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SUPPLEMENTARY MATERIAL

New Cytotoxic Norditerpenes from the Australian Nudibranchs *Goniobranchus Splendidus* and *Goniobranchus Daphne.*

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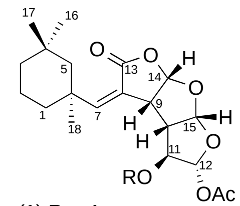
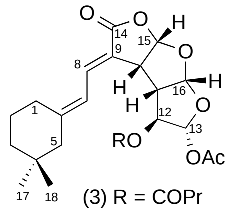
Figure **S1**. Structures of terpenes **1** – **7** and **16**



(1) R = Ac
(2) R = COPr



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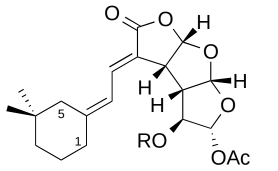

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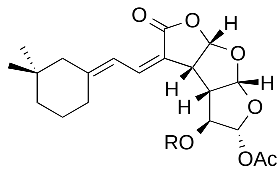
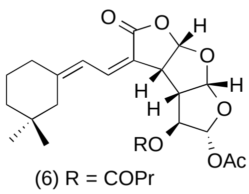
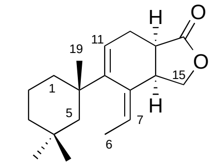


(5) R = COPr



(6) R = COPr



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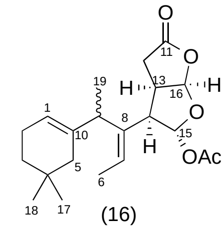


(16)

Figure **S2**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin G (**1**)

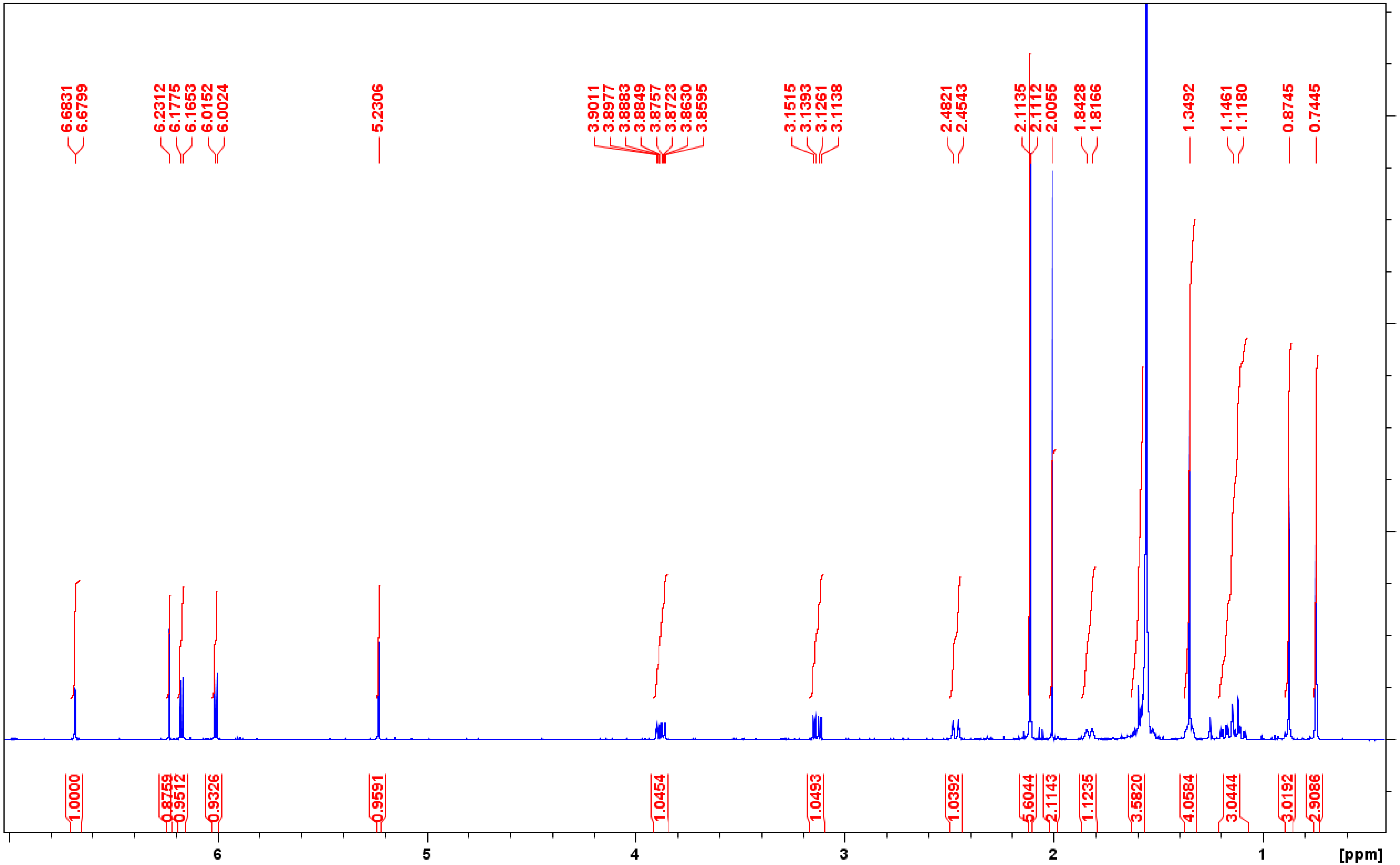


Figure **S3**. COSY spectrum (500 MHz, $CDCl_3$) for gracilin G (**1**)

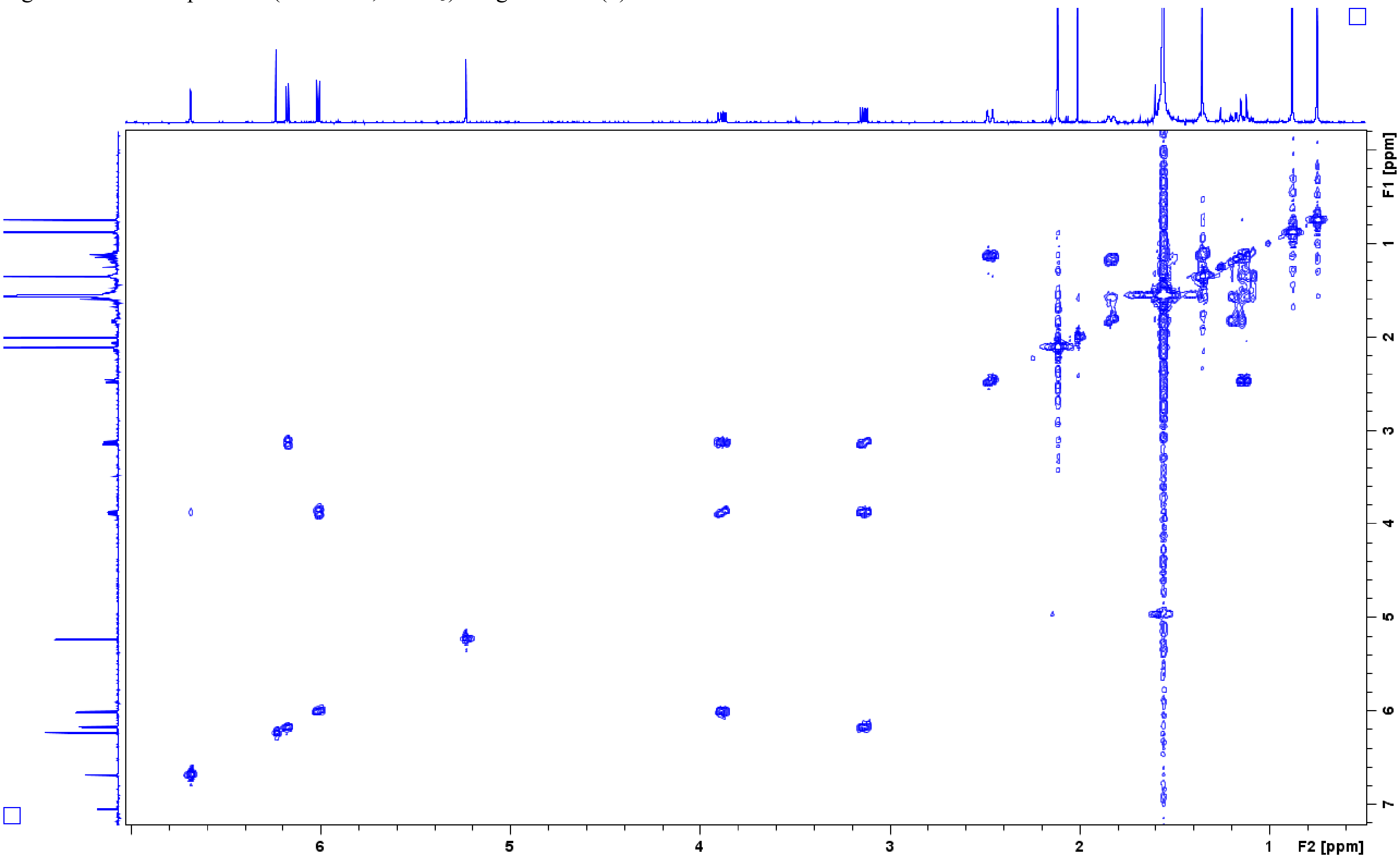


Figure **S4**. HSQC spectrum (500 MHz, $CDCl_3$) for gracilin G (**1**)

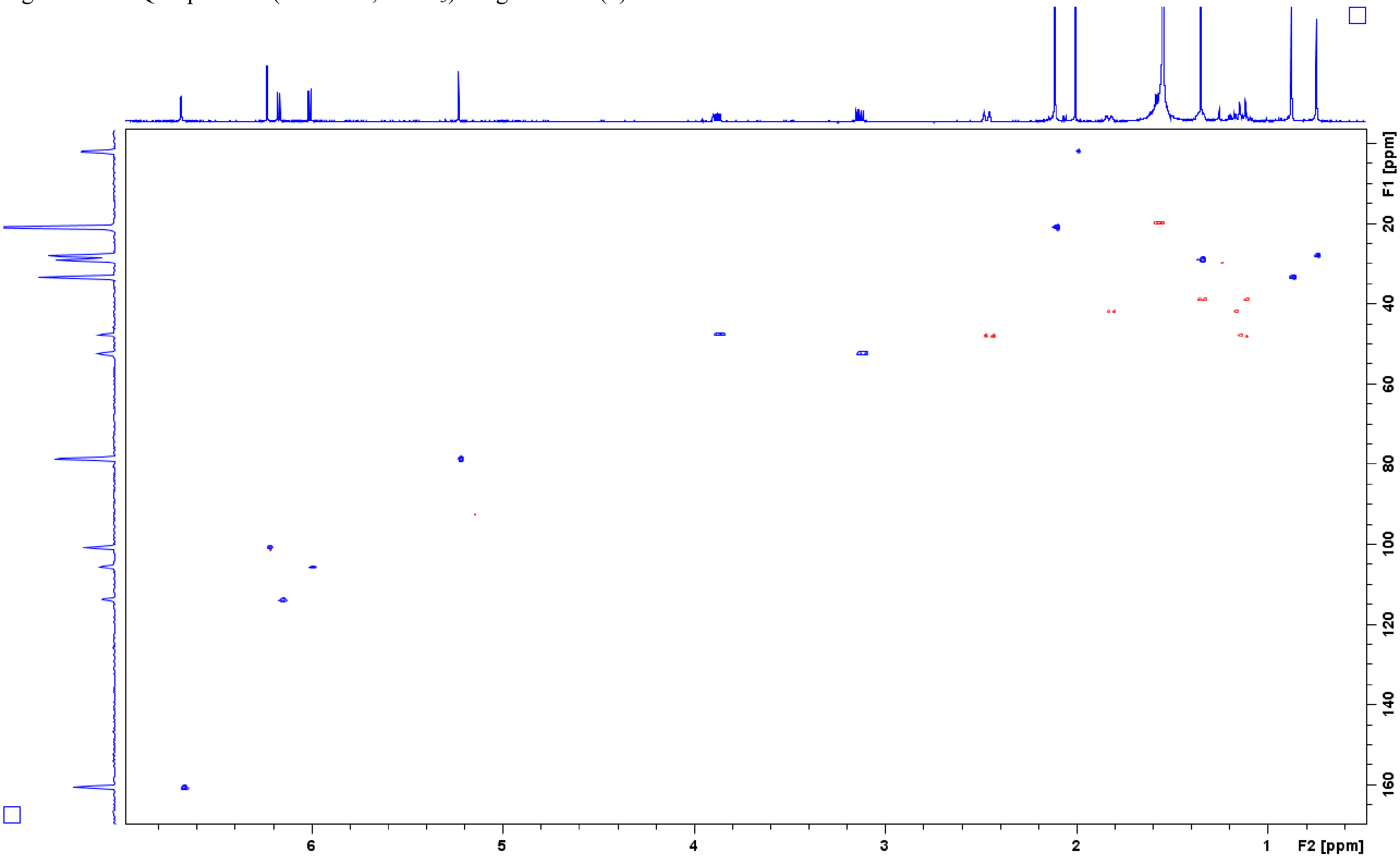


Figure **S5**. HMBC spectrum (500 MHz, $CDCl_3$) for gracilin G (**1**)

