

Supplementary Information

Cyclamenols E and F, two diastereoisomeric bicyclic macrolactams with cyclopentane moiety from an Antarctic *Streptomyces* species

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Theory and Calculation Details. The calculations were performed by using the density functional theory (DFT) as carried out in the Gaussian 09.^{S1} The preliminary conformational distributions search was performed by HyperChem Release 8.0 software. All ground-state geometries were optimized at the B3LYP/6-31G(d) level. Solvent effects of methanol solution were evaluated at the same DFT level by using the SCRF/PCM method.^{S2} TDDFT^{S3} at B3LYP/6-31G(d) was employed to calculate the electronic excitation energies and rotational strengths in methanol. The stable conformations obtained at the B3LYP/6-31G(d) level were further used in magnetic shielding constants at the B3LYP/6-311++G(2d,p) level. The overall calculated ECD curves were weighted by Boltzmann distribution (with a half-bandwidth of 0.35 eV) with a UV correction of -13 nm. The calculated ECD spectrum were produced by SpecDis 1.70.1 software.^{S4}

Cytotoxicity Assay. By the Cell Titer Glo (CTG) assay,^{S5} compounds **1** and **2** were evaluated for cytotoxicity against A431 (Epidermoid carcinoma cell line), A673 (rhabdomyoma cell line), U87 (glioblastoma cell line), U251 (glioblastoma cell line), HCC1954 (grade 3 invasive ductal carcinoma cell line), MCF-7 (human breast adenocarcinoma cell line), MKN-45 (human gastric cancer cell line), Hep3B (human liver cancer cell line), H1975 (human non-small cell lung carcinoma with L858R and T790M mutation cell line), DU145 (human prostate cancer cell line), MV-4-11 (biphenotypic B myelomonocytic leukemia cell line), K562 (human erythroleukemic cell line), A549 (lung cancer cell line), N87 (gastric carcinoma cell line), H1299 (human non-small cell lung carcinoma cell line), HUCCT1 (bile duct carcinoma cell line), 143B (human bone osteosarcoma cell line), B16F10 (highly metastatic mouse melanoma cell line), SPC-A1 (human lung cancer cell line overexpressing maspin cell line), HCT116 (colon carcinoma cell line), BT474 (hormone-sensitive breast cancer cell line), H2228 (non-small cell lung cancer cell line), MDA-MB-231 (breast cancer cell line), MDA-MB-468 (basal breast cancer cell line), Karpas299 (human T cell lymphoma cell line), HL60 (human promyelocytic leukemia cell line), HEK-293F (human embryonic kidney-293F cell line) and L02 (human liver cell line). In the CTG assay, 26 cell lines above were grown in DMEM supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin solution under a humidified atmosphere of 5% CO₂ and 95% air at 37 °C. 90 µL of culture solution (containing fetal bovine serum) and 100 µL of cell suspension at a density of 2 × 10³ cell/mL was plated in 96-well microtiter plates, allowed to attach overnight, and then exposed to 10 µL varying concentrations (0.032–100 µM) of compounds for 72 h. The CTG solution (100 µL) was then added to each well and incubated for 10 min. Absorbance was then determined on a Spectra Max Plus plate reader at 500 nm.

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Table S1. DFT-optimized structures and thermodynamic parameters for low-energy conformers of **1**

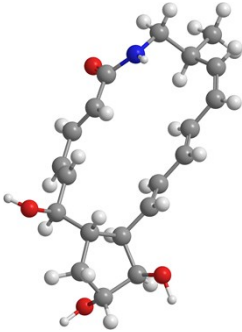
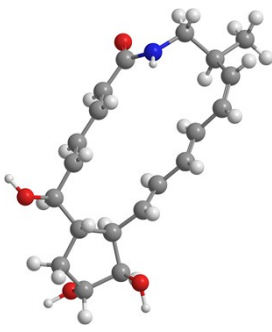
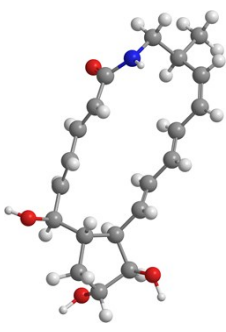
Conformers	Conf. A	Conf. B	Conf. C
DFT-optimized structures			
Population	46.2%	31.9%	21.9%
Total energy (a.u.)	-1133.93990984	-1133.93955867	-1133.93920460
Gibbs free energy (a.u.)	-1133.55013584	-1133.54129767	-1133.5490586
Sum of electronic and zero-point energies (a.u.)	-1133.495869	-1133.495785	-1133.495185
Sum of electronic and thermal energies (a.u.)	-1133.470621	-1133.470444	-1133.469978
Sum of electronic and thermal enthalpies (a.u.)	-1133.469676	-1133.469500	-1133.469034
Sum of electronic and thermal free energies (a.u.)	-1133.550136	-1133.550298	-1133.549059

Table S2. DFT-optimized structures and thermodynamic parameters for low-energy conformers of **2**

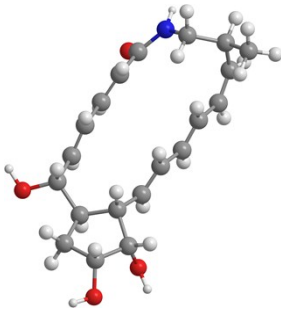
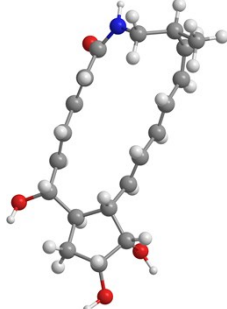
Conformers	Conf. A	Conf. B
DFT-optimized structures		
Population	99.0%	1.0%
Total energy (a.u.)	-1133.93099988	-1133.92667507
Gibbs free energy (a.u.)	-1133.54154388	-1133.53760607
Sum of electronic and zero-point energies (a.u.)	-1133.486937	-1133.482970
Sum of electronic and thermal energies (a.u.)	-1133.461616	-1133.457516
Sum of electronic and thermal enthalpies (a.u.)	-1133.460672	-1133.456572
Sum of electronic and thermal free energies (a.u.)	-1133.541544	-1133.537606

Table S3. DFT-optimized structures and thermodynamic parameters for low-energy conformers of 18-*epi*-2

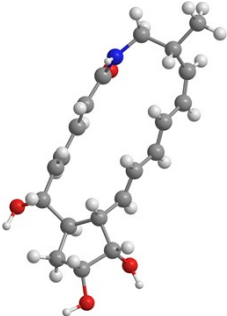
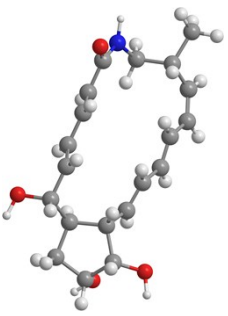
Conformers	Conf. A	Conf. B
DFT-optimized structures		
Population	91.8%	8.2%
Total energy (a.u.)	-1133.93257627	-1133.93030495
Gibbs free energy (a.u.)	-1133.54337027	-1133.54114795
Sum of electronic and zero-point energies (a.u.)	-1133.489049	-1133.486448
Sum of electronic and thermal energies (a.u.)	-1133.463621	-1133.461089
Sum of electronic and thermal enthalpies (a.u.)	-1133.462677	-1133.460145
Sum of electronic and thermal free energies (a.u.)	-1133.543370	-1133.541148

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

Conf. A				Conf. B				Conf. C			
C	-2.1449	-2.2045	-1.5098	C	-1.9898	-2.2963	-1.7481	C	-1.9688	-0.774	-4.5809
C	-1.2106	-2.8379	-2.5192	C	-1.4055	-2.5371	-3.1237	C	-0.8082	-1.7377	-4.4621
C	0.2224	-2.2346	-2.4127	C	0.0871	-2.0928	-3.1802	C	-0.2072	-1.7851	-3.0224
C	-3.2573	-1.5562	-1.9032	C	-3.0178	-1.4491	-1.5623	C	-3.1153	-0.9277	-3.8945
C	1.1728	-2.7987	-3.5118	C	0.7023	-2.2731	-4.6009	C	1.1357	-2.5735	-2.9957
C	-4.1917	-0.8708	-0.9949	C	-3.5137	-1.1353	-0.2148	C	-4.1762	0.0825	-3.9939
C	-3.9076	-0.5416	0.2796	C	-4.5033	-0.2397	-0.0475	C	-5.1583	0.1524	-3.0778
C	-4.8474	0.2263	1.1136	C	-5.0144	0.1861	1.2661	C	-6.1758	1.2149	-3.1104
O	-5.968	0.5095	0.6858	O	-6.0445	0.8629	1.269	O	-6.2889	1.9329	-4.1058
N	-4.3992	0.7721	2.3441	N	-4.2579	0.0584	2.4625	N	-6.8917	1.5252	-1.926
C	-4.968	1.9973	2.894	C	-4.4008	1.0003	3.5676	C	-7.4166	2.863	-1.6779
C	-4.2289	3.2521	2.3443	C	-3.3213	2.1188	3.4874	C	-6.3052	3.8091	-1.1371
C	-2.8029	3.3015	2.8594	C	-1.96	1.5813	3.8859	C	-5.7758	3.2992	0.1894
C	-1.7142	2.8749	2.1903	C	-0.9962	1.1736	3.0379	C	-4.6048	2.6585	0.3721
C	-4.9726	4.5497	2.7604	C	-3.6938	3.3042	4.4185	C	-6.8522	5.2503	-0.958
C	-1.7307	2.2848	0.8423	C	-1.1116	1.1559	1.571	C	-3.6274	2.3569	-0.6869
C	-0.683	1.5644	0.4038	C	-0.1726	0.5473	0.8247	C	-2.6637	1.442	-0.4788
C	-0.6979	0.9191	-0.9161	C	-0.3102	0.4411	-0.6337	C	-1.6844	1.1046	-1.5217
C	0.2626	0.0425	-1.2597	C	0.4971	-0.3709	-1.3398	C	-0.8742	0.0407	-1.3759
C	0.252	-0.6822	-2.5878	C	0.3092	-0.5899	-2.8246	C	0.1229	-0.3718	-2.438
C	1.5176	-0.3846	-3.4369	C	1.5538	-0.173	-3.6512	C	1.5746	-0.4573	-1.8861
C	1.5881	-1.5972	-4.3989	C	1.3441	-0.9157	-4.9958	C	2.2494	-1.5165	-2.7937
O	0.6664	-1.4061	-5.4849	O	0.4619	-0.1483	-5.8317	O	2.6371	-0.9142	-4.0393
O	2.6963	-0.318	-2.616	O	2.7693	-0.603	-3.0148	O	1.5954	-0.8855	-0.5134
O	-1.1446	-4.253	-2.2727	O	-1.4914	-3.9386	-3.4321	O	-1.2267	-3.0603	-4.8424
H	-1.9001	-2.2729	-0.4899	H	-1.5508	-2.7737	-0.9189	H	-1.8522	0.067	-5.2039
H	-1.5871	-2.6754	-3.533	H	-1.9699	-1.9768	-3.8742	H	-0.028	-1.4085	-5.1553
H	0.6418	-2.4992	-1.4372	H	0.664	-2.7124	-2.486	H	-0.9143	-2.2999	-2.3655
H	-3.4816	-1.5231	-2.9317	H	-3.4427	-0.9614	-2.3924	H	-3.2346	-1.7476	-3.2466
H	2.0619	-3.2177	-3.0346	H	1.474	-3.0451	-4.5636	H	1.1324	-3.2578	-2.1438
H	0.6948	-3.5752	-4.1091	H	-0.0525	-2.5639	-5.3325	H	1.2974	-3.1474	-3.9081
H	-5.1185	-0.5766	-1.3993	H	-3.0649	-1.5949	0.6167	H	-4.1323	0.7951	-4.7671
H	-2.9722	-0.7897	0.6893	H	-4.9377	0.1953	-0.9033	H	-5.1709	-0.5359	-2.2817
H	-3.5354	0.4444	2.7231	H	-3.4941	-0.581	2.492	H	-6.8135	0.9028	-1.1487
H	-6.0265	2.0592	2.6315	H	-5.3929	1.4555	3.5366	H	-7.8213	3.2744	-2.6054
H	-4.891	1.9666	3.9834	H	-4.3089	0.4591	4.5122	H	-8.2316	2.7933	-0.9535
H	-4.2394	3.2123	1.2538	H	-3.2951	2.5091	2.4683	H	-5.5048	3.858	-1.8765
H	-2.6515	3.6581	3.8401	H	-1.757	1.4898	4.9167	H	-6.3942	3.4155	1.0357
H	-0.7884	2.9366	2.6899	H	-0.1063	0.8055	3.4663	H	-4.3881	2.3273	1.3489
H	-4.4432	5.4205	2.3692	H	-2.9255	4.0773	4.3582	H	-6.0597	5.9023	-0.586
H	-5.9849	4.5439	2.3524	H	-4.6473	3.7348	4.1073	H	-7.2012	5.6361	-1.9174
H	-5.028	4.6248	3.8478	H	-3.7777	2.9643	5.4523	H	-7.6818	5.2575	-0.2489
H	-2.5713	2.3981	0.2228	H	-1.9471	1.5814	1.0978	H	-3.6803	2.8448	-1.6154
H	0.1518	1.4302	1.031	H	0.6528	0.0955	1.2964	H	-2.62	0.9393	0.4451
H	-1.484	1.1239	-1.5846	H	-1.0837	0.9625	-1.1202	H	-1.6344	1.6871	-2.3962
H	1.0345	-0.1671	-0.5747	H	1.2529	-0.9066	-0.8393	H	-0.9555	-0.5465	-0.5054
H	-0.6187	-0.3707	-3.1722	H	-0.545	-0.0074	-3.1821	H	0.124	0.3631	-3.248
H	1.3984	0.5503	-3.9875	H	1.5745	0.9088	-3.7953	H	2.0727	0.5102	-1.9742
H	2.5974	-1.7291	-4.792	H	2.2945	-1.0672	-5.5101	H	3.123	-1.9534	-2.3078
H	0.7821	-2.1763	-6.0817	H	0.4064	-0.6283	-6.6857	H	3.0855	-1.6175	-4.5559
H	3.436	-0.083	-3.2162	H	3.5042	-0.2644	-3.5696	H	2.5348	-0.8605	-0.2313
H	-2.0445	-4.6056	-2.4435	H	-2.4481	-4.1533	-3.4783	H	-1.4924	-3.0062	-5.7857

Table S5. Optimized Z-matrixes of **2** in the gas phase (Å) at B3LYP/6-31G(d) level

Conf. A				Conf. B			
C	-1.9927	-2.6121	-0.1016	C	-0.9883	-3.2748	-0.1151
C	-2.1993	-2.9951	1.3482	C	-0.9391	-3.6256	1.3555
C	-0.8289	-3.1705	2.0683	C	0.3649	-3.0709	2.0093
C	-2.3682	-1.4123	-0.5794	C	-1.9227	-2.449	-0.6193
C	-0.9813	-3.6843	3.5306	C	0.5021	-3.4445	3.515
C	-2.0605	-1.0237	-1.9627	C	-1.8901	-2.0518	-2.0336
C	-2.2261	0.2465	-2.3737	C	-2.671	-1.0549	-2.4874
C	-1.8514	0.6846	-3.7288	C	-2.6053	-0.5844	-3.8811
O	-1.7718	-0.1454	-4.6364	O	-2.1713	-1.3345	-4.7573
N	-1.6342	2.0486	-4.0563	N	-3.0895	0.6895	-4.2772
C	-1.2422	3.064	-3.0853	C	-3.1764	1.8366	-3.3805
C	0.1815	3.621	-3.3798	C	-2.2035	2.9742	-3.8088
C	1.2414	2.5592	-3.6182	C	-0.7805	2.5199	-4.0851
C	1.6013	1.5483	-2.8025	C	0.0544	1.8594	-3.2583
C	0.637	4.6475	-2.3082	C	-2.2366	4.1705	-2.8203
C	1.0245	1.2572	-1.4822	C	-0.2506	1.4324	-1.8854
C	1.2465	0.0739	-0.8829	C	0.5264	0.531	-1.2588
C	0.6083	-0.2516	0.3994	C	0.182	0.046	0.0842
C	0.7306	-1.4754	0.9442	C	0.8821	-0.9448	0.6653
C	-0.0095	-1.8526	2.2076	C	0.4741	-1.5165	2.0044
C	0.9436	-2.1367	3.3981	C	1.5152	-1.2192	3.1158
C	0.0238	-2.8814	4.4023	C	1.124	-2.2174	4.2383
O	0.7676	-3.7205	5.2972	O	2.2459	-2.5753	5.0579
O	2.051	-2.9536	2.9803	O	2.851	-1.4517	2.6362
O	-2.9245	-4.2356	1.4009	O	-0.9936	-5.0611	1.4301
H	-1.4994	-3.2917	-0.7369	H	-0.2431	-3.6621	-0.7504
H	-2.7795	-2.2265	1.8654	H	-1.8116	-3.2093	1.8655
H	-0.2314	-3.9047	1.5181	H	1.2283	-3.4882	1.4808
H	-2.8355	-0.7199	0.0605	H	-2.6534	-2.0383	0.0167
H	-0.7561	-4.7517	3.568	H	1.1415	-4.3225	3.6201
H	-1.9935	-3.518	3.9033	H	-0.474	-3.6552	3.9555
H	-1.6557	-1.7383	-2.6206	H	-1.2094	-2.5209	-2.6846
H	-2.6078	0.9551	-1.6966	H	-3.328	-0.5771	-1.8191
H	-1.6392	2.3049	-5.0222	H	-3.2651	0.8429	-5.2489
H	-1.2855	2.674	-2.0712	H	-4.2003	2.218	-3.4224
H	-1.9598	3.8863	-3.1523	H	-2.9775	1.5454	-2.3518
H	0.0998	4.178	-4.3214	H	-2.5858	3.356	-4.7635
H	1.7637	2.6246	-4.5327	H	-0.3976	2.7537	-5.0402
H	2.3564	0.9023	-3.1549	H	1.0065	1.6178	-3.6412
H	-0.0824	5.4666	-2.2543	H	-1.8996	3.8677	-1.8294
H	0.7114	4.18	-1.3268	H	-1.5884	4.9689	-3.1863
H	1.6117	5.0566	-2.5807	H	-3.2549	4.5557	-2.7431
H	0.4176	1.9645	-1.0015	H	-1.0896	1.8147	-1.3857
H	1.8451	-0.6485	-1.3598	H	1.3651	0.1314	-1.7531
H	0.0026	0.4688	0.8701	H	-0.6578	0.4464	0.5761
H	1.3253	-2.1994	0.4644	H	1.7145	-1.3532	0.1667
H	-0.6858	-1.0426	2.4972	H	-0.4869	-1.0929	2.3117
H	1.3107	-1.2014	3.8246	H	1.4191	-0.1879	3.4606
H	-0.5274	-2.1366	4.9842	H	0.3583	-1.75	4.8647
H	0.1134	-4.1006	5.922	H	1.8922	-3.1534	5.7675
H	2.6575	-3.0119	3.7489	H	3.4565	-1.1456	3.3445
H	-3.8108	-4.0541	1.0203	H	-1.14	-5.2939	2.3706

Table S6. Optimized Z-matrixes of 18-*epi*-2 in the gas phase (Å) at B3LYP/6-31G(d) level

Conf. A				Conf. B			
C	-0.9026	-2.4751	-0.2372	C	-2.2418	-0.2958	1.4718
C	-0.8743	-3.2883	1.0389	C	-2.2208	-1.4443	2.4577
C	0.0449	-2.6285	2.1159	C	-0.8984	-2.2702	2.3888
C	0.0755	-2.5418	-1.1616	C	-2.2559	-0.4798	0.1389
C	-0.1132	-3.2838	3.5224	C	-0.8083	-3.3303	3.5242
C	0.1469	-1.6828	-2.3587	C	-2.2929	0.6708	-0.7749
C	-0.8074	-0.8024	-2.7161	C	-2.1585	0.5133	-2.1041
C	-0.6627	0.1078	-3.8645	C	-2.211	1.6576	-3.0299
O	0.3434	0.0679	-4.5744	O	-2.8309	2.6729	-2.7079
N	-1.6142	1.148	-4.0199	N	-1.6763	1.5904	-4.343
C	-1.3608	2.361	-4.7861	C	-0.4364	0.8814	-4.6357
C	-0.9733	3.5395	-3.8446	C	0.8025	1.7846	-4.3655
C	0.4893	3.4537	-3.4502	C	2.0462	0.9227	-4.2669
C	0.9726	2.8839	-2.3296	C	2.4656	0.3226	-3.1358
C	-1.2308	4.9026	-4.543	C	0.985	2.8598	-5.47
C	0.1607	2.2141	-1.3014	C	1.782	0.4387	-1.8375
C	0.7534	1.4493	-0.3669	C	1.9652	-0.4851	-0.8784
C	-0.0338	0.6822	0.608	C	1.2513	-0.3917	0.4017
C	0.5617	-0.2283	1.3994	C	1.183	-1.45	1.2281
C	-0.2249	-1.1076	2.3472	C	0.398	-1.4033	2.5231
C	0.161	-0.8625	3.8304	C	1.2027	-2.0005	3.7137
C	-0.3768	-2.1353	4.5316	C	0.6992	-3.4593	3.8483
O	0.2492	-2.3627	5.8019	O	1.3691	-4.3166	2.9102
O	1.5861	-0.7379	3.9781	O	2.6237	-1.9124	3.5311
O	-0.438	-4.6246	0.7299	O	-3.3677	-2.2722	2.1931
H	-1.6884	-1.7869	-0.3512	H	-2.2489	0.6854	1.8542
H	-1.8995	-3.3374	1.4181	H	-2.3243	-1.0169	3.4597
H	1.087	-2.7558	1.8051	H	-0.8752	-2.8052	1.4342
H	0.8742	-3.2092	-1.0018	H	-2.241	-1.4553	-0.2548
H	0.8093	-3.8076	3.7814	H	-1.2307	-4.2843	3.2081
H	-0.9449	-3.9887	3.5507	H	-1.333	-2.9794	4.4155
H	1.0205	-1.7478	-2.9429	H	-2.4239	1.6363	-0.3769
H	-1.6812	-0.7175	-2.1392	H	-2.0113	-0.4521	-2.4951
H	-2.4398	1.1215	-3.4577	H	-1.9881	2.2698	-5.0061
H	-0.5743	2.1997	-5.5256	H	-0.3716	-0.0131	-4.0139
H	-2.2815	2.6088	-5.3206	H	-0.4448	0.5607	-5.6799
H	-1.6084	3.51	-2.9571	H	0.6537	2.3137	-3.422
H	1.1977	3.8449	-4.1266	H	2.5854	0.7251	-5.1506
H	2.0195	2.8823	-2.2076	H	3.3153	-0.297	-3.1981
H	-0.6521	4.9727	-5.4657	H	1.1075	2.3864	-6.4457
H	-0.9428	5.7191	-3.8781	H	1.8687	3.4633	-5.254
H	-2.2914	5.0036	-4.7799	H	0.1142	3.5164	-5.4998
H	-0.8871	2.2858	-1.3205	H	1.1227	1.2367	-1.6572
H	1.8017	1.3534	-0.3664	H	2.6014	-1.3041	-1.0575
H	-1.0772	0.8099	0.6485	H	0.761	0.5035	0.6568
H	1.6044	-0.3606	1.3344	H	1.6469	-2.3525	0.9468
H	-1.2958	-0.9128	2.2385	H	0.1472	-0.3684	2.7657
H	-0.3336	0.033	4.2109	H	0.9298	-1.4514	4.6206
H	-1.4556	-2.025	4.6753	H	0.8516	-3.8268	4.8644
H	-0.1837	-3.1577	6.1805	H	1.0276	-5.2216	3.0741
H	1.7474	-0.4967	4.915	H	3.027	-2.2705	4.3508
H	-0.5805	-5.1661	1.5341	H	-3.4459	-2.8988	2.9429

