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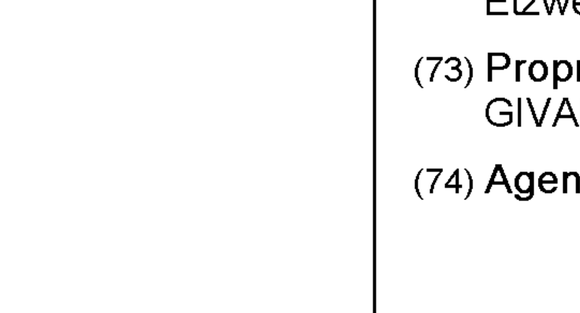
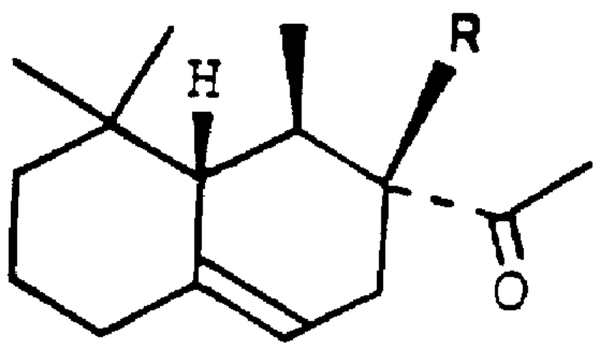
(54) Titre : ACETYLE-TRI ET TETRAMETHYLE-OCTAHYDRONAPHTALENES ET COMPOSITIONS DE FRAGRANCES LES CONTENANT

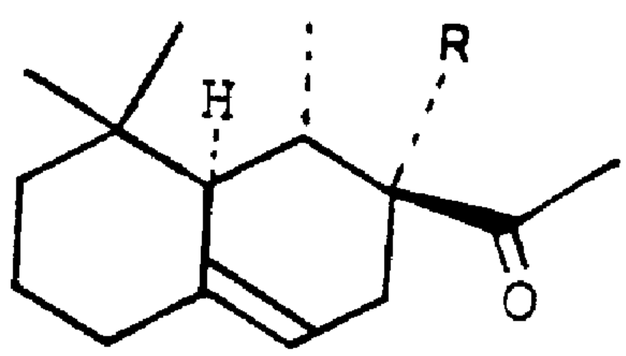
(54) Title: ACETYL-TRI- AND TETRAMETHYL-OCTAHYDRONAPHTHALENES AND FRAGRANCE COMPOSITIONS CONTAINING THE SAME



I



Ia



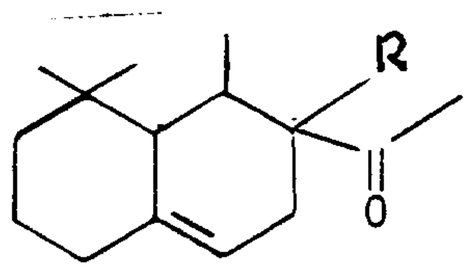
Ib

(57) Abrégé/Abstract:
The invention relates to odorants. More particularly, the invention relates to compounds of the general formula (see formula I) wherein R is hydrogen or methyl. Formula I should in particular embrace the two enantiomers (see formulas Ia and Ib) as the racemate.

Abstract

The invention relates to odorants.

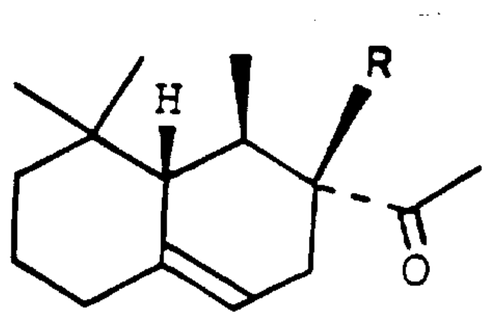
More particularly, the invention relates to compounds of the general formula



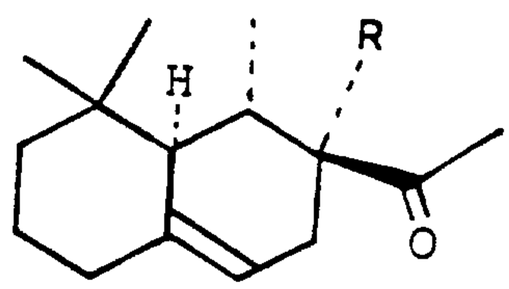
I

wherein R is hydrogen or methyl.

