United States Patent Office 3,268,589 Patented August 23, 1966

3,268,589

PROCESS FOR PREPARING 4-(2-BUTENYLIDENE)-3,5,5-TRIMETHYL-2-CYCLOHEXENE-1-ONE

Ralph Lawrence Rowland, Winston-Salem, N.C., assignor to R. J. Reynolds Tobacco Company, Winston-Salem, N.C., a corporation of New Jersey

No Drawing. Original application May 29, 1963, Ser. No. 283,970, now Patent No. 3,211,157, dated Oct. 12, 1965. Divided and this application Dec. 8, 1964, Ser. No. 416,909

3 Claims. (Cl. 260—586)

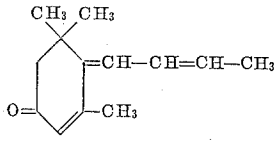
This application is a division of my copending application Serial No. 283,970, filed May 29, 1963, now Patent No. 3,211,157, which in turn is a continuation-in-part of my prior United States application Serial No. 209,778, filed July 13, 1962, now abandoned.

This invention relates to tobacco and has for an object the provision of a tobacco composition having an improved aroma and flavor. The invention relates specifically to the synthesis of a tobacco additive.

It is well known in the tobacco art that the domestic tobaccos which are exemplified by burley, Maryland, flue-cured, bright leaf or Virginia tobaccos are low in flavor as compared with so-called oriental or aromatic tobaccos which are imported from Turkey, Greece, Bulgaria, Yugoslavia, Rhodesia and Russia. Accordingly, it has been common practice in the tobacco industry to prepare blends of domestic and oriental tobaccos in order to provide cigarettes which have desired flavor and aroma characteristics. Accordingly, it is a further object of this invention to provide a domestic tobacco which has an enhanced flavor and aroma.

An additional object of this invention is to provide a tobacco which has been treated in such a manner as to impart a desired peppery spicy odor which is pleasing to the smoker.

In accordance with one embodiment of this invention a domestic tobacco is provided to which has been added a small amount of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one. The above chemical, herein referred to as Compound I, may be represented by the following formula:



Several isomeric forms of the above Compound I exist with both the cis and trans isomers being eminently suited, either separately or in mixtures for addition to tobacco to impart a pleasing flavor thereto. Accordingly, Compound I as used herein includes the cis and trans isomers as well as mixtures thereof.

The chemical Compound I indicated above can be synthesized from dehydroionone which is known to the art. In this synthesis dehydroionone is reduced to the corresponding alcohol, β-dehydroionol, which by treating with acids undergoes rearrangement to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol. This rearrangement product is then oxidized to form Compound I.

A detailed description of the synthesis of Compound I is as follows:

EXAMPLE A

A. *Synthesis of dehydroionol [4-(2,6,6-trimethyl-1,3-cyclohexadien-1-yl)-3-buten-2-ol].*—To a solution of 16 grams of dehydroionone in 70 milliliters of methyl alcohol was added a solution of 1.5 grams of sodium borohydride in 7 milliliters of water. After one hour, a mixture of 200 milliliters of water and 15 milliliters of 2 N sulfuric acid was added to the reaction mixture. The resultant acid mixture was extracted with two 100-milliliter portions of pentane. The combined pentane extracts were washed with two 50-milliliter portions of water. Concentration of the pentane solution yielded 14–15 grams of dehydroionol characterized by its infrared spectrum accompanied by small amounts of isomerized compounds which result from acidification during the processing procedure.

B. *Acid rearrangement of dehydroionol to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol.*—To a cold solution of 30 grams of crude dehydroionol in 700 milliliters of acetone was added a mixture of 240 milliliters of water and 80 milliliters of 2 N sulfuric acid. The mixture was kept at a temperature of 5–25° for 16 to 48 hours, after which time it was added to 400 milliliters of 5 percent sodium bicarbonate solution. The resultant mixture was extracted with two 300-milliliter portions of pentane. The pentane extracts were washed with two 200-milliliter portions of water. The pentane solutions were chromatographed on silicic acid, using pentane-ether mixtures, to separate dehydroionol from the rearrangement product. The procedure yields a 45–60 percent conversion to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol with 20–25 percent recovery of the starting material (dehydroionol which can be utilized in subsequent rearrangement reactions). The rearrangement product which is readily distinguished from dehydroionol by its infrared absorption, is a mixture of cis-trans isomers.

