Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Naphthomycins-Derived Macrolactams with Two New Carbon Skeletons from an Endophytic *Streptomyces*

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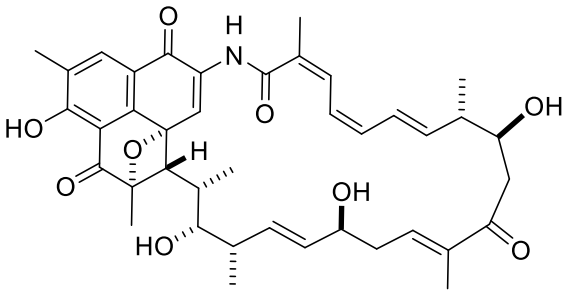
Supplementary Information

Contents

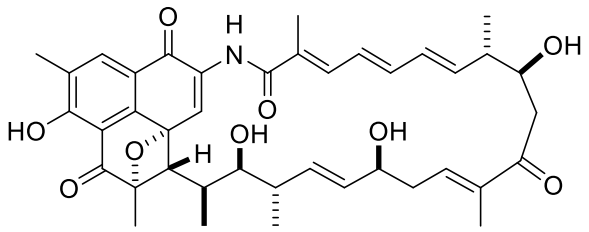
Table S1. Cytotoxic activity of compounds **1**-**3** (μM).

Compounds	IC_{50} ± SD (μM)				
	HL-60	A549	SMMC-7721	MCF-7	SW480
1	19.82 ± 1.65	16.98 ± 2.40	20.35 ± 1.38	16.49 ± 0.45	18.70 ± 0.50
2	15.85 ± 1.05	16.86 ± 1.22	22.47 ± 1.31	10.68 ± 0.16	18.71 ± 0.57
3	18.38 ± 1.14	32.55 ± 1.16	>40	>40	>40
cisplatin	1.81 ± 0.35	9.62 ± 0.19	8.58 ± 0.19	13.93 ± 0.29	13.73 ± 0.51

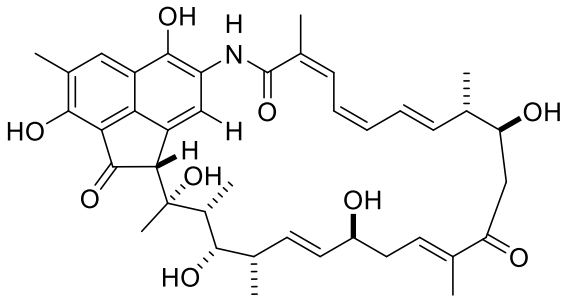
Figure S1. The chemical structures of compounds **1**-**3** and **1a**-**3a**.



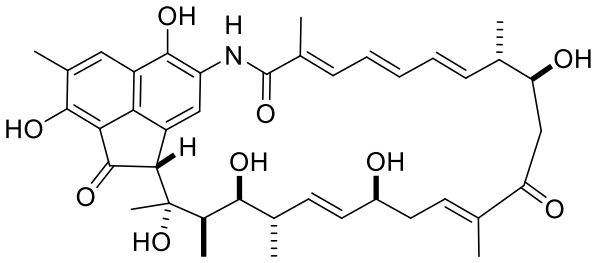
naphthomycin O (**1**)



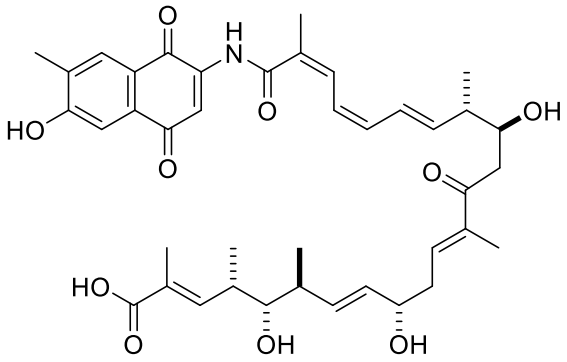
1a



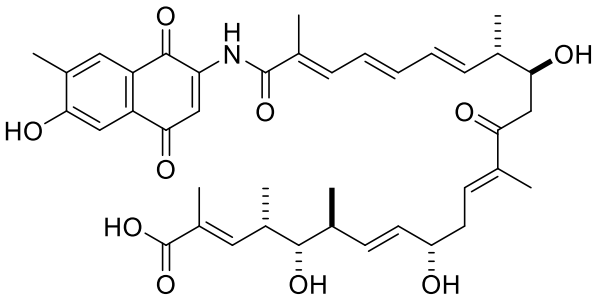
naphthomycin P (**2**)



2a



naphthomycin Q (**3**)



3a

Table S2. NMR spectral data for naphthomycin O (**1**) in $CDCl_3$[a].

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	168.2, C				
2	131.2, C				
2-Me	21.1, CH_3	2.16, s	3	1, 2, 3, 4	3, 4, NH
3	130.1, CH	6.73, d (11.9)	2-Me, 4	1, 2, 4, 5	2-Me, 5, 6, 7
4	123.5, CH	6.59, overlap	3, 5	2, 3, 6	2-Me, NH
5	133.4, CH	6.13, t (11.2)	4, 6	3, 4, 6, 7	3, 15
6	125.9, CH	6.58, overlap	5, 7	4, 5, 8	3, 8, 8-Me
7	139.7, CH	5.90, dd (15.3, 7.0)	6, 8	5, 8-Me, 9	8, 8-Me, 9
8	43.0, CH	2.57, m	7, 8-Me, 9	5, 6, 9	6, 7, 8-Me, 9
8-Me	15.1, CH_3	1.09, d (6.9)	8	7, 8, 9	6, 8
9	72.7, CH	3.86, m	8, 10a, 10b	7, 8, 10, 11	8
10a	38.6, CH_2	2.87, overlap	9, 10b	8, 9, 11	10, 13
10b		2.60, dd (15.6, 5.8)	9, 10a	8, 9, 11	10
11	202.9, C				
12	140.1, C				
12-Me	11.6, CH_3	1.68, s	13	11, 12, 13	14a, 14b
13	143.6, CH	6.43, dd (8.7, 5.0)	12-Me, 14a 14b	11, 14, 15	10a, 14b, 15
14a	38.0, CH_2	2.37, m	13, 14b, 15	12, 13, 15	12-Me, 13
14b		2.20, m	13, 14a, 15	12, 13, 15	12-Me, 14, 15
15	74.3, CH	3.91, m	14a, 14b, 16	13, 16, 17	5, 7, 13, 14b, 17
16	132.7, CH	5.25, overlap	15, 17	17, 18	14a, 14b, 18, 18a
17	137.8, CH	5.24, overlap	16, 18	16, 18	15
18	42.1, CH	1.84, m	17, 18-Me, 19	16, 17, 19	16, 18-Me, 20-Me
18-Me	16.2, CH_3	1.07, d (7.0)	18	17, 18, 19	19, 20
19	74.0, CH	3.82, d (8.9)	18, 20	17, 18, 20, 20-Me, 21	16, 20, 21, 30
20	31.3, CH	2.88, overlap	19, 20-Me, 21	21, 22, 31	18-Me, 19, 20-Me, 21, 22-Me, 30
20-Me	10.2, CH_3	0.80, d (6.6)	20	19, 20, 21, 31	20, 21, 22-Me
21	72.5, CH	3.32, d (11.8)	20	19, 20, 22, 23, 31, 31a	19, 20, 20-Me, 22-Me, 30
22	88.0, C				
22-Me	16.3, CH_3	1.60, s		21, 22, 23	20, 20-Me
23	202.7, C				
24	117.2, C				
25	164.7, C				
26	129.0, C				
26-Me	15.3, CH_3	2.34, s	27	25, 26, 27, 31a,	27
27	134.0, CH	7.99, s	26-Me	25, 27a, 31, 31a, 26-Me	26-Me
27a	110.5, C				
28	177.1, C				
29	133.0, C				
30	121.6, CH	8.16, s		21, 24, 25, 27a, 28, 29, 31, 31a	18-Me, 19, 20, 21, NH
31	77.8, C				
31a	150.2, C				
25-OH		11.14, s			
NH		8.59, s		1, 28, 30, 31	2-Me, 4, 30

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Table S3. NMR spectral data for **1a** in $CDCl_3$ [a].

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	167.6, C				
2	129.3, C				
2-Me	12.9, CH_3	2.15, s	3	1, 2, 3	4, 16, NH
3	136.1, CH	7.19, d (11.4)	2-Me, 4	1, 2-Me, 5	
4	126.3, CH	6.52, dd (14.7, 11.3)	3, 5	5, 6	2-Me, 6
5	139.4, CH	6.63, dd (14.9, 10.7)	4, 6	3, 4, 6, 7	7
6	131.5, CH	6.32, dd (15.4, 10.6)	5, 7	4, 5, 8	8, 8-Me
7	141.0, CH	5.81, dd (15.2, 8.6)	6, 8	5, 8-Me, 9	5, 8, 9
8	44.0, CH	2.43, overlap	7, 8-Me, 9	6, 7, 8-Me, 9, 10	
8-Me	16.1, CH_3	1.13, d (6.6)	8	7, 8, 9	9
9	73.4, CH	3.45, m	8, 10a, 10b	7, 8, 8-Me, 11	7, 8-Me
10a	40.0, CH_2	2.41, overlap	9, 10b	9, 11	
10b		3.15, brd (13.9)	9, 10a	9, 11	
11	202.7, C				
12	139.5, C				
12-Me	11.4, CH_3	1.74, s	13, 14a	11, 12, 13	14b
13	142.2, CH	6.47, dd (9.3, 4.3)	12-Me, 14a, 14b	11, 12-Me, 15	9, 15
14a	37.7, CH_2	2.22, brd (16.2)	12-Me, 13, 14b, 15	13, 15	15
14b		2.46, overlap	13, 14a, 15	15	12-Me
15	73.4, CH	3.89, t (9.4)	14a, 14b, 16	13, 14, 16, 17	6, 14a, 16
16	133.2, CH	5.47, dd (15.3, 8.0)	15, 17	14, 15, 17, 18, 18-Me	15, 18, 18-Me
17	137.3, CH	5.34, dd (15.3, 9.0)	16, 18	15, 16, 18, 18-Me	15, 18, 18-Me
18	42.0, CH	2.11, m	17, 18-Me, 19	18-Me, 19	
18-Me	16.3, CH_3	1.17, d (6.7)	18	17, 18, 19	20
19	73.5, CH	4.01, d (9.0)	18, 20	17, 18, 20, 20-Me	16, 21, 30
20	31.4, CH	2.93, m	19, 20-Me, 21	20-Me, 21, 22	19, 20-Me, 22-Me, 30
20-Me	10.3, CH_3	0.91, d (6.5)	20	20, 21	18, 20, 21,22-Me
21	73.0, CH	3.28, d (11.7)	20	20, 20-Me, 23, 31, 31a	19, 20-Me, 22-Me, 30
22	87.7, C				
22-Me	15.7, CH_3	1.63, s		21, 22, 23	20, 20-Me, 21
23	202.3, C				
24	116.9, C				
25	164.7, C				
26	128.9, C				
26-Me	15.2, CH_3	2.35, s	27	25, 26, 27	27
27	133.9, CH	7.99, s	26-Me	25, 26-Me, 28, 31, 31a	26-Me
27a	110.3, C				
28	177.0, C				
29	133.1, C				
30	121.1, CH	8.24, s		21, 27a, 28, 29, 31a	19, 20
31	78.1, C				
31a	149.9, C				
NH		8.78, s		1, 28, 30, 31	18

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Table S4. NMR spectral data for naphthomycin P (**2**) in $CDCl_3$ [a]

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	169.1, C				
2	133.8, C				
2-Me	21.2, CH_3	2.12, s	3	1, 2, 3	3, 4
3	125.7, CH	6.64, d (12.2)	2-Me, 4	1, 2, 2-Me	2-Me, 5, NH
4	123.6, CH	6.25, t (12.6)	3, 5	2, 3	2-Me, 7, NH
5	131.5, CH	6.06, t (11.6)	4, 6, 7	6, 7	3, 7, 8
6	125.1, CH	6.38, dd (14.9, 11.5)	5, 7	4, 5	3, 7, 8
7	140.8, CH	5.57, dd (14.9, 10.3)	6, 8	5, 8, 8-Me, 9	5, 8-Me, 9, 10
8	44.7, CH	2.55, m	7, 8-Me, 9	6, 7, 9	6, 7, 8-Me
8-Me	18.2, CH_3	1.22, d (6.5)	8	7, 8, 9	7, 8
9	74.6, CH	3.57, m	8, 10a, 10b	8-Me, 11	7
10a	40.0, CH_2	2.72, overlap	9, 10b	8, 11, 12	10b, 12-Me
10b		3.18, dd (17.6, 3.3)	9, 10a	11	7, 10a, 13
11	203.5, C				
12	141.3, C				
12-Me	11.1, CH_3	1.86, s		11, 12, 13	14a
13	138.5, CH	6.54, dd (9.4, 4.2)	14	11, 12-Me	10b, 14a, 14b, 15
14a	39.1, CH_2	2.72, overlap	13, 14b, 15	12, 13, 15	16
14b		2.36, d (14.5, 4.2)	13, 14a, 15	12, 13 ,15	8-Me, 13, 15
15	74.9, CH	4.27, t (9.3)	14a, 14b, 16	13, 16, 17	13, 14b, 16
16	131.2, CH	5.88, dd (15.5, 8.2)	15, 17	15, 18	15, 18, 20
17	135.8, CH	5.85, dd (15.3, 9.5)	15, 18	15, 18, 18-Me	15, 18, 20
18	39.0, CH	2.95, m	1.19, 5.85	16, 17, 18-Me	18-Me, 19, 22
18-Me	19.1, CH_3	1.19, d (6.7)	18	17, 18, 19	18, 19
19	77.1, CH	4.10, d (10.3)	18, 20	17, 18-Me, 20, 20-Me	18, 18-Me, 20, 22
20	47.9, CH	1.72, m	19, 20-Me	20-Me, 21, 22, 31	20-Me, 22, 30
20-Me	11.8, CH_3	0.76, d (6.6)	20	19, 20, 21	19, 20
21	76.0, C				
21-Me	30.9, CH_3	1.30, s		21, 22, 23	22
22	49.2, CH	3.55, s		20, 20-Me, 21, 21-Me, 23, 30, 31, 31a	18, 19, 20, 21-Me, 30
23	206.1, C				
24	106.2, C				
25	162.0, C				
26	127.5, C				
26-Me	16.0, CH_3	2.43, s		25, 26, 27	27
27	133.7, C	8.42, s		25, 26-Me, 28, 31a	26-Me
27a	119.9, C				
28	142.9, C				
29	120.2, C				
30	123.3, CH	7.23, s		22, 27a, 28, 29, 31a	20, 22, NH
31	126.4, C				
31a	128.7, C				
25-OH		12.41, s		23, 24, 25, 26	
28-OH		9.90, s		29	
NH		8.82, s		1, 28, 29, 30	3, 4 ,30

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Table S5. NMR spectral data for **2a** in $CDCl_3$ [a].

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	170.7, C				
2	131.8, C				
2-Me	13.6, CH_3	2.05, s		1, 2, 3	4
3	133.2, CH	6.69, d (8.8)	2-Me, 4	1, 2-Me, 5	5, 7, NH
4	126.4, CH	6.38, overlap	3, 5	2	2-Me, NH
5	138.2, CH	6.37, overlap	4, 6	7	7
6	130.8, CH	6.05, dd (15.2, 9.5)	5, 7	4, 5, 8	8
7	140.9, CH	5.58, dd (15.1, 10.1)	6, 8	2, 8, 8-Me	3, 9, 8-Me, 10b
8	45.3, CH	2.41, overlap	7, 8-Me, 9	7, 8-Me, 9	6
8-Me	18.3, CH_3	1.22, d (6.6)	8	7, 8, 9	8
9	75.3, CH	3.68, m	8, 9-OH, 10a, 10b	8-Me	7, 8
10a	41.1, CH_2	2.79, dd (16.8, 4.3)	9, 10b	8, 9 ,11	10b
10b		2.99, dd (16.8, 4.1)	9, 10a	11	10a, 13
11	202.6, C				
12	140.2, C				
12-Me	11.8, CH_3	1.79, s		11, 12 , 13	14b
13	138.4, CH	6.58, t (7.2)	14a, 14b	11, 14, 15, 12-Me	15, 18
14a	39.4, CH_2	2.42, overlap	13, 14b	12, 15	13, 15, 27
14b		2.63, dt (16.8, 4.3)	13, 14a, 15	12, 13, 15, 16	12-Me, 16
15	75.2, CH	4.38, brs	14b, 16	16	13, 14a, 17
16	135.1, CH	5.88, overlap	15, 17	15, 18	13-Me, 22
17	132.4, CH	5.89, overlap	16, 18	15, 18	14b, 15, 18, 30
18	39.2, CH	2.95, overlap	17, 18-Me, 19	16, 17, 18-Me	16, 18-Me, 19, 22
18-Me	19.4, CH_3	1.18, d (6.7)	18	16, 18, 19	17, 19, 22
19	77.4, CH	4.08, d (9.9)	18, 20	16, 18-Me, 20, 20-Me	18, 20
20	48.5, CH	1.70, m	19, 20-Me	21, 22, 31	20-Me, 22, 30
20-Me	12.0, CH_3	0.73, d (6.9)	20	21, 22	19, 20
21	76.1, CH				
21-Me	31.3, CH_3	1.29, s		21, 22 ,23	22
22	49.7, CH	3.59, s		20, 20-Me, 21, 23, 30, 31, 31a	16, 18, 19, 20, 21-Me, 30
23	206.1, C				
24	106.3, C				
25	162.1, C				
26	127.6, C				
26-Me	16.1, CH_3	2.43, s	27	25, 26, 27	27
27	133.9, CH	8.41, s	26-Me	25, 26-Me, 31a	26-Me
27a	120.3, C				
28	142.9, C				
29	120.1, C				
30	123.6, CH	7.15, s		22, 28, 29, 31a	17, 20, 22, NH
31	126.4, C				
31a	128.8, C				
9-OH		3.41, d (9.0)	9	8, 9, 10	8
21-OH		3.97, s		21, 22, 23	21-Me
25-OH		12.37, s		23, 24, 25, 26	26-Me
28-OH		10.03, s		27a, 28	
NH		8.40, s		1, 28, 30	3, 17, 28-OH, 30

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Table S6. NMR spectral data for naphthomycin Q (**3**) in CD_3OD [a].

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	170.1, C				
2	131.7, C				
2-Me	20.9, CH_3	2.13, s	3	1, 2, 3	3
3	132.3, CH	6.94, d (12.0)	2-Me, 4	1, 2-Me, 5	2-Me, 6
4	124.0, CH	6.47, t (11.5)	3, 5	2, 6	
5	135.5, CH	6.18, t (11.1)	4, 6	3, 6, 7	7
6	126.7, CH	6.71, dd (15.0, 11.4)	5, 7	4, 5, 8	3, 8, 8-Me
7	142.1, CH	5.80, dd (15.0, 8.5)	6, 8	5, 8, 8-Me, 9	5, 8, 8-Me, 9, 10
8	45.2, CH	2.38, m	7, 8-Me, 9	6, 7, 8-Me, 9	6, 7, 8-Me, 9, 10
8-Me	16.6, CH_3	1.11, d (6.73)	8	7, 8, 9	7, 8, 9, 10
9	73.2, CH	3.97, m	8, 10		7, 8, 8-Me, 10, 13
10a	43.4, CH_2	2.79, dd (16.1, 5.1)	9, 10b	8, 9, 11	8-Me, 10, 13
10b		2.83, dd (16.1, 7.7)	9, 10a	8, 9, 11	7, 8
11	202.7, C				
12	139.8, C				
12-Me	11.8, CH_3	1.75, s	13	11, 12, 13	14
13	141.4, CH	6.76, t (7.1)	12-Me, 14	11, 12-Me, 14, 15	10, 14, 15
14	38.0, CH_2	2.47, m	13, 15	12, 13, 15, 16	12-Me, 13, 15, 16
15	72.5, CH	4.18, m	14, 16	13, 17	13, 14, 16, 17
16	134.6, CH	5.41, dd (15.5, 6.6)	15, 17	14, 15, 18	14, 15, 18, 18-Me
17	133.6, CH	5.65, dd (15.5, 8.6)	16, 18	15, 18, 18-Me, 19	14, 15, 18, 18-Me
18	41.9, CH	2.22, m	17, 18-Me, 19		16, 18-Me, 19
18-Me	19.1, CH3	1.05, d (6.9)	18	17, 18, 19	18, 19
19	79.9, CH	3.26, dd (8.5, 3.1)	18, 20	17, 18, 18-Me, 20, 20-Me, 21	16, 20, 21,
20	38.9, CH	2.59, m	19, 20-Me, 21	19, 20-Me, 21, 22	16, 20, 20-Me, 21, 22-Me
20-Me	16.4, CH_3	1.03, d (6.7)	20	18, 19, 20, 21	4, 20
21	145.9, CH	6.57, d (10.2)	20	19, 20, 22, 22-Me, 23	
22	128.5, C				
22-Me	13.2, CH_3	1.82, s		21, 22, 23	18-Me, 20
23	172.2, C				
24	116.8, CH	7.63, s		26, 28, 31a	
25	163.5, C				
26	133.9, C				
26-Me	16.3, CH_3	2.26, s		25, 26, 27	
27	131.1, CH	7.79, s		24, 25, 26, 26-Me, 28, 31	
27a	123.4, C				
28	180.5, C				
29	132.2, C				
30	112.1, CH	7.29, s		25, 27a, 28, 29, 31	
31	187.4, C				
31a	142.0, C				

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Table S7. NMR spectral data for **3a** in CD_3OD [a].

No.	δ_C (mult.) [b]	δ_H (mult., *J* in Hz)	COSY	HMBC	ROESY
1	169.3, C				
2	129.9, C				
2-Me	12.8, CH_3	2.07, s		1, 2, 3	4
3	138.1, CH	7.09, d (11.1)	4	1, 2, 5	5
4	127.3, CH	6.57, overlap	3, 5	6	2-Me, 6
5	142.1, CH	6.65, dd (14.7, 10.5)	4, 6	3, 4, 7	2-Me, 3, 7
6	132.1, CH	6.32, dd (15.2, 10.5)	5, 7	4, 5, 8	4, 8, 8-Me
7	142.8, CH	5.92, dd (15.2, 8.3)	6, 8	5, 8-Me, 9	5, 8, 8-Me, 9, 10
8	45.1, CH	2.36, m	7, 8-Me, 9	7, 8-Me, 9	6, 7, 8-Me, 9, 10
8-Me	16.4, CH_3	1.11, d (6.8)	8	7, 8, 9	6, 7, 8, 9, 10
9	73.1, CH	3.97, m	8, 10		13, 7, 8, 8-Me, 10
10a	43.3, CH_2	2.79, dd (16.1, 4.4)	9, 10b	8, 9, 11	8, 9, 13
10b		2.83, dd (16.1, 8.4)	9, 10a	8, 9, 11	7, 8-Me,13
11	202.7, C				
12	139.8, C				
12-Me	11.8, CH_3	1.75, s		11, 12, 13	14
13	141.4, CH	6.76, t (7.0)	14	11, 12-Me, 14, 15	9, 10, 14, 15, 16, 18-Me
14	38.0, CH_2	2.47, m	13, 15	12, 13, 15, 16	12-Me, 13, 15, 16, 17
15	72.5, CH	4.18, dt (6.5, 6.5)	14, 16	13, 17	13, 14, 16, 17
16	134.6, CH	5.41, dd (15.6, 6.5)	15, 17	15, 18	13, 14,15, 18, 18-Me, 22-Me
17	133.6, CH	5.66, dd (15.5, 8.6)	16, 18	15, 18, 18-Me	13, 15, 18, 18-Me, 19, 20
18	41.8, CH	2.24, m	17, 18-Me, 19	18-Me	16, 18-Me, 19, 21
18-Me	19.1, CH_3	1.05, d (6.9)	18	17, 18, 19	7, 13, 16, 17, 20
19	80.0, CH	3.26, dd (8.5, 3.0)	18, 20	17, 18, 20, 21	17, 18, 18-Me, 20, 20-Me, 21
20	38.9, CH	2.58, dq (7.1, 7.0)	19, 20-Me, 21	19, 20-Me, 21, 22	20-Me, 22-Me
20-Me	16.4, CH_3	1.03, d (6.7)	20	19, 20, 21	12-Me, 18, 19, 20, 21
21	145.1, CH	6.53, dd (11.0, 3.9)	20	19, 20, 22-Me, 23	3, 6, 18, 19, 20
22	129.3, C				
22-Me	13.4, CH_3	1.82, s		21, 22, 23	18-Me, 20
23	173.1, C				
24	116.2, CH	7.57, s		26, 28, 31a	2-Me
25	163.6, C				
26	133.9, C				
26-Me	16.4, CH_3	2.26, s		25, 29	27
27	131.1, CH	7.80, s		25, 26, 26-Me, 28, 31	15, 26-Me
27a	123.3, C				
28	180.7, C				
29	132.2, C				
30	112.1, CH	7.28, s		25, 27a, 28, 29, 31	
31	187.4, C				
31a	142.2, C				

[a] 600 MHz for ^1H NMR and 150 MHz for ^{13}C NMR. [b] Numbers of attached protons were determined by analysis of 2D NMR spectra.

