Supplementary Information

Two new seco-Polycyclic Polyprenylated Acylphloroglucinol from *Hypericum sampsonii*

Zi-Zhen Zhang,[a,b,c] Yan-Rong Zeng,[a,c] Ya-Nan Li,[a,c] Zhan-Xing Hu,[a,c] Lie-Jun Huang,[a,b,c] Wei Gu,[a,b,c] Xiao-Jiang Hao,[a,b,c,d]*, Chun-Mao Yuan[a,b,c,]*

[a] *State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, Guiyang 550014, China.*

[b] School of Pharmaceutical Sciences, Guizhou Medical University, Guiyang 550025, China

[c] *The Key Laboratory of Chemistry for Natural Products of Guizhou Province and Chinese Academy of Sciences, Guiyang 550014, China.*

[d.] *State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Boanty, Chinese Academy of Science, Kunming 650201, China.*

* Corresponding author.

E-mail address: haoxj@mail.kib.ac.cn (X.J. Hao);

yuanchunmao01@126.com (C.M. Yuan)

Contents

1. Detail experimental procedures.

1.1 General experimental procedures

NMR spectra were performed on Bruker Avance NEO 600 MH with TMS as internal standard. UV spectra were measured on a Shimadzu UV-2401PC spectrometer. Optical rotations were detected on a JASCOP-1020 polarimeter. IR spectra were determined on a Bruker FT-IR Tensor-27 infrared spectrophotometer with KBr disks. CD spectra were recorded with an Applied Photophysics Chirascan instrument. HR-ESIMS analysis was carried out on Agilent 1290 UPLC/ 6540 Q-TOF mass spectrometers. Column chromatography was performed on silica gel (40-80, 200-300 and 300–400 mesh; Qingdao Marine Chemical Co. Ltd., China), RP-C18 gel (40-63μm, Merck, Darmstadt, Germany), and Sephadex LH-20 (40-70 μm, Amersham Pharmacia Biotech AB, Uppsala, Sweden). HPLC separation was performed on an instrument consisting of a Waters 600 controller, a Waters 600 pump, and a Waters 2487 dual λ absorbance detector with a YMC-C_{18} (250 × 10 mm) preparative column. The solvents used for HPLC were HPLC grade (Xinlanjing International Corporation, Pennsylvania, USA). Fractions were detected by TLC (GF 254, Qingdao Marine Chemical Co., Ltd.) and 5% H_2SO_4 in ethanol was used as chromogenic reagent.

1.2 Plant material

The aerial parts of *H. sampsonii* were collected from the Ziyun Country, Guizhou Province of China and identified by Mr. Jun Zhang. A voucher specimen (NO. 20191108) was deposited in the Key Laboratory of Chemistry for Natural Products of Guizhou Province and Chinese Academy of Sciences.

1.3 Extraction and isolation

The air-dried aerial parts of *H. sampsonii* (30 kg) were extracted with MeOH (150 L × 3) at room temperature (each time 5 days), and the MeOH extracts were combined and evaporated under reduced pressure to give a crude residue (3.3 kg), which was applied to a silica gel column chromatography eluted with petroleum ether-ethyl acetate (from 1:0 to 0:1) to obtain nine fractions (Fr. A–G). Fr. C (110 g) was applied to a RP-C18 column (MeOH: H_2O, 60% → 100%) to get nine subfractions (Fr. C1–Fr. C9). Compound **1** (20 mg) was isolated from Fr. C1 after repeated silica gel column chromatography. Fr.C3 was applied to a silica gel column and then was purified from HPLC to get **2** (13 mg, t_R = 43.3 min, CH_3OH: H_2O = 90: 10, v/v). Fr.C7 was subjected to HPLC to get **3** (15 mg, t_R = 54.9 min, CH_3CN: H_2O = 94: 6, v/v).

Hypsampsone A (1) Colorless oil, $[\alpha]^{20}_D$ +71.49 (*c* 0.7, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.26) and 256 (3.08) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 222 (+1.4), 252 (+20.1), 294 (-3.3) nm; IR (KBr) ν_{max} 3328, 2967, 2920, 2850, 1791, 1731, 1660, 1597, 1447, 1294, 1243, 1194, 1006,694 cm^{-1}; ^1H NMR (600 MHz) and ^{13}C NMR (150 MHz) data, see Table 1; HR-ESIMS *m*/*z*: $[M + H]^+$ 533.2898 (calcd. for $C_{33}H_{41}O_6$, 533.2893).

Hyperhexanone F (2) Light yellow oil, $[\alpha]^{20}_D$ –40 (*c* 0.3, MeOH); UV (MeOH) λ_{max} (log ε)

205 (4.56) and 247 (4.23) nm; IR (KBr) ν_{max} 3366, 2958, 2918, 2852,1758, 1719, 1680, 1594, 1445, 1376, 1234, 1183,1129, 1091, 979, 701 cm^{-1}; ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) data, see Table S1 in Supplementary Information; HR-ESIMS *m/z*: $[M + Na]^+$ 573.3187 (calcd. for $C_{34}H_{46}O_6Na$, 573.7177).

1.4 Theory and calculation details

The calculations were performed by using the density functional theory (DFT) as carried out in the Gaussian 09.[1-3] The preliminary conformational distributions search was performed by HyperChem Release 8.0 software.[1,2] Selected conformers with distributions higher than 1% were further optimized by the DFT (density functional theory) method at the B3LYP/6-311+g (d) level in Gaussian 09 program package.[2,3] The ECD of the conformer of selected conformers was then calculated by the TD-DFT method at the CAM-B3LYP/tzvp levels with the PCM model in methanol solution. The overall calculated ECD curves were weighted by Boltzmann distribution. The calculated ECD spectra were produced by SpecDis 1.604.[4]

1.5. MDR reversal activity

HepG2/ADR or MCF-7/ADR cells were seeded into 96-well plates at a density of 5×10^3/well. After 24h, incubated with premeditated concentration of reversal agents and ADR (6 concentration gradients) for an additional 48 h. The cytotoxicities of ADR with or without reversal agents were analyzed using the MTT assay. Verapamil (Solarbio, China) was used as a positive control, and DMSO was used as a negative control. The reversal fold is calculated as a ratio of $IC_{50(ADR)}$ to $IC_{50(reversal\ agent+ADR)}$. Two cancer cell lines, HepG2/ADR or MCF-7/ADR, were obtained from Sun Yat-Sen University.

2. The key 2D NMR correlations of hyperhexanone F (2) and ^{1}H and ^{13}C NMR data of compound 2 in $CDCl_3$.

Fig. S1 The key HMBC(↷), ^{1}H–^{1}H COSY (—), and NOESY (⇢) correlations of hyperhexanone F (**2**).

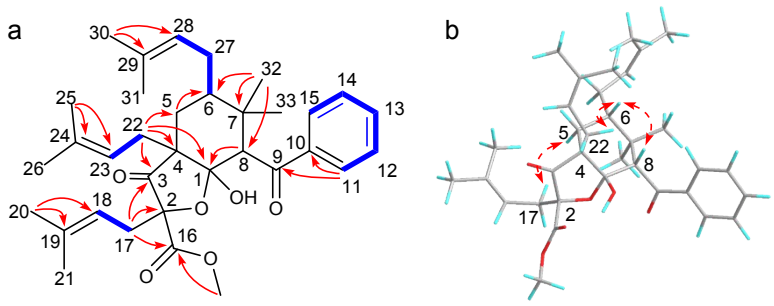
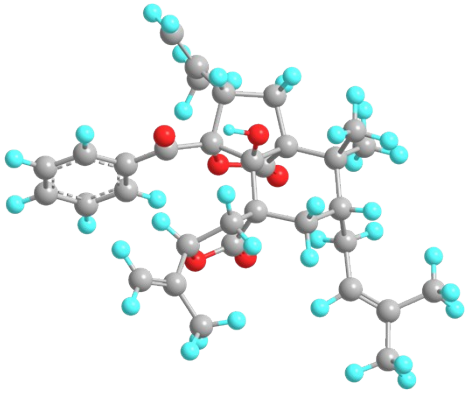


Table S1 ^{1}H and ^{13}C NMR data of compound **2** in $CDCl_3$ (600 MHz for ^{1}H and 150 MHz for ^{13}C, δ in ppm)

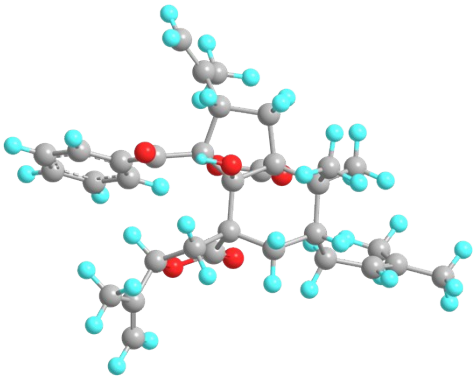
Pos.	δ_H (J in Hz)	δ_C	Pos.	δ_H (J in Hz)	δ_C
1		105.8	18		116.9
2		87.5	19		136.7
3		211.2	20	1.73 s	26.1
4		55.4	21	1.65 s	17.9
a	1.37 d (13.7)	31.5	22	2.42 d (8.7)	29.2
5b	1.72 overlap		23		119.9
6	1.43 m	44.3	24		134.3
7		38.7	25	1.80 s	
8	3.97 s	56.7	26	1.70 s	
9		200.2	27a	2.14 dd (14.3, 6.0)	27.8
10		141.1	27b	1.52 m	
11	7.99 d (8.5)	128.5	28		123.1
12	7.46 t (7.7)	128.6	29		133.1
13	7.54 t (7.4)	132.7	30	1.70 s	26.1
14	7.46 t (7.7)	128.6	31	1.56 s	18.1
15	7.99 d (8.5)	128.5	32	0.87s	28.9
16		171.3	33	1.17 s	15.5
17a	3.03 dd (14.6, 9.0)	36.5	OCH3	3.70 s	56.7
17b	2.60 dd (14.6, 6.0)				

3. ECD computation of hypsampsone A (1)

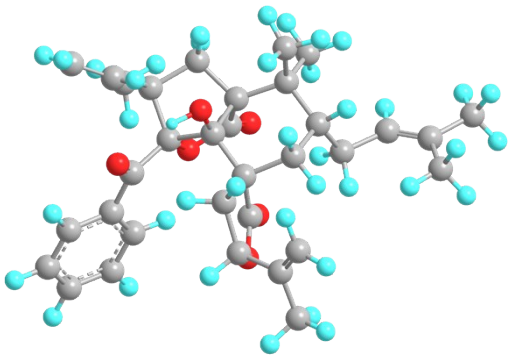
Fig. S2 DFT-optimized structures for low-energy conformers of compound **1** (**1a–1c**)



Conf 1a: 88.16%



Conf 1b: 11.52%



Conf 1c: 0.32%

Three stable conformers of optimized geometries of **1** at the B3LYP/6-311+g (d) level in the gas phase.

Table S2 Standard orientation of **1a** at B3LYP/6-311+g (d) level in gas phase:
Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.329462	0.489685	-0.971920
2	6	0	0.816722	0.763457	-0.730455
3	6	0	-0.035958	-0.517990	-1.031600
4	6	0	0.579095	-1.844360	-0.494211
5	6	0	2.078611	-2.086666	-0.829249
6	6	0	2.953446	-0.833691	-0.450817
7	6	0	0.581501	1.392057	0.632178
8	8	0	-0.198161	2.500743	0.562859
9	6	0	-0.430867	2.876224	-0.787463
10	6	0	0.464710	1.986198	-1.621633
11	6	0	3.446503	-0.779444	1.019226
12	6	0	-1.374138	-0.806439	-0.289730
13	6	0	-1.788726	-2.211670	-0.874583
14	6	0	-0.424365	-2.944950	-0.959208
15	6	0	-2.474768	0.191205	-0.644603
16	6	0	-3.522069	0.542111	0.346491
17	8	0	-2.551732	0.651715	-1.787542
18	6	0	-4.840733	0.659045	-0.112409
19	6	0	-5.864479	0.996551	0.773433
20	6	0	-5.573032	1.230074	2.115987
21	6	0	-4.258594	1.134358	2.571971
22	6	0	-3.230051	0.796393	1.689016
23	8	0	-0.952701	-0.980332	1.045689
24	6	0	-2.899445	-2.975637	-0.166213
25	6	0	-4.014178	-3.325950	-0.832763
26	6	0	-2.749802	-3.349408	1.285491
27	6	0	0.201008	-1.727823	0.983286
28	8	0	0.704936	-2.271395	1.946279
29	6	0	4.344850	0.391792	1.327581
30	6	0	5.681342	0.460075	1.172131
31	6	0	6.438253	1.701382	1.563677
32	6	0	6.538590	-0.641247	0.612405
33	8	0	0.998270	0.968774	1.695621
34	6	0	-0.170201	4.357067	-0.960949
35	6	0	-1.023033	5.141197	-1.643787
36	6	0	1.067315	4.932435	-0.324472
37	8	0	-0.193009	-0.618808	-2.460495
38	6	0	2.608318	-3.382869	-0.167745
39	6	0	2.284026	-2.333461	-2.357010
40	1	0	2.915341	1.341751	-0.604963
41	1	0	2.494101	0.497343	-2.059363
42	1	0	3.889824	-0.936060	-1.022466
43	1	0	-1.483668	2.676506	-0.997659
44	1	0	1.376080	2.531972	-1.900406
45	1	0	-0.008360	1.742295	-2.576552
46	1	0	2.614961	-0.753528	1.721861
47	1	0	3.990250	-1.697463	1.266801
48	1	0	-2.125332	-2.059796	-1.911738
49	1	0	-0.257550	-3.260873	-1.993174
50	1	0	-0.378734	-3.841136	-0.331089
51	1	0	-5.077370	0.483372	-1.159903

52	1	0	-6.887972	1.080463	0.416261
53	1	0	-6.369161	1.495781	2.807502
54	1	0	-4.030739	1.331110	3.617420
55	1	0	-2.215064	0.763262	2.075419
56	1	0	-4.818892	-3.873070	-0.348388
57	1	0	-4.161848	-3.083267	-1.881292
58	1	0	-3.555198	-4.013878	1.618554
59	1	0	-1.810137	-3.879089	1.463123
60	1	0	-2.785979	-2.461732	1.922518
61	1	0	3.822426	1.250601	1.750735
62	1	0	7.184786	1.464388	2.328753
63	1	0	5.781581	2.478234	1.969279
64	1	0	6.952466	2.122065	0.693392
65	1	0	5.965968	-1.513824	0.288777
66	1	0	7.094239	-0.278362	-0.258779
67	1	0	7.258695	-0.977484	1.365518
68	1	0	-1.925283	4.743620	-2.100416
69	1	0	-0.846956	6.206692	-1.761926
70	1	0	1.024792	4.826425	0.764185
71	1	0	1.182163	5.999193	-0.545552
72	1	0	1.965568	4.425054	-0.688737
73	1	0	-0.996336	-0.116274	-2.722062
74	1	0	2.538399	-3.373204	0.921408
75	1	0	3.664005	-3.543923	-0.417982
76	1	0	2.056334	-4.262683	-0.517279
77	1	0	1.969356	-1.490973	-2.975327
78	1	0	3.344557	-2.503694	-2.582105
79	1	0	1.751979	-3.223606	-2.705954

