

Genome-based analysis of the type II PKS biosynthesis pathway of xanthonenes in *Streptomyces caelestis* and their antifungal activity

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Figure S1. ^1H and ^{13}C NMR spectra of citreamicin ϵ (1) in $\text{DMSO-}d_6$.

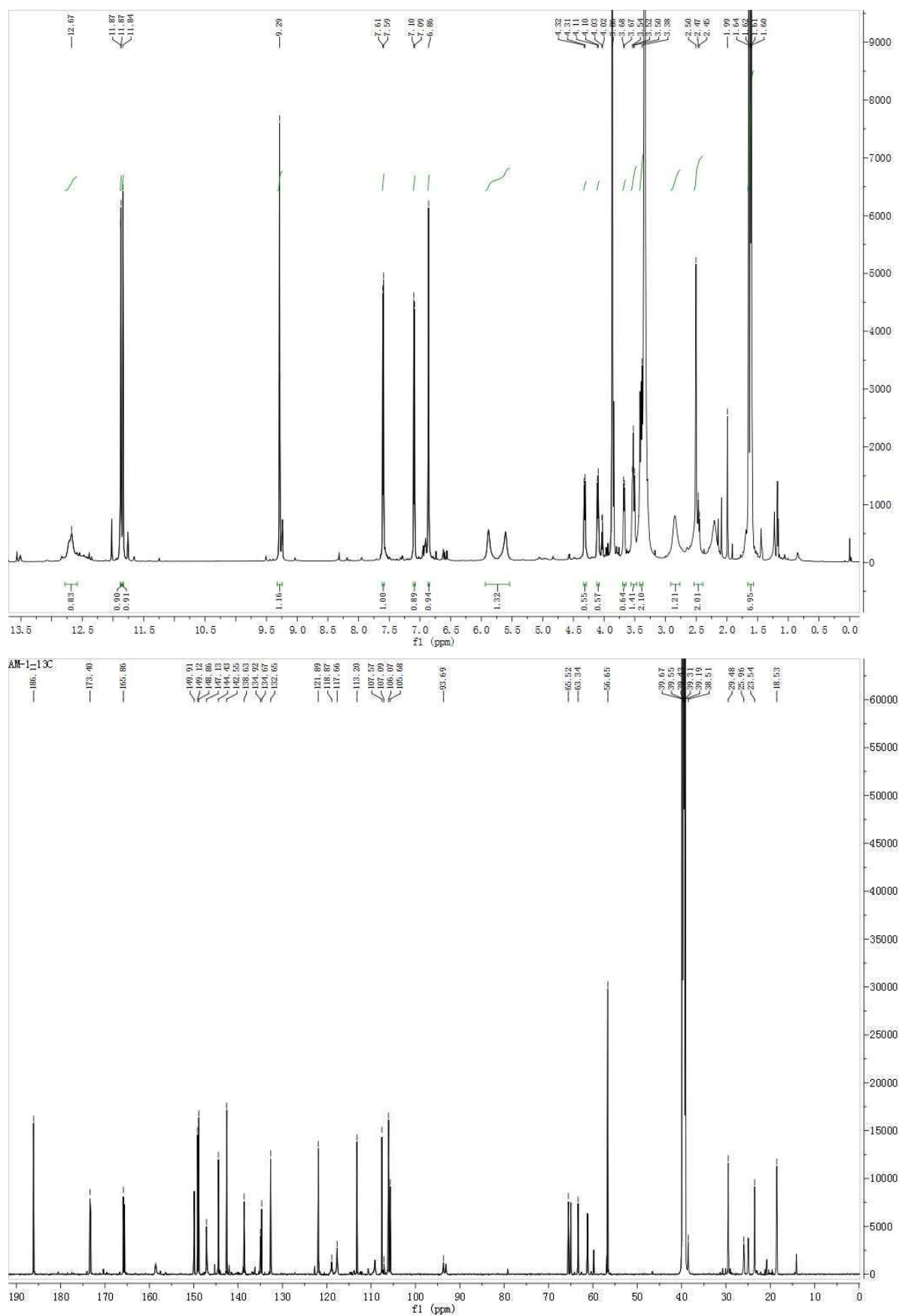


Figure S2. HR-ESI-MS spectrum of citreamicin ϵ (1).

