Supplementary Information

Molecular networking and whole genome analysis aid discovery of an angucycline that inactivates mTORC1/C2 and induces programmed cell death

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SI Table 1: Biosynthetic Gene cluster predicted by antiSMASH

Cluster No	antiSMASH prediction	Start position	End position	Size (bases)
1	Bacteriocin-NRPS	158063	168356	10294
2	Siderophore	3858	15315	11458
3	Terpene-Isorenieratene	170849	195592	24744
4	Terpene-Albaflavenone	95951	116388	20438
5	Terpene-Carotenoid	160551	195472	34922
6	NRPS-Coelichelin	100747	134072	33326
7	Indole-Antimycin	95706	116674	20969
8	NRPS -Coelibactin	11199	45591	34393
9	T3PKS-Salinomycin	65988	90501	24514
10	Bacteriocin	57647	66835	9189
11	NRPS -Griseoviridin / viridogrisein	1888	68844	66957
12	T2PKS-Saquayamycin Z /galtamycin B	3	61076	61074

13	Siderophore	13013	23885	10873
14	Terpene-Hopene	6140	27839	21700
15	T3PKS-Other	3330	63373	60044
16	Melanin-Lactonamycin	44571	55467	10897
17	Bacteriocin-Pimaricin	11288	17790	6503
18	Ectoine	56771	66914	10144
19	Butyrolactone A-factor	16323	26811	10489

SI Table 2: 1H and 13C NMR spectral data of compound 1 and 2

Annotation	δc ppm	δ_H ppm	multiplicity	Couplings (Hz)	HMBC
1	203.49		Q		2.77-2.55,1.22
7	188.96		Q		6.52
12	182.59		Q		7.60,6.52
5	164.47		Q		6.54,2.5,2.20-2.07
8	157.3		Q		7.85
9	137.27		Q		4.88
6a	137.22		Q		7.59
11a	134.04		Q		6.52
10	133.06	7.8	CH	d, *J* = 7.9 Hz, 1H	7.58
12a	131.41		Q		7.84
11	118.68	7.56	CH	d, *J* = 7.9 Hz, 1H	7.84
6a	114.17		Q		7.54
6	104.69	6.99	CH	S	2.5
4a	83.31		Q		6.52,2.06-2.22
12b	82.14		Q		6.52
3	75.4		Q		2.77-2.55,1.22
13	28.62	1.2	CH3		
2	53.59	2.77-2.55	CH2		
4	44.69	2.22-2.06	CH2		6.52
14	13.16	2.5	CH3		
1’	70.94	4.89	CH		3.52,2.21,1.55
2’	36.34	1.26-2.55	CH2		
3’	76.33	3.8	CH	m	
4’	75.41	3.19	CH	t,9.07	
5’	70.91	3.52	CH	q, 2.58	
6’	17.41	1.39	CH3	d,6.6.1Hz	3.52,3.19
1’’	93.77	4.96	CH	qd,6.22	3.8
2’’	24.16	1.30-2.55	CH2	m	
3’’	24	1.96-1.40	CH2	m	
4’’	76.37	3.58	CH	broad singlet	4.58
5’’	66.38	4.22	CH	qd,6.22	
6’’	15.98	1.16	CH3	d,6.75	

1’’’	101.46	4.58	CH	dd,9.65,1.9	3.24,2.23-1.59
2’’’	39.2	2.23-1.58	CH2	m	
3’’’	76.41	3.52	CH	dd,5.22	
4’’’	77.05	2.9	CH	t,8.9	1.28
5’’’	71.9	3.24	CH	q,6.3	
6’’’	17.12	1.28	CH3	d,6.3	3.24,2.91
1a	94.5	5.3	CH	broad singlet	
2a	22.84	1.86	CH2	m	
3a	25.1	1.57	CH2	m	
4a	66.38	3.34	CH	m	
5a	66.9	3.65	CH	qd,6.55,0.9	
6a	15.6	0.54	CH3	d,6.54	66.9

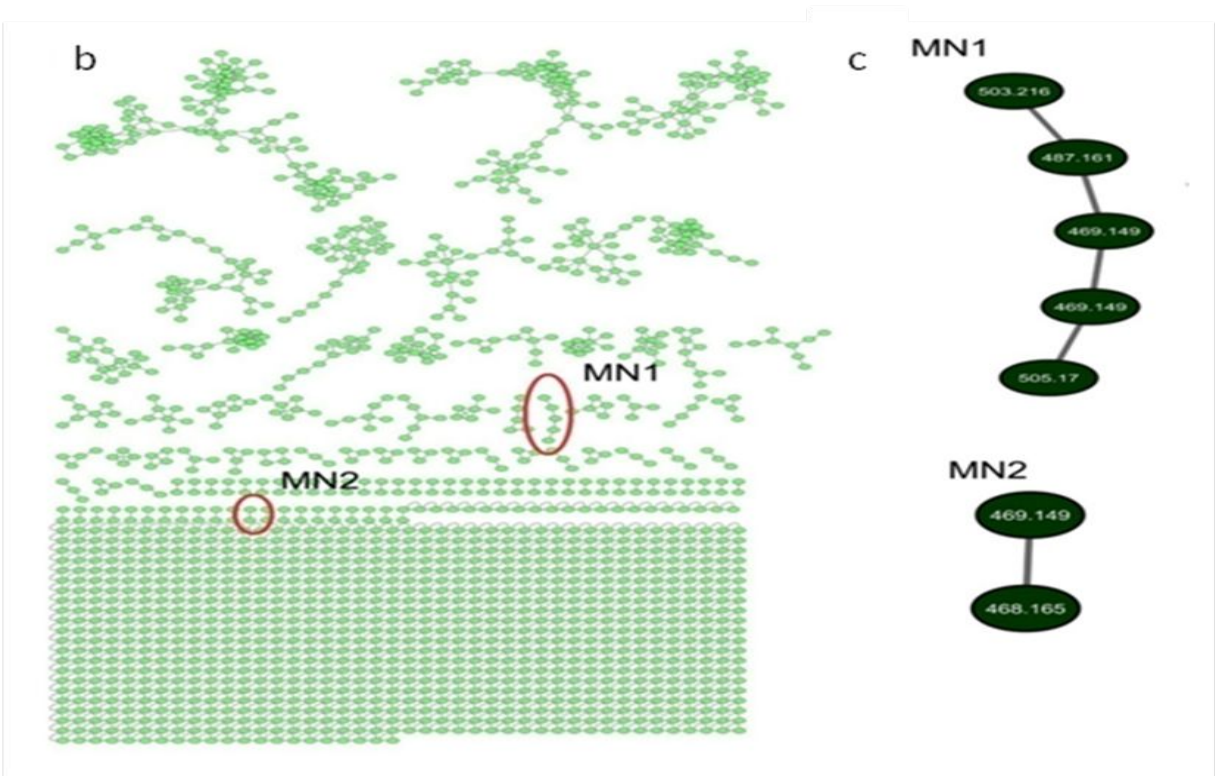


Figure SI.-1 Whole genome analysis and molecular networking: **a**.antiSMASH prediction identified type II polyketide synthase in *Streptomyces* sp OA293 that is similar in sequence to

Saquayamycin gene cluster. **b**.Massive Molecular Network **c**. subnetwork of compound dereplicated from GNPS Database

