Polycyclic Polyprenylated Acylphloroglucinols: Natural Phosphodiesterase - 4 inhibitors from *Hypericum sampsonii*

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Contents:

S1. Experimental Section.

1.1. Expression and purification of PDE4D2 protein.

The cDNAs for expression of human PDE4D2 (catalytic domain, residues 86–413) were subcloned into the expression vector pET15b. All these resultant plasmids were transformed into *E. coli* strain BL21 (Codonplus) for over expression. The *E. coli* cells carrying these plasmids were grown in LB medium at 37 °C to OD_{600} = 0.7, and then 0.1 mM isopropyl *β*-D-thiogalactopyranoside was added for further growth at 16 °C for 20–40 h. The recombinant protein was purified by Ni-NTA column (Qiagen). The purity of PDE4D2 protein was greater than 95% as shown by SDS–PAGE. A typical batch of purification yielded over 50 mg of PDE4D2 (catalytic domain) from 1 L cell culture.

1.2. Enzymatic assay.

The enzymatic activities of PDE4D catalytic domain and the inhibition of PDE4D by extracted compounds were assayed by using ^{3}H-cAMP as substrates (20000–30000 cpm/assay) and the reactions were occured in mixture containing 50 mM Tris/HCl (pH 7.5), 10 mM $MgCl_2$, 0.5 mM DTT at room temperature (25 °C) for 15 min. The reactions were terminated by addition of 0.2 M $ZnSO_4$ and $Ba(OH)_2$. The reaction product ^{3}H-cAMP was precipitated out, while unreacted ^{3}H-cAMP remained in the supernatant. Radioactivity in the supernatant was measured in 2.5 mL Ultima Gold liquid scintillation cocktails

(PerkinElmer) by a PerkinElmer 2910 liquid scintillation counter. Each measurement was repeated at least three times. The IC_{50} values were calculated by nonlinear regression. As a reference compound, rolipram purchased from Sigma was measured its IC_{50} value before other assays.

S2. Detailed information for ECD calculations of 1

The absolute configuration of **1** was determined by quantum chemical TDDFT calculations of its theoretical ECD spectrum. Firstly, conformational analysis of the 1*S*, 5*R*, 7*S*, 23*R*, 24*R*, 28*R* stereoisomer was carried out via Monte Carlo searching using molecular mechanism with MMFF94 force field in the Spartan 08 program, resulting 14 conformers with relative energy within 2.0 kcal/mol. These conformers included conformational possibilities on the directions of the O-H bond at C-28 (three directions), and isopentenyl side chains on C-7 (two directions), and C-3 (three directions). The conformers with different directions of the O-H bond were ignored because of the far distance between the O-H bond and the chromophore, which will has little influence on the carbon skeleton and ECD spectrum. Then six conformers with different directions of the two isopentenyl side chains (**1a**-**1f**, Figure S1) were selected for further calculation. In addition, a simplified model with the absence of the two isopentenyl side chains (**1g**, Figure S1) was also designed and calculated. The conformers were reoptimized using DFT at the B3LYP/6-31G(d) level in vacuum by the Gaussian 09 program.[1] The B3LYP/6-31G(d) harmonic vibrational frequencies were further calculated to confirm their stability. The energies, oscillator strengths, and rotational strengths of the first 60 electronic excitations were calculated using the TDDFT methodology at the B3LYP/6-311++G(2d,2p) level in vacuum. The ECD spectra were simulated by the overlapping Gaussian function (δ = 0.4 eV),[2] in which velocity rotatory strengths of the first 50 exited states were adopted. To get the overall ECD spectra, the simulated spectra of the lowest energy conformers were averaged according to the Boltzmann distribution theory and their relative Gibbs free energy (ΔG).

1. *Gaussian 09*, Revision A.1, 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.; 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, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

2. Stephens, P. J.; Harada, N. ECD cotton effect approximated by the Gaussian curve and other methods. *Chirality* **2010**, *22*, 229–233.

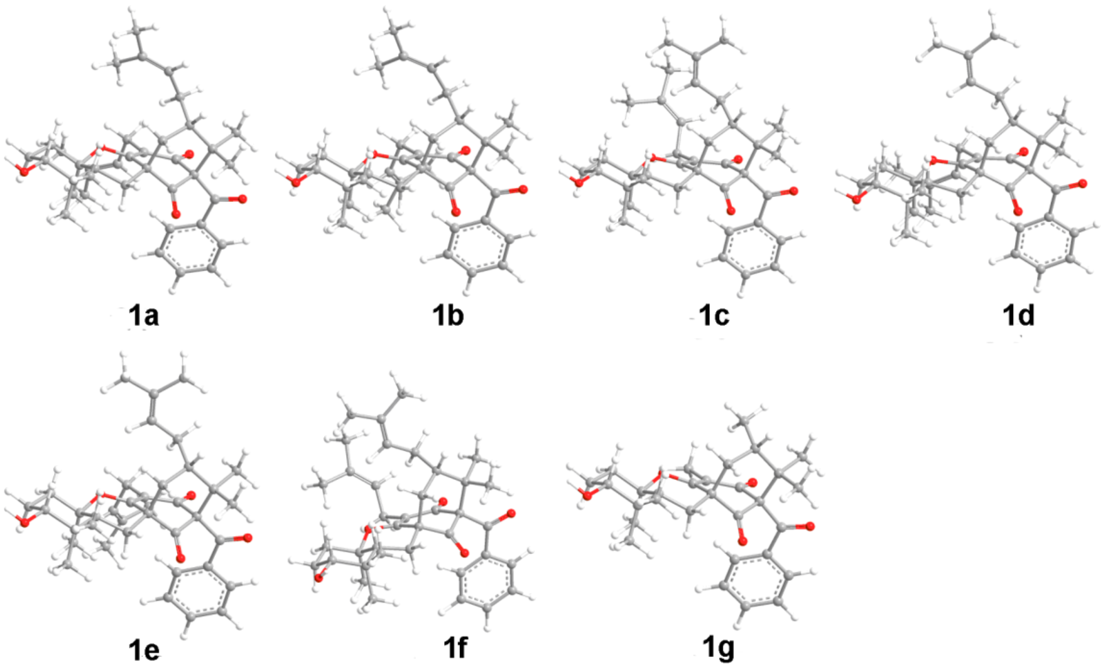


Figure S1. B3LYP/6-31G(d) optimized lowest energy 3D conformers (**1a**–**1f**) of **1** and model conformer (**1g**).

ECD simulation:

ECD spectrum of each conformation is simulated according to the overlapping Gaussian functions expressed as:

$$\Delta\varepsilon(E) = \frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{A}\Delta E_i R_i e^{[-(E-\Delta Ei)^2/\sigma^2]}$$

Where σ is half the bandwidth at 1/e peak height and expressed in energy units. The parameters ΔE_i and R_i are the excitation energies and rotational strengths for the transition *i*, respectively.

The above function is converted to Δε, λ (wavelength) correlations as:

$$\Delta\varepsilon(\lambda) = \frac{1}{2.296\times10^{-39}\sqrt{\pi}\sigma}\sum_{i}^{A}\Delta E_i R_i e^{[-(1240/\lambda-\Delta Ei)^2/\sigma^2]}$$

and then simulation were accomplished by using the Excel 2003 and the Origin 7.0 software.

To get the final spectra, all the simulated spectra of conformations of each compound were averaged according to their energy and the Boltzmann distribution theory expressed as:

$$\frac{N_i^*}{N} = \frac{g_i e^{-\varepsilon_i/k_B T}}{\sum g_i e^{-\varepsilon_i/k_B T}}$$

Energy analyses:

conf.	Gibbs free energy (298.15 K)		
	G (Hartree)	ΔG (Kcal/mol)	Boltzmann Distribution
1a	-1853.495399	0	0.524415
1b	-1853.494841	0.35015058	0.290323
1c	-1853.493329	1.2989457	0.058486
1d	-1853.493421	1.24121478	0.064475
1e	-1853.492856	1.59575793	0.035431

1f	-1853.492595	1.75953804	0.02687

ECD Data:

State	1a		1b		1c	
	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*
1	3.6817	4.2424	3.6714	10.4602	3.673	10.4996
2	3.7463	10.8801	3.7342	25.8871	3.7338	28.5458
3	4.0752	-23.4828	4.0085	-48.8488	4.0007	-49.5255
4	4.1645	1.9394	4.105	0.0113	4.1028	-0.2199
5	4.1938	4.7141	4.1757	2.5215	4.1675	1.8589
6	4.2458	4.8644	4.2597	0.9162	4.2437	9.038
7	4.2696	-2.6224	4.2763	2.4225	4.2742	24.7606
8	4.2859	11.7323	4.295	13.2729	4.3028	0.7336
9	4.4534	3.9283	4.4447	4.0002	4.468	8.1404
10	4.5155	5.5042	4.5201	6.2349	4.5321	0.6914
11	4.5715	2.9623	4.5404	10.4566	4.5497	-3.994
12	4.581	11.2795	4.5728	-14.206	4.5682	-11.113
13	4.6652	35.358	4.6443	51.3677	4.6513	39.8063
14	4.7356	46.5797	4.7205	49.6296	4.7189	40.3379
15	4.74	-6.2093	4.7401	-6.4608	4.7382	-4.6131
16	4.8275	-2.7606	4.825	-5.4607	4.809	20.5223
17	4.9083	-8.0979	4.8903	-5.789	4.91	-24.4969
18	4.9225	-67.7908	4.9185	-96.5237	4.9211	-78.101
19	4.9626	-18.9566	4.9668	-23.0462	4.9744	-33.1479
20	4.9898	8.8131	5	8.0209	5.0099	73.4003
21	5.0121	71.6569	5.0265	67.5889	5.0225	8.8909
22	5.2441	0.8841	5.239	-1.6946	5.2356	-2.8391
23	5.2851	-3.5032	5.2493	0.2981	5.2522	2.1615
24	5.293	-3.1384	5.2794	-3.6334	5.2769	-2.2964
25	5.3336	5.1425	5.3275	11.2161	5.3299	0.3895
26	5.4274	-1.1872	5.3366	-7.4824	5.3406	-4.7154
27	5.4593	-40.4331	5.4355	3.5338	5.4345	3.5764
28	5.4787	-1.5472	5.4621	-43.3117	5.4721	-41.5268
29	5.5601	-19.3415	5.5828	0.1711	5.5944	-3.6448
30	5.5882	-0.9433	5.606	-5.4031	5.5968	-14.4199
31	5.5993	2.862	5.6123	-9.6957	5.6021	0.2961
32	5.6875	-2.3808	5.646	-2.8584	5.6045	2.1549
33	5.7123	0.4724	5.6995	-1.3044	5.6728	-4.4176
34	5.7251	5.3903	5.7274	-26.6106	5.7103	-14.9093
35	5.7898	2.3572	5.7342	-1.5743	5.7192	-1.6022

36	5.7926	-0.4089	5.8074	3.6138	5.8057	0.3797
37	5.8048	6.0992	5.8204	-0.9348	5.8171	-2.4658
38	5.8167	-2.635	5.8232	-3.008	5.8192	-1.1124
39	5.8284	-6.0468	5.8432	-3.297	5.8397	1.828
40	5.8381	4.7233	5.8531	-7.2726	5.8497	-26.0247
41	5.8393	-21.2366	5.8619	-0.3667	5.8698	5.9161
42	5.8511	-3.7135	5.8672	-4.5406	5.8814	-20.1067
43	5.8977	17.21	5.8817	2.7084	5.8956	5.7089
44	5.9165	-17.4631	5.9136	-15.799	5.8975	-22.4807
45	5.9502	1.6618	5.9184	-6.9406	5.9209	1.9637
46	5.9788	-4.33	5.9352	-38.7385	5.9288	1.3844
47	5.9904	12.2748	5.9449	12.0626	5.9436	0.9563
48	6.0239	11.5336	5.9589	-2.6686	5.9839	2.657
49	6.0335	-9.5806	6.0195	-12.745	6.0102	-17.908
50	6.0549	0.3076	6.033	-0.8293	6.0286	-10.961
51	6.0676	-19.9138	6.0671	-28.7026	6.0402	2.1604
52	6.0734	10.58	6.0717	5.6315	6.0464	-0.6568
53	6.0797	-1.1437	6.0865	47.4198	6.0692	-12.5495
54	6.0953	-27.7796	6.0903	-46.3584	6.0829	-0.4593
55	6.1073	13.8332	6.1007	10.5947	6.0979	37.0584
56	6.1116	7.8838	6.1159	8.2675	6.1052	-2.2068
57	6.1429	7.2296	6.1281	-0.2002	6.1154	4.2504
58	6.1525	-7.5526	6.137	-1.89	6.1205	3.3443
59	6.1592	18.3205	6.1378	5.518	6.1273	-3.4638
60	6.1693	17.2632	6.1502	6.2374	6.1324	-1.9149

* R(velocity) 10**-40 erg-esu-cm

State	**1d**		**1e**		**1f**	
	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*	Excitation energies(eV)	Rotatory Strengths*
1	3.6832	3.6541	3.6791	3.8182	3.68	4.117
2	3.751	12.7144	3.7195	3.6906	3.717	2.4853
3	4.0652	-23.2655	4.0073	28.0583	3.9938	29.3959
4	4.1584	0.2888	4.1332	-6.5929	4.1257	-6.5634
5	4.189	10.3233	4.1781	15.4926	4.1772	14.0636
6	4.2322	11.9334	4.2244	11.4701	4.2225	12.2862
7	4.2701	12.9963	4.2602	8.5388	4.2599	9.4592
8	4.2944	0.259	4.333	-8.8779	4.3314	-9.7382
9	4.4791	8.1718	4.362	1.8673	4.3567	2.4452
10	4.5399	-4.131	4.5457	-9.8021	4.5407	-9.3793
11	4.5628	-4.4135	4.5676	-4.9028	4.5654	-6.4267
12	4.5771	4.0108	4.6011	-4.9723	4.5936	-6.5991

13	4.6768	33.4389	4.6964	10.3165	4.6825	14.9332
14	4.7343	25.7949	4.7115	6.7342	4.702	2.8278
15	4.7415	13.9554	4.7395	6.1331	4.7386	7.849
16	4.8142	9.5155	4.7836	52.479	4.7794	51.4175
17	4.9215	-57.8699	4.8676	2.7874	4.8519	6.7983
18	4.9296	-0.4034	4.909	-67.8113	4.9108	-72.3244
19	4.9679	-34.4353	4.9633	-26.9802	4.9652	-22.9718
20	5	81.6729	4.9893	74.8427	4.9906	71.9482
21	5.0118	-0.5363	5.0671	2.1004	5.0511	3.0712
22	5.2421	0.5567	5.2371	4.7658	5.2472	-1.5452
23	5.2844	-2.8293	5.2595	-1.2246	5.2756	5.3924
24	5.2913	-4.2876	5.2837	-1.1769	5.293	-2.4602
25	5.3458	0.1262	5.306	-2.2993	5.2945	-1.293
26	5.4287	-1.0137	5.4705	-44.2073	5.4621	-42.7263
27	5.471	-38.9166	5.5031	6.3156	5.4944	4.5383
28	5.4841	0.062	5.5152	3.0612	5.5175	0.1899
29	5.5458	-21.0351	5.5292	0.3126	5.5229	-0.1992
30	5.5964	0.3309	5.5366	-1.9693	5.5603	0.6205
31	5.6013	1.0562	5.5469	-11.0696	5.5823	-7.7174
32	5.6511	-1.1288	5.5887	-3.1462	5.6126	-1.8551
33	5.6983	1.8495	5.6126	-0.7468	5.6404	-4.4108
34	5.7031	1.0433	5.6954	6.0745	5.6623	0.7371
35	5.7592	2.3285	5.7436	2.3427	5.7223	1.5265
36	5.7885	-0.3061	5.7691	-5.9461	5.7304	1.224
37	5.793	0.7624	5.7838	-3.7079	5.738	4.2662
38	5.8063	-2.7914	5.7922	-5.0876	5.7561	-4.9738
39	5.8226	-0.2598	5.7993	-0.4307	5.7776	-0.1517
40	5.8612	1.5502	5.8122	2.9377	5.792	-9.2302
41	5.8731	-12.8464	5.8172	-5.2271	5.7961	-2.6672
42	5.8869	-3.2829	5.8468	4.1583	5.8159	0.5807
43	5.9118	-3.136	5.8587	1.759	5.871	1.2777
44	5.9191	0.1478	5.8911	-3.4031	5.9097	-2.606
45	5.9362	9.397	5.9143	-1.5221	5.9361	-5.0161
46	5.9702	20.5472	5.9511	-11.863	5.954	-13.0075
47	5.9862	-3.7763	5.9639	2.339	5.9626	-3.512
48	6.0111	-12.352	5.9674	0.204	5.9754	19.9451
49	6.0347	-1.6369	5.9789	-2.1738	5.9956	-4.7338
50	6.0374	1.0285	6.0146	-0.1808	6.0151	0.5724
51	6.0524	-12.6943	6.0286	1.2448	6.0426	4.3389
52	6.0614	6.1023	6.0485	-11.6207	6.053	-15.2939
53	6.0723	3.3038	6.0617	10.5643	6.0745	6.9784
54	6.0868	-41.6722	6.0654	-1.3995	6.0847	-16.0367
55	6.0989	11.5113	6.077	-2.8302	6.089	5.0938

56	6.1071	0.1782	6.0922	-19.9738	6.0982	-8.6321
57	6.1161	-0.629	6.0965	-7.7518	6.1126	10.5911
58	6.1226	17.4225	6.1085	-1.8849	6.1202	-11.2178
59	6.1298	6.2731	6.1124	6.4244	6.1279	0.3522
60	6.1417	5.2152	6.1327	-4.4655	6.1486	-3.3443

* R(velocity)　10**-40 erg-esu-cm

1g					
State	Excitation energies(eV)	Rotatory Strengths*	State	Excitation energies(eV)	Rotatory Strengths*
1	3.6797	1.6927	31	6.0496	-3.5756
2	3.7768	25.1112	32	6.0546	-1.5279
3	4.1746	-7.2378	33	6.0787	-16.2536
4	4.2431	18.3063	34	6.0912	9.2806
5	4.3086	-4.4531	35	6.0952	-6.7571
6	4.3746	5.2548	36	6.1235	2.864
7	4.5656	-10.0639	37	6.1462	1.6754
8	4.5995	10.3276	38	6.1583	2.78
9	4.7198	8.8114	39	6.1666	2.2705
10	4.7633	17.2866	40	6.1905	-3.0802
11	4.7918	73.0747	41	6.2161	14.3322
12	4.8693	15.0187	42	6.223	1.4462
13	4.9054	-57.068	43	6.2275	3.9964
14	4.9672	-57.8083	44	6.268	-4.4908
15	5.0024	76.4673	45	6.2689	-8.5479
16	5.2403	0.2589	46	6.2882	3.6955
17	5.2843	-4.1949	47	6.293	-5.347
18	5.4362	-40.1212	48	6.3014	0.1319
19	5.519	0.8166	49	6.3082	-2.6412
20	5.535	3.4306	50	6.348	-14.5332
21	5.5678	-17.4361	51	6.3614	-3.7526
22	5.768	3.1233	52	6.3772	-4.3291
23	5.7927	-0.1152	53	6.405	-9.5676
24	5.8043	0.5422	54	6.42	8.4767
25	5.8183	0.9853	55	6.4217	4.6146
26	5.8236	-6.5668	56	6.4274	5.6291
27	5.8357	-14.1568	57	6.4299	8.7586
28	5.8506	0.2128	58	6.4679	-4.1629
29	5.8804	-0.4416	59	6.4721	27.142
30	6.0445	4.0087	60	6.4748	10.0743

* R(velocity)　10**-40 erg-esu-cm

S3. CD spectra of compounds **2–7**.

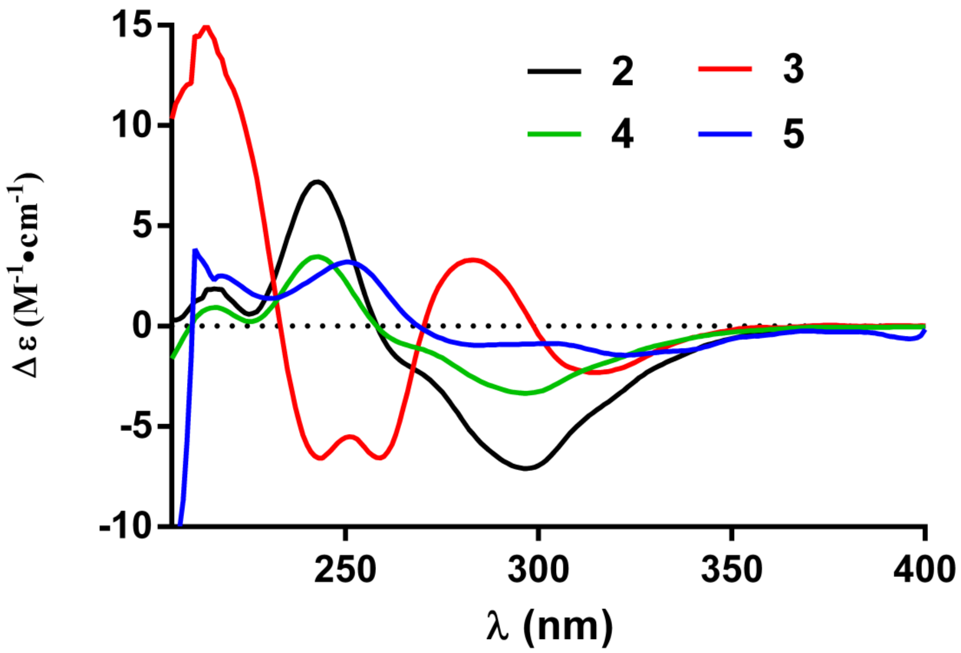


Figure S2A. CD spectra of homoadamantyl type PPAPs (compounds **2**–**5**).

