conversion of large prochiral ketone substrate compounds of Formula **(II)** to the corresponding chiral amine product compounds of Formula **(I)**.

[0016] Accordingly, in one aspect, the present invention provides an engineered polypeptides having transaminase activity, comprising ~~where the engineered polypeptide comprises~~ an amino acid sequence (a) having at least 80% identity to SEQ ID NO: 2, (b) comprising ~~and one or more~~ residue differences as compared to SEQ ID NO:2 at residue positions ~~selected from X19, X21,~~ X34, ~~X53,~~ X56, ~~X73, X86,~~ X88, ~~X107, X113, X147,~~ X155, and~~X165, X171, X178, X233, X251, X259, X268, X277, X286, X312, X316, X317, X358, X366, X383, X399, X414, X415,~~ X417, ~~X426, X434, and X450,~~ wherein the residue differences at residue positions ~~X21,~~ X56, and ~~X86,~~ X88, ~~X107, X113, X133, X147, X233, X286, X312, X316, X383, X415, X417, and X434,~~ are selected from: ~~X21H,~~ X56A/C, and (c) further comprising residue differences as compared to SEQ ID NO:2 at residue positions X31M, X57F/L, X153C, X163F, and X323T~~X86C, X88H/Y, X107G, X113L/P, X147H/V, X233V, X286C/H, X312N, X316C/P/G/N/S/T, X383C/F/I/M/T, X415A/G/H/L/V, X417V, and X434T~~. In some embodiments , the residue differences at the residue positions X19, X34, X53, X73, X155, X165, X171, X178, X251, X259, X268, X277, X317, X358, X366, X399, X414, X426, and X450 are selected from X19W, X34A, X53M, X73R, X155V, X165F, X171Q, X178W, X251V, X259V, X268A, X277A, X317L, X358K, X366H, X399A, X414I, X426R, and X450S.

[0017] In some embodiments of the engineered polypeptides having transaminase activity, the amino acid sequence comprises at least one or more residue differences as compared to SEQ ID NO: 2 selected from: X34A, X56A, X88H, X107G, X113L, X147H, X153C, X155V, X233V, X315G, X316N, X383I, and X450S. In some embodiments, the amino acid sequence further comprises one or more residue differences selected from: X31M, X57F/L, X86N/S, X153A, X233T, X323T, X383V, and X417T.

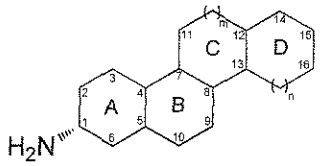
[0018] In some embodiments of the engineered polypeptides having transaminase activity, the amino acid sequence comprises at least a combination of residue differences as compared to SEQ ID NO: 2 comprising X34A, X56A, X57L, X86S, X88A; X153C, X155V, X163F, X315G, and X417T. In some embodiments, the amino acid sequence further comprises the residue difference X316N. In some embodiments, the amino acid sequence further comprises the residue difference X316N and one or more residue differences selected from X31M, X57F, X323T, X383I/T, X415H, and X450S.

[0019] In some embodiments of the engineered polypeptides having transaminase activity, the amino acid sequence comprises the residue differences as compared to SEQ ID NO: 2 X34A, X56A, X57L, X86S, X88A; X153C, X155V, X163F, X315G, X316N, and X417T and further comprises a combination of residue differences selected from: (a) X31M, X57F, X323T, and X383V; (b) X31M, X57F, X107G, X113L, X233T, X415H, and X450S; (c) X31M, X57F, X233V, X323T, X383I, X415H, and X450S; and (d) X31M, X57F, X147H, X323T, X383I, X415H, and X450S.

[0020] In some embodiments of the engineered polypeptides having transaminase activity, the engineered polypeptide has at least 1.2 fold increased stability as compared to the polypeptide of SEQ ID NO: 4, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X34T, X107G, X113L, X147H, X155V, X233T/V, X323T,

[0029] The structural features of the engineered transaminase polypeptides allow for the conversion of large prochiral ketone substrate compounds, other than compound **(2)**, to their corresponding amine product compounds, optionally in stereomeric excess of one chiral amine product over another chiral amino product. Thus the present disclosure also provides processes using the engineered transaminase polypeptides to catalyze a reaction in which an amino group from an amino donor is transferred to an amino acceptor, wherein the process comprises contacting an engineered transaminase polypeptide of the disclosure with an amino acceptor (*e.g.*, a ketone substrate compound) in the presence of an amino donor (*e.g.*, isopropylamine) under reaction conditions suitable for converting the amino acceptor to an amine compound.

In one aspect, the present invention provides a process for preparing an amine compound of Formula (I),



(I)

wherein

Ring A is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond between positions 2 and 3 and/or positions 5 and 6, and/or optionally substituted independently positions 2, 3, 4, 5 and 6 with a group selected from halo, hydroxy, and methyl;

Ring B is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond between positions 5 and 10, and/or optionally substituted independently at one or more of positions 9 and 10 with a group selected from halo, hydroxy, and methyl;

Ring C is a 5- or 6-membered carbocyclic ring (*i.e.*, m = 0 or 1), optionally substituted at position ~~10~~ 11 with a group selected from halo, hydroxy, methyl, ethyl, and carbonyl;

Ring D is a 5-, 6-, or 7-membered carbocyclic ring (*i.e.*, n = 0, 1, or 2), optionally including 1, 2, or 3 unsaturated C-C bonds, and/or optionally substituted independently as follows:

at position 14 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, straight-chain or branched (C_1-C_3)alkylamino, and cyclopropyl bridging to position 12;

at position 15 or position 16 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, aminocarbonyl(C_1-C_6)alkyl, optionally substituted cycloalkyl, optionally

What is claimed is:

1. An engineered polypeptide having transaminase activity, comprising an amino acid sequence (a) having at least 80% identity to SEQ ID NO: 2, (b) comprising residue differences as compared to SEQ ID NO: 2 at residue positions X34, X56, X88, X155, and X417, wherein the residue differences at residue positions X56, andX88, are selected from: X56A/C, and X88H/Y, and (c) further comprising residue differences as compared to SEQ ID NO:2 at residue positions X31M, X57F/L, X153C, X163F, and X323T.

