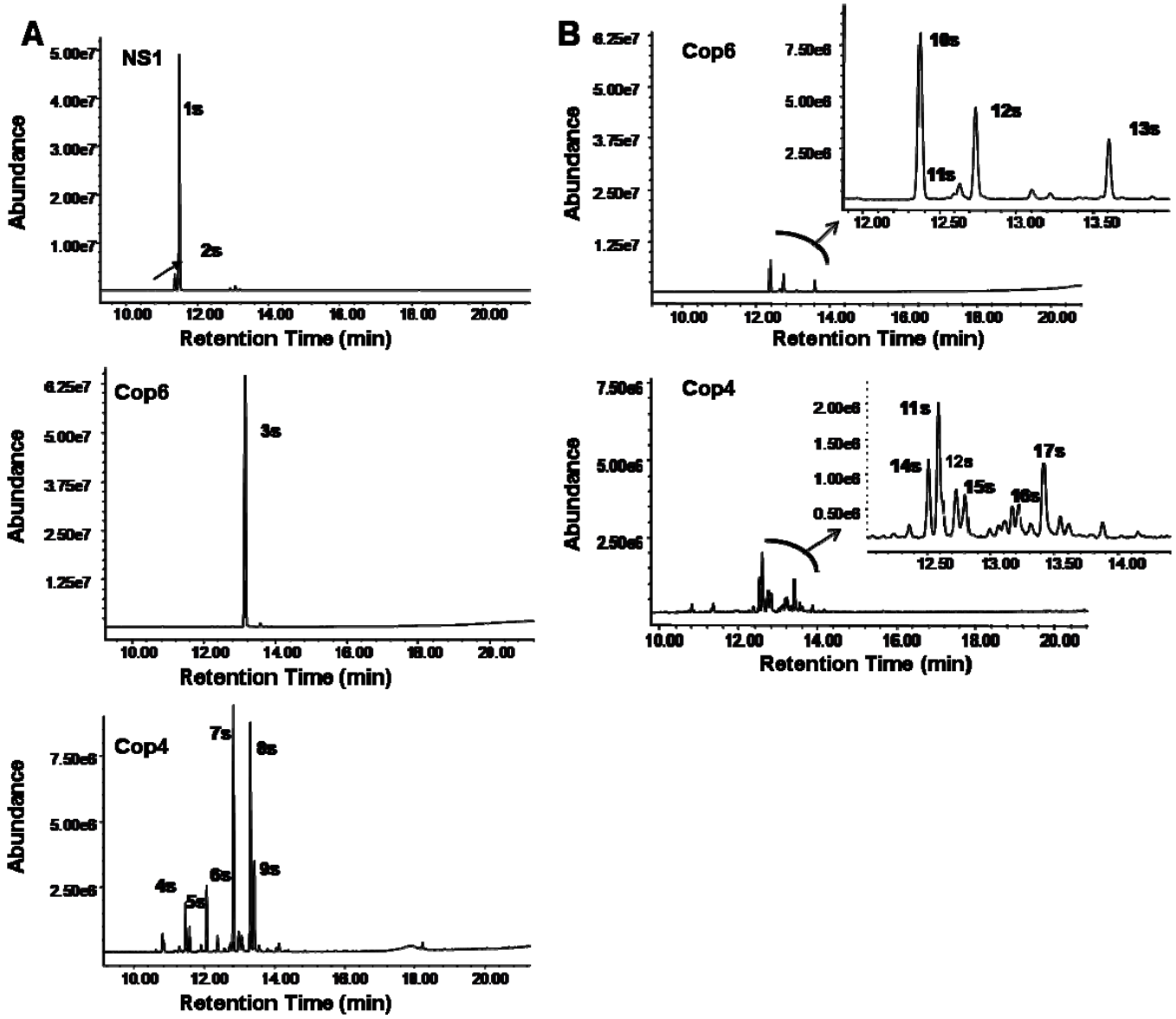
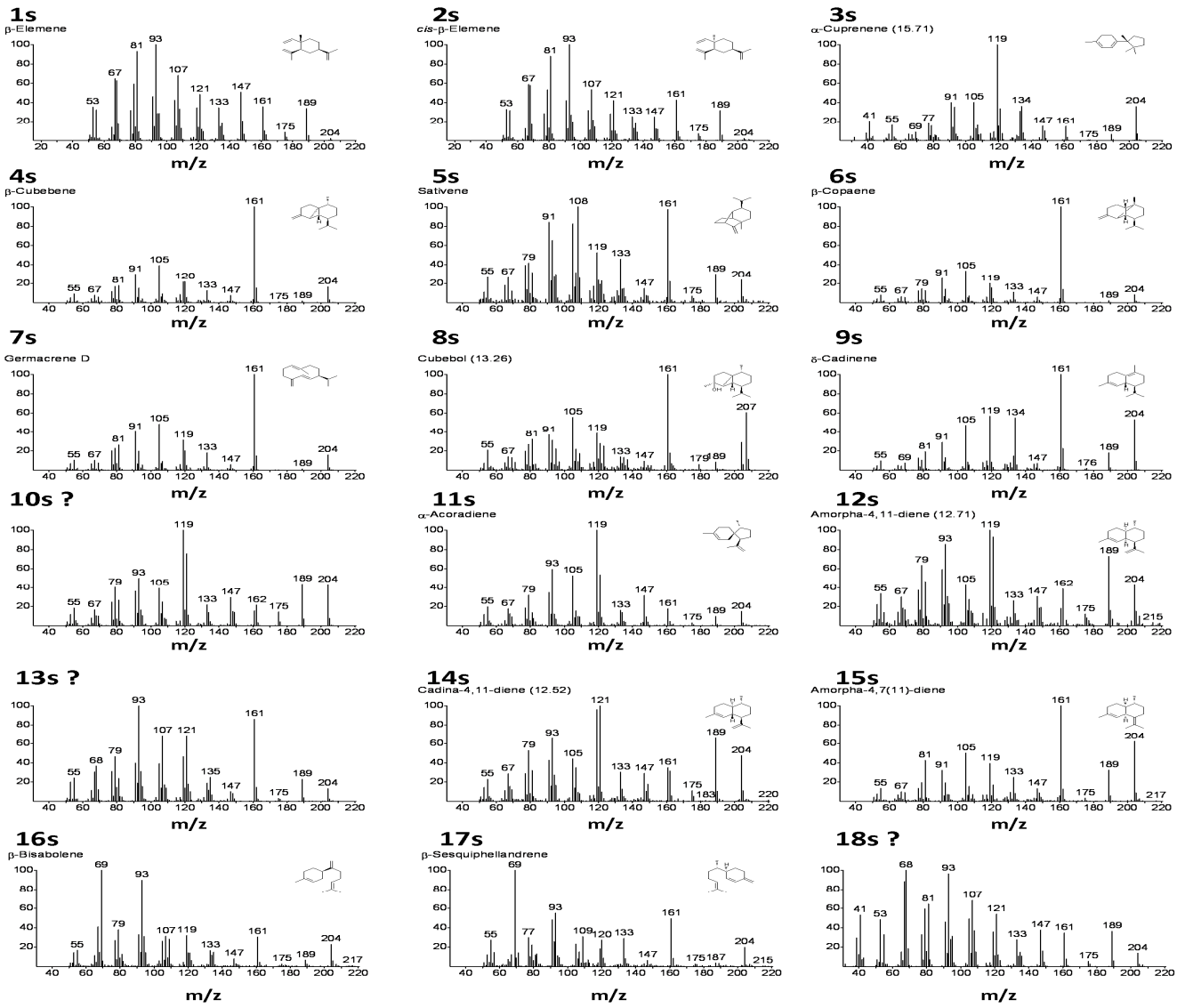
SUPPLEMENTARY INFORMATION

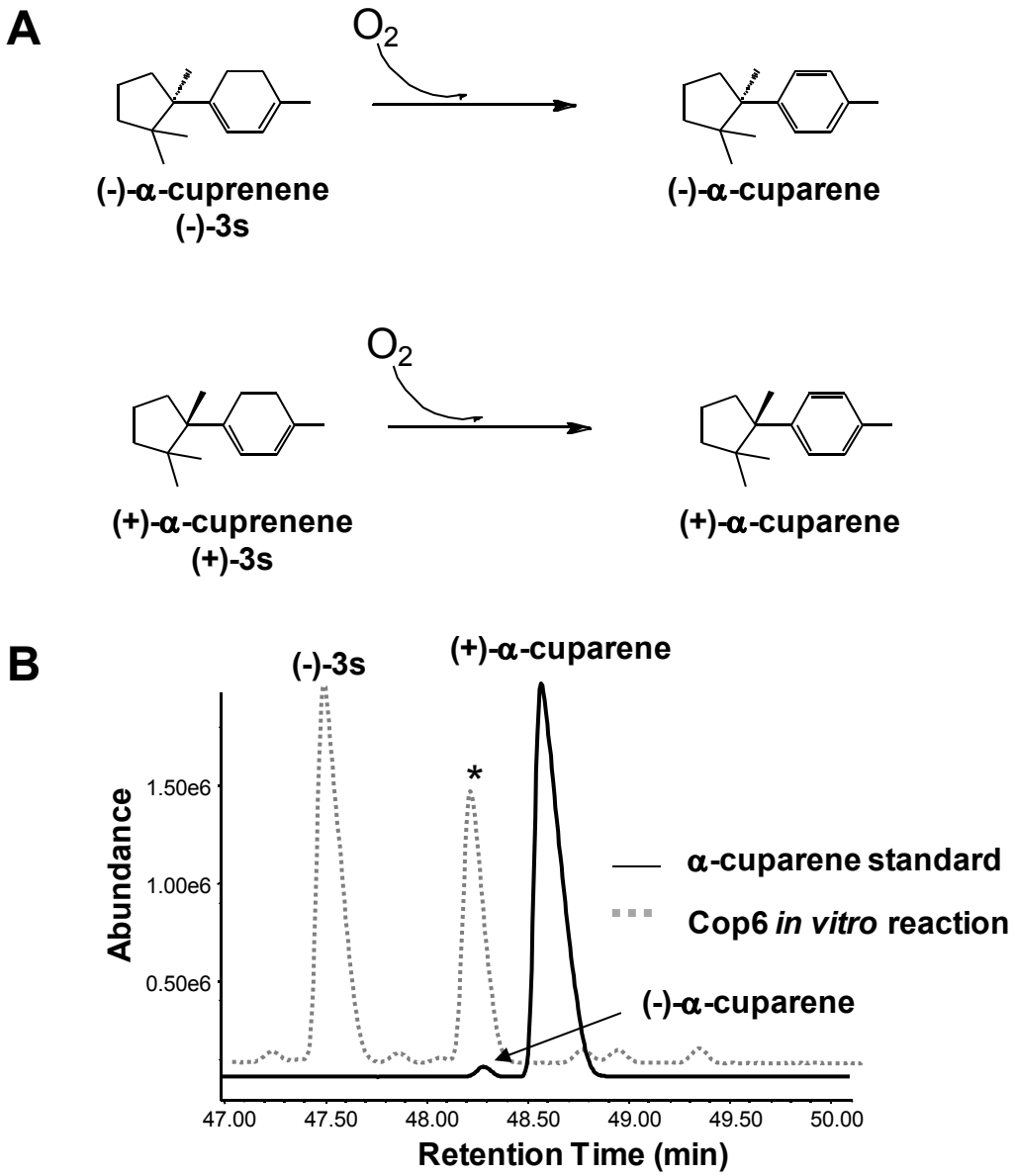
Supplemental Figure 1. GC/MS analysis of reaction products of *in vitro* assays of purified Cop4, Cop6 and NS1with *(E,E)*-FPP (A) and *(Z,E)*-FPP (B). Peaks are labeled with numbers that correspond to their identified structures in Schemes 1 and 2. Compounds were identified by comparison of their mass spectra and RI values with data from published reference (MassFinder3, terpene library [46] and authentic standards (Supplemental Table 1).



