

[54] **PRECURSOR OF SESQUITERPINE  
DERIVATIVES OF THE EREMOPHILANE  
GROUP**

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[22] Filed: **June 21, 1971**

[21] Appl. No.: **154,960**

[30] **Foreign Application Priority Data**

June 19, 1970 Netherlands ..... 7009040

[52] U.S. Cl. .... **260/586 R, 252/522, 260/586 C,**  
260/631.5, 260/675.5

[51] Int. Cl. .... **C07c 49/44**

[58] **Field of Search** ..... 260/587

[56] **References Cited**

## UNITED STATES PATENTS

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[57] **ABSTRACT**

Sesquiterpene derivatives of the eremophilane group  
e.g.,  $\alpha$ -vetivone and nootkatone which are useful  
aroma chemicals are prepared from 5,6-dimethyl-8-  
isopropyl-tricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one.

**1 Claim, 23 Drawing Figures**

FIG. 1.

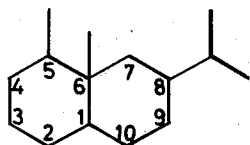


FIG. 2.

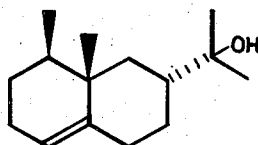


FIG. 3.

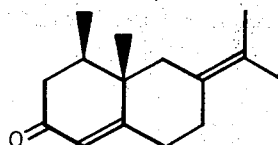


FIG. 4.

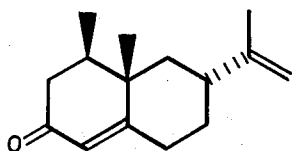


FIG. 5.

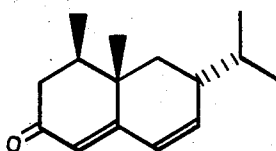


FIG. 6.

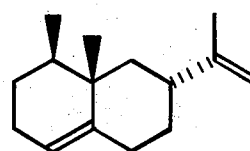
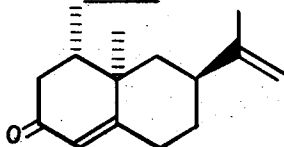


FIG. 7.



REACTION 1.

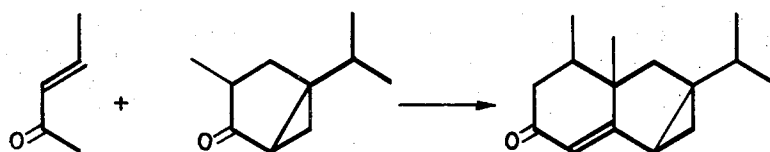


FIG. 9.

FIG. 10.

FIG. 8.

REACTION 2.

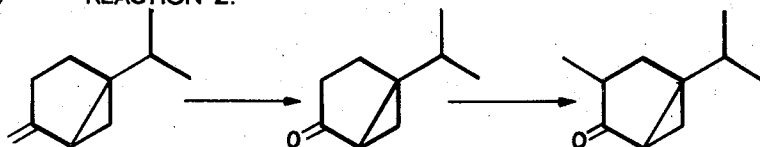


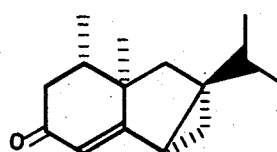
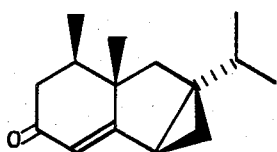
FIG. 11.

FIG. 12.

FIG. 10.

FIG. 13.

FIG. 14.



