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(54) PROCESS FOR THE PRODUCTION OF PINOCARVEOL

(71) We, INTERNATIONAL FLAVORS & FRAGRANCES INC., a Corporation organised and existing 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:—

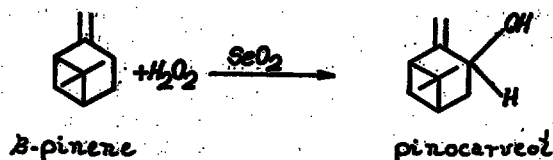
This invention relates to a process for the production of pinocarveol.

In view of the limited availability of natural pine oils and their commercial importance in producing high-grade olfactory agents, synthetic substitutes therefor have become desirable. Pinocarveol, also known as 2(10)-pinen-3-ol, constitutes a significant part of the fragrance impression of pine aromas and is an important constituent of such aromas. Accordingly, a commercially feasible synthesis for this alcohol has been sought.

A number of routes for the production of pinocarveol from various starting materials are available, but they are rather cumbersome and generally uneconomical. For instance, one of the known methods of synthesis of pinocarveol shown by Joshel et al., J.A.C.S. 64, 1008 (1942), employs the oxidation reaction of a quantity of selenium dioxide with β -pinene to form the pinocarveol. However, such a treatment of the β -pinene is uneconomical because of the quantity of the relatively toxic selenium dioxide required and the required purification of the end product to eliminate the toxic selenium compounds.

Briefly, the process of this invention for selectively oxidizing a terpene comprises treating β -pinene with an oxidizing agent, such as hydrogen peroxide and a small quantity of selenium dioxide to obtain pinocarveol. The pinocarveol so formed is then separated from the reaction mass as further disclosed hereinafter.

The pinocarveol obtained according to the present invention can be used as separated from the reaction mixture, or it can be further purified to obtain the substantially pure material. As is known, pinocarveol has a pine-like fragrance and has great utility in the preparation of perfumes and the like, as further described hereinafter. The reaction of the present invention to provide pinocarveol can be illustrated as follows:



β -Pinene widely occurs in nature in the wood and leaf oils of many higher plants, particularly those of the order Coniferae. It can accordingly readily be obtained from certain products obtained from pine trees, and is conveniently obtained by fractionation of turpentine. It is preferred that the β -pinene used in the practice of this invention be relatively pure to obviate the production of unwanted by-products and to facilitate purification of the end product. It has particularly been found that the presence

of other terpenes in the β -pinene produces unwanted by-products and substantially lowers the yield of pinocarveol.

Accordingly, the substantially pure natural levorotatory or $(-)$ β -pinene is preferred. The pure material has an $[\alpha]_D^{20} = -22.4^\circ$, boiling point at 1 atm. of $166.0^\circ \text{C} \pm 1^\circ \text{C}$, $n_D^{20} = 1.4768$, and $d_4^{20} = 0.8667$. Such material is readily obtained by conventional methods, fractional distillation being generally preferable.

When the levorotatory β -pinene is utilized as the starting material, the pinocarveol reaction product is the dextrorotatory *trans*-pinocarveol. This structure is confirmed by its nuclear magnetic resonance (NMR) spectrum and infrared (IR) spectral analysis.

The selenium dioxide utilized in the practice of this process should be substantially free of inorganic oxide impurities. It has been found that the presence of quantities of such oxide impurities in the selenium dioxide produces relatively large quantities of undesired by-products and substantially lowers the yield of pinocarveol. The selenium dioxide is utilized in relatively small, or catalytic, amounts, and it is preferred that substantially less than an equimolar quantity of selenium dioxide be utilized. The quantity of selenium dioxide should not be more than 12% based on the weight of β -pinene used, and it is preferred to use from 0.3 to 12% of the selenium dioxide, based on the β -pinene. Excellent results have been obtained with 3–10% of selenium dioxide. All parts, proportions, percentages and ratios herein are by weight, unless otherwise indicated.

The hydrogen peroxide is furnished to the reaction as an aqueous solution of the peroxide. The yield of the reaction is affected by the quantity of peroxide present in the reaction mixture. If an inadequate amount of the peroxide is utilized, yields are lower and more purification (e.g., removal of β -pinene) is required if a high quality pinocarveol is desired.

