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PROCESS FOR PREPARING OPTICALLY ACTIVE 2-HYDROXY-4-PHENYL-3-BUTENOIC ACID.

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Description

[Background of the Invention]

This invention relates to a process for the production of optically active 2-hydroxy-4-phenyl-3-butenolic acid. More particularly, it relates to a process for the production of optically active 2-hydroxy-4-phenyl-3-butenolic acid which comprises treating 2-oxo-4-phenyl-3-butenolic acid with a microorganism which may be optionally ground, treated with acetone, lyophilized or immobilized, capable of asymmetrically reducing the 2-oxo-4-phenyl-3-butenolic acid into (R)-2-hydroxy-4-phenyl-3-butenolic acid or (S)-2-hydroxy-4-phenyl-3-butenolic acid to thereby asymmetrically reduce the same into (R)-2-hydroxy-4-phenyl-3-butenolic acid or (S)-2-hydroxy-4-phenyl-3-butenolic acid, wherein said microorganism capable of asymmetrically reducing 2-oxo-4-phenyl-3-butenolic acid into (R)-2-hydroxy-4-phenyl-3-butenolic acid is selected from among those belonging to the genera Leuconostoc, Sporolactobacillus, Pediococcus, Arthrobacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthoasus, Aureobacterium, Bacillus, Botryoasus, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluveromyces, Lipomyces, Loderomyces, Proteins, Pseudomonas, Saccharomycopsis, Schizosaccharomyces, Stephanoascus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella and Xanthomonas and wherein said microorganism capable of asymmetrically reducing 2-oxo-4-phenyl-3-butenolic acid into (S)-2-hydroxy-4-phenyl-3-butenolic acid is selected from among those belonging to the genus Leuconostoc.

Optically active 2-hydroxy-4-phenyl-3-butenolic acid is an important intermediate in the production of various drugs, optically active and physiologically active substances and derivatives thereof.

Further, optically active 2-hydroxy-4-phenyl-butyric acid, which is an important intermediate in the production of drugs such as ACE inhibitors, can be readily obtained by bringing optically active 2-hydroxy-4-phenyl-3-butenolic acid into contact with a hydrogenation catalyst such as palladium in a hydrogen atmosphere.

[Prior Art]

Known methods for the production of optically active 2-hydroxy-4-phenyl-3-butenolic acid include one which comprises treating a racemic mixture of said acid with bornylamine to thereby form diastereomers and then optically resolving the same [cf. Chem. Ber., 89, 671 - 677 (1956)] and another one comprising optical resolution through liquid chromatography with the use of a packing comprising a carrier containing a metal salt of an optically active amino acid bound thereto (cf. Japanese Patent Laid-Open No. 87640/1986). However, the former method requires a complicated procedure, which makes it undesirable from the industrial viewpoint. On the other hand, the latter method is disadvantageous from the economic viewpoint. Thus it has been demanded to develop a simple and economical method therefor. In addition, there has been known no process for the production of optically active 2-hydroxy-4-phenyl-3-butenolic acid from 2-oxo-4-phenyl-3-butenolic acid by using a microorganism capable of asymmetrically reducing the 2-oxo-4-phenyl-3-butenolic acid.

According to JP-A-63-32493 optically active hydroxy acid is produced by reducing an alpha-keto acid of the formula RCOCOOH by means of reduced type of nicotinamide-adenine-dinucleotide in the presence of benzoyl formic acid reductase extracted from Streptococcus bacteria to give the corresponding alpha-hydroxy acid optically active isomer. R is 2-4 C alkyl, chloromethyl, bromoethyl or benzyl.

