

Supplementary Information

Hypoestins A-D: highly modified fusicoccane diterpenoids with promising Ca_v3.1 calcium channel inhibitory activity from *Hypoestes purpurea*

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ECD calculation method of compounds 2 and 4-6

Theoretical calculations of ECD spectra for compounds **2** and **4-6** were performed with the Gaussian 09 program package¹. The conformations of **2** and **4-6** were searched by the CHARMM force field and then optimized at the b3lyp/6-311g+(d,p) level of theory with CPCM solvent model in Methanol. All conformers were checked and none of them possess imaginary frequencies. The ECD computation of compounds **2** and **4-6** were performed with time-dependent density functional theory (TDDFT) calculations at the b3lyp/6-311+g(d,p) level with CPCM solvent model in Methanol. For fitting of the calculated curves and experimental CD spectra, the program SpecDis 1.62 was used with σ value of 0.35 eV and UV shift of 15 nm².

References

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2. T. Bruhn, A. Schaumlöffel, Y. Hemberger, G. Bringmann, *Chirality* 2013, **25**, 243–249.

Table S1. Optimized geometries of predominant conformers of compound **2** at the b3lyp/6-311+g(d,p) level.

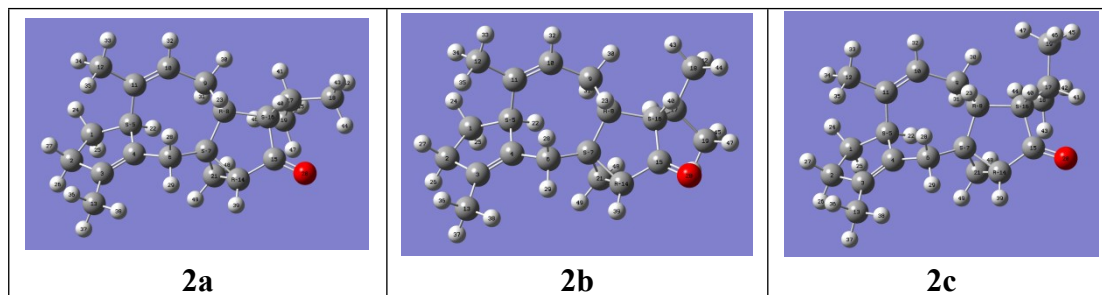


Table S2. Boltzmann distribution of conformers **2a-2c**.

Conformer	E (Hartree)	ΔG (Kcal/mol)	Proportion (%)
2a	-853.844869	0.591741	25.67
2b	-853.845812	0	69.69
2c	-853.843254	1.605169	4.64

Table S3. Cartesian coordinates of conformers **2a** and **2b**.

Atomic Type	2a			2b		
	X	Y	Z	X	Y	Z
C	-3.44131	-0.78922	1.456483	3.403287	0.81743	1.500326
C	-4.34627	0.321925	0.873199	4.304867	-0.32375	0.971397
C	-3.39564	1.192038	0.073876	3.365153	-1.19729	0.163072
C	-2.18515	0.616183	-0.05947	2.16732	-0.60773	-0.01626
C	-2.11931	-0.74499	0.635898	2.097394	0.764748	0.654459
C	-1.00562	1.138072	-0.84984	1.009062	-1.11993	-0.84149
C	0.369447	0.820896	-0.253	-0.38516	-0.82465	-0.27902
C	1.136057	-0.43736	-0.73583	-1.15828	0.43515	-0.75012
C	0.6525	-1.77254	-0.11219	-0.65349	1.774081	-0.15455
C	-0.65343	-2.26604	-0.70191	0.65783	2.249864	-0.74541
C	-1.89519	-1.85215	-0.38871	1.894713	1.850024	-0.39694
C	-3.09965	-2.38914	-1.12692	3.1126	2.371802	-1.12343
C	-3.87747	2.494501	-0.49679	3.846818	-2.51686	-0.36694
C	1.394874	1.942749	-0.07478	-1.40657	-1.97165	-0.19027
C	2.739537	1.411877	-0.38821	-2.71385	-1.42594	-0.60143
C	2.675919	-0.10332	-0.639	-2.68573	0.108175	-0.55746
C	3.623924	-0.96699	0.251693	-3.42389	0.736307	0.681861
C	5.095487	-0.77113	-0.15786	-4.16641	2.020184	0.268908
C	3.47063	-0.77287	1.769257	-4.41078	-0.21923	1.376054
O	3.7474	2.101459	-0.52136	-3.65174	-2.09225	-1.03174
C	0.683195	1.307033	1.122035	-0.76104	-1.36664	1.058083
H	-1.26672	-0.75961	1.322703	1.231717	0.793241	1.324701
H	0.922508	-0.50975	-1.80973	-0.99956	0.489268	-1.83556
H	-3.9173	-1.77317	1.447231	3.893551	1.793788	1.467173
H	-3.20988	-0.56057	2.50195	3.148657	0.628024	2.548124
H	-4.86383	0.891334	1.656685	4.788464	-0.88262	1.783622
H	-5.13538	-0.0809	0.219955	5.120023	0.049567	0.332922
H	-1.03022	0.730844	-1.8707	1.056543	-0.69265	-1.85334
H	-1.10198	2.22345	-0.95803	1.114528	-2.20207	-0.96858
H	1.409042	-2.54146	-0.29725	-1.40408	2.545471	-0.34992
H	0.579935	-1.66826	0.976876	-0.58015	1.685683	0.935773
H	-0.55192	-3.00375	-1.4989	0.566938	2.965753	-1.56322
H	-2.80077	-3.08112	-1.91972	2.827951	3.042774	-1.93917
H	-3.78587	-2.92201	-0.45774	3.782787	2.923874	-0.45349
H	-3.67575	-1.57469	-1.58451	3.701087	1.548551	-1.5485
H	-4.69865	2.325508	-1.20689	4.693764	-2.37313	-1.05184
H	-4.27947	3.142166	0.293354	4.212871	-3.15415	0.448709
H	-3.0932	3.045719	-1.02216	3.072828	-3.068	-0.90731
H	1.184271	2.982403	-0.306	-1.16099	-2.99354	-0.4609
H	3.077912	-0.21815	-1.65385	-3.23486	0.436043	-1.44688
H	3.372788	-2.01098	0.02771	-2.66693	1.012138	1.424322
H	5.735333	-1.46718	0.395905	-4.59487	2.518075	1.145944
H	5.24032	-0.95879	-1.22781	-3.51162	2.736231	-0.23607
H	5.43482	0.247398	0.052401	-4.98824	1.780375	-0.41717
H	4.18067	-1.41762	2.298737	-4.89124	0.294808	2.215602
H	2.470381	-1.03462	2.124552	-3.91685	-1.11173	1.774257
H	3.683546	0.260645	2.067542	-5.19605	-0.55176	0.68911
H	1.254801	0.694846	1.809165	-1.37153	-0.78373	1.739869
H	-0.04975	1.949439	1.601799	-0.04388	-2.01689	1.550711

Table S4. Cartesian coordinates of conformers **2c**.

Atomic Type	2c		
	X	Y	Z
C	3.393637	0.85011	1.455505
C	4.356671	-0.15496	0.78084
C	3.44041	-1.06307	-0.01672
C	2.186328	-0.57484	-0.07944
C	2.050915	0.749302	0.675435
C	1.020606	-1.15325	-0.8522
C	-0.36073	-0.93325	-0.22594
C	-1.2162	0.285419	-0.66684
C	-0.80776	1.608389	0.037721
C	0.444805	2.218123	-0.55821
C	1.720438	1.879472	-0.29461
C	2.863474	2.529006	-1.04022
C	3.992609	-2.30098	-0.66255
C	-1.29862	-2.12393	-0.03183
C	-2.68332	-1.68659	-0.29788
C	-2.72507	-0.18238	-0.61045
C	-3.85969	0.540269	0.175872
C	-3.62077	0.713887	1.684916
C	-4.30858	1.856882	-0.48322
O	-3.66346	-2.42499	-0.34076
C	-0.61988	-1.43557	1.155431
H	1.222897	0.67773	1.38781
H	-0.99629	0.432798	-1.73093
H	3.794103	1.866747	1.489631
H	3.216668	0.544907	2.492095
H	4.956207	-0.71301	1.512264
H	5.076802	0.34081	0.112268
H	0.998181	-0.72961	-1.86643
H	1.181136	-2.22858	-0.98279
H	-1.6141	2.336384	-0.067
H	-0.68787	1.433562	1.112716
H	0.270685	2.978375	-1.32097
H	2.495035	3.223599	-1.80085
H	3.525594	3.088124	-0.36822
H	3.486008	1.775755	-1.53993
H	4.762253	-2.04111	-1.40239
H	4.481641	-2.9443	0.080611
H	3.228094	-2.89193	-1.1737
H	-1.01906	-3.14751	-0.26129
H	-3.07633	-0.17085	-1.65194
H	-4.70735	-0.15077	0.074401
H	-4.52536	1.112053	2.158082
H	-3.39568	-0.24104	2.172048
H	-2.8047	1.408894	1.901547
H	-5.2258	2.219878	-0.0058
H	-4.52123	1.711984	-1.5485
H	-3.56187	2.652064	-0.39749
H	-1.22599	-0.8542	1.843165
H	0.158307	-2.02312	1.634028

Table S5. Optimized geometries of predominant conformers of compound **4** at the b3lyp/6-311+g(d,p) level.

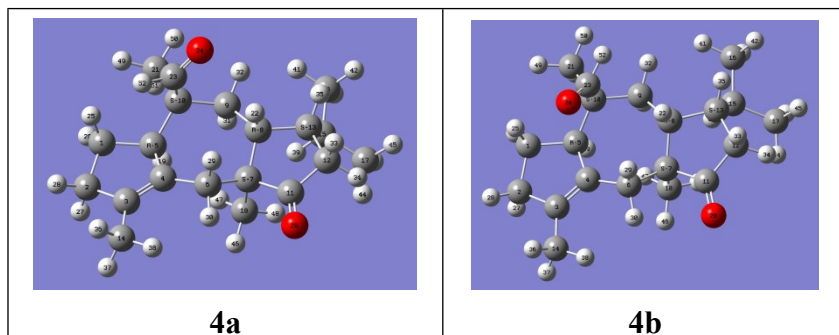


Table S6. Boltzmann distribution of conformers **4a** and **4b**.

Conformer	E (Hartree)	ΔG (Kcal/mol)	Proportion (%)
4a	-930.289373	0	66.01
4b	-930.288721	0.409136	33.09

Table S7. Cartesian coordinates of conformers **4a** and **4b**.

Atomic Type	4a			4b		
	X	Y	Z	X	Y	Z
C	3.433072	-1.09989	-0.821873	3.398497	-1.1247	-0.76089
C	4.155898	0.246553	-1.00928	4.094318	0.217679	-1.05276
C	3.244531	1.235717	-0.31311	3.165061	1.238866	-0.42928
C	2.022791	0.709674	-0.0855	1.959188	0.704894	-0.14651
C	1.938305	-0.72018	-0.64427	1.898256	-0.75805	-0.61636
C	0.878945	1.434444	0.588608	0.817433	1.446526	0.509165
C	-0.53562	1.135141	0.046842	-0.6032	1.098688	0.014086
C	-1.07047	-0.24656	0.526774	-1.10264	-0.27337	0.558304
C	-0.47209	-1.5121	-0.09717	-0.51015	-1.54593	-0.05622
C	1.048275	-1.76057	0.110017	1.019487	-1.78352	0.154225
C	-1.56972	2.085504	0.672063	-1.64007	2.05836	0.621074
C	-2.82333	1.313042	1.048502	-2.85865	1.280117	1.088078
C	-2.63649	-0.13685	0.534027	-2.66911	-0.18346	0.618458
C	3.747225	2.616652	-0.00986	3.643199	2.647644	-0.23016
C	-3.3697	-0.526	-0.79727	-3.43902	-0.62705	-0.67504
C	-3.82003	-1.99922	-0.74752	-3.88433	-2.0976	-0.55269
C	-4.58629	0.353357	-1.13616	-4.66674	0.235943	-1.01566
C	-0.61321	1.412709	-1.47887	-0.71452	1.30522	-1.52079
H	1.496853	-0.66843	-1.65209	1.469436	-0.75737	-1.63245
O	-1.41178	3.285843	0.838862	-1.50745	3.269781	0.710755
C	1.354051	-3.18389	-0.44767	1.310261	-3.21949	-0.3735
H	-0.80684	-0.28419	1.592176	-0.7992	-0.27154	1.617024
C	1.419635	-1.83601	1.582346	1.278813	-1.85901	1.649492
O	0.660775	-2.16568	2.480525	2.150607	-1.2813	2.27487
H	3.814819	-1.58612	0.08325	3.770576	-1.52899	0.185995
H	3.592771	-1.79082	-1.65412	3.575304	-1.87243	-1.53934
H	4.254643	0.5083	-2.07468	4.190019	0.3984	-2.13567
H	5.172255	0.2452	-0.59579	5.110561	0.268378	-0.64109
H	0.879024	1.199347	1.664149	0.846661	1.262482	1.593426
H	1.044455	2.514068	0.52247	0.961585	2.523808	0.382757
H	-0.66279	-1.54994	-1.17639	-0.7057	-1.59987	-1.13324
H	-0.99808	-2.36774	0.337936	-1.0328	-2.40068	0.388666
H	-2.86338	1.31635	2.14658	-2.84126	1.322021	2.18621
H	-3.71923	1.837886	0.712163	-3.78121	1.77524	0.780681
H	-3.0159	-0.82152	1.301638	-3.01238	-0.84674	1.420968
H	4.581953	2.576087	0.70281	4.479771	2.67626	0.481339
H	4.139622	3.091228	-0.9192	4.025148	3.062289	-1.17292
H	2.981627	3.272844	0.410867	2.866426	3.319309	0.143407
H	-2.66595	-0.43233	-1.63206	-2.75873	-0.56503	-1.53193
H	-4.25804	-2.30428	-1.70459	-4.35097	-2.44112	-1.48272
H	-2.9927	-2.67951	-0.52845	-3.04981	-2.76872	-0.33228
H	-4.58198	-2.14078	0.029659	-4.62143	-2.20821	0.252843
H	-5.0812	-0.02883	-2.03579	-5.18305	-0.18271	-1.8865
H	-4.31289	1.394787	-1.33392	-4.40223	1.269451	-1.26119
H	-5.32449	0.345542	-0.32454	-5.38403	0.257794	-0.18582
H	-0.15791	2.385227	-1.69055	-0.29666	2.282751	-1.78019
H	-0.08152	0.655163	-2.05744	-0.16073	0.542835	-2.07184
H	-1.64258	1.445545	-1.84468	-1.74906	1.284807	-1.87255
H	2.382606	-3.49909	-0.25288	2.350762	-3.51322	-0.21593
H	0.682033	-3.92036	0.002296	0.670131	-3.95685	0.121787
H	1.198211	-3.18952	-1.53192	1.101126	-3.26146	-1.44778
H	2.477889	-1.61454	1.824148	0.589954	-2.54927	2.185203

Table S8. Optimized geometries of predominant conformers of compound **5** at the b3lyp/6-311+g(d,p) level.

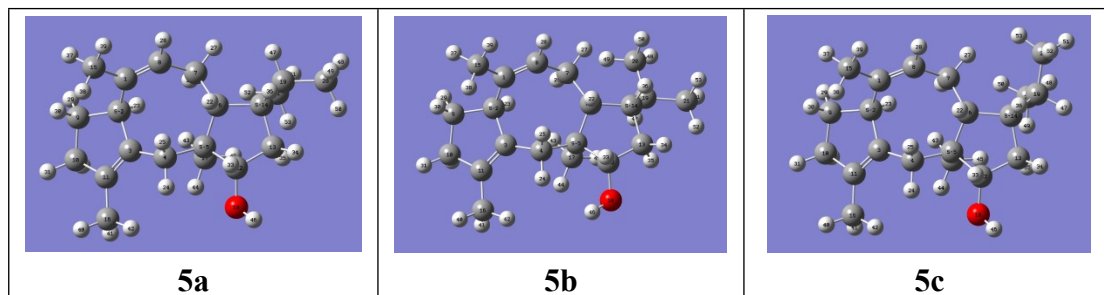


Table S9. Boltzmann distribution of conformers **5a-5c**.

Conformer	E (Hartree)	ΔG (Kcal/mol)	Proportion (%)
5a	-856.231495	0	76.94
5b	-856.230274	0.766189	21.11
5c	-856.228022	2.179340	1.94

Table S10. Cartesian coordinates of conformers **5a** and **5b**.

Atomic Type	5a			5b		
	X	Y	Z	X	Y	Z
C	-1.8217	-2.07915	-0.5055	-1.85058	-2.00881	-0.64798
C	-2.25977	-0.97393	0.445249	-2.24717	-1.00096	0.41976
C	-2.10647	0.457486	-0.10278	-2.09932	0.464007	-0.02448
C	-0.92697	0.888177	-0.9396	-0.95	0.928142	-0.8828
C	0.496939	0.773028	-0.30091	0.497313	0.811927	-0.29962
C	1.194997	-0.60325	-0.57908	1.221977	-0.538	-0.61528
C	0.645463	-1.85395	0.15431	0.635853	-1.85016	-0.03975
C	-0.53191	-2.45293	-0.58488	-0.56124	-2.34926	-0.82053
C	-3.73193	-1.00225	0.926375	-3.7002	-1.05525	0.952731
C	-4.07266	0.471261	1.222252	-4.01681	0.396374	1.365779
C	-3.11017	1.243366	0.340262	-3.07702	1.224556	0.509682
C	1.48374	1.69236	-1.06747	1.440956	1.753142	-1.10577
C	2.883856	1.199949	-0.6743	2.863064	1.263307	-0.81309
C	2.756485	-0.3442	-0.55912	2.766407	-0.25482	-0.45674
C	-2.85113	-2.69892	-1.42339	-2.91569	-2.5386	-1.57979
C	-3.31948	2.71623	0.136917	-3.27893	2.709398	0.418935
C	0.442827	1.195789	1.18069	0.499061	1.194434	1.192139
O	1.246646	3.076095	-0.77325	1.355324	3.148457	-0.78651
C	3.639122	-1.00209	0.536179	3.552757	-0.56247	0.855411
C	5.128984	-0.77459	0.216372	3.479641	-2.01466	1.361924
C	3.35111	-0.60016	1.991736	5.040389	-0.20748	0.644081
H	0.981842	-0.78939	-1.64055	1.109002	-0.64518	-1.70531
H	-1.61564	-1.04762	1.33423	-1.56759	-1.14967	1.272291
H	-1.0694	1.938716	-1.21132	-1.12402	1.98454	-1.11982
H	-0.91766	0.322411	-1.88189	-0.96806	0.395261	-1.84334
H	0.39069	-1.61695	1.192824	0.401399	-1.73693	1.024955
H	1.433704	-2.61252	0.201567	1.406887	-2.62202	-0.10521
H	-0.27005	-3.21092	-1.32491	-0.32062	-3.01964	-1.64724
H	-3.87777	-1.66377	1.786687	-3.81983	-1.77441	1.769652
H	-4.3835	-1.35965	0.123495	-4.3843	-1.35161	0.151964
H	-5.12363	0.714749	1.019479	-5.0713	0.661413	1.215158
H	-3.89522	0.726411	2.279588	-3.8038	0.572435	2.432493
H	1.32455	1.532269	-2.14508	1.207105	1.624745	-2.17305
H	3.643164	1.507311	-1.40102	3.536371	1.46376	-1.6519
H	3.156734	1.654456	0.284446	3.24212	1.83779	0.039409
H	3.134727	-0.77977	-1.49295	3.267595	-0.84752	-1.23486
H	-3.61863	-3.25349	-0.86965	-3.65618	-3.15202	-1.05182
H	-3.37867	-1.93214	-2.00628	-3.47079	-1.72014	-2.05705
H	-2.37844	-3.39114	-2.12634	-2.47302	-3.15272	-2.36966
H	-4.29912	2.910172	-0.3201	-4.27221	2.942841	0.012816
H	-3.31883	3.242664	1.101468	-3.23795	3.166254	1.417387
H	-2.55556	3.17584	-0.4948	-2.53361	3.207477	-0.206
H	-0.1071	0.47487	1.789973	0.010889	0.42902	1.801531
H	-0.06652	2.159157	1.272109	-0.04392	2.131957	1.344578
H	1.435834	1.306306	1.61759	1.50844	1.33722	1.583147
H	1.778816	3.610045	-1.37812	0.529658	3.503755	-1.14287
H	3.46596	-2.08458	0.463263	3.170281	0.085173	1.655201
H	5.765306	-1.33301	0.912266	4.208371	-2.1609	2.167829
H	5.374568	-1.10177	-0.80062	2.498886	-2.27602	1.761802
H	5.398358	0.285178	0.301387	3.72623	-2.72818	0.565385
H	4.007093	-1.16146	2.667345	5.606471	-0.35966	1.569703
H	2.319151	-0.80919	2.284917	5.190003	0.830364	0.333066
H	3.543968	0.464489	2.167102	5.482028	-0.85395	-0.12586

Table S11. Cartesian coordinates of conformer **5c**.

Atomic Type	5c		
	X	Y	Z
C	-1.59036	-2.12945	-0.53312
C	-2.13946	-1.08265	0.426074
C	-2.09716	0.366216	-0.09581
C	-0.95411	0.904666	-0.92061
C	0.473844	0.911675	-0.27895
C	1.299122	-0.39345	-0.56817
C	0.839271	-1.68491	0.159639
C	-0.27019	-2.37833	-0.60238
C	-3.61218	-1.24108	0.877661
C	-4.07243	0.192886	1.203924
C	-3.16575	1.059266	0.350543
C	1.367498	1.931583	-1.03085
C	2.802648	1.567102	-0.6385
C	2.834325	0.016193	-0.5621
C	-2.54941	-2.83104	-1.46772
C	-3.49295	2.513816	0.172788
C	0.375892	1.302332	1.209041
O	0.99798	3.282522	-0.72012
C	3.861733	-0.49956	0.491827
C	3.459247	-0.36799	1.969888
C	4.378355	-1.92131	0.194488
H	1.101758	-0.59275	-1.6299
H	-1.50839	-1.11722	1.326657
H	-1.18675	1.941295	-1.18359
H	-0.89272	0.351811	-1.86854
H	0.543435	-1.46622	1.190883
H	1.680073	-2.37769	0.226743
H	0.069798	-3.09847	-1.34851
H	-3.72085	-1.93483	1.71791
H	-4.21876	-1.62607	0.052403
H	-5.13731	0.357114	0.994382
H	-3.92629	0.435225	2.269059
H	1.227055	1.769626	-2.11087
H	3.539757	1.960842	-1.34734
H	3.026149	2.015003	0.336542
H	3.233317	-0.34804	-1.51693
H	-3.2694	-3.45664	-0.92589
H	-3.13808	-2.10976	-2.05007
H	-2.00999	-3.47245	-2.17096
H	-4.47908	2.636435	-0.29485
H	-3.54812	3.01836	1.14739
H	-2.76078	3.047376	-0.43799
H	-0.11464	0.526265	1.800563
H	-0.21349	2.217231	1.315463
H	1.353559	1.486639	1.655575
H	1.477282	3.872772	-1.31682
H	4.731371	0.161051	0.350522
H	4.2898	-0.68546	2.611116
H	3.21944	0.6642	2.241357
H	2.594704	-0.99163	2.217276
H	5.255053	-2.14285	0.814406
H	4.67783	-2.02236	-0.85509
H	3.632727	-2.69478	0.404081

Table S12. Optimized geometries of predominant conformer of compound **6** at the b3lyp/6-311+g(d,p) level.

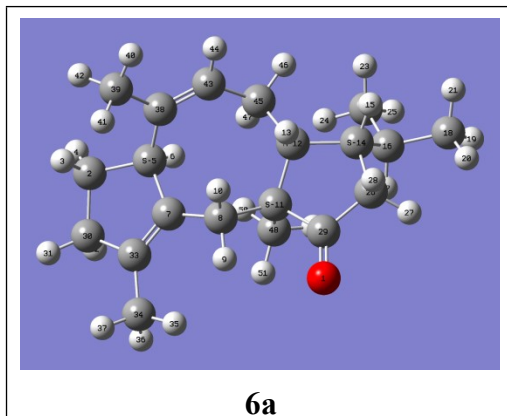


Table S13. Boltzmann distribution of conformer **6a**.

Conformer	E (Hartree)	ΔG (Kcal/mol)	Proportion (%)
6a	-855.055214	0	100

Table S14. Cartesian coordinates of conformer **6a**.

Atomic Type	6a		
	X	Y	Z
O	1.293623	2.954068	-1.11514
C	-3.70957	-0.98824	0.879934
H	-4.36452	-1.28057	0.053877
H	-3.86835	-1.70227	1.694545
C	-2.23615	-0.95209	0.403216
H	-1.59425	-1.09342	1.285928
C	-2.0629	0.508713	-0.05142
C	-0.88348	0.96949	-0.87066
H	-1.0032	2.034959	-1.08608
H	-0.881	0.451459	-1.83898
C	0.533799	0.791075	-0.23467
C	1.231469	-0.56706	-0.56249
H	1.057565	-0.69368	-1.64247
C	2.779213	-0.30436	-0.51818
H	3.243131	-1.06863	-1.15529
C	3.598765	-0.29193	0.807292
H	3.387371	0.644135	1.341374
C	5.103743	-0.28443	0.469407
H	5.703055	-0.17114	1.379412
H	5.377561	0.528793	-0.21018
H	5.39472	-1.22906	-0.00755
C	3.315017	-1.44928	1.777767
H	3.463958	-2.42212	1.294253
H	2.299234	-1.42128	2.177927
H	4.004964	-1.39673	2.627649
C	2.837546	1.078131	-1.21532
H	3.683313	1.712178	-0.93523
H	2.873523	0.970486	-2.30824
C	1.524319	1.775313	-0.89022
C	-4.02667	0.468327	1.272585
H	-5.07294	0.741898	1.085455
H	-3.84633	0.650285	2.344198
C	-3.05129	1.281968	0.443601
C	-3.23646	2.767471	0.33273
H	-2.46337	3.253833	-0.267
H	-3.23105	3.231703	1.328489
H	-4.21141	3.004687	-0.11343
C	-1.81024	-1.99481	-0.62097
C	-2.84573	-2.53224	-1.58211
H	-2.38226	-3.1774	-2.33421
H	-3.36306	-1.71774	-2.10617
H	-3.62028	-3.11555	-1.06934
C	-0.52513	-2.37941	-0.72252
H	-0.26808	-3.08626	-1.51276
C	0.653069	-1.85599	0.072097
H	1.432935	-2.62401	0.071951
H	0.384932	-1.69146	1.120408
C	0.493332	1.164883	1.269364
H	1.48722	1.202038	1.719346
H	-0.10319	0.448032	1.837489
H	0.034962	2.151102	1.389179

Table S15. Crystallographic data of compound **1**.

Empirical formula	C20H28O
Formula weight	284.42
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P1211
Unit cell dimensions	a = 10.0477(2) Å $\alpha = 90^\circ$ b = 7.16210(10) Å $\beta = 91.8680(10)^\circ$ c = 11.3732(2) Å $\gamma = 90^\circ$
Volume	818.01(2) Å ³
Z	2
Calculated density	1.155 Mg/m ³
Absorption coefficient	0.518 mm ⁻¹
F(000)	312
Crystal size	0.560 x 0.290 x 0.200 mm ³
Theta range for data collection	3.89 to 72.33°
Indices ranges	-12 ≤ h ≤ 12, -8 ≤ k ≤ 8, -12 ≤ l ≤ 14
Reflections collected	12142
Independent reflections	3212 [R(int) = 0.0353]
Completeness to theta = 67.679°	99.1 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3212/1/194
Goodness-of-fit on F ²	1.052
Final R indices [I > 2σ(I)]	R ₁ = 0.0327, wR ₂ = 0.0841
R indices (all data)	R ₁ = 0.0328, wR ₂ = 0.0842
Absolute structure parameter	-0.03(8)
Largest diff. peak and hole	0.211 and -0.208 e.Å ⁻³

Table S16. Crystallographic data of compound **3**.

Empirical formula	C20H30O4
Formula weight	334.44
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
Unit cell dimensions	$a = 6.5674(2)$ Å $\alpha = 90^\circ$ $b = 15.9608(6)$ Å $\beta = 90^\circ$ $c = 16.7628(6)$ Å $\gamma = 90^\circ$
Volume	1757.09(11) Å ³
Z	4
Calculated density	1.264 Mg/m ³
Absorption coefficient	0.691 mm ⁻¹
F(000)	728
Crystal size	0.770 x 0.620 x 0.220 mm ³
Theta range for data collection	5.28 to 72.12°
Indices ranges	-8 ≤ h ≤ 8, -15 ≤ k ≤ 19, -20 ≤ l ≤ 20
Reflections collected	19975
Independent reflections	3453 [R(int) = 0.0333]
Completeness to theta = 67.679°	99.5 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3453 / 0 / 224
Goodness-of-fit on F ²	1.098
Final R indices [I > 2σ(I)]	R ₁ = 0.0287, wR ₂ = 0.0731
R indices (all data)	R ₁ = 0.0287, wR ₂ = 0.0732
Absolute structure parameter	0.09(3)
Largest diff. peak and hole	0.455 and -0.164 e.Å ⁻³

Table S17. Crystallographic data of compound **6**.

