

Supplementary Materials

Streptomyces alleviate abiotic stress in plant by producing pteridic acids

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Table S1. The biosynthetic gene clusters in *S. iranensis* HM 35 predicted by antiSMASH 6.0.

Cluster	Type	Position		Most similar known cluster	Similarity
Cluster 1	lassopeptide	47,826	67,848	SSV-2083	18%
Cluster 2	NRPS-like, T1PKS, NRPS	89,243	264,517	argimycins	10%
Cluster 3	terpene, NRPS	310,755	369,526	carotenoid	63%
Cluster 4	NRPS	584,615	633,798	coelichelin	100%
Cluster 5	butyrolactone	920,071	929,026	cyphomycin	9%
Cluster 6	phosphonate, acyl_amino_acids, butyrolactone, NRPS-like, T1PKS, hserlactone	983,576	1,129,298	lydicamycin	20%
Cluster 7	T1PKS	1,216,733	1,353,478	azalomycin F3a	100%
Cluster 8	T1PKS	1,525,866	1,708,371	nigericin	100%
Cluster 9	T1PKS	1,812,276	1,890,013	elaiophylin	87%
Cluster 10	redox-cofactor	1,914,682	1,936,746		
Cluster 11	hserlactone	2,054,025	2,074,780	daptomycin	4%
Cluster 12	butyrolactone	2,085,494	2,096,426		
Cluster 13	T1PKS, NRPS	2,274,879	2,327,099	meilingmycin	
Cluster 14	NRPS, T3PKS, other	2,383,216	2,482,446	feglymycin	
Cluster 15	NRPS, T1PKS	2,535,309	2,739,409	α -lipomycin	
Cluster 16	terpene	2,985,464	3,007,479	hopene	76%
Cluster 17	T1PKS	3,153,626	3,235,531	macbecin / macbecin II	34%
Cluster 18	T2PKS	3,304,807	3,374,688	spore pigment	83%
Cluster 19	T1PKS	3,499,162	3,559,357	s56-p1	11%
Cluster 20	RiPP-like	3,612,469	3,622,637		
Cluster 21	siderophore	3,792,665	3,803,134		
Cluster 22	T2PKS	4,140,701	4,213,204	isoindolinomycin	61%
Cluster 23	NRPS-like	4,442,739	4,484,596	echosides	100%
Cluster 24	siderophore	5,229,788	5,240,857	desferrioxamin B	100%
Cluster 25	terpene	6,441,503	6,461,832	geosmin	100%
Cluster 26	ladderane, arylpolyene, NRPS	6,705,172	6,807,080	atratumycin	57%
Cluster 27	NRPS	7,345,535	7,387,933	ochronotic pigment	75%
Cluster 28	ladderane	7,449,836	7,489,866	atratumycin	34%
Cluster 29	RRE-containing	7,510,172	7,530,691	granaticin	10%
Cluster 30	T1PKS	7,664,407	7,848,116	mediomycin A	68%
Cluster 31	terpene	8,396,931	8,416,950		
Cluster 32	ectoine	9,062,415	9,072,819	ectoine	100%
Cluster 33	siderophore	9,237,702	9,251,453		
Cluster 34	terpene	9,301,372	9,319,391	BE-43547s	25%
Cluster 35	nucleoside	9,535,814	9,572,869	toyocamycin	40%
Cluster 36	nucleoside, NRPS, T1PKS, NRPS-like	9,677,504	9,821,457	rapamycin	82%
Cluster 37	PKS-like	9,909,290	9,950,318	rustmicin	33%
Cluster 38	terpene	10,000,500	10,020,321	2-methylisoborneol	100%
Cluster 39	terpene	10,464,893	10,484,016	pristinol	100%
Cluster 40	T1PKS, ladderane, arylpolyene	10,578,295	10,629,355	atratumycin	28%

Cluster 41	T1PKS, NRPS-like	10,835,982	10,918,034	hygrocins	83%
Cluster 42	lanthipeptide-class-ii	11,011,708	11,035,079	reveromycin A	9%
Cluster 43	hglE-KS, T1PKS, RiPP-like	11,062,970	11,124,110		
Cluster 44	T1PKS, NRPS	11,127,758	11,269,230	X-14547	21%
Cluster 45	terpene	11,320,894	11,341,820	brasilicardin A	38%
Cluster 46	terpene	11,470,415	11,491,323		
Cluster 47	T1PKS, NRPS-like	11,577,719	11,624,306	niphimycins C-E	9%
Cluster 48	betalactone	11,818,784	11,847,595	Sch-47554 / Sch-47555	7%
Cluster 49	NRPS, NRPS-like, T1PKS	12,040,448	12,123,871	echosides	11%
Cluster 50	lassopeptide	12,143,153	12,165,683	SSV-2083	18%

Table S2. The annotation of pteridic acids core biosynthetic genes in *S. iranensis* HM35.

ORF	Size ^a	Proposed functions	SI/ID ^b	Protein homologue and origin
<i>Pta5</i>	1041	3-oxoacyl-ACP synthase III	98/97	WP_210951575.1, <i>Streptomyces</i> sp. MK37H
<i>pta4</i>	572	3-hydroxyacyl-CoA dehydrogenase	98/97	WP_020866330.1, <i>Streptomyces rapamycinicus</i>
<i>pta3</i>	958	LuxR family transcriptional regulator	99/99	WP_020866329.1, <i>Streptomyces rapamycinicus</i>
<i>pta2</i>	316	glucose-1-phosphate thymidyltransferase	99/99	RLV74943.1, <i>Streptomyces rapamycinicus</i> NRRL 5491
<i>pta1</i>	324	TDP glucose 4,6 dehydratase	98/98	WP_214665150.1, <i>Streptomyces javensis</i>
<i>ptaA</i>	4535	Type I PKS	90/88	WP_214609358.1, <i>Streptomyces malaysiensis</i>
<i>ptaB</i>	1746	Type I PKS	91/89	WP_037957959.1, <i>Streptomyces</i> sp. PRh5
<i>ptaC</i>	1655	Type I PKS	95/94	WP_138910801.1, <i>Streptomyces</i> sp. DASNCL29
<i>ptaD</i>	3395	Type I PKS	96/95	WP_020866322.1, <i>Streptomyces rapamycinicus</i>
<i>ptaE</i>	2112	Type I PKS	95/95	WP_201848053.1, <i>Streptomyces</i> sp. 110
<i>pta1*</i>	261	Thioesterase	97/95	GDY58888.1, <i>Streptomyces violaceusniger</i>
<i>pta2*</i>	417	Glycosyltransferase	99/98	MBP8534388.1, <i>Streptomyces</i> sp. MK37H
<i>pta3*</i>	196	dTDP-4-dehydrorhamnose 3,5-epimerase	97/97	WP_210946413.1, <i>Streptomyces</i> sp. MK37H
<i>pta4*</i>	304	Exporter (membrane domain)	100/99	WP_138910796.1, <i>Streptomyces</i> sp. DASNCL29
<i>pta5*</i>	245	Exporter (ATPase domain)	99/99	WP_020866316.1, <i>Streptomyces rapamycinicus</i>
<i>pta6*</i>	420	Two-component regulator (sensor/kinase domain)	97/97	WP_199334865.1, <i>Streptomyces</i> sp. GMR22
<i>pta7*</i>	223	Two-component regulator (effector domain)	98/98	WP_138910795.1, <i>Streptomyces</i> sp. DASNCL29
<i>pta8*</i>	321	NAD(P)-dependent oxidoreductase	96/96	WP_164428021.1, <i>Streptomyces rhizosphaericus</i>
<i>pta9*</i>	328	aldo/keto reductase	98/98	WP_191066610.1, <i>Streptomyces</i> sp. 5-10
<i>pta10*</i>	469	NDP-hexose 2,3 dehydratase	97/95	GDY58900.1, <i>Streptomyces violaceusniger</i>
<i>pta11*</i>	446	Crotonyl-CoA reductase	99/99	WP_020866310.1, <i>Streptomyces rapamycinicus</i>

a, The size of amino acids; b, similarity-identity ratio.

Table S3. Alignment of conserved motifs in the active site of AT domains.

domain name	specificity	198	199	200	201
ave_AT5	Malonyl-CoA	H	A	F	H
nid_AT3	Malonyl-CoA	H	A	F	H
epo_AT2	Malonyl-CoA	H	A	F	H
amp_AT18	Malonyl-CoA	H	A	F	H
rif_AT2	Malonyl-CoA	H	A	F	H
pta_LD	Malonyl-CoA	H	A	F	H
pta_AT2	Malonyl-CoA	H	A	F	H
pta_AT6	Malonyl-CoA	H	A	F	H
pta_AT7	Malonyl-CoA	I	A	A	H
ave_AT1	Methylmalony-CoA	Y	A	S	H
nid_AT4	Methylmalony-CoA	Y	A	S	H
ery_AT4	Methylmalony-CoA	Y	A	S	H
amp_AT2	Methylmalony-CoA	Y	A	S	H
rif_AT7	Methylmalony-CoA	Y	A	S	H
pta_AT3	Methylmalony-CoA	Y	A	S	H
pta_AT4	Methylmalony-CoA	Y	A	S	H
pta_AT5	Methylmalony-CoA	Y	A	S	H
nid_AT5	Ethylmalonyl-CoA	T	A	G	H
tyl_AT5	Ethylmalonyl-CoA	T	A	G	H
pta_AT1	Ethylmalonyl-CoA	T	A	G	H
ery_LD	Propionyl-CoA	M	A	A	H
meg_LD	Propionyl-CoA	M	A	A	H
epo_AT3	Flexible	H	A	S	H

* Abbreviations: LD, loading module; ave, avermectin; nid, niddamycin; epo, epothilone; amp, amphotericin; rif, rifamycin; ery, erythromycin; tyl, tylactone; meg, megalomicin; pta, pteridic acids.

Table S4. The *Streptomyces* strains that can produce elaiophylin, pteridic acids, or harbor *pta* BGC.

NO	Strain name	Geographic location	Source	Reference/Assembly
1	<i>Streptomyces iranensis</i> HM 35	Isfahan City, Iran	rhizosphere	This study
2	<i>Streptomyces</i> sp. 219807	Sanya, Hainan, China	mangrove soil	1
3	<i>Streptomyces</i> sp. SCSGAA 0027	South China Sea, China	gorgonian-associated	2
4	<i>Streptomyces</i> sp. 7-145	Heishijiao Bay, Dalian, China	marine-sediment	3
5	<i>Streptomyces melanosporofaciens</i>	Italy	soil	4
6	<i>Streptomyces autolyticus</i> CGMCC 0516	Yunnan, China	soil	5
7	<i>Streptomyces</i> sp. DSM 3816	Kypcerissia, Greece	soil	6
8	<i>Streptomyces</i> sp. BCC 71188	Nakhon Si Thammarat Province, Thailand	soil	7
9	<i>Streptomyces</i> sp. BCC 72023	Chumphon province, Thailand	plant-associated	8
10	<i>Streptomyces</i> sp. BS 1261	New Zealand	soil	9
11	<i>Streptomyces</i> sp. ICBB 9297	Jatiroto, East Java, Indonesia	soil	10
12	<i>Streptomyces</i> sp. SNA-4606	Towada-shi, Aomori Prefecture, Japan	soil	11
13	<i>Streptomyces</i> sp. MCY-846	cheju-island, Korea	soil	12
14	<i>Streptomyces albiflaviniger</i> SCSIO ZJ28	South China Sea, China	marine-sediment	13
15	<i>Streptomyces</i> sp. USC-16018	Hastings Point, NSW, Australia	marine	14
16	<i>Streptomyces</i> sp. SPMA113	Prajinburi Province, Thailand	soil	15
17	<i>Streptomyces</i> sp. LZ35	Ji'mei, Xia'men, China	soil	16
18	<i>Streptomyces malaysiensis</i> DSM 4137	Germany	soil	17
19	<i>Streptomyces</i> sp. BCa1	Borra Caves, India	soil	18
20	<i>Streptomyces</i> sp. IFM11958	Sakuragi cemetery, Chiba city, Japan	soil	19
21	<i>Streptomyces malaysiensis</i> OUCMDZ-2167	South China Sea, China	marine	20
22	<i>Streptomyces</i> sp. 11-1-2	Newfoundland, Canada	plant-associated	21
23	<i>Streptomyces</i> sp. HNM0561	Hainan, China	marine-sediment	22
24	<i>Streptomyces</i> sp. GMR 22	Wanagama Forest, Indonesia	soil	23
25	<i>Streptomyces</i> sp. NTK 935	Canary Basin	marine sediment	24
26	<i>Streptomyces</i> sp. NTK 937	Canary Basin	marine sediment	24
27	<i>Streptomyces</i> sp. RJA 2928	Papua New Guinea	marine sediment	25
28	<i>Streptomyces rapamycinicus</i> NRRL 5491	Easter island, Fiji	soil	26
29	<i>Streptomyces pseudouerticillus</i> YN 17707	Xishuangbanna, Yunnan, China	soil	27
30	<i>Streptomyces</i> sp. SCSIO ZS0520	Okinawa, Japan	marine sediment	28
31	<i>Streptomyces hygrosopicus</i> NND-52	Suqian, Jiangsu, China	soil	29
32	<i>Streptomyces hygrosopicus</i> NO.662	Sapporo-city, Hokkaido, Japan	soil	30
33	<i>Streptomyces hygrosopicus</i> TP-A0451	Toyama, Japan	plant-associated	31
34	<i>Streptomyces hygrosopicus</i> CH-7	Vojvodina, Serbia	soil	32
35	<i>Streptomyces hygrosopicus</i> 17997	Yunnan, China	soil	33
36	<i>Streptomyces hygrosopicus</i> ACTMS-9H	Amazon, Brazil	rhizosphere	34
37	<i>Streptomyces hygrosopicus</i> XM 201	Xiamen, Fujian, China	soil	35
38	<i>Streptomyces yatensis</i> DSM 41771	New Caledonia	Ultramafic soil	36
39	<i>Streptomyces solisilvae</i> HNM0141	Bawangling, Hainan, China	soil	37
40	<i>Streptomyces</i> sp. NA02950	Hainan, China	marine-sediment	38

