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Drug intermediates isovaleric acid synthesis method

FIELD OF THE INVENTION

The present invention relates to drug intermediates isovaleric acid synthesis method.

GENERAL BACKGROUND

Isovaleric acid is used for the production of sedative hypnotics bromoisovaleride, but more for the production of spices, the isovalerate used as a perfume mainly includes isovalerate hexahydrate, isovalerate, isopentyl isovalerate, geranyl isovalerate, benzyl isovalerate and cinnamyl isovalerate. Lower isovalerate esters is used for edible spices, and higher isovalerate esters for cosmetics. Isovalic acid natural stored in valerian oil, vanilla oil, hops oil, bay leaf oil, spearmint oil, etc., the Chinese national standard GB2760-86 provides for the use of food spices, mainly for the preparation of cheese and cream flavor, but also trace for fruit flavor. However, most of the existing synthetic methods are using isoamyl alcohol oxidation synthesis, it is complicated and the final yield is not very high. Therefore, it is necessary to propose a new synthetic method for further improving the quality and yield of the product and reducing the byproduct content, it has important economic significance.

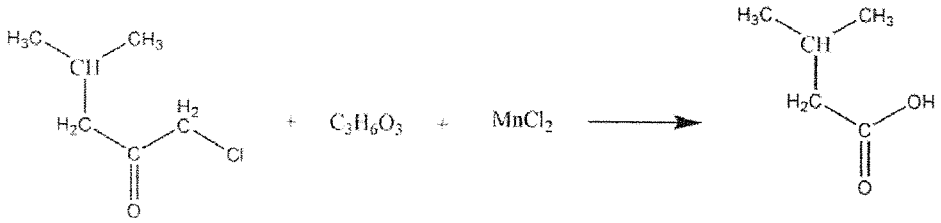
SUMMARY

The purpose of the present invention is to provide drug intermediates isovaleric acid synthesis method, comprises the following steps:

(i) 2 mol 1-chloro-3-isopropylacetone and 4-5 mol dimethyl carbonate solution were added to the reaction vessel, control the stirring speed at 110-140 rpm, the solution temperature was raised to 30-40 ℃, and then added 3-4 mol manganese chloride, reacted for 70-90 min, added 900 ml potassium chloride solution, reduced the temperature of the solution to 20-25 ℃, added potassium hydrogen sulfate solution to adjust the pH to 4-5, standing for 50-70 min, the solution was layered, washed with a methyl carbitol solution, washed with a methyl hydrazine solution, recrystallized from

1-methylpiazepine solution, and dehydrated with the dehydrating agent, finally obtained the product isovaleric acid; wherein, the mass fraction of the dimethyl carbonate solution in step (i) is 70 to 76%, the mass fraction of the potassium chloride solution in step (i) is 10 to 16%, the mass fraction of the potassium bisulfate solution described in step (i) is 20 to 25% , the mass fraction of the methyl carbitol solution in step (i) is 60 to 68%, the mass fraction of the methylhydrazine solution in step (i) is 80 to 87%, the 1- the methylpyrazine solution has a mass fraction of 90-95%.

Throughout the reaction process can be the following reaction formula:



Advantage of the present invention is that: reducing intermediate links reaction, decreasing the reaction time and improving the reaction yield.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

The following examples with reference to specific embodiments of the present invention are further illustrated:

drug intermediates isovaleric acid synthesis method.

Embodiment 1

2 mol 1-chloro-3-isopropylacetone and 4mol dimethyl carbonate solution with a mass fraction of 70%, were added to the reaction vessel, controlled the stirring speed at 110 rpm, the solution temperature was raised to 30 ℃, and then added 3 mol manganese chloride, reacted for 70 min, added 900 ml potassium chloride solution with a mass fraction of 10%, reduced the temperature of the solution to 20 ℃, added potassium hydrogen sulfate solution with a mass fraction of 20% to adjust the pH to 4, standing for 50 min, the solution was layered, washed with a methyl carbitol solution with a mass fraction of 60%,, washed with a methyl hydrazine solution with a mass fraction of 80%, recrystallized from 1-methylpiazepine solution with a mass fraction of

90%, and dehydrated with the anhydrous calcium chloride dehydrating agent, finally obtained the product isovaleric acid 181.56 g, yield of 89%.

Embodiment 2

2 mol 1-chloro-3-isopropylacetone and 4.5mol dimethyl carbonate solution with a mass fraction of 73%, were added to the reaction vessel, controlled the stirring speed at 120 rpm, the solution temperature was raised to 35 ℃, and then added 3.5 mol manganese chloride, reacted for 80 min, added 900 ml potassium chloride solution with a mass fraction of 13%, reduced the temperature of the solution to 23 ℃, added potassium hydrogen sulfate solution with a mass fraction of 23% to adjust the pH to 4.5, standing for 60 min, the solution was layered, washed with a methyl carbitol solution with a mass fraction of 64%,, washed with a methyl hydrazine solution with a mass fraction of 83%, recrystallized from 1-methylpiazepine solution with a mass fraction of 92%, and dehydrated with the anhydrous magnesium sulfate dehydrating agent, finally obtained the product isovaleric acid 187.68 g, yield of 92%.

Embodiment 3

2 mol 1-chloro-3-isopropylacetone and 5mol dimethyl carbonate solution with a mass fraction of 76%, were added to the reaction vessel, controlled the stirring speed at 140 rpm, the solution temperature was raised to 40 ℃, and then added 4 mol manganese chloride, reacted for 90 min, added 900 ml potassium chloride solution with a mass fraction of 16%, reduced the temperature of the solution to 25 ℃, added potassium hydrogen sulfate solution with a mass fraction of 25% to adjust the pH to 5, standing for 70 min, the solution was layered, washed with a methyl carbitol solution with a mass fraction of 65%,, washed with a methyl hydrazine solution with a mass fraction of 87%, recrystallized from 1-methylpiazepine solution with a mass fraction of 95%, and dehydrated with the anhydrous calcium chloride dehydrating agent, finally obtained the product isovaleric acid 191.76 g, yield of 94%.

Claims

1. Drug intermediates isovaleric acid synthesis method, comprises the following steps:

(i) 2 mol 1-chloro-3-isopropylacetone and 4-5 mol dimethyl carbonate solution were added to the reaction vessel, control the stirring speed at 110-140 rpm, the solution temperature was raised to 30-40 ℃, and then added 3-4 mol manganese chloride, reacted for 70-90 min, added 900 ml potassium chloride solution, reduced the temperature of the solution to 20-25 ℃, added potassium hydrogen sulfate solution to adjust the pH to 4-5, standing for 50-70 min, the solution was layered, washed with a methyl carbitol solution, washed with a methyl hydrazine solution, recrystallized from 1-methylpiazepine solution, and dehydrated with the dehydrating agent, finally obtained the product isovaleric acid; wherein, the mass fraction of the dimethyl carbonate solution in step (i) is 70 to 76%, the mass fraction of the potassium chloride solution in step (i) is 10 to 16%, the mass fraction of the potassium bisulfate solution described in step (i) is 20 to 25% , the mass fraction of the methyl carbitol solution in step (i) is 60 to 68%.

2. Drug intermediates isovaleric acid synthesis method according to claim 1 wherein the mass fraction of the methylhydrazine solution in step (i) is 80 to 87%.

3. Drug intermediates isovaleric acid synthesis method according to claim 1 wherein the 1- the methylpyrazine solution has a mass fraction of 90-95%.