

Figure S1 Concentrations of methylperillate and pathway intermediates in *Salvia dorisiana* plant parts. Highest concentrations were found in the small leaves. Error bars indicate standard deviations (n=3).

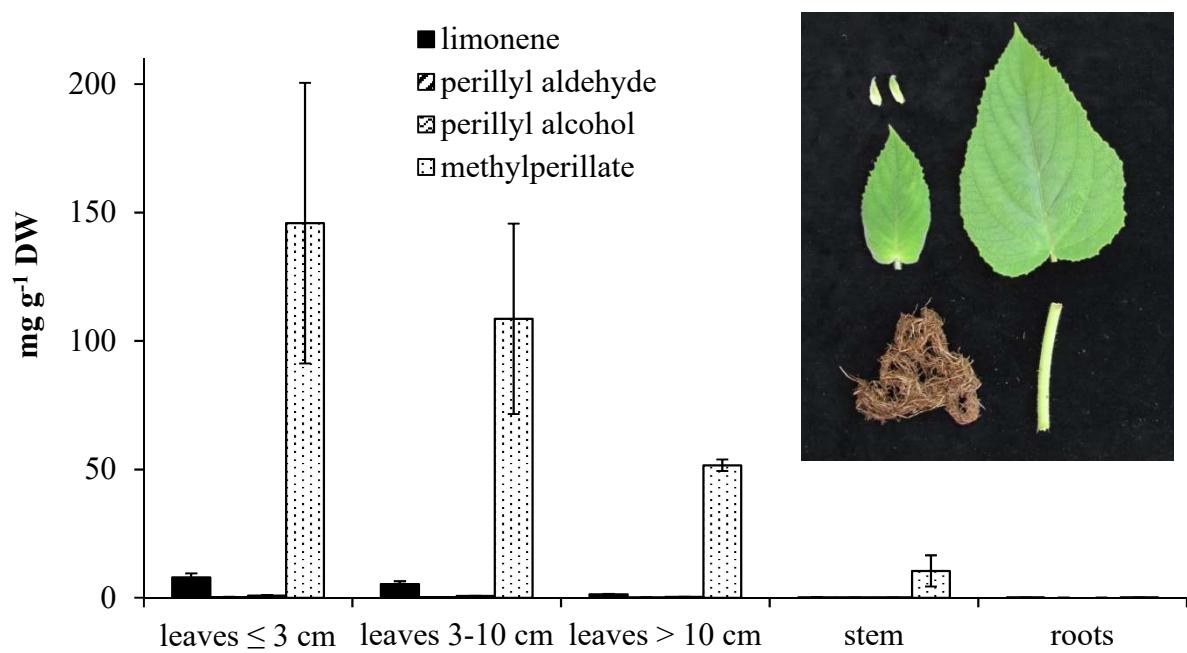


Fig. S2 GC-MS chromatograms on enantioselective column. *Salvia dorisiana* trichomes and young leaves contain exclusively the (-)-limonene enantiomer. m/z 68-69+136-137. RT 10.32-10.37 (-)-limonene, RT 11.22-11.25 (+)-limonene, RT 11.37-11.39 phellandrene peak visible in *Salvia dorisiana* chromatograms. Phellandrene was identified by its mass spectrum. In both (-)- and (+)-limonene standards a minor contamination from the other enantiomer is visible.

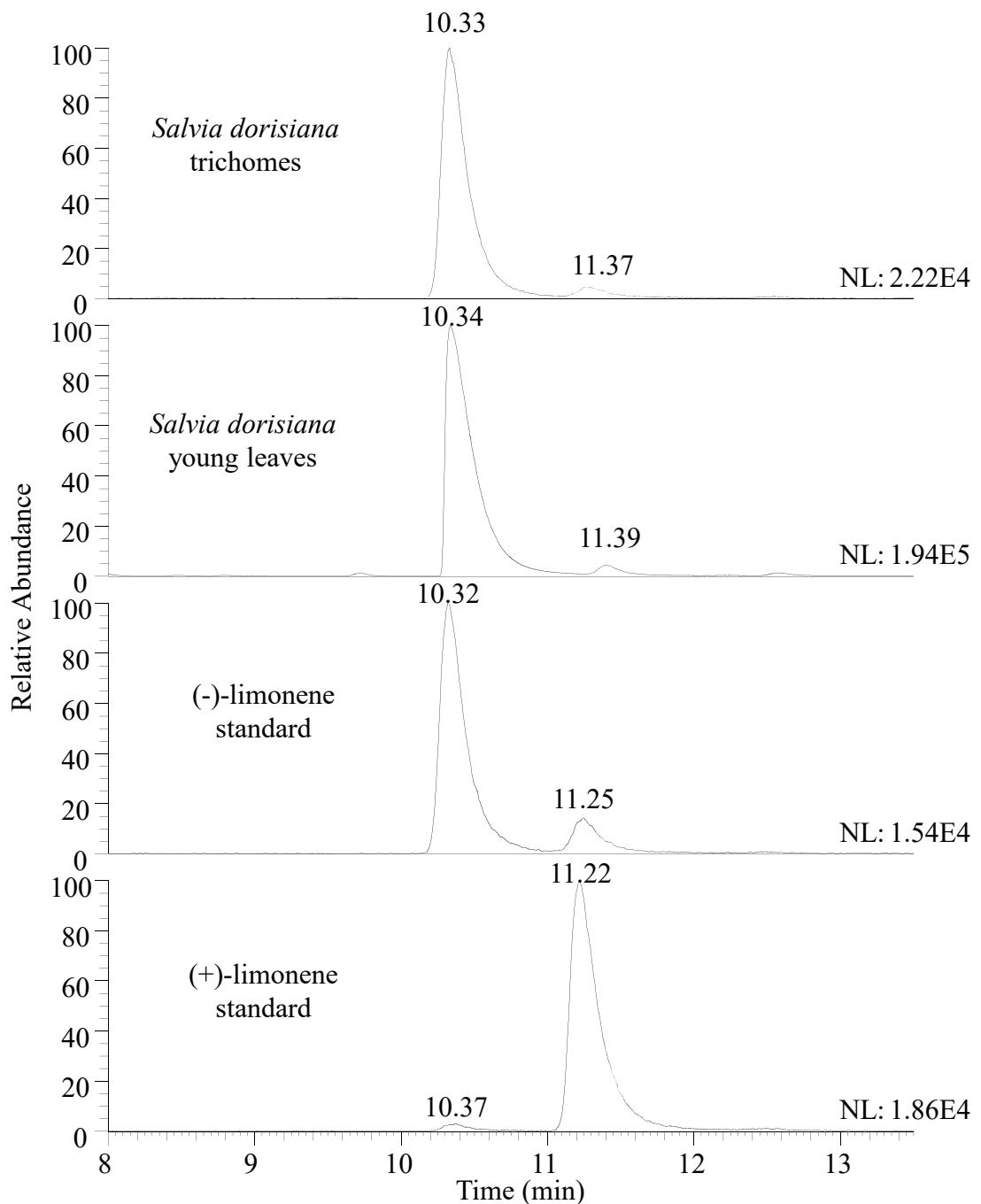
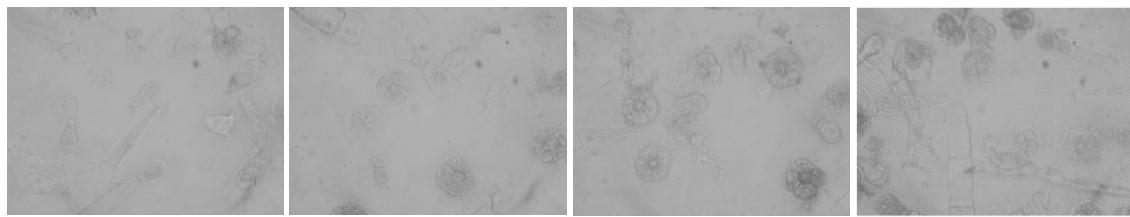
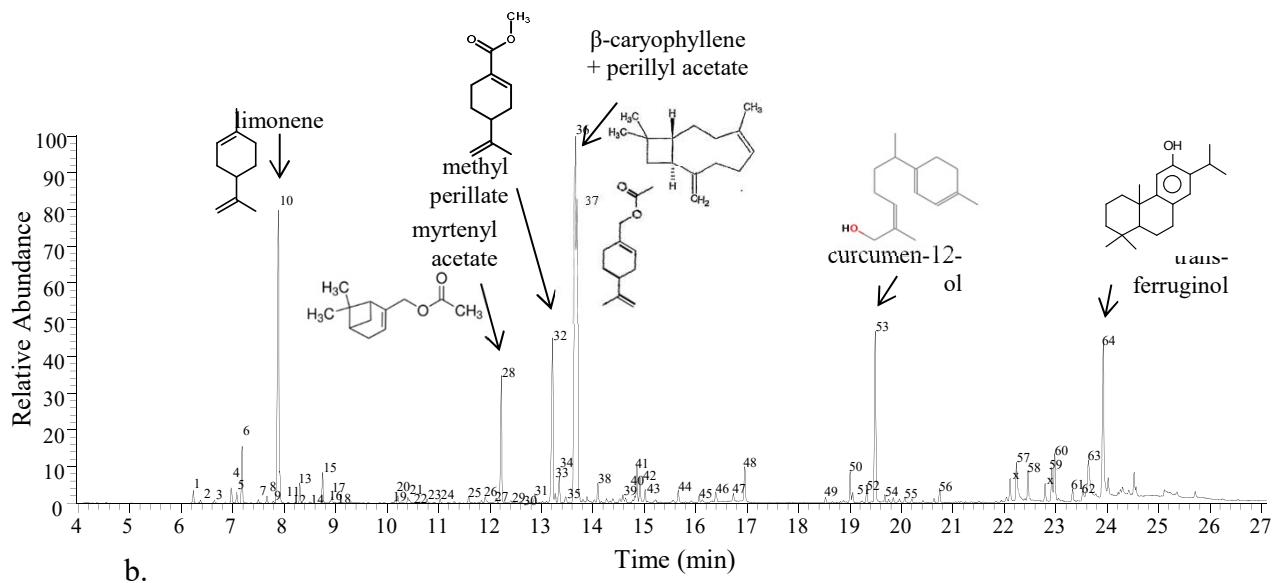


Fig. S3 Isolated *S. dorisiana* trichomes. a. light microscopy analysis, b. GC-MS chromatogram of isolated trichomes TIC NL 2.90E7. Peak annotations are provided below. Peaks have been identified by their MS spectrum by comparison to the NIST library. Peaks 10, 25, 26, 32 have additionally been identified by comparison to original standards.



a.



b.

1 α -thujene, 2 α -pinene, 3 camphene, 4 sabinene, 5 β -pinene, 6 myrcene, 7 α -phellandrene, 8 α -terpinene, 9 p-mentha-1,3,8-triene, 10 limonene, 11 trans-B-ocimene, 12 2-methylbutyl butanoate, 13 γ -terpinene, 14 trans-4-thujanol, 15 terpinolene, 16 linalool, 17 butanoic acid, 2-methyl-, 2-methylbutyl ester, 18 cis-4-thujanol, 19 isopinocamphone, 20 terpinen-4-ol (internal standard), 21 α -terpineol, 22 8,9-epoxy limonene, 23 B-cyclocitral, 24 p-mentha-1,8-dien-10-ol, 25 perillyl aldehyde, 26 perillyl alcohol, 27 methylgeranate, 28 myrtenyl acetate, 29 bicycloelemene, 30 α -copaene, 31 geraniol acetate, 32 methyl perillate, 33 3-carene, 34 limonene-10-ol, 35 α -gurjunene, 36 B- β -caryophyllene, 37 perillyl acetate, 38 α -humulene, 39 dicyclogermacrene, 40 d-amorphene, 41 α -thujopsan-2-ol, 42 farnesol, 43 α -bisabolene, 44 caryophyllene oxide, 45 limonene-10-ol, 46 α -longipinene, 47 α -bisabolol, 48 6-A-hydroxy-germacra-1(10),4-dienepropanolyl-1H-inene ate, 49 1,6,10,14-Hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (E,E)-, 50 trans-bergamota-2,12-dien-14-ol, (E)-, 51 1,6,10,14-Hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (E,E)-, 52 9(11),15-isopimaradiene, 53 Z- γ -curcumen-12-ol, 54 1,6,10,14-Hexadecatetraen-3-ol, 3,7,11,15-tetramethyl-, (E,E)-, 55 thujopsene, 56 16-kaurene, 57 diterpene, 58 4,5,6,7-Tetrahydroxy-1,8,8,9-tetramethyl-8,9-dihydrophenalenol[1,2-b]furan-3-one, 59 Podocarpa-1,8,11,13-tetraen-3-one, 14-isopropyl-1,13-dimethoxy-, 60 cis-ferruginol, 61 retinoic acid, 62 carnosol, 63 carnosic acid, 64 trans-ferruginol, x background (column material)

Figure S4 Separated *Salvia dorisiana* trichome fractions

Fresh *Salvia dorisiana* leaves of intermediate size were harvested (1-10 cm), and trichomes were isolated as described previously (Sallets et al. 2014), with following modifications: cutted leaves were shaken for 20 min 115 rpm. Trichomes were separated on size on different meshes, and flushed with washing buffer (Sallets et al. 2014): 350 um, 100 um, washed (100 um fraction was harvested: “type III and IV fraction”), 75 um and 45 um, and washed. The 45 um fraction was further separated by Percoll layers 10-30-60-80%, trichomes were harvested from the 30-60% interface and loaded on a 10-60% continuous sucrose gradient, trichome layer was visible in the light and harvested “type VI fraction”.

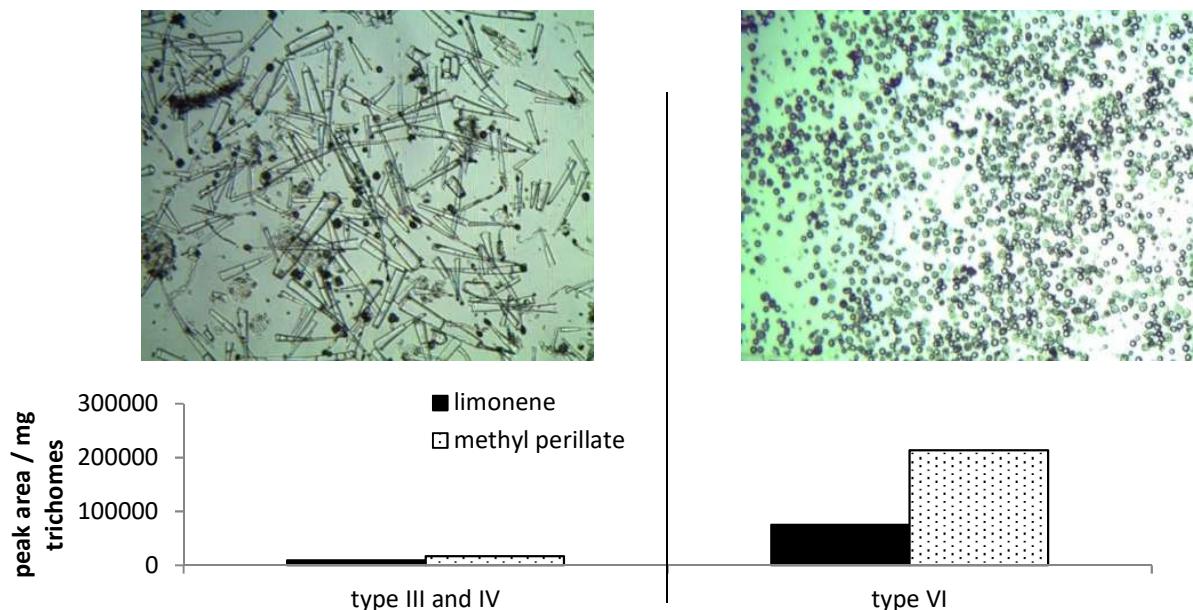


Figure S5 Protein sequence alignment and phylogenetic tree of monoterpene synthases. Colored lines indicate typical monoterpene synthase elements: green: plastid targeting signal (absent in SdSaS which has an in-frame stop codon 3 amino acids upstream of Met in the 5'UTR), orange RRX₈W motif and blue DDXXD metal binding motif

Sequence alignment of monoterpene synthases (SdLS, SdEuS, PfLS_KM015, SdPS, SdPCS, SdLis, CLLS_AF514, SdSaS) showing conserved regions and motifs. Colored bars indicate specific motifs: green for plastid targeting signal, orange for RRX₈W motif, and blue for DDXXD metal binding motif. Asterisks indicate conserved positions.

