

Labdane-Type Diterpenoids from *Streptomyces griseorubens* and Their Antimicrobial and Cytotoxic Activities

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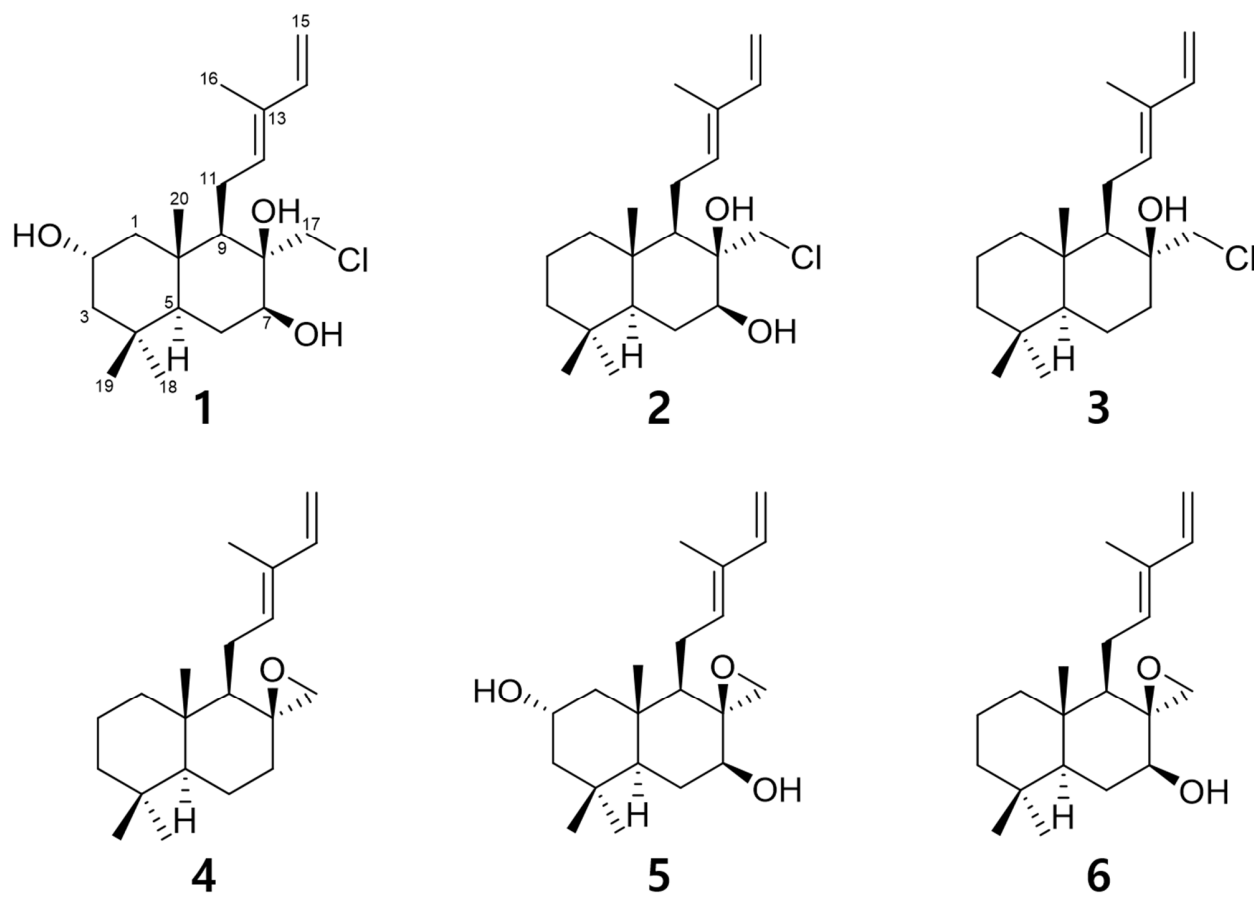


Figure S1. Structures of **1-6** isolated from *Streptomyces griseorubens* 2210JJ-087.

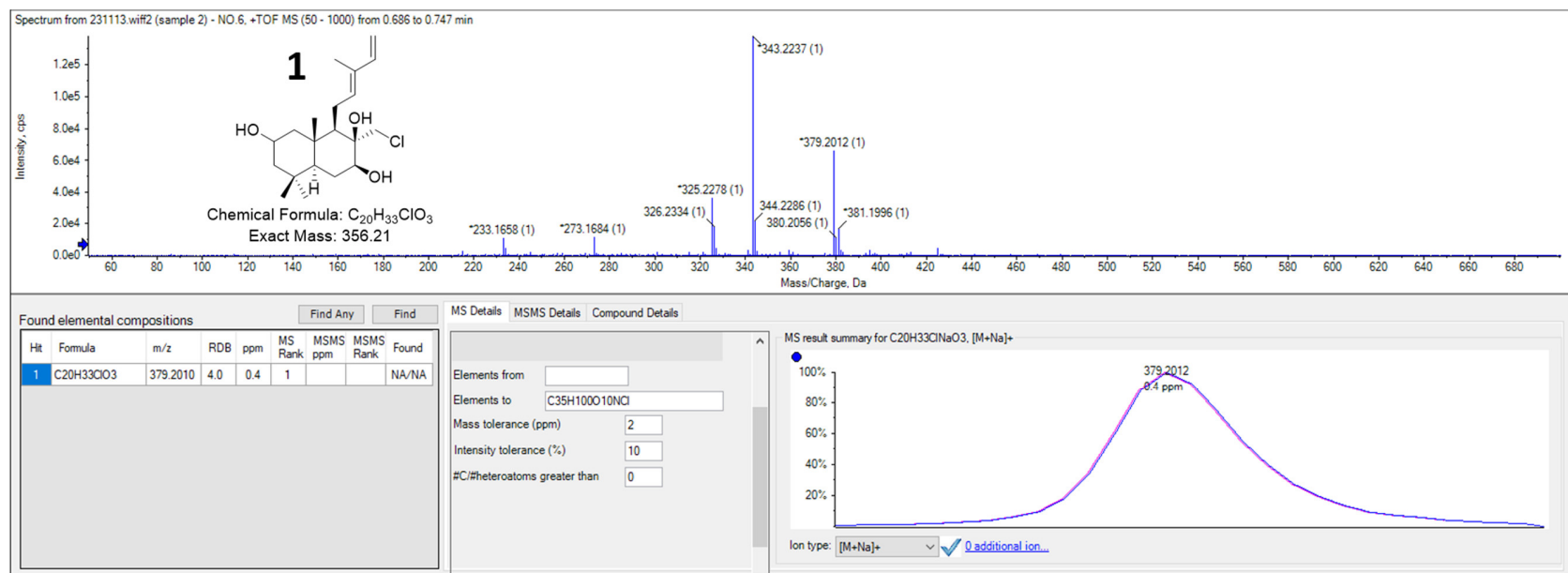


Figure S2. HRESIMS data of 1.

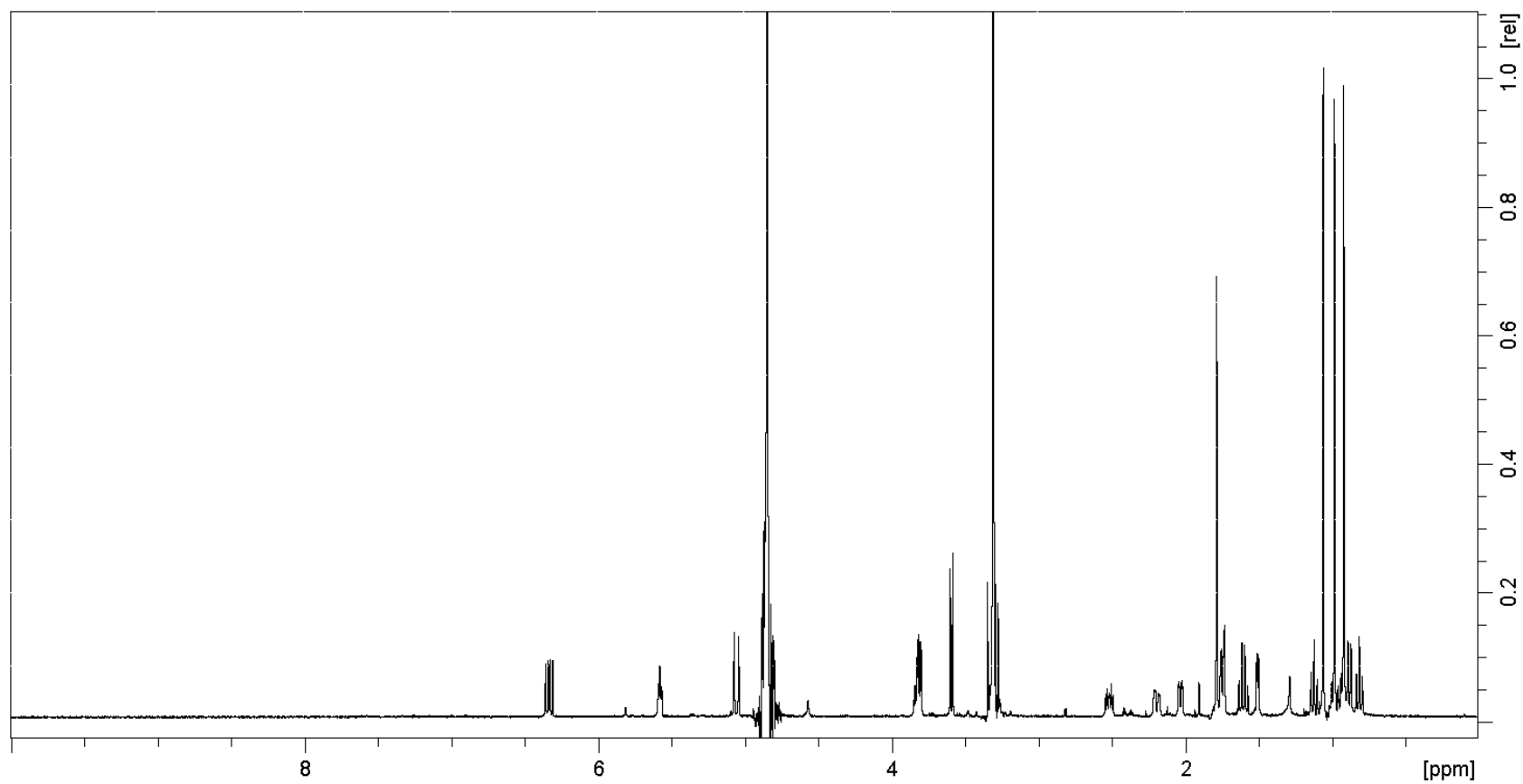


Figure S3. ^1H NMR spectrum of **1** (CD_3OD).

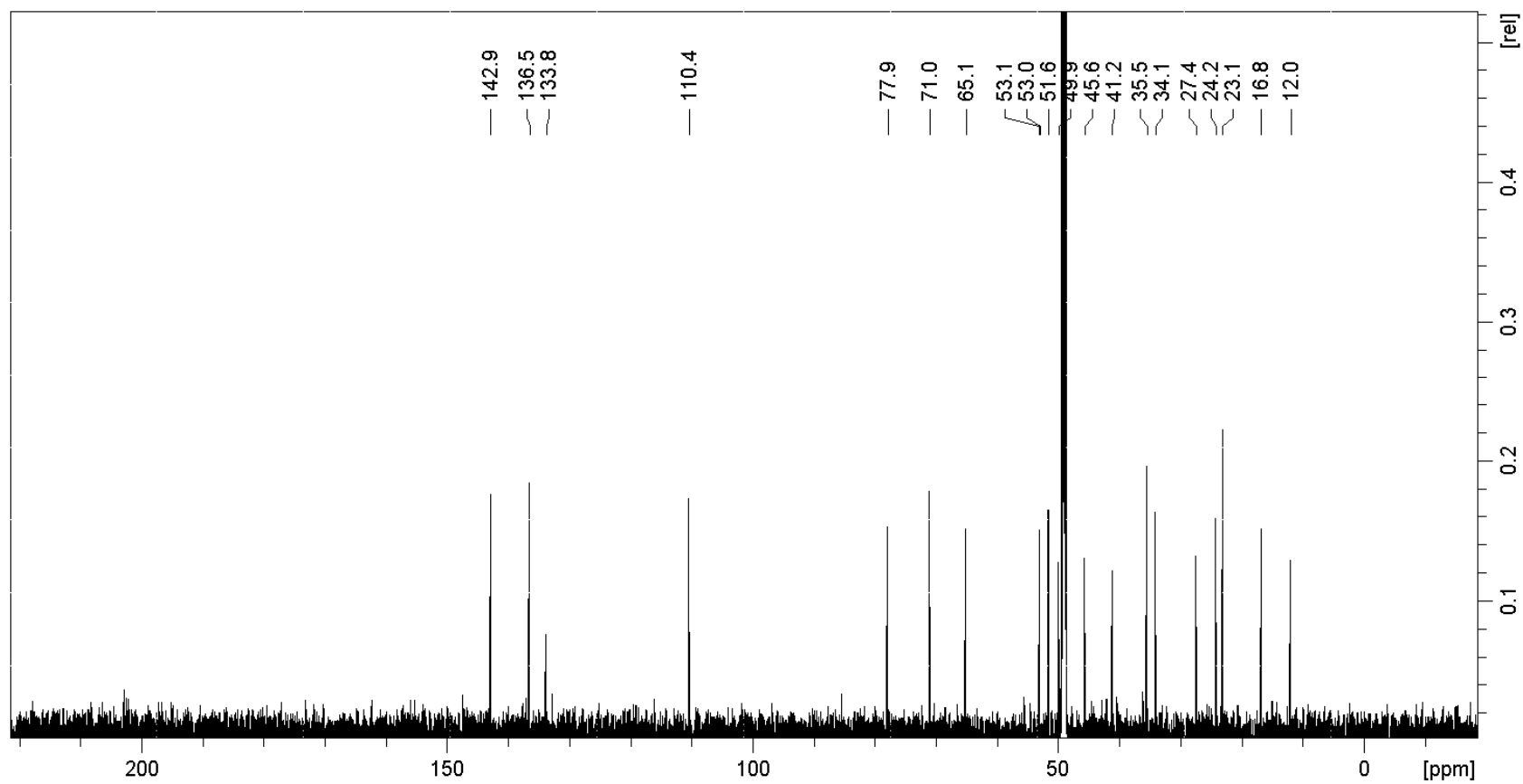


Figure S4. ¹³C NMR spectrum of **1** (CD₃OD).

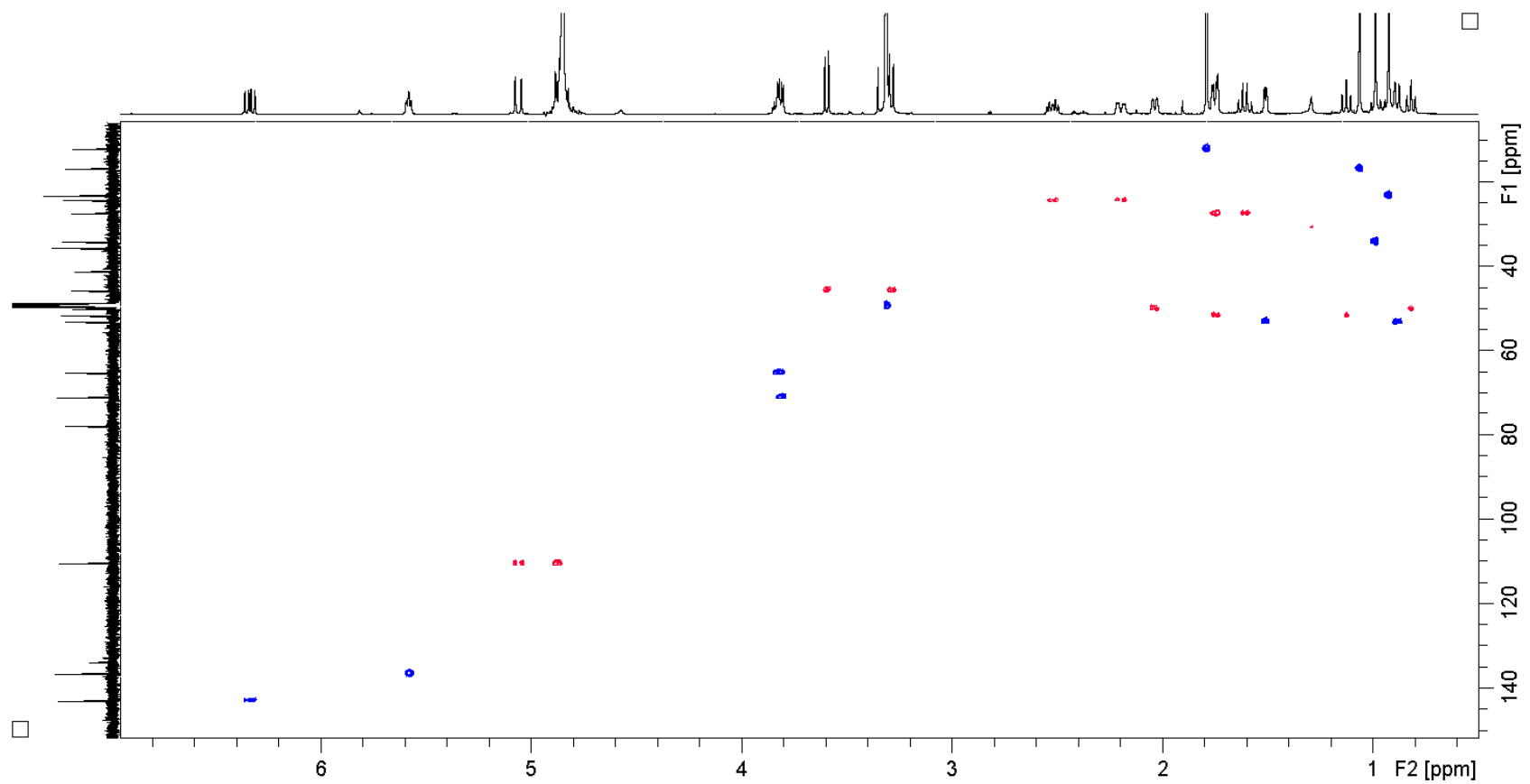


Figure S5. HSQC spectrum of **1** (CD_3OD).



Figure S6. ^1H - ^1H COSY spectrum of **1** (CD_3OD).

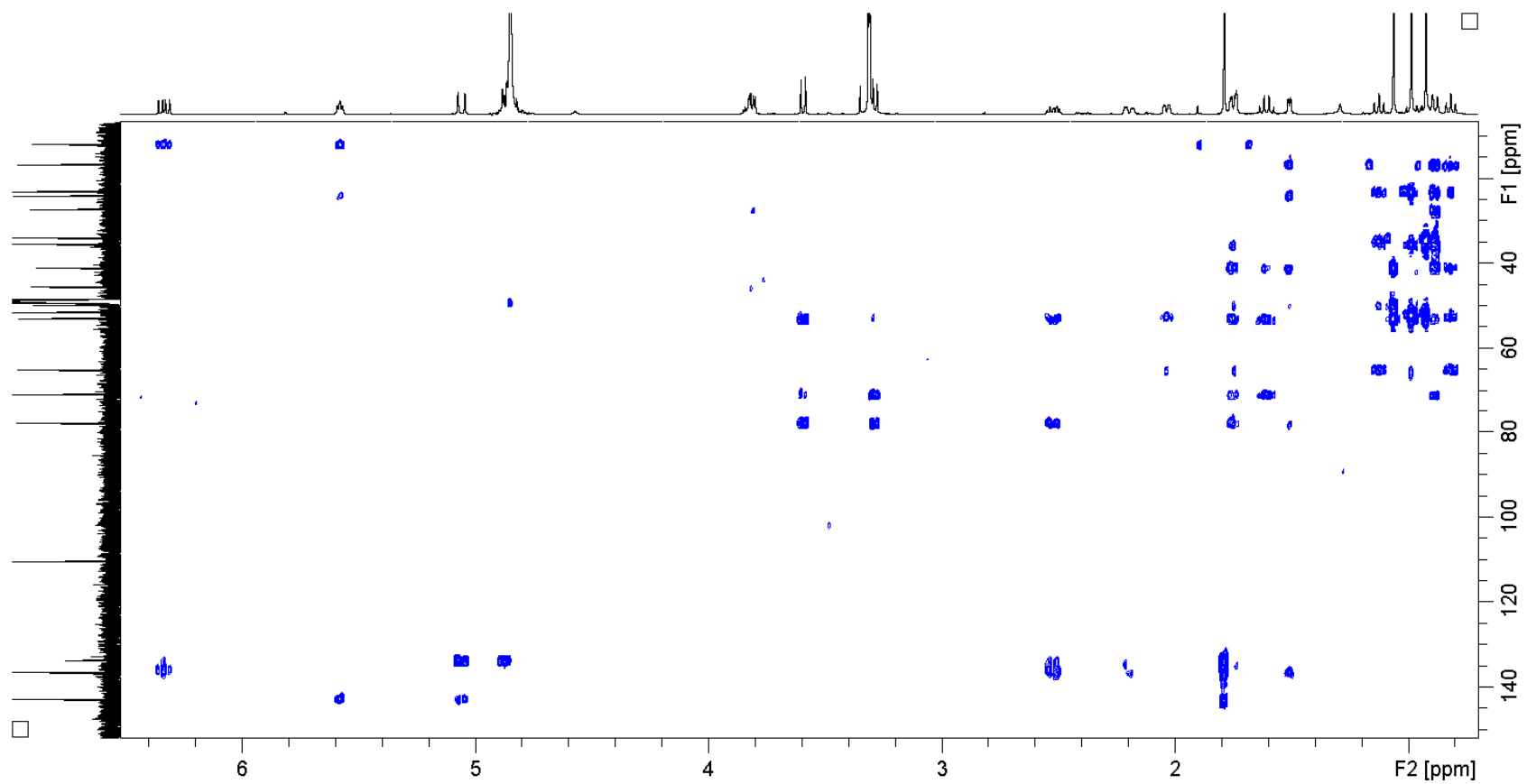


Figure S7. HMBC spectrum of **1** (CD_3OD).

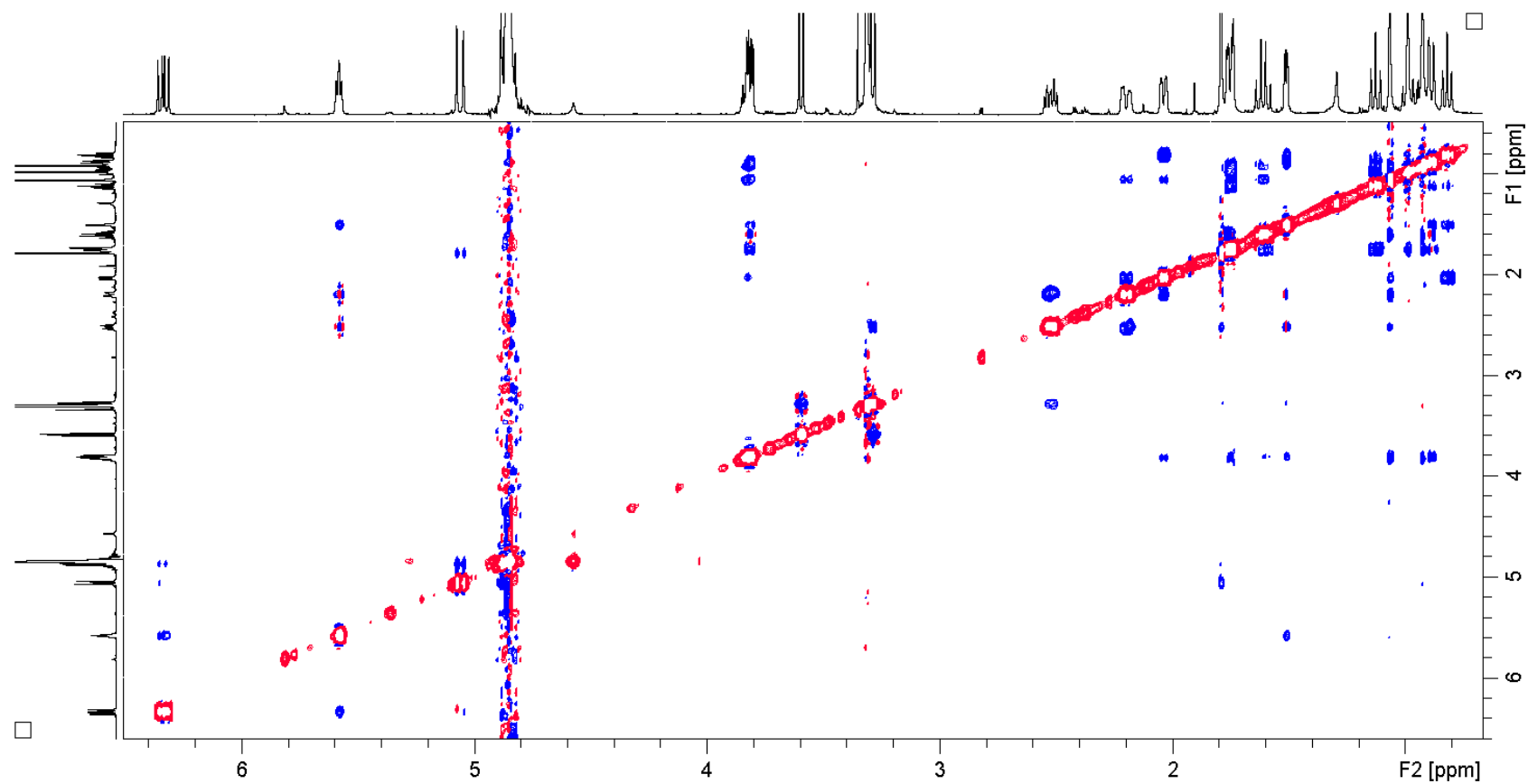


Figure S8. NOESY spectrum of **1** (CD₃OD).

