Supporting Information

Multigram Scale Synthesis of A21, a New Antibiotic Equally Effective and Less Toxic Than Amphotericin B.

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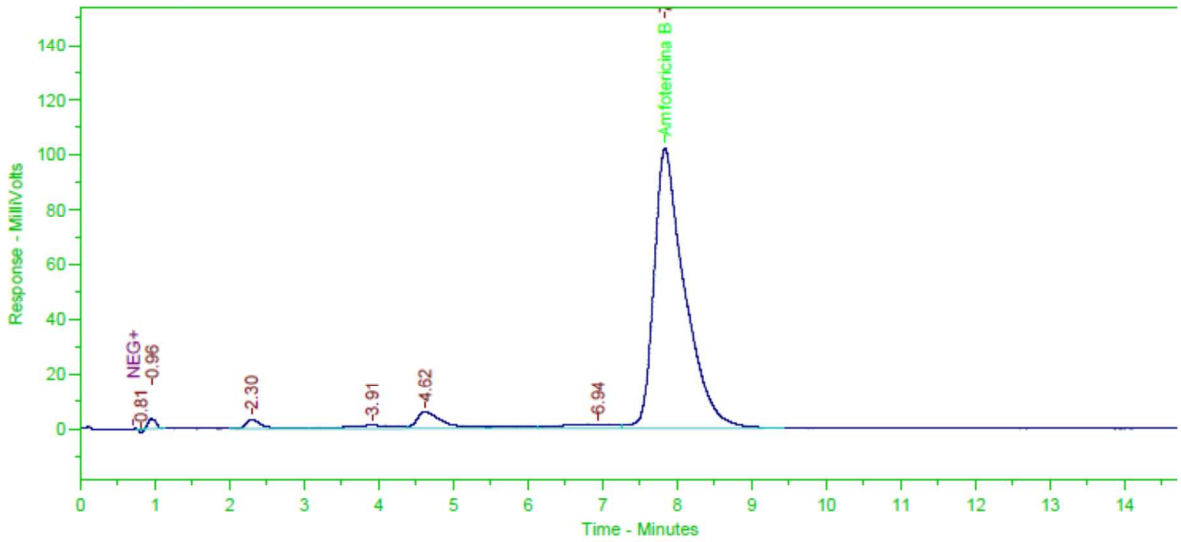
Sample Name = **Amfotericina USP 1**

Instrument = Instrument 1
Heading 1 = CH3CN/ Buffer AcOH/Et3N 30 mmolar pH4, (30:70)
Heading 2 = A-21, 0.125 mg/mL, 1 mL/min 383 nm

Symmetry C18 3.5 µm 4.6x75mm



Peak #	Ret. Time	Amount	Amt %	Area	Area %	Type	Width
1	0.81	0.00	N/A	4290	0.131	BB N	0.06
2	0.96	0.00	N/A	25881	0.789	BB	0.12
3	2.30	0.00	N/A	50911	1.552	BV	0.19
4	3.91	0.00	N/A	56141	1.712	VV	0.79
5	4.62	0.00	N/A	146860	4.477	VV	0.30
6	6.94	0.00	N/A	79745	2.431	VV	0.78
7	7.84	0.00	N/A	2916392	88.908	SBB	0.42

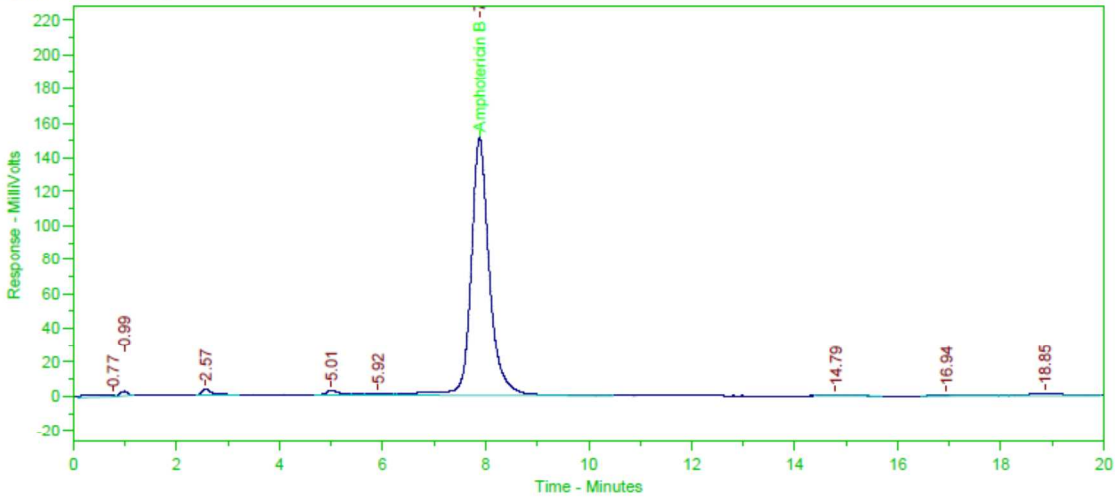
Total Area = 3280220 Total Height = 118770.8 Total Amount = 0

Figure S1. HPLC analysis of AmB **(1)**

Sample Name = **Amphotericin B lote 093M4011 SIGMA**

Instrument = Instrument 1
Heading 1 = CH3CN/ Buffer AcOH/Et3N 30 mmolar pH4, (30:70)
Heading 2 = A-21, 0.125 mg/mL, 1 mL/min 383 nm

