Instruction Manual Summary

The present invention relates to the technical field of chemical synthesis, and provides a preparation process and application of γ-butyl betaine ethyl ester , wherein the preparation process of γ-butyl betaine ethyl ester comprises the following steps: S1, adding γ- butyrolactone, thionyl chloride and a catalyst into a reactor, adding anhydrous ethanol under heating and stirring conditions, pouring into deionized water after heating and stirring, extracting , filtering, drying the extract, rotary evaporation, and vacuum distillation to obtain γ- chlorobutyric acid ethyl ester for standby use; S2, mixing the γ- chlorobutyric acid ethyl ester obtained in step S1 with trimethylamine and anhydrous ethanol, heating, sealing and heat-insulating the reaction, returning to room temperature, discharging, rotary evaporation, cooling to 0-5 °C for precipitation, filtering, washing, and drying to obtain γ-butyl betaine ethyl ester . The γ-butyl betaine ethyl ester obtained by the preparation process provided by the present invention has the characteristics of high yield and can be applied to L-carnitine .

Claims

1. A process for preparing γ-butyl betaine ethyl ester , characterized in that it comprises the following steps:

S1. Add γ -butyrolactone, thionyl chloride and a catalyst into a reaction kettle, add anhydrous ethanol under heating and stirring conditions, pour into deionized water after heating and stirring, extract , filter, dry the extract, rotary evaporate, and distill under reduced pressure to obtain ethyl γ- chlorobutyrate for use;

the ethyl gamma-chlorobutyrate obtained in step S1 with trimethylamine and anhydrous ethanol, heat, seal and keep warm for reaction, return to room temperature, discharge, rotary evaporate, cool to 0-5 °C for precipitation, filter, wash and dry to obtain gamma-butyl betaine ethyl ester .

2. The process for preparing γ-butyl betaine ethyl ester according to claim 1 , characterized in that in the step S1, the molar ratio of γ- butyrolactone, thionyl chloride and anhydrous ethanol is 1:(1.2-2):(1-2) .

3 . The process for preparing γ-butyl betaine ethyl ester according to claim 1 , characterized in that, in the step S1 , the mass ratio of γ- butyrolactone to the catalyst is 1:(0.02-0.04) .

4. The process for preparing γ-butyl betaine ethyl ester according to claim 1 , characterized in that the preparation method of the catalyst comprises the following steps:

(1) Wash the peeled walnut green peel with distilled water, dry, crush, sieve, and carbonize to obtain walnut green peel activated carbon for later use;

(2) mixing the walnut peel activated carbon and N-hydroxymethyl acrylamide prepared in step (1), and ball milling the mixture to obtain a carrier for later use;

(3) Mix zinc chloride and n-octanoic acid, heat at 85-95°C until liquid is obtained, and set aside for use;

(4) Add the liquid of step (3) and the carrier of step (2) into a reaction vessel, stir, heat, immerse, stir, filter, wash and dry to obtain a catalyst.

5 . The process for preparing γ-butyl betaine ethyl ester according to claim 4 , characterized in that, in the step (2), the mass ratio of walnut green peel activated carbon to N-hydroxymethyl acrylamide is 1:(0.15-0.4) .

6 . The process for preparing γ-butyl betaine ethyl ester according to claim 4 , characterized in that in the step (3), the mass ratio of zinc chloride to n-octanoic acid is 1:(0.2-0.6) .

7 . The process for preparing γ-butyl betaine ethyl ester according to claim 4 , characterized in that, in the step (4), the mass ratio of the liquid to the carrier is 1:(0.2-0.4) .

8 . The process for preparing γ-butyl betaine ethyl ester according to claim 1 , wherein the molar ratio of γ- butyrolactone to trimethylamine is 1:(1.5-2.5) .

9. The process for preparing γ- butyl betaine ethyl ester according to any one of claims 1 to 8 , characterized in that in the step S2, the yield of γ- butyl betaine ethyl ester is not less than 95 % .

of γ -butyl betaine ethyl ester according to any one of claims 1 to 9 in L-carnitine.

A preparation process and application of γ-butyl betaine ethyl ester

Technical Field

The invention relates to the technical field of chemical synthesis , and in particular to a preparation process and application of gamma-butyl betaine ethyl ester .

