

Supporting information

Neuroprotective Caffeoylquinic Acid Derivatives from the Flowers of *Chrysanthemum morifolium*

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Table of Contents

Figures	Contents	Compound	Page
1	The UV Spectrum in MeOH	1	S3
2	The ECD Spectrum in MeOH	1	S3
3	The IR Spectrum (KBr)	1	S4
4	The HR-ESI-MS Data	1	S4
5	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S5
6	The ¹³ C NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S5
7	The HSQC Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S6
8	The HMBC Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S6
9	The ¹ H- ¹ H COSY Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S7
10	The ROESY Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1	S7
11	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1a	S8
12	The ¹³ C NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1a	S8
13	The ECD Spectrum in MeOH	1a	S9
14	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	1b	S9
15	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	4- <i>O</i> -caffeoylquinic acid	S10
16	The UV Spectrum in MeOH	2	S10
17	The ECD Spectrum in MeOH	2	S11
18	The IR Spectrum (KBr)	2	S11
19	The HR-ESI-MS Data	2	S12
20	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S12
21	The ¹³ C NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S13
22	The HSQC Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S13
23	The HMBC Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S14
24	The ¹ H- ¹ H COSY Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S14
25	The ROESY Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2	S15
26	The ¹ H NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2a	S15
27	The ¹³ C NMR Spectrum in MeOH- <i>d</i> ₄ (500 Hz)	2a	S16
28	The ECD Spectrum in MeOH	2a	S16
29	The UV Spectrum in MeOH	3	S17
30	The ECD Spectrum in MeOH	3	S17
31	The IR Spectrum (KBr)	3	S18

32	The HR-ESI-MS Data	3	S18
33	The ^1H NMR Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S19
34	The ^{13}C NMR Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S19
35	The HSQC Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S20
36	The HMBC Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S20
37	The $^1\text{H-}^1\text{H}$ COSY Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S21
38	The ROESY Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3	S21
39	$^1\text{H-}^1\text{H}$ COSY and Key HMBC	3	S22
40	The ^1H NMR Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3a	S22
41	The ^{13}C NMR Spectrum in $\text{MeOH-}d_4$ (500 Hz)	3a	S23
42	The ECD Spectrum in MeOH	3a	S23
	ECD Calculation of 1a		S24

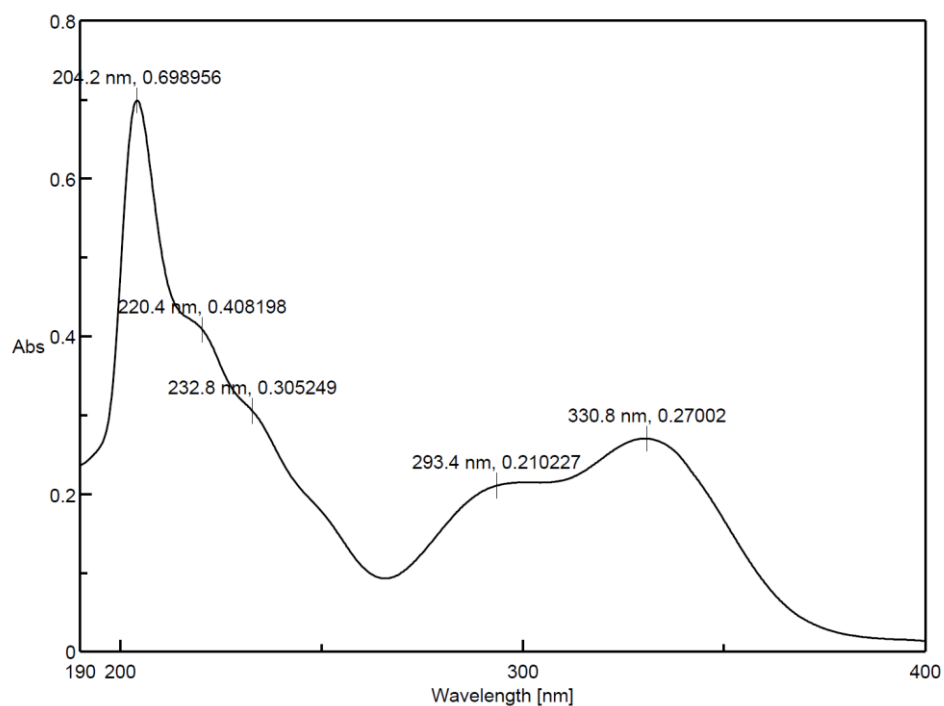


Figure 1. The UV Spectrum of compound **1** in MeOH

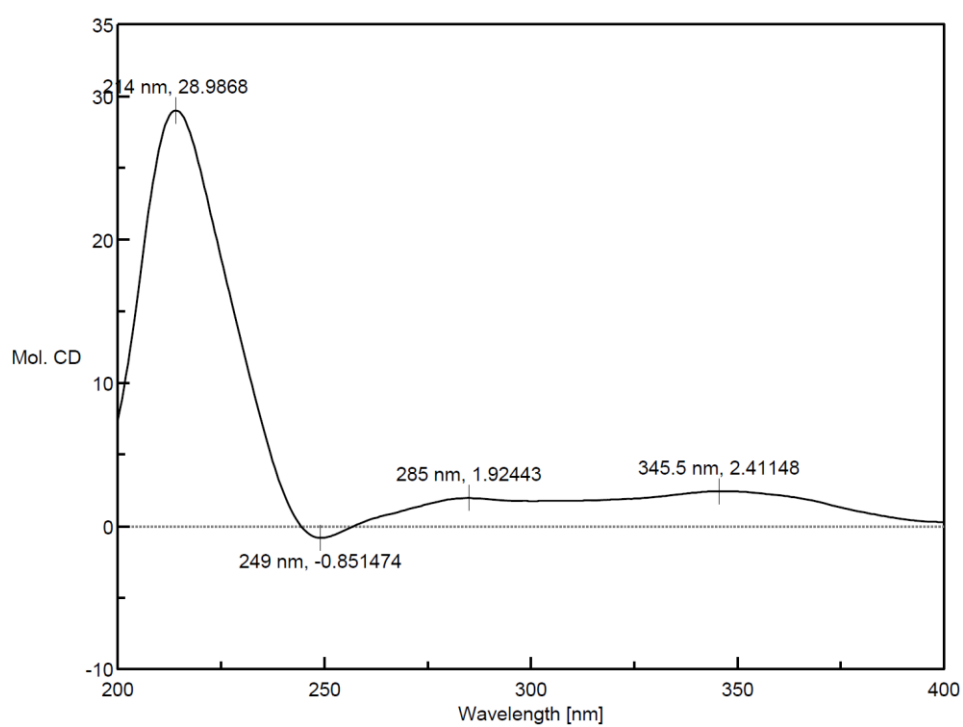


Figure 2. The ECD Spectrum of compound **1** in MeOH

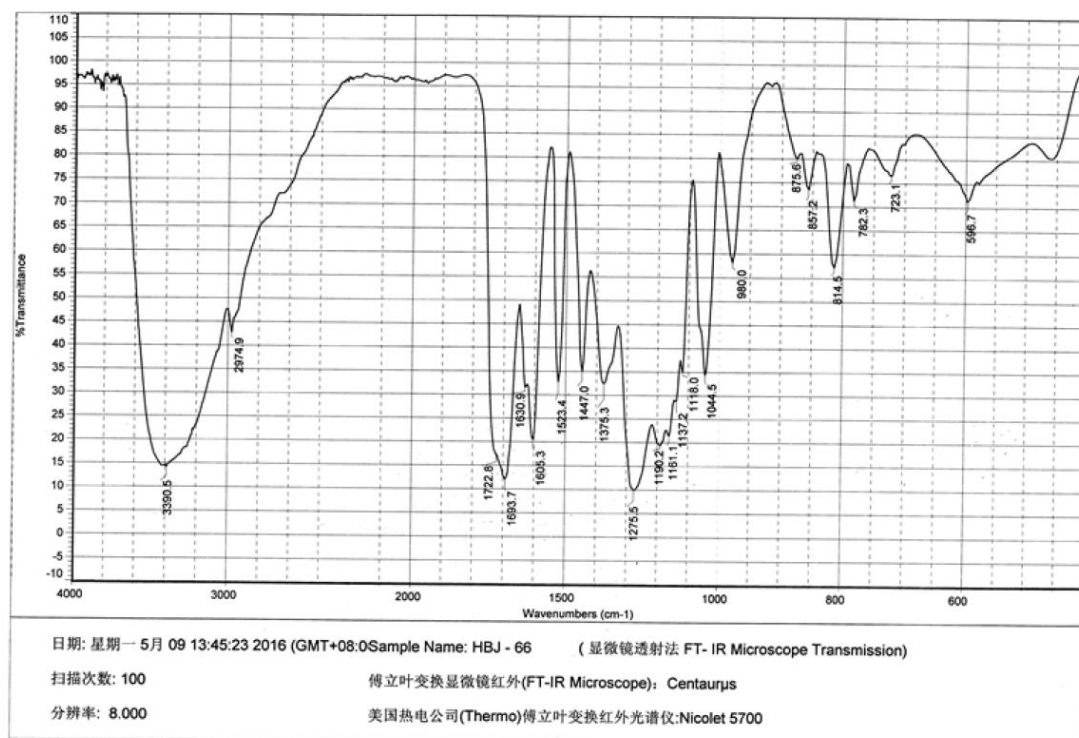


Figure 3. The IR Spectrum (KBr) of compound 1

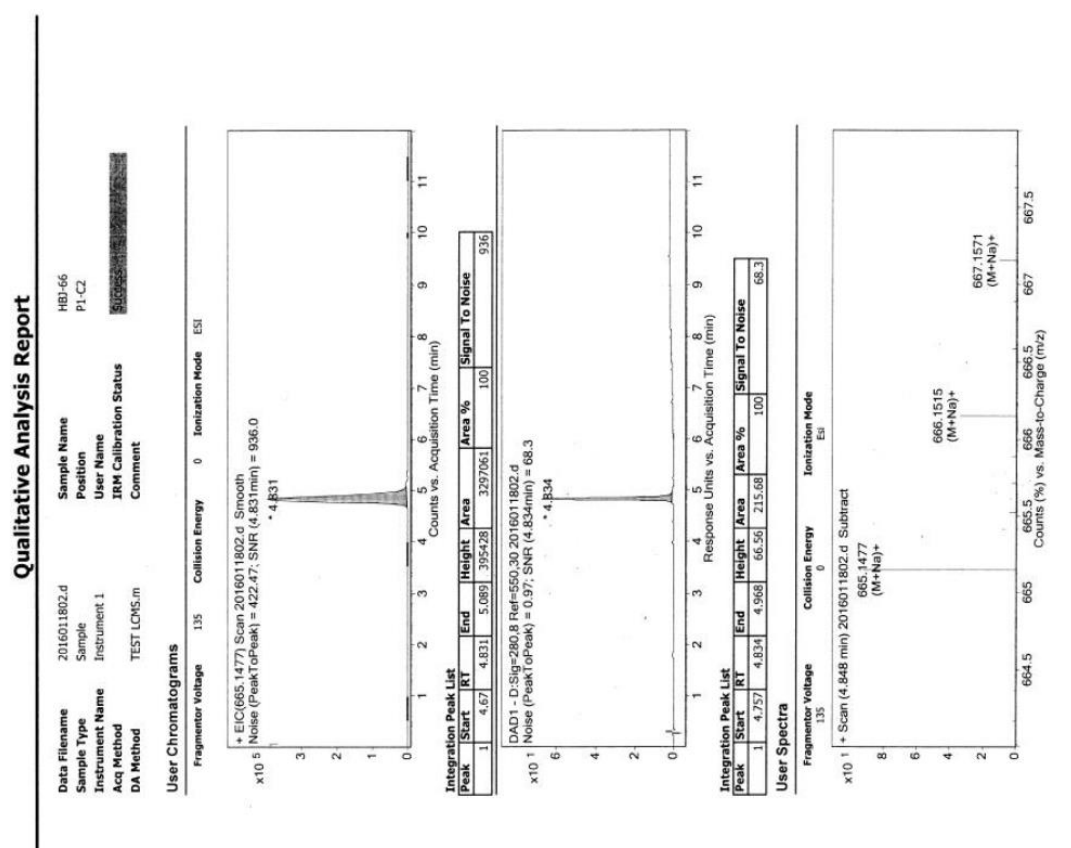


Figure 4. The HR-ESI-MS Data of compound 1

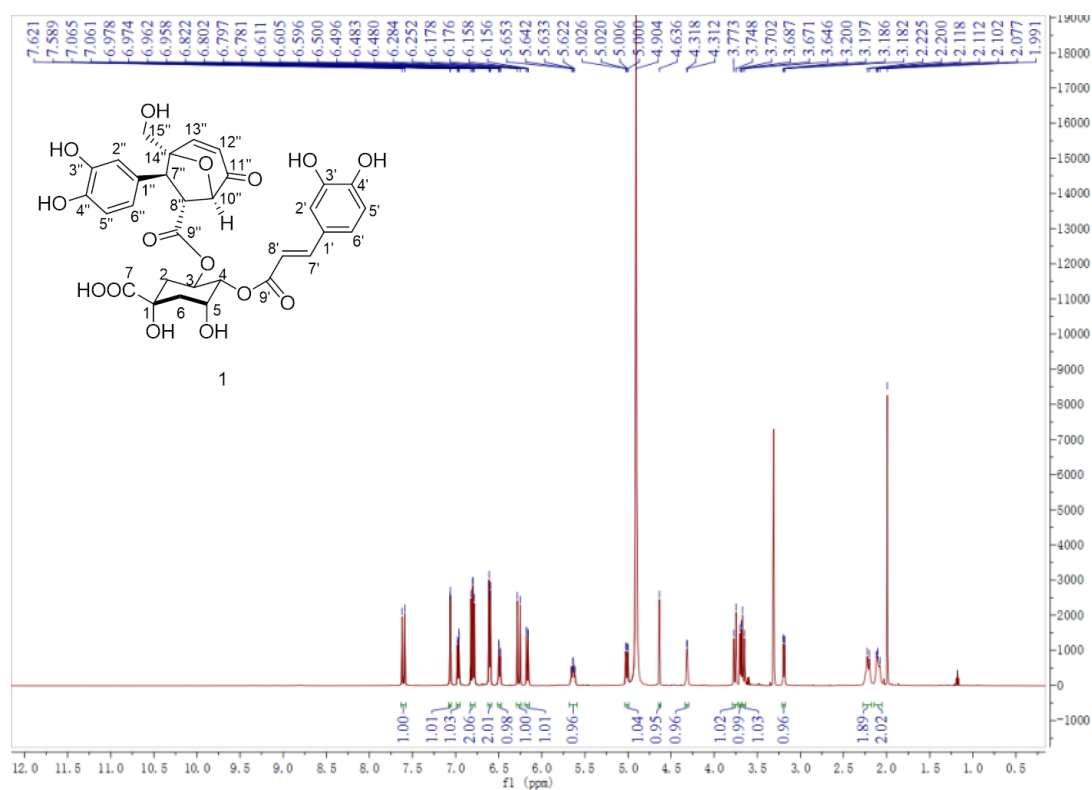


Figure 5. The ¹H NMR Spectrum of Compound **1** in MeOH-*d*₄ (500 Hz)