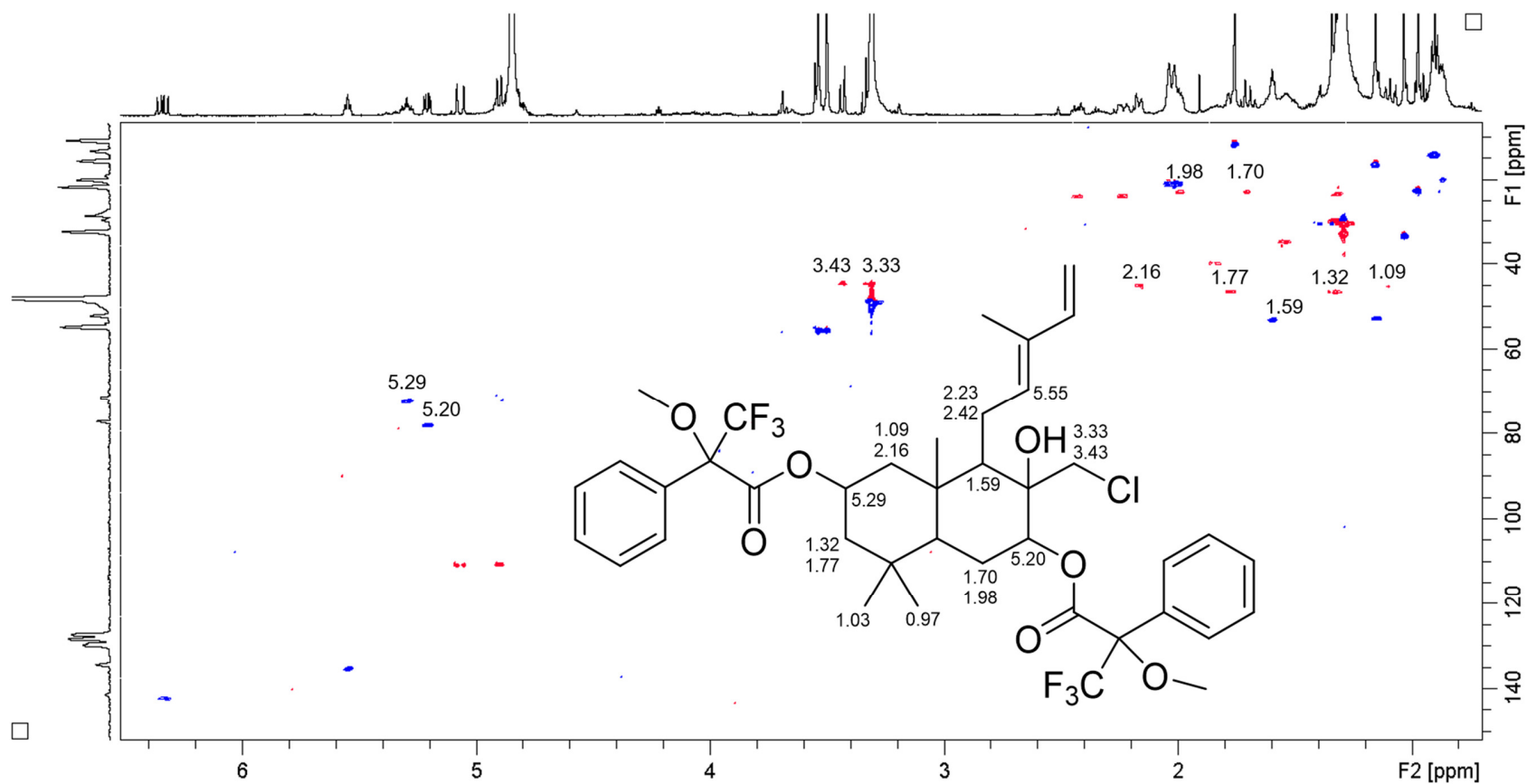


Figure S9. HSQC spectrum of (*S*)-di-MTPA esters of **1** (**1a**) (CD₃OD).

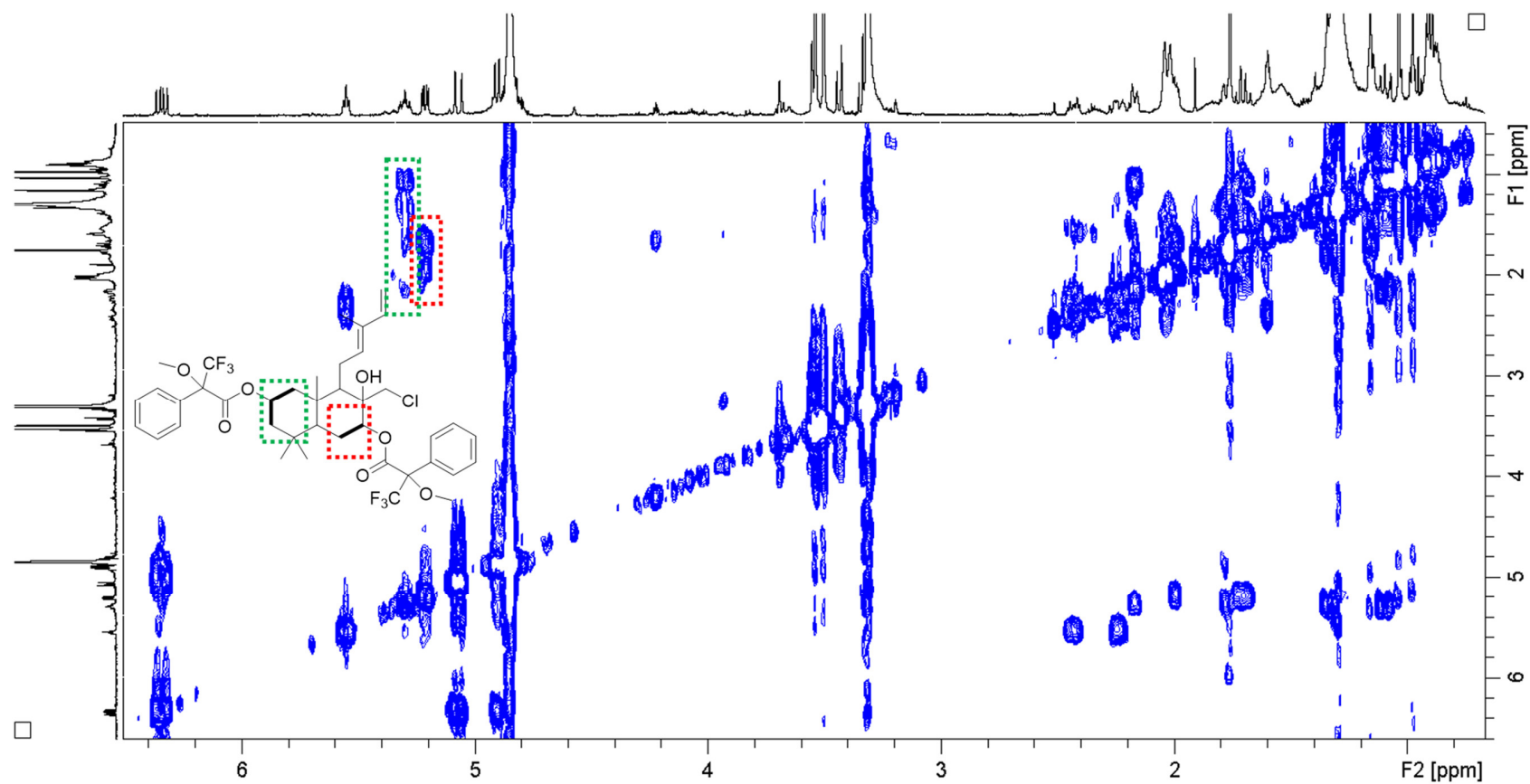


Figure S10. ^1H - ^1H COSY spectrum of (S)-di-MTPA esters of **1** (**1a**) (CD_3OD).

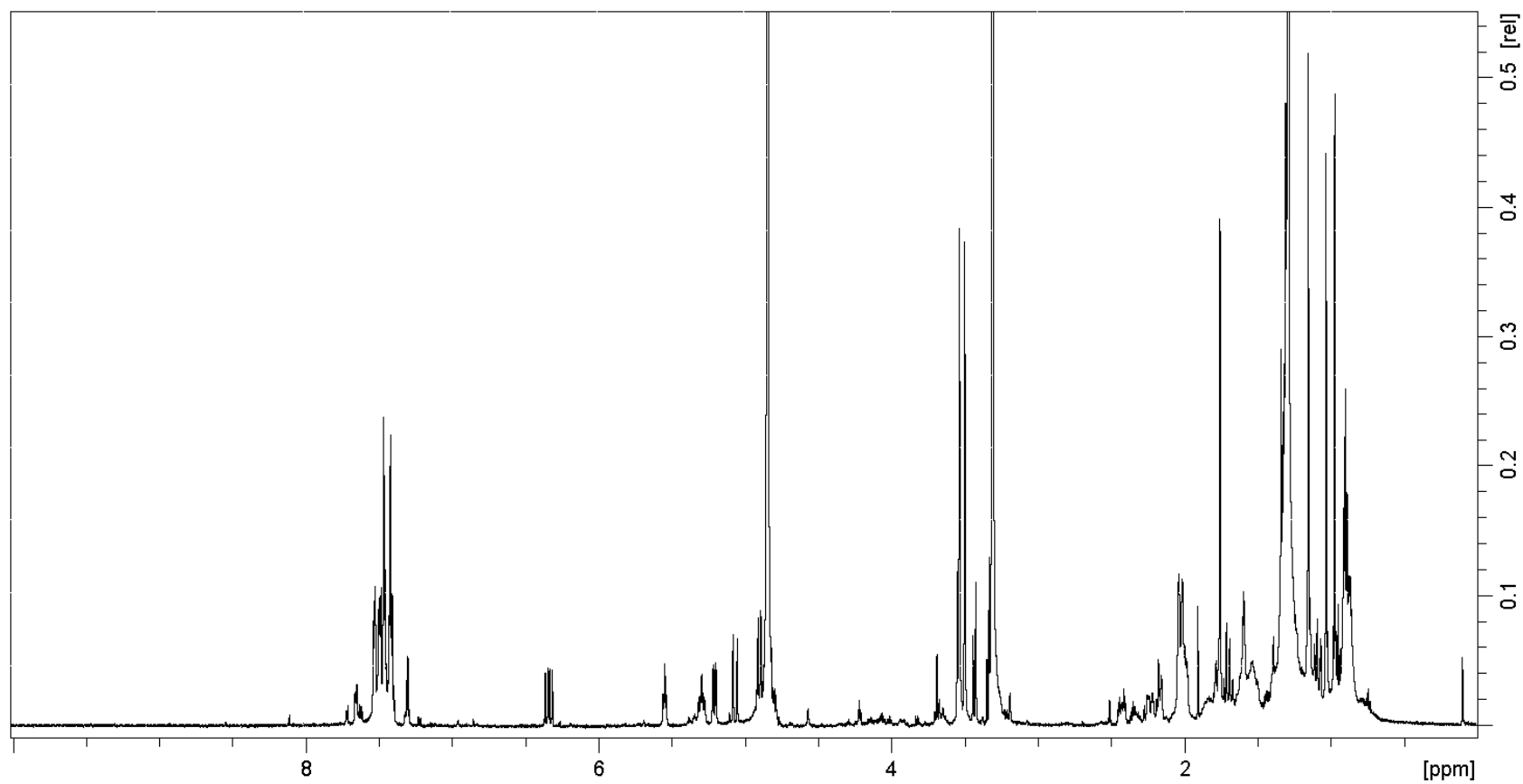


Figure S11. ^1H NMR spectrum of (S)-di-MTPA esters of 1 (1a) (CD_3OD).

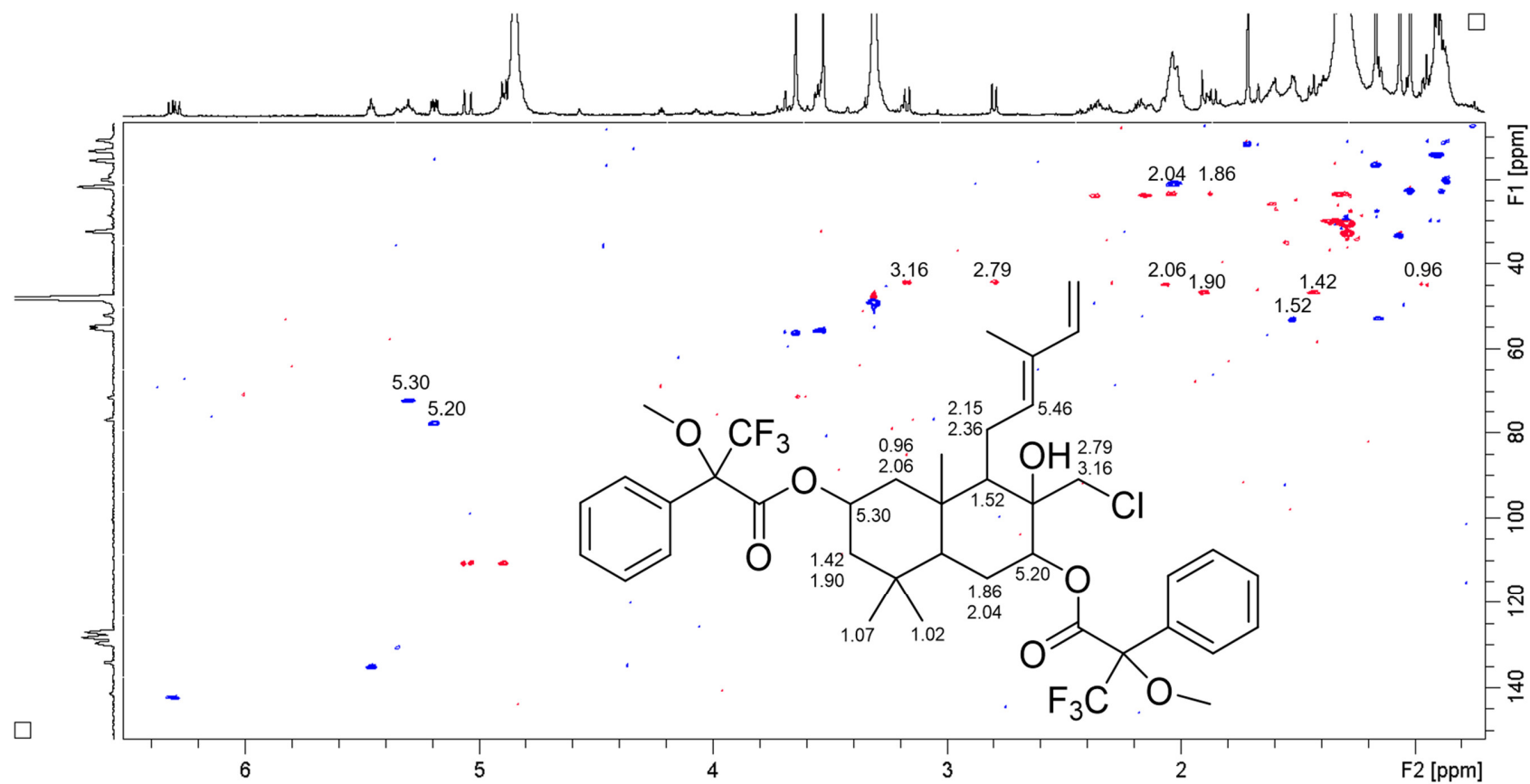


Figure S12. HSQC spectrum of (*R*)-di-MTPA esters of **1** (**1b**) (CD_3OD).

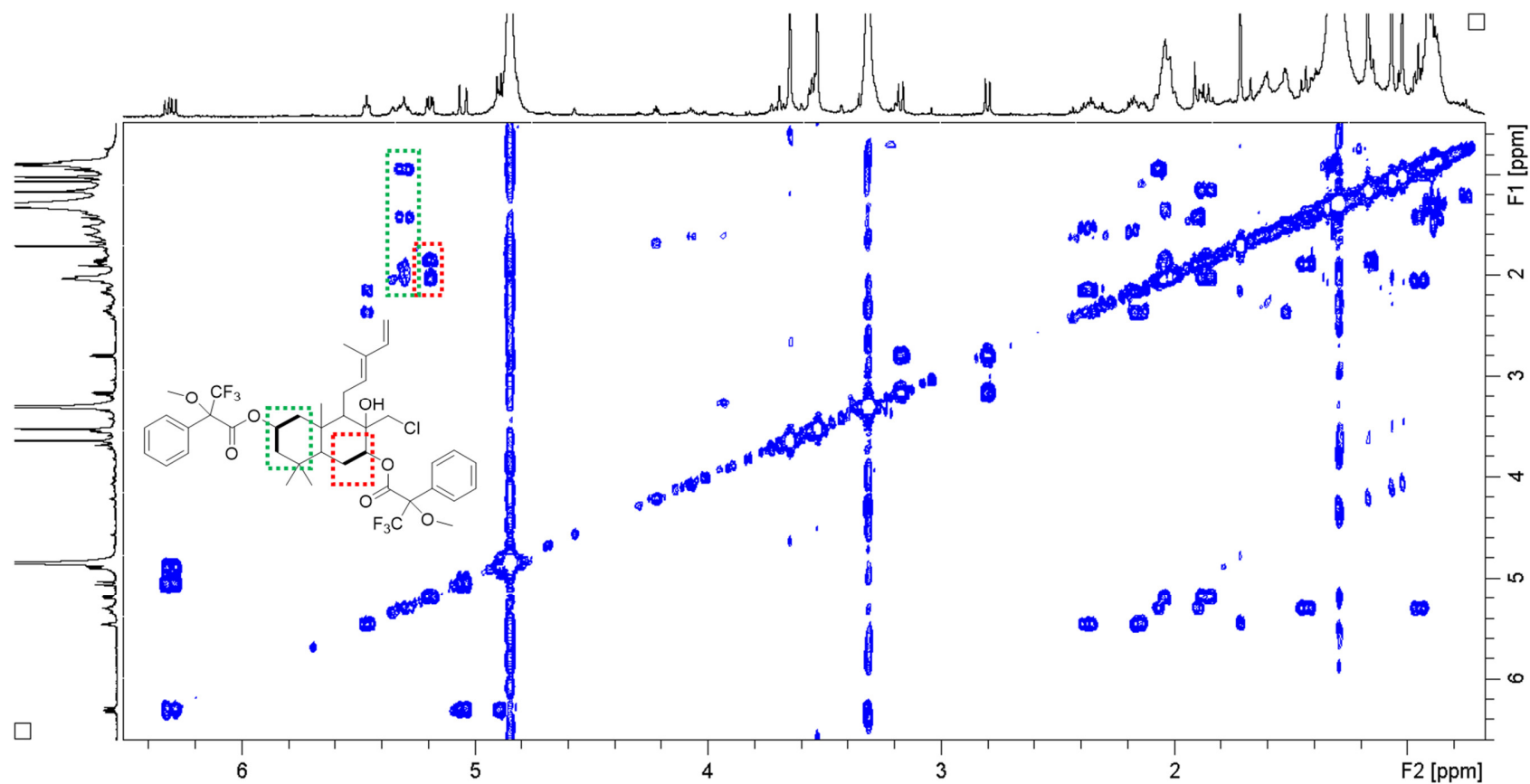


Figure S13. ^1H - ^1H COSY spectrum of (*R*)-di-MTPA esters of **1** (**1b**) (CD_3OD).

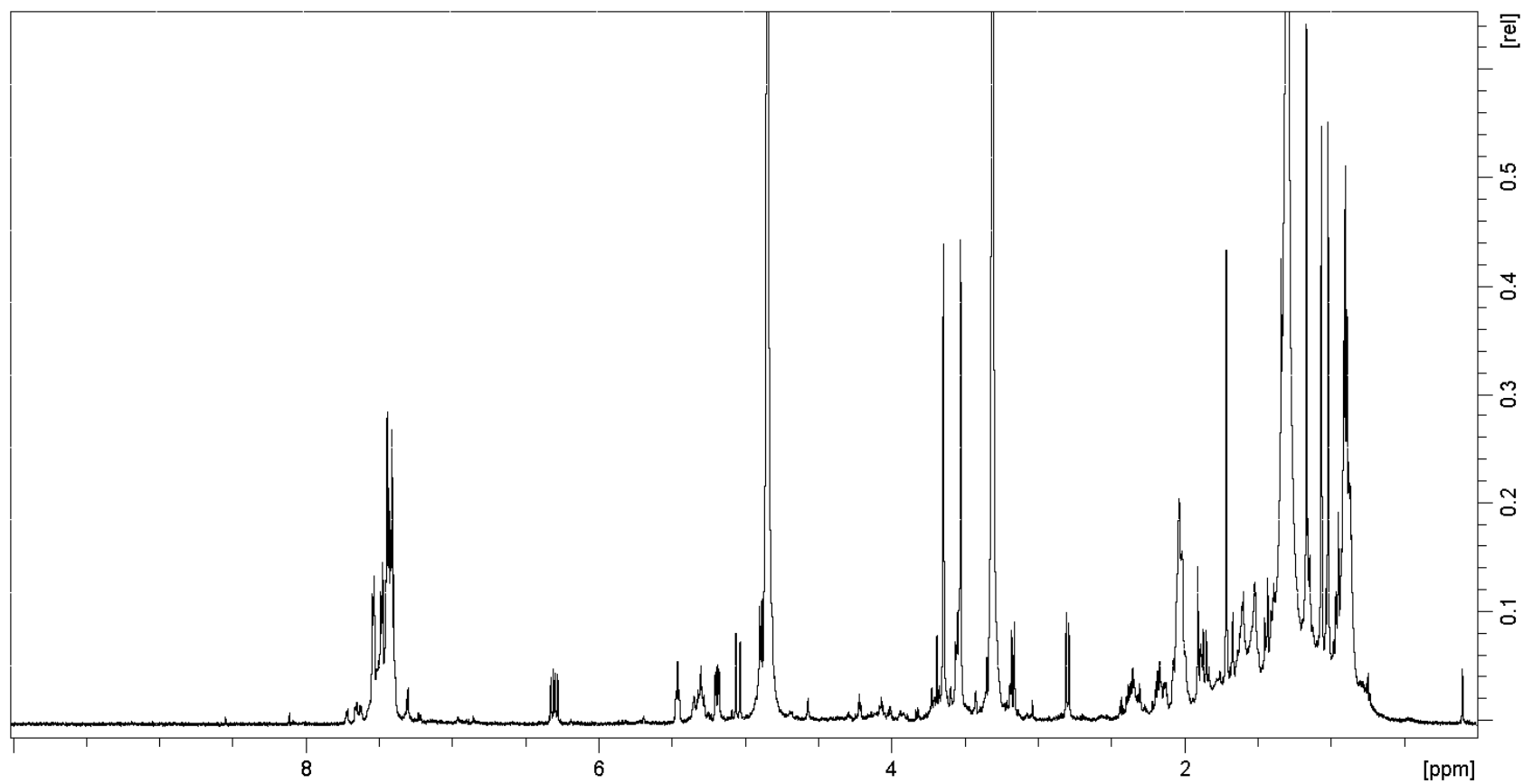


Figure S14. ^1H NMR spectrum of (*R*)-di-MTPA esters of **1** (**1b**) (CD_3OD).

