

Supporting Information

Neuroprotective azaphilones from a deep-sea derived fungus *Penicillium* sp. SCSIO41030

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^c University of Chinese Academy of Sciences, 19 Yuquan Road, Beijing 100049, China

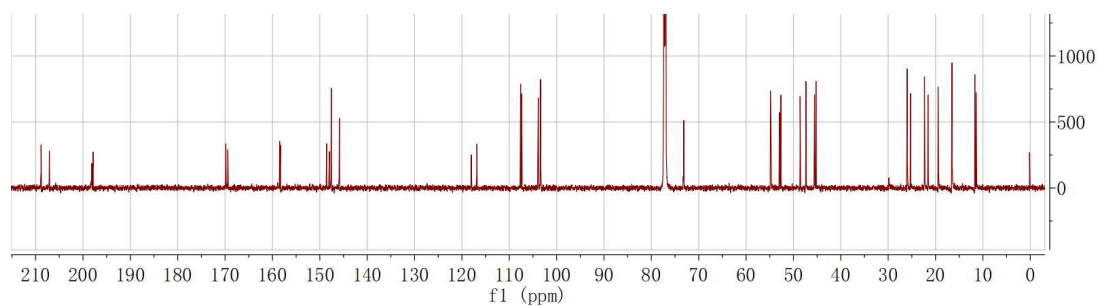
^d Sanya Institute of Marine Ecology and Engineering, Yazhou Scientific Bay, Sanya 572000, China

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Figure S1. The ^{13}C NMR spectrum of **P1** in Chloroform-*d* and its chiral HPLC profile.



(Daicel Chiralpak IC, 4.6×250 mm, $5\mu\text{m}$) using ethanol/n-hexane (v/v: 55:65)

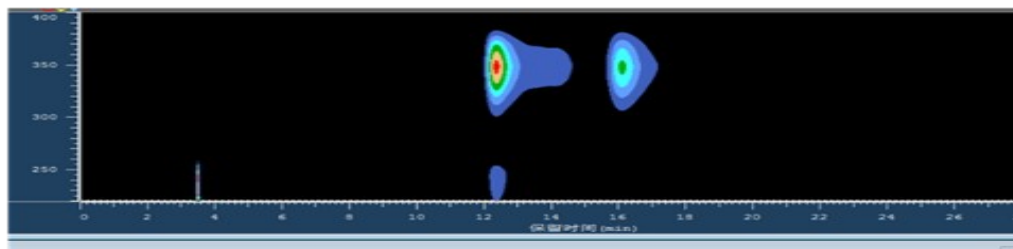


Figure S2. The ^1H NMR spectrum of **1** in Chloroform-*d*.

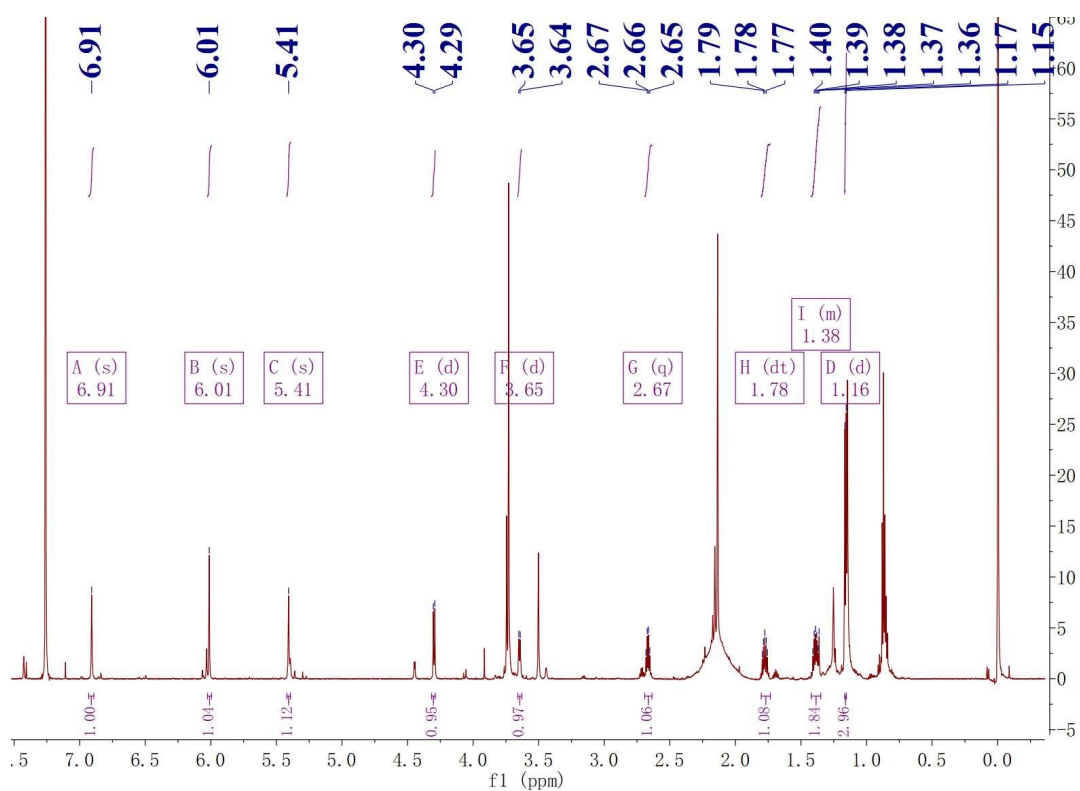


Figure S3. The ^{13}C NMR spectrum of **1** in Chloroform-*d*.

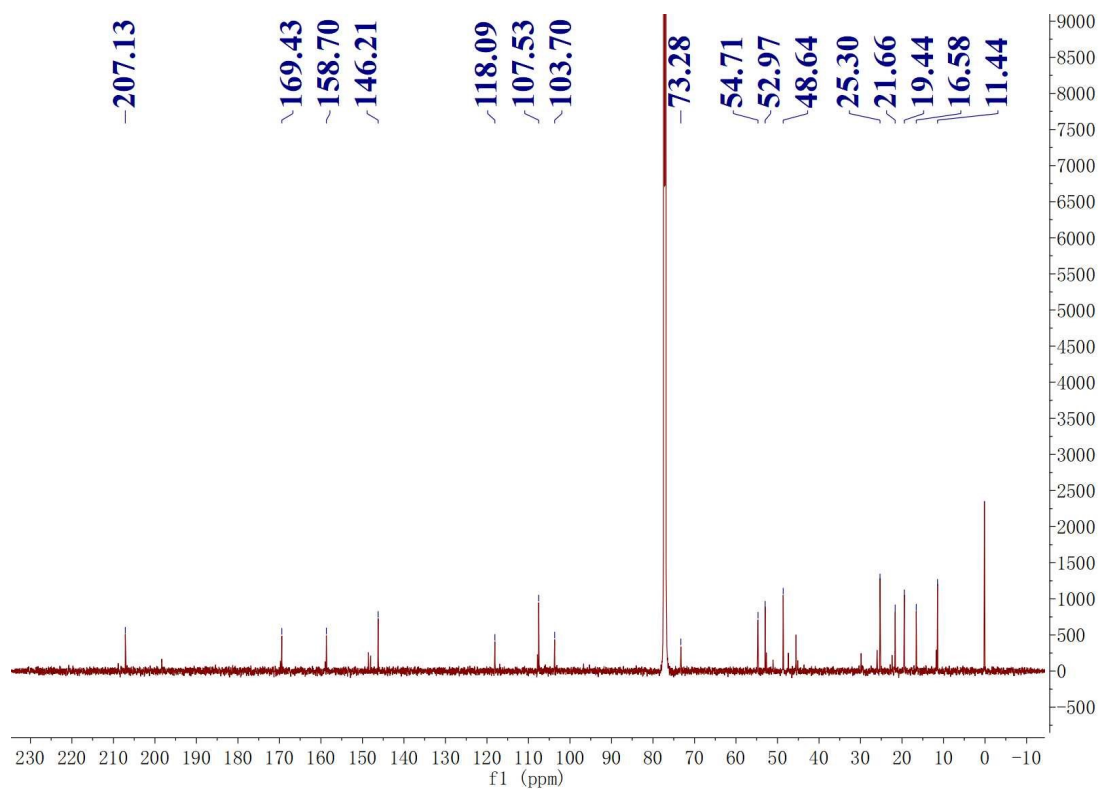


Figure S4. The HSQC spectrum of **1** in Chloroform-*d*.

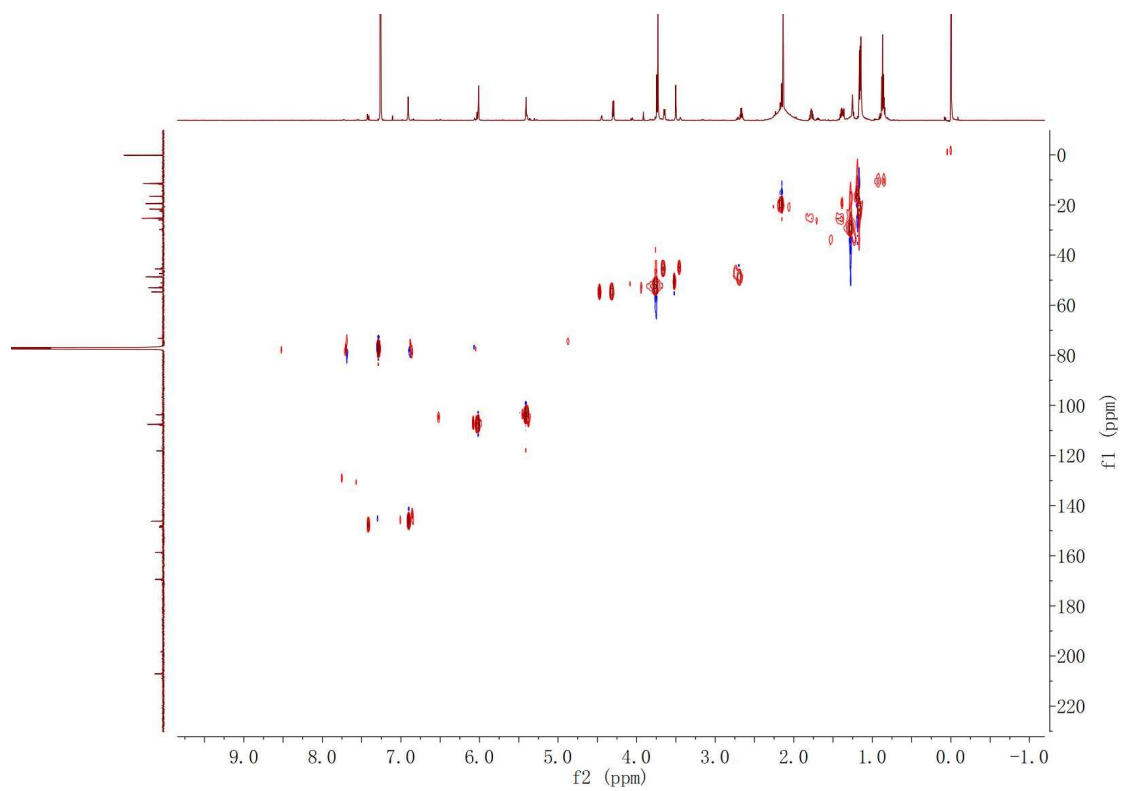


Figure S5. The HMBC spectrum of **1** in Chloroform-*d*.

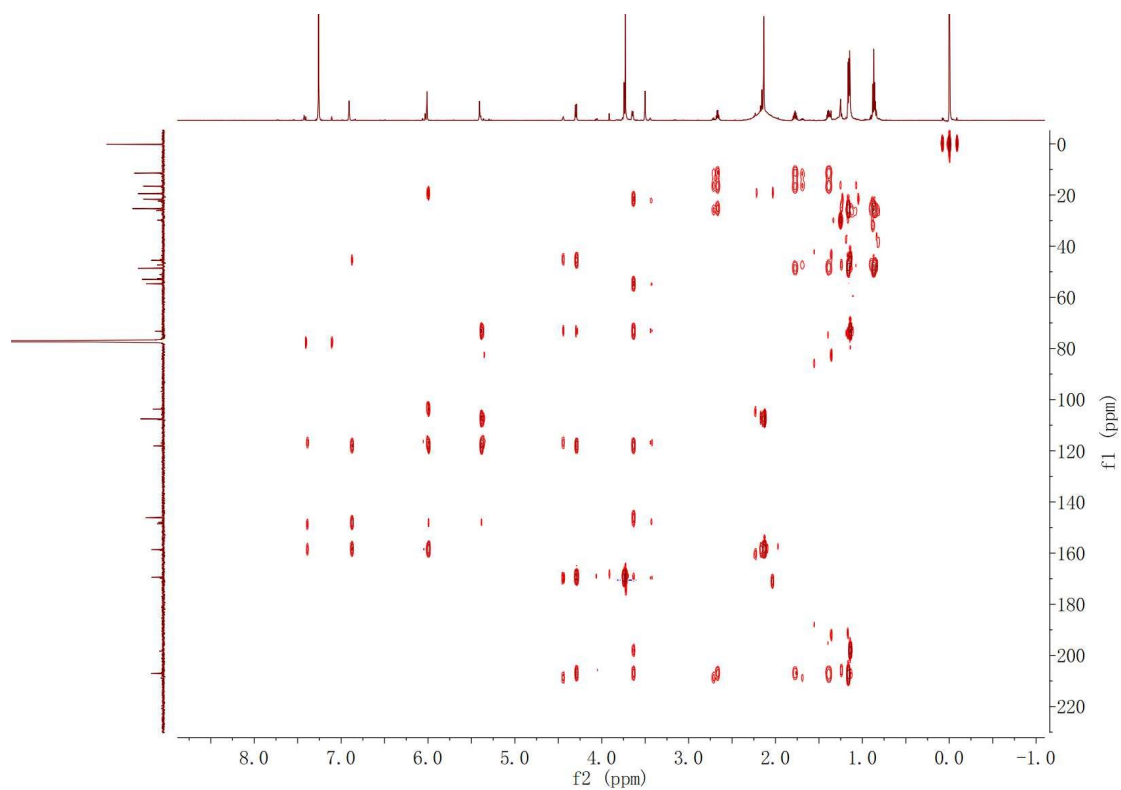


Figure S6. The COSY spectrum of **1** in Chloroform-*d*.

