

Supporting information for

Antiplasmodial Sesquiterpenoid Lactones from *Trichospira verticillata*: Structure Elucidation by Spectroscopic Methods and Comparison of Experimental and Calculated ECD Data

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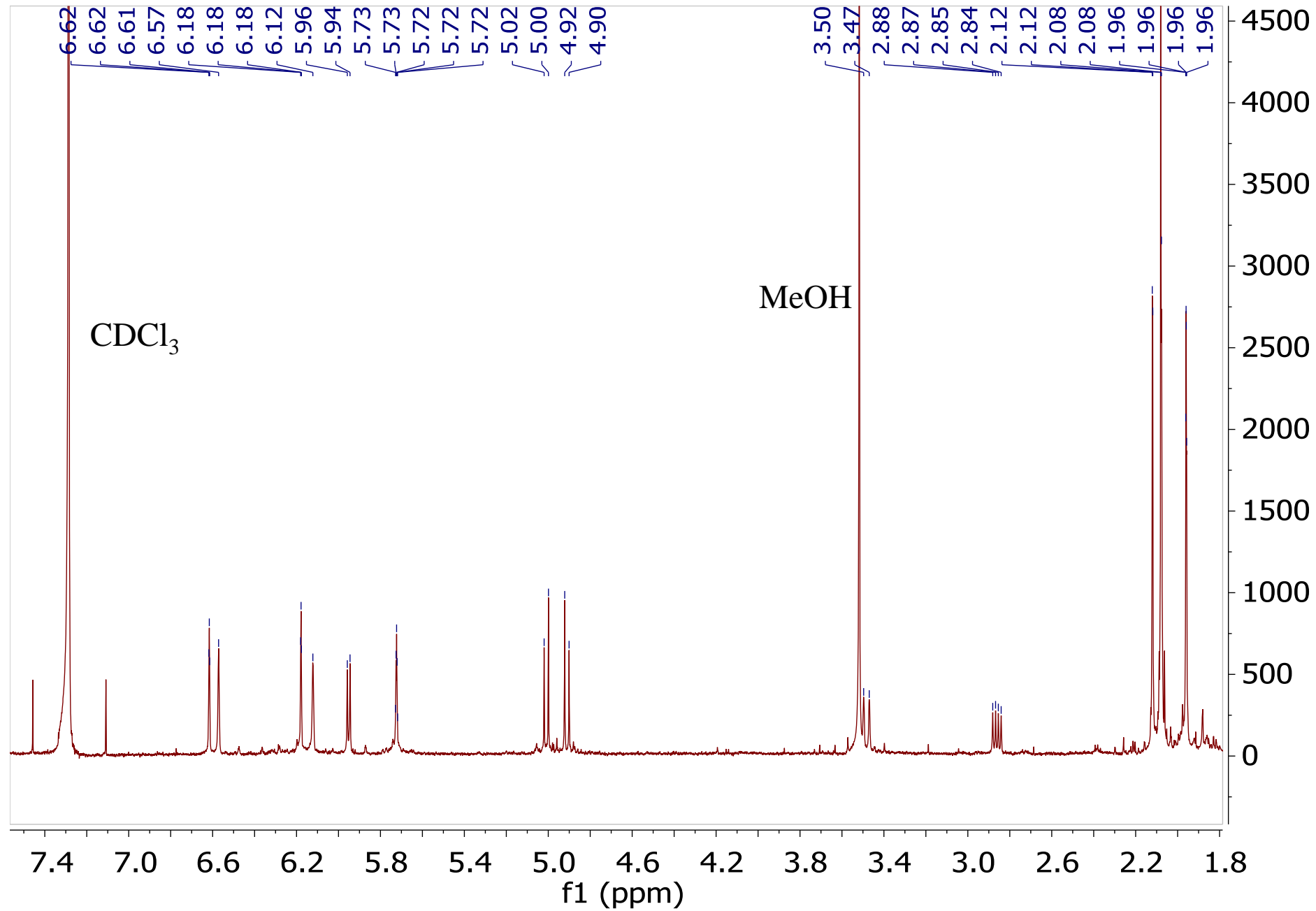
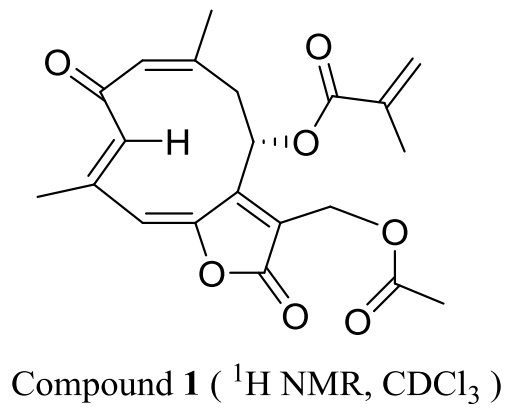
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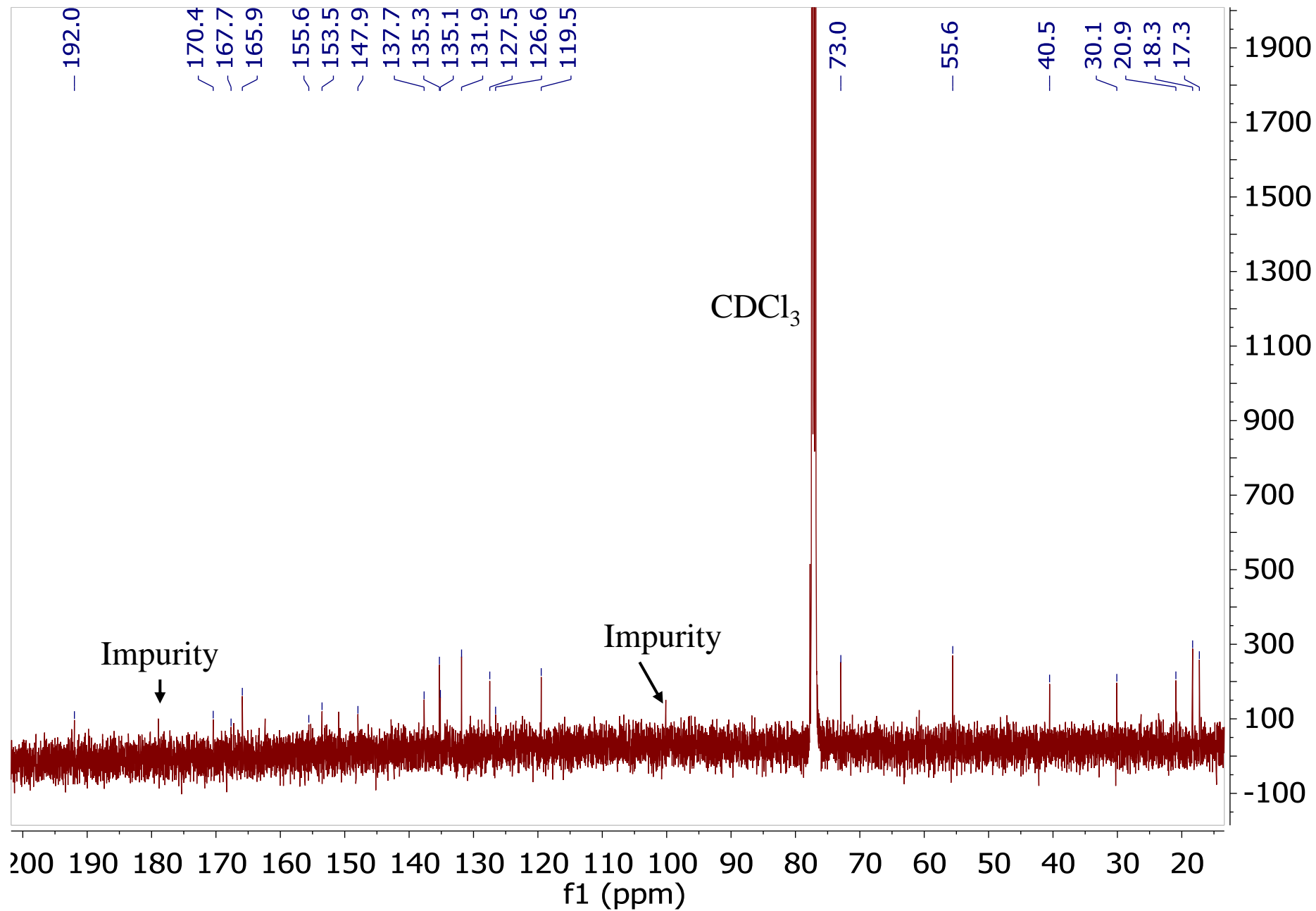
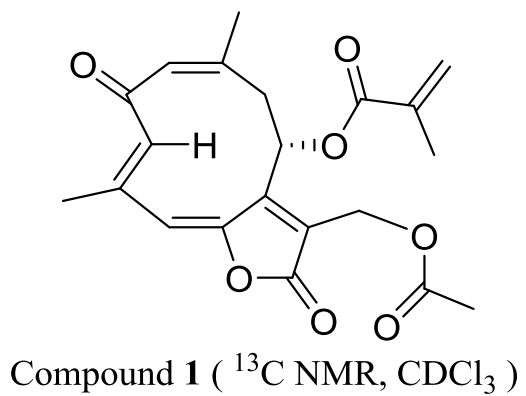
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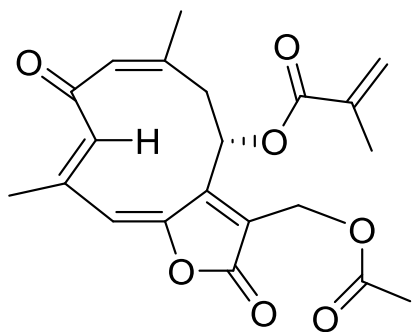
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Comparison of Experimental and calculated UV Spectra for all Possible Stereoisomers

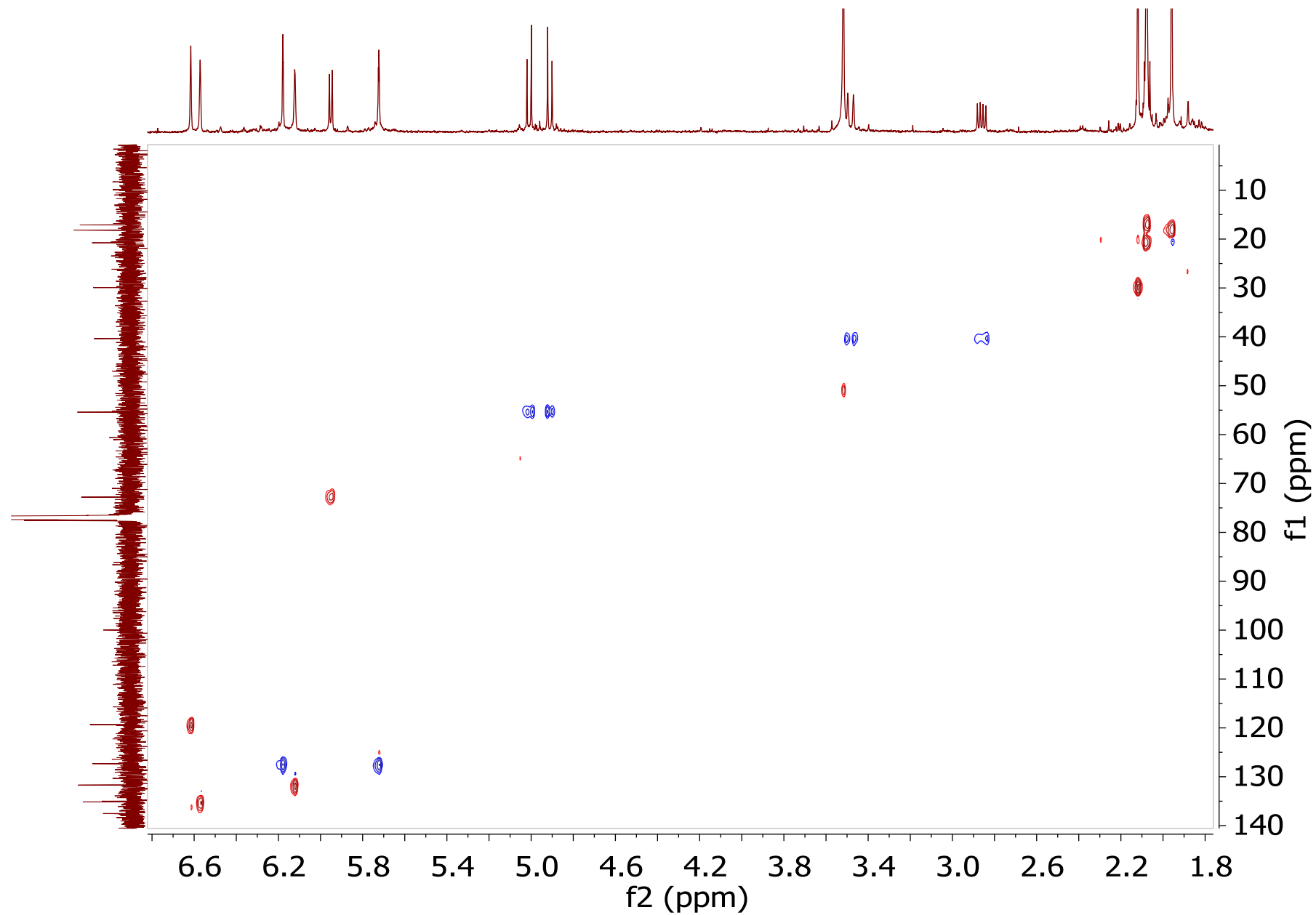
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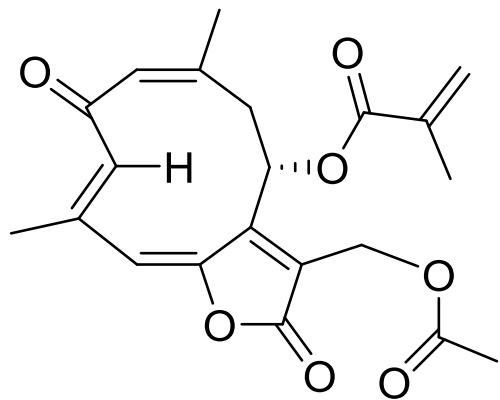




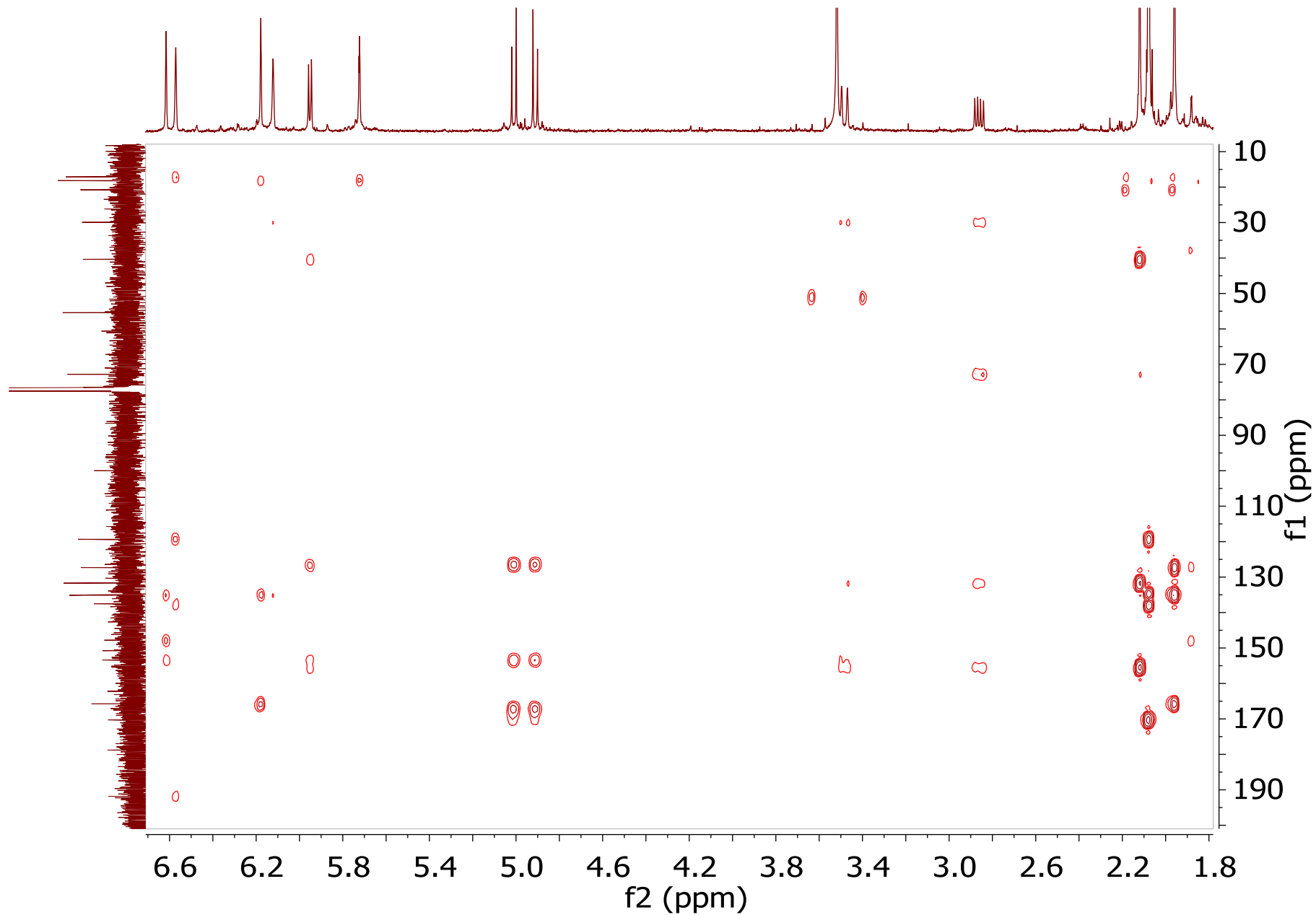


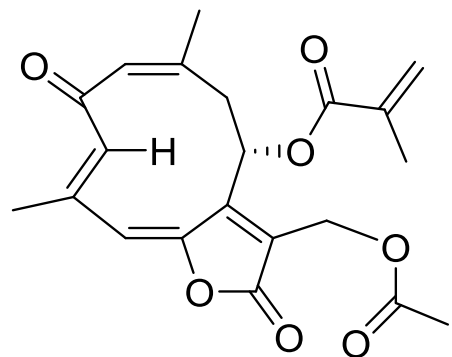
Compound 1 (gHSQC, CDCl₃)



