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FORM-02

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Complete After Provisional Specification

Section 10

TITLE

“A Method for Preparing 4-Hexene-3-one”

APPLICANT

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The following specification describes the invention

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FIELD OF INVENTION:

[001] The present invention relates to the field of preparing a method of 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of a base followed by dehydration in acidic medium

DESCRIPTION OF THE RELATED ART:

[002] 4-Hexen-3-one (CAS: 2497-21-4) is a unique spice (China GB 2760-2007), mainly used for blending food flavors such as old, white, horseradish and so on.

[003] The hydroxy compound dehydration reaction is a reaction in which a hydroxyl group and a hydrogen atom on the adjacent atoms of the reactant molecule are removed as water in the presence of a catalyst. Since the oxygen atom of the hydroxyl group contains a lone pair of electrons, it can combine with the proton (H^{+}) to form an oxonium ion. Since the oxygen atom has a positive charge, it becomes a strong electron-withdrawing group and the C-O bond is easily dissociated. The entire dehydration reaction involves the formation of a protonated oxonium salt ($R-OH_2^{+}$), the oxonium salt slowly dissociates into a positive carbon ion and a hydrogen ion is quickly eliminated from the normal carbon ion to form an olefin, which occurs as per the β -elimination reaction. In the reaction of dehydration of α -hydroxyketone to α, β -unsaturated ketone, the formation of oxonium ions by the α -hydroxy group is difficult due to the influence of the carbonyl group and the reaction is difficult to occur.

Reference may be made to the following:

[004] Patent No. US5300654 relates to (beta)-hydroxyketones prepared by reacting an aldehyde with acetone in the presence of perhydroisoindole or pyrrolidine and water. The resulting (beta)-hydroxyketone is further reacted in the presence of a solvent mixture to produce (alpha)-(beta)-unsaturated ketones.

[005] Publication No. CN103030541 relates to a production method of 4-hexen-3-one by catalyzed dehydration of 4-hydroxy-3-hexanone, and mainly solves the

problem of low catalyst activity, high reaction temperature and low space velocity in the prior art. According to the invention, 4-hydroxy-3-hexanone is used as a raw material, and the reaction raw material is in contact with a catalyst to produce 4-hexen-3-one at the conditions of a reaction temperature of 200-450 °C and the
5 airspeed of 0.5-15 hr-1 with respect to the mass of 4-hydroxy-3-hexanone liquid, wherein the catalyst is WO₃/ZrO₂-SiO₂ or MoO₃/ZrO₂-SiO₂ and the molar ratio of W or Mo:Zr:Si is (0.05-0.3):1:(5-50). The technical solution solves the problem preferably. The method can be used in the industrial production of 4-hexen-3-one from 4-hydroxy-3-hexanone.

10 [006] Patent No. US4245122 relates to the preparation of allyl acetone (5-hexen-2-one) according to the reaction: wherein R is methyl or ethyl; X is chloro or bromo; M is sodium or potassium; and Q is sodium or potassium, the reaction being carried out (i) using a phase transfer agent and (ii) in a two phase system.

15 [007] In order to overcome the above listed prior art, the present invention provides a method of preparing 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of a base followed by dehydration in acidic medium.

OBJECTS OF THE INVENTION:

20 [008] The principal object of the present invention is to provide a method for preparing 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of base followed by dehydration in acidic medium.

[009] Another object of the present invention is to provide a simple and eco-friendly process with very minimum by-products for preparing 4-Hexen-3one

25 [010] Yet another object of the present invention is to provide a method of preparing 4-Hexen-3-one which enhances the yield of the production

SUMMARY OF THE INVENTION:

[011] The present invention relates to a method of preparing 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of base. The process is a simple two-step synthesis providing 4-Hexen-3-one in high yields.

