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(54) PROCESS FOR THE PRODUCTION OF LACTONES

(71) We, INTERNATIONAL FLAVORS & FRAGRANCES INC., a Corporation organised under the laws of the State of New York, United States of America, of 521 West 57th Street, New York, New York, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention relates to a process for the preparation of an unsaturated δ-decalactone by reacting a pentynylcyclopentanone with an aliphatic percarboxylic acid at 10° to 50°C and, of desired, partially hydrogenating the δ-pentynyllactone so obtained to produce a δ-pentynyllactone.

In view of the limited availability of natural jasmin, and its commercial importance in producing high grade fragrances, synthetic substitutes have become desirable. Since certain lactones constitute part of the fragrance impression of jasmin, and 2' - (cis - penten - 2' - yl - 1') pentanolide, the δ-lactone of 5 - hydroxy - 7 - decenoic acid, is known to constitute an important constituent of the essence of Italian jasmin, a commercially feasible synthesis for this lactone has been sought.

A number of routes for the production of such lactones from various starting materials are available, although they are rather complicated. One of the known methods of synthesis for the δ-lactone of 5 - hydroxy - 7 - decenoic acid begins with the reaction of cyclopentanone with pyrrolidine to form pyrrolidylcyclopentene, and subsequent treatment of the unsaturated alicyclic ring with bromopentyne to provide pentynylcyclopentanone. The prior art proposes (but then discards) that a Baeyer-Villiger reaction could be used to produce the lactone from the pentynylcyclopentanone, but the prior art further demonstrated that treating alkynylcyclopentanone with peracids such as perbenzoic, metachlorobenzoic or trifluoroacetic acids provided a mixture of materials without the formation of any detectible amounts of the desired lactone. In order to produce the desired intermediate, a multistep method was devised by E. Demole et al and reported in *Helvetica Chemica Acta* 45, 1256 (1962).

In showing a synthesis for the lactone, Demole et al disclosed that attempts to oxidize the material to the lactone directly utilizing either perbenzoic acid, metachloroperbenzoic acid, or trifluoroperacetic acid, all of which were thought to be reagents specific to oxidize the ring and thereby produce the lactones, were unsuccessful. Accordingly, the synthesis finally arrived at by Demole et al utilized a complex multistep process involving reduction of the acetylenic bond in the pentynylcyclopentanone, formation of the cyclic alcohol, bromination and lactone formation, followed by a reduction to obtain the unsaturated lactone ring.

The invention accordingly comprises the novel processes and steps of processes, specific embodiments of which are described hereinafter by way of example and in accordance with which it is now preferred to practice the invention.

The process of this invention comprises treating pentynylcyclopentanone with unsubstituted aliphatic percarboxylic acids at temperatures in the range of from 10° to 50°C to form the pentynyl δ-lactone. The pentynyllactone so form can be further selectively hydrogenated to provide the pentynyl derivatives. Such δ-pentynyllactones are useful in the preparation of perfumes and fragrance compositions, as further described herein.

The pentynylcyclopentanone treated according to the present invention is 2 - (pentyn - 2' - yl)cyclopentanone. It is preferred that the starting material be relatively pure to avoid the formation of unwanted by-products and

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to facilitate purification of the desired lactone. Said pentynylcyclopentanone can readily be prepared by treating cyclopentanone with a secondary amine such as pyrrolidine or piperidine under acidic conditions to form the corresponding enamine such as 1 - pyrrolidylcyclopentene - 1 and subsequently alkylating the enamine so obtained with 1 - bromopentyne - 2.

The choice of the percarboxylic acid is most important in obtaining any significant yield of the desired product from the reaction, and accordingly aliphatic, namely alkyl percarboxylic acids are used. The lower aliphatic percarboxylic acids having up to four carbon atoms are most desirable, and performic, peracetic, and perpropionic acids are preferred. The best results are generally obtained with peracetic acid. The term "aliphatic" as used herein to described the percarboxylic acids utilized in the practice of this process will be taken to exclude substituted percarboxylic acids such as mono- or polyfluoro-, hydroxy, methoxy, and amino-substituted acids.