Figure S2. Key COSY and HMBC correlations of naphthomycin O (**1**).

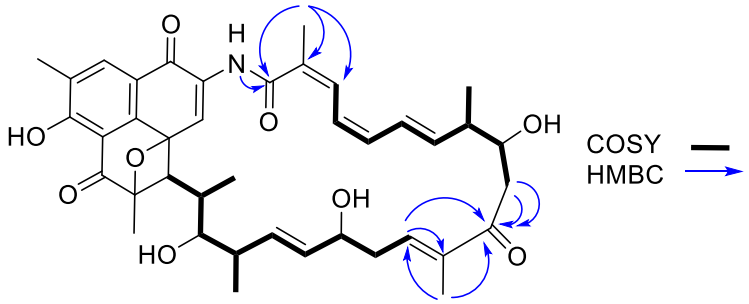


Figure S3. Key ROESY correlations of naphthomycin O (**1**).

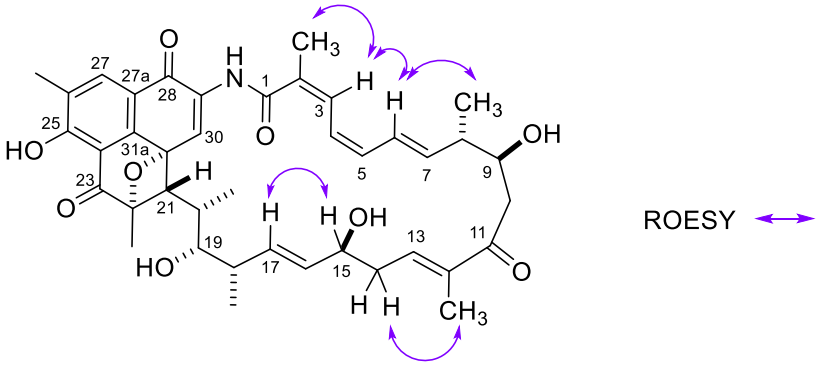


Figure S4. Key COSY and HMBC correlations of **1a**.

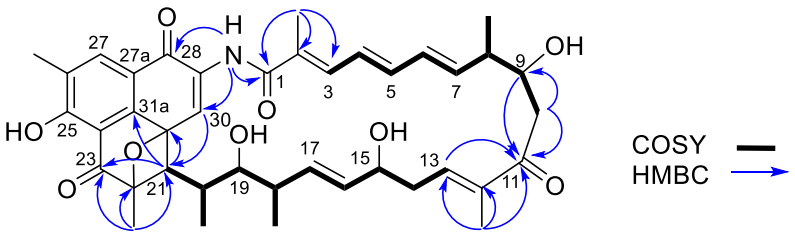


Figure S5. Key ROESY correlations of **1a**.

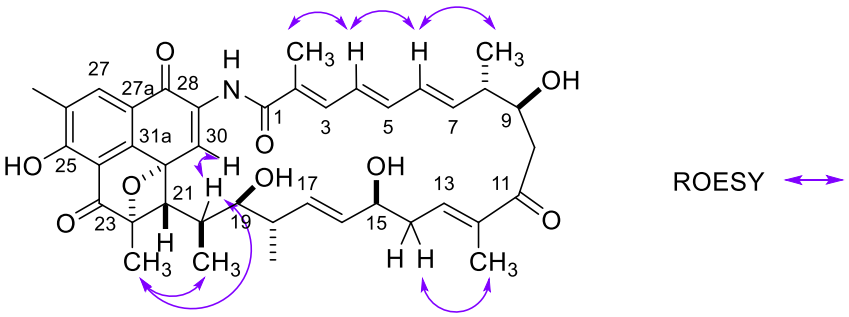


Figure S6. Key COSY and HMBC of naphthomycin P (**2**).

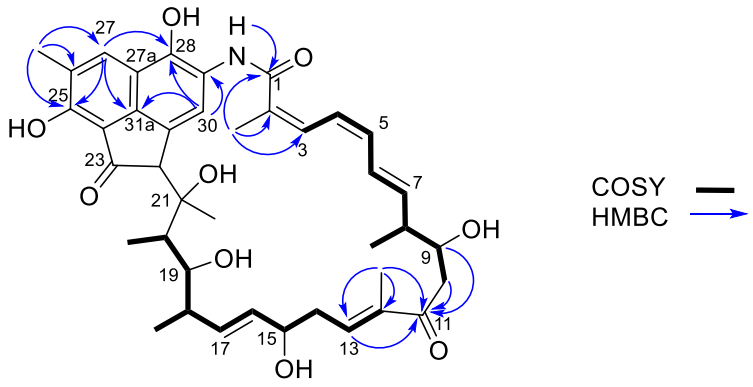


Figure S7. Key ROESY correlations of naphthomycin P (**2**).

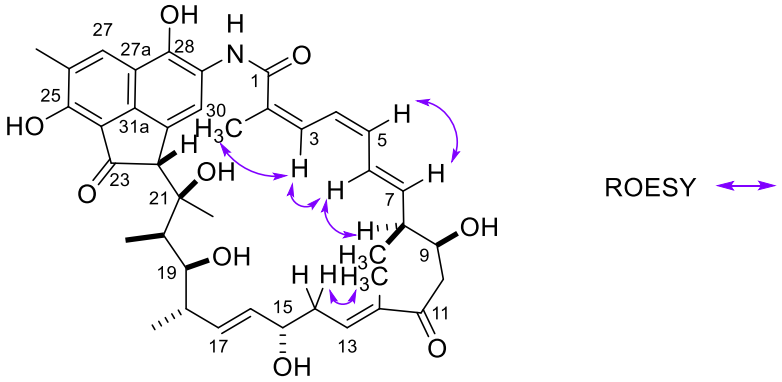
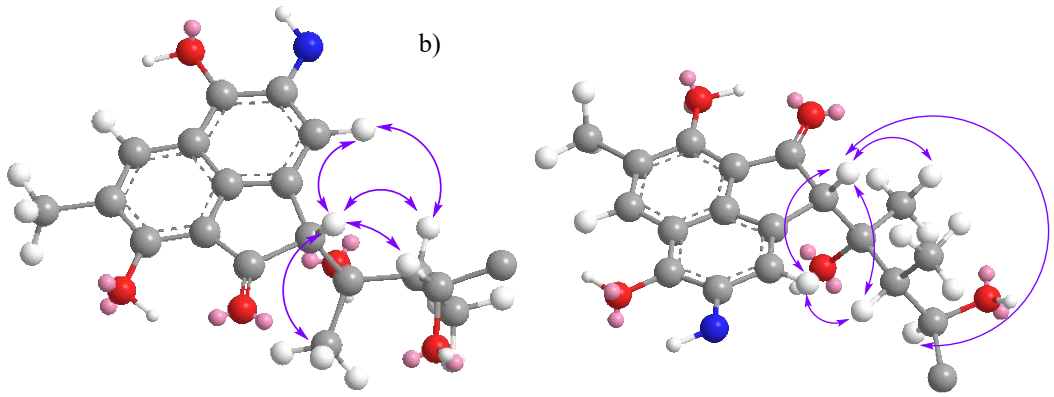


Figure S8. Energy minimized model of simplified naphthomycin P (**2**) a) model of 21*S**, 22*R**, b) model of 21*R**, 22*S** (calculated by Chem3D ver 15.0, red = oxygen, blue = nitrogen, white = hydrogen, gray = carbon, pink = lone pair, double solid arrow = ROESY correlation).

a) b)



21*S**, 22*R**	21*R**, 22*S**
H-20-H-30: 2.179 Å	H-20-H-30: 2.166
H-20-H-22: 2.559 Å	H-20-H-22:3.287 Å
H-22-21-Me: 3.009 Å	H-22-21-Me: 2.759 Å
H-19-H-22: 2.250 Å	H-19-H-22: 4.819 Å

Figure S9. Key COSY and HMBC correlations of **2a**.

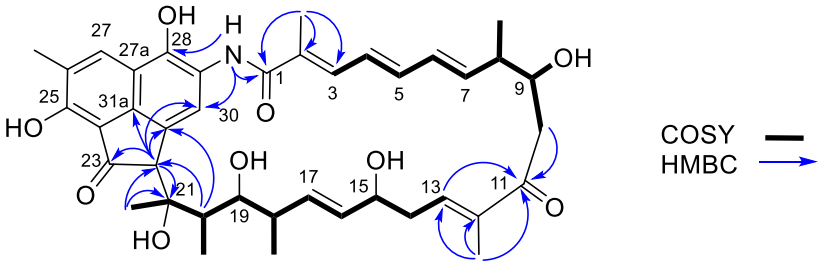


Figure S10. Key ROESY correlations of **2a**.

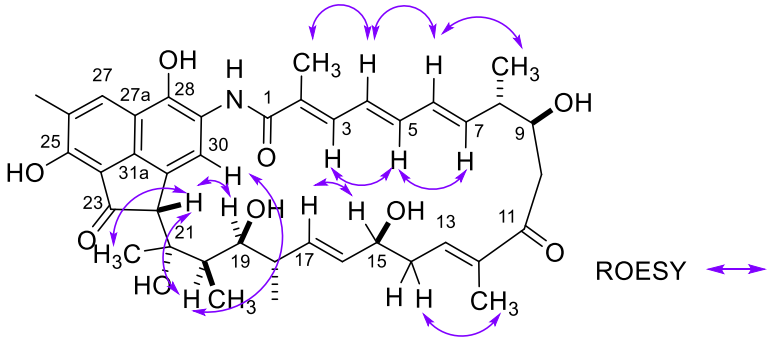


Figure S11. Key COSY and HMBC correlations of naphthomycin Q (**3**).

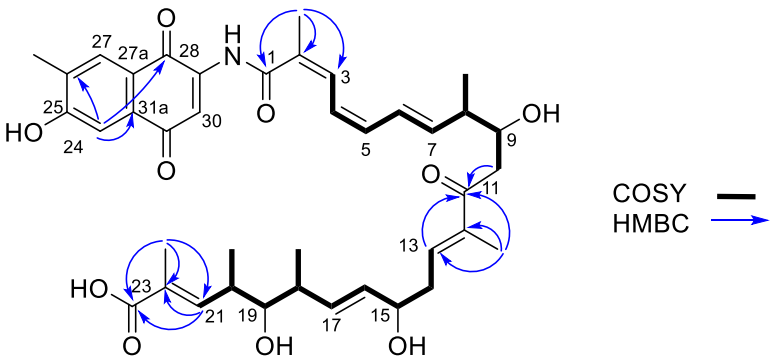


Figure S12. Key ROESY correlations of naphthomycin Q (**3**).

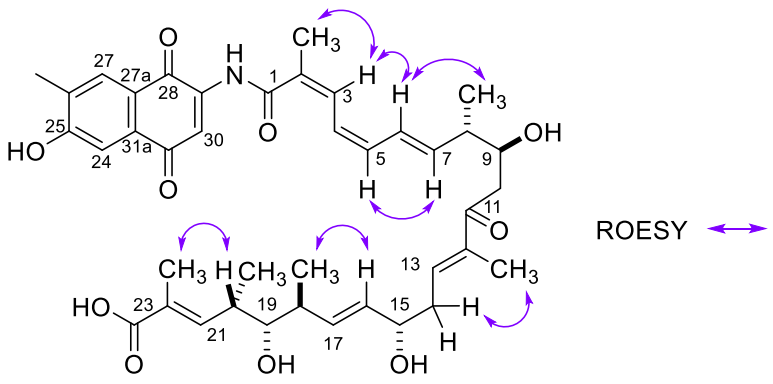


Figure S13. Key COSY and HMBC correlations of **3a**.

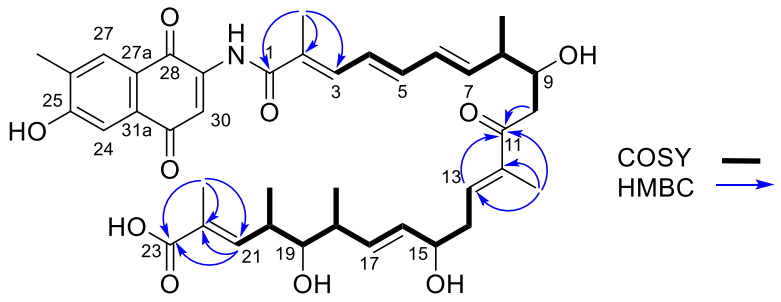


Figure S14. Key ROESY correlations of **3a**.

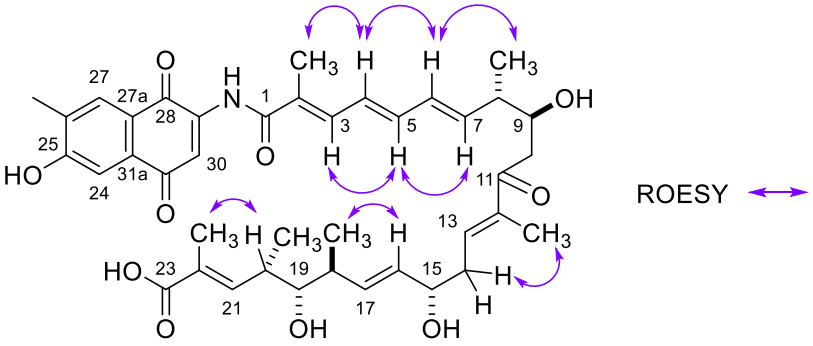
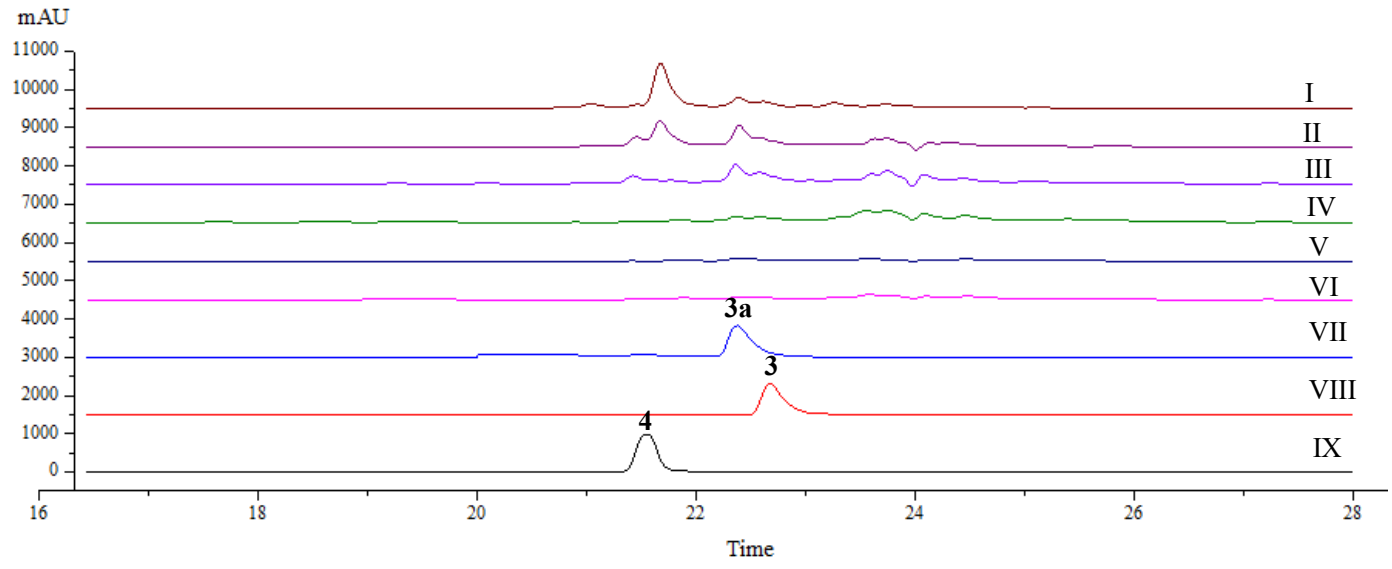


Figure S15. HPLC analysis of retro-Friedel-Crafts acylation reaction of naphthomycin E (**4**), with the aid of a Lewis acid, SnCl4. (I) reaction time of 10 min; (II) reaction time of 20 min; (III) reaction time of 35 min; (IV) reaction time of 50 min; (V) reaction time of 80 min; (VI) reaction time of 110 min; (VII) standard **3a**; (VIII) standard **3**; (IX) standard **4**.



2. NMR and HRESIMS spectra of compounds 1-3 and 1a-3a

Figure S16. ^{1}H NMR spectrum (600 MHz) of naphthomycin O (**1**) in $CDCl_3$.

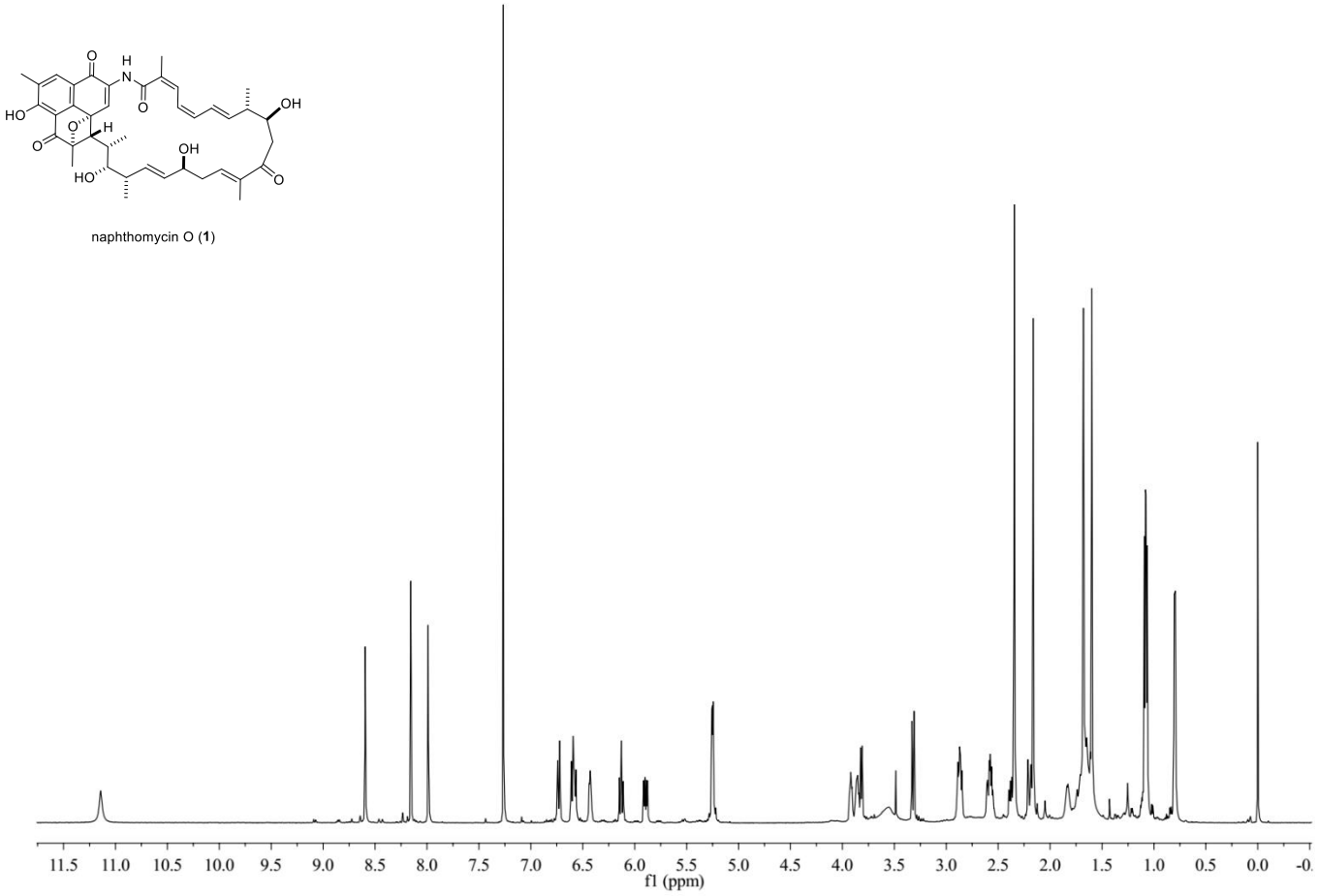


Figure S17. ^{13}C NMR spectrum (150 MHz) of naphthomycin O (**1**) in $CDCl_3$.