Symmetry C18 3.5 µm 4.6x75mm



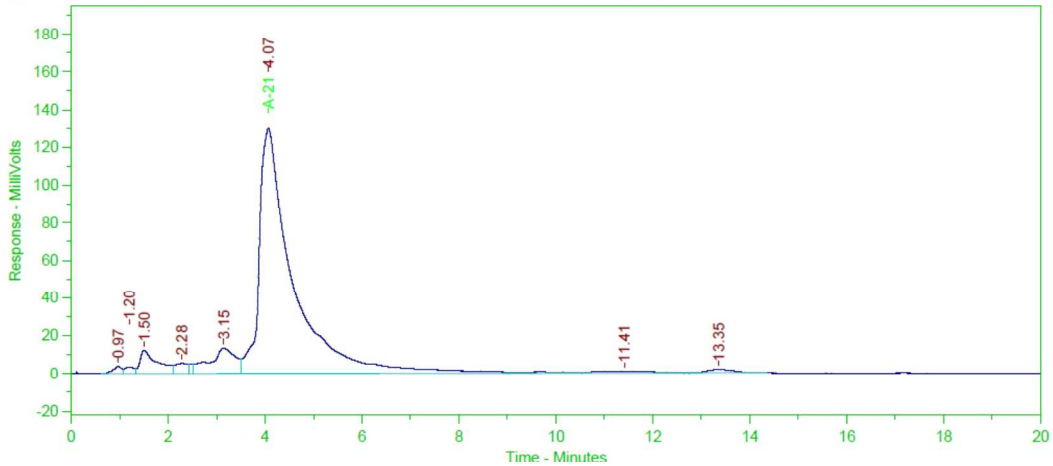
Peak #	Ret. Time	Amount	Amt %	Area	Area %	Type	Width
1	0.77	0.00	N/A	31142	0.775	BB	0.70
2	0.99	0.00	N/A	24938	0.621	BB	0.17
3	2.57	0.00	N/A	42220	1.051	BB	0.18
4	5.01	0.00	N/A	47060	1.172	BV	0.27
5	5.92	0.00	N/A	19444	0.484	VV	0.25
6	7.88	0.00	N/A	3744531	93.238	VB	0.34
7	14.79	0.00	N/A	18779	0.468	BB	0.59
8	16.94	0.00	N/A	19637	0.489	BV	0.93
9	18.85	0.00	N/A	68335	1.702	VB	0.76

Total Area = 4016085 Total Height = 163169.7 Total Amount = 0

Figure S2. HPLC analysis of AmB (**1**), batch 093M4011/Sigma

Instrument = Instrument 1
Heading 1 = CH3CN/ Buffer AcOH/Et3N 30 mmolar pH4, (30:70)
Heading 2 = A-21, 0.125 mg/mL, 1 mL/min 383 nm

Symmetry C18 3.5 µm 4.6x75mm



Peak #	Ret. Time	Amount	Amt %	Area	Area %	Type	Width
1	0.97	0.00	N/A	48572	0.661	BV	0.23
2	1.20	0.00	N/A	46332	0.630	VV	0.13
3	1.50	0.00	N/A	305811	4.161	VV	0.24
4	2.28	0.00	N/A	97534	1.327	VV	0.23
5	3.15	0.00	N/A	485277	6.603	VV	0.34
6	4.07	0.00	N/A	6203265	84.408	VV	0.54
7	11.41	0.00	N/A	90306	1.229	VV	1.27
8	13.35	0.00	N/A	72014	0.980	VB	0.61

Total Area = 7349112 Total Height = 170613.3 Total Amount = 0

Elaboró: M. en C. Manuel López Ortiz
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Figure S3. HPLC of A21 **(2)**

Table S1. ^{1}H NMR signals for A21 (**2**)

^{1}H NMR	Assignment	HSQC	DEPT
8.55 (*d*, *J* = 7.1, 1H)	H-51	117.15	CH
8.33 (br, 1H)			
7.21 (*s*, 1H)	H-52	133.9	CH
6.48 – 6.07 (*m*, 12H)	H-21 - H-32	12 C(133.94 - 128.58)	CH
5.95 (*dd*, *J* = 15.1, 8.8 Hz, 1H)	H-20	133.94	CH
5.82 (s, 1H)			
5.45 (*dd*, J = 14.9, 9.9 Hz, 1H)	H-33	136.8	CH
5.37 (*s*, 1H)			
5.22 (*s*, 1H)	H-37	68.91	CH
4.8 - 4.72 (*m*, 2H)			
4.45 (*m*, 2H)	H-48, H-13	97.09, 52.21	CH, CH
4.35 (*br*, 1H)	H-41	96.04	CH
4.31 (*br*, 1H)	H-19	75.21	CH
4.24 (*br*, 1H)		67.67	CH
4.18 (*t*, J = 9.6 Hz, 1H)		65.11	CH
4.09 – 3.99 (*m*, 2H)	H-3	66.2, 65.04	CH, CH
3.86 (*s*, 1H)		67.1	CH
3.65 (*s*, 3H)	H-54	52.07	CH_3
3.54 (*br*, 1H)	H-5	69.14	CH
3.48 (*br*, *J*= 9.0 Hz, 1)		73.72	CH
3.27 (*m*, 2H)	H-45, H-42	72.55, 68.7	CH, CH
3.15 - 3.09 (*m*, 5H)	H-35, H-49	77.1, 73.6, 48.72, 26.83	CH, CH, CH, CH_2
2.96 (*d*, J = 8.5 Hz, 1H)	H-44	55.5	CH
2.29 (*m*, 1H)	H-34	42.36	CH
2.18 (*d*, *J* = 5.9 Hz, 1H)	H-2	42.06	CH_2
2.02 (*t*, *J* = 10.2 Hz, 1H)		56.44	CH
1.9 (*d*, *J* = 7.8 Hz, 1H)		44.69	CH_2
1.73 (*m*, 1H)	H-36	40.02	CH
1.68 (*m*, 1H)		36.33	CH_2
1.62 - 1.51 (*m*, 4H)		46.22, 39.0, 28.97	CH_2, CH_2, CH_2
1.44 - 1.26 (*m*, 8H)	H-4	44.75, 39.0, 36.33, 35.05, 28.97	CH_2, CH_2, CH_2, CH_2, CH_2
1.19 (*d*, *J* = 5.3 Hz, 3H)	H-46	17.72	CH_3
1.11 (*m*, 5H)	H-38	44.69, 16.98	CH_2, CH_3
1.04 (*d*, *J* = 6.2 Hz, 3H)	H-40	18.48	CH_3
0.92 (*d*, *J* = 7 Hz, 3H)	H-39	12.06	CH_3