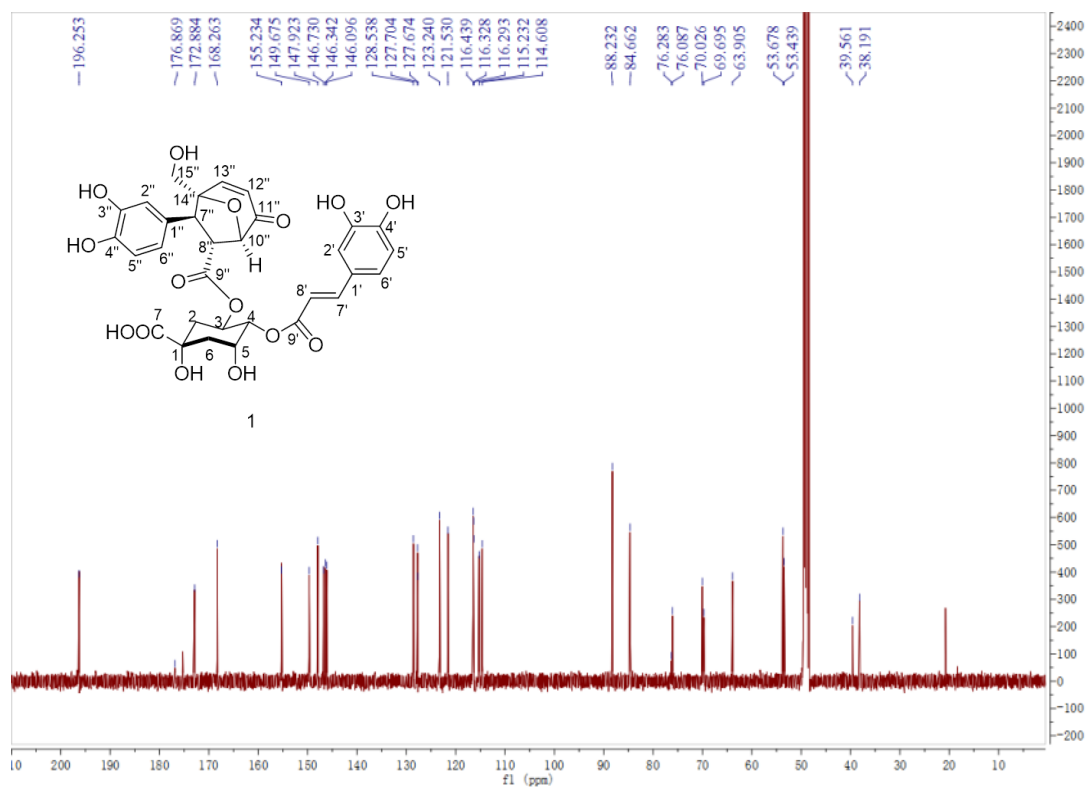


Figure 6. The ¹³C NMR Spectrum of Compound **1** in MeOH-*d*₄ (500 Hz)

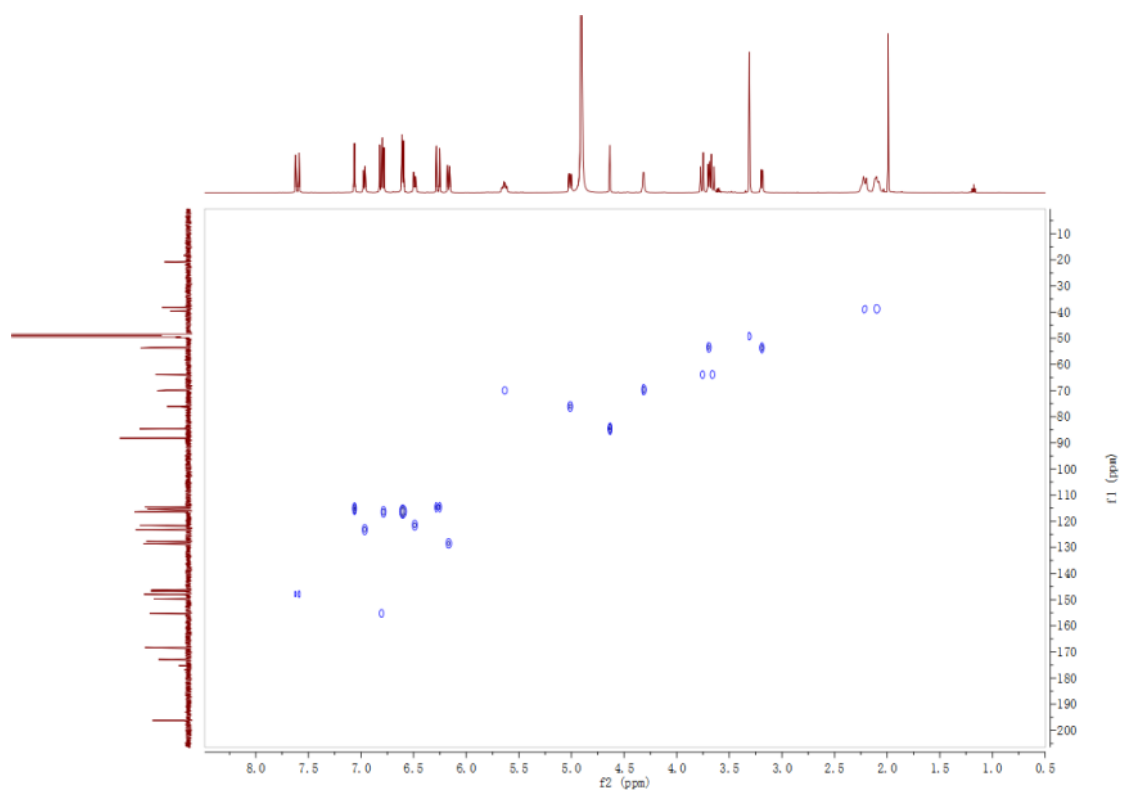


Figure 7. The HSQC Spectrum of Compound **1** in $\text{MeOH-}d_4$ (500 Hz)

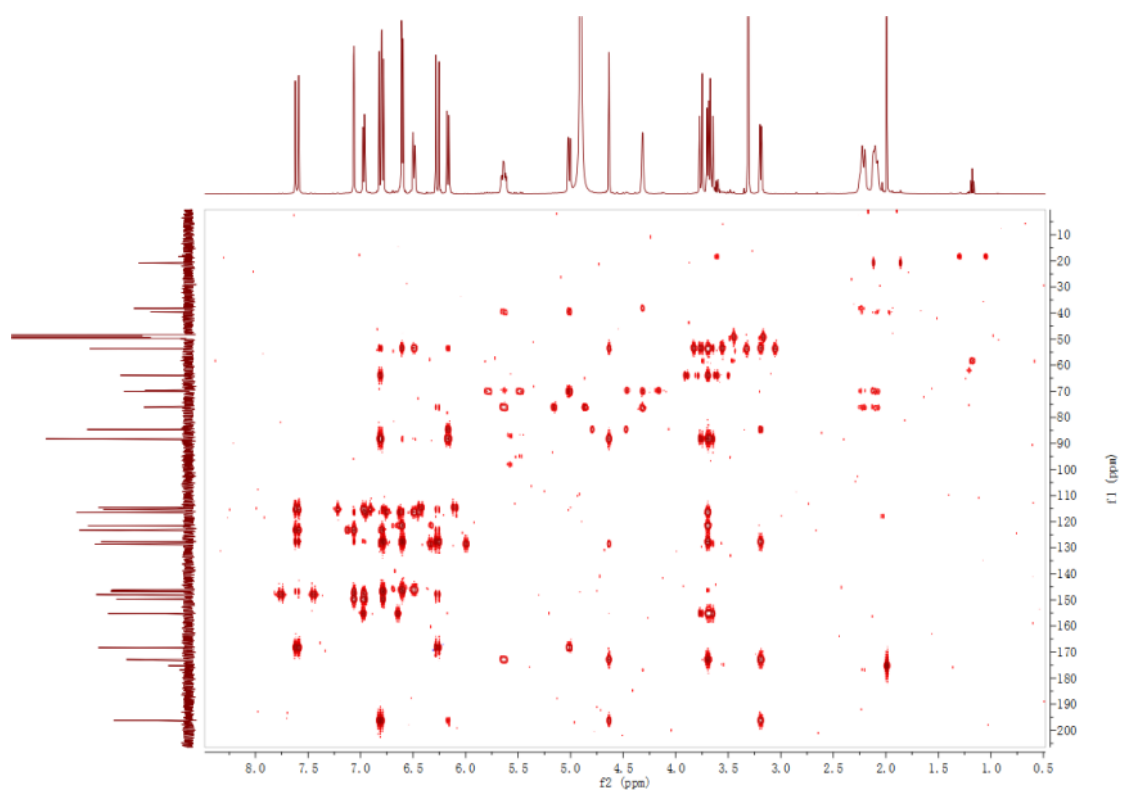


Figure 8. The HMBC Spectrum of Compound **1** in $\text{MeOH-}d_4$ (500 Hz)

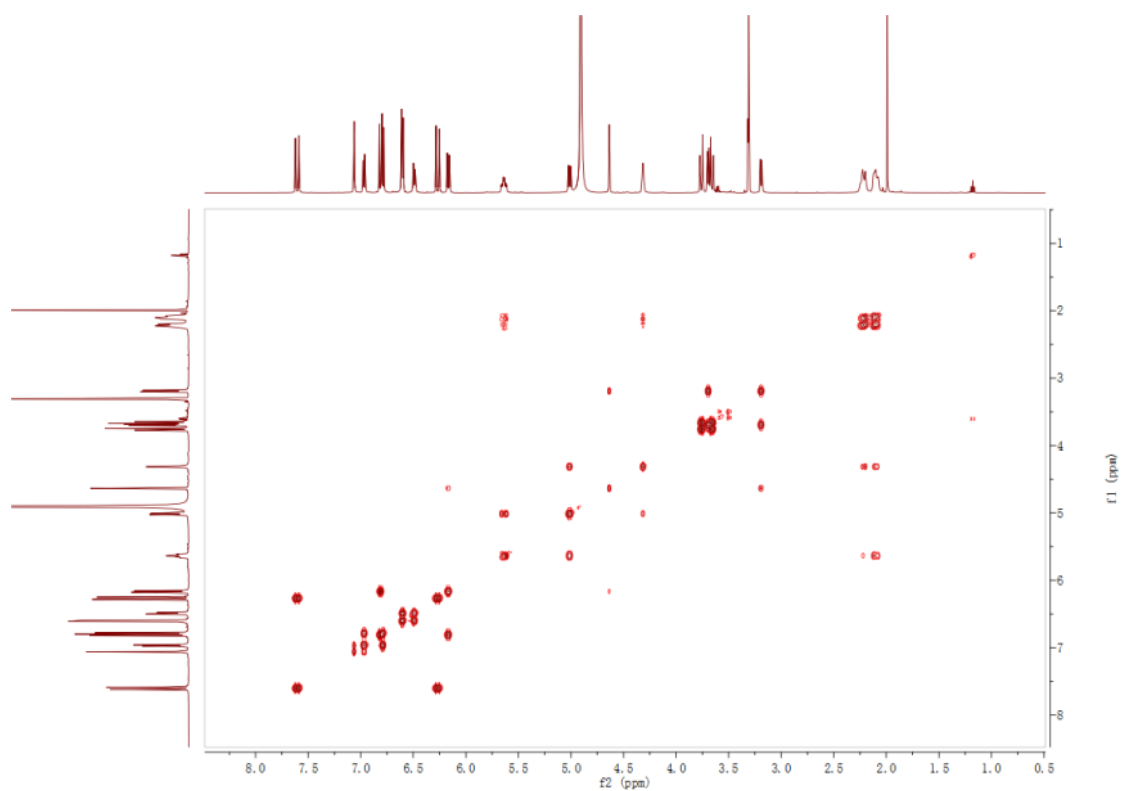


Figure 9. The ^1H - ^1H COSY Spectrum of Compound **1** in $\text{MeOH-}d_4$ (500 Hz)

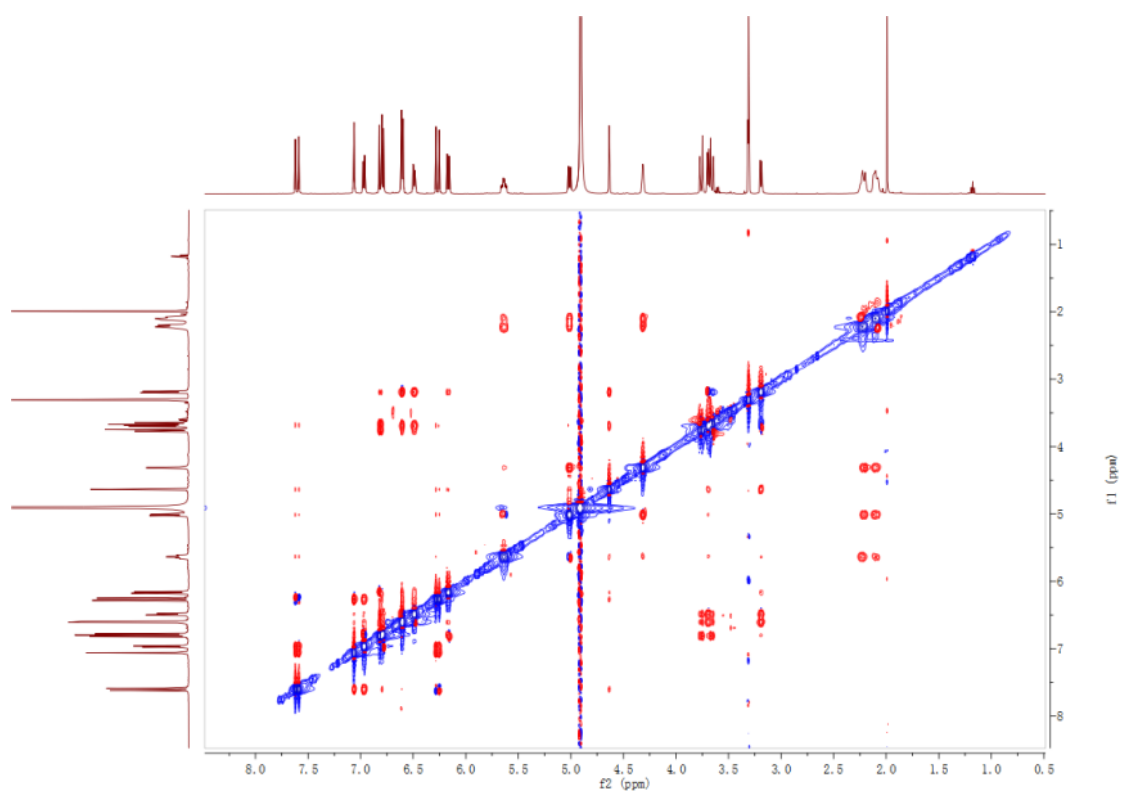


Figure 10. The ROESY Spectrum of Compound **1** in $\text{MeOH-}d_4$ (500 Hz)