41	<i>Streptomyces</i> sp. PRh5	Dongxiang, China	plant-associated	39
42	<i>Streptomyces albus</i> DSM 41398	Fuji City, Shizuoka Pref, Japan	soil	GCA_000827005.1
43	<i>Streptomyces samsunensis</i> SA31	Songkhla, Thailand	soil	GCA_013345665.1
44	<i>Streptomyces</i> sp. MK37H	Antalya, Turkey	soil	GCA_018035285.1
45	<i>Streptomyces</i> sp. 4503	Guangxi, China	mangrove sediment	GCA_018883605.1
46	<i>Streptomyces</i> sp. t39	Austin, Texas, USA	soil	GCA_008042045.1
47	<i>Streptomyces</i> sp. 5-10	Hainan, China	plant-associated	GCA_014712245.1
48	<i>Streptomyces antioxidans</i> MUSC164	Malaysia	mangrove	GCA_000968685.2
49	<i>Streptomyces malaysiensis</i> F913	Chongqing, China	soil	GCA_002891865.1
50	<i>Streptomyces</i> sp. DASNCL29	Unkeshwar, India	soil	GCA_005938145.1
51	<i>Streptomyces</i> sp. WAC05858	Germerby	soil	GCA_003949695.1
52	<i>Streptomyces rhizosphaericus</i> 0250	Taian, China	soil	GCA_010892295.1
53	<i>Streptomyces</i> sp. NEAU-YJ-81	Harbin, China	soil	GCA_017592595.1
54	<i>Streptomyces rhizosphaericus</i> NRRL B-24304	Indonesia	rhizosphere	GCA_002155885.1
55	<i>Streptomyces malaysiensis</i> TY049-057	Bidor Perak, Malaysia	soil	GCA_008033485.1
56	<i>Streptomyces malaysiensis</i> DSM 14702	Germany	soil	GCA_011800555.1
57	<i>Streptomyces cangkringensis</i> DSM 41769	South Korea	-	GCA_019059395.1
58	<i>Streptomyces endocoffeicus</i> CA3R110	Lampang, Thailand	plant-associated	GCA_016741935.1
59	<i>Streptomyces indonesiensis</i> DSM 41759	Yogyakarta, Indonesia	rhizosphere	GCA_018138705.1
60	<i>Streptomyces rhizosphaericus</i> DSM 41760	Yogyakarta, Indonesia	rhizosphere	GCA_017942185.1
61	<i>Streptomyces asiaticus</i> DSM 41761	Yogyakarta, Indonesia	rhizosphere	GCA_018138715.1
62	<i>Streptomyces</i> sp. RCU064	Nong Jum Rung, Thailand	Peat swamp forest soil	GCA_024505145.1
63	<i>Streptomyces violaceusniger</i> Tu 4113	-	soil	GCA_000147815.3
64	<i>Streptomyces antimycoticus</i> NBRC 100767	-	soil	GCA_009936315.1
65	<i>Streptomyces antimycoticus</i> NBRC 12839	-	soil	GCA_005405925.1
66	<i>Streptomyces</i> sp. AgN23	-	rhizosphere	GCA_001598115.2
67	<i>Streptomyces</i> sp. NRRL 30748	-	soil	39
68	<i>Streptomyces</i> sp. M56	-	termite-associated	40
69	<i>Streptomyces</i> sp. CWJ-256	-	plant-associated	41
70	<i>Streptomyces</i> sp. 92JF-1	-	marine	42
71	<i>Streptomyces</i> sp. KIB-H869	-	plant-associated	43
72	<i>Streptomyces hygroscopicus</i> MSU-625	-	soil	44
73	<i>Streptomyces hygroscopicus</i> MSU-616	-	soil	45
74	<i>Streptomyces hygroscopicus</i> OUPS-N92	-	marine	46
75	<i>Streptomyces</i> sp. CBR53	-	-	47
76	<i>Streptomyces violaceusniger</i> NBRC 13459	-	-	GCA_005405945.1
77	<i>Streptomyces violaceusniger</i> NRRL F-8817	-	-	GCA_001509775.1
78	<i>Streptomyces</i> sp. HKI-0113	-	-	48
79	<i>Streptomyces</i> sp. HKI-0114	-	-	48
80	<i>Streptomyces</i> sp. 57-13	-	-	49
81	<i>Streptomyces javensis</i>	-	-	GCA_016103505.1

“-”: information missing.

Table S5. Summary of strains and plasmids used in this study.

Strains	Description	Source/[Ref]
One Shot™ Mach1™ T1 Phage-Resistant Chemically Competent <i>E. coli</i>	For routine plasmids maintenance and cloning	Thermo Fisher Scientific
<i>E. coli</i> ET12567/pUZ8002	For conjugating plasmids into <i>Streptomyces</i>	[50]
<i>Streptomyces iranensis</i> HM35	Wild-type strain	DSMZ
<i>Streptomyces iranensis</i> HM35/ Δ ptaA	Δ ptaA mutant strain	In this work
<i>S. rapamycinicus</i> NRRL 5491	Wild-type strain	DSMZ
<i>S. violaceusniger</i> Tu 4113	Wild-type strain	DSMZ
<i>S. albus</i> DSM 41398	Wild-type strain	DSMZ
Plasmids		
pCRISPR-cBEST	For C to T base editing	[51]
pCRISPR-cBEST/ Δ ptaA	Modified plasmid for inactivation of <i>ptaA</i>	In this work

Table S6. ^1H (800 MHz) NMR data for **1–2** (in MeOD).

position	ΔH (J in Hz)	
	1	2
1	-	-
2	5.90 (d, 15.4)	5.97 (d, 15.1)
3	7.33 (dd, 15.4, 11.1)	7.16 (dd, 15.1, 10.9)
4	6.26 (dd, 15.2, 10.8)	6.25 (dd, 15.1, 10.9)
5	6.13 (dd, 15.3, 8.8)	6.07 (dd, 15.1, 8.6)
6	2.48 (m)	2.49 (m)
7	3.85 (dd, 10.2, 2.2)	3.32 (m)
8	2.01 (m)	2.02 (m)
9	3.69 (not determined)	3.56 (dd, 11.5, 4.7)
10	1.61 (m)	1.69 (m)
11	-	-
12	2.29 (dd, 14.9, 6.1), 1.64 (dd, 14.9, 1.9)	2.19 (dd, 13.1, 4.3) 1.32 (dd, 13.2, 11.2)
13	3.59 (m)	3.66 (td, 10.8, 4.3)
14	1.49 (m)	1.02 (m)
15	3.43 (m)	3.88 (m)
16	1.21 (d, 6.1)	1.14 (d, 6.2)
17	1.01 (d, 6.8)	1.02 (d, 6.8)
18	0.91 (d, 7.0)	0.95 (d, 6.9)
19	0.96 (d, 6.8)	0.98 (d, 6.8)
20	1.52 (m), 1.21 (m)	1.60 (m), 1.44 (m)
21	0.93 (t, 7.3)	0.82 (t, 7.6)

Table S7. ^{13}C (200 MHz) NMR data for **1–2** (in MeOD).

position	Δ_c , type	
	1	2
1	168.7	170.2
2	120.6	122.9
3	146.7	148.1
4	129.6	129.6
5	151.0	148.1
6	40.4	40.5
7	75.5	78.0
8	37.5	38.0
9	70.3	74.7
10	42.2	42.1
11	103.2	103.2
12	37.4	33.8
13	70.1	66.3
14	51.3	52.2
15	72.8	66.3
16	20.9	20.4
17	16.0	15.9
18	5.0	5.3
19	12.1	12.7
20	24.8	19.7
21	10.1	10.5

Table S8. Summary of primers used in this study.

Primer name	Sequence (5' → 3')	Description
Del- <i>ptaA</i>	CGGTTGGTAGGATCGACGGC GCACCCAGGCGG TATGCGTAG TTTTAGAGCTAGAAATAGC	Inactivation of <i>ptaA</i> , the base marked in red is sgRNA sequence
Mut- <i>ptaE</i>	CCGTTGGTAGGATCGACGG GGTCCTCCATCA TGGTGAAG TTTTAGAGCTAGAAATAGC	Site-directed mutagenesis of TE domain in <i>ptaE</i> , the base marked in red is sgRNA sequence
ID-sgRNA-F	TGTGTGGAATTGTGAGCGGATA	Forward primer for screening plasmid
ID-sgRNA-R	CCCATTCAAGAACAGCAAGCA	Reverse primer for screening plasmid
ID- <i>ptaA</i> -F	TTGCACAGCTCGACGGACAT	Forward primer for screening <i>ptaA</i> mutants
ID- <i>ptaA</i> -R	GTGTCACCCGCTTTGTCTGA	Reverse primer for screening <i>ptaA</i> mutants
ID- <i>ptaE</i> -F	CAACGCCATGATCGTCGTTC	Forward primer for screening <i>ptaE</i> mutants
ID- <i>ptaE</i> -R	CGTTCGAGACCGGGAAATG	Reverse primer for screening <i>ptaE</i> mutants

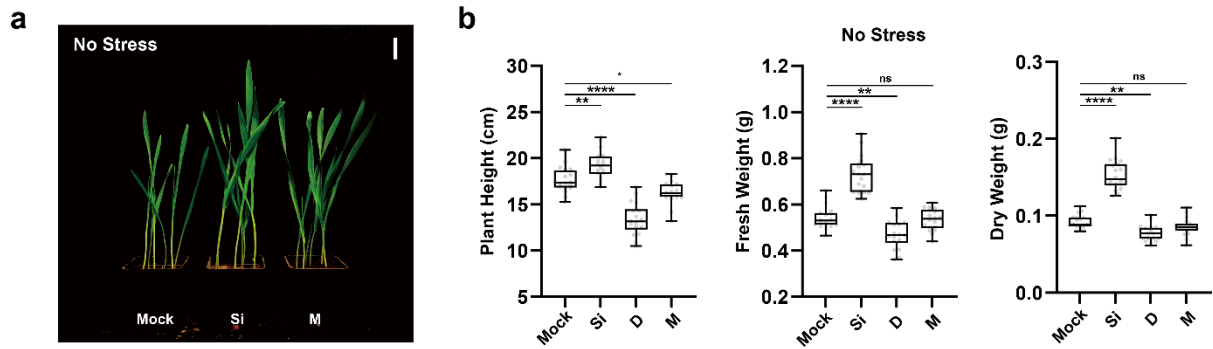


Figure S1. Barley experiments of *S. iranensis* HM 35 and *S. iranensis* HM 35/ Δ *ptaA* treatment under non-stress condition. **a**, *S. iranensis* HM 35 and its plant growth-promoting activity on barley seedlings growth (bars = 2 cm); **b**, the box-plot (middle bar = median, box limit = upper and lower quartile, extremes = Min and Max values) depicts the plant height, fresh weight and dry weight of barley seedlings growing on non-stress condition (n =18); Abbreviation: CK, control; Si, treatment of *S. iranensis* HM 35 culture broth; D, treatment of *S. iranensis* HM 35/ Δ *ptaA* culture broth; M, treatment of blank medium (ISP2). Asterisks indicate the level of statistical significance: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ and **** $P < 0.0001$.

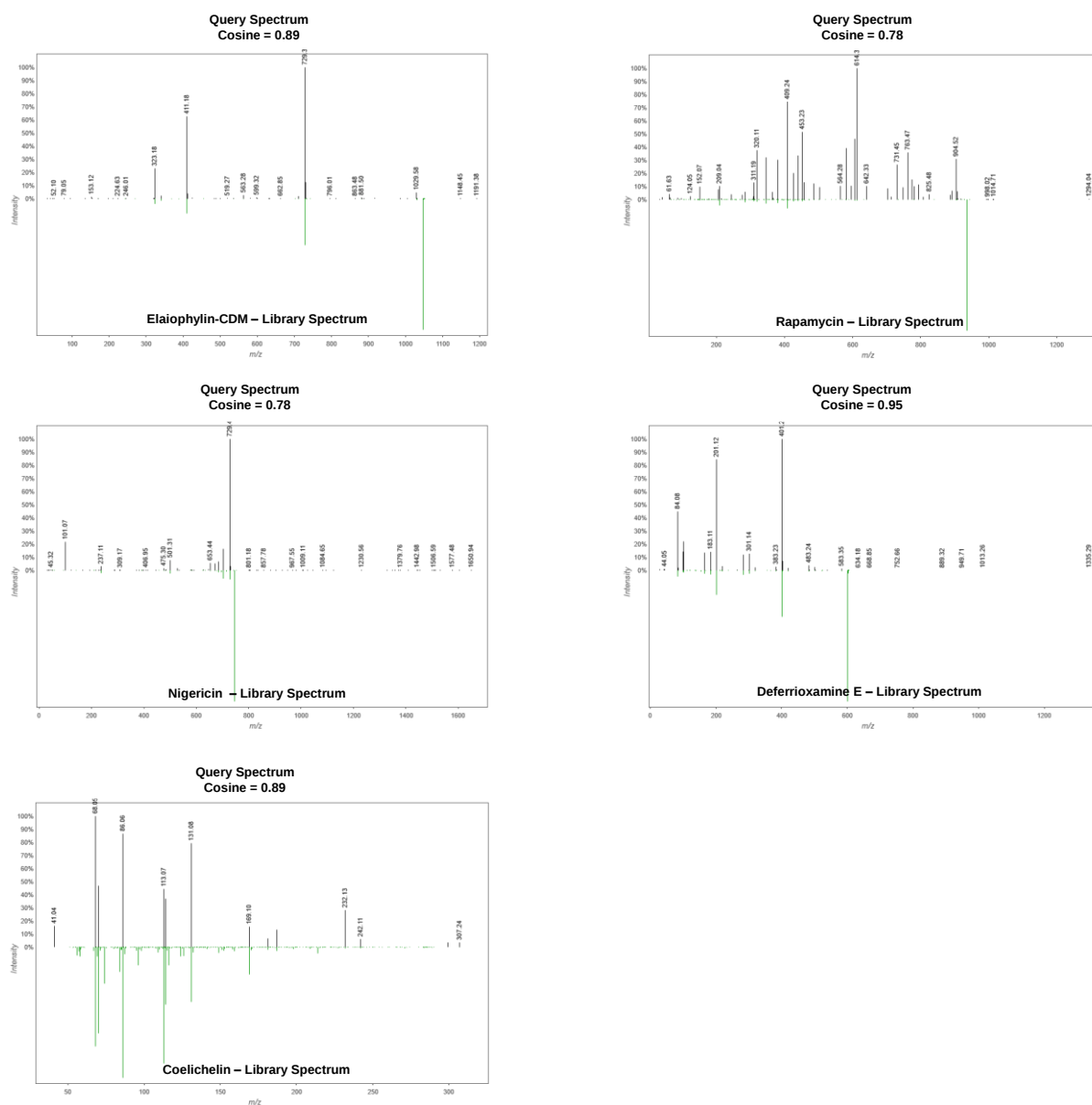


Figure S2. Mirror plots comparing spectra from known metabolites from *S. iranensis* HM 35 to standard spectra deposited in GNPS. In the upper part of the plot (black lines) is represented the MS spectra of the candidate feature and in the lower part (green lines) is the MS spectra of the standard compound. Mirror plots have been generated using <https://metabolomics-usi.ucsd.edu/>.

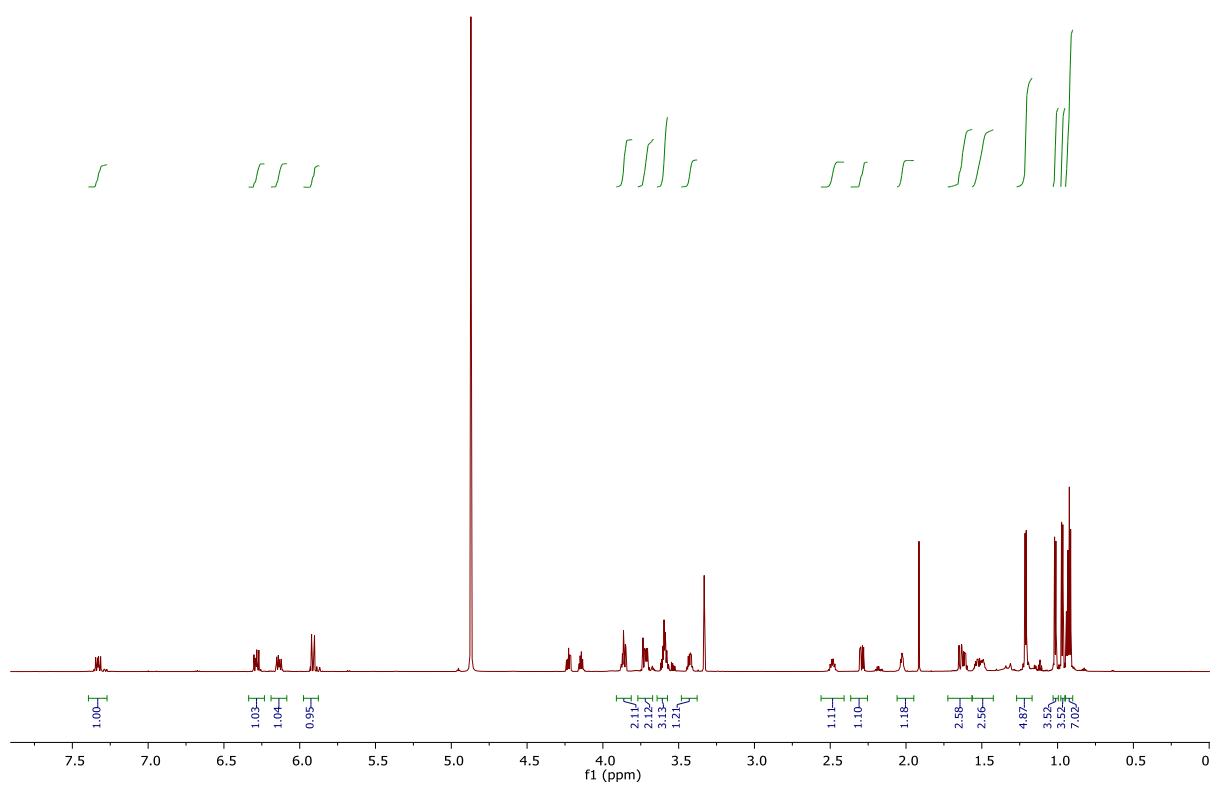


Figure S3. ^1H NMR spectrum of **1**.

