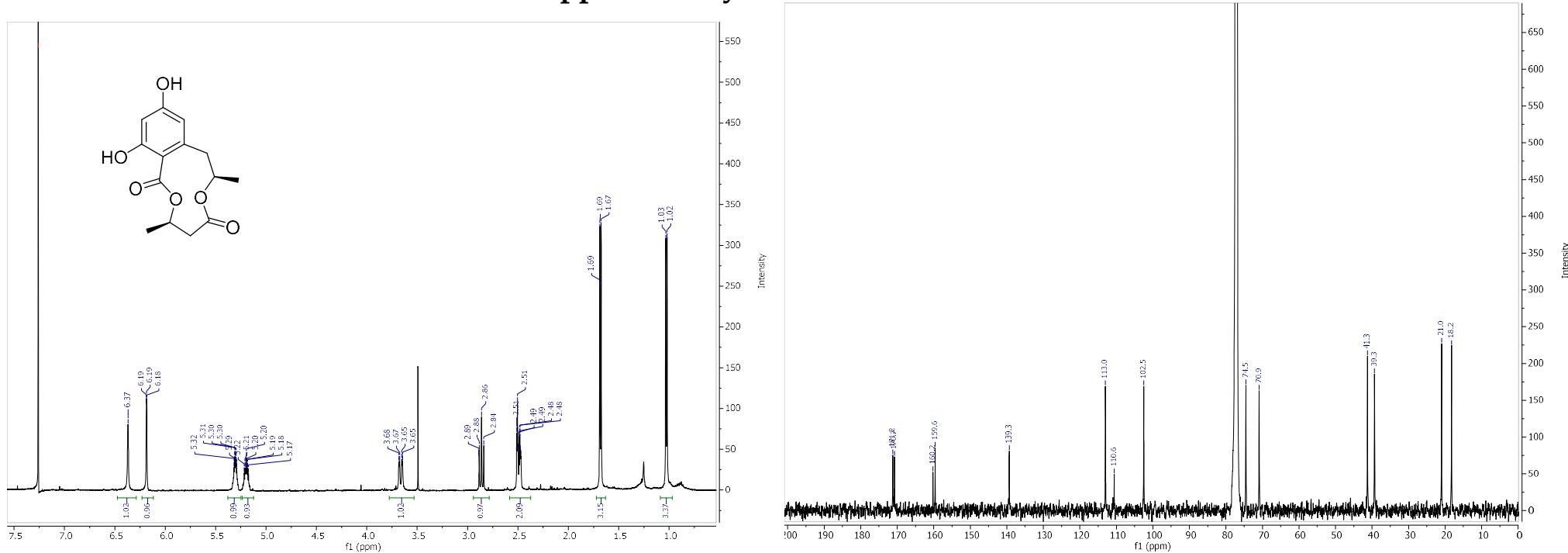


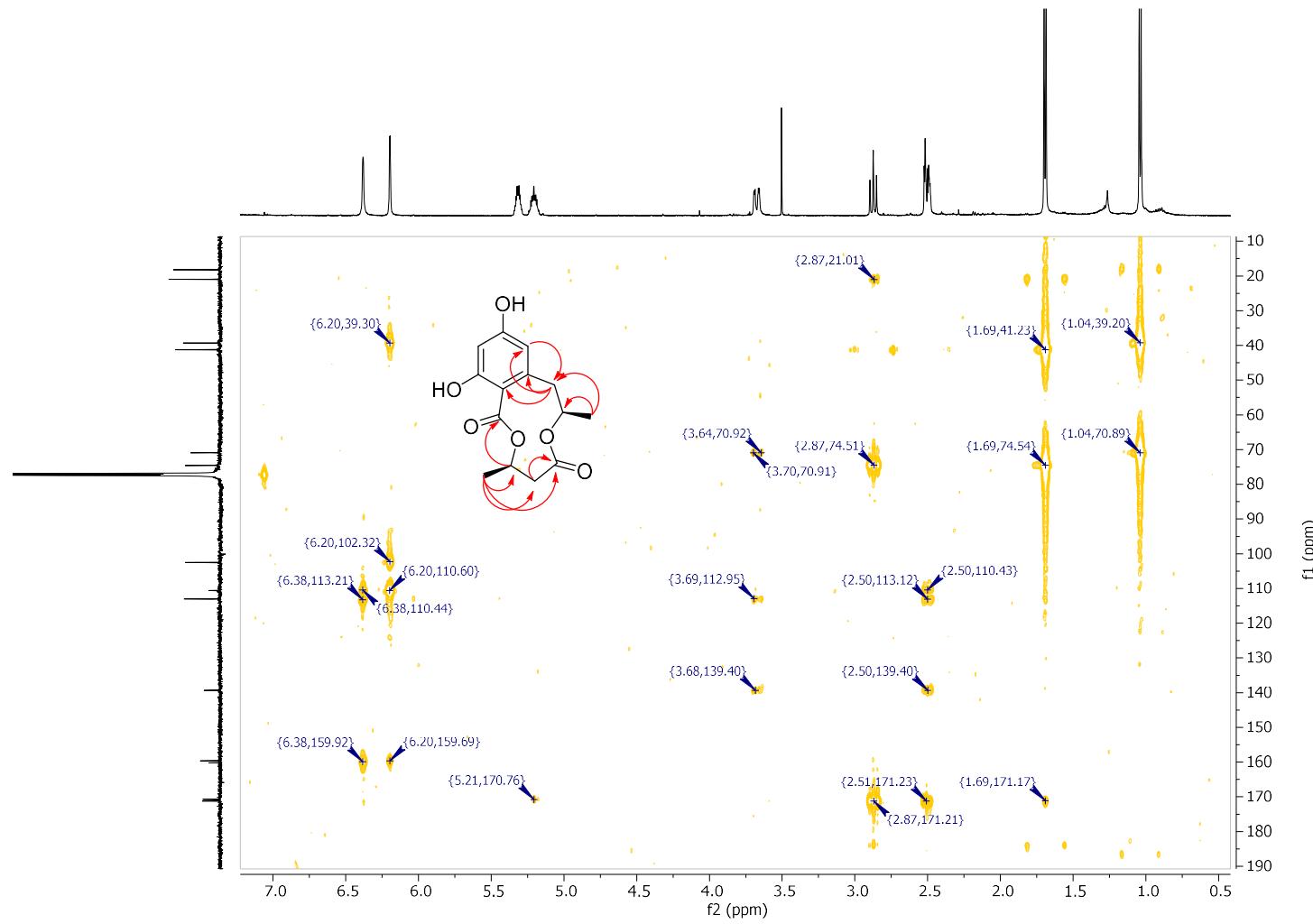
# Putative Biosynthesis of Talarodioxadione & Talarooxime from *Talaromyces stipitatus*