Block 1 (Amino acid positions 20-40):

*	20	*	40	*
SdLS	: -----	MSSIIIMQFAIPRGTSFISKVSSKQRRFTAASATSRG		
SdEuS	: MVDLQAAANSLVIM	SSIIIQFSIPRNTSFISNVSSKQRRFTAASATSQG		
PfLS_KM015	: -----	MHMAIPIKPAHYLHNNSGRSYASQLCGFSSTSTRAAIARLPL		
SdPS	: ----MSSFVMKMEI	PSGLPNHLHSSN-NESSKLY--SRRISTNAVSGPRL		
SdPCS	: ----MSSIIMMSMAI	PNKPTKHVNHYAKKYP-----KTQIASSQTGWRQS		
SdLis	: ----MSTISMHVPI	FSMPLNSLHNSKRRLS-----KPWPVCSILPAA		
CLLS_AF514	: -----MSSC	NPSTLVTSVNAFKCLP-----LATNKAIRIMAKY		
SdSaS	: -----			

Block 2 (Amino acid positions 60-100):

60	*	80	*	100
SdLS	: SQRARCSLQVDNEIEAERRTGGYQPTLWDFD	SIQSFEFEYKDKKKYPKKAA		
SdEuS	: SQRARCSLQVDNEIQTERRTGGYQPTLWNF	DSIQSFEEFYKDKEYPKKAA		
PfLS_KM015	: CLRFRCSLQASD---	QRRSGNYSPSFWNADYIILSINS	SHYKDKSHMKRAG	
SdPS	: CLRCSSQLSADQL-QIERRSGNYSPSRWDVDF	IQLSDFYKEERHMRRAG		
SdPCS	: CSLKRTADQTSDQIQSTRSGNYKPTLWD	DFRIQSITSVYTDEKYATRAS		
SdLis	: RLRAASCSSQQEE-AHQFERRSGNYQPSLWDF	NYIQSIKTPYKEEWHLNREA		
CLLS_AF514	: KPVQCLISAKYDNLTVDRRSANYQPSIWDH	DELQSINSNYTDEAYKRAAE		
SdSaS	: -----MEEVIRRSANYEASVWDDYIQSIALASP	YTGEKYAREAE		

Block 3 (Amino acid positions 120-140):

*	120	*	140	*
SdLS	: ALIEKVKMILLKEQ----	RLELIDDIRRLGISCHFRNEIDQILKSKYLE-		
SdEuS	: ALIEKVKMILLKEQ----	RLELIDDIRRLGISCHFRNEIDQILKSKYLE-		
PfLS_KM015	: ELIVQVKVMVMGKETDPVVQLELIDDIQKLALSHHVEKEIKEILFKISTY-			
SdPS	: ELIMQVKMMINNETGSVRQLELIDEIQLRLGSDHFQKEFKEIILNSIYLDN			
SdPCS	: ELVVQLKKLICQESNWIMQLELIDDIHKLGVSYHEDNEINQVILNRIYLEH			
SdLis	: ELIVQVKILLIKEKLEFVQQLELIDDIKYLGLSYFFHDEIKEILGFIHRCF			
CLLS_AF514	: EIRGKVKIAIKDVIEPIDQLELIDNIQRLGLAHRFETEIRNIIINNIYNNN			
SdSaS	: RIKDIVNILLINDTEKEIDQQLHLDINVQRLGLSGHFKDQIAKMDNDNIYEEQ			

Block 4 (Amino acid positions 160-200):

160	*	180	*	200
SdLS	: -----KNELDERDLYSTAIRFRILLRQYGENVSQDVFDCFKN-----	YKAN		
SdEuS	: -----KNELDERDLYSTAIRFRILLRQYGENVSQDVFDCFKN-----	YKAN		
PfLS_KM015	: -----DHKIMVERDLYSTAIAFRILLRQYGEKVPQEVFDCFKNNDNG-EFKRS			
SdPS	: KYKNEETKEERDLYSTAIAFRILLREHGFHVVAQEVLCKNEKG-DFKPN			
SdPCS	: -----KYCNNEERDLYSTAIAFR-LRQNGERVTQDVFDFFKNDDED-EFEES			
SdLis	: -----HDKEVDGSDLYLT-IGFRILLRQHGENVSQEVFDCFKNEGSDFKAS			
CLLS_AF514	: KD-----YNWRKENLYATSIEFRILLRQHGYPVSQEVFNGFKDDQG-GF---			
SdSaS	: E-----WLQNDLHFTSIKFRLRQHGYHVPQEVECSLMDEDG-NEKAS			

Block 5 (Amino acid positions 220-240):

*	220	*	240	*
SdLS	: -DFDTKGILLQLYEASFIA	THGEETLEIAKEFATKSILKKRVVDHEIDD---		
SdEuS	: -DFHTKGILLQLYEASFIA	THGEE---IAKEFATKSIMKRVVDHEIDD---		
PfLS_KM015	: ISSDTKGILLQLYEASF	FILTEGEMTLELAREFATKSIQEKINEKTIDDDDD		
SdPS	: LVDDTRGILLQLYEASF	FILTKGENTLELAREFATKHIQDKIDNKTD---		
SdPCS	: LGGDTIEGVILQLYEASF	FILTEGETSLEQARLFSENLIKKEIDDEVLDE---		
SdLis	: LGQDTKGMLQLYEASF	FILREGEDTLELARQFATENIQTIDDERGDEID--		
CLLS_AF514	: ICDDFKGILSIHEASYYS	LEGESIMEAWQFTSKHIKEVMISKMEED--		
SdSaS	: LSEDVRGLVSLYEASYI	SVEGESIMDLAKEESLTHITRRILDQITEPR---		

260 * 280 * 300

SdLS	: --IHFLSSVESALEFPShWRVQMPYAKSFIDAYKNRQDMNPVVLELAILD
SdEuS	: --IHFLSSVEAALEFPShWRVQMPNAKSFIDAYKRRPDMNPVVLELAILD
PfLS_KM015	: ADTNIISCVRHSLDIPHIHWRIQRPNASWWIDAYKRRSHMNPLVLELAILD
SdPS	: ---NLSTWIQYSLDIPHIHWRIQRANASMWINAYKERPDMDPVVLLELAILD
SdPCS	: ---FLSSLVRHSLELPLHWSQRPNARWEANAYSKKSQANPILLELAILD
SdLis	: --KNLISLWIQHSLEIPLHWRTPNLEAKWMIDAYSRRPDFNPTIL-LAKLD
CLLS_AF514	: --VFVAEQAKRALELPLHWKVPMLEARWFIFIHIERREDKNHLLLELAKE
SdSaS	: ---IKEQVRHALEVPLHWRLQKLEARWFIQAYEDTAEANRTLVELAKLE

* 320 * 340 *

SdLS	: INIVQAQFLEELKETSRWWESTGIAQELEFVRDRIVECYWTTGVIERRE
SdEuS	: INIVQAQFLEELKETSRWWESTGIAQELEFVRDRIVECYWTTGVVERRE
PfLS_KM015	: LNIEQAQFQQELKQDLGWWKNTCLAEKLEFVRDRIVECYFWCTGIIQPLQ
SdPS	: INVVQAQFQDELKQDLGWWRNTSFVEKLFARDRDLVECYFWTTGIVQPRQ
SdPCS	: FNIVQATYQQELKEISRWWKETELAEEKLSEARDRDRVVENYIWNVGLIFKPQ
SdLis	: FNIVQATQIEELKDISRWWNNSCI SEKLFVRDRDLVESYFWAIGLFETHQ
CLLS_AF514	: FNTLQATYQEEELKEISGWWKDGTGEKLSFARNRLVASFLWSMGIAFEPO
SdSaS	: YNMVQAAYQQELKLISSWYKETGIPKELEFARHQLAVSYLWAIGFIPEHH

360 * 380 * 400

SdLS	: HGFERIMLTKVFALIAAIDDIYDVYGTLEEQLIFTDAIRRWDIE-SIDKL
SdEuS	: HGFERIMLTKINALVTTIDDIYEIYGTLEEQLIFTDAIRRWDIE-SIDKL
PfLS_KM015	: HENARVTLAKVNALITTLDDIYDVYGTLEEQLIFTDAIRRWDVS-SIDHL
SdPS	: HTNPRITVGKVNALITTIDDVYDVYGTLEEQLIFTDAIRRWDIS-TIDQL
SdPCS	: YGYARIMTTKLFILITVIDDVYDVYGTLEEQLIFTDAIRRWDDE-AIDQL
SdLis	: HCYERKTAAKIITLITSLDDVYDIYGTIDLELEVFTLTQQRWDTE-AINRL
CLLS_AF514	: FAYCRRVLTISIALITVIDDIYDVYGTIDLEEIFDTAVERWDINYALKHL
SdSaS	: LVYSREILSKIAVMITIIDDIYDVYGTLEEQLFTHTERWDIN-SLDSL

* 420 * 440 *

SdLS	: PPYMKVCYLALYNFVNEMGYYTLDKKGENSIPFLRKVWVDIVERYLIEAN
SdEuS	: PPYMKVCYLALYNFVNEMGYYTLDKKGFSIPFLRKTVWVDIVERYLIEAN
PfLS_KM015	: PNYMQLCFLALNNFVDDTAYDVMKEKDINIIPYLRKSWLDDIAETYLVEAK
SdPS	: PSYMQLCFLALDNFVNDDTAYDVLKHKGNAIPYLRKSWRDLIVEAYLIEAK
SdPCS	: PYYMKICYMVLDSFINEMAYHVLKEKDVLVIQDLRKTWGDICSAYAKEAE
SdLis	: PYYLQLFYLVIIHFVFEIYH-ILKEEGVISIPYIQLPWVDIIVEAYIQEAK
CLLS_AF514	: PGYMKMCFLALYNFVNFFAYYVLKQQDFLILISIKNAWLGIIQAYLVEAK
SdSaS	: PEYMKICFLALENTVNEFAYHILRDQGENIISNLRNWLAEICRAYYLEAT

460 * 480 * 500

SdLS	: WYHKGYKPSLEEYINNAWITVGGIPGLSHLFERVTDSIDEDEAAESVHKYH
SdEuS	: WYHKGYKPSLEEYINNAWMSIGGPVILSHLFERVTDSIEEEASESVHEYH
PfLS_KM015	: WFYSGHKPNLEEYLNNAWISISIGPVMICHVFERVTDSITRETVESILFKYH
SdPS	: WYHSAHKPNLEEYLNISWISISIGATVILTHAFEGVTPAITKDACDALYGYH
SdPCS	: WYHTGYKPTMEEYINVAWISISAHTILTHVFLISNPIEKEAAESIRNYH
SdLis	: WYYGGYTPSLEEYLNNSSSISIGTPTVIAQVELTSKD-----KLYKDN
CLLS_AF514	: WYHSKYTPKLEEYIENGIVSITGPLIITISYLSGTNPPIIKKELEFILESNP
SdSaS	: WFHSGYFPTTNEYLNWISISGPLLIFYGYET-TNPINQKELKSIEQYP

	*	520	*	540	*
SdLS	:	EIVRASCTITRLADDMGTS LAEVKRGDVPKS VQCYMN ESNASEEEA RENV			
SdEuS	:	DIVRASCMILRLADDMGTS LDEVERGDVPKS VQCYMN ENNASEEEA RKHV			
PfLS_KM015	:	DLIRYSSTILRLADDLGT SLEEVSRGDVPKS IQCYMNDNN ASEE EARH I			
SdPS	:	DIVRWSAIIIRLTDLGT SLEEVSRGDVPKS IQCYMNDNN ASEE ARAHV			
SdPCS	:	DTIRYSAMVLRLADDLGT SPHEMQRGDVPKA VECYMN ETGASREE AREHV			
SdLiS	:	HIIHLSGMLVRLFDDLGT LVFEMKRGDVA KSIQCYMKERNAS MEEAEHV			
CILS_AF514	:	DIVHWSSKIERLQDDLGTS SDEIQRGDVPKS IQCYMHETGASEEVARQHI			
SdSaS	:	GIIRWPATVRLADDLGTS SDEM KRGDVPKS IQCYMKETGCSEEDARKHI			

	560	*	580	*	600
SdLS	:	QSLIEETWKTMNKEMM--DSPFSTCFVEVCANIARMAQI IYQKDS DGF GM			
SdEuS	:	RSLIEQTWKMMNKEMM--DSQFAIYFVEVCANLGRMAQFIYQKES DGF GM			
PfLS_KM015	:	RWLIAETWKKINNEEVWSVDSPFCKDFIACAADMGRMAQF MYHN-GDGHGI			
SdPS	:	KWMIGETWKKMNEARVAKDSPFCEDFVGCAVDLGRMAQYMYHY-GDGHGI			
SdPCS	:	MFMIREIWMKTNGERFR-ESPFSDDFIRSAADLGRQAQYMYQH-GDGHGI			
SdLiS	:	RELIREAWKEMNTAGG---CPVRDDLVETAANFGRAAQF MYLD-GDGN--			
CILS_AF514	:	KDMMRQMWKKVNAYTADKDSPLTGTTTEFLINIVRM SHF MYLH-GDGHGV			
SdSaS	:	KQLIDTALKRMNKEILMEN-PIKNFG-QTAMNLGRISLCMYQH-GDGFGL			

	*	620	*	
SdLS	:	QHSVWNKQI RSLLFEEYE-----		
SdEuS	:	QHSIVNKQI RSLLFEEYE-----		
PfLS_KM015	:	QNPQIHQQMTDILFEQWL-----		
SdPS	:	QHPIIHQQMTDCLEHEIA-----		
SdPCS	:	SNPEMEERILGLIFQPPIV-----		
SdLiS	:	-HSKLHQRRIASLLFQPCD-----		
CILS_AF514	:	QNQETIDVGFTLLFQPIPLEDKHMAFTASPGTKG		
SdSaS	:	PYSETKKNIMSLLVQPF SMP-----		

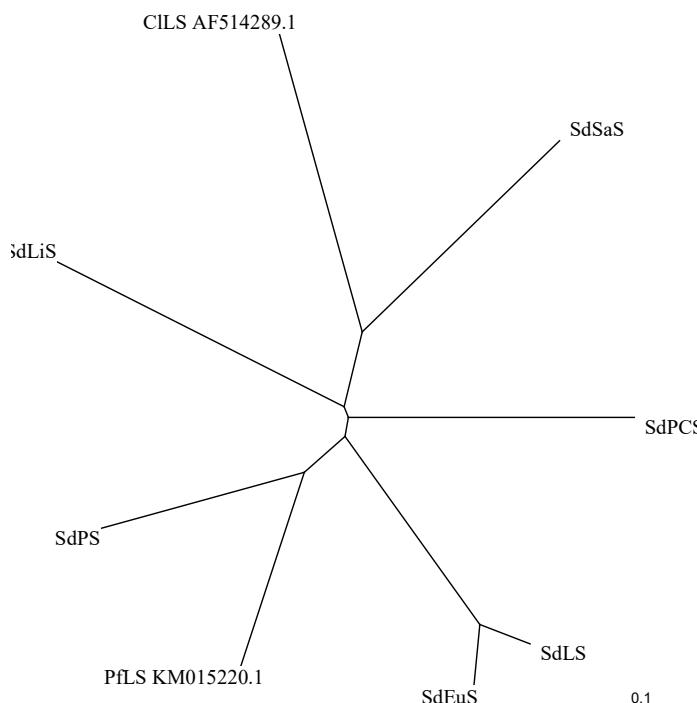
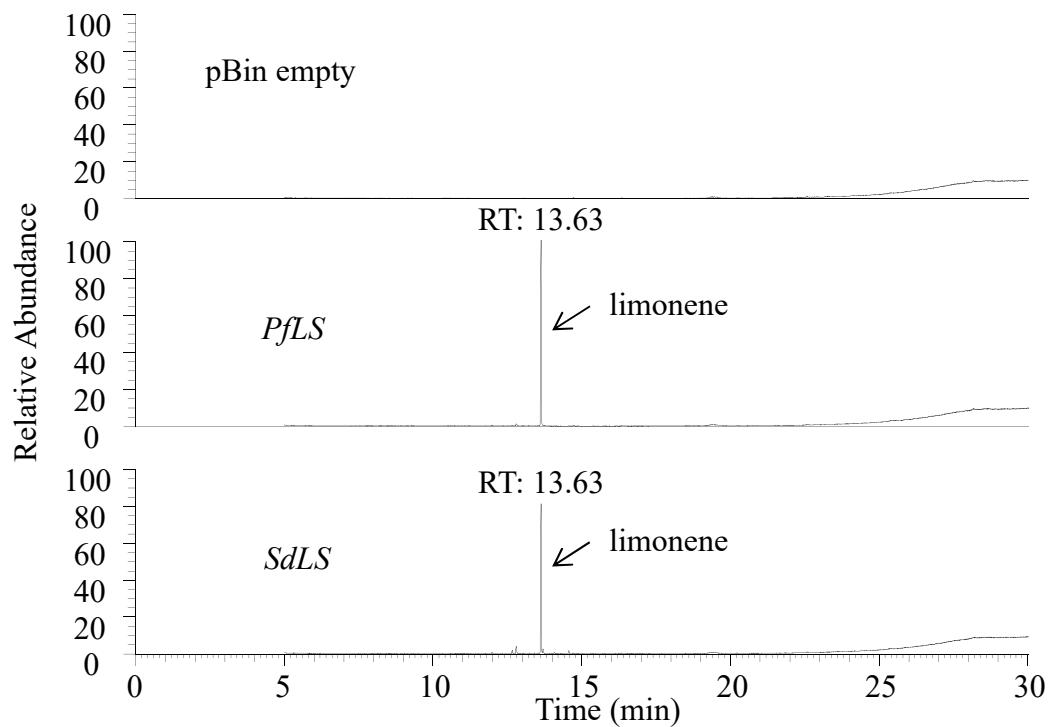