Table S7. The calculated ^{13}C NMR data for **2** and 18-*epi*-**2**

no.	δ_{exp}	δ_{cal}		δ_{scal}		corrected error		t distribution		probability	
		2	18- <i>epi</i> - 2	2	18- <i>epi</i> - 2	2	18- <i>epi</i> - 2	2	18- <i>epi</i> - 2	2	18- <i>epi</i> - 2
1	165.7	172.21	168.60	163.52	163.54	-2.18	-2.16	0.82	0.82	0.18	0.18
2	124.6	128.55	125.57	120.47	119.84	-4.13	-4.76	0.95	0.97	0.05	0.03
3	138.5	150.25	146.80	141.87	141.40	3.37	2.90	0.91	0.88	0.09	0.12
4	126.5	137.74	129.35	129.53	123.68	3.03	-2.82	0.89	0.88	0.11	0.12
5	143.9	151.83	144.24	143.43	138.80	-0.47	-5.10	0.58	0.98	0.42	0.02
6	76	85.80	83.10	78.31	76.71	2.31	0.71	0.83	0.62	0.17	0.38
7	49	51.60	61.42	44.58	54.69	-4.42	5.69	0.96	0.98	0.04	0.02
8	35.1	40.57	40.91	33.70	33.87	-1.40	-1.23	0.72	0.70	0.28	0.30
9	72.9	79.59	80.37	72.19	73.94	-0.71	1.04	0.62	0.67	0.38	0.33
10	76.3	83.64	83.53	76.18	77.15	-0.12	0.85	0.52	0.64	0.48	0.36
11	48.1	59.06	56.42	51.94	49.61	3.84	1.51	0.94	0.74	0.06	0.26
12	135.7	144.21	143.16	135.91	137.70	0.21	2.00	0.54	0.80	0.46	0.20
13	132.7	142.48	139.40	134.21	133.88	1.51	1.18	0.74	0.69	0.26	0.31
14	132.8	141.13	139.59	132.87	134.08	0.07	1.28	0.51	0.70	0.49	0.30
15	127.2	135.56	133.42	127.38	127.81	0.18	0.61	0.53	0.60	0.47	0.40
16	130	140.62	137.68	132.38	132.14	2.38	2.14	0.84	0.81	0.16	0.19
17	134.2	137.62	142.61	129.42	137.15	-4.78	2.95	0.97	0.89	0.03	0.11
18	32.3	43.35	41.88	36.45	34.85	4.15	2.55	0.95	0.85	0.05	0.15
19	45	53.90	47.31	46.86	40.36	1.86	-4.64	0.78	0.97	0.22	0.03
20	18.7	20.58	21.33	14.00	13.98	-4.70	-4.72	0.97	0.97	0.03	0.03
Product of probabilities										3.99E-17	3.03E-18
Bayes's theorem probability (%)										93	7

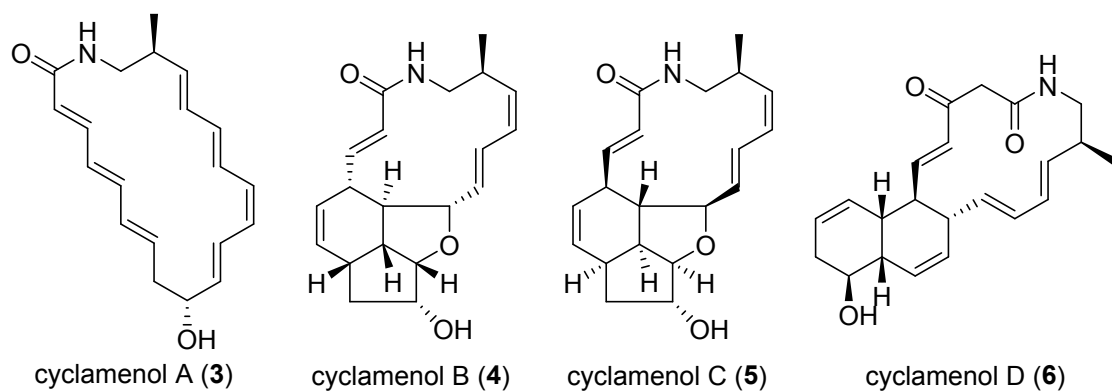


Figure S1. Structures of cyclamenols A–D

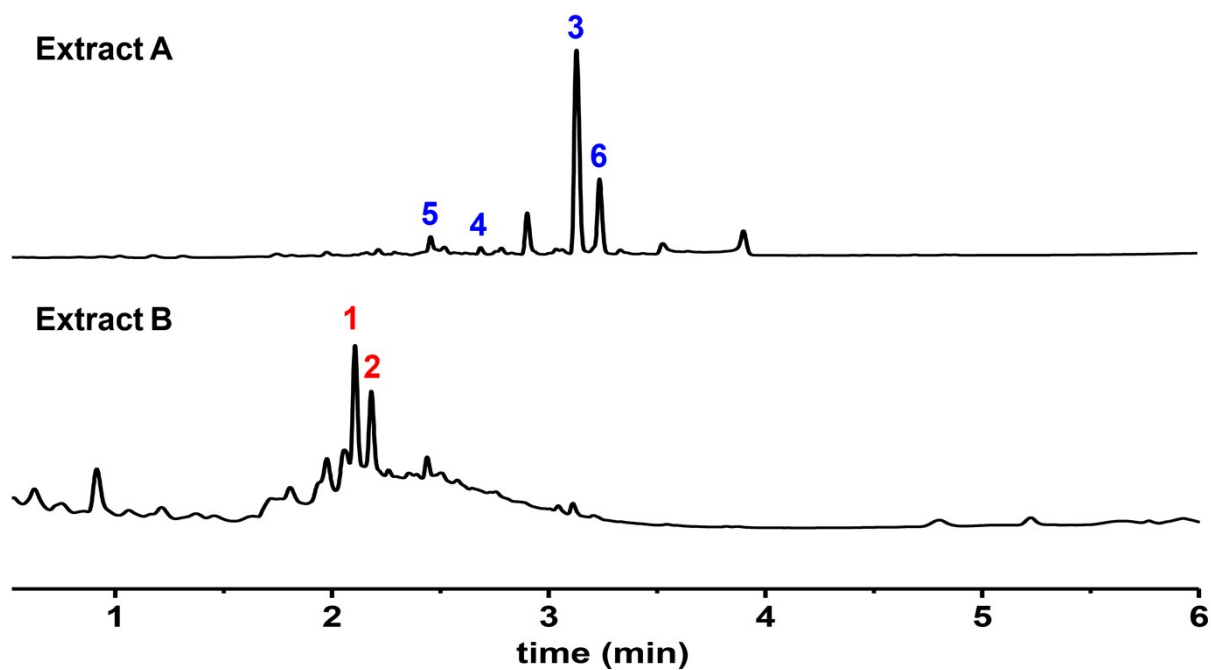
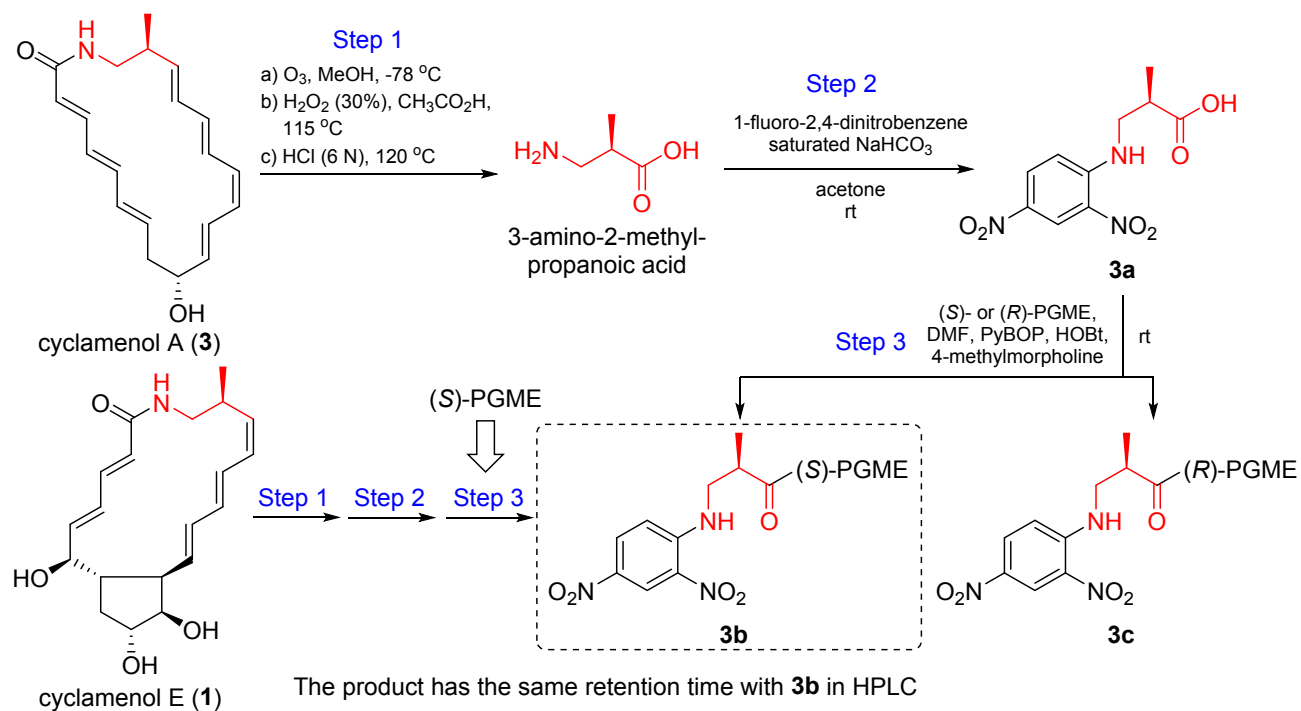


Figure S2. HPLC profiles of crude extracts of *Streptomyces* sp. OUCMDZ-4348. **Extract A (previous work):** After 7 days of cultivation, the whole broth was extracted three times with EtOAc to give the crude extract A. **Extract B (this work):** After 7 days of cultivation, XAD-16N resin (20 g/L) was added to the culture to adsorb the organic products. The resin was filtered through gauze, eluted with acetone/H₂O (80%). The acetone was removed under reduced pressure. The remaining part was extracted three times with EtOAc, and then the water layer was dried *in vacuo* to yield extract B.



Scheme S1. Chemical reactions for the identification of the absolute configuration at C-18 of **1**

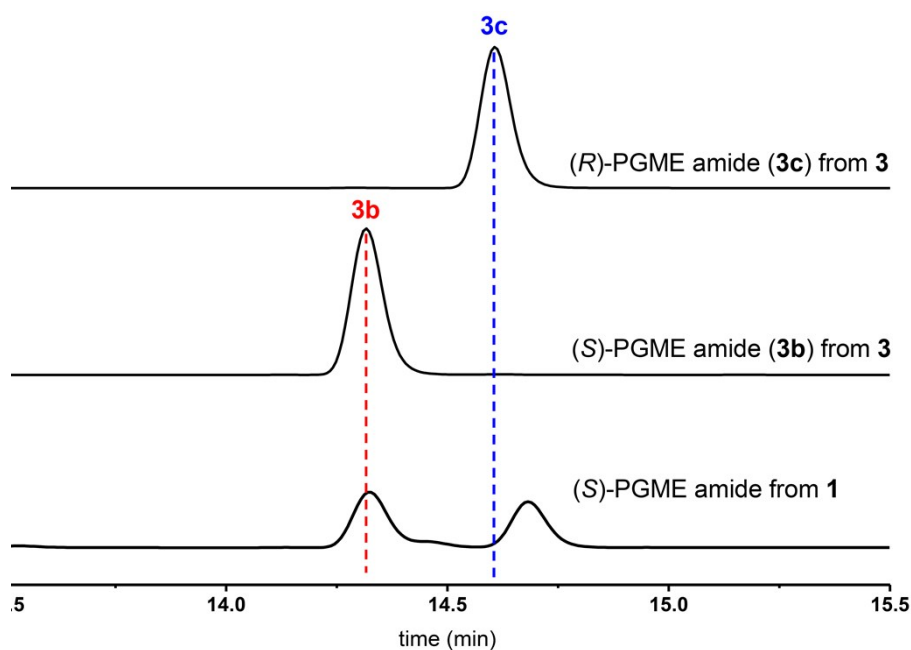


Figure S3. HPLC profiles of PGME amide products derived from compounds **1** and **3**

Figure S4. HRESIMS spectrum of cyclamenol E (**1**)

20190304-SJJ-B-10_190304101224 #53 RT: 0.46 AV: 1 SB: 17 0.10-0.25 NL: 1.92E7

T: FTMS + p ESI Full ms [100.00-2000.00]

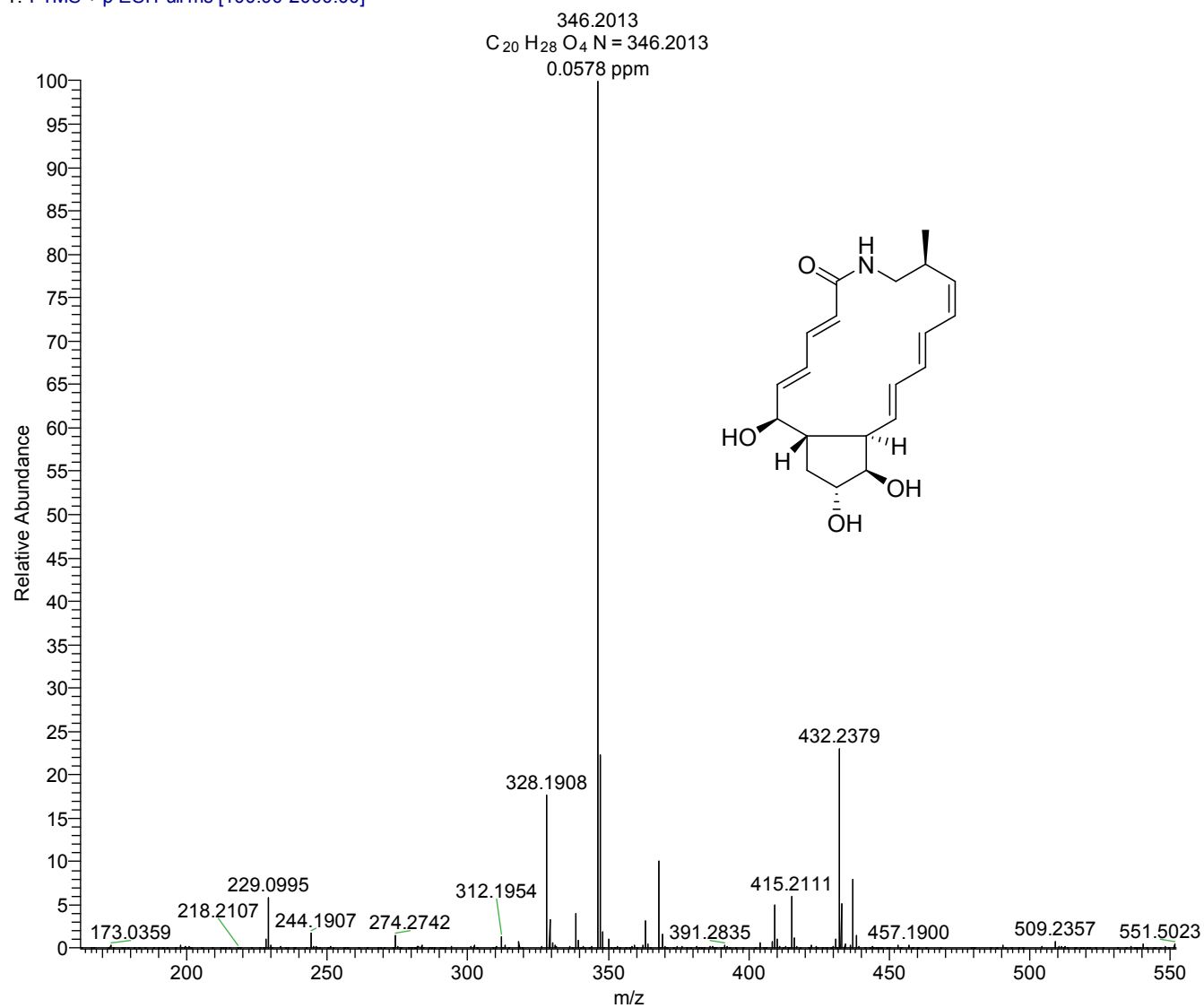


Figure S5. ^1H -NMR spectrum of cyclamenol E (**1**) in $\text{DMSO}-d_6$ (500 MHz)

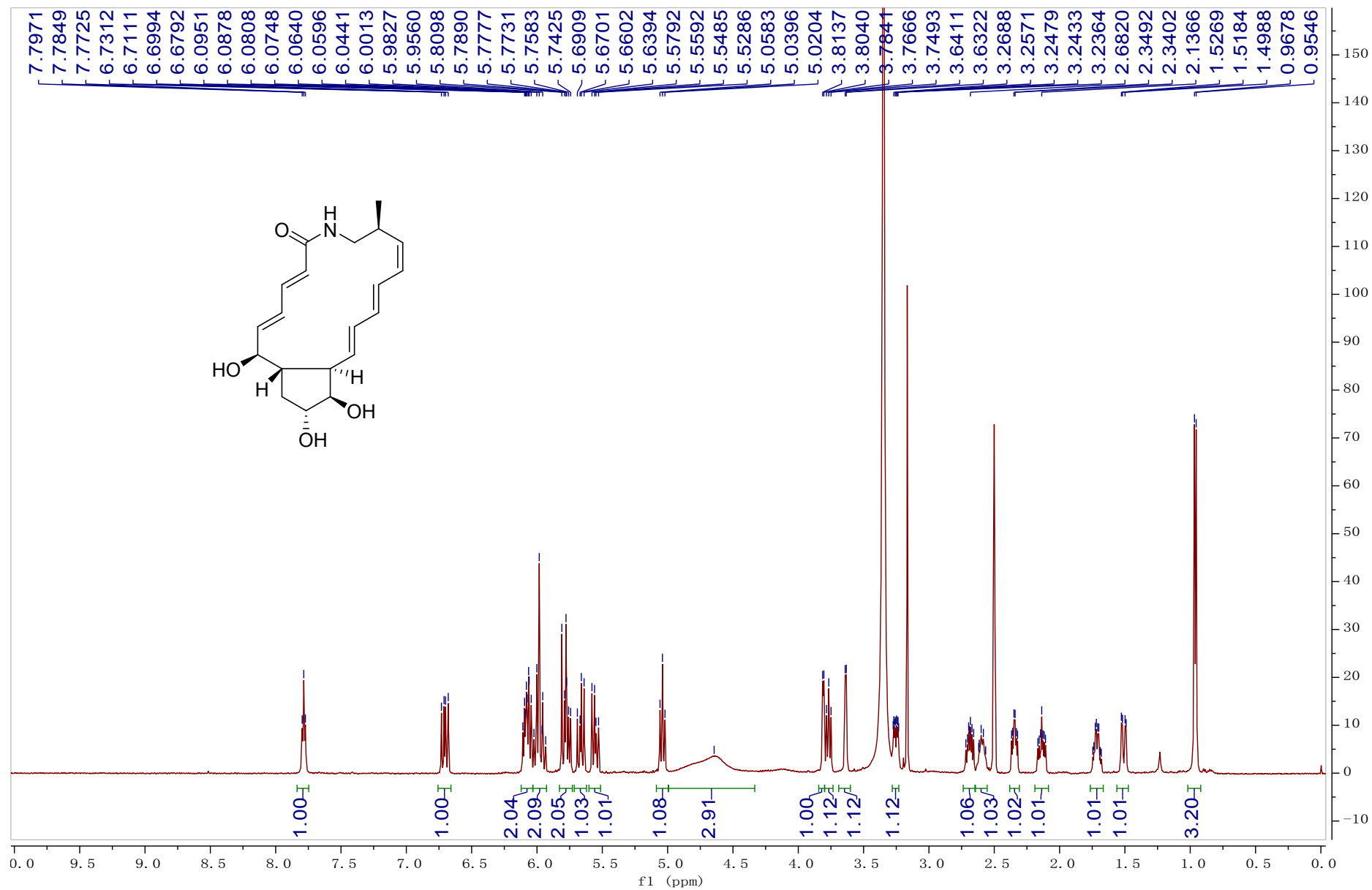
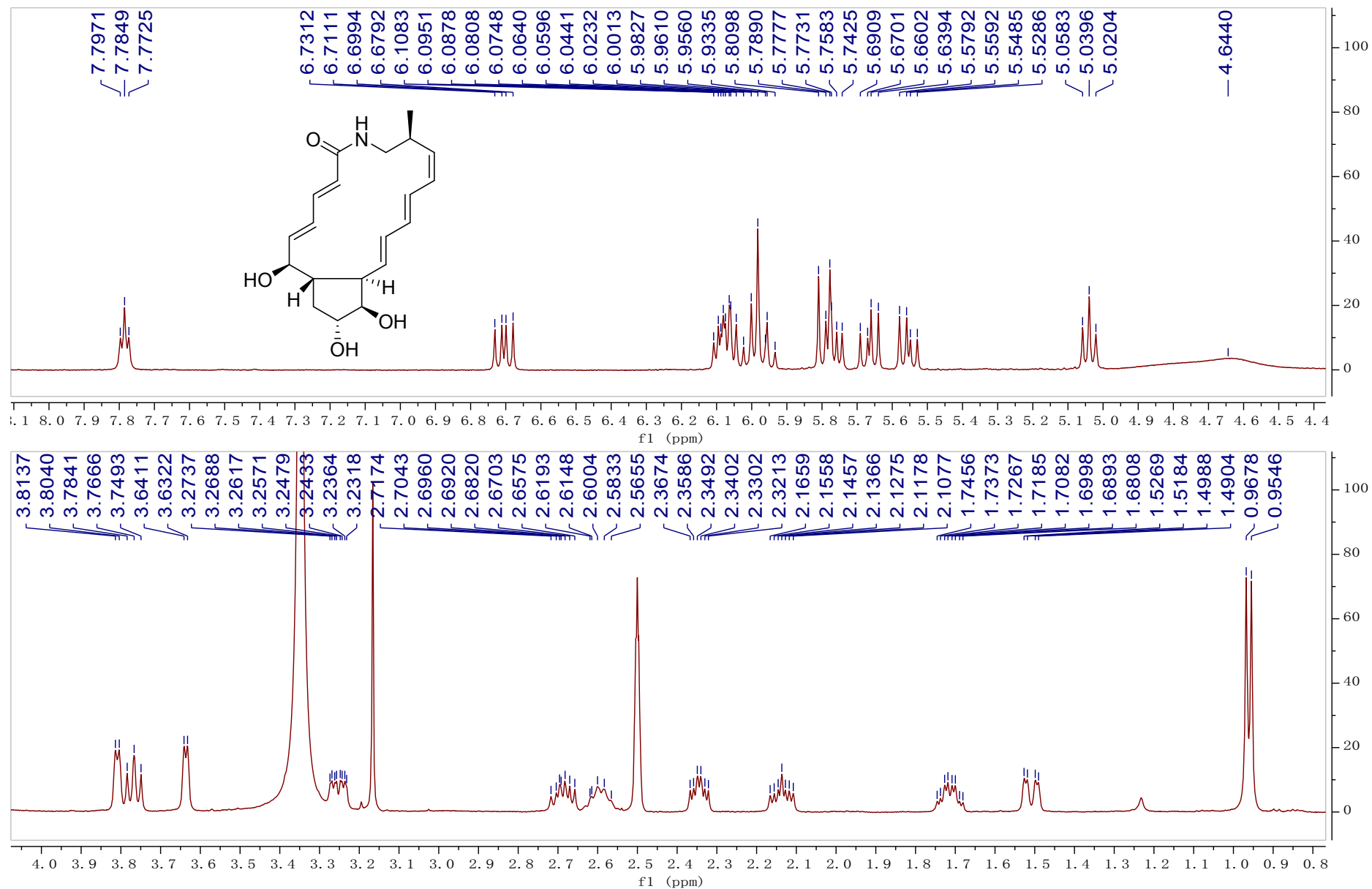


Figure S6. Expanded ^1H -NMR spectrum of cyclamenol E (1) in $\text{DMSO}-d_6$ (500 MHz)



The figure displays the ¹³C NMR spectrum of a complex molecule, with the chemical structure shown above the spectrum. The x-axis represents the chemical shift in ppm, ranging from 180 to 0. The spectrum shows several sharp peaks, with the most prominent ones in the aliphatic region (30-50 ppm) and the carbonyl region (165 ppm). The chemical structure is a complex polycyclic molecule with multiple hydroxyl groups, a carbonyl group, and a long chain with a double bond.