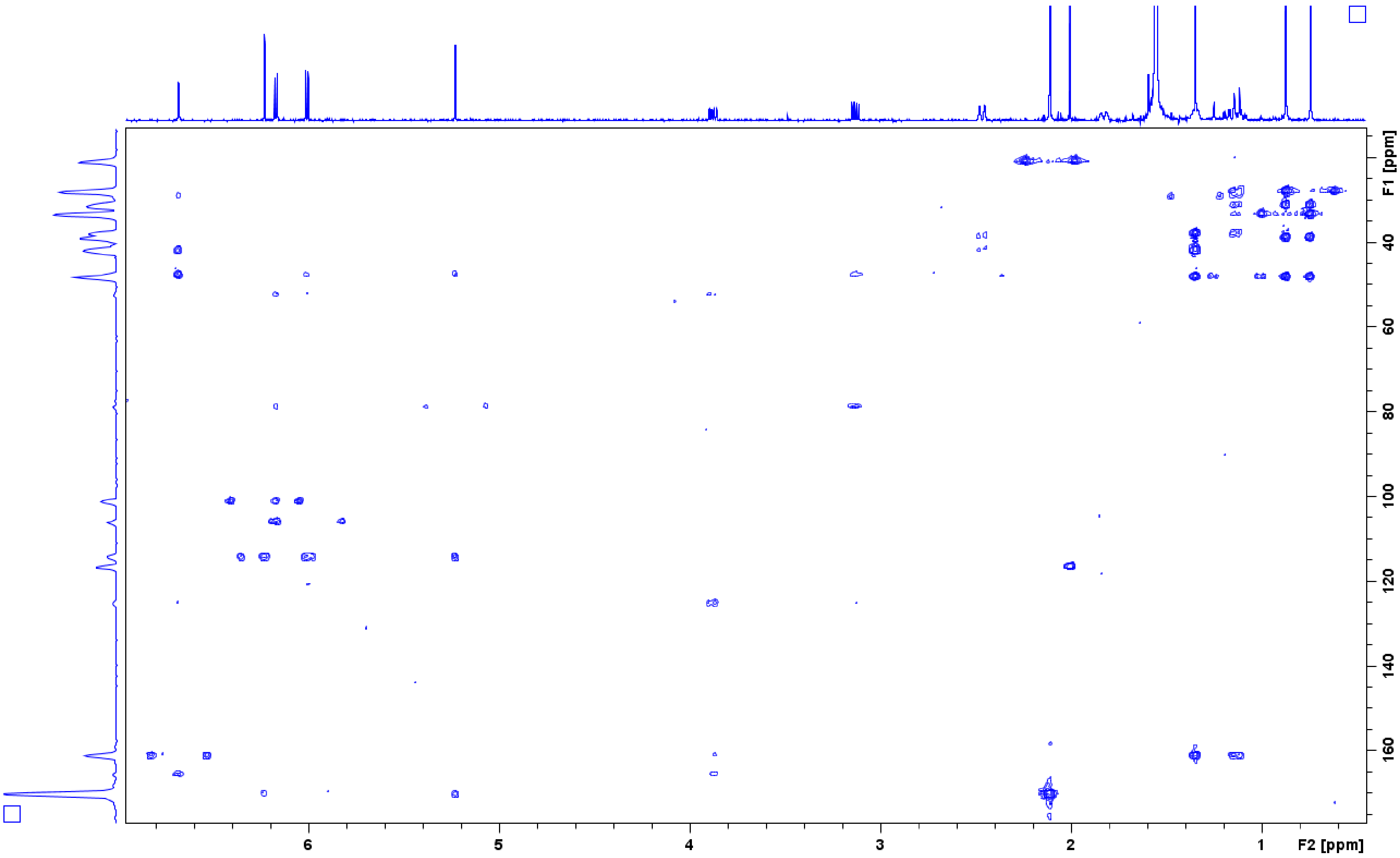


Figure **S6**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin M (**2**)

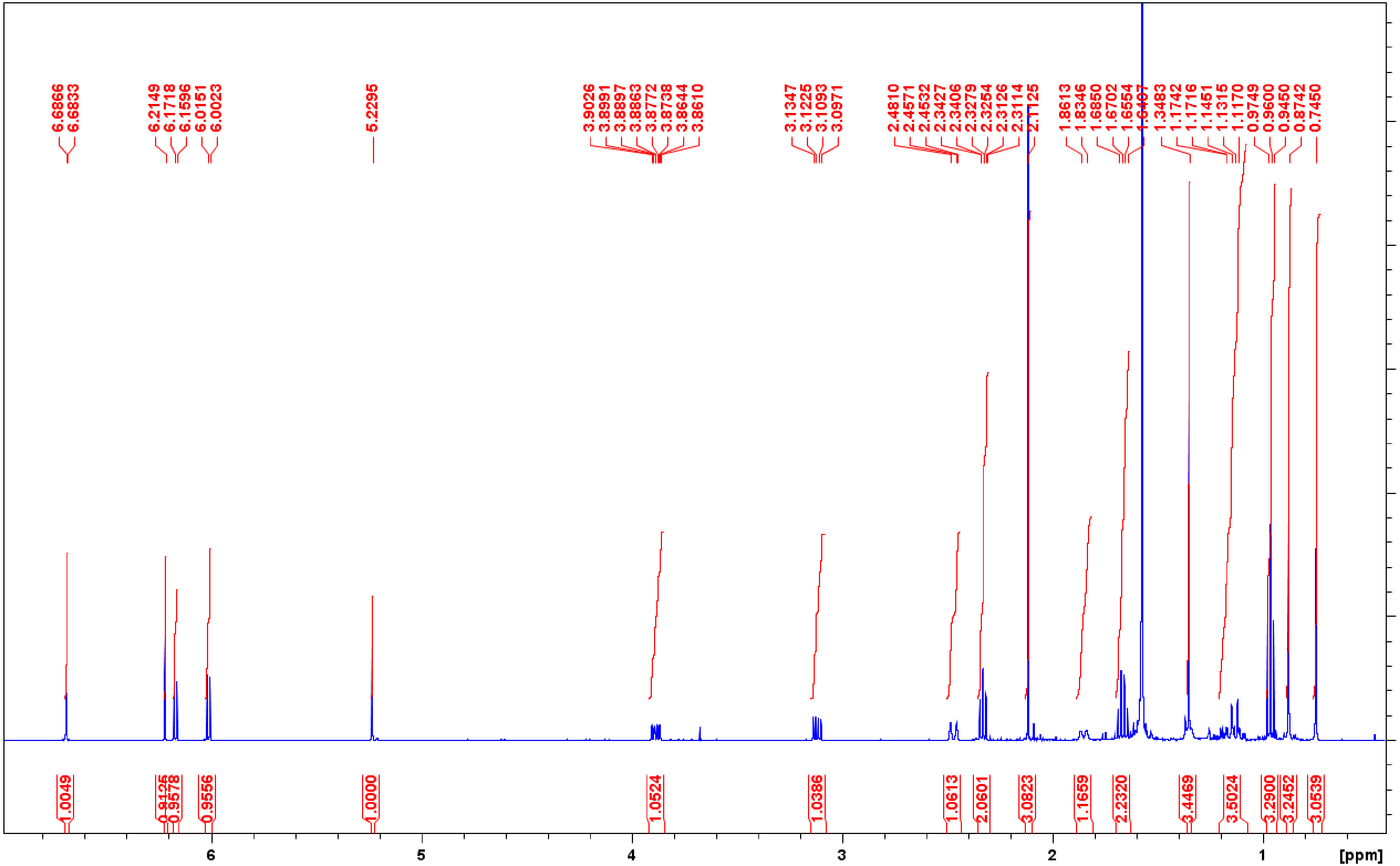


Figure **S7**. COSY spectrum (500 MHz, $CDCl_3$) for gracilin M (**2**)

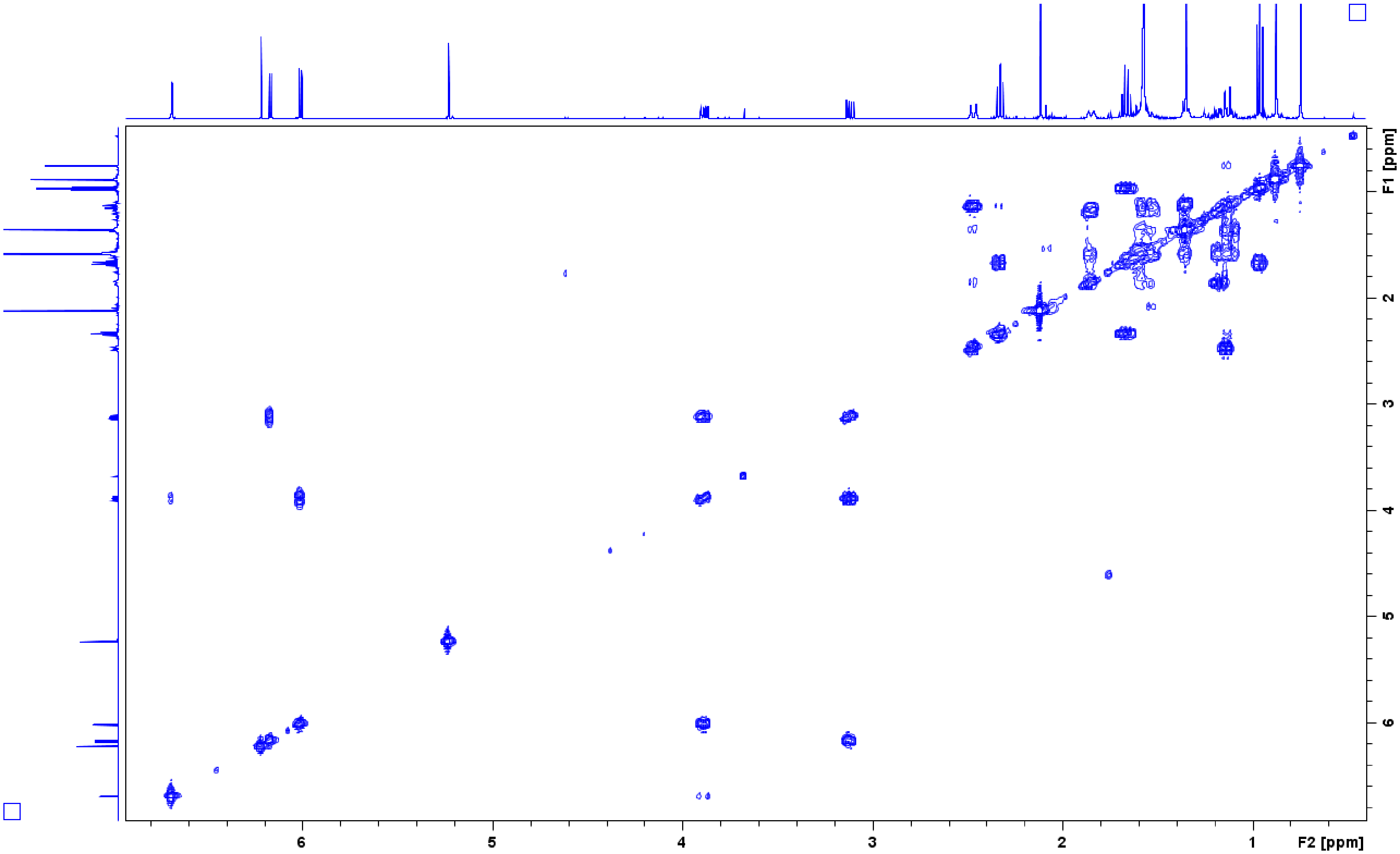


Figure **S8**. HSQC spectrum (500 MHz, $CDCl_3$) for gracilin M (**2**)

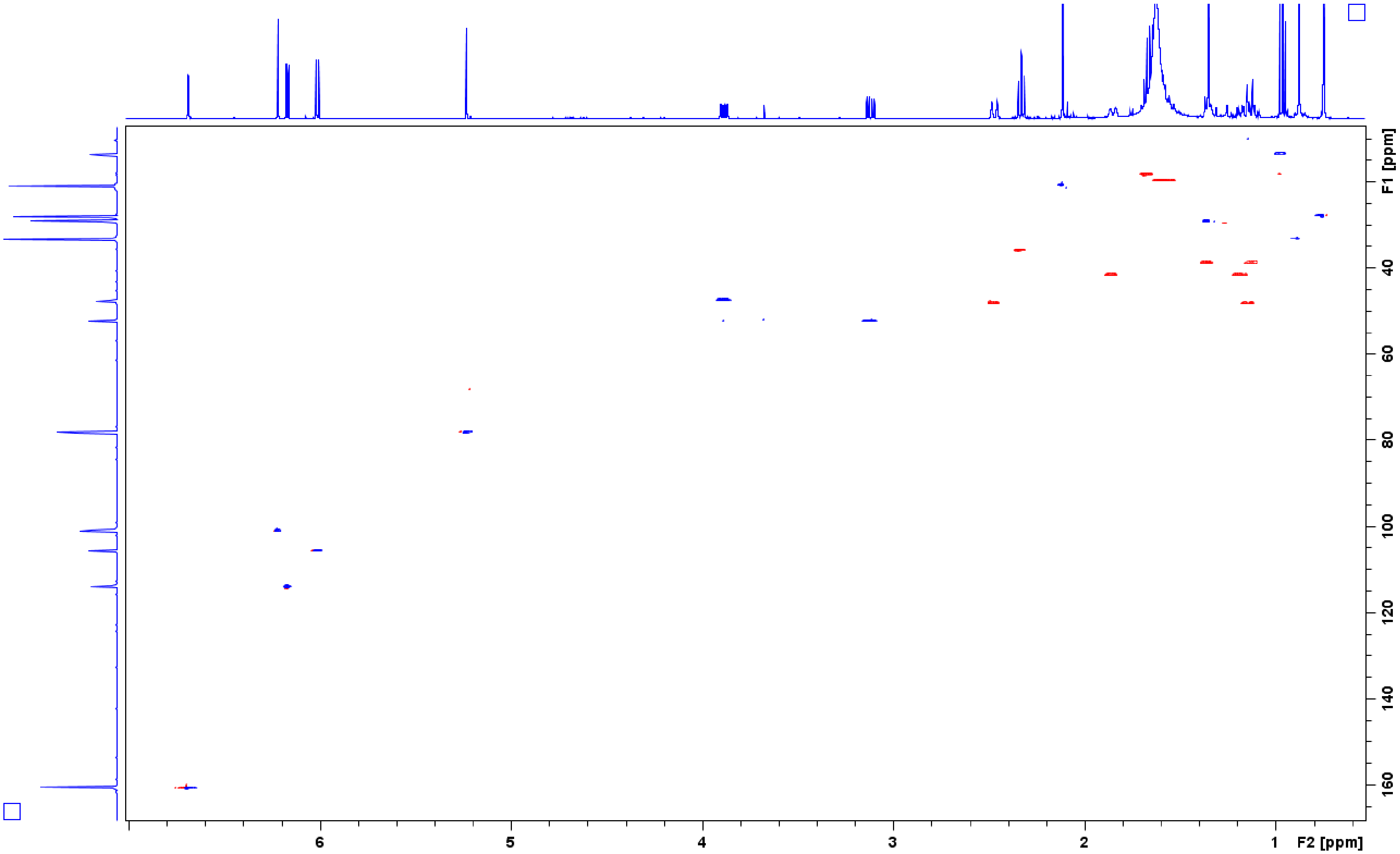


Figure **S9**. HMBC spectrum (500 MHz, $CDCl_3$) for gracilin M (**2**)

