Apratoxin H and Apratoxin A Sulfoxide from the Red Sea Cyanobacterium *Moorea producens*

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Contents

Table S1. NMR Spectroscopic Data for Apratoxin H (**1**) in $CDCl_3$ (500 MHz).

unit	position	δ_C, mult.	δ_H (J in Hz)[a]	COSY	HMBC	ROESY
Pip	1	172.2, C				
	2	54.4, CH	4.60, dd (7.0, 3.6)	H-3a, H-3b	1, 3, 4, 6	H-3a, H-3b
	3a	25.7, CH_2	1.82, m	H-2, H-3b		H-2
	3b		2.03, m	H-2, H-3a	1, 5	H-2, H_3-42/43/44
	4a	19.2, CH_2	1.36, m	H-4b		H-4b
	4b		1.62, m	H-4a	1, 5	H-4a
	5a	24.3, CH_2	1.56, m	H-5a, H-6b		H-5b
	5b		1.82, m	H-5b, H-6b	6 (w)[c]	H-5a, H-6a
	6a	43.1, CH_2	3.50, m	H-5a, H-5b, H-6b	4 (w)[c], 5 (w)[c]	H-5b
	6b		4.35, m	H-6a	4, 5	H-8
N-Me-Ile	7	169.7, C				
	8	54.4, CH	5.48, d (11.5)	H-9	7, 9	H-6a, H_3-12, H_3-13
	9	31.8, CH	2.29, m	H-8, H-10b, H_3-12	11	H-10b, H_3-12, H_3-13
	10a	24.6, CH_2	0.99, m	H-9, H_3-11	8, 11, 12	H-10b, H-9
	10b		1.33, m	H-9, H_3-11		H-10a, H_3-13
	11	9.0, CH_3	0.91, ob	H-10b		
	12	14.5, CH_3	0.92, ob	H-9	8	H-8, H-9
	13	30.4, CH_3	2.71, s		8, 14	H-8, H-9, H-10b, H-15, H-19, OH
N-Me-Ala	14	169.6[b], C				
	15	60.8, CH	3.31, br m	H_3-16		H_3-13, H_3-17
	16	14.0, CH_3	1.25, d (6.7)	H-15	14, 15	H_3-17
	17	36.7, CH_3	2.79, s		15, 18	H-15, H_3-16, H-19, H-22/26
O-Me-Tyr	18	170.5, C				
	19	50.6, CH	5.06, ddd (10.9, 9.5, 4.8)	H-20a, H-20b, NH	18, 20, 21	H_3-17, H-20a, NH
	20a	37.3, CH_2	2.88, dd (-12.4, 4.8)	H-19, H-20b	18, 19, 21, 22/26	H-20b, H-22/26
	20b		3.14, dd (-12.4, 4.8)	H-19, H-20a	18, 19, 21, 22/26	H-20a, H-22/26
	21	128.3, C				
	22/26	130.6, CH	7.17, d (8.5)	H-23/25	22/26, 23/25, 24	H_3-17, H-19, H-20a, H-20b, H-23/25
	23/25	113.9, CH	6.82, d (8.6)	H-22/26	21, 23/25, 24	H-22/26, H_3-27
	24	158.7, C				
	27	55.3, CH_3	3.79, s		24	H-23/25
	NH		6.05, d (9.4)	H-19	28	H-19, H_3-33
moCys	28	169.6[b], C				
	29	130.5, C				
	30	136.4, CH	6.36, br d (9.6)	H-31, H_3-33	28, 32, 33	H-31, H-32a, H-35
	31	72.6, CH	5.23, ddd (9.4, 9.1, 4.5)	H-30, H-32a, H-32b	29, 30	H-30, H-32b, H_3-33
	32a	37.6, CH_2	3.13, dd (-10.9, 4.7)	H-31, H-32b	29, 31, 34	H-30, H-32b
	32b		3.47, dd (-10.9, 8.7)	H-31, H-32a	30, 31, 34	H-31, H-32a
	33	13.4, CH_3	1.97, s	H-30	28, 29, 30, 31d, 32	H-31, NH
polyketide	34	177.1, C				
	35	48.8, CH	2.65, ob	H-36, H3-45	34, 36, 45	H-30, H-36, H-37b, H_3-45
	36	71.7, CH	3.56, dddd (10.9, 10.6, 10.4, 3.0)	H-35, H-37a, H-37b, OH		H-35, H_3-45, H_3-46
	37a	38.5, CH_2	1.11, ddd (-13.8, 10.9, 3.0)	H-36, H-37b, H-38	38	H-37b, H-38
	37b		1.46, ddd (-13.7, 11.1, 4.0)	H-36, H-37a	35, 36, 38, 46	H-35, H-37a, H-38, H-40

38	24.5, CH	2.11, br m	H-37a, H-39a, H_3-46		H-37a, H-37b, H-39b, H_3-46, OH
39a	37.8, CH_2	1.26, ob	H-38, H-39b, H-40	38	H-39b, H-40, H_3-42/43/44
39b		1.79, m	H-39a, H-40	37, 38, 40	H-38, H-39a, H-40, H_3-42/43/44
40	77.4, CH	4.90, dd (12.7, 2.2)	H-39a, H-39b	1, 39, 42/43/44	H-37b, H-39a, H-39b, H_3-42/43/44
41	34.9, C				
42/43/44	3 × 26.1, CH_3	3 × 0.89, s		40, 41, 42/43/44	H-3b, H-39a, H-39b, H-40
45	16.7, CH_3	1.06, d (6.9)	H-35	34, 35, 36	H-35, H-36
46	19.9, CH_3	1.01, d (6.7)	H-38	36d, 37, 38, 39	H-36, H-38
OH		4.40, d (10.9)	H-36	36	H_3-13, H-38

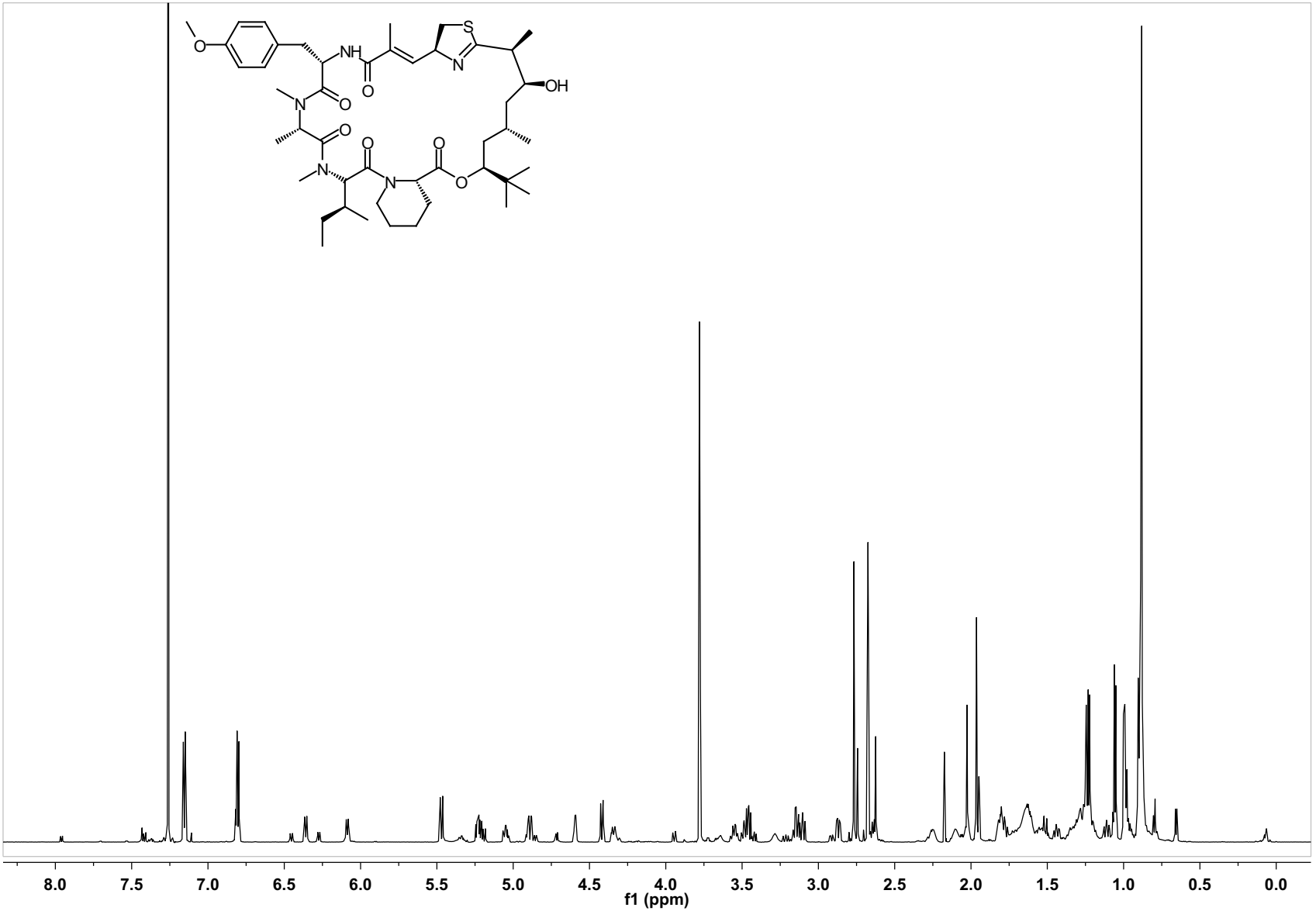
[a] *J* values obtained from ^{1}H spectrum recorded at 700 MHz. [b] These carbons have the same chemical shift. [c](w) indicates a weak correlation. [d] Four-bond HMBC correlation. ob = obscured.

Table S2. NMR Spectroscopic Data for Apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz).

