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A Process for the Production of Optically Active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane

Field of the Invention

This invention relates to a process for the production of optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane, to the product obtainable by this process and to its use as a perfume.

Prior Art

Judging by demand, many natural perfumes are available in totally inadequate quantities. For example 5000 kg of rose blossoms are required to produce 1 kg of rose oil. The consequences are extremely limited annual world production and a high price. Accordingly, it is clear that there is a constant need in the perfume industry for new perfumes with interesting fragrance notes in order to extend the range of naturally available perfumes, to make the necessary adaptations to changing fashion trends and to be able to meet the steady increasing demand for odor enhancers for products of everyday use, such as cosmetics and cleaners.

Accordingly, it is clear that there is a constant need in the perfume industry for new perfumes with interesting fragrance notes in order to extend the range of naturally available perfumes, to make the necessary adaptations to changing fashion trends and to be able to meet the steadily increasing demand for odor enhancers for products of everyday use, such as cosmetics and cleaners.

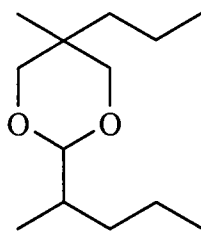
In addition, there is generally a constant need for synthetic perfumes which can be favorably produced in a consistent quality and which have



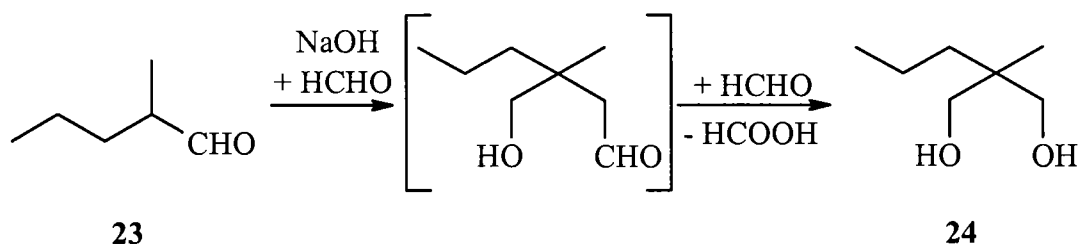
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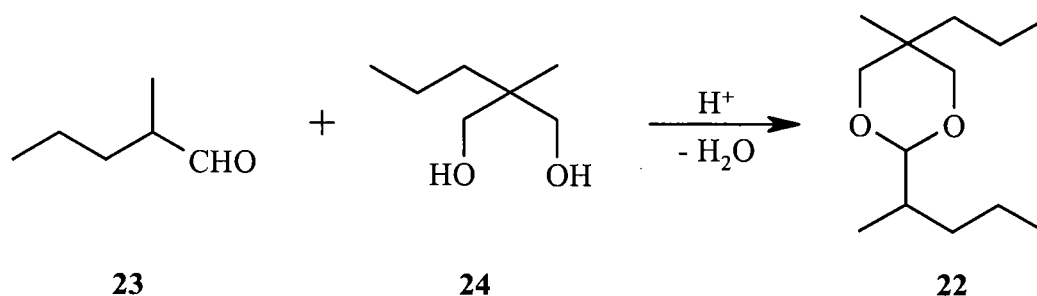
desirable olfactory properties, i.e. pleasant, near-natural and qualitatively new odor profiles of adequate intensity, and which are capable of advantageously influencing the fragrance of cosmetic and consumer products. In other words, there is a constant need for compounds which have characteristic new odor profiles coupled with high staying power, intensity of odor and emanative power.

5-Methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane **22** (trade name Troënan[®])

**22**

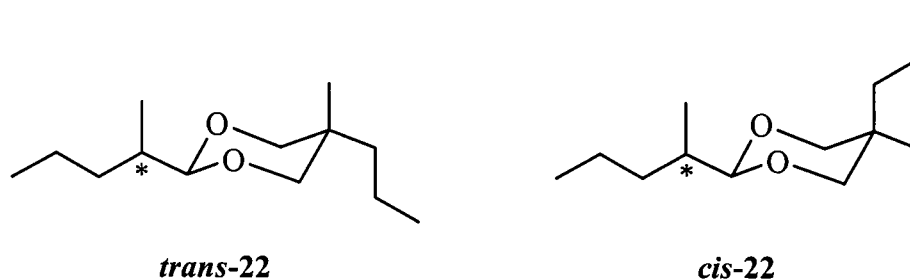
is a known synthetic perfume obtainable from 2-methyl pentanal **23** (cf. following scheme). The educt **23** is reacted with 2 equivalents of formaldehyde in a crossed Canizzaro reaction to form 2-methyl-2-propylpropane-1,3-diol **24**. The diol **24** may then be acetalized with 2-methylpentanal **23** to form Troënan[®] **22**.





By virtue of its privet blossom note, Troënan[®] is valued for flowery and aromatic formulations, more particularly lily-of-the-valley compositions. It has the advantage over other lily-of-the-valley components that it is stable to alkalis.