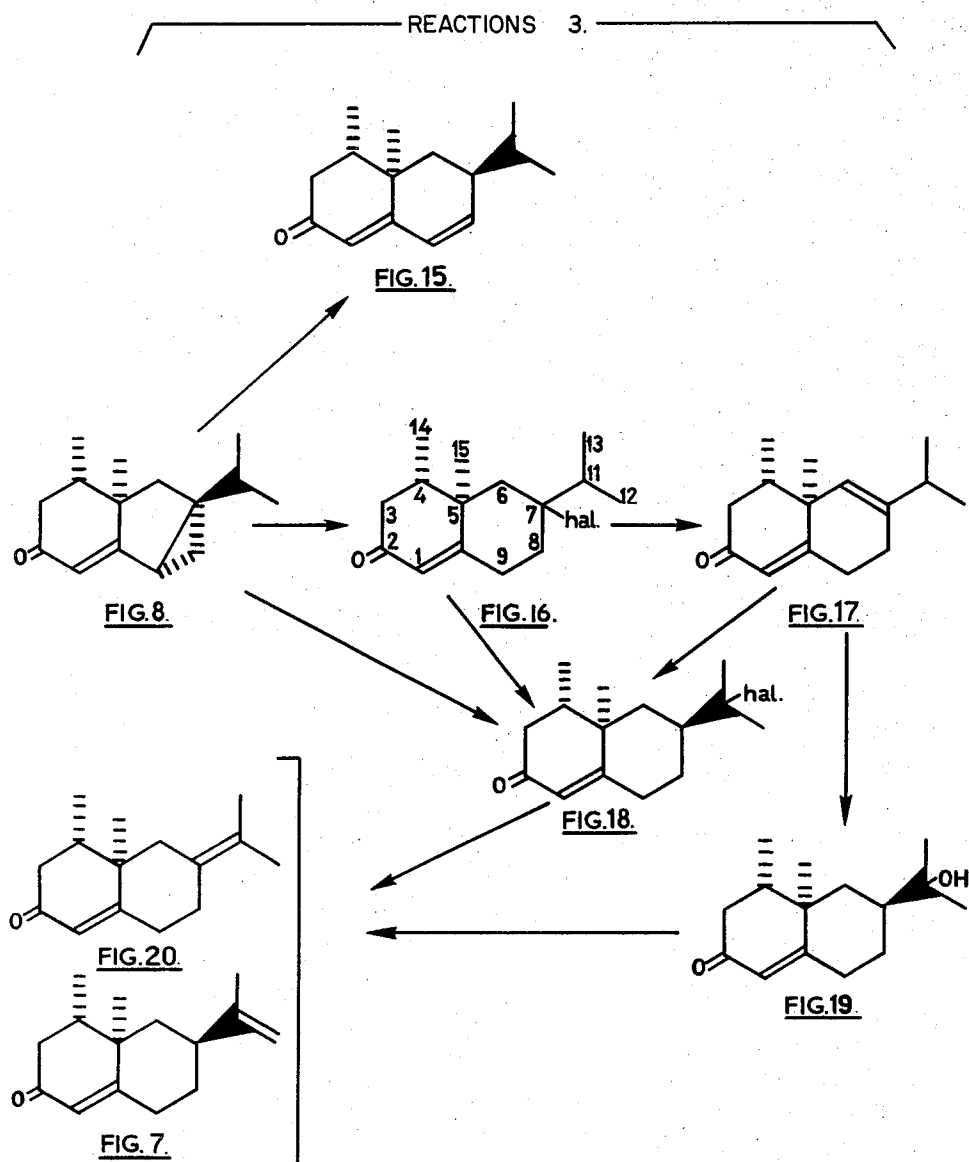
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# PRECURSOR OF SESQUITERPINE DERIVATIVES OF THE EREMOPHILANE GROUP

The invention relates to product and process for the preparation of sesquiterpene derivatives of the eremophilane group.

Sesquiterpenes having an eremophilane skeleton are characterized by a bicyclo [4.4.0] decane structure, as shown in the formula of FIG. 1, with methyl substituents at the positions 5 and 6, and a branched chain C<sub>3</sub> substituent at the position 8.

The invention relates more particularly to those structures in which both methyl groups are disposed on the same side of the molecule (i.e., on the same side of a plane drawn through the carbons of the six-membered rings), while the substituent at C<sub>8</sub> is either disposed at the opposite side or connected with the C<sub>8</sub> by means of a double bond. Said group of compounds will be referred to hereinafter by the name of nootkatane group.

Several members of said group are important components of essential oils [cf., for example, Perf. & Ess. Oil Rec., 59, 280 (1968)].

Valerianol (formula of FIG. 2) occurs in the oil of *Valeriana officinalis*,  $\alpha$ -Vetivone (formula of FIG. 3) is found in vetiver oil (from *Vetiveria zizanioides*), nootkatone (formula of FIG. 4) is found in the oil of the Alaska yellow cedar (*Chamaecyparis nootkatensis*) and in a great number of citrus oils, specifically grapefruit oil (from *Citrus paradisi*).

Nardostachone (formula of FIG. 5) is a constituent of spikenard oil (from *Nardostachis jatamansi*).

Nootkatone (formula of FIG. 4) may be prepared by oxidation of valencene (formula of FIG. 6) with tertiary butyl chromate [cf. J. Food Sci., 30, 876 (1965)]. If (+)-valencene is used as the starting material, it will yield optically active nootkatone which is dextrorotatory, as is the natural isomer, and has the absolute configuration which is shown in the formula of FIG. 4.

A disadvantage of the aforementioned method for the preparation of nootkatone is that valencene is not sufficiently commercially available in an economical way to warrant its use.

Nootkatone may also be prepared from nootkatene by a process consisting of various steps (see the Dutch Pat. Application No. 69,14545, laid open for public inspection), a substance which, in accordance with Acta Chim. Scand., 11, 1157 (1957), may be isolated from the wood of *Chamaecyparis nootkatensis*, giving a yield of about 0.25 percent.

For the synthesis of nootkatone (FIG. 4) and  $\alpha$ -vetivone (FIG. 3), respectively, there have been described a series of chemical processes on a laboratory scale which, it is true, are of scientific interest, but are not suitable for a technical preparation. As starting materials there were used: 4,4-dicarboethoxypimelic-acid-dinitrile [see Chem. Comm., 26 (1969)], 4-ethoxy  $\Delta^3$ -tetra-hydroacetophenone [see Chem. Comm., 1,152 (1968)], and dimethyl  $\gamma$ -ketopimelate [see *Tetrahedron Letters*, 1,239 (1970)] and 2-carbomethoxy-4-isopropylidenecyclohexanone [see Chem. Comm., 753 (1967)], respectively.

The sesquiterpenes thus obtained are not optically active, but are mixtures of equal amounts of optical antipodes; for example, of (+)-nootkatone (FIG. 4) and (−)-nootkatone (FIG. 7).