[Disclosure of the Invention]

The present inventors have noticed asymmetric reduction with a microorganism as a process for readily producing optically active 2-hydroxy-4-phenyl-3-butenolic acid of a high optical purity and attempted to search for microorganisms suitable for this purpose. As a result, they have found out that a microorganism belonging to the genus Leuconostoc, , Sporolactobacillus, Pediococcus, Arthrobacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthoasus, Aureobacterium, Bacillus, Botryoasus, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluveromyces, Lipomyces, Loderomyces, Proteins, Pseudomonas, Saccharomycopsis, Schizosaccharomyces, Stephanoascus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella or Xanthomonas can asymmetrically reduce 2-oxo-4-phenyl-3-butenolic acid to thereby give (R)-2-hydroxy-4-phenyl-3-butenolic acid and that a microorganism belonging to the genus Leuconostoc can asymmetrically reduce 2-oxo-4-phenyl-3-butenolic acid to thereby give (S)-2-hydroxy-4-phenyl-3-butenolic acid, thus completing the present invention.
In the present invention, therefore, any microorganism belonging to the genus Leuconostoc, Sporolactobacillus, Pediciococcus, Arthrobacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthrobacceus, Aerobacterium, Bacillus, Botryococcus, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluveromyces, Lipomyces, Lodderomyces, Proteins, Pseudomonas, Saccharomyces, Schizosaccharomyces, Stephanasceus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella or Xanthomonas and capable of asymmetrically reducing 2-oxo-4-phenyl-3-butenolic acid to thereby give (R)-2-hydroxy-4-phenyl-3-butenolic acid or any one belonging to the genus Leuconostoc and capable of asymmetrically reducing 2-oxo-4-phenyl-3-butenolic acid to thereby give (S)-2-hydroxy-4-phenyl-3-butenolic acid can be used.

Particular examples of the microorganism capable of producing (R)-2-hydroxy-4-phenyl-3-butenolic acid from 2-oxo-4-phenyl-3-butenolic acid include Leuconostoc mesenteroides subsp. dextranicum IFO 3349, Pediciococcus acidilactici NRIC 1102, Sporolactobacillus inulinus NRIC 1133, Arthrobacter citreus IAM 12341, Agrobacterium radiobacter IFO 12864, Ambrosiozyma cicatricosa IFO 1848, Ambrosiozyma platypodi IFO 1471, Achromobacter pestifer ATCC 23584, Arthrobacceus javanensis IFO 1848, Aureobacterium testaceum IFO 12675, Bacillus licheniformis IFO 12200, Botryococcus synnaedendrus IFO 1804, Brevibacterium iodinum IFO 3558, Candida parapsilosis IFO 1396, Candida rugosa IFO 0750, Clavispora lusitaniae IFO 1019, Corynebacterium glutanicum ATCC 13032, Flavobacterium suaveolens IFO 3752, Geotrichum candidum IFO 4601, Hansenula fabianii IFO 1253, Kluveromyces lactis IFO 1903, Lipomyces starkeyi IFO 1289, Lodderomyces elongioporus IFO 1676, Proteus vulgaris IFO 3167, Pseudomonas aureotheciens IFO 3522, Saccharomyces lipolytica IFO 1550, Saccharomyces fibuliger IFO 0103, Schizosaccharomyces octosporus IFO 0353, Stephanasceus ciferii IFO 1854, Torulaspora delbrueckii IFO 0381, Trigonopsis variabilis IFO 0755, Wickerhamiella domecquii IFO 1857, Enterobacter aerogenes AHU 1338, Klebsiella pneumoniae IAM 1063 and Xanthomonas oryzae IAM 1857.

On the other hand, examples of the microorganism capable of producing (S)-2-hydroxy-4-phenyl-3-butenolic acid from 2-oxo-4-phenyl-3-butenolic acid include Leuconostoc mesenteroides AHU 1416.

These microorganisms may be either wild strains, variants or recombinants obtained through genetic engineering techniques such as cell fusion or gene manipulation.

The microorganisms having IFO numbers assigned thereto are described in the List of Cultures, 8th ed., vol. 1 (1988) published by the Institute for Fermentation, Osaka (IFO) and are available therefrom. Those having AHU numbers are described in the Catalogue of Cultures, 4th ed. (1987) published by Japan Federation of Culture Collection (JFCC) and are available from the Faculty of Agriculture, Hokkaido University. Further, those having ATCC numbers are described in the Catalogue of Bacteria Phages rDNA Vectors, 16th ed. (1985) published by American Type Culture Collection (ATCC) and are available therefrom. Those having NRIC numbers are described in the Culture Collection of NODAI No. 1 (1985) published by Tokyo University of Agriculture and are available therefrom. Those having IAM numbers are available from the Institute of Applied Microbiology, the University of Tokyo.