Chemical structure (SMILES): CC(C)(O)C1C(C(C1O)O)C(C(C(C2=CC=CC=C2)C(=O)NCC3=CC=CC=C3)C(=O)O)C

Peak list (ppm):

- 165.7099
- 144.2209
- 138.5230
- 135.4673
- 134.1303
- 132.9325
- 132.8961
- 130.0421
- 127.0674
- 126.4384
- 124.6210
- 80.5168
- 77.1499
- 76.7535
- 49.6179
- 48.5667
- 45.0210
- 36.9309
- 32.4350
- 18.7737

Figure S8. Expanded ^{13}C -NMR spectrum of cyclamenol E (**1**) in $\text{DMSO}-d_6$ (125 MHz)

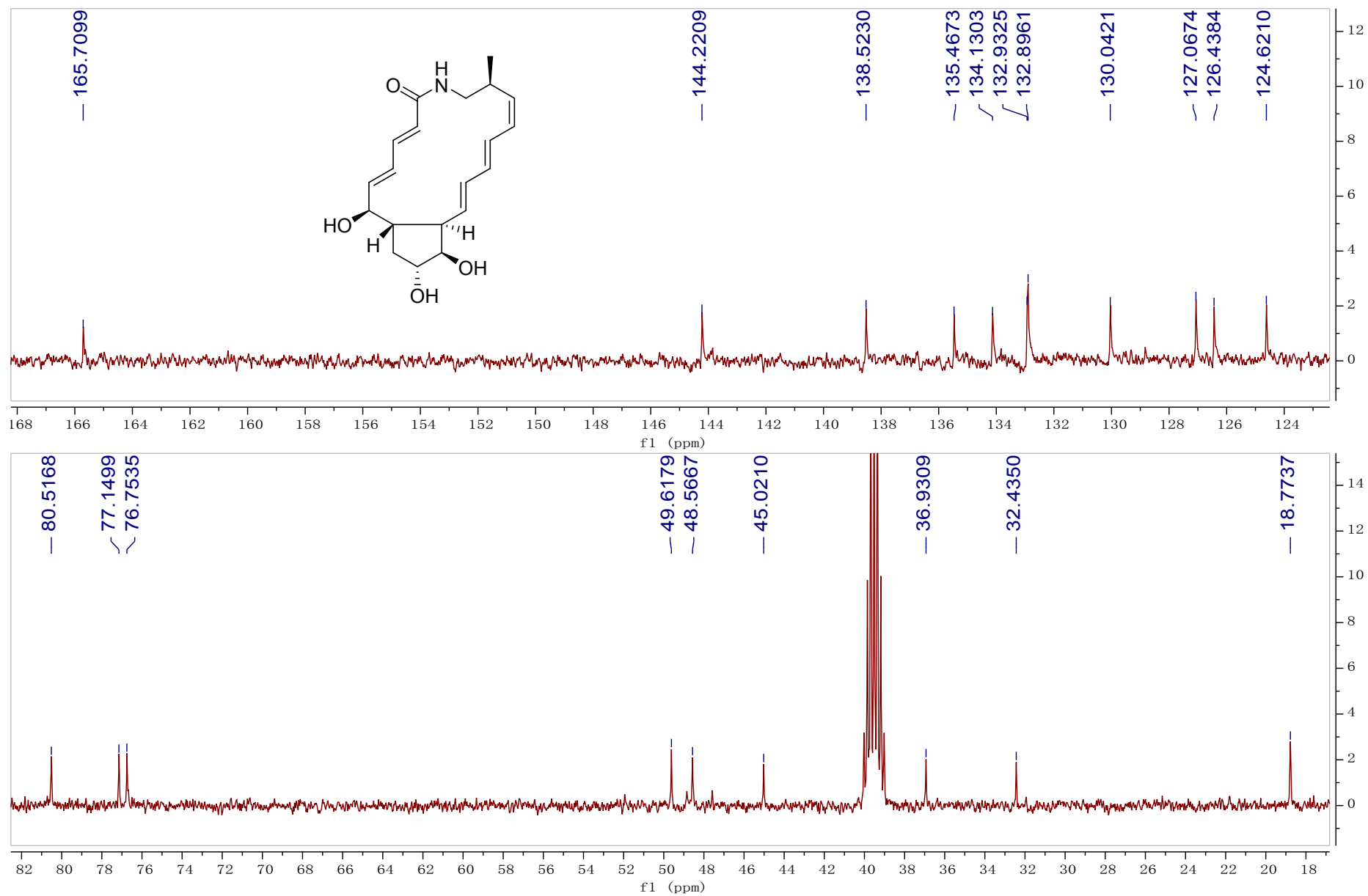


Figure S9. HSQC spectrum of cyclamenol E (**1**) in DMSO- d_6 (500 $\times$ 125 MHz)

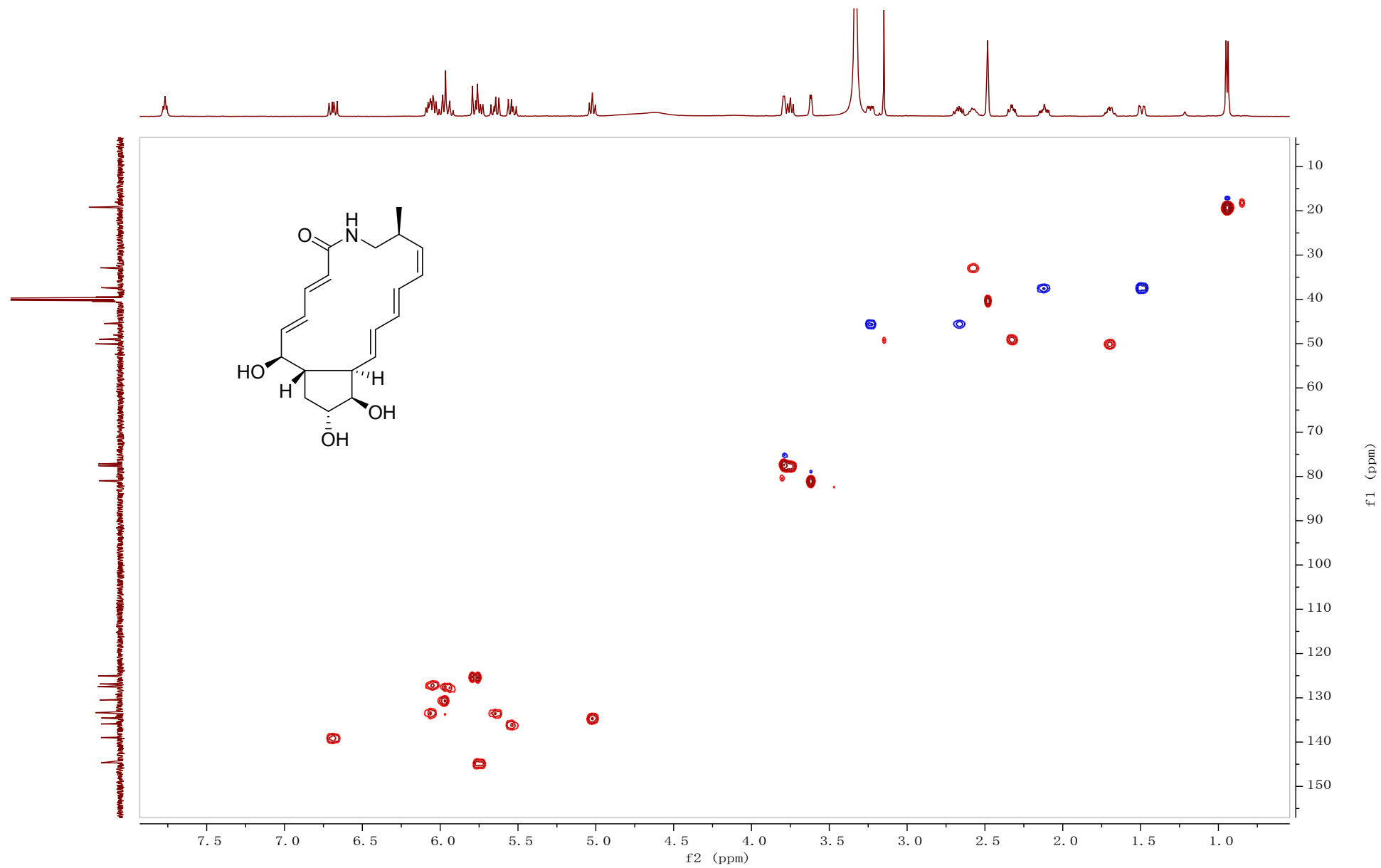


Figure S10. ^1H - ^1H COSY spectrum of cyclamenol E (**1**) in $\text{DMSO}-d_6$ (500 MHz)

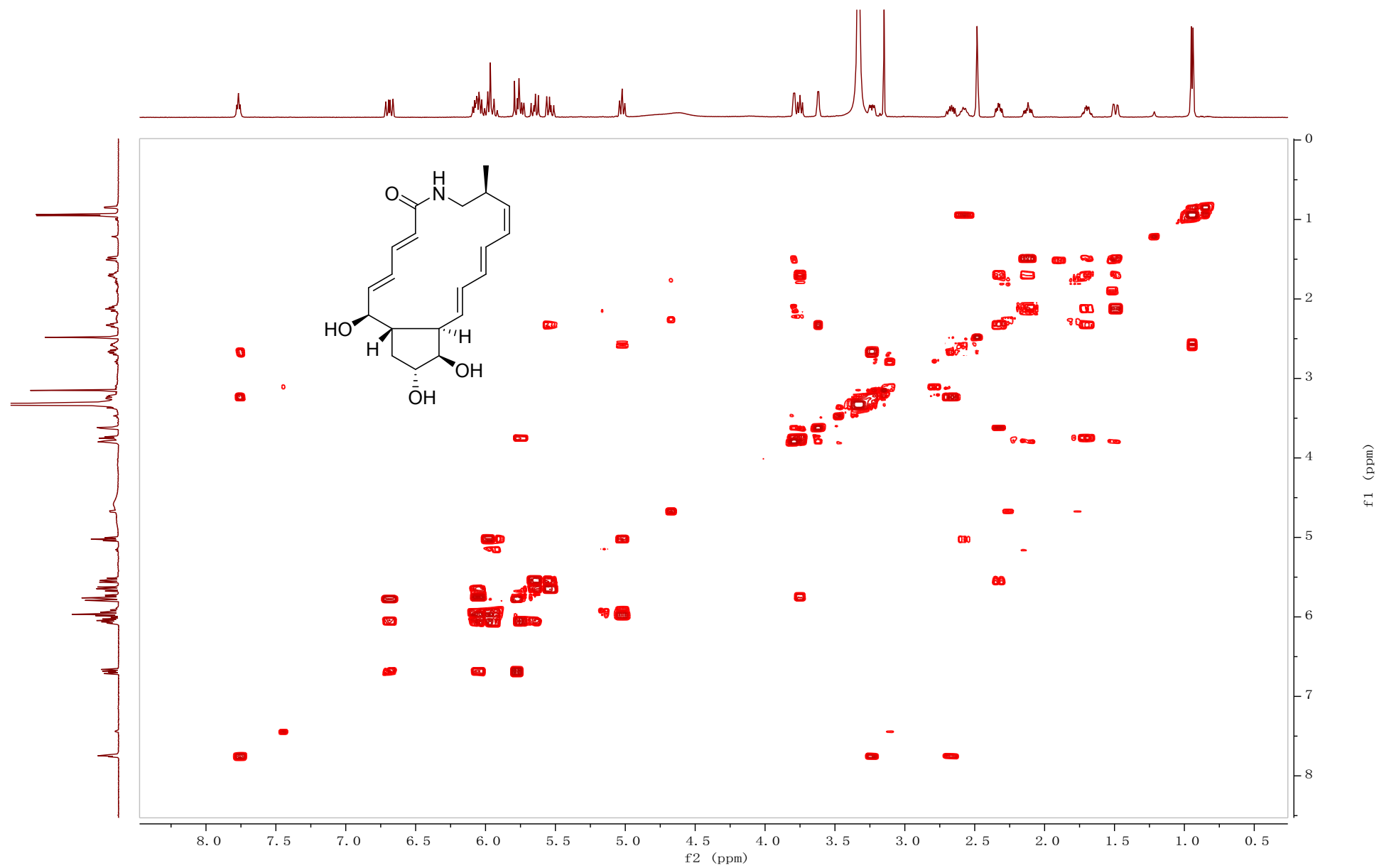


Figure S11. HMBC spectrum of cyclamenol E (**1**) in DMSO-*d*₆ (500 × 125 MHz)

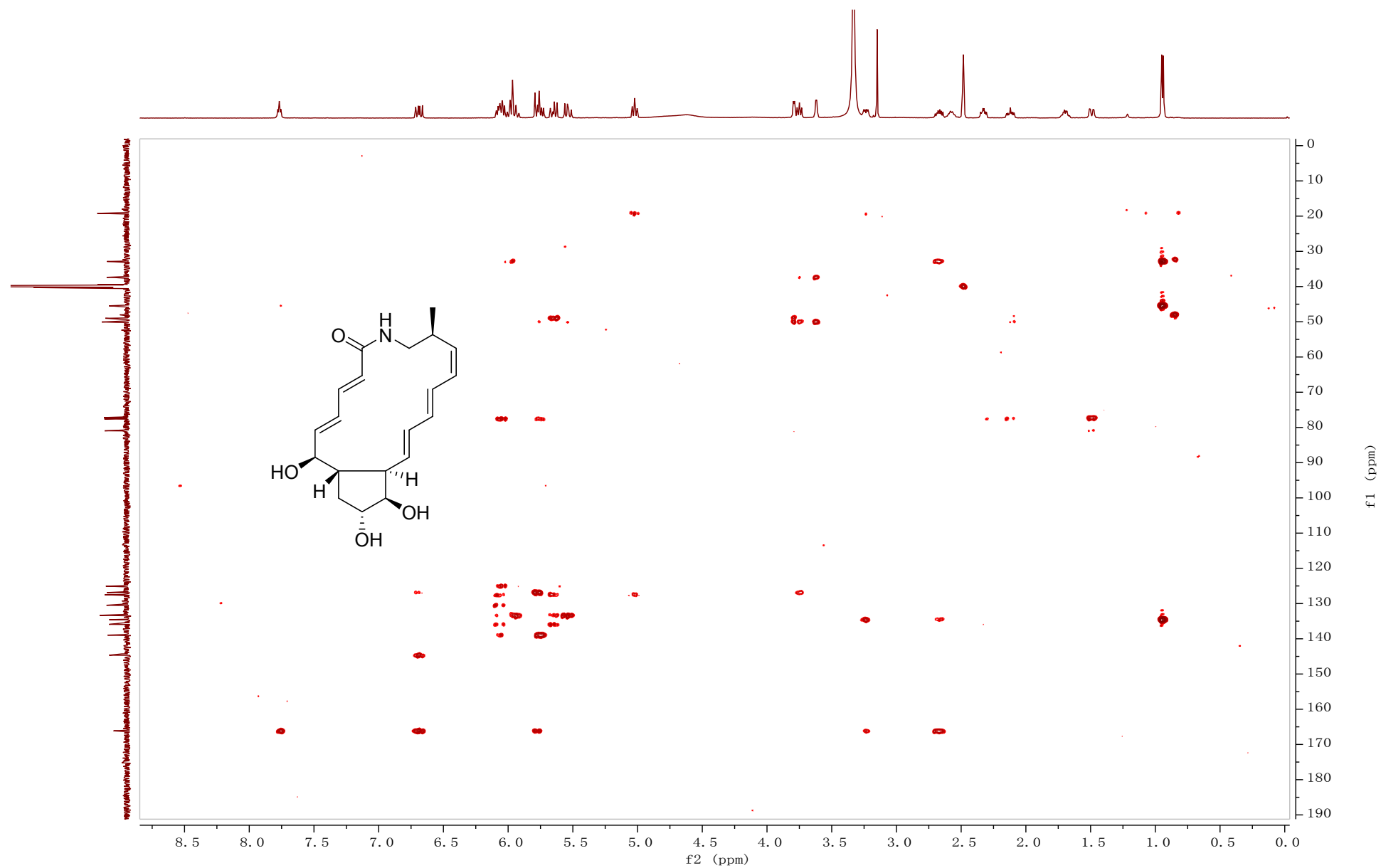


Figure S12. NOESY spectrum of cyclamenol E (1) in DMSO- d_6 (500 MHz)

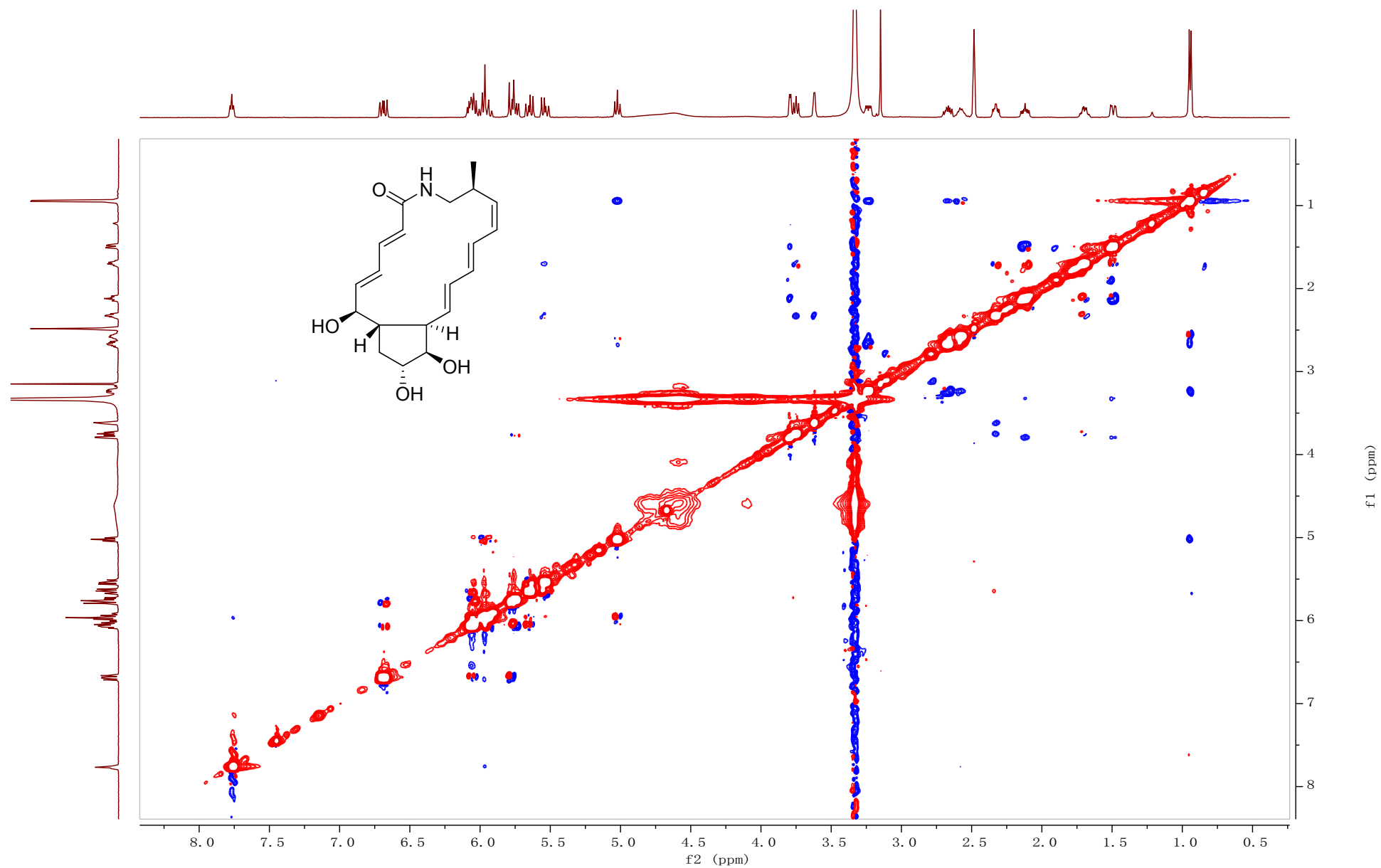


Figure S13. ^1H -NMR spectrum of cyclamenol E (**1**) in methanol- d_4 (500 MHz)

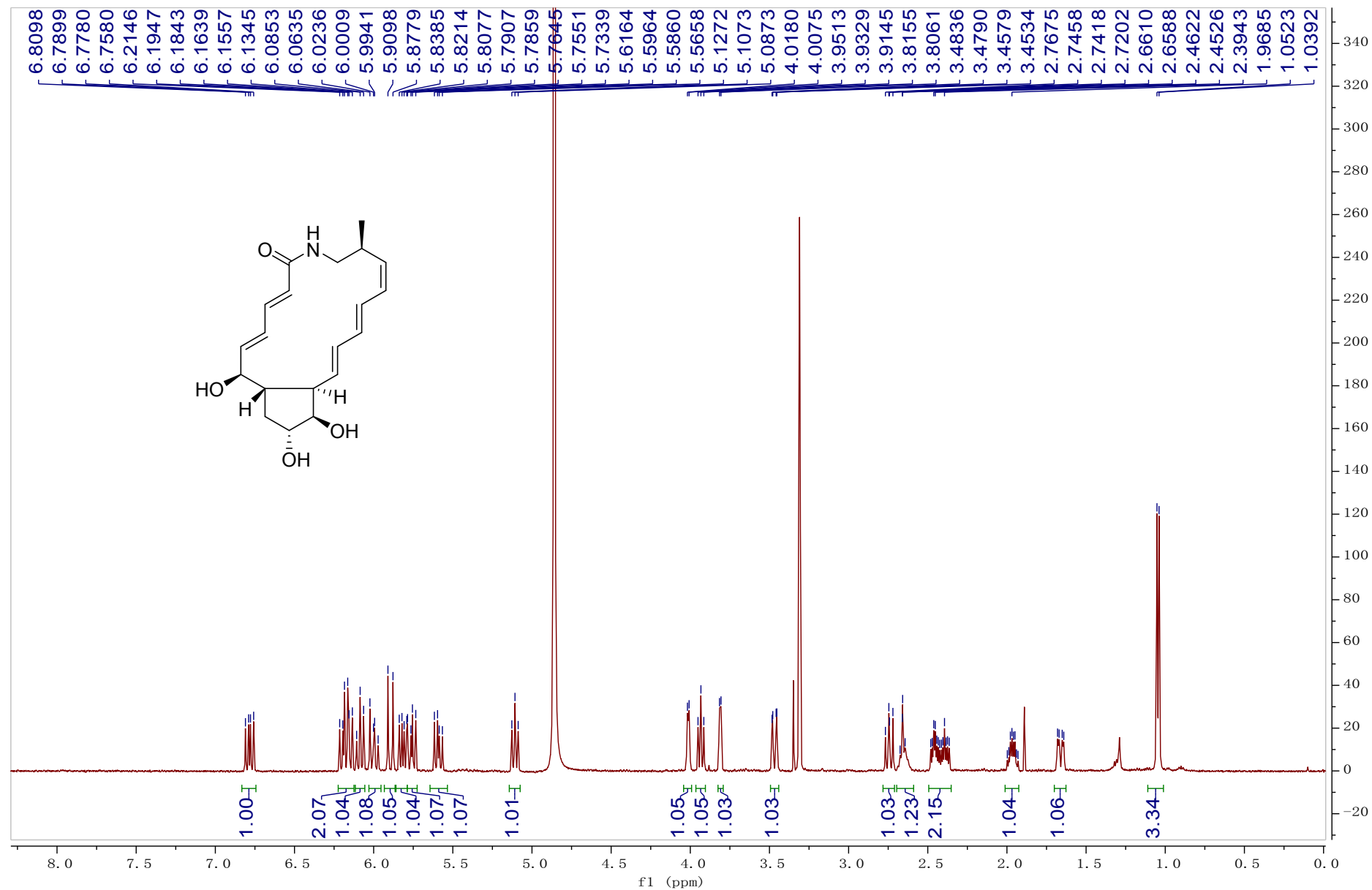


Figure S14. Expanded ^1H -NMR spectrum of cyclamenol E (**1**) in methanol- d_4 (500 MHz)