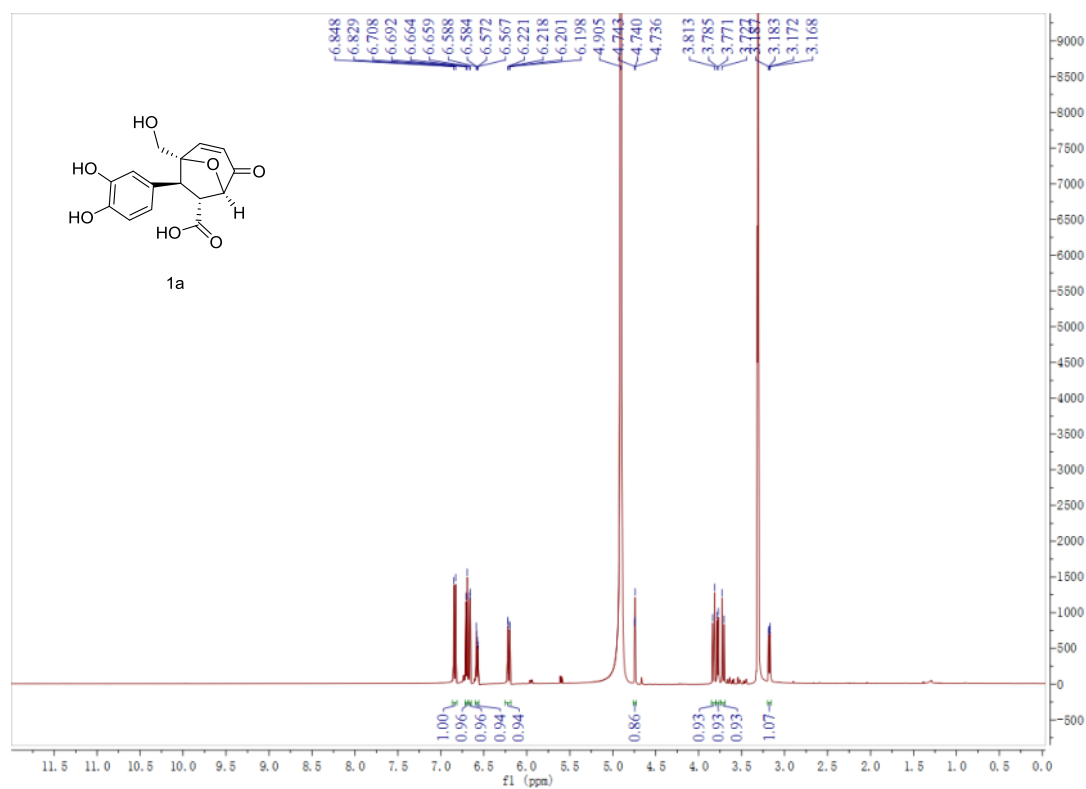


Figure 11. The ^1H NMR Spectrum of Compound **1a** in $\text{MeOH-}d_4$ (500 Hz)

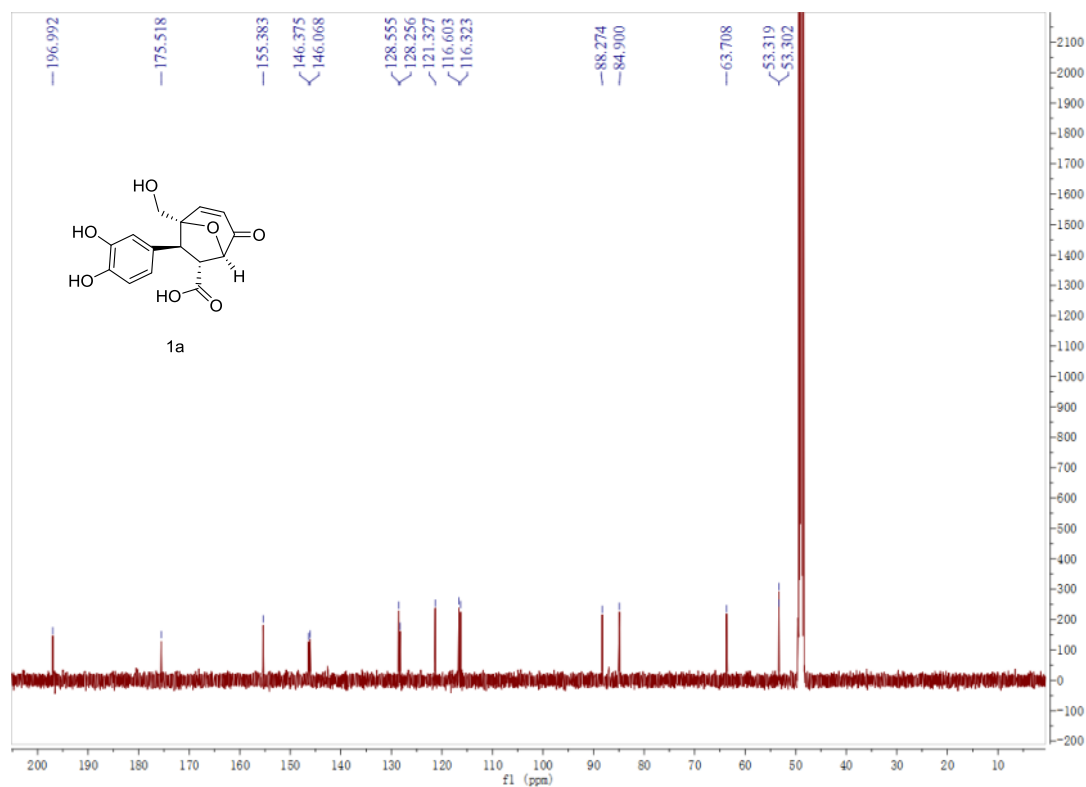


Figure 12. The ^{13}C NMR Spectrum of Compound **1a** in $\text{MeOH-}d_4$ (500 Hz)

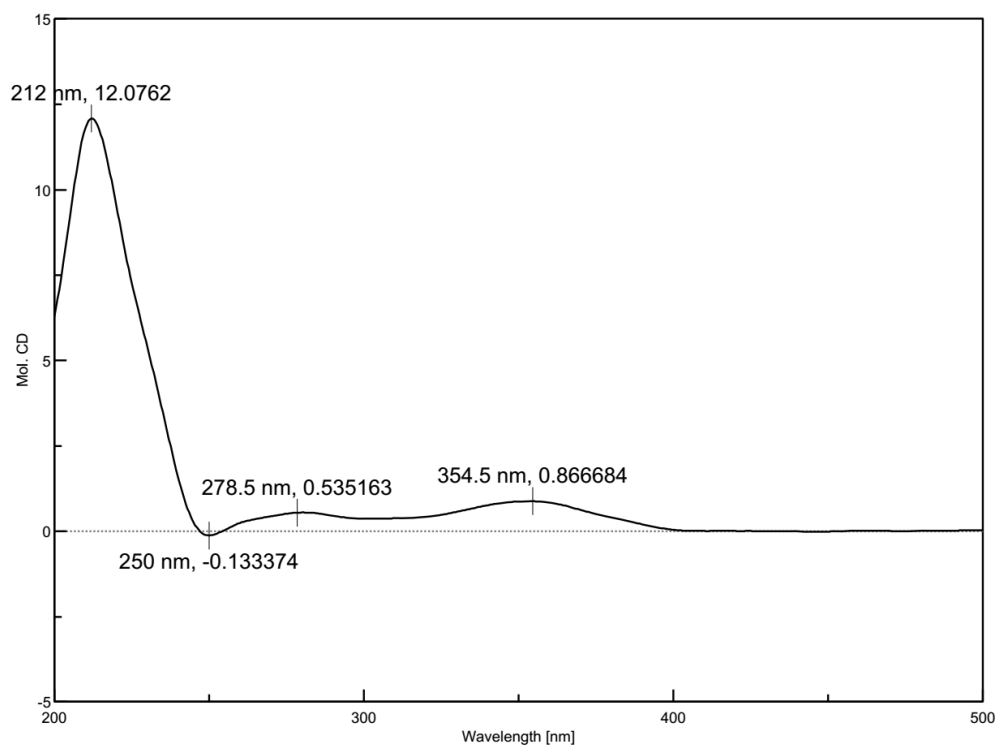


Figure 13. The ECD Spectrum of compound **1a** in MeOH

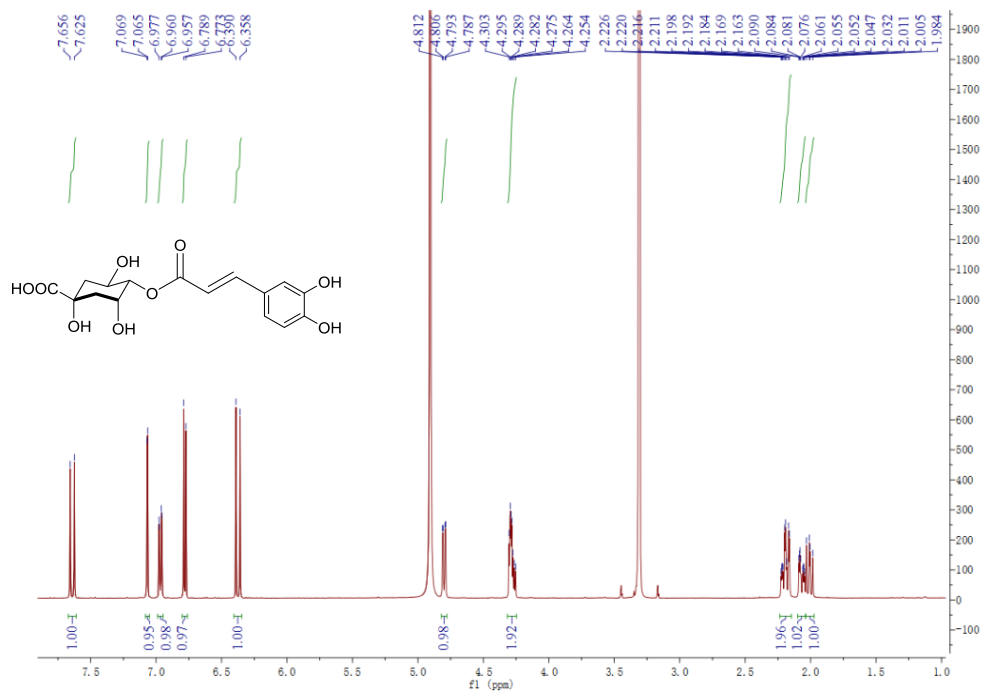


Figure 14. The ^1H NMR Spectrum of Compound **1b** in $\text{MeOH-}d_4$ (500 MHz)

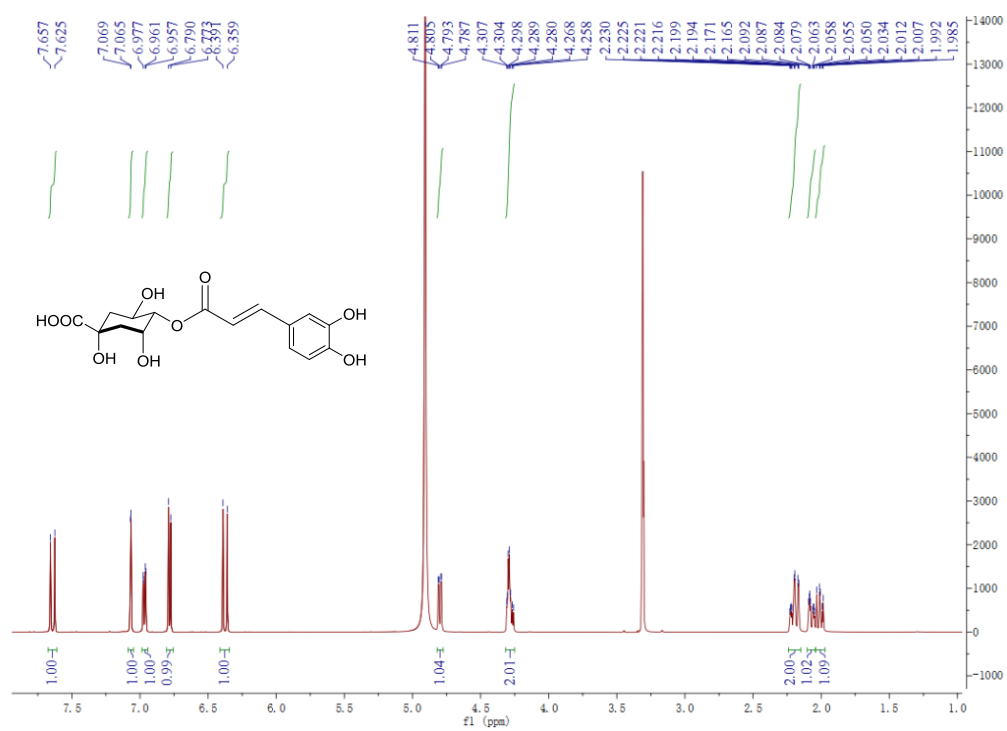


Figure 15. The ¹H NMR Spectrum of standard 4-O-caffeoylquinic acid in MeOH-d₄ (500 Hz)