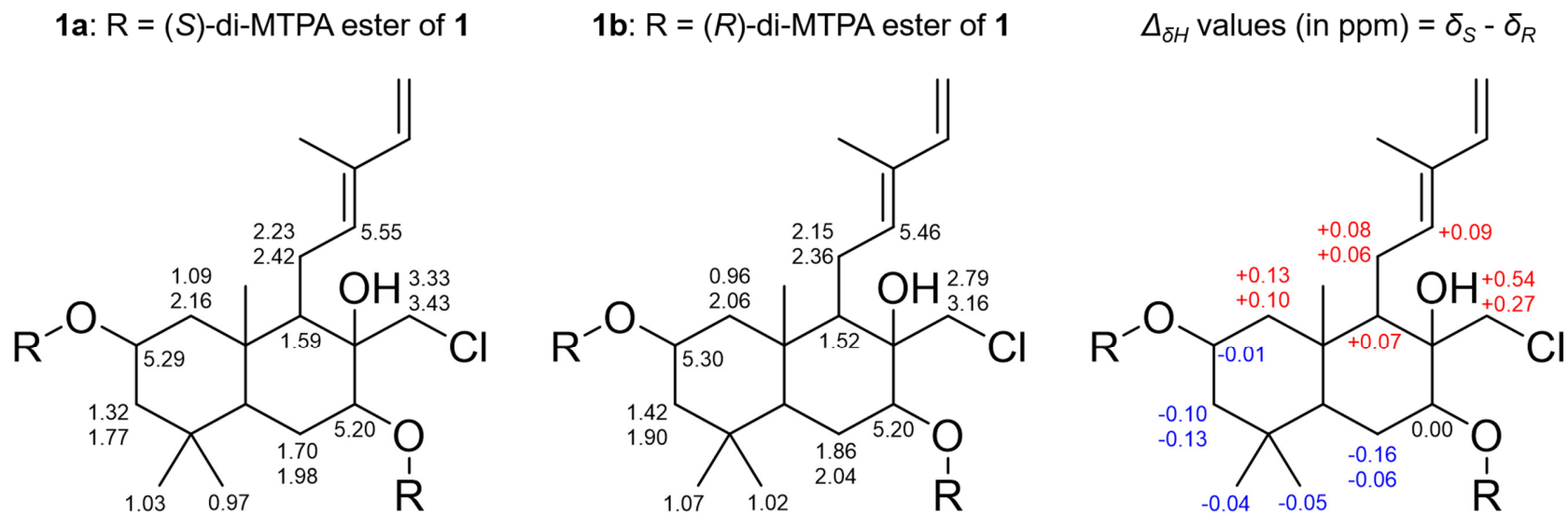


Figure S15. Summarized $\Delta\delta$ values (in ppm) = $\delta_S - \delta_R$ obtained for (*S*)- and (*R*)-di-MPTA esters of **1**.

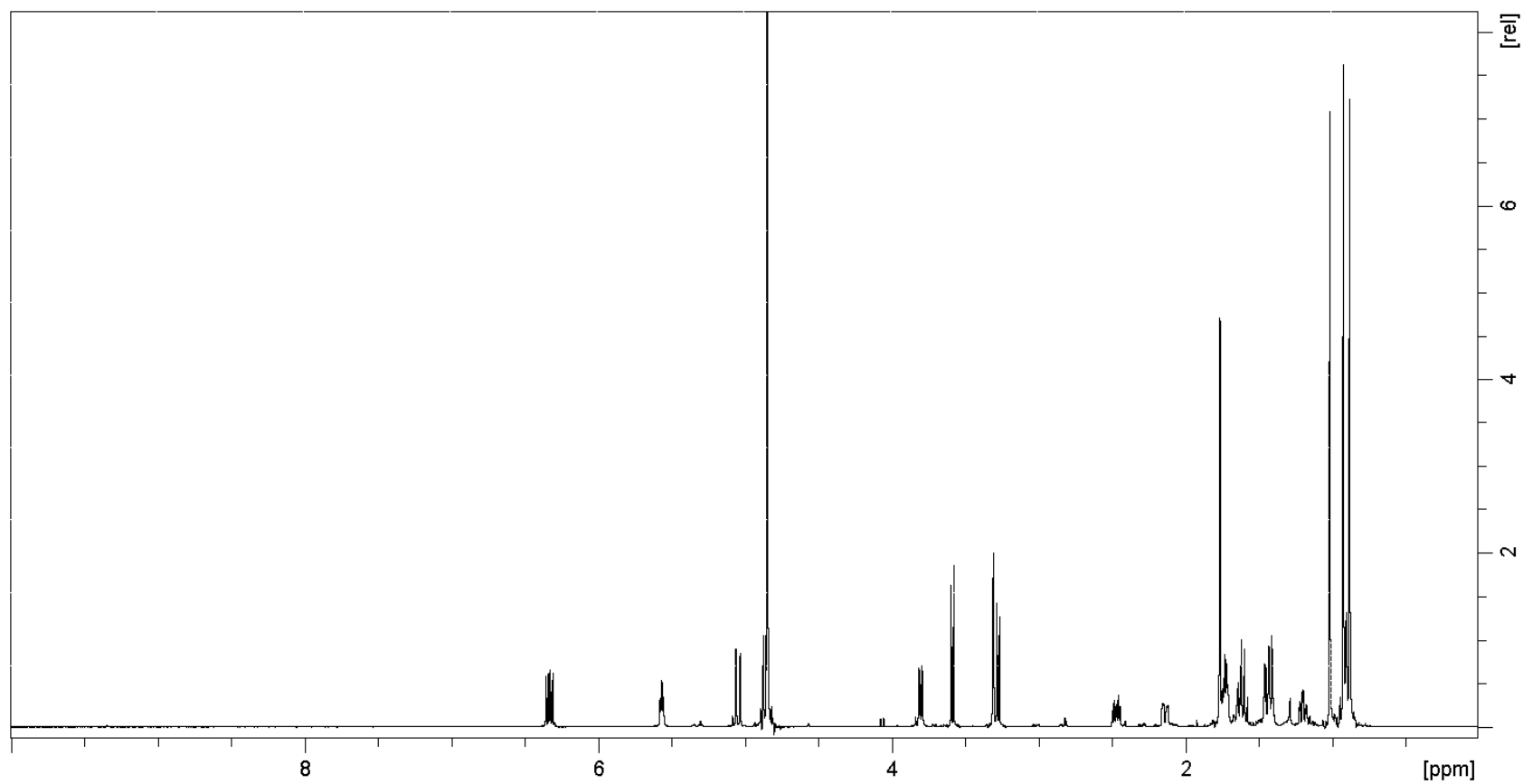


Figure S17. ^1H NMR spectrum of **2** (CD_3OD).

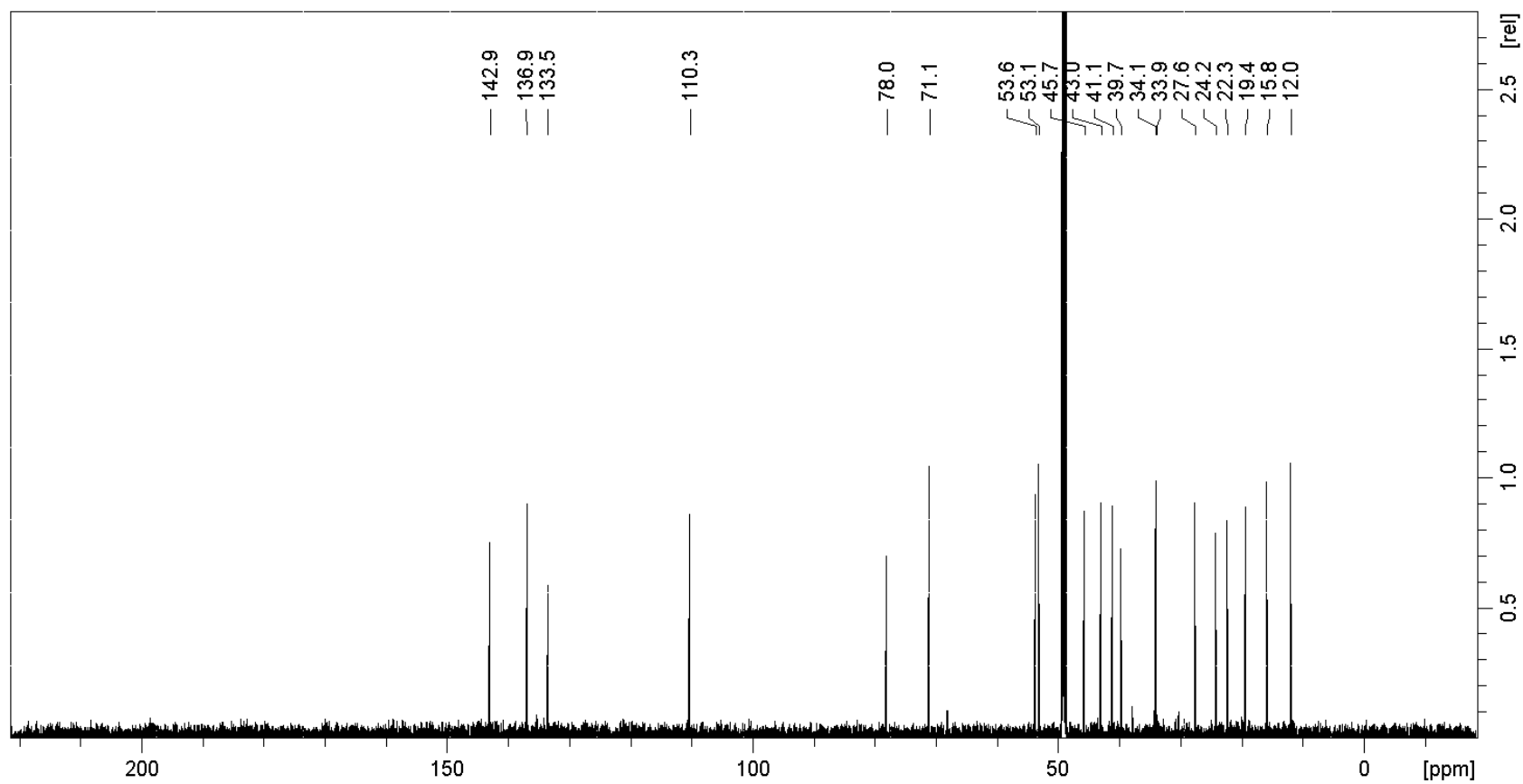


Figure S18. ¹³C NMR spectrum of **2** (CD₃OD).

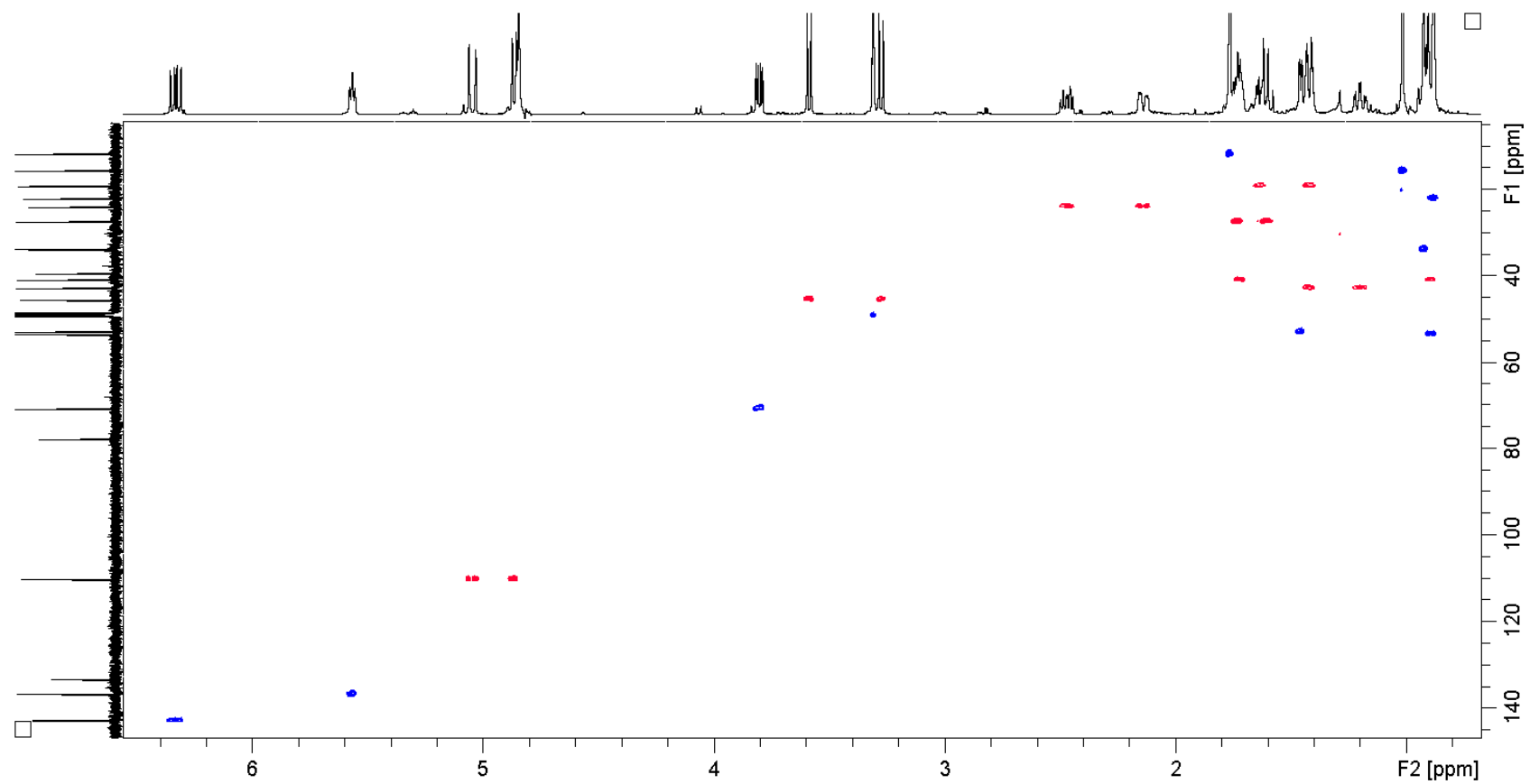


Figure S19. HSQC NMR spectrum of **2** (CD_3OD).

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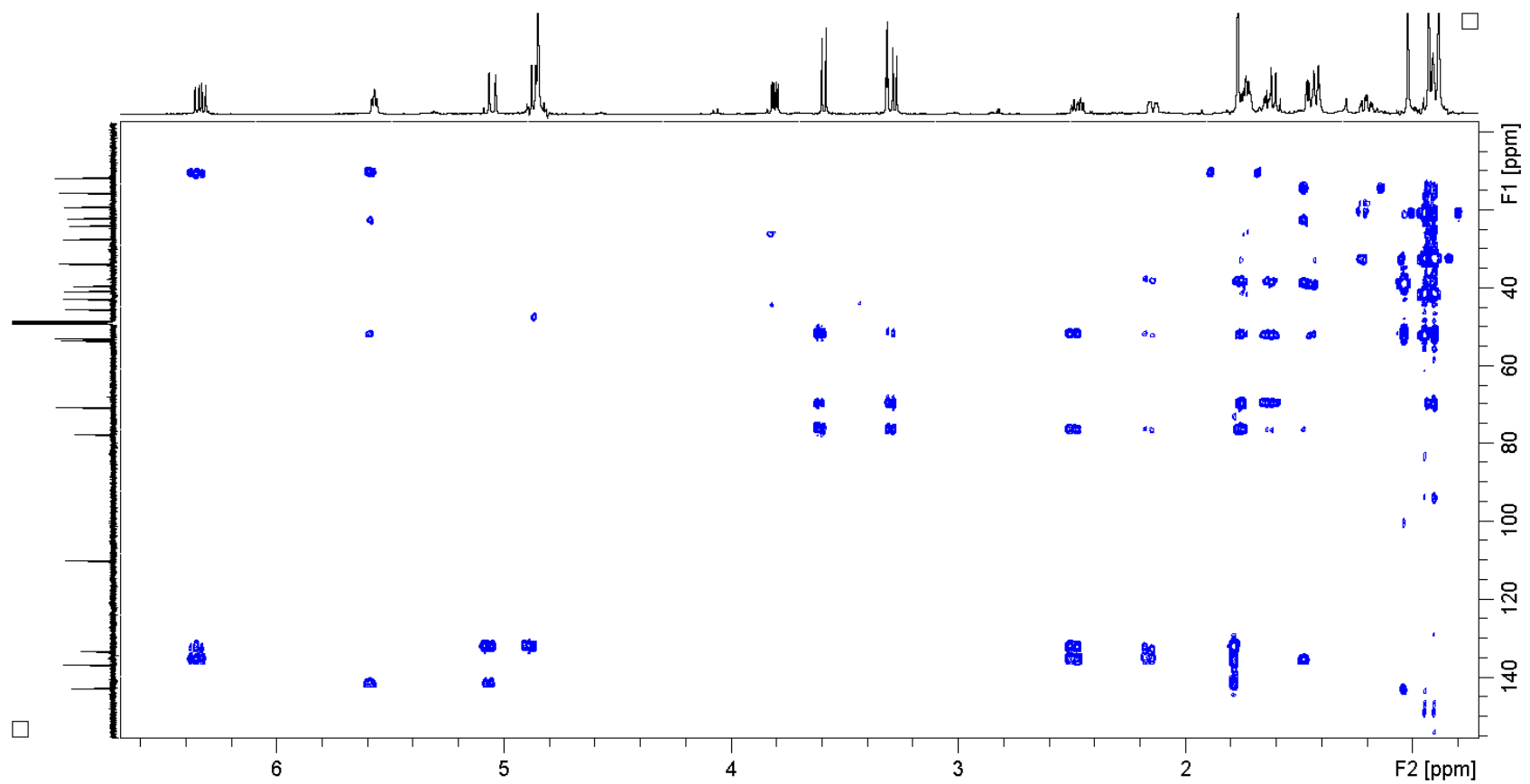


Figure S21. HMBC NMR spectrum of **2** (CD₃OD)..

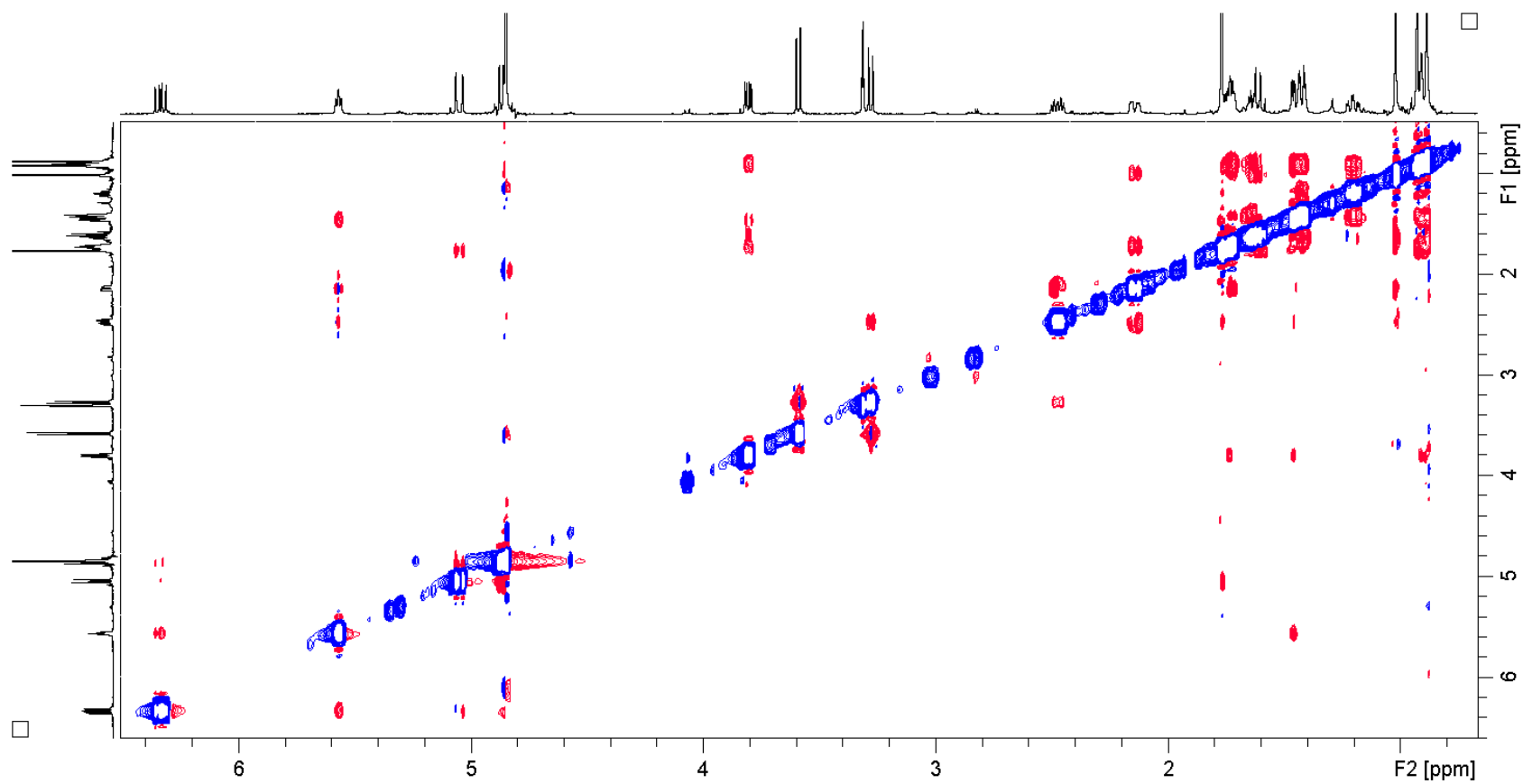


Figure S22. NOESY NMR spectrum of **2** (CD₃OD).

