SUMMARY OF THE INVENTION

[0006] The ~~invention~~disclosure provides non-naturally occurring microbial organisms having a (2-hydroxy-3-methyl-4-oxobutoxy)phosphonate pathway, p- toluate pathway, and/or terephthalate pathway. The ~~invention~~disclosure additionally provides methods of using such organisms to produce (2-hydroxy-3-methyl-4-oxobutoxy)phosphonate pathway, p- toluate pathway or terephthalate pathway.

[0006a] In a first aspect, the present invention refers to a non-naturally occurring microbial organism having carbon monoxide dehydrogenase or hydrogenase activity and a reductive tricarboxylic acid (rTCA) pathway, wherein said microbial organism comprises (1) at least one exogenous nucleic acid encoding a rTCA pathway enzyme expressed in a sufficient amount to convert CO, CO_2 or H_2 to acetyl-CoA, wherein said rTCA enzyme is selected from the group consisting of an ATP citrate-lyase, a citrate lyase, an aconitase, an isocitrate dehydrogenase, an alpha-ketoglutarate:ferredoxin oxidoreductase, a succinyl-CoA synthetase, a succinyl-CoA transferase, a fumarate reductase, a fumarase, and a malate dehydrogenase; and (2) at least one exogenous nucleic acid encoding a biosynthetic product pathway enzyme expressed in a sufficient amount to produce said biosynthetic product, wherein the microbial organism does not require light for growth.

[0006b] In a second aspect, the present invention refers to a non-naturally occurring microbial organism comprising

a rTCA pathway comprising at least one exogenous nucleic acid encoding a rTCA pathway enzyme expressed in a sufficient amount to convert (i) CO, (ii) CO_2 and H_2, (iii) CO and CO_2, (iv) synthesis gas comprising CO and H_2, or (v) synthesis gas comprising CO, CO_2, and H_2; to acetyl-CoA; wherein said at rTCA pathway enzyme is selected from the group consisting of an ATP citrate-lyase, a citrate lyase, an aconitase, an isocitrate dehydrogenase, an alpha-ketoglutarate:ferredoxin oxidoreductase, a succinyl-CoA synthetase, a succinyl-CoA transferase, a fumarate reductase, a fumarase and a malate dehydrogenase;

a reducing equivalent producing pathway comprising at least one exogenous nucleic acid encoding a reducing equivalent producing enzyme selected from the group consisting of a carbon monoxide dehydrogenase, a hydrogenase and a NAD(P)H:ferredoxin oxidoreductase; and

at least one exogenous nucleic acid encoding a biosynthetic product pathway enzyme expressed in a sufficient amount to produce a biosynthetic product, wherein the microbial organism does not require acetyl-CoA synthase.

[0006c] In a third aspect, the present invention refers to a non-naturally occurring microbial organism comprising a reducing equivalent producing pathway comprising at least one exogenous nucleic acid encoding a reducing equivalent producing enzyme selected from the group consisting of a carbon monoxide dehydrogenase, a hydrogenase and a NAD(P)H:ferredoxin oxidoreductase; and

at least one exogenous nucleic acid encoding a biosynthetic product pathway enzyme expressed in a sufficient amount to produce said biosynthetic product, wherein the microbial organism does not require acetyl-CoA synthase.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] Figure 1 shows a schematic depiction of an exemplary pathway to (2-hydroxy-3-methyl-4-oxobutoxy)phosphonate (2H3M4OP) from glyceraldehyde-3-phosphate and pyruvate. G3P is glyceraldehyde-3-phosphate, DXP is 1-deoxy-D-xylulose-5-phosphate and 2ME4P is C-methyl-D-erythritol-4-phosphate. Enzymes are (A) DXP synthase; (B) DXP reductoisomerase; and (C) 2ME4P dehydratase.

[0008] Figure 2 shows a schematic depiction of an exemplary alternate shikimate pathway to p-toluate. Enzymes are: (A) 2-dehydro-3-deoxyphosphoheptonate synthase; (B) 3-dehydroquinate synthase; (C) 3-dehydroquinate dehydratase; (D) shikimate dehydrogenase; (E) Shikimate kinase; (F) 3-phosphoshikimate-2-carboxyvinyltransferase; (G) chorismate synthase; and (H) chorismate lyase. Compounds are: (1) (2-hydroxy-3-methyl-4-oxobutoxy)phosphonate; (2) 2,4-dihydroxy-5-methyl-6-[(phosphonooxy)methyl]oxane-2-carboxylate; (3) 1,3-dihydroxy-4-methyl-5-oxocyclohexane-1-carboxylate; (4) 5-hydroxy-4-methyl-3-oxocyclohex-1-ene-1-carboxylate; (5) 3,5-dihydroxy-4-methylcyclohex-1-ene-1-carboxylate; (6) 5-hydroxy-4-methyl-3-(phosphonooxy)cyclohex-1-ene-1-carboxylate; (7) 5-[(1-carboxyeth-1-en-1-yl)oxy]-4-methyl-3-(phosphonooxy)cyclohex-1-ene-1-carboxylate; (8) 3-[(1-carboxyeth-1-en-1-yl)oxy]-4-methylcyclohexa-1,5-diene-1-carboxylate; and (9) p-toluate.

[0009] Figure 3 shows an exemplary pathway for conversion of p-toluate to terephthalic acid (PTA). Reactions A, B and C are catalyzed by p-toluate methyl-monooxygenase reductase, 4-carboxybenzyl alcohol dehydrogenase and 4-carboxybenzyl aldehyde dehydrogenase, respectively. The compounds shown are (1) p-toluic acid; (2) 4-carboxybenzyl alcohol; (3) 4-carboxybenzaldehyde and (4) terephthalic acid.