CLAIMS

1. A recombinant host cell capable of producing oxygenated diterpenoid compounds, wherein the host cell
    i. is capable of producing miltiradiene and/or dehydroabietadiene; and
    ii. comprises a first heterologous nucleic acid encoding a first enzyme having cytochrome P450 activity, wherein the first enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP82D274 as set forth in SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 74 or SEQ ID NO: 75, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof, whereby the host cell is capable of converting miltiradiene and/or dehydroabietadiene into 14-hydroxydehydroabietadiene.

2. The recombinant host cell according to claim 1, wherein the recombinant host cell further comprises a second heterologous nucleic acid encoding a second enzyme having cytochrome P450 activity, wherein the second enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP71BE86 as set forth in SEQ ID NO: 4, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

3. The recombinant host cell according to claim 2, wherein the recombinant host cell comprises and expresses said first heterologous nucleic acid and said second heterologous nucleic acid, whereby the cell is capable of producing 14-hydroxydehydroabietadiene, 3,14-dihydroxydehydroabietadiene, 3,14-dihydroxyabeodiene and 14-hydroxy-18-aldo-abeodiene.

4. The recombinant host cell according to any one of the preceding claims, wherein the recombinant host cell further comprises a third heterologous nucleic acid encoding a third enzyme having cytochrome P450 activity, wherein the third enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP71BE85 as set forth in SEQ ID NO: 3, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

5. The recombinant host cell according to claim 4, wherein the recombinant host cell comprises and expresses said first heterologous nucleic acid and said third heterologous nucleic acid, whereby the cell is capable of producing 14-hydroxydehydroabietadiene.

6. The recombinant host cell according to claim 4, wherein the recombinant host cell comprises and expresses said first heterologous nucleic acid, said second heterologous nucleic acid and said third heterologous nucleic acid, whereby the cell is capable of producing 14-hydroxydehydroabietadiene, 3,14-dihydroxydehydroabietadiene, 3,14-dihydroxyabeodiene, 14-hydroxy-18-aldo-abeodiene and triptophenolide.

7. The recombinant host cell according to any one of the preceding claims, wherein the recombinant host cell further comprises a fourth heterologous nucleic acid encoding a fourth enzyme having cytochrome P450 activity, wherein the fourth enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP82D213 as set forth in SEQ ID NO: 5 or SEQ ID NO: 76, or a functional homologue thereof having at least 80 % sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

8. The recombinant host cell according to claim 7, wherein the recombinant host cell comprises and expresses said first heterologous nucleic acid, said second heterologous nucleic acid, said third heterologous nucleic acid and said fourth heterologous nucleic acid, whereby the cell is capable of producing 14-hydroxydehydroabietadiene, 3,14-dihydroxydehydroabietadiene, 3,14-dihydroxyabeodiene, 14-hydroxy-18-aldo-abeodiene, triptophenolide and triptonide.

9. The recombinant host cell according to any one of the preceding claims, wherein the host cell further comprises a fifth heterologous nucleic acid encoding a fifth enzyme having cytochrome P450 activity, wherein the fifth enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP82D217 as set forth in SEQ ID NO: 6, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

10. The recombinant host cell according to any one of the preceding claims, wherein the host cell further comprises a sixth heterologous nucleic acid encoding a sixth enzyme having cytochrome P450 activity, wherein the sixth enzyme having cytochrome P450 activity is the cytochrome P450 enzyme TwCYP82D275 as set forth in SEQ ID NO: 7, or a functional homologue thereof having at least 80 % sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

11. The recombinant host cell according to any one of the preceding claims, wherein the host cell further comprises a seventh heterologous nucleic acid encoding an enzyme having cytochrome B5 activity, wherein the enzyme having cytochrome B5 activity is the cytochrome B5 TwB5#1 as set forth in SEQ ID NO: 8, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto, or the mature polypeptide thereof.

12. The recombinant host cell according to any of the preceding claims, wherein the recombinant host cell expresses one or more of:
    i. a geranylgeranyl diphosphate synthase;
    ii. a diterpene synthase capable of converting geranyl-geranyl-diphosphate (GGPP) into miltiradiene;
    iii. a combination of two or more diterpene synthases that in combination are capable of converting GGPP into miltiradiene; or
    iv. a copalyl diphosphate synthase and a miltiradiene synthase

whereby the cell is capable of producing miltiradiene and/or dehydroabietadiene.

