Claims

1. A modified terpene synthase comprising at least one modified amino acid residue as compared to the amino acid sequence corresponding to an unmodified wild type terpene synthase according to any one of SEQ ID NOs: 1 to 5, wherein said at least one modified amino acid residue is located in an α-helix structure being part of or close to an active site pocket of the terpene synthase, and wherein said at least one modified amino acid residue is an amino acid with a hydrophobic side chain, such as alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, or tryptophan, and/or an amino acid with a polar uncharged side chain, such as threonine, cysteine, asparagine, glutamine, or serine.

2. The modified terpene synthase according to claim 1, wherein the modified terpene synthase has at least 75% sequence identity to the unmodified wild type terpene synthase according to any one of SEQ ID NOs: 1 to 5, preferably wherein the modified terpene synthase has at least 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the unmodified wild type terpene synthase according to any one of SEQ ID NOs: 1 to 5.

3. The modified terpene synthase according to claim 1 or 2, wherein the modified terpene synthase catalyzes the production of at least one pseudopterosin intermediate, such as Elisabethatriene, Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or the production of at least one pseudopterosin, such as Pseudopterosin A, from Geranylgeranyl pyrophosphate (GGPP) in a host cell in an amount that is greater than the amount of said pseudopterosin intermediate and/or said pseudopterosin produced from GGPP by the unmodified wild type terpene synthase having the amino acid sequence according to any one of SEQ ID NOs: 1 to 5 in the same host cell and under the same conditions, and/or wherein the modified terpene synthase catalyzes the production of at least one side product, such as Hydropyrene (HP) or Hydropyrenol (HP-ol), from GGPP in a host cell in an amount that is smaller than the amount of said side product, such as HP or HP-ol produced from GGPP by the unmodified wild type terpene synthase having the amino acid sequence according to any one of SEQ ID NOs: 1 to 5 in the same host cell and under the same conditions.

4. The modified terpene synthase according to any one of the preceding claims, wherein the terpene synthase is a Hydropyrene synthase (HpS) comprising the amino acid sequence according to SEQ ID NO: 1, a class I terpene synthase, such as CotB2 from Streptomyces melanosporofaciens comprising the amino acid sequence according to SEQ ID NO: 2, a Diterpene synthase comprising the amino acid sequence according to SEQ ID NO: 3, a Trichodiene synthase comprising the amino acid sequence according to SEQ ID NO: 4, or a Clavulatriene synthase comprising the amino acid sequence according to SEQ ID NO: 5.

5. The modified terpene synthase according to any one of the preceding claims, wherein said at least one modified amino acid residue is a substitution of a wild type amino acid residue selected from:

   (i) methionine at position 71,

   (ii) methionine at position 75,

   (iii) glycine at position 182,

   (iv) histidine at position 184,

   (v) methionine at position 300, and

   (vi) methionine at position 304,

   in the amino acid sequence of the unmodified wild type HpS according to SEQ ID NO: 1, or wherein said at least one modified amino acid residue is a substitution of a wild type amino acid residue located at an equivalent position of any of (i) to (vi) in the amino acid sequence of an unmodified wild type terpene synthase according to any one of SEQ ID NOs: 2 to 5.

6. The modified terpene synthase according to any one of the preceding claims, wherein the modified terpene synthase comprises at least one substitution selected from the group consisting of:

   (i) a substitution of methionine for tyrosine at position 71,

   (ii) a substitution of methionine for phenylalanine at position 75,

   (iii) a substitution of methionine for leucine at position 75,

   (iv) a substitution of glycine for alanine at position 182,

   (v) a substitution of glycine for phenylalanine at position 182,

   (vi) a substitution of histidine for alanine at position 184,

   (vii) a substitution of histidine for phenylalanine at position 184,

(viii) a substitution of methionine for isoleucine at position 300,

(ix) a substitution of methionine for isoleucine at position 304,

(x) a substitution of methionine for threonine at position 304, and

(xi) a substitution of methionine for cysteine at position 304,

in the amino acid sequence of the unmodified wild type HpS according to SEQ ID NO: 1, or wherein said modified terpene synthase comprises at least one substitution at an amino acid residue located at an equivalent position of any of (i) to (xi) in the amino acid sequence of an unmodified wild type terpene synthase according to any one of SEQ ID NOs: 2 to 5.

