Design, Synthesis and Structure-Odor Correlation of Novel Spiro[4.5]-decan-2-ones

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Abstract: Dehydration and Rupe rearrangement of 2-(3,3-dimethylcyclohexyl)hex-3-yne-2,5-diol (**9**) furnished as a 3% byproduct the intense vetiver-like smelling 4,7,7-trimethyl-1-methylenespiro[4.5]decan-2-one (**11**). Motivated by the commercial importance of vetiver oil and the lack of synthetic substitutes as well as the lack of insight into the structural requirements for vetiver odorants, an efficient synthetic route to vetiver-like smelling compounds was developed. It consists of Wittig–Horner–Emmons reaction of diverse cycloalkanones with triethyl 2-phosphonopropionate, subsequent Grignard reaction with in situ conversion to the trienolate, and classical Nazarov cyclization of the resulting dienones. This route not only leads to **11** in 61% yield in the final Nazarov cyclization, but also to 16 analogs, which provide insight into both, the Nazarov reaction and the structure-odor relationship of vetiver odorants. Other vetiver-like smelling compounds discovered include (1*RS*,4*SR*,5*SR*)-1,4,7,7-tetramethylspiro[4.5]decan-2-one (**16**), 4-methyl-1-methylenespiro[4.6]undecan-2-one (**30**) and 4-methyl-1-methylenespiro[4.7]dodecan-2-one (**31**).

Key words: cyclizations, khusimone, odor-structure correlation, spiro compounds, vetiver

Introduction

Despite its commercial importance, vetiver oil continues to be one of the few natural perfumery raw materials, for which no synthetic substitutes are available to the perfumer. It is produced by steam distillation of the roots of *Vetiveria zizanoides* (L.) Nash, a tufted grass of the Graminaceae family, which is cultivated in Haiti, Java, Réunion, Madagascar and China. On average, 1000 kg of dried roots yield about 10–15 kg ethereal oil (ca. 50 t/a),[1] which is priced around € 35–100 depending on the origin and quality. The bourbon quality (10% of total production) possesses an additional rosy tonality with sulfury aspects, while vetiver oil from Haiti (50% of total production) shows additional aspects reminiscent of jute and roasted peanuts, and the Java and China qualities (together 35% of total production) have harsh and smoky bynotes.[1] All vetiver oils share, however, a characteristic and distinctive suave and sweet woody-earthy odor with green, grapefruit- and rhubarb-type facets that is much appreciated in perfumery.[2] Vetiver oil is used in feminine fragrances like »Mitsouko« (Guerlain, 1919) and »Chanel N°5« (Chanel, 1921),[3] but is more important in masculine perfumery, e.g. »Aramis« (Lauder, 1965) and »Déclaration« (Cartier, 1998).[4] It is even the main theme of a number of masculine fragrances: »Vetiver« (Creed, 1948), »Vétiver Carven« (Carven, 1957), »Vetiver de Guerlain« (Guerlain, 1959), »Vetiver de Givenchy« (Givenchy, 1959), »Vetyver Lanvin« (Lanvin, 1964), »Vetiver de Puig« (Puig, 1978), »Eau de Vétiver« (Yves Rocher, 1982), »Vetyver Dry« (Carven, 1988), »Imperial Vetiver« (Yardley, 1997), »Pure Vetiver« (Azzaro, 2000), »Vétiver Extraordinaire« (Editions de Parfums Frédéric Malle, 2002), and »Vetiver Oriental« (Les Salons du Palais Royal Shiseido, 2002), to give just a dozen examples.

But while there is no question about the importance of vetiver oil in perfumery, there is no agreement upon the constituents responsible for this typical odor.[2] Mookherjee et al. [5] of IFF claimed β-vetivone (**1**, Figure 1), which makes up 2.9% of the neutral part of Haitian vetiver oil,[6] to be the key odorant, but the recent work of Spreitzer et al. on (–)- and (+)-β-vetivone (**1**),[7] as well as on chiral partial structures,[8,9] clearly established that neither β-vetivone (**1**) nor its partial structures exhibit typical vetiver notes. Also Maurer[10] at Firmenich found β-vetivone (**1**) relatively weak and uninteresting. According to him, khusimone (**2**) and the two dimethyloctalones **3** and **4** (Figure 1) are responsible for the typical odor characteristics of vetiver oil.[10] Yet Mookherjee et al. resynthesized the dimethyloctalones **3** and **4**,[5] and ascribed them only a weak woody odor, with green, rooty and ambery nuances. Weyerstahl et al.[6] described *rac*-**4** as minty, fruity (plum/fig), peppery and tobacco-like. But like Maurer, Weyerstahl et al. regard khusimone (**2**) as one of the most important constituents for the odor of vetiver oils.[6] Besides, they considered the zizaenone **5** close to but weaker than khusimone (**2**), and reported eremophiladienal (**6**) and the new 1,7-cyclogerma-1(10),4-dien-15-al (**7**)[11] as valuable, typical vetiver-type odorants reminiscent of khusimone (**2**). However, the norsesquiterpene khusimone (**2**), present in about 2%,[6] is the only constituent on which both perfumers and chemists agree to possess a typical vetiver odor, and thus also served as the lead in a recent structure-odor relationship study of Spreitzer et al.[12–14]

Incitation and Modeling

We thus were very excited when we discovered a byproduct, which emanated typical vetiver odor characteristics. In the course of our synthetic work on new damascones,[15]

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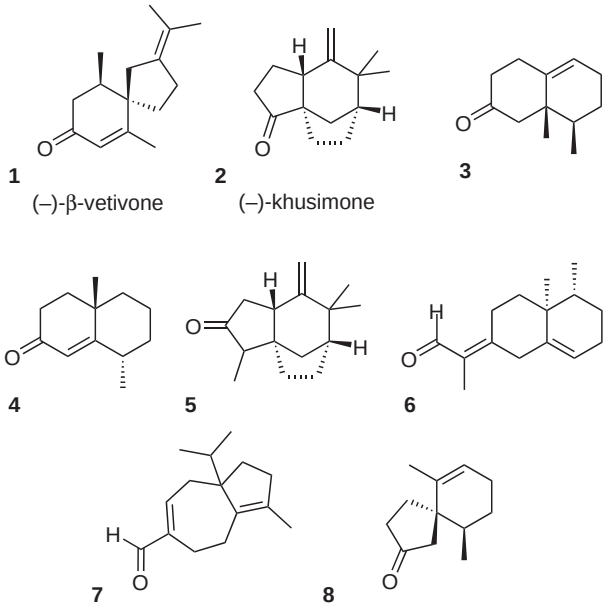
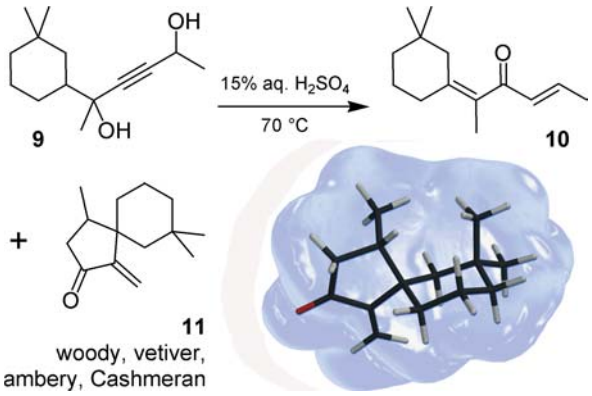


Figure 1 Some important constituents of vetiver oil and the spiroketone **8**

we had submitted 2-(3,3-dimethylcyclohexyl)hex-3-yne-2,5-diol (**9**) to dehydration/Rupe rearrangement, and, besides the desired dienone **10**, isolated in 3% yield the consecutive Nazarov product **11** (Scheme 1). This spiro[4.5]decanone possessed a woody-vetiver odor.



Scheme 1

Interestingly, **11** was structurally related to a desisopropyl spirovetiv-3-en-7-one[16] that Büchi et al.[17,18] had reported to also possess a typical vetiver odor: 6,10-dimethylspiro[4.5]dec-6-en-2-one (**8**). Although structurally related to some of the constituents of vetiver, **8** has not yet been found in essential oils. It was first reported by Marshall et al.[19,20] as an intermediate in the revision of the wrong hydroazulene structure for β-vetivone proposed by Pfau and Plattner.[21] The use of **8** in perfumery was later patented by Firmenich.[22] But neither **8** nor its derivatives described in the patent[22] were introduced into perfumery, perhaps due to their laborious syntheses.

Superimposing the energy-minimized structures (PM3) of 4,7,7-trimethyl-1-methylenespiro[4.5]decan-2-one (**11**, cf. Figure 2) and 6,10-dimethylspiro[4.5]dec-6-en-2-one (**8**, cf. Figure 3) on that of khusimone (**2**), we found a better degree of overlap with the former. The hydrophobic *gem*-dimethyl motives superimpose well, and also the steric bulk around the quarternary C-3a atom (azulene numbering) of khusimone is better mimicked by **11**.

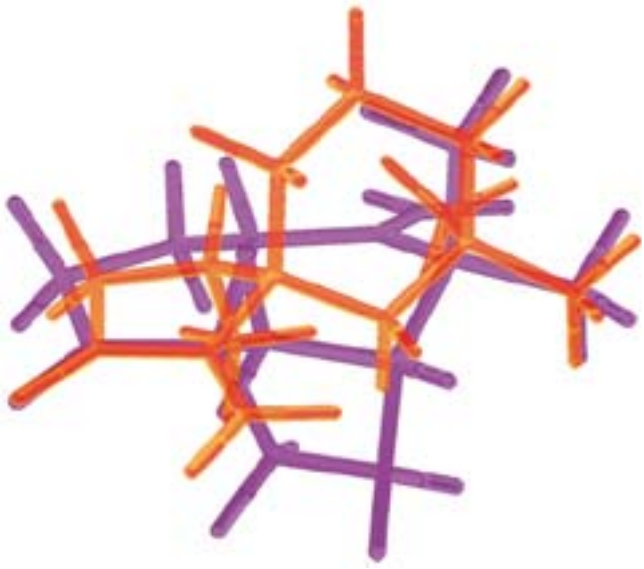


Figure 2 Energy minimized structure of **11** superimposed on **2**

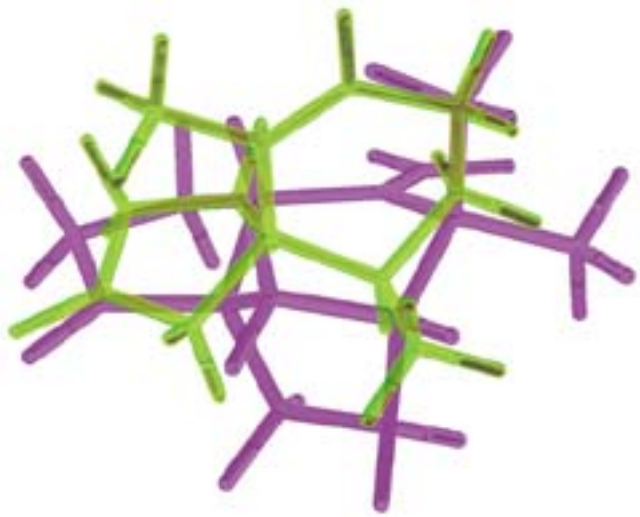


Figure 3 Energy minimized structure of **8** superimposed on **2**

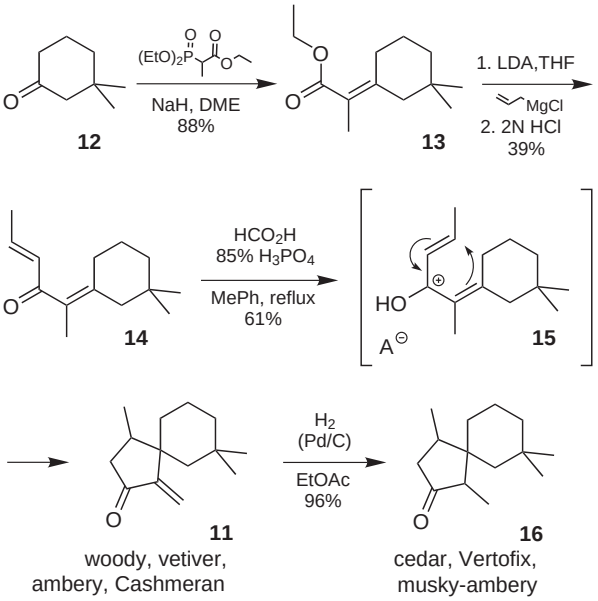
Is khusimone (**2**) a valid template for the design of novel spirocyclic vetiver odorants? This was the crucial question. To answer it, we designed a number of target compounds around the lead **11**. But first of course, we needed a directed synthetic access to our lead compound **11**.