2. The engineered polypeptide of **claim** 1 in which the residue differences at the residue positions X34, and X155, are selected from X34A, and X155V .

3. The engineered polypeptide of **claim** 1 or **2** in which the amino acid sequence comprises at least one or more residue differences as compared to SEQ ID NO: 2 selected from: X34A, X56A, X88H, X153C, and X155V.

4. The engineered polypeptide of **claim** 1, 2, or **3** in which the amino acid sequence further comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X86N/S, X233T, X383V, and X417T.

5. The engineered polypeptide of **claim 4** in which the amino acid sequence comprises at least the combination of residue differences as compared to SEQ ID NO: 2 comprising X34A, X56A, X57L, X86S, X153C, X155V, X163F, and X417T.

6. The engineered polypeptide of claim 5 in which the amino acid sequence further comprises the residue difference as compared to SEQ ID NO: 2 of X316N.

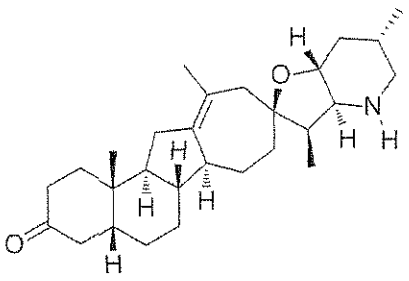
7. The engineered polypeptide of **claim 6** in which the amino acid sequence further comprises a residue difference as compared to SEQ ID NO: 2 selected from X383I/T, X415H, and X450S.

8. The engineered polypeptide of **claim 7** in which the amino acid sequence further comprises a residue difference or combination of residue differences as compared to SEQ ID NO: 2 selected from:

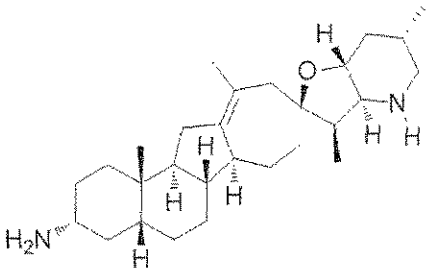
   X107G, X113L, X233T, and;
   X383I; and
   X147H, and X383I.

9. The engineered polypeptide of **claim** 1 in which the transaminase has at least 1.2 fold increased stability as compared to the polypeptide of SEQ ID NO: **4**, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X34T, X155V, and X323T.

10. The engineered polypeptide of **claim** 1 in which the transaminase has at least 1.2 fold increased activity as compared to the polypeptide of SEQ ID NO: **4** in converting compound **(2),**



(2) to compound **(1),**



(1), wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X56A, X88H, X153C, and X417T.

11. The engineered polypeptide of **claim** 1 in which the transaminase has increased enantioselectivity as compared to the polypeptide of SEQ ID NO: **4** in converting compound **(2)** to compound **(1)**, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X57F, and X153C.

12. The engineered polypeptide of any one of **claims** 1 to **11** in which the amino acid sequence further comprises a residue difference as compared to SEQ ID NO: **2** selected from: X18A, X19W, X21H, X34A, X53M, X73R, X86C/N/S/Y, X107G, X113C/L/P, X146L, X147H/K/V, X155A/V, X165F, X171Q, X178W, X190K, X206K, X228G, X233T/V, X235P, X244T, X251V, X259V, X268A, X277A, X286C/H, X312N, X314N, X315G, X316A/C/F/N/S/T, X317L, X319N, X358K, X366H, X383C/F/I/L/M/T/V, X395P, X399A, X414I, X415A/G/H/L/V, X417T/V, X424A, X426R, X427Y, X434T, and X450S.

13. The engineered polypeptide of any one of **claims** 1 to **12** in which the amino acid sequence does not comprise a residue difference as compared to SEQ ID NO: **2** at positions X9, X45, X177, X211, X294, X324, and X391.

14. The engineered polypeptide of **claim 1** in which the amino acid sequence comprises a sequence selected from SEQ ID NO: 148, 150, 156, 158, 160, 162, 164, 166, 170, 172, 178, 180, 182, 184, 190, and 192.

15. The engineered polypeptide of any one of **claims** 1 to **14** in which the polypeptide is immobilized on a solid support.

16. The engineered polypeptide of **claim 15** in which the solid support is a bead or resin comprising polymethacrylate with epoxide functional groups, polymethacrylate with amino epoxide functional groups, styrene/DVB copolymer or polymethacrylate with octadecyl functional groups

17. A polynucleotide encoding the engineered transaminase polypeptide of any one of **claims** 1 to **14**.

18. A polynucleotide encoding the engineered transaminase polypeptide of **claim** 1, comprising a nucleotide sequence selected from SEQ ID NO: 147, 149, 155, 157, 159, 161, 163, 165, 169, 171, 177, 179, 181, 183,189, and 191.

19. An expression vector comprising the polynucleotide of **claim 17** or **18**.

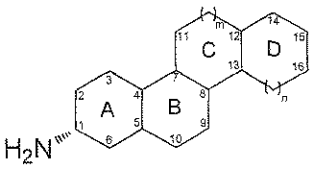
20. The expression vector of **claim 19** comprising a control sequence

21. A host cell comprising the polynucleotide of **claim 17** or **18** or the expression vector of **claim 19** or **20**.

22. A method of preparing the engineered polypeptide of any one of **claims** 1 to **14**, comprising culturing the host cell of **claim 21** under conditions suitable for expression of the polypeptide.

