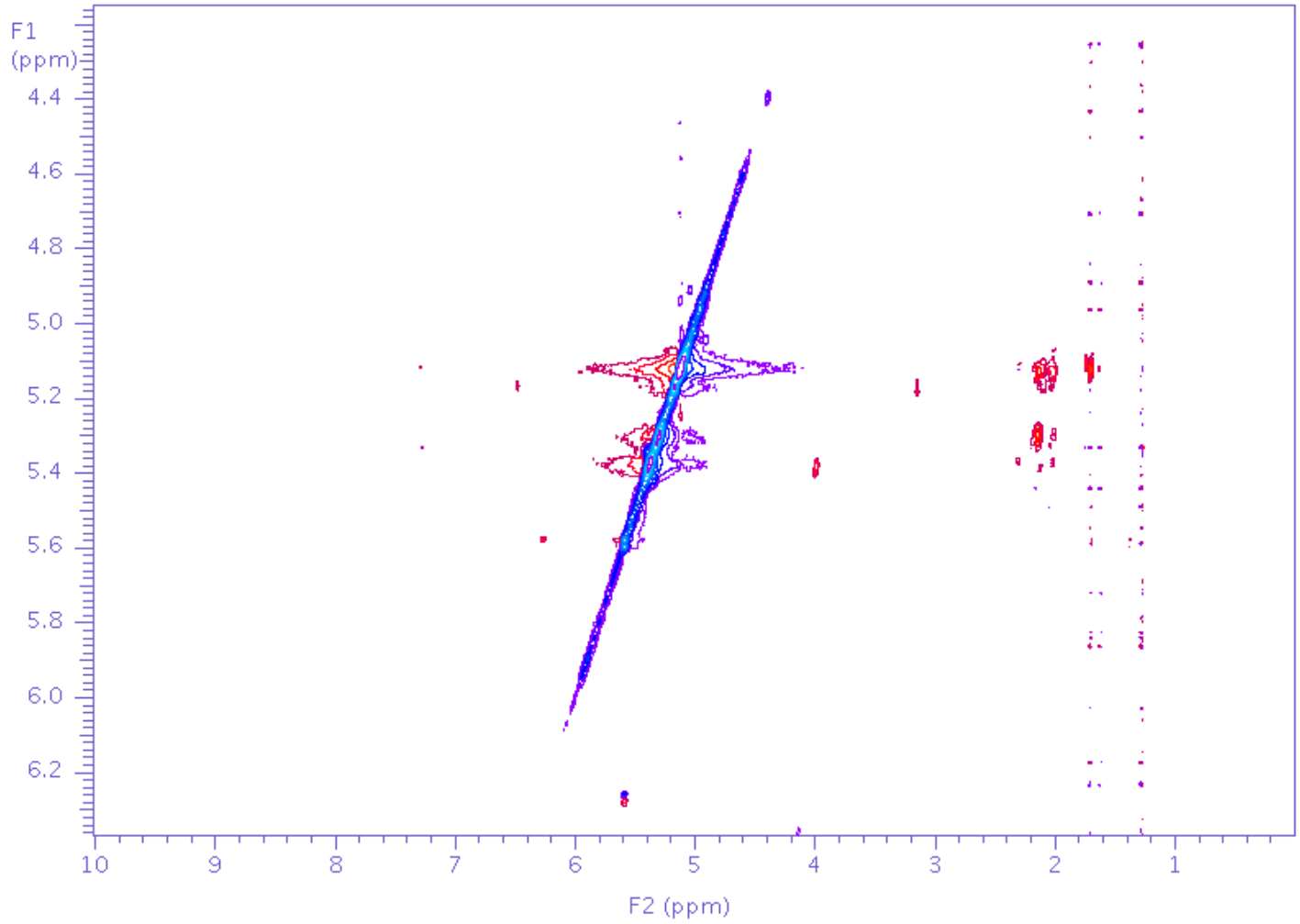


Figure S63. Band selective NOESY NMR spectrum (500 MHz, $CDCl_3$) of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture showing the irradiation between δ_H 4.30–7.30.