Syntheses and Olfactory Properties

Kuroda et al.[23] recently synthesized related spiro[4.5]decane and spiro[4.4]nonane systems employing the $FeCl_3$-mediated silicon-directed Nazarov conditions of Denmark et al.,[24] which required the synthesis of β-trimethylsilyl substituted divinyl ketones. They however observed that the position of the double bond in the product was not determined by the β-silyl substituent, but rather by α-effects of alkyl groups. And even at –15 °C, with desilylated substrates and $FeCl_3$ as catalyst, moderate yields (32–39%) were obtained.

We thus reasoned that the proximate perpendicular spirocyclic cyclohexane ring probably hindered the alignment of the C–Si bond and the empty *p*-orbital necessary for hyperconjugation.[25] The selectivities reported by Kuroda et al.[23] were probably due only to the α-effects of the methyl substituents. Thus, the conditions of Denmark et al. should not bring any advantage to classical Nazarov conditions. Instead, they would elongate the synthetic access.

Instead of the Rupe alkyne carbinol rearrangement of the initial synthesis, we chose a Grignard reaction with allylmagnesium chloride and in situ conversion of the formed dienone into its trienolate.[26] The required ethyl 2-(3,3-dimethylcyclohexylidene)propionate (**13**) was prepared by a standard Wittig–Horner–Emmons reaction[27] of 3,3-dimethylcyclohexanone (**12**) with triethyl 2-phosphonopropionate in 88% yield (Scheme 2). Both a solution of the α,β-unsaturated ester **13** and a solution of the reactive allylic Grignard reagent were added simultaneously to a solution of LDA in THF. The formed lithium trienolate was then quenched with 2 N aqueous hydrochloric acid, ensuring isomerization of the terminal double bond into conjugation. By flash chromatography, we isolated the pivotal intermediate **14** in 39% yield. Submitting **14** to classical Nazarov conditions,[28] i.e. formic acid and 85% phosphoric acid (1:1) in refluxing toluene, GC monitoring indicated 80% conversion after 8 hours of reaction time. After workup and chromatographic purification, we obtained olfactorily pure **11** in 61% yield, emanating indeed a pleasant woody, vetiver-type odor with ambery nuances and aspects reminiscent of Coniferane and Cashmerane. By multidimensional preparative GC, we were able to separate the diastereomers of **11** and attribute their relative configurations. For these two isomers we found odor thresholds of 2.2 ng/L (4*RS*,5*SR*; 56%) and 3.2 ng/L air (4*RS*,5*RS*; 44%), respectively; better but in the same range as (–)-khusimone (**2**; 4.7 ng/L). Hydrogenation of the diastereomeric mixture of **11** afforded in 96% the saturated ketone **16**, with a more cedarwood odor and vetiver nuances being present reminiscent of Vertofix.[29] The threshold of the mixture **16** was determined to be 12.6 ng/L air; the most powerful diastereomer was isolated by preparative GC and assigned the 1*RS*,4*SR*,5*SR*-configuration by 2D NMR techniques (see Experimental); it possessed an odor threshold of 3.3 ng/L air.



Scheme 2

To study the importance of the 7,7-dimethyl substitution on the odor, we then applied this synthetic sequence to 2-, 3-, and 4-methylcyclohexanone. In the case of 2-methylcyclohexanone, the corresponding target molecule **17** (Figure 4) was obtained diastereoselectively as the 4*RS*,5*RS*,6*RS*-isomer; however only in 8%, while the main product of the Nazarov cyclization was the isomeric (1*RS*,5*RS*,6*RS*)-1,4,6-trimethylspiro[4.5]dec-3-en-2-one (**34**). In the case of a 7-methyl substitution, the target molecule **19** was already the main product (29%), accompanied by only 19% of the endocyclic isomer (cf. Experimental). The next target compound **21** was clearly the dominant product (62%) of the Nazarov cyclization of 2-(4′-methylcyclohexylidene)hex-4-en-3-one, accompanied by 17% of the isomeric 1,4,8-trimethylspiro[4.5]dec-3-en-2-one. Hydrogenation of **17**, **19** and **21** furnished **18**, **20** and **22** (Figure 4), the latter two being almost odorless. Compound **18**, which was obtained stereoselectively as 1*RS*,4*SR*,5*SR*,6*SR*-isomer, possessed a woody-ambery note, while the corresponding enone **17** was mainly moss- and fir-like with a metallic pineapple note. The 7-methyl analog **19** was still fruity, but a woody-resinous part prevailed. Its odor threshold (21.4 ng/L air) was however almost ten times weaker than that of the 7,7-dimethyl lead **11**. The 8-methyl substituted **21** surprisingly possessed in addition to the fruity-woody note, a patchouli and oakmoss character; yet was even weaker (52.5 ng/L air).

Next on our agenda were the 7,9-dimethylspiro[4.5]cycles **23** and **24** (Figure 4). Standard Nazarov reaction provided the 4*RS*,5*rs*,7*RS*,9*SR*-configured **23** in 17% yield, while the main product was the endocyclic isomer (39%). Astonishingly, no woody character was present in the odor profile of **23**; instead it emanated an earthy, metallic scent with damascone-like nuances. Its odor threshold was poor (159 ng/L air), but again the hydrogenated derivative **24** was even weaker, only vaguely woody-nutty.

Starting from 3,3,5-trimethylcyclohexanone, we then introduced a 9-methyl group into the original lead structure **11**. The projected target **25** was the only cyclization product we could isolate from the Nazarov cyclization (31%), and we could attribute its ambery-woody odor to the 4*RS*,5*SR*,9*RS*-diastereoisomer (63%). Due to unambiguous NOE attributions between 1-CH_3 and 2′-H_{eq} and 6′-H_{eq}, respectively, we were even able to determine the diastereomer ratio of the employed 2-(3′,3′,5′-trimethylcyclohexylidene)hex-4-en-3-one as 55:45 (2*E*/2*Z*, cf. Experimental). The hydrogenated ketone **26** possessed an earthy, patchouli-type odor with salicylate-like and slightly cinnamic nuances. With odor thresholds of 4.4 ng/L air (**25**) and 6.8 ng/L air (**26**), both compounds were almost as strong as the leads **11** and **16**, but with strongly diminished vetiver character.

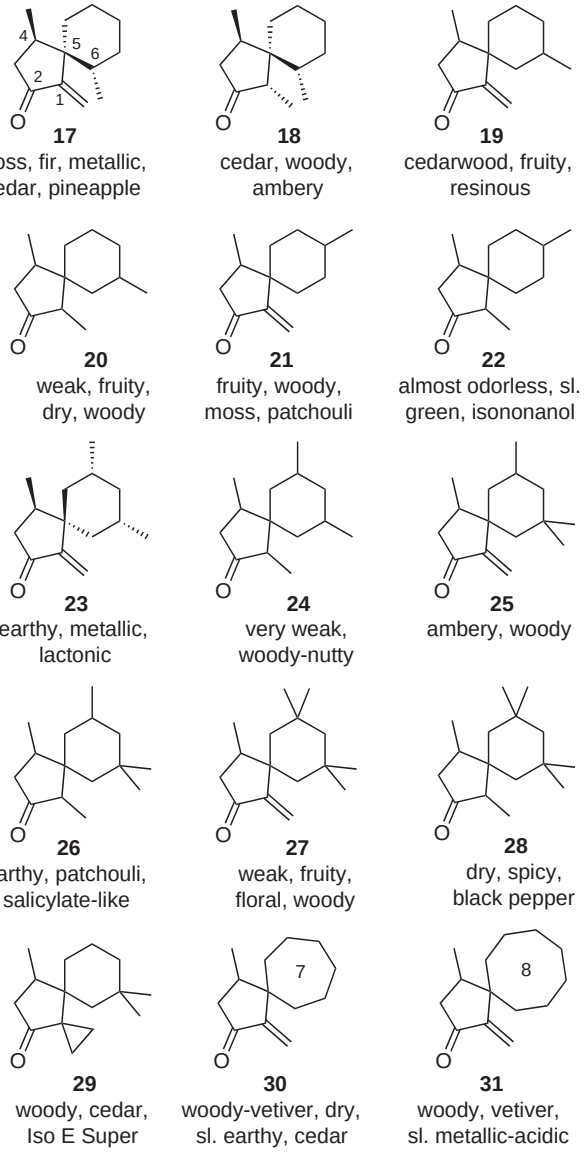


Figure 4 Compounds **17**–**31** prepared for structure-odor correlation

The 7,7,9,9-tetramethyl analog **27** and **28** were also obtained via the elaborated synthetic sequence, whereby Nazarov cyclization provided just the desired *exo*-methylene isomer **27** in 66% yield. Both **27** and **28** were, however, weak, maybe due to their low vapor pressure; yet, **28** showed an interesting dry-spicy, peppery character. However, so far only **11** was really vetiver-like in smell.We therefore were interested in the cyclopropanated derivative **29**. Simmons–Smith reaction of **11** provided **29**, but again the vetiver character was lost, and the odor was described as woody, cedarwood, reminiscent of Iso E Super.

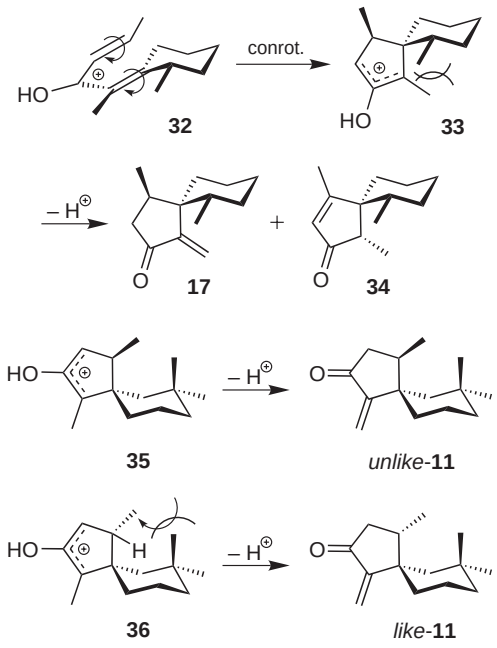
The last two projected target molecules of our series were the spiro[4.6]undecanone **30** and the spiro[4.7]dodecanone **31** (Figure 4). A cyclooctane ring is very well able to mimic the steric bulk of a dimethylcyclohexane ring, as we had observed in the synthesis of violet odorants,[30] and as was also reported for theaspirane analog by Weyerstahl et al.[31] and for Ambrox® derivatives by Sandermann et al.[32] Thus, especially **31** seemed to be an interesting synthetic target, and with 2.5 ng/L air it indeed possessed a threshold similar to **11** while also being close in odor to this lead. Even the spiro[4.6]undecanone **30** possessed a pronounced vetiver character with a moderate threshold of 9.4 ng/L air. The Nazarov cyclization of 2-cycloheptylidenehex-4-en-3-one went smoothly and good yields of **30** (58%) and its *endo*-isomer (31%) were obtained; yet, in the case of the cyclooctyl derivatives, the endocyclic ethyl 2-cyclooctenylpropionate and the corresponding 2-cyclooct-1-enylhex-4-en-3-one were formed, and the Nazarov cyclization of the latter went sluggishly, with large amounts of 1,4-dimethyl-3,5,6,7,8,9,10,10a-octahydro-1*H*-benzocycloocten-2-one being formed from the endocyclic 2-cyclooct-1-enylhex-4-en-3-one. This octahydrobenzocyclooctenone was impossible to separate from **31** by repeated flash chromatography, and therefore, we employed preparative HPLC to obtain a pure sample of **31** for spectral characterization and olfactory evaluation.