Troënan[®] **22** contains two *cis/trans* isomers which in turn consist of two enantiomers:



Description of the Invention

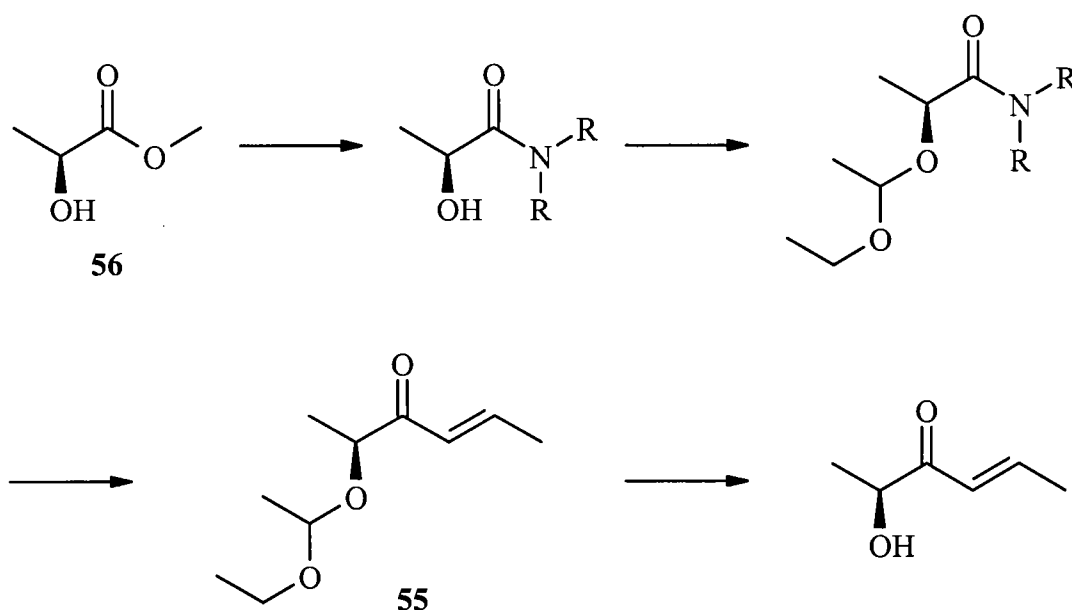
In exploratory investigations conducted by applicants using the technique of "GC Sniffing", it was surprisingly found that the *trans* isomer of Troënan[®] has the typical privet note while the *cis* isomer has a weak flowery-bergamotish note.

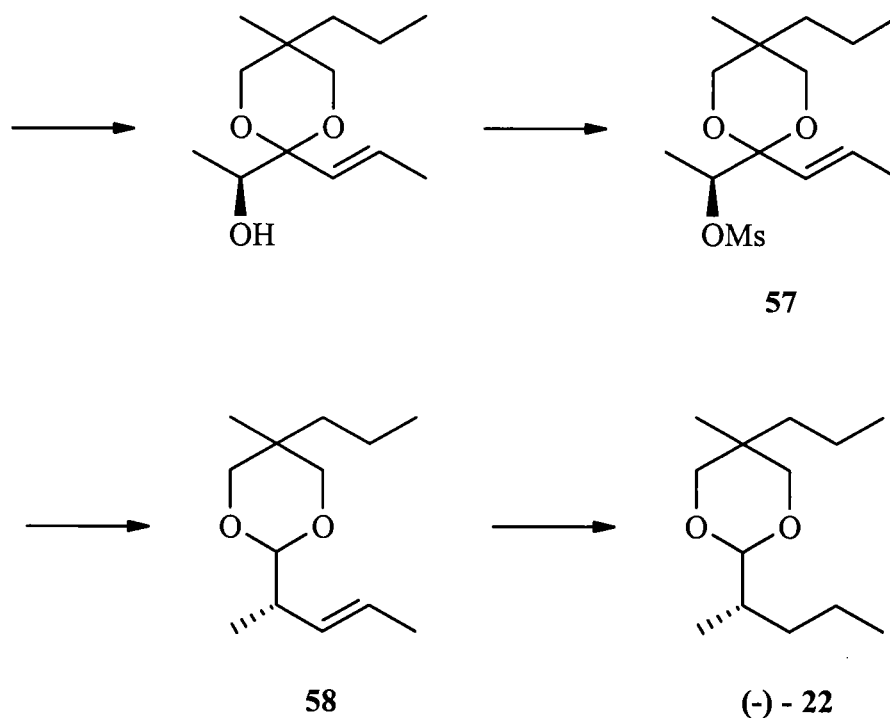
The problem addressed by the present invention was to provide a 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane with a more attractive odor than the known commercial product Troënan[®].

The problem stated above has been solved by an optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane which was obtained by

multistage chiral pool synthesis from enantiomeric (S)-(-)-lactic acid methyl ester **56**.

The synthesis according to the invention starts out from commercially obtainable enantiomeric (S)-(-)-lactic acid methyl ester **56** which, in a first step, is reacted to form an N,N-disubstituted amide. After protection of the OH function, the amide group is converted by a Grignard reaction into an α,β -unsaturated ketone **56**. After removal of the protective group and subsequent acetalization, the hydroxy group is converted into the mesylate **57**. After the reductive 1,2-rearrangement with the stereochemistry intact, a "dehydro-Troënan" **58** is converted by catalytic hydrogenation into the optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane (-)-**22**.





