United States Patent Office 3,050,532 Patented Aug. 21, 1962

3,050,532

TWO STAGE OXIDATION OF SCLAREOL

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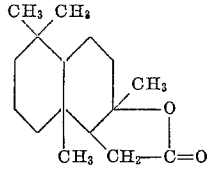
No Drawing. Filed June 19, 1959, Ser. No. 821,345
7 Claims. (Cl. 260—343.3)

This invention relates to oxidation and has for an object the provision of a process for oxidizing sclareol to form decahydro - 3a,6,6,9a - tetramethylnaphtho[2,1-b]-furan-2(1H)-one.

As well known in the art, the terpene-like compound sclareol is known to be a component of clary sage (*Salvia sclarea*) and it may be obtained from clary sage by extraction of the flowering parts of the plant with a suitable solvent such as hexane. It is also known, as set forth in the copending application of Joseph N. Schumacher, Serial No. 708,987, filed January 15, 1958, now Patent No. 2,905,576, issued September 22, 1959, that sclareol may be converted to decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan - 2(1H) - one (compound I) which has the following structural formula:



(I)

This compound I as disclosed in said Schumacher application has been found to be particularly useful for incorporation into domestic tobaccos in order to increase the odor and flavor of the tobacco smoke.

Accordingly, an object of this invention is the provision of a process for oxidizing sclareol to produce compound I whereby high yields of compound I are obtainable.

A further object of this invention is the provision of a process for producing compound I from sclareol which is simple and safe to carry out in a commercial scale operation.

A still further object of this invention is the provision of a sclareol oxidation process carried out under conditions whereby the major proportion of the sclareol is oxidized to produce compound I and only small amounts of undesired reaction products are produced.

Further and additional objects will appear from the following description and the accompanying claims.

Thus in accordance with one embodiment of this invention, compound I is produced from sclareol in high yields when the oxidation is carried out in two separate steps. In the first step the sclareol is partially oxidized with an alkali metal permanganate under alkaline conditions and then the oxidation of the reaction mixture is completed in a second step under acid conditions. In the second step either an alkali metal permanganate or chromic acid may be used as the oxidizing agent. Furthermore, it has been found that about six moles of permanganate or chromic acid are theoretically required to oxidize sclareol whereby to produce the desired compound I. Usually some excess of the oxidizing agent is employed. Thus it is preferred in accordance with one embodiment of this invention that the molar ratio of sclareol to permanganate in the first step of the oxidation should be between about 1 to 2 and about 1 to 5 and then in the second step the balance of the oxidizing agent is employed so that the total amount of oxidizing agent

used in both steps corresponds to between about 6 to 8 moles of the oxidizing agent per mole of sclareol.

Sclareol and its related oxidation products are insoluble in water and perhaps for this reason organic solvents have been employed in carrying out reactions of this general type. However, the alkali metal salts, such as the potassium salts, of certain acidic intermediate oxidation products are water soluble and in accordance with this invention it has been discovered that water may be very effectively used as the menstruum for carrying out both steps (and particularly the first step) of the oxidation. By utilizing water many operating hazards are avoided which are known to be incident to carrying out oxidation procedures in the presence of organic solvents, such as acetone, alcohols, ether or the like.

For a more complete understanding of this invention, reference will now be made to examples for preparing compound I by the two step oxidation of sclareol.

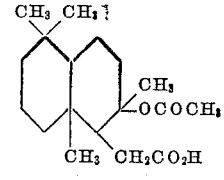
Example I

To 205.6 g. (0.67 mole) of sclareol and 1435 ml. of water in a jacketed reaction vessel is added 379.5 g. of 2.4 moles) of $KMnO_4$ over three hours. The reaction mixture is agitated vigorously during the addition. The reaction temperature is maintained between 30° and 35° C. and the reaction medium is alkaline during this stage of the oxidation due to the KOH liberated in the reaction. Agitation is continued for an additional two hours and the first step of the reaction is completed.

To the partially oxidized reaction mixture is added 1435 ml. of glacial acetic acid. With vigorous agitation, an adidtional 254 g. (1.6 moles) of $KMnO_4$ is added together with 104 ml. of glacial acetic acid over a two-hour period. The temperature is maintained over the range 8–10° C. Stirring is continued for an additional 20 to 30 minutes at the same temperature. The mixture is then allowed to stand at room temperature for 15 hours. Stirring is resumed and continued for two hours at room temperature. At this stage the second oxidation step is completed.

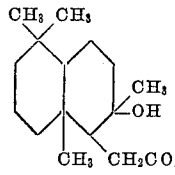
A liter of water is then added and the mixture is acidified to pH 2 with H_2SO_4. Normally, one liter of 7 N H_2SO_4 is required. The mixture is cooled to 10° C. and SO_2 is added to convert the precipitated MnO_2 to the water soluble $MnSO_4$. The SO_2 is added over a 70 minute period and at a temperature below 15° C.