7. The modified terpene synthase according to any one of the preceding claims, wherein the amino acid sequence of said modified terpene synthase further comprises one or more amino acid deletions, substitutions, and/or additions at positions other than at position 71, 75, 182, 184, 300, and/or 304 according to the amino acid sequence of the unmodified wild type terpene synthase according to SEQ ID NO: 1, or other than the at least one substitution at said equivalent position of an unmodified wild type terpene synthase according to any one of SEQ ID NOs: 2 to 5.

8. The modified terpene synthase according to any one of the preceding claims, wherein the modified terpene synthase comprises an amino acid sequence according to any one of SEQ ID Nos. 8 to 18, or wherein the modified terpene synthase has at least 75% sequence identity to an amino acid sequence according to any one of SEQ ID Nos. 8 to 18, preferably at least 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to an amino acid sequence according to any one of SEQ ID Nos. 8 to 18, or wherein the modified terpene synthase consists of an amino acid sequence according to any one of SEQ ID Nos. 8 to 18.

9. A nucleic acid, encoding for a modified terpene synthase according to any one of claims 1 to 8, or an expression vector capable of expressing said nucleic acid.

10. A recombinant host cell comprising the modified terpene synthase according to any one of claims 1 to 8, or the nucleic acid or the expression vector according to claim 9.

11. A method for producing a modified terpene synthase according to any one of claims 1 to 8, the method comprising culturing the host cell according to claim 10 that comprises the modified terpene synthase according to any one of claims 1 to 8, or expresses the nucleic acid according to claim 9, or comprises the expression vector according to claim 9, and isolating the modified terpene synthase from the host cell or its culture medium.

12. A modified terpene synthase according to any one of claims 1 to 8, a nucleic acid or an expression vector according to claim 9, or a host cell according to claim 10, when used in the production of at least one pseudopterosin intermediate, such as Elisabethatriene, Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or when used in the production of at least one pseudopterosin, such as Pseudopterosin A, wherein said use is an *in vitro* use.

13. A method for producing at least one pseudopterosin intermediate, such as Elisabethatriene, Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or for producing at least one pseudopterosin, such as Pseudopterosin A, the method comprising the steps of:

a) Providing an intermediate generated from a Geranylgeranyl pyrophosphate (GGPP);

b) Providing a modified terpene synthase comprising at least one modified amino acid residue as compared to the amino acid sequence corresponding to an unmodified wild type terpene synthase according to any one of SEQ ID NOs: 1 to 5, wherein said at least one modified amino acid residue is located in an α-helix structure being part of or close to an active site pocket of the terpene synthase, and wherein said at least one modified amino acid residue is an amino acid with a hydrophobic side chain, such as alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, or tryptophan, and/or an amino acid with a polar uncharged side chain, such as threonine, cysteine, asparagine, glutamine, or serine, and

c) Destabilizing the intermediate of step a) by said at least one modified amino acid residue of the modified terpene synthase,

thereby producing at least one pseudopterosin intermediate, such as Elisabethatriene, Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or for producing at least one pseudopterosin, such as Pseudopterosin A.

14. The method according to claim 13, wherein said method further comprises the step of modifying said at least one pseudopterosin intermediate, such as Elisabethatriene,

Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or said at least one pseudopterosin, such as Pseudopterosin A, wherein said modifying preferably comprises a modification selected from a functionalization, oxidation, hydroxylation, methylation, glycosylation, lipid-conjugation, or combinations thereof.

15. A pseudopterosin intermediate, such as Elisabethatriene, Isoelisabethatriene A, Isoelisabethatriene B, Erogorgiaene, or Seco-Pseudopterosin, and/or a pseudopterosin, such as Pseudopterosin A, produced by a method according to claim 13 or 14.