Empirical formula	C20H30O
Formula weight	286.44
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	P1211
Unit cell dimensions	$a = 10.8483(7) \text{ \AA}$ $\alpha = 79.290(2)^\circ$ $b = 6.9259(4) \text{ \AA}$ $\beta = 101.620(2)^\circ$ $c = 11.4177(7) \text{ \AA}$ $\gamma = 75.423(2)^\circ$
Volume	840.28(9) Å ³
Z	2
Calculated density	1.132 Mg/m ³
Absorption coefficient	0.505 mm ⁻¹
F(000)	316
Crystal size	0.660 x 0.170 x 0.050 mm ³
Theta range for data collection	3.95 to 72.23°
Indices ranges	-12 ≤ h ≤ 13, -8 ≤ k ≤ 8, -14 ≤ l ≤ 13
Reflections collected	11725
Independent reflections	3271 [R(int) = 0.0722]
Completeness to theta = 67.679°	99.7 %
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3271 / 1 / 195
Goodness-of-fit on F ²	1.078
Final R indices [I > 2σ(I)]	R ₁ = 0.0472, wR ₂ = 0.1200
R indices (all data)	R ₁ = 0.0497, wR ₂ = 0.1232
Absolute structure parameter	-0.35(19)
Largest diff. peak and hole	0.216 and -0.298 e.Å ⁻³

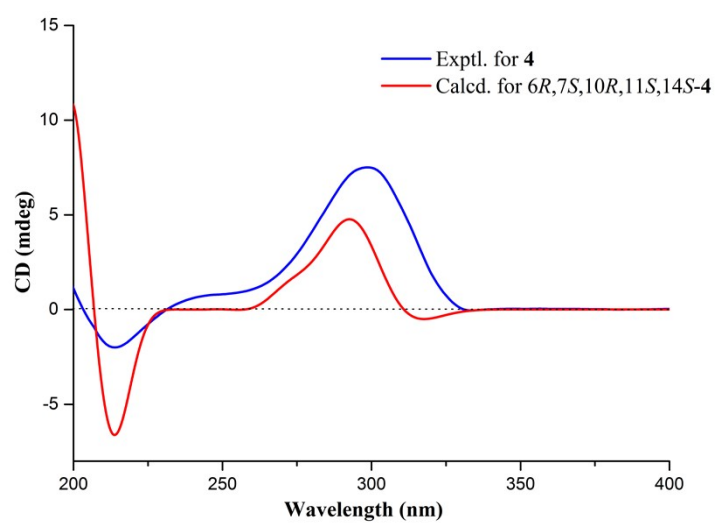


Figure S1. Experimental and calculated ECD spectra for compound **4**.

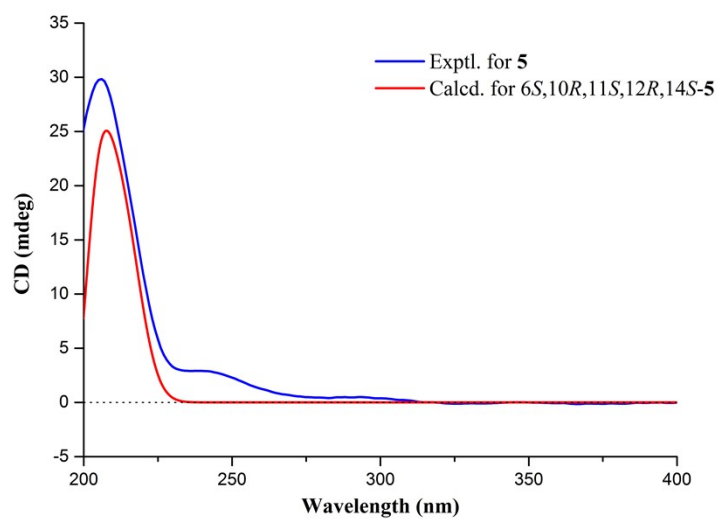


Figure S2. Experimental and calculated ECD spectra for compound **5**.

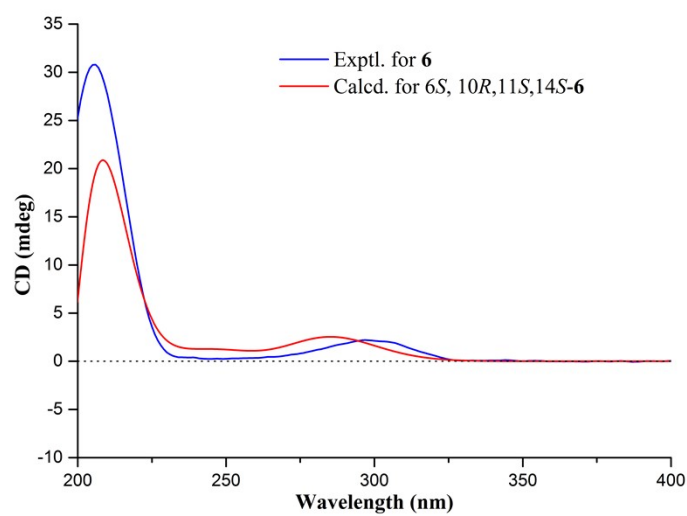


Figure S3. Experimental and calculated ECD spectra for compound **6**.

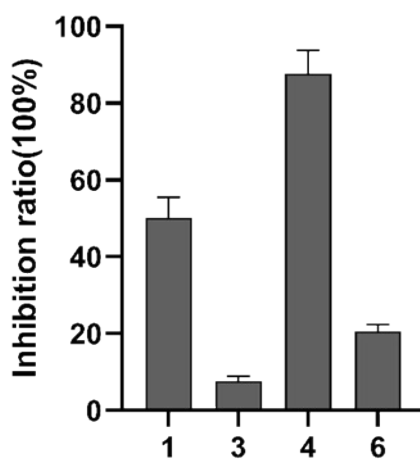


Figure S4. Effects of compounds **1**, **3**, **4**, and **6** on current of human $Ca_v3.1$ low-voltage-gated calcium channel at $25 \mu\text{M}$. All the data were represented as mean \pm SD ($n = 3$).

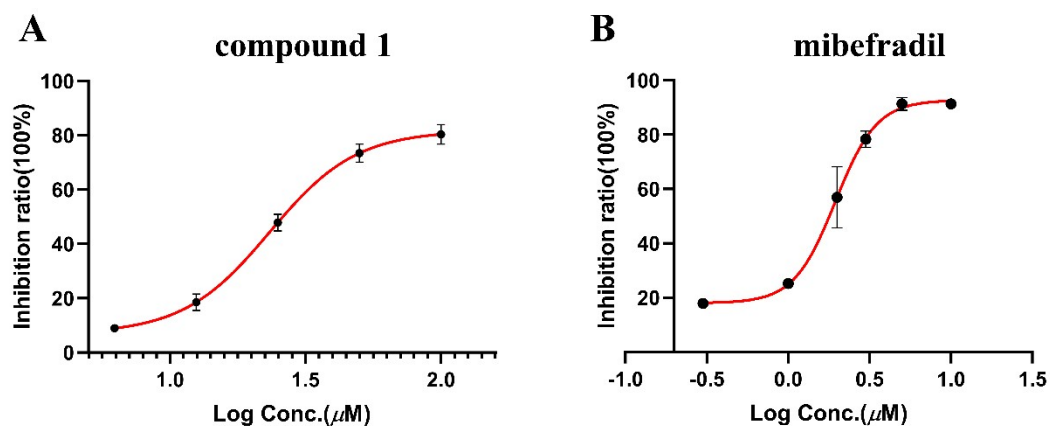


Figure S5. Dose-response curves of inhibition of compound **1** (A) and the positive control, mibefradil (B), on peak current of $Ca_v3.1$. Data were fit using a Hill equation and the points represent mean \pm SD ($n = 4$).

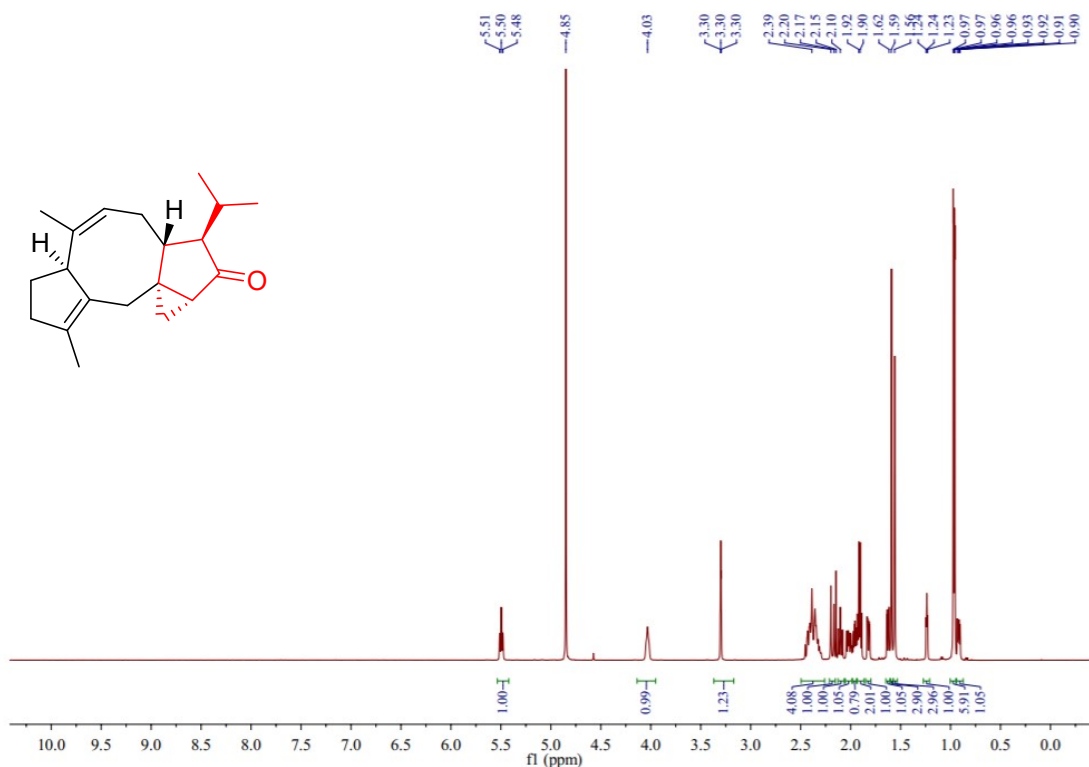


Figure S6. ^1H NMR (500 MHz) spectrum of hypoestin A (**1**) in methanol- d_4 .

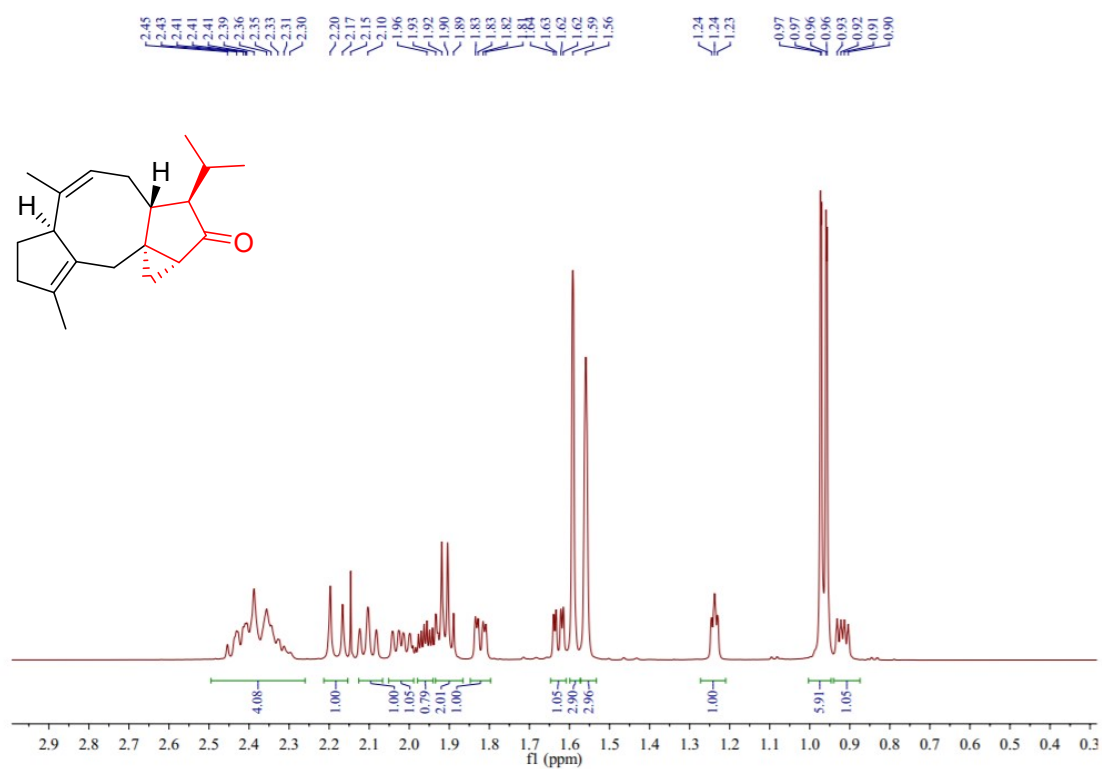


Figure S7. Expanded ^1H NMR spectrum of hypoestin A (**1**).

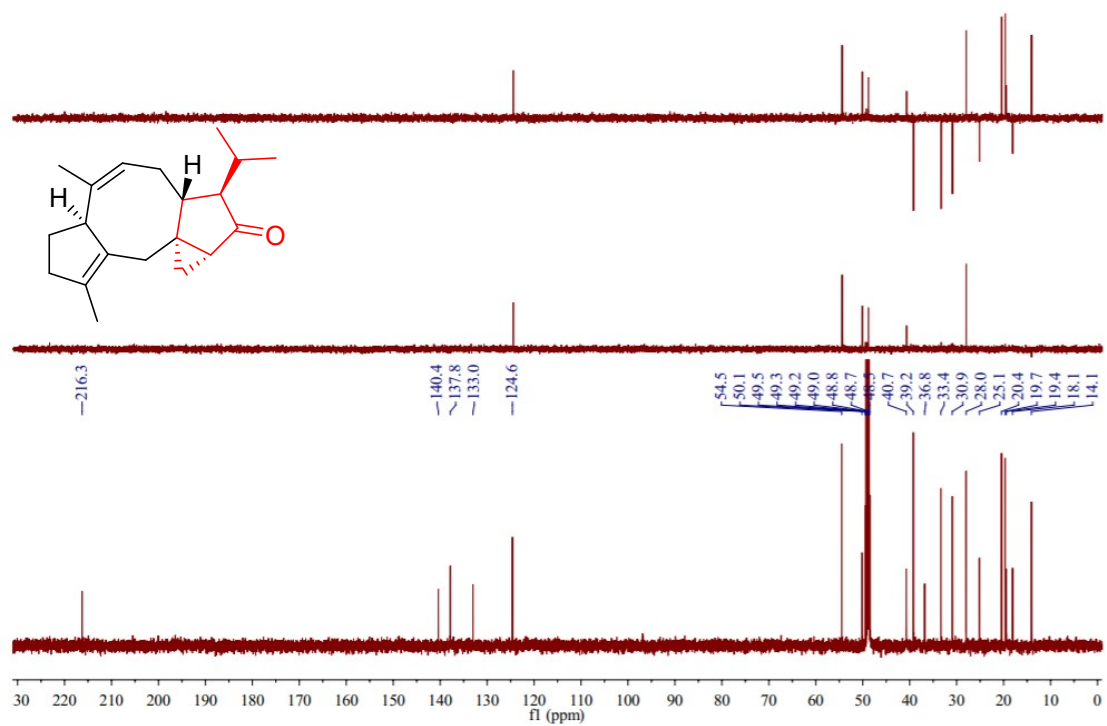


Figure S8. ^{13}C NMR and DEPT (125 MHz) spectra of hypoestin A (**1**) in methanol- d_4 .

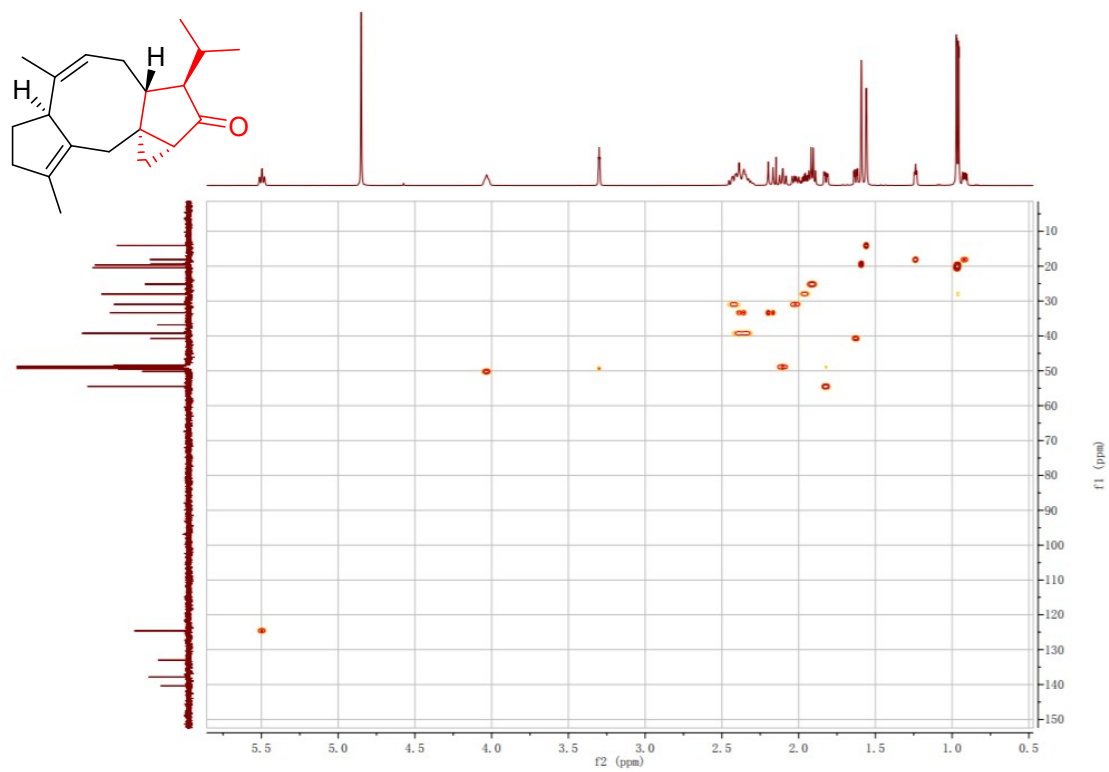


Figure S9. HSQC spectrum of hypoestin A (**1**).

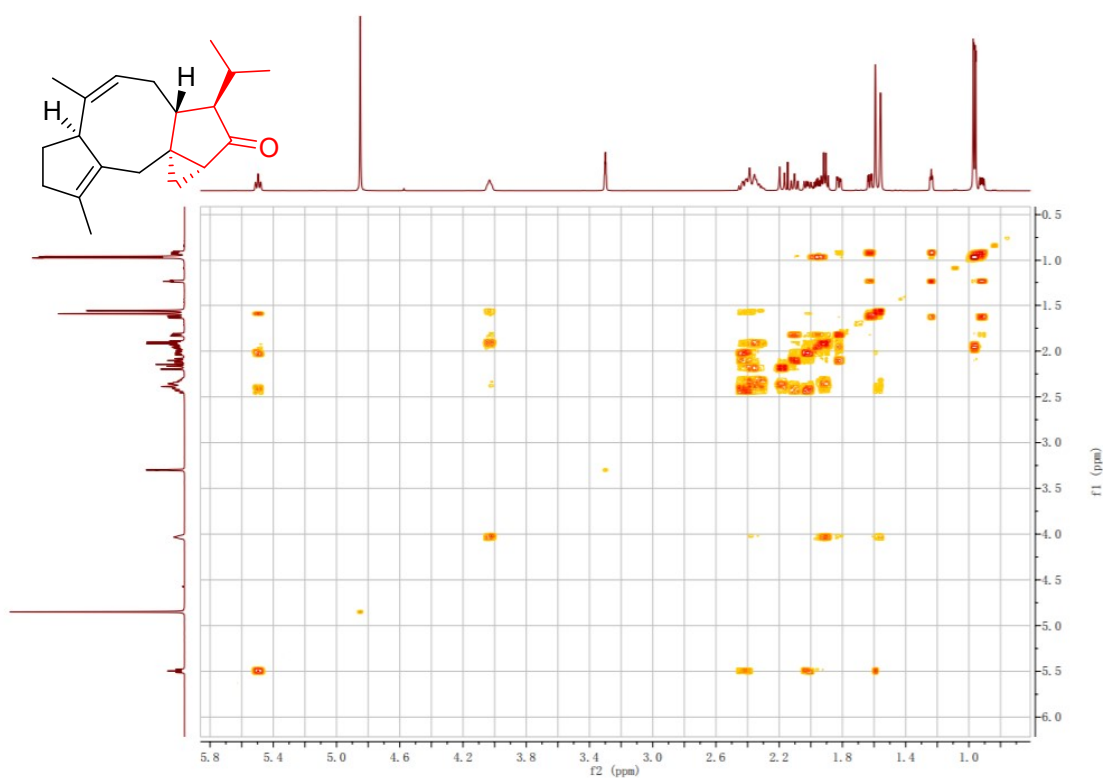


Figure S10. ^1H - ^1H COSY spectrum of hypoestin A (**1**).

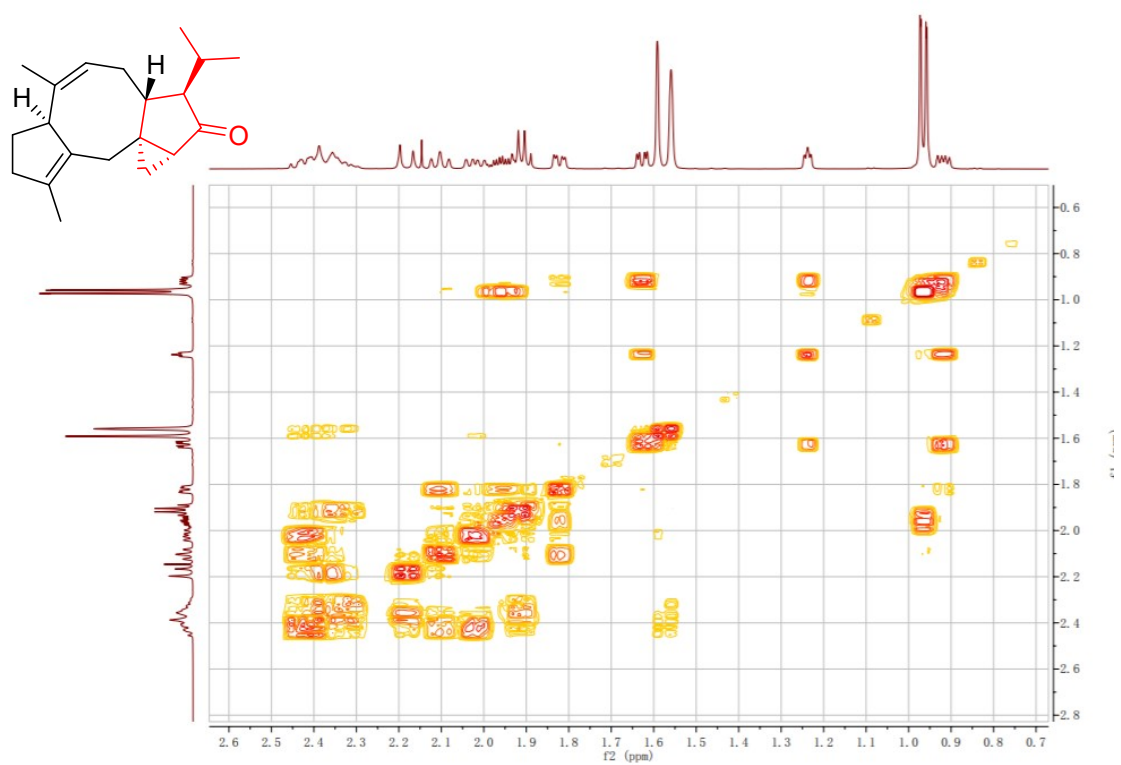


Figure S11. Expanded ^1H - ^1H COSY spectrum of hypoestin A (**1**).

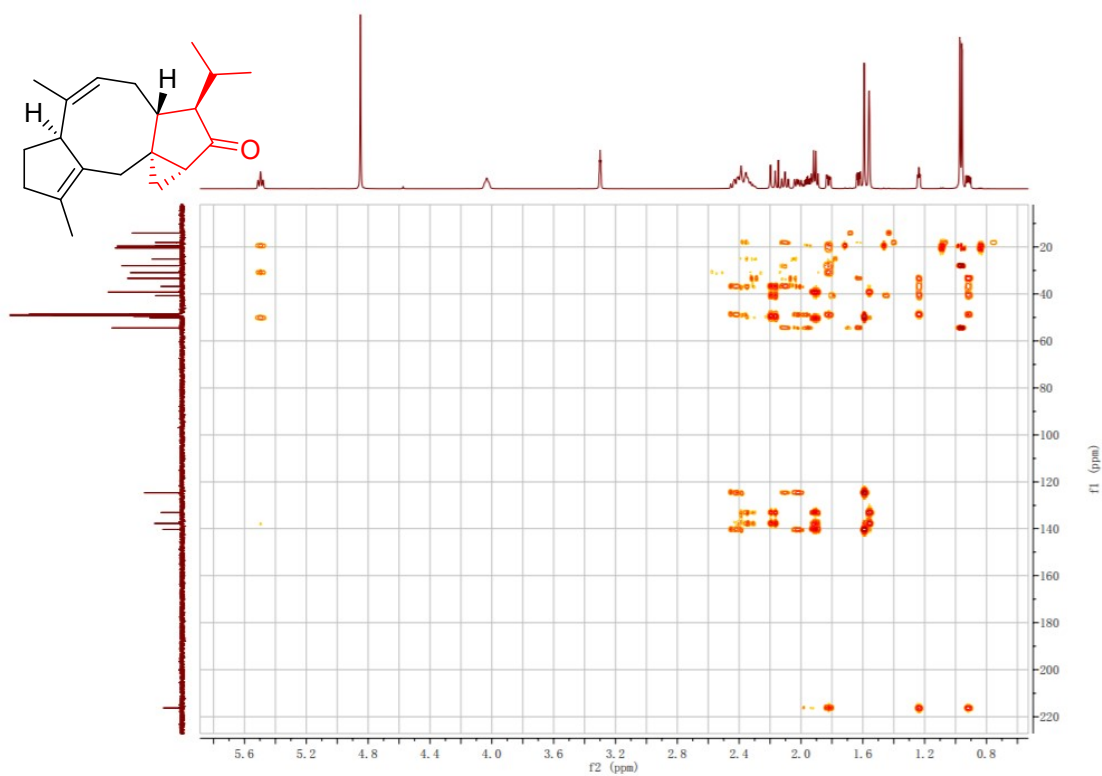


Figure S12. HMBC spectrum of hypoestin A (**1**).

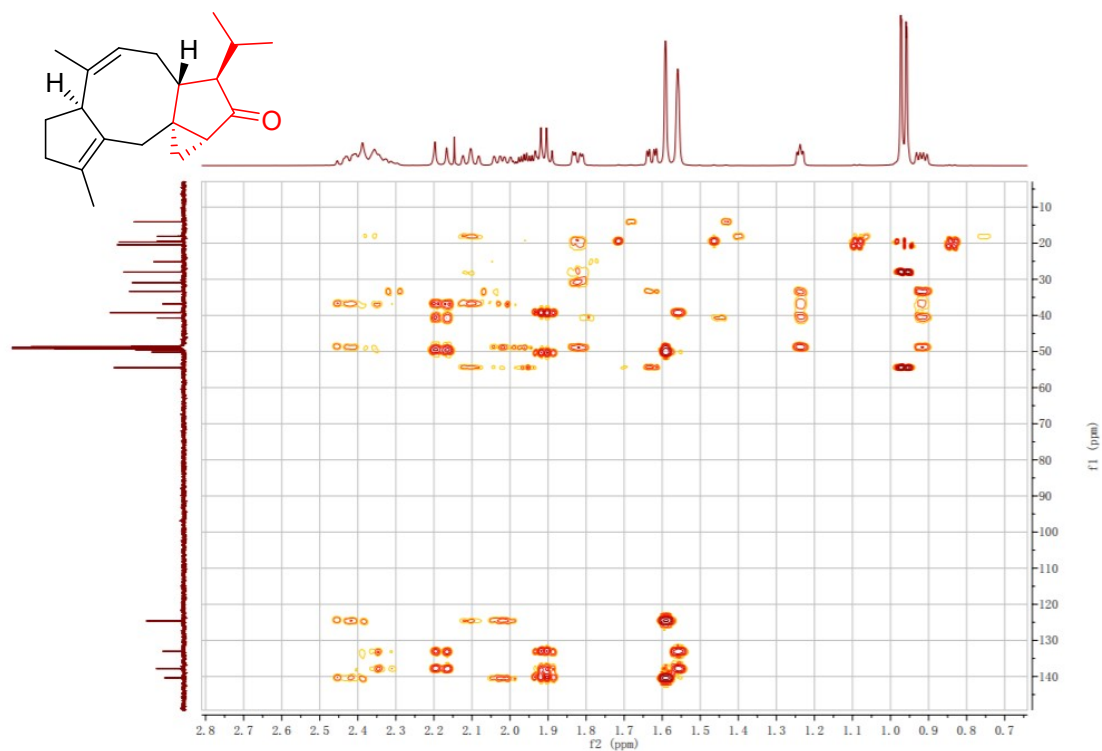


Figure S13. Expanded HMBC spectrum of hypoestin A (**1**).

