Supporting Information

Diterpenoids with novel 6/5-5 spiro tricyclic skeleton from *Orthosiphon wulfenioides* and their NLRP3 inflammasome inhibitory activity

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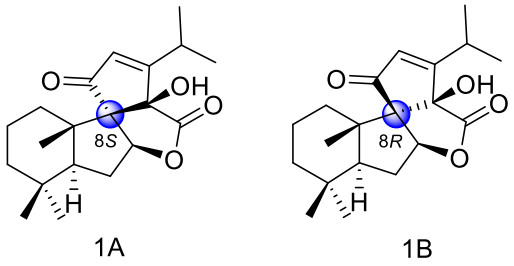

Figure S1. Possible isomers **1A** and **1B** for compound **1**

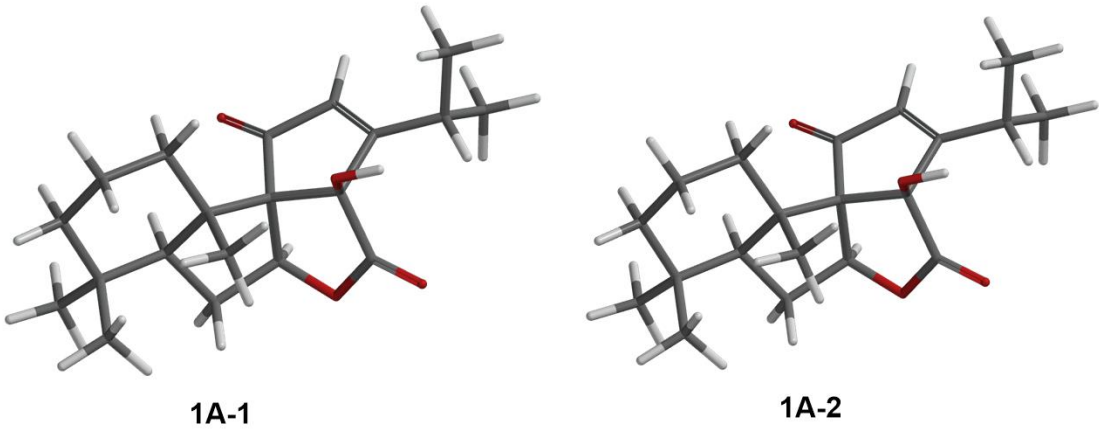

Figure S2. Conformers of isomer **1A**

Table S1. Important thermodynamic parameters and Boltzmann distributions of the optimized isomer **1A** at B3LYP/6-31+ G (d, p) level in gas phase.

Conformations	Energy (a.u)	ΔG(kcal/mol)	%	Number of imaginary frequencies
1A-1	-1079.680290	0	50.1	0
1A-2	-1079.680288	0	49.9	0

Table S2. Optimized Z-matrixes of isomer **1A** in the gas phase (Å) at B3LYP/6-31+ G (d, p) level.

1A-1				**1A-2**			
C	3.08277	-1.34019	1.711662	C	3.082751	-1.34016	1.711686
C	3.943443	-1.15487	0.451776	C	3.943332	-1.15496	0.451738
C	2.071615	0.064263	-0.62393	C	2.071564	0.064246	-0.62392
C	1.148694	-0.12049	0.619327	C	1.148676	-0.12037	0.619367
C	1.576795	-1.38151	1.390263	C	1.57674	-1.38135	1.390416
C	3.599601	0.102223	-0.3908	C	3.599547	0.102143	-0.39085
C	4.137176	1.379703	0.283026	C	4.137146	1.379646	0.282868
C	4.298205	-0.02238	-1.76013	C	4.298149	-0.02254	-1.76017
C	1.160514	1.091317	1.579178	C	1.160394	1.091557	1.579101
C	1.387983	1.185575	-1.424	C	1.387957	1.18558	-1.42399
C	-0.1029	0.850598	-1.27195	C	-0.10292	0.850566	-1.27198
C	-0.23034	-0.20639	-0.11181	C	-0.23033	-0.20637	-0.11175
C	-1.5368	0.241331	0.572235	C	-1.53678	0.241376	0.57223

C	-1.64475	1.722524	0.217976	C	-1.64462	1.72255	0.217999
O	-2.29291	2.537135	0.83626	O	-2.29255	2.537196	0.83651
O	-0.89821	2.008293	-0.86044	O	-0.8983	2.008255	-0.86055
O	-1.63113	0.057223	1.973824	O	-1.63106	0.057401	1.973851
C	-2.63163	-0.6156	-0.08375	C	-2.63161	-0.61553	-0.08382
C	-2.08269	-1.64194	-0.75685	C	-2.08265	-1.64192	-0.75684
C	-0.6144	-1.54901	-0.77366	C	-0.61434	-1.54903	-0.77353
O	0.148337	-2.34486	-1.29727	O	0.148447	-2.34498	-1.29691
C	-4.08521	-0.29571	0.118714	C	-4.08519	-0.29561	0.11853
C	-4.59486	0.585461	-1.04447	C	-4.59491	0.585024	-1.04502
C	-4.9453	-1.55833	0.269765	C	-4.94522	-1.55823	0.270136
H	1.919844	-0.85406	-1.20347	H	1.919703	-0.85409	-1.20344
H	3.297961	-0.54501	2.434945	H	3.298084	-0.54497	2.434913
H	3.368423	-2.27655	2.204675	H	3.368356	-2.27652	2.204732
H	5.00603	-1.12291	0.72491	H	5.005949	-1.12312	0.724772
H	3.811383	-2.03784	-0.18841	H	3.811112	-2.03792	-0.18843
H	0.990251	-1.47651	2.311136	H	0.990256	-1.47617	2.311342
H	1.37845	-2.26773	0.781108	H	1.378258	-2.26763	0.78138
H	3.75745	2.28333	-0.20516	H	3.758245	2.283185	-0.20613
H	5.229846	1.400206	0.204623	H	5.229892	1.399599	0.205375
H	3.89038	1.445275	1.342866	H	3.889431	1.445887	1.34244
H	3.918271	-0.8822	-2.32287	H	3.918331	-0.88248	-2.3228
H	4.149121	0.876203	-2.36899	H	4.14894	0.875941	-2.36915
H	5.377749	-0.15601	-1.62767	H	5.377714	-0.15601	-1.62771
H	2.124435	1.187779	2.072654	H	2.124101	1.187713	2.073064
H	0.962987	2.041396	1.077386	H	0.963427	2.041643	1.077108
H	0.410472	0.952661	2.356761	H	0.409902	0.953212	2.3563
H	1.686375	1.204352	-2.4745	H	1.686364	1.20435	-2.47448
H	1.582587	2.176688	-1.00586	H	1.582575	2.176697	-1.00585
H	-0.5493	0.500268	-2.20534	H	-0.54927	0.500167	-2.20537
H	-2.07353	0.845594	2.331722	H	-2.07472	0.845284	2.331311
H	-2.60558	-2.45202	-1.25048	H	-2.60552	-2.45202	-1.25046
H	-4.16873	0.291749	1.040566	H	-4.16878	0.292238	1.040127
H	-5.63734	0.867387	-0.86615	H	-5.63735	0.867111	-0.86676
H	-4.01399	1.505554	-1.14673	H	-4.01398	1.50503	-1.14778
H	-4.5431	0.035374	-1.98991	H	-4.54325	0.034505	-1.99022
H	-5.98375	-1.28262	0.47789	H	-5.98366	-1.28249	0.478226
H	-4.58407	-2.18718	1.088595	H	-4.58387	-2.18672	1.08919
H	-4.93883	-2.15496	-0.64876	H	-4.93876	-2.15521	-0.64815

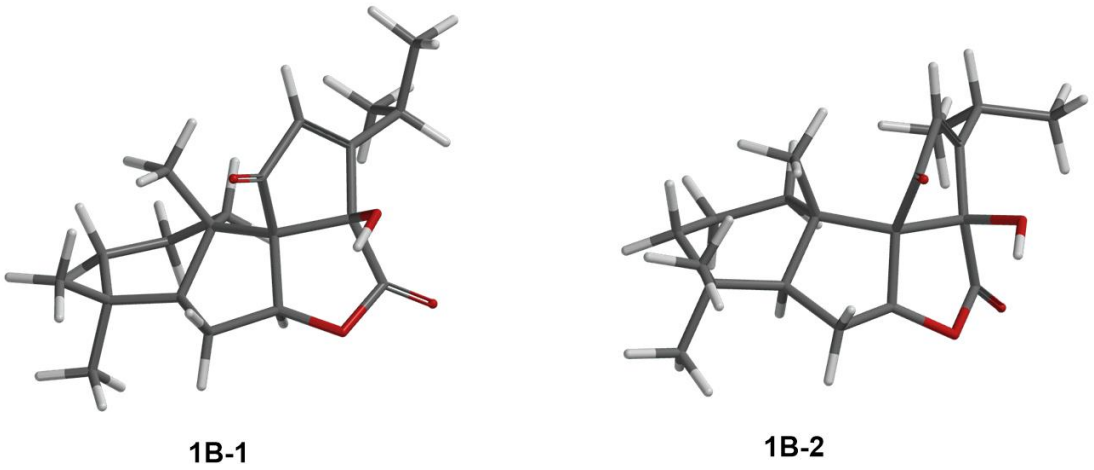

Figure S3. Conformers of isomer **1B**

Table S3. Important thermodynamic parameters and Boltzmann distributions of the optimized isomer **1B** at B3LYP/6-31+ G (d, p) level in gas phase.

Conformations	Energy (a.u)	ΔG(kcal/mol)	%	Number of imaginary frequencies
1B-1	-1079.513778	0	41.0	0
1B-2	-1079.51412	-0.21	59.0	0

Table S4. Optimized Z-matrixes of isomer **1B** in the gas phase (Å) at B3LYP/6-31+ G (d, p) level.

1B-1				**1B-2**			
C	2.178301	-1.72619	-1.80749	C	-2.30866	2.071928	-1.3265
C	3.373828	-1.6275	-0.81725	C	-3.51872	1.613477	-0.46309
C	2.117778	0.404761	-0.18025	C	-2.10725	-0.41198	-0.33671
C	0.858735	-0.55866	0.054363	C	-0.94477	0.543972	0.215007
C	0.751782	-1.35591	-1.26027	C	-0.871	1.676516	-0.82794
C	3.503377	-0.25653	-0.05329	C	-3.54866	0.079972	-0.10583
C	4.51521	0.633439	-0.80724	C	-4.45729	-0.64489	-1.1223
C	4.033138	-0.4419	1.377349	C	-4.1317	-0.17455	1.293105
C	1.037592	-1.59814	1.183397	C	-1.24623	1.219459	1.571509
C	1.752962	1.841208	0.335893	C	-1.63205	-1.90253	-0.2138
C	0.350916	1.732729	-0.24615	C	-0.22909	-1.52983	-0.67055
C	-0.29698	0.534043	0.428461	C	0.290114	-0.5186	0.339123
C	-1.77751	0.800818	0.013916	C	1.80189	-0.55013	-0.04909
C	-1.70712	1.853966	-1.08814	C	1.859632	-1.26135	-1.39816
O	-2.35264	2.074017	-2.06953	O	2.557319	-1.15676	-2.36313
O	-0.68401	2.718918	-0.60525	O	0.89872	-2.29722	-1.22855
O	-2.35445	1.71184	1.043064	O	2.417742	-1.66625	0.724337
C	-2.47622	-0.49074	0.384988	C	2.370531	0.63836	0.701061
C	-1.89962	-0.79815	1.571399	C	1.730642	0.559163	1.89116
C	-0.74634	0.147809	1.878259	C	0.654931	-0.5179	1.86344

O	-0.28512	0.432022	2.960555	O	0.182636	-1.12525	2.79774
C	-3.63173	-1.09677	-0.34529	C	3.493059	1.515764	0.250703
C	-3.21407	-1.45921	-1.78602	C	4.763245	0.684537	-0.01657
C	-4.22665	-2.30035	0.391057	C	3.080716	2.304939	-1.00794
H	2.155508	-2.74358	-2.21143	H	-2.36401	3.159806	-1.43708
H	2.397264	-1.07878	-2.66412	H	-2.44531	1.670455	-2.33695
H	4.291467	-1.79702	-1.39276	H	-4.43073	1.862796	-1.0181
H	3.332021	-2.44943	-0.09861	H	-3.57053	2.207864	0.45225
H	2.100586	0.575046	-1.25961	H	-2.04486	-0.27641	-1.41928
H	0.152526	-2.25798	-1.09732	H	-0.35896	2.543108	-0.39659
H	0.229149	-0.7701	-2.02624	H	-0.27732	1.365326	-1.69612
H	4.59831	1.624049	-0.34784	H	-4.46644	-1.72663	-0.95205
H	5.509933	0.175625	-0.79164	H	-5.48823	-0.28613	-1.03415
H	4.225179	0.770138	-1.85554	H	-4.12725	-0.46746	-2.1525
H	3.407157	-1.09228	1.986612	H	-3.58209	0.33035	2.086226
H	5.037829	-0.87918	1.349726	H	-5.16969	0.175151	1.334221
H	4.108165	0.525153	1.886829	H	-4.13565	-1.24689	1.517648
H	1.790424	-2.33162	0.911888	H	-2.05224	1.939453	1.46892
H	1.314787	-1.16241	2.140566	H	-1.51174	0.519801	2.360636
H	0.107742	-2.15627	1.318999	H	-0.37269	1.788696	1.899414
H	2.384315	2.60383	-0.12414	H	-2.18032	-2.55438	-0.89666
H	1.754505	1.948296	1.423289	H	-1.65508	-2.3058	0.801438
H	0.539984	1.358784	-1.25675	H	-0.42014	-0.90754	-1.5497
H	-1.91646	2.577317	0.978755	H	2.05346	-2.50897	0.404732
H	-2.21304	-1.56307	2.271768	H	1.956177	1.12773	2.786814
H	-4.39823	-0.3105	-0.41736	H	3.698469	2.227468	1.060186
H	-4.07372	-1.85088	-2.33854	H	5.586089	1.346778	-0.30492
H	-2.83883	-0.58434	-2.32423	H	5.061202	0.120846	0.871384
H	-2.43354	-2.22773	-1.77892	H	4.596525	-0.0255	-0.83209
H	-5.08079	-2.69995	-0.16358	H	3.894004	2.968333	-1.31892
H	-4.5705	-2.0274	1.393362	H	2.191109	2.914824	-0.82363
H	-3.48625	-3.10256	0.489906	H	2.86883	1.622755	-1.83807

Table S5. Experimental and calculated ^{13}C NMR data for compound **1A** (Δ in ppm)

		1A (gas phase)				**1A (PCM)**			
NO.	δe(exp)	δu(unsacled)	δs(sacled)	δu-δe	δs-δe	δu(unsacled)	δs(sacled)	δu-δe	δs-δe
1	31.9	32.3008	32.9431	0.4008	1.0431	33.3024	33.9647	1.4024	2.0647
2	19	21.9772	22.4143	2.9772	3.4143	22.4051	22.8506	3.4051	3.8506
3	40.4	40.5021	41.3076	0.1021	0.9076	41.1735	41.9923	0.7735	1.5923
4	33.1	36.0196	36.7360	2.9196	3.6360	36.7204	37.4507	3.6204	4.3507
5	52.6	52.4447	53.4877	-0.1553	0.8877	53.4415	54.5043	0.8415	1.9043
6	30.3	31.7388	32.3700	1.4388	2.0700	32.2433	32.8845	1.9433	2.5845

7	85.1	86.5693	88.2910	1.4693	3.1910	87.5816	89.3235	2.4816	4.2235
8	68.3	69.7779	71.1656	1.4779	2.8656	70.8134	72.2217	2.5134	3.9217
9	45.3	48.9450	49.9184	3.6450	4.6184	49.6829	50.6710	4.3829	5.3710
10	203.8	201.0637	205.0624	-2.7363	1.2624	203.3524	207.3966	-0.4476	3.5966
11	127.8	124.1684	126.6378	-3.6316	-1.1622	125.5617	128.0589	-2.2383	0.2589
12	179.5	182.9270	186.5650	3.4270	7.0650	184.9751	188.6539	5.4751	9.1539
13	85.5	86.3601	88.0776	0.8601	2.5776	87.3040	89.0402	1.8040	3.5402
14	175.6	173.8034	177.2599	-1.7966	1.6599	175.6099	179.1024	0.0099	3.5024
15	27.2	30.3813	30.9855	3.1813	3.7855	31.3402	31.9635	4.1402	4.7635
16	22.8	24.6703	25.1610	1.8703	2.3610	24.8720	25.3666	2.0720	2.5666
17	22.9	22.1259	22.5660	-0.7741	-0.3340	22.3783	22.8234	-0.5217	-0.0766
18	34	33.4670	34.1326	-0.5330	0.1326	33.8242	34.4968	-0.1758	0.4968
19	22.1	22.7745	23.2274	0.6745	1.1274	23.1837	23.6448	1.0837	1.5448
20	16.2	16.1710	16.4926	-0.0290	0.2926	16.6784	17.0100	0.4784	0.8100
		MAE = 2.07, and CMAE = 0.74 ppm. R^2 = 0.9990				MAE = 3.00, and CMAE =1.65 ppm. R^2 = 0.9989			

Table S6. Experimental and calculated ^{13}C NMR data for compound **1B** (Δ in ppm)

		1B (gas phase)				**1B (PCM)**			
NO.	δe(exp)	δu(unsacled)	δs(sacled)	δu-δe	δs-δe	δu(unsacled)	δs(sacled)	δu-δe	δs-δe
1	31.9	38.4728	39.2379	6.5728	7.3379	38.6888	39.4582	6.7888	7.5582
2	19	23.8331	24.3071	4.8331	5.3071	24.2430	24.7251	5.2430	5.7251
3	40.4	41.4318	42.2558	1.0318	1.8558	41.8837	42.7166	1.4837	2.3166
4	33.1	39.6545	40.4431	6.5545	7.3431	40.4373	41.2415	7.3373	8.1415
5	52.6	64.3267	65.6060	11.7267	13.0060	64.3961	65.6768	11.7961	13.0768
6	30.3	28.8953	29.4700	-1.4047	-0.8300	29.7344	30.3257	-0.5657	0.0257
7	85.1	88.9202	90.6886	3.8202	5.5886	89.7270	91.5115	4.6270	6.4115
8	68.3	82.8889	84.5373	14.5889	16.2373	84.5926	86.2749	16.2926	17.9749
9	45.3	53.1488	54.2058	7.8488	8.9058	54.3955	55.4773	9.0955	10.1773
10	203.8	189.1033	192.8642	-14.6967	-10.9358	192.7415	196.5747	-11.0585	-7.2253
11	127.8	138.4043	141.1569	10.6043	13.3569	138.9320	141.6951	11.1320	13.8951
12	179.5	166.2388	169.5449	-13.2612	-9.9551	168.5058	171.8570	-10.9942	-7.6430
13	85.5	93.7152	95.5790	8.2152	10.0790	94.6738	96.5566	9.1738	11.0566
14	175.6	167.4266	170.7564	-8.1734	-4.8436	169.6705	173.0449	-5.9295	-2.5551
15	27.2	36.7267	37.4571	9.5267	10.2571	37.2865	38.0280	10.0865	10.8280
16	22.8	24.7412	25.2332	1.9412	2.4332	25.2253	25.7270	2.4253	2.9270
17	22.9	23.5896	24.0588	0.6896	1.1588	23.8777	24.3525	0.9777	1.4525
18	34	27.5129	28.0600	-6.4871	-5.9400	27.8182	28.3715	-6.1818	-5.6285
19	22.1	35.4180	36.1224	13.3180	14.0224	35.5508	36.2578	13.4508	14.1578
20	16.2	29.8841	30.4784	13.6841	14.2784	30.2610	30.8628	14.0610	14.6628
		MAE = 4.93, and CMAE =3.55 ppm. R^2 = 0.9842				MAE =5.87, and CMAE =4.46 ppm. R^2 = 0.9851			

Table S7. Experimental chemical shifts of compound **1**, calculated shielding tensors and chemical shifts of isomer **1** in gas phase with TMS as reference.

