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(54) Title: TOTALLY RECYCLABLE CATALYSTS FOR ESTERIFICATION REACTIONS

(57) Abstract: The invention relates to a catalytic esterification process for the synthesis of an ester of a fatty acid using zinc oxide (ZnO) or zinc(II) based salts with basic anions, as totally and immediately recyclable catalysts for esterification reactions. The process includes the esterification of fatty acids (C₄-C₂₂) with mono-alcohols (C₆-C₂₂) and poly-alcohols (C₃-C₁₂) (di-hydroxy, tri-hydroxy, tetra-hydroxy, penta-hydroxy) obtaining the corresponding acyl-derivatives.

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Totally recyclable catalysts for esterification reactions

Description

5 Technical field of the invention

The present invention relates to the production process of fatty acid esters.

10 In particular, the developed method allows the production of esters through esterification reaction between saturated, mono-unsaturated and poly-unsaturated C₄-C₂₂ fatty acids (for example butyric acid, valeric acid, capronic acid, enanthic acid, caprylic acid, nonanoic acid, capric acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, palmitic acid, margaric acid, stearic acid, nonadecanoic acid, arachic acid, behenic acid, myristoleic acid, sapienic acid, palmitoleic acid, heptadecenoic acid, oleic acid, elaidinic acid, vaccenic acid, asclepic acid, petroselinic acid, petroselaidic acid, gadoleic acid, gondoic acid, cetoleic acid, erucic acid, linoleic acid, rumenic acid, α-linolenic acid, γ-linolenic acid, stearidonic acid, arachidonic acid, thymnodonic acid, cervonic acid) and linear, branched or cyclic, primary or secondary C₆-C₁₆ mono-alcohols (e.g. 1-hexanol, 1-heptanol, 1-octanol, 2-octanol, 1-nonanol, 1-decanol, 1-undecanol, 1-dodecanol, 1-tridecanol, 1-tetradecanol, 1-pentadecanol, 1-hexadecanol, 11-undecene-1-ol, 3-methyl-3-pentanol, 2-methyl-1-pentanol, 2-ethyl-1-hexanol, 2-propyl-1-heptanol, 2-butyl-1-octanol, 2-pentyl-1-nonanol, 2-hexyl-1-decanol, cyclohexanol, menthol), and C₃-C₁₂ polyalcohols with a number of hydroxyls between 2 and 5 (e.g. propylene glycol, 1,3-butylene glycol, glycerol, erythritol, pentaerythritol, arabitol, xylitol).

25 The present method uses zinc oxide or zinc salts with basic anions (for example carboxylates and carbonate) as esterification catalyst between carboxylic acids and alcohols or poly-alcohols. The catalyst is introduced as a powder into the reactant system. Once the reaction is complete and the ester is obtained, after the reaction mixture has been cooled to room temperature, a precipitate is separated from the mixture by simple filtration. The precipitate, used as a catalyst in subsequent reactions, showed without further treatments a catalytic activity comparable to the original catalyst.

30 Background of the invention

Organic esters are a family of chemical compounds of very wide industrial use (solvents, surfactants, lubricants, biofuels, monomers). They are typically produced by esterification reactions starting from a carboxylic acid and an alcohol. This reaction is generally acid catalyzed and in equilibrium. Sulfuric acid is an effective esterification catalyst and, coupled with systems for removing water from the reaction environment, allows for convenient conversions. However, its use is problematic due to its strong corrosive action, and due to the intolerance of many functional groups to Brønsted's acidity. Furthermore, the purification of the product often requires complex operations, which involve washing with aqueous solutions and resulting wastewater to be disposed of. A partial solution to these drawbacks is represented by its substitution with Lewis acids, mainly inorganic salts of metal cations, such as Zn(II) [1], Sn(II) [2], Fe(III) [3]. They are capable of catalyzing the reaction in less aggressive conditions and are better tolerated by organic functions, but, acting in the homogeneous phase, they also present the problem of difficult separation from the reaction product: in patent US589,807,7 [4] reference is made to catalytic processes of esterification of C₅-C₃₅ carboxylic acids with alcohols and polyalcohols (bp > 120°C) with catalysts based on Zn(II) and Sn(II). However, a product purification strategy is proposed which involves the use of aqueous solutions with complexing agents such as nitrilotriacetic acid, ion exchange resins, water washing and a phase separation and a dehydration procedure of the aqueous phase.