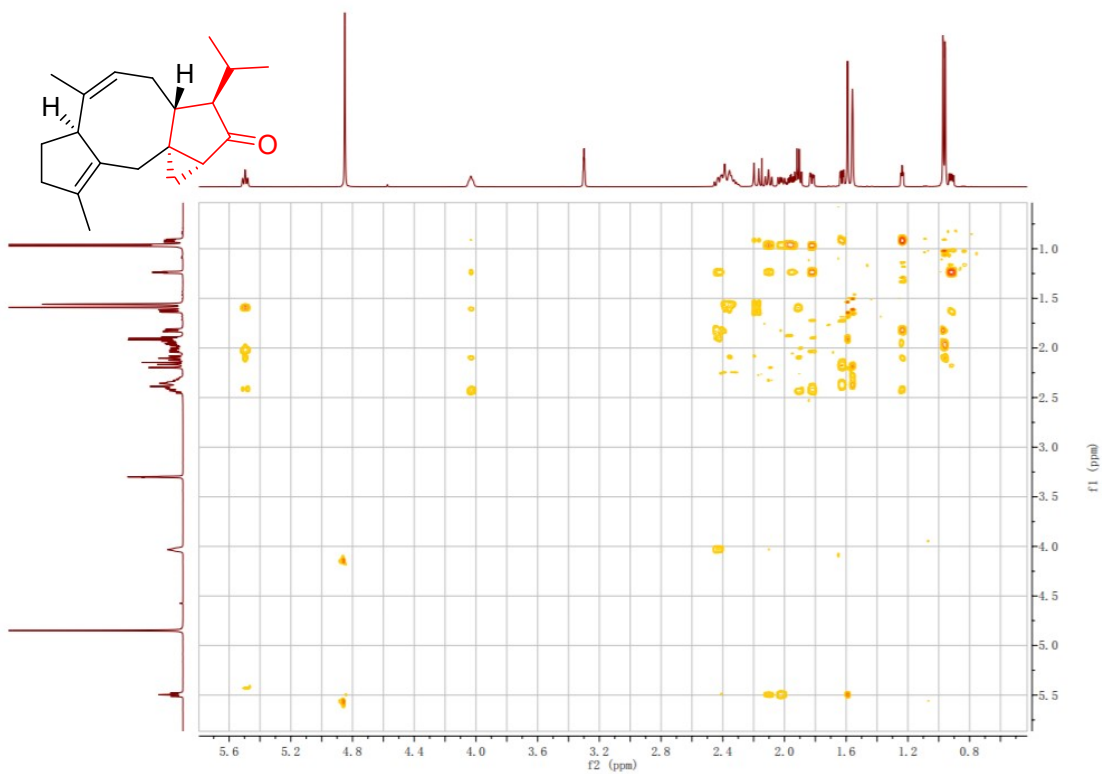


Figure S14. ROESY spectrum of hypoestin A (**1**).

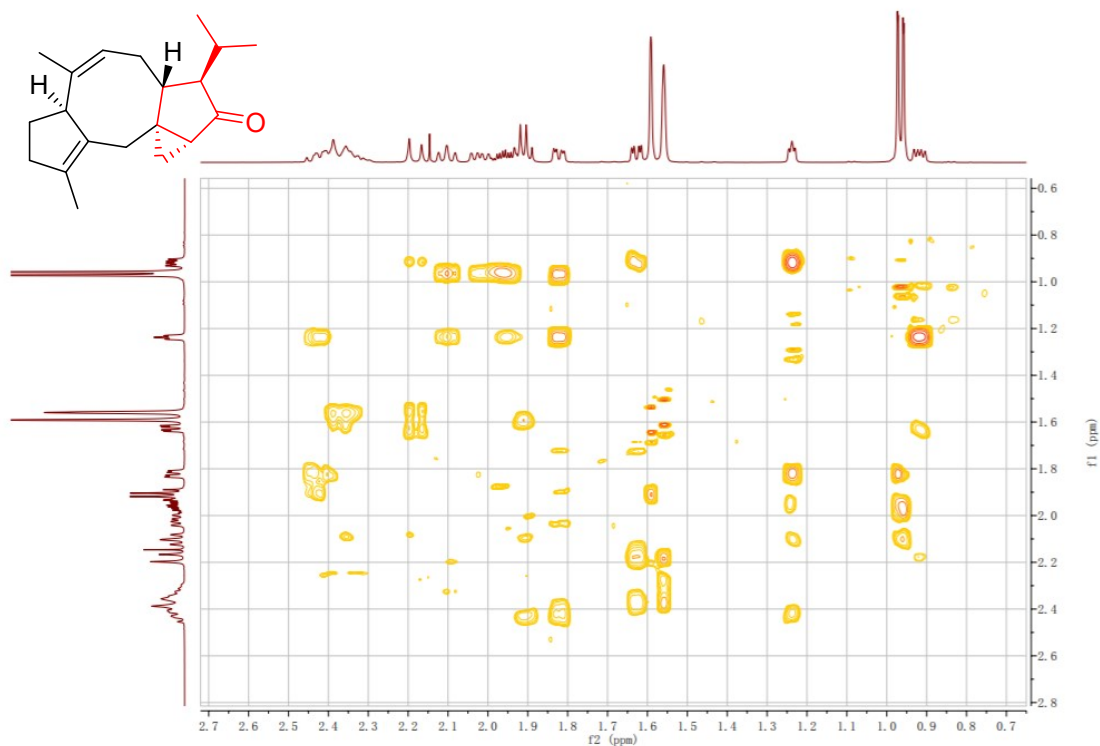


Figure S15. Expanded ROESY spectrum of hypoestin A (1).

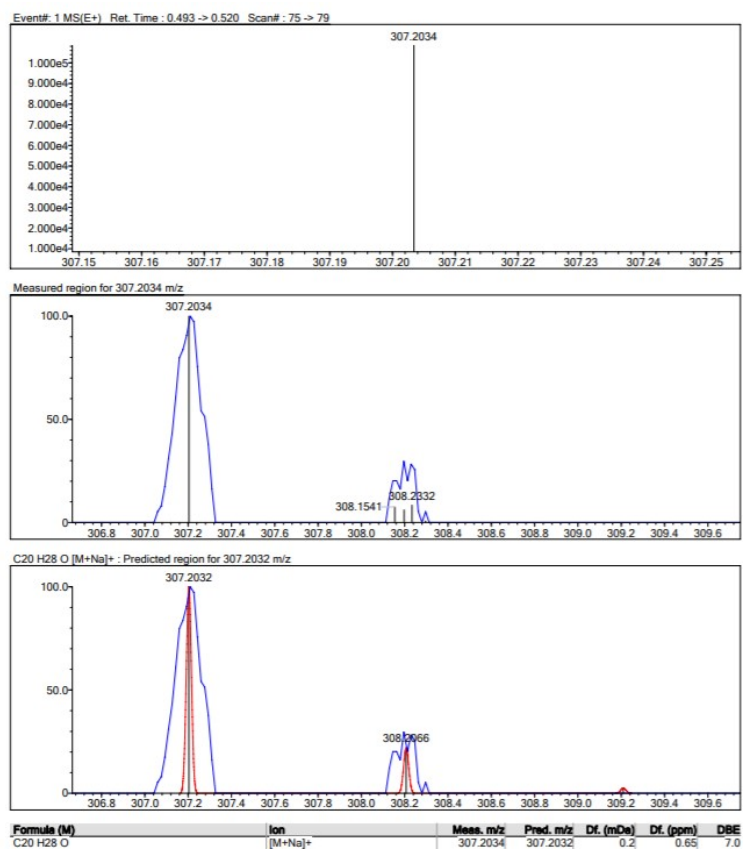


Figure S16. HRESIMS spectrum of hypoestin A (1).

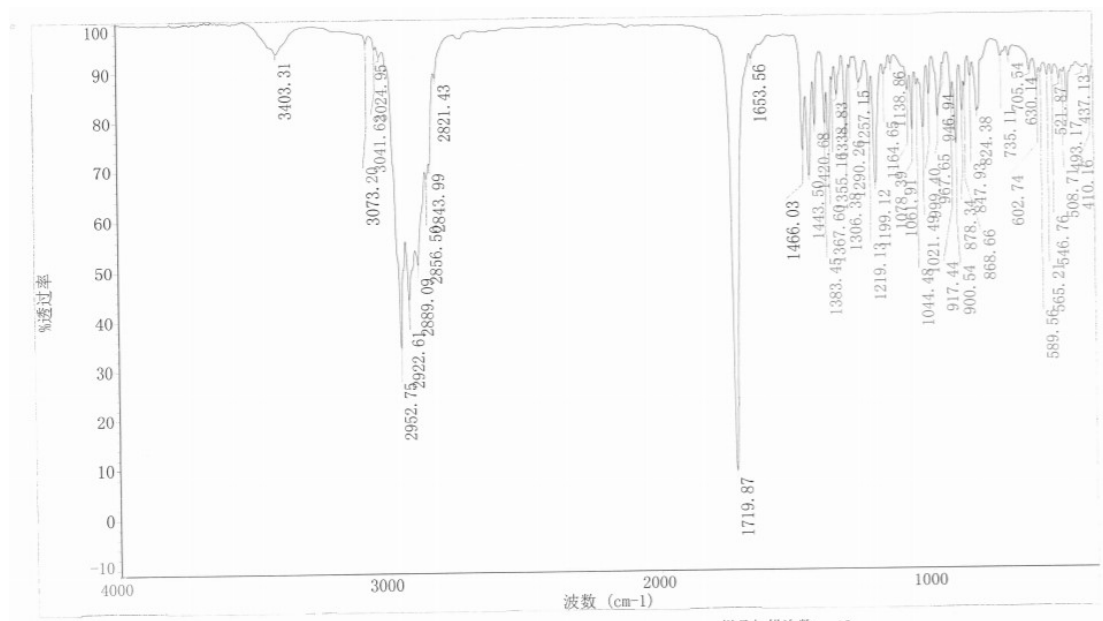


Figure S17. IR spectrum of hypoestin A (1).

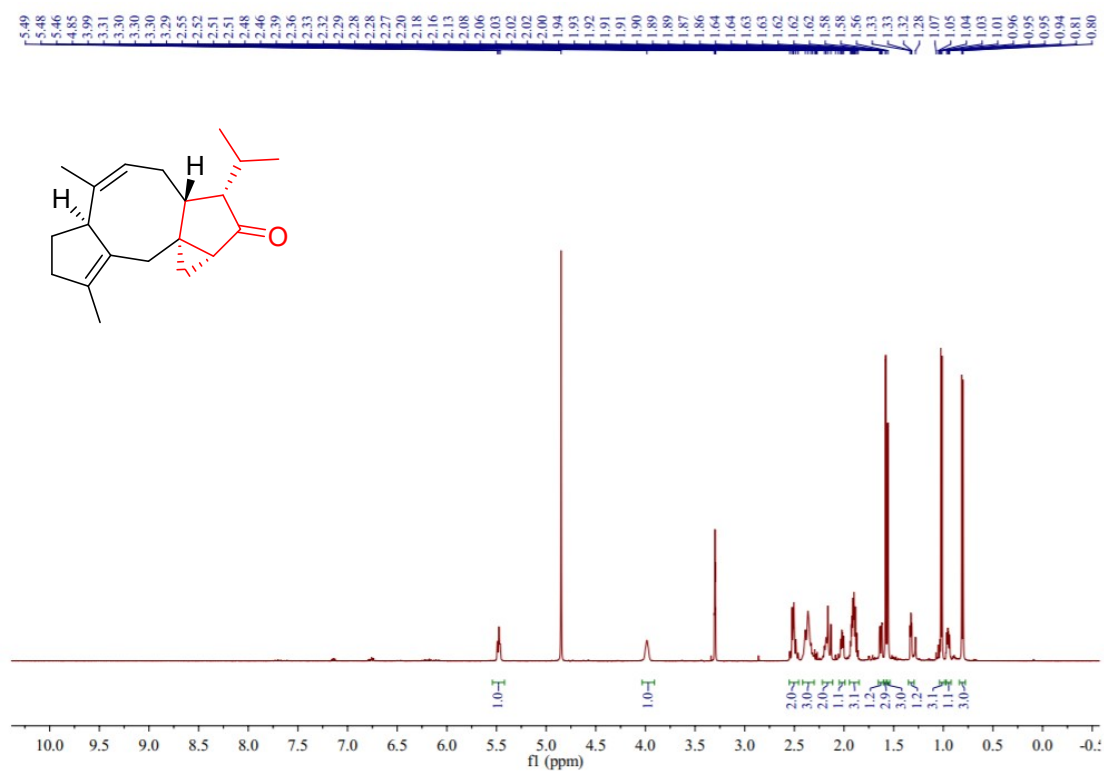


Figure S18. ^1H NMR (500 MHz) spectrum of hypoestin B (2) in methanol- d_4 .

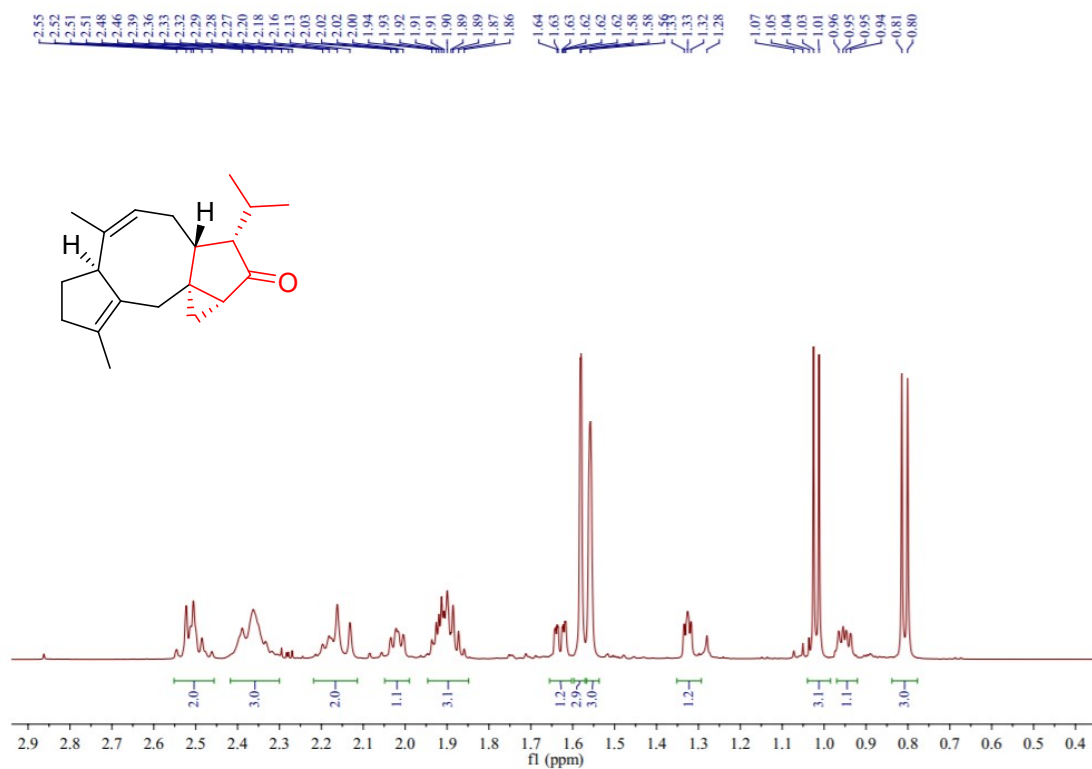


Figure S19. Expanded ¹H NMR spectrum of hypoestin B (2).

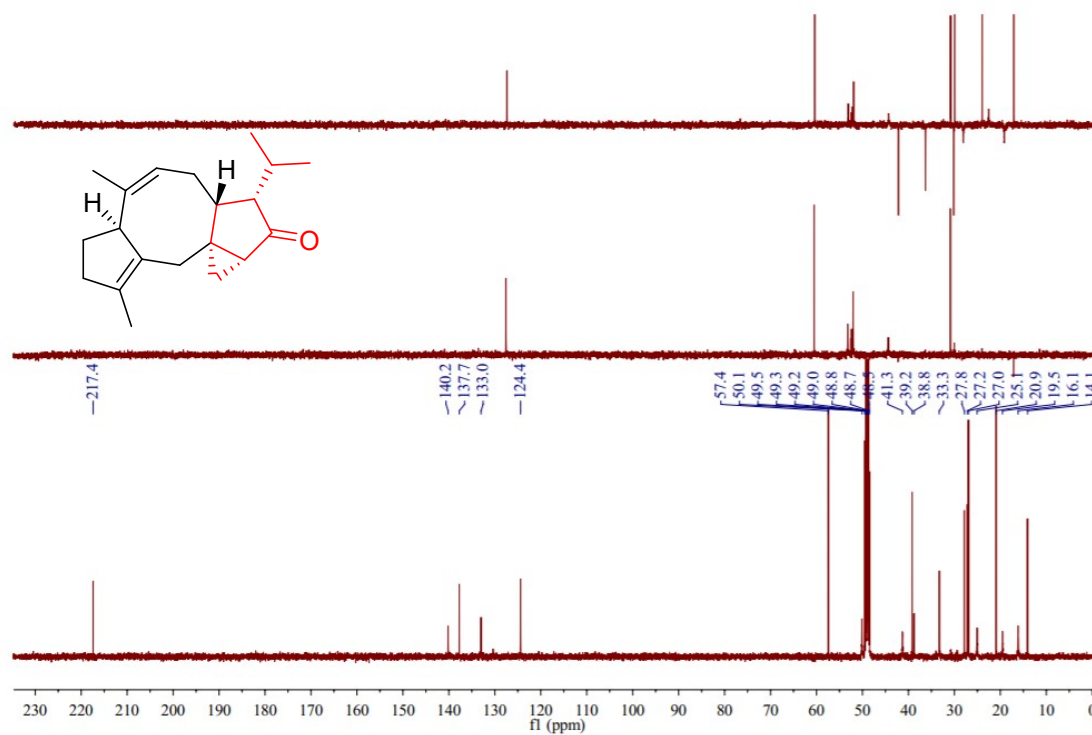


Figure S20. ¹³C NMR and DEPT (125 MHz) spectra of hypoestin B (2) in methanol-*d*₄.

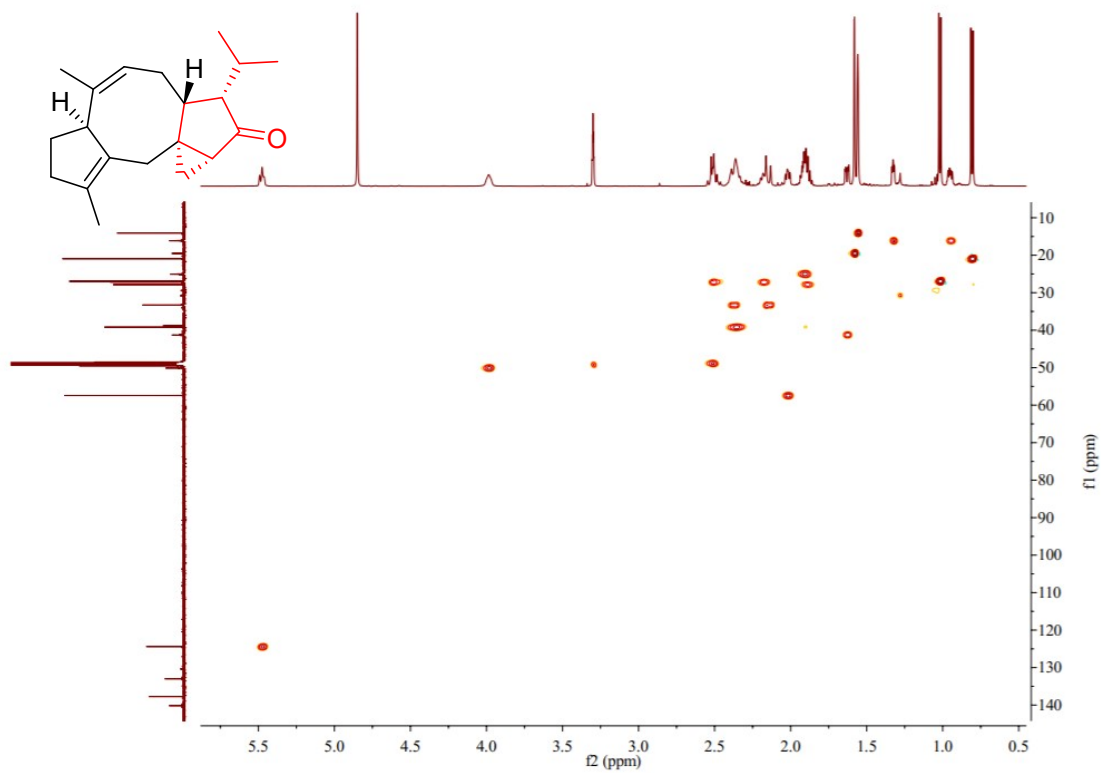


Figure S21. HSQC spectrum of hypoestin B (2).

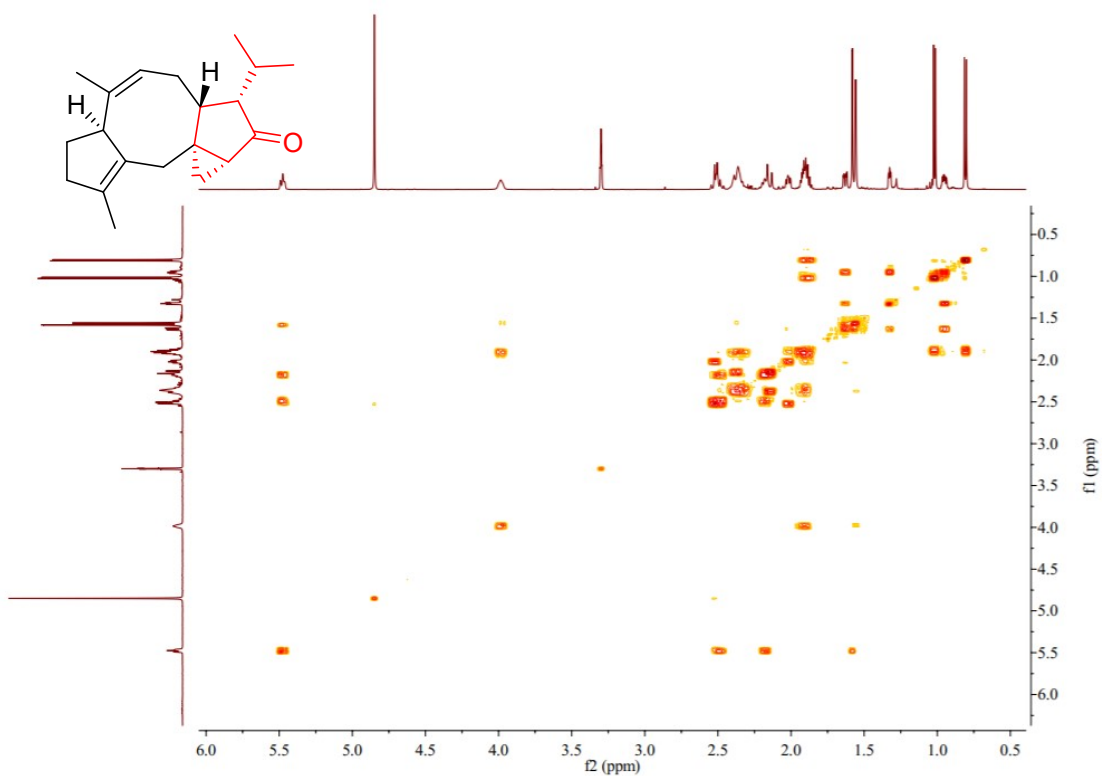


Figure S22. ^1H - ^1H COSY spectrum of hypoestin B (2).

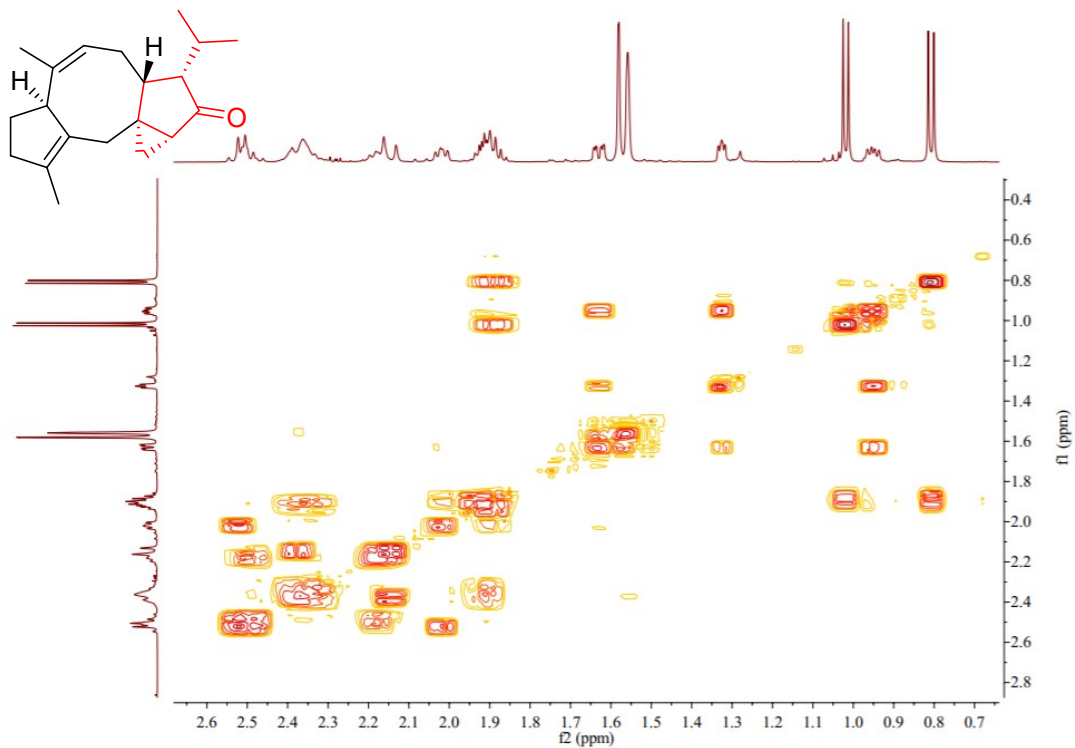


Figure S23. Expanded ^1H - ^1H COSY spectrum of hypoestin B (**2**).

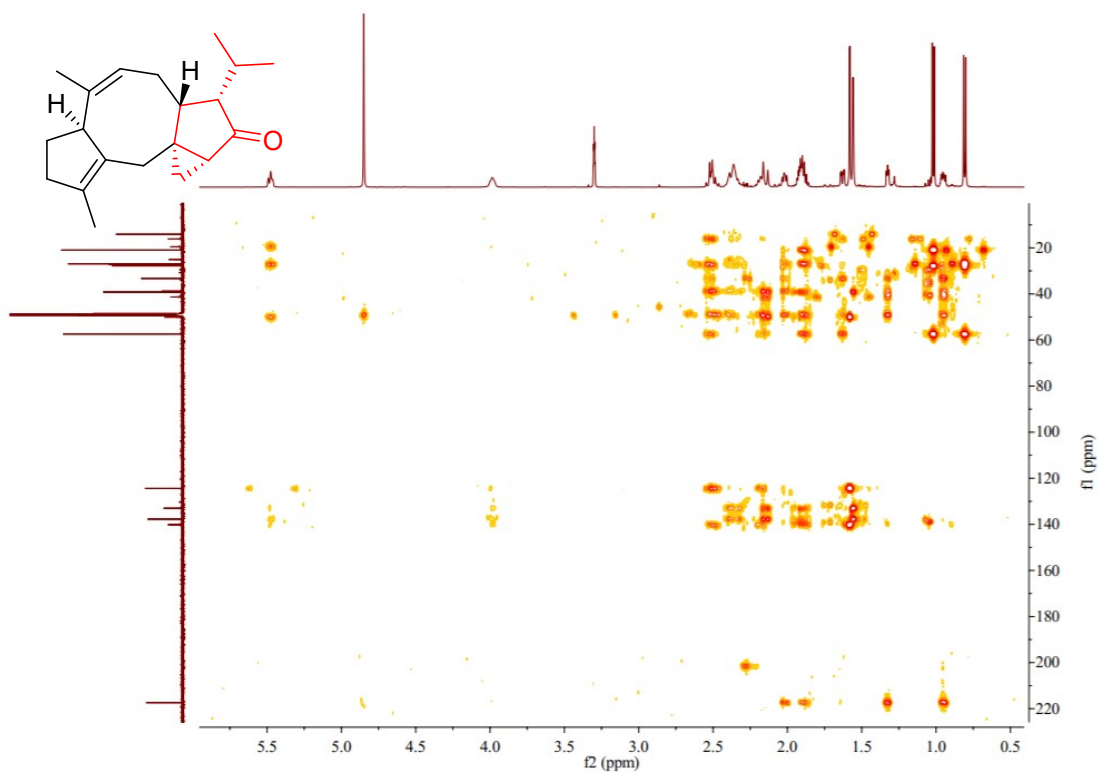


Figure S24. HMBC spectrum of hypoestin B (**2**).