C. *Manganese dioxide oxidation of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol.*—To a solution of 15 grams of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol in 750 milliliters of 85:15 pentane-ether solution was added 90 grams of activated manganese dioxide and the mixture was stirred at room temperature for 16 to 30 hours. The manganese dioxide was removed by filtration and the filtrate was chromatographed using silicic acid. The desired products were separated by collection of the fractions eluted by pentane-ether mixtures. A mixture of cis-trans isomers of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one was obtained in 70 percent yield. The mixture boiled at 75° C. at 0.2 millimeter pressure and at 62° C. at 0.095 millimeter pressure.

EXAMPLE B

To a solution of 10.1 grams of dehydroionol in 200 milliliters of acetone was added 80 milliliters of 0.25 N hydrochloric acid. The mixture was kept at 24° C. for 5 hours, after which time it was added to 200 milliliters of 5 percent sodium bicarbonate solution. The resultant mixture was extracted with 300 milliliters of ether. The ether extract was washed with two 200-milliliter portions of water after which it was dried over anhydrous magnesium sulfate for 3 days. The residue from concentration of the dried ethereal extract was chromatographed on silicic acid. The procedure yielded a 40 percent conversion to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol and a 46 percent recovery of dehydroionol. The 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol is then treated as in Example A.

EXAMPLE C

Chromic oxide-pyridine oxidation of 4-(2-bentenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol.—To a suspension prepared from the addition of 20 grams of chromic oxide to 190 milliliters of pyridine cooled in an ice bath was added 8.5 grams of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol. The mixture was stirred for 2 hours

after which it was diluted with 900 milliliters of water and was extracted with two 300-milliliter portions of pentane. The combined pentane extracts were washed with three 200-milliliter portions of water, with 200 milliliters of 2 N hydrochloric acid, and finally with 200 milliliters of water. The pentane extracts were subjected to chromatography using silicic acid to give 3.6 grams (42 percent yield) of 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one (I).

The mixture of cis-trans isomers comprising Compound I can be employed in tobacco as a flavoring material. Nevertheless, separation of the isomers comprising the mixture has been accomplished by vapor phase chromatography and characterized as follows:

Isomer 1

The infrared spectrum showed absorption at 6.03(s), 6.13(sh), 6.25(m), 6.9(m), 7.06(m), 7.32(s), 7.62(s), 7.9(m), 8.0(m), 8.4(w), 8.86(w), 9.0(w), 9.7(w), 10.1(w), 10.3(w), 10.82(m), 11.0(m), 11.3(m), 11.85(w), 12.1(w) and 13.75(m) μ.

Maximum ultraviolet absorption occurred at 320 mμ, ϵ 17,000 and 234 mμ, ϵ 12,000. The NMR spectrum showed peaks at 8.76 p.p.m. (6 protons, geminal dimethyl), 8.09 and 8.22 p.p.m. (3 protons, $C\underline{H}_3CH{=}C$), 7.72 p.p.m. (3 protons, $C\underline{H}_3C{=}CCO$), 7.65 p.p.m. (2 protons, $C\underline{H}_2CO$), and 3.35–3.95 p.p.m. (4 olefinic protons).

The dinitrophenylhydrazone melted at 156–158°.

