Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

SUPPORTING INFORMATION

Resorculins: hybrid polyketide macrolides from Streptomyces sp. MST-91080

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Supplementary Figures

Figure S1. Fractionation and isolation schematic for MST-91080.

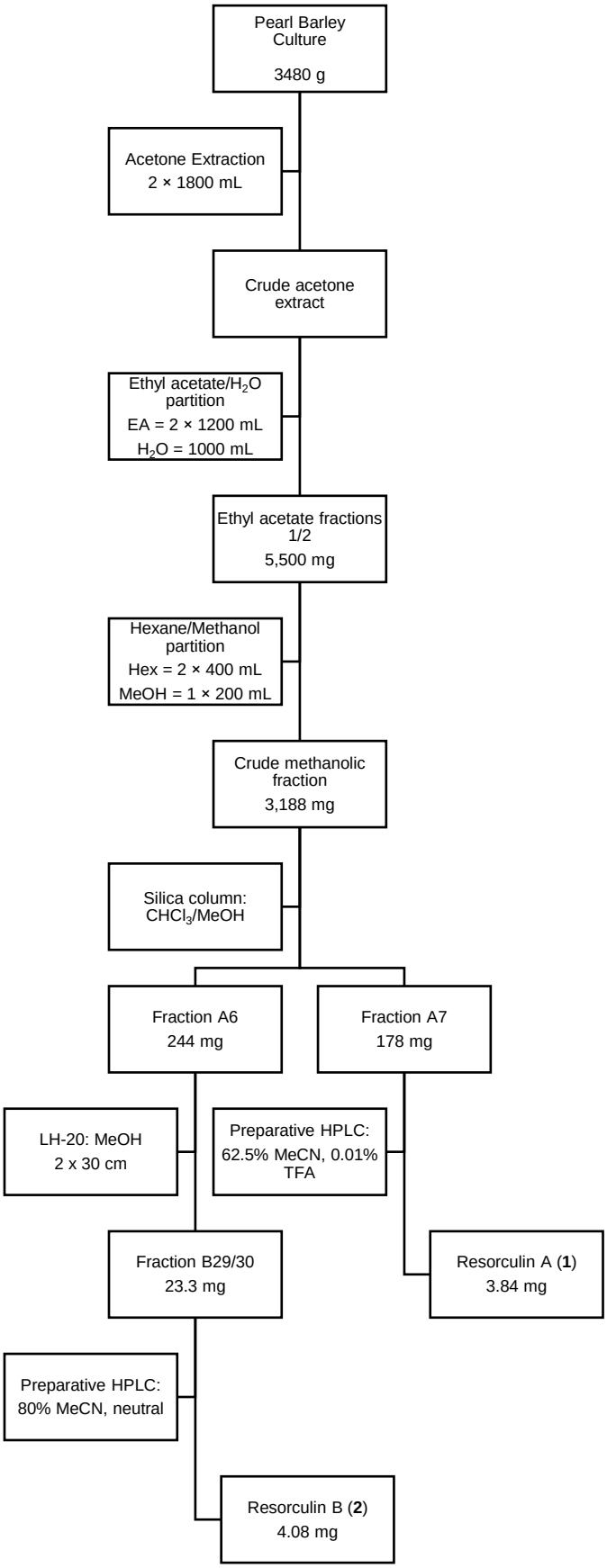
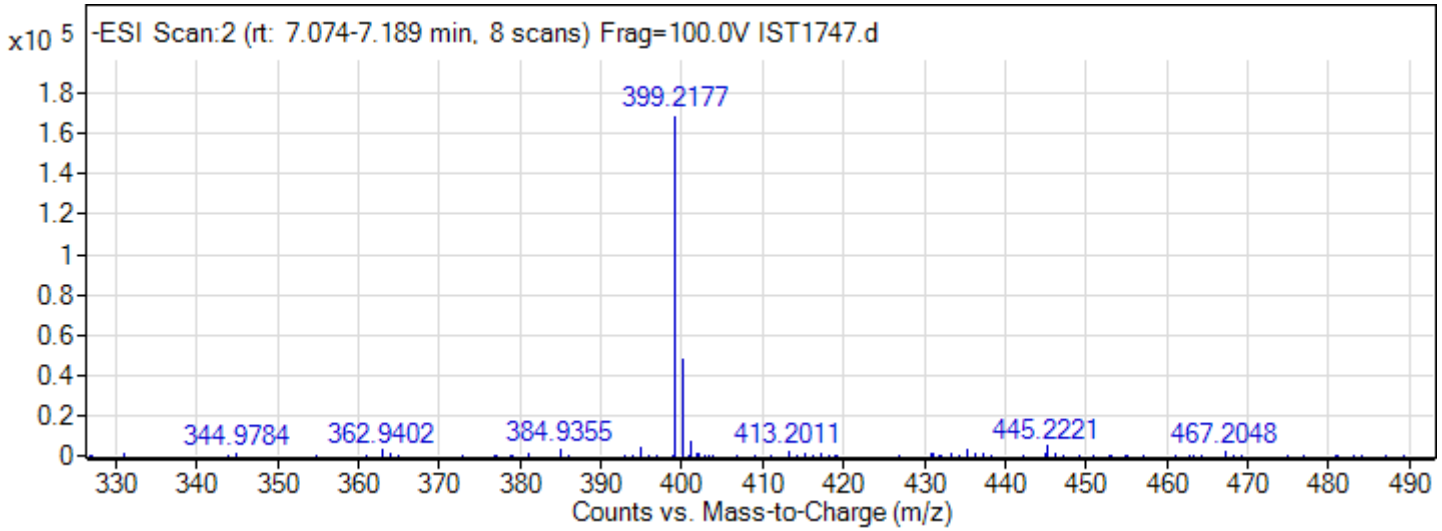


Figure S2. HRESI spectra for resorculin A and resorculin B.

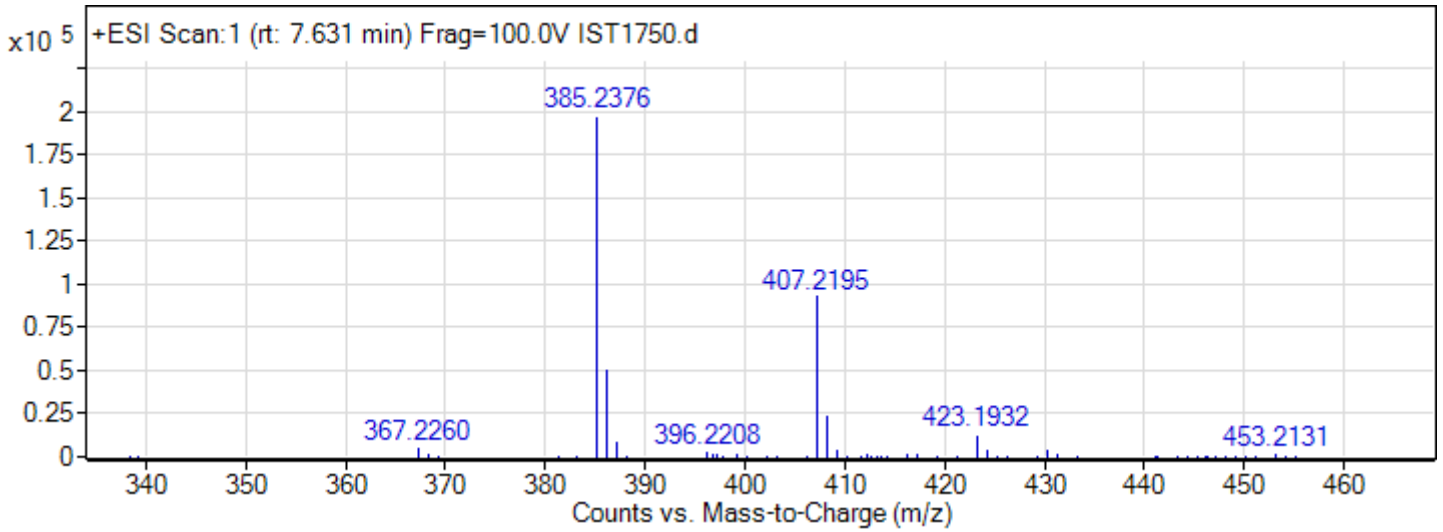
a) HRESI(−)MS spectrum of resorculin A (**1**).



b) Elemental composition report for peak 399.2177.

Formula	Species	m/z	Score	Diff (ppm)	Diff (mDa)
C24 H32 O5	(M-H)-	399.2177	99.39	0.01	0
C23 H26 N7	(M-H)-	399.2177	99.46	-0.38	-0.15
C17 H32 N6 O3 S	(M-H)-	399.2177	86	0.63	0.25
C25 H36 S2	(M-H)-	399.2177	82.8	1.35	0.54
C10 H32 N12 O S2	(M-H)-	399.2177	68.48	1.46	0.59
C16 H36 N2 O7 S	(M-H)-	399.2177	79.28	-2.45	-0.98
C15 H30 N9 O2 S	(M-H)-	399.2177	79.84	-2.98	-1.19
C25 H28 N4 O	(M-H)-	399.2177	95.73	3.16	1.26
C22 H30 N3 O4	(M-H)-	399.2177	93.53	-3.53	-1.41
C11 H30 N9 O7	(M-H)-	399.2177	73.51	3.74	1.5