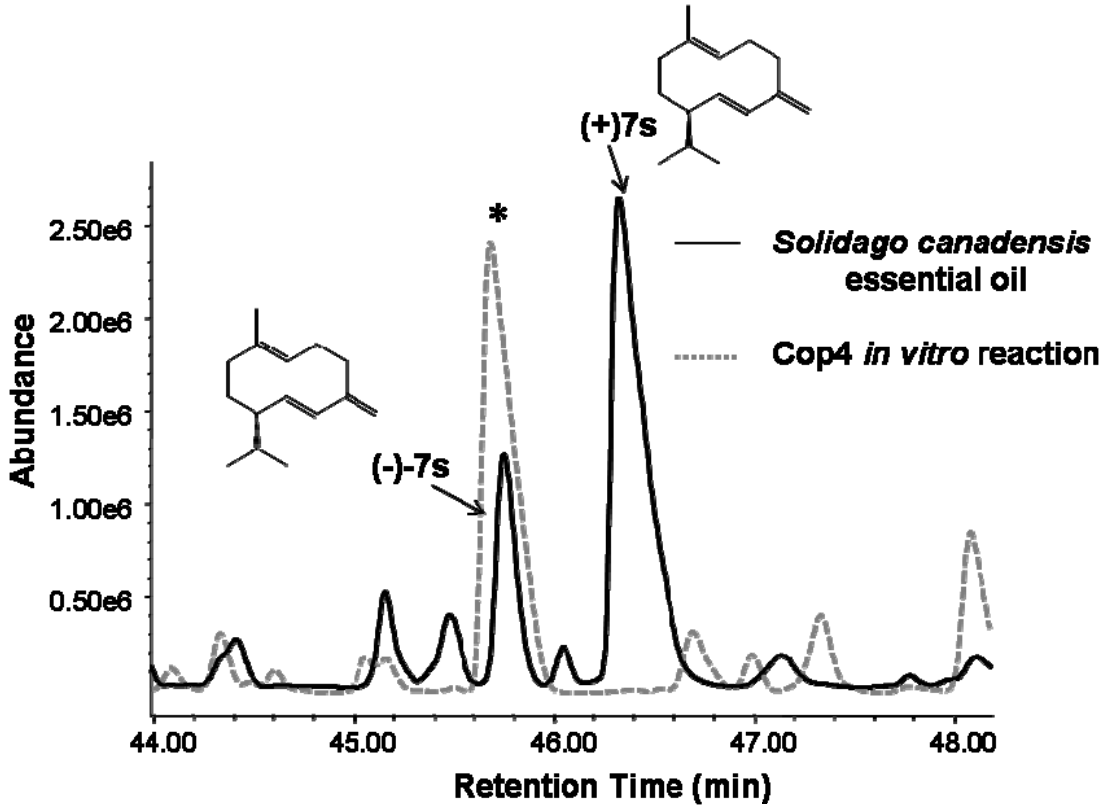
Supplemental Figure 2: Mass spectra of identified sesquiterpenoids. Numbers correspond to compound names shown in Schemes 1.



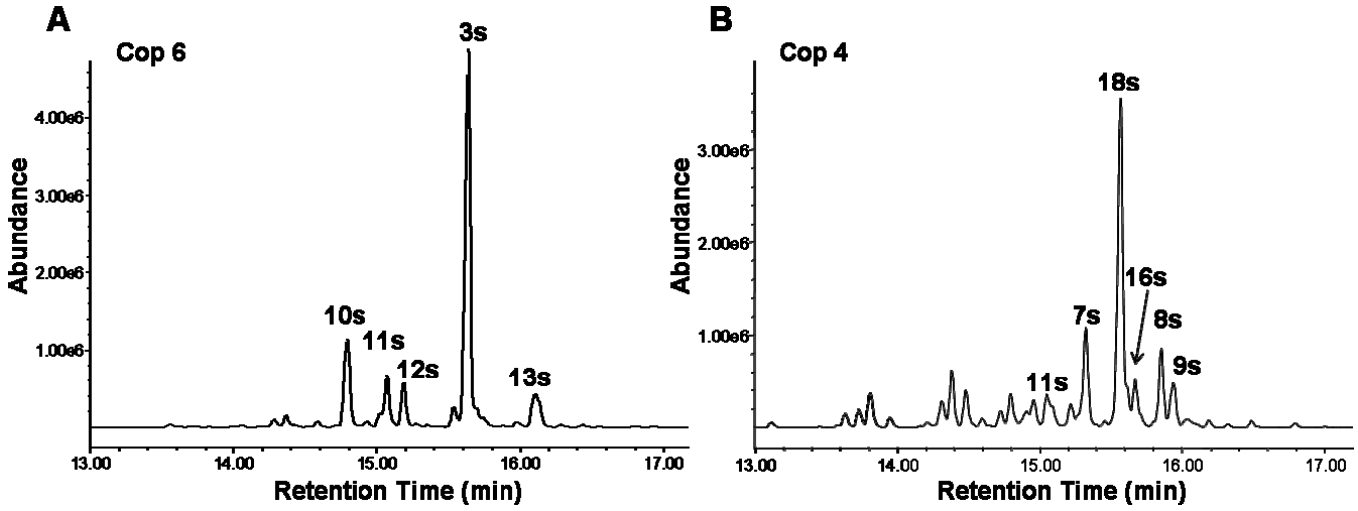
Supplemental Figure 3. Absolute configuration determination of α-cuprenene (3s). (A) The absolute configuration of the Cop6 reaction product α-cuprenene was indirectly determined by comparison of its oxidation product α-cuparene with a synthetic standard compound containing 98% (+)-α-cuparene, 2% (-)-α-cuparene. Dauben and Oberhänsli [73] report the isolation and synthesis of cuprenenes that under retention of absolute configuration slowly convert into the corresponding aromatic cuparenes after prolonged air exposure. *In vitro* reactions of Cop6 with (*E,E*)-FPP as a substrate were left standing for up to 30 days at 30 °C with periodic analysis of products formed. Air oxidation yields α-cuparene from α-cuprenene (**3s**). (B) Chiral GC-MS analysis of Cop6 reaction products (grey dotted line) after 30 days of air exposure and of synthetic α-cuparene (black solid line). Asterisk indicates (-)-α-cuparene as the oxidation product of (-)-α-cuprenene (**3s**) synthesized by Cop6.



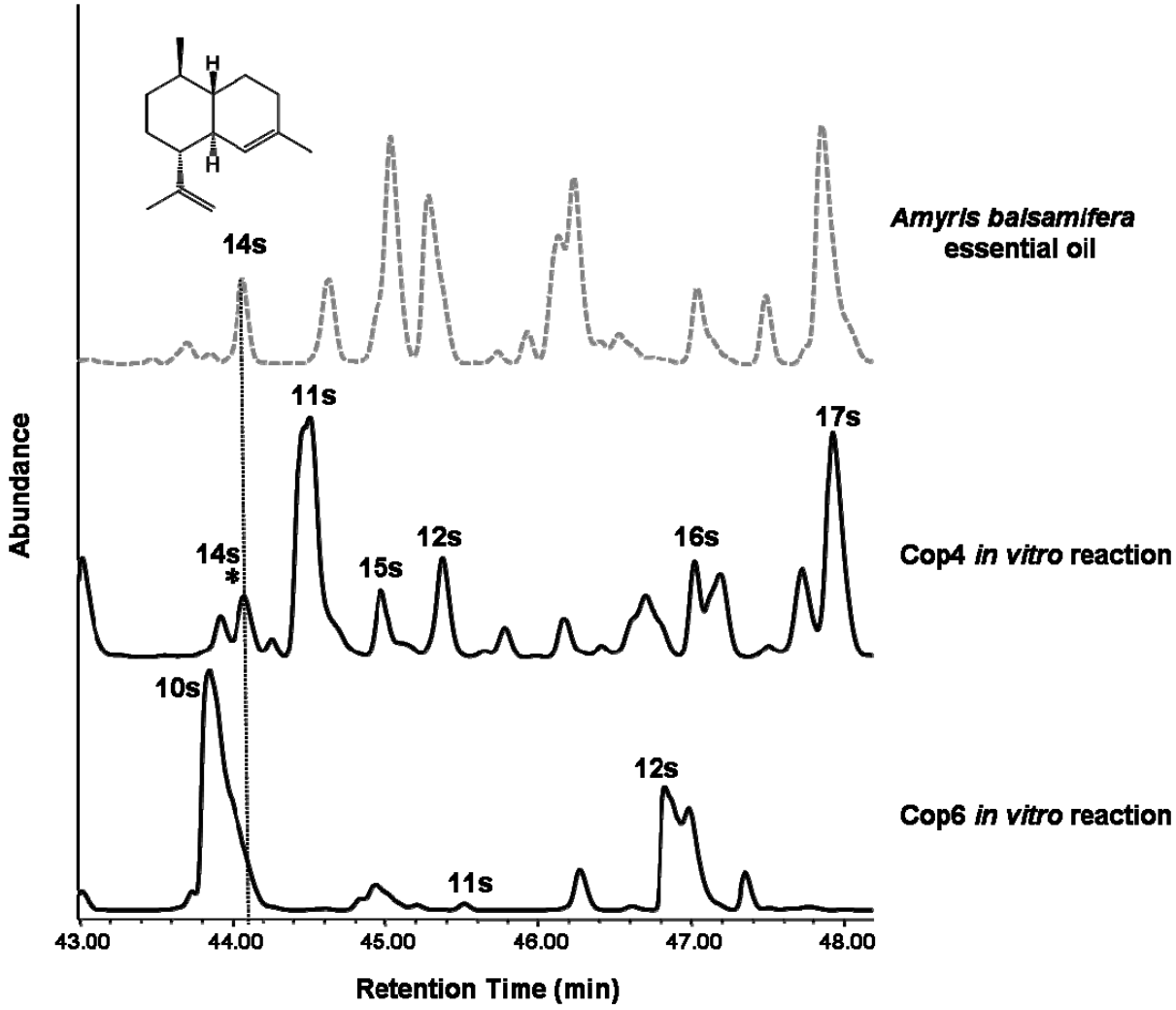
Supplemental Figure 4. Absolute configuration determination of germacrene D (7s). The essential oil of *Solidago canadensis* contains both germacrene D (**7s**) enantiomers, with (+)-germacrene D (**(+)-7s**) as the more abundant enantiomere [46]. Chiral GC-MS analysis of Cop4 *in vitro* reaction