

SUPPLEMENTARY MATERIAL

Bis-nor-diterpene from *Cnidoscolus quercifolius* (Euphorbiaceae) induces tubulin depolymerization-mediated apoptosis in BRAF-mutated melanoma cells

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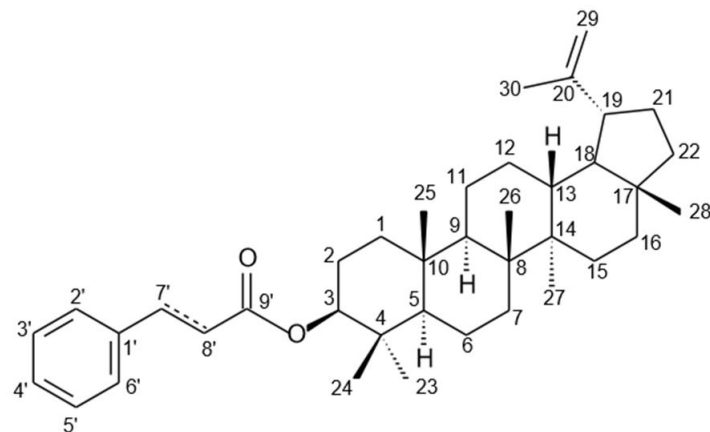
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1. NMR data from compounds 1 and 2



1: lupeol-3 β -*O*-cinnamate
2: lupeol-3 β -*O*-dihydrocinnamate

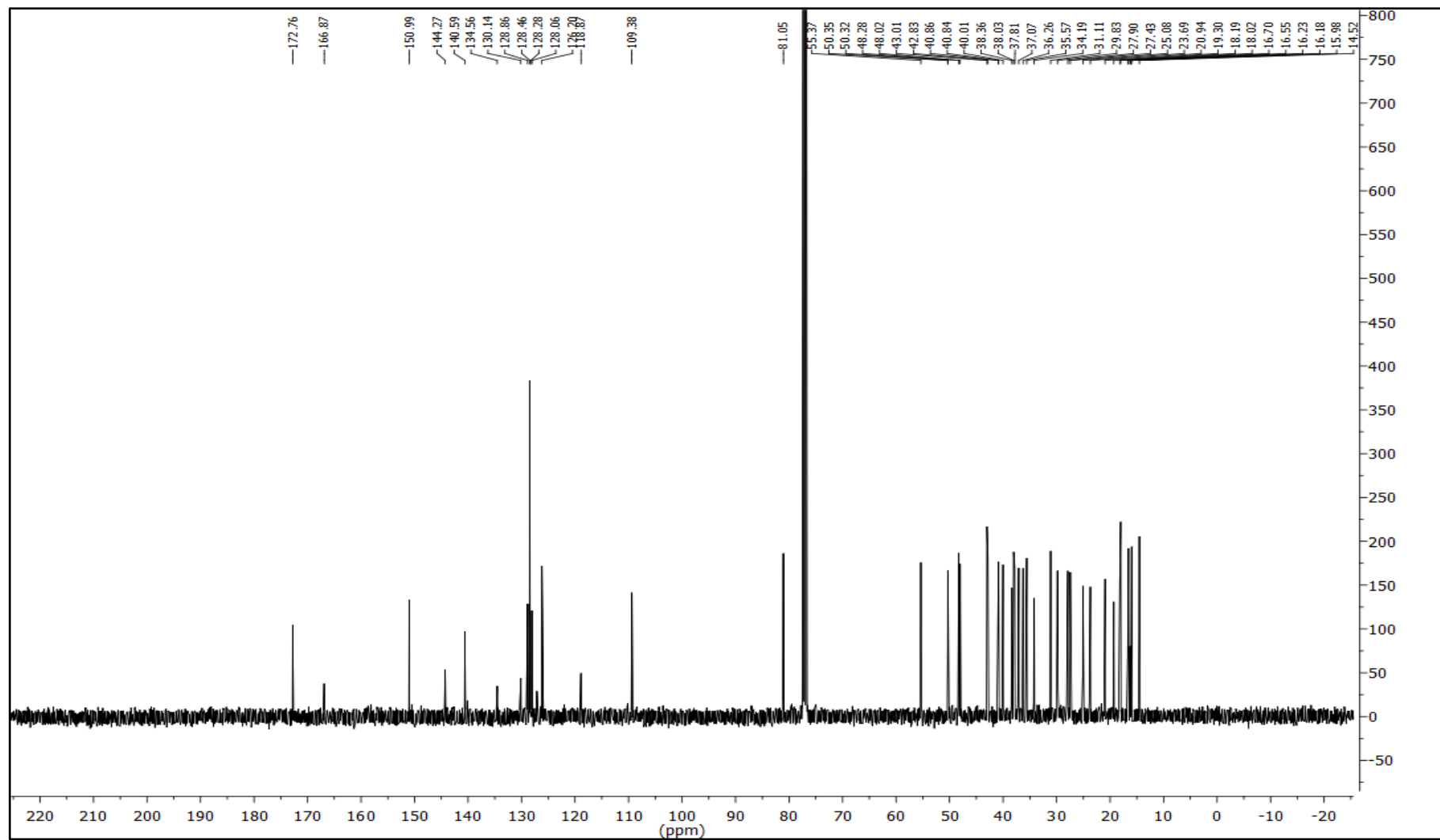
Table S1. NMR data (δ , ppm) of compounds 1 and 2 in CDCl₃ (400 MHz).

Position	Compound 1				Compound 2			
	HSQC (<i>J</i> , Hz)		HMBC		HSQC (<i>J</i> , Hz)		HMBC	
	¹³ C	¹ H	² <i>J</i> _{CH}	³ <i>J</i> _{CH}	¹³ C	¹ H	² <i>J</i> _{CH}	³ <i>J</i> _{CH}
C								
4	37.8	-	H-23, H-24		37.8	-	H-23, H-24	
8	40.9	-	H-26	H-27	40.9	-	H-26	H-27
10	37.0	-	H-27	H-26	37.1	-	H-27	H-26
14	42.8	-	H-25		42.8	-	H-25	

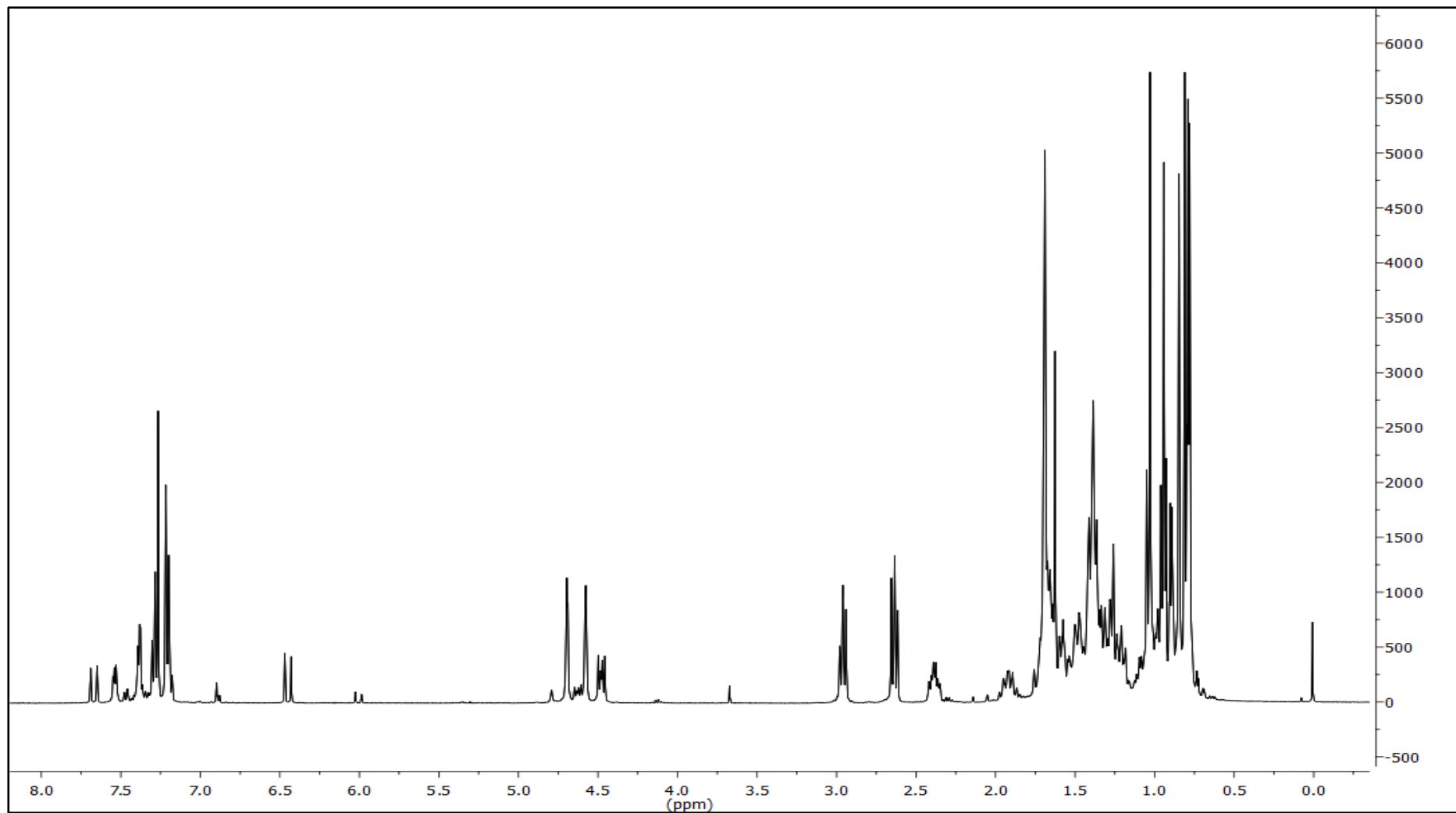
17	43.0	-	H-28		43.0	-	H-28	
20	150.9	-	H-19, H-30	H-18	150.9	-	H-19, H-30	H-18
1'	134.6	-	H-8'	H-3'/5'	140.6	-	H-8'	H-7'
9'	166.9	-	H-7'	H-8', H-3	172.8	-	H-7'	H-8', H-3
CH								
3	81.0	4.63 dd (10.4; 5.2)	H-2	H-23, H-24	81.0	4.48 dd (10; 5.6)	H-2	H-23, H-24
5	55.3	0.84 m		H-23, H-24, H-25	55.4	0.84 m		H-23, H-24, H-25
9	50.3	1.30 m		H-25, H-26	50.3	1.30 m		H-25, H-26
13	38.0	1.66 m		H-27	38.0	1.66 m		H-27
18	48.3	1.37 m	H-19	H-28	48.3	1.33 m	H-19	H-28
19	48.0	2.38 m		H-30	48.0	2.38 m		H-30
7'	144.3	7.67 d (16)			-	-		
8'	118.9	6.45 d (16)	H-7'		-	-		
2'/6'	128.3	7.53 m			128.1	7.19 m		
3'/5'	128.5	7.28 m			128.9	7.38 m		
4'	130.1	7.39 m		H-2'/6'	126.2	7.20 m		
CH₂								
1	38.4	1.73; 0.98 m		H-25	38.3	1.73; 0.98 m		H-25