Background Art

L-carnitine is an important biologically active substance that is widely present in animal tissues, especially in muscles and livers . It plays a key role in energy metabolism and fatty acid transport . In recent years, L-carnitine has been widely used in medicine, nutrition and sports science. As a precursor for the synthesis of L-carnitine, the research on the preparation process of γ-butylbetaine ethyl ester is crucial.

At present, the preparation process of γ -butyl betaine ethyl ester is more common abroad, but less studied in China. The more common preparation process is to use γ- bromobutyric acid ethyl ester or γ -chlorobutyric acid ethyl ester and trimethylamine as raw materials. Among them, the cost of γ- bromobutyric acid ethyl ester raw materials is relatively high, and the preparation process using γ-chlorobutyric acid ethyl ester and trimethylamine as raw materials still has the following two major problems: first, the yield of γ-butyl betaine ethyl ester prepared by this process is still low; second, γ-chlorobutyric acid ethyl ester, one of the raw materials, has few sources for purchase and often needs to be synthesized by itself. The synthesis of γ-chlorobutyric acid ethyl ester has the problems of long reaction time and low yield, which leads to limitations in the yield of the prepared γ-butyl betaine ethyl ester.

Patent CN 101538215A discloses a method for producing γ-butyl betaine ester, which uses ethyl γ-chlorobutyrate and trimethylamine as raw materials and alcohol as raw material to prepare γ-butyl betaine methyl ester or γ-butyl betaine ethyl ester. Although the method uses ethyl γ-chlorobutyrate to replace ethyl γ-bromobutyrate, which reduces the synthesis cost, the yield obtained by the method is 89-93%, which still does not meet the high yield requirement.

Therefore, there is an urgent need to develop a preparation process for γ-butyl betaine ethyl ester in the market that can meet the requirement of high yield .

Summary of the invention

In view of the problems existing in the prior art, the invention starts from the preparation

process of ethyl gamma-chlorobutyrate , adopts gamma -butyrolactone, thionyl chloride and anhydrous ethanol as raw materials, and designs to add a catalyst to synthesize ethyl gamma -chlorobutyrate in a "one-step method", and then reacts ethyl gamma-chlorobutyrate with trimethylamine, and solves the problem of low yield in the existing preparation process of ethyl gamma-butyl betaine by controlling appropriate reaction conditions .

In order to achieve the above object, the technical solution adopted by the present invention is as follows:

The present invention provides a process for preparing γ-butyl betaine ethyl ester , comprising the following steps:

S1. Add γ -butyrolactone, thionyl chloride and a catalyst into a reaction kettle, add anhydrous ethanol under heating and stirring conditions, pour into deionized water after heating and stirring, extract , filter, dry the extract, rotary evaporate, and distill under reduced pressure to obtain ethyl γ- chlorobutyrate for use;

the ethyl gamma-chlorobutyrate obtained in step S1 with trimethylamine and anhydrous ethanol, heat, seal and keep warm for reaction, return to room temperature, discharge, rotary evaporate, cool to 0-5 °C for precipitation, filter, wash and dry to obtain gamma-butyl betaine ethyl ester .

Wherein, the temperature of heating and stirring in step S1 is 50-60 °C ; and the extraction solvent is ether.

The applicant controlled the reaction temperature during the preparation of ethyl γ -chlorobutyrate to 50-60 °C , which not only ensured a moderate reaction time, but also reduced the occurrence of side reactions during the reaction of thionyl chloride and anhydrous ethanol, thereby improving the yield of ethyl γ- chlorobutyrate to a certain extent and avoiding an overly intense reaction.

The applicant selected ether as the extraction solvent, which can effectively separate the target product and the catalyst, thereby increasing the yield of ethyl γ- chlorobutyrate.

In some embodiments of the present invention, in step S1, the molar ratio of γ-butyrolactone, thionyl chloride and anhydrous ethanol is 1:(1.2-2):(1-2) .

Preferably, in step S1, the molar ratio of γ- butyrolactone, thionyl chloride and anhydrous ethanol is 1:1.5:1.5 .

In some embodiments of the present invention, in step S1, the mass ratio of γ -butyrolactone to the catalyst is 1:(0.02-0.04) .

