CLAIMS

What is claimed is:

1. An engineered polypeptide having imine reductase activity and comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO: 16, wherein said engineered polypeptide comprises a phenylalanine residue or an isoleucine residue at position 222 in said polypeptide sequence, and wherein the amino acid positions of said polypeptide sequence are numbered with reference to SEQ ID NO: 16.

2. The engineered polypeptide of Claim 1, wherein said polypeptide comprises a polypeptide sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more identical to the sequence of at least one engineered polypeptide set forth in Table 5.1, 6.1, 7.1, 8.1, 9.1 and/or 10.1.

3. The engineered polypeptide of Claim 1, comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO:16, comprising at least one substitution or substitution set at one or more positions selected from 29/94/184/223/232/288/293, 29/94/184/232/287/288/293/311, 29/94/184/232/287/288/311, 29/94/184/232/287/293/332, 29/94/184/232/288/293/311/324/353, 29/94/184/232/288/311/324/332, 29/94/184/232/293, 29/94/184/232/311, 29/94/184/287/293, 29/94/184/287/293/311/353, 29/94/184/287/311, 29/94/184/288/293/324, 29/94/184/288/293/332/353, 29/94/184/288/298/332, 29/94/184/288/353, 29/94/184/293/311, 29/94/184/324, 29/94/223/232/287, 29/94/223/232/293/311/324, 29/94/223/288/293, 29/94/232/287/288/311, 29/94/232/288/293, 29/94/287/288/293, 29/94/287/288/293/353, 29/94/287/311, 29/94/293/311/324, 29/94/293/332/353, 29/94/311, 29/94/324/353, 29/184, 29/184/223/288/293/324, 29/184/232/288, 29/184/287, 29/184/287/288/293, 29/184/287/288/293/311, 29/184/287/311/332, 29/184/288/293, 29/184/288/293/311, 29/184/293, 29/184/293/311, 29/184/293/324, 29/184/353, 29/223/287/288/293/353, 29/232/287/288/293/332/353, 29/287/288/293, 29/287/288/293/324/353, 29/288/293, 29/311, 29/311/332, 29/353, 72/94/184/288/311, 86, 94/96/223/287/288/293/311/324/332, 94/99/184/293/311/332/353, 94/184/223, 94/184/223/232/287/311, 94/184/223/288/293, 94/184/223/293, 94/184/232/287/288, 94/184/232/287/288/324/332, 94/184/232/287/293, 94/184/232/287/293/332, 94/184/287/288/293, 94/184/287/288/311, 94/184/287/293/311/324/353, 94/184/287/311, 94/184/287/353, 94/184/288/293, 94/184/288/293/311, 94/184/288/293/311/332, 94/184/293, 94/184/293/311, 94/184/293/332/353, 94/223/232/311/353/355/356/357/358/359, 94/223/287/288/293, 94/223/288/293/311, 94/232/287/288/293/353, 94/232/288/293/353, 94/232/293, 94/232/293/324/332, 94/232/311, 94/287/288/293, 94/287/288/311/324, 94/288/293, 94/288/293/324, 94/293/324, 94/311/324, 153,

184/223, 184/223/287/288/353, 184/232/287/288/293/311, 184/232/287/288/324/353, 184/232/287/293/332, 184/287/288, 184/287/288/293, 184/287/288/293/324/353, 184/287/293, 184/287/293/311, 184/288/293/311/324, 184/332/353, 205, 223/232/287/288/332/353, 223/287/288, 223/287/288/293/311, 223/287/311/353, 223/288/293, 232/287/288/293, 232/287/288/293/311, 232/287/288/293/321, 232/287/311, 232/288/293, 232/288/293/332, 234/287/288/293/311, 287/288/293, 287/288/311/324, 287/293, 287/311, 287/311/332, 287/324, 288/293, 288/293/311/324/353, 288/293/324, 293/311, and 311/332, wherein said positions are numbered with reference to SEQ ID NO:16.