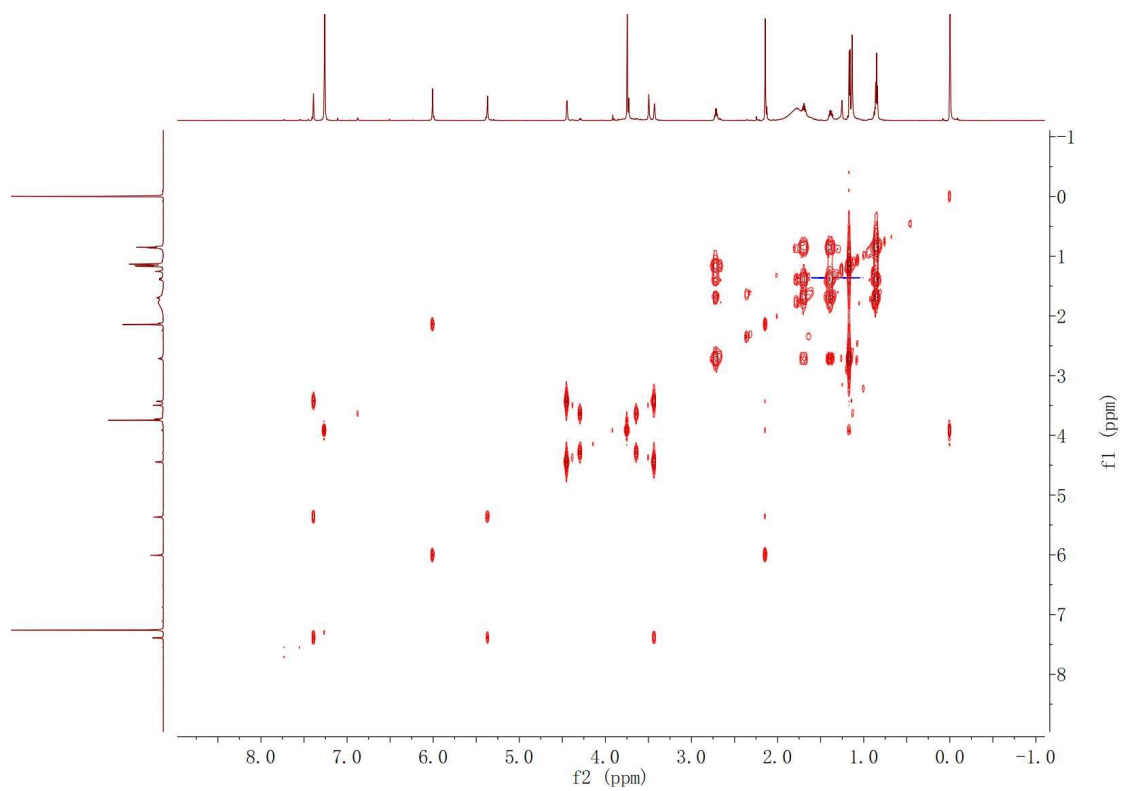


Figure S7. The UV spectrum of **1** in MeOH

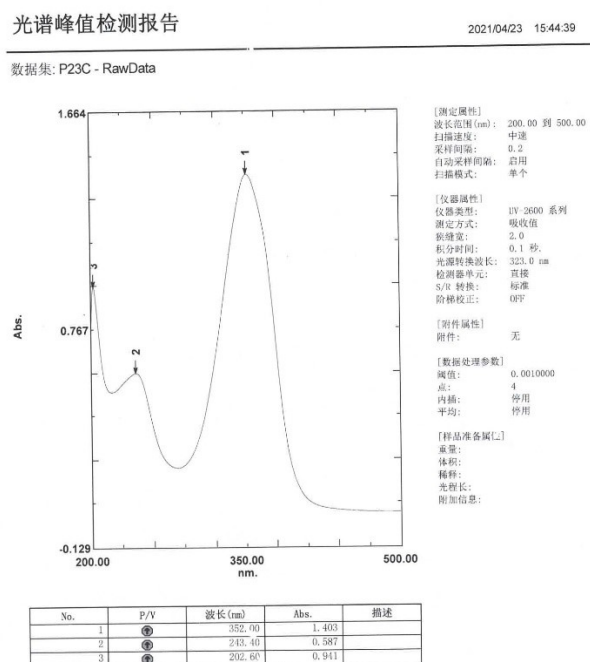


Figure S8. The IR spectrum of **1**

IR Spectrum report

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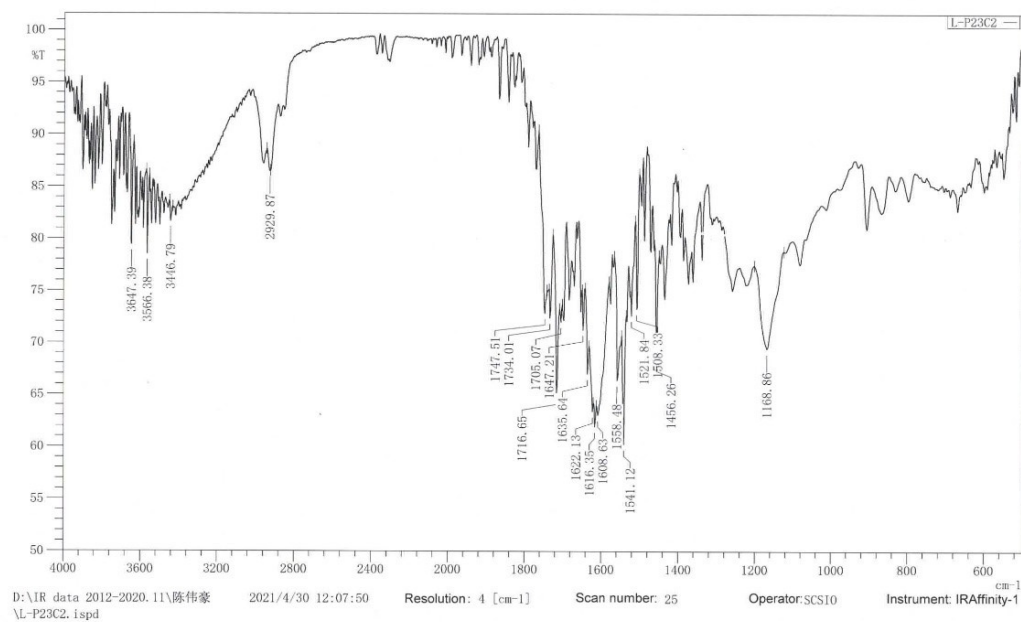
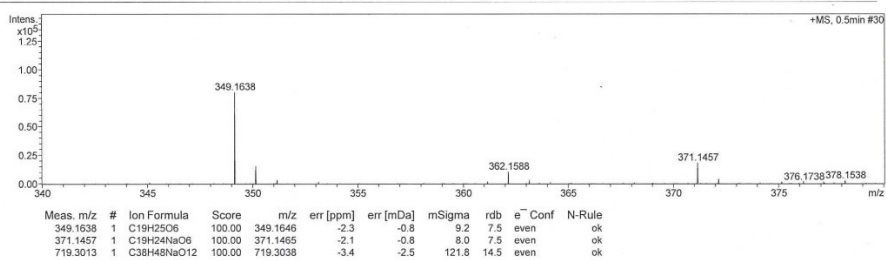


Figure S9. The HRESIMS spectrum of 1

Mass Spectrum SmartFormula Report

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Comment					

Acquisition Parameter					
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		Set Corona	0 nA	Set APCI Heater	0 °C



chenweihao_P23A_pos_72_01_10410.d
 Bruker Compass DataAnalysis 4.1 printed: 4/8/2021 2:51:07 PM by: SCSIO Page 1 of 1

Figure S10. The ¹H NMR spectrum of **2** in Chloroform-*d*.

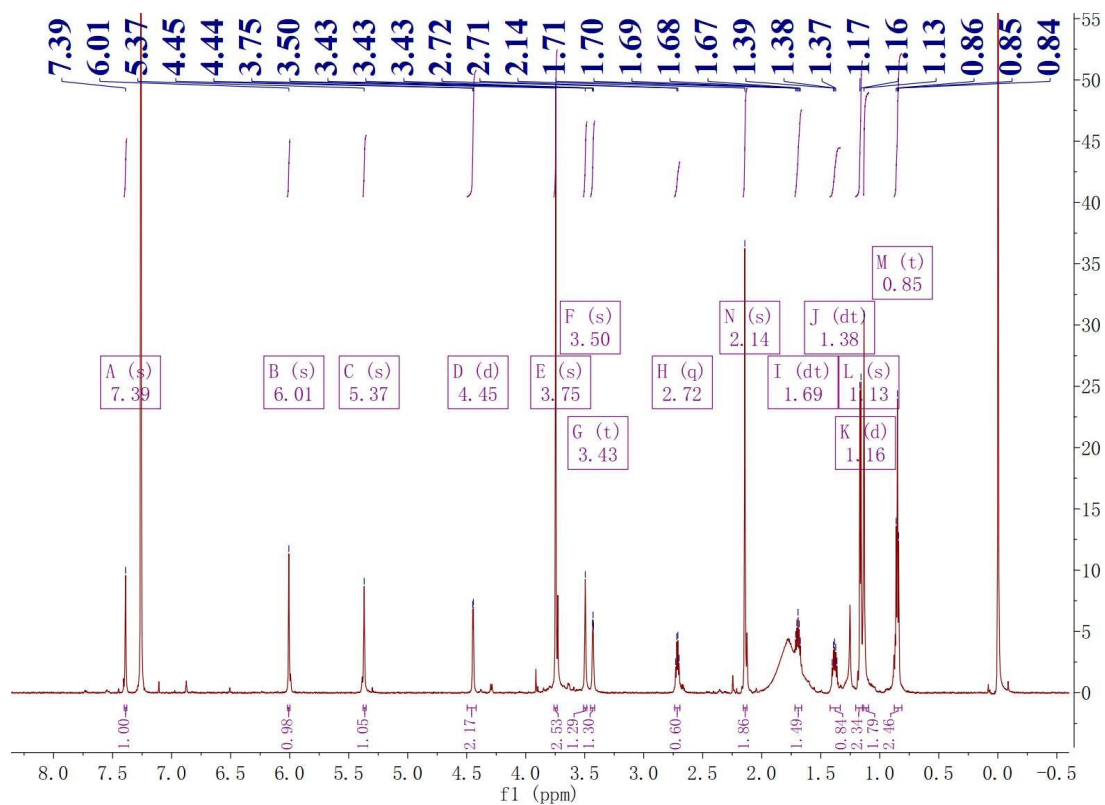


Figure S11. The ^{13}C NMR spectrum of **2** in Chloroform-*d*.