13. The recombinant host cell of claim 12, wherein the geranylgeranyl diphosphate synthase is a polypeptide comprising the amino acid sequence of SEQ ID NO: 73 or SEQ ID NO: 81, or a functional homologue thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto.

14. The recombinant host cell according to any one of claims 12 to 13, wherein the combination of two or more diterpene synthases, that is capable of converting GGPP into miltiradiene, is the combination of CfTPS1 as set forth in SEQ ID NO: 67 and CfTPS3 as set forth in SEQ ID NO: 68, or CftTPS1 as set forth in SEQ ID NO: 77 and CftTPS3 as set forth in SEQ ID NO: 78, or a combination of the respective functional homologues thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto; or is the combination of TwTPS9 as set forth in SEQ ID NO: 69 and TwTPS27 as set forth in SEQ ID NO: 70, or a combination of the respective functional homologues thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto.

15. The recombinant host cell according to any one of claims 12 to 14, wherein the combination of a copalyl diphosphate synthase and a miltiradiene synthase is the combination of SmCPS as set forth in SEQ ID NO: 71 and SmKSL as set forth in SEQ ID NO: 72, or a combination of the respective functional homologues thereof having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, more preferred at least 98% sequence identity thereto.

16. The recombinant host cell according to any one of the preceding claims, wherein the recombinant host cell is a prokaryotic or a eukaryotic cell.

17. The recombinant host cell according to any one of the preceding claims, wherein the recombinant host cell is a eukaryotic cell of a species selected from the group consisting of *Saccharomyces*, *Schizosaccharomyces*, *Klyveromyces*, *Pichia*, *Candida* and *Yarrowia*.

18. The recombinant host cell according to any one of the preceding claims, wherein the recombinant host cell is a *S. cerevisiae* cell.

19. The recombinant host cell according to any one of claims 1 to 16, wherein the recombinant host cell is a prokaryotic cell of a species selected from the list consisting of *Escherichia, Bacillus, Lactobacillus and Corynebacterium*.

20. The recombinant host cell according to any one of claims 1 to 16, wherein the recombinant host cell is a plant cell or comprised in a plant, wherein the plant may be *Nicotiana tabacum*, and/or the host cell is a cell from another multi-cellular host.

21. A method for production of an oxygenated diterpenoid compound, such as triptonide, said method comprising the steps of
    i. providing a recombinant host cell according to any one of the preceding claims; and
    ii. culturing said recombinant host cell under conditions suitable for production of said oxygenated diterpenoid compound.

22. The method according to claim 21, wherein the oxygenated diterpenoid compound is selected from the list consisting of 14-OH-dehydroabietadiene, triptophenolide and triptonide.

23. The method according to any one of claims 21 to 22, wherein the oxygenated diterpenoid compound is triptonide.

24. The method according to any one of claims 22 to 23, further comprising a step of recovering and, optionally, purifying the triptonide.

25. A method of producing triptolide said method comprising
    i. producing triptonide according to the method of any one of claims 22 to 24, and
    ii. converting the triptonide into triptolide and,
    iii. optionally, recovering and/or purifying the triptolide.

26. Use of a recombinant host cell according to any of claims 1 to 20 for the production of an oxygenated diterpenoid compound.

27. The use of claim 26, wherein the oxygenated diterpenoid compound is selected from the list consisting of 14-OH-dehydroabietadiene, triptophenolide and triptonide.

28. The use of claim 26, wherein the oxygenated diterpenoid compound is triptonide, wherein the triptonide is further converted into triptolide.

29. The use according to any one of claims 26 to 28, wherein the oxygenated diterpenoid compound is recovered using one or more separation and/or chromatographic steps.

30. A polypeptide having cytochrome P450 enzyme activity and comprising an amino acid sequence having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, preferably at least 96% sequence identity, preferably at least 97% sequence identity, preferably at least 98% sequence identity, or even 100% sequence identity to one of the sequences SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, or the mature polypeptide thereof or a polypeptide having cytochrome B5 enzyme activity and comprising an amino acid sequence having at least 80% sequence identity, preferably at least 85% sequence identity, preferably at least 90% sequence identity, preferably at least 95% sequence identity, preferably at least 96% sequence identity, preferably at least 97% sequence identity, preferably at least 98% sequence identity, or even 100% sequence identity to SEQ ID NO:8.