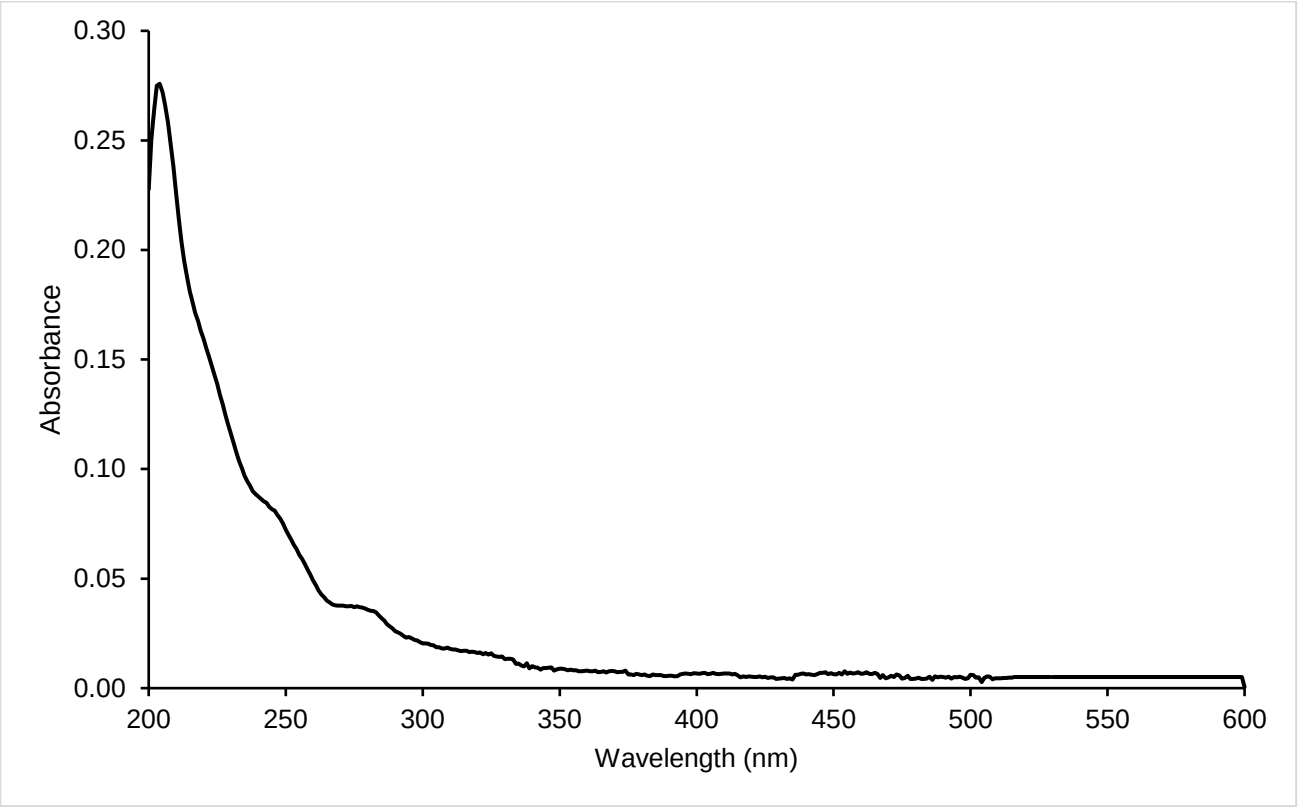
c) HRESI(+)MS spectrum of resorculin B (**2**).



d) Elemental composition report for peak 385.2376.

Formula	Species	m/z	Score	Diff (ppm)	Diff (mDa)
C24 H32 O4	(M+H)+	385.2376	99.51	-0.48	-0.18
C25 H28 N4	(M+H)+	385.2376	95.04	2.81	1.08
C22 H30 N3 O3	(M+H)+	385.2376	93.28	-4.16	-1.6
C17 H32 N6 O2 S	(M+H)+	385.2376	90.38	0.21	0.08
C19 H34 N3 O3 S	(M+H)+	385.2376	85.88	3.94	1.51
C15 H30 N9 O S	(M+H)+	385.2376	83.45	-3.54	-1.36
C27 H30 N O	(M+H)+	385.2376	82.58	6.47	2.49
C16 H36 N2 O6 S	(M+H)+	385.2376	82.43	-3.02	-1.16
C20 H28 N6 O2	(M+H)+	385.2376	79.83	-7.85	-3.02
C11 H30 N9 O6	(M+H)+	385.2376	79.13	3.45	1.33

Figure S3: UV-vis spectra of resorculin A (**1**) and resoculin B (**2**).
a) UV-vis spectrum of resorculin A (**1**) in MeCN



b) UV-vis spectrum of resorculin B (**2**) in MeCN

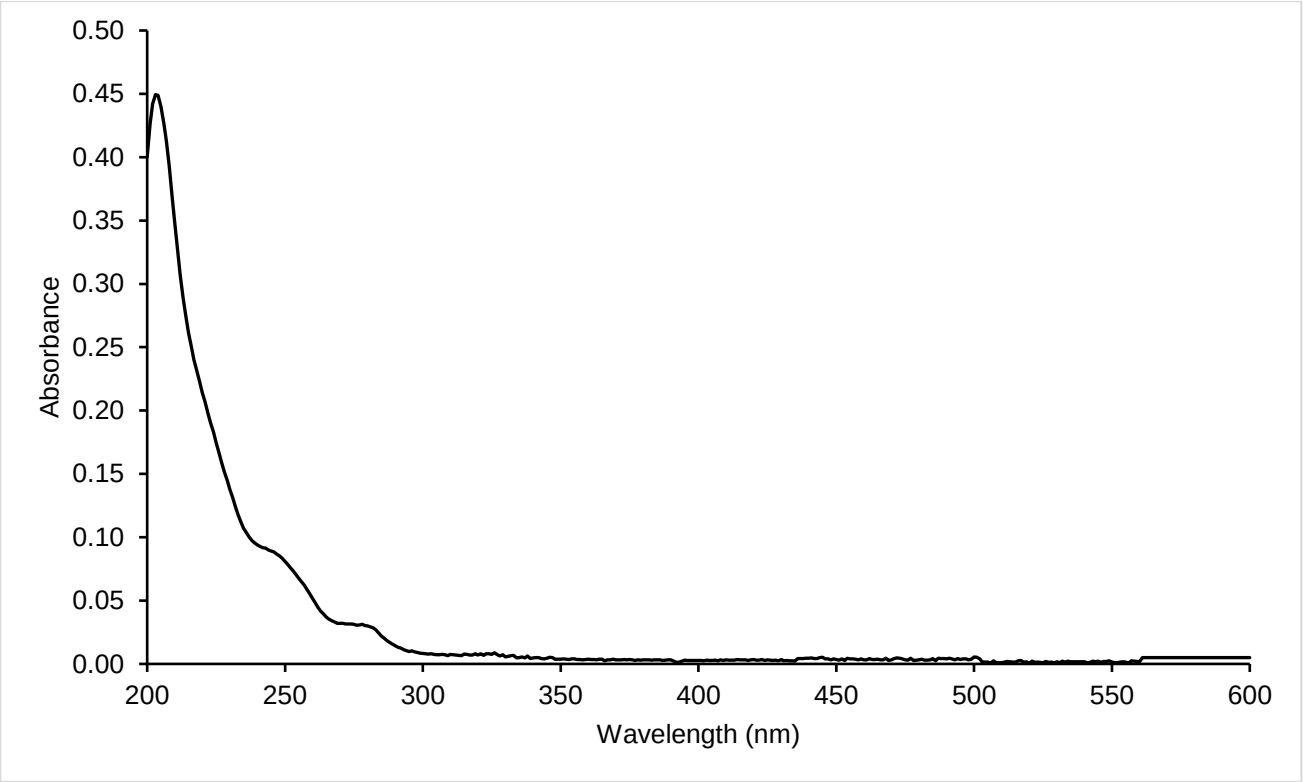


Figure S4. ^{1}H NMR spectrum (600 MHz, DMSO-*d6*) of resorculin A (**1**).

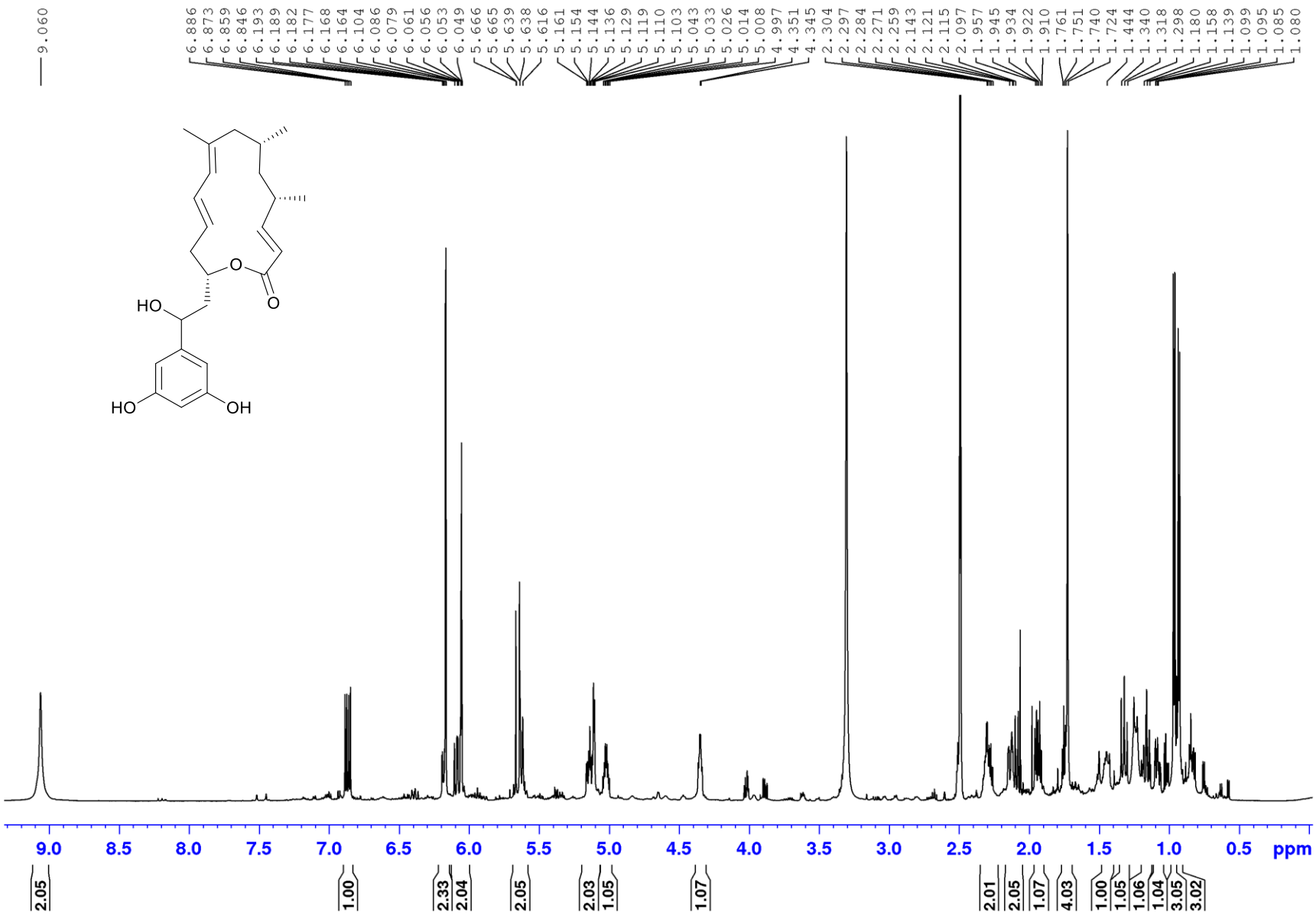


Figure S5. ^{13}C NMR spectrum (150 MHz, DMSO-*d6*) of resorculin A (**1**).