		1A-1		**1A-2**		**1B-1**		**1B-2**	
Nuclie	exptl.	σiso	*Δ*	σiso	*Δ*	σiso	*Δ*	σiso	*Δ*
1	31.9	163.94	32.30	163.94	32.30	160.54	35.70	155.84	40.40
2	19	174.26	21.98	174.26	21.98	175.15	21.09	170.50	25.74
3	40.4	155.74	40.50	155.74	40.50	157.72	38.52	152.79	43.45
4	33.1	160.22	36.02	160.22	36.02	159.77	36.47	154.37	41.87
5	52.6	143.79	52.45	143.80	52.44	135.08	61.16	129.71	66.53
6	30.3	164.50	31.74	164.50	31.74	169.48	26.76	165.86	30.38
7	85.1	109.67	86.57	109.67	86.57	110.49	85.75	105.12	91.12
8	68.3	126.46	69.78	126.46	69.78	116.33	79.91	111.28	84.96
9	45.3	147.29	48.95	147.30	48.94	146.31	49.93	140.85	55.39
10	203.8	-4.82	201.06	-4.82	201.06	9.57	186.67	5.44	190.80
11	127.8	72.07	124.17	72.07	124.17	59.85	136.39	56.44	139.80
12	179.5	13.31	182.93	13.32	182.93	32.04	164.20	28.58	167.66
13	85.5	109.88	86.36	109.88	86.36	105.16	91.08	100.69	95.55
14	175.6	22.44	173.80	22.44	173.80	31.03	165.21	27.27	168.97
15	27.2	165.86	30.38	165.86	30.38	164.46	31.78	156.08	40.17
16	22.8	171.57	24.67	171.57	24.67	173.69	22.55	169.98	26.26
17	22.9	174.12	22.12	174.11	22.13	177.03	19.21	169.61	26.63
18	34	162.77	33.47	162.77	33.47	170.88	25.36	167.23	29.01
19	22.1	173.47	22.77	173.47	22.78	163.09	33.15	159.25	36.99
20	16.2	180.07	16.17	180.07	16.17	168.74	27.50	164.70	31.54
H-1α	1.95	29.55	2.05	29.55	2.05	30.11	1.48	30.12	1.48
H-1β	1.53	30.10	1.49	30.10	1.49	30.28	1.32	30.31	1.29
H-2α	1.44	30.26	1.34	30.26	1.34	30.32	1.28	30.38	1.21
H-2β	1.63	29.87	1.73	29.87	1.73	29.85	1.75	29.86	1.74
H-3α	1.45	30.27	1.32	30.27	1.32	29.78	1.81	29.83	1.76
H-3β	1.26	30.29	1.31	30.29	1.31	29.65	1.94	29.68	1.92
H-5	2.3	28.93	2.67	28.93	2.67	30.12	1.47	30.15	1.44
H-6α	2.26	29.50	2.09	29.50	2.09	29.71	1.88	29.81	1.79
H-6β	1.81	29.73	1.87	29.73	1.87	29.18	2.42	29.27	2.33
H-7α	4.43	27.35	4.25	27.35	4.25	27.26	4.34	27.29	4.31
H-11	5.99	25.56	6.03	25.56	6.03	25.55	6.04	25.70	5.89
H-15	2.76	28.88	2.72	28.88	2.71	28.69	2.90	29.04	2.55
H-16a	1.12	30.42	1.18	30.42	1.18	30.41	1.19	30.58	1.01
H-16b		30.38	1.22	30.38	1.22	29.81	1.78	30.42	1.17
H-16c		31.01	0.58	31.01	0.58	30.96	0.63	30.00	1.59
H-17a	1.27	30.43	1.17	30.43	1.17	30.50	1.10	30.46	1.14
H-17b		30.40	1.20	30.40	1.20	30.26	1.33	30.69	0.91
H-17c		30.38	1.22	30.38	1.22	30.64	0.95	30.23	1.36
H-18a	0.92	30.89	0.70	30.89	0.70	30.29	1.31	30.35	1.25

H-18b		30.50	1.10	30.50	1.10	30.82	0.78	30.88	0.71
H-18c		30.87	0.72	30.87	0.72	30.70	0.89	30.77	0.82
H-19a	0.94	30.62	0.98	30.62	0.98	30.40	1.20	30.44	1.15
H-19b		31.10	0.49	31.10	0.49	30.89	0.70	30.96	0.64
H-19c		30.28	1.32	30.28	1.32	30.58	1.02	30.64	0.96
H-20a	1.18	30.31	1.28	30.31	1.28	30.33	1.26	30.41	1.18
H-20b		30.96	0.64	30.96	0.64	30.15	1.45	30.16	1.44
H-20c		29.91	1.69	29.91	1.69	30.70	0.89	30.82	0.77
OH	2.96	28.83	2.76	28.83	2.76	27.88	3.72	27.86	3.73

Table S8. Experimental chemical shifts of compound **1**, calculated shielding tensors and chemical shifts of isomer **1** in chloroform with TMS as reference.

		1A-1		**1A-2**		**1B-1**		**1B-2**	
Nuclie	exptl.	σ iso	Δ	σ iso	Δ	σ iso	Δ	σ iso	Δ
1	31.9	163.57	33.30	163.57	33.30	160.96	35.91	156.26	40.62
2	19	174.47	22.41	174.47	22.41	175.39	21.48	170.71	26.16
3	40.4	155.70	41.17	155.70	41.17	157.92	38.96	152.96	43.92
4	33.1	160.15	36.72	160.15	36.72	159.62	37.25	154.22	42.65
5	52.6	143.43	53.44	143.43	53.44	135.64	61.23	130.28	66.60
6	30.3	164.63	32.24	164.63	32.24	169.28	27.60	165.65	31.22
7	85.1	109.29	87.58	109.29	87.58	110.31	86.56	104.95	91.93
8	68.3	126.06	70.82	126.06	70.81	115.28	81.60	110.20	86.67
9	45.3	147.19	49.69	147.19	49.68	145.70	51.17	140.24	56.64
10	203.8	-6.48	203.35	-6.48	203.35	6.58	190.29	2.43	194.44
11	127.8	71.31	125.56	71.31	125.56	60.00	136.88	56.51	140.36
12	179.5	11.90	184.98	11.90	184.97	30.34	166.53	27.00	169.88
13	85.5	109.57	87.31	109.57	87.30	104.83	92.05	100.38	96.50
14	175.6	21.26	175.61	21.26	175.61	29.38	167.50	25.69	171.18
15	27.2	165.53	31.34	165.54	31.34	164.09	32.79	156.46	40.41
16	22.8	172.00	24.87	172.00	24.87	174.13	22.74	169.92	26.95
17	22.9	174.50	22.38	174.49	22.38	177.44	19.43	169.91	26.97
18	34	163.05	33.83	163.05	33.82	171.22	25.65	167.55	29.32
19	22.1	173.47	23.41	173.92	22.96	163.61	33.27	159.74	37.14
20	16.2	180.20	16.68	180.20	16.68	169.01	27.86	164.95	31.93
H-1α	1.95	29.64	1.95	29.64	1.95	30.04	1.55	30.04	1.55
H-1β	1.53	30.13	1.46	30.13	1.46	30.21	1.38	30.25	1.34
H-2α	1.44	30.24	1.35	30.24	1.35	30.27	1.32	30.34	1.25
H-2β	1.63	29.81	1.78	29.81	1.78	29.78	1.81	29.79	1.79
H-3α	1.45	30.34	1.25	30.33	1.25	29.65	1.94	29.70	1.89
H-3β	1.26	30.23	1.36	30.23	1.36	29.63	1.96	29.66	1.93
H-5	2.3	29.04	2.55	29.04	2.55	30.08	1.51	30.12	1.47
H-6α	2.26	29.36	2.23	29.36	2.23	29.56	2.03	29.66	1.93

H-6β	1.81	29.69	1.90	29.69	1.90	29.25	2.33	29.34	2.25
H-7α	4.43	27.15	4.44	27.15	4.44	27.09	4.50	27.11	4.48
H-11	5.99	25.40	6.19	25.40	6.19	25.43	6.16	25.57	6.01
H-15	2.76	28.83	2.76	28.83	2.76	28.68	2.91	28.87	2.72
H-16a	1.12	30.33	1.26	30.33	1.26	30.32	1.26	30.45	1.14
H-16b		30.51	1.08	30.51	1.08	29.95	1.64	30.49	1.09
H-16c		30.89	0.70	30.89	0.70	30.81	0.78	30.20	1.39
H-17a	1.27	30.35	1.24	30.35	1.24	30.43	1.16	30.39	1.20
H-17b		30.44	1.15	30.44	1.15	30.27	1.32	30.56	1.03
H-17c		30.27	1.32	30.27	1.32	30.55	1.04	30.36	1.23
H-18a	0.92	30.94	0.65	30.94	0.65	30.32	1.27	30.38	1.21
H-18b		30.43	1.15	30.43	1.15	30.79	0.80	30.86	0.72
H-18c		30.85	0.74	30.85	0.74	30.72	0.87	30.79	0.80
H-19a	0.94	30.57	1.01	30.57	1.01	30.39	1.20	30.44	1.15
H-19b		31.08	0.51	31.08	0.51	30.88	0.71	30.95	0.64
H-19c		30.27	1.32	30.27	1.32	30.51	1.08	30.58	1.01
H-20a	1.18	30.23	1.35	30.23	1.35	30.18	1.40	30.27	1.32
H-20b		30.95	0.64	30.95	0.64	30.30	1.29	30.32	1.27
H-20c		29.93	1.66	29.93	1.66	30.66	0.93	30.78	0.81
OH	2.96	28.58	3.01	28.57	3.02	27.72	3.87	27.71	3.88

Functional	Solvent?	Basis Set	Type of Data
mPW1PW91	PCM	6-31+G(d,p)	Unscaled Shifts

	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5	Isomer 6
sDP4+ (H data)	100.00%	0.00%	–	–	–	–
sDP4+ (C data)	100.00%	0.00%	–	–	–	–
sDP4+ (all data)	100.00%	0.00%	–	–	–	–
uDP4+ (H data)	100.00%	0.00%	–	–	–	–
uDP4+ (C data)	100.00%	0.00%	–	–	–	–
uDP4+ (all data)	100.00%	0.00%	–	–	–	–
DP4+ (H data)	100.00%	0.00%	–	–	–	–
DP4+ (C data)	100.00%	0.00%	–	–	–	–
DP4+ (all data)	100.00%	0.00%	–	–	–	–

Figure. S4. Detailed DP4+ probability of compound **1** (calculated at mPW1PW91/6-31G (d, p) level in gas with PCM model.

Functional	Solvent?	Basis Set	Type of Data
mPW1PW91	Gas Phase	6-31+G(d,p)	Unscaled Shifts

	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5	Isomer 6
sDP4+ (H data)	100.00%	0.00%	–	–	–	–
sDP4+ (C data)	100.00%	0.00%	–	–	–	–
sDP4+ (all data)	100.00%	0.00%	–	–	–	–
uDP4+ (H data)	100.00%	0.00%	–	–	–	–
uDP4+ (C data)	100.00%	0.00%	–	–	–	–
uDP4+ (all data)	100.00%	0.00%	–	–	–	–
DP4+ (H data)	100.00%	0.00%	–	–	–	–
DP4+ (C data)	100.00%	0.00%	–	–	–	–
DP4+ (all data)	100.00%	0.00%	–	–	–	–

Figure. S5. Detailed DP4+ probability of compound **1** (calculated at mPW1PW91/6-31G (d, p) level in chloroform with PCM model.

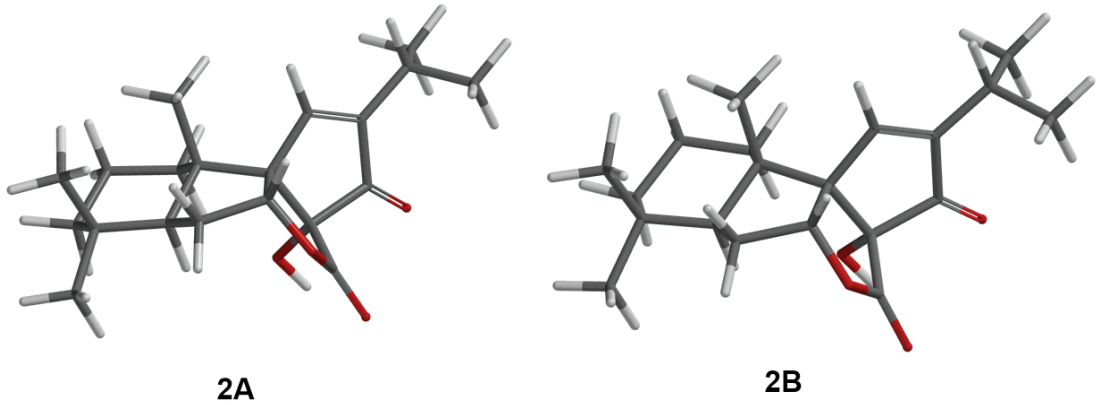

Figure S6. Possible conformers of **2** for ECD calculation.

Table S9. Important thermodynamic parameters and Boltzmann distributions of the optimized isomer **2** at B3LYP/6-31 + G (d, p) level in the gas phase.

Conformations	Energy (a.u)	ΔG(kcal/mol)	%	Number of imaginary frequencies
2A	-1079.574196	0	72.6	0
2B	-1079.573275	0.58	27.4	0

Table S10. Optimized Z-matrixes of compound **2** in the gas phase (Å) at B3LYP/6-31+ G (d, p) level

2A				**2B**			
C	2.375072	-2.144281	1.415352	C	-2.518732	-2.244428	1.138663
C	3.457398	-1.049382	1.382599	C	-3.521408	-1.089087	1.309422
C	2.071052	0.244816	-0.232781	C	-2.107397	0.330796	-0.171744
C	0.934553	-0.827411	-0.207758	C	-1.046763	-0.804652	-0.344679
C	0.962594	-1.586788	1.134051	C	-1.081197	-1.745381	0.876584
C	3.52254	-0.228337	0.063153	C	-3.57665	-0.085371	0.121528
C	4.203231	-1.045816	-1.057634	C	-4.351001	-0.68836	-1.071269

C	4.397631	1.022062	0.309592	C	-4.352776	1.170019	0.580463
C	1.003153	-1.855055	-1.366308	C	-1.224024	-1.654015	-1.630446
C	1.77278	1.076777	-1.495795	C	-1.796028	1.30904	-1.320999
C	0.232049	1.081529	-1.588226	C	-0.262308	1.233008	-1.474998
C	-0.311166	0.10616	-0.488172	C	0.24978	0.078122	-0.547379
C	-0.847836	1.059897	0.625478	C	0.889687	0.825588	0.664611
C	-2.26286	0.534232	0.938851	C	2.27834	0.173284	0.838509
C	-2.668886	-0.378155	-0.138004	C	2.586894	-0.586079	-0.382533
C	-1.587229	-0.586106	-0.921612	C	1.460776	-0.619546	-1.129043
C	-4.063554	-0.943921	-0.245747	C	3.921086	-1.215232	-0.70456
C	-4.40006	-1.43755	-1.65976	C	5.042794	-0.159293	-0.76787
C	-4.276583	-2.06081	0.800616	C	4.268506	-2.345515	0.286237
O	-2.864073	0.861765	1.953054	O	2.916021	0.298554	1.87527
C	-0.927039	2.435188	-0.086495	C	1.035872	2.281453	0.15274
O	-1.410881	3.448206	0.370067	O	1.602043	3.186307	0.726794
O	-0.330434	2.394077	-1.286761	O	0.396456	2.451125	-1.014128
O	-0.10975	1.233246	1.815332	O	0.210301	0.870856	1.899779
H	1.841181	0.894588	0.62061	H	-1.802826	0.839425	0.751542
H	2.621183	-2.940399	0.702494	H	-2.84607	-2.911443	0.332277
H	2.378028	-2.618438	2.40421	H	-2.520568	-2.855438	2.049427
H	4.442259	-1.494372	1.576423	H	-4.527452	-1.492695	1.483866
H	3.265248	-0.350715	2.20935	H	-3.250772	-0.529062	2.216028
H	0.231007	-2.404646	1.126032	H	-0.410761	-2.599733	0.718945
H	0.686078	-0.910615	1.946236	H	-0.728021	-1.213928	1.763075
H	4.128878	-0.543258	-2.02798	H	-4.282943	-0.052603	-1.960512
H	5.269405	-1.15587	-0.828133	H	-5.412222	-0.770544	-0.809379
H	3.796187	-2.052013	-1.170707	H	-4.012767	-1.687933	-1.349045
H	3.95479	1.675786	1.070052	H	-3.839517	1.678841	1.404741
H	5.394333	0.727557	0.65858	H	-4.473473	1.888746	-0.23795
H	4.528085	1.608581	-0.606968	H	-5.354834	0.892872	0.928231
H	1.000064	-1.391999	-2.357536	H	-2.144552	-2.23366	-1.603357
H	1.898721	-2.4691	-1.302617	H	-1.245267	-1.055977	-2.546365
H	0.149041	-2.53699	-1.31473	H	-0.403948	-2.372512	-1.719655
H	2.153393	2.099954	-1.439402	H	-2.107373	2.336158	-1.112958
H	2.192362	0.622655	-2.398125	H	-2.272926	1.008412	-2.258339
H	-0.134258	0.84321	-2.587886	H	0.055348	1.118794	-2.512532
H	-1.603867	-1.1903	-1.821655	H	1.411773	-1.097412	-2.102312
H	-4.752513	-0.126065	0.006424	H	3.82318	-1.662475	-1.701634
H	-5.443694	-1.764614	-1.70179	H	5.985606	-0.633646	-1.059617
H	-4.26124	-0.647787	-2.405431	H	4.81333	0.61989	-1.502052
H	-3.775063	-2.291496	-1.945108	H	5.1921	0.319252	0.205367
H	-5.314941	-2.407309	0.772012	H	5.210577	-2.820052	-0.007966
H	-4.063244	-1.708019	1.813613	H	3.489369	-3.114532	0.298412

H	-3.62451	-2.915546	0.588523	H	4.384966	-1.957457	1.302595
H	-0.756851	1.446577	2.511566	H	0.898774	0.917848	2.588004

Table S11. Key transitions, oscillator strengths, and rotatory strengths in the ECD spectra of conformers **2A** at the B3LYP/6-31 + G (d, p) level in MeOH with PCM.