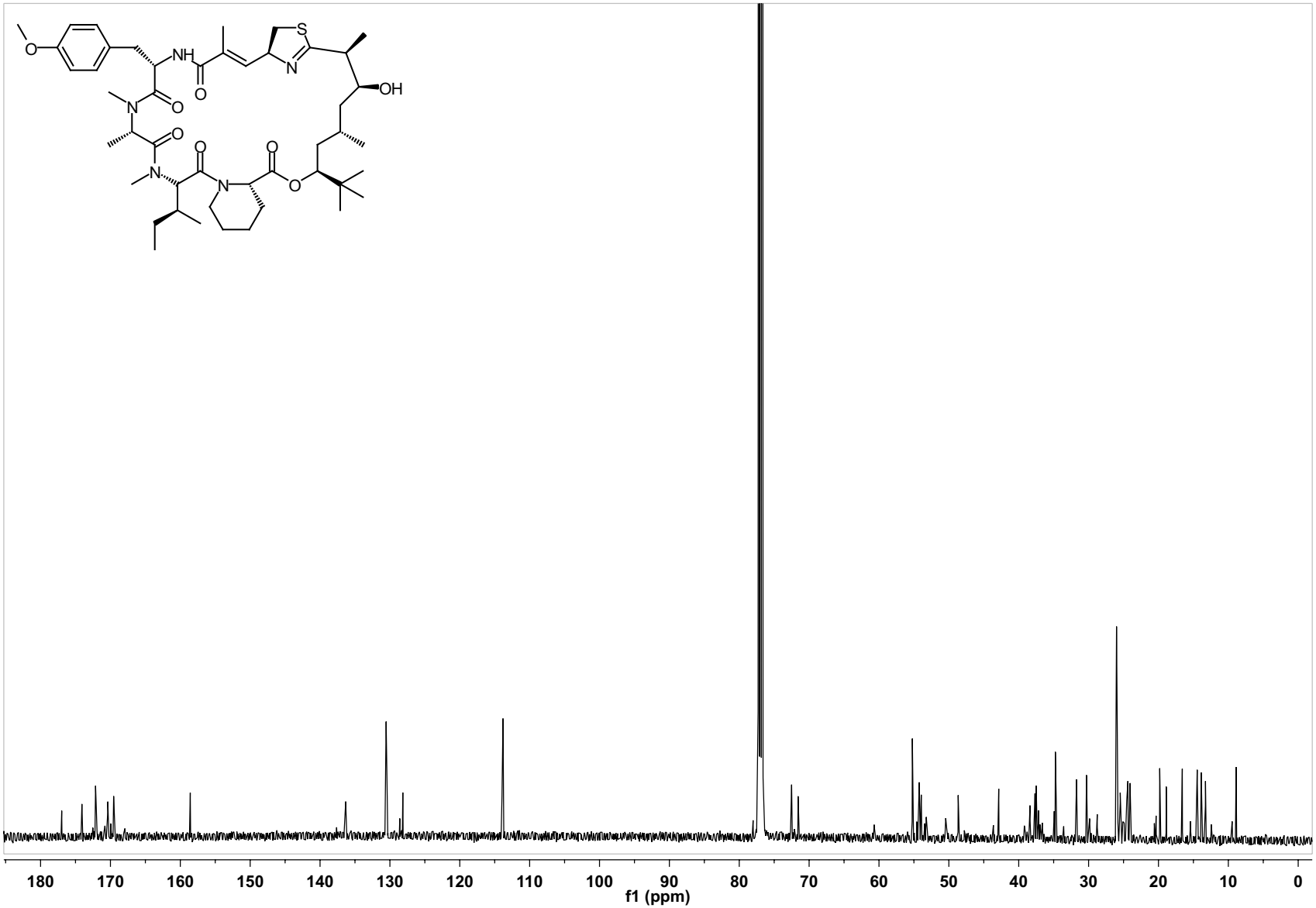
unit	position	δ_C, mult.	δ_H (*J* in Hz)	COSY	HMBC	ROESY
Pro	1	172.6, C				
	2	59.8, CH	4.22, br t (7.4)	H-3a, H-3b	1, 3	H-3a, H-3b, H-4b
	3a	29.5, CH_2	1.90, m	H-2, H-3b	1, 4	H-2
	3b		2.26, m	H-2, H-3a	1, 4, 5	H-2
	4a	25.7, CH_2	1.92, m	H-5a, H-5b		H-5b
	4b		2.06, m	H-5a, H-5b	2, 3	H-2, H-5b
	5a	48.0, CH_2	3.69, m	H-4a, H-4b, H-5b	3, 4	H-5b, H-7
	5b		4.18, m	H-4a, H-4b, H-5a	3, 4	H-4a, H-4b, H-5a, H-7
N-Me-Ile	6	170.5, C				
	7	57.3, CH	5.23, d (11.5)	H-8	6, 8	H-5a, H-5b, H-8, H_3-12
	8	32.2, CH	2.18, m	H-7 H_3-11	11	H-7, H_3-11, H_3-12
	9a	25.0, CH_2	0.99, m	H-9b	10, 11	H-9b
	9b		1.36, m	H-9a, H_3-10		H-9a, H_3-10
	10	9.6, CH_3	0.95, d (7.5)	H-9b	8, 9	H-9b
	11	14.5, CH_3	0.97, d (7.3)	H-8	7, 8, 9	H-8
	12	30.5, CH_3	2.66, s		7, 13	H-7, H-8, H-14, H-29, OH
N-Me-Ala	13	170.2, C				
	14	60.8, CH	3.31, m	H_3-15	13, 15	H_3-12, H_3-15, H_3-16
	15	14.1, CH_3	1.23, d (6.6)	H-14	13, 14	H-14, H_3-16
	16	36.9, CH_3	2.82, s		14, 17	H-14, H-18, H_3-15, OH
O-Me-Tyr	17	170.5, C				
	18	50.8, CH	5.05, m	H-19a, H-19b, NH	17, 19	H_3-16, H-19a, H-19b, H-21/25, NH
	19a	37.2, CH_2	2.88, dd (-12.5, 4.5)	H-18, H-19b	17, 18, 20, 21/25	H-18, H-19b
	19b		3.14, m	H-18, H-19a	17, 18, 20, 21/25	H-18, H-19a, NH
	20	128.4, C				
	21/25	130.8, CH	7.17, d (8.5)	H-22/24	19, 21/25, 22/24, 23	H-18, H_3-26
	22/24	114.1, CH	6.80, d (8.5)	H-21/25	20, 22/24, 23	H_3-26
	23	158.9, C				
	26	55.5, CH_3	3.79, s		23	H-21/25, H-22/24
	NH		6.05, d (9.5)	H-18	27	H-18, H-19b, H_3-32
moCys	27	169.5, C				
	28	133.8, C				
	29	135.0	5.90, d (9.9)	H-30, H_3-32	27, 30, 31, 32	H_3-12, H-30, H-31a, H-32
	30	71.8, CH	5.70, m	H-29, H-31a, H-31b	28, 29, 31, 33	H-29, H-31a, H-31b
	31a	57.0, CH_2	2.78, dd (-13.9, 5.7)	H-30, H-31b	29, 30, 33	H-29, H-30, H-31b
	31b		3.32, dd (-14.0, 5.9)	H-31a	29, 33	H-30, H-31a
	32	13.6, CH_3	2.0, s	H-29	27, 28, 29	H-29, H-30, NH
polyketide	33	177.2, C				
	34	48.7, CH	2.84, dq (10.5, 7.0)	H-35, H_3-44	33, 35, 44	H-35, H-36b, H_3-44, OH
	35	70.8, CH	3.89, dddd (11.1, 0.8, 10.5, 3.5)	H-34, H-36a, H-36b, OH		H-34, H-36a H_3-44, H_3-45, OH
	36a	37.9, CH_2	1.24, m	H-35, H-36b, H-37	38	H-35, H-36b
	36b		1.61, m	H-35, H-36a, H-37	34, 36, 45	H-34, H-36a, H-39, OH
	37	24.7, CH	2.12, m	H-36a, H-36b, H-38b, H_3-45		H-39, H_3-45
	38a	37.6, CH_2	1.31, ob	H-38b, H-39	37	H-38b, H-39
	38b		1.82, m	H-37, H-38a	36	H-38a, H-39
	39	77.7, CH	4.98, dd (12.6, 2.2)	H-38a	1, 40, 41/42/43	H-36b, H-37, H-38a,

					H-38b, H_3-41/42/43
40	35.1, C				
41/42/43	3 × 26.3, CH_3	3 × 0.89, s		39, 40, 41/42/43	H-39
44	15.7, CH_3	1.35, d (7.0)	H-34	33, 34, 35	H-34, H-35
45	20.0, CH_3	1.01, d (6.5)	H-37	37, 38	H-35, H-37
OH		4.65, d (11.5)	H-35	35	H_3-12, H_3-16, H-34, H-35, H-36b, H-37

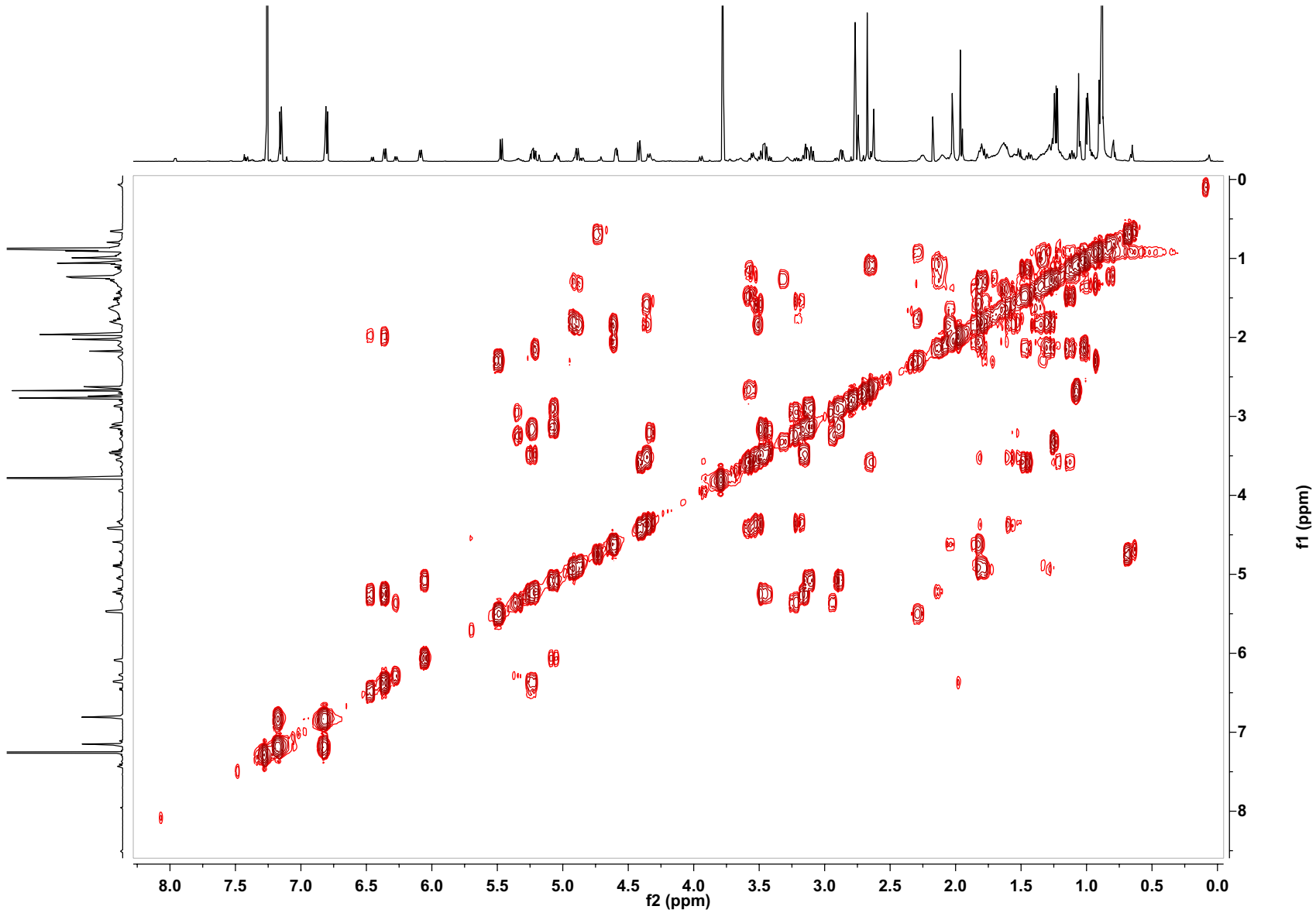
ob = obscured.