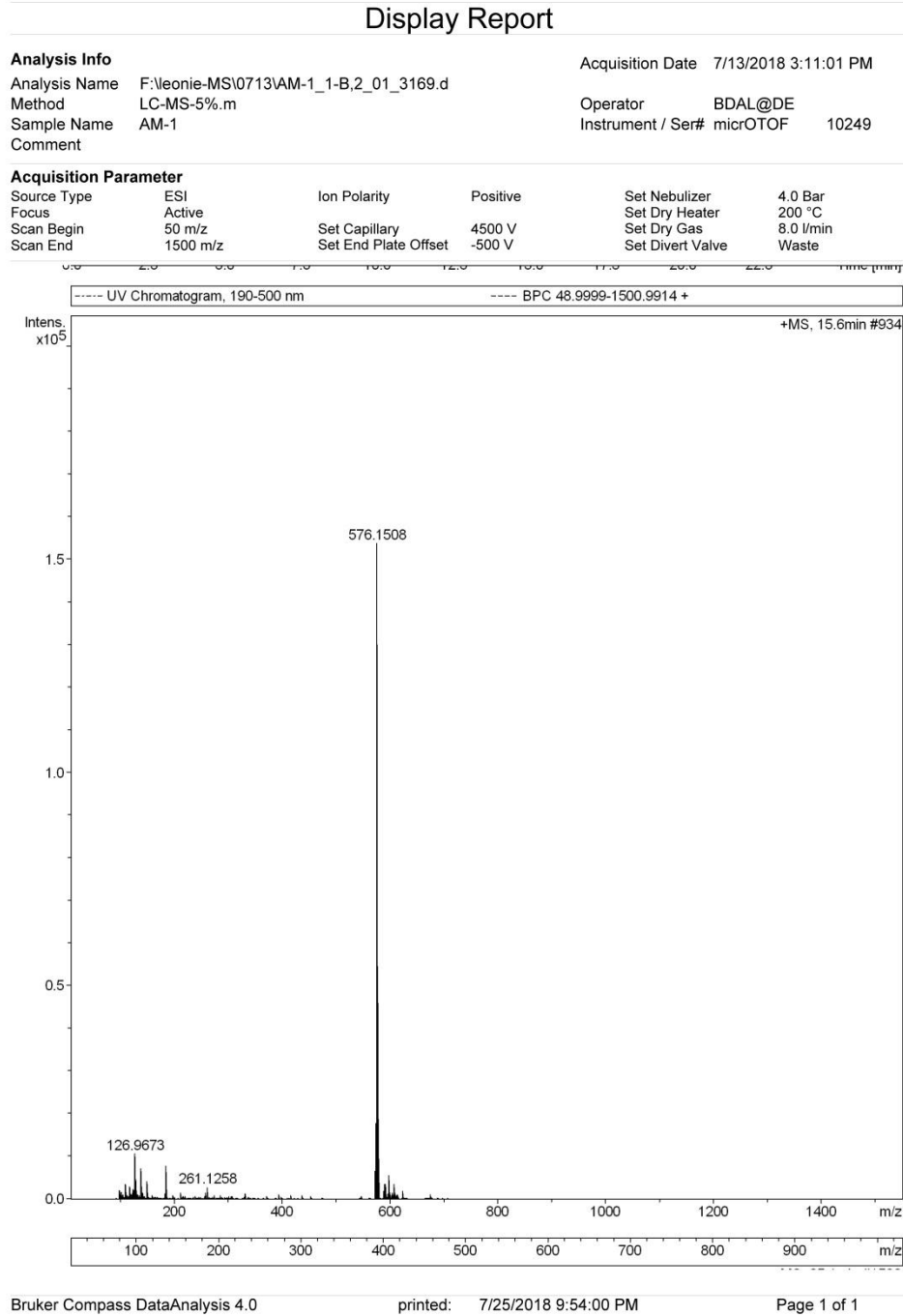


Figure S3. ^1H and ^{13}C NMR spectra of Citreamicin θ (2) in $\text{DMSO-}d_6$

