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SCIENCE DIRECT
European Journal of Medicinal Chemistry 41 (2006) 905–913
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY
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Original article

Syntheses and odor of "bulky group"-modified sandalwood odorants: isophorono-β-santalol analogues

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Received in revised form 7 March 2006; accepted 10 March 2006
Available online 27 April 2006

Abstract

Three osmophoric points have been found to be necessary for the scent of sandalwood odorants. One of these points is the bulky group in a certain distance from the osmophoric hydroxyl group. Such a hydrophobic moiety is part of the trimethylcyclopentenyl derivatives, the so called campholenals, among them many are known to exert a strong and long lasting sandalwood odor. In continuation of our SAR-studies of sandalwood odorants four isophorone analogues of β-santalol have been synthesized. The hydrophobic region of these new isophorone derivatives is now a trimethylcyclohexene nucleus, so to speak an extension of the cyclopentene part of the campholenals by one methylene group. This modification changes the sandalwood odor drastically to woody odor notes, reminiscent only to sandalwood odor. The environs of the crowded trimethylcyclohexene nucleus demonstrate the sensitivity of sandalwood odor on the shape of the hydrophobic, bulky part of β-santalol analogues.

Keywords: Campholene homologues; Hydrophobic moiety; Isophorone; β-Santalol; Structure–odor-relationship

1. Introduction

In continuation of our studies on structure–odor-relationship of fragrance compounds emitting the sandalwood odor [1–7] it seemed worthwhile to study the influence of another modified "bulky group" on the sandalwood character. The "bulky group" [3] has been the focus of recent efforts to find out how far a structure modification can be done without loss of the precious sandalwood scent of the standard molecule β-santalol (**1**) [1,4–6,8–11].

In this paper we report on the synthesis of (*Z*)-2-isophorono-β-santalol (**2**), (*Z*)-2-dihydroisophorono-β-santalol (**3**), (*Z*)-6-isophorono-β-santalol (**4**) and (*Z*)-2-methyl-6-isophorono-β-santalol (**5**). All these new analogues show the typical, *Z*-configurated 2-methyl-2-penten-1-ol side chain, but possess the isophorone nucleus as the necessary hydrophobic part of such an odorous molecule [12–19]. Isophorone (**6**) is a cheap, terpenoid like ketone with a rather flat structure, however rendered bulky by the geminal dimethyl group and possessing the same characteristic structural features as the known campholenic derivatives Brahmanol® (**7**), or Sandacore®, resp. Madrol® (**8**) which belong to the most powerful synthetic sandalwood odorants [12,13,18,20]. The isophorone moiety is similar in its shape to these molecules also showing a geminal, bulky dimethyl group and an endocyclic double bond carrying a methyl group: thus, the isophorone nucleus is a homologue of the campholenic one extended by a methylene group (Fig. 1a–c).

2. Results

2.1. Syntheses

In the following chart (Fig. 2)—showing the general synthetic procedure for the synthesis of **2**–**5** starting from the unsaturated, cyclic ketone **6**—the letters x and y mean the residues at the isophorone nucleus. In each case the first step was an alkylation into the α-position of the keto group using 2-(2-

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doi:10.1016/j.ejmech.2006.03.016

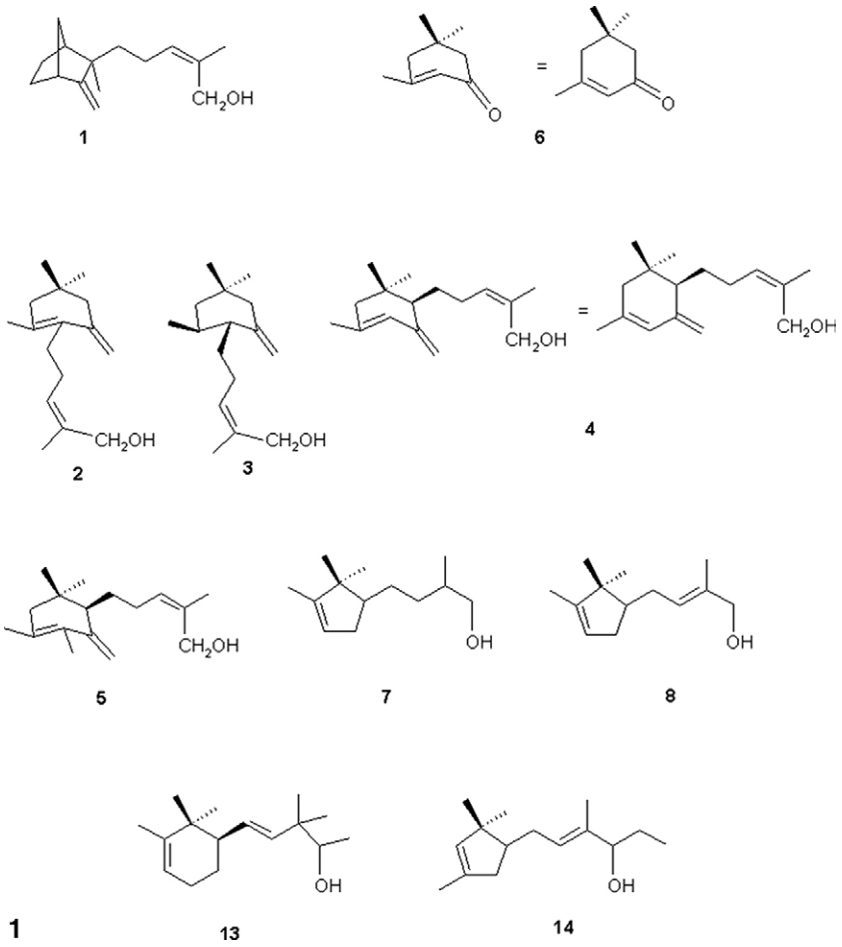
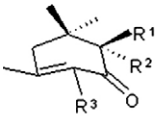


Fig. 1a. Target molecules, part 1.

bromoethyl)-1,3-dioxolane, $NaNH_2$ and hexamethyl disilazane according to Krotz and Helmchen [21], followed by an acidic acetal-cleavage using diluted sulfuric acid. This more or less drastic condition furnished better yields and cleaner products, leading to the corresponding aldehydes as suitable synthons for the following carbonyl olefination. On account of the instability of these aldehydes (autoxidation) they were used without further purification in the sequent *Horner-Emmons* variant of the *Wittig*-reaction with triethyl-2-phosphonopropionate/18-crown-6/K-bis(trimethylsilyl)amide ($KN(TMS)_2$) furnishing the corresponding *Z*/*E*-ester mixtures out of which the pure *Z*-isomers could be obtained by column chromatography (CC). By using such a strongly dissociated base system the *Z*-isomer could be achieved in a synthetic useful level [22]. Transformation of the ketone function of the isophorone nucleus into the exocyclic methylene group was accomplished using the Tebbe-reagent which proved itself successful especially in the case of sterically more voluminous and hindered ketones [23,24]. Finally, the target allyl alcohols **2**–**5** were obtained by reduction of the *Z*-esters with diisobutylaluminium hydride (DIBAH) in CH_2Cl_2 at −78 °C [25,26]. As already described in [1,2] the proof of the existence of the *Z*-alcohols could be given by the ^{1}H-NMR spectrum: the allylic proton of the side chain forms a triplet and could be found characteristically upfield shifted in the region of about 5.24 ppm in comparison to the same signal of the *E*-isomer [27].