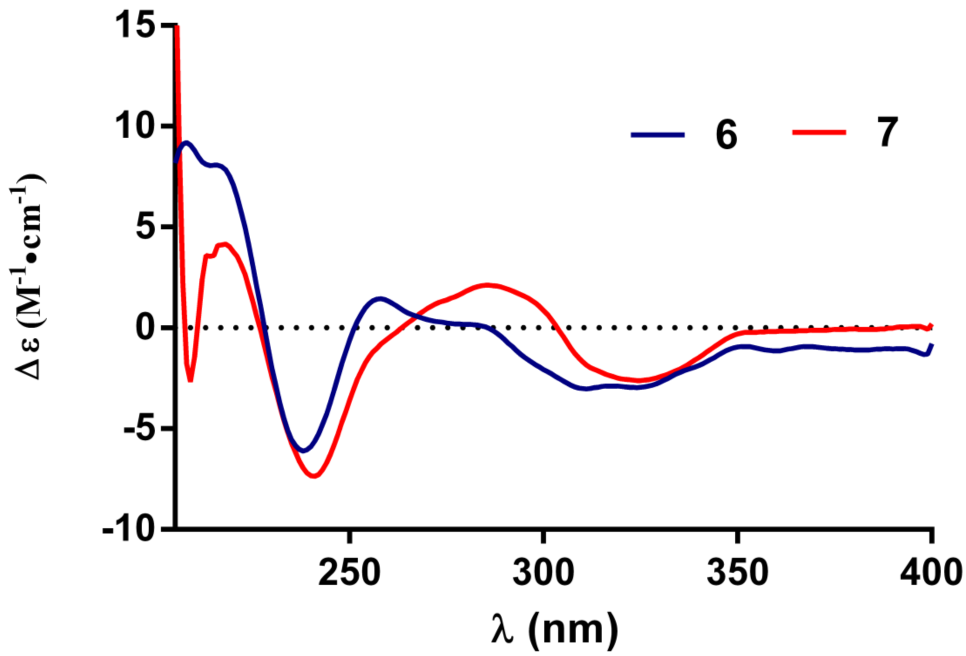
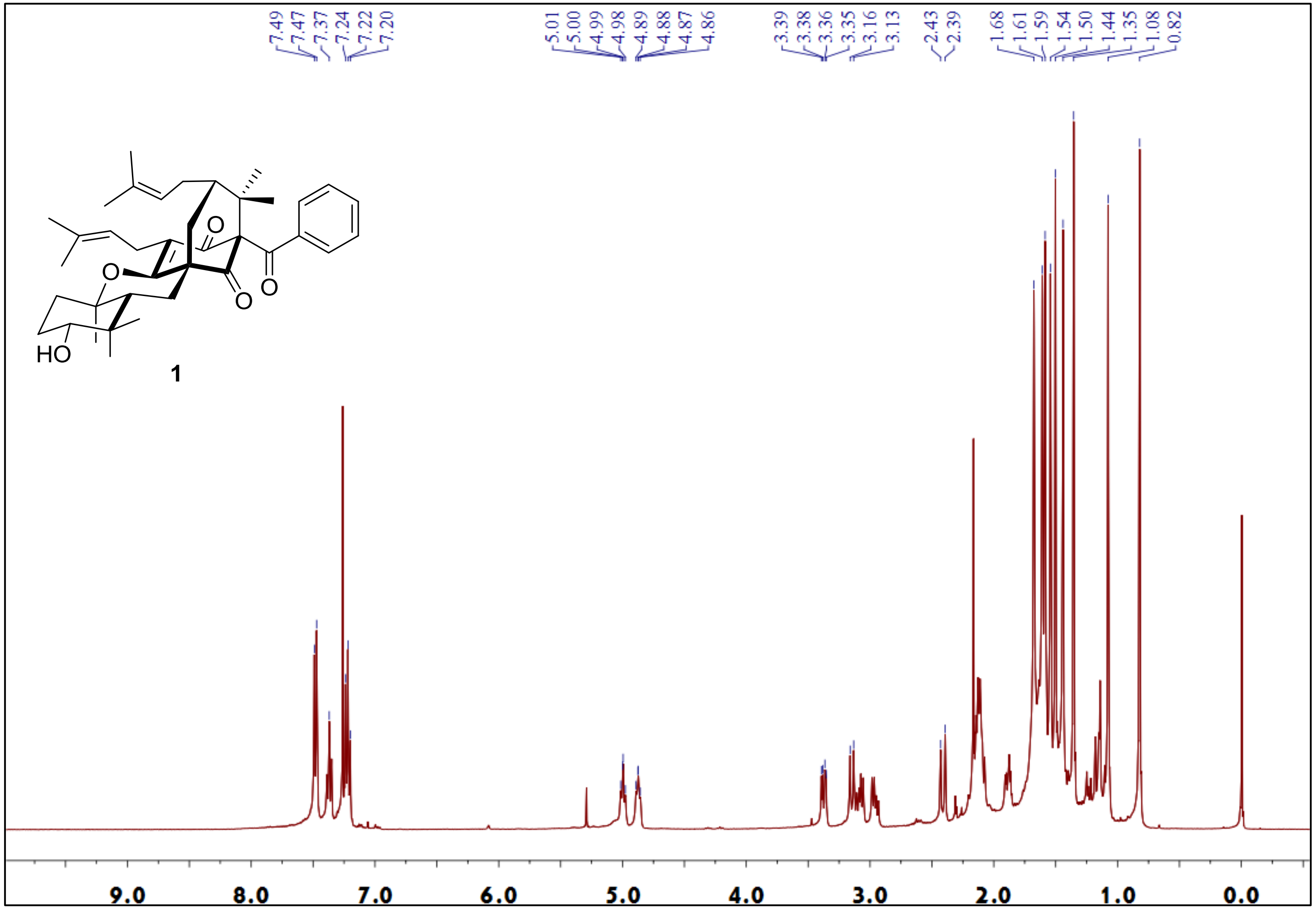
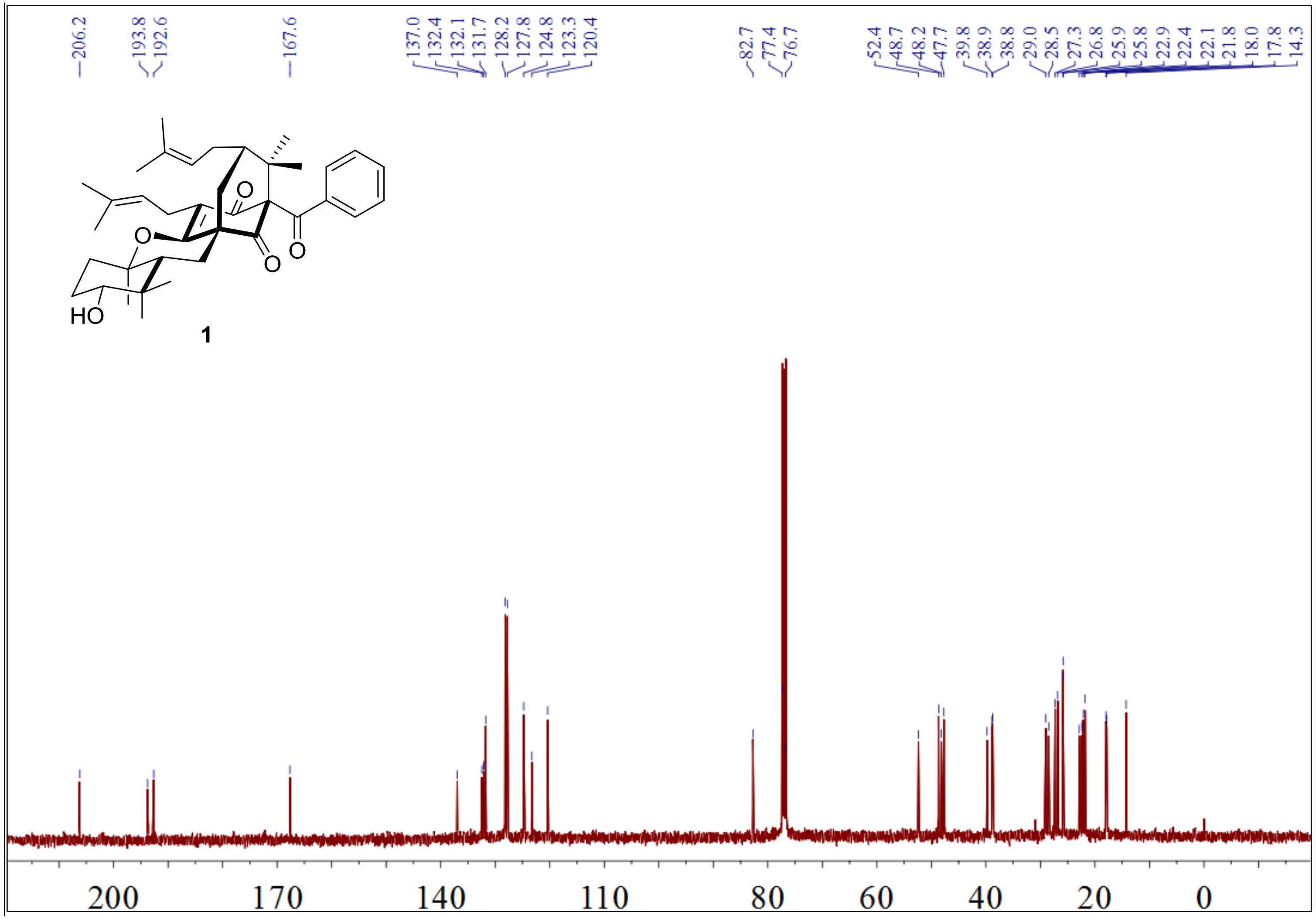


Figure S2B. CD spectra of adamantane type PPAPs (compouns **6** and **7**).

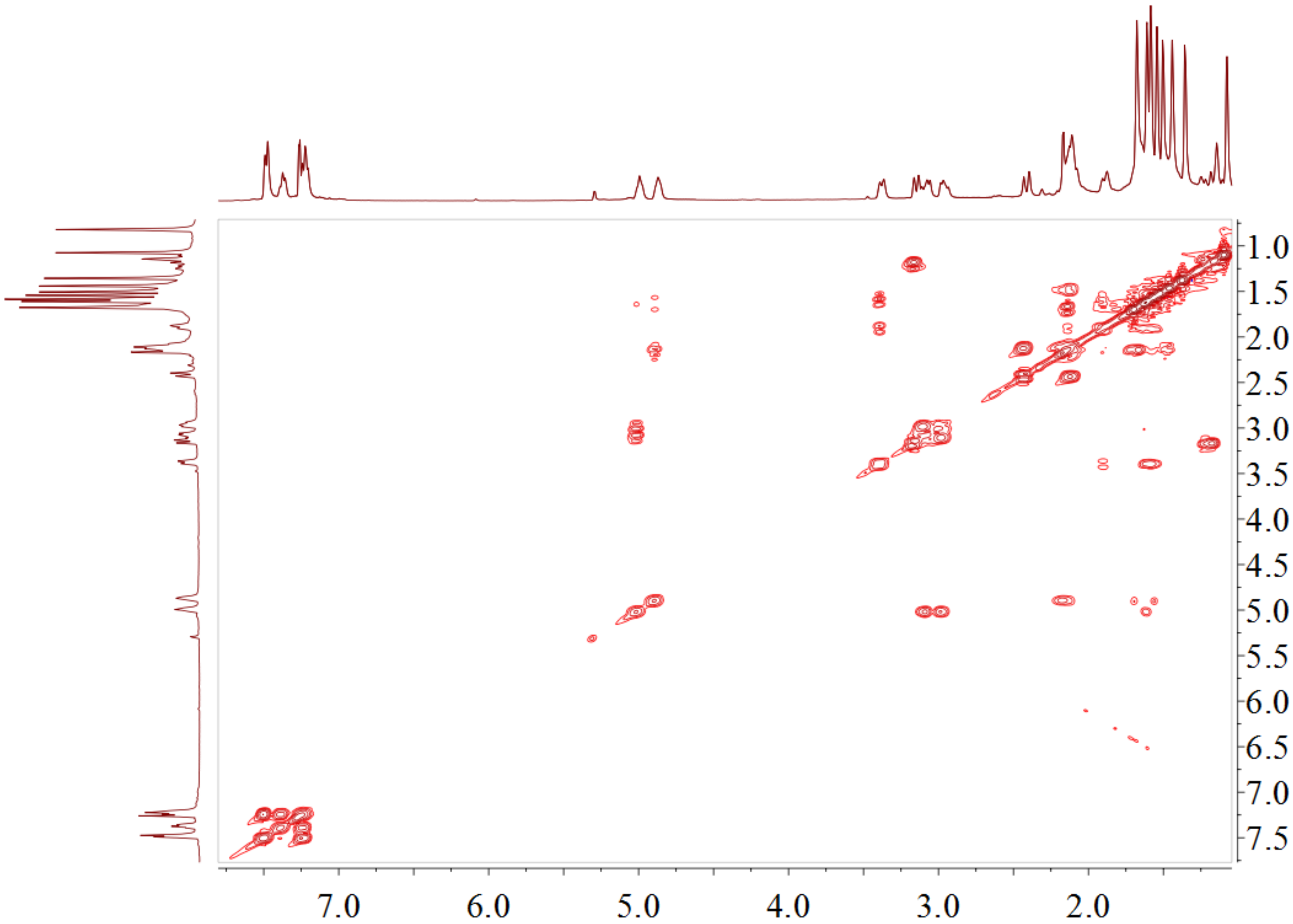
S4. [1]H NMR Spectrum of **1** in $CDCl_3$



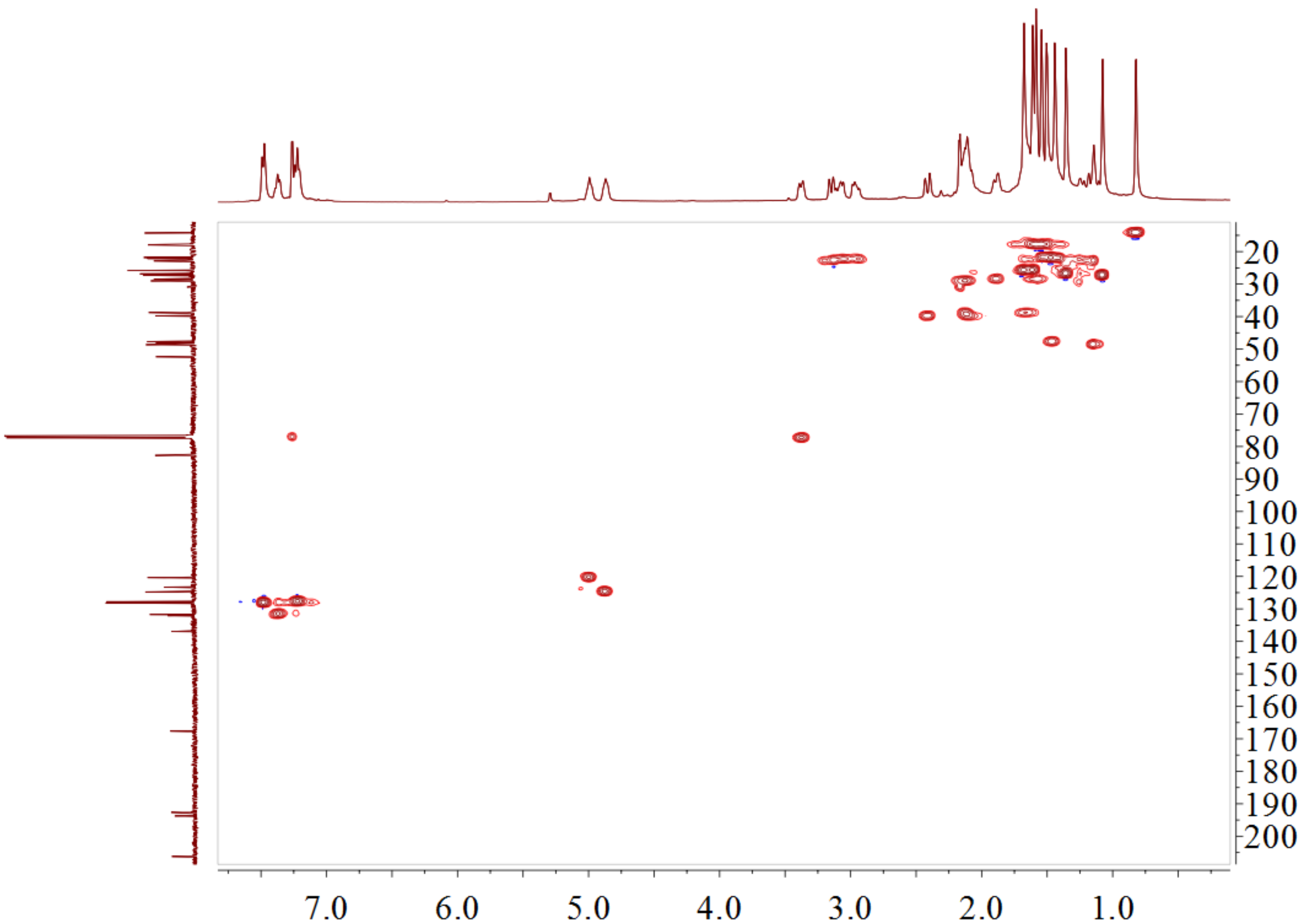
S5. ^{13}C NMR Spectra of **1** in $CDCl_3$



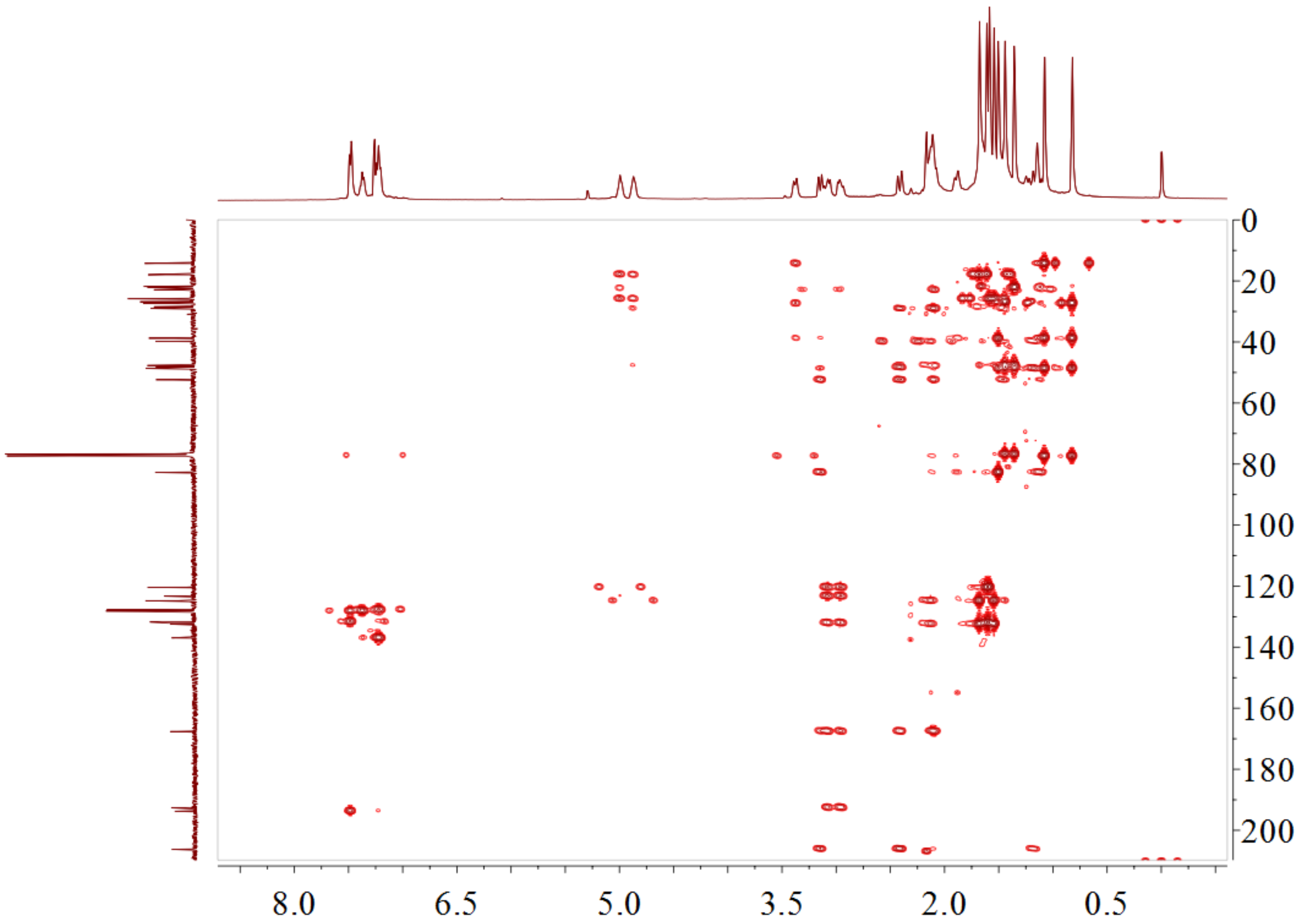
S6. ^{1}H-^{1}H COSY Spectrum of **1** in $CDCl_3$