Table S2. ^{13}C NMR signals for A21 **(2)**

^{13}C NMR					
□ (ppm)	DEPT	Assignment	□ (ppm)	DEPT	Assignment
172.19	C	C-47	68.7	CH	C-45
171.21	C	C-53	67.67	CH	
170.53	C	C-1	67.1	CH	
136.8	2 (CH)	C-33, C-20	66.2	CH	C-3
133.94	CH	Olefinic	65.11	CH	
133.9	CH	C-52	65.04	CH	
133.69	CH	Olefinic	56.44	CH	
133.5	CH	Olefinic	55.5	CH	C-44
133.2	CH	Olefinic	52.21	CH	C-48
132.44	CH	Olefinic	52.07	CH_3	C-54
132.38	CH	Olefinic	48.72	CH	
132.17	CH	Olefinic	46.22	CH_2	
131.86	CH	Olefinic	44.75	CH_2	
131.76	CH	Olefinic	44.69	CH_2	C-4
131.18	CH	Olefinic	42.36	CH	C-34
128.58	CH	Olefinic	42.06	CH_2	C-2
117.15	CH	C-51	40.02	CH	C-36
97.09	CH	C-13	39	CH_2	
96.04	CH	C-41	36.33	CH_2	
77.11	CH		35.05	CH_2	
75.21	CH		28.97	CH_2	
73.72	CH	C-19	26.83	CH_2	C-49
73.6	CH		18.48	CH_3	C-40
72.55	CH	C-42	17.72	CH_3	C-46
69.14	CH	C-5	16.98	CH_3	C-38
68.91	CH	C-37	12.06	CH_3	C-39