Ahmed J. al Fahad<sup>1</sup>

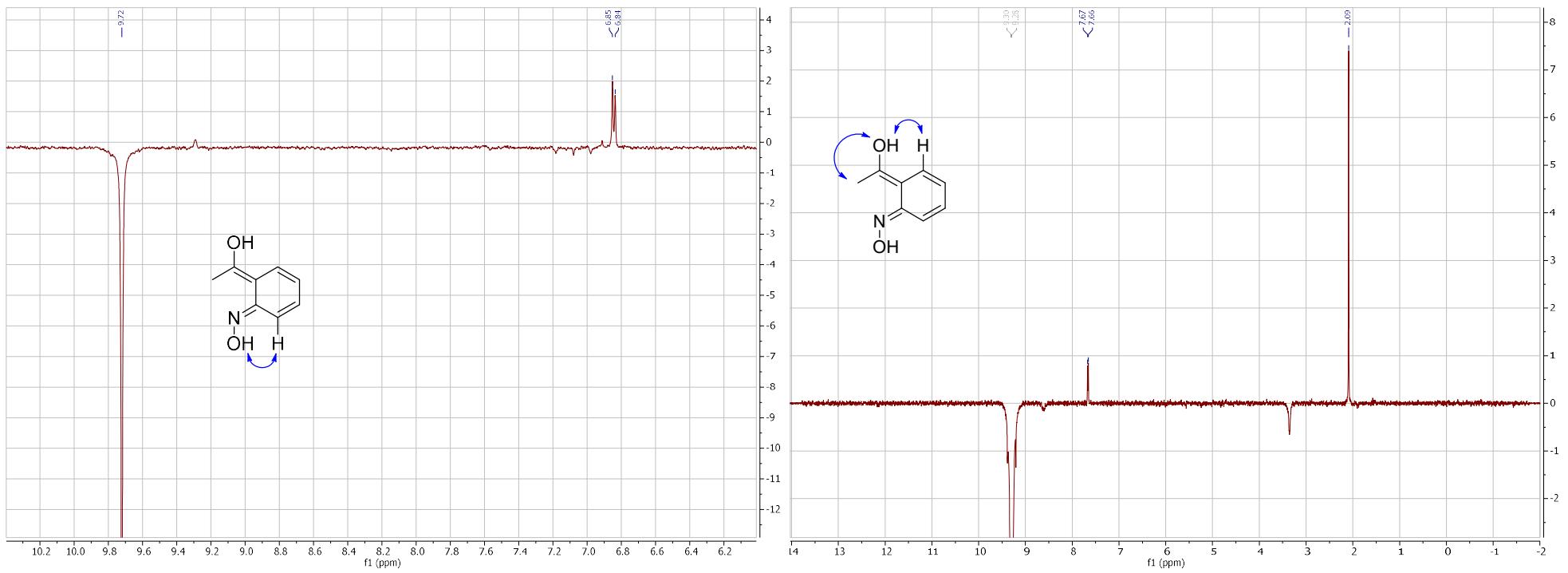
## Supplementary Information



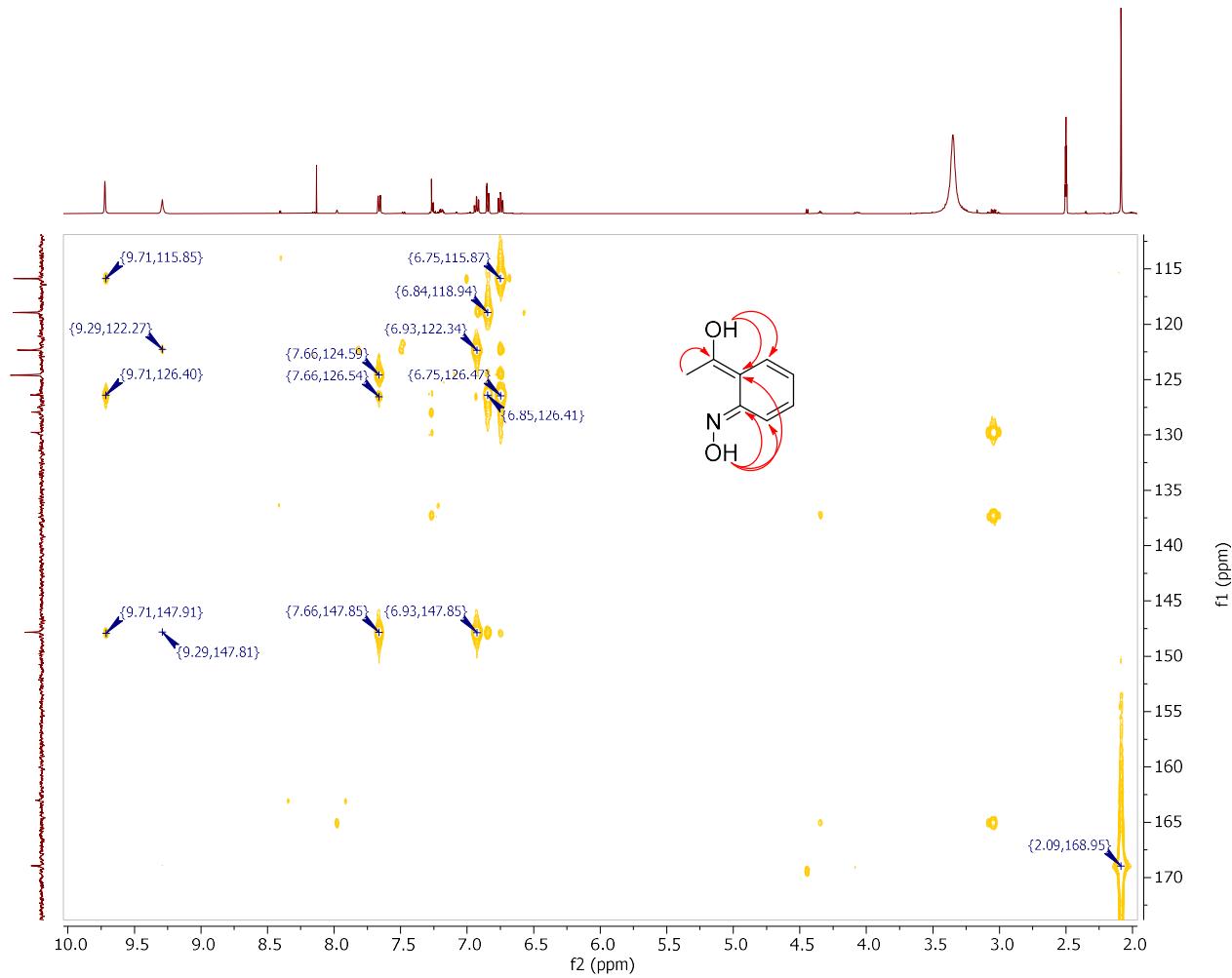
**Figure S1.** <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra of Talarodioxadione 1 (CDCl<sub>3</sub>, 600 and 150 MHz).