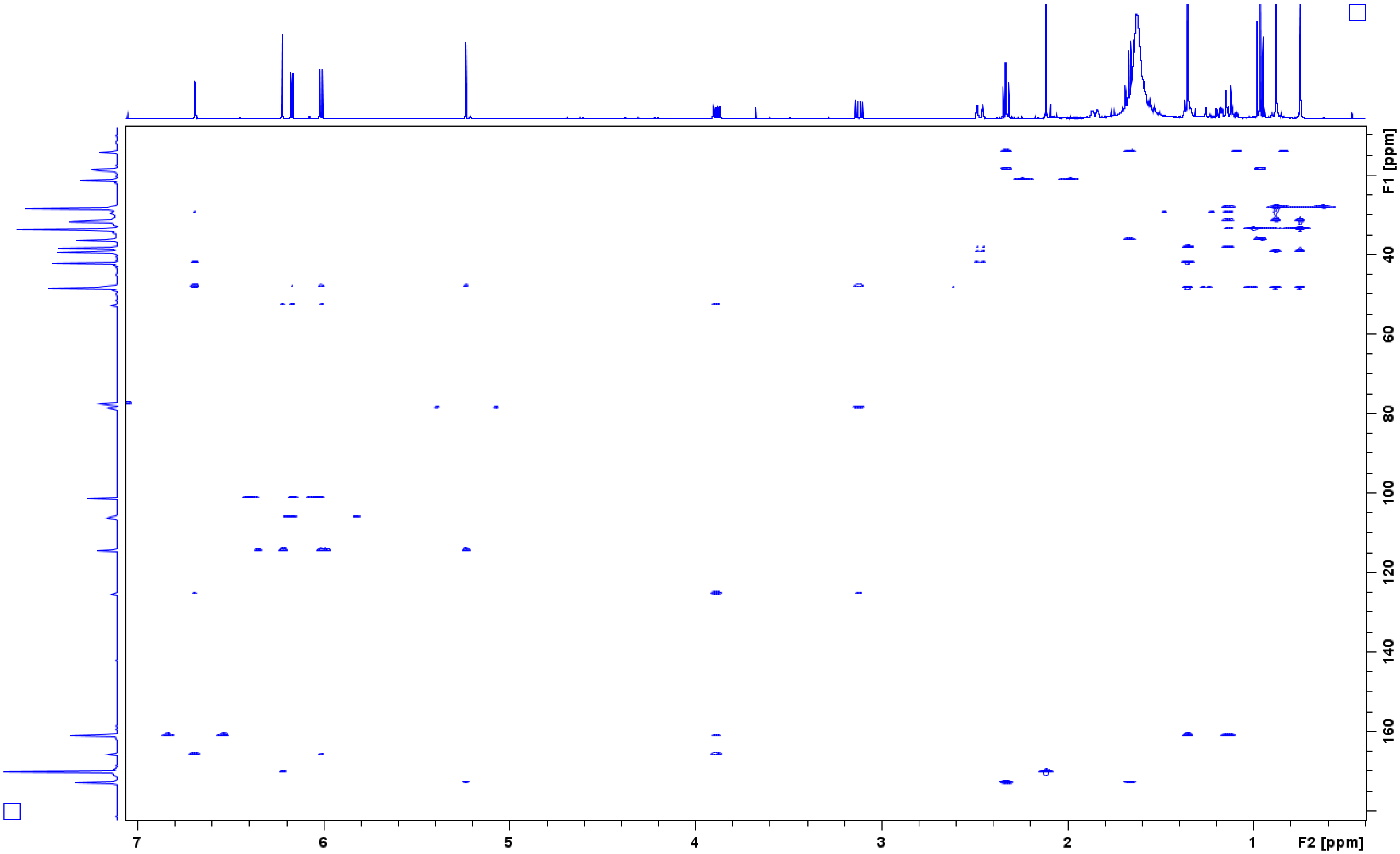


Figure **S10**. NOESY spectrum (500 MHz, $CDCl_3$) for gracilin M (**2**)

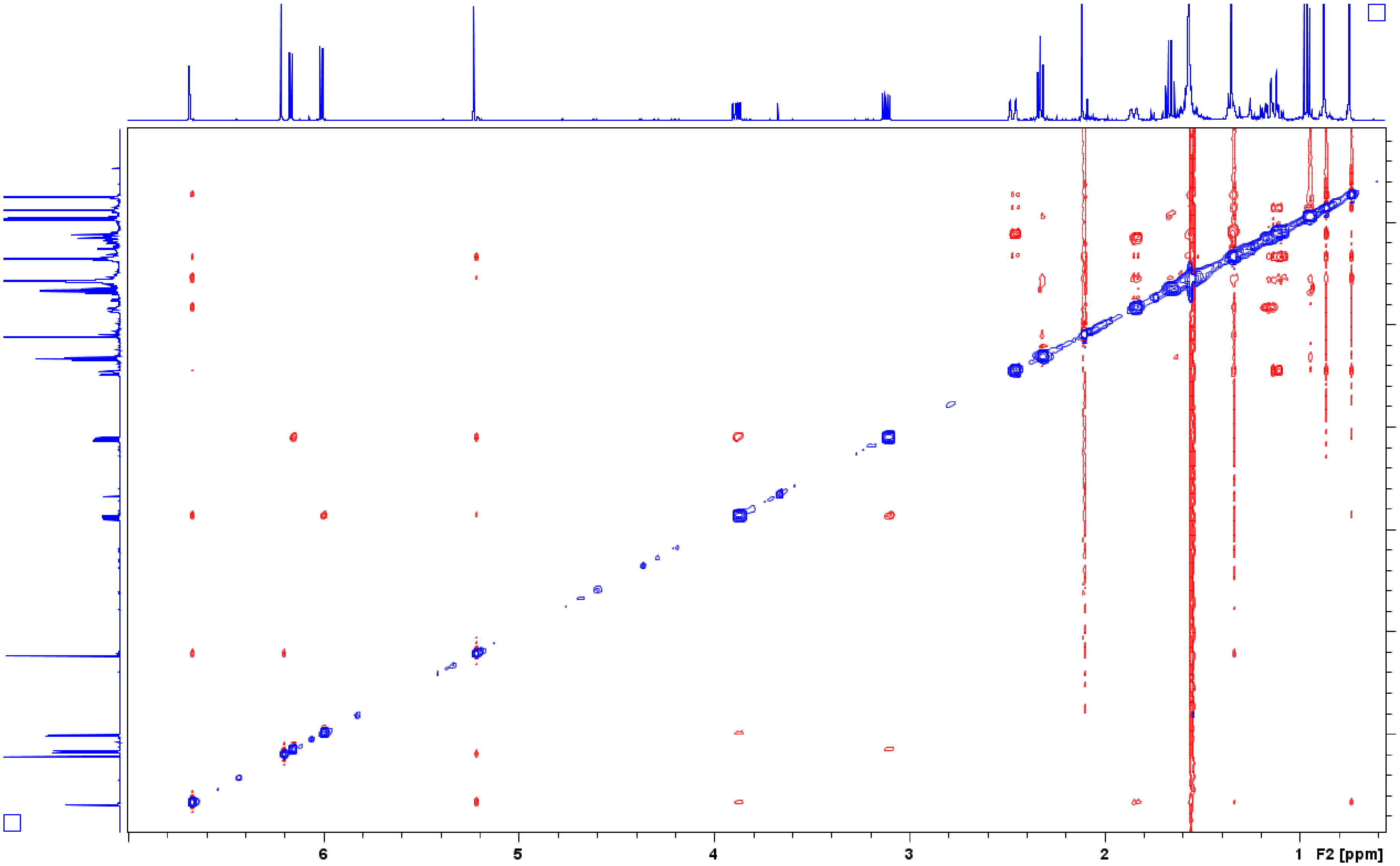


Figure **S11**. EXSIDE spectrum (750 MHz, $CDCl_3$) for gracilin M (**2**); (A) signal for H-7 with ^3J interaction to C-1 and to C-5; (B) expansion showing ^3J interaction to C-1

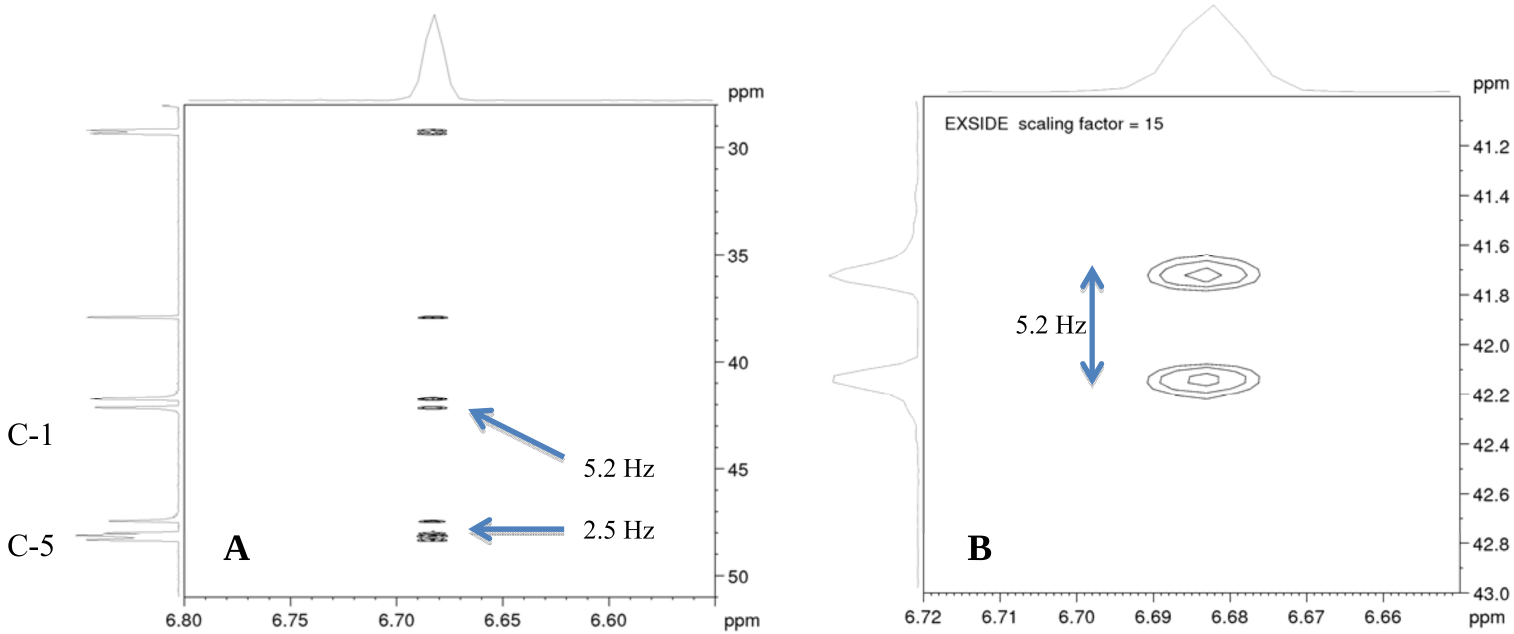


Figure **S12**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin N (**3**)

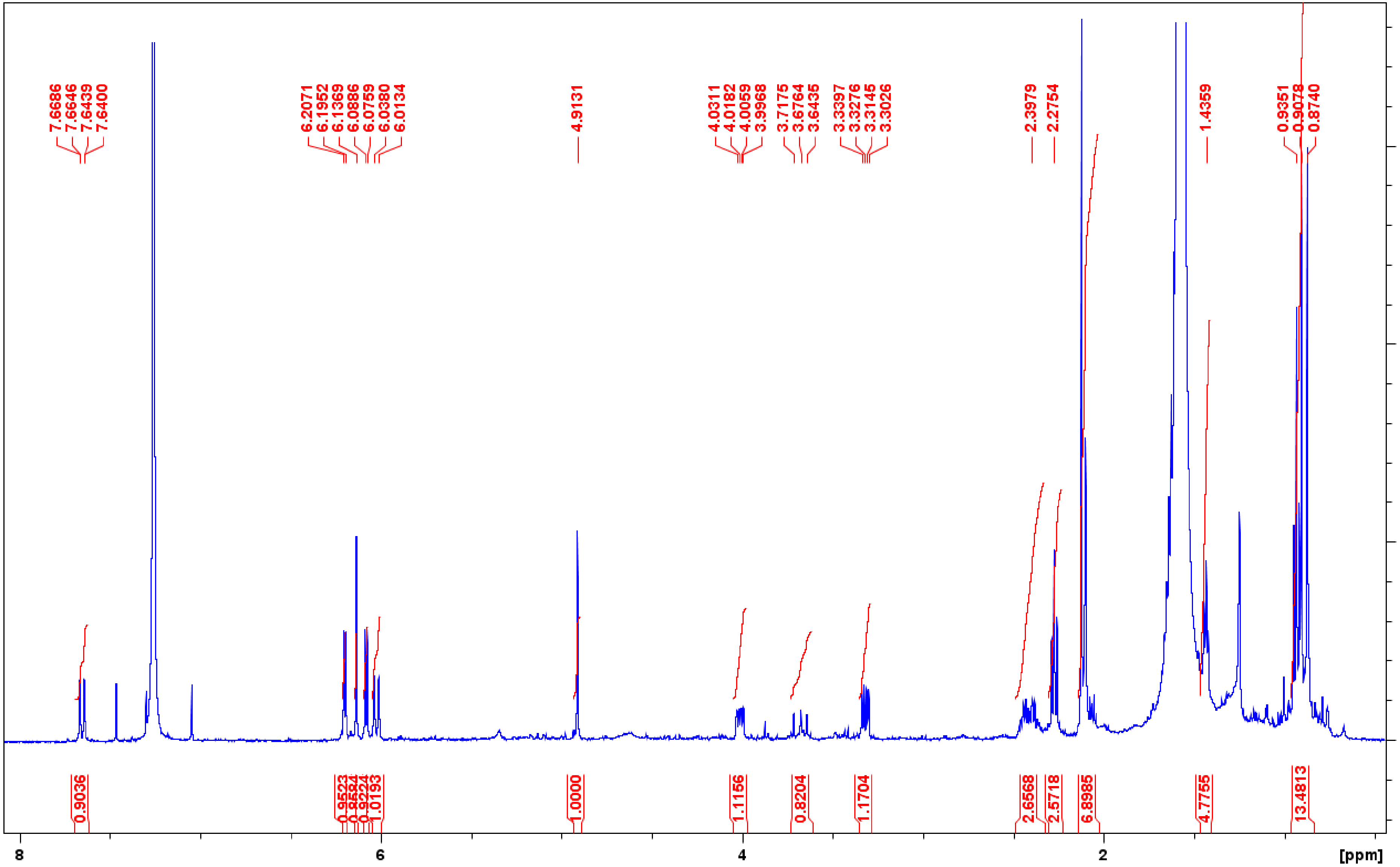


Figure **S13**. COSY spectrum (500 MHz, $CDCl_3$) for gracilin N (**3**)