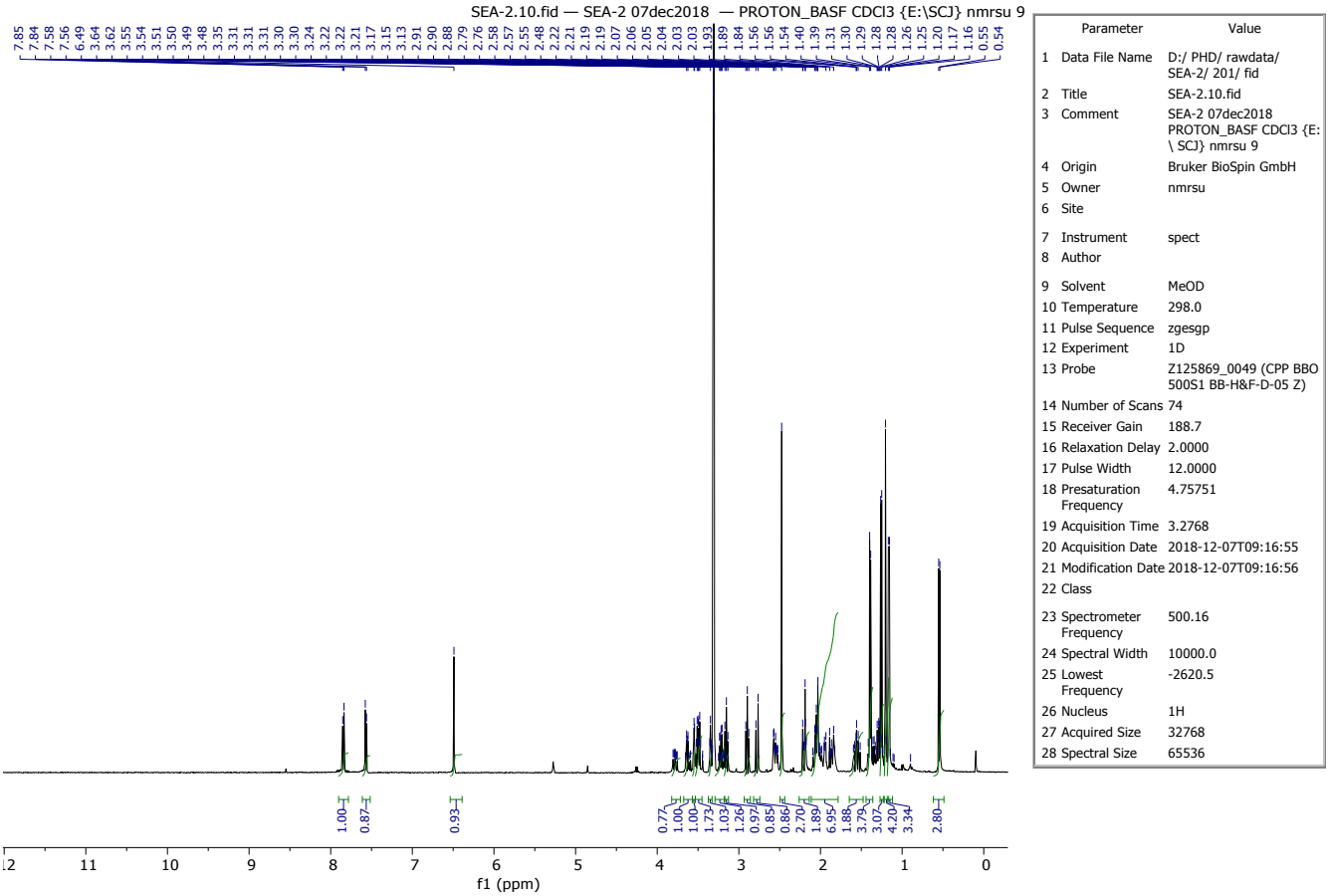
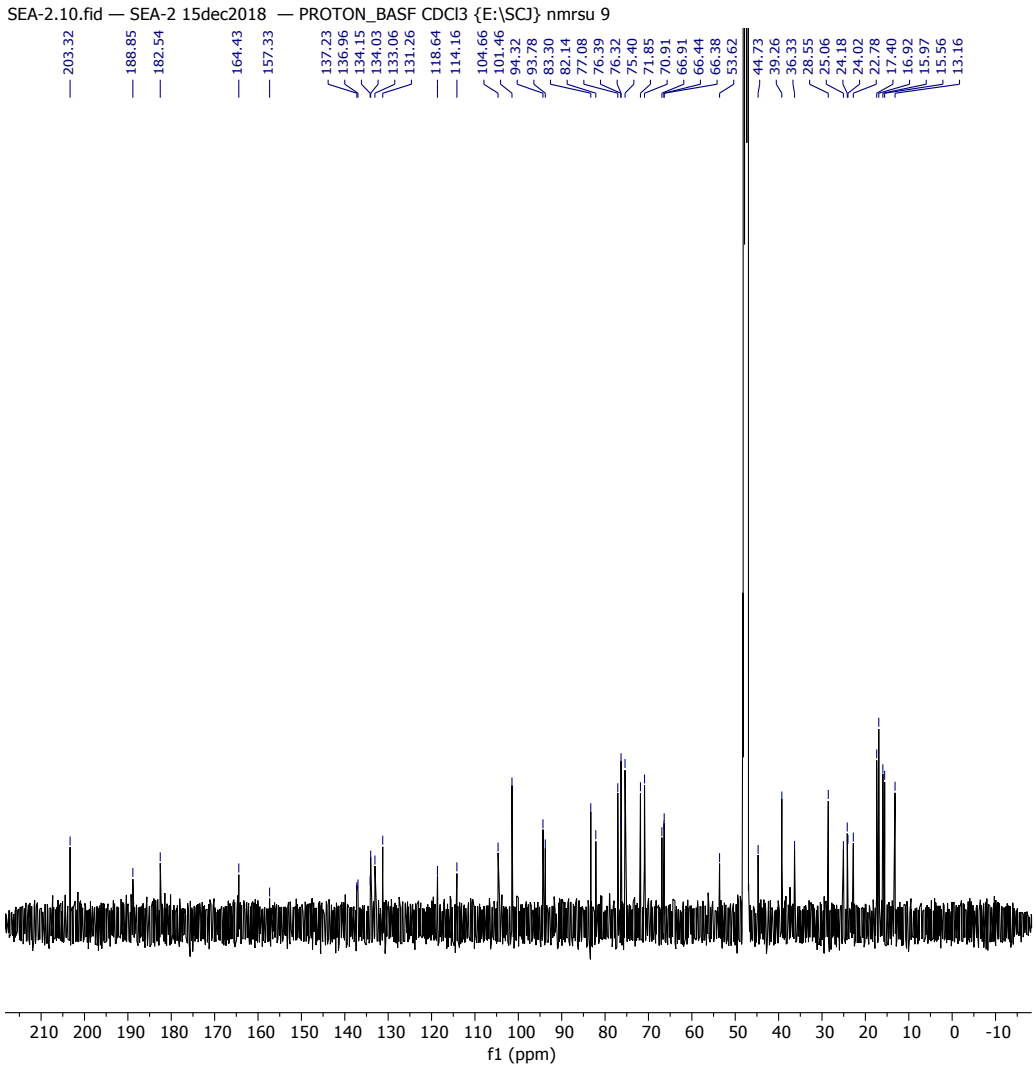