Table S3 Standard orientation of 1b at B3LYP/6-311+g (d) level in gas phase:

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	1.718858	1.810914	-1.222205
2	6	0	0.270112	1.413651	-0.810001
3	6	0	0.024001	-0.073432	-1.291151
4	6	0	1.219736	-1.033913	-0.960671
5	6	0	2.648339	-0.585174	-1.380147
6	6	0	2.911671	0.879874	-0.882660
7	6	0	0.039352	1.653950	0.699248
8	8	0	-1.136559	2.297538	0.905710
9	6	0	-1.782671	2.700459	-0.324393
10	6	0	-0.728584	2.437093	-1.418638
11	6	0	3.427868	1.060187	0.576439
12	6	0	-1.011137	-0.982045	-0.530301
13	6	0	-0.868098	-2.341498	-1.320660
14	6	0	0.681561	-2.388068	-1.537769
15	6	0	-2.460599	-0.524592	-0.514710
16	6	0	-3.359107	-0.664248	0.663567
17	8	0	-2.871399	-0.098431	-1.586609
18	6	0	-4.718434	-0.906410	0.408012
19	6	0	-5.620512	-1.017178	1.456940
20	6	0	-5.182797	-0.853794	2.772919
21	6	0	-3.840659	-0.584821	3.033545
22	6	0	-2.923622	-0.502939	1.988720
23	8	0	-0.394144	-1.149807	0.749669
24	6	0	-1.495848	-3.580914	-0.708309
25	6	0	-2.413560	-4.242435	-1.419038
26	6	0	-1.054280	-4.079357	0.647488
27	6	0	0.969514	-1.266194	0.544617
28	8	0	1.698136	-1.574915	1.434678
29	6	0	4.927845	0.957761	0.707378
30	6	0	5.648113	0.314657	1.632622
31	6	0	7.157689	0.377156	1.620018
32	6	0	5.069366	-0.524747	2.744354
33	8	0	0.751569	1.366569	1.618140
34	6	0	-2.262845	4.130644	-0.248959
35	6	0	-1.979760	4.925291	0.779855
36	6	0	-3.092003	4.565419	-1.431661
37	8	0	-0.255635	-0.058715	-2.680005
38	6	0	3.700669	-1.577421	-0.848128
39	6	0	2.789037	-0.591223	-2.927621
40	1	0	1.918894	2.796301	-0.793331
41	1	0	1.686213	1.956846	-2.304485
42	1	0	3.719884	1.255634	-1.521236
43	1	0	-2.652308	2.050099	-0.457900
44	1	0	-0.186149	3.362543	-1.624498
45	1	0	-1.170196	2.115143	-2.357941
46	1	0	3.143312	2.074372	0.881805
47	1	0	2.914985	0.404079	1.272463
48	1	0	-1.347267	-2.188011	-2.283928
49	1	0	0.891915	-2.452504	-2.600383
50	1	0	1.147740	-3.241207	-1.046193
51	1	0	-5.049787	-1.014871	-0.617491

52	1	0	-6.665196	-1.223626	1.250775
53	1	0	-5.889246	-0.932647	3.592776
54	1	0	-3.501040	-0.443233	4.053386
55	1	0	-1.886437	-0.293181	2.203583
56	1	0	-2.867955	-5.155882	-1.048847
57	1	0	-2.741414	-3.902014	-2.396784
58	1	0	0.032544	-4.175829	0.722372
59	1	0	-1.354097	-3.400081	1.447237
60	1	0	-1.490468	-5.059071	0.850899
61	1	0	5.484076	1.531719	-0.037648
62	1	0	7.548134	0.804091	2.551727
63	1	0	7.536058	0.979038	0.790566
64	1	0	7.595130	-0.625669	1.535929
65	1	0	5.367047	-1.575402	2.636693
66	1	0	5.458202	-0.196096	3.715307
67	1	0	3.982011	-0.495200	2.792869
68	1	0	-1.401423	4.579873	1.627578
69	1	0	-2.335891	5.950136	0.807735
70	1	0	-3.437325	5.592484	-1.309193
71	1	0	-3.971996	3.924739	-1.559624
72	1	0	-2.529157	4.511478	-2.370607
73	1	0	-1.209764	0.084128	-2.774678
74	1	0	3.694705	-1.667534	0.234211
75	1	0	4.697219	-1.257504	-1.156991
76	1	0	3.530801	-2.572851	-1.269770
77	1	0	2.683638	-1.594832	-3.342464
78	1	0	2.068504	0.046392	-3.435018
79	1	0	3.795081	-0.249683	-3.183774

Table S4 Standard orientation of **1c** at B3LYP/6-311+g (d) level in gas phase:
Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-2.089862	0.705055	0.955927
2	6	0	-0.581916	0.970074	0.697915
3	6	0	0.262800	-0.295466	1.065057
4	6	0	-0.330174	-1.653410	0.587523
5	6	0	-1.847354	-1.872771	0.864601
6	6	0	-2.694633	-0.620328	0.420914
7	6	0	-0.402066	1.576695	-0.681891
8	8	0	-0.254775	2.927629	-0.633069
9	6	0	-0.413908	3.419533	0.698105
10	6	0	-0.154025	2.193456	1.550944
11	6	0	-3.064505	-0.484533	-1.081155
12	6	0	1.629807	-0.620894	0.393784
13	6	0	2.024956	-1.979035	1.096457
14	6	0	0.656699	-2.714398	1.172854
15	6	0	2.724936	0.405263	0.685236
16	6	0	3.713076	0.769352	-0.360984
17	8	0	2.856627	0.878832	1.817188
18	6	0	5.052924	0.903106	0.027449
19	6	0	6.025022	1.249813	-0.911709
20	6	0	5.660955	1.475945	-2.237804
21	6	0	4.325865	1.363394	-2.623813
22	6	0	3.349083	1.016000	-1.687322
23	8	0	1.274693	-0.910689	-0.940267
24	6	0	3.170562	-2.783453	0.495671
25	6	0	4.256724	-3.073602	1.234567
26	6	0	3.088188	-3.263175	-0.929830
27	6	0	0.117421	-1.647233	-0.875422
28	8	0	-0.338342	-2.266346	-1.817233
29	6	0	-4.278787	-1.278267	-1.492611
30	6	0	-5.569690	-0.913893	-1.362416
31	6	0	-6.675027	-1.806544	-1.861106
32	6	0	-6.039811	0.366274	-0.729263
33	8	0	-0.409381	0.972533	-1.739195
34	6	0	-1.728419	4.168611	0.812966
35	6	0	-2.611925	4.040008	1.818814
36	6	0	-1.991769	5.167082	-0.288342
37	8	0	0.374512	-0.308362	2.507109
38	6	0	-2.359246	-3.183957	0.224667
39	6	0	-2.111116	-2.076360	2.390315
40	1	0	-2.694365	1.529052	0.559884
41	1	0	-2.263738	0.726646	2.040032
42	1	0	-3.662306	-0.703420	0.939718
43	1	0	0.386624	4.149252	0.874803
44	1	0	-0.608203	2.226170	2.545225
45	1	0	0.923554	2.173241	1.724121
46	1	0	-3.251238	0.566228	-1.335346
47	1	0	-2.238508	-0.779197	-1.727493
48	1	0	2.314909	-1.751958	2.133776
49	1	0	0.445774	-2.956769	2.218737
50	1	0	0.641907	-3.652847	0.608308

51	1	0	5.345906	0.731924	1.061317
52	1	0	7.064851	1.344768	-0.608922
53	1	0	6.417009	1.746259	-2.971261
54	1	0	4.041104	1.550242	-3.657186
55	1	0	2.316972	0.961127	-2.022597
56	1	0	5.085211	-3.647624	0.827910
57	1	0	4.356097	-2.751819	2.267397
58	1	0	2.158867	-3.809774	-1.110500
59	1	0	3.152013	-2.424013	-1.627803
60	1	0	3.909468	-3.945766	-1.176231
61	1	0	-4.054342	-2.226732	-1.980010
62	1	0	-7.330821	-2.096401	-1.033642
63	1	0	-6.293294	-2.724624	-2.320058
64	1	0	-7.273928	-1.283232	-2.613640
65	1	0	-6.583660	0.971286	-1.462041
66	1	0	-6.713452	0.146858	0.105892
67	1	0	-5.224652	0.977931	-0.334683
68	1	0	-2.466732	3.364881	2.654540
69	1	0	-3.527757	4.625859	1.841674
70	1	0	-1.150164	5.861478	-0.380419
71	1	0	-2.890755	5.763740	-0.099552
72	1	0	-2.131501	4.655744	-1.246130
73	1	0	1.166634	0.213769	2.763733
74	1	0	-1.804873	-4.051671	0.599974
75	1	0	-2.272726	-3.197371	-0.862100
76	1	0	-3.415822	-3.350888	0.465769
77	1	0	-1.625562	-2.979386	2.773660
78	1	0	-1.779958	-1.235137	3.001413
79	1	0	-3.183928	-2.200639	2.584877

---

4. ACD/Labs calculated method of hypsampsone A (1).

Correlation Spectroscopy Based Structure Generator options:

Keep Generated Molecules = Yes

Clear Generated Molecules List Before Generation = Yes

Add Structures Already Existing in Generated Molecules List = No

Transfer Spectra to Generated Structures = Yes

Use Assignment when Removing Duplicates = Yes

Allow Filter during Generation = Yes

Use Only 1000 First MCD(s)

Allow "Fuzzy" Generation = Yes

"Fuzzy" Generation Options were Determined Automatically

2D NMR Spectral Data Must Contain Connectivities = Real spectrum

Increase Connectivity Length when Merging Connectivities = No

Allow Bonds between Heteroatoms = Yes

Allow Bonds between Heteroatoms of the Same Atom Type = Yes

Use NMR Shifts Correlation Table = 2

Maximum bond multiplicity = 3

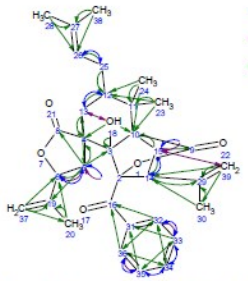
MCD #1 (ID = 0): (200/0) structures have been generated.

2729 molecule(s) have been generated by Correlation Spectroscopy Based Generator and 200 molecule(s) have been stored.

Generation time: 14 s (Check: 0 s, Generation: 14 s 017 ms)

1 (from No) connectivities have been extended during generation

1 (from 0 possible) connectivity combination(s) have been used during generation



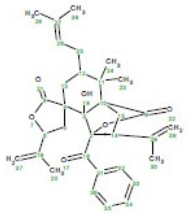
COSY
NOESY
HMBC

Date (dd/mm/yyyy): 29 06 2020

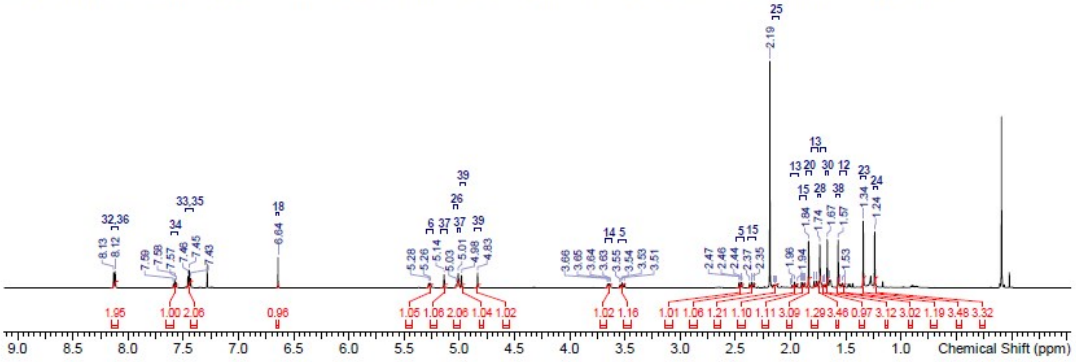
#	Atom#	C Label	C Shift	X Shift	XHn	H Label	H Shift	C Calc Shift (HOSE)	H Calc Shift (Neural Net)	H Multiplicity	COSY	NOESY	H HMBC	C HMBC	Non-Negative H Volume
1	23	M02	17.031		CH3	H 2	1.343	23.930	1.240	s				11, 12, 10	3.476
2	38	M03	17.763		CH3	H 4	1.571	17.940	1.613	s				26, 27	3.022
3	20	M04	18.387		CH3	H 9	1.838	18.730	1.773	s			37, 37	6, 19	3.087
4	30	M05	23.525		CH3	H 5	1.668	22.530	1.855	s			39, 39	14, 29	3.115
5	24	M06	24.553		CH3	H 1	1.237	25.870	1.240	s				11, 12, 10	3.318
6	28	M07	25.983		CH3	H 7	1.737	25.970	1.677	m				26, 27	3.462
7	25	M08	26.493		CH2	H 6	1.714	28.240	2.012	br d (8.54)	26			12	0.972
8	25	M08	26.493		CH2	H 12	2.141	28.240	2.012	br dd (14.08, 5.36)	26			26	1.212
9	15	M09	28.589		CH2	H 10	1.884	30.090	2.014	dd (14.35, 4.72)	15	15, 39		14, 9	1.106
10	15	M09	28.589		CH2	H 13	2.353	30.090	2.014	dd (14.26, 10.63)	15, 14	15		10, 9	1.055
11	5	M11	33.185		CH2	H 15	3.526	35.860	2.536	m	5, 6	5, 6	13	13, 4, 6, 3, 19	1.158
12	5	M11	33.185		CH2	H 14	2.458	35.860	2.536	dd (12.53, 2.91)	5	5	13	8	1.010
13	11	M12	34.426		C			40.530					24, 23		
14	13	M13	34.607		CH2	H 11	1.985	34.390	2.274	m	12, 13	18	5	5, 12, 4	1.095
15	13	M13	34.607		CH2	H 8	1.780	34.390	2.274	dd (13.81, 2.54)	13		5	12	1.290
16	12	M14	40.748		CH	H 3	1.532	40.740	1.816	m	13		24, 23, 25, 13, 13		1.191
17	4	M15	46.248		C			56.190					13, 5, 18		
18	14	M16	50.350		CH	H 16	3.647	45.560	3.705	dd (10.54, 4.54)	15		30, 15, 39, 39	29	1.015
19	10	M17	61.432		C			60.690					24, 23, 15, 18		
20	6	M18	78.926		CH	H 22	5.271	78.000	4.818	br d (9.26)	5	5	20, 5, 37, 37		1.049