The $^1\text{H-NMR}$ spectrum of **(-)-22** agrees with that of the *cis/trans* mixture of Troënan[®] **22**.

Determination of the angle of rotation produced a specific rotation angle $[\alpha]_{\text{D}}^{20} = -2.43^\circ$.

An optically active **(-)-22** was obtained as a *cis/trans* mixture by the chiral pool synthesis. It was found that this **(-)-22** was surprisingly superior in its olfactory properties to commercially available Troënan[®] both from the qualitative point of view (typical odor profile) and from the odor intensity point of view (quantitative aspect).

Accordingly, the present invention relates to a process for the production of optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane by

- converting lactic methyl ester into the corresponding N,N-disubstituted amide (aminolysis with piperidine and/or pyrrolidine),
- protecting its free OH function by reaction with ethyl vinyl ether in

the presence of p-pyridinium tosylate,

- subjecting the N-pentamethylene or N-tetramethylene lactamide thus obtained to a Grignard reaction in known manner to form the corresponding α,β -unsaturated ketone,
- removing the protective group introduced in the second stage in known manner (for example by stirring with acetic acid),
- acetalizing the ketone function in known manner (for example by reaction with 2-methyl-2-propylpropane-1,3-diol),
- mesylating the free OH function by reaction with methane sulfonic acid chloride in pyridine,
- subjecting the intermediate product thus obtained to a reductive 1,2-rearrangement in the presence of diisobutyl aluminium hydride and triethyl aluminium with the stereochemistry intact and
- converting the dehydro compound thus obtained into the optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane by catalytic hydrogenation.

The optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane obtainable by the process according to the invention has a surprisingly strong emanative power and captivates by its intensive privet and muguet note.

The present invention also relates to optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane obtainable by the process according to the invention.

The present invention also relates to the use of the optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane obtainable by the process according to the invention as a perfume.

The following Examples are intended to illustrate the invention without limiting it in any way.

Examples

1.1 General observations

The following instruments and materials were used:

Melting points:

The melting points mentioned were determined with a melting point microscope (Reichert Thermovar) and are not corrected.

Rotation angles:

The rotation angles were measured with a Perkin-Elmer 241 polarimeter. The concentration c shown in connection with the specific rotation angle is defined as the quantity of substance (in g) per 100 ml of solution.

IR spectroscopy:

The IR spectra were recorded with a Perkin-Elmer 983 spectrometer.

The intensities of the absorption bands mentioned are described by the symbols s (strong), m (medium) and w (weak).

NMR spectroscopy:

The NMR spectra were recorded with Bruker ARX 400, AMX 400 and AC 200 F spectrometers. The chemical shifts are shown in δ -values, based on the standard. In the case of the ARX 400 spectrometer, the solvent used was employed as the standard; in the case of the AMX 400 and AC 200 F spectrometers, TMS was used as the internal standard.

The signal multiplicities are characterized by the symbols s (singlet), d (doublet), t (triplet), Ψ -t (pseudotriplet), q (quartet) and m (multiplet). To enable the hydrogen and carbon atoms to be unequivocally assigned, 2-D-

COSY spectra ($^1\text{H}/^1\text{H}$ and $^1\text{H}/^{13}\text{C}$) and DEPT spectra were recorded.

The individual atoms were numbered in the same way in order to illustrate structural similarities and variations even in the spectrum. Accordingly, they do not always correspond to IUPAC rules.

In the case of compounds present in the form of *cis/trans* mixtures, the signals were characterized by c for *cis* and t for *trans* where assignment was possible.

Mass spectroscopy:

The mass spectra were recorded with a Varian MAT 311 A.

Elemental analysis:

The elemental analysis was carried out with a Perkin-Elmer 240B microelemental analyzer.

Chromatographic processes:

The gas-chromatographic reaction control was carried out with a Hewlett-Packard GC 5710 A in conjunction with a DB-5 capillary column (l = 30 m).

The chiral GC column investigations were carried out using a Shimadzu GC 14A in conjunction with a Cyclodex-beta-I/P capillary column (l = 25 m).

The chiral HPLC column measurements were carried out with a Merck L7100/L7400 in conjunction with an OD-R column (l = 250 mm, d = 4 mm). A mixture of acetonitrile and water (50:50) was used as the mobile solvent (flow = 0.8 ml/min.). Detection was carried out with a UV detector at 254 nm.

1.2 General procedures

The syntheses described in 1.3 were carried out inter alia by the

following general procedures (AAV 1 to AAV 3). These procedures are as follows:

AAV 1: acetalization

1 Equivalent of the aldehyde and 1 equivalent of the diol are dissolved in cyclohexane with 0.025 equivalent of p-toluene sulfonic acid hydrate and the resulting solution is heated under reflux in a Dean-Stark apparatus (water separator), the water formed separating off. On completion of the reaction, the cooled solution is extracted by shaking with saturated sodium hydrogen carbonate solution until the washing water is no longer alkaline. The solution is dried over sodium sulfate and the solvent is removed under reduced pressure in a rotary evaporator. The residue is fractionated in an oil pump vacuum.

