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Supplementary Information

Chemical constituents from the seeds of *Nigella glandulifea* Freyn et Sint and their hypoglycemic activities

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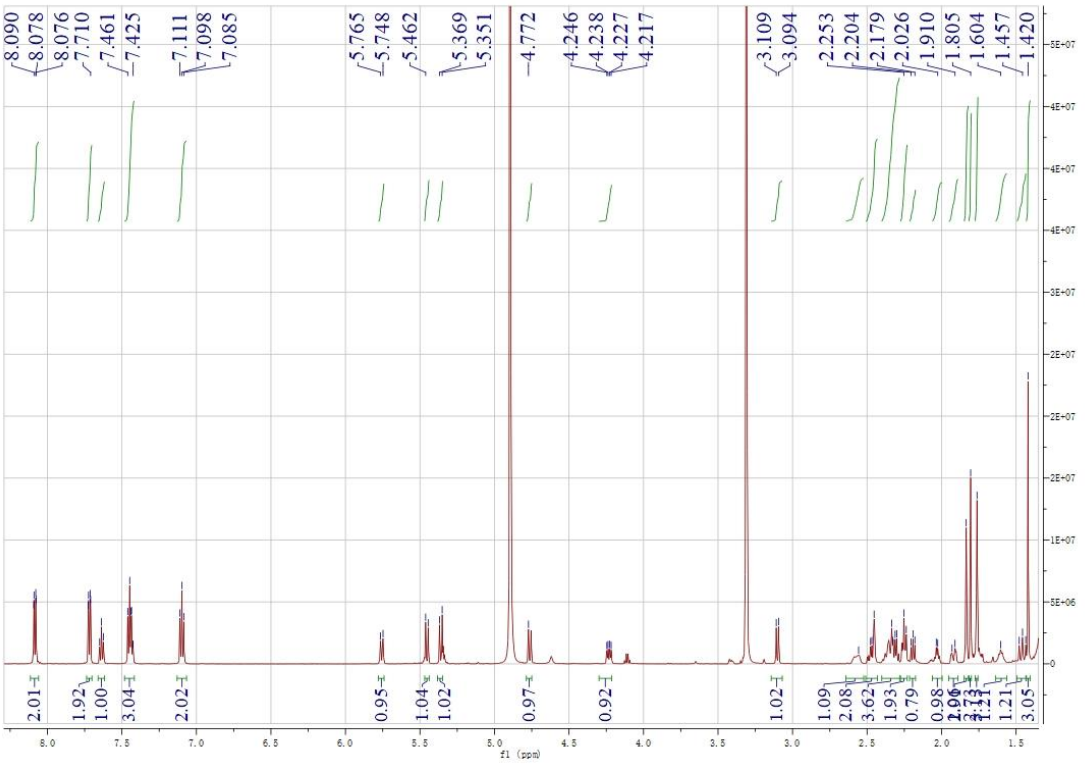