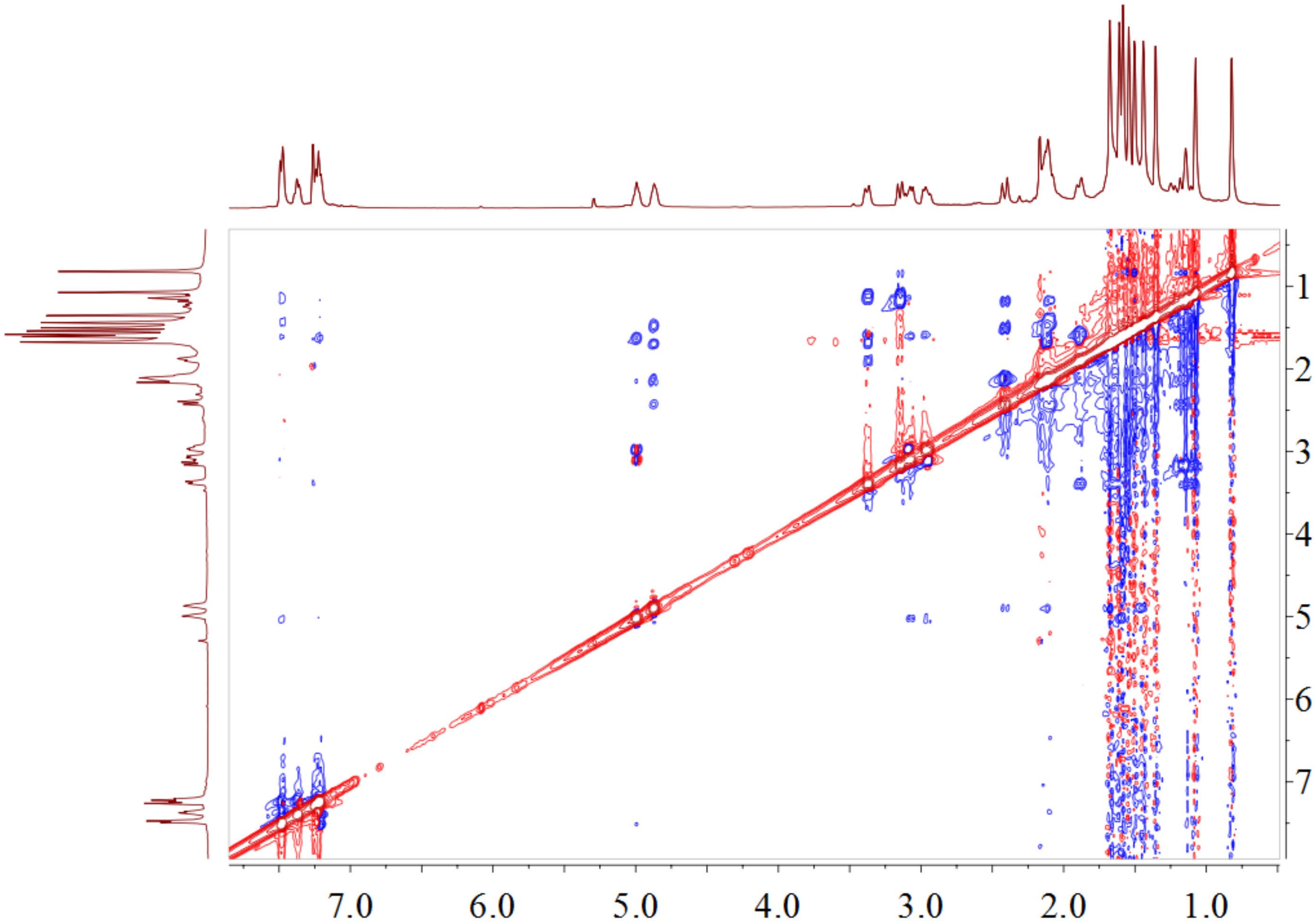
S7. HSQC Spectrum of **1** in $CDCl_3$



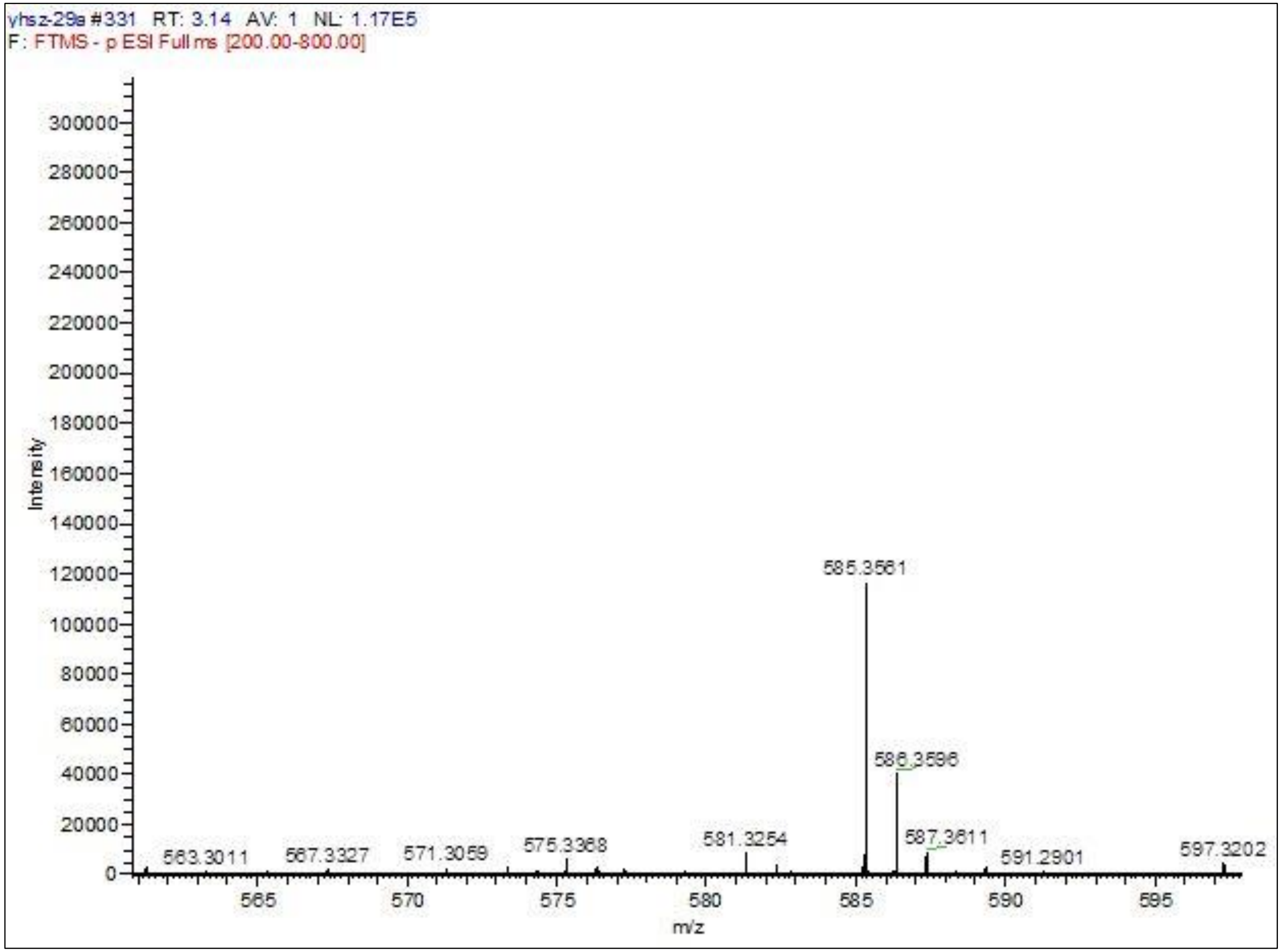
S8. HMBC Spectrum of **1** in $CDCl_3$



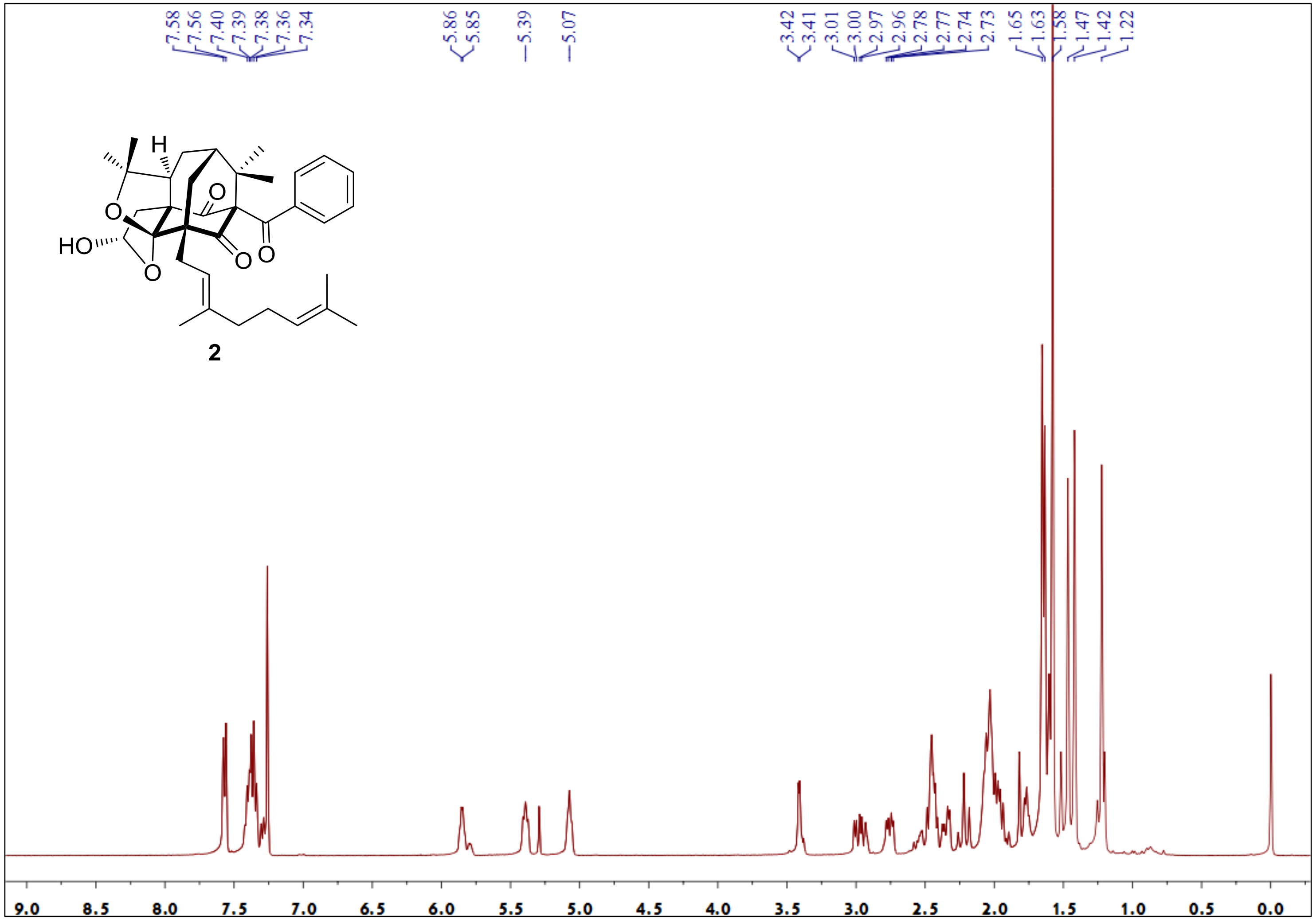
S9. NOESY Spectrum of **1** in $CDCl_3$



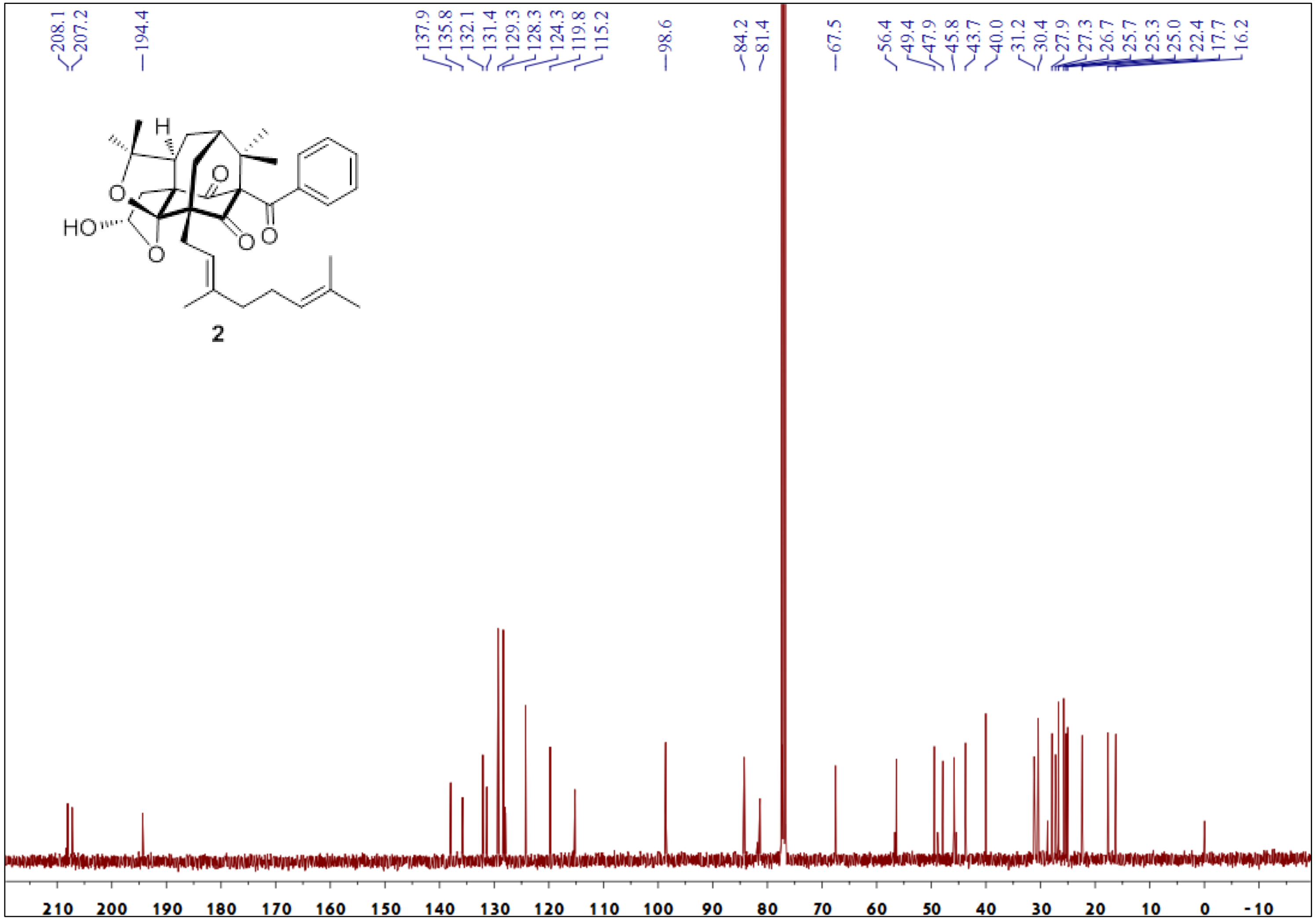
S10. HRESIMS spectrum of **1**



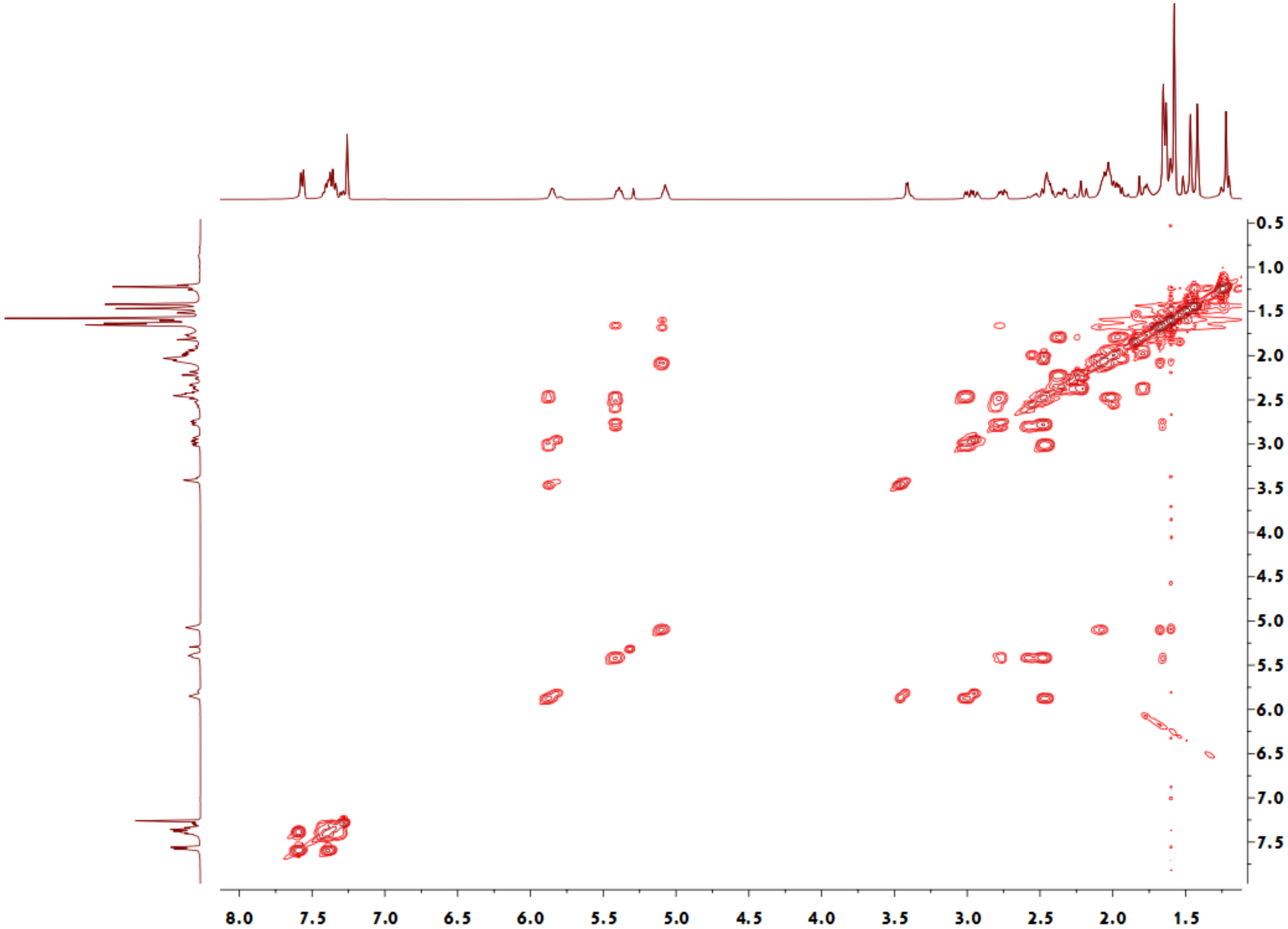
S11. [1]H NMR Spectrum of **2** in $CDCl_3$



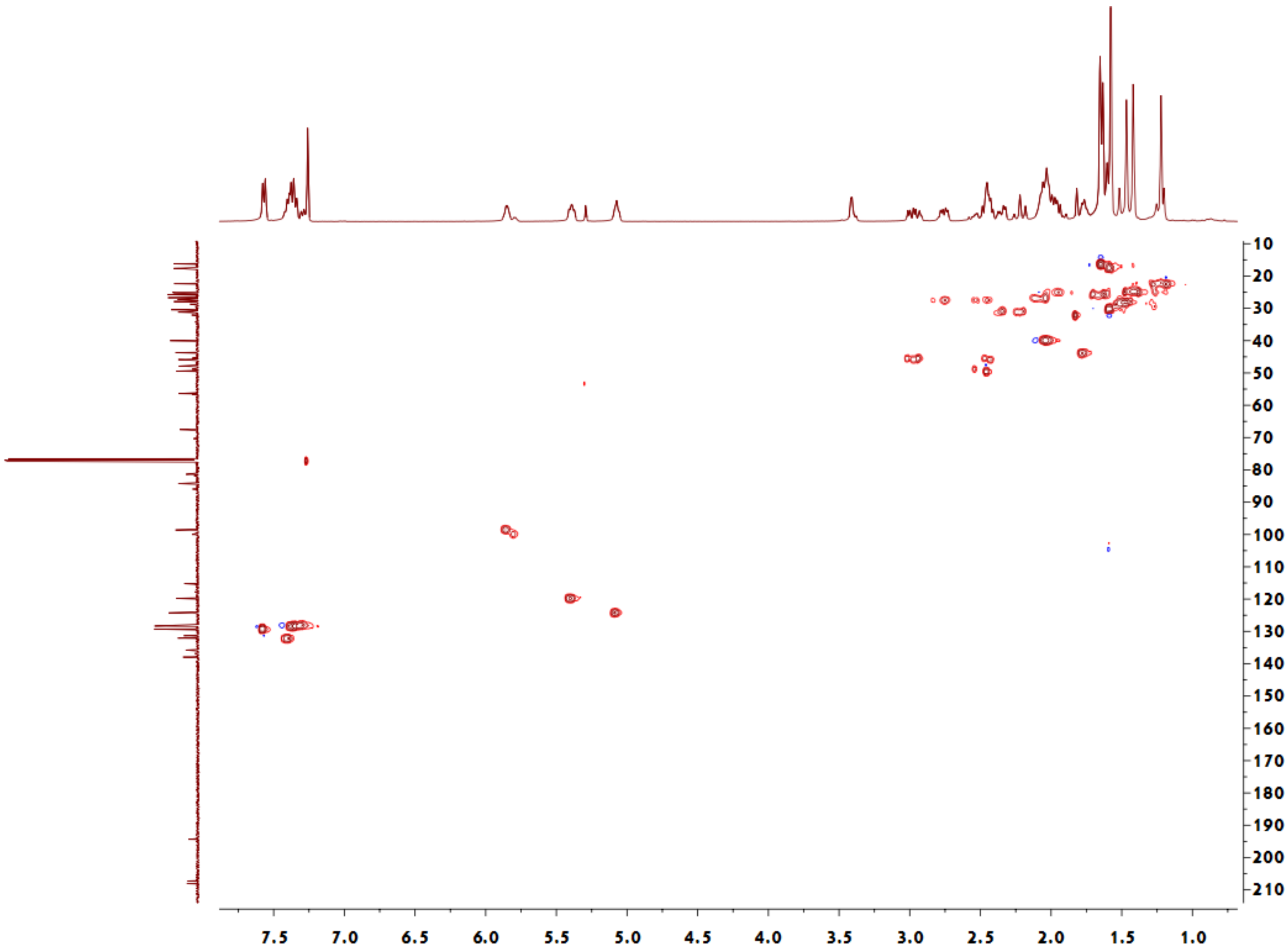
S12. ^{13}C NMR Spectra of **2** in $CDCl_3$



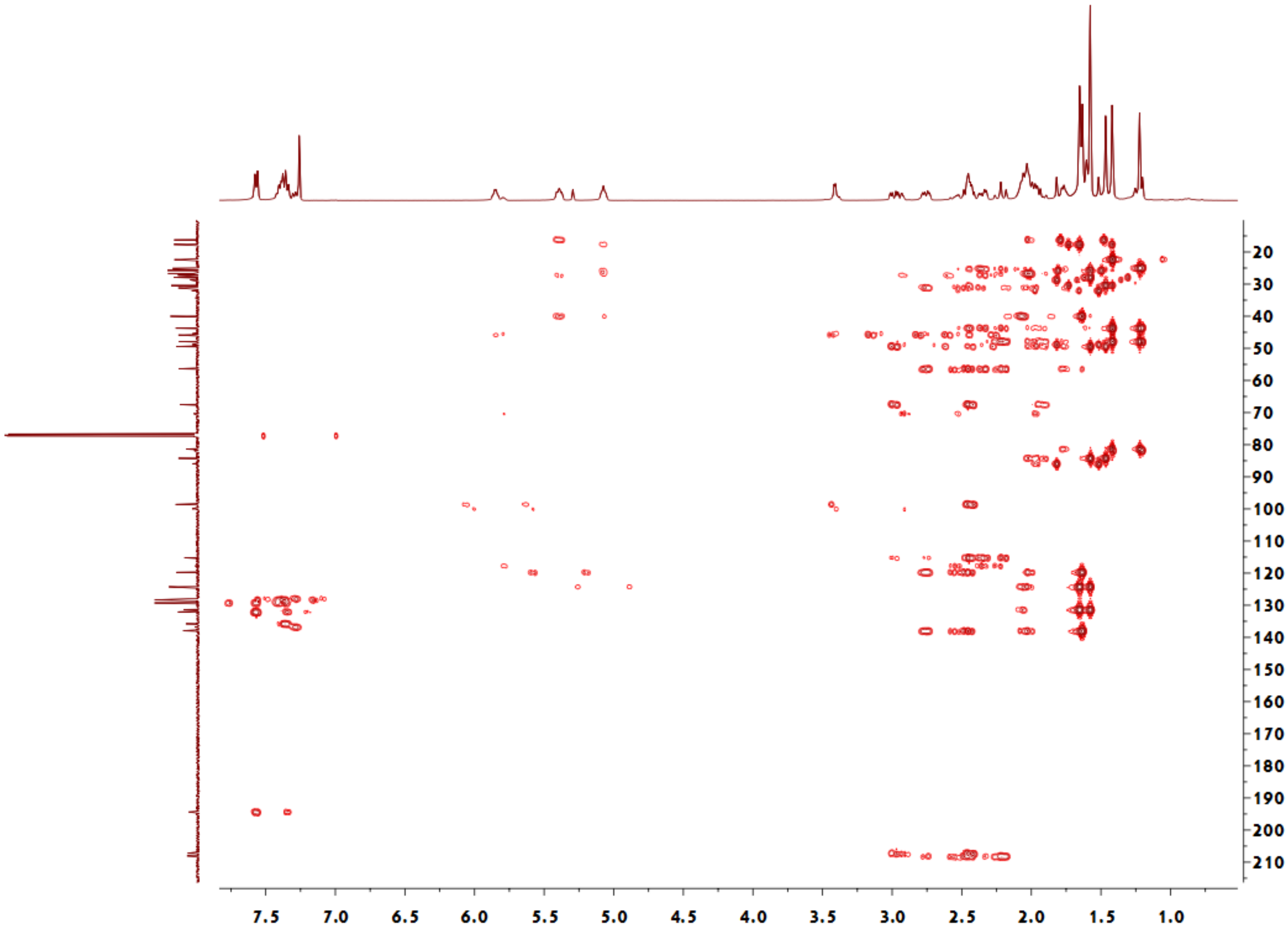
S13. ^{1}H-^{1}H COSY Spectrum of **2** in $CDCl_3$