[012] MEK is employed in large excess such that, it acts as a solvent as well as reactant for the condensation with Acetaldehyde in presence of catalytic base. The reaction can be carried out at a temperature varying from -15 to 45 °C to afford mixture of crossed Aldol product. The base is selected from the series of alkali group, metal alkoxides & organic bases but not limited to Sodium methoxide, Sodium ethoxide, Potassium methoxide, Potassium ethoxide, NaOH, KOH, Sodium Carbonate, Triethanol amine, Triethyl amine, Ammonia etc. In particular, the Aldol mixture is then subjected to dehydration utilizing the Organic acids and or Carboxylic acids such as Formic acid, Acetic acid, Oxalic acid, Salicylic acid etc and or Zeolites and Ion Exchange resins, but not limited to these, such that a double bond is generated, selectively at 4th carbon atom in the chain. This upon purification afforded the selective Hexenone in satisfactory yields. The process accordingly is very simple, eco-friendly with very minimum by-products and provides high yield.

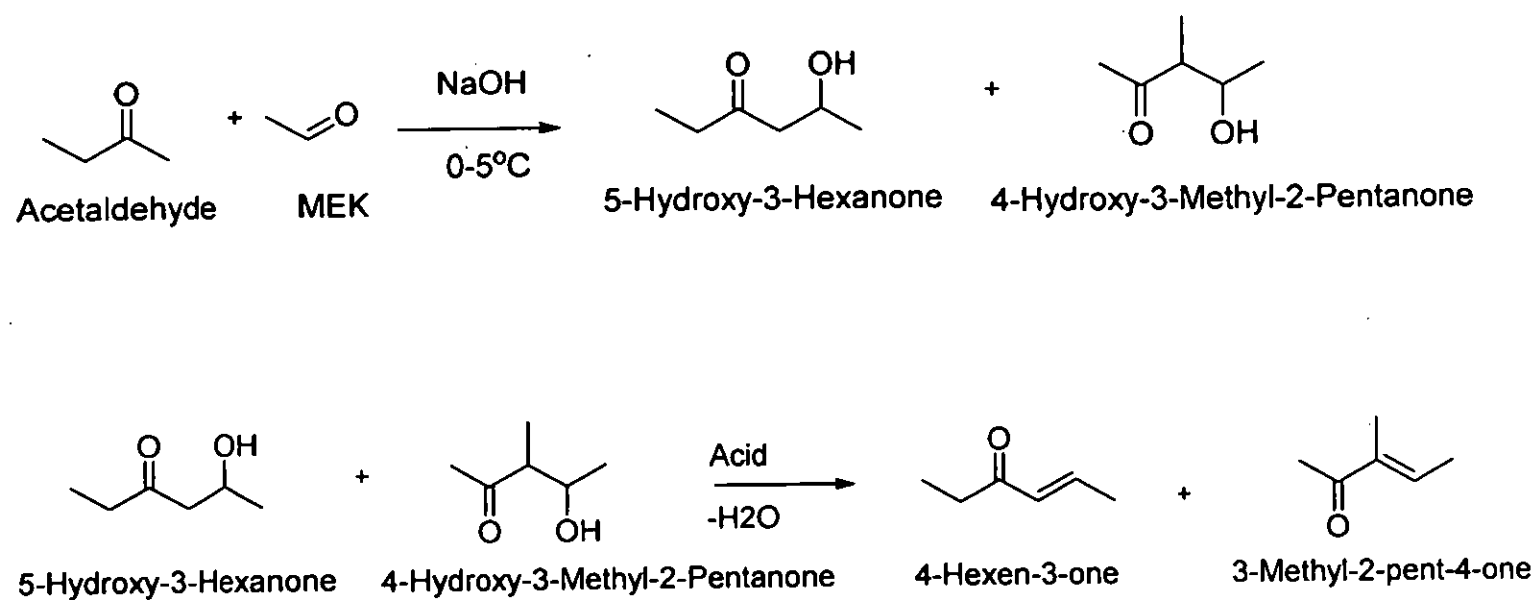
DETAILED DESCRIPTION OF THE INVENTION:

[013] The present invention provides a method of preparing 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of base. The process is a simple two-step synthesis process providing 4-Hexen-3-one in high yields.