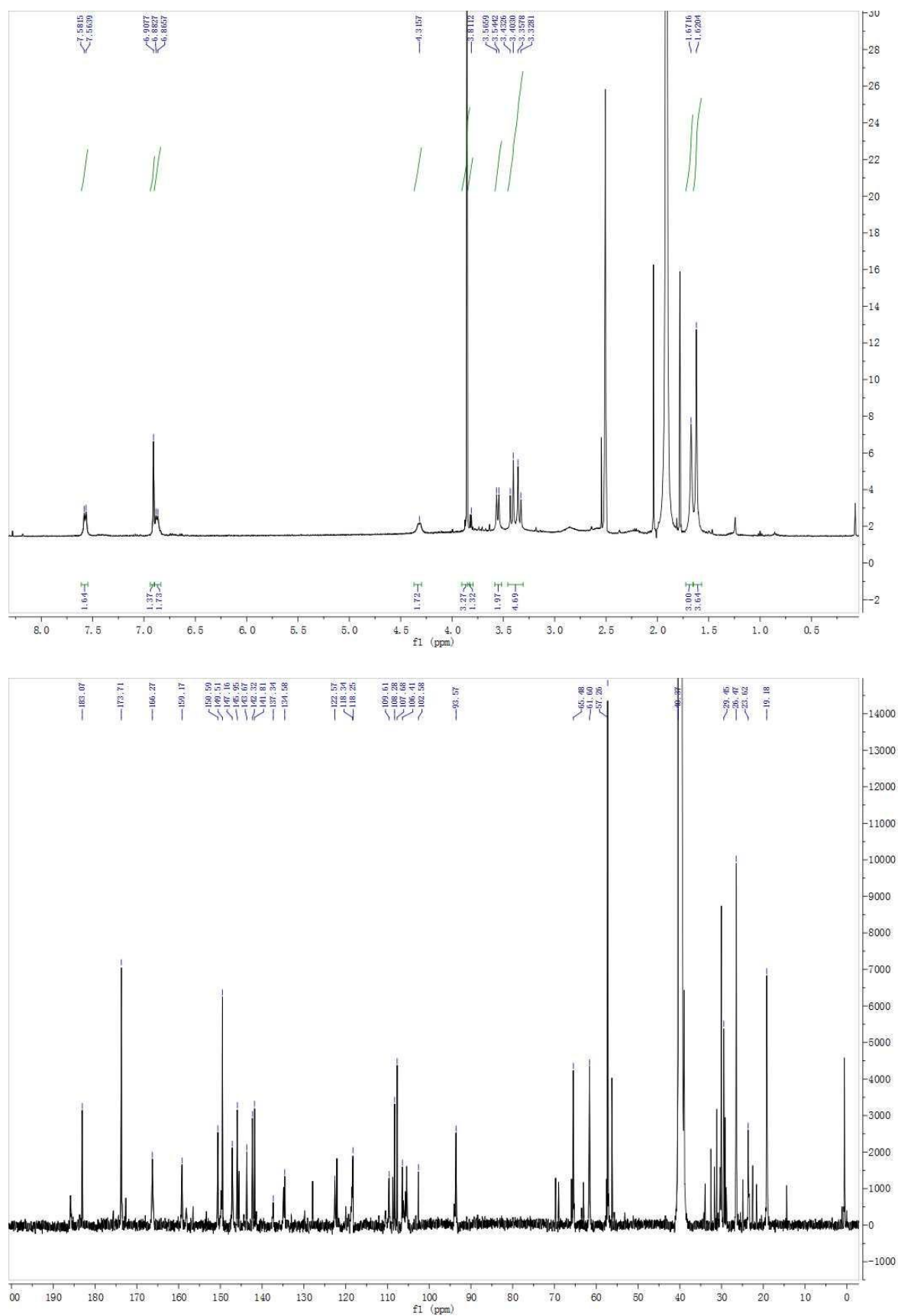


Figure S4. HR-ESI-MS spectrum of citreamicin θ (2).