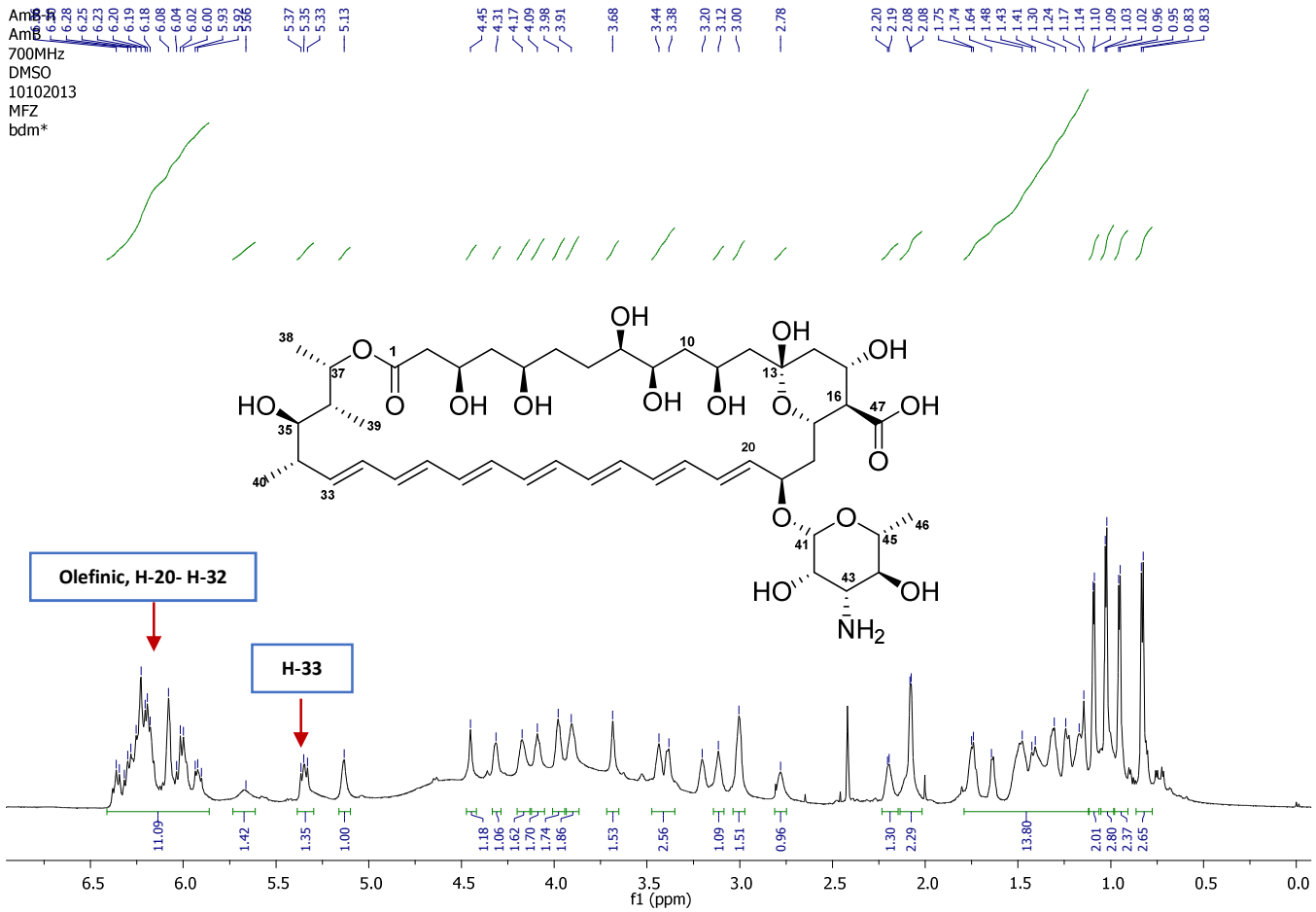

Figure S4. ^{1}H NMR (700 MHz, $DMSO_{d-6}$) of AmB **(1).**

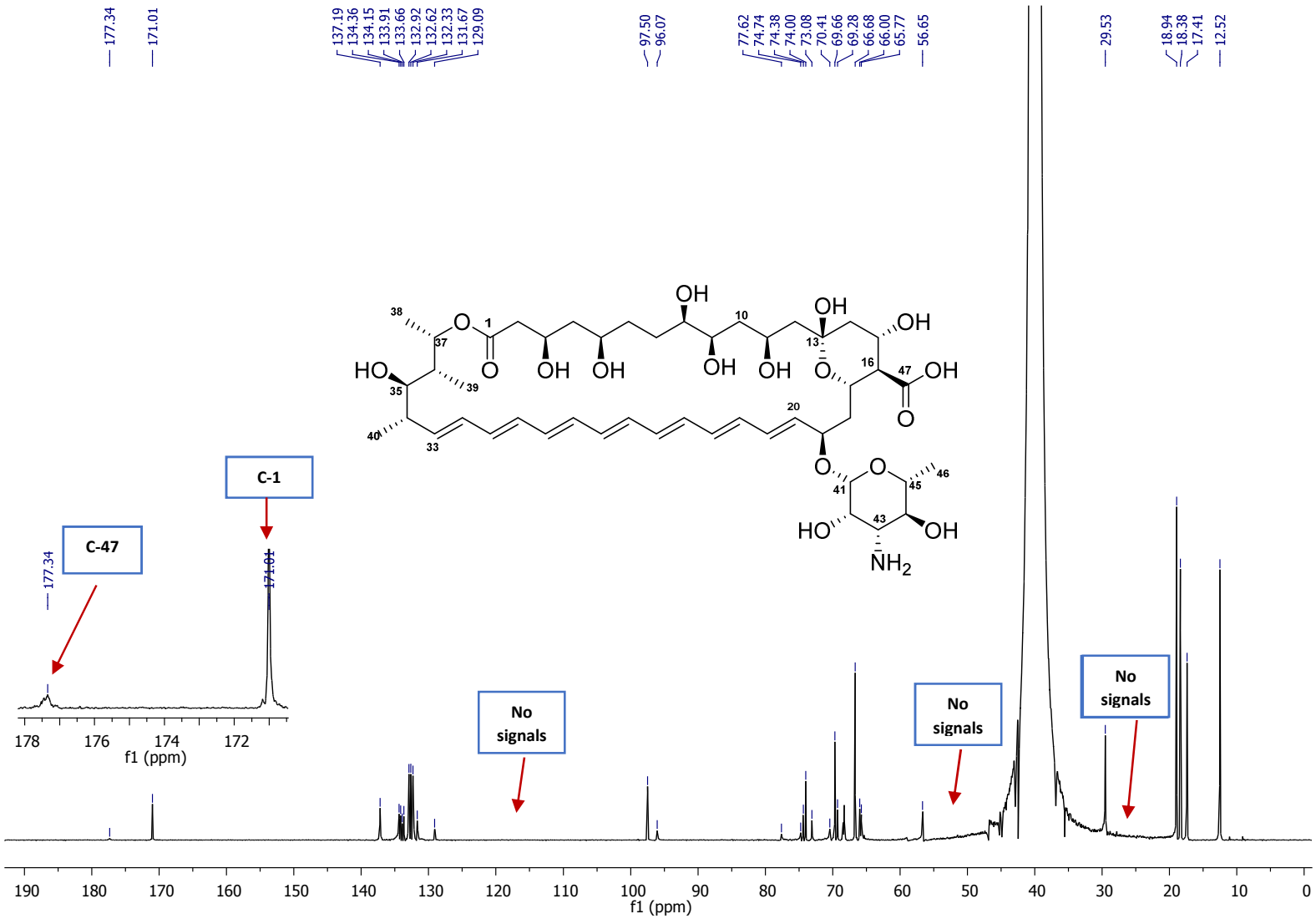