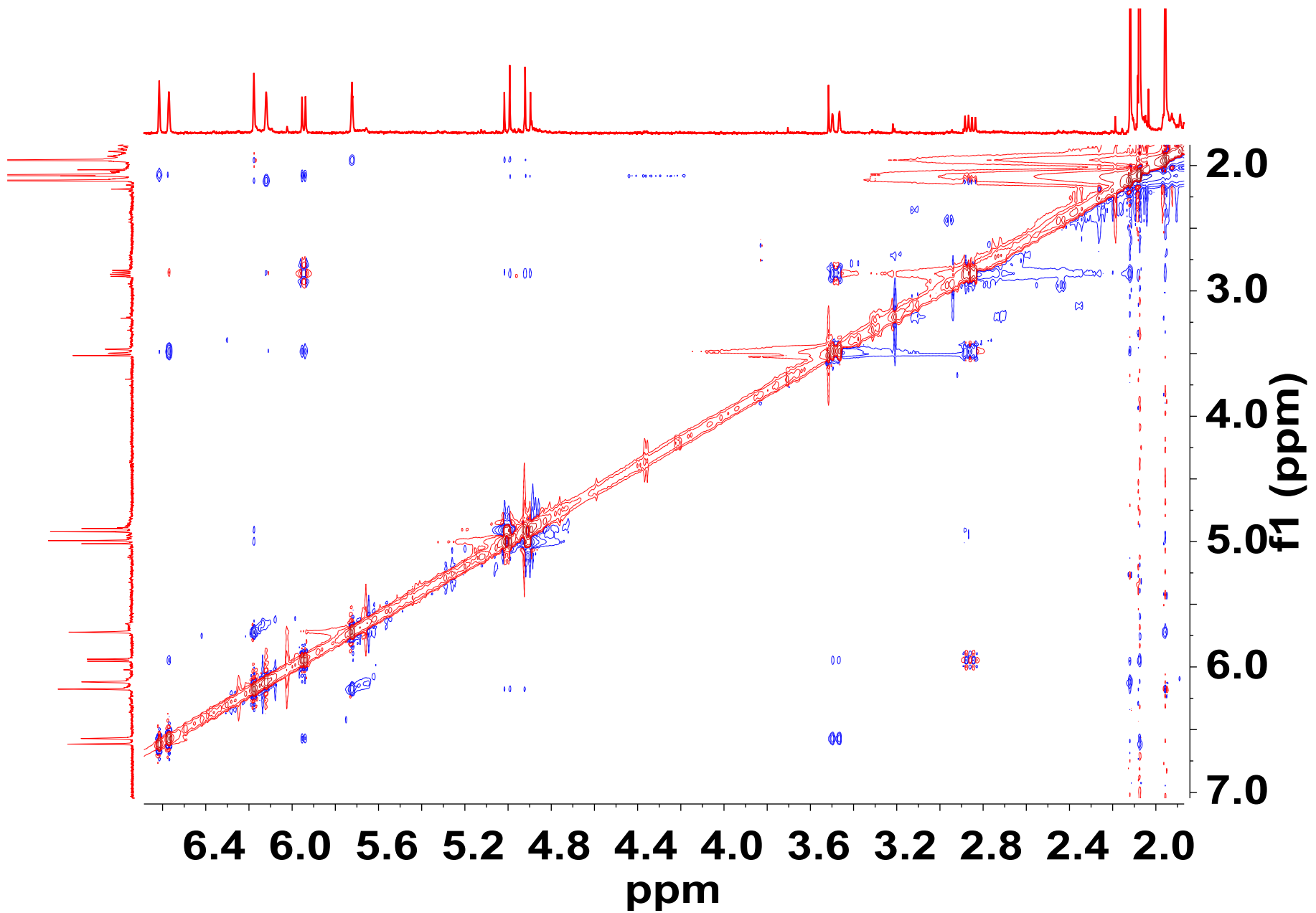


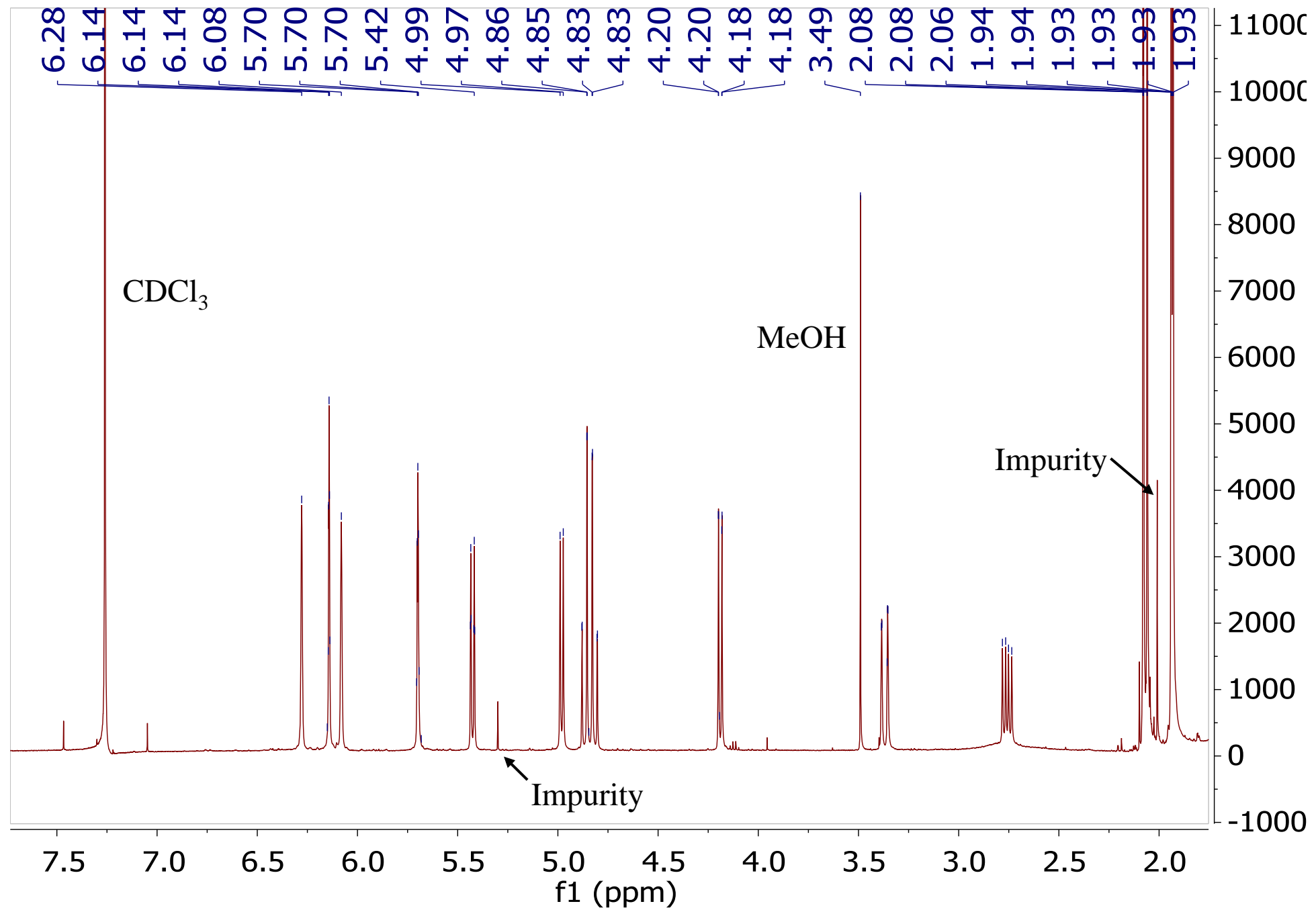
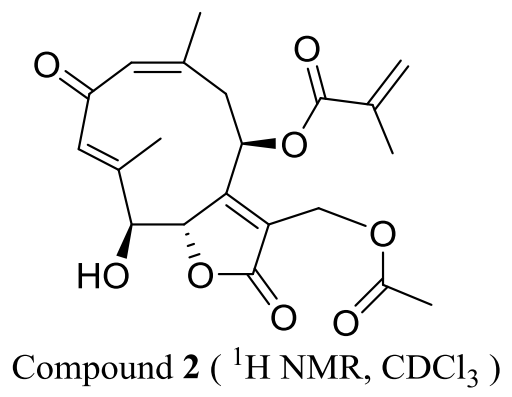
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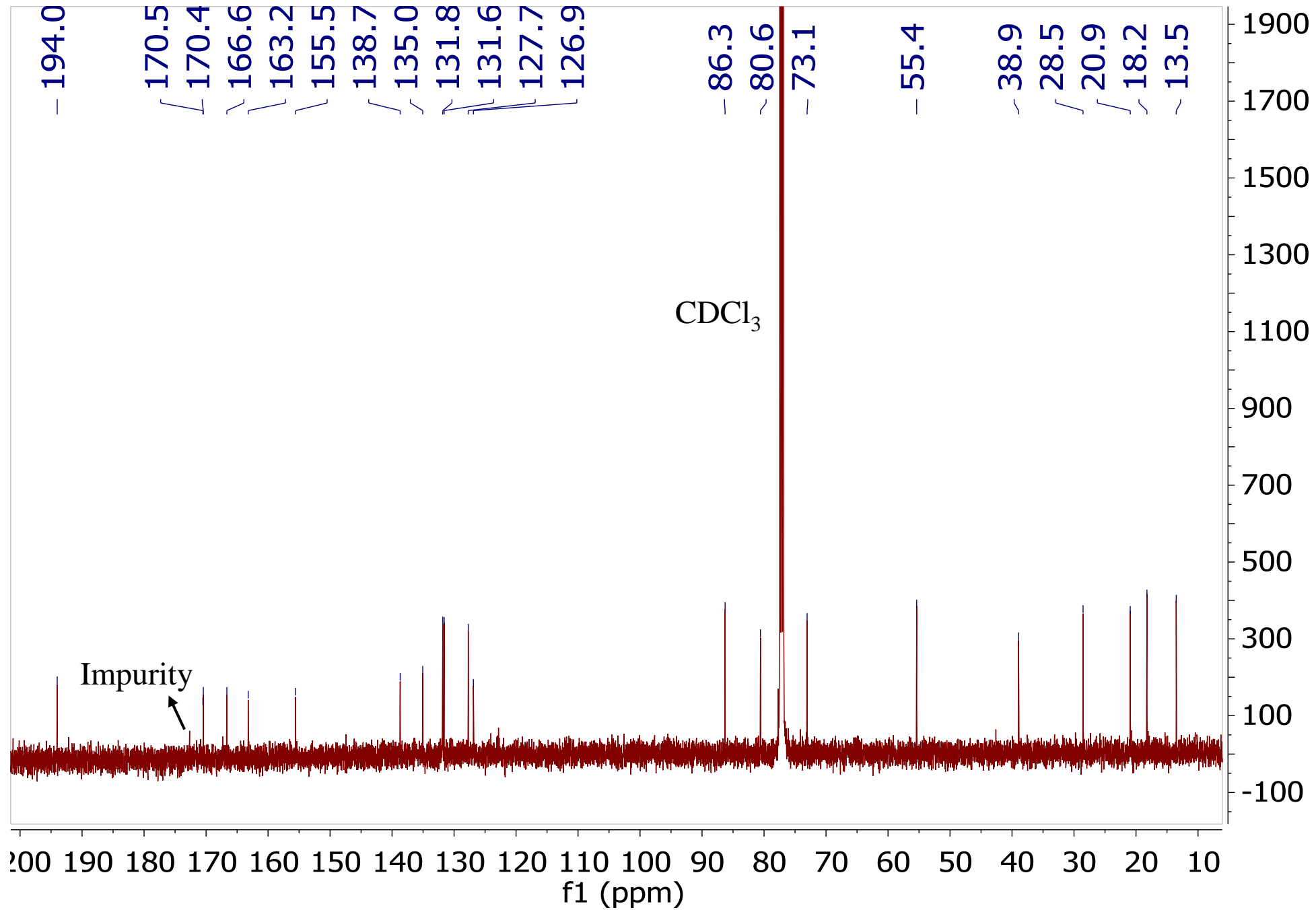
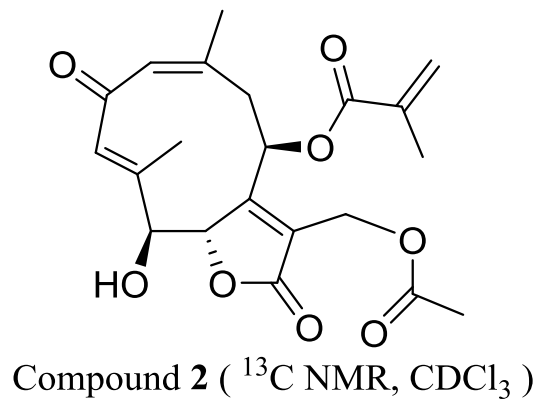


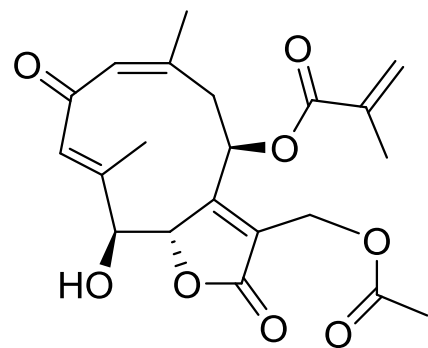


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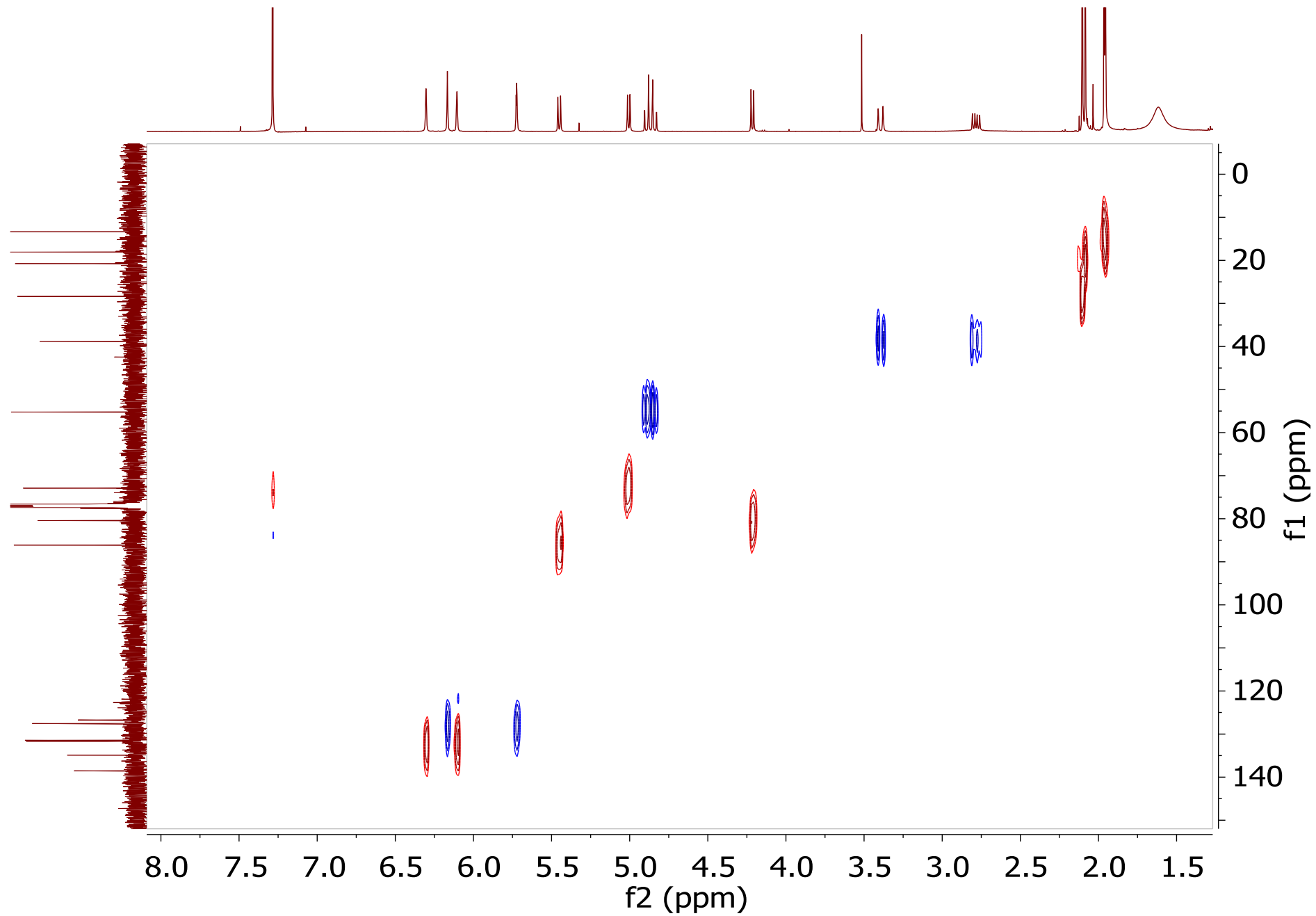


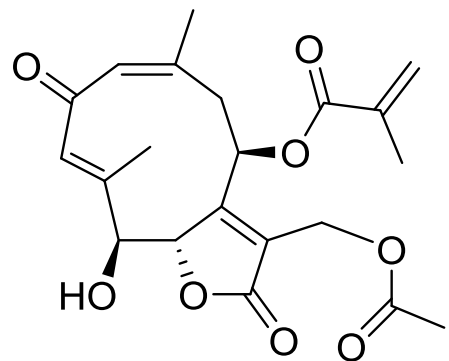




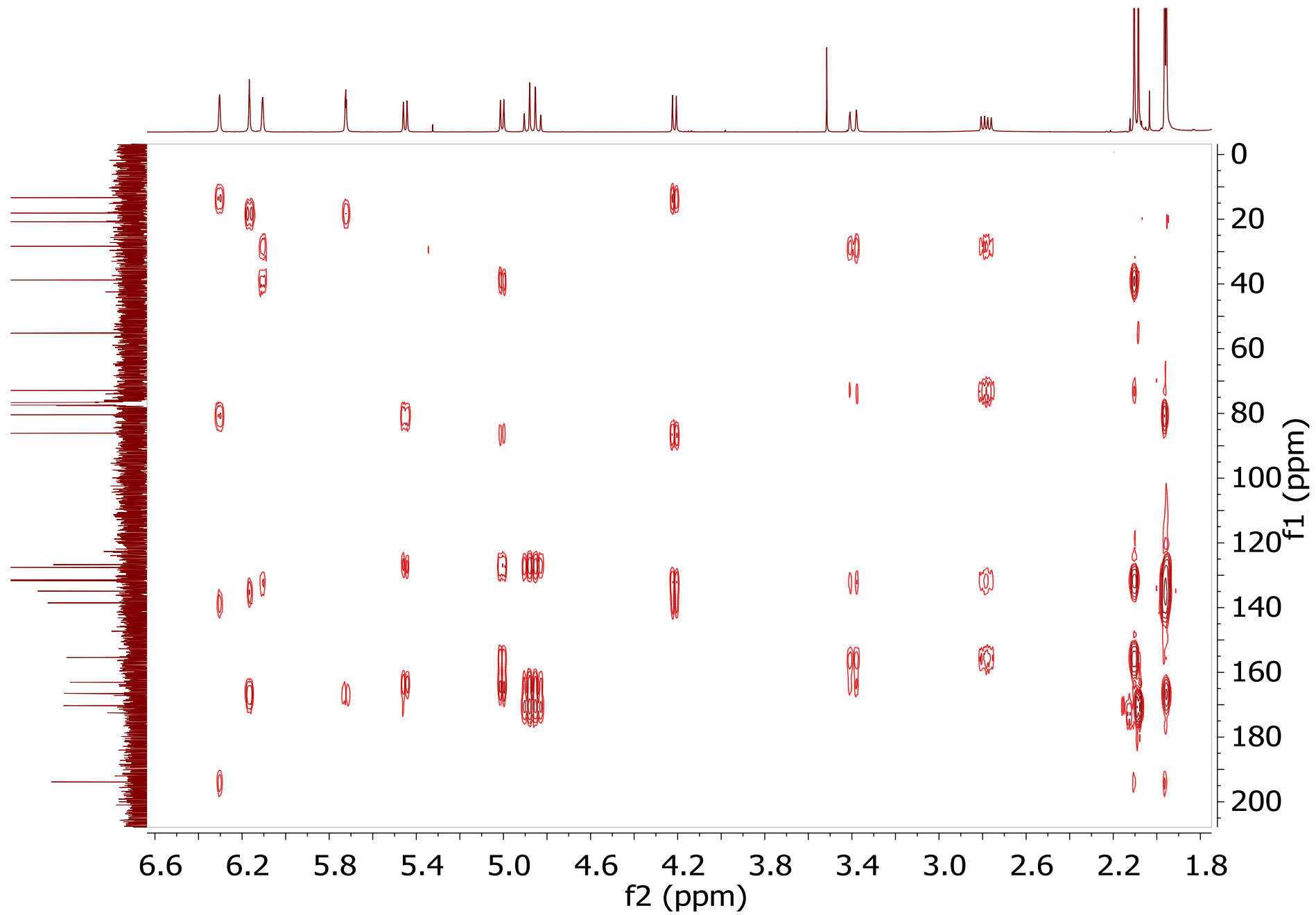


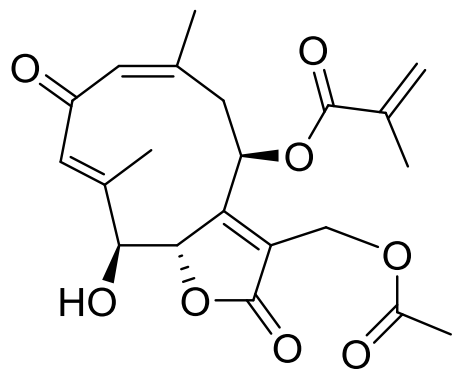
Compound **2** (gHSQC, CDCl₃)



