Phylogenetic analysis

General overview

Table S1: Detailed information about the enzymes used in the phylogenetic analysis

Lable	Species	Accession Numbers / Peptide reference	Main Product
	Antrodia cinnamomea [1]		
AcTPS4		EIW57364	zonarene
AcTPS5		EJF64719	T-cadinol
AcTPS7		EIW53985	nerolidol
AcTPS9		EIW57365	1-epi-cubenol
	Armillaria gallica [2]		
ArmGa1		P0DL13.1	Δ-6 protoilludene
	Boreostereum vibrans [3]		
BvCS		AMW90891	δ-cadinol
	Coprinus cinereus [4]		
Cop1		XP_001832573	germacrene A
Cop2		XP_001836556	germacrene A
Cop3		XP_001832925	α-muurolene
Cop4		XP_001836356	δ-cadinene
Cop6		XP_001832549	α-cuprenene
	Coniophora puteana		
Copu1		XP_007772164	---
Copu2		XP_007771895	β-copaene
Copu3		XP_007765978	cubebol
	Fomitopsis pinicola [5]		
Fompi_84944		EPT01290	α-cuprenene
	Lignosus rhinocerus [6]		
GME3634		KX281943 / ASK39765	α-cadinol
GME3638		KX281944 / ASK39768	δ-cadinol
GME9210		KX281945	2H-2,4a-ethanonaphthalene
	Omphalotus olearius [5]		
Omp1		MUStwsD_GLEAN_10001317	α-muurolene
Omp3		MUStwsD_GLEAN_10003938	germacrene A
Omp4		MUStwsD_GLEAN_10005581	δ-cadinene
Omp5a		MUStwsD_GLEAN_10000810	γ-cadinene
Omp5b		MUStwsD_GLEAN_10000811	γ-cadinene
Omp6		MUStwsD_GLEAN_10003820	Δ-6 protoilludene
Omp7		MUStwsD_GLEAN_10000831	Δ-6 protoilludene
Omp9		MUStwsD_GLEAN_10000543	α-barbatene
Omp10		MUStwsD_GLEAN_10000292	trans-daucadiene
	Stereum hirsutum [7]		
Stehi_128017		XP_007299839	δ-cadinene
Stehi_159379		XP_007306912	β-barbatene
Stehi2		XP_007301467	Δ-6 protoilludene
Stehi6		XP_007308318	Δ-6 protoilludene
Stehi7		XP_007299456	Δ-6 protoilludene

Detailed amino acid sequences

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KQLPSFGAAALDDAVAKYVAAMEHWVIGNLEWSFESQRYFGAEHTRVKATRVVVLSPADEN

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PQRVRA

>AcTPS7
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RLVPFNELDRVVTAELLSLHRGQGLELLWRDSLQCPTEEEYVSMVNNKTGGLFRVAVKLMMACSTTNI
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>AcTPS9
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DN

>ArmGa1
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VDGFHL

>BvCS
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>Cop1
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DTSGCKPCWALIEYANNLDLPDEVMDHPVVRSLGEAANDLVTWSNDIFSFNVEQSKGDTHNMIPVVMH
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TPAVRVLA

>Cop3
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>Copu2
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SESE
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>Stehi2
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>Stehi6
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Sequence analysis

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Copu2           -MSTMDPSEFILPDFFATCPFAFGRTNPHADVVIPEAHAWIVKHVPFVDRKRDEFIQDGF 59
Copu3           MSATPAPTEFILPNLFSVCPLTFGRSNPYYDEVIPEARAWIAKYNPFVDSKRAEFVQGCN 60
                        :* **::*: **:  . :**  . .  *::*** ..  *
                                           D(D/E)xxD
Cop4            ELLCSHVYAYAGYEQFRTCCDFVNLLFVVDEISDDQNGQDARATGRIFVNAMRDAHWDDG 117
Copu1           -GLAWHCDPWAGKEGFRTICDFQNLLFLMDELTDEMSGEDARVVGESFIRVLKDPSVDNE 106
Copu2           QDLMPHCYPWAGKETLRTMCYLNNLLFLVDDLTDDMNSDEARGFGESFIRVLNDPAVHDS 119
Copu3           ELLCSRVWPYAGREEFRTCCDFVNLLFVLDELSDDMGGADARSTCDSFIRVLNDPDAPDT 120
                  *  :   :** * :** * : ****::*:::*: .. :**     *:..:.*    :