23. The method of **claim 22**, further comprising isolating the engineered polypeptide.

24. A process for preparing an amine compound of Formula (**I**),



(I)

wherein

Ring A is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond between positions 2 and 3 and/or positions 5 and 6, and/or optionally substituted independently positions 2, 3, 4, 5 and 6 with a group selected from halo, hydroxy, and methyl;

Ring B is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond

between positions 5 and 10, and/or optionally substituted independently at one or more of positions 9 and 10 with a group selected from halo, hydroxy, and methyl;

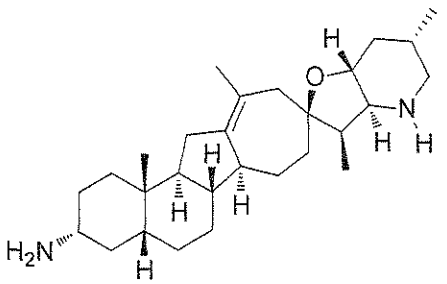
Ring C is a 5- or 6-membered carbocyclic ring (*i.e.*, m = 0 or 1), optionally substituted at position 11 with a group selected from halo, hydroxy, methyl, ethyl, and carbonyl;

Ring D is a 5-, 6-, or 7-membered carbocyclic ring (*i.e.*, n = 0, 1, or 2), optionally including 1, 2, or 3 unsaturated C-C bonds, and/or optionally substituted independently as follows:

at position 14 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, straight-chain or branched (C_1-C_3)alkylamino, and cyclopropyl bridging to position 12;

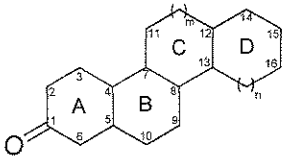
at position 15 or position 16 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, aminocarbonyl(C_1-C_6)alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted arylamino, optionally substituted arylthio, optionally substituted arylsulfonyl, optionally substituted arylsulfinyl, optionally substituted aryloxycarbonyl, optionally substituted arylcarbonyloxy, optionally substituted heteroaryloxy, optionally substituted heteroarylamino, optionally substituted heteroarylthio, optionally substituted heteroarylsulfonyl, optionally substituted heteroarylsulfinyl, optionally substituted heteroaryloxycarbonyl, optionally substituted heteroarylcarbonyloxy, alkylaminosulfonyl(C_1-C_6)alkyl, arylsulfonyl(C_1-C_6)alkyl, and heteroarylsulfonyl(C_1-C_6)alkyl;

with the proviso that the compound of Formula (**I**) is not compound (**1**)



(1)

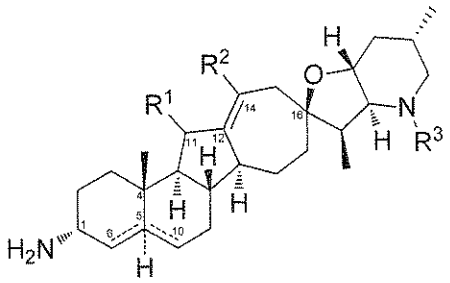
wherein the method comprises contacting the ketone substrate compound of Formula (**II**),



(II)

wherein rings A, B, C, and D are as defined above for the compound of formula **(I)**, with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

25. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound of Formula (Ia)



(Ia)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

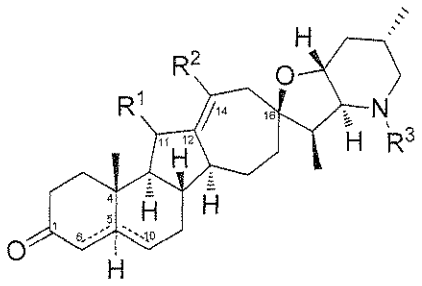
Ring D comprises an unsaturated C-C bond between positions 12 and 14;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl(C_1-C_6)alkyl;

and wherein the method comprises contacting the ketone substrate compound of Formula **(IIa)**,

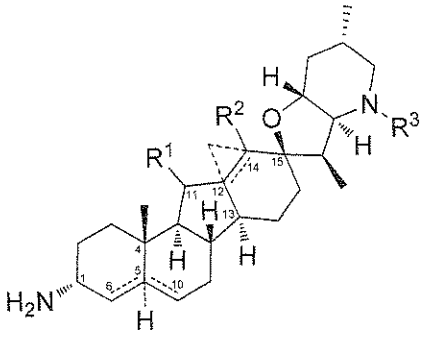


(IIa)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of Formula **(Ia)**,

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

26. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound of Formula **(Ib)**



(Ib)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

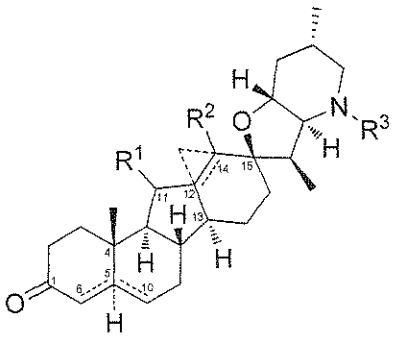
Ring D comprises an unsaturated C-C bond between positions 12 and 14, or a bridging cyclopropyl between positions 12 and 14;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl(C_1-C_6)alkyl;

and wherein the method comprises contacting the ketone substrate compound of Formula **(IIb)**,

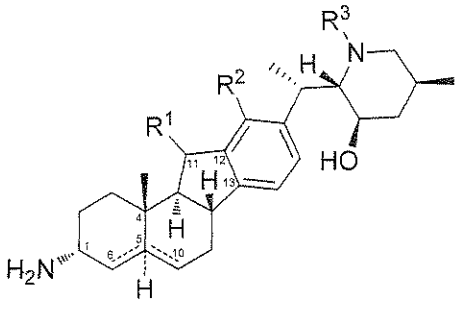


(IIb)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of Formula **(Ib)**,

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

27. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound Formula **(Ic)**



(Ic)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

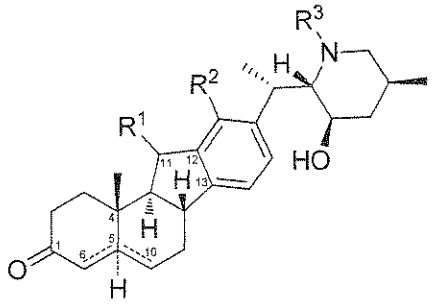
Ring D is aromatic;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl(C_1-C_6)alkyl;

wherein the method comprises contacting the ketone substrate compound of Formula (**IIc**),

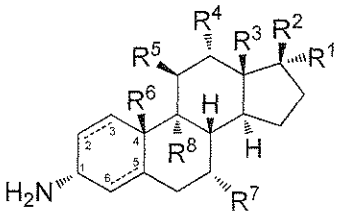


(IIc)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of Formula (**Ic**),

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

28. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound of Formula **(Id)**



(Id)

wherein

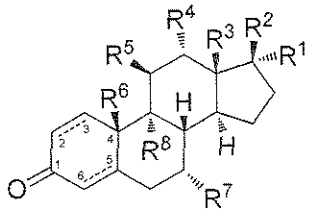
Ring A comprises an unsaturated C-C bond between positions 2 and 3, or positions 5 and 6;