#	Atom#	C Label	C Shift	X Shift	XHn	H Label	H Shift	C Calc Shift (HOSE)	H Calc Shift (Neural Net)	H Multiplicity	COSY	NOESY	H HMBC	C HMBC	Non-Negative H Volume
21	3	M19	90.312		C			89.130					5, 18		
22	2	M20	98.376		C			93.460							
23	37	M21	111.998		CH2	H 19	5.010	114.210	4.696	br s				20, 6	1.338
24	37	M21	111.998		CH2	H 21	5.139	114.210	4.852	s				20, 6, 19	1.058
25	39	M22	114.719		CH2	H 18	4.981	114.820	4.597	s		39		30, 14	1.044
26	39	M22	114.719		CH2	H 17	4.836	114.820	4.590	s		15, 39		30, 14, 29	1.019
27	26	M23	122.932		CH	H 20	5.024	124.820	5.105	br s	25, 25		38, 28, 25		0.777
28	33, 35	M24	128.366		CH	H 24	7.447	128.640	7.346	t (7.90, 7.90)	34, 32, 36	32, 36		31	2.062
29	32, 36	M25	130.290		CH	H 26	8.123	129.570	7.830	m	33, 35	33, 35	34	34, 16	1.949
30	27	M26	133.800		C			132.910					38, 28		
31	34	M27	133.833		CH	H 25	7.578	133.090	7.407	m	33, 35		32, 36	32, 36	1.000
32	31	M28	136.266		C			135.670					33, 35		
33	29	M29	141.010		C			143.280					30, 14, 39		
34	19	M30	142.210		C			143.870					20, 5, 37		
35	9	M31	173.737		C			176.170					15, 15		
36	8	M32	181.465		C			179.050					5		
37	16	M33	198.794		C			195.570					32, 36		
38	18	O 1		100.000	OH	H 23	6.640		3.303	s		13		4, 10, 3	0.961

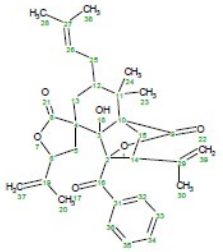
Acquisition Time (sec)	2.7525	Comment	Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)		
D	0.0002	D1	1	DE	7.729705
DS	2	Date	04 Jan 2020 07:08:05 (GMT+08:00)		
Date Stamp	04 Jan 2020 07:08:05 (GMT+08:00)			ExpNo	1
File Name	D:\ACD\结构解析\贵州天然产物重点实验室 苑老师\HSH-12b\1\PDATA\1\1r				
Frequency (MHz)	600.1300	GB	0	INSTRUM	<Avance>
LB	0.3	NS	16	Nucleus	1H
Number of Transients	16	Origin	Avance	Original Points Count	32768
Owner	nmrsu	PC	1		
PROBHD	<Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)>			PULPROG	<zg30>
Points Count	65536	Pulse Sequence	zg30	Receiver Gain	92.31
SF	600.13	SFO1	600.133705802		
SI	65536	SSB	0	SW(cyclical) (Hz)	11904.76
SWH	11904.7619047619			Solvent	CHLOROFORM-d
Spectrum Offset (Hz)	3705.7993	Spectrum Type	standard	Sweep Width (Hz)	11904.58
TD	65536	TD0	1	TE	298.0051
Temperature (degree C)	25.005	UNC1	<1H>	WDW	1

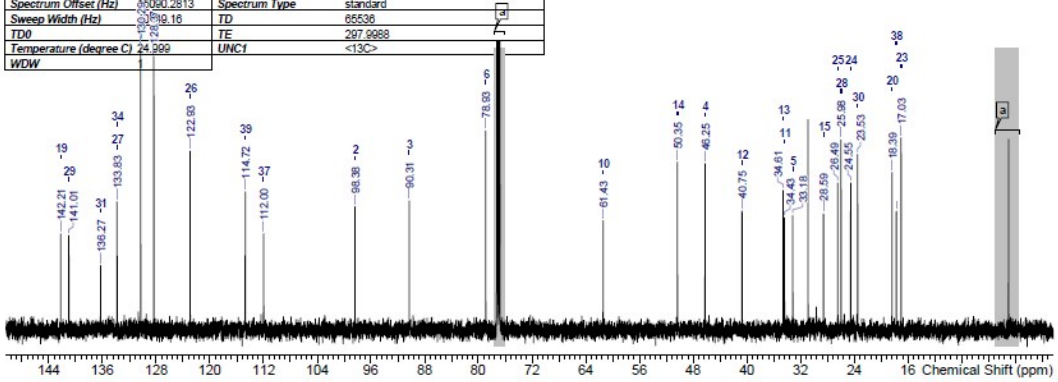


^{1}H NMR (600 MHz, CHLOROFORM-*d*) δ ppm 1.24 (s, 3 H) 1.34 (s, 3 H) 1.50 - 1.55 (m, 1 H) 1.57 (s, 3 H) 1.67 (s, 3 H) 1.70 (br d, *J*=8.54 Hz, 1 H) 1.73 - 1.75 (m, 3 H) 1.78 (dd, *J*=13.81, 2.54 Hz, 1 H) 1.84 (s, 3 H) 1.89 (dd, *J*=14.35, 4.72 Hz, 1 H) 1.93 - 2.00 (m, 1 H) 2.14 (br dd, *J*=14.08, 5.36 Hz, 1 H) 2.35 (dd, *J*=14.26, 10.63 Hz, 1 H) 2.45 (dd, *J*=12.53, 2.91 Hz, 1 H) 3.49 - 3.57 (m, 1 H) 3.65 (dd, *J*=10.54, 4.54 Hz, 1 H) 4.83 (s, 1 H) 4.98 (s, 1 H) 5.01 (br s, 1 H) 5.02 (br s, 1 H) 5.14 (s, 1 H) 5.27 (br d, *J*=9.26 Hz, 1 H) 6.64 (s, 1 H) 7.45 (t, *J*=7.90 Hz, 2 H) 7.55 - 7.61 (m, 1 H) 8.09 - 8.16 (m, 2 H)

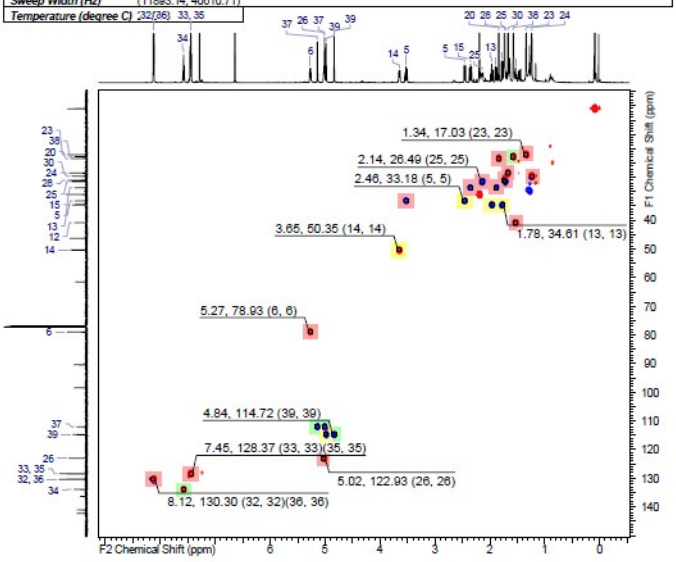


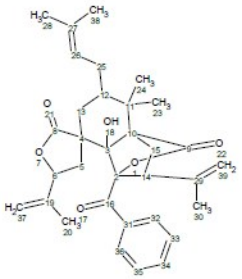
Acquisition Time (sec)	0.8061		
Comment	Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)		
D	0.03	D1	2
DE	6.5	DS	2
Date	24 Dec 2019 17:35:17 (GMT+08:00)		
Date Stamp	24 Dec 2019 17:35:17 (GMT+08:00)		
ExpNo	6		
File Name	D:\ACD\结构解析\贵州天然产物重点实验室 苑老师\HSH-12b\6\PDATA\1\1r		
Frequency (MHz)	150.9028	GB	0
INSTRUM	<Avance>	LB	1
NS	1024	Nucleus	13C
Number of Transients	1024	Origin	Avance
Original Points Count	32768	Owner	nmrsu
PC	1.4		
PROBHD	<Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)>		
PULPROG	<zgpg30>	Points Count	32768
Pulse Sequence	zgpg30	Receiver Gain	101.00
SF	150.902808526		
SFO1	150.917898807		
SI	32768	SSB	0
SW(cyclical) (Hz)	40650.41	SWH	40650.406504065
Solvent	CHLOROFORM-d		
Spectrum Offset (Hz)	45090.2813	Spectrum Type	standard
Sweep Width (Hz)	39.16	TD	65536
TD0	1	TE	297.9968
Temperature (degree C)	24.999	UNC1	<13C>
WDW	1		



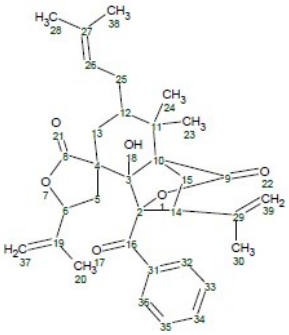


Acquisition Time (sec)	(0.0430, 0.0063)	*Comment*	Z114607 0334 (PA BBO 600S3 BBF-H-D-05 Z SP)
Date	04 Jan 2020 11:12:10		
ExpNo	4		
File Name	D:\ACD\结构解析\贵州天然产物重点实验室 殷老师\HSH-12b\4\PDATA\1\2rr		
Frequency (MHz)	(600.1300, 150.9028)		
Mixing Time	0	*Nucleus*	(1H, 13C)
Number of Transients	8	*Origin*	Avance
Original Points Count	(512, 256)	*Owner*	nmrsu
Points Count	(1024, 1024)	*Pulse Sequence*	hsqcedetgpsp.3
Solvent	CHLOROFORM-d	*Spectrum Type*	HSQC-DEPT
Sweep Width (Hz)	(11893.14, 40610.71)		
Temperature (degree C)	32(36) 33, 35		

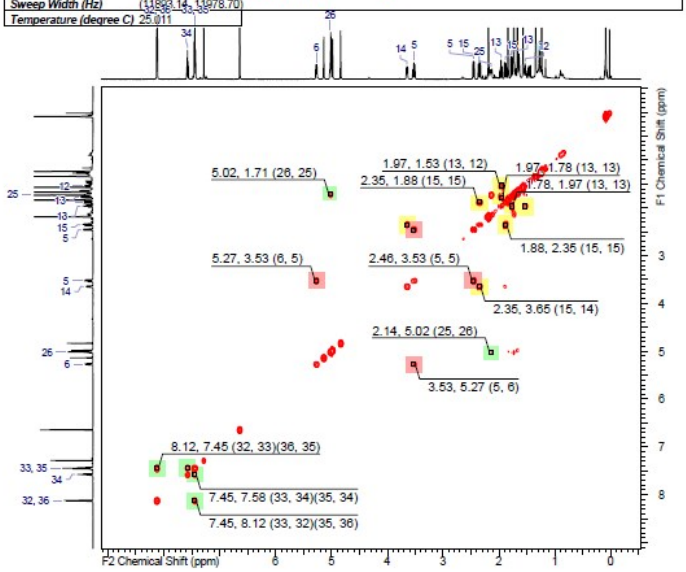


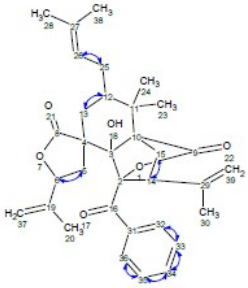


No.	F2 Atom	F1 Atom	F2 (ppm)	F1 (ppm)
1	5	5	2.46	33.18
2	5	5	3.53	33.18
3	6	6	5.27	78.93
4	12	12	1.53	40.75
5	13	13	1.78	34.61
6	13	13	1.97	34.61
7	14	14	3.65	50.35
8	15	15	1.88	28.59
9	15	15	2.35	28.59
10	20	20	1.84	18.39
11	23	23	1.34	17.03
12	24	24	1.24	24.55
13	25	25	1.71	26.49
14	25	25	2.14	26.49
15	26	26	5.02	122.93
16	28	28	1.74	25.98
17	30	30	1.67	23.53
18	32	32	8.12	130.30
19	33	33	7.45	128.37
20	34	34	7.58	133.83
21	35	35	7.45	128.37
22	36	36	8.12	130.30
23	37	37	5.01	112.00
24	37	37	5.14	112.00
25	38	38	1.57	17.76
26	39	39	4.84	114.72
27	39	39	4.98	114.72

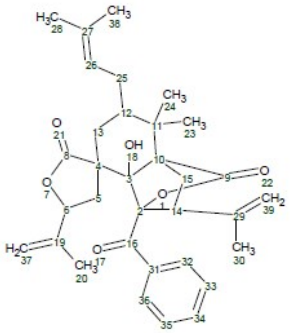


Acquisition Time (sec)	(0.0860, 0.0214)	*Comment*	Z114607 0334 (PA BBO 600S3 BBF-H-D-05 Z SP)
Date	04 Jan 2020 11:11:52		
ExpNo	2		
File Name	D:\ACD\结构解析\贵州天然产物重点实验室 简老师\HSH-12b\2\PDATA\1\2rr		
Frequency (MHz)	(600.1300, 600.1300)		
Mixing Time	0	*Nucleus*	(1H, 1H)
Number of Transients	4	*Origin*	Avance
Original Points Count	(1024, 256)	*Owner*	nmrsu
Points Count	(1024, 1024)	*Pulse Sequence*	cosygpppqf
Solvent	CHLOROFORM-d	*Spectrum Type*	COSY
Sweep Width (Hz)	(11993.14, 11978.70)		
Temperature (degree C)	25.011		