Cop4            SILAKITHEFRERFVRLA--GPKTVRRFADLCESYTDCVAREAELRERNQVLGLNDFIAL 175
Copu1           SIIAQATREFRTRIADDVATKSVWFGRFVAICKSYADATYIEAEHRENNRVLDLDDFVIA 166
Copu2           SQVMQATREFRSRITGTGVTESRWFGRFLAIFKLYINAVCAEAEDRENKRILDLDTFTVA 179
Copu3           SLIAQMTREFRARVAERA--KPGCLRRFIALCGTYVEAVCVEAELREQGRVLDLRSFILL 178
                * : : *:*** *..         . **  :   * :..  *** **. ::*.*  *
        Pyrophosphate sensor                            (N/D)Dxx(S/T)xxxE (NSE)
Cop4            RRQNSAVLLCYSLVEYILGIDLDDEVYEDPTFAKAYWAACDFVCWANDVYSYDMEQAKGH 235
Copu1           RRENSAVRCCFSINEHALGIDLPDSVFEDPEFLRMYFDAVDMIVIVNDVYSYNMEQAKGL 226
Copu2           RRENSAVMVFFAITEYALGIDLPDAVYEDPTFLRVYADSADMVILVNDVFSYNREQAKGL 239
Copu3           RRENSAVRCCLALAEYALGLELPDAVFNDPAFQSVYFCAADMVCWSNDVYSYNMEQAKGH 238
                **:****    :: *: **::* * *::** *   *  : *::   ***:**: *****

Cop4            TGNNVVTVLMKEKDLSLQEASDYIGRECEKQMRDYLEAKSQLLQ-STDLPQEAVRYIEAL 294
Copu1           AGNNVVTVLEQALGVDLQAAVNRGGEMFAQKMEGYVRGRGVPPSWGAKVDADVEHFFDSV 286
Copu2           DGNNNITVLMQTLDLDLQAAVDHVGEMFSQKMEGCMRGRAMLPSWGVKVDADVERFFDAL 299
Copu3           TGNNVVTVLMQEHGIDLQAAADRVGEVFGQLMEHYTSGSRSLPTWGGKVDADAARFLEAA 298
                 *** :*** :  .:.** * :  *.   : *.    .       . .:  :. :::::