Num	*Exited states*	*CI Coefficient*	*ΔE (eV)*	*λ (nm)*	*f*	*R(vel)*	*R(len)*
1	90 -> 91	0.68854	3.7506	330.57	0.0031	1.1290	0.8739
2	85 -> 91	-0.11957	4.5610	271.84	0.0596	-63.2649	-65.2745
	87 -> 91	-0.33194					
	88 -> 91	0.18138					
	89 -> 91	0.54876					
3	87 -> 91	-0.37692	4.7198	262.69	0.0723	-25.4010	-26.3873
	88 -> 91	0.41571					
	89 -> 91	-0.39282					
4	87 -> 91	0.44646	4.9223	251.88	0.0159	15.9468	16.7064
	88 -> 91	0.52501					
	89 -> 91	0.10716					
5	84 -> 91	-0.13039	5.2027	238.31	0.0037	-0.8148	-1.0630
	85 -> 91	-0.14670					
	86 -> 91	0.62950					
	90 -> 92	-0.17213					
6	83 -> 91	-0.14746	5.3194	233.08	0.0053	12.6055	14.4323
	85 -> 91	0.39348					
	85 -> 92	-0.12980					
	86 -> 91	0.26500					
	87 -> 91	-0.16009					
	87 -> 92	-0.21283					
	88 -> 92	0.10387					
	90 -> 92	0.32561					
7	85 -> 91	-0.45442	5.4441	227.74	0.0102	11.0716	10.2373
	90 -> 92	0.51116					
8	84 -> 91	0.66078	5.4756	226.43	0.0133	25.9151	26.8282
	86 -> 91	0.12162					
9	83 -> 91	-0.28613	5.6326	220.12	0.0129	-17.7370	-18.6423
	85 -> 91	-0.18426					
	85 -> 92	-0.12761					
	87 -> 92	-0.25494					
	88 -> 92	0.17851					
	89 -> 92	0.42162					
	90 -> 92	-0.20252					
10	83 -> 91	0.49923	5.7578	215.33	0.0285	-22.4658	-23.3540
	89 -> 92	0.44486					
11	79 -> 91	0.10299	5.9170	209.54	0.0724	60.7137	61.7753

	83 -> 91	-0.34285					
	85 -> 92	0.13880					
	87 -> 92	0.34972					
	88 -> 92	-0.24362					
	89 -> 92	0.30840					
	90 -> 92	0.16689					
12	80 -> 91	0.27808	5.9706	207.66	0.0152	17.1066	16.8753
	81 -> 91	0.20178					
	82 -> 91	0.58168					
	85 -> 91	0.11254					
13	80 -> 91	0.51087	6.0096	206.31	0.0010	-1.6082	-1.6473
	81 -> 91	0.30454					
	82 -> 91	-0.34134					
14	77 -> 91	0.19315	6.0673	204.35	0.0096	5.1855	4.8184
	78 -> 91	0.39314					
	79 -> 91	0.28073					
	80 -> 91	-0.24486					
	81 -> 91	0.25931					
	83 -> 91	-0.12264					
	85 -> 91	-0.12978					
	87 -> 92	-0.12040					
	88 -> 92	0.12590					
15	75 -> 91	0.10509	6.2008	199.95	0.0051	-10.8210	-11.7822
	79 -> 91	0.28285					
	80 -> 91	0.11973					
	81 -> 91	-0.21689					
	87 -> 92	0.22497					
	88 -> 92	0.51627					
16	75 -> 91	0.12229	6.2296	199.02	0.0077	6.5419	6.7815
	77 -> 91	0.12152					
	79 -> 91	0.40779					
	80 -> 91	0.13400					
	81 -> 91	-0.30331					
	87 -> 92	-0.27090					
	88 -> 92	-0.30913					
17	75 -> 91	-0.19227	6.3102	196.48	0.0012	-2.5279	-2.0594
	77 -> 91	0.17826					
	78 -> 91	0.43347					
	79 -> 91	-0.21880					
	80 -> 91	0.21324					
	81 -> 91	-0.36194					
18	77 -> 91	0.58772	6.4455	192.36	0.0010	6.1099	5.9449
	78 -> 91	-0.26145					

	86 -> 92	-0.17537					
19	77 -> 91	0.15097	6.5009	190.72	0.0161	-1.0888	-1.5062
	85 -> 92	-0.12204					
	86 -> 92	0.65384					
20	77 -> 91	-0.10291	6.5444	189.45	0.0112	5.9038	5.4923
	85 -> 92	-0.14662					
	87 -> 92	0.10856					
	90 -> 93	0.54211					
	90 -> 94	-0.30354					
	90 -> 95	0.12527					

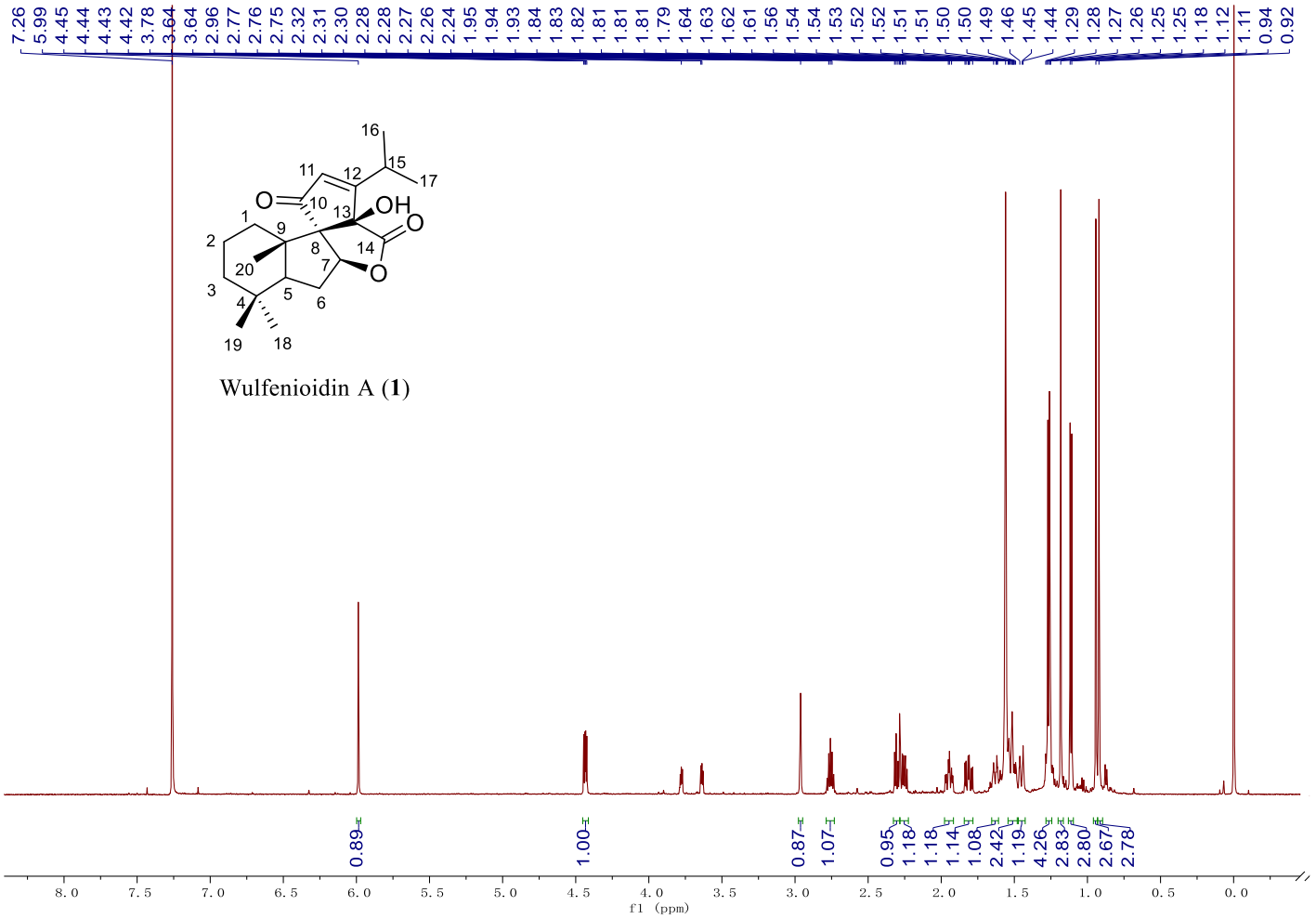

Figure S7. ^{1}H NMR spectrum of wulfenioidin **A** (**1**) in chloroform (600 MHz)

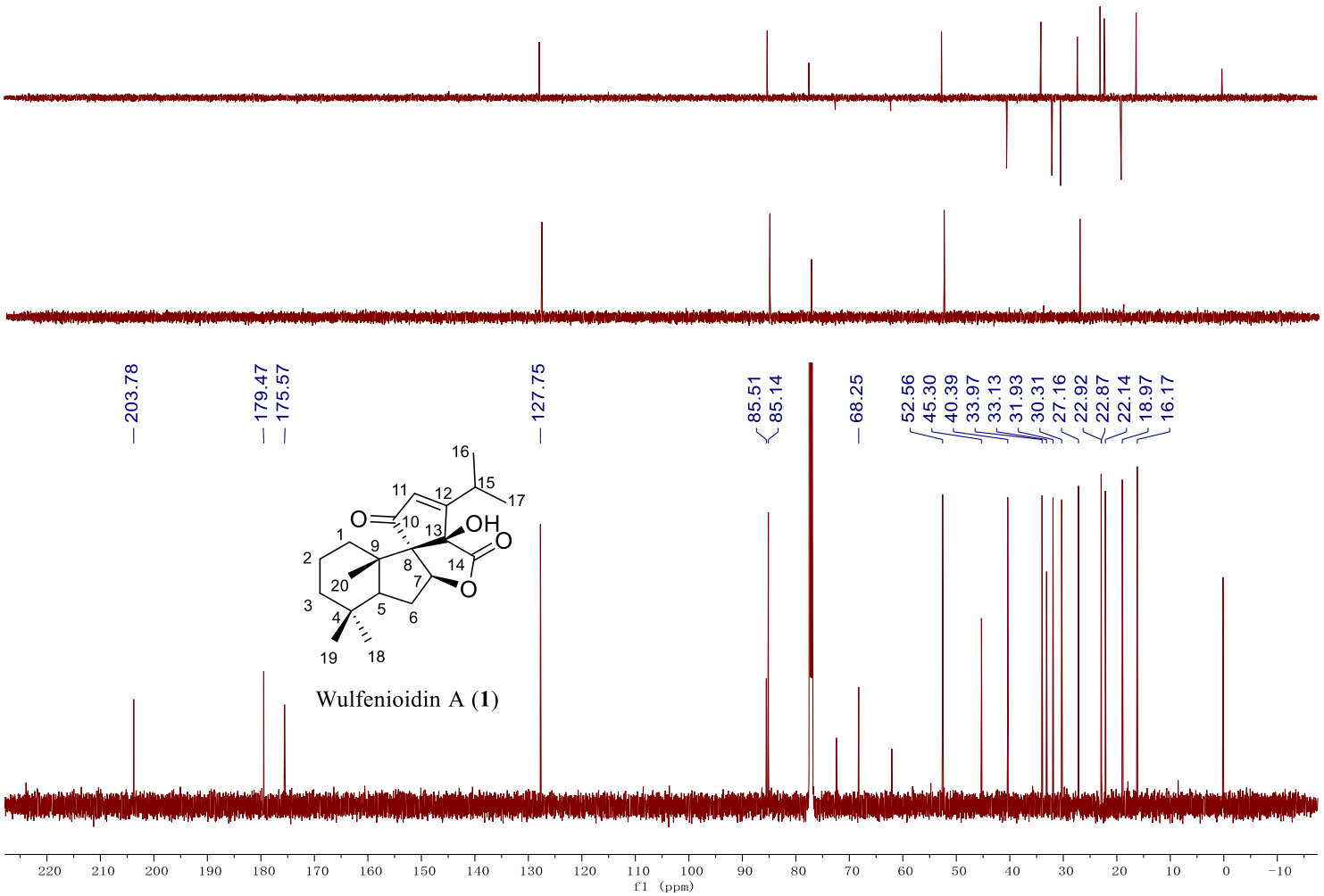

Figure S8. ^{13}C and DEPT NMR spectra of wulfenioidin **A** (**1**) in chloroform (150 MHz)

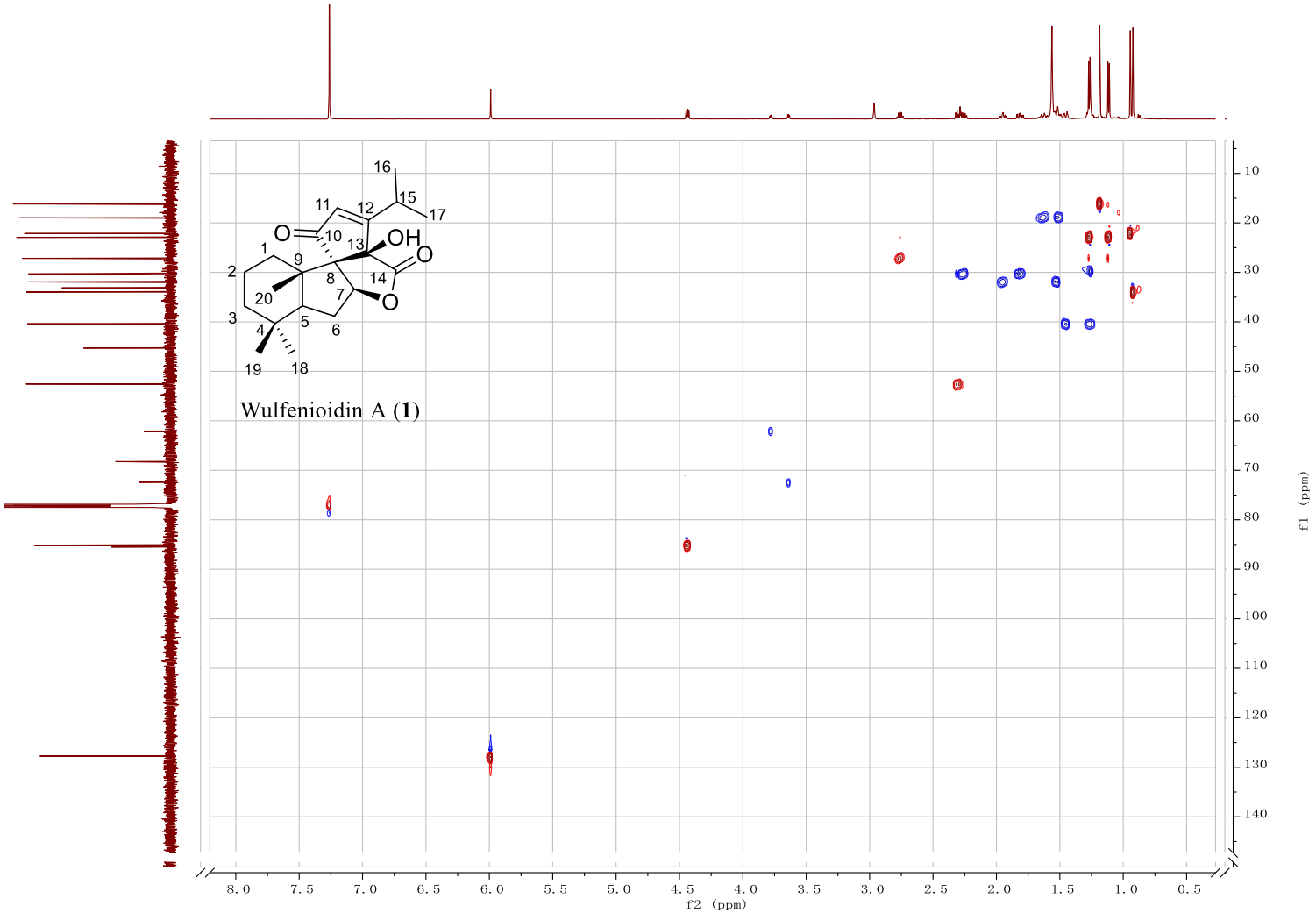

Figure S9. HSQC spectrum of wulfenioidin **A** (**1**) in chloroform (600 MHz)

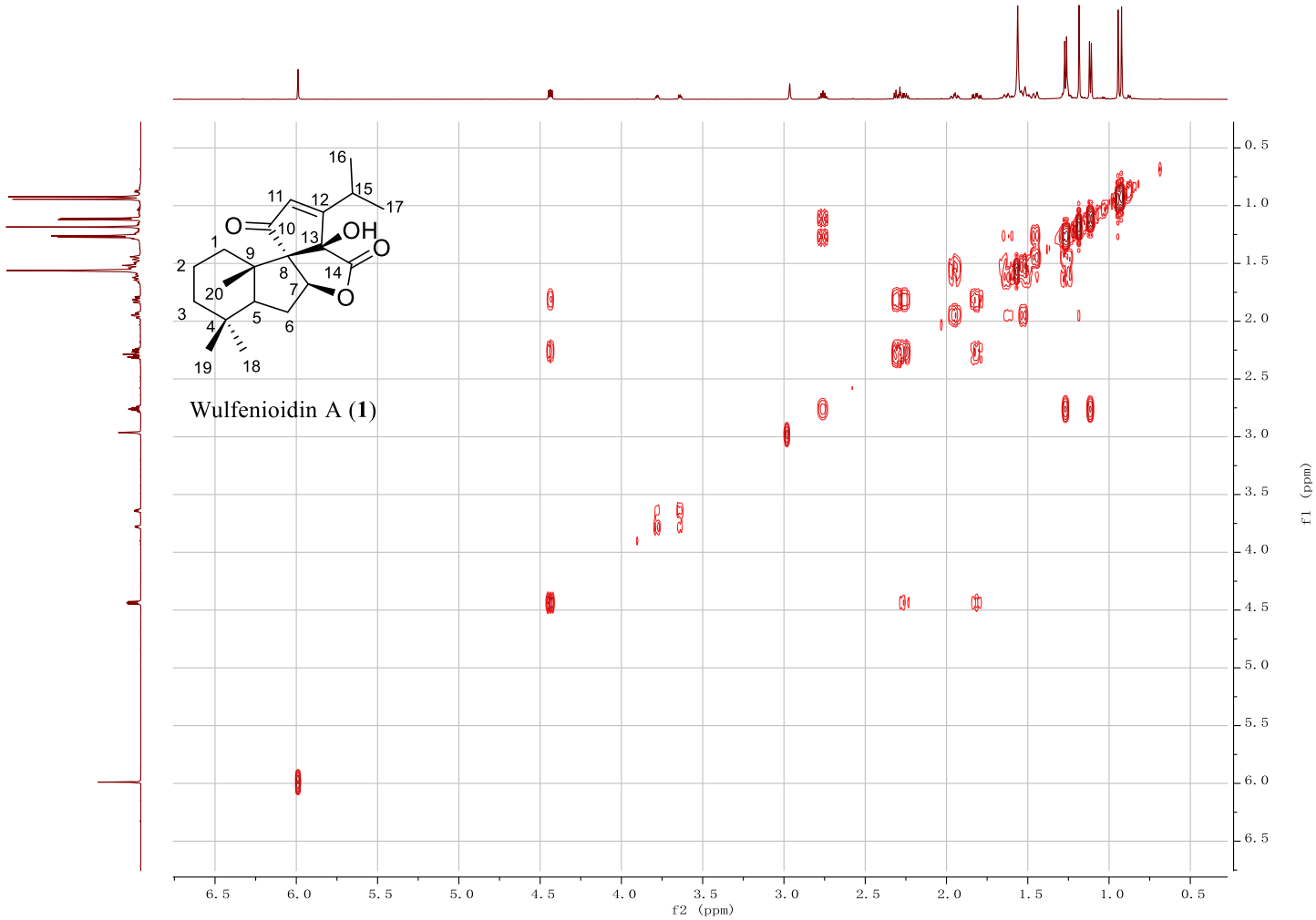

Figure S10. ^{1}H-^{1}H COSY spectrum of wulfenioidin **A** (**1**) in chloroform (600 MHz)