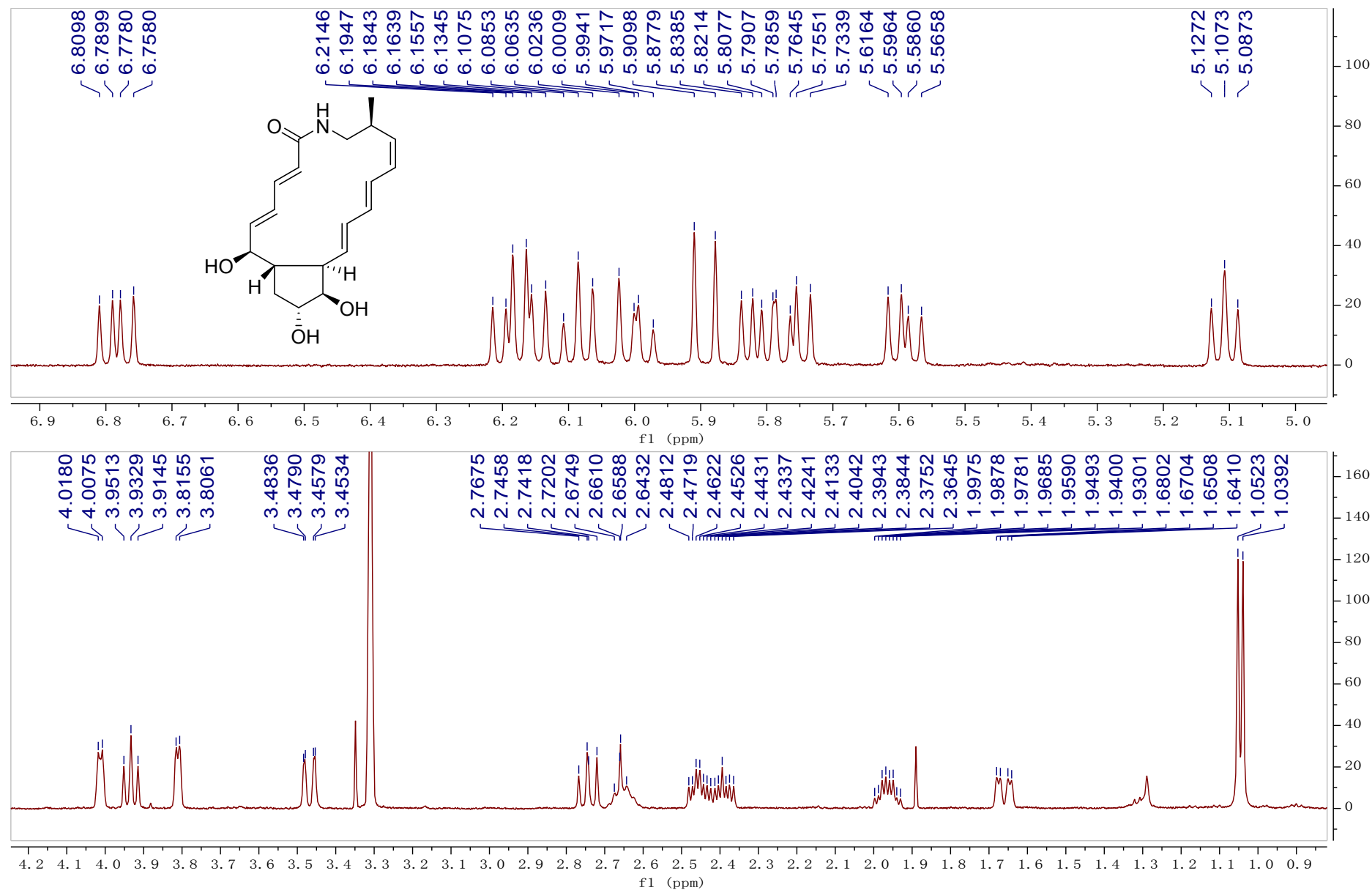


Figure S15. ^1H - ^1H COSY spectrum of cyclamenol E (**1**) in methanol- d_4 (500 MHz)

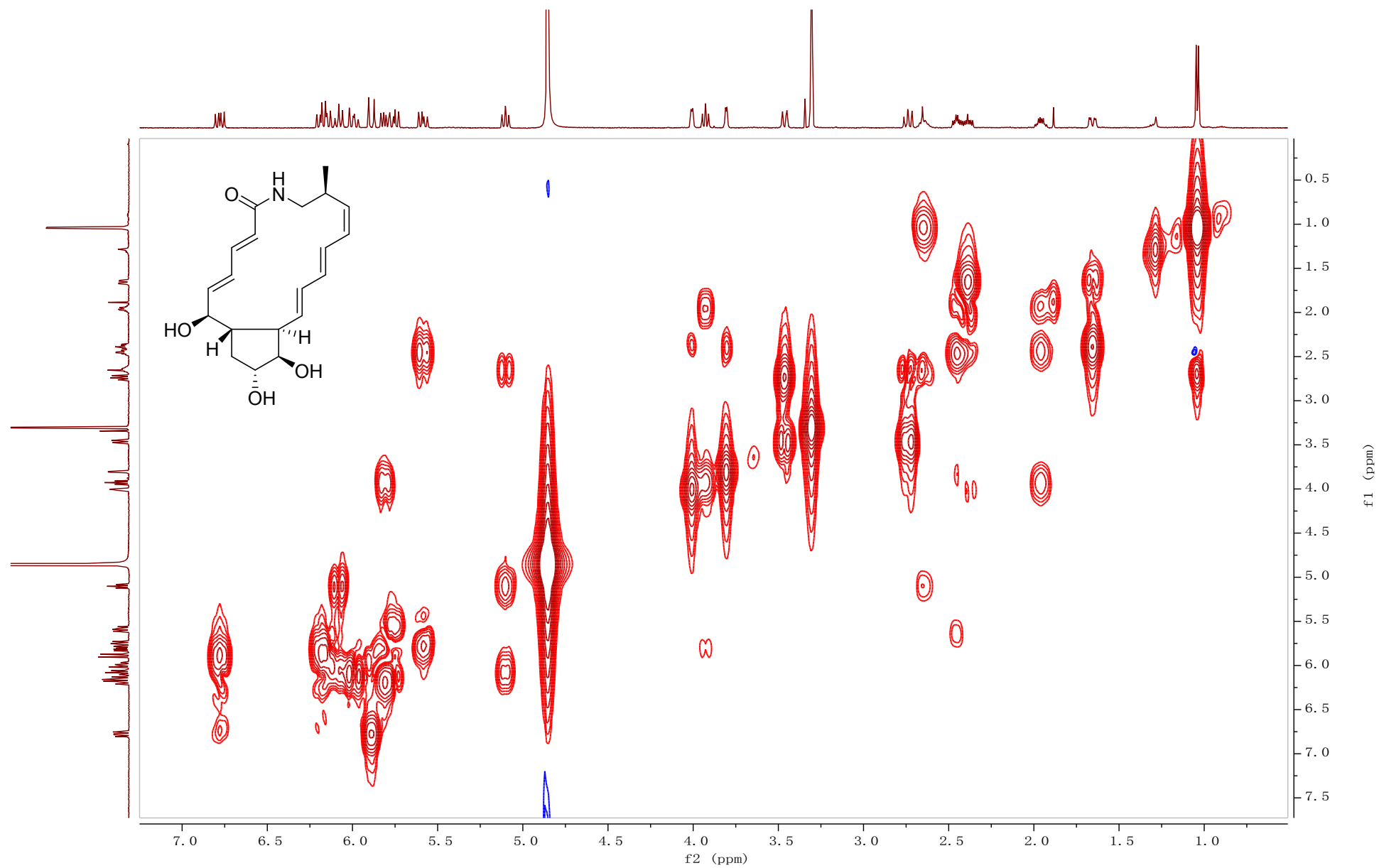


Figure S16. NOESY spectrum of cyclamenol E (**1**) in methanol- d_4 (500 MHz)

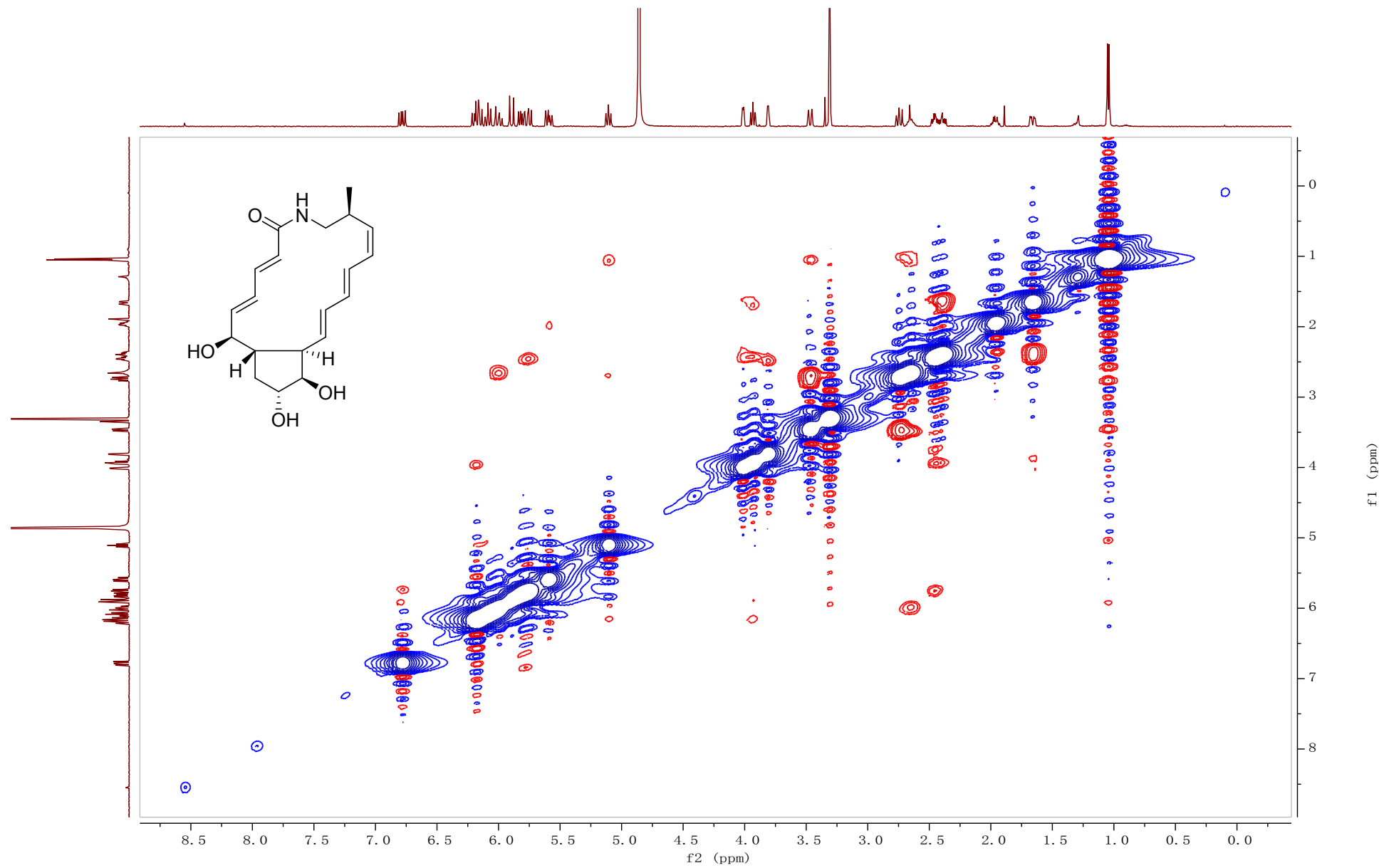


Figure S17. HRESIMS spectrum of cyclamenol F (2)

20190710-sjj-b-sx-1_190710103908 #41-43 RT: 0.32-0.34 AV: 3 NL: 1.56E7
T: FTMS + p ESI Full ms [150.00-1000.00]

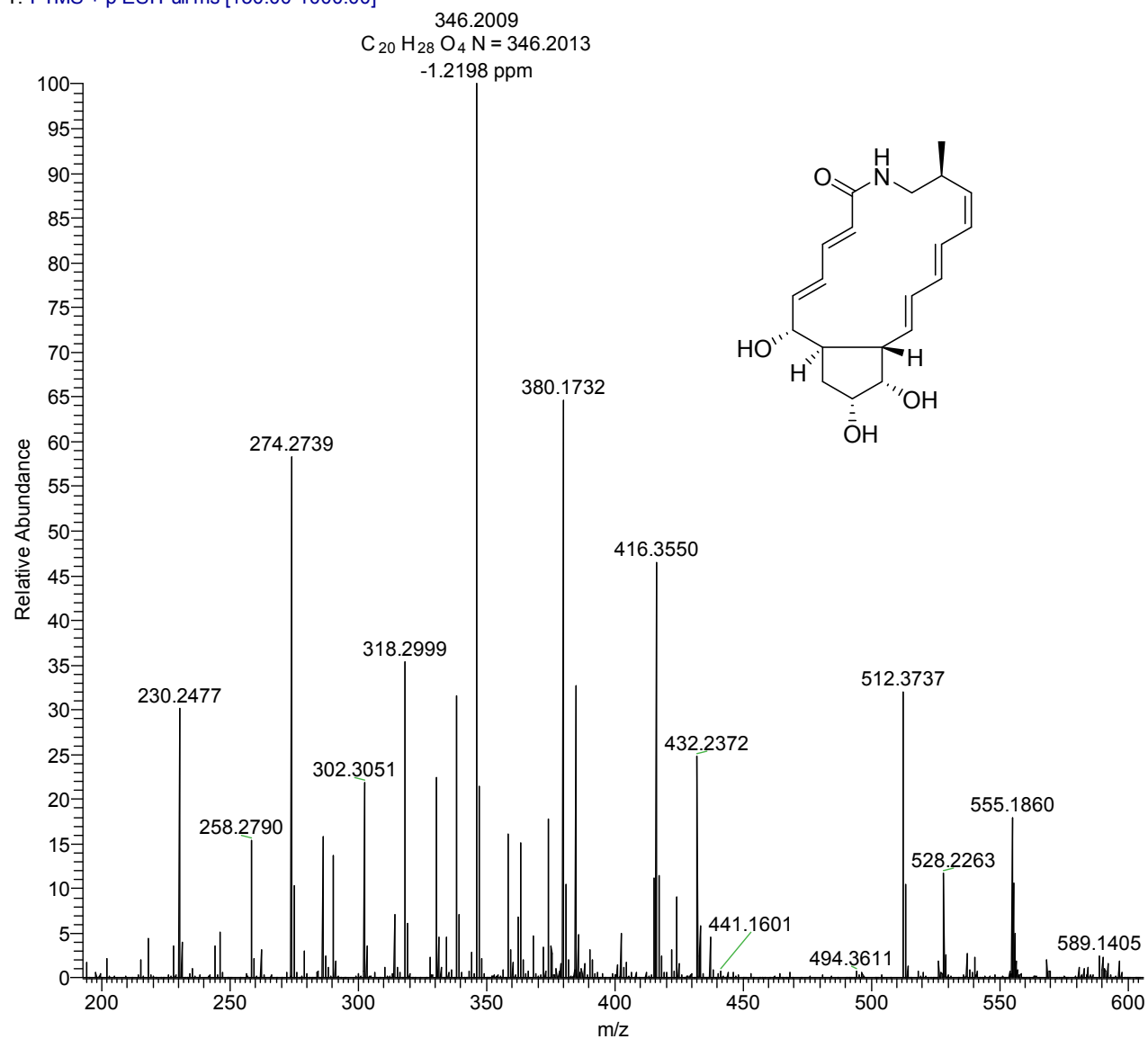


Figure S18. ^1H -NMR spectrum of cyclamenol F (**2**) in $\text{DMSO}-d_6$ (600 MHz)

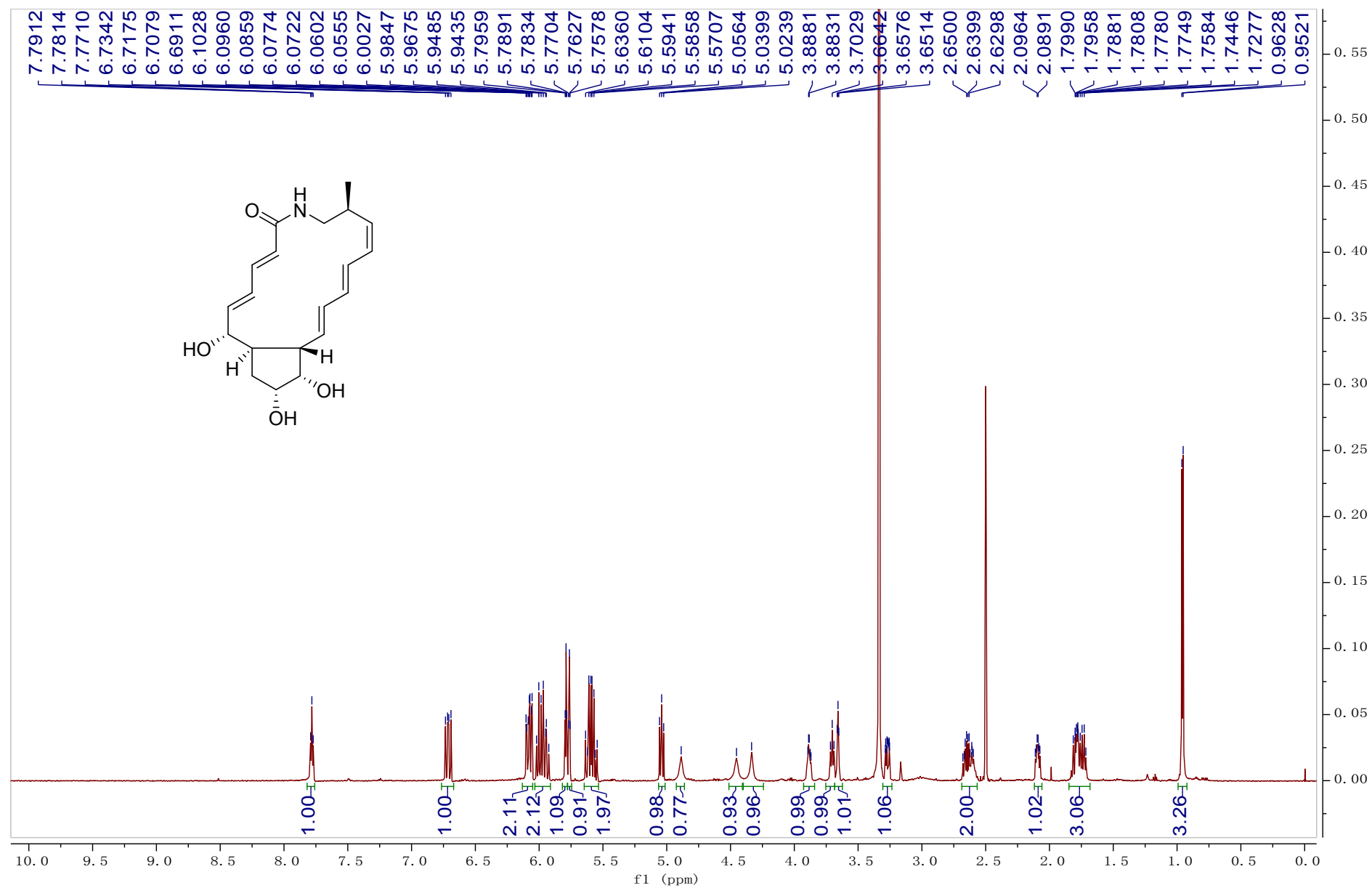


Figure S19. Expanded ^1H -NMR spectrum of cyclamenol F (**2**) in $\text{DMSO}-d_6$ (600 MHz)

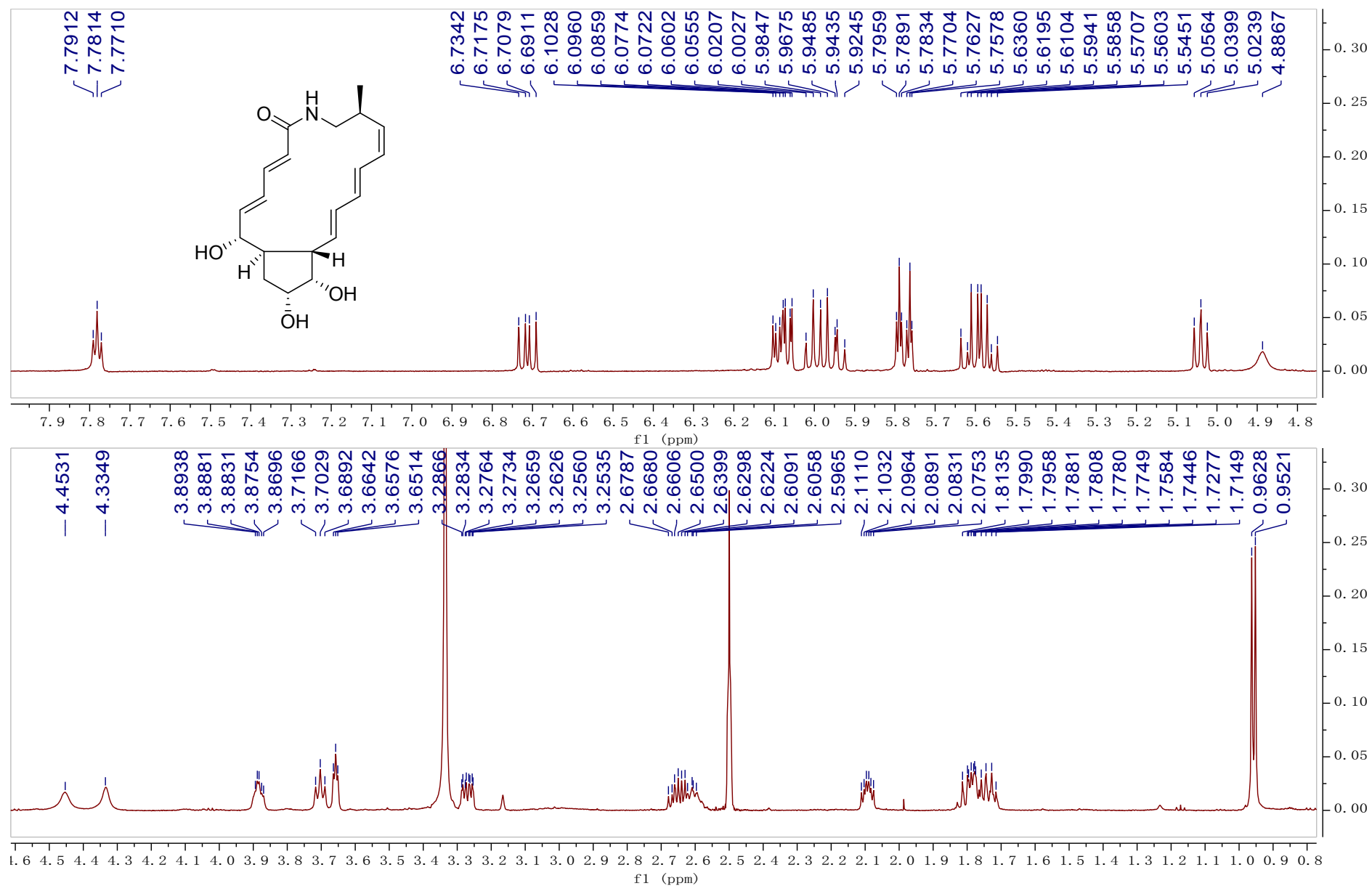


Figure S20. ^{13}C -NMR spectrum of cyclamenol F (**2**) in $\text{DMSO}-d_6$ (150 MHz)