The yield of pentynyl lactone can be improved or the rate of reaction can be increased by incorporating catalytic amounts of certain strong protonic acids into the reaction system. These protonic acids may be added directly into the system or may first be mixed with the peracid material. When such protonic acids are used, only small amounts are required, that is, up to 0.5% of the percarboxylic acid. It is especially preferred to utilize as strong protonic materials sulfuric acid and organic sulfonic acids such as methane sulfonic acid and *p*-toluene sulfonic acid. Unless otherwise indicated, all ratios, proportions, parts, and percentages herein are by weight.

The yield of the reaction is also affected by the amount of aliphatic percarboxylic acid present in the reaction mixture. If too small a quantity of the percarboxylic acid is present the yields are lower and the pentynylcyclopentanone starting material must be recovered. On the other hand, the use of too much percarboxylic acid causes side reactions which lower the yield. Accordingly, an approximately equimolar quantity of the percarboxylic acid may be used although an excess of the percarboxylic acid up to 40 molar percent is preferred.

It has been found that a temperature below 10°C the quantity of the desired material formed is generally insignificant. As the temperature is increased to 10°C and above, however, it has been discovered that the yields are substantially increased, and a temperature of 25°C or more is preferred. At temperatures in excess of 50°C, the acetylenic bond is attacked and the yields once again become less satisfactory. Accordingly, in the practice of this invention to the reaction is conducted at temperatures of from 10°C to 50°C, and it is especially preferred to conduct the reaction at temperatures of from 25°C to 45°C.

It is preferred to carry out the lactone formation under atmospheric pressure. The reaction can be carried out in the presence of an inert atmosphere such as nitrogen although this is not generally necessary or advantageous. If desired, an inert vehicle, for example an aromatic material such as toluene, can also be incorporated in the reaction mixture.

The time of the reaction varies according to the temperature at which the reaction is carried out, the purity of the ingredients, the completeness of reaction desired, the presence of inert vehicle, if any, and the agitation utilized. It is desirable to conduct the reaction for times ranging from two to ten hours, shorter times producing lower yields, and longer times giving no further advantage in the production of the desired lactone. The reaction is conveniently carried out by adding the percarboxylic acid slowly over a period of time and then holding the reaction mixture under agitation until the desired completeness of reaction is obtained. The progress of the reaction can be readily followed by analyzing small quantities of the reaction mixture, for example, by gas-liquid chromatography (GLC).

The pentynyllactone is extracted with water-benzene mixture to remove water-soluble impurities, and the organic layer so obtained is washed with an alkaline material, preferably the salt of a strong base and a weak acid, for excess acid removal. The material can then be washed with salt solution for further purification. It can thereafter be dried, filtered, and stripped of the benzene or other solvent. The pentynyllactone product can further be treated, as by hydrogenation, or it can be purified by conventional techniques such as selective extraction or fractional distillation.

The pentynyllactone so produced can be selectively hydrogenated in high yield to produce the corresponding pentynyllactone. In order to obtain the preferred pentynyl material having a preponderance of cis isomers in good yield, it is desirable to add not more than one mole of hydrogen per mol of pentynyllactone. The hydrogenation reaction is carried out in the presence of Lindlar catalysts such as palladium on calcium carbonate, which are selective in maximizing the yield of pentynyl material and minimizing the yield of other hydrogenation products such as pentynyl-lactone and trans-pentynyl-lactones. Suitable pressures are in the range of from 2 to 50 psig. The temperatures suit-

able in carrying out the reaction are in the range of from 25°C to 60°C.

It is generally preferred to perform the hydrogenation at a relatively low temperature while hydrogen is slowly added, and then to maintain the temperature of the reaction mass after the hydrogen has been introduced so as to insure completeness of reaction. It is frequently desirable to carry out the hydrogenation in the presence of an inert vehicle, such as an alcohol.

The cis-pentynyllactone obtained by hydrogenation is filtered to remove the hydrogenation catalyst and can be washed or further treated as desired to provide a substantially pure material.

The decenoic acid δ-lactone produced according to the present invention has a pronounced jasmin fragrance and is suitable for use as a fragrance material itself, as a component of fragrance compositions, or as a component of perfume compositions. Thus, the materials of this invention are useful as olfactory agents and fragrances.

