

[54] **ISOLONGIFOLENE PROCESSES AND PRODUCT**

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[58] Field of Search**260/587**, 586 B

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[57] **ABSTRACT**

Novel processes for producing isolongifolene ketone and its epimer which comprise treating isolongifolene with a peroxygen compound under acidic conditions to obtain a substantially fully saturated ketone, as well as the saturated epimer, and perfume compositions containing such products.

11 Claims, No Drawings

ISOLONGIFOLENE PROCESSES AND PRODUCT

BACKGROUND OF THE INVENTION

This disclosure relates to improved processes for the production of perfume materials, as well as to materials so obtained and their use in perfume compositions and the like.

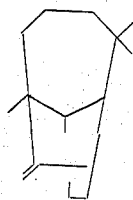
It has been suggested in Netherlands Pat. application No. 6,815,455 that isolongifolene can be oxidized with sodium dichromate in acetic acid to provide a mixture of saturated and unsaturated ketones. It was further suggested in this Netherlands specification that the mixture of compounds so obtained could be used in perfume compositions. The mixture so formed contained relatively small amounts of the saturated ketone.

THE INVENTION

It has been found that, of the saturated and unsaturated isolongifolene ketones provided by the Netherlands patent application process mentioned above, the unsaturated material has only a very slight aroma in its pure form, and accordingly is not useful to impart a definite aroma to a perfume composition. It is accordingly desirable to obtain the saturated ketone in as pure a form as possible.

Briefly, the present invention provides a process for the production of a fully saturated isolongifolene ketone which is substantially free of unsaturated material. The process comprises treating isolongifolene with a peroxygen compound in an acidic medium to produce saturated ketone. This saturated ketone can also be epimerized as hereinafter disclosed to provide a more stable perfume ingredient. The invention also contemplates certain products of the process and the use of such products in perfume and fragrance compositions.

The ultimate starting material in the practice of the invention is longifolene, a cyclic terpene having the structural formula



Longifolene is widely distributed in nature, notably among species of the genus *Pinus*. One of these sources of longifolene is so-called Indian turpentine oil obtained from *Pinus longifolia* Roxb. It occurs in such Indian turpentine oil in amounts of about 30 percent, and is preferably purified before use herein to higher purities of 80 percent or more. All parts, percentages, proportions and ratios herein are by weight unless otherwise indicated.

The specific starting material for use in the present invention is isolongifolene having the formula



This isomer of longifolene is readily obtained according to methods known in the art. For example, it can be ob-

tained by treating longifolene with boron trifluoride. Since the purity of the ultimate product can more readily be obtained with relatively pure isolongifolene, it is desirable that the isolongifolene used herein have a purity of the 80 percent or more.

The process is carried out by treating isolongifolene with a peroxygen source such as hydrogen peroxide in the presence of an acidic material which is desirably an organic anhydride or acid. The peroxygen source preferably has a substantial content of active oxygen, and hydrogen peroxide of at least 30% H_2O_2 content is desirable. A percarboxylic acid can also be used as the source of peroxygen, and is herein considered the equivalent of hydrogen peroxide. Lower peralkanoic acids are preferred peracids in the practice of this invention. Such peracids desirably have strengths of 30 percent or more. An especially preferred peroxygen source for use in this invention is 50 percent or stronger hydrogen peroxide.

The acidic medium utilized for the reaction is desirably a lower alkanoic acid or the anhydride thereof. The lower alkanoic acids containing from one to four carbon atoms and their corresponding anhydrides are preferred. The reaction proceeds at a more satisfactory rate with the anhydrides when a catalytic amount, desirably from about one to five percent of the weight of the anhydride, of a strong protonic acid is present. Preferred protonic acids for use herein are sulfuric acid and strong protonic sulfonic acids such as methanesulfonic acid, p-toluenesulfonic acid, and the like. When carboxylic acids other than formic acid are used, the acid medium should contain a catalytic amount of a strong protonic acid, as described herein.

The reaction can, if desired, be carried out in the presence of an inert vehicle. Such vehicles include mobile liquid alkanes such as propane, hexane, octane and the like; and liquid aryl hydrocarbons such as benzene, toluene, xylene, and the like. It has been found that such vehicles are generally unnecessary, however, and since the separation from the reaction mixture can add extra processing costs, a reaction vehicle (in addition to the alkanoic acid or anhydride) is not generally utilized.