Figure S1: ^{1}H-NMR (600 MHz, CD_3OD) spectrum of compound 1

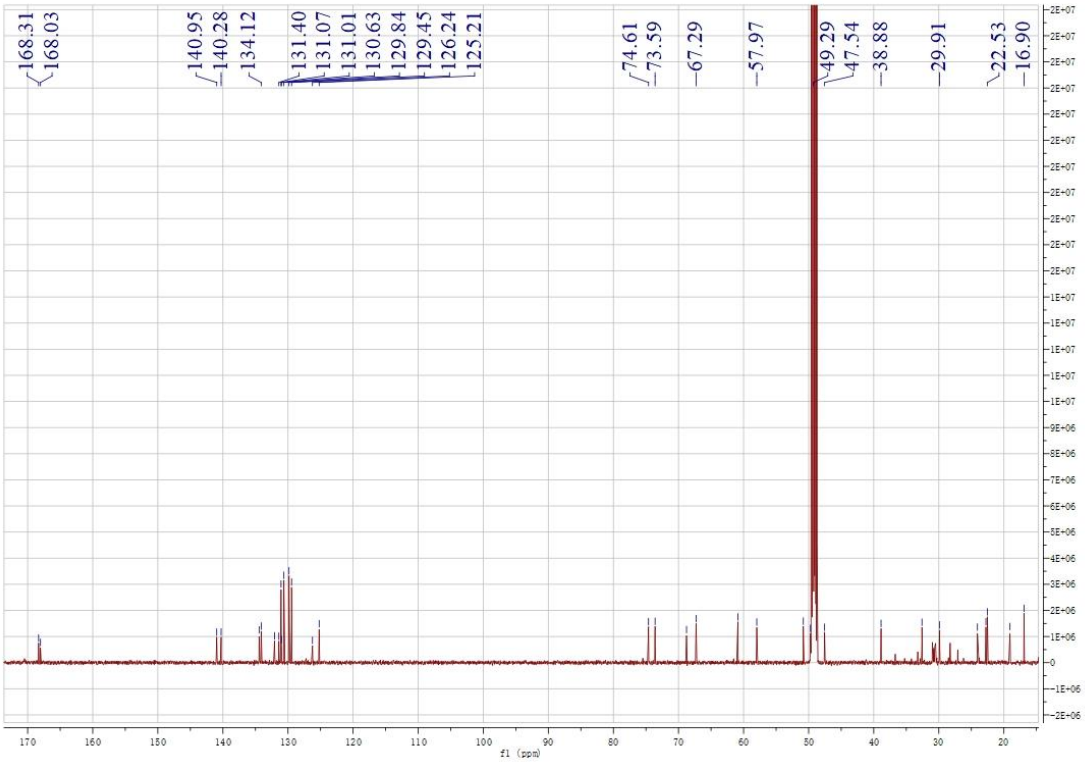


Figure S2: ^{13}C-NMR (150 MHz, CD_3OD) spectrum of compound 1

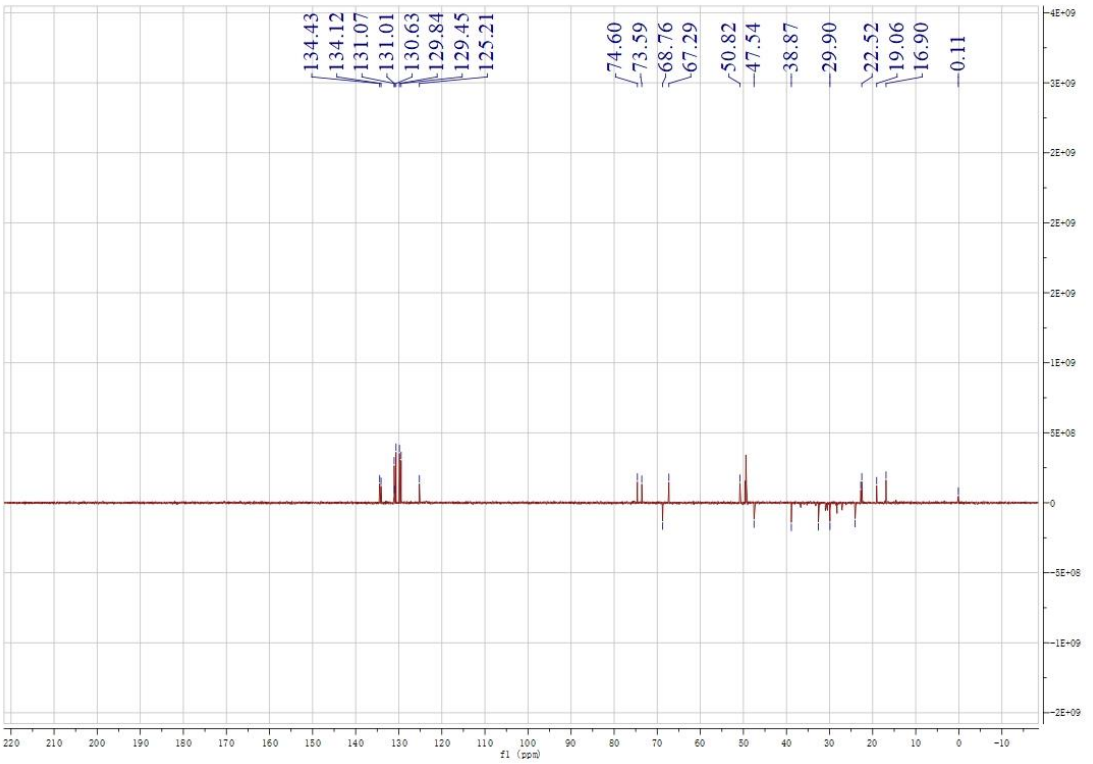


Figure S3: ^{13}C-NMR-DEPT (θ=135 °) spectrum of compound 1

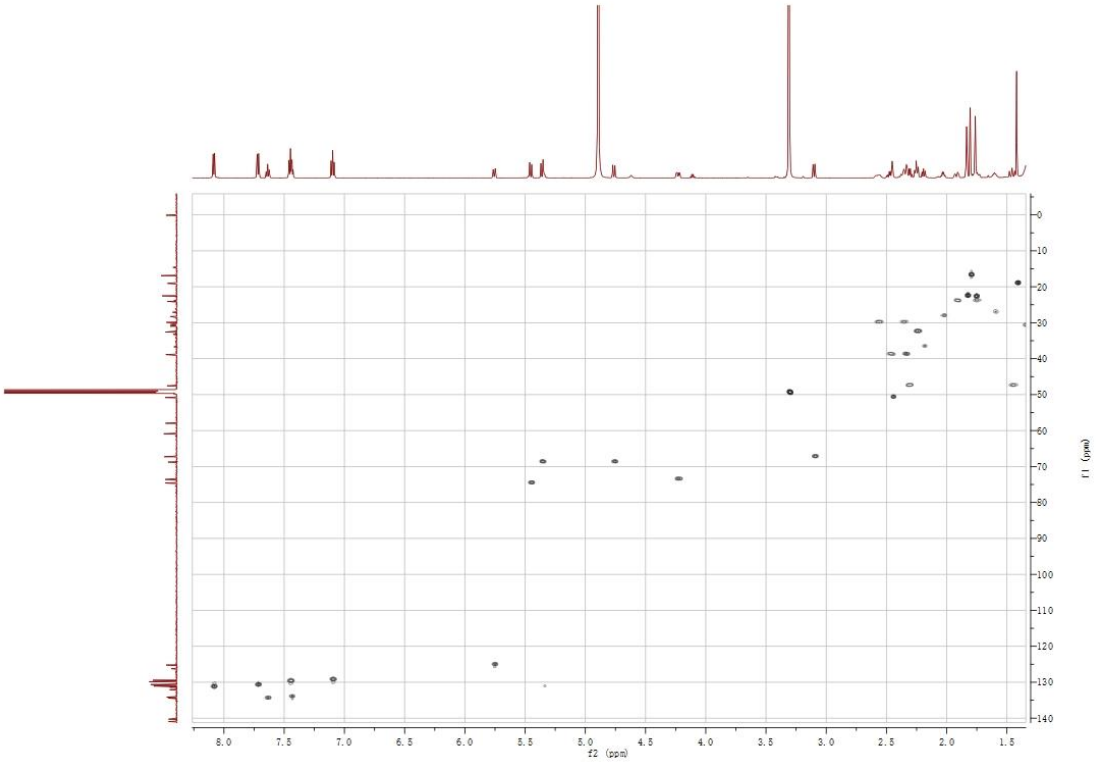


Figure S4: HSQC spectrum of compound 1

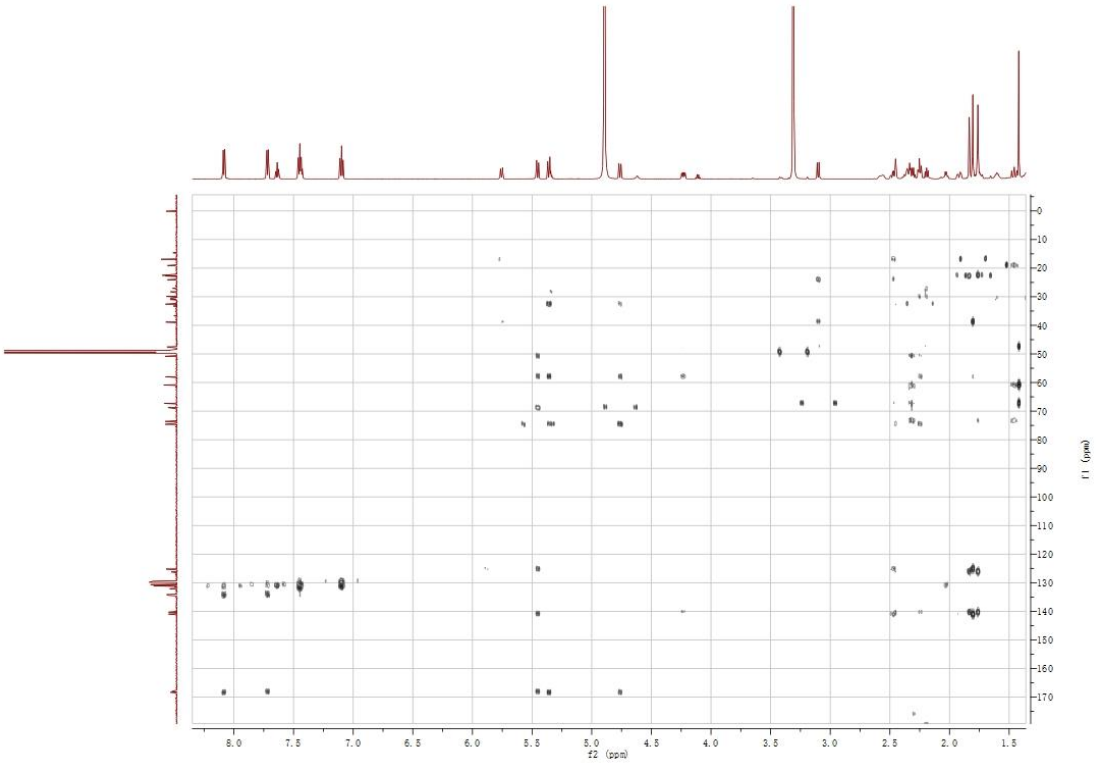