Figure S5. ^{13}C NMR (175 MHz, $DMSO_{d-6}$) of AmB **(1).**

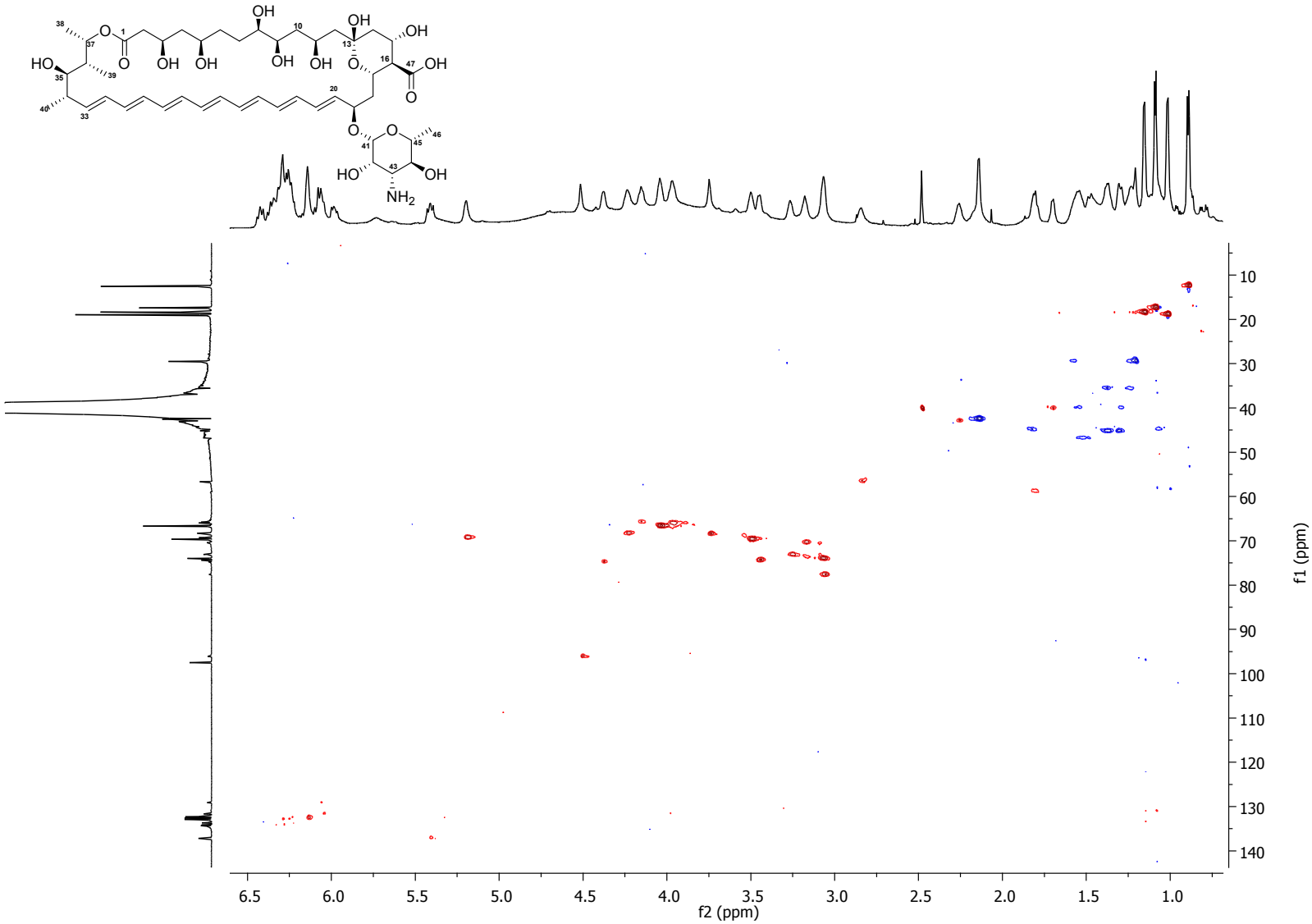

Figure S6. 1H-13C HSQC (700 MHz, DMSOd-6) of AmB (1).