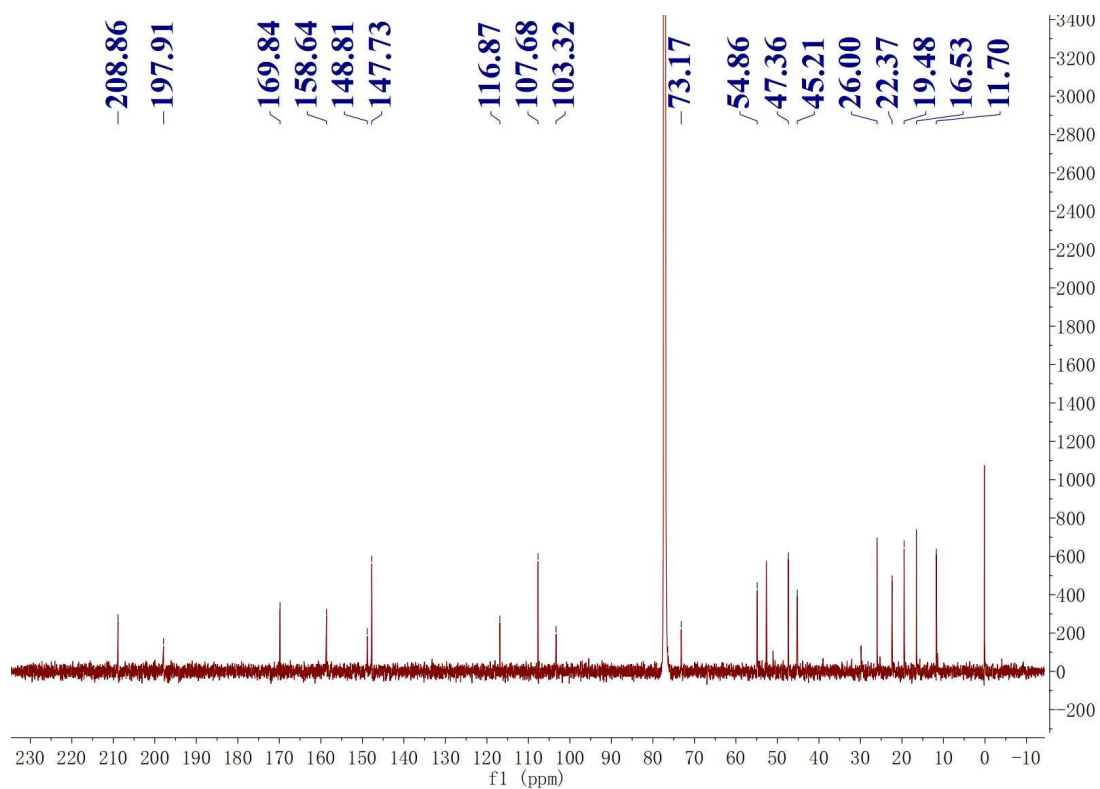


Figure S12. The HSQC NMR spectrum of **2** in Chloroform-*d*.

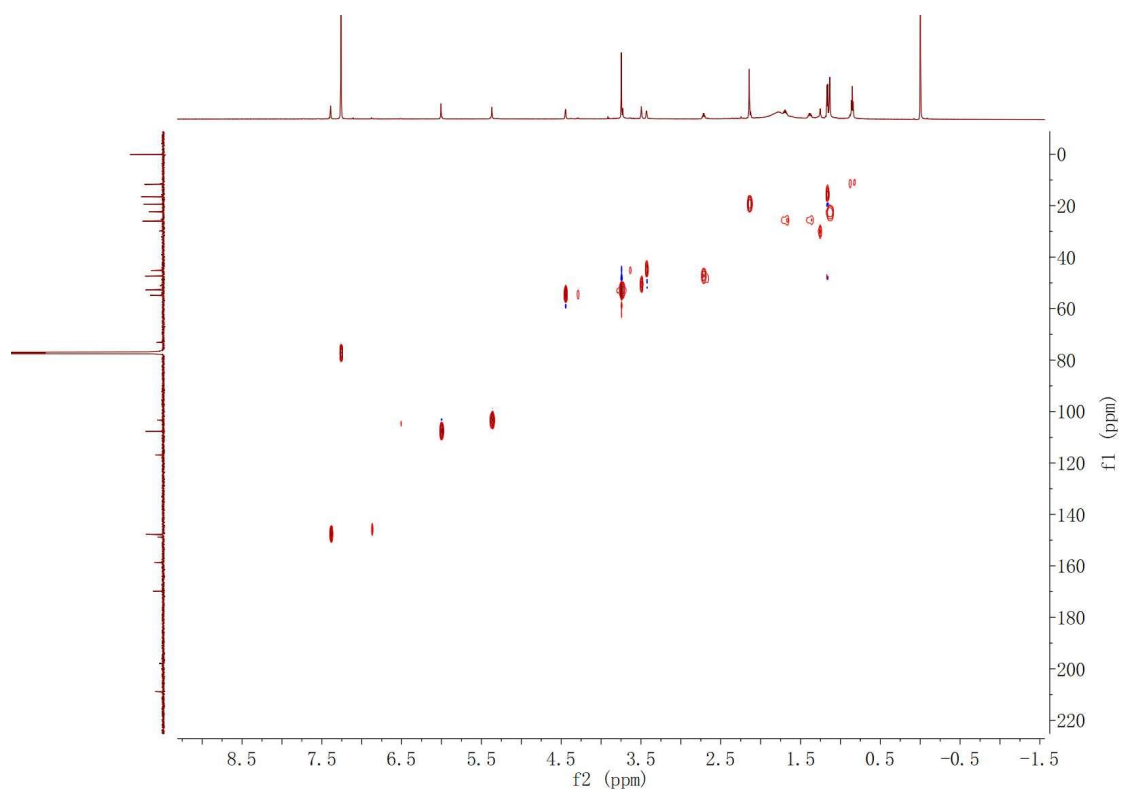


Figure S13. The HMBC NMR spectrum of **2** in Chloroform-*d*.

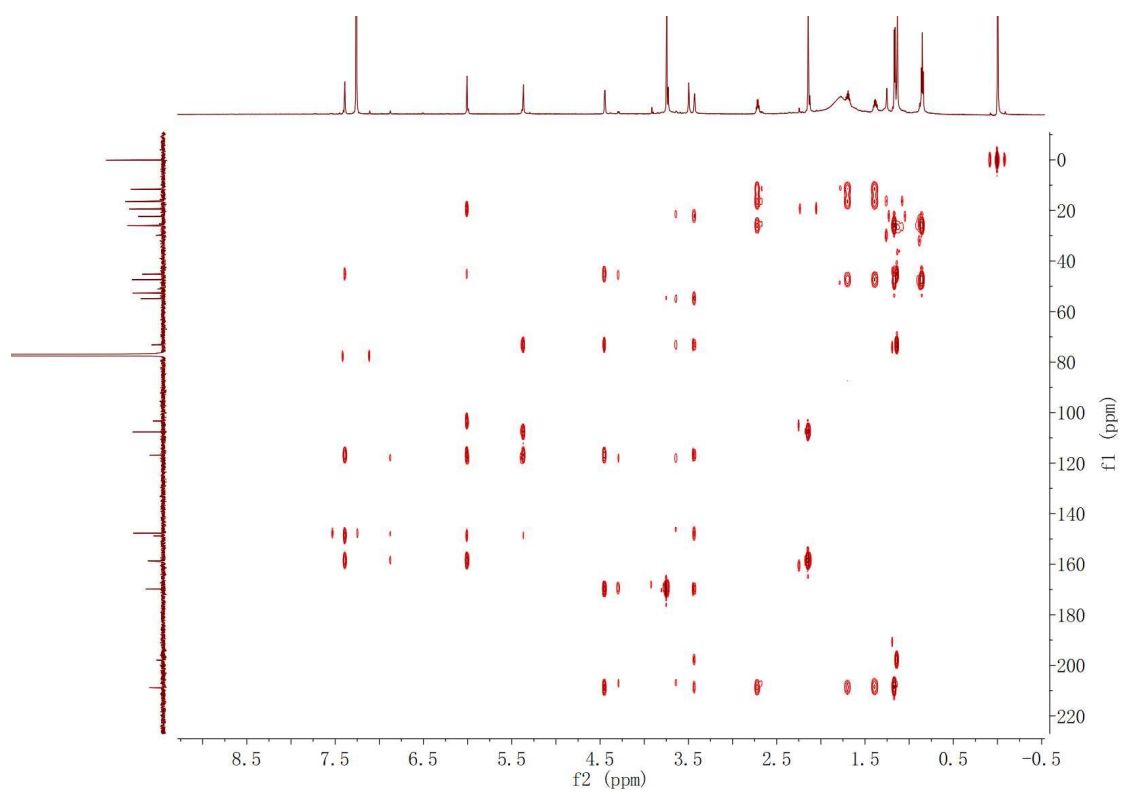


Figure S14. The COSY NMR spectrum of **2** in Chloroform-*d*.

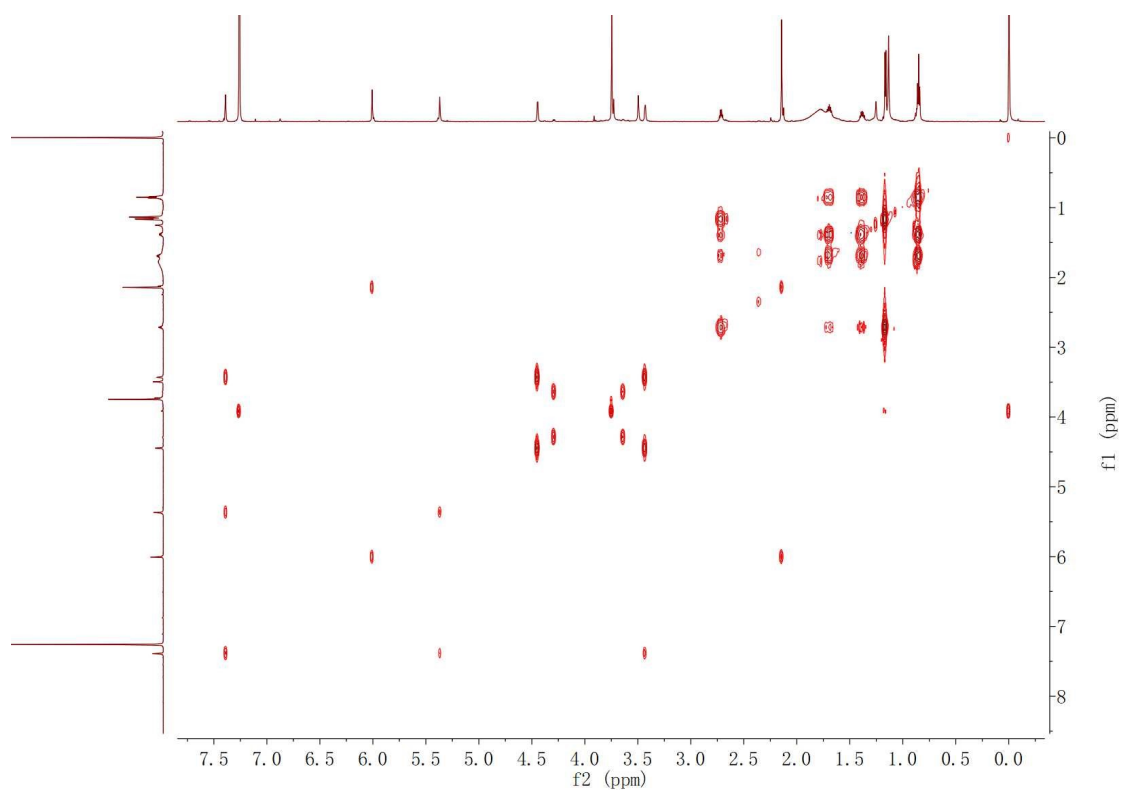


Figure S15. The NOESY spectrum of **2** in Chloroform- d_6 .

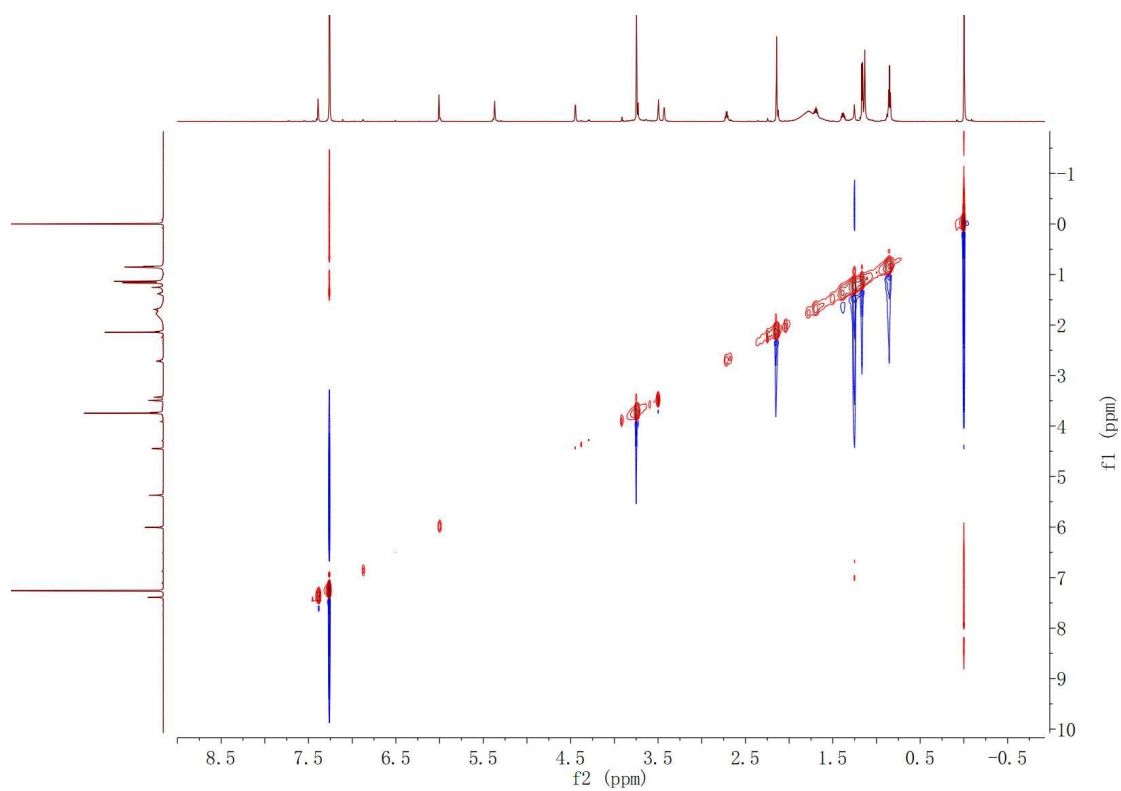


Figure S16. The UV spectrum of **2** in MeOH.