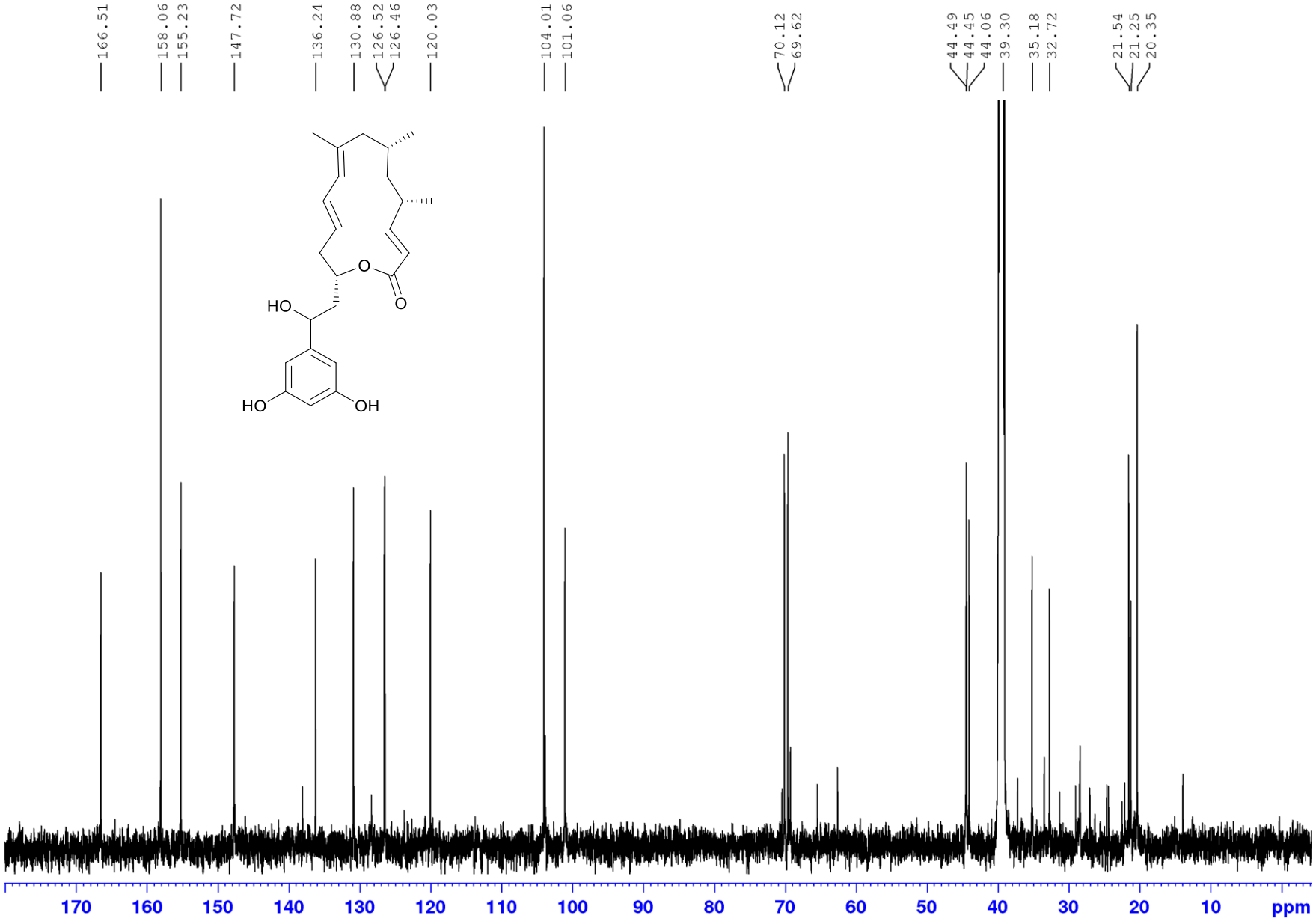


Figure S6. ^{1}H – ^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of resorculin A (**1**).

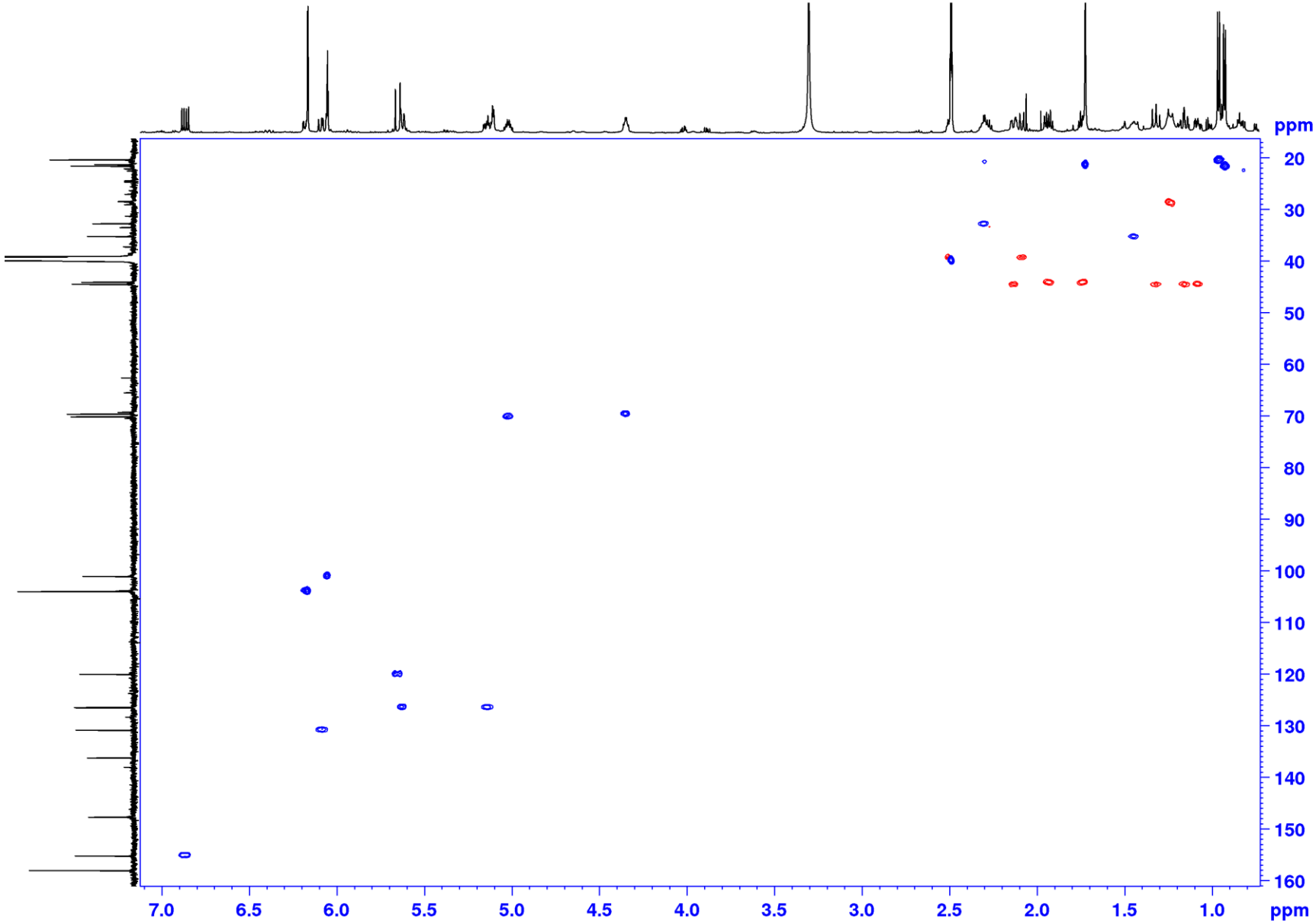


Figure S7. ^{1}H – ^{1}H COSY NMR spectrum (600 MHz, DMSO-*d6*) of resorculin A (**1**).