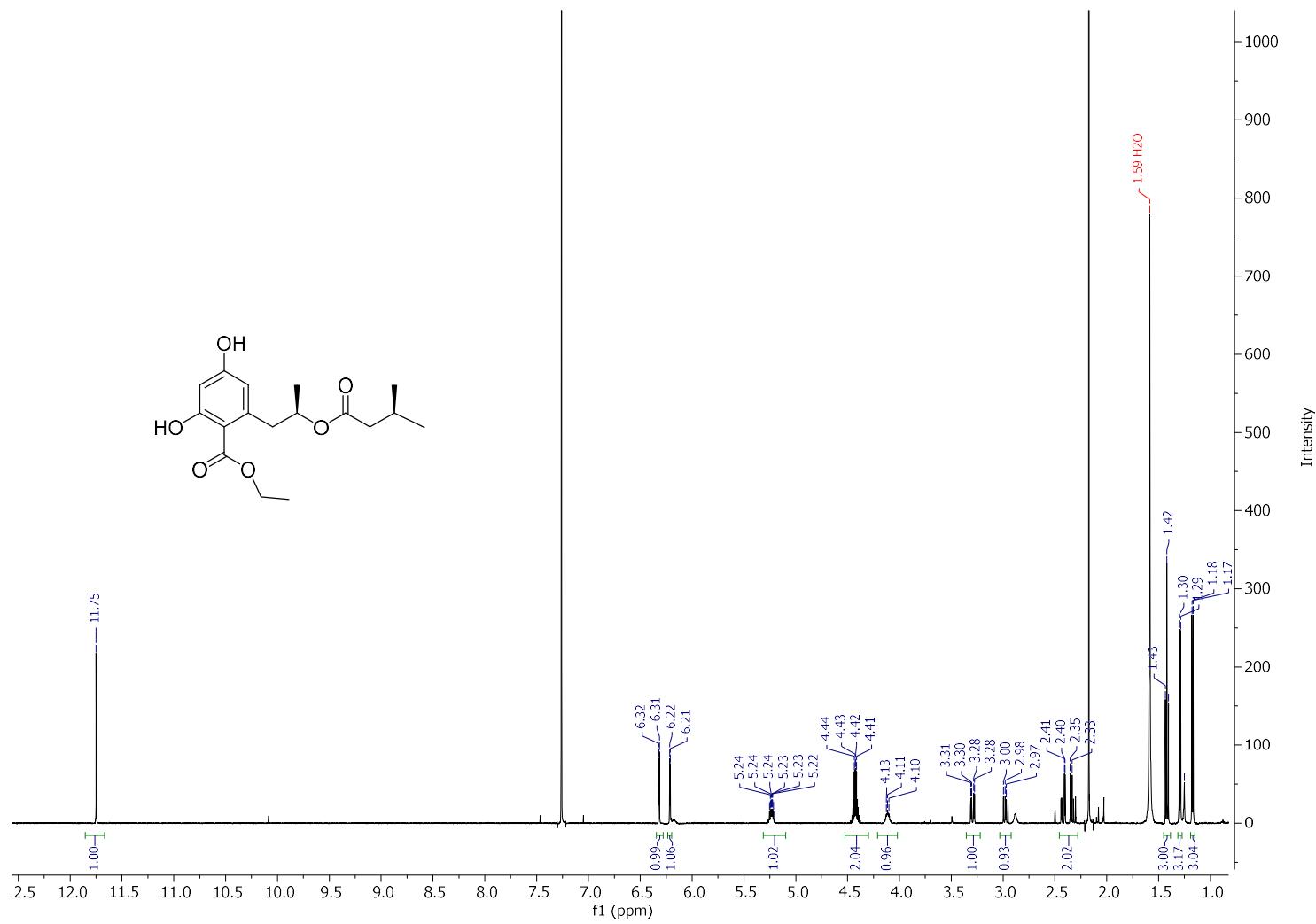
**Figure S2.** HMBC spectrum of Talarodioxadione **1** ( $\text{CDCl}_3$ , 600 MHz).



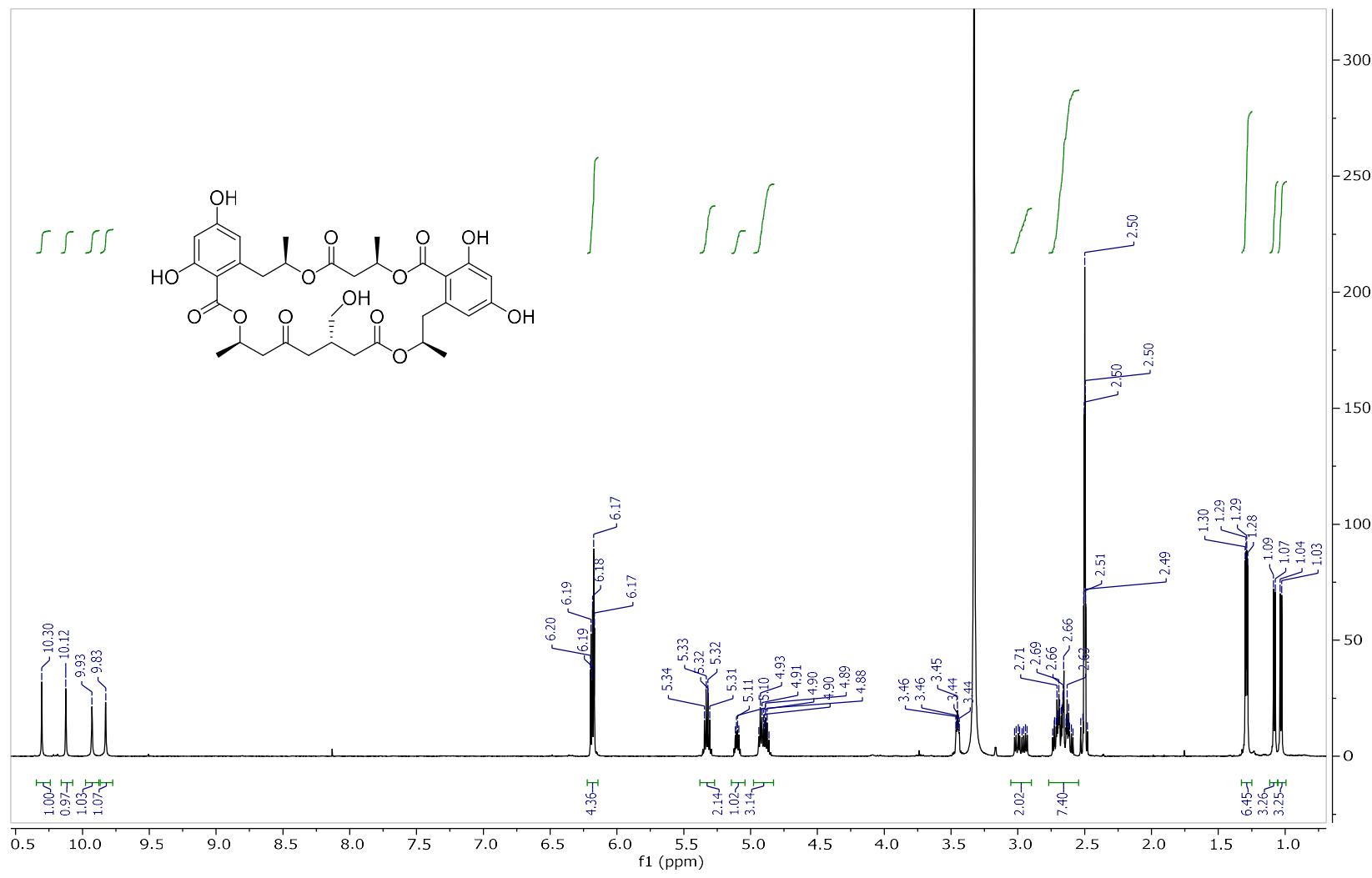
**Figure S3.** 1D-NOESY spectrum of Talarooxime 5 (DMSO- $d_6$ , 600 MHz).