Figure S6 GC-MS TIC chromatograms of *N. benthamiana* headspace after agro-infiltration. pBin empty (empty vector control), PfLS *Perilla frutescens* limonene synthase (positive control), SdLS the newly identified limonene synthase from *Salvia dorisiana*



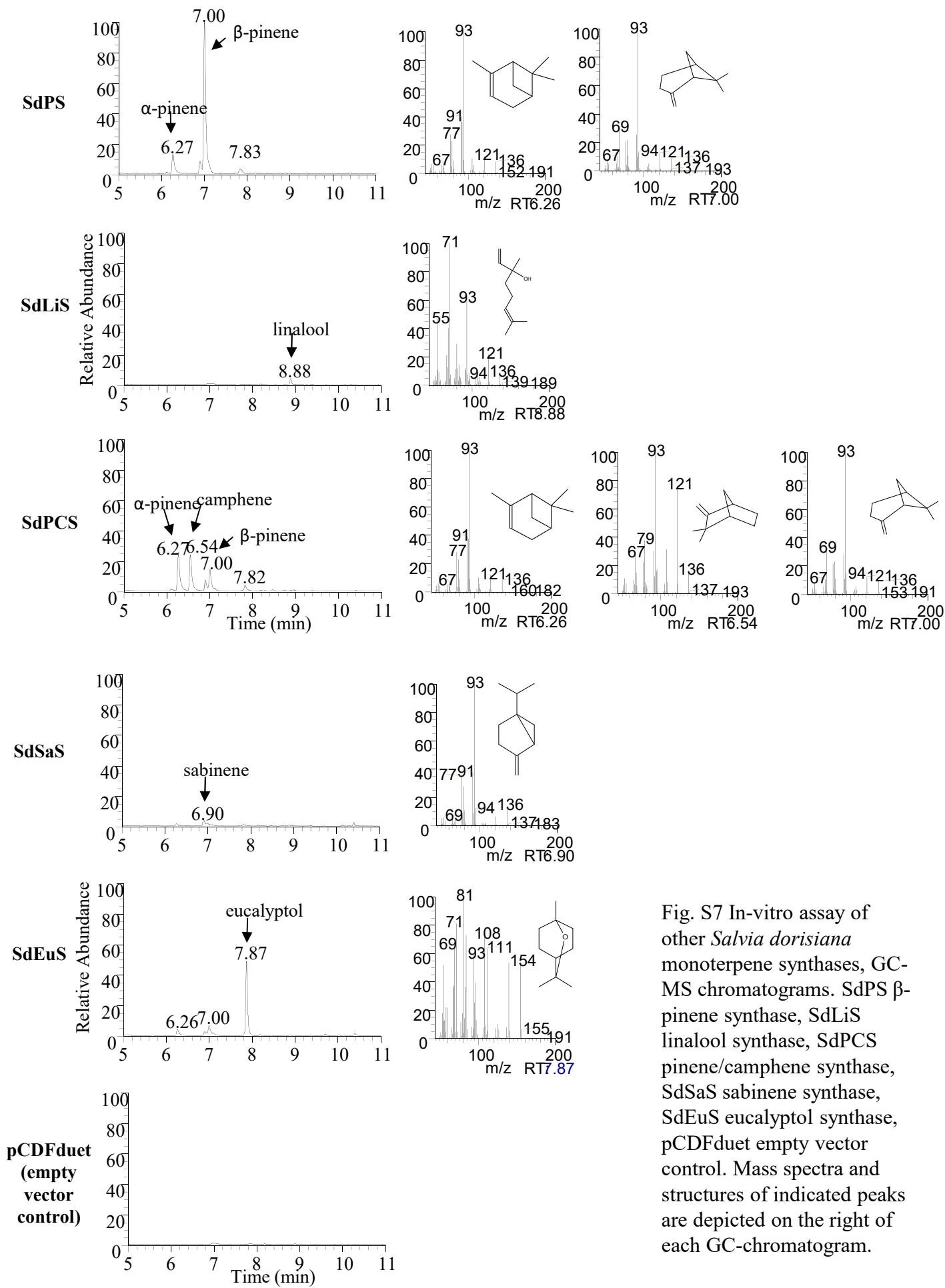
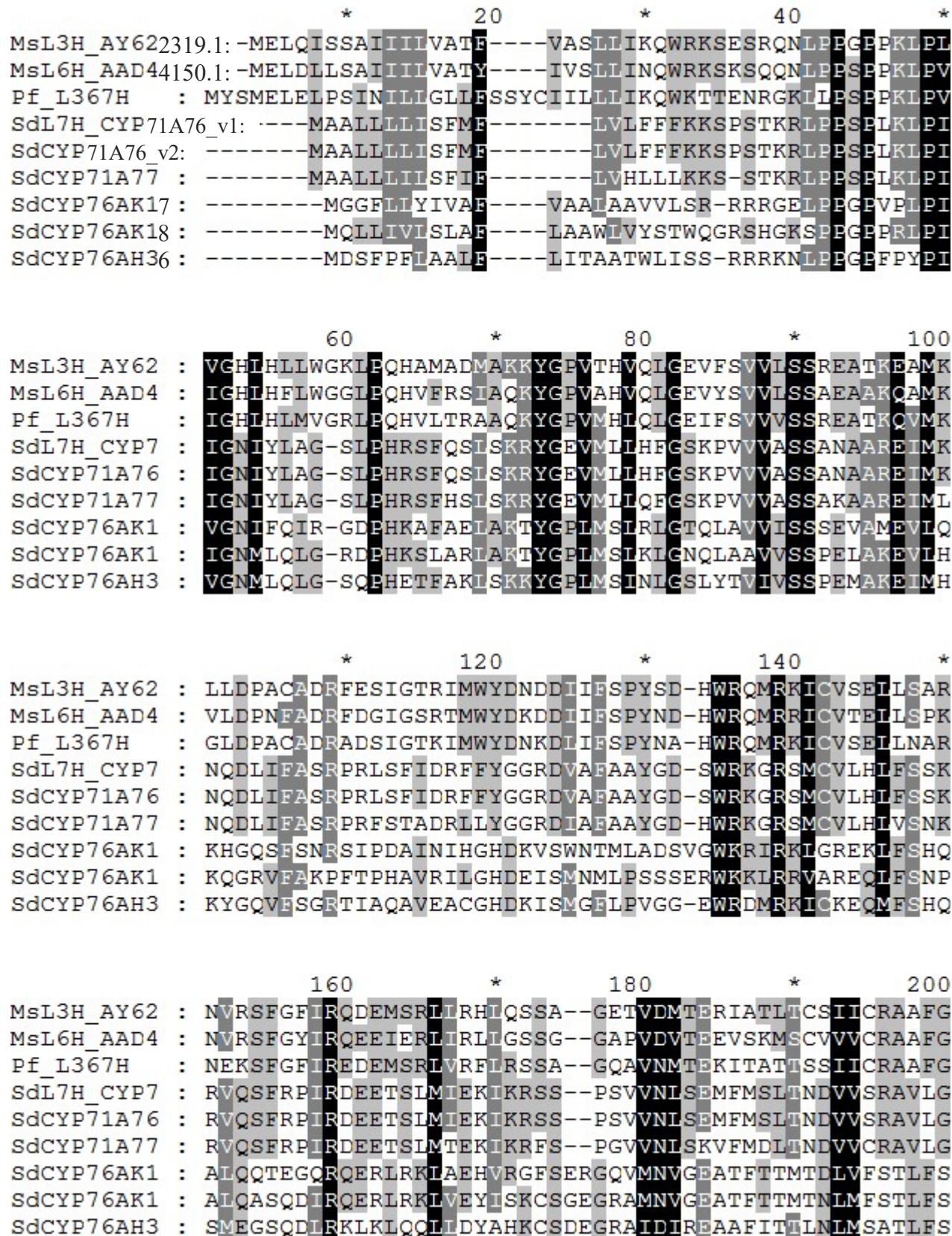


Fig. S7 In-vitro assay of other *Salvia dorisiana* monoterpenes synthases, GC-MS chromatograms. SdPS β -pinene synthase, SdLiS linalool synthase, SdPCS pinene/camphene synthase, SdSaS sabinene synthase, SdEuS eucalyptol synthase, pCDFduet empty vector control. Mass spectra and structures of indicated peaks are depicted on the right of each GC-chromatogram.

Figure S8 Protein sequence alignment of P450s. SdL7H and other cloned *S. dorisiana* P450 enzymes are indicated with systematic names (Nelson, 2009), L3H *Mentha spicata* (Lucker et al., 2004), L6H *Mentha spicata* (Lupien et al., 1999), PfL367H *Perilla frutescens*, sequence based on genbank GQ120438.1, cDNA from *P. frutescens* leaves isolated, 5'-race pcr, full length gene amplified and sequenced.



* 220 * 240 *

MsL3H_AY62	:	AIINDHEE-----LVELVKDSLSMASGFEIADLFESSKILNLLCWN
MsL6H_AAD4	:	SVLKDKQGS-----LAELVKESELALASGFEIADLYPSSWILNLNSLN
Pf_L367H	:	SVVRDDEV-----LIGLVKTASGMANGFEIADLFPSKILNLLCLN
SdL7H_CYP7	:	RTYGGDDDG-----EKNFNQILKKIVEILQSYNVGDFVAWLGINRVNGV
SdCYP71A76	:	RTYGGDDDG-----EKNFNQILKKIVEILQSYNVGDFVAWLGINRVNGV
SdCYP71A77	:	RKYGGGDDR-----EKPFNQILKMINEMIQRYNVGDFVWLGINRVNGV
SdCYP76AK1	:	IDLTDYGATDSIANK-EFKEHINSFTRYIGVPNVSDFYPILAFLDLQGVR
SdCYP76AK1	:	IELVEYASTDAATPKSKFREHVNAITRYMGVPNVADFFPIFAPFLDPQGMR
SdCYP76AH3	:	LQATEFDS---KATMEFKIEEVVASIVGVPNFADFFPILRPFDPPQGVK

260 * 280 * 300

MsL3H_AY62	:	KSKLWRMRRRVETILEAIVDEHKIKKS--GEFGGEDIIDVIIFRMQKDSQI
MsL6H_AAD4	:	KYRLQRMRRRLDHLDFLEEHREKKS--GEFGGEDIDVVIIFRMQKGSDI
Pf_L367H	:	KYRLWKMRRRELDAILEGVVEEHKIKQS--GEFGGEDIDVVLIRMQKNSQL
SdL7H_CYP7	:	EAQVEKIFEMTDEFMEALLREYRKKS--SGDAVVNFADALLELQGESKD
SdCYP71A76	:	EAQVEKIFEMTDEFMEALLREYRKKS--SGDAVVNFADALLELQGESKD
SdCYP71A77	:	EAQVEKIFKMTDQFMEGILLREYREKKS--SDDAVVNFA DALIQLQRESKD
SdCYP76AK1	:	RKIGHHLGKLLDFVEDMIQKRMRERRE-SDYQNKNDFLDTILLEIAEETE-
SdCYP76AK1	:	RKLTYHIGSVLELVQGFIEQRLQARTT-SSYQKKTDFLDTLIDSEGNE-
SdCYP76AH3	:	RRADVYFGRLGLIEGYINERIQSRKANPNAPKKDDFLETLVLDILEAND-

* 320 * 340 *

MsL3H_AY62	:	KVPIITTAIAKAFIFDTFSAGTETSSSTTIWVMAELMRNPAVMAKAQAEVR
MsL6H_AAD4	:	KIPIITSNCIKGFIFDTFSAGAETSSSTTISWALSELMRNPAKMAKVQAEVR
Pf_L367H	:	QFEITTDTIKGFIFDTFAAGTETSSSTTVWAMAELMKNPRVMANVQAEVR
SdL7H_CYP7	:	SDFVEDDVVIKALILDTEFAAGTDTTFTALEWTMAELIRNPRTMKLLQKEVR
SdCYP71A76	:	SDFVEDDVVIKALILDTEFAAGTDTTFTALEWTMAELIRNPRTMKLLQKEVR
SdCYP71A77	:	SDFVEDDVVIKALILDMEGGGTDTTFTALEWTMAELIRNPRTMKLLQKEVR
SdCYP76AK1	:	-YDLTIKEIRHFCVDILIAGSDTSAAATTWAMVELLILHPDKMAKIKAEKL
SdCYP76AK1	:	-YDLSVKEIKHMFDVIIIAAGSDTSAAATSEWAMVELLILHPDKMAKIKAEKL
SdCYP76AH3	:	-YKLKTEHLTHIMLDLEVGGSETSTTIEIEWIMEELMSSPDKMAKVKAELK

360 * 380 * 400

MsL3H_AY62	:	AALKGKTSVDVD--DVQELKYMKSVVKETMRMHPPIPLIP-RSCREECEV
MsL6H_AAD4	:	EALKGKTWVDLS--EVQELKYLRSVLKETLRLHPPPEPLIP-RQSREECEV
Pf_L367H	:	EGLKGKKSVDAS--DVQQLKYLKSVKETLRLHPPPEPLIP-RKCREDIEV
SdL7H_CYP7	:	EVARNKNGIDINEDDLEKMPYLKAVSKESLRLHPPPIPLALPRELNQDTNL
SdCYP71A76	:	EVARNKNGIDINEDDLEKMPYLKAVSKESLRLHPPPIPLALPRELNQDTNL
SdCYP71A77	:	EVARNKNGIDINEDDLDKMPYLKAVSKESLRLHPPPIPLALPRELNQDTNL
SdCYP76AK1	:	SVLGDKSTVEGS--DISKLPYIQTATNEVFRHFPVAPII LGPREAAEDTQI
SdCYP76AK1	:	SVLGSKKMVEEA--DISRLPYI RATVKEVFRYHPEAAPMLAPHAAEEQTEV
SdCYP76AH3	:	SVMGEQKVWDER--QMPNLPYIQA VVKESMRLHPPGPILLLPRKAESDQVV

* 420 * 440 *

MsL3H_AY62 :	NGYKIPNKARIMINVWSMGRNPLYWEKPETEWPEREDQVSRDEMGSDFEF
MsL6H_AAD4 :	NGYTIPAKTRIFINVWAIGRDPQQWEDPDTFRPERFDEVSRDEMGNDFEF
Pf_L367H :	EGYSIPSNSRIVINVWSILGRDPLYWEEPEIEWPEREDHISTDYVGNNFEF
SdL7H_CYP7 :	IGYDIPRGAIIVLVNCWAISRDPLIWINPNEFRPERFFDSSIDYKGLHFEM
SdCYP71A76 :	IGYDIPRGAIIVLVNCWAISRDPLIWINPNEFRPERFFDSSIDYKGLHFEM
SdCYP71A77 :	IGYDIPRGAIIVLVNCWAISRDPLIWINPNEFRPERFFNTSIDYKGLHFEM
SdCYP76AK1 :	NGYTIPKNVKVIVNEWAITRDRSIWKNPESFEPEPERELGTDINFEGQHFEL
SdCYP76AK1 :	NGYIIIAKNTKIEINFWAITRDESIWKNPESFEPEPERELDSEIDEFGGQHYEL
SdCYP76AH3 :	NGYLIPKGSQVIINAWAMGRDETIWKNPNSFEPEPERELDQKIDEKGQDYEL

460 * 480 * 500

MsL3H_AY62 :	IPFGAGRRICPGLNFGLANVEVPIAQQLIYHFDWKLAECMKPSDMDMSEA
MsL6H_AAD4 :	IPFGAGRRICPGLHFGLANVEIPIAQQLIYHFDWKLPQ-GMTDADLDMTET
Pf_L367H :	IPFGGGRRICPGLNLGVanVEVPIAQQLIYHFDWKILGEPCMSPVHMDMTVA
SdL7H_CYP7 :	VPFGAGRRGCPGIAFAMSMYELAVSRLVKEFDFGLPN-GVREEDIDMTEA
SdCYP71A76 :	VPFGAGRRGCPGIAFAMSMYELAVSRLVKEFDFGLPN-GVREEDIDMTEA
SdCYP71A77 :	IPFGAGRRGCPGIGFAMSLYELAISRLVNEFDFGMPN-GGREEDIDMTEA
SdCYP76AK1 :	IPFGSGRRICPGMPLASRMLFCMVATLCHNFDWELEG-GVESKLREREDV
SdCYP76AK1 :	IPFSSGRRICPGMPLAGRMLHCMVGTMCNFDWELEK-GAESKQIQREAV
SdCYP76AH3 :	IPFGSGRRVCPGMPLANRILHTVTATLVHNFEWKLER-PDASDAERQGVL

* 520

MsL3H_AY62 :	EGITGIRKNNLLLVPTLYKSP---
MsL6H_AAD4 :	PGISGPKKKNVCLVPTLYKSP---
Pf_L367H :	KGLSGPRKTPLFLVPSIYIPTQPN
SdL7H_CYP7 :	PGFVVHKKSPLIVVTTPRAY---
SdCYP71A76 :	PGFVVHKKSPLIVVATPRASL---
SdCYP71A77 :	PGFAVHKKSPLIVVATPRASL---
SdCYP76AK1 :	FGLALQKKFPLRAKPIKV-----
SdCYP76AK1 :	FGLALQKKIPLRAIPIKVE-----
SdCYP76AH3 :	FGFAVRRAVPLKVIPFKK-----

Fig. S9 Characterization of *SdL7H* in yeast. Mass spectra of the peaks shown in Fig. 4. a. POH peak from yeast strain ScPftLS + *SdL7H* at RT 11.3 min, b. POH standard at RT 11.3 min.