R^1 and R^2 are selected independently from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, aminocarbonyl(C_1-C_6)alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted arylamino, optionally substituted arylthio, optionally substituted arylsulfonyl, optionally substituted arylsulfinyl, optionally substituted aryloxycarbonyl, optionally substituted arylcarbonyloxy, optionally substituted heteroaryloxy, optionally substituted heteroarylamino, optionally substituted heteroarylthio, optionally substituted heteroarylsulfonyl, optionally substituted heteroarylsulfinyl, optionally substituted heteroaryloxycarbonyl, optionally substituted heteroarylcarbonyloxy, alkylaminosulfonyl(C_1-C_6)alkyl, arylsulfonyl(C_1-C_6)alkyl, and heteroarylsulfonyl(C_1-C_6)alkyl;

R^3, R^4, and R^5 are selected independently from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^6, R^7, and R^8 are selected independently from hydrogen, halo, hydroxy, and methyl;

wherein the method comprises contacting the ketone substrate compound of Formula (**IId**),



(IId)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 are as defined above for the compound of Formula (**Id**),

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of

an amino donor under suitable reaction conditions.

29. The process of any one of **claims 24** to **28** in which the substrate compound of Formula **(II)** is at a loading of 0.5 to 200 g/L, 1 to 200 g/L, 5 to 150 g/L, 10 to 100 g/L, or 20 to 100 g/L.

30. The process of **claim 29** in which the substrate compound of Formula **(II)** is at a loading of at least about 0.5 g/L, 1 g/L, 5 g/L, 10 g/L, 20 g/L, 30 g/L, 40 g/L, 50 g/L, 100 g/L, 150 g/L, or 200 g/L.

31. The process of any one of **claims 24** to **30** in which the amino donor is selected from the group consisting of isopropylamine, L-lysine, α-phenethylamine, D-alanine, L-alanine, or D,L-alanine, or D,L-ornithine.

32. The process of **claim 31** in which the amino donor is isopropylamine (IPM).

33. The process of **claim 32** in which the isopropylamine is at a concentration of 0.1 to 3 M, 0.2 to 2.5 M, 0.5 to 2 M, or 1 to 2 M.

34. The process of **claim 33** in which the isopropylamine is at a concentration of about 0.1 M, 0.2 M, 0.3 M, 0.4 M, 0.5 M, 0.6 M, 0.7 M, 0.8 M, 1 M, 1.5 M, 2 M, 2.5 M, or 3 M.

35. The process of any one of **claims 24** to **34** in which the suitable reaction conditions comprise a buffer.

36. The process of **claim 35** in which the buffer is selected from borate, phosphate, carbonate, triethanolamine (TEA), and Tris.

37. The process of **claim 36** in which the buffer comprises TEA, wherein the TEA concentration is 0.01 to 0.4 M, 0.05 to 0.4 M, 0.1 to 0.3 M, or 0.1 to 0.2 M.

38. The process of **claim 37** in which the TEA concentration is about 0.01 M, 0.02 M, 0.03 M, 0.04 M, 0.05 M, 0.07 M, 0.1 M, 0.12 M, 0.14 M, 0.16 M, 0.18 M, 0.2 M, 0.3 M, or 0.4 M.

39. The process of any one of **claims 24** to **38** in which the suitable reaction conditions comprise a pH from 6 to 12, pH from 6 to 10, pH from 6 to 8, pH from 7 to 10, pH from 7 to 9, or pH from 7 to 8.

40. The process of **claim 39** in which the suitable reaction conditions comprise a pH of about 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10. 10.5, 11, 11.5, or 12.

41. The process of any one of **claims 24** to **40** in which the suitable reaction conditions comprise a temperature of 10°C to 70°C, 10°C to 65°C, 15°C to 60°C, 20°C to 60°C, 20°C to 55°C, 30°C to 55°C, or 50°C to 60°C.

42. The process of **claim 41** in which the suitable reaction conditions comprise a temperature of at least about 10°C, 15°C, 20°C, 25°C, 30°C, 35°C, 40°C, 45°C, 50°C, 55°C, 60°C, 65°C, or 70°C.

43. The process of any one of **claims 24** to **42** in which the suitable reaction conditions comprise a pyridoxal cofactor, pyridoxal-5'-phosphate (PLP), at a concentration from 0.1 g/L to 10 g/L, 0.2 g/L to 5 g/L, or 0.5 g/L to 2.5 g/L.

44. The process of **claim 43** in which the suitable reaction conditions comprise a PLP concentration of about 0.1 g/L, 0.2 g/L, 0.5 g/L, 1 g/L, 2.5 g/L, 5 g/L, or 10 g/L.

45. The process of any one of **claims 24** to **44** in which the suitable reaction conditions comprise a co-solvent.

46. The process of **claim 45** in which the co-solvent comprises a polar co-solvent.

47. The process of **claim 46** in which the co-solvent is selected from a polyol, DMSO, or lower alcohol.

48. The process of **claim 47** in which the co-solvent is DMSO

49. The process of **claim 44** in which the DMSO is present at a concentration of from 1% to 40% v/v; 2% to 30% v/v; or 5% to 25% v/v.

50. The process of **claim 49** in which the DMSO is present at a concentration of about 1% v/v, 2% v/v, 5% v/v, 10% v/v, 15% v/v, 20% v/v, 25% v/v, 30% v/v, 35% v/v, 35% v/v, or 40% v/v.

51. The process of **claims 24** to **50** in which the transaminase polypeptide is at a concentration of 0.01 to 50 g/L, 0.05 to 50 g/L, 0.1 to 40 g/L, 1 to 40 g/L, 2 to 40 g/L, 5 to 40 g/L, 5 to 30 g/L, 0.1 to 10 g/L, 0.5 to 10 g/L, 1 to 10 g/L, 0.1 to 5 g/L, 0.5 to 5 g/L, or 0.1 to 2 g/L.

