CLAIMS:

1. A method for making an oxygenated product of a sesquiterpene, comprising, contacting the sesquiterpene with *Stevia rebaudiana* Kaurene Oxidase (*Sr*KO) or derivative thereof having sesquiterpene oxidizing activity, and recovering the oxygenated product.

2. The method of claim 1, wherein the *Sr*KO derivative comprises an amino acid sequence having from 1 to 50 mutations independently selected from substitutions, deletions, or insertions relative to *Sr*KO (SEQ ID NO: 37, 38, or 55).

3. The method of any one of claims 1 to 2, wherein the *Sr*KO derivative comprises an amino acid sequence having at least 70% sequence identity to *Sr*KO (SEQ ID NO: 37, 38, or 55), and has valencene oxidase activity.

4. The method of any one of claims 2 to 3, wherein one or more mutations relative to *Sr*KO (SEQ ID NO: 37, 38, or 55) are selected from Table 2 or Table 6.

5. The method of claim 2, wherein the *Sr*KO is a derivative having a deletion of at least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

6. The method of claim 5, wherein the SrKO is a derivative having a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from *E. coli* yhcB or derivative thereof.

7. The method of claim 6, wherein the N-terminal transmembrane domain from yhcB comprises the amino acid sequence of SEQ ID NO: 118, or an amino acid sequence having from 1 to 5 amino acid mutations with respect to SEQ ID NO: 118.

8. The method of any one of claims 1 to 7, wherein the SrKO is a derivative having one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37.

9. The method of claim 8, wherein the SrKO is a derivative having one or more mutations selected from R76K, M94V, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

10. The method of claim 1, wherein the SrKO is a derivative comprising an amino acid sequence selected from SEQ ID NOS:55-61, 104, and 105 or an amino acid sequence having from one to twenty mutations relative to a sequence selected from SEQ ID NOS: 55-61, 104 and 105.

11. The method of any one of claims 1 to 10, wherein the sesquiterpene is valencene, germacrene (A, B, C, D, or E), farnesene, farnesol, patchoulol, cadinene, cedrol, humulene, longifolene, and/or bergamotene, β-Ylangene, β-santalol, β-santalene, α-santalene, α-santalol, ß-vetivone, a-vetivone, khusimol, bisabolene, β-aryophyllene, Longifolene; α-sinensal; α-bisabolol, (-)-β-Copaene, (-)-α-Copaene, 4(Z),7(Z)-ecadienal, cedrol, cedrene, cedrol, guaiol, (-)-6,9-guaiadiene, bulnesol, guaiol, ledene, ledol, lindestrene, and alpha-bergamotene.

12. The method of claim 1 to 11, wherein the predominant sesquiterpene is valencene, germacrene (A, B, C, D, or E), farnesene, farnesol, patchoulol, cadinene, cedrol, humulene, longifolene, and/or bergamotene, β-Ylangene, β-santalol, β-santalene, α-santalene, α-santalol, ß-vetivone, a-vetivone, khusimol, bisabolene, β-aryophyllene, Longifolene; α-sinensal; α-bisabolol, (-)-β-Copaene, (-)-α-Copaene, 4(Z),7(Z)-ecadienal, cedrol, cedrene, cedrol, guaiol, (-)-6,9-guaiadiene, bulnesol, guaiol, ledene, ledol, lindestrene, and alpha-bergamotene.

13. The method of claim 12, wherein the predominant sesquiterpene is valencene.

14. The method of claim 13, wherein the predominant oxygenated product is nootkatone.

15. The method of any one of claims 1 to 14, wherein the contacting takes place in a host cell, which is a bacterium.

16. The method of claim 15, wherein the host cell is *E. coli*, *Bacillus subtillus*, or *Pseudomonas putida*.

17. The method of any one of claims 1 to 14, wherein the contacting takes place in a host cell which is a yeast.

18. The method of claim 17, wherein the host cell is a species of *Saccharomyces*, *Pichia*, or *Yarrowia*, including *Saccharomyces cerevisiae*, *Pichia pastoris*, and *Yarrowia lipolytica*.

19. The method of any one of claims 15 to 18, wherein isopentyl pyrophosphate (IPP) is produced by the host cell by metabolic flux through an endogenous or heterologous MEP or MVA pathway.

20. The method of any one of claims 15 to 19, wherein the sesquiterpene is produced at least in part by metabolic flux through an MEP pathway, and wherein the host cell has at least one additional copy of a dxs, ispD, ispF, and/or idi gene.

21. The method of any one of claims 15 to 20, wherein the host cell further expresses a farnesyl pyrophosphate synthase.

22. The method of any one of claims 15 to 21, wherein the host cell further expresses a heterologous sesquiterpene synthase.

23. The method of claim 22, wherein the sesquiterpene synthase is a valencene synthase.

24. The method of claim 23, wherein the valencene synthase is *Citrus sinensis* valencene synthase (CsVS) or *Vitis vinfera* valencene synthase (VvVS) or derivative thereof.

25. The method of claim 24, wherein the VvVS comprises an amino acid sequence having from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to VvVS (SEQ ID NO:1).

26. The method of claim 24, wherein the CsVS comprises an amino acid sequence having from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to CsVS (SEQ ID NO:12).

27. The method of any one of claims 1 to 26, wherein the SrKO is expressed in a host cell that co-expresses a cytochrome P450 reductase.

28. The method of claim 27, wherein the P450 reductase is a CPR from *Stevia sp.*

29. The method of any one of claims 1 to 28, wherein the *Sr*KO is expressed as a fusion with a cytochrome P450 reductase partner.