AAV 2: mesylation

1 Equivalent of the alcohol is dissolved in n ml of pyridine and the resulting solution is cooled to 0°C. 1.1 Equivalents of methane sulfonic acid chloride are added dropwise and the mixture is left in a refrigerator for 24 h at 4°C. It is then poured onto 2 n ml of ice and neutralized with semiconcentrated hydrochloric acid. The solution is extracted with ethyl acetate. After washing with saturated sodium hydrogen carbonate solution and drying over sodium sulfate, the solvent is removed in a rotary evaporator.

AAV 3: aminolysis

1 Equivalent of (S)-(-)-methyl lactate **56** and 2 equivalents of the amine are heated to 105°C in a distillation assembly. The methanol formed is distilled off via a 15 cm Vigreux column. On completion of the reaction, the excess amine is distilled off and the product is fractionated at 0.1 mbar in the same assembly.

1.3 Chiral pool synthesis

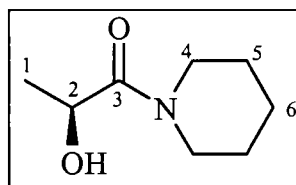
1.3.1 Synthesis of N-pentamethylene lactamide 59

47.6 g of (S)-(-)-methyl lactate **56** (0.46 mole) are reacted with 78.2 g of piperidine (0.92 mole) by AAV 3. A clear colorless liquid is obtained after distillation.

Yield: 73%

Bp.: 111°C/0.8 mbar

Rotation angle: $[\alpha]_{\text{D}}^{20} = -1.13^{\circ}$ (c = 12.7)



¹H-NMR (CDCl₃, 200 MHz): δ = 4.4 (q, 1H; H-2), 3.6/3.35 (t, 4H, H-4 diastereotopic), 1.6 (m, 6H, H-5/H-6), 1.3 (d, 3H, H-1)

¹³C-NMR (CDCl₃, 50 MHz): δ = 173.9 (C-3), 64.0 (C-2), 45.8/43.5 (C-4), 26.2/25.5 (C-5), 24.4 (C-6), 21.4 (C-1)

MS (70 eV): m/z (%) = 157 (18) [M⁺], 114 (12) [C₅H₈O₂N⁺], 113 (65) [C₆H₁₁ON⁺], 112 (100) [C₆H₁₀ON⁺], 85 (13) [C₅H₁₁N⁺], 84 (15) [C₅H₁₀N⁺], 69 (83) [C₅H₉⁺], 56 (13) [C₃H₆N⁺], 55 (12) [C₃H₃O⁺], 45 (33) [C₂H₅O⁺], 42 (18) [C₂H₄N⁺], 41 (63) [C₃H₅⁺]

IR (Film):	$\tilde{\nu}$ [cm ⁻¹]	vibration type
	3415, s	O-H stretching vibration
	2940, s	C-H stretching vibration
	1635, s	C=O stretching vibration, amide
	1480, s + 1400, s	C-H deformation vibration
	1115, s	C-O stretching vibration

EA: $C_8H_{15}NO_2$ $M = 157.21$ g/mole
 calculated: C = 61.12 % H = 9.62 % N = 8.91 %
 observed: C = 60.31 % H = 9.63 % N = 8.79 %

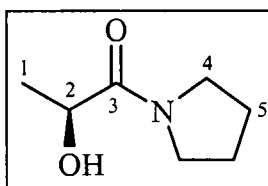
1.3.2 Synthesis of N-tetramethylene lactamide 60

31.2 g of (S)-(-)-methyl lactate **56** (0.3 mole) are reacted with 42.7 g of pyrrolidine (0.6 mole) by AAV 3. A clear colorless liquid is obtained after distillation.

Yield: 97%

Bp.: 95°C/0.1 mbar

Rotation angle: $[\alpha]_D^{20} = -48.67^\circ$ (c = 12.8)



^1H -NMR ($CDCl_3$, 200 MHz): $\delta = 4.35$ (q, 1H; H-2), 3.65/3.3 (m, 4H, H-4 diastereotopic), 2.1-1.8 (m, 4H, H-5), 1.35 (d, 3H, H-1)

^{13}C -NMR ($CDCl_3$, 50 MHz): $\delta = 173.5$ (C-3), 65.6 (C-2), 46.2/46.0 (C-4), 26.1/23.9 (C-5), 20.6 (C-1)

MS (70 eV): m/z (%) = 157 (18) [M^+], 114 (12) [$C_5H_8O_2N^+$], 113 (65) [$C_6H_{11}ON^+$], 112 (100) [$C_6H_{10}ON^+$], 85 (13) [$C_5H_{11}N^+$], 84 (15) [$C_5H_{10}N^+$], 69 (83) [$C_5H_9^+$], 56 (13) [$C_3H_6N^+$], 55 (12) [$C_3H_3O^+$], 45 (33) [$C_2H_5O^+$], 42 (18) [$C_2H_4N^+$], 41 (63) [$C_3H_5^+$]