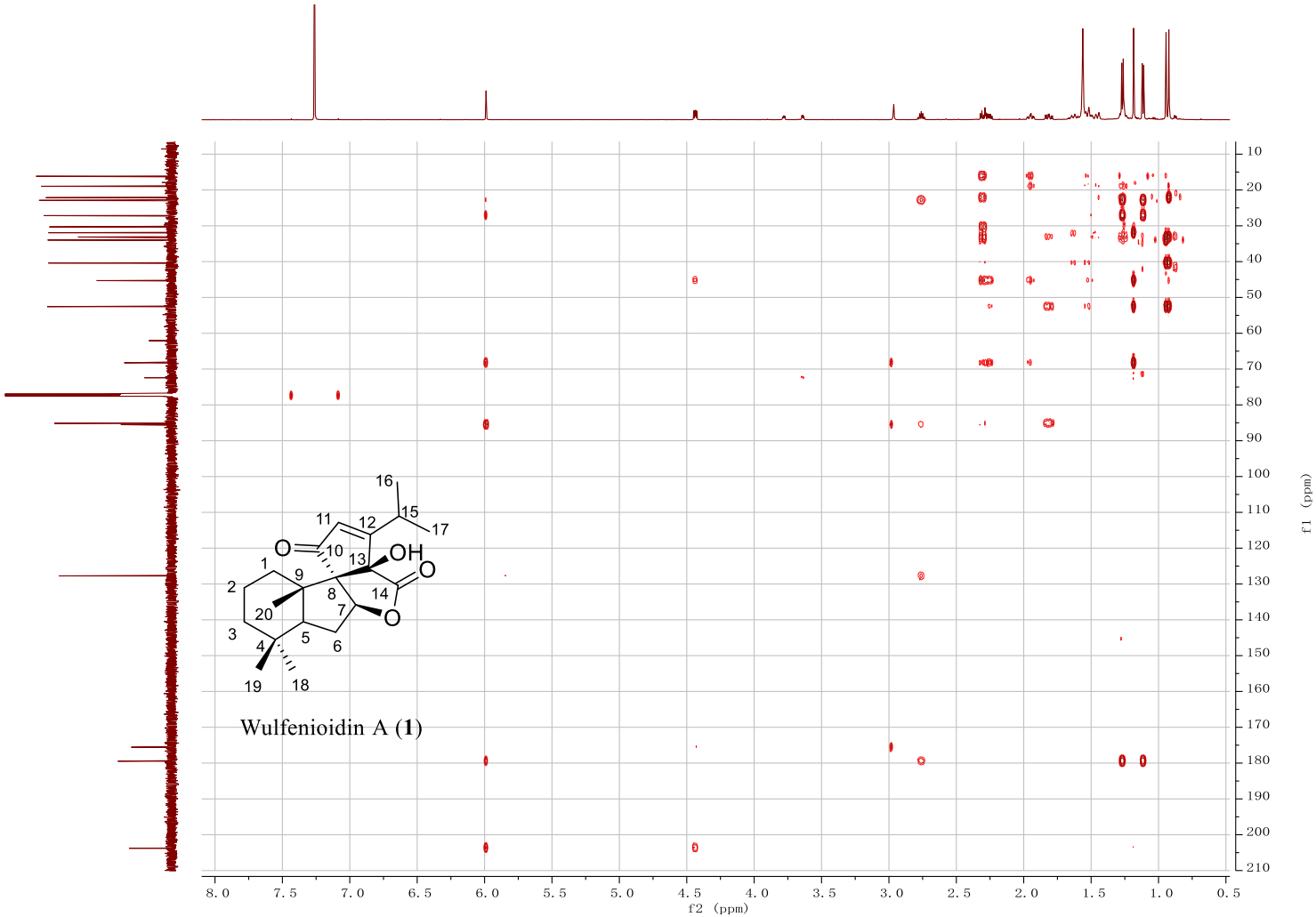

Figure S11. HMBC spectrum of wulfenioidin **A** (**1**) in chloroform (600 MHz)

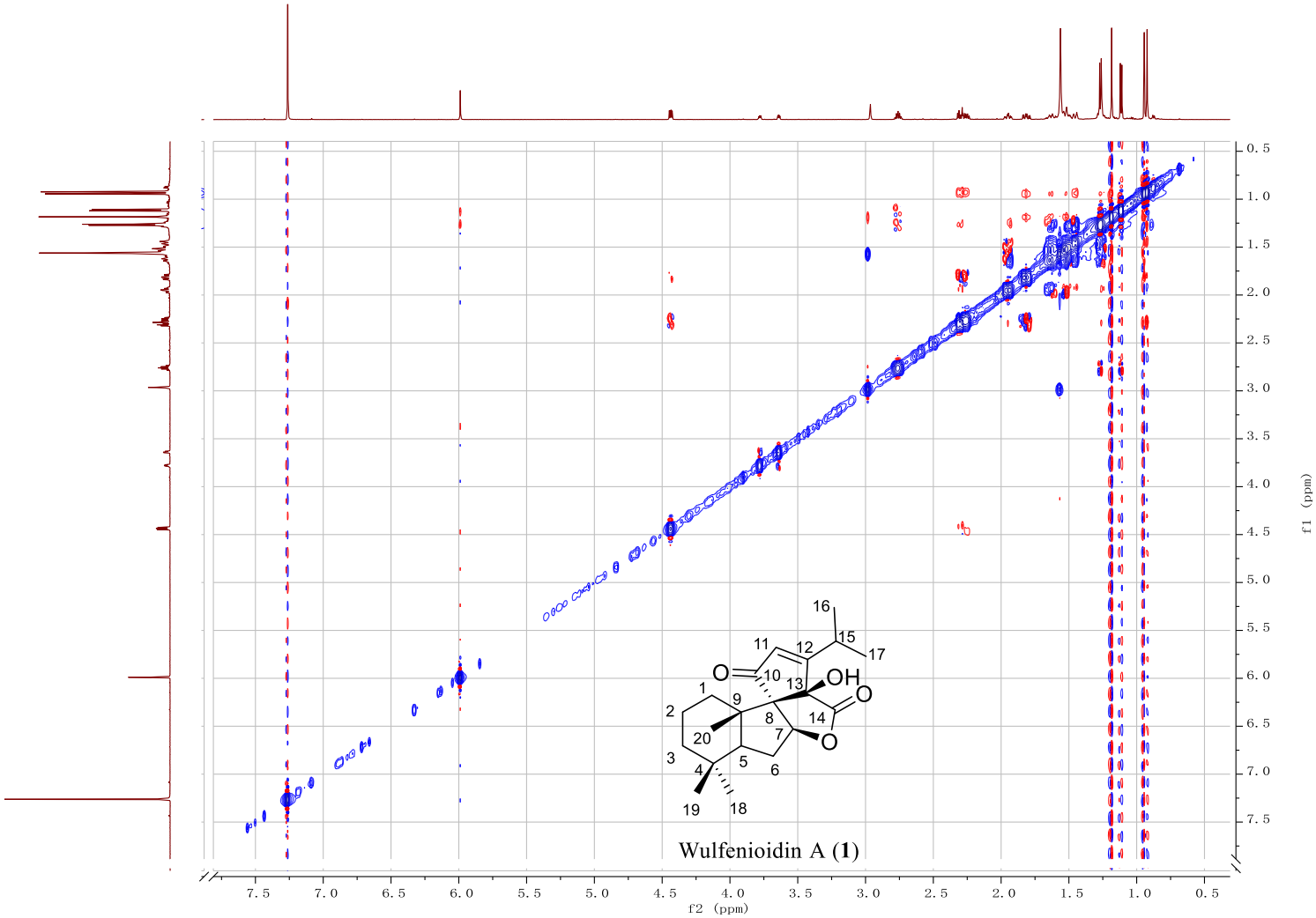

Figure S12. ROESY spectrum of wulfenioidin **A** (**1**) in chloroform (600 MHz)

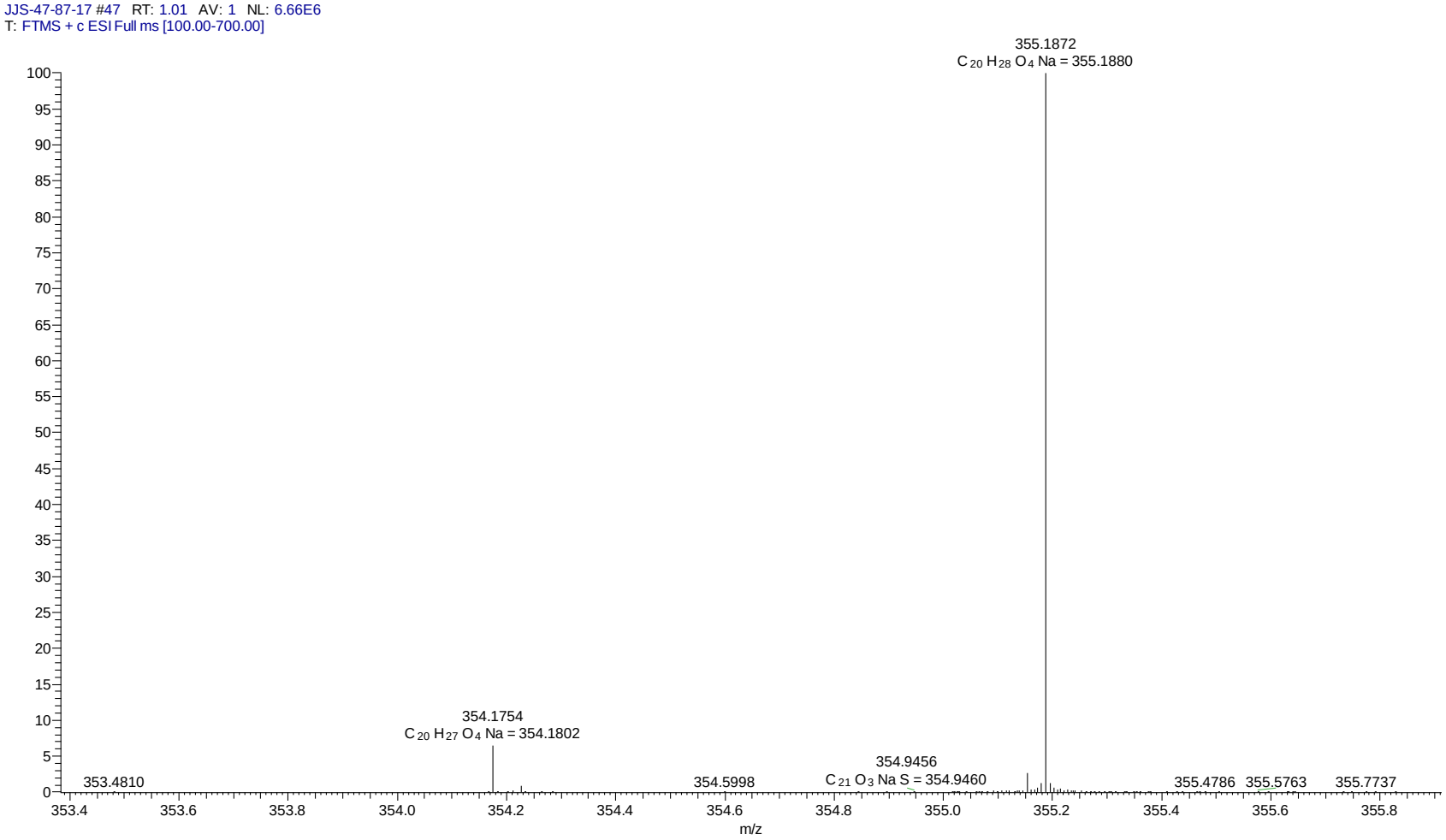

Figure S13. HRESIMS spectrum of wulfenioidin **A** (**1**)

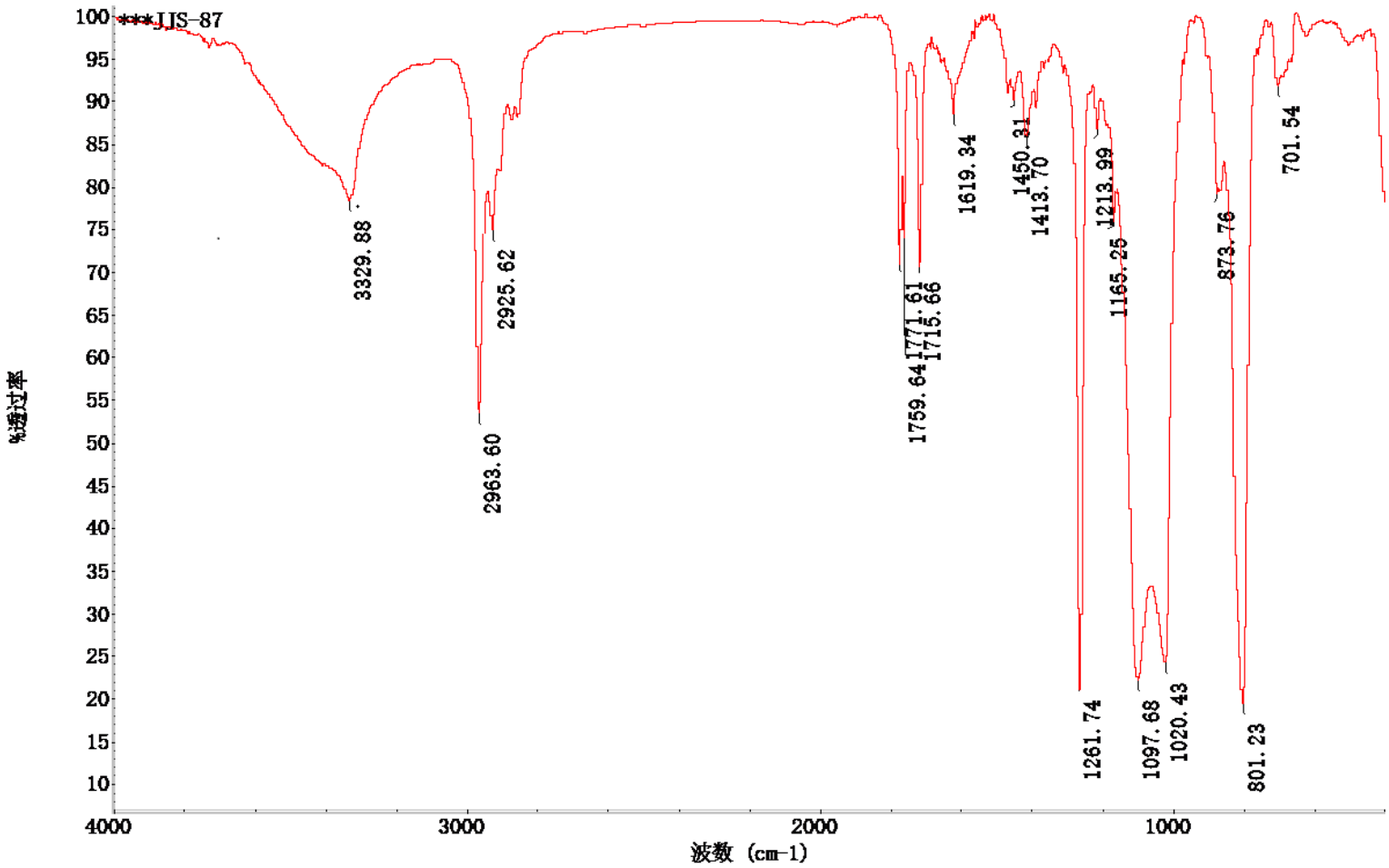

Figure S14. IR spectrum of wulfenioidin **A** (**1**)

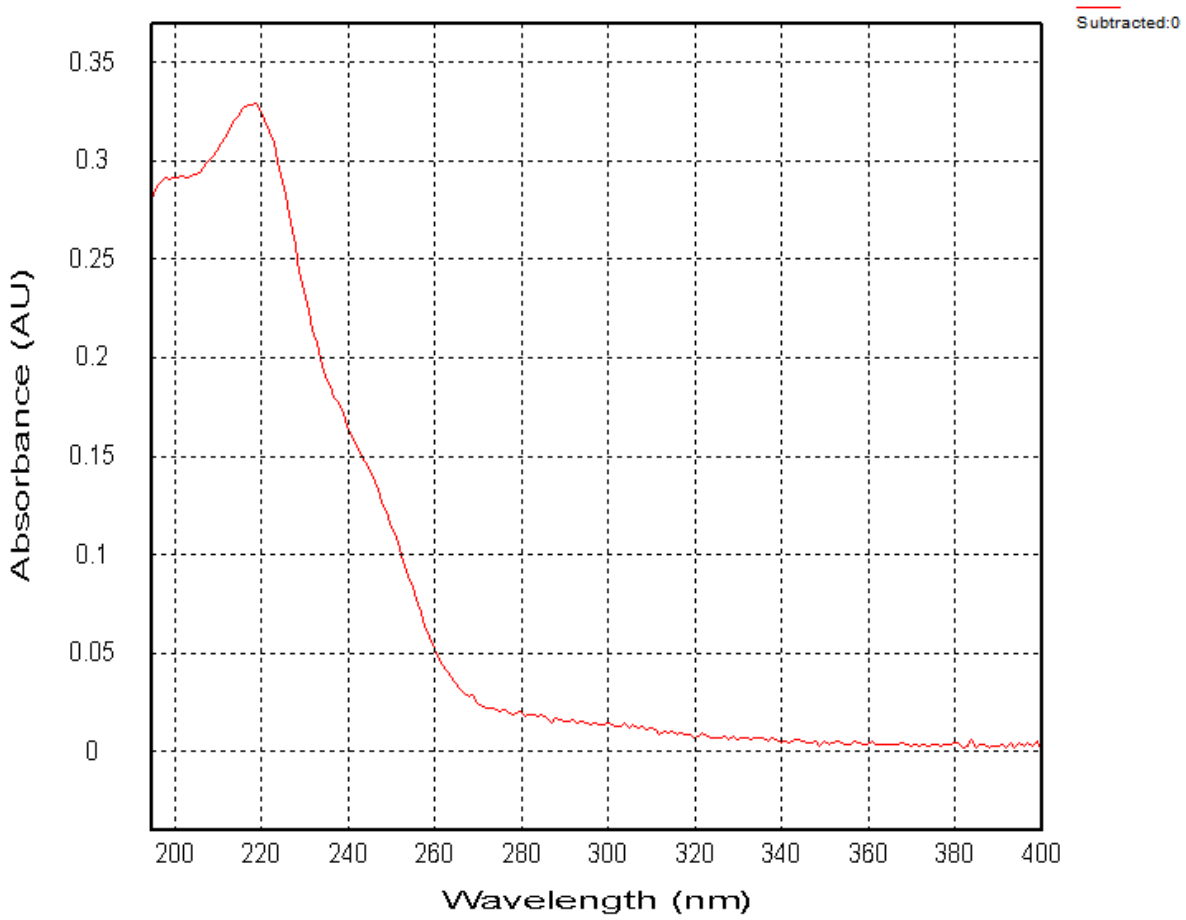

Figure S15. UV spectrum of wulfenioidin **A** (**1**)

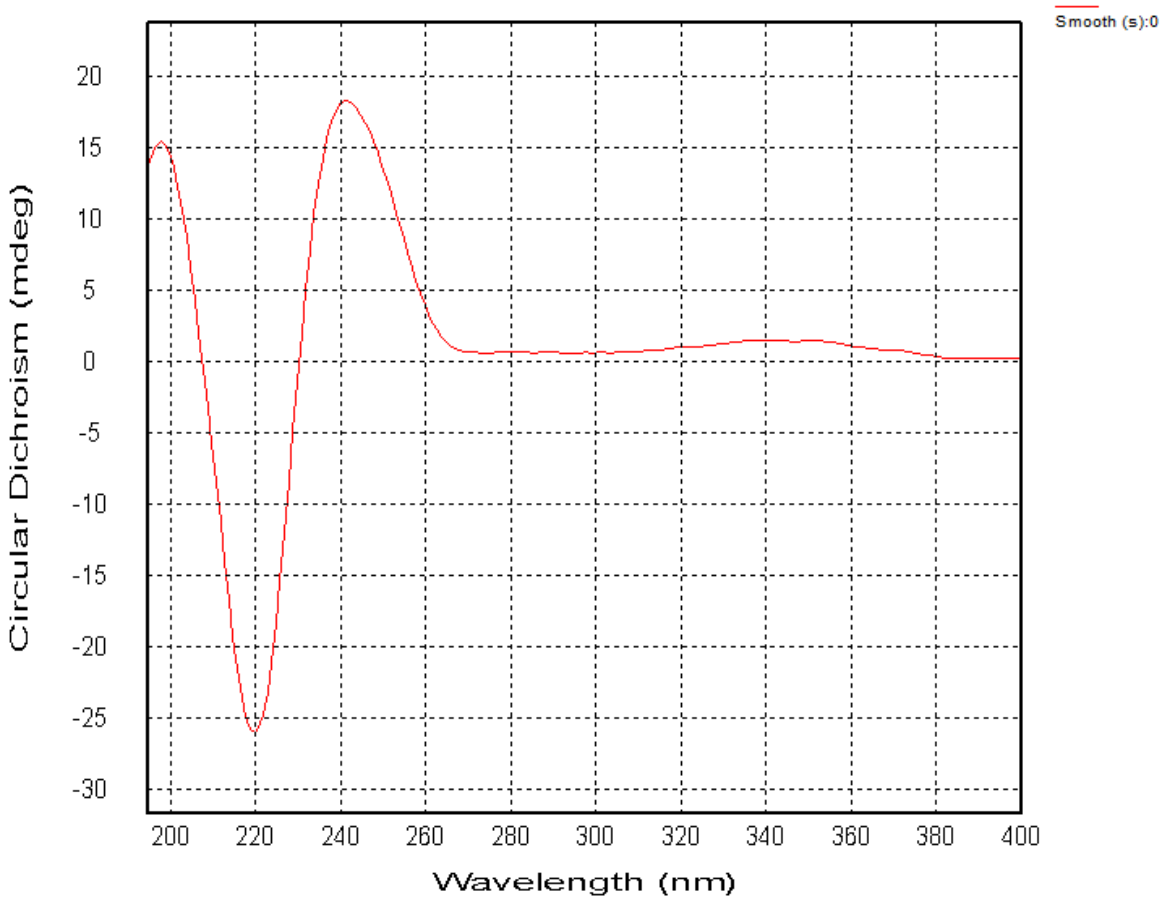

Figure S16. CD spectrum of wulfenioidin **A** (**1**)