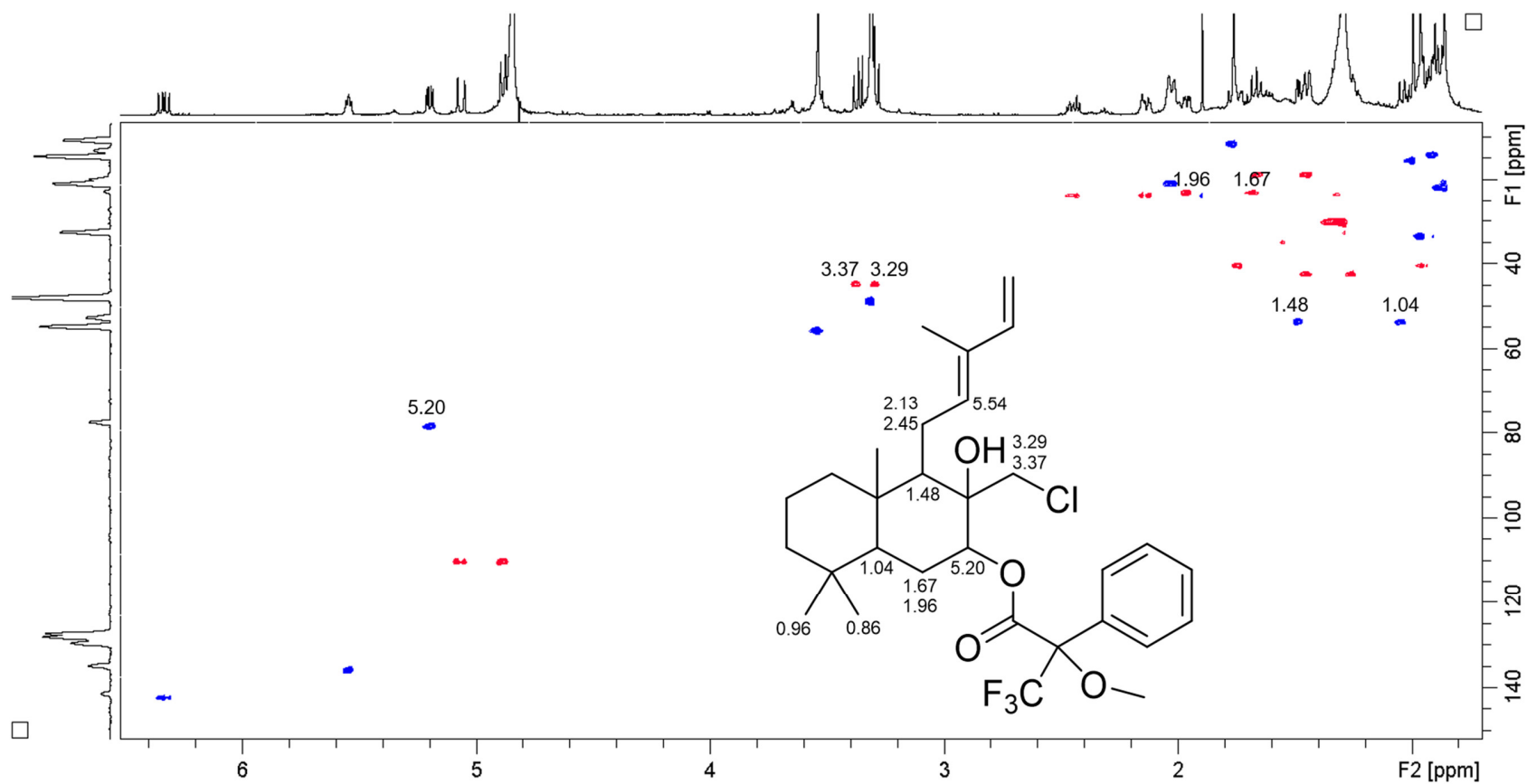


Figure S23. HSQC spectrum of (S)-MTPA esters of 2 (2a) (CD₃OD).

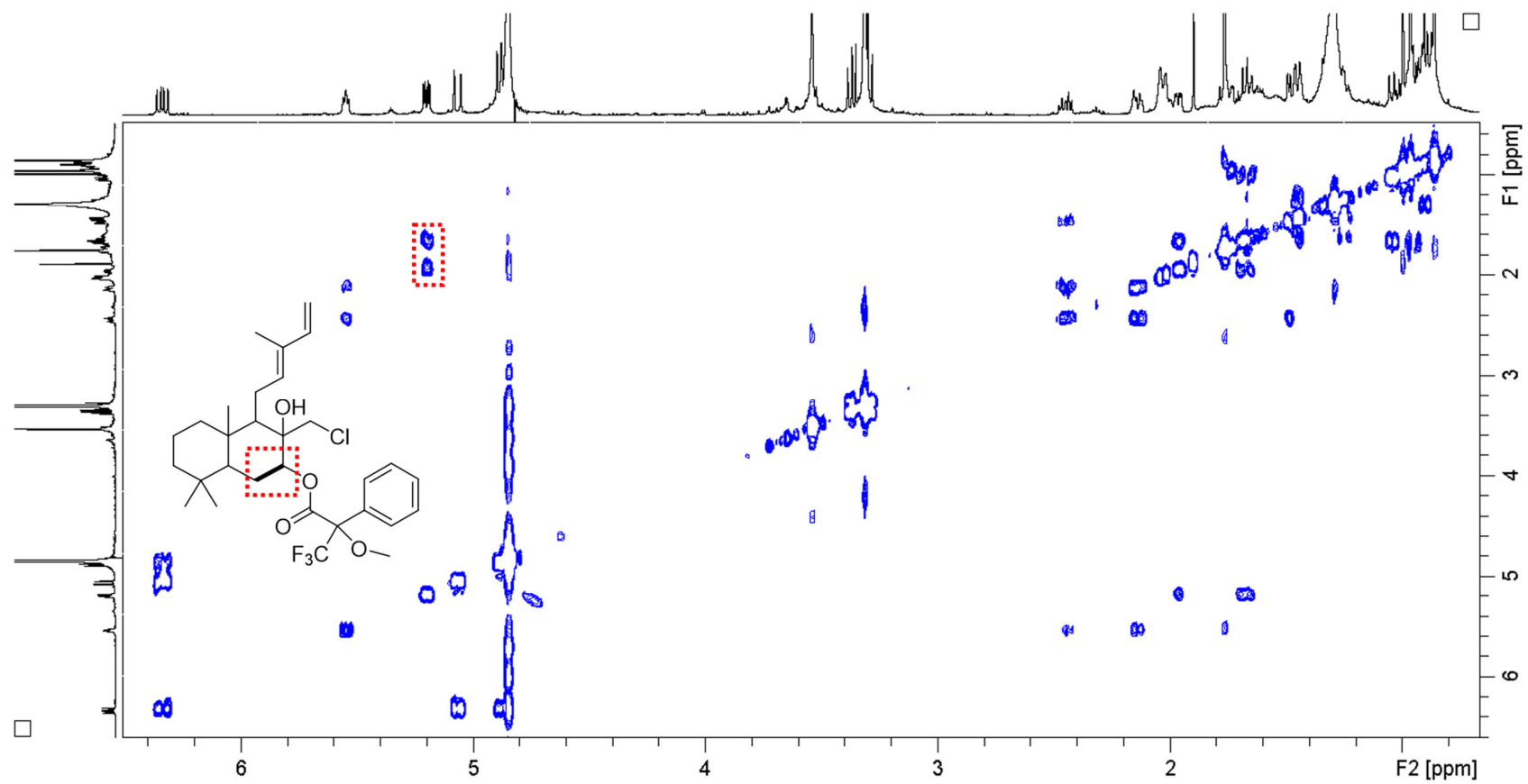


Figure S24. ^1H - ^1H COSY spectrum of (*S*)-MTPA esters of **2** (**2a**) (CD_3OD).

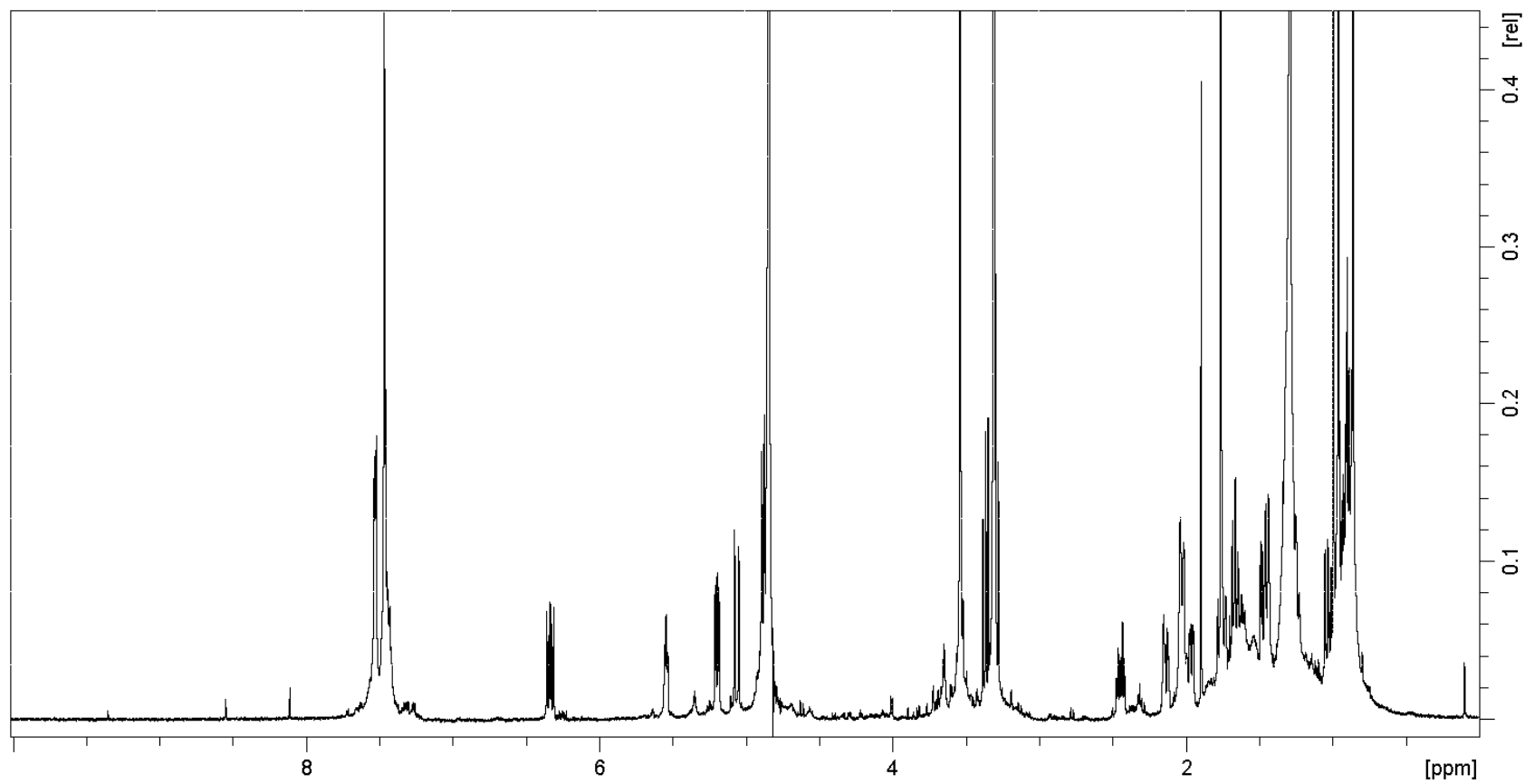


Figure S25. ^1H NMR spectrum of (*S*)-MTPA esters of **2** (**2a**) (CD_3OD).

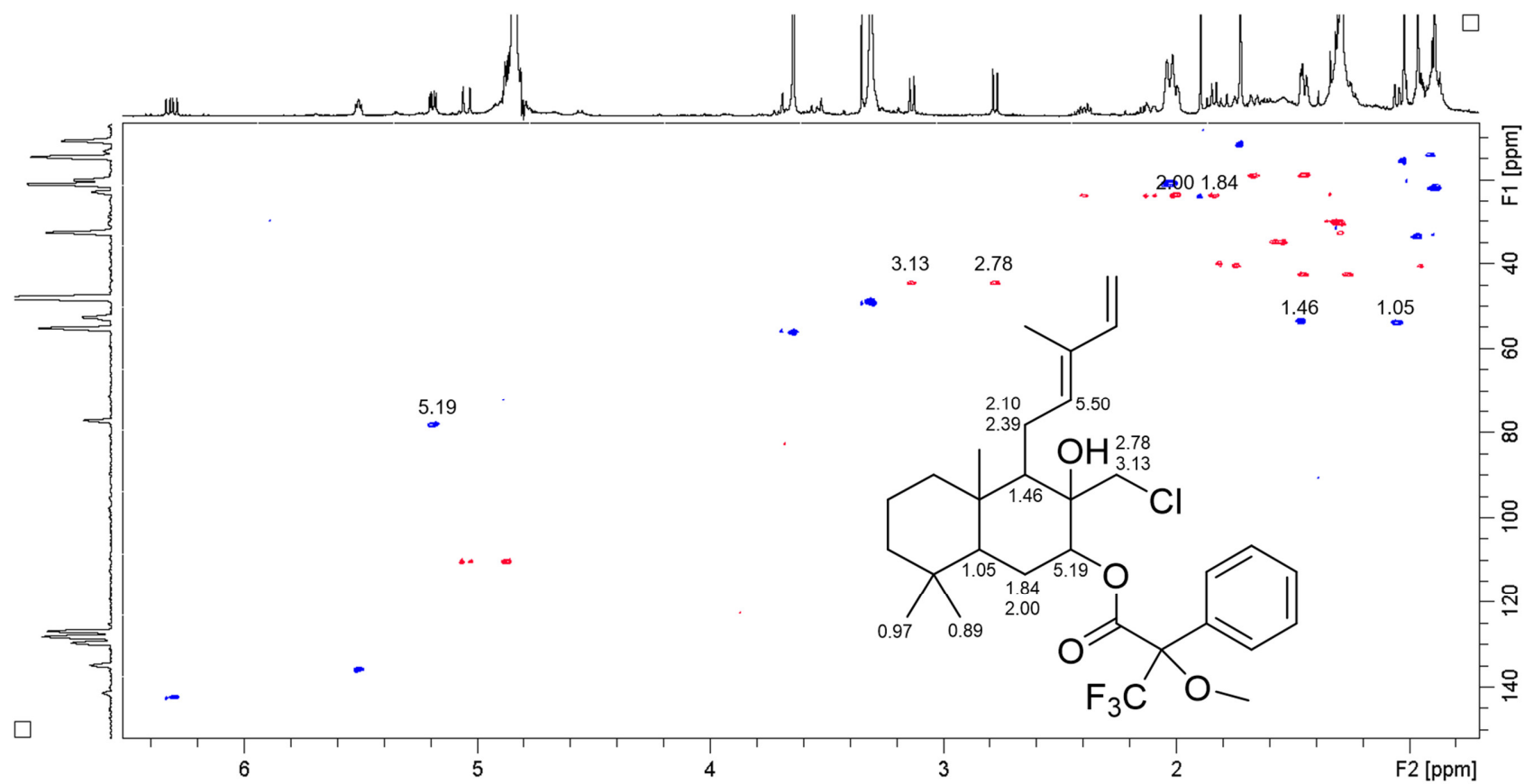


Figure S26. HSQC spectrum of (*R*)-MTPA esters of **2** (**2b**) (CD₃OD).

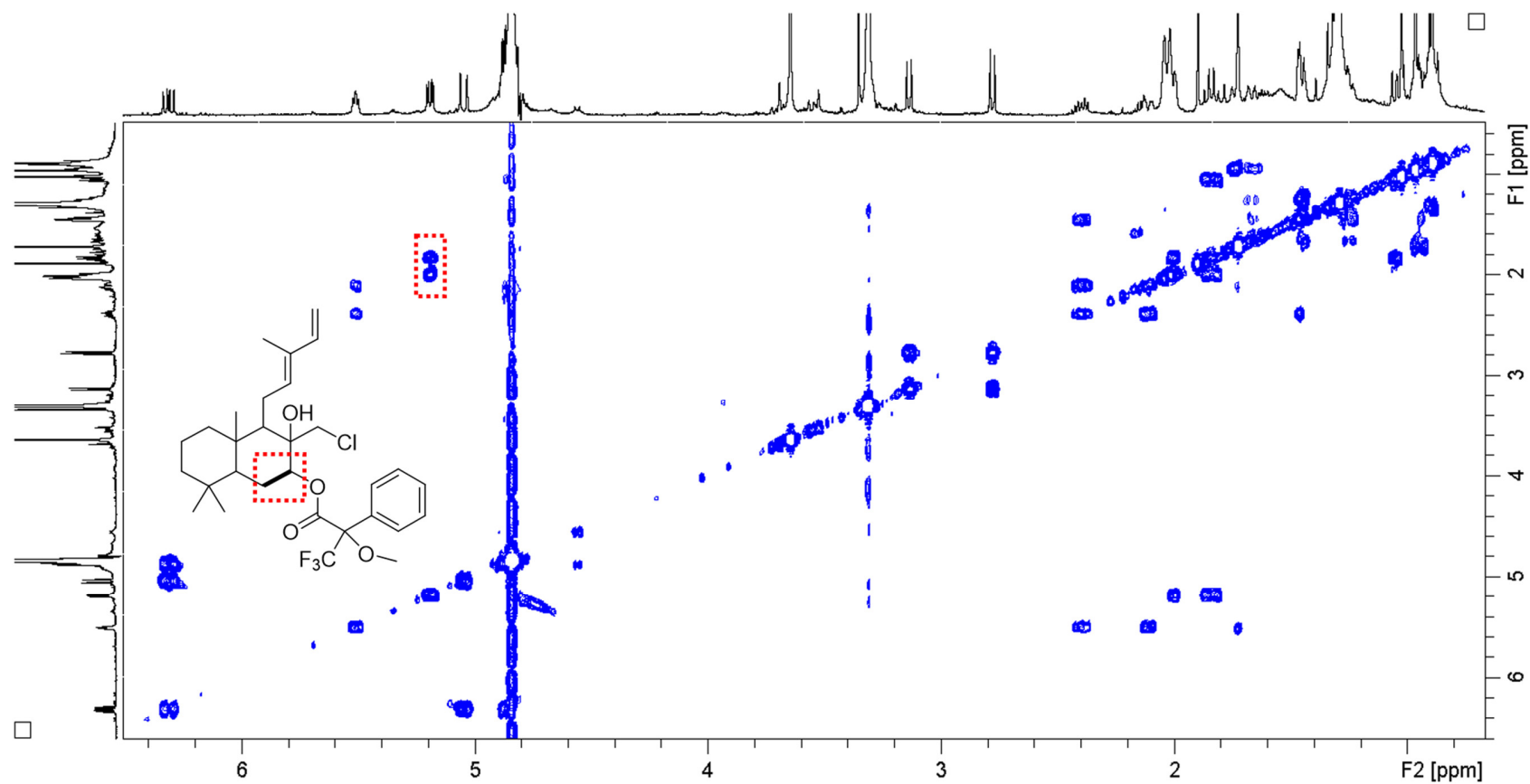


Figure S27. ^1H - ^1H COSY spectrum of (*R*)-MTPA esters of **2** (**2b**) (CD_3OD).

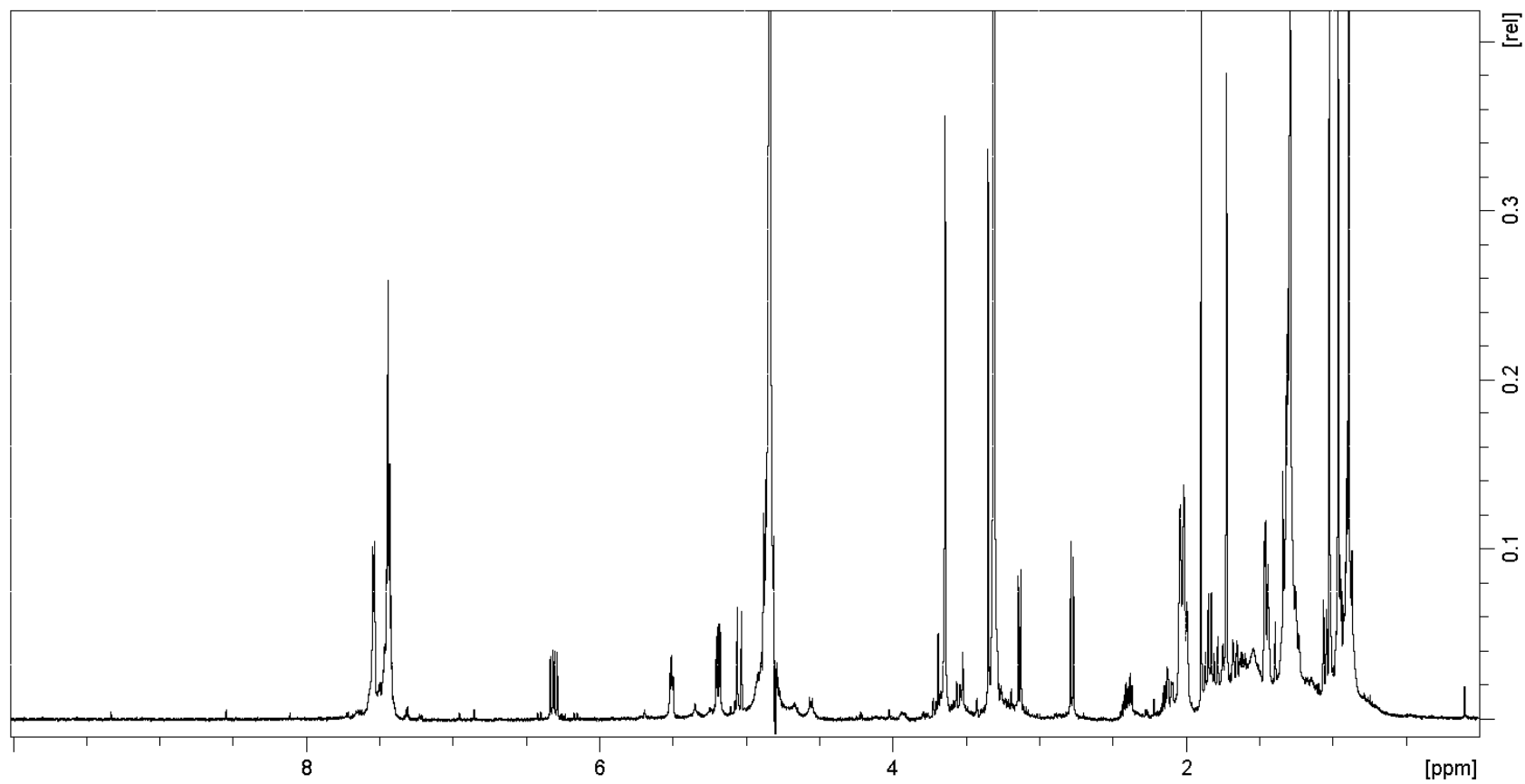
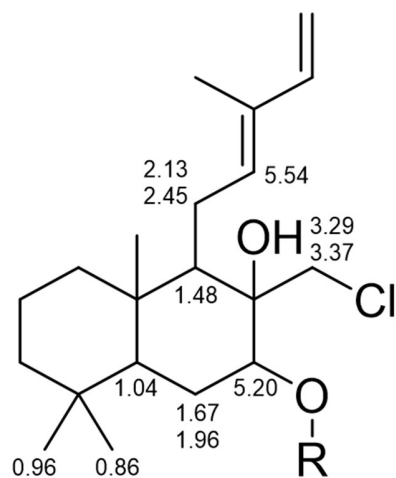
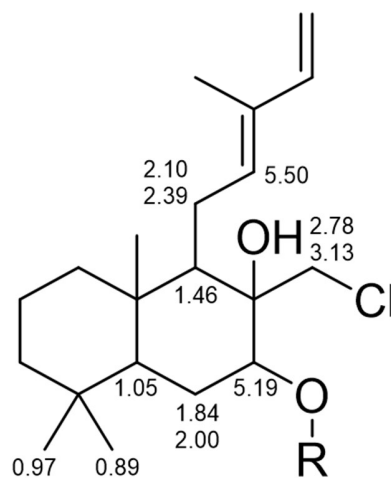


Figure S28. ^1H NMR spectrum of (*R*)-MTPA esters of **2** (**2b**) (CD_3OD).

2a: R = (S)-MTPA ester of **2**



2b: R = (R)-MTPA ester of **2**



$\Delta\delta_H$ values (in ppm) = $\delta_S - \delta_R$

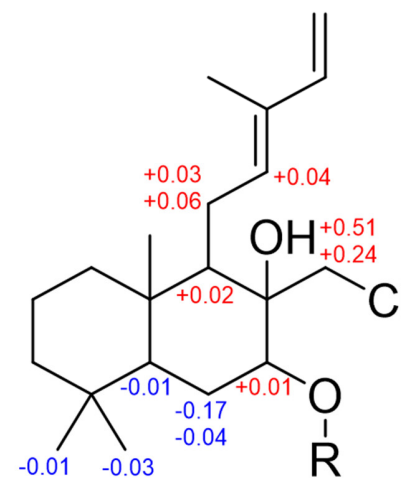


Figure S29. Summarized $\Delta\delta$ values (in ppm) = $\delta_S - \delta_R$ obtained for (S)- and (R)-MPTA esters of **2**.