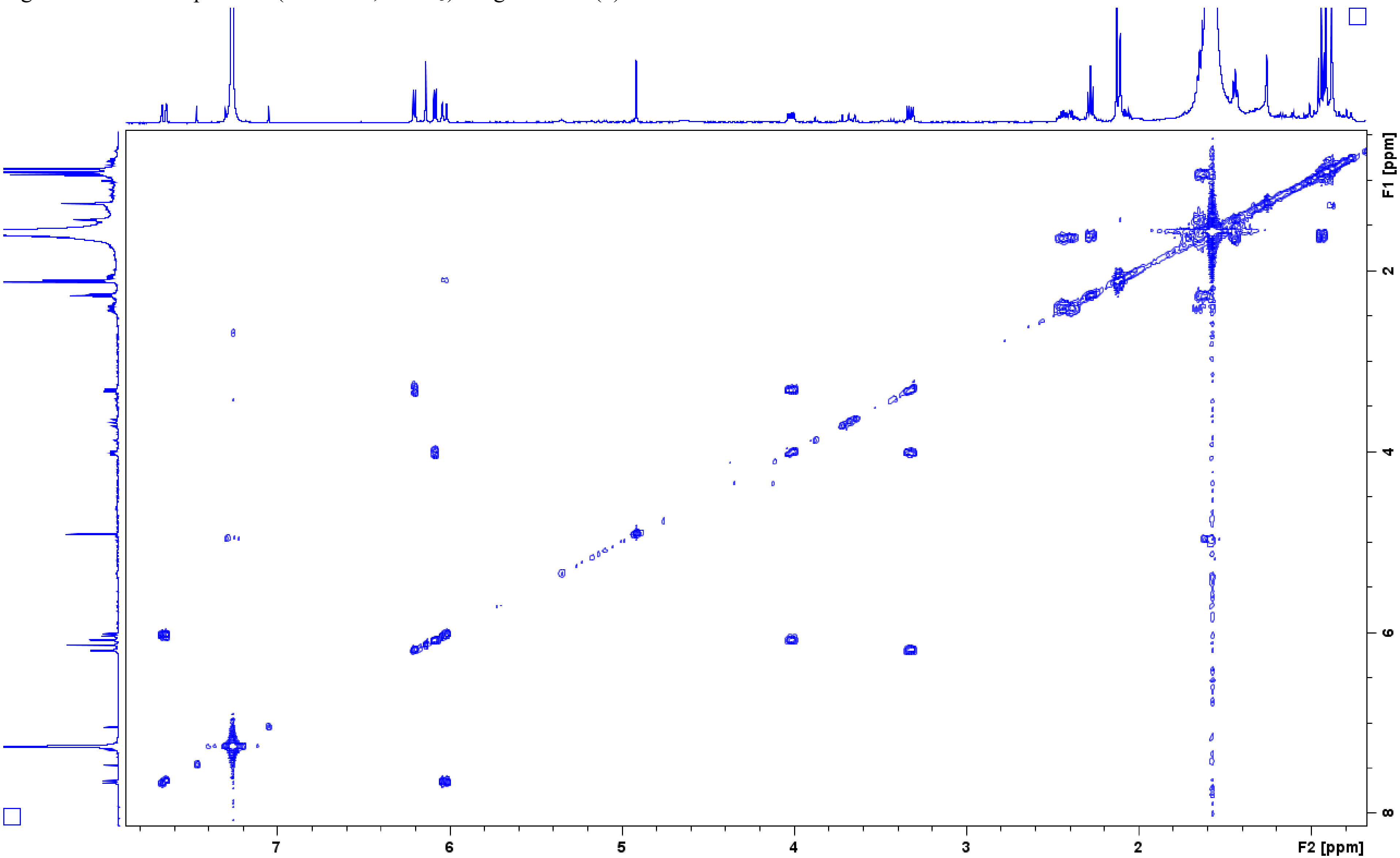


Figure **S14**. HSQC spectrum (500 MHz, $CDCl_3$) for gracilin N (**3**)

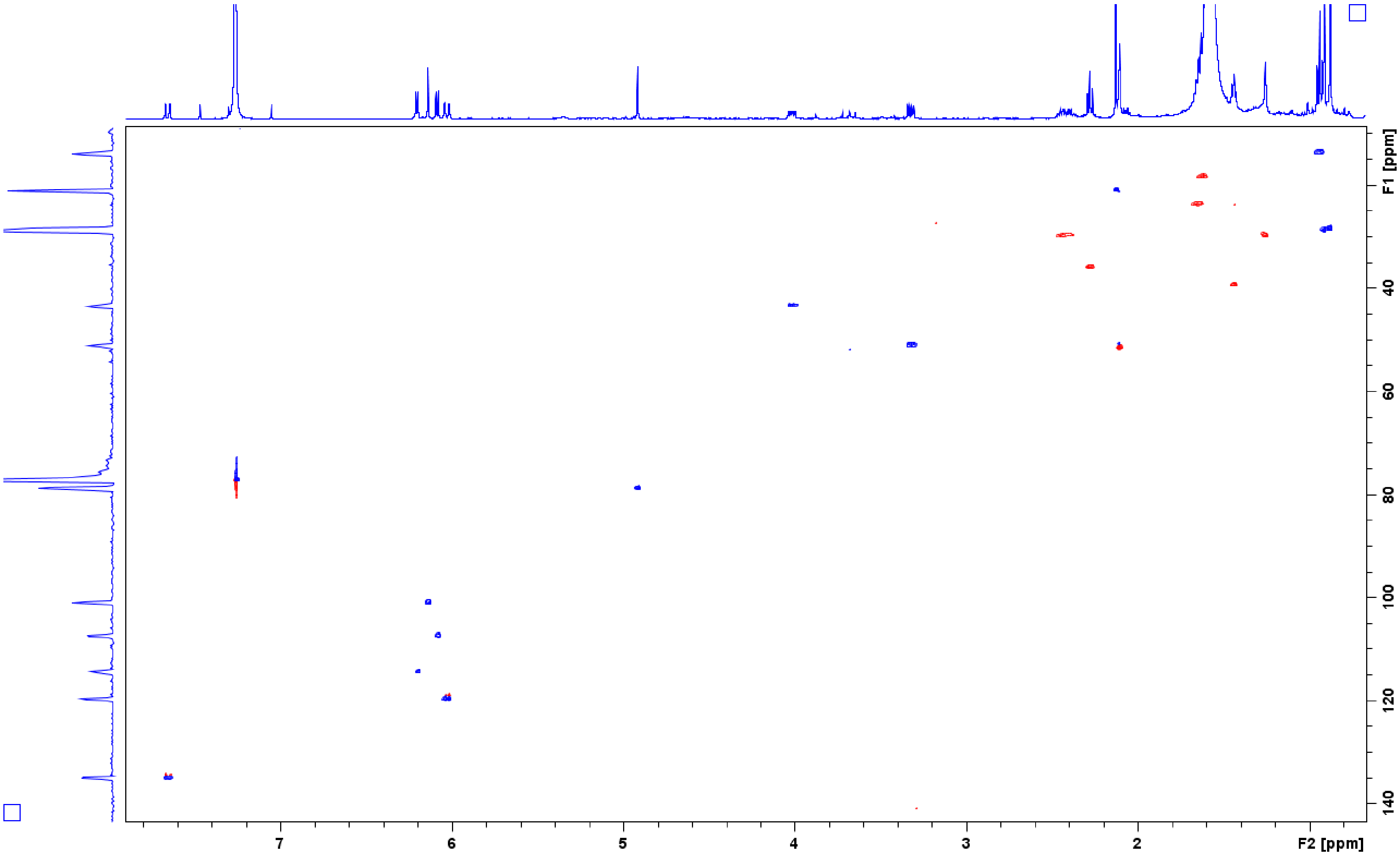


Figure **S15**. HMBC spectrum (500 MHz, $CDCl_3$) for gracilin N (**3**)

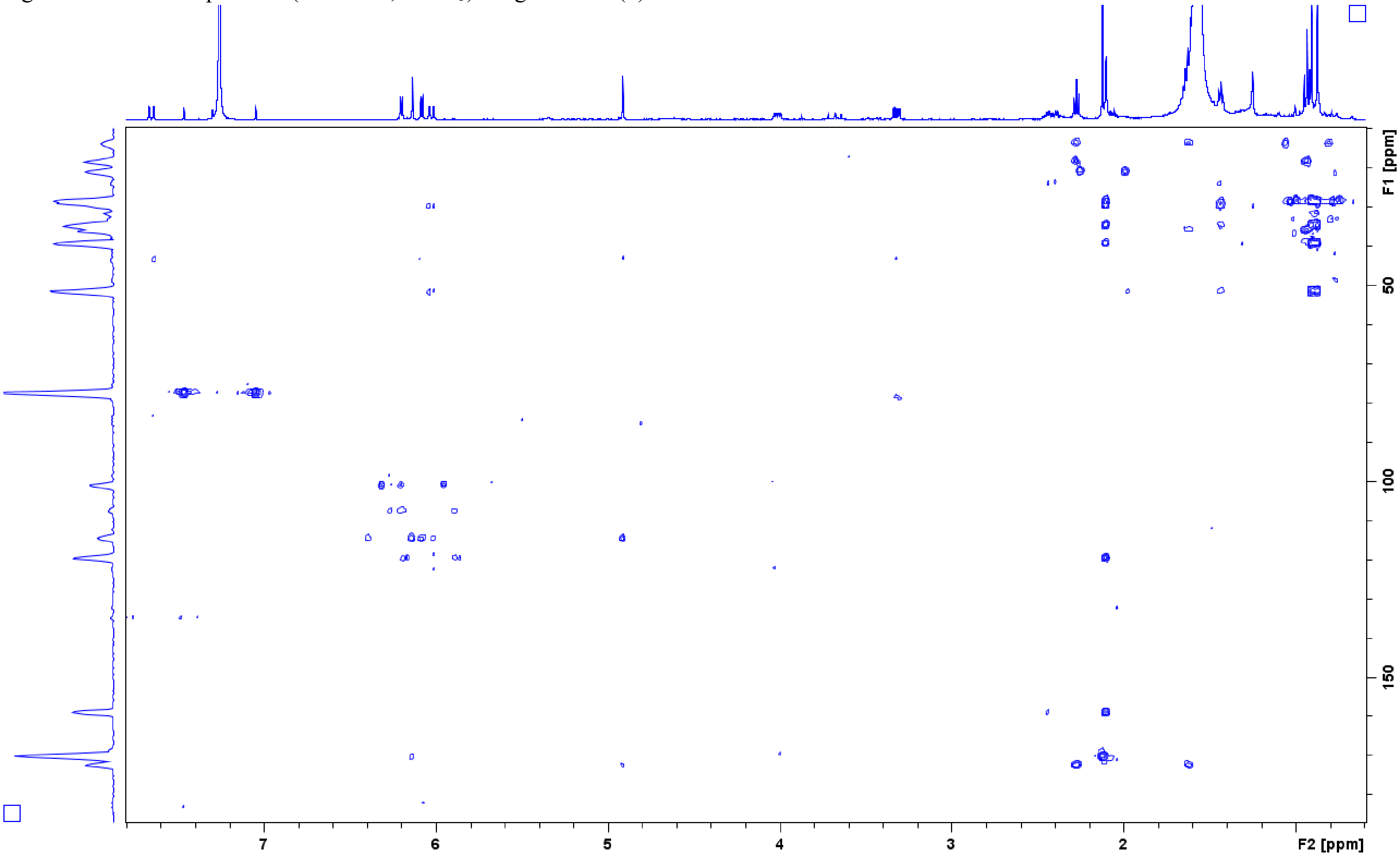


Figure **S16**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin O (**4**)

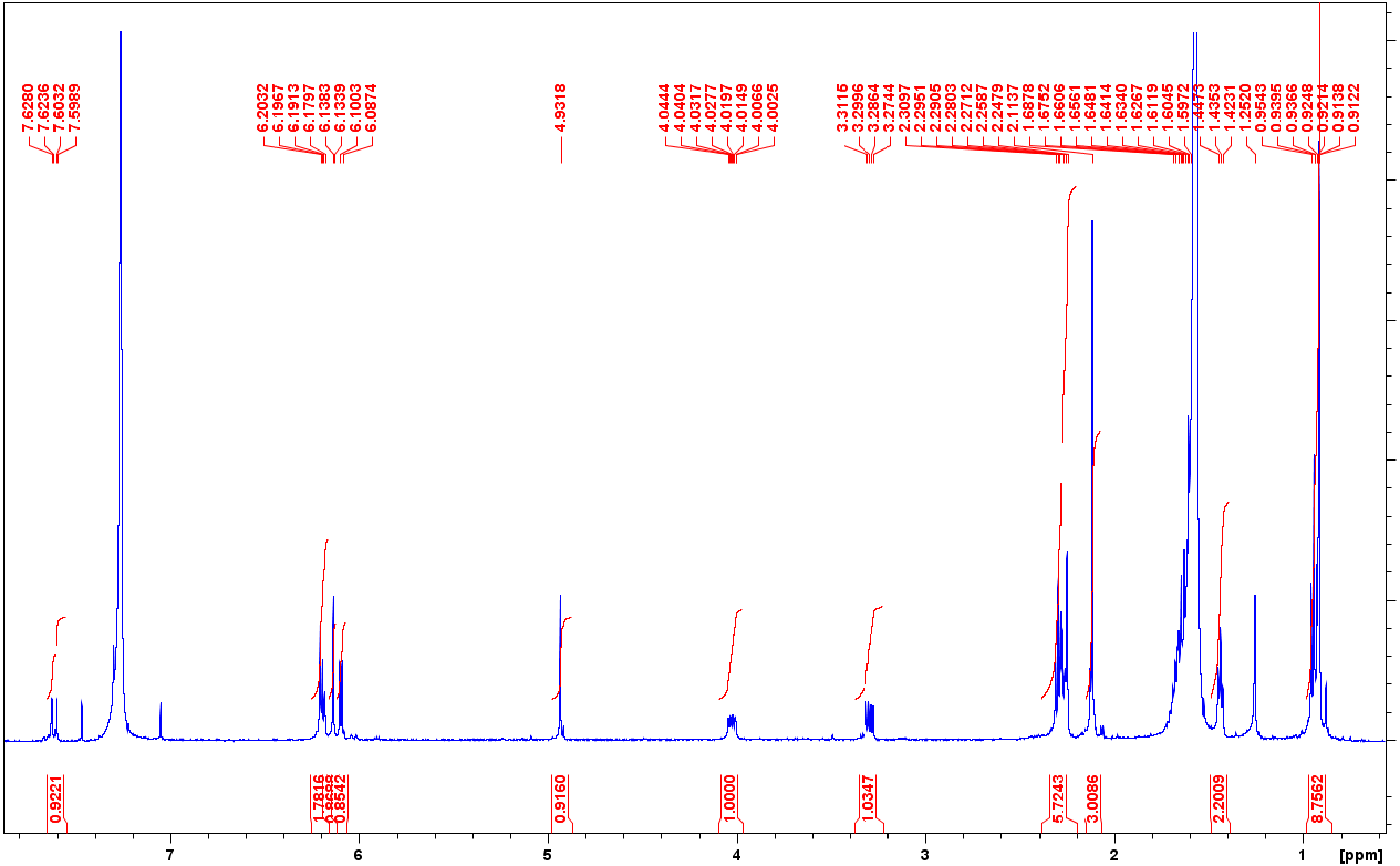


Figure **S17**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin P (**5**)