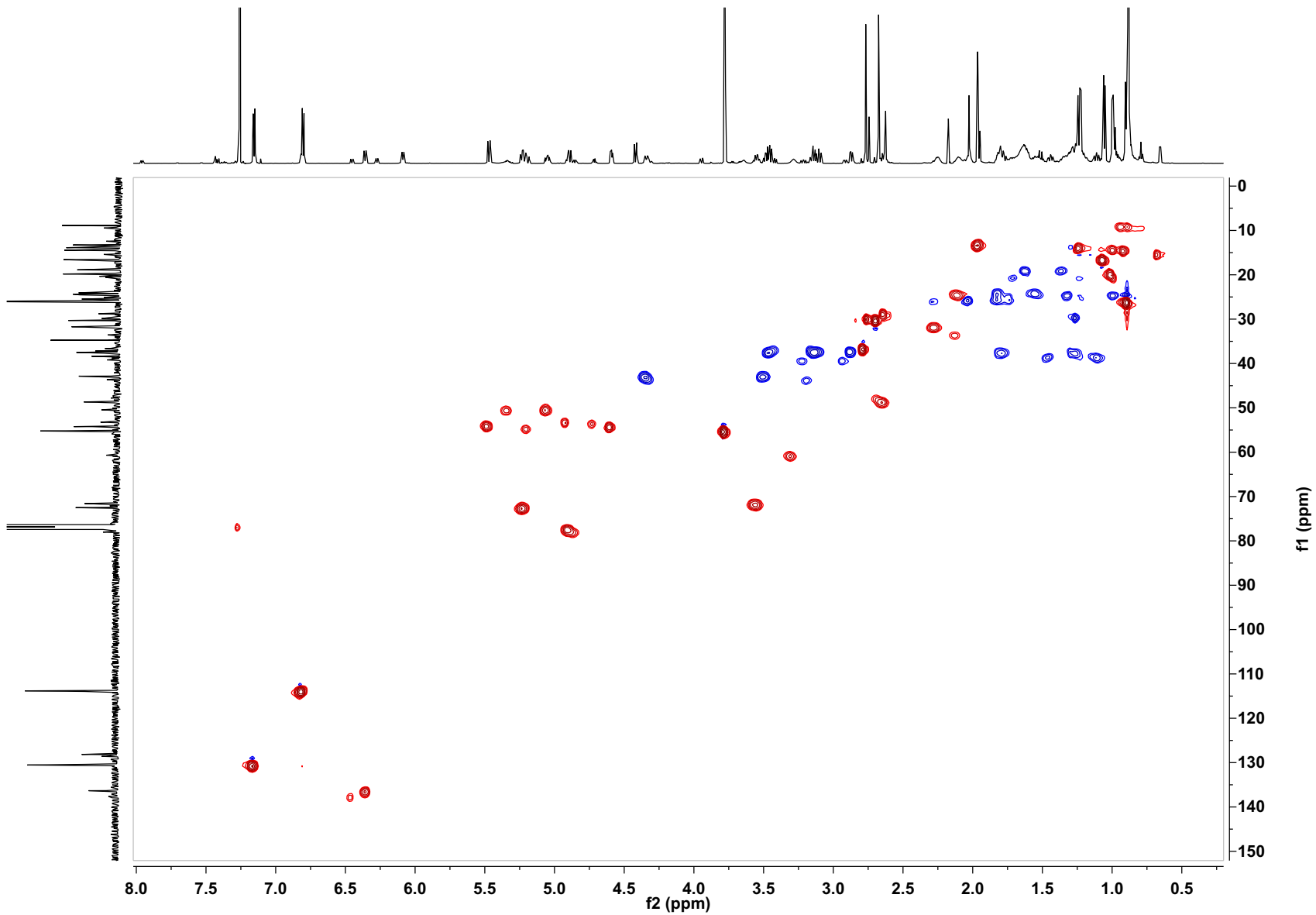
S3. ^{1}H NMR spectrum for apratoxin H (**1**) in $CDCl_3$ (500 MHz)



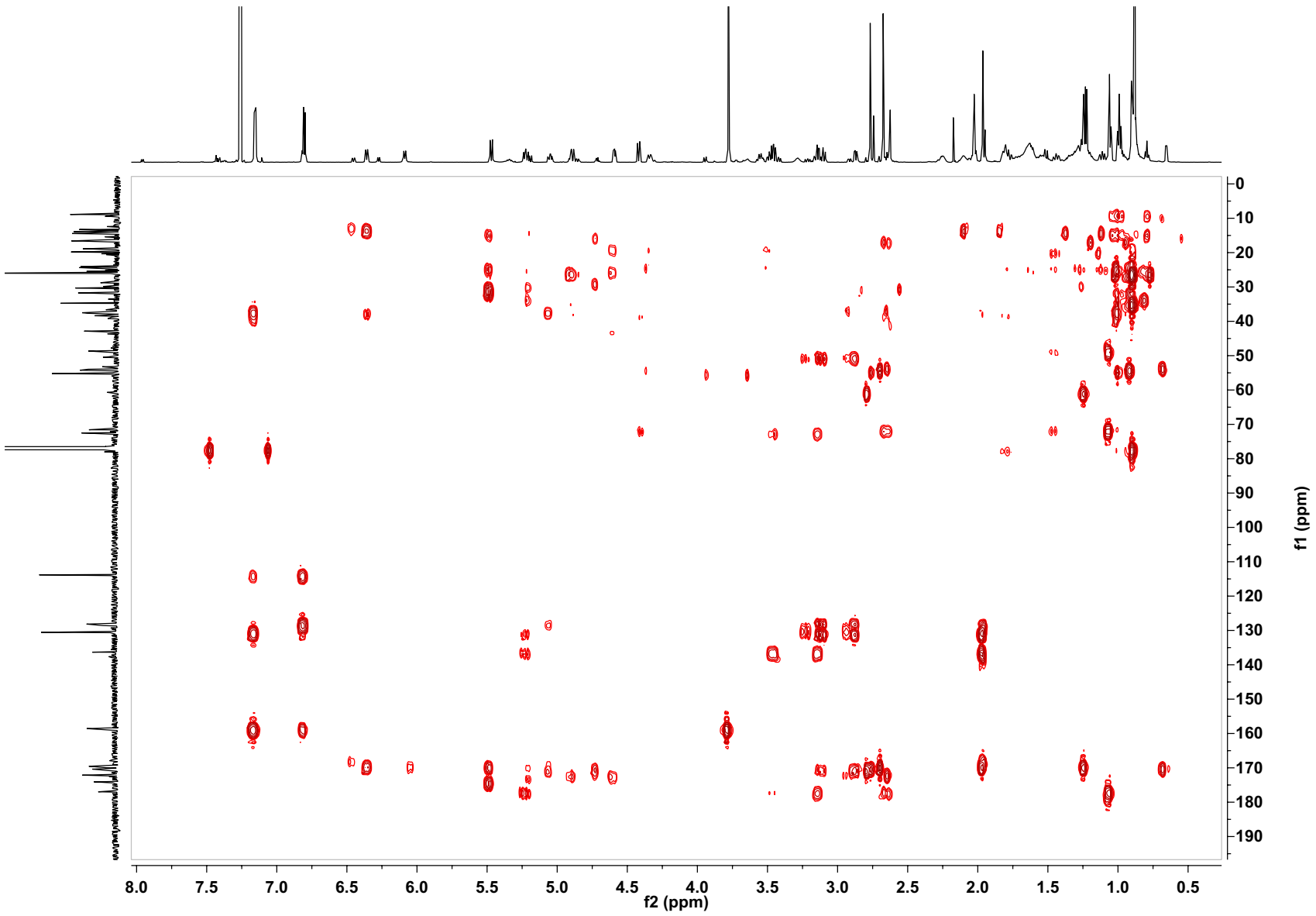
S4. ^{13}C NMR spectrum for apratoxin H (**1**) in $CDCl_3$ (125 MHz)



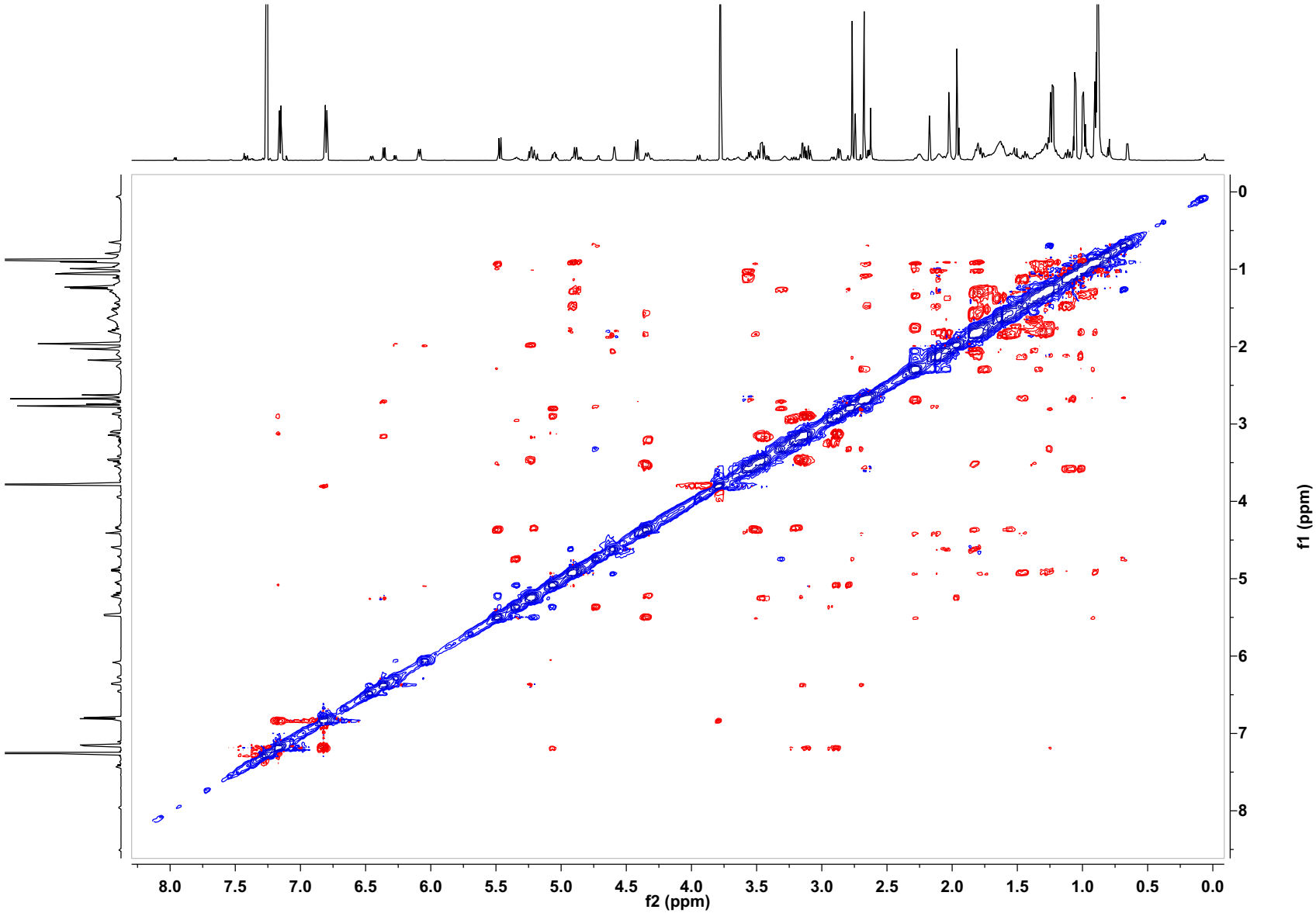
S5. DQF COSY spectrum for apratoxin H (**1**) in $CDCl_3$ (500 MHz)