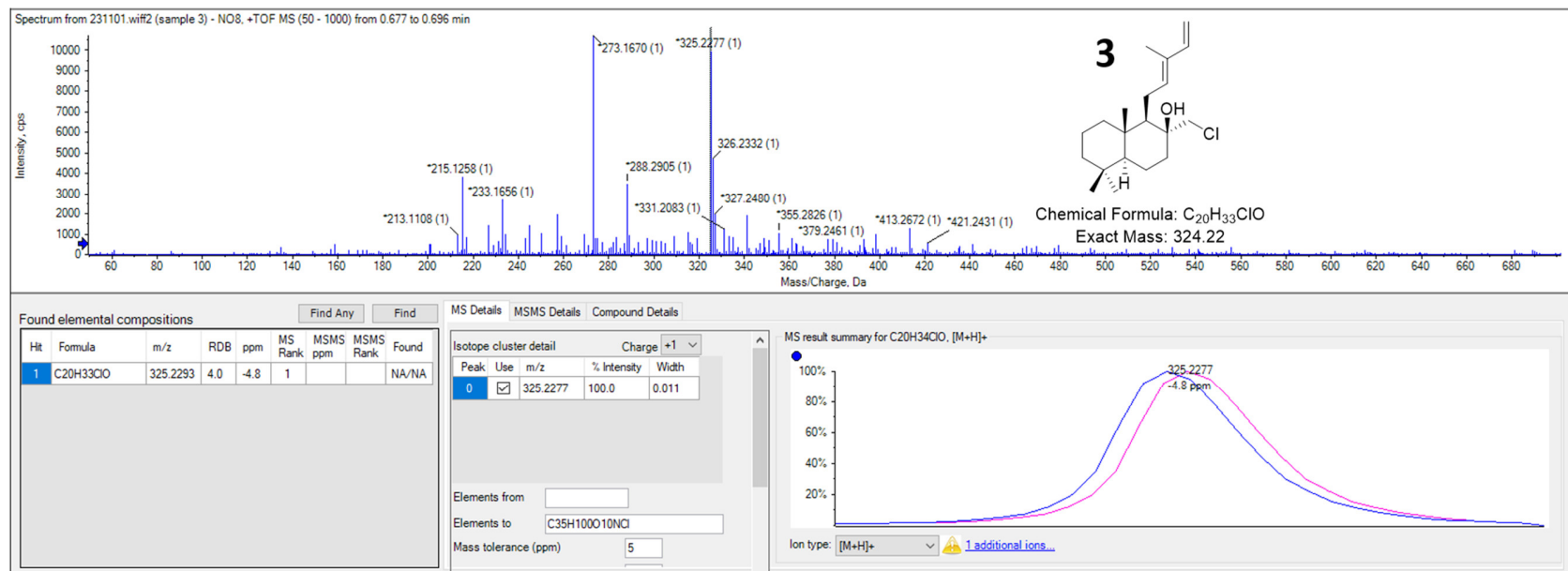


Figure S30. HRESIMS data of 3.

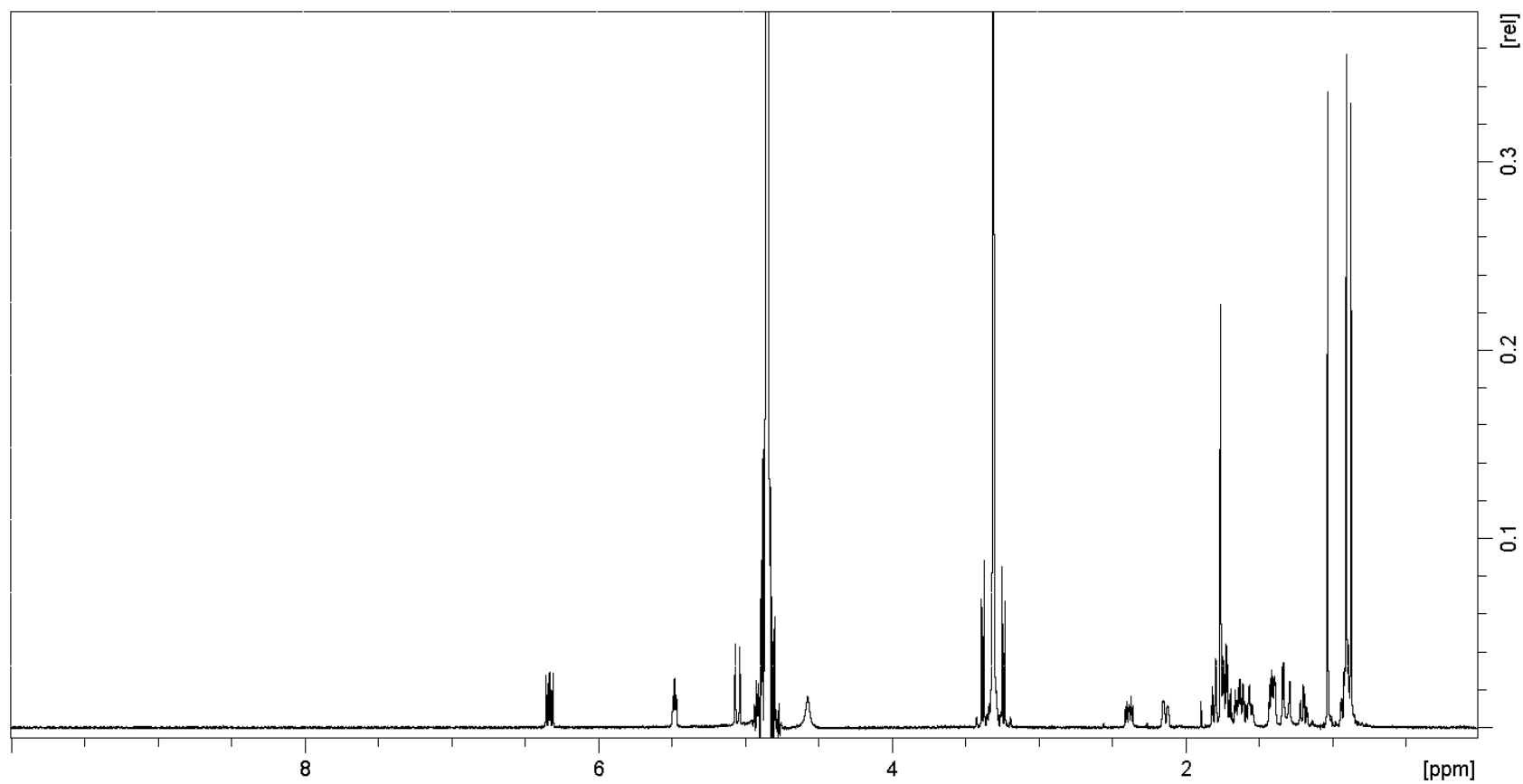


Figure S31. ^1H NMR spectrum of **3** (CD_3OD).

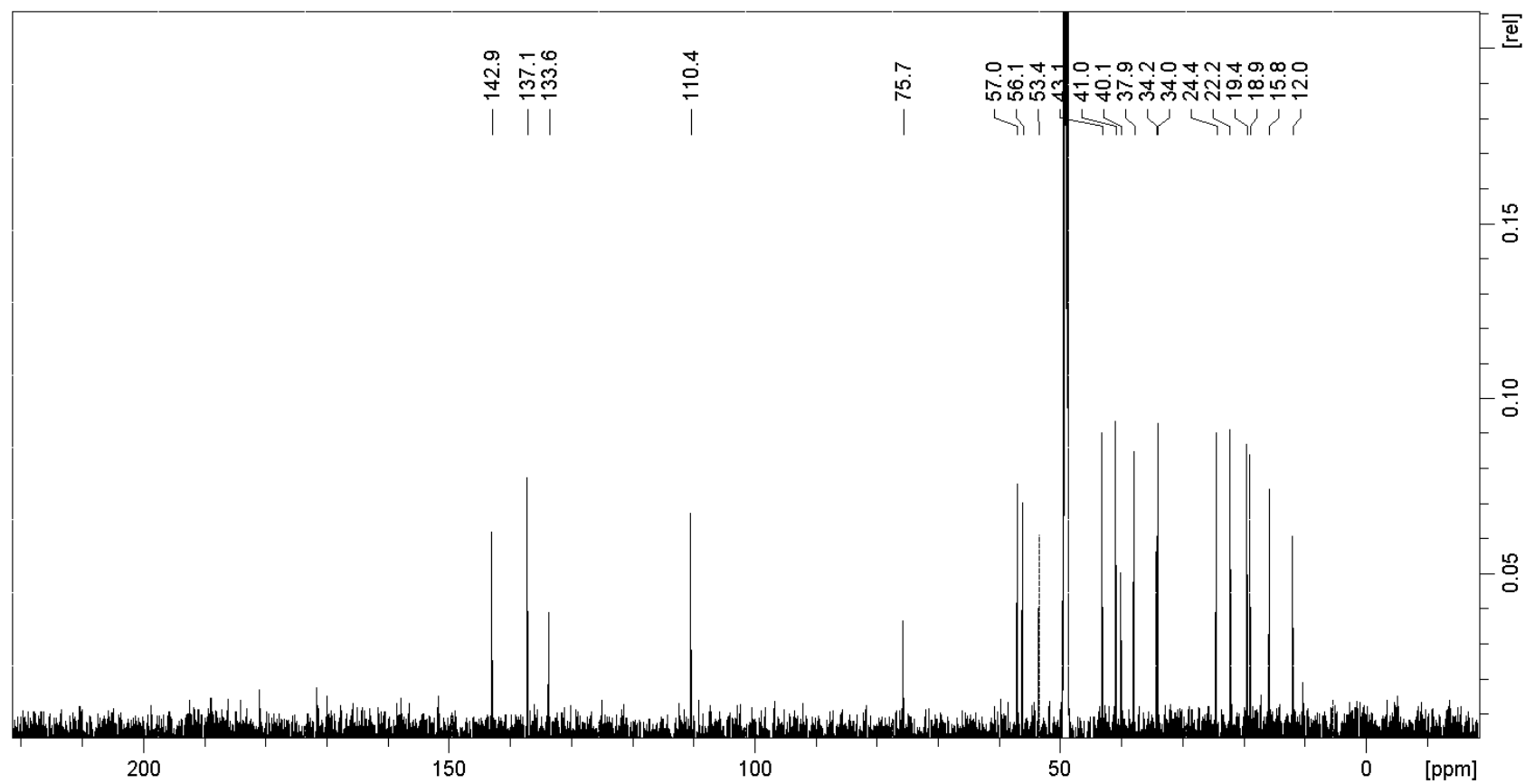


Figure S32. ^{13}C NMR spectrum of **3** (CD_3OD).

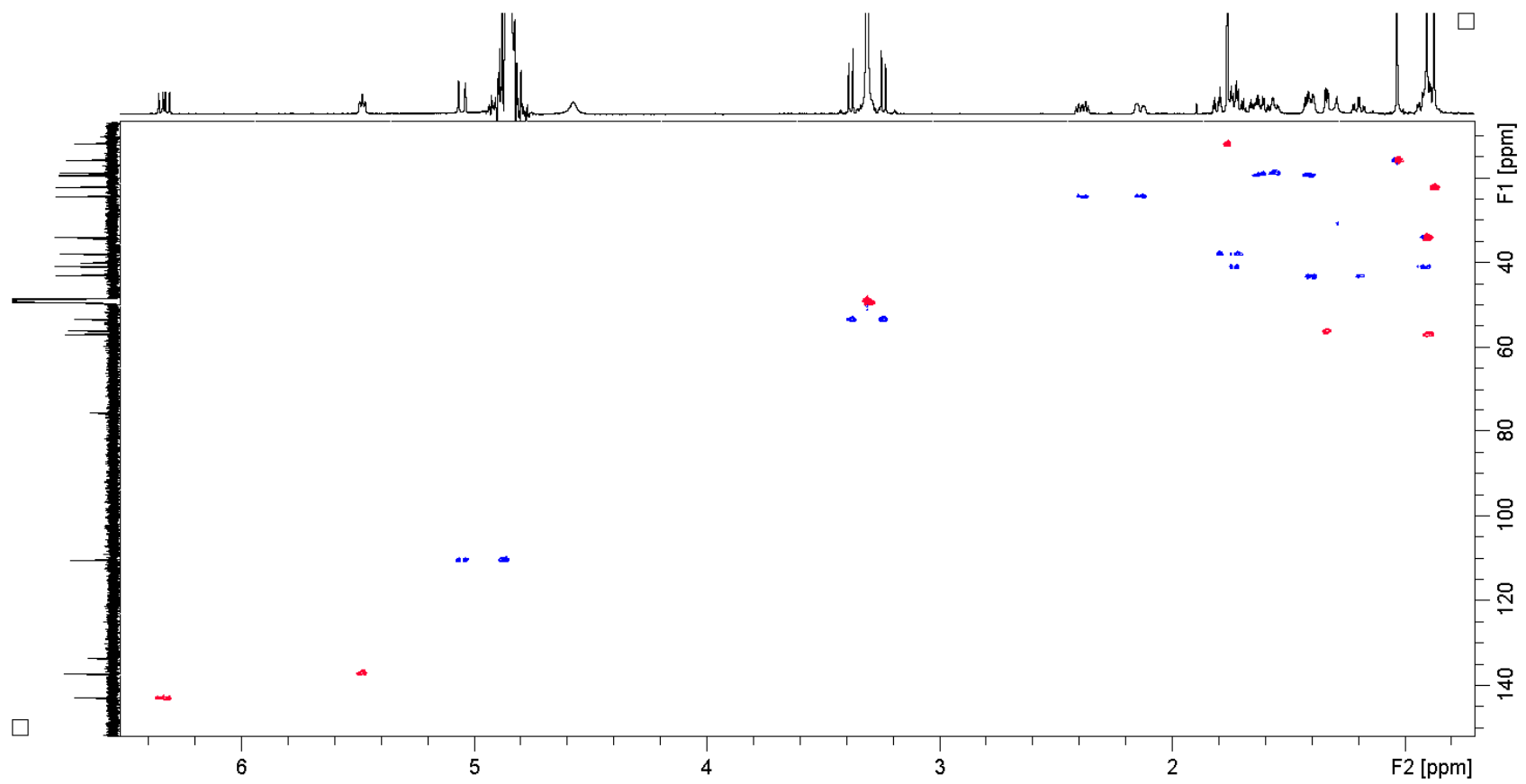


Figure S33. HSQC NMR spectrum of **3** (CD₃OD).

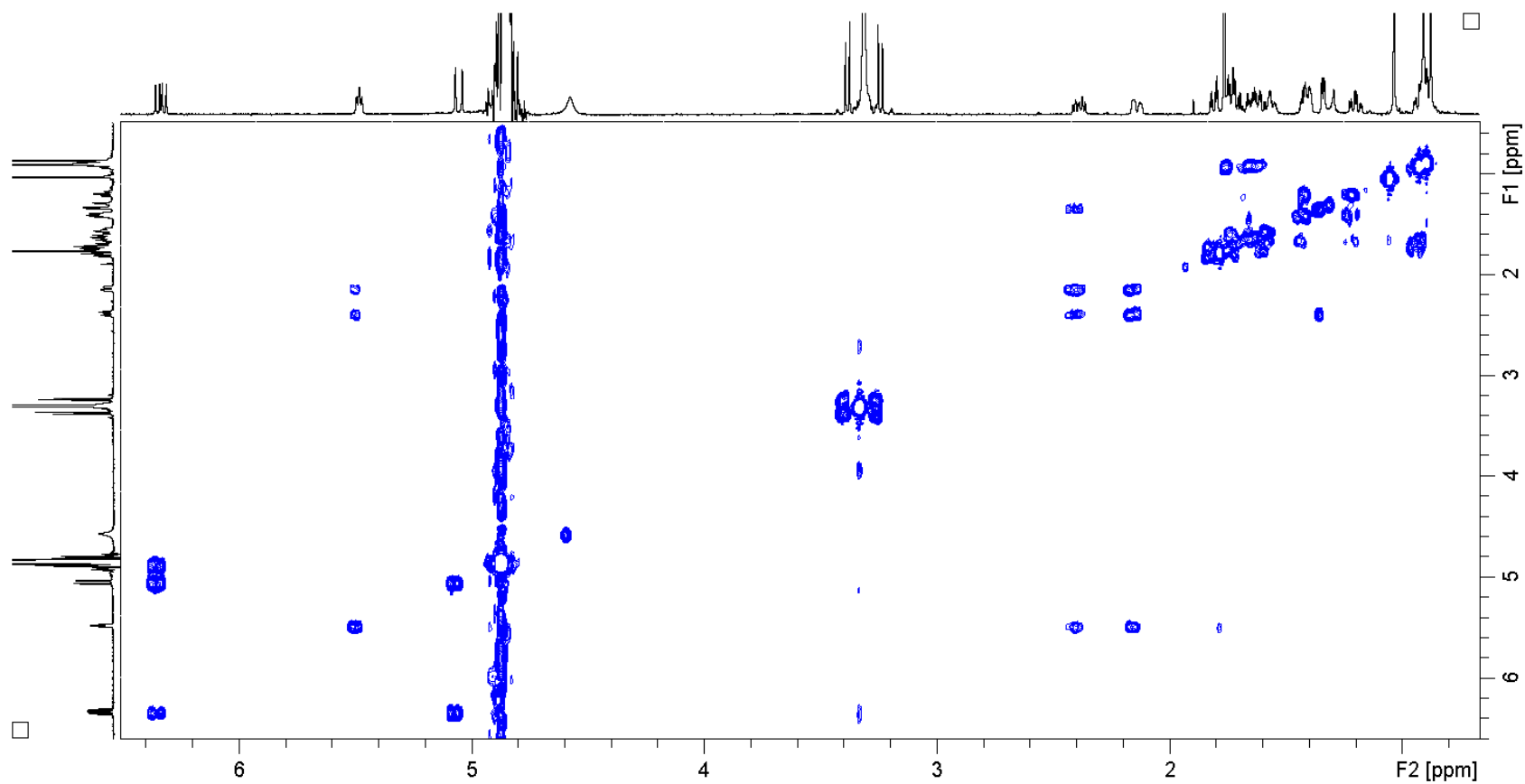


Figure S34. ^1H - ^1H COSY NMR spectrum of **3** (CD_3OD).

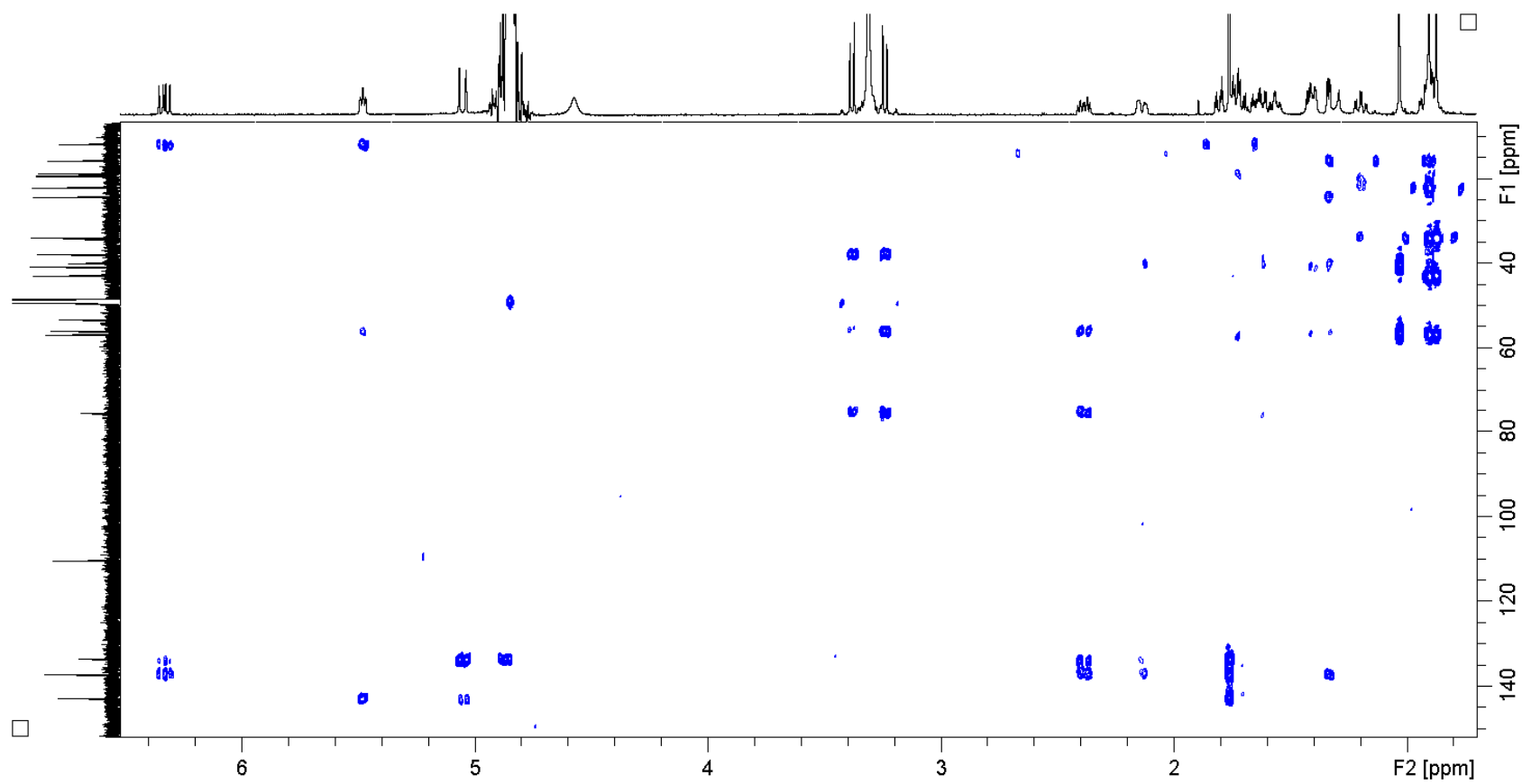


Figure S35. HMBC NMR spectrum of **3** (CD₃OD).

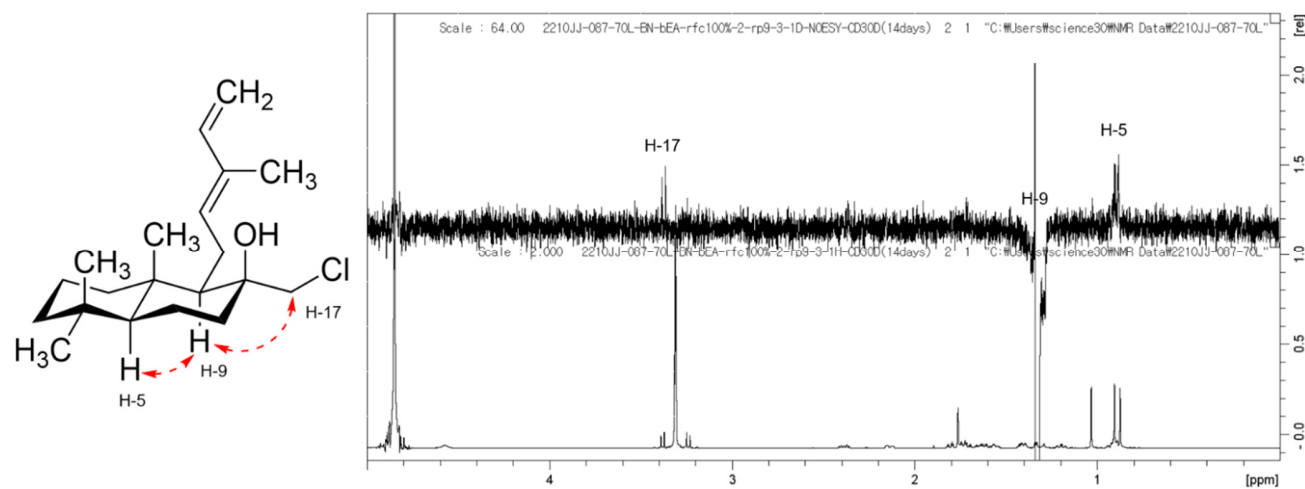


Figure S36. 1D selective NOESY data of **3** (irradiated H-9) (CD₃OD).