Surprisingly, it has now been found that sesquiterpenes having a bicyclo [4.4.0] decane skeleton can readily be prepared if the cyclopropane ring in 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (formula of FIG. 8) is opened or cleaved and the compounds thus obtained can be further converted, if desired.

The compound having the formula of FIG. 8 is new. According to the invention it can be produced easily on a technical scale if methylpropenyl ketone (formula of FIG. 9), in accordance with the reaction 1, is condensed with 2-methylsabinone (formula of FIG. 10) under the influence of a strong base, such as sodium hydride or sodium amide.

2-Methyl-sabina ketone (formula of FIG. 10) has been described [see J. Prakt. Chem., 90, 314 (1915)] and can easily be prepared from the monoterpene sabinene having the formula of FIG. 11, a natural and common product (see, for example, E. Gildemeister and Fr. Hoffmann "Die ätherischen Öle," Band IIIa, page 114 and following).

For this purpose, sabinene is oxidized with a strong oxidizing agent, such as ozone, into sabina ketone having the formula of FIG. 12, and into this sabina ketone a methyl group is introduced in the activated  $\alpha$ -position, for instance, by direct methylation with methyl iodide or dimethylsulphate, or by the introduction of a group which by means of reduction can be converted into a methyl group, such as a methylene group or a hydroxymethylene group (see reaction 2). Sabina ketone may be prepared by means of a synthetic process as well [see J. Org. Chem., 33, 1656 (1968)].

The process makes it possible to prepare optically active sesquiterpenes of the nootkatane series. If the reaction 1 is carried out with optically active and dextrorotatory 2-methyl-sabina ketone (which is derived from laevorotatory 1-sabinene), there is obtained optically active and laevorotatory 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one having the absolute configuration, as shown in the formula of FIG. 13. However, if the reaction is carried out with laevorotatory 2-methyl-sabina ketone (from dextrorotatory d-sabinene), the dextrorotatory optical antipode having the absolute configuration, shown in the formula of FIG. 14, is obtained. If optically inactive 2-methyl-sabina ketone (from natural or synthetic d.1-sabinene) is used as starting material, there is also obtained optically inactive 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one which is a mixture of equal parts of the optical antipodes having the formulae of FIGS. 13 and 14.

In order to obtain sesquiterpenes of the nootkatane group, the compound having the formula of FIG. 8 is treated with acid, as described in the examples. Compounds having a carbon skeleton, as in the formula of FIG. 1, representing the desired configuration are formed upon opening of the cyclopropane ring. This process is shown in the reaction scheme 3, if dextrorotatory 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (FIG. 8) is used as the starting material. If the laevorotatory isomer is used as the starting material, it is understood that in this instance the optical antipodes will be formed. Reaction of the compound having the formula of FIG. 8 with sulphuric acid in an aqueous medium leads to ring opening and yields 5,6-dimethyl-8-isopropylbicyclo [4.4.0] 1,9-decadiene-3-one, having the formula of FIG. 15. Reac-

tion with a hydrohalogenic acid, e.g., hydrogen chloride in the presence or the absence of a polar solvent, such as ethanol or ether, on the other hand, leads to ring opening with substitution at C<sub>8</sub>, there is thus formed 7-halodihydronootkatone, e.g., 7-chloro-dihydro-nootkatone having the formula of FIG. 16. From this product other sesquiterpenes of the nootkatone group may be prepared in a simple manner. This will be illustrated by means of a number of examples which follow.

By splitting off hydrohalic acid from 7-halogen-dihydro-nootkatone by treatment with a base, e.g., an organic base, such as dimethylaniline, there is formed as the major product 5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,7-decadiene-3-one, having the formula of FIG. 17, while in addition thereto there is formed  $\alpha$ -vetivone having the formula of FIG. 20 and a small quantity of 5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,9-decadiene-3-one, having the formula of FIG. 15. Upon treatment with hydrohalic acid, the compound of FIG. 17 yields 11-halodihydro-nootkatone, having the formula of FIG. 18, identical with the product which can be obtained from nootkatone (having the formula of FIG. 7) by the addition of hydrohalic acid. This product may also be formed directly from 7-halodihydro-nootkatone (having the formula of FIG. 16), e.g., by treatment with a moderately concentrated sulphuric acid in the presence of hydrohalic acid or a halide. A conversion of the compound of FIG. 8 into the compound of FIG. 18 in high yield and directly may be effected by adding hydrohalic acid in ethanol, followed by addition of sulphuric acid and water. 11-Hydroxydihydronootkatone (FIG. 19) is also formed upon treatment of the compound of FIG. 17 with water in acid medium.

Dehydrohalogenation of 11-halodihydronootkatone or dehydration of 11-hydroxydihydronootkatone (FIG. 19) yields mixtures of  $\alpha$ -vetivone (FIG. 20) and nootkatone (FIG. 7) which can be separated from one another. The relative quantities of the compounds of FIGS. 20 and 7 will vary depending on the method of dehydrohalogenation or dehydration employed in the process. Dehydrohalogenation with sodium acetate in glacial acetic acid will afford a nearly complete conversion into nootkatone. This is also true if the acetate of 11-hydroxydihydronootkatone is subjected to pyrolysis. On being treated with a catalytic amount of a strong acid, such as p-toluene-sulphonic acid, at an elevated temperature, 11-hydroxydihydronootkatone will mainly yield the  $\alpha$ -vetivone.