数据集: P23A - RawData

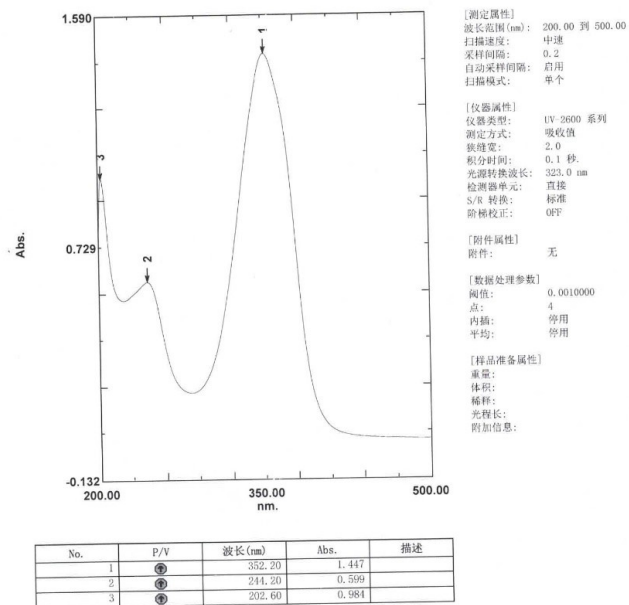


Figure S17. The IR spectrum of 2.

IR Spectrum report

SHIMADZU

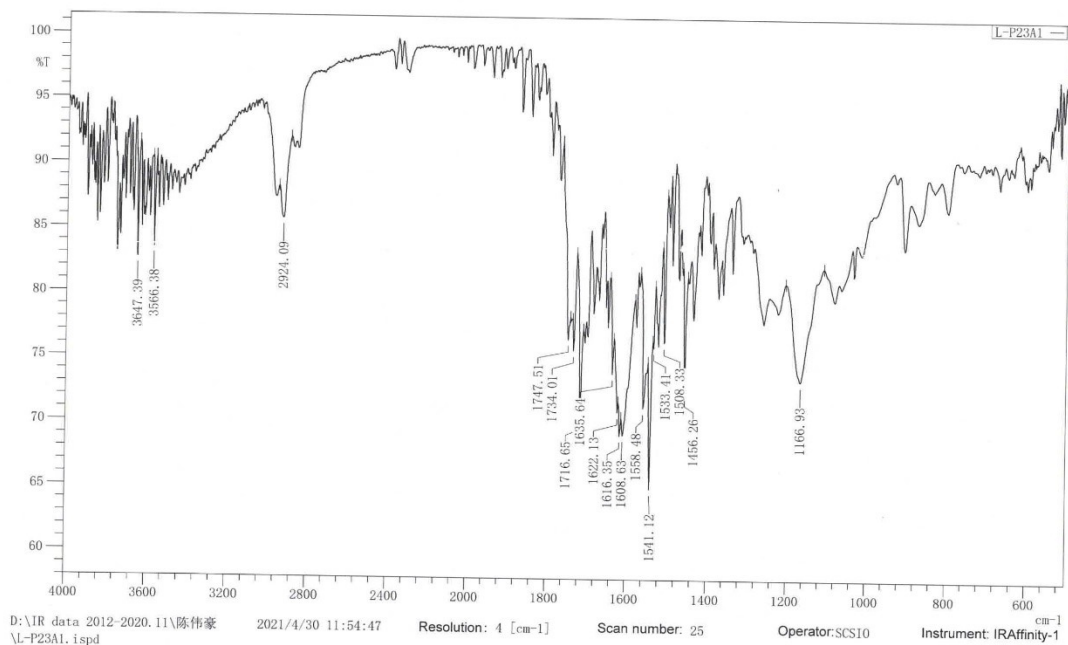
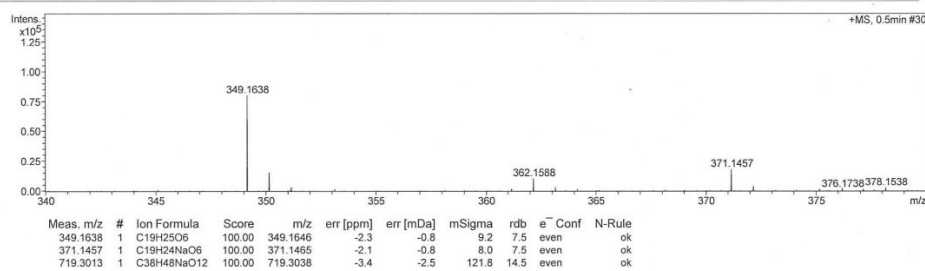


Figure S18. The HRESIMS spectrum of 2

Mass Spectrum SmartFormula Report

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Sample Name	chenweihao_P23A_pos	Instrument	maxis
Comment			255552.00029

Acquisition Parameter					
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chenweihao_P23A_pos_72_01_10410.d
Bruker Compass DataAnalysis 4.1

printed: 4/8/2021 2:51:07 PM

by: SCSIO

Page 1 of 1

Figure S19. The ¹H NMR spectrum of **3** in DMSO-*d*₆.

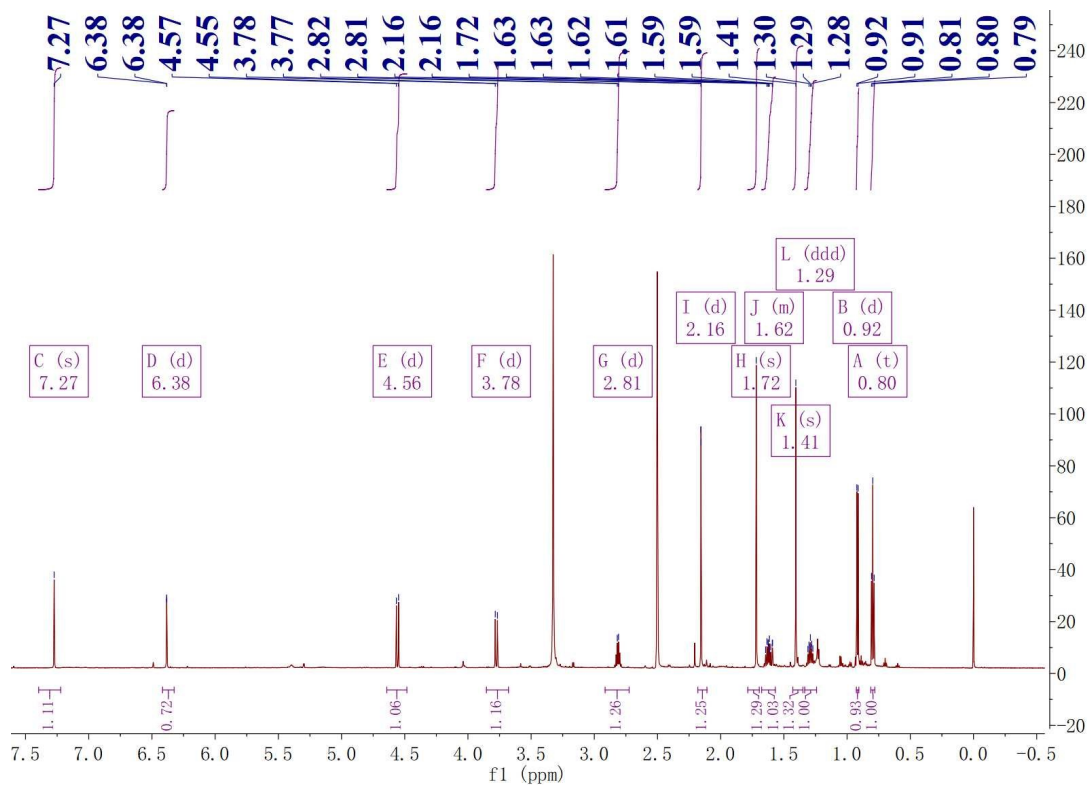


Figure S20. The ^{13}C NMR spectrum of **3** in $\text{DMSO-}d_6$.

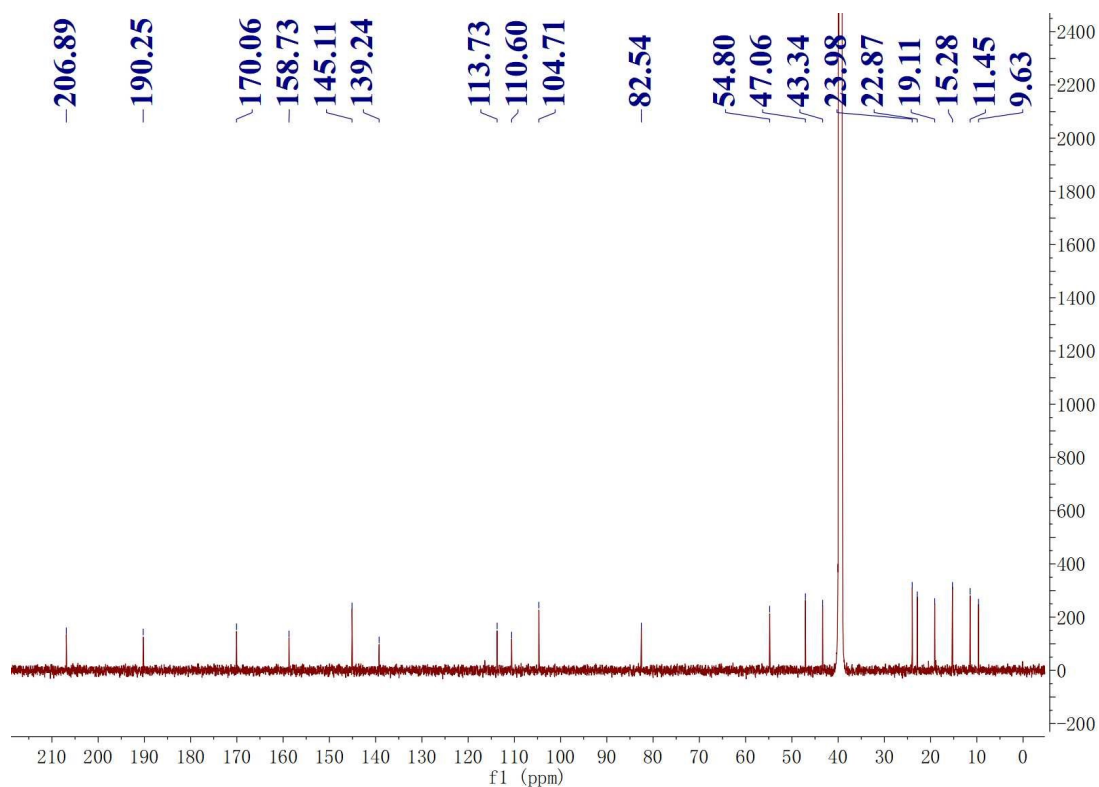


Figure S21. The HSQC NMR spectrum of **3** in $\text{DMSO-}d_6$.

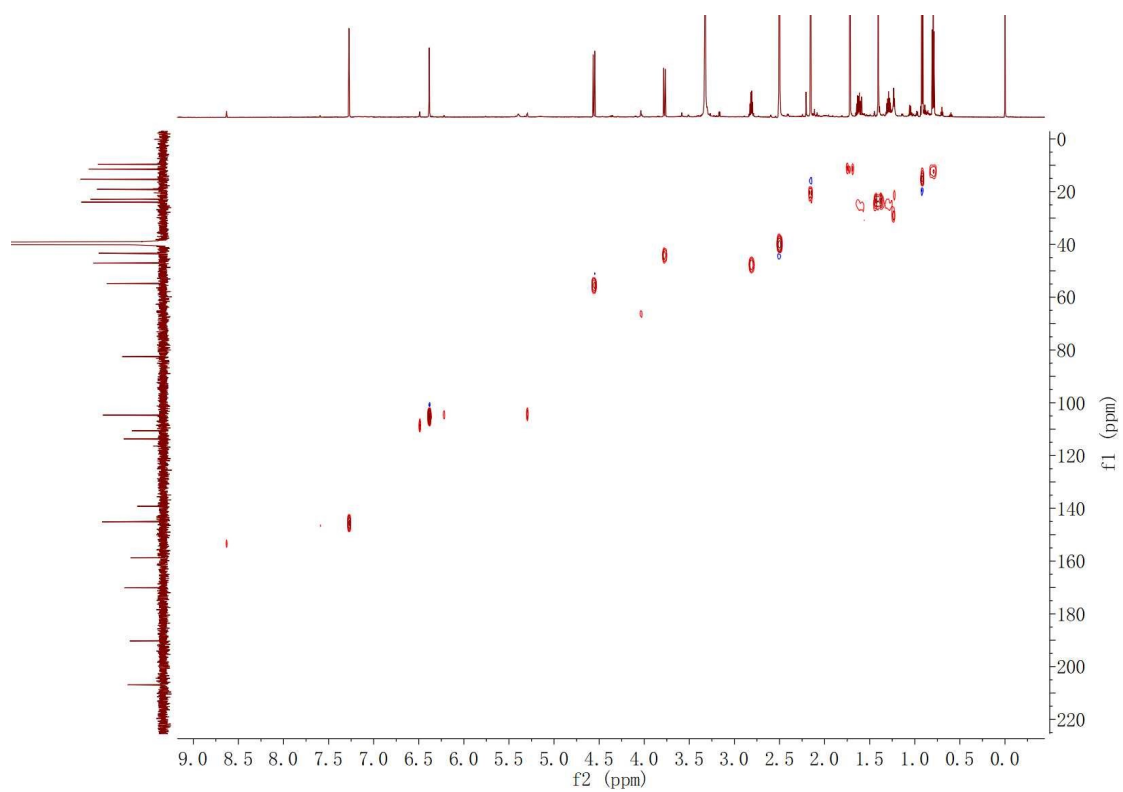


Figure S22. The HMBC NMR spectrum of **3** in DMSO- d_6 .