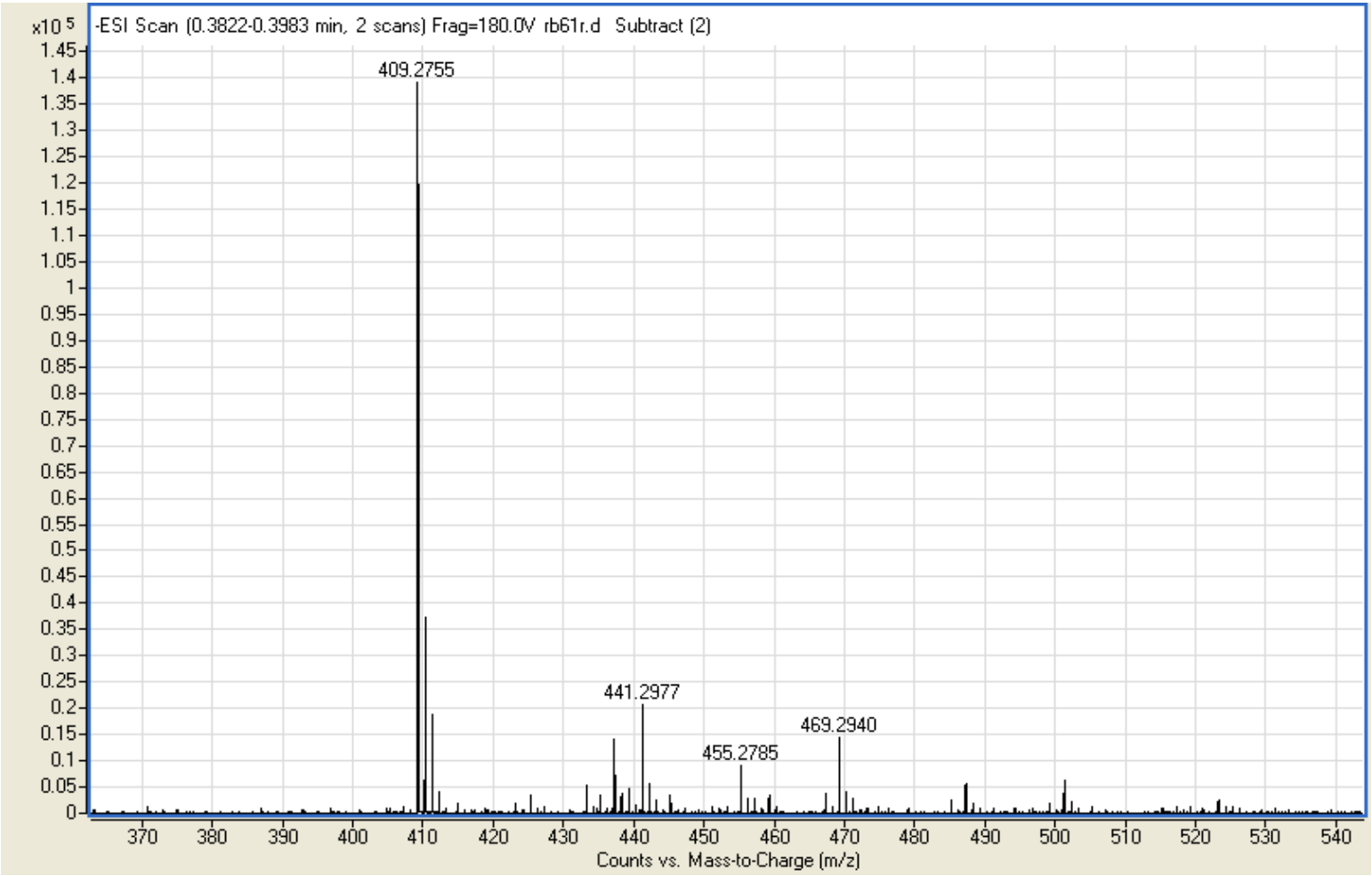
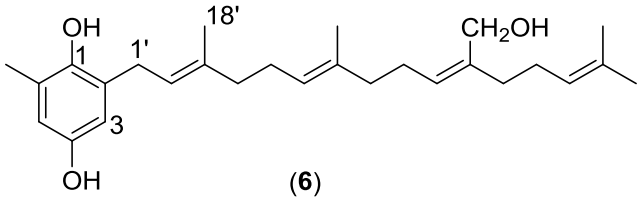


Figure S64. High resolution negative ESI-MS of (2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**) and paradoxquinone (**15**) mixture.

Table S1. NMR data (500 MHz, $CDCl_3$) of 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzenediol (**6**).