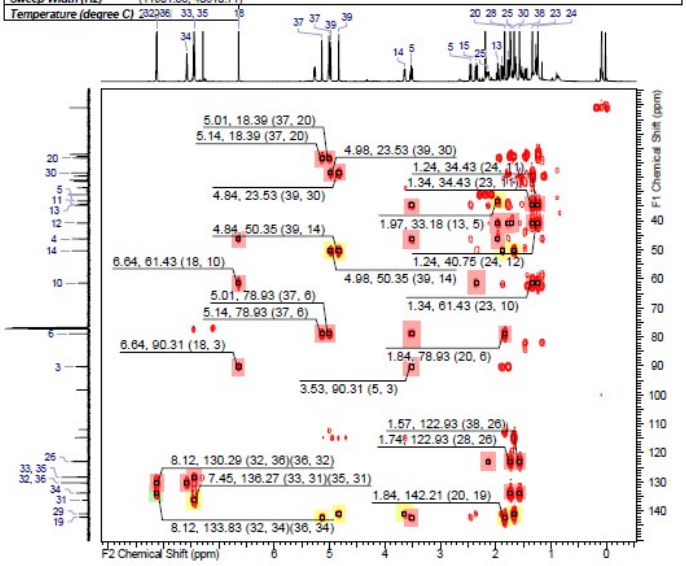


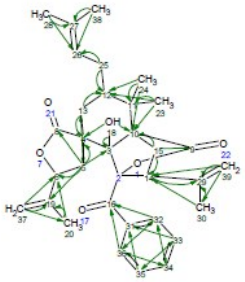


No.	F2 Atom	F1 Atom	F2 (ppm)	F1 (ppm)
1	5	5	3.53	2.46
2	5	5	2.46	3.53
3	6	5	5.27	3.53
4	5	6	3.53	5.27
5	13	12	1.97	1.53
6	12	13	1.53	1.97
7	13	13	1.97	1.78
8	13	13	1.78	1.97
9	15	14	2.35	3.65
10	14	15	3.65	2.35
11	15	15	2.35	1.88
12	15	15	1.88	2.35
13	26	25	5.02	1.71
14	25	26	2.14	5.02
15	33	32	7.45	8.12
16	32	33	8.12	7.45
17	34	33	7.58	7.45
18	33	34	7.45	7.58
19	35	34	7.45	7.58
20	34	35	7.58	7.45
21	36	35	8.12	7.45
22	35	36	7.45	8.12



Acquisition Time (sec)	(0.1613, 0.0040)	*Comment*	Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)
Constant (Hz)	10.0	*Date*	04 Jan 2020 11:12:18
ExpNo	5		
File Name	D:\ACD结构解析\贵州天然产物重点实验室 晏老师\HSH-12b\5\PDATA\1\2rr		
Frequency (MHz)	(600.1300, 150.9028)		
Mixing Time	0	*Nucleus*	(1H, 13C)
Number of Transients	8	*Origin*	Avance
Original Points Count	(1920, 183)	*Owner*	nmrsu
Points Count	(4096, 1024)	*Pulse Sequence*	hmbcgplpndqf
Solvent	CHLOROFORM-d	*Spectrum Type*	HMBC
Sweep Width (Hz)	(11901.86, 40610.71)		
Temperature (degree C)	32.936		

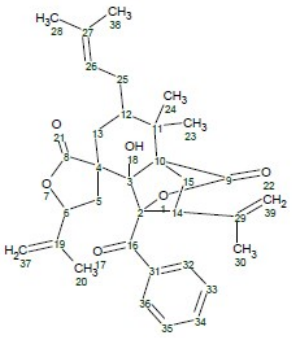




Date (dd/mm/yyyy): 29 06 2020
Page: 9

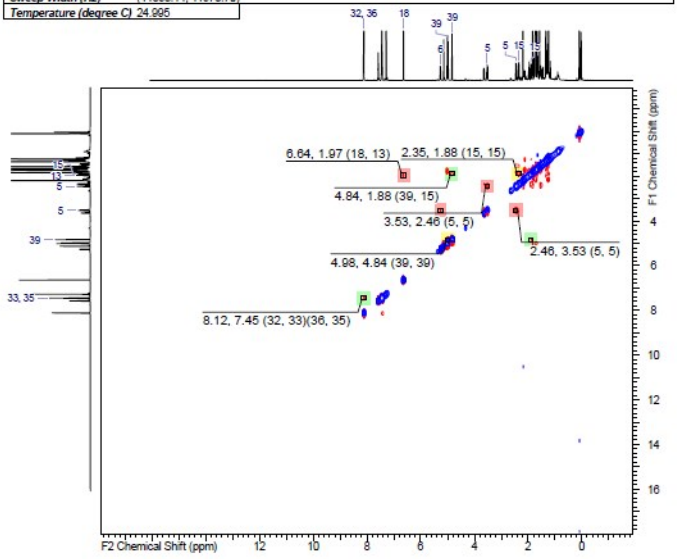
No.	F2 Atom	F1 Atom	F2 (ppm)	F1 (ppm)
1	5	3	3.53	90.31
2	18	3	6.64	90.31
3	5	4	3.53	46.25
4	13	4	1.97	46.25
5	18	4	6.64	46.25
6	13	5	1.97	33.18
7	5	6	3.53	78.93
8	20	6	1.84	78.93
9	37	6	5.01	78.93
10	37	6	5.14	78.93
11	5	8	2.46	181.46
12	15	9	1.88	173.74
13	15	9	2.35	173.74
14	15	10	2.35	61.44
15	18	10	6.64	61.43
16	23	10	1.34	61.43
17	24	10	1.24	61.43
18	23	11	1.34	34.43
19	24	11	1.24	34.43
20	13	12	1.78	40.75
21	13	12	1.97	40.75
22	23	12	1.34	40.75
23	24	12	1.24	40.75
24	25	12	1.71	40.75
25	5	13	3.53	34.61
26	15	14	1.88	50.35
27	30	14	1.67	50.35
28	39	14	4.84	50.35
29	39	14	4.98	50.35
30	32	16	8.12	198.79
31	36	16	8.12	198.79
32	5	19	3.53	142.21
33	20	19	1.84	142.21
34	37	19	5.14	142.21
35	37	20	5.01	18.39
36	37	20	5.14	18.39
37	25	26	2.14	122.93
38	28	26	1.74	122.93

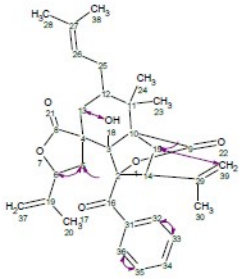
No.	F2 Atom	F1 Atom	F2 (ppm)	F1 (ppm)
39	38	26	1.57	122.93
40	28	27	1.74	133.80
41	38	27	1.57	133.80
42	14	29	3.65	141.01
43	30	29	1.67	141.01
44	39	29	4.84	141.01
45	39	30	4.84	23.53
46	39	30	4.98	23.53
47	33	31	7.45	136.27
48	35	31	7.45	136.27
49	34	32	7.58	130.29
50	36	32	8.12	130.29
51	35	33	7.45	128.37
52	32	34	8.12	133.83
53	36	34	8.12	133.83
54	33	35	7.45	128.37
55	32	36	8.12	130.29
56	34	36	7.58	130.29



Date (dd/mm/yyyy): 29 06 2020
Page: 10

Acquisition Time (sec)	(0.0860, 0.0214)	*Comment*	Z114607_0334 (PA BBO 600S3 BBF-H-D-05 Z SP)
Date	04 Jan 2020 11:12:02		
ExpNo	3		
File Name	D:\ACD\结构解析\贵州天然产物重点实验室 苑老师\HSH-12b\3\PDATA\1\2rr		
Frequency (MHz)	(600.1300, 600.1300)		
Mixing Time	0.3	*Nucleus*	(1H, 1H)
Number of Transients	4	*Origin*	Avance
Original Points Count	(1024, 256)	*Owner*	nmrsu
Points Count	(1024, 1024)	*Pulse Sequence*	noesygpph
Solvent	CHLOROFORM-d	*Spectrum Type*	NOESY
Sweep Width (Hz)	(11893.14, 11978.70)		
Temperature (degree C)	24.995		





No.	F2 Atom	F1 Atom	F2 (ppm)	F1 (ppm)
1	5	5	3.53	2.46
2	5	5	2.46	3.53
3	6	5	5.27	3.53
4	18	13	6.64	1.97
5	15	15	2.35	1.88
6	39	15	4.84	1.88
7	32	33	8.12	7.45
8	36	35	8.12	7.45
9	15	39	1.88	4.84
10	39	39	4.98	4.84

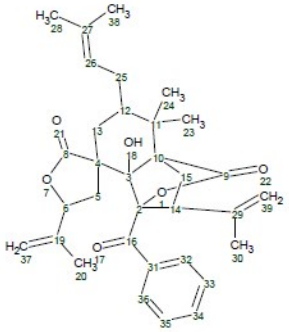


Fig. S3 The top ranked structures of the output file generated by the ACD/Labs software for compound **1**.

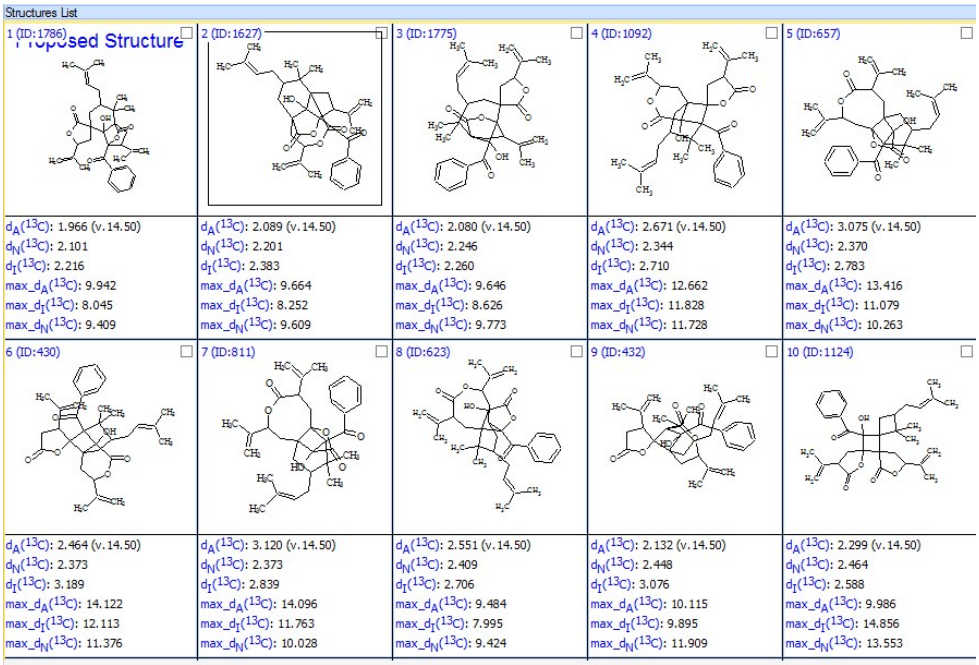


Table S5 ^{13}C NMR calculation of **1**

No.	Experiment Shift (ppm)	HOSE Shift (ppm)	Difference (ppm)	Neural Network Shift (ppm)	Difference (ppm)
1	61.432	60.69	-0.742	60.38	-1.052
2	28.589	30.09	1.501	30.671	2.081
3	50.35	45.58	-4.77	45.43	-4.92
4	98.376	93.46	-4.916	93.549	-4.828
5	90.312	89.13	-1.182	89.266	-1.046
6	46.248	56.19	9.942	55.657	9.409
7	34.607	34.39	-0.217	35.324	0.716
8	40.748	40.74	-0.008	40.85	0.102
9	34.426	40.53	6.104	40.624	6.198
10	173.737	176.17	2.433	173.561	-0.176
11	181.465	179.05	-2.415	178.499	-2.966
12	24.553	25.87	1.317	24.755	0.202
13	17.031	23.93	6.899	24.755	7.724
14	141.01	143.28	2.27	144.253	3.243
15	114.719	114.82	0.101	113.808	-0.912
16	23.525	22.53	-0.995	22.785	-0.74
17	33.185	35.86	2.675	38.009	4.824
18	78.926	78	-0.926	77.912	-1.014
19	142.21	143.87	1.66	141.209	-1.001
20	111.998	114.21	2.212	113.217	1.219
21	18.387	18.73	0.343	18.19	-0.197
22	26.493	28.24	1.747	28.243	1.75
23	122.932	124.82	1.888	123.795	0.863
24	133.833	133.09	-0.743	132.727	-1.106
25	17.763	17.94	0.177	18.009	0.246
26	25.983	25.97	-0.013	26.166	0.183
27	198.794	195.57	-3.224	193.555	-5.239
28	136.266	135.67	-0.596	136.705	0.439
29,33	130.29	129.57	-0.72	128.914	-1.375
30,32	128.366	128.64	0.274	128.882	0.516
31	133.8	132.91	-0.89	132.646	-1.154

5. Spectra of physico-chemical properties of hypsampsone A (1).

Fig. S4 ^{1}H NMR spectrum of hypsampsone A (**1**).

