[0007a] In one aspect, there is provided a ketoreductase polypeptide capable of converting the substrate, methyl-2-benzamidomethyl-3-oxobutyrate, to the product, 2*S*, 3*R*-methyl-2-benzamidomethyl-3-hydroxybutyrate, with a percent stereomeric excess of at least 60%, which comprises an amino acid sequence that is at least 85% identical to a reference sequence of SEQ ID NO:2 or 4 or 86 having the following features: residue corresponding to X94 is threonine; residue corresponding to X199 is a histidine and residue corresponding to X202 is valine or leucine; with the proviso that the ketoreductase polypeptide has an amino acid sequence in which the residue corresponding to X94 is an aliphatic or polar residue; residue corresponding to X199 is an aliphatic, constrained or polar residue; and residue corresponding to X202 is valine or leucine.

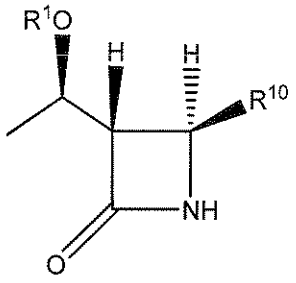
[0007b] In another aspect, there is provided a polynucleotide encoding a polypeptide as defined above.

[0007c] In yet another aspect, there is provided an expression vector comprising the polynucleotide as defined above operably linked to control sequences suitable for directing expression in a host cell.

[0007d] In still another aspect, there is provided a host cell comprising the expression vector as defined above.

[0007e] In a further aspect, there is provided a composition comprising a ketoreductase as defined above and compound methyl-2-benzamidomethyl-3-oxobutyrate or compound 2*S*,3*R*-methyl-2-benzamidomethyl-3-hydroxybutyrate.

[0007f] In yet a further aspect, there is provided a method for the synthesis of the intermediate of formula (IVa),

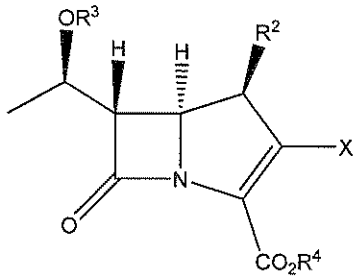


(IVa)

wherein R^1 is H or a hydroxyl protecting group, and R^{10} is a halogen, or –OAc, where Ac is acetate,

characterized in that a step in the method comprises contacting or reacting the substrate methyl-2-benzamidomethyl-3-oxobutyrate with a ketoreductase as defined above under reaction conditions suitable for reducing or converting the substrate to product 2*S*,3*R*-methyl-2-benzamidomethyl-3-hydroxybutyrate.

[0007g] In still a further aspect, there is provided a method for the synthesis of the intermediate of structural formula (IX),

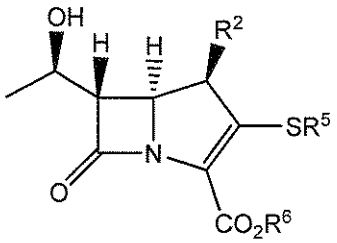


(IX)

wherein R^2 is H or a C1-C4 alkyl; R^3 is H, or a hydroxyl protecting group; R^4 is H, carboxy protecting group, ammonia group, alkali metal, or alkaline earth metal; and X is OH or a leaving group,

characterized in that a step in the method comprises contacting or reacting the substrate methyl-2-benzamidomethyl-3-oxobutyrate with a ketoreductase as defined above under reaction conditions suitable for reducing or converting the substrate to product 2*S*,3*R*-methyl-2-benzamidomethyl-3-hydroxybutyrate.

[0007h] In another aspect, there is provided a method for the synthesis of a carbapenem of structural formula (V):



(V)

or solvates, hydrates, salts, and prodrugs thereof, wherein R^2 is H or $-CH_3$; R^5 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted heterocycloalkyl, and substituted or unsubstituted heteroarylalkyl; and R^6 is H or a progroup,

characterized in that a step in the method comprises contacting or reacting the substrate methyl-2-benzamidomethyl-3-oxobutyrate with a ketoreductase as defined above under reaction conditions suitable for reducing or converting the substrate to product 2*S*,3*R*-methyl-2-benzamidomethyl-3-hydroxybutyrate.