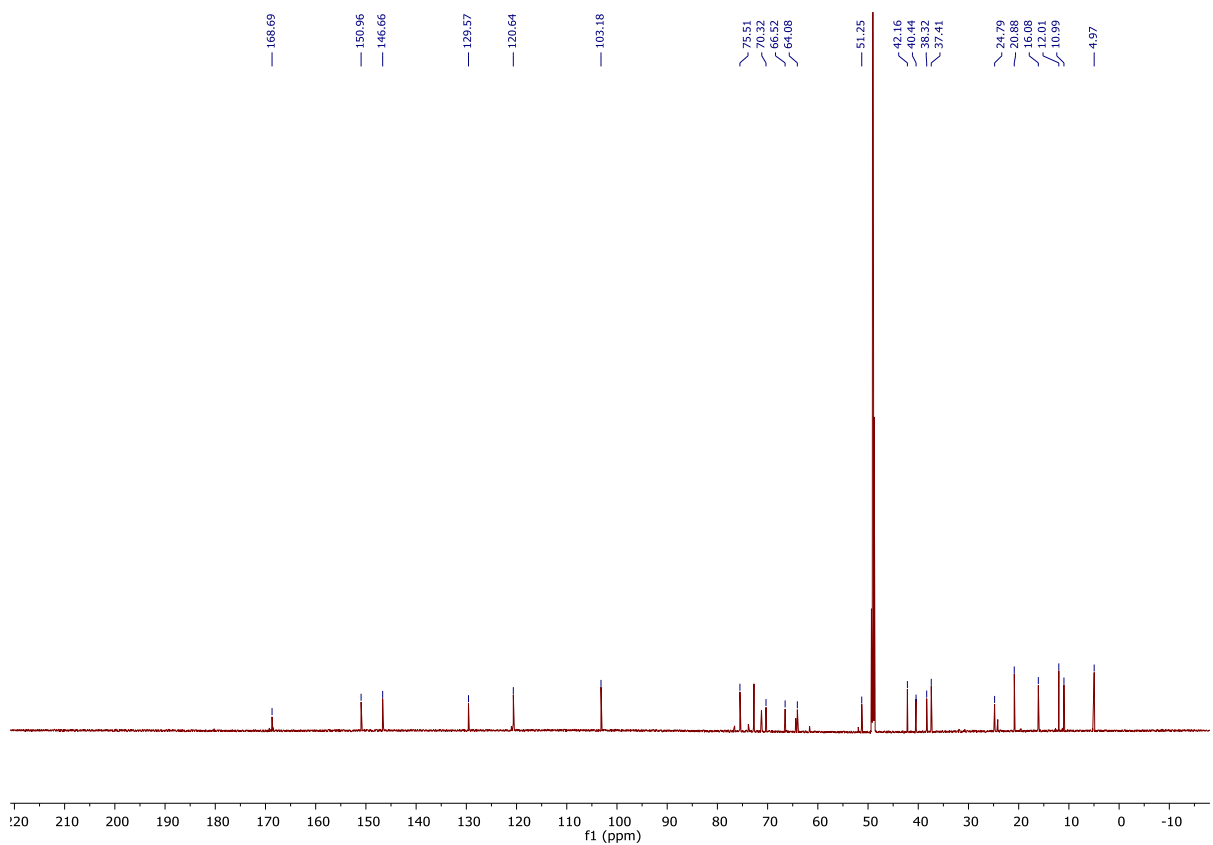


Figure S4. ^{13}C NMR spectrum of **1**.

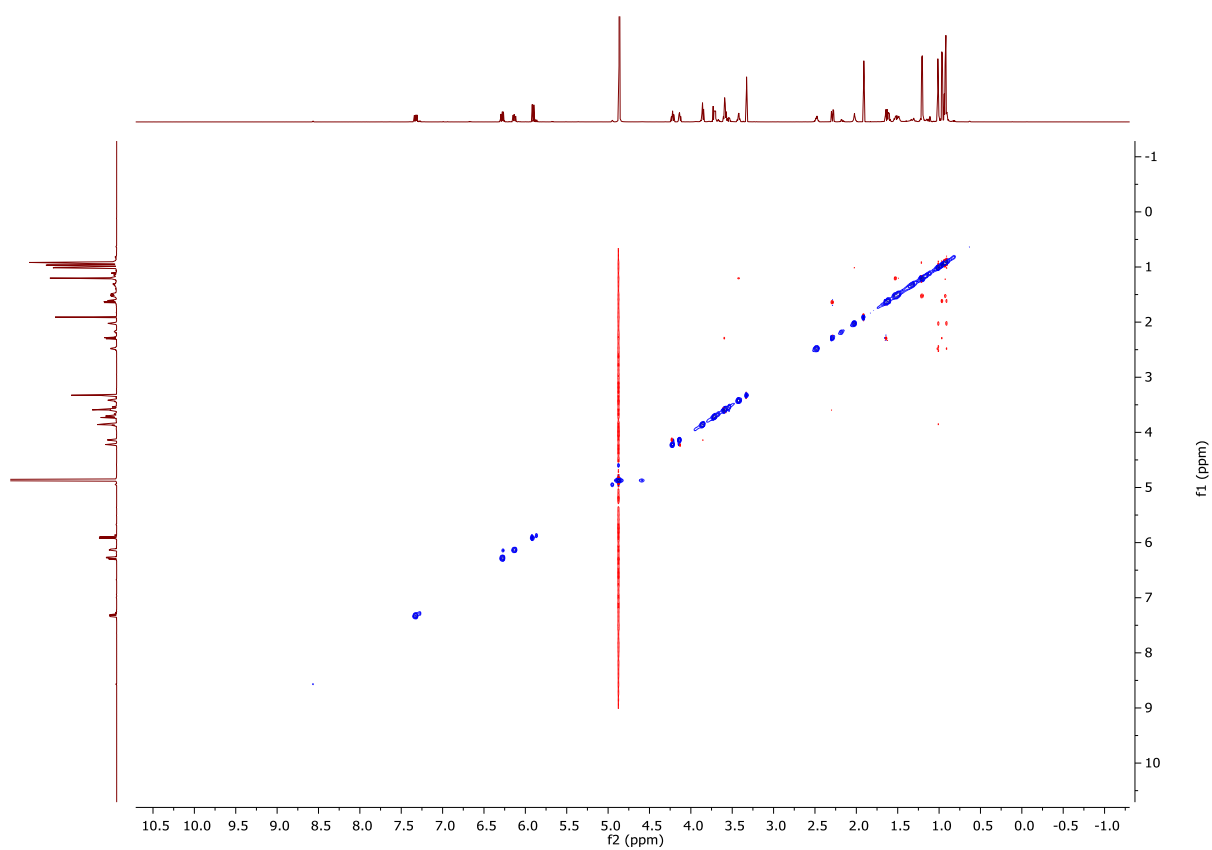


Figure S5. NOESY spectrum of **1**.

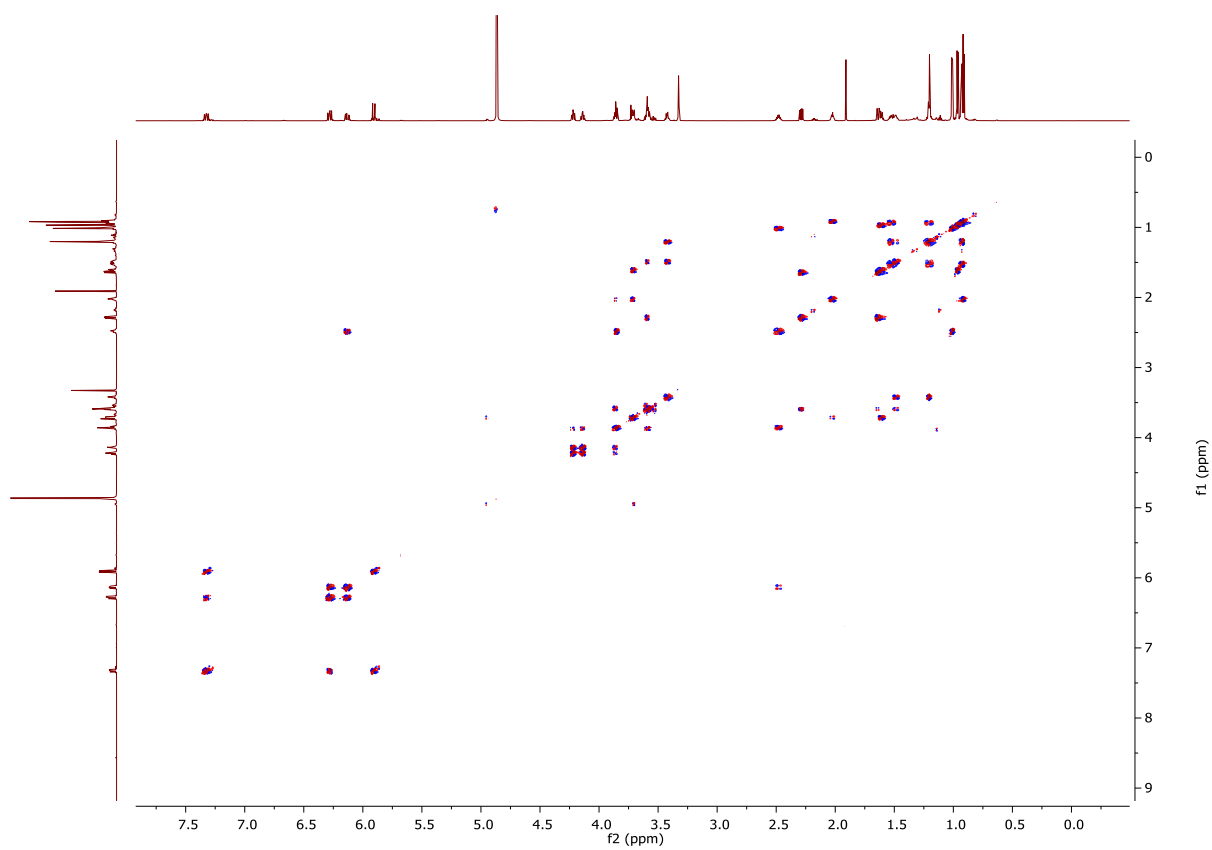


Figure S6. COSY spectrum of **1**.

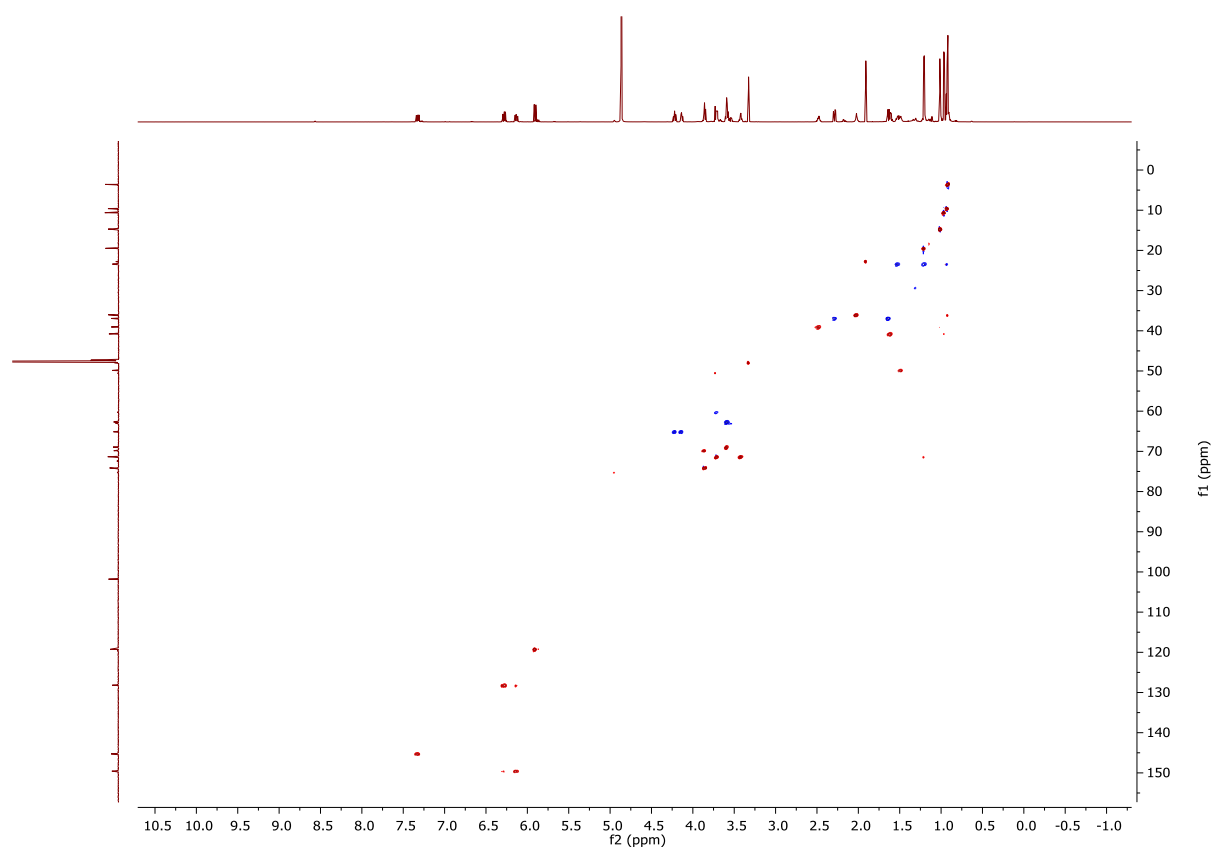


Figure S7. HSQC spectrum of **1**.