In order to culture the microorganism to be used in the present invention, any medium may be used without restriction, so long as said microorganism can grow therein. For example, any carbon source available for said microorganism may be used. Examples thereof include sugars such as glucose, fructose, sucrose and dextrin; alcohols such as sorbitol, ethanol and glycerol; organic acids such as fumaric acid, citric acid, acetic acid and propionic acid and salts thereof; hydrocarbons such as paraffin; and mixtures thereof. Examples of a nitrogen source include ammonium salts of inorganic acids, such as ammonium chloride, ammonium sulfate and ammonium phosphate; ammonium salts of organic acids, such as ammonium fumarate and ammonium citrate; organic or inorganic nitrogen-containing compounds such as meat extract, yeast extract, corn steep liquor, casein hydrolyzate and urea; and mixtures thereof. The medium may further contain appropriate nutritional sources commonly employed in culturing microorganisms, for example, inorganic salts, trace metal salts and vitamins. Furthermore, a growth promoter for the microorganism, a factor capable of elevating the productivity of the target compound of the present invention or a substance effective in maintaining the pH value of the medium at a desired level may be added thereto.

The culture may be conducted at a pH value of from 3.5 to 9.5, preferably from 4 to 8, at a temperature of from 20 to 45°C, preferably from 25 to 37°C, under aerobic or anaerobic conditions suitable for each microorganism for from 5 to 120 hours, preferably from 12 to 72 hours.

The reduction may be conducted by using the culture medium as such. Alternately, the cells may be separated by, for example, centrifuging, and optionally washed. Then the cells are resuspended in a buffer solution or water and 2-oxo-4-phenyl-3-butenolic acid is added to the suspension thus obtained and reacted therewith. In this reaction, it is sometimes preferable to add a carbon source such as glucose or sucrose to thereby supply energy. The cells may be used as such in the form of viable cells. Alternately, they may be
those which have been ground, treated with acetone or lyophilized. These optionally treated cells may be
immobilized prior to the use by a conventional method, for example, the polyacrylamide gel method, the
sulfur-containing polysaccharide gel method (the carrageenan gel method), the alginic acid gel method
or the agar gel method. Furthermore, an enzyme obtained from said treated cells by combining known
methods may be used therefor.

The 2-oxo-4-phenyl-3-butenoic acid may be used as such. Alternately, it may be dissolved in water or
an inert organic solvent or dispersed in a surfactant. It may be added either at once at the initiation of the
reaction or in portions. The 2-oxo-4-phenyl-3-butenoic acid may be used in the form of various salts such
as ammonium, sodium, calcium or potassium salt.

The reaction may be conducted at a pH value of from 3 to 9, preferably from 5 to 8, at from 10 to
60 °C, preferably from 20 to 40 °C, for from 1 to 120 hours with or without stirring. It is preferable that the
concentration of the substrate ranges from 0.1 to 10%, though it is not restricted thereby.

The optically active 2-hydroxy-4-phenyl-3-butenoic acid thus formed may be collected directly from the
reaction mixture or after separating the cells. It may be extracted with an organic solvent and then purified
by a common method such as column chromatography or recrystallization.

According to the process of the present invention for the production of optically active 2-hydroxy-4-
phenyl-3-butenoic acid by using a microorganism, optically active 2-hydroxy-4-phenyl-3-butenoic acid of a
high optical purity can be readily produced. Thus it is highly advantageous as an industrial process.

[Examples]

To further illustrate the present invention, and not by way of limitation, the following Examples will be
given.

In the following Examples, the absolute configuration and optical purity of a reaction product were
determined by extracting the reaction product with ethyl acetate and subjecting the product to high-
performance liquid chromatography with the use of an optical resolution column [column: Chiral-pack WH
(mfd. by Daicel Chemical Industries, Ltd., packed with silica gel containing copper salt of L-proline bound
thereto), 4.6 mm (i.d.) x 250 mm, solvent: 0.5 mM CuSO4/acetonitrile = 4 : 1, flow rate: 1.5 ml/min,
detection: at 254 nm]. The reaction yield was determined by high-performance liquid chromatography with
the use of a reverse-phase column [column: Nucleosil 10C18, 4.6 mm (i.d.) x 250 mm, solvent: 40 mM
potassium phosphate solution (pH 3.0)/acetonitrile = 4 : 1, flow rate: 1 ml/min, detection: at 254 nm].