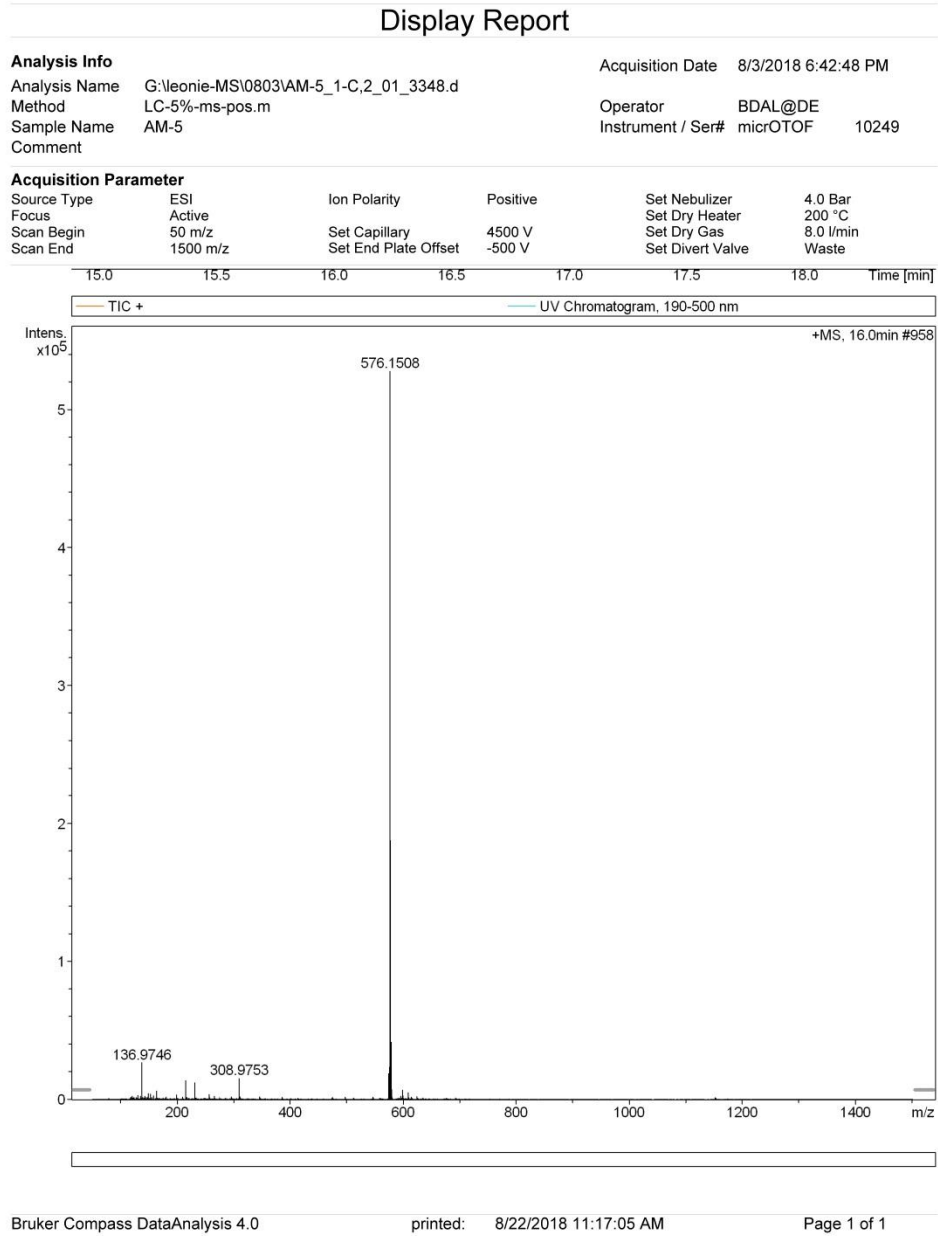


Figure S5. UPLC-MS analysis of the intermediates in citreamicins biosynthesis pathway.