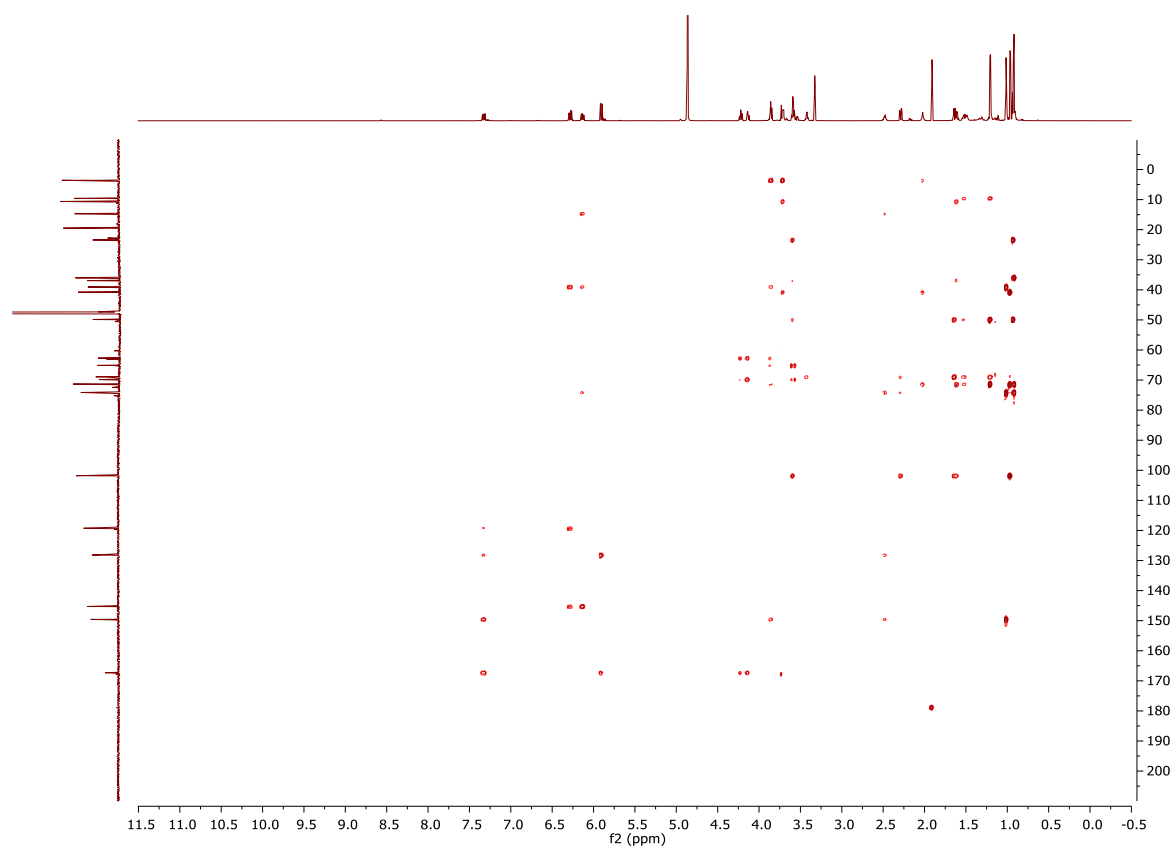


Figure S8. HMBC spectrum of **1**.

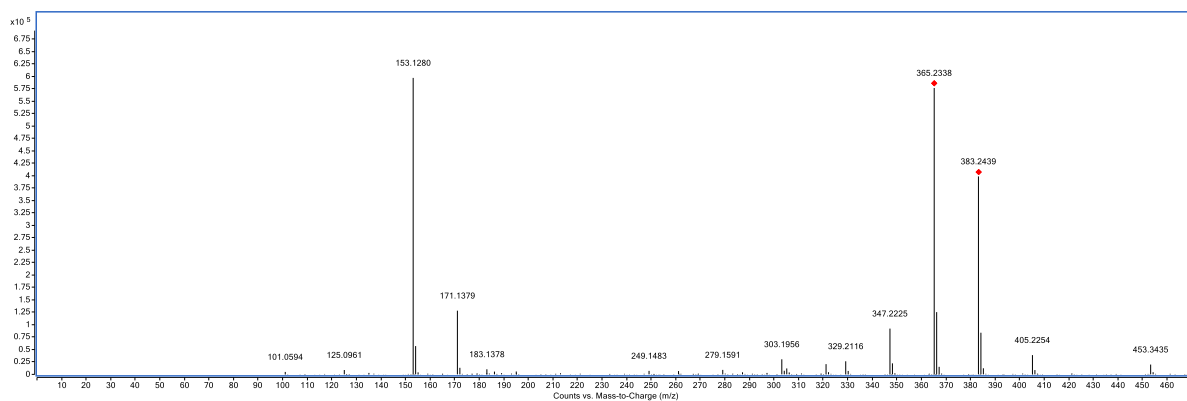


Figure S9. Mass spectrum of **1**. Its formula of $C_{21}H_{34}O_6$ was deduced by m/z 383.2439 $[M+H]^+$ (calculated for 383.2428, Δ 2.84 ppm).

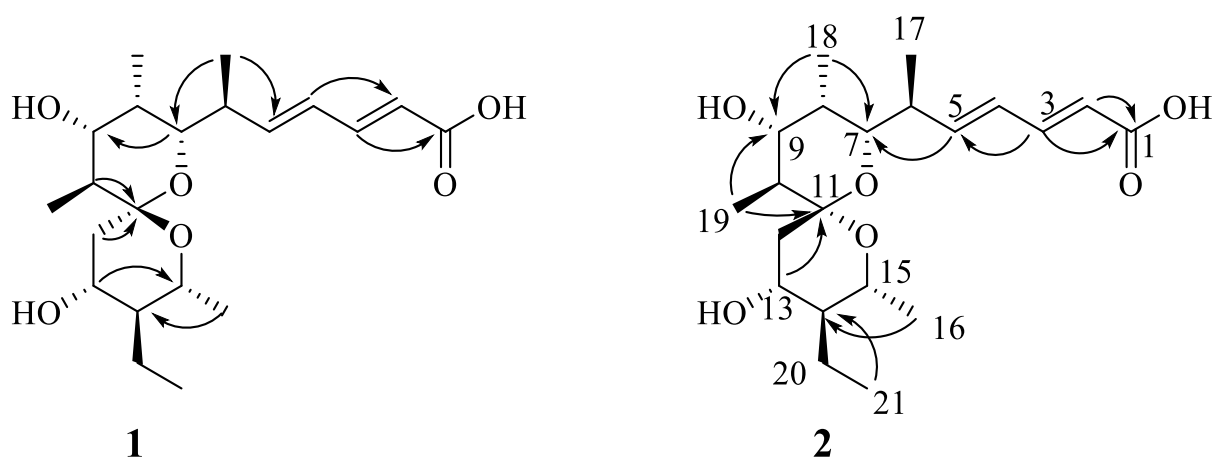


Figure S10. Selected HMBC correlations for **1** and **2**.

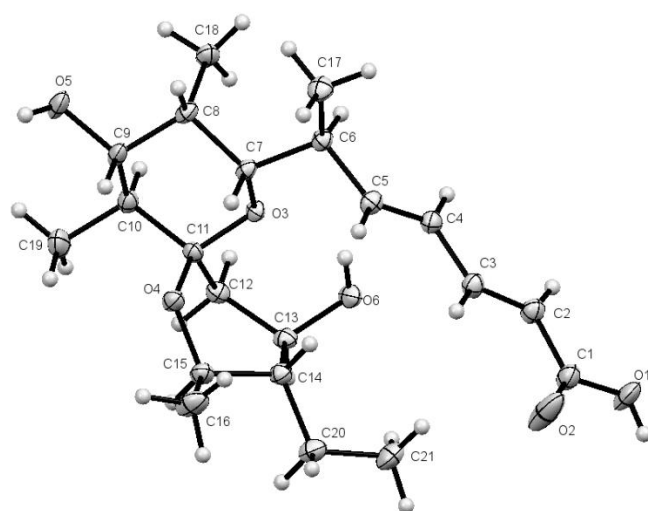


Figure S11. Crystal structure of **1**. ORTEP diagram showing the atom-numbering scheme and solid-state conformation of **1**.

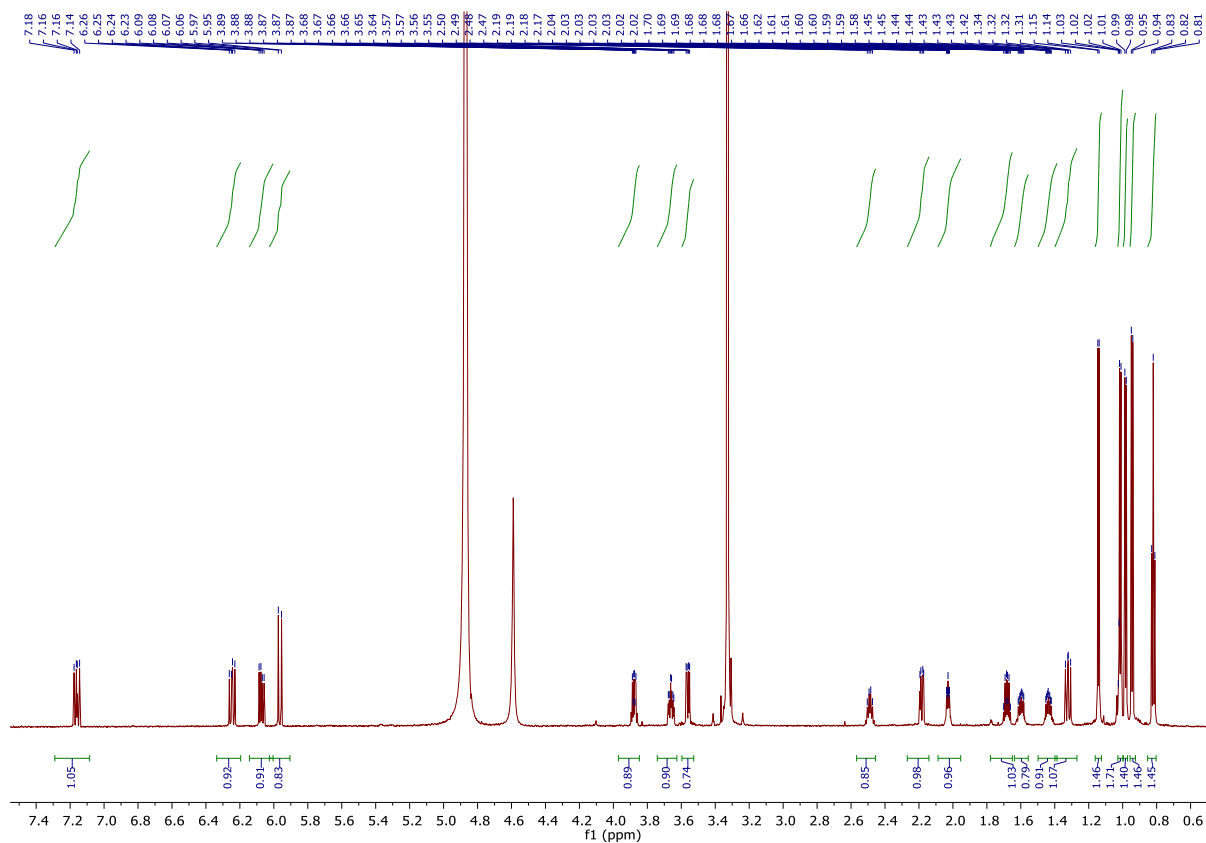


Figure S12. ^1H NMR spectrum of **2**.

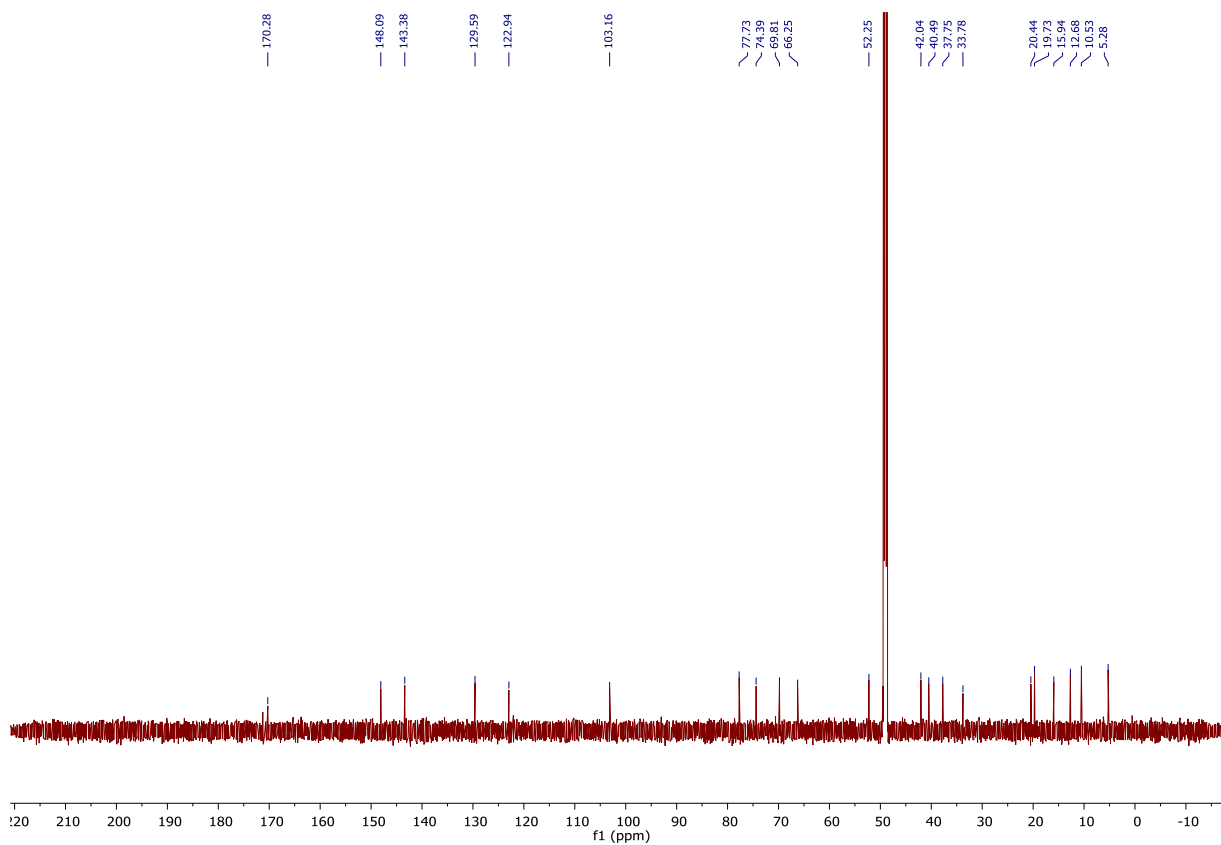


Figure S13. ^{13}C NMR spectrum of **2**.