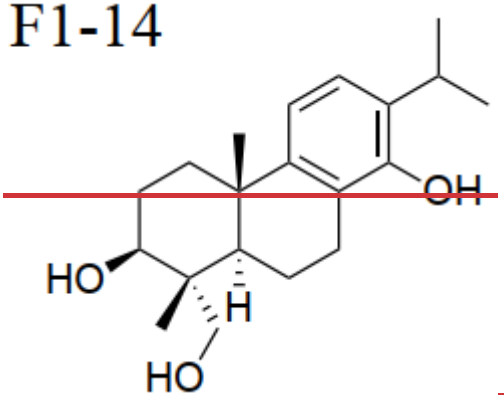
31. A polynucleotide encoding the polypeptide of claim 30.

32. A plasmid, expression vector, expression construct or recombinant host cell comprising the polynucleotide of claim 31.

33. The compound 14-OH-dehydroabietadiene.

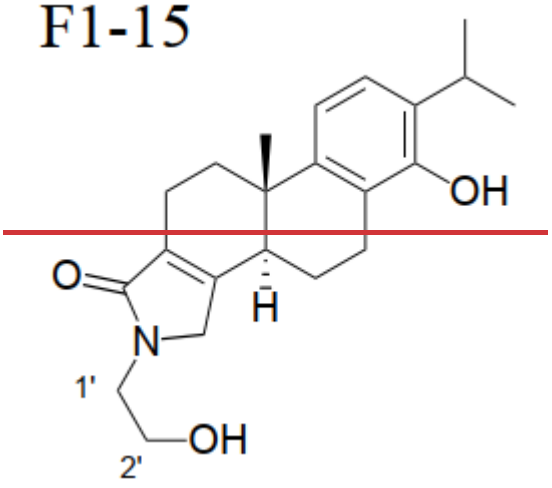
~~34. A compound selected from the group consisting of the following formulas (1) to (17):~~

F1-14



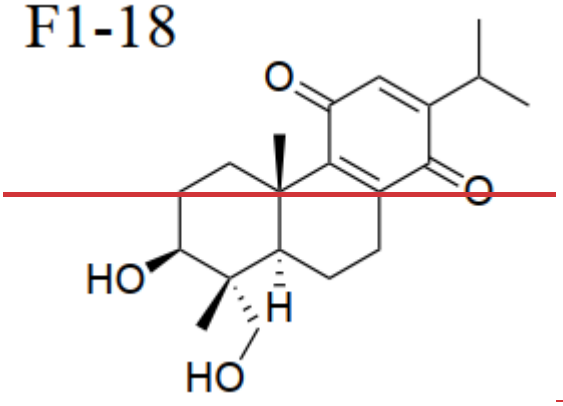
~~(1)~~

F1-15



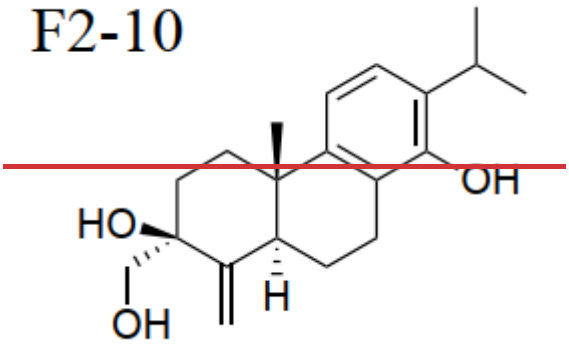
~~(2)~~

F1-18



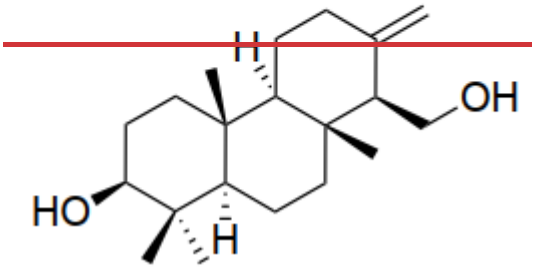
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F2-10