Formula I should in particular embrace the two enantiomers



Ia



Ib

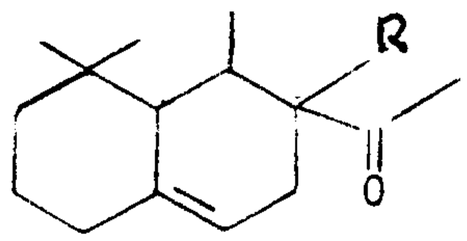
as the racemate.

25561-166

Acetyl-Tri- and Tetramethyl-Octahydronaphthalenes and Fragrance Compositions Containing the Same

The invention relates to odorants.

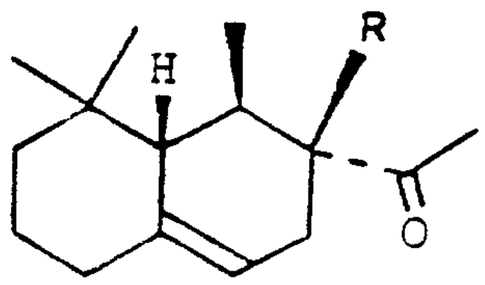
More particularly, the invention relates to compounds of the general formula



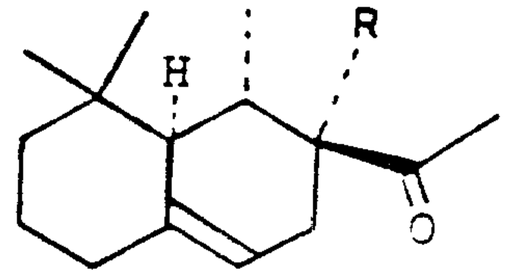
I

wherein R is hydrogen or methyl.

Formula I should in particular embrace the two enantiomers



Ia

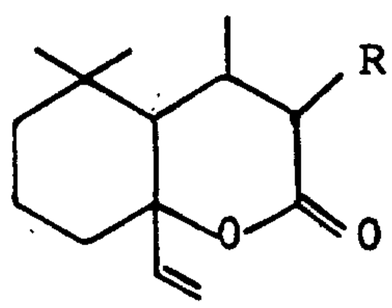


Ib

as the racemate.

The invention relates furthermore to a process for the manufacture of the compounds I, in particular compounds Ia or Ib.

This process comprises subjecting a compound

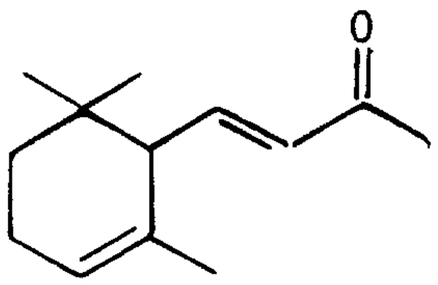


II

wherein R is as above,
preferably in the form of its corresponding silyl enol ether, to a Ireland-Claisen-rearrangement, followed by a methylation of the formed 3-carboxyl group.

The access to the novel compounds I can be visualized as follows:

Reaction Scheme

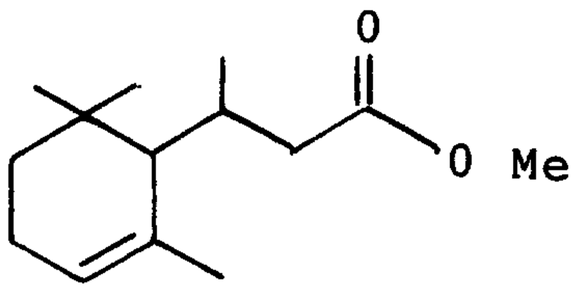


VI

methylation via conjugative Grignard reaction, e.g. addition of dimethyl CuLi to α-ionone