The solid product dispersed in the aqueous medium at this stage comprises a mixture of compound I and a substantial amount of an acetoxy acid (2-acetoxy-2,5,5,8a-tetramethyldecahydro naphthalene acetic acid) having the structure:



The organic mixture is separated from the aqueous phase by filtration and is dried in the air to constant weight. The dried product is then hydrolyzed or saponified under reflux over 3 hours in a solution consisting of 110 g. of KOH, 150 ml. of water, and 1500 ml. of methanol. The methanol is removed by distillation at reduced pressure. The residue from the distillation is dissolved in 2 liters of water and the solution is washed with 2500 ml. of hexane. The washed aqueous layer is then acidified with 6 N H_2SO_4 to a pH of 2. The hydroxy acid (2-hy-

droxy-2,5,5,8a-tetramethyldecahydro naphthalene acetic acid) which precipitates has the formula



and is isolated by filtration. The solid is dried in the air and is then heated at 135–145° C. for 1.5 to 2 hours to convert it to the desired lactone product (compound I). The lactone is purified by crystallization from hexane. The yield of pure product by this process has averaged 108 g.; yield, basis starting sclareol, 65%; melting point, 123–124° C.

Example II

In this example the process is essentially the same as disclosed in Example I except that an equivalent amount of chromic acid is substituted for the permanganate employed in the acid oxidizing step. Essentially the same yields of compound I are obtained.

Thus it will be apparent that a simple process has been devised for preparing high yields of compound I from sclareol. The process is carried out in two oxidation steps but it is not required to subject the product from the first step to any purification and the entire reaction mixture from the first step is treated directly in the second oxidizing step. The alkali metal permanganate in the first step and when used in the second step may be either sodium or potassium permanganate, but other salts of permanganic acid may be used, such as calcium, magnesium or other salt-forming cations. The temperatures employed in the first step may be between about 0° and 50° C., preferably about 30° to 40° C., and in the second step may be between about 0° and 20° C., preferably about 0° to 10° C. In the second step acetic or propionic acid may be used to provide the acid conditions; however, any suitable nonoxidizing acid may be used.

While particular embodiments of this invention are shown above, it will be understood, of course, that the invention is not to be limited thereto, since many modifications may be made, and it is contemplated, therefore, by the appended claims, to cover any such modifications as fall within the true spirit and scope of this invention.

We claim:

1. A process of preparing the compound decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan - 2(1H) - one which comprises the first step of intimately contacting an aqueous dispersion of sclareol with an alkali metal permanganate oxidizing agent under alkaline oxidizing conditions to partially oxidize the sclareol, the second step of acidifying the resulting aqueous reaction mixtures and intimately contacting it with an oxidizing agent selected from the group consisting of a permanganate and chromic acid under acid oxidizing conditions whereby the oxidation is completed, separating a solid mixture of said compound and an intermediate 2-acetoxy-2,5,5,8a-tetramethyldecahydronaphthalene acetic acid from the reaction medium and thereafter subjecting the last mentioned mixture successively to saponification, acidifying and dehydrating conditions whereby to form said compound.

2. The process recited in claim 1 in which chromic acid is the oxidizing agent used in the second step.

3. The process recited in claim 1 in which a permanganate is the oxidizing agent used in the second step.

4. A process of preparing the compound decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan - 2(1H) - one which comprises the first step of intimately contacting an aqueous dispersion of sclareol with an alkali metal permanganate oxidizing agent under alkaline oxidizing conditions at a temperature between about 0° and about 50° C. to partially oxidize the sclareol, the second step of acidifying the resulting aqueous reaction mixture and intimately contacting it with an oxidizing agent selected from the group consisting of a permanganate and chromic acid under acid oxidizing conditions at a temperature between about 0° and about 20° C. whereby the oxidation is completed, separating a solid mixture of said compound and an intermediate 2-acetoxy-2,5,5,8a-tetramethyldecahydronaphthalene acetic acid from the reaction medium and thereafter subjecting the last mentioned mixture successively to saponificaion, acidifying and dehydrating conditions whereby to form said compound.

5. The process recited in claim 4 wherein the molar ratio of sclareol to permanganate in said first step is between about 1 to 2 and about 1 to 5 and the total molar ratio of sclareol to the total amount of oxidizing agents employed in both said first and second steps being between about 1 to 6 and about 1 to 8.

6. The process of preparing the compound decahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan - 2(1H) - one which comprises the first step of intimately contacting an aqueous dispersion of sclareol with an alkali metal permanganate oxidizing agent under alkaline oxidizing conditions to partially oxidize the sclareol, the second step of acidifying the resulting aqueous medium and intimately contacting it with an oxidizing agent selected from the group consisting of a permanganate and chromic acid under acid oxidizing conditions whereby the oxidation is completed, further acidifying the resulting aqueous reaction mixture if necessary whereby a solid comprising manganese dioxide, said compound and an intermediate 2-acetoxy-2,5,5,8a-tetramethyldecahydronaphthalene acetic acid is dispersed in the mixture, treating the aqueous mixture with sulfur dioxide to convert the manganese dioxide to the water soluble salts of manganese, separating the remainder of said solid from the sulfur dioxide-treated mixture, and subjecting the separated substances successively to saponification, acidifying and dehydrating conditions whereby to form said compound.

7. The process recited in claim 6 wherein the first oxidizing step is carried out at a temperature between about 0° and about 50° C. and wherein the second oxidizing step is carried out at a temperature between about 0° and about 20° C.

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