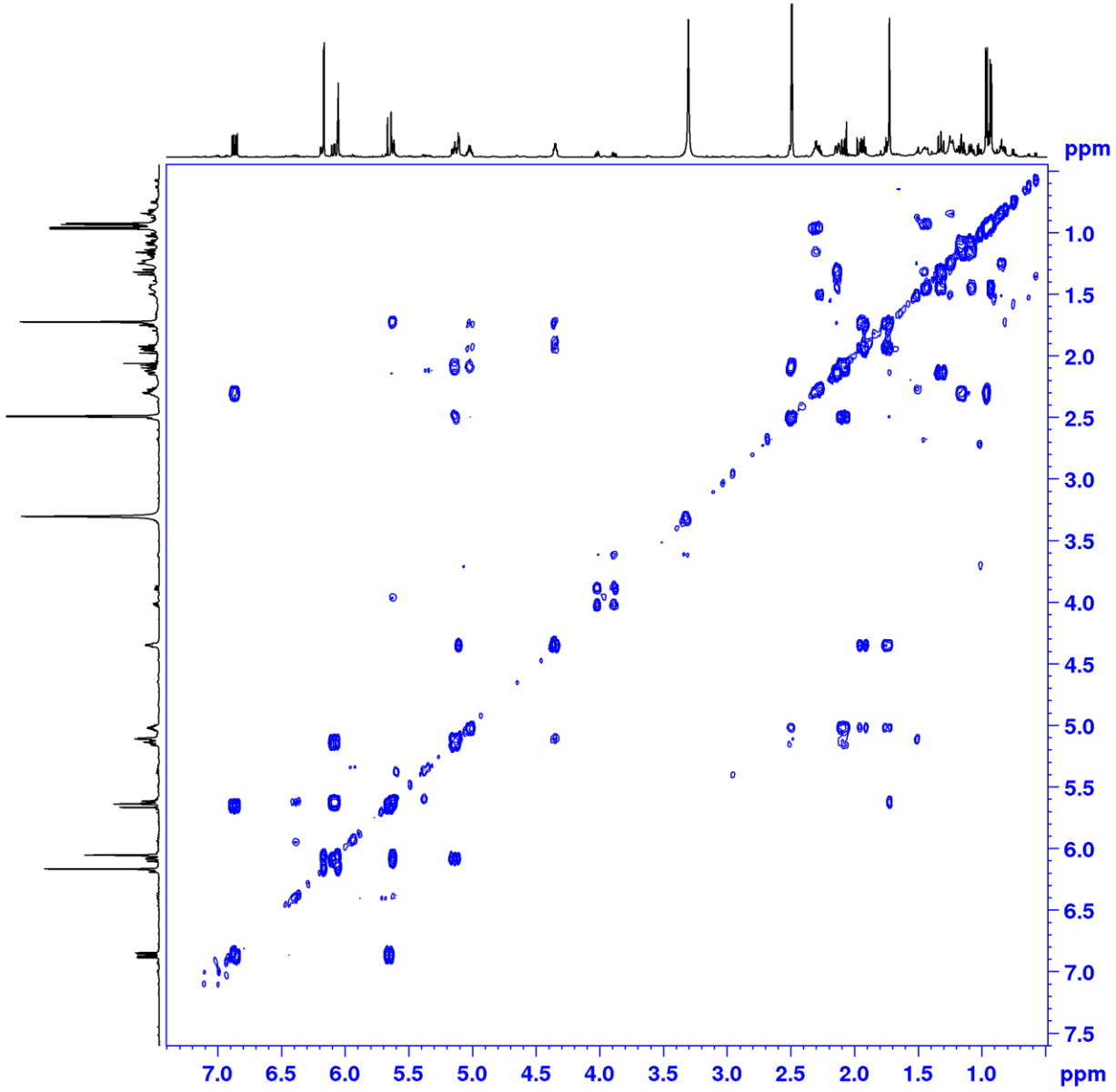


Figure S8. ^{1}H – ^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of resorculin A (**1**).

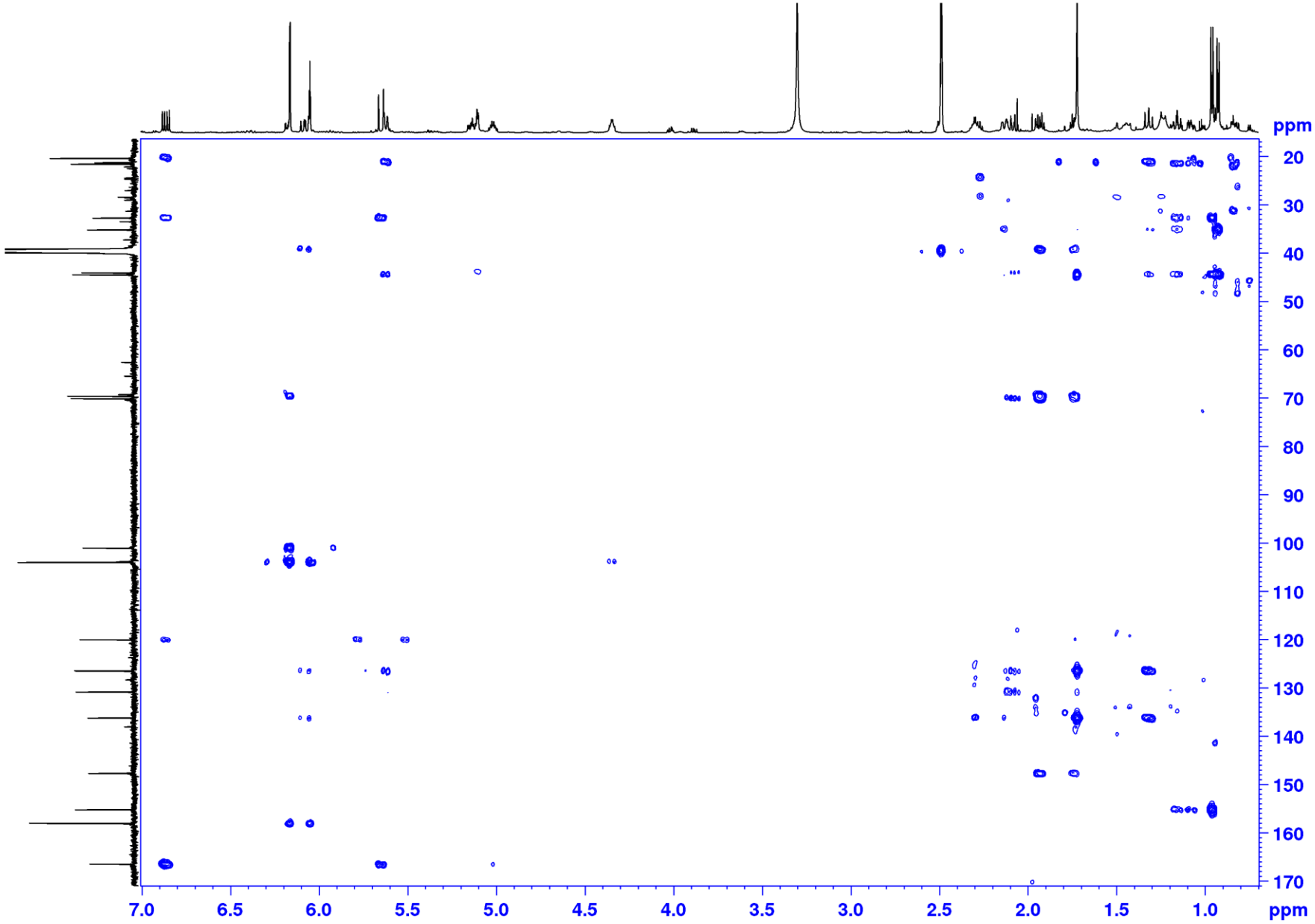


Figure S9. ^{1}H – ^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of resorculin A (**1**).

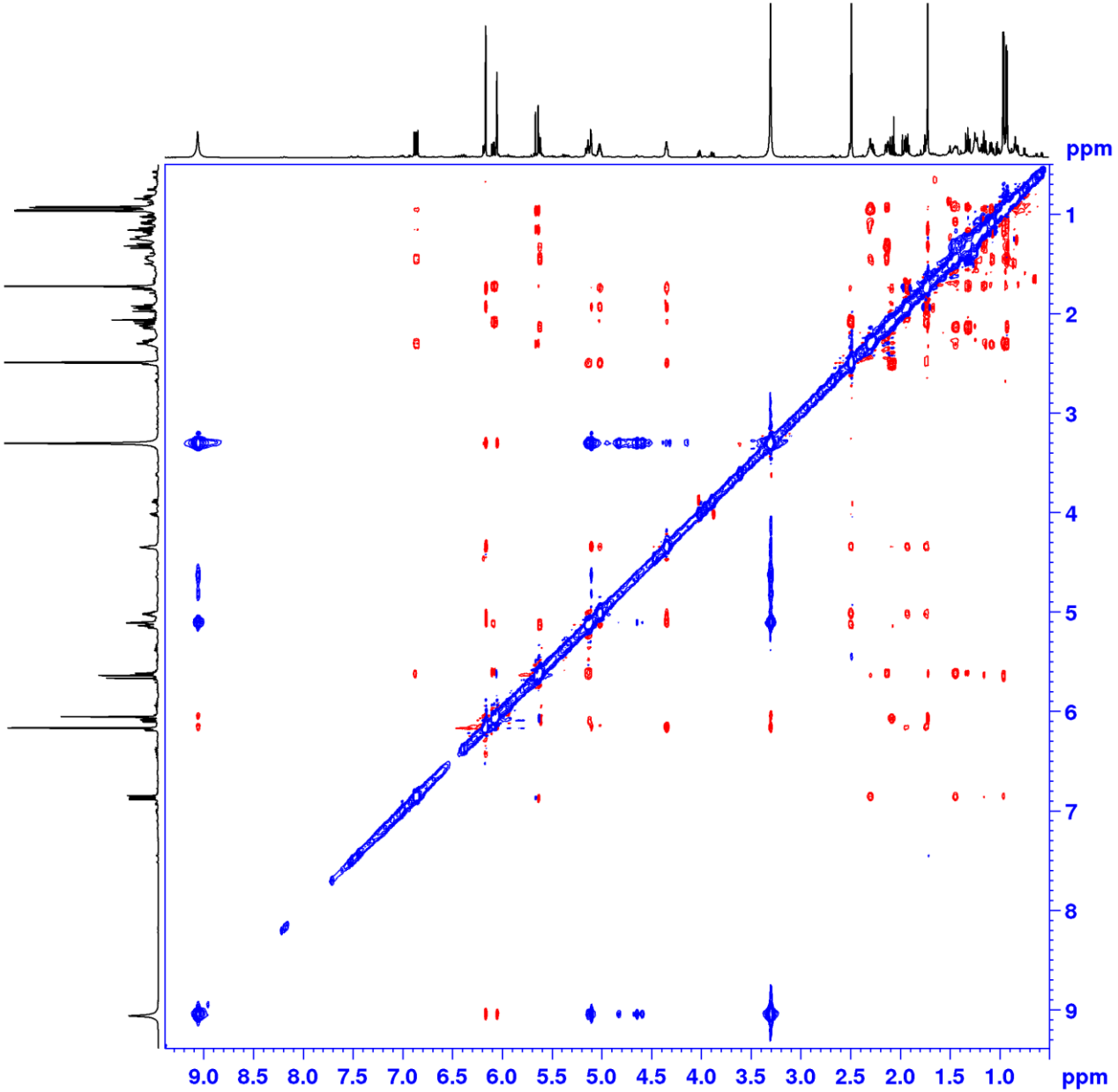


Figure S10. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of resorculin B (**2**).