The fact that the first alkylation leads to a substitution in position 2 of the isophorone nucleus instead of position 6—where moreover the shield effect by the geminal dimethyl group at C5 renders the bonding with the ethyldioxolane side chain more difficult—, forced us to use another strategy to obtain the corresponding ethyldioxolane at C6. By introduction of an formic ester moiety into position 6 [28,29] the geminal proton has become more acidic and thus enabled also this α-alkylation to **9**. The resulting reaction mixture consisted of the C2 and the desired C6 derivatives (nearly 1:1) which could be separated by CC. Decarboxylation of the β-ketoester yielded finally the pure dioxolanylethylisophorone **10**. Alkylation of **10** with CH_3I/Li-cyclohexylisopropylamide (CIPA) resulted in a product mixture of five alkylation products, out of which **11** could be isolated in moderate yield. **10** and **11** served as starting products for the synthesis of the target alcohols **4** and **5** according to the reaction scheme depicted in Fig. 2. The geminal methyl ethyldioxolanyl isophorone **12**, also an alkylation product, could not be transformed into the corresponding β-santalol analogue, probably due to steric reasons.

The stereochemical position of the ethyldioxolanyl side chain of the starting product for the alcohols **4** and **5** was as-



2

15 $R^1 = R^2 = H$; $R^3 = CH_2CH_2$–(dioxolanyl)

16 $R^1 = R^2 = H$; $R^3 = CH_2CH_2CHO$

17 $R^1 = R^2 = H$; $R^3 = CH_2CH_2CH{=}C(CH_3)COOC_2H_5$

9 $R^1 = CH_2CH_2$–(dioxolanyl); $R^2 = COOC_2H_5$; $R^3 = H$

10 $R^1 = CH_2CH_2$–(dioxolanyl); $R^2 = R^3 = H$

12 $R^1 = CH_2CH_2$–(dioxolanyl); $R^2 = CH_3$; $R^3 = H$

21 $R^1 = CH_2CH_2CHO$; $R^2 = R^3 = H$

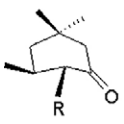
22 $R^1 = CH_2CH_2CH{=}C(CH_3)COOC_2H_5$; $R^2 = R^3 = H$

11 $R^1 = CH_2CH_2$–(dioxolanyl); $R^2 = H$; $R^3 = CH_3$

23 $R^1 = CH_2CH_2CHO$; $R^2 = H$; $R^3 = CH_3$

24 $R^1 = CH_2CH_2CH{=}C(CH_3)COOC_2H_5$; $R^2 = H$; $R^3 = CH_3$

Fig. 1b. Target molecules, part 2.



3

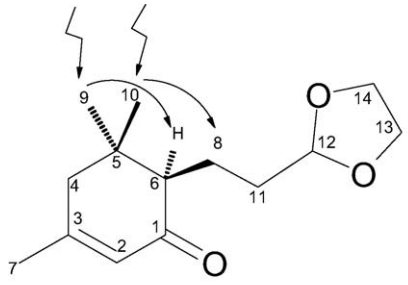
18 R = CH_2CH_2–(dioxolanyl)

19 R = CH_2CH_2CHO

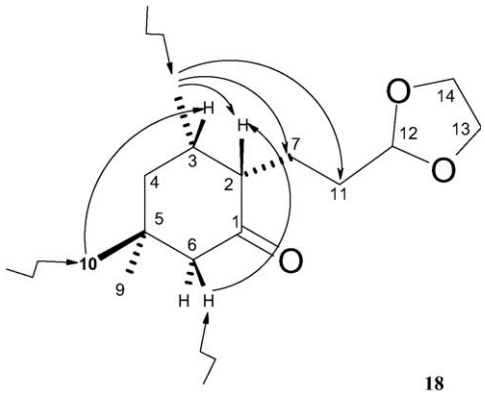
20 R = $CH_2CH_2CH{=}C(CH_3)COOC_2H_5$

Fig. 1c. Target molecules, part 3.

certained by measuring a *NOE*: irradiation upon C6-H resulted in a positive influence on the equatorial CH_3-group as well as irradiation upon the adjacent CH_2-group of the side chain showed an influence on the axial CH_3-group. Thus the ethyl-



10



18

Fig. 3. NOE measurement on compounds **10** and **18**.

dioxolanyl side chain is in axial position and the geminal C6-proton equatorial (see Fig. 3). Also by *NOE* measurement the cis equatorial substitution pattern at C2 and C3 of the hydrogenated isophorone nucleus of **18** was ascertained (Fig. 3).

2.2. Olfactory evaluation

The odor analysis of the target compounds **2**–**5** is given in Table 1. The alcohols **3**–**5** show a woody odor with various tonalities, only **2** is devoid of any note in this direction. Interestingly, the methyl-isophorono analogue **5** possesses a long lasting woody scent which later on develops also a weak note which reminds faintly of sandalwood. Probably the more crowded and bulky hydrophobic part by the additional olefinic methyl group at C2 of **5** causes the weak sandalwood note. Also the distance of about 6 Å of the side chain hydroxyl group from the quaternary C-atom is more similar to the standard [3]. Concerning the chirality of odor molecules, it is known that if one enantiomer shows sandalwood odor, the racemate possesses in most cases this fragrance too [2,18,21].

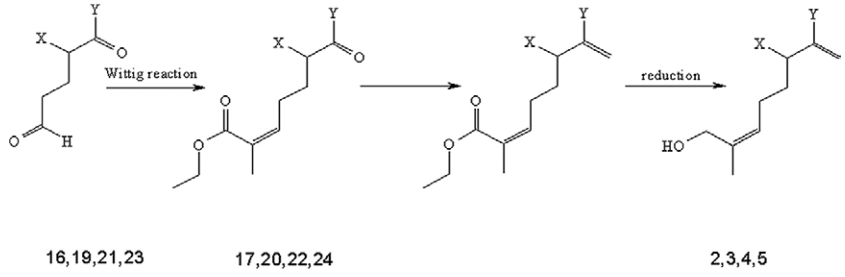


Fig. 2. General synthetic pathway for the synthesis of the target compounds.

Table 1
Odor characterization of the newly synthesized target compounds

Compounds	Odor impression
(*Z*)-2-Methyl-5-(6-methylen-2,4,4-trimethyl-1-cyclohex-1-enyl)-2-penten-1-ol (**2**)	Weak coconut like ("aldehyde C18"), lactonic, creamy
(*Z*)-2-Methyl-5-(6-methylen-2,4,4-trimethyl-1-cyclohexyl)-2-penten-1-ol (**3**)	At the beginning cinnamon like, later cedar wood like-woody-amber note
(*Z*)-2-Methyl-5-(2-methylen-4,6,6-trimethyl-1-cyclohex-3-enyl)-2-penten-1-ol (**4**)	Long lasting woody, cedarwood like
(*Z*)-2-Methyl-5-(2-methylen-3,4,6,6-tetra-methyl-1-cyclohex-3-enyl)-2-penten-1-ol (**5**)	Weak woody, later on strong woody with a weak sandalwood note

Table 2
Spearman- and SOMFA-coefficients of the newly synthesized target compounds

Compounds	*Spearman*-coefficient	SOMFA-coefficient
2	0.3912	0.0123
3	0.5377	0.0070
4	0.4459	0.1392
5	0.6503	0.3194

Therefore, olfactory evaluation has been performed on the racemates only.