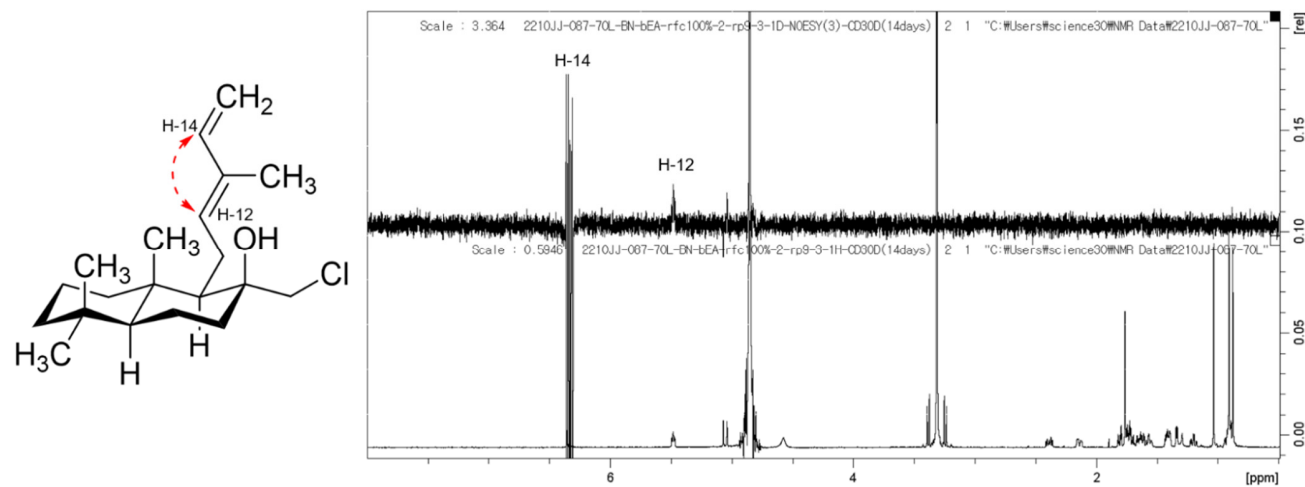


Figure S37. 1D selective NOESY data of **3** (irradiated H-14) (CD₃OD).

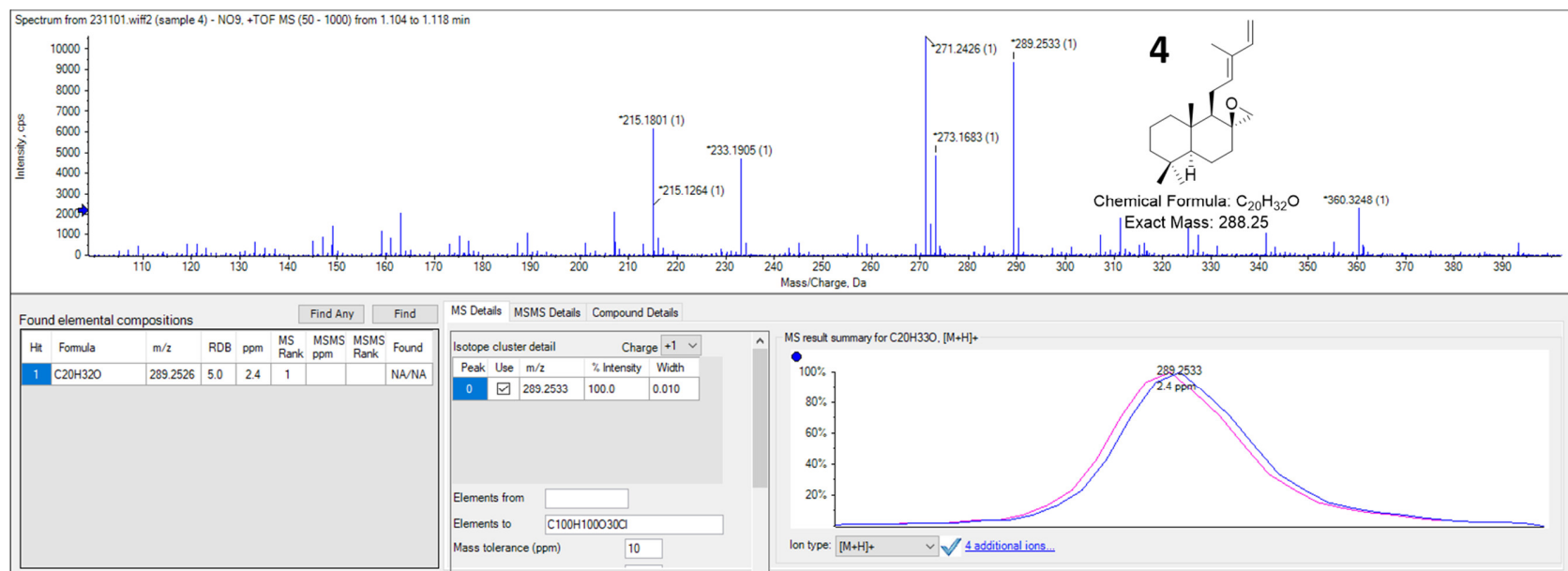


Figure S38. HRESIMS data of **4**.

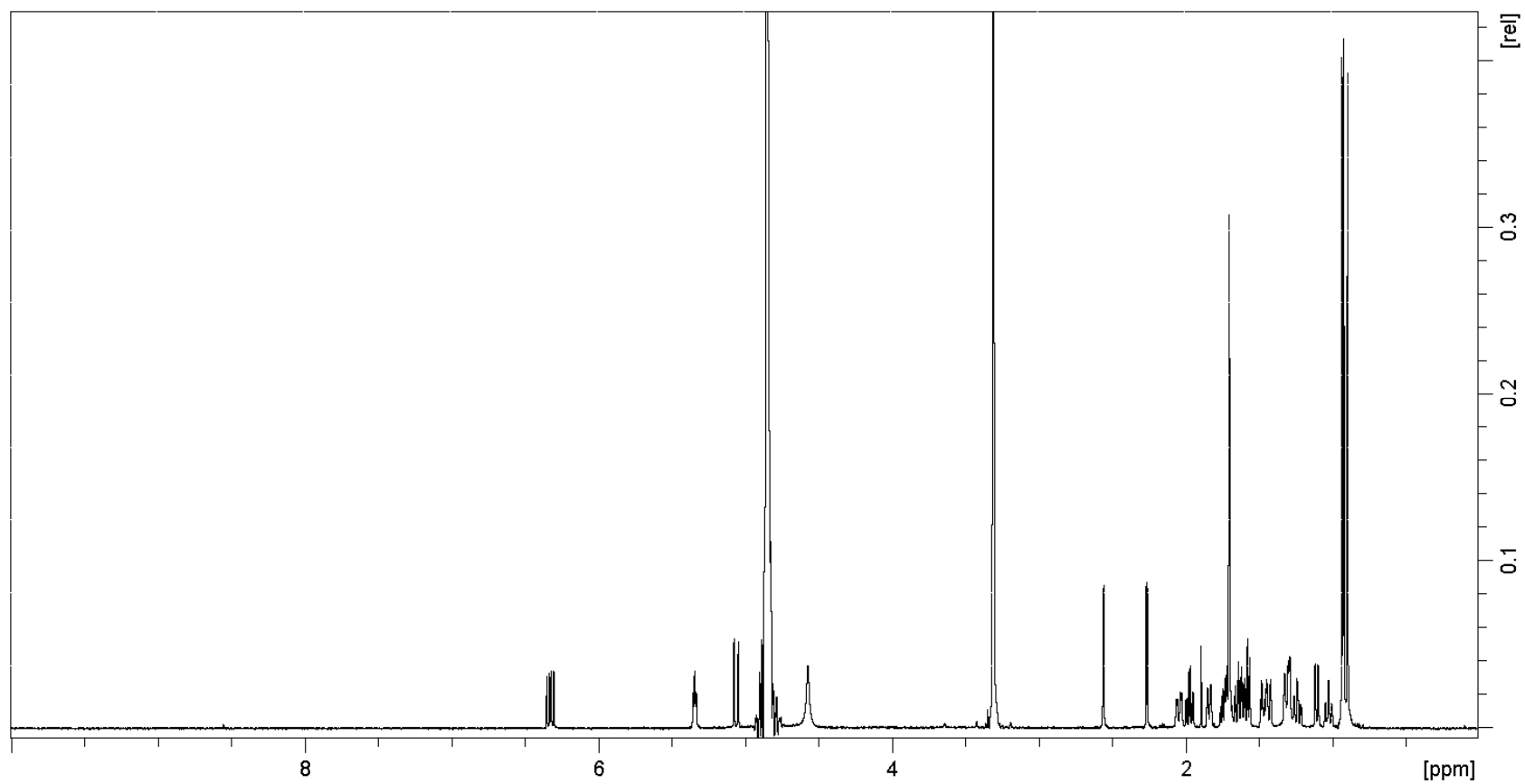


Figure S39. ^1H NMR spectrum of **4** (CD_3OD).

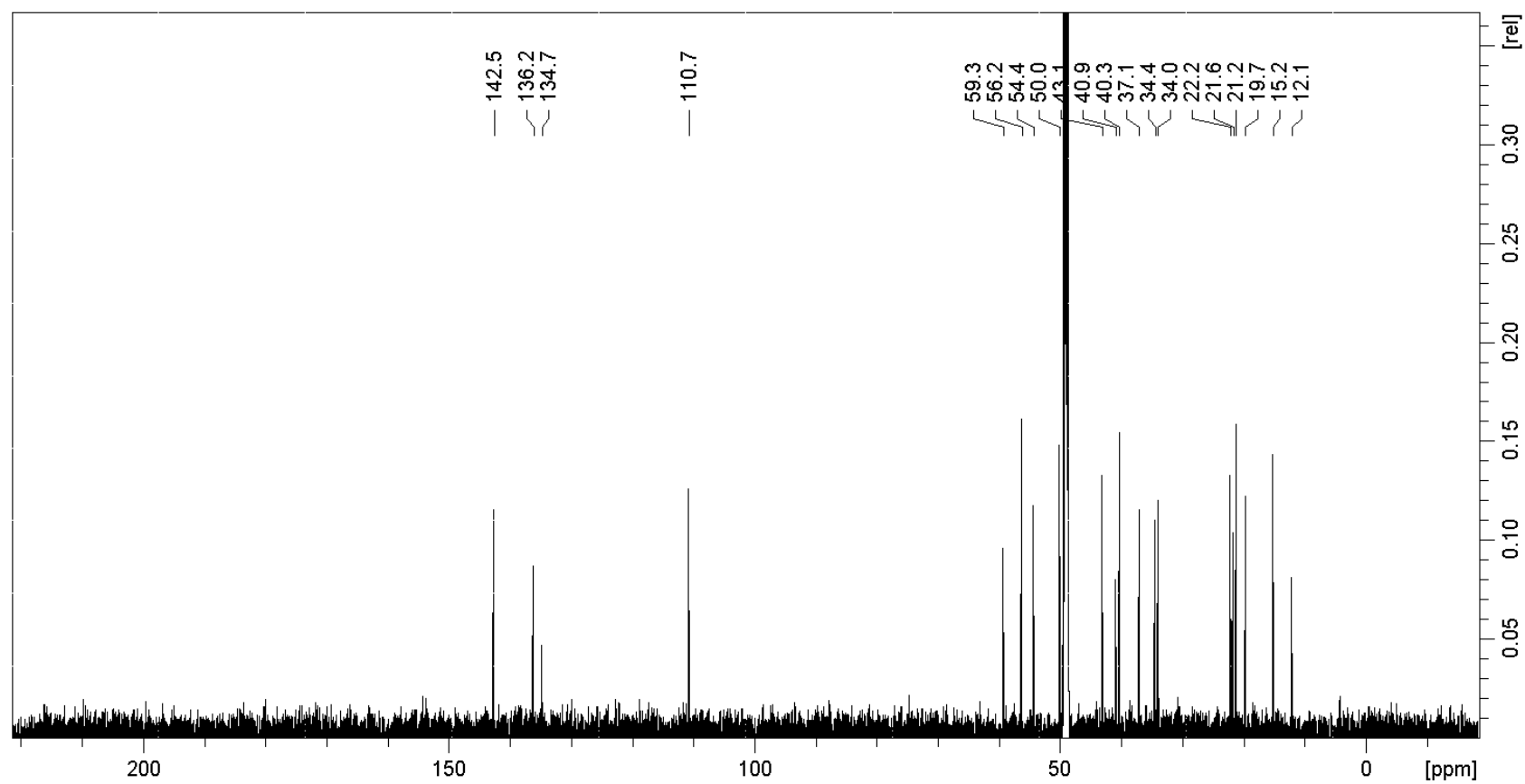


Figure S40. ^{13}C NMR spectrum of **4** (CD_3OD).

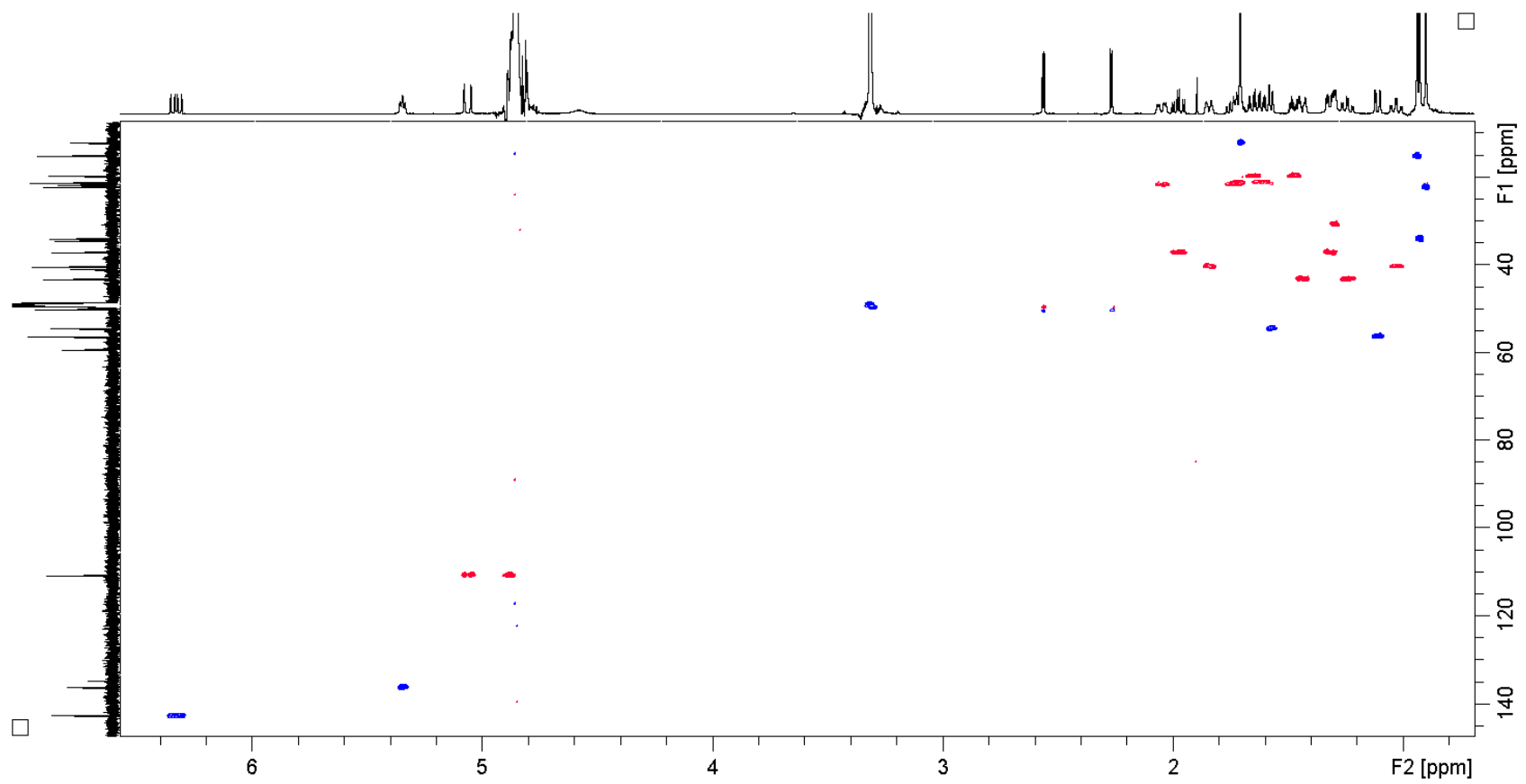


Figure S41. HSQC NMR spectrum of **4** (CD₃OD).

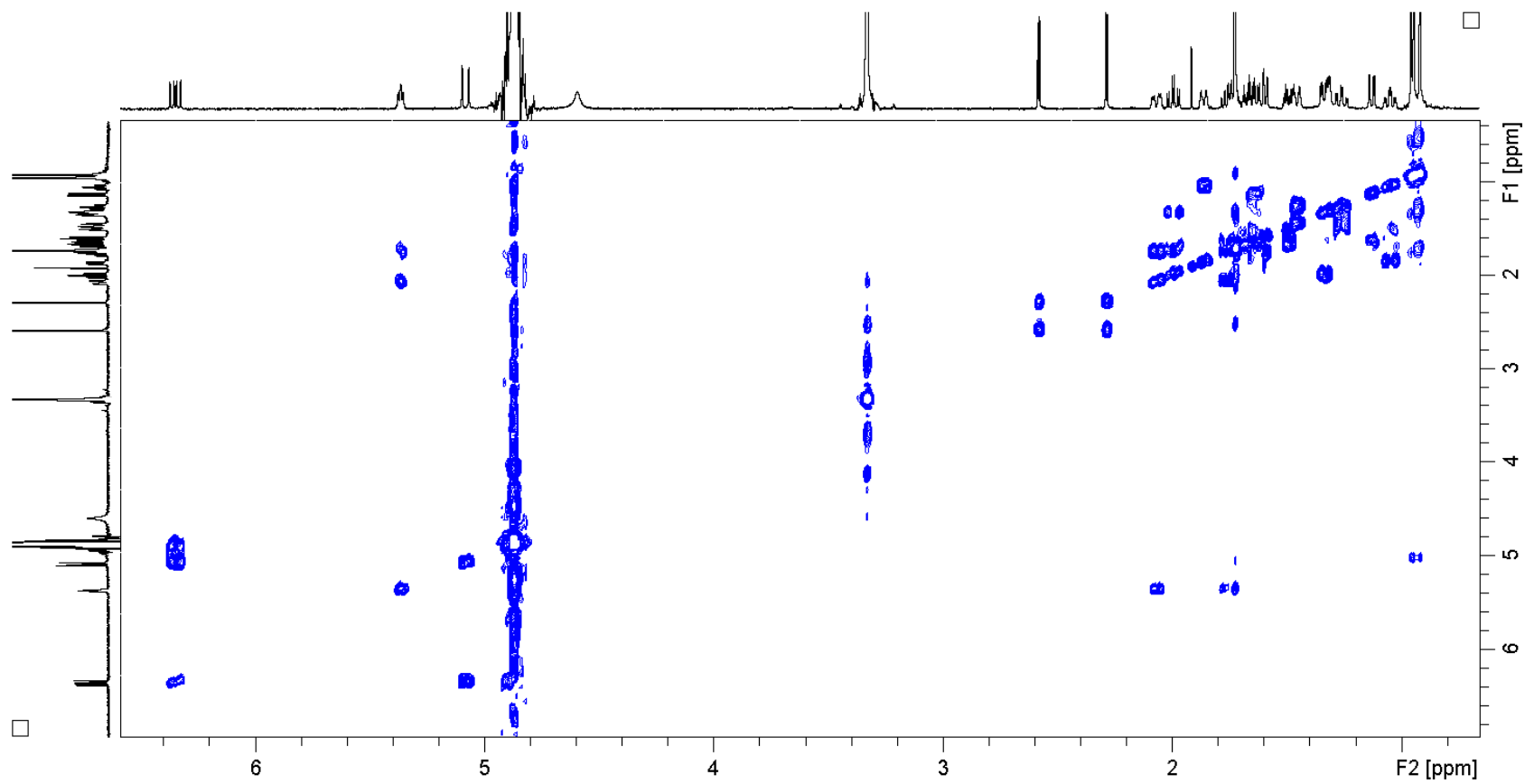


Figure S42. ^1H - ^1H COSY NMR spectrum of **4** (CD_3OD).

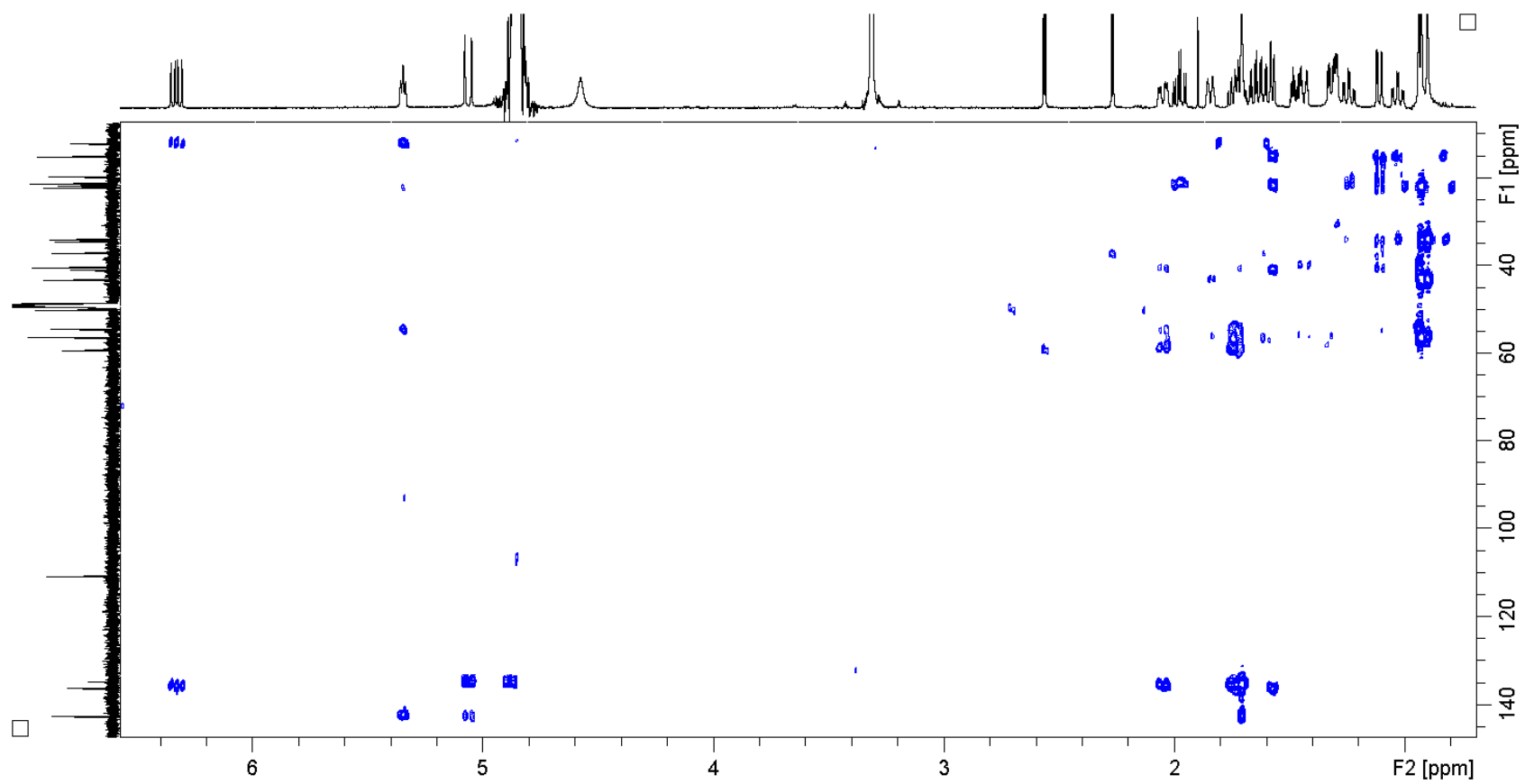


Figure S43. HMBC NMR spectrum of **4** (CD₃OD).