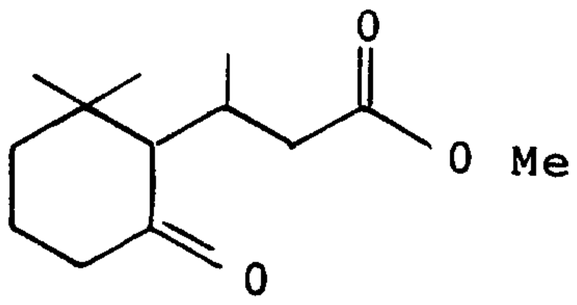
V

1) haloform reaction
2) esterification



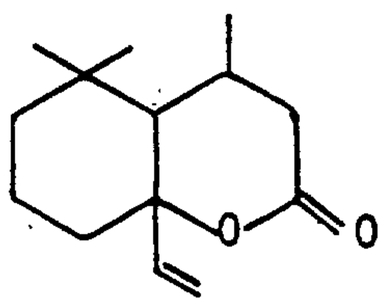
IV

oxydative demethylation e.g. with OCl^- leading to the allyl chloride / O_3



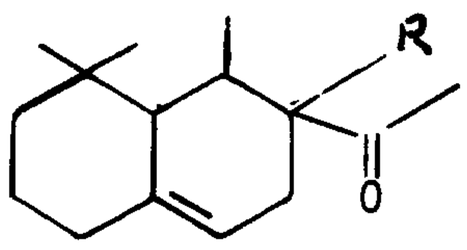
III

cyclisation
e.g. acetylene Mg Br,
sponaneous cyclisation
(lactonisation) of the
carbinol, hydrogenation of
the triple bond



II'

Ireland-Claisen-rearrange-
ment [thermic rearrange-
ment, e.g. at approx.
100-120°, e.g. in toluene]
1) base catalyzed
methylation (optional)
2) silylation preceding
rearrangement
3) methylation of the
formed 3-carboxyl group



I

As it will be obvious from the Examples, reactions VI→V and III→II are stereoselective.

1) S.L. Schreiber et al., J. Org. Chem., 54 (1989) 9, 10

The particular, individual steps involved are based on chemistry known to the man skilled in the art.

The details of the methods are outlined in the Examples. It is a matter of course that modifications concerning the reagents and reaction conditions are possible. Such are embraced by the claims, since the originality of the access to, e.g. compound I resides in the selection of the various steps and its linkage together.

In the course of the present investigations it has been found that the novel compounds I possess valuable odorant properties and can accordingly be used as odorants.

The invention is accordingly also concerned with the use of I as odorants.

The olfactory notes of I can be characterized as follows: ambra, and also woody, flowery.

On the basis of its olfactory notes the compounds of formula I are especially suitable for modifying and intensifying known compositions. In particular, its extraordinary olfactory strength, which contributes quite generally to the refinement of the compositions, should be emphasized.

The enormously low threshold value of the tetramethyl derivative I is worth mentioning, namely 5pg/1 air.

In contradistinction thereto, the threshold value of the closely related 1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetra-methyl-2-acetonaphthone, Example 5 of Canadian Patent No.

1,029,036 is 500 ng/1 air, i.e. 10000 x the former value.

The compounds I combine with numerous known odorant ingredients of natural or synthetic origin, whereby the

range of the natural odorants can embrace not only readily-volatile, but also moderately-volatile and difficultly-volatile components, and that of the synthetics can embrace representatives from practically all classes of substances, as will be evident from the following compilation:

- Natural products, such as tree moss absolute, basil oil, tropical fruit oils (such as bergamot oil, mandarin oil, etc.), mastix absolute, myrtle oil, palmarosa oil, patchouli oil, petitgrain oil, Paraguay, wormwood oil,

- alcohols, such as farnesol, geraniol, linalool, nerol, phenylethyl alcohol, rhodinol, cinnamic alcohol, Sandalore [3-methyl-5-(2,2,3-trimethylcyclopent-3-en--1-yl)pentan-2-ol], Sandela [3-isocamphyl-(5)-cyclo-hexanol],

- aldehydes, such as citral, Helional®, α-hexyl-cinnamaldehyde, hydroxycitronellal, Lilial® (p-tert.butyl-α-methyl-dihydrocinnamaldehyde), methylnonylacetaldehyde,

- ketones, such as allylionone, α-ionone, ß-ionone, isoraldein (isomethyl-α-ionone), methylionone,