2	23.7	1.60; 1.58 m		23.8	1.60; 1.58 m	
6	18.2	1.50; 1.30 m		18.1	1.50; 1.30 m	
7	34.2	1.39 m	H-26	34.2	1.39 m	H-26
11	20.9	1.41; 1.25 m		20.9	1.41; 1.25 m	
12	25.1	1.66; 1.09 m		25.1	1.66; 1.09 m	
15	27.4	1.64; 1.03 m	H-27	27.4	1.64; 1.03 m	H-27
16	35.6	1.50; 1.47 m	H-28	35.6	1.50; 1.47 m	H-28
21	29.8	1.92; 1.34 m		29.8	1.92; 1.34 m	
22	40.0	1.39; 1.21 m	H-28	40.0	1.39; 1.21 m	H-28
29	109.4	4.70 s; 4.58 s		109.4	4.70 s; 4.58 s	
7'	-	-		31.1	2.96 t	H-8'
8'	-	-		36.3	2.63 t	H-7'
CH₃						
23	27.9	0.90 s	H-23	28.0	0.78 s	H-23
24	16.5	0.95 s	H-24	16.7	0.82 s	H-24
25	16.1	0.84 s		16.2	0.89 s	
26	15.9	1.04 s		15.9	1.06 s	
27	14.5	0.95 s	H-15	14.5	0.97 s	H-15
28	18.0	1.00 s		18.0	0.81 s	
30	19.3	1.69 s	H-19, H-29	19.3	1.68 s	H-19, H-29

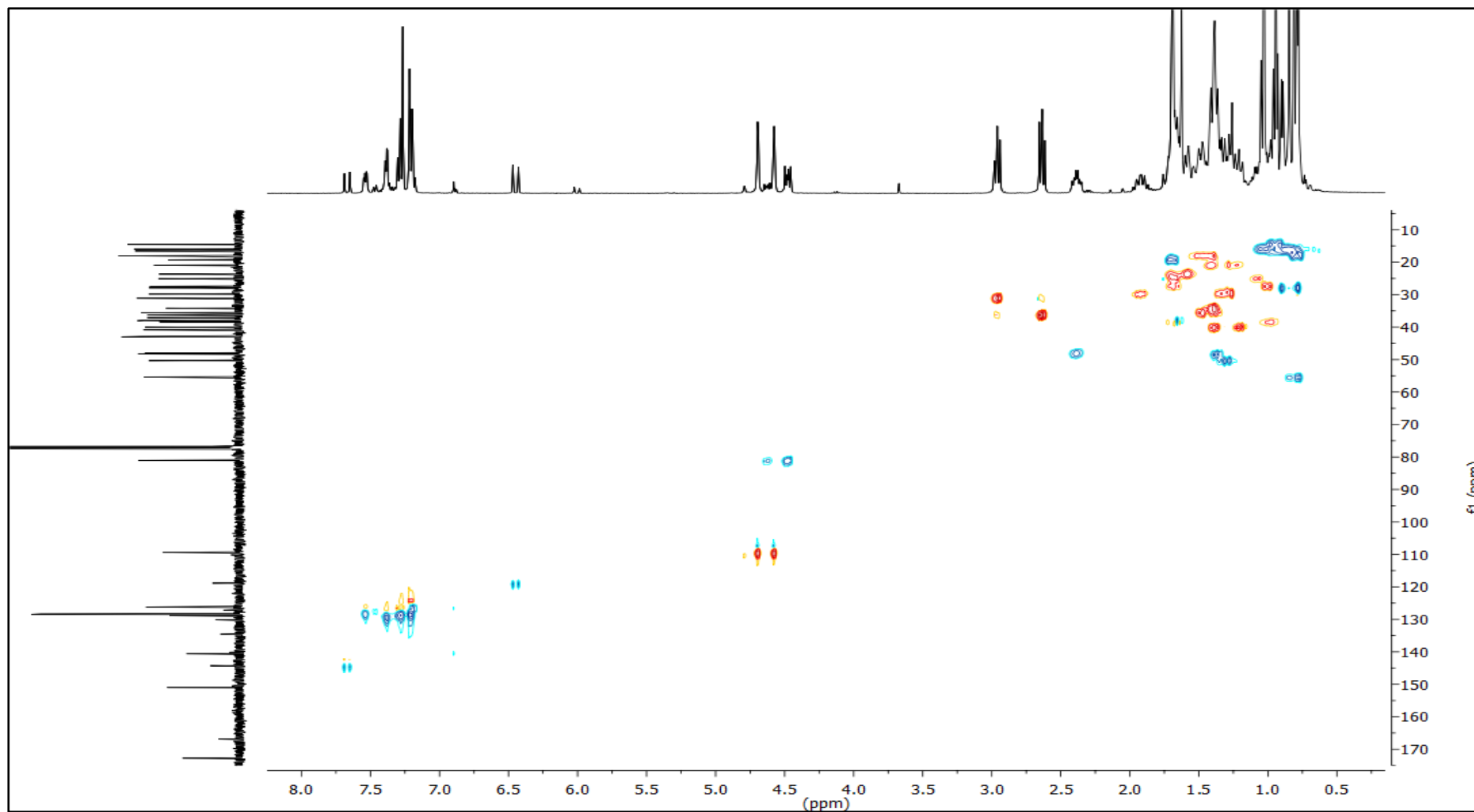
^{13}C NMR spectrum of compounds 1/2 in CDCl_3 (100 MHz).



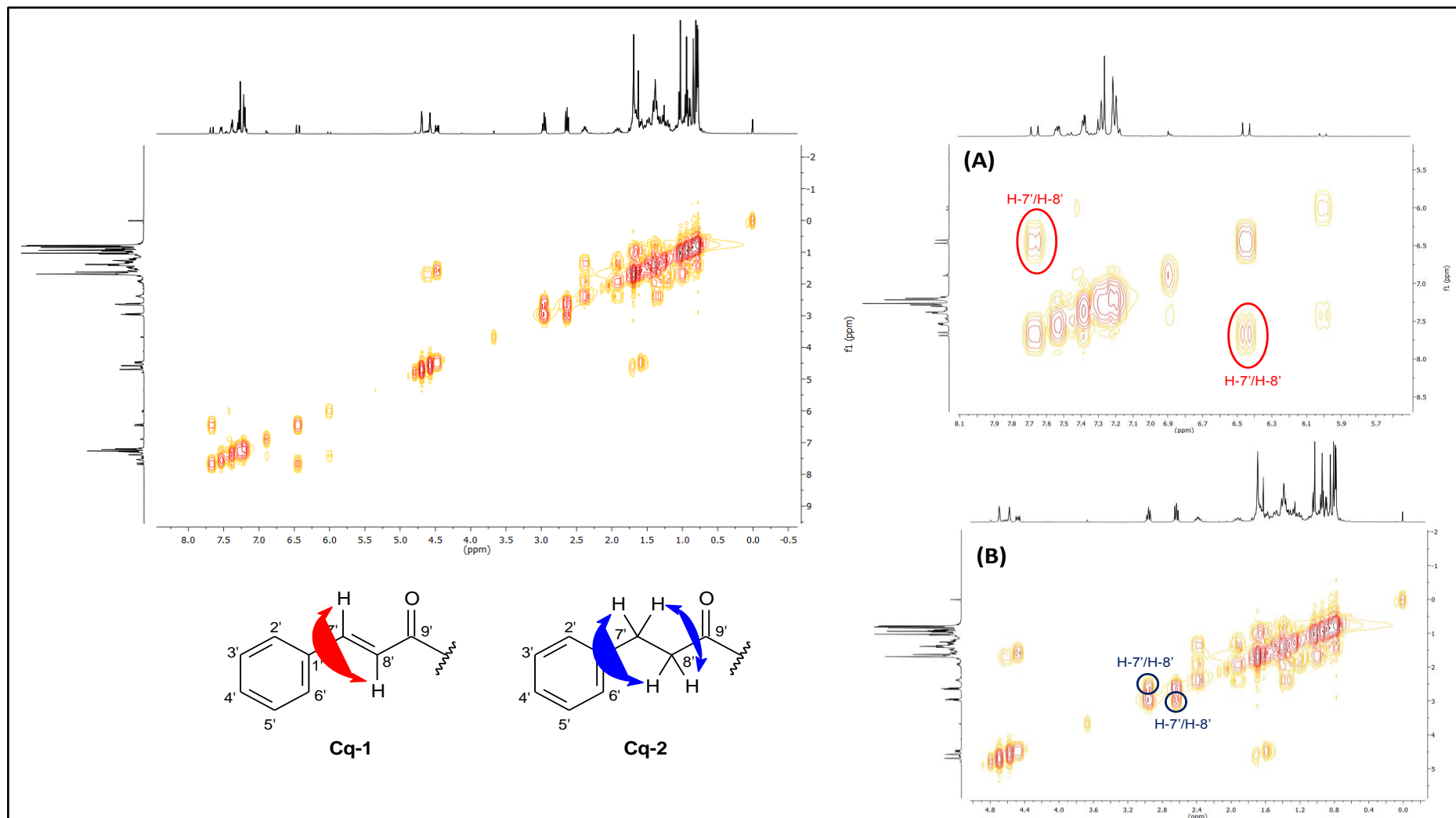
^1H NMR spectrum of compounds **1/2** in CDCl_3 (400 MHz).



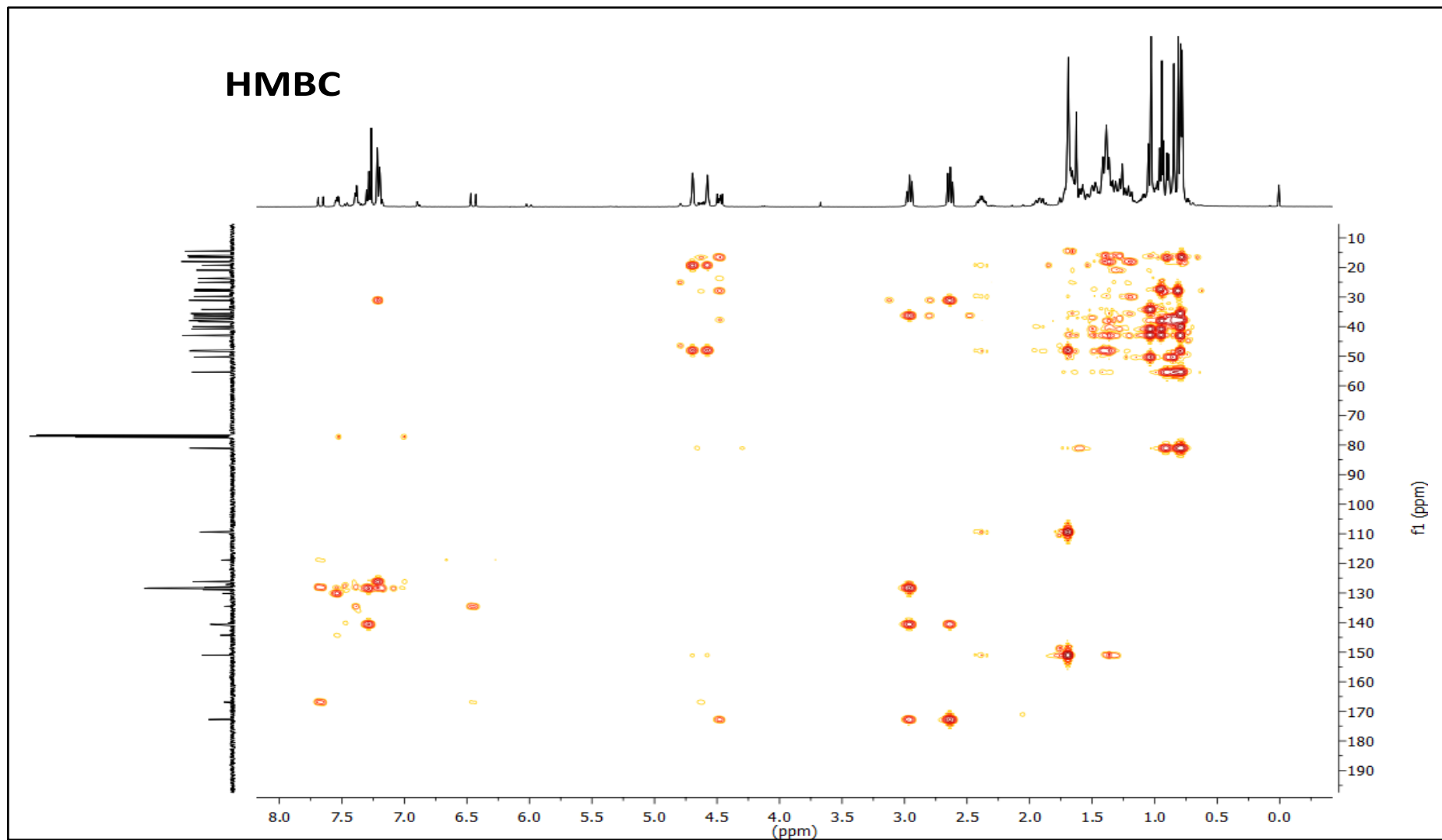
HSQC spectrum of compounds **1/2** in CDCl_3 (400 MHz).