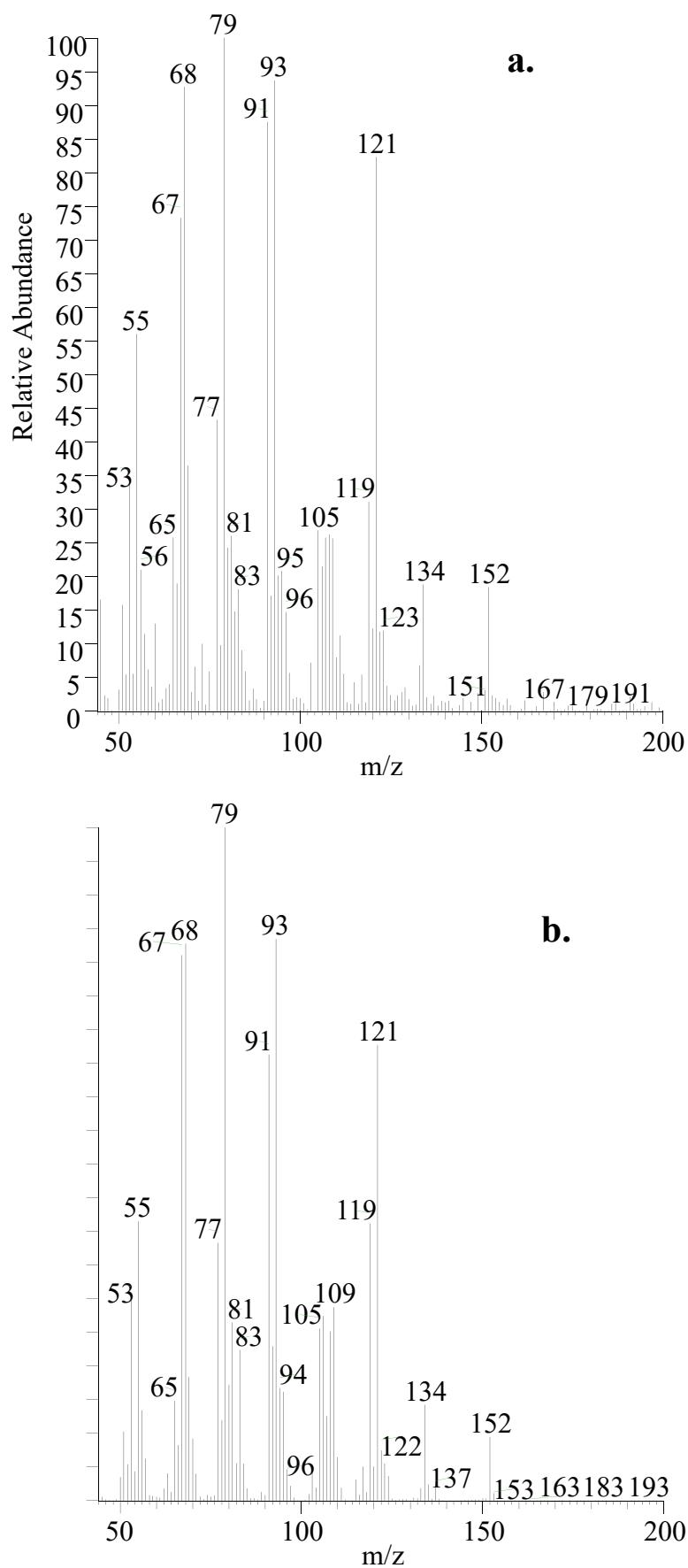
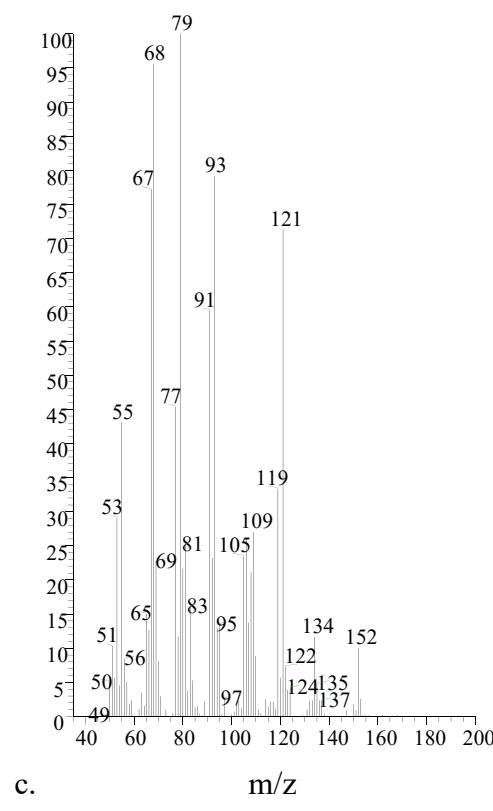
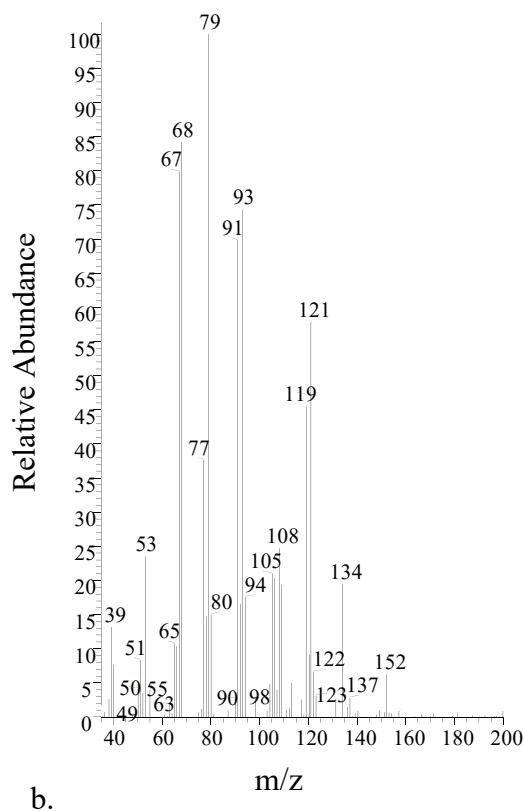
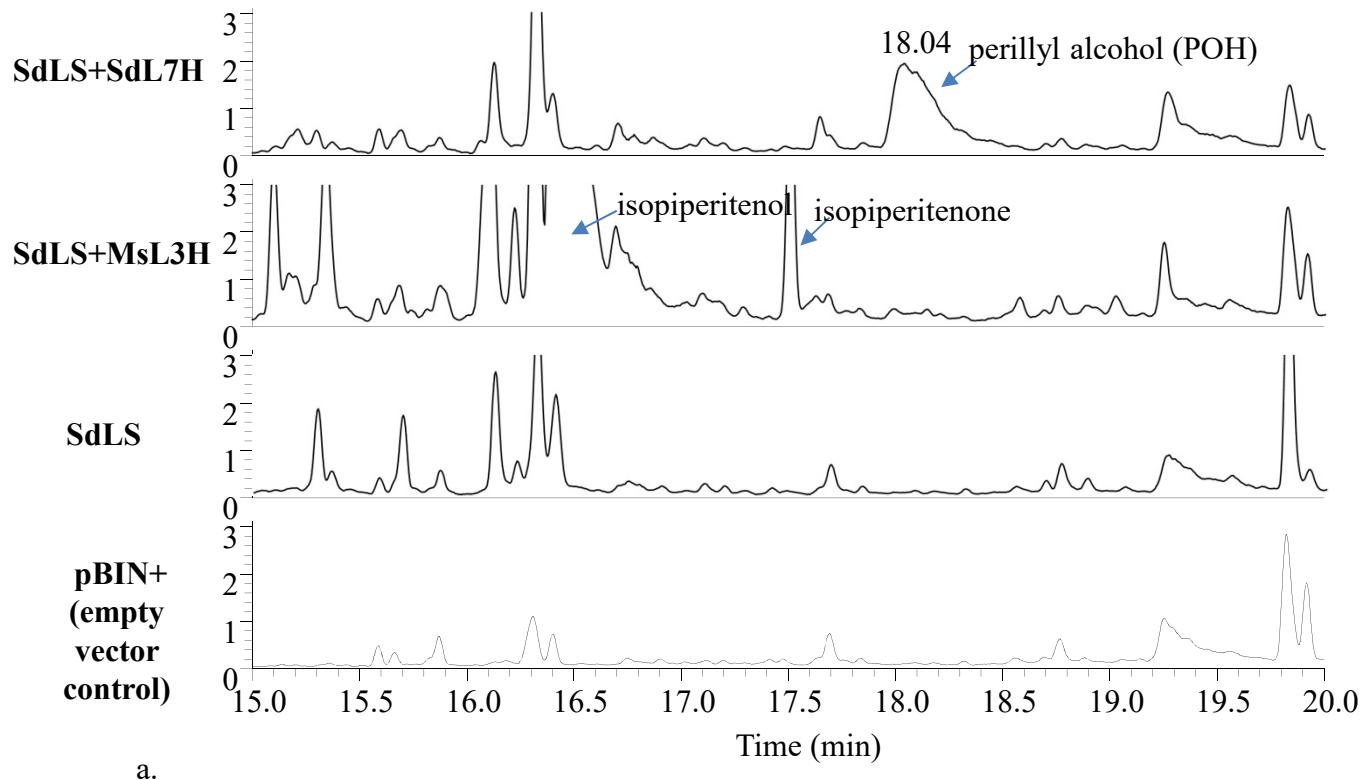


Fig. S10 a. GC-MS chromatograms of *N. benthamiana* leave headspace after agro-infiltration of constructs, b. Mass spectrum of perillyl alcohol peak in SdLS+SdL7H at RT 18.04 +c Full ms [35.00-400.00], c. Mass spectrum of perillyl alcohol reference compound. NL 5.17E7, m/z = 92.5-93.5+120.5-121.5+151.5-152.5 MS. d. LC-MS chromatograms of *N. benthamiana* agro-infiltrated leaves. m/z 355.1760-355.1770 (perillyl alcohol marker POH-M1 at RT 41.93) FTMS - c ESI Full ms [95.00-1300.00] MS NL: 100% = 4.38E6 e. GC-MS peak area of limonene peak in *N. benthamiana* leaf headspace after agro-infiltrations. *SdLS* *Salvia dorisiana* limonene synthase, *SdL7H* *S. dorisiana* P450 limonene-7-hydrogenase, *MsL3H* *Mentha spicata* limonene-3-dehydrogenase (P450, isopiperitenol synthase, control)



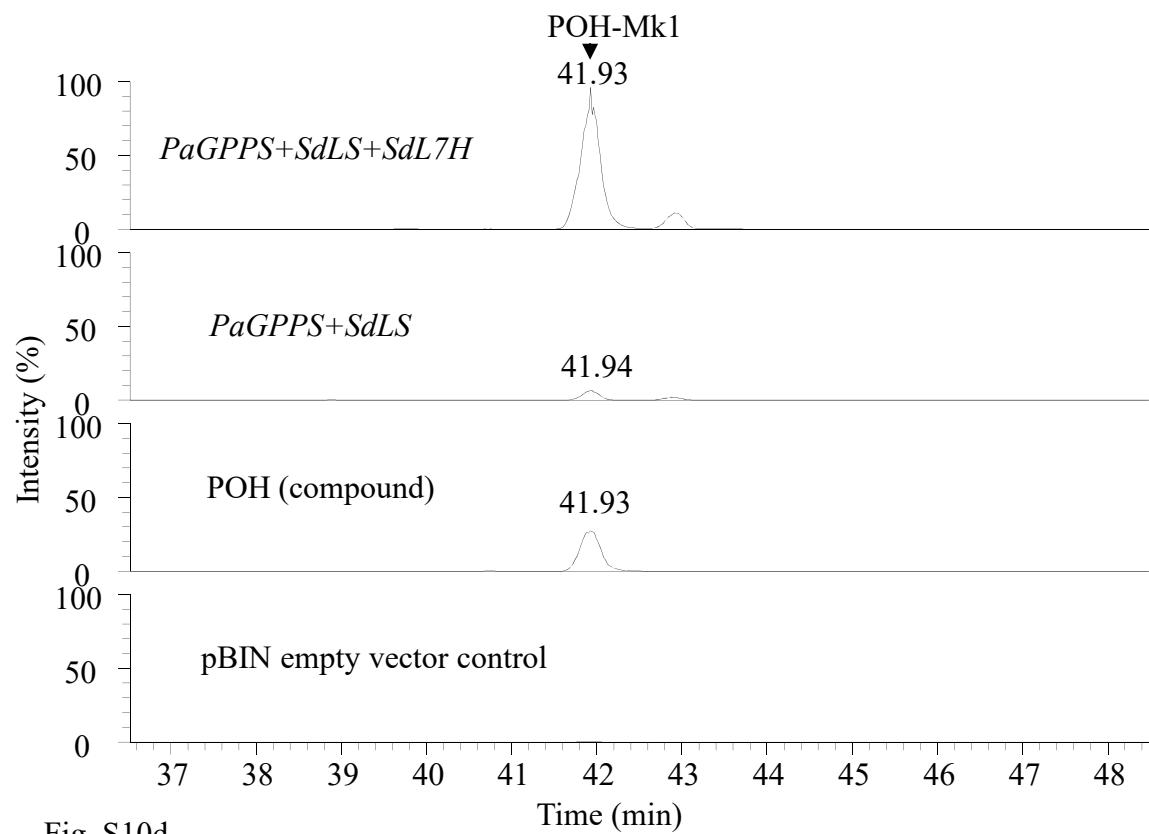


Fig. S10d.

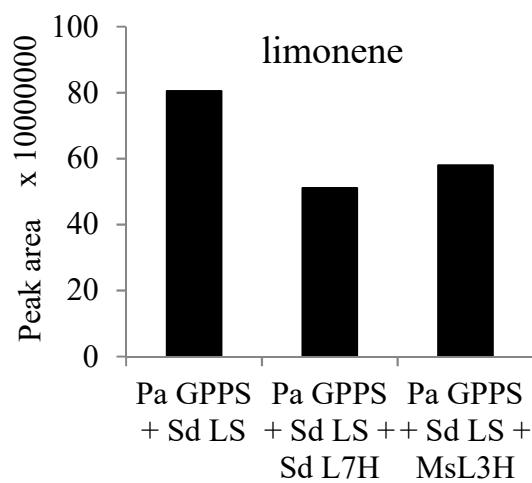


Fig. S10e.

Figure S11 Alcohol dehydrogenases (ADH) protein sequence alignment and phylogenetic tree. SdADH characterized *Salvia dorisiana* perillyl alcohol dehydrogenase, Cr8HGO *Catharanthus roseus* 8-hydroxygeraniol oxidoreductase (Miettinen et al. 2014), AaAdh2 *Artemisia annua* ADH2 monoterpane alcohol dehydrogenase Genbank No. GU253890.1 (Polichuk et al 2010), PfAKR and PfGeDH *Perilla frutescens* perilla alcohol dehydrogenases Genbank No. AFV99148 and AFY63472 (Matsumoto and Ito 2014), Sdclust... other *Salvia dorisiana* cloned ADHs that did not convert perillyl alcohol to perillyl aldehyde.