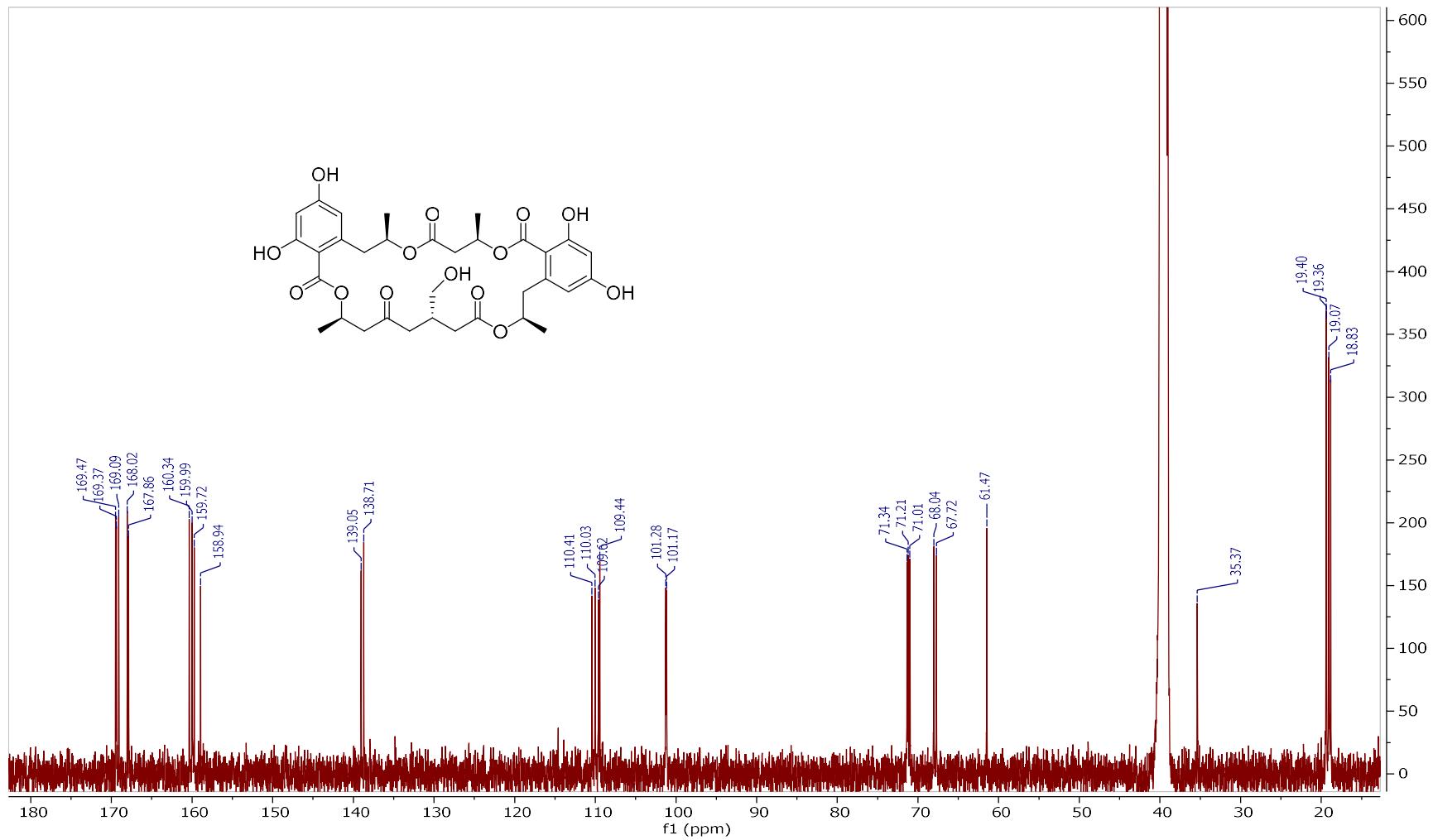
**Figure S4.** HMBC spectrum of Talarooxime 6 (DMSO- $d_6$ , 600 MHz).



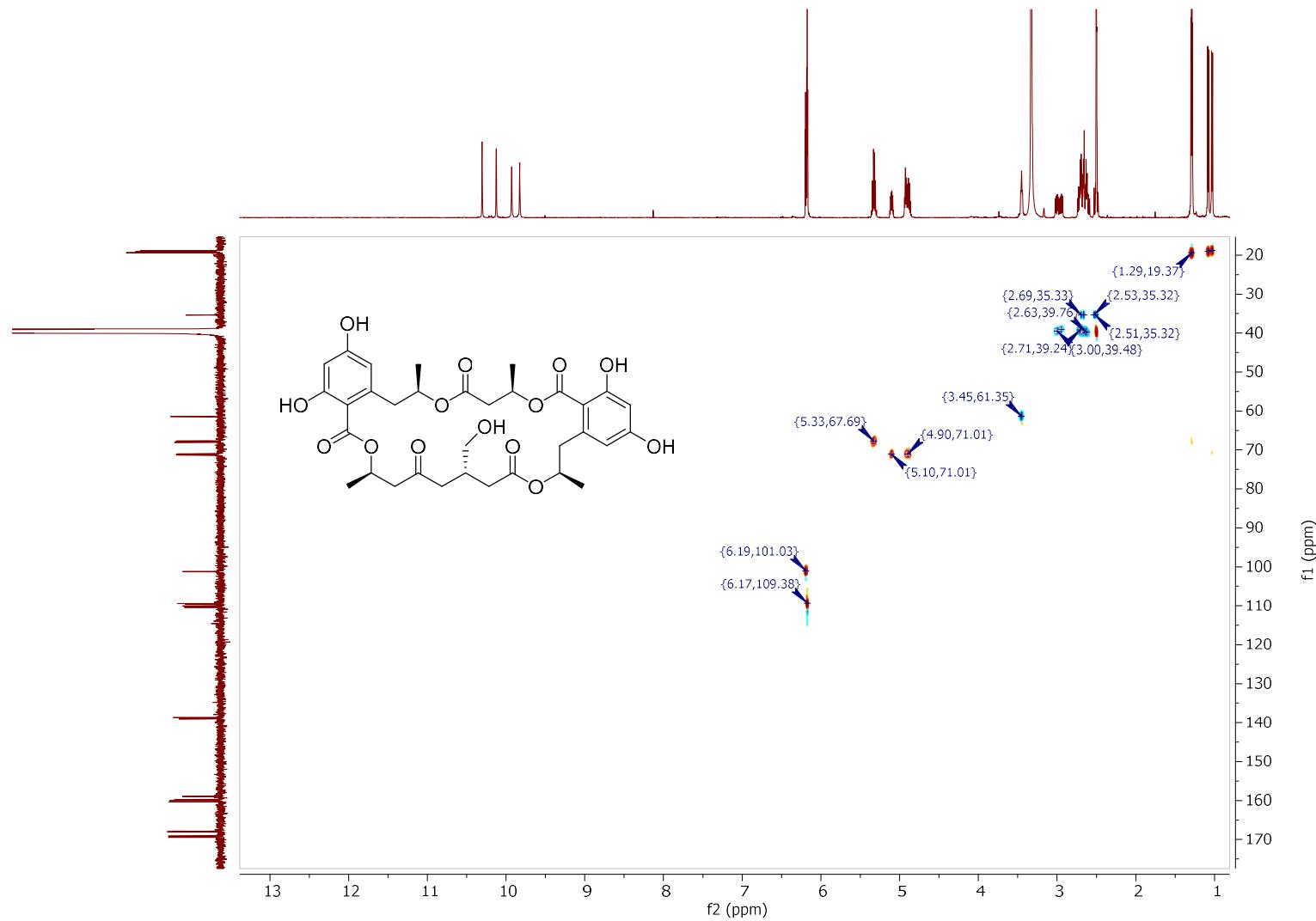
**Figure S5.**  $^1\text{H}$ -NMR spectrum of Talopolyester G **2** ( $\text{CDCl}_3$ , 600 MHz).