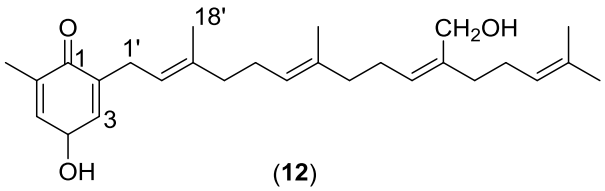


(**6**)

Position	δ_C [a], mult	δ_H (*J* in Hz)	gCOSY	gHMBC
1	146.4, s			
2	127.6, s			
3	114.0, d	6.46, d (2.5)	5, 1′	1, 4, 5, 1′
4	149.0, s			
5	115.5, d	6.50, d (2.5)	3, 7	1, 3, 4, 7
6	125.5, s			
7	16.1, q	2.18, s	5	1, 5, 6
1′	30.0, t	3.28, d (7.0)	3, 2′, 4′ [w], 18′ [w]	1, 2, 3, 2′, 3′
2′	122.0, d	5.26, t (7.0)	1′, 4′, 18′	1′, 4′, 18′
3′	138.1, s			
4′	39.5, t	2.08, m	1′ [w]	5′, 18′
5′	26.1, t	2.13, m		4′, 7′
6′	124.4, d	5.09, m		4′, 5′, 19′
7′	135.1, s			
8′	39.8, t	2.00, m	9′	7′, 9′, 10′ 19′
9′	26.1, t	2.13, m	8′	7′, 10′
10′	128.9, d	5.30, t (7.5)	9′, 20′	8′, 9′, 12′, 20′
11′	138.2, s			
12′	35.2, t	2.12, m		11′, 13′, 14′
13′	27.1, t	2.11, m		11′, 12′, 14′, 15′
14′	124.4, d	5.09, m	13′, 16′, 17′	
15′	131.8, s			
16′	17.7, q	1.60, s	13′	14′, 15′, 17′
17′	25.7, q	1.68, s	13′, 14′	14′, 15′, 16′
18′	16.2, q	1.75, s	1′, 2′	2′, 3′, 4′
19′	16.1, q	1.59, s	5′, 6′	7′, 8′
20′	60.4, t	4.11, s	10′	10′, 11′, 12′
1-OH		ND [b]		
4-OH		ND [b]		
20′-OH		ND [b]		

[a] Carbon assignments made on the basis of gHSQCAD and gHMBCAD experiments. [b] indicates signal not detected. [w] Indicates weak or long range correlation.

Table S2. NMR data (500 MHz, $CDCl_3$) of 2-[11-(hydroxymethyl)-3,7,15-trimethyl-2,6,10,14-hexadecatetraen-1-yl]-6-methyl-1,4-benzoquinone (**12**).



(**12**)

Position	δ_C [a], mult	δ_H (*J* in Hz)	gCOSY	gHMBCAD	bsNOESY
1	188.0, s				
2	148.5, s				
3	132.3, d	6.46, bs	5, 1′	1, 4, 5	
4	188.0, s				
5	133.2, d	6.54, bs	3, 7	1, 3, 4	
6	145.9, s				
7	16.0, q	2.05, s	5	1, 5, 6	
1′	27.5, t	3.13, d (7.5)	3, 2′, 18′	1, 2, 3, 2′, 3′	
2′	118.1, d	5.15, t (7.5)	1′, 18′	1′, 4′, 18′	5, 1′, 4′
3′	139.8, s				
4′	39.6, t	2.07, m		2′, 3′, 5′, 18′	
5′	26.2, t	2.11, m	6′, 18′ [w], 19′ [w]	3′, 4′, 6′	
6′	124.2, d	5.10, m	5′	4′, 5′, 19′	5′, 8′
7’	135.1, s				
8′	39.8, t	2.01, m		6′, 10′	
9′	26.2, t	2.16, m	10′	8′, 10′, 11′	
10′	128.5, d	5.30, t (7.0)	9′, 20′	8′, 9′, 12′, 20′	12′
11′	138.4, s				
12′	35.2, t	2.12, m		11′, 13′, 14′, 15′	
13′	27.1, t	2.12, m	14′, 17′ [w]	11′, 12′, 14′, 15′	
14′	124.2, d	5.10, m	13′, 16′		17′
15′	131.7, s				
16′	17.7, q	1.60, s		14′, 15′	
17′	25.7, q	1.68, s	13′ [w]	14′, 15′, 16′	
18′	16.1, q	1.61, s		2′, 3′	
19′	16.1, q	1.61, s			
20′	60.3, t	4.11, s		10′, 11′, 12′	
20′-OH		ND [b]			

[a] Carbon assignments made on the basis of gHSQCAD and gHMBCAD experiments. [b] indicates signal not detected. [c] bs stands for band selective (Selective NOESY experiment). [w] Indicates weak or long range correlation.