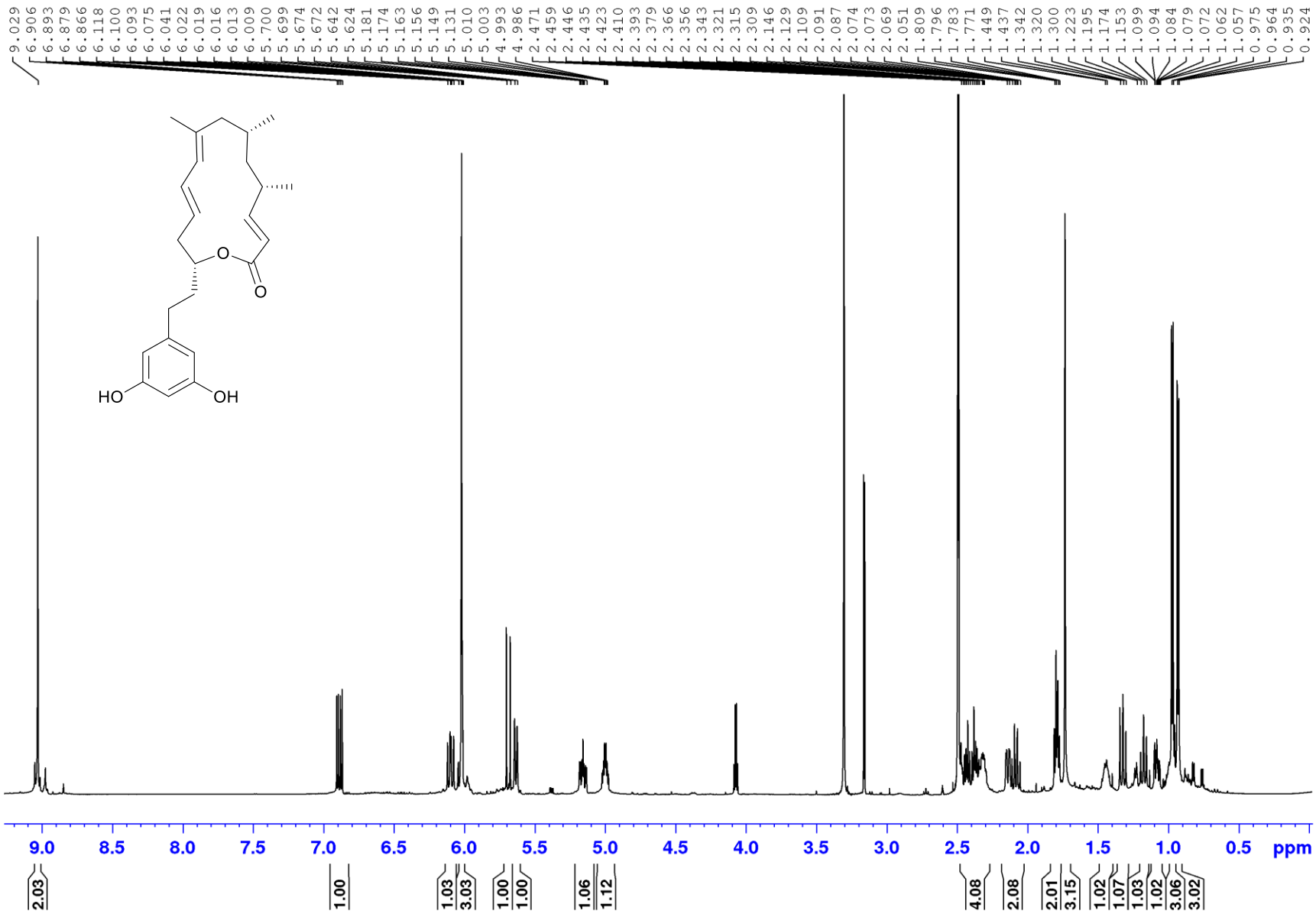


Figure S11. ^{13}C NMR spectrum (150 MHz, DMSO-*d6*) of resorculin B (**2**).

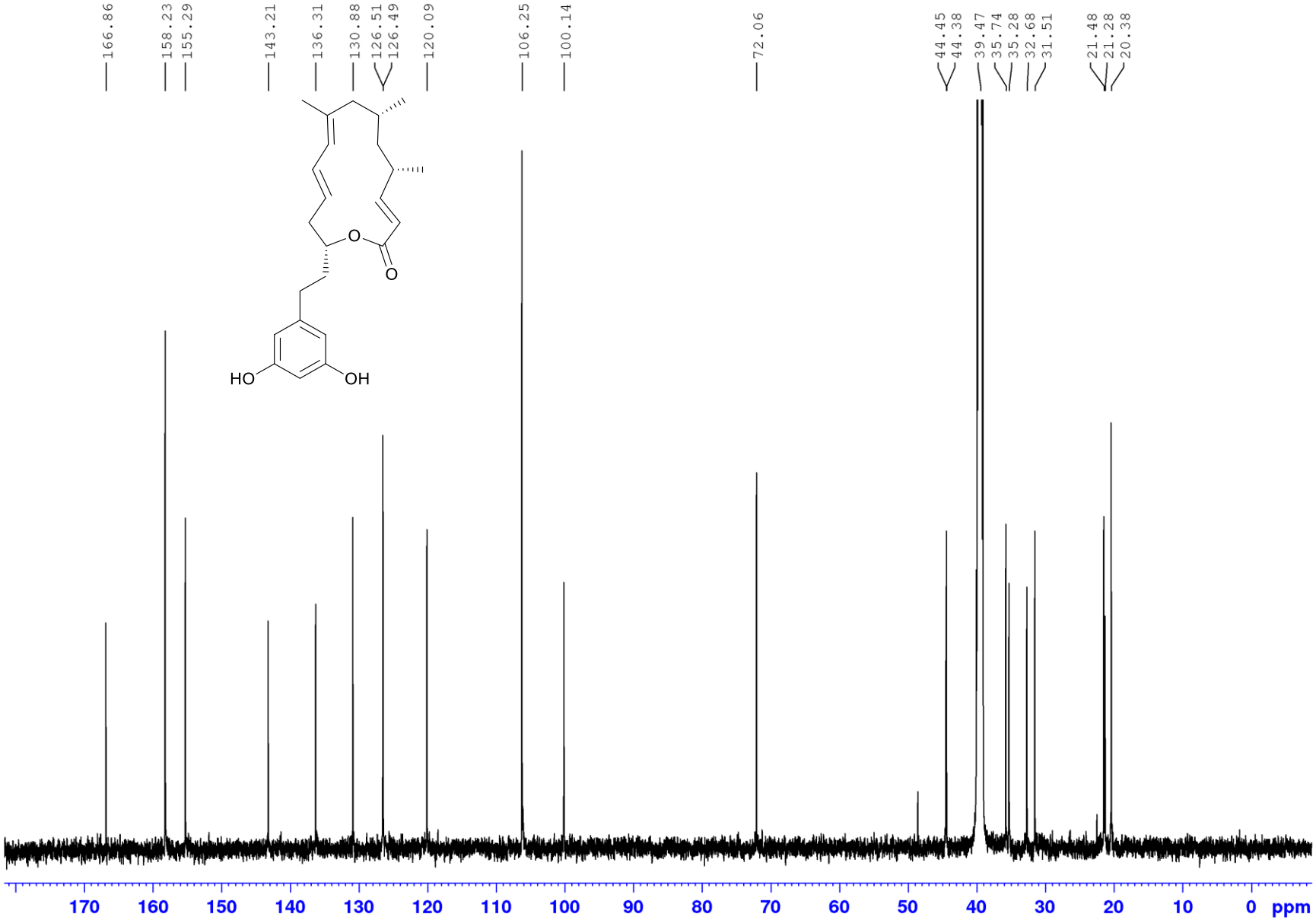


Figure S12. ^{1}H – ^{13}C HSQC NMR spectrum (600 MHz, DMSO-d_6) of resorculin B (**2**).

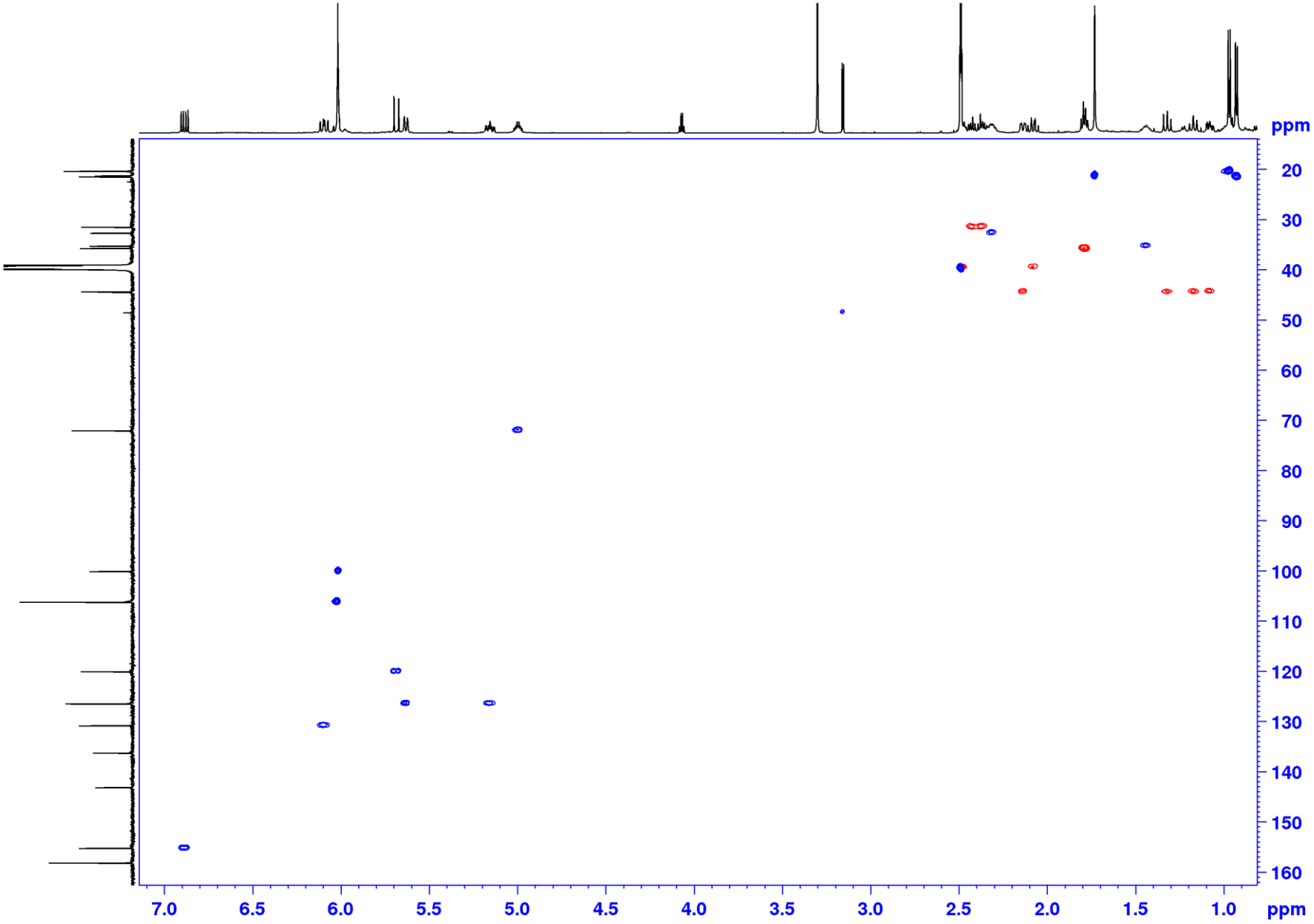


Figure S13. ^{1}H – ^{1}H COSY NMR spectrum (600 MHz, DMSO-d_6) of resorculin B (**2**).