52. The process of **claim 51** in which the transaminase polypeptide is at a concentration of about 0.01 g/L, 0.05 g/L, 0.1 g/L, 0.2 g/L, 0.5 g/L, 1 g/L, 2 g/L, 5 g/L, 10 g/L, 15 g/L, 20 g/L, 25 g/L, 30 g/L, 35 g/L, 40 g/L, or 50 g/L.

53. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:

(a) substrate loading at 5 g/L to 200 g/L;

(b) 0.1 to 50 g/L of engineered transaminase polypeptide;

(c) 0.1 to 4 M of isopropylamine (IPM);

(d) 0.1 to 10 g/L of pyridoxal phosphate (PLP) cofactor;

(e) pH of 6 to 9; and

(f) temperature of 30 to 65°C.

54. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:

(a) substrate loading at 10 g/L to 150 g/L;

(b) 0.5 to 20 g/L of engineered transaminase polypeptide;

(c) 0.1 to 3 M of isopropylamine (IPM);

(d) 0.1 to 10 g/L of pyridoxal phosphate (PLP) cofactor;

(e) 0.05 to 0.20 M triethanolamine (TEA) buffer;

(f) 1% to 45% DMSO;

(g) pH of 6 to 9; and

(h) temperature of 30 to 65°C.

55. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:

(a) substrate loading at 20 to 100 g/L;

(b) 1 to 5 g/L of engineered transaminase polypeptide;

(c) 0.5 to 2 M of isopropylamine (IPM);

(d) 0.2 to 2 g/L of pyridoxal phosphate (PLP) cofactor;

(e) about 0.1 M TEA buffer;

(f) about 25% DMSO;

(e) pH of about 8; and

(f) temperature of 45 to 60°C.

What is claimed is:

1. An engineered polypeptide having transaminase activity, comprising an amino acid sequence having at least 80% identity to SEQ ID NO: 2 and one or more residue differences as compared to SEQ ID NO:2 at residue positions selected from: X19, X21, X34, X53, X56, X73, X86, X88, X107, X113, X147, X155, X165, X171, X178, X233, X251, X259, X268, X277, X286, X312, X316, X317, X358, X366, X383, X399, X414, X415, X417, X426, X434, and X450, wherein the residue differences at residue positions X21, X56, X86, X88, X107, X113, X133, X147, X233, X286, X312, X316, X383, X415, X417, and X434, are selected from: X21H, X56A/C, X86C, X88H/Y, X107G, X113L/P, X147H/V, X233V, X286C/H, X312N, X316C/F/G/N/S/T, X383C/F/I/M/T, X415A/G/H/L/V, X417V, and X434T.

2. The engineered polypeptide of **claim** 1 in which the residue differences at the residue positions X19, X34, X53, X73, X155, X165, X171, X178, X251, X259, X268, X277, X317, X358, X366, X399, X414, X426, and X450 are selected from X19W, X34A, X53M, X73R, X155V, X165F, X171Q, X178W, X251V, X259V, X268A, X277A, X317L, X358K, X366H, X399A, X414I, X426R, and X450S.

3. The engineered polypeptide of **claim** 1 or **2** in which the amino acid sequence comprises at least one or more residue differences as compared to SEQ ID NO: 2 selected from: X34A, X56A, X88H, X107G, X113L, X147H, X153C, X155V, X233V, X315G, X316N, X383I, and X450S.

4. The engineered polypeptide of **claim** 1, 2, or **3** in which the amino acid sequence further comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X31M, X57F/L, X86N/S, X153A, X233T, X323T, X383V, and X417T.

5. The engineered polypeptide of **claim** 4 in which the amino acid sequence comprises at least the combination of residue differences as compared to SEQ ID NO: 2 comprising X34A, X56A, X57L, X86S, X88A; X153C, X155V, X163F, X315G, and X417T.

6. The engineered polypeptide of claim 5 in which the amino acid sequence further comprises the residue difference as compared to SEQ ID NO: 2 of X316N.

7. The engineered polypeptide of **claim** 6 in which the amino acid sequence further comprises a residue difference as compared to SEQ ID NO: 2 selected from X31M, X57F, X323T, X383I/T, X415H, and X450S.

8. The engineered polypeptide of **claim 7** in which the amino acid sequence further comprises a combination of residue differences as compared to SEQ ID NO: 2 selected from:

X31M, X57F, X323T, and X383V;

X31M, X57F, X107G, X113L, X233T, X415H, and X450S;

X31M, X57F, X233V, X323T, X383I, X415H, and X450S; and

X31M, X57F, X147H, X323T, X383I, X415H, and X450S.

9. The engineered polypeptide of **claim** 1 in which the transaminase has at least 1.2 fold increased stability as compared to the polypeptide of SEQ ID NO: 4, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X34T, X107G, X113L, X147H, X155V, X233T/V, X323T, X383I/V, and X450S.

10. The engineered polypeptide of **claim** 1 in which the transaminase has at least 1.2 fold increased activity as compared to the polypeptide of SEQ ID NO: 4 in converting compound **(2)** to compound **(1)**, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X56A, X86S, X88H, X153C, X415H, and X417T.

11. The engineered polypeptide of **claim** 1 in which the transaminase has increased enantioselectivity as compared to the polypeptide of SEQ ID NO: 4 in converting compound **(2)** to compound **(1)**, wherein the amino acid sequence comprises one or more residue differences as compared to SEQ ID NO: 2 selected from: X57F, X153C, and X316N.

12. The engineered polypeptide of any one of **claims** 1 to **11** in which the amino acid sequence further comprises a residue difference as compared to SEQ ID NO: 2 selected from: X18A, X19W, X21H, X31M, X34A, X53M, X56A/C, X57C/F/L, X73R, X86C/N/S/Y, X88H/Y, X107G, X113C/L/P, X146L, X147H/K/V, X153A/C/V, X155A/V, X163L, X165F, X171Q, X178W, X190K, X206K, X228G, X233T/V, X235P, X244T, X251V, X259V, X268A, X277A, X286C/H, X312N, X314N, X315G, X316A/C/F/N/S/T, X317L, X319N, X323T, X358K, X366H, X383C/F/I/L/M/T/V, X395P, X399A, X414I, X415A/G/H/L/V, X417T/V, X424A, X426R, X427Y, X434T, and X450S.