2.3. Molecular modeling calculations (Spearman- and SOMFA-coefficients)

Molecular similarity calculations which hitherto have been performed on β-santalol analogues [30] showing sandalwood odor yielded a *Spearman*-coefficient of > 0.6 and a SOMFA-coefficient [31] of > 0.5. As can be seen in Table 2 no one of the four target compounds meets both conditions, therefore the shift from pure and distinct sandalwood odor to more woody tonalities can be easily explained. Only the isophorono analogue **5** showing a trace of a sandalwood note is at least in line with the condition of a *Spearman* coefficient above 0.6, however, the SOMFA-coefficient is below the necessary level of 0.5.

3. Discussion

The bulky and hydrophobic part of the newly synthesized molecules is not large enough to meet the steric conditions to emanate a sandalwood odor, even if the condition of the distance parameter of nearly 6 Å from the side chain hydroxyl group to the quaternary carbon atom with the geminal dimethyl group is met. Other factors are not in favor of the desired scent. SOMFA-shape graphics show that none of the necessary three centers of a sandalwood odorant (osmophoric oxygen function, adjacent to it a tiny methyl group and in the distance to it by a "flexible spacer" a large hydrophobic group) [2,3,8,32–35] create in these four isophorono analogues the suitable molecular shape for an easy docking onto the receptor site. The extension of the trimethylcyclopentenyl (= campholene) nucleus by a methylene-group to the isophorone nucleus as in our case (ortho to the geminal dimethyl group), does not lead to new sandalwood odorants, whereas another trimethylcyclohexene nucleus (a β-ionone nucleus with the side chain at C5 and thus ortho to the geminal dimethyl group) of the sandalwood analogue **13** exerts a strong sandalwood odor indeed [36]. Thus we can conclude that in trimethylcyclohexene derivatives the olefinic methyl group has to be positioned ortho to the geminal dimethyl group and not meta, whereas this does not matter in trimethylcyclopentenyl derivatives as in the fencholene derivative **14** [37]. The overcrowded region in the "upper part" of the β-ionone-derivative **13** is obvious. The molecular shape of all newly synthesized compounds does not allow a sufficient association of the molecules to related receptor sites.

It has to be assumed that for sandalwood odor recognition a specific combination of the association at different odorant receptors leads to the typical scent. If the association at some of these receptors is changed by geometry modifications of the ligand under investigation, other tonalities of the same family will become more dominant. In the present case the modifications of the molecular shape leads to fragrances, where the woody tonalities can be recognized mainly. In only one molecule (**5**) some sandalwood odor note remains.

4. Experimental protocols

Melting points were investigated on a *Kofler* apparatus and are uncorrected. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance DPX-200 NMR-spectrometer (200 MHz, $CDCl_3$, 28 °C) (Karlsruhe, Germany) or on a Varian Unityplus 300 NMR-spectrometer (300 MHz, $CDCl_3$, 28 °C) (Palo Alto, CA). Chemical shifts are given in ppm relative to tetramethylsilane (TMS) as internal standard (= 0 ppm). Infrared (IR) spectra were performed on a Perkin–Elmer FT-IR-spectrophotometer Spectrum 2000 (Oak Brook, IL) (cm^{-1}). Mass spectra were recorded on a Hewlett–Packard MSD (GC: 5890, MS: 5970, column: HP-5MS 30m × 0.25 mm × 0.25 μm, HP-Part No. 19091S-433) (Corvallis, OR) or on a Shimadzu DI-QP5000 instrument (Kyoto, Japan). Purifications were performed either on preparative thin layer chromatography (PTLC) plates (silica gel 60 F_{254}, 2 mm layer thickness, No. 5717), on thin layer chromatography (TLC) plates (silica gel 60 F_{254}, 0.25 mm layer thickness, No. 5554), or with CC (KG 60 F 354, 70–230 mesh ASTM, No. 7734) from Merck (Darmstadt, Germany).

4.1. 2-[2-(1,3-Dioxolan-2-yl)-ethyl]-3,5,5-trimethylcyclohex-2-en-1-one (*15*)

A mixture consisting of 1.70 g (43.6 mmol) $NaNH_2$, 6.35 g (39.3 mmol) hexamethyl disilazane and 50 ml absolute THF was refluxed in argon atmosphere. After 5 h isophorone (**6**) (5.00 g, 36.2 mmol) was added and the refluxing continued for another 2 h. Finally, an amount of 13.10 g (72.4 mmol) 2-(2-bromoethyl)-1,3-dioxolane was added and the mixture stirred at 100 °C for 10 h. The reaction was stopped by cooling

and mixing with water. This mixture was extracted with ether, the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Upon bulb-to-bulb distillation the crude product was submitted to CC (pentane/ethyl acetate 80:20) yielding 1.84 g (21.4%) of a light yellow oil. IR (NaCl, liquid film): ν = 1739, 1664, 1633, 1140 cm^{-1}. MS: (*m*/*z*; r.I.) = 238 (M^+, 5), 223 (1), 193 (7), 178 (4), 166 (7), 135 (3), 123 (3), 110 (12), 86 (20), 73 (100), 67 (12), 53 (11), 45 (28), 43 (12), 41 (21). ^{1}H-NMR ($CDCl_3$): δ = 0.93 (s, 6H, 9 und 10), 1.62 (m, 2H, 11), 1.86 (s, 3H, 8), 2.14 (m, 4H, 4 und 6), 2.35 (t, 2H, 7), 3.75–3.92 (m, 4H, 13 und 14), 4.77 (t, 1H, 12). ^{13}C-NMR ($CDCl_3$): δ = 19.67 (7), 21.19 (8), 28.17 (9, 10), 32.65 (5), 32.96 (11), 46.99 (4), 51.26 (6), 64.79 (13, 14), 104.28 (12), 133.72 (2), 152.87 (3), 198.56 (1). $C_{14}H_{22}O_3$ (238.33).

*4.2. 3-(2,4,4-Trimethyl-6-oxo-1-cyclohex-1-enyl)-propanal (**16**)*

A solution of 1.30 g (5.5 mmol) **15** in 25 ml diethyl ether was stirred with 15 ml 2 N H_2SO_4 at RT for 25 h and afterwards extracted three times with ether. The organic layers were washed with water, dried ($MgSO_4$) and freed from the solvent in vacuo. The crude **16** (0.92 g), a yellowish oil, was directly used for the next step, the carbonyl olefination. MS: (*m*/*z*; r.I.) = 194 (M^+, 17), 179(4), 166(71, 151(11), 135(12), 123(15), 110(100), 95(22), 82(38), 67(42), 55(18), 53(27). $C_{12}H_{28}O_2$ (204.34).