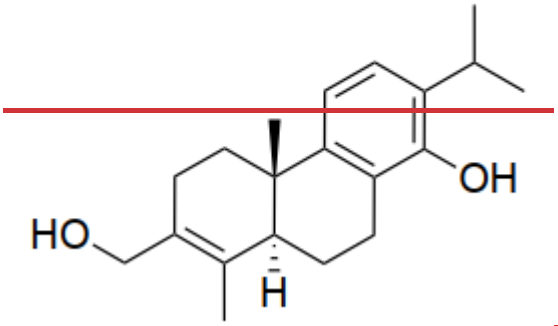
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F20P1



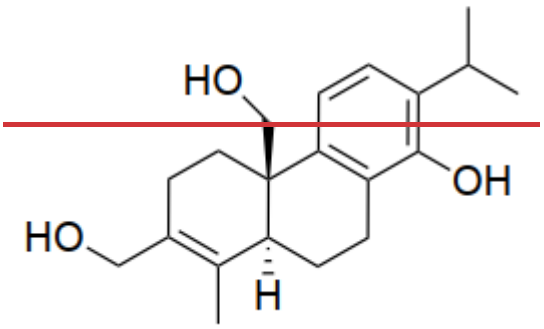
~~(5)~~

F20P2



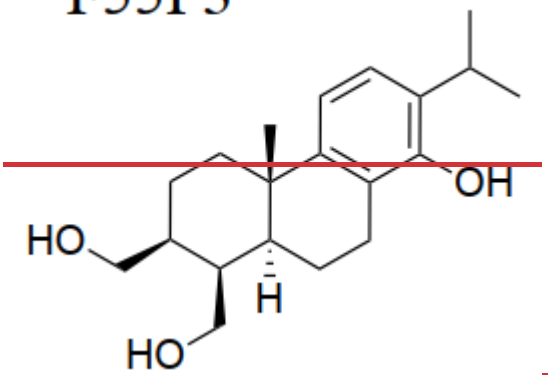
~~(6)~~

F55P2



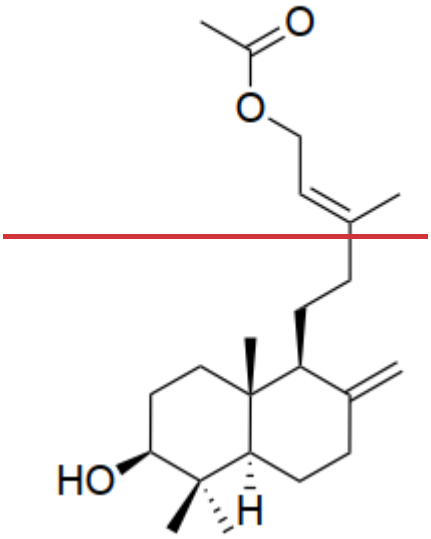
~~(7)~~

F55P3



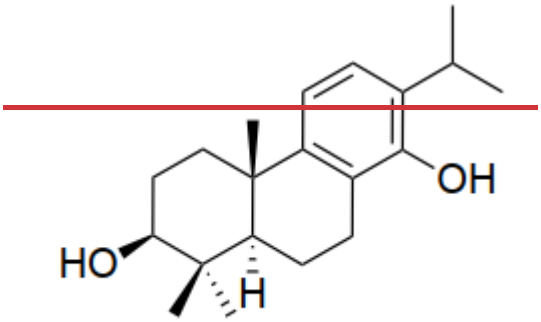
~~(8)~~

F15P4



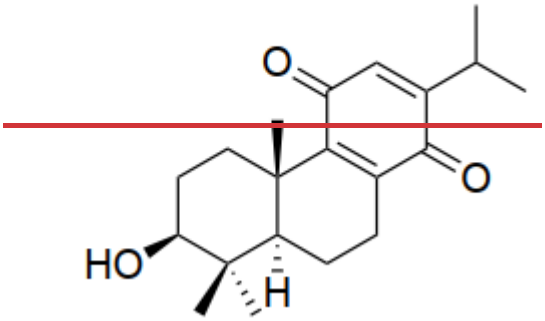
~~(9)~~

F15P1



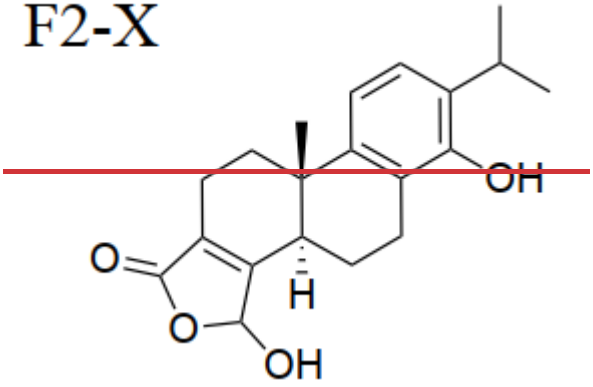
~~(10)~~

F1-31 (F2-35)



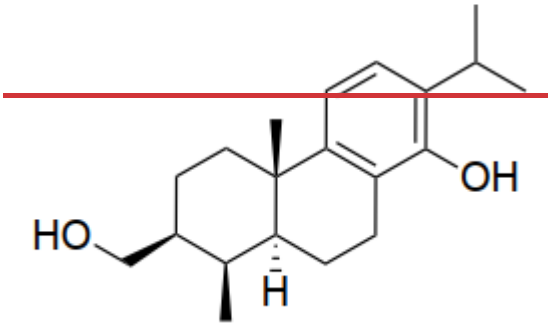
~~(11)~~

F2-X



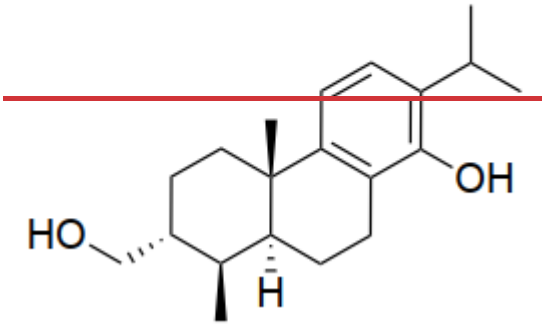
~~(12)~~

