Supplementary Material

Two new triterpenoid-chromones hybrids from the rhizomes of *Cimicifuga foetida* and their cytotoxic activity

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Abstract: Two new triterpenoid-chromones hybrids Cimitriteromone H (**1**) and I (**2**) and one known analogue were isolated from the phytochemical research on the *n*-Butyl alcohol extracts of *Cimicifuga foetida* rhizoma. The new compounds were elucidated by spectroscopic experiments and chemical method. The cytotoxic activity of the isolated compounds were tested on A-549/Taxol cell line. Cimitriteromone I (**2**) showed cytotoxicity with IC_{50} value of 27.14 $\pm$1.38 μM comparable to positive control group cisplatin (IC_{50} value of 25.80 $\pm$1.15 μM).

Keywords: *Cimicifuga foetida*; Triterpenoid-chromones hybrid; Cytotoxicity

Contents

Table 1S. ^{1}H NMR Spectroscopic Data of Compounds 1-3 (δ in ppm, J in Hz)

No.	1[b]	2[b]	3[c]	No.	1[b]	2[b]	3[c]
1	1.49 m 1.10 m	1.51 m 1.10 m	1.42[a] 1.03 m	30	1.02 s	1.01 s	0.96 s
2	2.28 m 1.89 m	2.28 m 1.88 m	2.23 m 1.81 m	Xyl-1	4.85 d (7.8)	4.85 d (7.7)	4.85 d (7.6)
3	3.47 dd (11.6 4.2)	3.45 dd (11.7 4.3)	3.45 dd (11.5 4.5)	Xyl-2	4.03[a]	4.03 m	4.02 m
5	1.24 m	1.23 m	1.21 m	Xyl-3	4.16[a]	4.15 m	4.16 m
6	1.45 m 0.69 m	1.45 m 0.70 m	1.43 m 0.55 m	Xyl-4	4.21 m	4.22[a]	4.21 m
7	1.24 m	1.22 m	1.13 m	Xyl-5	4.35 dd (11.2	4.36[a]	4.34[a]
	0.93 m	0.95 m	0.79 m		5.2)	3.74 t (10.7)	3.73 m
					3.73 t (10.7)		
8	1.60 m	1.70 m	1.54[a]	-OAc	2.09 s	2.10 s	2.06 s
11	2.72 m	2.63 dd (16.0 9.1)	2.67 dd (16.0 9.0)	2´	4.90 m	4.87[a]	4.96 m
	1.16 m	1.15 m	1.07 m				
12	5.10 dd (9.0 3.7)	5.30 dd (9.2 4.2)	5.07[a]	3´	3.61 dd (15.9	3.60 dd (15.8 7.4)	3.68 dd (15.9 7.8)
					7.7)	3.32 dd (15.8 7.7)	3.42 dd (15.9 7.8)
					3.34 dd (15.8		
					9.4)		
15	1.95 m	2.00 dd (13.9 7.0)	1.99 m	6´	6.85 s	6.78 s	6.67 s
	1.72[a]	1.89 m	1.78[a]				
16	4.77 m	4.18 m	4.89 m	9´	6.64 s	6.59 s	6.77 s
17	1.75 m	2.08 m	1.78[a]	4-OCH_3	4.03 s	4.01 s	4.10 s
18	1.35 s	1.33 s	1.33 s	2´´	1.40 s	1.38 s	1.42[a]
19	0.58 d (4.2)	0.61 d (4.2)	0.46 d (4.2)	3´´	1.49 s	1.48 s	1.51 s
	0.22 d (4.2)	0.18 d (4.3)	0.16 d (4.2)				
20	1.89 m	2.44 m	2.33 m	4´´	4.98[a]	4.87[a]	4.91 m
					4.87 d (14.6)	4.72 d (14.6)	4.56 m
21	0.97 d (6.3)	1.13 d (6.8)	1.09 d (6.6)	Glc-1	4.95 d (7.8)	4.97[a]	4.95 d (7.4)
22	2.70 m	5.19 d (3.1)	2.61 dd (13.4 3.3)	Glc-2	4.16[a]	4.09 m	4.15 m
	1.44 m		1.50 m				
24	3.75 m	4.52 s	4.13 m	Glc-3	4.16[a]	4.22[a]	4.18 m
26	1.62 s	1.61 s	1.65 s	Glc-4	3.99 m	4.18 m	4.09 m
27	1.72 s	1.47 s	1.53 s	Glc-5	3.98 m	3.98 m	3.96 m
28	0.85 s	0.87 s	0.75 s	Glc-6	4.40 m 4.03[a]	4.36[a] 4.15[a]	4.53 m 4.34[a]
29	1.32 s	1.31 s	1.34 s				

[a]Signals overlapped. [b]Recorded at 600 MHz in pyridine-d_5. [c]Recorded at 800 MHz in pyridine-d_5.

Table 2S. ^{13}C NMR Spectroscopic Data of Compounds 1-3 (δ in ppm, J in Hz)

No.	1[a]	2[a]	3[b]	No.	1[a]	2[a]	3[b]
1	31.9, CH_2	31.9, CH_2	31.8, CH_2	30	15.2, CH_3	15.2, CH_3	15.2, CH_3
2	29.6, CH_2	29.8, CH_2	29.8, CH_2	Xyl-1	107.5, CH	107.5, CH	107.4, CH
3	88.0, CH	88.0, CH	87.8, CH	Xyl-2	75.5, CH	75.5, CH	75.5, CH
4	41.1, C	41.1, C	41.1, C	Xyl-3	78.5, CH	78.5, CH	78.5, CH
5	47.0, CH	46.9, CH	47.1, CH	Xyl-4	71.2, CH	71.1, CH	71.1, CH
6	20.4, CH_2	20.3, CH_2	20.5, CH_2	Xyl-5	67.0, CH_2	67.0, CH_2	67.0, CH_2
7	25.8, CH_2	25.7, CH_2	25.6, CH_2	-OAc	170.5, C	170.6, C	170.4, C
					21.6, CH_3	21.1, CH_3	21.5, CH_3
8	45.8, CH	46.4, CH	46.0, CH	2´	92.2, CH	92.2, CH	92.4, CH
9	20.0, C	20.5, C	19.8, C	3´	27.8, CH_2	27.8, CH_2	27.9, CH_2
10	26.6, C	27.0, C	26.5, C	3a´	118.4, C	118.4, C	118.5, C
11	36.7, CH_2	36.4, CH_2	36.7, CH_2	4´	156.2, C	156.1, C	156.3, C
12	77.2, CH	76.9, CH	77.2, CH	4a´	112.8, C	112.7, C	112.9, C
13	48.7, C	48.8, C	48.8, C	5´	176.3, C	176.3, C	176.2, C
14	47.8, C	47.8, C	47.2, C	6´	111.2, CH	111.1, CH	111.5, CH
15	43.8, CH_2	45.6, CH_2	43.4, CH_2	7´	162.6, C	162.5, C	162.1, C
16	71.1, CH	74.6, CH	70.7, CH	8a´	159.9, C	159.8, C	159.9, C
17	56.8, CH	52.4, CH	55.7, CH	9´	94.1, CH	94.0, CH	94.1, CH
18	13.5, CH_3	12.9, CH_3	13.5, CH_3	9a´	165.2, C	165.2, C	165.4, C
19	29.8, CH_2	30.0, CH_2	29.9, CH_2	4-OCH_3	60.9, CH_3	60.8, CH_3	60.9, CH_3
20	26.0, CH	24.6, CH	26.9, CH	1´´	70.7, C	70.6, C	70.6, C
21	21.1, CH_3	25.7, CH_3	21.1, CH_3	2´´	26.2, CH_3	26.1, CH_3	26.0, CH_3
22	41.9, CH_2	106.0, CH	41.5, CH_2	3´´	25.6, CH_3	25.7, CH_3	25.6, CH_3
23	101.9, C	152.9, C	104.2, C	4´´	66.3, CH_2	66.5, CH_2	66.3, CH_2
24	77.7, CH	75.9, CH	83.1, CH	Glc-1	103.9, CH	104.3, CH	101.7, CH
25	81.3, C	78.2, C	79.1, C	Glc-2	74.8, CH	74.9, CH	74.5, CH
26	23.7, CH_3	22.3, CH_3	19.4, CH_3	Glc-3	78.2, CH	78.1, CH	79.1, CH
27	24.9, CH_3	23.1, CH_3	29.8, CH_3	Glc-4	72.0, CH	71.9, CH	69.3, CH
28	19.5, CH_3	20.7, CH_3	19.4, CH_3	Glc-5	76.8, CH	76.7, CH	78.4, CH
29	25.6, CH_3	25.6, CH_3	25.6, CH_3	Glc-6	62.9, CH_2	62.7, CH_2	62.4, CH_2