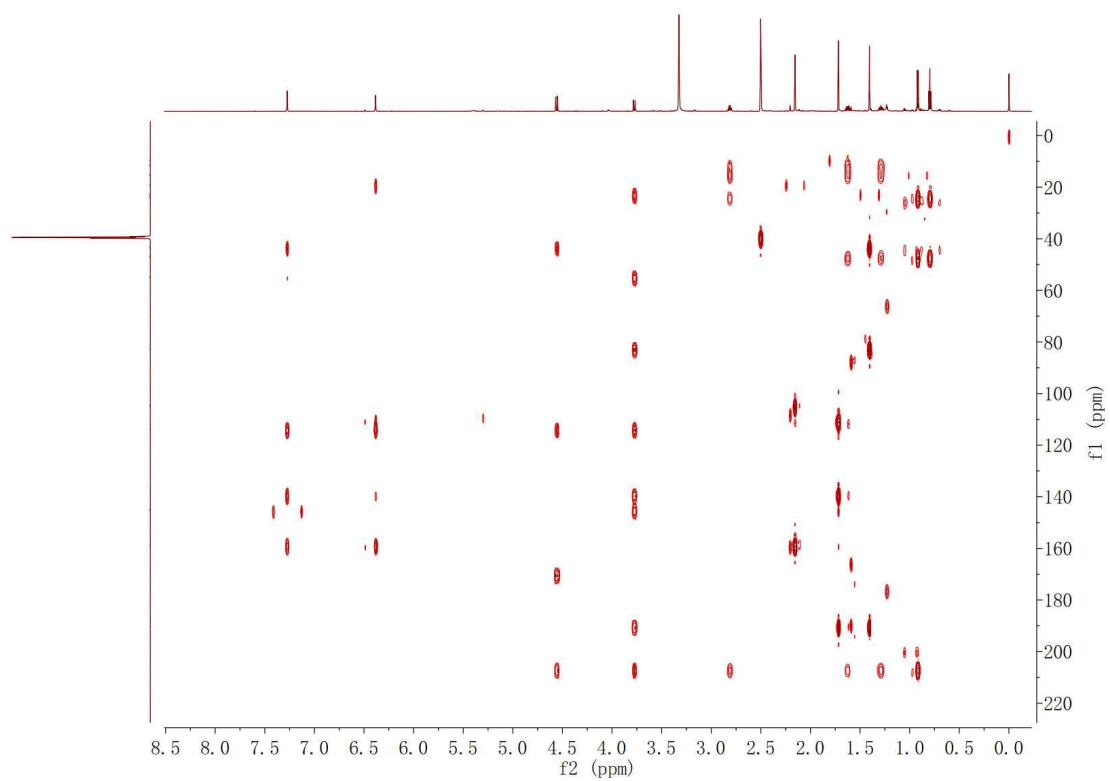


Figure S23. The COSY NMR spectrum of **3** in DMSO- d_6 .

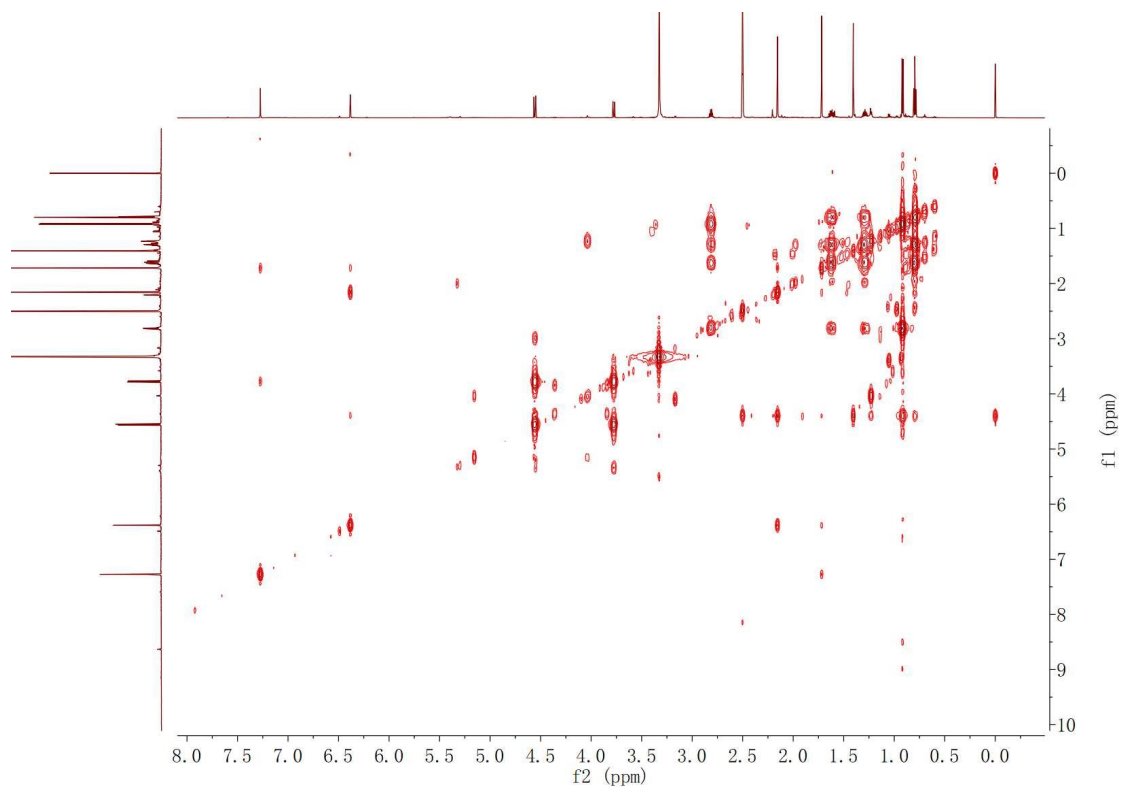


Figure S24. The NOESY spectrum of **3** in DMSO- d_6 .

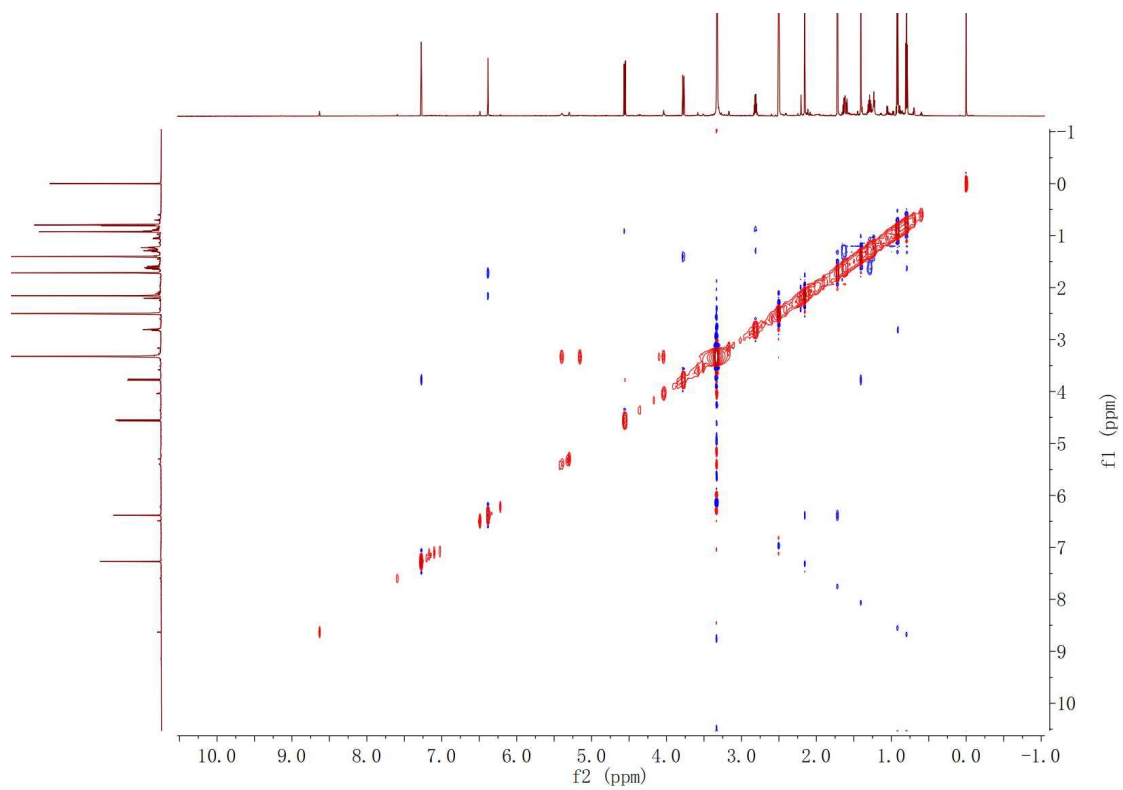
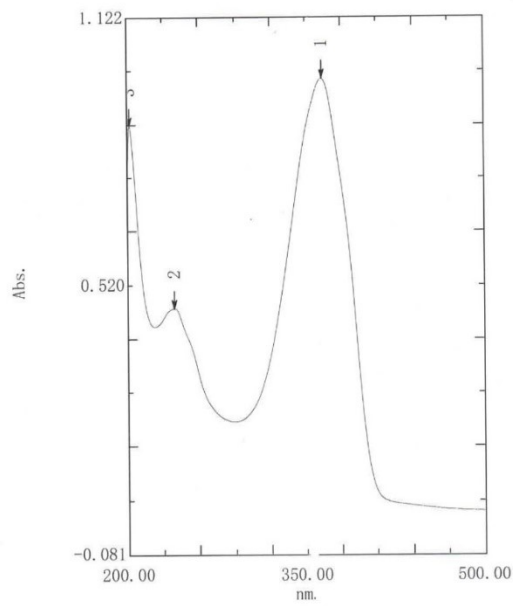


Figure S25. The UV spectrum of **3** in MeOH.

数据集: L-P6 - RawData



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1	①	363.80	0.984	
2	②	239.20	0.468	
3	③	201.80	0.877	

Figure S26. The HRESIMS spectrum of **3**

Mass Spectrum SmartFormula Report

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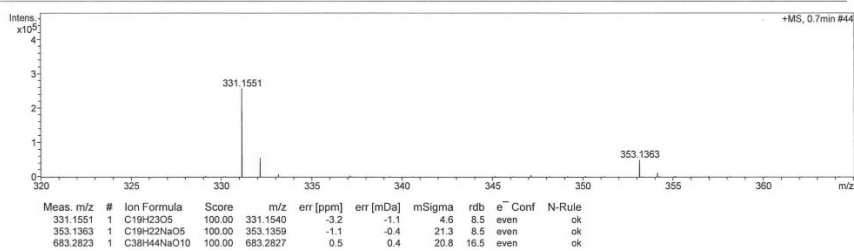


Figure S27. The ¹H NMR spectrum of **4** in DMSO-*d*₆.