Figure SI-2: ^{1}H NMR spectra of Compound **1(Urdamycin E)**



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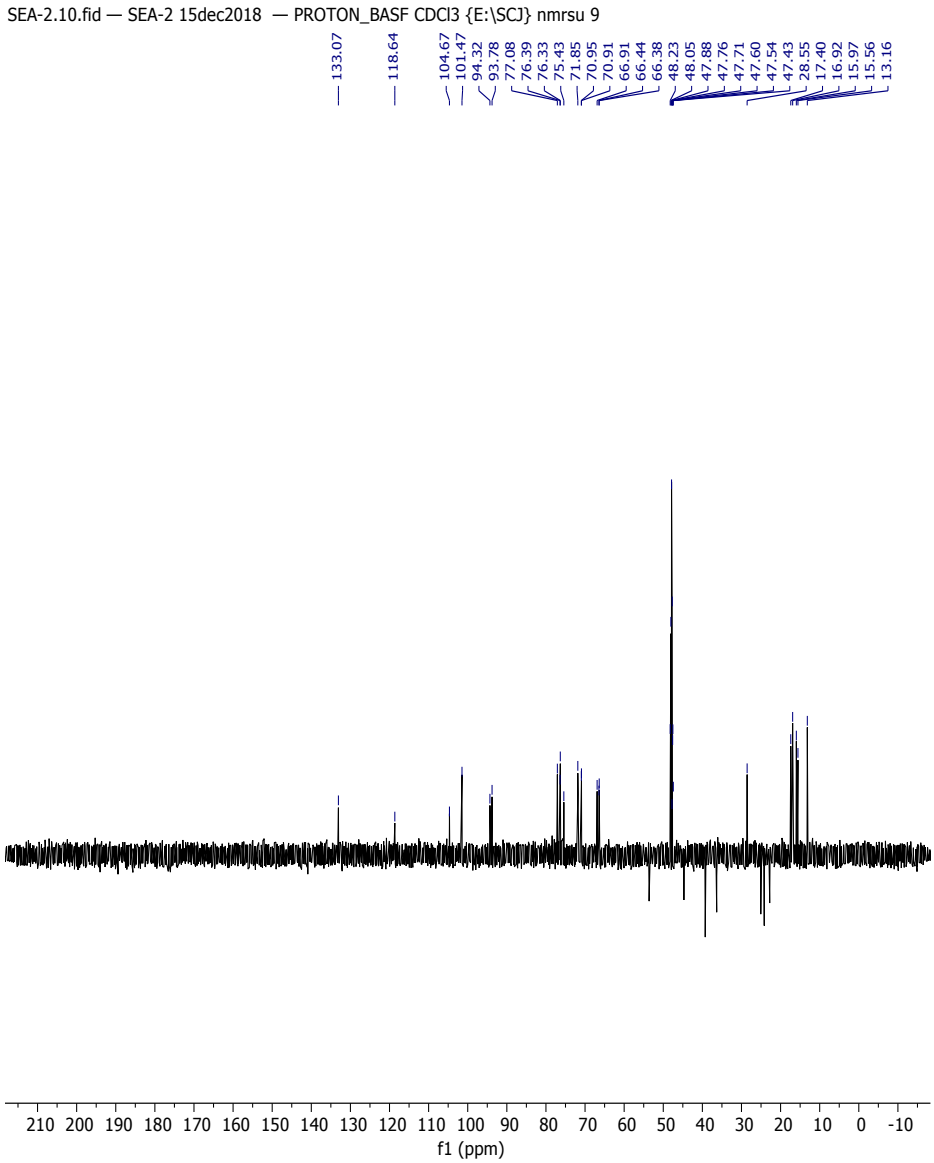
5	Owner	nmrsu
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	296.3
11	Pulse Sequence	zgpg30
12	Experiment	1D
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	40960
15	Receiver Gain	188.7
16	Relaxation Delay	2.0000
17	Pulse Width	10.0000
18	Presaturation Frequency	
19	Acquisition Time	3.2768
20	Acquisition Date	2018-12-26T02:58:36
21	Modification Date	2018-12-26T02:58:36
22	Class	
23	Spectrometer Frequency	125.78
24	Spectral Width	29761.9
25	Lowest Frequency	-2304.4
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536

Figure SI-3 ^{13}C NMR spectra of Compound **1**



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4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	298.0
11	Pulse Sequence	deptsp135
12	Experiment	DEPT-135
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	10240
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16	Relaxation Delay	2.0000
17	Pulse Width	10.0000
18	Presaturation Frequency	
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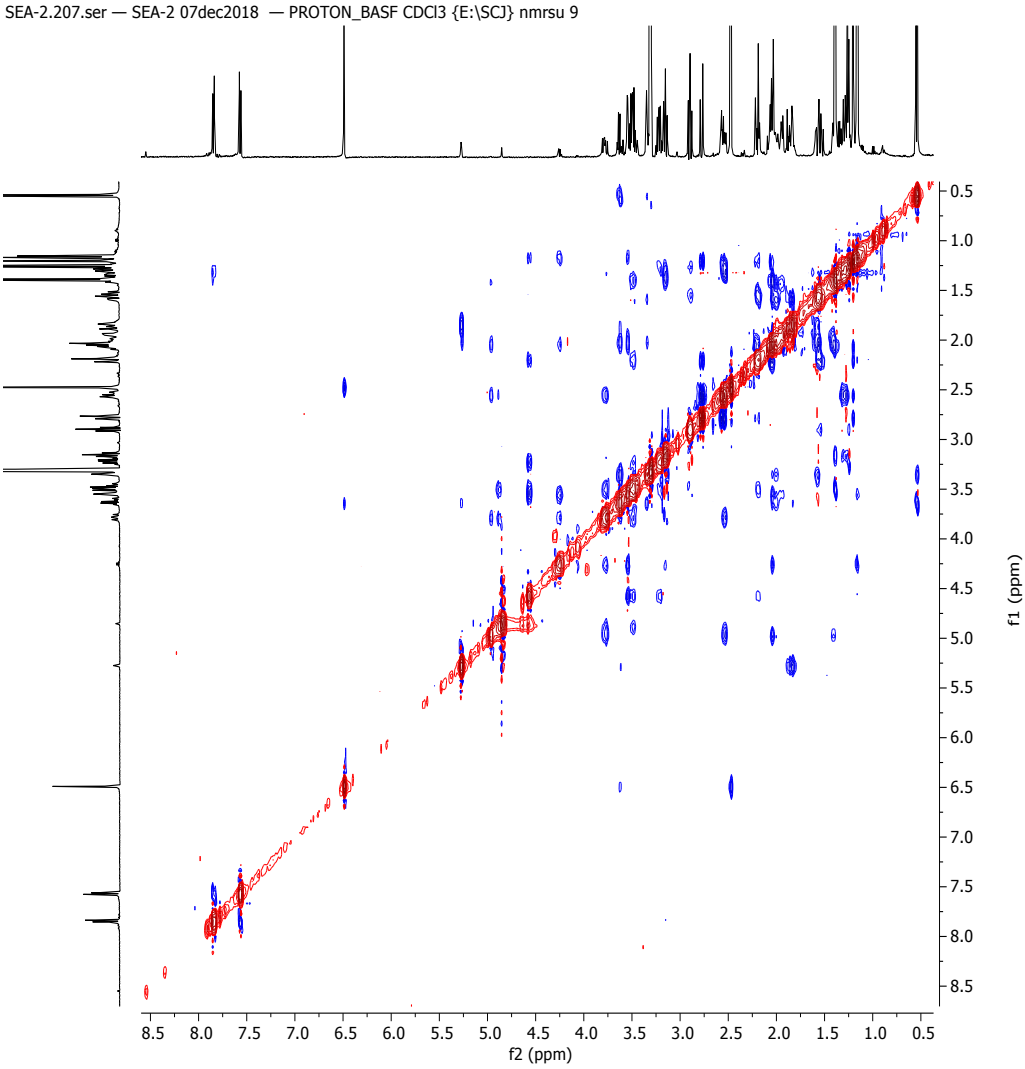
22	Class	
23	Spectrometer Frequency	125.78
24	Spectral Width	29761.9
25	Lowest Frequency	-2304.4
26	Nucleus	13C
27	Acquired Size	32768
28	Spectral Size	65536