*4.3. (Z)-Ethyl-2-methyl-5-(2,4,4-trimethyl-6-oxo-1-cyclohex-1-enyl)-2-pentenoate (**17**)*

A solution of triethyl-2-phosphonopropionate (1.52 ml, 7.0 mmol) and freshly re-crystallized 18-crown-6 (8.5 g, 32.2 mmol) in 120 ml distilled THF was cooled down to –78 °C in argon atmosphere and mixed with $KN(TMS)_2$ (0.5 M in THF, 13.5 ml, 6.8 mmol). Afterwards a solution of **16** (1.25 g, 6.4 mmol) in 20 ml dry THF was added drop-wise and the mixture stirred for 4 h at –78 °C and finally for 12 h at RT. Upon quenching with saturated NH_4Cl-solution extraction with ether followed. The combined ethereal layers were dried ($MgSO_4$) and freed from the solvent by evaporation. The residue, a yellowish-brown oil was purified by CC (ligroin/ethyl acetate 80:20) yielding in total: 1.14 g (63.7%); pure (*Z*)-product **17**: 0.62 g (34.6%), pure (*E*)-product: 0.09 g (6.7%). IR (NaCl, liquid film): ν = 2957, 1714, 1665, 1632 cm^{-1}. MS: (*m*/*z*; r.I.) [(*Z*)-isomer] = 278 (M^+, 1), 232 (21), 217 (7), 189 (15), 148 (18), 133 (23), 105 (18), 95 (51), 79 (25), 67 (100), 55 (37). [(*E*)-isomer] = 278 (M^+, 1), 232 (20), 217 (7), 189 (13), 148 (17), 133 (20), 105 (15), 95 (44), 83 (23), 67 (100), 53 (33). ^{1}H-NMR ($CDCl_3$) [(*Z*)-isomer]: δ = 0.92 (s, 6H, CH_3 9 and 10), 1.21 (t, 3H, CH_3 17), 1.79 (s, 3H, CH_3 14), 1.86 (s, 3H, CH_3 8), 2.15 (m, 4H, CH_2 3 and 5), 2.31-2.45 (m, 4H, CH_2 7 and 11), 4.09 (q, 2H, CH_2 16), 5.88 (t, 1H, CH 12). ^{13}C-NMR ($CDCl_3$) [(*Z*)-isomer]: δ = 14.20 (C17), 20.57 (C14), 21.26 (C8), 24.35 (C7), 28.10 (C9 and 10), 28.75 (C11), 32.59 (C4), 46.95 (C3), 51.20 (C5), 59.91 (C16), 127.28 (C13), 133.50 (C1), 142.06 (C12), 153.30 (C2), 167.98 (C15), 198.67 (C6). ^{1}H-NMR ($CDCl_3$) [(*E*)-isomer]: δ = 0.93 (s, 6H, CH_3 9 and 10), 1.22 (t, 3H, CH_3 17), 1.74 (s, 3H, CH_3 14), 1.85 (s, 3H, CH_3 8), 2.17 (m, 6H, CH_2 3, 5 and 7), 2.36 (t, 2H, CH_2 11), 4.10 (q, 2H, CH_2 16), 6.68 (t, 1H, CH 12). ^{13}C-NMR ($CDCl_3$) [(*E*)-isomer]: δ = 12.24 (C17), 14.27 (C14), 21.387 (C8), 24.04 (C7), 27.94 (C9 and 10), 32.65 (C4), 47.02 (C3), 51.28 (C5), 60.33 (C16), 128.09 (C13), 133.30 (C1), 141.44 (C12), 153.38 (C2), 168.22 (C15), 198.76 (C6). $C_{17}H_{26}O_3$ (278.39).

*4.4. (Z)-2-Methyl-5-(2,4,4-trimethyl-6-methylen-1-cyclohex-1-enyl)-2-penten-1-ol (**2**)*

A solution of **17** (0.55 g, 2.0 mmol) in 20 ml absolute THF was cooled down with ice to 0 °C in argon atmosphere, mixed drop-wise with *Tebbe*-reagent (0.5 M in toluene, 7 ml, 3.5 mmol) and afterwards stirred at this temperature for 6 h. Quenching was accomplished by slowly injecting a 1:1-mixture of ether/CH_3OH by a syringe till the end of gas-evolution. The reaction mixture was filtered through a layer of Celite/Al_2O_3 (1:1) and washed with 1 l of ether. The resulting dark-red oil (0.44 g crude product) was directly used for the next reaction in order to avoid decomposition on the stationary phase of a CC.

A solution of the just obtained crude methylene pentenoate (0.44 g, ≈ 1.6 mmol) in 10 ml anhydrous CH_2Cl_2 was cooled down to –78 °C in argon atmosphere and slowly mixed with 7 ml (7 mmol) DIBAH (1 M solution in n-hexane). The resulting mixture was stirred overnight slowly getting warm to RT, then again cooled down to –20 °C and hydrolyzed with 2 ml of a mixture of CH_3OH/H_2O (1:1) and stirred for another 3 h at RT. Afterwards, the solution was mixed with Celite, filtered through Celite, washed with ethyl acetate and evaporated. The crude yellowish-brown oil was purified by prep. TLC (Al_2O_3, petroleum ether/ethyl acetate 90:10) furnishing 50 mg (13.5%) of an almost colorless oil of (*Z*)-**2**. IR (NaCl, liquid film): ν = 3335, 3087, 2951, 1632, 1605, 1453, 1365, 1006 cm^{-1}. MS: (*m*/*z*; r.I.) = 234 (M^+, 5), 216 (5), 201 (9), 175 (100), 162 (17), 145 (13), 133 (21), 119 (28), 107 (53), 91 (56), 77 (32), 69 (18), 55 (28). ^{1}H-NMR ($CDCl_3$): δ = 0.80 (s, 6H, CH_3 9 and 10), 1.65 (s, 3H, CH_3 16), 1.72–1.72 (m, 3H, CH_3 8), 1.84 (s, 2H, CH_2 3), 1.99 (s, 2H, CH_2 5), 2.13 (t, 2H, CH_2 11), 2.23–2.28 (m, 2H, CH_2 12),4.02 (s, 2H, CH_2 15), 4.63 and 4.82 (m, 2H, =CH_2), 5.28 (t, 1H, CH 13). ^{13}C-NMR ($CDCl_3$): δ = 20.36 and 21.30 (C8 and 16), 27.06 and 27.88 (C11 and 12), 28.04 (C10 and 9), 30.02 (C4), 46.727 and 47.49 (C3 and C5), 61.52 (C15), 107.10 (C7), 128.52 (C13), 129.49 (C2), 132.59 (C6), 143.47 (C1). $C_{16}H_{26}O$ (234.38).

*4.5. 2-[2-(1,3-Dioxolan-2-yl)-ethyl]-3,5,5-trimethyl-cyclohexan-1-one (**18**)*

A mixture consisting of 0.8 g (3.4 mmol) **15**, 0.52 g (5.2 mmol) triethylamine, 380 mg Pt on activated carbon (10%) and 80 ml absolute ethanol was hydrogenated at RT for 20 h. Afterwards the solution was filtered and the solvent evaporated. Purification of the residue was accomplished by CC (ligroin/ethyl acetate 80:20) yielding 0.59 g (72.6%) **18**