The term "perfume composition" is used herein to mean a mixture of compounds, including, for example, natural oils, synthetic oils, alcohols, aldehydes, ketones, esters, other lactones, and frequently hydrocarbons which are admixed so that the combined odors of the individual components produce a pleasant and desired fragrance. Such perfume compositions usually contain: (a) the main note (the "bouquet" or foundation-stone) of the composition; (b) modifiers which round off and accompany the main note; (c) fixatives including 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. Such perfume compositions of this invention can be used in conjunction with carriers, vehicles, solvents, dispersants, emulsifiers, surface-active agents and aerosol propellants.

In perfume compositions the individual components contribute their particular olefactory characteristics, but the overall effect of the perfume composition can be more than the sum of the effect of each ingredient. Thus, the individual compounds prepared according to this invention or mixtures thereof, may be used to alter the aroma characteristics of a perfume composition, for example, by high-lighting or moderating the olfactory contribution of another ingredient in the composition.

The amount of the compounds obtained 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 a little as 0.5% by weight of the compounds produced according to the process of this invention, or even less, can be used to impart a jasmin odor to soaps, cosmetics and similar products. The amount employed will depend on considerations of cost, nature of the end product, the effect desired on the finished product and the particular fragrance sought.

The materials disclosed herein can be used alone, in a fragrance-modifying composition, or in a perfume composition as olfactory components in detergents and soaps; space deodorants; perfumes; colognes; both 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; powders such as talcs, dusting powders, and face powders.

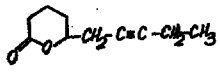
The following examples serve to illustrate embodiments of the invention as it is now preferred to practice it. It will be understood that these examples are illustrative.

EXAMPLE I

Preparation of Pentynyllactone

A 50 ml. Erlenmeyer flask is fitted with a stirrer, a thermometer, and cooling means, and 15 g. (0.1 mol) of 2 - (pentyn - 2' - yn)-cyclopentanone is introduced into a flask .The flask is cooled to maintain a temperature of 20—25°C while 21 g. (0.11 mol) of 40% peracetic acid containing about 1% sulfuric acid is added over a 45-minute period. The mass is then maintained under agitation for three hours, at which point the GLC monitoring indicates formation of the desired product with a small amount of the original starting material still present. Accordingly, 7 g. (0.037 mol) of 40% peracetic acid is added, and the mixture is stirred for an additional one hour.

At the end of the additional one-hour stirring period, the reaction mixture is transferred to a separatory funnel, and an equal volume of water and 50 ml. of benzene are added. After mixing, the upper organic layer is separated from the aqueous layer and washed three times with 50 ml. of 5% aqueous sodium bicarbonate. The organic layer is further washed twice with 50 ml. of aqueous saturated sodium chloride, dried over anhydrous magnesium sulfate and filtered. The benzene is then removed on a rotary evaporator. Instrumental analysis shows the major product formed is the δ-lactone of 5 - hydroxy - 7 - decynoic acid having the structure



Example II

Preparation of Pentynyllactone

Two equal portions of 28.5 g. (0.16 mol) of 2 - (pentyn - 2' - yl)cyclopentanone are treated with 35 g. (0.18 mol) of 40% peracetic acid containing about 1% sulfuric acid so that the peracetic acid is in approximately 16 molar % excess over the theoretical amount. In each instance the peracetic acid is added to the cyclopentanone at 20—25°C over a one-hour interval. The reaction mixtures are stirred for approximately five hours, while the course of the reaction is monitored by GLC analysis of the reaction mixture.

After the five-hour period 50 ml. of an aqueous 50% saturated salt solution is added to each reaction mixture together with 25 ml. of benzene. The organic layers in each of the two vessels are separated and washed three times with 100 ml. of aqueous 50% saturated sodium chloride solution and then once with saturated sodium chloride solution. The washed mixtures are dried over anhydrous magnesium sulfate and filtered. The fractions are then distilled on a micro still to obtain pure product.

This material is substantially the pure δ-lactone of 5 - hydroxy - 7 - decynoic acid.

Similar results are obtained by substitution of perpropionic acid for peracetic acid.