Example 1

A medium comprising 2% of glucose, 1% of yeast extract, 1% of peptone, 10 ppm of MnSO4 and 1%
of calcium carbonate was used for lactic acid bacteria; a medium comprising 1% of glucose, 0.5% of yeast
extract, 0.5% of peptone, 0.5% of meat extract and 0.5% of NaCl (pH 7) was used for other bacteria; and a
medium comprising 2% of glucose, 0.3% of yeast extract, 0.5% of peptone and 0.3% of malt extract (pH 6)
was used for yeasts. 100 ml of each medium was introduced into a 500-ml Erlenmeyer flask and sterilized.

Then one platinum loopful of each strain listed in Table 1 was inoculated to the corresponding medium and
subjected to rotary shaking culture for 48 hours. After the completion of the culture, the cells were
separated by centrifuging and washed with a physiological saline solution once to thereby give viable cells.
50 ml of distilled water was introduced into a 500-ml Erlenmeyer flask and the above-mentioned viable cells
were suspended therein. After adding 5 g of sucrose and 0.5 g of calcium carbonate thereto, the mixture
was shaken at 30 °C for 10 minutes. Then 0.5 g of potassium 2-keto-4-phenyl-3-butenoate was added
thereto and the mixture was allowed to react under shaking at 30 °C for 40 hours. After the completion of the
reaction, the pH value of the reaction mixture was adjusted to 1 or below with sulfuric acid. Then it was
extracted with 100 ml of ethyl acetate and the solvent was removed from the extract. Then the amount and
optical purity of the (R)-2-hydroxy-4-phenyl-3-butenoic acid thus formed were determined by high-perfor-
mance liquid chromatography.
Table 1 summarizes the results.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Yield of (R)-2-hydroxy-4-phenyl-3-butenoic acid (%)</th>
<th>Optical purity of (R)-2-hydroxy-4-phenyl-3-butenoic acid (% e.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Leuconostoc mesenteroides</em> subsp. <em>dextranicum</em> IFO 3349</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td><em>Pediococcus acidilactici</em> NRIC 1102</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td><em>Sporolactobacillus inulinus</em> NRIC 1133</td>
<td>16</td>
<td>68</td>
</tr>
<tr>
<td><em>Leuconostoc dextranicum</em> ATCC 17072</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td><em>Leuconostoc mesenteroides</em> AHU 1067</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td><em>Arthrobacter citreus</em> IAM 12341</td>
<td>20</td>
<td>100</td>
</tr>
<tr>
<td><em>Agrobacterium radiobacter</em> IFO 12664</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td><em>Ambrosiozyma cicatricosa</em> IFO 1846</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td><em>Ambrosiozyma platypodis</em> IFO 1471</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Strain</td>
<td>Yield of (R)-2-hydroxy-4-phenyl-3-butenolic acid (%)</td>
<td>Optical purity of (R)-2-hydroxy-4-phenyl-3-butenolic acid (%)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>-----------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>Achromobacter pestifer ATCC 23584</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Arthrobotryum javanensis IFO 1848</td>
<td>12</td>
<td>32</td>
</tr>
<tr>
<td>Aureobacterium testaceum IFO 12675</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Bacillus licheniformis IFO 12200</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Botryosphaeria synnaedendrus IFO 1604</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>Brevibacterium iodinum IFO 3558</td>
<td>15</td>
<td>100</td>
</tr>
<tr>
<td>Candida parapsilosis IFO 1396</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Saccharomycopsis lipolytica IFO 1550</td>
<td>12</td>
<td>100</td>
</tr>
<tr>
<td>Saccharomycopsis fibuligera IFO 0103</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>Schizosaccharomyces octosporus IFO 0353</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Stephanoascus ciferrii IFO 1854</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Torulaspora delbrueckii IFO 0381</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Trigonopsis variabilis IFO 0755</td>
<td>15</td>
<td>100</td>
</tr>
</tbody>
</table>
Table 1 (cont'd)