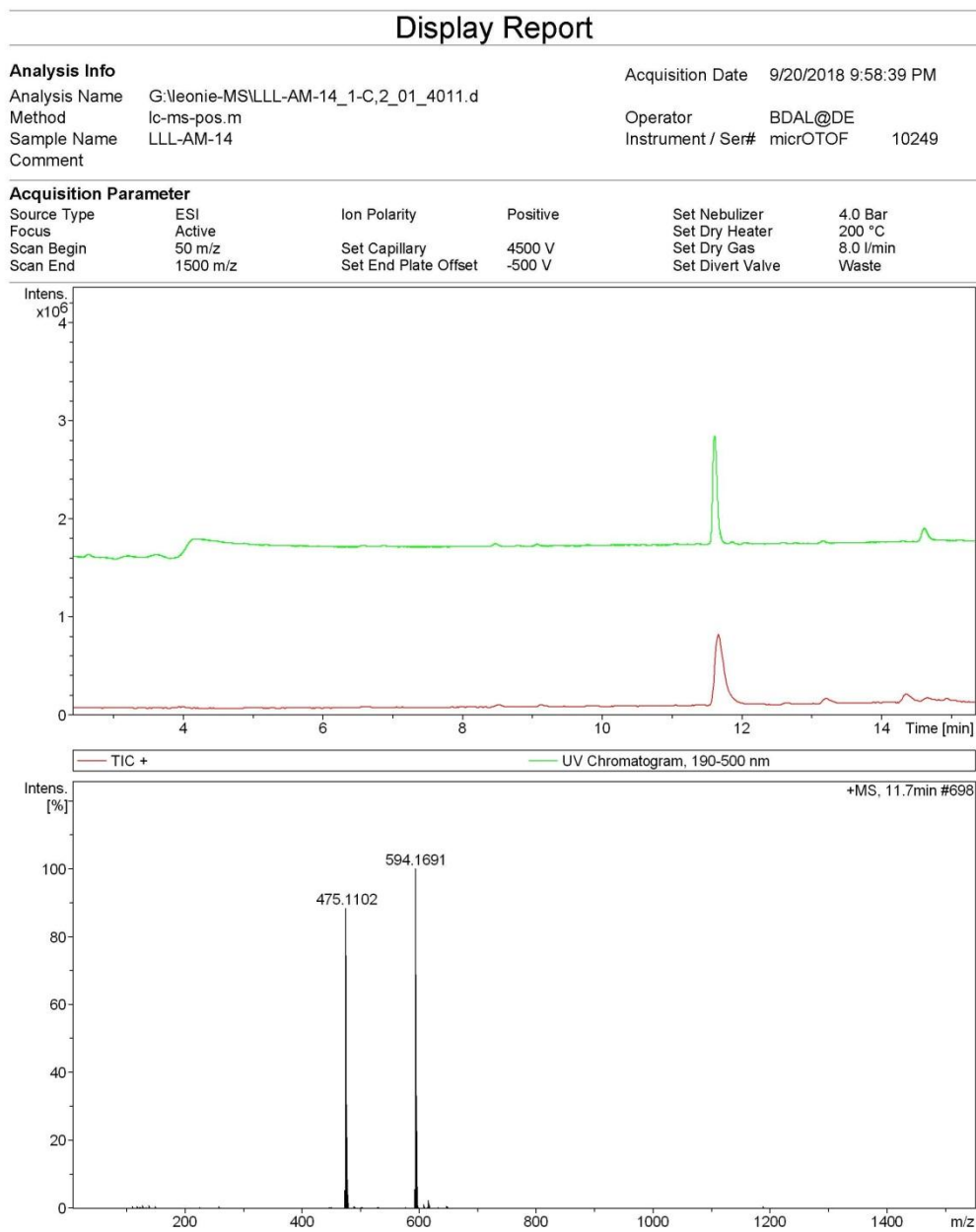


Table S1. Gene clusters encoding secondary metabolite biosynthesis in the draft genome sequences of *Streptomyces caelestis* Aw99c.