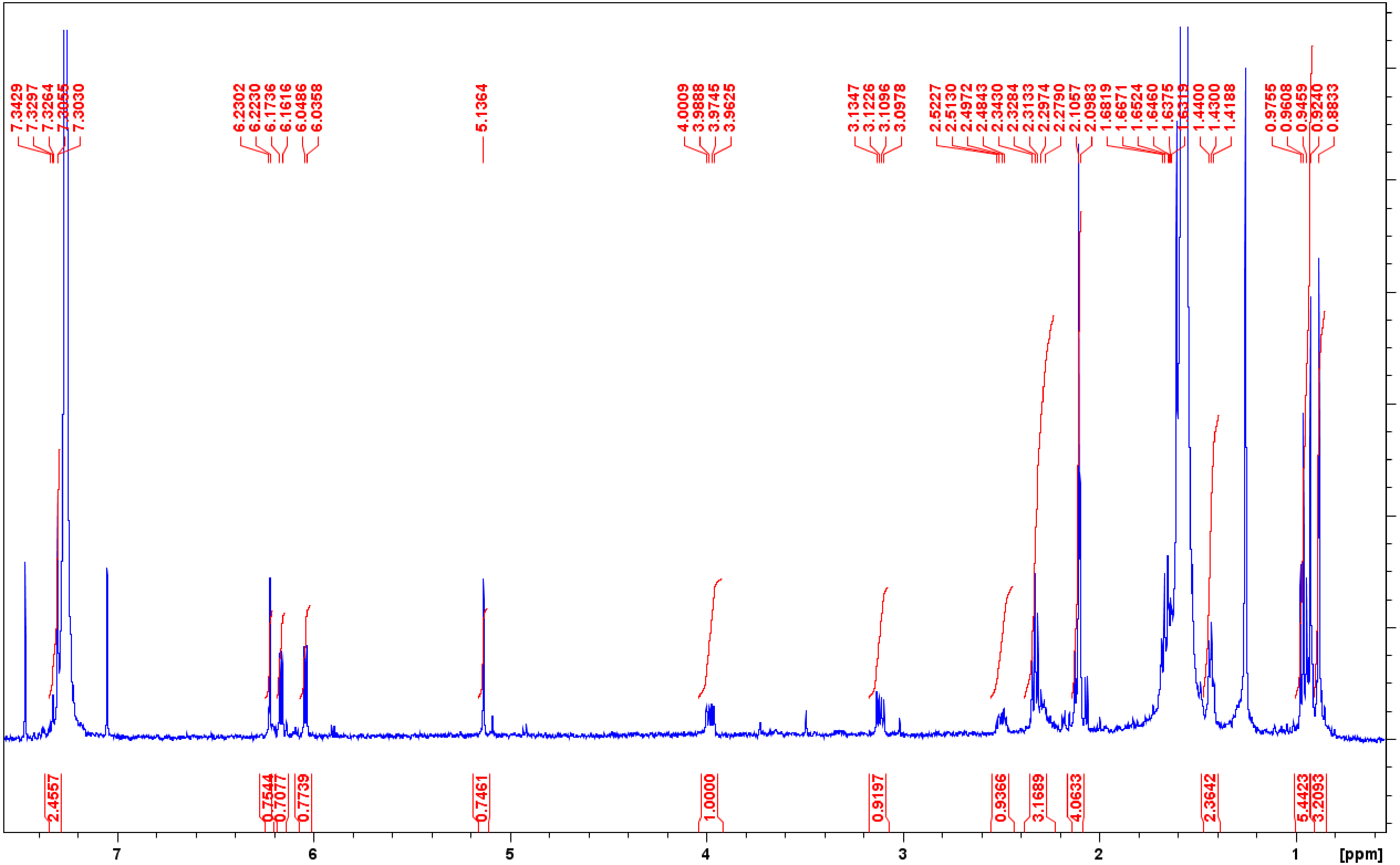


Figure **S18**. [1]H NMR spectrum (500 MHz, $CDCl_3$) for gracilin Q (**6**)

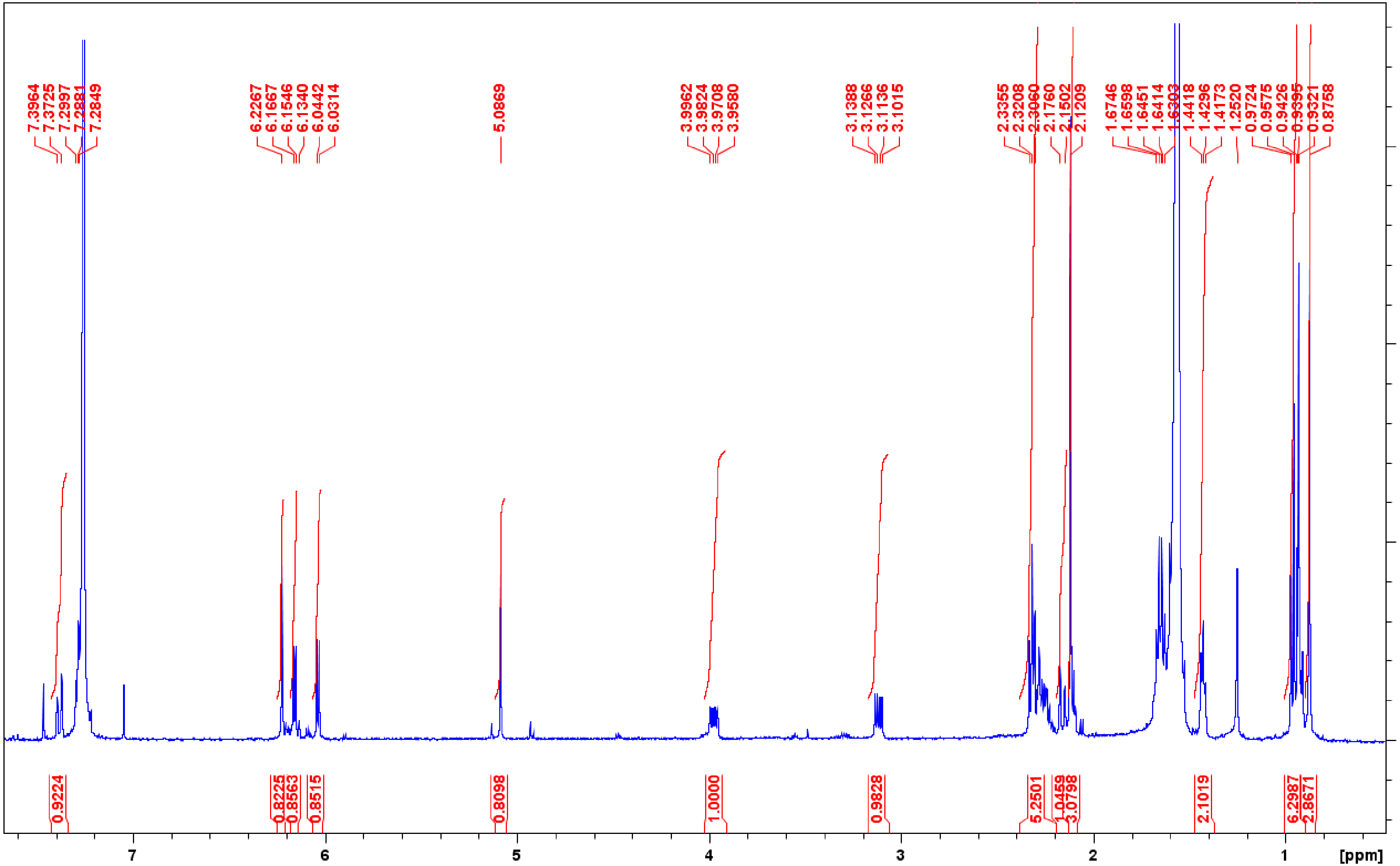


Figure **S19**. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) for aplytandiene-3 (**7**)

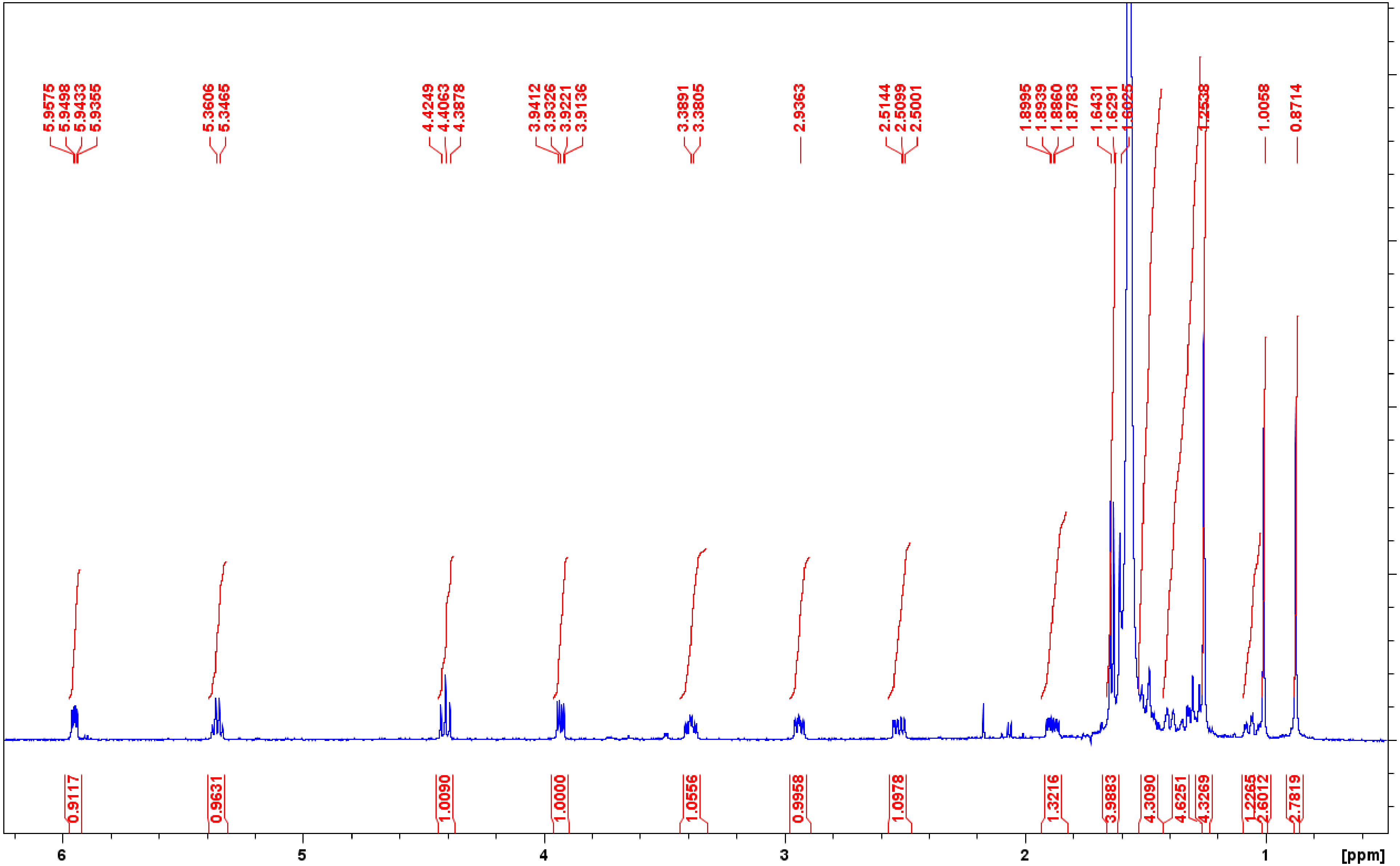


Figure **S20**. COSY spectrum (500 MHz, $CDCl_3$) for aplytandiene-3 (**7**)