as a nearly colorless oil. IR (NaCl, liquid film): ν = 2957, 1709, 1463, 1138, 942 cm^{-1}. MS: (*m*/*z*; r.I.) = 240 (M^+, 2), 225 (1), 195 (1), 178 (4), 163 (1), 136 (1), 125 (2), 99 (11), 83 (6), 73 (100), 55 (16). ^{1}H-NMR ($CDCl_3$): δ = 0.82 (s, 3H, CH_3 10), 1.01 (s, 3H, CH_3 9), 1.03 (d, 3H, CH_3 8) [^3J (H-3,3-Me) = 6.2 Hz], 1.41 (m, 1H, H4ax) [^3J (H3ax, H4ax) = 12.1 Hz], 1.53 and 1.70 (m, 2H, CH_2 11), 1.55 (m, 1H, 4aq.) [^2J (H4eq, H4ax) = 13.2 Hz], 1.64 (m, 2H, CH_2 7), 1.71 (m, 1H, 3ax), 1.91 (m, 1H, 2ax), 2.05 (dd, 1H, 6eq.) [^2J (H6eq., H6ax) = 12.6 Hz, ^4J (H6eq., H4eq.) = 2.6 Hz], 2.20 (d, 1H, 6ax) [^2J (H6eq., H6ax) = 12.6 Hz, ^4J (H6ax, H4eq.) = 0.9 Hz], 3.82 and 3.93 (m, 4H, CH_2 13 and 14), 4.83 (t, 1H, H 12). ^{13}C-NMR ($CDCl_3$): δ = 20.00 (C7), 20.72 (C8), 25.51 (C10), 31.20 (C11), 32.06 (C9), 34.12 (C3), 35.44 (C5), 48.21 (C4), 54.84 (C6), 55.75 (C2), 64.70 (C14). 64.80 (C13), 104.79 (C12), 211.68 (C1). $C_{14}H_{24}O_3$ (240.34).

*4.6. 3-(2,4,4-Trimethyl-6-oxo-1-cyclohexyl)-propanal (**19**)*

A solution of 0.80 g (3.3 mmol) **18**, 8 ml 2 N H_2SO_4 and 50 ml ether was stirred at RT for 48 h and hereupon extracted with ether three times. The combined ethereal layers were washed with water, dried ($MgSO_4$) and finally freed from the solvent in vacuo. The crude product **19**, a yellowish oil (yield 0.63 g, 70%) was directly used for the next reaction. MS: (*m*/*z*; r.I.) = 196 (M^+, 10), 181(15), 168(6), 163(5), 153(9), 140(26), 125(90), 112(12), 97(15), 83(100), 69(47), 55(70), 41(94). $C_{12}H_{22}O_2$ (196.29).

*4.7. (Z)-Ethyl-2-methyl-5-(2,4,4-trimethyl-6-oxo-1-cyclohexyl)-2-pentenoate (**20**)*

A solution of triethyl-2-phosphono-propionate (0.84 g, 3.5 mmol) and freshly re-crystallized 18-crown-6 (4.25 g, 16.0 mmol) in 50 ml absolute THF was treated in the same manner as already described for the preparation of **17** and then mixed with $KN(TMS)_2$ (0.5 M in THF, 6.4 ml, 3.2 mmol). Afterwards a solution of **19** (0.63 g, 3.2 mmol) in 20 ml dry THF was added drop-wise and stirred at –78 °C for 4 h. Quenching and work up followed the instructions for the preparation of **17**. Yield in total: 0.56 g (62.5%); pure (*Z*)-**20**: 0.45 g (50.0%), pure (*E*)-**20**: 0.05 g (5.6%). IR (NaCl, liquid film): ν = 2958, 1710, 1650, 1462, 1265, 1122 cm^{-1}. MS: (*m*/*z*; r.I.) = 280 (M^+, 1), 265 (1), 234 (20), 219 (4), 207 (7), 191 (6), 177 (2), 164 (4), 150 (3), 140 (23), 125 (100), 113 (12), 95 (18), 84 (17), 69 (15), 55 (27), 41 (17). ^{1}H-NMR ($CDCl_3$) [*Z*-isomer]: δ = 0.78 (s, 3H, CH_3 10), 0.96 (s, 3H, CH_3 9), 0.98 (m, 3H, CH_3 8), 1.21 (t, 3H, CH_3 16, ^3J = 7.0 Hz), 1.41 (t, 3ax), 1.52–1.77 (m, 6H, H1, H2, CH_2 7, H3eq.), 1.82 (s, 3H, CH_3 17), 2.04 (dd, 1H, H5eq., ^3J = 2.5 Hz, ^2J = 12.8 Hz), 2.12 (d, 1H, H5ax, ^3J = 12.5 Hz), 2.36 (m, 2H, CH_2 11), 4.09 (q, 2H, CH_2 15), 5.85 (t, 1H, H12, ^3J = 7.52 Hz). ^{13}C-NMR ($CDCl_3$) [*Z*-isomer]: δ = 14.23 (C16), 20.60 and 20.78 (C8 and C17), 25.06 (C11), 25.505 (C10), 27.37 (C7), 32.06 (C9), 34.17 (C2), 35.47 (C4), 48.20 (C3), 54.84 (C5), 55.66 (C1), 59.98 (C15), 127.21 (C13), 142.47 (C12), 168.15 (C14), 211.83 (C6). ^{1}H-NMR ($CDCl_3$) [*E*-isomer]: δ = 0.79 (s, 3H, CH_3 10), 0.97 (s, 3H, CH_3 9), 0.98 (m, 3H, CH_3 8), 1.22 (t, 3H, CH_3 16), 1.37 (t, 1H, H3ax, ^2J = 12.2 Hz), 1.49 (m, 1H, H3eq.), 1.53–1.73 (m, 4H, H1, H2 and CH_2 7), 1.76 (s, 3H, CH_3 17), 2.04 (dd, 2H, CH_2 5, ^2J = 12.4 Hz, ^4J = 2.3 Hz), 2.15 (d, 2H, CH_2 11, ^3J = 12.4 Hz), 4.10 (q, 2H, CH_2 15, ^3J = 12.4 Hz), 6.68 (t, 1H, H12, ^3J = 7.3 Hz). ^{13}C-NMR ($CDCl_3$) [*E*-isomer]: δ = 12.28 (C16), 14.25 and 20.77 (C8 and C17), 24.53 (C11), 25.52 (C10), 26.37 (C7), 32.05 (C9), 34.20 (C2), 35.55 (C4), 48.16 (C3), 54.92 (C5), 55.64 (C1), 60.32 (C15), 127.02 (C13), 142.04 (C12), 168.28 (C14), 211.91 (C6). $C_{17}H_{28}O_3$ (280.41).

*4.8. (Z)-2-Methyl-5-(2,4,4-trimethyl-6-methylen-1-cyclohexyl)-2-penten-1-ol (**3**)*

A mixture of 0.3 g (1.1 mmol) **20** in 13 ml absolute THF and 2.64 ml (1.3 mmol) *Tebbe*-reagent (0.5 M in toluene) was treated as already described for the preparation of **2** (first step). Yield: 0.36 g (crude product) of a dark-red oily liquid.