IR (Film):	$\tilde{\nu}$ [cm^{-1}]	vibration type
	3405, s	O-H stretching vibration
	2975, s	C-H stretching vibration
	1635, s	C=O stretching vibration, amide

1435, s + 1380, s C-H deformation vibration

1128, s C-O stretching vibration

EA: $C_7H_{13}NO_2$ $M = 143.19$ g/mole
calculated: C = 58.72 % H = 9.15 % N = 9.78 %
observed: C = 58.29 % H = 9.23 % N = 9.58 %

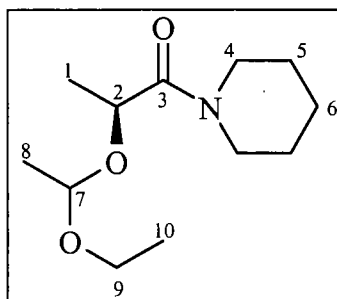
1.3.3 Synthesis of the EE-protected N-pentamethylene lactamide **62**

46.0 g of N-pentamethylene lactamide **59** (293 mmoles), 76.6 g of ethylvinyl ether and 7.53 g of p-pyridinium tosylate (30 mmoles) are dissolved in 200 ml of absolute dichloromethane. The solution is refluxed for 3 h. After cooling, the solution is washed with distilled water and saturated sodium hydrogen carbonate solution. The solvent is removed in a rotary evaporator and the residue is fractionated via a 15 cm Vigreux column. A clear colorless liquid is obtained.

Yield: 45%

Bp.: 78°C/0.08 mbar

Rotation angle: $[\alpha]_D^{20} = -47.77^\circ$ (c = 17.6)



^1H -NMR ($CDCl_3$, 200 MHz): $\delta = 4.80/4.70$ (q, 1H; H-2), 4.6/4.5 (q, 1H, H-7), 3.55 (m, 6H, H-4/H-9), 1.65 (m, 6H, H-5/H-6), 1.45-1.30 (m, 6H, H-1/H-8), 1.2 (m, 3H, H-10)

The protons at C² and C⁷ break up under the effect of the diastereomer mixture present.

$^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz): δ = 170.8 (C-3), 99.3/98.9 (C-7), 70.4 (C-2), 61.3/60.3 (C-9), 46.1/43.2 (C-4), 26.4/25.7 (C-5), 24.6 (C-6), 20.2 (C-8), 18.8/18.4 (C-1), 15.3 (C-10)

IR (Film):	$\tilde{\nu}$ [cm^{-1}]	vibration type
	2935, s	C-H stretching vibration
	1640, s	C=O stretching vibration, amide
	1440, s + 1375, m	C-H deformation vibration
	1080, s	C-O stretching vibration

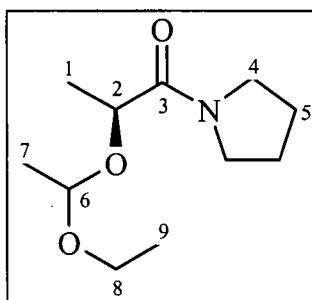
1.3.4 Synthesis of the EE-protected N-tetramethylene lactamide 61

34.7 g of N-tetramethylene lactamide **60** (243 mmol), 36.0 g of ethylvinyl ether (0.5 mmol) and 2.3 g of p-pyridinium tosylate (9 mmol) are dissolved in 150 ml of absolute dichloromethane. The solution is stirred for 3 h at room temperature and then washed with distilled water and saturated sodium hydrogen carbonate solution. The solvent is removed in a rotary evaporator and the residue is fractionated via a 15 cm Vigreux column. A clear colorless liquid is obtained.

Yield: 76%

Bp.: 78°C/0.1 mbar

Rotation angle: $[\alpha]_{\text{D}}^{20} = -76.84^\circ$ ($c = 10.2$)



$^1\text{H-NMR}$ (CDCl_3 , 200 MHz): δ = 4.80/4.75 (q, 1H; H-2), 4.5/4.35 (q, 1H, H-6), 3.7-3.3 (m, 6H, H-4/H-8), 2.05-1.75 (m, 4H, H-5), 1.4 (m, 6H, H-1/H-7), 1.15 (m, 3H, H-9)

The protons at C² and C⁶ break up under the effect of the diastereomer mixture present.

