- Reaction of isobutene and formaldehyde
- Reaction of acetone and acetylene
- Propylene dimerization

WO 2009/076676 reports a metabolic pathway to isoprene. The pathway is based on the dephosphorylation-dehydration of downstream intermediates in the mevalonate pathway, i.e. isoprenyl-pyrophosphate or prenyl-pyrophosphate. This process has the drawback of requiring going through the whole mevalonate pathway: double phosphorylation of mevalonate, followed by a decarboxylation-dehydration into isoprenyl-pyrophosphate, further isomerised into prenyl-pyrophosphate, and finally double dephosphorylation/dehydration into isoprene.

Isoamyl alcohol is a very important chemical commonly used as solvents for fats, oils, resins and alkaloids. There is a demand for isoamyl alcohol in perfumery industry, for example in the manufacture of isoamyl salicylate used in soap and cosmetic fragrances. It is also used in the manufacture of phosphoric acid. Furthermore, it is used in the synthesis of pyrethroids. Commercial processes for the production of isoamyl alcohol include fractionation of fusel oils, chlorination of alkanes with subsequent hydrolysis to produce a mixture of isomers and a low pressure oxo-process or hydroformylation of n-butenes followed by hydrogenation of the resulting iso-valeraldehyde.

WO 2011/076261 describes a process for producing isoprenol by enzymatic conversion of mevalonate with an enzyme having the activity of a decarboxylase. Although the method described in WO 2011/076261 allows to produce isoprenol by enzymatically converting mevalonate, there is still a need for improvements, in particular as regards efficiency of the process so as to make it suitable for industrial purposes. The present application addresses this need.

Summary

In one aspect, the present invention provides a method for producing isoprenol, characterized in that it comprises the conversion of mevalonate into isoprenol by

(i) a first enzyme having an activity of converting mevalonate into mevalonate 3-phosphate, wherein said first enzyme is a Mevalonate Diphosphate Decarboxylase; and

(ii) a second enzyme being different from the first enzyme and having an activity of converting said mevalonate 3-phosphate into isoprenol, wherein said second enzyme is a Mevalonate Diphosphate Decarboxylase,

wherein the production of isoprenol by use of the combination of enzymes as defined in (i) and (ii) is higher than the production of isoprenol achieved by either enzyme alone or the addition of the production which either enzyme achieves in isolation.

In another aspect, the present invention provides a composition comprising

(a) mevalonate; and

(b) at least two enzymes, wherein one enzyme is selected from (i) and the other enzyme is selected from (ii), wherein (i) and (ii) are as follows:

(i) a first enzyme having an activity of converting mevalonate into mevalonate 3-phosphate, wherein said first enzyme is a Mevalonate Diphosphate Decarboxylase; and

(ii) a second enzyme being different from the first enzyme and having an activity of converting said mevalonate 3-phosphate into isoprenol, wherein said second enzyme is a Mevalonate Diphosphate Decarboxylase,

wherein the production of isoprenol by use of the combination of enzymes as defined in (i) and (ii) is higher than the production of isoprenol achieved by either enzyme alone or the addition of the production which either enzyme achieves in isolation.

In yet another aspect, the present invention provides a composition comprising

(a) mevalonate; and

(b) a multicellular organism or a microorganism which produces at least two enzymes, wherein one enzyme is selected from (i) and the other enzyme is selected from (ii), wherein (i) and (ii) are as follows:

(i) a first enzyme having an activity of converting mevalonate into mevalonate 3-phosphate, wherein said first enzyme is a Mevalonate Diphosphate Decarboxylase; and

(ii) a second enzyme being different from the first enzyme and having an activity of converting said mevalonate 3-phosphate into isoprenol, wherein said second enzyme is a Mevalonate Diphosphate Decarboxylase

wherein the production of isoprenol by use of the combination of enzymes as defined in (i) and (ii) is higher than the production of isoprenol achieved by either enzyme alone or the addition of the production which either enzyme achieves in isolation.

In yet another aspect, the present invention provides the use of a combination of at least two enzymes, wherein one enzyme is selected from the following (i) and the other enzyme is selected from the following (ii) or of a composition as defined herein or of a microorganism as defined herein, for producing isoprenol from mevalonate,

wherein (i) and (ii) are as follows:

(i) a first enzyme having an activity of converting mevalonate into mevalonate 3-phosphate, wherein said first enzyme is a Mevalonate Diphosphate Decarboxylase; and

(ii) a second enzyme being different from the first enzyme and having an activity of converting said mevalonate 3-phosphate into isoprenol, wherein said second enzyme is a Mevalonate Diphosphate Decarboxylase,

wherein the production of isoprenol by use of the combination of enzymes as defined in (i) and (ii) is higher than the production of isoprenol achieved by either enzyme alone or the addition of the production which either enzyme achieves in isolation.

In yet another aspect, the present invention provides a method for producing isoprenol comprising the step of enzymatically converting mevalonate 3-phosphate into isoprenol by use of an enzyme which can catalyze the conversion via decarboxylation and dephosphorylation, said enzyme being a Mevalonate Diphosphate Decarboxylase, and wherein said mevalonate-3-phosphate has been produced by a different enzyme.

In yet another aspect, the present invention provides a method for producing isoprene from mevalonate comprising the method as defined herein and further comprising the step of converting the produced isoprenol into isoprene.

In yet another aspect, the present invention provides a method for producing isoamyl alcohol from mevalonate comprising the method as defined herein and further comprising the step of converting the produced isoprenol into isoamyl alcohol.

Description

Thus, in a first aspect, the present invention relates to a method for producing isoprenol from mevalonate. In particular, the present invention relates to a method for producing isoprenol from mevalonate through a biological process, in particular an enzymatic process, in which two types of enzymes are combined in order to increase the efficiency of the production rate. More specifically, the present invention relates to a method for producing isoprenol, characterized in that it comprises the conversion of mevalonate into isoprenol by

(i) a first enzyme having an activity of converting mevalonate into mevalonate 3-