[014] MEK is employed in large excess (More than 4 molar equivalents) such that, it acts as a solvent as well as reactant for the condensation with Acetaldehyde in presence of catalytic base. The reaction can be carried out at temperature varying from -15 to 45 °C, preferably -10 to + 35 °C to afford a mixture of crossed Aldol products. The base is selected from the series of alkali group, metal alkoxides & organic bases but not limited to Sodium methoxide, Sodium ethoxide, Potassium

methoxide, Potassium ethoxide, NaOH, KOH, Sodium Carbonate, Triethanol amine, Triethyl amine, Ammonia etc. In particular, the Aldol mixture is then subjected to dehydration utilizing the Inorganic acids, Organic acids and or Carboxylic acids or in combination such as Sulfuric acid, Phosphoric acid, Formic acid, Acetic acid, Oxalic acid, Salicylic acid etc and Zeolites and Ion Exchange resins, but not limited to these, such that a double bond is generated, selectively at 4th carbon atom in the chain. This upon purification afforded the selective Hexenone in satisfactory yields. The process accordingly is simple, eco-friendly with very minimum by-products and provides high yield.

10 Scheme



[015] The invention is described in detail with reference to the examples given below. The examples are provided just to illustrate the invention and therefore, should not be construed to limit the scope of the invention.

EXAMPLES

[016] Example 1: Preparation of Mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone

[017] 1636 g of MEK, 22 g of Methanol and 5.5 g of Sodium hydroxide were added to a reactor and cooled to 15 - 20 °C. 100 g of acetaldehyde is dosed over a period of 4.0 hr to the reaction mixture, maintaining the temp of 15 - 20 °C. The reaction mixture was stirred for another 2.0 hr at 15 - 20 °C. 7.0 g of Oxalic acid was

charged to the reaction mass and stirred for 15 minutes, The crude was filtered and the then taken for solvent recovery followed by vacuum distillation to get 165 g mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone showing the sum of these two isomers together to 92% by GLC.

5 **[018] Example 2: Dehydration of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone**

[019] 1650 g of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone were refluxed with 1650 ml of 0.1N H₂SO₄ for 2.0 hr. The mass was cooled and allowed for the layers to settle. The layers were separated to obtain a
10 950 g mixture of 4-Hexen-3-one and 3-Methyl-2-pent-4-one of which was then neutralized by Caustic soda and further washed water to get neutral washed crude. The crude on high vacuum slow fractionation gave 675 gm pure 4-Hexen-3-one of 92%.

15 **[020] Example 3: Preparation of Mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone**

[021] 1400 g of MEK, 25 g of Methanol and 5.5 g of Sodium hydroxide were added to a reactor and cooled to 10 - 180 °C. 100 g of acetaldehyde is dosed over a period of 3.0 hr to the reaction mixture, maintaining the temp of 15 – 20 °C. The reaction mixture was stirred for another 2.0 hr at 15 – 20 °C. 7.0 g of Oxalic acid was
20 charged to the reaction mass and stirred for 15 minutes, The crude was filtered and the then taken for partial solvent recovery followed by flash distillation to get 325 g mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone showing the sum of these two isomers together to 43% and remaining being MEK and other high boiler peaks, by GLC.