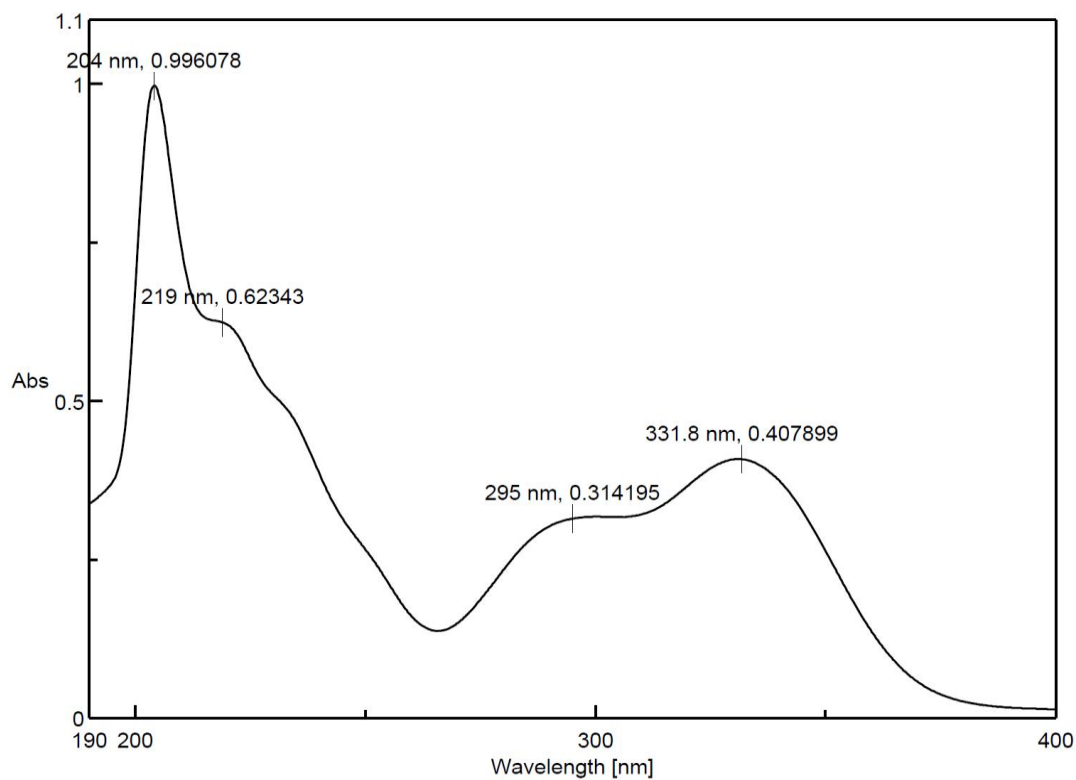


Figure 16. The UV Spectrum of compound **2** in MeOH

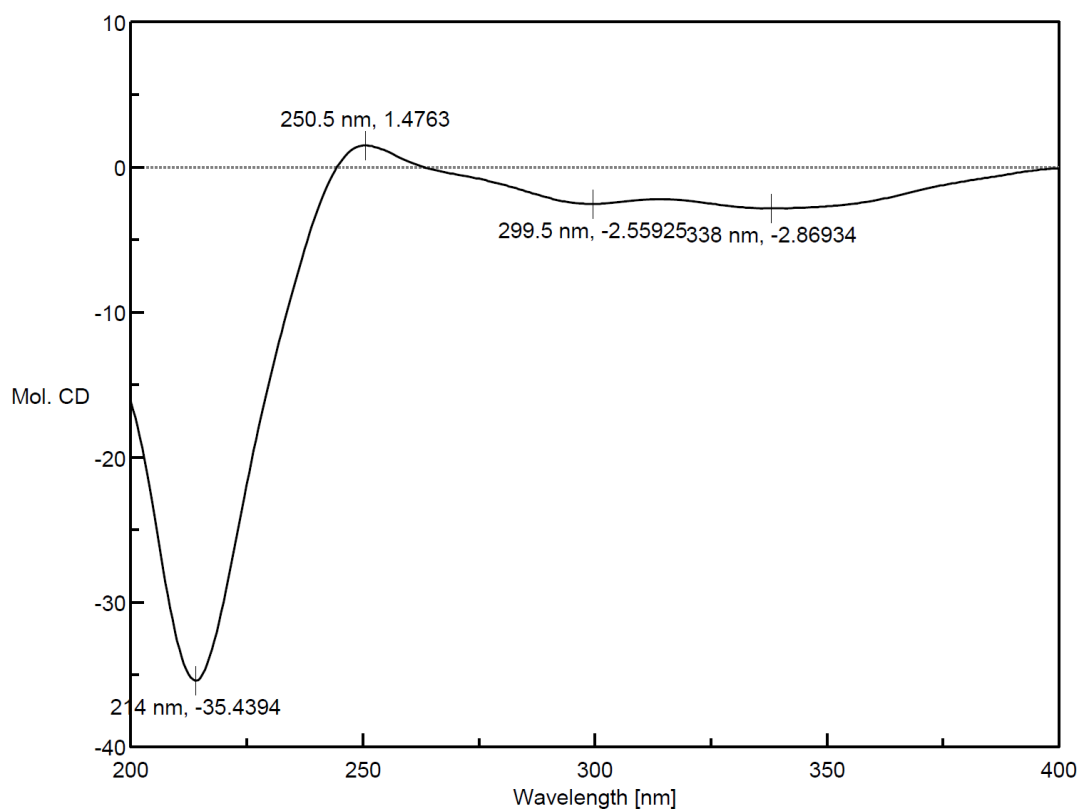


Figure 17. The ECD Spectrum of compound **2** in MeOH

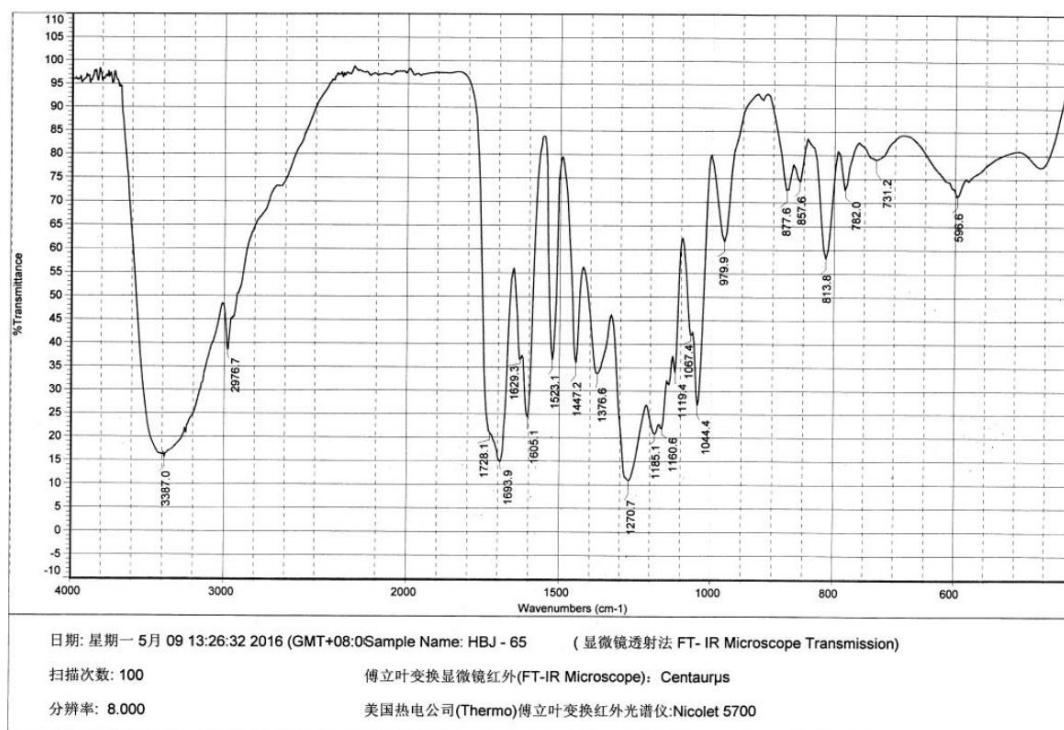
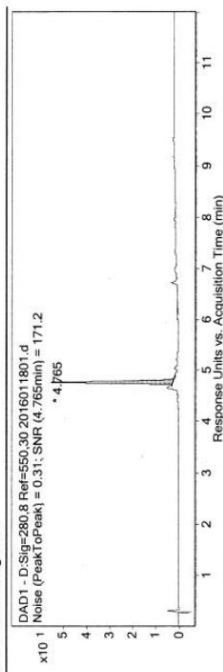


Figure 18. The IR Spectrum (KBr) of compound **2**

Qualitative Analysis Report

Data Filename 2016011801.d
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Instrument Name Instrument 1
Acq Method TEST LCMS.m
DA Method
Sample Name HBI-65
Position P1-C1
User Name
IRM Calibration Status
Comment

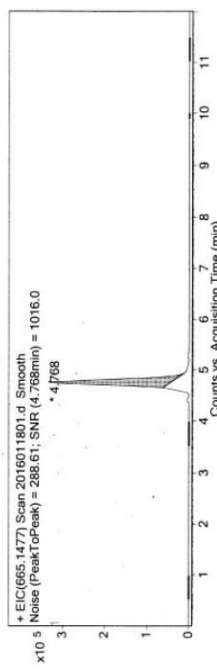
User Chromatograms



Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	4.711	4.765	4.898	52.58	162.91	100	171.2

Fragmentor Voltage 135 Collision Energy 0 Ionization Mode ESI



Integration Peak List

Peak	Start	RT	End	Height	Area	Area %	Signal To Noise
1	4.655	4.768	4.945	293212	2163305	100	1016

User Spectra

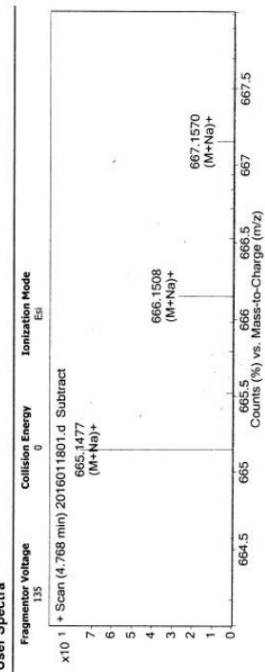


Figure 19. The HR-ESI-MS Data of compound **2**

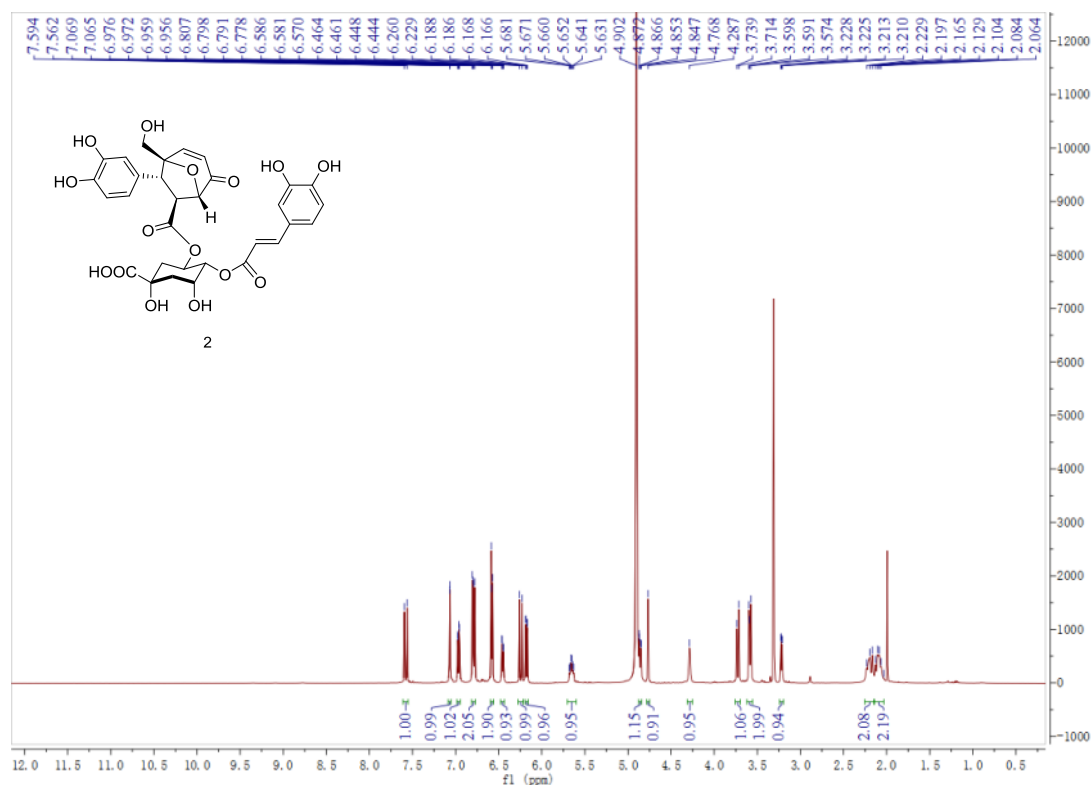


Figure 20. The ^1H NMR Spectrum of Compound **2** in $\text{MeOH-}d_4$ (500 Hz)

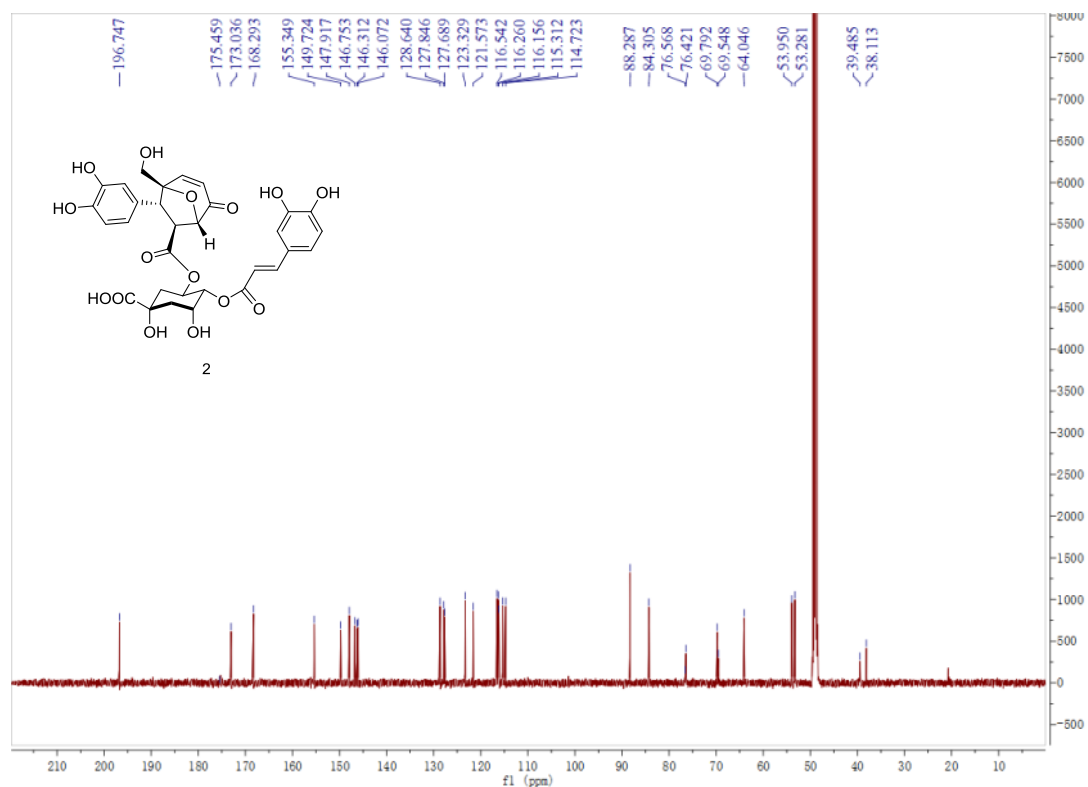


Figure 21. The ^{13}C NMR Spectrum of Compound 2 in $\text{MeOH-}d_4$ (500 Hz)

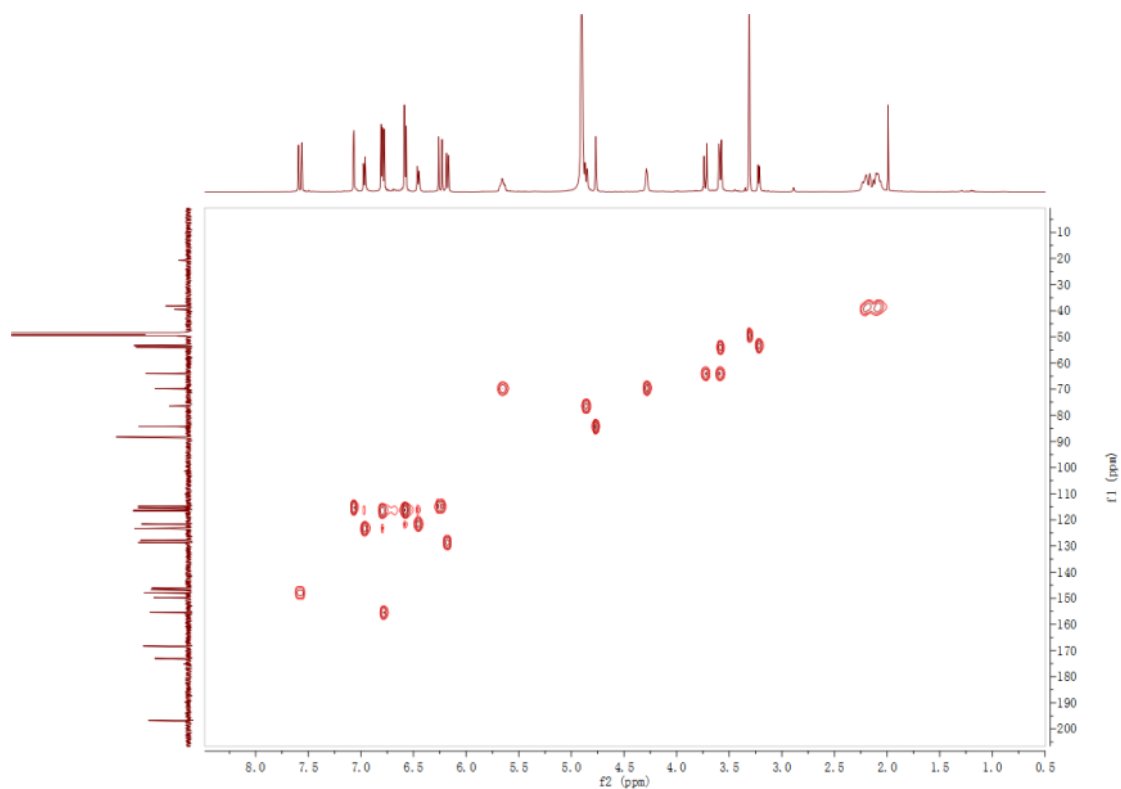


Figure 22. The HSQC Spectrum of Compound 2 in $\text{MeOH-}d_4$ (500 Hz)