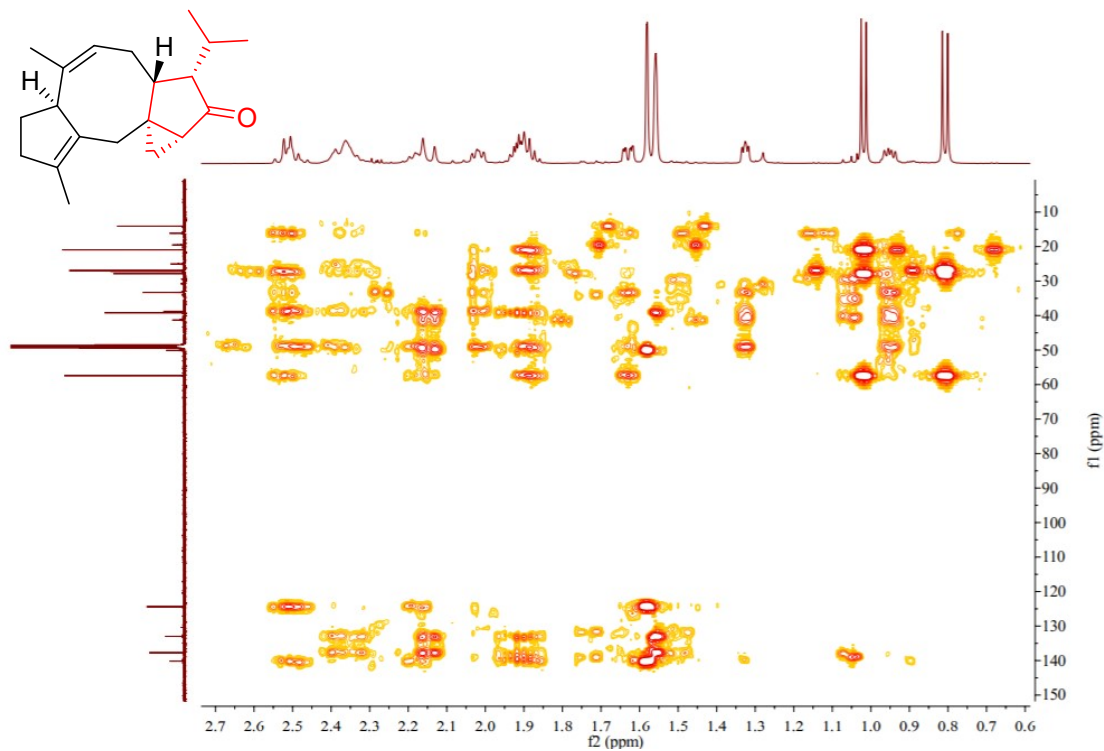


Figure S25. Expanded HMBC spectrum of hypoestin B (2).

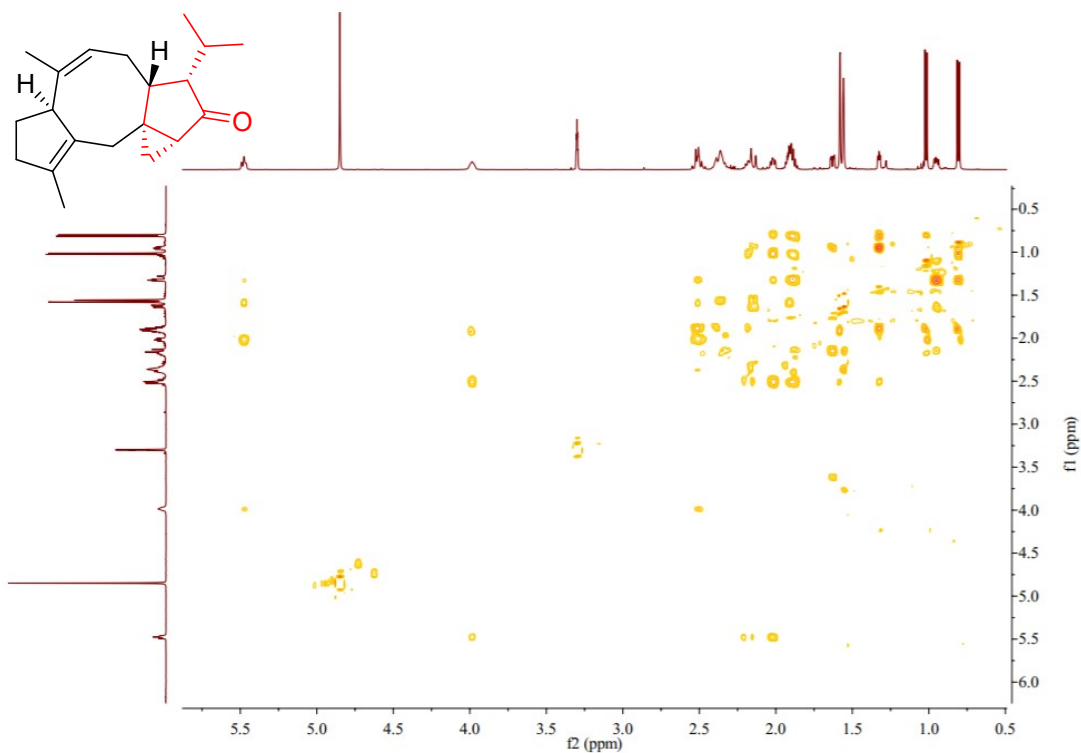


Figure S26. ROESY spectrum of hypoestin B (2).

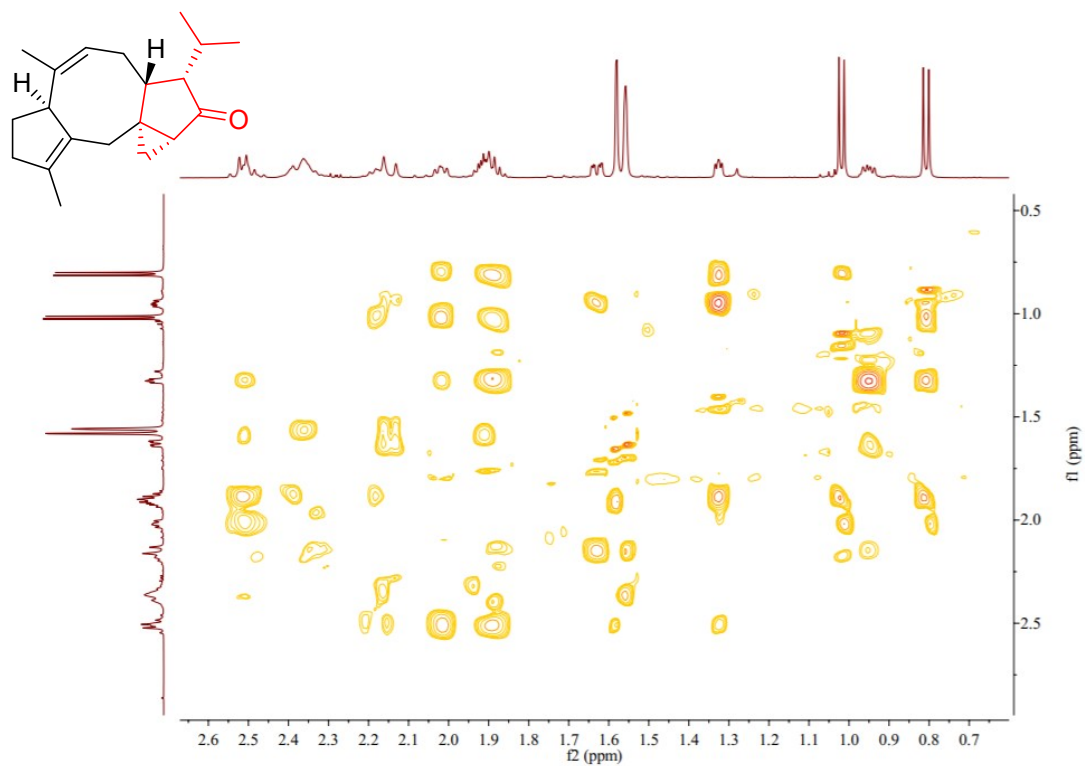


Figure S27. Expanded ROESY spectrum of hypoestin B (2).

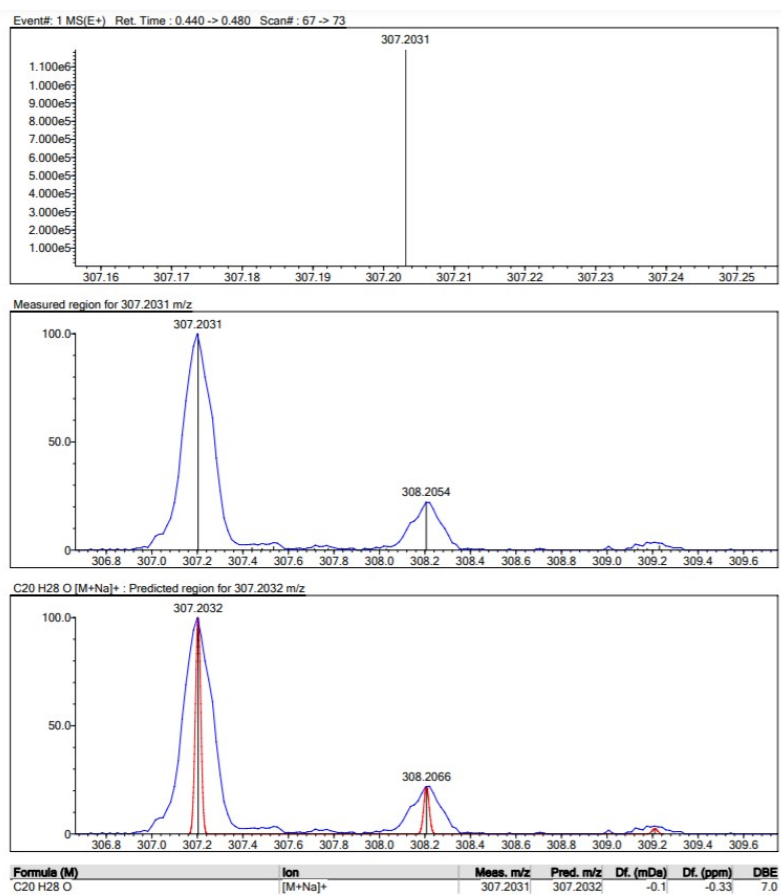


Figure S28. HRESIMS spectrum of hypoestin B (2).

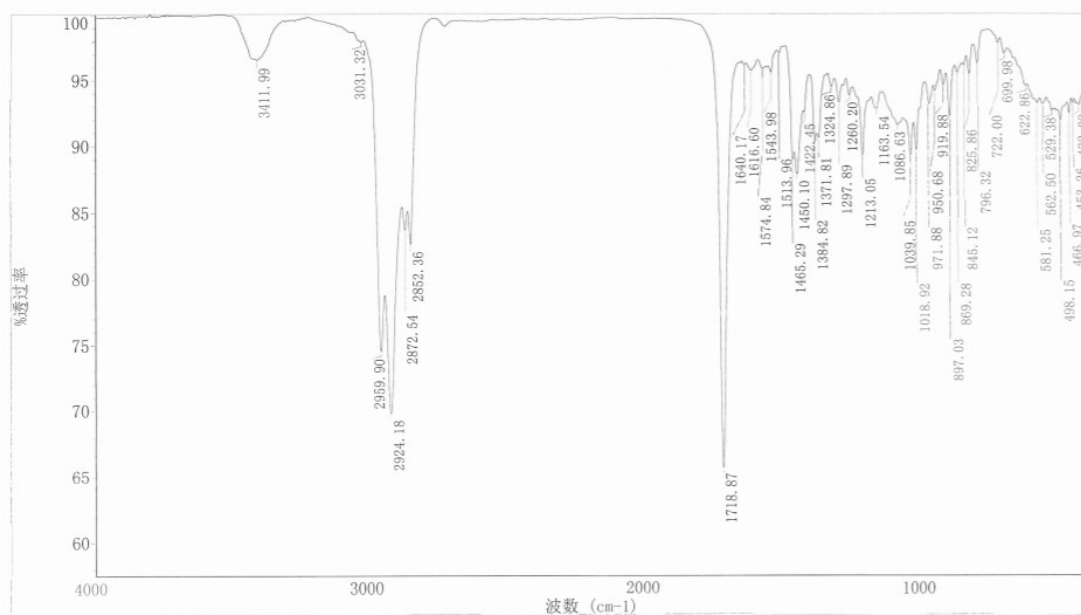


Figure S29. IR spectrum of hypoestin B (2).

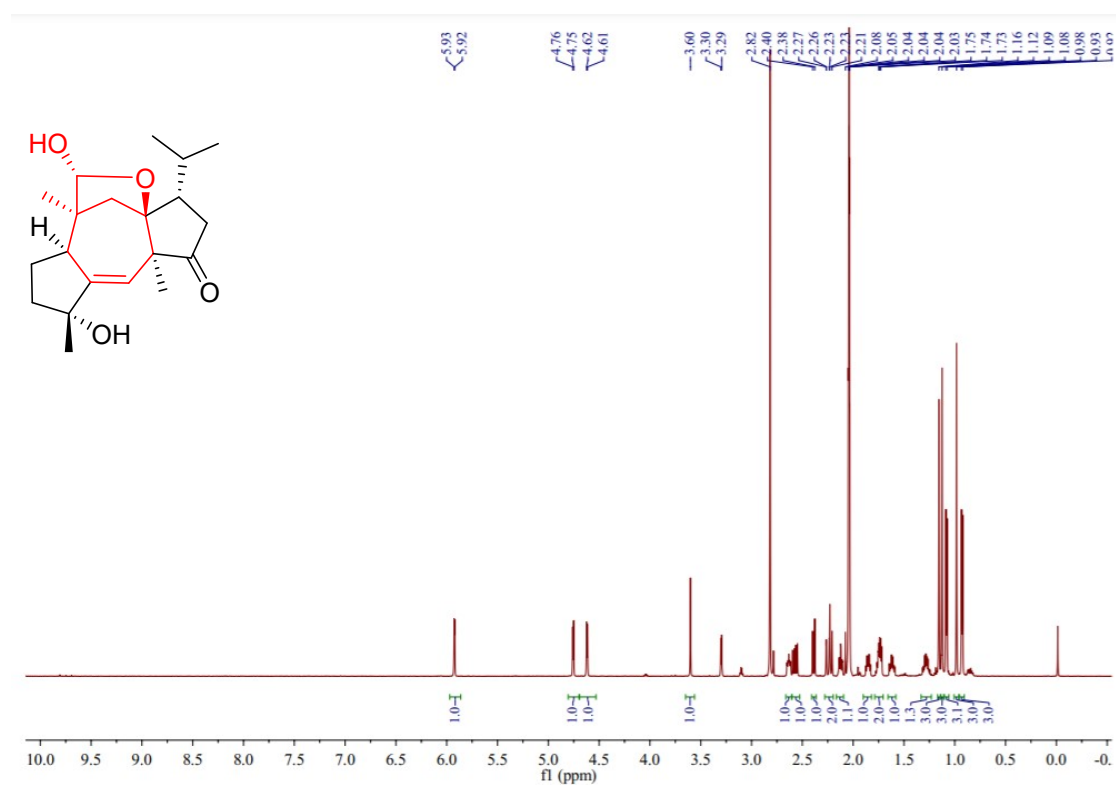


Figure S30. ¹H NMR (500 MHz) spectrum of hypoestin C (3) in acetone-*d*₆.

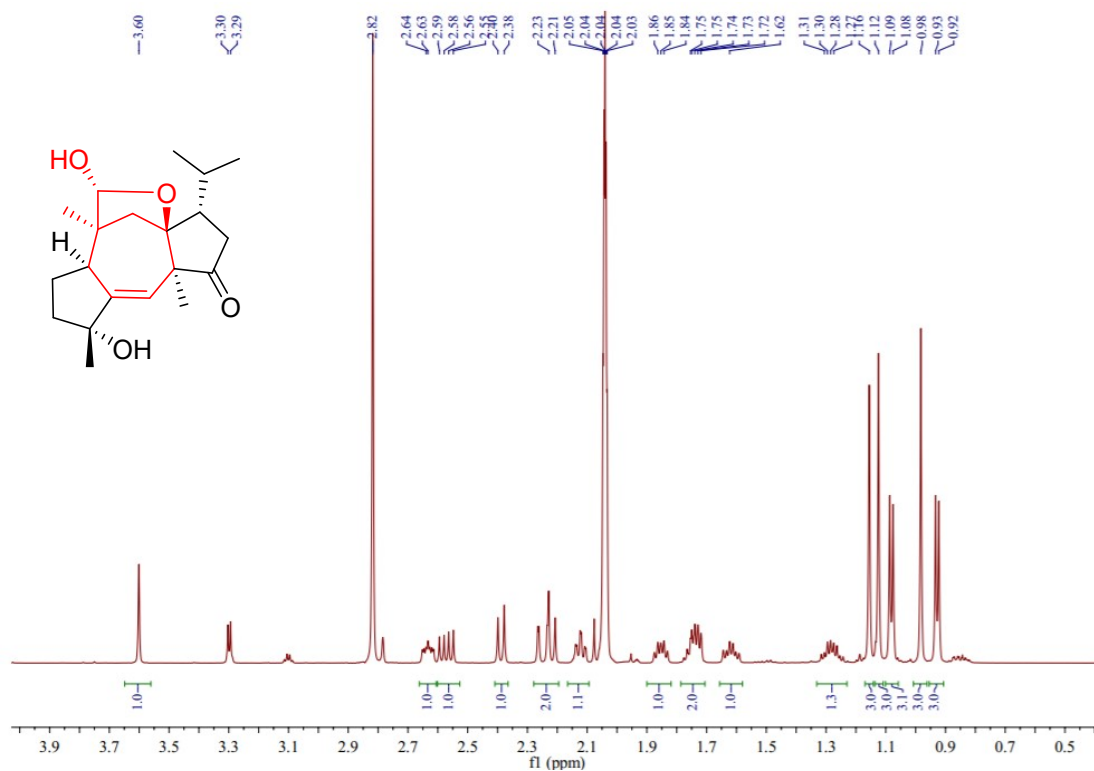


Figure S31. Expanded ^1H NMR spectrum of hypoestin C (**3**).

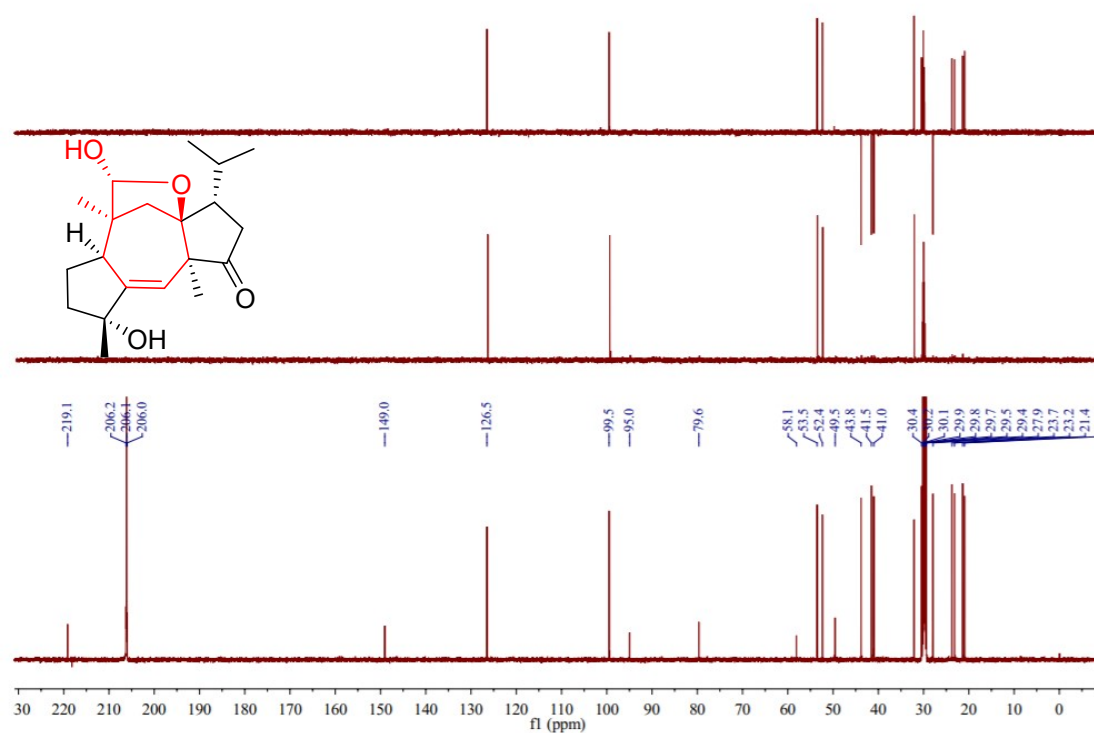


Figure S32. ^{13}C NMR and DEPT (125 MHz) spectra of hypoestin C (**3**) in acetone- d_6 .

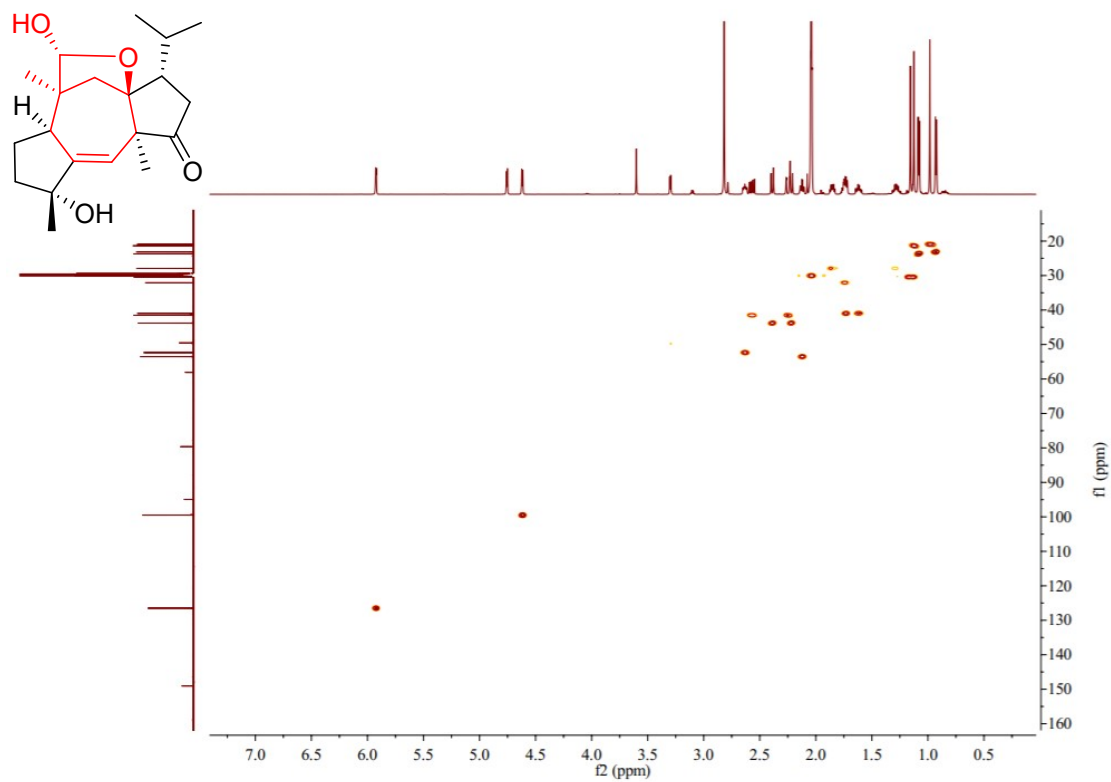


Figure S33. HSQC spectrum of hypoestin C (**3**).

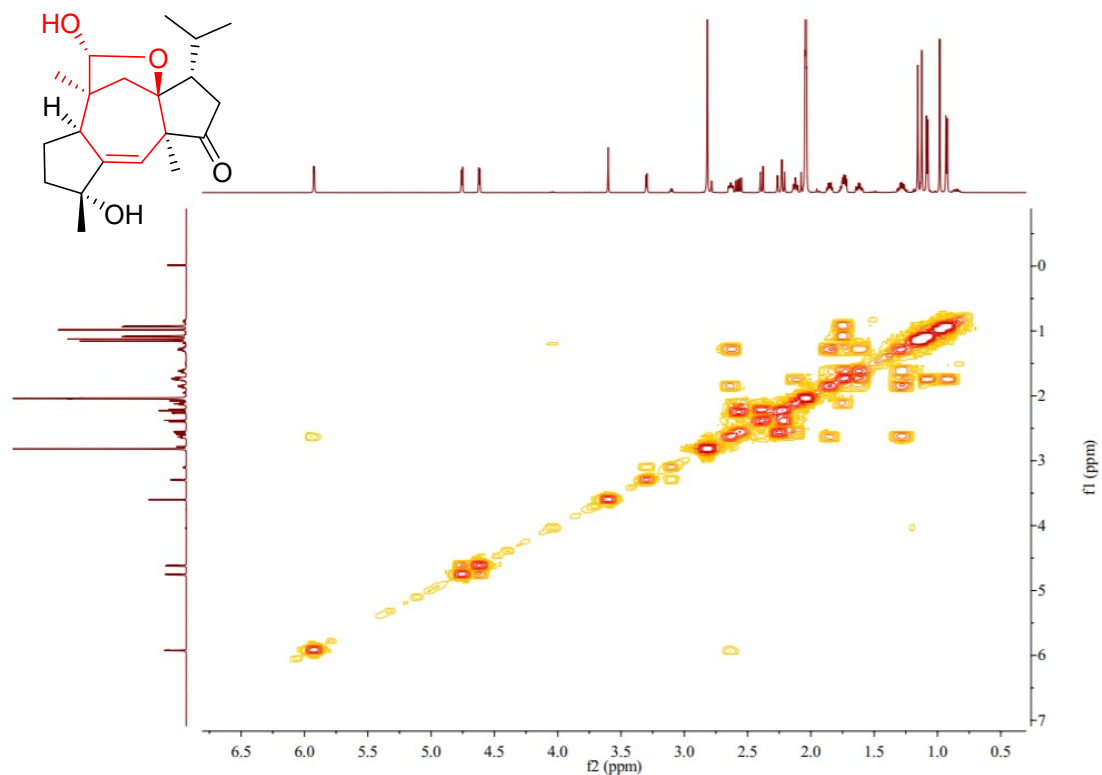


Figure S34. ^1H - ^1H COSY spectrum of hypoestin C (**3**).

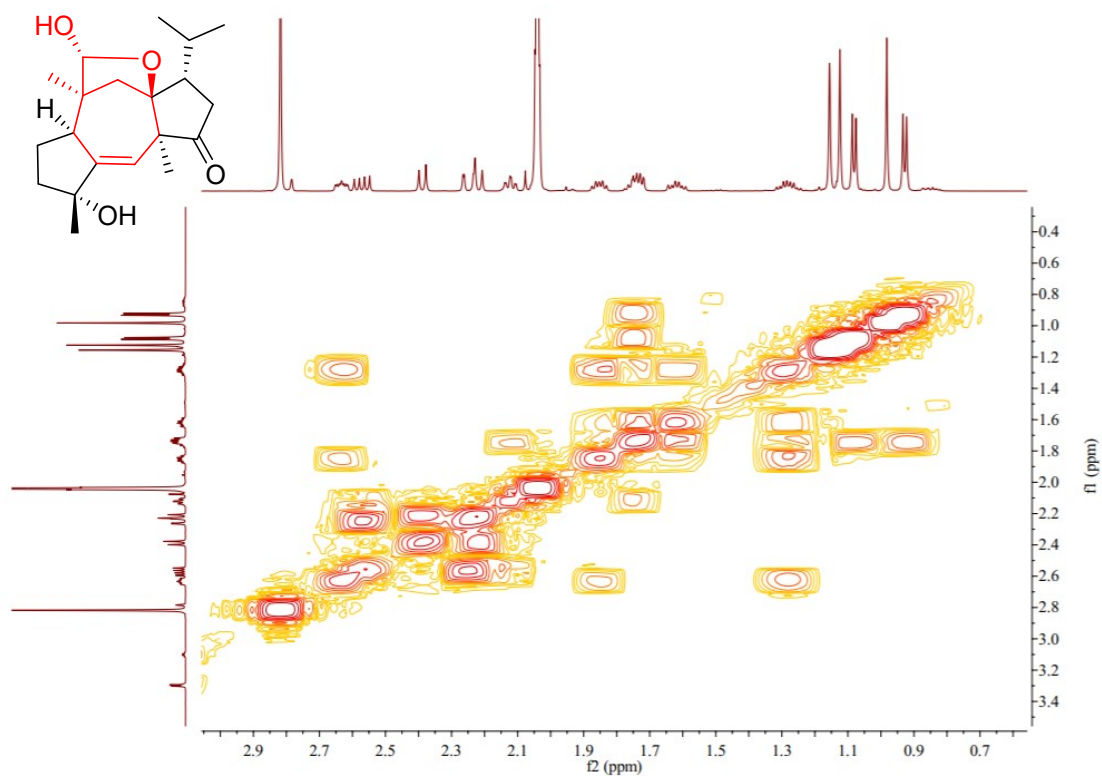


Figure S35. Expanded ^1H - ^1H COSY spectrum of hypoestin C (3).