<table>
<thead>
<tr>
<th>Strain</th>
<th>Yield of (R)-2-hydroxy-4-phenyl-3-butenoic acid (%)</th>
<th>Optical purity of (R)-2-hydroxy-4-phenyl-3-butenoic acid (% e.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wickerhamiella domercquii IFO 1857</td>
<td>11</td>
<td>95</td>
</tr>
<tr>
<td>Enterobacter aerogenes AHU 1338</td>
<td>13</td>
<td>94</td>
</tr>
<tr>
<td>Klebsiella pneumoniae IAM 1063</td>
<td>12</td>
<td>70</td>
</tr>
<tr>
<td>Xanthomonas oryzae AIM 1657</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td>Leuconostoc mesenteroides AHU 1416</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Candida rugosa IFO 0750</td>
<td>17</td>
<td>100</td>
</tr>
<tr>
<td>Clavispora lusitaniae IFO 1019</td>
<td>16</td>
<td>100</td>
</tr>
<tr>
<td>Corynebacterium glutamicum ATCC 13032</td>
<td>11</td>
<td>93</td>
</tr>
<tr>
<td>Flavobacterium suaveolens IFO 3752</td>
<td>11</td>
<td>70</td>
</tr>
<tr>
<td>Geotrichum candidum IFO 4601</td>
<td>19</td>
<td>100</td>
</tr>
<tr>
<td>Hansenula fabianii IFO 1253</td>
<td>13</td>
<td>100</td>
</tr>
<tr>
<td>Kluyveromyces lactis IFO 1903</td>
<td>14</td>
<td>100</td>
</tr>
</tbody>
</table>
Table 1 (cont'd)

<table>
<thead>
<tr>
<th>Strain</th>
<th>Yield of (R)-2-hydroxy-4-phenyl-3-butoenoic acid (%)</th>
<th>Optical purity of (R)-2-hydroxy-4-phenyl-3-butoenoic acid (% e.e.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipomyces starkeyi IFO 1289</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>Lodderomyces elongisporus IFO 1676</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>Proteus vulgaris IFO 3167</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Pseudomonas aureotaciens IFO 3522</td>
<td>11</td>
<td>100</td>
</tr>
</tbody>
</table>

Example 2

2 l of the same medium as that used in Example 1 contained in 5-l jar fermenter was inoculated with Leuconostoc mesenteroides subsp. dextranicum IFO 3349. The strain was cultured at 30°C under stirring at 100 rpm for 40 hours. After the completion of the culture, the cells were collected by centrifuging and washed with 1 l of water. Then these cells were suspended in 500 ml of water, and 5 g of potassium 2-keto-4-phenyl-3-butoenate, 50 g of glucose and 4 g of calcium carbonate were added thereto. The obtained mixture was allowed to react at 30°C under stirring for 48 hours and then the pH value thereof was adjusted to 1 or below with sulfuric acid. Then it was extracted with the same amount of ethyl acetate twice. The ethyl acetate phase was dehydrated over anhydrous Galuber’s salt and the solvent was removed therefrom under reduced pressure. Thus 4.0 g of 2-hydroxy-4-phenyl-3-butoenoic acid was obtained in the form of crude crystals. By recrystallizing from ethanol, 3.8 g of crystals of (R)-2-hydroxy-4-phenyl-3-butoenoic acid were obtained (optical purity: 100% e.e., yield: 93%).

Claims

1. A process for the production of optically active 2-hydroxy-4-phenyl-3-butoenoic acid which comprises treating 2-oxo-4-phenyl-3-butoenoic acid with a microorganism which may be optionally ground, treated with acetone, lyophilized or immobilized, capable of asymmetrically reducing the 2-oxo-4-phenyl-3-butoenoic acid into (R)-2-hydroxy-4-phenyl-3-butoenoic acid or (S)-2-hydroxy-4-phenyl-3-butoenoic acid to thereby asymmetrically reduce the same into (R)-2-hydroxy-4-phenyl-3-butoenoic acid or (S)-2-hydroxy-4-phenyl-3-butoenoic acid, wherein said microorganism capable of asymmetrically reducing 2-oxo-4-phenyl-3-butoenoic acid into (R)-2-hydroxy-4-phenyl-3-butoenoic acid is selected from among those belonging to the genera Leuconostoc, Sporolactobacillus, Pediococcus, Arthrobacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthosascus, Aureobacterium, Bacillus, Botryosphaeria, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluyveromyces, Lipomyces, Lodderomyces, Proteins, Pseudomonas, Saccharomyces, Schizosaccharomyces, Stephanoascus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella and Xanthomonas and wherein said microorganism capable of asymmetrically reducing 2-oxo-4-phenyl-3-butoenoic acid into (S)-2-hydroxy-4-phenyl-3-butoenoic acid is selected from among those belonging to the genus Leuconostoc.
Patentansprüche