It is accordingly desirable to use an amount ranging from semimolar (based on β -pinene) up to 100 molar percent excess. In general, larger quantities of peroxide do not increase the yield of desired products and unnecessarily increase the cost of carrying out the reaction. It is desirable to use from 5 to 60 mol percent aqueous solutions of the hydrogen peroxide.

It is preferred to conduct the reaction at temperatures of from -10°C up to 100°C and it is especially preferred to conduct the reaction at temperatures of from about 25° up to about 80°C . The use of lower temperatures gives rise to long reaction periods required to attain desired yields. The use of higher reaction temperatures provides higher reaction rates, but the reaction can become difficult to control and undesired side reactions occur.

The reaction mass is a two-phase liquid mixture, the β -pinene reactant and pinocarveol being in the organic phase and the hydrogen peroxide and SeO_2 oxidizing agent being in the organic aqueous liquid phase. The intermixing of the two liquid phases during the reaction is facilitated by addition to the reaction mass of a small quantity of non-ionic emulsifier such as Triton X-100, (Triton is a Trade Mark) a straight chain polyalkylene ether manufactured by the Rohm and Haas Co., of Philadelphia, Pa. Triton X-100 is described in detail in U.S. Patent 2,819,996, and is *t*-octyl phenoxypolyethoxyl ethanol, wherein the ethoxyl group is taken from 9 up to 10 times.

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, other than water, can also be incorporated into the reaction mixture, or the reaction can be run in the absence of any such inert vehicle.

The time of reaction varies according to the temperature at which the reaction is carried out, the concentration of hydrogen peroxide, the purity of the ingredients (β -pinene, hydrogen peroxide and selenium dioxide), the completeness of reaction desired, the presence of an inert solvent, if any, and nature of the agitation utilized. The reaction being a two-phase reaction, higher agitation rates and high dispersion of one liquid phase within the second liquid phase give rise to higher reaction rates. It is desirable to conduct the reaction under conditions such that the reaction is complete in a period of from about five up to about ten hours, although satisfactory results are obtained with reaction times of up to about 24 hours.

The reaction is conveniently carried out by adding the aqueous hydrogen peroxide solution slowly over a period of time to the other reaction ingredients, and then holding the reaction mixture under agitation until the desired completeness of reaction is obtained. The progress of the reaction can be readily monitored by analyzing small quantities of the reaction mixture, for example, by the use of gas-liquid chromatography (GLC).

The reaction mass is extracted with aqueous sodium chloride solution to remove water-soluble impurities and the organic layer so obtained can be washed with a slightly acidic reducing material, preferably a salt such as ferrous sulfate for removal of excess hydrogen peroxide. The material can then be dried, filtered, and stripped of any inert solvent used in the reaction or work-up procedure. The pinocarveol product can be further treated, as by oxidation, or it can be purified by conventional techniques such as selective extraction and fractional distillation.

The term "perfume composition" is used herein to mean a mixture of compounds, including, for example, natural oils, synthetic oils, aldehydes, ketones, esters, lactones, other alcohols, and frequently hydrocarbons which are admixed so that the combined odors of the individual components produce a pleasant or 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 or the materials produced by the process 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 olfactory characteristics, but the overall effect of the perfume composition can be more than the sum of the effect of each ingredient. Thus, the individual compound produced by the process of this invention 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 of the composition.

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

The pinocarveol produced by the process of the instant invention 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; bath preparations, such as bath oil and bath salts; hair preparations, such as lacquers, brillian-tines, pomades and shampoos; cosmetic preparations such as creams, deodorants, hand lotions, and sun screens; powders such as talcs, dusting powers 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 and the invention is to be considered restricted thereto only as indicated in the appended claims.

EXAMPLE I

Preparation of Pinocarveol from β -Pinene

Into a five-liter reaction vessel equipped with a stirrer, thermometer, reflux condenser, dropping funnel, and heating mantle are placed the following ingredients:

β -Pinene	1000 g.
Water	1000 g.
Selenium Dioxide	10 g.