Discussion and Evaluation

Based on conformational calculations (MMFF94, PM3) and the NMR data, we rationalize the obtained yields and isomeric ratios with the mechanistic considerations detailed in Scheme 3: The diastereoselective formation of the cationic intermediate **33** can be explained by the conrotatory electrocyclization of **32**. The steric interactions of the methyl groups on C-1 and C-6 in **33** favor the formation of the endocyclic isomer **34**, and thus, the exocyclic isomers become more favored in the series **17** → **19** → **21**. Therefore, the closer the substituent is located to the spiro-atom, the lower the yields are and the more favored is the formation of the endocyclic isomers.

Severe 1,3-diaxial strain is unavoidable in all *gem*-dimethyl compounds studied, and this favors the formation of the methylene isomers, although actually the mode differs

for the different diastereoisomers. In the case of **35**, for instance, there is no steric hindrance between 4-Me and 7-Me$_{ax}$, but elimination of 4-H would bring 4-Me and 7-Me$_{ax}$ in close proximity; thus, the *unlike* (*u*) exomethylene product is formed. For the same reason, the formation of the *like* (*l*) exomethylene diastereomer instead of the endomethylene product seems, however, rather unfavorable; one may even call this another form of a *masochistic steric effect*.[33] However, the close proximity of 4-Me and 7-Me$_{ax}$ forces 4-H into an almost *pseudoequatorial* position. Therefore, C-4 can not attain the necessary 2p$_z$-character to allow an elimination transition state; and thus, no endocyclic isomer is formed, but the sterically crowded *like*-**11** diastereomer.



Scheme 3

Quite astonishingly, in terms of odor, the relative configuration of C-4 seems to be of little influence, as both *like*- and *unlike*-**11** share the desired vetiver tonality and their odor thresholds are comparable (2.2 and 3.2 ng/L air, respectively): In the range of, or even slightly better than that of khusimone (**2**; 4.7 ng/L air). This is in agreement with the superposition analysis in Figure 2, in which the configuration of C-4 also does not affect the overall fit of **11** on khusimone (**2**). However, for individual persons sensitivities towards *like*- and *unlike*-**11** can vary extensively, with some being more sensitive towards *like*-**11** and some more towards *unlike*-**11**. In terms of odor threshold, the most powerful hydrogenated 1*RS*,4*SR*,5*SR*-isomer of **16** is comparable in strength to the diastereoisomers of **11**, but has only slight vetiver nuances. Noteworthy is that its 1-Me group does not superimpose with that of khusimone (**2**); and maybe this is the reason for the diminished vetiver quality? In general, the hydrogenated mixtures were very weak, not only because they were diluted by inactive isomers.

The position of the substituents on the cyclohexyl moiety is most important. Of the monomethyl derivatives, only the 7-substituted **19** was typical woody in smell, while both the 6-substituted **17** and the 8-substituted **21** shared a dominant moss- and fir-like note. The additional symmetrical methyl-group in **23** shifted the odor of **19** towards an earthy-metallic tonality, but the 7,7,9-trimethyl substituted **25** smelled again mainly woody – its hydrogenated analog **26** was patchouli-like. The 7,7,9,9-tetramethyl spirocycle **27** finally becomes very weak; weaker in fact than the hydrogenated **28**, which is of spicy, peppery tonality. Thus, it seems that different receptors respond to **26** and **28**. The cyclopropyl moiety of **29** did not improve the vetiver note of **11** but instead shifted the olfactory impression towards cedarwood. Both **30** and **31** were able to mimic **11**, yet were inferior in terms of odor threshold.

Therefore, the importance of the 7,7-dimethyl substitution pattern on the pleasant vetiver odor of **11** is apparent. As vetiver is a complex odor note, designing vetiver odorants is a tricky balancing act. Nevertheless, khusimone (**2**) seems a valid template for vetiver odorants, and our novel spiro[4.5]decanones established the importance of a quarternary carbon atom at a distance of 5.0 Å to a carbonyl carbon atom – the steric bulk of which can be mimicked by a larger ring. In conclusion, we postulate a hydrophobic binding site 5.0 Å apart from the carbonyl carbon of an α-methyl or α-methylene substituted C_{13}–C_{16} ketone or aldehyde to be a structural key feature for vetiver odor. Compounds **5** (4.9 Å), **6** (5.3 Å) and **7** (4.7 Å) meet this structural criterion, while **1** (6.1 Å), **3** (2.5 Å) and **4** (3.0 Å) do not; yet, obviously many more vetiver-smelling compounds need to be synthesized in order to validate this hypothesis.

All mps and bps are uncorrected. All reactions were performed under N_2 using reagents and solvents (puriss. or purum) from Fluka or Aldrich without further purification. The required cycloalkylidenepropionates were synthesized from commercially available cycloalkanones by standard Wittig–Horner–Emmons reaction,[27] but employing ethylene glycol dimethyl ether instead of benzene. Flash Chromatography (FC): Merck Kieselgel 60 (particle size 0.040–0.063 mm). Thin layer chromatography (TLC): Merck Kieselgel 60 F_{254} (particle size 0.005–0.020 mm, layer thickness 0.25 mm on glass); detection by spraying Merck PMA spray solution for TLC (Cat. No. 1.00480.0100). Attenuated-total-reflection (ATR) IR spectroscopy: Bruker VECTOR 22 with Harrick SplitPea micro ATR (Si), frequencies ordered according to intensity (Abbr. oop = out of plane). NMR: Bruker AVANCE DPX-400 ($CDCl_3$); ^{1}H: chemical shifts δ in ppm relative to tetramethylsilane (=0 ppm); ^{13}C: δ in ppm relative to $CDCl_3$ (=77 ppm); multiplicities assigned by DEPT experiments. MS: Finnigan MAT 95 or HP Chemstation 6890 GC/5973 Mass Sensitive Detector. Elemental analyses: F. Hoffmann-La Roche AG, Basel, PRPI-S, and Eidgenössische Materialprüfungs- und Forschungsanstalt (EMPA), Überlandstrasse 129, Dübendorf. (–)-Khusimone (**2**) was kindly provided by Dr. R. Kaiser, Givaudan Dübendorf. Odor threshold: 4.7 ng/L air.

[2(1′)*E*/*Z*,4*E*]-2-(3′,3′-Dimethylcyclohexylidene)hex-4-en-3-one (14); Typical Procedure

At 0 °C, a 1.6 M BuLi solution in hexane (37.2 mL, 59.5 mmol) was added dropwise to a stirred solution of diisopropylamine (6.02 g, 59.5 mmol) in THF (100 mL). After stirring for 10 min, a solution

of **13** (10.0 g, 47.5 mmol) in THF (10 mL) and a 1 M allylmagnesium chloride solution in Et_2O (59.5 mL, 59.5 mmol) were added simultaneously at this temperarture from two dropping funnels over a period of 30 min. After stirring for another 2 h at this temperature, 2 N aq HCl (100 mL) was added dropwise with stirring. The reaction mixture was poured into H_2O (300 mL), the organic layer separated, and the aqueous layer extracted with Et_2O (2 × 500 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in a rotary evaporator. Silica gel FC (pentane–Et_2O, 19:1, R_f 0.21) of the resulting residue provided **14** (3.81 g, 39%) as a colorless liquid.

IR (neat): 1651, 1682 (ν C=O, double unsat.), 972 (δ C=C–H oop), 1442 cm^{-1} (δ H–C–H).

^{1}H NMR ($CDCl_3$): δ = 0.83/0.94 [s, 6 H, $C(CH_3)_2$], 1.33–2.16 (m, 6 H, 4′-CH_2 to 6′-CH_2), therein 1.77/1.81 (s, 3 H, 1-CH_3), 1.88/1.99 (s, 2 H, 2′-H_2), and 1.91/1.93 (dd, *J* = 7.0, 2.0 Hz, 3 H, 6-H_3), 6.11/6.15 (dq, *J* = 15.5, 2.0 Hz, 1 H, 4-H), 6.76/6.81 (dq, *J* = 15.5, 7.0 Hz, 1 H, 5-H).

^{13}C NMR ($CDCl_3$): δ = 15.3/15.4 (q, C-1), 18.2/18.3 (q, C-6), 22.8/23.6 (t, C-5′), 28.3/28.4 [q, $C(CH_3)_2$], 29.1/32.0 (t, C-6′), 33.2/33.7 [s, $C(CH_3)_2$], 39.2/39.3 (t, C-4′), 42.9/45.0 (t, C-2′), 128.5/128.6 (s, C-2), 132.2/132.6 (d, C-4), 137.8/138.2 (s, C-1′), 145.0/145.2 (d, C-5), 201.6/201.4 (s, C-3).

MS: *m*/*z* (%) = 41 (80) $[C_2HO]^+$, 69 (85) $[C_4H_5O]$, 95 (24) $[M - C_4H_5O - C_3H_6]^+$, 107 (20) $[C_7H_7O]^+$, 121 (100) $[C_{10}H_{14}O - C_2H_5]^+$, 135 (53) $[C_{10}H_{14}O - CH_3]^+$, 150 (33) $[C_{10}H_{14}O]^+$, 163 (7) $[M - C_3H_7]^+$, 177 (5) $[M - C_2H_5]^+$, 191 (30) $[M - CH_3]^+$, 206 (25) $[M]^+$.

Anal. Calcd for $C_{14}H_{22}O$ (206.33): C, 81.50; H 10.75. Found: C, 81.50; 10.55.

4,7,7-Trimethyl-1-methylenespiro[4.5]decan-2-one (11)

Formic acid (100 mL) and 85% H_3PO_4 (100 mL) were added to a stirred solution of **14** (12.0 g, 58.2 mmol) in toluene (100 mL), and the mixture was refluxed for 8 h, prior to pouring into H_2O (400 mL) and extracting with Et_2O (2 × 500 mL). The combined organic extracts were washed with sat. aq $NaHCO_3$ (2 × 300 mL) and brine (300 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by silica gel FC (pentane–Et_2O, 19:1, R_f 0.37) to provide 7.62 g (61%) of **11** as a colorless odoriferous liquid.

IR (neat): 1725 (ν C=O), 1638 (ν C=C), 1456 (δ H–C–H), 935 cm^{-1} (δ C=C–H oop).

MS: *m*/*z* (%) = 41 (92) $[C_2HO]^+$, 79 (59), 93 (98), 107 (70) $[C_nH_{2n-5}]^+$, 121 (100) $[C_9H_{12}O - CH_3]^+$, 136 (66) $[M - C_3H_6 - CO]^+$, 149 (22) $[M - C_3H_6 - CH_3]^+$, 164 (55) $[M - C_3H_6]^+$, 191 (89) $[M - CH_3]^+$, 206 (21) $[M]^+$.

Anal. Calcd for $C_{14}H_{22}O$ (206.33): C, 81.50; H, 10.75. Found: C, 81.41; H, 10.73.

Odor Description: woody, vetiver, ambery, aspects of Coniferane/Cashmerane.

The diastereoisomers were separated by preparative multidimensional GC on Supelcowax 10 (30 m, 0.53 mm, 1 μm).

(±)-(4*RS*,5*SR*)-11

Content: 56%; Odor Threshold: 2.2 ng/L air.

^{1}H NMR ($CDCl_3$): δ = 0.82 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.88 (s, 3 H, 7-CH_{3eq}),1.04 (s, 3 H, 7-CH_{3ax}), 1.18 (d, *J* = 14.0 Hz, 1 H, 6-H_{ax}), 1.37 (m_c, 2 H, 8-CH_2), 1.49 (d, *J* = 14.0 Hz, 1 H, 6-H_{eq}), 1.62 (m_c, 4 H, 9-, 10-CH_2), 1.93 (d, *J* = 18.5 Hz, 1 H, 3-H_b), 2.48 (quint, *J* = 7.0 Hz, 1 H, 4-H), 2.70 (dd, *J* = 18.5, 7.0 Hz, 1 H, 3-H_a), 5.25 (s, 1 H, H_bC=), 6.02 (s, 1 H, H_aC=).