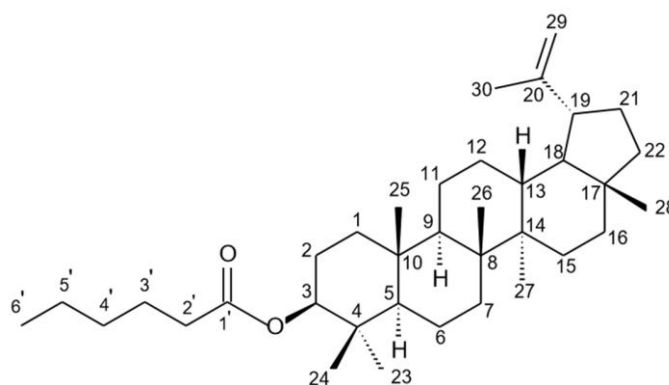
COSY spectrum of compounds **1/2** in CDCl_3 (400 MHz).



HMBC spectrum of compounds **1/2** in CDCl₃ (400 MHz).



2. NMR data from compound 3



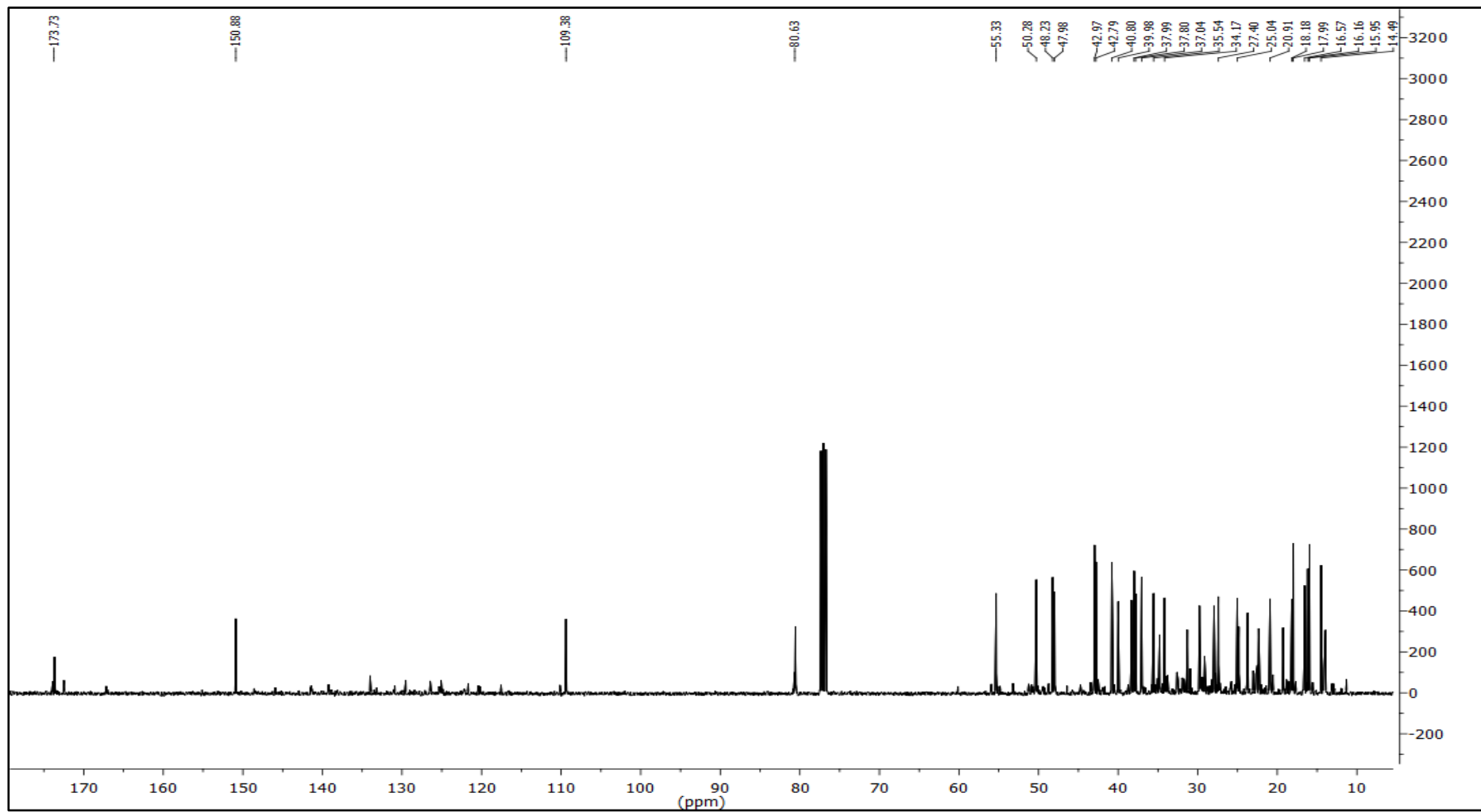
3: lupeol-3β-*O*-hexanoate

Table S2. NMR data (δ , ppm) of compound **3** in CDCl_3 (400 MHz).

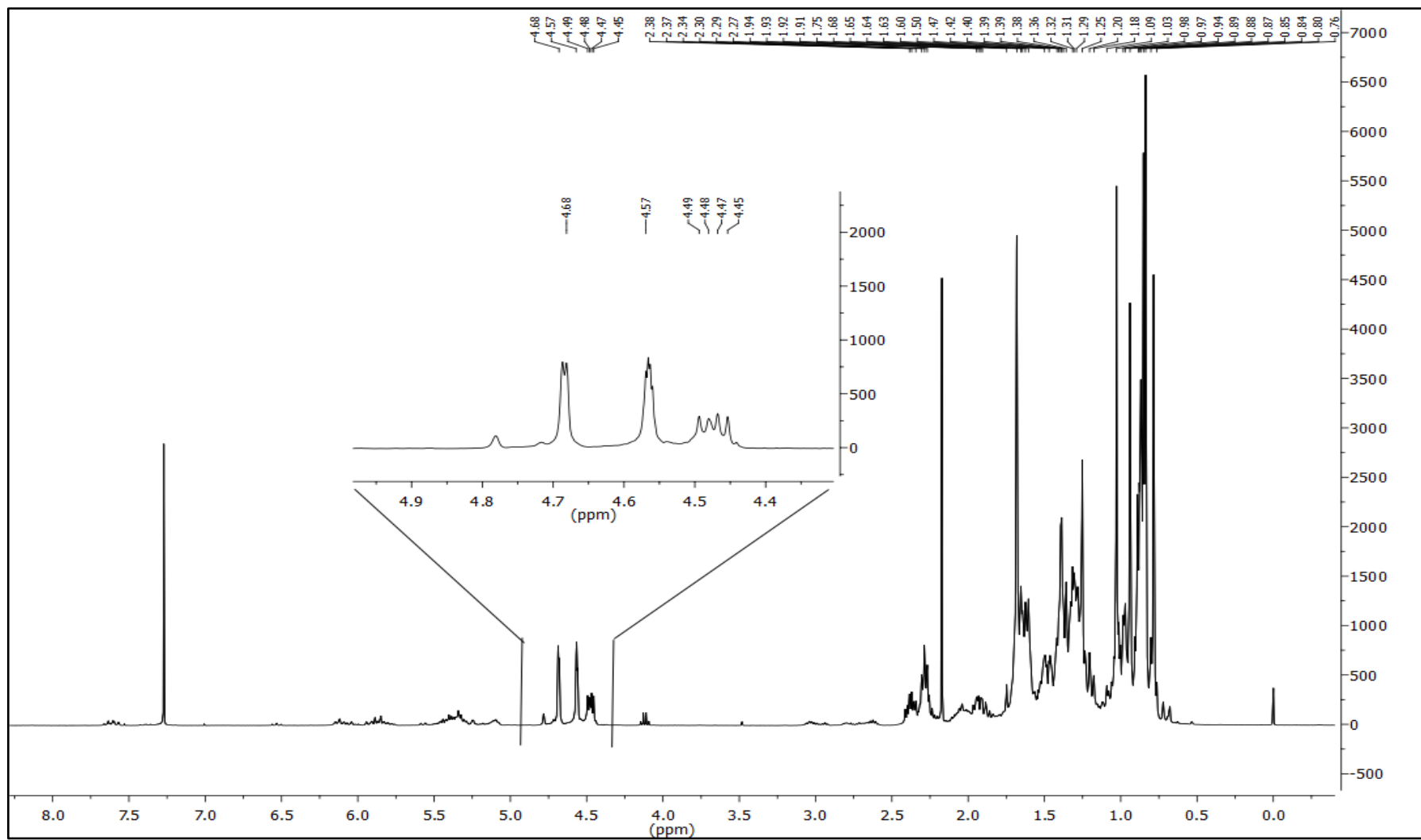
Position	Compound 3			
	HSQC (J , Hz)		HMBC	
	^{13}C	^1H	$^2J_{\text{CH}}$	$^3J_{\text{CH}}$
C				
4	37.8	-	H-23, H-24	
8	40.8	-	H-26	H-27
10	37.0	-	H-1, H-25	
14	42.8	-	H-27	H-18, H-26
17	43.0	-	H-28	
20	150.9	-	H-19, H-30	H-18
1'	173.7	-	H-2'	H-3, H-3'
CH				
3	80.5	4.47 dd (40; 8.0)		H-23, H-24
5	55.3	0.76 m		H-23, H-24, H-25
9	50.3	1.29 m		H-25, H-26
13	38.0	1.65 m		H-27
18	48.2	1.35 m	H-19	H-28
19	48.0	2.38 m	H-18	H-29, H-30
CH₂				
1	38.3	0.98 m		H-25
2	23.7	1.62 m		

6	18.2	1.52 m		
7	34.2	1.39 m		H-26
11	20.9	1.41; 1.0 m		
12	25.0	1.74; 1.08 m		
15	27.4	1.65; 1.05 m		H-27
16	35.5	1.49; 1.46 m		H-28
21	29.8	1.91; 1.25 m		
22	40.0	1.38; 1.20 m		H-19, H-28
29	109.4	4.68; 4.57 s		H-19 e H-30
2'	34.8	2.28 t	H-3'	
3'	24.8	1,62 m	H-2', H-4'	
4'	31.3	1,30 m	H-3', H-5'	
5'	22.3	1,25 m	H-4', H-6'	
<hr/>				
CH₃				
23	27.9	0.83-0.86 s		H-24
24	16.6	0.83-0.86 s		H-3, H-23
25	16.2	0.83-0.86 s		
26	15.9	0.94 s		
27	14.5	1.02 s		
28	18.0	0.83-0.86 s		
30	19.3	1.68 s		H-19, H-29
6'	13.9	0.78 s	H-5'	
<hr/>				