Through the dropping funnel, 1130 ml. of a 30% aqueous solution of hydrogen peroxide is added during one hour, while the temperature of the reaction mass is maintained in the range of 19°C to 22°C. The reaction mass is then heated to 40°C and maintained with stirring at that temperature for eight hours. At this stage, GLC analysis indicates that most of the β -pinene has reacted (GLC conditions: 6' $\times$ 1/8" stainless steel column packed with 20% "Carbowax 20 M" (Carbowax is a Trade Mark) polyoxyethylene glycol coated on "Chromosorb" (Chromosorb is a Trade Mark) diatomaceous earth treated with dimethyl chlorosilane; column temp. = 150°C; flow rate, 30 ml./min.; chart speed, 1.25"/min.).

The reaction mass exists in two phases: an aqueous phase and an organic phase. The mass is transferred to a separatory funnel, and the lower aqueous phase is separated from the upper organic layer. The organic layer is then washed with three volumes

of saturated NaCl solution and with a dilute solution of ferrous sulfate to reduce the hydrogen peroxide content to less than 0.05%.

The washed mixture is then distilled with a packed fractionation column (1:1 reflux ratio) at 62–68°C and 2 mm. Hg pressure. The distillate has a refractive index (at 20°C) of 1.4955, an average specific rotation of +60°, and a purity of 99%. The IR and NMR analyses indicate that the product has the chemical structure of pinocarveol. The amount of pinocarveol produced is 403 g. This is a conversion of 36%, based upon the 100% β -pinene. As used herein, "conversion" is the percentage of product based upon the total amount of pure β -pinene fed to the reaction, and "yield" is the percentage of product based upon unrecovered β -pinene.

Similar results are obtained at reaction temperatures of 20°C, 30°C, and 50°C and using H_2O_2 concentrations of 5, 15, 40 and 50%.

EXAMPLE II

Preparation of Pinocarveol from β -Pinene

Into a 12-liter reaction vessel equipped with a stirrer, thermometer, reflux condenser, dropping funnel and heating mantle are introduced the following ingredients:

β -Pinene	2000 g.
Water	2000 g.
Selenium Dioxide	10 g.
"Triton X-100" Emulsifier	7 ml.

Through the dropping funnel 2260 ml. of a 30% aqueous solution of hydrogen peroxide is added over a period of 2-1/2 hours, while the temperature of the reaction mass is maintained at 22–33°C. After eight hours of continuous agitation, the reaction mass is heated to 40°C and maintained at this temperature for another 12 hours.

At this stage, GLC analysis shows that most of the β -pinene has reacted. A sample of the aqueous phase reveals a 2.43% concentration of peroxide. The organic phase is thereupon washed with four volumes of saturated sodium chloride solution. The washings are extracted with benzene, and the benzene extracts and the organic phase are then combined.

The benzene is evaporated and the remaining organic material is distilled without fractionation. The distillate consists of a forerun of β -pinene (87 g.) followed by 1160 g. of pinocarveol having a purity of 87.5%, a boiling point range of 45–51°C at 0.8 mm. Hg pressure, $[\alpha]_D^{20} = +46.06^\circ$, and $n_D^{20} = 1.4959$. The conversion is 51.5%.

EXAMPLE III

Into a 12-liter reaction vessel equipped with a stirrer, thermometer, dropping funnel, and reflux condenser is introduced 5440 g. (38.2 moles) of 93.5% pure β -pinene. The contents of the vessel are heated to 60°C and 27.2 g of selenium dioxide is added. An exothermic reaction ensues and after it has subsided the reaction mass is stirred for one-half hour at 60°C. To the stirred mixture is then added 2693 g. (40 moles) of 50.5% hydrogen peroxide.

The course of the reaction is monitored by determining the quantity of hydrogen peroxide in the water layer after 1, 2, and 3 hours. The aqueous phase is then separated from the organic phase and the organic phase is washed twice with saturated aqueous sodium chloride solution, once with sodium carbonate solution, and finally with saturated aqueous sodium chloride solution.

The washings and washed organic solutions are then worked up and distilled as in Example I to yield the pinocarveol.

When the procedures set forth in Examples I, II and III are duplicated using oxides of tungsten, molybdenum, or vanadium, no significant yields of pinocarveol are obtained. Similarly, treatment of terpenes other than β -pinene, for instance, α -pinene, cedrene, and limonene, with hydrogen peroxide and small quantities of selenium dioxide does not give rise to allylic hydroxylation, as is the case with β -pinene.