1. Verfahren für die Herstellung von optisch aktiver 2-Hydroxy-4-phenyl-3-butensäure, welches das Behalten von 2-Oxo-4-phenyl-3-butensäure mit einem Mikroorganismus umfaßt, der wahlweise gemahlen, mit Aceton behandelt, lyophilisiert oder immobilisiert sein kann und fähig ist, 2-Oxo-4-phenyl-3-butensäure asymmetrisch zu (R)-2-Hydroxy-4-phenyl-3-butensäure oder (S)-2-Hydroxy-4-phenyl-3-butensäure zu reduzieren, um dadurch dieselbe asymmetrisch zu (R)-2-Hydroxy-4-phenyl-3-butensäure oder (S)-2-Hydroxy-4-phenyl-3-butensäure zu reduzieren, worin der besagte Mikroorganismus, der fähig ist, 2-Oxo-4-phenyl-3-butensäure asymmetrisch zu (R)-2-Hydroxy-4-phenyl-3-butensäure zu reduzieren, ausgewählt ist aus solchen, die zu den Gattungen Leuconostoc, Sporolactobacillus, Pediococcus, Arthroabacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthrobacter, Aureobacterium, Bacillus, Botryoascus, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluyveromyces, Lipomyces, Lodderomyces, Proteus, Pseudomonas, Saccharomyces, Schizosaccharomyces, Stephanoascus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella und Xanthomonas gehören und worin der besagte Mikroorganismus, der fähig ist, 2-Oxo-4-phenyl-3-butensäure asymmetrisch zu (S)-2-Hydroxy-4-phenyl-3-butensäure zu reduzieren, ausgewählt ist aus solchen, die zu der Gattung Leuconostoc gehören.

Revendications

1. Procédé de préparation de l’acide 2-hydroxy-4-phényl-3-buténoïque optiquement actif, comprenant le traitement de l’acide 2-oxo-4-phényl-3-butynoïque avec un microorganisme qui peut être éventuellement broyé, traité avec de l’acétone, lyophilisé ou immobilisé, capable de réduire l’acide 2-oxo-4-phényl-3-butyroïque de façon asymétrique pour donner l’acide (R)-2-hydroxy-4-phényl-3-butyroïque ou l’acide (S)-2-hydroxy-4-phényl-3-butyroïque, pour réduire ainsi celui-ci de façon asymétrique et donner l’acide (R)-2-hydroxy-4-phényl-3-butyroïque ou l’acide (S)-2-hydroxy-4-phényl-3-butyroïque, ledit micro-organisme capable de réduire l’acide 2-oxo-4-phényl-3-butyroïque de façon asymétrique en acide (R)-2-hydroxy-4-phényl-3-butyroïque étant choisi parmi les micro-organismes appartenant aux genres Leuconostoc, Sporolactobacillus, Pediococcus, Arthroabacter, Agrobacterium, Ambrosiozyma, Achromobacter, Arthrobacter, Aureobacterium, Bacillus, Botryoascus, Brevibacterium, Candida, Clavispora, Corynebacterium, Flavobacterium, Geotrichum, Hansenula, Kluyveromyces, Lipomyces, Lodderomyces, Proteus, Pseudomonas, Saccharomyces, Schizosaccharomyces, Stephanoascus, Torulaspora, Trigonopsis, Wickerhamiella, Enterobacter, Klebsiella et Xanthomonas, et ledit micro-organisme capable de réduire asymétriquement l’acide 2-oxo-4-phényl-3-butyroïque en acide (S)-2-hydroxy-4-phényl-3-butyroïque étant choisi parmi les micro-organismes appartenant au genre Leuconostoc.