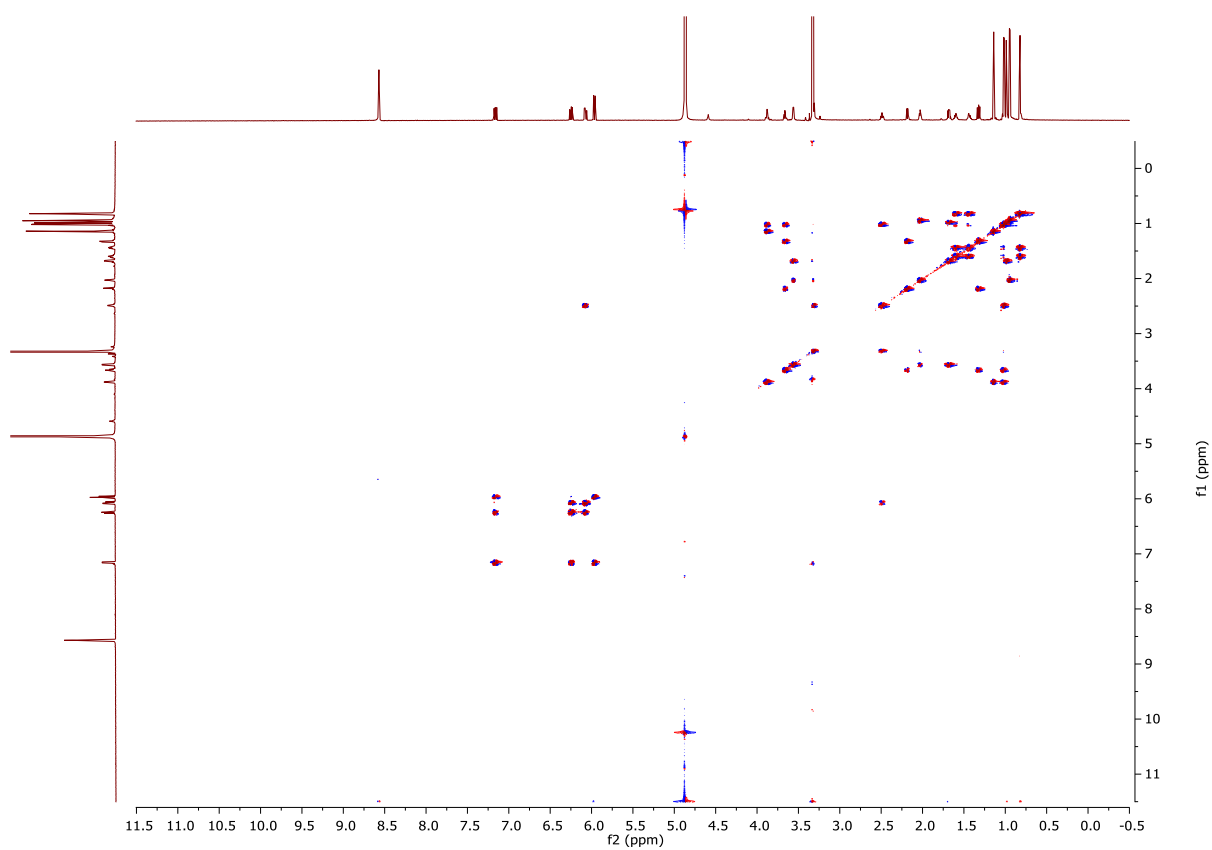


Figure S14. COSY spectrum of **2**.

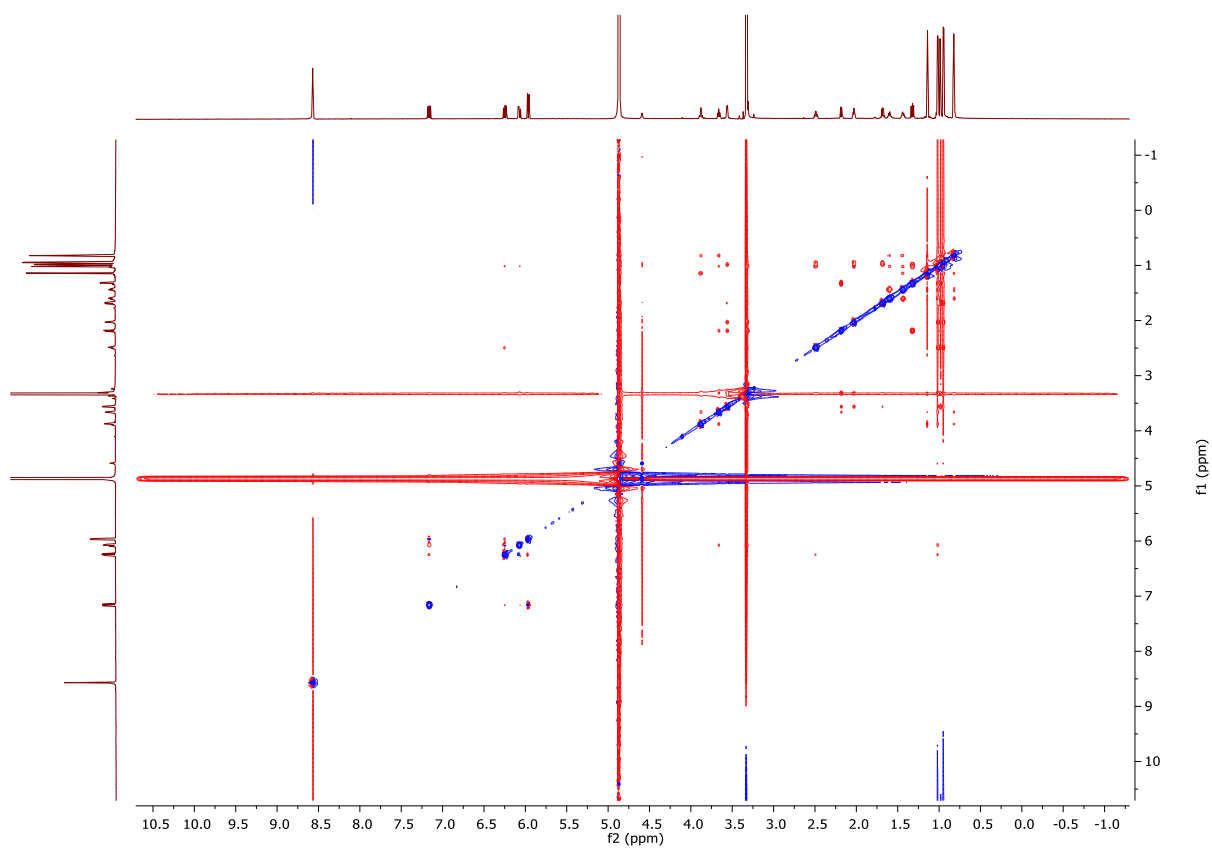


Figure S15. NOESY spectrum of **2**.

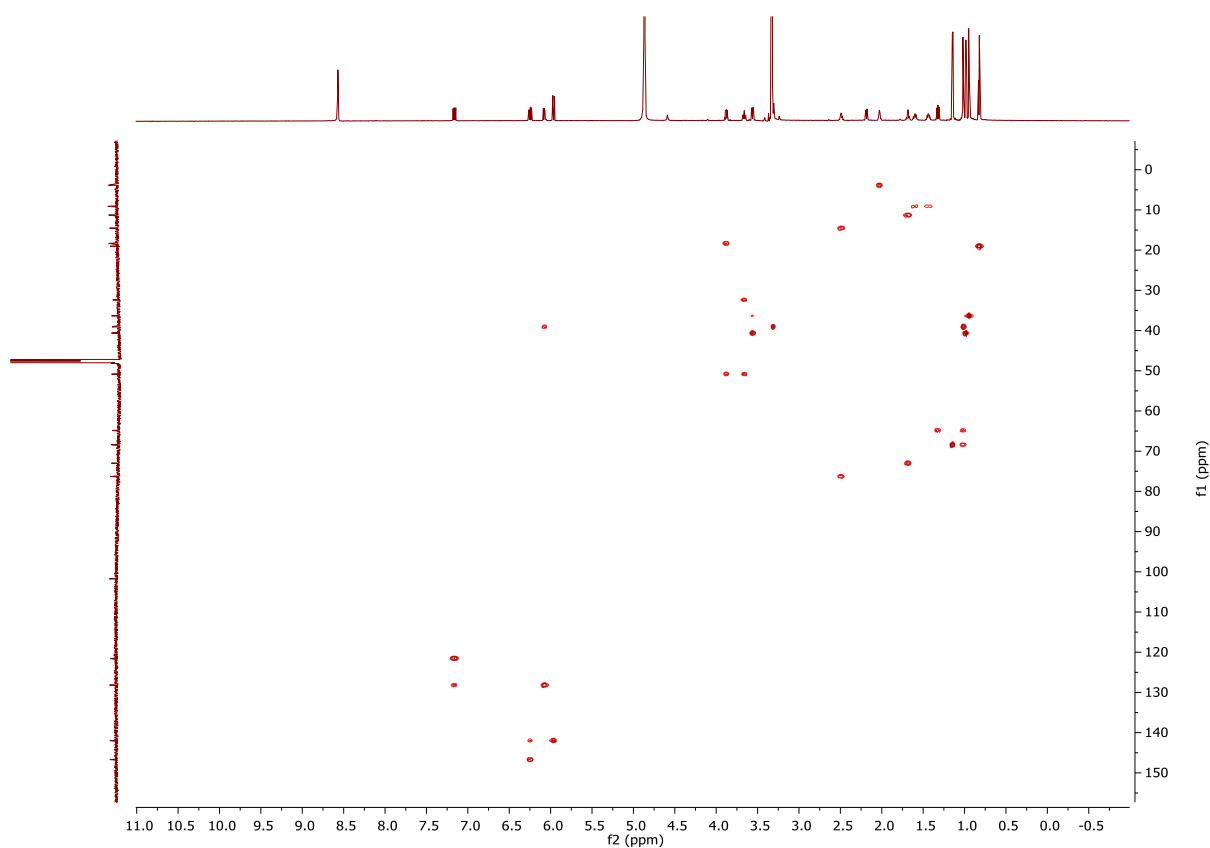


Figure S16. H2BC spectrum of compound **2**.

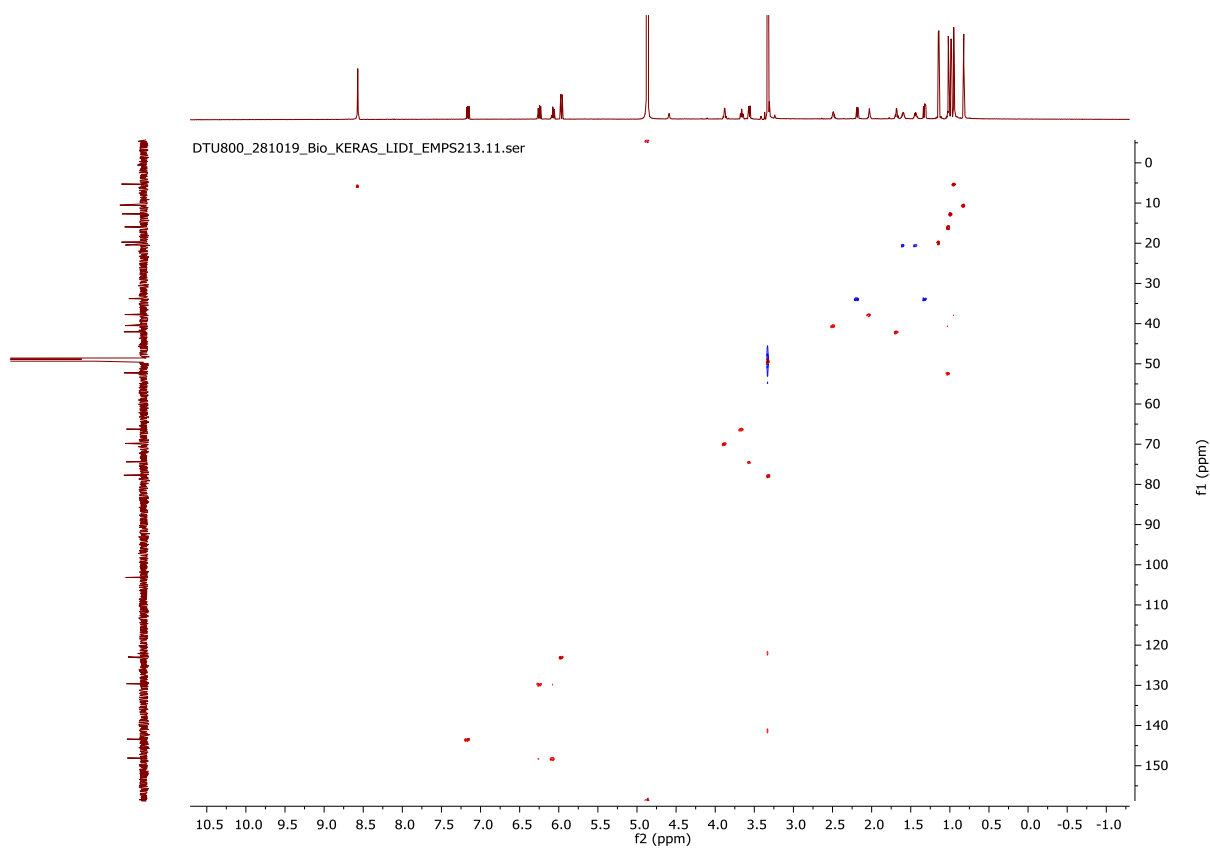


Figure S17. HSQC spectrum of **2**.

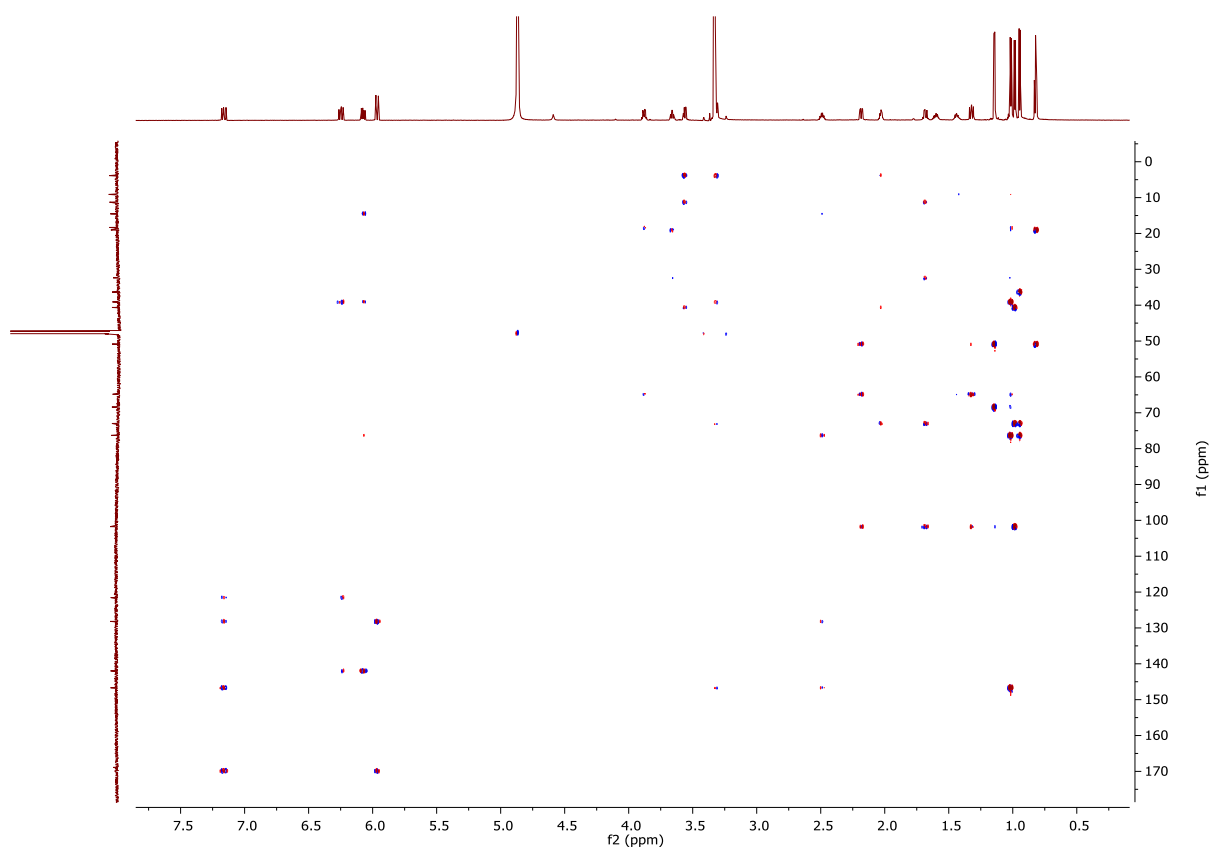


Figure S18. HMBC spectrum of **2**.