It will also be understood by those skilled in the art that other surface active agents can be used as emulsifiers in the practice of this invention. The emulsifiers should be substantially inert under the reaction conditions, and nonionic polyglycols are particularly preferred.

EXAMPLE IV
Perfume Composition

The following mixture is prepared:

	<i>Ingredient</i>	<i>Grams</i>	
5	Borneol	50	5
	Bornyl Acetate	100	
	Cedarwood	100	
	Lavender, Spike	200	
	Methyl Anthranilate	50	
10	Rosewood	100	10
	Terpineol	200	
	Pinocarveol produced in Example I	50	
	Terebene	50	
	Musk Residues	30	
15	Coumarin	20	15

The foregoing perfume formulation is an important part of the fragrance of absolute essence of pine needle oil. This perfume is incorporated into a soap at the 0.1% level to provide an excellent pine scent in the soap. The pinocarveol gives to this fragrance a natural and distinctly pine-like top note.

20 Further quantities of pinocarveol are prepared by reacting β -pinene with hydrogen peroxide and a small amount of selenium dioxide as set forth in Table I. The pinocarveol so produced is satisfactory for use in perfume compositions. 20

TABLE I

Example	β -Pinene (93%)		H_2O_2 (50%)		SeO_2		Temperature $^{\circ}C$		Recovered β -Pinene		Pinocarveol Produced		Conversion		Yield	
	g.	moles	g.	g.	g.	g.	$^{\circ}C$	$^{\circ}C$	g.	moles	g.	moles	%	%	%	%
IV	1813	12.4	897.7	9.06	786	5.4	40	40	471	3.1	25.0	44.4				
V	1813	12.4	897.7	54.4	766	5.0	40	40	649	4.3	34.7	63.1				
VI	1813	12.4	897.7	163.2	276	1.9	40	40	1078	7.1	57.3	67.6				
VII	1813	12.4	897.7	163.2	330	2.3	60	60	1038	6.8	54.8	67.5				
VIII	5440	37.2	2693.0	54.4	3532	24.2	60	60	1091	7.2	19.4	55.5				
IX	1813	12.4	897.7	217.6	—	—	40	40	1125	7.4	59.7	59.7				
X	1813	12.4	897.7	108.8	232	1.6	20	20	742	4.9	39.5	45.5				
XI	1813	12.4	897.7	163.2	103	0.7	20	20	1084	7.1	57.3	60.7				
XII	1813	12.4	897.7	108.8	416	2.8	40	40	917	6.0	48.4	62.5				
XIII	1813	12.4	1122.1	108.8	382	2.6	40	40	994	6.5	52.9	66.3				
XIV	1813	12.4	673.3	108.8	594	4.1	40	40	859.5	5.7	46.0	62.6				
XV	1813	12.4	448.8	108.8	416	2.8	40	40	683	4.5	36.3	46.8				

WHAT WE CLAIM IS:—

1. A process for oxidizing a terpene which comprises reacting β -pinene with hydrogen peroxide and a small amount of selenium dioxide to produce pinocarveol.
- 5 2. The process of Claim 1 wherein the amount of selenium dioxide is not greater than 12 per cent, based on the weight of β -pinene. 5
3. The process of Claim 1 wherein the amount of selenium dioxide is from 0.3% to 12%, based on the weight of β -pinene.
4. The process of Claim 1 wherein the amount of selenium dioxide is from 3% to 10% based on the weight of β -pinene.
- 10 5. The process of Claim 1 wherein the temperature is from -10°C to 100°C . 10
6. The process of Claim 1 wherein from a semimolar quantity to a 100 molar per cent excess of hydrogen peroxide is used, based upon the amount of β -pinene.
7. The process of Claim 1 wherein the hydrogen peroxide is an aqueous solution containing from five to about 60 mole percent of hydrogen peroxide.
- 15 8. The process of Claim 1 wherein the pinocarveol is recovered by distillation. 15
9. The process of Claim 1 wherein an emulsifier is additionally present.
10. A process for the production of pinocarveol substantially as hereinbefore described in any of Examples I to III herein.
11. Pinocarveol when produced by the process of any one of Claims 1 to 10.
- 20 12. A composition comprising the pinocarveol of Claim 11. 20

For the Applicants.

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