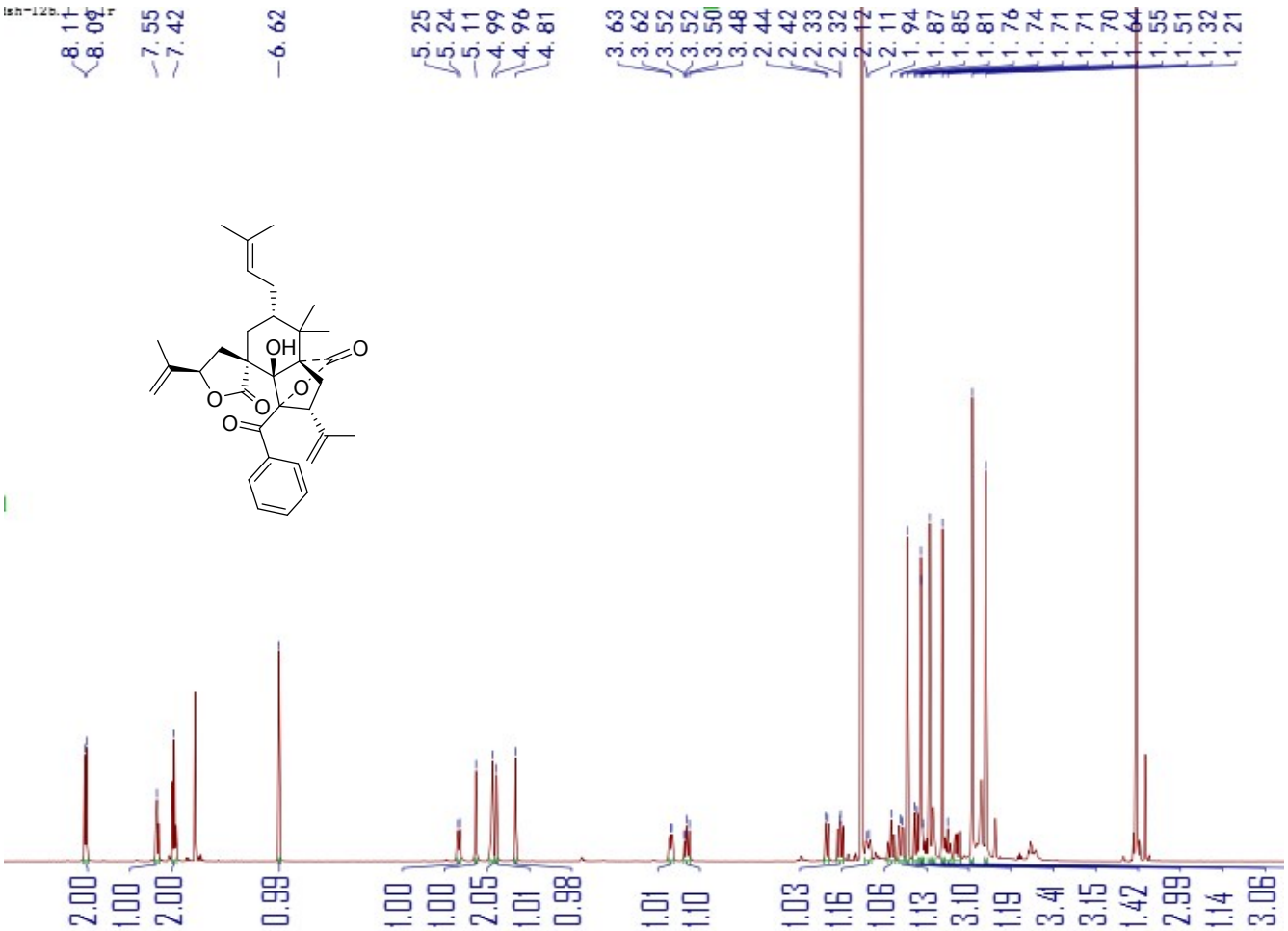


Fig. S5 ^{13}C NMR spectrum of hypsampsone A (**1**).

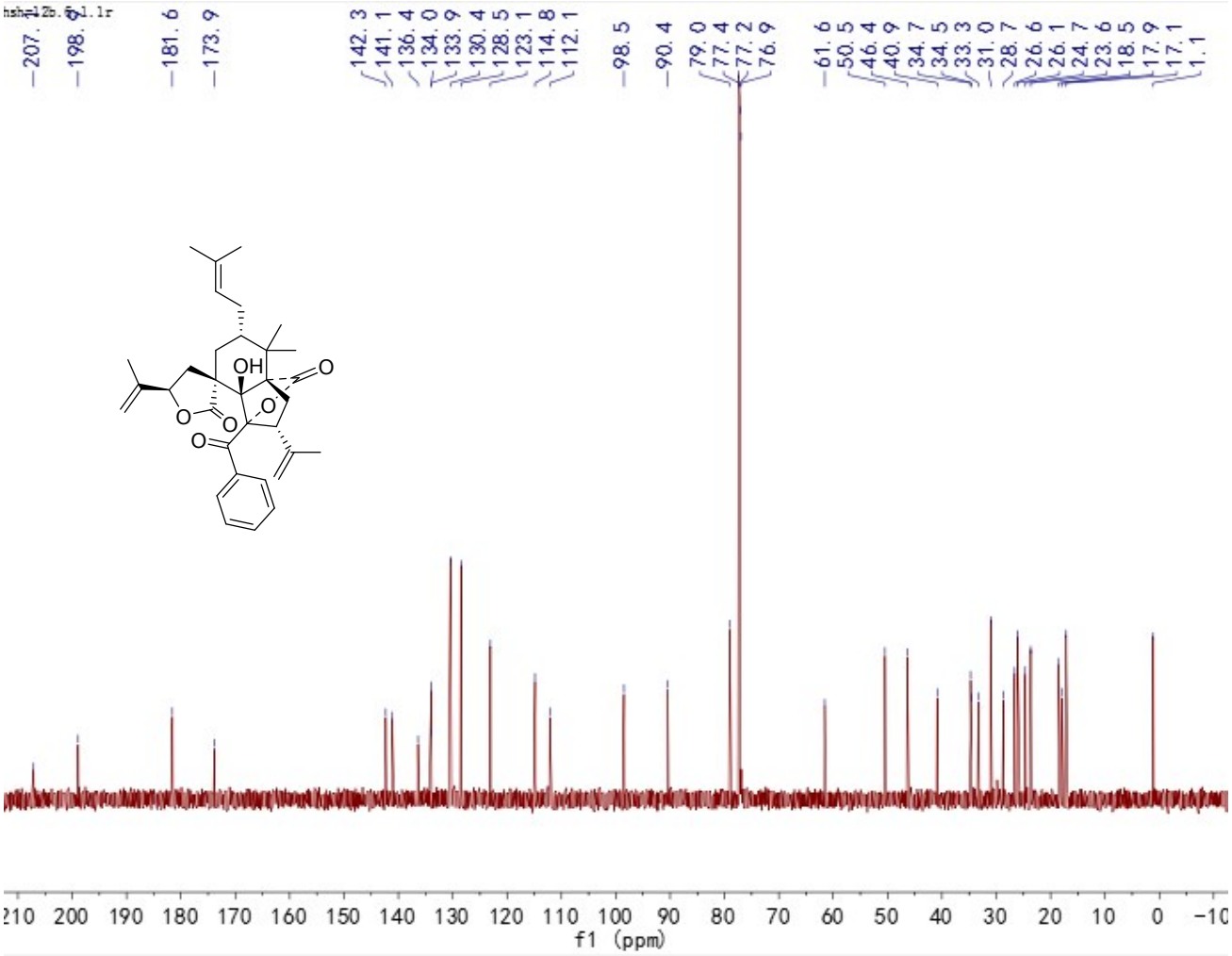


Fig. S6 HSQC spectrum of hypsampsone A (**1**).

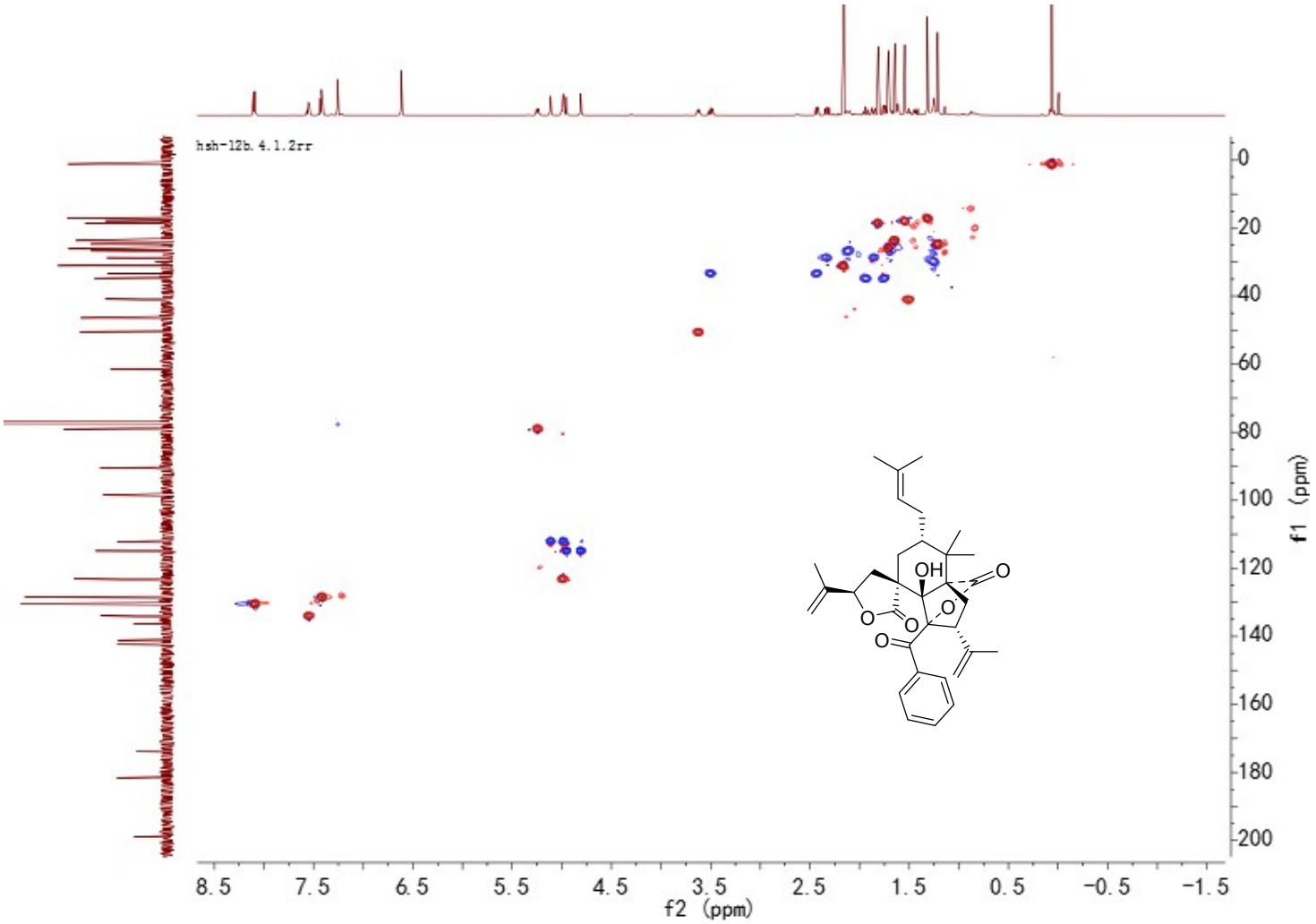


Fig. S7 HMBC spectrum of hypsampsone A (**1**).

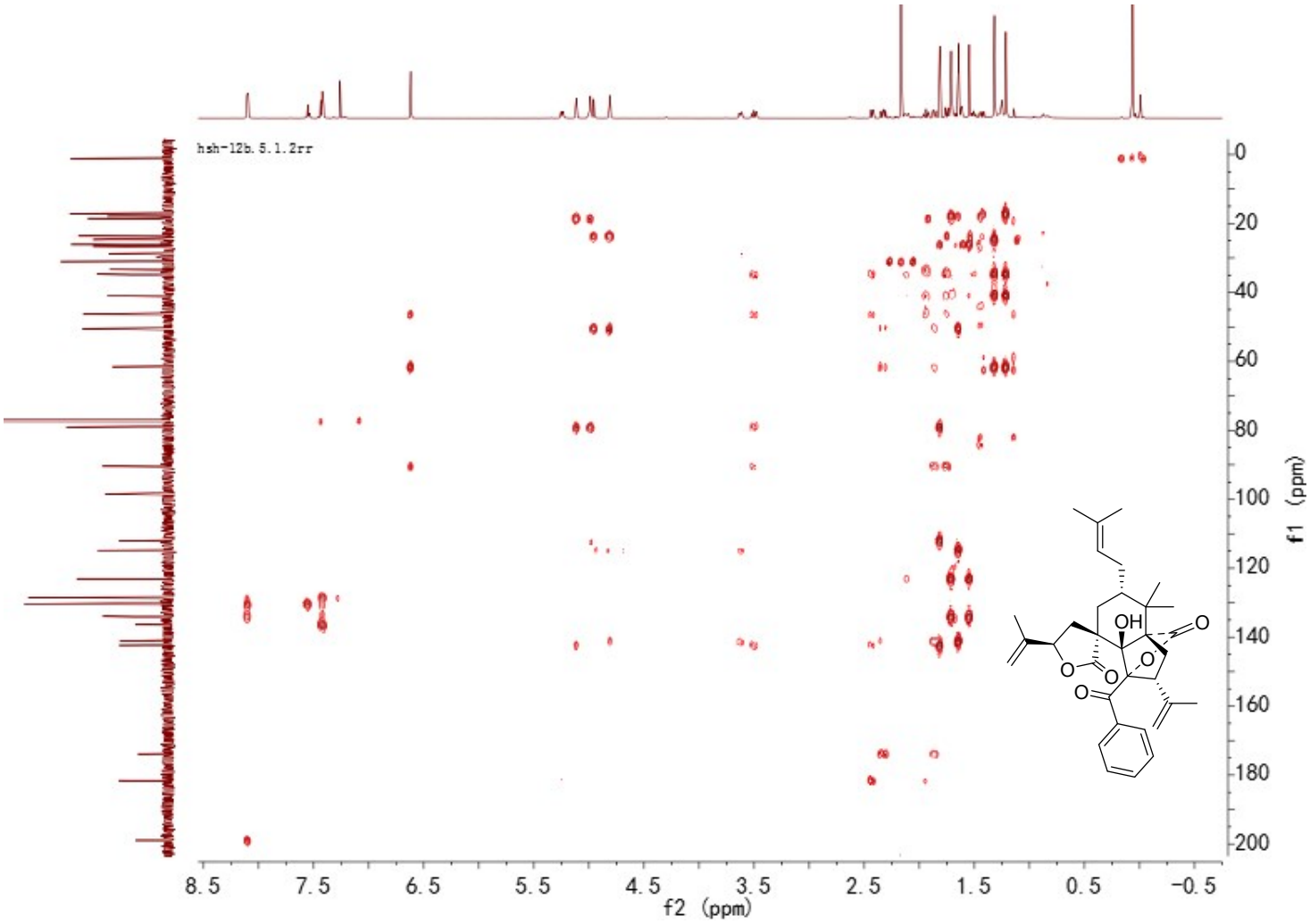


Fig. S8 ^{1}H–^{1}H COSY spectrum of hypsampsone A (**1**).