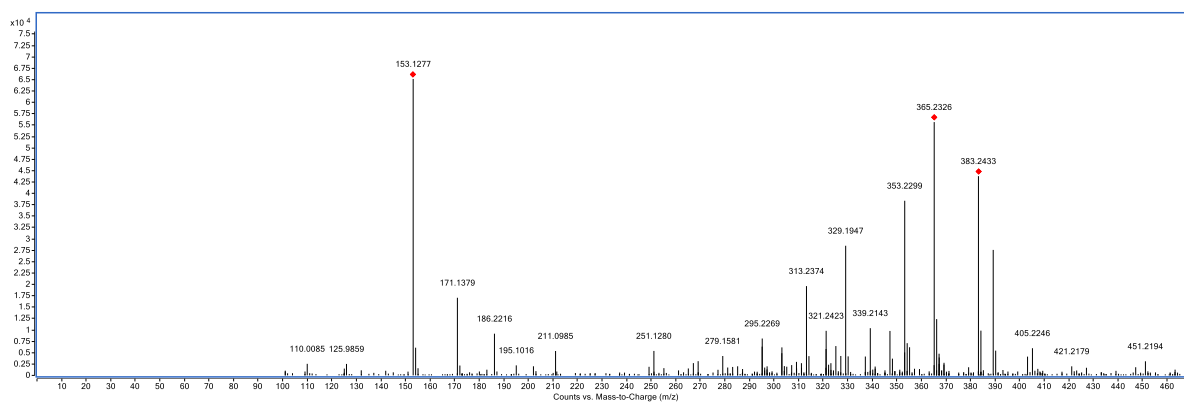


Figure S19. Mass spectrum of **2**. Its formula of $C_{21}H_{34}O_6$ was deduced by m/z 383.2433 $[M+H]^+$ (calculated for 383.2428, Δ 1.27 ppm).



Figure S20. Pteridic acid H and ABA at 10 nM help barley against drought stress (mediated by 20% PEG-6000). PH, pure pteridic acid H treatment; ABA, abscisic acid treatment; Mock, control in drought stress; Ctrl, control in non-stress growth condition.

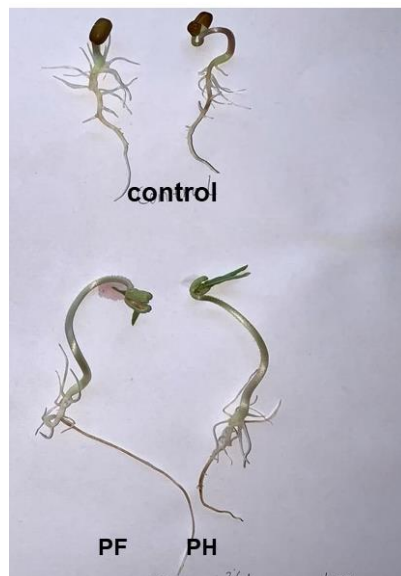


Figure S21. Effect of pteridic acid H and F on Mung bean root growth under normal condition. PF, pure pteridic acid F; PH, pure pteridic acid H.

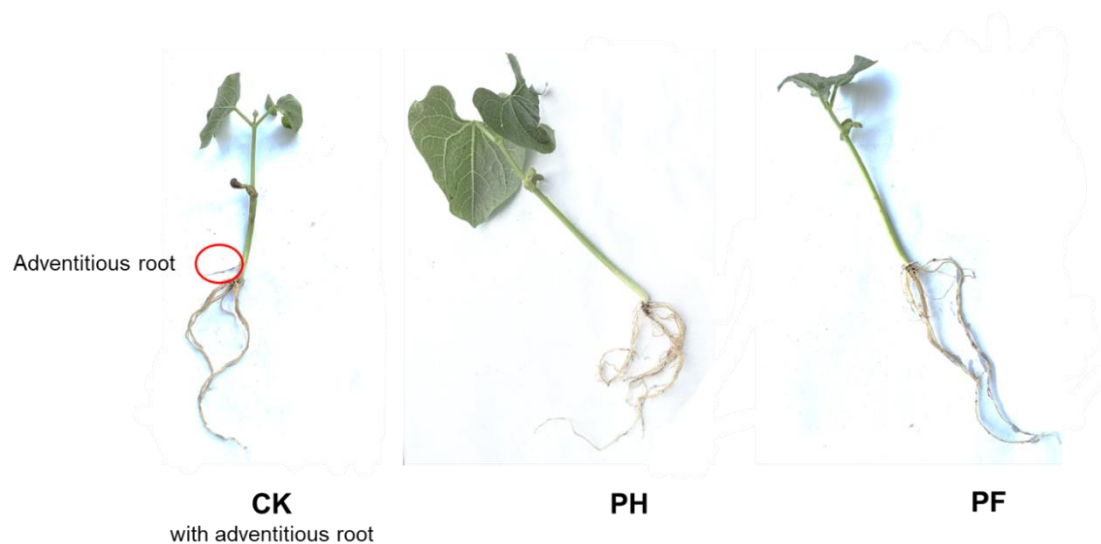


Figure S22. Kidney beans growth experiment with pure pteridic acids at 1 ng/mL. $N = 10$ plants per treatment group. Abbreviation: *CK*, control; *PH*, treatment of pure pteridic acid H; *PF*, treatment of pure pteridic acid F.



Figure S23. Pteridic acid H and ABA at 1 ng/mL help Mung beans against heavy metal stress. Abbreviation: *PH*, treatment of pure pteridic acid H; *ABA*, treatment of abscisic acid.

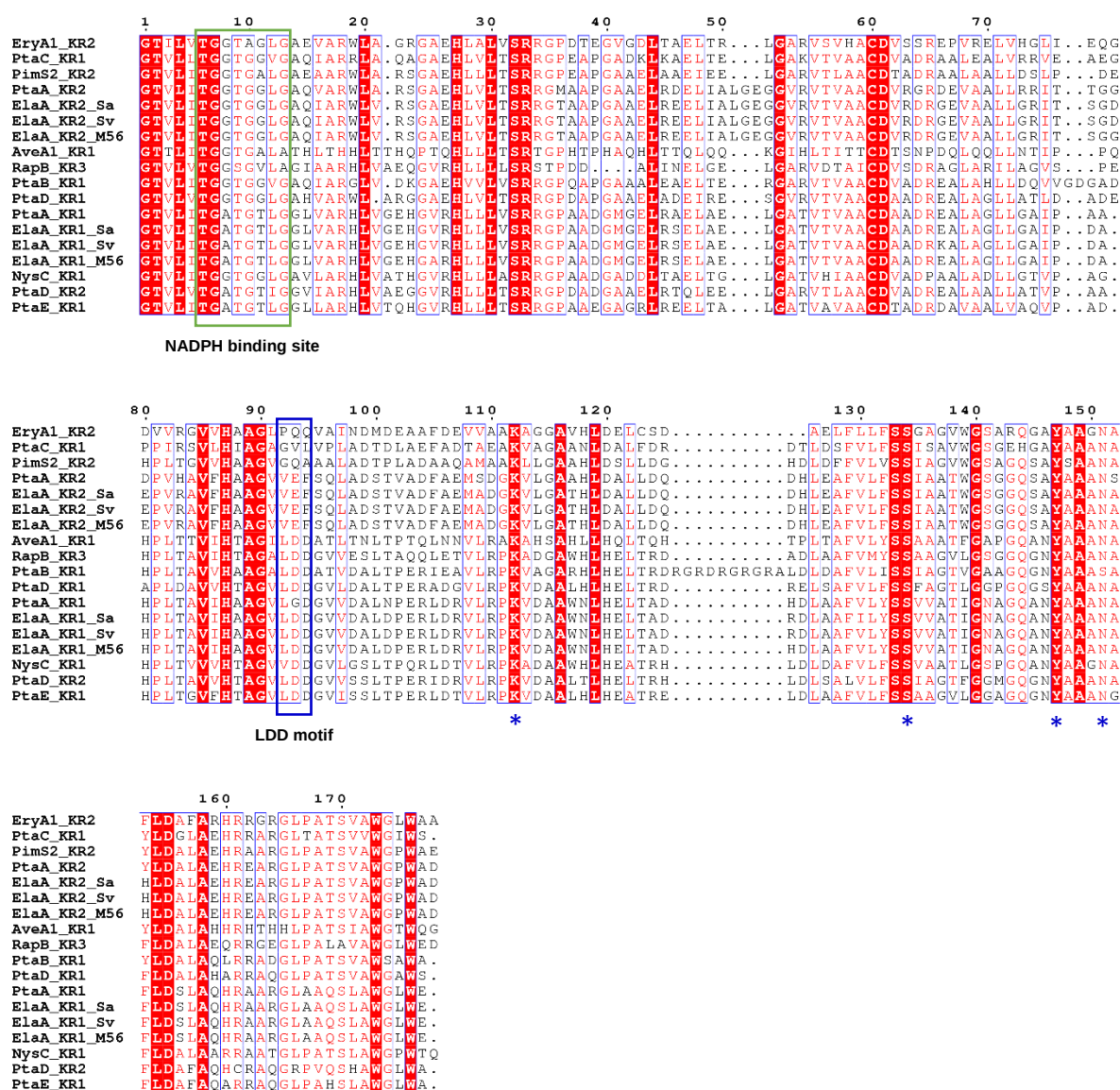


Figure S24. Multiple sequence alignment of KR domains. Green box indicates NADPH binding site and blue box indicates the LDD motif. Abbreviation: Ery, erythromycin; Pta, pteridic acids; Pim, pimarinic; Ave, avermectin; Rap, rapamycin; Nys, nystatin.

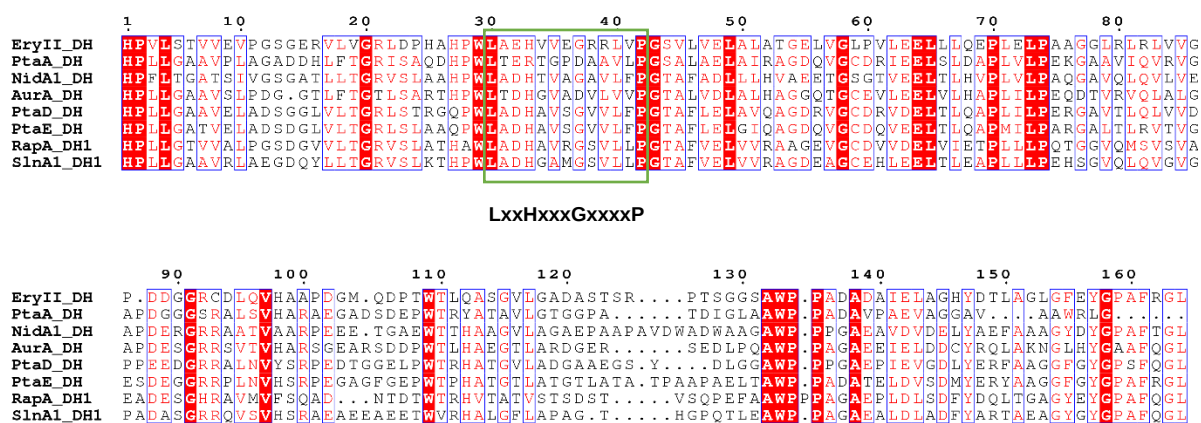


Figure S25. Multiple sequence alignment of DH domains. The green box indicates the conserved LxxHxxxGxxxxP motif. Abbreviation: Ery, erythromycin; Pta, pteridic acids; Nid, niddamycin; Aur, aureothin; Rap, rapamycin; Sln, salinomycin.

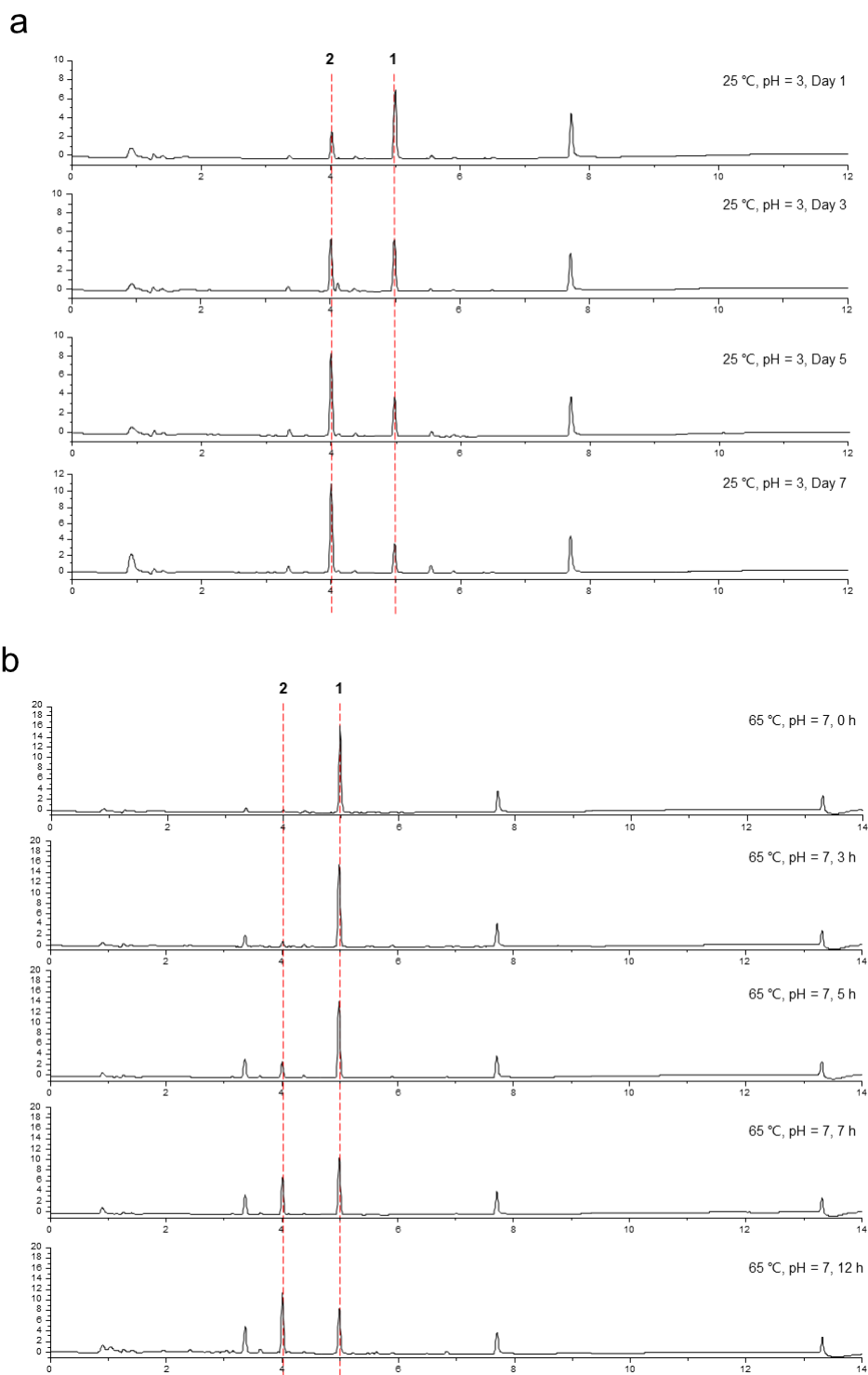


Figure S26. Stability test of pteridic acids. Abbreviation: **1**, pteridic acid H; **2**, pteridic acid F. **1** was tested unstable in pH 3 buffer solution at 25 °C. **a**, **1** was transformed to **2** fast, after 3 days the contents of them were as equal. The transformation rate is approximately 12.5%, 25%, 37.5%, 50% in 1 d, 3 d, 5 d and 7 d in pH 3 buffer solution at 25 °C. **b**, **1** was unstable in water with 65 °C and transformed to **2** fast, after 12 hours, the content of **1** exceeded **2**. The transformation rate is approximately 7 %, 33 % and 47 % in 3 h, 7 h and 12 h, 65 °C.