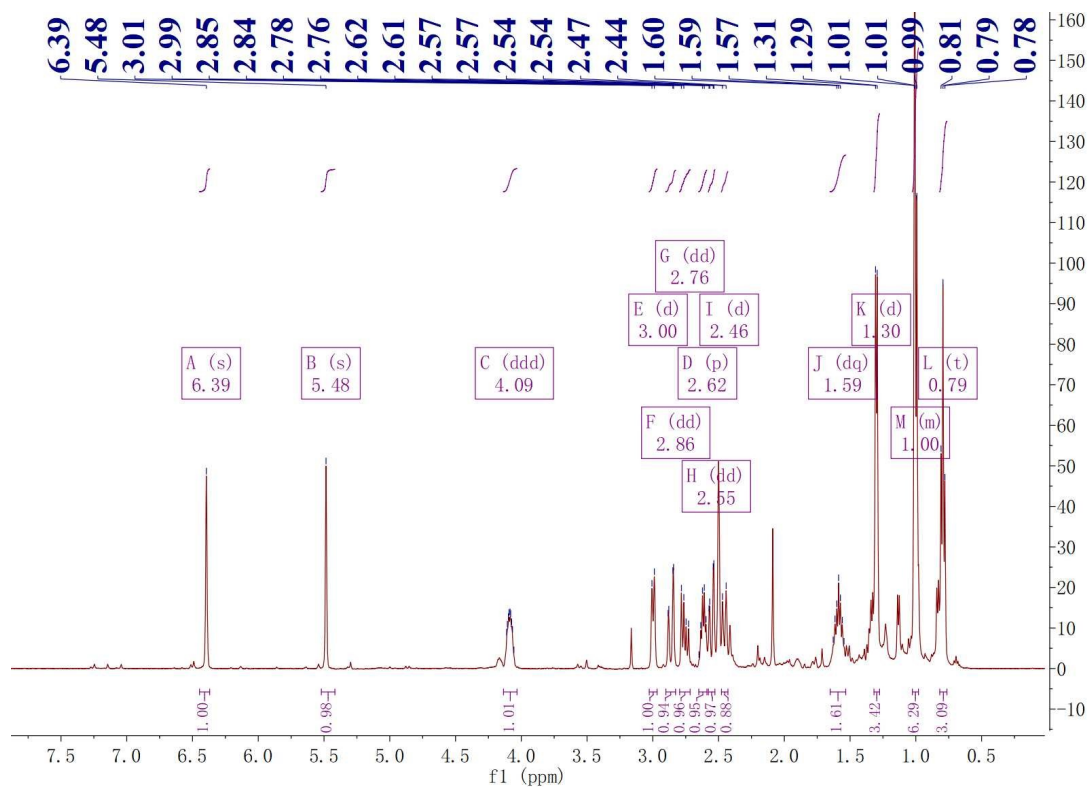


Figure S28. The ^{13}C NMR spectrum of **4** in $\text{DMSO-}d_6$.

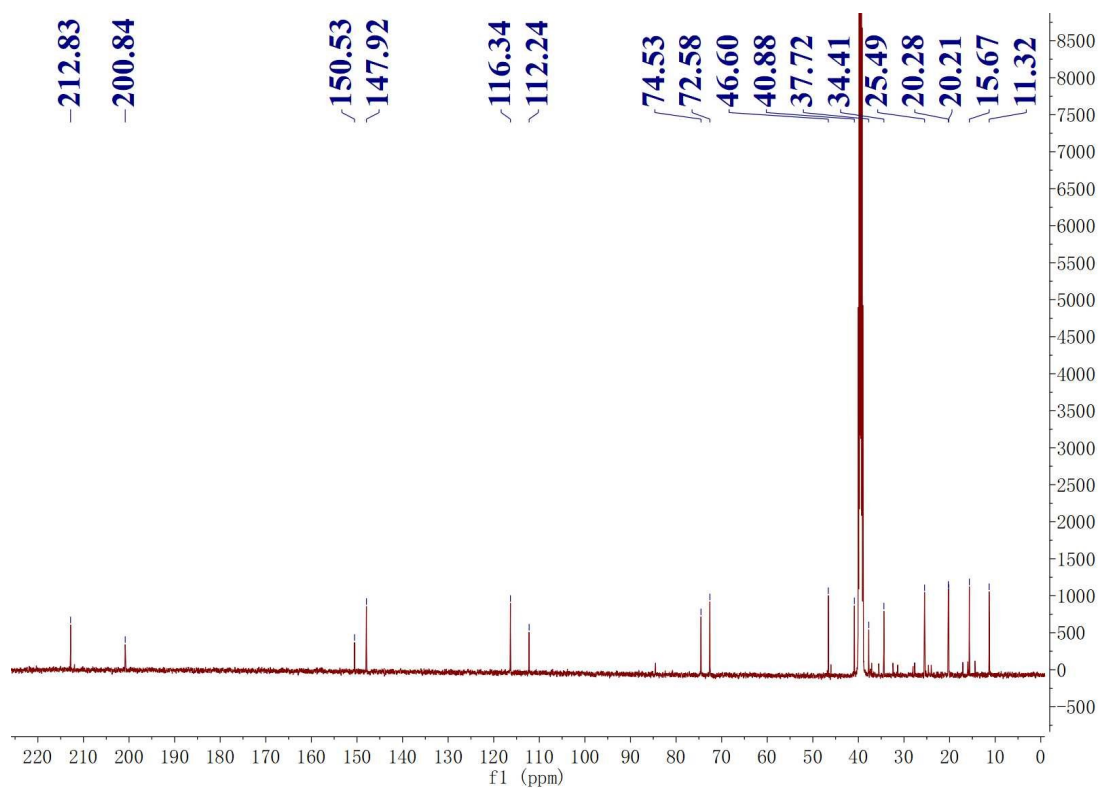


Figure S29. The HSQC NMR spectrum of **4** in DMSO- d_6 .

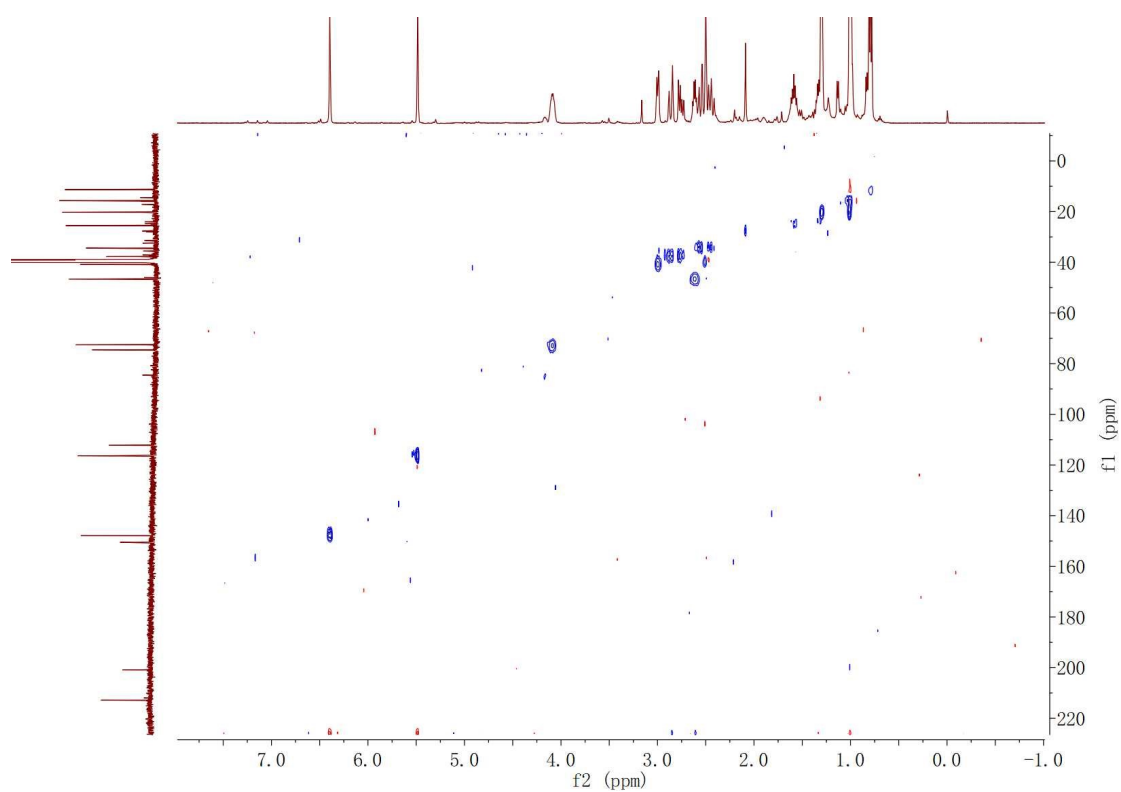


Figure S30. The HMBC NMR spectrum of **4** in DMSO- d_6 .

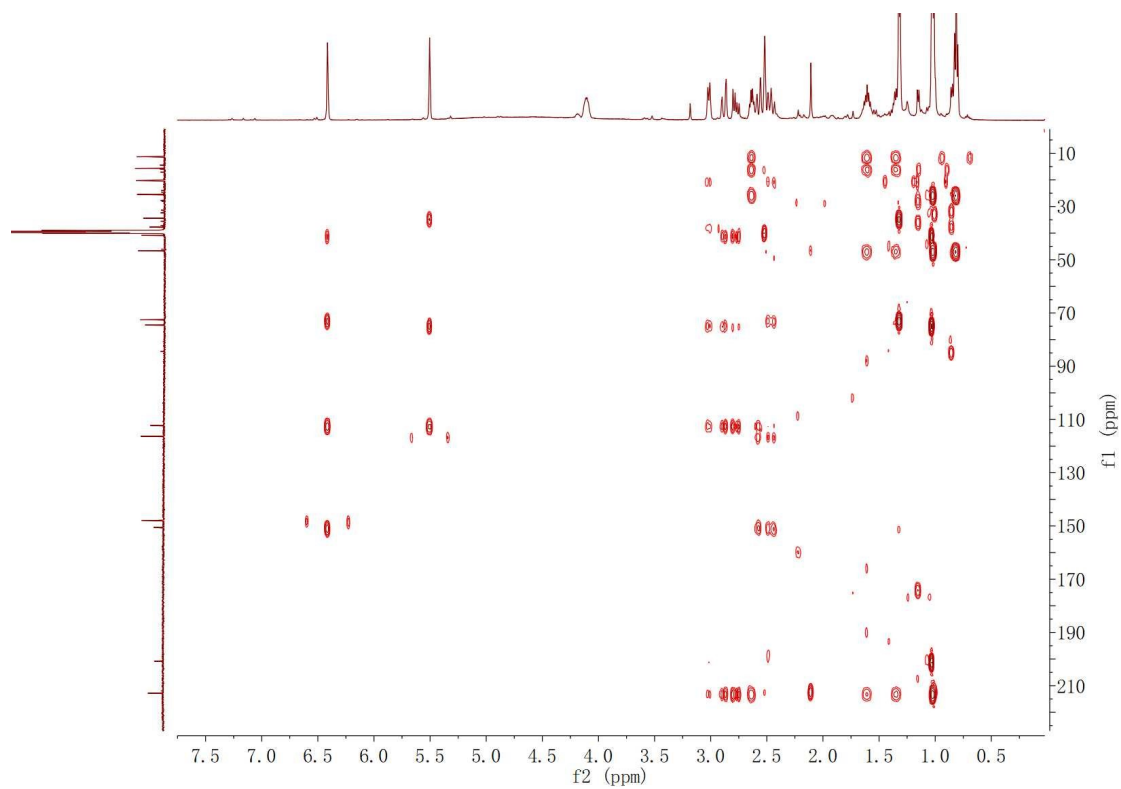


Figure S31. The COSY NMR spectrum of **4** in DMSO- d_6 .

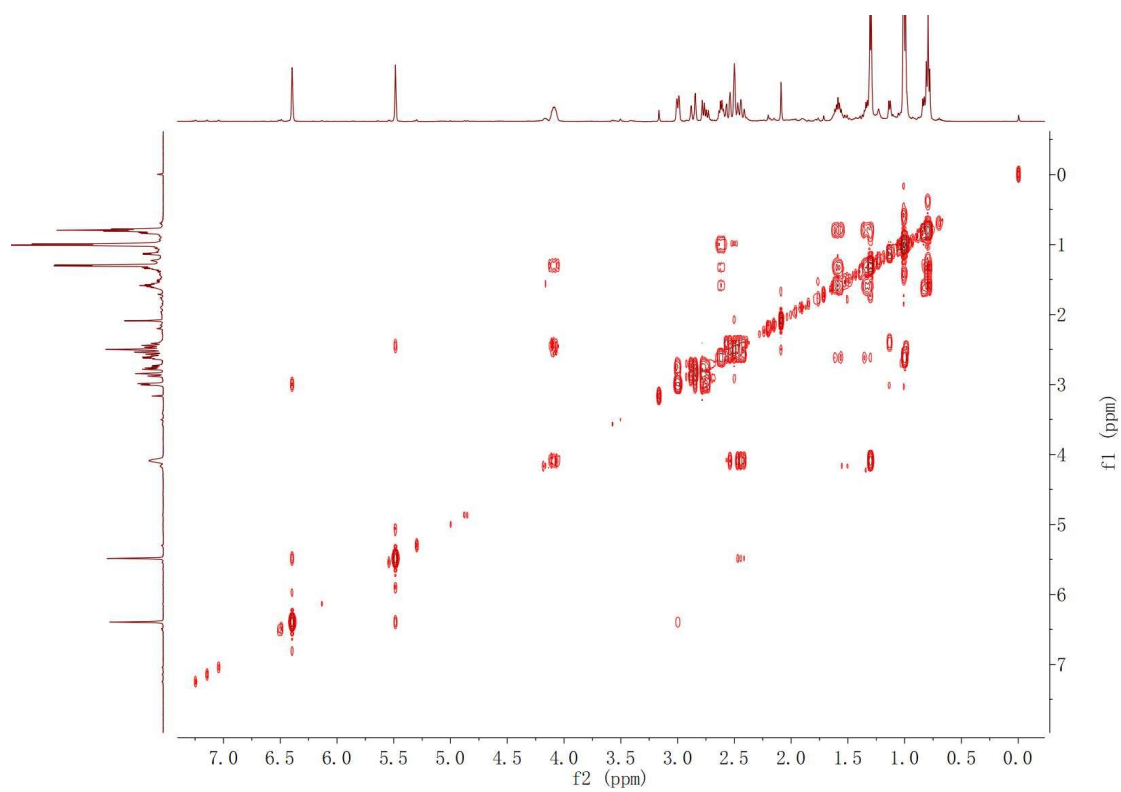


Figure S32. The NOESY spectrum of **4** in DMSO-*d*₆.