The applicant adjusted the traditional method of first ring-opening γ-butyrolactone and thionyl chloride to generate γ-chlorobutyryl chloride and then reacting with alcohol to prepare

γ-chlorobutyric acid ethyl ester into a "one-step method" in step S1 to synthesize γ-chlorobutyric acid ethyl ester, that is, γ-butyrolactone, thionyl chloride and anhydrous ethanol are used as raw materials, and the reaction conditions are controlled to synthesize γ-chlorobutyric acid ethyl ester. Compared with the traditional preparation method, the addition of a small amount of anhydrous ethanol and the reaction of thionyl chloride to generate hydrogen chloride can catalyze the ring-opening reaction of γ-butyrolactone and thionyl chloride, and the generated γ-chlorobutyryl chloride will immediately react with anhydrous ethanol to generate esters. The generation of esters will rapidly move the reaction toward the direction of generating products, thereby accelerating the reaction process to a certain extent.

In some embodiments of the present invention, the method for preparing the catalyst comprises the following steps:

(1) Wash the peeled walnut green peel with distilled water, dry, crush, sieve, and carbonize to obtain walnut green peel activated carbon for later use;

(2) mixing the walnut peel activated carbon and N-hydroxymethyl acrylamide prepared in step (1), and ball milling the mixture to obtain a carrier for later use;

(3) Mix zinc chloride and n-octanoic acid, heat at 85-95°C until liquid is obtained, and set aside for use;

(4) Add the liquid of step (3) and the carrier of step (2) into a reaction vessel, stir, heat, immerse, stir, filter, wash and dry to obtain a catalyst.

In some embodiments of the present invention, in step (2), the mass ratio of walnut peel activated carbon to N-hydroxymethyl acrylamide is 1:(0.15-0.4) .

Preferably, in step (2), the mass ratio of walnut peel activated carbon to N-hydroxymethyl acrylamide is 1:0.3 .

In some embodiments of the present invention, in step (3), the mass ratio of zinc chloride to n-octanoic acid is 1:(0.2-0.6) .

Preferably, in step (3), the mass ratio of zinc chloride to n-octanoic acid is 1:0.4 .

In some embodiments of the present invention, in step (4), the mass ratio of the liquid to the carrier is 1:(0.2-0.4) .

Preferably, in step (4), the mass ratio of the liquid to the carrier is 1:0.33 .

The first step in the preparation process of γ-butyl betaine ethyl ester is the ring-opening reaction of γ-butyrolactone and thionyl chloride to generate γ-chlorobutyric acid ethyl ester. This step often requires the addition of catalysts such as zinc chloride to ensure the reaction rate and yield, but the stability and dispersibility of zinc chloride still need to be improved.

The applicant first uses natural, environmentally friendly and abundant walnut peel as a

raw material to prepare walnut peel activated carbon, and then introduces N-hydroxymethyl acrylamide to modify it to obtain a carrier. Without destroying the original morphology and structure of the activated carbon, hydroxyl groups are introduced to the surface of the activated carbon, which can increase the surface activity of the activated carbon and remove trace impurities in the activated carbon. Further, the applicant selects octanoic acid and zinc chloride as raw materials to prepare a low eutectic solvent, which is used as the active ingredient of the catalyst. It has the advantages of being non-volatile, recyclable and biodegradable. At the same time, octanoic acid as an acid and zinc chloride as a Lewis acid have good synergistic catalytic activity for the ring-opening reaction of γ-butyrolactone and thionyl chloride. Finally, the above-mentioned active ingredients are loaded in the carrier, so that the active ingredients are well dispersed, thereby improving its catalytic activity and stability. In addition, the hydroxyl groups introduced into the carrier by N-hydroxymethyl acrylamide can also enhance the adsorption of zinc ions in the active ingredient zinc chloride by the carrier, thereby further enhancing the overall stability of the catalyst.

In some embodiments of the present invention, the molar ratio of γ-butyrolactone to trimethylamine is 1:(1.5-2.5).

Preferably, the molar ratio of γ-butyrolactone to trimethylamine is 1: 2 .

In some embodiments of the present invention, in step S2, the yield of γ- butyl betaine ethyl ester is not less than 95 % .

of the present invention provides the use of γ-butyl betaine ethyl ester obtained by the preparation process of γ-butyl betaine ethyl ester in L-carnitine.