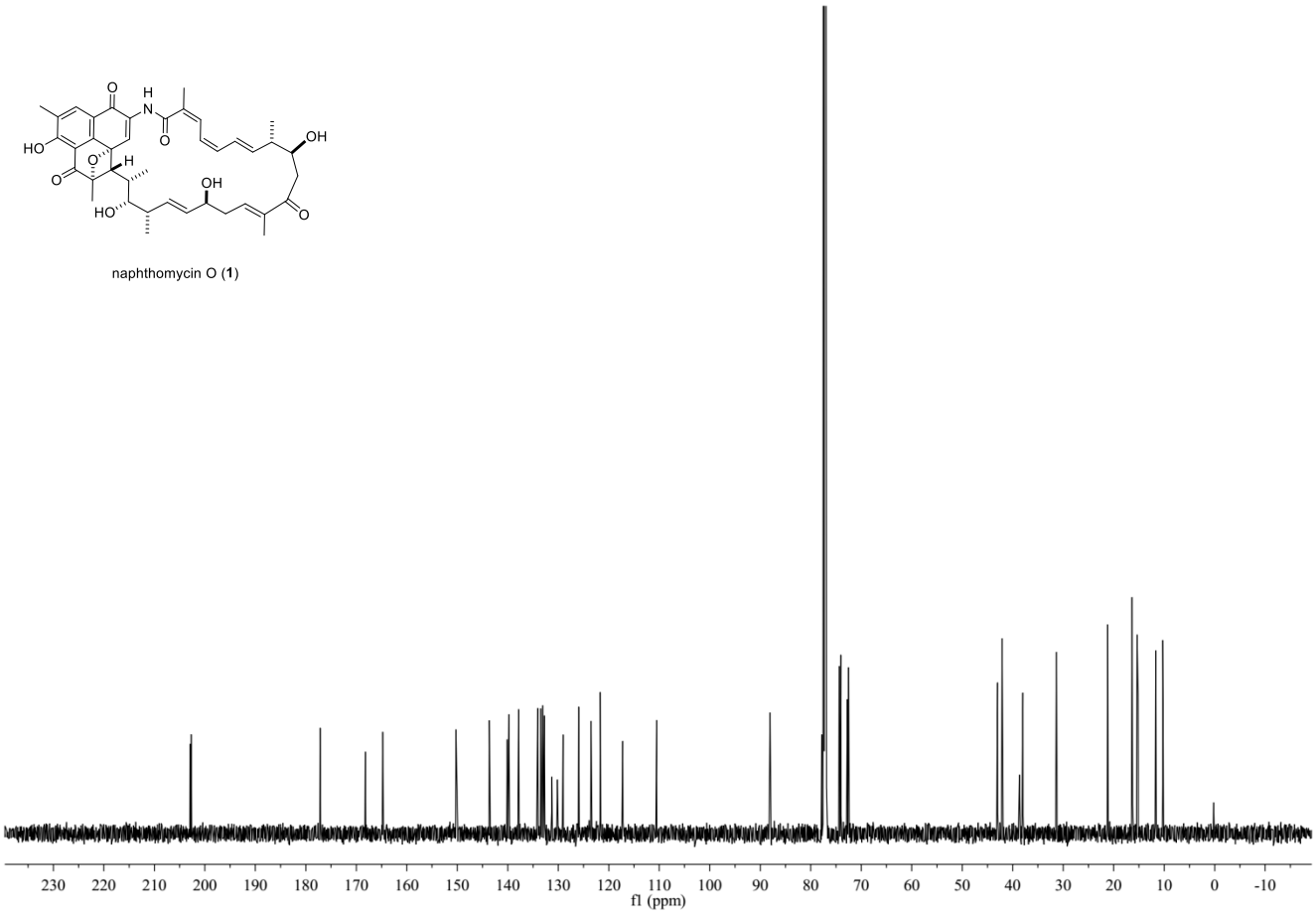


Figure S18. COSY spectrum (600 MHz) of naphthomycin O (**1**) in $CDCl_3$

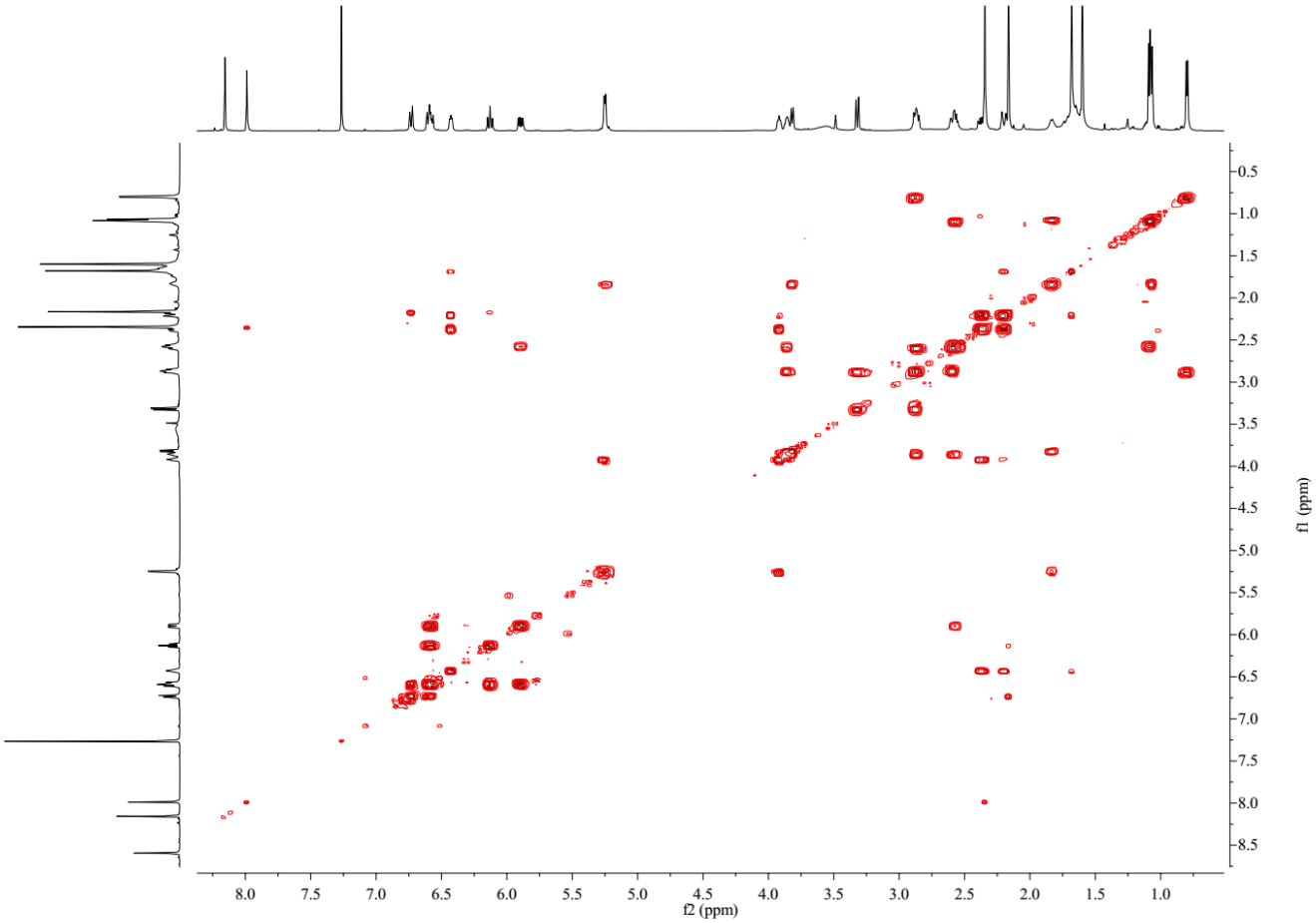


Figure S19. HSQC spectrum (600 MHz) of naphthomycin O (**1**) in $CDCl_3$

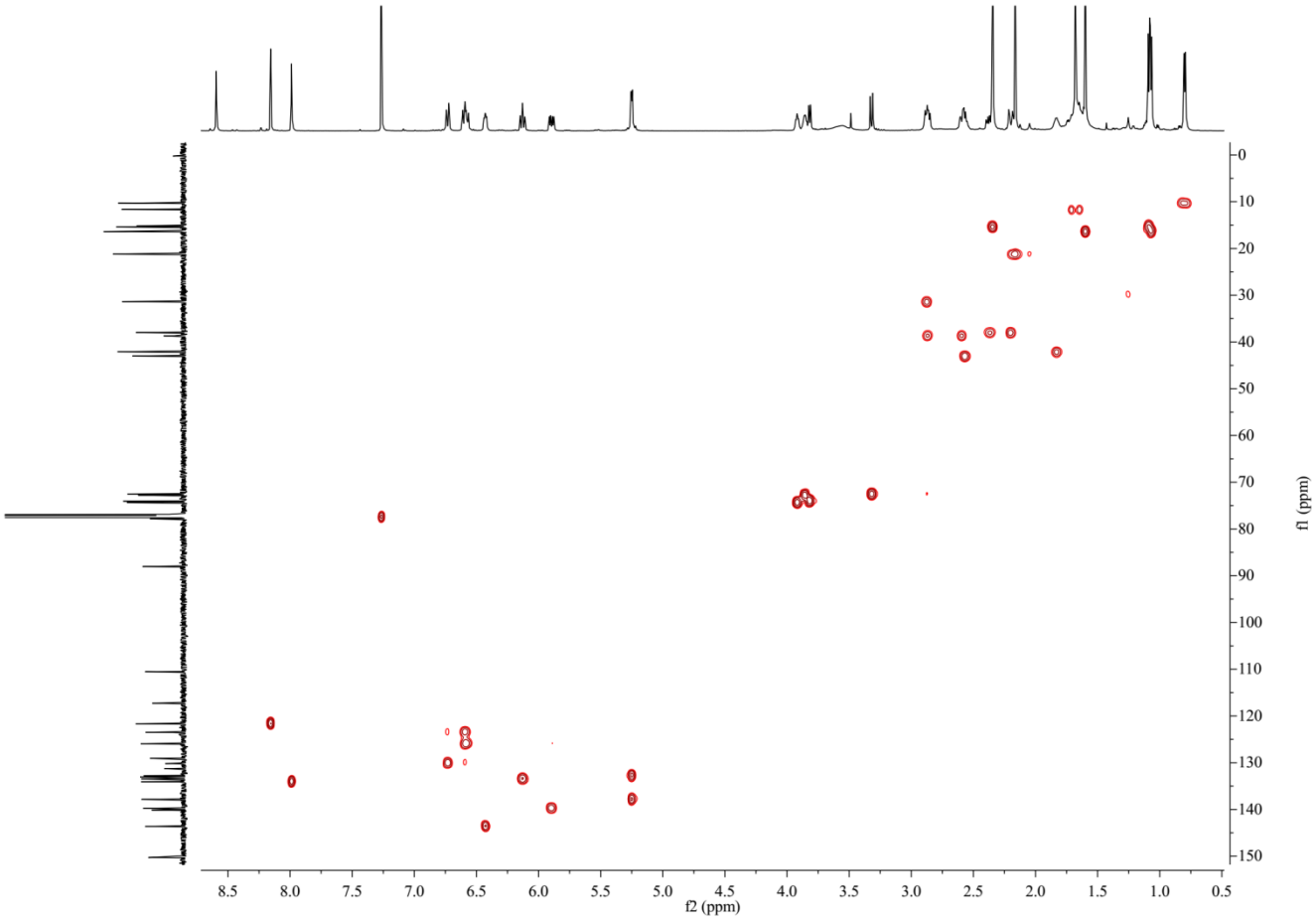


Figure S20. HMBC spectrum (600 MHz) of naphthomycin O (**1**) in $CDCl_3$

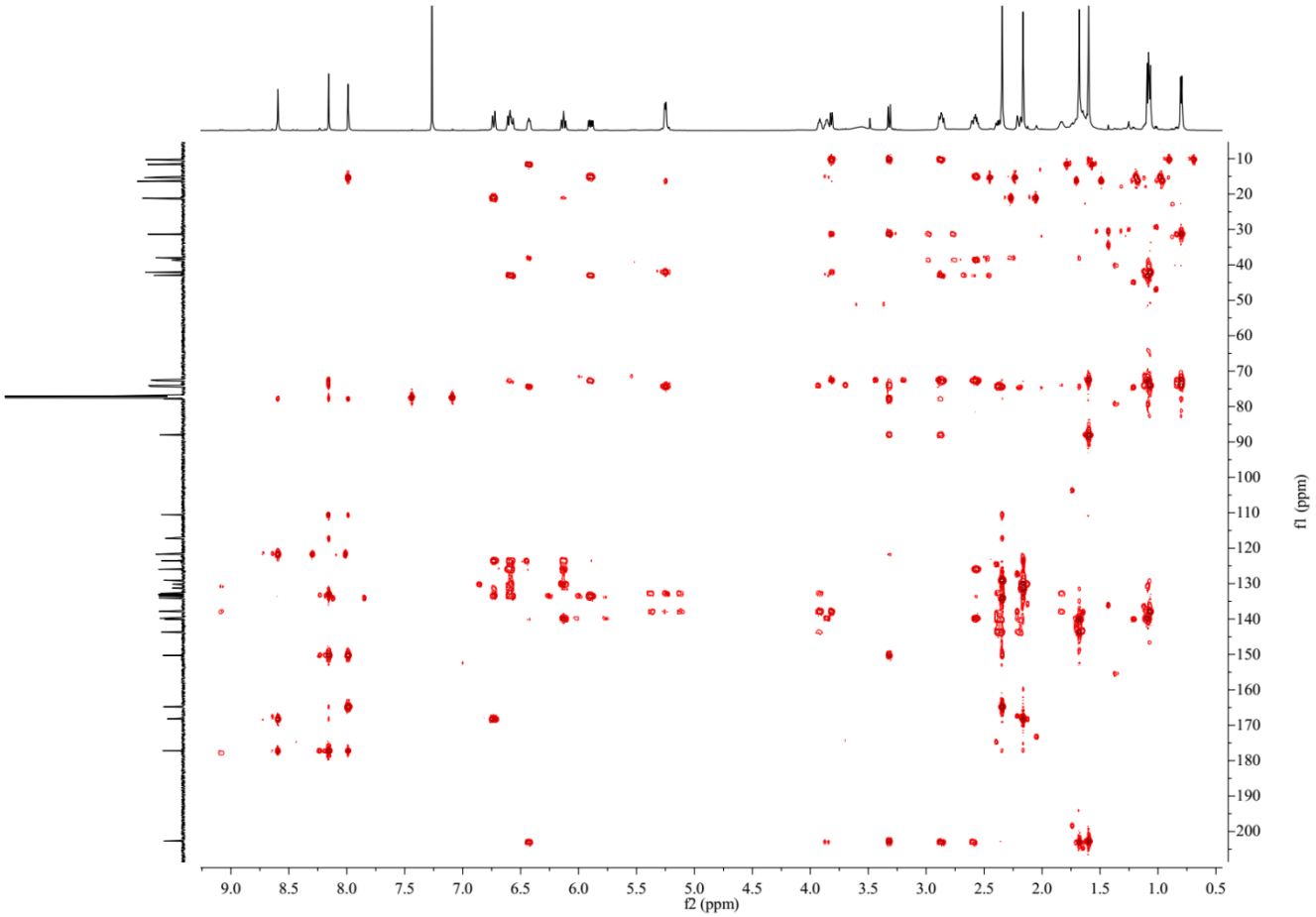


Figure S21. ROESY spectrum (600 MHz) of naphthomycin O (**1**) in $CDCl_3$

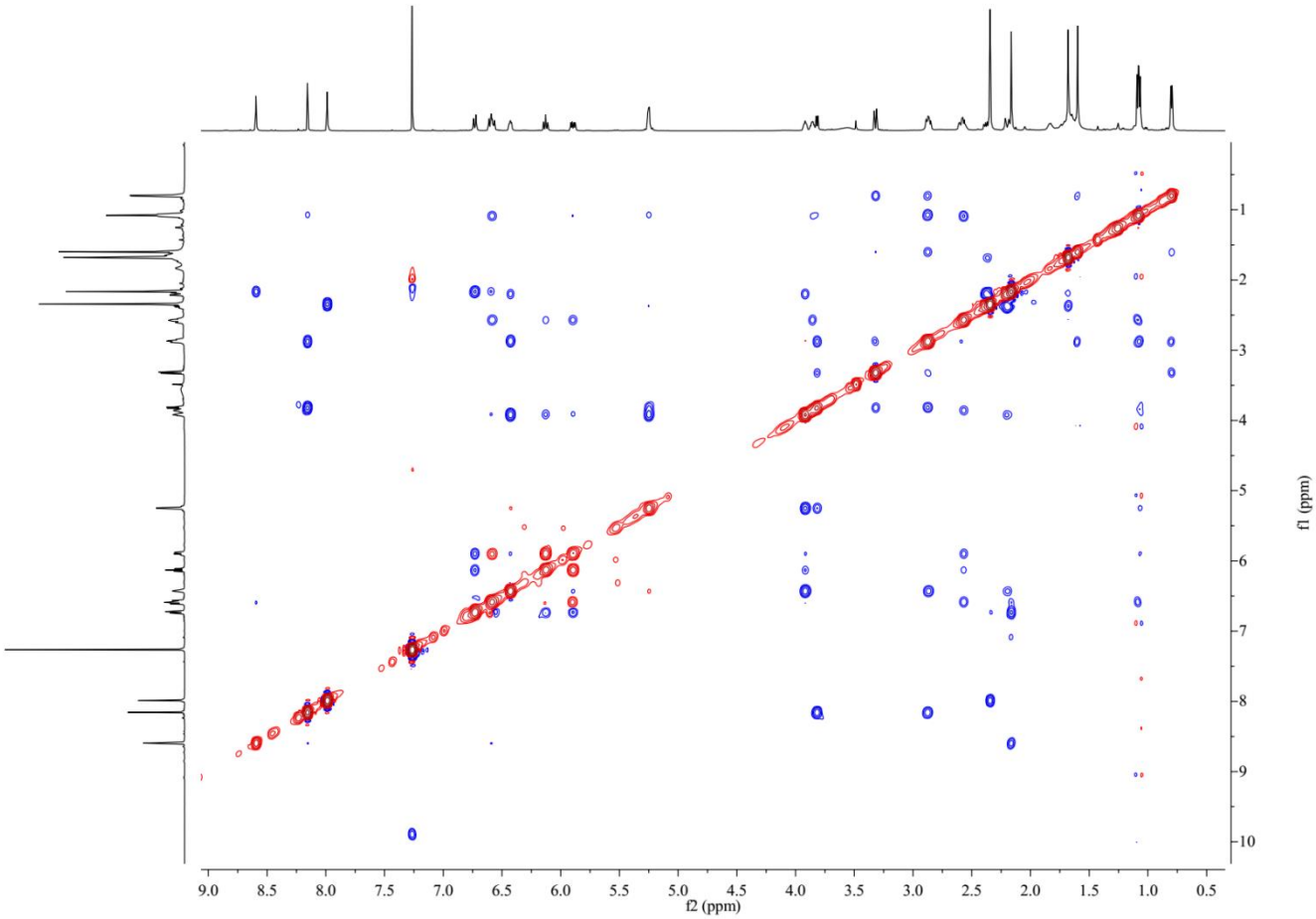


Figure S22. HRESIMS spectrum of naphthomycin O (**1**).

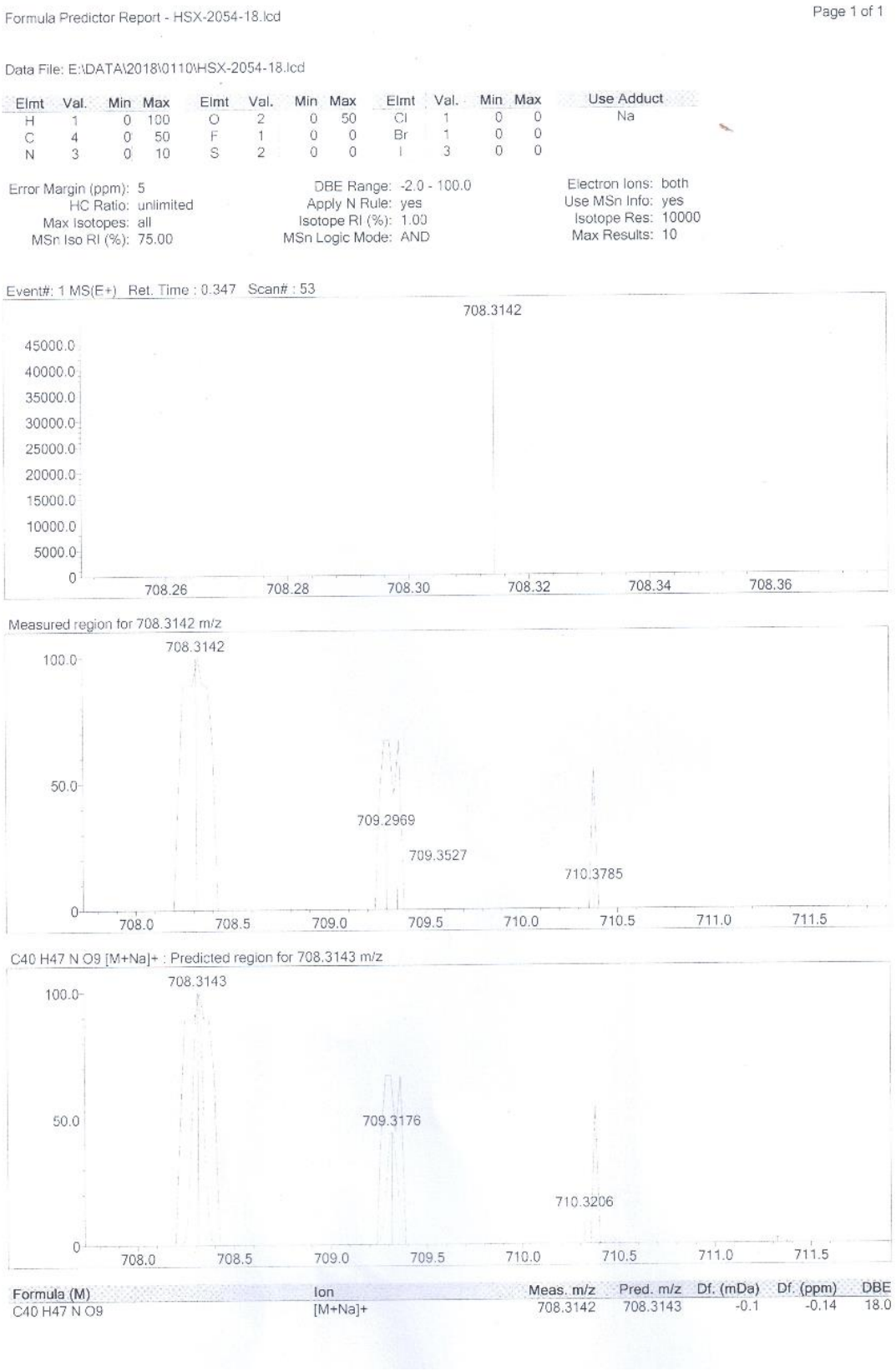


Figure S23. ^{1}H NMR spectrum (600 MHz) of **1a** in $CDCl_3$.

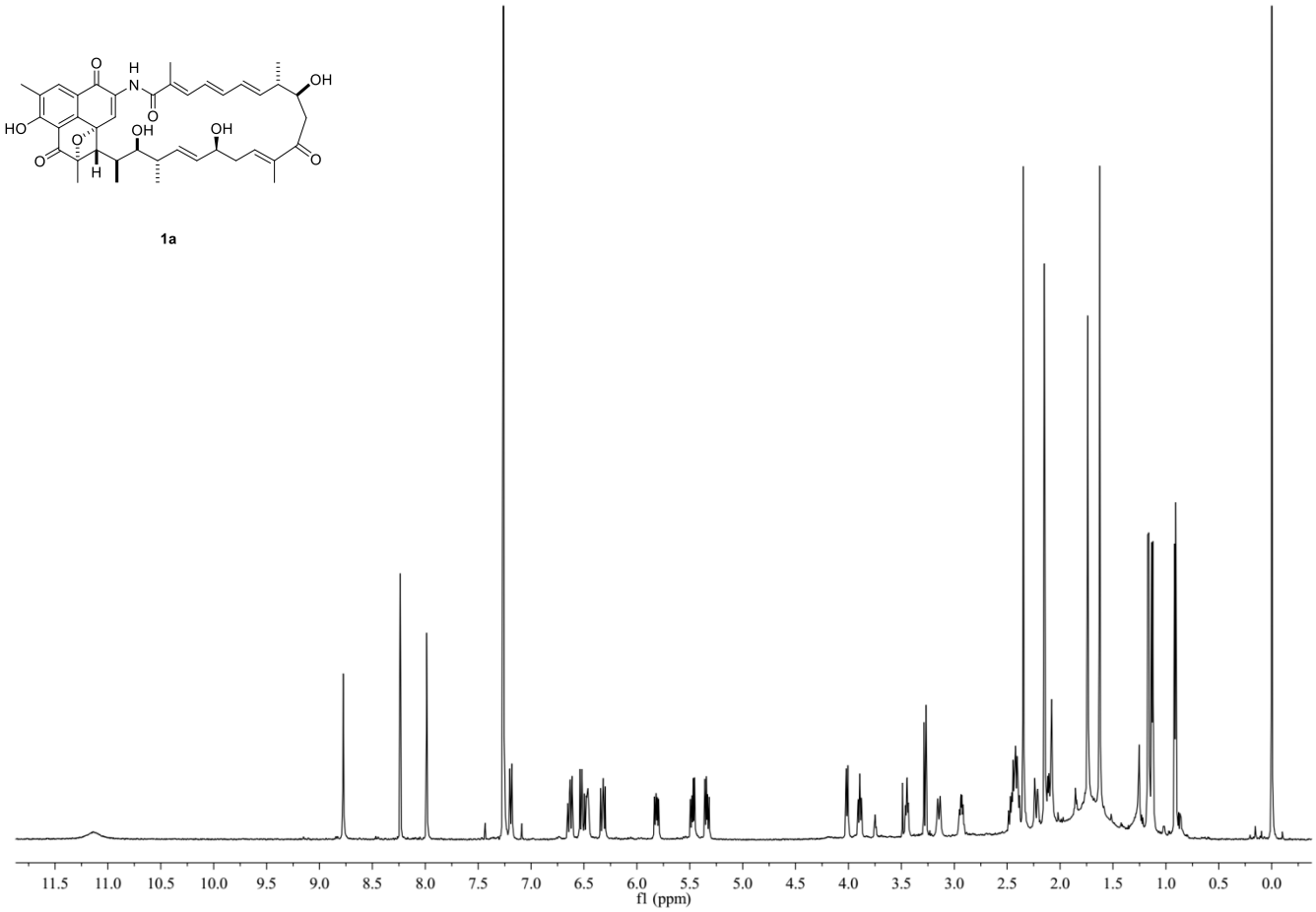


Figure S24. ^{13}C NMR spectrum (150 MHz) of **1a** in $CDCl_3$.