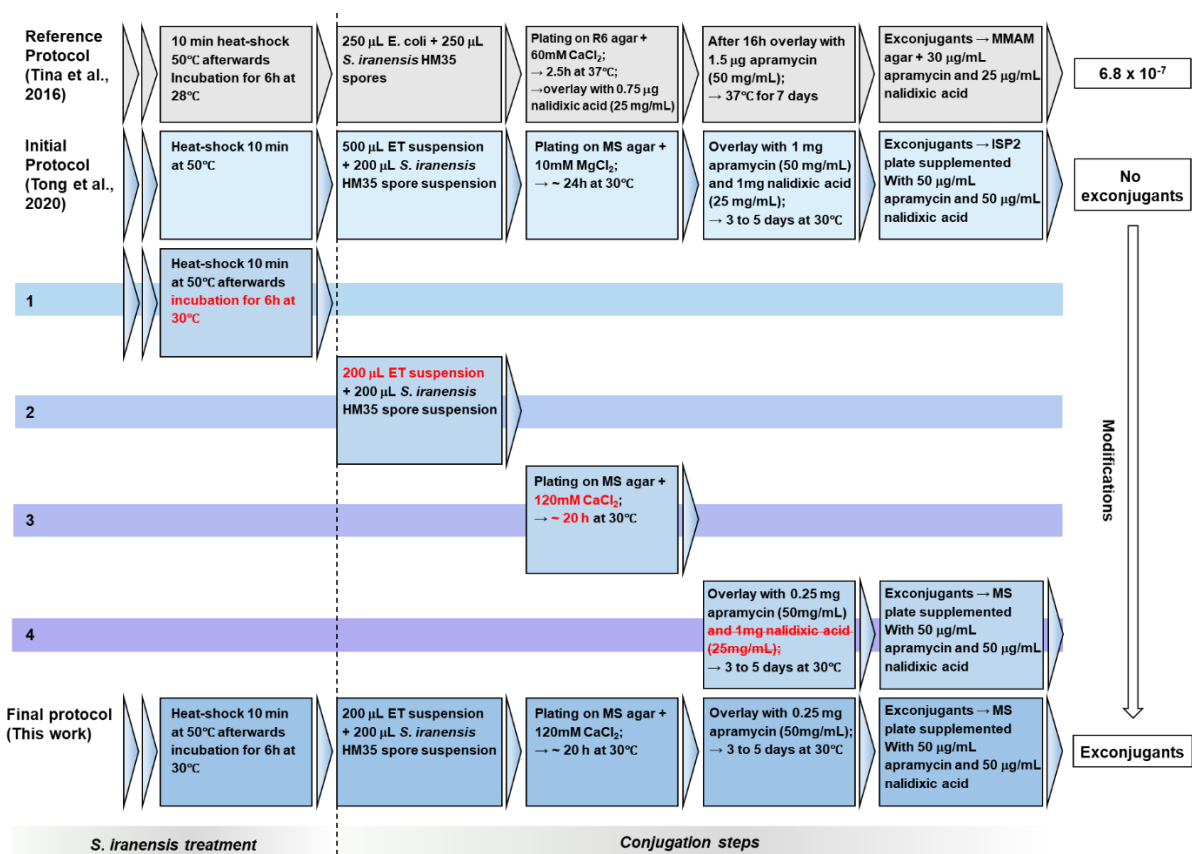


Figure S27. The schematic of optimized genetic manipulation in *S. iranensis* HM 35 by using CRISPR-cBEST system.

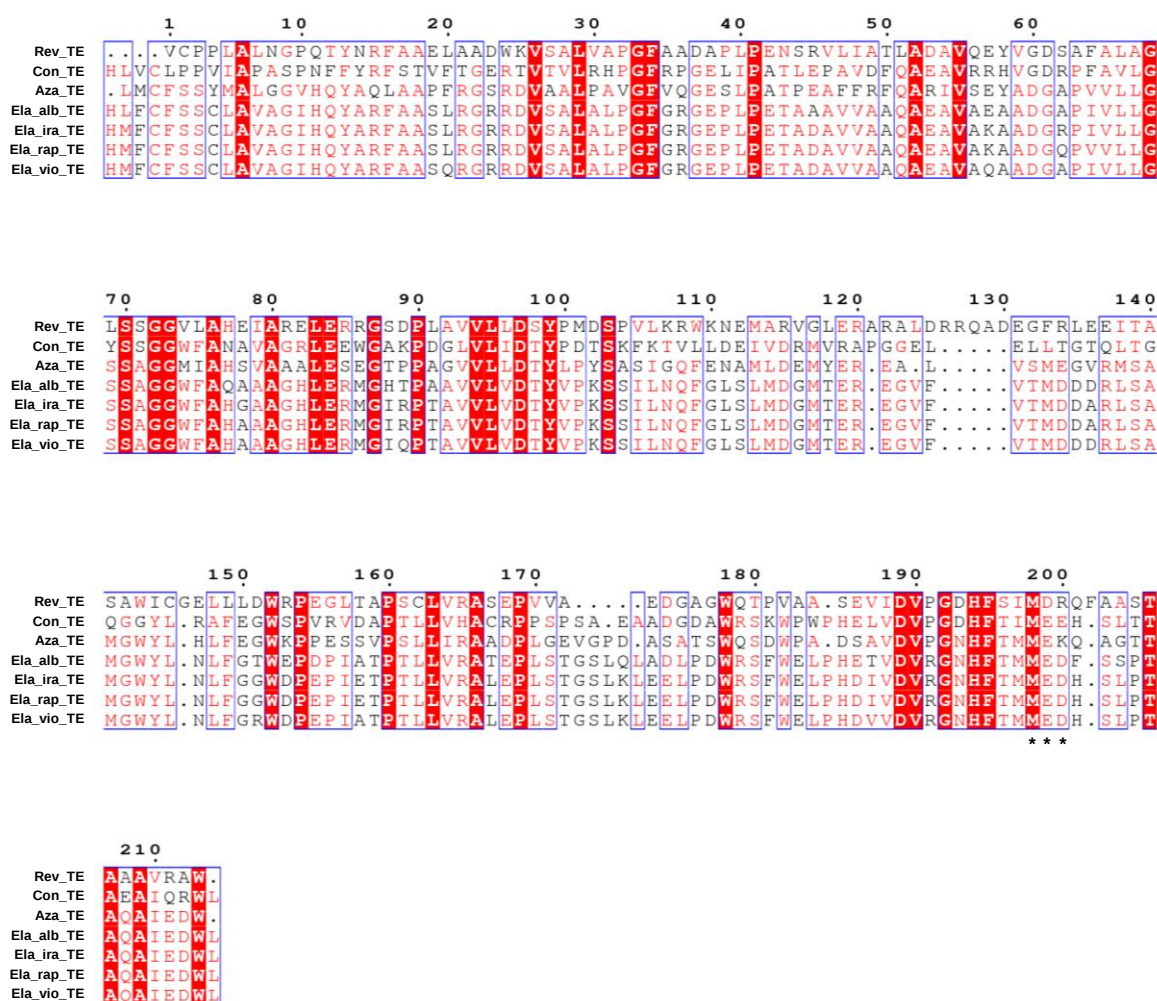


Figure S28. Multiple sequence alignment of TE domains. The three amino acids marked with an asterisk were mutated in this study. Abbreviation: Rev_TE, the TE domain in reveromycin A biosynthesis from *Streptomyces* sp. SN-593; Con_TE, the TE domain in conglobatin biosynthesis from *Streptomyces conglobatus*; Aza_TE, the TE domain in azalomycin F3a biosynthesis from *Streptomyces* sp. 211726; Ela_alb_TE, the TE domain in elaiophylin biosynthesis from *S. albus* DSM 41398; Ela_ira_TE, the TE domain in elaiophylin biosynthesis from *S. iranensis* HM 35; Ela_rap_TE, the TE domain in elaiophylin biosynthesis from *S. rapamycinicus* NRRL 5491; Ela_vio_TE, the TE domain in elaiophylin biosynthesis from *S. violaceusniger* Tu 4113.

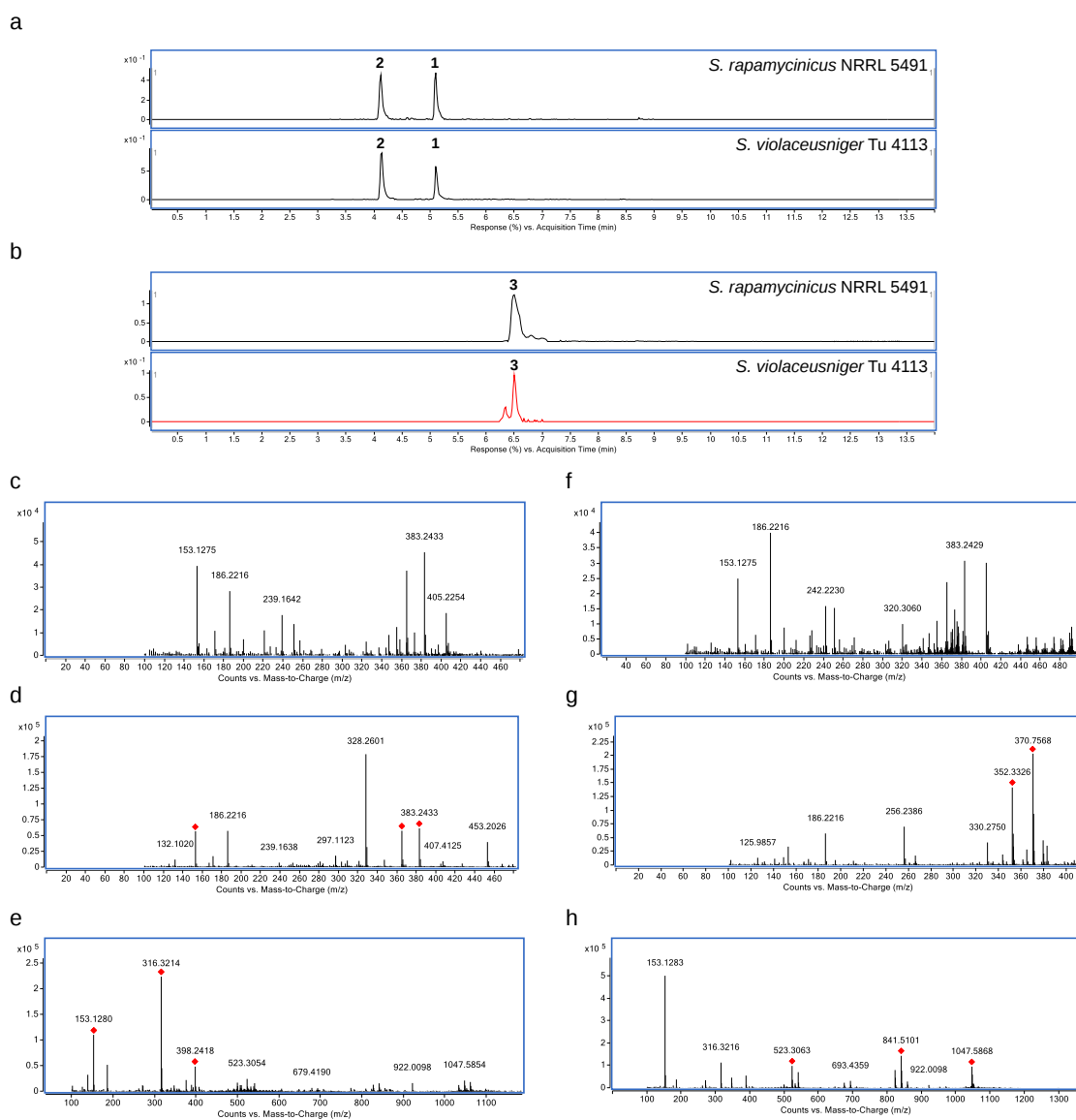


Figure S29. The HPLC and mass spectrum analysis of metabolites in *S. rapamycinicus* NRRL 5491 and *S. violaceusniger* Tu 4113. **a**, the Extracted Ion Chromatography (EIC) of m/z 383.2428 $[M+H]^+$ in wild-type *S. rapamycinicus* NRRL 5491 and *S. violaceusniger* Tu 4113. The single m/z expansion for the chromatogram is ± 5 ppm. **b**, the Extracted Ion Chromatography (EIC) of m/z 1047.5863 $[M+Na]^+$ in wild-type *S. rapamycinicus* NRRL 5491 and *S. violaceusniger* Tu 4113. The single m/z expansion for the chromatogram is ± 5 ppm. **c**, the LC-ESI-MS spectrum of 1 in wild-type *S. violaceusniger* Tu 4113. **d**, the LC-ESI-MS spectrum of 1 in wild-type *S. rapamycinicus* NRRL 5491. **e**, the LC-ESI-MS spectrum of 2 in wild-type *S. violaceusniger* Tu 4113. **f**, the LC-ESI-MS spectrum of 2 in wild-type *S. rapamycinicus* NRRL 5491. **g**, the LC-ESI-MS spectrum of 3 in wild-type *S. violaceusniger* Tu 4113. **h**, the LC-ESI-MS spectrum of 3 in wild-type *S. rapamycinicus* NRRL 5491.

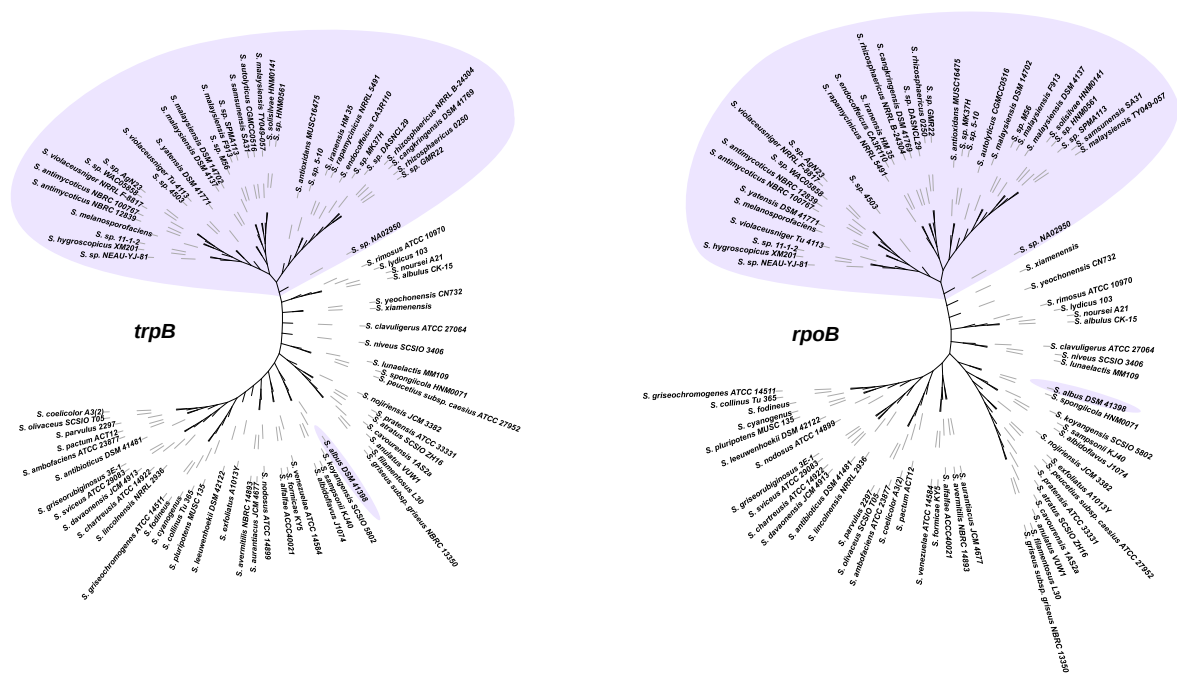


Figure S30. The phylogenetic analysis of potential pteridic acids *Streptomyces* producers. The high-resolution *Streptomyces* sp. housekeeping genes: *trpB* (tryptophan synthase subunit beta) and *rpoB* (RNA polymerase subunit beta) were used in this analysis.