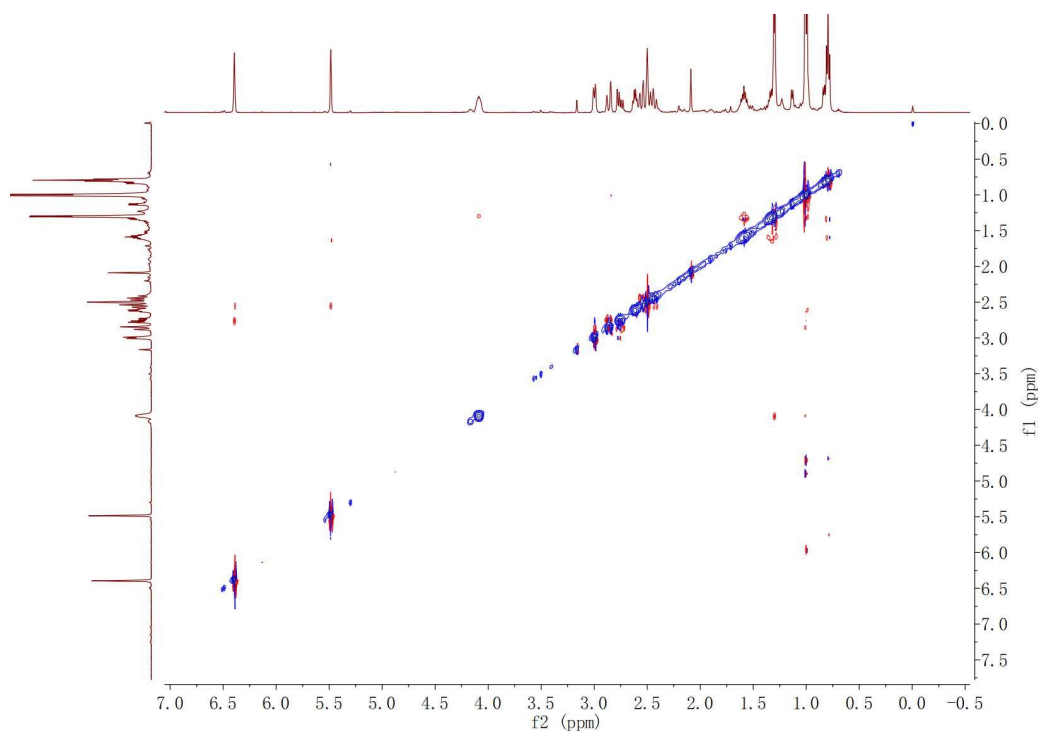
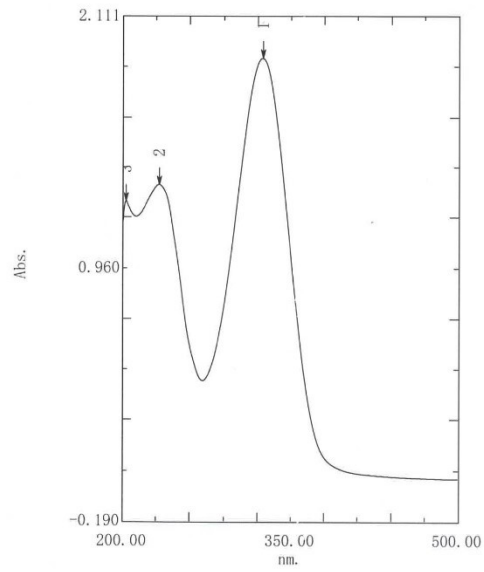


Figure S33. The UV spectrum of **4** in MeOH.

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 S/R 转换: 标准
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3	●	202.80	1.264	

Figure S34. The HRESIMS spectrum of 4.

Mass Spectrum SmartFormula Report

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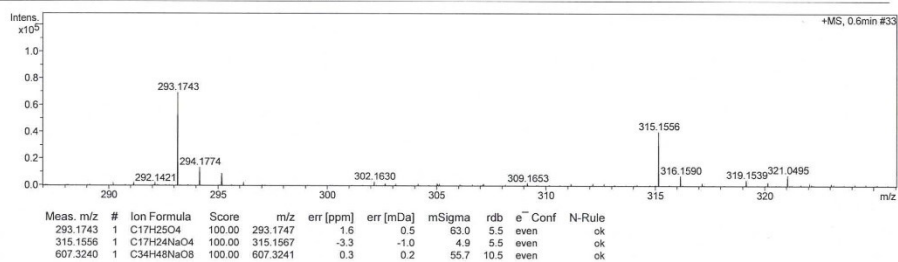


Figure S35. The ¹H NMR spectrum of **5** in DMSO-*d*₆.

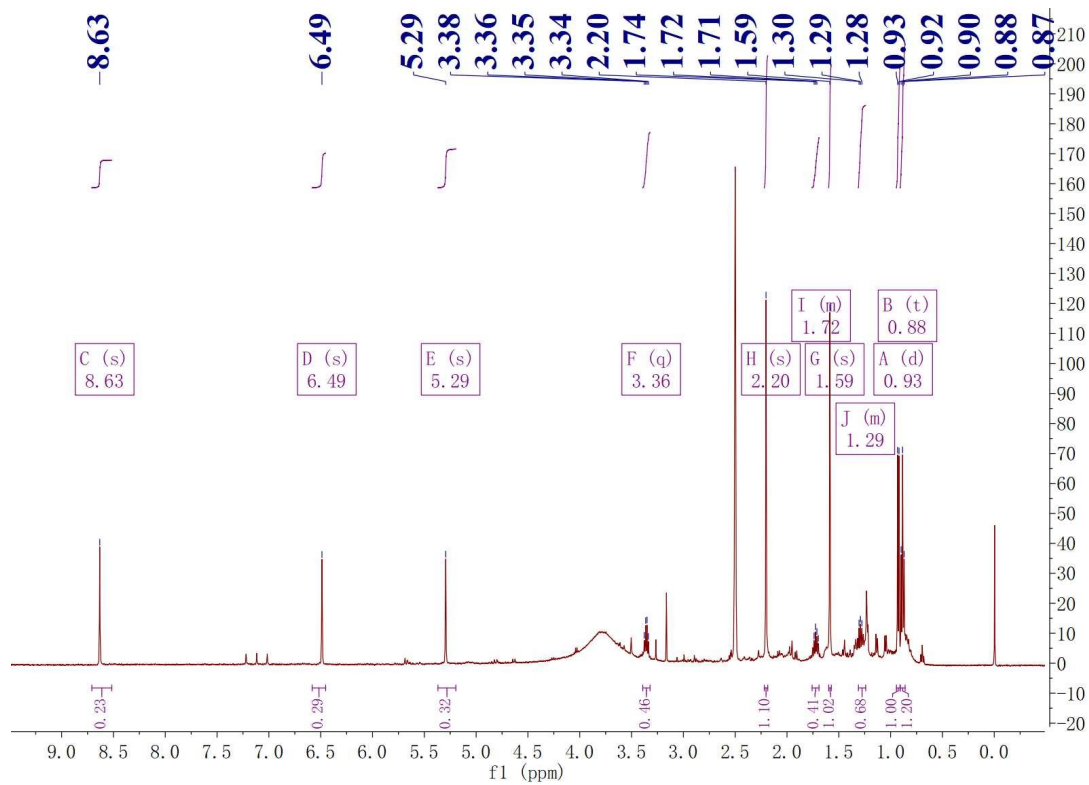
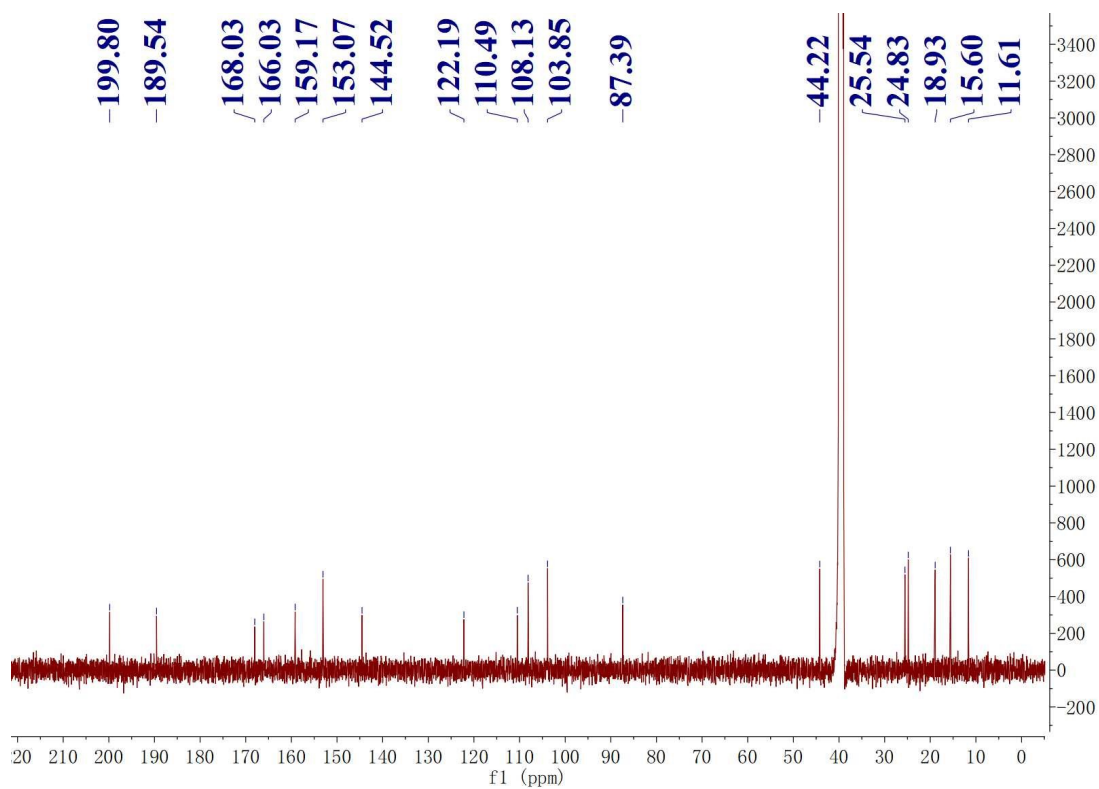
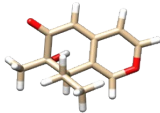
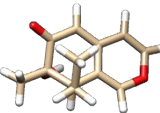
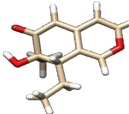
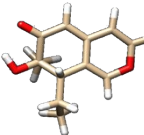

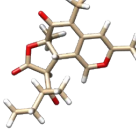
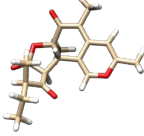
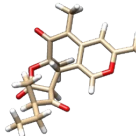
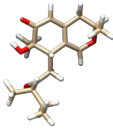
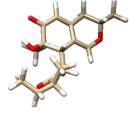


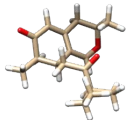
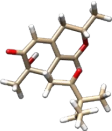
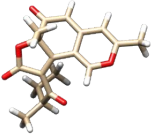

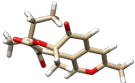
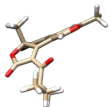
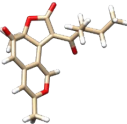
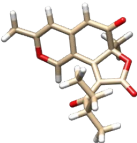
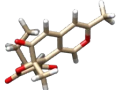
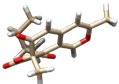
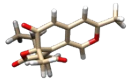
Figure S36. The ^{13}C NMR spectrum of **5** in $\text{DMSO-}d_6$.



The optimized conformers and equilibrium populations of calculated compounds

Table S1. Energies of all calculated conformers at B97-3c level in methanol.