	*	20	*	40	*
AaAdh2	:	M-----ASLTPKARLENKV-----			AIVTGG
Sdclust305	:	M-----WLFMNRNGPSGFSSASTAAEVNGIDAS-----			GLTAIVTGA
Sdclust316	:	M-----ADAVDQYPAP-----			RRYALVSGA
PfAKR	:	M-----ATAAMTVAVP-----			RIKLGVDGL
SdADH	:	M-----ADNTITCKAAVAWNQSEPLKVEEVEVDPPNSTQVRRIKMVYASM			
Cr8HGO	:	MTKTNSPAPSVITCKAAVVWKSGEPPKVEEIQVDPPKASEVRIKMI CASL			
PfGeDH	:	MAKTPETEHPVKAFGWAARDNSGTLSFNFSSRDTGER-DVQFKVLYCGV			
Sdclust424	:	M-----ENQGKRVLLTS			
Sdclust351	:	MAEKILIIGGTGHIGKFLVEASAKSGHPTFALMRESSLSDPPKAO VEGW			

	60	*	80	*	100
AaAdh2	: A-RGI GECIVRLFVKHG-----AKVVIAADVND-				
Sdclust305	: S-SGI GLETARVLAKG-----VNVVMGIRNMG-				
Sdclust316	: N-RGI GFEICRQLASKG-----MVVILAARDEK-				
PfAKR	: EVSKI GLGCVGGMSETYGPPRPEPEMVLQLIHHAVDSGVTFFDTSDFYGPHT				
SdADH	: CHTDI -TCWNGSLFPFAFPRILGHEGAGVI-ESVGEDVKNLKVGDSV-MLF				
Cr8HGO	: CHTDF-LACNGLPVPLFPRIPGHEGVGMI-ESVGENVTNLKEGDIV-MPL				
PfGeDH	: CHSDI HMVKNEWGVTHYPVVPGHEIVGVV-TEVGSKVEKVKAGDKVGVGV				
Sdclust424	: NGDQISLSIARTLARRTCRL-----VIMGNEGQ-				
Sdclust351	: NKSGVTTI-TGTGDLNDHASIVKAIKHVDIVISTVVG-----FM				

	*	120	*	140	*
AaAdh2	:	----LGKLLCQDL----	GSKFACFVHCDVTIESDIENL---	INTTIAK	
Sdclust305	:	----VGEKVKGIIKENPAAKIDA-	IQLDLSSMQSVRNF---	ASHFKSS	
Sdclust316	:	---RGIEARERLKDFFNNV---	VFHPLDVADAASVAAV---	AHFVRQE	
PfAKR	:	NEILLGRAILKGMREKVQIATKFGARLKGDVVEICGHPAY---	VR--EAC		
SdADH	:	YVGECGECAYCASGKTNVCLRYPPTISD--	DGTTSRIYAKGQRRIHMFSS		
Cr8HGO	:	YLGECGECILNCKSGRTNLCHKYPLGFSGLLL	DGTTSRMSIGEQKVYHHFSC		
PfGeDH	:	IVGSCRQCDQCSNDLENYC	SKQILTYGAPYIDGT-----	ITR	
Sdclust424	:	-----LRTAAEKIKGSLN	GAVFVEVVGLMED-----	ER	
Sdclust351	:	QIADQHKIIAAIKEAGNVKREL	PSEFGNDWQSHP-----	ENPLSONFOQ	

	160	*	180	*	200
AaAdh2	: HGQLDIMVNNAGTV-----		-DEPKI	SILDNEKS-----	
Sdclust305	: GLPLNILINNAGIM-----		-VPPFTLSPDNIEL-----		
Sdclust316	: FGRLDILVNNAASI GLLQIDGDVLVLHEHLLADAASVSSGELQELVHPKA				
PfAKR	: EASLKRLETNYIDI-----YYIHRIDTRVPIEITMGEKKLVVEEGK				
SdADH	: STWAEYAVVESNYV-----VKVDPRVPL-SHACLLTGCG-				
Cr8HGO	: STWSEYIVIVAAAYA-----VKVDPRVSL-PHASFLCCG-				
PfGeDH	: GGYSNIMVADEHFI-----IRWPENI PLDAGAPLLCAG-				
Sdclust424	: EGAFDDAVEKARRILGGLDALVNCYSYEGKMQDPLSIAEDEFKKI-----				
Sdclust351	: KVQTBRRAIEAOGT-----				

	*	220	*	240	*
AaAadh2	:	-----DFDRVVSINLAGVELGT-----	KHAARVMIPKCS---	GS	
Sdclust305	:	-----QF---ATNYLGHELLTHLLLDTMKKTARDT--KRE---GR			
Sdclust316	:	NGTLIEAFEHAEECINTNNYGLKRVTEALIPLLKLSESPTIVNVSSLG			
PfAKR	:	IKHVGLSEACPSTIRRAHAVHPLAAVELEWSLWSRDSEDEIIPTCRALCI			
SdADH	:	-----FTTGYGGVWK-----	ELKAGKGS		
Cr8HGO	:	-----FTTGFEGATWR-----	DVNWKGS		
PfGeDH	:	-----ITYSPLRYY-----	GLDK-PGL		
Sdclust424	:	-----MRTNFMAAWYLLKAVGKVMRD-----	QKSGGS		
Sdclust351	:	-----PYTYISCNLFAGYSLSNLLQ-----	VGATAPPRD		

	260	*	280	*	300
AaAadh2	:	IITTAS-----IC---SVTGGVA---SHA---YTSSK-----			
Sdclust305	:	IVNLSS-----IAHRNSYRECIRFDKINDE-----KSYSK-----			
Sdclust316	:	LVLQPNE---WVKGVLSSEDCLKEERIDEVVQEYLKNYKE GSLRENKWP			
PfAKR	:	GIVAYSPLGRGFLAAGPSFVENLSESDFRKRFPRFQOPENIEQNKKIYERL			
SdADH	:	SVAVIGLGA VGLGAVKASQILGATRIFGIDVN-DMKRDIA R-----			
Cr8HGO	:	TVAVLGLGA VGLGAVQGAKSQGASRIIGLDIN-DKKREKGE-----			
PfGeDH	:	SVGVNGLGGLGHAVKFAKAFC-TKVTVIESTLGKKK EAIE-----			
Sdclust424	:	IVFLTSVIGAERGLYPGAAAYESCLAGVQQQLVRTSALEIGKHQ-----			
Sdclust351	:	KVVI PG-----DENVKAVFNEEH-----			

	*	320	*	340	*
AaAadh2	:	--HGVVGIAKNA---AAE-LGKY-----NIRVCVSPYFVPTKIAFKF			
Sdclust305	:	--FSAYGQS KLANILHANE-LARRIKEEGADITAN SVHPGVITTNL-FRH			
Sdclust316	:	LHMSAYKVSKAA---VNA-YTRIMAKKHDTFYINSVCPGYTRTELT-RN			
PfAKR	:	CEMAARRECSPAQLALAWV-LAR-----GIDVCPIPGTTKID---			
SdADH	:	----AFGVTDVFVNPKHSNKPISQLILEATGGLGVDYC---VECTGVASLL			
Cr8HGO	:	----AFGMTEFINPKGSNKSISELTNEATGGLGIDYV---YECTGV PALL			
PfGeDH	:	----HLGVDEF LV--SSDP--QQM QAAVGTL--IGI---IDTVSAEHPL			
Sdclust424	:	----IRVNGIARGLHLEDEFPVSVGKERAERLVNDANPLRRWL DVE--			
Sdclust351	:	-DVGTYT KAAVDPRTL NKIVYFR-----PHN IYSFNELVA WEKK			

	360	*	380	*	400
AaAadh2	:	LNMDE-TSSFYSNLQGKTLGPQDIANATLFLASDESGYVSGHNLVVDGGY			
Sdclust305	:	LGIFEGLVSSVGRVLV LKNV--QQGASTTCYVA-----			
Sdclust316	:	FGLLTDAEGAVAPVKLA-LAPEGGPSGSIFLRAE-----			
PfAKR	:	-NLNQNMEAFLLELT----PEEKADLESYASPD-----			
SdADH	:	NEAIASTKMGVGETVLISAPPEEKGELNYIPMILGR-TIKGTTF---GG			
Cr8HGO	:	NEAIESSKVGLGTAVLIGAGLETSGEIKFIPLLCGR-TVKGSIY---GG			
PfGeDH	:	VPLMSLLKPH-GKLIVVGAP-EKPLQLHAFSLIQRKTVAGSAI---GG			
Sdclust424	:	-----NDLASTVIYLISDGARYMTGTTIFVDGGQ			
Sdclust351	:	INK-TLEKIYVPEQELLKQIQESPIPVNIILCINHCIFVKG-----			

	* 420 * 440 *
AaAadh2	: SVLNPAFGLFSWKP*TLSISPQCSCVLYVRFLE*GHILLVMIVKTTL*HF
Sdclust305	: -----IHPQLKGVSGQYFSDNN--IDKADAKATDKDL
Sdclust316	: -----
PfAKR	: -MVKGERHAFMSQTWINSETPQLSNWKLENHIDDG-----
SdADH	: VKIHSDVPKIVEKCINKEI-----NLGDLITHEVS---LAD
Cr8HGO	: VRPKSDLPTLIEKCINKEI-----PMDELMTHEVS---LSE
PfGeDH	: MK---ETQEMIDFAAKKNIIPDVEVIPIDYINTAMDRLLKSDVKYRFVID
Sdclust424	: SLVRPRMKSIM*-----
Sdclust351	: -----DQMNEFEIDPKIGVE

	460 *
AaAadh2	: ITS*FIYVY-----LIIIV
Sdclust305	: AAKLWDYTMD-----LINK*
Sdclust316	: VLSIFG-----TN*
PfAKR	: -----V*
SdADH	: INKGFLAYMKQPKCVKVIIKF*
Cr8HGO	: INKGFL-EYLKHEDCVKVVIKF-
PfGeDH	: VNKSFNAH*-----
Sdclust424	: -----
Sdclust351	: VSQIYPDVKYTTVDEYLNQFV*

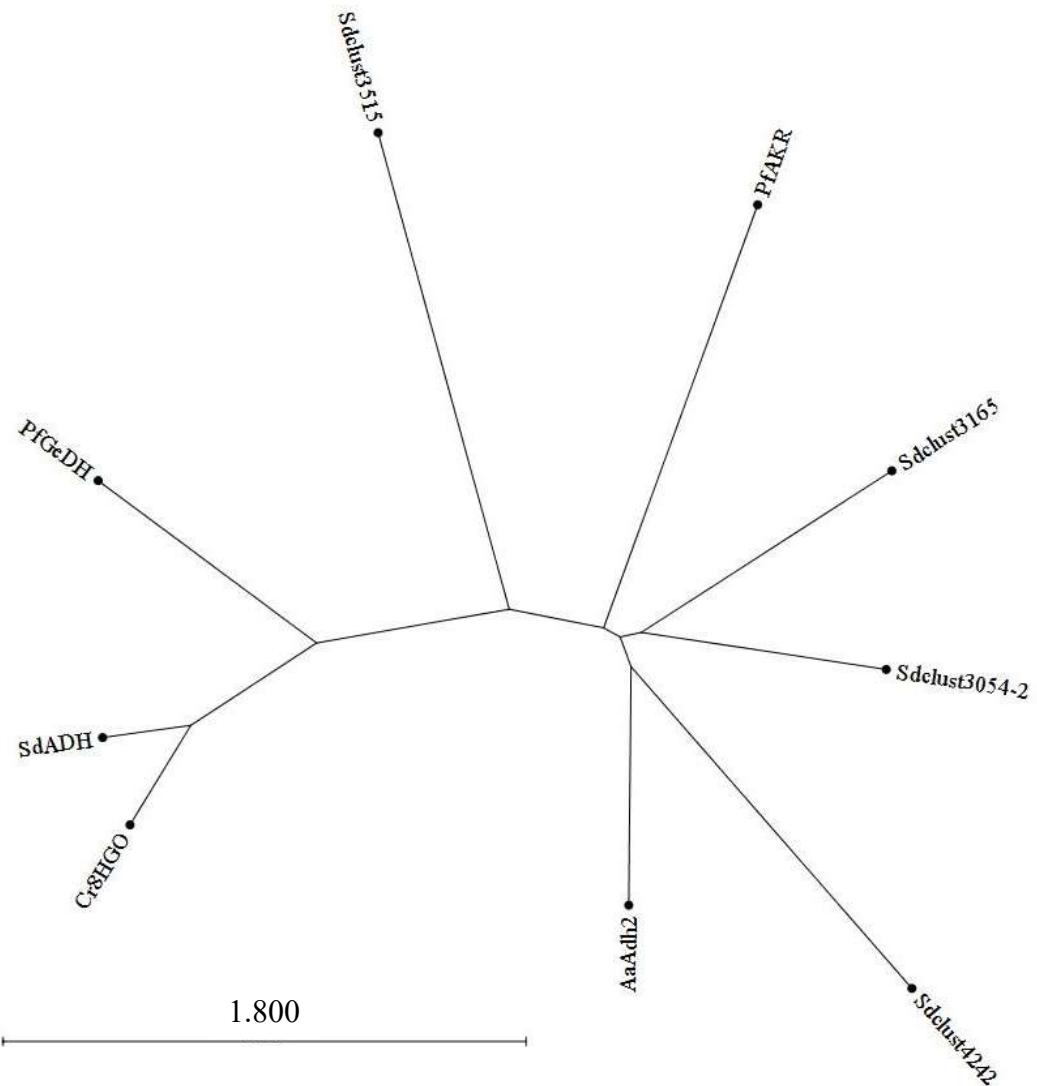


Figure S12 Characterization of *SdPOHDH* activity. a. LC-MS chromatograms of *N. benthamiana* leaves agro-infiltrated with *SdPOHDH* and perillyl alcohol. m/z range 355.1760-355.1770 + 458.1960-458.1970 (perillyl aldehyde marker PAldH-M1 at RT 28.11; perillyl alcohol marker POH-M1 at RT 41.93) FTMS - c ESI Full ms [95.00-1300.00] MS NL: 100% = 1.20E6 b. Quantification of peak areas of POH and PAldH markers POH-M1 and PAldH-M1 from chromatograms. POH perillyl alcohol, PAldH perillyl aldehyde, pBIN empty vector control, *SdPOHDH Salvia dorisiana* alcohol dehydrogenase.

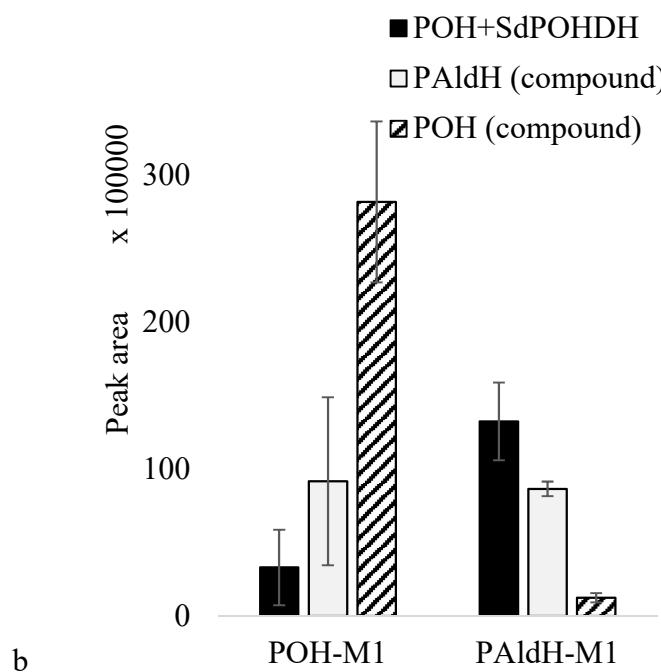
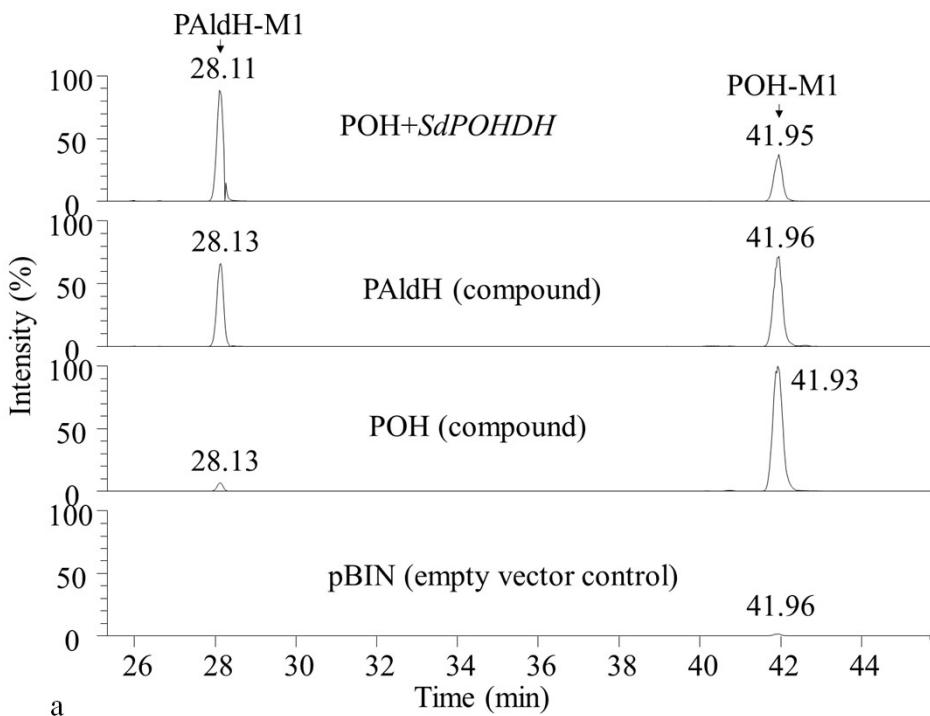
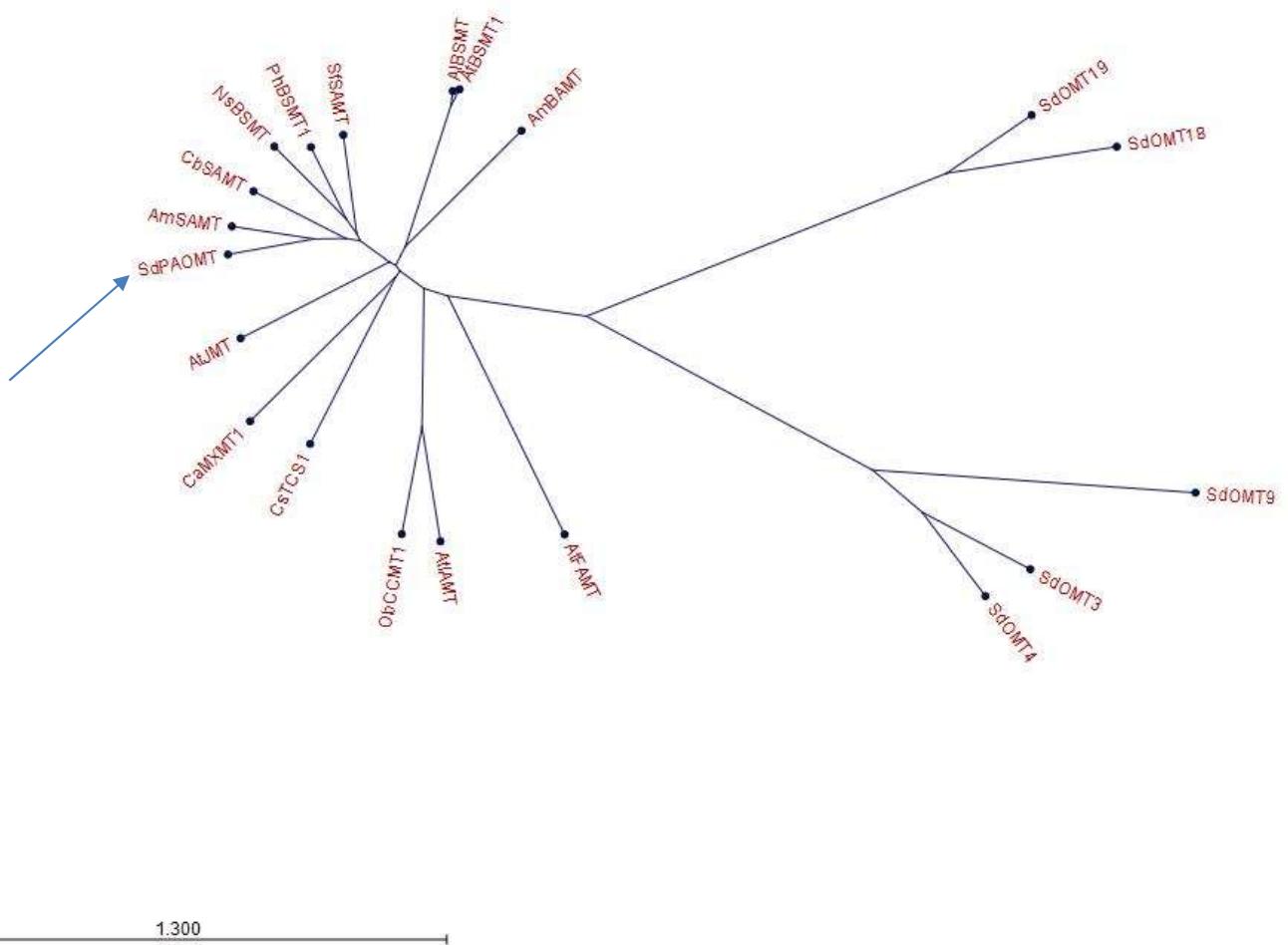