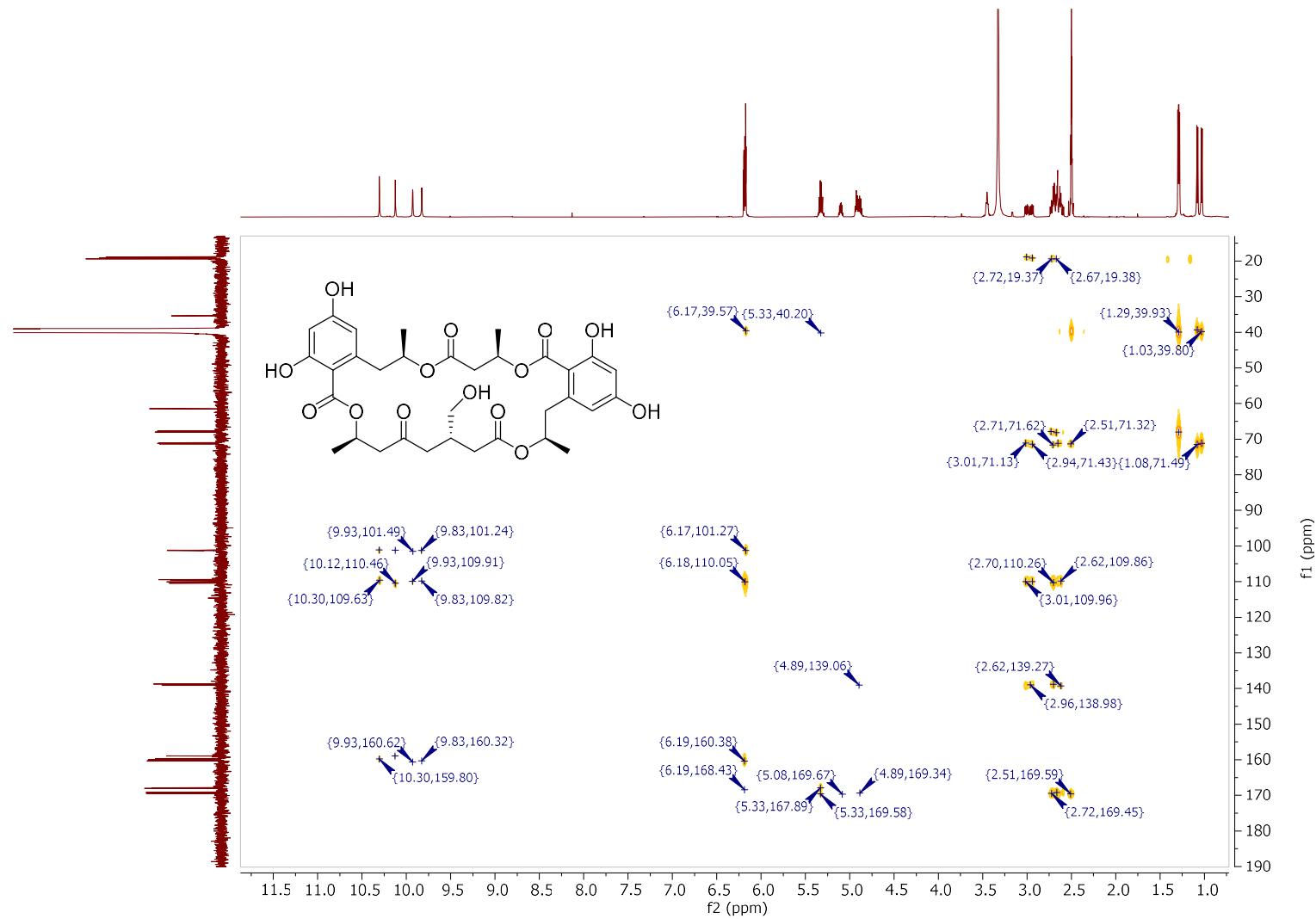
**Figure S6.**  $^1\text{H}$ -NMR spectrum of 15G256 $\alpha$  3 (DMSO- $d_6$ , 600 MHz).



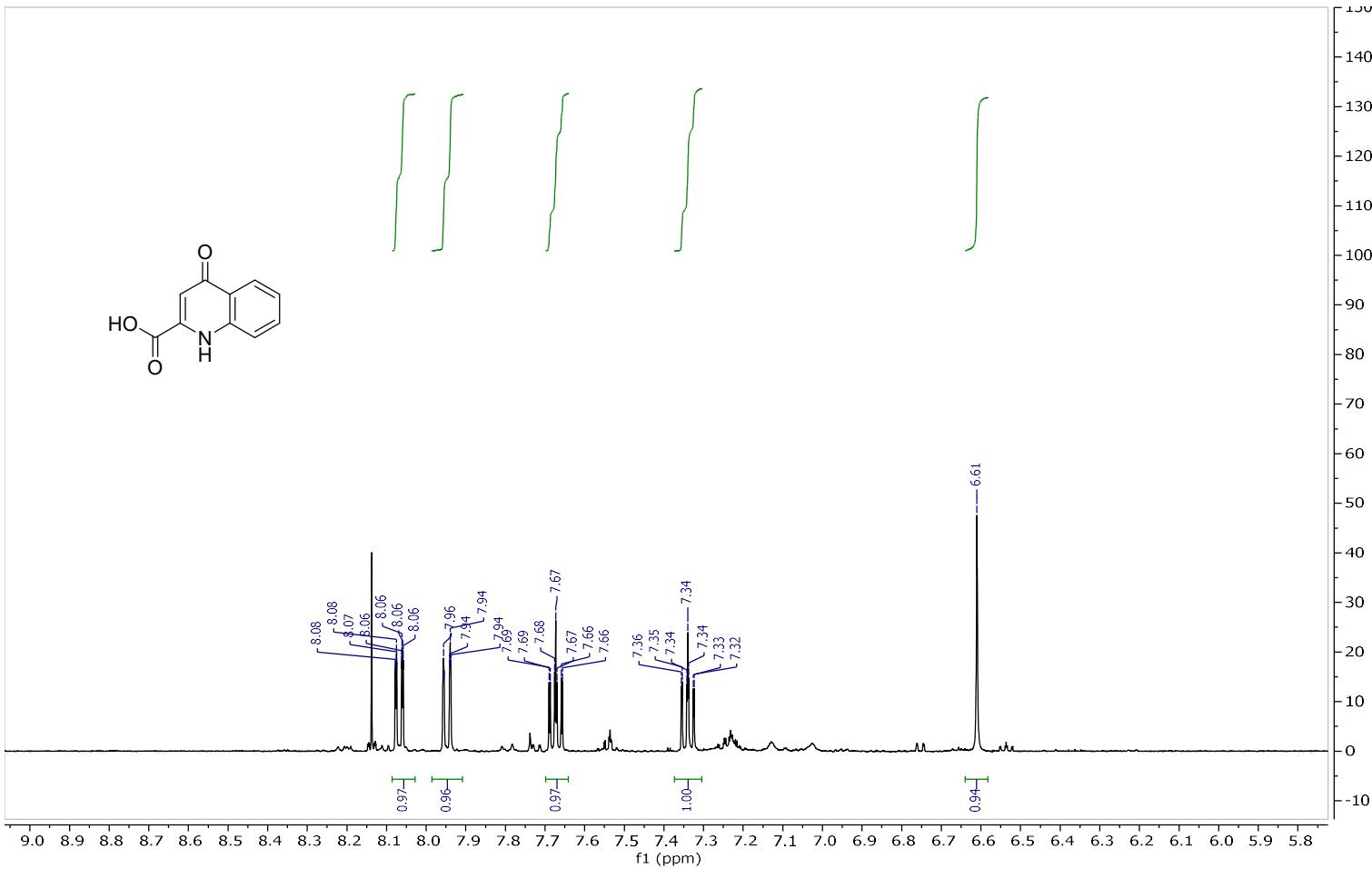
**Figure S7.**  $^{13}\text{C}$ -NMR spectrum of 15G256 $\alpha$  3 (DMSO- $d_6$ , 150 MHz).