Configurations	Conformers	E (Hartree)	ΔE (kcal/mol)	Population (%)
6 <i>S</i> ,7 <i>R</i> - a1		-690.840080	0.00	87.9
6 <i>S</i> ,7 <i>R</i> - a2		-690.838208	1.17	12.1
6 <i>R</i> ,7 <i>S</i> - b1		-690.843390	0.00	82.77
6 <i>R</i> ,7 <i>S</i> - b2		-690.841908	0.93	17.23
6 <i>S</i> ,7 <i>R</i> ,10 <i>R</i> - c1		-992.543770	0.00	100
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> - d1		-1112.892630	0.00	64.7
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> - d2		-1112.891726	0.57	24.84
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> - d3		-1112.890909	1.08	10.46
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a		-691.906009	0.00	100
2 <i>S</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4b		-691.906933	0.00	100

2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c		-691.904997	0.00	100
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d		-691.907267	0.00	100
6 <i>R</i> ,13 <i>S</i> -5a1		-1072.390590	0.00	68.77
6 <i>R</i> ,13 <i>S</i> -5a2		-1072.389723	0.54	27.44
6 <i>R</i> ,13 <i>S</i> -5a3		-1072.387855	1.72	3.79
6 <i>R</i> ,13 <i>R</i> -5b1		-1072.389826	0.00	68.90
6 <i>R</i> ,13 <i>R</i> -5b2		-1072.388863	0.60	24.84
6 <i>R</i> ,13 <i>R</i> -5b3		-1072.387561	1.42	6.26
6 <i>S</i> ,13 <i>S</i> -5c1		-1072.388531	0.00	62.08
6 <i>S</i> ,13 <i>S</i> -5c2		-1072.387861	0.42	30.53
6 <i>S</i> ,13 <i>S</i> -5c3		-1072.386521	1.26	7.39

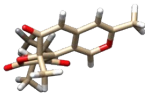
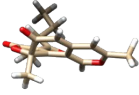
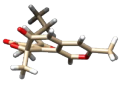
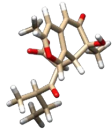
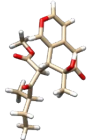
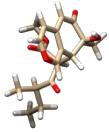
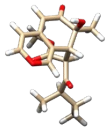
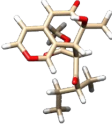
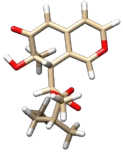
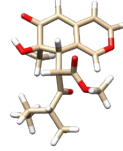
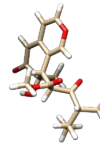
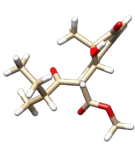
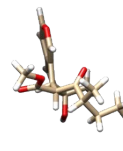
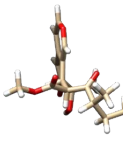
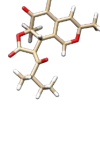
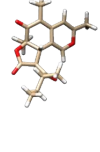
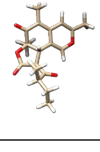
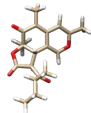
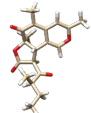
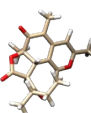
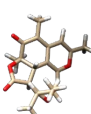
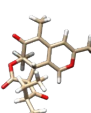
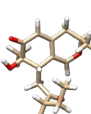
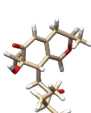
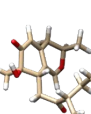
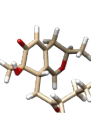
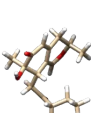
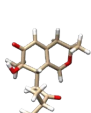
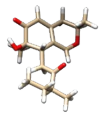
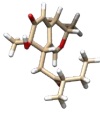
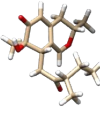
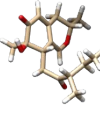
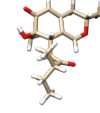
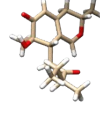
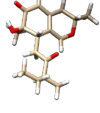
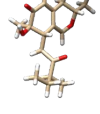
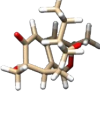
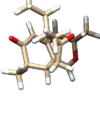
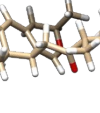
6 <i>S</i> ,13 <i>R</i> -5d1		-1072.391651	0.00	66.38
6 <i>S</i> ,13 <i>R</i> -5d2		-1072.390463	0.75	18.86
6 <i>S</i> ,13 <i>R</i> -5d3		-1072.390231	0.89	14.75

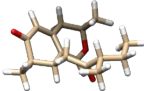
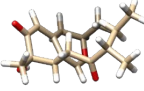
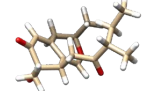
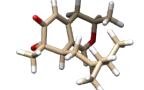
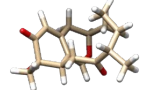
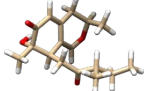
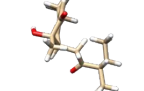
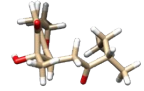
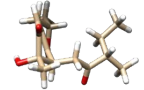
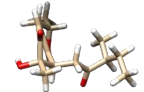
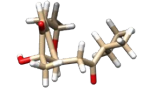
Table S2. Energies of all calculated conformers at B3LYP/6-31+G (d,p) level in PCM model.

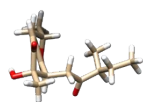
Configurations	Conformers	E (Hartree)	ΔE (kcal/mol)	Population (%)
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,12 <i>S</i> -1a1		-1149.660672	0.00	94.75
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,12 <i>S</i> -1a2		-1149.657941	1.71	5.25
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,12 <i>R</i> -1b1		-1149.653468	0.00	55.18
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,12 <i>R</i> -1b2		-1149.652824	0.40	27.90
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,12 <i>R</i> -1b3		-1149.652352	0.7	16.92

6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>S</i> - 2a1		-1150.152390	0.00	73.74
6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>S</i> - 2a2		-1150.150918	0.92	15.51
6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>S</i> - 2a3		-1150.150572	1.14	10.75
6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>R</i> - 2b1		-1150.152390	0.00	64.97
6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>R</i> - 2b2		-1150.151340	0.66	21.37
6 <i>R</i> ,7 <i>S</i> ,10 <i>R</i> ,12 <i>R</i> - 2b3		-1150.150918	0.92	13.67
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>S</i> - 3a1		-1112.711345	0.00	57.40
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>S</i> - 3a2		-1112.710118	0.77	15.65
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>S</i> - 3a3		-1112.709880	0.92	12.16

6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>S</i> - 3a4		-1112.709574	1.11	8.80
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>S</i> - 3a5		-1112.709211	1.34	5.99
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>R</i> - 3b1		-1112.711196	0.00	72.72
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>R</i> - 3b2		-1112.709838	0.85	17.74
6 <i>R</i> ,7 <i>S</i> ,10 <i>S</i> ,13 <i>R</i> - 3b3		-1112.709030	1.36	7.54
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a1		-962.638810	0.00	76.74
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a2		-962.636556	1.41	7.05
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a3		-962.635945	1.80	3.69
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a4		-962.635858	1.85	3.37
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a5		-962.635825	1.87	3.25
2 <i>R</i> ,6 <i>R</i> ,7 <i>S</i> ,12 <i>S</i> - 4a6		-962.635810	1.88	3.20

<i>2R,6R,7S,12S-4a7</i>		-962.635650	1.98	2.70
<i>2S,6R,7S,12S-4b1</i>		-962.639570	0.00	78.89
<i>2S,6R,7S,12S-4b2</i>		-962.636873	1.69	4.48
<i>2S,6R,7S,12S-4b3</i>		-962.636840	1.71	4.32
<i>2S,6R,7S,12S-4b4</i>		-962.636800	1.74	4.15
<i>2S,6R,7S,12S-4b5</i>		-962.636564	1.89	3.23
<i>2S,6R,7S,12S-4b6</i>		-962.636491	1.93	2.99
<i>2S,6R,7S,12S-4b7</i>		-962.636479	1.94	2.95
<i>2R,6S,7R,12S-4c1</i>		-962.630461	0.00	39.79
<i>2R,6S,7R,12S-4c2</i>		-962.629578	0.55	15.62
<i>2R,6S,7R,12S-4c3</i>		-962.629418	0.65	13.19

2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c4		-962.629356	0.69	12.35
2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c5		-962.628459	1.26	4.78
2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c6		-962.628449	1.26	4.73
2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c7		-962.628204	1.42	3.65
2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c8		-962.628173	1.44	3.53
2 <i>R</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4c9		-962.627797	1.67	2.37
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d1		-962.292042	0.00	36.89
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d2		-962.291891	0.09	31.44
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d3		-962.291296	0.47	16.74
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d4		-962.290597	0.91	7.98
2 <i>S</i> ,6 <i>S</i> ,7 <i>R</i> ,12 <i>S</i> -4d5		-962.290110	1.21	4.77



-962.289373

1.67

2.18

	1a			1b			2a			2b		
	DP4+	TAD	MAE	DP4+	TAD	MAE	DP4+	TAD	MAE	DP4+	TAD	MAE
H	99.91%	3.32	0.24	0.09%	4.63	0.36	100.0%	1.65	0.13	0.0%	4.24	0.33
C	100%	51.71	2.72	0.0%	51.37	2.70	68.74%	54.27	2.86	31.26%	56.03	2.95
Both	100%	55.03	2.96	0.0%	56.00	3.06	100%	55.92	2.99	0.0%	60.27	3.28

Figure S37 NMR calculation results of **1** and **2**.

DP4⁺ probability (sarotti-nmr.weebly.com), total absolute deviation (TAD), and mean absolute error (MAE) analysis for four candidate diastereomers, **1a/1b** and **2a/2b** (PCM/B3LYP/6-31+G (d,p) level).

 SUMMARY OF ISOTROPIC COUPLING CONSTANTS (Hz)

	25 H	26 H	27 H	28 H	29 H	30 H
25 H	0.000	0.428	-3.104	0.075	0.000	0.000
26 H	0.428	0.000	0.000	-0.329	0.039	0.000
27 H	-3.104	0.000	0.000	0.430	0.000	0.043
28 H	0.075	-0.329	0.430	0.000	0.272	-1.401
29 H	0.000	0.039	0.000	0.272	0.000	-15.497
30 H	0.000	0.000	0.043	-1.401	-15.497	0.000
31 H	0.000	0.000	0.074	-1.591	-15.713	-19.445
32 H	-0.006	-0.057	-0.015	0.012	0.000	0.000
33 H	-0.498	0.000	0.014	0.000	0.000	0.000
34 H	2.327	0.179	0.000	0.000	0.000	0.000
35 H	-0.088	0.030	0.000	0.000	0.000	0.000
36 H	6.439	0.000	-0.277	0.000	0.000	0.000
37 H	0.086	0.000	0.058	0.000	0.000	0.000
38 H	0.000	0.000	0.138	0.000	0.000	0.000
39 H	0.033	0.000	0.077	0.000	0.000	0.000
40 H	0.000	0.000	0.041	0.000	0.000	0.000
41 H	0.000	0.000	0.040	0.000	0.000	0.000
42 H	0.000	0.000	0.000	0.000	0.000	0.000
43 H	0.000	0.000	0.000	0.000	0.000	0.000
44 H	0.000	0.000	0.000	0.000	0.000	0.000
45 H	0.000	0.000	0.001	0.000	0.000	0.000
46 H	0.000	0.000	0.000	0.000	0.000	0.000
47 H	0.000	0.000	0.000	0.000	0.000	0.000
48 H	-0.069	0.000	0.000	0.000	0.000	0.000

Figure S38 Calculation results of the spin-spin coupling constants of **1**.

“25 H” and “36 H” corresponds respectively to H-7 and H-10 in the structure of **1**. (B972/pcJ-1 level). (*J. Chem. Theory Comput.* 2017, 13, 11, 5231–5239)

SUMMARY OF ISOTROPIC COUPLING CONSTANTS (Hz)						
	25 H	26 H	27 H	28 H	29 H	30 H
25 H	0.000	0.411	-2.851	0.070	0.000	0.000
26 H	0.411	0.000	0.000	-0.273	0.042	0.000
27 H	-2.851	0.000	0.000	0.416	0.000	0.032
28 H	0.070	-0.273	0.416	0.000	0.292	-1.286
29 H	0.000	0.042	0.000	0.292	0.000	-15.489
30 H	0.000	0.000	0.032	-1.286	-15.489	0.000
31 H	0.000	0.000	0.099	-1.705	-15.656	-19.293
32 H	-0.672	0.075	-0.028	0.029	0.000	0.000
33 H	-0.140	0.445	0.052	0.000	0.000	0.000
34 H	-2.928	-0.021	0.000	0.000	0.000	0.000
35 H	0.064	-0.025	0.000	0.000	0.000	0.000
36 H	2.610	0.000	-0.498	0.000	0.000	0.000
37 H	0.298	0.000	0.094	0.000	0.000	0.000
38 H	0.000	0.000	0.000	0.000	0.000	0.000
39 H	0.000	0.000	0.141	0.000	0.000	0.000
40 H	0.000	0.000	0.000	0.000	0.000	0.000
41 H	0.000	0.000	0.000	0.000	0.000	0.000
42 H	0.000	0.000	0.000	0.000	0.000	0.000
43 H	0.000	0.000	0.000	0.000	0.000	0.000
44 H	0.000	0.000	0.000	0.000	0.000	0.000
45 H	0.000	0.000	0.000	0.000	0.000	0.000
46 H	0.012	0.000	0.000	0.000	0.000	0.000
47 H	0.269	0.000	0.000	0.000	0.000	0.000
48 H	-0.003	0.000	0.000	0.000	0.000	0.000

Figure S39 Calculation results of the spin-spin coupling constants of 2.

“25 H” and “36 H” corresponds respectively to H-7 and H-10 in the structure of **2**. (B972/pcJ-1 level). (*J. Chem. Theory Comput.* 2017, 13, 11, 5231–5239)