Figure S13 O-methyltransferases protein sequence phylogenetic tree of *Salvia dorisiana* methyltransferase candidates. SdPAOMT characterized *Salvia dorisiana* perillic acid methyltransferase (indicated with an arrow), SdOMT3,4,9,18,19 are alternative candidates from *S. dorisiana*, CrLAMT *Catharanthus roseus* loganic acid methyltransferase, ObCCMT *Ocimum basilicum* cinnamate carboxyl methyltransferase, SfSAMT *Stephanotis floribunda* salicylic acid carboxyl methyltransferase (Pott et al., 2002), AtIAMT *Arabidopsis thaliana* indole-3-acetic acid carboxyl methyltransferase (Zubieta et al., 2003), AtFAMT *Arabidopsis thaliana* Farnesoic acid methyl transferase (Yang et al., 2006), PhBSMT *Petunia hybrida* benzoic acid/salicylic acid carboxyl methyltransferase (Underwood et al., 2005), CbSAMT *Clarkia breweri* salicylic acid methyl transferase (Ross et al., 1999), CaMXMT1 *Coffea arabica* 7-methylxanthine methyltransferase (Ogawa et al., 2001), NsBSMT *Nicotiana suaveolens* benzoic acid/salicylic acid carboxyl methyltransferase (Roeder et al., 2009), AmSAMT *Antirrhinum majus* salicylic acid carboxyl methyltransferase (Negre et al., 2002), AtJMT *Arabidopsis thaliana* jasmonic acid carboxyl methyltransferase (Seo et al., 2001), AmBAMT *Antirrhinum majus* benzoic acid carboxyl methyltransferase (Dudareva et al., 2000), AtBSMT *Arabidopsis thaliana* benzoic acid/salicylic acid carboxyl methyltransferase (Chen et al., 2003), AlBSMT *Arabidopsis lyrata* benzoic acid/salicylic acid carboxyl methyltransferase (Chen et al., 2003), CsTCS1 *Camellia sinensis* caffeine synthase (Kato et al., 2000). Reference methyltransferase sequences were adapted from (Kapteyn et al., 2007).

Fig. S13.



20 | EVVE -- VLRMN - GGLGE - | 40 | TSYANNSSLVQRKVILMTPMITEEAITQVYRS - - - 46
 SdPAOMT M----- | -EVVE-- VLHMN - GGGND - | -SSYANNSSLVQKVLIMLTKPITEQAMIDLYSS - - - 46
 PhBSMT1 M----- | -EVVE-- VLHMN - GGTGD - | -ASYANSLSLQQVKVILLTKPITEEAITELYTR - - - 46
 SfSAMT M----- | -EVAK - VLHMN - EGIGK - | -ASYANSLSLQQVKVILMTHKSIRDEAIALYRS - - - 46
 CbSAMT M----- | -DVRQ - VLHMK - GGAGE - | -NSYAMNSFIQRQVISITKPIIEEAMTEFYTR - - - 57
 AmSAMT M----- | -TKQTQKQNKRMLKAQ - VLHMN - GGLGK - | -SSYASNSLVLQRKVVISITKPIIEEAMTEFYTR - - - 57
 AJMT M----- | -EVMR - VLHMN - KGNGE - | -TSYAKNSTAQSNIISLGRVMDEALKLKLMM - - - 46
 AmBAMT M----- | -KV----- MKK - LLCMNIAGDGE - | -TSYANNSGLQKVMMMSKSLHVLDETLKDIIGD - - - 48
 CaMXMT1 M----- | -ELQE - VLHMN - EGGED - | -TSYAKNASY - NLALAKVKFLEQCICRELLRA - - - 45
 AIBSMT1 MDPRFINTIPSLRYDDDKCDEYAFVK - ALCMS - GGDGA - | -NSYSANSRLQKVKVLSMAKPVLVRNTEEMMMN - - - 68
 AIBSMT MDPRFINTIPSLSYNDDKCDEYAFVK - ALCMS - GGDGT - | -NSYSANSRLQRKVLTMAKPVLVKTTEEMMMS - - - 68
 CsTCS1 MELATAG - - - KVNE - VLFMN - RGEGE - | -SSYAQNSNSLVLQRKVFTQVVASMAQPALENAVETLFSR - - - 52
 ObCCMT1 MARK-ENYVVS - - - NMNVES - VLCMK - GGGKE - | -DSYDNNSKMQEIQHARSVLHLLMEALDGVGL - - - 56
 AJMT MGSKGDNVAVC - - - NMKLER - LLSMK - GGGKQ - | -DSYANNSQAAQMHSRSMHLLLEETLENVHLN - - - 58
 AIFAMT M----- | -S - TSFTMIGGEG - | -NSYREHSKYQGALVIAAKEKINEAISTKL - - - 42
 SdOMT4 MEV----- KMWSDEEEEVRLTALKLASGAVLPMLKAVALDLFELIKNAESNISAQALAVQLPTTPNAASMLDRVRLLAANSILICSLHGAND - - - 92
 SdOMT3 MATNSATTNPQGEEEEENFLFAMQLASASVLPMLVKAAILD - - - - RIRLRLASAYAVLECRELETLESQAV 66
 SdOMT9 MASS----- SQDVLEAQAHVWNHIFSYIKSMALRSAVELRIPDAIHKGKPMTLSQLAESLSINNEKTNGLY - - - 90
 SdOMT18 MKDK ----- YY - - - GSILQSE - - - ALAKYILETSVYPREHEQLT 33
 SdOMT19 METK ----- VVINTTSSTEKGVLQTA - - - ELYNYVMDTSVYPREHECLK 41

100 | -VDA - ITNCFCIAELGCSSGPNSLVVGAELISTVHQLRSQGRQ - LP-EFQIFLNDLPGNDNFNSIQFSLLPQFRAQLNRE - - - MGS-ESAP - CLV 132
 PhBSMT1 -----L-FPETLCIADLGCSLGANTFLVVSQQLVKEKERKKHGFK - SPEFYFHNDLPGNDNFNTLQFSL-GAFQEDLRKH - - - IGG-ESFG-PCFF 129
 SfSAMT -----L-FPKSICIAADMGCSSGPNTFLAVSELINKVEKKRTSLGHE - SPEYQIHLNDLPSDNDFNTIIFRSL-PSFQKSFSKQ - - - MG-SGFG-HCFV 129
 NsBSMT -----L-SPEAICIAADLGCSGPNTFLTISELIKTYEESINKQK-QSPEFQVFLNDLPGNDNFNTIIFRSL-PALYEDLRKH - - - MG-DGFGTNCFV 131
 CbSAMT -----DT - VTRRLAIADLGCSGPNALFAVTELIKTVEELRKKMGRE - NSPEYQIFLNDLPGNDNFNAIFRSL-P - - - IE-NDVDGVCF 123
 AmSAMT -----MLP-SPHTSIADLGCSGPNTLLVAEALVKIVLRLQKLDRE-PPPEFQVFLNDLPGNDNFNTIIFRSL-PSFQVFLNDLPGNDNFNTIIFRSL- - - IGGEEAGRRCFV 147
 AJMT -----NSE-1-SSGICIAADLGCSGPNSLSSISNVTIHLNCPDLDR - PVPFLRVLSDNLSDFNVIASL-PEFYDVRNNNEKGGLGFRGGGESCFV 136
 AmBAMT -----HVQ-FPKCFKMMMDMGCGSGPNALLVMSGIINTIEDLYTEKNIN-ELPEFEVFLNDLPGNDNFNTIIFRSL- - - SHENGNCFV 123
 CaMXMT1 -----NLPNINKCIVKADLGCSGPNTLLTVRDVQSVIDKVGQEEKKNERLEPTQIIFLNDLQFQNDNFNSVFKLPSFYRKLEKNGRKIG - - - SCLI 133
 AIBSMT1 -----L-DFPTYIKVAELGCSSGQNSFLAIFEINTINVLCOHVNKN - SPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - MITSKACFV 149
 CsTCS1 -----DFHL - QALNAADLGCAAGPNTFAVISTIKRMMEKKCRELNCQ-TLELQVYLNLDLFGNDNFNTLFGKLSSEVIGNKCEEV - - - PCYV 132
 ObCCMT1 -----SSA-AAGAFVFLDGCSSGQNSFLAIFEINTINVLCOHVNKN - SPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - SDGSSGSYFT 133
 AJMT -----SSA-SPPPFATVLDGCSSGQNTFLAISEINTISVLCOHVNKN - PPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - MITSKACFV 149
 AIFAMT -----DIDFTSNLVNIAFDGCSSGPNTTAVQTLIDAVENKYKKS - NIEGIEFQVFFNDNSNDFNTLFLCKLTP - - - ARLYFA 117
 SdOMT4 - RRYALSPVGKFFTENEDGGSCRAVTLTQDKVL - - - MEGWYNLKDAILEG-GNPFERA - - - HGMS-IFG 153
 SdOMT3 GRRYGLAPVCKFLTKNDGVSMAPLAQMNDQKV - - - MESWYHLKDAVLDG-GIPFNKA - - - YGMATAF 128
 SdOMT9 -----YSLTRASRLLI-SDEPLSLAPALLLTDPAV - - - IDPFHHMSEWYRDECPTAFTITK - - - NGMDHWY 149
 SdOMT18 EIRKATVDKYQFWSV - - MNISADEGQFLSM - - LLKIMNAKKTLEVGVTGYSLLTTALALPDDAIIAIDP - - - DREAYE 106
 SdOMT19 ELRAITSTHPR - - AV - - MGTPSPDVQFMAL - - LLTTINAKKTEIEGVFTGYSLLQTLAIPDDGKITAIDV - - - NRSWYE 112