The temperature of the reaction is sufficiently high to provide a good rate of reaction, but it has been found that temperatures which are too high can result in a rapid, uncontrolled reaction which may actually be destructive of the starting material. It is accordingly desirable to conduct the reaction at temperatures of at least 25°C, but temperatures in excess of 75°C are desirably not utilized. Accordingly, the reaction is generally carried out at temperatures from 25 to 75°C. The reaction rate will also depend upon the particular peroxygen compound used, the solvent system, the presence of any inert vehicles, and the ratios of reactants. However, it has been found that best results are obtained in many aspects of this invention by using temperatures in the preferred range of from 30° to 60°C.

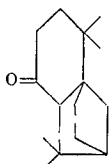
The peroxygen compound is preferably added to the isolongifolene and acidic material at a low rate to permit control of the temperature within the limits set forth herein. The peroxygen material is accordingly added dropwise when small quantities of isolongifolene are being treated and is added on a proportionate scale in large reaction vessels.

It has been found that the yields of the reaction can be improved by a holding period following addition of all the peroxygen compound. The length of this holding period will vary according to the quantities and ratios of reactants used, the amount of agitation and mixing available, and similar factors. The course of the reaction can, if desired, be followed by observing disappearance of the isolongifolene starting material by gas-liquid chromatography (GLC). Generally, it is desirable to provide at least thirty minutes of agitation after the addition of the peroxygen compound is complete, and with modern processing equipment the use of times in excess of four hours is generally unnecessary. Accordingly, the agitation is desirably carried out for from 30 minutes to four hours after peroxygen addition is complete, and times of from one to three hours are generally preferred.

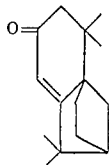
The amount of peroxygen compound used is desirably in molar excess, preferably slight excess, of the quantity of isolongifolene, since the use of lesser quantities will result in increasing amounts of unreacted isolongifolene, and large excesses are deleterious because of the formation of increasing amounts of unsaturated lactones. The amount of lower alkanolic acid used is desirably at least equivalent on a molar basis to the quantity of isolongifolene, and molar excesses of three or more times can be used. It is preferred to use a four to six times molar excess of alkanolic acid over molar quantity of isolongifolene. When anhydrides are used in lieu of acids, the same molar proportion is desirable.

The reaction can be carried out under subatmospheric or superatmospheric pressures. It is generally preferred to carry out the reaction under normal atmospheric pressures.

The process described herein provides substantially entirely a saturated ketone having the formula



The material so produced is substantially free of unsaturated ketone, such as that having the formula



shown in the prior art. The saturated isolongifolene ketone provided according to the present invention is a colorless liquid having a distinctive rich, woody fragrance.

The saturated isolongifolene ketone can also be isomerized to provide a more stable ketone. The isomerization is carried out by treating the saturated ketone with aqueous or alcoholic solutions of alkali metal hydroxides or carbonates. Such alkaline solutions of hydroxides used for epimerization desirably contain from about two to about ten percent of hydroxide. Solutions containing the lower alkanols, e.g., methanol, ethanol, propanol, and isopropanol are preferably used to obviate solubility problems.

The isomerization is carried out by contacting the alkaline solution with the saturated isolongifolene ketone, as produced above, for from about 30 minutes to about 6 hours. It is preferred that the alkaline treatment be carried out for from one to three hours. The temperature of treatment can be from 40°C to 100°C, and excellent results are obtained at temperatures in the range of 60° to 80°C.

The saturated ketones and/or isomers produced according to the processes herein disclosed can be separated from the vehicle and any unreacted materials, or unwanted by-products can be removed, by conventional means including washing, distillation, extraction, preparative chromatography, and the like. It is preferred to fractionally distill the washed reaction product under a relatively high vacuum so as to obtain a pure product. Product purities of 80 percent are readily obtained, and much higher purities can also be provided by suitable treatment. Such fractional distillation readily separates the saturated ketone from any lactones which may be formed as by-products.

The saturated isolongifolene ketones of this invention are useful as fragrances. They can be used to contribute a rich, precious wood fragrance. As olfactory agents the saturated ketones produced according to this invention can be formulated into or used as components of a "perfume composition."

The term "perfume composition" is used herein to mean a mixture of organic compounds, including, for example, alcohols, aldehydes, other ketones, esters, and frequently hydrocarbons which are admixed so that the combined odors of the of the individual components produce a pleasant or desired fragrance. Such perfume compositions usually contain: (a) the main note or the "bouquet" or foundation-stone of the composition; (b) modifiers which round-off and accompany the main note; (c) fixatives which include odorous substances which lend a particular note to the perfume throughout all stages of evaporation, and substances which retard evaporation; and (d) top-notes which are usually low-boiling fresh-smelling materials.