For this reason, the use of insoluble solid catalysts in the reaction environment, based on organic or inorganic matrix, is sometimes used, with the aim of separating the product through simple filtration [5]. In this case, the heterogeneity of the system can depress the performance of the catalyst, high temperatures are required and reaction times are lengthened, the catalyst is more expensive and easily subject to leaching or deactivation [5]. Furthermore, the conversion is often impaired by the establishment of equilibria within the particles of the solid: in US patent 807,649,7 [6] a system for the production of di-acylglycerol and tri-acylglycerol is reported, which uses an acid ion exchange resin as a heterogeneous catalyst. In this case, a distribution of mono-, di- and tri-acylglycerol products is obtained, and the product isolation procedure requires sequential distillations at high

temperatures (between 200°C and 260°C). Furthermore, the possibility and costs of catalyst recycling are not investigated.

Among the heterogeneous catalysts, zinc oxide has also been proposed [7]. In Fernandes's work, data are reported in which ZnO is active as a catalyst for the esterification of acetic acid with butanol. In an attempt to repeat the experiments reported in the cited work it has been pointed out that at the end of the reaction there is a complete dissolution of the catalyst and its recovery by filtration is not possible (see example 1).

It is therefore necessary to find a catalyst that is active in mild conditions (temperature <180°C) and that is completely and immediately recyclable.

Summary of the invention

The present invention relates to a catalytic esterification process between carboxylic acids (C₄-C₂₂) and monoalcohols (C₆-C₂₂) or polyalcohols (C₃-C₁₂) using zinc(II)-based catalysts that are completely and immediately recyclable, avoiding reactivation operations. The catalyst, preferably zinc oxide or zinc(II) salts with basic anions (for example carboxylates and carbonate), is introduced as a powder into the reagent system. At the end of the reaction, through simple filtration a solid is recovered which has the same catalytic performance as the originally introduced zinc(II) species.

This methodology has proved surprisingly effective and has the following advantages:

1. Zinc-based catalysts are readily available, inexpensive catalysts with a low ecotoxicological profile.
2. The precipitate obtained at the end of the reaction is insoluble in the product and can be separated through simple solid/liquid filtration.
3. The recovered solid can be recycled into the same reaction several times as a catalyst without any loss of activity.

Further objects of the invention will be evident from the detailed description of the invention.

Detailed description of the invention

Contrary to what was found in the reaction between acetic acid and butanol [7], surprisingly, using ZnO as catalyst, it was found that by reaction of C₄-C₂₂ saturated, mono-unsaturated and poly-unsaturated fatty acids (for example butyric acid, capric acid, nonanoic acid, oleic acid, linoleic acid, arachidonic

acid) with linear or branched C₆-C₁₆ monoalcohols, primary or secondary, and C₃-C₁₂ polyalcohols with a number of hydroxyls between 2 and 5 (for example 1-hexanol, 2-ethyl-1-hexanol, 1-octanol, 2-octanol, 1-hexadecanol, geraniol, glycerol, erythritol, xylitol), at the end of the reaction it is possible to separate a solid, which in subsequent uses has shown the same catalytic activity as the zinc(II) species originally introduced as a catalyst.

Subsequently, zinc salts containing basic anions (carboxylates and carbonate) were used as catalysts for esterification reaction of C₄-C₂₂ saturated, mono-unsaturated and poly-unsaturated fatty acids (for example butyric acid, capric acid, nonanoic acid, oleic acid, linoleic acid, arachidonic acid) with linear or branched C₆-C₁₆ monoalcohols, primary or secondary, and C₃-C₁₂ polyalcohols with a number of hydroxyls between 2 and 5 (for example 1-hexanol, 2-ethyl-1-hexanol, 1-octanol, 2-octanol, 1-hexadecanol, geraniol, glycerol, erythritol, xylitol). Also in this case at the end of the reaction a solid was separated from the reaction mixture, which in subsequent uses showed the same catalytic activity as the zinc(II) species originally introduced as a catalyst.