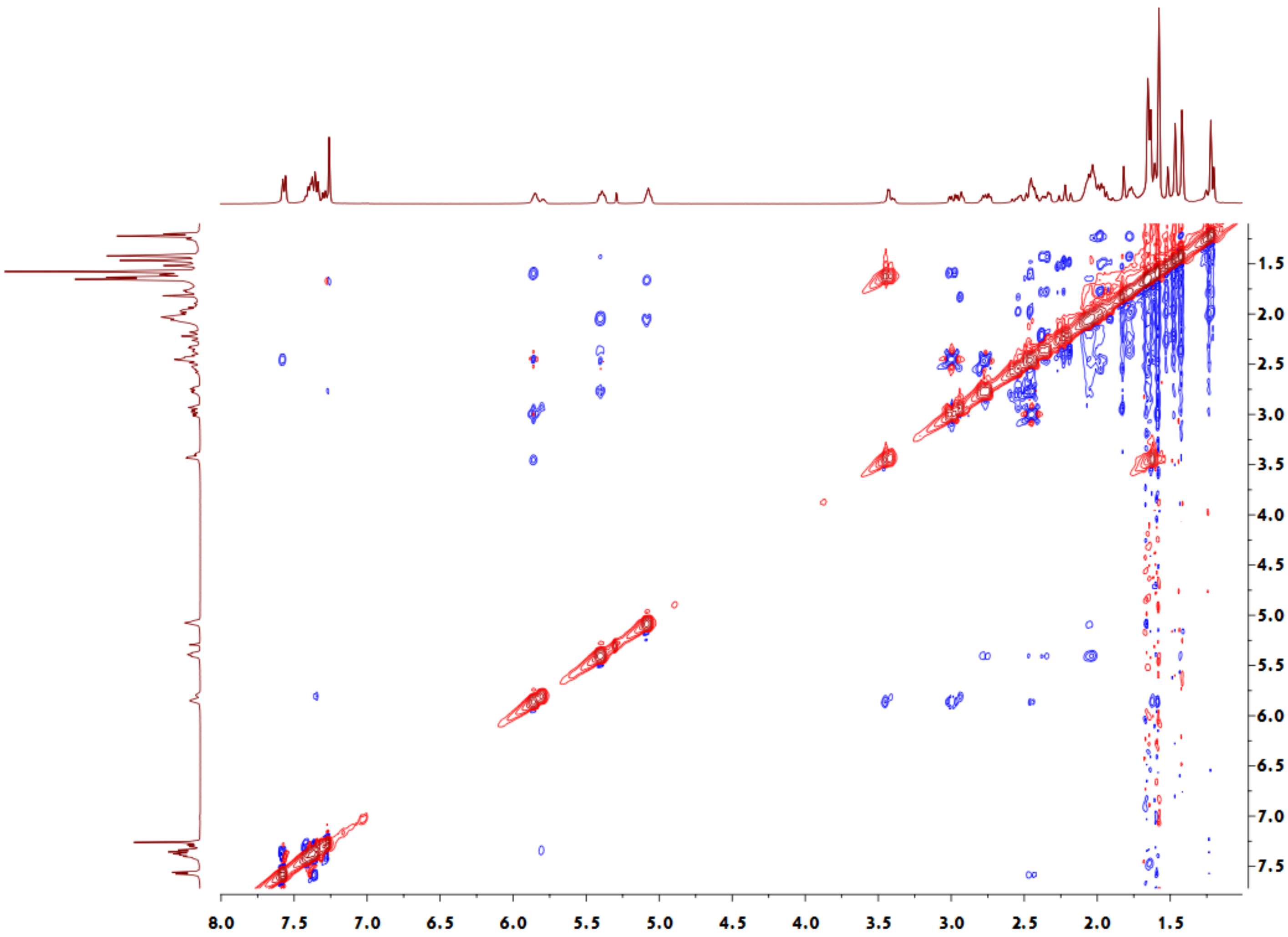
S14. HSQC Spectrum of **2** in $CDCl_3$



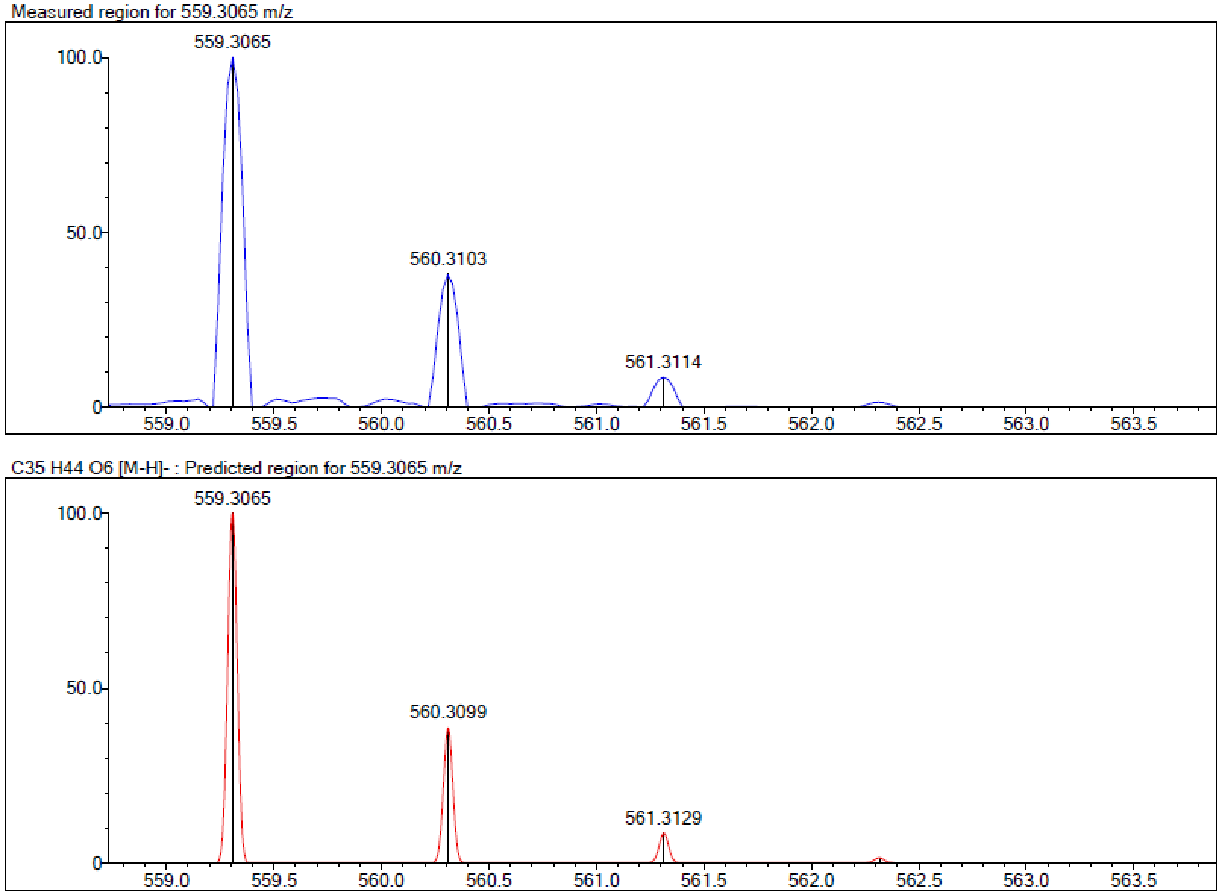
S15. HMBC Spectrum of **2** in $CDCl_3$



S16. NOESY Spectrum of **2** in $CDCl_3$

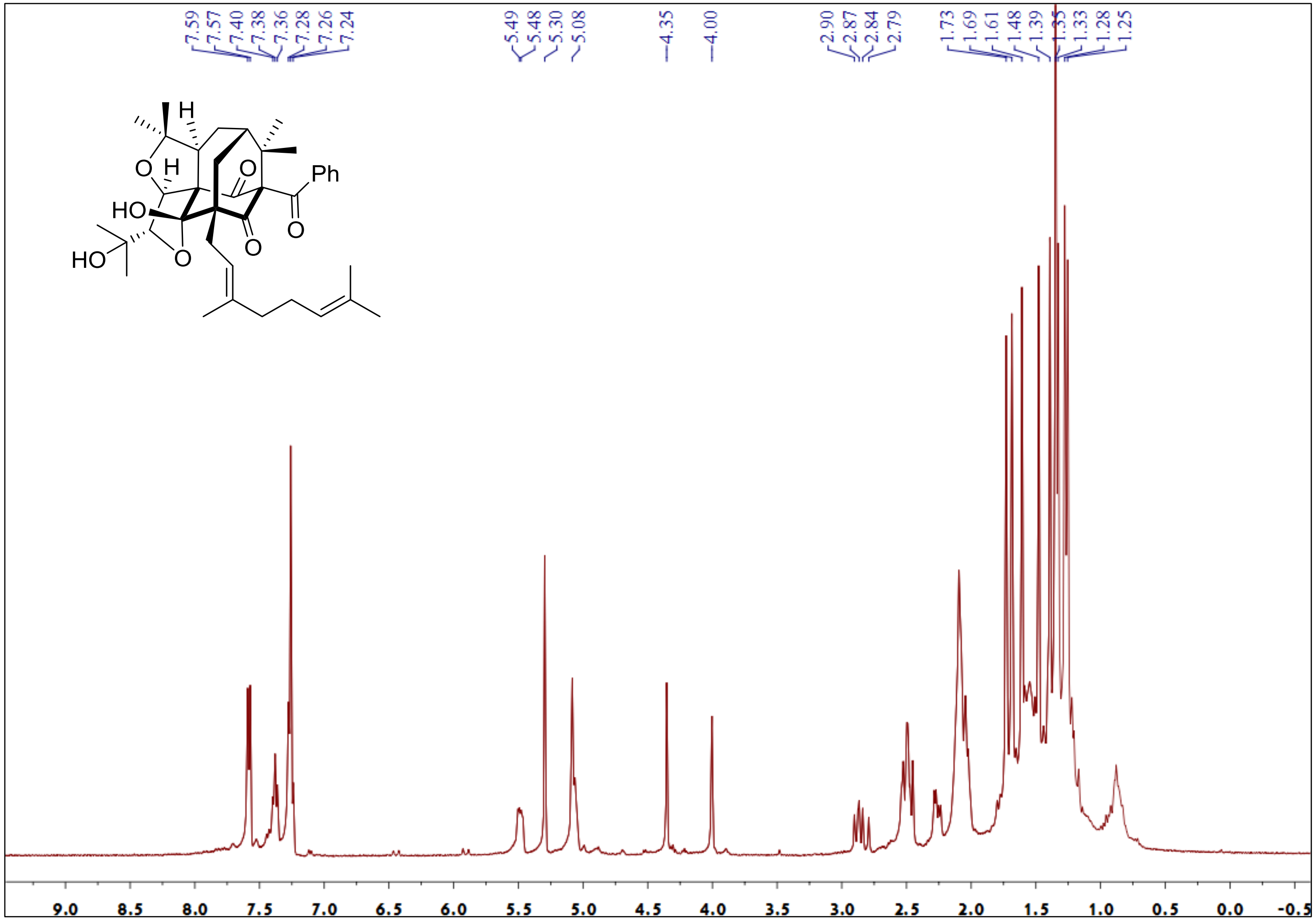


S17. HRESIMS spectrum of **2**

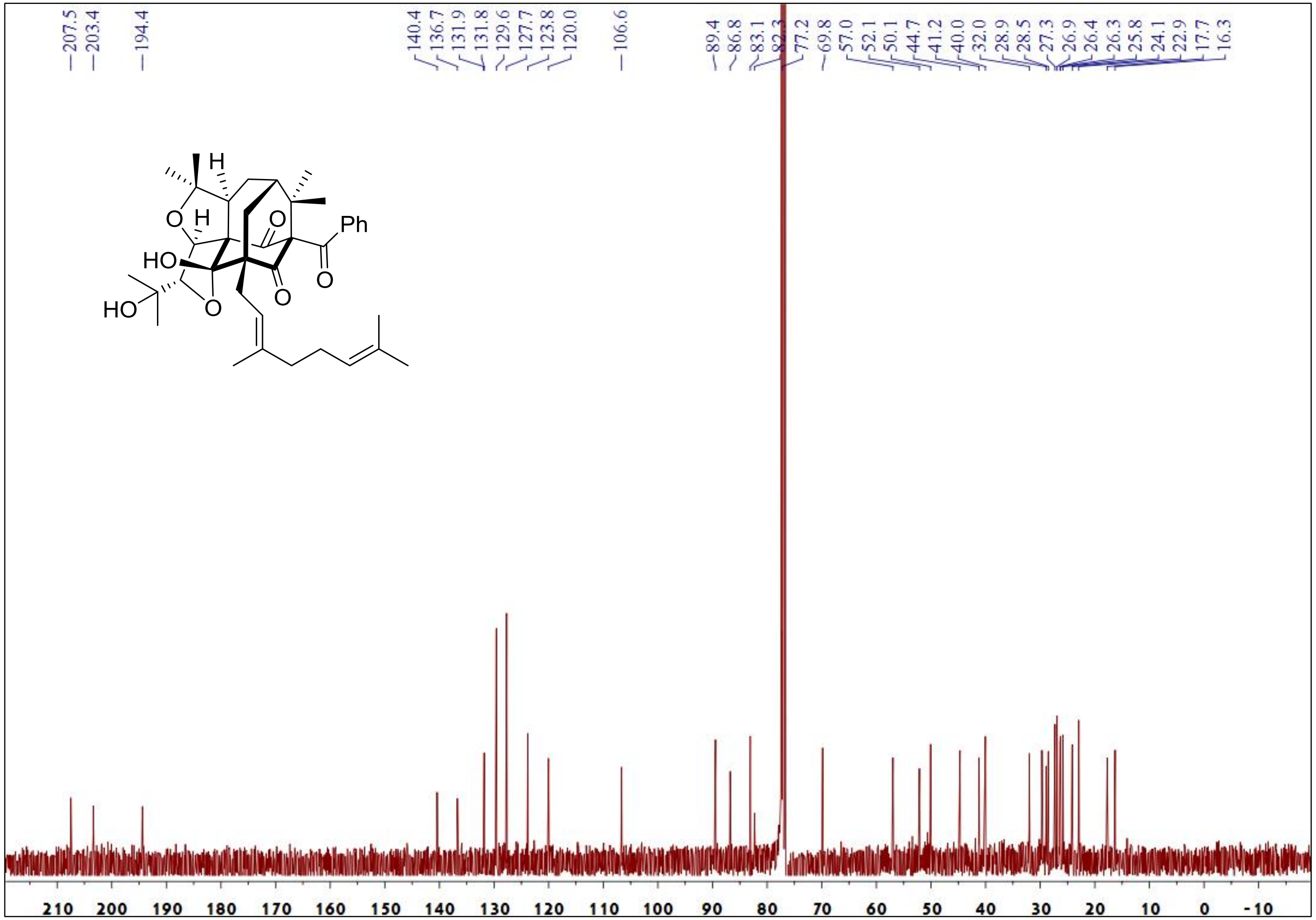


Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
1	99.52	C35 H44 O6	[M-H]-	559.3065	559.3065	-0.0	0.00	99.52	14.0

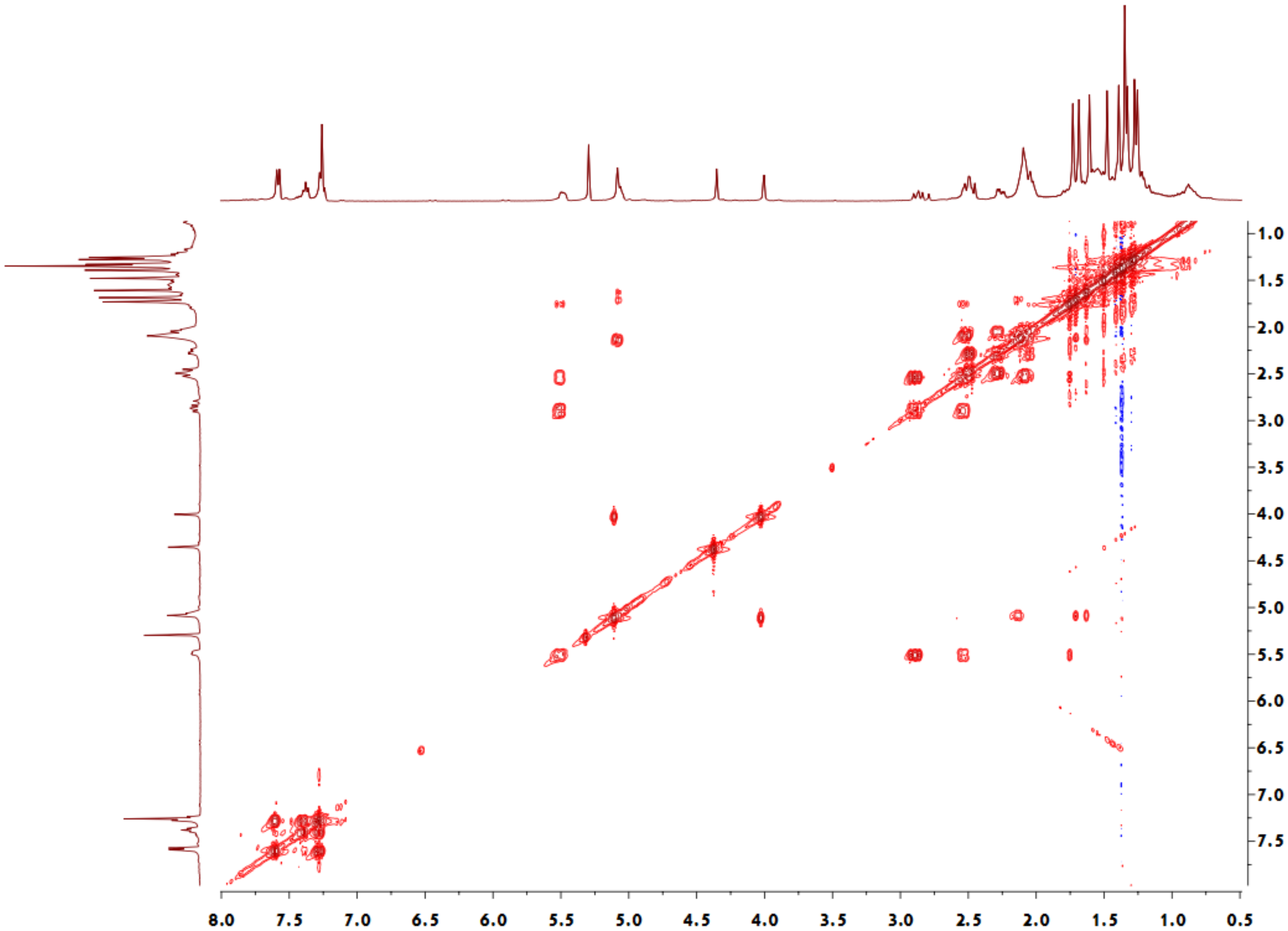
S18. ^{1}H NMR Spectrum of **3** in $CDCl_3$



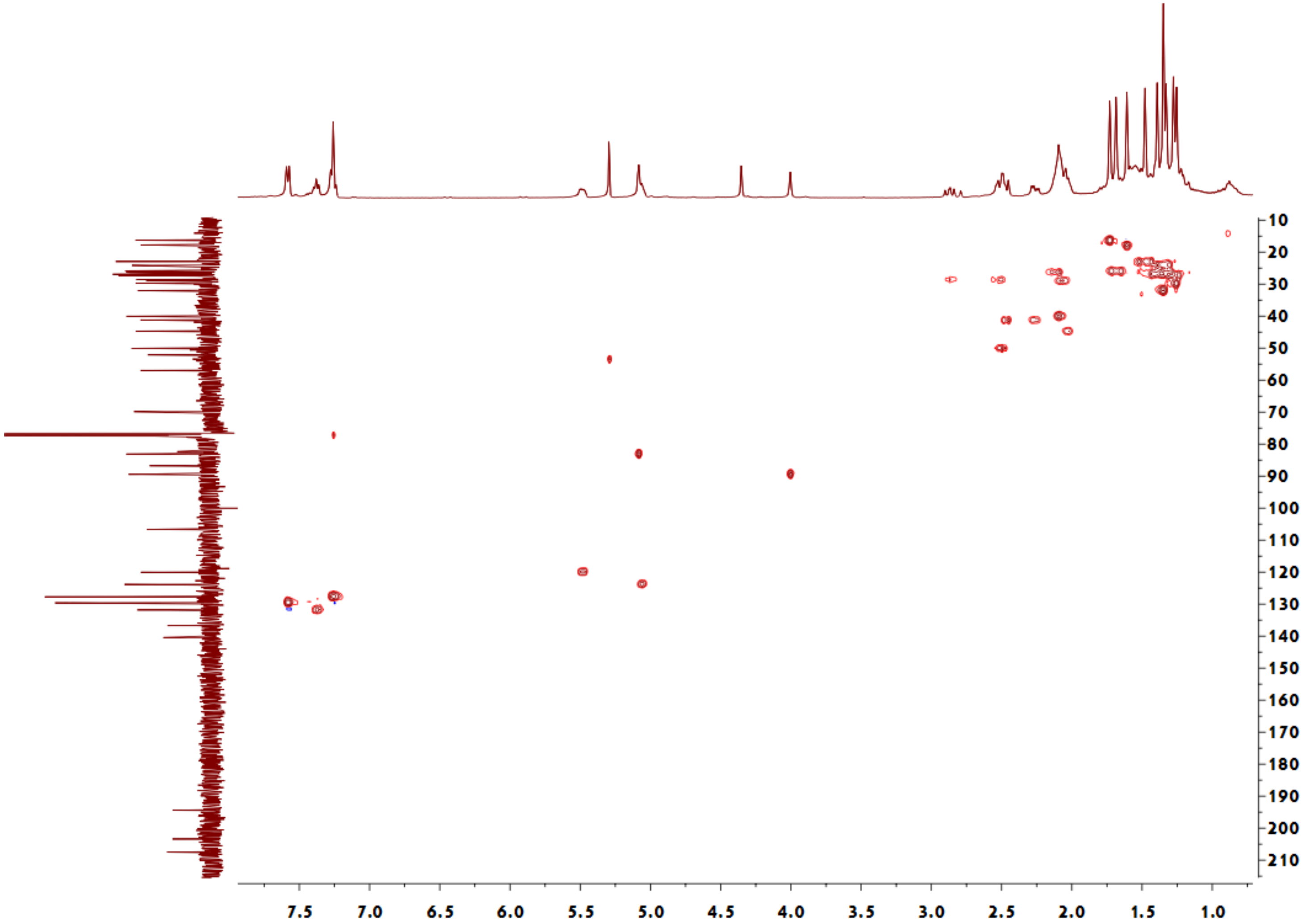
S19. ^{13}C NMR Spectra of **3** in $CDCl_3$



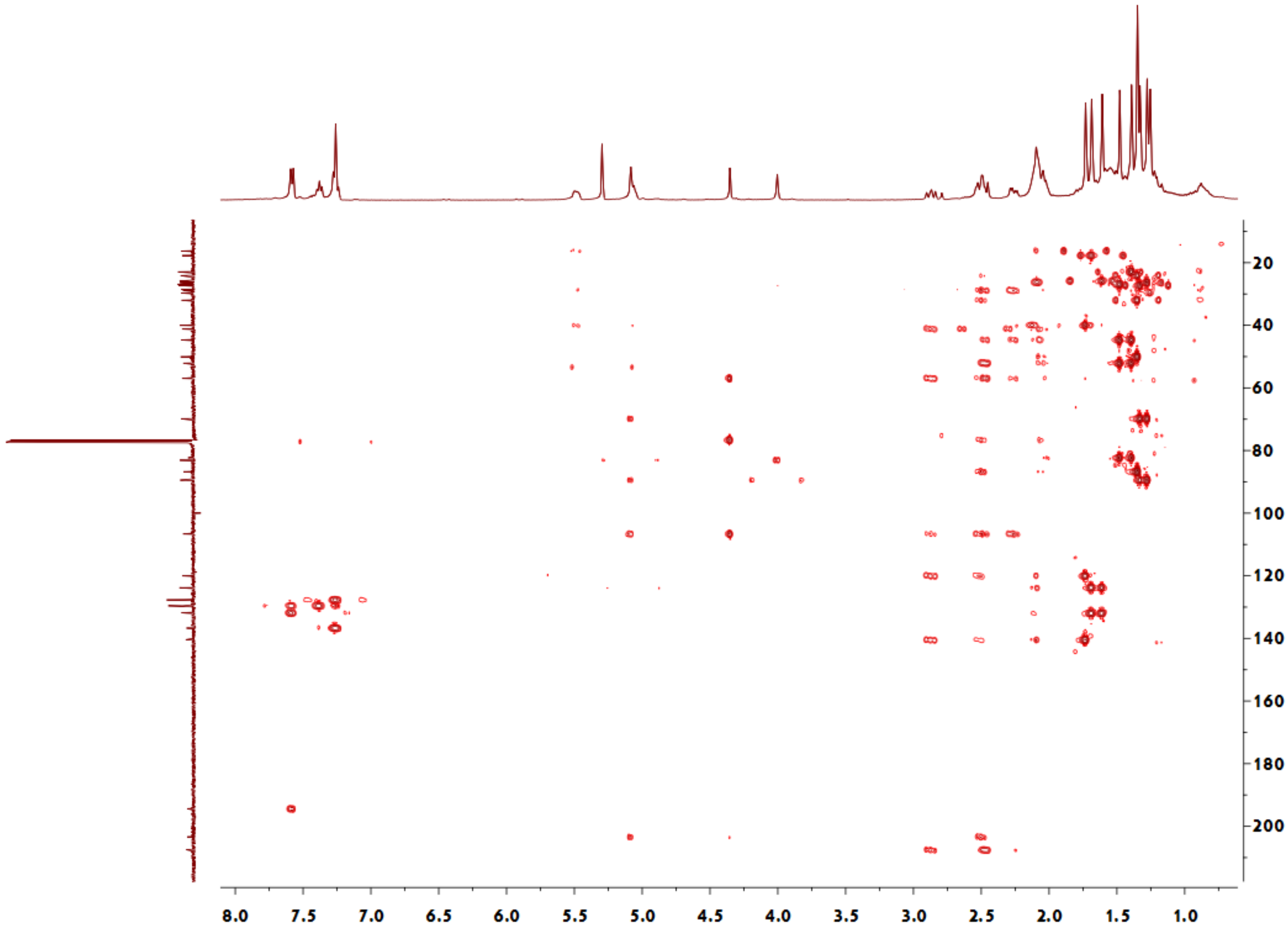
S20. ^{1}H-^{1}H COSY Spectrum of **3** in $CDCl_3$