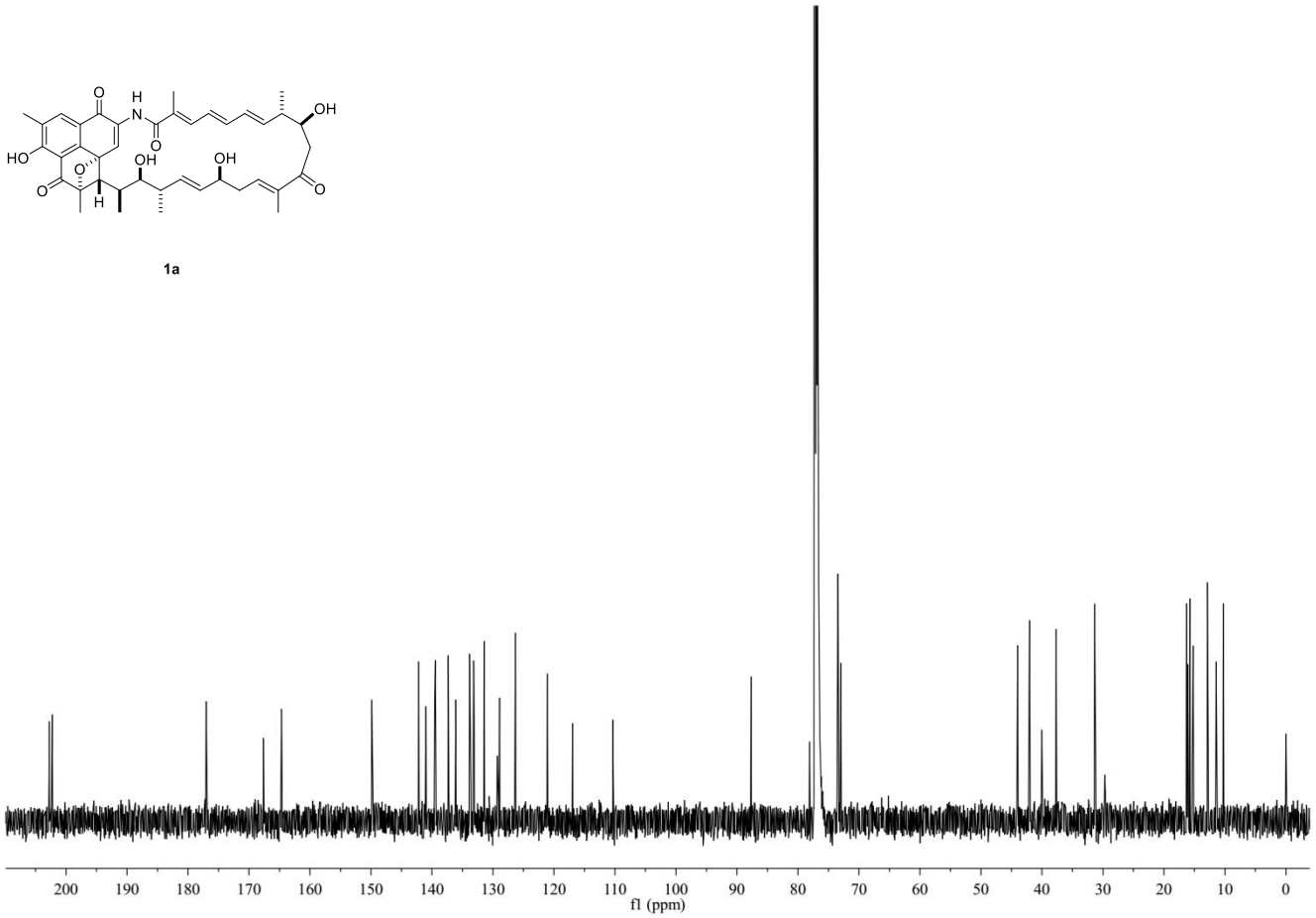


Figure S25. COSY spectrum (600 MHz) of **1a** in $CDCl_3$

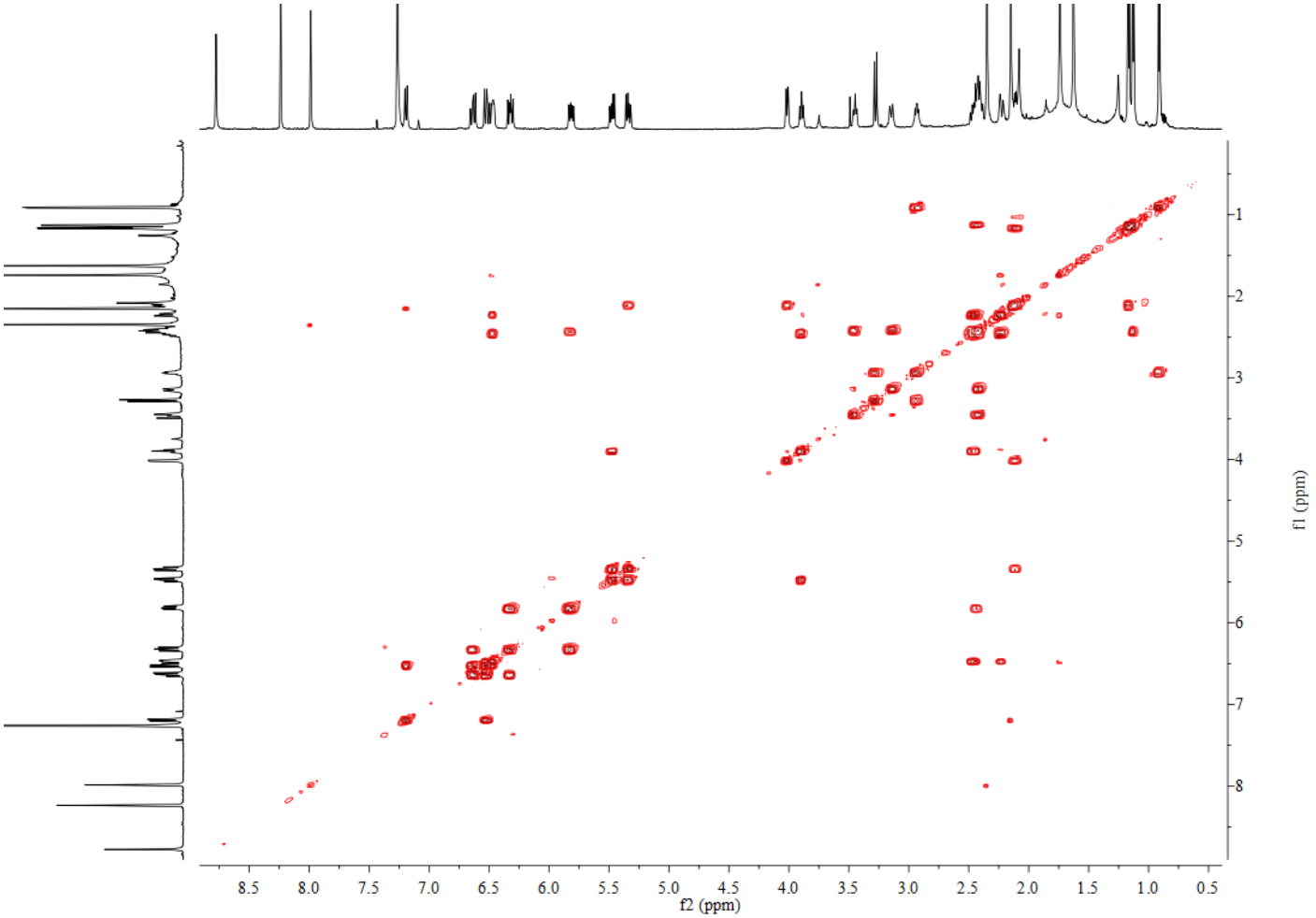


Figure S26. HSQC spectrum (600 MHz) of **1a** in $CDCl_3$

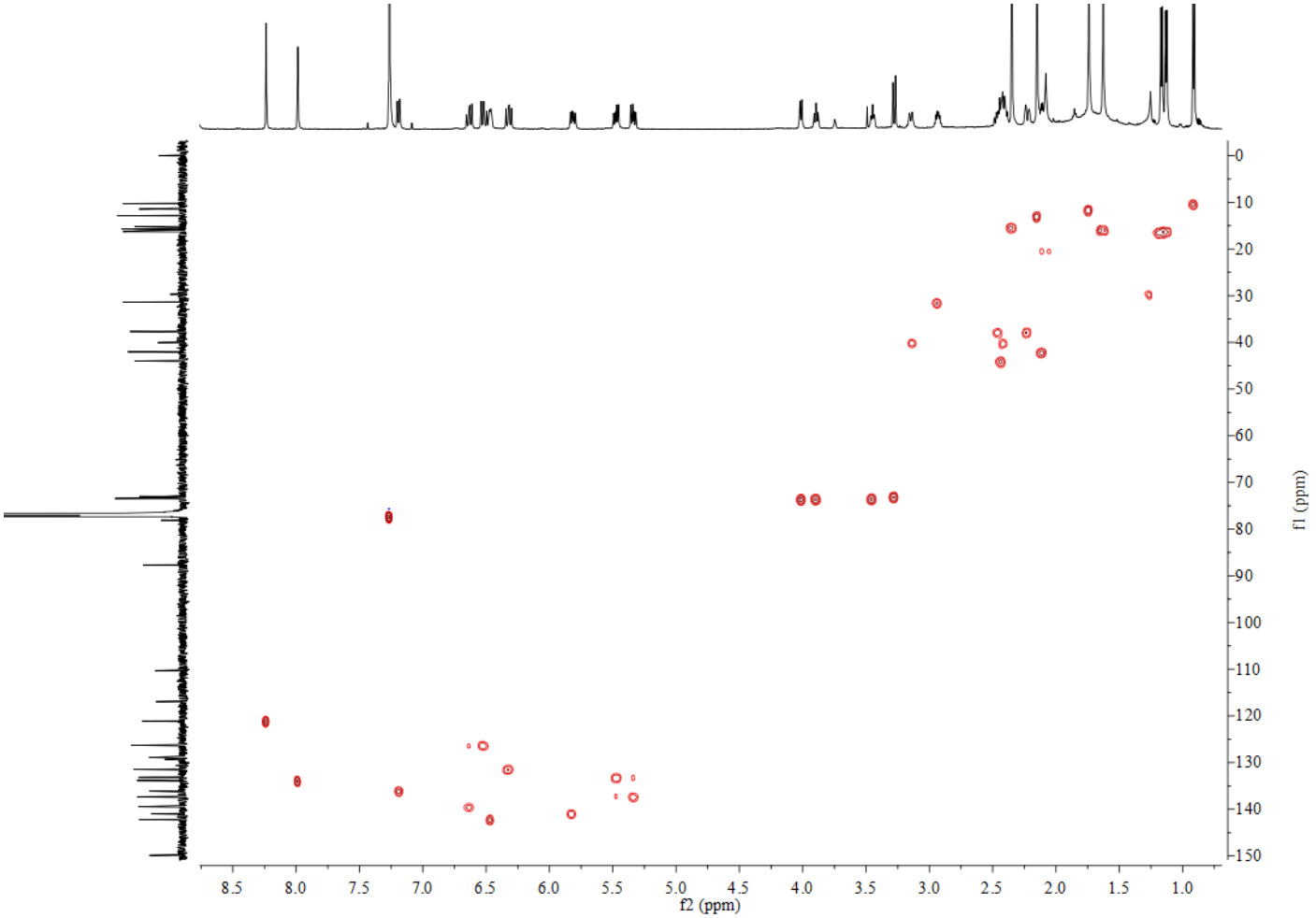


Figure S27. HMBC spectrum (600 MHz) of **1a** in $CDCl_3$

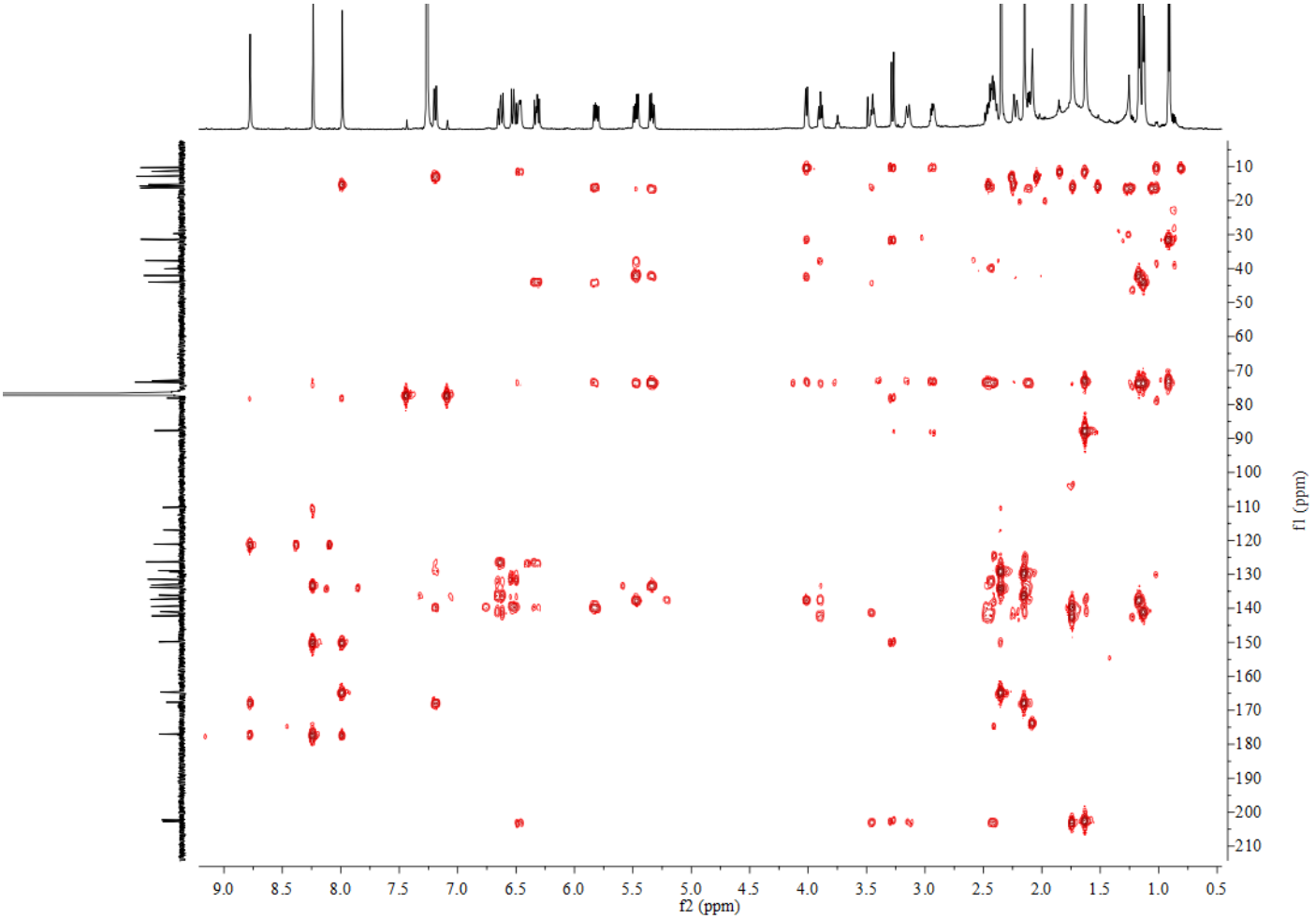


Figure S28. ROESY spectrum (600 MHz) of **1a** in $CDCl_3$

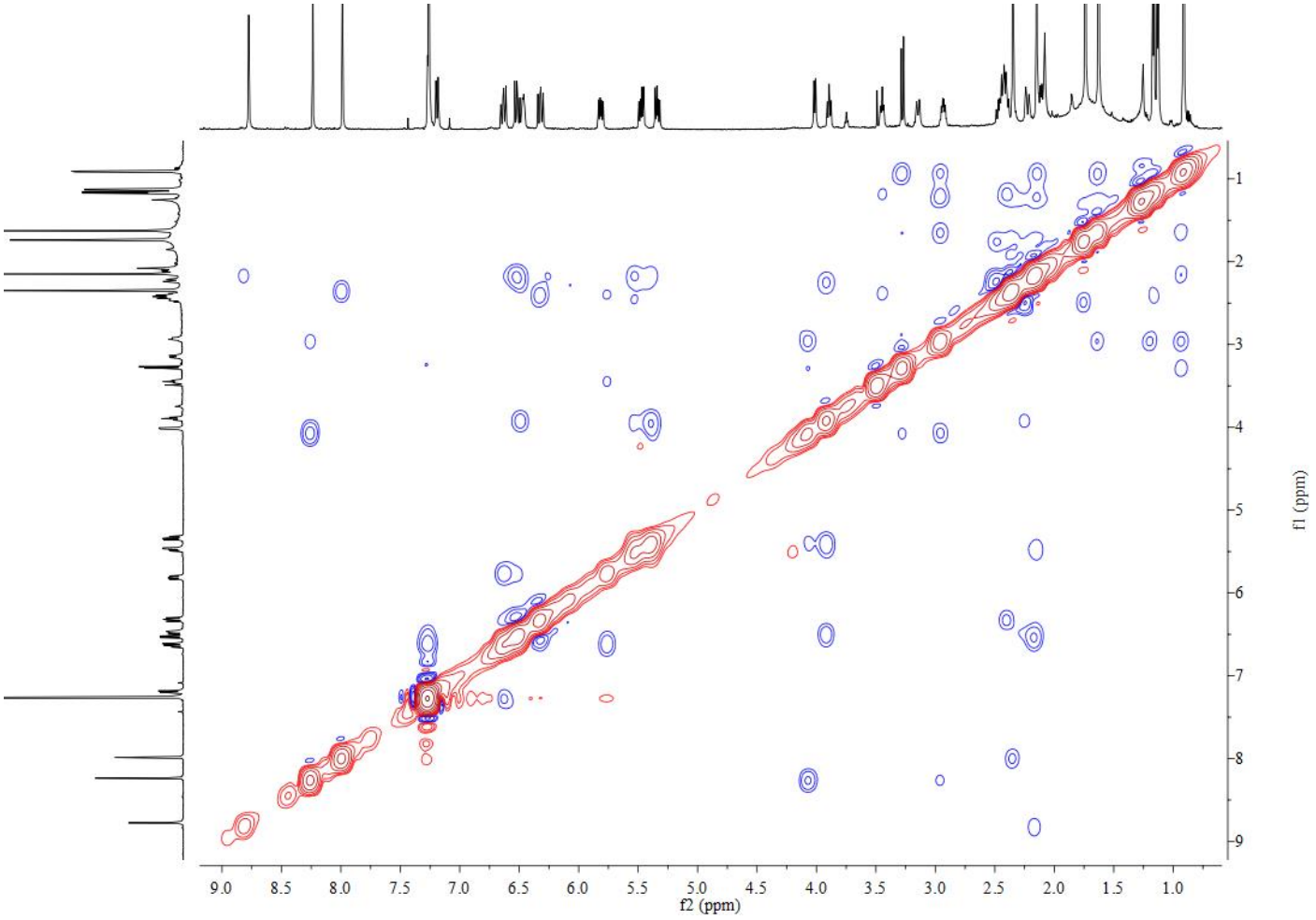


Figure S29. HRESIMS spectrum of **1a**.

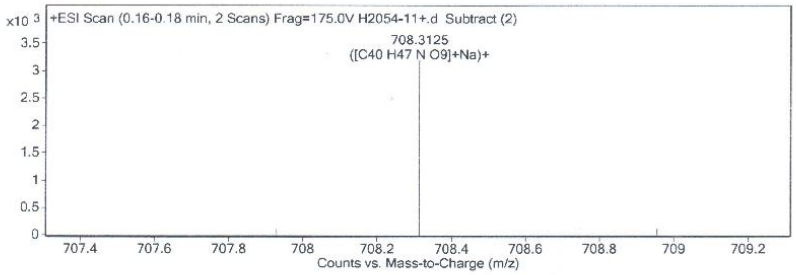
Qualitative Analysis Report

Data Filename	H2054-11+.d	**Sample Name**	H2054-11
Sample Type	Sample	**Position**	P1-E2
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	4/6/2017 3:42:23 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



Peak List

m/z	z	Abund
102.967		5848.29
154.9312		8907.25
214.9531		6367.04
228.968		7217.94
242.9474	1	26469.23
256.963	1	84544
414.953	1	9236.09
740.3388	1	10308.18

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C40 H47 N O9	685.3251	708.3143	708.3125	1.2	1.7	18.0000

--- End Of Report ---

Figure S30. ^{1}H NMR spectrum (600 MHz) of naphthomycin P (**2**) in $CDCl_3$.

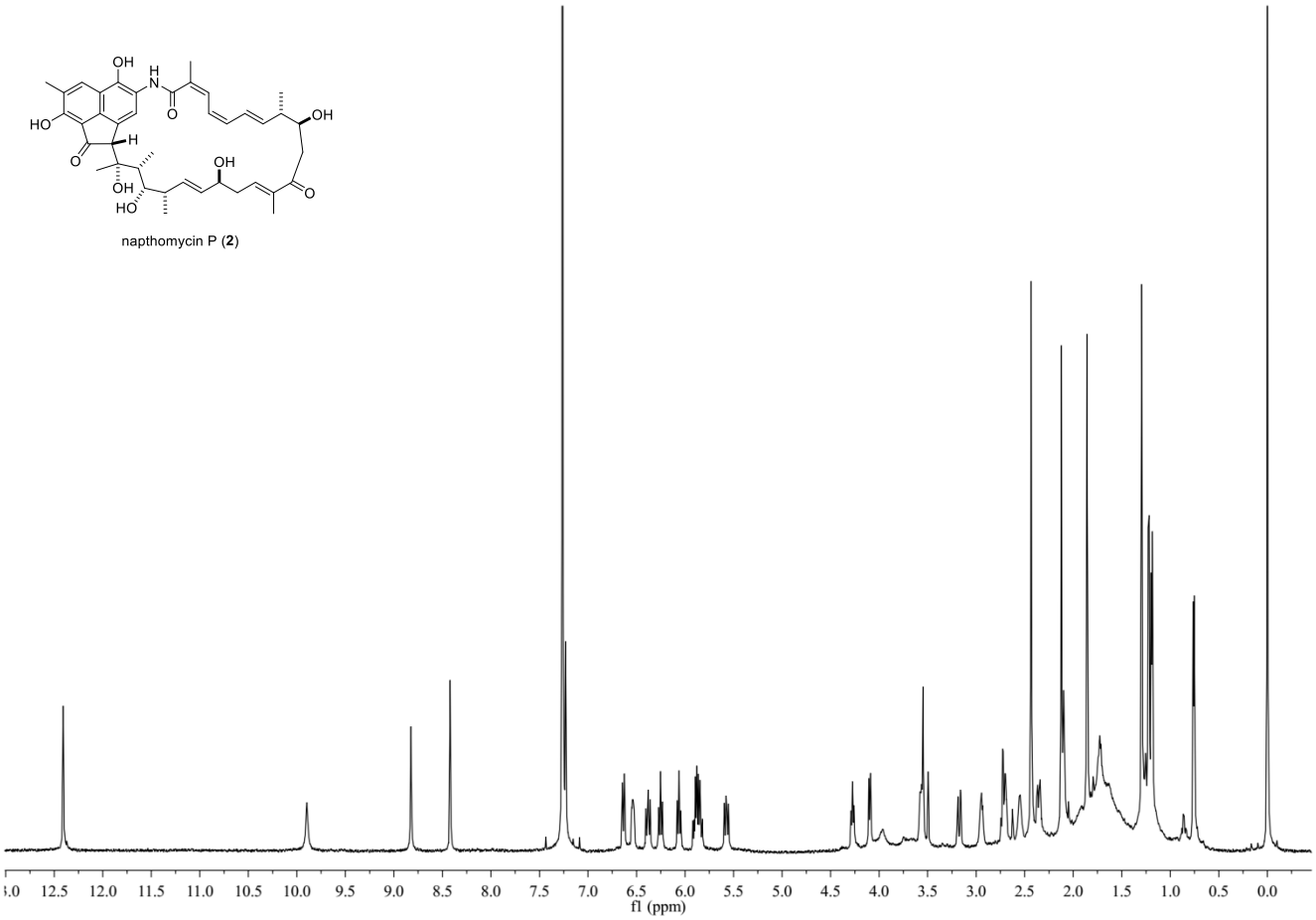


Figure S31. ^{13}C NMR spectrum (150 MHz) of naphthomycin P (**2**) in $CDCl_3$.