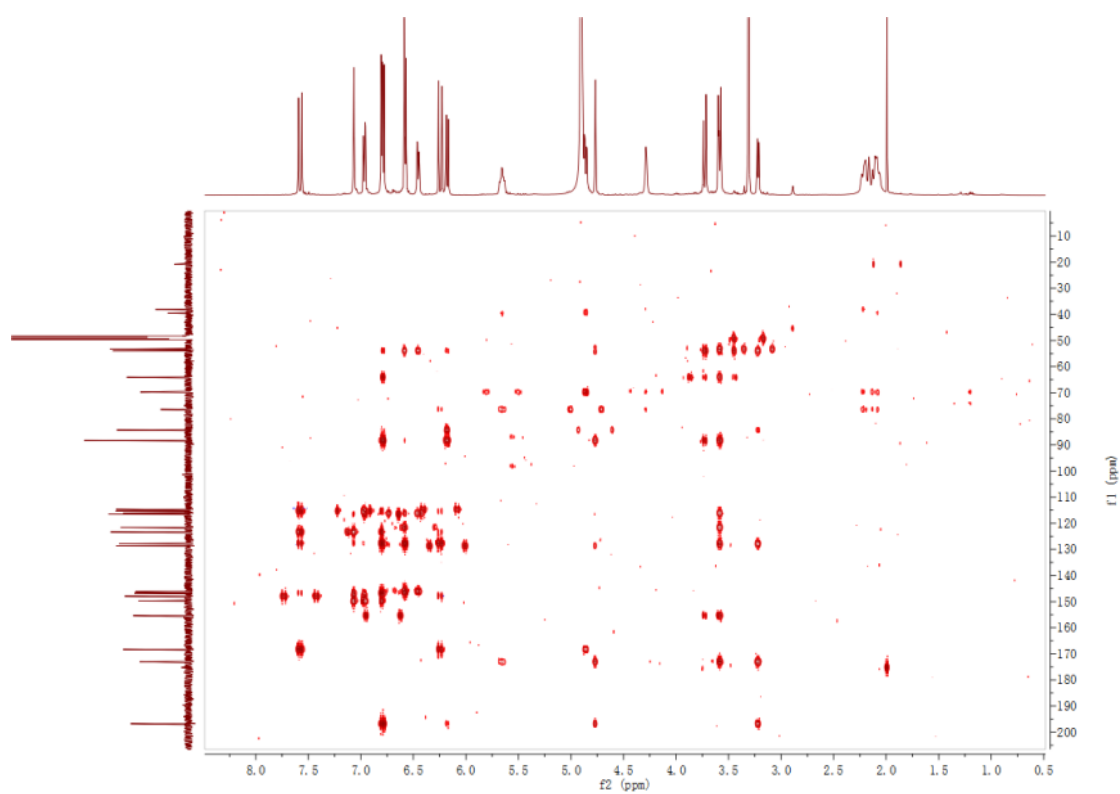


Figure 23. The HMBC Spectrum of Compound **2** in MeOH- d_4 (500 Hz)

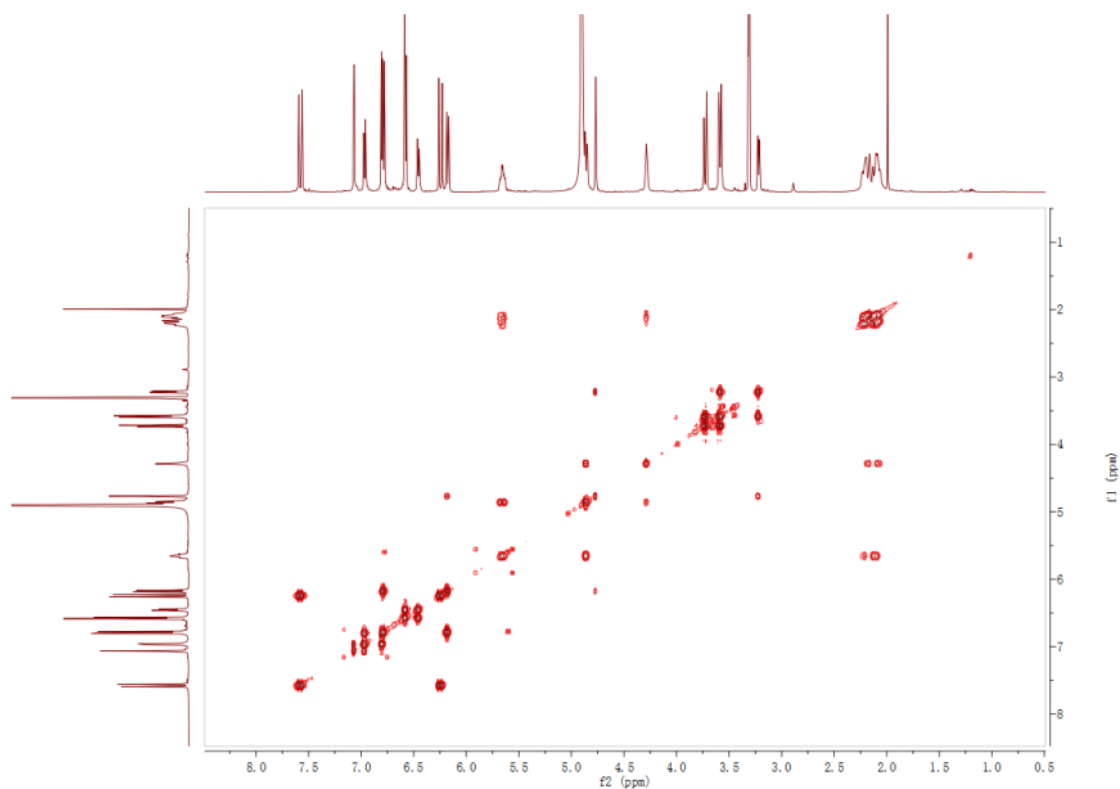


Figure 24. The ^1H - ^1H COSY Spectrum of Compound **2** in MeOH- d_4 (500 Hz)

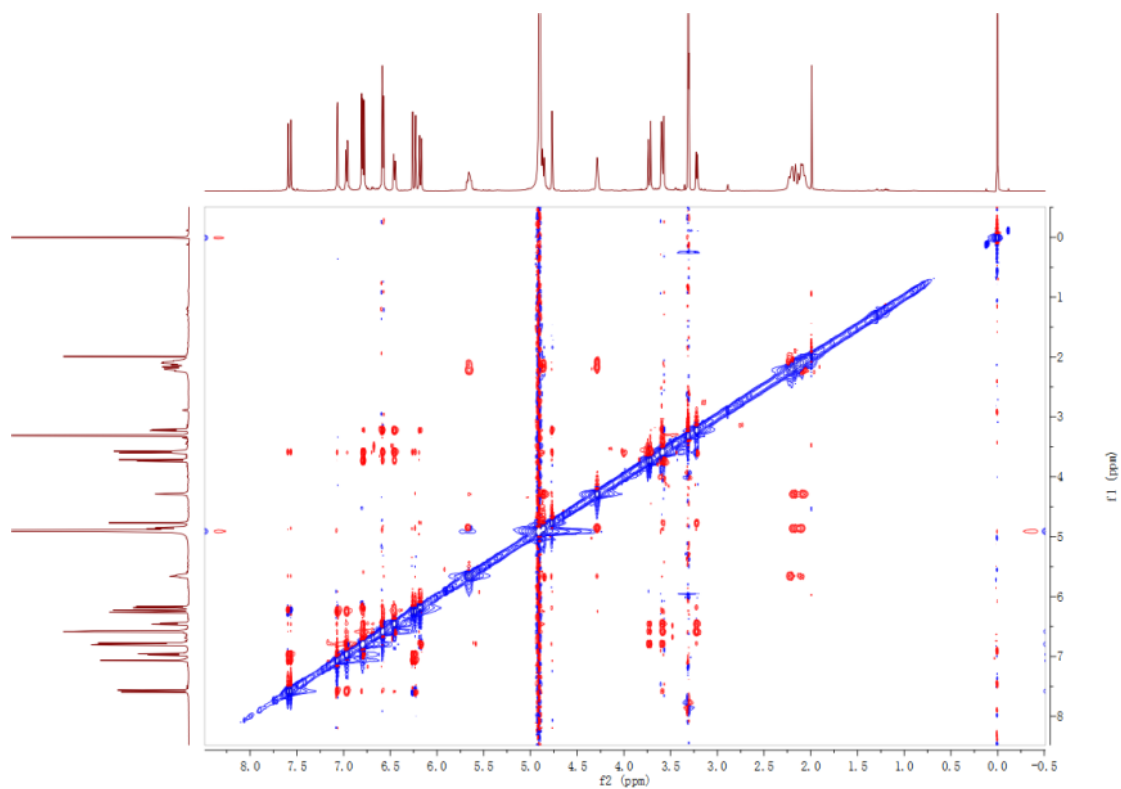


Figure 25. The ROESY Spectrum of Compound **2** in MeOH-*d*₄ (500 Hz)

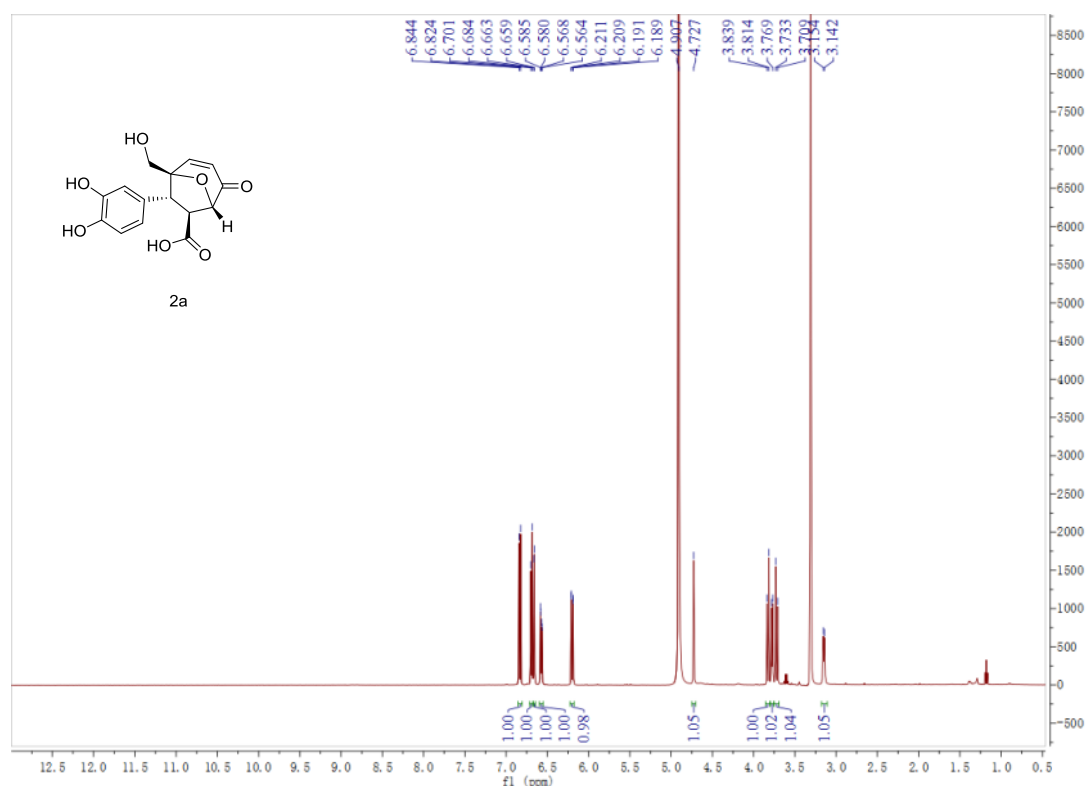


Figure 26. The ¹H NMR Spectrum of Compound **2a** in MeOH-*d*₄ (500 Hz)

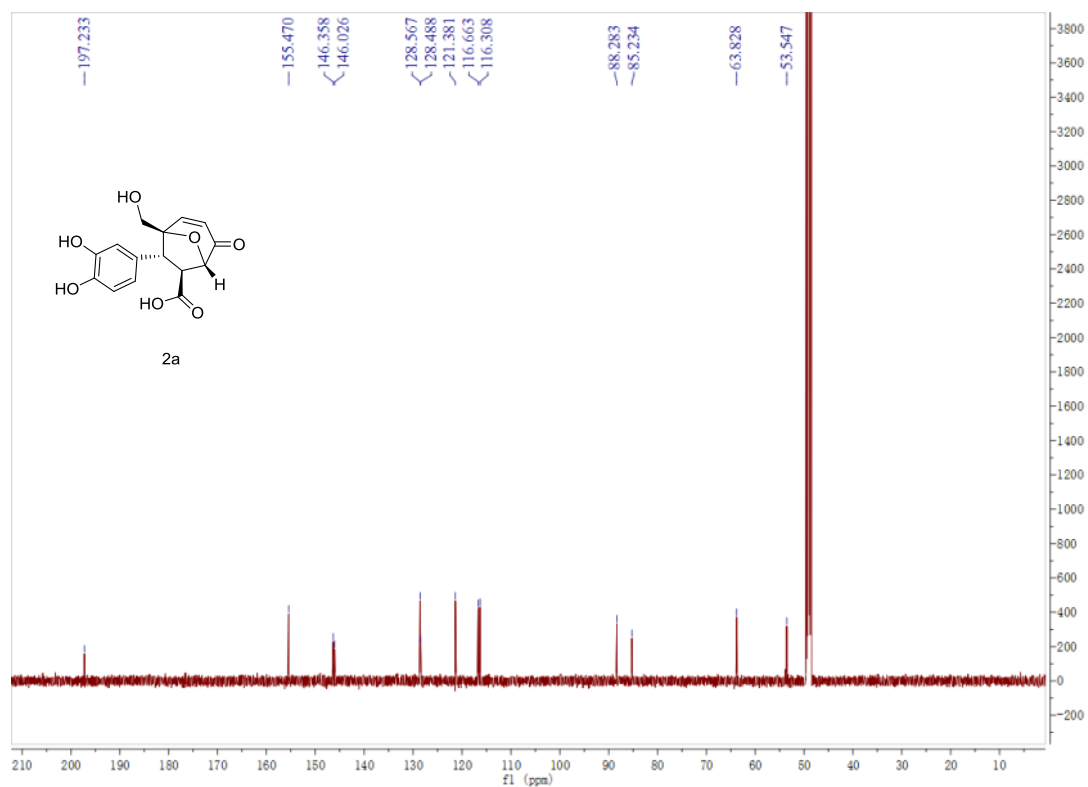


Figure 27. The ^{13}C NMR Spectrum of Compound **2a** in $\text{MeOH-}d_4$ (500 Hz)