Figure SI-4 DEPT spectra of Compound **1**



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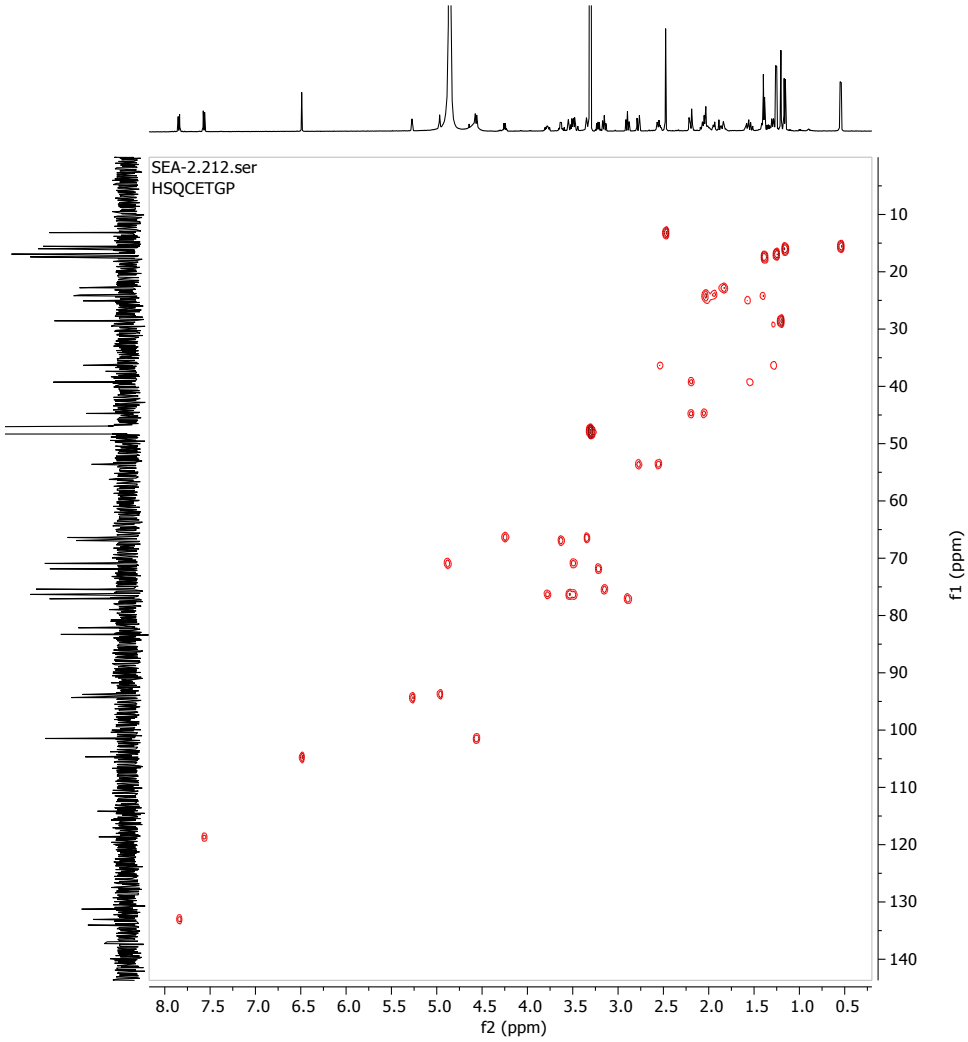
5	Owner	nmrsu
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	298.0
11	Pulse Sequence	roesyphpr
12	Experiment	ROESY
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	32
15	Receiver Gain	188.7
16	Relaxation Delay	2.0000
17	Pulse Width	12.0000
18	Presaturation Frequency	
19	Acquisition Time	0.2925
20	Acquisition Date	2018-12-09T04:32:11
21	Modification Date	2018-12-09T10:23:41
22	Class	
23	Spectrometer Frequency	(500.16, 500.16)
24	Spectral Width	(7002.8, 7002.8)
25	Lowest Frequency	(-1122.1, -1116.3)
26	Nucleus	(1H, 1H)
27	Acquired Size	(2048, 256)
28	Spectral Size	(2048, 256)

Figure SI-5 ROESY spectra of Compound **1**



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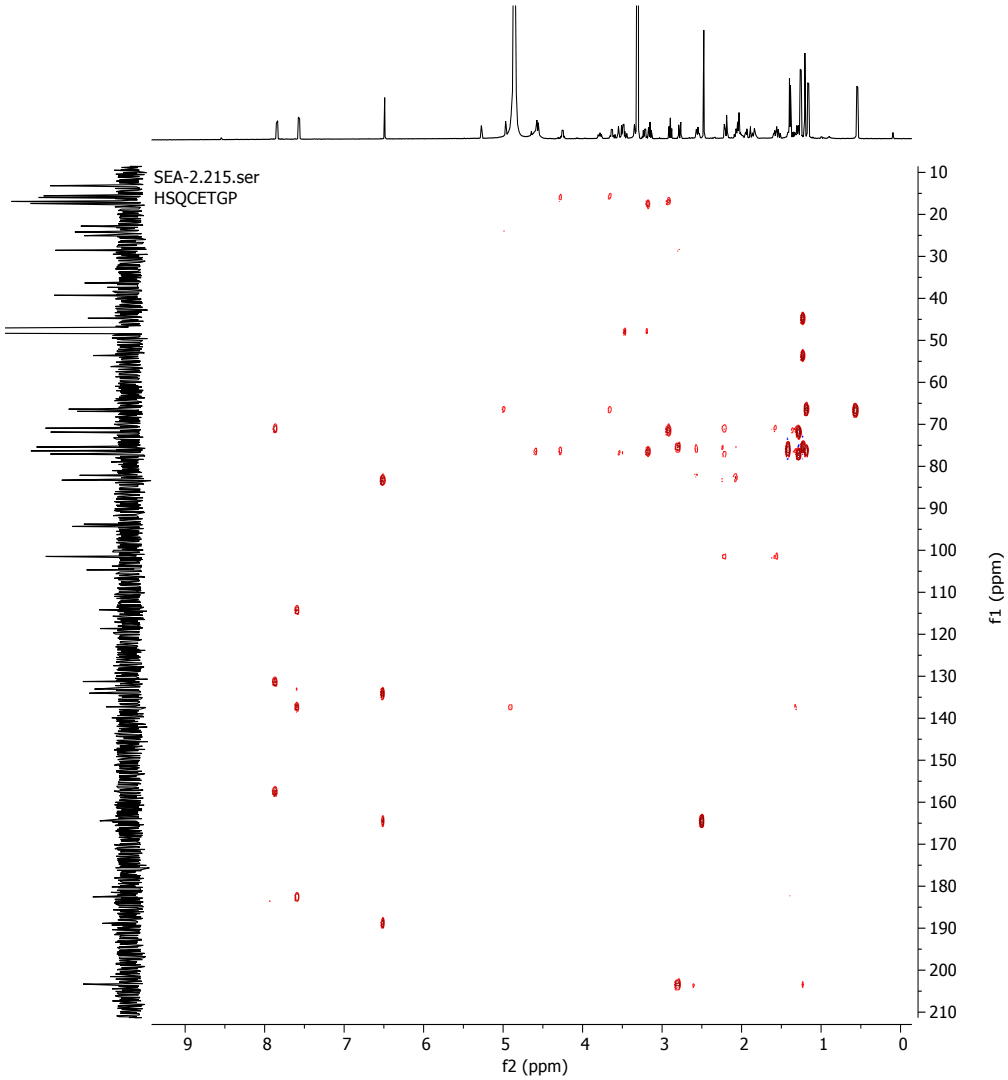
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	298.0
11	Pulse Sequence	hsqcetgp
12	Experiment	HSQC
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	32
15	Receiver Gain	188.7
16	Relaxation Delay	1.5000
17	Pulse Width	12.0000
18	Presaturation Frequency	
19	Acquisition Time	0.0786
20	Acquisition Date	2018-12-16T14:50:41
21	Modification Date	2018-12-16T18:27:30
22	Class	
23	Spectrometer Frequency	(500.16, 125.77)
24	Spectral Width	(6510.4, 20746.9)
25	Lowest Frequency	(-178.7, -941.0)
26	Nucleus	(1H, 13C)
27	Acquired Size	(512, 256)
28	Spectral Size	(512, 512)