NOESY (^{1}H/^{1}H): 3-H_a/6-H_{eq}, 4-H/6-H_{eq}, 4-H/7-CH_{3ax}.

^{13}C NMR ($CDCl_3$): δ = 17.1 (q, 4-CH_3), 19.3 (t, C-9), 31.6 (s, C-7), 29.8 (q, 7-CH_{3ax}), 31.5 (t, C-10), 32.0 (q, 7-CH_{3eq}), 34.8 (d, C-4), 38.9 (t, C-8), 43.6 (t, C-3), 46.7 (s, C-5), 49.7 (t, C-6), 116.7 (t, 1-H_2C=), 154.3 (s, C-1), 207.8 (s, C-2).

(±)-(4*RS*,5*RS*)-11

Content: 44%; Odor Threshold: 3.2 ng/L air.

^{1}H NMR ($CDCl_3$): δ = 0.91 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.98 (s, 3 H, 7-CH_{3eq}), 1.01 (s, 3 H, 7-CH_{3ax}), 1.03 (m_c, 1 H, 10-H_{ax}), 1.37 (d, *J* = 14.0 Hz, 1 H, 6-H_{ax}), 1.50–1.62 (m, 3 H, 8-CH_2-, 9-H_{eq}), 1.55 (d, *J* = 14.0 Hz, 1 H, 6-H_{eq}), 1.65 (m_c, 1 H, 9-H_{ax}), 1.82 (m_c, 1 H, 10-H_{eq}), 1.95 (dd, *J* = 18.5, 2.0 Hz, 1 H, 3-H_b), 2.42 (quint d, *J* = 7.0, 2.0 Hz, 1 H, 4-H), 2.64 (dd, *J* = 18.5, 7.0 Hz, 1 H, 3-H_a), 5.19 (s, 1 H, H_bC=), 6.01 (s, 1 H, H_aC=).

NOESY (^{1}H/^{1}H): H_bC=/6-H_{ax}, 3-H_a/10-H_{eq}, 3-H_b/4-CH_3, 4-CH_3/6-H_{eq}, 4-H/7-CH_{3ax}, 4-H/9-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 17.7 (q, 4-CH_3), 19.6 (t, C-9), 31.0 (s, C-7), 27.6 (q, 7-CH_{3eq}), 33.9 (q, 7-CH_{3ax}), 33.4 (d, C-4), 37.4 (t, C-10), 39.7 (t, C-8), 43.9 (t, C-3), 46.9 (s, C-5), 40.9 (t, C-6), 115.9 (t, 1-H_2C=), 154.8 (s, C-1), 207.4 (s, C-2).

1,4,7,7-Tetramethylspiro[4.5]decan-2-one (16); Typical Procedure

A suspension of **11** (0.30 g, 1.45 mmol) and 10% Pd/C (0.02 g, 0.19 mmol) in EtOAc (10 mL), was twice evacuated and flushed with N_2. Following two cycles of evacuation and flushing with H_2, the reaction mixture was stirred at r.t. overnight under a positive pressure of H_2. The catalyst was removed by vacuum filtration over a pad of Celite, and the filtrate was concentrated in a rotary evaporator. The resulting residue was purified by Kugelrohr distillation to provide **16**; boiling range 50–80 °C/0.05 mbar (0.29 g, 96%). The most powerful diastereoisomer was detected by GC-olfactometry and isolated by preparative multidimensional GC on Supelcowax 10 (30 m, 0.53 mm, 1 μm).

Odor Description: cedarwood, Vertofix, musky-ambery. Odor Threshold (isomeric mixture): 12.6 ng/L air.

IR (neat): 1738 (ν C=O), 1456 (δ H–C–H), 1381 cm^{-1} (δ CH_3).

^{1}H NMR ($CDCl_3$): δ = 0.92/0.93/0.94/0.94/0.95/0.96/0.99/1.03 [s, 6 H, $C(CH_3)_2$], 0.91/0.99/1.00/1.14 (d, *J* = 7.5 Hz, 3 H, 1-CH_3), 0.95/1.04/1.06/1.15 (d, *J* = 7.5 Hz, 3 H, 4-CH_3), 1.19–2.45 (m, 12 H, 1-, 4-H and 3-, 6-, 8-, 9-,10-CH_2).

^{13}C NMR ($CDCl_3$): δ = 7.9/11.2/13.3/13.9 (q, 1-CH_3), 14.6/16.8/17.6/18.9 (q, 4-CH_3), 18.4/18.6/19.3/20.0 (t, C-9), 28.1/28.6/28.9/29.9/31.6/32.6/33.0/33.5 [q, $C(CH_3)_2$], 30.8/30.9/31.0/31.1 (s, C-7), 33.7/35.7/39.9/40.8 (d, C-4), 29.2/29.3/29.4/38.8/39.7/39.8/39.9/40.3/40.6/41.2/41.6/41.8 (t, C-6, -8, -10), 43.2/43.4/43.6/44.3 (s, C-5), 43.9/44.2/44.7/51.9 (t, C-3), 51.0/51.2/51.8/52.3 (d, C-1), 220.7/222.1/223.3/224.2 (s, C-2).

MS: *m*/*z* (%) = 41 (64) $[C_2HO]^+$, 69 (62) $[C_5H_9]^+$, 81 (35), 95 (100), 109 (40), 123 (31), 137 (54), 151 (25), 165 (9) $[C_nH_{2n-3}]^+$, 179 (7) $[M - CHO]^+$, 193 (16) $[M - CH_3]^+$, 208 (14) $[M]^+$.

Anal. Calcd for $C_{14}H_{24}O$ (208.35): C, 80.71; H, 11.61. Found: C, 80.69; H, 11.53.

(±)-(1*RS*,4*SR*,5*SR*)-16 (Most Powerful Isomer)

Yield: 27%; Odor Threshold: 3.3 ng/L air.

^{1}H NMR ($CDCl_3$): δ = 0.91 (d, *J* = 7.5 Hz, 1 H, 3 H, 1-CH_3), 0.96 (s, 3 H, 7-CH_{3ax}), 1.03 (s, 3 H, 7-CH_{3eq}), 1.06 (d, *J* = 7.5 Hz, 3 H, 4-CH_3), 1.16 (m_c, 1 H, 8-H_{ax}), 1.17 (m_c, 1 H, 6-H_{ax}), 1.18 (m_c, 2 H, 10-CH_2), 1.40 (m_c, 1 H, 8-H_{eq}), 1.48 (m_c, 1 H, 9-H_{ax}), 1.52 (m_c, 1 H, 6-H_{eq}), 1.62 (m_c, 1 H, 9-H_{eq}), 1.95 (dd, *J* = 18.0, 5.0 Hz, 1 H, 3-H_b), 2.20 (q, *J* = 7.5 Hz, 1 H, 1-H), 2.48 (m_c, 1 H, 4-H), 2.51 (dd, *J* = 18.0, 8.0 Hz, 1 H, 3-H_a).

NOESY (^{1}H/^{1}H): 1-H/4-CH_3, 1-H/6-H_{eq}, 1-H/6-H_{ax}, 4-H/6-H_{ax}, 4-H/3-H_b, 1-CH_3/6-H_{ax}, 4-CH_3/6-H_{eq}, 7-H_{ax}/9-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 7.9 (q, 1-CH_3), 16.8 (q, 4-CH_3), 18.6 (t, C-9), 28.1 (q, 7-CH_{3eq}), 29.2 (t, C-10), 31.1 (s, C-7), 33.5 (q, 7-CH_{3ax}), 33.7 (d, C-4), 39.8 (t, C-8), 41.8 (t, C-6), 44.3 (s, C-5), 44.2 (t, C-3), 51.2 (d, C-1), 220.7 (s, C-2).

(±)-(4*RS*,5*RS*,6*SR*)-4,6-Dimethyl-1-methylenespiro[4.5]decan-2-one (17)

In analogy to the synthesis of **14**, the Grignard reaction of ethyl 2-(2′-methylcyclohexylidene)propionate (19.6 g, 100 mmol) with allylmagnesium chloride in the presence of LDA (300 mmol) afforded 2-(2′-methylcyclohexylidene)hex-4-en-3-one (5.98 g, 31%). This compound (4.50 g, 23.4 mmol) was dissolved in toluene (40 mL), and formic acid (40 mL) and 85% H_3PO_4 (40 mL) were added with stirring. The reaction mixture was refluxed for 4 h, prior to pouring into H_2O–Et_2O mixture (500 mL). After separation of the organic layer, the aqueous layer was extracted with Et_2O (2 × 250 mL), and the combined organic extracts were washed with H_2O (200 mL), sat. aq $NaHCO_3$ (2 × 200mL) and brine (200 mL). After drying ($MgSO_4$) and evaporation of the solvent, silica gel FC (pentane–Et_2O, 19:1, R_f 0.30) afforded the target compound **17** (0.34 g, 8%), while the main compound (2.83 g, 63%; R_f 0.09) was the isomeric (±)-(1*RS*,5*RS*,6*RS*)-1,4,6-trimethylspiro[4.5]dec-3-en-2-one (**34**).

Odor Description: moss, fir, cedar, pineapple-metallic. Odor Threshold: 9.6 ng/L air.

IR (neat): 1724 (ν C=O), 941 (δ C=C–H oop), 1452 (δ H–C–H), 1624 cm^{-1} (ν C=C).

^{1}H NMR ($CDCl_3$): δ = 0.71 (d, *J* = 7.0 Hz, 3 H, 6-CH_3), 1.14 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 1.26–1.75 (m, 9 H, 6-H, 7-, 8-, 9-, 10-CH_2), 1.97 (m_c, 1 H, 4-H), 2.16 (dd, *J* = 19.0, 12.5 Hz, 1 H, 3-H_b), 2.46 (dd, *J* = 19.0, 9.0 Hz, 1 H, 3-H_a), 5.65 (s, 1 H, H_bC=), 6.14 (s, 1 H, H_aC=).

NOESY (^{1}H/^{1}H): 4-CH_3/6-CH_{3eq}, H_bC=/7-H_{ax}, H_bC=/9-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 13.2 (q, 4-CH_3), 18.9 (q, 6-CH_3), 22.6 (t, C-8), 25.4 (t, C-9), 30.3 (t, C-7), 35.5 (d, C-6), 37.1 (t, C-10), 40.4 (d, C-4), 44.8 (t, C-3), 47.9 (s, C-5), 118.9 (t, 1-H_2C=), 151.6 (s, C-1), 207.5 (s, C-2).

MS: *m*/*z* (%) = 41 (73) $[C_2HO]^+$, 79 (100) $[C_8H_{10}O - C_3H_7]^+$, 93 (80) $[C_8H_{10}O - C_2H_5]^+$, 107 (77) $[C_8H_{10}O - CH_3]^+$, 122 (63) $[C_8H_{10}O]^+$, 124 (82) $[C_8H_{12}O]^+$, 135 (59) $[M - C_4H_9]^+$, 149 (50) $[M - C_3H_7]^+$, 163 (52) $[M - C_2H_5]^+$, 177 (39) $[M - CH_3]^+$, 192 (29) $[M]^+$.

Anal. Calcd for $C_{13}H_{20}O$ (192.30): C, 81.20; H, 10.48. Found: C, 81.35; H, 10.32.

(±)-(1*RS*,5*RS*,6*RS*)-1,4,6-Trimethylspiro[4.5]dec-3-en-2-one (34)

Odor Description: very weak, slightly fruity-agrestic.

IR (neat): 1701 (ν C=O), 1618 cm^{-1} (ν C=C).