Figure S5: HMBC spectrum of compound 1

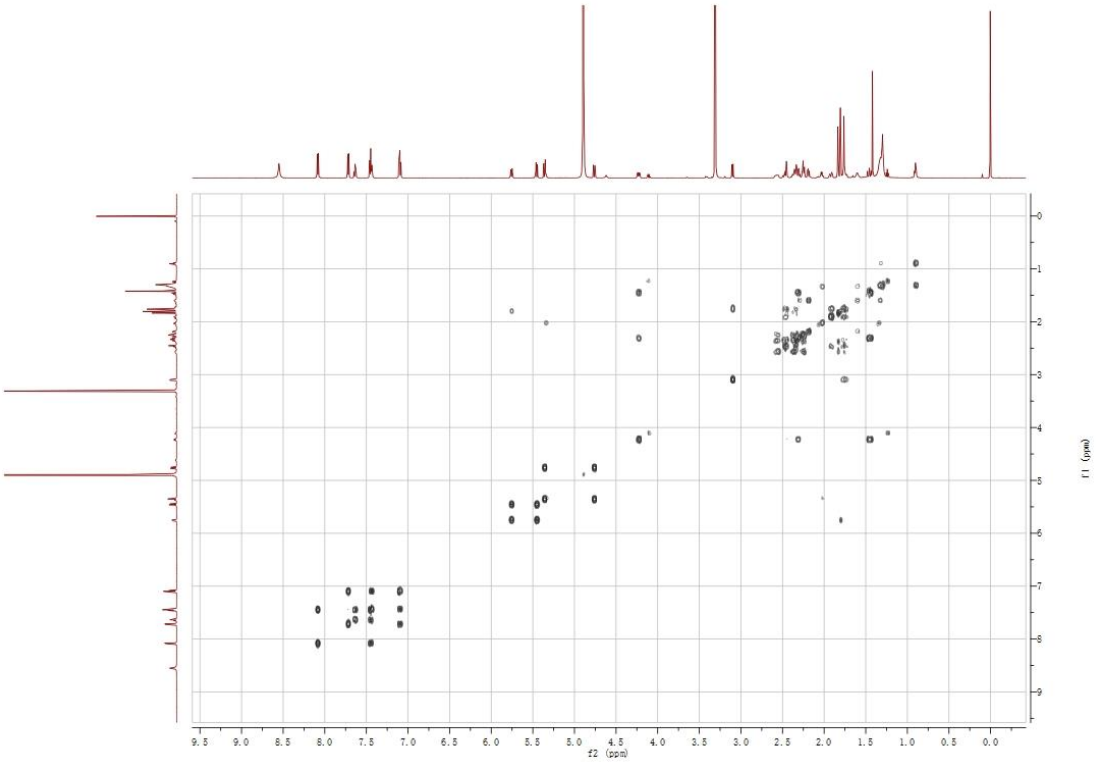


Figure S6: ^{1}H-^{1}H COSY spectrum of compound 1

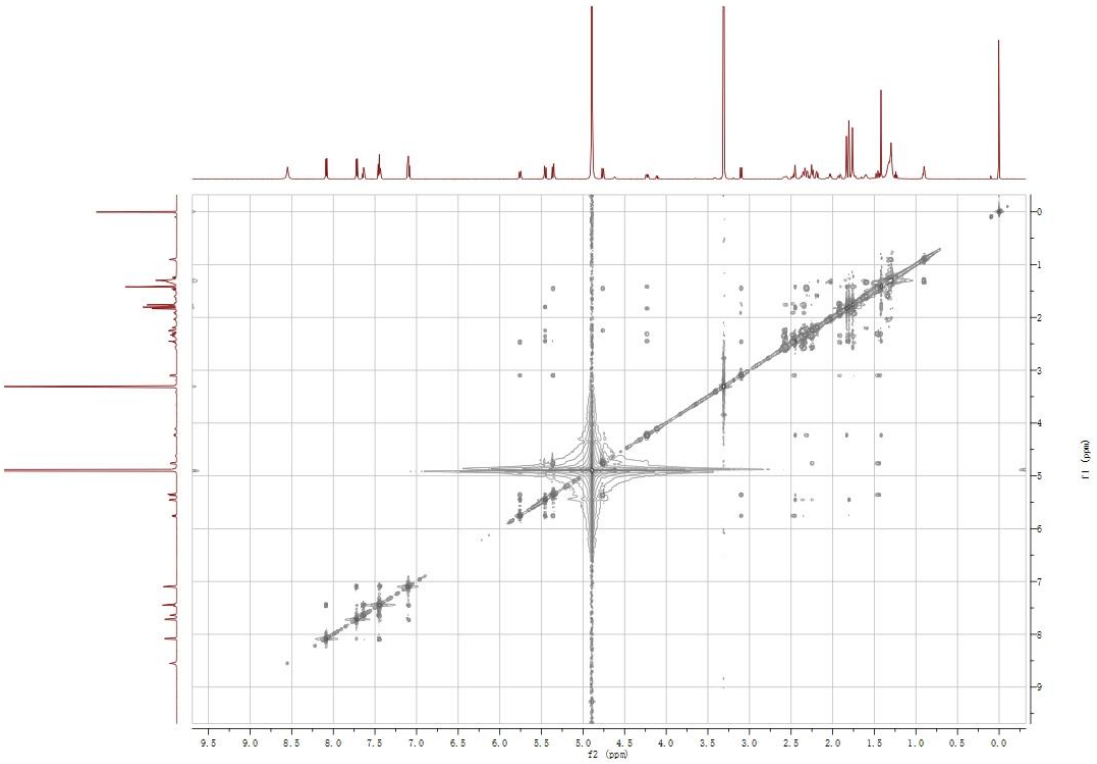


Figure S7: ROESY spectrum of compound 1

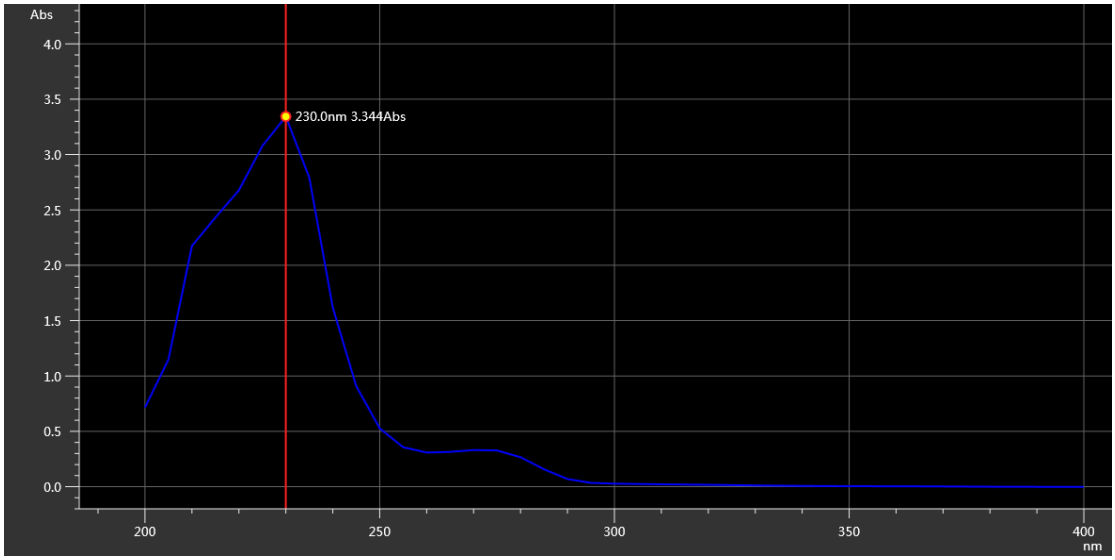


Figure S8: UV spectrum of compound 1

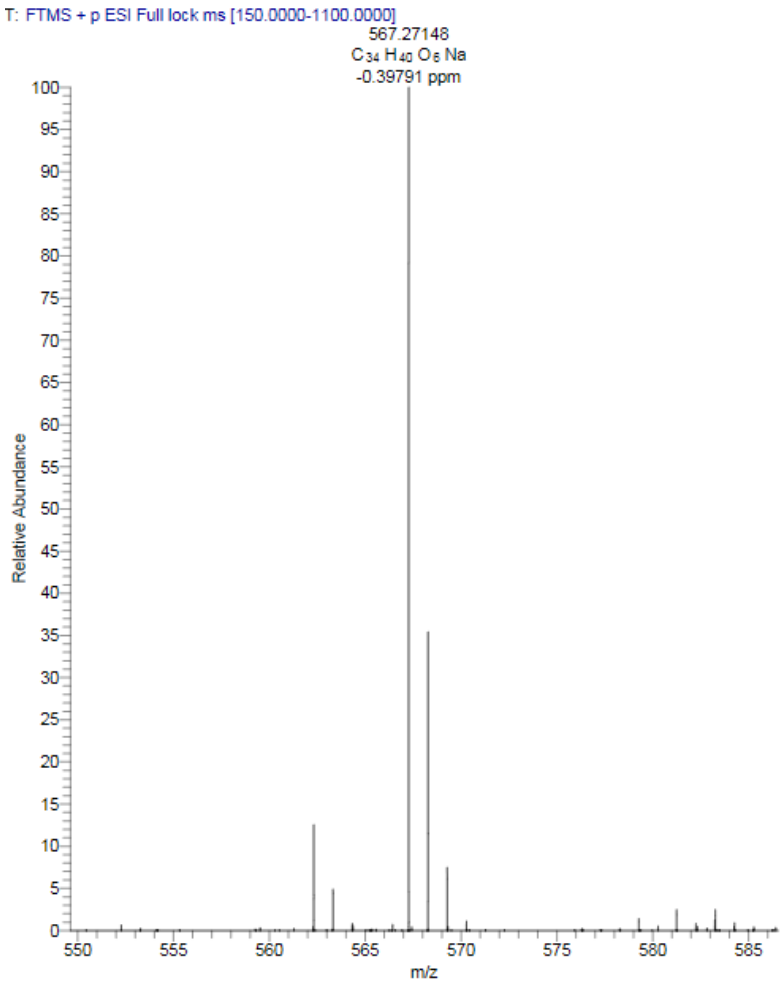


Figure S9: HR-ESI-MS of compound 1

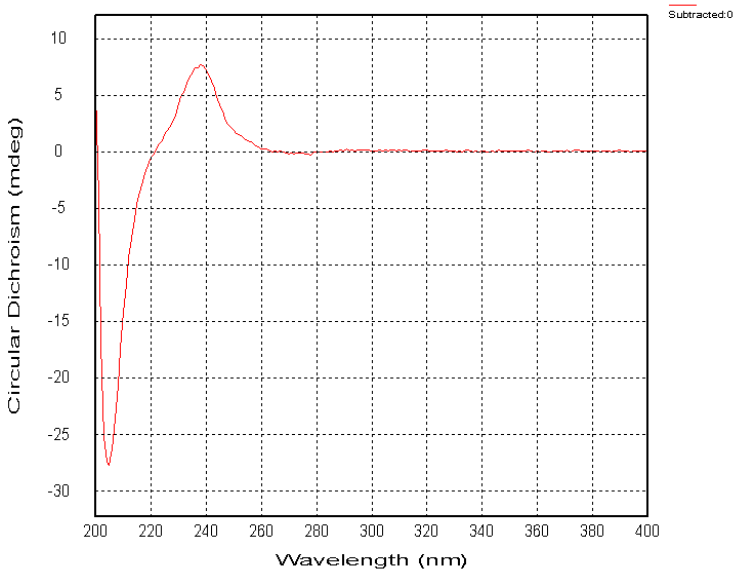