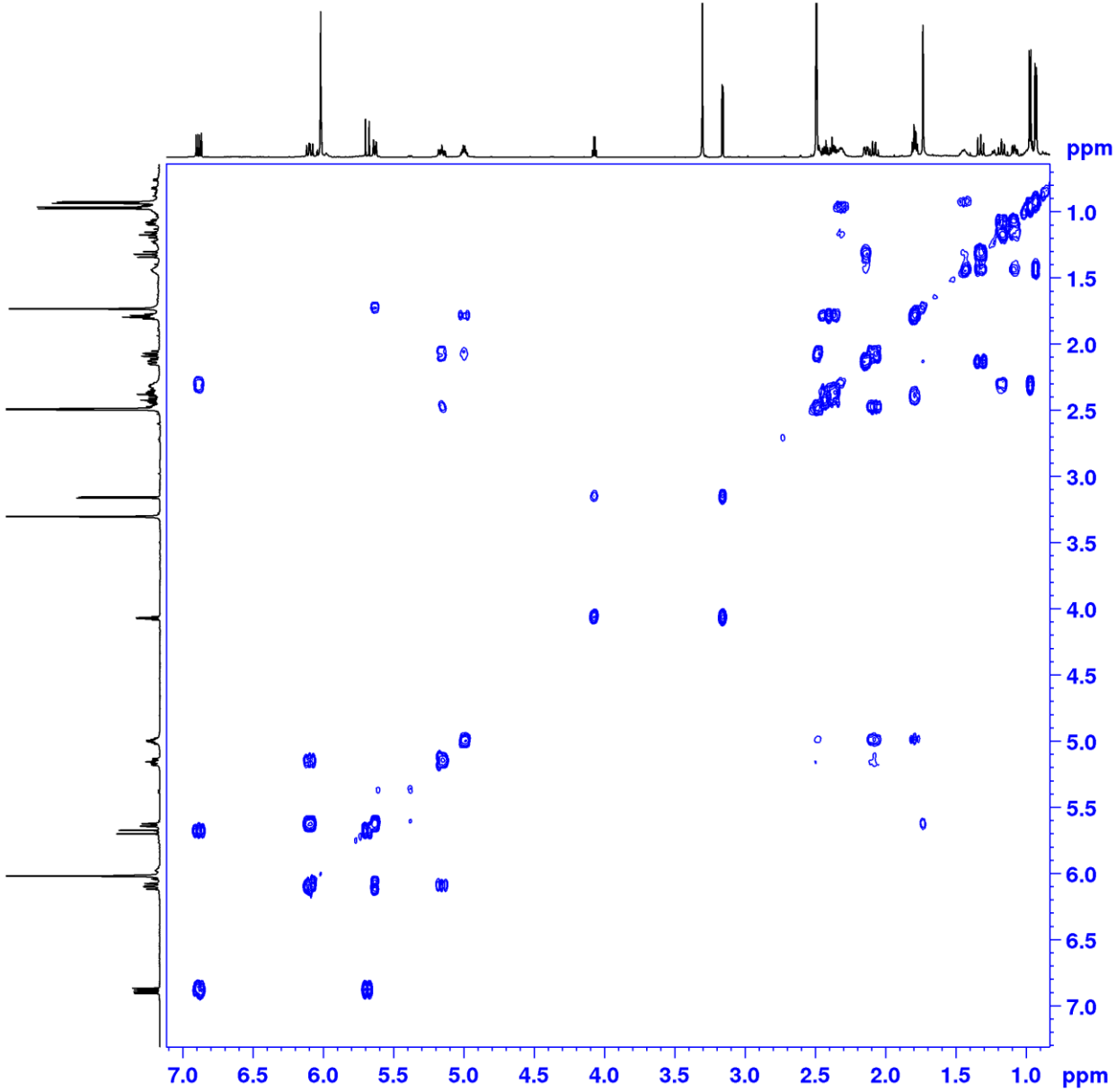


Figure S14. ^{1}H – ^{13}C HMBC NMR spectrum (600 MHz, DMSO-d_6) of resorculin B (**2**).

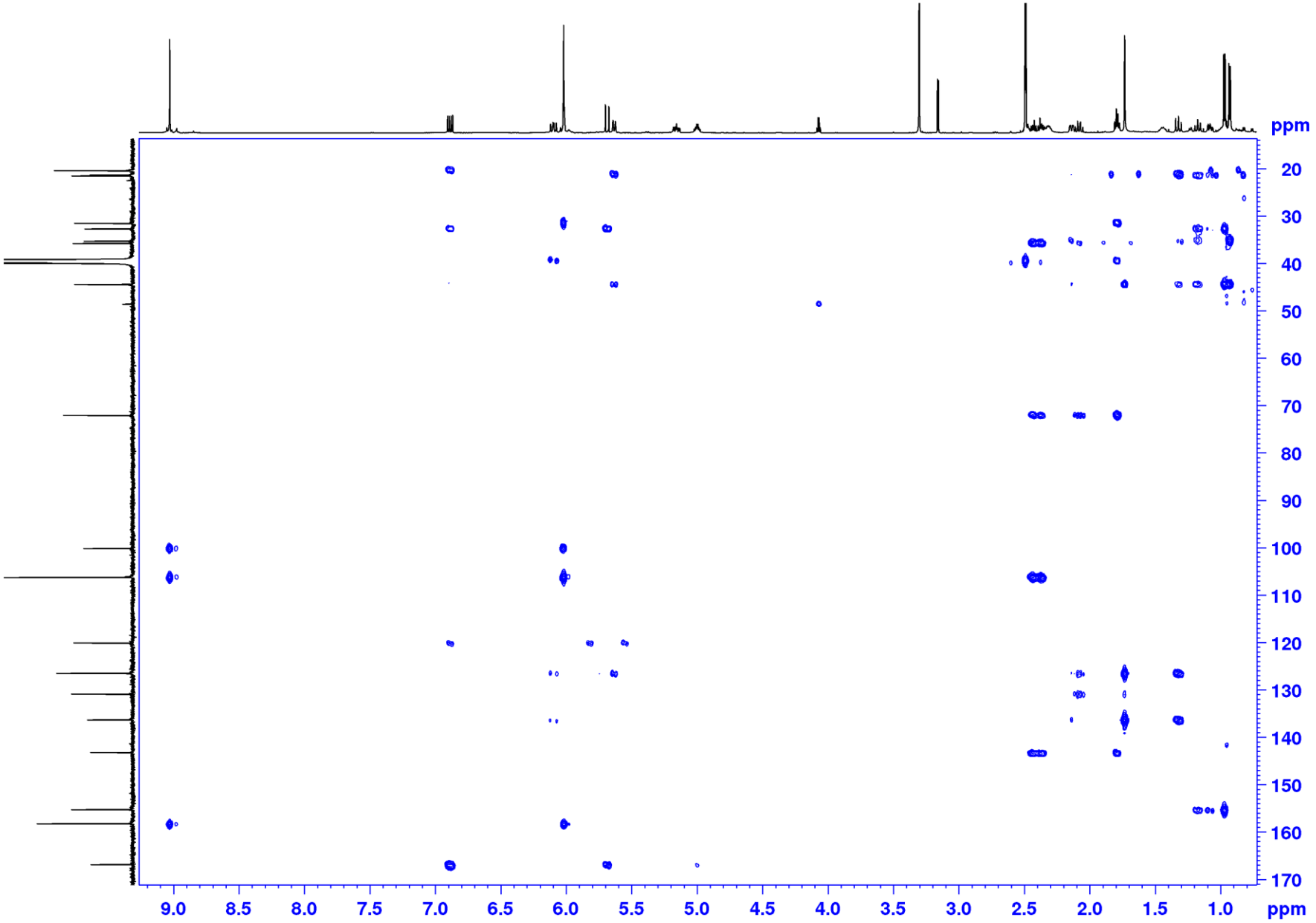


Figure S15. ^{1}H – ^{1}H ROESY NMR spectrum (600 MHz, DMSO-d_6) of resorculin B (**2**).