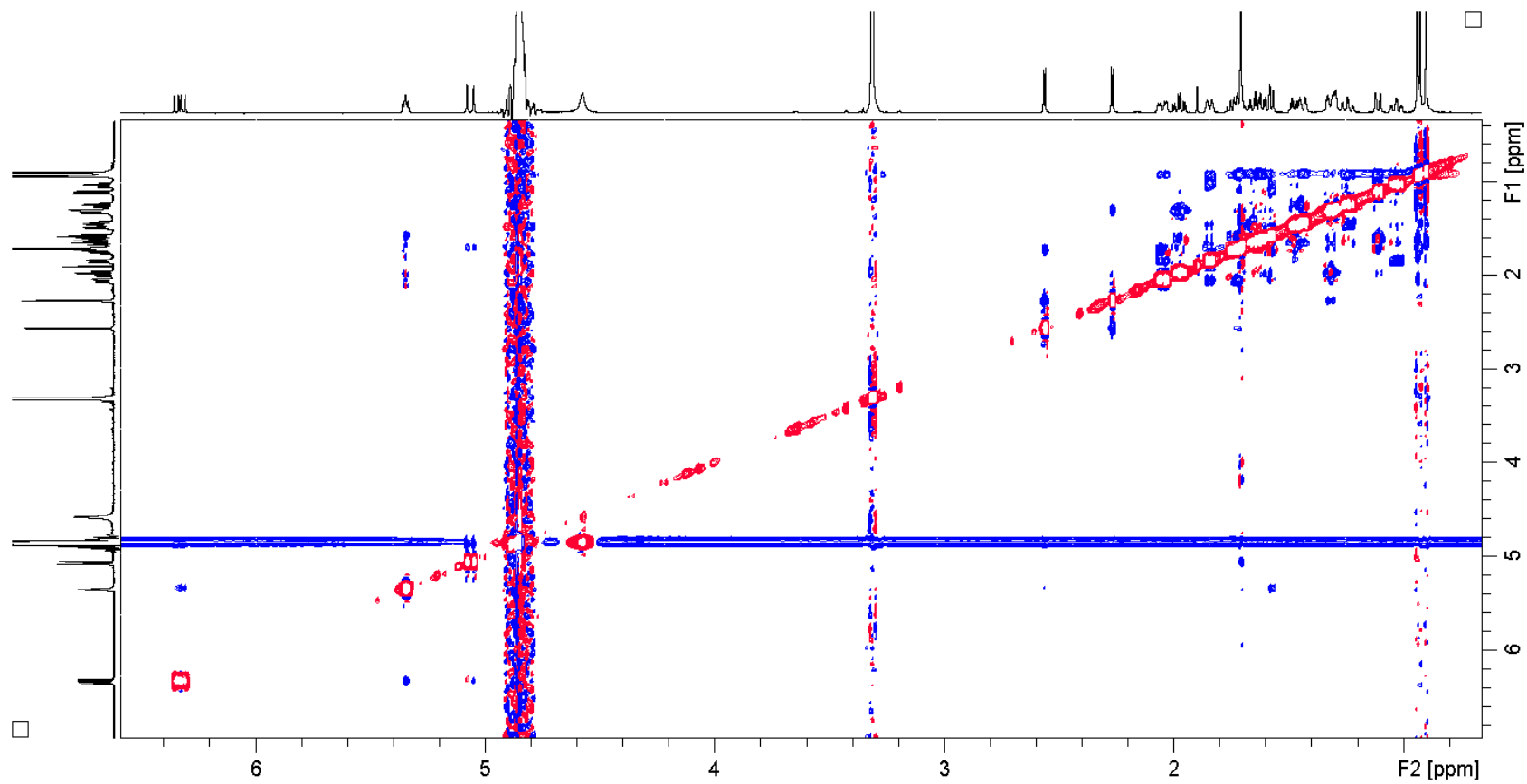


Figure S44. NOESY NMR spectrum of **4** (CD₃OD).

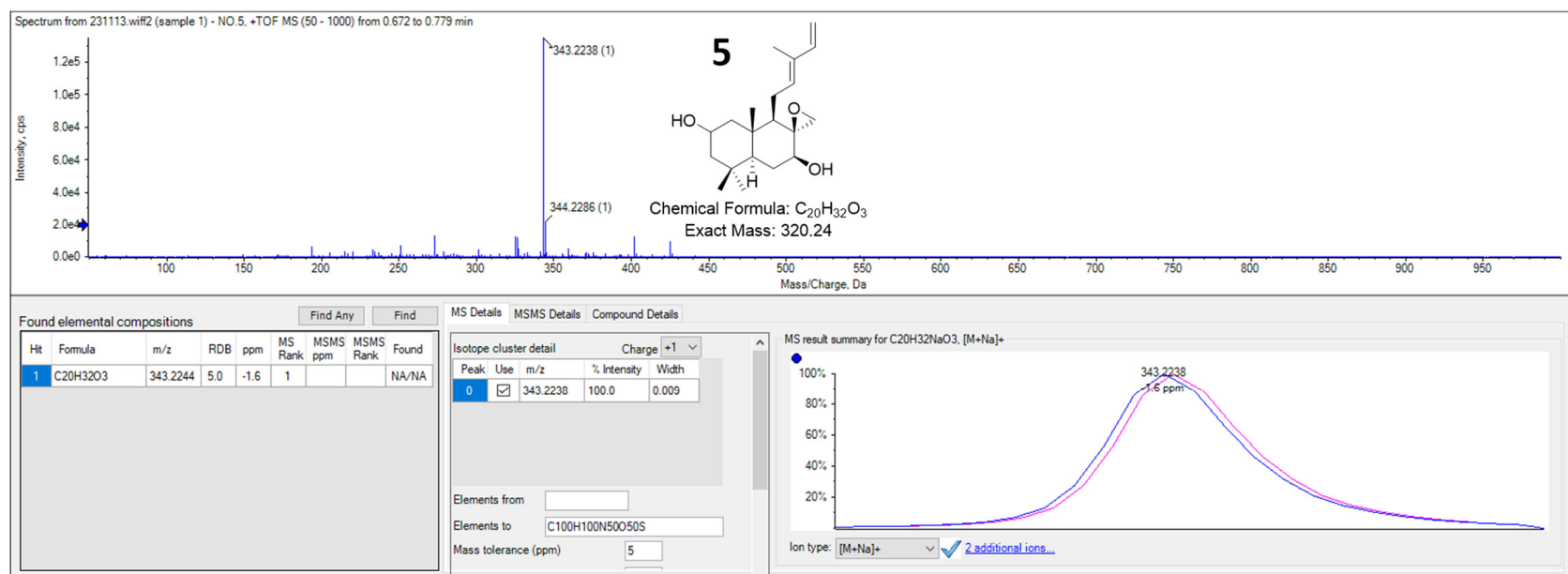


Figure S45. HRESIMS data of **5**.

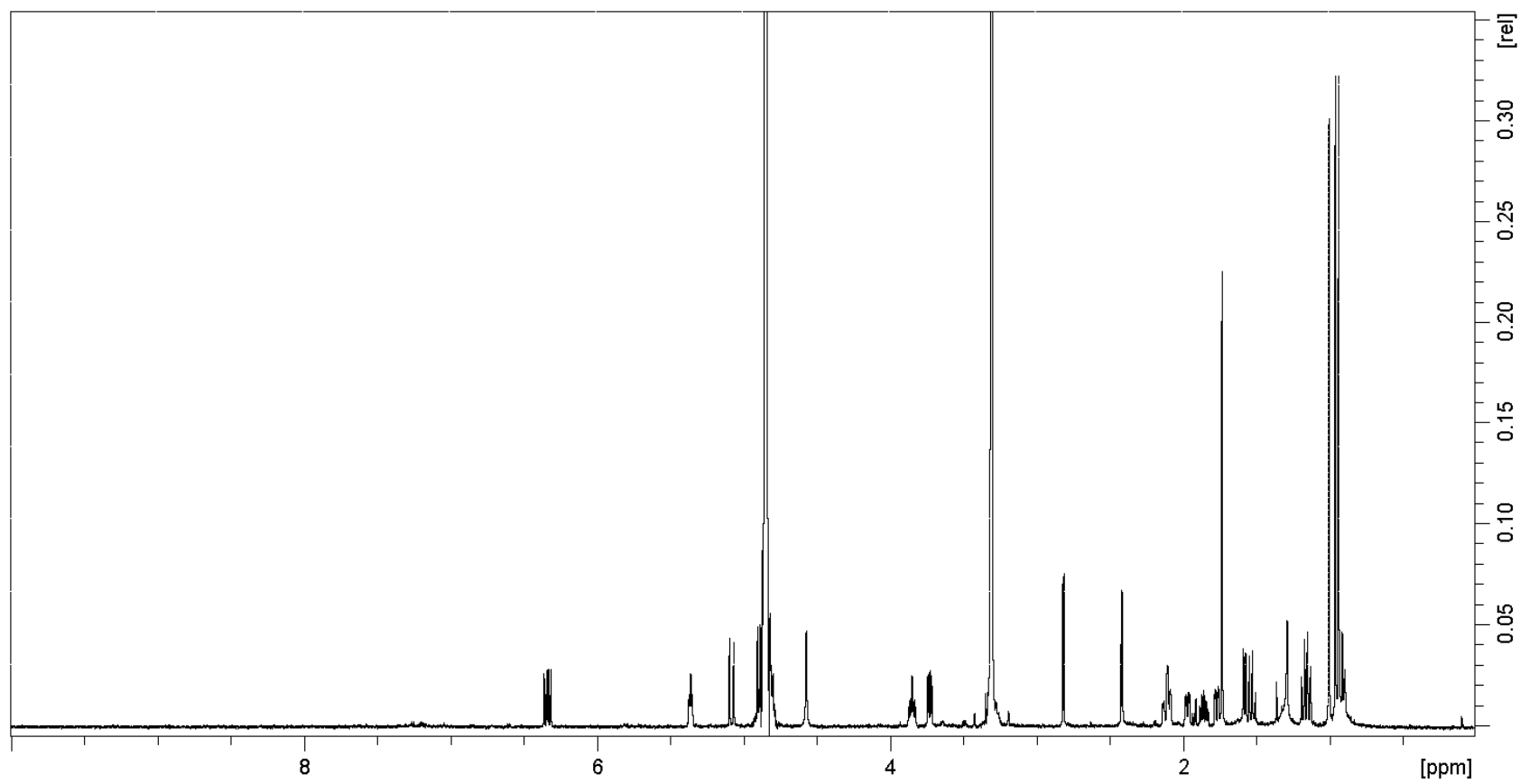


Figure S46. ^1H NMR spectrum of **5** (CD_3OD).

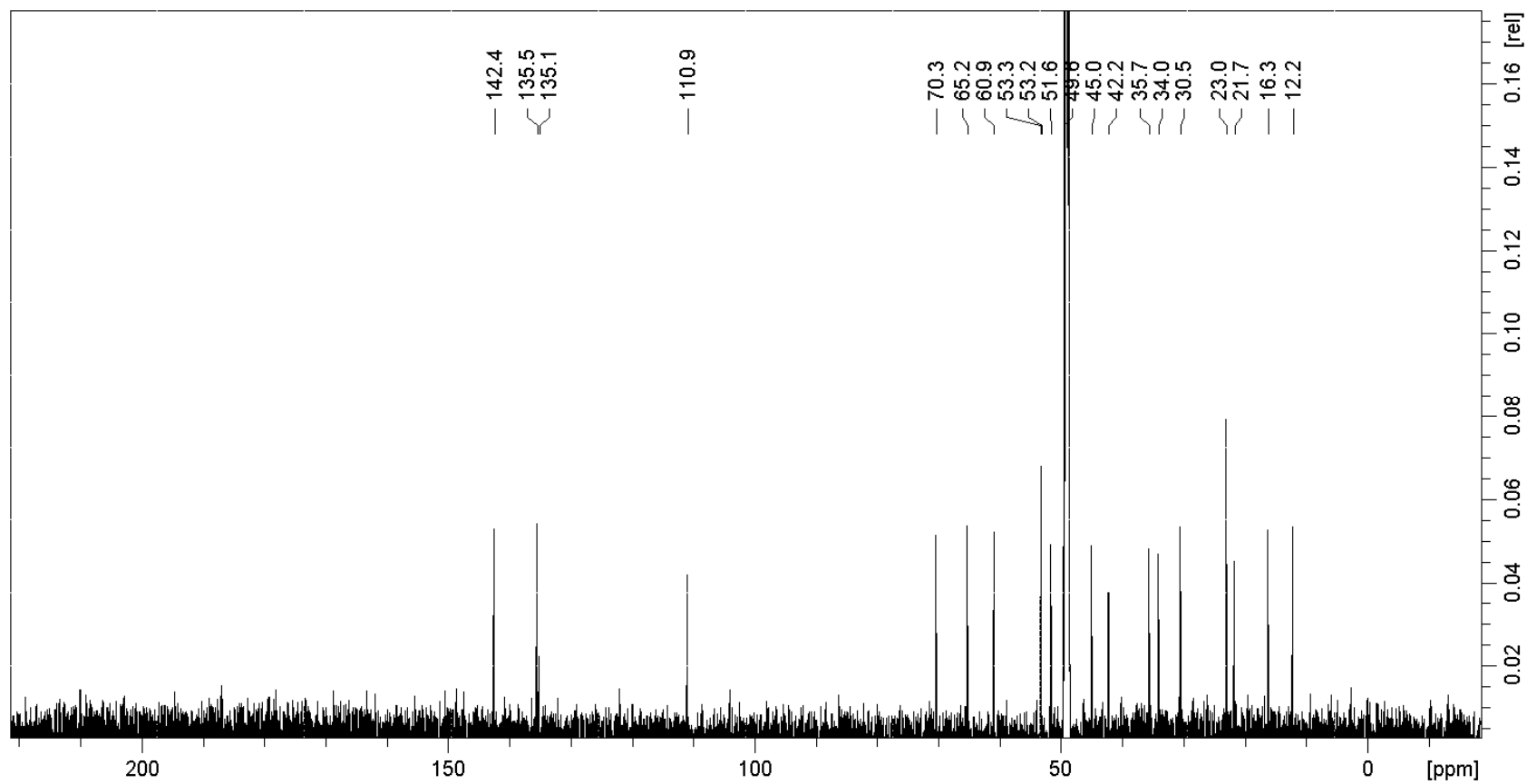


Figure S47. ^{13}C NMR spectrum of **5** (CD_3OD).

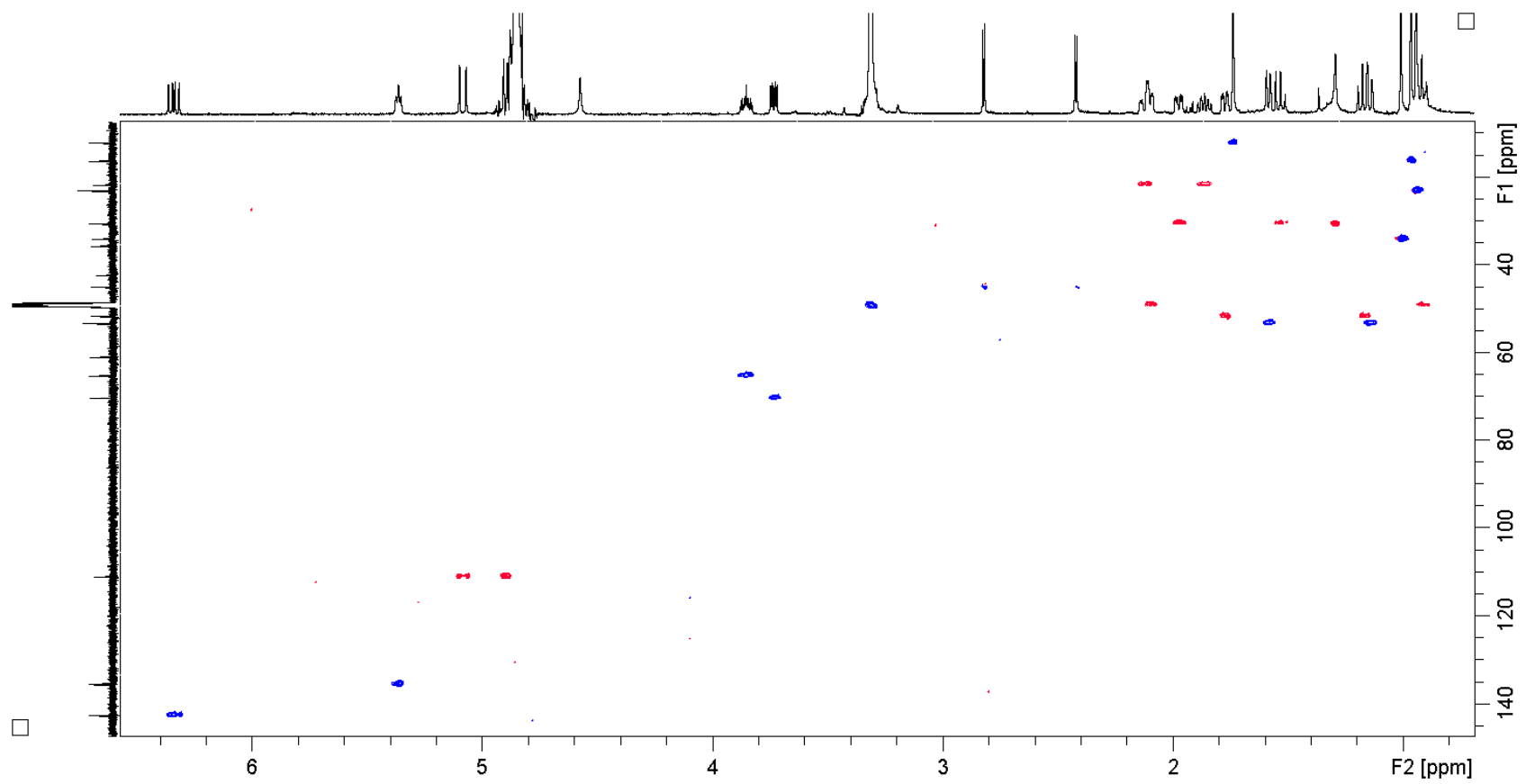


Figure S48. HSQC NMR spectrum of **5** (CD₃OD).

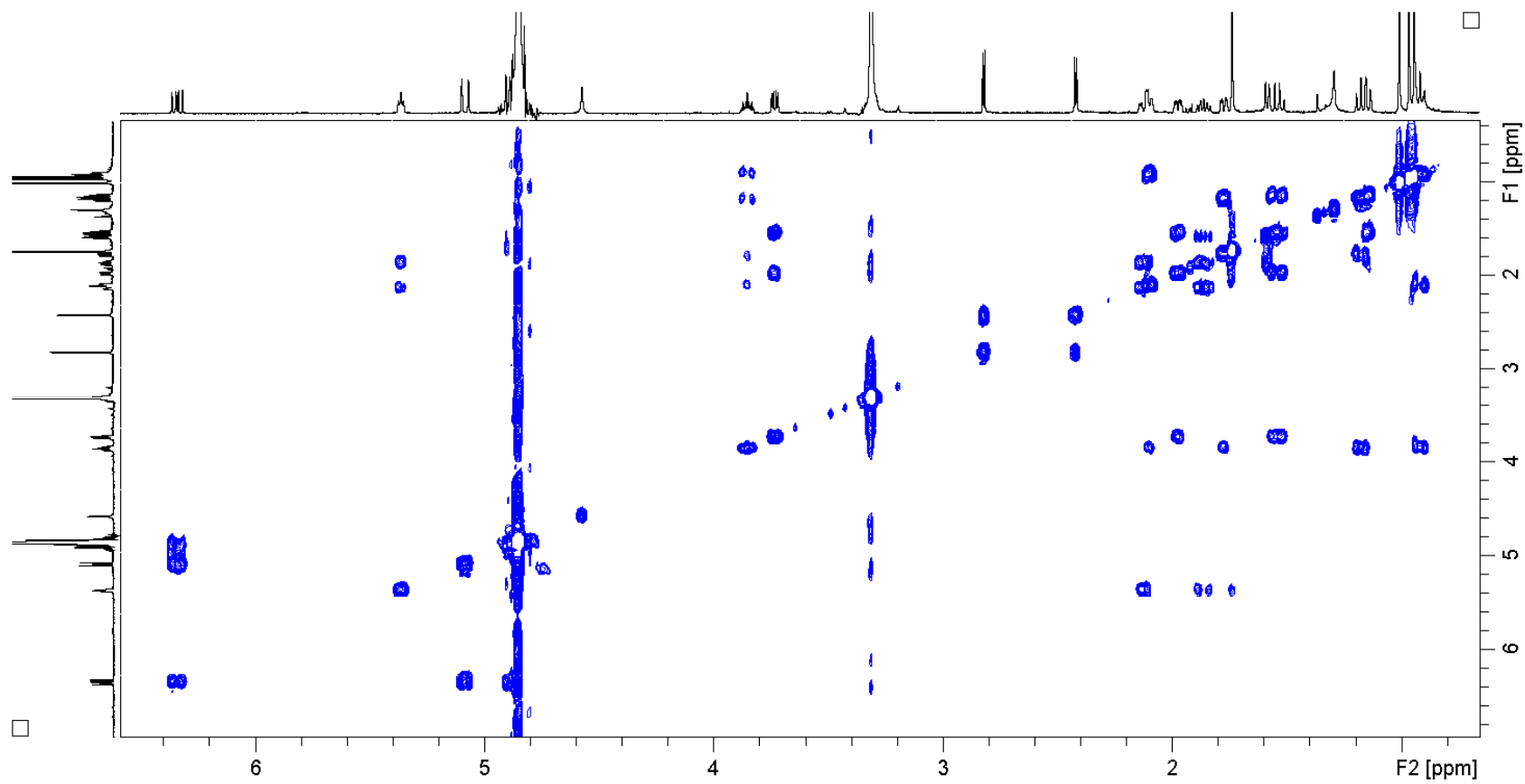


Figure S49. ^1H - ^1H COSY NMR spectrum of **5** (CD_3OD).

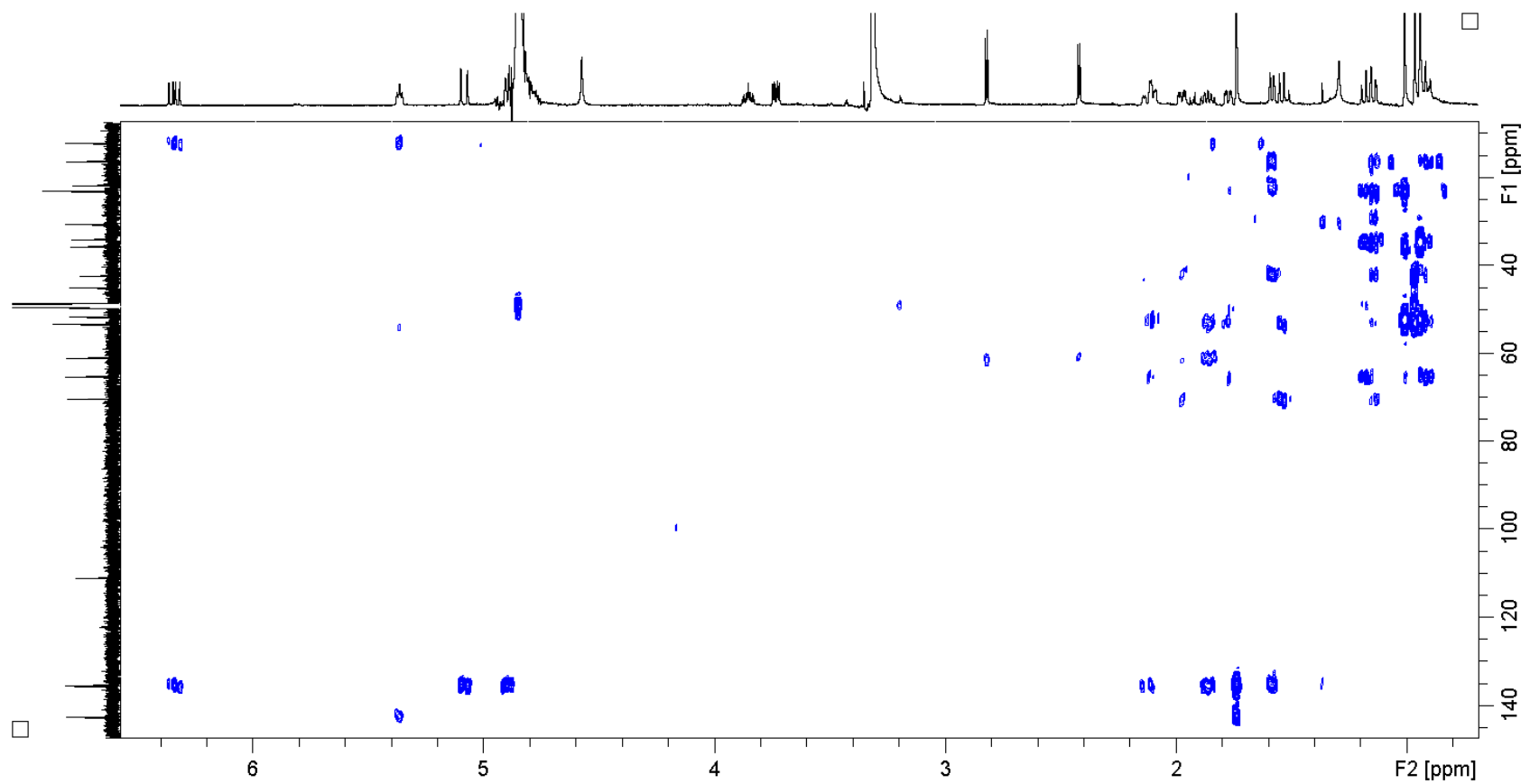


Figure S50. HMBC NMR spectrum of **5** (CD₃OD).