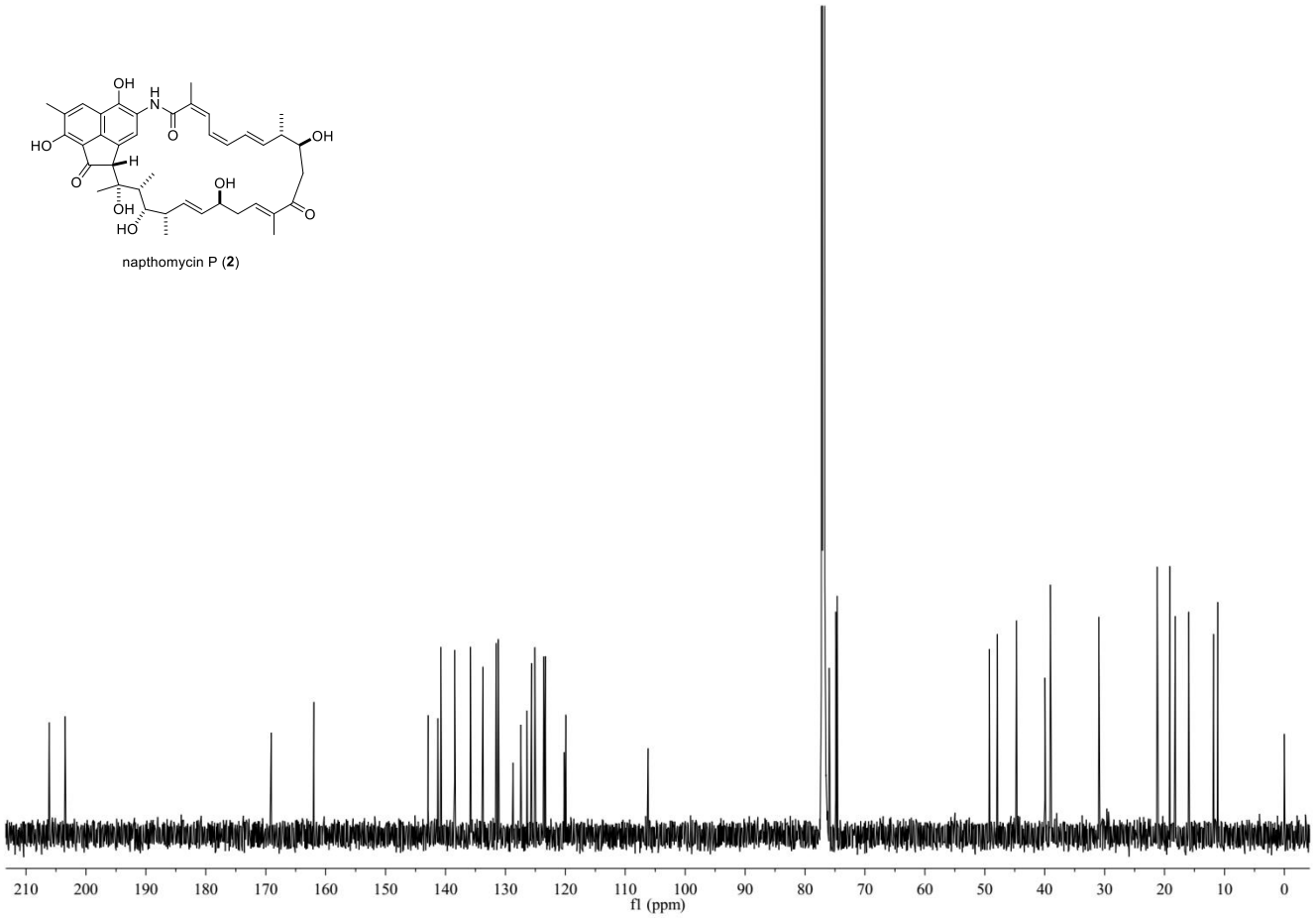


Figure S32. COSY spectrum (600 MHz) of naphthomycin P (**2**) in $CDCl_3$

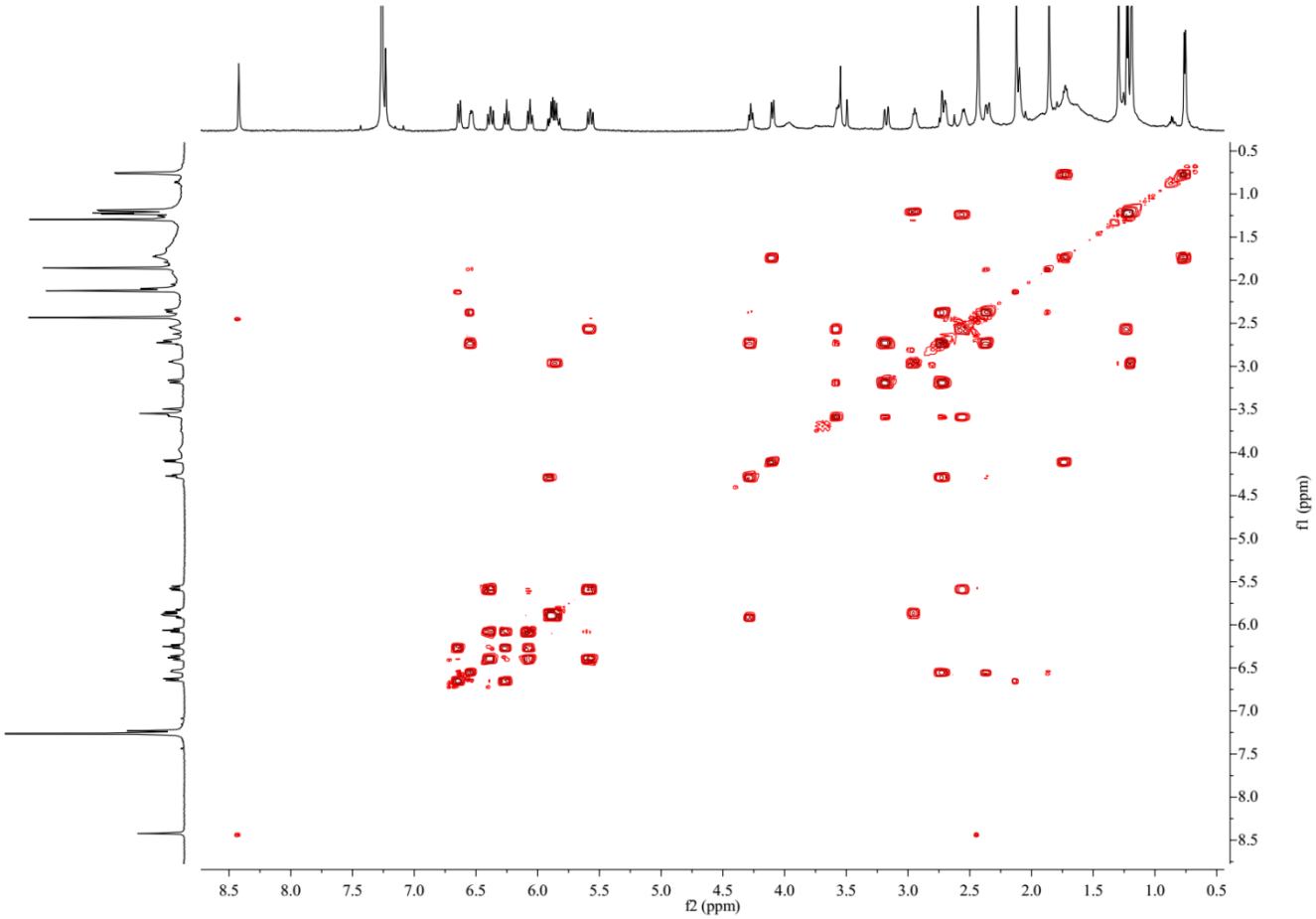


Figure S33. HSQC spectrum (600 MHz) of naphthomycin P (**2**) in $CDCl_3$

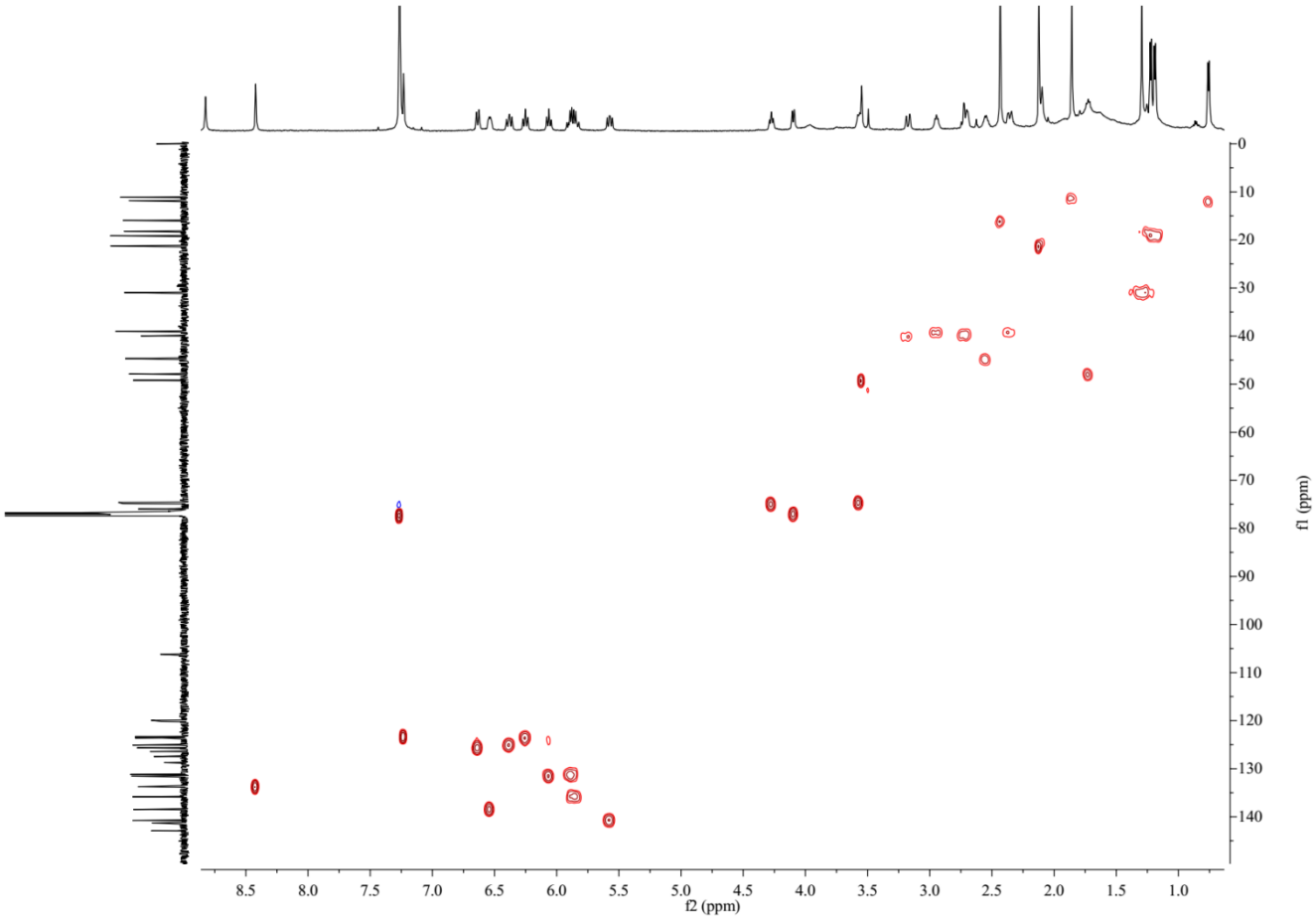


Figure S34. HMBC spectrum (600 MHz) of naphthomycin P (**2**) in $CDCl_3$

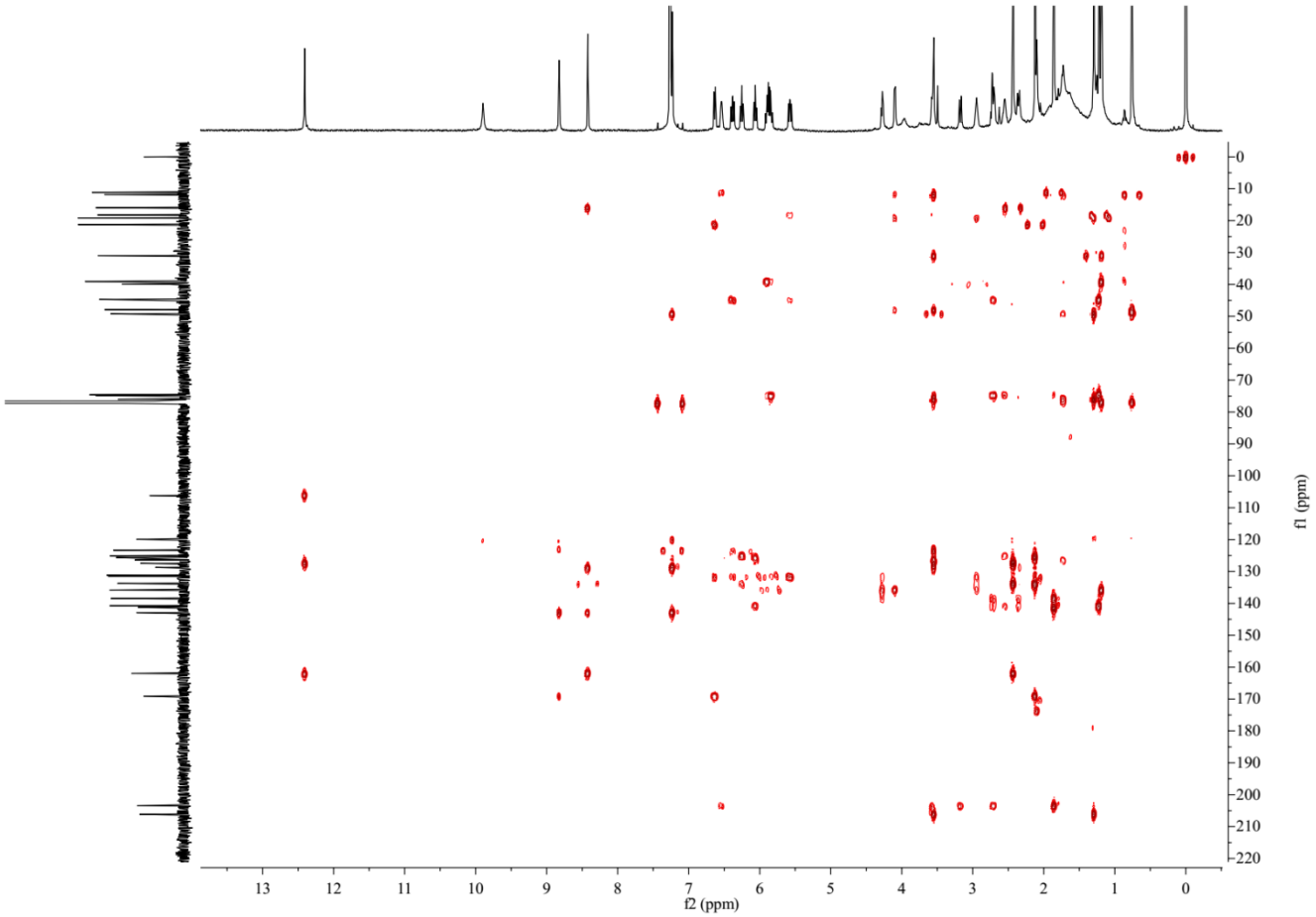


Figure S35. ROESY spectrum (600 MHz) of naphthomycin P (**2**) in $CDCl_3$

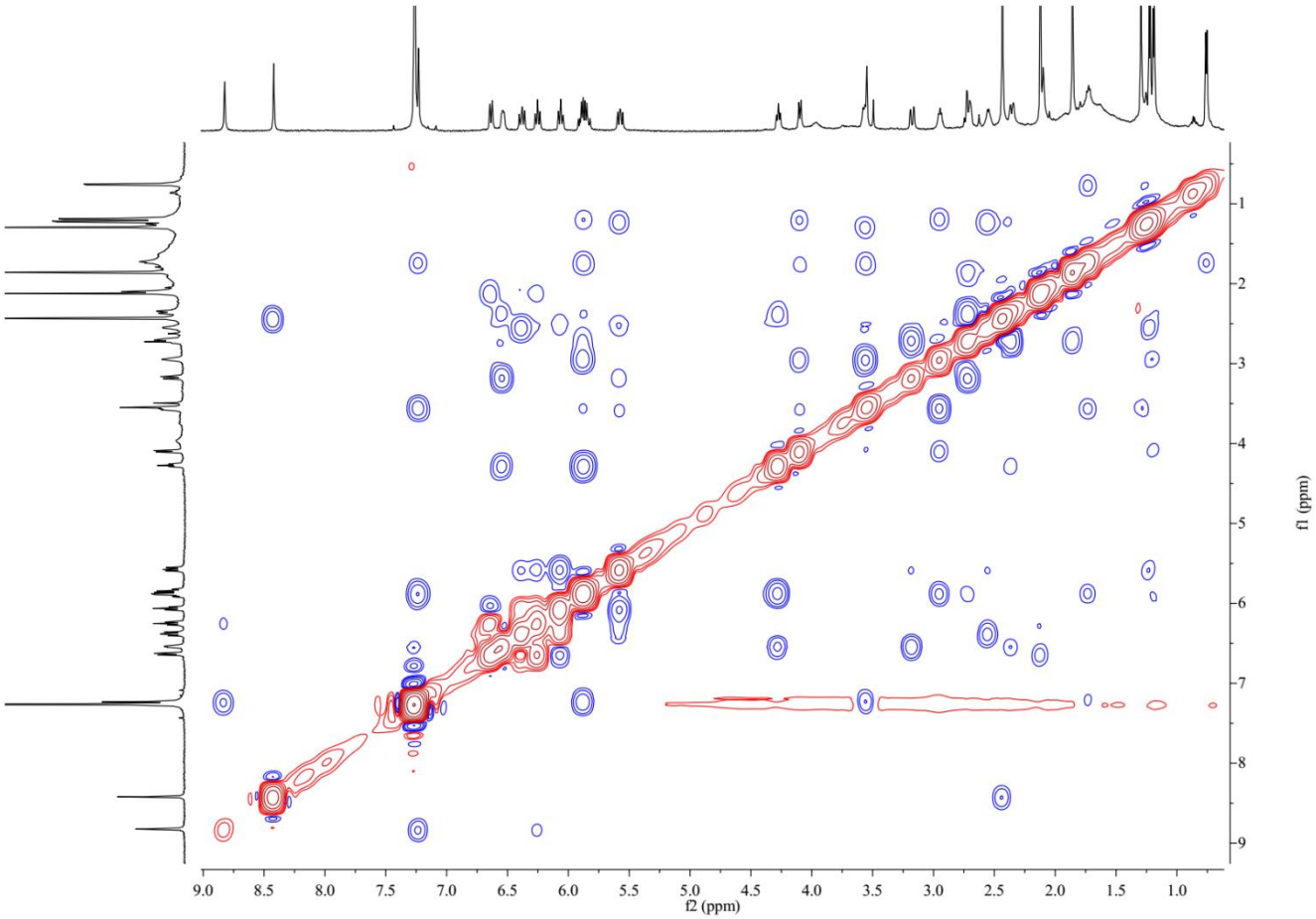


Figure S36. HRESIMS spectrum of naphthomycin P (**2**).

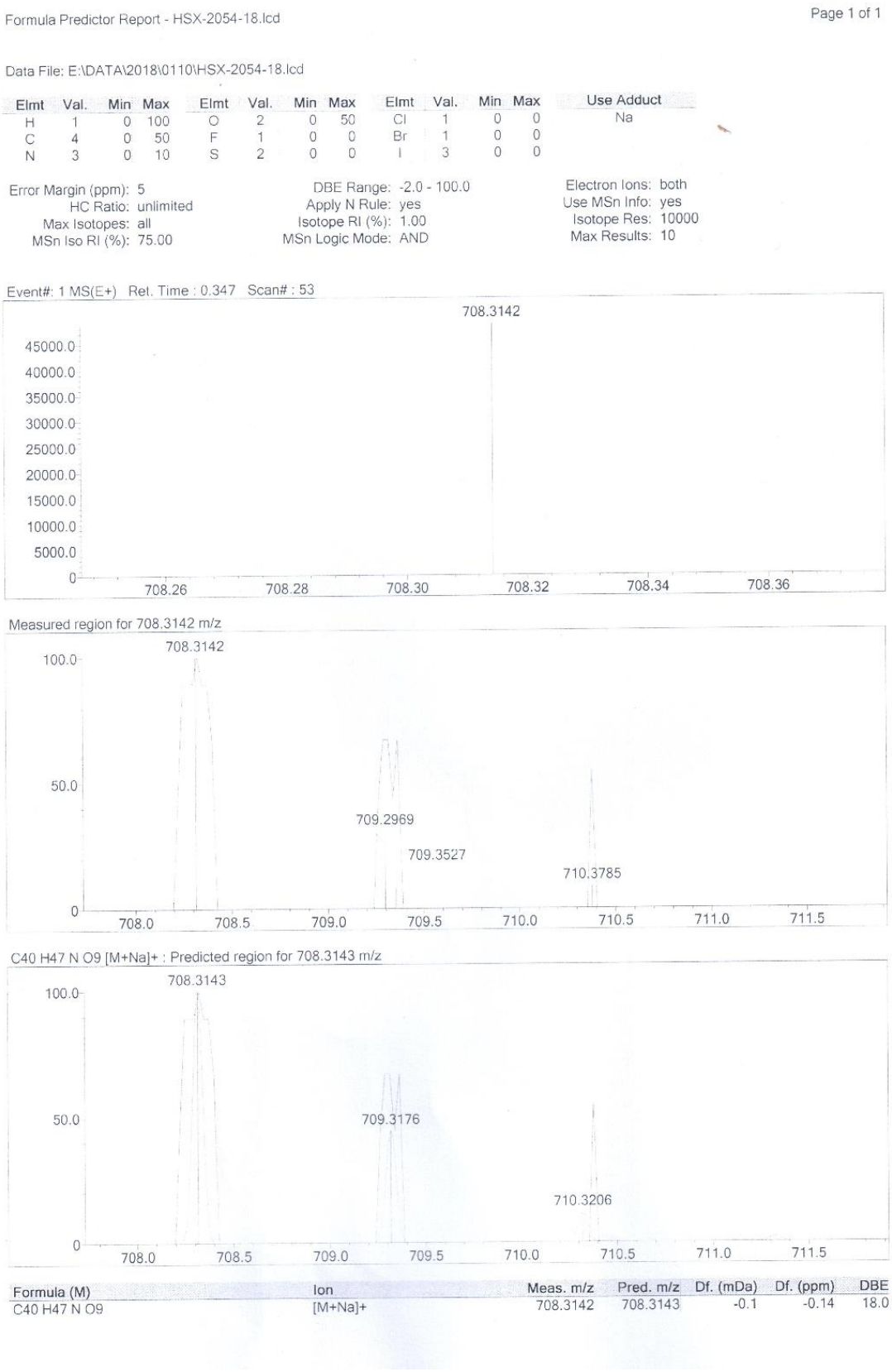


Figure S37. ^{1}H NMR spectrum (600 MHz) of **2a** in $CDCl_3$.

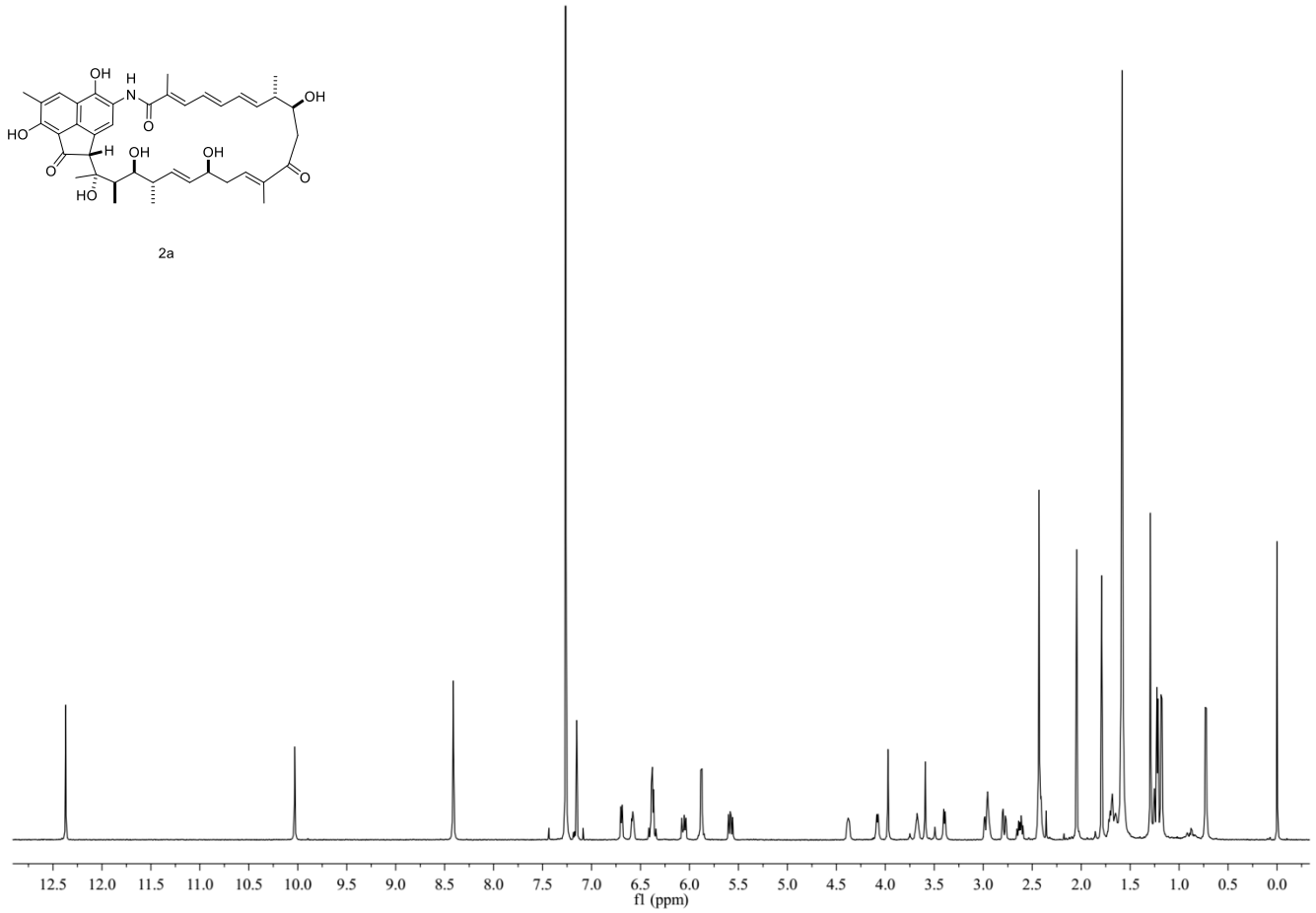


Figure S38. ^{13}C NMR spectrum (150 MHz) of **2a** in $CDCl_3$.