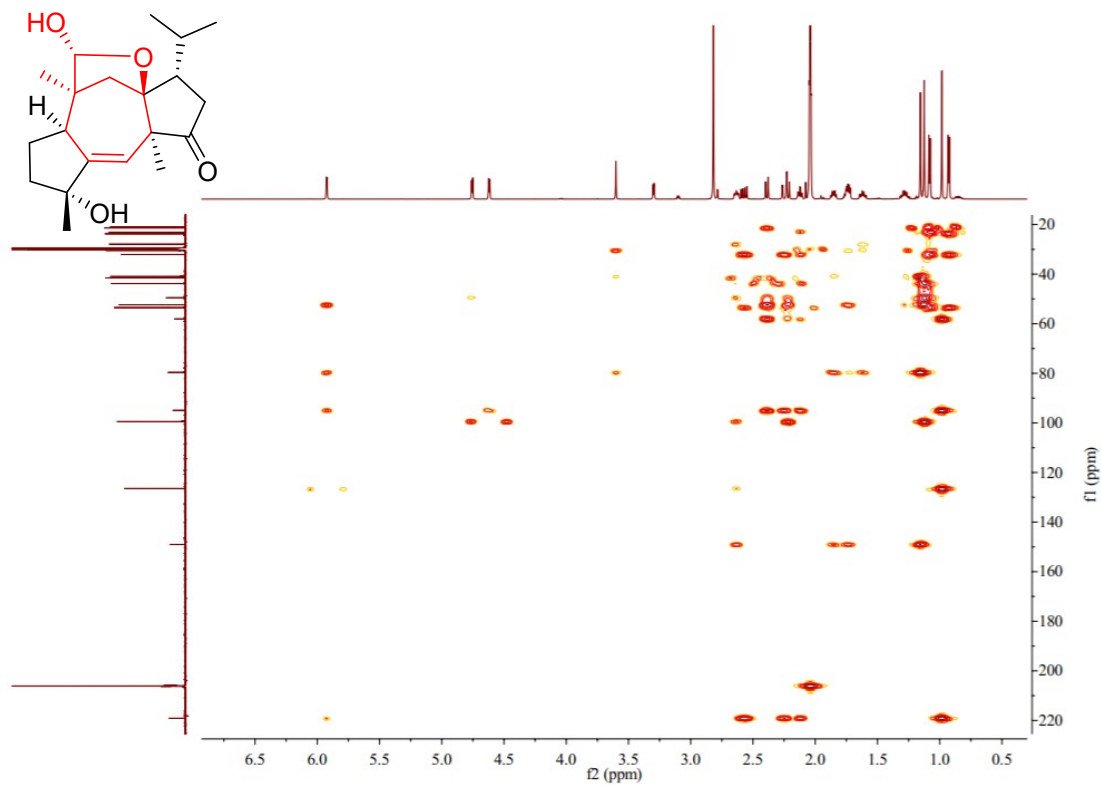


Figure S36. HMBC spectrum of hypoestin C (3).

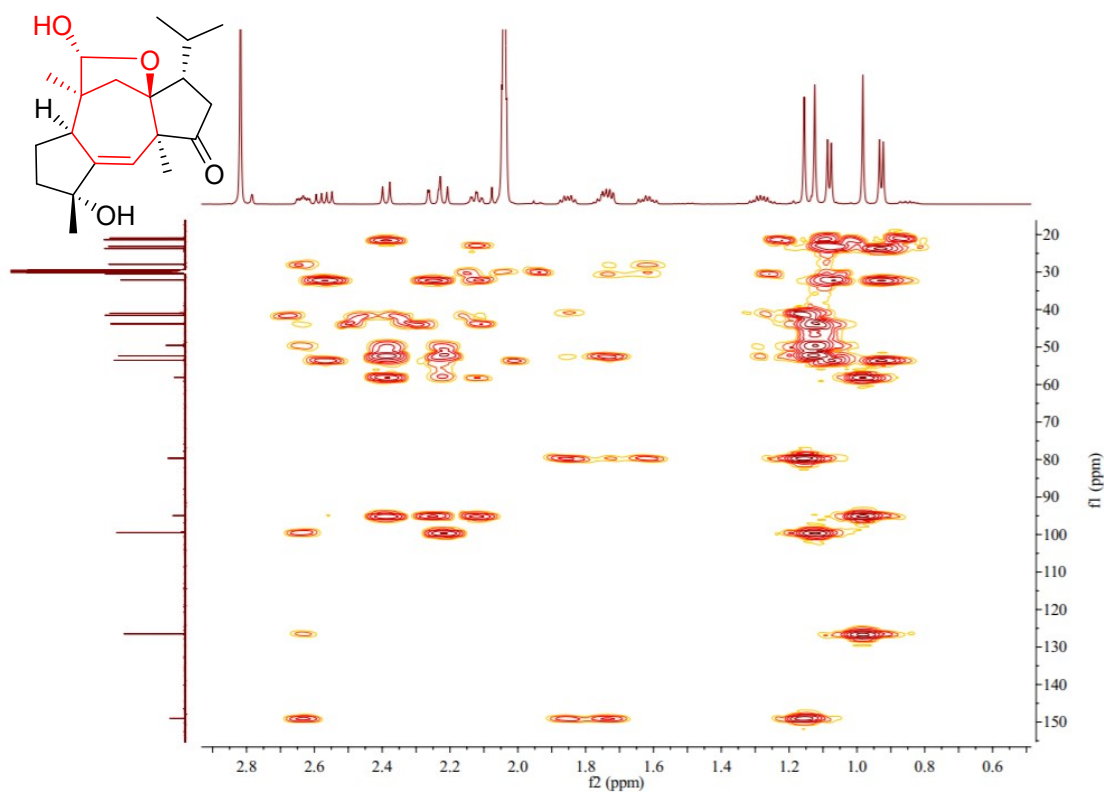


Figure S37. Expanded HMBC spectrum of hypoestin C (**3**).

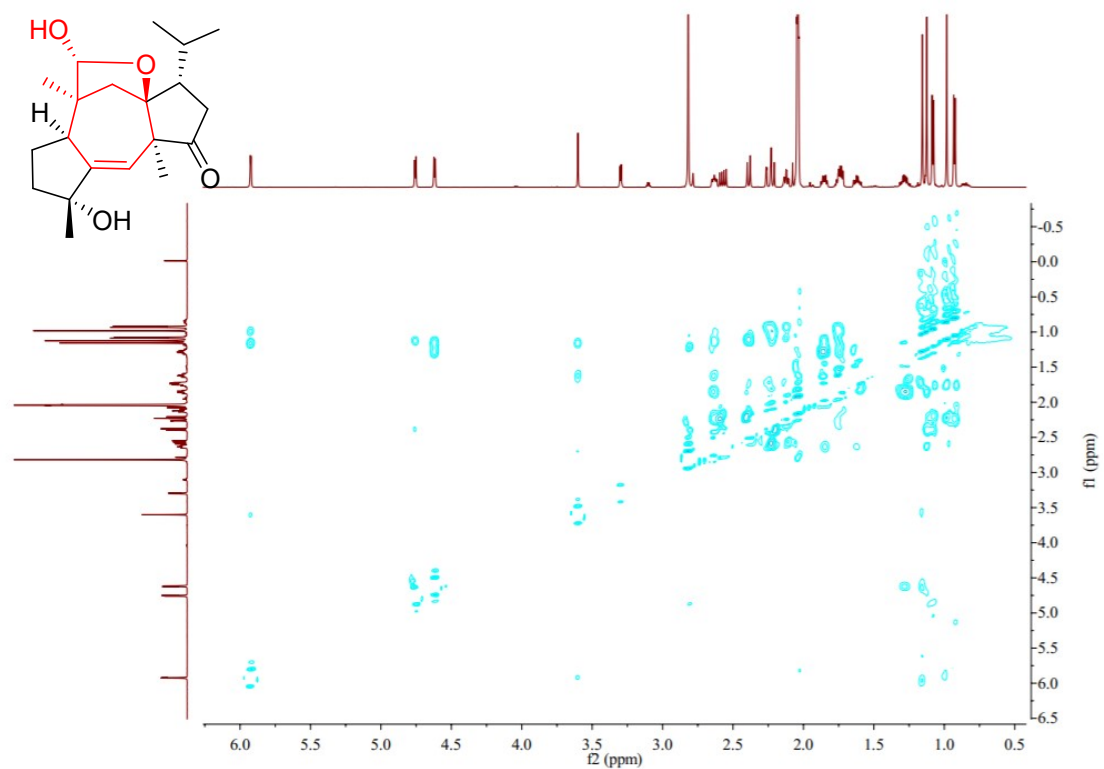


Figure S38. ROESY spectrum of hypoestin C (**3**).

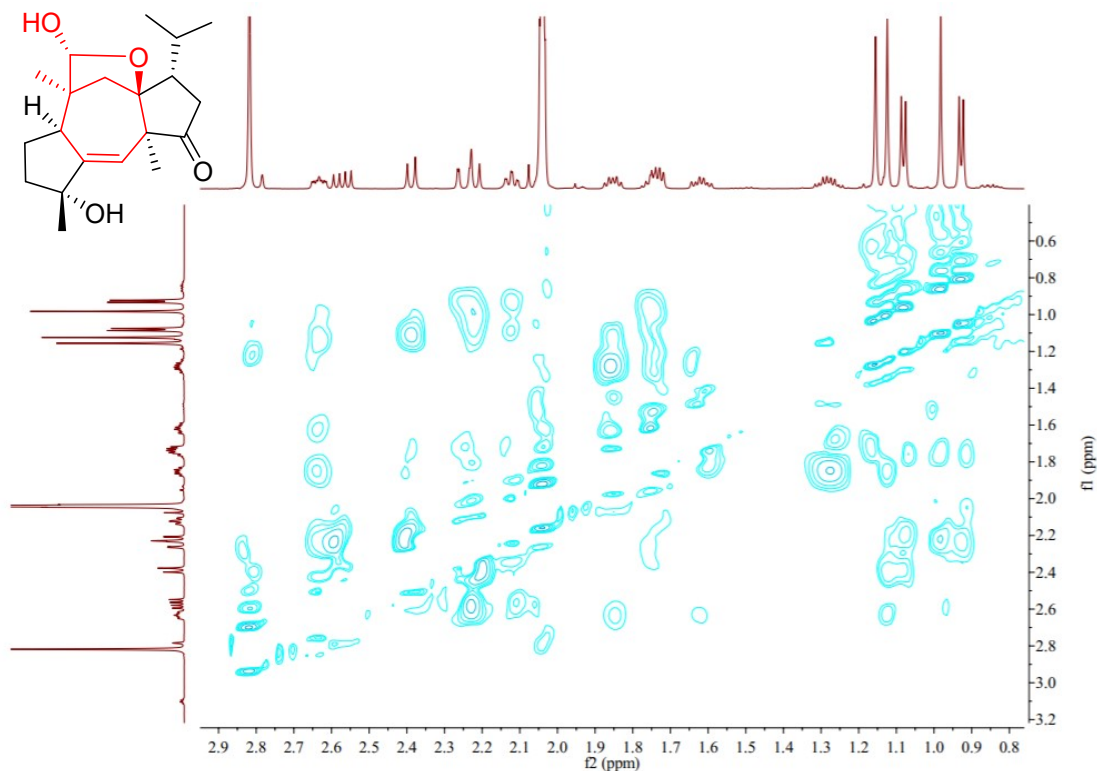
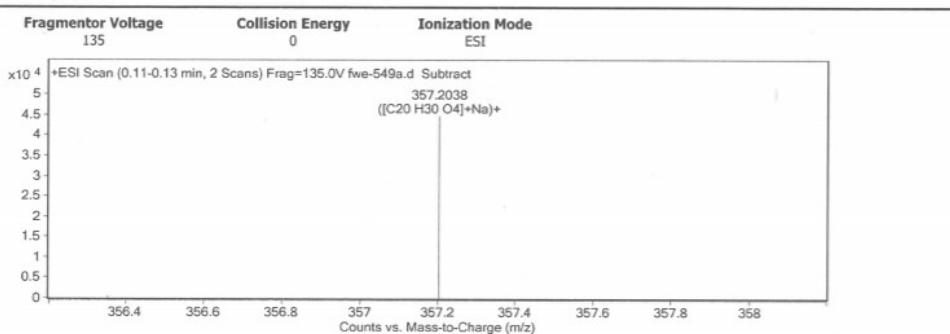


Figure S39. Expanded ROESY spectrum of hypoestin C (3).

User Spectra



Peak List

m/z	z	Abund	Formula	Ion
271.2057	1	63990.41		
272.2096	1	12761.14		
299.2007	1	73951.92		
300.2038	1	15003.91		
317.2117	1	140210.34		
318.2151	1	28337.52		
357.2038	1	44674.82	C ₂₀ H ₃₀ O ₄	(M+Na) ⁺
373.1786	1	12506.43		
455.1791	1	9210.98		
691.4183	1	9094.21		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C ₂₀ H ₃₀ O ₄	334.2144	357.2036	357.2038	0.0	0.1	6.0000

Figure S40. HRESIMS spectrum of hypoestin C (3).

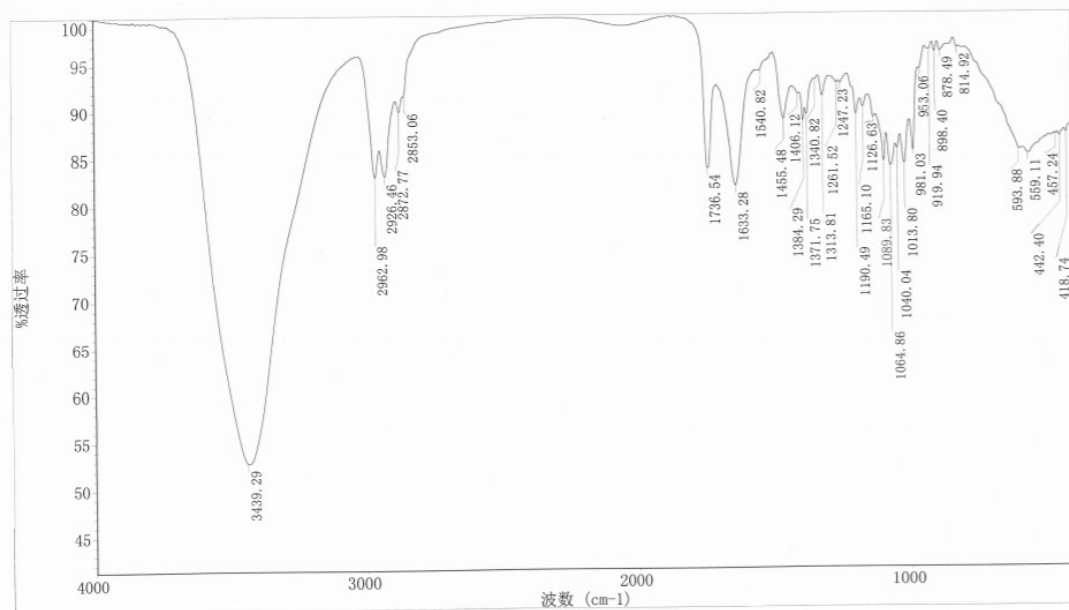


Figure S41. IR spectrum of hypoestin C (3).

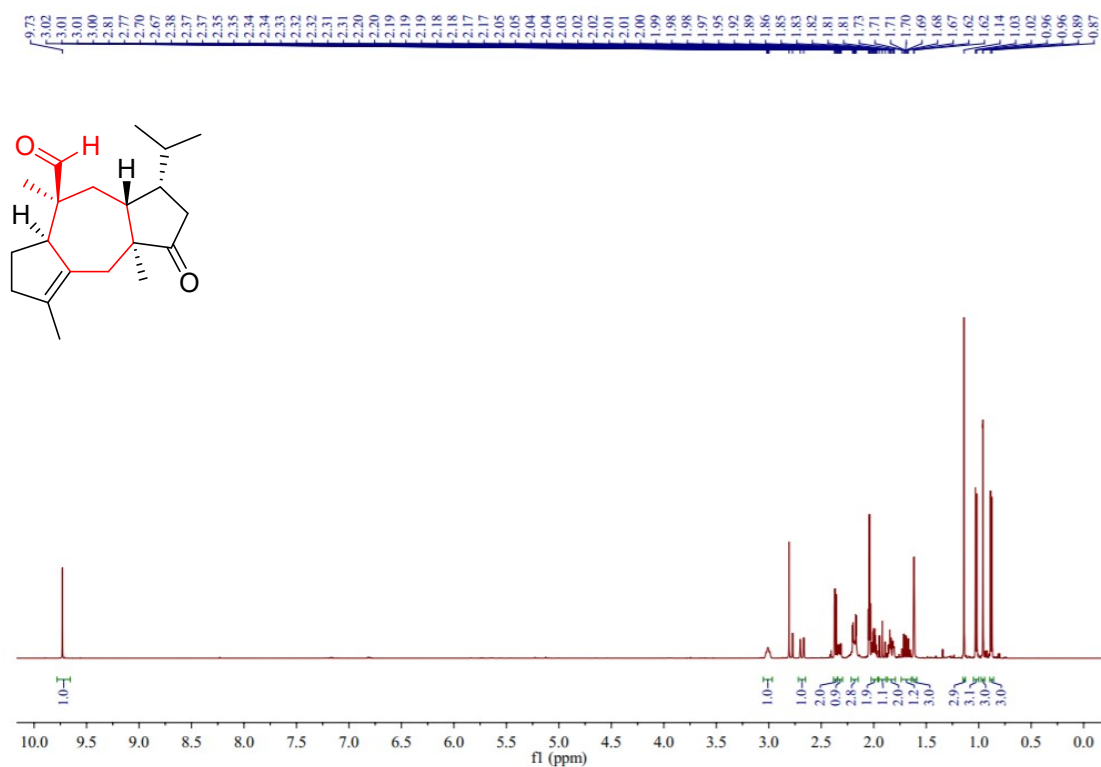


Figure S42. ¹H NMR (500 MHz) spectrum of hypoestin D (4) in acetone-*d*₆.

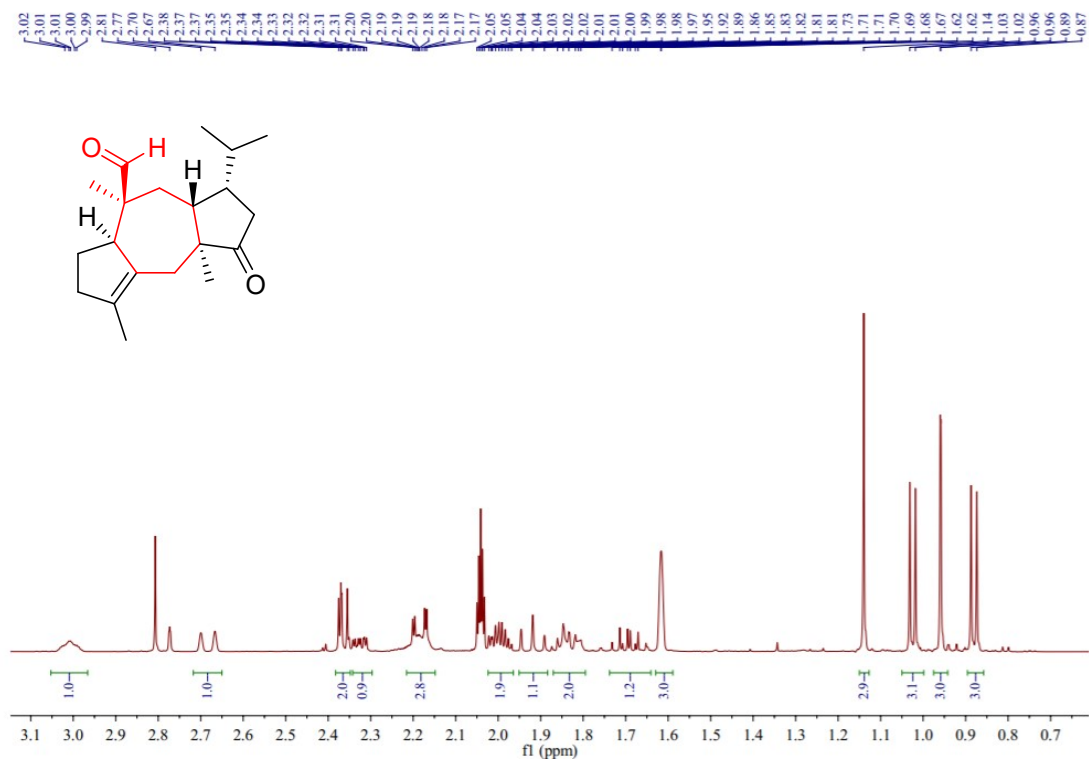


Figure S43. Expanded ¹H NMR spectrum of hypoestin D (4).

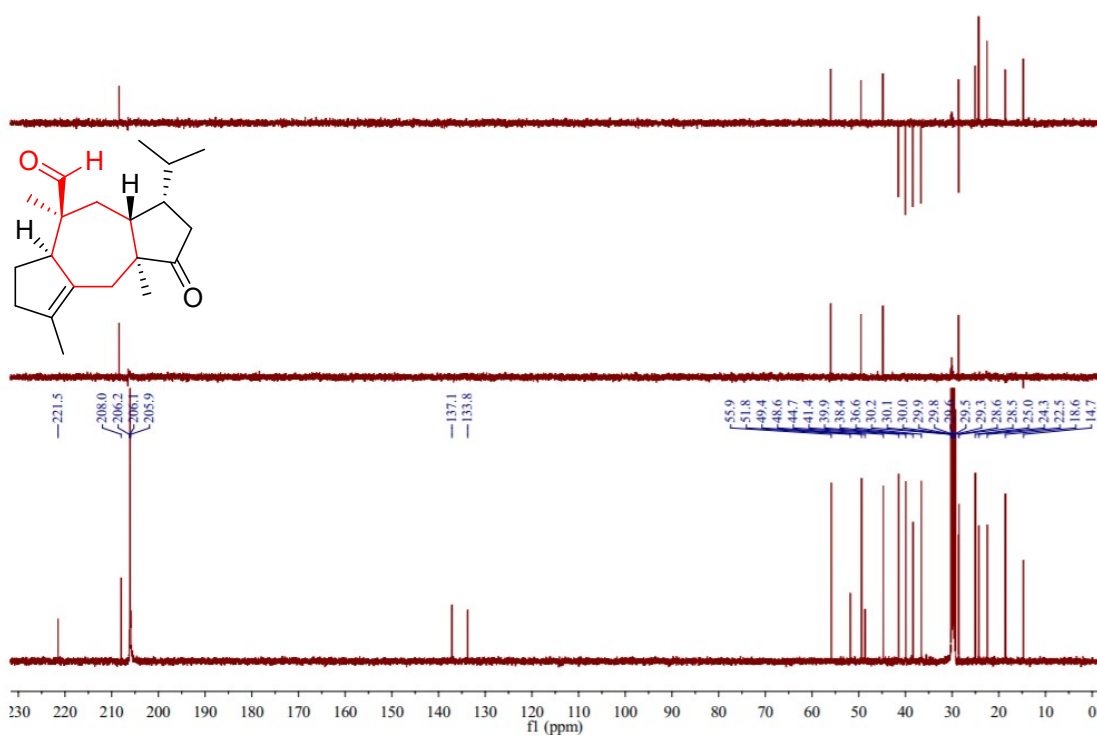


Figure S44. ¹³C NMR and DEPT (125 MHz) spectra of hypoestin D (4) in acetone-*d*₆.

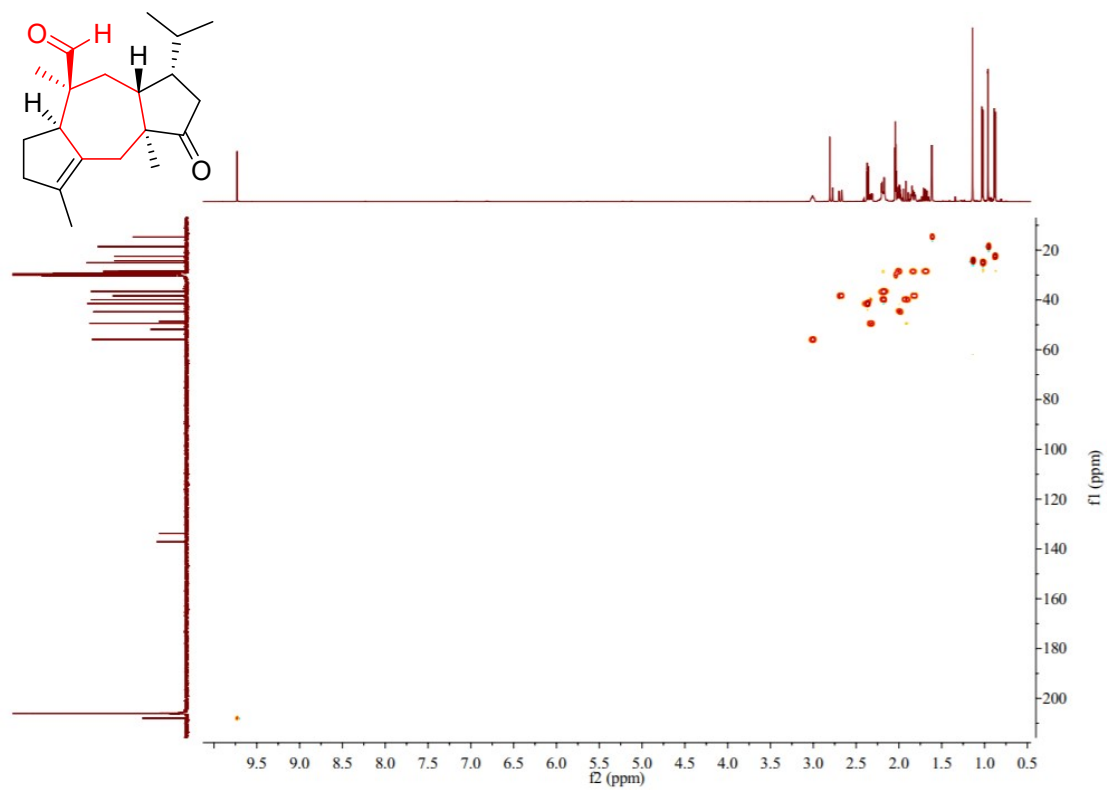


Figure S45. HSQC spectrum of hypoestin D (4).

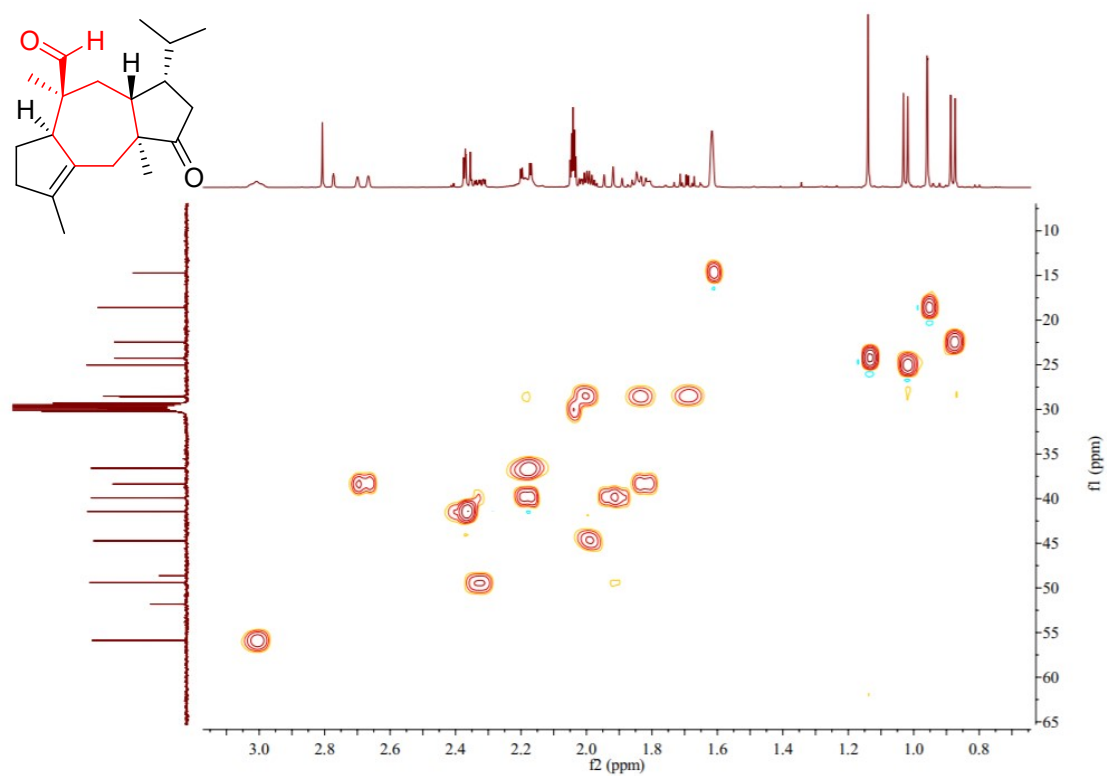


Figure S46. Expanded HSQC spectrum of hypoestin D (4).