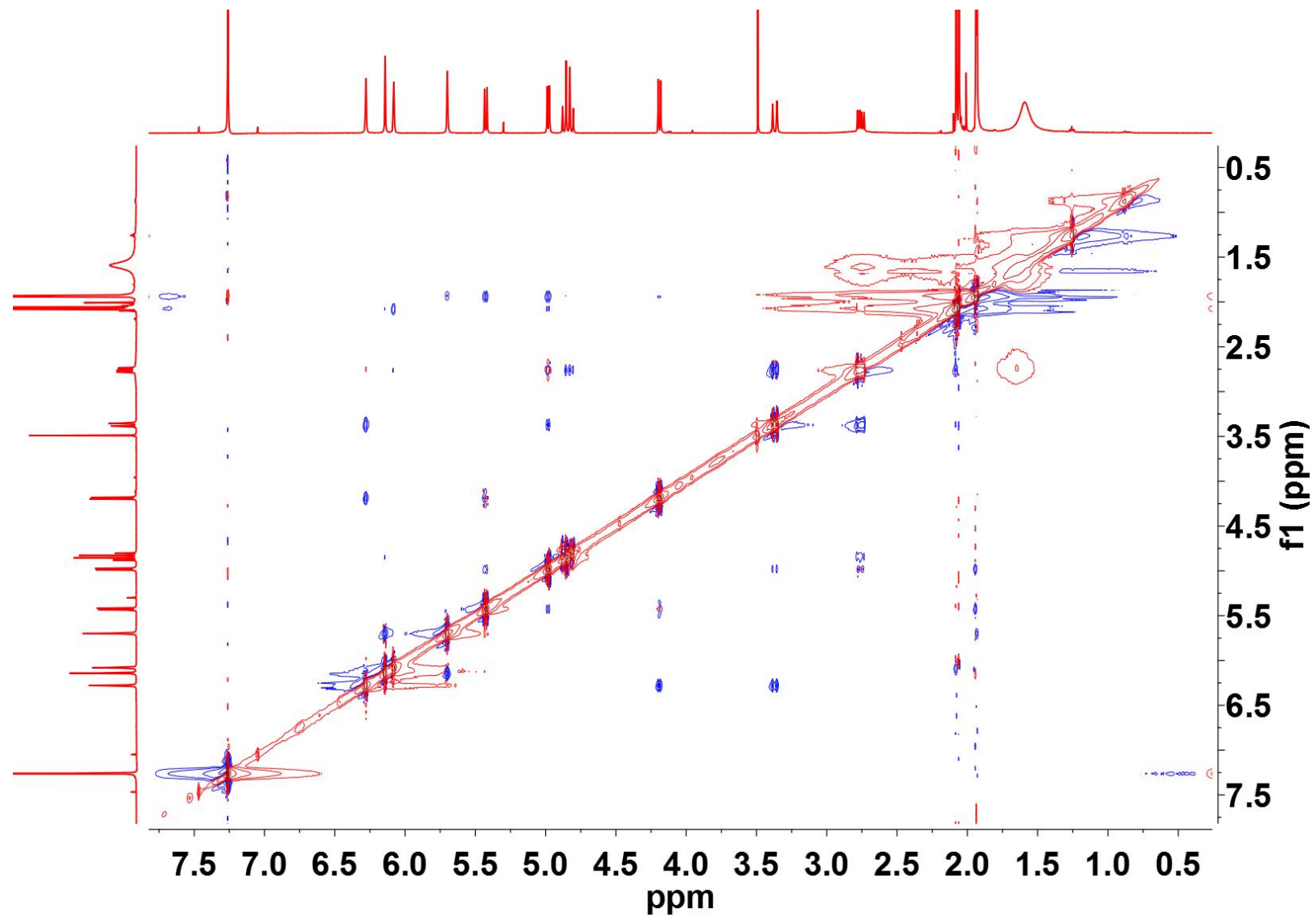


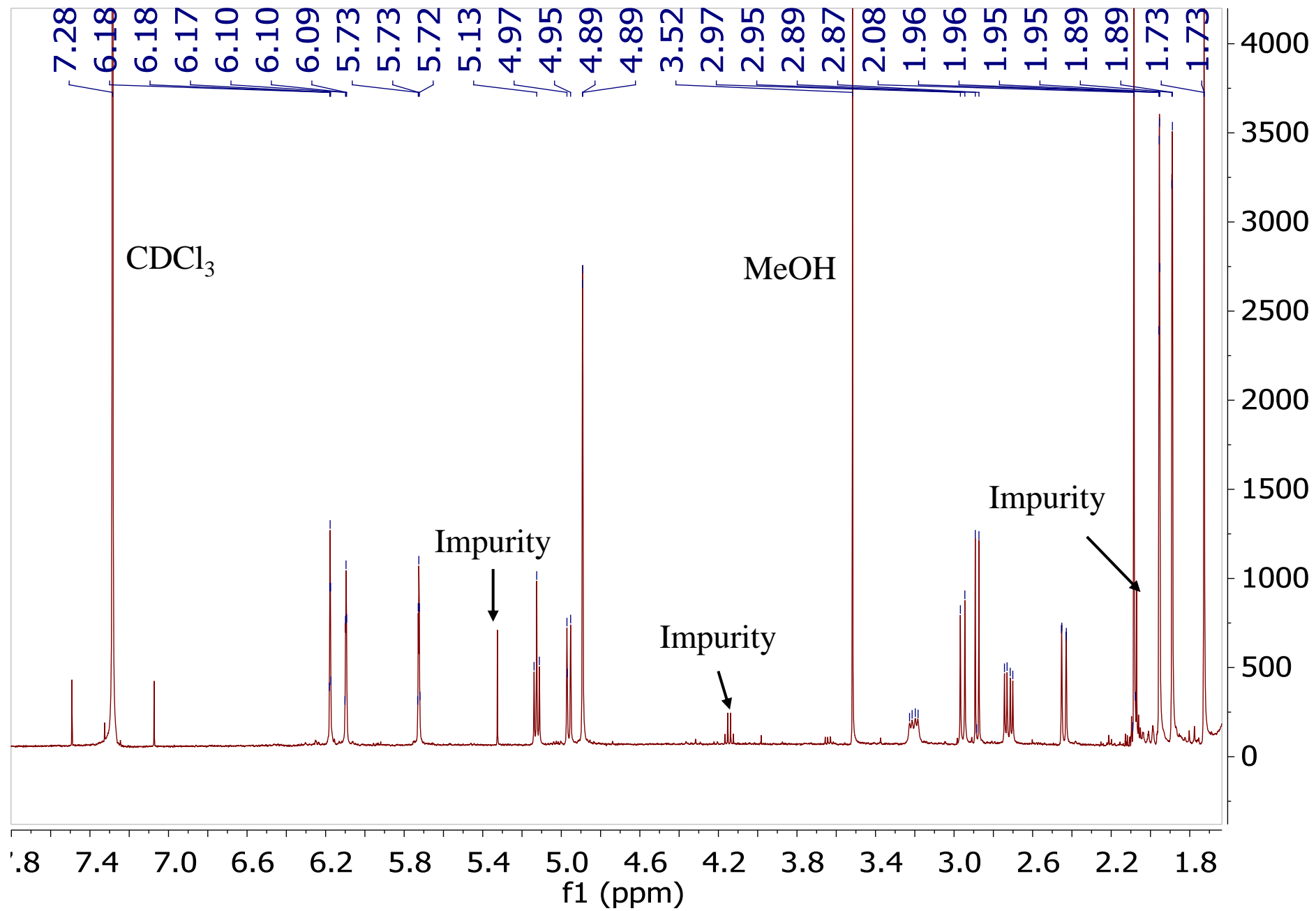
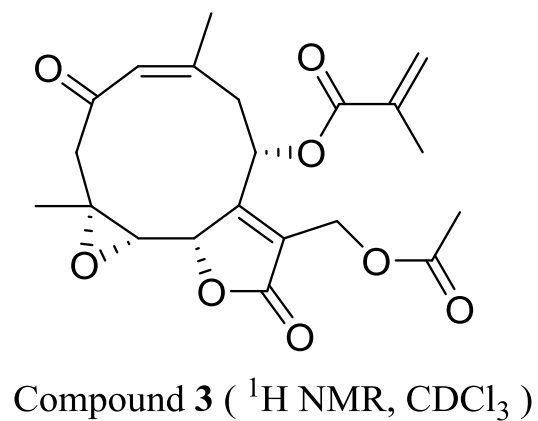
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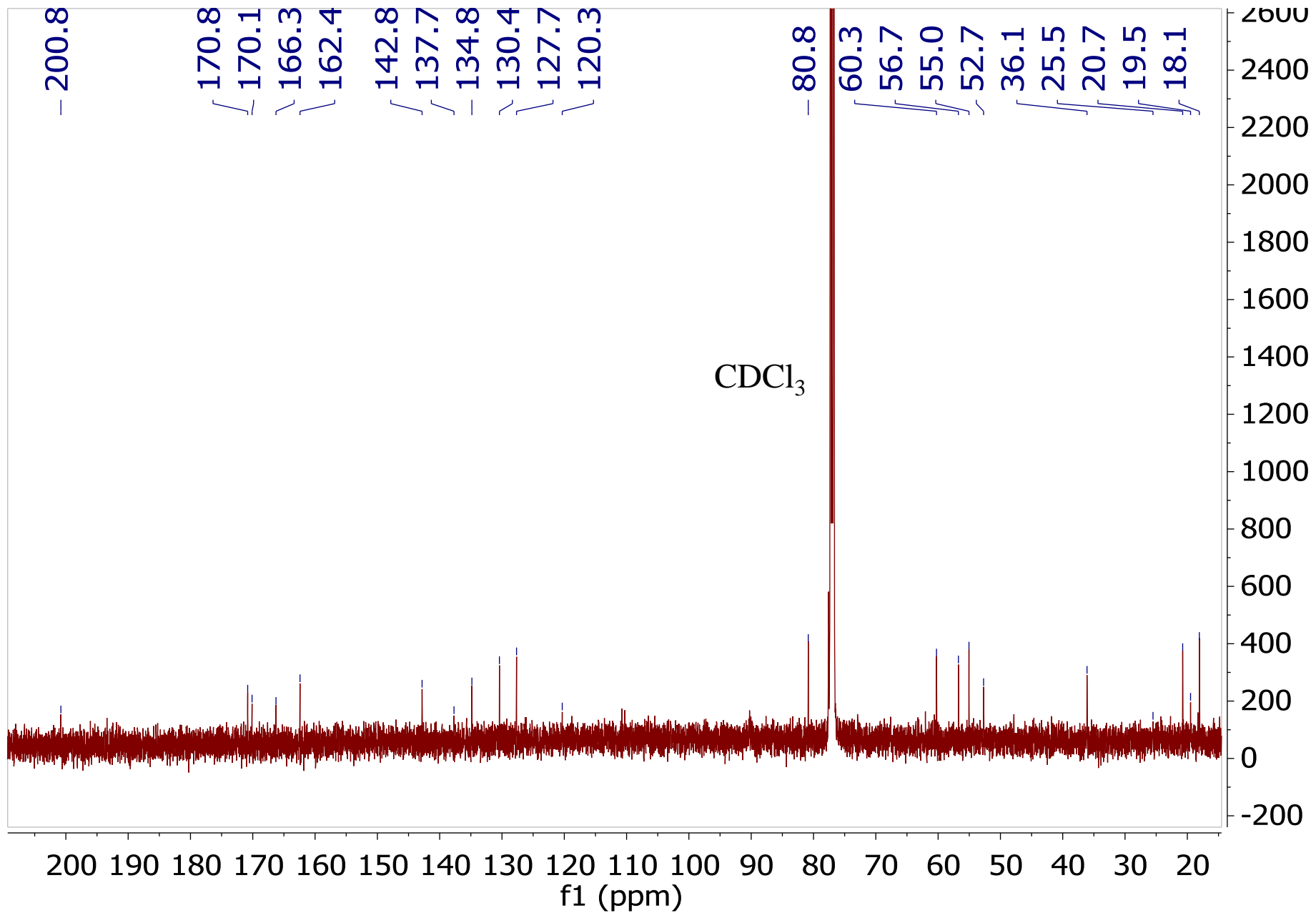
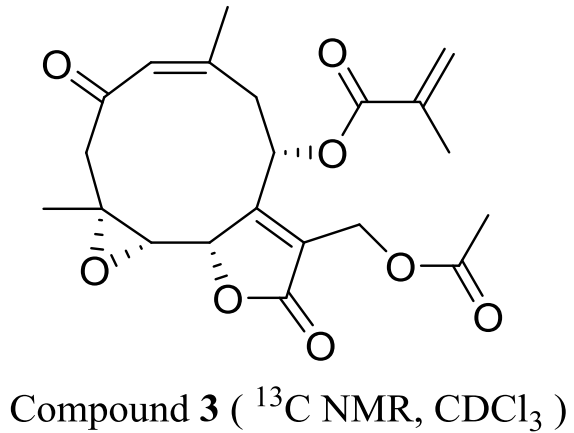


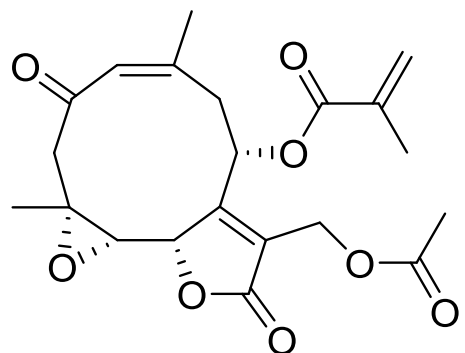


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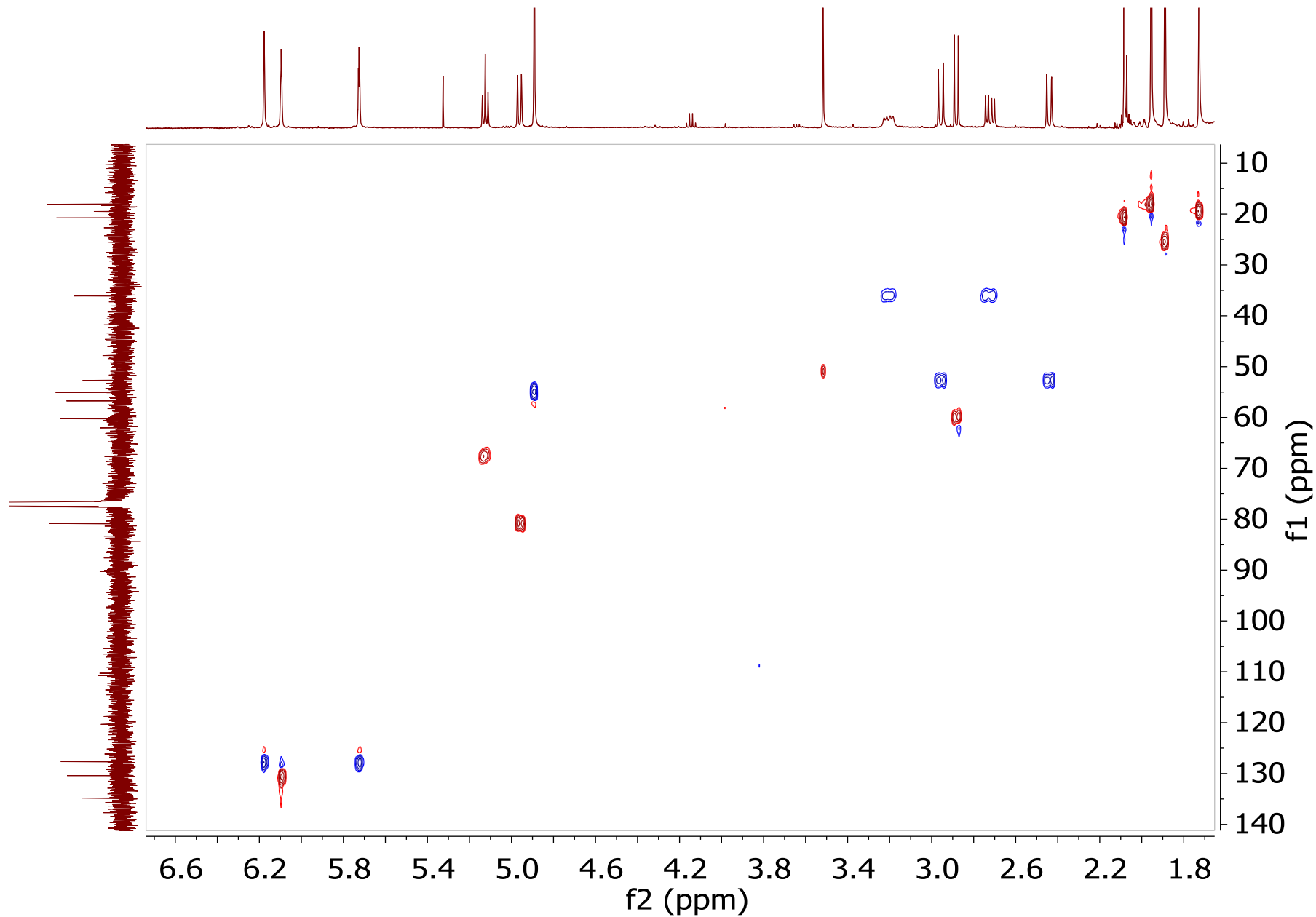