Rudolph Research Analytical

This sample was measured on an Autopol VI, Serial #91058
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Measurement Date : Thursday, 21-JUL-2022

Set Temperature : OFF

Time Delay : Disabled

Delay between Measurement : Disabled

n	Average	Std.Dev.	% RSD	Maximum	Minimum
5	46.20	0.45	0.97	47.00	46.00

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG.nm	Lg.mm	Conc.g/100ml	Temp.
1	jjs-87	03:37:26 PM	46.00	SR	0.046	589	100.00	0.100	25.6
2	jjs-87	03:37:33 PM	46.00	SR	0.046	589	100.00	0.100	25.6
3	jjs-87	03:37:39 PM	47.00	SR	0.047	589	100.00	0.100	25.6
4	jjs-87	03:37:45 PM	46.00	SR	0.046	589	100.00	0.100	25.6
5	jjs-87	03:37:51 PM	46.00	SR	0.046	589	100.00	0.100	25.6

Figure S17. OR report of wulfenioidin **A** (**1**)

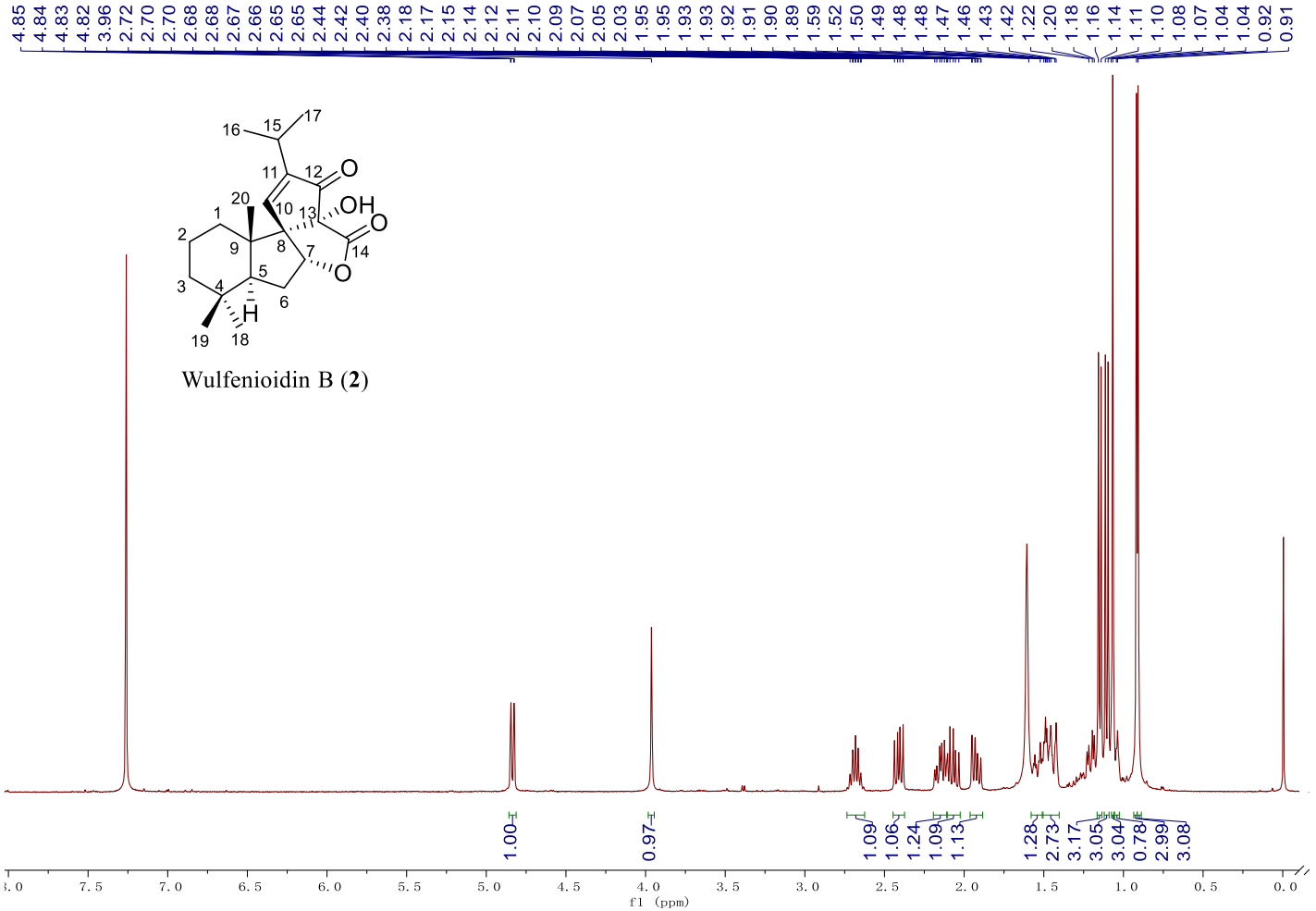

Figure S18. ^{1}H NMR spectrum of wulfenioidin **B** (**2**) in chloroform (400 MHz)

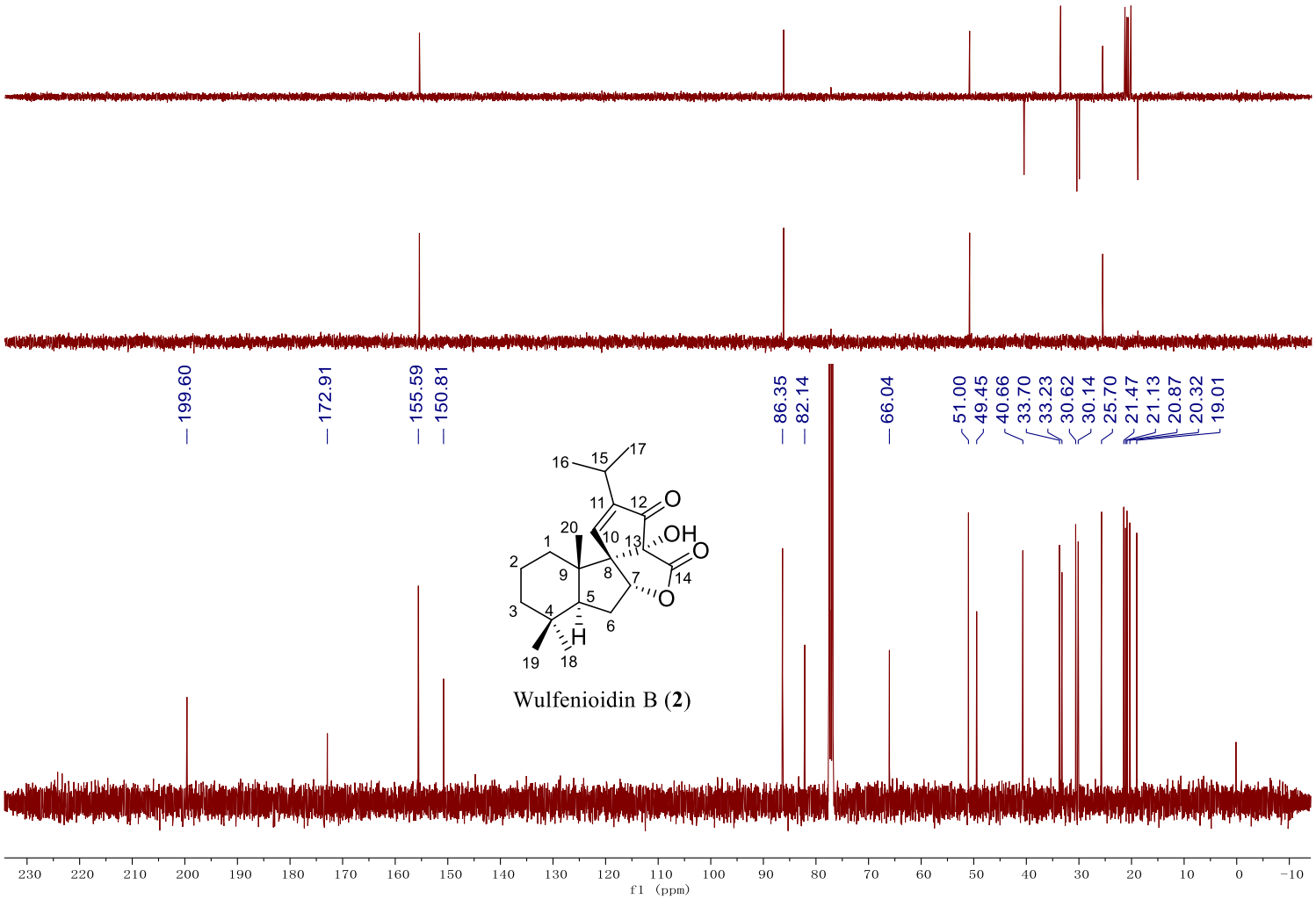

Figure S19. ^{13}C and DEPT NMR spectra of wulfenioidin **B** (**2**) in chloroform (100 MHz)

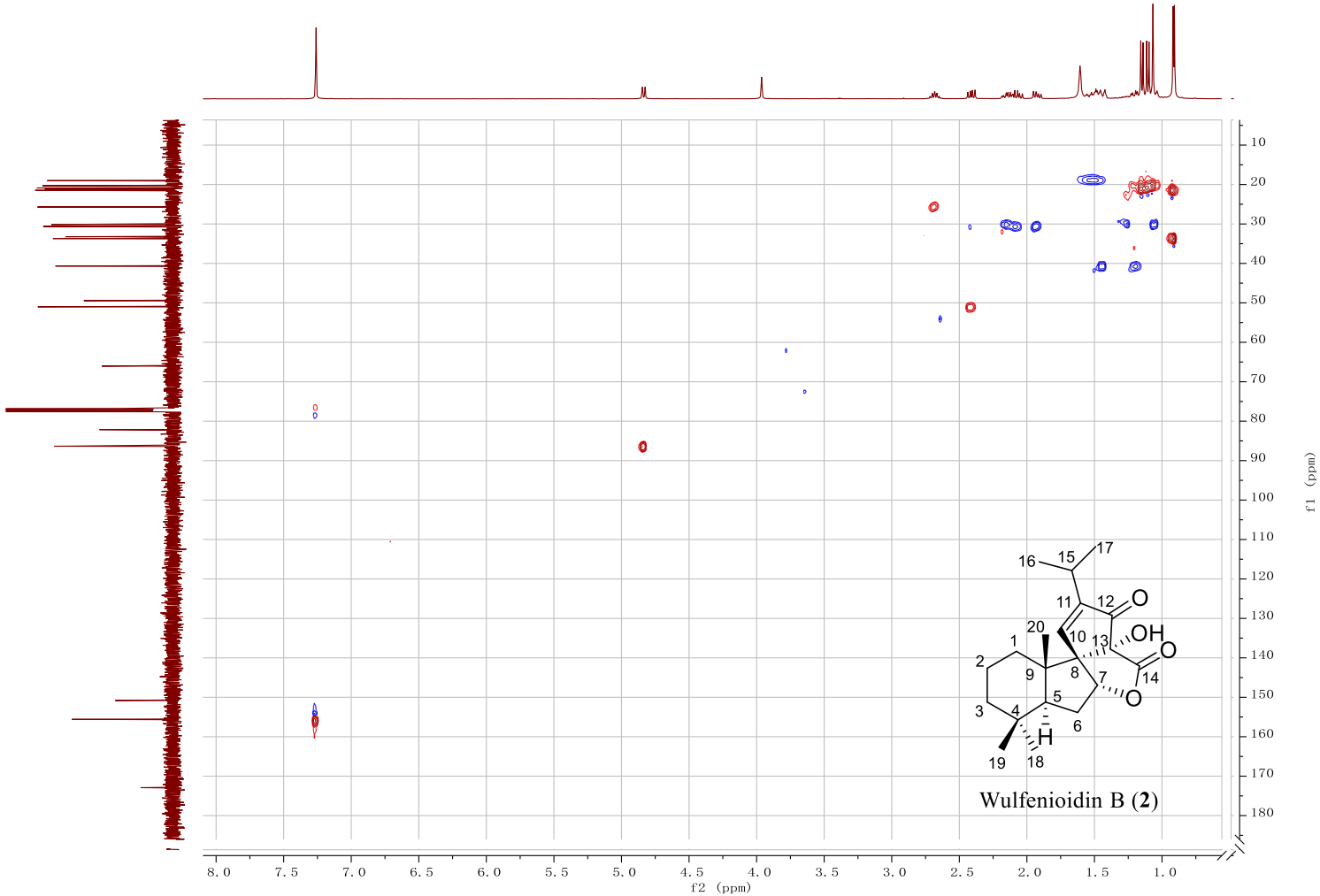

Figure S20. HSQC spectrum of wulfenioidin **B** (**2**) in chloroform (600 MHz)

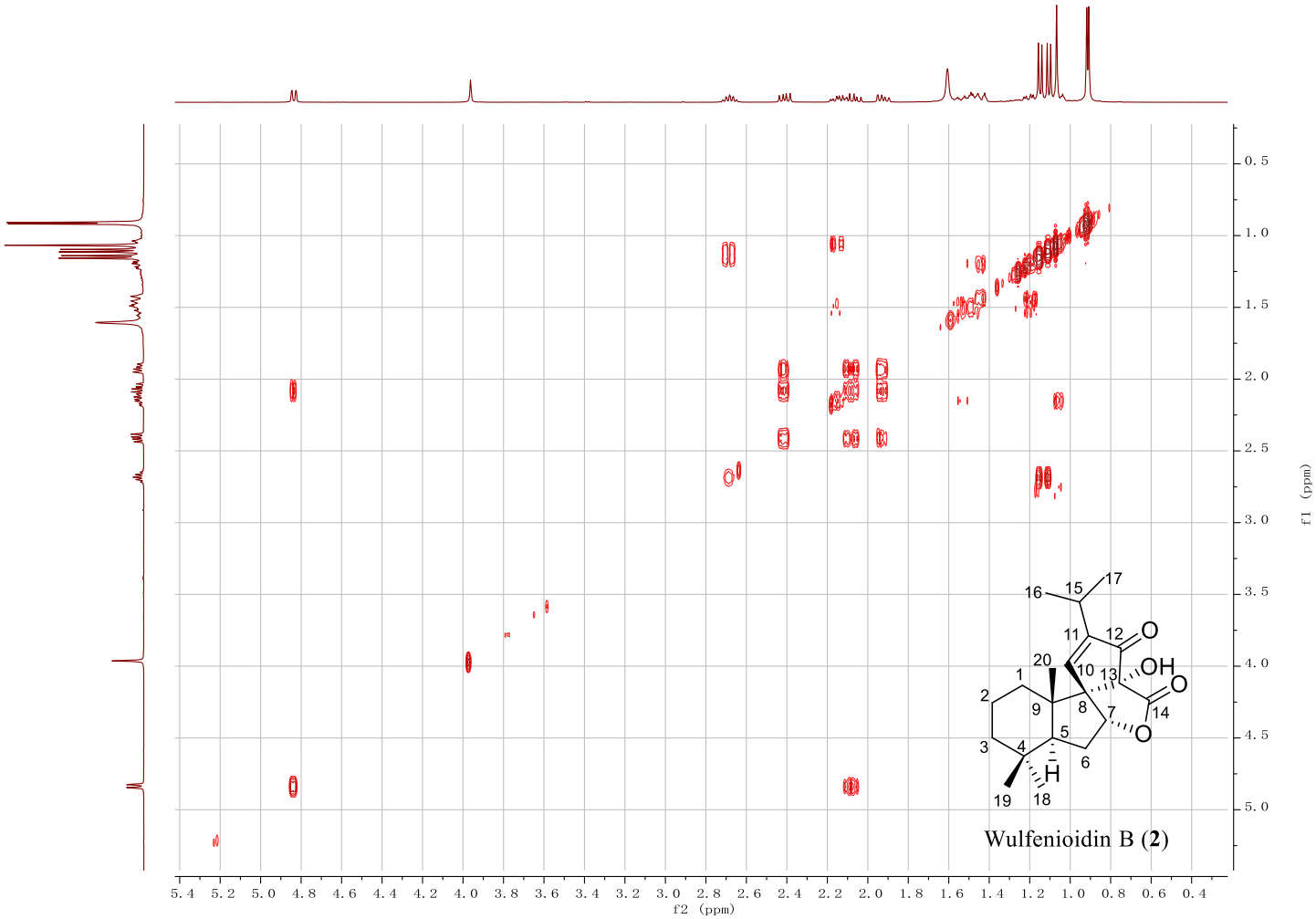

Figure S21. ^{1}H-^{1}H COSY spectrum of wulfenioidin **B** (**2**) in chloroform (600 MHz)

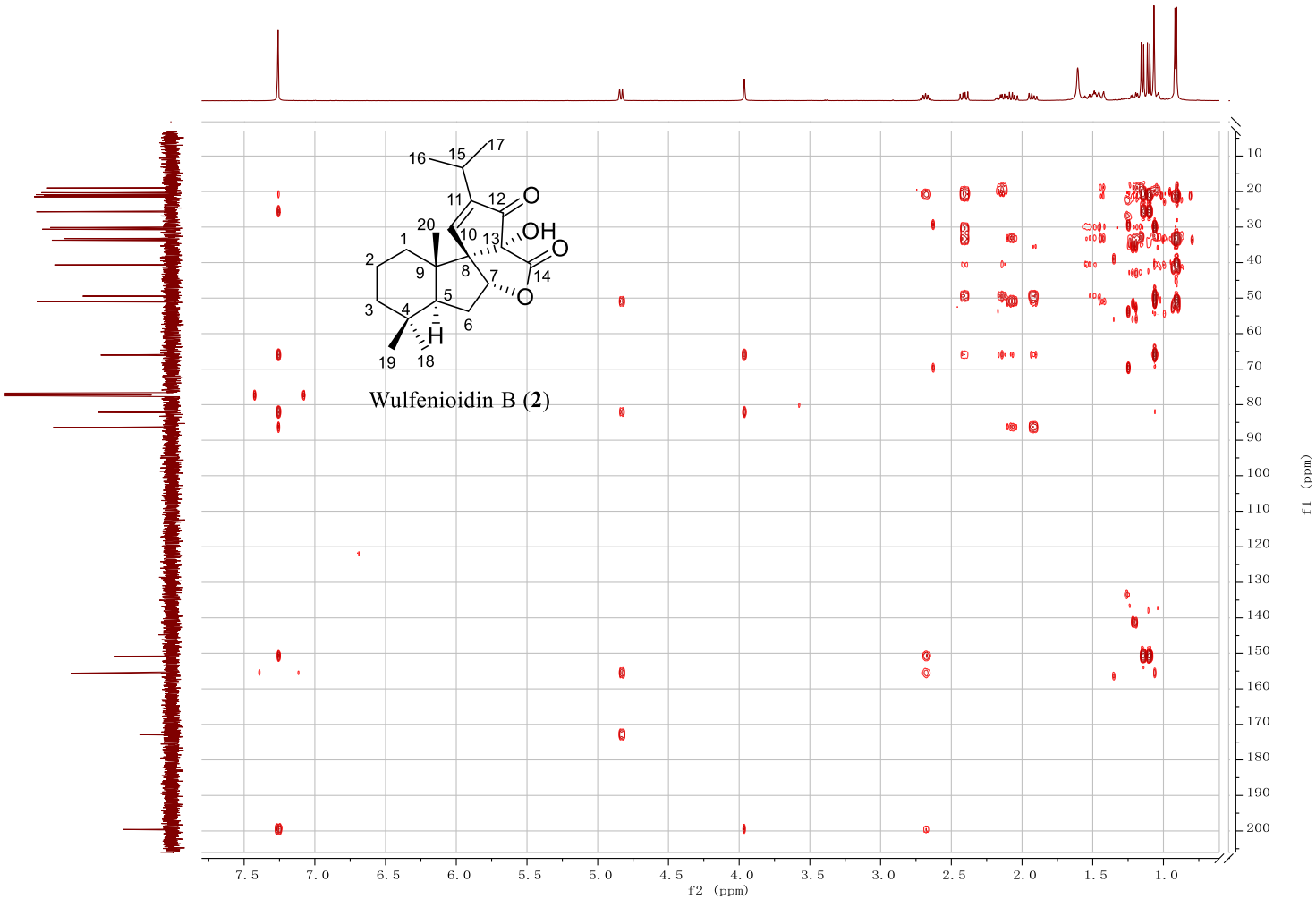

Figure S22. HMBC spectrum of wulfenioidin **B** (**2**) in chloroform (600 MHz)