                            RY-dimer
Cop4            GYWMVGNLVWSFESQRYFGAQHERVKATHVVHLRPSSVLEASCDSDSDSDC          345
Copu1           DQWIVGNLEWSTETSRYLGPDHEEIMKTGRVVLRKIESKTK----------          327
Copu2           DQWVVGNLEWSSQSPRYLGPEHEEIMRTRRVVLRKVETEIE----------          340
Copu3           GQWVVGNLEWSFETPRYFGPDHDEVRDTHRVLLK-----------------          332
                . *:**** ** :: **:* :*:.:  *  * *:
```

***Figure S1**: Alignment of Copu1-3 and Cop4 (as reference) amino acid protein sequences. Typical signature motifs for class I terpene cyclases such as the highly conserved NSE-triad and the aspartate-rich D(D/E)xxD motif are highlighted. Additionally, a highly conserved arginine residue 46 AA downstream of the NSE motif, which is indicated as pyrophosphate sensor and a common conserved RY-dimer ~80 AA downstream of the NSE motif, close to the C-terminus is found in all four sequences [8–11].*

Enzyme modelling

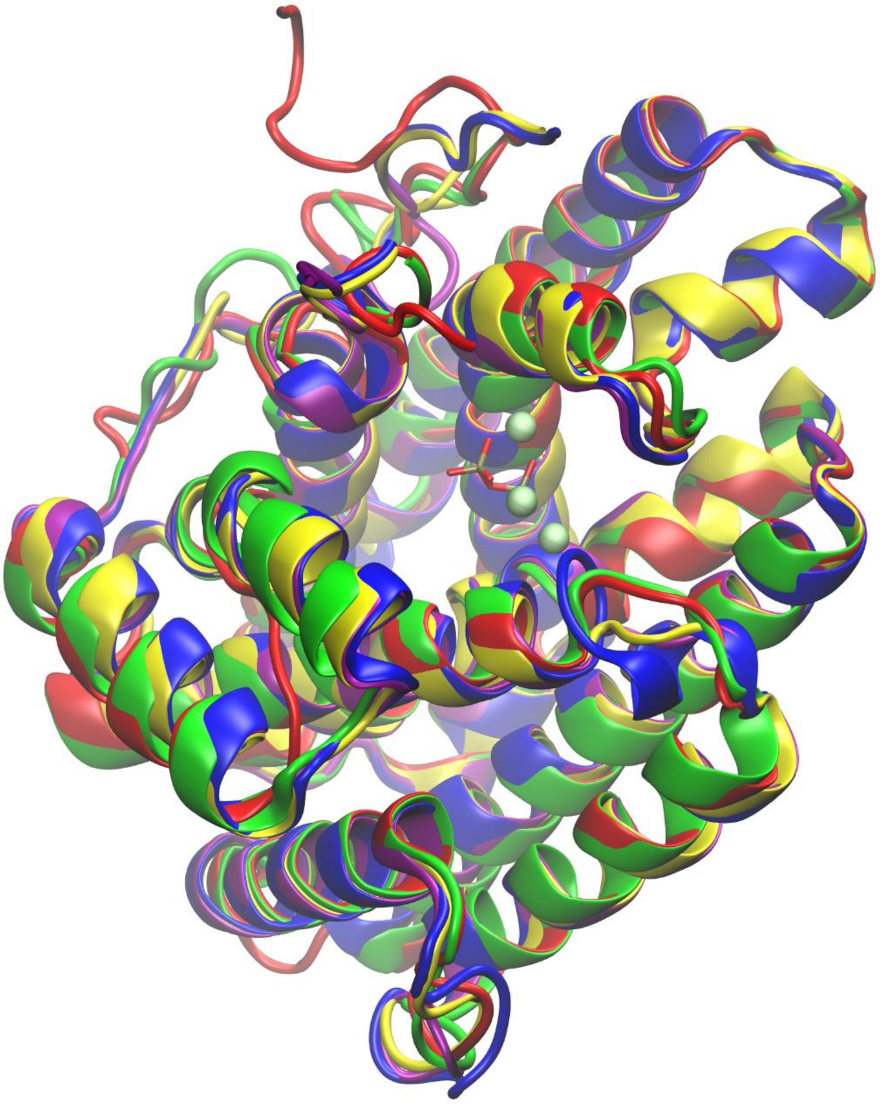