Figure SI-6 HSQC spectra of Compound **1**



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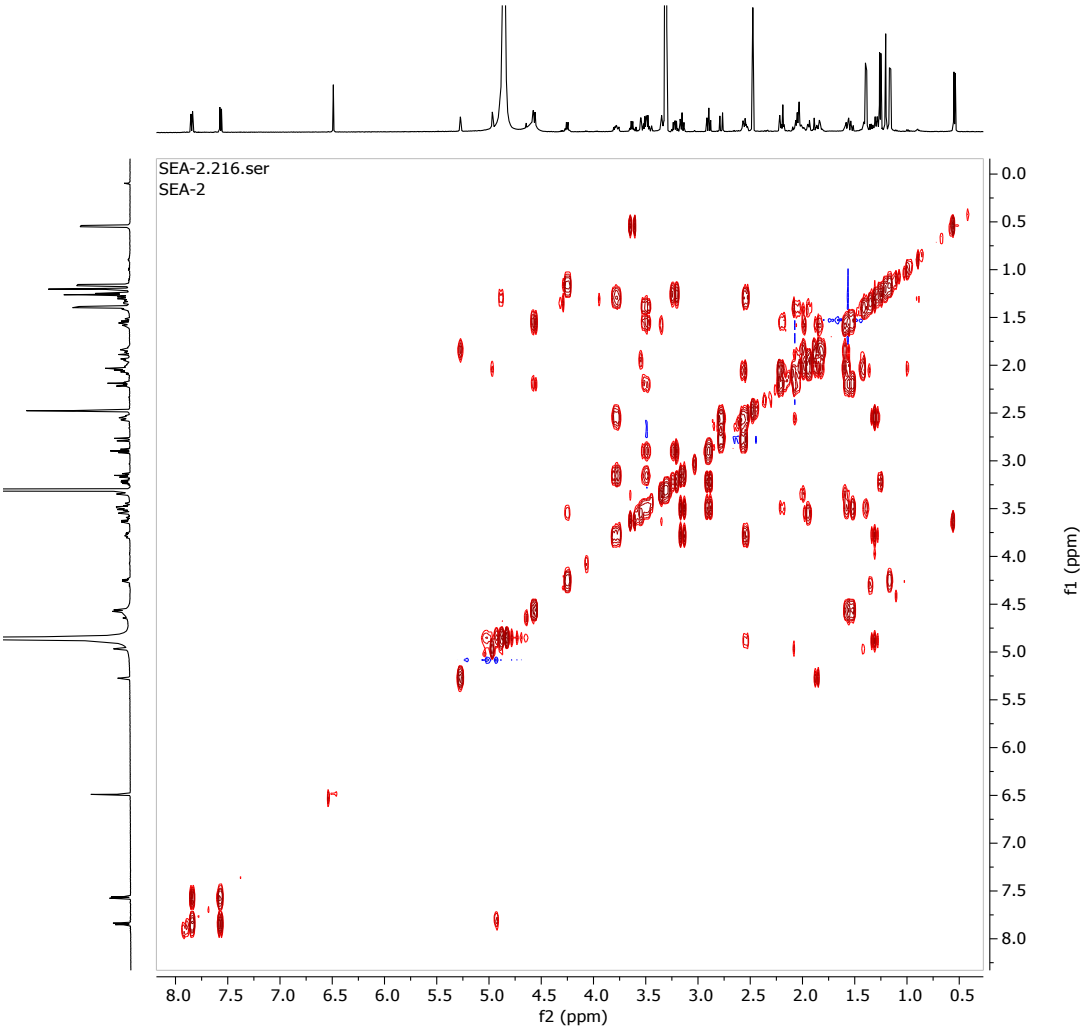
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	298.0
11	Pulse Sequence	hmbcetgpl3nd
12	Experiment	HMBC
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	128
15	Receiver Gain	188.7
16	Relaxation Delay	1.5000
17	Pulse Width	12.0000
18	Presaturation Frequency	
19	Acquisition Time	0.2731
20	Acquisition Date	2018-12-22T19:52:31
21	Modification Date	2018-12-23T12:42:09
22	Class	
23	Spectrometer Frequency	(500.16, 125.78)
24	Spectral Width	(7500.0, 27624.3)
25	Lowest Frequency	(-499.0, 22.0)
26	Nucleus	(1H, 13C)
27	Acquired Size	(2048, 256)
28	Spectral Size	(4096, 1024)

Figure SI-7 HMBC spectra of Compound **1**



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3	Comment	SEA-2
4	Origin	Bruker BioSpin GmbH
5	Owner	nmrsu
6	Site	
7	Instrument	spect
8	Author	
9	Solvent	MeOD
10	Temperature	298.0
11	Pulse Sequence	cosygpppqf
12	Experiment	COSY
13	Probe	Z125869_0049 (CPP BBO 500S1 BB-H&F-D-05 Z)
14	Number of Scans	64
15	Receiver Gain	188.7
16	Relaxation Delay	2.0201
17	Pulse Width	12.0000
18	Presaturation Frequency	
19	Acquisition Time	0.2744
20	Acquisition Date	2018-12-23T12:45:26
21	Modification Date	2018-12-23T23:25:54
22	Class	
23	Spectrometer Frequency	(500.16, 500.16)
24	Spectral Width	(7462.7, 7462.7)
25	Lowest Frequency	(-547.8, -547.8)
26	Nucleus	(1H, 1H)
27	Acquired Size	(2048, 256)
28	Spectral Size	(2048, 256)

Figure SI-8 COSY spectra of Compound **1**

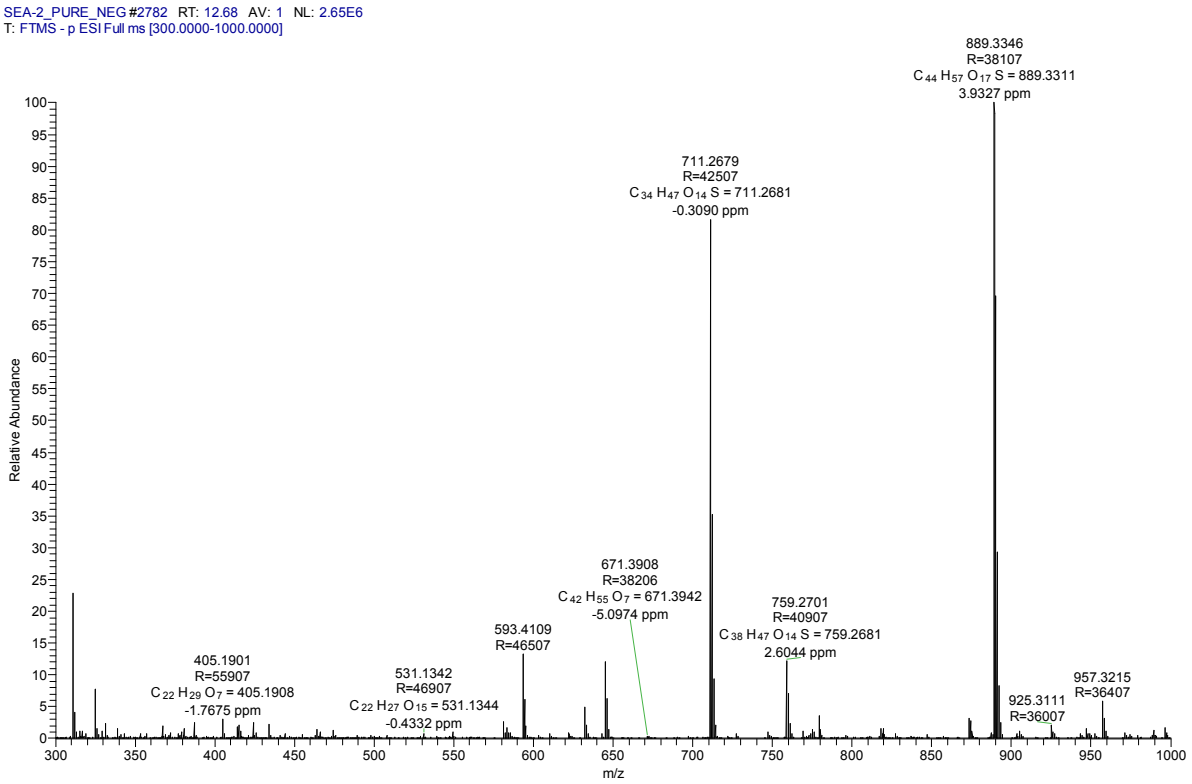
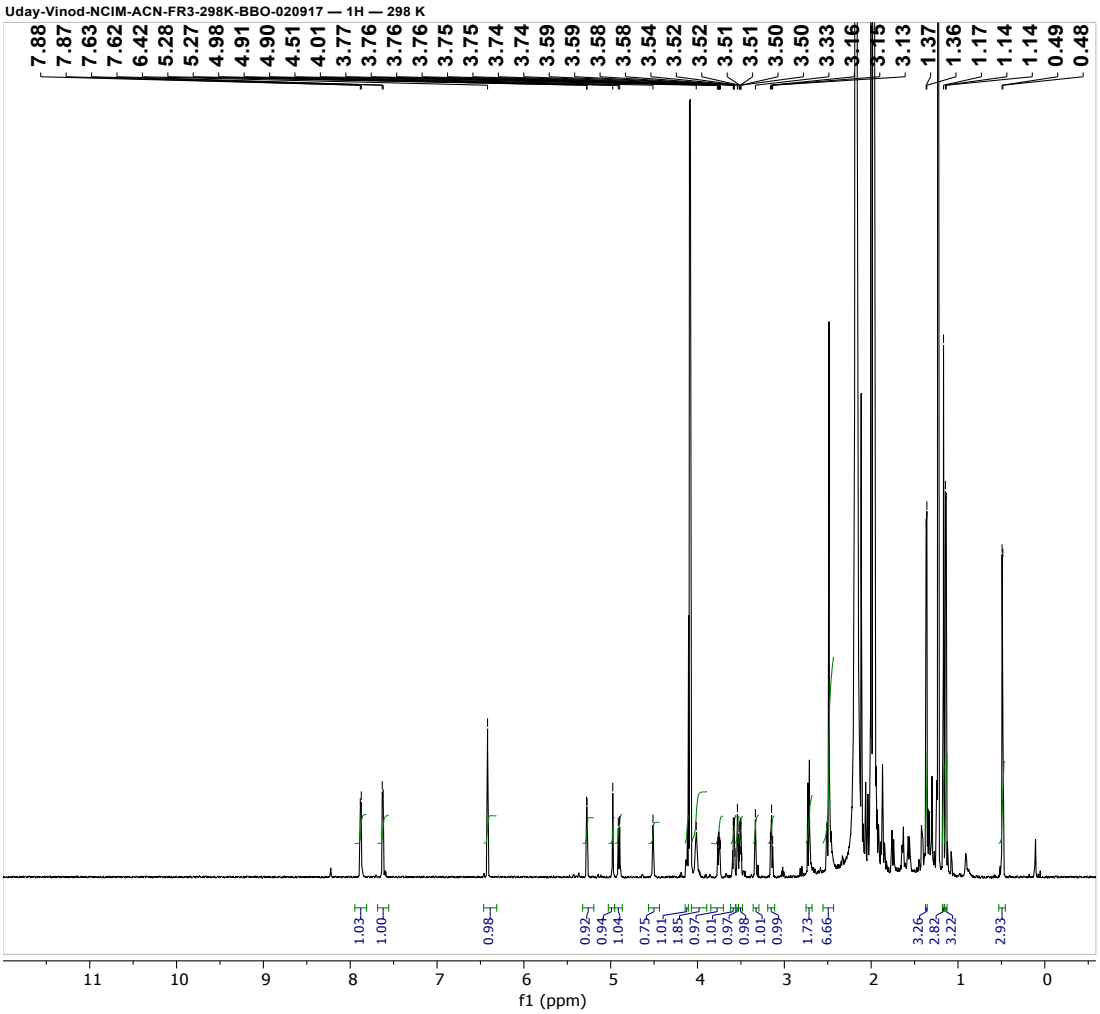