Compared with the prior art, the present invention has the following beneficial effects:

(1) The present invention provides a preparation process of γ-butyl betaine ethyl ester , which uses γ- butyrolactone, thionyl chloride and anhydrous ethanol as raw materials, and is designed to add a catalyst to synthesize γ- chlorobutyric acid ethyl ester in a "one-step method" , and then reacts γ- chlorobutyric acid ethyl ester with trimethylamine, and optimizes the synthesis steps and reaction conditions of the process , so that the γ-butyl betaine ethyl ester obtained by the preparation process has the characteristics of high yield and can be used in L-carnitine .

(2) The present invention designs a catalyst for the synthesis process of ethyl γ-chlorobutyrate . First, natural, environmentally friendly and abundant walnut peel is used as a raw material to prepare walnut peel activated carbon, and then N-hydroxymethyl acrylamide is introduced to modify it to obtain a carrier. Furthermore, the applicant selects n-octanoic acid and zinc chloride as raw materials to prepare a low eutectic solvent, which is used as the active

ingredient of the catalyst; finally, the active ingredient is loaded in the carrier to obtain a catalyst, and then the active ingredient is well dispersed, thereby improving its catalytic activity and stability, so that the yield of ethyl γ -chlorobutyrate is improved, and thus the yield of ethyl γ -chlorobutyrate is high .

(3) The yield of γ-butyl betaine ethyl ester obtained by the preparation process of the present invention is not less than 95 % , which has the characteristic of high yield .

DETAILED DESCRIPTION

The present invention will be described below in conjunction with specific embodiments. It should be noted that the following embodiments are examples of the present invention and are only used to illustrate the present invention, but not to limit the present invention. Other combinations and various modifications within the concept of the present invention may be performed without departing from the spirit or scope of the present invention.

In the following examples, except for the catalyst , the other compound monomers and related reagents used can be purchased from the market.

Preparation Example 1

catalyst A comprises the following steps:

(1) 20 g of peeled walnut green peel was washed with distilled water, dried at 100°C for 2 h, crushed, passed through an 80-mesh sieve, and carbonized at 500°C for 2.5 h to obtain walnut green peel activated carbon for later use;

(2) Mix 10 g of the walnut peel activated carbon prepared in step (1) and 3 g of N-hydroxymethyl acrylamide, and ball mill for 20 min to obtain a carrier for use;

(3) Mix 15 g of zinc chloride and 6 g of n-octanoic acid, heat at 90°C until liquid is obtained, and set aside for use;

(4) Add 15 g of the liquid from step (3) and 5 g of the carrier from step (2) into a reaction vessel, stir evenly, heat to 115°C, soak for 4 h, stir every 20 min, filter, wash with deionized water, and dry at 110°C for 4 h to obtain catalyst A.

Preparation Example 2

Catalyst B, the specific implementation method is the same as that of catalyst A, except that in step (2), the mass of N-hydroxymethyl acrylamide is replaced by 1 g .

Preparation Example 3

Catalyst C, the specific implementation method is the same as that of Catalyst A, except that in step (3), the mass of n-octanoic acid is replaced with 2.5 g .

Preparation Example 4

Catalyst D, the specific implementation method is the same as that of Catalyst A, except that in step (4), the mass of the carrier is replaced with 2.5 g .

Preparation Example 5

Catalyst E , the specific implementation method is the same as that of Catalyst A, except that in step (4), the mass of the carrier is replaced with 6.5 g .

Example 1

A preparation process of γ-butyl betaine ethyl ester comprises the following steps:

S1. Add 0.1 mol of γ-butyrolactone, 0.15 mol of thionyl chloride and 0.3 g of catalyst A into a reaction kettle, add 0.15 mol of anhydrous ethanol dropwise under heating and stirring at 55°C (addition is completed within 15 min), heat and stir at 60 ° C for 3.5 h, pour into deionized water, extract with ether, filter, dry the extract with anhydrous sodium sulfate, remove the solvent by rotary evaporation, and distill under reduced pressure to obtain ethyl γ-chlorobutyrate for use;

S2. Mix the ethyl γ-chlorobutyrate obtained in step S1 with 0.2 mol of trimethylamine and 18 g of anhydrous ethanol, heat to 85° C., seal and keep warm for 10 h, return to room temperature, discharge, rotary evaporate, cool to 0° C. to precipitate, filter, wash with acetone, and dry at 70° C. for 5 h to obtain ethyl γ-butyl betaine.