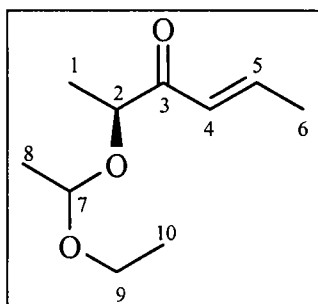
¹³C-NMR (CDCl₃, 50 MHz): δ = 171.3 (C-3), 99.2/98.5 (C-6), 70.4/69.9 (C-2), 61.0/60.0 (C-8), 46.1 (C-4), 26.4/23.8 (C-5), 20.0 (C-7), 18.2/17.9 (C-1), 15.4/15.2 (C-9)

IR (Film):	$\tilde{\nu}$ [cm ⁻¹]	vibration type
	2980, s	C-H stretching vibration
	1655, s	C=O stretching vibration, amide
	1430, s + 1370, m	C-H deformation vibration
	1085, s	C-O stretching vibration

1.3.5 Synthesis of 2-hydroxyhex-4-en-3-one 63

3.6 g of magnesium turnings (150 mmoles) are introduced into 25 ml of THF, after which 18.2 g of 1-bromo-1-propene (150 mmoles) in 50 ml of THF are added dropwise over a period of 30 minutes. After stirring for 30 minutes at 35°C, 10.75 g of the EE-protected N-tetramethylene lactamide **61** (50 mmoles) in 25 ml of THF are added dropwise, followed by stirring for 3 h at 40°C. After the solution has been cooled, it is hydrolyzed with 2 n hydrochloric acid. The phases are separated and the aqueous phase is extracted with diethyl ether. The combined organic phases are neutralized with saturated sodium hydrogen carbonate solution. After the solvent has been removed in a rotary evaporator, part of the EE-protected 2-hydroxyhex-4-en-3-one **55** can be isolated from the residue. It is characterized as follows:

Bp.: 62°C/0.1 mbar



¹H-NMR (CDCl₃, 200 MHz): δ = 7.0 (dq, 1H; H-5), 6.5 (ψ -t, 1H, H-4), 4.75/4.65 (q, 1H, H-7), 4.35/4.2 (q, 1H, H-2), 3.65-3.35 (m, 2H, H-9), 1.95 (d, 3H, H-6), 1.35 (m, 6H, H-1/H-8), 1.15 (ψ -q, 3H, H-10)

The protons at C² and C⁷ break up under the effect of the diastereomer mixture present.

¹³C-NMR (CDCl₃, 50 MHz): δ = 200.5 (C-3), 144.5/143.5 (C-5), 126.6 (C-4), 99.8/99.5 (C-6), 76.1 (C-2), 61.7/60.7 (C-9), 20.1 (C-8), 18.4 (C-1), 16.1/15.3 (C-10)

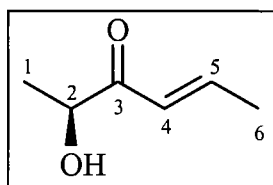
IR (Film):	$\tilde{\nu}$ [cm ⁻¹]	vibration type
	2980, s	C-H stretching vibration, aliphatic
	1695, s	C=O stretching vibration, α,β -unsaturated ketone
	1630, s	C=C stretching vibration, α,β -unsaturated ketone
	1445, s + 1375, m	C-H deformation vibration
	1080, s	C-O stretching vibration

The protected compound **55** is refluxed for 30 minutes with 40 ml of 10% acetic acid. After cooling, the mixture is extracted with dichloromethane. After drying over potassium carbonate, the solvent is removed and the residue is fractionated via a 15 cm Vigreux column. A clear light yellow liquid is obtained.

Yield: 54%

Bp.: 98°C/40 mbar

Rotation angle: $[\alpha]_D^{20} = + 40.25^\circ$ (c = 3.5)



$^1\text{H-NMR}$ (CDCl_3 , 200 MHz): $\delta = 7.05$ (dq, 1H; H-5),
 6.25 (d, 1H,
 H-4), 4.45 (q, 1H, H-2), 1.95 (d, 3H, H-6), 1.40 (d, 3H,
 H-1)

$^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz): $\delta = 201.1$ (C-3), 145.5 (C-5), 126.4
 (C-4), 71.3 (C-2), 20.5 (C-6), 18.2 (C-1)

IR (Film):	$\tilde{\nu}$ [cm^{-1}]	vibration type
	3445, s	O-H stretching vibration
	3025, w	C-H stretching vibration, olefinic
	2980, s	C-H stretching vibration, aliphatic
	1690, s	C=O stretching vibration α,β -unsaturated ketone
	1630, s	C=C stretching vibration α,β -unsaturated ketone
	1440, s + 1375, s	C-H deformation vibration
	1070, s	C-O stretching vibration

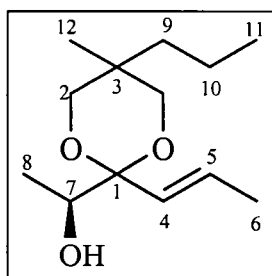
1.3.6 Synthesis of 2-hydroxyethyl-5-methyl-2-(1-propenyl)-5-propyl-1,3-dioxane **64**

2.9 g of 2-hydroxyhex-4-en-3-one **63** (25 mmol) and 3.3 g of 2-methyl-2-propylpropane-1,3-diol **24** (25 mmol) are acetalized in 50 ml of cyclohexane by AAV 1. After distillation through a spinning band column, a

clear light yellow oil is obtained.