^{1}H NMR ($CDCl_3$): δ = 0.61 (d, *J* = 7.0 Hz, 3 H, 6-CH_3), 1.16 (m_c, 1 H, 7-H_{ax}), 1.21 (d, *J* = 7.5 Hz, 3 H, 4-CH_3), 1.34 (m_c, 1 H, 8-H_{ax}), 1.47 (m_c, 1 H, 9-H_{ax}), 1.52 (m_c, 1 H, 10-H_{ax}), 1.61 (m_c, 1 H, 10-H_{eq}), 1.62 (m_c, 1 H, 7-H_{eq}), 1.63 (m_c, 1 H, 6-H), 1.67 (m_c, 1 H, 9-H_{eq}), 1.77 (m_c, 1 H, 8-H_{eq}), 1.97 (s, 3 H, 1-CH_3), 2.30 (q, *J* = 7.5 Hz, 1 H, 1-H), 5.73 (br s, 1 H, 3-H).

NOESY (^{1}H/^{1}H): 1-H/7-H_{ax}, 1-H/6-CH_{3eq}, 1-CH_3/9-H_{ax}, 4-CH_3/10-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 14.5 (q, 1-CH_3), 14.6 (q, 4-CH_3), 15.6 (q, 6-CH_3), 23.0 (t, C-9), 26.1 (t, C-8), 30.2 (t, C-10), 31.7 (t, C-7), 37.1 (d, C-6), 44.6 (d, C-1), 53.3 (s, C-5), 128.6 (d, C-3), 182.3 (s, C-4), 212.0 (s, C-2).

MS: *m*/*z* (%) = 122 (100) $[C_8H_{10}O]^+$, 135 (34) $[M - C_4H_9]^+$, 192 (31) $[M]^+$.

(±)-(1*RS*,4*SR*,5*SR*,6*SR*)-1,4,6-Trimethylspiro[4.5]decan-2-one (18)

Following the procedure described for the synthesis of **16**, the enone **17** (1.50 g, 7.80 mmol) was hydrogenated in the presence of 10% Pd/C catalyst. After the usual workup, Kugelrohr distillation provided **18**; boiling range 50–80 °C/0.05 mbar (1.28 g, 85%).

Odor Description: cedar, woody, ambery. Odor Threshold: 9.6 ng/L air.

IR (neat): 1738 (ν C=O), 1459 (δ H–C–H), 1379 cm^{-1} (δ CH_3).

^{1}H NMR (C_6D_6): δ = 0.75 (d, *J* = 7.0 Hz, 3 H, 6-CH_{3eq}), 0.81 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 1.02 (d, *J* = 8.0 Hz, 3 H, 1-CH_3), 0.93–1.13 (m, 4 H, 7-H_{ax} to 10-H_{ax}), 1.20–1.31 (m, 2 H, 7-H_{eq},10-H_{eq}), 1.32–1.48 (m, 3 H, 6-H, 8-, 9-H_{eq}), 1.79 (dd, *J* = 18.5, 7.5 Hz, 1 H, 3-H_b), 1.86 (m_c, 1 H, 4-H), 2.17 (q, *J* = 8.0 Hz, 1 H, 1-H), 2.33 (dd, *J* = 18.5, 9.0 Hz, 1 H, 3-H_a).

NOESY (^{1}H/^{1}H): 1-H/6-CH_{3eq}.

^{13}C NMR (C_6D_6): δ = 12.0 (q, 1-CH_3), 13.8 (q, 4-CH_3), 17.6 (q, 6-CH_3), 23.0 (t, C-9), 23.7 (t, C-8), 30.4 (t, C-10), 31.2 (t, C-7), 35.1 (d, C-6), 36.2 (d, C-4), 43.8 (t, C-3), 45.8 (s, C-5), 47.3 (d, C-1), 219.4 (s, C-2).

MS: *m*/*z* (%) = 41 (44) $[C_2HO]^+$, 55 (34) $[C_4H_7]^+$, 67 (37), 81 (43), 95 (98), 109 (25), 123 (100), 137 (10), 151 (6), 165 (5) $[C_nH_{2n-3}]^+$, 147 (10) $[M - CHO - H_2O]^+$, 179 (10) $[M - CH_3]^+$, 194 (20) $[M]^+$.

Anal. Calcd $C_{13}H_{22}O$ (194.32): C, 80.35; H, 11.41. Found: C, 80.14; H, 11.16.

4,7-Dimethyl-1-methylenespiro[4.5]decan-2-one (19)

Following the synthesis of **14**, the Grignard reaction of ethyl 2-(3′-methylcyclohexylidene)propionate (19.6 g, 100 mmol) with allylmagnesium chloride in the presence of LDA (300 mmol) afforded 2-(3′-methylcyclohexylidene)hex-4-en-3-one (8.25 g, 43%). In analogy to the synthesis of **11**, this material (8.00 g, 41.6 mmol) was refluxed in a solvent mixture of formic acid (70 mL), 85% H_3PO_4 (70 mL) and toluene (100 mL) for 6 h. After the usual workup, silica gel FC (pentane–Et_2O, 19:1, R_f 0.21) afforded the target structure **19** (2.35 g, 29%), besides the isomeric 1,4,7-trimethylspiro[4.5]dec-3-en-2-one (1.50 g, 19%).

Odor Description: cedarwood, fruity, resinous. Odor Threshold: 21.4 ng/L air.

IR (neat): 1726 (ν C=O), 1455 (δ H–C–H), 937 (δ C=C–H oop), 1633 cm^{-1} (ν C=C).

^{1}H NMR ($CDCl_3$): δ = 0.88/0.89 (d, *J* = 6.5 Hz, 3, 7-CH_3), 0.97 (2 d, *J* = 6.5 Hz, 3 H, 4-CH_3), 1.10–1.77 (m, 9 H, 7-H, 6-, 8-, 9-, 10-CH_2), 1.89 (pseudo sext, *J* = 7.5 Hz, 1 H, 4-H), 2.00/2.05 (dd, *J* = 7.5, 3.0 Hz, 1 H, 3-H_b), 2.50/2.54 (dd, *J* = 7.5, 4.0 Hz, 1 H, 3-H_a), 5.48 (s, 1 H, H_bC=), 6.04 (s, 1 H, H_aC=).

^{13}C NMR ($CDCl_3$): δ = 14.5/17.0 (q, 4-CH_3), 21.7/22.4 (t, C-9), 22.8/22.9 (q, 7-CH_3), 27.6/28.3 (d, C-7), 29.2/34.3/34.4/34.5/38.4/43.5 (t, C-6, -8, -10), 39.5/39.6 (d, C-4), 43.0/43.0 (t, C-3), 46.2/46.2 (s, C-5), 117.5/117.6 (t, 1-H_2C=), 153.2/153.3 (s, C-1), 207.2/207.3 (s, C-2).

MS: *m*/*z* (%) = 41 (59) $[C_2HO]^+$, 79 (73) $[C_8H_{10}O - C_3H_7]^+$, 93 (94) $[C_8H_{10}O - C_2H_5]^+$, 107 (84) $[C_8H_{10}O - CH_3]^+$, 122 (92) $[C_8H_{10}O]^+$, 124 (100) $[C_8H_{12}O]^+$, 136 (36) $[M - C_4H_8]^+$, 150 (45) $[M - C_3H_6]^+$, 164 (10) $[M - CO]^+$, 177 (26) $[M - CH_3]^+$, 192 (30) $[M]^+$.

Anal. Calcd for $C_{13}H_{20}O$ (192.30): C, 81.20; H, 10.48. Found: C, 81.24; H, 10.48.

1,4,7-Trimethylspiro[4.5]decan-2-one (20)
Following the synthesis of **16**, compound **19** (1.00 g, 5.15 mmol) was hydrogenated in EtOAc (10 mL) in the presence of 10% Pd/C (0.12 g, 2 mol%). Silica gel FC (pentane–Et_2O, 19:1, R_f 0.38) provided the target compound **20** (0.80 g, 80%).

Odor Description: weak, fruity, dry, woody.

IR (neat): 1737 (ν C=O), 1456 (δ H–C–H), 1376 cm^{-1} (δ CH_3).

^1H NMR ($CDCl_3$): δ = 0.87/0.87/0.88/0.88 (d, *J* = 6.5 Hz, 3 H, 4-CH_3), 0.99/0.99/1.01/1.01 (d, *J* = 7.0 Hz, 3 H, 1-CH_3), 1.00/1.02/1.18/1.19 (d, *J* = 7.5 Hz, 3 H, 7-CH_3), 1.09–2.55 (m, 13 H, 1-H to 10-CH_2).

^{13}C NMR ($CDCl_3$): δ = 11.5/11.6/13.5/13.6 (q, 1-CH_3), 12.9/13.0/15.8/16.0 (q, 4-CH_3), 22.7/22.8/22.8/23.1 (q, 7-CH_3), 21.7/22.9/23.0/23.2/26.8/28.3/30.0/34.3/34.4/34.5/34.6/36.5/37.9/38.0/39.3/47.4 (t, C-6, -8, -9, -10), 27.9/28.9/29.1/29.4 (d, C-7), 36.9/37.2/40.8/40.9 (d, C-4), 43.8/43.9/43.9/44.0 (s, C-5), 42.6/42.7/43.6/43.7 (t, C-3), 50.0/50.4/52.9/55.9 (d, C-1), 222.0/222.2/222.4/222.5 (s, C-2).

MS: *m*/*z* (%) = 41 (34) $[C_2HO]^+$, 55 (27) $[C_4H_7]^+$, 67 (32), 81 (40), 95 (100), 109 (12) $[C_nH_{2n-3}]^+$, 122 (82) $[C_8H_{10}O]^+$,123 (46), 137 (7), 151 (8), 165 (2) $[C_nH_{2n-3}]^+$, 179 (4) $[M - CH_3]^+$, 194 (16) $[M]^+$.

Anal. Calcd for $C_{13}H_{22}O$ (194.32): C, 80.35; H, 11.41. Found: C, 80.51; H, 11.40.

4,8-Dimethyl-1-methylenespiro[4.5]decan-2-one (21)
Following the synthesis of **14**, the Grignard reaction of ethyl 2-(4′-methylcyclohexylidene)propionate (39.2 g, 199.7 mmol) with allylmagnesium chloride in the presence of LDA (600 mmol) afforded 2-(4′-methylcyclohexylidene)hex-4-en-3-one (21.3 g, 55%), a part of which (4.45 g, 23.1 mmol) was submitted to the Nazarov cyclization conditions described for the synthesis of **11**. After the usual workup, silica gel FC (pentane–Et_2O, 19:1, R_f 0.54) furnished the title compound **21** (2.75 g, 62%), besides the isomeric 1,4,8-trimethylspiro[4.5]dec-3-en-2-one (0.76 g, 17%).

Odor Description: fruity, woody, oakmoss, patchouli, slightly earthy. Odor Threshold: 52.5 ng/L air.

IR (neat): 1726 (ν C=O), 933 (δ C=C–H oop), 1457 (δ H–C–H), 1638 cm^{-1} (ν C=C).

^1H NMR ($CDCl_3$): δ = 0.93 (d, *J* = 6.5 Hz, 3 H, 8-CH_3), 0.95 (d, *J* = 6.0 Hz, 3 H, 4-CH_3), 1.13–1.27 (m, 2 H, 7-, 9-H_b), 1.39–1.71 (m, 7 H, 6-, 10-CH_2, 7-, 9-H_a, 8-H_{ax}), 1.98 (m_c, 1 H, 4-H), 2.00 (m_c, 1 H, 3-H_b), 2.52 (m_c, 1 H, 3-H_a), 5.45 (s, 1 H, H_bC=), 6.04 (s, 1 H, H_aC=).

NOESY ($^1H/^1H$): H_bC=/8-CH_3, H_bC=/7-H_{ax}, H_bC=/9-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 14.9 (q, 4-CH_3), 21.7 (q, 8-CH_3), 30.1/30.8 (t, C-7, -9), 31.4 (d, C-8), 29.1/34.5 (t, C-6, -10), 38.3 (d, C-4), 43.2 (t, C-3), 45.2 (s, C-5), 117.5 (t, 1-H_2C=), 153.1 (s, C-1), 207.2 (s, C-2).