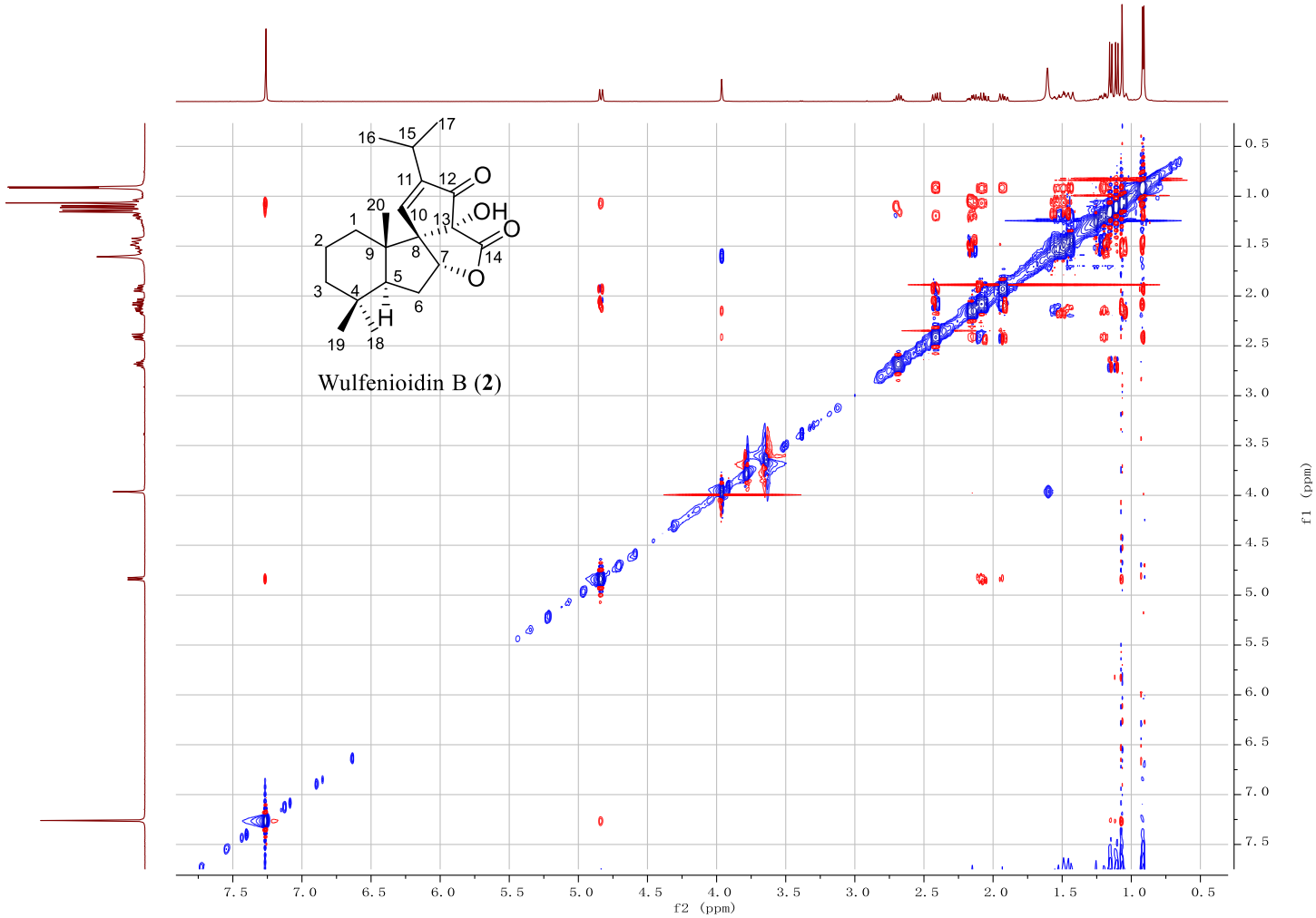

Figure S23. ROESY spectrum of wulfenioidin **B** (**2**) in chloroform (600 MHz)

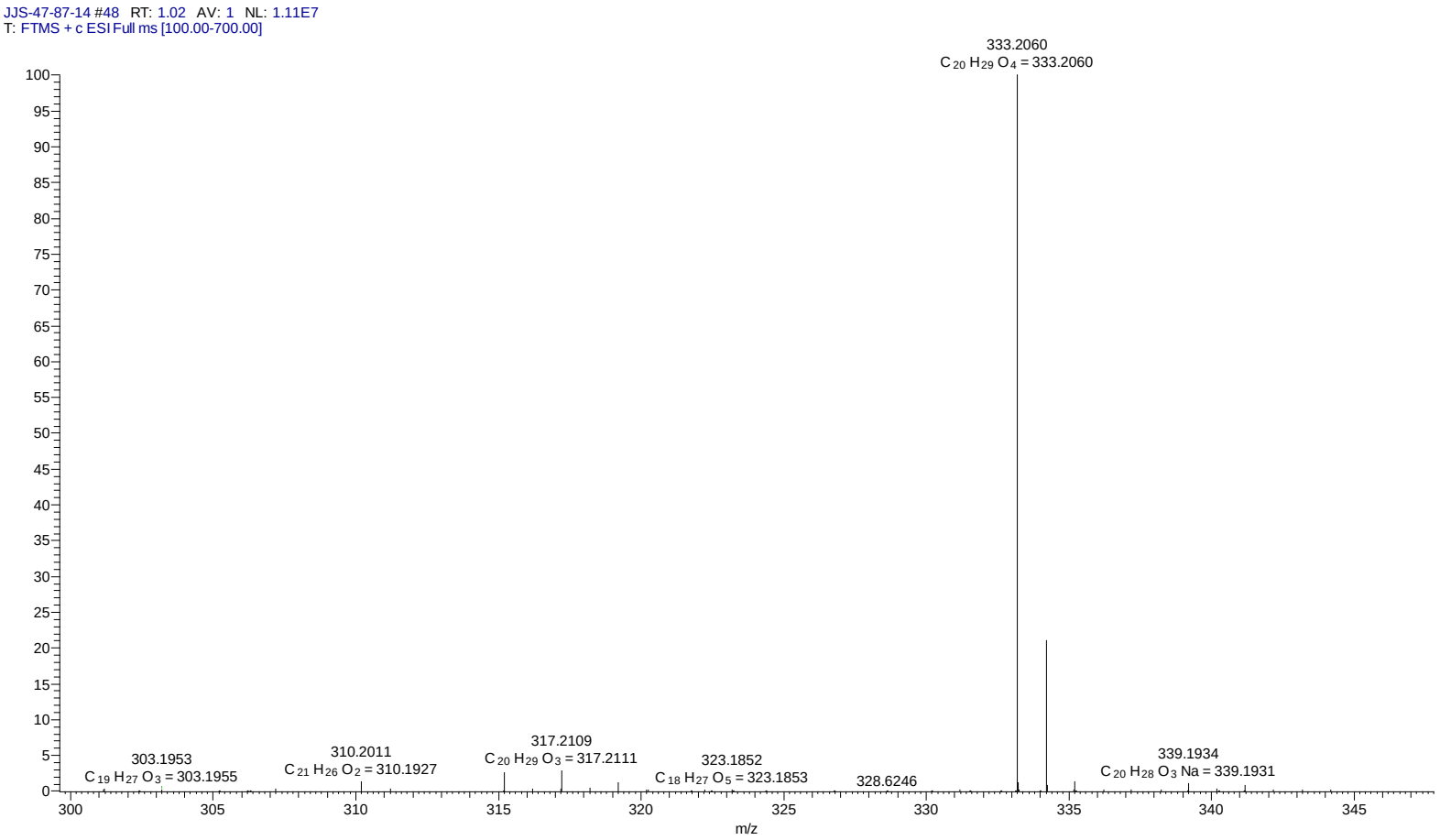

Figure S24. HRESIMS spectrum of wulfenioidin **B** (**2**)

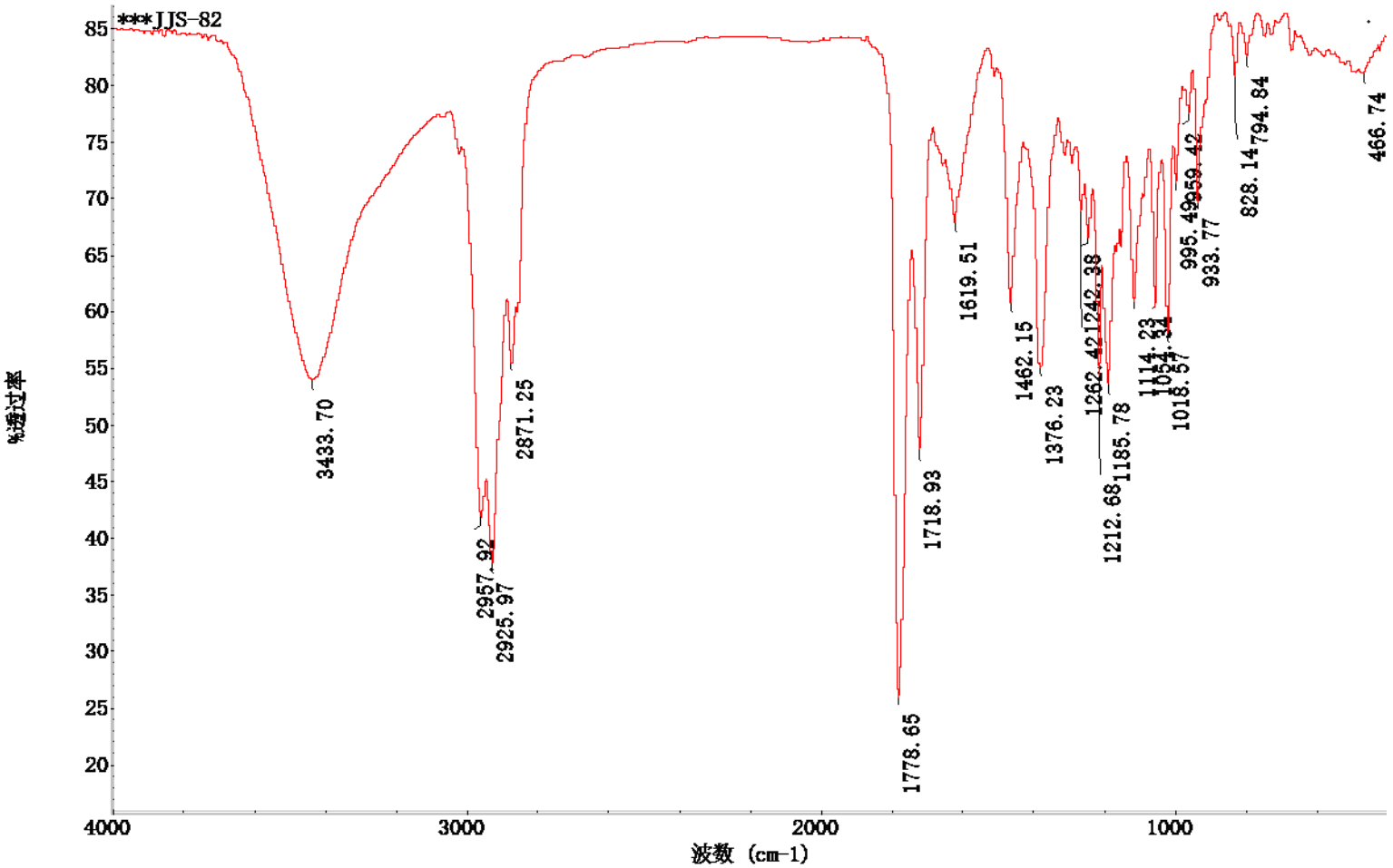

Figure S25. IR spectrum of wulfenioidin **B** (**2**)

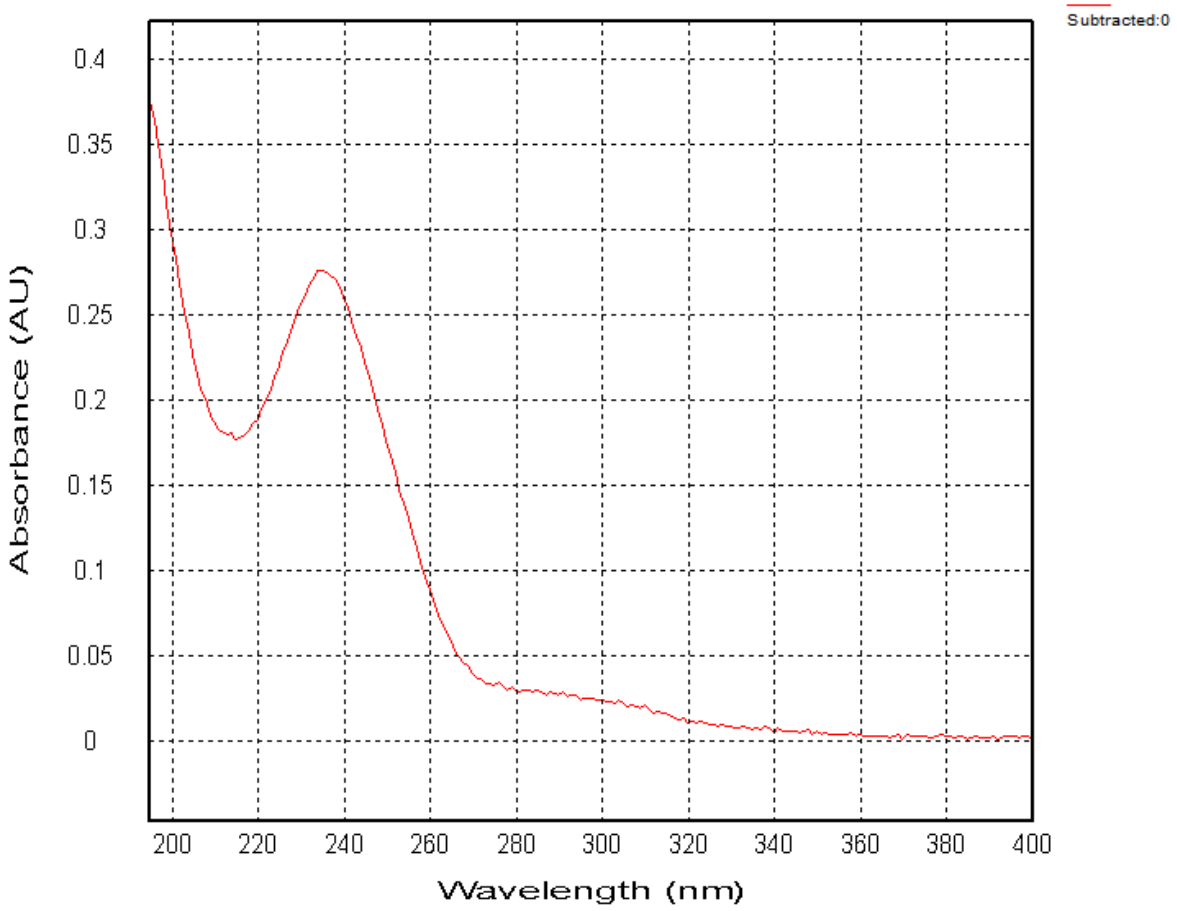

Figure S26. UV spectrum of wulfenioidin **B** (**2**)

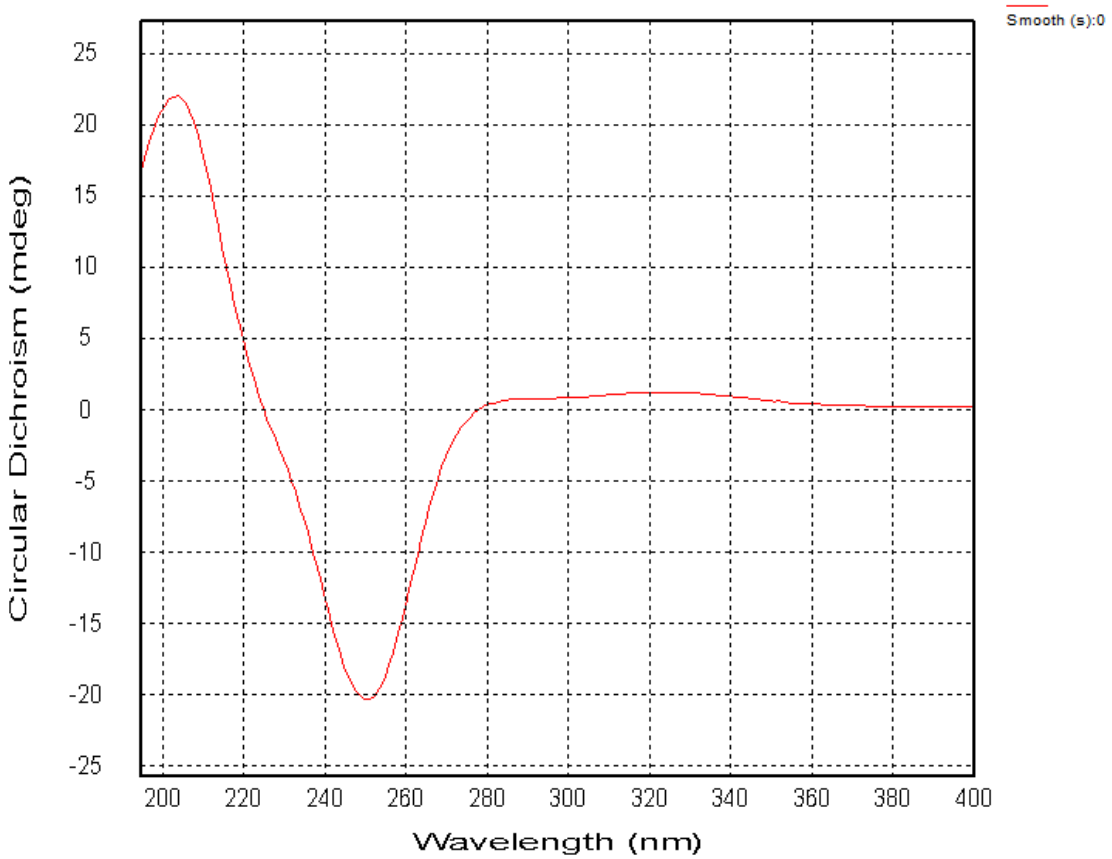

Figure S27. CD spectrum of wulfenioidin **B** (**2**)

Rudolph Research Analytical

This sample was measured on an Autopol VI, Serial #91058
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Measurement Date : Thursday, 21-JUL-2022