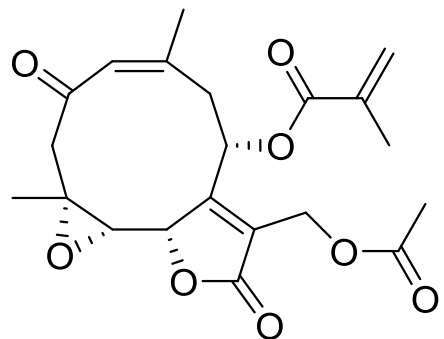




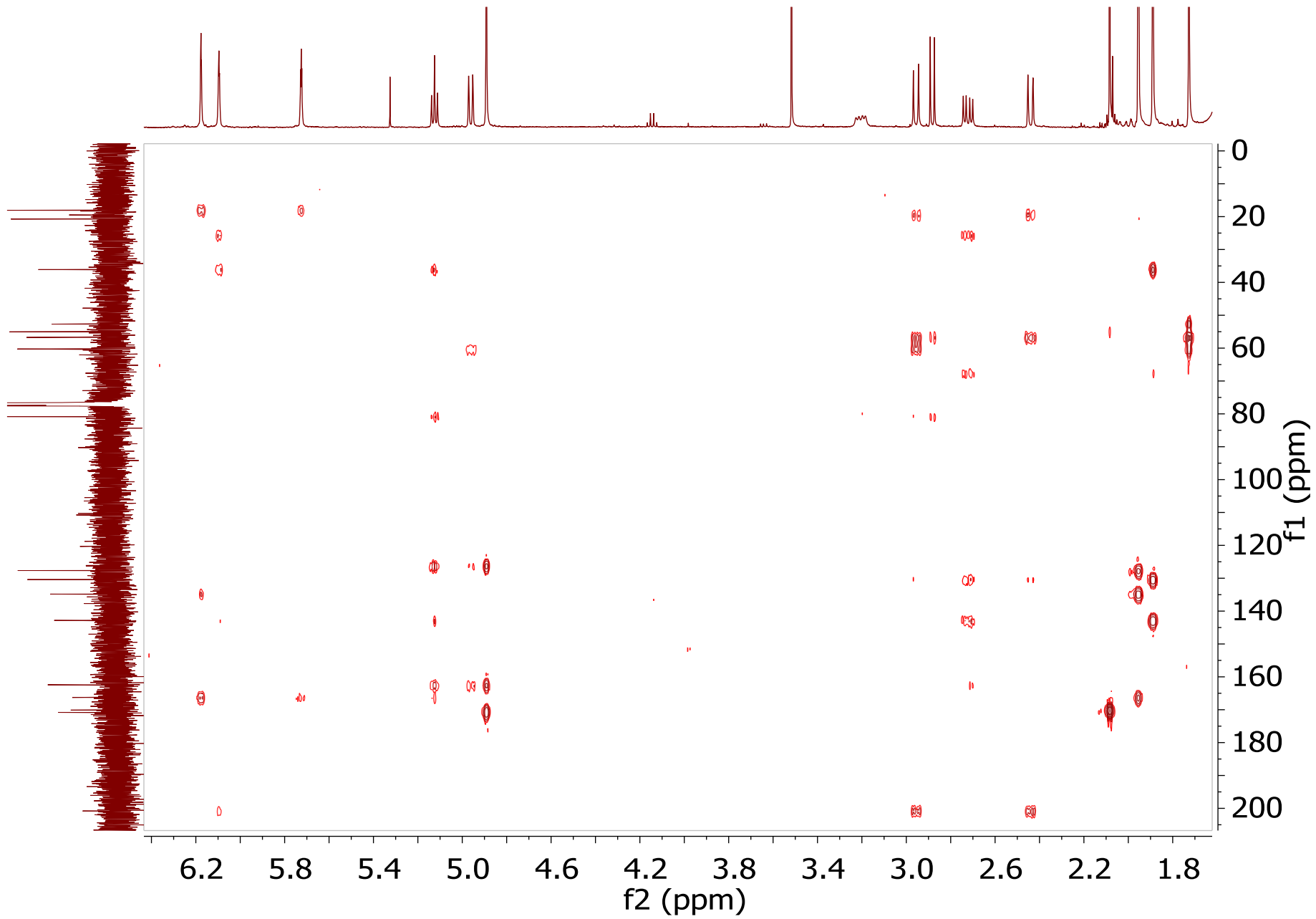


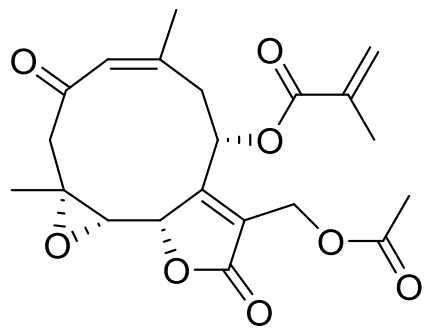
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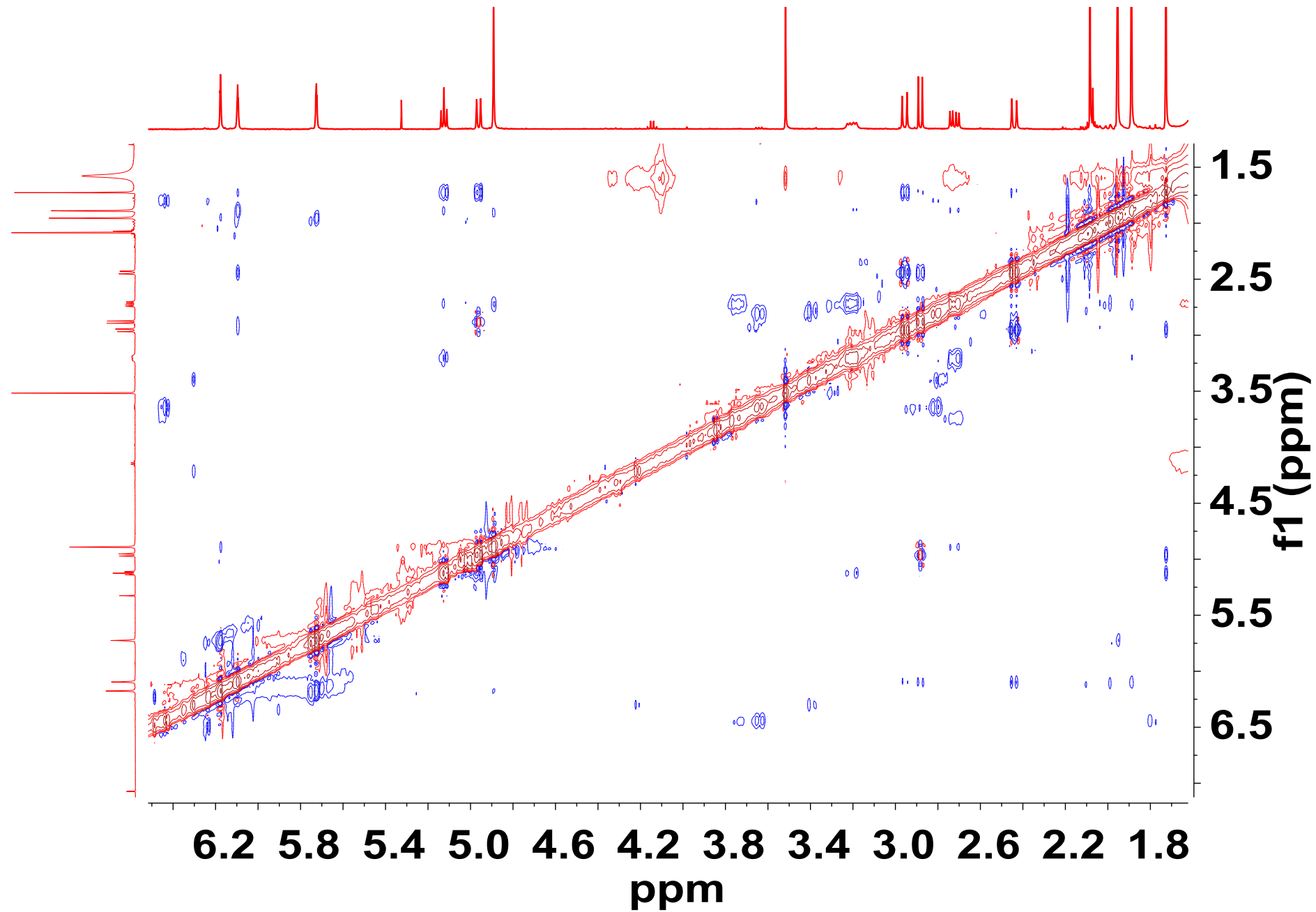


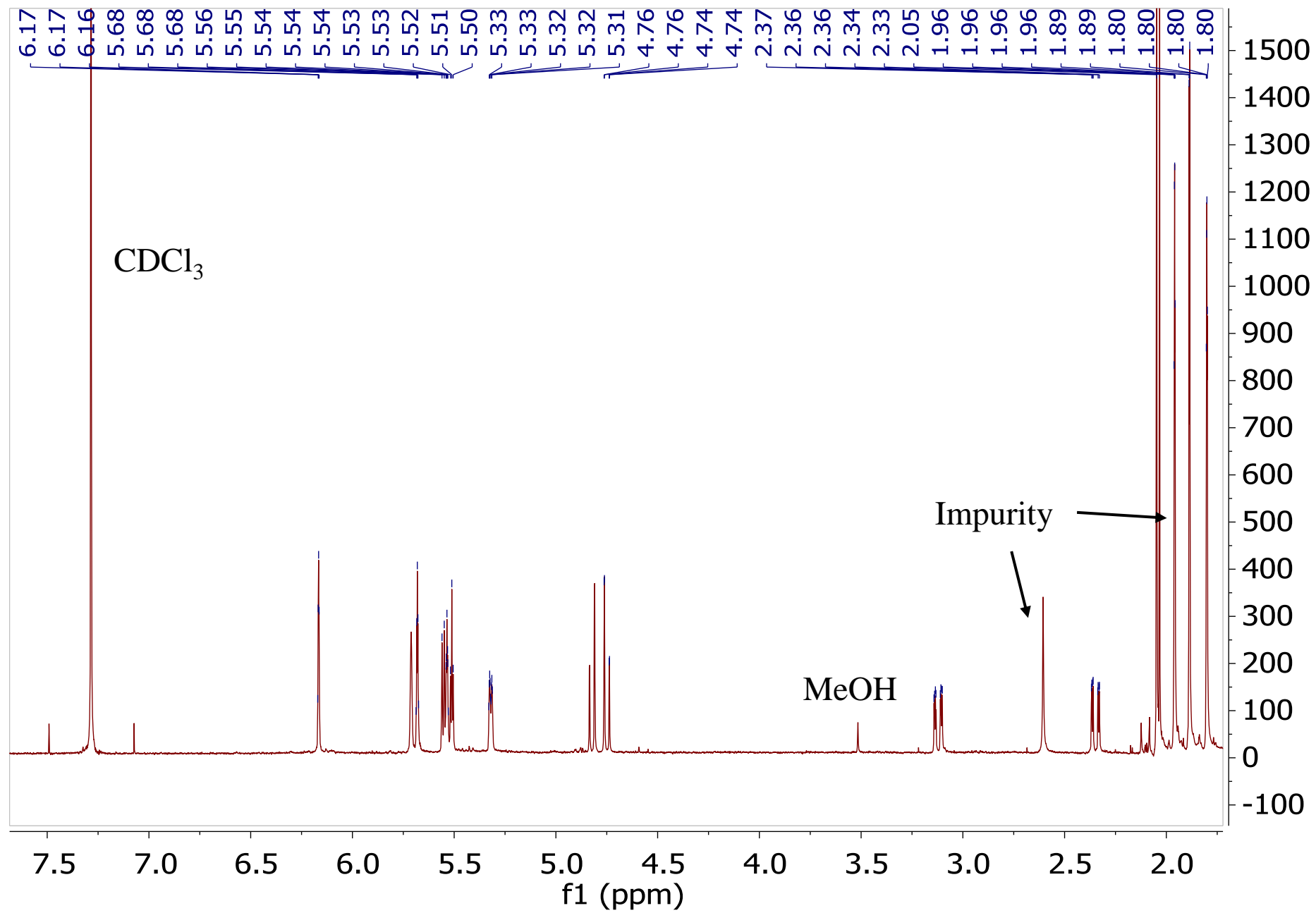
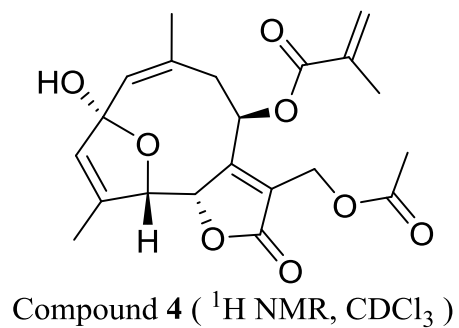
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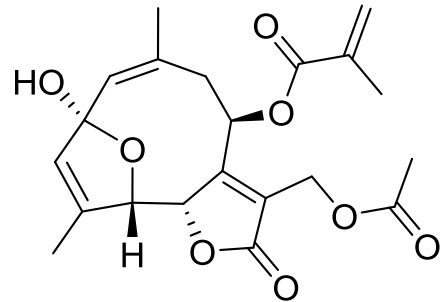




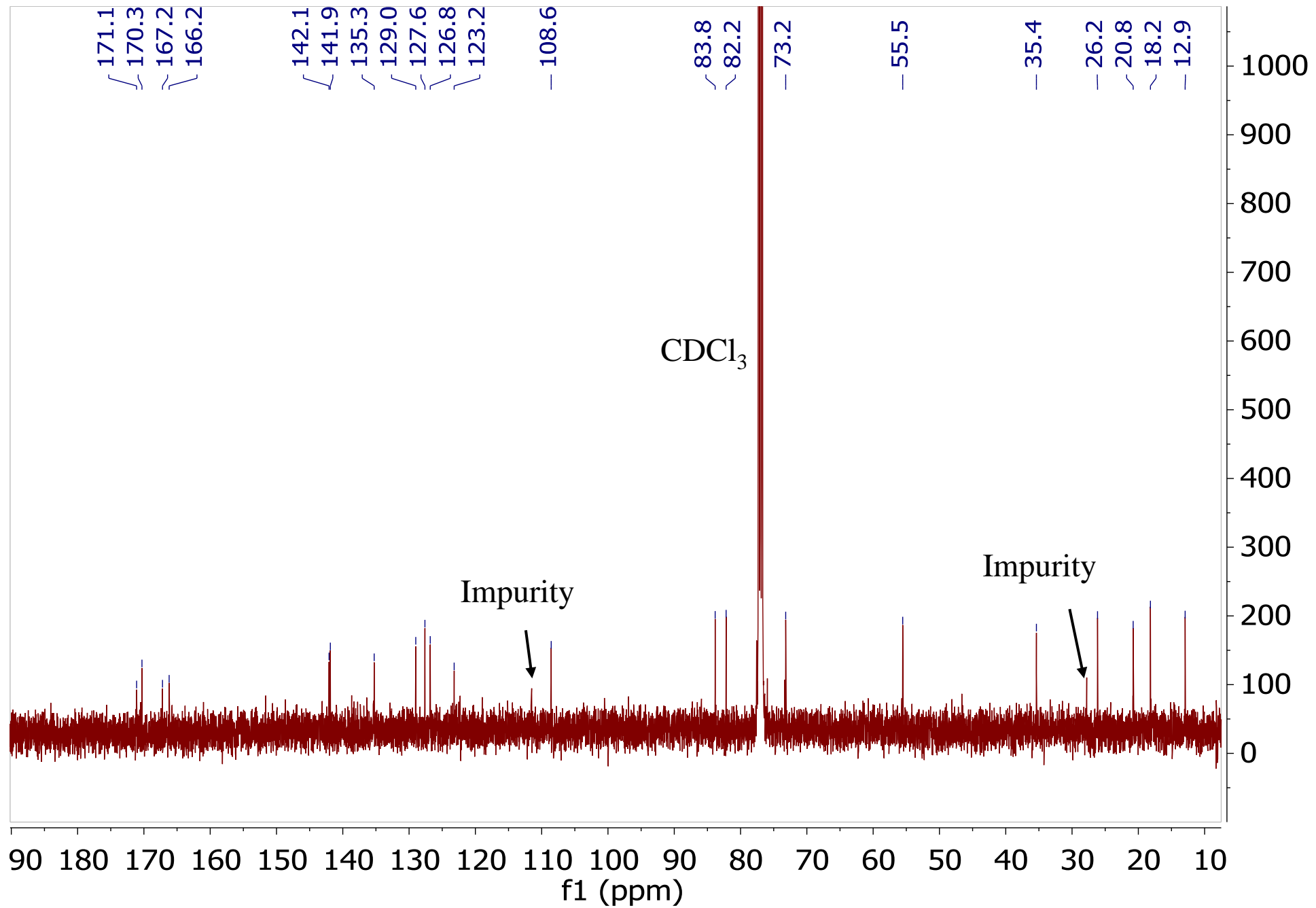
Compound **3** (NOESY, CDCl_3)

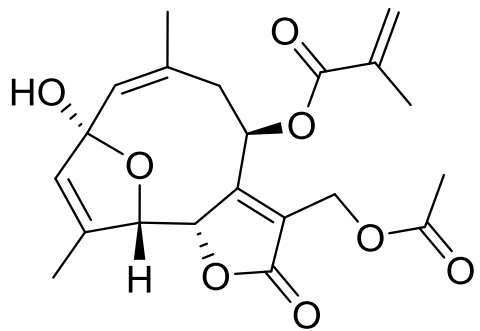




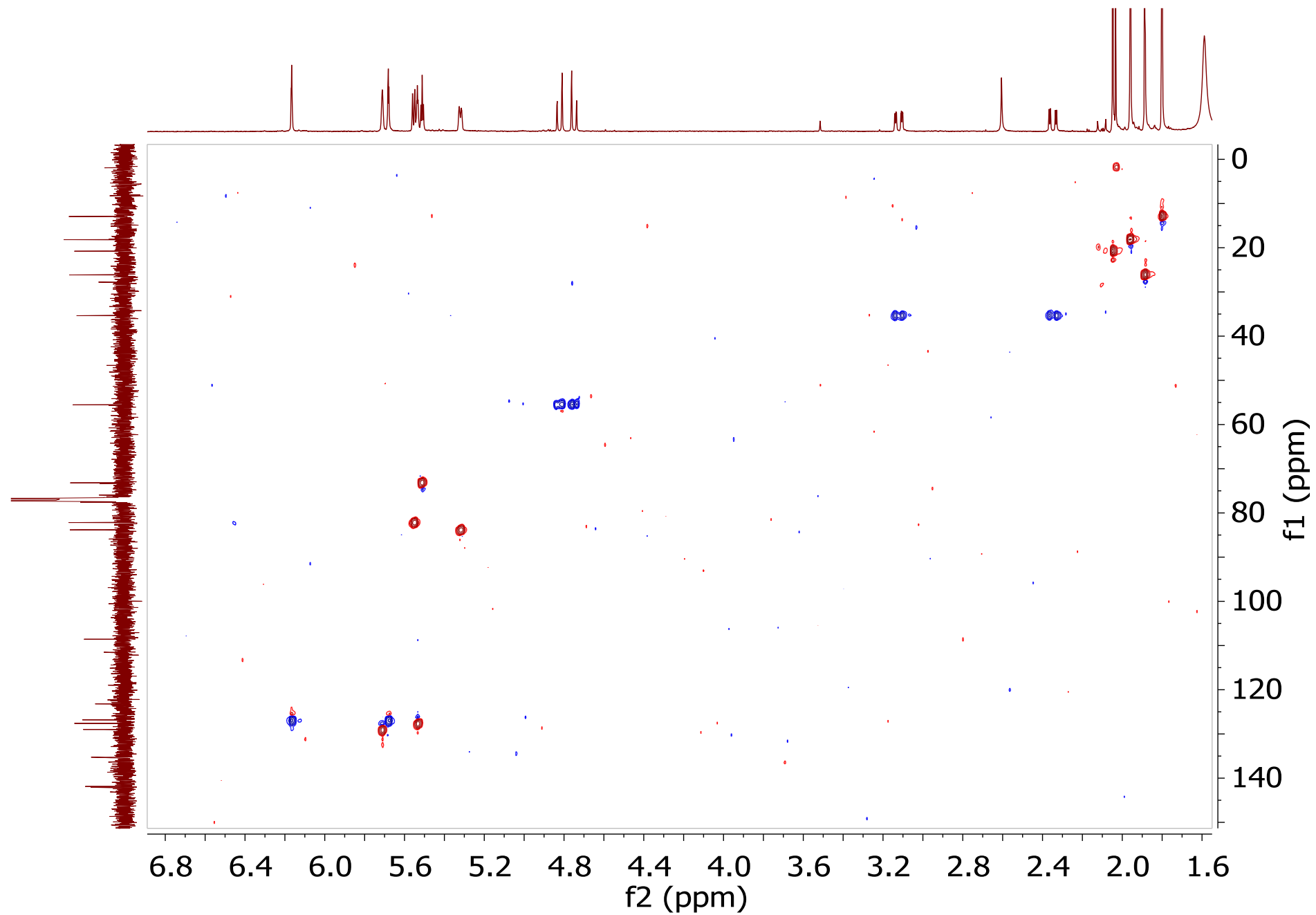


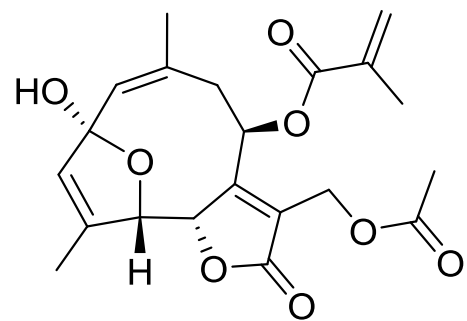
Compound 4 (^{13}C NMR, CDCl_3)



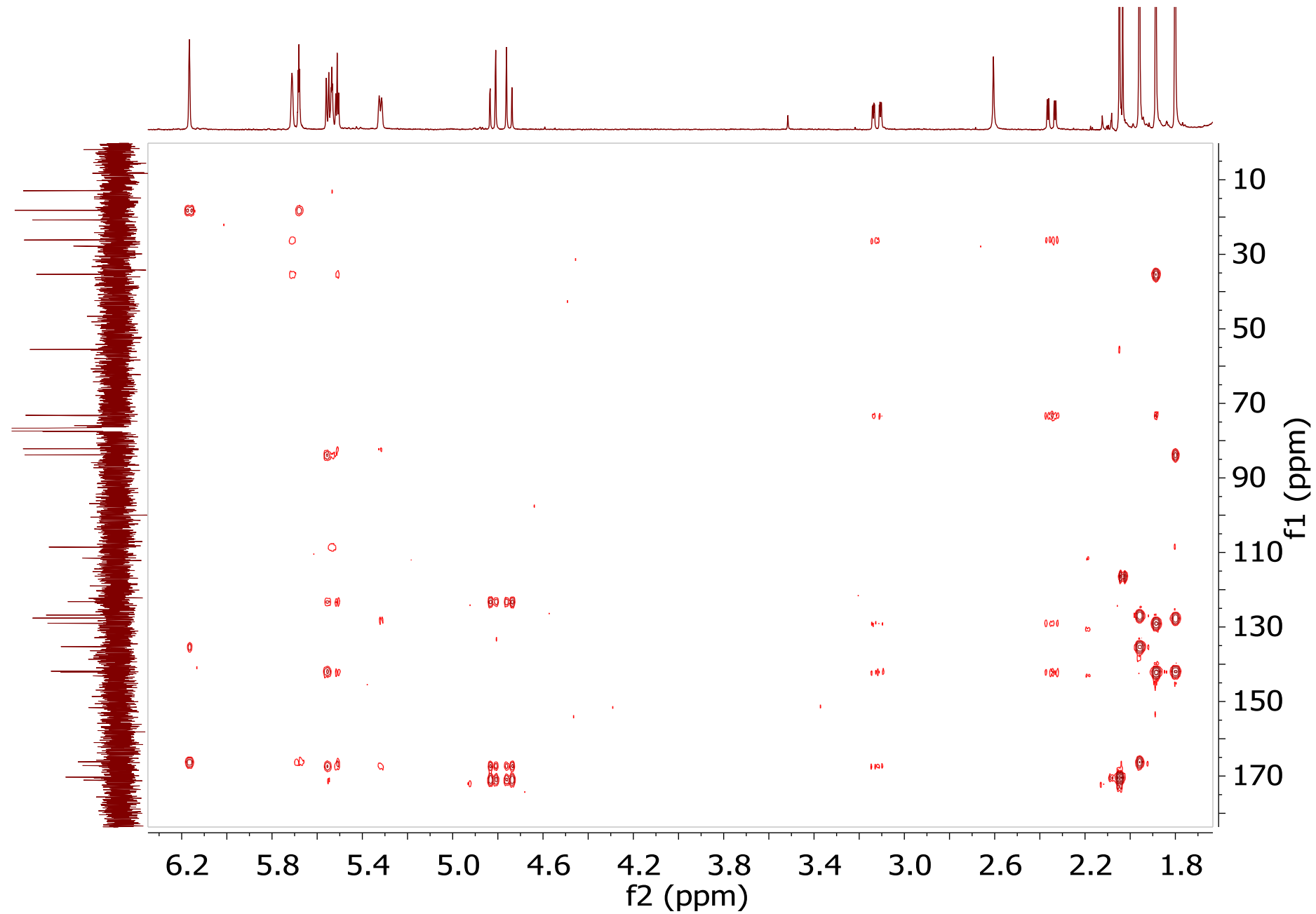


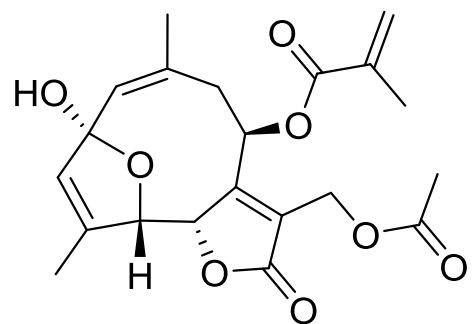
Compound 4 (gHSQC, CDCl₃)





Compound 4 (gHMBC, CDCl₃)