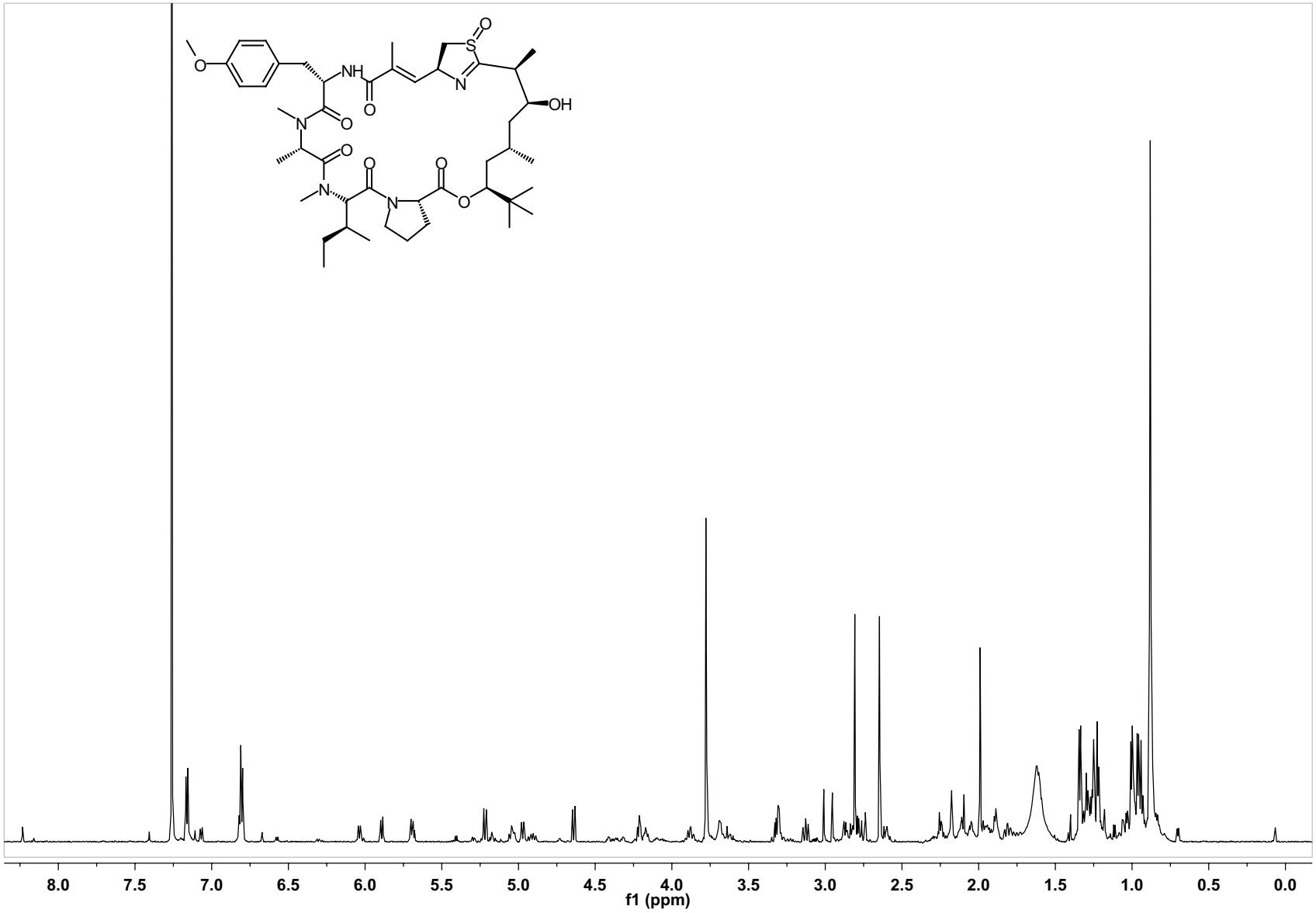
S.6. Multiplicity-edited HSQC spectrum for apratoxin H (**1**) in $CDCl_3$ (500 MHz)



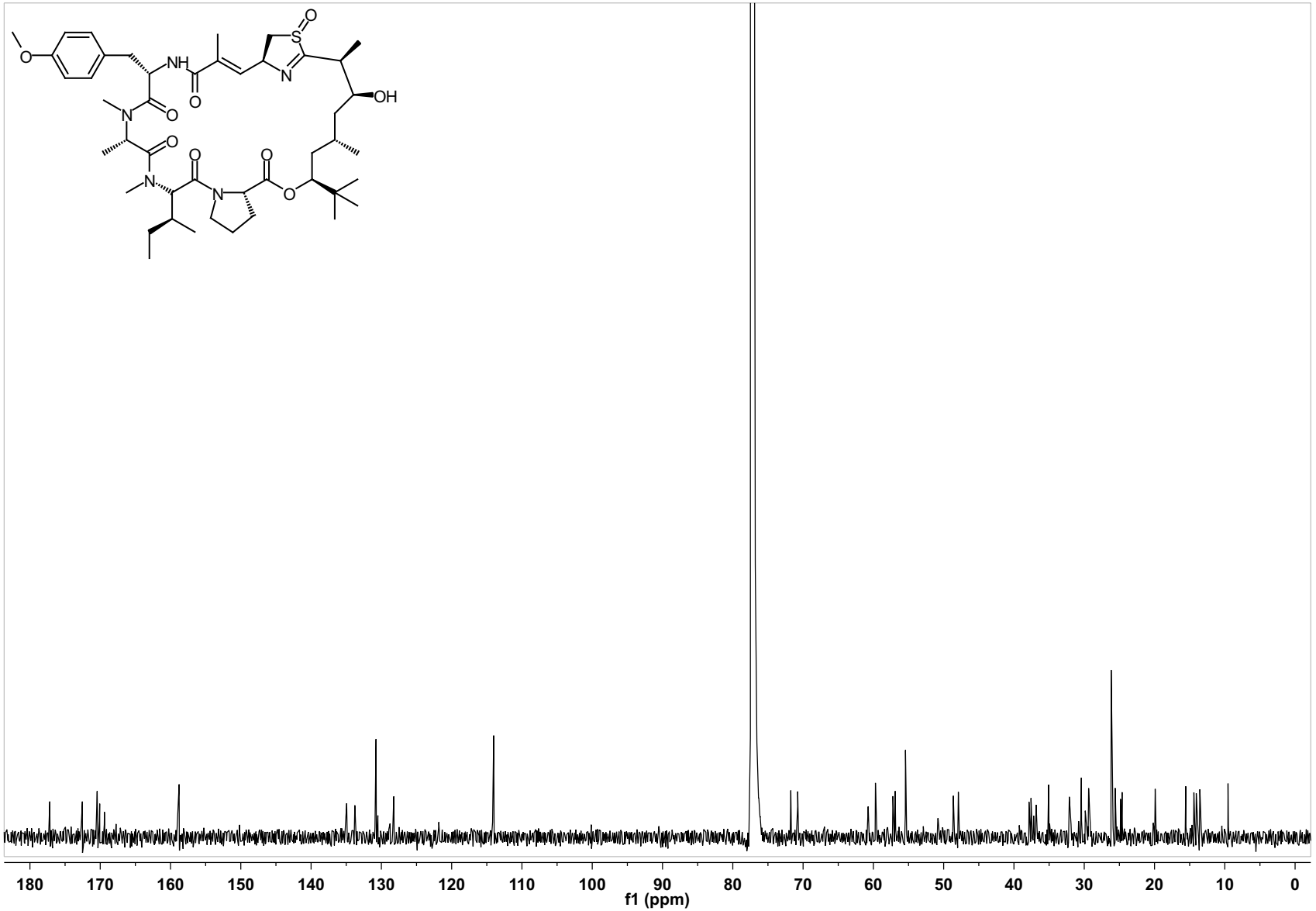
S7. HMBC spectrum for apratoxin H (**1**) in $CDCl_3$ (500 MHz)



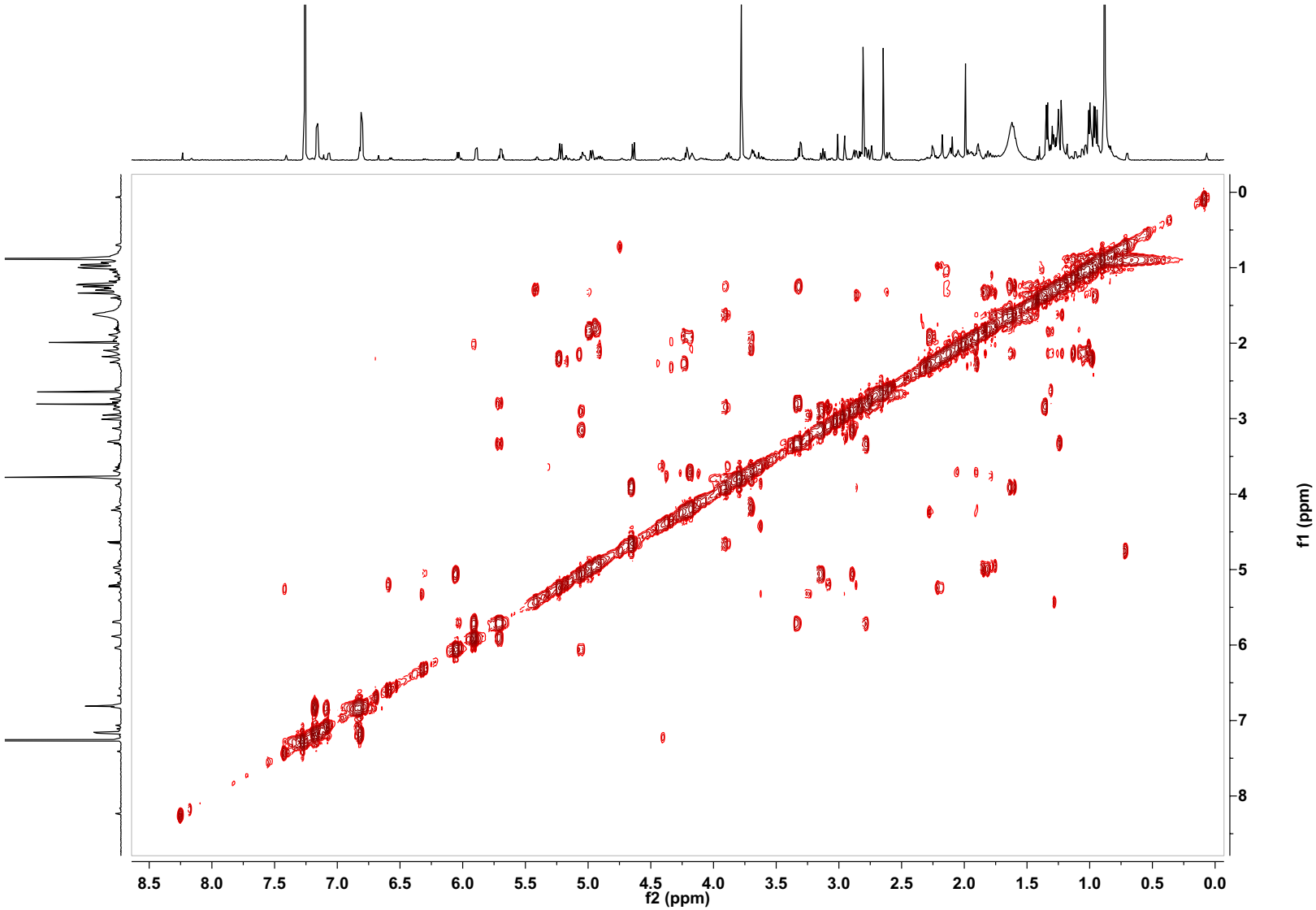
S8. ROESY spectrum for apratoxin H (**1**) in $CDCl_3$ (500 MHz)