If zinc(II) salts with non-basic anions (for example chloride) are used, at the end of the reaction, a non-negligible quantity of zinc remains in solution and any solid recovered does not have the same performance as the fresh catalyst used.

Examples

Example 1. Synthesis of butyl acetate [7]

The synthesis was repeated as described in reference 7. Glacial acetic acid (26.3 g; 25 mL), butanol (16.2 g; 20 mL) and zinc oxide (0.050 g) were introduced into a flask. After 2 hours under stirring at 95°C, the measured conversion is comparable to those reported in the reference [7] (40%) but in the mixture cooled to room temperature, no precipitate is observed.

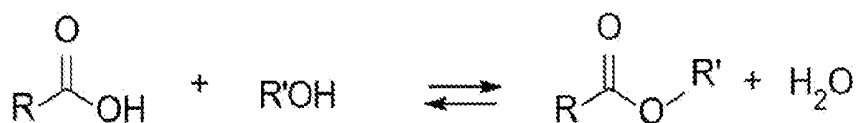
Example 2. Synthesis of esters using ZnO as catalyst

In tests 2.1-2.6 and 3.1-3.3 the following general procedure was used.

In a flask equipped with a Claisen head fitted with a heating band, the carboxylic acid, alcohol or polyalcohol are introduced in the appropriate stoichiometric ratio, in which the ratio in moles between the RCOOH fatty acid and (i) the mono-alcohol R'OH is between 1:1.01 and 1:2, more preferably

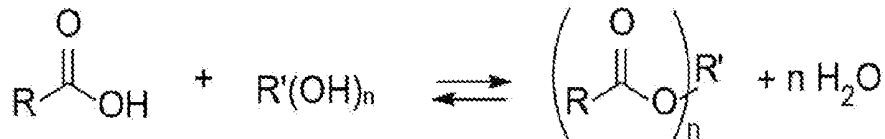
between 1:1.1 and 1:1.2 (ii) the polyalcohol $R'(OH)_n$ is between 1:1 and 5:1, with n between 1 and 5.

The zinc(II) catalyst is added to the system in a stoichiometric ratio between fatty acid and zinc(II) between 1:0.02 and 1:0.001, more preferably between 1:0.01 and 1:0.005. The reactor and the Claisen head are heated to 150-180°C and 100°C-120°C respectively. The reaction time is between 4 and 6h and the working pressure during the reaction time is 760 mmHg. The following reactions occur:



R = represents an alkyl group, saturated or unsaturated, linear or branched, containing from 4 to 22 carbon atoms;

R' = represents a group containing from 6 to 16 carbon atoms;



R = represents an alkyl group, saturated or unsaturated, linear or branched, containing from 4 to 22 carbon atoms,

R' = represents a group containing from 3 to 12 carbon atoms, n is a value between 2 and 5,

In its course, downstream of the head is observed some condensation of water, which is collected in the graduated test tube. At the end of the reaction, there is a distillation phase at 100 mmHg lasting between 30 and 60 minutes, to recover further aqueous fraction and excess alcohol; the system is subsequently brought first to atmospheric pressure (760 mmHg) and then cooled to room temperature (25°C); when 25°C temperature is reached, precipitation of a crystalline solid is observed. A simple filtration at reduced pressure between 1.5 and 100 mmHg on porosity 2 septum (P2-nominal porosity between 40-100 μm) allows to separate the liquid phase from the solid one: the first is the pure ester, the second is the recovered catalyst. To

check if the solid contains most of the zinc introduced, an ICP analysis of the liquid phase is performed. The solid thus separated can be fed back into the reactor for a subsequent cycle of catalysis under the same conditions.

Test 2.1 For the synthesis of 2-ethylhexyl nonanoate, 125 mmol of nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99%), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol zinc oxide (0.102 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling from the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater than 99% (¹H and ¹³C NMR analysis). The content of zinc(II) in the product is lower than 2 ppm.

Test 2.2 For the synthesis of 2-ethylhexyl oleate, 125 mmol of oleic acid (35.3 g; 39.7 mL; supplied by Carlo Erba, purity 99%), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol zinc oxide (0.102 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a

thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 6 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling from the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexyl oleate product is obtained with a purity greater than 96% (¹H and ¹³C NMR analysis). The content of zinc(II) in the product is lower than 10 ppm. The double bond of oleic acid does not undergo chemical transformations and is inert during the process.