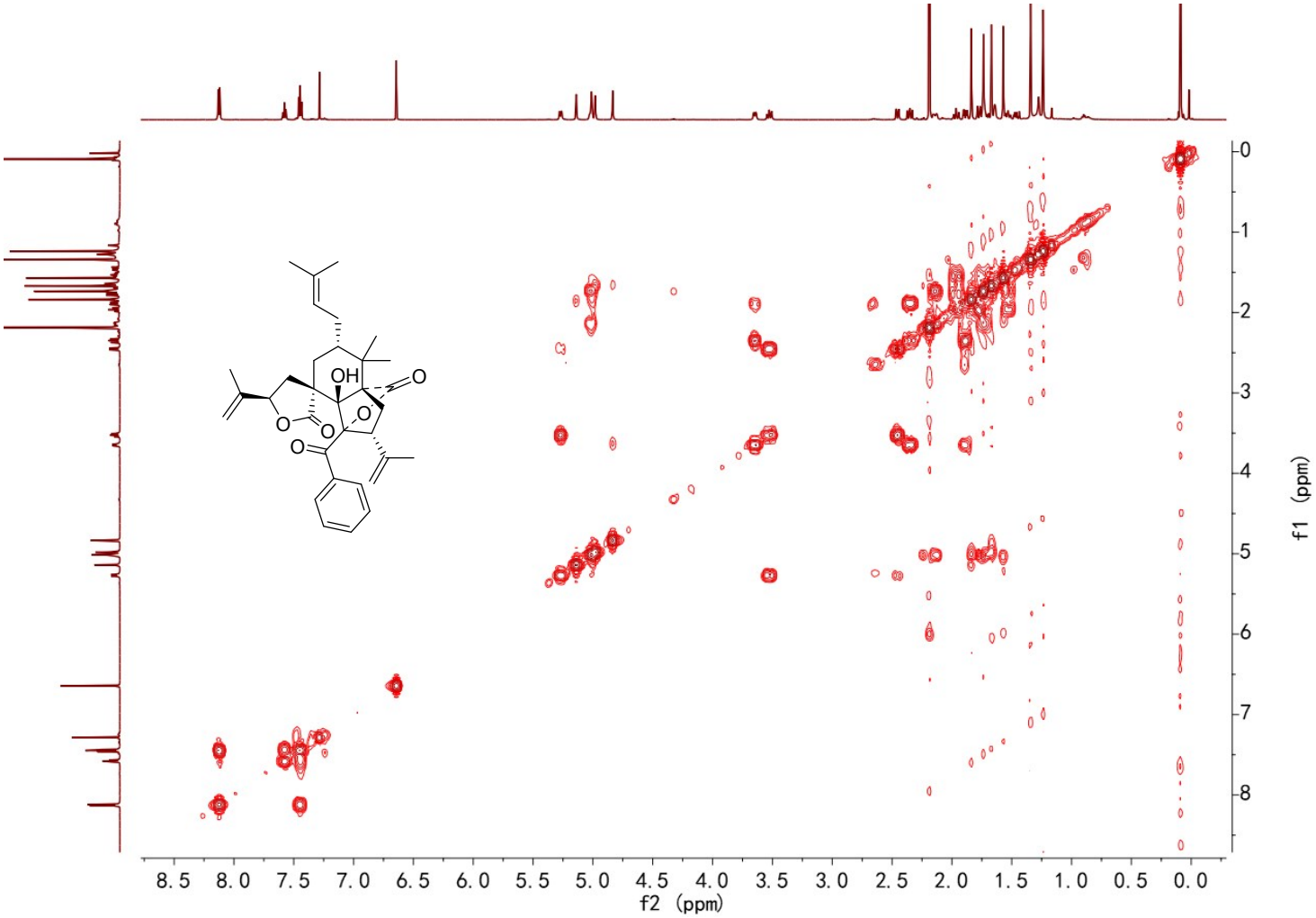


Fig. S9 NOESY spectrum of hypsampsone A (**1**).

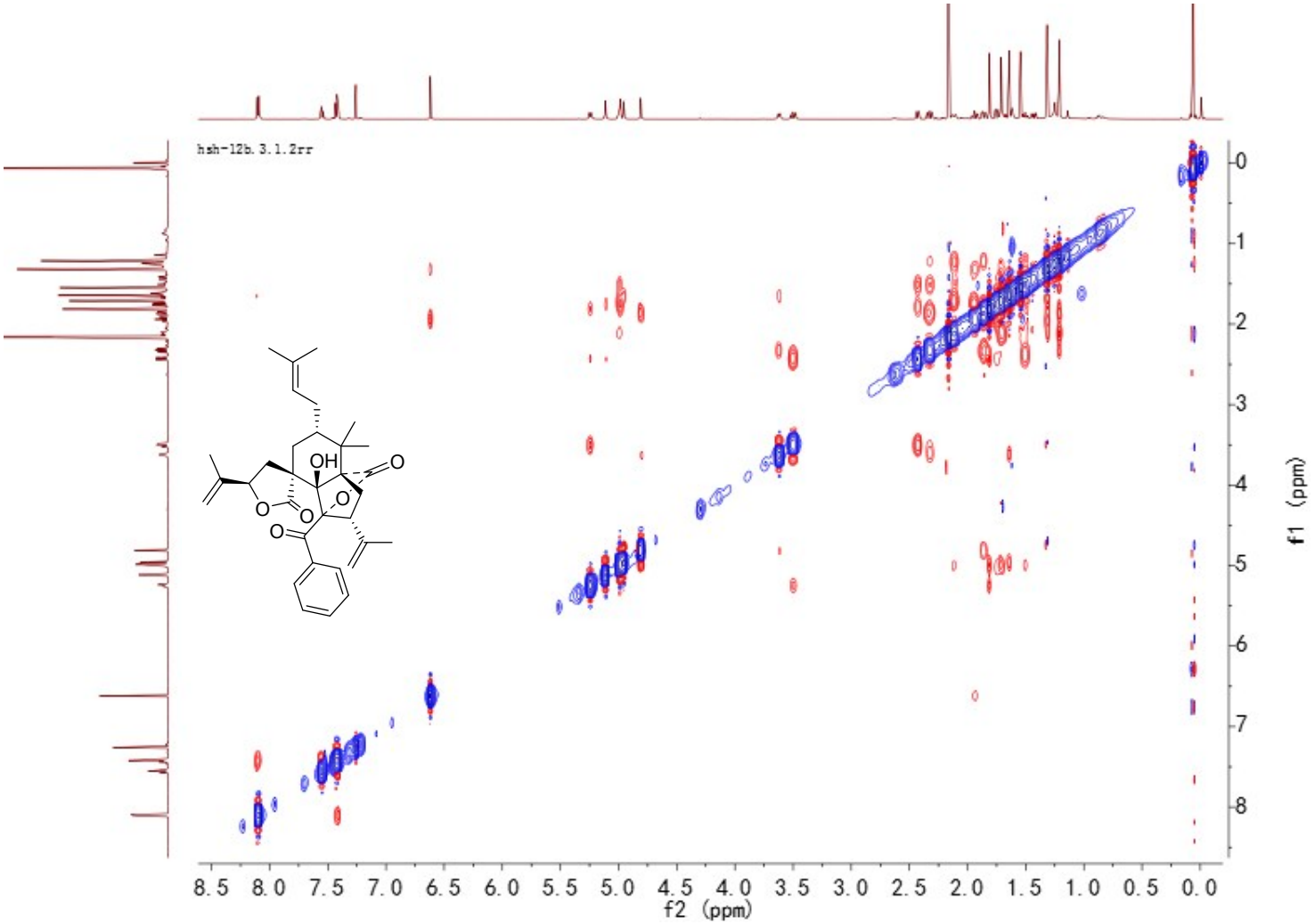


Fig. S10 HR-ESI-MS spectrum of hypsampsone A (**1**).

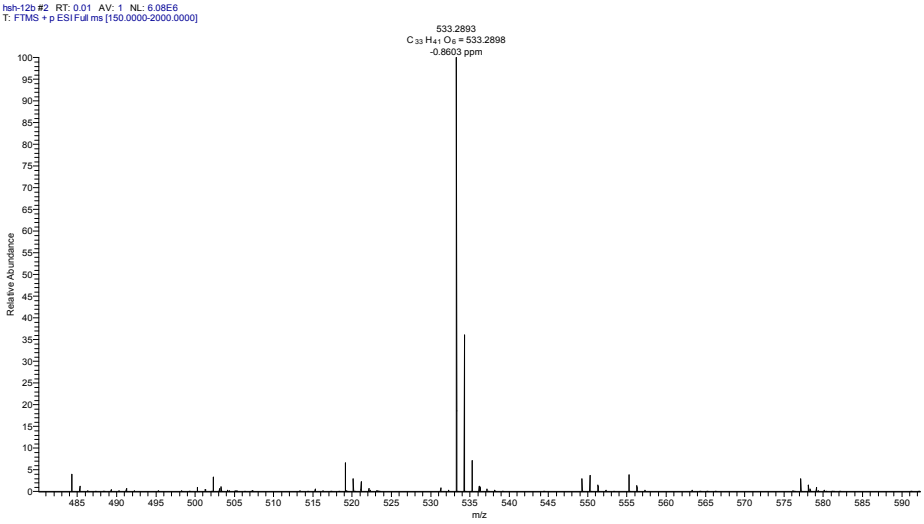
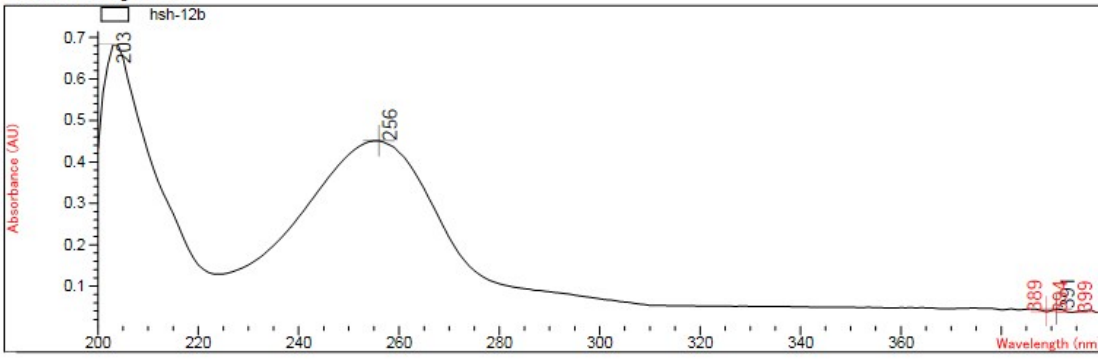


Fig. S11 UV spectrum of hypsampsone A (**1**).

Spectrum/Peak Report Date 8/3/2020 Time 15:43:34 Page 1 of 1

Method file : <method not saved>
Information : Default Method
Data File : D:\ZHANGZIZHEN\HSH-12B-1.STD Created : 8/3/20 14:28:42

Overlaid Spectra:



#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1	hsh-12b	203.0	0.68265	399.0	3.6026E-2
1		256.0	0.45092	394.0	3.6446E-2
1		391.0	4.5233E-2	389.0	3.8589E-2

Report generated by : system Signature: .....

*** End Spectrum/Peak Report ***

Fig. S12 IR spectrum of hypsampsone A (**1**).

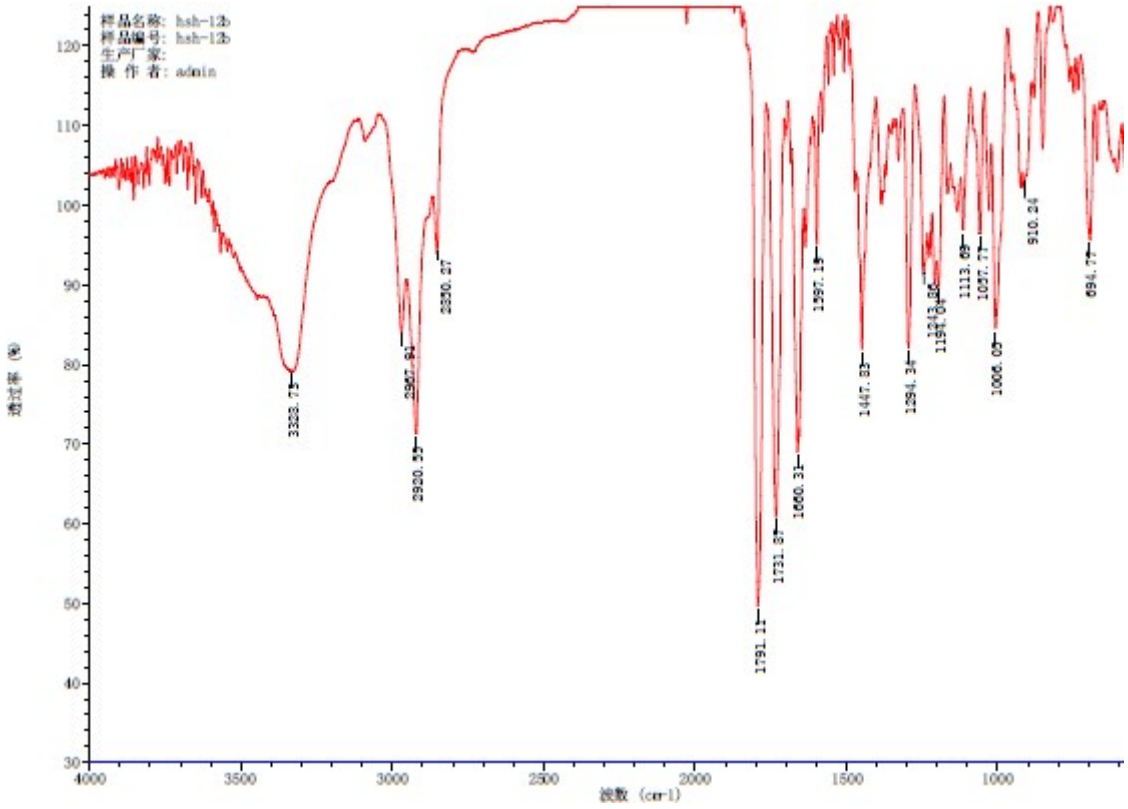


Fig. S13 ^{1}H NMR spectrum of hyperhexanone F (**2**).