[a]Recorded at 150 MHz in pyridine-d_5. [b]Recorded at 200 MHz in pyridine-d_5

Table 3S. Comparison of the chemical shifts of compounds 2, 4, cimifoetidanoside G and (16*S*,20*S*,24*R*)-12*β*-acetoxy-16,23-epoxy-24,25-dihydroxy-3*β*-(*β*-*D*-xylopyranosyloxy)-9,19-cyclolanost-22(23)-ene

No.	**2**[a]		**4**[a]		**cimifoetidanoside G**[a]		**(16*S*,20*S*,24*R*)**[a]	
	δ_H[b] (*J* in Hz)	δ_C[c]	δ_H[b] (*J* in Hz)	δ_C[c]	δ_H[d] (*J* in Hz)	δ_C[e]	δ_H[f] (*J* in Hz)	δ_C[g]
20	2.44 m	24.6, CH	2.45 m	24.6, CH	2.45 m	24.6, CH	2.48 m	25.1, CH
21	1.13 d (6.8)	25.7, CH_3	1.15 d (7.1)	25.4, CH_3	1.12 d (7.2)	25.6, CH_3	1.16 d (7.2)	26.3, CH_3
22	5.19 d (3.1)	106.0, CH	5.21 d (3.2)	105.8, CH	5.19 d (3.1)	105.8, CH	5.22 d (3.3)	106.3, CH
23		152.9, C		153.6, C		153.6, C		154.2, C
24	4.52 s	75.9, CH	4.32 s	79.4, CH	4.32 d (4.6)	79.4, CH	4.34 d (4.3)	80.0, CH
25		78.2, C		72.8, C		72.9, C		73.4, C
26	1.61 s	22.3, CH_3	1.66	27.4, CH_3	1.65 s	27.4, CH_3	1.68 s	28.0, CH_3
27	1.47 s	23.1, CH_3	1.61	25.9, CH_3	1.60 s	25.9, CH_3	1.62 s	26.4, CH_3

[a]Recorded in pyridine-d_5. [b]600 MHz. [c]150 MHz. [d]400 MHz. [e]100 MHz. [f]500 MHz. [g]125 MHz.

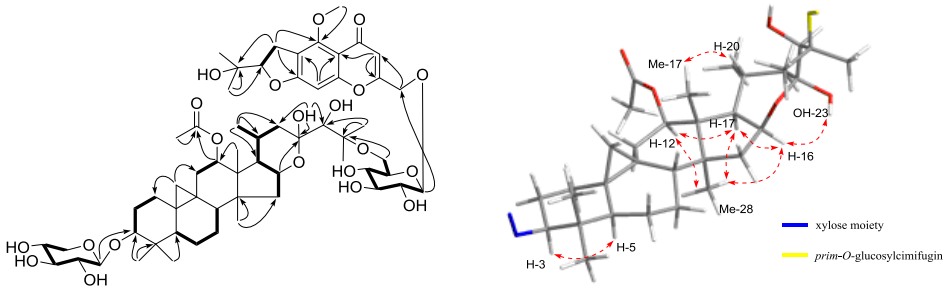


Fig. 1S Key HMBC ( ), ^{1}H–^{1}H COSY ( ) and ROESY ( ) correlations of cimitriteromone H (**1**)

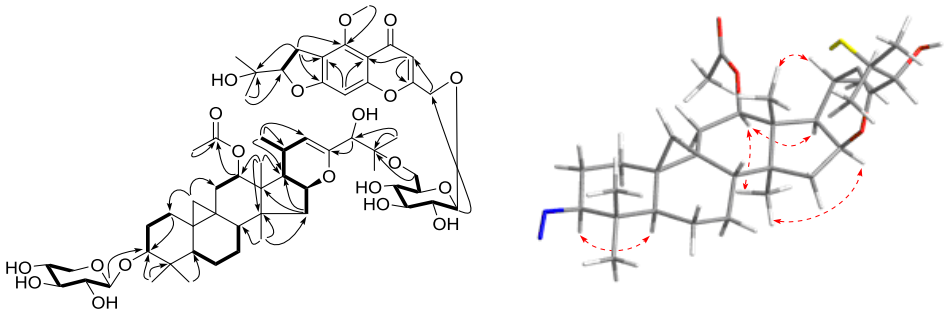


Fig. 2S Key HMBC ( ), ^{1}H–^{1}H COSY ( ) and ROESY ( ) correlations of cimitriteromone I (**2**)

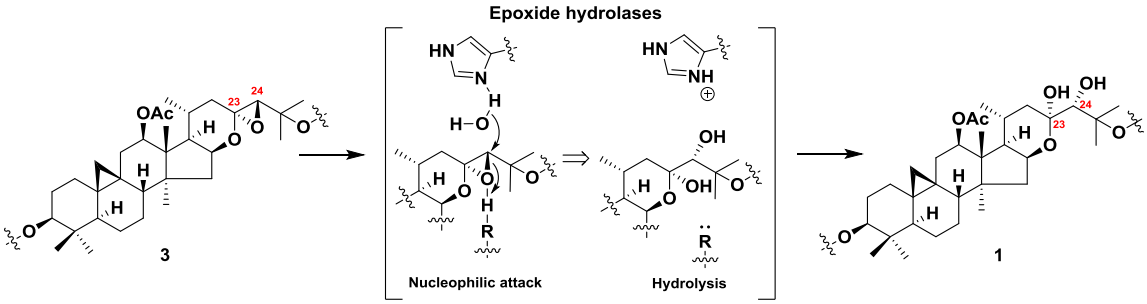


Figure 3S. The cleavage pattern of the epoxy ring in **3**

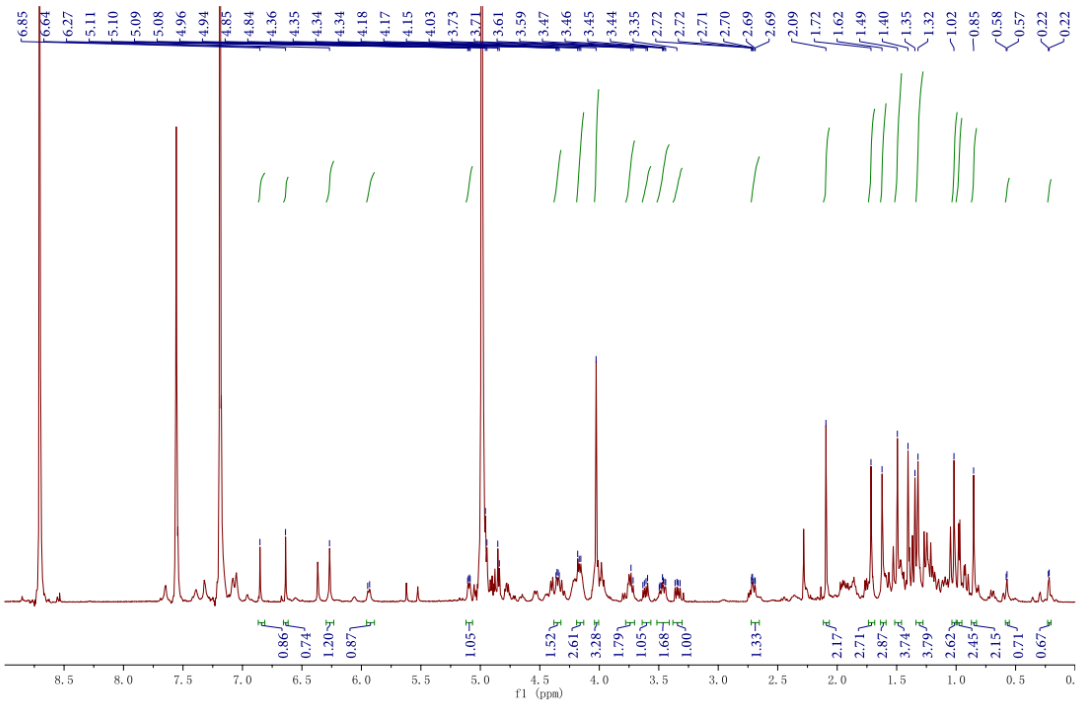


Figure 4S. ^{1}H NMR spectrum of cimitriteromone H (1) in pyridine-d_5 (600 MHz).