Test 2.3. For the synthesis of 1-hexyl nonanoate, 125 mmol of nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99%), 150 mmol of 1-hexyl alcohol (15.3 g; 18.8 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol zinc oxide (0.102 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4

h; the working pressure is 760 mmHg. The complete conversion is verified by sampling from the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 1-hexyl nonanoate product is obtained with a purity greater than 96% (^1H and ^{13}C NMR analysis). The content of zinc(II) in the product is lower than 10 ppm.

Test 2.4. For the synthesis of triolein, 40.0 mmol of glycerol (3.68 g; 2.92 mL; supplied by Sigma Aldrich, 99% purity), 122 mmol of oleic acid (34.6 g; 38.4 mL; supplied by Sigma Aldrich, 99% purity) and 1.2 mmol of zinc oxide (0.098 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction parameters are the same as described in example 2.1. After 4 h of reaction the glycerol conversion is complete, and triolein is produced with a selectivity greater than 98% (^1H and ^{13}C NMR analysis). The content of zinc(II) in the product is 1.4 ppm. The double bond of oleic acid does not undergo chemical transformations and is inert during the process.

Test 2.5 For the synthesis of 2-ethylhexyl nonanoate, 125 mmol of nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99%), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol zinc acetate dihydrate (0.275 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water

produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling from the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater than 99% (^1H and ^{13}C NMR analysis). The content of zinc(II) in the product is 2.5 ppm.

Test 2.6 For the synthesis of 2-ethylhexyl nonanoate, 125 mmol of nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99%), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol zinc carbonate (0.156 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of

alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater than 99% (^1H and ^{13}C NMR analysis). The zinc(II) content in the product is 7.6 ppm.

Example 3. Recycling of the catalyst in the synthesis of 2-ethylhexylnonanoate

Test 3.1 To demonstrate the feasibility of using the recovered catalyst after ester synthesis described in Test 2.1, for the synthesis of 2-ethylhexyl nonanoate, 125 mmol nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99 %), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and the solid recovered in Test 2.1 without further treatment are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater

than 99% (^1H and ^{13}C NMR analysis).

Test 3.2 To demonstrate the feasibility of using the recovered catalyst after ester synthesis described in Test 3.1, for the synthesis of 2-ethylhexyl nonanoate, 125 mmol nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99 %), 150 mmol 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and the solid recovered in Test 3.1 without further treatment are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater than 99% (^1H and ^{13}C NMR analysis).

Test 3.3 To demonstrate the feasibility of using the recovered catalyst after ester synthesis described in Test 2.5, for the synthesis of 2-ethylhexyl nonanoate, 125 mmol nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99 %), 150 mmol 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and the solid recovered in Test 2.5 without further treatment are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is

heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. At this point, the reaction mixture appears as a suspension of the solid insoluble catalyst in the ester. The catalyst is easily separated by filtration at a reduced pressure between 1.5 and 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity greater than 99% (¹H and ¹³C NMR analysis).

Example 4. Synthesis of 2-ethylhexyl nonanoate using ZnCl₂ as catalyst

125 mmol of nonanoic acid (19.8 g; 22.0 mL; supplied by Sigma Aldrich, purity 99%), 150 mmol of 2-ethylhexyl alcohol (19.5 g; 23.5 mL; supplied by Sigma Aldrich, purity 99%) and 1.25 mmol of zinc chloride (0.170 g; supplied by Sigma Aldrich, purity 99%) are vigorously mixed in a 100 mL flask equipped with a Claisen head fitted with a thermo-electric heating band. The reaction vessel is heated to a temperature of 170°C, using a thermostated diathermic oil bath, while the temperature of the heating band on the Claisen head is set at 110°C using a thermocouple. Downstream of the Claisen head, a graduated 5 mL Schlenk tube is mounted to monitor the reaction conversion by collecting the water produced by the reaction. The reaction time is considered from the moment in which the catalyst is added, and the mixture is left to react at the set temperatures for 4 h; the working pressure is 760 mmHg. The complete conversion is verified by sampling the reaction mixture and NMR analysis (400 MHz Bruker). At the end of the reaction, the volume of water collected in the