MS: *m*/*z* (%) = 41 (52) $[C_2HO]^+$, 79 (81) $[C_8H_{10}O - C_3H_7]^+$, 93 (82) $[C_8H_{10}O - C_2H_5]^+$, 107 (81) $[C_8H_{10}O - CH_3]^+$, 122 (100) $[C_8H_{10}O]^+$, 135 (38) $[M - C_3H_6 - CH_3]^+$, 150 (57) $[M - C_3H_6]^+$, 164 (32) $[M - CO]^+$, 177 (29) $[M - CH_3]^+$, 192 (17) $[M]^+$.

Anal. Calcd for $C_{13}H_{20}O$ (192.30): C, 81.20; H, 10.48. Found: C, 81.25; H, 10.54.

1,4,8-Trimethylspiro[4.5]decan-2-one (22)
Following the procedure described for the synthesis of **16**, the enone **21** (700 mg, 3.64 mmol) was hydrogenated in the presence of 10% Pd/C catalyst. Standard workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.29) furnished the trimethylketone **22** (550 mg, 78%).

Odor Description: almost odorless, slightly green, isononanol-like.

IR (neat): 1738 (ν C=O), 1457 (δ H–C–H), 1379 cm^{-1} (δ CH_3).

^1H NMR ($CDCl_3$): δ = 0.89/0.90 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.98/1.17 (d, *J* = 7.0 Hz, 3 H, 1-CH_3), 0.99/1.01 (d, *J* = 6.5 Hz, 3 H, 8-CH_3), 1.03–1.63 (m, 9 H, 6-H_2 to 10-CH_2), 1.91/1.94 (pseudo d, *J* = 19.0 Hz, 1 H, 3-H_b), 1.87/2.12 (m_c, 1 H, 4-H), 2.09/2.38 (dd, *J* = 19.0, 8.0 Hz, 1 H, 3-H_a), 2.32/2.53 (q, *J* = 8.0 Hz, 1 H, 1-H).

^{13}C NMR ($CDCl_3$): δ = 11.2/13.6 (q, 1-CH_3), 13.2/16.2 (q, 4-CH_3), 22.0/22.2 (q, 8-CH_3), 27.3/28.4/29.8/30.3/31.6/31.7/31.9/38.4 (t, C-6, -7, -9, -10), 31.7/31.8 (d, C-8), 36.3/40.6 (d, C-4), 42.7/43.0 (s, C-5), 42.9/43.8 (t, C-3), 49.7/52.7 (d, C-1), 222.2/222.3 (s, C-2).

MS: *m*/*z* (%) = 41 (52) $[C_2HO]^+$, 55 (34) $[C_4H_7]^+$, 67 (52), 81 (79), 95 (100), 109 (24), 123 (67), 137 (53), 151 (11), 165 (15) $[C_nH_{2n-3}]^+$, 176 (9) $[M - H_2O]^+$, 179 (11) $[M - CH_3]^+$, 194 (31) $[M]^+$.

Anal. Calcd for $C_{13}H_{22}O$ (194.32): C, 80.35; H, 11.41. Found: C, 80.30; H, 11.61.

(±)- (4*RS*,5*rs*,7*RS*,9*SR*)-4,7,9-Trimethyl-1-methylenespiro-[4.5]decan-2-one (23)
Analogous to the preparation of **14**, the Grignard reaction of (±)-(3′*RS*,5′*SR*)-ethyl 2-(3′,5′-dimethylcyclohexylidene)propionate (18.0 g, 85.6 mmol) with allylmagnesium chloride in the presence of LDA (260 mmol) afforded (±)-(3′*RS*,5′*SR*)-2-(3′,5′-methylcyclohexylidene)hex-5-en-3-one (7.82 g, 44%), a part of which (7.50 g, 36.3 mmol) was submitted to the Nazarov conditions of the procedure for the synthesis of **11**. Standard workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.52) provided **23** (1.30 g, 17%), besides the isomeric 1,4,7,9-tetramethylspiro[4.5]dec-3-en-2-one (2.93 g, 39%).

Odor Description: earthy, metallic, lactonic, with damascone aspects. Odor Threshold: 159 ng/L air.

IR (neat): 1726 (ν C=O), 1455 (δ H–C–H), 936 (δ C=C–H oop), 1623 cm^{-1} (ν C=C).

^1H NMR ($CDCl_3$): δ = 0.53 (pseudo q, *J* = 12.0 Hz, 1 H, 8-H_{ax}), 0.88/0.89 (d, *J* = 6.5 Hz, 6 H, 7-/9-CH_3), 0.96 (t, *J* = 15.0 Hz, 1 H, 6-H_{ax}), 0.97 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 1.07 (t, *J* = 15.0 Hz, 1 H, 10-H_{ax}), 1.44 (dquint, *J* = 15.0, 2.0 Hz, 1 H, 6-H_{eq}), 1.56 (dquint, *J* = 15.0, 2.0 Hz, 1 H, 10-H_{eq}), 1.59–1.76 (m, 3 H, 7-, 9-H_{ax}, 8-H_{eq}), 1.89 (pseudo sext, *J* = 7.5 Hz, 1 H, 4-H), 1.89 (dd, *J* = 18.5, 8.0 Hz, 1 H, 3-H_b), 2.37 (dd, *J* = 18.0, 7.5 Hz, 1 H, 3-H_a), 5.44 (s, 1 H, H_bC=), 6.02 (s, 1 H, H_aC=).

NOESY ($^1H/^1H$): H_bC=/7-H_{ax}, H_bC=/9-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 14.5 (q, 4-CH_3), 22.6 (q, 7-CH_{3eq}), 22.7 (q, 9-CH_{3eq}), 27.7 (d, C-7), 28.3 (d, C-9), 38.0 (t, C-6), 39.5 (d, C-4), 43.0 (t, C-3), 43.1 (t, C-10), 43.4 (t, C-8), 46.9 (s, C-5), 117.4 (t, 1-H_2C=), 153.4 (s, C-1), 207.2 (s, C-2).

MS: *m*/*z* (%) = 41 (58) $[C_2HO]^+$, 83 (100) $[C_9H_{16} - C_3H_5]^+$, 93 (64) $[C_9H_{12}O - C_3H_7]^+$, 107 (87) $[C_9H_{12}O - C_2H_5]^+$, 124 (80) $[C_9H_{16}]^+$, 136 (77) $[C_9H_{12}O]^+$, 150 (43) $[C_{10}H_{14}O]^+$, 164 (22) $[M - C_3H_6]^+$, 177 (4) $[M - C_2H_5]^+$, 191 (20) $[M - CH_3]^+$, 206 (16) $[M]^+$.

Anal. Calcd for $C_{14}H_{22}O$ (206.33): C, 81.50; H, 10.75. Found: C, 81.65; H, 10.68

1,4,7,9-Tetramethylspiro[4.5]decan-2-one (24)
Following the synthesis of **16**, the enone **23** (1.20 g, 5.82 mmol) was hydrogenated in the presence of 10% Pd/C catalyst. Standard workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.29) furnished the tetramethylketone **24** (790 mg, 65%).

Odor Description: very weak, woody-nutty.

IR (neat): 1738 (ν C=O), 1456 (δ H–C–H), 1375 cm^{-1} (δ CH_3).

^1H NMR ($CDCl_3$): δ = 0.48/0.49 (pseudo q, *J* = 12.0 Hz, 1 H, 8-H_{ax}), 0.77–1.11 (m, 2 H, 6-, 10-H_{ax}), 0.88 (br d, *J* = 6.5 Hz, 6 H, 7-/9-CH_3), 0.98/0.99 (d, *J* = 8.0 Hz, 3 H, 4-CH_3), 1.01/1.16 (d, *J* = 7.5 Hz, 3 H, 1-CH_3), 1.35–1.67 (m, 5 H, 6-, 8-, 10-H_{eq}, 7-, 9-H_{ax},), 1.87–

2.12 (m, 2 H, 3-H_b, 4-H), 2.30/2.37 (dd, *J* = 18.5, 8.0 Hz, 1 H, 3-H_a), 2.50–2.54 (m, 1 H, 1-H).

^{13}C NMR ($CDCl_3$): δ = 11.6/12.9 (q, 1-CH_3), 13.5/15.9 (q, 4-CH_3), 22.5/22.6/22.7/23.0 (q, 7-, 9-CH_{3eq}), 27.8/28.9/29.1/29.2 (d, C-7, -9), 36.9/40.7 (d, C-4), 35.8/37.4/38.9/42.7/43.3/43.5/43.6/47.0 (t, C-3, -6, -8, -10), 44.4/44.6 (s, C-5), 50.7/53.8 (d, C-1), 222.0/222.5 (s, C-2).

MS: *m*/*z* (%) = 41 (40) $[C_2HO]^+$, 81 (31) $[C_6H_9]^+$, 95 (26) $[C_{10}H_{18} - C_3H_7]^+$, 109 (100) $[C_{10}H_{18} - C_2H_5]^+$, 123 (17) $[C_9H_{15}]^+$, 136 (85) $[C_{10}H_{16}]^+$, 138 (40) $[C_{10}H_{18}]^+$, 151 (4) $[M - C_4H_9]^+$, 165 (6) $[M - C_3H_7]^+$, 193 (2) $[M - CH_3]^+$, 208 (15) $[M]^+$.

Anal. Calcd for $C_{14}H_{24}O$ (208.34): C, 81.71; H, 11.61. Found: C, 81.58; H, 11.74.

[(2(1′)*E*/*Z*,4*E*]-2-(3′,3′,5′-Trimethylcyclohexylidene)hex-4-en-3-one

Following the procedure described for the preparation of **14**, the Grignard reaction of ethyl 2-(3′,3′,5′-trimethylcyclohexylidene)-propionate (44.9 g, 200 mmol) with allylmagnesium chloride in the presence of LDA (600 mmol) furnished the title compound (28.9 g, 66%) as a 2*E*:2*Z* mixture (55:45).

IR (neat): 1651 (ν C=O, double unsat.), 972 (δ C=C–H oop), 1456 cm^{-1} (δ H–C–H).

^{1}H NMR ($CDCl_3$): δ = 0.75/0.87 (s, 3 H, 3′-CH_{3ax}), 0.84/0.94 (d, *J* = 6.5 Hz, 3 H, 5′-CH_3), 0.90/1.00 (s, 3 H, 3′-CH_{3eq}), 0.96 (m_c, 1 H, 4′-H_{ax}), 1.32 (m_c, 1 H, 6′-H_{ax}), 1.41 (m_c, 1 H, 4′-H_{eq}), 1.57–1.67 (m, 2 H, 2′-H_{ax}, 5′-H), 1.77/1.81 (s, 3 H, 1-CH_3), 1.91/1.93 (dd, *J* = 7.0, 1.5 Hz, 3 H, 6-CH_3), 2.06/2.30 (dt, *J* = 13.0, 2.0 Hz, 1 H, 2′-H_{eq}), 2.31/2.57 (dquint, *J* = 13.5, 2.0 Hz, 1 H, 6′-H_{eq}), 6.12/6.14 (dq, *J* = 15.5, 2.0 Hz, 1 H, 4-H), 6.77/6.79 (dq, *J* = 15.5, 7.0 Hz, 1 H, 5-H).

NOESY (^{1}H/^{1}H): 1-CH_3/2′-H_{eq} (2*E*-isomer, 55%), 1-CH_3 /6′-H_{eq} (2*Z*-isomer, 45%).

^{13}C NMR ($CDCl_3$): δ = 15.4/15.5 (q, C-1), 18.1/18.2 (q, C-6), 22.4/22.7 (q, 5′-CH_3), 25.0/25.1 (q, 3′-CH_{3ax}), 29.0/29.8 (d, C-5′), 32.2/32.3 (q, 3′-CH_{3eq}), 33.3/33.7 (s, C-3′), 37.8/40.5 (t, C-6′), 42.4/44.5 (t, C-2′), 48.3/48.4 (t, C-4′), 128.5/128.6 (s, C-2), 132.2/132.6 (d, C-4), 137.6/138.0 (s, C-1′), 144.9/145.2 (d, C-5), 201.3/201.5 (s, C-3).