Selective Hydrogenation

The lactone prepared above in the amount of 27.5 g. is then placed in a Parr reaction vessel with 20 g. of isopropanol and 0.3 g. of a palladium on calcium carbonate catalysts. The mixture is hydrogenated with 0.15 mol of hydrogen at 27—55°C with a pressure falling from 49 to 36 psig over the reaction period.

After hydrogenation the material from the Parr apparatus is filtered to remove solids, and the isopropanol is recovered on a rotary separator. The mixture is then distilled on a micro still at a temperature of 108—117°C at 0.5 mm Hg. GLC analysis shows the reaction products to be approximately 60% of the desired cis isomer and 30% of the trans isomer of the δ - lactone of 5 - hydroxy - 7 - decenoic acid. The liquid pure cis isomer has an n_D^{20} of 1.4860.

In other hydrogenations conducted according to the foregoing procedure, the product assayed 90% cis isomer with smaller amounts of the trans isomer and saturated material.

Example III

The procedure of Example II is repeated with 40% peracetic acid containing no sulfuric acid. Substantially the same yields are obtained, and the reaction velocity appears to be somewhat lower.

Example IV

To a 500 ml. reaction flask containing 143 g. of 2 - (pentyn - 2' - yl)cyclopentanone is added 200 g. of 40% peracetic acid containing about 1% sulfuric acid during a three hour and fifty-three minute period at 24—30°C. The reaction mixture is constantly stirred and mild cooling is applied to maintain the temperature at approximately 30°C. Thereafter the reaction mass is stirred for three hours at 27—44°C while the course of the reaction is monitored by GLC.

The reaction mixture is then treated with 250 ml. of ether and 250 ml. of 50% saturated aqueous sodium chloride solution, washed, and settled to separate the organic layer. The organic layer is washed five more times with 250 ml. of 50% saturated aqueous sodium chloride solution and then twice with 250 ml. of saturated aqueous sodium chloride solution. The washed material is dried over magnesium sulfate and filtered, and the solvent is stripped off with a rotary evaporator.

The mixture is then distilled at 159—186°C at 0.8—2.1 mm Hg. The reaction yields 87 g. (0.525 mol) of the δ - lactone of 5 - hydroxy - 7 - decynoic acid of 97% purity.

It will further be understood from the present disclosure that the percarboxylic acid can be formed *in situ* from an aliphatic carboxylic acid and a peroxygen compound such as hydrogen peroxide. This technique can be used to obtain any of the percarboxylic acids according to the present invention and it is especially useful when the aliphatic percarboxylic acid is not readily available or when the percarboxylic acid is relatively unstable so that it cannot conveniently be handled in the form of the peracid. Thus, percarboxylic acids such as performic and the higher aliphatic percarboxylic acids are conveniently prepared by adding hydrogen peroxide to the aliphatic acid. In such instances an equilibrium mixture of hydrogen peroxide, the percarboxylic acid and the aliphatic carboxylic acid, is obtained.

Example V

Lactone Preparation with Carboxylic Acid and Peroxide Mixture

A 200 ml. reaction flask is equipped with a stirrer, dropping funnel, and thermometer, and 15 g. (0.1 mol) of 2 - (pentyn - 2' - yl)-cyclopentaone and 50 g. of 100% formic acid are introduced into the flask. The flask and its contents are then cooled to 20°C and 7.8 g. of 50% hydrogen peroxide is added to the cooled contents during a forty-five minute period. The temperature of the reaction mixture is then allowed to rise to 35°C, and the contents are stirred for an additional 2.5 hours.

Instrumental analysis shows the formation of substantial quantities of the δ-lactone of 5 - hydroxy - 7 - decyonoic acid.

EXAMPLE VI

The following perfume composition illustrates the use of compositions made by the process of this invention.

Ingredient	Amount (by weight)
Phytol	25 %
Phytyl acetate	10 %
Hexyl cinnamic aldehyde	6 %
Benzyl acetate	30 %
Benzyl alcohol	5 %
Benzyl benzoate	10 %
Indole	0.5%
Hexenyl pentanone	1.5%
Linalool	10 %
δ-Lactone of 5-hydroxy-7-decenoic acid	2 %

produced according to the process of Example II.