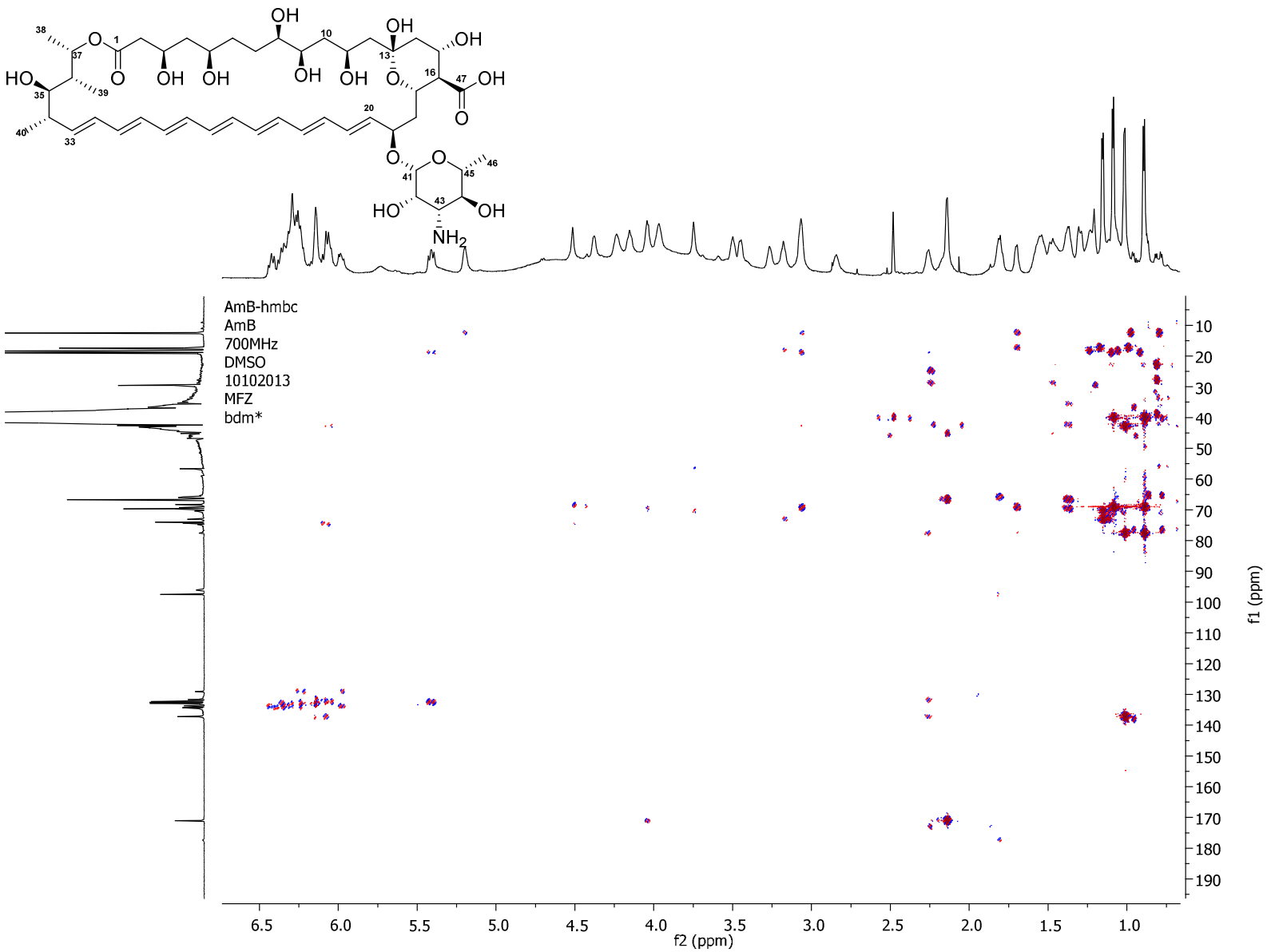

Figure S7. ^{1}H- ^{13}C HMBC (700 MHz, $DMSO_{d-6}$) of AmB **(1).**

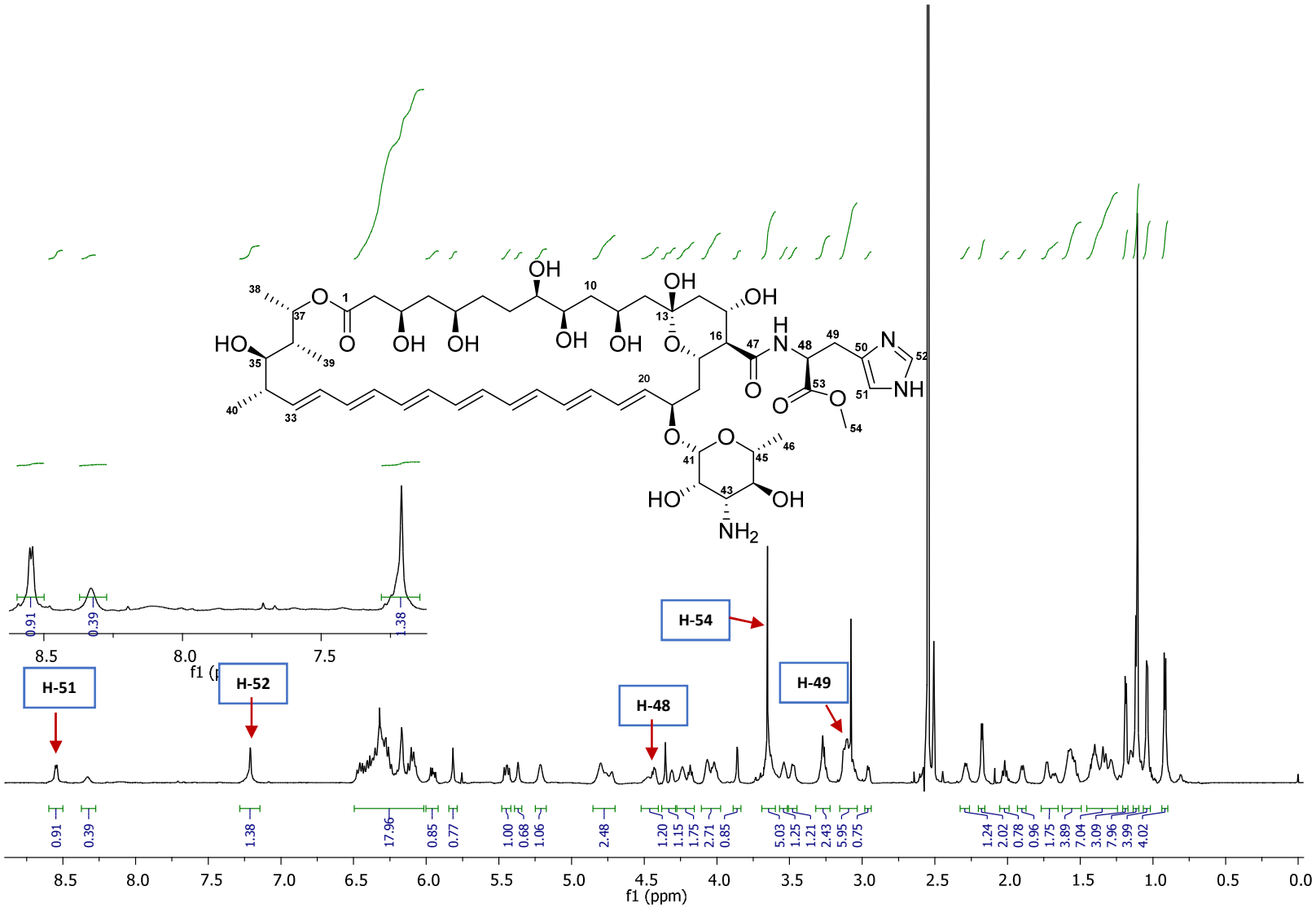

Figure S8. ^{1}H NMR (700 MHz, $DMSO_{d-6}$) of A21 **(2).**