Compound 4 (NOESY, CDCl_3)

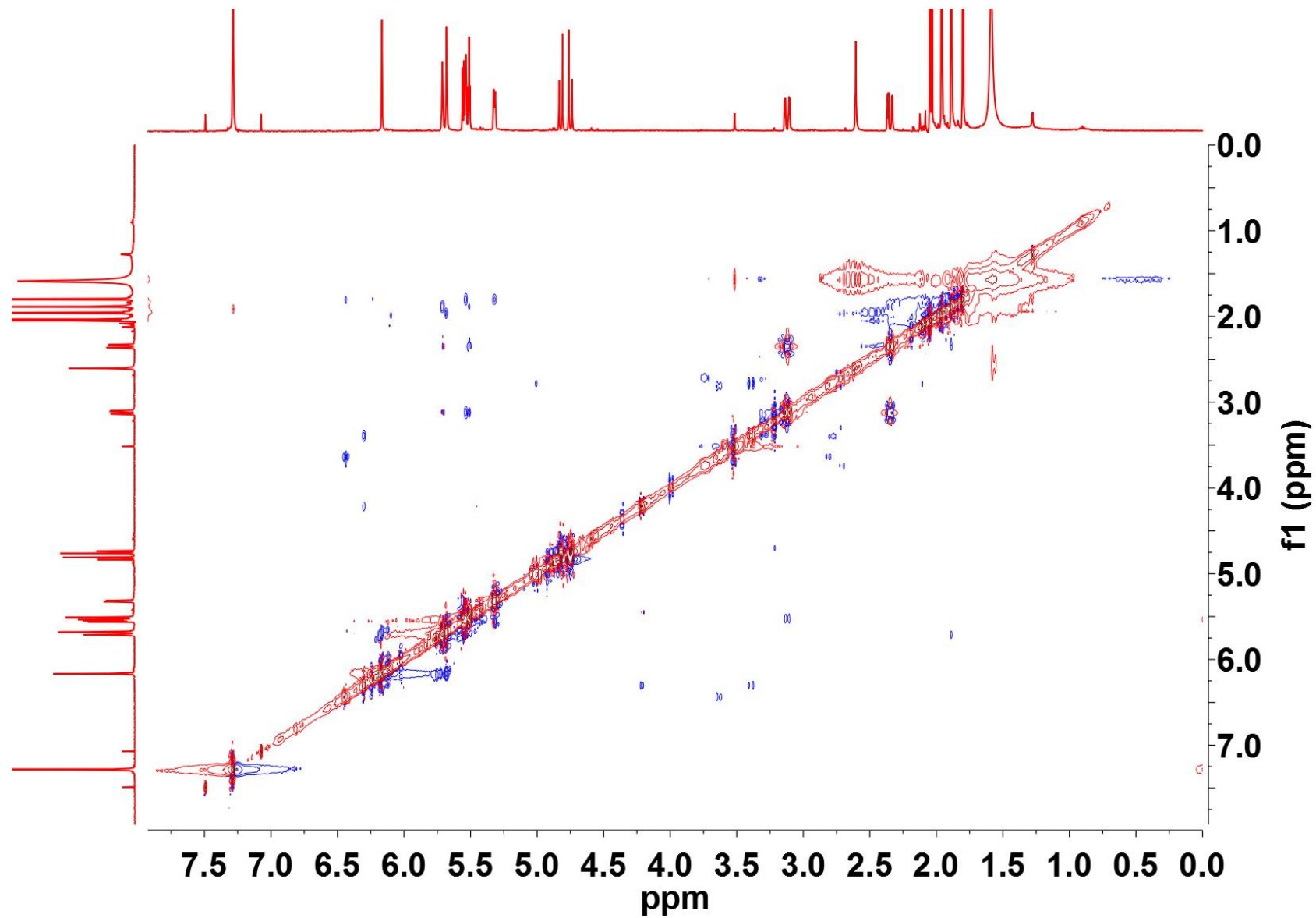


Table S1 Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide A (**1**)^a

Conf. #	R	
	ΔG^b	% ^c
1	0.0000	23.36
2	0.1268	18.86
3	0.1537	18.02
4	0.3991	11.91
5	0.5359	9.46
6	0.6306	8.06
7	0.8013	6.04
8	1.0059	4.28
9	5.1242	0.00
10	5.1380	0.00
11	5.5271	0.00
12	5.5560	0.00
13	5.7241	0.00
14	5.9733	0.00
15	6.1006	0.00

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

Figure S1. Comparison of Experimental (red) and calculated (blue) ECD Spectra for All Possible Stereoisomers of Trichospirolide A (**1**).

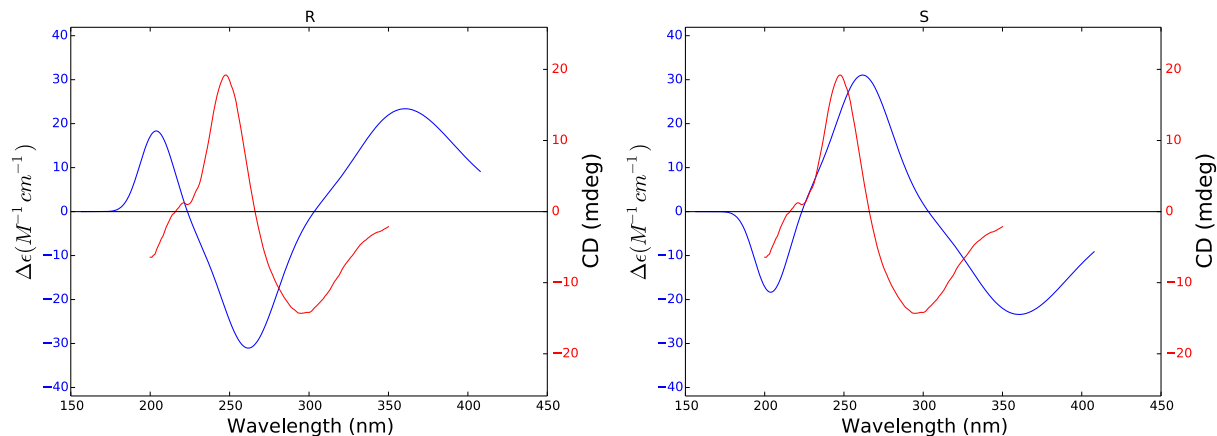


Figure S2. Comparison of Experimental (red) and calculated (blue) UV Spectra for Enantiomerically Unique Stereoisomers of Trichospirolide A (**1**)

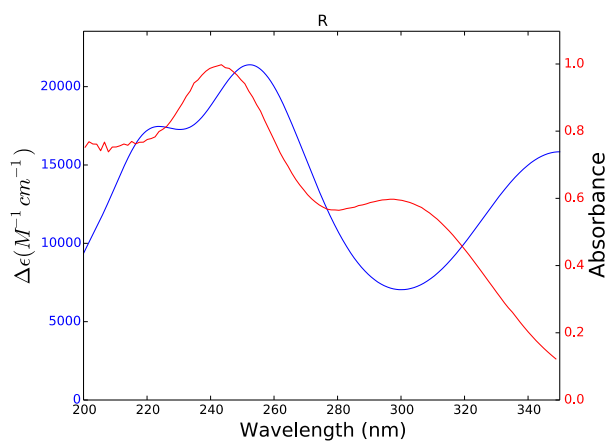


Table S2. Calculated Weighted Average Internuclear Distances for Enantiomerically Unique Stereoisomers of Trichospirolide A (**1**)

Proton Pair	R WA Distance (Å) ^a	NOESY Signal
H5-H15	3.19	medium
H3-H9a	1.94	strong
H3-H8	2.65	strong
H1-H14	3.01	medium
H8-H15	3.85	medium

^a Weighted average internuclear distances are reported. In the case of methyl hydrogens, a simple average of the three individual weighted average distances is reported.

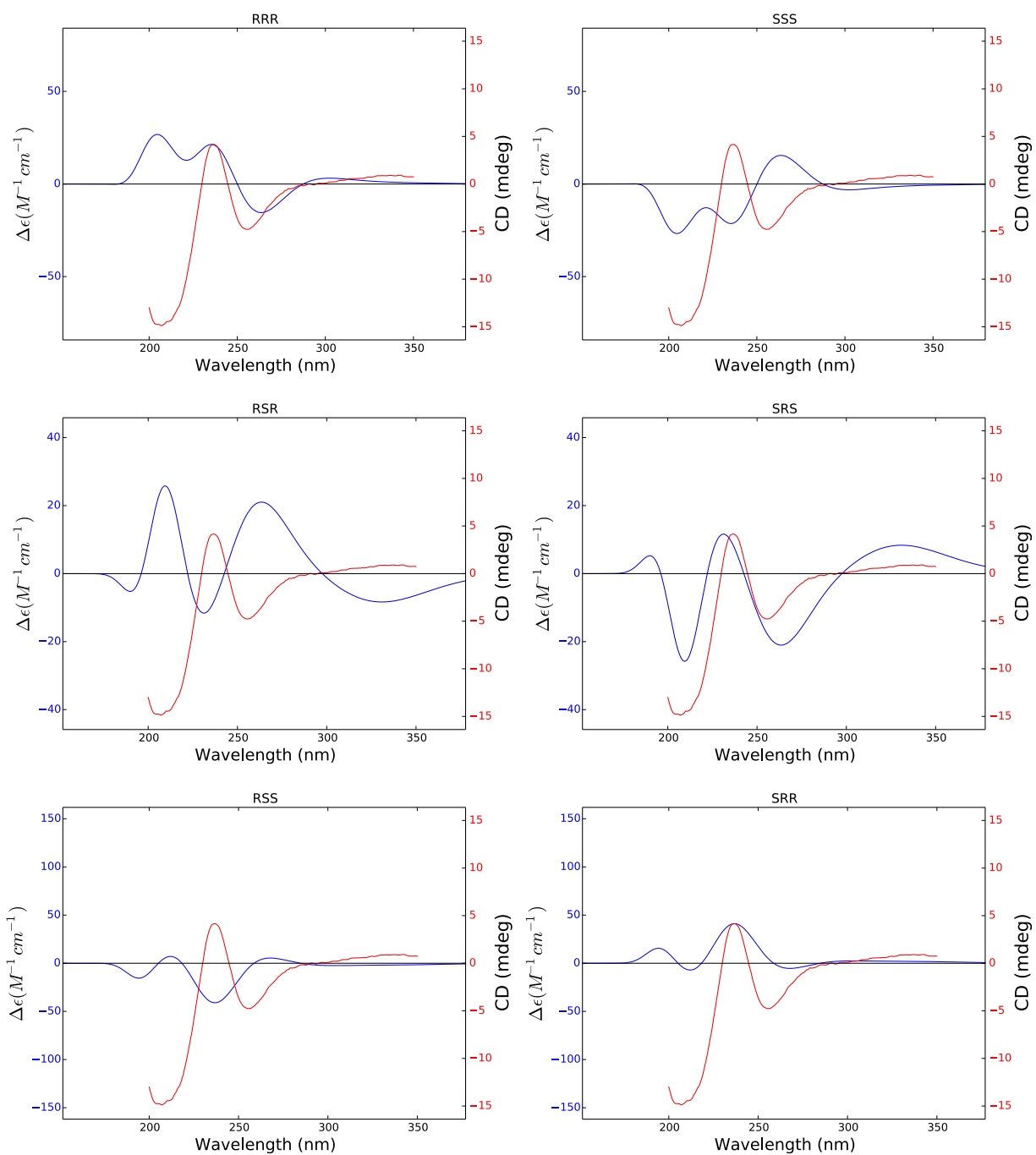
Table S3. Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide B (**2**)^a

Conf. #	RRR		RSR		SRR		SSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
1	0.0000	25.90	0.0000	23.81	0.0000	82.94	0.0000	45.72
2	0.1381	20.52	0.4644	10.87	1.4232	7.51	0.8566	10.77
3	0.4255	12.63	0.6783	7.58	1.9798	2.93	0.8911	10.16
4	0.4656	11.80	0.6783	7.58	2.0300	2.70	0.9024	9.97
5	0.4913	11.30	0.7034	7.26	2.2427	1.88	1.0360	7.96
6	0.8358	6.32	0.7034	7.26	2.6864	0.89	1.3015	5.08
7	1.0197	4.63	0.9814	4.54	3.2273	0.36	1.7206	2.51
8	1.3316	2.74	0.9814	4.54	3.3283	0.30	2.1825	1.15
9	1.3510	2.65	1.2287	2.99	3.5831	0.20	2.1862	1.14
10	1.9152	1.02	1.2293	2.99	3.5981	0.19	2.2942	0.95
11	2.8200	0.22	1.5104	1.86	4.3744	0.05	2.2942	0.95
12	2.8326	0.22	1.5267	1.81	4.5074	0.04	2.3299	0.90
13	4.3656	0.02	1.5274	1.81	5.3138	0.01	2.4730	0.70
14	4.5250	0.01	1.5487	1.74	8.2743	0.00	2.7523	0.44
15	4.7251	0.01	1.5499	1.74	8.4883	0.00	2.9430	0.32
16	4.8638	0.01	1.6485	1.47	8.9169	0.00	3.3616	0.16
17	5.1437	0.00	1.6623	1.44	8.9527	0.00	3.4664	0.13
18	5.6758	0.00	1.7075	1.33	9.3041	0.00	3.4664	0.13
19	5.7649	0.00	1.7269	1.29	9.6800	0.00	3.5072	0.12
20	6.3146	0.00	1.7326	1.28	9.7760	0.00	3.7826	0.08
21	6.3328	0.00	1.9447	0.89	9.8287	0.00	3.7833	0.08
22	6.3799	0.00	1.9472	0.89	9.9711	0.00	3.8008	0.07
23	6.6083	0.00	2.1950	0.59	10.1663	0.00	3.8008	0.07
24	6.7545	0.00	2.2157	0.57	10.4989	0.00	3.8473	0.07
25	6.7551	0.00	2.4529	0.38	10.5089	0.00	3.9031	0.06
26	6.8097	0.00	2.6104	0.29	10.7285	0.00	3.9709	0.06
27	6.8505	0.00	2.6939	0.25	10.9551	0.00	4.0600	0.05
28	6.9453	0.00	2.6939	0.25	11.1879	0.00	4.0600	0.05
29	7.6054	0.00	2.8100	0.21	11.7878	0.00	4.1171	0.04
30	7.7422	0.00	3.0447	0.14	11.8304	0.00	4.1328	0.04
31	7.9656	0.00	3.0553	0.14	11.8712	0.00	4.2275	0.04
32	9.1761	0.00	3.2467	0.10	12.0061	0.00	4.9329	0.01
33	9.2520	0.00	3.3929	0.08	12.0752	0.00	5.1556	0.01
34	9.5306	0.00	4.1918	0.02	12.2879	0.00	14.2288	0.00
35	9.5883	0.00	12.8445	0.00	12.3161	0.00	14.5463	0.00
36	9.9448	0.00	13.5209	0.00	12.3168	0.00	19.5720	0.00
37	10.0558	0.00	13.7525	0.00	12.3563	0.00	19.9084	0.00
38	10.1267	0.00	14.0637	0.00	12.4586	0.00		
39	10.3727	0.00	14.7741	0.00	12.4774	0.00		
40	10.4681	0.00	16.9591	0.00	12.6437	0.00		
41	10.6262	0.00			12.6556	0.00		
42	10.8766	0.00			12.6644	0.00		
43	11.8537	0.00			12.8777	0.00		
44	11.9716	0.00			13.0196	0.00		
45	12.2829	0.00			13.1162	0.00		
46	12.4498	0.00			13.1840	0.00		

Conf. #	RRR		RSR		SRR		SSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
47	12.8137	0.00			13.2448	0.00		
48	12.8539	0.00			13.3816	0.00		
49	12.8916	0.00			13.5184	0.00		
50	13.2041	0.00			13.6766	0.00		
51	13.4312	0.00			14.7364	0.00		
52	13.4620	0.00			14.7973	0.00		
53	13.4726	0.00			14.8563	0.00		
54	13.5498	0.00			15.0100	0.00		
55	13.7801	0.00			15.2221	0.00		
56	13.9489	0.00			15.3859	0.00		
57	14.2212	0.00			15.6162	0.00		
58	14.7898	0.00			15.7191	0.00		
59					16.2192	0.00		
60					16.3592	0.00		

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

Figure S3. Comparison of Experimental (red) and calculated (blue) ECD Spectra for All Possible Stereoisomers of Trichospirolide B (2)



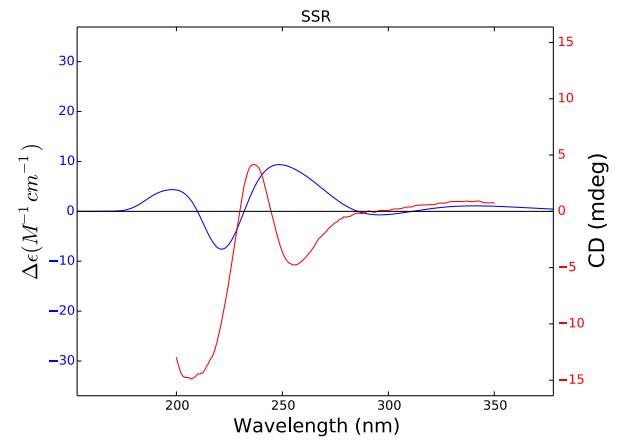
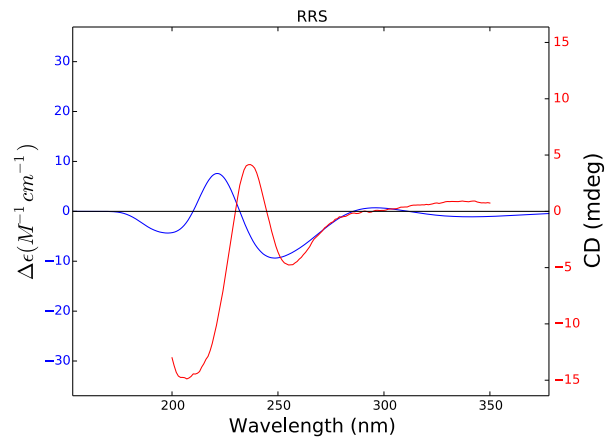


Figure S4. Comparison of Experimental (red) and calculated (blue) UV Spectra for Enantiomerically Unique Stereoisomers of Trichospirolide B (**2**)

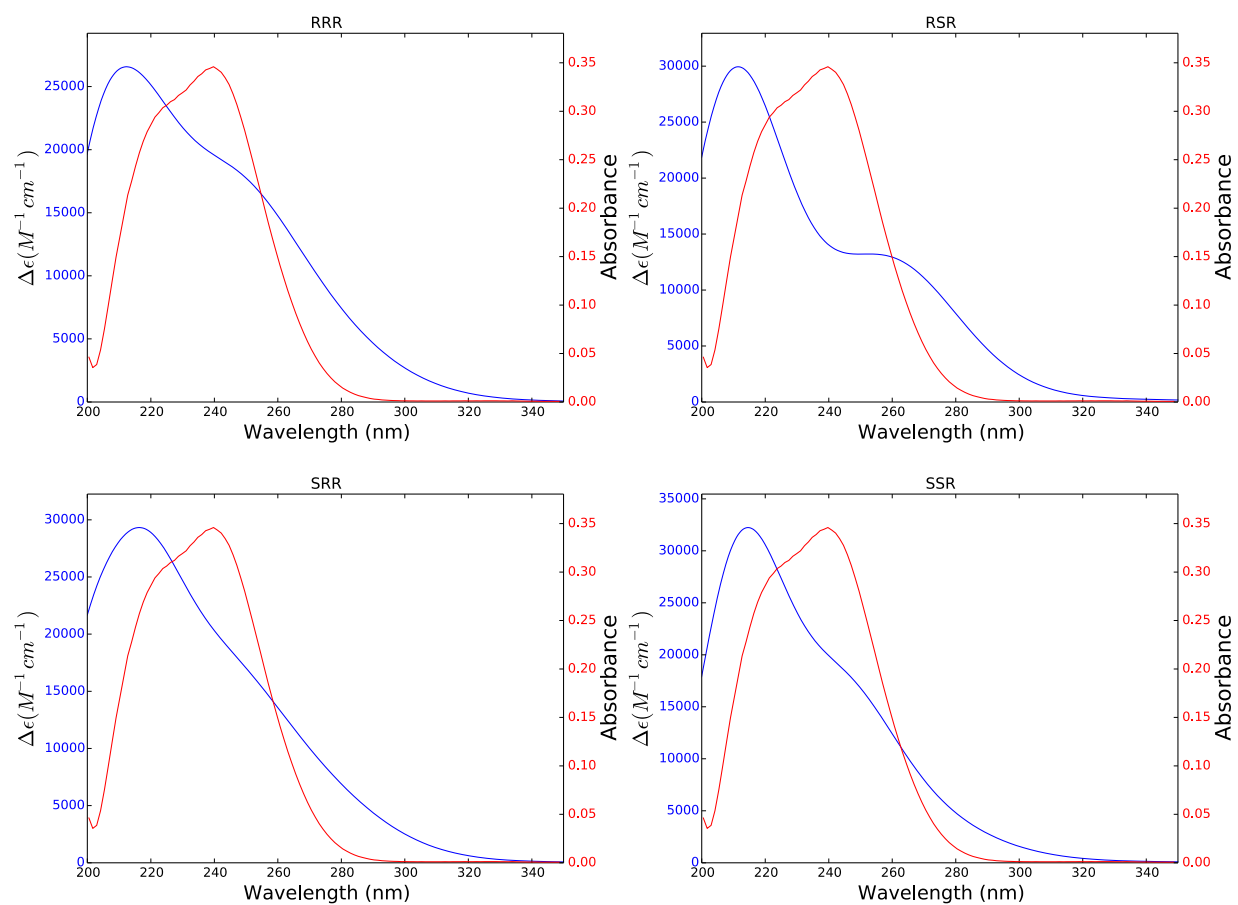


Table S4. Calculated Weighted Average Internuclear Distances for Enantiomerically Unique Stereoisomers of Trichospirolide B (**2**)

Proton Pair	RRR WA Distance (Å) ^a	RSR WA Distance (Å) ^a	SRR WA Distance (Å) ^a	SSR WA Distance (Å) ^a	NOESY Signal
H3-H9a	1.99	3.00	1.98	2.16	strong
H3-H9b	3.68	4.18	3.67	3.86	medium
H3-H5	2.22	3.50	3.52	3.71	strong
H3-H8	3.21	2.09	3.17	3.26	v. weak
H1-H14	3.02	3.03	3.02	3.02	medium
H3'b-H4'	3.16	3.15	3.16	3.15	medium
H6-H15	3.23	3.35	3.13	4.72	medium
H6-H8	2.71	3.47	2.69	3.35	medium
H8-H15	3.44	4.69	3.35	3.01	strong
H5-H15	3.98	3.12	3.11	2.93	weak

^a Weighted average internuclear distances are reported. In the case of methyl hydrogens, a simple average of the three individual weighted average distances is reported.