- esters, such as allyl phenoxyacetate, benzyl salicylate, cinnamyl propionate, citronellyl acetate, citronellyl ethoxolate (citronellyl . O-CO-CO . OC_2H_5), decyl acetate, dimethylbenzylcarbinyl acetate, dimethylbenzylcarbinyl butyrate, ethyl aceto-acetate, ethyl acetylacetate, hexenyl isobutyrate, linalyl acetate, methyl dihydrojasmonate, styrallyl acetate, vetiveryl acetate, 2-ethyl-6,6-dimethyl (and 2,3,6,6-tetramethyl)-2-cyclohexene-1-carboxylic acid ethyl ester ("Givescone"), Rosacetol (trichloromethyl-

benzyl acetate), Vetynal (acetylated caryophyllene),

- lactones, such as γ-undecalactone,

- various components often used in perfumery, such as musk ketone, indole, p-menthane-8-thiol-3-one, methyl-eugenol.

Further, the manner in which the compounds I round-off and harmonize the olfactory notes of a wide range of known compositions without, however, dominating in an unpleasant manner is remarkable. There are to be mentioned in this connection: compositions with flowery, e.g. jasmine or rose, notes as well as woody, chypre, animalic, tobacco-like and patchouli compositions, etc.

The compounds of formula I can be used in wide limits which can extend in compositions, for example, from about 0.1 (detergents) - about 5% (alcoholic solutions), without these values being, however, limiting values, since the experienced perfumer can also achieve effects with even lower concentrations or can synthesize novel complexes with even higher amounts. The preferred concentrations range between about 0.1% and about 3%. The compositions manufactured with I can be used for all kinds of perfumed consumer goods (eau de cologne, eau de toilette, extracts, lotions, creams, shampoos, soaps, salves, powders, toothpastes, mouth washes, deodorants, detergents, tobacco, etc.).

The compounds I can accordingly be used in the manufacture of compositions and, as the above compilation shows, a wide range of known odorants or odorant mixtures can be used. In the manufacture of such compositions the known odorants enumerated above can be used according to methods known to the perfumer, such as e.g. from W. A. Poucher, Perfumes, Cosmetics and Soaps 2, 7th

edition, Chapman and Hall, London, 1974.

Example 1

To a suspension of 91.1 g (0.48 mol) of CuI in 3 l of dry Et_2O were added at -10° 600 ml of 1.6M MeLi (0.96 mol) in Et_2O during 20 minutes. The mixture was stirred for 1 h at 0° and then cooled to -10°. A solution of 84.5 g (0.44 mol) of α-ionone in 100 ml of Et_2O was added at -10° during 30 minutes and the resulting solution warmed up to room temperature. The reaction mixture was poured carefully on ice/water under N_2. The organic phase was separated, washed with brine, dried ($MgSO_4$) and evaporated. Distillation afforded 74.0 g (81%) of (4SR,1'SR)-4-(2',6',6'-trimethyl-2'-cyclohexen -1'-yl)pentan-2-one (1 diastereomer) (88% pure by GLC) as a colorless liquid.

bp.: 92°/0.4 Torr.

Odor: woody, floral (violet).

IR ($CHCl_3$): 1712 s.

MS: 208 (1, M^+), 190(2), 150(51), 123(100), 85(57), 81(73), 43(94).

^{1}H-NMR ($CDCl_3$, 400 MH_3): 0.87 (s,CH_3); 0.99 (s,CH_3); 1.03 (d,J=7,CH_3); 1.07-1.15 (m,1H); 1.32-1.44 (m,2H); 1.70 (q,J=2,CH_3); 1.93-2.01 (m,2H); 2.11 (s,CH_3CO); 2.20 (dd,J=10.5 and 16.5,1H); 2.35-2.45 (m,H-C(4)); 2.51 (dd,J=3 and 16.5,1H); 5.38 (m,wl/2 = 8,1H).