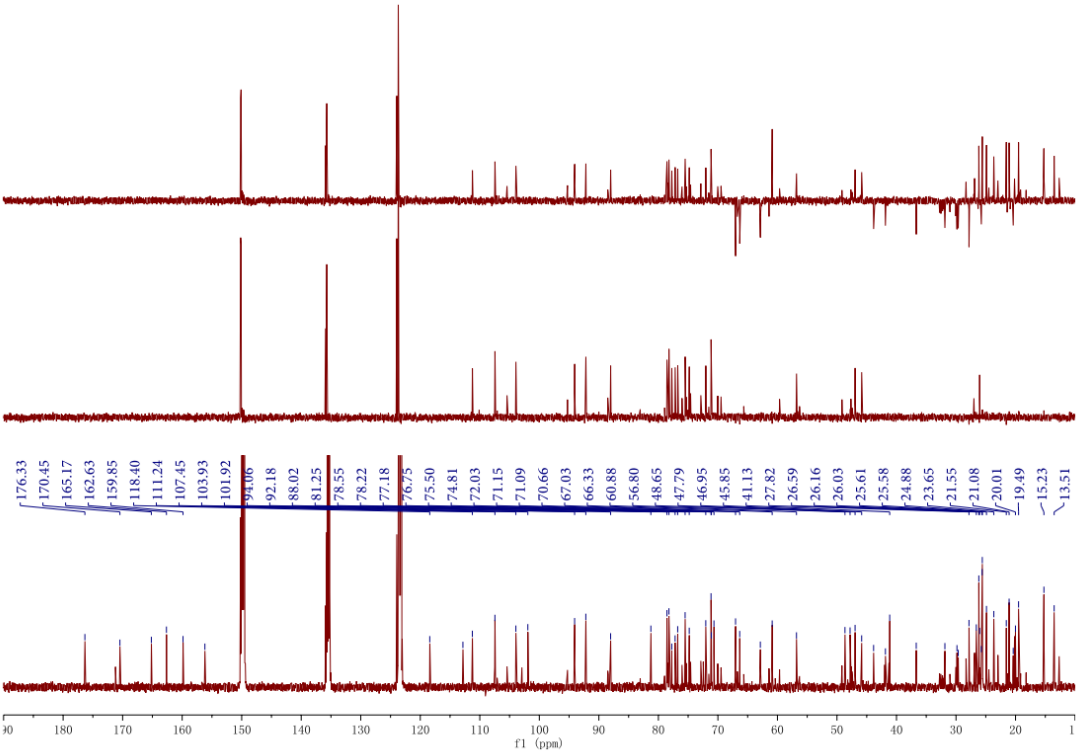


Figure 5S. ^{13}C NMR spectrum of cimitriteromone H (1) in pyridine-d_5 (150 MHz).

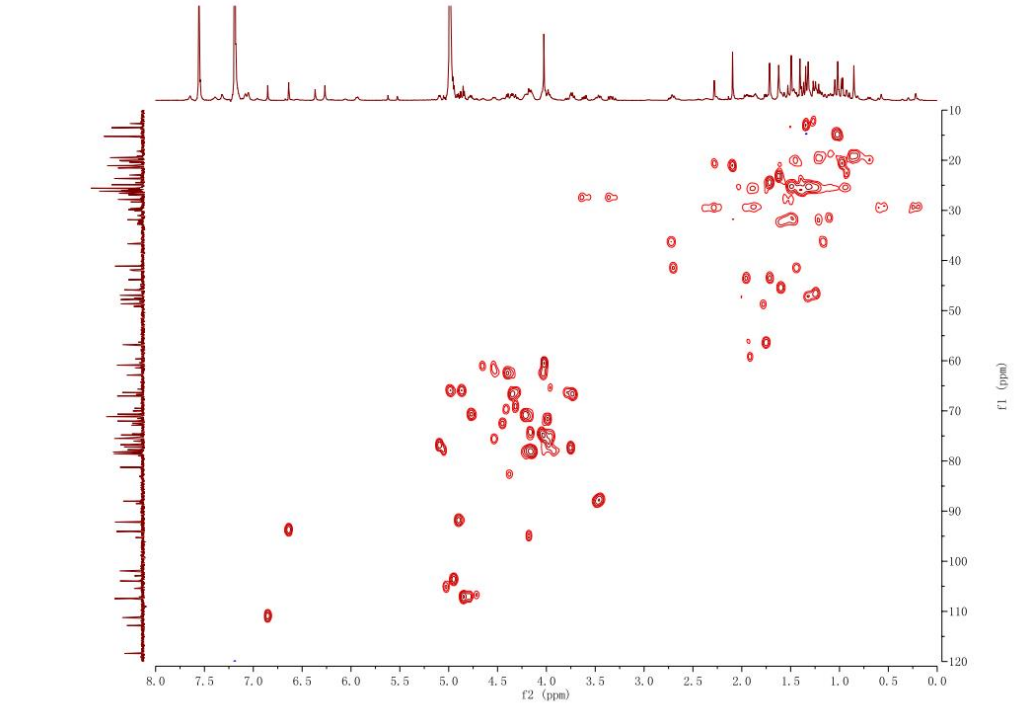


Figure 6S. HSQC spectrum of cimitriteromone H (1) in pyridine-d_5.

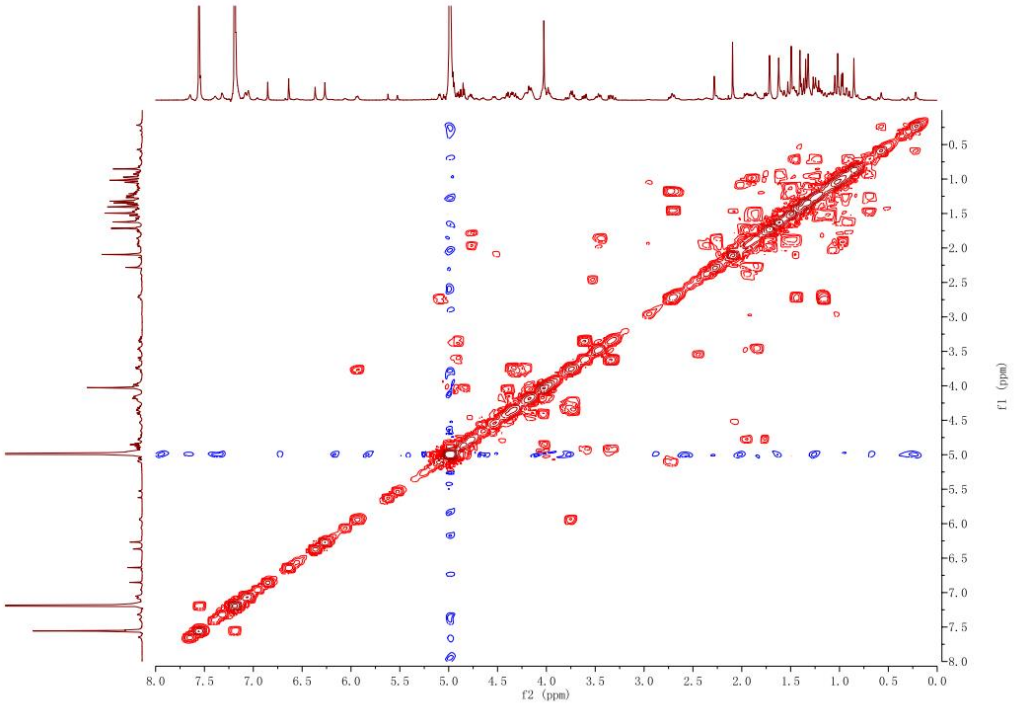


Figure 7S. ^{1}H-^{1}H COSY spectrum of cimitriteromone H (1) in pyridine-d_5.