Other suitable methods are, for example, dehydrohalogenation by heating with a base, such as potassium hydroxide or potassium methoxide in methanol or with an organic nitrogen base, such as dimethylaniline or picoline and dehydration by treating with phosphorus oxychloride or thionyl-chloride in pyridine.

On using dextrorotatory 5,6 dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (FIG. 14) there is obtained optically active and laevorotatory  $\alpha$ -vetivone, as well as laevorotatory nootkatone. If laevorotatory compound of FIG. 14 is used as the starting material, there is obtained dextrorotatory  $\alpha$ -vetivone and dextrorotatory nootkatone.

The process and compounds according to the invention open up new pathways for the technically and economically feasible synthesis of nootkatane type sesquiterpenes and derivatives, which are useful aroma chemi-

cals in the compounding of perfume and flavour concentrates, for use in the industry of foods, drinks and perfumed articles.

#### EXAMPLE I

2-methyl-sabina ketone (formula of FIG. 10)

172 g of Sabinene,  $[\alpha]_D^{20} + 93.1$  percent, content 83 percent, shown by gas chromatographic analysis, was dissolved in 100 ml of ethyl acetate. The ozone was introduced into the mixture at  $-70^\circ\text{C}$ . until saturation. The solvent was eliminated under reduced pressure and the ozonide thus obtained was decomposed by the addition of a 20 percent solution of sodium sulphite. The oil layer was separated off and the aqueous layer was extracted with 200 ml of ether. Oil layer and ethereal extracts were combined, washed with 50 ml of water, dried over calcium chloride and filtered. After removal of the solvent, the crude sabina ketone was fractionated. There was thus obtained 128 g of sabina ketone (formula of FIG. 12), boiling point  $79^\circ\text{--}80^\circ\text{C}$ . at 8 mm,

$[\alpha]_D^{20} - 37.8$  ( $\text{C}_2\text{H}_5\text{OH}$ ),  $n_D^{20} = 1.4705$ . Gas chromatographic analysis showed a content of 98 percent.

A solution of 128 g of sabina ketone in 160 ml of glacial acetic acid and 200 g of N-piperidinemethanol was refluxed for 15 hours (reaction temperature  $75^\circ\text{C}$ .). After cooling the reaction mixture was poured out onto a mixture of water, ice and hydrochloric acid. The oil layer was separated and the aqueous layer was extracted three times with 200 ml of pentane each time. Oil layer and extracts were combined, washed until neutral, dried and filtered off. After removal of the solvent and distillation, there was thus obtained 30 g of 2-methylene-sabina ketone. B.p.  $67^\circ\text{C}$ . at 2 mm. A considerable quantity of the reaction product was present in the aqueous layer in the form of a salt of the Mannich base. The acid aqueous layer was rendered alkaline with sodium carbonate and was extracted three times with 100 ml of carbon tetrachloride each time. After drying and evaporation of the solvent there was thus obtained 142 g of Mannich base. The Mannich base was quaternized by boiling with 100 g of methyl iodide. The solid was sucked off and washed with toluene. There was thus obtained 150 g of quaternary ammonium salt. This salt was boiled with 60 g of sodium carbonate in a mixture of 500 ml of methanol and 60 ml of water for 2.5 hours. The reaction mixture was poured out into water and extracted four times with 200 ml of pentane.

The combined extracts were washed with water, dried and filtered. After the removal of the solvent and distillation there was obtained an additional 60 g of 2-methylenesabina ketone. B.p.  $66^\circ\text{--}67^\circ\text{C}$ . at 2 mm,  $n_D^{20} = 1.4881$   $[\alpha]_D^{20} - 64.6^\circ$  ( $\text{C}_2\text{H}_5\text{OH}$ )  $l_{\text{max}} 226$  mm ( $\text{C}_2\text{H}_5\text{OH}$ )  $\epsilon_{\text{max}} = 9.400$ .

The I.R. spectrum showed bands at:

$3.25 - 5.82 - 6.08 - 7.00 - 7.16 - 7.34 - 7.52 - 7.88 - 10.80 - 11.08 - 11.59 - 11.83$  and  $12.52$  micron.

90 g of 2-methylene-sabina ketone were dissolved in 100 ml of hexane and, after the addition of 1 g of a 5 percent platina on carbon catalyst, hydrogenated at  $45^\circ\text{C}$ . and a hydrogen pressure of 0.35 at. The catalyst was filtered off and the filtrate was evaporated and distilled. There was thus obtained 72 g of 2-methyl-sabina ketone (formula of FIG. 10). B.p.  $60^\circ\text{--}62^\circ\text{C}$ . at 1 mm,  $n_D^{20} = 1.4666$ ,  $[\alpha]_D^{20} - 30.8^\circ$  ( $\text{C}_2\text{H}_5\text{OH}$ ).

The I.R. spectrum showed bands at:

3.25 - 5.80 - 7.23 - 7.31 - 7.34 - 7.51 - 8.47 - 10.65 - 11.27 - 11.62 - 11.89 micron.

#### EXAMPLE II

5,6-dimethyl-8-isopropyl-tricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (formula of FIG. 8)

In a 5-litre-three-necked reaction flask, equipped with stirrer, dropping funnel and cooler (cooling agent ethanol at -60°C.) there was prepared a solution of sodium amide in liquid ammonia from 3.9 g (0.17 gr. atom) of sodium and 750 ml of liquid solid ammonia in the presence of a catalytic amount of ferric nitrate.