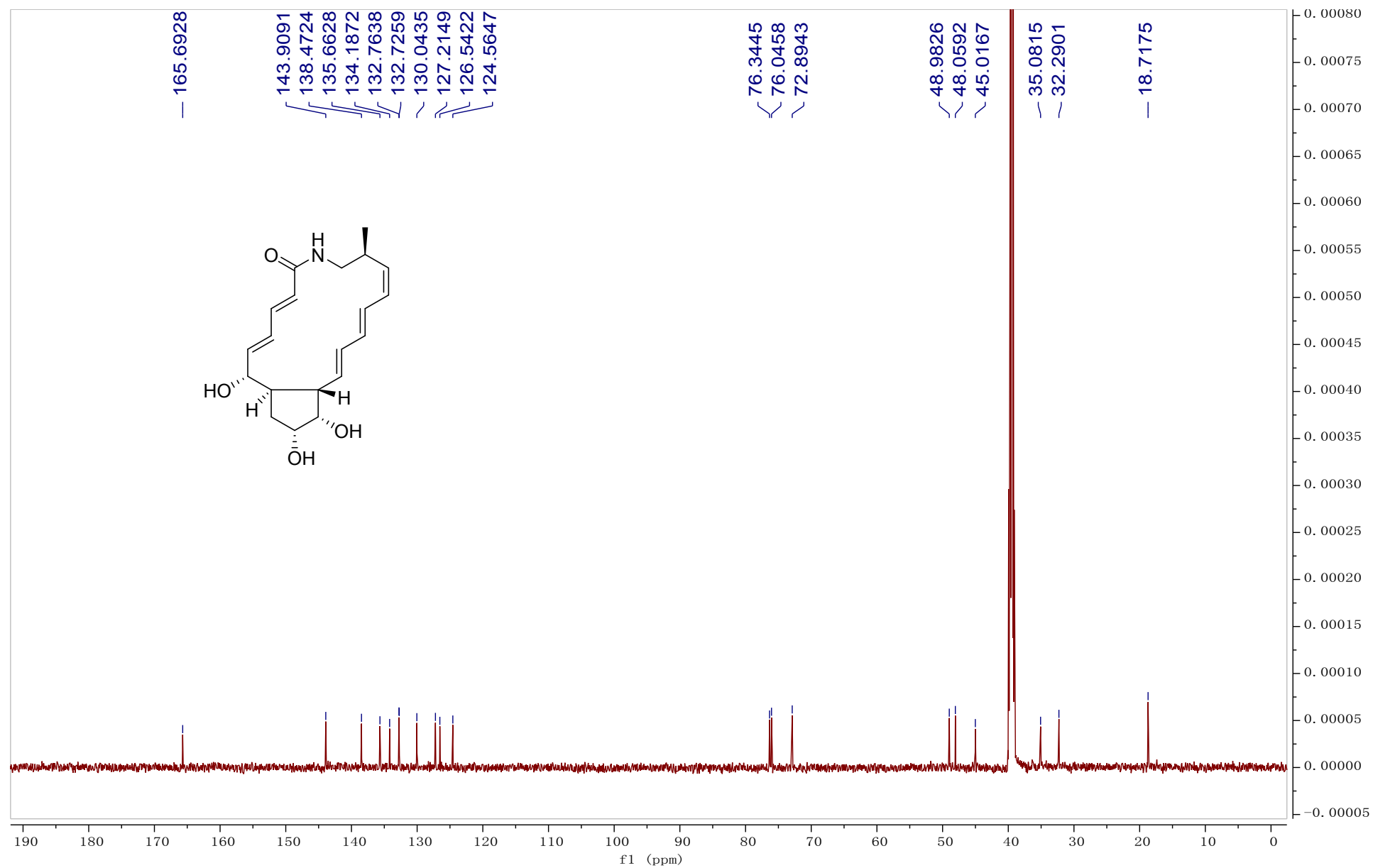


Figure S21. Expanded ^{13}C -NMR spectrum of cyclamenol F (**2**) in $\text{DMSO-}d_6$ (150 MHz)

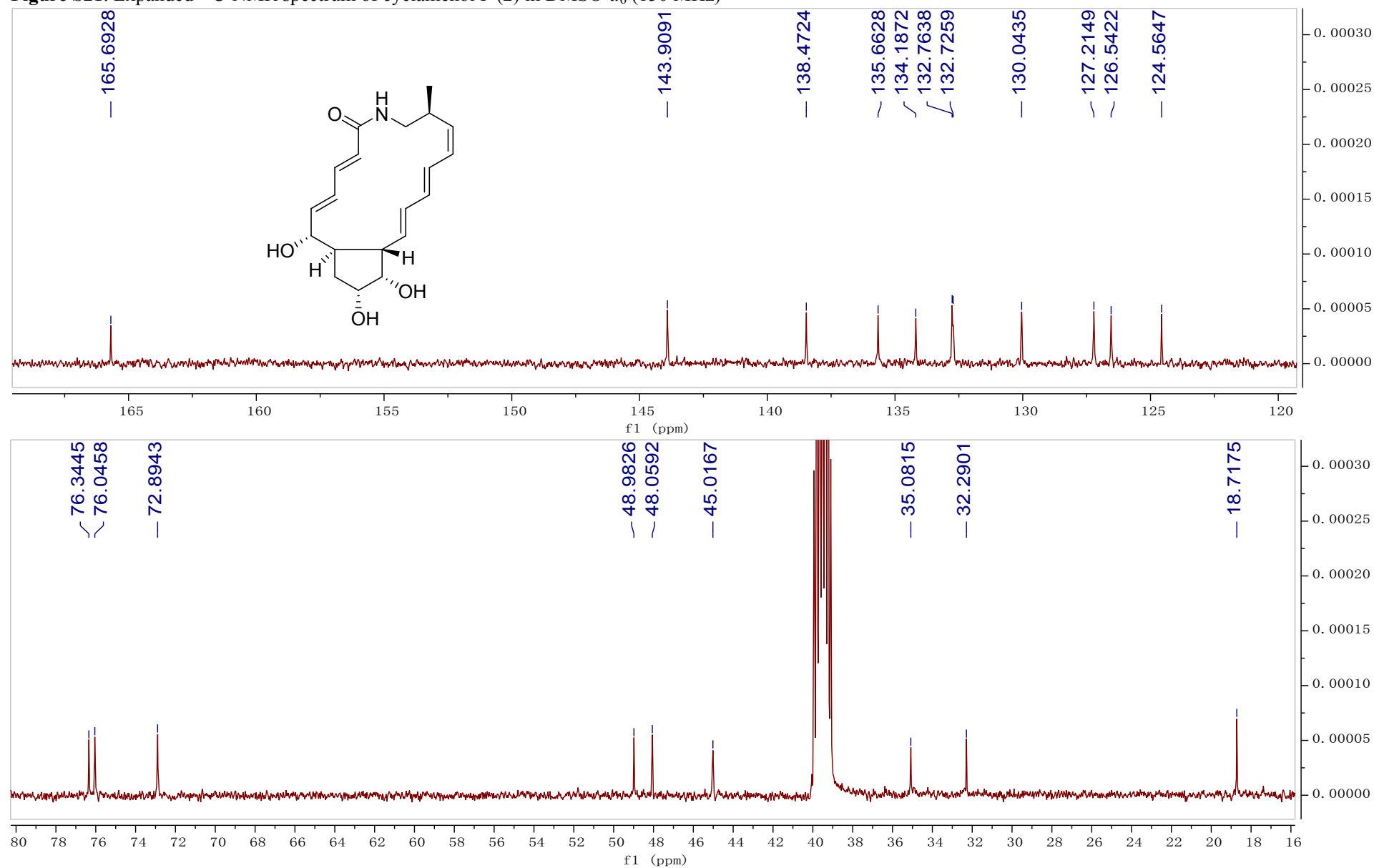


Figure S22. HSQC spectrum of cyclamenol F (**2**) in DMSO- d_6 (600 $\times$ 150 MHz)

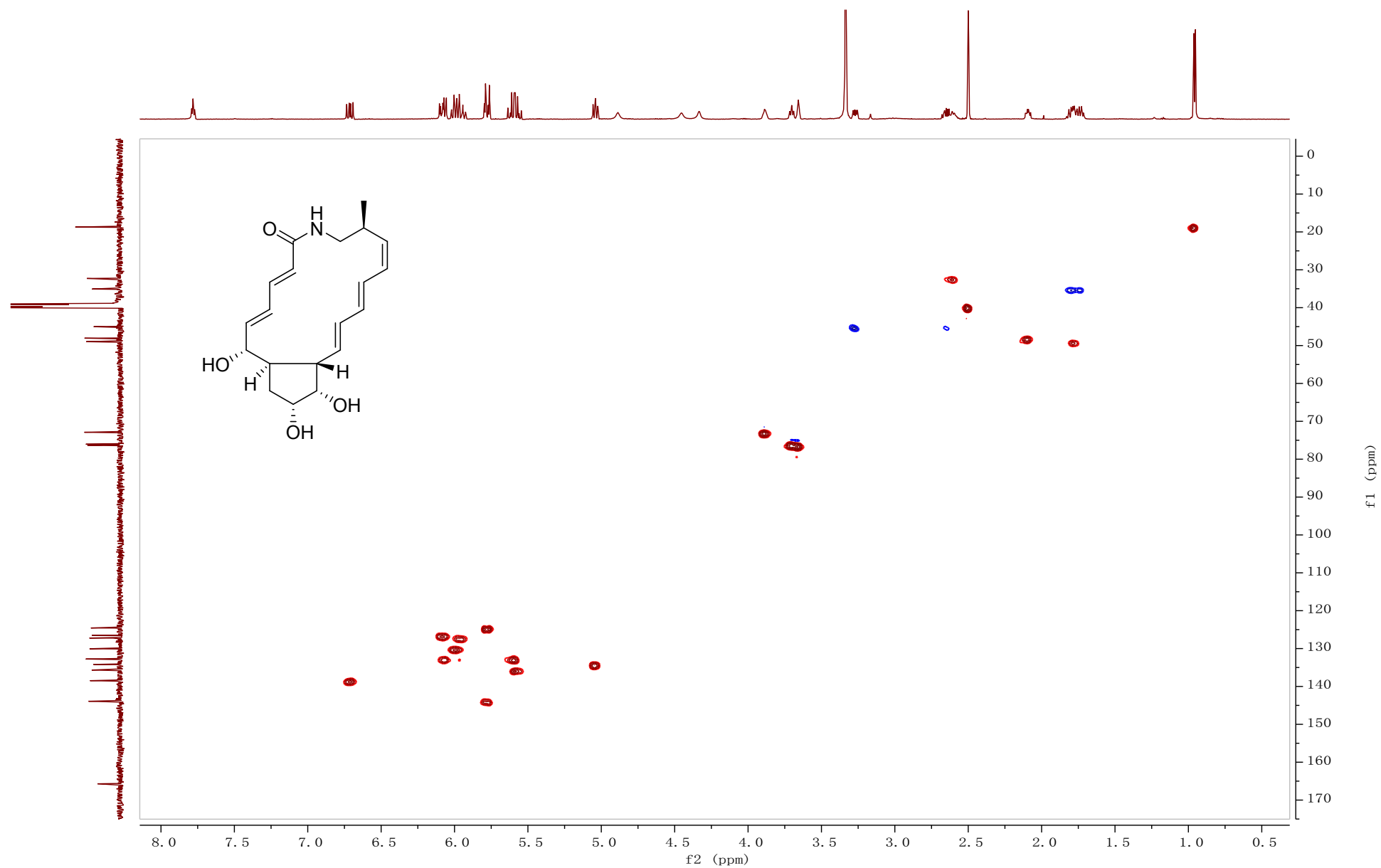


Figure S23. ^1H - ^1H COSY spectrum of cyclamenol F (**2**) in $\text{DMSO}-d_6$ (600 MHz)

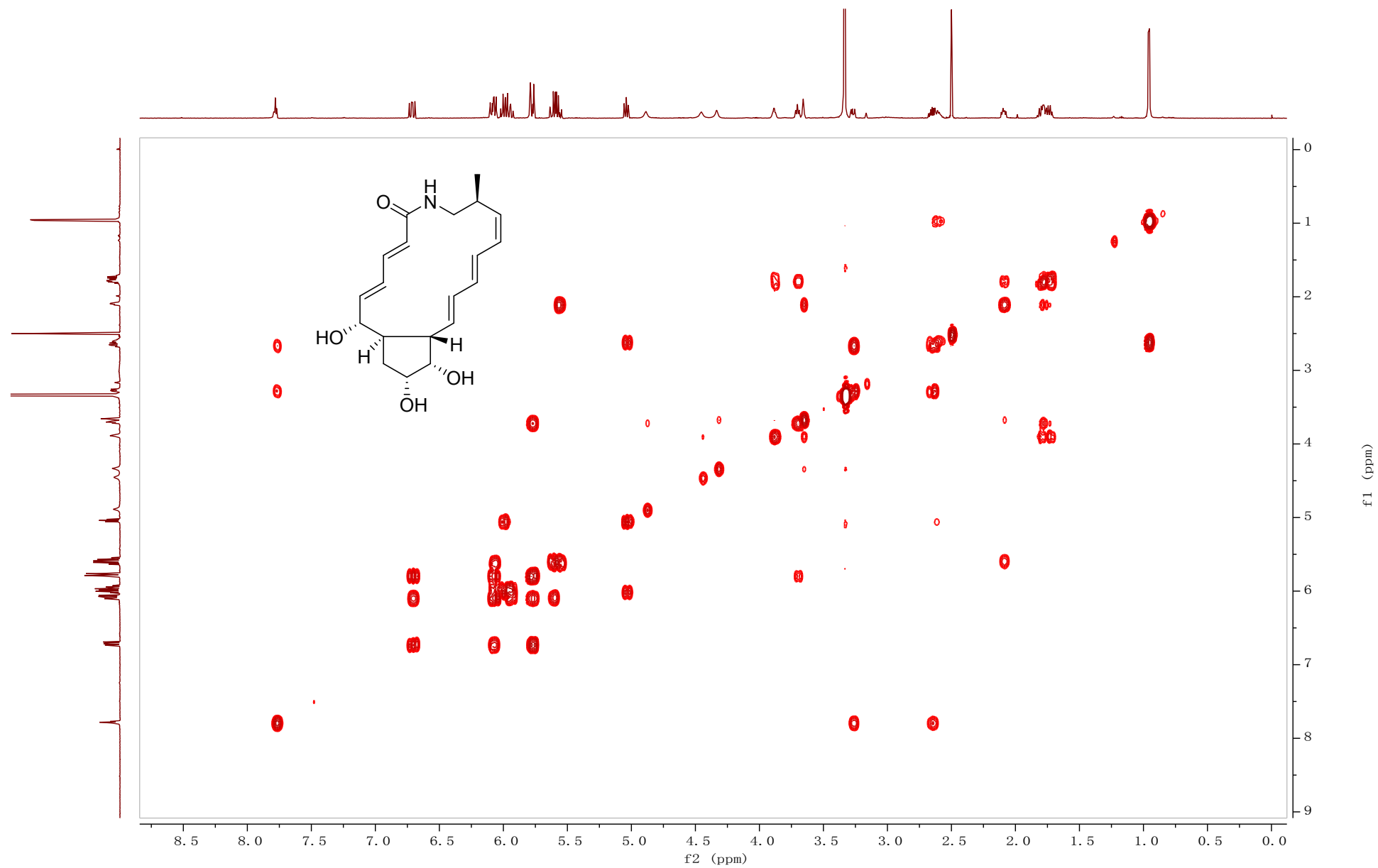


Figure S24. HMBC spectrum of cyclamenol F (2) in DMSO- d_6 (600 $\times$ 150 MHz)

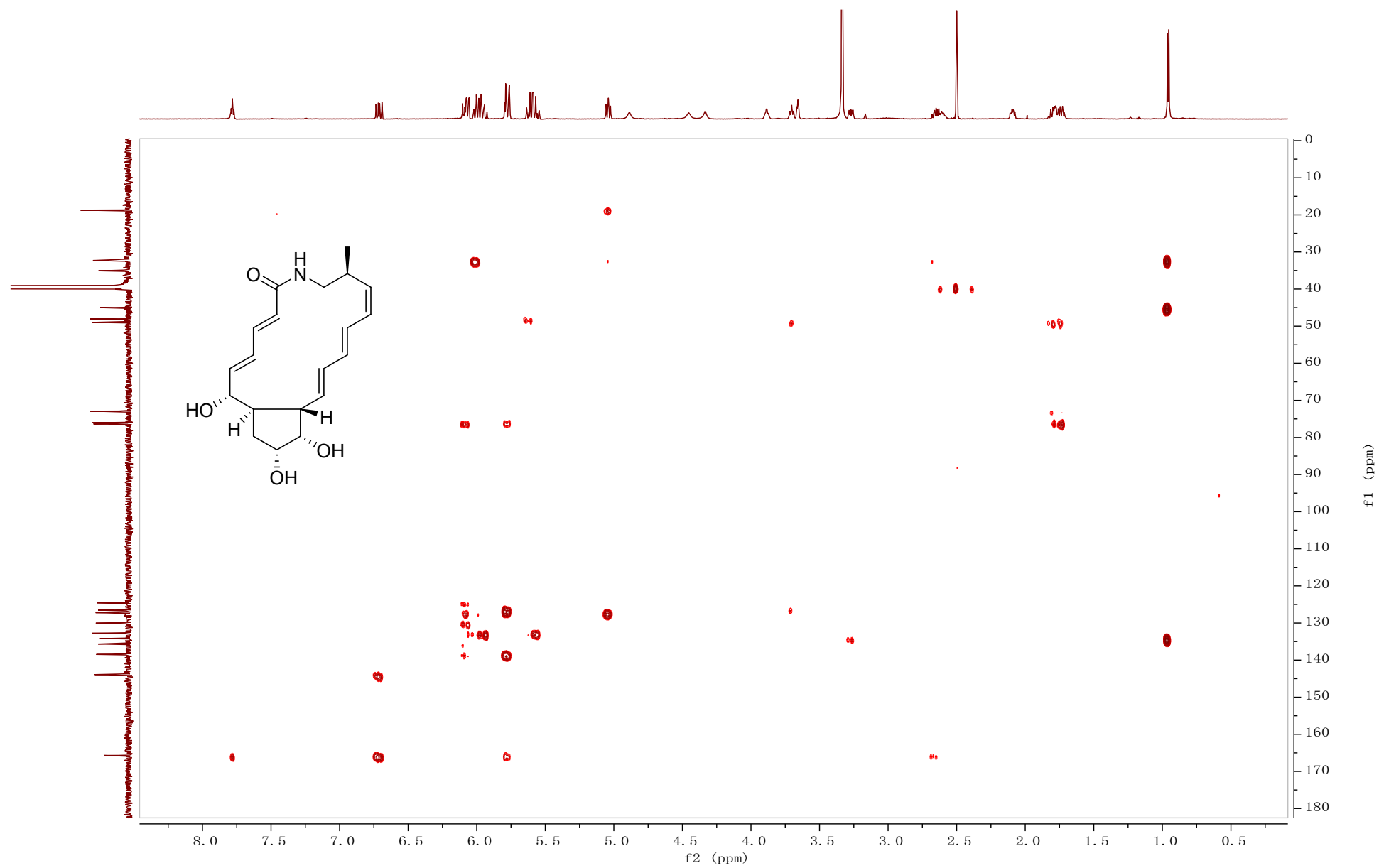


Figure S25. NOESY spectrum of cyclamenol F (**2**) in DMSO- d_6 (600 MHz)

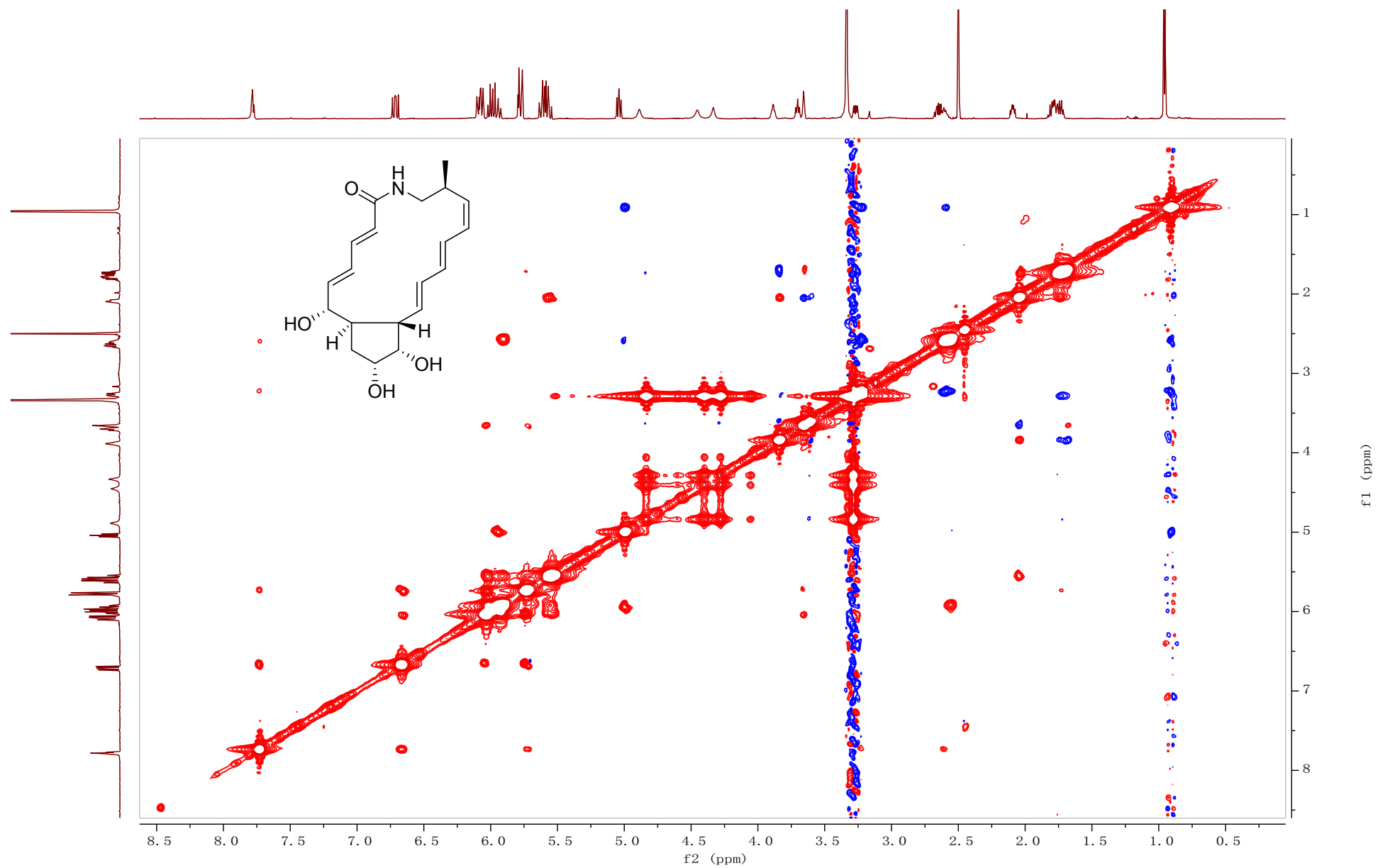


Figure S26. HRESIMS spectrum of compound **1a**

20190911-SJJ-B-10-BCHA1_190911144823 #24 RT: 0.19 AV: 1 NL: 8.53E5

T: FTMS + c ESI Full ms [50.00-2000.00]