4. The engineered polypeptide of Claim 1, comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO: 16, comprising at least one substitution or substitution set at one or more positions selected from 29/57/94/153/184/205/261/265/287, 29/57/94/153/205/265, 29/57/94/184/205/277/353, 29/57/94/205/259/261/265, 29/57/94/205/261/353, 29/57/153/184/205/259/261/265/277, 29/57/153/184/205/353, 29/57/153/205/261/265, 29/57/153/205/261/265/277, 29/57/153/205/265/277, 29/57/153/205/277/353, 29/57/184/205/259/261/265/277/287/357, 29/57/184/205/259/261/265/287, 29/57/205/259/261/265, 29/57/205/259/261/265/287, 29/57/205/261/265/353, 29/94/153/184/205, 29/94/153/205/259/261/265, 29/94/153/205/259/261/287, 29/94/153/205/259/261/287/353, 29/94/184/205/259/261, 29/94/184/205/261, 29/94/205, 29/94/205/259/261/287, 29/94/205/261, 29/94/261/265/287/353, 29/153/184/205, 29/153/205, 29/153/205/259/261/265/277/287, 29/153/261/265/287/353, 29/184/205, 29/184/205/259/261/277, 29/184/205/353, 29/184/261/265, 29/184/265, 29/205, 29/205/259/261, 29/205/259/261/265/287, 29/205/259/261/287, 29/205/261, 29/205/261/265, 29/205/261/265/353, 29/205/261/353, 29/205/277, 29/205/287, 29/205/287/353, 29/259/261/265, 29/261/353, 57/94/153/184/205/259/261, 57/94/153/205/261/265, 57/94/153/259/261/265, 57/94/153/261/265, 57/94/184/205/261/265/287, 57/94/184/261/265/287, 57/94/205/259, 57/94/205/259/261/265/277/287, 57/94/205/261/265, 57/94/205/277, 57/153/205/259/261/265/287, 57/153/205/259/265/277, 57/153/205/261, 57/153/205/261/265, 57/153/205/265, 57/153/261/265, 57/153/261/265/287/353, 57/205, 57/205/259/261, 57/205/259/261/265/277/287/353, 57/205/259/261/287/353, 57/205/259/265, 57/205/261, 57/205/261/265/277/287/353, 57/205/261/277, 57/205/261/277/353, 57/261/265/353, 94/126/184/205/259/261/265, 94/153/184/205, 94/153/184/259/261/265, 94/153/205/259/261/265/353, 94/153/205/287, 94/153/205/287/353, 94/153/205/353, 94/184/205/259/261, 94/184/205/259/261/265/287, 94/184/205/259/261/353, 94/184/205/261/265/287/353, 94/184/353, 94/205, 94/205/259/261/265, 94/205/259/261/265/277/287, 94/205/259/261/265/353, 94/205/259/261/287/353, 94/205/261/265/277, 94/205/261/265/353, 94/205/261/353, 94/205/277, 94/259/261/265, 153/184/205/261/277/287, 153/184/261/265/287, 153/205, 153/205/261, 153/205/261/265/287, 153/259/261/265, 153/259/265/287, 153/261/265, 153/261/265/287/353, 153/265, 153/265/277/287/353, 184/205, 184/205/259/261/287, 184/205/261, 184/205/261/265, 184/205/261/287,

184/205/277, 184/205/287/353, 184/261/265/287, 202, 205, 205/259/261, 205/259/261/265, 205/259/261/265/277/287/353, 205/259/261/277/287, 205/259/265, 205/261, 205/261/265, 205/261/265/274, 205/261/265/287, 205/261/265/287/353, 205/261/277, 205/261/353, 205/277/287, 205/287, 223, 225, 256, 259/261/265, 261/265/287, 265/287, 283, and 294, wherein said positions are numbered with reference to SEQ ID NO: 16.

5. The engineered polypeptide of Claim 1, comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO: 16, comprising at least one substitution or substitution set at one or more positions selected from 197/198/201/259, 198/201/259/280, 202/205/221/223/225/261, 202/205/221/223/261/294, 202/221/222/225/256/261/294, 202/221/223/225/283/294, 205/221/222, 205/221/223/225/256/261/283, 219, 221/222/223/225, 221/223, 221/223/225, 221/223/225/256/261, 221/223/225/261, 221/223/225/294, 221/225, 221/225/256, 221/225/256/261, 221/225/256/261/283/294, 223/225/256/261, 225/256/261, 280, and 280/306, wherein said positions are numbered with reference to SEQ ID NO: 16.

6. The engineered polypeptide of Claim 1, comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO: 16, comprising at least one substitution or substitution set at one or more positions selected from 17/198/259/280, 197, 197/198, 197/198/223/259, 197/223/277/280, 197/259, 197/277, 198, 198/223, 198/223/259/277/280, 198/259, 198/259/277, 198/259/277/280, 198/277/280, 223/259, 223/259/280, 258, 259, 259/268/277/280, 259/277, 259/280, 263, 277, and 280, wherein said positions are numbered with reference to SEQ ID NO: 16.

7. The engineered polypeptide of Claim 1, comprising an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% sequence identity to a reference sequence of SEQ ID NO: 16, comprising at least one substitution or substitution set at one or more positions selected from 141, 154, 197, 197/198, and 278, wherein said positions are numbered with reference to SEQ ID NO: 16.

8. The engineered polypeptide of Claim 1, wherein said engineered polypeptide comprises a polypeptide sequence that is at least 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more identical to SEQ ID NO: 16.

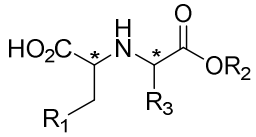
9. The engineered polypeptide of Claim 1, wherein said engineered polypeptide comprises SEQ ID NO: 16.

10. The engineered polypeptide of Claim 1, wherein said polypeptide comprises an amino acid sequence with at least 90% sequence identity to any even-numbered sequence set forth in SEQ ID NO: 16, 38-646, 650-684, 688-700, and 704-802 .

11. The engineered polypeptide of Claim 1, wherein said engineered polypeptide comprises a polypeptide sequence set forth in the even numbered sequences of SEQ ID NO: 16, 38-646, 650-684, 688-700, and 704-802 .