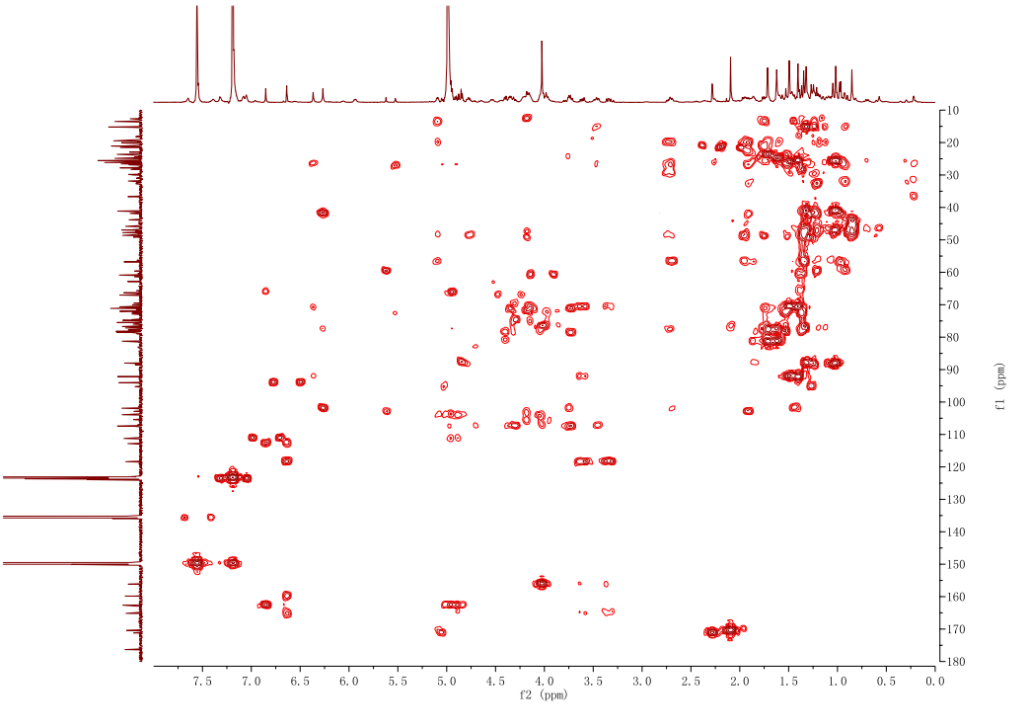


Figure 8**S. HMBC spectrum of cimitriteromone H (1) in pyridine-d_5.**

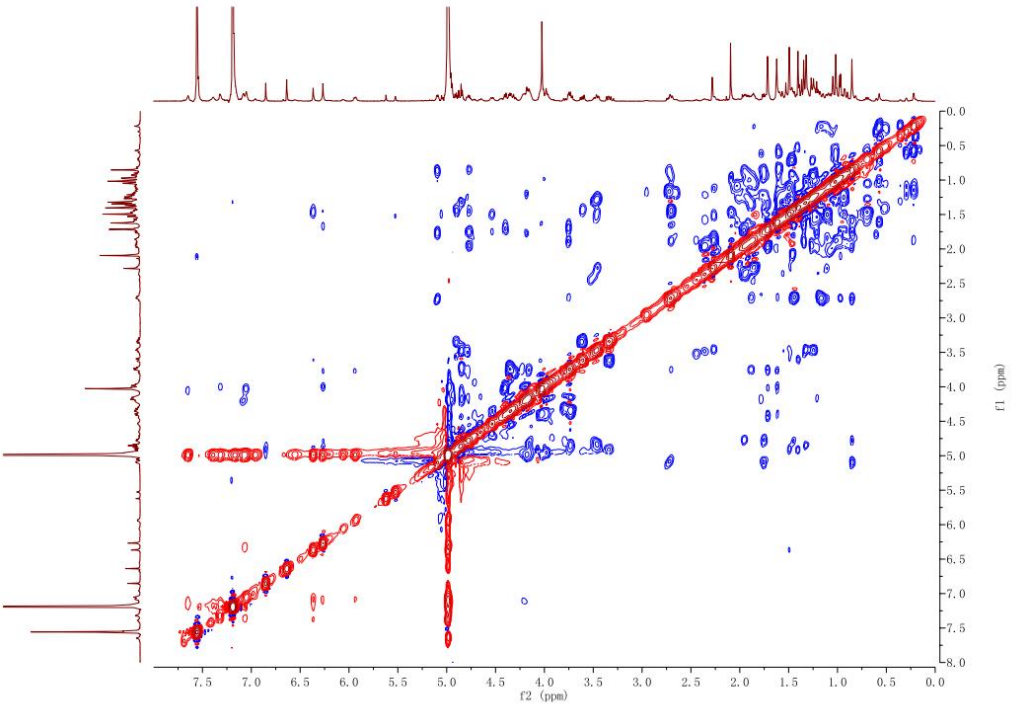


Figure 9**S. ROESY spectrum of cimitriteromone H (1) in pyridine-d_5.**

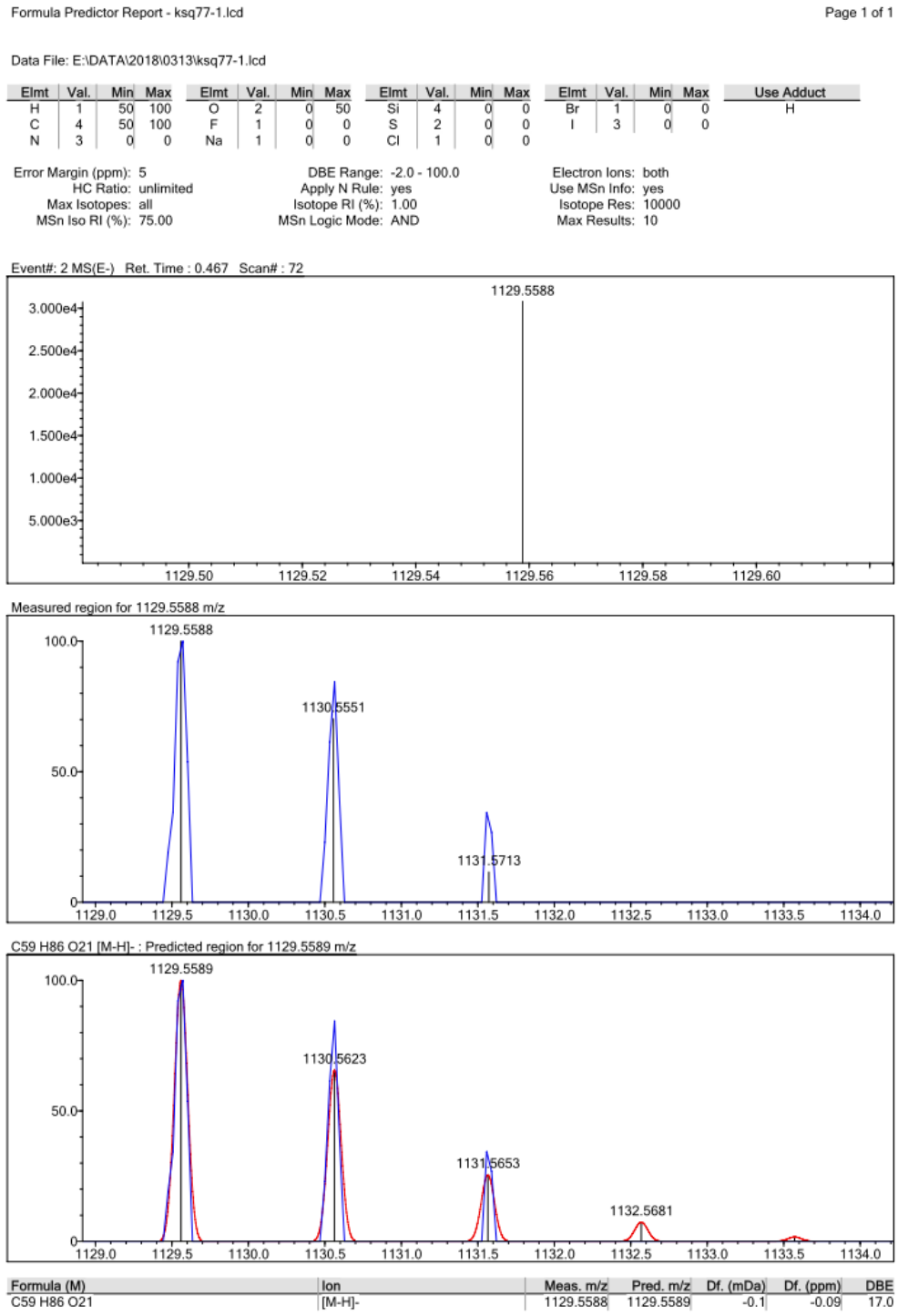
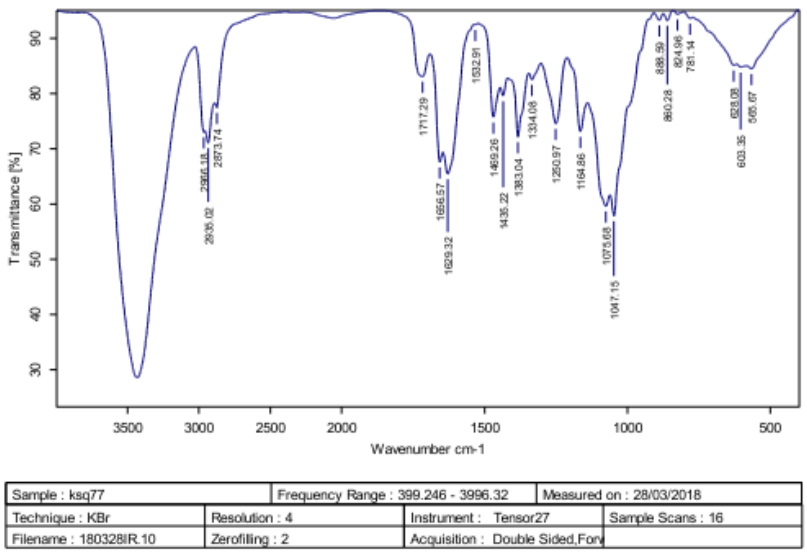