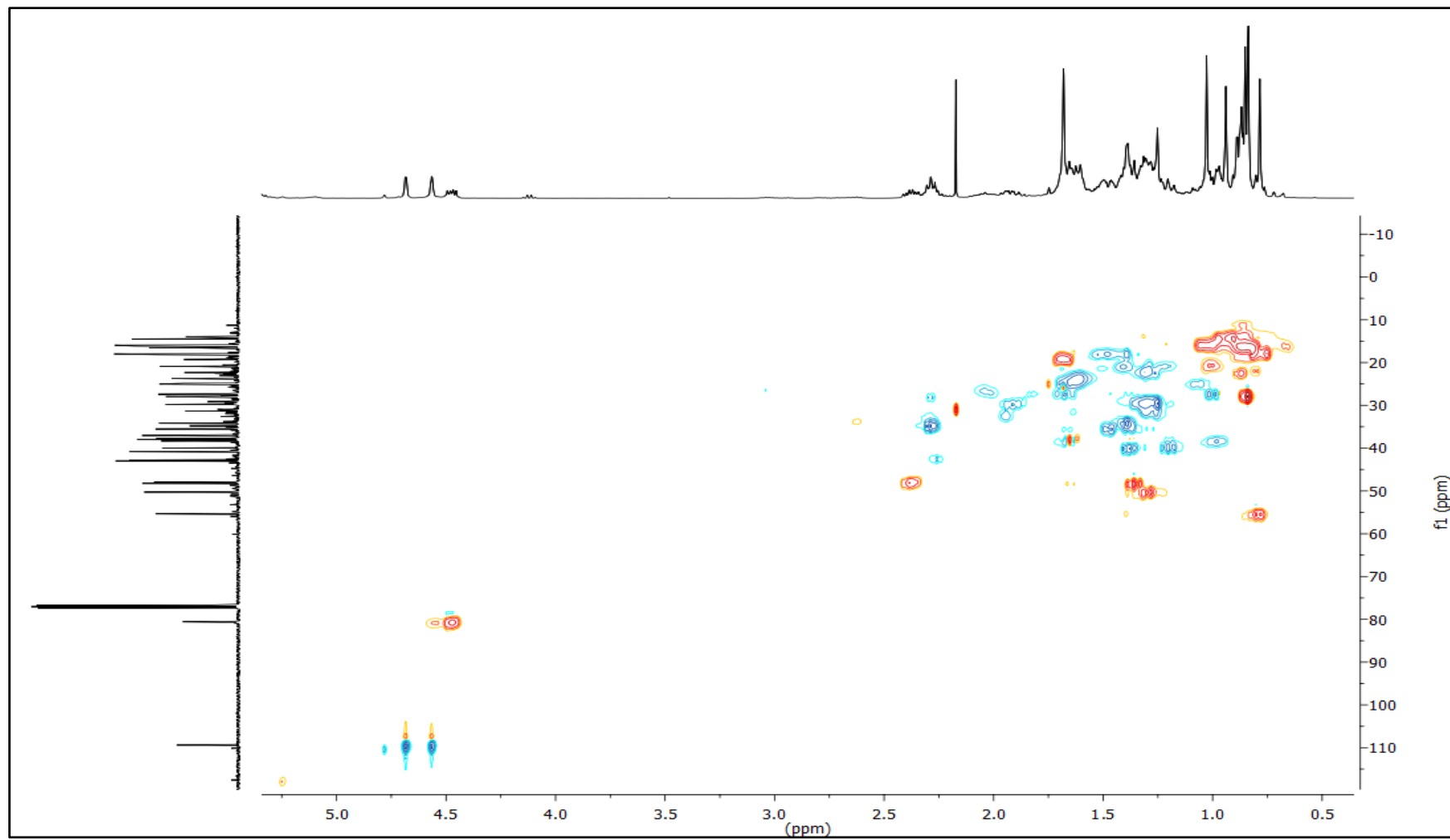
^{13}C NMR spectrum of compound **3** in CDCl_3 (100 MHz).



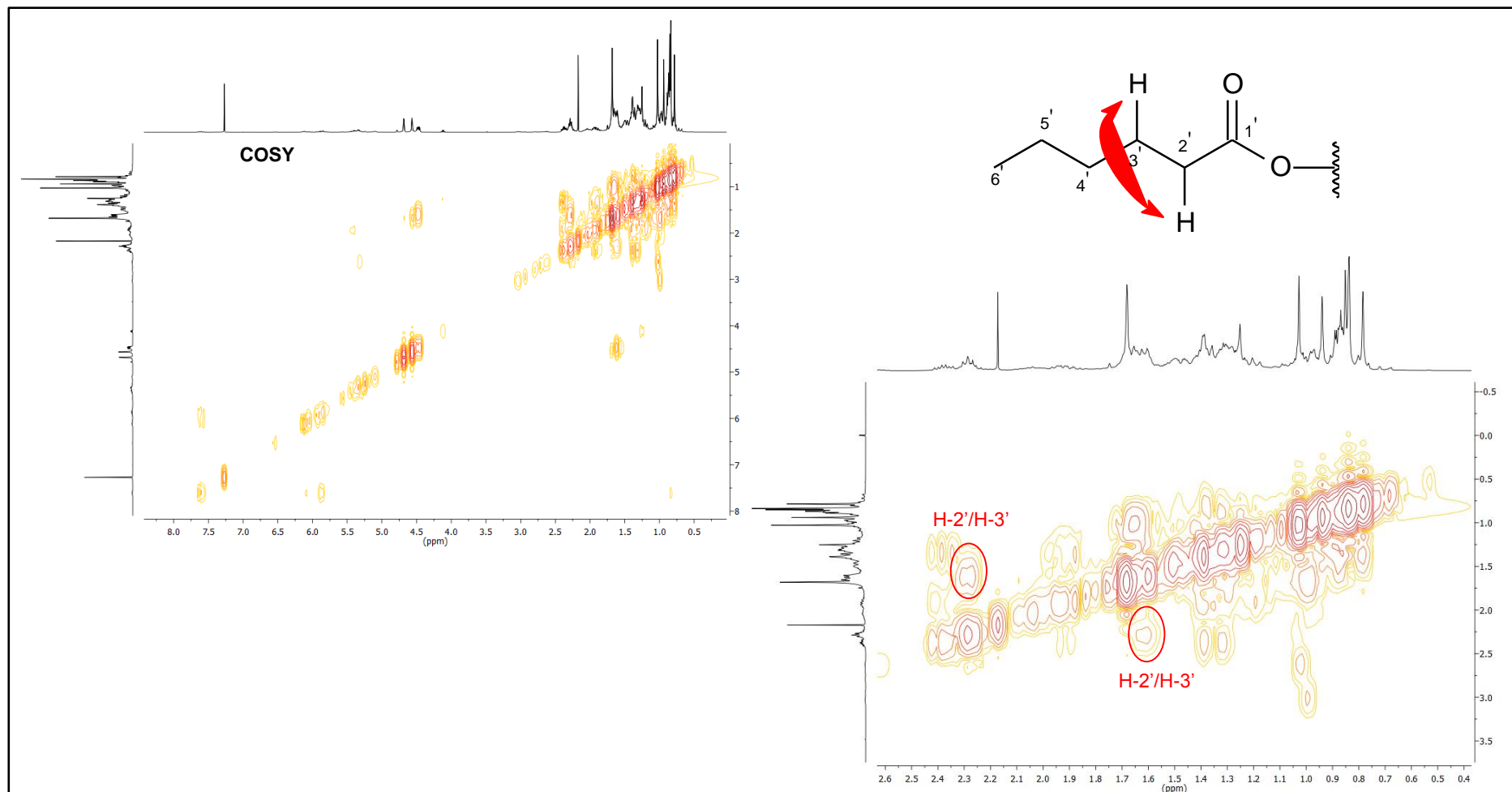
^1H NMR spectrum of compound **3** in CDCl_3 (400 MHz).



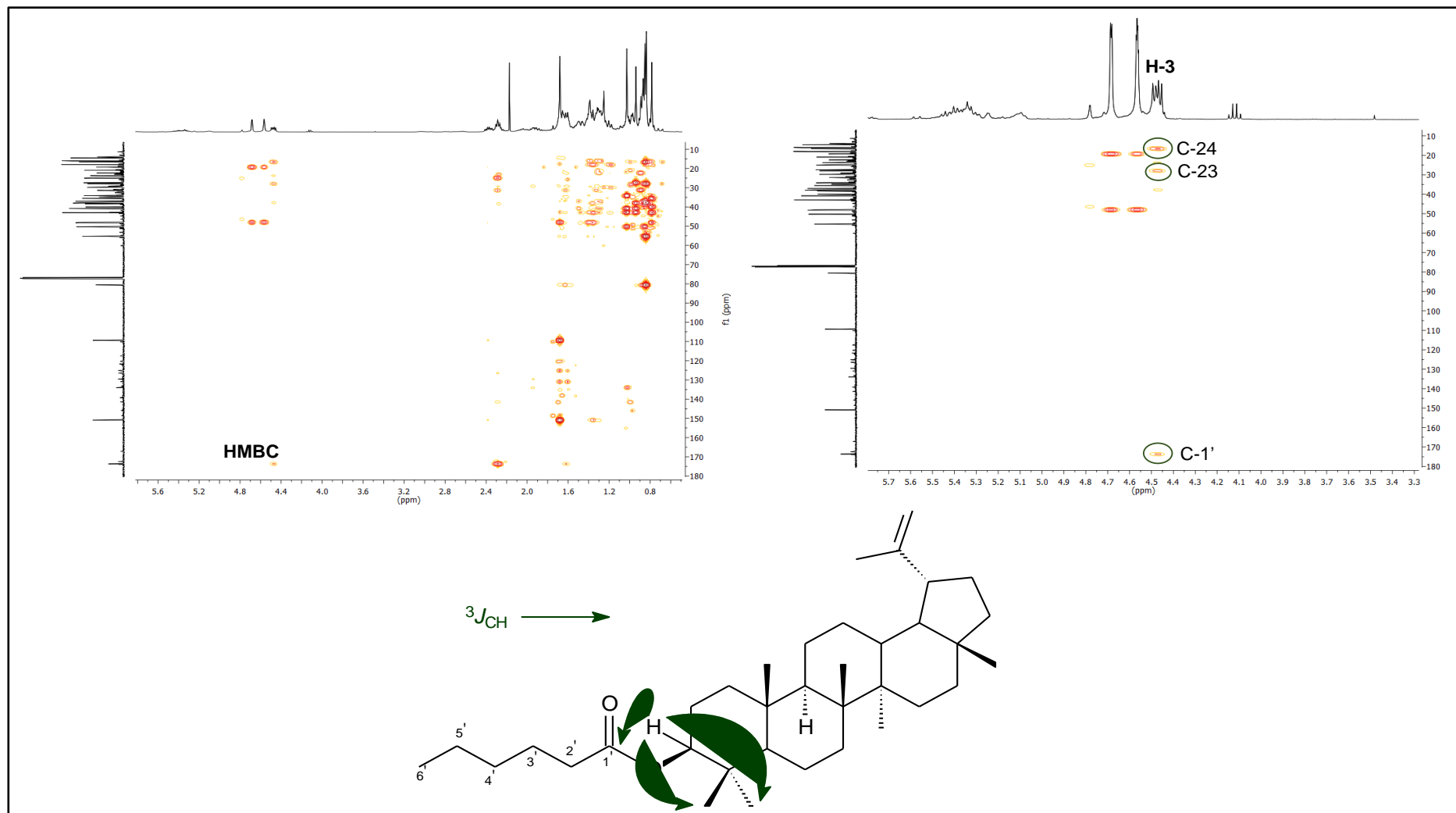
HSQC NMR spectrum of compound **3** in CDCl₃ (400 MHz).