In perfume compositions the individual component will contribute its particular olfactory characteristics, but the overall effect of the perfume composition will be the sum of the effect of each ingredient. Thus, the individual compounds produced according to this invention, or mixtures thereof, can be used to alter the aroma characteristics of a perfume composition, for example, by highlighting or moderating the olfactory reaction contributed by another ingredient in the composition.

The amount of the saturated ketone produced according to this invention which will be effective in perfume compositions depends on many factors, including the other ingredients, their amounts and the effects which are desired. It has been found that perfume compositions containing as little as 2 percent of the compound of this invention, or even less, can be used to impart a woody amber odor to soaps, cosmetics, and other products. The amount employed can range up to 7 percent or higher and will depend on considerations of cost, nature of the end product, the effect desired on the finished product and the particular fragrance sought.

EXAMPLE II

A 5 liter flask equipped with a stirrer, thermometer, reflux condenser and dropping funnel is charged with 1500 g (7.35 moles) of isolongifolene, 1650 g (27.5 moles) of glacial acetic acid, and 41 g (0.38 moles) of concentrated sulfuric acid. The flask contents are heated to 45°C, and 500 g (7.35 moles) of 50 percent hydrogen peroxide is added during one and one-half hours, during which addition the temperature is maintained at 44°–49°C by cooling. After addition is complete, the reaction mass is stirred for 3 additional hours at 44°–49°C. The reaction can be monitored by GLC so that the quantity of isolongifolene remaining is about 3 percent.

The reaction is washed with 500 ml of 10 percent aqueous sodium chloride solution and then twice with 250 ml of 10 percent aqueous sodium hydroxide. The aqueous layers obtained from the washes are extracted with 250 ml of toluene. The toluene is stripped away to yield 55 g of organic material, and this material is combined with the washed oil to obtain washed isolongifolene ketone product.

Epimerization

A 5-liter reaction flask fitted with a stirrer, thermometer, dropping funnel, and reflux condenser is charged with 1641 g of the washed isolongifolene ketone, 720 g (22.5 moles) of methanol, and 102 g of 50 percent aqueous sodium hydroxide (1.2 moles), and the mixture is refluxed for 3 hours. Thereupon 680 g of water is added, and the methanol is recovered by gradually raising the temperature to 85°C. The organic phase of the resulting mixture is then separated from the aqueous phase, the aqueous phase is extracted with toluene, and the extract and organic phase are combined.

The combined phase is then washed four times with 500 ml portions of 10 percent aqueous sodium chloride to obtain a final pH of 6–7. The aqueous wash liquids are extracted with toluene, and the extract is combined with the washed crude material. One hundred grams of Primol mineral oil is added to the washed crude, and the mixture is flash-distilled at a pot temperature of 135°–208°C and a head temperature of 115°–154°C at 2 mm Hg to obtain 1316 g of product.

The product is obtained is combined with 50 g of Primol mineral oil and 5 g of Ionox antioxidant and fractionated through a 12-inch Goodloe column at 2–3 mm Hg. The light fractions are separated by employing a 9:1 reflux ratio, and the remainder of the distillation is carried out with a 2:1 reflux ratio. During this distillation the pot temperature is 150°–235°C and the head temperature is 110°–115°C. The product is stable isolongifolene ketone epimer having an excellent full-bodied, precious wood fragrance note.

EXAMPLE III

A 500 ml reaction flask equipped with a stirrer, thermometer, reflux condenser and addition funnel is charged initially with 204 g (1.0 mole) of isolongifolene and then with 195 g (1.91 moles) of acetic anhydride. The flask contents are heated to 40°C, and 68 g (1.0 mole) of 50 percent hydrogen peroxide is added dropwise to maintain the temperature at 40°C. The addition requires about 1 hour and 20 minutes.

The reaction mass is maintained at 40°–50°C for 3 hours, after which 250 ml of water and 50 ml of toluene are added. The aqueous layer so obtained is separated from the organic layer, extracted once with 50 ml of toluene, and discarded. The toluene extract is combined with the organic layer and washed twice with 250 ml of water.

The resulting isolongifolene ketone is epimerized by refluxing at about 100°C with 250 ml of 5 percent aqueous sodium hydroxide and washed twice with 250 ml portions of 5 percent aqueous sodium chloride solution.

Gas-liquid chromatography and IR analysis indicate that the stable epimer of isolongifolene ketone is obtained.