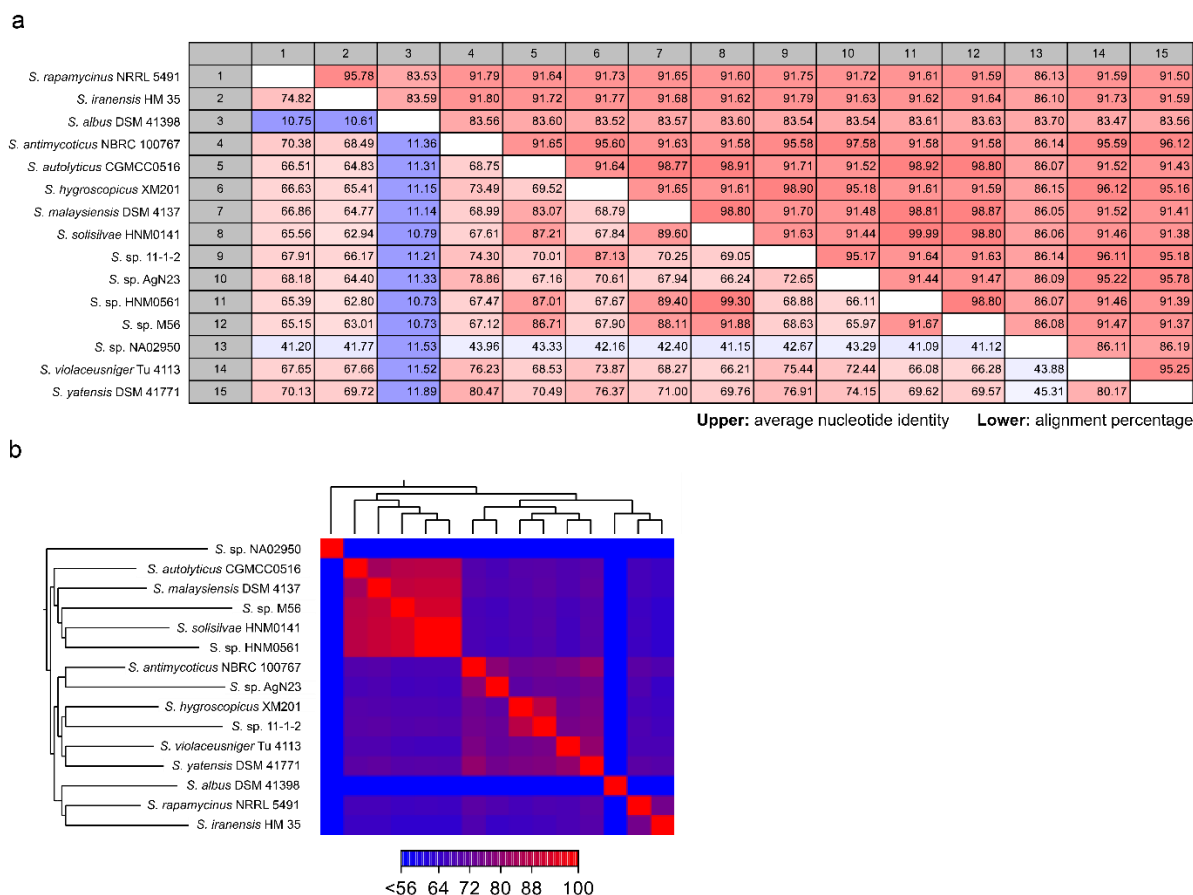


Figure S31. Genome similarity analysis based on the alignment of 15 sequenced *pta*-containing *Streptomyces* genomes. **a**, AP (alignment percentage) and ANI (average nucleotide identity) values between genomes. The AP value represents the average percentage of aligned genomic regions between two genomes, whereas the ANI value stands for the percentage of exactly matching nucleotides for these aligned regions. **b**, Heat map showing genetic similarity between genomes based on AP values.

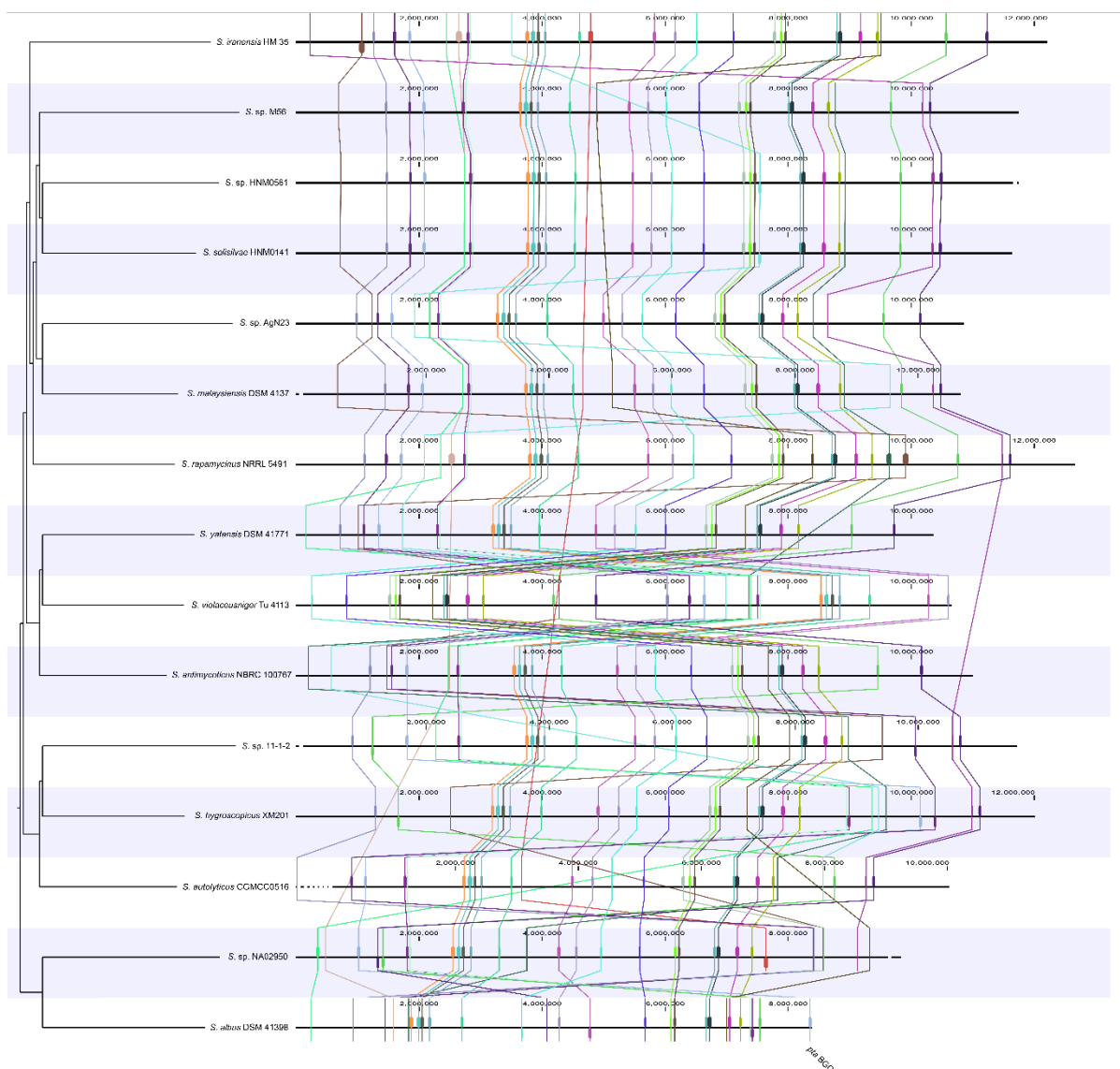


Figure S32. The genome synteny analysis of selected 15 *pta*-containing *Streptomyces* strains. The colored squares each represent local alignment synteny blocks that are linked together among different genomes by lines with the same colors. The pteridic acids (*pta*) BGC is located in the end of *S. albus* DSM 41398 chromosome.

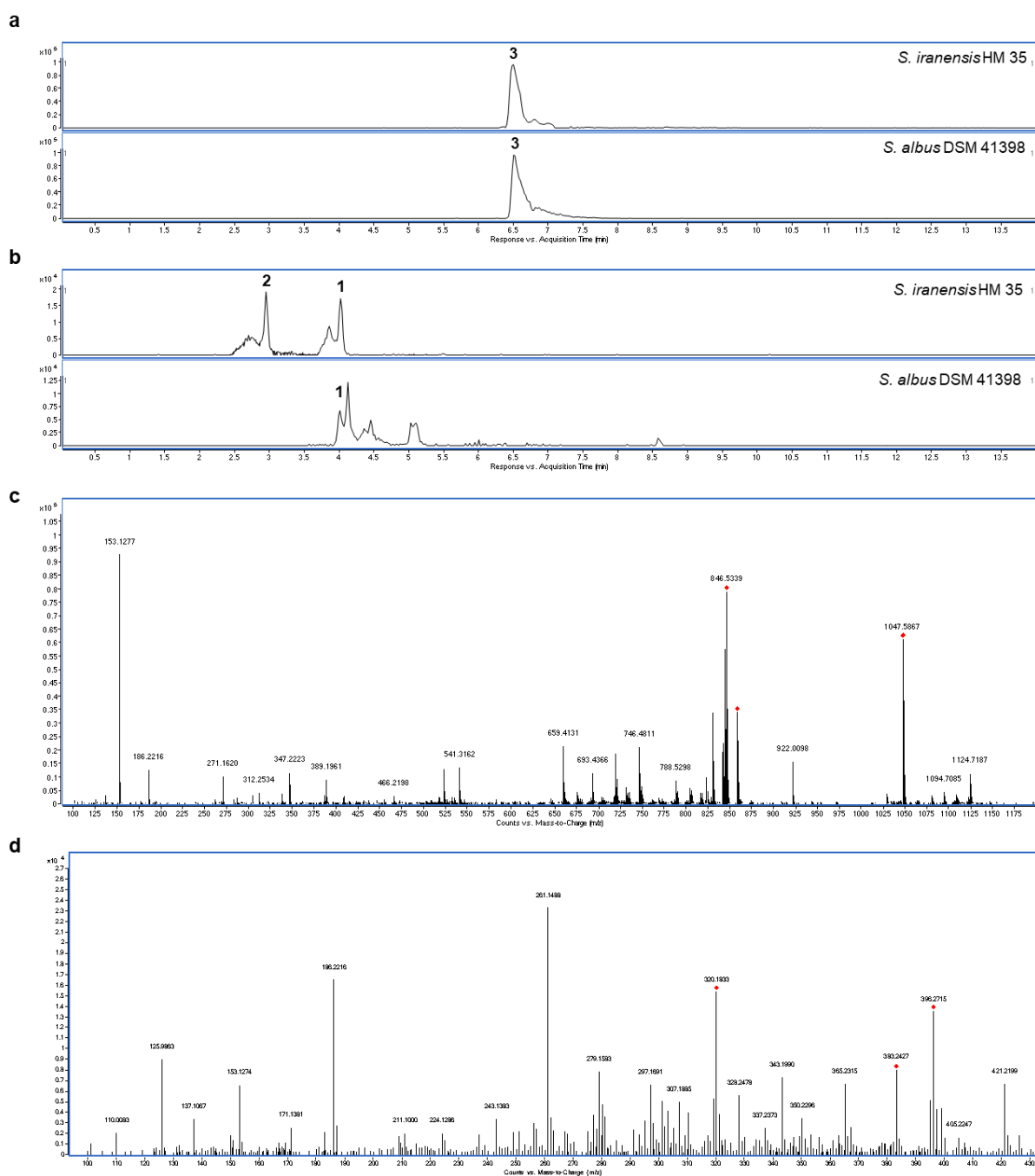


Figure S33. The HPLC and mass spectrum analysis of metabolites in *S. albus* DSM 41398. **a**, the Extracted Ion Chromatography (EIC) of m/z 383.2428 $[M+H]^+$ in wild-type *S. iranensis* HM 35 and wild-type *S. albus* DSM 41398. The single m/z expansion for the chromatogram is ± 5 ppm. **b**, the Extracted Ion Chromatography (EIC) of m/z 1047.5863 $[M+Na]^+$ in wild-type *S. iranensis* HM 35 and wild-type *S. albus* DSM 41398. The single m/z expansion for the chromatogram is ± 5 ppm. **c**, the LC-ESI-MS spectrum of **3** in wild-type *S. albus* DSM 41398. **d**, the LC-ESI-MS spectrum of **1** in wild-type *S. albus* DSM 41398.

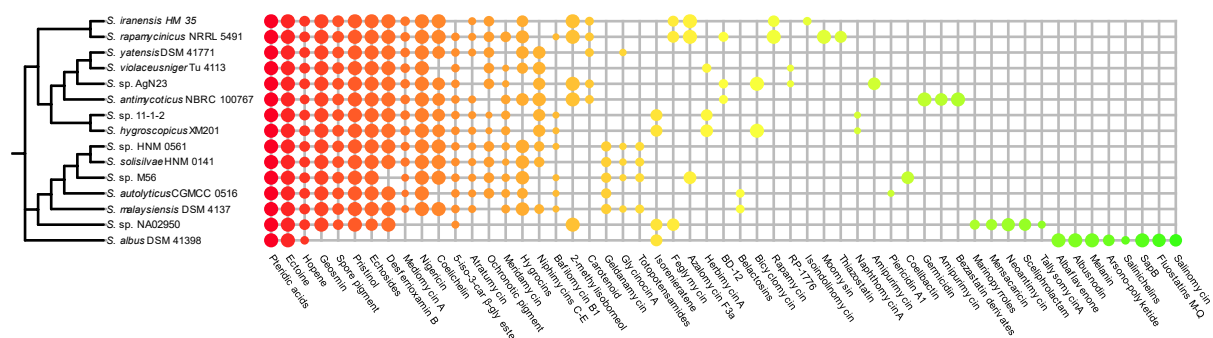


Figure S34. The secondary metabolites biosynthetic gene clusters profiles of 15 *pta*-containing *Streptomyces* strains with complete genome information. BGCs with a similarity greater than 45% are displayed, and the size of the nodes represents the level of similarity *, 5-isoprenylindole-3-carboxylate β -glycosyl ester.

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