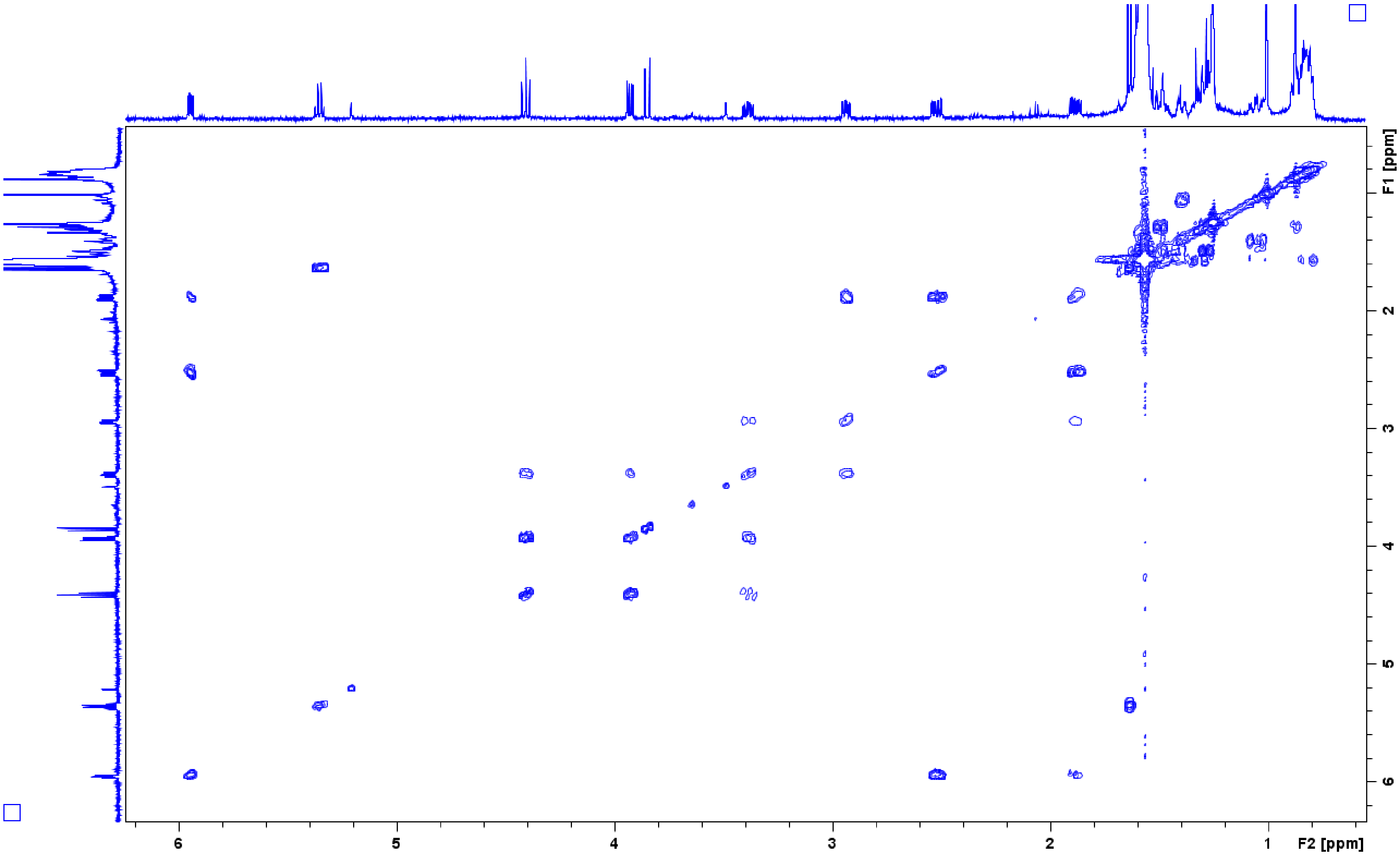


Figure **S21**. HSQC spectrum (500 MHz, $CDCl_3$) for aplytandiene-3 (**7**)

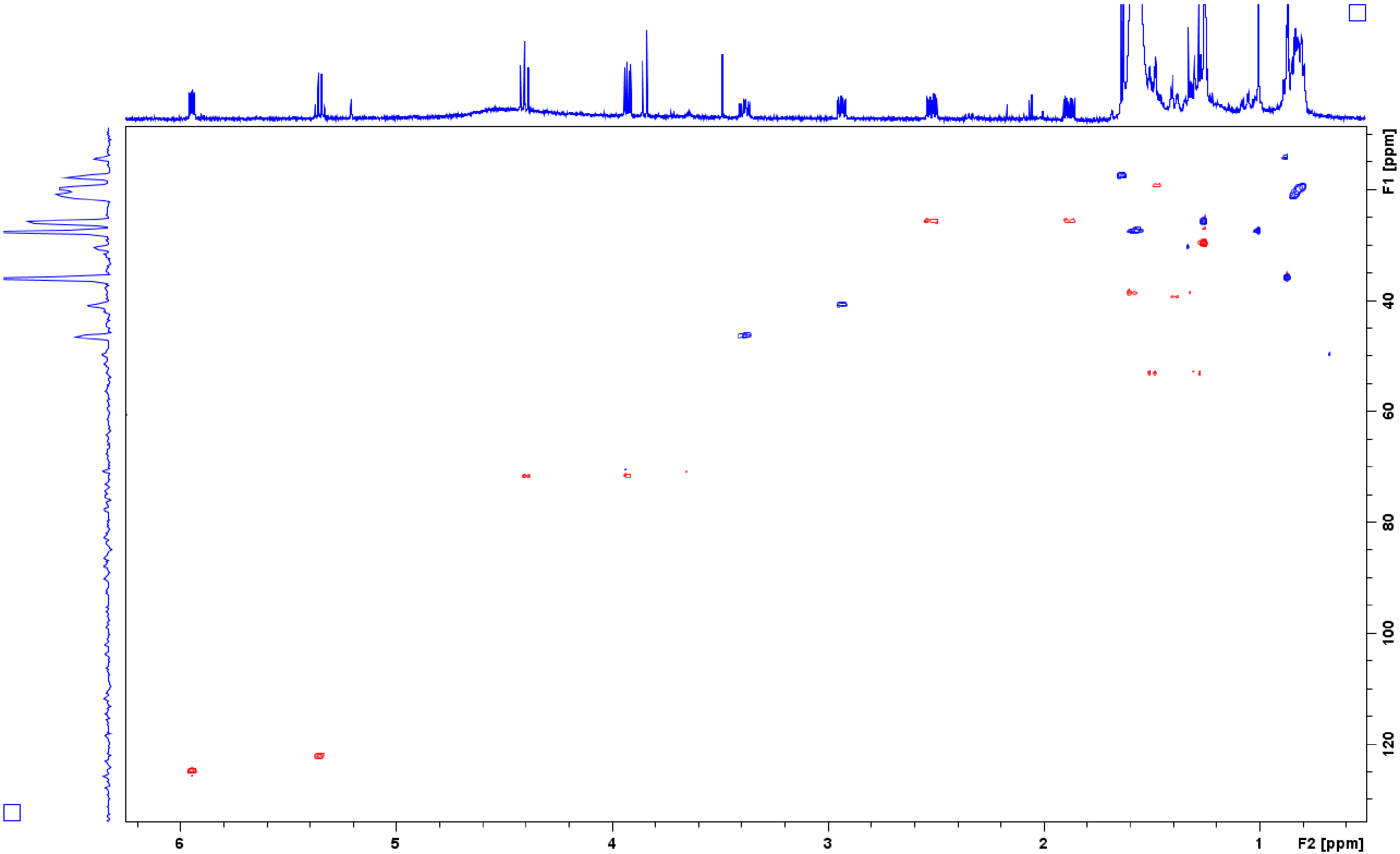


Figure **S22**. HMBC spectrum (500 MHz, $CDCl_3$) for aplytandiene-3 (**7**)

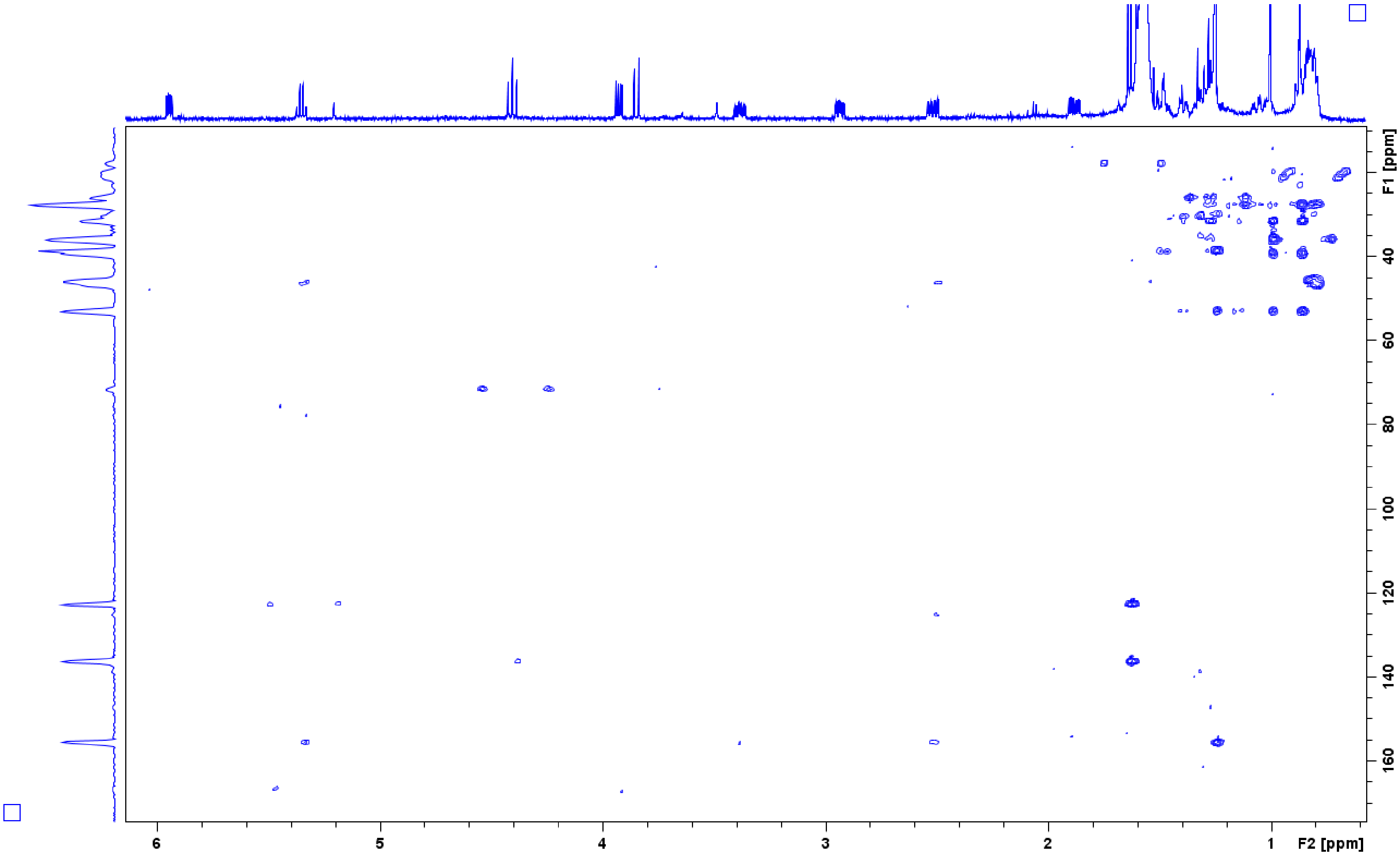


Figure **S23**. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) for daphnelactone (**16**)

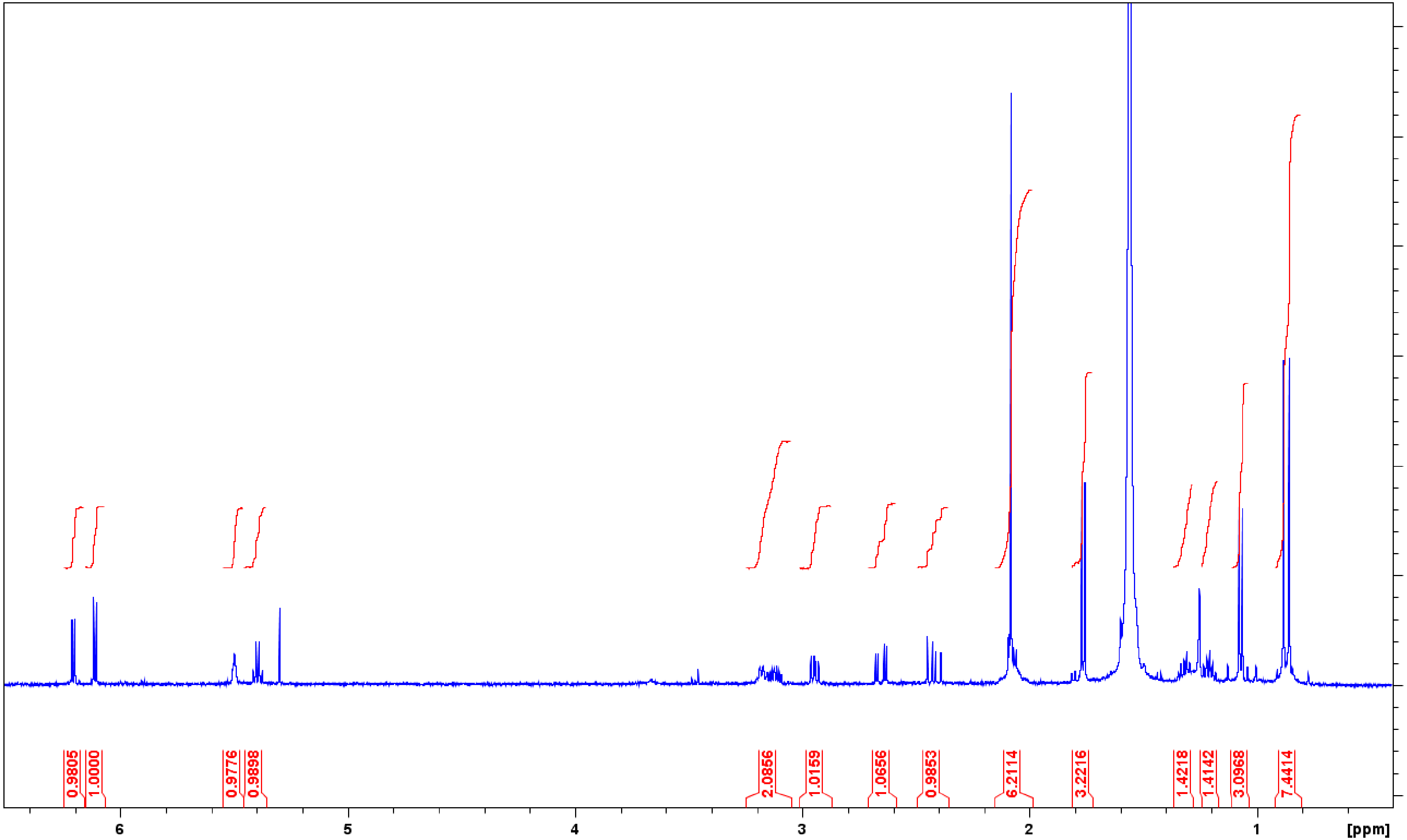


Figure **S24**. [1]H NMR spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)