Figure S2*: Homology modeling and structural alignment of selinadiene cyclase (blue), Copu1 (red), Copu2 (green), Copu3 (yellow) and Cop4 (purple).*

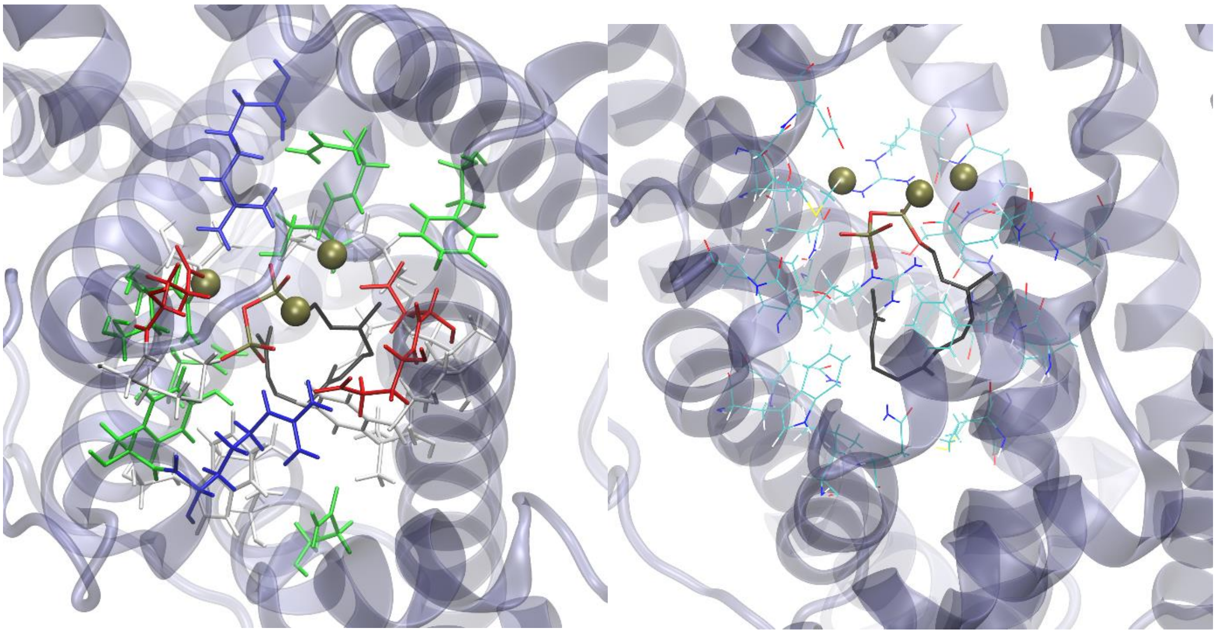

***Figure S3**: Structure function analyses of copu3 revealed reliable positioning of FPP in the active sites cleft. Amino acid sidechains in close proximity (5 Angstrom) to the docked FPP molecules (black) are shown. Sidechains are colored based on their physico-chemical characteristics (hydrophobic - white, alkaline - blue, acidic -red, polar - green).*

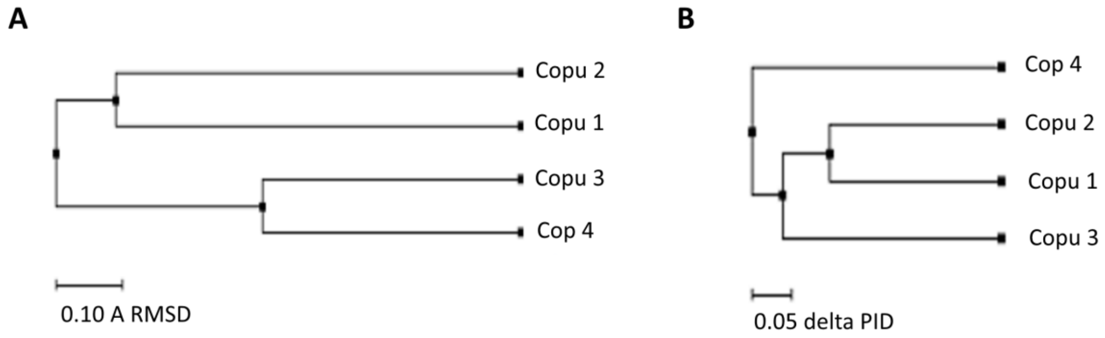

***Figure S4**: Structural identity analysis (RMSD calculation) (**A**) and sequence identity analyses (**B**) of the Copu1-3 and Cop4 sequences. Sequence identity analysis strictly differentiate sequences from distinct organisms while the structural analysis (RMSD calculation) revealed a close structural relation between Cop4 and Copu3.*

Structure analysis and quantification

NMR spectra

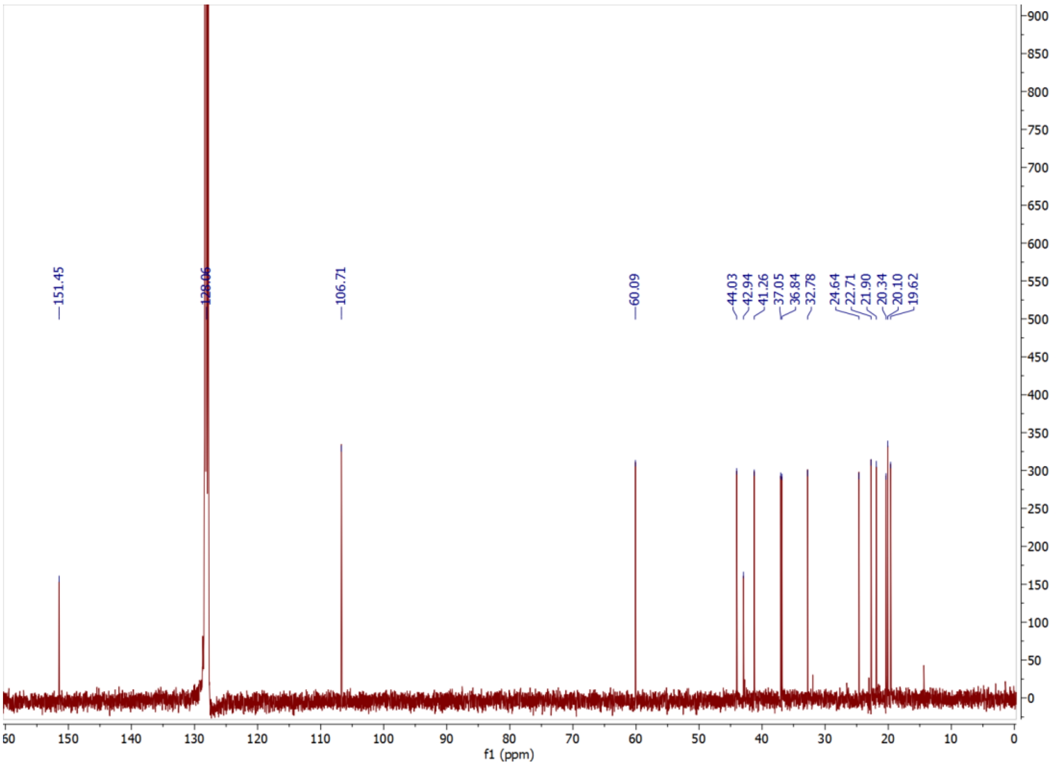