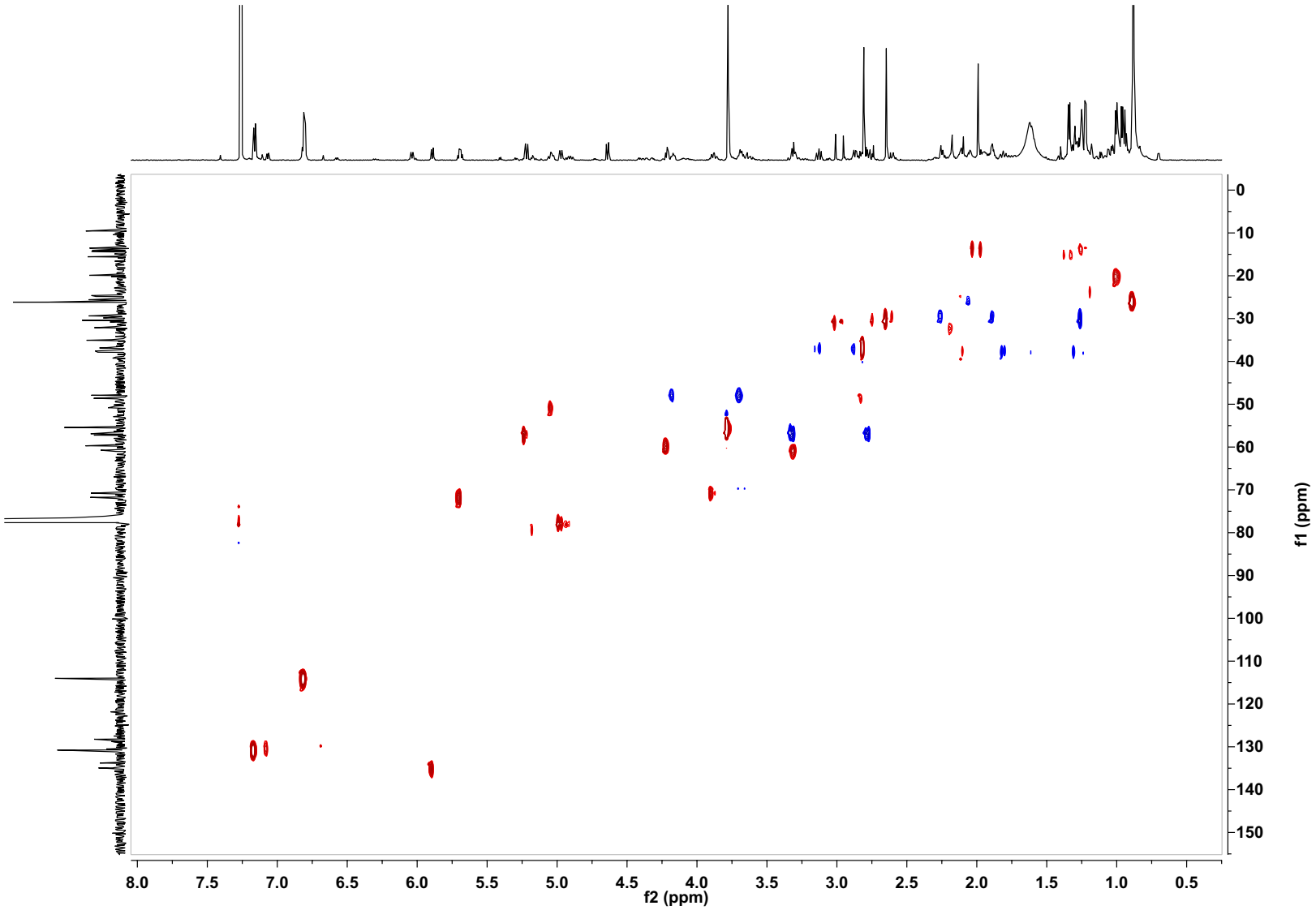
S9. ^{1}H NMR spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz)



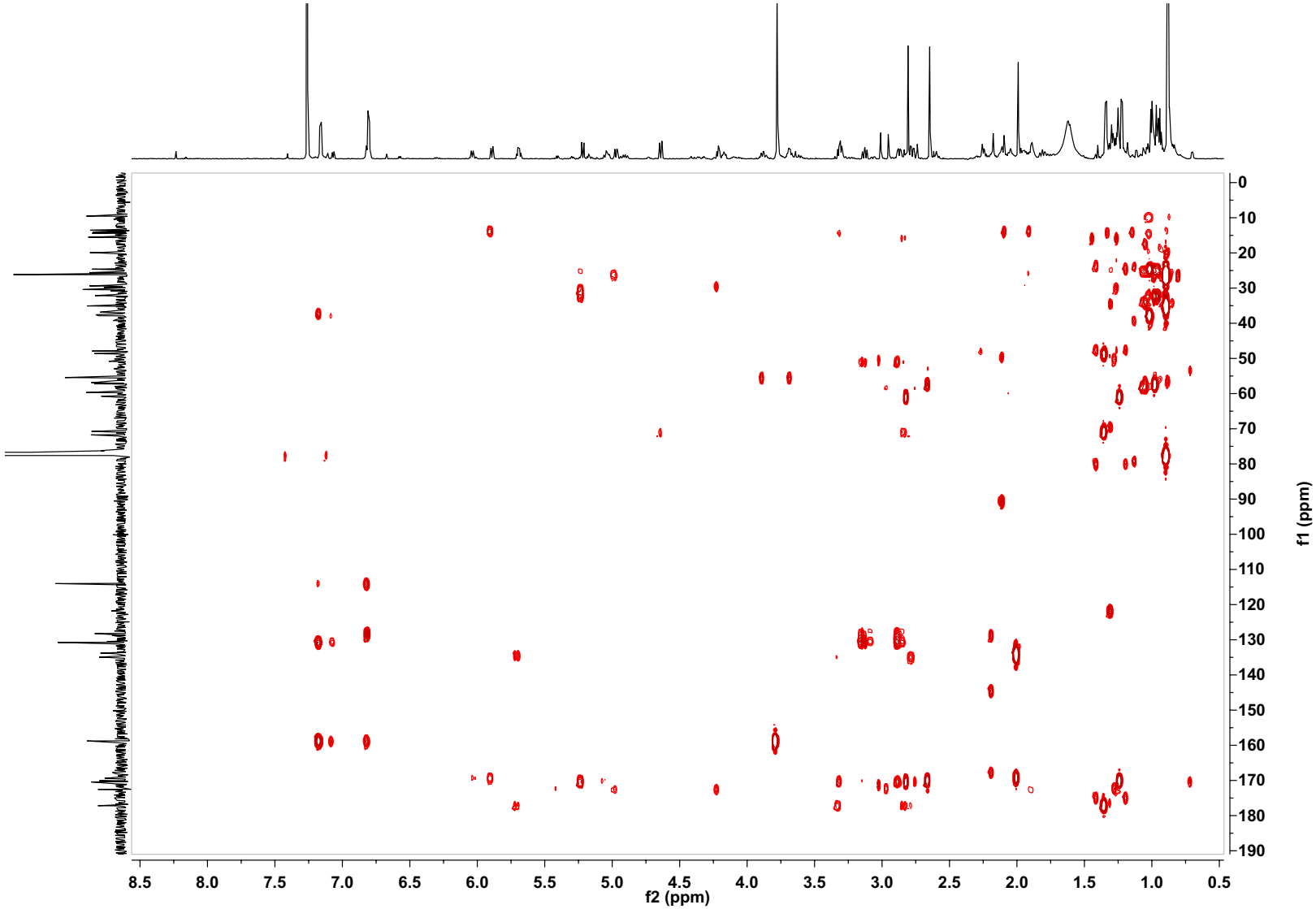
S10. ^{13}C NMR spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (175 MHz)



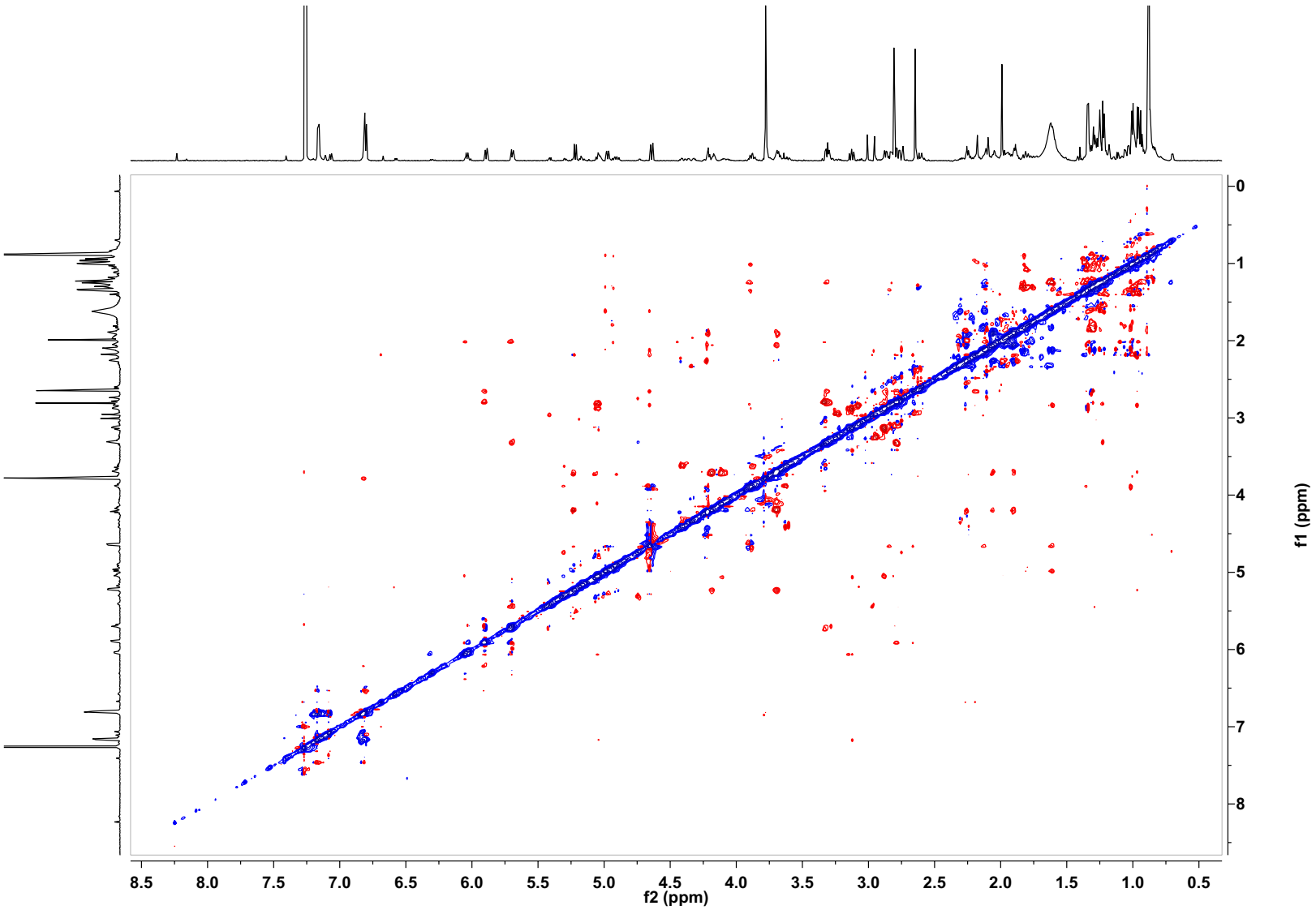
S11. COSY spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz)