Table S5. Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide C (**3**)^a

Conf. #	RRRR		RRSR		RSRR		RSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
1	0.0000	26.76	0.0000	67.66	0.0000	19.88	0.0000	34.82
2	0.5936	9.83	0.6890	21.15	0.1889	14.45	0.1311	27.91
3	0.5936	9.83	1.5067	5.32	0.3382	11.23	0.7919	9.15
4	0.8515	6.36	1.9792	2.40	0.4091	9.96	0.8534	8.25
5	0.8515	6.36	1.9917	2.35	0.4738	8.93	1.1433	5.06
6	0.8628	6.24	2.9330	0.48	0.6783	6.33	1.3002	3.88
7	0.9664	5.24	3.5831	0.16	0.8013	5.14	1.5248	2.66
8	1.0542	4.52	3.8931	0.09	0.8026	5.13	1.7081	1.95
9	1.0548	4.51	4.0186	0.08	0.9105	4.27	1.7338	1.87
10	1.0699	4.40	4.1685	0.06	1.0272	3.51	1.7489	1.82
11	1.2914	3.03	4.3122	0.05	1.1860	2.69	1.9265	1.35
12	1.3598	2.70	4.3612	0.04	1.5481	1.46	2.4448	0.56
13	1.3598	2.70	4.4547	0.04	1.6949	1.14	2.5753	0.45
14	1.6209	1.74	4.5074	0.03	1.7351	1.06	4.2376	0.03
15	2.0501	0.84	4.5294	0.03	1.7671	1.01	4.2545	0.03
16	2.0651	0.82	4.7063	0.02	2.1593	0.52	4.4277	0.02
17	2.0852	0.79	5.3702	0.01	2.1906	0.49	4.4428	0.02
18	2.1674	0.69	5.5164	0.01	2.2408	0.45	4.4716	0.02
19	2.2459	0.60	5.5735	0.01	2.2804	0.42	4.5683	0.02
20	2.6054	0.33	5.6746	0.00	2.4071	0.34	4.5996	0.01
21	2.6475	0.31	5.7756	0.00	2.5213	0.28	4.7565	0.01
22	2.6475	0.31	5.7825	0.00	2.5220	0.28	4.7841	0.01
23	2.7887	0.24	6.2927	0.00	2.6738	0.22	4.7848	0.01
24	2.8872	0.20	6.4759	0.00	2.8320	0.17	4.8801	0.01
25	2.8878	0.20	6.7489	0.00	3.0422	0.12	4.8971	0.01
26	2.9066	0.20	9.2175	0.00	3.1426	0.10	4.9391	0.01
27	2.9066	0.20	9.6850	0.00	3.1645	0.10	4.9642	0.01
28	3.6402	0.06	10.9369	0.00	3.3440	0.07	4.9674	0.01
29	4.4710	0.01	11.6284	0.00	3.3747	0.07	5.0182	0.01
30	4.8362	0.01	11.6365	0.00	3.4990	0.05	5.1048	0.01
31	5.2692	0.00	11.9729	0.00	3.5674	0.05	5.1155	0.01
32	5.5108	0.00	12.0545	0.00	3.7368	0.04	5.1744	0.01
33	6.6905	0.00	12.4002	0.00	3.7638	0.03	5.1882	0.01
34	7.2666	0.00	12.6167	0.00	4.9768	0.00	5.2253	0.01
35	7.4328	0.00	13.6446	0.00	5.1167	0.00	5.3520	0.00
36	7.4617	0.00	13.9577	0.00	5.1374	0.00	5.4349	0.00
37	7.4674	0.00	15.7599	0.00	5.8471	0.00	5.4424	0.00
38	7.5985	0.00	15.8791	0.00	5.9149	0.00	5.5742	0.00
39	7.6933	0.00	16.4100	0.00	5.9174	0.00	5.5905	0.00
40	7.7002	0.00	16.4351	0.00	6.5041	0.00	5.6112	0.00
41	7.7974	0.00	16.4853	0.00	6.8637	0.00	5.6382	0.00
42	8.0409	0.00	16.6936	0.00	6.9133	0.00	5.7135	0.00
43	8.0792	0.00	16.7125	0.00	6.9359	0.00	5.7957	0.00
44	8.7575	0.00	16.9139	0.00	7.1028	0.00	5.8164	0.00
45	8.9621	0.00	16.9290	0.00	7.1467	0.00	5.8421	0.00

Conf. #	RRRR		RRSR		RSRR		RSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
46	9.3336	0.00	16.9773	0.00	7.1837	0.00	5.8528	0.00
47	9.4773	0.00	17.0344	0.00	7.2000	0.00	5.8747	0.00
48	9.5344	0.00	17.0670	0.00	7.2170	0.00	5.9933	0.00
49	9.8544	0.00	18.2241	0.00	7.3676	0.00	6.0511	0.00
50	10.3294	0.00	18.2273	0.00	7.3858	0.00	6.1251	0.00
51	10.6865	0.00	18.5404	0.00	7.4203	0.00	6.1766	0.00
52	10.7285	0.00	18.5969	0.00	7.4398	0.00	6.3115	0.00
53	10.8760	0.00	18.6144	0.00	8.0949	0.00	6.5650	0.00
54	11.1358	0.00	18.8416	0.00	8.1997	0.00	6.6139	0.00
55	11.2324	0.00	18.8579	0.00	8.2499	0.00	6.7194	0.00
56	11.7859	0.00	18.9790	0.00	8.5605	0.00	6.7206	0.00
57	17.7817	0.00	19.1177	0.00	9.9128	0.00	6.7922	0.00
58	18.2988	0.00	19.1805	0.00	13.1714	0.00	6.8919	0.00
59	18.5197	0.00	19.3737	0.00			6.9020	0.00
60	19.0022	0.00	19.4691	0.00			6.9051	0.00
61	19.6185	0.00	19.5877	0.00			7.2132	0.00
62	20.0213	0.00	20.0878	0.00			7.3638	0.00
63	20.1255	0.00	20.4524	0.00			7.7021	0.00
64	20.8019	0.00	20.5516	0.00			7.8037	0.00
65			23.1375	0.00			7.8357	0.00
66			23.2850	0.00			7.9236	0.00
67			23.5002	0.00			7.9280	0.00
68			23.9941	0.00			7.9744	0.00
69			24.1033	0.00			8.1520	0.00
70			24.1227	0.00			8.3848	0.00
71			24.1648	0.00			8.7688	0.00
72			24.1654	0.00			8.8504	0.00
73			24.2288	0.00			11.4326	0.00
74			24.2683	0.00			14.1918	0.00
75			24.3060	0.00				
76			24.8770	0.00				
77			24.8895	0.00				
78			25.0621	0.00				
79			25.0803	0.00				
80			25.0822	0.00				
81			25.4832	0.00				
82			25.6168	0.00				

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

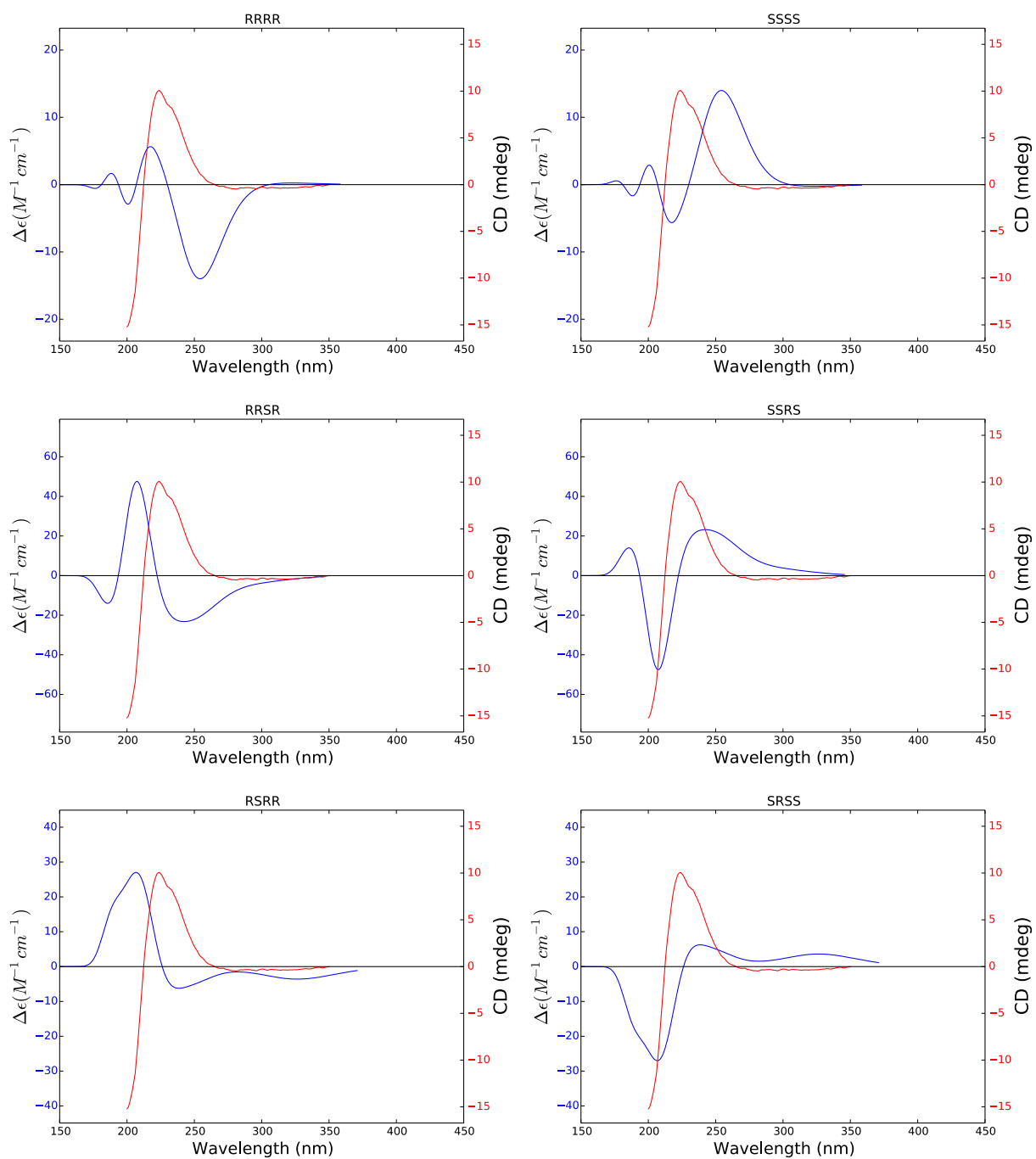
Table S6. Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide C (**3**)^a

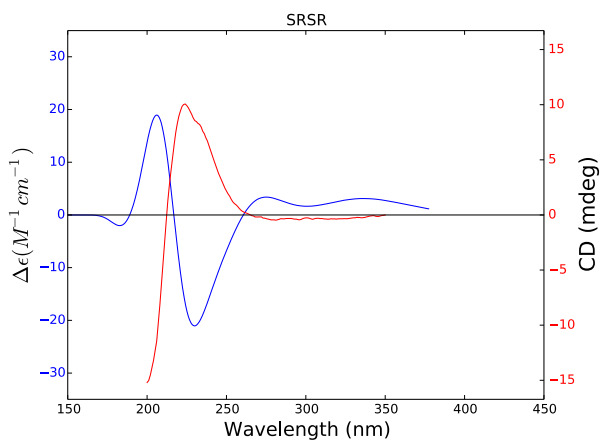
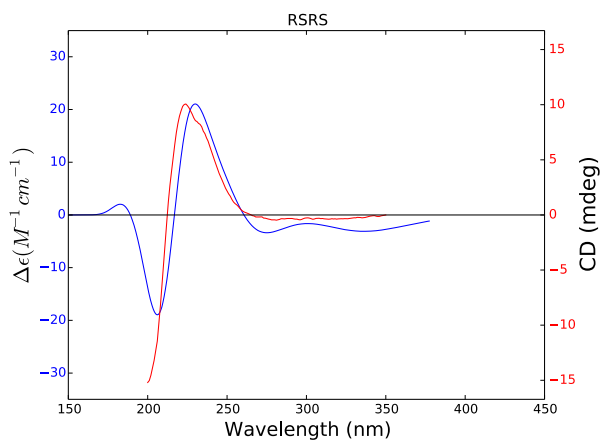
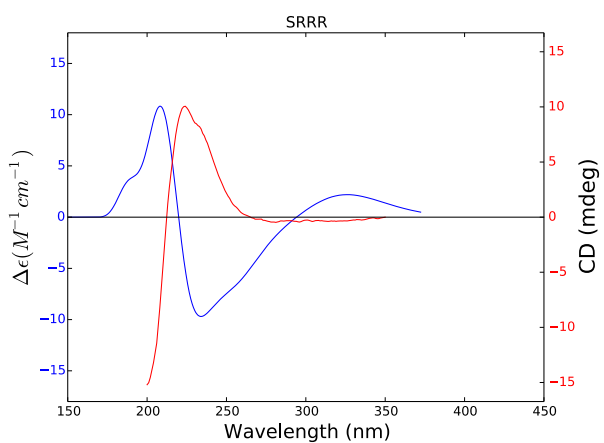
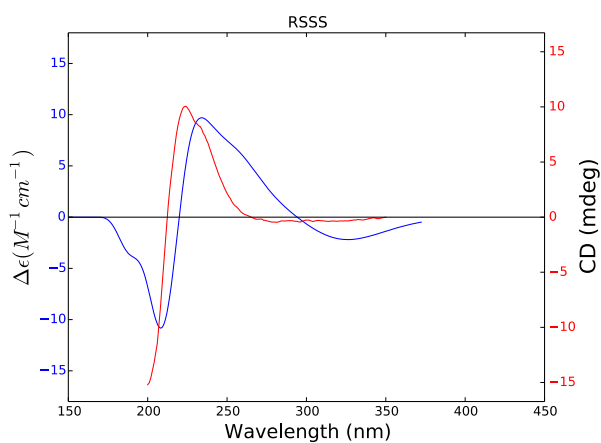
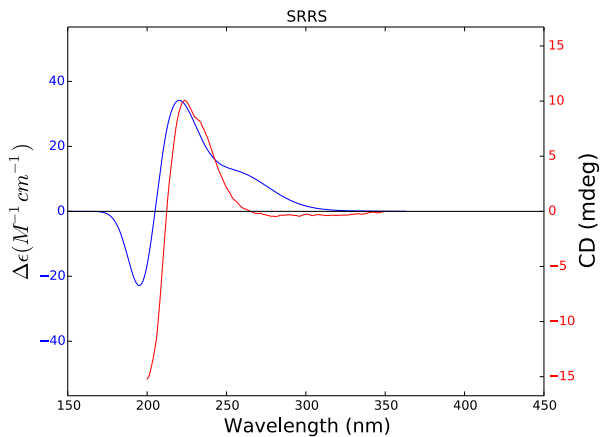
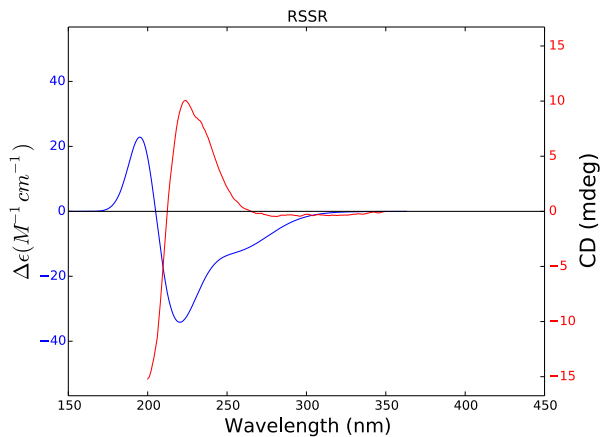
Conf. #	SRRR		SRSR		SSRR		SSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
1	0.0000	14.35	0.0000	32.32	0.0000	26.70	0.0000	27.45
2	0.0195	13.89	0.0289	30.78	0.2039	18.93	0.2698	17.41
3	0.5522	5.65	0.5453	12.87	0.3257	15.41	0.3533	15.12
4	0.6049	5.17	0.7932	8.47	0.6551	8.84	0.7919	7.21
5	0.7016	4.39	1.1176	4.90	0.7700	7.28	1.0624	4.57
6	0.7179	4.27	1.6114	2.13	0.8848	6.00	1.1992	3.63
7	0.7455	4.08	1.6943	1.85	1.0875	4.26	1.2732	3.20
8	0.7593	3.99	1.9447	1.21	1.1370	3.92	1.3071	3.02
9	0.7882	3.80	1.9647	1.17	1.5600	1.92	1.3906	2.63
10	0.8082	3.67	2.4925	0.48	1.5669	1.90	1.6146	1.80
11	0.8327	3.52	2.5232	0.46	2.0745	0.81	1.7206	1.50
12	0.9111	3.08	2.5803	0.42	2.0877	0.79	1.7539	1.42
13	0.9720	2.78	2.6004	0.40	2.1342	0.73	1.9848	0.96
14	1.0680	2.37	2.8332	0.27	2.2145	0.64	2.0783	0.82
15	1.0831	2.31	2.8752	0.25	2.6136	0.32	2.1505	0.73
16	1.1841	1.95	3.0403	0.19	2.6663	0.30	2.1605	0.72
17	1.3473	1.48	3.1168	0.17	2.7372	0.26	2.1630	0.71
18	1.3642	1.44	3.2147	0.14	3.0008	0.17	2.1712	0.70
19	1.3811	1.40	3.3045	0.12	3.0729	0.15	2.2396	0.63
20	1.4703	1.20	3.3114	0.12	3.1457	0.13	2.2935	0.57
21	1.4847	1.17	3.3189	0.12	3.2919	0.10	2.3168	0.55
22	1.5299	1.09	3.3202	0.12	3.2988	0.10	2.3475	0.52
23	1.5405	1.07	3.4162	0.10	3.3559	0.09	2.5201	0.39
24	1.6171	0.94	3.4438	0.10	3.6383	0.06	2.5339	0.38
25	1.7495	0.75	3.4745	0.09	3.8215	0.04	2.5753	0.36
26	1.8348	0.65	3.5649	0.08	3.9125	0.04	2.6493	0.31
27	1.8367	0.65	3.6101	0.07	4.1391	0.02	2.7636	0.26
28	1.9064	0.57	3.6163	0.07	4.1673	0.02	2.7686	0.26
29	1.9183	0.56	3.7067	0.06	4.2727	0.02	2.7692	0.26
30	1.9559	0.53	3.7851	0.05	4.7226	0.01	2.8062	0.24
31	1.9823	0.51	3.7971	0.05	4.7433	0.01	2.8752	0.21
32	1.9848	0.50	3.8686	0.05	4.7647	0.01	2.9750	0.18
33	2.0080	0.48	3.9577	0.04	4.8858	0.01	2.9819	0.18
34	2.0269	0.47	4.1428	0.03	5.0383	0.01	3.0240	0.17
35	2.0733	0.43	4.1434	0.03	5.1230	0.00	3.1482	0.14
36	2.1197	0.40	4.1623	0.03	5.2328	0.00	3.2078	0.12
37	2.1260	0.40	4.2231	0.03	5.3163	0.00	3.2662	0.11
38	2.1693	0.37	4.3009	0.02	5.3301	0.00	3.3540	0.10
39	2.1919	0.36	4.3072	0.02	5.4236	0.00	3.5699	0.07
40	2.1988	0.35	4.4798	0.02	5.6049	0.00	3.6709	0.06
41	2.2710	0.31	4.5143	0.02	5.6388	0.00	3.7989	0.05
42	2.3274	0.28	4.6053	0.01	6.4891	0.00	3.8755	0.04
43	2.3362	0.28	4.6260	0.01	7.0814	0.00	3.9006	0.04
44	2.4542	0.23	4.6561	0.01	7.1185	0.00	4.0148	0.03
45	2.5163	0.21	4.8306	0.01	7.1706	0.00	4.1491	0.02
46	2.5477	0.19	5.0471	0.01	7.5665	0.00	4.3016	0.02