13. The engineered polypeptide of any one of **claims** 1 to **12** in which the amino acid sequence does not comprise a residue difference as compared to SEQ ID NO: 2 at positions X9, X45, X177, X211, X294, X324, and X391.

14. The engineered polypeptide of **claim 1** in which the amino acid sequence comprises a sequence selected from SEQ ID NO: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38,40, 42,

44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, and 204.

15. The engineered polypeptide of any one of **claims** 1 to **14** in which the polypeptide is immobilized on a solid support.

16. The engineered polypeptide of **claim 15** in which the solid support is a bead or resin comprising polymethacrylate with epoxide functional groups, polymethacrylate with amino epoxide functional groups, styrene/DVB copolymer or polymethacrylate with octadecyl functional groups

17. A polynucleotide encoding the engineered transaminase polypeptide of any one of **claims** 1 to **14**.

18. A polynucleotide encoding the engineered transaminase polypeptide of **claim** 1, comprising a nucleotide sequence selected from SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, and 203.

19. An expression vector comprising the polynucleotide of **claim 17** or **18**.

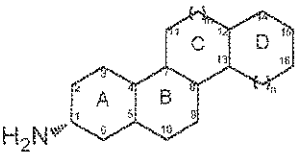
20. The expression vector of **claim 19** comprising a control sequence

21. A host cell comprising the polynucleotide of **claim 17** or **18** or the expression vector of **claim 19** or **20**.

22. A method of preparing the engineered polypeptide of any one of **claims** 1 to **14**, comprising culturing the host cell of **claim 21** under conditions suitable for expression of the polypeptide.

23. The method of **claim 22**, further comprising isolating the engineered polypeptide.

24. A process for preparing an amine compound of Formula (I),



(I)

wherein

Ring A is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond between positions 2 and 3 and/or positions 5 and 6, and/or optionally substituted independently positions 2, 3, 4, 5 and 6 with a group selected from halo, hydroxy, and methyl;

Ring B is a 6-membered carbocyclic ring, optionally including an unsaturated C-C bond between positions 5 and 10, and/or optionally substituted independently at one or more of positions 9 and 10 with a group selected from halo, hydroxy, and methyl;

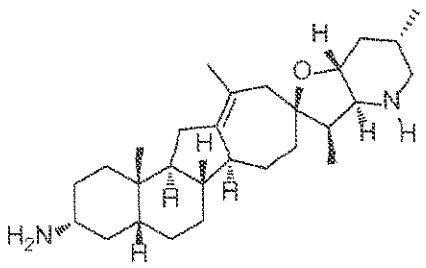
Ring C is a 5- or 6-membered carbocyclic ring (*i.e.*, m = 0 or 1), optionally substituted at position 10 with a group selected from halo, hydroxy, methyl, ethyl, and carbonyl;

Ring D is a 5-, 6-, or 7-membered carbocyclic ring (*i.e.*, n = 0, 1, or 2), optionally including 1, 2, or 3 unsaturated C-C bonds, and/or optionally substituted independently as follows:

at position 14 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, straight-chain or branched (C_1-C_3)alkylamino, and cyclopropyl bridging to position 12;

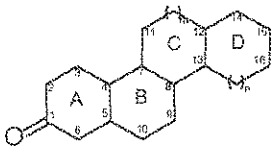
at position 15 or position 16 with a group selected from halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, *optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally* substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, aminocarbonyl(C_1-C_6)alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted arylamino, optionally substituted arylthio, optionally substituted arylsulfonyl, optionally substituted arylsulfinyl, optionally substituted aryloxycarbonyl, optionally substituted arylcarbonyloxy, optionally substituted heteroaryloxy, optionally substituted heteroarylamino, optionally substituted heteroarylthio, optionally substituted heteroarylsulfonyl, optionally substituted heteroarylsulfinyl, optionally substituted heteroaryloxycarbonyl, optionally substituted heteroarylcarbonyloxy, alkylaminosulfonyl(C_1-C_6)alkyl, arylsulfonyl(C_1-C_6)alkyl, and heteroarylsulfonyl(C_1-C_6)alkyl;

with the proviso that the compound of Formula (I) is not compound (1)



(1)

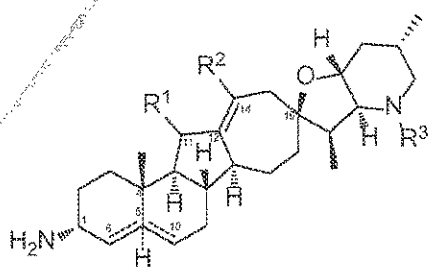
wherein the method comprises contacting the ketone substrate compound of Formula (II),



(II)

wherein rings A, B, C, and D are as defined above for the compound of formula (I), with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

25. The process of **claim 24**, wherein the amine compound of Formula (I) is the compound of Formula (Ia)



(Ia)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

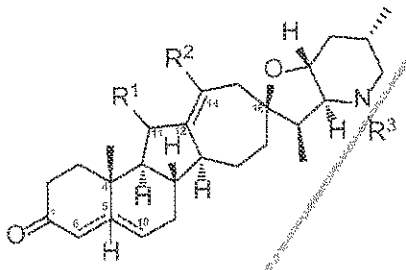
Ring D comprises an unsaturated C-C bond between positions 12 and 14;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl(C_1-C_6)alkyl;

and wherein the method comprises contacting the ketone substrate compound of Formula **(IIa)**,