EXAMPLE IV

A 1-liter reaction flask equipped with a stirrer, thermometer reflux condenser, addition funnel, and drying tube is charged with 204 g (1.0 mole) of isolongifolene and 24.6 g (0.3 mole) anhydrous sodium acetate. The mixture is heated to 60°C and 190 g (1.0 mole) of 40 percent peracetic acid is added dropwise while the temperature is maintained at 55°–60°C. After the addition is completed in 1 hour and 10 minutes, stirring is continued in 1 hour and 10 minutes, stirring is continued for 3 hours while the temperature is maintained at 60°C.

After the additional stirring period the reaction mass is washed once with 400 ml of water and once with 100 ml of water. The water separated from the reaction mixture after washing is extracted once with 100 ml of toluene, and the extract is added to the organic layer.

The organic layer is washed twice with 500 ml of water, and the toluene is stripped off under vacuum to provide 216 g of a mixture of isolongifolene ketone, the corresponding lactone, and a sesquiterpenic alcohol. The pure ketone is obtained by distillation, as taught hereinabove.

EXAMPLE V

The epimer produced in Example I is used to prepare a chypre perfume according to the following formula:

Ingredient	Amount (Parts)
Santalol	60
Couarin	90
Musk ketone	30
Musk ambrette	20
Ambreine absolute	25
Tarragon oil	25
Angelica root oil	5
Clary sage	30
Epimer from Example I	60
Linalol oil	30
Patchouli oil	20
Iso-eugenol	35
Methyl ionone	50
Oakmoss absolute	60
Bergamot oil	225
Jasmin absolute	20
Rose absolute	15
Methyl salicylate	2
Lavender oil	3
Vanillin	15
Heliotropin	35
Ylang oil, Manila	70
Cinnamyl acetate	25
Benzoin resinoid	50

The presence of the epimer in the foregoing perfume composition provides a full bodied, rich, precious wood

The saturated ketones can be used alone or in a perfume composition as an olfactory component in detergents and soaps; space deodorants; perfumes; colognes; bath preparations such as bath oil and bath salts; hair preparations such as lacquers, brilliantines, pomades, and shampoos; cosmetic preparations such as creams, deodorants, hand lotions, and sun screens; powder such as talcs, dusting powders, face powder, and the like. When used as an olfactory component of a perfumed article, as little as 0.01 percent of the ketone or ketones will suffice to impart a full-bodied, rich, precious wood odor.

In addition, the perfume composition can contain a vehicle or carrier for the other ingredients. The vehicle can be a liquid such as alcohol, glycol, or the like. The carrier can be an absorbent solid such as a gum or components for encapsulating the composition.

It will be appreciated that the saturated ketones obtained according to this invention can be used to enhance, alter, modify, vary, or supplement the fragrance properties of natural or synthetic fragrance compositions. Thus, such ketones can be used in fragrance compositions for addition to perfume compositions or directly to products such as soap, detergents, cosmetics, and the like. The fragrance compositions so prepared do not entirely provide the olfactory properties to the finished perfume or other article, but they do furnish a substantial part of the overall fragrance impression.

The following examples are given to illustrate embodiments of the invention as it is presently preferred to practice it. It will be understood that these examples are illustrative, and the invention is not to be considered as restricted thereto except as indicated in the appended claims.

EXAMPLE I

Preparation of Isolongifolene

A clean, dry 50-gallon stainless steel reactor is charged with 250 pounds of longifolene, agitated, and swept with nitrogen. The nitrogen pressure is maintained at 5 psig, and 2.8 pounds of boron trifluoride etherate is charged to the reactor during one hour. During this time, the reactor temperature is maintained at 25°–30°C by a water jacket. After all of the etherate is added, the reaction is maintained at 30°C for 1 hour.

The reaction mixture is then neutralized with 200 pounds of 5 percent aqueous sodium hydroxide solution and washed at room temperature (20°–30°C) for one-half hour. The aqueous and organic layers so formed are separated, and the lower aqueous layer is discarded. The organic layer is then washed with 40 pounds of 10 percent aqueous sodium chloride at room temperature for one half hour.

The lower aqueous layer is separated to provide a washed organic phase containing isolongifolene.

Preparation of Saturated Isolongifolene Ketone

A 12-liter reaction flask fitted with a stirrer, thermometer and condenser is charged with 3264 g (16 moles) of isolongifolene and 3600 g (70 moles) of formic acid (90 percent). The mixture is agitated while 1088 g (16 moles) of 50 percent hydrogen peroxide is added at 44°–49°C during 1 hour. The mixture is then stirred for another 3 hours at 44°–49°C.

The reaction mass is then washed with 2.5 liters of 10 percent aqueous sodium chloride and then with 1 liter of 5 percent aqueous sodium hydroxide.