Figure S10: CD spectrum of compound 1

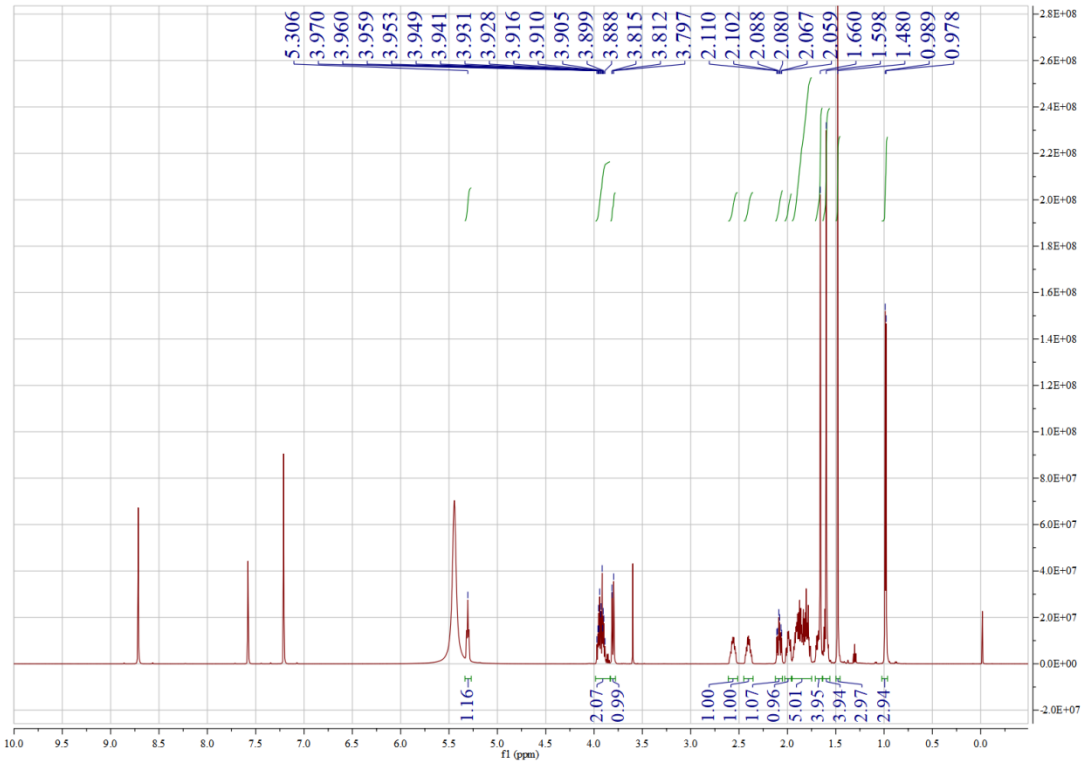


Figure S11: ^{1}H-NMR (600 MHz, C_5D_5N) spectrum of compound 3

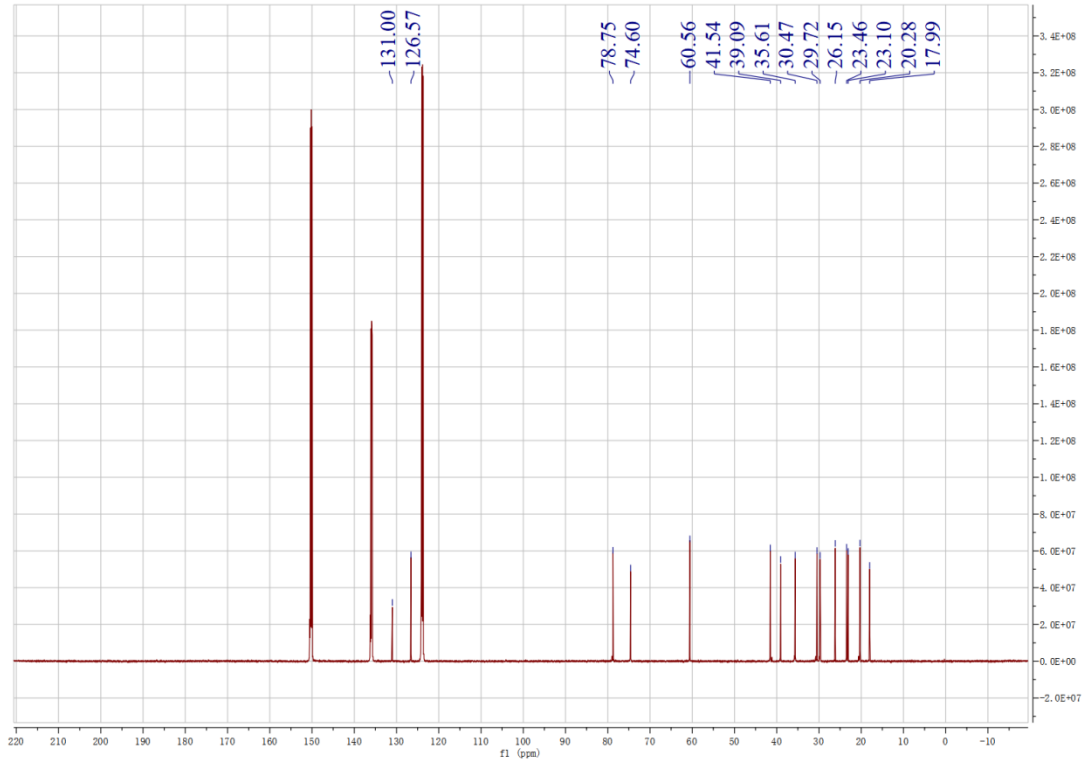


Figure S12: ^{13}C-NMR (150 MHz, C_5D_5N) spectrum of compound 3

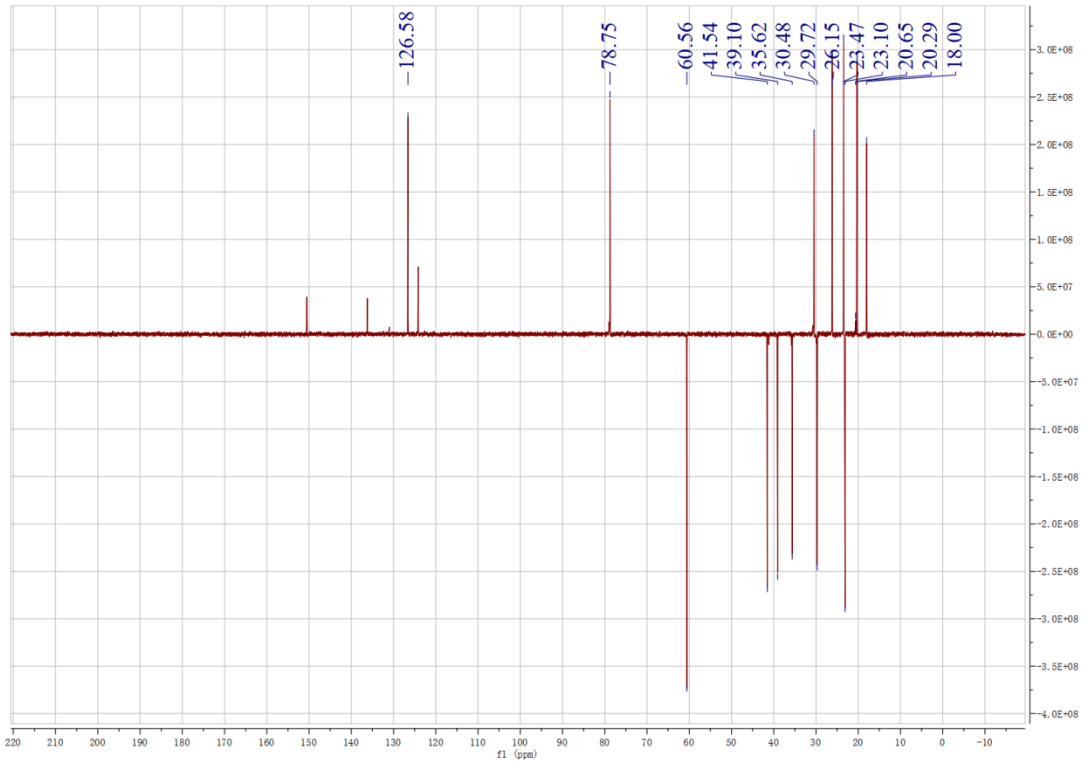


Figure S13: ^{13}C-NMR-DEPT (θ=135 ◦) spectrum of compound 3

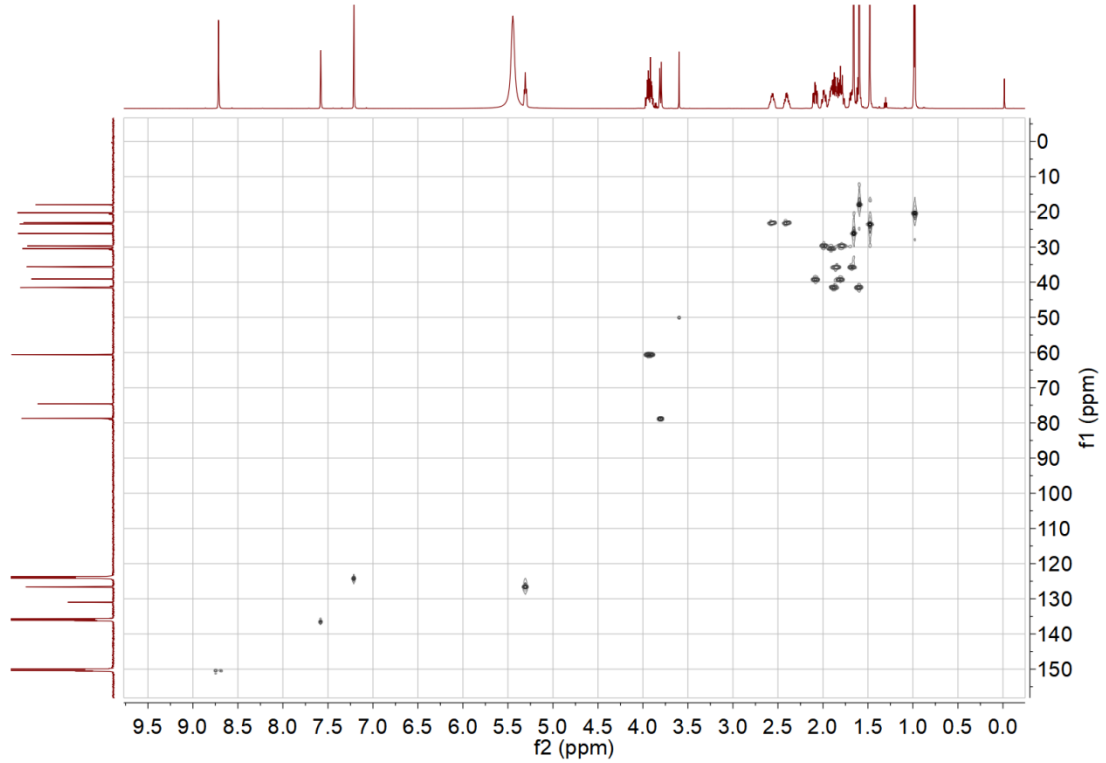


Figure S14: HSQC spectrum of compound 3