Isomer 2

The infrared spectrum showed peaks at 6.03(s), 6.10(sh), 6.28(m), 6.9(s), 7.10(w), 7.28(s), 7.56(s), 7.82(s), 7.96(m), 8.4(w), 8.85(w), 9.0(w), 9.73(w), 10.1(w), 10.35(s), 10.78(m), 11.0(m), 11.3(w), 11.9(w), 12.1(w) and 13.75(m) μ. Maximum ultraviolet absorption occurred at 320 mμ, ϵ 13,000 and 231 mμ, ϵ 9,100. The NMR spectrum showed peaks at 8.80 p.p.m. (6 protons, geminal dimethyl), 8.08 and 8.20 p.p.m. (3 protons, $C\underline{H}_3CH{=}C$), 7.71 p.p.m. (5 protons, $C\underline{H}_3C{=}CCO$ and $C\underline{H}_2CO$), and 3.2–4.3 p.p.m. (4 olefinic protons).

Anal.—Calcd. for $C_{13}H_{18}O$: C, 82.05; H, 9.53; mol. wt., 190. Found: C, 81.98, 81.92; H, 9.58, 9.66; mol. wt. (mass spectrum), 190.

The dinitrophenylhydrazone of isomer 2 melted at 156–157°. *Anal.*—Calcd. for $C_{19}H_{22}N_4O_4$: C, 61.61; H, 5.99. Found: C, 61.73; H, 6.07.

Isomer 3

The infrared spectrum of isomer 3 showed absorption at 6.02(s), 6.14(sh), 6.32(s), 6.94(m), 7.34(s), 7.54(w), 7.65(m), 7.85(s), 7.93(sh), 8.05(sh), 8.4(m), 9.02(w), 9.75(w), 10.08(w), 10.37(m), 11.23(m), 12.1(w) and 13.8(m) μ. Maximum ultraviolet absorption of an ethanol solution occurred at 320 mμ, ϵ 25,500 and 231 mμ, ϵ 9,100. The NMR spectrum showed bands at 8.63 p.p.m. (6 protons, geminal dimethyl), 8.06 and 8.18 p.p.m. (3 protons, $C\underline{H}_3CH{=}C$), 7.83 p.p.m. (3 protons,

$C\underline{H}_3C{=}CCO$)

7.57 p.p.m. (2 protons, $C\underline{H}_2CO$), and 3.2–4.05 p.p.m. (4 olefinic protons).

The dinitrophenylhydrazone melted at 147–149°.

Isomer 4

The infrared spectrum showed absorption at 6.05(s), 6.13(s), 6.30(s), 6.92(s), 7.25(s), 7.35(s), 7.45(s), 7.65(m), 7.8(s), 7.93(s), 8.03(m), 8.36(m), 9.0(m), 9.7(m), 10.08(m), 10.37(s), 10.75(w), 11.2(m) and 12.1(w) μ. Maximum ultraviolet absorption in ethanol occurred at 320 mμ, ϵ 23,000 and at 230 mμ, ϵ 8,100. The NMR spectrum showed peaks at 8.66 p.p.m. (6 protons, geminal dimethyl), 8.07 and 8.20 p.p.m. (3 protons, $C\underline{H}_3CH{=}C$), 7.93 p.p.m. (3 protons, $C\underline{H}_3C{=}CCO$), 7.67 p.p.m. (2 protons, $C\underline{H}_2CO$), and 3.2–4.2 p.p.m. (4 olefinic protons).

Anal.—Calcd. for $C_{13}H_{18}O$: C, 82.05; H, 9.53; mol. wt., 190. Found: C, 81.78, 81.69; H, 9.55, 9.42; mol. wt. (mass spectrum), 190.

The dinitrophenylhydrazone melted at 170–172°. *Anal.*—Calcd. for $C_{19}H_{22}N_4O_4$: C, 61.61; H, 5.99. Found: C, 61.52; H, 6.08.

From this data it is evident that these isomers are represented by the formula given in column 1 of this application.