Figure S5: *β-Copaene ^{13}C NMR data recorded in C_6D_6.*

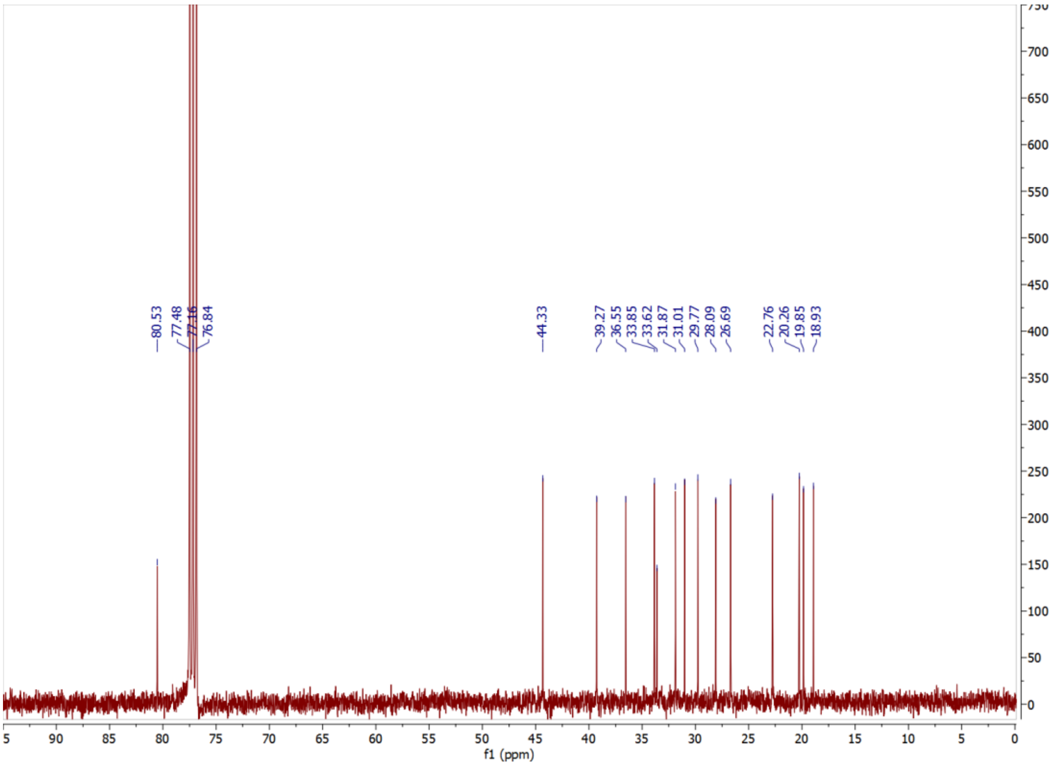

Figure S6*: Cubebol ^{13}C NMR data recorded in $CDCl_3$.*

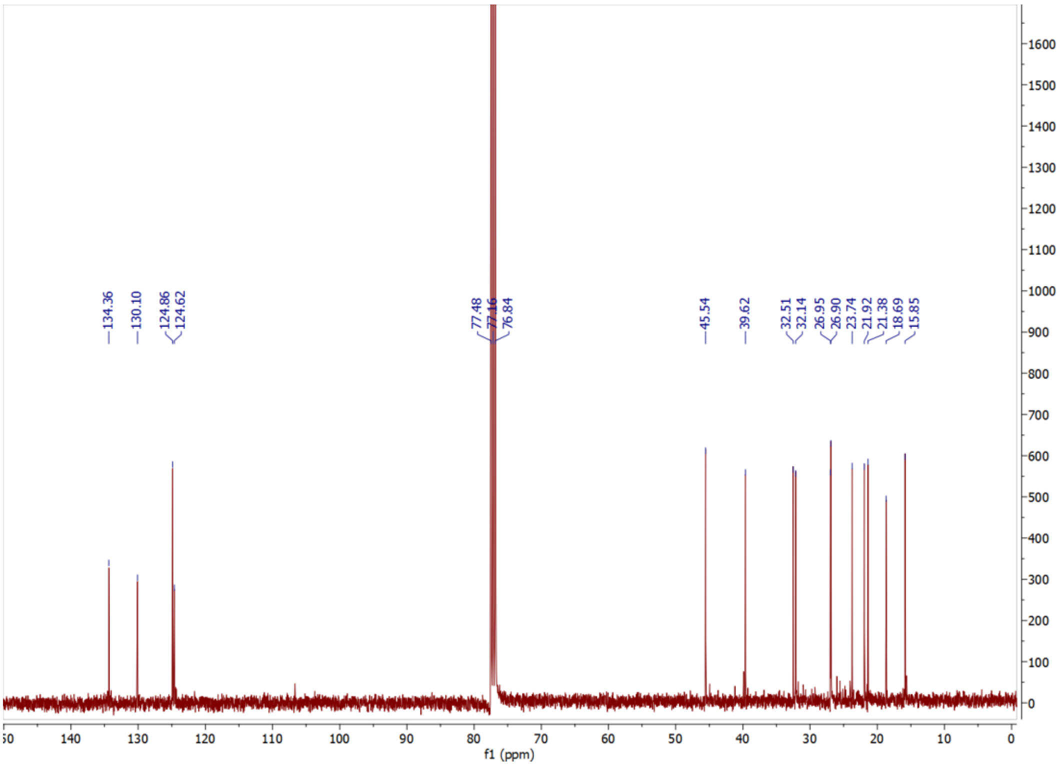

Figure S7: *δ-Cadinene ^{13}C NMR data recorded in $CDCl_3$.*

Terpene quantification

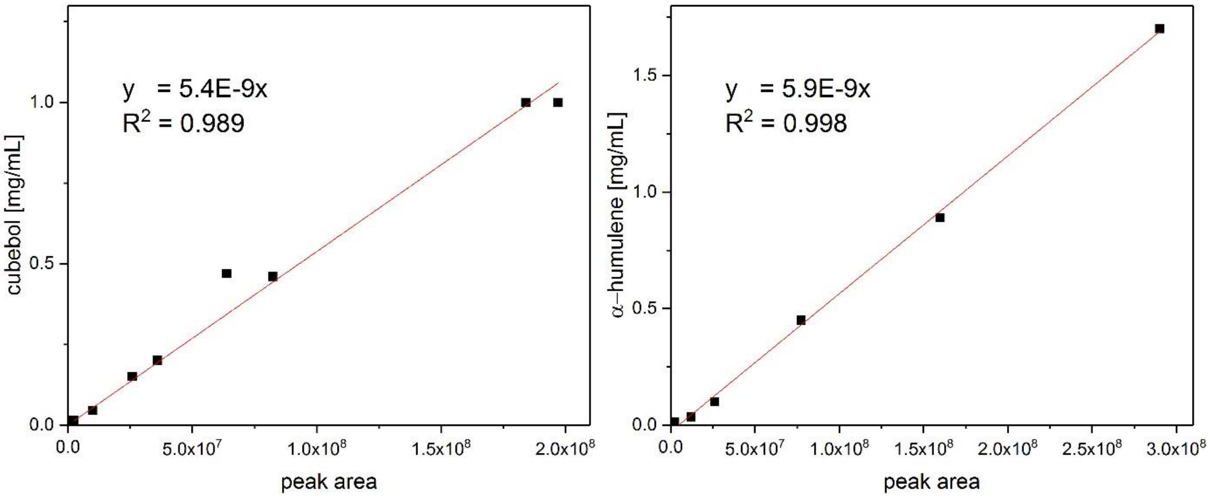

Figure S8: *Calibration curves for GC-FID based sesquiterpene quantification. Different concentrations of cubebol and α-humulene were used for peak-area evaluation via GC-FID.*

References

1. Lin Y-L, Ma L-T, Lee Y-R, Shaw J-F, Wang S-Y, Chu F-H. Differential Gene Expression Network in Terpenoid Synthesis of Antrodia cinnamomea in Mycelia and Fruiting Bodies. J Agric Food Chem. 2017;65:1874–86. doi:10.1021/acs.jafc.6b05386.
2. Engels B, Heinig U, Grothe T, Stadler M, Jennewein S. Cloning and characterization of an Armillaria gallica cDNA encoding protoilludene synthase, which catalyzes the first committed step in the synthesis of antimicrobial melleolides. J Biol Chem. 2011;286:6871–8. doi:10.1074/jbc.M110.165845.