Figure SI-9 HRMS spectrum of Compound **1** (Urdamycin E)

Compound 2 (Urdamycin V) Structure details



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6	Author	
7	Solvent	CD3CN
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10	Experiment	1D
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12	Number of Scans	128
13	Receiver Gain	140.9
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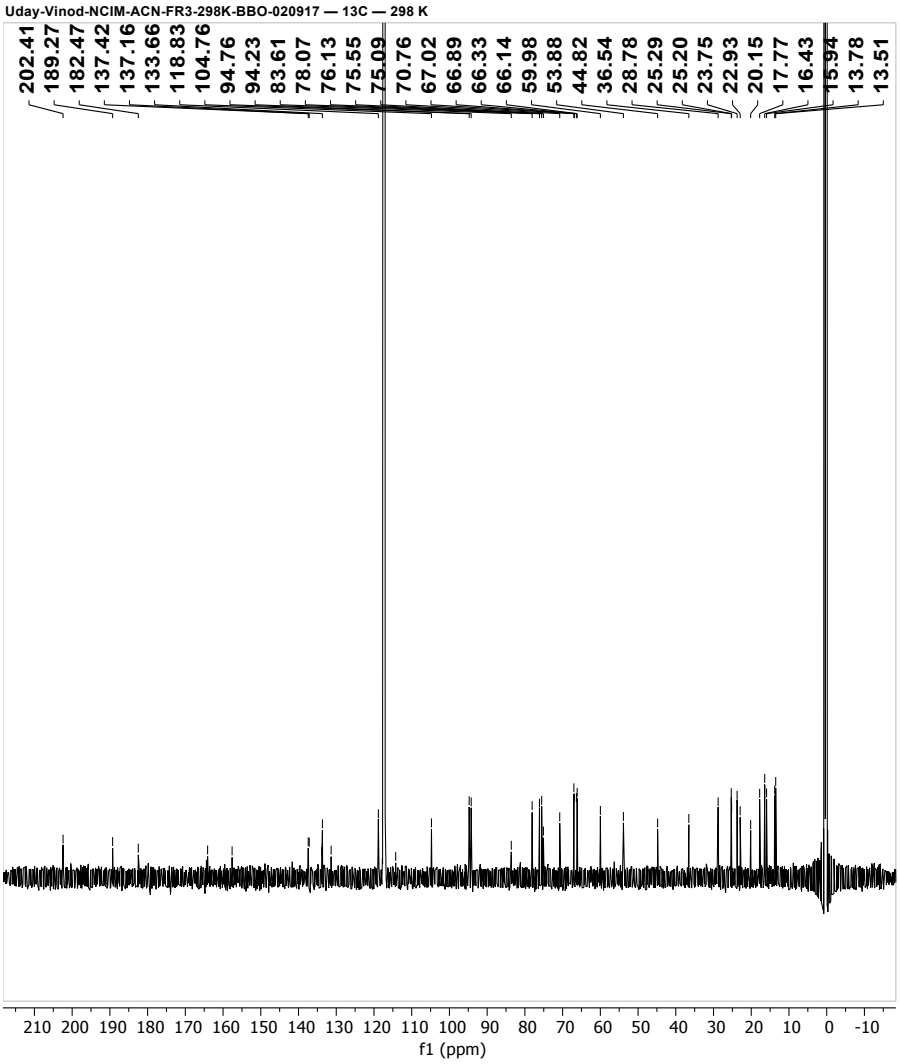
20	Class	
21	Spectrometer Frequency	700.13
22	Spectral Width	14097.7
23	Lowest Frequency	-3761.1
24	Nucleus	1H

Figure SI-10 ^{1}H NMR spectra of Compound **2**



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6	Author	
7	Solvent	CD3CN
8	Temperature	298.0
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10	Experiment	1D
11	Probe	Z123726_0018 (PA BBO 700S3 BB-H-D-05 Z)
12	Number of Scans	12288
13	Receiver Gain	2050.0
14	Relaxation Delay	1.5000
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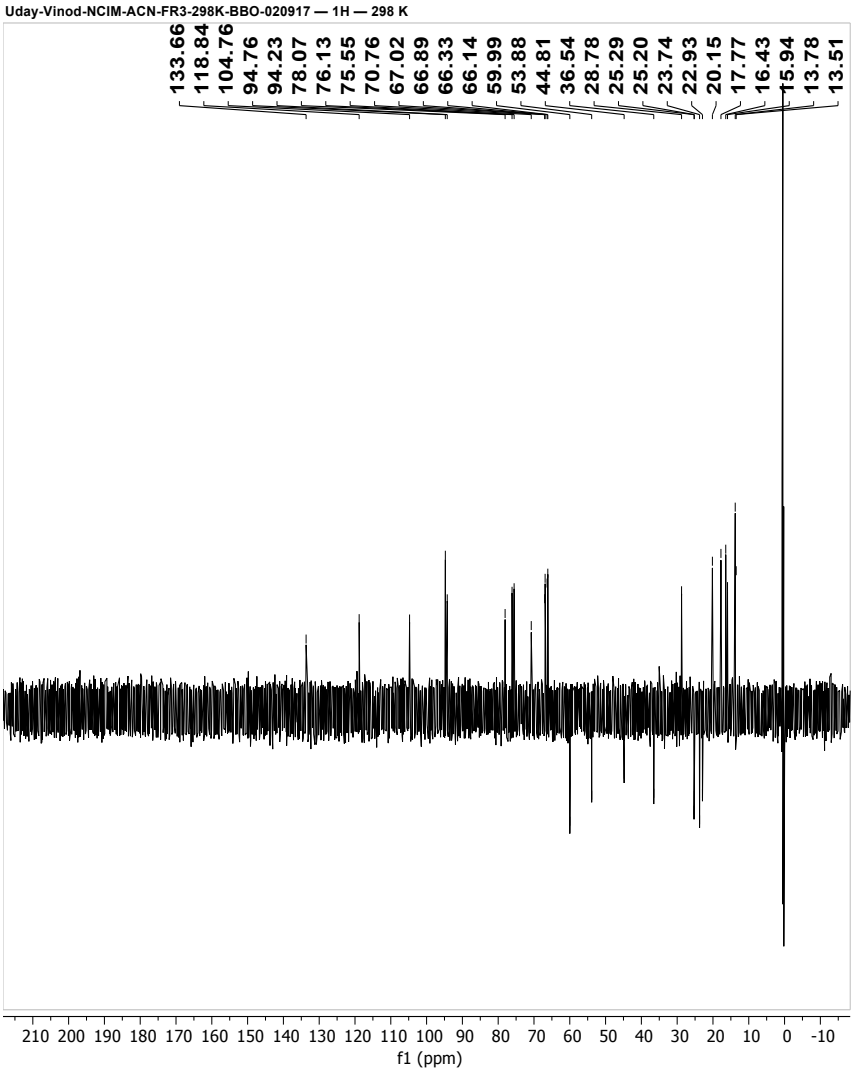
16	Presaturation Frequency	
17	Acquisition Time	0.3932
18	Acquisition Date	2017-09-05T07:00:57
19	Modification Date	2017-09-05T07:00:56
20	Class	
21	Spectrometer Frequency	176.07
22	Spectral Width	41666.7
23	Lowest Frequency	-3229.9
24	Nucleus	13C
25	Acquired Size	16384
26	Spectral Size	65536