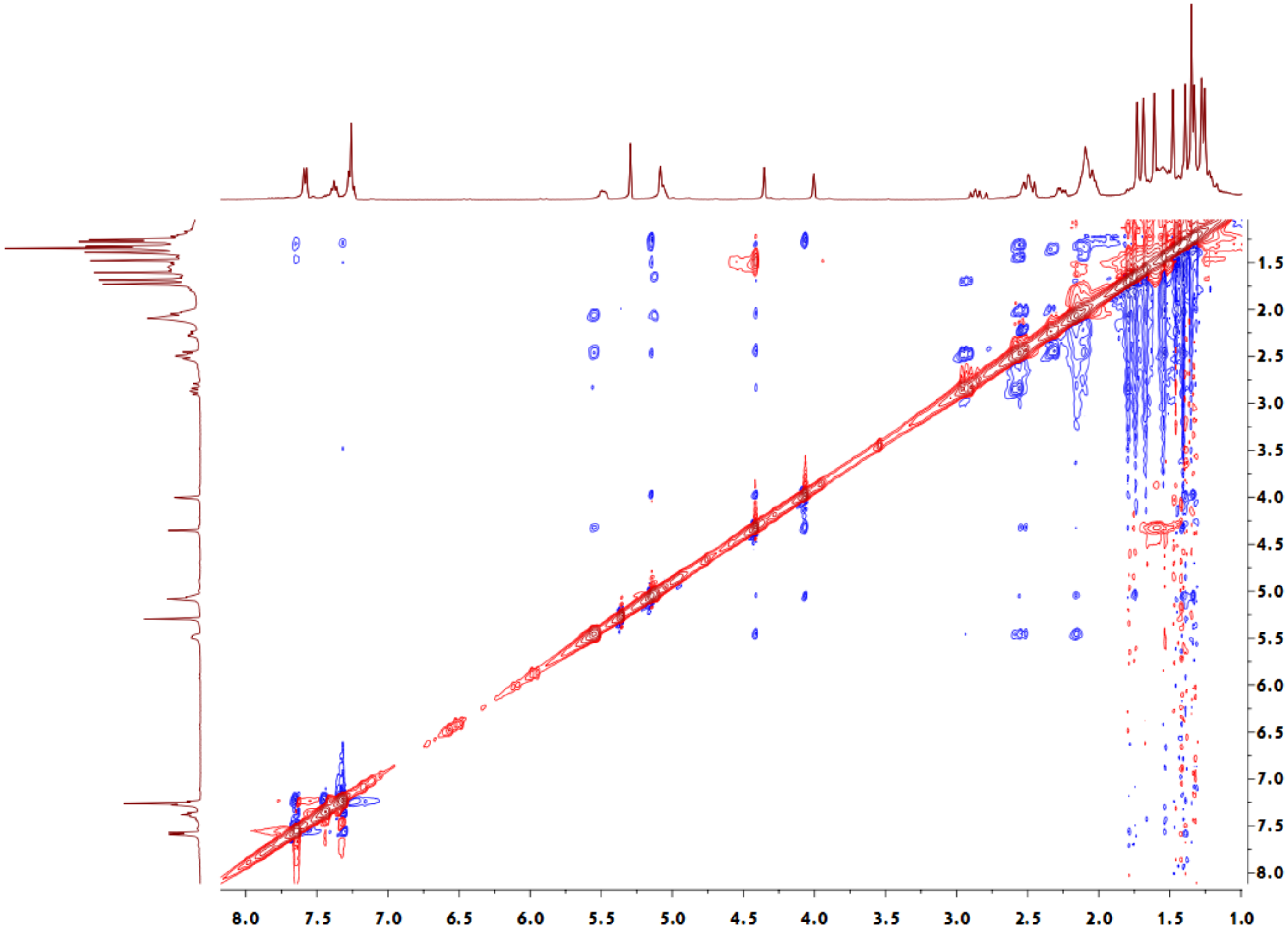
S21. HSQC Spectrum of **3** in $CDCl_3$



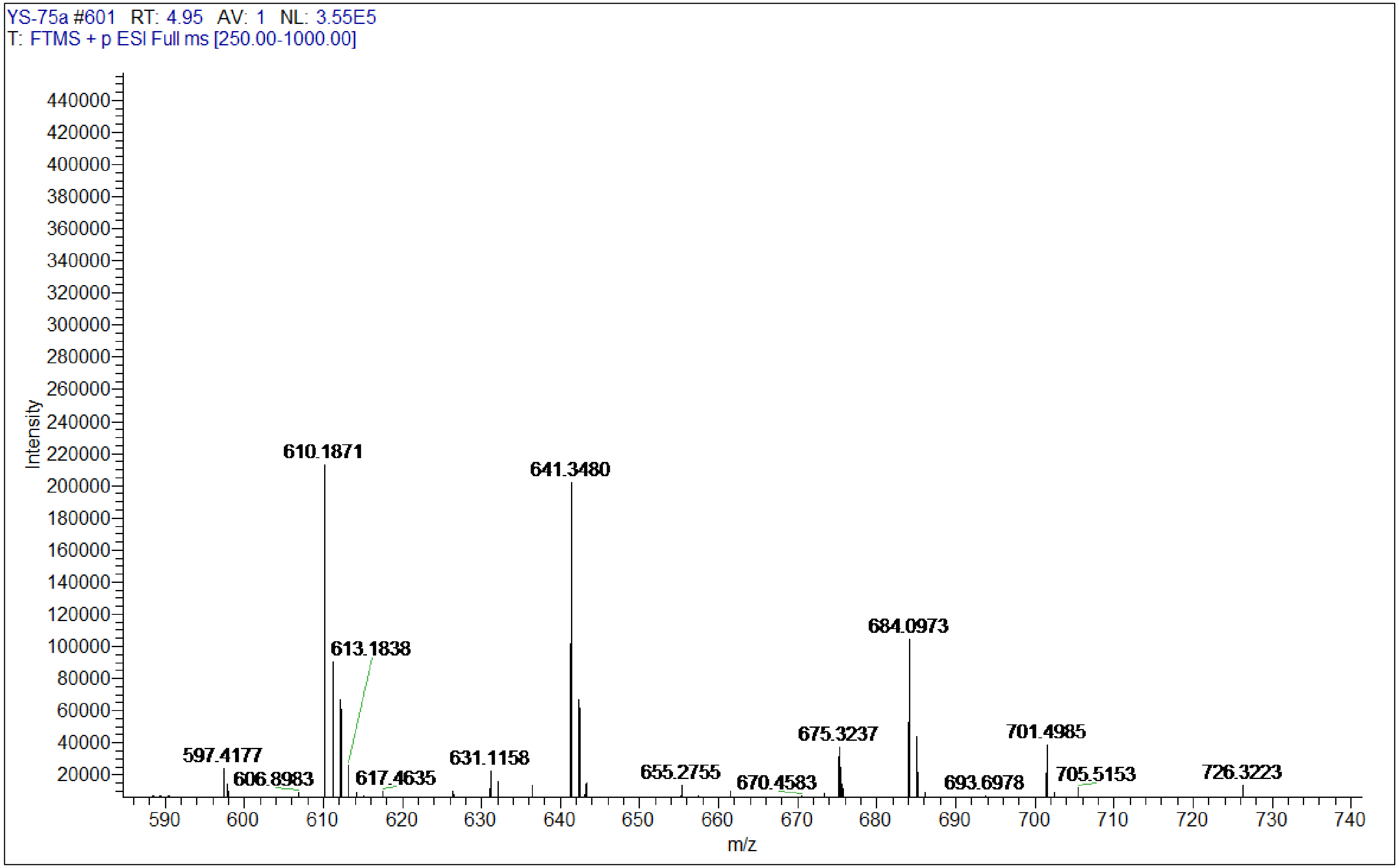
S22. HMBC Spectrum of **3** in $CDCl_3$



S23. NOESY Spectrum of **3** in $CDCl_3$



S24. HRESIMS spectrum of **3**



S25. Selected ^{1}H–^{1}H COSY and HMBC correlations of **3**

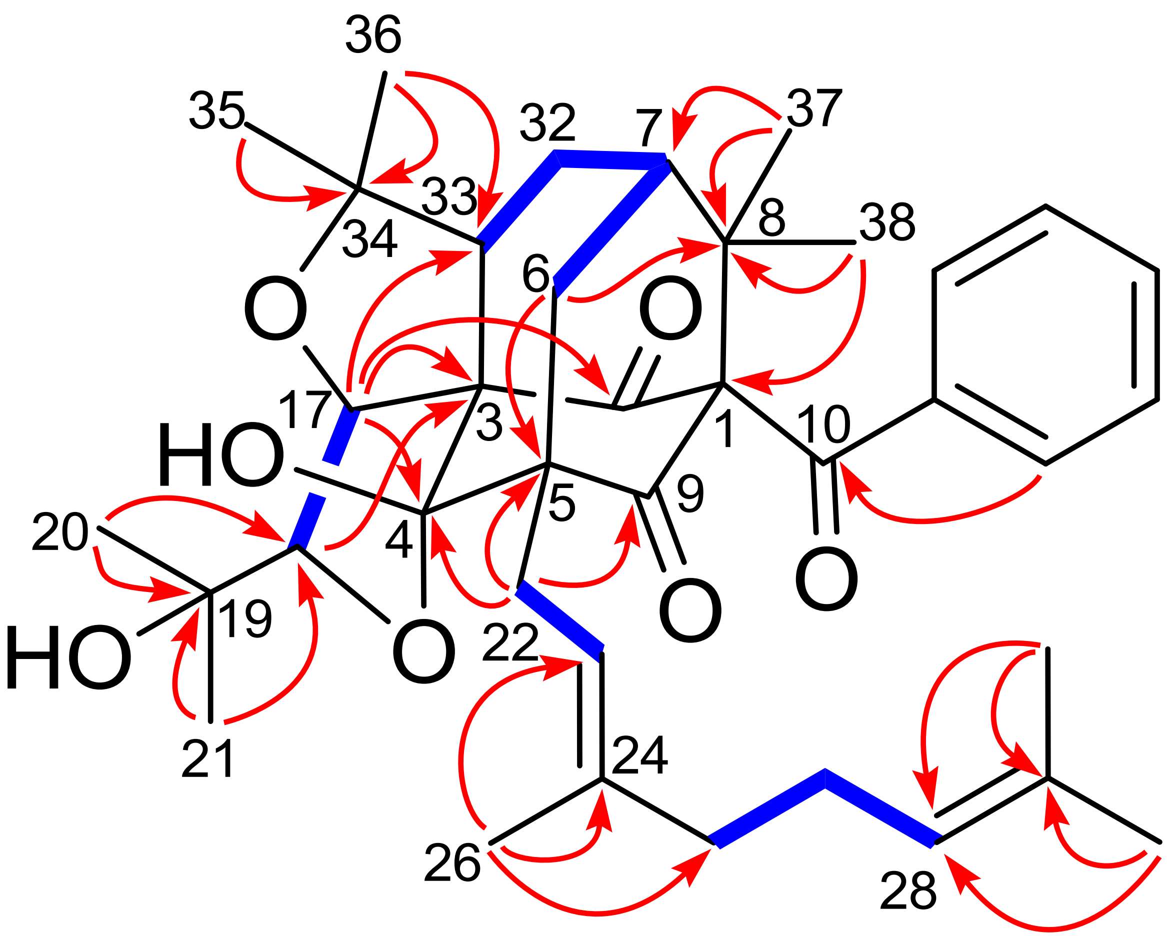
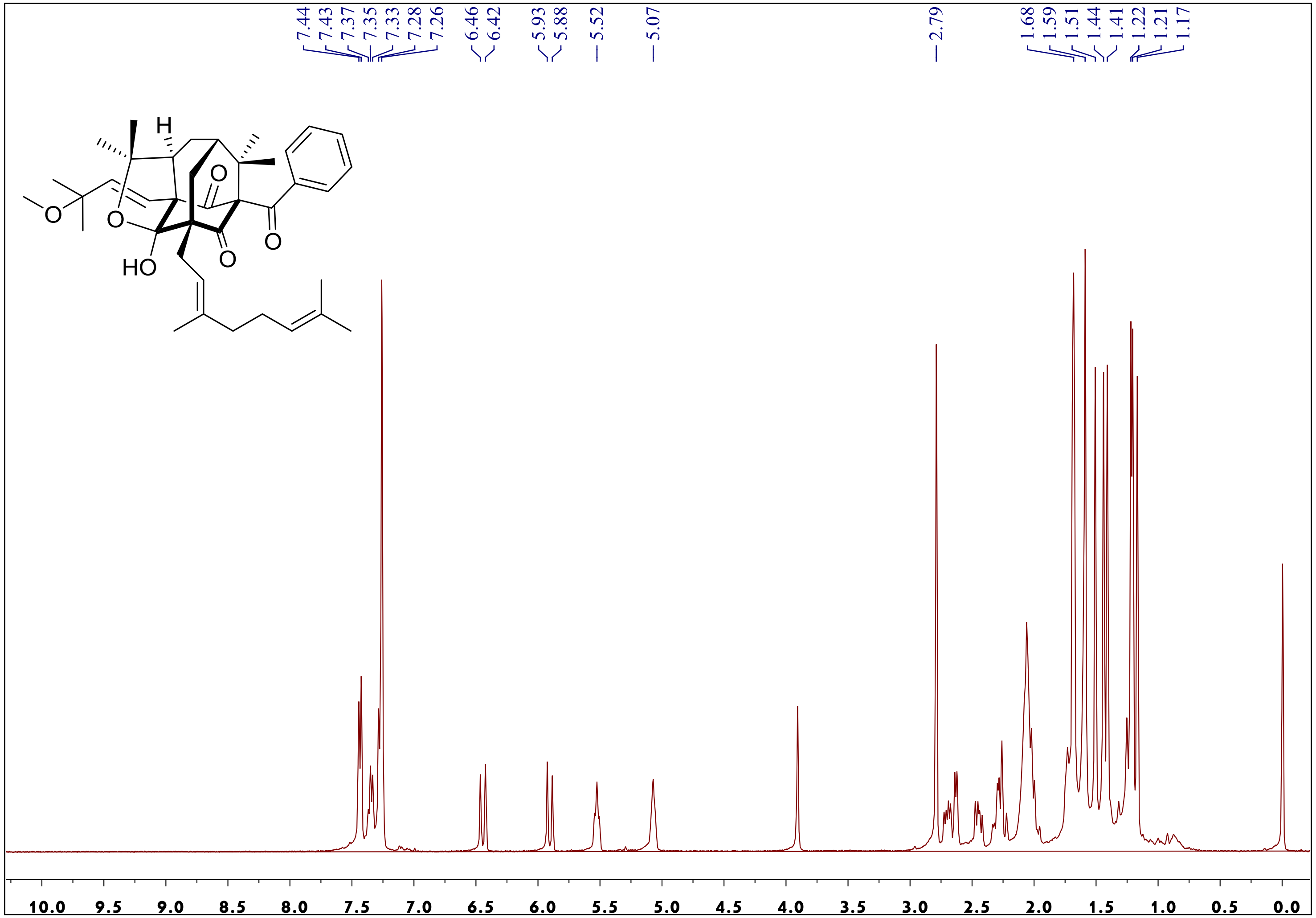
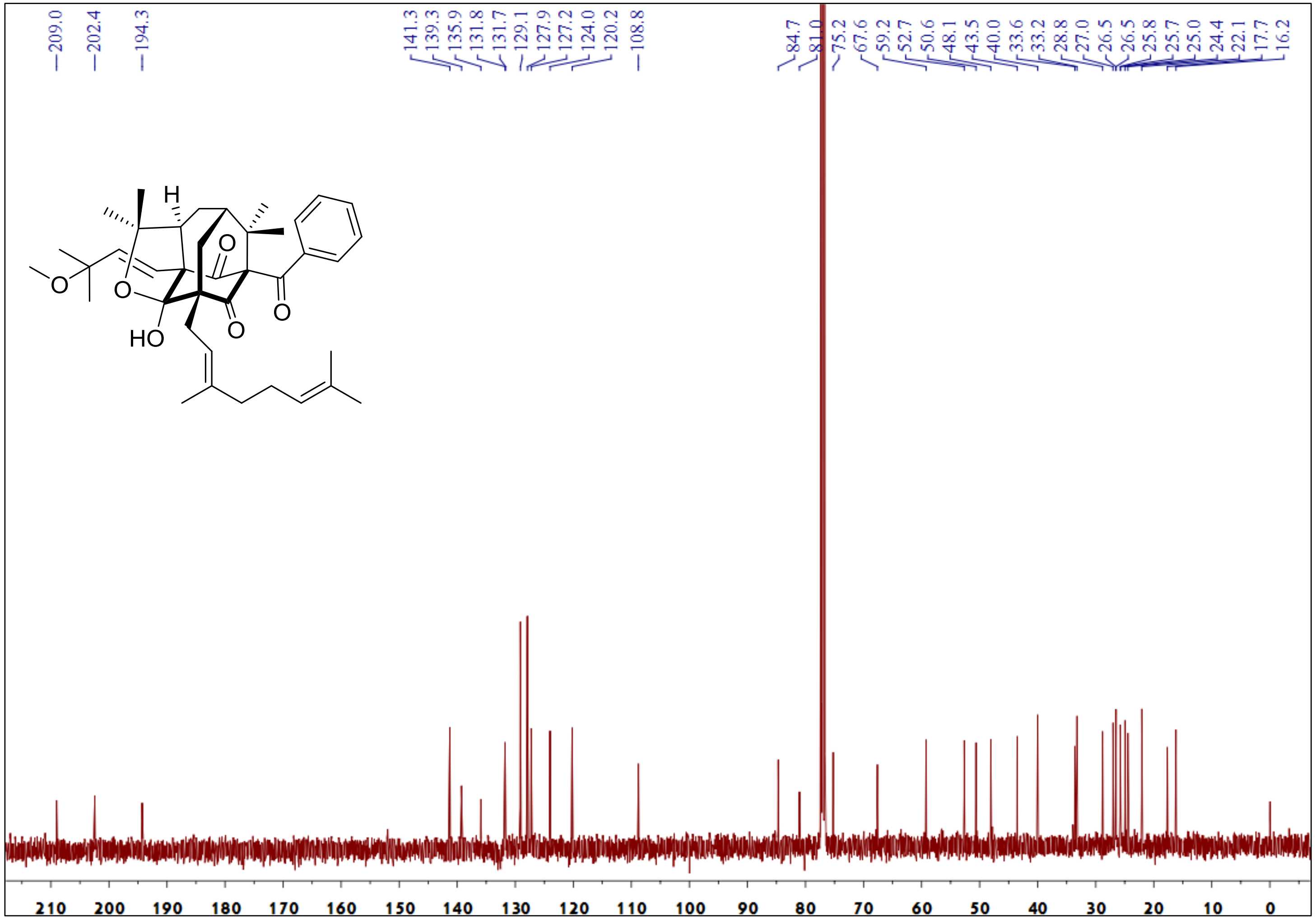


Figure S3. Selected ^{1}H–^{1}H COSY (—) and HMBC (→) correlations of **3**

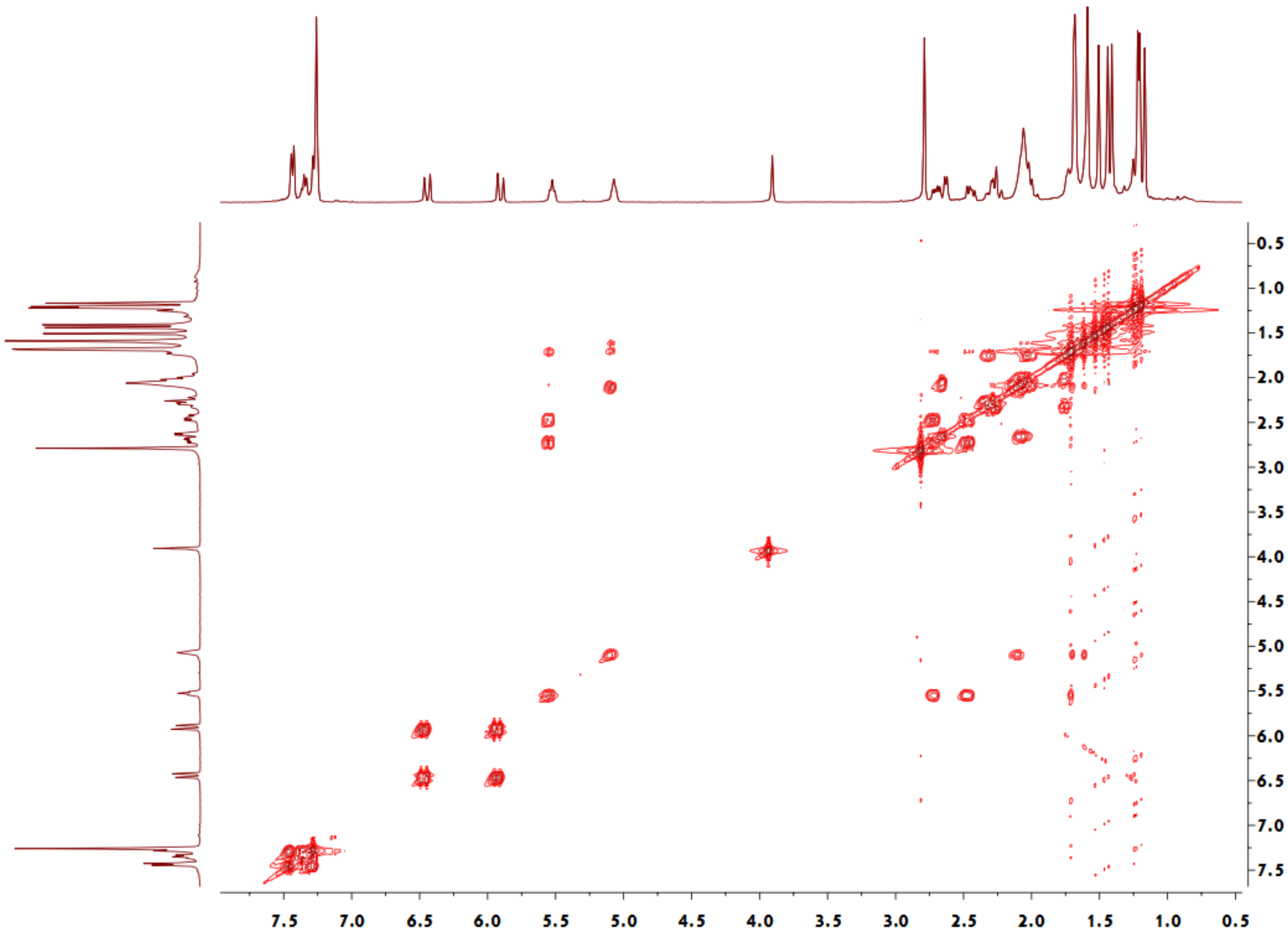
S26. ^{1}H NMR Spectrum of **4** in $CDCl_3$



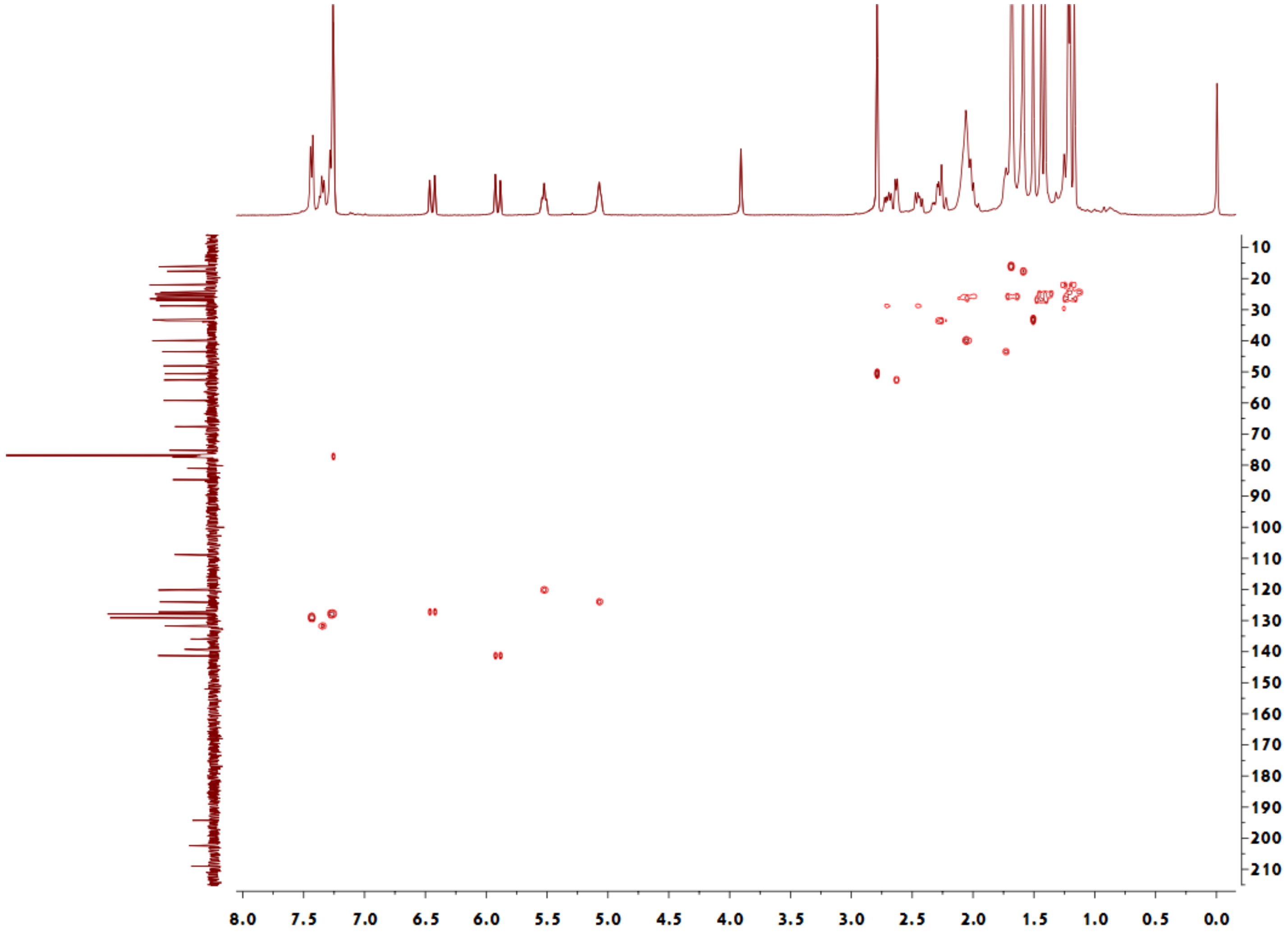
S27. ^{13}C NMR Spectra of **4** in $CDCl_3$



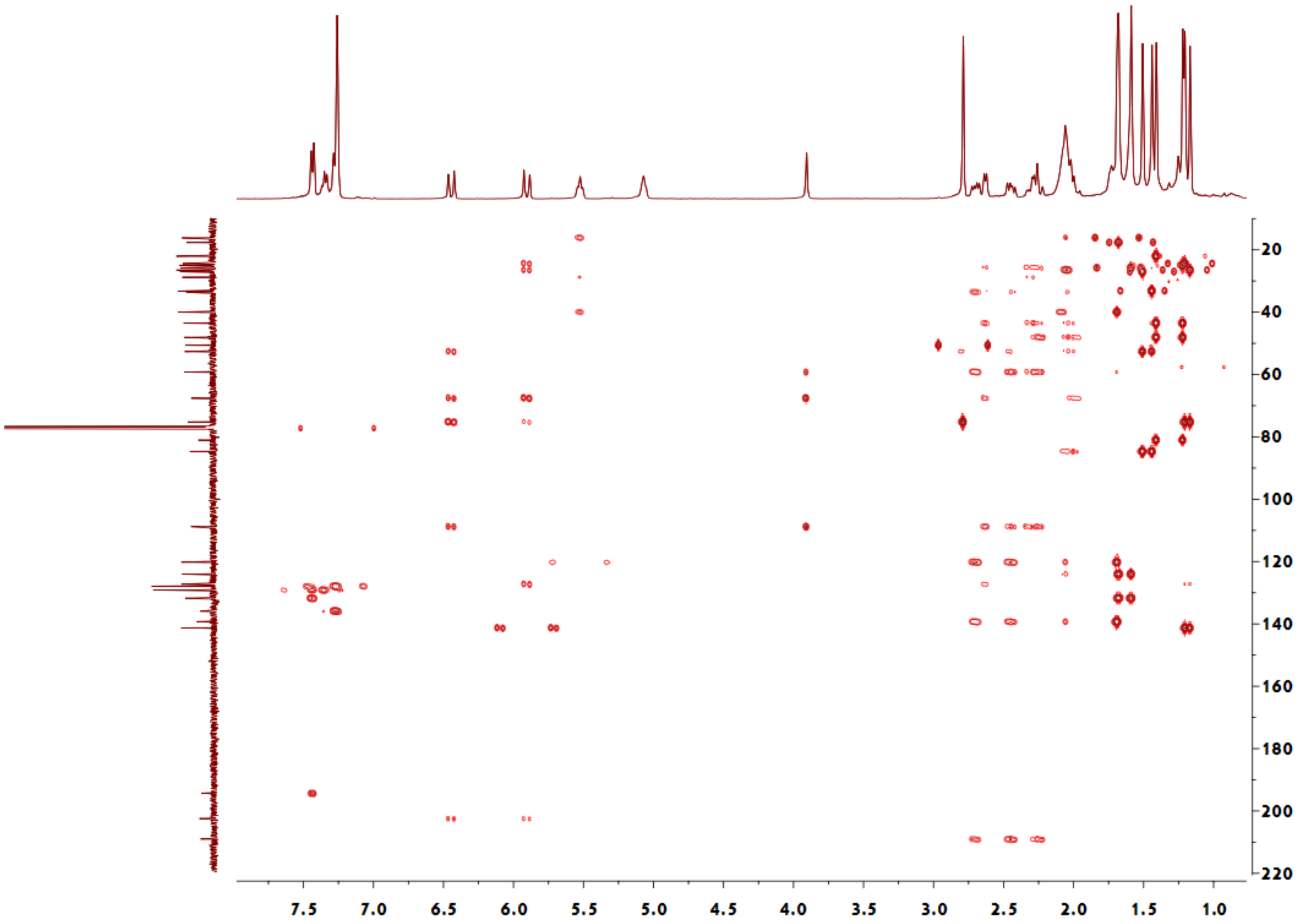
S28. [1]H-[1]H COSY Spectrum of **4** in $CDCl_3$