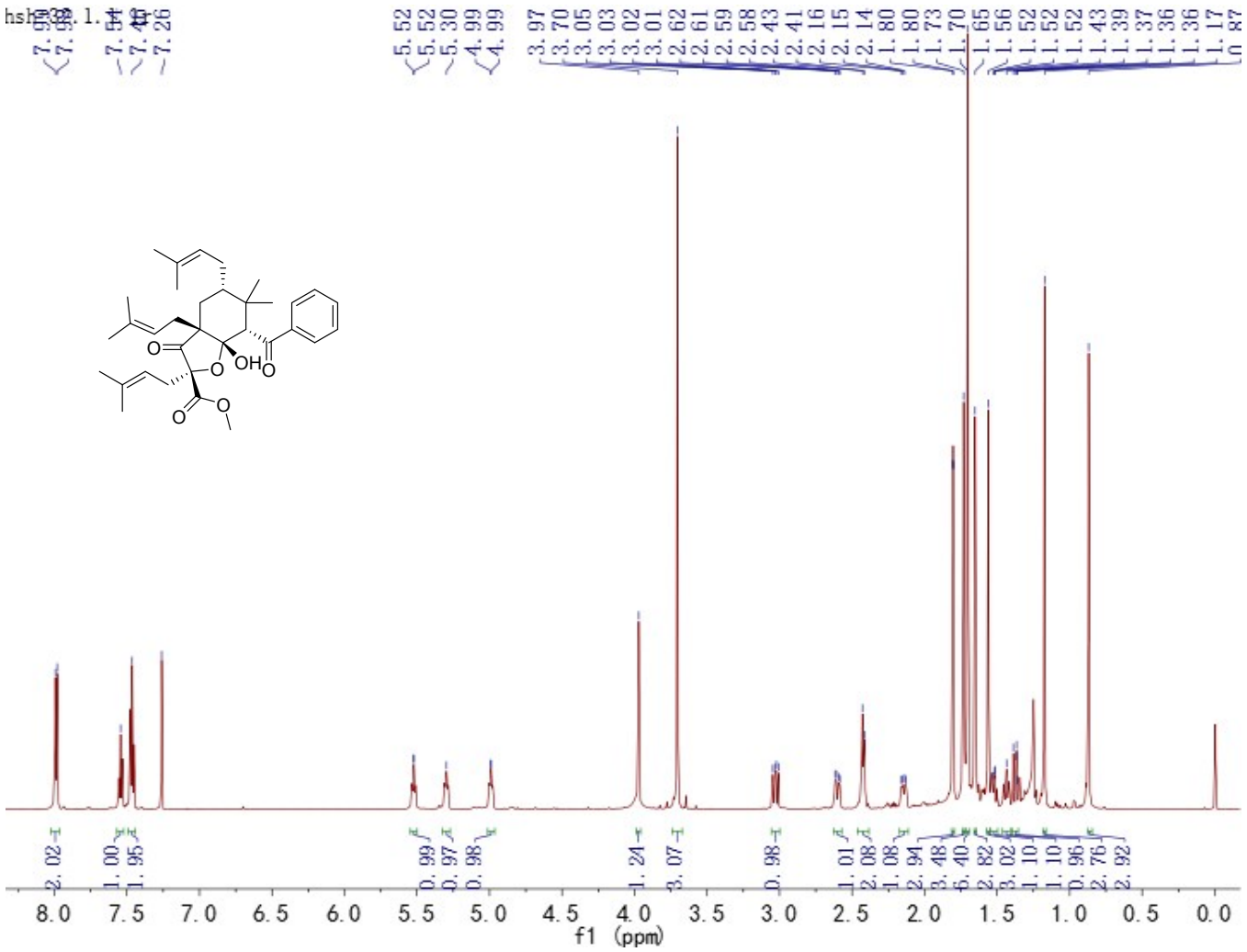


Fig. S14 ^{13}C NMR spectrum of hyperhexanone F (**2**).

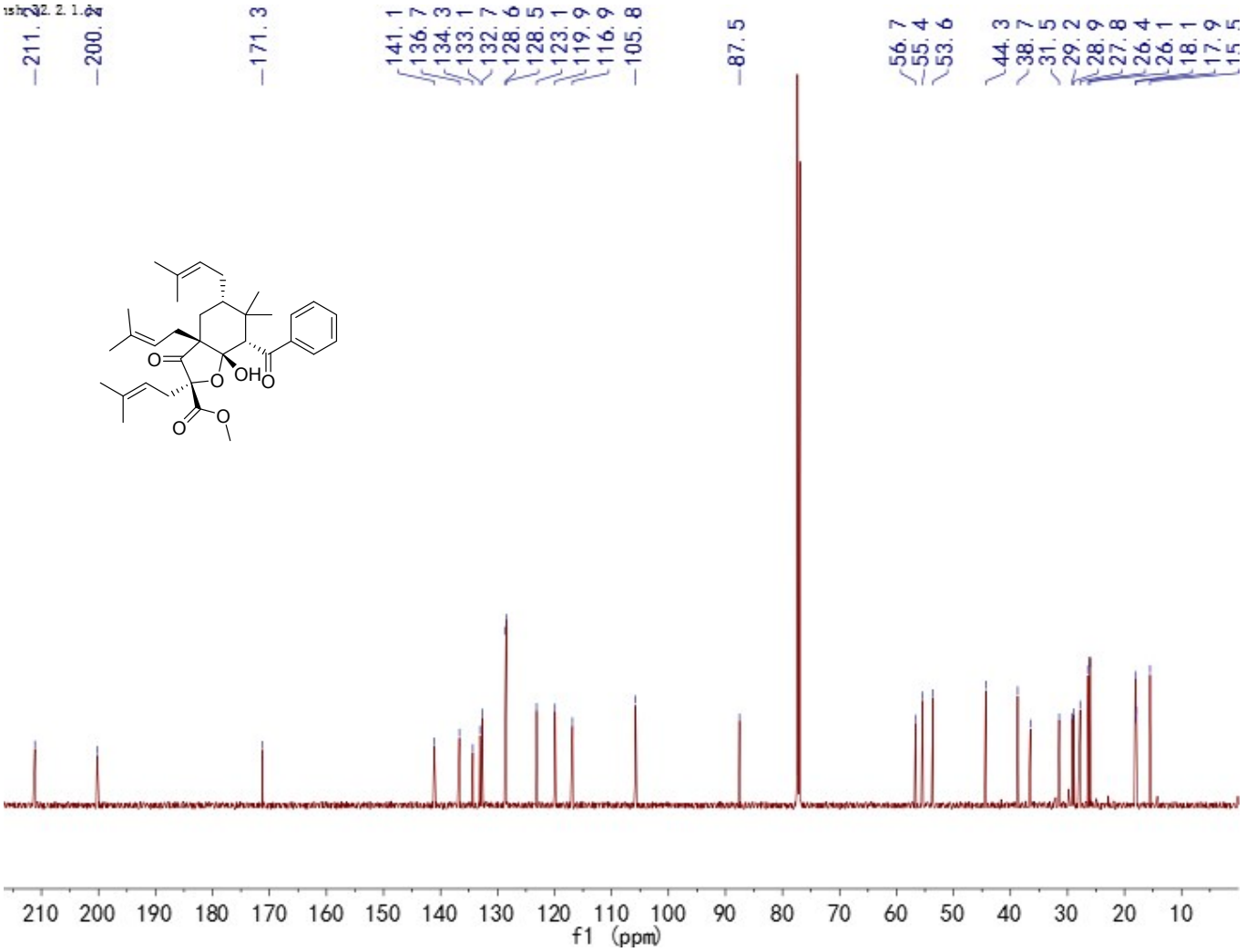


Fig. S15 HSQC spectrum of hyperhexanone F (**2**).

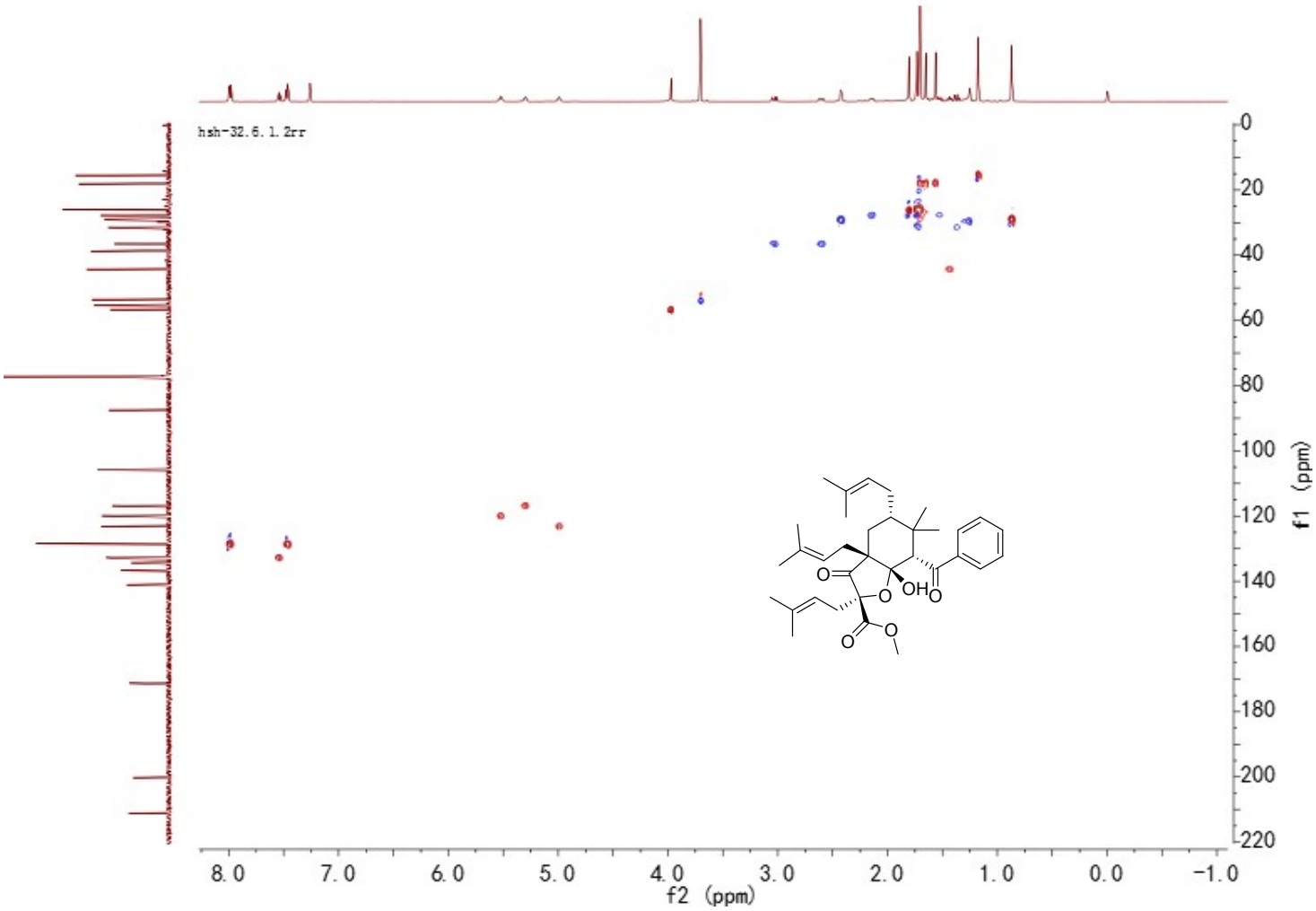


Fig. S16 HMBC spectrum of hyperhexanone F (**2**).

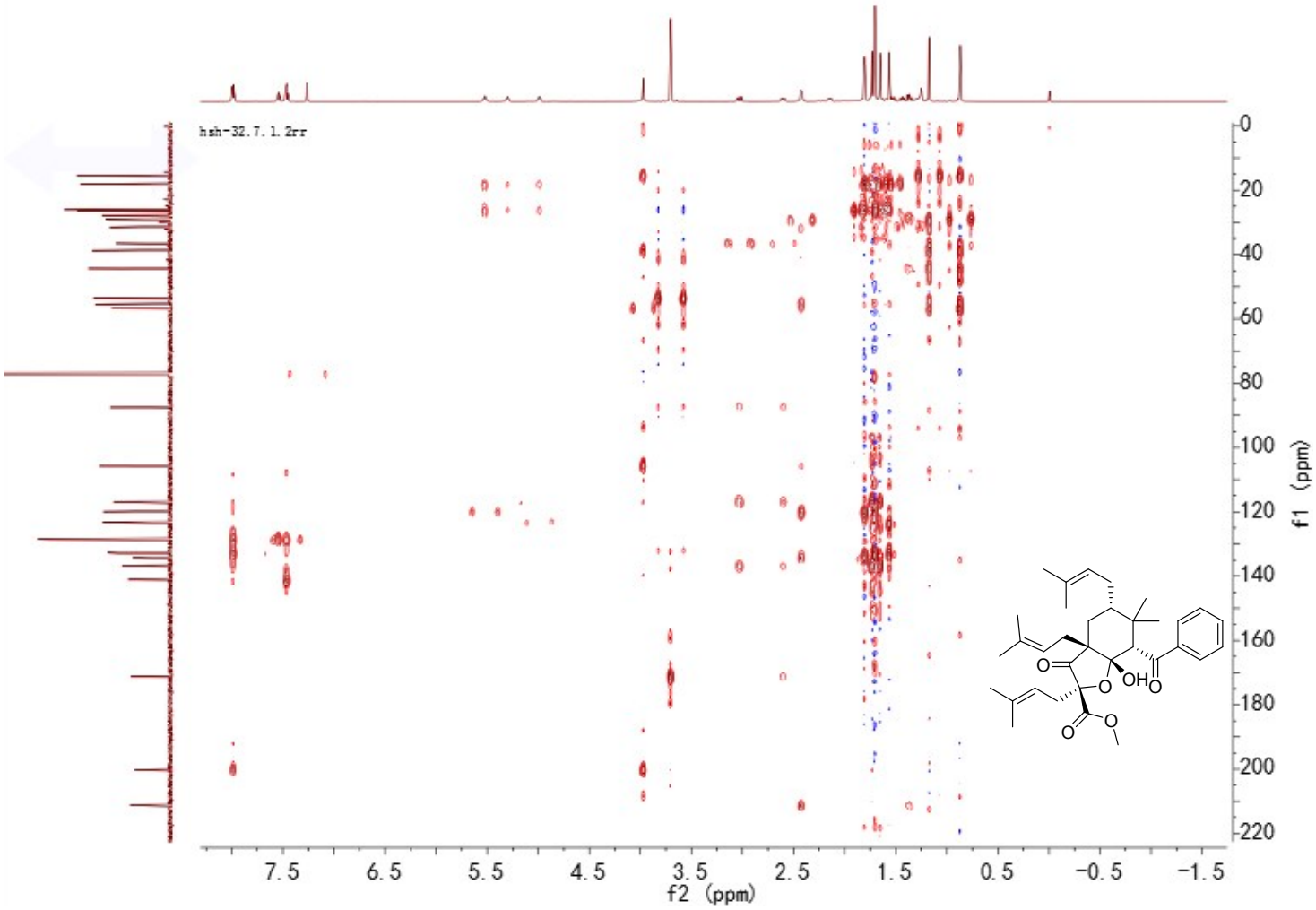


Fig. S17. ^{1}H-^{1}H COSY spectrum of hyperhexanone F (**2**).