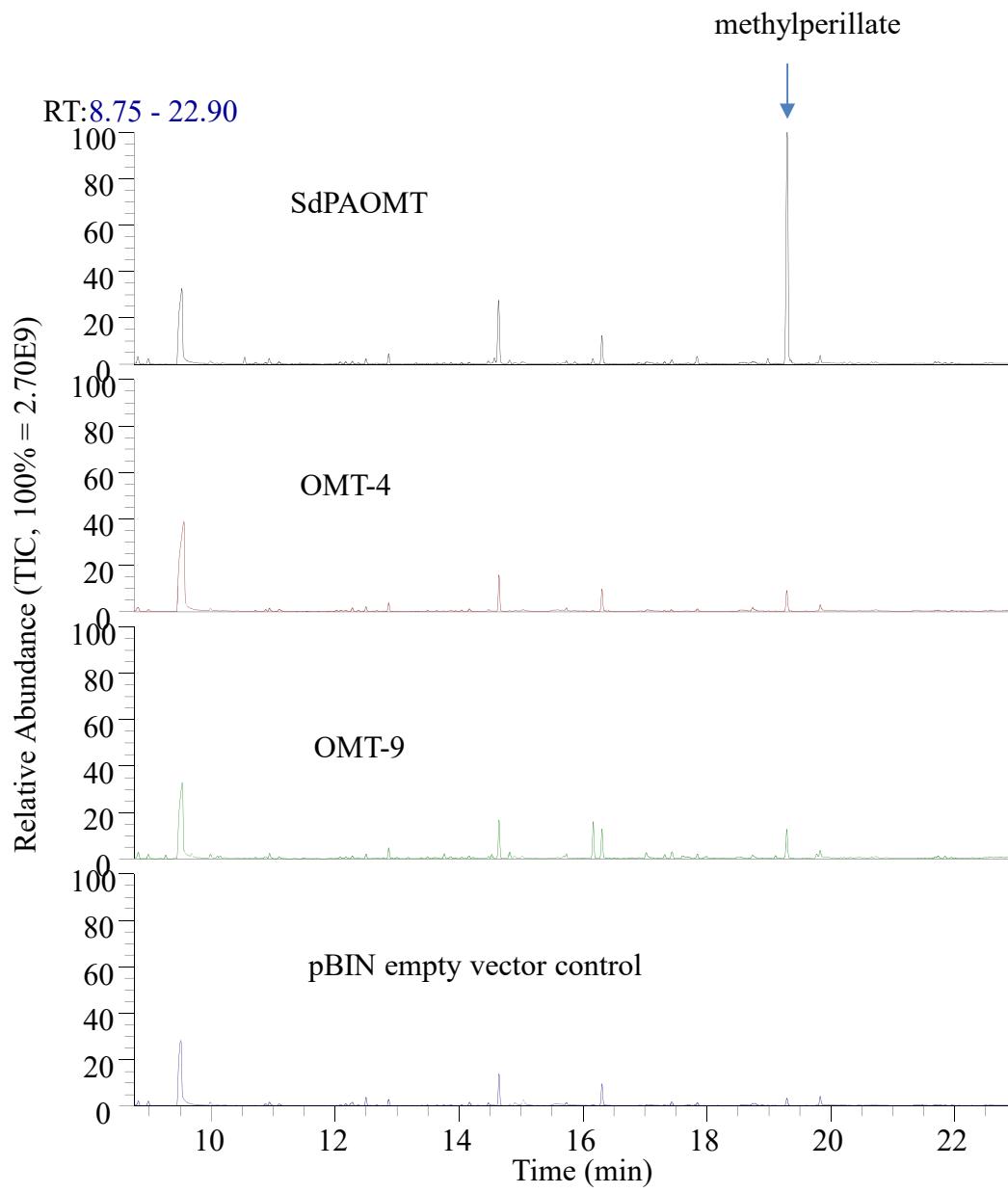
200 | -VDA - ITNCFCIAELGCSSGPNSLVVGAELISTVHQLRSQGRQ - LP-EFQIFLNDLPGNDNFNSIQFSLLPQFRAQLNRE - - - MGS-ESAP - CLV 132
 PhBSMT1 -----L-FPETLCIADLGCSLGANTFLVVSQQLVKEKERKKHGFK - SPEFYFHNDLPGNDNFNTLQFSL-GAFQEDLRKH - - - IGG-ESFG-PCFF 129
 SfSAMT -----L-FPKSICIAADMGCSSGPNTFLAVSELINKVEKKRTSLGHE - SPEYQIHLNDLPSDNDFNTIIFRSL-PSFQKSFSKQ - - - MG-SGFG-HCFV 129
 NsBSMT -----L-SPEAICIAADLGCSGPNTFLTISELIKTYEESINKQK-QSPEFQVFLNDLPGNDNFNTIIFRSL-PALYEDLRKH - - - MG-DGFGTNCFV 131
 CbSAMT -----DT - VTRRLAIADLGCSGPNALFAVTELIKTVEELRKKMGRE - NSPEYQIFLNDLPGNDNFNAIFRSL-P - - - IE-NDVDGVCF 123
 AmSAMT -----MLP-SPHTSIADLGCSGPNTLLVAEALVKIVLRLQKLDRE-PPPEFQVFLNDLPGNDNFNTIIFRSL-PSFQVFLNDLPGNDNFNTIIFRSL- - - IGGEEAGRRCFV 147
 AJMT -----NSE-1-SSGICIAADLGCSGPNSLSSISNVTIHLNCPDLDR - PVPFLRVLSDNLSDFNVIASL-PEFYDVRNNNEKGGLGFRGGGESCFV 136
 AmBAMT -----HVQ-FPKCFKMMMDMGCGSGPNALLVMSGIINTIEDLYTEKNIN-ELPEFEVFLNDLPGNDNFNTIIFRSL- - - SHENGNCFV 123
 CaMXMT1 -----NLPNINKCIVKADLGCSGPNTLLTVRDVQSVIDKVGQEEKKNERLEPTQIIFLNDLQFQNDNFNSVFKLPSFYRKLEKNGRKIG - - - SCLI 133
 AIBSMT1 -----L-DFPTYIKVAELGCSSGQNTFLAISEINTISVLCOHVNKN - PPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - MITSKACFV 149
 CsTCS1 -----DFHL - QALNAADLGCAAGPNTFAVISTIKRMMEKKCRELNCQ-TLELQVYLNLDLFGNDNFNTLFGKLSSEVIGNKCEEV - - - PCYV 132
 ObCCMT1 -----SSA-AAGAFVFLDGCSSGQNSFLAIFEINTINVLCOHVNKN - SPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - SDGSSGSYFT 133
 AJMT -----SSA-SPPPFATVLDGCSSGQNTFLAISEINTISVLCOHVNKN - PPEIDCCCLNDLPENDFNTTFKPV-PFFNKEL - - - ADGNR-SYFV 146
 AIFAMT -----DIDFTSNLVNIAFDGCSSGPNTTAVQTLIDAVENKYKKS - NIEGIEFQVFFNDNSNDFNTLFLCKLTP - - - ARLYFA 117
 SdOMT4 - RRYALSPVGKFFTENEDGGSCRAVTLTQDKVL - - - MEGWYNLKDAILEG-GNPFERA - - - HGMS-IFG 153
 SdOMT3 GRRYGLAPVCKFLTKNDGVSMAPLAQMNDQKV - - - MESWYHLKDAVLDG-GIPFNKA - - - YGMATAF 128
 SdOMT9 -----YSLTRASRLLI-SDEPLSLAPALLLTDPAV - - - IDPFHHMSEWYRDECPTAFTITK - - - NGMDHWY 149
 SdOMT18 EIRKATVDKYQFWSV - - MNISADEGQFLSM - - LLKIMNAKKTLEVGVTGYSLLTTALALPDDAIIAIDP - - - DREAYE 106
 SdOMT19 ELRAITSTHPR - - AV - - MGTPSPDVQFMAL - - LLTTINAKKTEIEGVFTGYSLLQTLAIPDDGKITAIDV - - - NRSWYE 112

200 | YGVPGSFYGRFLFAANSLHFVHSSYSLMWLSKVP - - - EGVEKWNLKEEYIYGSGSPPTVINAYYSQFRLDFDTFLKCRSEEVVGGAVALTILG 221
 PhBSMT1 SGVPGSFYTRLFPKSLSLHFVYSSYSLMWLSQVP - - - NGIEN-NKGNIYMARSTSPLSVIKAYYKQYEIDFSNFLKYLQKREELMKGGMVLTLLG 217
 SfSAMT TGVPGSFYGRFLFPNKSLSLHFVYSSYSLMWLSRVP - - - DLEEV-NKGNIYLSSTSPLSVIRAYLQKQRFDTFTLQCRRAELVPGGVMVLTLMG 217
 NsBSMT AGVAGSFYNRLLFPSSNSVHFVHSSYSLMWLSRVP - - - HGIEN-NKGNIQVASTSPQDQVVEAYEYQERDFVNFLKLRSIELVKGRMVLTVMG 219
 CbSAMT NGVPGSFYGRFLFPNLTGHFIHSSYSLMWLSQVP - - - IGIES-NKGNIYMANTCPSQVNLNAYYKOFQEDHALFLRCRAEVVPGGRMVLTILG 211
 AmSAMT SGVPGSFYGRFLFPKTSLSLHFVHSSYSLMWLSKVP - - - EGV-KMNNIYASTSPQNVINAYEQFQQRDFSSFLICRSEEVIGGRMVLTFLG 235
 AJMT SAVPGSFYGRFLFPKTSLSLHFVHSSYSLMWLSQVP - - - EGLEDNNRNQIYMATESPPEVYKAKYQERDFSTFLKLRGEEIVPGGRMVLTENG 212
 AmBAMT YGLPGSFYGRFLFPKKSLSLHFAYSSYSLWLSQVP - - - EGLEDNNRNQIYMATESPPEVYKAKYQERDFSTFLKLRGEEIVPGGRMVLTENG 212
 CaMXMT1 SAMPGSFYGRFLPEESMFLHSCSYVHWSLQVPSGLVIELGIGA - - - NKGSIYSSKGCRPPVQKAYLQDFTKFTFLRHSKELFSRGRMLLTIC 227
 AIBSMT1 YGAPGFSYFRLFSRNSLHIIHSSYALHWLSKVPKEKL - - - ENNKGNLYNTSSSPQSAKAYLQNFQDFKDMFLRSEEIVSNGRMVLTFIG 237
 AIBSMT YGAPGFSYFRLFSRNSLHIIHSSYALHWLSKVPKEKL - - - ENNKGNLYNTSSSPQSAKAYLQNFQDFKDMFLRSEEIVSNGRMVLTFIG 237
 CsTCS1 MGVPGSFHGRFLFPNSLHVFHSSYVHWSLQPKGLTSREGLAL - - - NKGKIYISKTSPVQHFEDFTMLNARSOEVVPNCMVLI LRG 226
 ObCCMT1 AGVAGSFYRRLFPAKSVDFYSAFLSHWLQSPQKIPKEVMEKGSAAY - - - NEGRVTI-NGAKESTVNAYKQFQSDLGVFLRSRSKELKPGGSMFLMLLG 226
 AJMT AGVPGSFYRRLFPARTIDFFHSAFSLHWLSQPSVTDRRSAAY - - - NGRVRTI-HGAGEKTTAYKRFQADLAEFLRARAEEVKRGAMFLVCLG 239
 AIFAMT SGVPGSFFGRVLPKNSLHVGSSYSLHFVSKVPEIKEKDRDSL - - - WNK-DIH-CSGSKSEVKKVLYLGQYKIDVGSFLTARAOELVSGGLLMLLG 209
 SdOMT4 YAAKDGRISSSL - - - NKVMSE-STFLVKKVIEEMYKG-FE - - - GGETVVDVGGGT - - - G 200
 SdOMT3 YHGTDPRFNKIF - - - NQGMSNSHSTITMKKILETYING-FD - - - GVKTVVVDVGGGT - - - G 176
 SdOMT9 FAAKDESWNQMY - - - NEAMAADARFVGSLVLLKECKHIFE - - - GLKTMVDVDAGGS - - - G 198
 SdOMT18 IGLP - - FIEKTNMTHKIQFIQSN-AMAVMKDLLS - - - KGE-EGADEF - - - AFVDADKENIYKHYEQLLKVVGIIAYD - - - 176
 SdOMT19 IGLP - - IDKARMTHKINFIESE-ALPVLDQLMK - - - DPNKGTFDF - - - AFVDADKDNYANYHERVELLKPGGIAYD - - - 183

300 | RKS-ENAASKECCCIWEL-LALSLSKEMVSEGAEIEEKVHSF-NIPEYTPSPAVERRSVEEEGSFATIRLEASERIW - - - AECCG - - - GG 301
 PhBSMT1 RES-EDPTSKECCYIWEL-LAMALNKLVEEGLIKEEKVDAF-NIPQYTPSPAVERVYIIVEKGSFTINRLETSRVHW - - - NASNNE - - - KNG 299
 SfSAMT RKG-EDHSKGESYALEL-LARALNLELVEGQIEEQLDCF-NVPQYTPSPAVERVYFVEEKGFSITREALLEIHW - - - TAYDHDTGHHHAFKDG 308
 NsBSMT RNN-EDRFSKASCYILEP-MYMLALNEIAEGSIEEEKVAAF-NIPVYPPSPAEVKYIVEKEGSFAIDVLTSEIHM - - - DSSNE - - - 297
 CbSAMT RRS-EDRASTECCLIWQL-LAMALNQMVSEGLIEEKKMDKF-NIPQYTPSPAVERVYIIVEKGSFLIDHIEASEIYW - - - SSCTKDGDGDDG - - - SVEEE 300
 AmSAMT RKS-ASARSKECCYIWEL-LSLALKQLVLEGIVEKEKLSHS-HIPQYTPSPAVERVYIIVEKGSFTIDRLEISPIDWEGGSISEESYDLAIRSKPEALAS 331
 AJMT RRS-LDPTTEESCYQWEL-LAQLALMSMAKEGIIEEEKIADF-NAPYYAASSEELKVMIEKEGSFSIDRLEISPIDWEGGSISEESYDLAIRSKPEALAS 331
 AmBAMT RSV-EDPSKSDLLAIFT-LAKTLDVMDVMAEGLVMDLDSYNSF-NIPIYSPCTREVEAII1SEGSFTLDRLEVFVRVCWDASDYTDF-DDDQQDPSIFGKQRS 307
 CaMXMT1 KVD-EFDEPNP - - - LDL-DMALINDLVEGLEELKDSL-NIPFTPSAEEVCKIIVEEGSCEIYLETFKAHYDAAF-S1DDDYPVRSHEQIKAE 317
 AIBSMT1 RNTLNDPLYRDCCHFWTL-LSNSLRDLYFEGLVSESKLDAF-NMPFYDPNVQELKEV1QKEGSFSEINELESHGFLDGHY-YEEDDFE - - - A 322
 AIBSMT RNTLNDPLYRDCCHFWTL-LSNSLRDLYFEGLVSESKLDAF-NMPFYDPNVQELKEV1RNEGETHGFQDLSHNSYEEEDDYE - - - A 322
 CsTCS1 RQ-CSDPDMQCSFTWEL-LAMALIAEVLSQGLIDEDKLDTF-NIPSYFASLEEVKIDVERDGSFTIDHIEQFDL - - - SVEMQENDKWR - - - 310
 ObCCMT1 RTSPDPADQGAWILTFSTRYQDAWNDLVOEGLISSEKRDFT-NIPYTPSLEEFKVERDGAIFIINKLQL-FHGSALIIDDPN - - - AVEI 314
 AJMT RTSPDPADQGAWILTFSTRYQDAWNDLVOEGLISSEKRDFT-NIPYTPSLEEFKVERDGAIFIINKLQL-FHGSALIIDDPN - - - AVEI 314
 AIFAMT RTSPDPADQGAWILTFSTRYQDAWNDLVOEGLISSEKRDFT-NIPYTPSLEEFKVERDGAIFIINKLQL-YKGGSPVLPVNEPD - - - ASEV 327
 SdOMT4 ATLSII1VAQNPS1KGINFDLPHV1QDAPSYPG1VHVGGMDFVNVP - - KADVFMKWLHWDGD - - AECVRI1LNKCKAALPENG - KVVIVERALSEIPM 293
 SdOMT3 ATLNM1LSKYP1KGINFDLPHV1EDAPSYPG1VHVGGMDFVNVP - - KDA1FMWKI CHDWSD - - EHCVKFLKWNHCDALPQNG - KV1AECVLPEAPD 269
 SdOMT9 EVSKALTGAFSGLCKIVLDLPHV1VARMEGSENVFRVSGDMFEPF1 - - PADAVFLWKW1MHDWKD - - EDC1K1LGCKEIAHNGNKKVII 1VDMVWDEEQK 293
 SdOMT18 - - - NTLWSGTVVAEEDEMDDYLRGCKH1LNLNLSFLAADSRIELAQLS1 - - - 223
 SdOMT19 - - - NTFWAGTVAMDEASPVESLASRKA-LIEFNKHIAGDARVQISQIPL - - - 229

400 | 420 | 440 | 460 | 480 | 500 |
 SdPAOMT SYDVAKCMRSVAEPLLMEHFGGS1-IDELFEKYERILTDRMS - - - KEEMKF1NTVTSILRR - - - 359
 PhBSMT1 GYVNSRCMRAVEAPLLVSFVSHDFKEL-MDLVFLHKEYE1VSDCMS - - - KENTEFINVINSL-TKIN - - - 357
 SfSAMT GYSLSNCRVAVPVEPLLVRHGEAI-MDEVFHRYRE1LTNCMT - - - KEKIEFINVTVSM-KRRV - - - 366
 NsBSMT - - - YNVTQCMRAFIEPLVNVNHFGE1LNMDQVHFHKCGE1FDNIIIA - - - KEKTTISINVVSL-TKTN - - - 355
 CbSAMT GYNVARCMRAVEAPLLDDHGEAI - - - IEDVFLHRYKLLI1IERSM - - - KEKTKFINVVISLIRKSD - - - 359
 AmSAMT EYNVAKCMRSVAEPLLIEHFGESV-IDRLFEKYERI1FDRMS - - - REETKFFNVTISMTRR-E - - - 383
 AJMT GRRVSNT1RAVVEPMLEPTFGENV-MDELFLERYAK1VGEYFY-VSSPRYAI1VILSLV-RTG - - - 389
 AmBAMT GKFVADCVRATEPMLASHFGST1-MDLLFGKYAK1VEHLS-VENSSYFSIVVSLSR - - - 364
 CaMXMT1 - - - YVASL1RSVYEP1LASHFGGEAI-MPDLFLHRLAKHAALKVH-MGKGCYNNL1IISLAKKPEKSDV 378
 AIBSMT1 GRNEANGIRAVSEPM1IAHFGE1-IDTFLDKYAHV1TQHAN-CRNLKTTVSLVSLTKK - - - 379
 AIBSMT GHDEANCIRAVSEPM1VAHFGE1-IDTFLDKYAHV1TQHAN-CRNLKTTVSLVSLTKK - - - 380
 CsTCS1 GEKFTKVRFAFTEPI1SNQFGE1-MDKLYDKFT1VVSDE-AKLPKTTT1ILVLSK - - - IDG 369
 ObCCMT1 SRAYVSLCRSLTGLV1DHA1GDLQLG-HELFSRLLSQAVDQAKELMDQFLVH1VSL - - - LA 373
 AJMT GRAFASSCRSVAQV1VAH1GEELS-RESRATSHAKDVLVNLQFFFHIVASLS - - - FT 386
 AIFAMT - - - YLTSIAFKVTVGGSV1FLQGQD-GMECTYELVKEK1QMLPQ1IAKAKPGMQLY1VLRN - - - 348
 SdOMT3 TGPANGEEGS-NYVMLVFNPGAKERTEKEF1RLGKAGFHFGRKVCTAAALWVMEFF - - - 349
 SdOMT3 TGLATKVNWHIDV1MLAHNPGKTERKEF1HNLAKAAGFHKFNKACAYNSWIMELL - - - K 327
 SdOMT9 THLL----MDVLMMMTHYPG-KERTETEWAFLTAAGFNNYK1THTLGVRS1IEVF - - - P 344
 SdOMT18 GDGLTLCRRL - - - T 234
 SdOMT19 GDGITYCRR - - - N 239

Fig. S14. Agro-infiltration of *Salvia dorisiana* methyltransferase candidates. Leaves of *N. benthamiana* were infiltrated with perillic acid and Agrobacterium cultures expressing several OMT candidates, or empty vector control. a. GC-MS chromatograms of leaf headspace; b. peak area of methylperillate m/z 180.1 extracted, quantified relative to pBIN peak empty vector control. Error bars indicate standard deviation. c. Mass spectrum of SdPAOMT product, +c Full ms [35.00-400.00], d. Mass spectrum of methylperillate reference compound, +c Full ms [35.00-500.00]