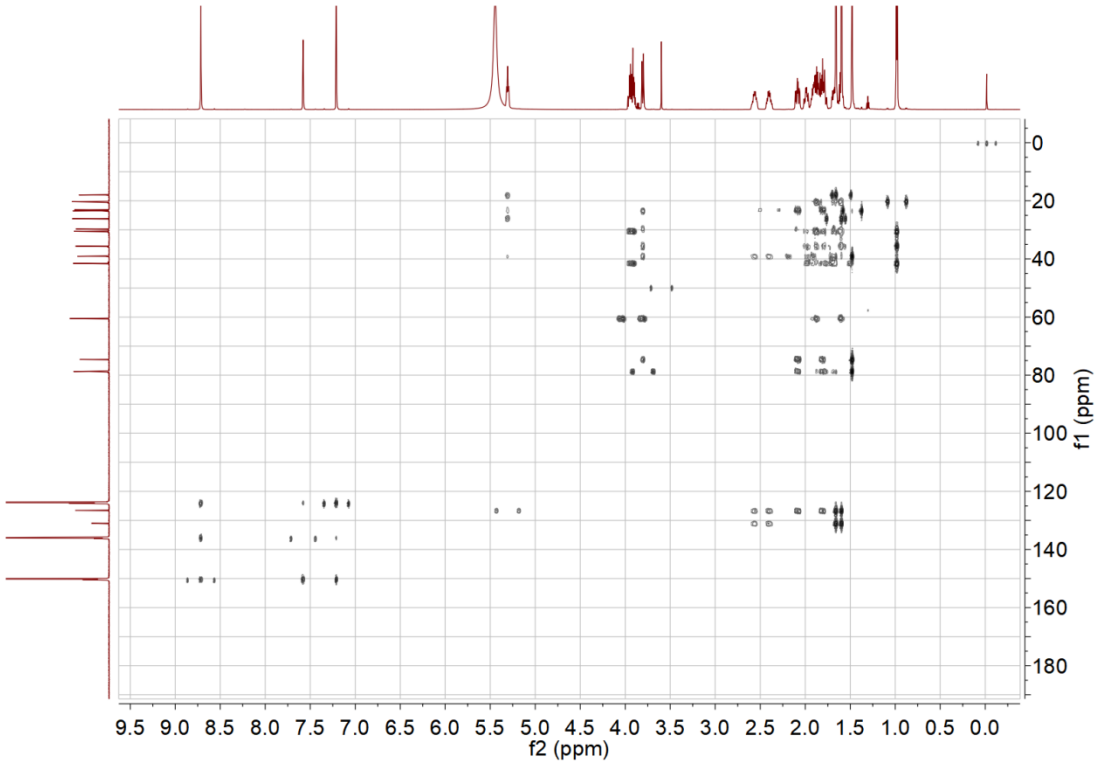


Figure S15: HMBC spectrum of compound 3

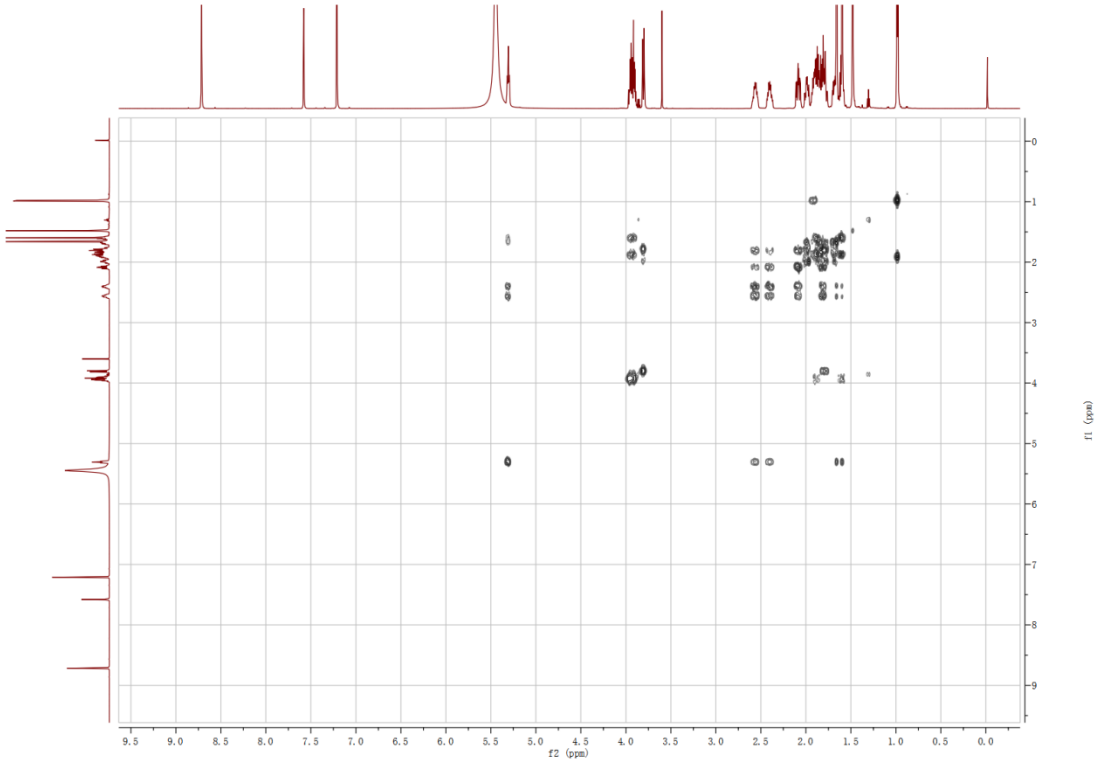


Figure S16: ^{1}H-^{1}H COSY spectrum of compound 3

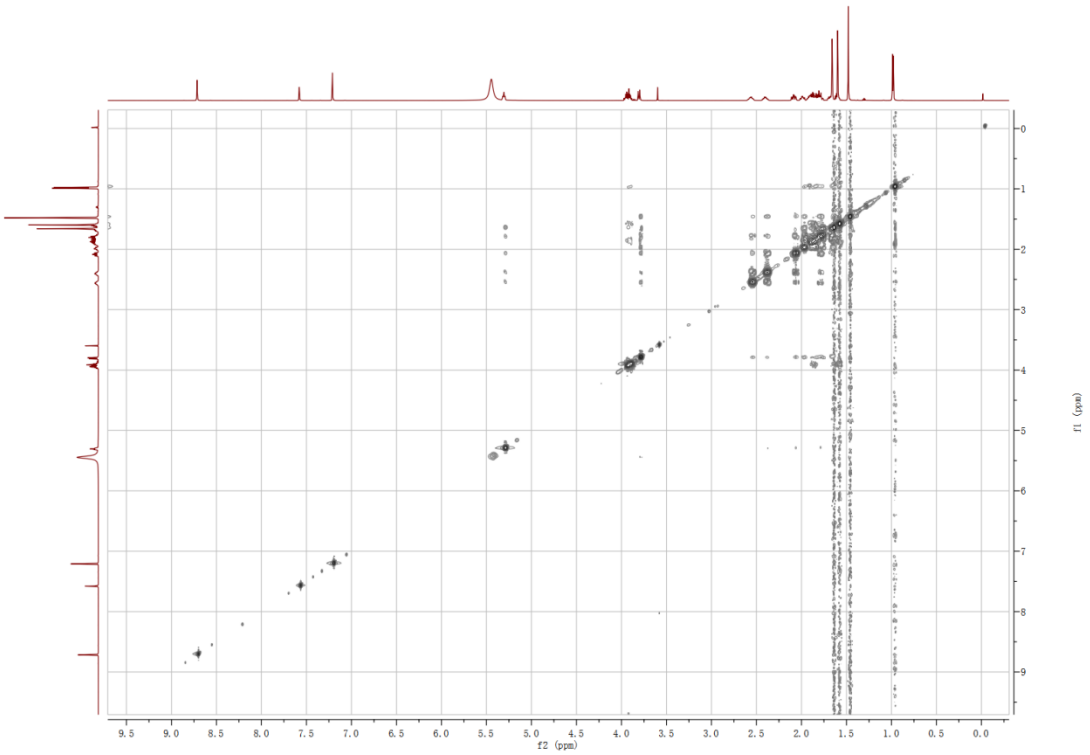


Figure S17: ROESY spectrum of compound 3

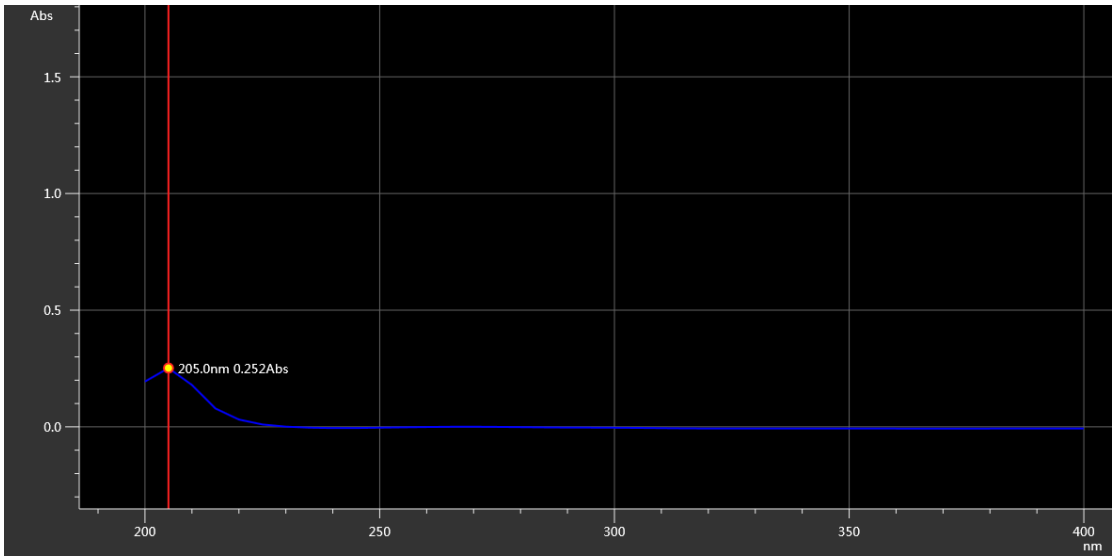


Figure S18: UV spectrum of compound 3

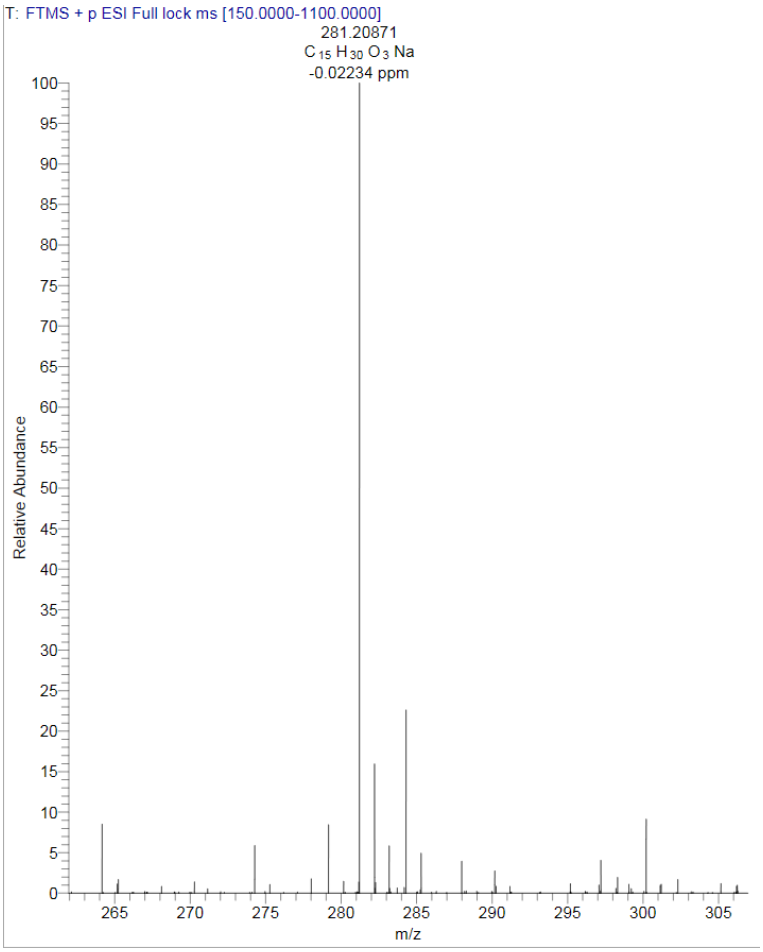