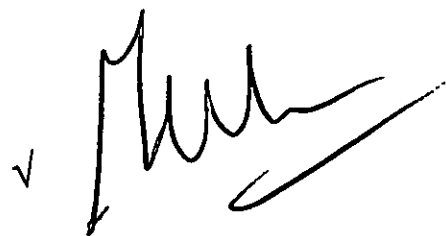
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[022] Example 4: Dehydration of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone

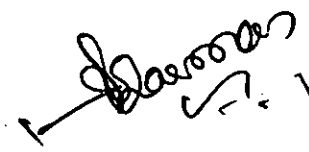
[023] 650 g of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone as stated in example 3 was refluxed with 500 ml of 0.1N H₂SO₄ for 2.0
5 hr and distilled. The organic distillate was then neutralized with 1.0 N NaOH solution to get the neutral crude of the mixture of 4-Hexen-3-one and 3-Methyl-2-pent-4-one which is then distilled under mild vacuum to remove the MEK (which is recycled) and 4-Hexene-3-one and 3-Methyl-2-pent-4-one mixture is further
10 subjected for the high vacuum fractionation to get 135 gm pure 4-Hexen-3-one of 91%.

Numerous modifications and adaptations of the system of the present invention will be apparent to those skilled in the art, and thus it is intended by the appended claims to cover all such modifications and adaptations which fall within the true spirit and scope of this invention.

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Datedday of, 2019



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We Claim:

1. A process for preparation of 4-Hexen-3-one in which Acetaldehyde is reacted with MEK in presence of a base and alcohol to give a mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone which on dehydration with an acid followed by distillation gives 4-Hexen-3-one wherein the dehydration is carried out in presence of inorganic acid or carboxylic acids from C1 - C6 carboxylic acid or dicarboxylic acid from C1 - C6 dicarboxylic acid or halogenated carboxylic acid from C1-C6 carboxylic acid or halogenated dicarboxylic acid from C1-C6 dicarboxylic acid or any combination thereof.
2. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the base is selected from alkali metal and alkaline earth metal.
3. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the preparation of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone includes following steps:
 - a) MEK, Methanol and Sodium hydroxide were added to a reactor and cooled to 15 - 20 °C. Acetaldehyde is dosed over a period of 4.0 hr to the reaction mixture, maintaining the temp of 15 - 20 °C.
 - b) The reaction mixture was stirred for another 2.0 hr at 15 - 20 °C. 7.0 g of Oxalic acid was charged to the reaction mass and stirred for 15 minutes,
 - c) The crude was filtered and then taken for solvent recovery followed by vacuum distillation to get mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone showing the sum of these two isomers together to 92% by GLC.
4. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the dehydration of mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone includes following step:

- a) Mixture of 5-Hydroxy-3-Hexanone and 4-Hydroxy-3-Methyl-2-Pentanone were refluxed with 1650 ml of 0.1N H₂SO₄ for 2.0 hr.
- b) The mass was cooled and allowed for the layers to settle.
- c) The layers were separated to obtain a mixture of 4-Hexen-3-one and 3-Methyl-2-pent-4-one of which was then neutralized by Caustic soda and further washed water to get neutral washed crude.
- d) The crude on high vacuum slow fractionation gave pure 4-Hexen-3-one of 92%.
5. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the alcohol is selected from C1 to C10 alcohol like Methanol, Ethanol, Propanol, Butanol and till Decanol, most preferably Menthanol to Butanol.
6. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the reaction is carried out at temperature varying from -15 to 45 °C, preferably -10 to + 35 °C to afford a mixture of crossed Aldol products.
7. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the dehydration is carried out in presence of Inorganic acid or Organic acid or acidic resin or zeolites or silica or any other known in art.
8. The process for preparation of 4-Hexen-3-one, as claimed in claim 1, wherein the condensation of acetaldehyde and MEK is carried out at 0-30 °C.


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Datedday of, 2019

ABSTRACT

A Method for Preparing 4-Hexene-3-one

The present invention relates to a method of preparing 4-Hexen-3-one by condensation of Acetaldehyde and Methyl Ethyl Ketone (MEK) in presence of a base followed by dehydration of the condensation product using an acid and slow fractionation. The process is a simple two-step synthesis for obtaining 4-Hexen-3-one with high yields.


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Datedday of, 2019