To this mixture there was added, with stirring, in 45 minutes a solution of 26 g (0.17 mol) of 2-methylsabin ketone (formula of FIG. 10) prepared by the same method as described in Example I, [ $\alpha$ ] 20°-30.8° (C<sub>2</sub>H<sub>5</sub>OH), in 75 ml of dry dimethoxyethane.

Upon simultaneous substitution with 300 ml of dry dimethoxyethane, the ammonia was for the greater part removed from the reaction mixture by evaporation. To the dark-coloured solution thus obtained there was added dropwise, with passing of dry nitrogen, 16 g (0.19 mol) of trans 3-pentene-2-one dissolved in 75 ml of dry dimethoxyethane at a temperature of -20° to -25° in 2.5 hours. After a further 30 minutes' stirring, at -20°C., the reaction mixture was poured out into a mixture of 100 ml of saturated ammonium chloride and 900 ml of water. The aqueous mixture thus obtained was extracted three times with 150 ml of ether. The ethereal extract was washed three times with 100 ml of a 10 percent solution of sodium chloride, dried over magnesium sulphate and filtered. After separation of the solvent, the residue was distilled under reduced pressure. There was thus obtained 25 g of 5,6-dimethyl-8-isopropyl-tricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (formula of FIG. 8). Yield 67.5 percent (theory) with a content of about 98 percent, (shown by gas chromatographic analysis). B.p. 131°-132°C. at 1 mm. A sample for analysis was crystallized from hexane. M.P. 70.7° - 71.6°

$l_{max}$  265 mm (C<sub>2</sub>H<sub>5</sub>OH)  $\epsilon_{max}$  19,500.

[ $\alpha$ ]<sub>D</sub><sup>20</sup> +216° (C<sub>2</sub>H<sub>5</sub>OH). The mass spectrum showed important peaks at  $m/e$  = 218 (55 percent) M<sup>+</sup>, 176 (69 percent), 175 (57 percent), 161 (49 percent), 147 (62 percent), 133 (100 percent), 105 (96 percent), 91 (58 percent), 43 (58 percent) and 41 (89 percent).

The I. R. spectrum showed important absorptions at: 3.23 - 5.99 - 6.12 - 6.97 - 7.08 - 7.25 - 7.30 - 7.35 - 7.46 - 7.85 - 8.00 - 9.48 - 9.68 - 11.45 - 11.85 - 12.10 - and 12.31  $\mu$ . The N.M.R. spectrum (60 Me, 10 percent solution in C<sub>6</sub>D<sub>6</sub>) gave signals at:

$\delta$  = 0.60 (3H, doublet, J = 6 centipoises); 0.67 (3H, singlet); 0.73 (3H, doublet, J = 5.5 centipoises); 0.78 (3H, doublet, J = 5.5 centipoises); 5.98 (1H, singlet).

#### EXAMPLE III

5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,9-decadiene-3-one (formula of FIG. 15)

1.0 g of 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one was dissolved in 10 ml of a mixture of 1 part by volume of sulphuric acid 96 percent and 1 part by volume of water at room temperature.

After 10 minutes' stirring at room temperature, the reaction mixture was poured out into water. The aqueous mixture was extracted with carbon tetrachloride (two times 25 ml). The combined extracts were washed two times with a 5 percent solution of sodium bicarbonate and two times with water.

After drying over magnesium sulphate and filtering, the solvent was removed under reduced pressure and the residue was distilled in a ball tube furnace. There was thus obtained 0.6 g of 5,6-dimethyl-8-isopropylbicyclo- [4.4.0] 1,9-decadiene-3-one (formula of FIG. 15).

The N.M.R. spectrum (60 Mc, 10 percent solution in carbon tetrachloride) gave the following signals:

80.80 - 1.10 (12H); 5.60 (1H, broadened singlet); 86.10 (2H), broadened singlet).

From a 10 percent solution in C<sub>6</sub>D<sub>6</sub> the following data could be obtained:

80.60 (3H, doublet), J = 6 centipoises); 0.70 (3H, singlet); 80.75 (6H, doublet), J = 6 centipoises); 5.75 - 5.9 (3H, multiplet).

The I.R. spectrum showed bands at: 3.30 - 6.01 - 6.15 - 6.29 - 7.08 - 7.23 - 7.32 - 7.37 - 7.75 - 7.80 - 8.33 - 11.06 - 11.42 - 11.73 - and 12.22 micron.

#### EXAMPLE IV

7-chloro-dihydronootkatone (formula of FIG. 16)

To 55 ml of a saturated solution of dry hydrochloric acid gas in absolute ethanol there was added with stirring at 20°C. 7.0 g of (0.032 mol) 5,6-dimethyl-8-isopropyl-tricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (formula of FIG. 8) (obtained by the method described in Example II). After all solids had dissolved, the mixture was stirred for another 5 minutes at 20°C. and then poured out into water. The aqueous mixture was extracted four times with 50 ml of chloroform each time.