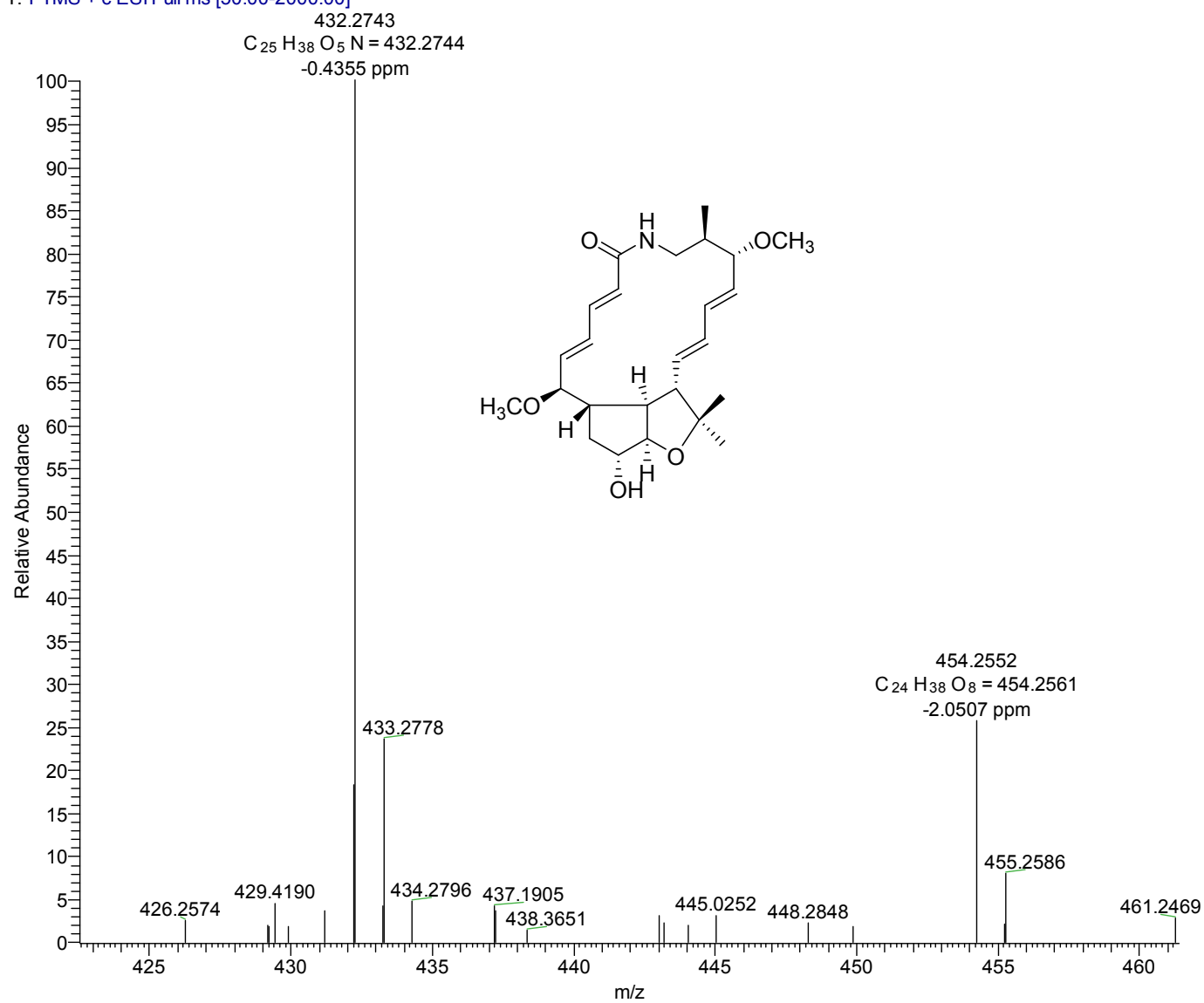


Figure S27. ^1H -NMR spectrum of compound **1a** in CDCl_3 (500 MHz)

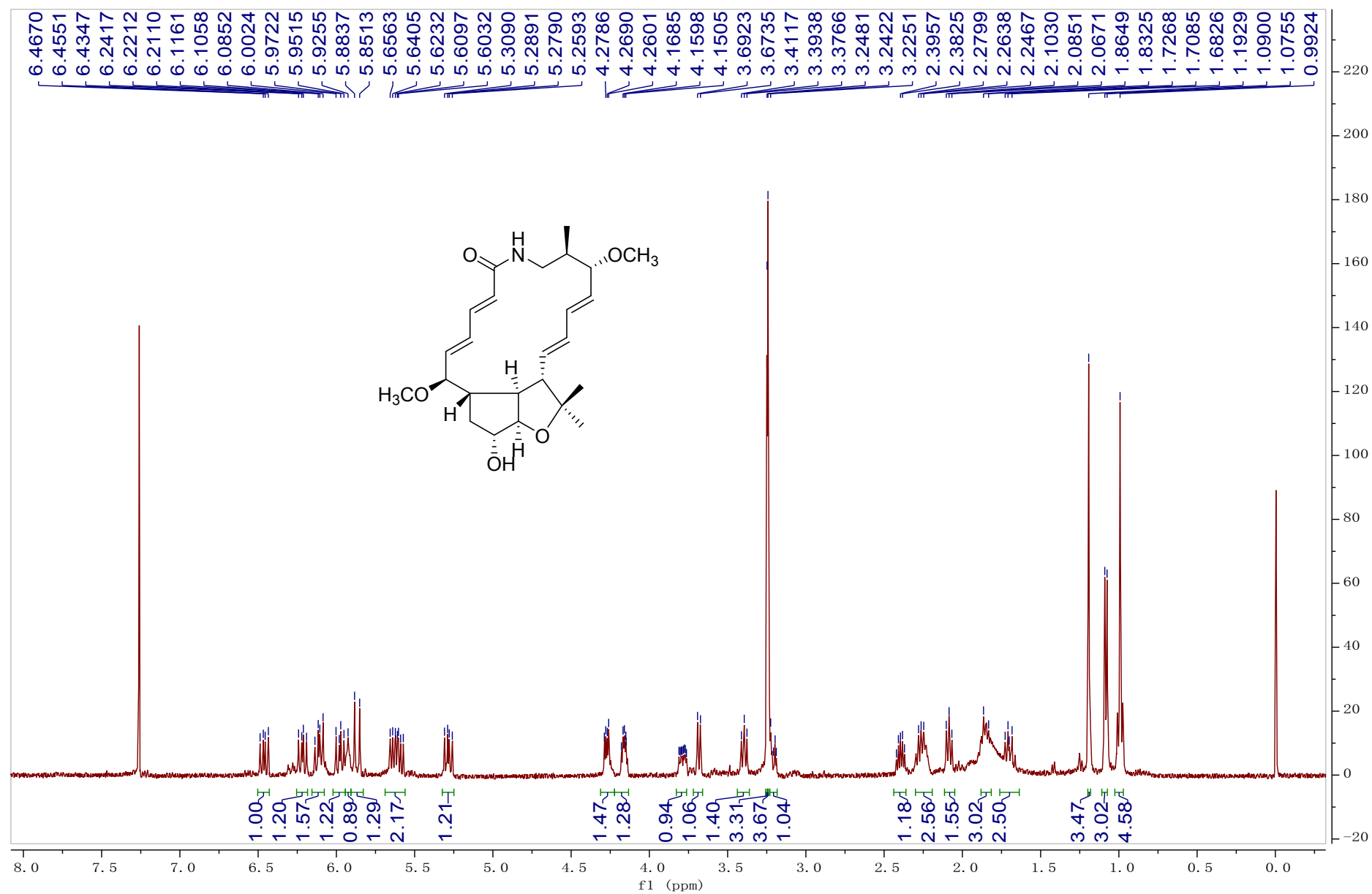


Figure S28. Expanded ^1H -NMR spectrum of compound **1a** in CDCl_3 (500 MHz)

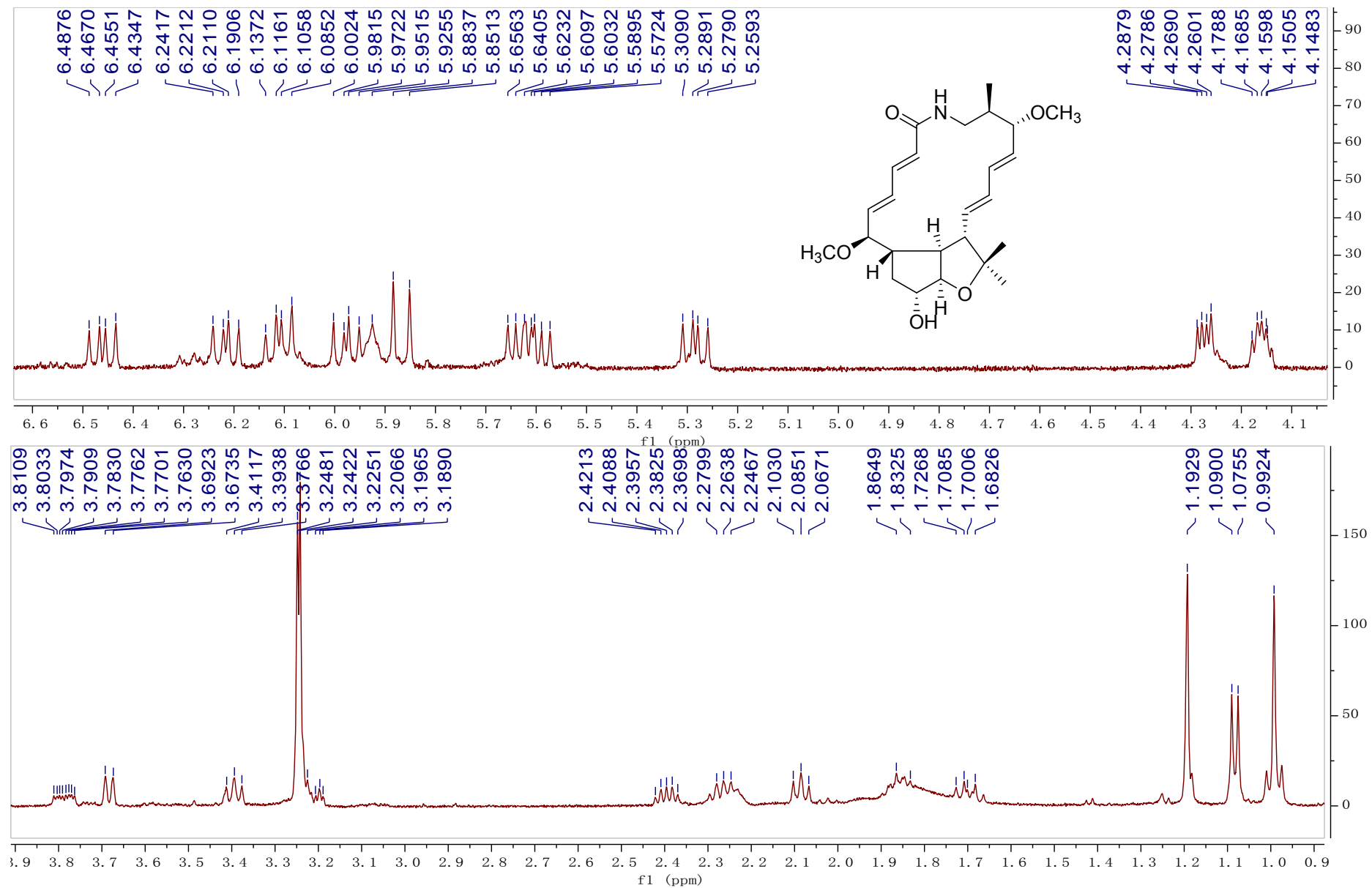


Figure S29. HSQC spectrum of compound **1a** in CDCl₃ (500 × 125 MHz)

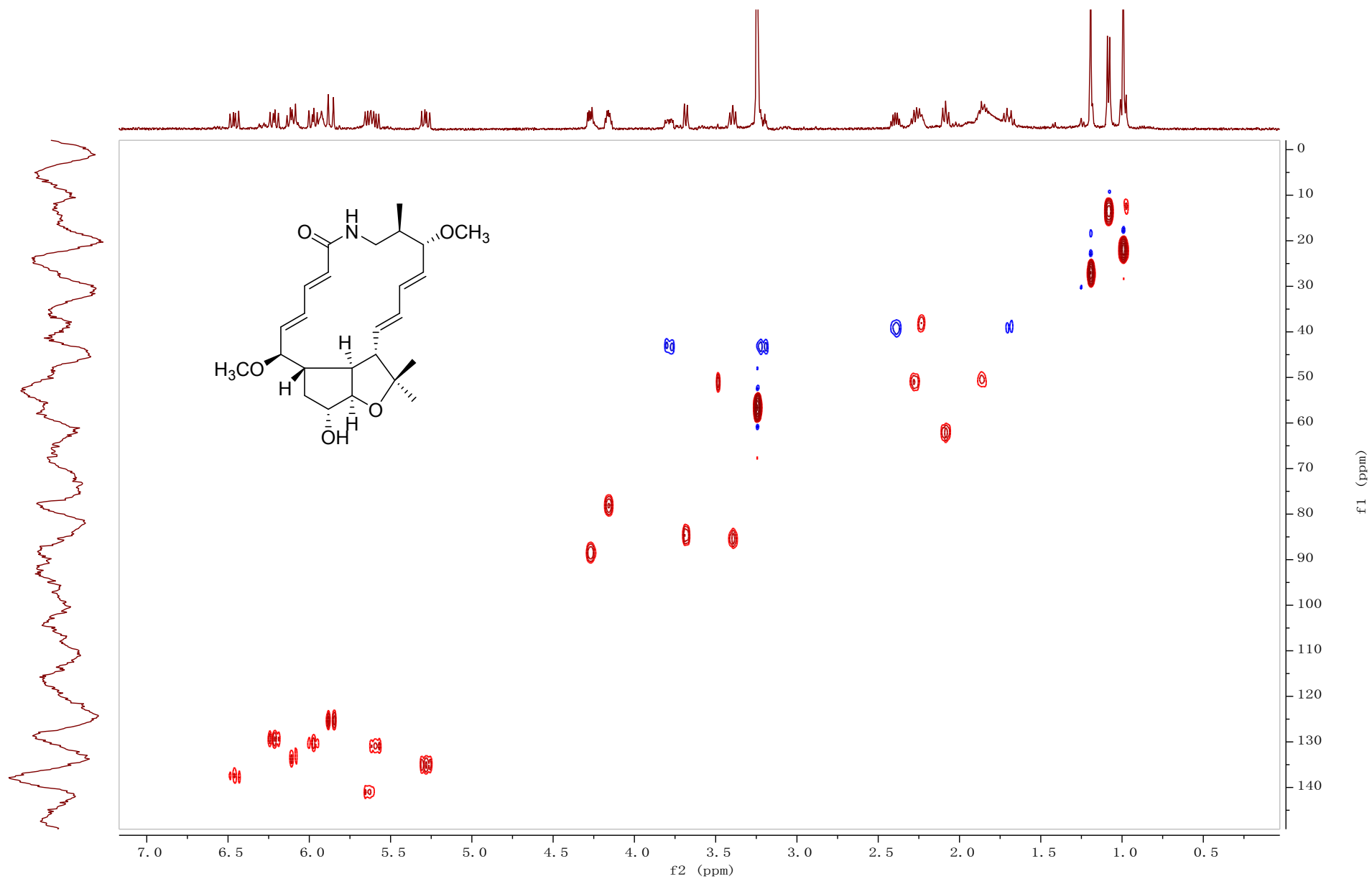


Figure S30. ^1H - ^1H COSY spectrum of compound **1a** in CDCl_3 (500 MHz)

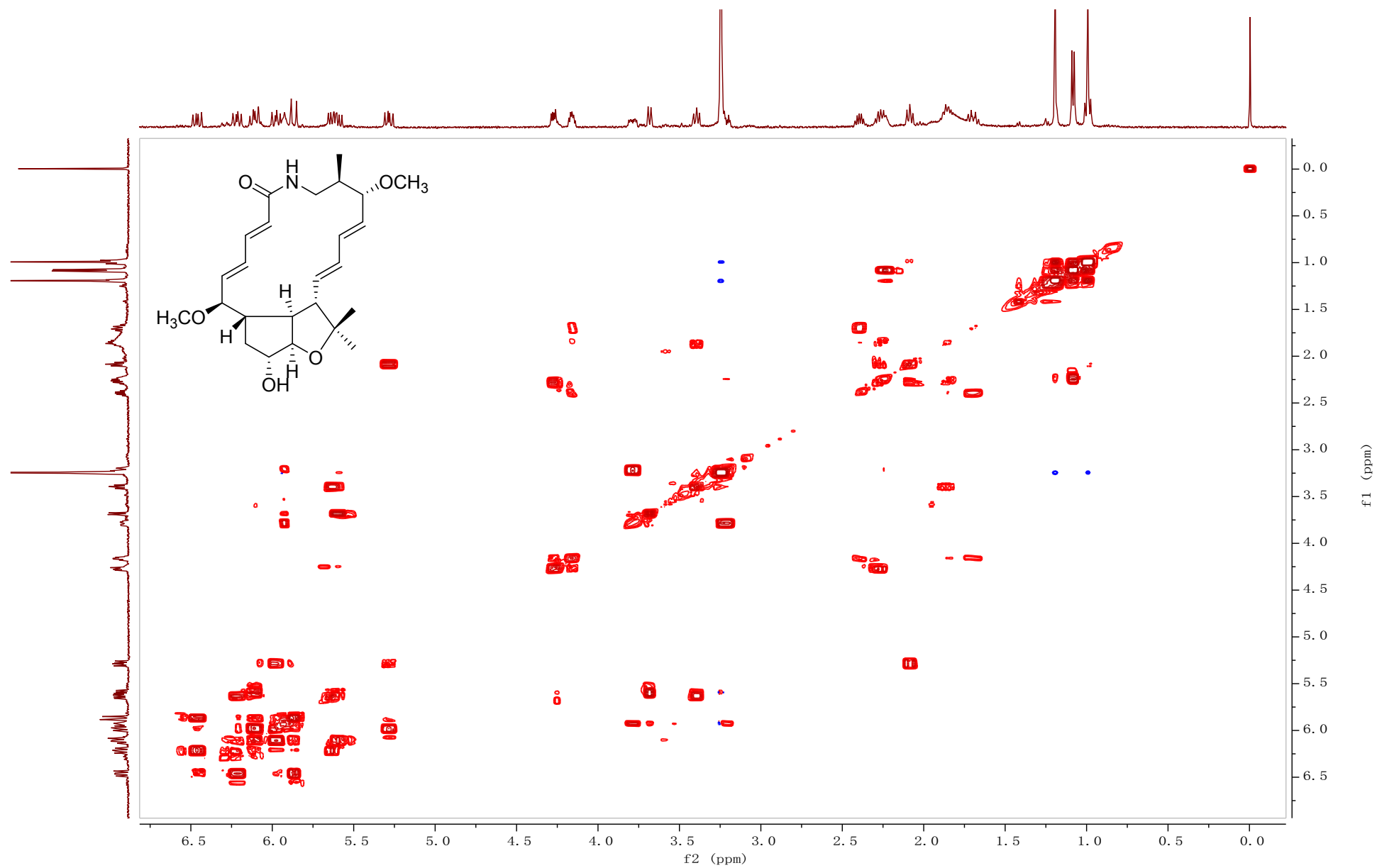


Figure S31. HMBC spectrum of compound **1a** in CDCl₃ (500 × 125 MHz)

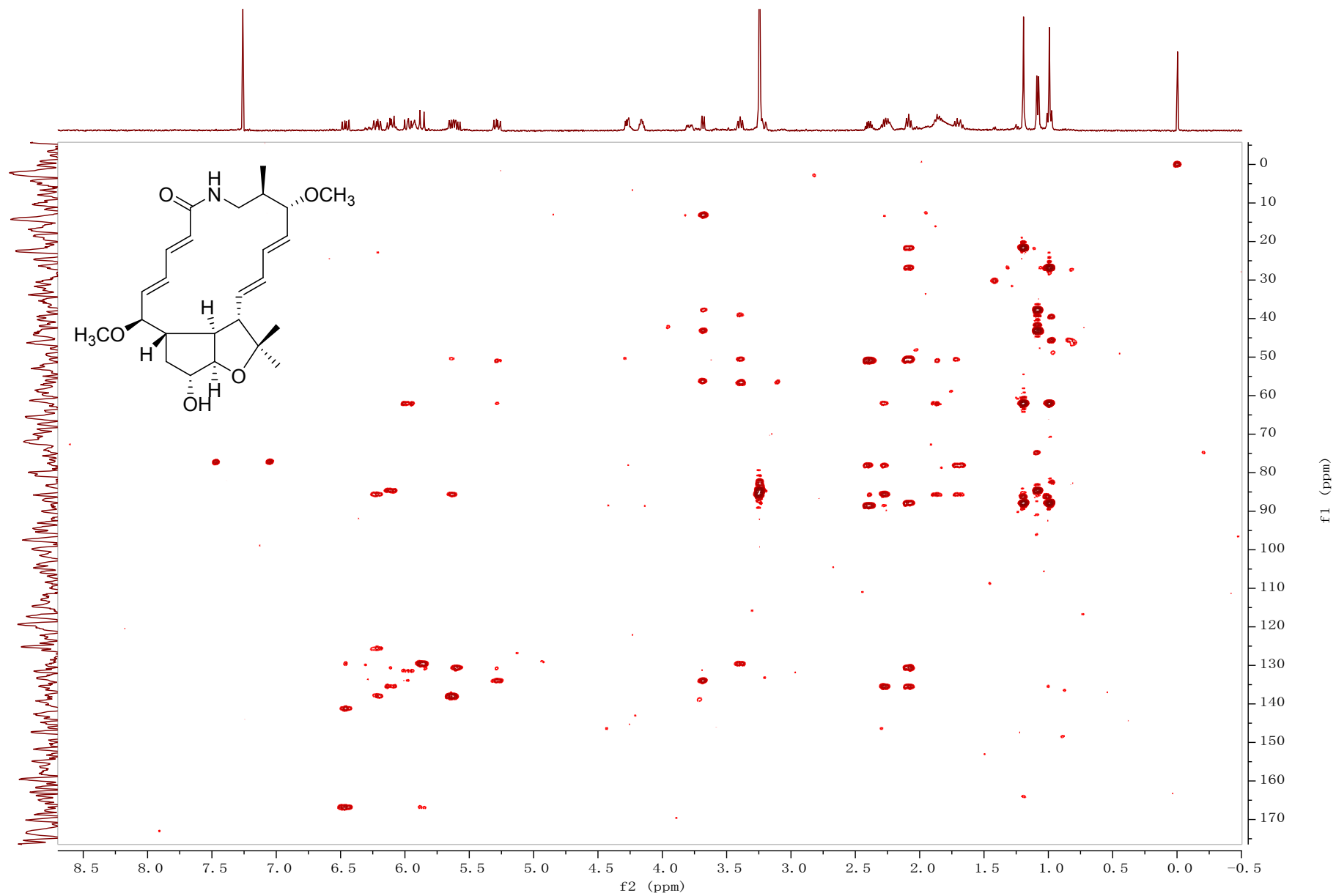


Figure S32. NOESY spectrum of compound **1a** in CDCl₃ (500 MHz)