A solution of the just obtained crude methylene pentenoate (0.36 g, ≈ 1.3 mmol) was treated according to the instructions for the preparation of **2** (second step). Yield: 25 mg (7%) 3 as a nearly colorless oil. IR (NaCl, liquid film): ν = 3348, 3082, 2951, 1643, 1455, 1382, 1239, 1009, 891 cm^{-1}. MS: (*m*/*z*; r.I.) = 218 (M^+ – 18, 5), 203 (10), 189 (2), 175 (17), 162 (5), 149 (7), 137 (21), 123 (42), 107 (29), 95 (44), 82 (84), 67 (58), 55 (80), 41 (100). ^{1}H-NMR ($CDCl_3$): δ = 0.73 (s, 3H, CH_3 11), 0.83 (s, 3H, CH_3 10), 0.85 (s, 3H, CH_3 9), 0.99–1.62 (m, 6H, H1, H2, CH_2 3, CH_2 8), 1.73 (s, 3H, CH_3 16), 1.81 (m, 2H, CH_2 5), 1.93–2.11 (m, 2H, CH_2 12), 4.03 (s, 2H, CH_2 15), 4.58 (d, 2H, olefin. CH_2 7, ^2J = 17.5 Hz), 5.24 (t, 1H, H13, ^3J = 7.7 Hz). ^{13}C-NMR ($CDCl_3$): δ = 20.80 (C9), 21.29 (C16), 24.96 (C12), 25.54 (C11), 28.40 (C8), 31.96 (C10), 32.74 (C4), 33.82 (C2), 48.79 (C1), 49.03 (C3), 50.22 (C5), 61.64 (C15), 107.09 (C7), 128.97 (C13), 134.16 (C14), 148.91 (C6). $C_{16}H_{28}O$ (236.40).

*4.9. Ethyl-1-[2-(1,3-dioxolan-2-yl)-ethyl]4,6,6-trimethyl-2-oxo-1-cyclohex-3-enyl-carboxylate (**9**)*

11.67 ml n-BuLi (1.6 M in n-hexane) were added slowly to a cooled solution (–20 °C) of 2.31 ml (18.6 mmol) diisopropyl amide in 45 ml absolute THF and stirred for 20 min whereupon this mixture was further cooled down to –78 °C and mixed with 2.0 g (14.5 mmol) **6**. After stirring for 1 h at 0 °C and cooling down again at –78 °C at first 2.1 g (16.5 mmol) dimethyl-propylene-urea (DMPU) and then 1.72 g (17.4 mmol) ethyl cyanoformiate were added and stirred using a mechanical stirring device (a stir bar is not suited enough to mix the at this temperature resinous mixture). To complete the reaction the mixture was allowed to get warm at RT overnight. Quenching with water, extraction with ether and drying the combined ethereal phases ($MgSO_4$) followed. The residue after evaporation of the solvent was purified by CC (ligroin/ethyl acetate 80:20) to yield 2.20 g (72%) of this intermediate isophorono ethyl-formiate. $C_{12}H_{18}O_3$ (210.27). IR (NaCl, liquid film): ν = 2975, 1723, 1674, 1441, 1378, 1274, 1209, 1190, 1067,

1026, 904, 862 cm^{-1}. MS: (*m/z*; r.I.) =: 210 (M^+, 18), 195 (6), 181 (4), 149 (38), 123 (25), 83 (25), 82 (100), 55 (16), 54 (17). ^{1}H-NMR ($CDCl_3$): δ = 1.01–1.06 (2s, 6H, CH_3 9 and 10), 1.19 (t, ^3J = 7.02 Hz, 3H, CH_3 12), 1.90 (s, 3H, CH_3 8), 1.97–2.50 (dd, 2H, CH_2 5), 3.057 (s, 1H, H1), 4.079 (q, ^3J = 7.02 Hz, 2H, CH_2 11), 5.855 (s, 1H, H3). ^{13}C-NMR ($CDCl_3$): δ = 14.10 (C12), 24.50–25.15 (C9 and C10), 28.22 (C8), 35.92 (C6), 44.03 (C5), 60.75 (C11), 63.41 (C1), 124.29 (C3), 161.29 (C4), 168.87 (C7), 194.29 (C2).

NaH (0.25 g, 6.3 mmol, 60% dispersion) was washed with absolute benzene three times and after each washing procedure the solvent evaporated. To this purified NaH was added carefully freshly distilled DMF (20 ml) and a solution of the just obtained isophorono ethyl-formiate (1.00 g, 4.8 mmol) in 10 ml of dry DMF, followed by stirring at about 40 °C for 1 h. Then freshly purified (filtration over Al_2O_3 *Wölm*®) 2-(2-bromoethyl)-1,3-dioxolane (1.72 g, 9.5 mmol) was added and stirred at RT for 48 h. Quenching with water, extraction with ether and drying the combined organic phases ($MgSO_4$) followed. The residue consisted roughly of two main compounds (~1:1), each showing a molecular ion peak at *m/z* 310 in the GC/MS. Subsequent CC (ligroin ethyl acetate 80:20) furnished finally pure **9** (0.52 g, 19%). IR (NaCl, liquid film): ν = 2978, 2886, 2750 1723, 1668, 1443, 1379, 1274, 1191, 1145, 1094, 1034, 946, 863 cm^{-1}. MS: (*m/z*; r.I.) = 310 (M^+, 2), 295 (1), 265 (4), 249 (2), 237 (8), 221 (7), 210 (9), 195 (14), 149 (9), 126 (9), 99 (28), 82 (24), 73 (100), 55 (9), 45 (18). ^{1}H-NMR ($CDCl_3$): δ = 0.93 and 1.13 (2s, 6H, CH_3 10 and 11), 1.17 (t, 3H, ^3J = 7.02 Hz, CH_3 13), 1.48–2.02 (m, 4H, CH_2 9 and 14), 1.83 (s, 3H, CH_3 8), 2.15 (s, 2H, CH_2 5), 3.72–3.92 (m, 4H, CH_2 16 and 17), 4.04–4.16 (dq, 2H, ^3J = 4.5 Hz, ^2J = 2.76 Hz, CH_2 12), 4.79 (t, ^3J = 4,5 Hz, 1H, H15), 5.80 (m, 1H, H3). ^{13}C-NMR ($CDCl_3$): δ = 14.06 (C13), 23.34 (C9), 23.82 (C10 and 11), 24.40 (C10 and 11), 24.40 (C8), 30.08 (C14), 38.91 (C6), 45.05 (C5), 60.53 (C12), 63.10 (C1), 64.66 (C16 and 17), 104.59 (C15), 125.57 (C3), 156.56 (C4), 170.53 (C7), 196.87 (C2). $C_{17}H_{26}O_5$ (310.42).

*4.10. 6-[2-(1,3-Dioxolan-2-yl)-ethyl]-3,5,5-trimethylcyclohex-2-en-1-one (**10**)*

A mixture of **9** (0.10 g, 0.3 mmol) and 1.20 ml of a 5% KOH-solution (EtOH/H_2O 1:1) was heated at 100–105 °C for 48–60 h and after cooling down to RT several extractions with ether followed. The combined ethereal phases were dried ($MgSO_4$) and then freed from the solvent by evaporation. Purification by CC (ligroin/ethyl acetate 70:30) furnished 0.020 g (20%) **10**. IR (NaCl, liquid film): ν = 2962, 2890, 1667, 1436, 1379, 1140, 1034, 1730, 1247, 733, 944, 846 cm^{-1}. MS: (*m/z*; r.I.) = 238 (M^+, 7), 223 (11), 195 (6), 178 (2), 161 (28), 151 (3), 138 (14), 123 (33), 107 (4), 99 (17), 82 (20), 73 (100), 55 (12), 45 (21), 41 (16).^{1}H-NMR ($CDCl_3$): δ = 0.88–0.96 (2s, 6H, CH_3 9 and 10), 1.48–1.76 (m, 4H, CH_2 8 and 11), 1.83 (s, 3H, CH_3 7), 1.87–2.21 (m, 3H, CH_2 4 and H6), 3.72–3.92 (m, 4H, CH_2 13 and 14), 4.76 (m, 1H, H12), 5.71 (m, 1H, H2). ^{13}C-NMR ($CDCl_3$): δ = 19.75 (C8), 23.93–28.32 (C7, 9 and 10), 32.43 (C11), 35.98 (C5), 44.01 (C4), 56.60 (C6), 64.61 (C13 and 14), 104.20 (C12), 124.43 (C2), 157.93 (C3), 202.28 (C1). $C_{14}H_{22}O_3$ (238.33).