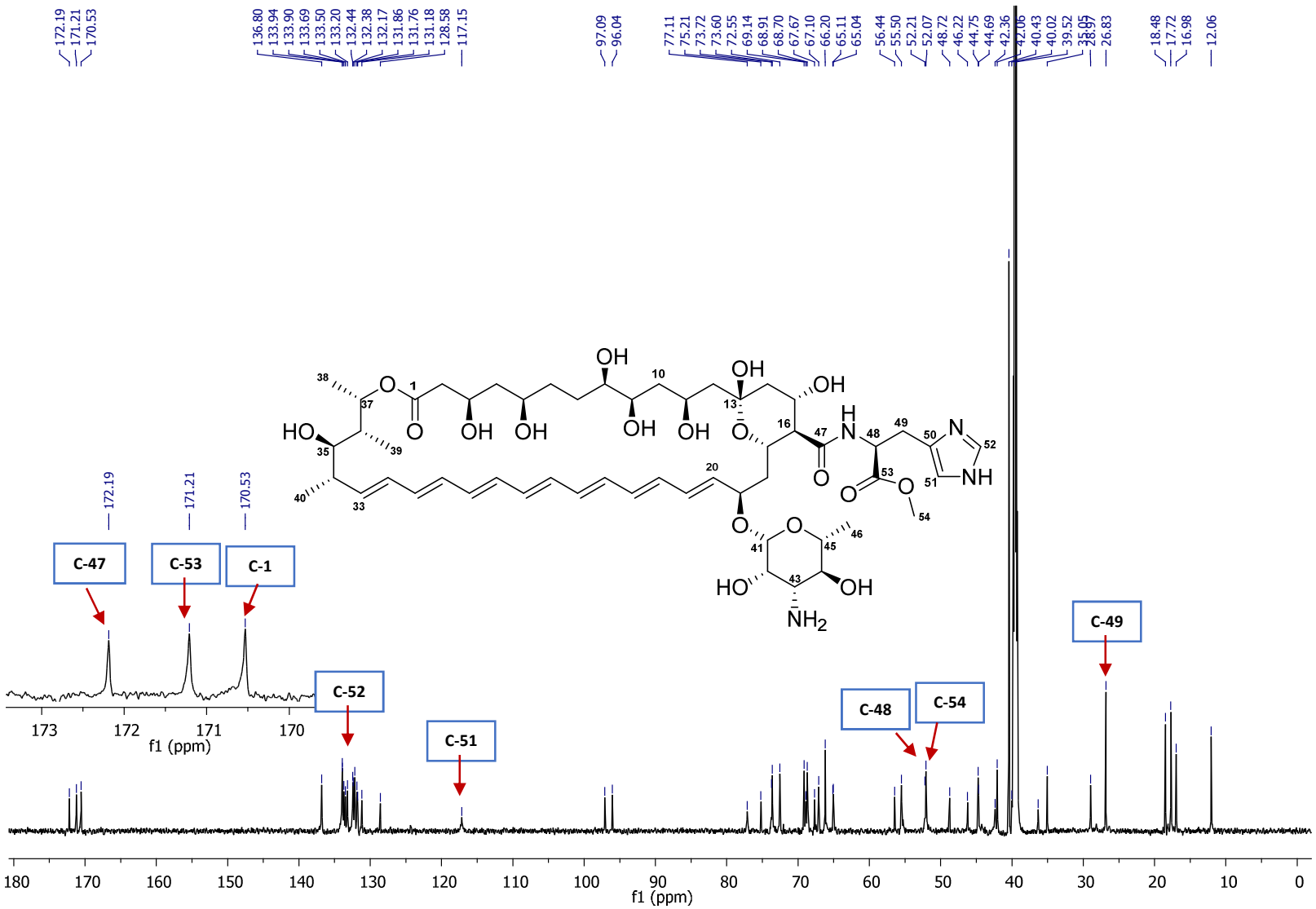

Figure S9. ^{13}C NMR (175 MHz, $DMSO_{d-6}$) of A21 **(2).**

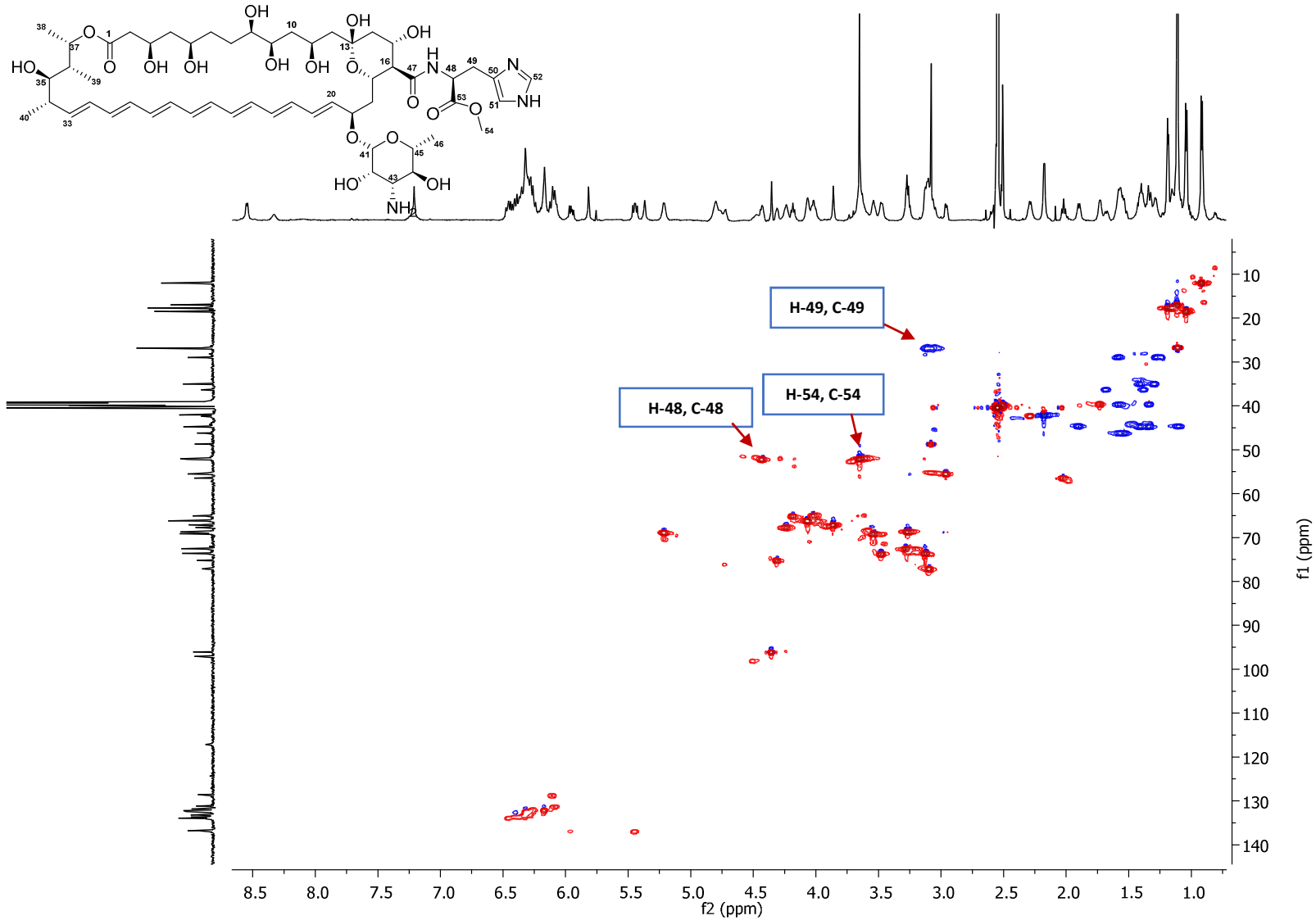

Figure S10. ^{1}H-^{13}C HSQC (700 MHz, $DMSO_{d-6}$) of A21 **(2).**