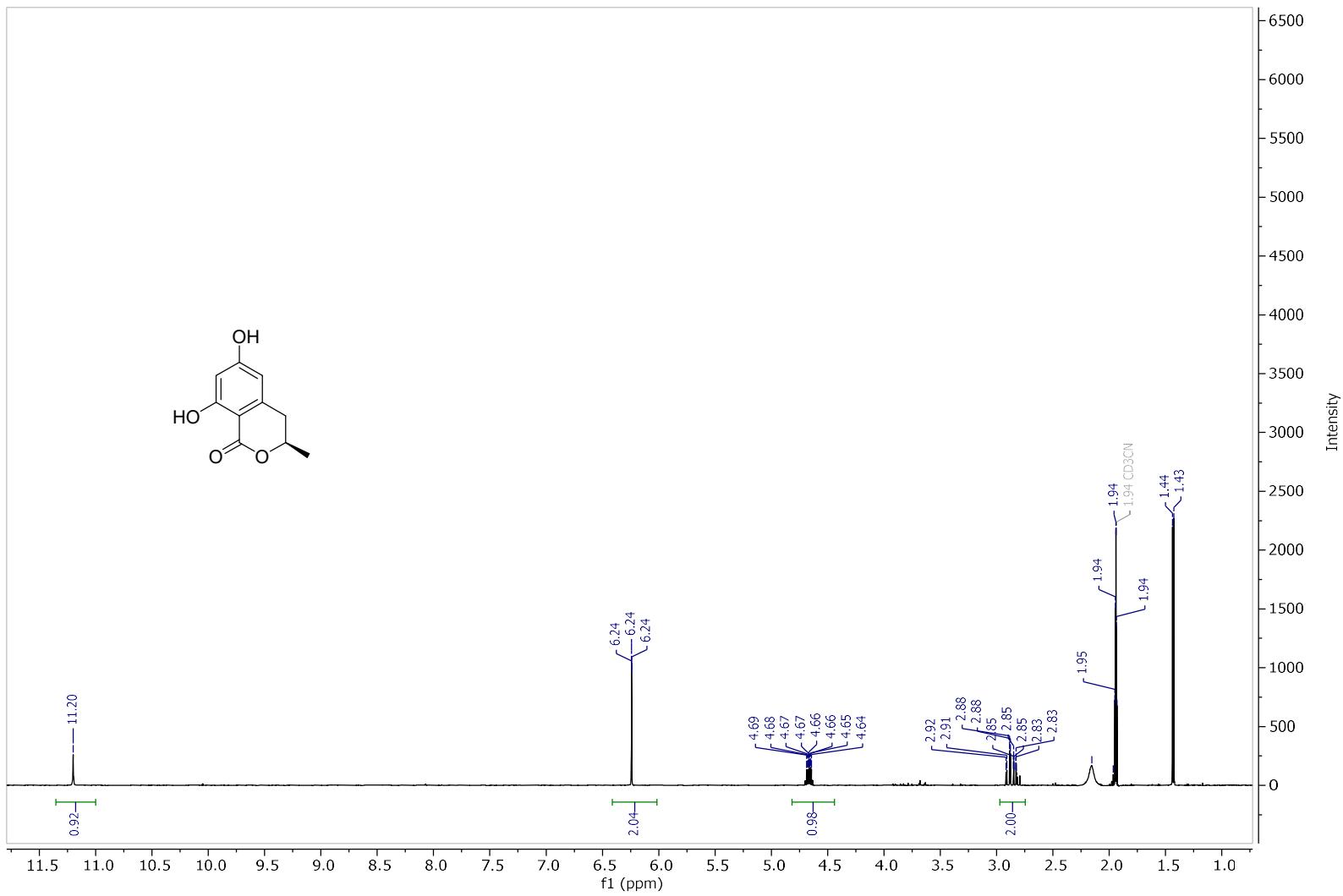
**Figure S8.** HSQC spectrum of 15G256 $\alpha$  3 (DMSO- $d_6$ , 600 MHz).



**Figure S9.** HMBC spectrum of **15G256 $\alpha$  3** ( $\text{DMSO}-d_6$ , 600 MHz).



**Figure S10.**  $^1\text{H}$ -NMR spectrum of 4 (DMSO- $d_6$ , 600 MHz).



**Figure S11.**  $^1\text{H}$ -NMR spectrum of **6** ( $\text{CD}_3\text{CN}$ , 600 MHz).

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Database nr [See details](#)  
Query ID CAB3277415.1 **Men1**  
Description Men1 [Menisporopsis theobromae]  
Molecule type amino acid  
Query Length 2598  
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	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident.	Acc. Len	Accession
<b>TpeA</b>	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	3048	3048	99%	0.0	59.07%	2521	XP_002488696.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	409	899	50%	1e-114	48.13%	3725	XP_002478535.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	404	889	81%	5e-113	47.37%	3968	XP_002486701.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	374	811	59%	4e-104	45.91%	2900	XP_002483871.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	389	1034	85%	6e-109	43.38%	2368	XP_002488004.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	340	822	79%	8e-94	41.94%	2347	XP_002480264.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	353	876	81%	8e-98	40.60%	2432	XP_002478229.1
	<input checked="" type="checkbox"/> malonyl CoA-acyl carrier protein transacylase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	39.3	39.3	2%	0.020	39.68%	2086	XP_002479408.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	294	294	16%	8e-80	38.62%	2635	XP_002339967.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	299	421	33%	1e-81	38.22%	1786	XP_002482902.1

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Database nr [See details](#)  
Query ID CAB3277416.1 **Men2**  
Description Men2 [Menisporopsis theobromae]  
Molecule type amino acid  
Query Length 2186  
Other reports [Distance tree of results](#) [Multiple alignment](#) [MSA viewer](#)

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<input checked="" type="checkbox"/> select all 10 sequences selected	Description	GenPept	Graphics	<a href="#">Distance tree of results</a>	<a href="#">Multiple alignment</a>	<a href="#">MSA Viewer</a>			
	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident.	Acc. Len	Accession
<b>TpeB</b>	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	3073	3073	99%	0.0	66.82%	2200	XP_002488697.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	1072	1072	98%	0.0	31.97%	2125	XP_002483594.1
	<input checked="" type="checkbox"/> conidal pigment polyketide synthase PksP/Alb1 [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	1032	1032	97%	0.0	32.31%	2142	XP_002481882.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	1012	1012	91%	0.0	32.19%	2157	XP_002478062.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	928	928	77%	0.0	33.31%	1786	XP_002482902.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	888	888	77%	0.0	31.85%	1809	XP_002482968.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	823	914	94%	0.0	31.85%	2051	XP_002483004.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	634	634	87%	0.0	27.30%	2104	XP_002486858.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	543	543	51%	6e-160	31.45%	1989	XP_002478017.1
	<input checked="" type="checkbox"/> polyketide synthase, putative [ <i>Talaromyces stipitatus</i> ATCC 10500]	<i>Talaromyces stipitatus</i> ATCC 10500	478	478	78%	1e-138	26.48%	1879	XP_002340065.1

**Figure S12.** The result of protein Blast searches of Men1 (left) and Men2 (right) amino acid sequences against *Talaromyces stipitatus* protein database.