Figure SI-11 ^{13}C NMR spectra of Compound **2**



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5	Instrument	spect
6	Author	
7	Solvent	CD3CN
8	Temperature	298.0
9	Pulse Sequence	deptsp135
10	Experiment	DEPT-135
11	Probe	Z123726_0018 (PA BBO 700S3 BB-H-D-05 Z)
12	Number of Scans	5120
13	Receiver Gain	2050.0
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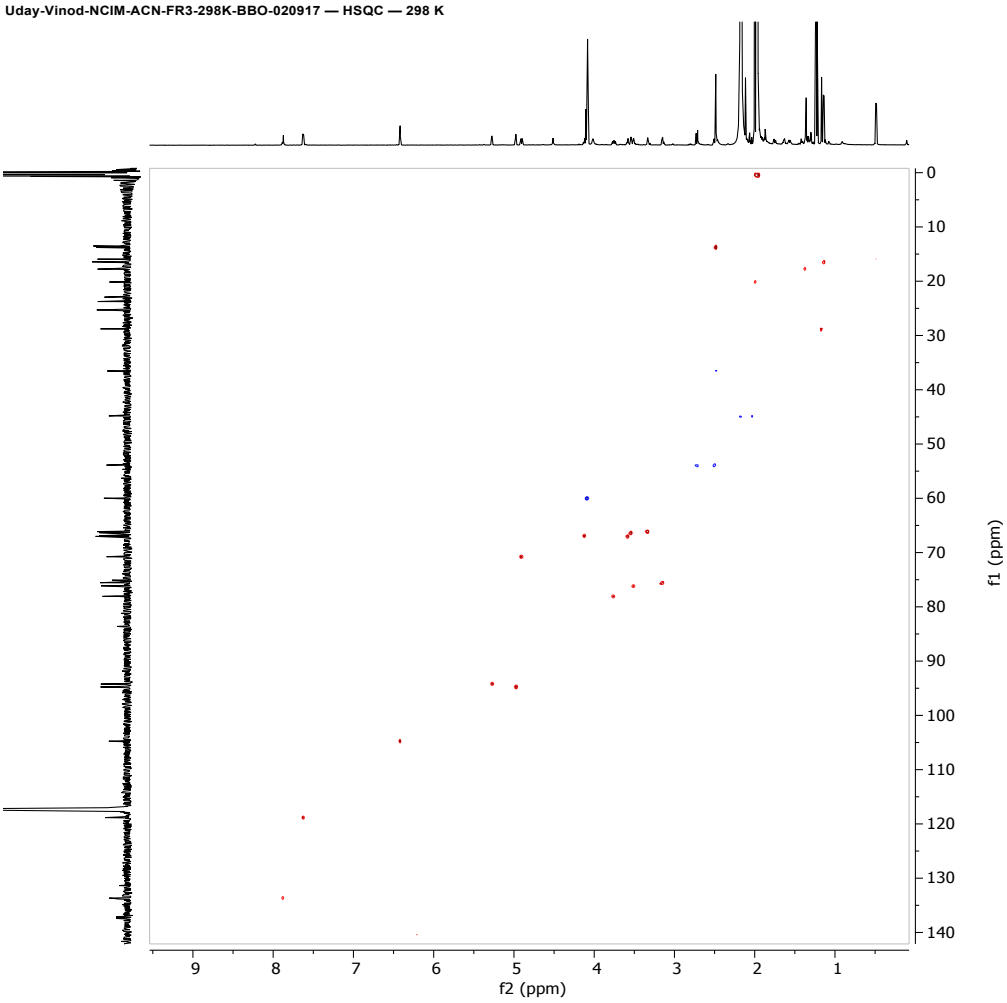
17	Acquisition Time	0.6999
18	Acquisition Date	2017-09-05T10:12:55
19	Modification Date	2017-09-05T10:12:54
20	Class	
21	Spectrometer Frequency	176.07
22	Spectral Width	41666.7
23	Lowest Frequency	-3229.9
24	Nucleus	13C
25	Acquired Size	29164
26	Spectral Size	65536

Figure SI-12 DEPT spectra of Compound **2**



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5	Instrument	spect
6	Author	
7	Solvent	CD3CN
8	Temperature	298.0
9	Pulse Sequence	hsqcedetgp
10	Experiment	HSQC-EDITED
11	Probe	Z123726_0018 (PA BBO 700S3 BB-H-D-05 Z)
12	Number of Scans	16
13	Receiver Gain	396.2
14	Relaxation Delay	1.5000
15	Pulse Width	14.2900
16	Presaturation Frequency	
17	Acquisition Time	0.2032
18	Acquisition Date	2017-09-06T13:04:03
19	Modification Date	2017-09-06T17:41:00
20	Class	
21	Spectrometer Frequency	(700.13, 176.06)
22	Spectral Width	(10080.6, 27322.4)
23	Lowest Frequency	(-614.0, -457.6)
24	Nucleus	(1H, 13C)
25	Acquired Size	(1024, 640)
26	Spectral Size	(1024, 1024)