Example 2

To a chilled (15°) solution of 37.0 g (0.18 mol) of (4SR,1'SR)-4-(2',6',6'-trimethyl-2'-cyclohexen -1'-yl)pentan-2-one in 700 ml of dioxane was added over a period of 15 minutes a cooled solution of NaOBr in H_2O (prepared by adding 40 ml of Br_2 to a solution of 124.3 g (3.11 mol) of NaOH in 1.1 l of H_2O). The resulting

mixture was stirred at 15° for 1 h, and then at 25° for 2 h. 250 ml of 1M aq. Na_2SO_3 were added and the solvent evaporated under reduced pressure. The residue was distributed between H_2O and Et_2O. The aqueous layer was acidified with 200 ml of 25% H_2SO_4 and extracted with Et_2O. The organic phase was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Yield: 36.5 g of (3SR,1'SR)-3-(2',6',6'-trimethyl-2'-cyclohexen-1'-yl)butanoic acid, as a single diastereoisomer, m.p. 41°.

The crude acid was heated in 330 ml of benzene/MeOH 10:1 (v/v) with 2.0 g of p-TsOH for 8 h with azeotropic removal of H_2O. Work up afforded 36.2 g (91%) of (3SR,1'SR)--methyl-3-(2',6',6'-trimethyl-2'-cyclohexene-1'-yl)butyrate (82% pure, GLC).

Odor: woody, ionone-like.

IR ($CHCl_3$): 1736s.

^{1}H-NMR ($CDCl_3$, 200 MHz): 0.87 (s,CH_3); 1.00 (s,CH_3); 1.04-1.60 (m,3H); overlapped by 1.09 (d,J=7,CH_3); 1.69 (q,J=2,CH_3); 1.90-2.06 (m,2H), overlapped by 2.04 (dd,J=10.5 and 14.5,1H); 2.22-2.40 (m,H-C(3)); 2.43 (dd,J=3.5 and 14.5,1H); 3.65 (s,OCH_3); 5.37 (m,wl/2=8,1H).

Example 3

To a chilled mixture of 31.1 g (0.14 mol) of (3SR,1'SR)-methyl-3-(2',6',6'-trimethyl-2'-cyclohexene-1'-yl)butyrate in 75 ml of hexane and 140 ml of 10% aqueous NaOCl were added during 20 minutes. 15 ml of 40% H_3PO_4 with cooling (pH 12.5→6.5). H_2O was then added and the product extracted with Et_2O. The organic extract was dried ($MgSO_4$) and concentrated in vacuo to give 31.1 g of a yellow liquid (82% pure by GLC).

^{1}H-NMR ($CDCl_3$, 200 MH_3): 4.54 (t,J=5,1H); 4.93 (br,s,1H); 5.33 (t,J=1,1H).

The crude allylchloride was dissolved in 700 ml of CH_3OH and cooled to -70°. O_3 was bubbled through the solution until the starting material had disappeared. Excess of O_3 was removed by purging the solution with N_2, and the reaction mixture was poured into 100 g Zn/300 ml H_2O. The mixture was stirred at room temperature for 24 h, filtered and concentrated in vacuo. The residue was equilibrated between Et_2O and H_2O. Work up afforded 24.8 g of (3SR,1'SR)-methyl-3-(6',6'--dimethyl-2'-oxo-cyclohex -1'-yl)butyrate (64% GLC). An analytically pure sample was obtained by chromatography on SiO_2 with hexane/methyl-tert.-butylether 10:1.
IR ($CHCl_3$): 1705s, 1735s.
MS: 226 (3,M^+), 211(4), 195(6), 179(29), 153(24), 126(24), 111(100).
^{1}H-NMR ($CDCl_3$, 200 MHz): 0.97 (s,CH_3); 1.06 (d,J=6.5,CH_3); 1.12 (s,CH_3); 1.52-2.70 (m,10H); 3.67 (s,OCH_3).

Example 4

To a solution of acetylene magnesium bromide (0.1 mol) in 100 ml of THF was added, at 0°, over a period of 15 minutes a solution of 8.0 g (35 mmol) of (3SR,1'SR)--methyl-3-(6',6'-dimethyl-2'-oxo-cyclohex -1'-yl)butyrate in 20 ml of THF during 15 minutes. The reaction mixture was warmed to room temperature during 4 h, poured into ice water/NH_4Cl and extracted with Et_2O to give 8.83 g of a red, viscuos liquid. This lactone was dissolved in 150 ml of ethanol and hydrogenated at room temperature in the presence of 0.5 g of Lindlar's catalyst. Filtration and evaporation of the solvent, followed by chromatography on SiO_2 with hexane/methyl-tert.-butylether 9:1 afforded 3.8 g (48%) of crystalline (±)-3,4,4aß,5,6,7,8a-octahydro--4ß,5,5-trimethyl -8aß-vinyl-coumarin, m.p. 84-88° (from hexane).
IR ($CHCl_3$): 1730 cm^{-1}.