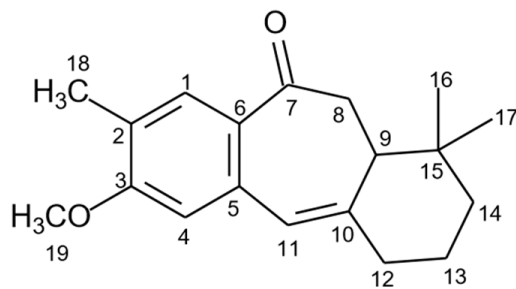
COSY NMR spectrum of compound **3** in CDCl₃ (400 MHz).



HMBC NMR spectrum of compound **3** in CDCl₃ (400 MHz).



3. NMR data from compound 4



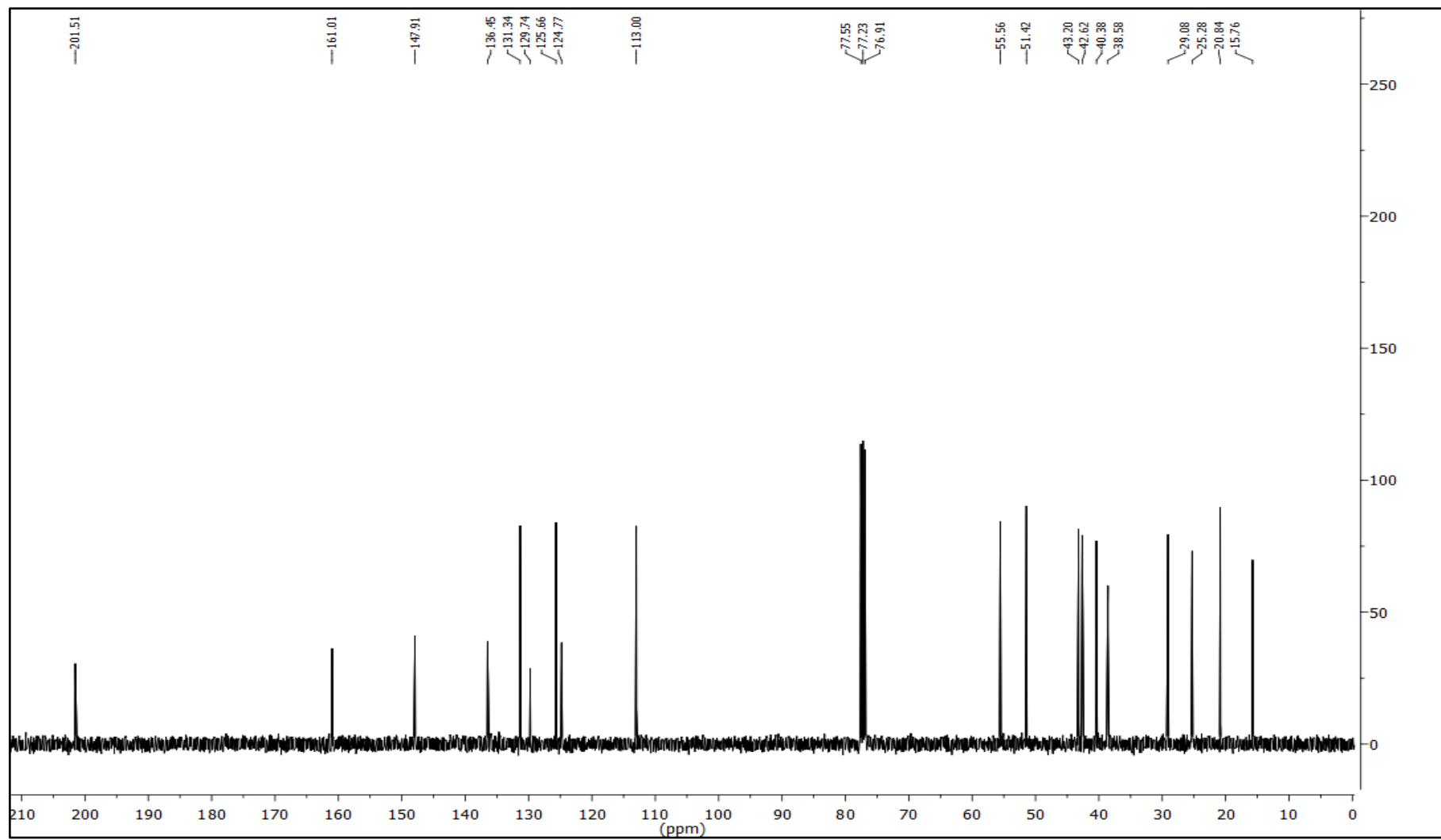
4: Phyllacanthone

Table S3. NMR data (δ , ppm) of compound 4 in CDCl₃ (400 MHz).

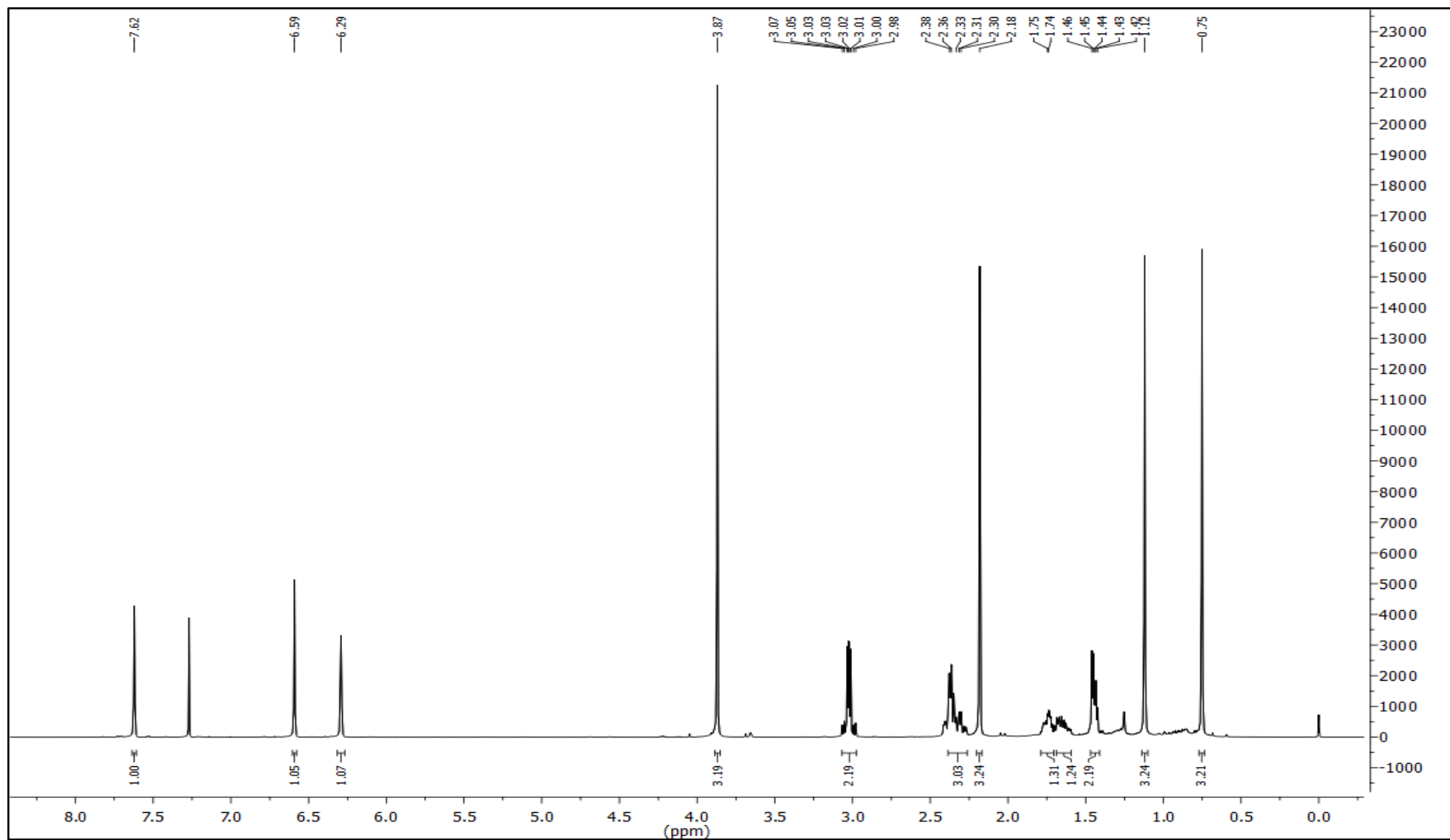
Position	Compound 4			
	HSQC (J , Hz)		HMBC	
	¹³ C	¹ H	² J_{CH}	³ J_{CH}
C				
2	124.8	-	H-18	H-4
3	161.0	-	H-4	H-1, H-18, H-19
5	136.4	-		H-1
6	129.7	-		H-4, H-11
7	201.5	-	H-8	H-1, H-9
10	147.9	-	H-9, H-11	H-8
15	38.5	-	H-9, H-14, H-16, H-17	H-8
CH				
1	131.3	7.62 s		H-18
4	113.0	6.59 s		H-11
9	51.4	2.36 m	H-8	H-11, H-16, H-17
11	125.7	6.29 s		H-4, H-9
CH₂				
8	42.6	3.02 d (5.6); 3.01 d (6.4)	H-9	
12	40.3	2.34 m; 2.30 m		
13	25.3	1.75 m; 1.66 m	H-14	
14	43.2	1.44 m		H-9, H-16, H-17

CH₃				
16	20.8	0.75 s		H-9, H-17
17	29.0	1.12 s		H-16
18	15.8	2.18 s		H-1
MeO (19)	55.5	3.87 s		