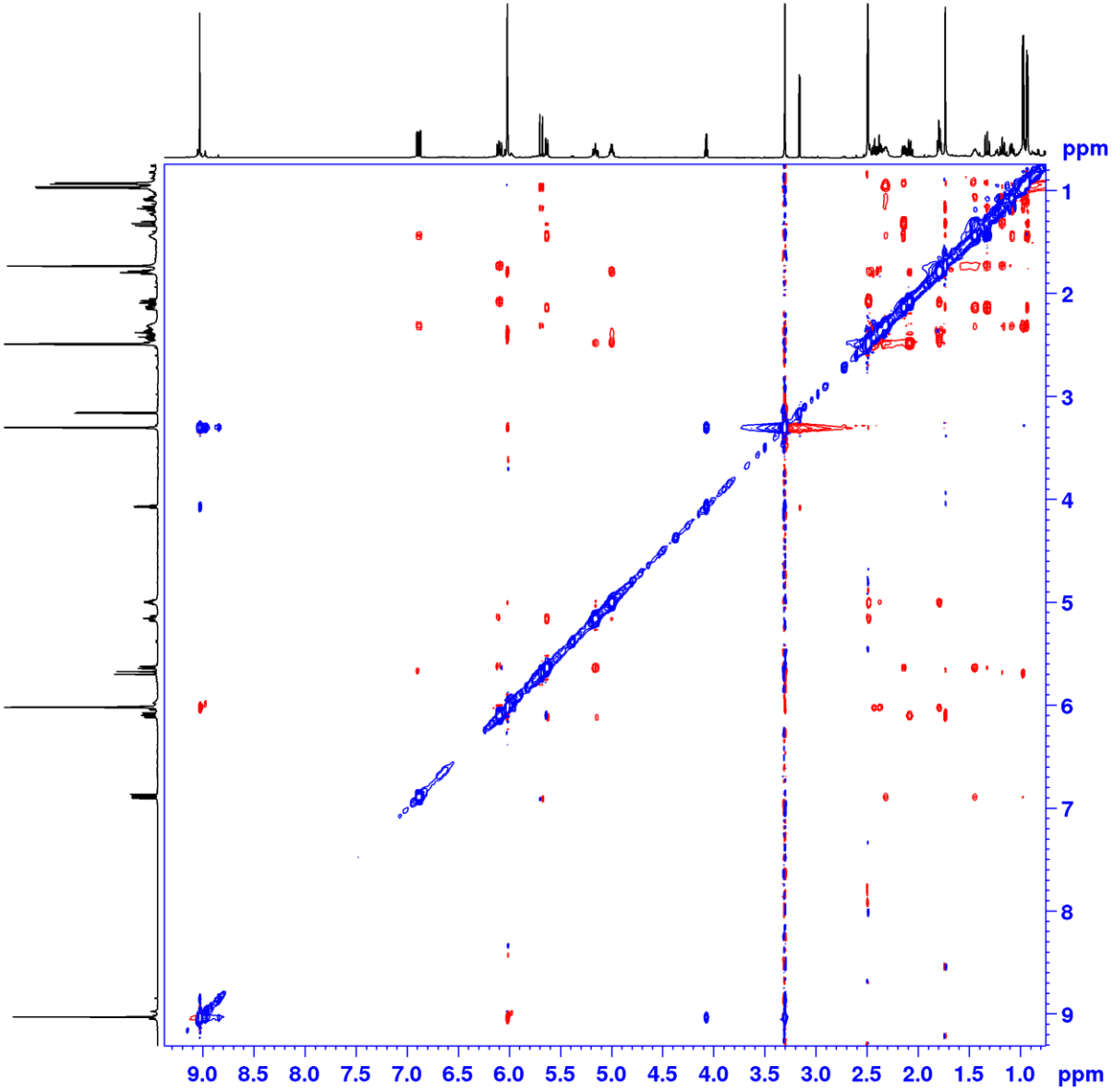


Figure S16. IR Spectrum of resorculin A (**1**).

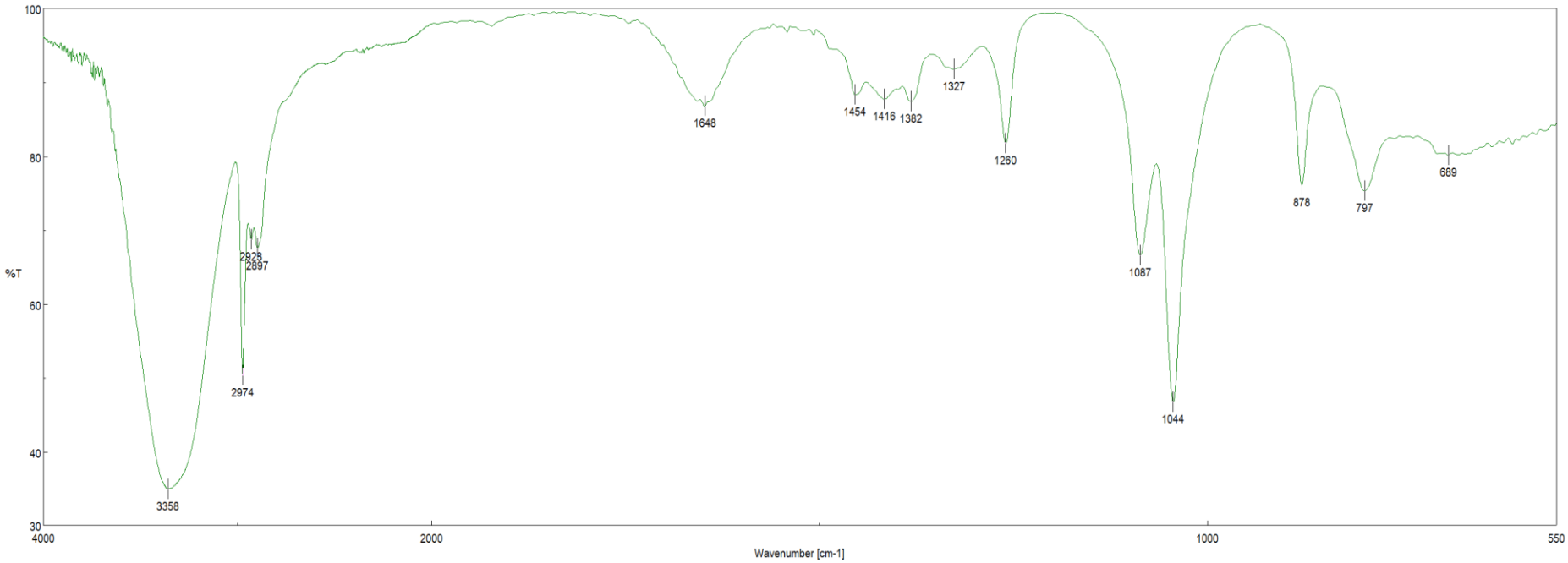
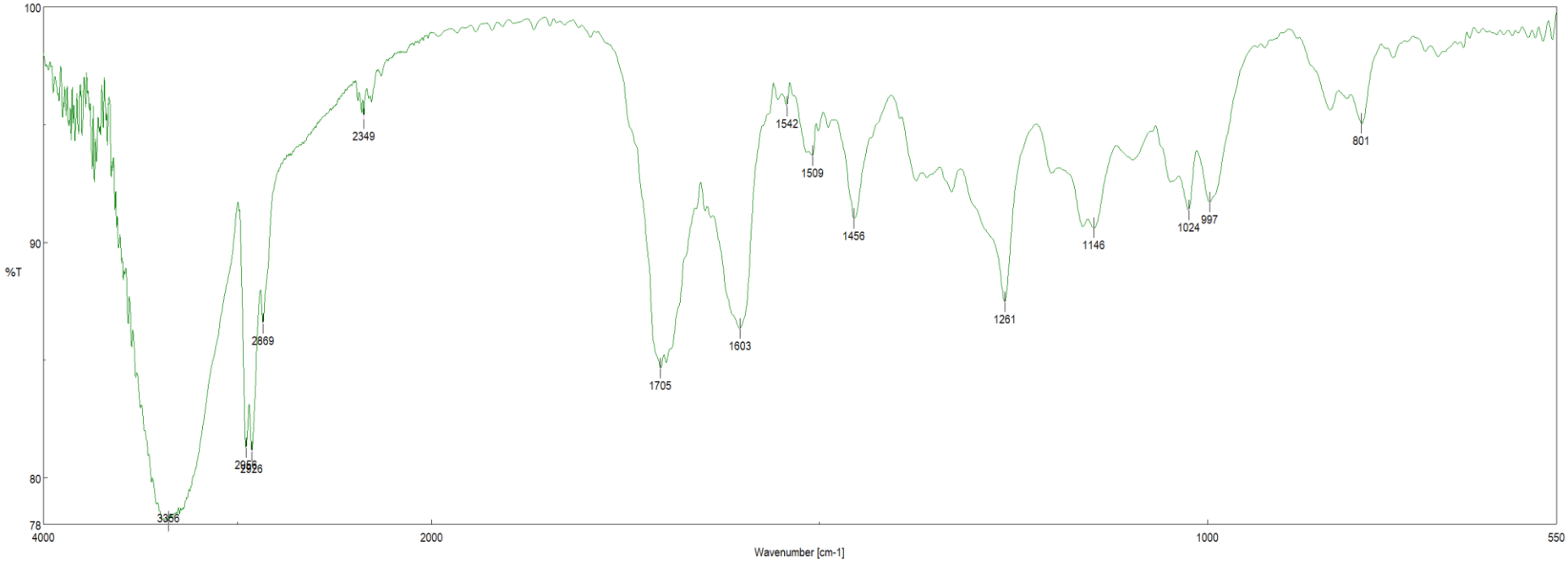


Figure S17. IR Spectrum of resorculin B (**2**).



Supplementary Tables

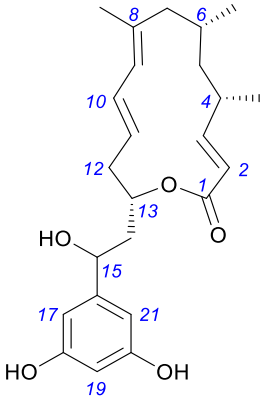


Table S1. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for resorculin A (**1**) in DMSO-*d*$_6$.

Pos	δ_C	δ_H, mult (*J* in Hz)	HMBC	COSY	ROESY
1	166.5				
2	120.0	5.65, dd (16.0, 0.8)	1, 4	3	4-Me, 5a
3	155.2	6.87, dd (16.0, 7.7)	1, 2, 4, 20	2, 4	6
4	32.7	2.31, m	8	3, 4-Me, 5a	6, 6-Me
4-Me	20.4	0.96, d (6.8)	3, 4, 5	4	2, 5a/b
5a	44.50[b]	1.17, dd (13.0, 12.1)	3, 6-Me	4, 5b	2, 4-Me, 7b, 8-Me
5b		1.08, ddd (13.0, 8.7, 2.9)	3, 6-Me	5a, 6	4-Me, 6-Me
6	35.2	1.45, m		5b, 7a/b, 6-Me	3, 4, 6-Me, 9
6-Me	21.5	0.93, d (6.5)	6, 7	6	4, 5b, 6, 7a
7a	44.45[b]	2.13, m	8	6, 7b	6-Me, 9
7b		1.32, dd (13.1, 12.3)		6, 7a	6-Me, 8-Me
8	136.2				
8-Me	21.3	1.72, s	7, 8, 9		5a, 7b, 10
9	126.46[c]	5.62, br d (11.1)	6-Me, 7, 8-Me, 11	10	6, 7a, 11
10	130.9	6.08, dd (15.0, 11.1)	8, 9, 11, 12	9, 11	8-Me, 12b
11	126.52[c]	5.14[d], ddd (15.0, 10.8, 4.3)	9	10, 12a/b	9, 12a, 13
12a	39.3[a]	2.50[a]	9, 10, 11	11, 12b, 13	11, 13, 14b, 15
12b		2.09, ddd (13.2, 10.9, 10.8)		11, 12a, 13	10, 14a/b, 15
13	70.1	5.02, dtd (10.9, 6.5, 4.1)	1, 14	12a/b, 14a/b	11, 12a
14a	44.1	1.93, ddd (13.7, 6.8, 6.5)		13, 14b, 15	12b, 17/21
14b		1.74, ddd (13.7, 6.5, 6.2)		13, 14a, 15	12a/b, 17/21
15	69.6	4.35, ddd (6.8, 6.2, 4.2)	14, 16, 17/21	14a/b, 15-OH	12a/b, 17/21
15-OH		5.11[d], d (4.2)		15	18/20-OH
16	147.7				
17/21	104.0	6.17, d (2.2)	15, 18, 19	19	14a/b, 15, 18/20-OH
18/20	158.1				
18/20-OH		9.06, s			15-OH, 17/21, 19
19	101.1	6.05, t (2.2)	17/21, 18	17/21	18/20-OH