^{1}H-NMR ($CDCl_3$, 200 MH_3): 0.88 (s,CH_3); 0.94 (s,CH_3); 1.15 (d,J=7,CH_3); 1.16-1.96 (m,7H); 1.98-2.22 (m,1H); 2.31 (dd,J=9.5 and 16,1H); 2.54 (dd,J=8.5 and 16,1H); 5.13 (d,J=11,1H); 5.21 (d,J=17.5,1H); 5.94 (dd,J=11 and 17.5,1H).

Example 5

A solution of 2.22 g (10 mmol) of (±)-3,4,4aß,5,6,7,8a-octahydro-4ß,5,5-trimethyl -8aß-vinyl-coumarin in 10 ml of THF was added at -70° to 30 ml of 0.37M (11 mmol) LDA (lithium diisopropylamide) (prepared from 20 ml of THF, 2 ml of diisopropylamine, 8 ml of 1.4M BuLi in hexane). The solution was stirred at -70°, then 0.75 ml (12 mmol) of CH_3I in 6 ml THF/DMPU 5:1 (v/v) were added. The solution was warmed up to 0°, cooled to -70° and treated with 10 ml of 1.4M BuLi in hexane. The mixture was stirred at -70° for 1 h, excess of trimethylchlorosilane was added and the solution warmed up to room temperature. The solvent was evaporated under reduced pressure, the residue taken up in hexane and filtered. The crude product was heated to reflux in 50 ml of toluene for 24 h. The solvent was stripped off, the residue dissolved in 50 ml of Et_2O and treated with 20 ml of 1.3M CH_3Li in Et_2O at 0°. The mixture was refluxed for 90 minutes, cooled and poured on 100 ml of cold 0.5N HCl with vigorous stirring. Work up, followed by chromatography on SiO_2 with hexane/ethylacetate (20:1) afforded 749 mg (32%) of (±)-3α-acetyl-3ß,4ß,5,5-tetramethyl-2,3,4,4aß,5,6,7,8 -octahydronaphthalene as a colorless oil.

IR ($CHCl_3$): 1700s.

MS: 234(23, M^+), 219(7), 191(100).

^{1}H-NMR ($CDCl_3$, 400 MHz): 0.84 (s,CH_3); 0.89 (d,J=6.5,CH_3); 1.01 (s,CH_3); 1.05 (s,CH_3); 1.32-1.62 (m,5H); 1.71 (ddm,J=7/15/<1,1H); 1.80-1.92 (m,1H); 2.04-2.26 (m,6H), overlapped by 2.15 (s,CH_3CO); 5.44 (dq,J=7 and ~1,1H).

The proper stereostructure of (±)-3α-acetyl-3ß,4ß,5,5-tetramethyl-2,3,4,4aß,5,6,7,8 -octahydronaphthalene could unambiguously be assigned by $^{1}H/^{13}C$-shift correlated -2D-NMR, 2D-$^{13}C/^{13}C$-inadequate NMR and NOE difference spectroscopy.

Example 6

The procedure given for the preparation of (±)-3α-acetyl-3ß,4ß,5,5-tetramethyl-2,3,4,4aß,5,6,7,8 -octahydronaphthalene was followed, exept that the initial methylation step was omitted.

Yield: 65% of (±)-3α-acetyl-4ß,5,5-trimethyl-2,3ß,4,4aß,5,6,7,8 -octahydronaphthalene as a colorless oil.

Odour: woody, amber, floral.

IR ($CHCl_3$): 1700s.

MS: 220 (9, $M^{+\cdot}$), 205(5), 177(28), 43(100).

^{1}H-NMR ($CDCl_3$, 400 MHz): 0.79 (s,CH_3); 0.98 (d,J=6.5,CH_3); 1.03 (s,CH_3); 1.34-2.23 (m,13H), overlapped by 2.17 (s,CH_3CO); 2.29 (td,J=11.5 and 4,H-C(3)); 5.58 (dq,J=7 and <1H).