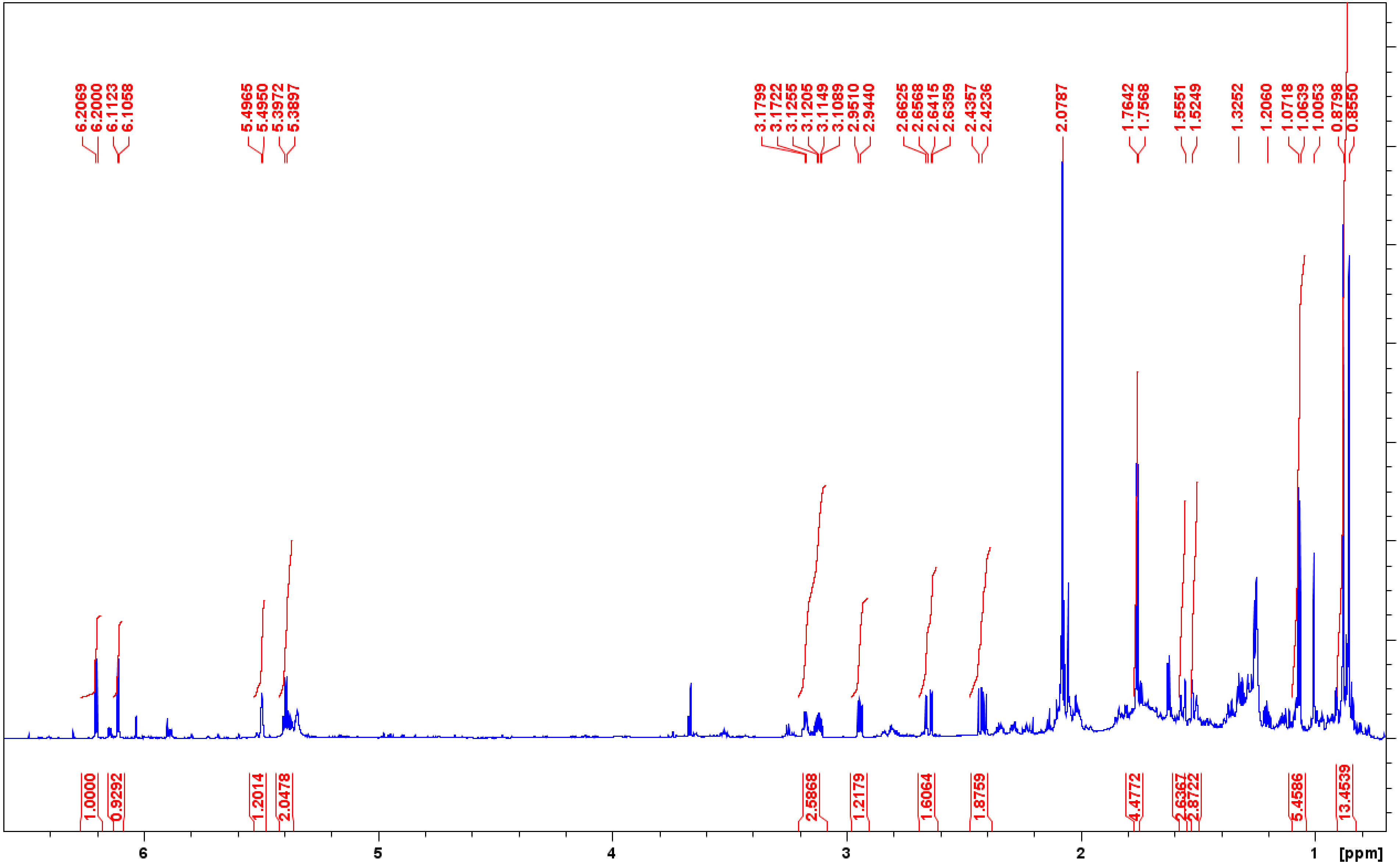


Figure **S25**. ^{13}C NMR spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)

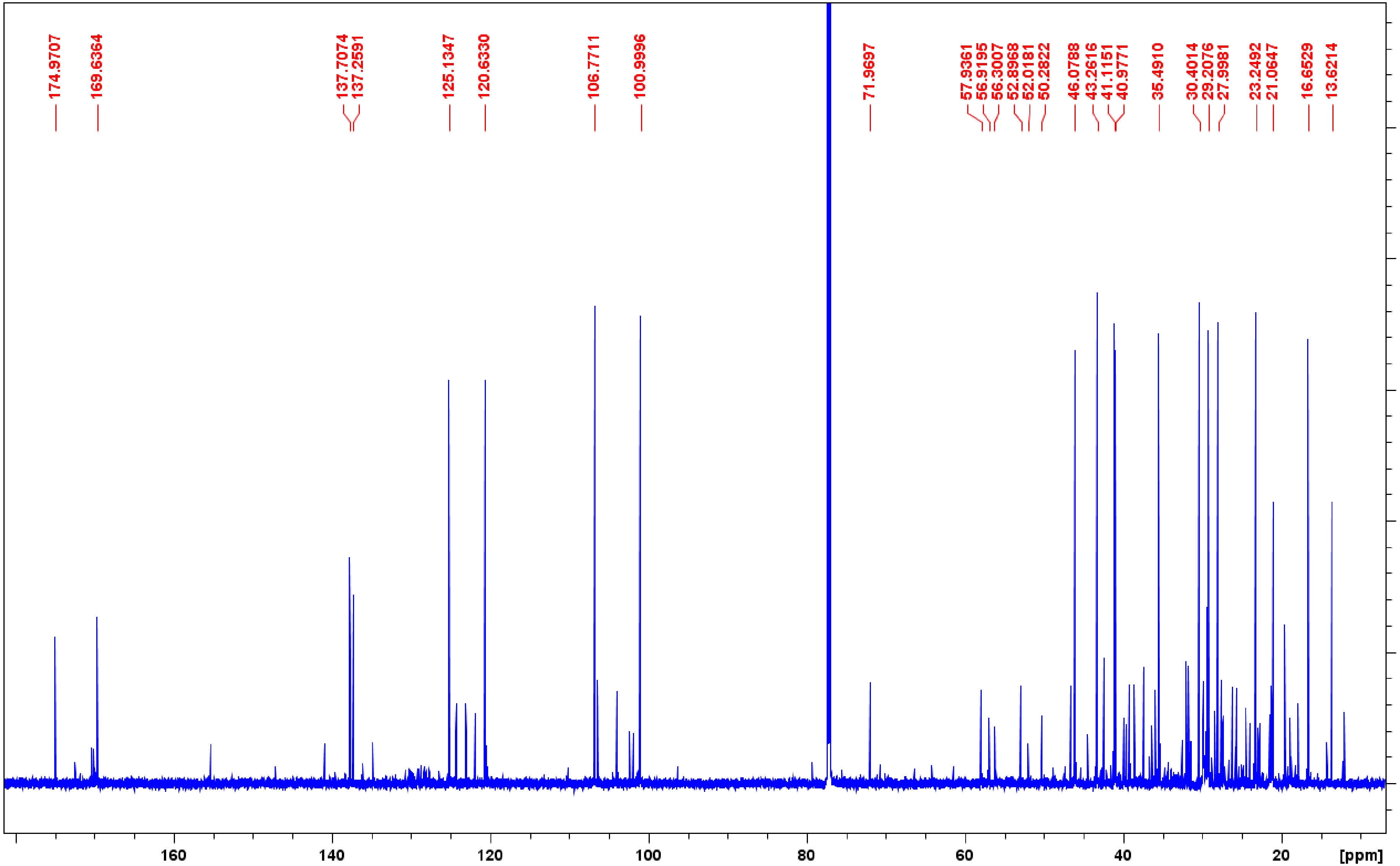


Figure **S26**. COSY spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)

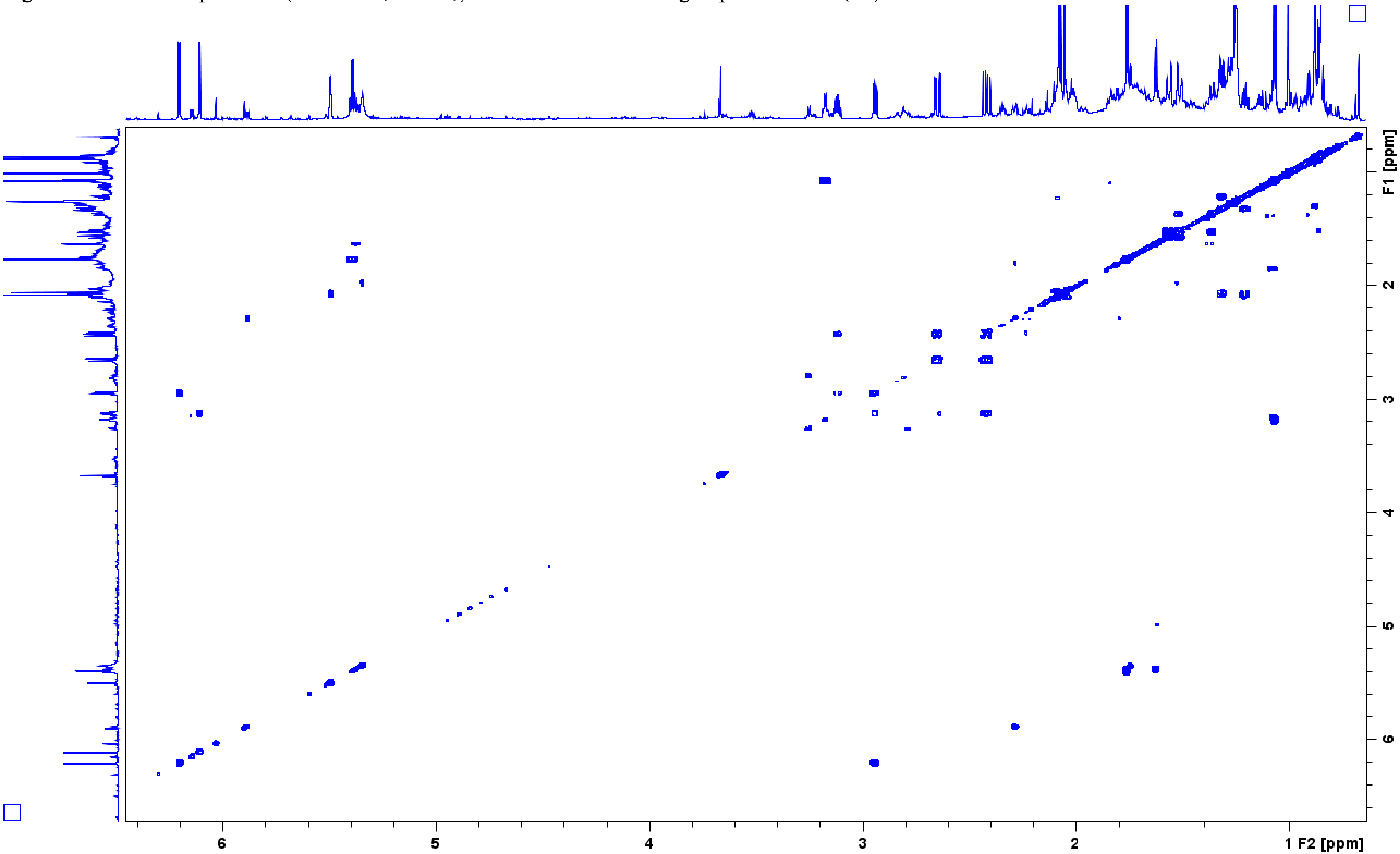


Figure **S27**. HSQC spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)

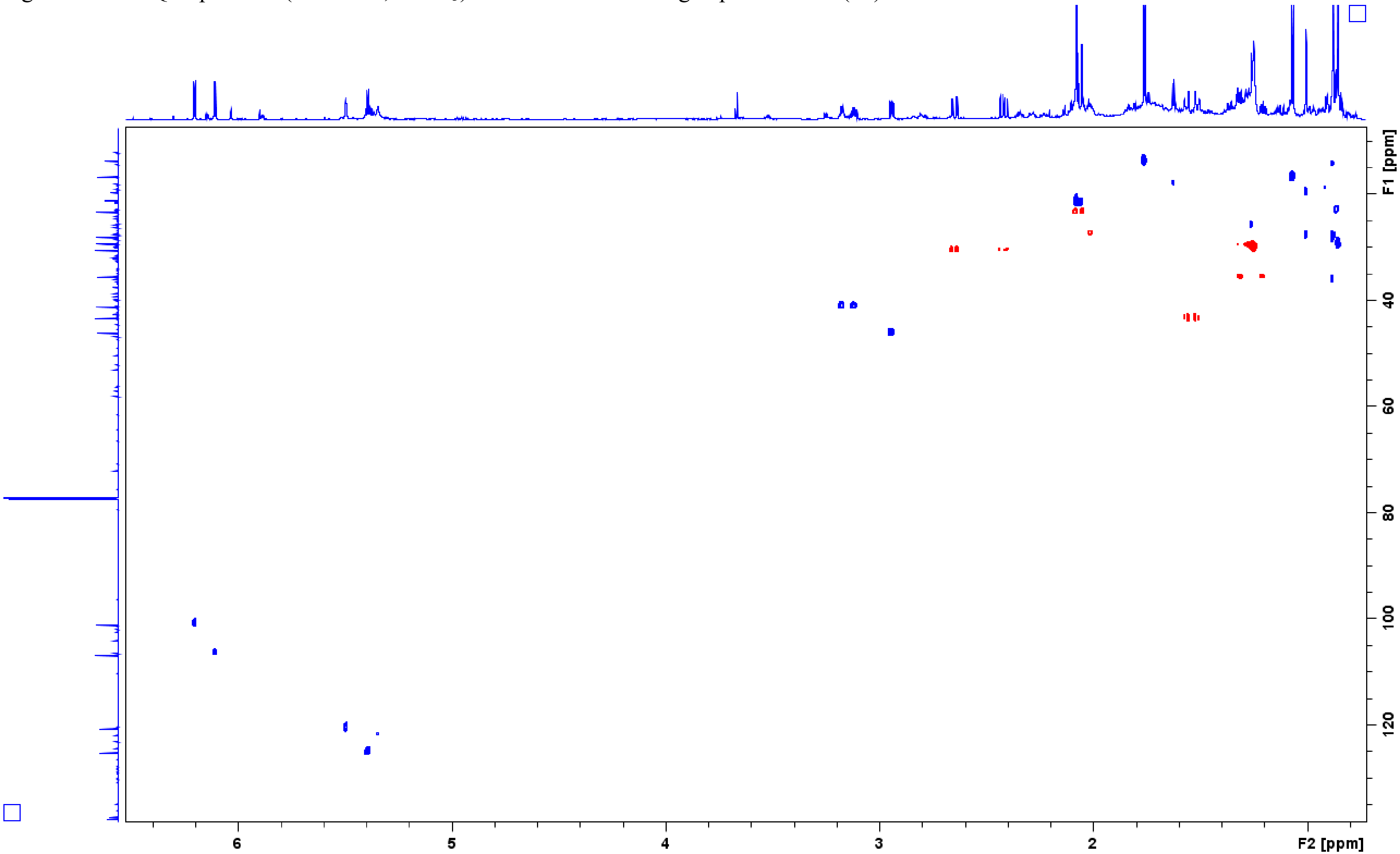


Figure **S28**. HMBC spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)