Figure S19: HR-ESI-MS of compound 3

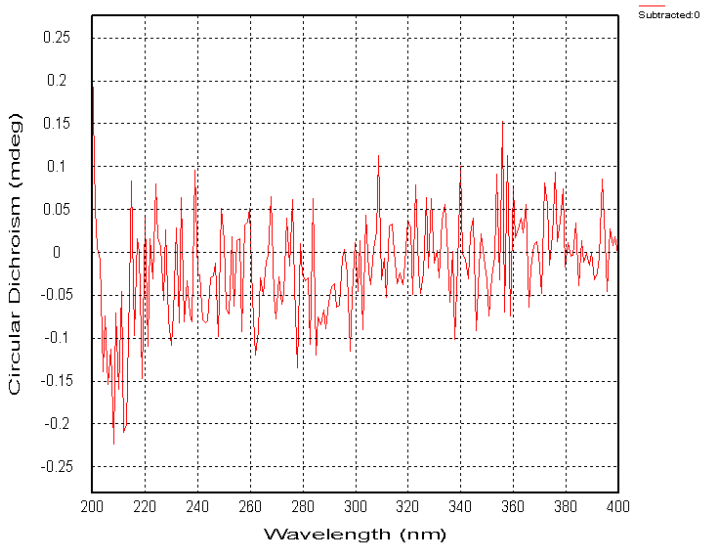


Figure S20: CD spectrum of compound 3

1. Computational methods

1.1 Conformational analysis

Conformational analysis for compound **1** (**Figure S**21) were performed in Yinfo Cloud Platform (http://cloud.yinfotek.com/) using Custom Search by Confab [1] at MMFF94 force field with RMSD threshold of 0.5 Å and energy window of 7 kcal/mol.