Set Temperature : OFF

Time Delay : Disabled

Delay between Measurement : Disabled

n	Average	Std.Dev.	% RSD	Maximum	Minimum
5	-54.00	0.00	0.00	-54.00	-54.00

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG.nm	Lg.mm	Conc.g/100ml	Temp.
1	jjs-82	03:30:07 PM	-54.00	SR	-0.081	589	100.00	0.150	25.4
2	jjs-82	03:30:13 PM	-54.00	SR	-0.081	589	100.00	0.150	25.4
3	jjs-82	03:30:19 PM	-54.00	SR	-0.081	589	100.00	0.150	25.4
4	jjs-82	03:30:25 PM	-54.00	SR	-0.081	589	100.00	0.150	25.4
5	jjs-82	03:30:30 PM	-54.00	SR	-0.081	589	100.00	0.150	25.4

Figure S28. OR report of wulfenioidin **B** (**2**)

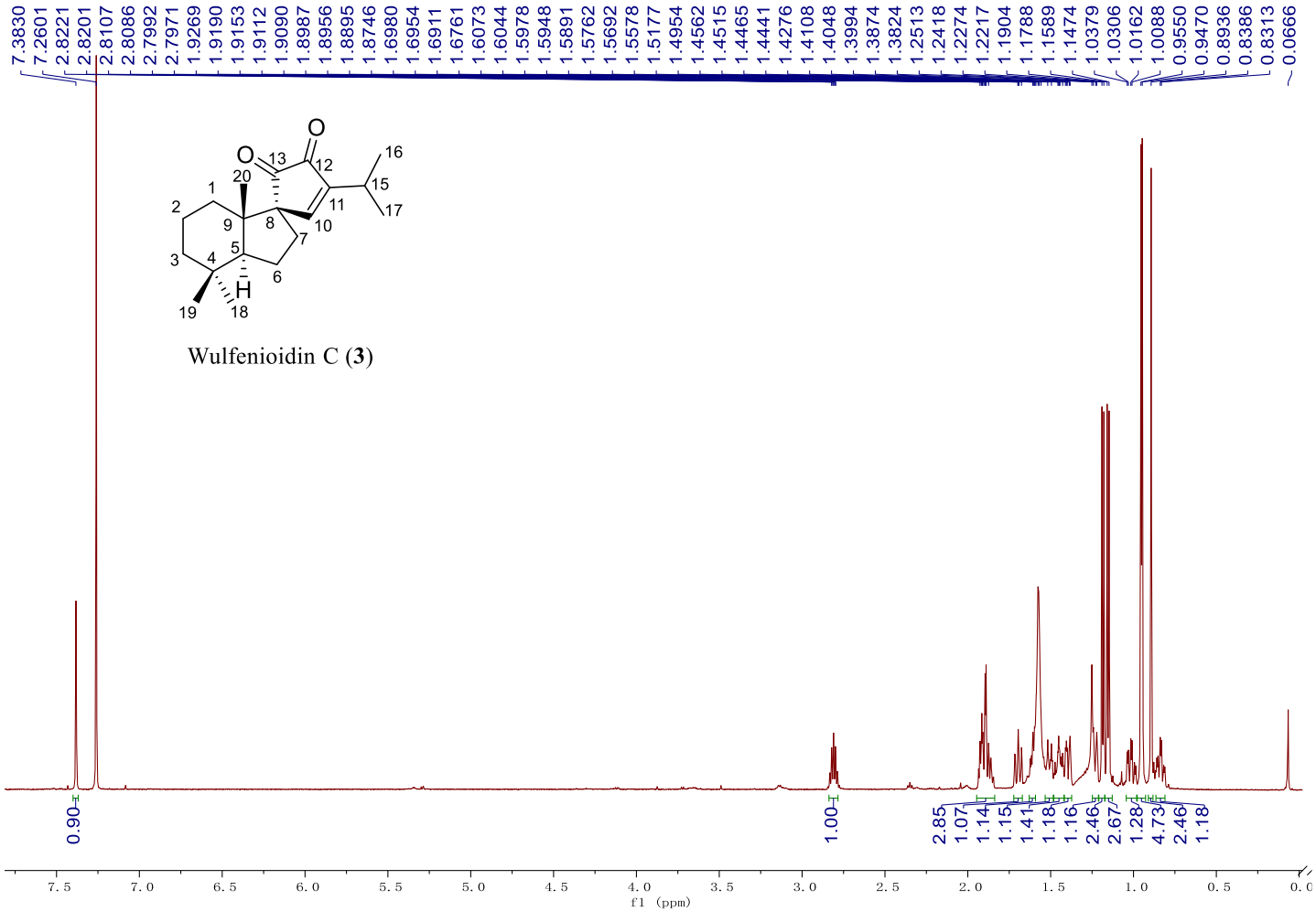

Figure S29. ^{1}H NMR spectrum of wulfenioidin **C** (**3**) in chloroform (600 MHz)

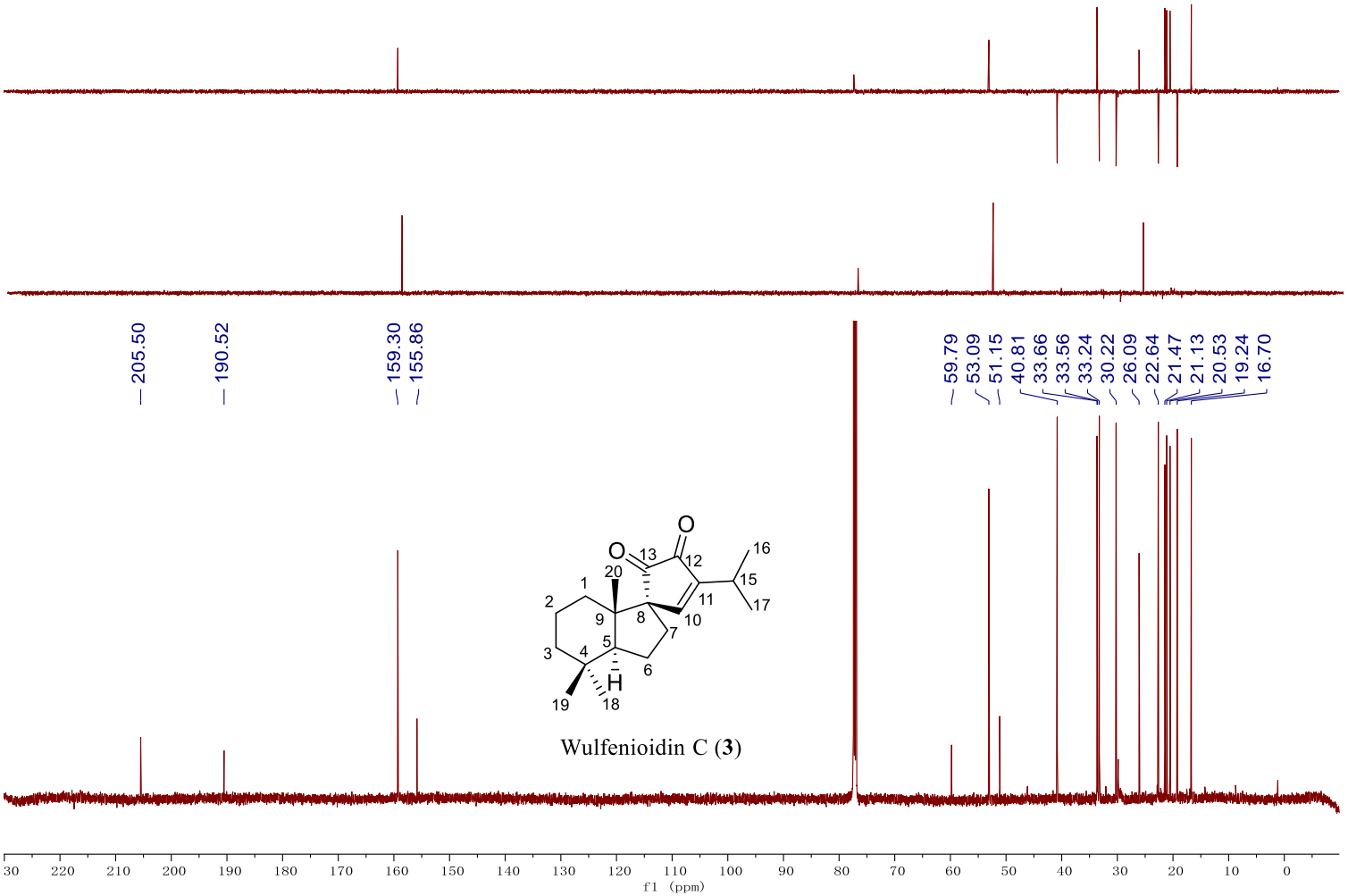

Figure S30. ^{13}C and DEPT NMR spectra of wulfenioidin **C** (**3**) in chloroform (150 MHz)

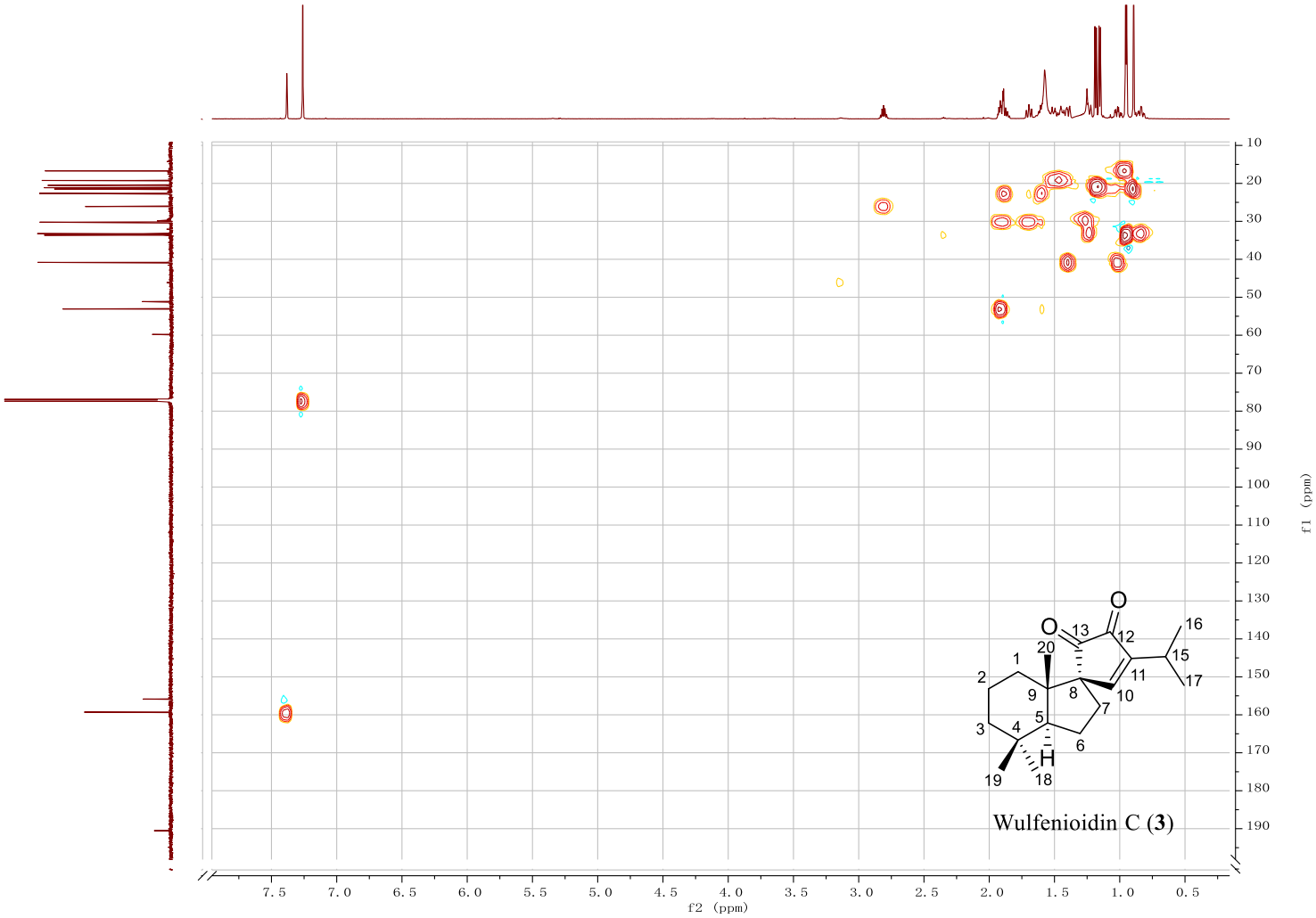

Figure S31. HSQC spectrum of wulfenioidin **C** (**3**) in chloroform (600 MHz)

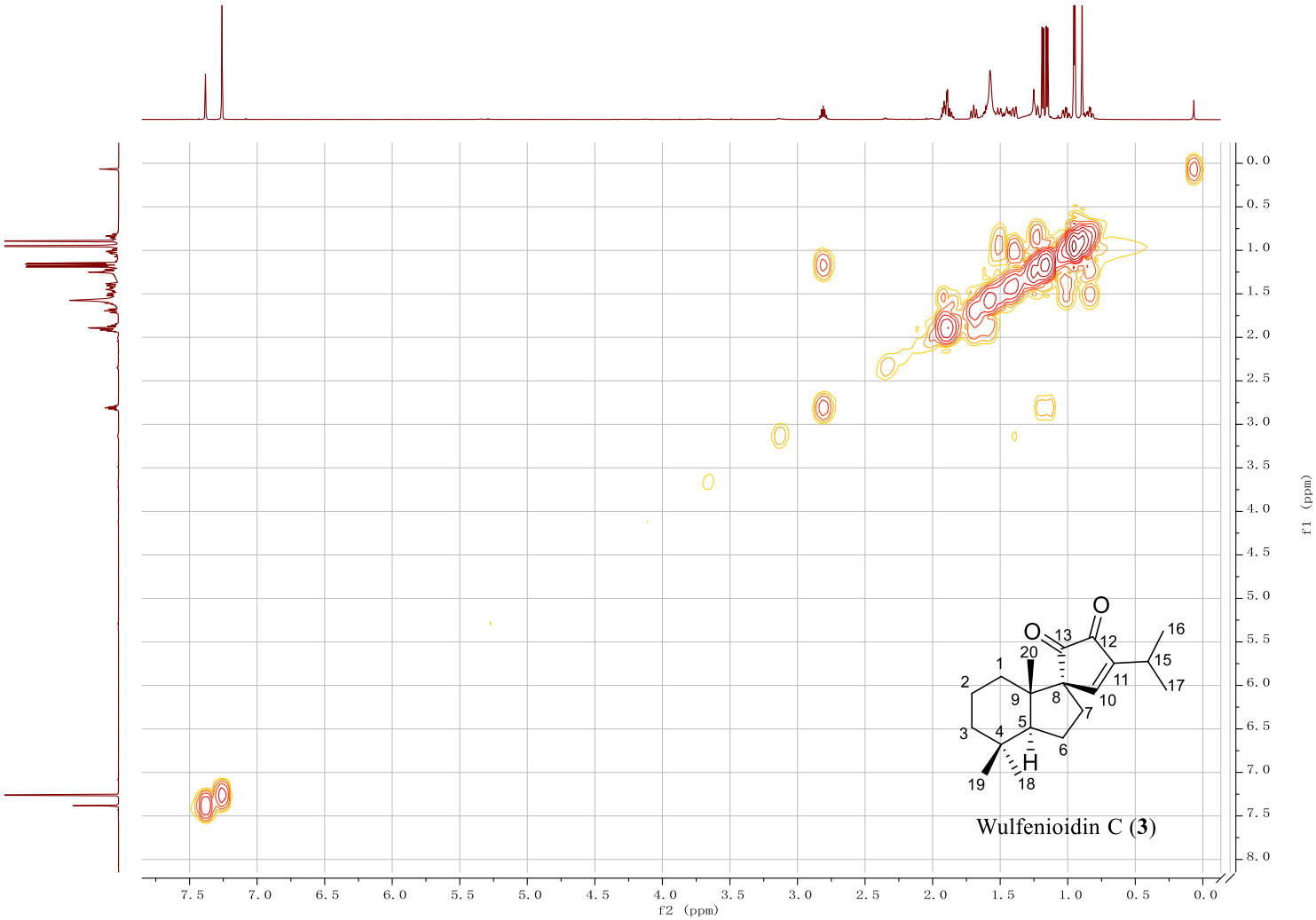

Figure S32. ^{1}H-^{1}H COSY spectrum of wulfenioidin **C** (**3**) in chloroform (600 MHz)

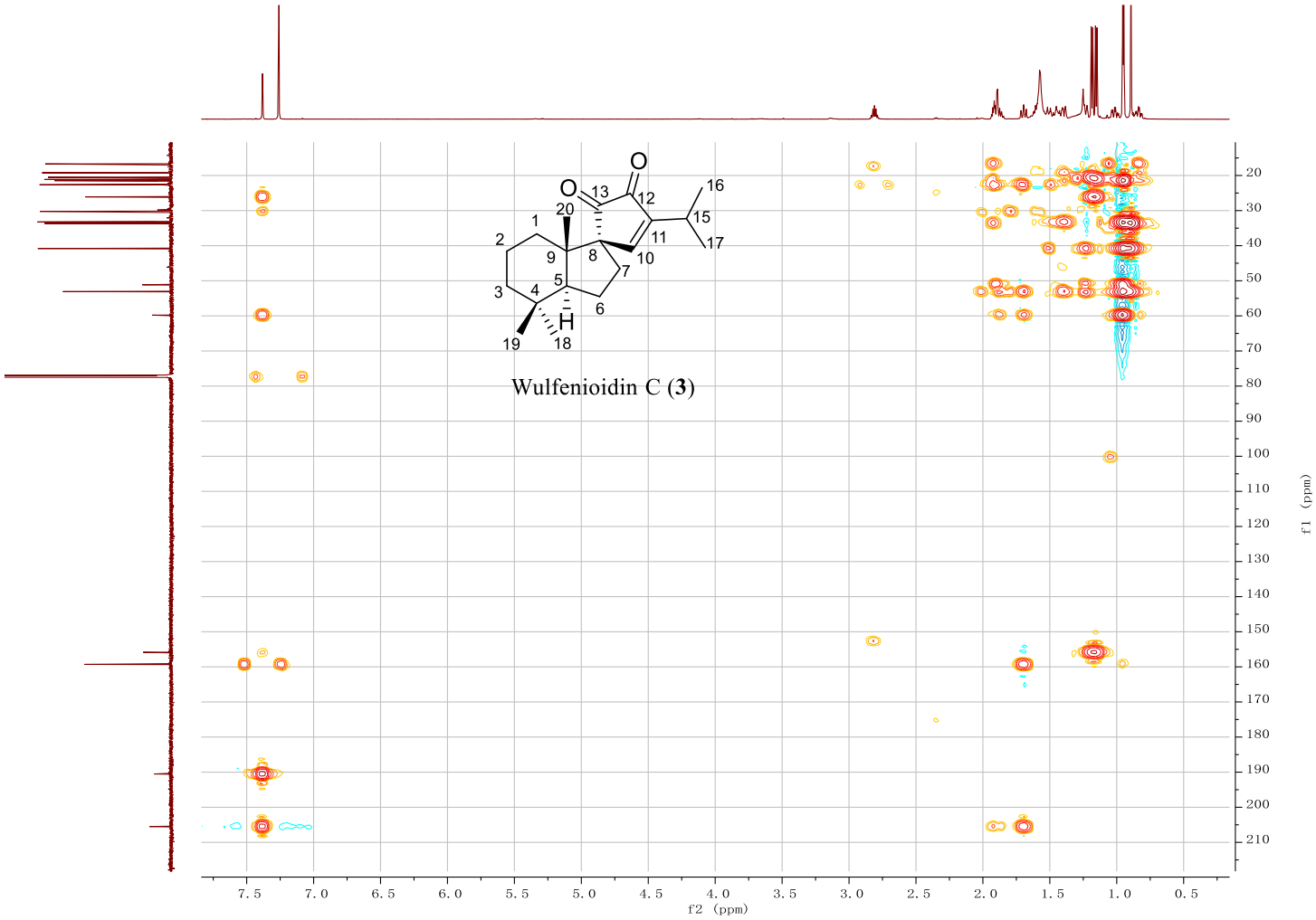

Figure S33. HMBC spectrum of wulfenioidin **C** (**3**) in chloroform (600 MHz)