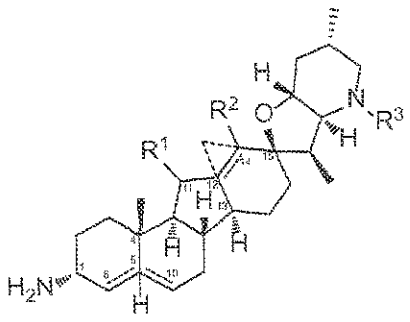


(IIa)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of Formula **(Ia)**,

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

26. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound of Formula **(Ib)**



(Ib)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

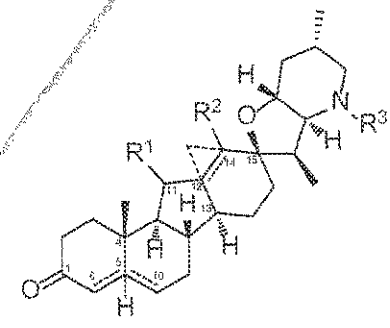
Ring D comprises an unsaturated C-C bond between positions 12 and 14, or a bridging cyclopropyl between positions 12 and 14;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched $(C_1$-$C_4)$alkyl, straight-chain or branched $(C_1$-$C_4)$alkenyl, and straight-chain or branched $(C_1$-$C_3)$alkylamino; and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, optionally substituted$(C_1$-$C_6)$alkyloxy, optionally substituted $(C_1$-$C_6)$alkylamino, optionally substituted $(C_1$-$C_6)$dialkylamino, optionally substituted $(C_1$-$C_6)$alkylthio, optionally substituted $(C_1$-$C_6)$alkylsulfonyl, optionally substituted $(C_1$-$C_6)$alkylsulfinyl, carboxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyloxycarbonyl, $(C_1$-$C_6)$alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl$(C_1$-$C_6)$alkyl;

and wherein the method comprises contacting the ketone substrate compound of Formula **(IIb)**,



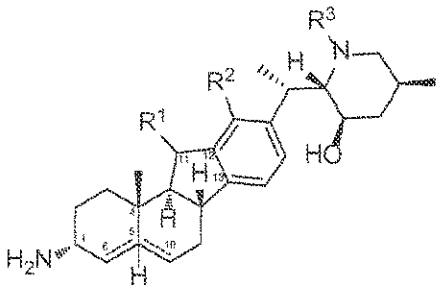
(IIb)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of Formula **(Ib)**,

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

27. The process of **claim 24**, wherein the amine compound of Formula **(I)** is the compound Formula

(Ic)



(Ic)

wherein

Rings A and B comprise one of the following:

(a) an unsaturated C-C bond between positions 5 and 6;

(b) an unsaturated C-C bond between positions 5 and 10;

(c) a hydrogen at position 5 *cis* to the methyl group at position 4; or

(d) a hydrogen at position 5 *trans* to the methyl group at position 4;

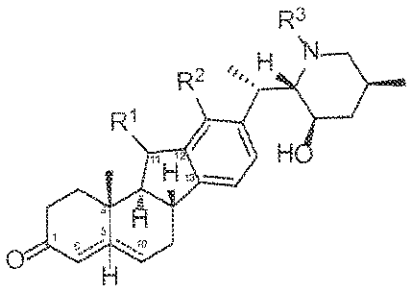
Ring D is aromatic;

R^1 is selected from hydrogen, halo, hydroxy, methyl, ethyl, and carbonyl;

R^2 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino: and

R^3 is selected from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, and aminocarbonyl(C_1-C_6)alkyl;

wherein the method comprises contacting the ketone substrate compound of Formula (IIc),

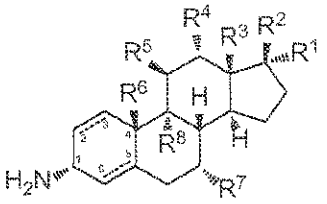


(IIc)

wherein rings A, B, C, and D, and R^1, R^2, and R^3 are as defined above for the compound of *Formula* (**Ic**),

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

28. The process of **claim 24**, wherein the amine compound of Formula (**I**) is the compound of Formula (**Id**)



(Id)

wherein

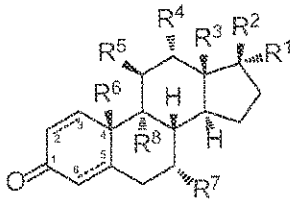
Ring A comprises an unsaturated C-C bond between positions 2 and 3, or positions 5 and 6;

R^1 and R^2 are selected independently from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, optionally substituted (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, optionally substituted(C_1-C_6)alkyloxy, optionally substituted (C_1-C_6)alkylamino, optionally substituted (C_1-C_6)dialkylamino, optionally substituted (C_1-C_6)alkylthio, optionally substituted (C_1-C_6)alkylsulfonyl, optionally substituted (C_1-C_6)alkylsulfinyl, carboxy(C_1-C_6)alkyl, (C_1-C_6)alkyloxycarbonyl, (C_1-C_6)alkylcarbonyloxy, optionally substituted aminocarbonyl, aminocarbonyl(C_1-C_6)alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted arylamino, optionally substituted arylthio, optionally substituted arylsulfonyl, optionally substituted arylsulfinyl, optionally substituted aryloxycarbonyl, optionally substituted arylcarbonyloxy, optionally substituted heteroaryloxy, optionally substituted heteroarylamino, optionally substituted heteroarylthio, optionally substituted heteroarylsulfonyl, optionally substituted heteroarylsulfinyl, optionally substituted heteroaryloxycarbonyl, optionally substituted heteroarylcarbonyloxy, alkylaminosulfonyl(C_1-C_6)alkyl, arylsulfonyl(C_1-C_6)alkyl, and heteroarylsulfonyl(C_1-C_6)alkyl;

R^3, R^4, and R^5 are selected independently from hydrogen, halo, hydroxy, amino, carboxy, cyano, nitro, thio, straight-chain or branched (C_1-C_4)alkyl, straight-chain or branched (C_1-C_4)alkenyl, and straight-chain or branched (C_1-C_3)alkylamino; and

R^6, R^7, and R^8 are selected independently from hydrogen, halo, hydroxy, and methyl;

wherein the method comprises contacting the ketone substrate compound of Formula (**IId**),



(IId)

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 are as defined above for the compound of Formula **(Id)**,

with an engineered transaminase polypeptide of any one of **claims** 1 to **16** in the presence of an amino donor under suitable reaction conditions.

29. The process of any one of **claims 24** to **28** in which the substrate compound of Formula **(II)** is at a loading of about 0.5 to about 200 g/L, 1 to about 200 g/L, 5 to about 150 g/L, about 10 to about 100 g/L, or about 20 to about 100 g/L.

30. The process of **claim 29** in which the substrate compound of Formula **(II)** is at a loading of at least about 0.5 g/L, 1 g/L, 5 g/L, 10 g/L, 20 g/L, 30 g/L, 40 g/L, 50 g/L, 100 g/L, 150 g/L, or 200 g/L.