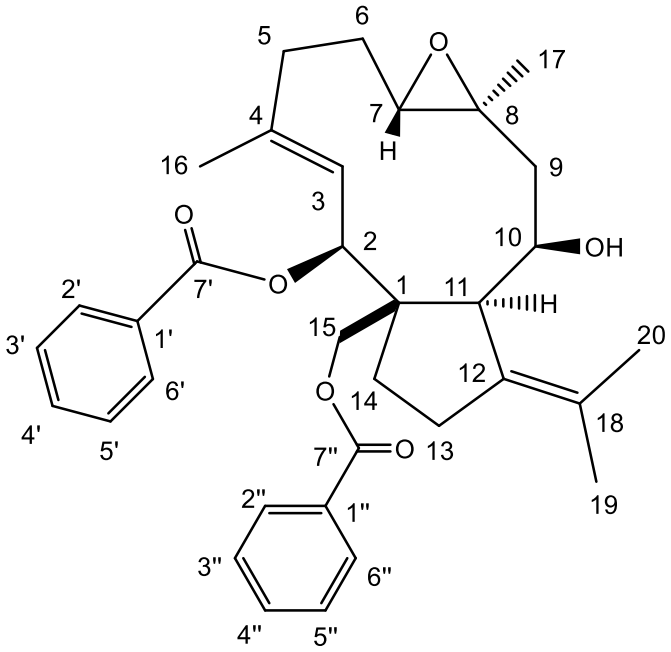


Figure S21 Chemical structure of compound **1a**.

1.2 ECD calculation

The theoretical calculations were carried out using Gaussian 09 [2]. At first, all conformers were optimized at PM6. Room-temperature equilibrium populations were calculated according to Boltzmann distribution law(**eq.1**), based on which dominative conformers of population over 1% were kept. The chosen conformers were further optimized at B3LYP/6-31G(d,p) in gas phase (**Table S2**). Vibrational frequency analysis confirmed the stable structures. ECD calculations were conducted at

B3LYP/6-311G(d,p) level in methanol with IEFPCM model using Time-dependent Density functional theory (TD-DFT) (**Table S1**). Rotatory strengths for 30 excited states were calculated. The ECD spectrum was simulated using the ECD/UV analysis tool in Yinfo Cloud Platform (https://cloud.yinfotek.com/) by overlapping Gaussian functions for each transition according to **eq.2**).

$$\frac{N_i}{N} = \frac{g_i e^{-\frac{E_i}{k_B T}}}{\sum g_i e^{-\frac{E_i}{k_B T}}} \qquad \textbf{(1)}$$

where N_i is the number of conformer i with energy E_i and degeneracy g_i at temperature T, and k_B is Boltzmann constant.

$$\Delta\varepsilon(E) = \frac{1}{2.297\times10^{-39}} \times \frac{1}{\sqrt{2\pi\sigma}} \sum_i^A \Delta E_i R_i e^{-\left(\frac{E-E_i}{2\sigma}\right)^2} \qquad \textbf{(2)}$$

where σ represents the width of the band at 1/e height, while ΔE_i and R_i are the excitation energies and rotatory strengths for transition i, respectively.

The σ and UV-shift values of compound **1** was set 0.20 eV and -34 nm, respectively. The spectrum of the enantiomers was produced directly by mirror inversion about the horizontal axis.

1.3 References

1. Noel M OBoyle, Tim V, ermeersch, Christopher J Flynn, Anita R Maguire Maguire, and Geoffey R Hutchison. Confab - systematic generation of diverse low-energy conformers. *Journal of Cheminformatics*, 3:3–8, March 2011.
2. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M.

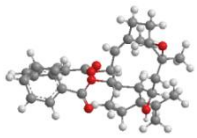
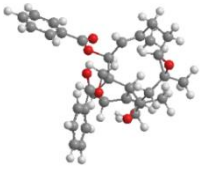
Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox. Gaussian 09 Revision D.01. Gaussian Inc. Wallingford CT 2009.

2. Energies and Coordinates

2.1 Energies at B3LYP theory level

Structures for ECD calculation were shown in **Table S1**

Table S1 Energies of configurations **1** at B3LYP/6-311G(d,p) in methanol.

Configuration	Conformer	Structure	E (Hartree)	E (kcal/mol)	Population (%)
1a	5		-1771.47992600	-1111620.43	5.4
1a	7		-1771.48264340	-1111622.13	94.6

2.2 Coordinates at B3LYP theory level

Table S2 Standard orientations of configurations **1**.

Conformer **1a-5**					
Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	0.702697	0.401300	1.766000
2	1	0	0.127599	-0.462702	2.096100
3	6	0	0.323795	0.898699	0.400200
4	1	0	0.814792	1.845601	0.177900
5	6	0	0.708698	-0.123900	-0.731900
6	6	0	2.258698	0.123605	-0.969500
7	6	0	3.176201	-1.070792	-1.376800
8	1	0	4.135100	-0.608089	-1.650400
9	6	0	3.501805	-2.155791	-0.323300
10	1	0	4.247607	-2.809488	-0.795100
11	1	0	2.630107	-2.787693	-0.143700
12	6	0	4.071403	-1.704189	1.021200
13	6	0	3.216604	-1.745892	2.234600
14	6	0	3.373301	-0.879591	3.474100
15	1	0	3.542703	-1.537091	4.336900
16	1	0	4.258699	-0.240088	3.395300
17	6	0	2.109798	-0.018795	3.747000
18	1	0	2.304496	0.614305	4.622700
19	1	0	1.283200	-0.688998	4.013600
20	6	0	1.709395	0.823004	2.550100
21	6	0	0.058497	0.263898	-2.081500
22	1	0	0.126700	-0.598502	-2.751800
23	1	0	-1.000804	0.506095	-1.972300
24	6	0	0.886093	1.430001	-2.625100
25	1	0	0.467890	2.392899	-2.300200
26	1	0	0.879393	1.449801	-3.721200
27	6	0	2.281294	1.244705	-2.036500
28	6	0	3.328891	2.023709	-2.370800
29	6	0	4.690792	1.976413	-1.719600
30	1	0	5.029188	2.994914	-1.485900
31	1	0	5.447993	1.547316	-2.391400
32	1	0	4.705293	1.405013	-0.791600
33	6	0	3.228488	3.097608	-3.432000
34	1	0	4.071988	3.028411	-4.132900
35	1	0	3.287585	4.096409	-2.976000
36	1	0	2.304888	3.053005	-4.011900

37	8	0	4.175407	-2.782188	1.983800
38	6	0	5.321001	-0.843385	0.980600
39	1	0	5.102197	0.201115	0.738800
40	1	0	6.018302	-1.224182	0.225000
41	1	0	5.830801	-0.871783	1.946200
42	1	0	2.192105	-2.096095	2.089200
43	6	0	2.544491	2.055706	2.299100
44	1	0	2.613589	2.646206	3.222200
45	1	0	2.123489	2.702505	1.526400
46	1	0	3.575892	1.804610	2.016100
47	8	0	-1.108506	1.157994	0.368300
48	6	0	-1.495810	2.441593	0.568600
49	6	0	-2.978910	2.592788	0.557400
50	6	0	-3.508615	3.875387	0.756300
51	1	0	-2.823717	4.702989	0.908800
52	6	0	-4.887615	4.068382	0.756900
53	1	0	-5.295219	5.063581	0.911500
54	6	0	-5.745112	2.982279	0.558800
55	1	0	-6.821512	3.133776	0.559500
56	6	0	-5.220408	1.703081	0.360200
57	1	0	-5.883105	0.855779	0.207700
58	6	0	-3.840507	1.505485	0.359000
59	1	0	-3.428404	0.515187	0.206700
60	8	0	-0.720713	3.366596	0.730100
61	6	0	0.346503	-1.575501	-0.384600
62	1	0	0.827504	-1.906799	0.533400
63	1	0	0.624705	-2.233700	-1.206400
64	8	0	-1.070496	-1.729706	-0.116400
65	6	0	-1.823494	-2.379308	-1.035100
66	6	0	-3.226894	-2.584313	-0.567800
67	6	0	-3.644395	-2.260814	0.731200
68	1	0	-2.933096	-1.837612	1.431400
69	6	0	-4.966494	-2.486918	1.113800
70	1	0	-5.286095	-2.238919	2.122300
71	6	0	-5.875592	-3.034521	0.205200
72	1	0	-6.904892	-3.210625	0.506700
73	6	0	-5.460991	-3.360820	-1.089100
74	1	0	-6.166490	-3.789222	-1.795600
75	6	0	-4.141092	-3.139416	-1.473800
76	1	0	-3.795391	-3.390414	-2.471100
77	8	0	-1.410793	-2.755907	-2.114600
78	1	0	2.692396	0.498707	-0.035900
79	8	0	2.676504	-1.786593	-2.508700