*4.11. 3-(4,6,6-Trimethyl-2-oxo-1-cyclohex-3-enyl)-propanal (**21**)*

10 (1.30 g, 5.5 mmol) was dissolved in 25 ml ether, mixed with 19 ml 2 N H_2SO_4 and stirred for 48 h. Work up as described before (see preparation of **16**) furnished 1 g (72%) of crude **21** which was used directly for the *Wittig* reaction at the free aldehyde group. MS: (*m/z*; r.I.) = 194 (M^+, 2), 179(6), 166 (4), 151(7), 138(23), 135(21), 123(100), 110(8), 91(8), 82(82), 67(10), 55(18), 54(17), 51(33). $C_{12}H_{18}O_2$ (194.27).

*4.12. (Z)-Ethyl-2-methyl-5-(4,6,6-trimethyl-2-oxo-1-cyclohex-3-enyl)-2-pentenoate (**22**)*

1.20 ml (5.5 mmol) triethyl-2-phosphono-propionate, 6.86 g (26.0 mmol, freshly re-crystallized) 18-crown-6, 100 ml absolute THF, then 10.85 ml (5.4 mmol) $KN(TMS)_2$ (0.5 M in THF) and 1 g (≈ 5.2 mmol) **21** in 20 ml absolute THF were treated as described for the preparation of **17**. Also the quenching of the reaction mixture with NH_4Cl and the work up followed the procedure as already quoted before. Yield: 0.58 g (40%) **22**. IR (NaCl, liquid film): ν = 2962, 1713, 1669, 1438, 1378, 1236, 1183, 1131, 1027, 886 cm^{-1}. MS: (*m/z*; r.I.) = 278 (M^+, 0), 263 (4), 232 (2), 217 (3), 205 (3), 189 (2), 175 (0), 161 (5), 151 (4), 138 (17), 124 (9), 123 (100), 82 (9), 69 (9), 67 (8), 41 (19), 39 (8). ^{1}H-NMR ($CDCl_3$): δ = 0.86–0.96 (2s, 6H, CH_3 9 and 10), 1.22 (t, 3H, ^3J = 7.2 Hz, CH_3 17), 1.45–1.59 (m, 2H, CH_2 7), 1.81–1.82 (m, 6H, CH_3 8 and 14), 1.87–1.93 (m, 1H, H1), 2.06–2.08 (d, 2H, ^4J = 3.9 Hz, CH_2 5), 2.31–2.43 (q, 2H, ^3J = 7.6 Hz, CH_2 11), 4.06–4.16 (q, 2H, ^3J = 7.1 Hz, CH_2 16), 5.72 (m, 1H, H3), 5.81–5.90 (t, 1H, ^3J = 7.4 Hz, H12). ^{13}C-NMR ($CDCl_3$): δ = 14.15 (C17), 20.54 (C14), 23.93-24.10 (C9 and 10), 25.02 (C7), 28.45 (C8), 28.61 (C11), 36.11 (C6), 44.42 (C5), 56.35 (C1), 59.95 (C16), 124.64 (C3), 127.56 (C13), 141.56 (C12), 157.79 (C4), 167.98 (C15), 202.11 (C2). $C_{17}H_{26}O_3$ (278.39).

*4.13. (Z)-2-Methyl-5-(4,6,6-trimethyl-2-methylen-1-cyclohex-3-enyl)-2-penten1-ol (**4**)*

A solution of **22** (0.30 g, 1.1 mmol) in 10 ml absolute THF was cooled down with ice to 0 °C in argon atmosphere, mixed drop-wise with 2.7 ml (1.4 mmol) *Tebbe*-reagent (0.5 M in toluene) and stirred at this temperature for 15 h. Quenching was accomplished by carefully injecting a 1:1 mixture of ether/MeOH by a syringe until the gas-evolution has stopped. The reaction mixture was filtered through a layer of Celite/Al_2O_3 (1:1) and washed with 1 l of ether. The resulting dark-red oil (0.4 g crude product) was directly used for the ester reduction in order to avoid decomposition on the stationary phase of the CC.

A solution of the just obtained crude methylene pentenoate (0.4 g, ≈ 1.4 mmol) in 7 ml absolute CH_2Cl_2 was cooled down to –78 °C in argon atmosphere and slowly mixed with 6.4 ml

(6.4 mmol) DIBAH (1 M solution in n-hexane). Further work up followed the procedure already described for the preparation of **2**. Yield of pure (*Z*)-**4**: 0.034 g (13.2%). IR (NaCl, liquid film): ν = 3340, 2929, 2868, 1650, 1610, 1436, 1379, 1008, 879 cm^{-1}. MS: (*m*/*z*; r.I.) = 234 (M^+, 3), 216 (1), 201 (8), 175 (7), 159 (5), 145 (20), 136 (17), 121 (100), 105 (16), 91 (14), 79 (11), 43 (12), 41 (18). ^{1}H-NMR ($CDCl_3$): δ = 0.76–0.88 (2s, CH_3 9 and 10), 1.33–2.04 (m, 13 H, H1, CH_2 5, 11and 12, CH_3 8 and 16), 4.05 (m, 2H, CH_2 15), 4.55–4.70 (d, 2H, ^2J = 30.5 Hz, =CH_2 7), 5.21 (t, 1H, ^3J = 7.3 Hz, H13), 5.72 (s, 1H, H3) .^{13}C-NMR ($CDCl_3$): δ = 21.21 (C16), 23.49 (C8), 25.94 (C11), 27.43–28.32 (C9 and 10), 28.58 (C12), 32.87 (C6), 41.44 (C5), 50.82 (C1), 61.71 (C15), 110.29 (C7), 122.62 (C13), 128.97 (C3), 134.00 (C14), 136.05 (C4), 146.25 (C2). $C_{16}H_{26}O$ (234.38).

*4.14. 6-[2-(1,3-Dioxolan-2-yl)-ethyl]-2,3,5,5-tetramethyl-cyclohex-2-en-1-one (**11**)*