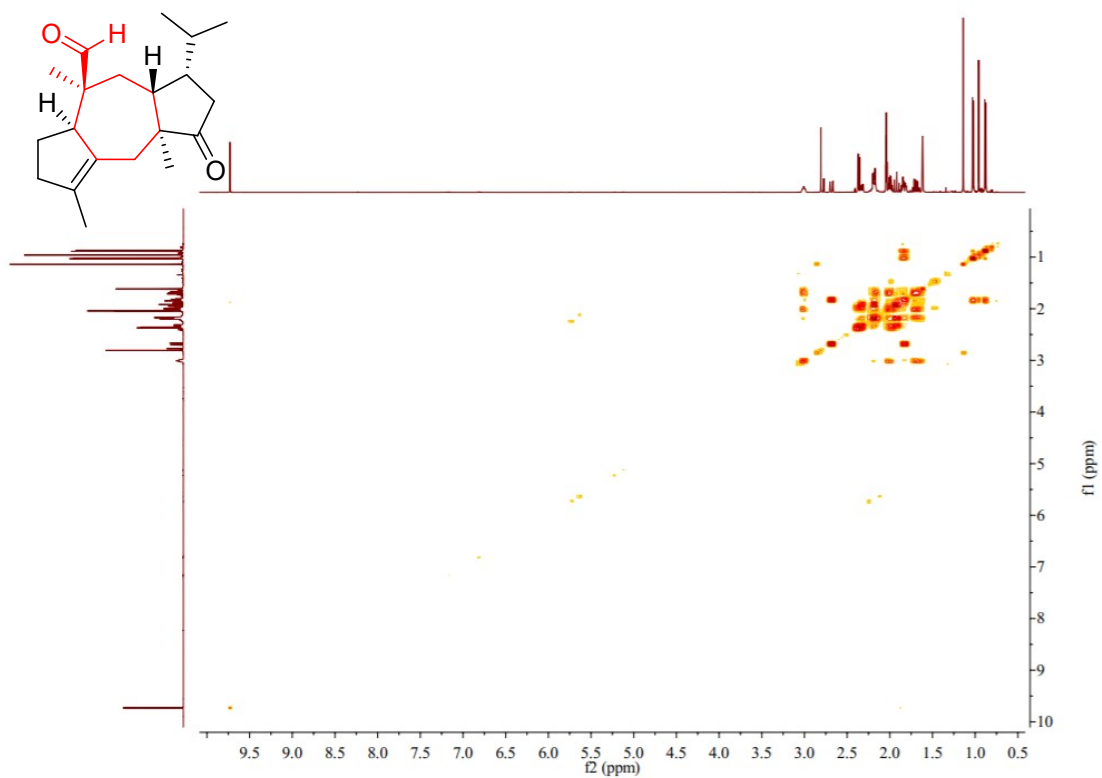


Figure S47. ^1H - ^1H COSY spectrum of hypoestin D (**4**).

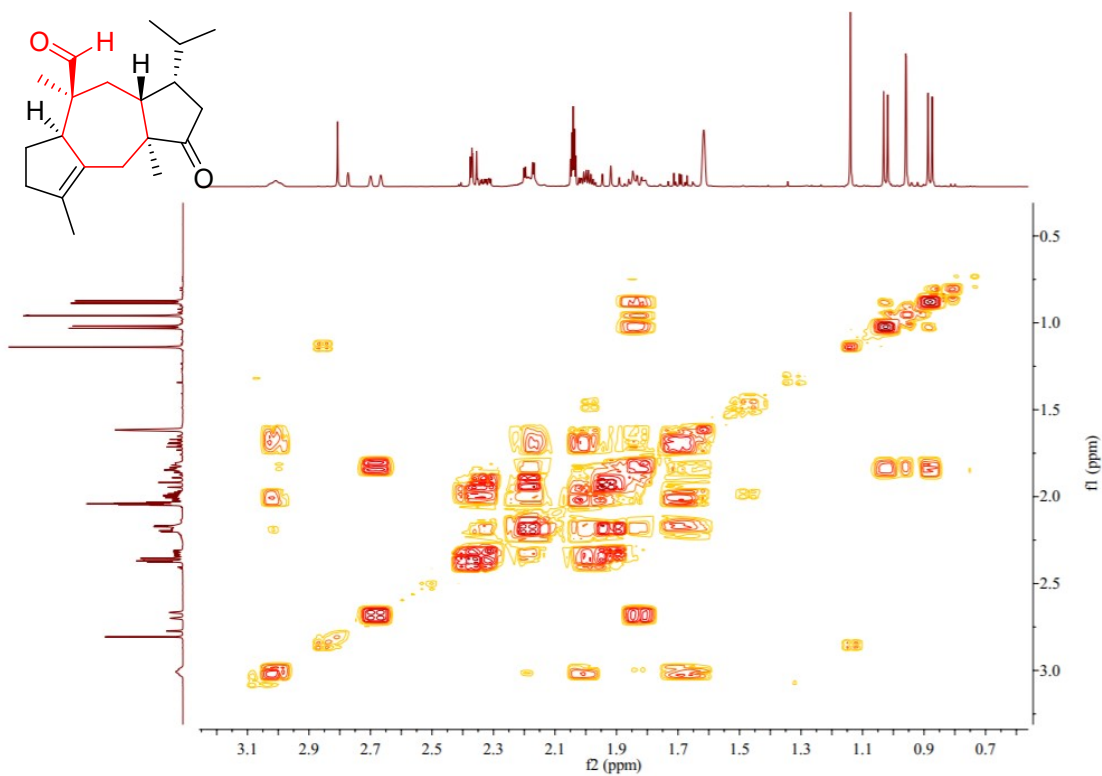


Figure S48. Expanded ^1H - ^1H COSY spectrum of hypoestin D (**4**).

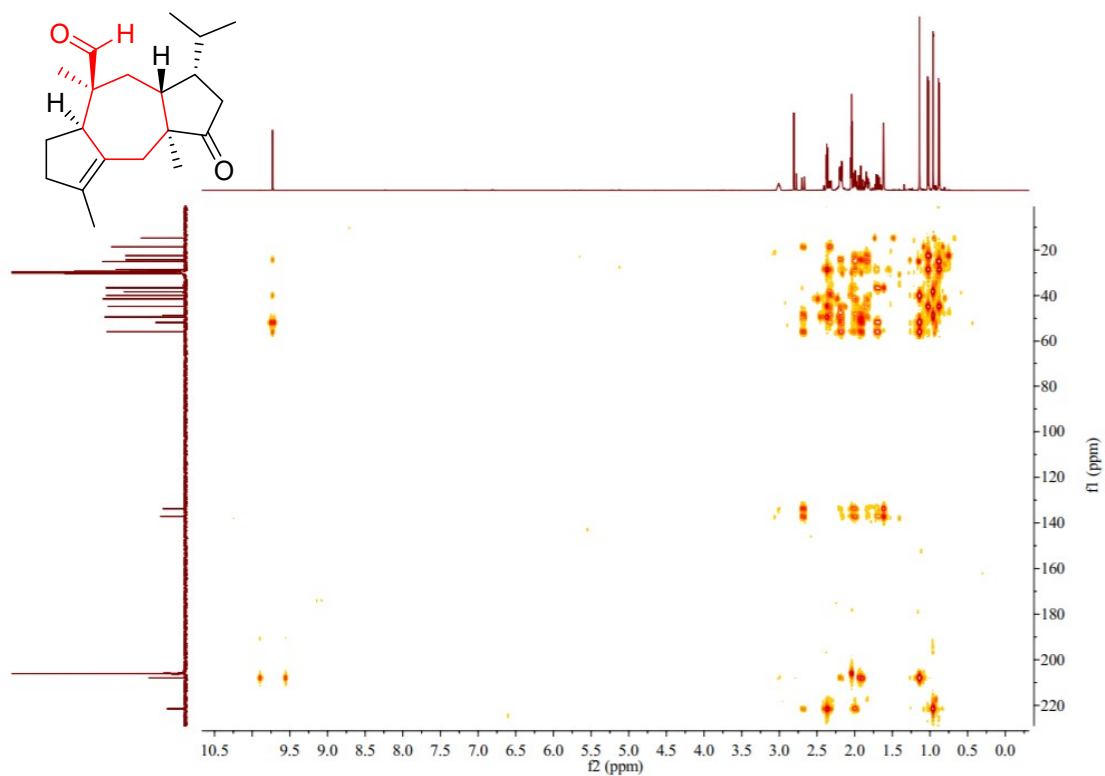


Figure S49. HMBC spectrum of hypoestin D (4).

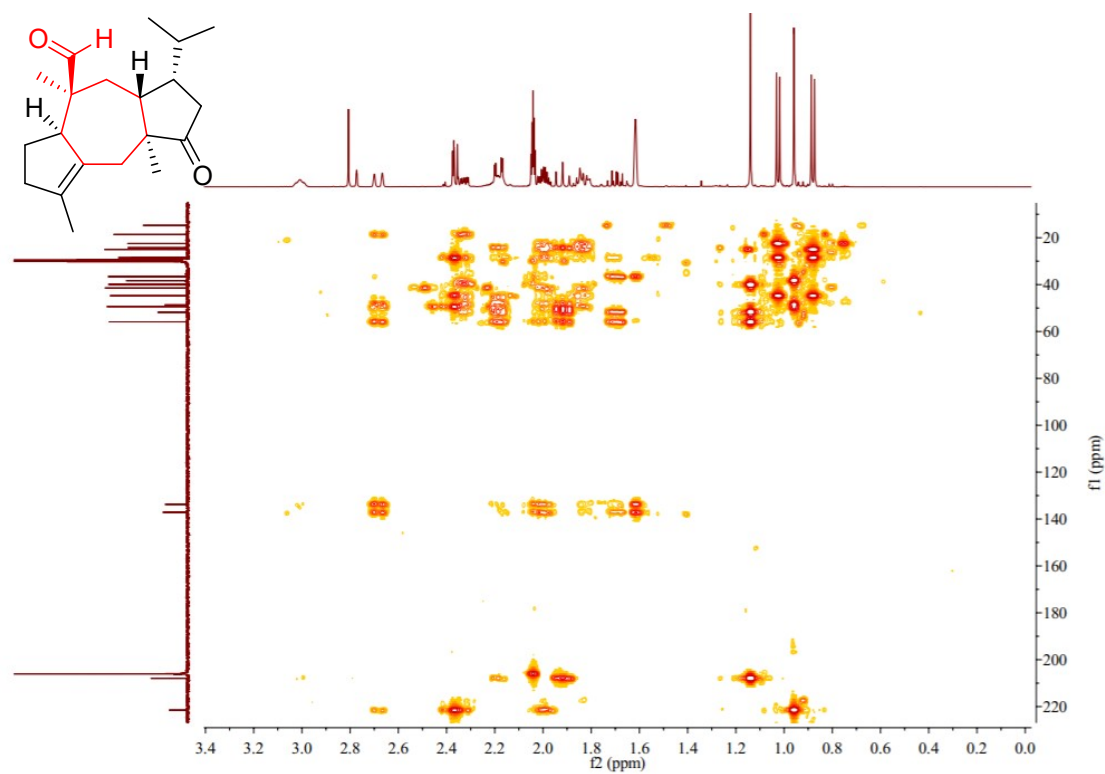


Figure S50. Expanded HMBC spectrum of hypoestin D (4).

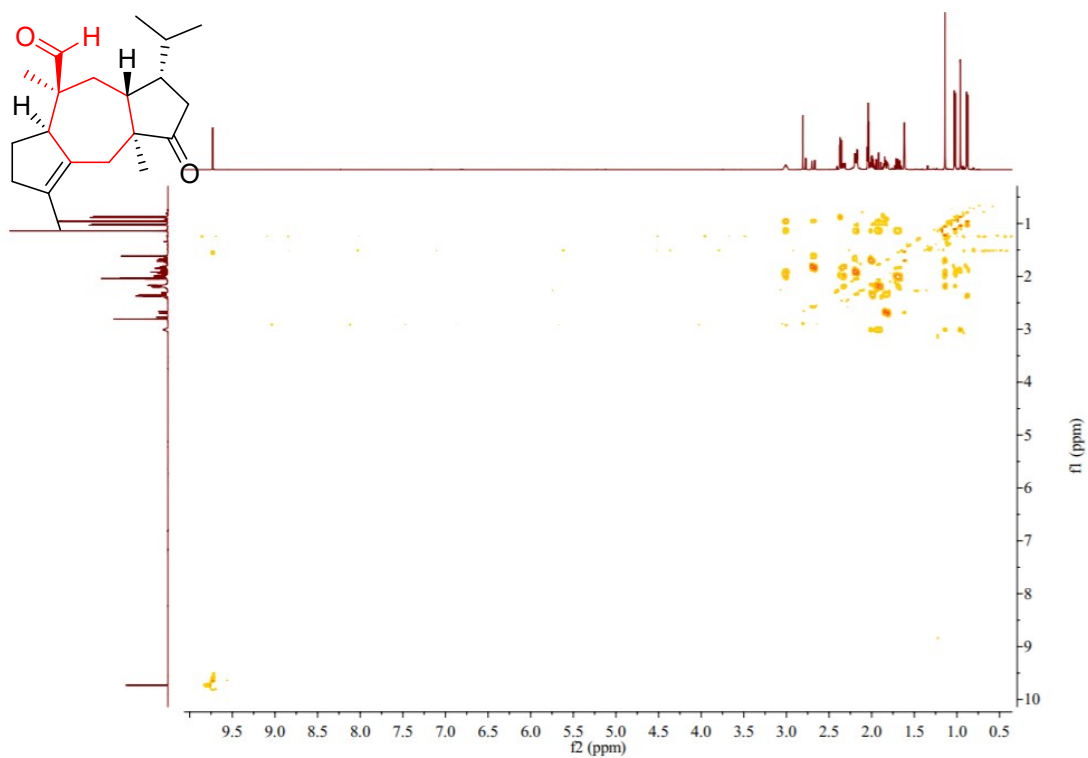


Figure S51. ROESY spectrum of hypoestin D (**4**).

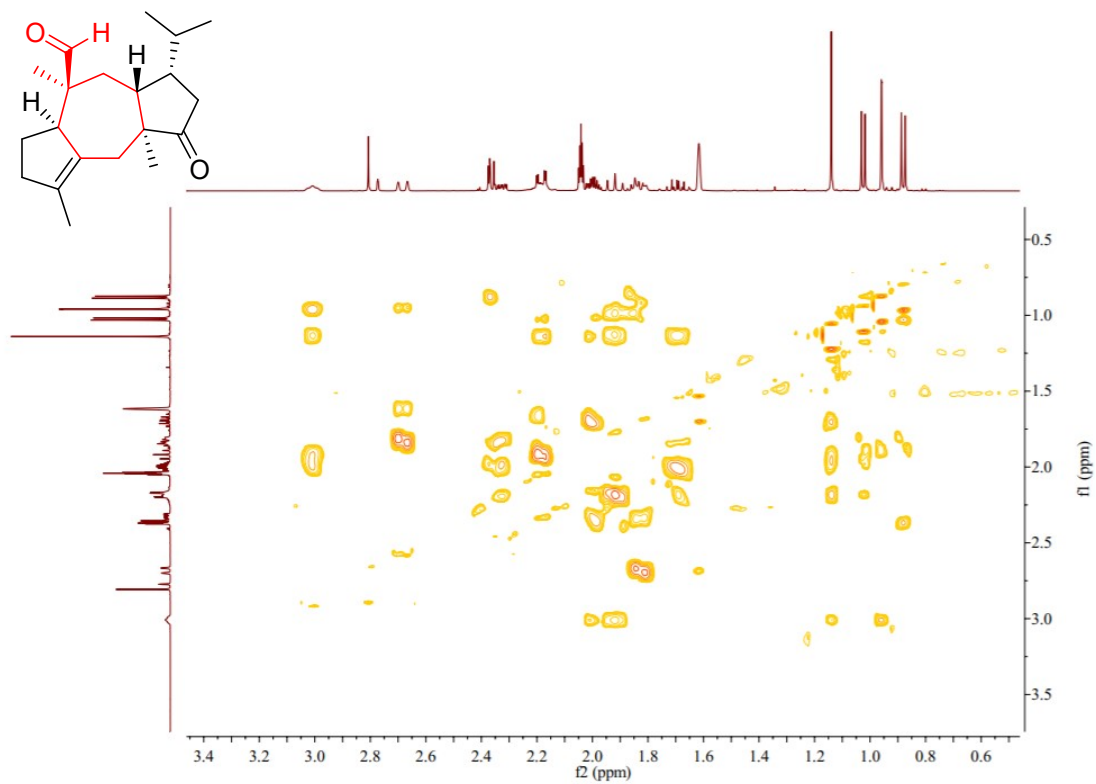


Figure S52. Expanded ROESY spectrum of hypoestin D (**4**).

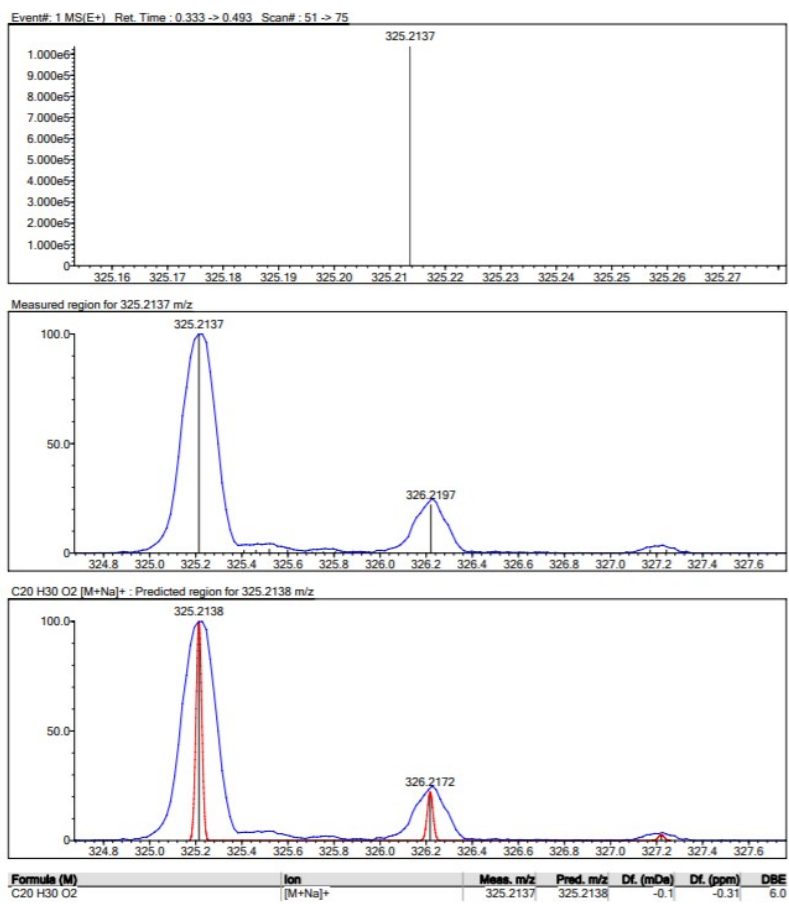


Figure S53. HRESIMS spectrum of hypoestin D (4).

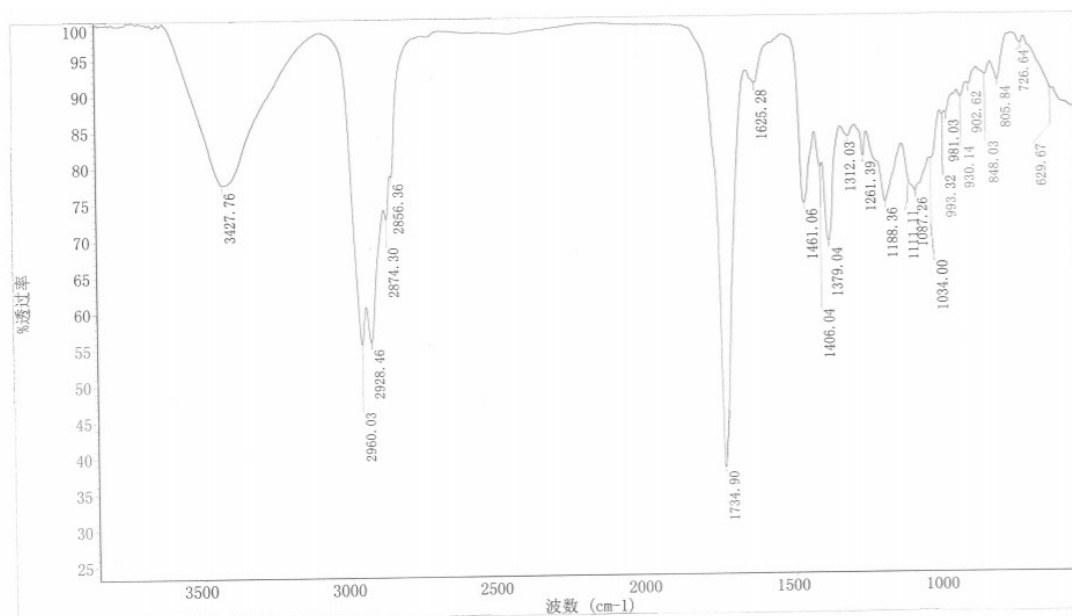


Figure S54. IR spectrum of hypoestin D (4).

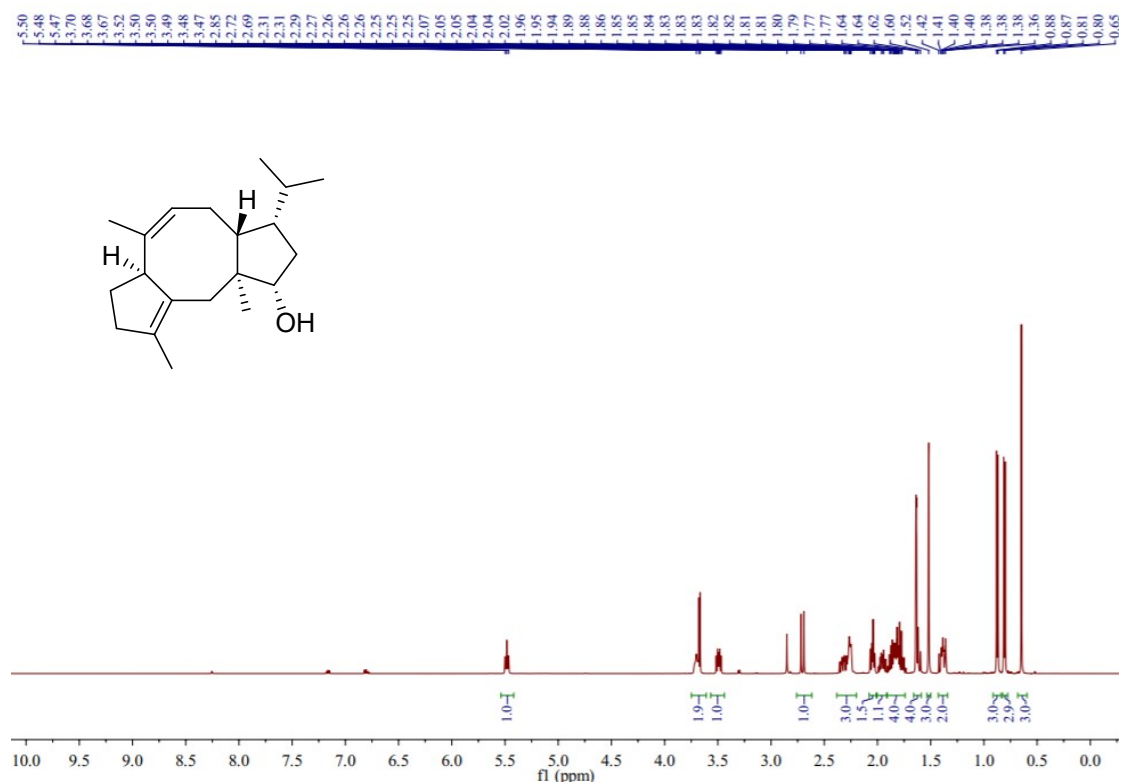


Figure S55. ^1H NMR (500 MHz) spectrum of hypoestin E (**5**) in acetone- d_6 .

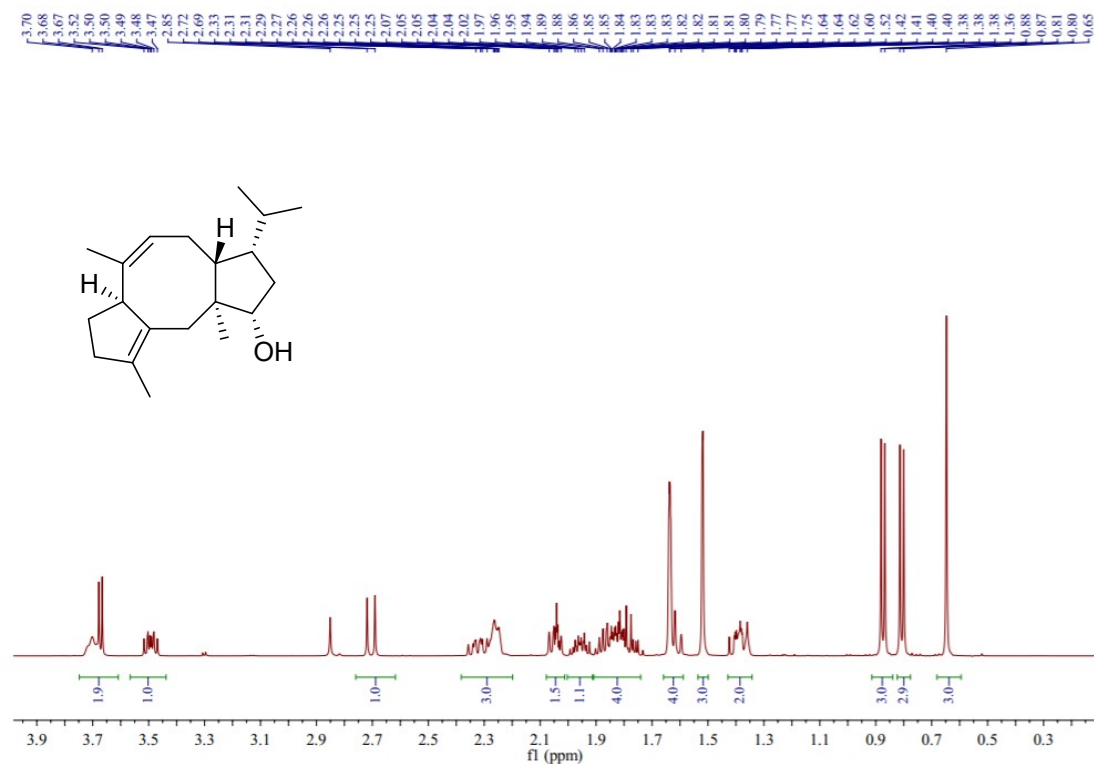


Figure S56. Expanded ^1H NMR spectrum of hypoestin E (**5**).