The organic layer is separated from the aqueous layer to obtain saturated isolongifolene ketone substantially free of unsaturated ketone. This ketone can be separated, if desired, from a smaller amount of lactone and unreacted starting material by distillation at 3 mm Hg and about 112°C to obtain a colorless liquid having a rich, woody odor.

The purified saturated isolongifolene ketone is subjected to infrared (IR) spectroscopy and shows a carbonyl absorption at 1695 cm^{-1} , gem-dimethyl absorption at 1368 and 1387 cm^{-1} , and an absorption attributable to a methylene group adjacent to a carbonyl group at 1410 cm^{-1} . Nuclear magnetic resonance (NMR) data show a singlet attributable to three methyl protons at 0.89 ppm, a singlet attributable to three methyl protons at 0.93 ppm, a singlet attributable to three methyl protons at 0.98 ppm, a singlet at 1.16 ppm attributable to three methyl protons, broad band attributable to methylene and methine protons at 1.23–2.04 ppm, and protons in a position alpha to a carbonyl group at 2.10–2.30 ppm. The foregoing parts refer to the frequency shift measured in a carbon tetrachloride solution on a Varian Model HA-100 spectrometer.

Preparation of Stable Saturated Isolongifolene

Ketone-Epimer

The crude saturated isolongifolene ketone obtained above is charged to the 12-liter reaction flask, together with 4 liters of methanol and 168 g of 50 percent aqueous sodium hydroxide. The reaction mixture is stirred at reflux for 2½ hours.

After addition of 1800 ml of water, the methanol is recovered under atmospheric pressure at 85°C. The water layer is extracted once with a liter of toluene, and the toluene extract is combined with the organic layer, which combination is then washed with one liter of 10 percent aqueous sodium chloride until it is neutral. The toluene is stripped, and 100 g of Primol refined mineral oil is added. The mixture is then flash-distilled at 2 mm Hg with a pot temperature of 135°–208°C and a head temperature of 115°–154°C. This yields 3916 g of distillate. The distillate is fractionated at 3 mm Hg and a 9:1 reflux ratio after 50 g of Primol and 8 g of Ionox antioxidant are added. The material boils at 121°C under 2.8 mm Hg.

The isomer product so obtained is a colorless liquid having a full-bodied, rich, precious wood fragrance note. It can be employed with tobacco fragrances, pine aromas, and sweet grass type aromas. IR spectroscopy of material shows a carbonyl absorption at 1715 cm^{-1} , gem dimethyl absorptions at 1370 and 1392 cm^{-1} , and a methyl group adjacent to a carbonyl group at 1420 cm^{-1} . NMR shows a singlet attributable to three methyl protons at 0.97 ppm, a singlet attributable to three methyl protons at 1.05 ppm, a singlet attributable to 6 methyl protons at 1.20 ppm, a [multiplet] at 1.25–2.00 attributable to methylene and methine protons, and a [multiplet] attributable to three protons alpha to a carbonyl group at 2.00–2.25 ppm. The NMR figures are obtained under the same conditions as set forth above.

note, and maintains a good formula balance, even in the absence of the vetivert oil customarily used in such formulations.

What is claimed is:

1. A process for the production of isolongifolene ketone which comprises reacting at a temperature of from 25° to 75°C. isolongifolene with a peroxide source selected from the group consisting of hydrogen peroxide and a peralkanoic acid having from two to four carbon atoms, said peroxide source having a strength of at least 30 per cent, in the presence of an acidic medium of a lower alkyl carboxylic acid or anhydride thereof to produce saturated isolongifolene ketone substantially free from unsaturated ketone.

2. A process according to claim 1 wherein the peroxide source has a strength of at least 50 percent.

3. A process according to claim 1 wherein there is additionally present a catalytic amount of a strong protonic acid.

4. A process according to claim 3 wherein the acid is sulfuric acid or a strong protonic sulfonic acid.

5. A process according to claim 1 wherein the carboxylic acid contains from one to four carbon atoms.

6. A process according to claim 5 wherein the acid contains from two to four carbon atoms and there is additionally present a strong protonic acid.

7. A process according to claim 1 wherein the carboxylic acid is formic acid.

8. A process according to claim 1 wherein the peroxide source is a peralkanoic acid having from two to four carbon atoms.

9. A process according to claim 1 wherein the saturated isolongifolene ketone so produced is isomerized at a temperature of from 40 to 100°C with aqueous, alcoholic, or aqueous alcoholic alkali metal hydroxide.

10. A process according to claim 9 wherein the aqueous hydroxide contains from two to ten percent hydroxide.

11. A process according to claim 1 wherein the peroxide source is hydrogen peroxide.

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