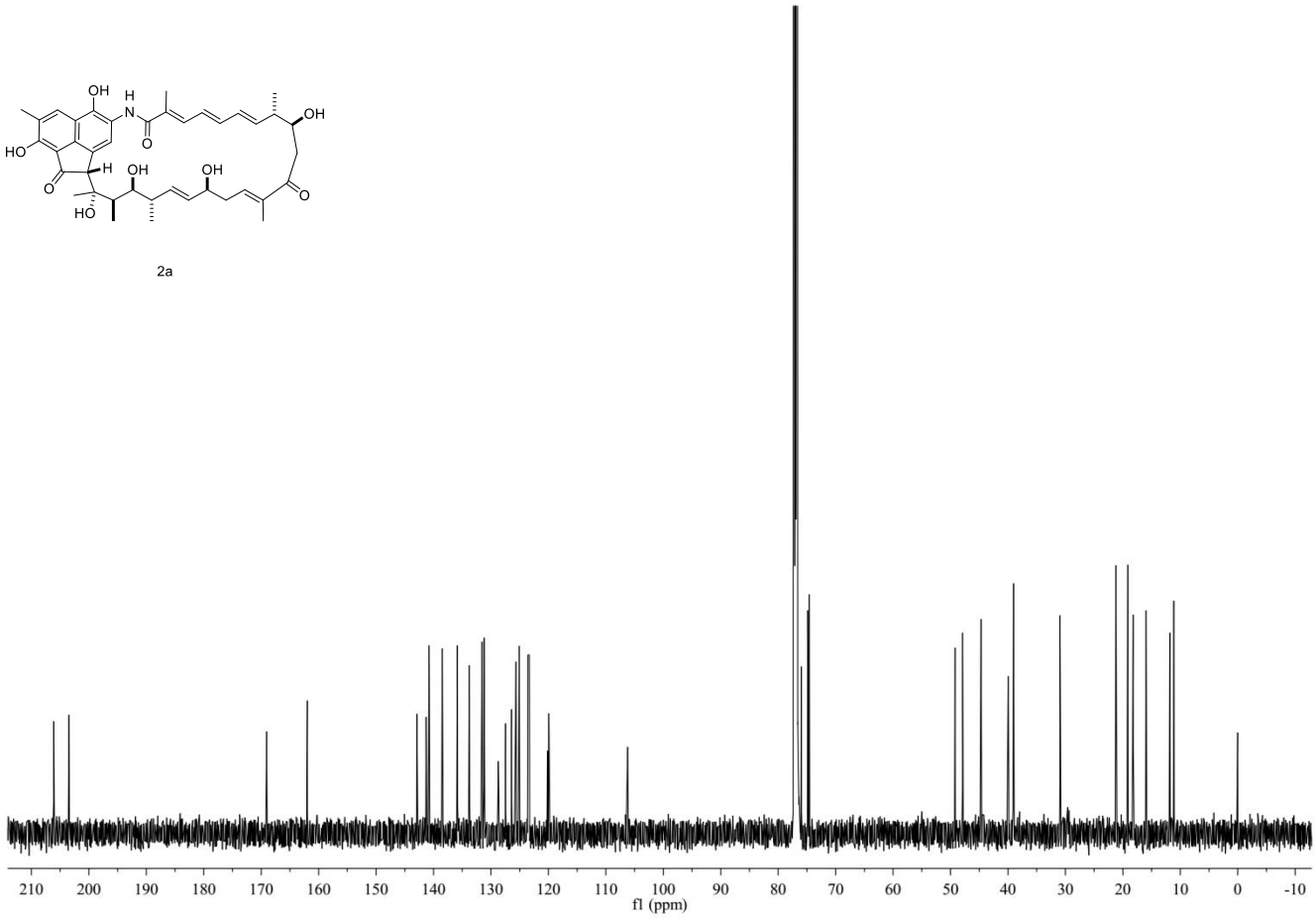


Figure S39. COSY spectrum (600 MHz) of **2a** in $CDCl_3$

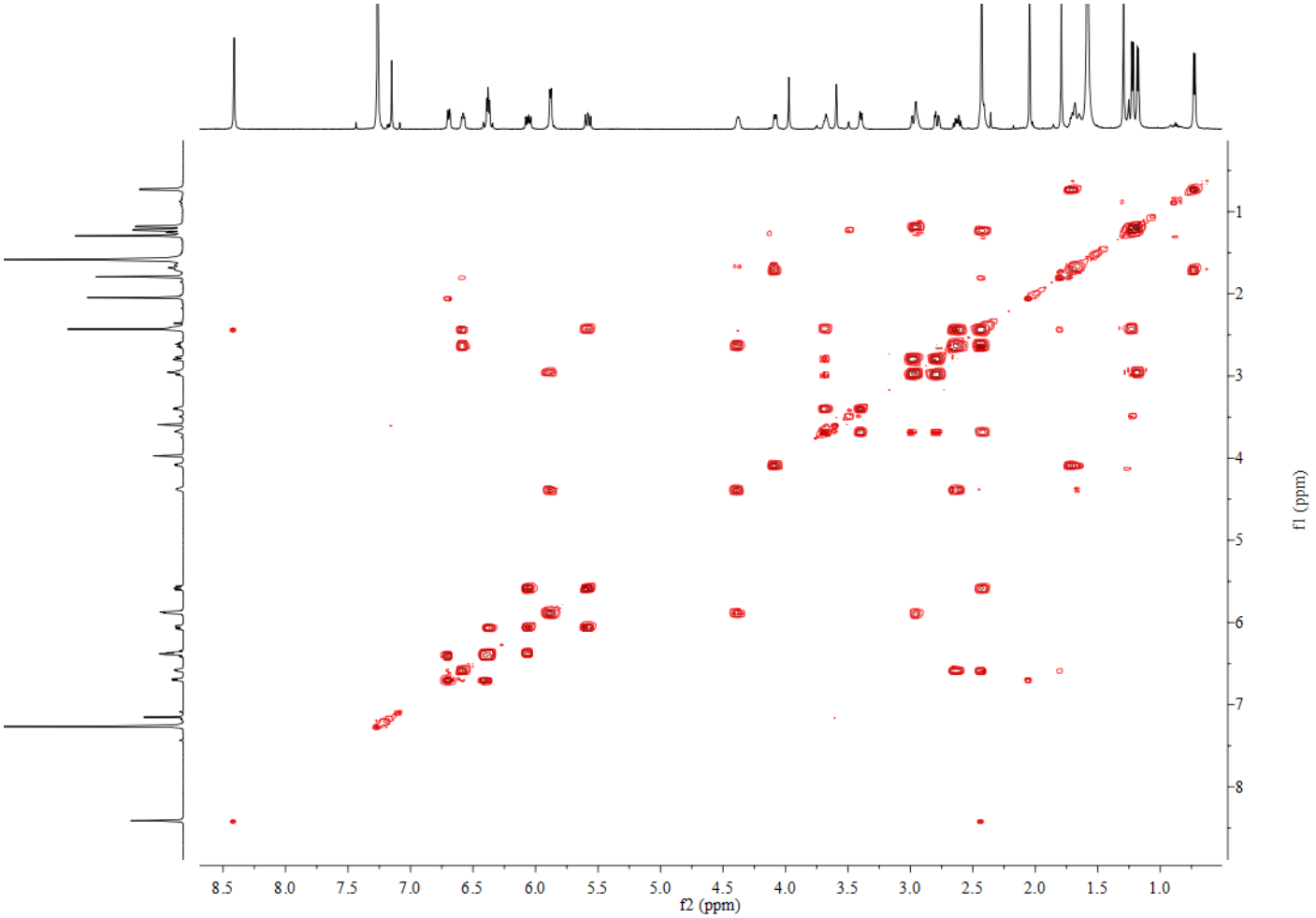


Figure S40. HSQC spectrum (600 MHz) of **2a** in $CDCl_3$

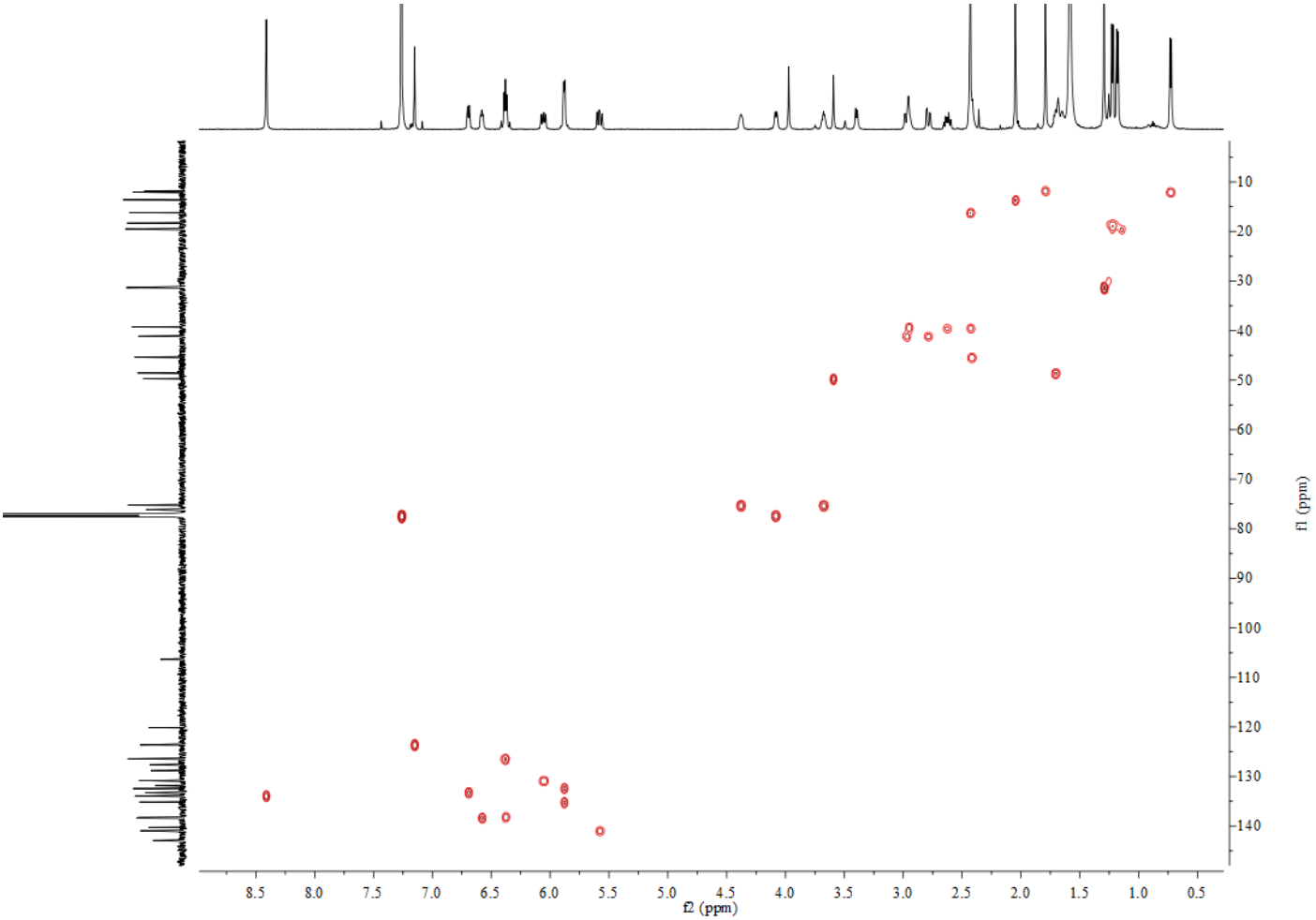


Figure S41. HMBC spectrum (600 MHz) of **2a** in $CDCl_3$

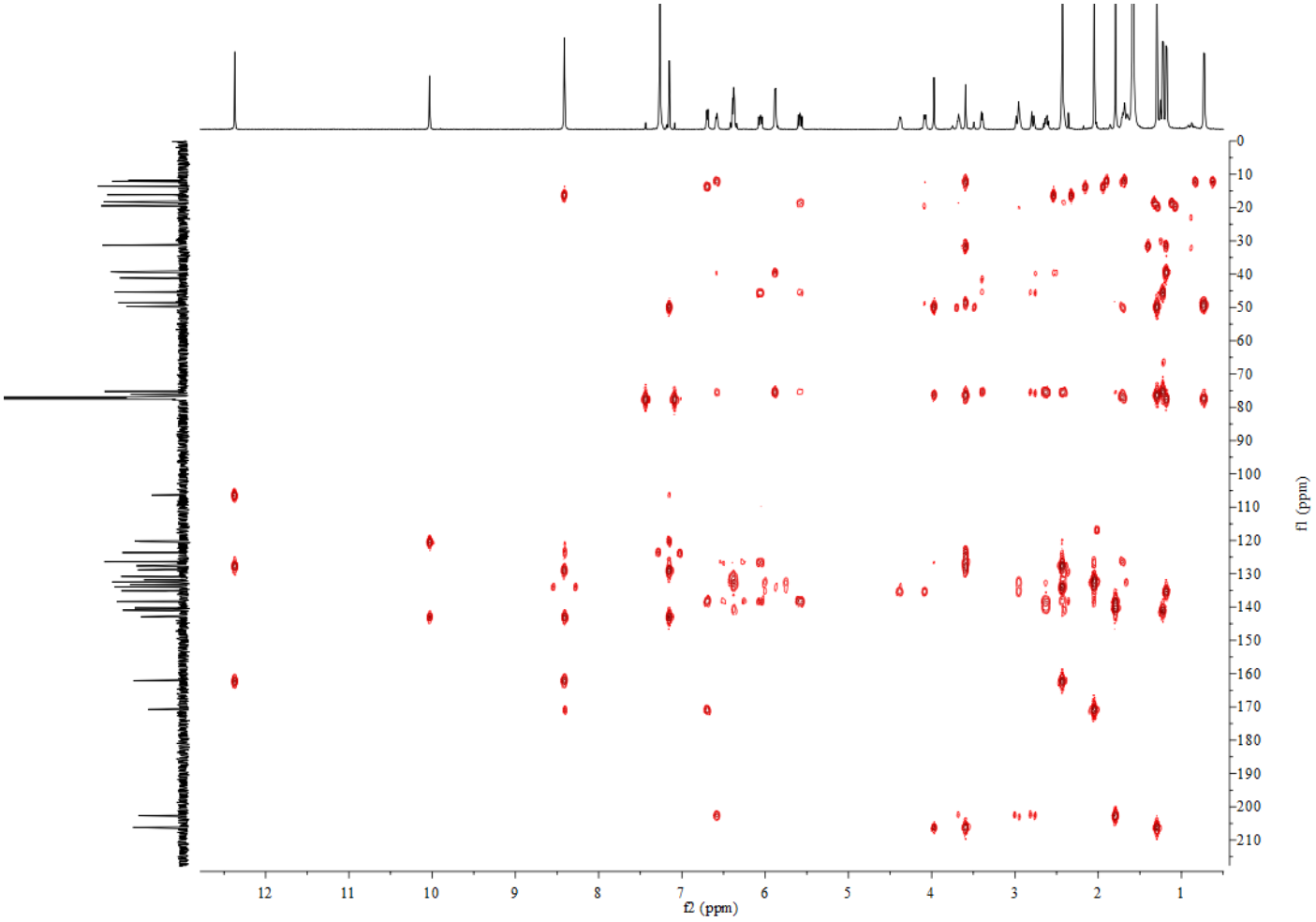


Figure S42. ROESY spectrum (600 MHz) of **2a** in $CDCl_3$

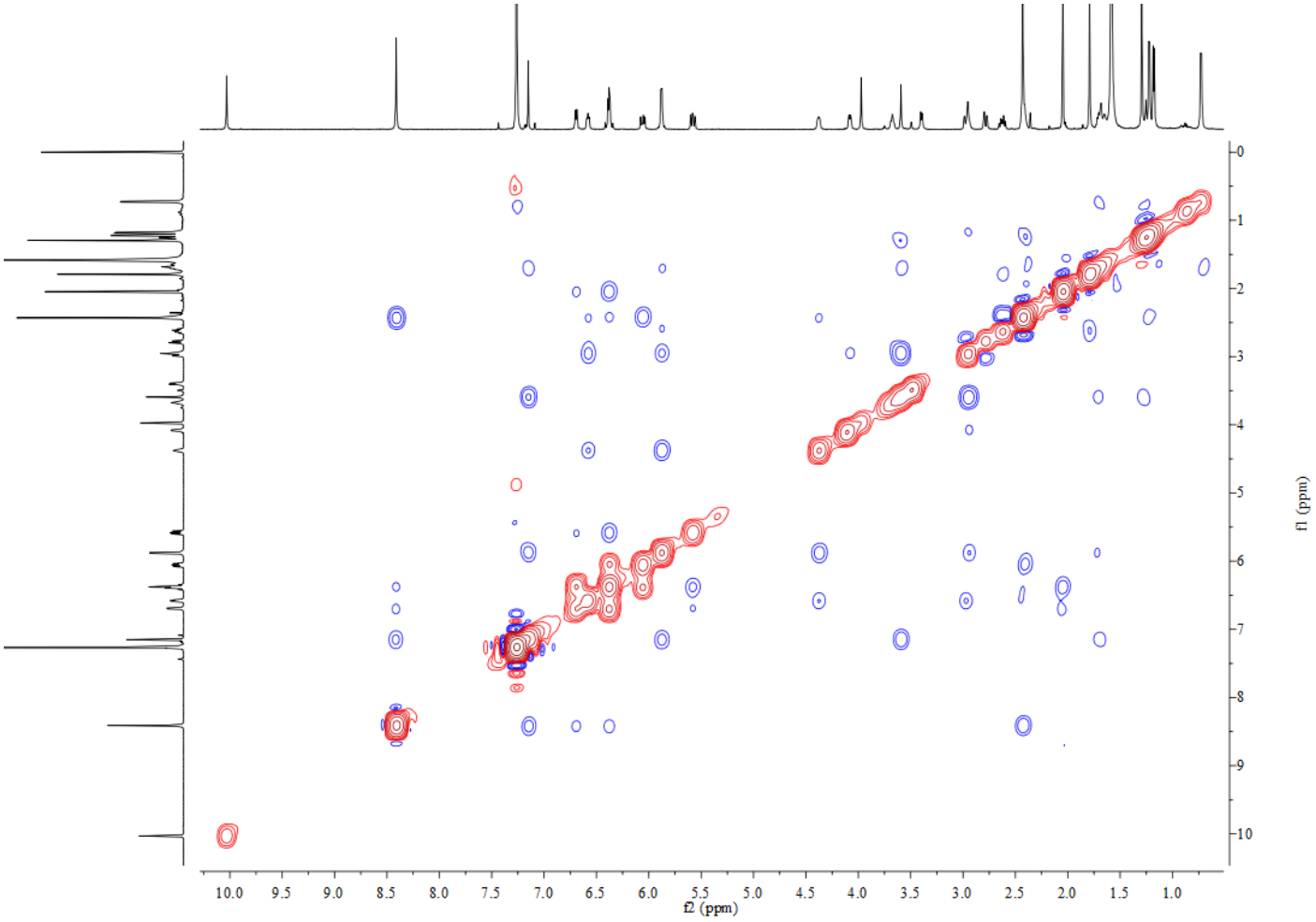


Figure S43. HRESIMS spectrum of **2a**.

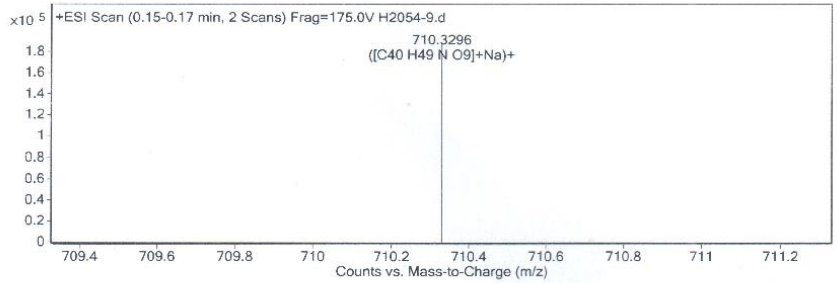
Qualitative Analysis Report

Data Filename	H2054-9.d	**Sample Name**	H2054-9
Sample Type	Sample	**Position**	P1-E1
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	4/6/2017 3:35:19 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
160.0496	1	13169.38		
345.2387	1	10345.73		
710.3296	1	189520.95	C40 H49 N O9	(M+Na)+
711.3326	1	79214.05	C40 H49 N O9	(M+Na)+
712.3356	1	18860.33	C40 H49 N O9	(M+Na)+
726.3032	1	53824.31		
727.3066	1	24458.73		
728.3053	1	9344.27		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C40 H49 N O9	687.3407	710.3300	710.3296	0.5	0.7	17.0000

--- End Of Report ---

Figure S44. ^{1}H NMR spectrum (600 MHz) of naphthomycin Q (**3**) in CD_3OD.

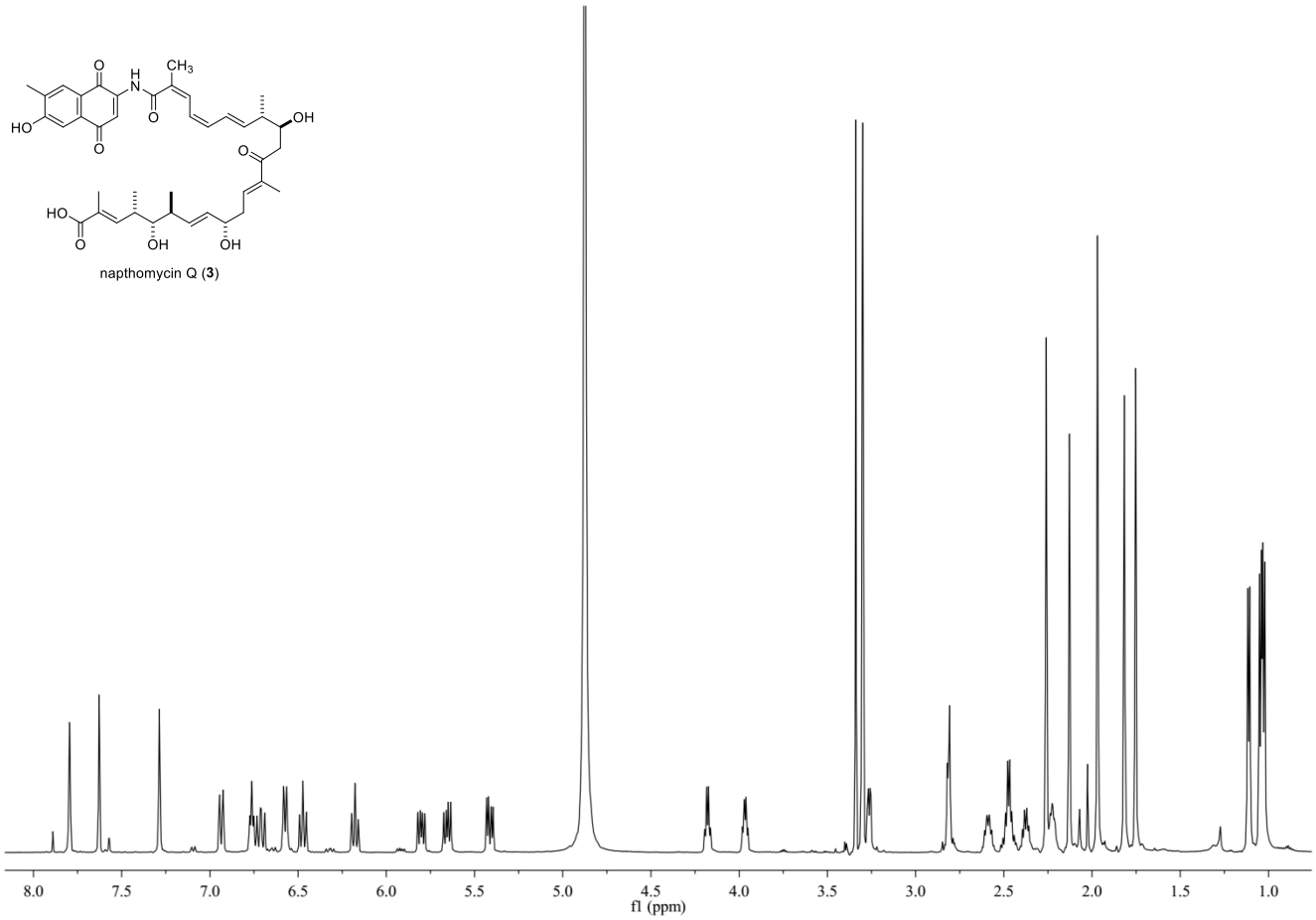


Figure S45. ^{13}C NMR spectrum (150 MHz) of naphthomycin Q (**3**) in CD_3OD.