5 tube is between 1.5 and 1.6 mL. At this point the recovery vessel is replaced with a new 5 mL graduated Schlenk tube and a pressure of 100 mmHg is applied. In this phase, lasting 40 minutes, about 0.5 mL of water and 3.5 mL of alcohol are collected. At the end of the distillation, the system is brought back to atmospheric pressure and is allowed to cool until it reaches room temperature. The residue is separated by filtration at a reduced pressure ranging from 1.5 to 100 mmHg on a P2 sintered glass filter, and the 2-ethylhexylnonanoate product is obtained with a purity of 91% (¹H and ¹³C NMR analysis). The content of zinc(II) in the product is equal to about 2000 ppm.

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CLAIMS

1. Catalytic esterification process for the synthesis of a fatty acid ester of general formula $\text{RCOO-R}'$ by reaction between a fatty acid of general formula RCOOH and a mono-alcohol of general formula $\text{R}'\text{OH}$, wherein:

- R represents an alkyl group, saturated or unsaturated, linear or branched, containing from 4 to 22 carbon atoms;

- R' represents a group containing from 6 to 16 carbon atoms;

wherein the catalyst is a zinc(II) salt with basic anions, preferably zinc oxide (ZnO), zinc carbonate (ZnCO_3), zinc acetate (Zn(OAc)_2), and which consists of the following five consecutive phases :

(i) a heating step of the reaction mixture at a temperature between $150\text{-}180^\circ\text{C}$ and at an operating pressure of 760 mmHg until the catalyst is dissolved;

(ii) a reaction step between the used species at a temperature between $150\text{-}180^\circ\text{C}$, at an operating pressure of 760 mmHg, for a time between 4 and 6h for the synthesis of the desired ester during which the temperature conditions used allow the removal by distillation of the water produced;

(iii) a distillation step of the alcohol fraction in excess and of the remaining traces of water at a pressure of 100 mmHg for a time between 30 and 60 minutes;

(iv) a cooling step of the reaction mixture containing the ester produced, at least 90% by mass, at room temperature and pressure, until precipitation of a solid containing Zn(II);

(v) a separation phase of the ester obtained by filtration of the solid at reduced pressure;

the process allowing to recycle the solid precipitated in the previous point (v) as a catalyst for the subsequent esterification reactions without loss of catalytic activity.

2. Catalytic esterification process for the synthesis of a ester fatty acid of general formula $\text{RCOO-R}'$ by reaction between a fatty acid of general formula RCOOH and a polyalcohol of general formula $\text{R}'(\text{OH})_n$, wherein:

- n is a value between 2 and 5,

- R represents an alkyl group, saturated or unsaturated, linear or branched, containing from 4 to 22 carbon atoms,

- R' represents a group containing from 3 to 12 carbon atoms,

wherein the catalyst is a zinc(II) salt with basic anions, preferably zinc oxide (ZnO), zinc carbonate (ZnCO₃), zinc acetate (Zn(OAc)₂), and which consists of
5 the following four consecutive phases :

(i) a heating step of the reaction mixture at a temperature between 150-180°C and at an operating pressure of 760 mmHg until the catalyst is dissolved;

10 (ii) a reaction step between the species used at a temperature between 150-180°C, at an operating pressure of 760 mmHg, for a time between 4 and 6h for the synthesis of the desired ester during which the used temperature conditions allow the removal by distillation of the water produced;

15 (iii) a cooling step of the reaction mixture containing the ester produced at least 90% by mass at room temperature and pressure, until precipitation of a solid containing Zn(II);

(iv) a separation step of the ester produced by filtration of the solid at reduced pressure;

20 this process allows the solid precipitated in the previous point (iv) to be recycled as a catalyst for the subsequent esterification reactions without loss of catalytic activity.

3. Catalytic process according to claim 1 wherein the molar ratio between the fatty acid RCOOH and the monoalcohol R'OH is comprised between 1:1.01 and 1:2, more preferably between 1:1.1 and 1:1.2, and the catalyst based on
25 zinc(II) is comprised between 1:0.02 and 1:0.001, more preferably between 1:0.01 and 1:0.005.