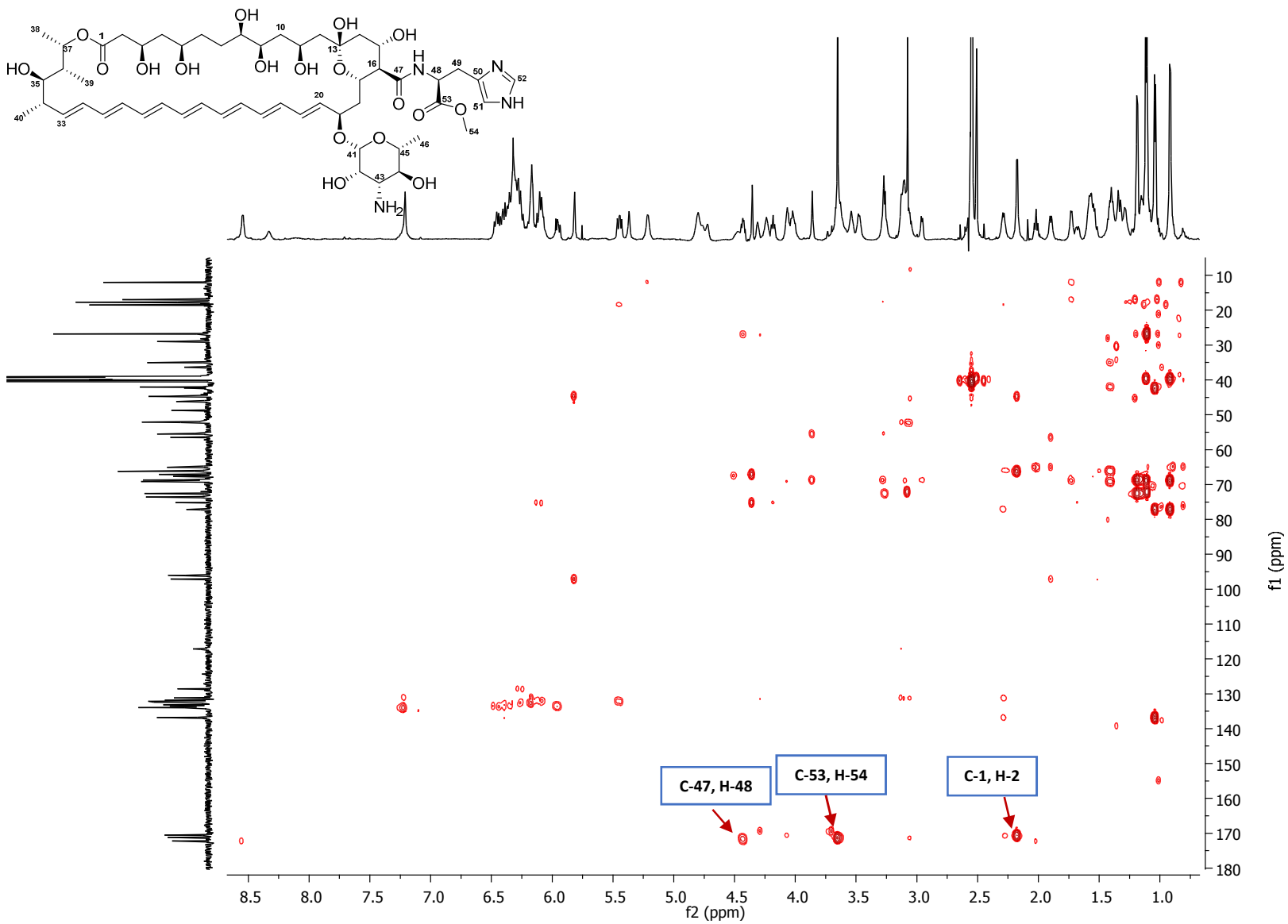

Figure S11. ^{1}H- ^{13}C HMBC (700 MHz, $DMSO_{d-6}$) of A21 **(2).**

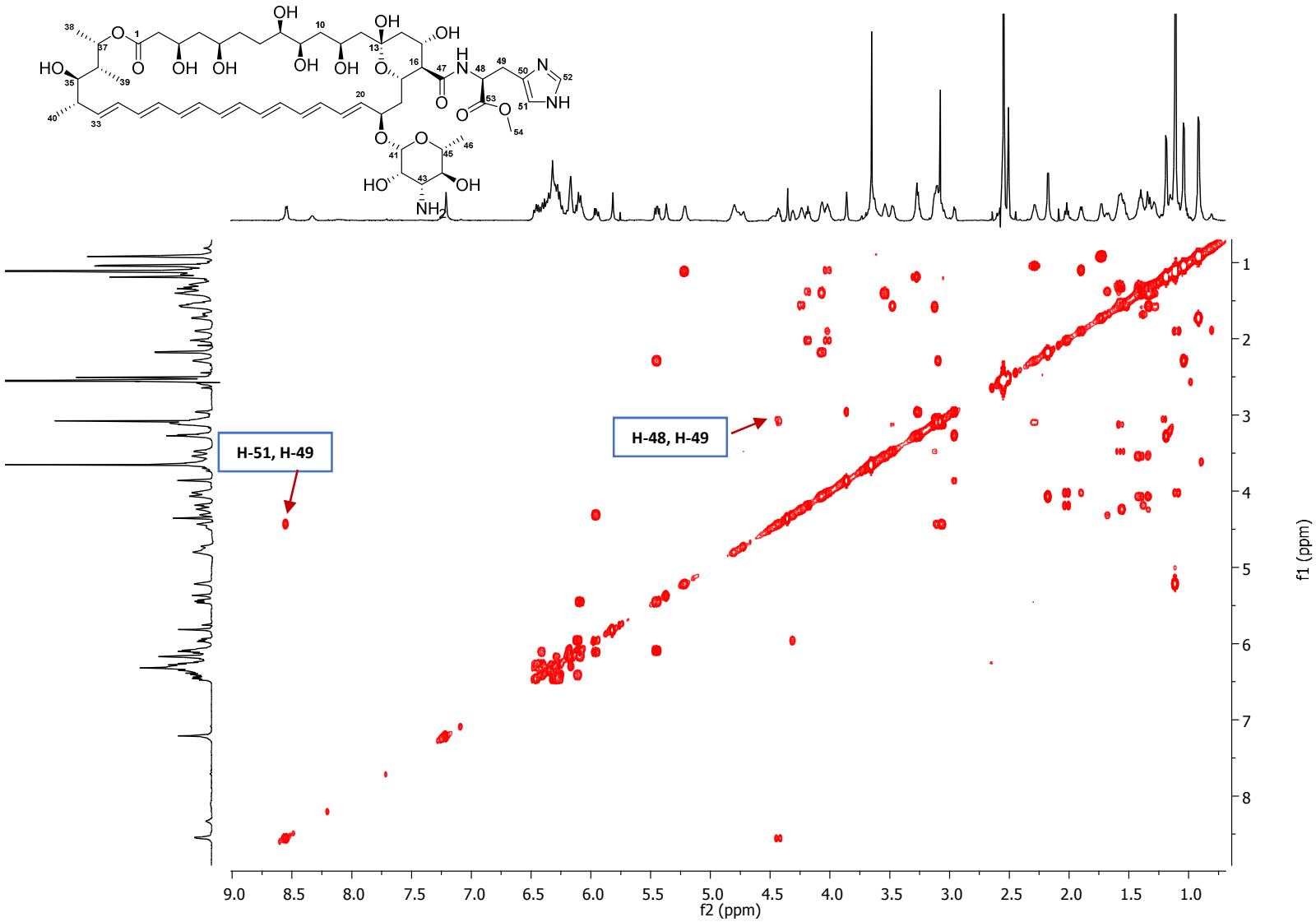

Figure S12. ^{1}H- ^{1}H COSY (700 MHz, $DMSO_{d-6}$) of A21 **(2).**