Yield: 40%

Bp.: 73°C/0.1 mbar



¹H-NMR (CDCl₃, 400.1 MHz): δ = 5.85 (dq, 1H; H-5), 5.25 (d, 1H, H-4), 3.7-3.3 (m, 5H, H-2/H-7), 1.8 (d, 3H, H-6), 1.3 (m, 2H, H-9), 1.20/0.60 (s, 3H, H-12), 1.15 (d, 3H, H-8), 1.0 (q, 2H, H-10), 0.9 (t, 3H, H-11)

¹³C-NMR (CDCl₃, 100.1 MHz): δ = 132.5 (C-5), 127.2 (C-4), 100.5 (C-1), 73.3 (C-7), 70.9/69.9 (C-2), 38.9/36.7 (C-9), 32.7 (C-3), 20.1/19.4 (C-12), 17.8 (C-6), 16.8 (C-10), 16.1 (C-8), 14.7 (C-11)

MS (70 eV): m/z (%) = 228 (1) [M⁺], 183 (65) [M⁺ - C₂H₅O⁺], 97 (22) [C₆H₉O⁺], 69 (100) [C₄H₅O⁺], 56 (14) [C₄H₈⁺], 55 (68) [C₃H₃O⁺], 45 (11) [C₂H₅O⁺], 43 (33) [C₃H₇⁺], 41 (27) [C₃H₅⁺]

IR (Film):	$\tilde{\nu}$ [cm ⁻¹]	vibration type
	3495, s	O-H stretching vibration
	3020, w	C-H stretching vibration, olefinic
	2960, s	C-H stretching vibration, aliphatic
	1670, w	C=C stretching vibration
	1470, m + 1390, m	C-H deformation vibration
	1120, s	C-O stretching vibration

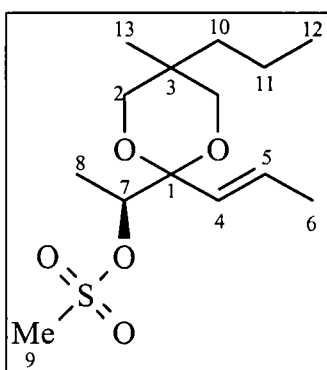
1.3.7 Mesylation of 2-hydroxyethyl-5-methyl-2-(1-propenyl)-5-propyl-

1,3-dioxane 64

12.6 g of 2-hydroxyethyl-5-methyl-2-(1-propenyl)-5-propyl-1,3-dioxane **64** (55 mmoles) are mesylated with 7.0 g of methane sulfonic acid chloride (61 mmoles) in 80 ml of pyridine by AAV 2. A clear light brown oil is obtained.

Yield: 92%

Bp.: decomposition at $T > 105^{\circ}\text{C}$



$^1\text{H-NMR}$ (CDCl_3 , 200 MHz): $\delta = 5.9$ (dq, 1H; H-5), 5.2 (d, 1H, H-4), 4.55 (q, 1H, H-7), 3.7-3.3 (m, 4H, H-2), 3.05 (s, 3H, H-9), 1.85 (d, 3H, H-6), 1.6 (m, 2H, H-10), 1.35 (d, 3H, H-8), 1.15/0.65 (s, 3H, H-13), 1.0 (q, 2H, H-11), 0.9 (t, 3H, H-12)

$^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz): $\delta = 133.9$ (C-5), 125.9 (C-4), 98.8 (C-1), 83.1 (C-7), 69.8 (C-2), 28.7/36.6 (C-10), 38.4 (C-9), 32.9 (C-3), 19.6/19.0 (C-13), 17.8 (C-6), 16.7/15.7 (C-11), 15.9 (C-8), 14.9 (C-12)

IR (Film):	$\tilde{\nu}$ [cm^{-1}]	vibration type
	3020, m	C-H stretching vibration, olefinic
	2960, s	C-H stretching vibration, aliphatic
	1670, w	C=C stretching vibration
	1440, s + 1360, s	C-H deformation vibration
	1415, m + 1175, s	sulfonate group
	1110, s	C-O stretching vibration

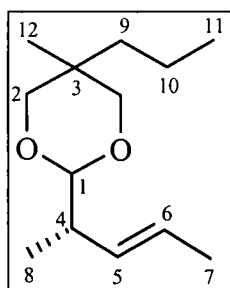
1.3.8 Reductive 1,2-rearrangement

4 g of the mesylate **57** (13 mmoles) were introduced under nitrogen into 40 ml of absolute toluene. The solution is cooled to -35°C , after which 30.5 ml of DI-BAH solution (1M in hexane) and 22.5 ml of triethyl aluminium solution (1M in hexane) are added through a syringe. The solution is stirred for 2 h at -30°C , followed by careful quenching with 15 ml of saturated sodium hydrogen carbonate solution at a temperature of -20°C . After addition of 10 ml of distilled water, the precipitate is filtered off under suction and the filtrate is extracted with diethyl ether. After drying over sodium sulfate, the solvent is removed in a rotary evaporator and the residue is distilled in a bulb-tube oven. A clear colorless liquid is obtained.