The combined extracts were washed with 50 ml of a 5 percent solution of sodium carbonate and two times with 50 ml of water. After drying over magnesium sulphate and filtering, the solvent was removed under reduced pressure. There was thus obtained 8.5 g of viscous oil which crystallized slowly. After recrystallization from hexane there was obtained 7.2 g of 7-chloro-dihydronootkatone (formula of FIG. 16), m.p. 67°-69°C. A sample for analysis was once again crystallized from hexane, m.p. 68.2° - 69.4°C. The N.M.R. spectrum (60 Mc, 10 percent solution in tetra) showed signals at:

80.97 (3H, doublet, J = about 6 centipoises); 81.07 (6H, doublet, J = 5.5 centipoises); 81.35 (3H, singlet) and 85.65 (1H, doublet, J = 1.7 centipoises).

The I.R. spectrum showed absorptions at:

5.96 - 6.14 - 6.98 - 7.07 - 7.23 - 7.32 - 7.37 - 7.42 - 7.78 - 8.32 - 8.44 - 11.07 - 11.29 - 11.43 - 11.85 - 12.26 and 12.64 micron.

#### EXAMPLE V

11-chlorodihydronootkatone (formula of FIG. 18) from the compound of FIG. 8

To 8 ml of a saturated solution of dry hydrochloric acid gas in absolute ethanol there was added with stirring at room temperature: 4 g (0.018 mol) of 5,6-dimethyl-8-isopropyltricyclo [4.4.0.0<sup>8,10</sup>] 1-decene-3-one (formula of FIG. 8) (obtained by the process de-

scribed in Example II, contents showed by gas chromatographic analysis, about 98 percent). Stirring was continued for another 5 minutes at 20°C. after all the crystals had dissolved. The solution was subsequently cooled to 10°C. and to this solution there was added dropwise 32 ml of a mixture of concentrated sulphuric acid and water (2:1, V/V), while the temperature was held between 5° and 10°C. The mixture thus obtained was stirred for 3 hours at room temperature and was subsequently poured out into water. The aqueous solution was extracted four times with 50 ml of carbon tetrachloride each time. The combined extracts were washed with a 5 percent solution of sodium bicarbonate and with water, and dried over magnesium sulphate. After separation of the solvent, the residue solidified. Crystallization of the residue from hexane/benzene yielded 4.1 g of 11-chloro-dihydronootkatone (formula of FIG. 18). m.p. 84°–85°C. A sample for analysis was once again crystallized from hexane/benzene. M.p. 84.5°–86.2°C. The N.M.R. spectrum (60 Mc, 10 percent solution in carbon tetrachloride) gave signals at:

80.99 (3H, doublet, J = 6 centipoises);

81.10 (3H, singlet);

81.57 (6H, singlet);

85.61 (1H, broadened singlet).

The I.R. spectrum showed absorptions at:

5.96 – 6.15 – 6.99 – 7.08 – 7.24 – 7.32 – 7.42 – 7.71 – 7.81 –

8.33 – 9.02 – 11.07 – 11.47 – 11.82 and 12.23 micron.

#### EXAMPLE VI

11-chlorodihydronootkatone (formula of FIG. 18) from the compound of FIG. 16

1.0 g of 7-chlorodihydronootkatone (formula of FIG. 16), obtained by the process described in Example IV, was mixed at room temperature with 10 ml of concentrated hydrochloric acid (38 percent). Subsequently, such an amount of glacial acetic acid was added that the mixture became clear (about 1.5 ml). After 2.5 hours' stirring at room temperature (20°C.) the mixture was poured out into water. The aqueous mixture was extracted twice with 25 ml of carbon tetrachloride. The combined extracts were washed until neutral and dried over magnesium sulphate. After removal of the solvent, the residue was crystallized from hexane. There was thus obtained 0.6 g of 11-chlorodihydronootkatone (formula of FIG. 18), m.p. 80°–84°C.

The N.M.R. spectrum showed that the sample contained some 5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,9-decadiene-3-one (formula of FIG. 15).

#### EXAMPLE VII

5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,7-decadiene-3-one (formula of FIG. 17) from compound of FIG. 16

9.0 g of 7-chlorodihydronootkatone (formula of FIG. 16), obtained by the process described in Example IV, was dissolved in 80 g of freshly distilled dimethylaniline. The solution was heated, with stirring, in 1.5 hour at 140°–150°C. After cooling, the mixture was poured out into 300 ml of water and acidified with 2N hydrochloric acid to pH 3. The aqueous mixture was extracted three times with 100 ml of carbon tetrachloride each time. The combined extracts were washed twice

with 50 ml of 2N hydrochloric acid, 50 ml of a 5 percent solution of sodium bicarbonate and twice with 50 ml of water successively. After drying over magnesium sulphate and filtering, the solvent was removed and the residue was distilled. (Boiling point 120°–125°C. at 2 mm). There was thus obtained 7 g of chlorine-free product, 70 percent of which, as shown by gas chromatographic and nuclear magnetic resonance analysis, consisted of 5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,7-decadiene-3-one (formula of FIG. 17), while in the remaining 30 percent about 20 percent  $\alpha$ -vetivone (formula of FIG. 20) and some percentages of 5,6-dimethyl-8-isopropyl-bicyclo [4.4.0] 1,9-decadiene-3-one (formula of FIG. 15) was discovered.