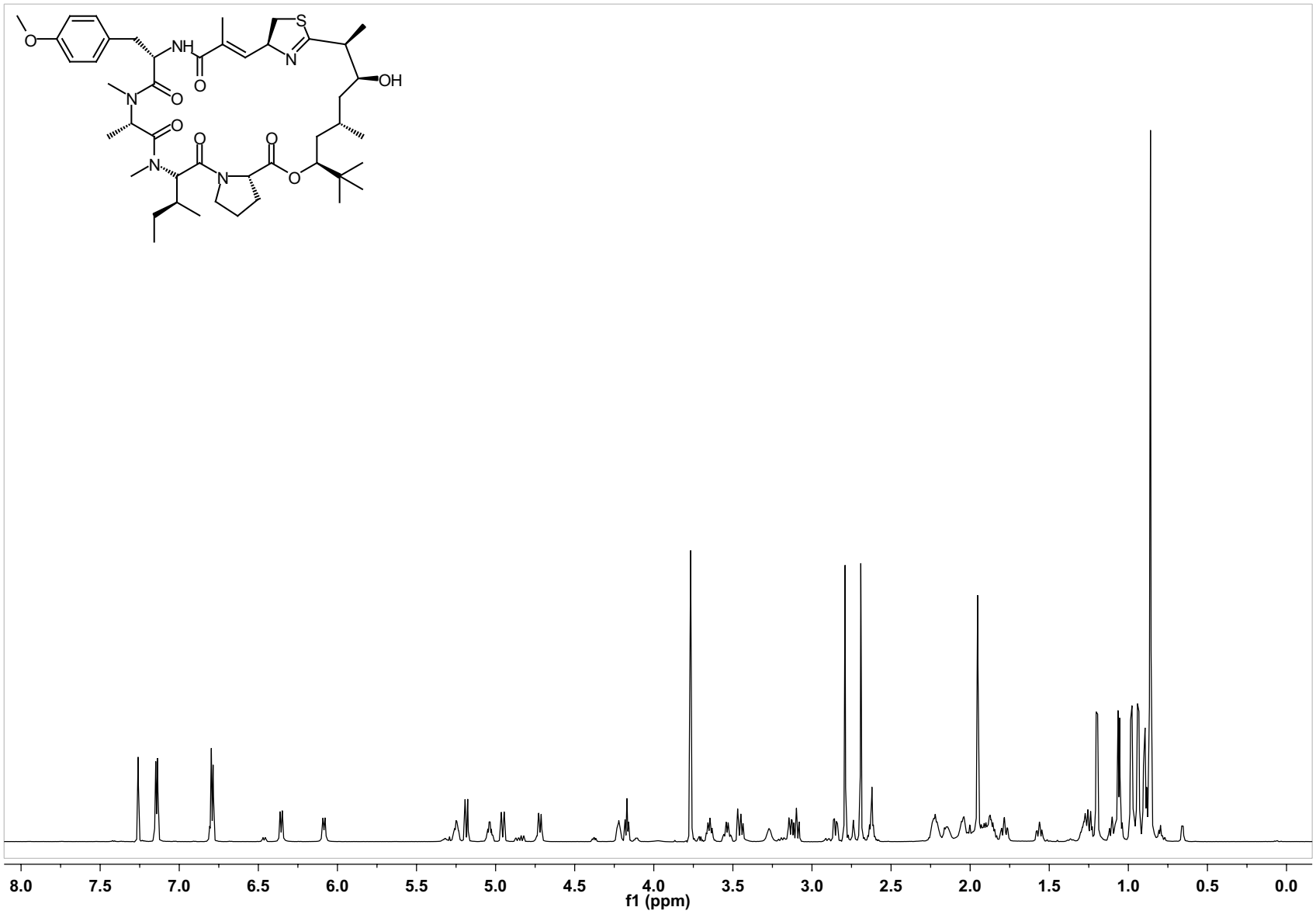
S12. Multiplicity-edited HSQC spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz)



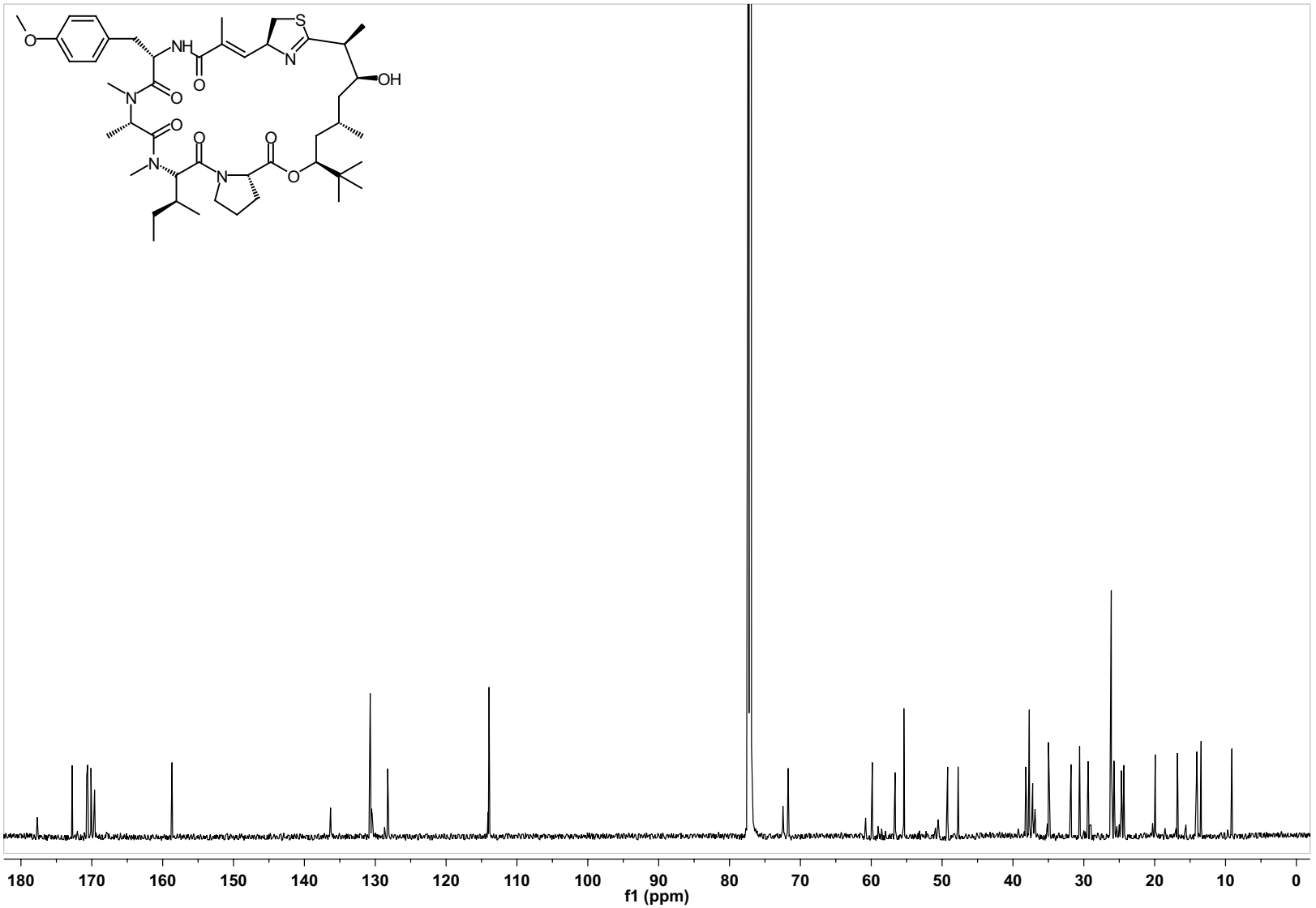
S13. HMBC spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz)



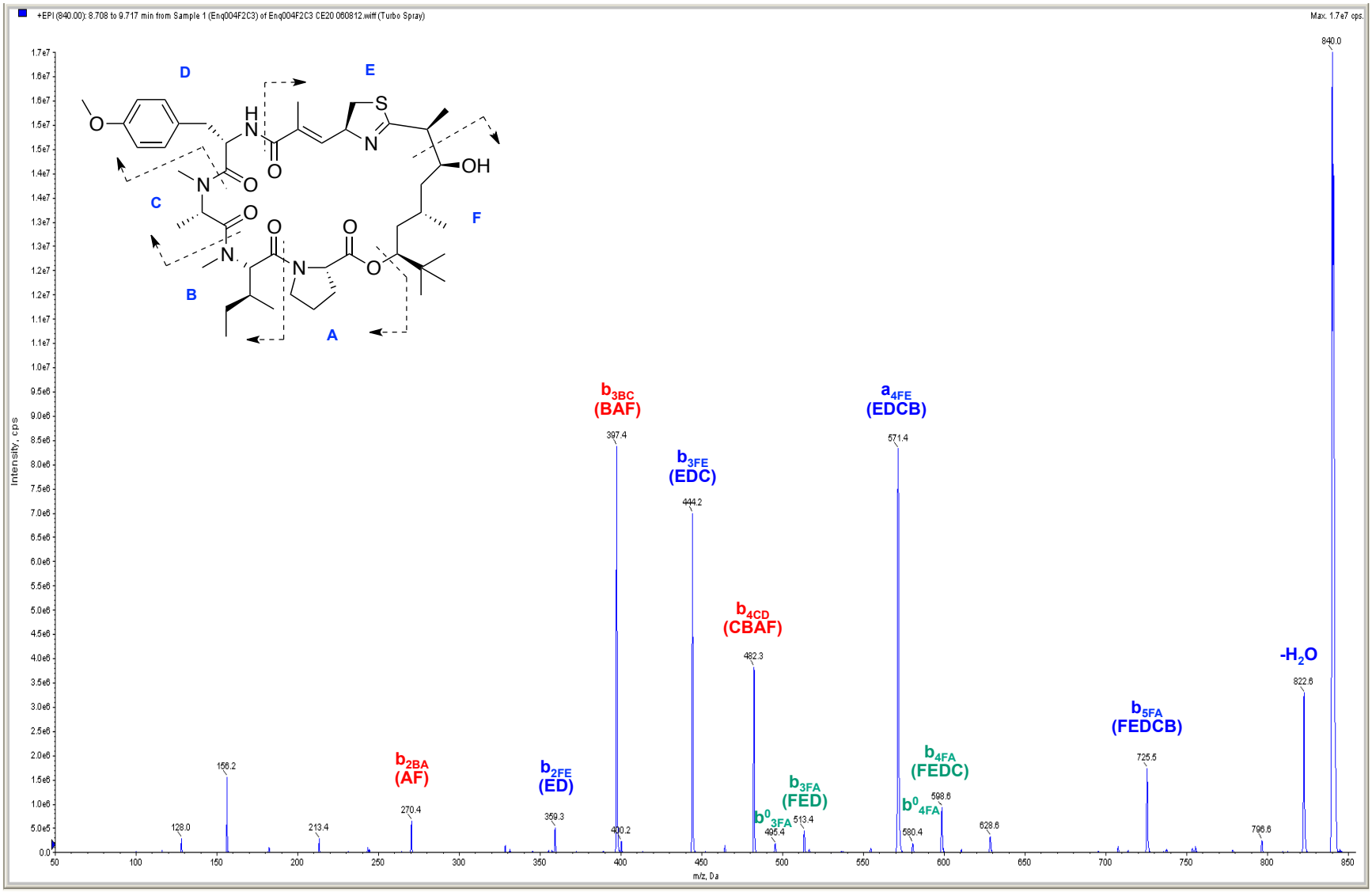
S14. ROESY spectrum for apratoxin A sulfoxide (**2**) in $CDCl_3$ (700 MHz)