products obtained with *(E,E)*-FPP as substrate (dotted grey line) and of terpenes in *Solidago canadensis* essential oil (solid black line) show that Cop4 synthesizes (-)-germacrene D (**(-)7s**) (peak labeled with an asterisk).



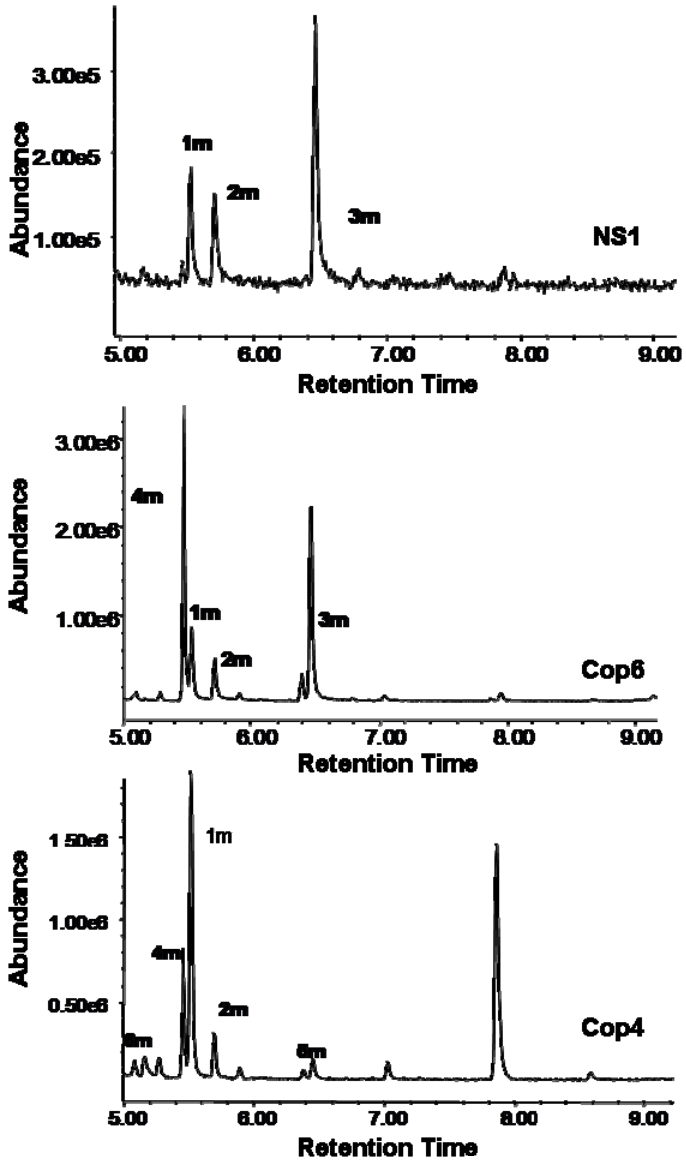
Supplemental Figure 5: GC/MS analysis of reaction products of *in vitro* assays of purified Cop6 (A), Cop4 (B) with a racemic mixture of nerolidyl diphosphate (NPP). Peaks are labeled with numbers that correspond to their identified structures in Scheme 3 and mass spectra in Supplemental Figure 2. Compounds were identified by comparison of their mass spectra and RI values with data from published reference (MassFinder3, terpene library [46]) and authentic standards (Supplemental Table 1).