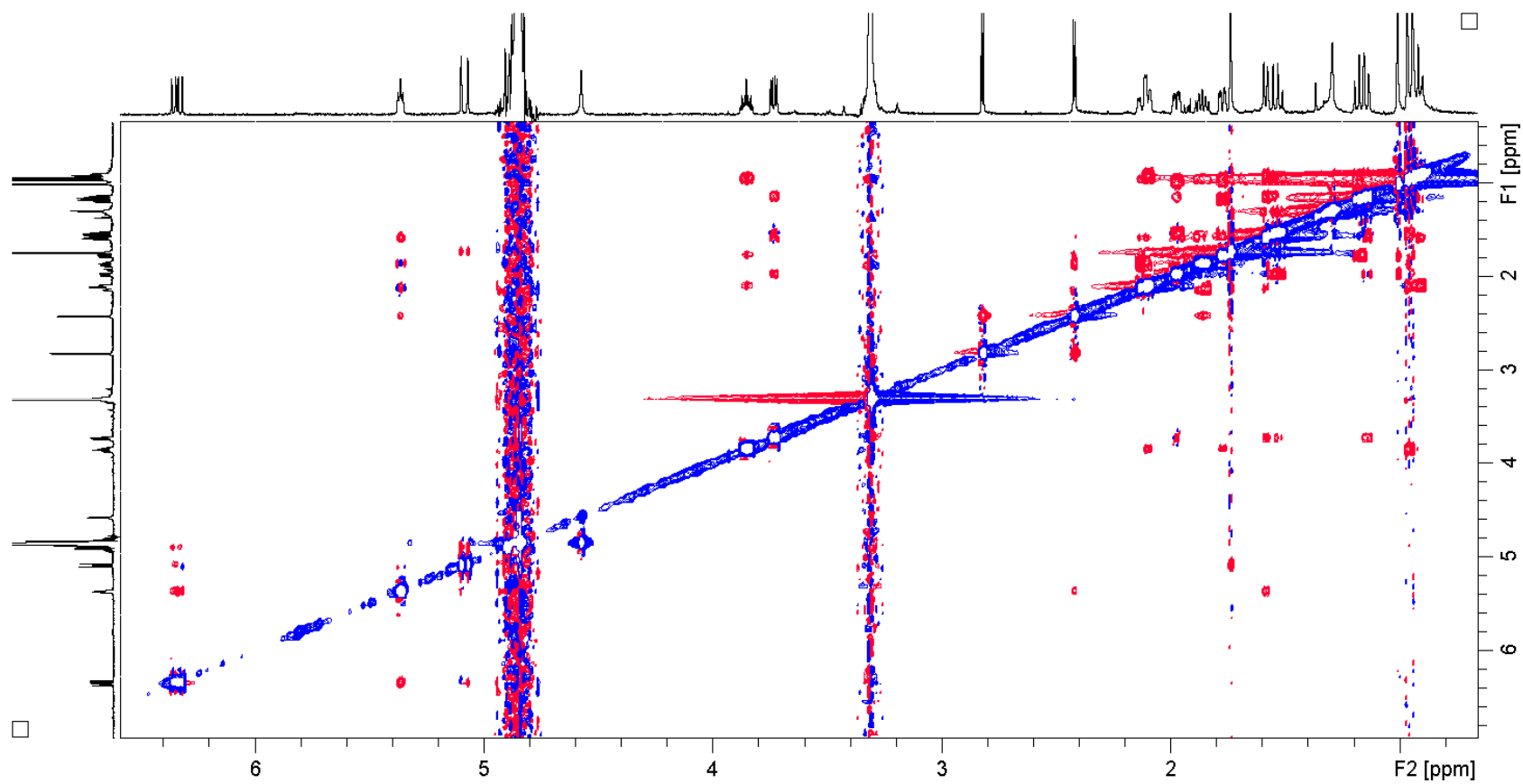


Figure S51. NOESY NMR spectrum of **5** (CD₃OD).

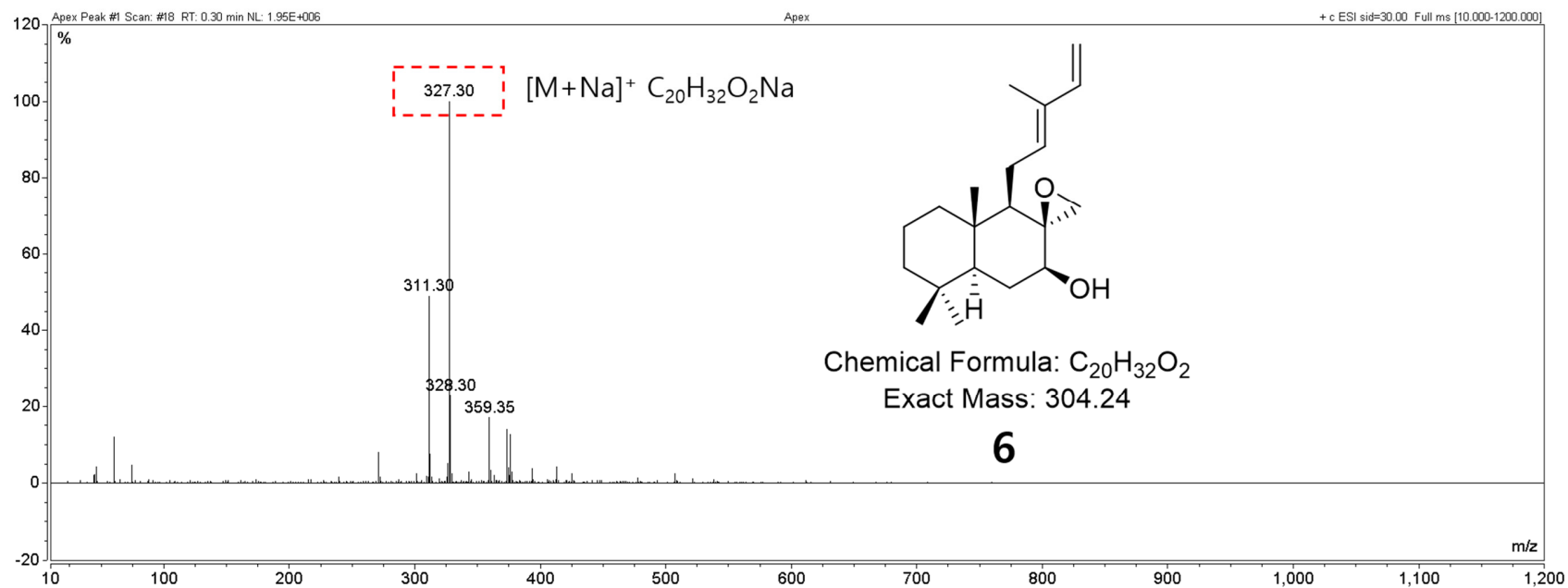


Figure S52. LRESIMS data of **6**.

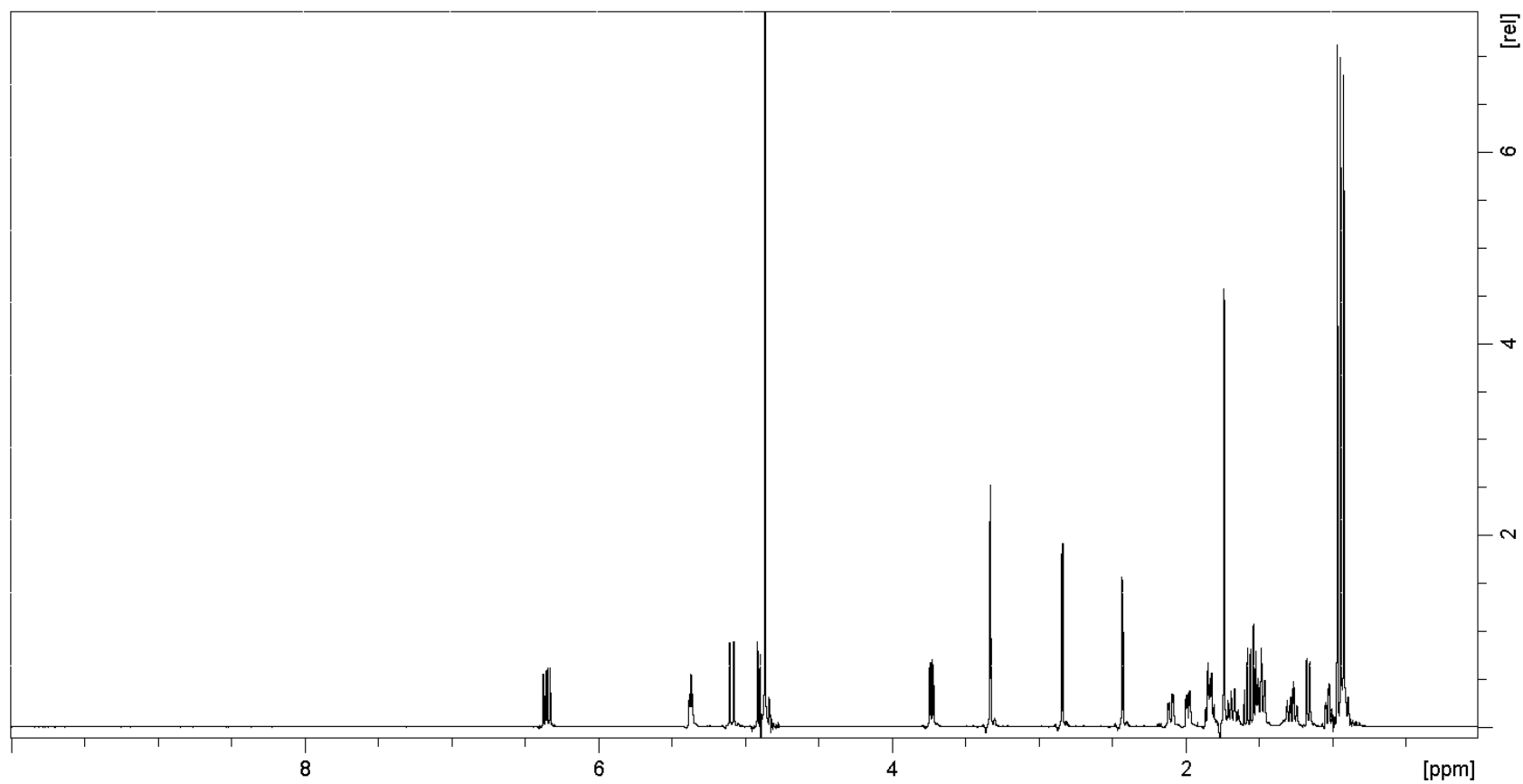


Figure S53. ^1H NMR spectrum of **6** (CD_3OD).

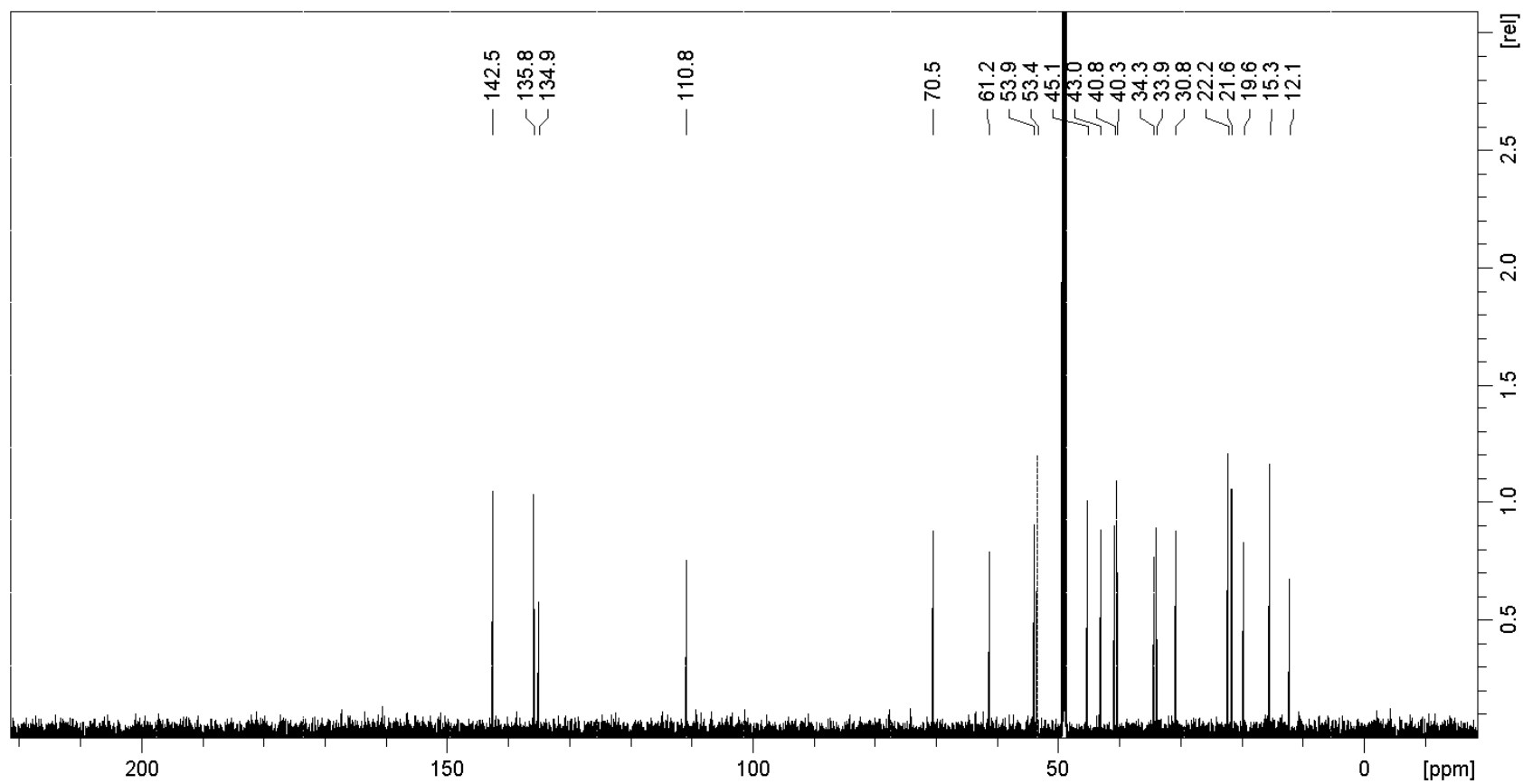


Figure S54. ¹³C NMR spectrum of **6** (CD₃OD).

HL-60	1		2		4		Doxorubicin				Raji	1		2		4		Doxorubicin	
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
0.1	97.7	1.9	80.0	3.0	93.3	1.3	1.6	0.2			0.1	27.4	2.6	0.1	0.1	30.1	6.4	0.8	0.2
0.03	102.6	2.8	95.1	0.7	92.2	2.1	30.0	3.3			0.03	67.7	5.5	10.1	5.3	73.6	8.6	22.0	2.5
0.01	99.6	1.6	99.1	4.3	94.9	2.4	75.2	3.6			0.01	86.5	7.4	64.5	7.3	79.1	9.3	52.5	1.2
0.003	96.8	1.9	98.5	2.6	94.7	2.1	90.5	4.6			0.003	92.9	7.5	79.3	6.5	92.5	4.0	85.7	3.2
0.001	94.6	2.4	96.2	1.1	84.6	4.2	85.8	2.7			0.001	102.4	6.4	82.4	8.0	94.3	8.2	88.9	9.9
IC50	>30		>30		>30		0.018				IC50	15.520		3.406		17.110		0.011	
WSU-DLCL2	1		2		4		Doxorubicin				NALM6 C. G5	1		2		4		Doxorubicin	
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
0.1	50.5	4.8	0.0	0.0	8.1	2.8	0.4	0.1			0.1	86.3	5.2	39.3	5.7	100.2	7.6	0.1	0.0
0.03	85.0	4.0	8.7	2.6	75.2	4.0	4.0	0.8			0.03	91.9	3.3	77.7	4.1	91.9	4.1	-0.1	0.0
0.01	93.7	6.0	43.1	7.8	82.1	8.0	20.9	0.6			0.01	102.8	2.3	88.6	1.8	94.3	5.9	2.5	1.1
0.003	100.1	6.4	56.4	3.7	89.2	3.9	90.1	8.9			0.003	110.6	0.6	99.5	2.8	96.0	4.9	64.0	4.7
0.001	101.2	7.7	66.5	8.0	92.1	3.6	94.8	8.4			0.001	99.8	3.9	107.0	2.6	87.4	6.2	82.8	6.8
IC50	>30(30.7)		1.182		14.170		0.006				IC50	>30		22.460		>30		0.003	
K562	1		2		4		Doxorubicin				RPMI-8402	1		2		4		Doxorubicin	
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
0.1	86.2	1.6	53.4	2.2	97.7	1.2	3.8	0.1			0.1	83.3	3.4	56.3	6.8	91.9	4.4	1.2	0.4
0.03	96.9	1.8	84.3	2.8	86.8	4.6	4.6	0.9			0.03	86.2	3.9	74.0	6.1	85.9	4.2	13.5	0.6
0.01	109.8	5.2	98.4	3.9	91.6	2.6	31.4	1.3			0.01	84.5	5.5	91.5	6.6	82.3	5.4	58.1	5.3
0.003	113.3	3.4	109.7	3.0	99.1	0.7	56.9	2.5			0.003	96.3	4.5	94.9	8.8	80.6	8.4	68.7	5.2
0.001	114.0	2.6	114.3	1.1	98.8	1.5	65.7	4.3			0.001	104.4	6.4	94.3	4.6	85.2	6.8	77.2	2.0
IC50	>30		>30		>30		0.003				IC50	>30		>30		>30		0.008	
U266	1		2		4		Doxorubicin				RPMI-1788	1		2		4		Doxorubicin	
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD			(μM)	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
0.1	101.0	4.2	83.6	1.6	99.0	7.8	17.2	1.4			0.1	89.9	4.9	60.9	4.1	97.2	9.2	3.2	0.4
0.03	96.3	3.3	92.7	5.4	89.3	4.5	68.1	4.2			0.03	95.2	1.4	88.3	4.6	92.1	6.0	14.0	0.9
0.01	99.2	4.1	96.4	1.9	92.8	4.0	84.4	3.5			0.01	99.1	5.0	94.2	1.2	96.0	4.0	38.6	6.0
0.003	100.3	2.0	100.1	4.5	93.4	4.5	88.9	4.4			0.003	99.0	2.2	94.0	1.7	94.5	3.1	85.7	5.0
0.001	97.5	4.6	97.7	2.8	90.6	1.9	86.8	4.5			0.001	96.1	1.8	96.6	7.2	89.4	2.6	99.9	2.8
IC50	>30		>30		>30		0.042				IC50	>30		>30		>30		0.008	

ACHN	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	72.06	6.94	72.00	5.82	81.94	4.42	3	-13.42	2.41
10	74.24	5.77	83.14	6.51	85.65	5.73	1	-4.90	6.19
3	86.68	7.11	89.39	2.48	90.98	5.35	0.3	12.82	5.58
1	87.08	6.98	93.12	5.49	95.41	6.17	0.1	30.04	2.04
0.3	94.02	3.03	99.14	3.93	98.72	1.13	0.03	92.15	7.02
GI50	>30		>30		>30		GI50	0.074	
PC-3	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	85.23	6.01	80.76	5.23	71.11	1.31	3	-10.58	3.74
10	86.14	3.39	82.94	7.49	76.59	7.90	1	-7.86	1.71
3	90.37	2.47	89.14	4.34	87.52	6.75	0.3	16.13	9.96
1	94.14	3.81	91.13	2.52	93.34	2.66	0.1	27.40	3.53
0.3	98.40	3.16	96.25	4.32	98.22	3.40	0.03	95.10	7.57
GI50	>30		>30		>30		GI50	0.073	
NCI-H23	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	73.68	5.34	72.20	6.69	78.62	7.31	3	-9.73	5.18
10	83.08	4.95	87.93	2.40	89.75	5.63	1	-6.45	2.12
3	87.02	4.74	88.07	0.81	90.41	3.68	0.3	16.90	8.45
1	95.45	7.56	96.23	4.02	92.36	6.61	0.1	27.58	2.13
0.3	100.36	2.31	98.57	6.77	94.13	5.84	0.03	96.57	7.31
GI50	>30		>30		>30		GI50	0.074	
MRC-9	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	80.62	6.81	85.72	3.97	74.81	8.01	3	-7.72	3.86
10	85.93	4.24	88.22	5.74	89.10	4.65	1	-4.38	3.80
3	88.28	5.42	90.65	5.28	91.80	7.86	0.3	19.26	6.64
1	97.15	4.12	95.54	4.32	93.31	3.99	0.1	39.69	8.11
0.3	100.00	1.62	97.15	5.80	96.06	3.46	0.03	94.36	4.23
GI50	>30		>30		>30		GI50	0.090	
MDA-MB-231	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	77.94	4.06	72.56	4.31	81.81	6.11	3	-11.01	7.44
10	80.43	2.07	77.83	4.53	88.19	7.42	1	-2.06	4.27
3	83.87	5.13	85.05	6.12	89.22	5.68	0.3	11.59	7.77
1	91.94	4.20	96.03	4.16	95.73	4.98	0.1	30.89	5.00
0.3	96.84	3.50	98.84	4.00	98.22	4.02	0.03	94.68	5.94
GI50	>30		>30		>30		GI50	0.076	
NUGC-3	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	75.75	6.55	76.07	2.78	71.34	4.23	3	-10.63	2.56
10	79.27	9.65	82.67	5.34	78.68	0.19	1	-5.42	8.59
3	85.43	7.30	88.71	6.11	89.75	6.00	0.3	18.29	9.25
1	92.73	2.49	92.48	6.47	93.55	5.00	0.1	43.64	7.94
0.3	94.27	2.49	98.26	4.35	97.32	2.77	0.03	93.91	5.80
GI50	>30		>30		>30		GI50	0.095	
HCT-15	1		2		4		Adriamycin		
(μM)	MEAN	SD	MEAN	SD	MEAN	SD	(uM)	MEAN	SD
30	75.84	8.94	77.84	4.60	75.49	6.52	3	-7.03	2.43
10	82.36	5.39	88.67	3.30	81.85	7.82	1	-3.82	3.78
3	84.01	6.82	91.35	2.47	84.38	0.68	0.3	19.05	4.66
1	90.80	0.61	92.46	3.51	96.86	1.49	0.1	35.19	2.10
0.3	96.50	3.57	100.50	4.90	98.37	4.05	0.03	98.35	3.87
GI50	>30		>30		>30		GI50	0.084	

Table S1. Results of the cytotoxicity test of 1, 2, and 4.