80	1	0	2.606202	-1.149994	-3.238500

Conformer **1a-7**

Center	Atomic	Atomic	Coordinates (Angstroms)		
Number	Number	Type	X	Y	Z
1	6	0	-1.503287	-1.175016	-1.407493
2	1	0	-1.241294	-0.492914	-2.215793
3	6	0	-1.575794	-0.515417	-0.056893
4	1	0	-2.058988	-1.157221	0.679107
5	6	0	-0.157297	-0.106104	0.496207
6	6	0	0.513015	-1.470697	0.932307
7	6	0	2.066717	-1.616783	0.885007
8	1	0	2.282225	-2.532381	1.445707
9	6	0	2.713318	-1.777377	-0.520293
10	1	0	3.785620	-1.929267	-0.337893
11	1	0	2.636309	-0.844078	-1.086593
12	6	0	2.215929	-2.916982	-1.408293
13	6	0	1.260326	-2.617490	-2.506093
14	6	0	0.230135	-3.564100	-3.103493
15	1	0	0.511037	-3.773397	-4.143493
16	1	0	0.232343	-4.528100	-2.583293
17	6	0	-1.198771	-2.950913	-3.090793
18	1	0	-1.901764	-3.700520	-3.477193
19	1	0	-1.219379	-2.104013	-3.787493
20	6	0	-1.616875	-2.479517	-1.710193
21	6	0	-0.297405	0.682895	1.822307
22	1	0	0.642191	1.204104	2.015407
23	1	0	-1.083612	1.440388	1.760307
24	6	0	-0.544795	-0.360707	2.919207
25	1	0	-1.613094	-0.432317	3.162107
26	1	0	-0.033498	-0.082502	3.848307
27	6	0	-0.038183	-1.682502	2.353007
28	6	0	-0.141872	-2.852003	3.010107
29	6	0	0.250140	-4.194100	2.439907
30	1	0	-0.489653	-4.956907	2.716907
31	1	0	1.215644	-4.540391	2.836607
32	1	0	0.319140	-4.186499	1.350607
33	6	0	-0.680371	-2.938308	4.420707
34	1	0	0.029334	-3.468202	5.071707
35	1	0	-1.615366	-3.516617	4.447707
36	1	0	-0.876980	-1.962610	4.869107
37	8	0	2.650928	-2.822678	-2.787293
38	6	0	2.386742	-4.317380	-0.854793
39	1	0	1.811043	-4.480985	0.059607

40	1	0	3.444143	-4.481470	-0.613493
41	1	0	2.096648	-5.070383	-1.591093
42	1	0	0.978016	-1.568193	-2.612493
43	6	0	-2.066465	-3.558021	-0.756493
44	1	0	-2.933261	-4.082229	-1.181193
45	1	0	-2.356869	-3.174624	0.223507
46	1	0	-1.288158	-4.318314	-0.607493
47	8	0	-2.381205	0.692576	-0.177693
48	6	0	-3.701504	0.580064	0.119007
49	6	0	-4.443515	1.854257	-0.100593
50	6	0	-5.810016	1.872744	0.212607
51	1	0	-6.266107	0.967440	0.599307
52	6	0	-6.554626	3.034138	0.025707
53	1	0	-7.613226	3.044028	0.270107
54	6	0	-5.939937	4.184443	-0.476493
55	1	0	-6.521245	5.090938	-0.623093
56	6	0	-4.579237	4.169956	-0.791593
57	1	0	-4.101245	5.063160	-1.183993
58	6	0	-3.829926	3.009363	-0.605293
59	1	0	-2.774426	2.993972	-0.851893
60	8	0	-4.213394	-0.444841	0.525407
61	6	0	0.507795	0.765203	-0.582393
62	1	0	-0.188013	1.545996	-0.897893
63	1	0	0.793600	0.201705	-1.469793
64	8	0	1.696889	1.424314	-0.072693
65	6	0	2.220480	2.395118	-0.876693
66	6	0	3.392273	3.084529	-0.268793
67	6	0	4.105565	3.975936	-1.083693
68	1	0	3.778464	4.118133	-2.108293
69	6	0	5.209059	4.656646	-0.577493
70	1	0	5.760652	5.342351	-1.214293
71	6	0	5.604961	4.457050	0.747807
72	1	0	6.466256	4.988658	1.143507
73	6	0	4.893569	3.576543	1.565507
74	1	0	5.197170	3.423146	2.597107
75	6	0	3.789675	2.890133	1.062207
76	1	0	3.237381	2.216228	1.707507
77	8	0	1.761377	2.650314	-1.970393
78	1	0	0.143423	-2.259901	0.270307
79	8	0	2.744807	-0.597577	1.611207
80	1	0	2.661400	0.213322	1.081607

3. Experimental and calculated ECD spectra

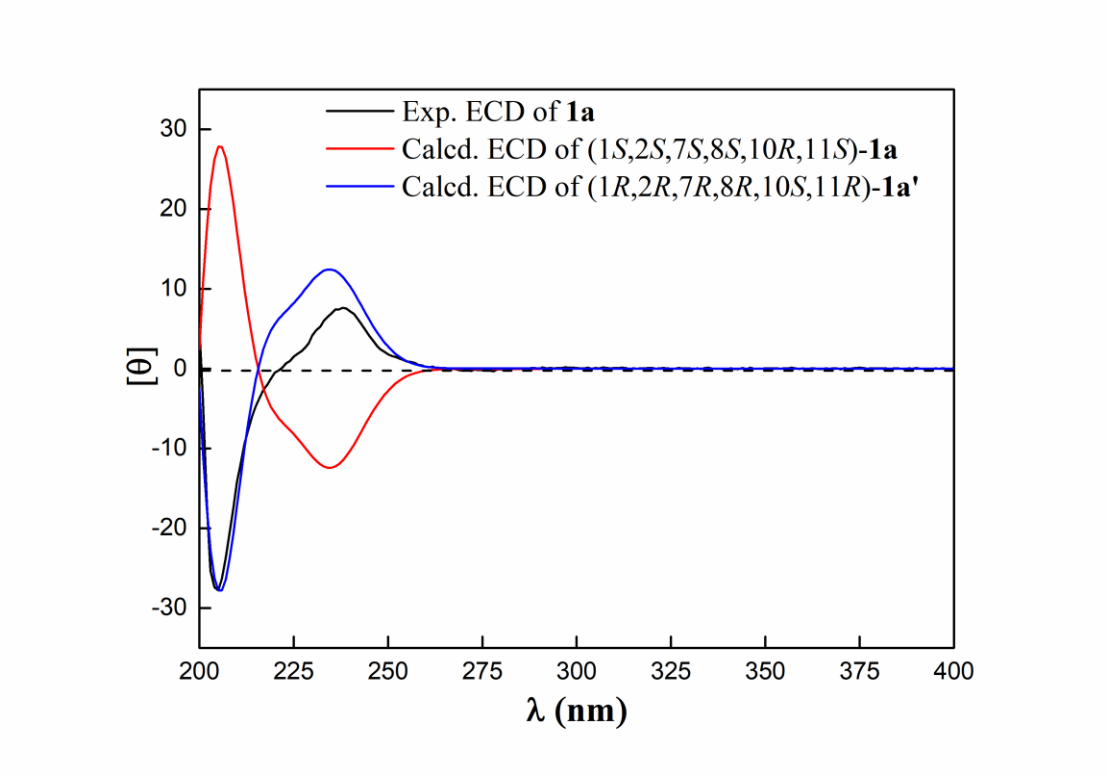


Figure S22 Calculated ECD spectra of compound **1** was compared with the experimental.