31. The process of any one of **claims 24** to **30** in which the amino donor is selected from the group consisting of isopropylamine, L-lysine, α-phenethylamine, D-alanine, L-alanine, or D,L-alanine, or D,L-ornithine.

32. The process of **claim 31** in which the amino donor is isopropylamine (IPM).

33. The process of **claim 32** in which the isopropylamine is at a concentration of about 0.1 to about 3 M, 0.2 to about 2.5 M, about 0.5 to about 2 M, or about 1 to about 2 M.

34. The process of **claim 33** in which the isopropylamine is at a concentration of about 0.1 M, 0.2 M, 0.3 M, 0.4 M, 0.5 M, 0.6 M, 0.7 M, 0.8 M, 1 M, 1.5 M, 2 M, 2.5 M, or 3 M.

35. The process of any one of **claims 24** to **34** in which the suitable reaction conditions comprise a buffer.

36. The process of **claim 35** in which the buffer is selected from borate, phosphate, carbonate, triethanolamine (TEA), and Tris.

37. The process of **claim 36** in which the buffer comprises TEA, wherein the TEA concentration is about 0.01 to about 0.4 M, about 0.05 to about 0.4 M, about 0.1 to about 0.3 M, or about 0.1 to about 0.2 M.

38. The process of **claim 37** in which the TEA concentration is about 0.01 M, 0.02 M, 0.03 M, 0.04 M, 0.05 M, 0.07 M, 0.1 M, 0.12 M, 0.14 M, 0.16 M, 0.18 M, 0.2 M, 0.3 M, or 0.4 M.

39. The process of any one of **claims 24** to **38** in which the suitable reaction conditions comprise a pH from about 6 to about 12, pH from about 6 to about 10, pH from about 6 to about 8, pH from about 7 to about 10, pH from about 7 to about 9, or pH from about 7 to about 8.

40. The process of **claim 39** in which the suitable reaction conditions comprise a pH of about 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10. 10.5, 11, 11.5, or 12.

41. The process of any one of **claims 24** to **40** in which the suitable reaction conditions comprise a temperature of about 10°C to about 70°C, about 10°C to about 65°C, about 15°C to about 60°C, about 20°C to about 60°C, about 20°C to about 55°C, about 30°C to about 55°C, or about 50°C to about 60°C.

42. The process of **claim 41** in which the suitable reaction conditions comprise a temperature of at least about 10°C, 15°C, 20°C, 25°C, 30°C, 35°C, 40°C, 45°C, 50°C, 55°C, 60°C, 65°C, or 70°C.

43. The process of any one of **claims 24** to **42** in which the suitable reaction conditions comprise a pyridoxal cofactor, pyridoxal-5'-phosphate (PLP), at a concentration from about 0.1 g/L to about 10 g/L, about 0.2 g/L to about 5 g/L, or about 0.5 g/L to about 2.5 g/L.

44. The process of **claim 43** in which the suitable reaction conditions comprise a PLP concentration of about 0.1 g/L, 0.2 g/L, 0.5 g/L, 1 g/L, 2.5 g/L, 5 g/L, or 10 g/L.

45. The process of any one of **claims 24** to **44** in which the suitable reaction conditions comprise a co-solvent.

46. The process of **claim 45** in which the co-solvent comprises a polar co-solvent.

47. The process of **claim 46** in which the co-solvent is selected from a polyol, DMSO, or lower alcohol.

48. The process of **claim 47** in which the co-solvent is DMSO

49. The process of **claim 44** in which the DMSO is present at a concentration of from about 1% to about 40% v/v; about 2% to about 30% v/v; or about 5% to about 25% v/v.

50. The process of **claim 49** in which the DMSO is present at a concentration of about 1% v/v, 2% v/v, 5% v/v, 10% v/v, 15% v/v, 20% v/v, 25% v/v, 30% v/v, 35% v/v, 35% v/v, or 40% v/v.

51. The process of **claims 24** to **50** in which the transaminase polypeptide is at a concentration of about 0.01 to about 50 g/L, about 0.05 to about 50 g/L, about 0.1 to about 40 g/L, about 1 to about 40 g/L, about 2 to about 40 g/L, about 5 to about 40 g/L, about 5 to about 30 g/L, about 0.1 to about 10 g/L, about 0.5 to about 10 g/L, about 1 to about 10 g/L, about 0.1 to about 5 g/L, about 0.5 to about 5 g/L, or about 0.1 to about 2 g/L.

52. The process of **claim 51** in which the transaminase polypeptide is at a concentration of about 0.01 g/L, 0.05 g/L, 0.1 g/L, 0.2 g/L, 0.5 g/L, 1 g/L, 2 g/L, 5 g/L, 10 g/L, 15 g/L, 20 g/L, 25 g/L, 30 g/L, 35 g/L, 40 g/L, or 50 g/L.

53. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:
    (a) substrate loading at about 5 g/L to 200 g/L;
    (b) about 0.1 to 50 g/L of engineered transaminase polypeptide;
    (c) about 0.1 to 4 M of isopropylamine (IPM);
    (d) about 0.1 to 10 g/L of pyridoxal phosphate (PLP) cofactor;
    (e) pH of about 6 to 9; and
    (f) temperature of about 30 to 65°C.

54. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:
    (a) substrate loading at about 10 g/L to 150 g/L;
    (b) about 0.5 to 20 g/L of engineered transaminase polypeptide;
    (c) about 0.1 to 3 M of isopropylamine (IPM);
    (d) about 0.1 to 10 g/L of pyridoxal phosphate (PLP) cofactor;
    (e) about 0.05 to 0.20 M triethanolamine (TEA) buffer;
    (f) about 1% to about 45% DMSO;
    (g) pH of about 6 to 9; and
    (h) temperature of about 30 to 65°C.

55. The process of any one of **claims 24** to **28** in which the suitable reaction conditions comprise:

(a) substrate loading at about 20 to 100 g/L;

(b) about 1 to 5 g/L of engineered transaminase polypeptide;

(c) about 0.5 to 2 M of isopropylamine (IPM);

(d) about 0.2 to 2 g/L of pyridoxal phosphate (PLP) cofactor;

(e) about 0.1 M TEA buffer;

(f) about 25% DMSO;

(e) pH of about 8; and

(f) temperature of about 45 to 60°C.