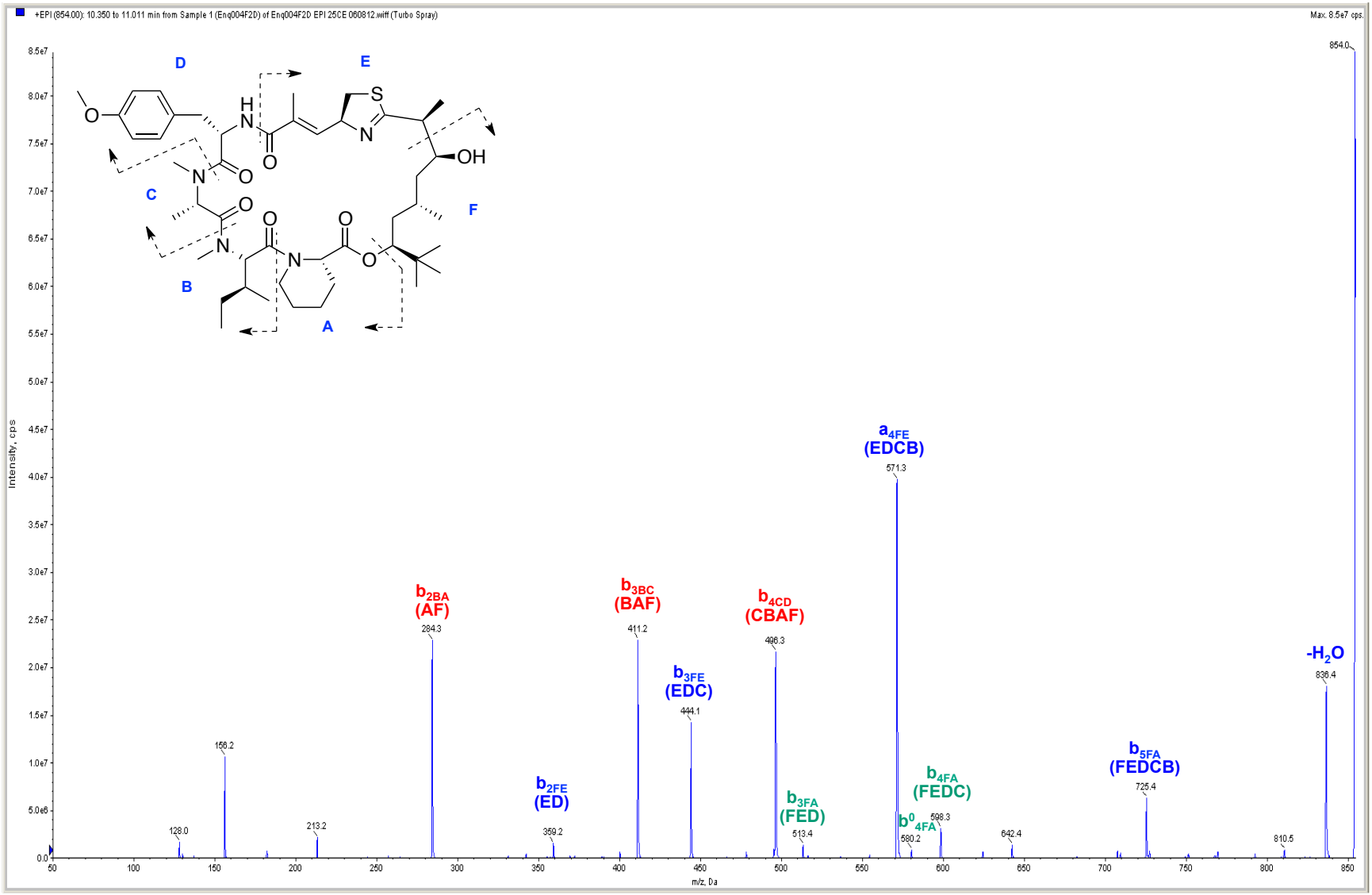
S15. ^{1}H NMR spectrum for apratoxin A in $CDCl_3$ (700 MHz)



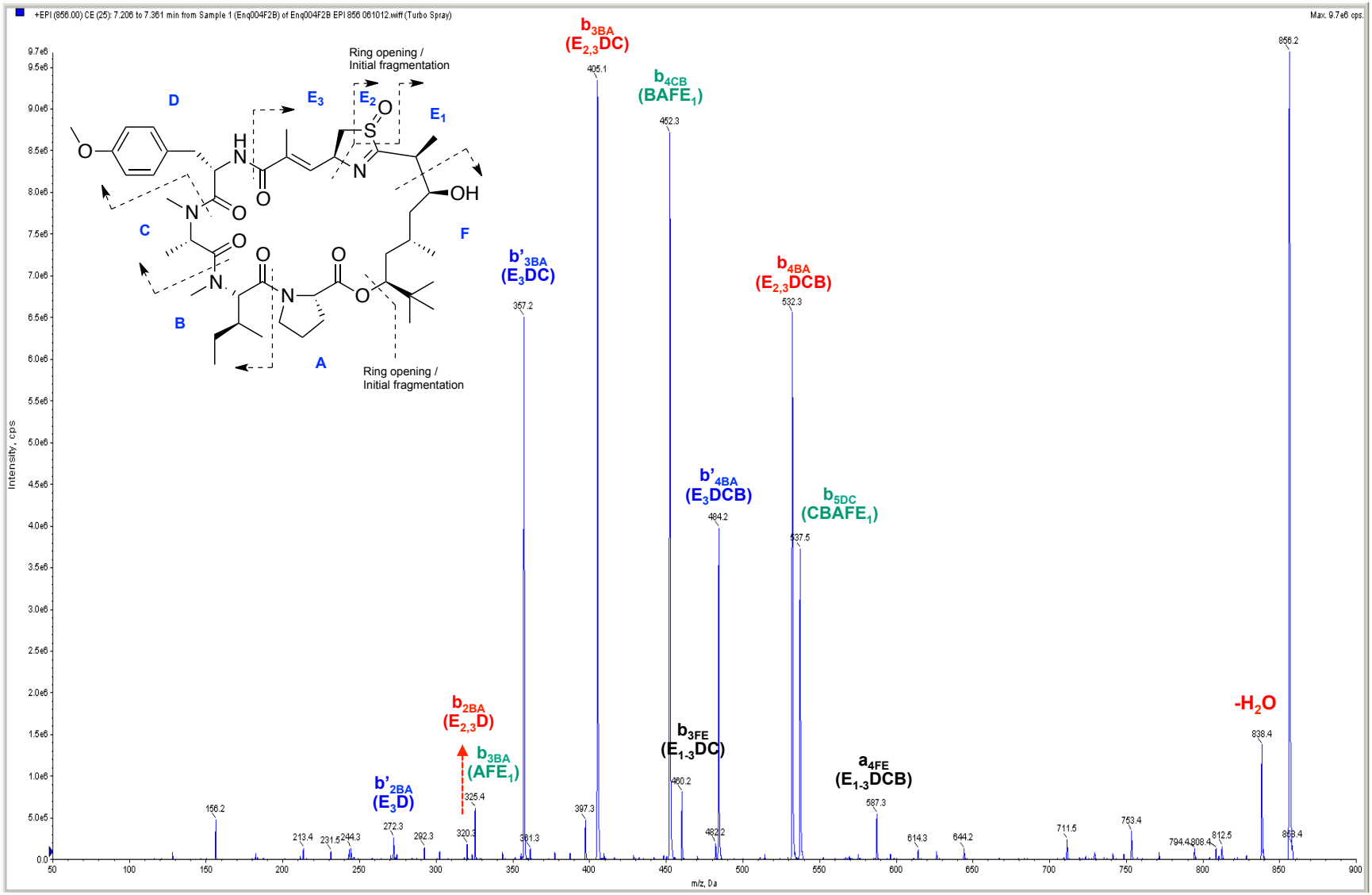
S16. ^{13}C NMR spectrum for apratoxin A in $CDCl_3$ (175 MHz)



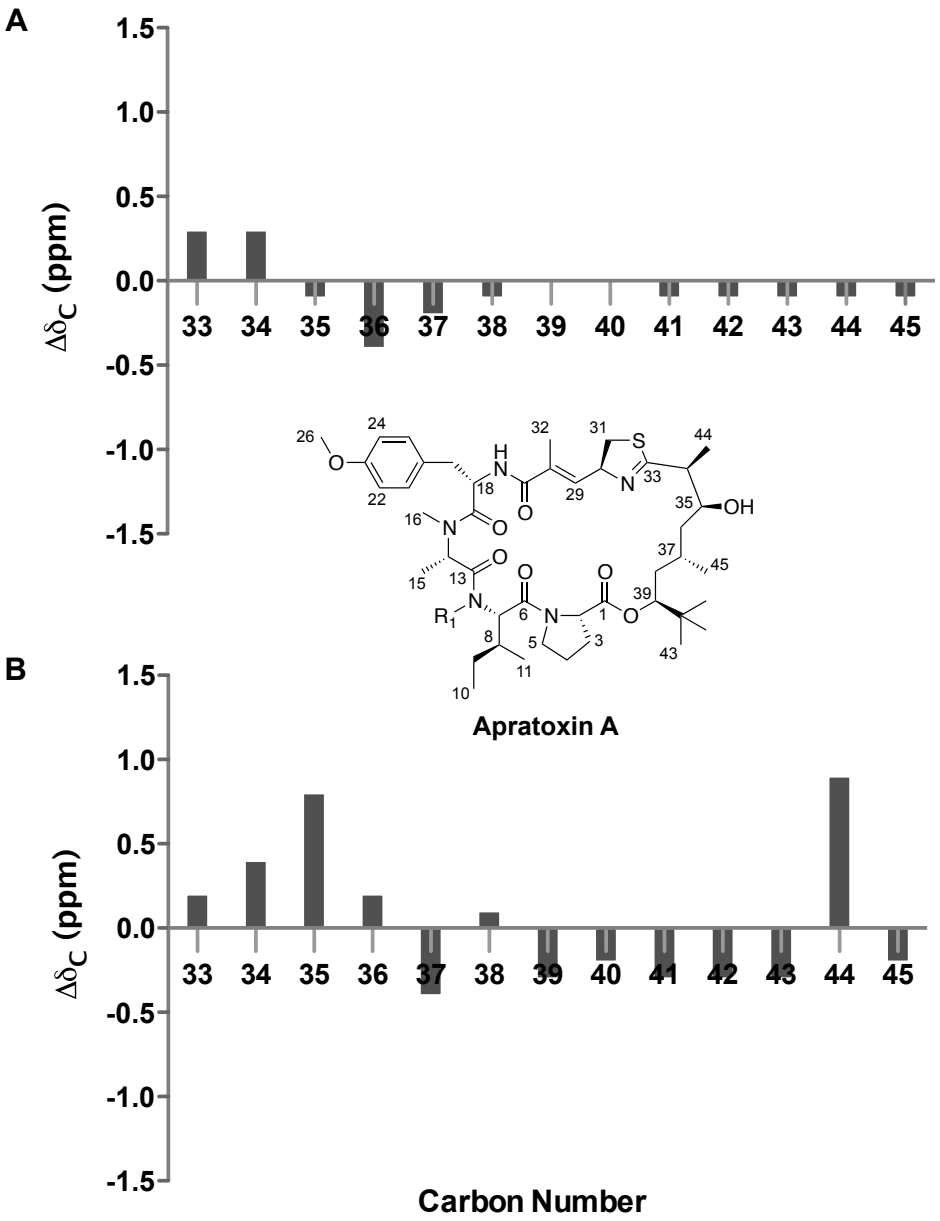
S17. Annotated MS/MS spectrum of apratoxin A



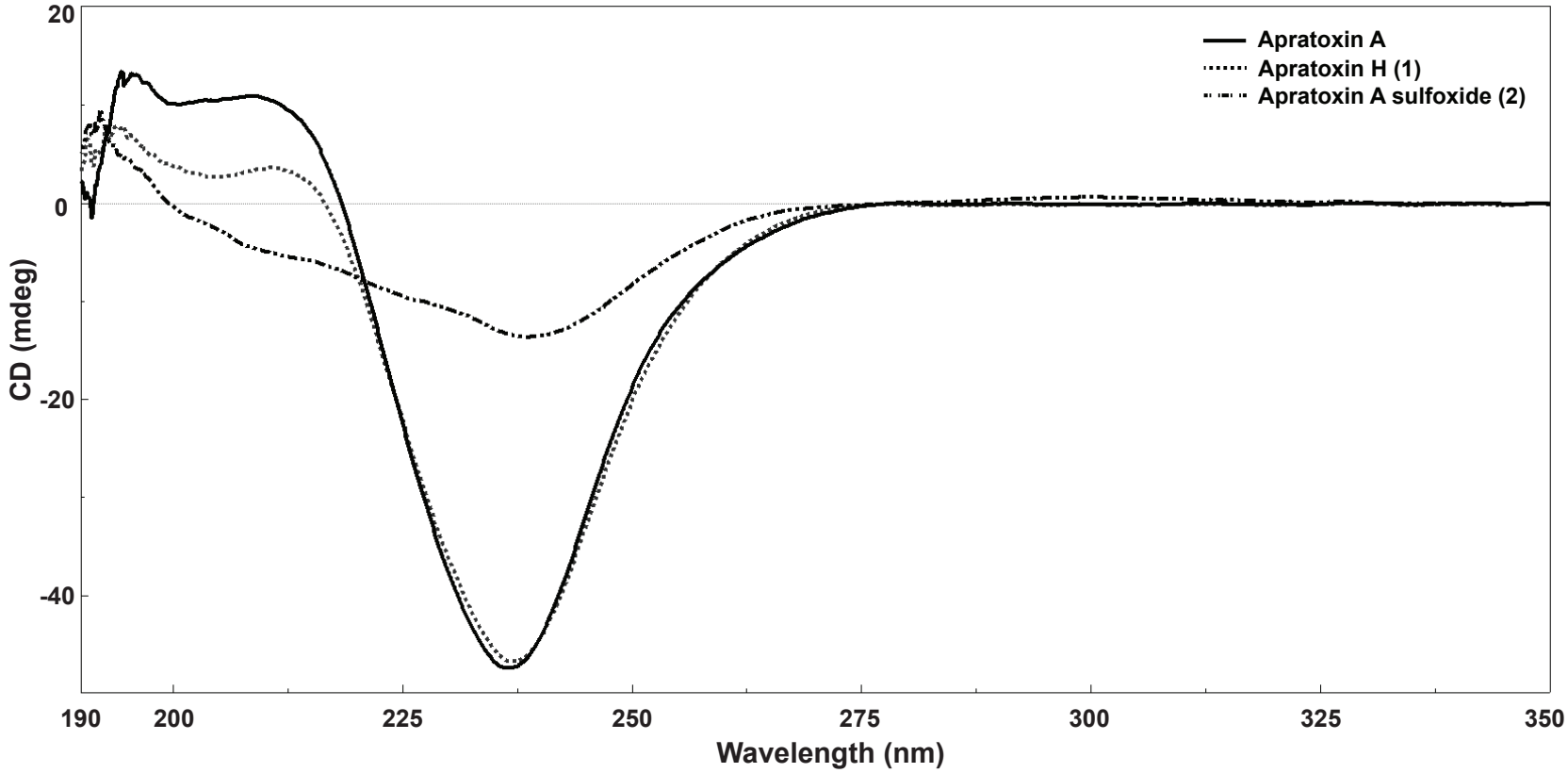
S18. Annotated MS/MS spectrum of apratoxin H (**1**)