Figure 10**S. HRESIMS spectrum of cimitriteromone H (1).**



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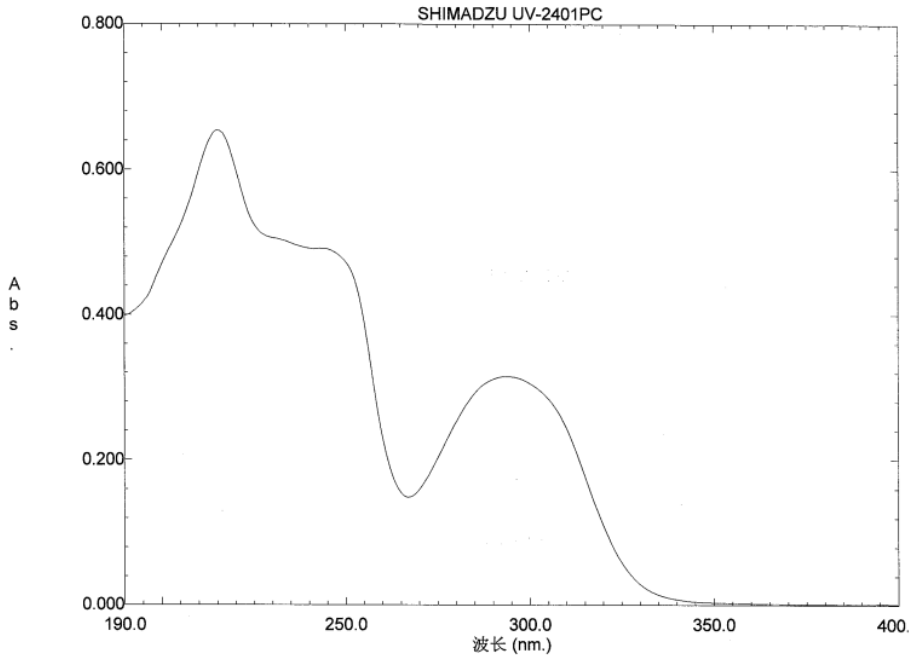
Filename : 180328IR.10	Zerofilling : 2	Acquisition : Double Sided,For	

Figure 11S. IR spectrum of cimitriteromone H (1).



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4	215.00	0.6534

Figure 12S. UV spectrum of cimitriteromone H (1).

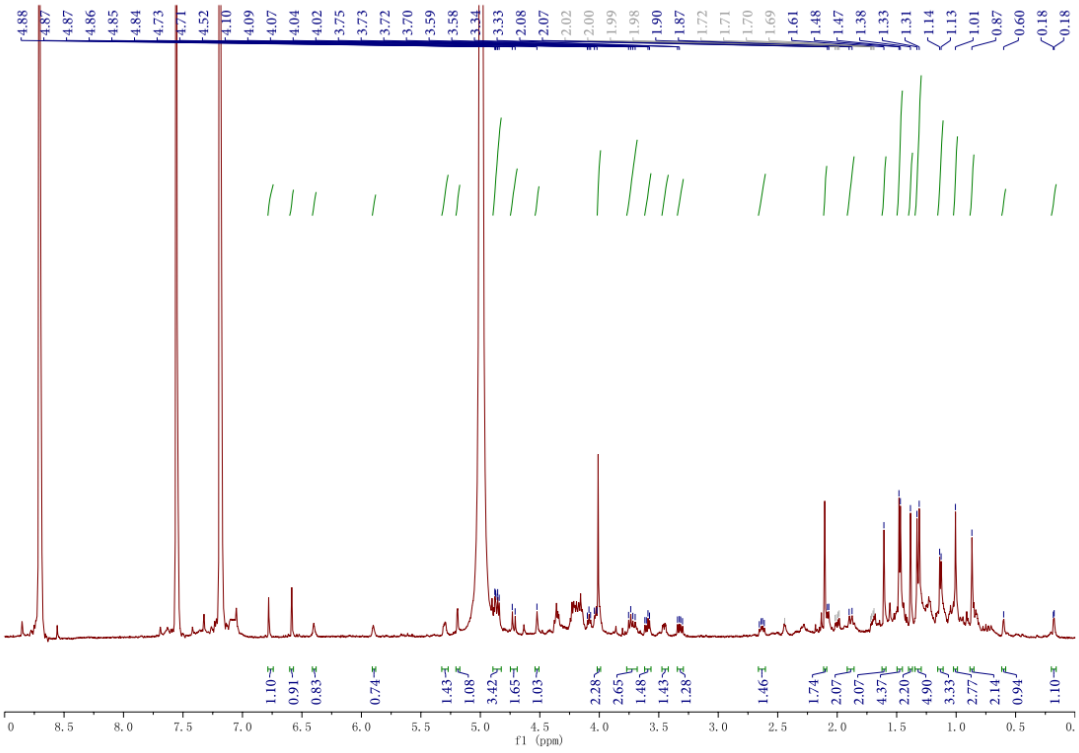

Figure 13S. ^{1}H NMR spectrum of cimitriteromone I (2) in pyridine-d_5 (600 MHz).

Figure S78. ^{13}C NMR spectrum of triteromone I (**9**) in Pyridine-d_5 (201 MHz).

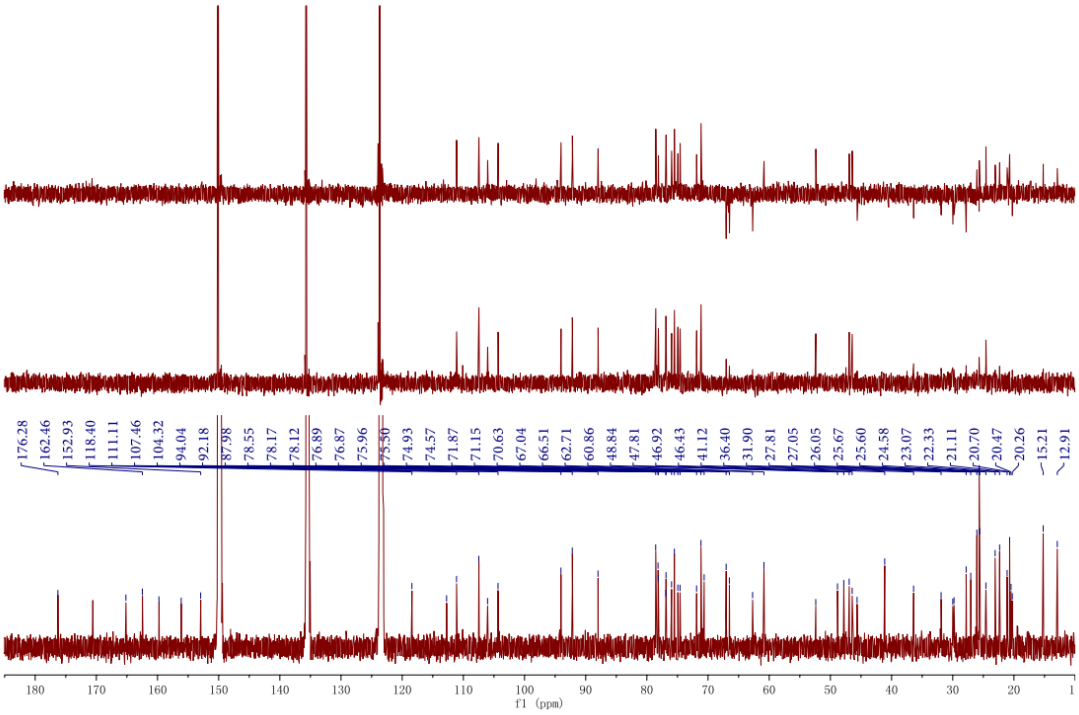

Figure 14S. ^{13}C NMR spectrum of cimitriteromone I (2) in pyridine-d_5 (150 MHz).