[a]Obscured by solvent signal; [b–d]Assignments interchangeable

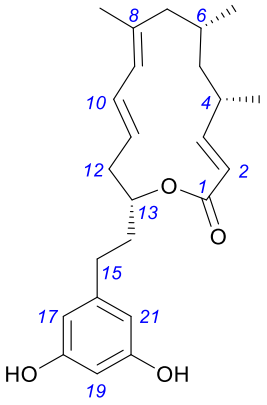


Table S2. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR data for resorculin B (**2**) in DMSO-d_6.

Pos	δ_C	δ_H, mult (*J* in Hz)	HMBC	COSY	ROESY
1	166.9				
2	120.1	5.69, dd (16.0, 0.8)	1, 4	3	4-Me, 5a
3	155.3	6.89, dd (16.0, 7.7)	1, 2, 4, 4-Me	2, 4	6
4	32.7	2.31, m		3, 4-Me, 5a	6, 6-Me
4-Me	20.4	0.97, d (6.8)	2, 4, 5	4	2, 5a/b
5a	44.45[b]	1.17, dd (13.0, 12.1)	3, 4, 6, 6-Me	4, 5b	2, 4-Me, 7b, 8-Me
5b		1.08, ddd (13.0, 8.8, 2.9)	3, 4-Me	5a, 6	4-Me, 6-Me
6	35.3	1.45, m		5b, 6-Me, 7a/b	3, 4, 6-Me, 9
6-Me	21.5	0.93, d (6.5)	3, 5, 6, 7	6	4, 5b, 6, 7a
7a	44.38[b]	2.14, dd (13.2, 3.1)	6, 8	7b	6-Me, 9
7b		1.32, dd (13.2, 12.1)	6-Me, 8, 8-Me, 9	7a	5a, 6, 8-Me
8	136.3				
8-Me	21.3	1.73, s	7, 8, 9		5a, 7b, 10
9	126.49[c]	5.63, d (11.0)	7, 8-Me	10	6, 7a, 11
10	130.9	6.10, dd (15.1, 11.0)	9, 11, 12	9, 11	8-Me, 12b, 14
11	126.51[c]	5.15, ddd (15.1, 10.8, 4.3)		10, 12a/b	9, 12a, 13
12a	39.5[a]	2.48[a]		11, 12b, 13	11, 13, 14
12b		2.08, ddd (13.2, 10.9, 10.8)	10, 11, 13, 14	11, 12a, 13	10, 14
13	72.1	4.99, dtd (10.9, 6.5, 4.1)		12a/b, 14	11, 12a
14	35.7	1.78, ddd (8.0, 7.6, 6.5)	12, 13, 15, 16	13, 15a/b	12a/b, 17/21
15a	31.5	2.43, dt (13.7, 7.6)	13, 14, 16, 17/21	14	17/21
15b		2.38, dt (13.7, 8.0)	13, 14, 16, 17/21	14	17/21
16	143.2				
17/21	106.3	6.02[c]	15, 18/20, 19		14, 15a/b, 18/20-OH
18/20	158.2				
18/20-OH		9.03, s	17/21, 18/20, 19		17/21, 19
19	100.1	6.02[c]	17/21, 18/20		18/20-OH

[a]Obscured by solvent signal; [b–c]Assignments interchangeable

Table S3. BLASTP hits for the resorculin (*rsn*) biosynthetic gene cluster.
The putative regulator and genes involved in polyketide and 3,5-dihydroxybenzoic acid (3,5-DHBA) biosynthesis are indicated. Top hits using BLASTP[1] versus the nr database.

Start	End	Gene	Top BLASTP Hit	Coverage (%)	Identity (%)	Predicted Role
394	1317	*−4*	ABC transporter ATP-binding protein [*Streptomyces albus* subsp. *albus*]	99	91	-
1314	2918	*−3*	ABC transporter permease [*Streptomyces albus* subsp. *albus*]	99	86	-
2994	3701	*−2*	LysR family transcriptional regulator *[Streptomyces palmae*]	99	96	-
3814	4209	*−1*	hypothetical protein ACZ90_64760 [*Streptomyces albus* subsp. *albus*]	95	96	-
4497	7289	*rsnR*	hypothetical protein ACZ90_64770 [*Streptomyces albus* subsp. *albus*]	74	91	Regulator
7651	9111	*rsnI*	benzaldehyde dehydrogenase [*Streptomyces albus* subsp. *albus*]	99	93	3,5-DHBA biosynthesis
9167	10834	*rsnH*	thiamine pyrophosphate-binding protein [*Streptomyces albus* subsp. *albus*]	98	93	3,5-DHBA biosynthesis
10831	12189	*rsnG*	enoyl-CoA hydratase [*Streptomyces albus* subsp. *albus*]	95	91	3,5-DHBA biosynthesis
12189	12992	*rsnF*	hypothetical protein ACZ90_64800 [*Streptomyces albus* subsp. *albus*]	86	90	3,5-DHBA biosynthesis
12997	14082	*rsnE*	stilbene synthase [*Streptomyces albus* subsp. *albus*]	99	94	3,5-DHBA biosynthesis
14351	28480	*rsnA*	type I polyketide synthase [*Streptomyces* sp. TSRI0107]	96	57	Macrolide biosynthesis
28507	39255	*rsnB*	type I polyketide synthase [*Streptomyces hygroscopicus*]	97	58	Macrolide biosynthesis
39255	45839	*rsnC*	PldAI [*Streptomyces platensis*]	98	58	Macrolide biosynthesis
45889	58506	*rsnD*	type I polyketide synthase [*Streptomyces caatingaensis*]	92	58	Macrolide biosynthesis
58604	59467	*+1*	hypothetical protein [*Streptomyces palmae*]	95	91	-
59924	61282	*+2*	M1 family metallopeptidase [*Streptomyces palmae*]	99	95	-
61494	62369	*+3*	hypothetical protein ACZ90_38515 [*Streptomyces albus* subsp. *albus*]	99	83	-
62524	64083	*+4*	hypothetical protein ACZ90_38515 [*Streptomyces albus* subsp. *albus*]	99	83	-

Table S4. Modules encoded by the resorculin (*rsn*) BGC.

Domains present in each module are shown (coenzyme A ligase (CAL), ketoreductase (KR), acyl carrier protein (ACP), ketosynthase (KS), acyltransferase (AT), dehydratase (DH), enoyl reductase (ER), docking (D) and thioesterase (TE)) along with predicted substrate specificity of AT domains (malonate (mal) or methylmalonate (mmal)) and the KR specificity according to Keatinge-Clay, 2007[2]. Predicted by antiSMASH[3].

Protein	Module	Domains	AT Specificity	KR Specificity
RsnA	Loading	CAL, KR, ACP	mal	C1
	1	KS, AT, DH, ER, KR, ACP	mal	B1
	2	KS, AT, KR, ACP	mal	B1
RsnB	3	KS, AT, DH, KR, ACP	mal	B1
	4	KS, AT, DH, KR, ACP, D	mmal	B1
RsnC	5	KS, AT, DH, ER, KR, ACP, D	mmal	B1
RsnD	6	KS, AT, DH, ER, KR, ACP	mmal	B1
	7	KS, AT, DH, KR, ACP, TE	mal	B1

Table S5. cblaster analysis of the resorculin (*rsn*) biosynthetic gene cluster.
Rsn proteins are shown in the top row; the number of homologues identified by cblaster[4] (> 30% identity) from each cluster in the MIBiG[5] are shown below and colour coded according to the number of homologues. The top 25 results are shown based on the number of hits.

MIBiG Accession	Product	Start	End	-4	-3	-2	-1	R	I	H	G	F	E	A	B	C	D	+1	+2	+3	+4
BGC0001662	mediomycin A	9319	165961	0	0	0	0	2	0	0	0	0	0	3	4	1	2	0	0	0	0
BGC0001932	mediomycin A	2426	159068	0	0	0	0	2	0	0	0	0	0	3	4	1	2	0	0	0	0
BGC0000052	ECO-02301	61851	138007	0	0	0	0	0	0	0	0	0	0	1	4	0	2	0	0	0	0
BGC0001819	venemycin	20093	29563	0	0	0	0	1	1	1	1	1	1	0	0	0	0	0	0	0	0
BGC0001066	kendomycin	5120	24752	0	0	0	0	0	1	1	1	1	1	0	0	0	1	0	0	0	0
BGC0000290	A-47934	49418	53393	0	0	0	0	0	0	0	2	1	1	0	0	0	0	0	0	0	0
BGC0001233	feglymycin	12001	15149	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000311	balhimycin	60178	63248	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001459	decaplanin	62840	65898	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000289	A40926	69670	72743	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001460	decaplanin	2063	4968	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001462	avoparcin	1986	5038	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0002034	perquinoline	5782	9399	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000419	ristomycin A	2035	5003	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000418	ristocetin	66546	69517	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001178	UK-68,597	75481	78566	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001955	keratinimicin	3434	6420	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000455	vancomycin	60010	63008	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000440	teicoplanin	73060	76142	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0000441	teicoplanin	66437	69519	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001461	nogabecin	62790	65758	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001635	kistamicin A	38928	41974	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001148	pheganomycin	11291	14547	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001183	lobophorin A	135187	138338	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0
BGC0001807	totopotensamide	64509	67744	0	0	0	0	0	0	0	1	1	1	0	0	0	0	0	0	0	0

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