MS: *m*/*z* (%) = 41 (97) $[C_2HO]^+$, 69 (98) $[C_4H_5O]^+$, 95 (35) $[M - C_4H_5O - C_4H_8]^+$, 109 (30) $[C_7H_9O]^+$, 121 (100) $[C_{10}H_{13}O - C_2H_4]^+$, 135 (84) $[C_9H_{11}O]^+$, 149 (39) $[C_{10}H_{13}O]^+$, 177 (20) $[M - C_3H_7]^+$, 191 (7) $[M - C_2H_5]^+$, 205 (86) $[M - CH_3]^+$, 220 (32) $[M]^+$.

4,7,7,9-Tetramethyl-1-methylenespiro[4.5]decan-2-one (25)

In analogy to the synthesis of **11**, 2-(3′,3′,5′-trimethylcyclohexylidene)hex-4-en-3-one (28.0 g, 127 mmol) was submitted to Nazarov cyclization. Usual workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.42) afforded **25** (8.29 g, 31%) as a mixture of 4*RS*,5*SR*,9*RS*- and 4*RS*,5*RS*,9*SR*-diastereomer (63:37).

Odor Description: ambery-woody.

IR (neat): 1727 (ν C=O), 935 (δ C=C–H oop), 1456 (δ H–C–H), 1642 cm^{-1} (ν C=C).

MS: *m*/*z* (%) = 41 (80) $[C_2HO]^+$, 79 (51), 93 (52), 107 (100) $[C_nH_{2n-5}]^+$, 121 (69) $[C_9H_{12}O - CH_3]^+$, 135 (86) $[C_9H_{11}O]^+$, 150 (56) $[M - C_3H_6 - CO]^+$, 163 (24) $[M - C_3H_6 - CH_3]^+$, 178 (42) $[M - C_3H_6]^+$, 191 (5) $[M - C_2H_5]^+$, 205 (73) $[M - CH_3]^+$, 220 (24) $[M]^+$.

Anal. Calcd for $C_{15}H_{24}O$ (220.36): C, 81.76; H, 10.98. Found: C, 81.80; H, 11.13.

(±)-(4*RS*,5*SR*,9*RS*)-25

Content: 63%; Odor Threshold: 4.4 ng/L air.

^{1}H NMR ($CDCl_3$): δ = 0.77 (m_c, 1 H, 8-H_b), 0.81 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.84 (s, 3 H, 7-CH_{3ax}), 0.86 (s, 3 H, 7-CH_{3eq}), 0.93 (m_c, 1 H, 10-H_{ax}), 0.97 (d, *J* = 6.5 Hz, 3 H, 9-CH_3), 1.14 (m_c, 1 H, 6-H_b), 1.43 (m_c, 1 H, 8-H_a), 1.62 (m_c, 1 H, 6-H_a), 1.81 (m_c, 1 H, 10-H_{eq}), 1.86 (pseudo d, *J* = 18.5, 1 H, 3-H_b), 1.91 (m_c, 1 H, 4-H), 2.70 (dd, *J* = 18.5, 7.5 Hz, 1 H, 3-H_a), 5.41 (s, 1 H, H_bC=), 6.04 (s, 1 H, H_aC=).

NOESY (^{1}H/^{1}H): 4-CH_3/10-H_{eq}.

^{13}C NMR ($CDCl_3$): δ = 16.0 (q, 4-CH_3), 23.2 (q, 9-CH_{3eq}), 25.7 (d, C-9), 25.9 (q, 7-CH_{3ax}), 32.4 (s, C-7), 34.8 (q, 7-CH_{3eq}), 41.0 (t, C-10), 41.9 (d, C-4), 42.9 (t, C-3), 46.9 (s, C-5), 47.7 (t, C-8), 48.5 (t, C-6), 117.2 (t, 1-H_2C=), 153.9 (s, C-1), 208.0 (s, C-2).

(±)-(4*RS*,5*RS*,9*SR*)-25

Content: 37%; Odor Threshold: >30 ng/L air.

^{1}H NMR ($CDCl_3$): δ = 0.75 (m_c, 1 H, 8-H_b), 1.01 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.87 (s, 3 H, 7-CH_{3ax}), 0.89 (s, 3 H, 7-CH_{3eq}), 0.94 (d, *J* = 7.0 Hz, 3 H, 9-CH_3), 1.13 (d, *J* = 13.5 Hz, 1 H, 6-H_b), 1.15 (m_c, 1 H, 10-H_{ax}), 1.20 (d, *J* = 13.5 Hz, 1 H, 6-H_a), 1.43 (m_c, 1 H, 8-H_a), 1.56 (m_c, 1 H, 10-H_{eq}), 1.74 (m_c, 1 H, 4-H), 2.06 (dd, *J* = 18.5, 12 Hz, 3-H_b), 2.35 (dd, *J* = 18.5, 7.5 Hz, 1 H, 3-H_a), 5.42 (s, 1 H, H_bC=), 5.92 (s, 1 H, H_aC=).

NOESY (^{1}H/^{1}H): 4-CH_3/6-H_{eq}, 4-CH_3/6-H_{ax}.

^{13}C NMR ($CDCl_3$): δ = 13.0 (q, 4-CH_3), 23.0 (q, 9-CH_{3eq}), 25.6 (d, C-9), 26.2 (q, 7-CH_{3ax}), 31.8 (s, C-7), 35.1 (q, 7-CH_{3eq}), 38.5 (t, C-6), 40.5 (d, C-4), 41.8 (t, C-10), 42.1 (t, C-3), 46.2 (s, C-5), 48.0 (t, C-8), 115.6 (t, 1-H_2C=), 157.4 (s, C-1), 207.2 (s, C-2).

1,4,7,7,9-Pentamethylspiro[4.5]decan-2-one (26)

Following the preparation of **16**, the enone **25** (4.00 g, 18.2 mmol) was hydrogenated. Standard workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.37) furnished the pentamethylketone **26** (3.69 g, 91%).

Odor Description: earthy, patchouli, salicylate, slightly cinnamic. Odor Threshold of the Isomeric Mixture: 6.8 ng/L air.

IR (neat): 1738 (ν C=O), 1456 (δ H–C–H), 1381 cm^{-1} (δ CH_3).

^{1}H NMR ($CDCl_3$): δ = 0.82/0.91 (d, *J* = 8.0 Hz, 3 H, 9-CH_{3eq}), 0.89/0.96 (s, 3 H, 7-CH_{3eq}), 0.93/1.06 (d, *J* = 8.0 Hz, 3 H, 4-CH_3), 0.92/0.94 (s, 3 H, 7-CH_{3ax}), 1.15/1.16 (d, *J* = 8.0 Hz, 3 H, 1-CH_3), 1.35–2.66 (m, 11 H, 1-, 4-, 9-H, 3- ,6-, 8-, 10-CH_2).

^{13}C NMR ($CDCl_3$): δ = 13.6/15.2 (q, 1-CH_3), 17.4/18.7 (q, 4-CH_3), 22.5/22.9 (q, 9-CH_3), 24.6/25.9 (d, C-9), 27.2/27.5/34.4/34.9 [q, $C(CH_3)_2$], 31.5/31.8 (s, C-7), 38.4/41.2/43.1/44.8 (t, C-6,-10), 43.2/43.3 (d, C-4), 43.9/44.0 (s, C-5), 49.5/50.4 (d, C-1), 47.8/48.8/49.4/51.6 (t, C-3,-8), 223.2/224.4 (s, C-2).

MS: *m*/*z* (%) = 41 (35) $[C_2HO]^+$, 55 (35) $[C_3H_3O]^+$, 83 (100) $[C_6H_{11}]^+$, 95 (24), 109 (27), 123 (39), 137 (13) $[C_nH_{2n-3}]^+$, 150 (71) $[C_{11}H_{18}]^+$, 179 (7) $[M - C_3H_7]^+$, 189 (2) $[M - CH_3 - H_2O]^+$, 207 (4) $[M - CH_3]^+$, 222 (7) $[M]^+$.

Anal. Calcd for $C_{15}H_{26}O$ (222.37): C, 81.02; H, 11.79. Found: C, 81.00; H, 11.59.

4,7,7,9,9-Pentamethyl-1-methylenespiro[4.5]decan-2-one (27)

According to the synthesis of **14**, the Grignard reaction of ethyl 2-(3′,3′,5′,5′-tetramethylcyclohexylidene)propionate (47.6 g, 200 mmol) with allylmagnesium chloride in the presence of LDA (600 mmol) provided 2-(3′,3′,5′,5′-tetramethylcyclohexylidene)hex-4-en-3-one (27.8 g, 59%). Part of this material (25.1 g, 107 mmol) was cyclized in formic acid (130 mL), 85% H_3PO_4 (130 mL) and toluene (250 mL) at 90 °C for 8 h. Standard workup and silica gel FC (pen-

tane–Et_2O, 19:1, R_f 0.37) furnished **27** (16.5 g, 66%) as a colorless solid; mp 46.5 °C.

Odor Description: weak, fruity, floral, woody.

IR (neat): 1720 (ν C=O), 935 (δ C=C–H oop), 1637 cm^{-1} (ν C=C).

^1H NMR ($CDCl_3$): δ = 0.89 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.89/1.00 (s, 6 H, 7-, 9-CH_{3eq}), 1.17 (s, 6 H, 7-, 9-CH_{3ax}), 0.95 (d, *J* = 14.0 Hz, 1 H, 6-H_{ax}), 1.18 (d, *J* = 12.5 Hz, 1 H, 8-H_{ax}), 1.34 (d, *J* = 14.0 Hz, 1 H, 10-H_{ax}), 1.38 (d, *J* = 12.5 Hz, 1 H, 8-H_{eq}), 1.67 (m_c, 2 H, 6-, 10-H_{eq}), 1.96 (m_c, 1 H, 3-H_b), 2.73 (m_c, 2 H, 3-H_a, 4-H), 5.15 (s, 1 H, H_bC=), 6.00 (s, 1 H, H_aC=).

^{13}C NMR ($CDCl_3$): δ = 18.1 (q, 4-CH_3), 29.1/29.2 (q, 7-/9-CH_{3ax}), 31.5/32.1 (s, C-7/-9), 34.3 (d, C-4), 36.0/36.4 (q, 7-/9-CH_{3eq}), 40.7/48.9 (t, C-6/-10), 43.7 (t, C-3), 47.9 (s, C-5), 51.5 (t, C-8), 115.8 (t, 1-H_2C=), 155.2 (s, C-1), 207.2 (s, C-2).

MS: *m*/*z* (%) = 41 (51) $[C_2HO]^+$, 55 (43) $[C_3H_3O]^+$, 79 (35), 93 (45), 107 (36) $[C_nH_{2n-5}]^+$, 121 (55) $[C_9H_{12}O - CH_3]^+$, 135 (22) $[C_9H_{11}O]^+$, 149 (54) $[C_{10}H_{13}O]^+$, 164 (24) $[C_{11}H_{16}O]^+$, 177 (14) $[M - C_3H_6 - CH_3]^+$, 192 (30) $[M - C_3H_6]^+$, 205 (5) $[M - C_2H_5]^+$, 219 (100) $[M - CH_3]^+$, 234 (11) $[M]^+$.

Anal. Calcd for $C_{16}H_{26}O$ (234.38): C, 81.99; H, 11.18. Found: C, 82.07; H, 11.36.

1,4,7,7,9,9-Hexamethylspiro[4.5]decan-2-one (28)

According to the procedure for the synthesis of **16**, the enone **27** (2.00 g, 8.53 mmol) was hydrogenated. Usual workup and silica gel FC (pentane–Et_2O, 19:1, R_f 0.32) afforded **28** (1.82 g, 90%) as a colorless solid with a diastereomeric ratio of 57:43 (*like*/*unlike*); mp 34.7 °C.

Odor Description: dry, spicy, black pepper.