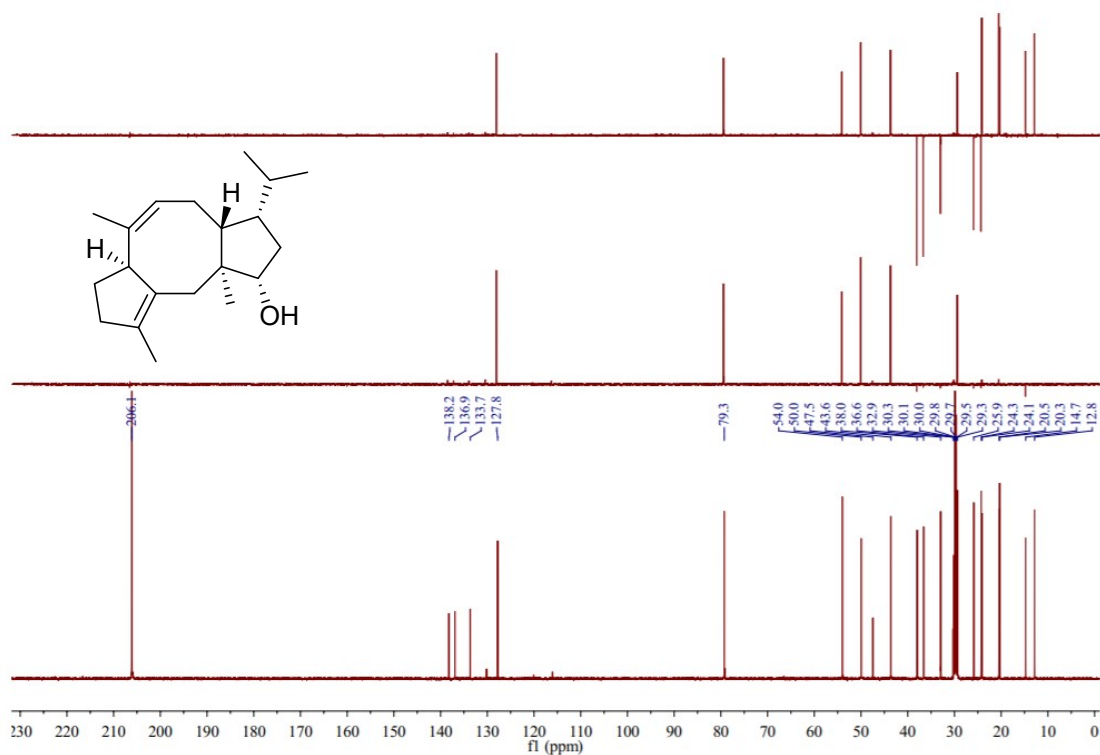


Figure S57. ^{13}C NMR and DEPT (125 MHz) spectra of hypoestin E (**5**) in acetone- d_6 .

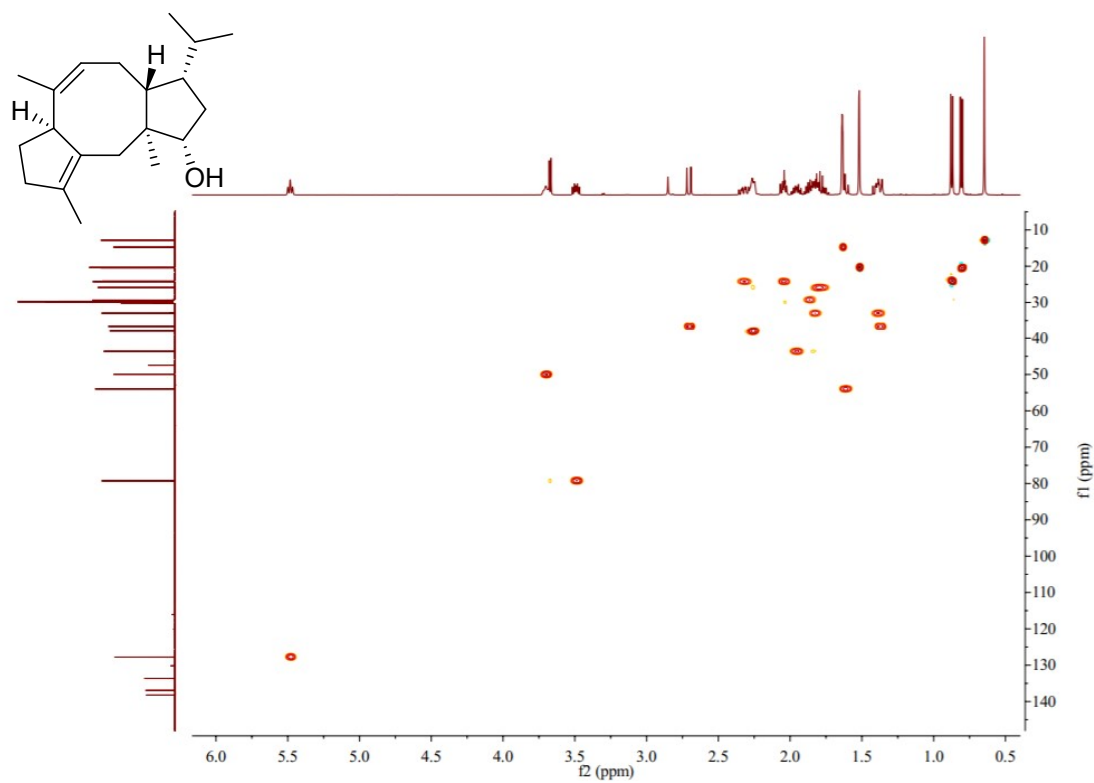


Figure S58. HSQC spectrum of hypoestin E (**5**).

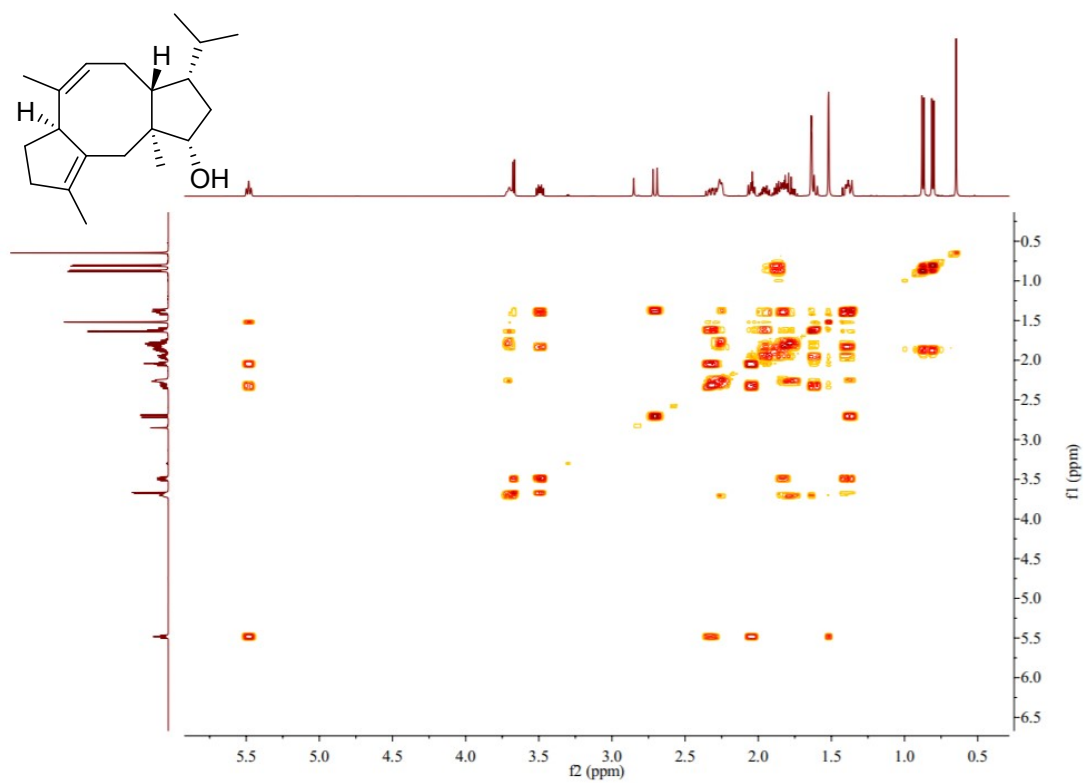


Figure S59. ^1H - ^1H COSY spectrum of hypoestin E (**5**).

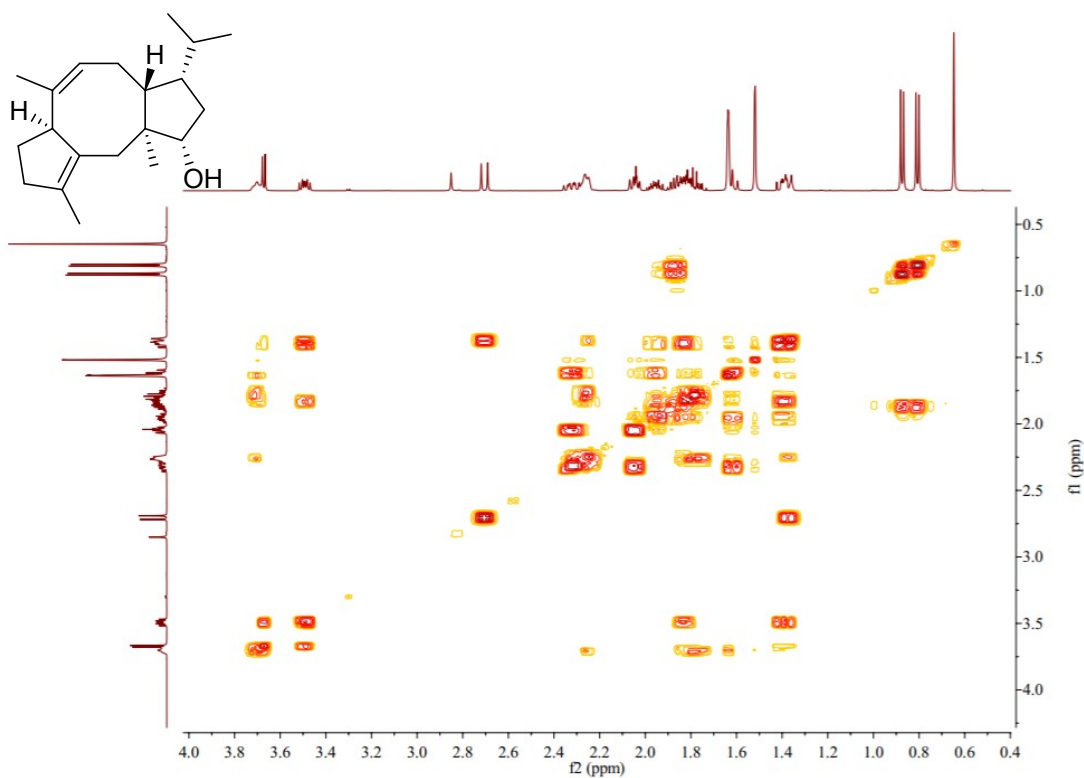


Figure S60. Expanded ^1H - ^1H COSY spectrum of hypoestin E (**5**).

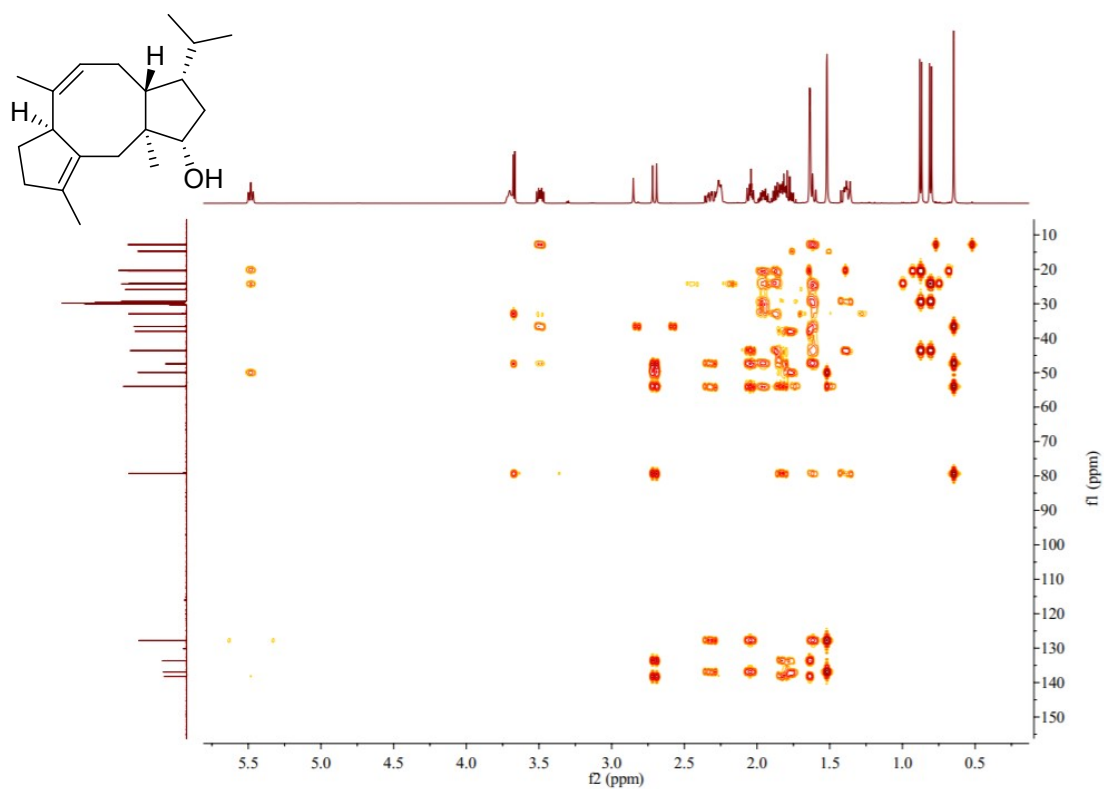


Figure S61. HMBC spectrum of hypoestin E (**5**).

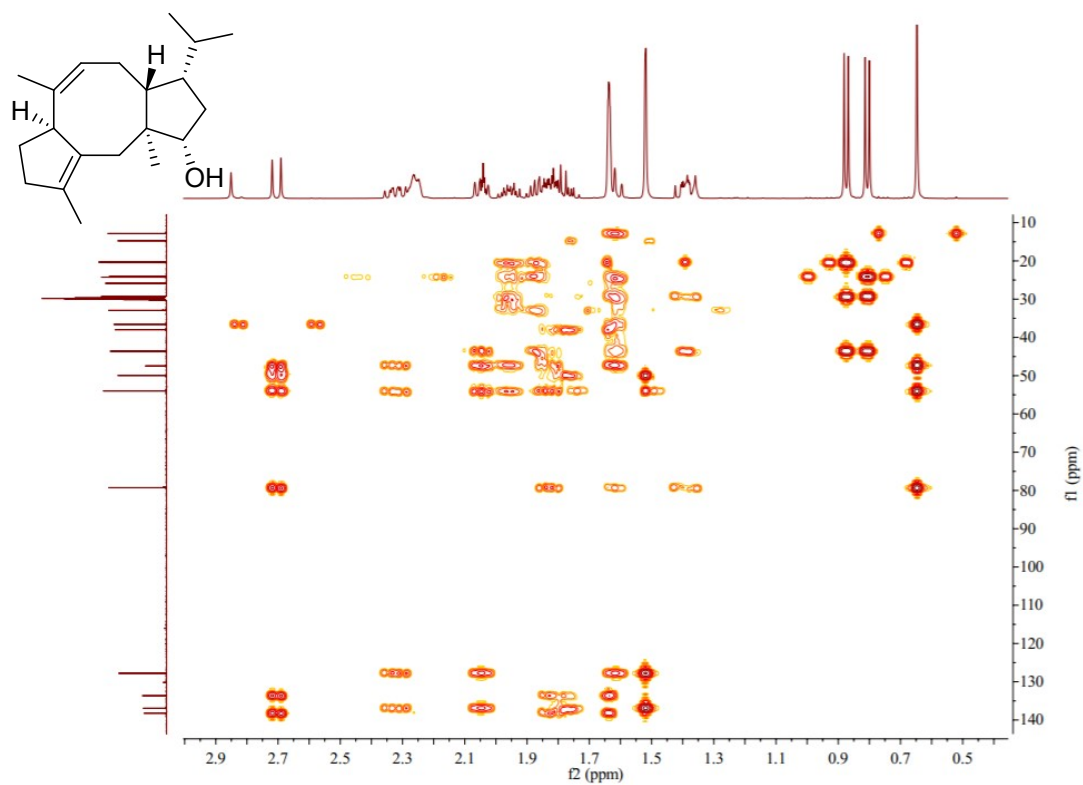


Figure S62. Expanded HMBC spectrum of hypoestin E (**5**).

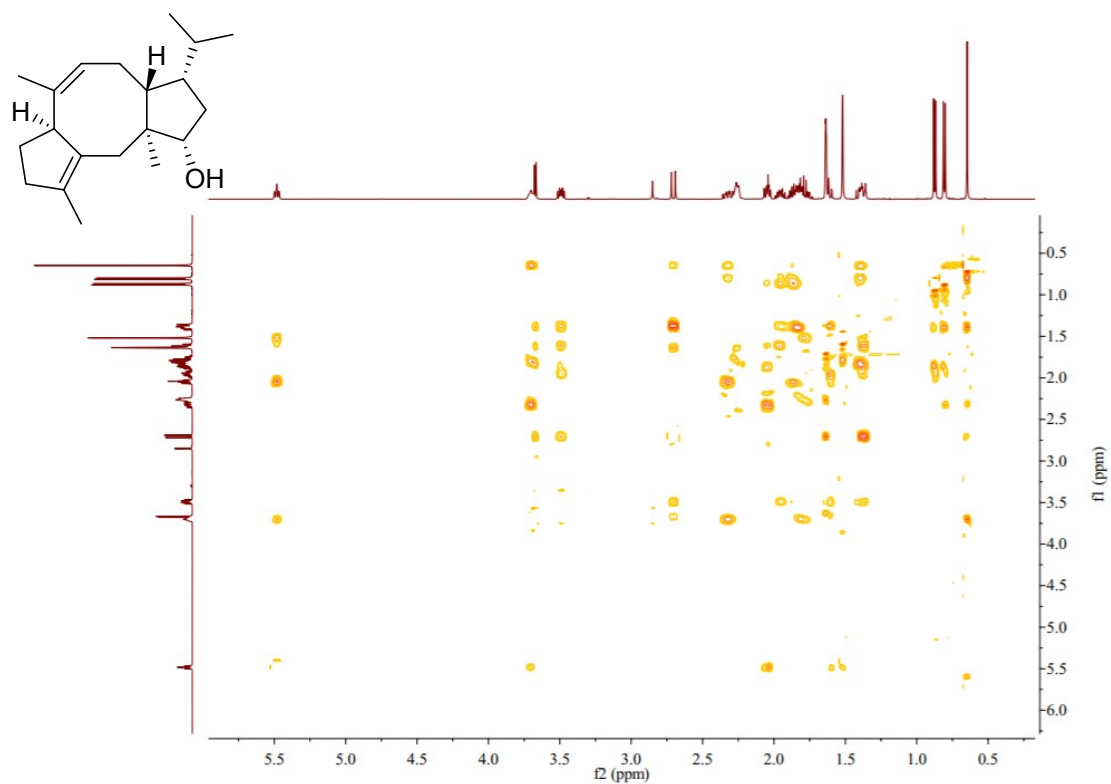


Figure S63. ROESY spectrum of hypoestin E (5).

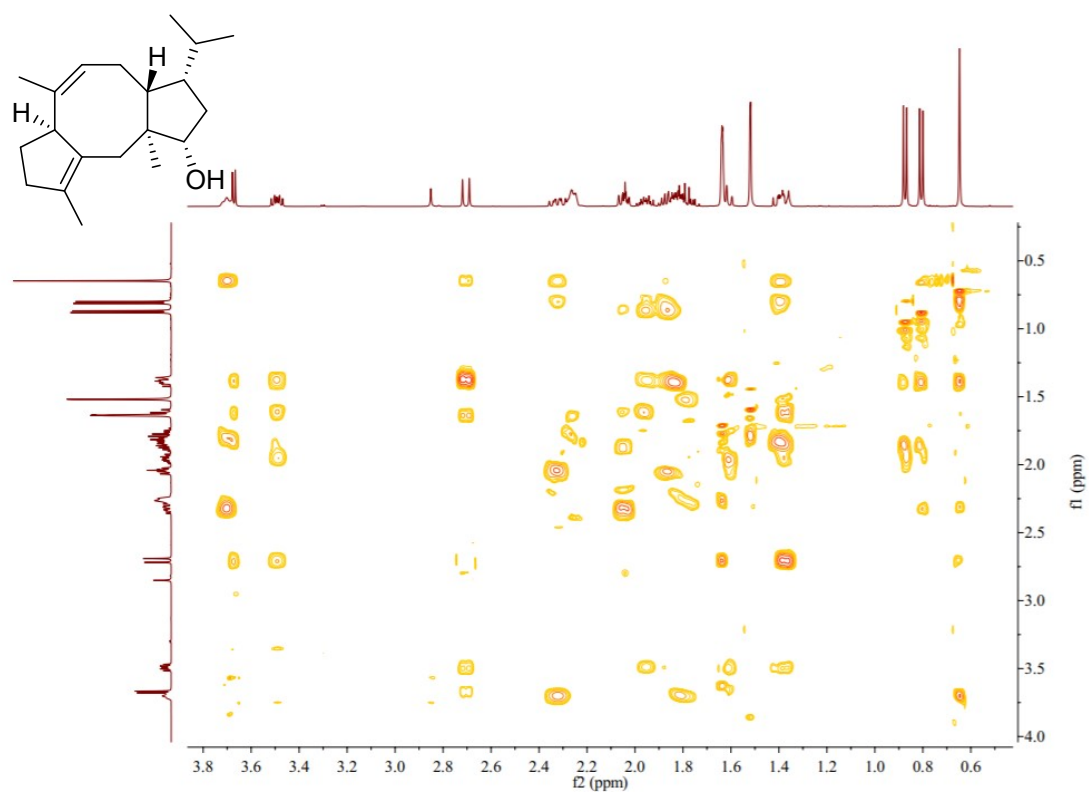


Figure S64. Expanded ROESY spectrum of hypoestin E (5).

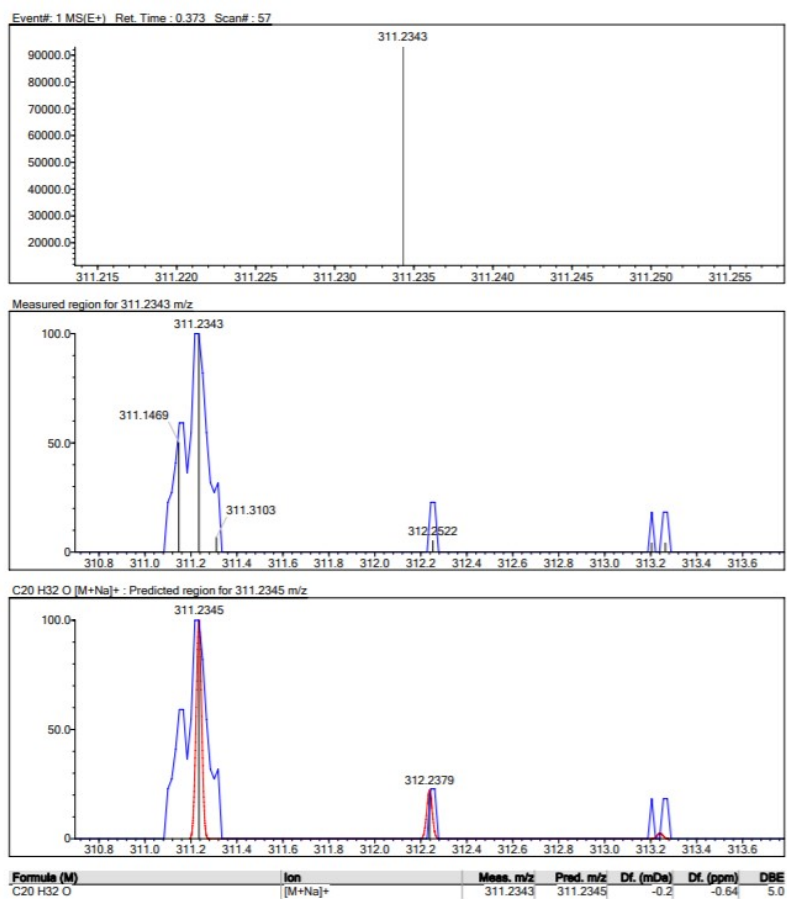


Figure S65. HRESIMS spectrum of hypoestin E (5).

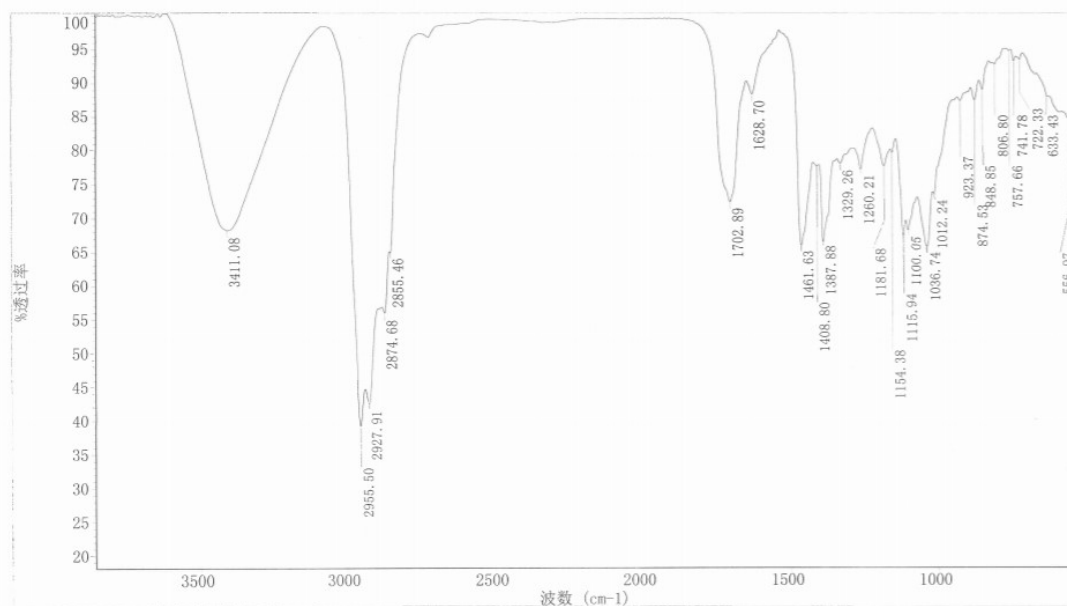


Figure S66. IR spectrum of hypoestin E (5).

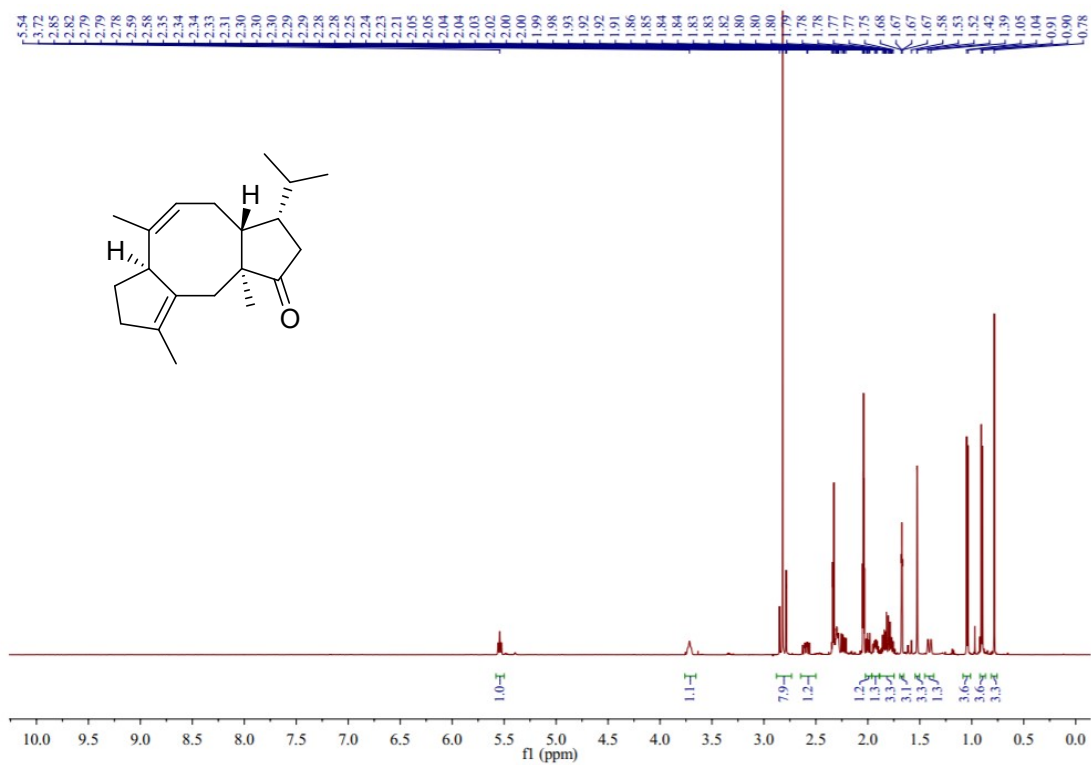


Figure S67. ^1H NMR (500 MHz) spectrum of hypoestin F (**6**) in acetone- d_6 .