Example 2

A preparation process of γ-butyl betaine ethyl ester comprises the following steps:

S1. Add 0.1 mol of γ-butyrolactone, 0.12 mol of thionyl chloride and 0.3 g of catalyst A into a reaction kettle, add 0.1 mol of anhydrous ethanol dropwise (addition is completed within 15 min) under heating and stirring at 55°C, heat and stir at 55°C for 4 h, pour into deionized water, extract with ether, filter, dry the extract with anhydrous sodium sulfate, remove the solvent by rotary evaporation, and distill under reduced pressure to obtain ethyl γ-chlorobutyrate for use;

S2. Mix the ethyl γ-chlorobutyrate obtained in step S1 with 0.15 mol of trimethylamine and 18 g of anhydrous ethanol, heat to 85°C, keep the mixture in a sealed container for reaction for 10 h, return to room temperature, discharge the mixture, perform rotary evaporation, cool to 0°C to precipitate, filter, wash with acetone, and dry at 70°C for 5 h to obtain ethyl γ-butyl betaine.

Example 3

A preparation process of γ-butyl betaine ethyl ester comprises the following steps:

S1. Add 0.1 mol of γ-butyrolactone, 0.2 mol of thionyl chloride and 0.3 g of catalyst A into a reaction kettle, add 0.2 mol of anhydrous ethanol dropwise (addition is completed within 15 min) under heating and stirring at 55°C , heat and stir at 50°C for 4.5 h, pour into deionized

water, extract with ether, filter, dry the extract with anhydrous sodium sulfate, remove the solvent by rotary evaporation, and distill under reduced pressure to obtain ethyl γ-chlorobutyrate for use;

S2. Mix the ethyl γ-chlorobutyrate obtained in step S1 with 0.25 mol of trimethylamine and 18 g of anhydrous ethanol, heat to 85°C, seal and keep warm for 10 hours, return to room temperature, discharge, rotary evaporate, cool to 0°C to precipitate, filter, wash with acetone, and dry at 70°C for 5 hours to obtain ethyl γ-butyl betaine.

Example 4

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that the mass of catalyst A is replaced with 0.12 g .

Example 5

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that the mass of catalyst A is replaced with 0.4 g .

Example 6

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that catalyst A is replaced by catalyst B in equal amounts.

Example 7

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that catalyst A is replaced by catalyst C in equal amounts.

Example 8

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that catalyst A is replaced by catalyst D in equal amounts.

Example 9

This embodiment provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that catalyst E replaces catalyst A in equal amounts.

Example 10

This comparative example provides a preparation process of γ-butyl betaine ethyl ester , and the specific implementation method is the same as that of Example 1, except that the

catalyst A is replaced by an equal amount of zinc chloride .

Performance Testing

The yield of γ-butyl betaine ethyl ester described in Examples 1-10 above was tested, and the test results are shown in Table 1.

The yield of γ-butyl betaine ethyl ester was measured by HPLC .

Table 1

Group	Yield (%)
Example 1	96.5
Example 2	95.9
Example 3	96.2
Example 4	94.2
Example 5	94.5
Example 6	93.6
Example 7	93.4
Example 8	93.1
Example 9	93.3
Example 10	92.5

the γ-butyl betaine ethyl ester in Examples 1-3 of the present invention has the characteristics of high yield as a whole . Among them, Examples 4-5 change the amount of catalyst A added, so that the first step of the preparation process of γ-butyl betaine ethyl ester, the ring-opening reaction of γ-butyrolactone and thionyl chloride to generate γ-chlorobutyric acid ethyl ester , is not well promoted , resulting in a decrease in the yield of γ-chlorobutyric acid ethyl ester, and then showing a phenomenon of a decrease in the yield of γ-butyl betaine

ethyl ester ; Examples 6-9 change the addition ratio of the key modifying components N-hydroxymethyl acrylamide and n-octanoic acid during catalyst synthesis and the ratio between the carrier and the active ingredient , so that the catalytic activity , stability and dispersibility of the catalyst decrease , resulting in a poor yield of γ-butyl betaine ethyl ester ; Example 10 is a conventional catalyst zinc chloride equivalent to replace catalyst A , and the test found that the yield of the prepared γ-butyl betaine ethyl ester showed a poor result.

The above implementation modes are only for illustrating the technical concept and features of the present invention, and their purpose is to enable people familiar with this technology to understand the content of the present invention and implement it, and they cannot be used to limit the protection scope of the present invention. Any equivalent changes or modifications made according to the spirit of the present invention should be included in the protection scope of the present invention.