The foregoing perfume formulation is an important part of the fragrance of absolute essence of jasmin flower. This perfume composition is incorporated into a soap formulation at the 0.1% level to provide an excellent jasmin scent in the soap.

WHAT WE CLAIM IS:—

1. A process for the production of an unsaturated lactone which comprises reacting 2 - (pentyn - 2' - yl)cyclopentanone with an aliphatic percarboxylic acid at a temperature of from 10°C to 50°C to obtain the δ-lactone of 5 - hydroxy - 7 - decynoic acid.

2. The process of claim 1, wherein the percarboxylic acid is performic acid, peracetic acid or perpropionic acid.

3. The process of claim 1, wherein the percarboxylic acid is peracetic acid and a catalytic amount of a strong proton acid is present.

4. The process of any one of claims 1 to 3, where the reaction is carried out at from 25° to 45°C.

5. The process of any one of claims 1 to 4, wherein an excess up to 40 molar percent of percarboxylic acid is present.

6. A process wherein the δ - lactone of 5 - hydroxy - 7 - decynoic acid obtained according to claim 1 is catalytically hydrogenated with not more than one mole of hydrogen per mol of pentynyllactone to produce the δ - lactone of 5 - hydroxy - 7 - decenoic acid.

7. A process according to claim 1 for the production of the δ - lactone of 5 - hydroxy - 7 - decynoic acid substantially as hereinbefore described with reference to the Examples I to V.

8. The δ - lactone of 5 - hydroxy - 7 - decynoic acid when produced by the process of any one of claims 1 to 7.

9. The δ - lactone of 5 - hydroxy - 7 - decenoic acid when produced by selective hydrogenation of the δ - lactone of 5 - hydroxy - 7 - decynoic acid of claim 8.

10. The δ - lactone of 5 - hydroxy - 7 - decenoic acid when produced by the process of claim 9 substantially as hereinbefore described with reference to Example II.

11. A perfume or fragrance composition containing the compound of claim 9 or claim 10.

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Instrumental analysis shows the formation of substantial quantities of the δ-lactone of 5 - hydroxy - 7 - decyonoic acid.

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The following perfume composition illustrates the use of compositions made by the process of this invention.

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Hexenyl pentanone	1.5%
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δ-Lactone of 5-hydroxy-7-decenoic acid	2 %

produced according to the process of Example II.

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WHAT WE CLAIM IS:—

1. A process for the production of an unsaturated lactone which comprises reacting 2 - (pentyn - 2' - yl)cyclopentanone with an aliphatic percarboxylic acid at a temperature of from 10°C to 50°C to obtain the δ-lactone of 5 - hydroxy - 7 - decynoic acid.

2. The process of claim 1, wherein the percarboxylic acid is performic acid, peracetic acid or perpropionic acid.

3. The process of claim 1, wherein the percarboxylic acid is peracetic acid and a catalytic amount of a strong proton acid is present.

4. The process of any one of claims 1 to 3, where the reaction is carried out at from 25° to 45°C.

5. The process of any one of claims 1 to 4, wherein an excess up to 40 molar percent of percarboxylic acid is present.

6. A process wherein the δ - lactone of 5 - hydroxy - 7 - decynoic acid obtained according to claim 1 is catalytically hydrogenated with not more than one mole of hydrogen per mol of pentynyllactone to produce the δ - lactone of 5 - hydroxy - 7 - decenoic acid.

7. A process according to claim 1 for the production of the δ - lactone of 5 - hydroxy - 7 - decynoic acid substantially as hereinbefore described with reference to the Examples I to V.

8. The δ - lactone of 5 - hydroxy - 7 - decynoic acid when produced by the process of any one of claims 1 to 7.

9. The δ - lactone of 5 - hydroxy - 7 - decenoic acid when produced by selective hydrogenation of the δ - lactone of 5 - hydroxy - 7 - decynoic acid of claim 8.

10. The δ - lactone of 5 - hydroxy - 7 - decenoic acid when produced by the process of claim 9 substantially as hereinbefore described with reference to Example II.

11. A perfume or fragrance composition containing the compound of claim 9 or claim 10.

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