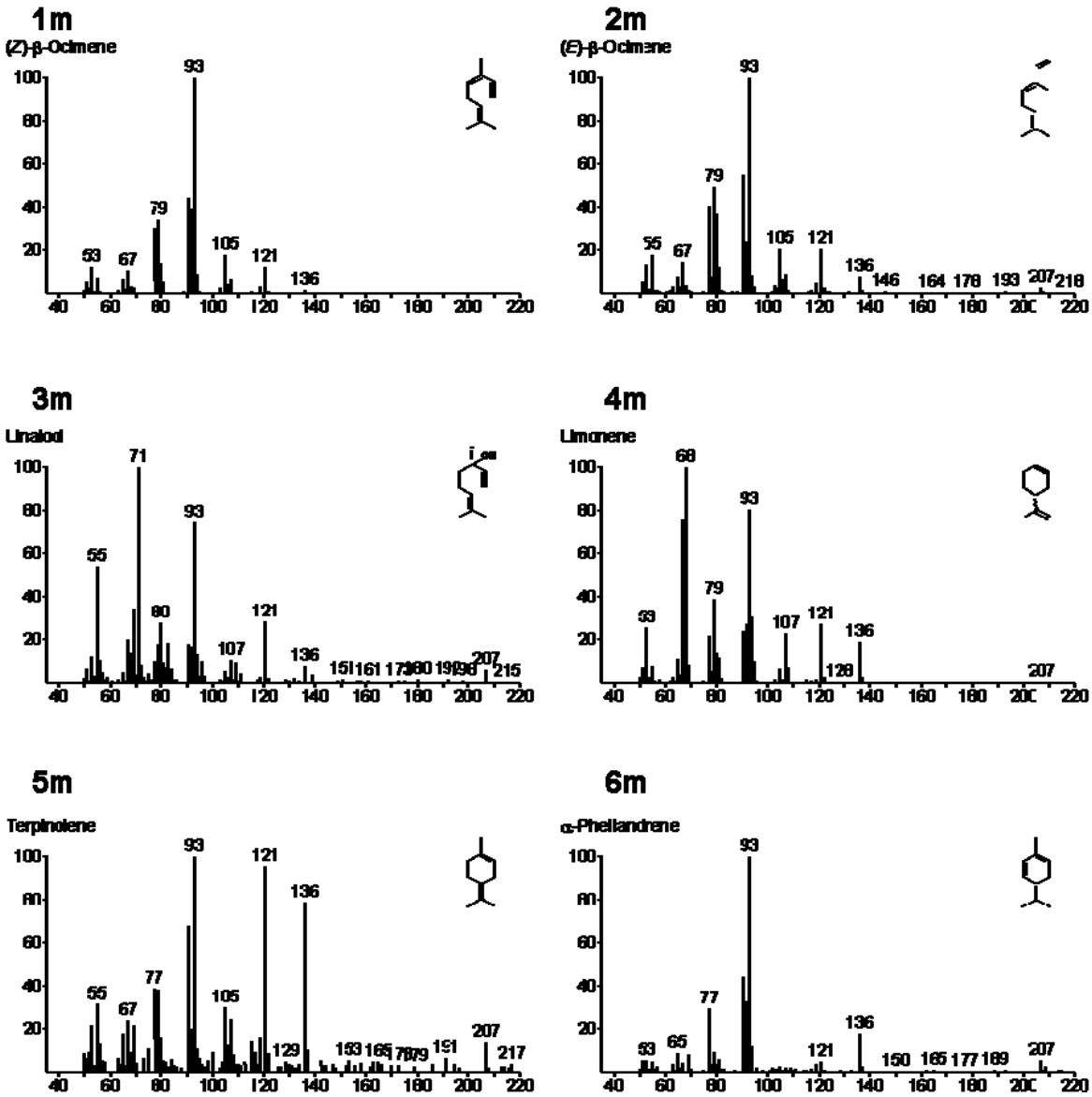
Suplemental Figure 6. Absolute configuration determination of cadina-4,11-diene (14s) and separation of Cop4 and Cop6 reaction products with (*Z,E*)-FPP by chiral GC-MS. To determine the absolute configuration of cadina-4,11-diene (**14s**) produced by Cop4, in vitro reaction products (black solid line, middle) were separated by chiral GC-MS and compared to of cadina-4,11-diene with known configuration present in the essential oil of *Amyris balsamifera* [46] (grey dotted line, top). Chiral GC-MS analysis of Cop4 *in vitro* reactions (middle) and Cop6 *in vitro* reaction (bottom) show that α-acoradiene (**11s**) and amorpha-4,11-diene (**12s**) are produced by Cop4 and Cop6 have different retention times, indicating that the two enzymes cyclize (*Z,E*)-FPP into opposite enantiomers of compounds **11s** and **12s**.



Supplemental Figure 7: GC/MS analysis of reaction products of *in vitro* assays of purified Cop4, Cop6 and NS1 with *E*-GPP. Peaks are labeled with numbers that correspond to their identified structures in Scheme 3. Compounds were identified by comparison of their mass spectra and RI values with data from published reference (MassFinder3, terpene library [46]) and authentic standards (Supplemental Table 1).



Supplemental Figure 8: Mass spectra of identified monoterpenoids. Numbers correspond to compound names shown in Scheme 3.