Irradiation of the d at 0.98→dd at 1.97 (J=6.5 and 11.5,H-C(4)).

Example 7

a) Composition with flowery note

	parts by weight	
Gardenol (α-phenyl ethyl acetate)	10.00	10.00
Geranyl acetate	30.00	30.00
Methyl isoeugenol	10.00	10.00
Geraniol	50.00	50.00
Hydroxycitronellal	50.00	50.00
Thibetolide (ω-pentadecanolide)	20.00	20.00
Eugenol	20.00	20.00
Hedione (methyl dihydrojasmonate)	40.00	40.00
Galaxolide 50% DIP	40.00	40.00

Heliotropine	20.00	20.00
Benzyl acetate	40.00	40.00
Dimethyl benzyl carbinyl acetate	40.00	40.00
Cyclohexal	40.00	40.00
Musk ketone	50.00	50.00
Cetone alpha (γ methyl ionone)	80.00	80.00
Phenyl ethyl alcohol	100.00	100.00
Benzyl salicylate	100.00	100.00
Bergamote essence	100.00	100.00
Dipropylene glycol	80.00	160.00
Compound of Example 5	80.00	xxx

b) Composition with flowery note — parts by weight

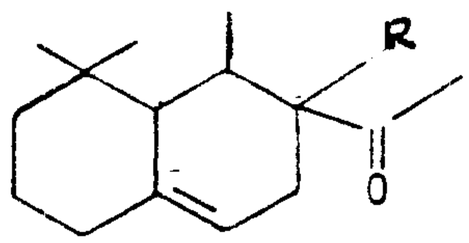
Cyclal C (2,4-dimethyl-3-cyclohexene-1-carboxaldehyde)	1.00	1.00
Geranium ess. Bourbon	5.00	5.00
Eugenol	5.00	5.00
Vanilline 10%/DIP	5.00	5.00
Indole 10%/DIP	4.00	4.00
Undecavertol	10.00	10.00
Coumarine (pure crist.)	10.00	10.00
Patchouli ess. Indonesia	20.00	20.00
Amyl salicylate	30.00	30.00
Dihydromyrcenol	60.00	60.00
Hedione (methyl dihydrojasmonate)	60.00	60.00
Sandalore	30.00	30.00
Mandarine ess.	50.00	50.00
Methyl cedryl cetone	100.00	100.00
Fixolide	100.00	100.00
Galaxolide 50% DIP	100.00	100.00
Bergamote essence	200.00	200.00
Lilial	60.00	60.00
Dipropylene glycol	xxx	150.00
Compound of Example 5	150.00	xxx

The novel compound I provides richness and volume; it wraps up the synthetic notes and provides elegance.

25561-166

CLAIMS:

1. Compounds of formula



I

wherein R is hydrogen or methyl.

2. (±)-3α-Acetyl-3β,4β,5,5-tetramethyl-2,3,4,4aβ,-5,6,7,8-octahydronaphthalene.

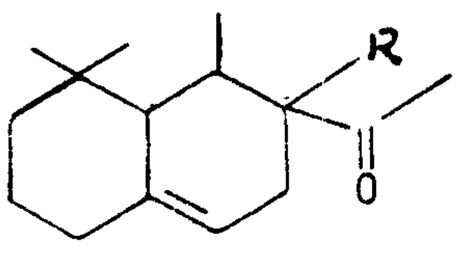
3. (±)-3α-Acetyl-4β,5,5-trimethyl-2,3β,4,4aβ,5,6,7,8-octahydronaphthalene.

4. (3SR,1'SR)-Methyl-3-(2',6',6'-trimethyl-2'-cyclohexen-1'-yl)butyrate.

5. (3SR,1'SR)-Methyl-3-(6',6'-dimethyl-2'-oxo-cyclohex-1'-yl)butyrate.

6. (±)-3,4,4aβ,5,6,7,8a-Octahydro-4β,5,5-trimethyl-8aβ-vinyl-coumarin.