MENSYDDQSIAVIGLSCRFPGDADNVERFWNLLREGQSAISTVPGNRWNSRRFQDDKNHSQNTSRNRAHFLKEDVSAFDANFFSISKSEAVSMDPQQRLMLEVSYEAFENAGLAVES  
 LAQSQMGCVSSFSQDWREMQFSDLQSVPKYAMSGMQPEMLANRVSYFFDLHGPSMALETACSGSLVGLHVACQSLRSGECDAAVLGGANLFLNPNMFLASNQNFLAPDGLSKA  
 FDASANGYGRGEGFAAVILPKVEKAIRDGDPPIRAVIRATGTNQDGRTKGTLMPNGDAQETLIRSTYRSAGLEKDTAYFEAHGTGTQVGDFEELSAIARTVADARKREGLEELWVGSAKTN  
 GHLEATAGLAGVLKAILYLENGVIPPNLHFKNPNPRIPFQEYHIRVPTQEVTVNPDTIRRVSVNSFGFGGSNAHAIIDNGKQYLHQRRSKATLVNGTHAADDKELKPEVPQIFVINSSDQEG  
 LGRQRSALRHylanFGKEGRANGWFRLAFTLGKKRCLPWRSFCTASTVLESEALETDFPKIRSGTAALRLAYVFTGQGAQWAQMGLELFQFPTFKQSVVAADSHLKKLGCPWSV  
 VEELQRSGAESNIHVSWYSQTLCTVLQVALVELLQSWGTPRSVVGHSSGEMAAAFAIGALAREDAWKIAYWRGKLSELTERAPDLSGAMMAVGASHEQAQKWVEGLTRGKCVVACI  
 NSPSSVTSGDDAGLDELAAMLKEKEVFARKLKVTAYHSHHMVKVAEAYHDVLKDVEVRNPDTGPQMFTSVSETLVNPSDLASHWVANLVSPVLFNSNTVAELARAKTPKDQATGS  
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 SSFI GLPMPSFVANEHIWRGFLRLEHPWPWVRRHHKMQSALFPAGGLAMAIEGASQFQGKDNRSVAKGYKLRDVRIDSATLVEESNIEHILQLRPHDTARSQQTDSYDGWWEFKISTSAGSD  
 ESLKCNCYGLTVFEEQLIHPHASKASSTTVQQAEAFYERLESVGLEYGPSFQAIKTILHSSGGQTEGEIEIMIDVNSTTPGGSDGRPYVHPTTLEALFQMAAYAFDNQSDGVKKALLVT  
 DIEELLDASISHTPGARLQT SARSSLRGFREMLADVTSPASNAGGISVRGLTC VEMPSTAGVNSDVGITGREGYDSMLS KFVWKPALNLLSATEREHLLIAATKVTDAETEAILAREAAD  
 FQNVKSALQASQRGKTGSLKLRNALWKISQELPDAKVFGKALENVSQDGQGAGPTGPIVDVLSGTSTPDVLLSGYGYGSTEKF LAALPGVKVSLQKMYQLSIMAHENPDLAVLEIGSGSSG  
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 TQASSLLWVTG IPEPHASTILGFARVVRFEIPSLDFRVLTD PATIEDAKNSI HISQVQR SKSPDKEYKELDSIVHIPRVTV DASLNHQ ISNLCLSE AIESKPLGSLERPQKLCIRNP GMLNTLCF  
 QADNVSENE LQDDEVE VRVMASGLNSKDV MVALGH ITDTHL GLEASGV VLRVGASV THLQLGD KVVM LANGA HRTT LRGKA AV CQKIP QDMTYEEAAGFPFAYCTAY TLLHVLRAQ  
 SGQS VLIHAAAGAVGQALVRLAQHLGLEVFTTAES ADDRAF VQELLGLFPD RIYHPQDKGLVQH VMRITGDVGVDFIVNPLS VEEIADSLNCLADFGTFV EMGMENDSRHSTLNTRLFR  
 DTTF VAVNLQ RVLELRPKLIGE ILQK ALGLF QDGQ KV SPSN VP SEAA AIQMFQ DNRHG KITL SYSS ED FV SVLQ NPKD SLK LSPD NTYLIAGGLGGI GRS LATLLVDCGARH IAMVS  
 RSGV TSVEQQQLIDNL SERGAKIGVYKCSIGDANALGRALTQCASEMPPIKGIIHS AVF RD AVLHNMTYK QW DELLDGKL RG SWNL HALTTSYNLDFFLCIGSFMAIIGGIQS NYAAGSA  
 FQDGLAHLRQSQGLPAV TIDLGIVKGF GAVEE QGAVGHTLE WREPFGVSE PEVHALIKG ALLGQ RGNW ALDV PAQMIN SIPTGGMVRSSGVSPYYFDDPRFSIMA KIGMDSEN SDTQ  
 ASVSLKELADAESSDDA VLFV TGA VISKVAKL M QVA EEE IDTG KSL HAYGV DLS VAVE YV SWAK KEVS ADITV FDV M ASK PIMS FARD LVKG KGK WGA AIPACKS

**Figure S13.** The amino acid sequence and domains of TpeA which were identified using SMART as follows: KS (green), AT (pink), DH (yellow), ER (cyan), KR (orange) and ACP (red).