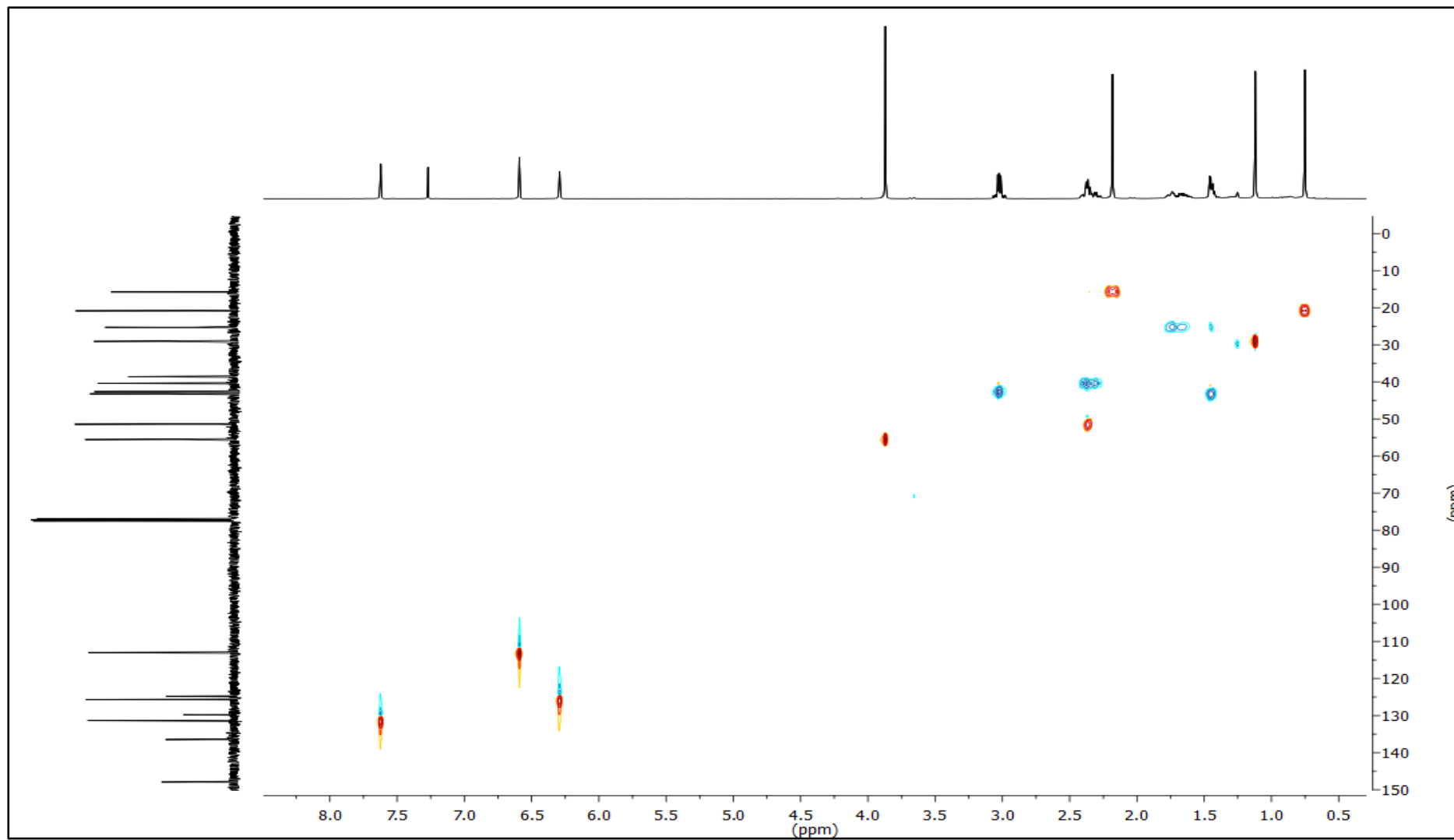
^{13}C NMR spectrum of compound **4** in CDCl_3 (100 MHz).



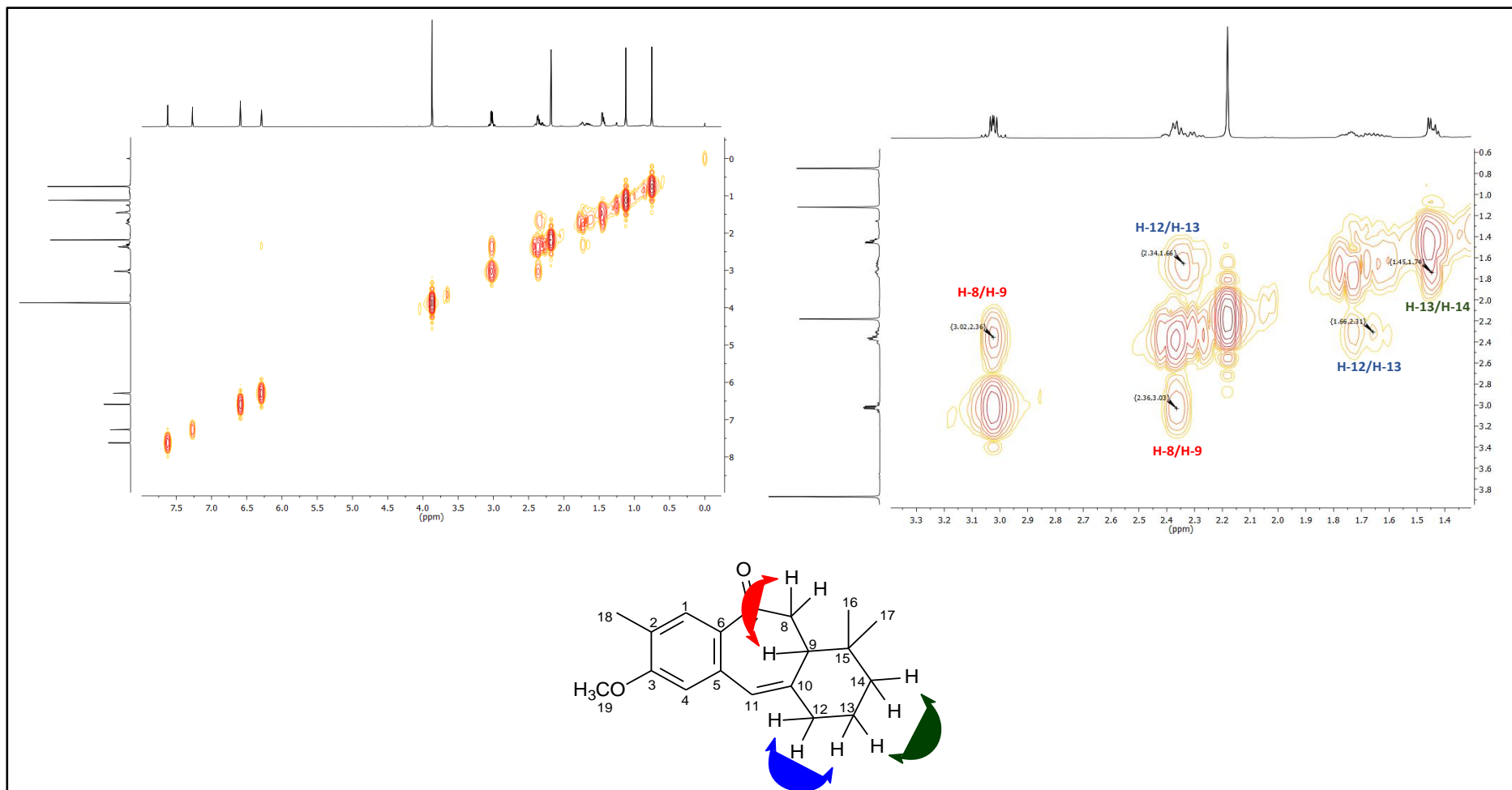
^1H NMR spectrum of compound **4** in CDCl_3 (400 MHz).



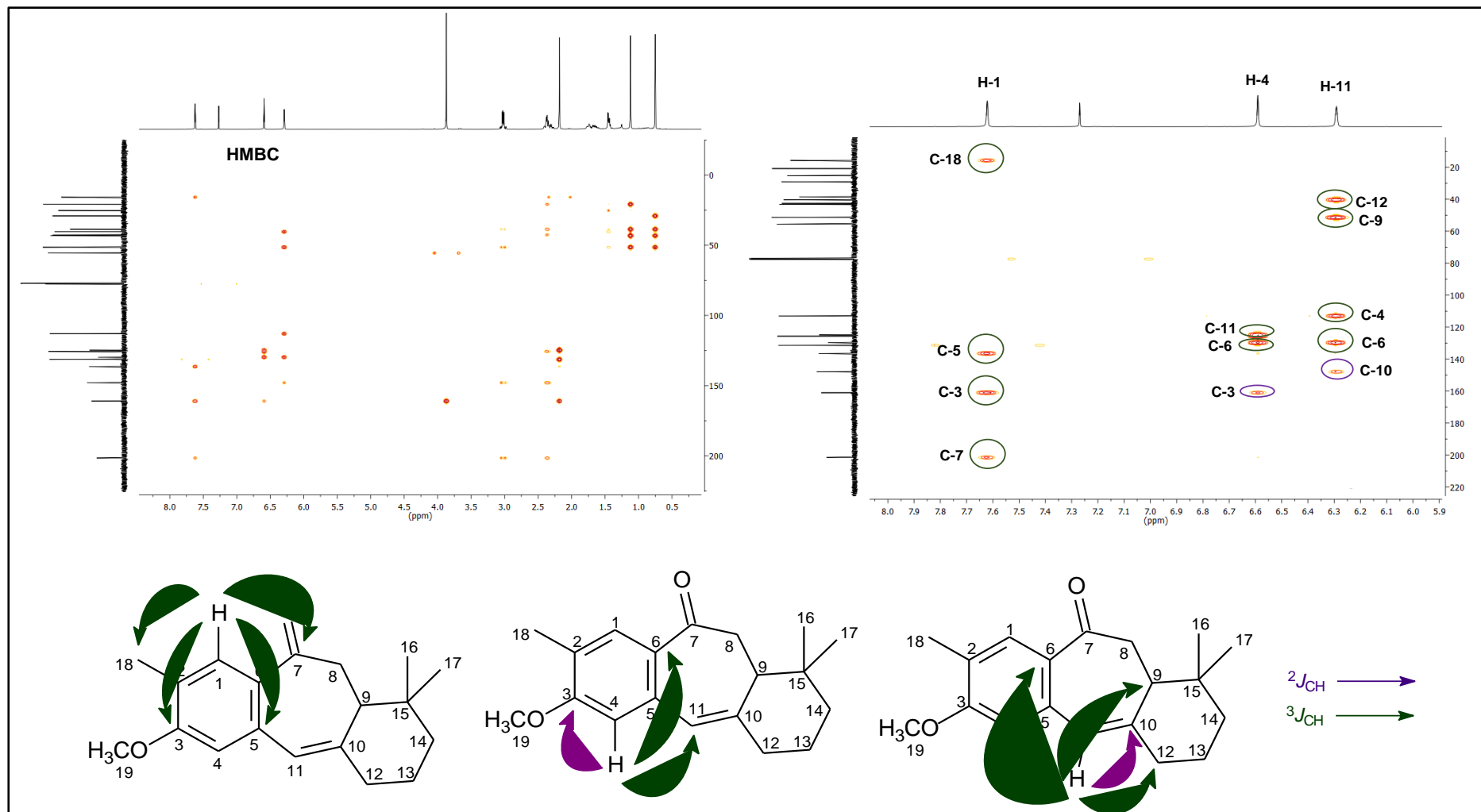
HSQC NMR spectrum of compound **4** in CDCl₃ (400 MHz).