3. Zhou H, Yang Y-L, Zeng J, Zhang L, Ding Z-H, Zeng Y. Identification and Characterization of a δ-Cadinol Synthase Potentially Involved in the Formation of Boreovibrins in Boreostereum vibrans of Basidiomycota. Nat Prod Bioprospect. 2016;6:167–71. doi:10.1007/s13659-016-0096-4.
4. Agger S, Lopez-Gallego F, Schmidt-Dannert C. Diversity of sesquiterpene synthases in the basidiomycete Coprinus cinereus. Mol Microbiol. 2009;72:1181–95. doi:10.1111/j.1365-2958.2009.06717.x.
5. Wawrzyn GT, Quin MB, Choudhary S, López-Gallego F, Schmidt-Dannert C. Draft genome of Omphalotus olearius provides a predictive framework for sesquiterpenoid natural product biosynthesis in Basidiomycota. Chem Biol. 2012;19:772–83. doi:10.1016/j.chembiol.2012.05.012.
6. Yap H-YY, Muria-Gonzalez MJ, Kong B-H, Stubbs KA, Tan C-S, Ng S-T, et al. Heterologous expression of cytotoxic sesquiterpenoids from the medicinal mushroom Lignosus rhinocerotis in yeast. Microb Cell Fact. 2017;16:103. doi:10.1186/s12934-017-0713-x.
7. Quin MB, Flynn CM, Wawrzyn GT, Choudhary S, Schmidt-Dannert C. Mushroom hunting by using bioinformatics: Application of a predictive framework facilitates the selective identification of sesquiterpene synthases in basidiomycota. Chembiochem. 2013;14:2480–91. doi:10.1002/cbic.201300349.
8. Dickschat JS. Bacterial terpene cyclases. Nat Prod Rep. 2016;33:87–110. doi:10.1039/c5np00102a.
9. Rabe P, Schmitz T, Dickschat JS. Mechanistic investigations on six bacterial terpene cyclases. Beilstein J Org Chem. 2016;12:1839–50. doi:10.3762/bjoc.12.173.
10. Baer P, Rabe P, Fischer K, Citron CA, Klapschinski TA, Groll M, Dickschat JS. Induced-fit mechanism in class I terpene cyclases. Angew Chem Int Ed Engl. 2014;53:7652–6. doi:10.1002/anie.201403648.
11. Leeper FJ, Vederas JC. Biosynthesis: Aromatic Polyketides, Isoprenoids, Alkaloids. Berlin, Heidelberg: Springer-Verlag Berlin Heidelberg; Springer e-books; 2000.