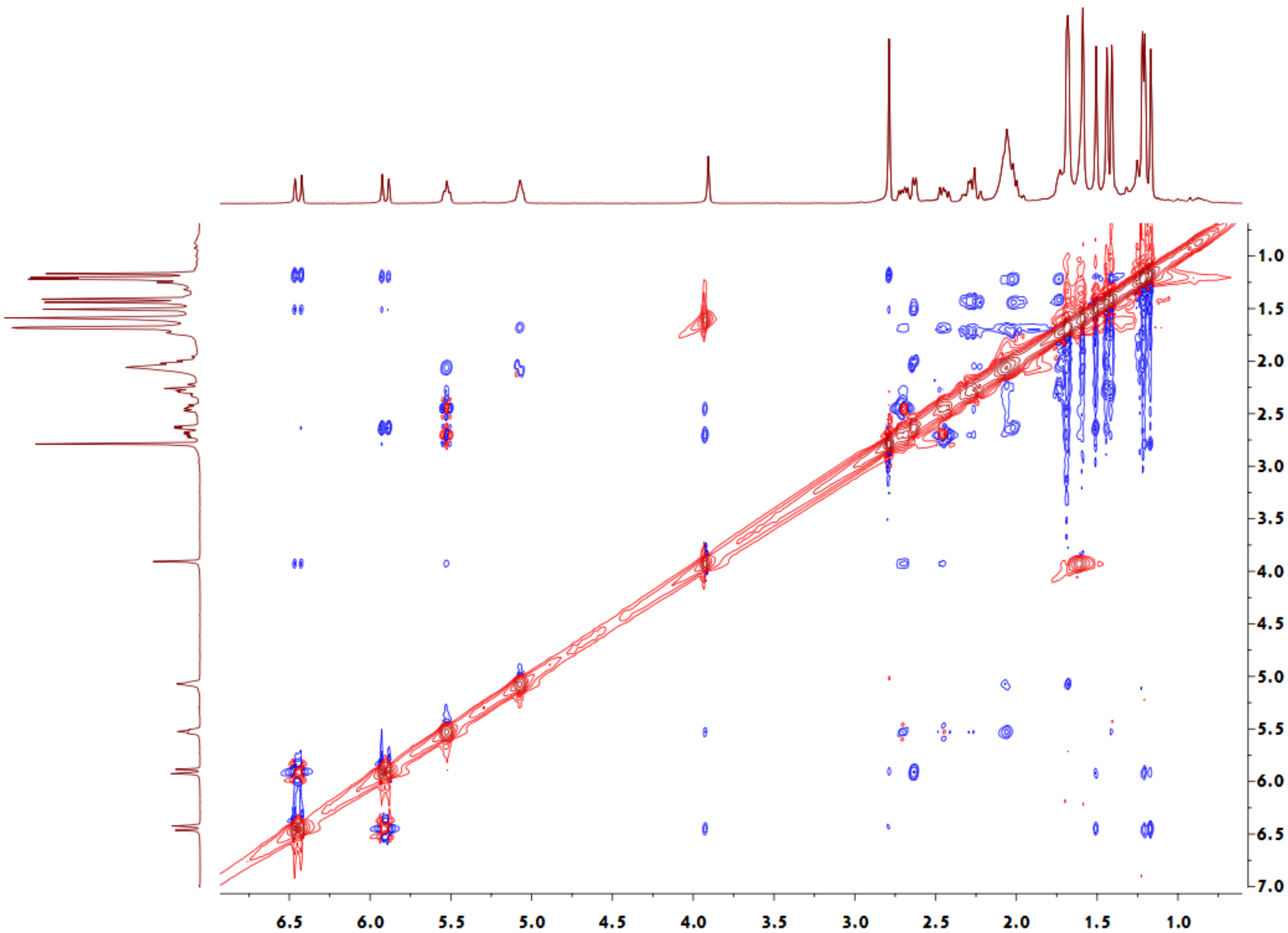
S29. HSQC Spectrum of **4** in $CDCl_3$



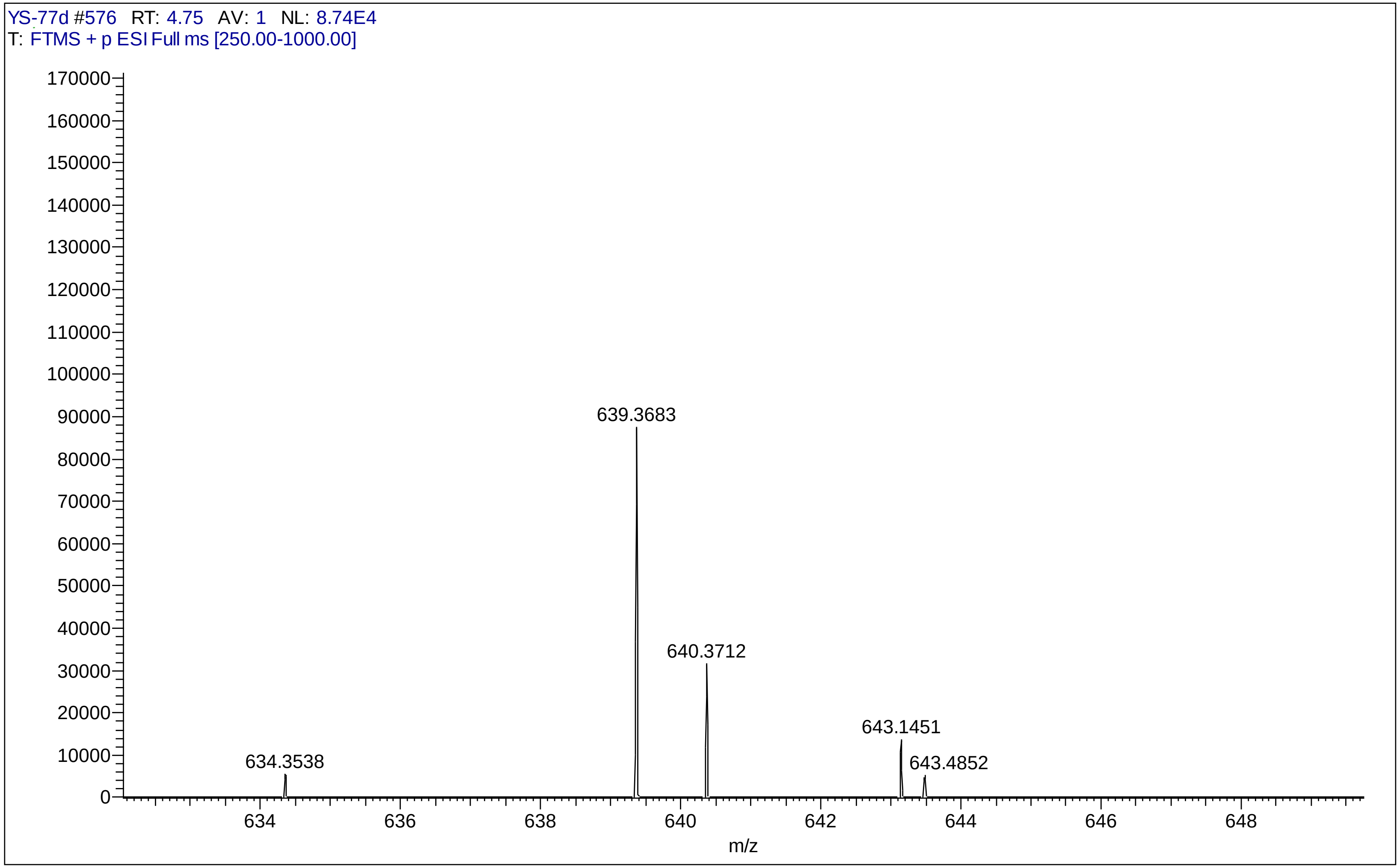
S30. HMBC Spectrum of **4** in $CDCl_3$



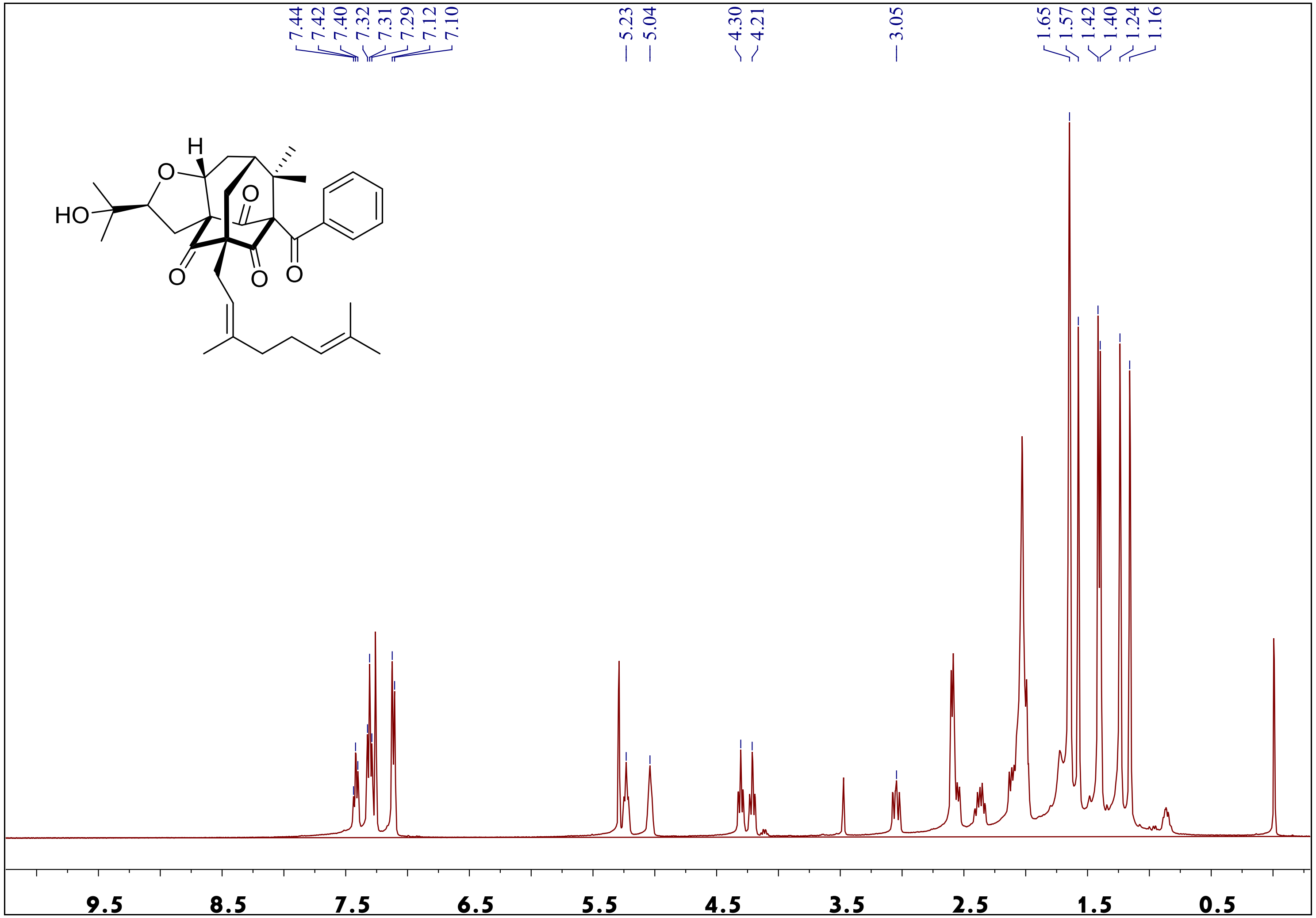
S31. NOESY Spectrum of **4** in $CDCl_3$



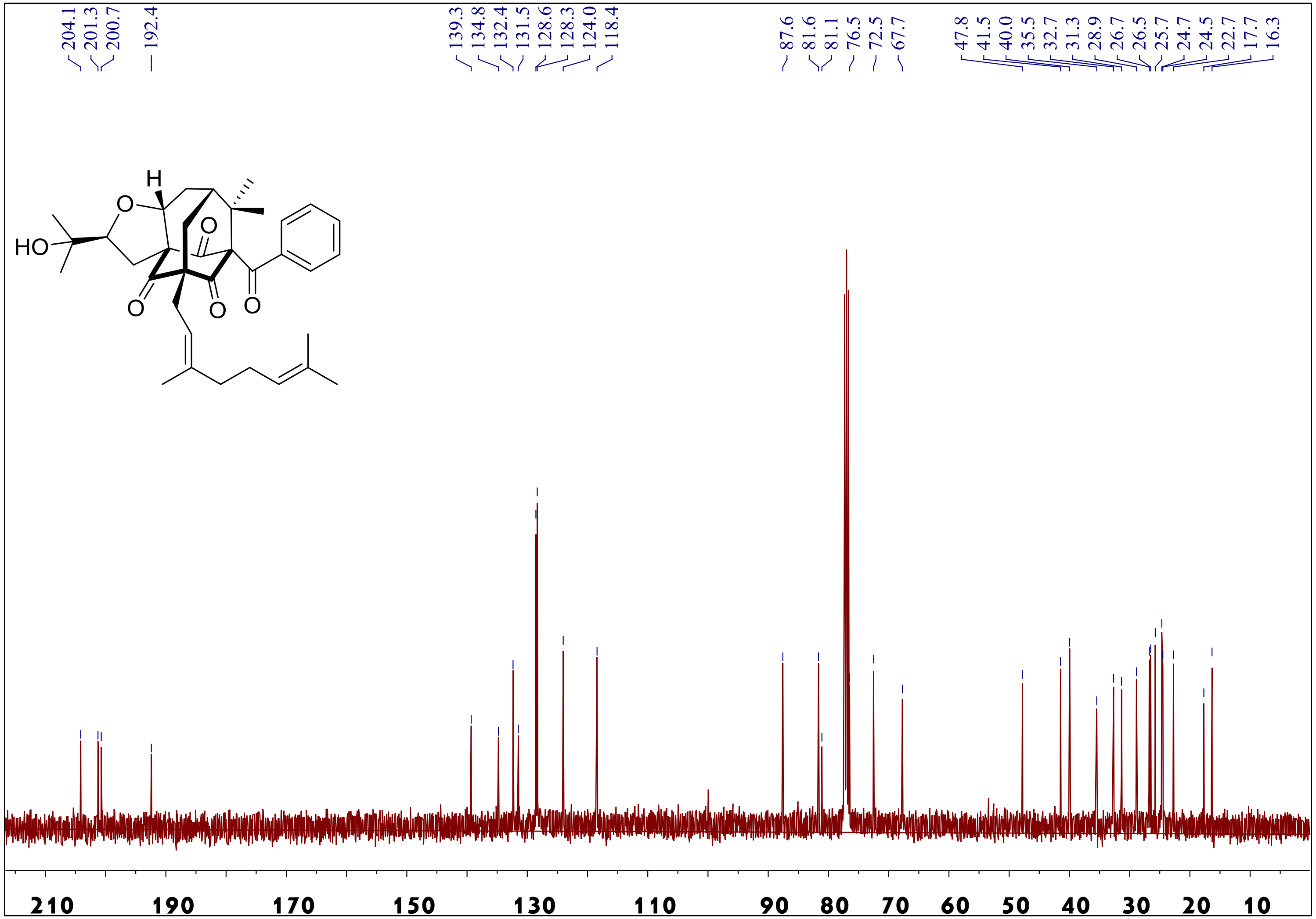
S32. HRESIMS spectrum of **4**



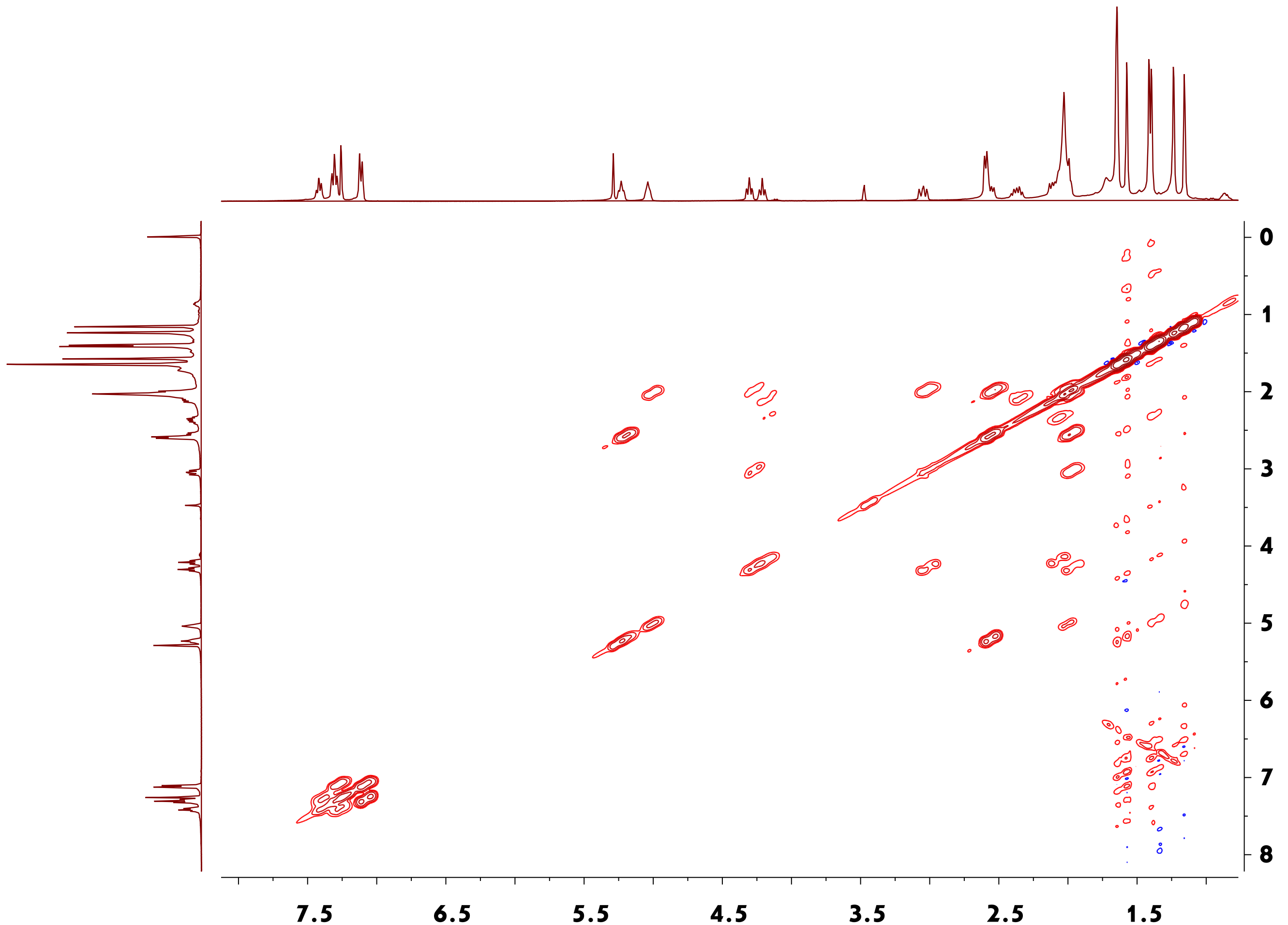
S33. ^{1}H NMR Spectrum of **5** in $CDCl_3$



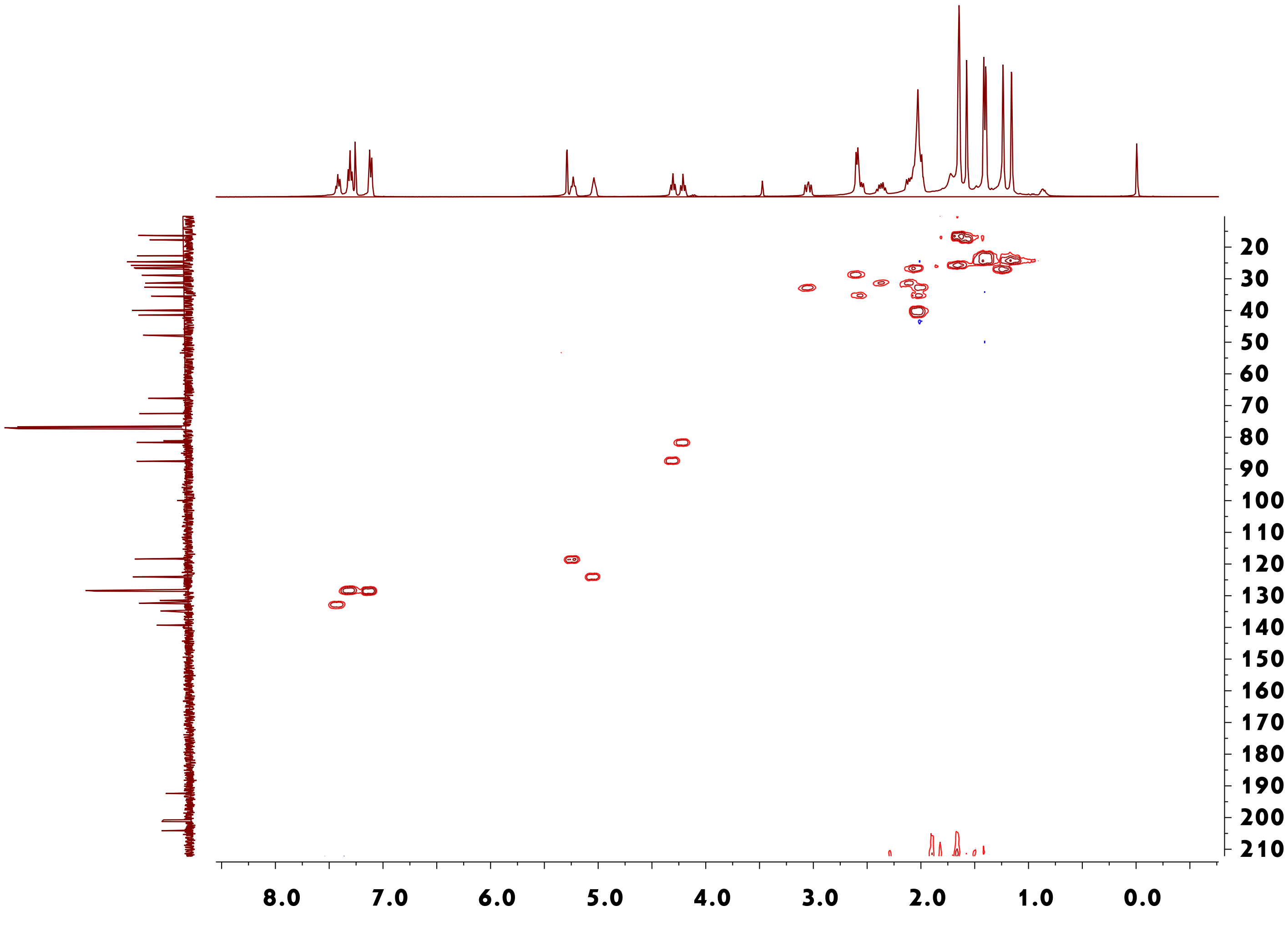
S34. ^{13}C NMR Spectra of **5** in $CDCl_3$



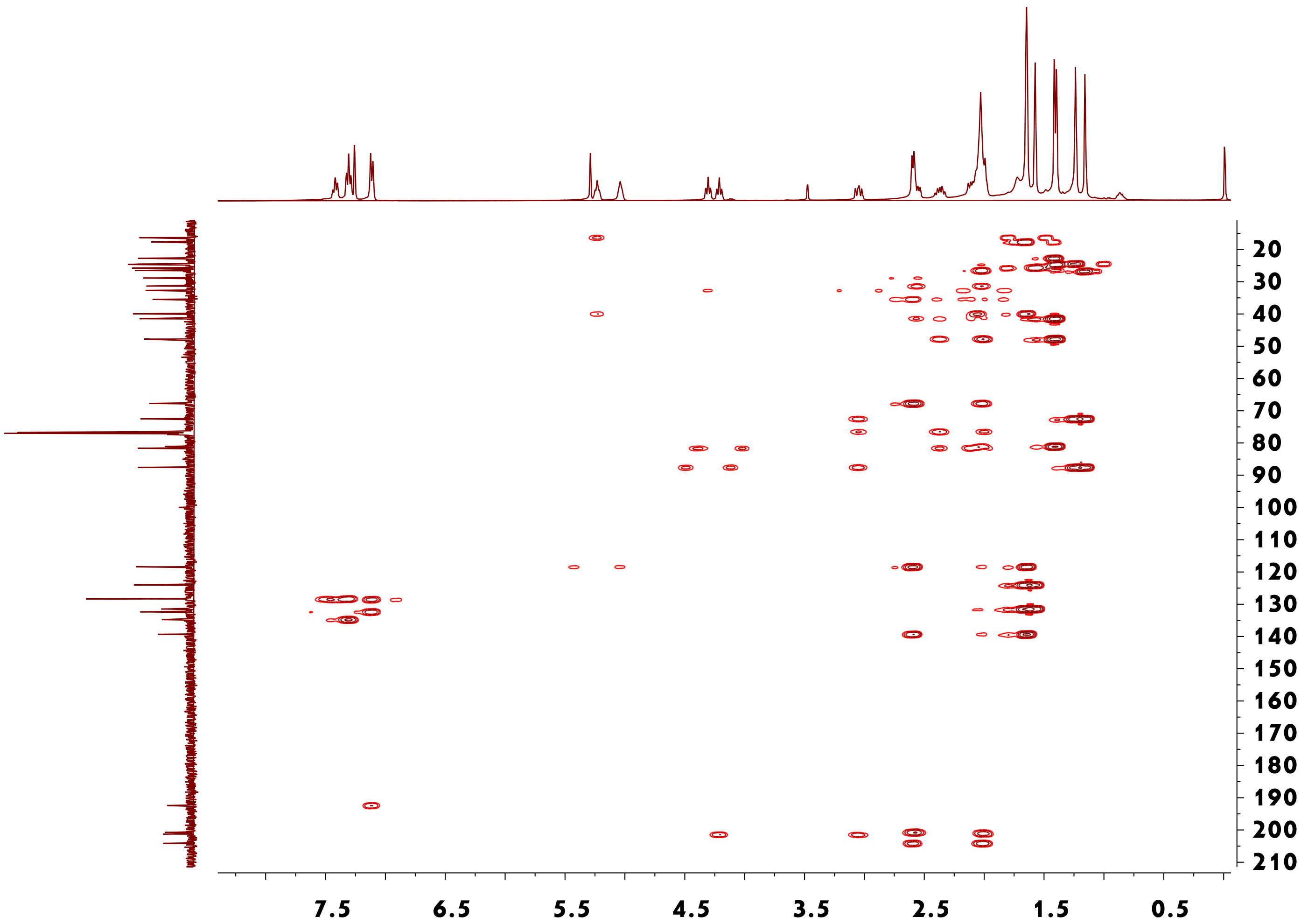
S35. ^{1}H-^{1}H COSY Spectrum of **5** in $CDCl_3$