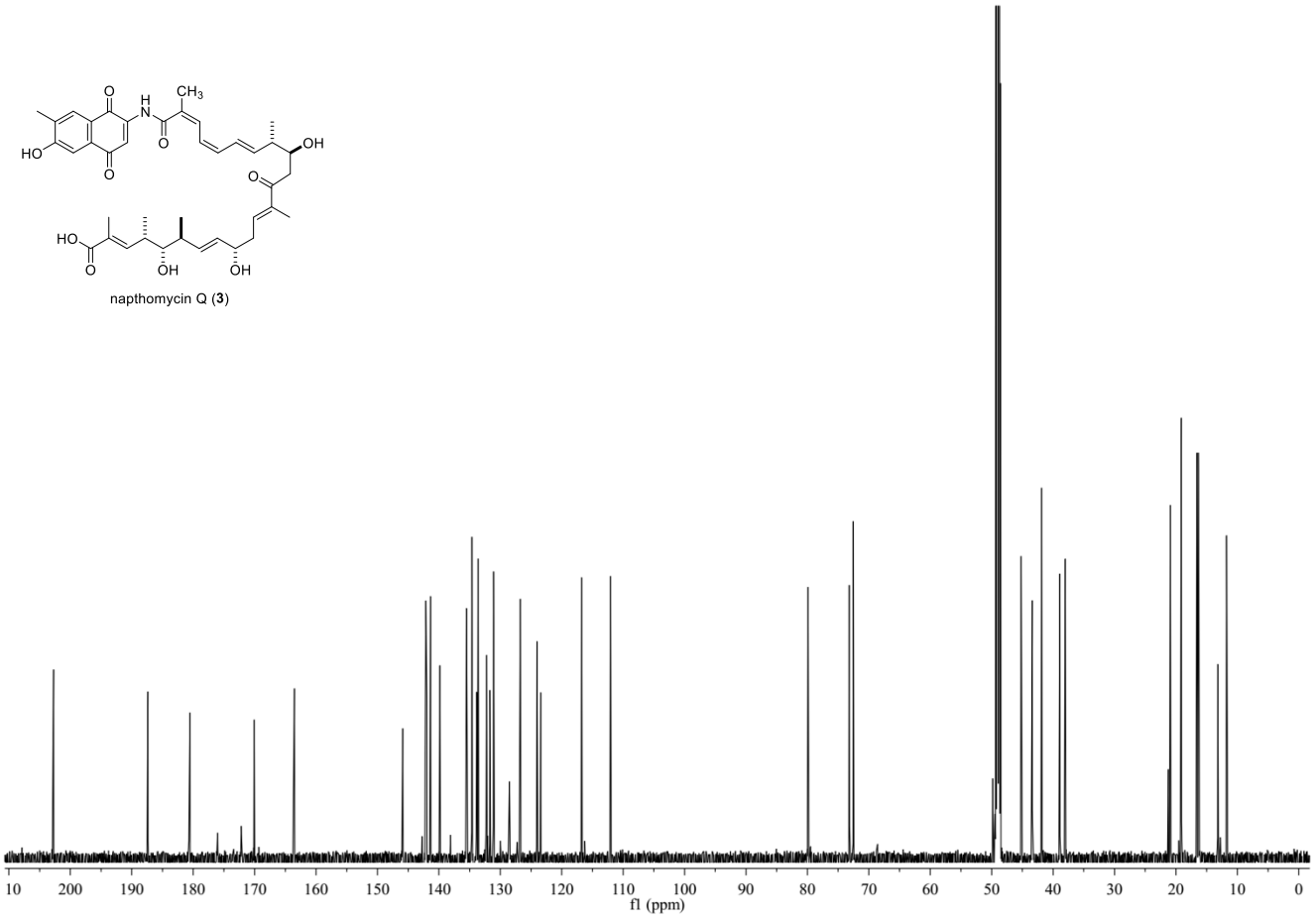


Figure S46. COSY spectrum (600 MHz) of naphthomycin Q (**3**) in CD_3OD

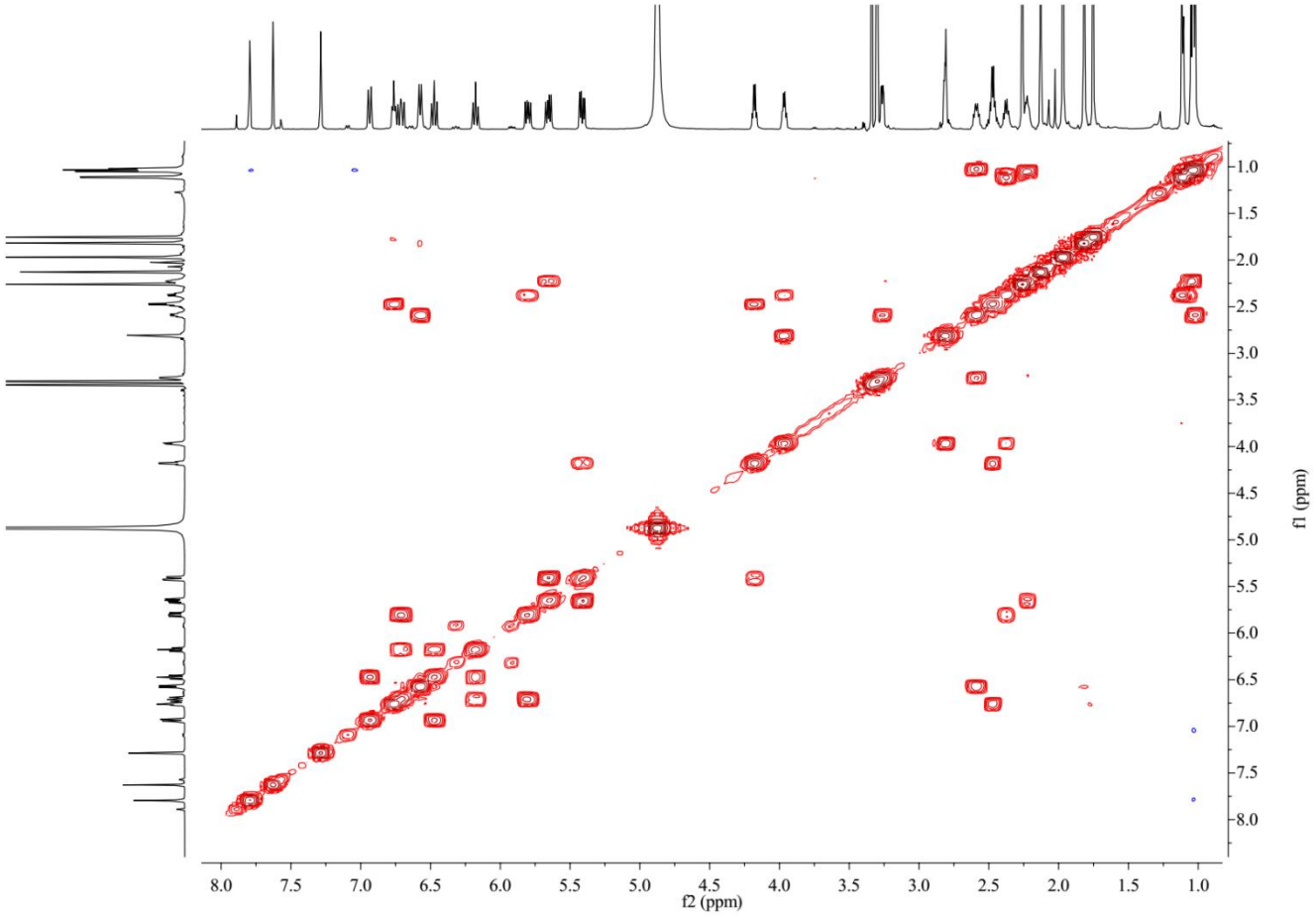


Figure S47. HSQC spectrum (600 MHz) of naphthomycin Q (**3**) in CD_3OD

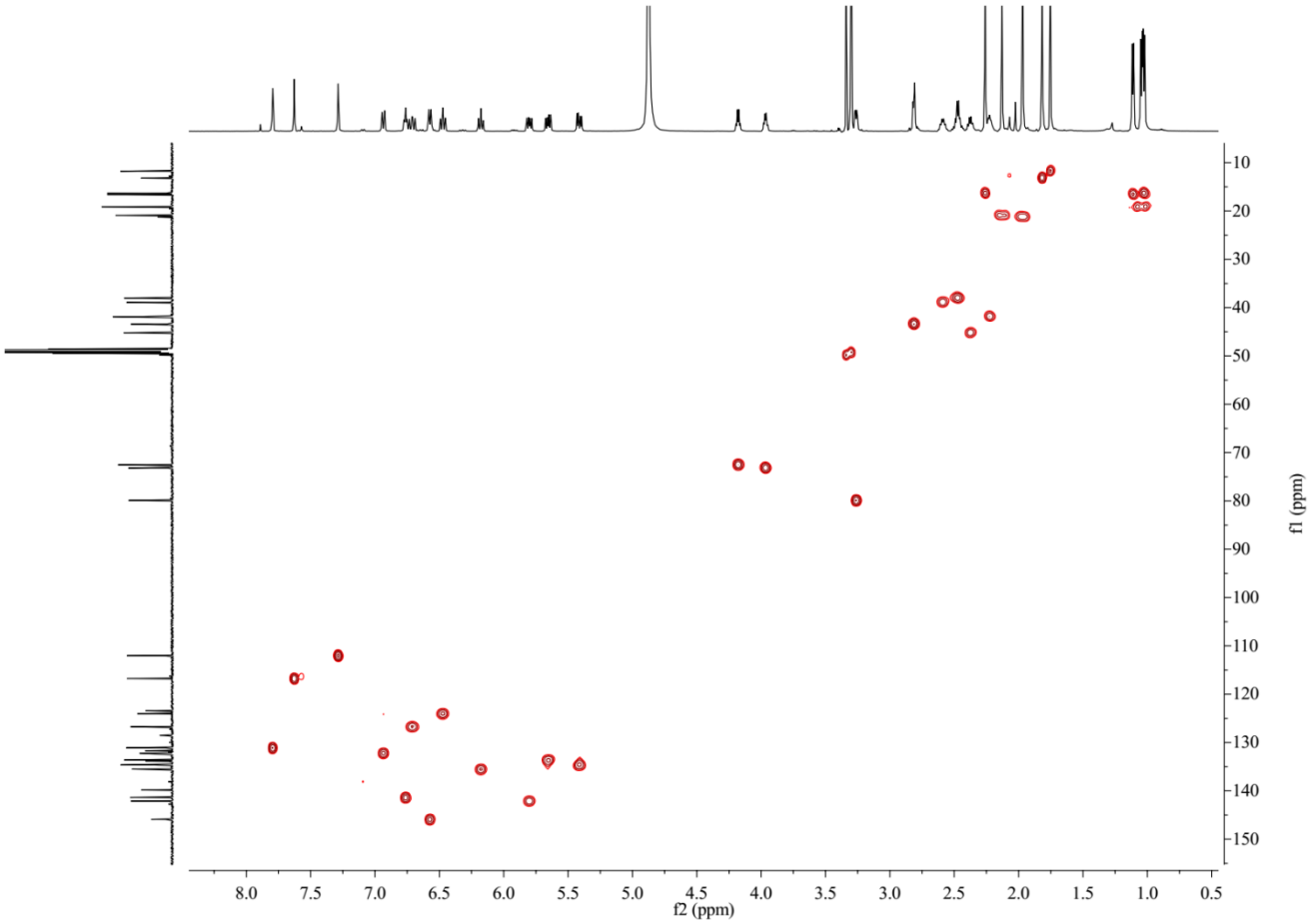


Figure S48. HMBC spectrum (600 MHz) of naphthomycin Q (**3**) in CD_3OD

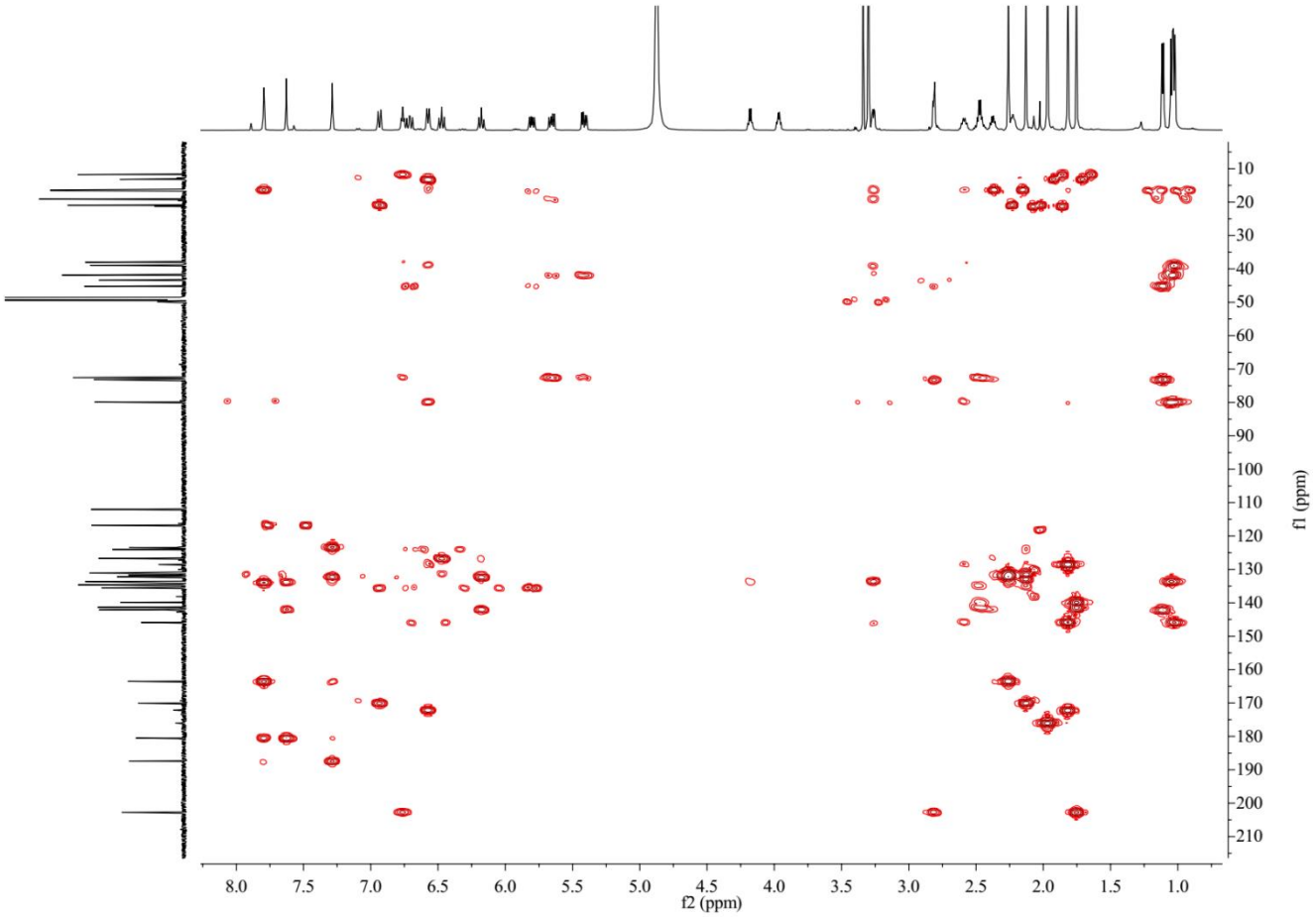


Figure S49. ROESY spectrum (600 MHz) of naphthomycin Q (**3**) in CD_3OD

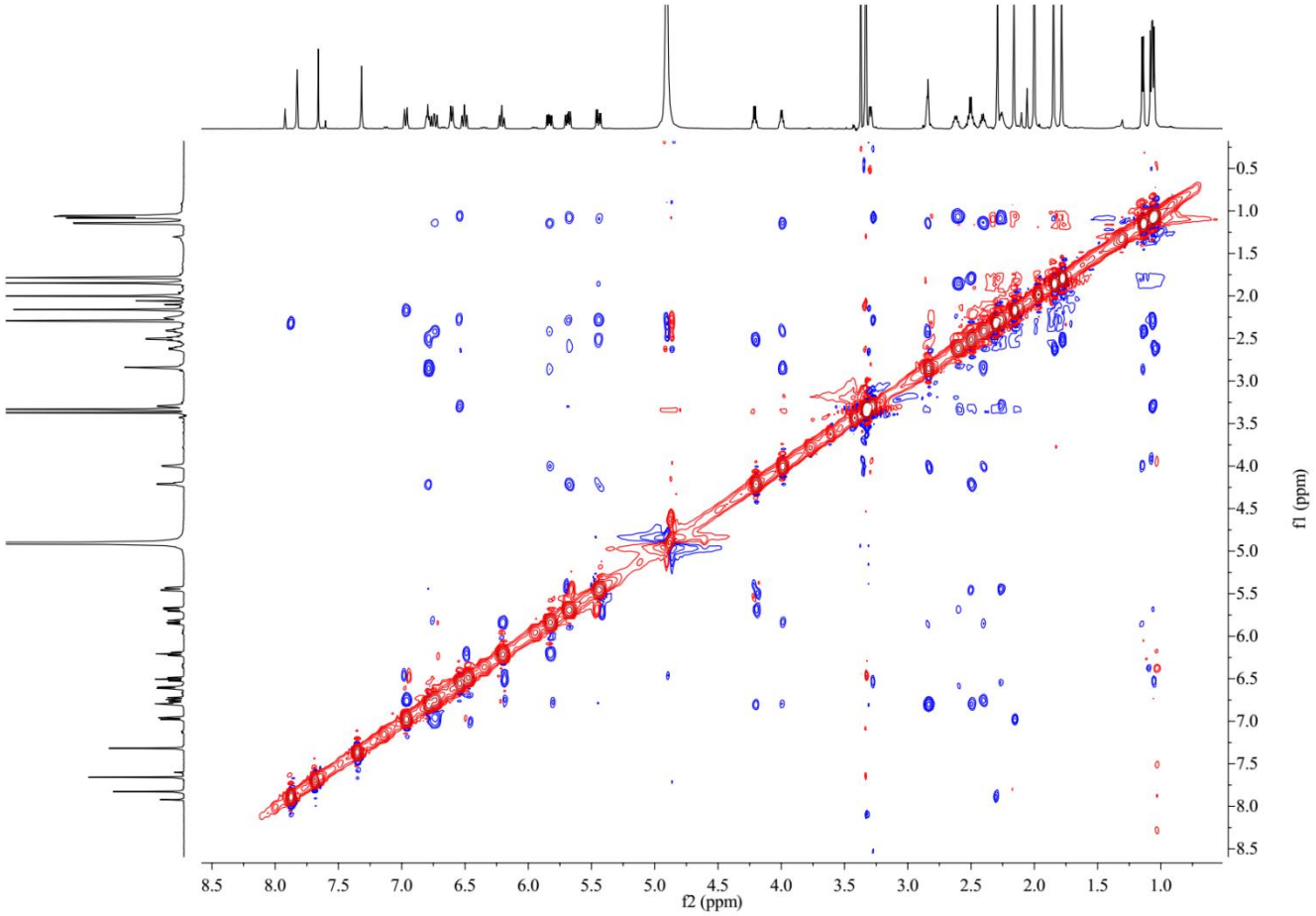


Figure S50. HRESIMS spectrum of naphthomycin Q (**3**).

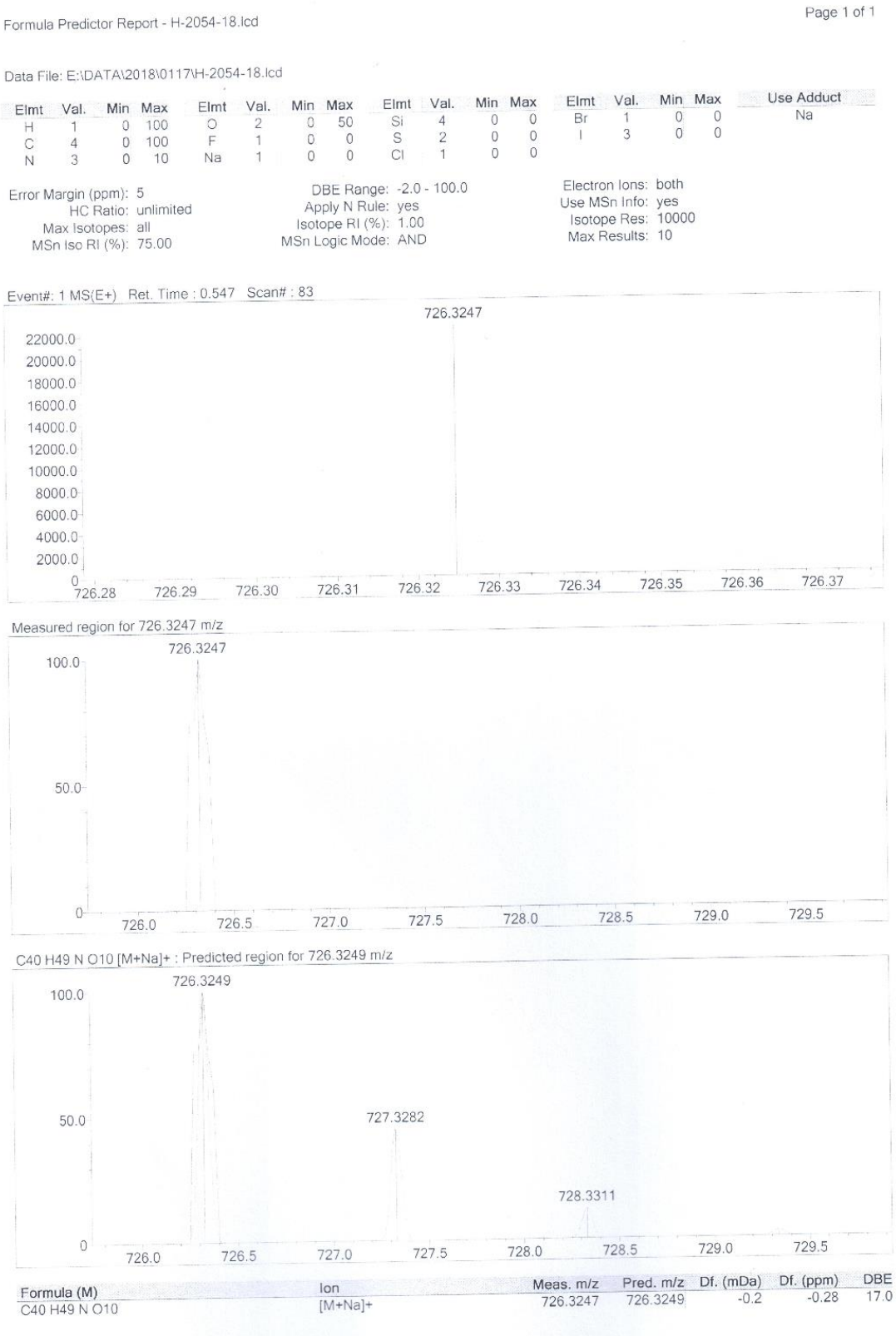


Figure S51. ^{1}H NMR spectrum (600 MHz) of **3a** in CD_3OD.