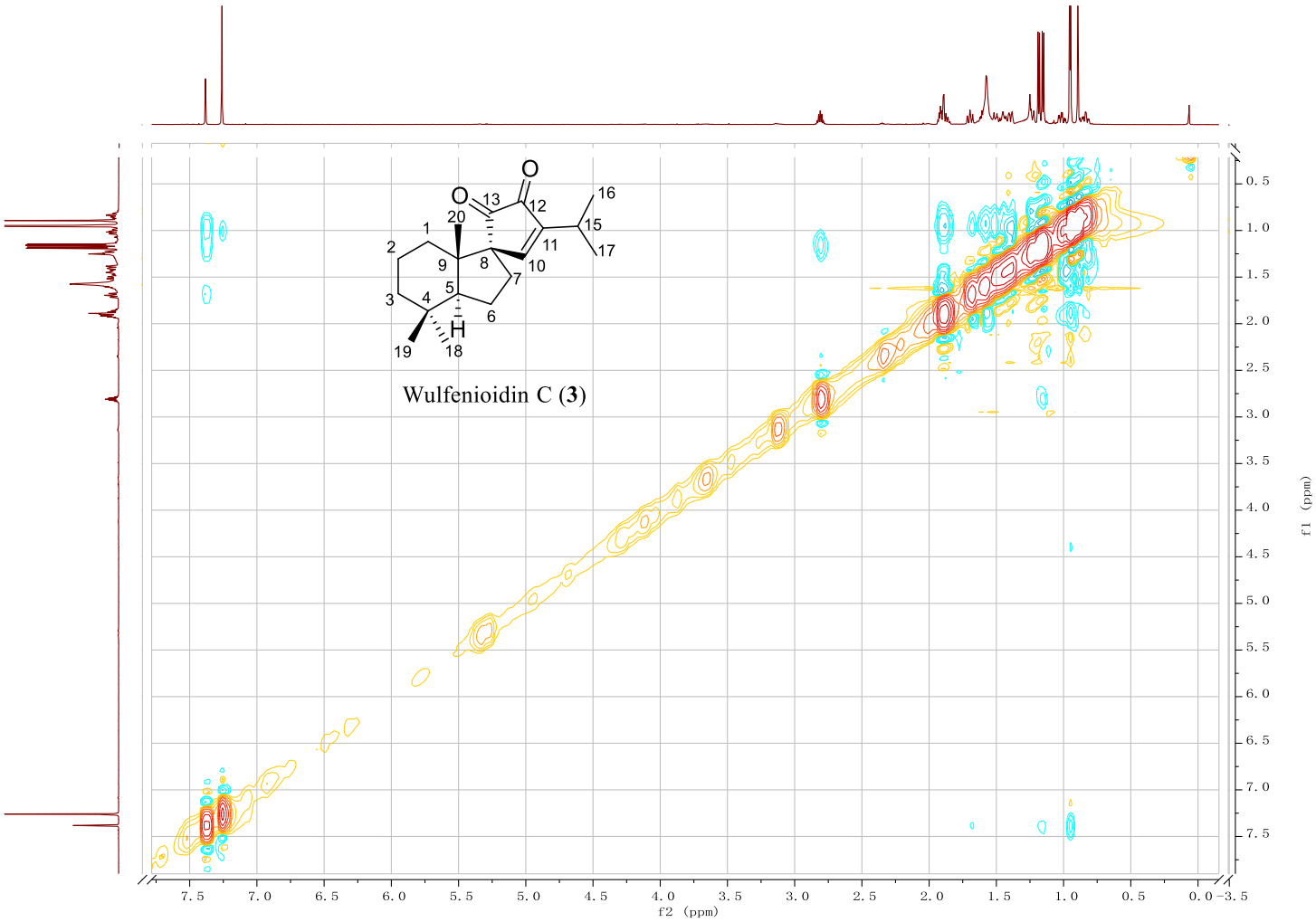

Figure S34. ROESY spectrum of wulfenioidin **C** (**3**) in chloroform (600 MHz)

m/z	Ion	Formula	Abundance
289.2167	(M+H)+	C19 H29 O2	460258.7

Best	Formula (M)	Ion Formula	Score	Cross Score	Calc m/z	Diff (ppm)	Mass Match	Abund Match	Spacing Match
☑	C19 H28 O2	C19 H29 O2	98.98		289.2162	-1.63	98.34	99.32	99.86

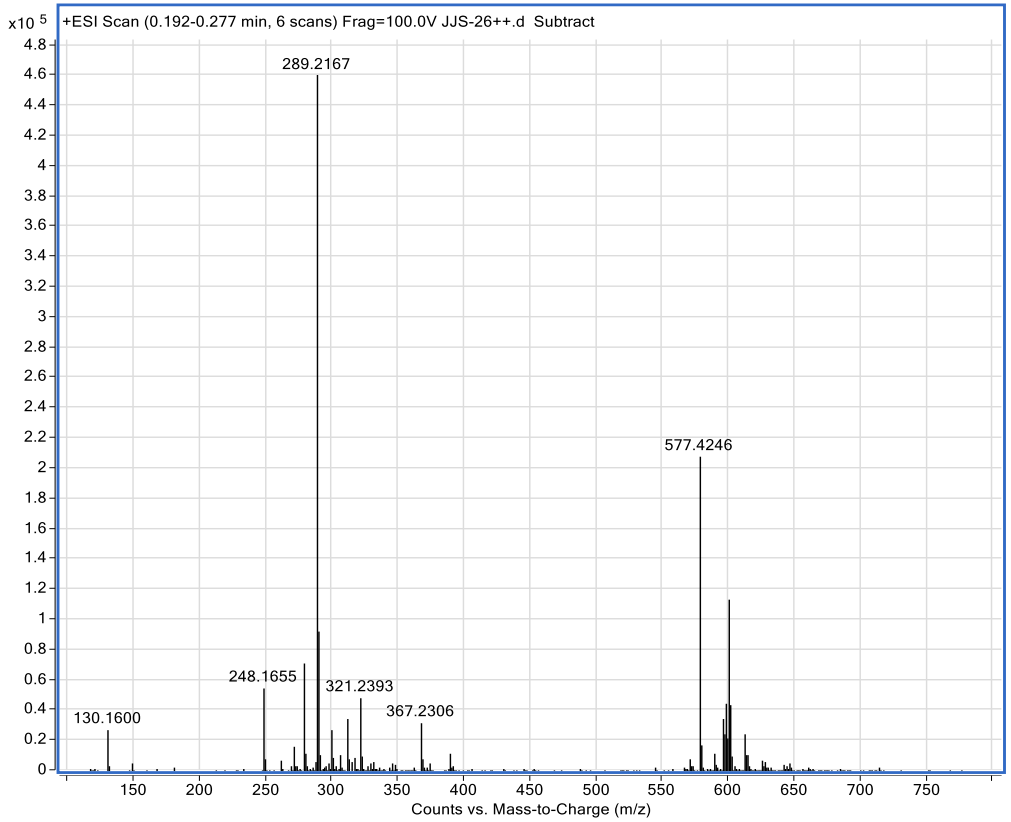

Figure S35. HRESIMS spectrum of wulfenioidin **C** (**3**)

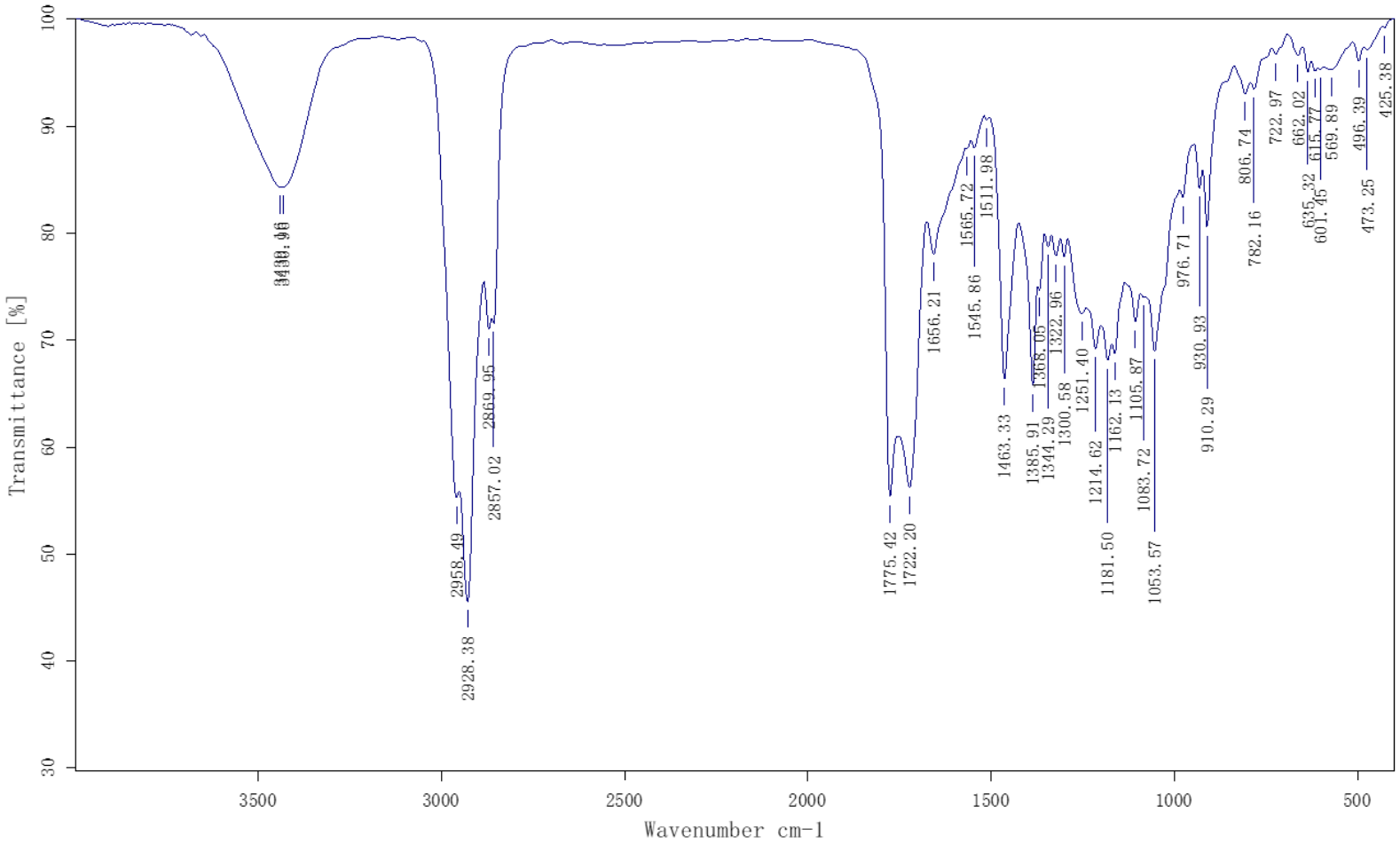

Figure S36. IR spectrum of wulfenioidin **C** (**3**)

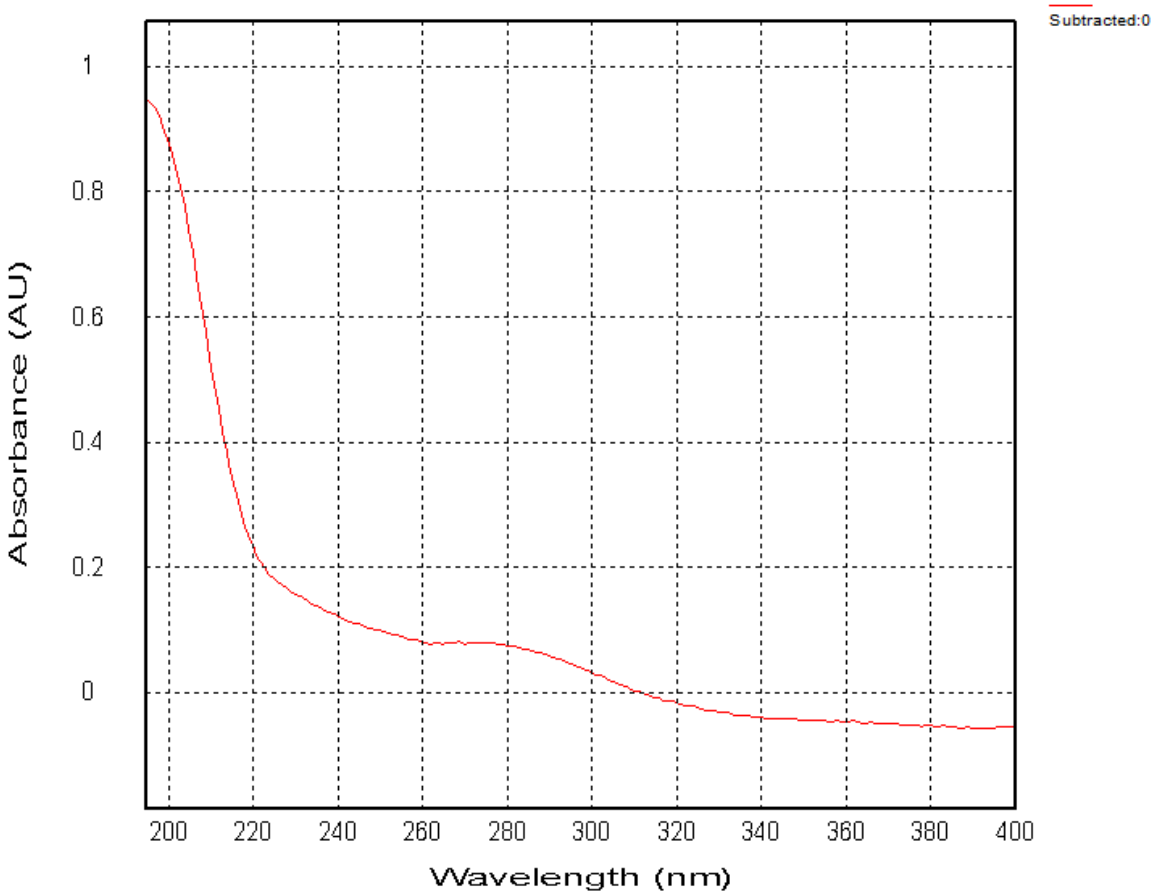

Figure S37. UV spectrum of wulfenioidin **C** (**3**)

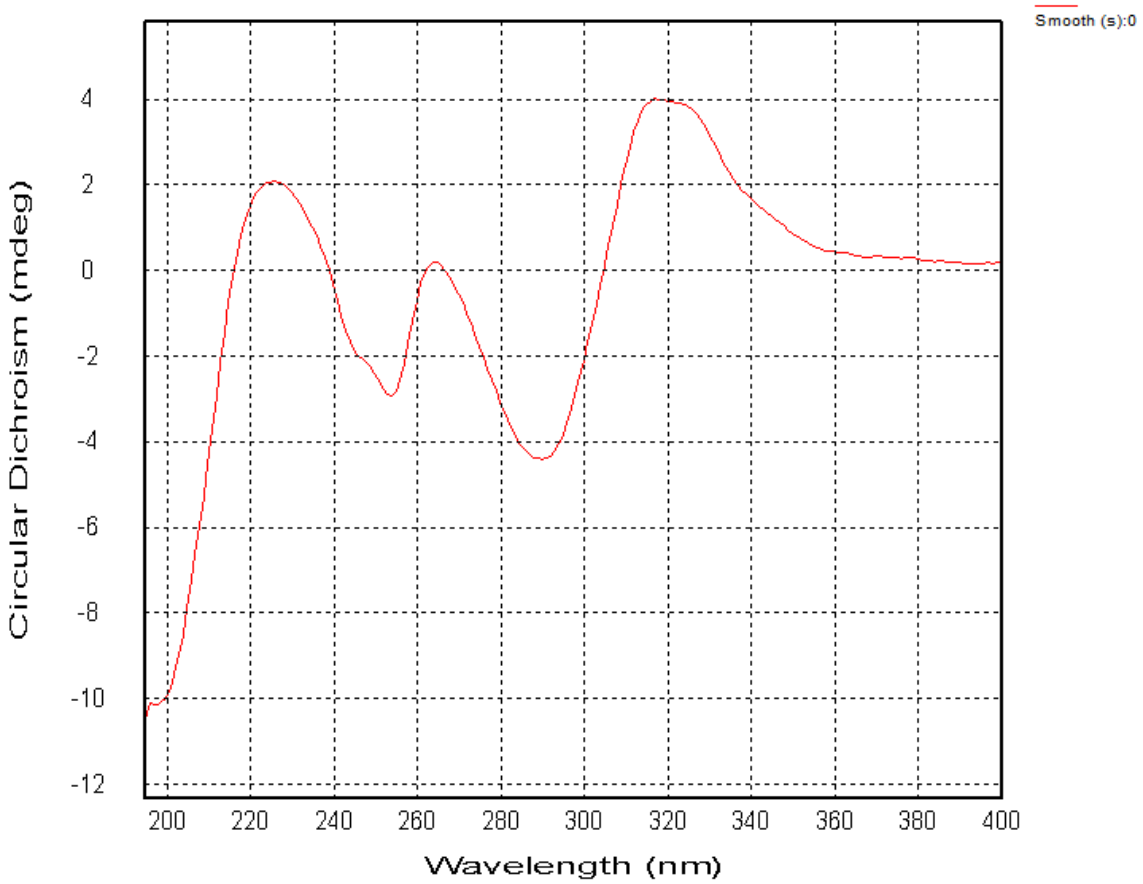

Figure S38. CD spectrum of wulfenioidin **C** (**3**)

Rudolph Research Analytical

This sample was measured on an Autopol VI, Serial #91058
Manufactured by Rudolph Research Analytical, Hackettstown, NJ, USA.

Measurement Date : Thursday, 24-FEB-2022

Set Temperature : 20.0

Time Delay : Disabled

Delay between Measurement : Disabled

n	Average	Std.Dev.	% RSD	Maximum	Minimum
5	-87.20	0.84	-0.96	-86.00	-88.00

S.No	Sample ID	Time	Result	Scale	OR °Arc	WLG.nm	Lg.mm	Conc.g/100ml	Temp.
1	JJS-26	02:31:57 PM	-87.00	SR	-0.087	589	100.00	0.100	20.0
2	JJS-26	02:32:03 PM	-88.00	SR	-0.088	589	100.00	0.100	20.0
3	JJS-26	02:32:09 PM	-88.00	SR	-0.088	589	100.00	0.100	20.0
4	JJS-26	02:32:16 PM	-87.00	SR	-0.087	589	100.00	0.100	20.0
5	JJS-26	02:32:22 PM	-86.00	SR	-0.086	589	100.00	0.100	20.0

Figure S39. OR report of wulfenioidin **C** (**3**)

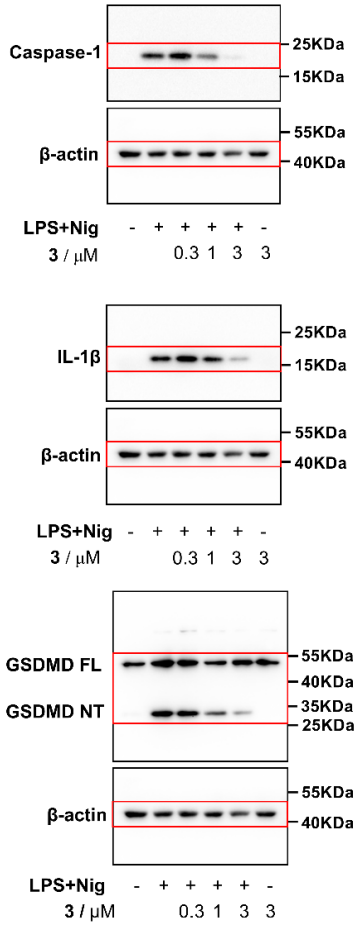

Figure S40. The full raw data of western blots (E, F, and G) of compound **3**