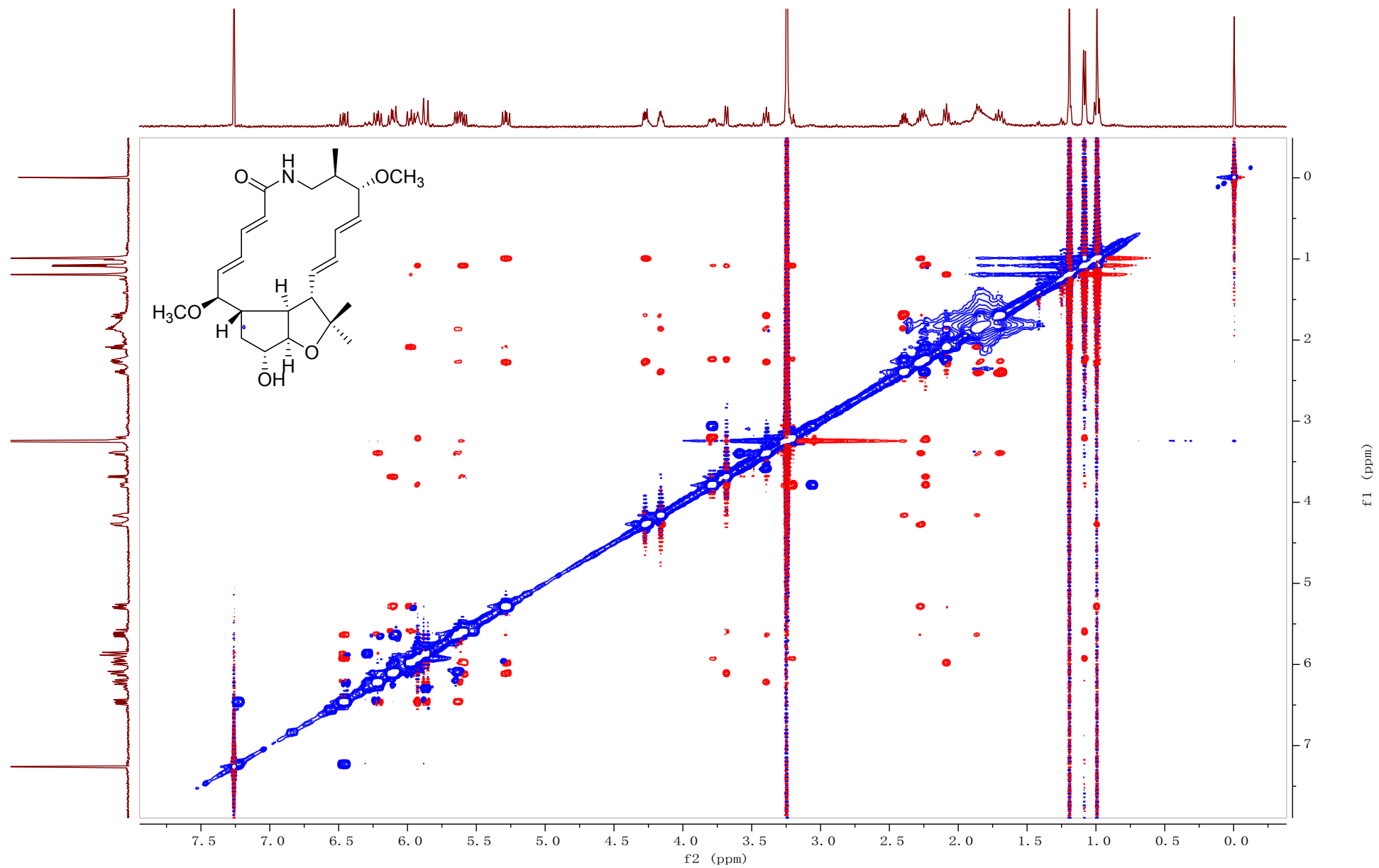


Figure S33. ^1H -NMR spectrum of (*S*)-MTPA ester (**1aa**) in CDCl_3 (500 MHz)

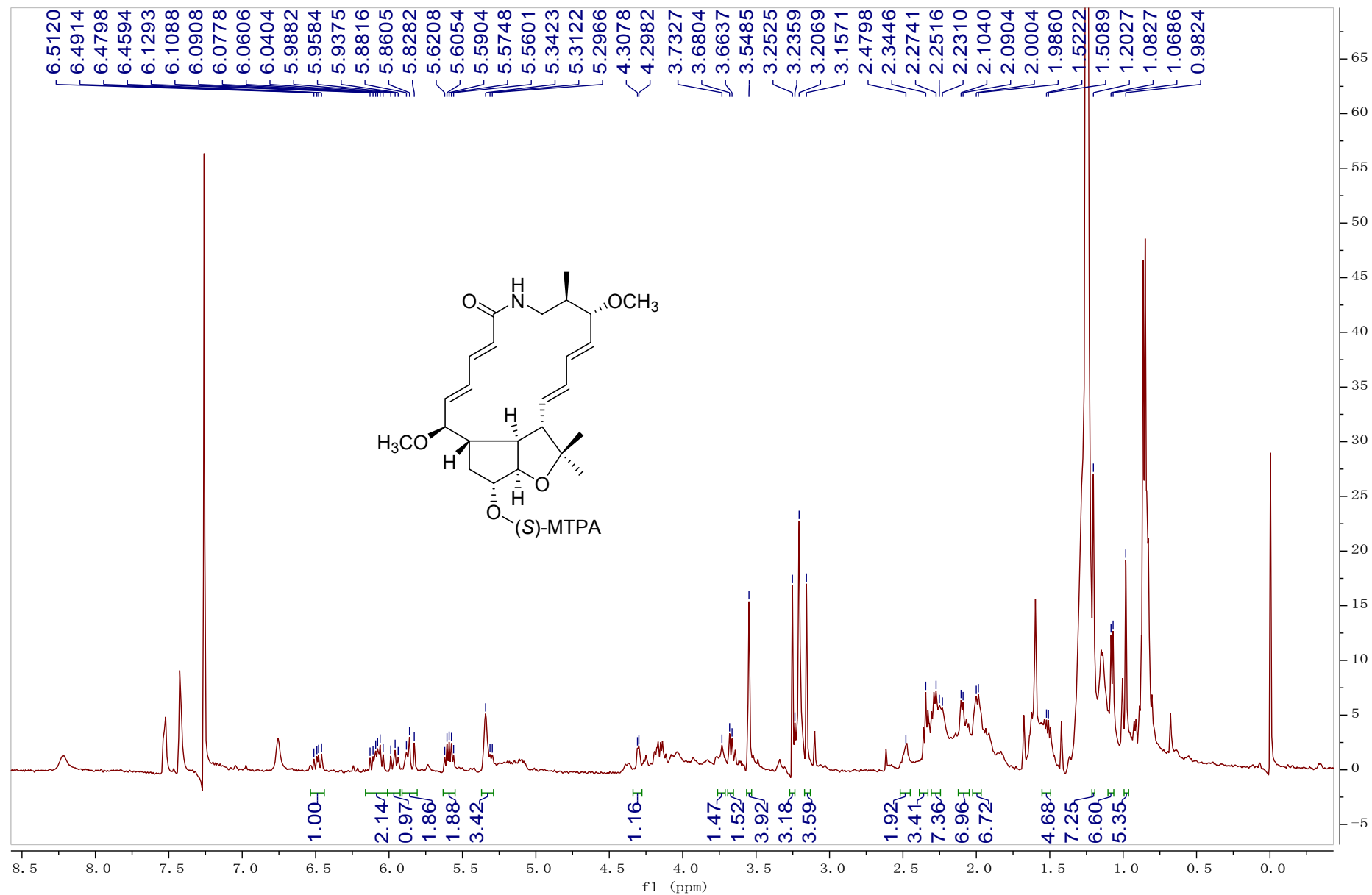
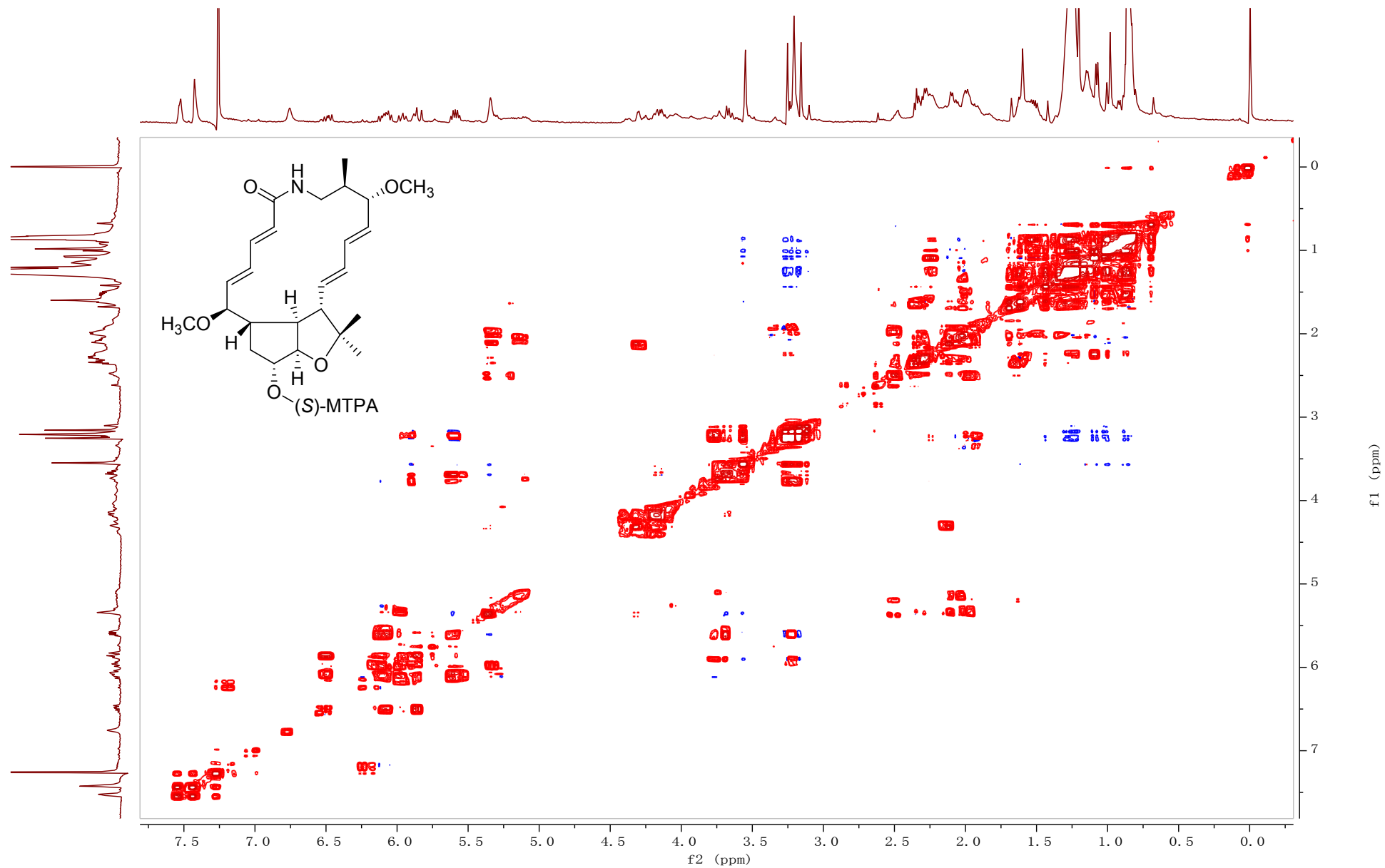


Figure S34. ^1H - ^1H COSY spectrum of (*S*)-MTPA ester (**1aa**) in CDCl_3 (500 MHz)



[illegible]

Figure S36. ^1H - ^1H COSY spectrum of (*R*)-MTPA ester (**1ab**) in CDCl_3 (500 MHz)

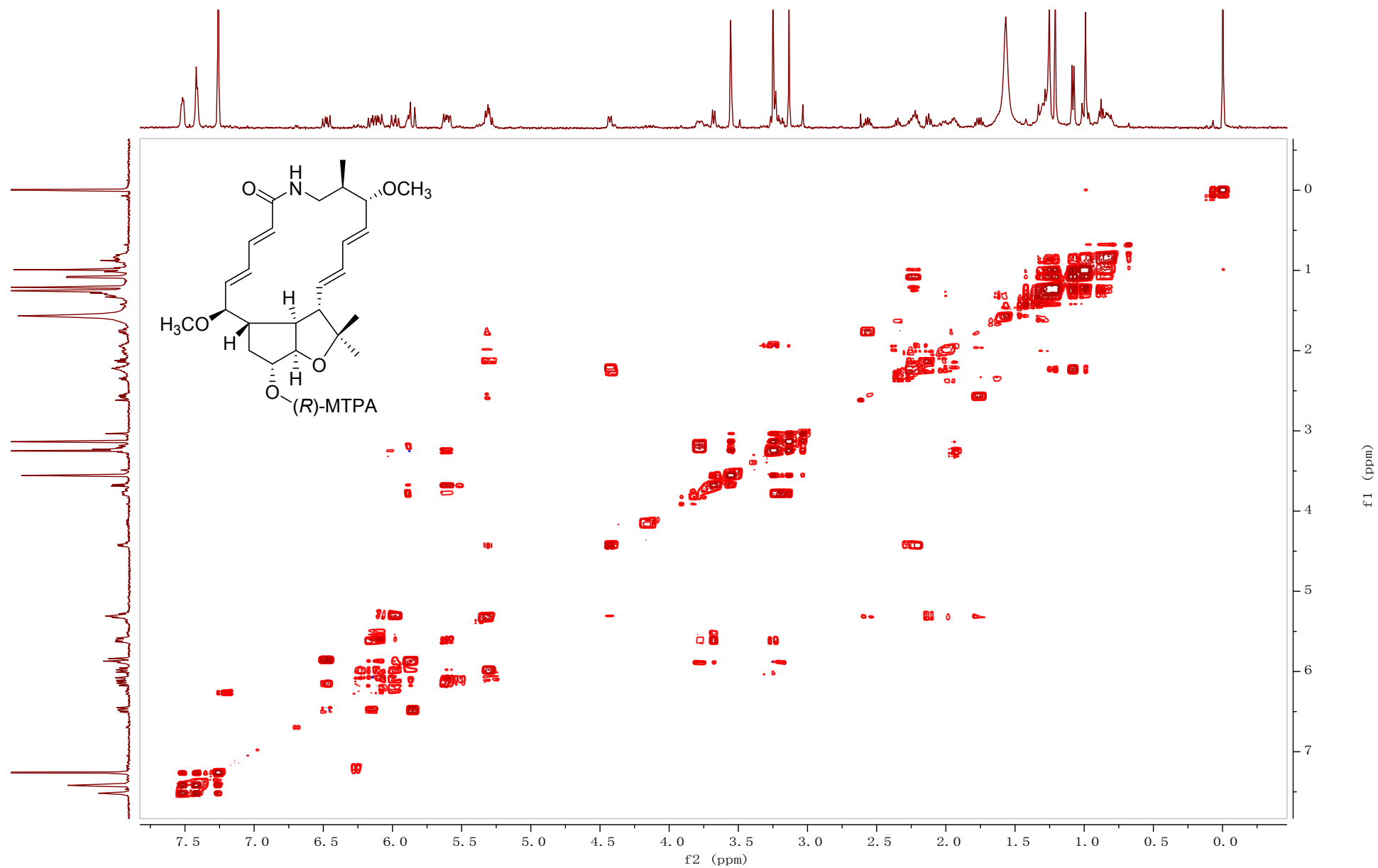


Figure S37. HRESIMS spectrum of compound **2a**

20190903-SJJ-B-SX-1-BCHA_190903153816 #41-42 RT: 0.35-0.36 AV: 2 SB: 7 0.05-0.10 NL: 2.47E7

T: FTMS + p ESI Full ms [180.00-1000.00]

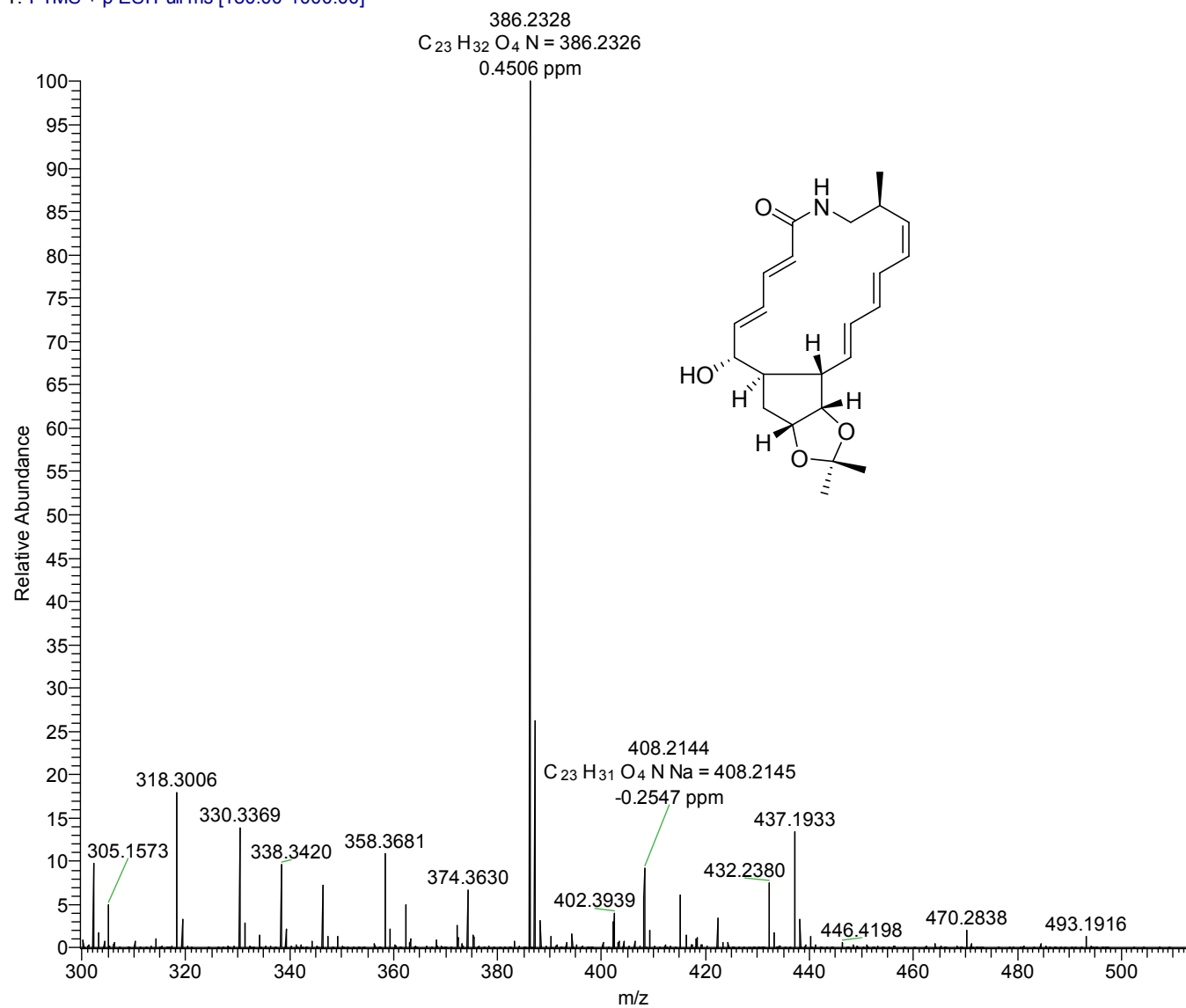
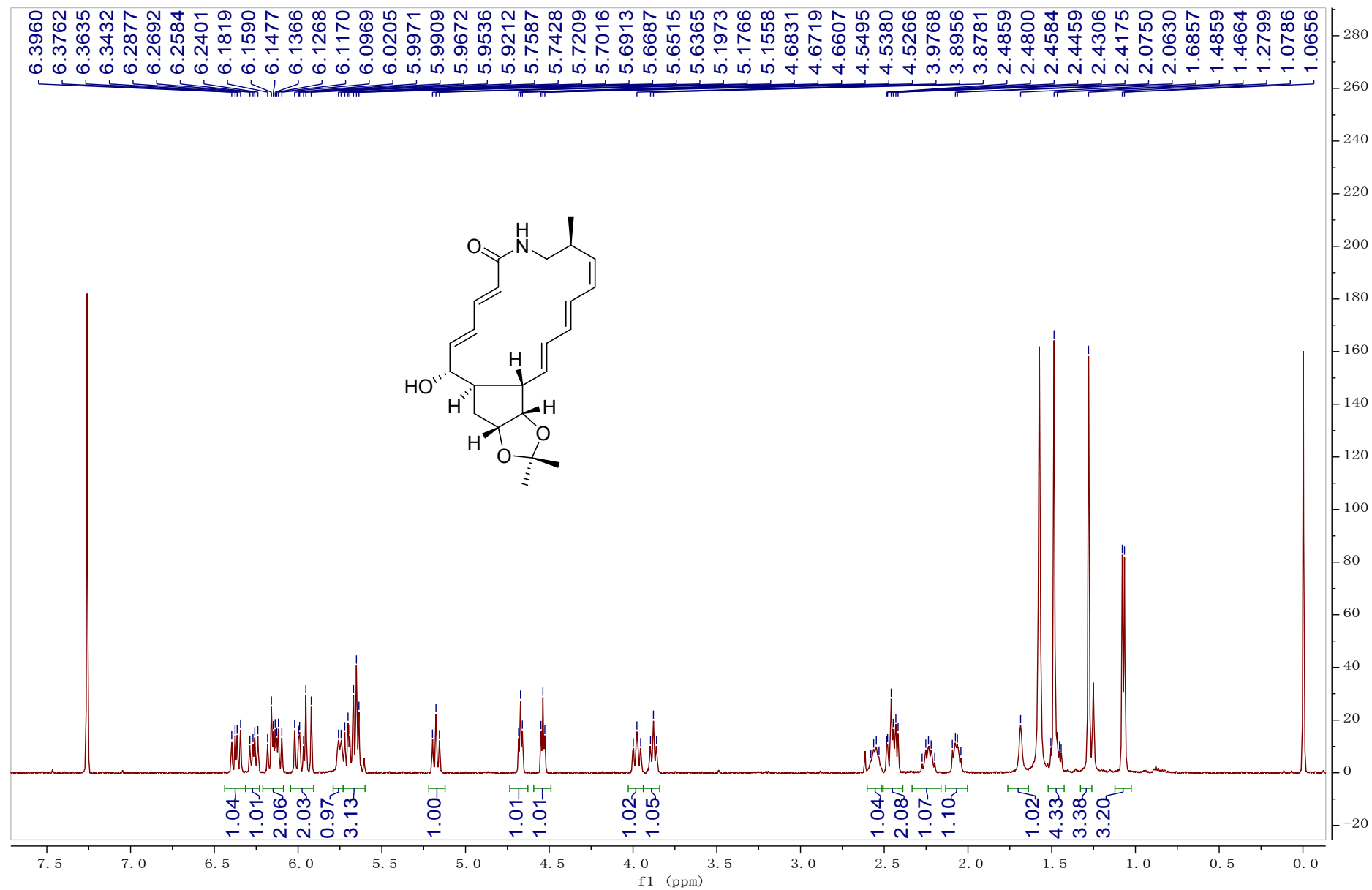


Figure S38. ^1H -NMR spectrum of compound **2a** in CDCl_3 (500 MHz)



The figure displays two stacked ¹H NMR spectra of compound 1, with the chemical structure of the compound shown in the center of the bottom spectrum.