The pure 1,7-dienone (formula of FIG. 17) was isolated by means of preparative gas chromatography (2 m, ¼ inch column with 10 percent DEGS at 200°C.). The N.M.R. spectrum (60 Mc, 10 percent solution in carbon tetrachloride) gave signals at:

81.02 (6H, doublet, J = 7 centipoises);

81.10 (3H, singlet);

80.85–1.2 (12H);

81.7–2.7 (8H);

85.40 (1H, singlet, w h/2 = 4 centipoises);

85.67 (1H, broadened singlet);

A 10 percent solution in C<sub>6</sub>D<sub>6</sub> gives the following data:

80.70 (3H, doublet, J = 6 centipoises);

80.82 (3H, singlet);

80.90 (6H, doublet, J = 7 centipoises);

81.5–2.5 (8H);

85.28 (1H, broadened singlet);

85.88 (1H, broadened singlet);

The I.R. spectrum showed absorptions at: 5.98 – 6.14 – 7.01 – 7.08 – 7.26 – 7.31 – 7.39 – 7.81 – 8.23 – 10.01 – 10.49 – 11.03 – 11.64 and 12.15 micron.

#### EXAMPLE VIII

11-chlorodihydronootkatone (formula of FIG. 18) from the compound of FIG. 17

5 g of the mixture of dienone obtained by the process described in Example VII was dissolved in a mixture of 20 ml of sulphuric acid (96 percent) and 10 ml of water, which mixture was cooled to 10°C. To this mixture there was added with stirring 10 ml of concentrated hydrochloric acid (38 percent), and the stirring was continued for another 30 minutes at 20°C. The reaction mixture was subsequently poured out into ice-water. The aqueous mixture was extracted three times with 50 ml of chloroform each time. The combined extracts were washed with 50 ml of a 5 percent solution of sodium bicarbonate, 50 ml of water and 50 ml of a saturated solution of sodium chloride successively. After drying and filtering, the solvent was removed under reduced pressure. The residue (5.6 g) solidified on standing. Crystallization from hexane with 10 percent of benzene yielded 4.1 g of 11-chlorohydronootkatone (formula of FIG. 18), m.p. 84.5°–85.5°C.

#### EXAMPLE IX

11-hydroxydihydronootkatone (formula of FIG. 19) from the compound of FIG. 17

4 g of the mixture of dienone obtained by the process described in Example VII was dissolved in 40 ml of a mixture of concentrated sulphuric acid and water (v/v, 1:1), cooled to 0°C. The solution was stirred for 15 minutes at 20°C. and poured out onto 200 ml of ice-

water. The acid aqueous mixture was washed once with 20 ml of hexane and was subsequently extracted three times with 60 ml of chloroform each time. The combined extracts were washed with 100 ml of a 5 percent solution of bicarbonate and two times with 50 ml of a saturated sodium chloride solution. After drying over magnesium sulphate and filtering, the solvent was removed and the residue was distilled. The main fraction (2.35 g) had a b.p. of 161°–163°C. at 2 mm and consisted of 11-hydroxydihydronootkatone (formula of FIG. 19) with a content of more than 95 percent (gas chromatographic analysis).  $[\alpha]_D^{20} = 155^\circ$  ( $C_2H_5OH$ ).

$l_{max} 238$  mm,  $\epsilon_{max} = 14,700$  ( $C_2H_5OH$ ). The I.R. spectrum showed absorptions at: 2.77 – 2.91 – 5.98 – 6.17 – 7.00 – 7.09 – 7.26 – 7.32 – 7.41 – 7.75 – 7.80 – 11.08 – 11.48 – 11.83 and 12.14  $\mu$ . The N.M.R. spectrum (60 Mc, 10 percent solution in tetra) showed signals at: 80.98 (3H, doublet,  $J = 6$  centipoises); 81.07 (3H, singlet); 81.10 (3H, singlet); 81.13 (3H, singlet) and 85.65 (1H, broadened singlet). The mass spectrum showed peaks at:  $m/e = 59$  (100 percent), 121 (36 percent), 178 (29 percent), 118 (27 percent), 41 (21 percent), 43 (21 percent), 136 (19 percent), 123 (13 percent), 91 (12 percent), and 163 (12 percent).

#### EXAMPLE X

$\alpha$ -vetivone (formula of FIG. 20) and nootkatone (formula of FIG. 7) from the compound of FIG. 18

2.0 g of 11-chlorodihydronootkatone (formula of FIG. 18), obtained by the process described in Example V, was dissolved in 20 ml of dimethylaniline and was heated with stirring at 145°C. for 2 hours. The reaction mixture was poured out into 100 ml of water and acidified with 2N hydrochloric acid to pH 5. The aqueous mixture was extracted with 30 ml of carbon tetrachloride four times. The combined extracts were washed five times with 20 ml of 2N hydrochloric acid, once with 20 ml of a 5 percent solution of sodium bicarbonate and once with water. After drying over magnesium sulphate and filtering, the solvent was removed and the residue distilled. There was thus obtained 1.2 g of viscous oil, b.p. 180°–112°C. at 1 mm, which consisted of  $\alpha$ -vetivone (formula of FIG. 20) and nootkatone (formula of FIG. 7) in a ratio of about 3:5, as was shown by gas chromatographic analysis.