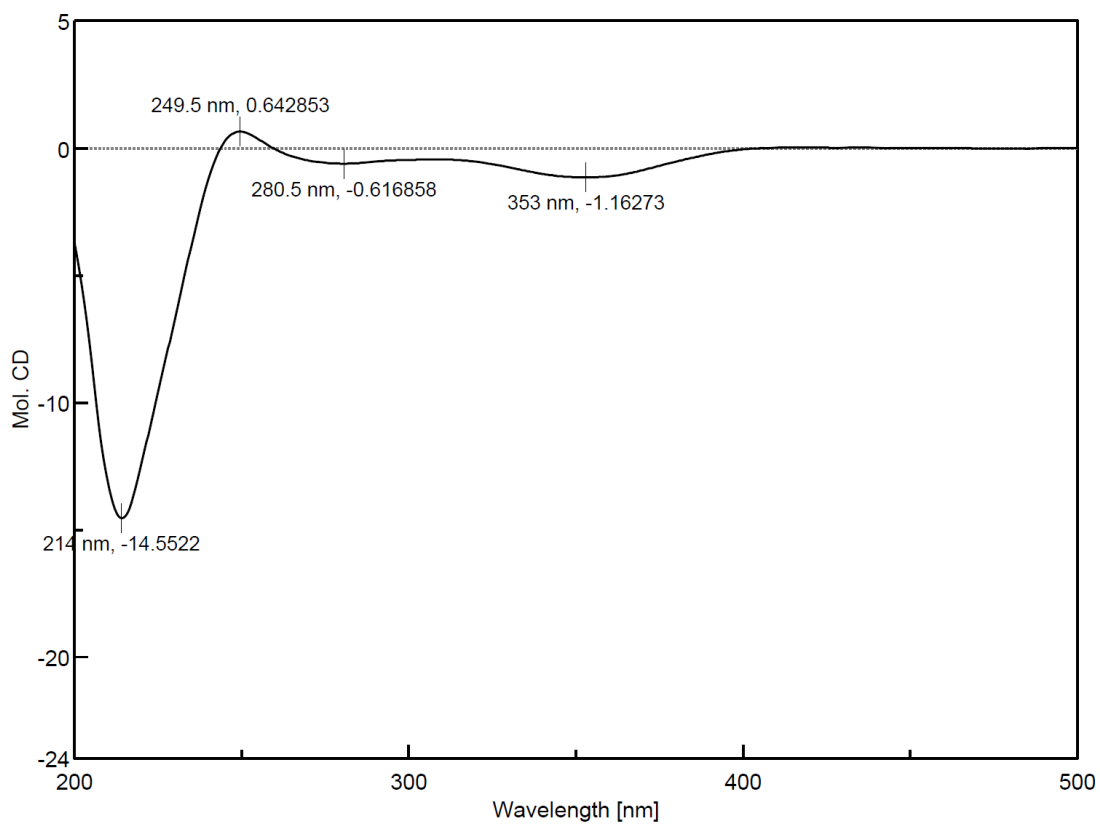


Figure 28. The ECD Spectrum of Compound **2a** in MeOH

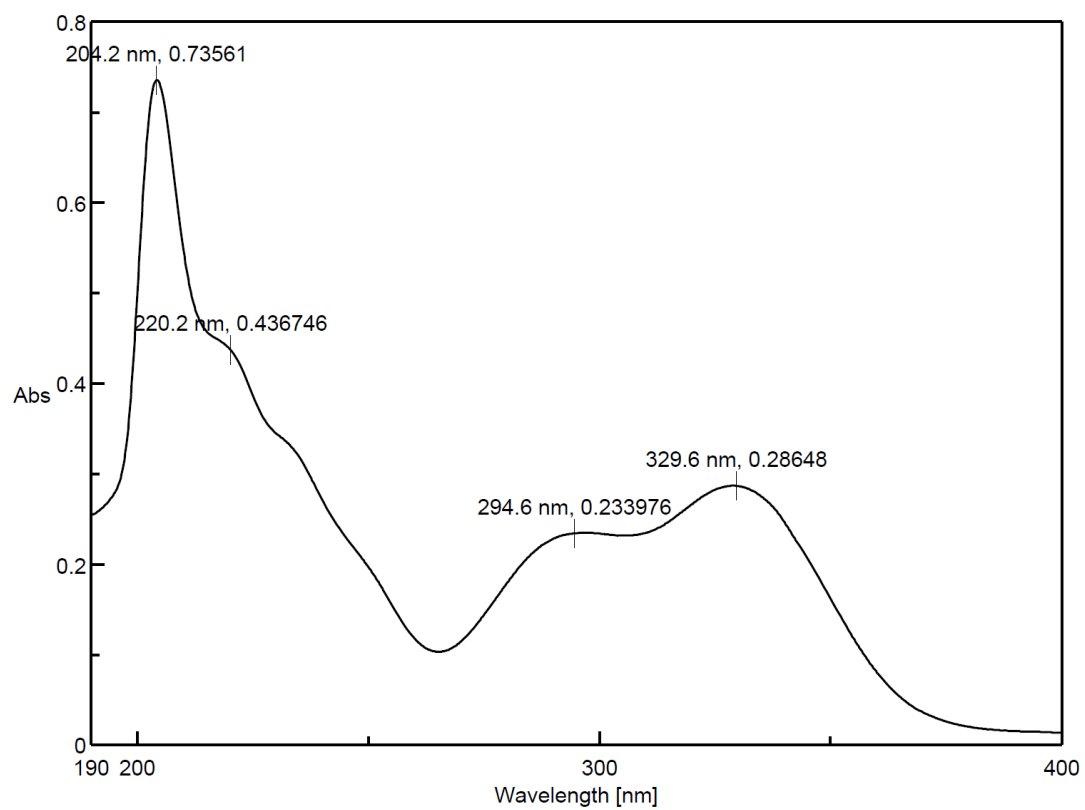


Figure 29. The UV Spectrum of Compound **3** in MeOH

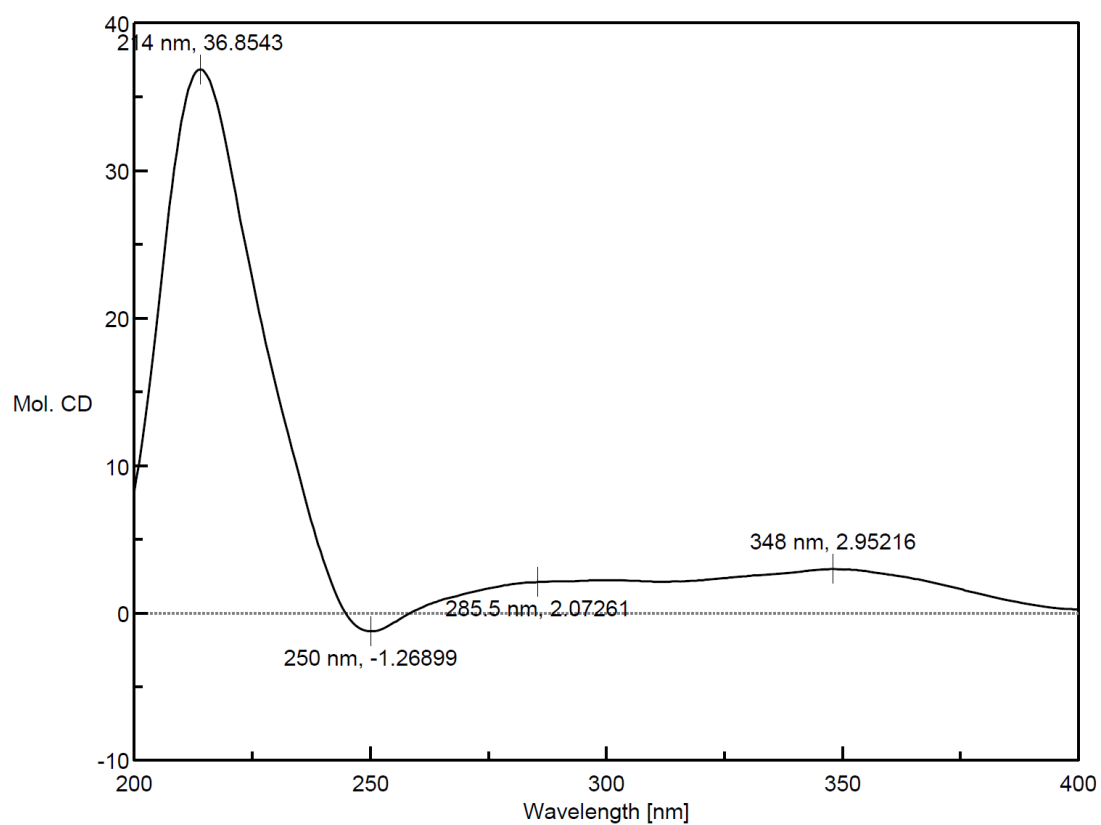


Figure 30. The ECD Spectrum of Compound **3** in MeOH

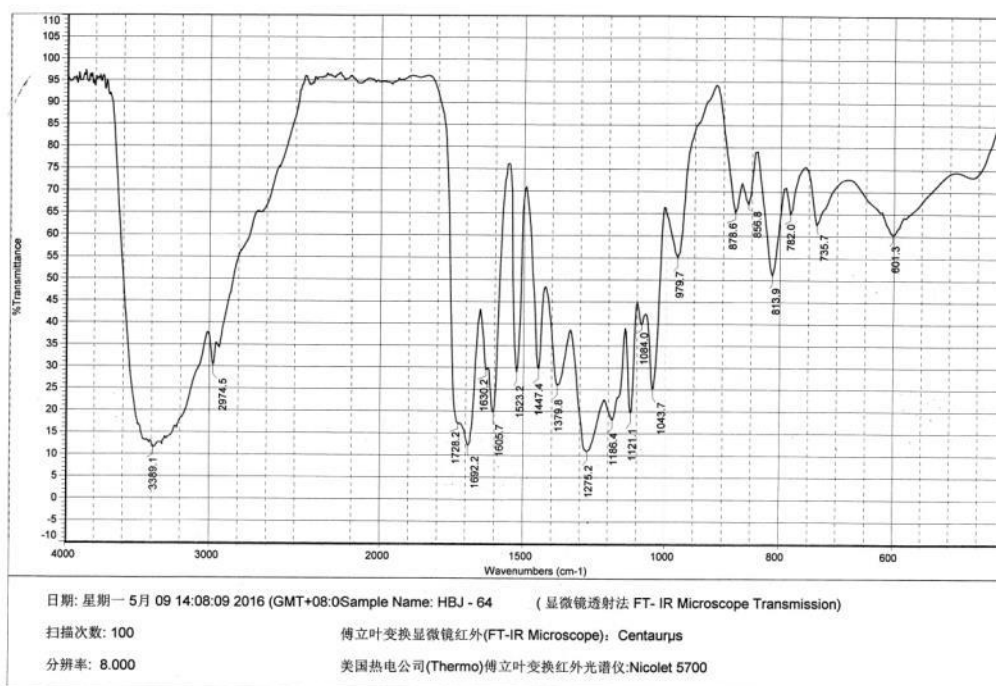


Figure 31. The IR Spectrum (KBr) of compound **3**

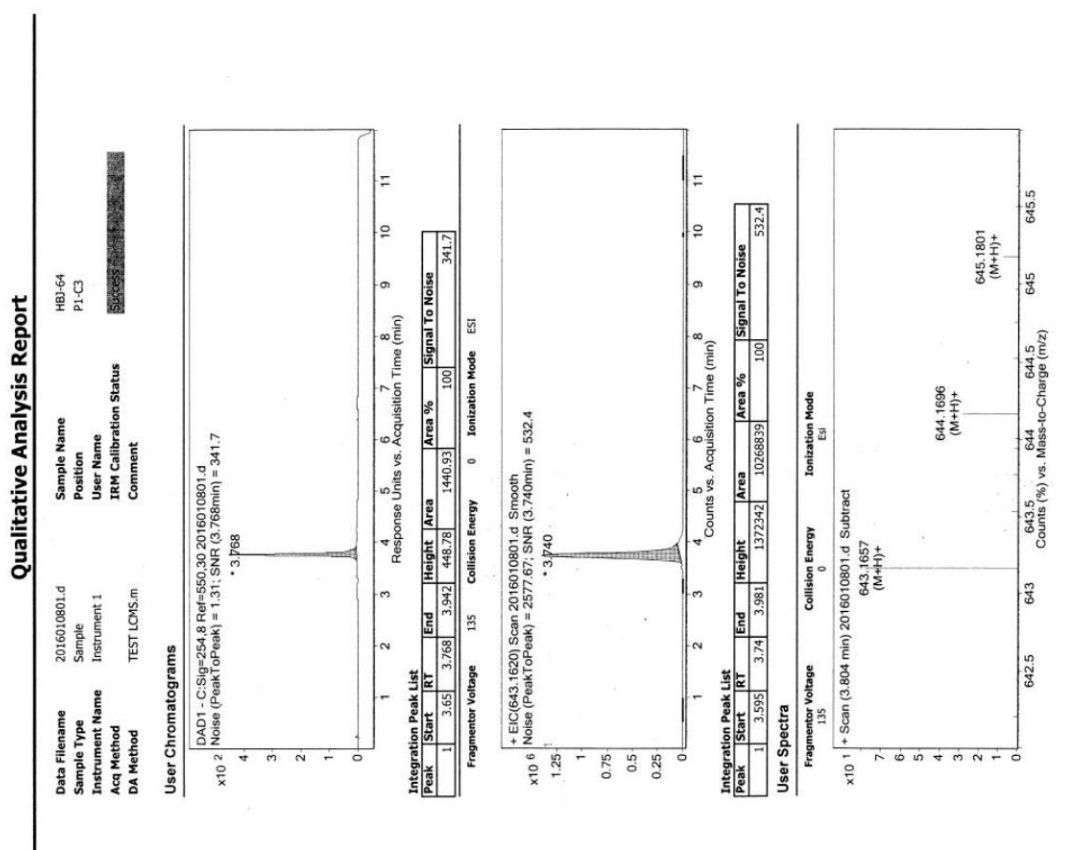


Figure 32. The IR Spectrum (KBr) of compound **3**

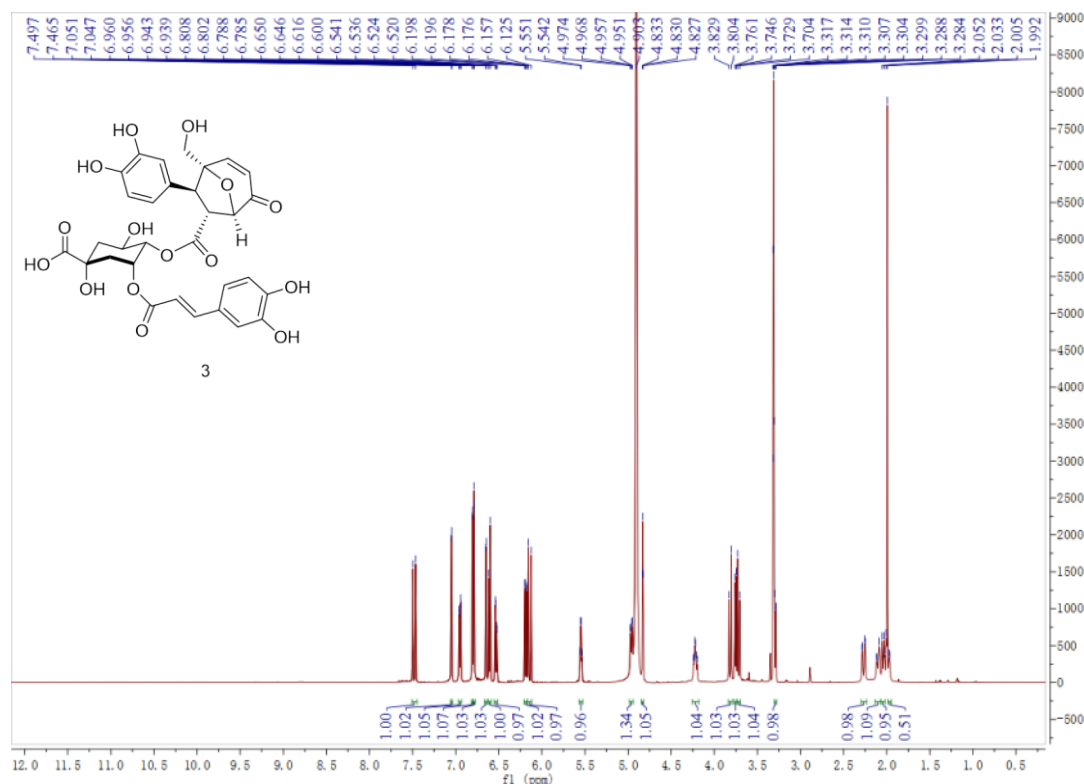


Figure 33. The ^1H NMR Spectrum of Compound **3** in $\text{MeOH-}d_4$ (500 Hz)