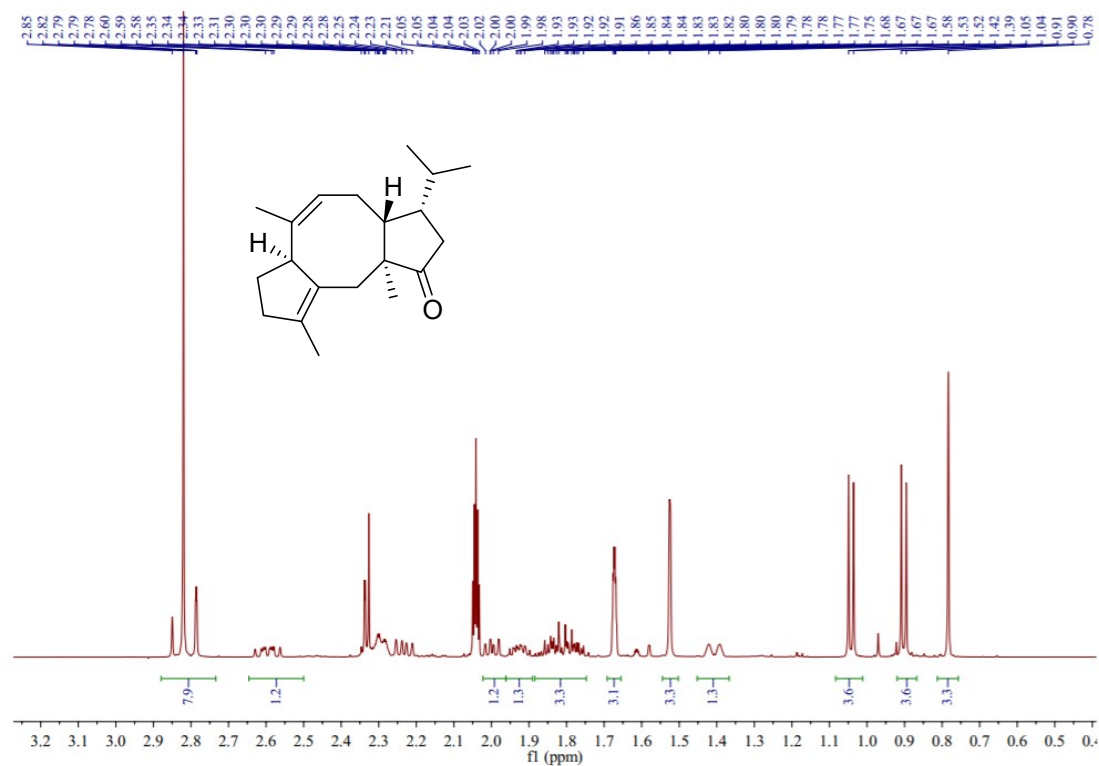


Figure S68. Expanded ^1H NMR spectrum of hypoestin F (**6**).

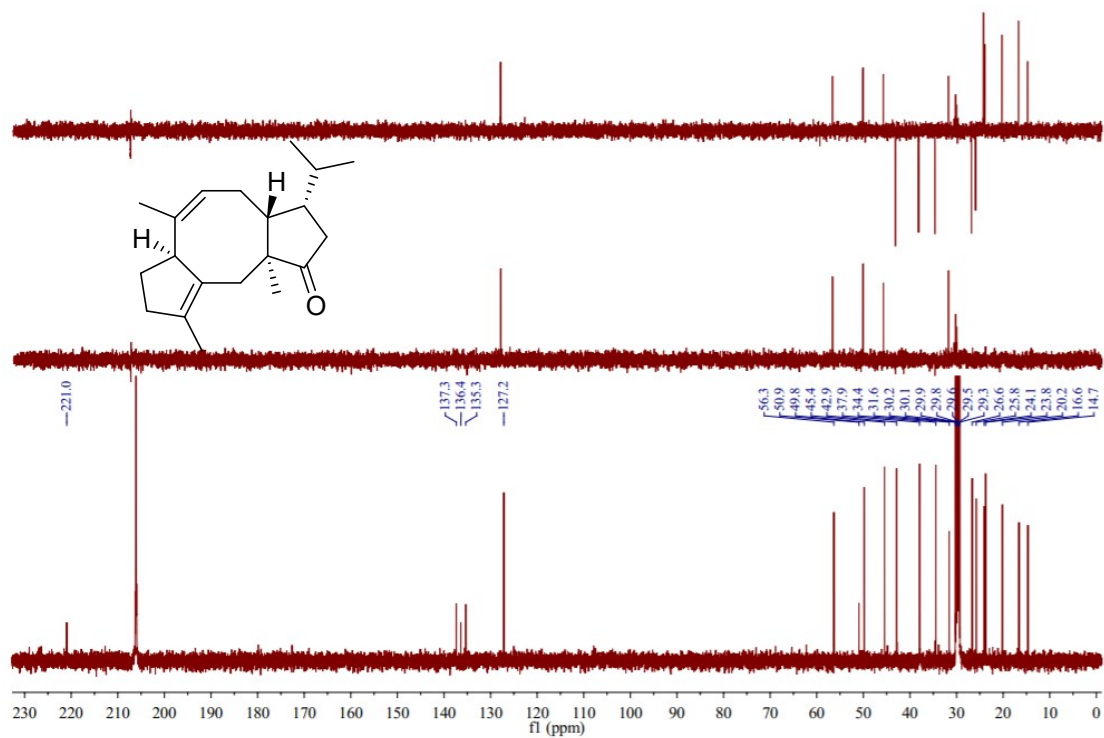


Figure S69. ^{13}C NMR and DEPT (125 MHz) spectra of hypoestin F (6) in acetone- d_6 .

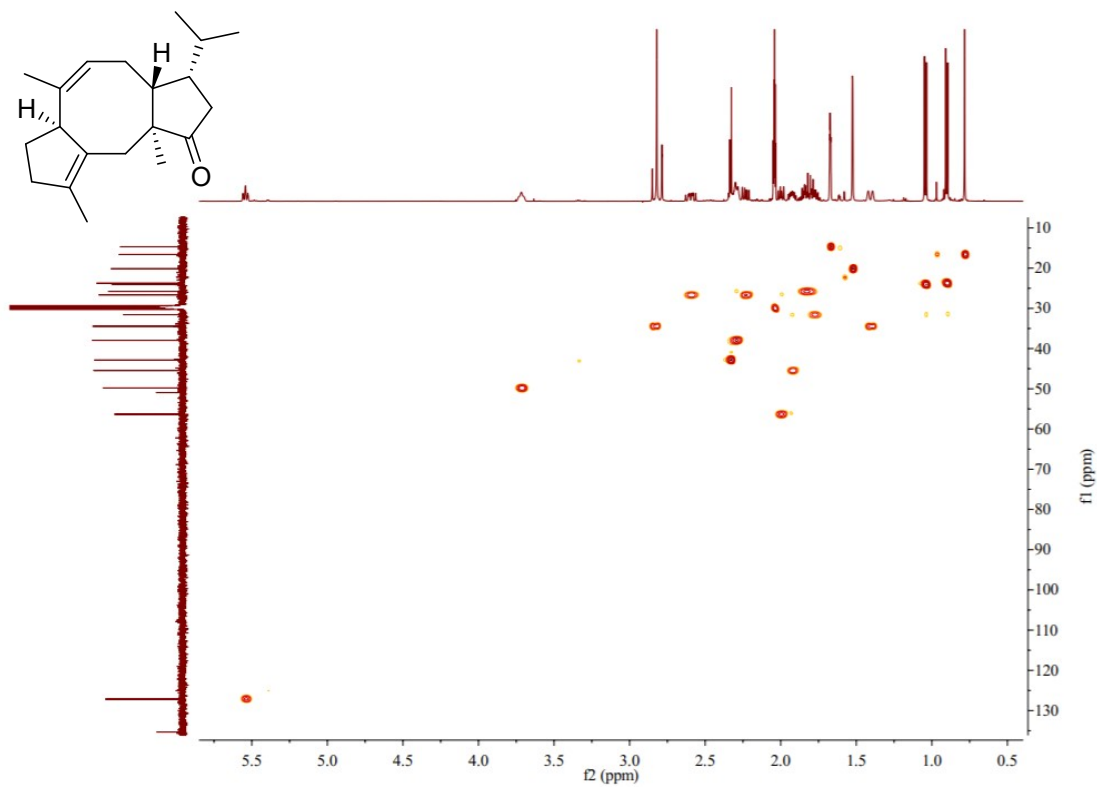


Figure S70. HSQC spectrum of hypoestin F (6).

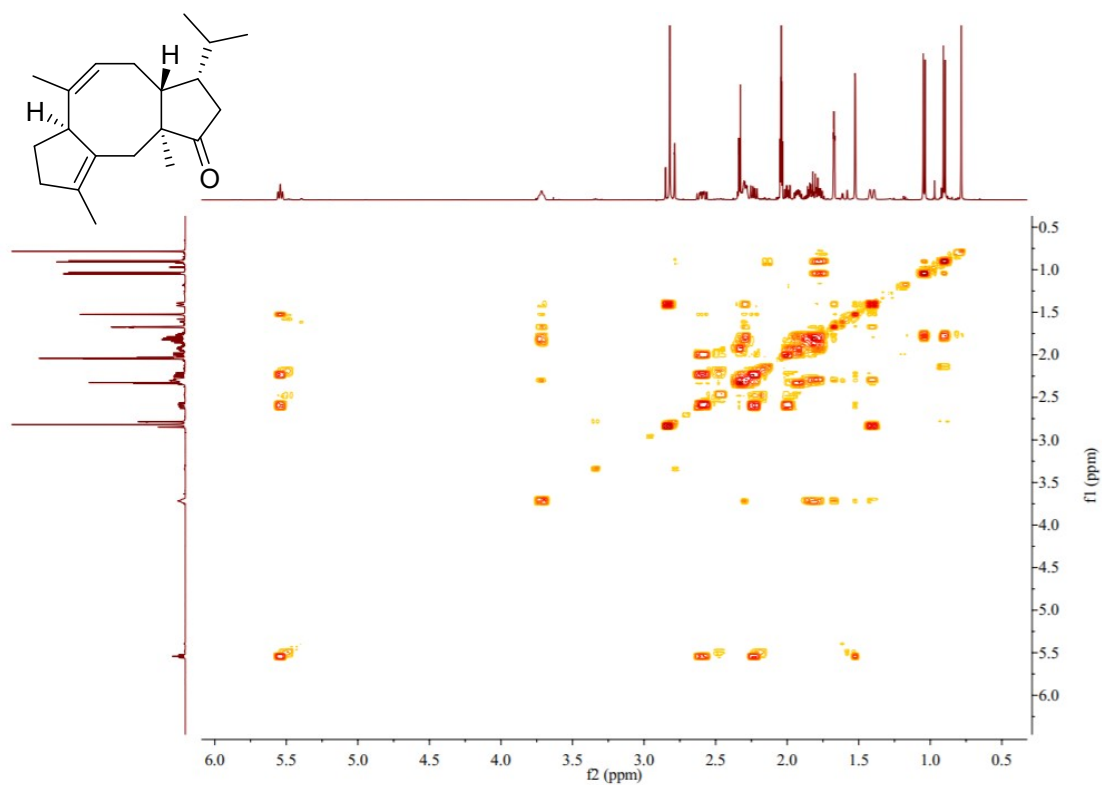


Figure S71. ^1H - ^1H COSY spectrum of hypoestin F (**6**).

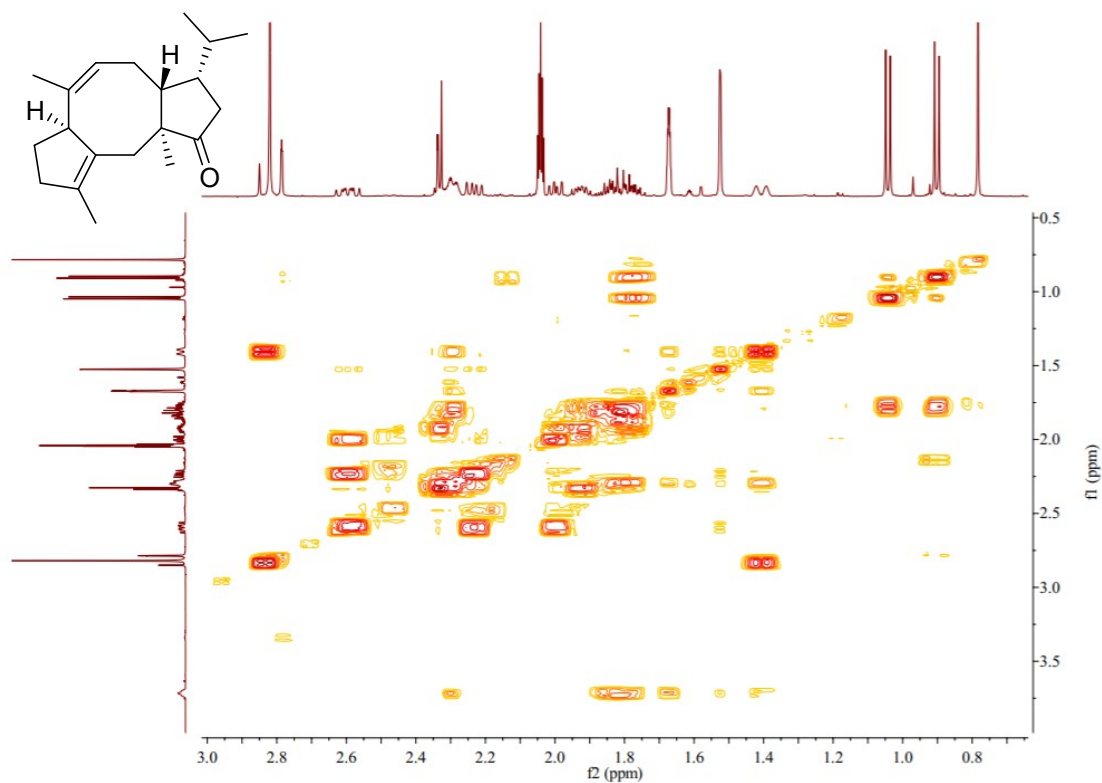


Figure S72. Expanded ^1H - ^1H COSY spectrum of hypoestin F (**6**).

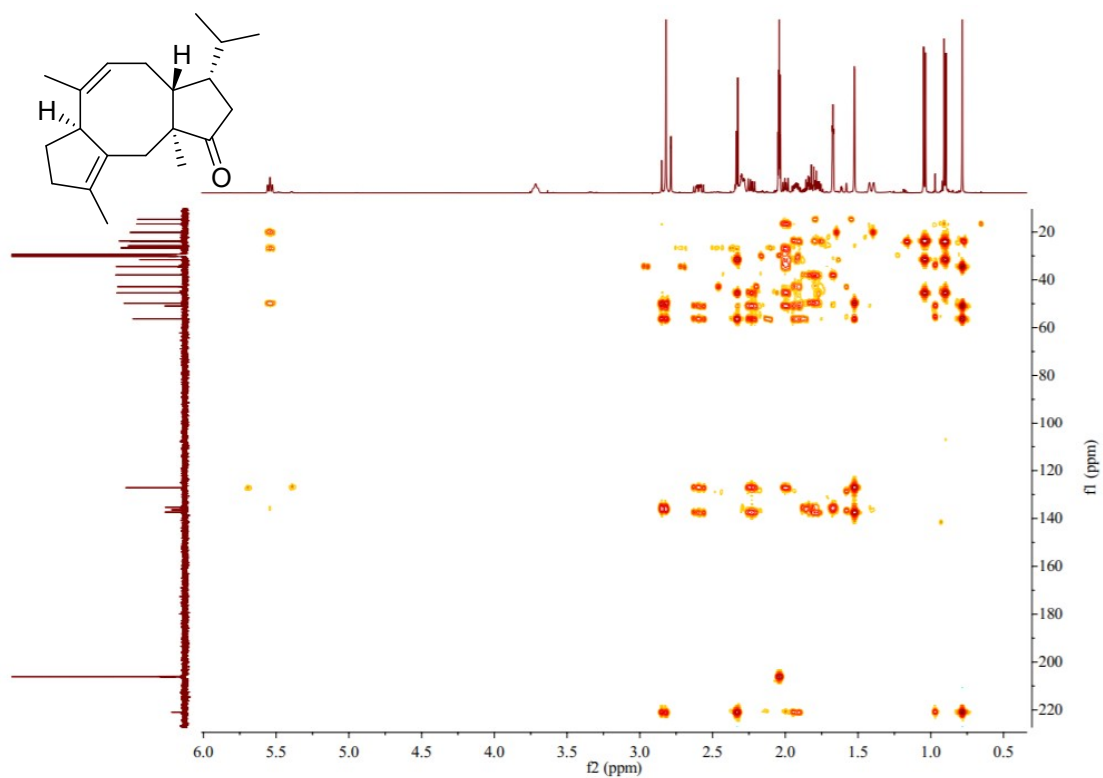


Figure S73. HMBC spectrum of hypoestin F (6).

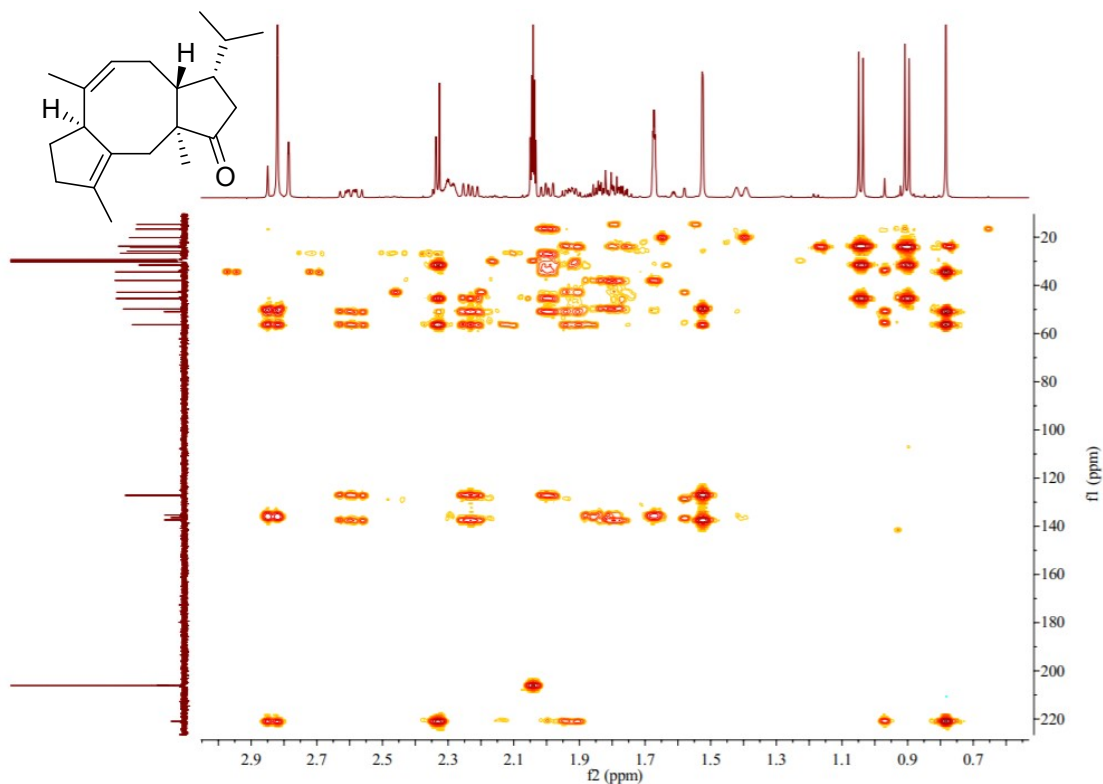


Figure S74. Expanded HMBC spectrum of hypoestin F (6).

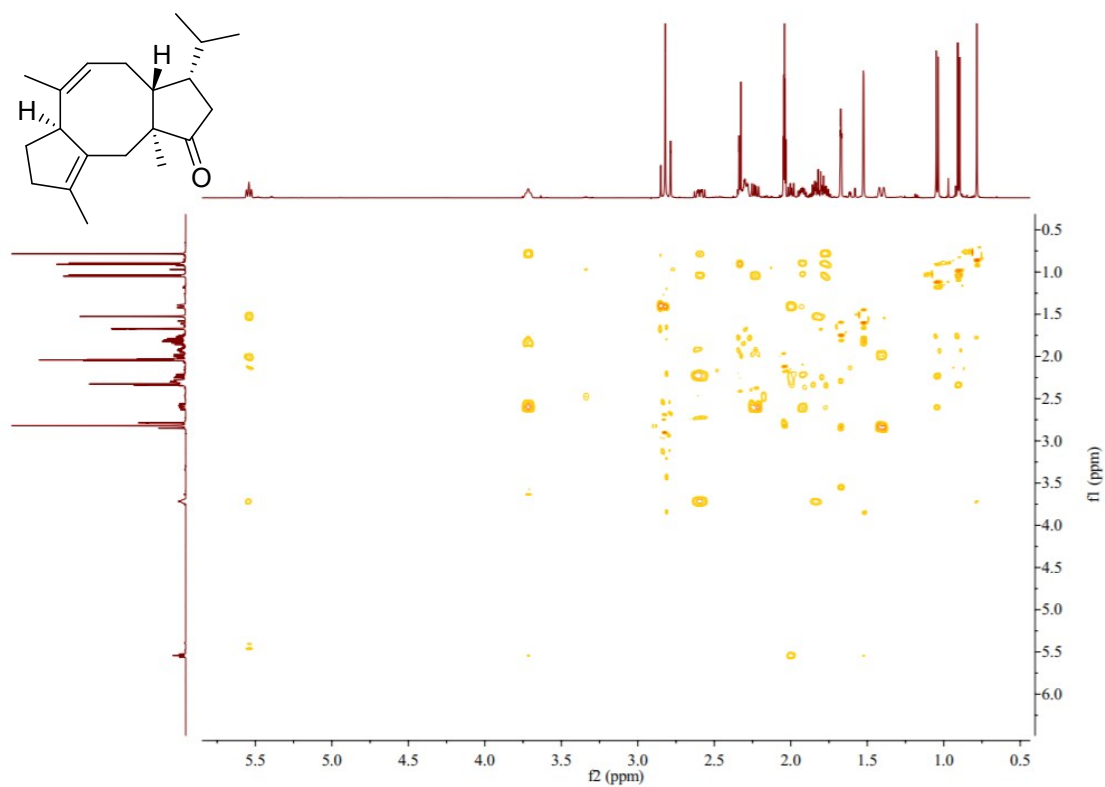


Figure S75. ROESY spectrum of hypoestin F (6).

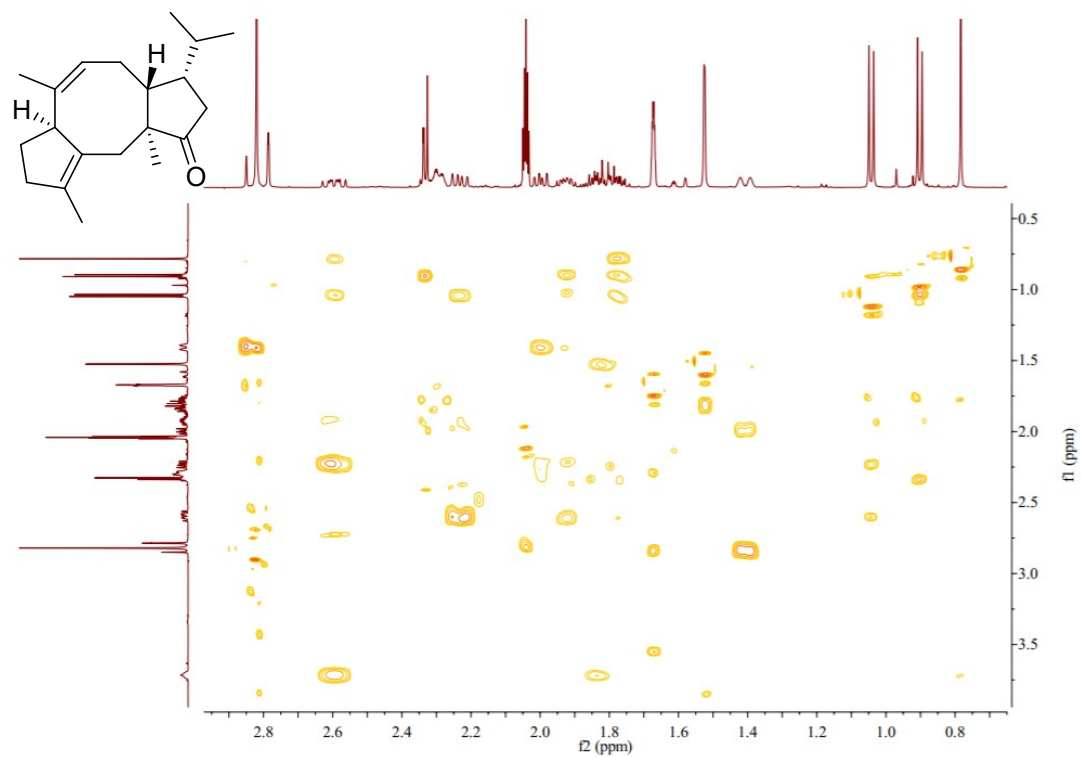


Figure S76. Expanded ROESY spectrum of hypoestin F (6).

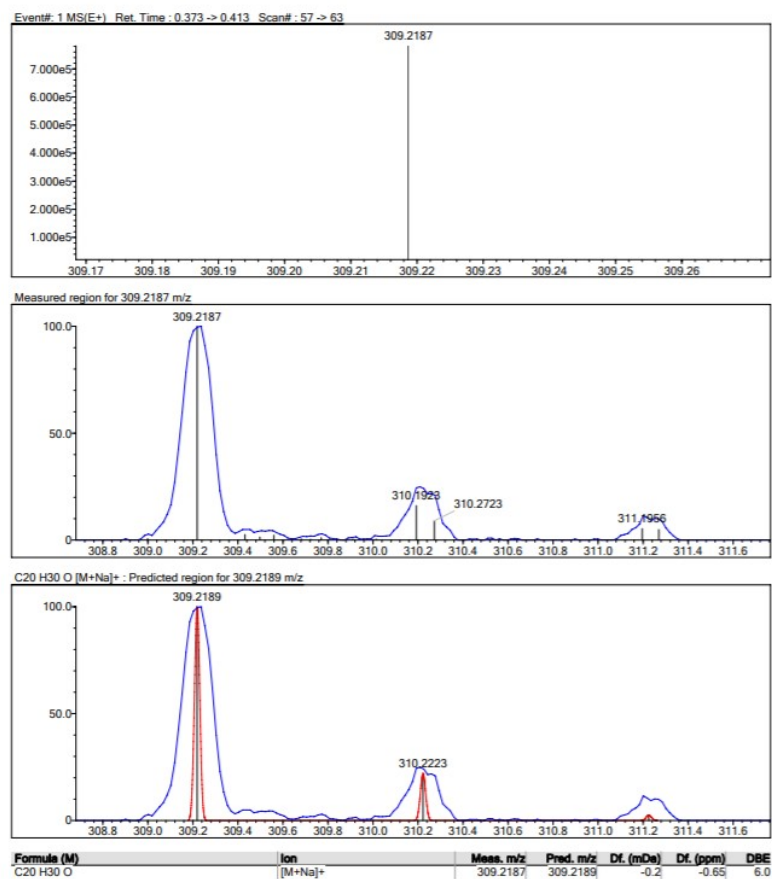


Figure S77. HRESIMS spectrum of hypoestin F (6).

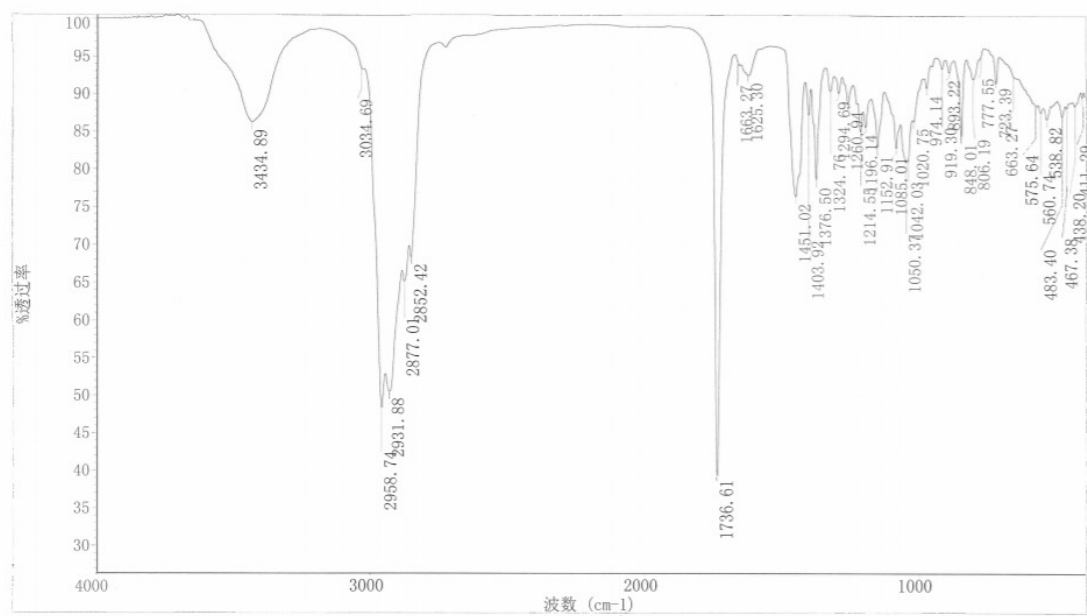


Figure S78. IR spectrum of hypoestin F (6).