The pure isomers were obtained by means of preparative gas chromatography. (Filling of column 20 percent OV 17, 3m  $\frac{1}{4}$  inch, isotherm at 200°). There was thus obtained: nootkatone, m.p. 35°–36°C.,  $l_{max} 237$  mm  $\epsilon_{max} = 16,200$ . I.R. spectrum: 3.25 – 5.99 – 6.16 – 7.08 – 7.25 – 7.30 – 7.41 – 11.82 and 12.22  $\mu$ . N.M.R. spectrum:

80.96 (3H, doublet,  $J = 6$  centipoises); 81.10 (3H, singlet); 81.70 (3H, broadened singlet); 84.68 (2H, broadened singlet) and 85.62 (1H, broadened singlet). Mass spectrum  $m/e$ : 218 (M+) (18 percent); 41 (100 percent); 79 (66 percent); 91 (64 percent); 147 (57 percent); 121 (55 percent); 93 (50 percent); 39 (50 percent); 55 (46 percent); 77 (46 percent); and 133 (35 percent);  $\alpha$ -Vetivone.

$l_{max} 233$  nm  $\epsilon_{max} = 12,800$  ( $C_2H_5OH$ ) I.R. spectrum: 5.98 – 6.16 – 7.00 – 7.08 – 7.25 – 7.30 – 7.41 – 11.08 – and 11.48  $\mu$ . N.M.R. spectrum:

80.96 (3H, singlet); 81.00 (3H, doublet,  $J =$  about 6 centipoises); 81.72 (6H, broadened singlet) and 85.62 (1H, broadened singlet). Mass spectrum:  $m/e$ : 218 (M+) (69 percent); 185 (100 percent); 41 (57 percent); 91 (31 percent); 147 (27 percent); 161 (26 percent); 203 (26 percent); 105 (25 percent); 121 (24 percent); and 55 (24 percent).

#### EXAMPLE XI

Nootkatone (formula of FIG. 7 from compound of FIG. 18

5 g (0.02 mol) of 11-chloronootkatone (formula of FIG. 18), obtained by the process described in Example V, was dissolved in 30 ml of glacial acetic acid, 2.1 g (0.025 mol) of dry powdered sodium acetate was added thereto and the resultant mixture was boiled for 20 minutes. After being poured out into water, the mixture was extracted three times with 50 ml of carbon tetrachloride each time. The combined extracts were washed two times with 30 ml of water, once with 30 ml of a 5 percent solution of sodium bicarbonate and finally two times with 20 ml of a saturated sodium chloride solution. After drying and filtering, the solvent was removed under reduced pressure. The residue (4.3 g) consisted, as shown by analysis by means of nuclear magnetic resonance spectrometry, of a mixture of about 85 percent nootkatone, 10 percent  $\alpha$ -vetivone and 5 percent of the acetate of 11-hydroxydihydronootkatone. This mixture was fractionated. There was thus obtained 3.4 g of nootkatone (formula of FIG. 7), b.p. 122°–123°C. at 1 mm. Content, shown by gas chromatographic analysis, 92 percent.  $l_{max} 237$  m ( $C_2H_5OH$ )  $\epsilon_{max} = 16,400$ . M.p. 33°–35°C.

#### EXAMPLE XII

Nootkatone (formula of FIG. 7) and  $\alpha$ -vetivone (formula of FIG. 20) from the compound of FIG. 19

To a solution of 15 g (0.064 mol) of 11-hydroxydihydronootkatone (formula of FIG. 19) in 100 ml of solid pyridine there was added dropwise with stirring and external cooling with ice-water 28 g of phosphorus oxychloride in 15 minutes. The stirring was continued for another three hours at 0°C., whereupon the mixture was poured out onto ice. After acidification with 4N sulphuric acid to pH 3, the mixture was extracted four times with 50 ml of carbon tetrachloride each time. The combined extracts were washed two times with 50 ml of 2N sulphuric acid, once with water, and once with a 5 percent solution of sodium bicarbonate, and once with a saturated solution of sodium chloride. After drying over magnesium sulphate and filtration, the solvent was removed under reduced pressure. The residue yielded on distillation 10.3 g of a colourless viscous oil, b.p. 115°–120°C/1 mm, which, as shown by gas chromatographic and nuclear magnetic resonance analysis appeared to consist of nootkatone (formula of FIG. 7) and  $\alpha$ -vetivone (formula of FIG. 20) in a ratio of about 6:4. The pure isomers could be isolated therefrom by preparative gas chromatography.

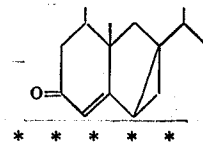
What is claimed is:



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1. The compound, 5,6-dimethyl-8-isopropyl-tricyclo  
[4.4.0.0<sup>8,10</sup>] 1-decene-3-one of the structural formula:

12



UNITED STATES PATENT OFFICE  
CERTIFICATE OF CORRECTION

PATENT NO. : 3,835,192

DATED : September 10, 1974

INVENTOR(S) : Leendert Maarten Van Der Linde, et al

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

[73] Change "N.V. Chemische Fabriek Naarden" to  
-- Naarden International N.V. --

[54] correct spelling of -- SESQUITERPENE --

Signed and Sealed this

Twenty-first Day of September 1976

[SEAL]

*Attest:*

**RUTH C. MASON**  
*Attesting Officer*

**C. MARSHALL DANN**  
*Commissioner of Patents and Trademarks*