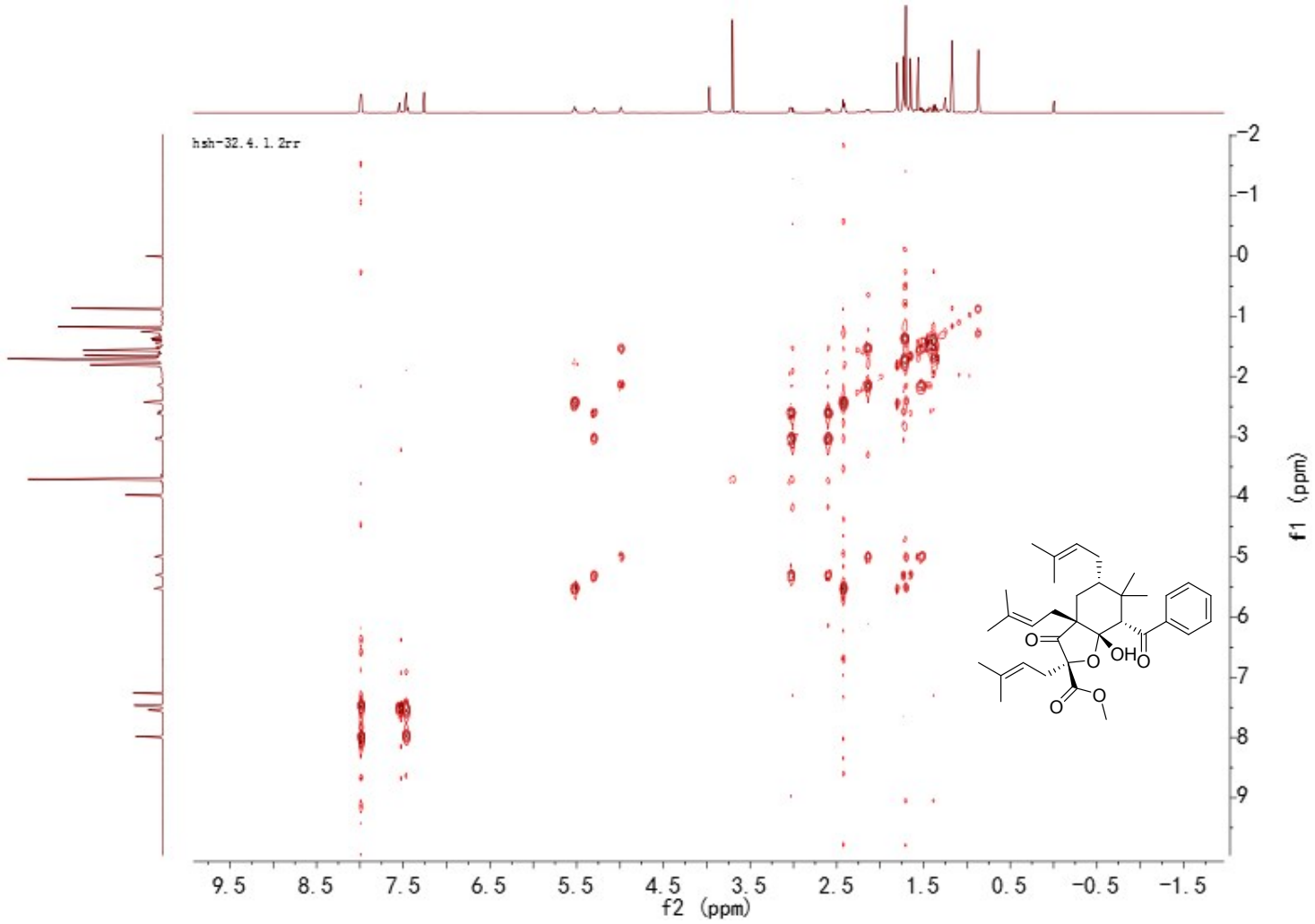


Fig. S18 NOESY spectrum of hyperhexanone F (**2**).

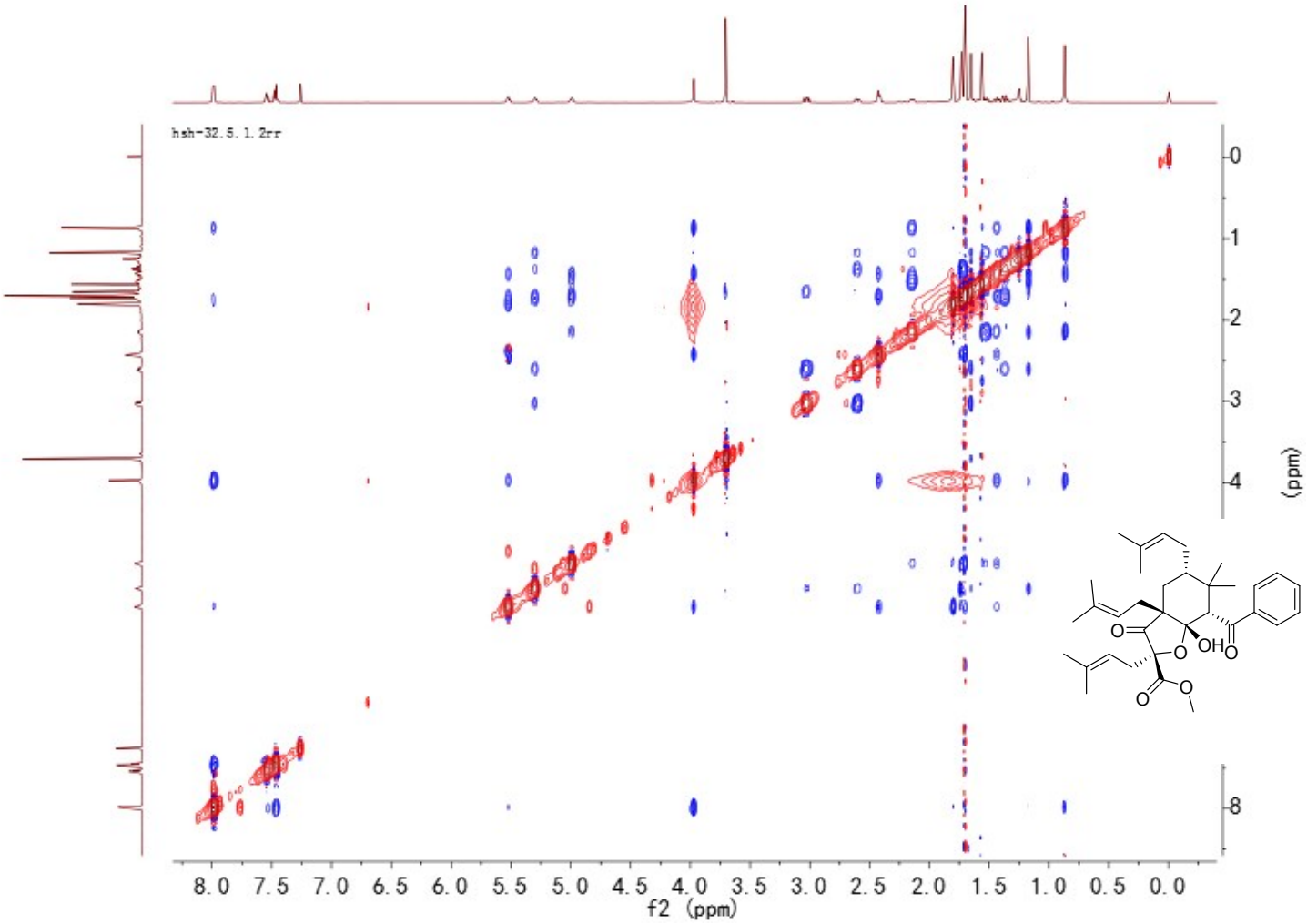


Fig. S19 HR-ESI-MS spectrum of hyperhexanone F (**2**).

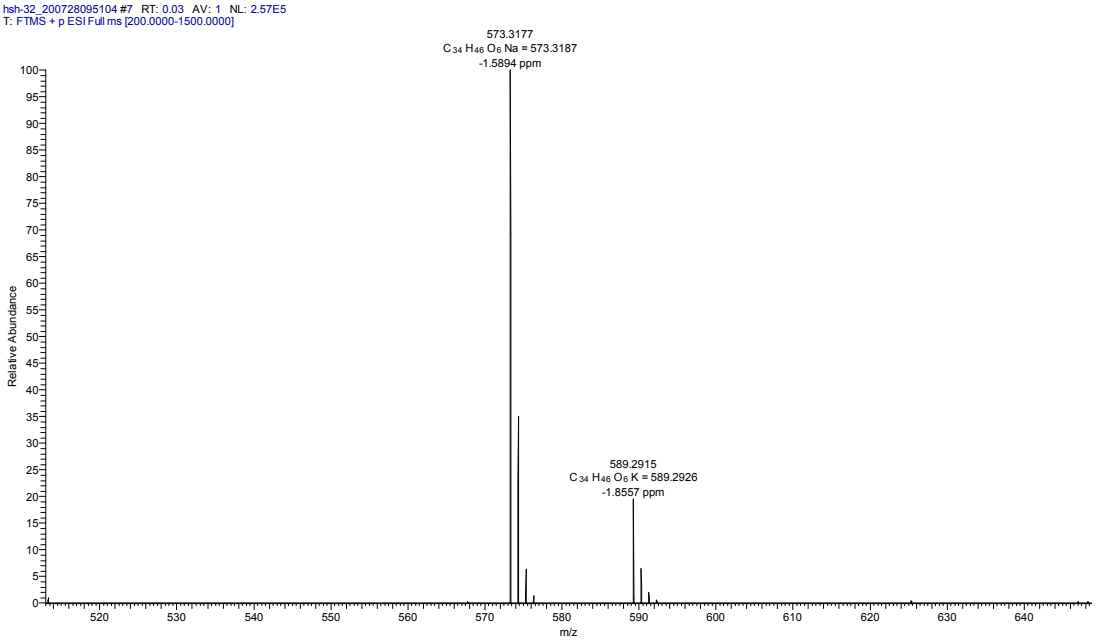
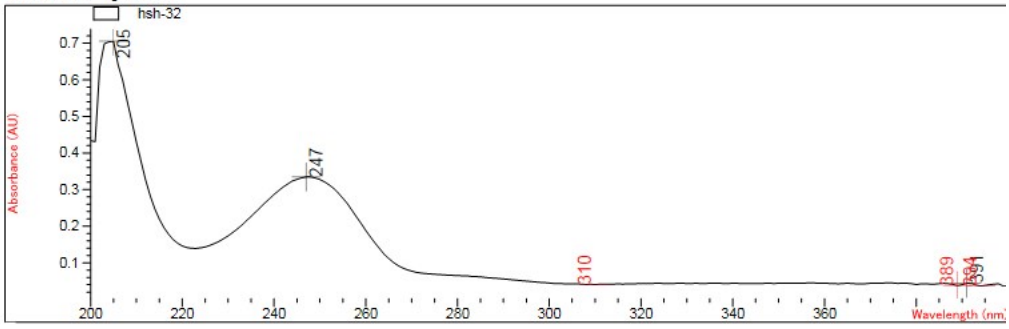


Fig. S20 UV spectrum of hyperhexanone F (**2**).

Spectrum/Peak Report Date 8/4/2020 Time 11:16:40 Page 1 of 1

Method file : <method not saved>
Information : Default Method
Data File : D:\ZHANGZIZHEN\HSH-32B.STD Created : 8/3/20 14:28:21

Overlaid Spectra:

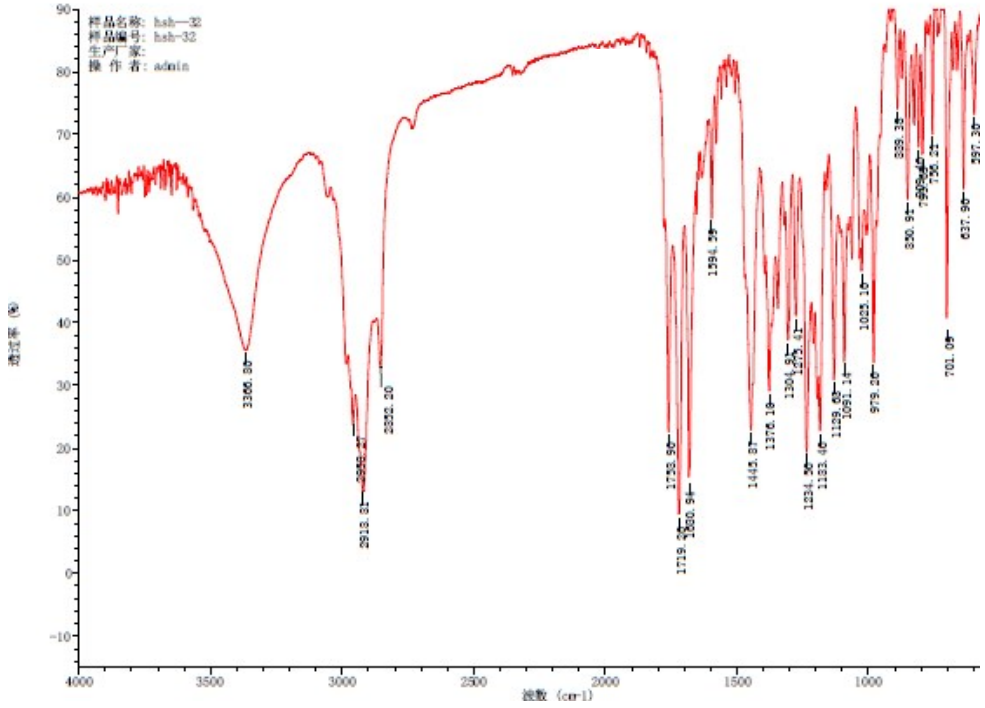


#	Name	Peaks(nm)	Abs(AU)	Valleys(nm)	Abs(AU)
1	hsh-32	205.0	0.70529	394.0	3.6696E-2
1		247.0	0.33455	389.0	3.7940E-2
1		391.0	4.4267E-2	310.0	4.1008E-2

Report generated by : system Signature: .....

*** End Spectrum/Peak Report ***

Fig. S21 IR spectrum of hyperhexanone F (**2**).



References:

(1) Goto, H.; Osawa, E. J. Am. Chem. Soc. 1989, 111, 8950–8951.

(2) Goto, H.; Osawa, E. J. Chem. Soc., Perkin Trans. 1993, 2, 187–198.

(3) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M.A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara,M.; Toyota, K.; Fukuda, R.;Hasegawa, J.; Ishida, M.;Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark,M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev,O.; Austin,A. J.; Cammi, R.; Pomelli,C.; Ochterski, J.W.; Martin,R. L.;Morokuma, K.; Zakrzewski,V. G.;Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.;Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, revision C.01; Gaussian, Inc.: Wallingford, CT, 2010.

(4) Bruhn, T.; Schaumlöffel, A.; Hemberger, Y.; Bringmann, G. Spec Dis, version 1.60, University of Wuerzburg, Germany, 2012.