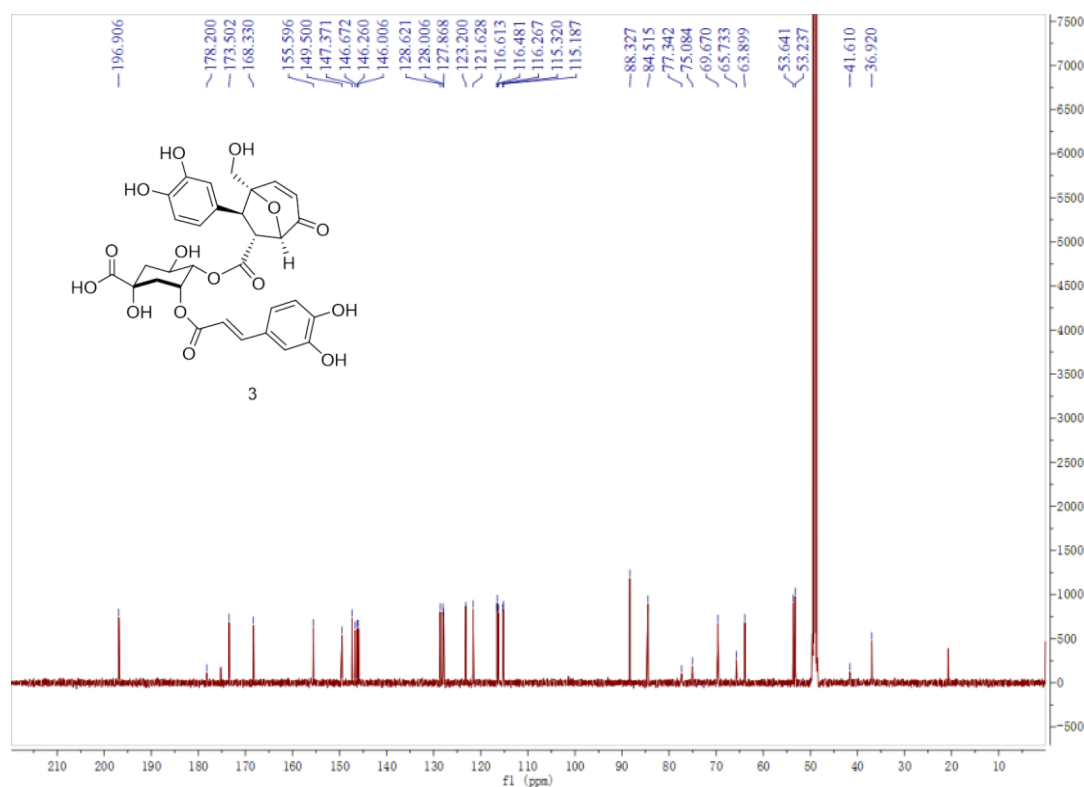


Figure 34. The ^{13}C NMR Spectrum of Compound **3** in $\text{MeOH-}d_4$ (500 Hz)

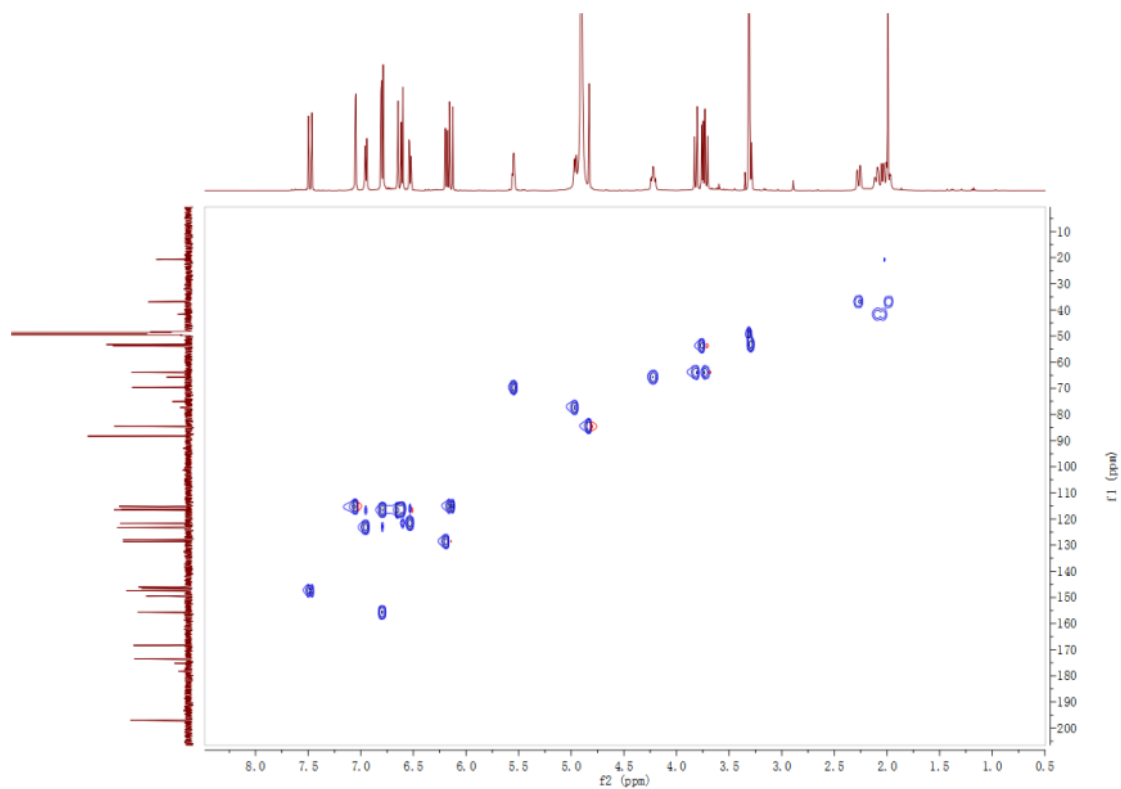


Figure 35. The HSQC Spectrum of Compound **3** in MeOH-*d*₄ (500 Hz)

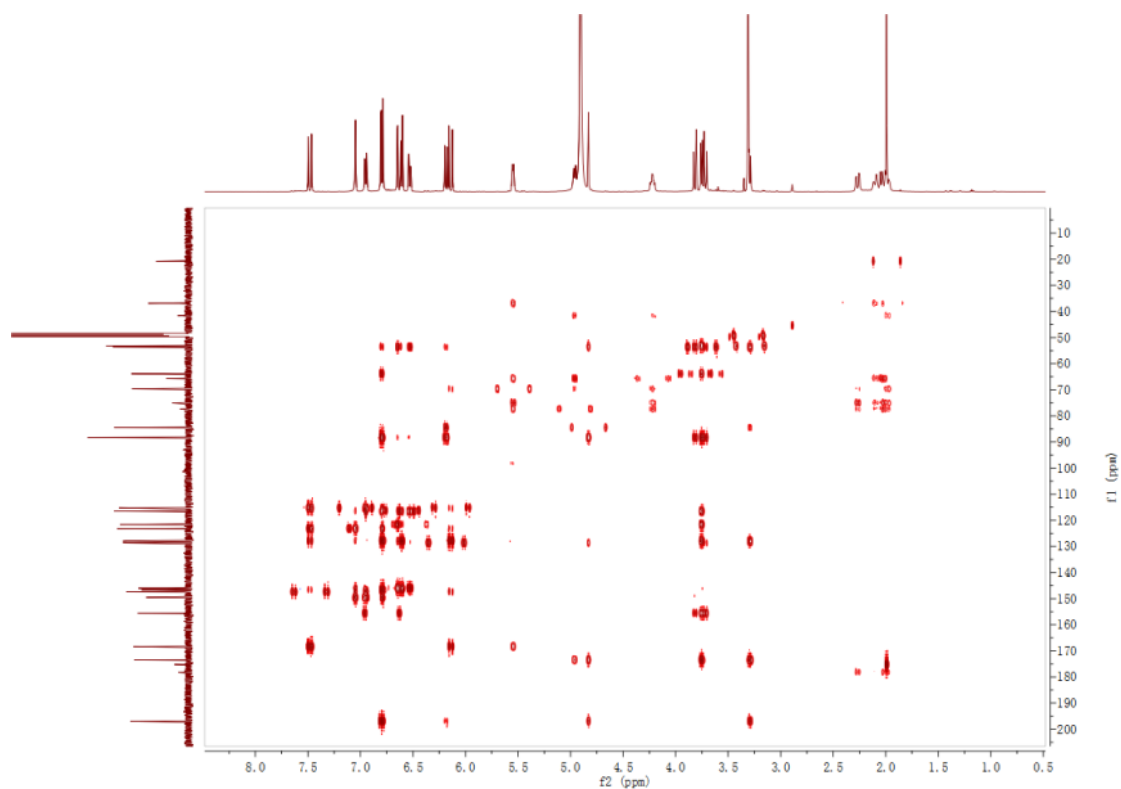


Figure 36. The HMBC Spectrum of Compound **3** in MeOH-*d*₄ (500 Hz)

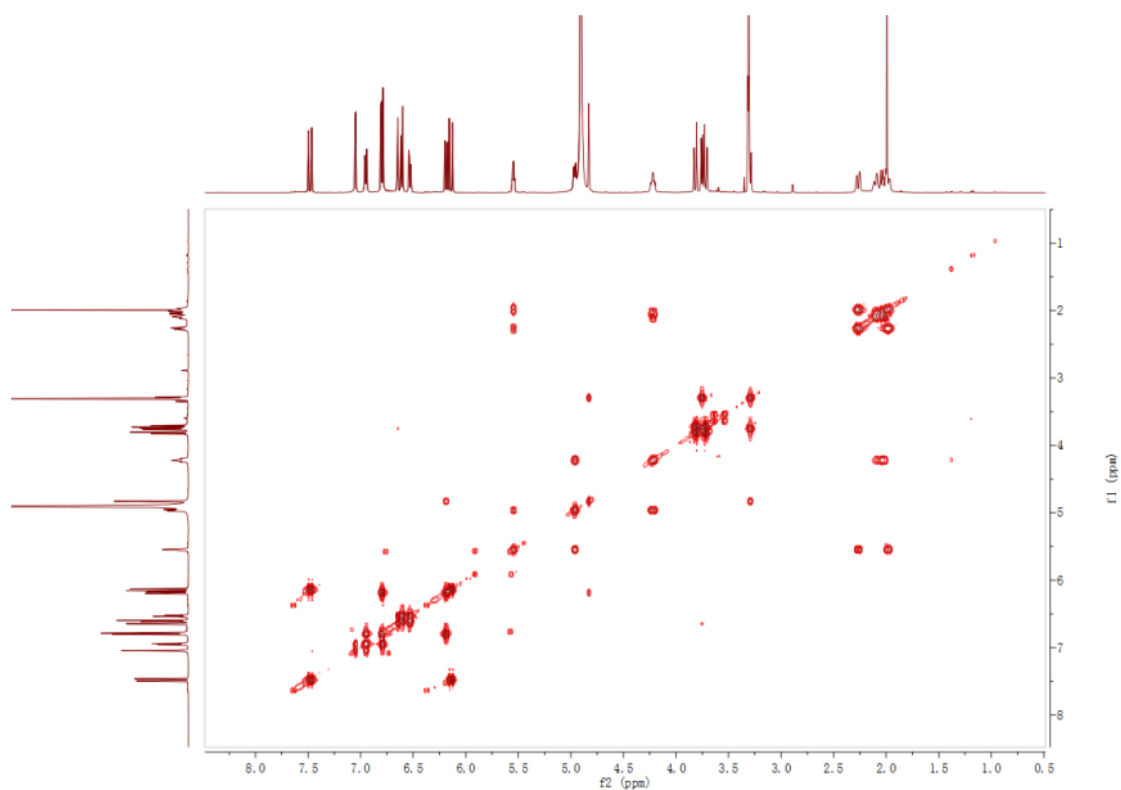


Figure 37. The ^1H - ^1H COSY Spectrum of Compound **3** in $\text{MeOH-}d_4$ (500 Hz)

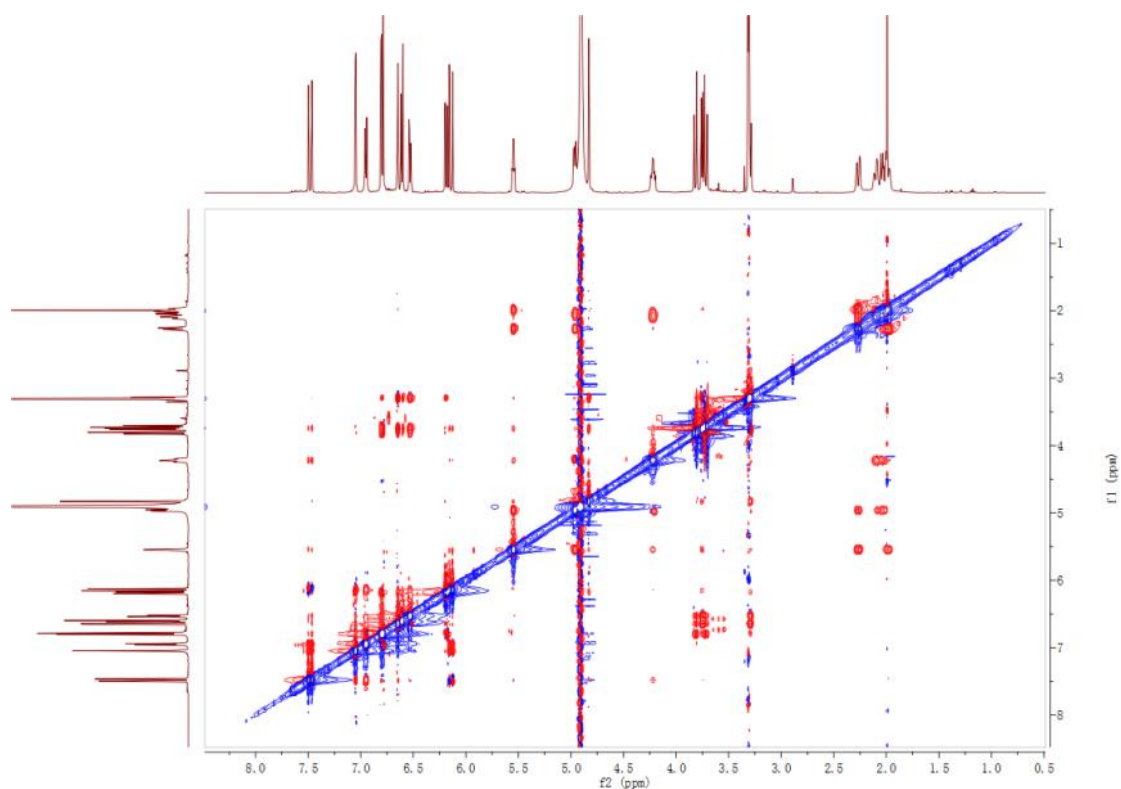


Figure 38. The ROESY Spectrum of Compound **3** in $\text{MeOH-}d_4$ (500 Hz)