Conf. #	SRRR		SRSR		SSRR		SSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
47	2.5998	0.18	5.5811	0.00	9.1541	0.00	4.3179	0.02
48	2.7604	0.14	5.9093	0.00	9.3555	0.00	4.3298	0.02
49	2.7930	0.13	6.0417	0.00			4.3675	0.02
50	2.8200	0.12	6.5016	0.00			4.6524	0.01
51	2.8282	0.12	6.5895	0.00			4.6655	0.01
52	2.8495	0.12	7.2785	0.00			4.6662	0.01
53	2.9744	0.09	7.6958	0.00			4.8174	0.01
54	2.9957	0.09	9.7634	0.00			4.9467	0.01
55	3.0403	0.08	10.7417	0.00			4.9542	0.01
56	3.1244	0.07					5.0627	0.01
57	3.1369	0.07					5.0734	0.01
58	3.1608	0.07					5.1625	0.00
59	3.4563	0.04					5.1744	0.00
60	3.6264	0.03					5.2297	0.00
61	3.7851	0.02					5.3200	0.00
62	3.8316	0.02					5.4267	0.00
63	3.9113	0.02					5.4367	0.00
64	4.0217	0.02					5.4838	0.00
65	4.0349	0.02					5.5177	0.00
66	4.2790	0.01					5.6237	0.00
67	4.9096	0.00					5.6997	0.00
68	5.1675	0.00					5.7172	0.00
69	5.2730	0.00					5.7210	0.00
70	6.4815	0.00					5.9745	0.00
71	8.4959	0.00					6.3353	0.00
72	8.5536	0.00					6.4094	0.00
73							6.6836	0.00
74							7.0143	0.00
75							7.0846	0.00
76							7.4404	0.00
77							7.5640	0.00
78							7.7322	0.00
79							7.7654	0.00
80							8.1896	0.00
81							8.4444	0.00
82							8.7280	0.00
83							9.1259	0.00
84							9.2966	0.00
85							9.4214	0.00
86							12.0940	0.00
87							13.7519	0.00
88							13.9602	0.00
89							14.9818	0.00
90							15.1958	0.00

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

Figure S5. Comparison of Experimental (red) and calculated (blue) ECD Spectra for All Possible Stereoisomers of Trichospirolide C (**3**)





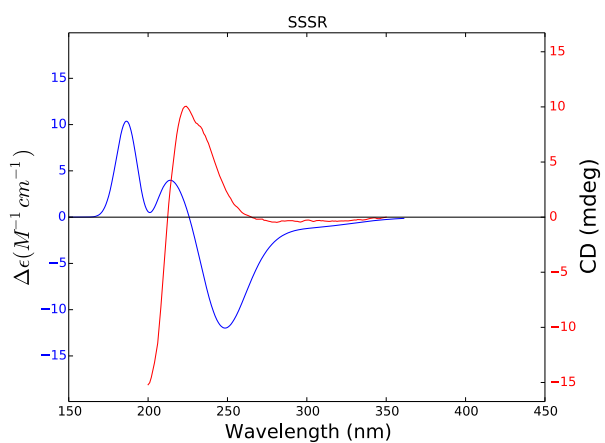
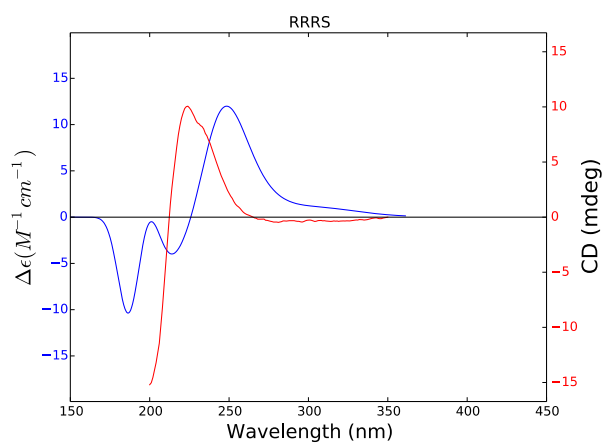
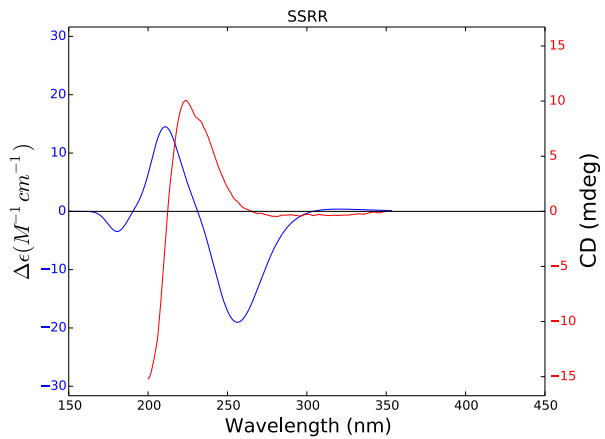
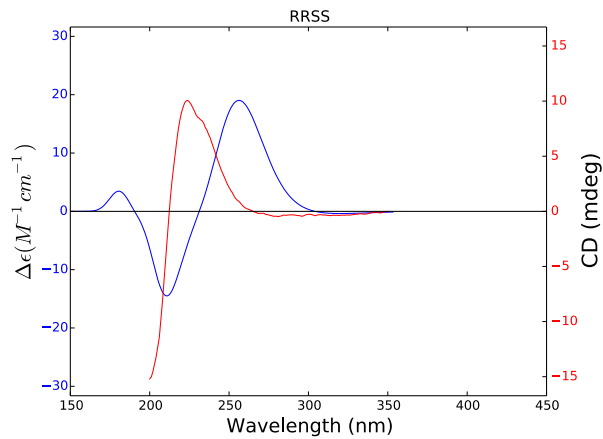
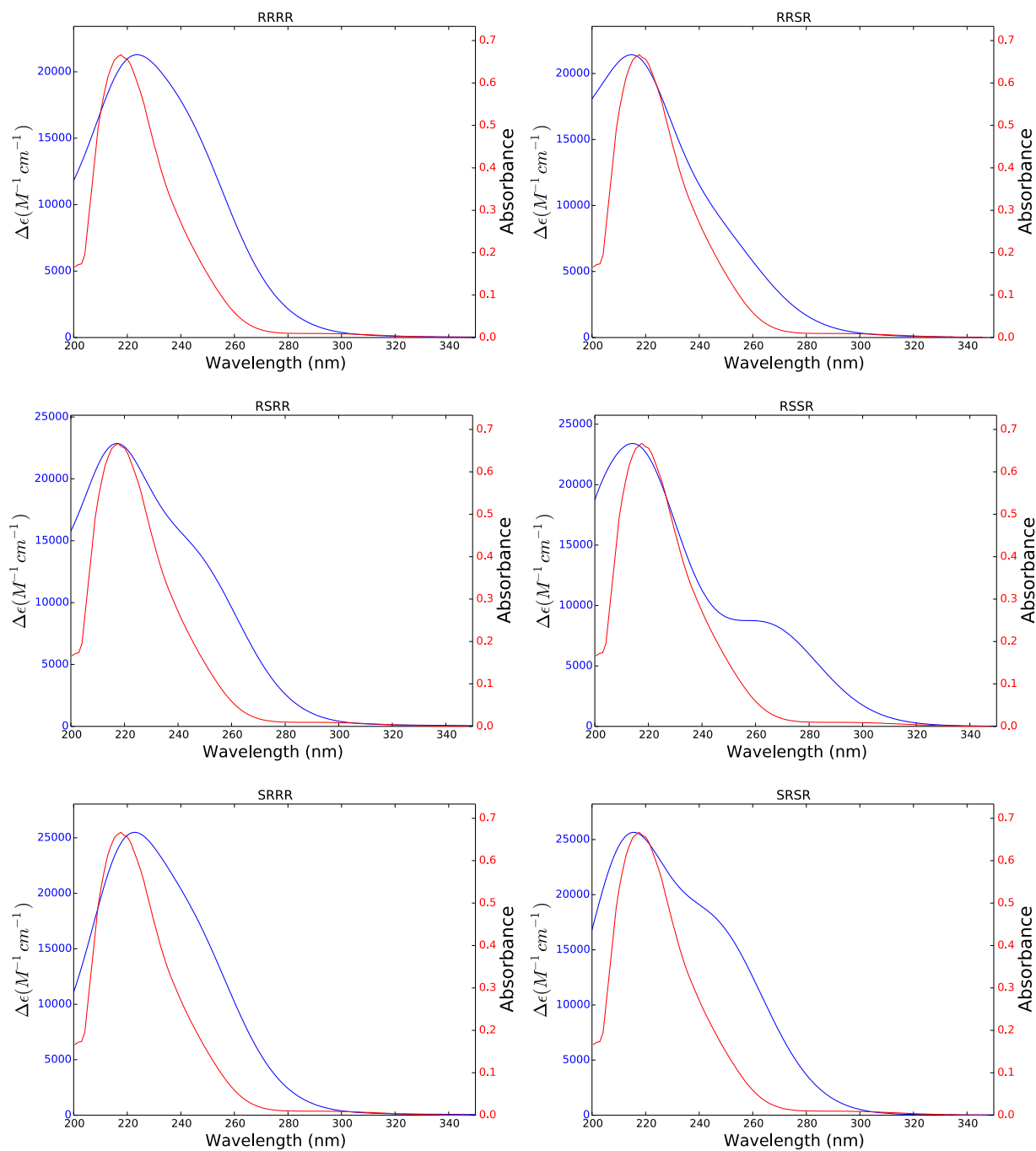


Figure S6. Comparison of Experimental (red) and calculated (blue) UV Spectra for Enantiomerically Unique Stereoisomers of Trichospirolide C (**3**)



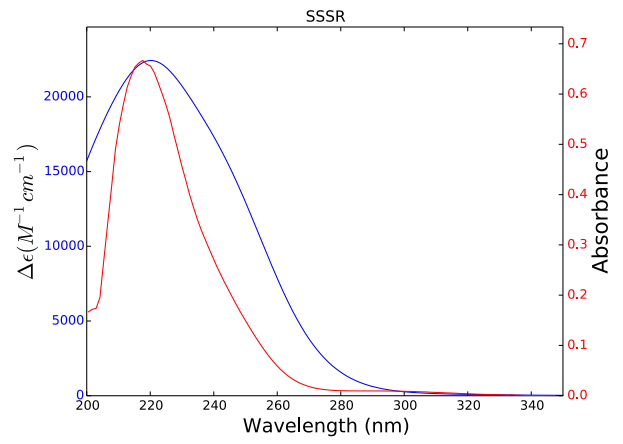
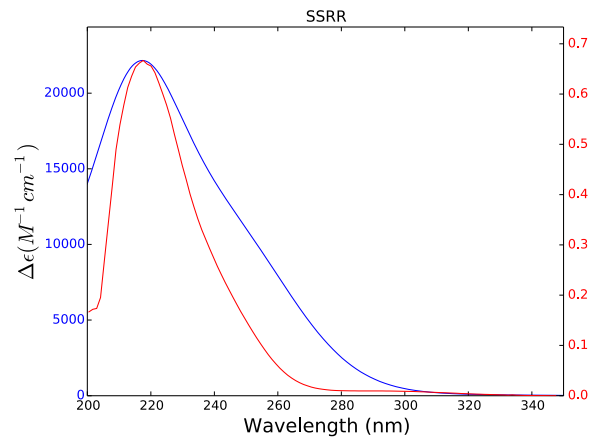


Table S7. Calculated Weighted Average Internuclear Distances for Enantiomerically Unique Stereoisomers of Trichospirolide C (**3**)

Proton Pair	RRRR WA Distance (Å) ^a	RRSR WA Distance (Å) ^a	RSRR WA Distance (Å) ^a	RSSR WA Distance (Å) ^a	NOESY Signal
H1-H14	3.07	3.08	3.07	3.07	medium
H1-H3a	2.53	2.76	3.12	2.56	medium
H1-H3b	3.59	3.82	3.81	3.77	medium
H8-H15	5.58	5.69	5.97	5.30	strong
H6-H15	4.62	3.07	4.78	4.70	strong
H3a-H15	3.92	3.96	3.96	3.01	strong
H3b-H5	3.71	3.72	4.31	3.92	strong

Proton Pair	SRRR WA Distance (Å) ^a	SRSR WA Distance (Å) ^a	SSRR WA Distance (Å) ^a	SSSR WA Distance (Å) ^a	NOESY Signal
H1-H14	3.03	3.01	3.09	3.06	medium
H1-H3a	3.65	4.09	2.68	2.78	medium
H1-H3b	3.81	3.84	3.83	3.73	medium
H8-H15	4.65	3.80	3.15	5.76	strong
H6-H15	4.44	4.80	3.09	4.63	strong
H3a-H15	3.16	3.32	2.99	2.95	strong
H3b-H5	3.81	3.82	2.69	2.79	strong

^a Weighted average internuclear distances are reported. In the case of methyl hydrogens, a simple average of the three individual weighted average distances is reported.

Table S8. Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide D (**4**)^a

Conf. #	RRRR		RRSR		RSRR		RSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
1	0.0000	23.20	0.0000	39.08	0.0000	42.34	0.0000	33.59
2	0.0646	20.80	0.3790	20.61	0.4474	19.90	0.5622	13.01
3	0.2736	14.62	0.6476	13.10	0.9808	8.09	0.6231	11.74
4	0.3263	13.37	1.6610	2.37	0.9852	8.03	0.8967	7.40
5	0.7467	6.58	1.7075	2.19	1.2249	5.36	0.9325	6.96
6	0.8509	5.52	1.7100	2.18	1.3466	4.36	0.9388	6.89
7	1.0680	3.82	1.7696	1.97	1.3749	4.16	1.0467	5.74
8	1.2318	2.90	1.8304	1.78	1.7169	2.33	1.0931	5.31
9	1.3429	2.40	1.9164	1.54	1.8894	1.74	1.2111	4.35
10	1.3755	2.28	1.9227	1.52	1.9472	1.58	1.3485	3.45
11	1.4357	2.06	1.9359	1.49	2.2691	0.92	1.8160	1.57
12	1.4715	1.94	2.1222	1.09	2.4987	0.62	8.0980	0.00
13	2.6657	0.26	2.1323	1.07	2.9305	0.30	8.8153	0.00
14	2.6770	0.25	2.1762	0.99	3.0547	0.24	8.9131	0.00
15	5.2956	0.00	2.1881	0.97	5.1299	0.01	8.9269	0.00
16	5.3012	0.00	2.2314	0.90	5.4637	0.00	8.9684	0.00
17	5.3715	0.00	2.2496	0.88	5.7781	0.00	9.2068	0.00
18	5.3752	0.00	2.3770	0.71	6.0141	0.00	9.2112	0.00
19	5.7386	0.00	2.4159	0.66	6.2048	0.00	9.2576	0.00
20	6.1170	0.00	2.4310	0.65	6.9691	0.00	9.3850	0.00
21	6.1239	0.00	2.5006	0.57	7.1881	0.00	9.5369	0.00
22	6.2776	0.00	2.5006	0.57	7.2377	0.00	9.5400	0.00
23	6.4232	0.00	2.5402	0.54	8.9483	0.00	9.8337	0.00
24	6.5801	0.00	2.5483	0.53	9.0650	0.00	10.1004	0.00
25	6.9045	0.00	2.6644	0.44	9.0744	0.00	10.3602	0.00
26	6.9271	0.00	2.7008	0.41	9.1478	0.00	10.5315	0.00
27	8.1319	0.00	2.7328	0.39	9.2043	0.00	10.5629	0.00
28	8.3452	0.00	2.9957	0.25	9.3744	0.00	10.6313	0.00
29	8.5078	0.00	3.0215	0.24	9.4986	0.00	10.8766	0.00
30	8.9050	0.00	3.0830	0.21	9.5413	0.00	10.9155	0.00
31	9.0142	0.00	4.4152	0.02	9.9316	0.00	10.9249	0.00
32	9.0292	0.00	4.4177	0.02	9.9423	0.00	11.1948	0.00
33	9.1679	0.00	4.6323	0.02	10.4462	0.00	11.2098	0.00
34	10.3589	0.00	4.7069	0.01	10.6275	0.00	11.2575	0.00
35	10.9871	0.00	5.3426	0.00	11.8750	0.00	11.2839	0.00
36	11.1019	0.00	5.5478	0.00	16.0919	0.00	11.2876	0.00
37	11.1370	0.00	5.7505	0.00	31.5531	0.00	11.3328	0.00
38	11.4420	0.00	5.7800	0.00	37.0921	0.00	11.4012	0.00
39	11.4797	0.00	5.8001	0.00			11.4822	0.00
40	11.6146	0.00	5.8973	0.00			11.5732	0.00
41	11.8505	0.00	6.3586	0.00			12.3249	0.00
42	11.9384	0.00	6.4194	0.00			12.5075	0.00
43	15.6846	0.00	6.4596	0.00			16.0322	0.00
44	17.6876	0.00	6.5907	0.00			17.3362	0.00
45			8.5950	0.00				
46			8.9521	0.00				

Conf. #	RRRR		RRSR		RSRR		RSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
47			11.5807	0.00				

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

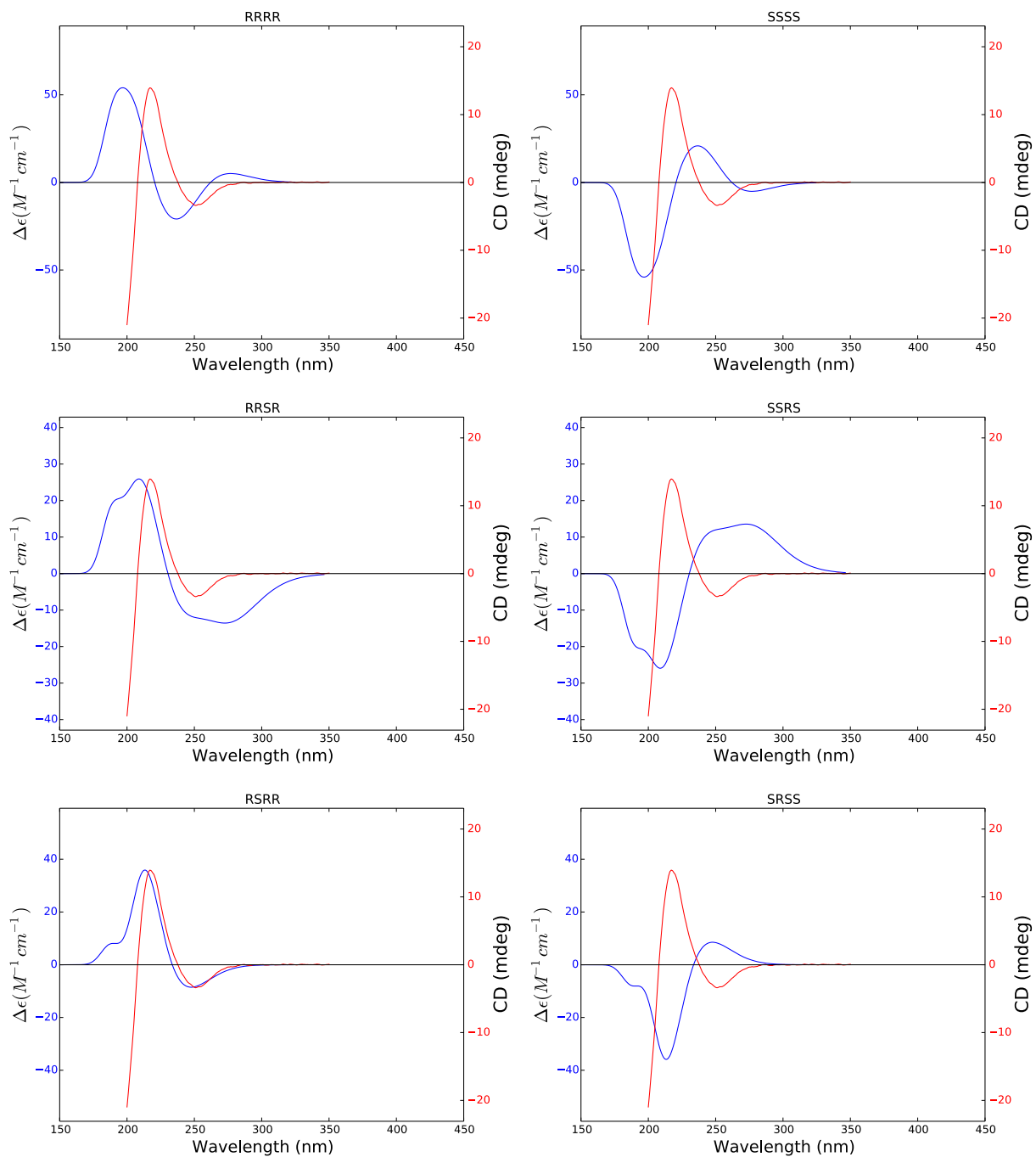
Table S9. Relative Free Energies and Room Temperature Boltzmann Population for Conformers of Enantiomerically Unique Stereoisomers of Trichospirolide D (**4**)^a