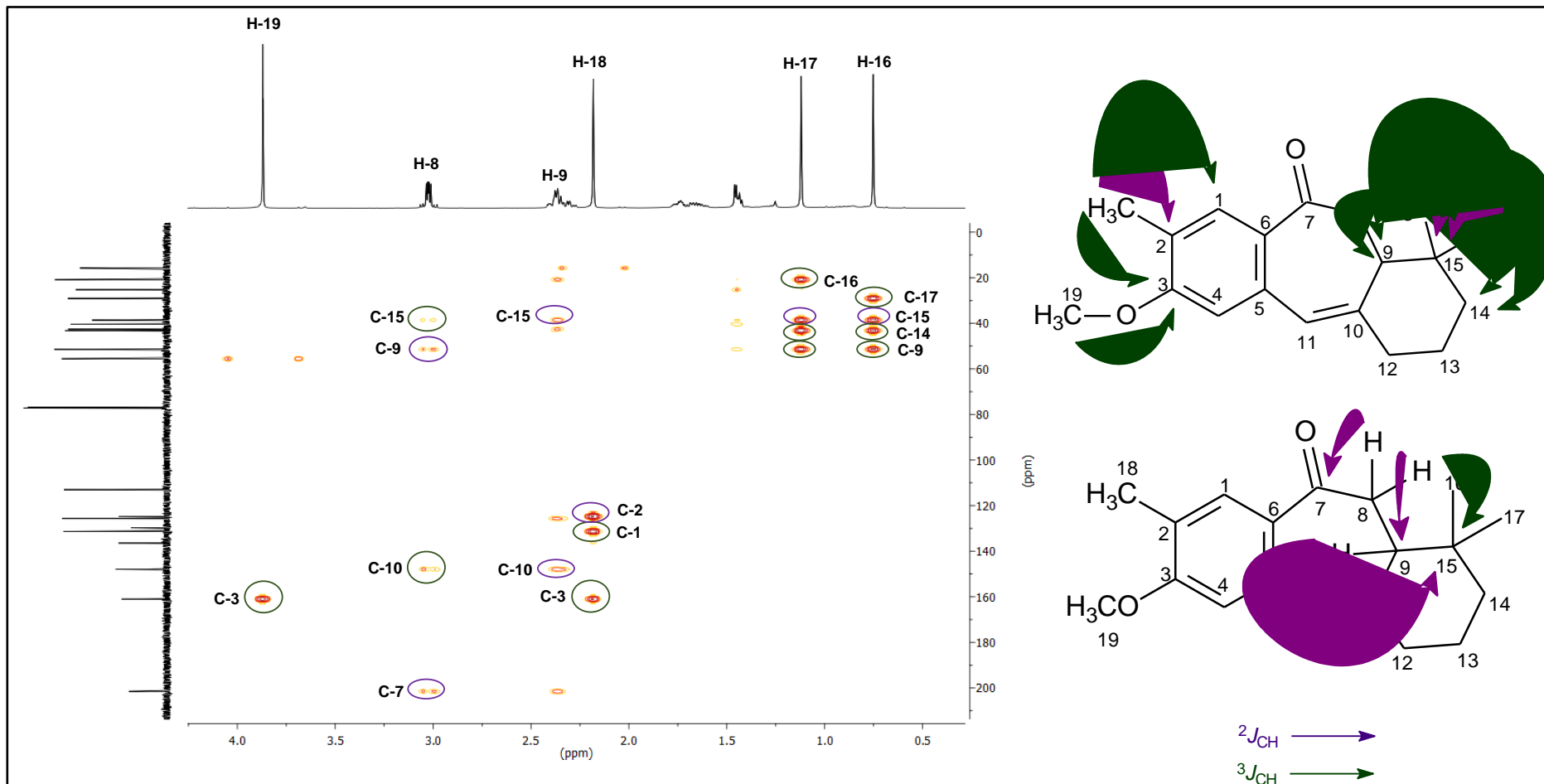


COSY NMR spectrum of compound **4** in CDCl₃ (400 MHz).

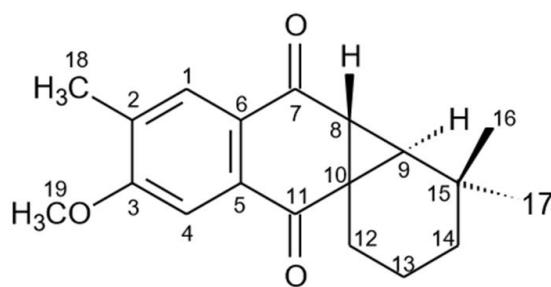


HMBC NMR spectrum of compound **4** in CDCl₃ (400 MHz).





4. NMR data from compound 4



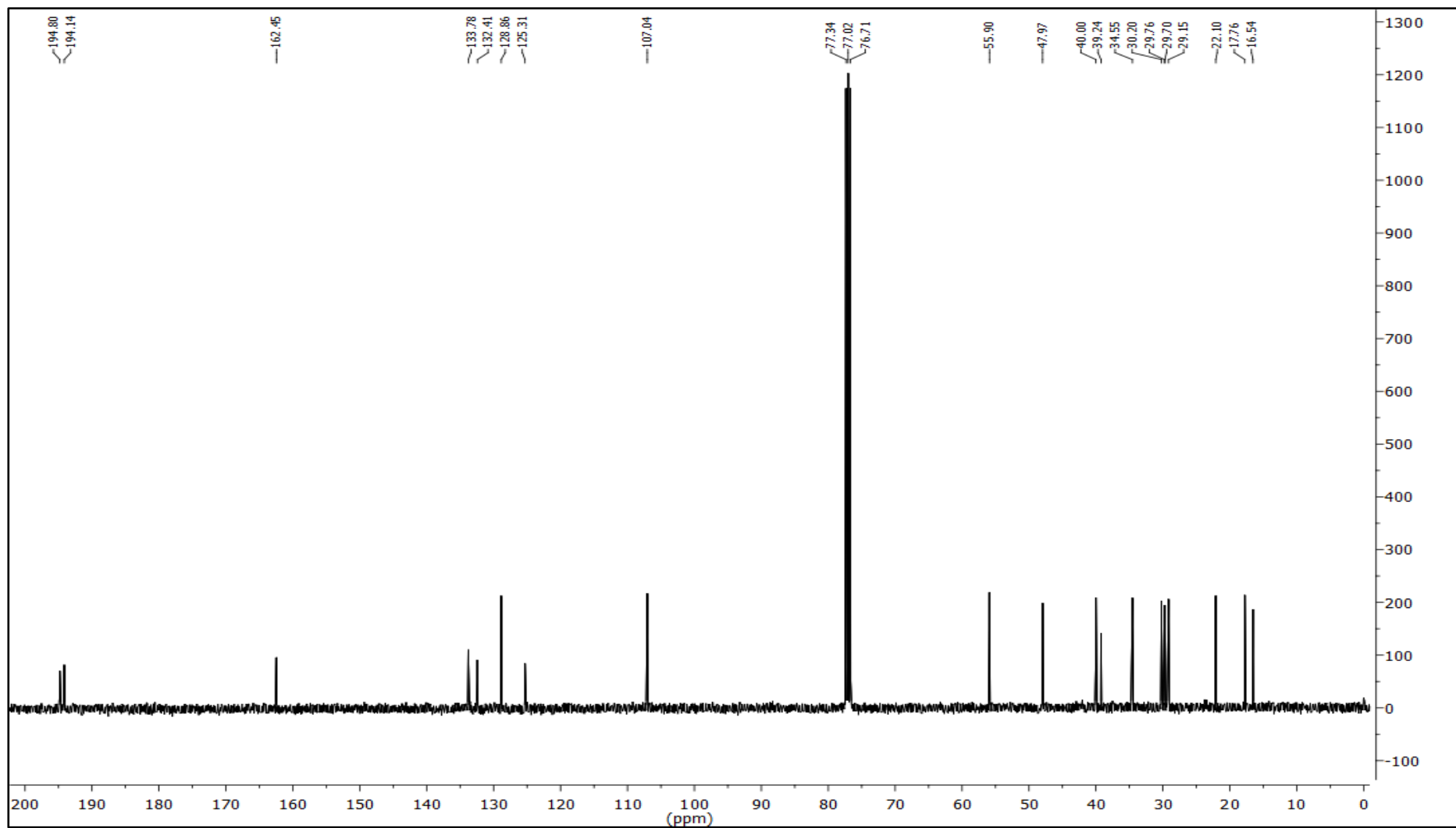
5: Favelanone

Table S4. NMR data (δ , ppm) of compound **5** in CDCl_3 (400 MHz).

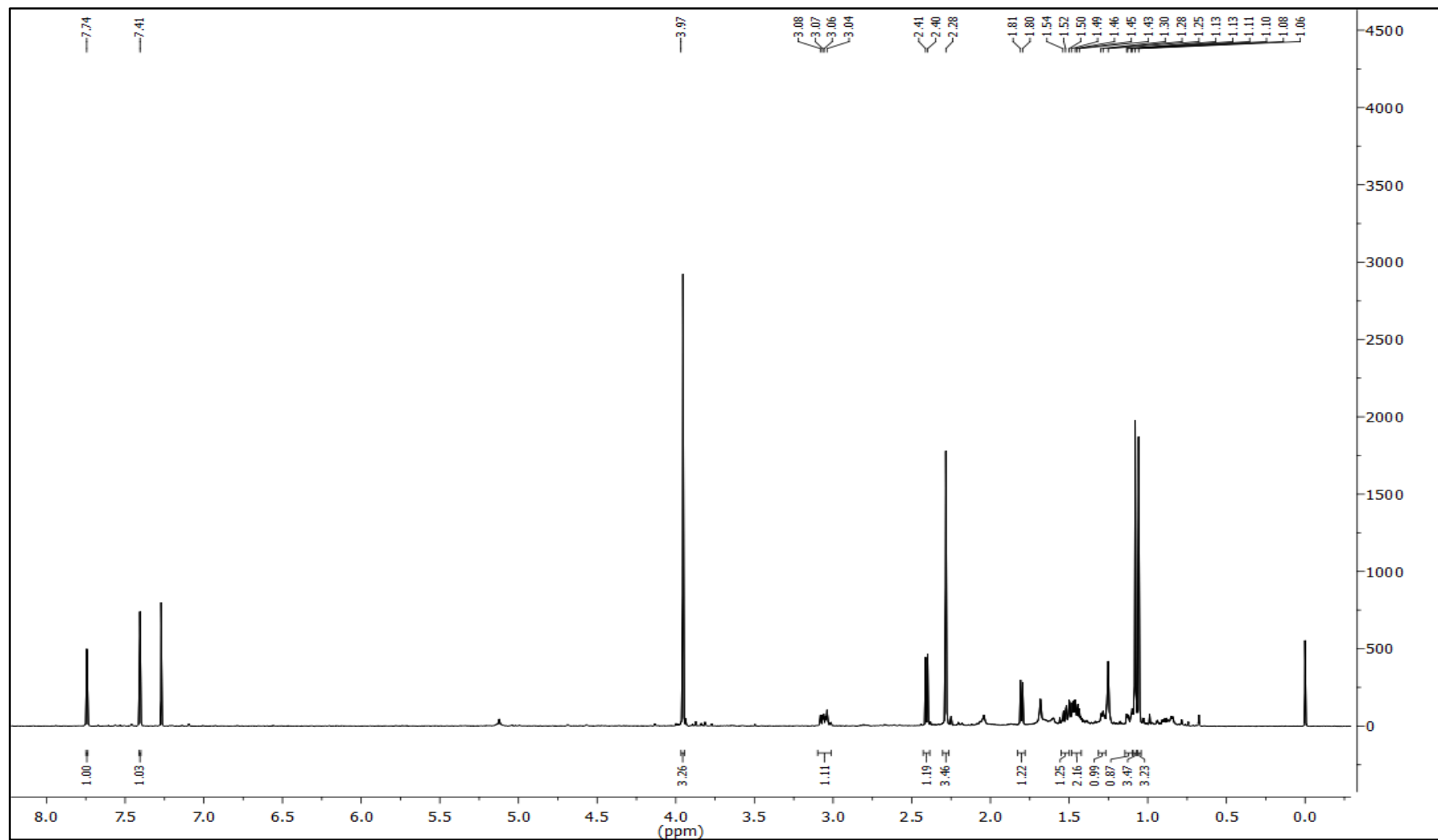
Position	Compound 5			
	HSQC (J , Hz)		HMBC	
	^{13}C	^1H	$^2J_{\text{CH}}$	$^3J_{\text{CH}}$
C				
2	133.8	-	H-18	H-4
3	162.4	-		H-1, H-18, H-19
5	132.4	-		H-1
6	125.3	-		H-4, H-8
7	194.1	-		H-1, H-9
10	39.2	-		
11	194.8	-		H-4, H-9
15	29.8	-	H-9, H-16, H-17	H-8
CH				
1	128.8	7.74 d (0.8)		H-18
4	107.0	7.41 s		
8	39.9	2.40 d (5.2)		H-12
9	47.9	1.80 d (5.2)		H-16, H-17
CH₂				
12	22.0	3.06 m; 1.51 m		
13	17.7	1.46 m; 1.44 m		
14	34.5	1.28 m; 1.11 m		H-9, H-12, H-16, H-17
CH₃				