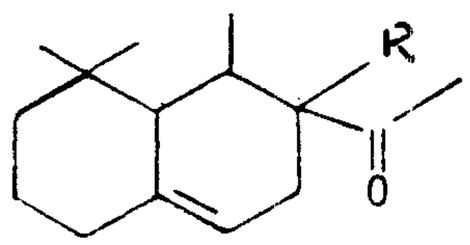
7. Odorant composition, comprising a compound of formula I



I

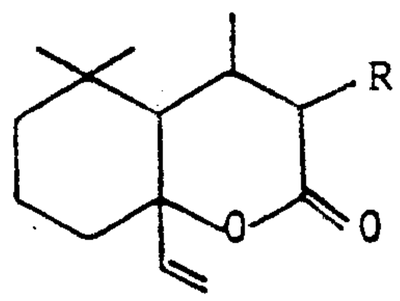
wherein R is hydrogen or methyl, and a further odiferous component.

8. Process for the manufacture of the compounds of formula



I

wherein R is hydrogen or methyl, comprising subjecting a compound



II

wherein R is as above, to a Ireland-Claisen-rearrangement, followed by a methylation of the formed 3-carboxyl group.

9. Process according to claim 8, wherein the compound cf formula II is used in the form of its corresponding silyl enol ether.

10. The use of the compounds of formula I of claim 1 as odorants.

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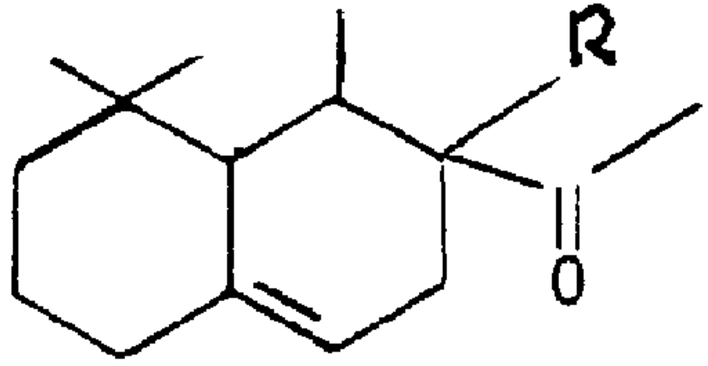
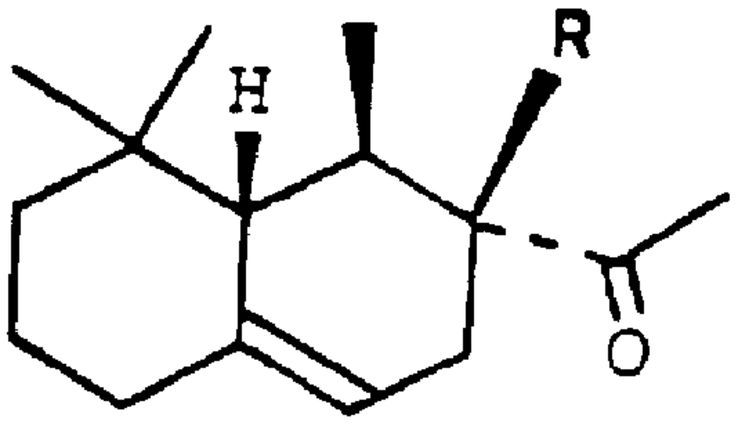
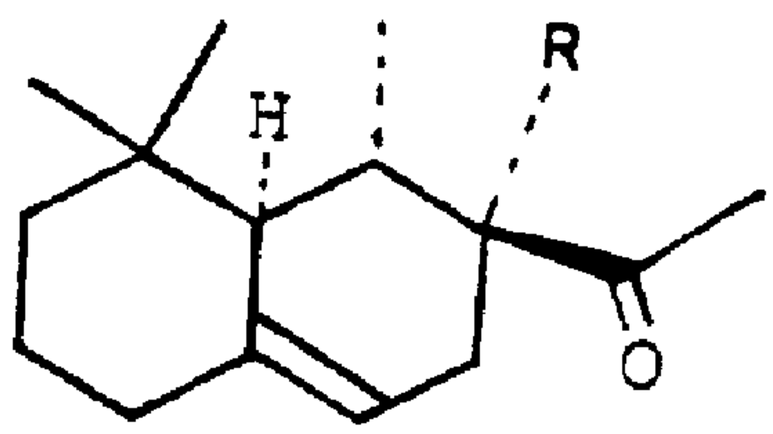


I



Ia



Ib