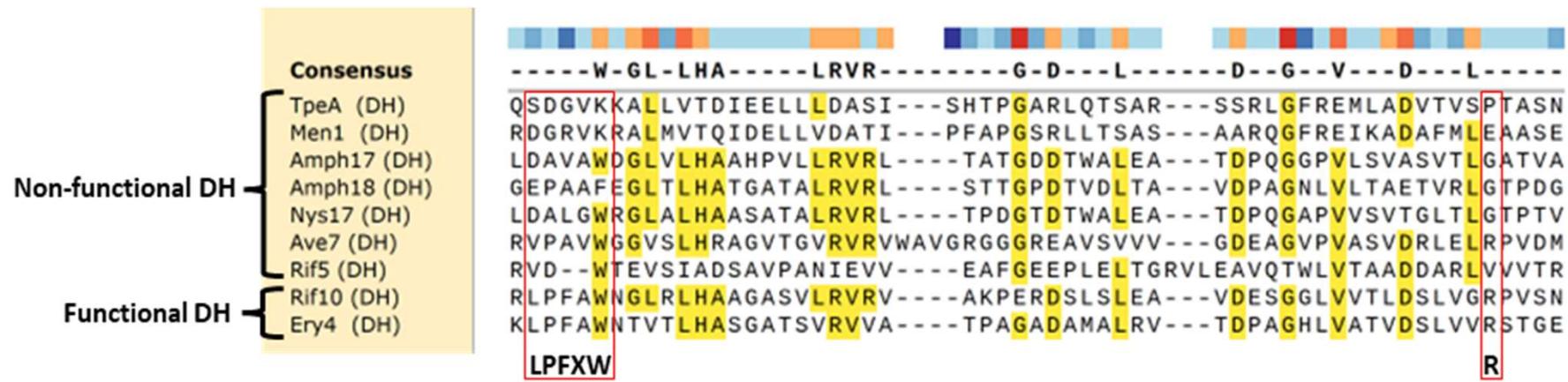


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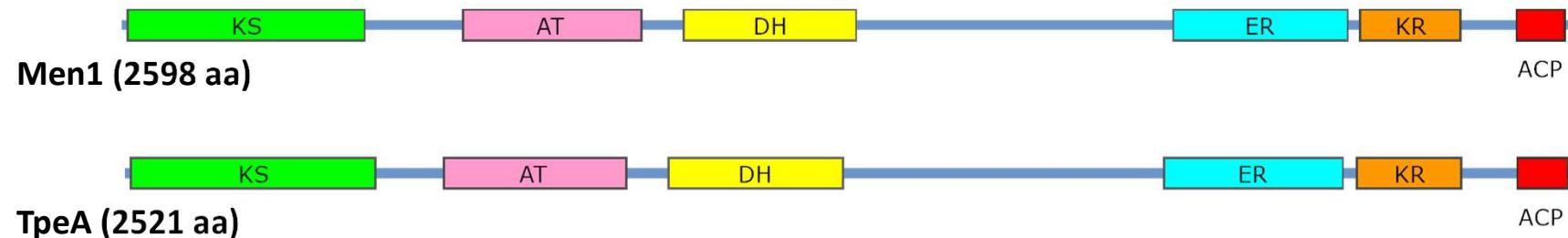
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DSAAQPTVVGVCGGLLLGA AAAATARDINELLDIGRKLVDFSNLGVAQWKRAMDIEGKPGRWAVAIVNVPPKQIRNIITAFNEDMAIPKHRQFYISFLAKGWAAISGPPS
IFPELWEYSSTLSSASKMDPLGTPAHAAHLRSLNIEELIGSGSVLDL PVRQDRLVISTSTCKPFESQTFGSLLSS LHDTGETLHIAGVNDYVASCLSRETLVQVSSFGPTSQIG
SFKA LE DSG LV DLDL SV PES KTPN LLKN PD AR DG SN MIA I VG QSV RL PG SDD V KTF WEN LKAG QTF ESE I PP SRFD LQ NY DTT GAK SS VTR FGH FLD R PGL FDC RL F
NVSPREAKQMDPIQRLLL MCSYEALQTAGYSPDSSLSTNRMRVATYFGQSGDDWRQGRASQDVDIYYIPGTIRSFA PGKLN YHYK WGGG NYSV DSACA ASTT SVIMAC
NALLGRECDMALAGGGQLHLE PENYAGLSRAGFLSKTTGGCTFREDADGYCRGEIGVVVLKRLEDALADNDNVLA VV RGA DRN YSWDASSI THPSANAQATVIQRV
LRNTGVEPADIGFVEMHGTTAGDSVEMKTVTTVFGSRPKDNPLYIGAVKANFGHGEAAAGITSLLKAVQMLGQKTIPRQPGFPGPKDPTFDHLDAMNIRIPDSSFPFP
TPTRPFSQDGKMRILVNNFDASGGNNCVLLEAPDKNVSQIQDPRQYYTAISARTTKSLQKNMERLSDYLVKHPDTPVADVAYTSTARRIHDLKRSYTVDSTESLVGLLQ
ADLKKDLTGIRPATPRSVVF AFTGQGSQYSGMTKQLFETCTPFR ES VQLHD LAVWQDFPSFLNLFTDDVTDEISASPIQTQLAIVVLEMS LANLWKS WGVEPD L VIGY SLG
EYVALYVSGVLSAHDVLFVGNRAQLMDERCEIGSYSMLAVQASPEDLEEPLKAYPTS NVACRGAPRSTV VSGP SEDIAKLHAE LKEK SI GTILNPVYGFHCAQVDP ILED F
RDLLDRVPFSKPRIPVASSLDGVITDDDVFSPSYMVRQTREP VAFV SALKAI ETSHL DNTSLW VIEGP KRV LNSFI KATLAVDHD RLLHSVDEK ASN WRTI AITACWQG
GVSIKWQNHFHQFTKHLRLV DLPTYAFDLKD YWI EPA API VQQRSAEPLRQV AVPAVPGFPTASLQ RV REERI QGDNA AVTFESTL SHPD LMGL IRGH QVNGV DLPAS
GWWD MAYTA AKYIH RI QPSR GAAP GLS MLD CSITHPL MPSASED QQK LVI VAKK QAG SSV E VSF KSQ EK SVE QDH GSCK IRF ESKADWEA EWSR AFIKA AKNNV
VTNATRPDG NGHKLPKPV VYTLFSNFVN YSGDFKG IQQV YLNADF QREV VADV VL PAGM YNF NLNP YWSD ALI HACG FMLH SDP DLPT QDCFLNG FEELRF LMDLL
PGV PYTSV FMHD TN SQEVPA KTRN VTGDI YIFQ GEKIV GTVQ GV V FQL T KRIL TT ILG KSQ DH HSNE VRNG NATT TNPPA HATT QSFF APPG IKPA VAFSSA PATV
GEETA EAVIA KILT KTGAN RASL SE TTLGEIGLDS LEWIELVGVFRS ALDIE VPASFFF EYPKV LRLR QIAEL PLEG EKEE SGSSSPD SPYGM LTPAT GRFT PIT ASR STH NSDG
PANYANIVLDIVLSQTGFDKDDVL PSTR FDDM GLDS LCTMEV VSLV RE QTGL DPAS FFHHPT VAD VRK NLG PNT EDK SKD SVK ASASIA VSEPATELV VV VH PGN SPAP
ESLPII DEDLKDYH CDF FLMQGSS DSAE IPMFL LPDG TGYP AVLLKLPV FKGD NPLFT CKS PLLH RAEG REVACTIEGL ALSY AE AIRR TRPH GPYLLAGY SLGA AYAYEVAKIL
ADAGEIVQG LLF VDFN MAAS VGLEH RER KPVPTN LVG VM EQV GWMNGI HNDE KNF HIPP APPKIKF HALS VF KSLTRYFPKPM TPS QR PRNTY ALWAGAG MEDLLG
PSNAGFLPEFGIIDWQMGSRRENNGPAGWENFIGGPVRCATVPCDHLSIMMSTDWV GTT ANI KDL LEDAL SNP GTP

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**Figure S14.** The amino acid sequence and domains of TpeB which were identified using SMART as follows: SAT (yellow), KS (green), AT (pink), PT (cyan), ACP1 (red), ACP2 (red) and TE (orange).

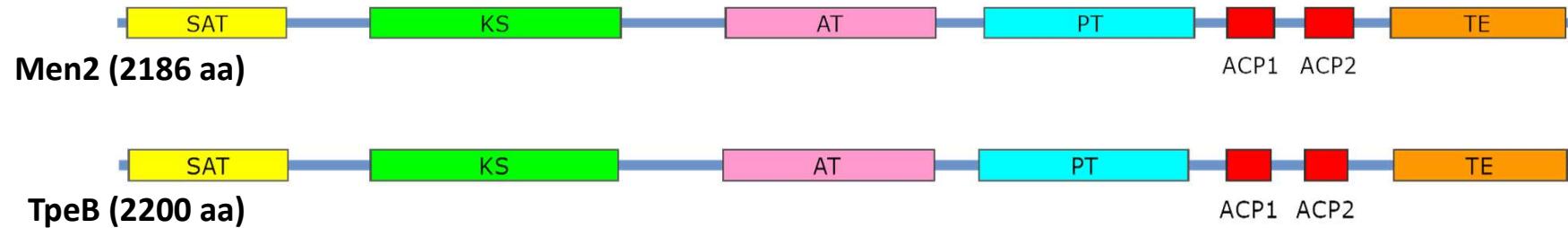


**Figure S15 :** Protein sequence alignment of the predicted site in DH domains for ACP interaction of TpeA and other functional and nonfunctional DH domains including Men1 and modular HR-PKs such as Amph17 (AJE44526) and Amph18 (AJE39059) from *Streptomyces nodosus*, Nys17 (AAF71767) from *Streptomyces noursei* ATCC 11455, Ave7 (BAA84478) from *Streptomyces avermitilis*, Rif5 (AAC01711) and Rif10 (AEK39124) from *Amycolatopsis mediterranei* S699 and finally Ery4 (CAM00064) from *Saccharopolyspora erythraea* NRRL 2338.



**Table S1.** The similarity of TpeA domains to their counterparts in Men1.

Domains	Size (aa)	Similarity to Men1 domains	E-value
KS	428	79.72%	0.0
AT	318	76.49%	5e-170
DH	302	50.00%	2e-89
ER	313	42.54%	2e-85
KR	181	77.90%	2e-93
ACP	85	70.59%	7e-32



**Table S2.** The similarity of TpeB domains to their counterparts in Men2.

Domains	Size (aa)	Similarity to Men2 domains	E-value
SAT	241	73.75%	7e-113
KS	376	79.79%	0.0
AT	320	68.75%	4e-159
PT	318	58.62%	5e-134
ACP1	67	64.18%	3e-27
ACP2	65	83.08%	8e-36
TE	262	78.16%	4e-132