Supplemental Table 1. Identification of sesquiterpenes and monoterpenes described in this study. Essential oils with known sesquiterpene compositions described at http://www.thegoodscentscompany.com and in the literature were used as authentic standards for product identification. Initial identification of terpene products from enzyme reactions was done by comparing mass spectra and RI values obtained by GC-MS with reference data in the MassFinder 3 terpene library using the MassFinder software calibrated with RI values obtained from different alkane standards. Compound identifications were then further confirmed by comparing RI values and mass spectra with those of reference compounds in various essential oils. Suppliers of essential oils are indicated by a number in the table: (1) Liberty natural products Inc. (http://www.libertynatural.com/), (2) Oshadhi Inc. (http://www.oshadhiusa.com/), (3) The Good Scents Company (http://www.thegoodsecentcompany.com/).

Terpenes	**RI observed**	**RI in MassFinder 3 terpene library**	**Occurrence in essential oil** (Supplier)
Sesquiterpenes			
1s	1393	1389	*Amyris balsamifera* oil (1)
2s	1386	1381	*Amyris balsamifera* oil (1)
3s	1498	1497	*Hypericum perforatum* oil (1)
4s	1385	1393	*Calamus* leaf oil (1)
5s	1393	1394	no commercial source found
6s	1425	1430	no commercial source found
7s	1473	1479	*Solidiago canadensis* oil (2)
8s	1501	1507	*Cubeb* oil (1)
9s	1509	1513	*Cubeb* oil (1)
11s	1457	1464	*Acorus calamus* oil (1)
12s	1466	1472	no commercial source found
14s	1453	1458	*Amyris balsamifera* oil (1)
15s	1470	1476	no commercial source found
16s	1496	1503	*Bergamot* oil (1)
17s	1511	1516	Ginger root oil from Brazil (3).
Monoterpenes			
1m	1036	1041	*Cubeb* oil (1)
2m	1025	1029	*Cubeb* oil (1)
3m	1084	1086	*Bergamot* oil (1)
4m	1021	1025	*Cubeb* oil (1)
6m	1079	1082	*Cubeb* oil (1)