Top Spectrum (Aromatic Region): The x-axis ranges from 3.8 to 6.5 ppm. The spectrum shows several multiplets in the aromatic region. The peak list (ppm) is: 6.3960, 6.3762, 6.3635, 6.3432, 6.2877, 6.2692, 6.2584, 6.2401, 6.1819, 6.1590, 6.1477, 6.1366, 6.1268, 6.1170, 6.0969, 6.0205, 5.9971, 5.9909, 5.9672, 5.9536, 5.9212, 5.7587, 5.7428, 5.7209, 5.7016, 5.6913, 5.6687, 5.6515, 5.6365, 5.1973, 5.1766, 5.1558, 4.6831, 4.6719, 4.6607, 4.5495, 4.5380, 4.5266, 3.9983, 3.9768, 3.9543, 3.8956, 3.8781, 3.8594.

Bottom Spectrum (Aliphatic Region): The x-axis ranges from 0.9 to 2.8 ppm. The spectrum shows several multiplets in the aliphatic region. The peak list (ppm) is: 2.5797, 2.5628, 2.5472, 2.5312, 2.4859, 2.4800, 2.4584, 2.4459, 2.4306, 2.4175, 2.2737, 2.2519, 2.2359, 2.2197, 2.1984, 2.0933, 2.0750, 2.0630, 2.0422, 1.6857, 1.5048, 1.4859, 1.4664, 1.4535, 1.4435, 1.2799, 1.0786, 1.0656.

Chemical Structure of Compound 1: The structure is a complex polycyclic molecule. It features a central five-membered ring with an oxygen atom. Attached to this ring are two side chains, each containing a double bond and a hydroxyl group. The structure is shown in a 3D representation with wedges and dashes indicating stereochemistry.

Figure S40. ^1H - ^1H COSY spectrum of compound **2a** in CDCl_3 (500 MHz)

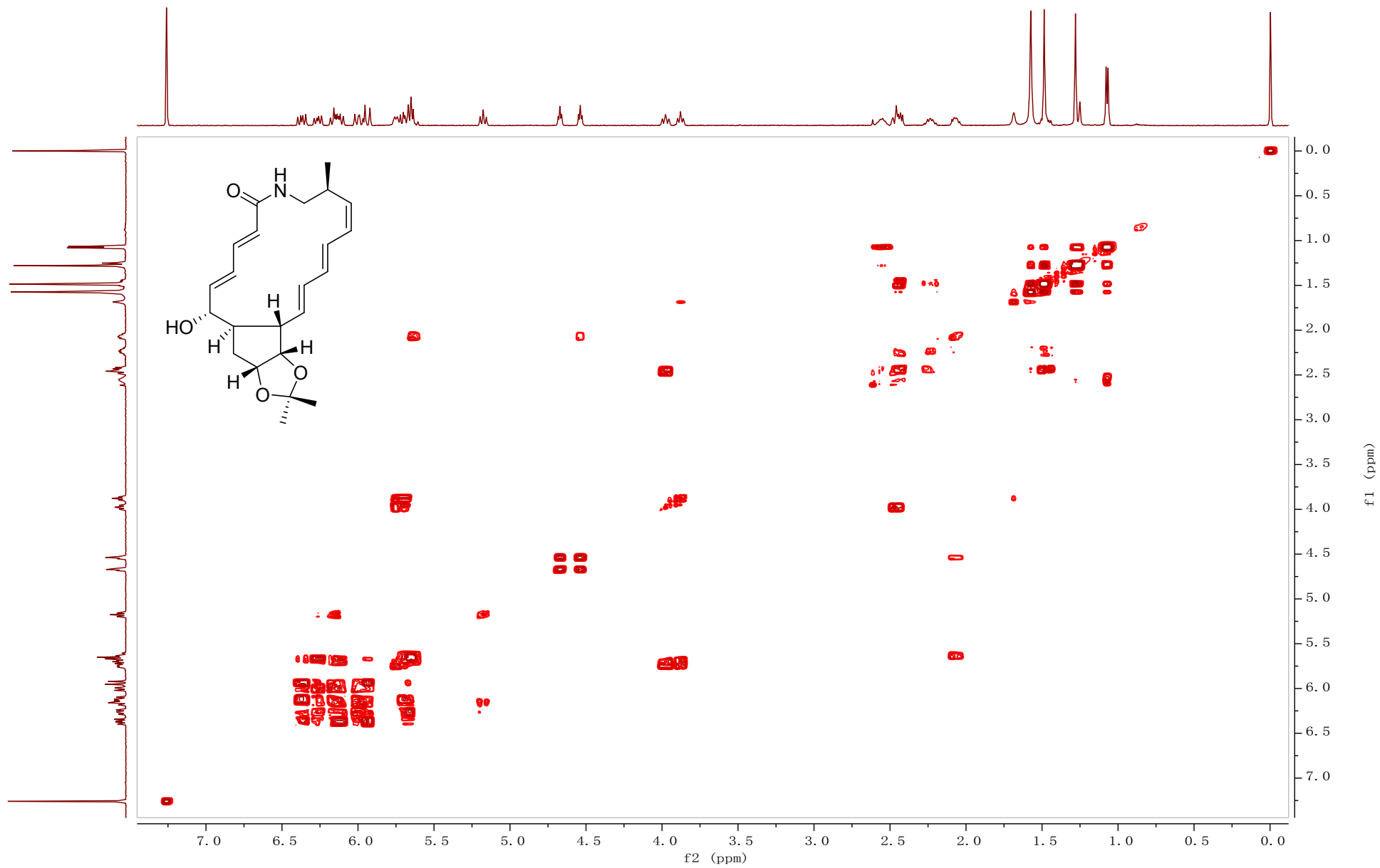


Figure S41. NOESY spectrum of compound **2a** in CDCl₃ (500 MHz)

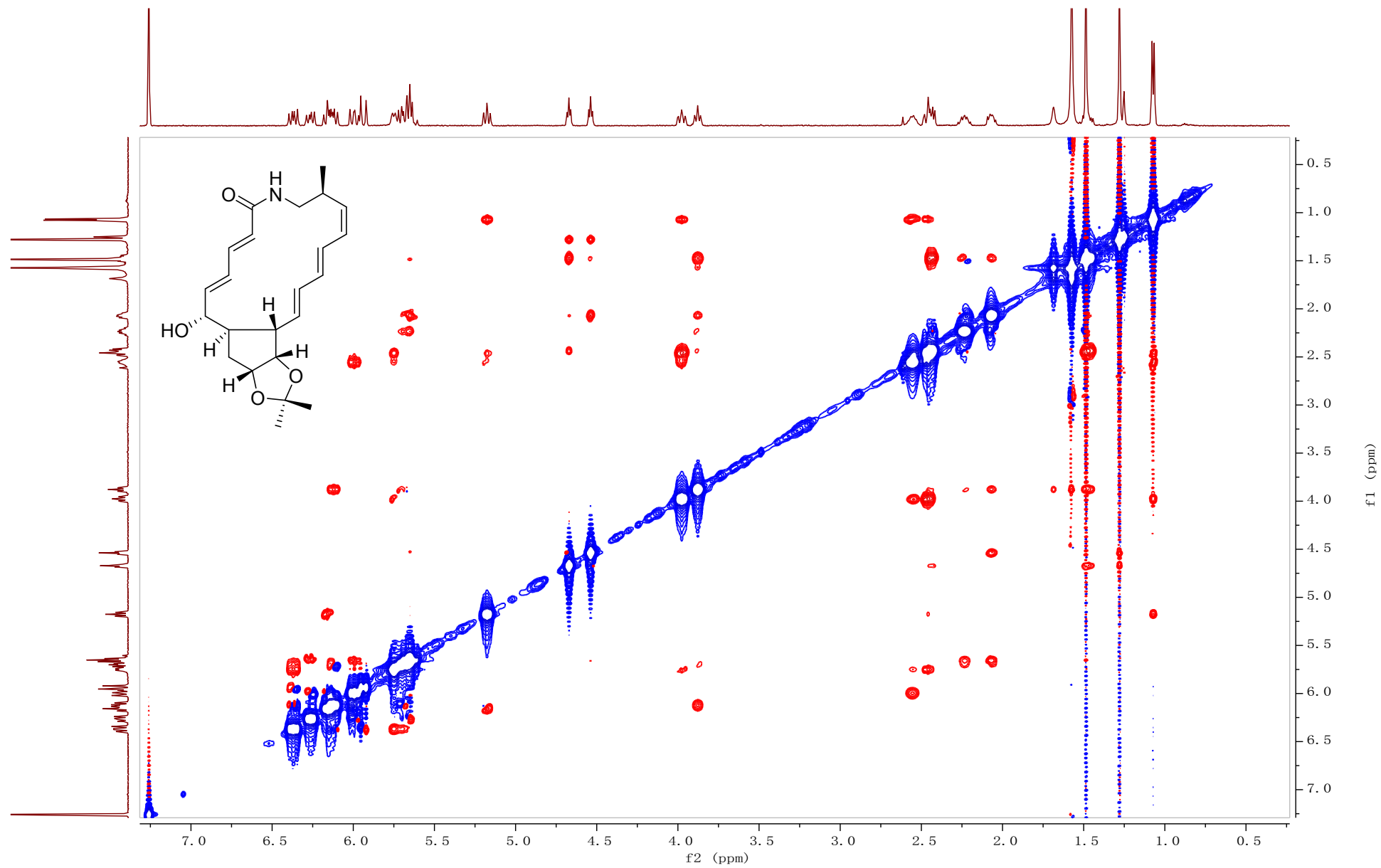


Figure S42. ^1H -NMR spectrum of (*S*)-MTPA ester (**2aa**) in CDCl_3 (500 MHz)

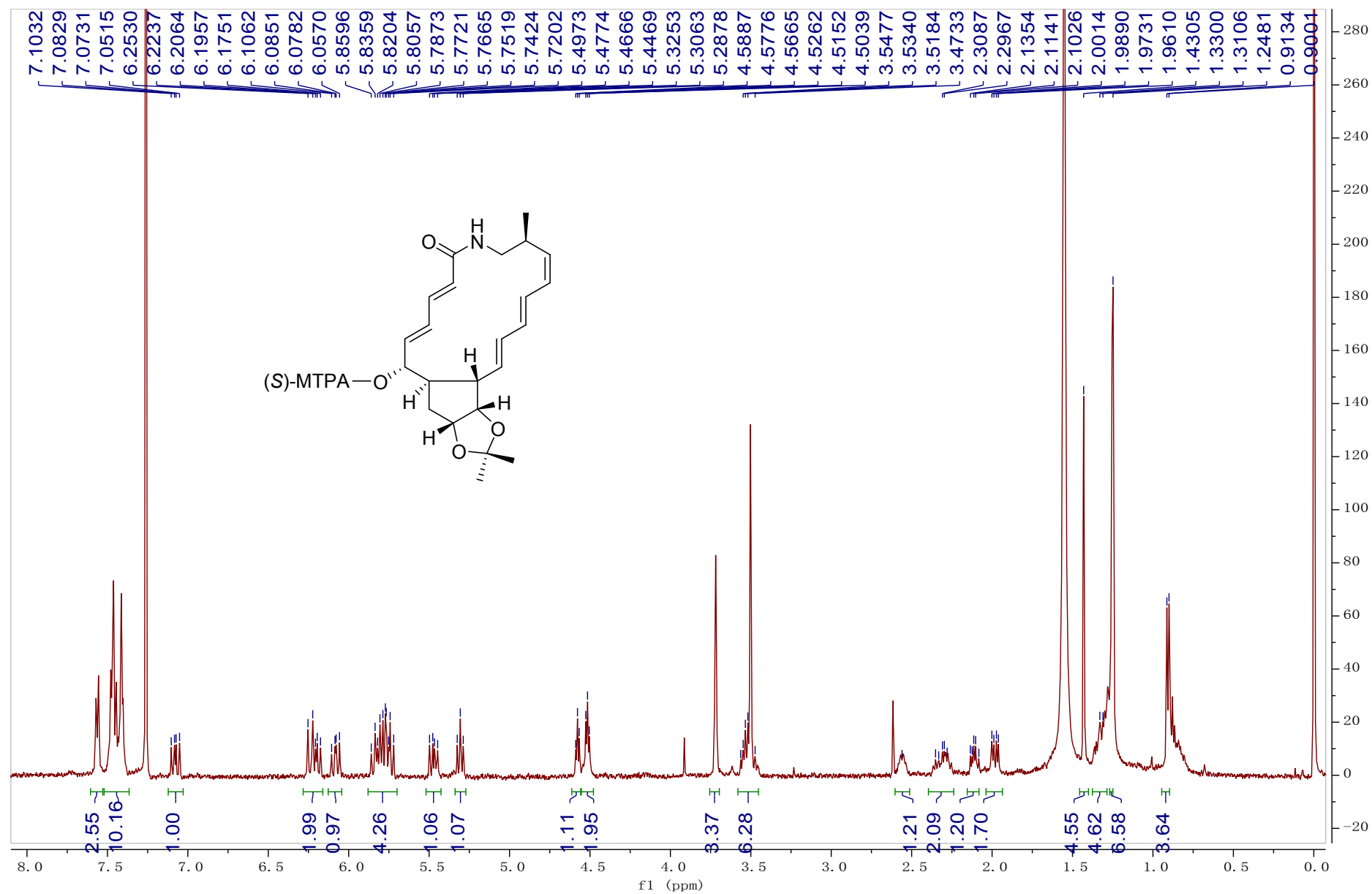
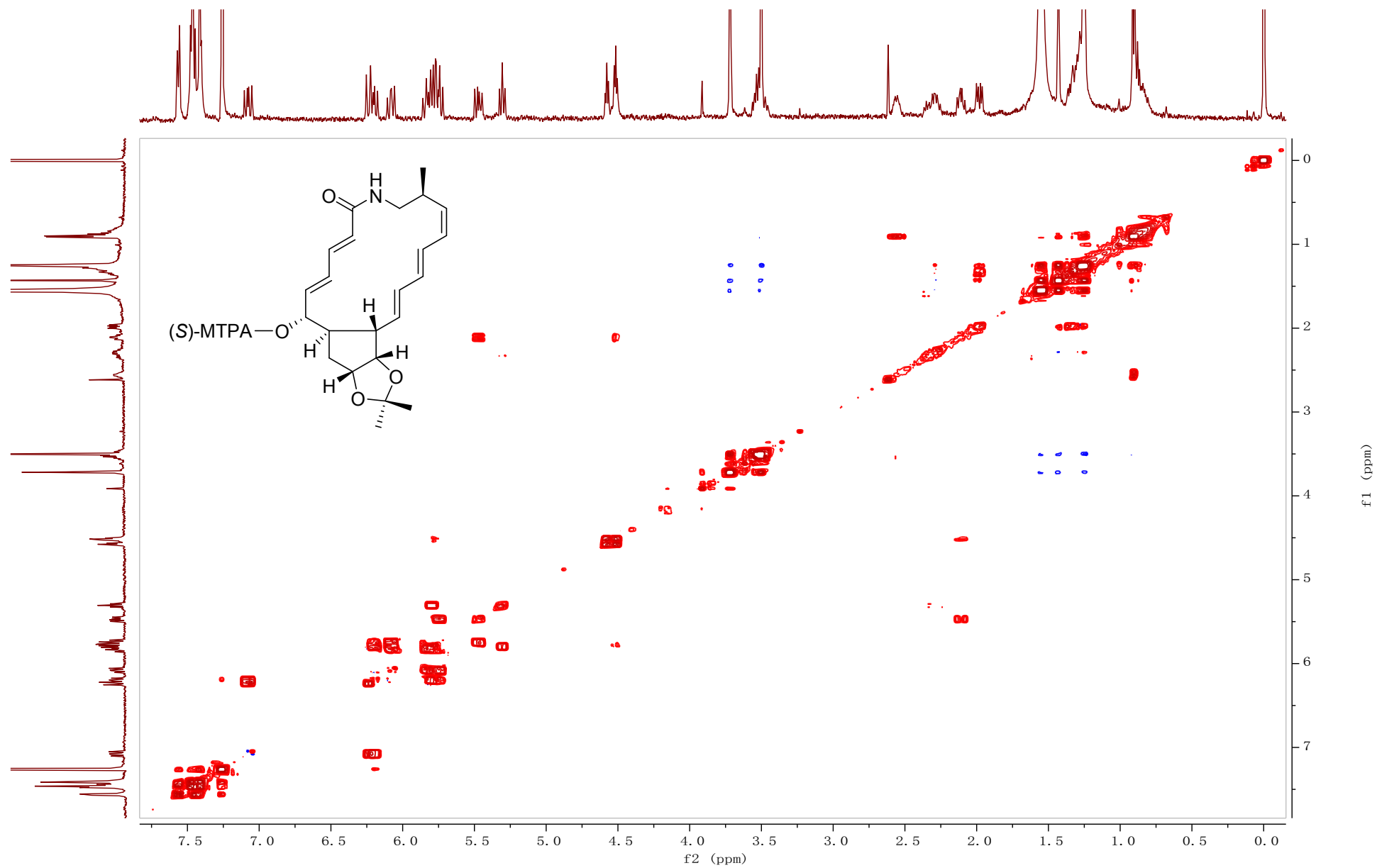


Figure S43. ^1H - ^1H COSY spectrum of (*S*)-MTPA ester (**2aa**) in CDCl_3 (500 MHz)



Chemical structure of the compound is shown above the spectrum. The structure is a bicyclic molecule with a methyl group, a hydroxyl group, and a (R)-MTPA-protected chiral center. The spectrum shows peaks from 0.0 to 6.9752 ppm. Integration values are provided for several peak groups: 5.22, 3.03, 2.03, 0.96, 1.00, 1.01, 0.98, 1.10, 0.96, 1.01, 1.03, 1.02, 0.99, 0.97, 0.99, 1.00, 2.01, 2.97, 3.15, 1.02, 2.10, 1.17, 3.69, 1.66, 4.11, and 3.18.

Figure S45. ^1H - ^1H COSY spectrum of (*R*)-MTPA ester (**2ab**) in CDCl_3 (500 MHz)

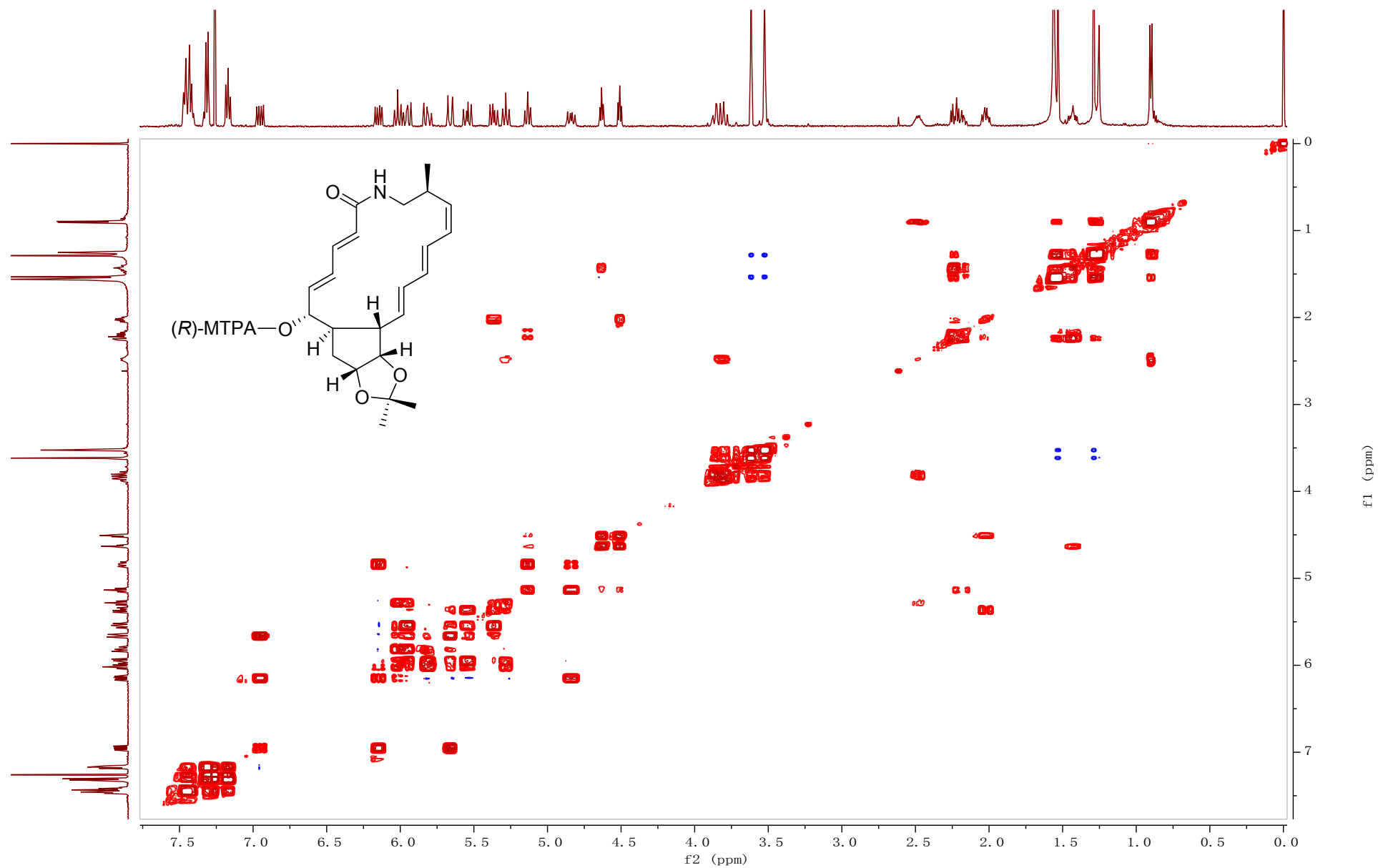


Figure S46. DFT-optimized structures of the lowest energy conformations for two MTPA esters of **1a**

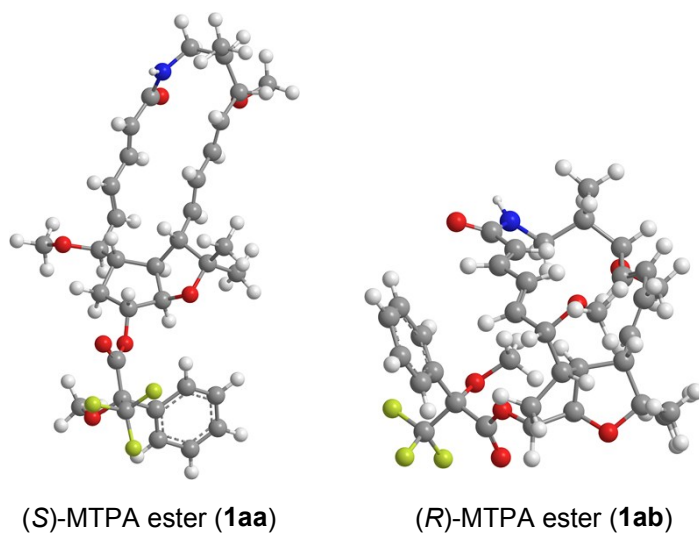


Figure S47. DFT-optimized structures of the lowest energy conformations for two MTPA esters of **2a**