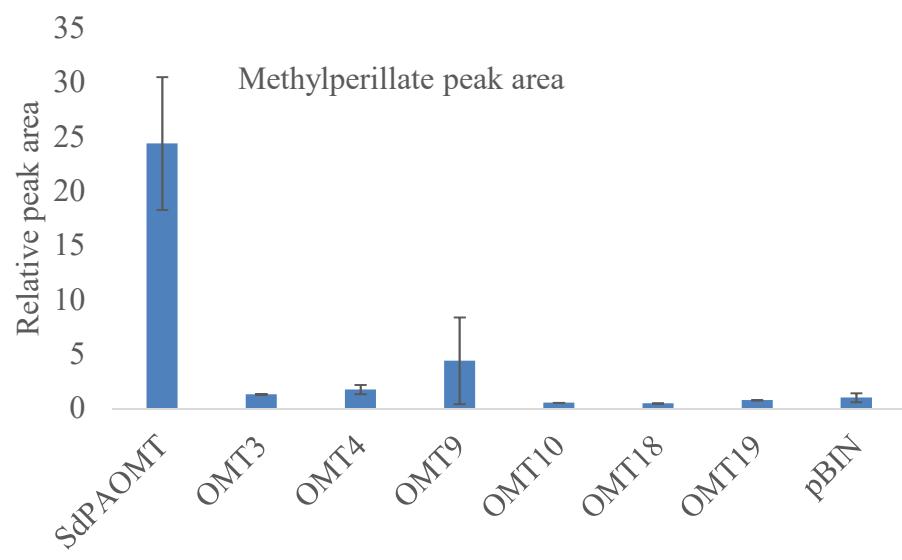


Figure S14b

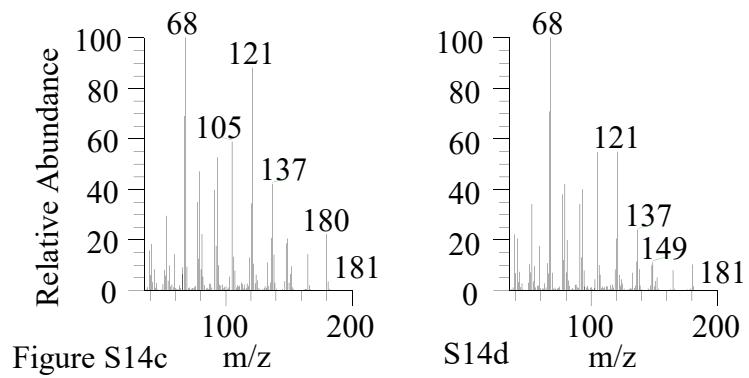
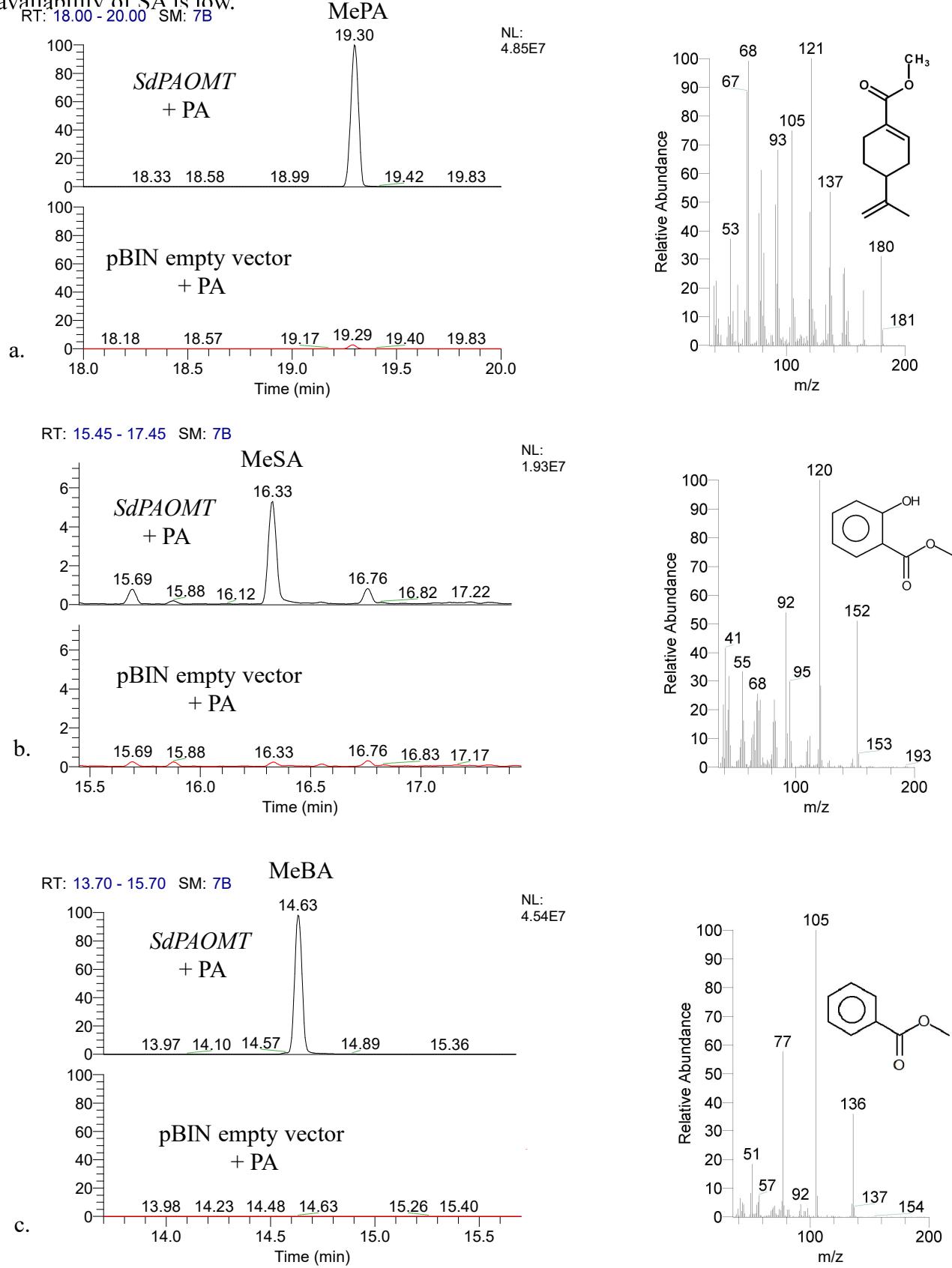


Figure S14c

S14d

Fig. S15 Headspace GC-MS analysis of *N. benthamiana* infiltrated with *SdPAOMT* and *S. dorisiana* leaves. Mass spectra are shown of MePA, MeSA and MeBA peaks. a. m/z 180-181 MS, MePA analysis, b. m/z 152-153, MeSA analysis, c. m/z 136-137, MeBA analysis, d. GC-MS chromatogram of *S. dorisiana* leaf headspace. Methyl perillate is indicated by an asterisk. When specific m/z 92-93+120-121+152-153 are extracted from the *S. dorisiana* chromatogram, a small MeSA peak becomes visible at RT 13.06, NL 1.91E6 (in TIC the methylsalicylate peak is covered by a decanal peak at RT 12.95). However, the ratio MeSA: MePA in *S. dorisiana* is much smaller than in *N. benthamiana*, so probably in *S. dorisiana* substrate availability of SA is low.



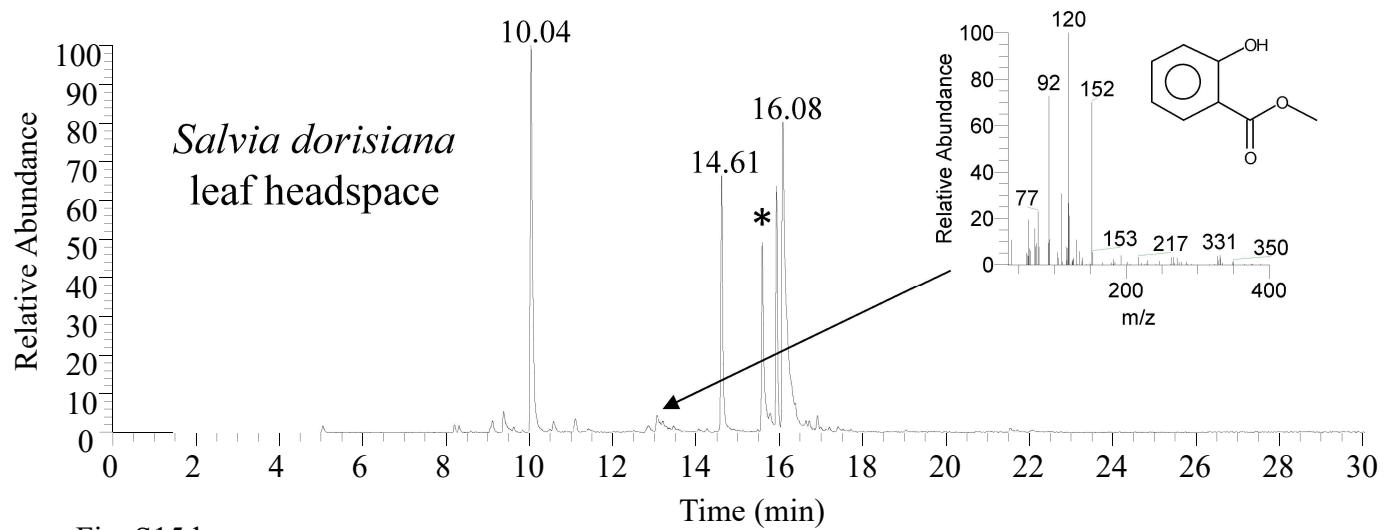


Fig. S15d.

Fig S16 Co-expression of *Picea abies* GPP synthase (*GPPS*) with *PfLS* in agroinfiltration of *N. benthamiana* increases limonene emission by 3-5 times

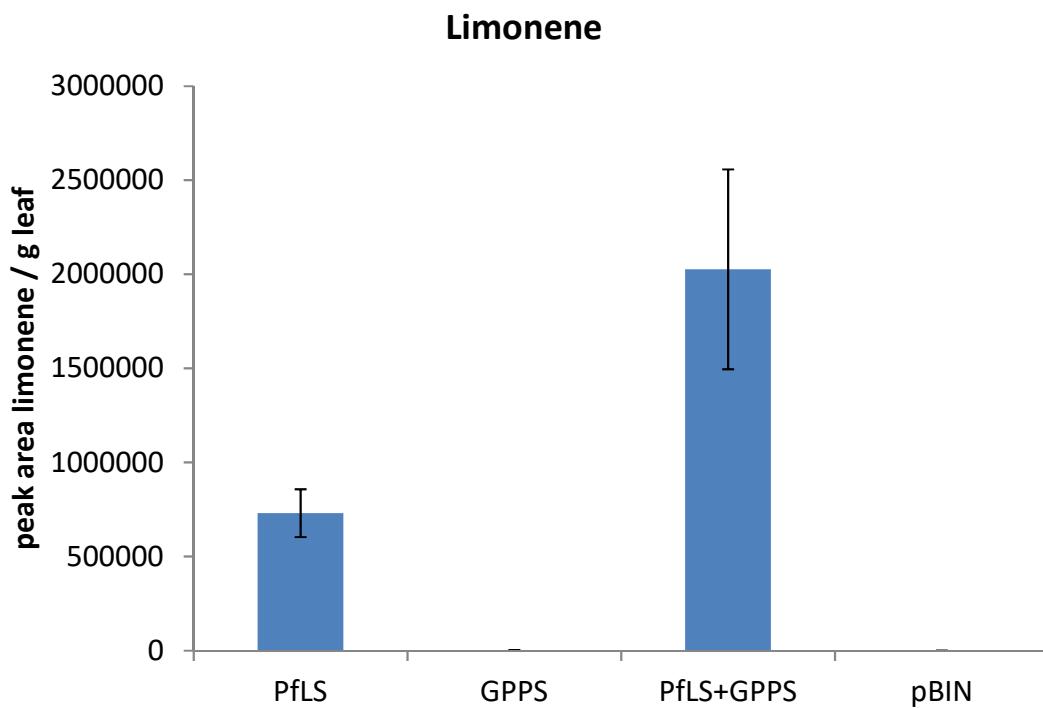


Figure S17. Agro-infiltration of methylperillate pathway genes (*SdLS*, *SdL7H*, *SdPOHDH* and *SdPAOMT*) results in production of perillyl aldehyde in the *N. benthamiana* leave headspace, which disappears when *SdPOHDH* is left out. a. GC-MS chromatograms of leave headspace m/z 149.5-150.5 NL 2.00E6, b. mass spectrum of perillyl aldehyde peak at RT 17.63, +c Full ms [35.00-400.00] c. mass spectrum of perillyl aldehyde reference compound

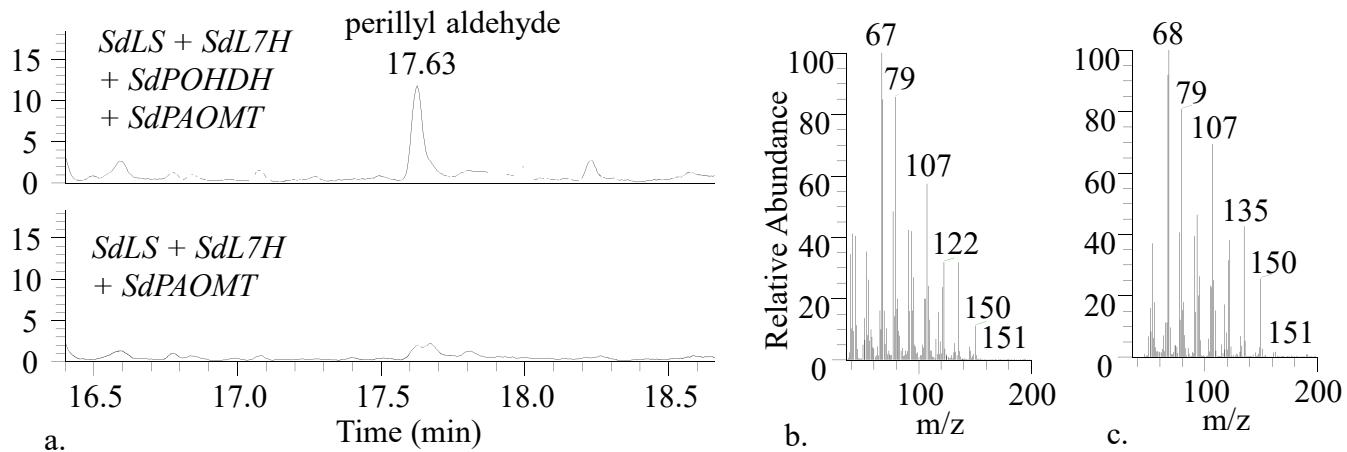


Figure S18 Methylperillate in agro-infiltrated *N. benthamiana* leaves headspace. GC-MS peak area methylperillate peak RT 19.26 m/z 180. Error bars indicate standard errors, N=3

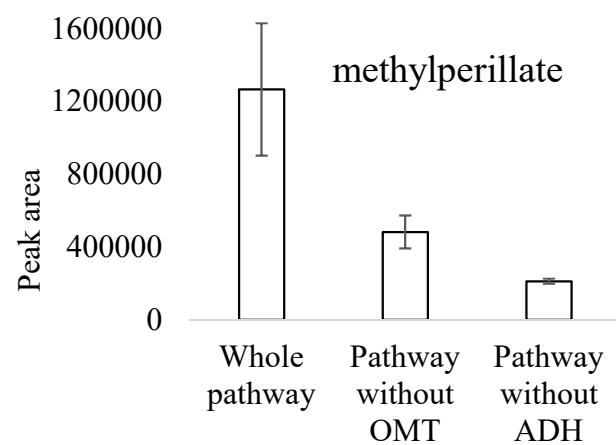


Figure S19: Reconstitution of the methylperillate biosynthesis pathway in *N. benthamiana*. Shown are LC-MS chromatograms of marker compounds representing plant metabolites of intermediates of the methylperillate pathway, and GC-MS chromatograms of methylperillate production in leaf headspace for different construct combinations. Marker compounds perillyl alcohol (POH-Mk1 and Mk2), perillyl aldehyde (PAldH-Mk1), perillic acid (PA-Mk1, Mk2 and Mk3) or methylperillate (MPA). Chromatogram characteristics: vertical scales are the same for each marker compound: POH-Mk1: 100% = 4.20E6 (m/z 355.1760-355.1770). POH-Mk2: 100% = 1.22E6 (m/z 491.2130-491.2150). PAldH-Mk1 100% = 6.86E4, (m/z 458.1950-458.1980). PA-Mk1: 100% = 1.11E6 (m/z 373.1500-373.1530). PA-Mk2: 100% = 4.67E5 (m/z 389.1450-389.1470). PA-Mk3: 100% = 6.98E5 (m/z 535.2030-535.2050). Methylperillate: 100% = 1.20E6, (m/z = 180-181).