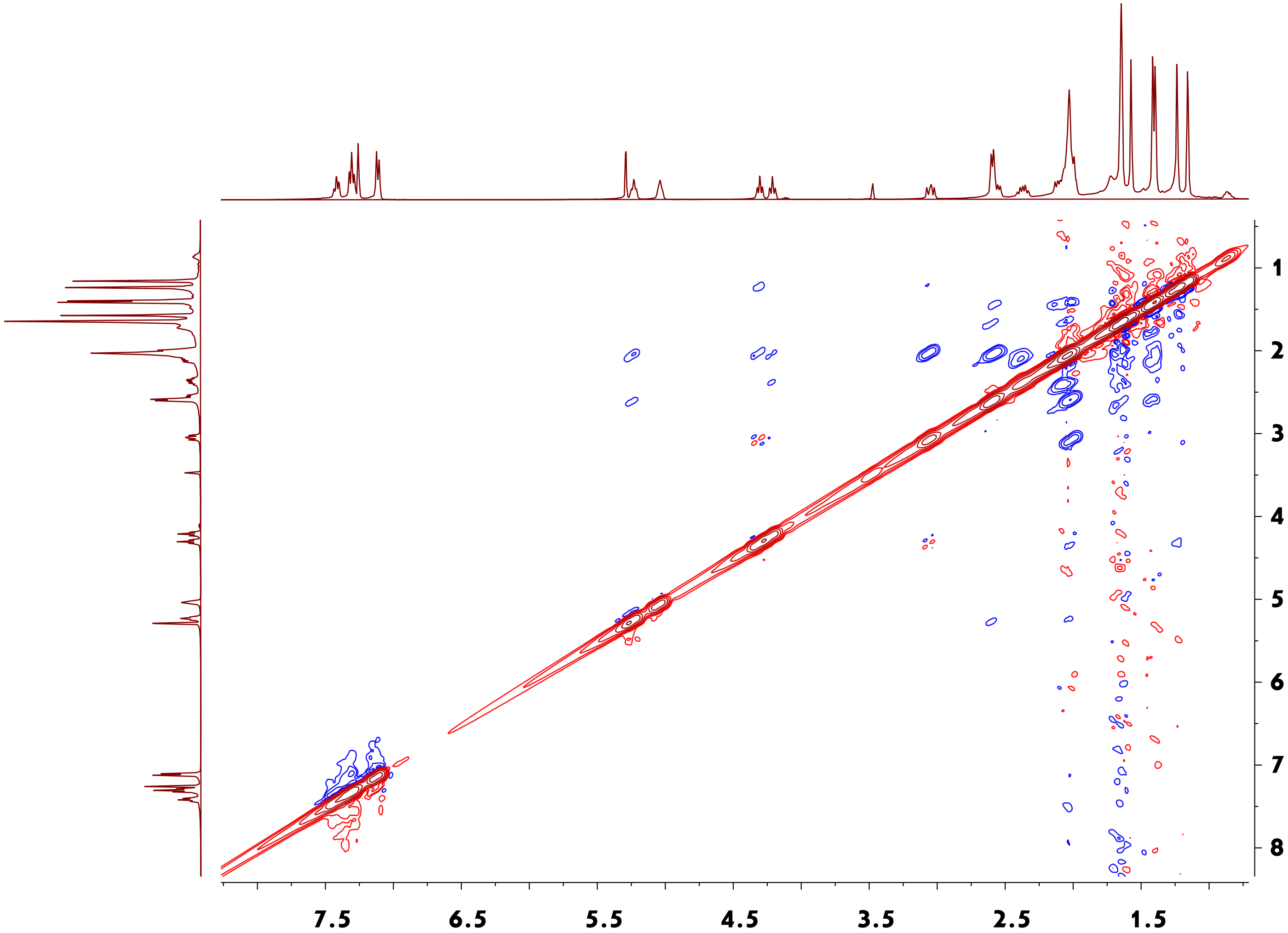
S36. HSQC Spectrum of **5** in $CDCl_3$



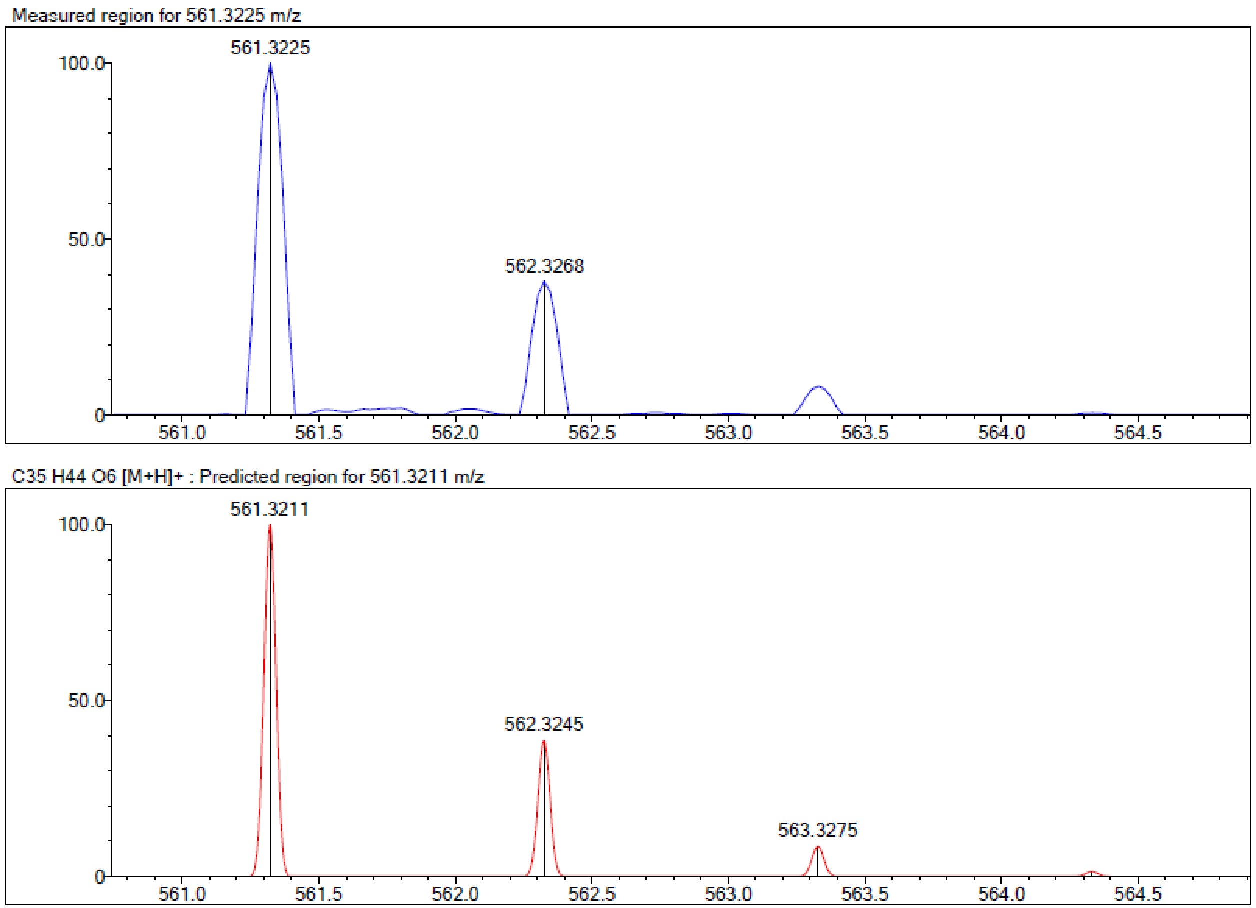
S37. HMBC Spectrum of **5** in $CDCl_3$



S38. NOESY Spectrum of **5** in $CDCl_3$

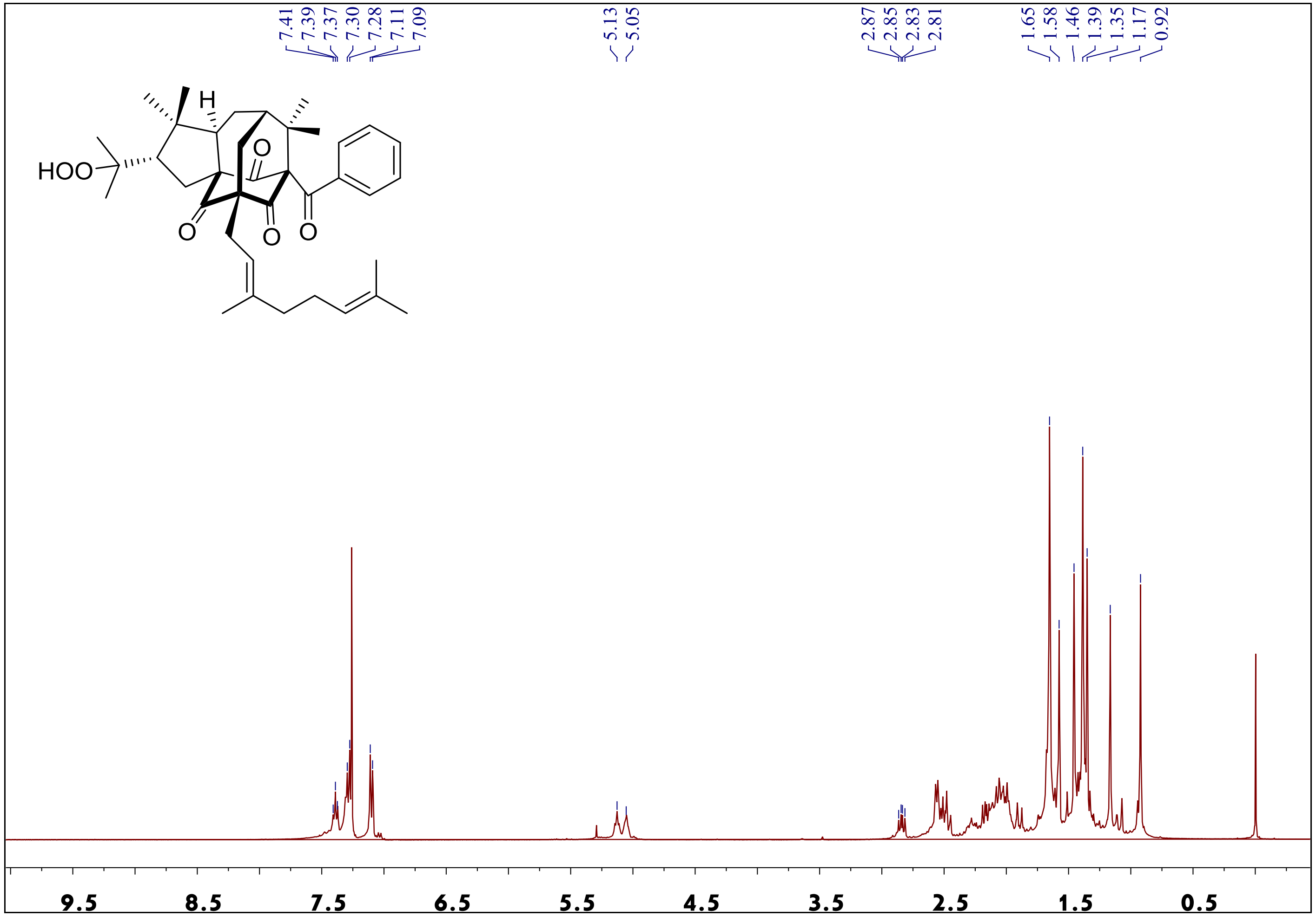


S39. HRESIMS spectrum of **5**

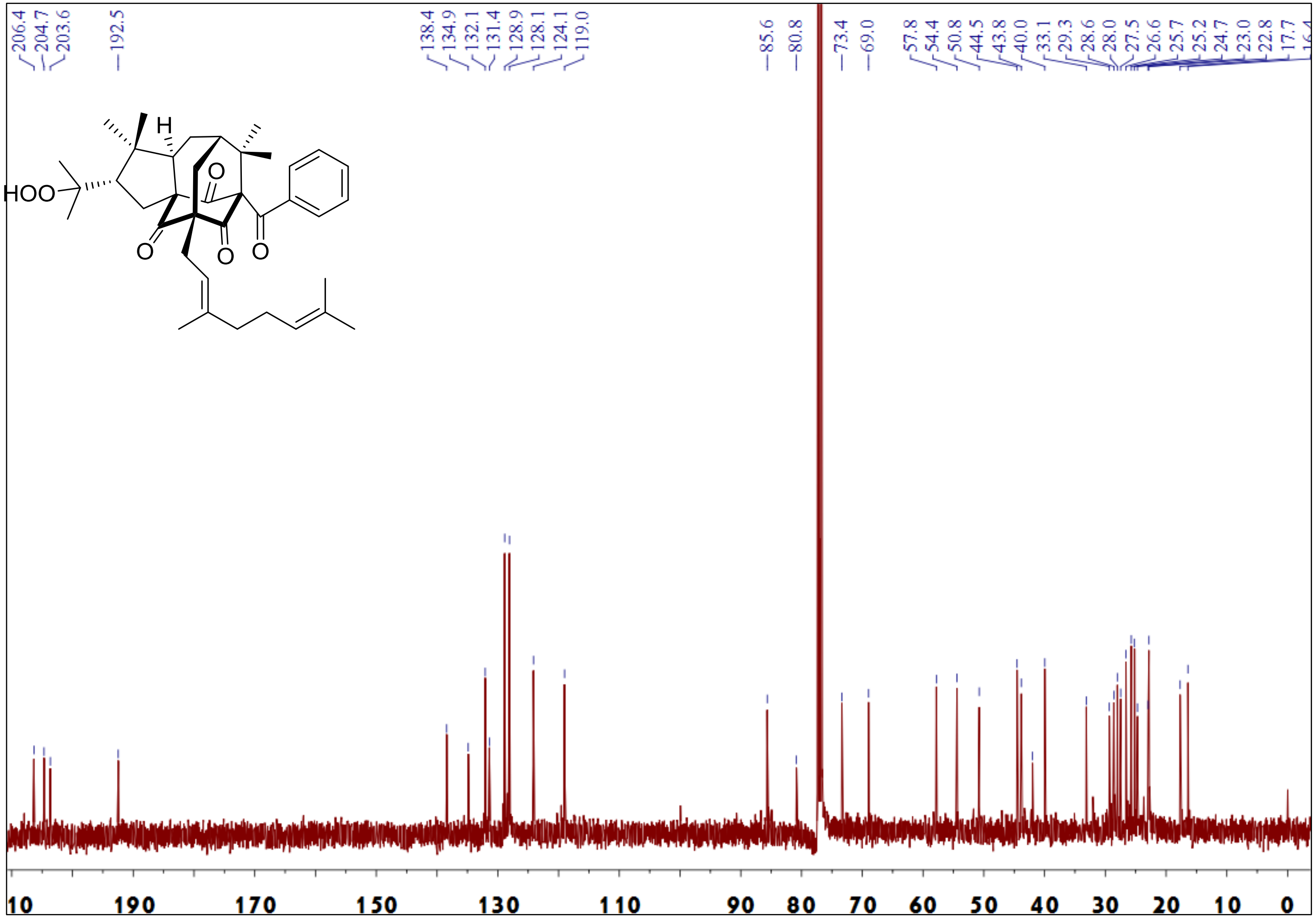


Rank	Score	Formula (M)	Ion	Meas. m/z	Pred. m/z	Df. (mDa)	Df. (ppm)	Iso	DBE
2	89.08	C35 H44 O6	[M+H]+	561.3225	561.3211	1.4	2.49	92.52	14.0

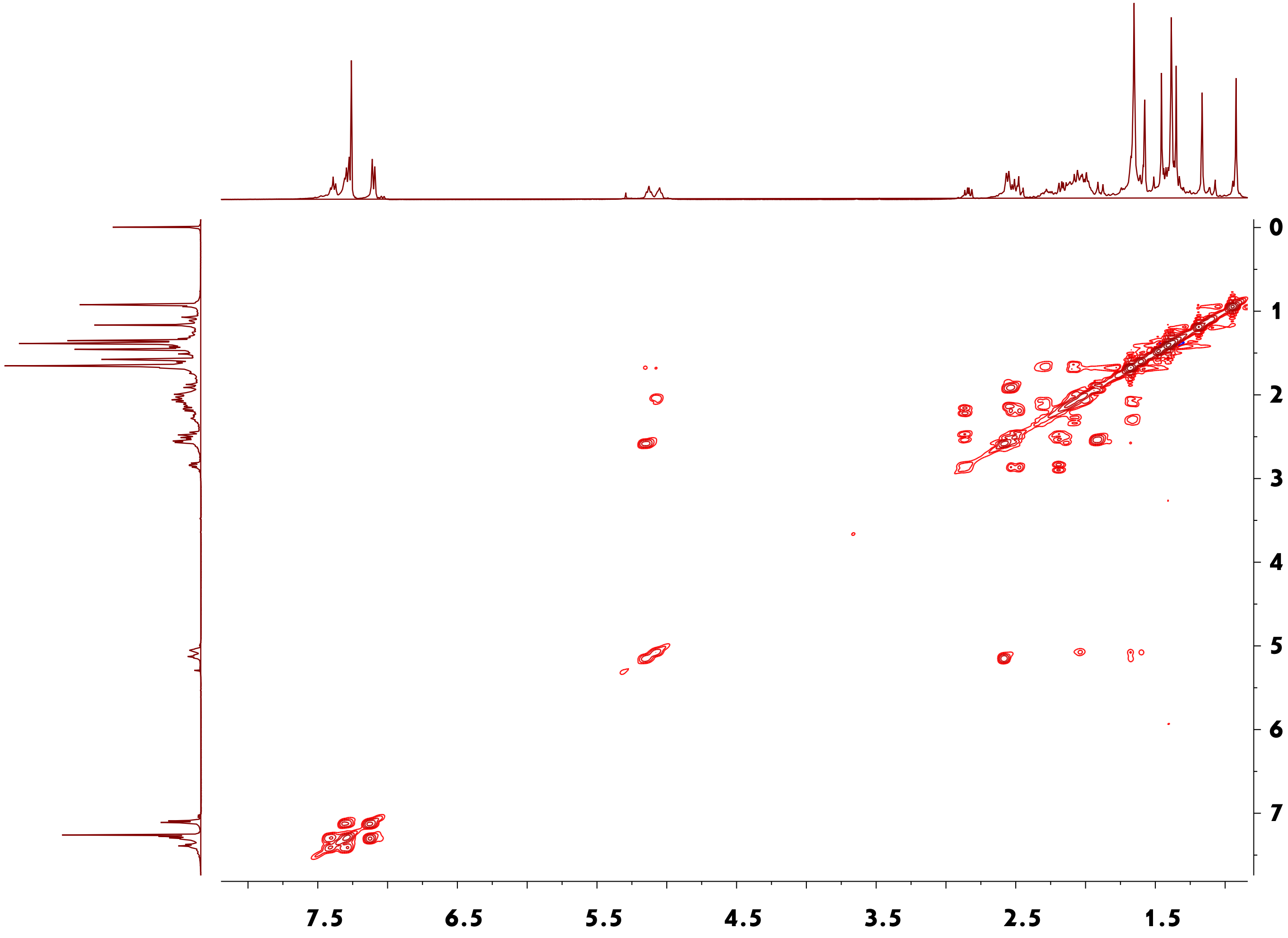
S40. ^{1}H NMR Spectrum of **6** in $CDCl_3$



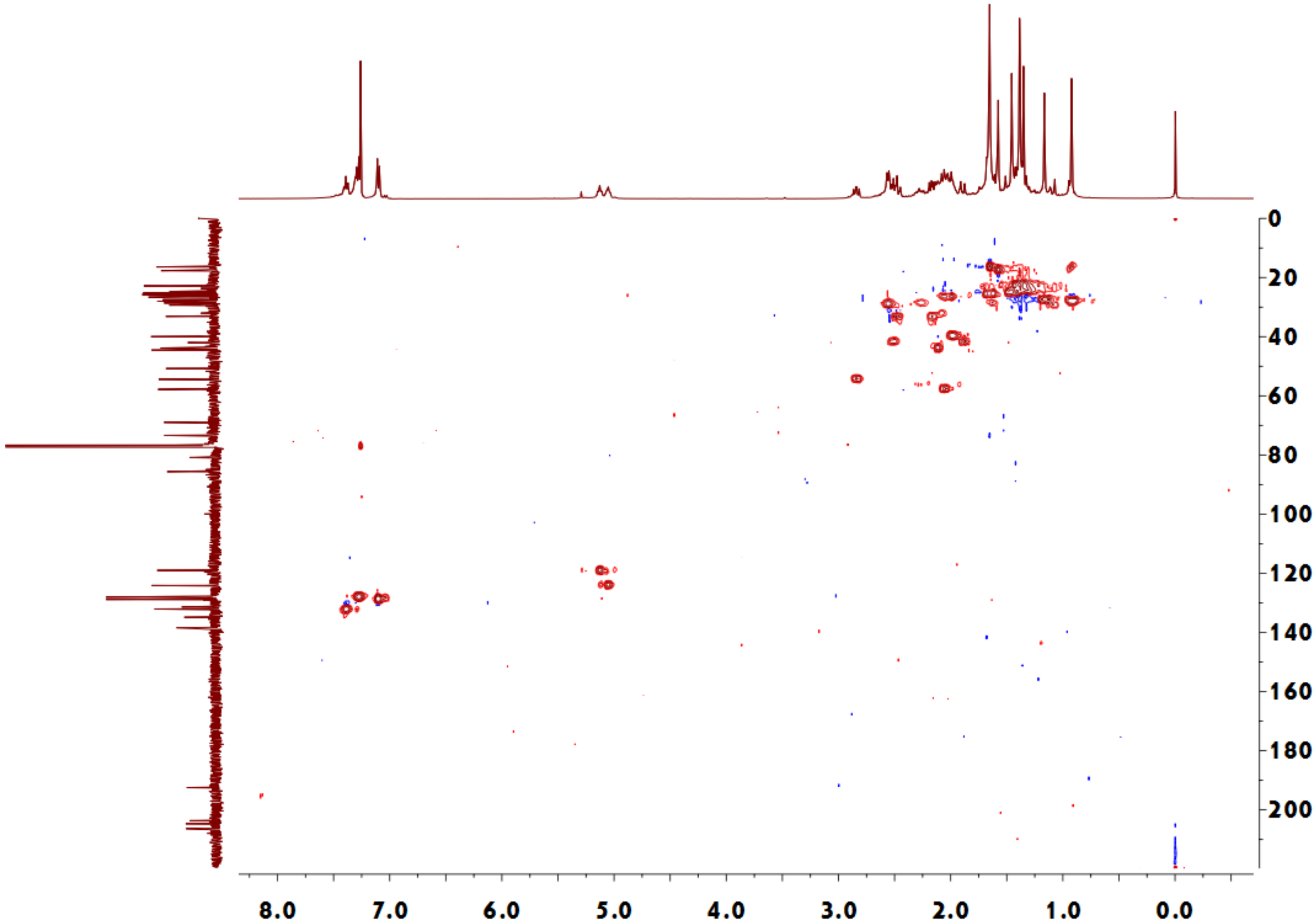
S41. ^{13}C NMR Spectra of **6** in $CDCl_3$



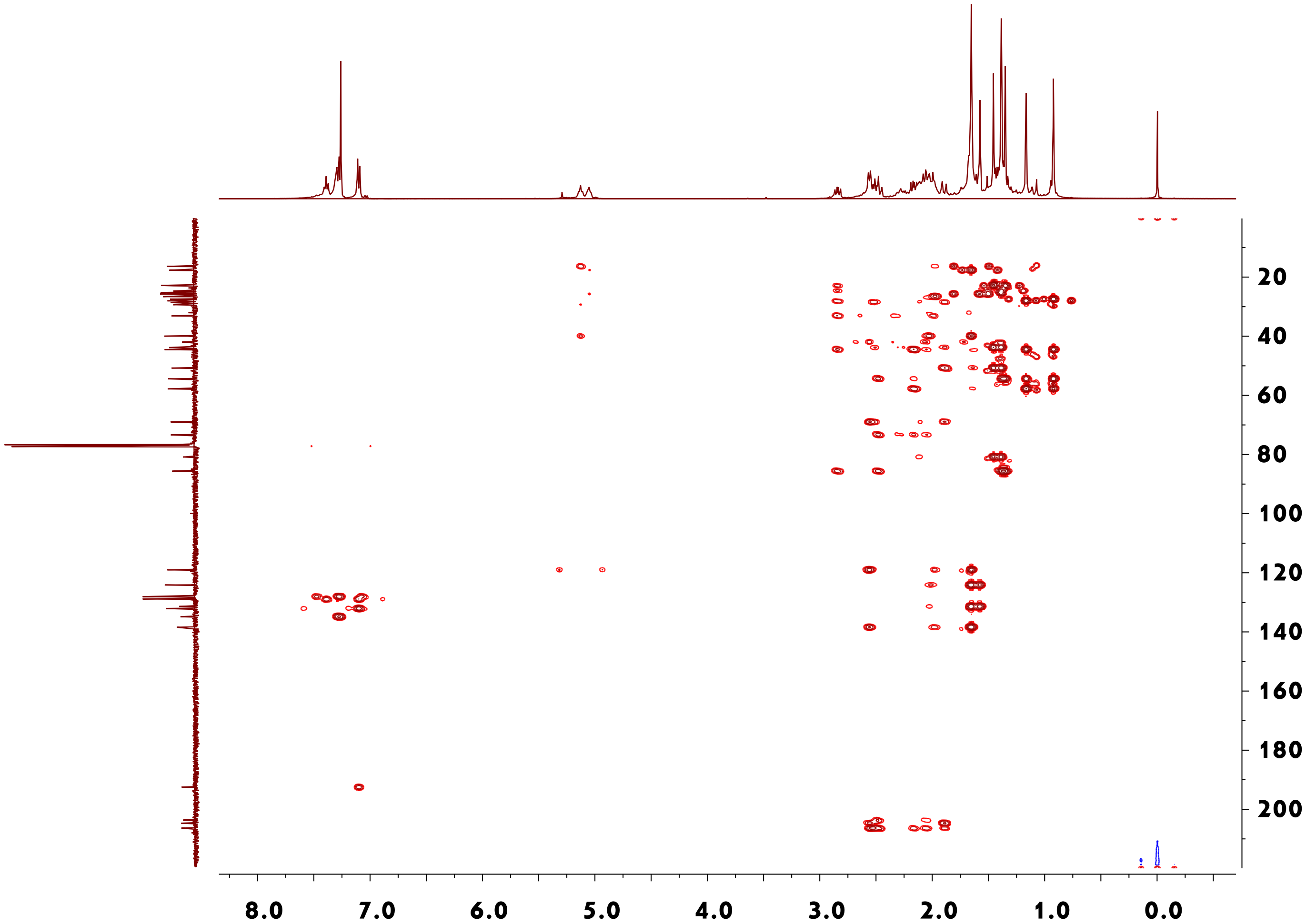
S42. [1]H-[1]H COSY Spectrum of **6** in $CDCl_3$