To a solution of 3.64 ml (3.1 mmol) cyclohexyl isopropyl amide (CIPA) in 30 ml absolute THF at 0 °C under inert gas atmosphere 13.3 ml (21.3 mmol) n-BuLi (1.6 M in n-hexane) were added carefully whereupon the mixture was allowed to get warm to RT. By controlling the ambient temperature (19–23 °C) **10** (1.72 g, 7.2 mmol) in 10 ml absolute THF and 10 ml (175 mmol) of CH_3I were slowly added in the course of which the color of the mixture turned from amber-like to dark brown after 20 min. After stirring for 20 h at RT the mixture was quenched by adding a saturated NH_4Cl solution. Extraction with ether, drying the combined ethereal phases ($MgSO_4$) and evaporation of the solvent followed. The crude residue consisted of five methylated products. Yields upon CC (ligroin/ethyl acetate 80:20): first: 100 mg (5.3%), second: 80 mg (4.15%), third: 250 mg (13.7%), fourth: 130 mg (7.2%) and finally the fifth as the main product **11**: 270 mg (14.9%). IR (NaCl, liquid film): ν = 2961, 2886, 1663, 1447, 1378, 1311, 1141, 1038, 944, 899 cm^{-1}. MS: (*m*/*z*; r.I.) = 252 (M^+, 8), 237 (4), 207 (2), 175 (22), 151 (14), 137 (28), 121 (4), 99 (24), 96 (17), 73 (100), 67 (17), 45 (26), 41 (23). ^{1}H-NMR ($CDCl_3$): δ = 0.84–0.93 (2s, 6H, CH_3 10 and 11), 1.45–1.63 (m, 4H, CH_2 9 and 12), 1.67 (s, 3H, CH_3 7), 1.78 (s, 3H, CH_3 8), 1.91–2.24 (2m, 3H, H6 and CH_2 4), 3.72–3.92 (m, 4H, CH_2 14 and 15), 4.78 (m, 1H, H13). ^{13}C-NMR ($CDCl_3$): δ = 10.84 (C7), 20.01 (C9), 21.01 (C8), 24.32–28.55 (C10 and 11), 32.66 (C12), 35.32 (C5), 45.78 (C4), 56.78 (C6), 64.69–64.73 (C14 and 15), 104.40 (C13), 128.71 (C2), 150.03 (C3), 201.98 (C1). $C_{15}H_{24}O_3$ (252.36).

*4.15. 3-(3,4,6,6-Tetramethyl-2-oxo-1-cyclohex-3-enyl)-propanal (**23**)*

0.30 g (1.2 mmol) **11**, 20 ml ether and 4.2 ml 2 N H_2SO_4 were stirred for 48 h followed by extraction with ether, collecting the ethereal phases, drying them with $MgSO_4$ and evaporating the solvent. The brown, oily residue (0.26 g) was directly used for the next reaction. MS: (*m*/*z*; r.I.) = 208 (6. M^+), 193 (4), 180(5), 164(1), 152(20), 149(23), 137(100), 124(14), 109 (6), 96(61), 68(28), 67(32), 41(37). $C_{13}H_{20}O_2$ (208.30).

*4.16. (Z)-Ethyl-2-methyl-5-(3,4,6,6-tetramethyl-2-oxo-1-cyclohex-3-enyl)-2-pentenoate (**24**)*

0.30 ml (1.4 mmol) Triethyl-2-phosphono propionate, 1.65 g (6.3 mmol) freshly re-crystallized 18-crown-6, 25 ml absolute THF, then 2.6 ml (1.3 mmol) $KN(TMS)_2$ (0.5 M in THF) and 0.26 g (1.3 mmol) **23** in 10 ml absolute THF were treated as described for the preparation of **17**. Also the quenching of the reaction mixture with NH_4Cl and the work up followed the procedure as already described before. This time the purification was accomplished by TLC (Al_2O_3, toluene/ethyl acetate 90:10). Yield: 0.20 g (54.4%) (*Z*)-**24**. IR (NaCl, liquid film): ν = 2959, 2930, 1714, 1665, 1454, 1377, 1309, 1235, 1186, 1129, 1097, 1026 cm^{-1}. MS: (*m*/*z*; r.I.) = 292 (M^+, 1), 247 (1), 246 (1), 219 (3), 203 (2), 175 (6), 152 (17), 138 (11), 137 (100), 122 (4), 109 (3), 96 (6), 91 (5), 67 (15), 55 (7), 53 (7), 43 (10), 41 (20). ^{1}H-NMR ($CDCl_3$): δ = 0.81–0.93 (2s, 6H, CH_3 10 and 11), 1.21 (t, ^3J = 7.18 Hz, 3H, CH_3 17), 1.44–1.60 (m, 2H, CH_2 9), 1.68 (m, ^4J = 0.62 Hz, 3H, CH_3 18), 1.78 (s, 3H, CH_3 7), 1.80 (m, ^4J = 1.26 Hz, 3H, CH_3 8), 1.91–1.97 (m, 1H, H1), 2.12 (s, 2H, CH_2 5), 2.97 (q, ^3J = 18.1 Hz, 2H, CH_2 12), 4.09 (q, ^3J = 7.08 Hz, 2H, CH_2 16), 5.85 (t, ^3J = 7.44 Hz, 1H, H13). ^{13}C-NMR ($CDCl_3$): δ = 10.86–28.61 (C7, 8, 10, 11, 17 and 18), 25.31 (C9), 28.72 (C12), 35.36 (C6), 46.02 (C5), 56.48 (C1), 59.94 (C16), 127.43–128.83 (C3 and 14), 141.86 (C13), 149.86 (C4), 168.03 (C15), 201.81 (C2). $C_{18}H_{28}O_3$ (292.42).

*4.17. (Z)-2-Methyl-5-(3,4,6,6-tetramethyl-2-methylen-1-cyclohex-3-enyl)-2-penten-1-ol (**5**)*

0.20 g (0.70 mmol) **24**, 10 ml absolute THF and 1.70 ml (0.85 mmol) *Tebbe*-reagent (0.5 M in toluene) were treated as described for the preparation of **2**. The dark-red oily reaction product (270 mg, ≈ 0.9 mmol) was dissolved in 8 ml absolute CH_2Cl_2 and the solution cooled down to –78 °C and finally mixed drop-wise with 5.30 ml (5.3 mmol) DIBAH (1 M in CH_2Cl_2). This mixture was stirred overnight whereupon it was allowed to warm to RT. The further work up followed the already described procedure for the preparation of **2**. The crude residue was purified by preparative TLC (Al_2O_3, toluene/ethyl acetate 95:5) and furnished 17 mg (7.4%) **5**. IR (NaCl, liquid film): ν = 3352, 2930, 1640, 1607, 1447, 1383, 1008, 878, 735 cm^{-1}. MS: (*m*/*z*; r.I.) = 248 (M^+, 7), 234 (0), 233 (1), 215 (8), 189 (3), 173 (6), 159 (25), 150 (14), 136 (12), 135 (100), 119 (14), 105 (11), 91 (14), 77 (8), 67 (5), 55 (8), 43 (13), 41 (18). ^{1}H-NMR ($CDCl_3$): δ = 0.75–0.85 (2s, 6H, CH_3 11 and 12), 0.87–1.13 (m, 2H, CH_2 10), 1.30–2.05 (m, 5H, H1, CH_2 5 and 13), 1.52–1.71 (3s, 9H, CH_3 8, 9 and 17), 4.02 (m, 2H, CH_2 16), 4.55–4.85 (2s, 2H, =CH_2 7), 5.21 (m, 1H, H14). ^{13}C-NMR ($CDCl_3$): δ = 14.23–28.58 (C8, 9, 11, 12, 17), 26.08 (C10), 28.58 (C13), 32.38 (C6), 43.96 (C5), 52.93

(C1), 61.74 (C16), 108.26 (C7), 123.702 (C4), 129.19 (C14), 130.48–133.87 (C3 and 15), 148.29 (C2). $C_{17}H_{28}O$ (248.41).

Acknowledgements

The authors want to thank the former chief perfumers of *Dragoco*-Vienna (now *Symrise*, Vienna) *V. Hausmann* and *W. Höppner* for the olfactory evaluation, and *Symrise*, Vienna for its continuing interest in our research. For cooperation with synthetic work we are grateful to Mag.pharm. *G. Schöberl*.

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