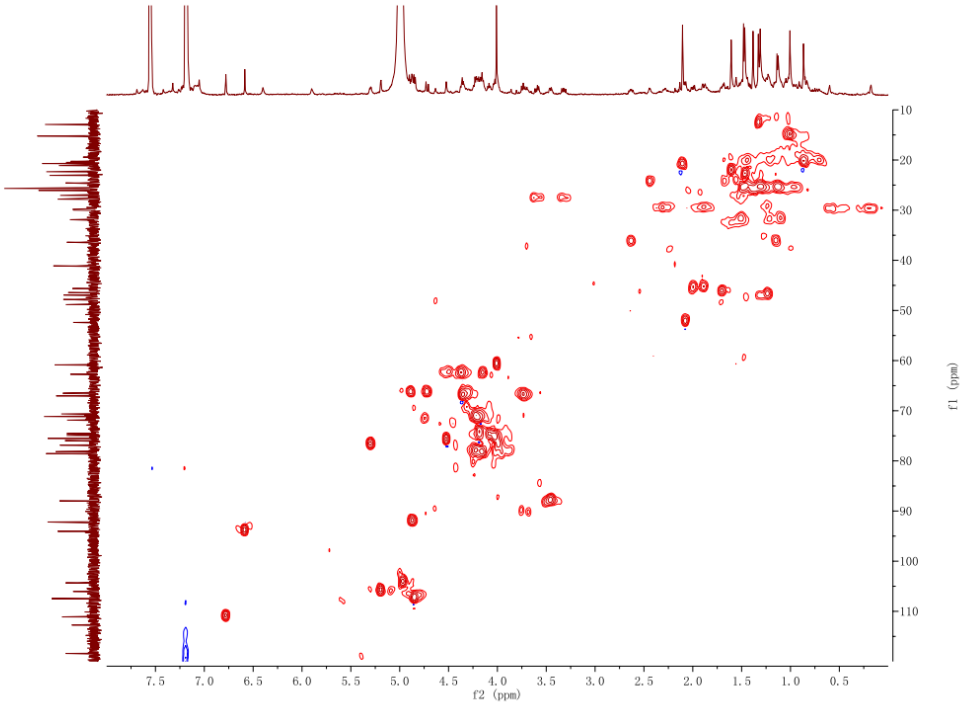

Figure 15S. HSQC spectrum of cimitriteromone I (2) in pyridine-d_5.

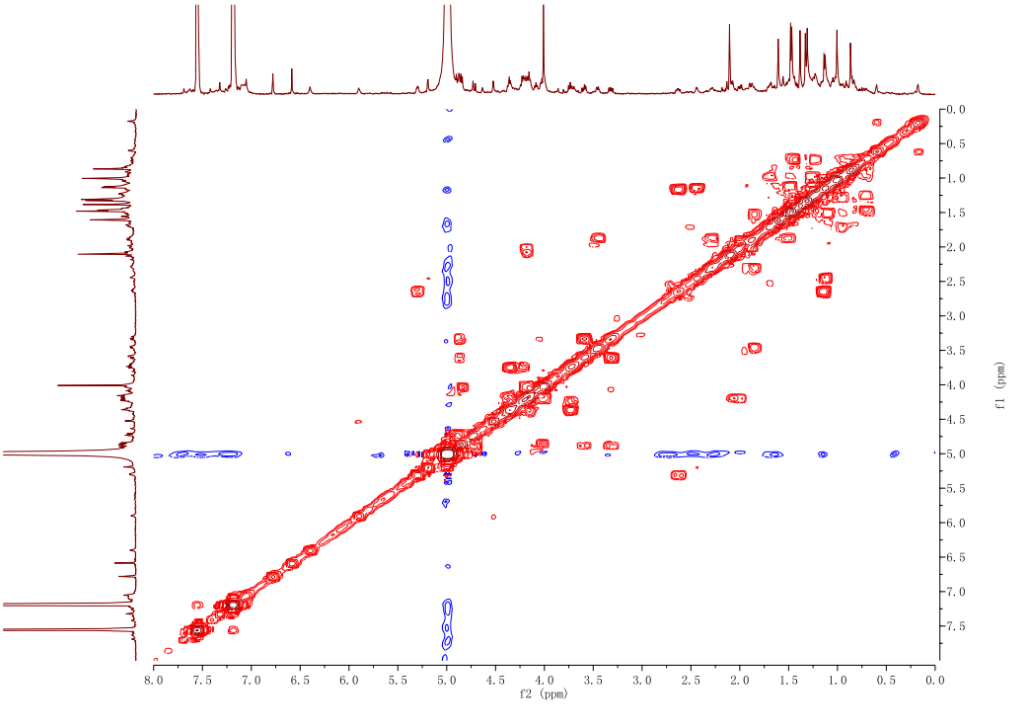

Figure 16S. ^{1}H-^{1}H COSY spectrum of cimitriteromone I (2) in pyridine-d_5.

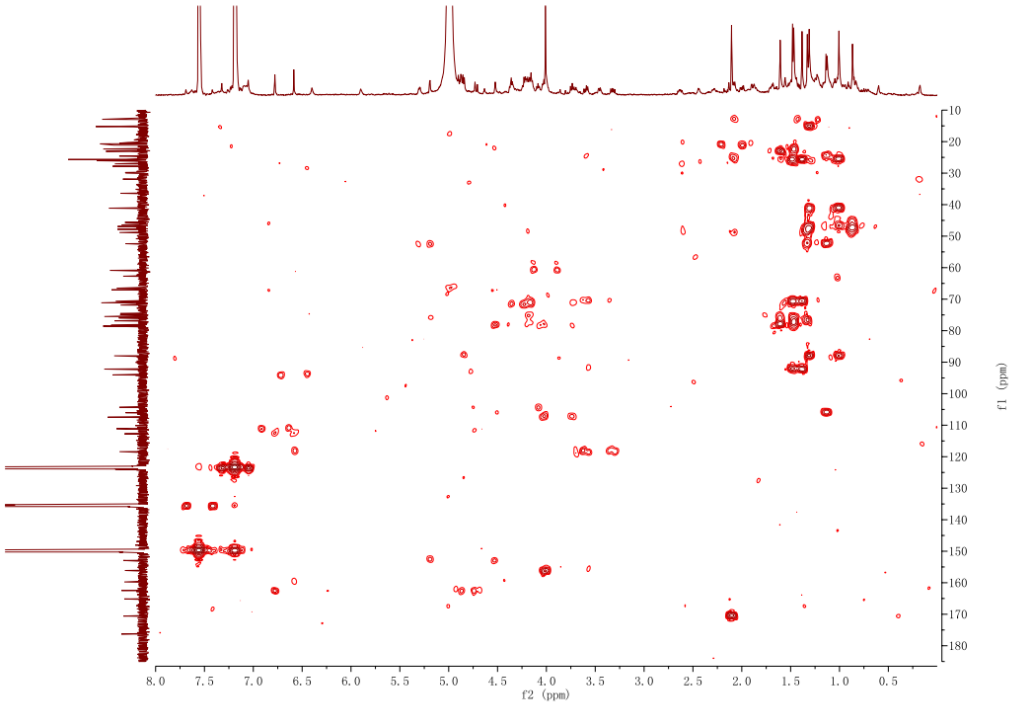

Figure 17S. HMBC spectrum of cimitriteromone I (2) in pyridine-d_5.