30. The method of any one of claims 1 to 29, wherein the host cell further expresses an alcohol dehydrogenase producing nootkatone.

31. The method of any one of claims 1 to 30, wherein oxidized oil is extracted from aqueous reaction medium followed by fractional distillation.

32. The method of claim 31, wherein the oxidized oil is extracted from aqueous reaction medium using an organic solvent.

33. The method of claim 31, wherein sesquiterpene and sesquiterpenoid components of fractions are measured quantitatively by GC/MS, followed by blending of the fractions to generate a desired nootkatone-containing ingredient.

34. The method of claim 31 or 32, wherein the nootkatone fraction is recovered.

35. A method for making a product containing an oxygenated sesquiterpene, comprising: incorporating the oxygenated sesquiterpene prepared by the method of any one of claims 1 to 34 into said product.

36. The method of claim 35, wherein the product is a flavor product, a fragrance product, a cosmetic, a cleaning product, a detergent or soap, or a pest control product.

37. The method of claim 36, wherein the product is a flavor product selected from a beverage, a chewing gum, a candy, or an artificial flavor.

38. The method of claim 36, wherein the product is an insect repellant.

39. An *Sr*KO derivative comprising at least one mutation with respect to SEQ ID NO: 37, 38, or 55 that increases valencene oxidase activity.

40. The SrKO derivative of claim 39, wherein the *Sr*KO derivative has a deletion of at least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

41. The *Sr*KO derivative of claim 40, wherein the *Sr*KO derivative has a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from *E. coli* yhcB or derivative thereof.

42. The *Sr*KO derivative of claim 41, wherein the N-terminal transmembrane domain comprises the amino acid sequence of SEQ ID NO: 118, or an amino acid sequence having from 1 to 5 amino acid mutations with respect to SEQ ID NO: 118.

43. The *Sr*KO derivative of claims 39 to 42, wherein the *Sr*KO derivative has one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37.

44. The *Sr*KO derivative of claim 43, wherein the *Sr*KO derivative has one or more mutations selected from R76K, M94V, L107M, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

45. The *Sr*KO derivative of claim 44, wherein the *Sr*KO derivative comprises an amino acid sequence selected from SEQ ID NOS:55-61, 104, and 105.

46. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and SrKO or derivative thereof having valencene oxidase activity, and wherein the *Sr*KO derivative has from 1 to 40 mutations relative to *Sr*KO (SEQ ID NO: 37, 38, or 55).

47. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and SrKO or derivative thereof having valencene oxidase activity, and wherein the *Sr*KO derivative comprises an amino acid sequence having at least 70% sequence identity to *Sr*KO (SEQ ID NO: 37, 38, or 55), and has valencene oxidase activity.

48. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and SrKO or derivative thereof having valencene oxidase activity, and wherein one or more mutations relative to *Sr*KO (SEQ ID NO:37 or 38) are selected from Table 2 or Table 6.

49. The host cell of claim 48, wherein at least 2 mutations are selected from Table 2 and/or Table 6.

50. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and SrKO or derivative thereof having valencene oxidase activity, and wherein the *Sr*KO derivative has a deletion of at

least a portion of its N-terminal transmembrane region, and the addition of an inner membrane transmembrane domain from *E. coli* yhcB or derivative thereof.

51. The host cell of claim 50, wherein the SrKO derivative has a deletion of from 15 to 35 amino acids of its N-terminal transmembrane domain, and the addition of from 15 to 25 amino acids of the transmembrane domain from E. coli yhcB or derivative thereof.

52. A host cell producing an oxygenated sesquiterpene: wherein the host cell produces isopentyl pyrophosphate (IPP); the host cell expresses a farnesyl pyrophosphate synthase, a sesquiterpene synthase, and SrKO or derivative thereof having valencene oxidase activity, wherein the *Sr*KO derivative comprises an amino acid sequence selected from SEQ ID NOS:55-61, 104, or 105; or an amino acid sequence having from one to twenty mutations relative to a sequence selected from SEQ ID NOS:55-61, 104, or 105 with the proviso that the amino acid sequence has one or more mutations at positions selected from 46, 76, 94, 131, 231, 284, 383, 390, 400, 444, 468, 488 and 499 relative to SEQ ID NO:37, or the proviso that the amino acid sequence has one or more of the mutations selected from R76K, M94V, T131Q, F231L, H284Q, R383K, I390L, T468I, and T499N relative to SEQ ID NO:37.

53. The host cell of any one of claims 46 to 52, wherein the host cell is an *E. coli* having at least one additional copy of a dxs, ispD, ispF, and/or idi gene and wherein the host cell produces nootkatone.

54. The host cell of of any one of claims 46 to 53, wherein the sesquiterpene synthase is a *Vitis vinifera* valencene synthase (VvVS) derivative having from 1 to 40 mutations independently selected from substitutions, deletions, or insertions with respect to VvVS (SEQ ID NO:1) and further one or more mutations selected from Table 3.

55. The host cell of any one of claims 46 to 54, wherein the SrKO or derivative thereof is expressed in a host cell that co-expresses a cytochrome P450 reductase and

wherein the P450 reductase comprises an amino acid sequence selected from SEQ ID NOS: 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, and 82, or a derivative thereof.

56. The host cell of any one of claims 46 to 55, wherein the host cell further expresses an alcohol dehydrogenase enzyme that converts nootkatol to nootkatone.

57. An Oxygenated sesquiterpene product obtainable by the method of any one of claims 1 to 38.

58. A Flavour or a Fragrance product comprising the oxygenated sesquiterpene product as defined in claim 57.