Figure SI-13 HSQC spectra of Compound **2**

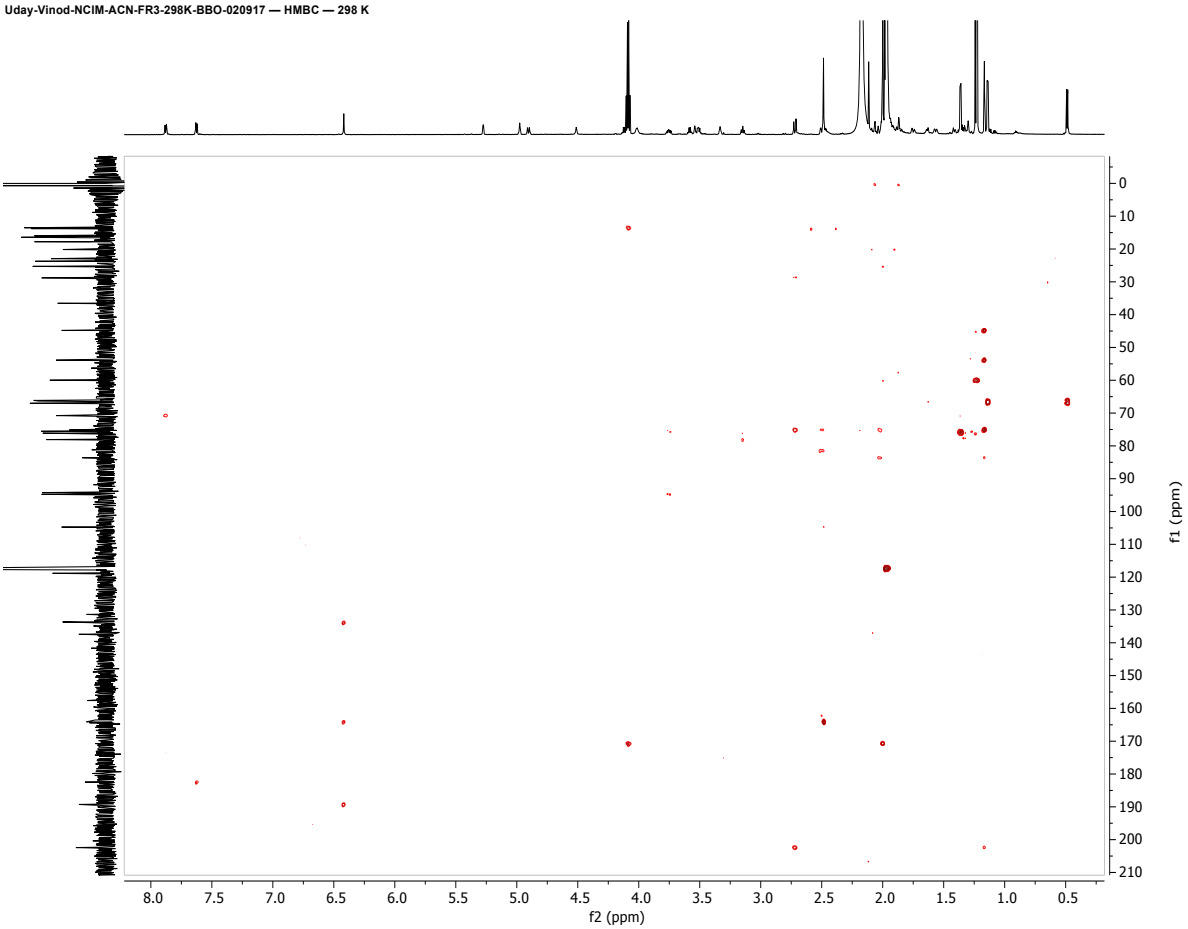
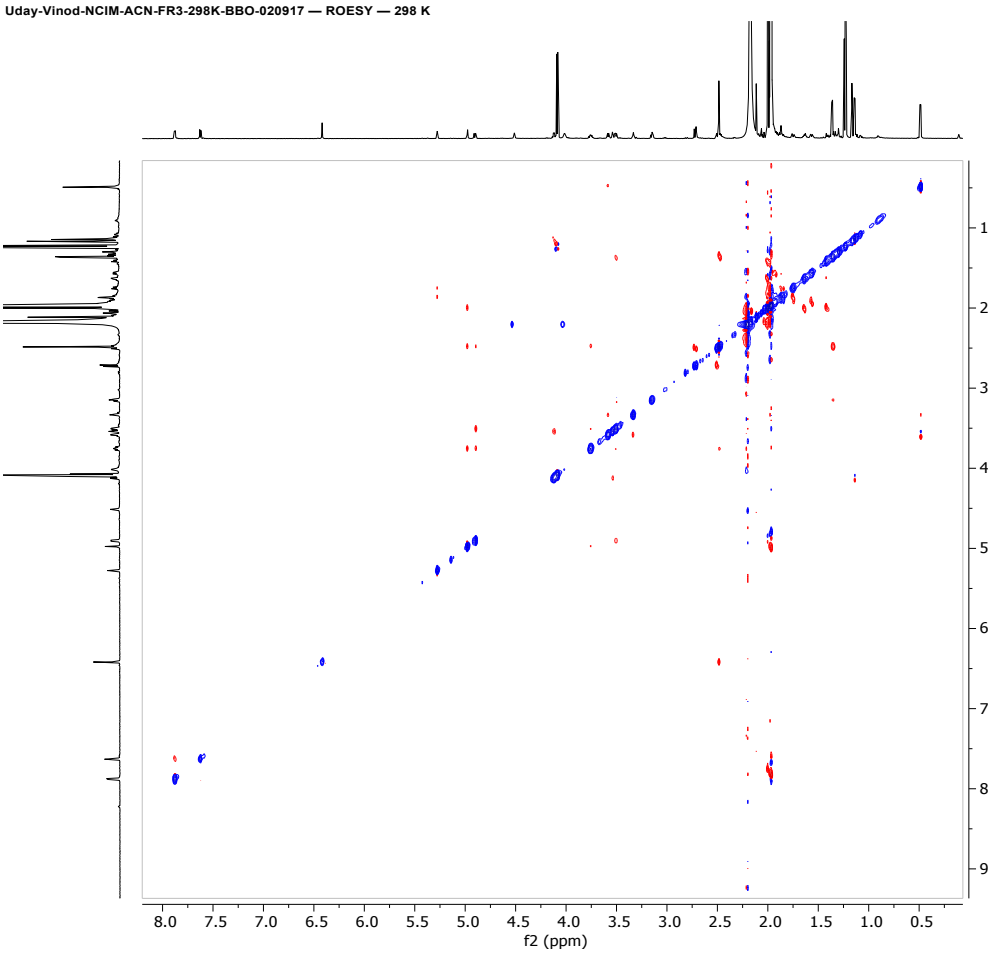


Figure SI-14 HMBC spectra of Compound **2**



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4	Site	
5	Instrument	spect
6	Author	
7	Solvent	CD3CN
8	Temperature	298.0
9	Pulse Sequence	roesyph
10	Experiment	ROESY
11	Probe	Z123726_0018 (PA BBO 700S3 BB-H-D-05 Z)
12	Number of Scans	16
13	Receiver Gain	543.2
14	Relaxation Delay	1.5000
15	Pulse Width	14.2900
16	Presaturation Frequency	
17	Acquisition Time	0.4063
18	Acquisition Date	2017-09-04T18:49:52
19	Modification Date	2017-09-05T00:19:56
20	Class	
21	Spectrometer Frequency	(700.13, 700.13)
22	Spectral Width	(10080.6, 10080.6)
23	Lowest Frequency	(-614.0, -614.0)
24	Nucleus	(1H, 1H)
25	Acquired Size	(4096, 512)
26	Spectral Size	(4096, 512)

Figure SI-15 ROESY spectra of Compound **2**

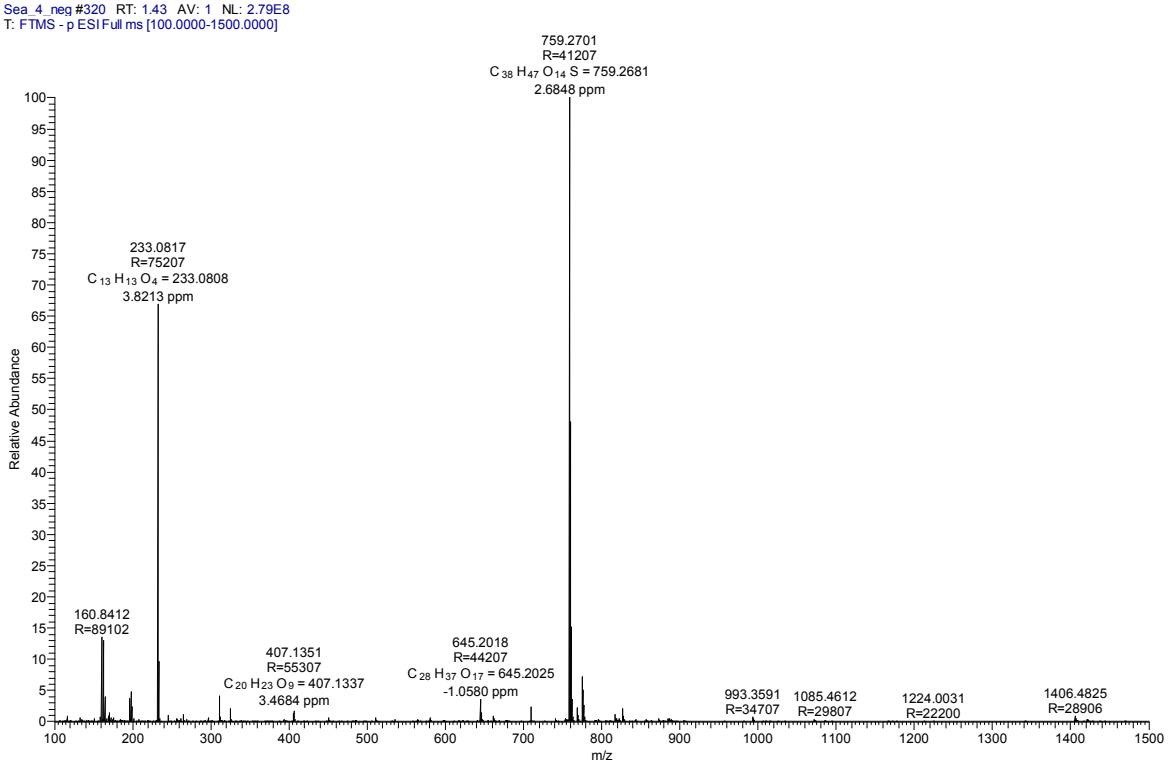

Figure SI-16. HRMS spectrum of Compound **2** (Urdamycin V)