4. Catalytic process according to claim 2 wherein the ratio (in moles) between the fatty acid RCOOH and the polyalcohol R'(OH)_n is between 1:1 and 5:1, the
30 zinc(II)-based catalyst is between 1:0.02 and 1:0.001, more preferably between 1:0.01 and 1:0.005.

5. Catalytic process according to claim 1 wherein the process step (v), isolation step, can be carried out by filtration at a reduced pressure, between

1.5 and 100 mmHg on sintered glass filters with nominal porosity between 40-100 μm (P2) until complete filtration of the synthesized product.

5 **6.** Catalytic process according to claim 2 wherein the process step (iv), isolation step, can be carried out by filtration at a reduced pressure, between 1.5 and 100 mmHg on sintered glass filters with nominal porosity between 40-100 μm (P2) until complete filtration of the synthesized product.

10 **7.** Process according to claim 1 or claim 2 wherein the fatty acid RCOOH belongs to the C₄-C₂₂ family of saturated fatty acids, mono-unsaturated fatty acids, poly-unsaturated fatty acids, for example: butyric acid, valeric acid, capronic acid, enanthic acid, caprylic acid, nonanoic acid, capric acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, palmitic acid, margaric acid, stearic acid, nonadecanoic acid, arachic acid, behenic acid, myristoleic acid, sapienic acid, palmitoleic acid, heptadecenoic acid, oleic acid, elaidinic acid, vaccenic acid, asclepic acid, petroselinic acid, petroselaidic acid, gadoleic acid, gondoic acid, cetoleic acid, erucic acid, linoleic acid, rumenic acid, α -linolenic acid, γ -linolenic acid, stearidonic acid, arachidonic acid, thymnodonic acid, cervonic acid.

15 **8.** Process according to claim 1 wherein the mono-alcohol R'OH belongs to the C₆-C₁₆ family of linear, branched or cyclic alcohols, for example: 1-hexanol, 1-heptanol, 1-octanol, 2-octanol 1-nonanol, 1-decanol, 1-undecanol, 20 1-dodecanol, 1-tridecanol, 1-tetradecanol, 1-pentadecanol, 1-hexadecanol, 11-undecene-1-ol, 3-methyl-3-pentanol, 2-methyl-1-pentanol, 2-ethyl-1-hexanol, 2-propyl-1-heptanol, 2-butyl-1-octanol, 2-pentyl-1-nonanol, 2-hexyl-1-decanol, cyclohexanol, menthol.

25 **9.** Process according to claim 2 wherein the polyalcohol belongs to the C₃-C₁₂ family of polyalcohols and alditols, for example: propylene glycol, 1,3-butylene glycol, glycerol, erythritol, pentaerythritol, arabitol, xylitol.

30 **10.** Use of a compound selected from zinc carbonate (ZnCO₃) and zinc acetate (Zn(OAc)₂) as catalyst in the catalytic process according to any one of claims 1-8.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/050551

A. CLASSIFICATION OF SUBJECT MATTER
INV. C11C3/00 C11C3/02 C11C3/12
ADD.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
C11C
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FR 2 752 242 A1 (INST FRANCAIS DU PETROLE [FR]) 13 February 1998 (1998-02-13) claims 1-17; examples 1,3, 4,10-12, 14 -----	1-10
A	US 2016/207871 A1 (KUBITSCHKE JENS [DE] ET AL) 21 July 2016 (2016-07-21) claims 1-20 -----	1-10
A	WO 2008/007231 A1 (A & A F LLI PARODI S R L [IT]; DP LUBRIFICANTI S R L [IT] ET AL.) 17 January 2008 (2008-01-17) claims 1-9; examples 1-3 -----	1-10
A	US 5 898 077 A (TAKAHARA ICHIRO [JP] ET AL) 27 April 1999 (1999-04-27) cited in the application the whole document ----- -/--	1-10

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
 "O" document referring to an oral disclosure, use, exhibition or other means
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
 "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
 "&" document member of the same patent family

Date of the actual completion of the international search 6 May 2021	Date of mailing of the international search report 20/05/2021
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Adechy, Miriam
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INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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A	FR 2 951 092 A1 (INST FRANCAIS DU PETROLE [FR]) 15 April 2011 (2011-04-15) the whole document -----	1-10
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