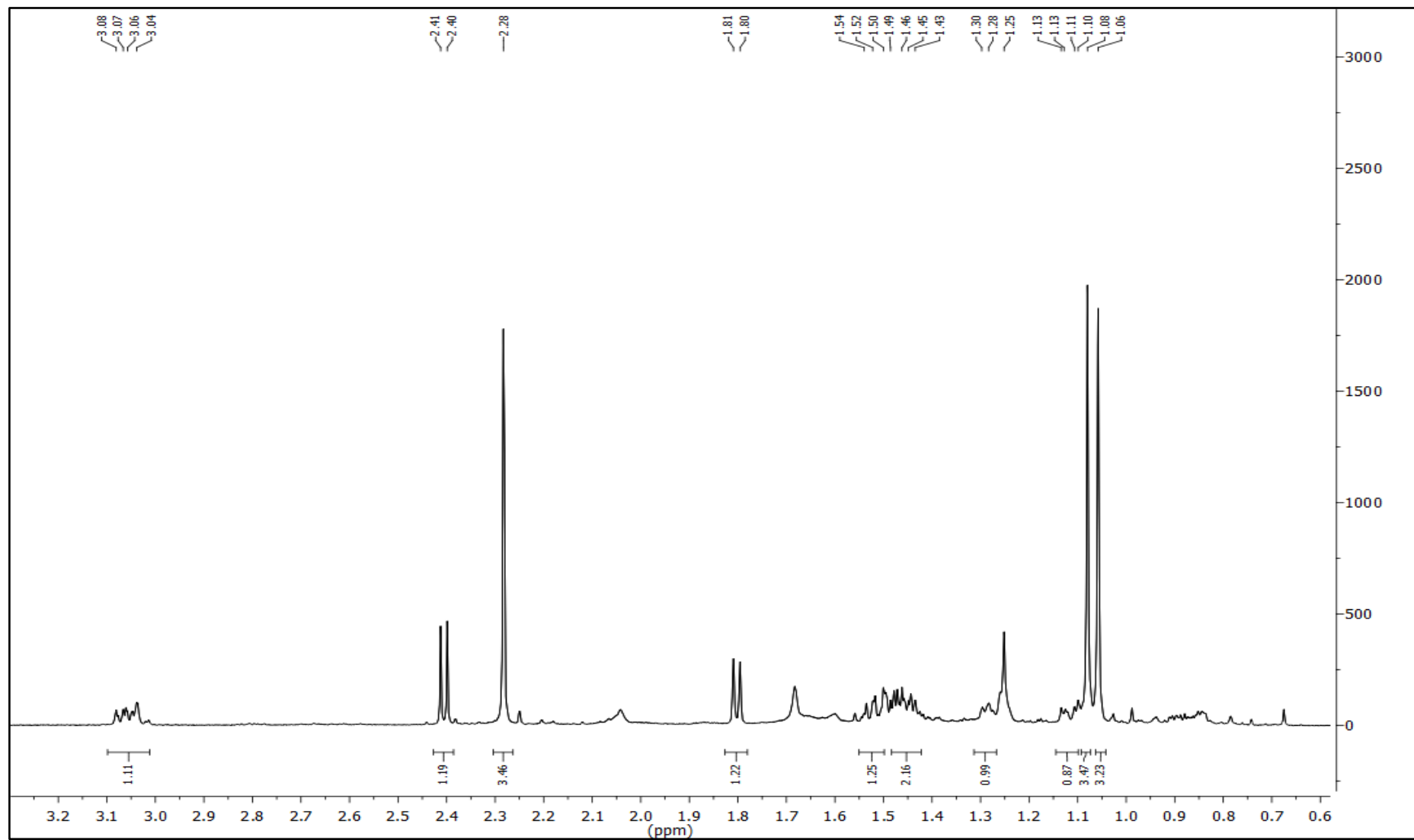
16	29.1	1.06 s	H-9	H-17
17	30.1	1.08 s		H-16
18	16.5	2.28 s		H-1
MeO (19)	55.8	3.95 s		

^{13}C NMR spectrum of compound **5** in CDCl_3 (100 MHz).

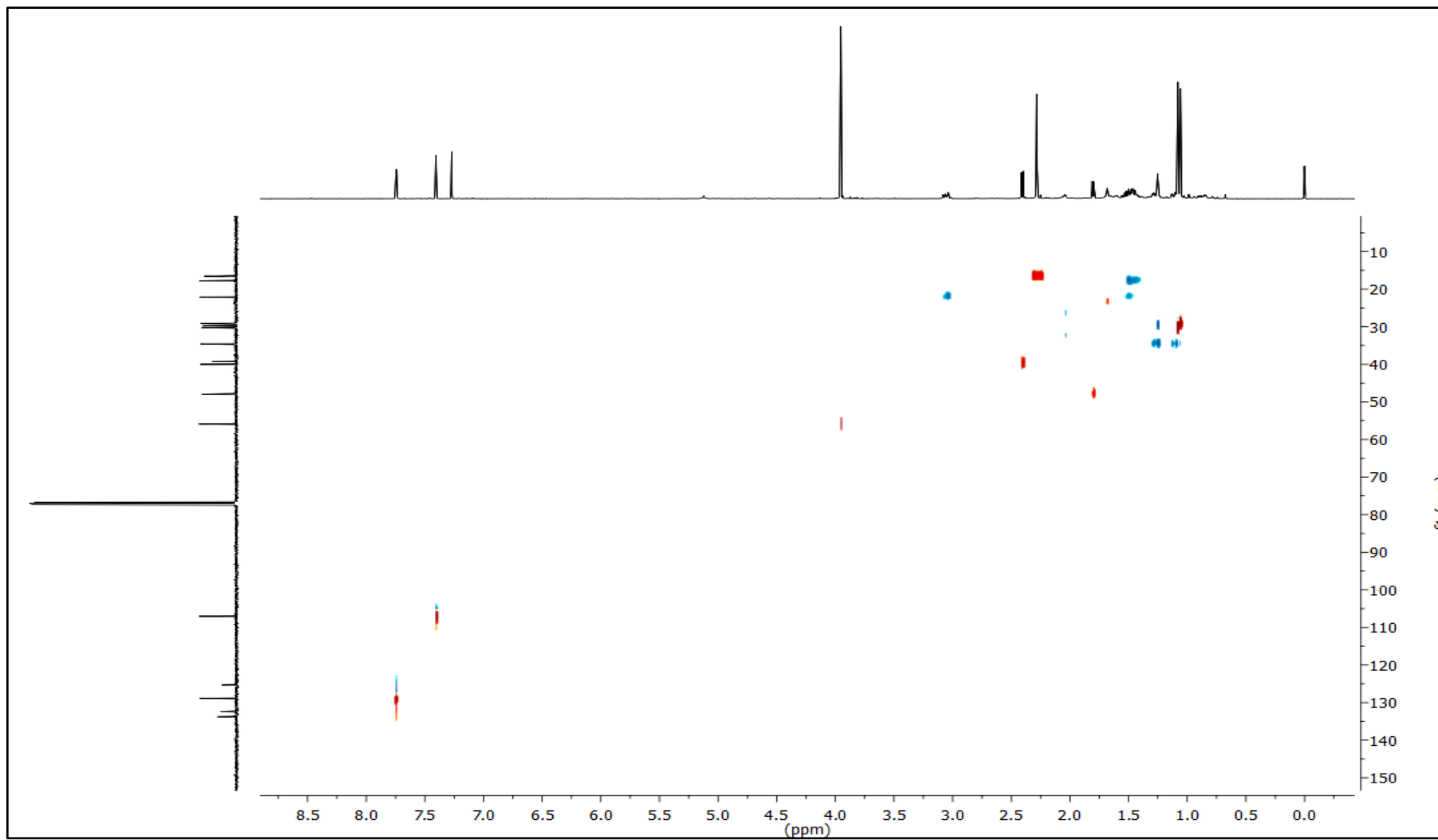


^1H NMR spectrum of compound **5** in CDCl_3 (400 MHz).

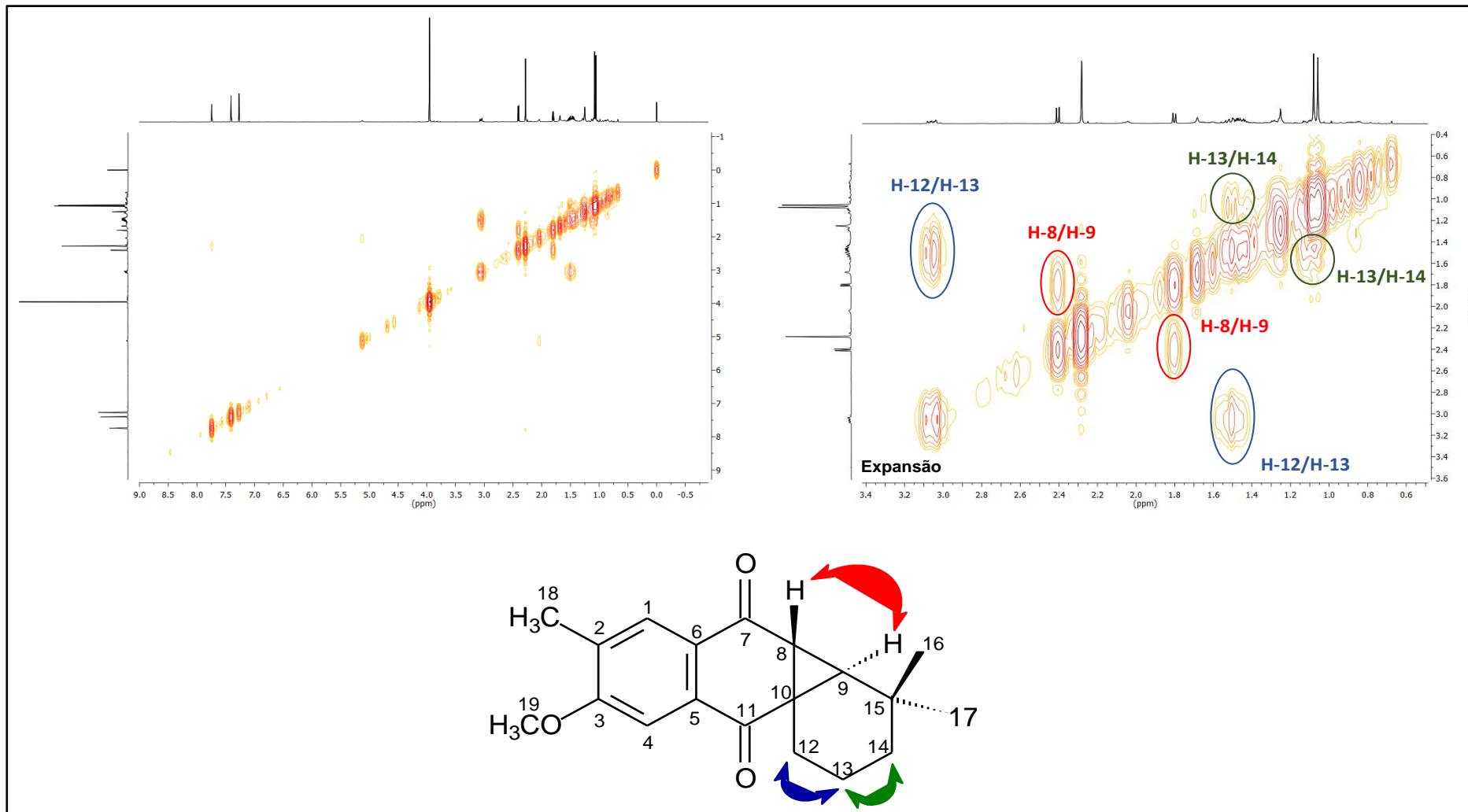




HSQC NMR spectrum of compound **5** in CDCl₃ (400 MHz).



COSY NMR spectrum of compound **5** in CDCl₃ (400 MHz).



HMBC NMR spectrum of compound **5** in CDCl₃ (400 MHz).