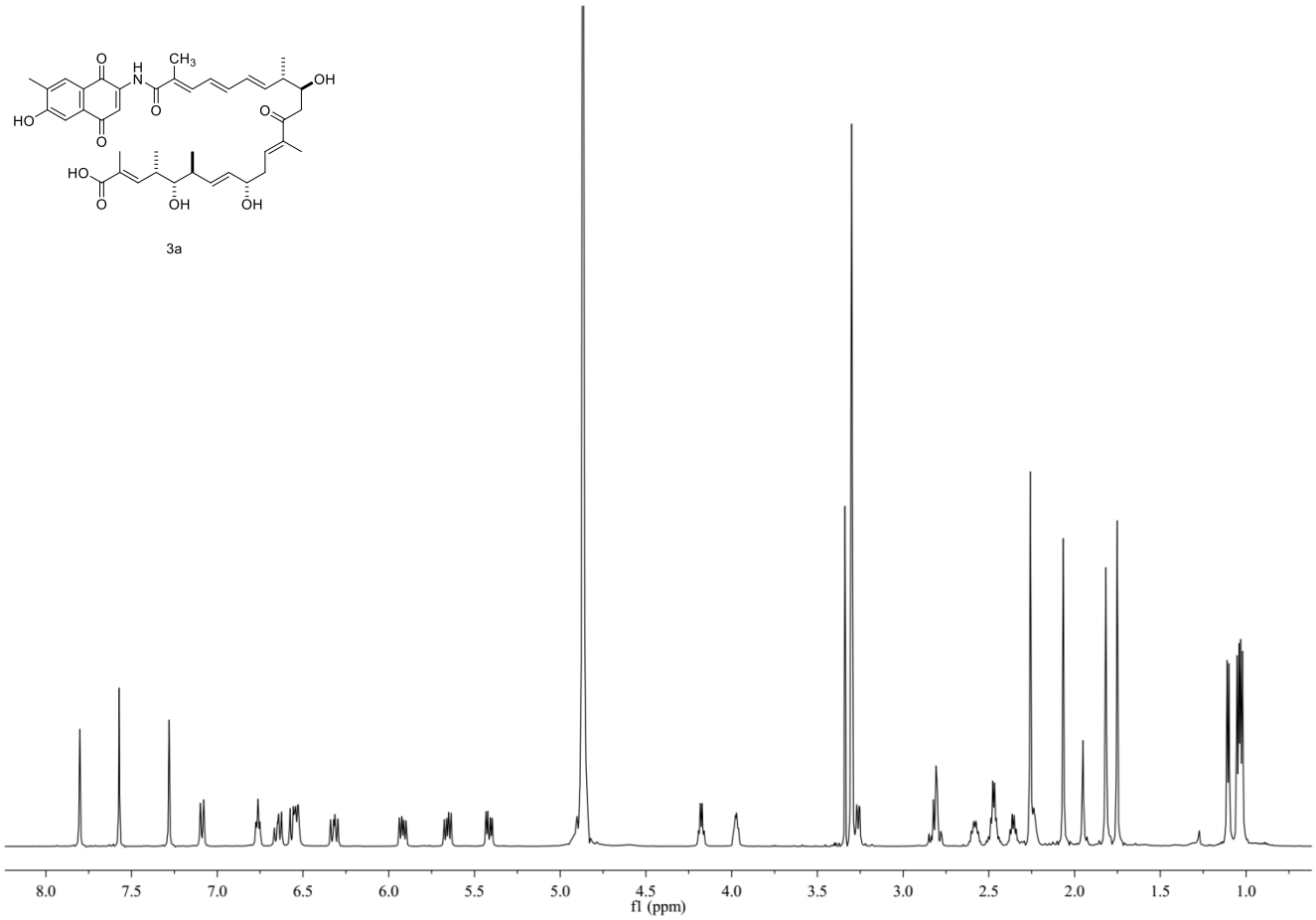


Figure S52. ^{13}C NMR spectrum (150 MHz) of **3a** in CD_3OD.

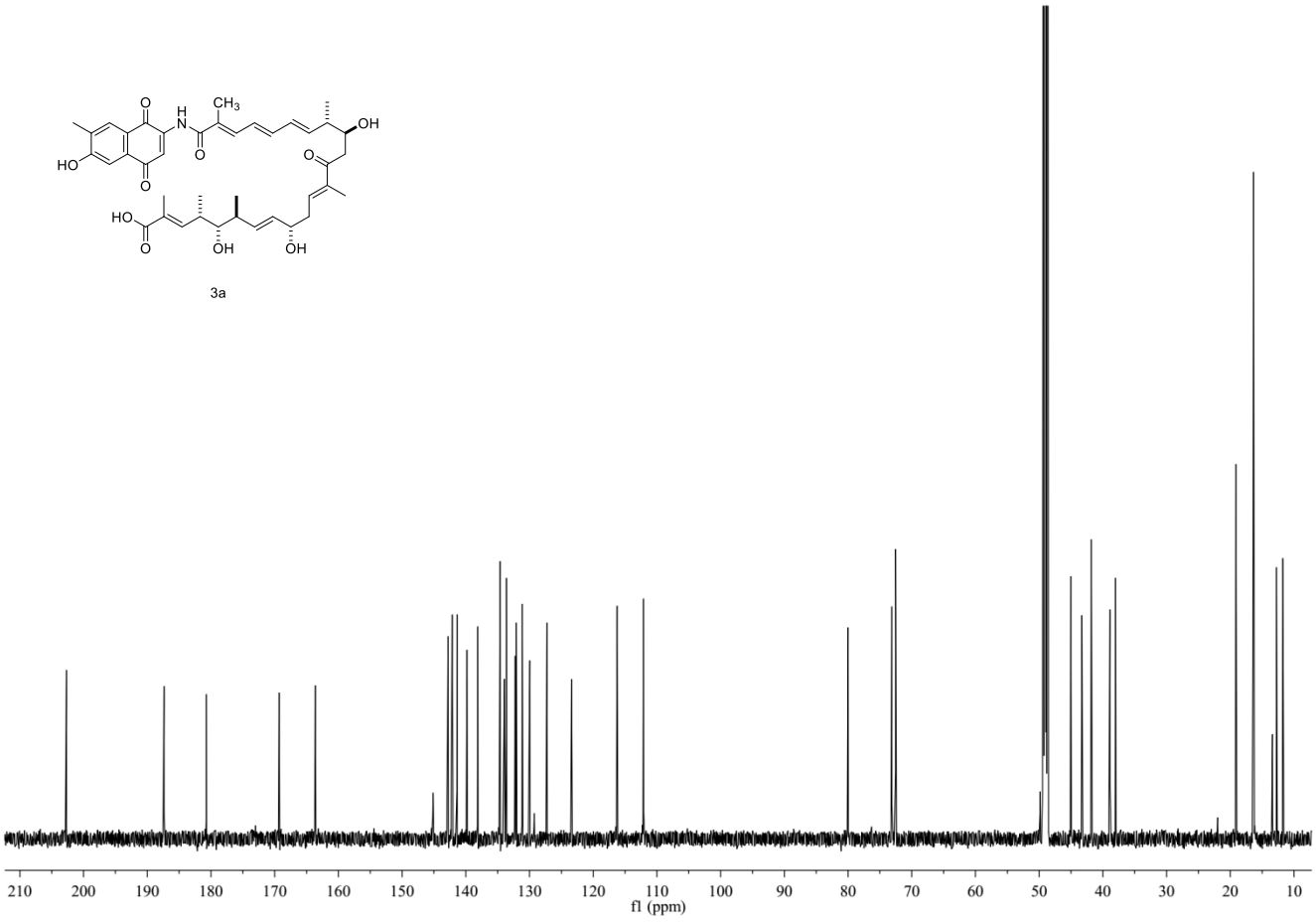


Figure S53. COSY spectrum (600 MHz) of **3a** in CD_3OD

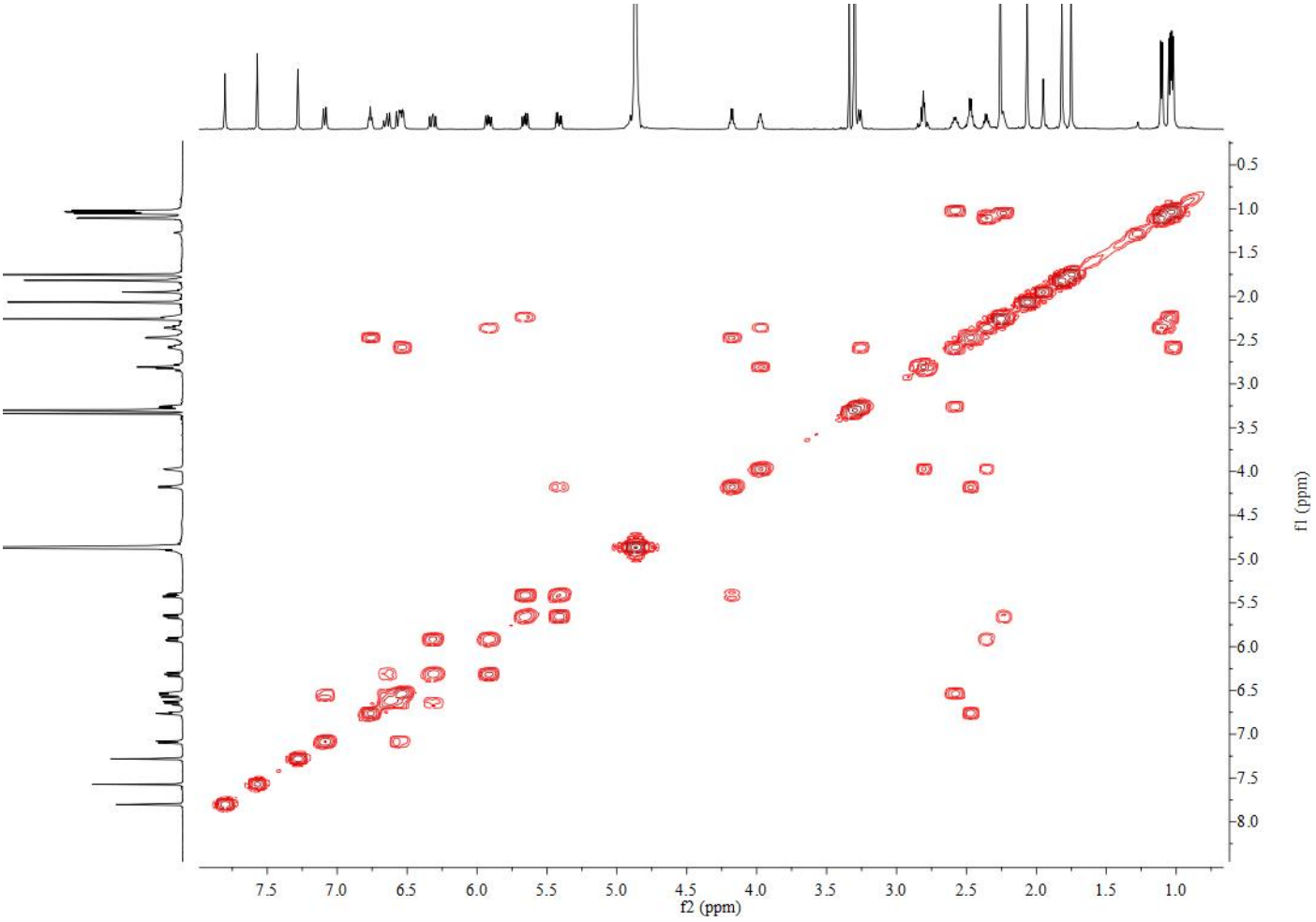


Figure S54. HSQC spectrum (600 MHz) of **3a** in CD_3OD

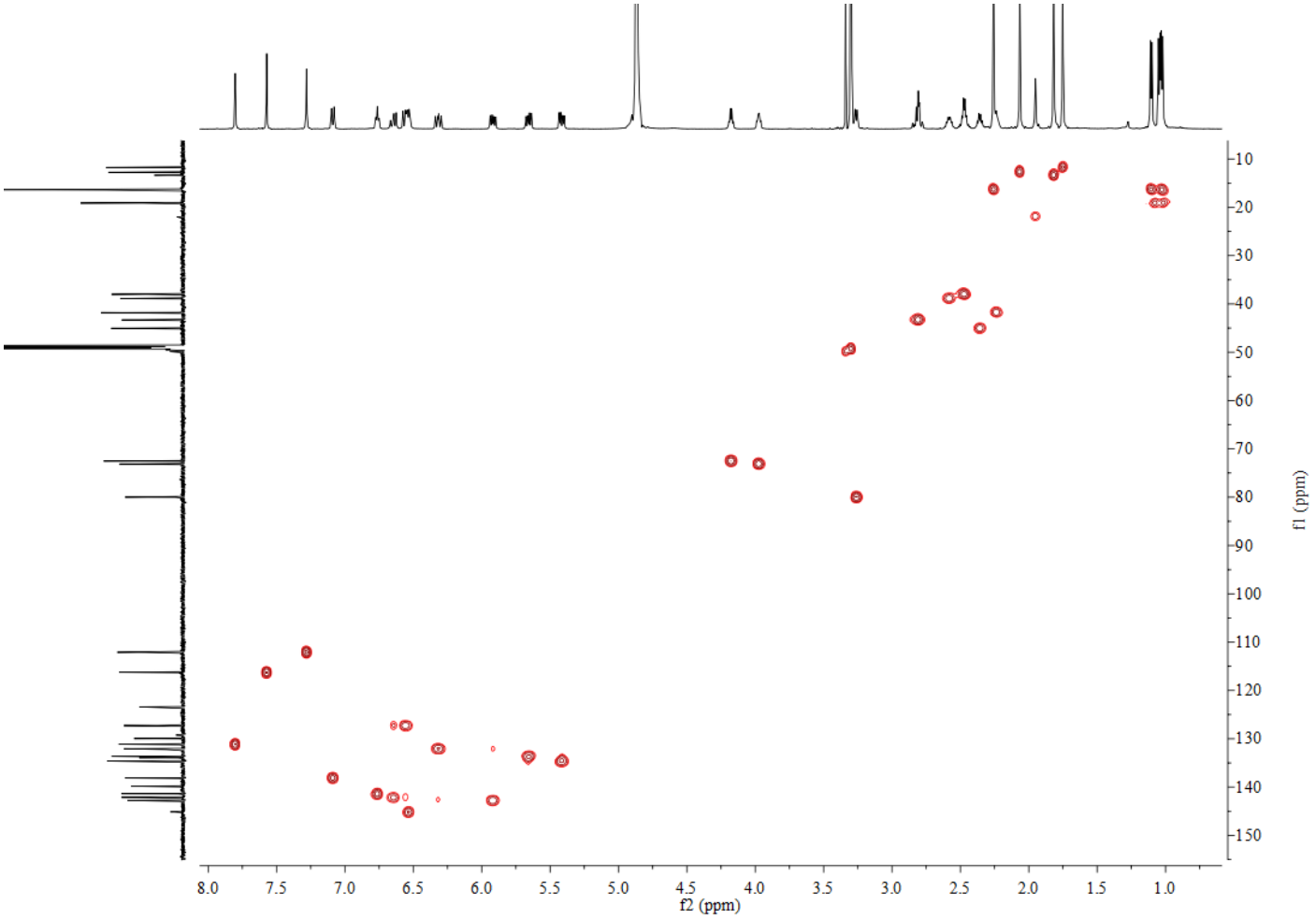


Figure S55. HMBC spectrum (600 MHz) of **3a** in CD_3OD

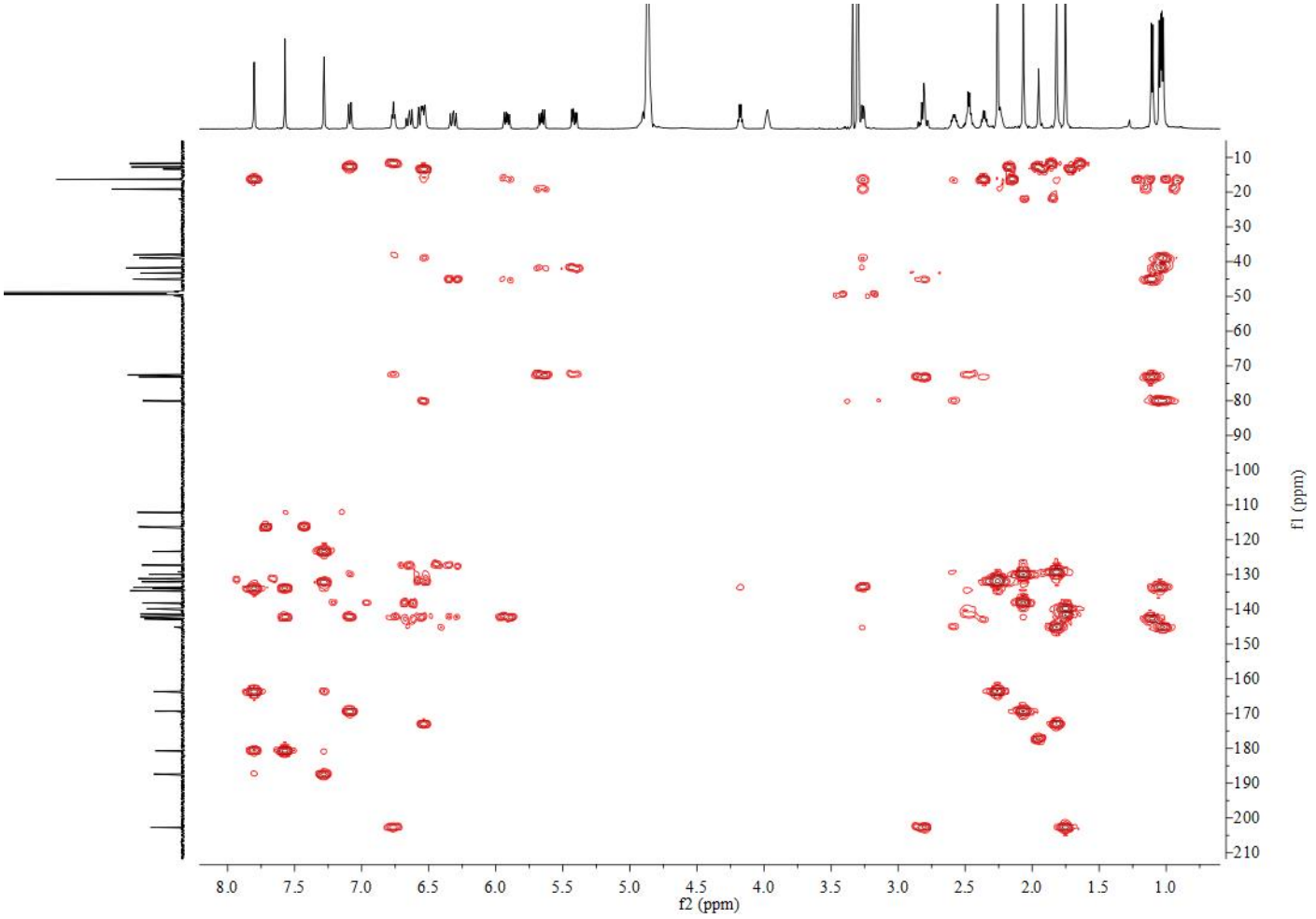


Figure S56. ROESY spectrum (600 MHz) of **3a** in CD_3OD

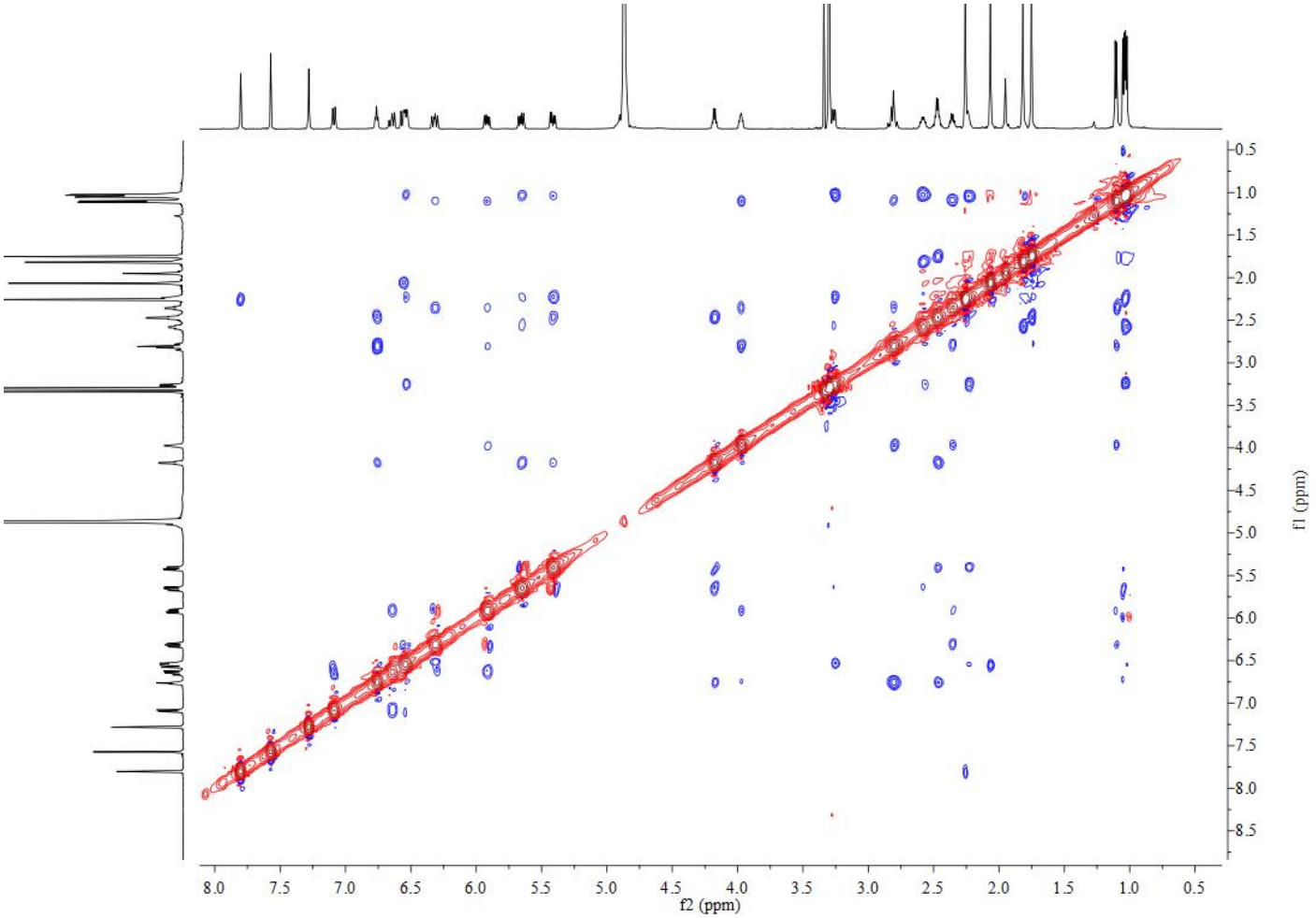


Figure S57. HRESIMS spectrum of **3a**.

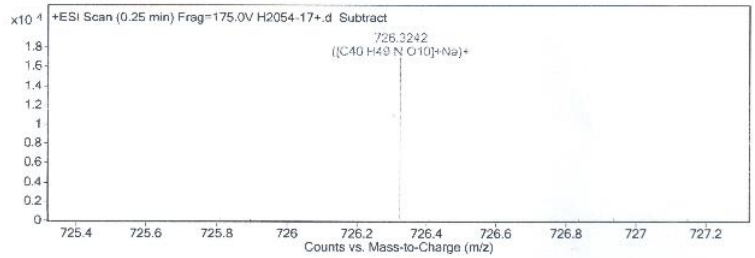
Qualitative Analysis Report

Data Filename	H2054-17+.d	**Sample Name**	H2054-17
Sample Type	Sample	**Position**	P1-E3
Instrument Name	Instrument 1	**User Name**	
Acq Method	SIBU.m	**Acquired Time**	4/6/2017 3:43:35 PM
IRM Calibration Status	Success	**DA Method**	Default.m
Comment			

Sample Group	**Info.**
Acquisition SW Version	6200 series TOF/6500 series Q-TOF B.05.01 (B5125.2)

User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
175	0	ESI



Peak List

m/z	z	Abund	Formula	Ion
242.9485	1	34088.71		
256.9641	1	96207.84		
338.9674		9093.67		
414.954		11086.17		
726.3242	1	17080.63	C40 H49 N O10	(M+Na)+
742.2913	2	30682.53		
742.7927	2	11454.71		
743.2939	2	12712.34		

Formula Calculator Element Limits

Element	Min	Max
C	3	60
H	0	120
O	0	30
N	0	3

Formula Calculator Results

Formula	CalculatedMass	CalculatedMz	Mz	Diff. (mDa)	Diff. (ppm)	DBE
C40 H49 N O10	703.3357	726.3249	726.3242	0.8	1.2	17.0000

--- End Of Report ---