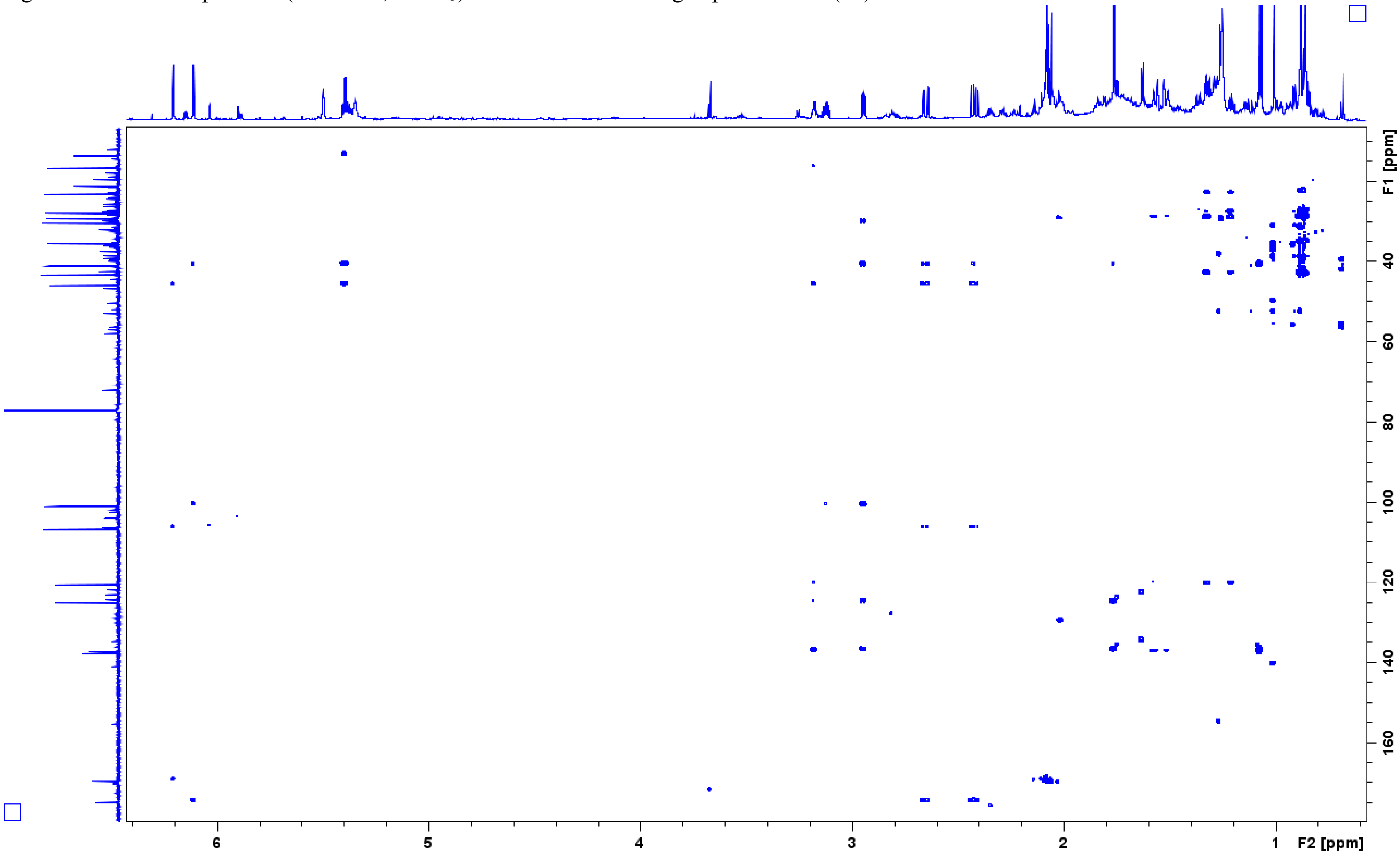
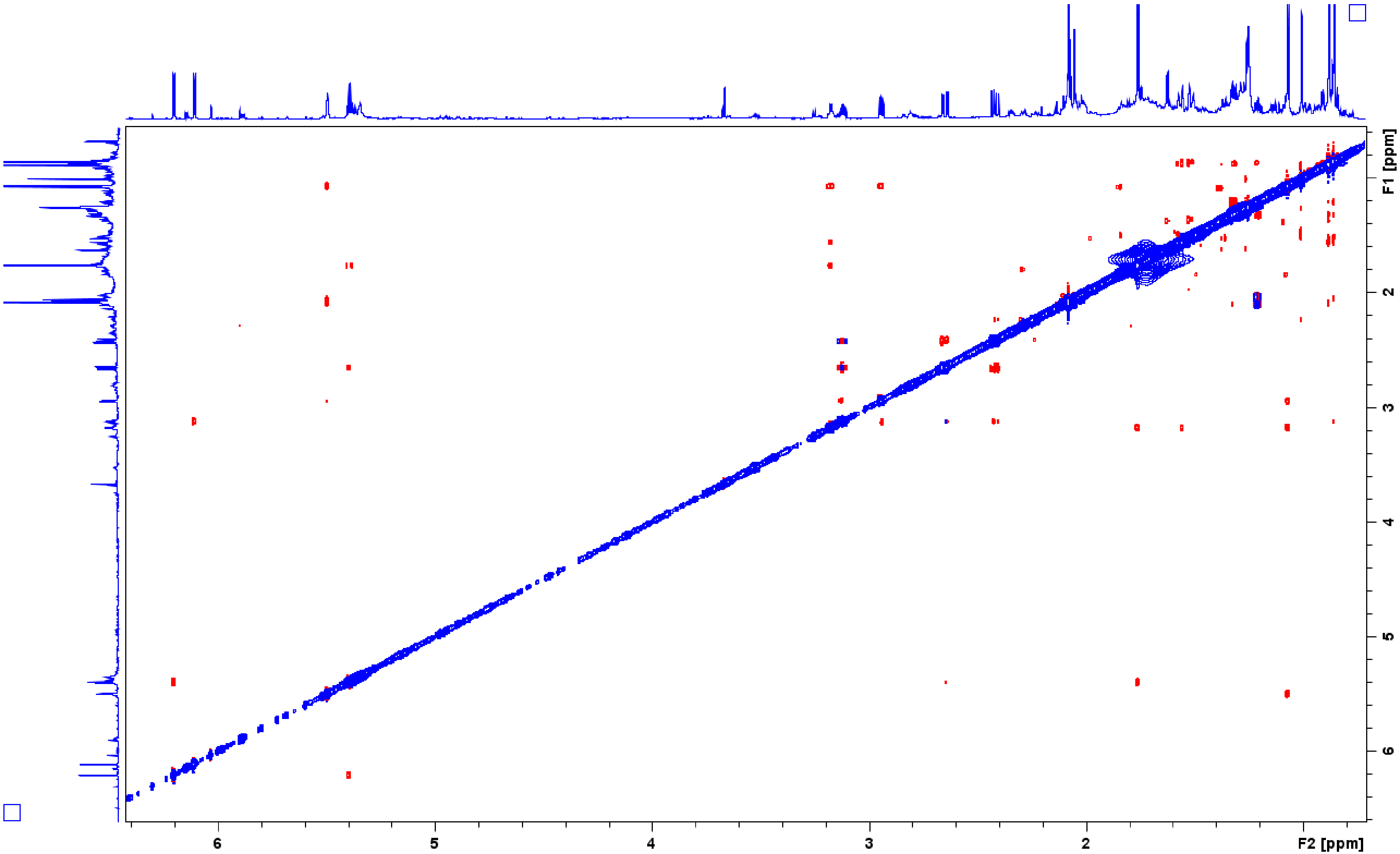


Figure **S29**. NOESY spectrum (900 MHz, $CDCl_3$) for fraction containing daphnelactone (**16**)



Molecular Modeling and DFT calculations.
Monte Carlo Conformational searching was performed using Macromodel v10.0(Schrodinger)[a] for diastereomers 1-6R and 1-6S. Torsional sampling (MCMM) was performed with 1000 steps per rotatable bond. Each step was minimised with the OPLS-2005 force field using TNCG method with maximum iterations of 50,000 and energy convergence threshold of 0.02. All other parameters were left as the default values. The lowest energy conformations (< 3 kcal/mol from global minimum, 10 and 8 conformers for 1-6R and 1-6S respectively) were further optimised using DFT calculations in Jaguar[b].

All conformers were optimised using B3LYP/6311+G(d,p) in vacuum using the Jaguar v8.0 (Schrodinger)[b]. All conformations were compared and any identical conformers removed. This resulted in 10 and 7 unique conformers for 1-6R and 1-6S respectively. The energies for each diastereomers were used to obtain a Boltzmann averaged torsion angle and this was used to calculate the coupling constant using equation 1 (Aydin[c]) and are details are shown in Tables S1 and S2.

$$^3J = 8.06\cos^2(\phi) - 0.87\cos(\phi) + 0.47, \qquad (1)$$

where ϕ is the torsion angle in radians

Table S1. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 - C1) for Diastereomer 6*R*-**2**

Diterpene **2** (6R)	Hartrees	Population (%)	Torsion H7-C1 (°)	Calculated 3J
1	-1458.63617	25.74	144.813	6.6
2	-1458.633809	2.11	10.060	7.4
3	-1458.636449	34.59	133.293	4.9
4	-1458.634268	3.43	2.673	7.6
5	-1458.635774	16.92	130.516	4.4
6	-1458.634479	4.29	129.238	4.2
7	-1458.633266	1.19	-117.009	2.5
8	-1458.634674	5.27	1.077	7.7
9	-1458.634307	3.57	0.817	7.7
10	-1458.634108	2.89	8.283	7.5
Boltzmann Averaged 3J coupling constant for H7-C1: 5.7 Hz				

Table S2. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 - C1) for Diastereomer 6*S*-**2**.

Diterpene **2** (6S)	Hartrees	Population (%)	Torsion H7-C1 (°)	Calculated 3J
1	-1458.637198	26.62	7.4	7.5
2	-1458.637510	37.04	1.7	7.7
3	-1458.634763	2.02	-124.5	3.5
4	-1458.637365	31.77	2.1	7.7
5	-1458.634324	1.27	9.4	7.5
6	-1458.634107	1.01	-114.7	2.2
7	-1458.632911	0.28	127.1	3.9
Boltzmann Averaged 3J coupling constant for H7-C1: 7.5 Hz				

Table S3. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 - C18) for Diastereomer 6*R*-**2**

Diterpene **2** (6R)	Hartrees	Population (%)	Torsion H7-C18 (°)	Calculated 3J
1	-1458.63617	25.74	-93.731889	0.6
2	-1458.633809	2.11	128.739849	4.2
3	-1458.636449	34.59	-105.31093	1.3
4	-1458.634268	3.43	120.873374	3.0
5	-1458.635774	16.92	-108.114953	1.5
6	-1458.634479	4.29	-108.671449	1.6
7	-1458.633266	1.19	1.246339	7.7
8	-1458.634674	5.27	119.103182	2.8
9	-1458.634307	3.57	117.166745	2.5
10	-1458.634108	2.89	125.343829	3.7
Boltzmann Averaged 3J coupling constant for H7-C18: 1.5 Hz				

Table S4. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 - C18) for Diastereomer 6*S*-**2**.

Diterpene **2** (6S)	Hartrees	Population (%)	Torsion H7-C18 (°)	Calculated 3J
1	-1458.637198	26.62	-109.568709	1.7
2	-1458.637510	37.04	-115.718426	2.4
3	-1458.634763	2.02	114.132071	2.2
4	-1458.637365	31.77	-115.279968	2.3
5	-1458.634324	1.27	-108.512206	1.6
6	-1458.634107	1.01	122.968375	3.3
7	-1458.632911	0.28	8.591968	7.5
Boltzmann Averaged 3J coupling constant for H7-C18: 2.2 Hz				

Table S5. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 – C5) for Diastereomer 6*R*-**2**

Diterpene **2** (6R)	Hartrees	Population (%)	Torsion H7-C5 (°)	Calculated 3J
1	-1458.63617	25.74	22.294	6.6
2	-1458.633809	2.11	-106.706	1.4
3	-1458.636449	34.59	11.632	7.4
4	-1458.634268	3.43	-114.514	2.2
5	-1458.635774	16.92	8.933	7.5
6	-1458.634479	4.29	11.544	7.4
7	-1458.633266	1.19	121.863	3.2
8	-1458.634674	5.27	-116.291	2.4
9	-1458.634307	3.57	-121.22	3.1
10	-1458.634108	2.89	-112.771	2.0
Boltzmann Averaged 3J coupling constant for H7-C5: 6.3 Hz				

Table S6. Energies, population percentages, torsion angles and weighted 3J coupling constants (H7 – C5) for Diastereomer 6*S*-**2**.

Diterpene **2** (6S)	Hartrees	Population (%)	Torsion H7-C5 (°)	Calculated 3J
1*	-1458.637198	26.62	128.959	4.2
2*	-1458.637510	37.04	122.662	3.3
3*	-1458.634763	2.02	-2.566	7.6
4*	-1458.637365	31.77	123.151	3.4
5	-1458.634324	1.27	127.279	4.0
6	-1458.634107	1.01	2.378	7.6
7	-1458.632911	0.28	-111.914	1.9
Boltzmann Averaged 3J coupling constant for H7-C5: 3.7 Hz				

* Me-18 is equatorial in each of conformers 1-4