Yield: 38%

Bp.: $90-100^{\circ}\text{C}/0.1\text{ mbar}$

Rotation angle: $[\alpha]_{\text{D}}^{20} = +6.28^{\circ}$ ($c = 6.2$)



$^1\text{H-NMR}$ (CDCl_3 , 200 MHz): $\delta = 5.5$ (m, 2H; H-5/H-6),

4.25 (ψ -t, 1H,

H-1), 3.75 (d, 1H, H-2_{cax}), 3.65 (d, 1H, H-2_{tax}), 3.40 (d,

1H, H-2_{teq}), 3.35 (d, 1H, H-2_{ceq}), 2.35 (m, 1H, H-4), 1.7

(d, 3H, H-7), 1.55 (m, 2H, H-9), 1.25 (m, 2H, H-10), 1.15

(s, 1.5H, H-12t), 1.05 (d, 3H, H-8), 0.9 (m, 3H, H-11),

0.65 (s, 1.5H, H-12c)

$^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz): $\delta = 132.6$ (C-6), 125.3 (C-5),

104.7 (C-1), 76.2/75.8 (C-2), 41.2 (C-4), 38.8/37.2 (C-10), 32.7 (C-3),

20.2/19.1

(C-12), 18.8 (C-7), 16.9/16.0 (C-10), 14.9 (C-11), 14.7 (C-8)

MS (70 eV): m/z (%) = 212 (2) $[M^+]$, 143 (60) $[C_8H_{15}O_2^+]$, 97 (39) $[C_6H_9O^+]$, 69 (22) $[C_5H_9^+]$, 56 (18) $[C_4H_8^+]$, 55 (100) $[C_4H_7^+]$, 43 (16) $[C_3H_7^+]$, 41 (29) $[C_3H_5^+]$

IR (Film):	$\tilde{\nu}$ [cm^{-1}]	vibration type
	3020, w	C-H stretching vibration, olefinic
	2960, s	C-H stretching vibration, aliphatic
	1465, m + 1385, m	C-H-deformation vibration
	1115, s	C-O stretching vibration

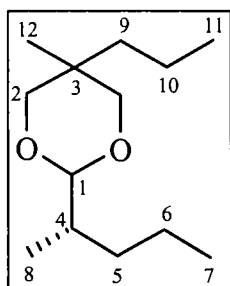
1.3.9 Synthesis of optically active (-)-22

4.0 g of 5-methyl-2-(1-methyl-2-butenyl)-5-propyl-1,3-dioxane **58** (19 mmoles) are dissolved in 80 ml of cyclohexane and, after addition of 0.4 g of hydrogenation catalyst (5% palladium on carbon), the resulting solution is transferred to a steel autoclave. The mixture is stirred for 7 h under a pressure of 10 bar hydrogen and at a temperature of 80°C. After the catalyst has been filtered off and the solvent distilled off, the residue is distilled in a bulb-tube oven. A clear colorless liquid is obtained.

Yield: 81%

Bp.: 75-90°C/0.1 mbar

Rotation angle: $[\alpha]_D^{20} = -2.43^\circ$ (c = 5.2)



¹H-NMR (CDCl₃, 200 MHz): δ = 4.25 (ψ -t, 1H; H-1), 3.75 (d, 1H, H-2_{c_{ax}}), 3.60 (d, 1H, H-2_{t_{ax}}), 3.40 (d, 1H, H-2_{t_{eq}}), 3.35 (d, 1H, H-2_{c_{eq}}), 1.75-1.1 (m, 9H, H-4/H-5/H-6/H-9/H-10), 1.15 (s, 1.5H, H-12_t), 1.05-0.8 (m, 9H, H-7/H-8/H-11), 0.65 (s, 1.5H, H-12_c)

¹³C-NMR (CDCl₃, 50 MHz): δ = 105.3 (C-1), 76.4/75.8 (C-2), 38.6/33.6 (C-9), 36.9 (C-4), 32.7 (C-3), 20.3 (C-6), 18.8/16.7 (C-12), 15.9 (C-10), 15.0 (C-11), 14.2 (C-7), 13.9 (C-8)

CLAIMS

1. A process for the production of optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane, characterized in that
 - lactic methyl ester is converted into the corresponding N,N-disubstituted amide (aminolysis with piperidine and/or pyrrolidine),
 - its free OH function is protected by reaction with ethyl vinyl ether in the presence of p-pyridinium tosylate,
 - the N-pentamethylene or N-tetramethylene lactamide thus obtained is subjected to a Grignard reaction in known manner to form the corresponding α,β -unsaturated ketone,
 - the protective group introduced in the second stage is removed in known manner (for example by stirring with acetic acid),
 - the ketone function is acetalized in known manner (for example by reaction with 2-methyl-2-propylpropane-1,3-diol),
 - the free OH function is mesylated by reaction with methane sulfonic chloride in pyridine,
 - the intermediate product thus obtained is subjected to a reductive 1,2-rearrangement in the presence of diisobutyl aluminium hydride and triethyl aluminium with the stereochemistry intact and
 - the dehydro compound thus obtained is converted into the optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane by catalytic hydrogenation.
2. Optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane obtainable by the process claimed in claim 1,
3. The use of optically active 5-methyl-2-(1-methylbutyl)-5-propyl-1,3-dioxane obtainable by the process claimed in claim 1 as a perfume.