F20P3



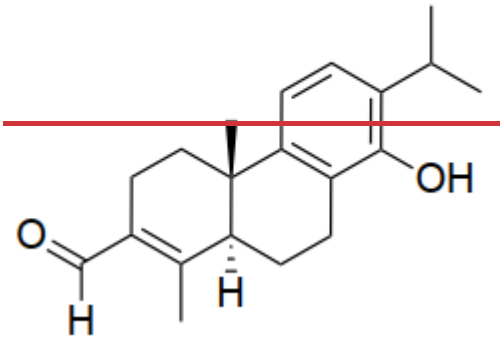
~~(13)~~

F20P4



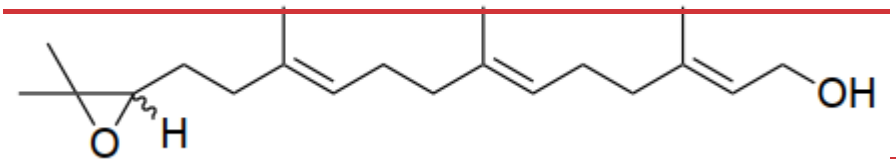
~~(14)~~

F15P2



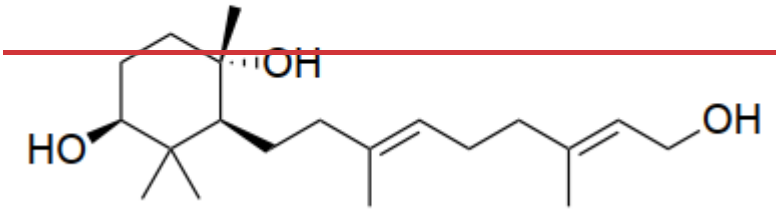
~~(15)~~

F20P5 (F15P3)



~~(16)~~

F60P1



~~(17).~~

~~35. The compound according to claim 34, wherein said compound is the compound according to formula (6) (F20P2).~~

~~36. The compound according to claim 34, wherein said compound is the compound according to formula (10) (F15P1).~~

~~37. The compound according to claim 34, wherein said compound is the compound according to formula (15) (F15P2).~~