In accordance with this invention, the designated Compound I is usually added to a domestic tobacco in amounts to provide a tobacco in which is dispersed about 0.001 to about 1.0 percent by weight of the additive. Preferably the amount of additive is between about 0.005 and about 0.03 percent by weight in order to form a domestic tobacco having a desired flavor and aroma. The preferred percentages may be somewhat less, however, if other flavorants imparting a desired aroma are also employed. The additive may be applied in any suitable manner and preferably in the form of a liquid solution or suspension by spraying, dipping or otherwise. The additive may be incorporated at any step in the treatment of the tobacco but is preferably added after aging, curing and shredding and before the tobacco is formed into cigarettes. Likewise, it will be apparent that only a portion of the domestic tobacco need be treated and the thus treated tobacco may be blended with other tobaccos before the cigarettes are formed. In such cases the tobacco treated may have the additive in excess of the amounts above indicated so that when blended with other tobaccos the final product will have the percentage within the indicated range.

In accordance with one specific example of this invention, an aged, cured and shredded burley tobacco is sprayed with a one percent ethyl alcohol solution of the above indicated compound in an amount to provide a tobacco composition containing 0.01 percent by weight of the additive on a dry basis. Thereafter the alcohol is removed by evaporation and the tobacco is manufactured into cigarettes by the usual techniques. The cigarette when treated as indicated has a desired and pleasing peppery spicy odor which is detectable to some extent when the cigarette is in its package but which is particularly detectable and pleasing in the main and side smoke streams when the cigarette is smoked.

It will be particularly apparent that the manner in which the additive is applied to the tobacco is not particularly important since, as indicated, it may be done in the form of spraying or dipping, utilizing suitable suspensions or solutions of the additive. Thus water or volatile organic solvents, such as alcohol, ether, acetone, volatile hydrocarbons and the like, may be used as the carrying medium for the additive while it is being applied to the tobacco. Also, other flavor and aroma producing additives, such as those disclosed in Jones United States Patent No. 2,766,145 and Schumacher United States Patent No. 2,978,365, may be incorporated into the tobacco with the additives of this invention.

While this invention is particularly useful in the manufacture of cigarette tobacco, it is also suitable for use in connection with the manufacture of pipe tobacco, cigars and other tobacco products formed from sheeted tobacco dust or fines which are well known to the art. Likewise, the additive of the invention being appreciably volatile can be incorporated with materials such as filter tip materials, seam paste, packaging materials and the like which are used along with tobacco to form a product adapted for smoking.

Those modifications and equivalents which fall within the spirit of the invention and the scope of the appended claims are to be considered part of the invention.

I claim:

1. A process of preparing the compound 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one which comprises contacting dehydroionone under reducing conditions with a reducing agent selected from the group consisting of

lithium aluminum hydride and sodium borohydride to form dehydroionol, contacting the so-formed dehydroionol with a dilute mineral acid to convert the dehydroionol to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol and then contacting the said 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol with an oxidizing agent selected from the group consisting of chromic oxide in pyridine and manganese dioxide to form 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one.

2. A process of preparing the compound 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one which comprises contacting dehydroionone under reducing conditions with a reducing agent selected from the group consisting of lithium aluminum hydride and sodium borohydride to form dehydroionol, contacting the so-formed dehydroionol with a dilute mineral acid to convert the dehydroionol to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol and then contacting the said 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol with manganese dioxide to form 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one.

3. A process of preparing the compound 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one which comprises

contacting dehydroionone under reducing conditions with a reducing agent selected from the group consisting of lithium aluminum hydride and sodium borohydride to form dehydroionol, contacting the so-formed dehydroionol with dilute sulfuric acid to convert the dehydroionol to 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol and then contacting the said 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-ol with an oxidizing agent selected from the group consisting of manganese dioxide and chromic oxide in pyridine to form 4-(2-butenylidene)-3,5,5-trimethyl-2-cyclohexen-1-one.

References Cited by the Examiner

Gaylord, "Reduction With Complex Metal Hydrides," pp. 172 and 290 (1956), QD63 R4 G3.

Oroshnik et al.: J. Am. Chem. Soc., vol 74, pp. 295–297 (1952).

Fieser et al.: "Steroids," pp. 206 and 224 (1959).

LEON ZITVER, *Primary Examiner.*

M. JACOB, *Assistant Examiner.*