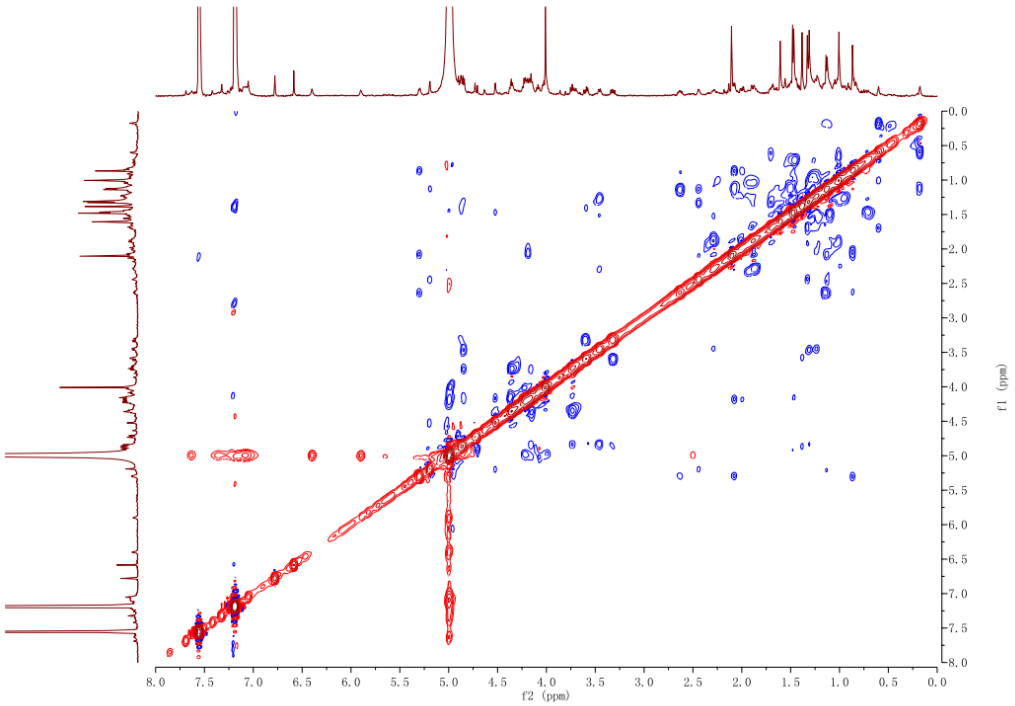

Figure 18S. ROESY spectrum of cimitriteromone I (2) in pyridine-d_5.

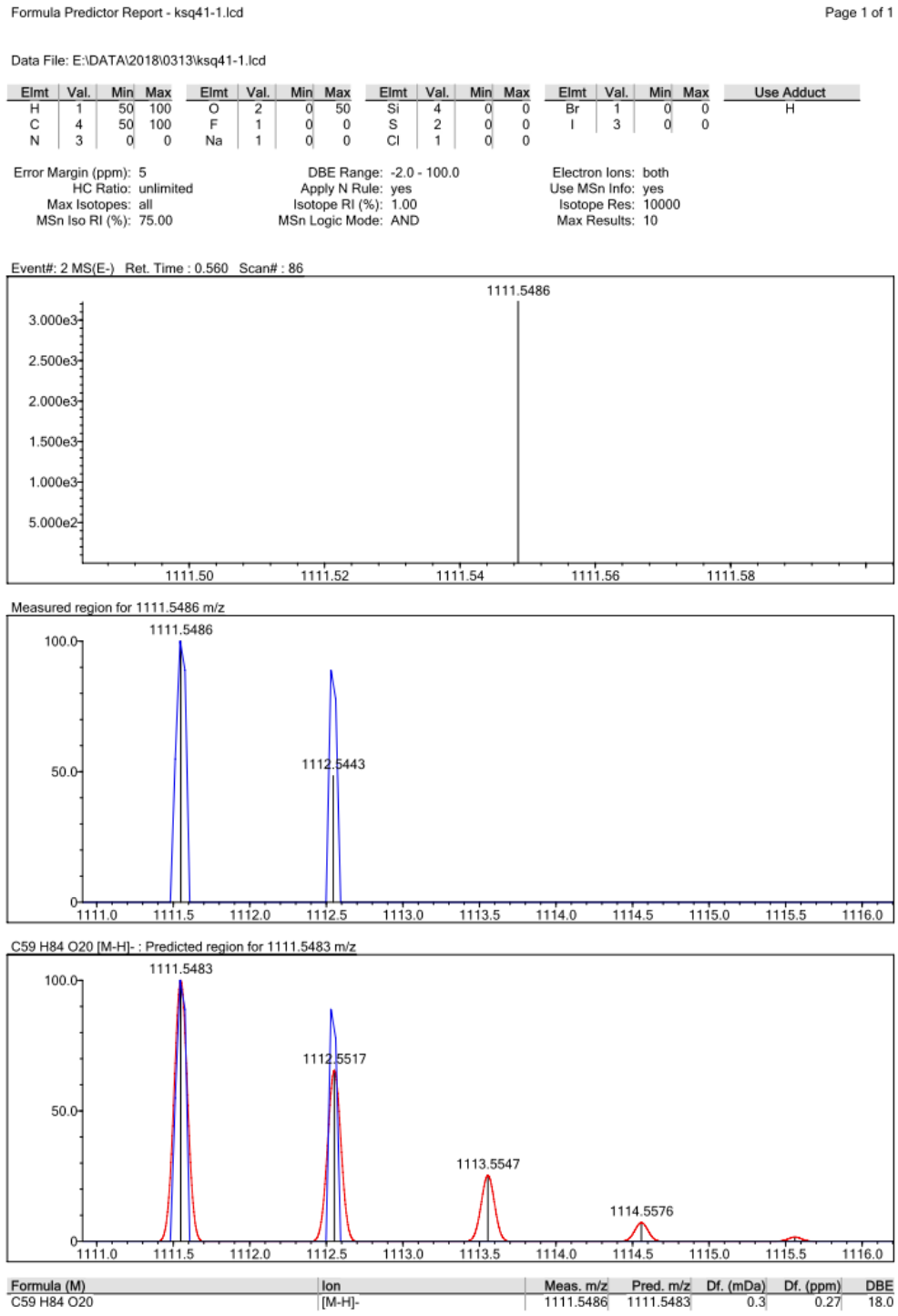

Figure 19S. HRESIMS spectrum of cimitriteromone I (2).