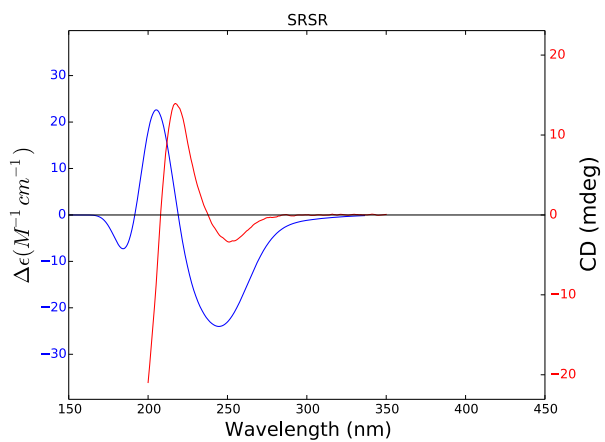
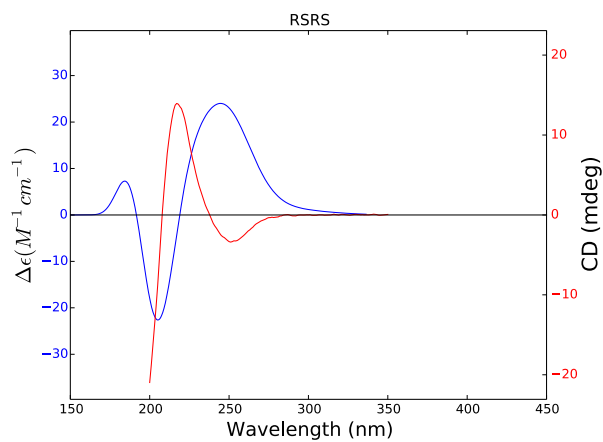
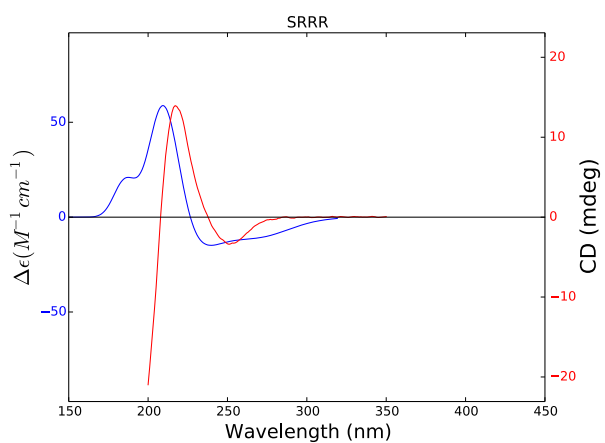
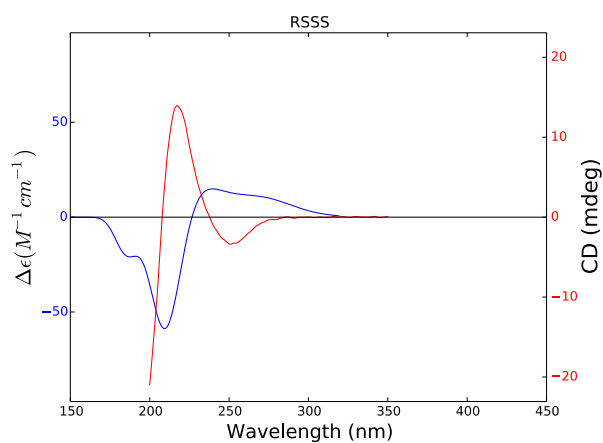
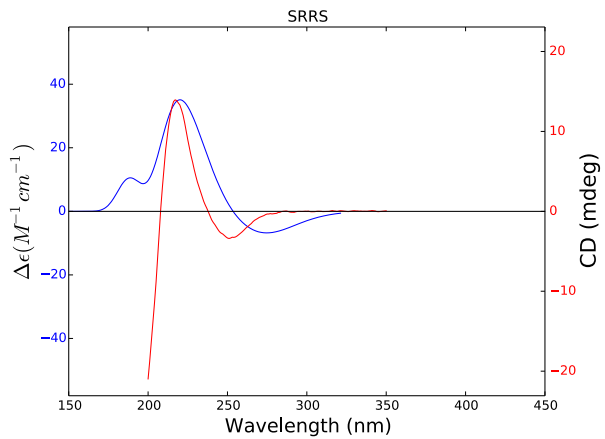
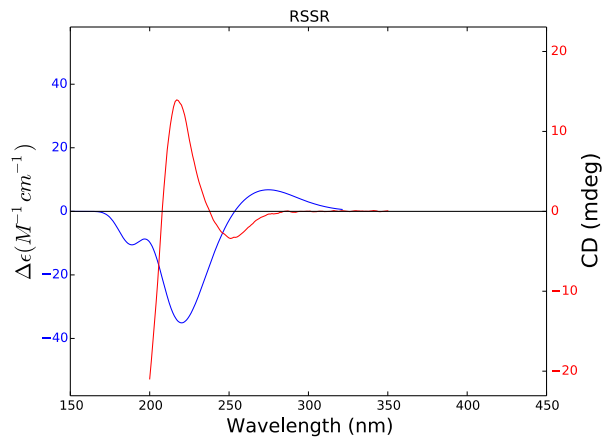
Conf. #	SRRR		SRSR		SSRR		SSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
1	0.0000	37.19	0.0000	19.06	0.0000	30.63	0.0000	33.31
2	0.5880	13.79	0.0232	18.33	0.1355	24.37	0.4123	16.61
3	0.8158	9.39	0.1399	15.05	0.4807	13.61	0.7656	9.15
4	0.8566	8.76	0.3313	10.90	0.6633	10.00	0.7743	9.02
5	1.0172	6.68	0.4826	8.44	0.9149	6.54	1.0398	5.76
6	1.2098	4.83	0.4970	8.24	1.2550	3.68	1.0894	5.30
7	1.2613	4.43	0.5692	7.29	1.3761	3.00	1.3630	3.34
8	1.3567	3.77	0.6451	6.42	1.4508	2.65	1.3956	3.16
9	1.5424	2.75	1.2720	2.23	2.2597	0.68	1.4634	2.82
10	1.6108	2.45	1.2883	2.17	2.2747	0.66	1.6271	2.14
11	1.8417	1.66	1.8173	0.89	2.3143	0.62	1.7991	1.60
12	1.9767	1.32	1.8267	0.87	2.3688	0.56	1.8700	1.42
13	2.0174	1.24	3.7870	0.03	2.3883	0.54	2.1473	0.89
14	2.2979	0.77	3.9778	0.02	2.4103	0.52	2.2879	0.70
15	2.4034	0.64	4.3298	0.01	2.4818	0.46	2.3638	0.62
16	2.8031	0.33	4.4578	0.01	2.8414	0.25	2.4862	0.50
17	9.0230	0.00	4.7496	0.01	2.9443	0.21	2.4969	0.49
18	10.7467	0.00	4.8431	0.01	3.0472	0.18	2.5489	0.45
19	12.2239	0.00	5.2974	0.00	3.0478	0.18	2.8219	0.28
20	12.2766	0.00	5.3727	0.00	3.0942	0.17	2.8527	0.27
21	12.6368	0.00	5.5666	0.00	3.1137	0.16	2.9192	0.24
22	12.6914	0.00	5.5742	0.00	3.3672	0.10	2.9480	0.23
23	13.0434	0.00	5.6564	0.00	3.7029	0.06	2.9957	0.21
24	13.0453	0.00	6.1151	0.00	4.1284	0.03	3.0001	0.21
25	13.0817	0.00	6.1383	0.00	4.3875	0.02	3.0415	0.20
26	13.1275	0.00	6.2174	0.00	4.4352	0.02	3.0986	0.18
27	13.3942	0.00	7.2013	0.00	4.4886	0.02	3.1106	0.17
28	13.4149	0.00	7.2182	0.00	4.5683	0.01	3.1495	0.16
29	13.7418	0.00	7.2597	0.00	4.6160	0.01	3.2988	0.13
30	15.2780	0.00	7.5000	0.00	4.7841	0.01	3.4337	0.10
31	29.6448	0.00	7.7516	0.00	4.8626	0.01	3.4595	0.10
32			7.8570	0.00	4.9015	0.01	3.9671	0.04
33			8.0058	0.00	4.9567	0.01	4.0167	0.04
34			8.1495	0.00	5.0835	0.01	4.3675	0.02
35			8.2442	0.00	5.1079	0.01	4.3857	0.02
36			8.2856	0.00	5.1970	0.00	4.4014	0.02
37			8.5153	0.00	5.2912	0.00	4.5582	0.02
38			8.6358	0.00	5.4148	0.00	4.5883	0.01
39			13.3164	0.00	5.8377	0.00	4.9021	0.01
40			13.9439	0.00	5.8622	0.00	4.9115	0.01
41					6.2180	0.00	5.0232	0.01
42					6.4521	0.00	5.0339	0.01
43					7.1655	0.00	5.0602	0.01
44					9.1516	0.00	5.0904	0.01
45					9.1604	0.00	5.1456	0.01
46					9.5858	0.00	5.2554	0.00

Conf. #	SRRR		SRSR		SSRR		SSSR	
	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c	ΔG^b	% ^c
47					15.4054	0.00	5.2679	0.00
48							5.2698	0.00
49							5.3891	0.00
50							5.5089	0.00
51							5.5585	0.00
52							5.8440	0.00
53							5.9864	0.00
54							6.5819	0.00
55							8.7048	0.00
56							11.3912	0.00

^a Conformers in bold were deemed significant and were selected for the computation of the UV and ECD spectra and optical rotations. ^b Relative Free energy in kcal mol⁻¹ calculated at the B3LYP/6-31G* level of theory. ^c Room temperature Boltzmann population in %.

Figure S7. Comparison of Experimental (red) and calculated (blue) ECD Spectra for All Possible Stereoisomers of Trichospirolide D (**4**)





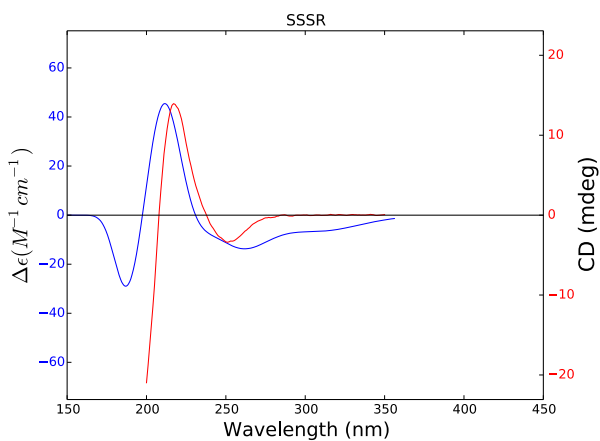
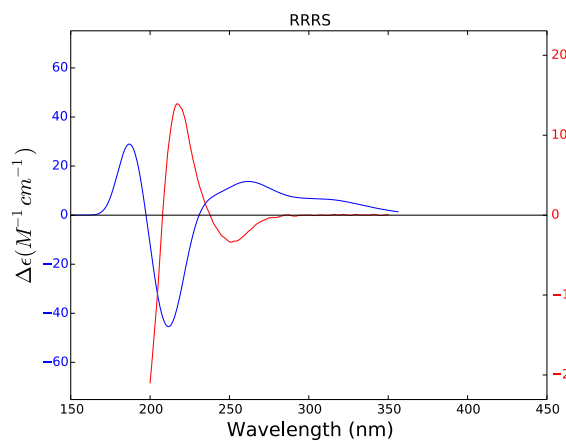
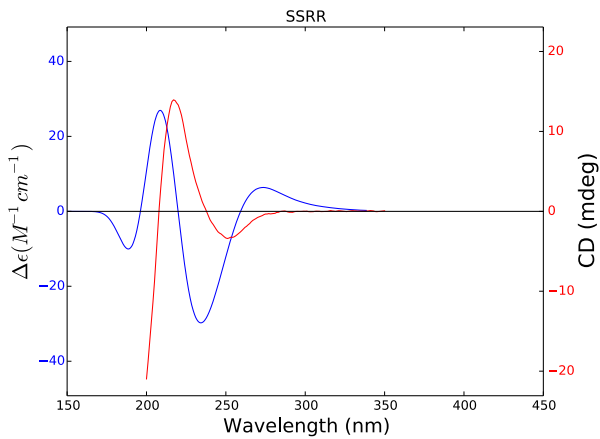
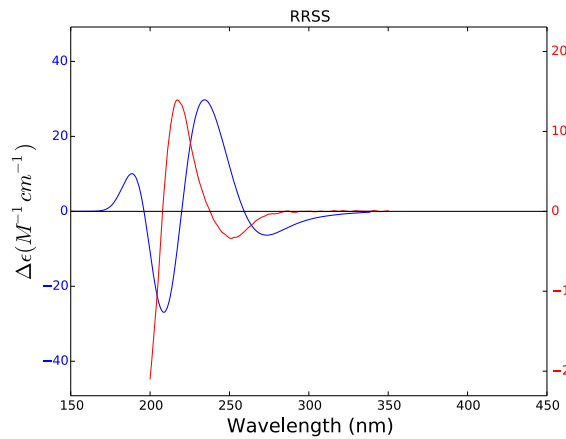
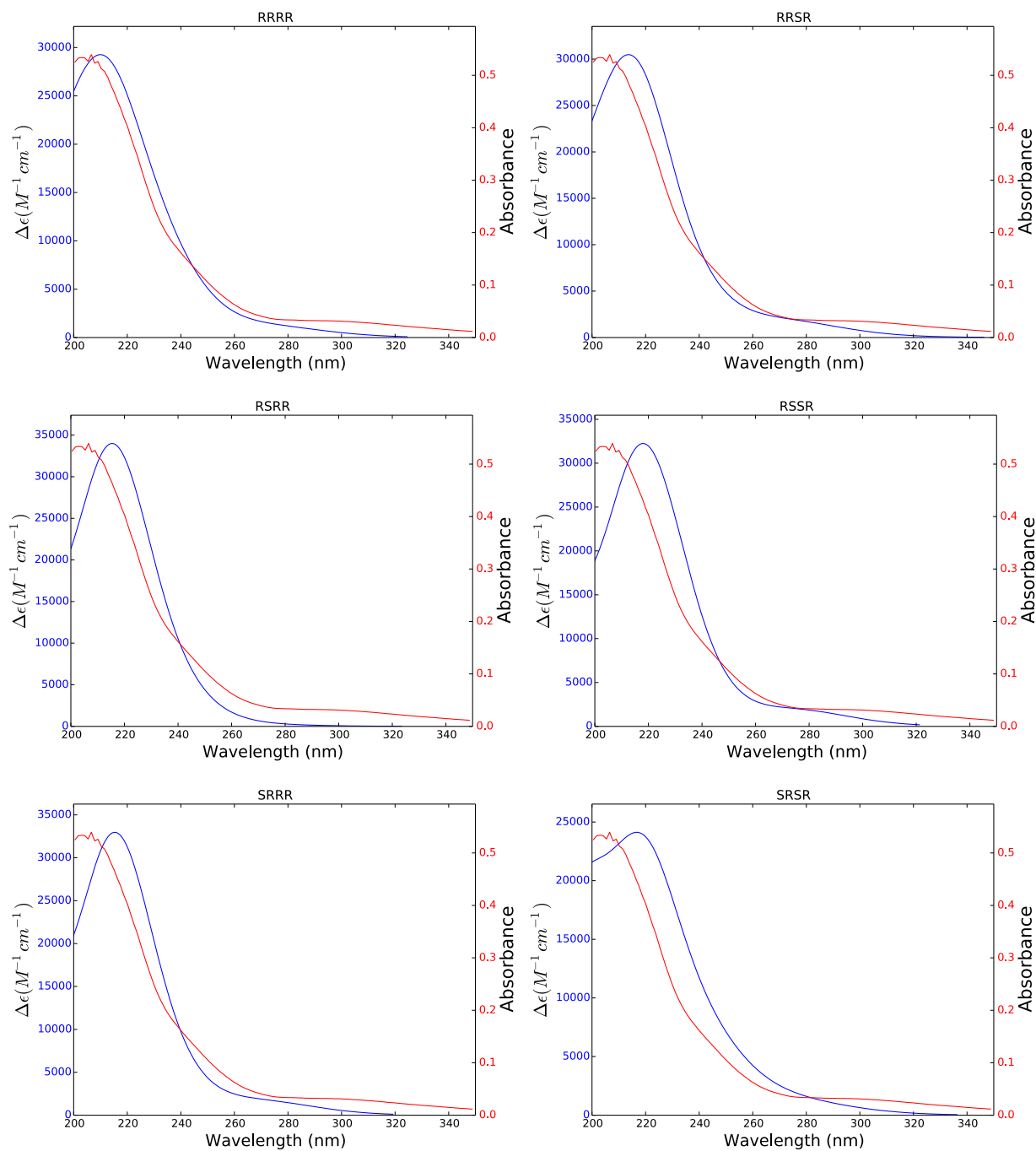


Figure S8. Comparison of Experimental (red) and Calculated (blue) UV Spectra for Enantiomerically Unique Stereoisomers of Trichospirolide D (**4**)



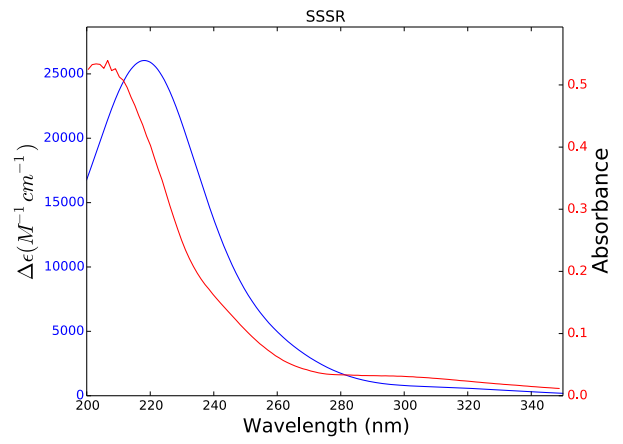
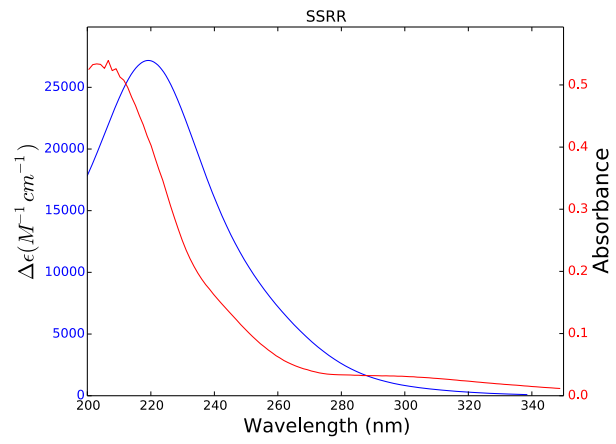


Table S10. Calculated Weighted Average Internuclear Distances for Enantiomerically Unique Stereoisomers of Trichospirolide D (**4**)^a

Proton Pair	RRRR WA Distance (Å) ^a	RRSR WA Distance (Å) ^a	RSRR WA Distance (Å) ^a	RSSR WA Distance (Å) ^a	NOESY Signal
H1-H14	3.07	3.04	2.94	3.02	medium
H3'b-H4'	3.15	3.16	3.16	3.15	medium
H3-H15	3.33	3.36	3.40	3.40	medium
H3-H9a	2.94	2.90	6.07	5.27	medium
H5-H15	3.38	3.33	3.53	3.55	medium

Proton Pair	SRRR WA Distance (Å) ^a	SRSR WA Distance (Å) ^a	SSRR WA Distance (Å) ^a	SSSR WA Distance (Å) ^a	NOESY Signal
H1-H14	3.03	3.06	3.05	3.03	medium
H3'b-H4'	3.15	3.15	3.16	3.15	medium
H3-H15	3.40	3.38	3.37	3.32	medium
H3-H9a	5.26	5.53	5.03	4.99	medium
H5-H15	3.54	3.33	3.35	3.35	medium

^a Weighted average internuclear distances are reported. In the case of methyl hydrogens, a simple average of the three individual weighted average distances is reported.