12. The engineered polypeptide of any one of Claims 1-11, wherein said engineered polypeptide comprises a polypeptide sequence that exhibits at least one improved property compared to the engineered polypeptide of SEQ ID NO:4.

13. The engineered polypeptide of Claim 12, wherein said improved property comprises improved production of a compound of structural Formula **(IV)**



(IV)

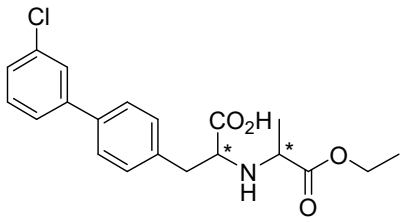
wherein

R_1 is selected from a hydrogen atom, or optionally substituted alkyl, alkenyl, alkynyl, alkoxy, arylalkoxy, hydroxyalkyl, heteroalkyl, heteroalkenyl, heteroalkynyl, haloalkyl, alkylthioalkyl, cycloalkyl, aryl, arylalkyl, heterocycloalkyl, heteroaryl, and heteroarylalkyl; and wherein

R_2 is independently selected from alkyl, alkenyl, alkynyl, hydroxyalkyl, carboxy, aminocarbonyl, heteroalkyl, heteroalkenyl, heteroalkynyl, carboxyalkyl, alkylamino, haloalkyl, alkylthioalkyl, cycloalkyl, aryl, arylalkyl, heterocycloalkyl, heteroaryl, and heteroarylalkyl; and wherein

R_3 is independently selected from methyl, d3-methyl and ethyl.

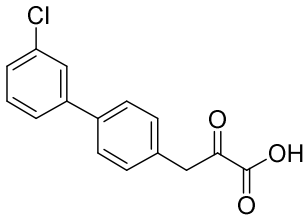
14. The engineered polypeptide of Claim 12, wherein said improved property comprises improved production of compound **(1)**



(1)

.

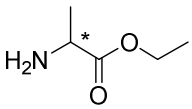
15. The engineered polypeptide of Claim 12, wherein said improved property comprises improved utilization of compound **(2)**



(2)

.

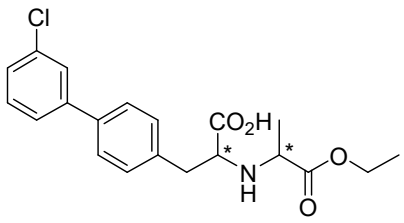
16. The engineered polypeptide of Claim 12, wherein said improved property comprises improved utilization of compound **(3)**



(3)

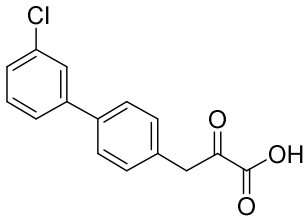
.

17. The engineered polypeptide of Claim 12, wherein said improved property comprises improved production of compound **(1)**



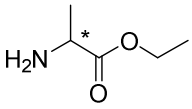
(1)

from compound **(2)**



(2)

and compound **(3)**



(3)

.

18. The engineered polypeptide of Claim 12, wherein said improved property comprises improved conversion of one or more of conversion reactions (A) to (E) in Table 2.

19. The engineered polypeptide of Claim 12, wherein said improved property comprises improved enantioselectivity.

20. The engineered polypeptide of Claim 12, wherein said improved property comprises improved stability.

21. The engineered polypeptide of any one of Claims 1-20, wherein said engineered polypeptide is purified.

22. A composition comprising at least one polypeptide provided in any one of Claims 1-21.

23. An engineered polynucleotide sequence encoding at least one engineered polypeptide of any one of Claims 1-21.

24. An engineered polynucleotide sequence encoding at least one engineered polypeptide of claim 1, wherein said polynucleotide sequence comprises at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity to SEQ ID NO: 15, wherein the polynucleotide sequence of said polypeptide comprises at least one substitution at one or more positions.

25. The engineered polynucleotide sequence of Claim 23 or 24, wherein said polynucleotide sequence comprises at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more sequence identity to SEQ ID NO: 15.

26. The engineered polynucleotide sequence of any one of Claims 23-25, wherein said polynucleotide sequence comprises SEQ ID NO: 15.

27. An engineered polynucleotide comprising the odd-numbered sequences set forth in any one of SEQ ID NO: 15, 37-645, 649-683, 687-699, and 703-801, and encoding an engineered polypeptide of claim 1 .

28. A vector comprising the engineered polynucleotide of any one of Claims 23 to 27.

29. The vector of Claim 28, further comprising at least one control sequence.

30. An *in vitro* host cell comprising the vector of Claim 28 or 29.

31. The host cell of Claim 30, wherein said host cell produces at least one engineered polypeptide of any one of Claims 1 to 21.

32. A method of producing an engineered polypeptide in a host cell, comprising culturing the host cell of Claim 30 or 31, in a culture medium under suitable conditions, such that at least one engineered polypeptide is produced.

33. The method of Claim 32, further comprising the step of recovering said engineered polypeptide.

34. The method of Claim 32 or 33, further comprising the step of purifying said at least one engineered polypeptide.