Type of secondary metabolite	Most similar known cluster	Similarity	MIBiG BGC-ID ^a
Lanthipeptide	SapB	75%	BGC0000551
Type II PKS	Xantholin	34%	BGC0000279
Siderophore	Desferrioxamine B	83%	BGC0000940
Type III PKS	Alkylresorcinol	100%	BGC0000282
Type II PKS	Spore pigment	83%	BGC0000271
Linaridin	Pentostatine / Vidarabine	9%	BGC0001735
Type I PKS	Oligomycin	38%	BGC0000117
<u>Phenazine</u>	Unknown		
Bacteriocin	Informatipeptin	28%	BGC0000518
Bacteriocin	Unknown		
Type I PKS	Micromonolactam	100%	BGC0000095
Lanthipeptide	Unknown		
Terpene	Geosmin	100%	BGC0001181
Type I PKS	Micromonolactam	100%	BGC0000095
Terpene	Isorenieratene	100%	BGC0000664
Terpene	Albaflavenone	100%	BGC0000660
Ectoine	Ectoine	100%	BGC0000853
Siderophore	Grincamycin	11%	BGC0000229
NRPS-PKS	Antimycin	100%	BGC0001455
Terpene	Carotenoid	54%	BGC0000633
NRPS	Naphthyridinomycin	64%	BGC0000394

Type of secondary metabolite	Most similar known cluster	Similarity	MIBiG BGC-ID ^a
Terpene	Hopene	53%	BGC0000663
NRPS-PKS	PM100117 / PM100118	8%	BGC0001359
Type I PKS	Unknown		
Type I PKS	Micromonolactam	100%	BGC0000095
Type I PKS	Unknown		
NRPS	Unknown		

^a MIBiG refers to “Minimum Information about a Biosynthetic Gene cluster” in the antiSMASH 5.0.

Table S2. Deduced function of the open reading frames in Figure 5

gene	Size (AA)	Proposed function	Protein homolog	Identity/ Similarity(%)	Protein accession
1	205	Uma2 family endonuclease	<i>Streptomyces sp.</i> NRRL F-5527	98/99	WP_031059834
2	285	AraC family transcriptional regulator	<i>Streptomyces sp.</i> NRRL F-5527	99/99	WP_031059832
3	309	putative inner membrane transporter YedA	<i>Streptomyces sp.</i> Go-475	86/90	AXE85492
4	150	hypothetical protein	<i>Streptomyces pseudogriseolus</i>	99/99	WP_086682316
5	224	O-methyltransferase	<i>Streptomyces gancidicus</i> BKS 13-15	96/96	EMF30210
6	111	hypothetical protein	<i>Streptomyces roseochromogenus</i>	77/86	WP_023544435
7	280	aminoglycoside phosphotransferase	<i>Streptomyces sp.</i> NTK 937	80/86	WP_037882343
8	645	ATP-binding protein	<i>Streptomyces sp.</i> NRRL S-1314	99/99	WP_031018592
9	153	Roadblock / LC7 domain-containing protein	<i>Streptomyces sp.</i> DH-12	94/96	WP_106414477
10	119	DUF742 domain-containing protein	<i>Streptomyces sp.</i> F-7	96/98	WP_093767843
11	205	ATP-binding protein	<i>Streptomyces sp.</i> CNH189	99/99	WP_024882742
12	426	cytochrome P450	<i>Streptomyces sp.</i> F-7	89/95	WP_093767845
13	408	cytochrome P450	<i>Streptomyces sp.</i> F-7	97/98	WP_093767846
14	71	DUF397 domain-containing protein	<i>Streptomyces sp.</i> NRRL F-5527	97/98	WP_031059799
15	97	ATP-binding protein	<i>Streptomyces sp.</i> DH-12	81/81	WP_106416448