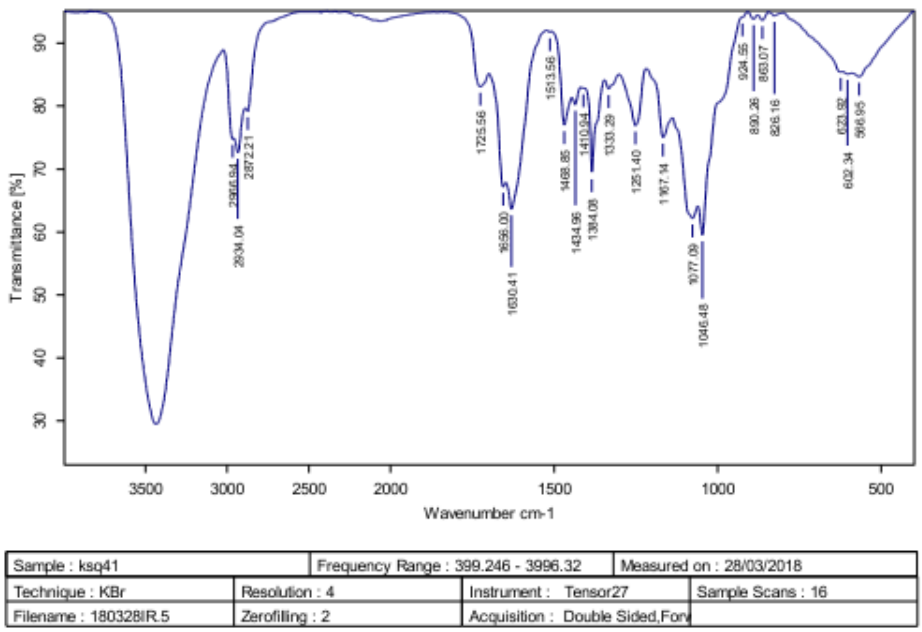

Figure 20**S. IR spectrum of cimitriteromone I (2).**

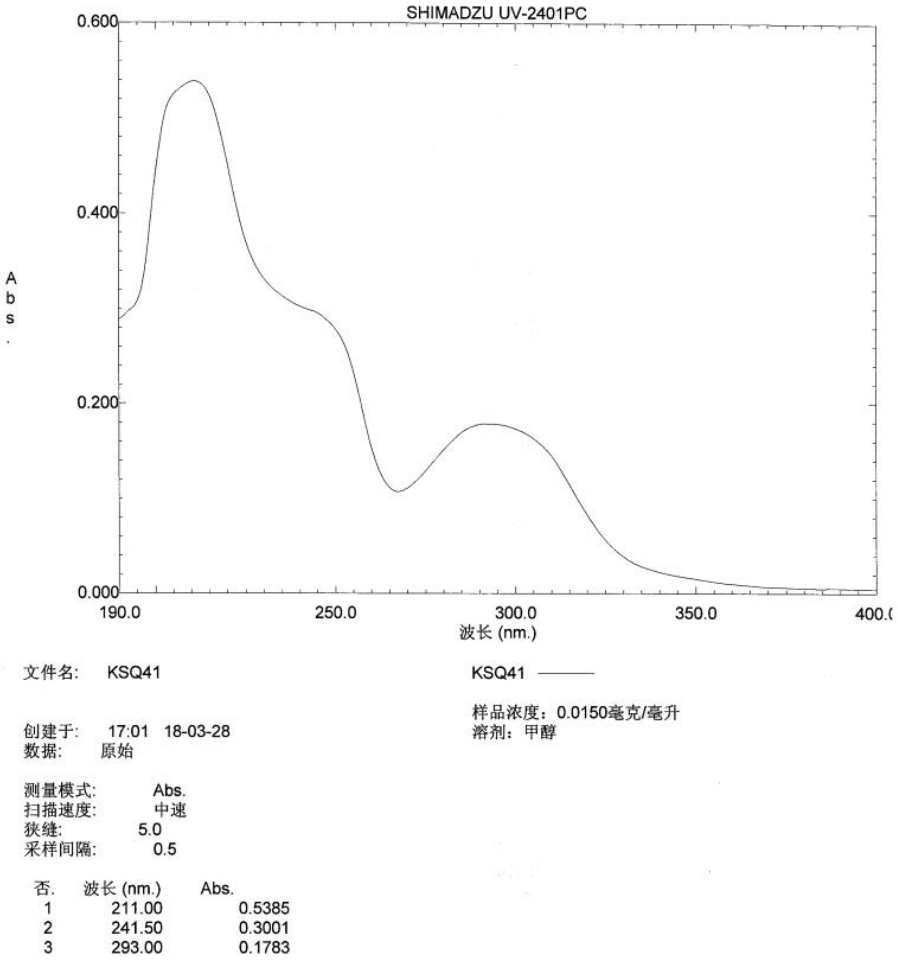

Figure 21**S. UV spectrum of cimitriteromone I (2).**

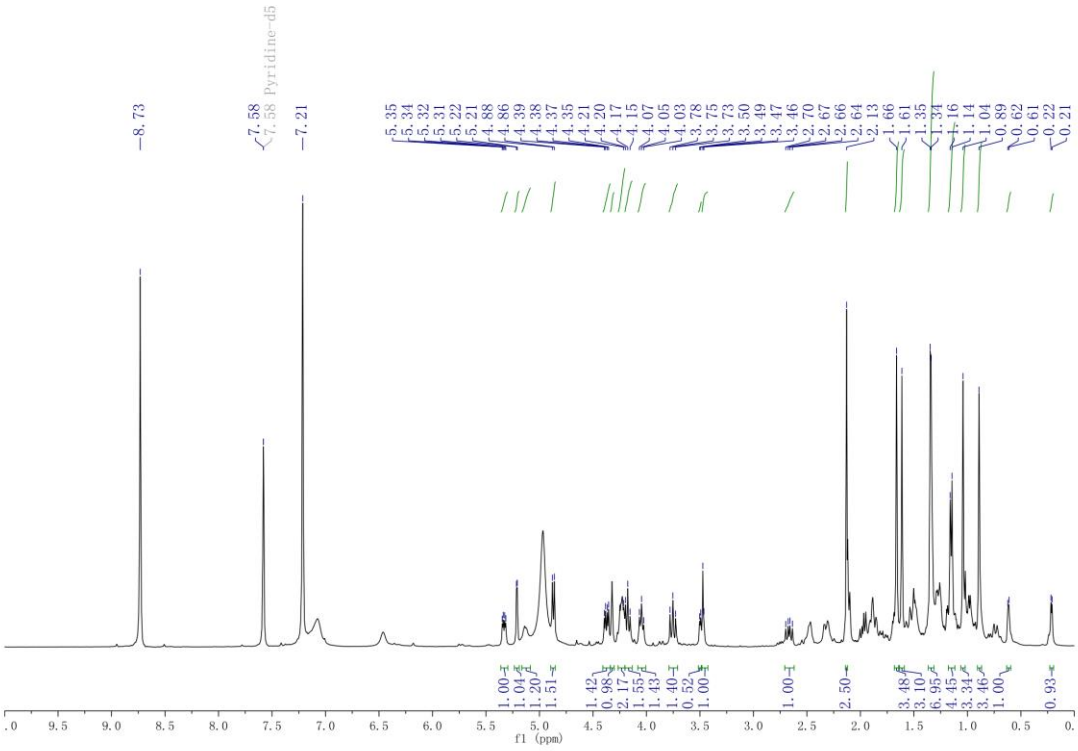

Figure 22S. ^{1}H NMR spectrum of compound 4 in pyridine-d_5 (600 MHz).

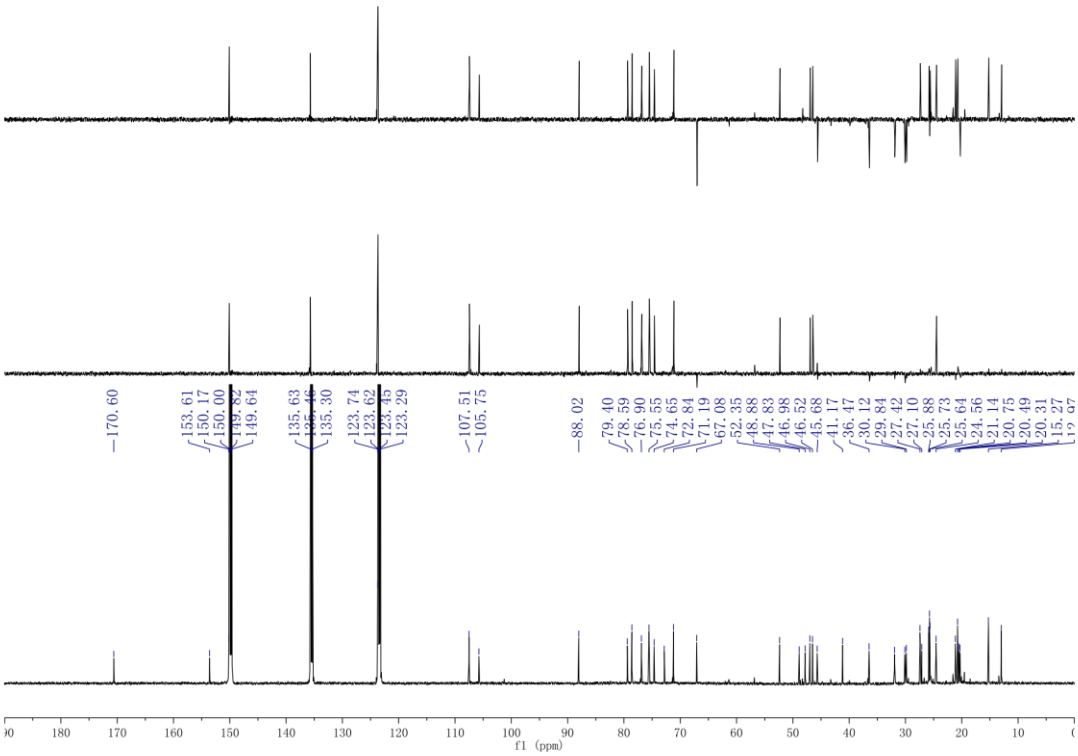

Figure 23S. ^{13}C NMR spectrum of compound 4 in pyridine-d_5 (150 MHz).