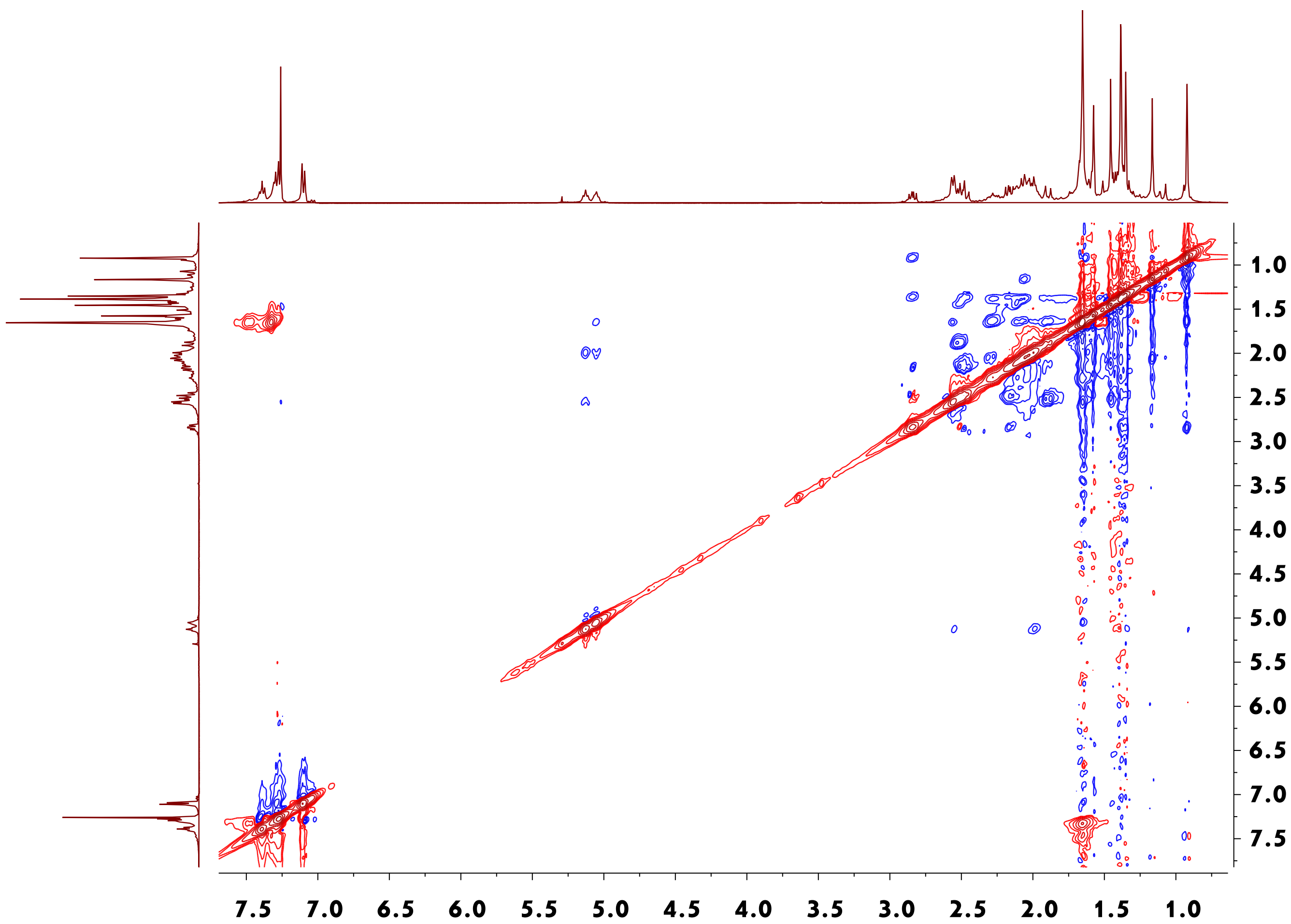
S43. HSQC Spectrum of **6** in $CDCl_3$



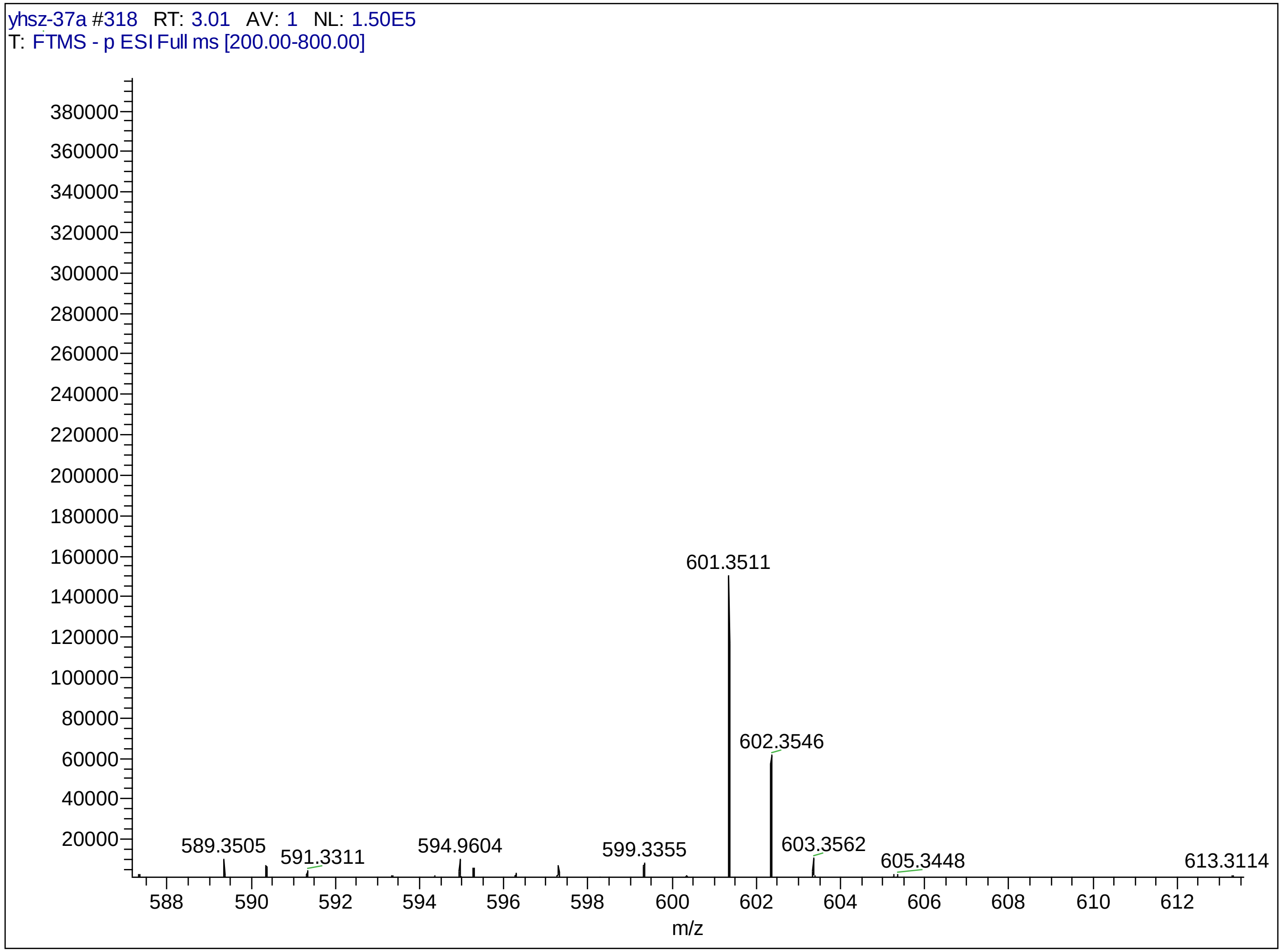
S44. HMBC Spectrum of **6** in $CDCl_3$



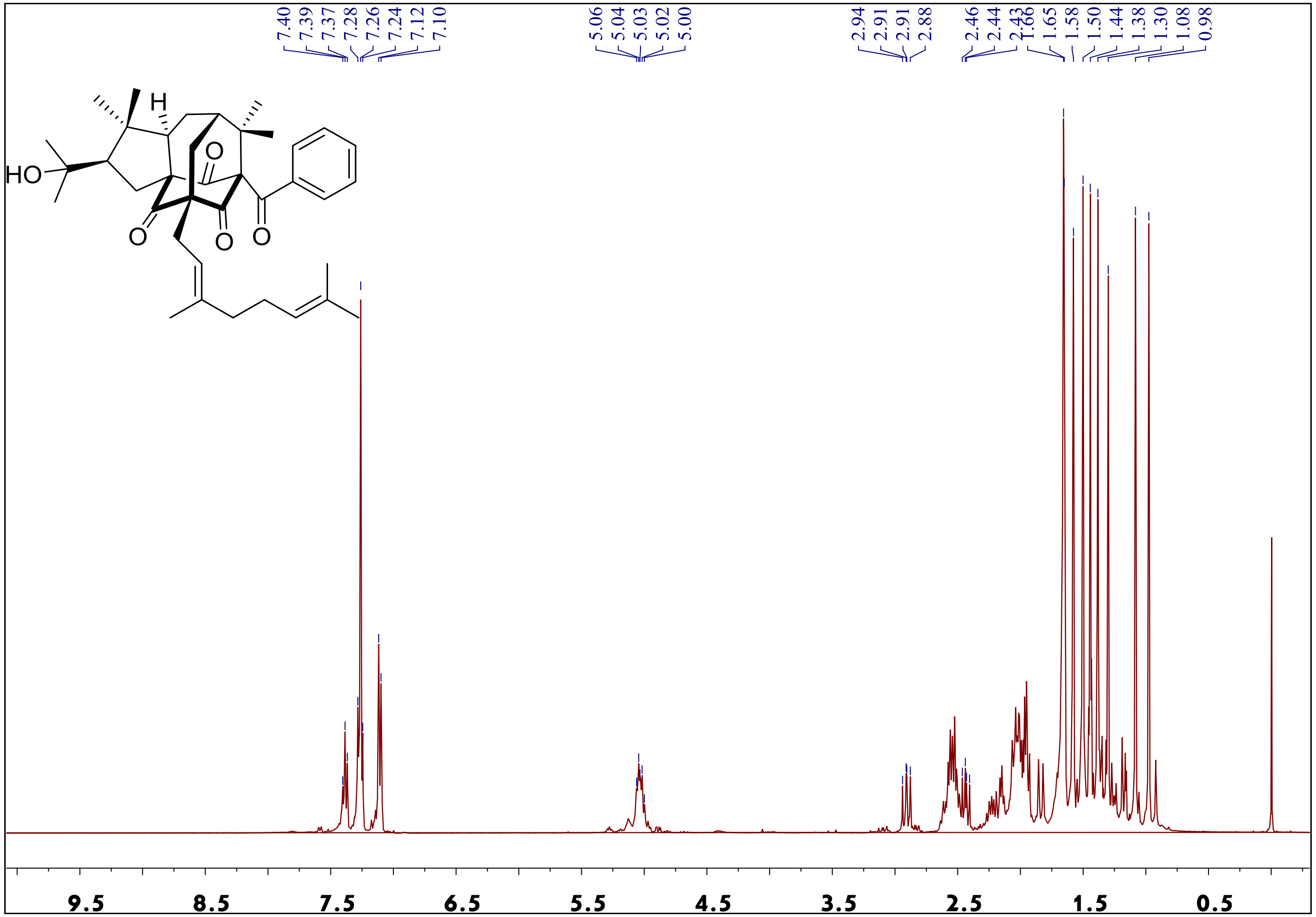
S45. NOESY Spectrum of **6** in $CDCl_3$



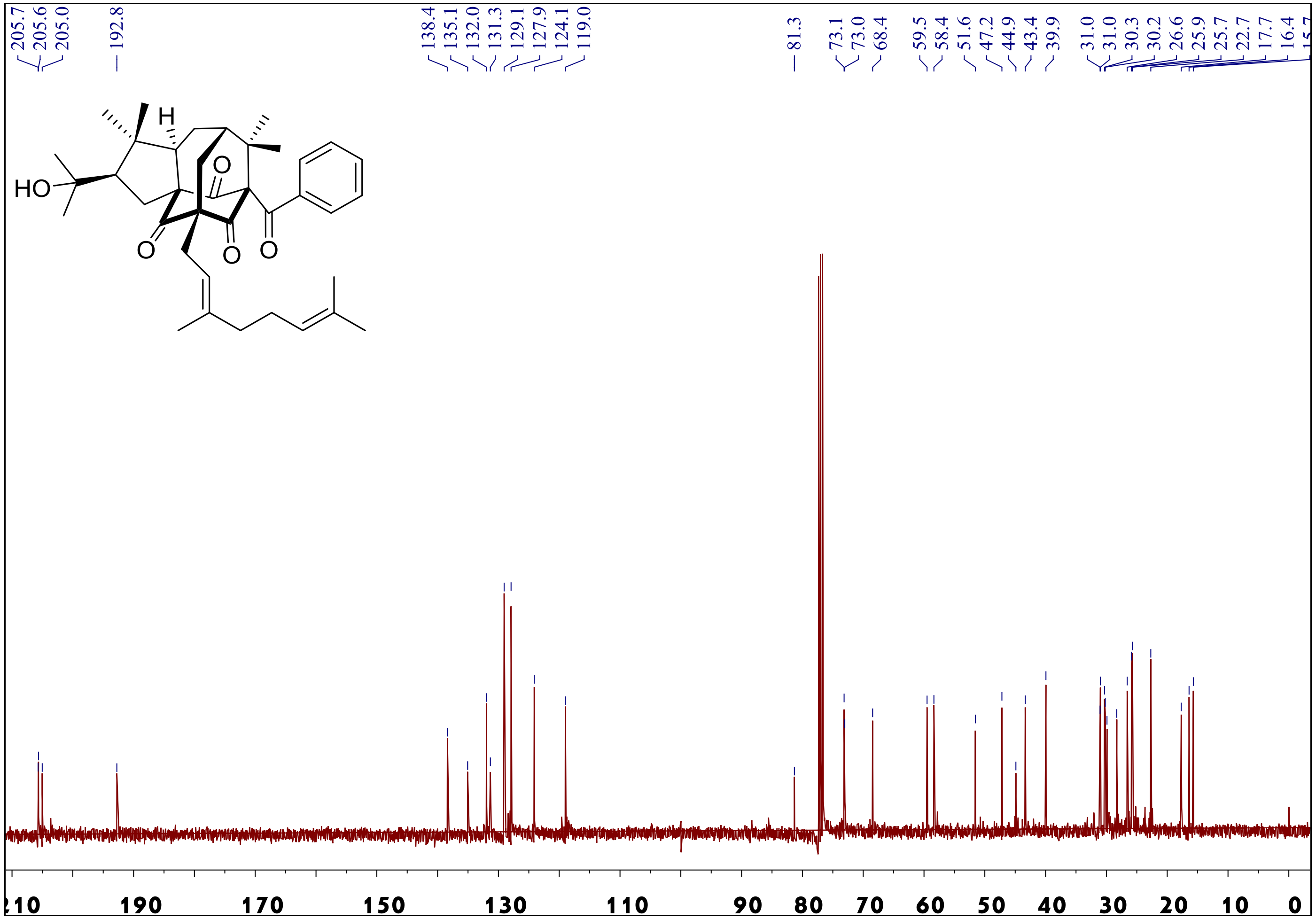
S46. HRESIMS spectrum of **6**



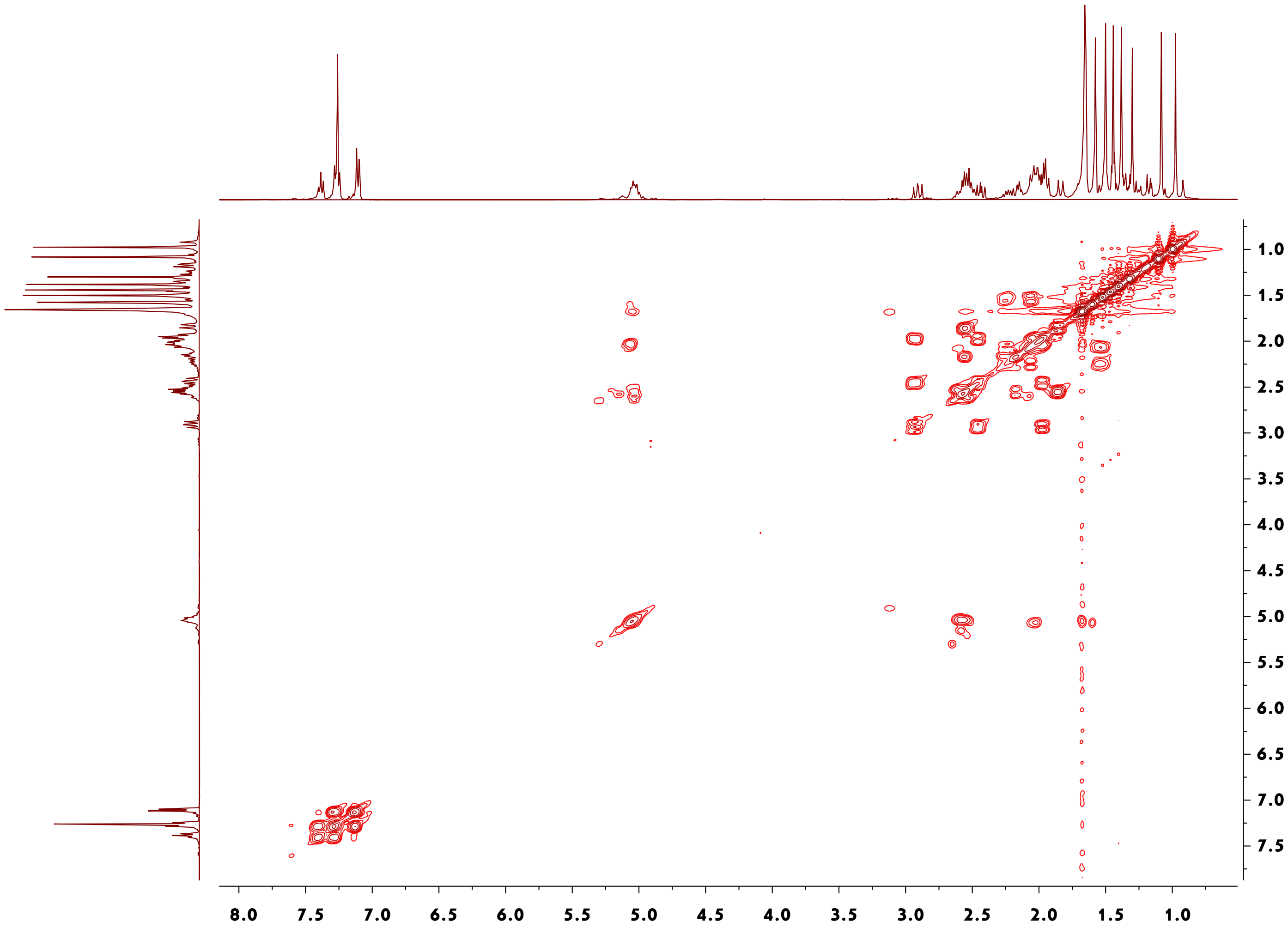
S47. ¹H NMR Spectrum of **7** in $CDCl_3$



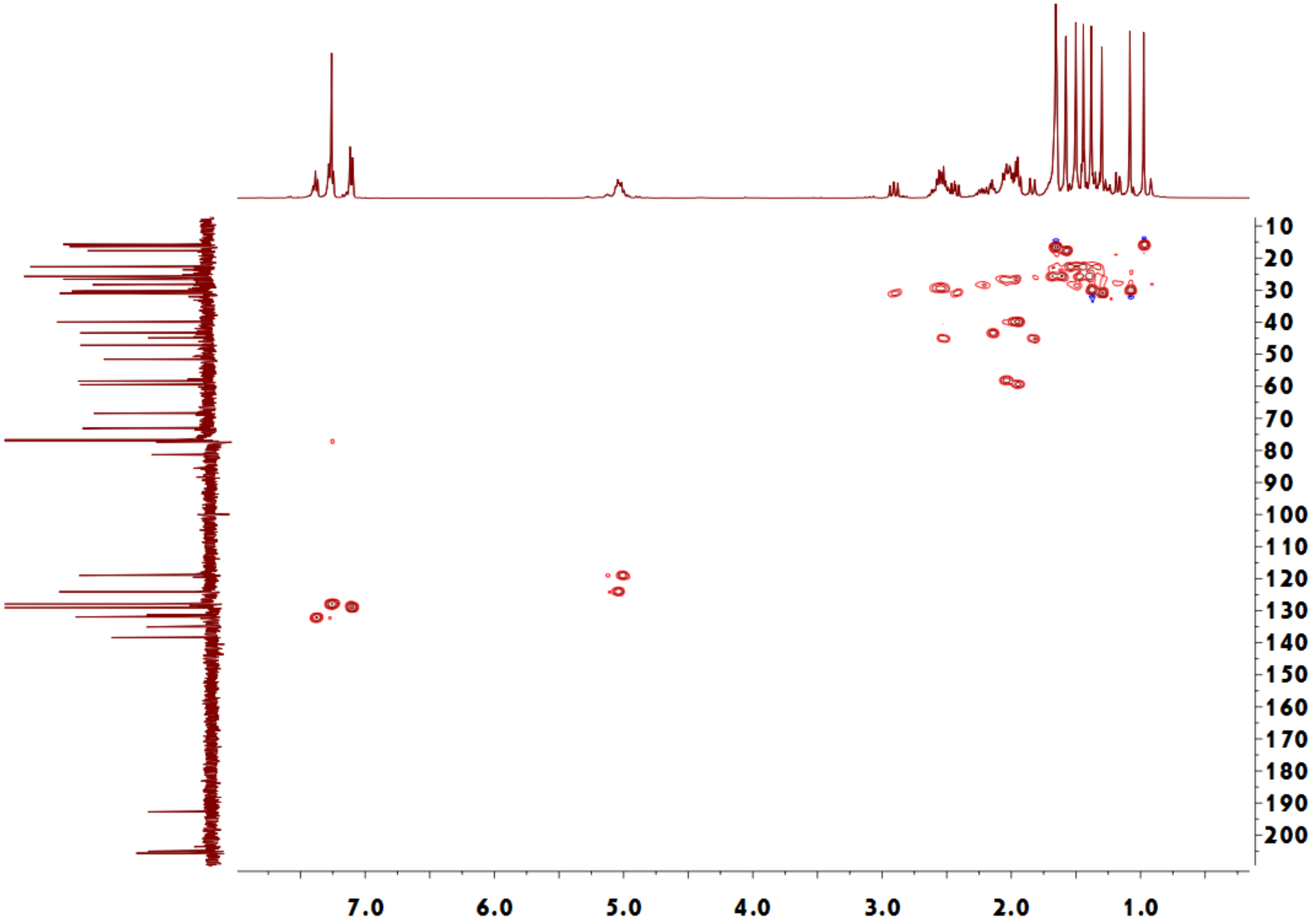
S48. ^{13}C NMR Spectra of **7** in $CDCl_3$



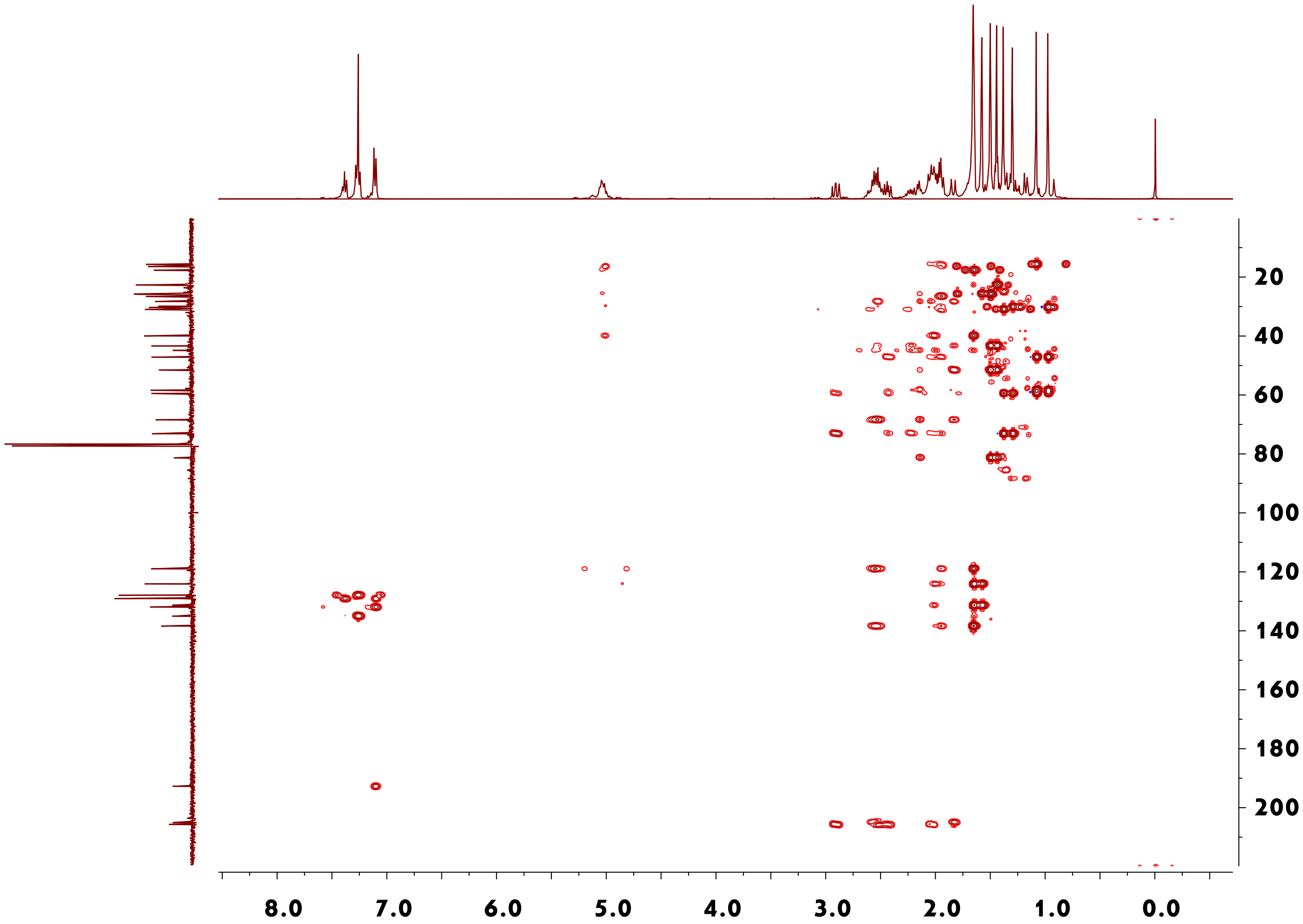
S49. ^{1}H-^{1}H COSY Spectrum of **7**in $CDCl_3$



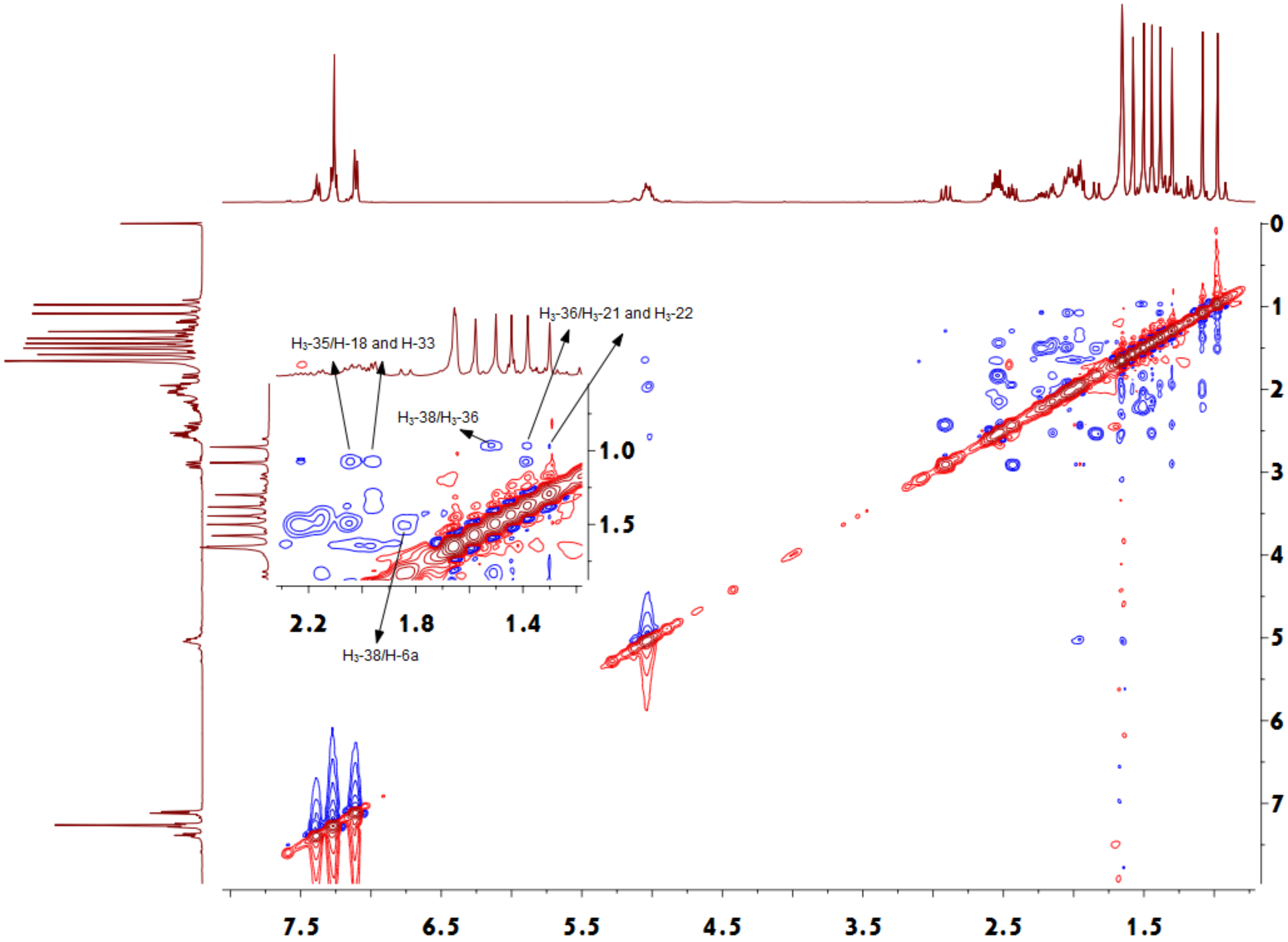
S50. HSQC Spectrum of **7** in $CDCl_3$



S51. HMBC Spectrum of **7** in $CDCl_3$



S52. NOESY Spectrum of **7** in $CDCl_3$



S53. HRESIMS spectrum of **7**