gene	Size (AA)	Proposed function	Protein homolog	Identity/ Similarity(%)	Protein accession
16	90	type II toxin-antitoxin system prevent-host-death family antitoxin	<i>Streptomyces sp.</i> NRRL F-5527	95/95	WP_051791764
17	243	hypothetical protein	<i>Streptomyces sp.</i> CNH189	96/99	WP_024882739
18	529	acyl-CoA carboxylase subunit beta	<i>Streptomyces pseudogriseolus</i>	100/100	WP_107481696
19	265	hypothetical protein	<i>Streptomyces sp.</i> NRRL S-1314	100/100	WP_031018585
20	83	hypothetical protein	<i>Streptomyces sp.</i> NRRL S-1314	100/100	WP_006130567
21	748	TOMM precursor leader peptide-binding protein	<i>Streptomyces sp.</i> NRRL S-1314	99/99	WP_031018582
22	396	histidine kinase	<i>Streptomyces sp.</i> BK335	79/85	WP_133048867
23	204	response regulator	<i>Streptomyces sp.</i> BK335	94/97	WP_133048866
24	416	acyltransferase domain-containing protein	<i>Streptomyces sp.</i> BK335	79/85	WP_133048865
25	587	fatty acyl-AMP ligase	<i>Streptomyces sp.</i> BK335	80/85	WP_133048864.
26	65	acyl-CoA carboxylase subunit epsilon	<i>Streptomyces sp.</i> BK335	72/78	WP_133048863
27	217	hypothetical protein	<i>Streptomyces sp.</i> BK335	62/74	WP_133048862
28	74	hypothetical protein	<i>Streptomyces sp.</i> BK335	61/68	WP_133048861
29	582	acyl-CoA dehydrogenase	<i>Streptomyces sp.</i> NRRL S-1314	99/99	WP_037816785
30	265	4'-phosphopantetheinyl transferase superfamily protein	<i>Streptomyces sp.</i> BK335	85/89	WP_133048909
31	271	thioesterase	<i>Streptomyces gancidicus</i>	99/99	WP_052034335

gene	Size (AA)	Proposed function	Protein homolog	Identity/ Similarity(%)	Protein accession
32	276	AfsR/SARP family transcriptional regulator	<i>Streptomyces sp.</i> BK335	91/93	WP_133048857
33	89	acyl carrier protein	<i>Streptomyces sp.</i> BK335	91/97	WP_133048856
34	242	SDR family oxidoreductase	<i>Streptomyces sp.</i> NRRL S-1314	99/99	WP_031018568
35	131	SchA/CurD	<i>Streptomyces sp.</i> BK335	85/92	WP_133048855
36	153	DUF1772 domain-containing protein	<i>Streptomyces sp.</i> BK335	86/90	WP_133048854
37	127	SchA/CurD	<i>Streptomyces sp.</i> BK335	87/92	WP_133048853
38	111	TcmI family type II polyketide cyclase	<i>Streptomyces sp.</i> BK335	85/94	WP_133048852
39	144	cupin domain-containing protein	<i>Streptomyces sp.</i> BK335	87/95	WP_133048851
40	429	beta-ketoacyl-ACP synthase II	<i>Streptomyces sp.</i> BK335	93/96	WP_133048850
41	406	ketosynthase chain-length factor	<i>Streptomyces sp.</i> RV15	86/91	WP_067021572
42	154	polyketide cyclase	<i>Streptomyces pseudogriseolus</i>	100/100	WP_086681953
43	153	putative membrane protein	<i>Streptomyces sp.</i> BK335	90/94	TCS44129.1
44	251	SDR family oxidoreductase	<i>Streptomyces sp.</i> BK335	92/97	WP_133048847
45	103	antibiotic biosynthesis monooxygenase	<i>Streptomyces sp.</i> BK335	83/88	WP_133048845

gene	Size (AA)	Proposed function	Protein homolog	Identity/ Similarity(%)	Protein accession
46	288	NAD(P)-dependent oxidoreductase	<i>Streptomyces sp.</i> BK335	90/95	WP_133048844
47	556	monooxygenase	<i>Streptomyces sp.</i> BK335	82/88	WP_133048843
48	113	antibiotic biosynthesis monooxygenase	<i>Streptomyces sp.</i> BK335	75/87	WP_133048842
49	521	copper oxidase	<i>Streptomyces sp.</i> BK335	81/87	WP_133048841
50	618	asparagine synthase (glutamine-hydrolyzing)	<i>Streptomyces sp.</i> BK335	92/94	WP_133048840
51	539	monooxygenase	<i>Streptomyces sp.</i> BK335	82/89	WP_133048839