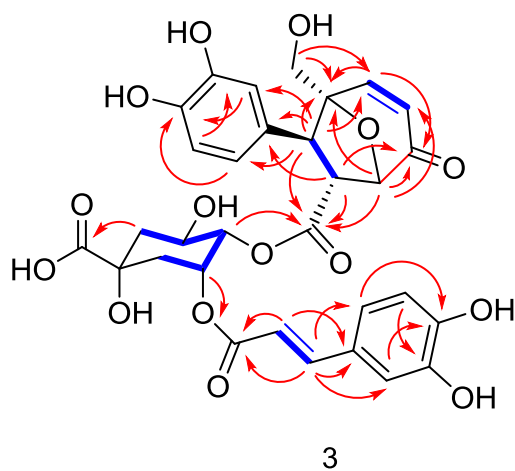


Figure 39. ^1H - ^1H COSY and Key HMBC of compound **3**

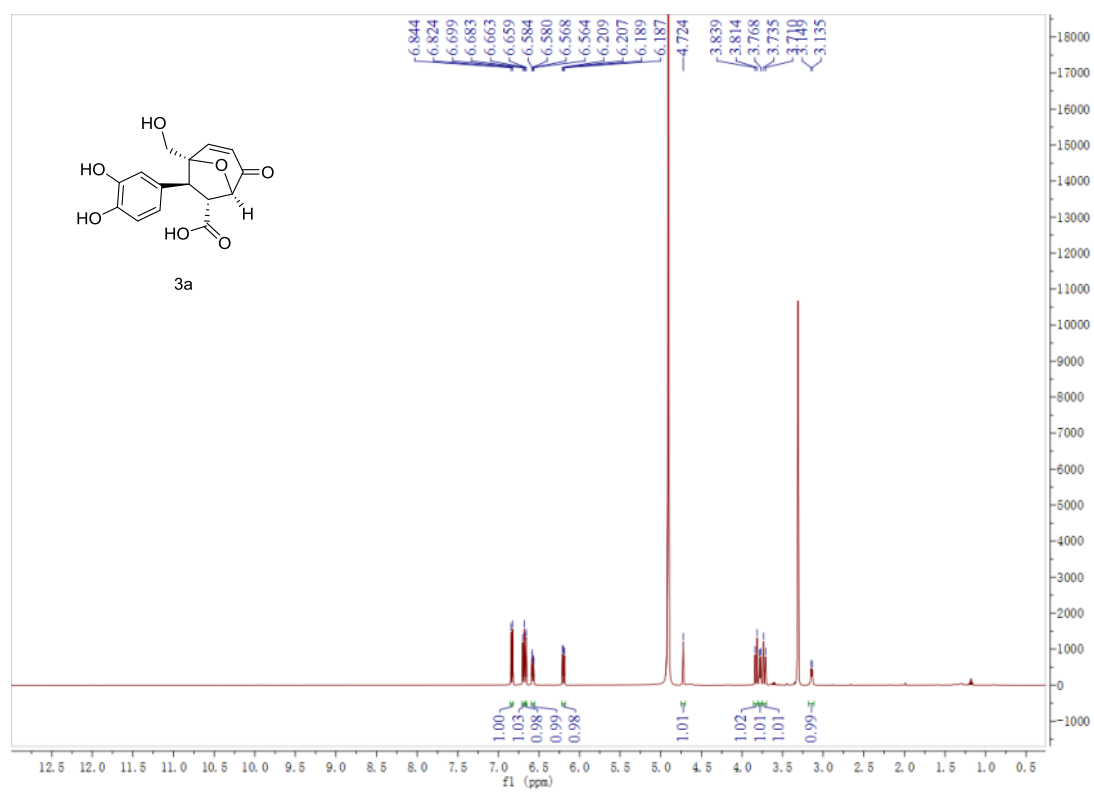


Figure 40. The ^1H NMR Spectrum of Compound **3a** in $\text{MeOH-}d_4$ (500 H_z)

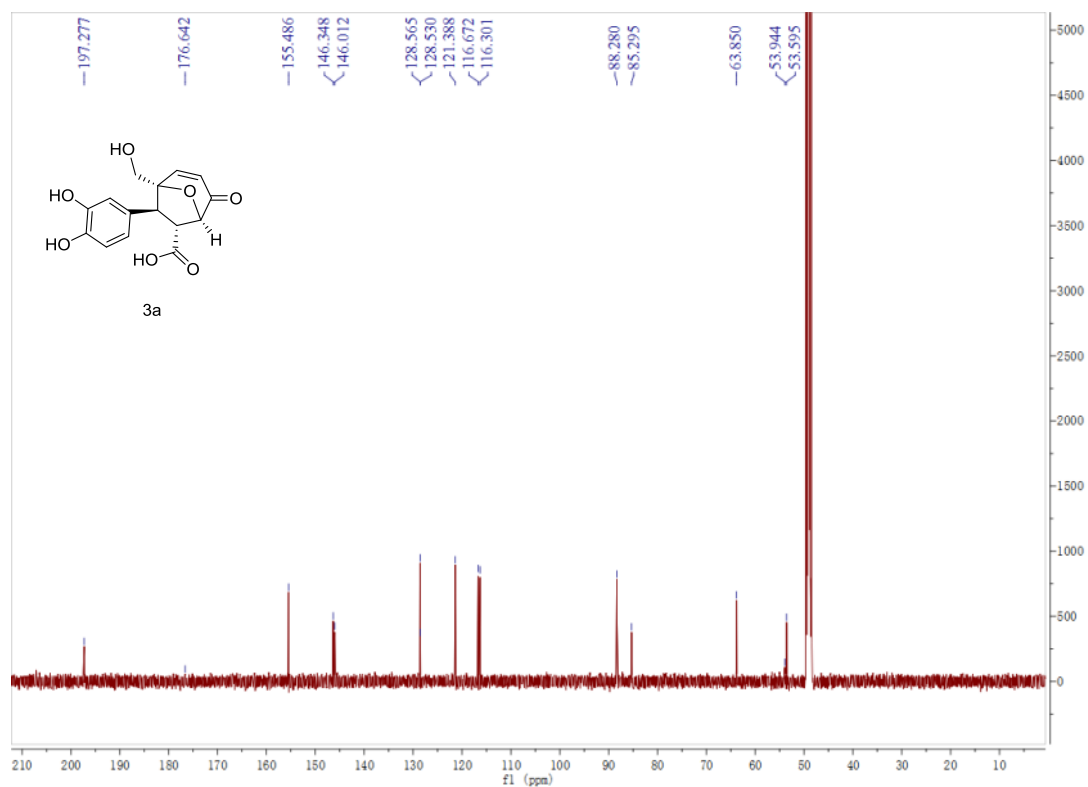


Figure 41. The ^{13}C NMR Spectrum of Compound **3a** in $\text{MeOH-}d_4$ (500 Hz)

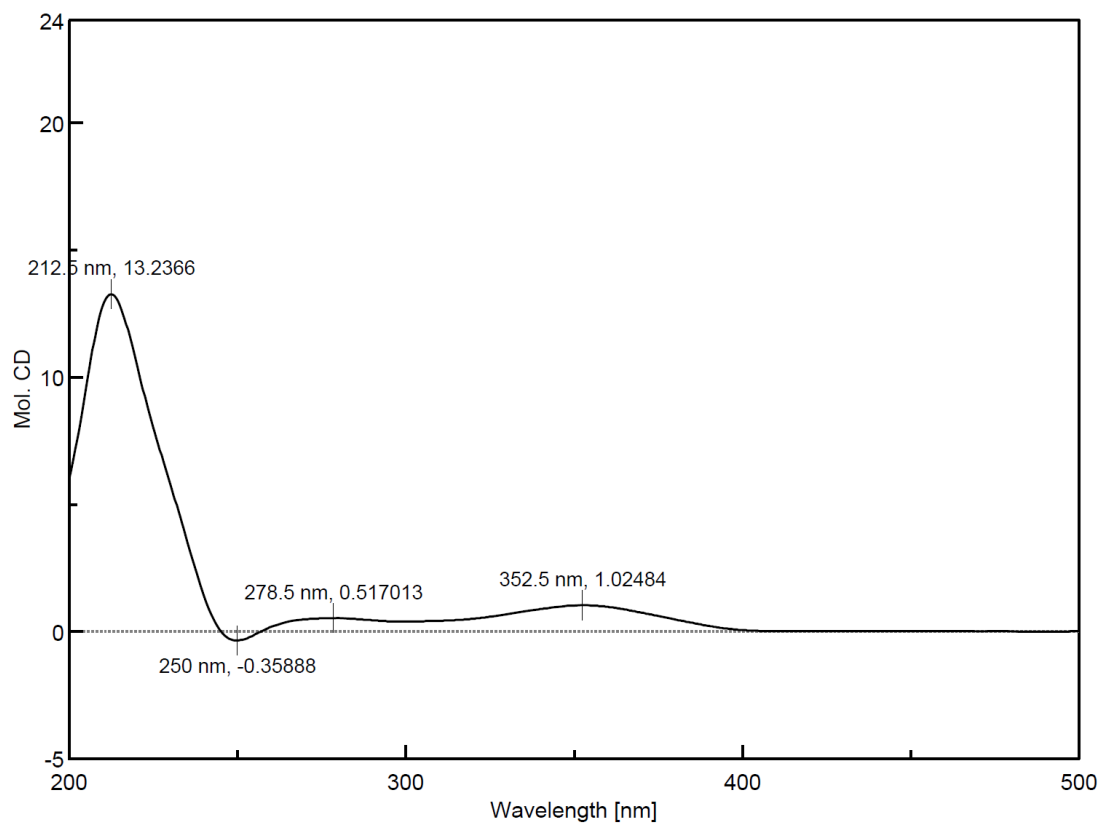
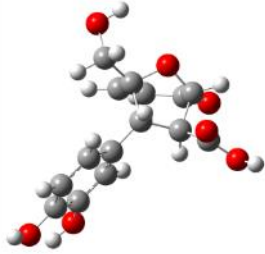
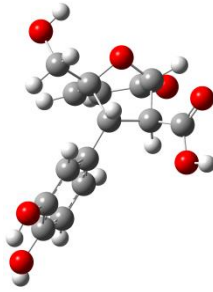
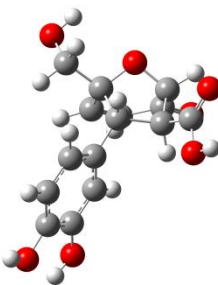
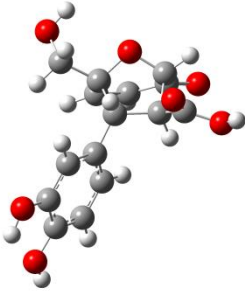
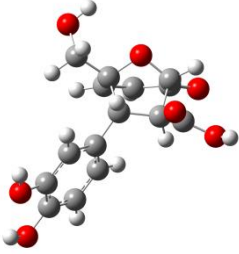


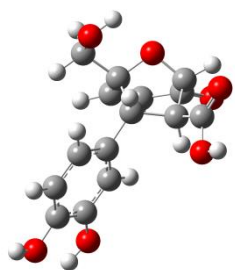
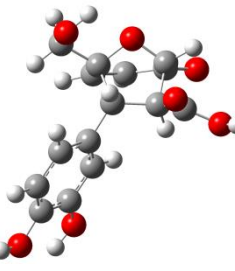
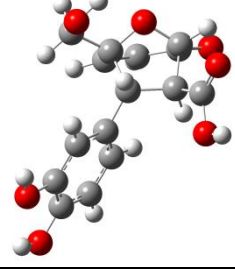
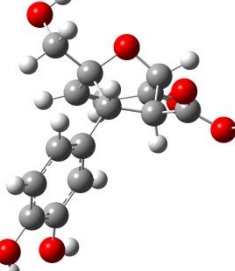
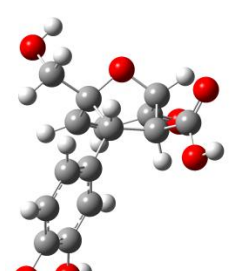
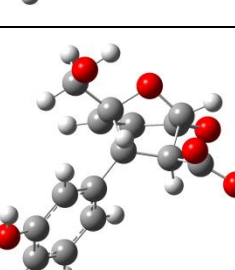
Figure 42. The ECD Spectrum of Compound **3a** in MeOH

ECD Calculation of (7''R, 8''S, 10''S, 14''S)-1a

Systematic conformational analyses of (7''R, 8''S, 10''S, 14''S)-**1a** were carried out via searching in the Discovery Studio (version 16.1.0.15350) using the MMFF94 force field. Conformers with Boltzmann distribution over 1% were chosen as the beginning for ECD calculations. Ground-state geometries were optimized at the B3LYP/6-311+G (d, p) level in gas phase by the Gaussian 09 program package (Gaussian Inc., Wallingford, CT, USA) and vibrational analysis were done to confirm these minima. All quantum computations were performed on an IBM cluster machine located at the High Performance Computing Center of Peking Union Medical College. The energies, oscillator strengths, and rotational strengths (velocity) of the first 50 electronic excitations were calculated using the TDDFT methodology at the B3LYP/6-311+G (d, p) level in methanol. The ECD spectra were simulated by the overlapping Gaussian function (half the bandwidth at 1/e peak height, 0.25 eV). The overall theoretical ECD spectra were obtained based on the Boltzmann weighting of each conformers. By comparison of the calculated and experimental ECD spectra, the configurations were resolved.

Table S1. 13 Conformers of (7''*R*, 8''*S*, 10''*S*, 14''*S*)-1a with Boltzmann Distribution over 1%.

No.	conformer	rel. E (kJ/mol)	Boltzmann Dist
1		0.00	0.279
2		2.35	0.108
3		2.46	0.103
4		2.65	0.096
5		3.10	0.080

6		3.58	0.066
7		4.32	0.049
8		4.90	0.039
9		4.93	0.038
10		5.48	0.031
11		5.53	0.030

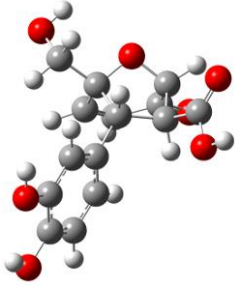
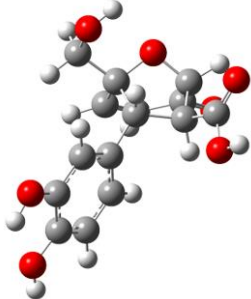
12		6.00	0.025
13		7.30	0.015

Table S2. Energies and Vibrational Analysis of (7''R, 8''S, 10''S, 14''S)-1a

Conformation	Energy (A.U.)	Energy (kcal/mol)	Boltzmann (%)	Number of imaginary frequencies
1	-1106.623446	-694599.6422292608	7.93	0
2	-1106.623143	-694599.370329774	5.01	0
3	-1106.623404	-694599.532164603	6.58	0
4	-1106.623262	-694599.522814704	6.48	0
5	-1106.623174	-694599.469539105	5.92	0
6	-1106.623818	-694599.903587772	12.33	0
7	-1106.623742	-694599.873655545	11.72	0
8	-1106.62356	-694599.696132966	8.68	0
9	-1106.62325	-694599.528713298	6.54	0
10	-1106.623236	-694599.429378465	5.53	0
11	-1106.623554	-694599.763966797	9.74	0
12	-1106.622998	-694599.284172651	4.33	0
13	-1106.623612	-694599.73152453	9.22	0

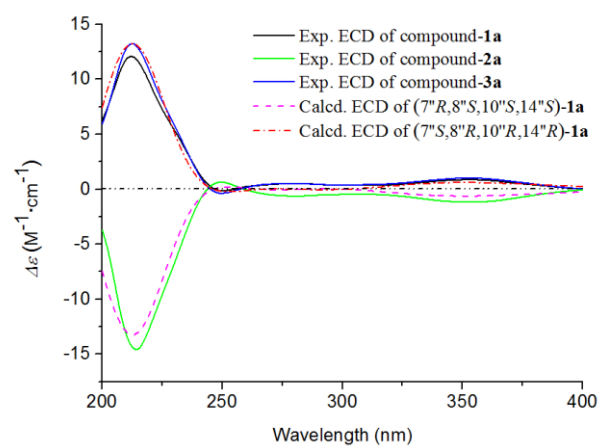


Figure 43. Calculated ECD spectra of (7''*S*, 8''*R*, 10''*R*, 14''*R*)-**1a** and (7''*R*, 8''*S*, 10''*S*, 14''*S*)-**1a** and the experimental ECD spectra of **1a**, **2a**, and **3a** in MeOH.