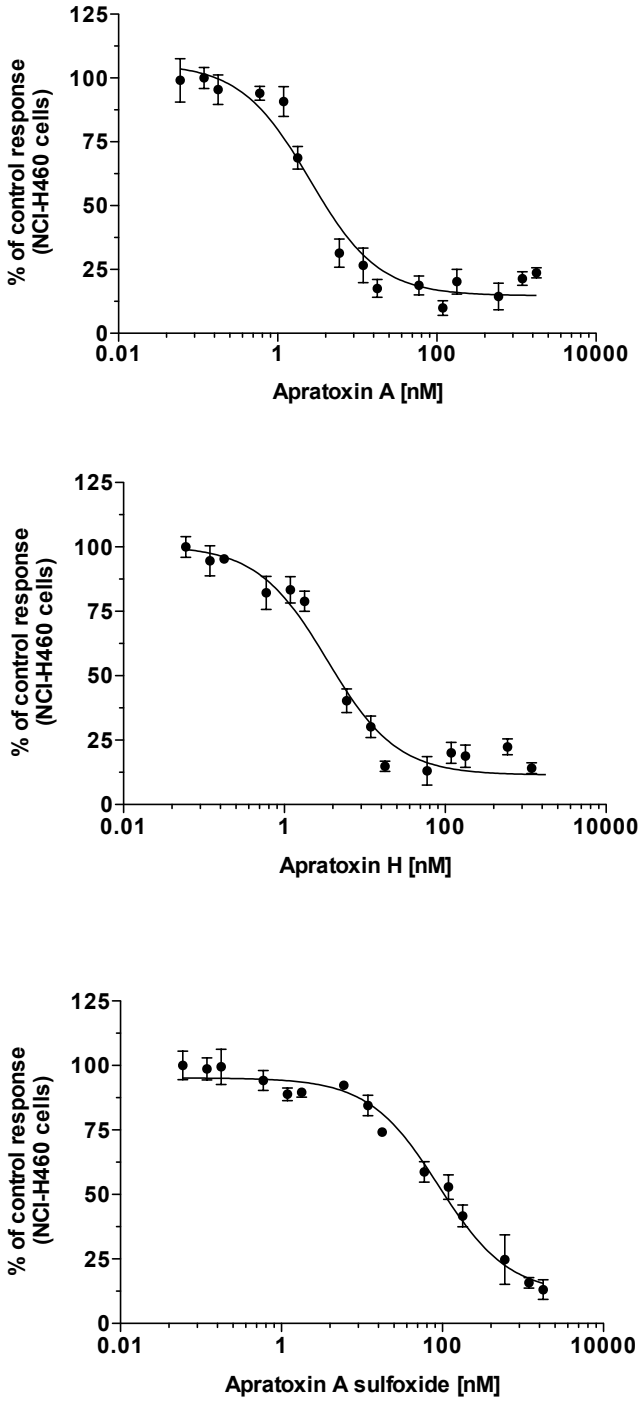
S19. Annotated MS/MS spectrum of apratoxin A sulfoxide (**2**)



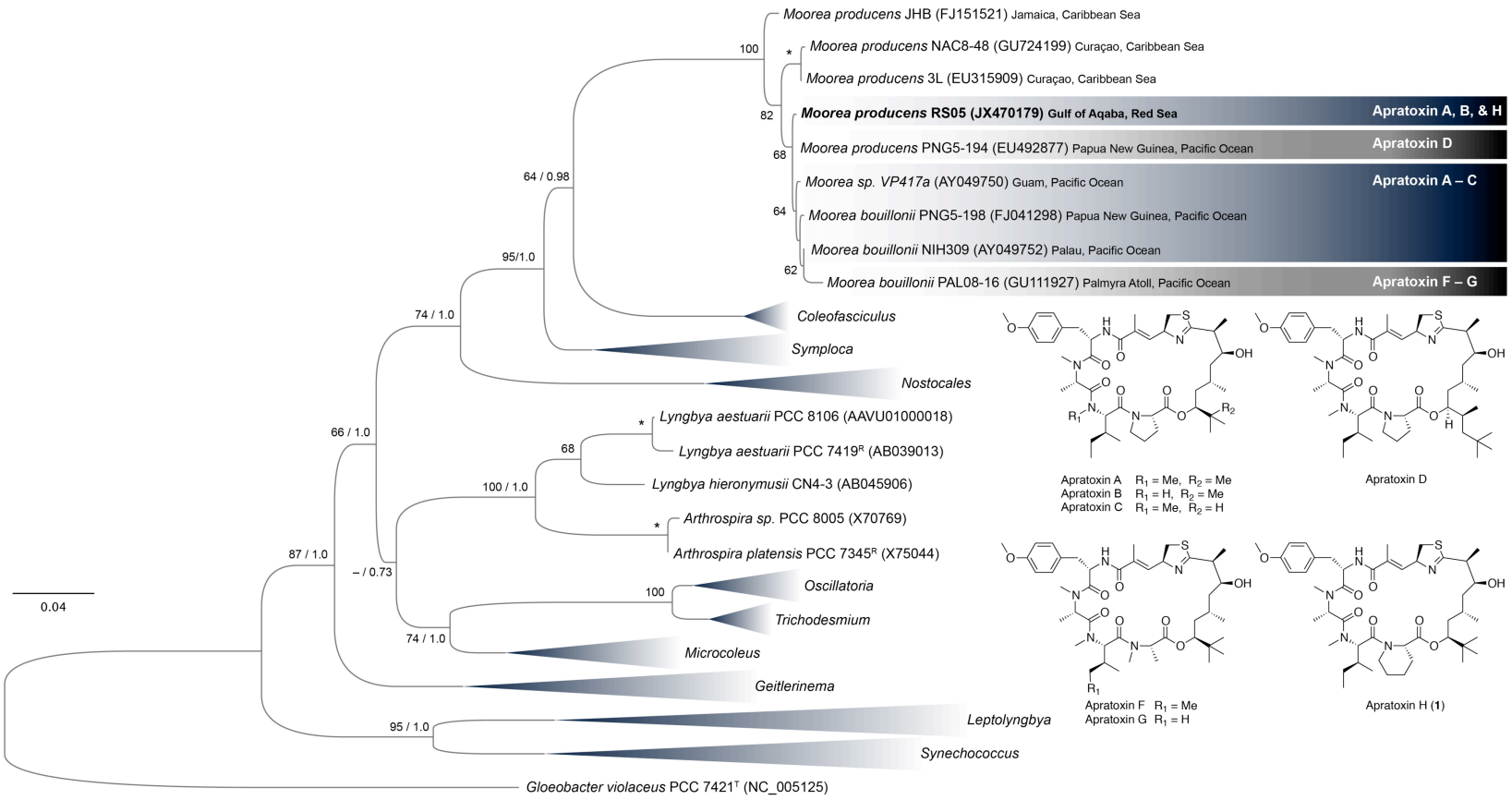
S20. Differential ^{13}C NMR chemical shifts of the polyketide moiety in apratoxin A versus: A) apratoxin H (**1**), and B) apratoxin A sulfoxide (**2**).



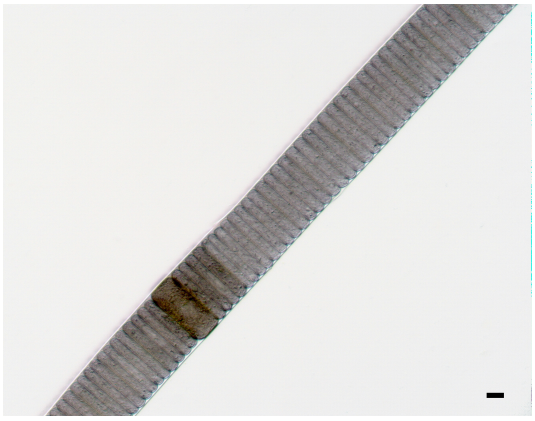
S21. CD spectra for apratoxins A, H (**1**) and apratoxin A sulfoxide (**2**).

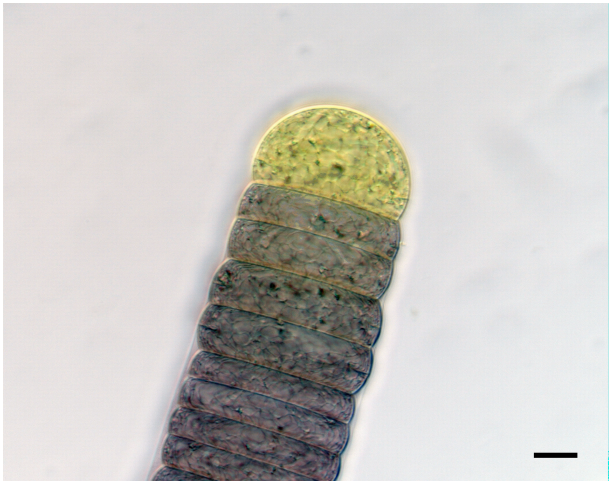


S22. Concentration-response profiles for apratoxin A, apratoxin H (1) and apratoxin A sulfoxide (2) against human NCI-H460 lung cancer cells. Cell viability was assessed after 48 hours using a colorimetric MTT cell viability. Data represent mean cell viability ± S.E. (n = 3) with the viability of vehicle-treated cells defined as 100 %.



S23. Phylogenetic relationship of the apratoxin-producing cyanobacteria with other marine filamentous cyanobacteria based on SSU (16S) rRNA gene sequences. Labels on the terminal nodes indicate the taxa, strain, GenBank accession numbers in parenthesis, and collection sites for relevant strains. Reference (^{R}) or type strains (^{T}) are included within each cyanobacterial group. The support values at important nodes are indicated as bootstrap and posterior probability for the maximum-likelihood (PhyML) and Bayesian inference (MrBayes) methods (* = bootstrap of > 98% and a posterior probability of 1.0). Support values < 60 are not indicated. The scale bar indicates 0.04 expected nucleotide substitutions per site.





S24. Laboratory cultured *Moorea* sp. RS05 (JX470179) and corresponding photomicrographs (x400 and x1000, respectively). Scale bar = 10 μm.