IR (neat): 1738 (ν C=O), 1456 (δ H–C–H), 1382 cm^{-1} (δ CH_3).

^1H NMR ($CDCl_3$): δ = 0.94/1.15 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 0.95/0.98/0.98/0.99/1.01/1.03/1.06/1.07 (s, 12 H, 7-, 9-CH_3), 1.02/1.06 (d, *J* = 7.5 Hz, 3 H, 1-CH_3), 1.13–1.47 (m, 6 H, C-6, -8, -10), 2.20/2.52 (quint, *J* = 8.0 Hz, 1 H, 4-H), 1.90/1.96 (dd, *J* = 19.0, 2.5 Hz, 1 H, 3-H_b), 2.17/2.39 (q, *J* = 7.5 Hz, 1 H, 1-H), 2.47/2.66 (dd, *J* = 19.0, 8.0 Hz, 1 H, 3-H_a).

^{13}C NMR ($CDCl_3$): δ = 9.5 (q, *u*-1-CH_3), 14.5 (q, *l*-1-CH_3), 15.5 (q, *u*-4-CH_3), 18.5 (q, *l*-4-CH_3), 31.3/31.3/31.4/31.5 (s, C-7-, 9), 31.7/32.0/32.0/32.3/33.3/33.3/33.7/33.9 [q, 7-, 9-C(CH_3)$_2$], 35.3 (d, *u*-C-4), 41.4 (d, *l*-C-4), 40.0 (*l*-C-6), 40.0/40.7 (t, *u*-C-6, *u*-C-10), 43.0 (t, *u*-C-3), 44.1 (t, *l*-C-3), 44.2 (s, *l*-C-5), 44.7 (s, *u*-C-5), 51.3/51.4 (t, *l*-C-8, *l*-C-10), 51.8 (t, *u*-C-8), 51.9 (d, *u*-C-1), 53.3 (d, *l*-C-1), 221.1 (s, *u*-C-2), 223.7 (s, *l*-C-2).

MS: *m*/*z* (%) = 41 (58) $[C_2HO]^+$, 55 (56) $[C_3H_3O]^+$, 97 (100) $[C_7H_{13}]^+$, 109 (54), 123 (36), 137 (64), 151 (27), 165 (52), 179 (5), 193 (7) $[C_nH_{2n-3}]^+$, 203 (8) $[M - CH_3 - H_2O]^+$, 221 (32) $[M - CH_3]^+$, 236 (11) $[M]^+$.

Anal. Calcd for $C_{16}H_{28}O$ (236.40): C, 81.29; H, 11.94. Found: C, 81.28; H, 11.93.

6,6,10-Trimethyldispiro[2.0.5.3]dodecan-12-one (29)

Zn powder (2.05 g, 31.4 mmol) was added in one dash into a stirred suspension of AgOAc (12.1 mg, 0.73 mmol) in refluxing AcOH (15 mL). After 15 min, the reaction mixture was allowed to cool down to r.t., and the AcOH was decanted. The resulting residue was washed with AcOH (15 mL) and Et_2O (5 × 25 mL), and then taken up in Et_2O (25 mL). A catalytic amount of Ag wool was added, followed by CH_2I_2 (4.22 g, 15.7 mmol). After stirring for 1 h at r.t., a solution of **11** (2.50 g, 12.1 mmol) in Et_2O (25 mL) was added dropwise, and the mixture was refluxed for 16 h. The mixture was then poured into ice-cold sat. aq NH_4Cl (200 mL), the organic layer was separated, and the aqueous layer extracted with Et_2O (2 × 200 mL). The combined organic extracts were washed with 40% aq $NaHSO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. Silica gel FC (pentane–Et_2O, 19:1, R_f 0.24) furnished the cyclopropanated target compound **29** (1.03 g, 39%).

Odor Description: woody, cedarwood, reminiscent of Iso E Super.

IR (neat): 1726 (ν C=O), 1097 (δ CH_3), 1319 (r_β H–C–H, cyclopropane), 1455 (δ H–C–H), 1413 (δ H–C–H, cyclopropane), 3078 cm^{-1} (ν C–H, cyclopropane).

^1H NMR ($CDCl_3$): δ = 0.29 (d, *J* = 14.0 Hz, 0.5 H, *l*-5-H_{ax}), 0.41 (m_c, 0.5 H, *u*-9-H_{ax}), 0.49/0.81 (m_c, 1 H, 1-, 2-H_b), 0.89/0.90 (s, 3 H, 6-CH_{3eq}), 0.96/1.03 (d, *J* = 7.0 Hz, 3 H, 10-CH_3), 1.05/1.09 (s, 3 H, 6-CH_{3ax}), 1.36 (dt, *J* = 14.0, 2.5 Hz, 0.5 H, *l*-5-H_{eq}), 1.59 (m_c, 0.5 H, *u*-9-H_{eq}), 0.91–1.11 and 1.39–1.73 (m, 10 H, 1-, 2-H_a, *u*-5-, 7-, 8-, *l*-9-CH_2, 11-H_b), 1.97/2.74 (dd, *J* = 18.0, 7.5 Hz, 1 H, 11-H_a), 2.64/2.86 (pseudo quint, *J* = 7.5 Hz, 1 H, 10-H).

^{13}C NMR ($CDCl_3$): δ = 8.4/8.9/16.6/17.0 (t, C-1, -2), 17.5/18.0 (q, 10-CH_3), 18.6/19.2 (t, C-8), 26.6/27.1 (q, 6-CH_{3ax}), 28.7/35.5/39.1/39.2 (t, C-7, -9), 30.9/31.1 (s, C-6), 32.6/34.0 (d, C-10), 34.7/35.4 (q, 6-CH_{3eq}), 38.4/38.6 (s, C-3), 41.6/42.1 (s, C-4), 39.8/47.1 (t, C-5), 44.4/44.8 (t, C-11), 219.5/219.8 (s, C-12).

MS: *m*/*z* (%) = 41 (91) $[C_2HO]^+$, 55 (53) $[C_3H_3O]^+$, 69 (32) $[C_4H_5O]^+$, 79 (54) $[C_5H_3O]^+$, 91 (50) $[C_7H_7]^+$, 107 (48) $[C_7H_7O]^+$, 124 (90) $[C_9H_{16}]^+$, 136 (44) $[M - C_5H_8O]^+$, 149 (100) $[C_{10}H_{13}O]^+$, 164 (99) $[M - C_2H_4 - CO]^+$, 177 (46) $[M - C_2H_4 - CH_3]^+$, 192 (94) $[M - C_2H_4]^+$, 205 (47) $[M - CH_3]^+$, 220 (9) $[M]^+$.

Anal. Calcd for $C_{15}H_{24}O$ (220.35): C, 81.76; H, 10.98. Found: C, 81.75; H, 11.02

4-Methyl-1-methylenespiro[4.6]undecan-2-one (30)

Following the synthesis of **14**, the Grignard reaction of ethyl 2-cycloheptylidenepropionate (39.2 g, 200 mmol) with allylmagnesium chloride in the presence of LDA (600 mmol) furnished 2-cycloheptylidenehex-4-en-3-one (17.8 g, 46%). In analogy to the synthesis of **11**, this compound (15.5 g, 80.9 mmol) was treated with formic acid (100 mL) and 85% H_3PO_4 (100 mL) in toluene (100 mL) at 90 °C for 2 h. After usual workup, the residue was purified by silica gel FC (pentane–Et_2O, 19:1, R_f 0.30) to furnish **30** (9.09 g, 58%), besides the isomeric 1,4-dimethylspiro[4.6]undec-3-en-2-one (4.87 g, 31%).

Odor Description: woody-vetiver, dry, slightly earthy, cedarwood, rhubarb. Odor Threshold: 9.4 ng/L air.

IR (neat): 1724 (ν C=O), 934 (δ C=C–H oop), 1458 (δ H–C–H), 1638 cm^{-1} (ν C=C).

^1H NMR ($CDCl_3$): δ = 0.97 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 1.50–1.74 (m, 12 H, 6-CH_2 to 11-CH_2), 2.00 (dd, *J* = 18.0, 6.0 Hz, 1 H, 3-H_b), 2.14 (pseudo sext, *J* = 6.5 Hz, 1 H, 4-H), 2.53 (dd, *J* = 18.0, 7.5 Hz, 1 H, 3-H_a), 5.26 (s, 1 H, H_bC=), 5.97 (s, 1 H, H_aC=).

^{13}C NMR ($CDCl_3$): δ = 16.0 (q, 4-CH_3), 23.0/23.7 (t, C-7, -10), 30.1/30.4 (t, C-8, -9),32.6/40.1 (t, C-6, -11), 38.0 (d, C-4), 43.7 (t, C-3), 48.9 (s, C-5), 115.5 (t, 1-H_2C=), 155.2 (s, C-1), 207.5 (s, C-2).

MS: *m*/*z* (%) = 41 (54) $[C_2HO]^+$, 79 (100) $[C_9H_{14} - C_3H_7]^+$, 93 (77) $[C_9H_{14} - C_2H_5]^+$, 107 (57) $[C_7H_7O]^+$, 122 (83) $[C_{10}H_{14}O - CO]^+$, 135 (30) $[C_{10}H_{14}O - CH_3]$, 150 (47) $[C_{10}H_{14}O]^+$, 164 (25) $[M - C_2H_4]^+$, 177 (14) $[M - CH_3]^+$, 192 (20) $[M]^+$.

Anal. Calcd for $C_{13}H_{20}O$ (192.30): C, 81.20; H, 10.48. Found C, 81.29; H, 10.56.

4-Methyl-1-methylenespiro[4.7]dodecan-2-one (31)

Following the synthesis of **14**, the Grignard reaction of ethyl 2-cyclooct-1-enylpropionate (28.0 g, 133 mmol) with allylmagnesium chloride in the presence of LDA (400 mmol) furnished 2-cyclooct-1-enylhex-4-en-3-one (8.64 g, 31%). In analogy to the synthesis of **11**, this compound (5.56 g, 26.9 mmol) was treated with formic acid (13 mL) and 85% H_3PO_4 (13 mL) in toluene (25 mL) at 90 °C for

16 h. After the usual workup, silica gel FC (pentane–Et_2O, 19:1, R_f 0.18) of the residue gave 41% (GC) pure **31** (1.31 g, 10%). The main component of this mixture was 1,4-dimethyl-3,5,6,7,8,9,10,10a-octahydro-1*H*-benzocycloocten-2-one, which was impossible to separate from **31** by repeated FC. A sample was purified by preparative HPLC (A: H_2O with 1% HCO_2H and 0.1% HCO_2NH_4, B: MeOH; 2 min: A/B, 20:80; 8 min: B, 100; R_f 5.82 min) on ZORBAX SB-AQ (250 × 4.6 mm, particle size 5 μm).

Odor Description: woody, vetiver, slightly metallic-acidic. Odor Threshold: 2.5 ng/L air.

IR (neat): 1722 (ν C=O), 1447 (δ H–C–H), 935 (δ C=C–H oop), 1636 cm^{-1} (ν C=C).

^{1}H NMR (C_6D_6): δ = 0.67 (d, *J* = 7.0 Hz, 3 H, 4-CH_3), 1.70 (pseudo sept, *J* = 7.0 Hz, 1 H, 4-H), 1.31–1.46 (m, 14 H, 6-CH_2 to 12-CH_2), 1.79 (dd, *J* = 18.0, 3.5 Hz, 1 H, 3-H_b), 2.33 (dd, *J* = 18.0, 8.0 Hz, 1 H, 3-H_a), 4.88 (s, 1 H, H_bC=), 6.21 (s, 1 H, H_aC=).

^{13}C NMR ($CDCl_3$): δ = 17.3 (q, 4-CH_3), 22.1/22.5 (t, C-7, -11), 25.0 (t, C-9), 27.4/28.3/28.8/34.2 (t, C-6, -8, -10, -12), 37.3 (d, C-4), 43.9 (t, C-3), 49.0 (s, C-5), 116.5 (t, 1-H_2C=), 152.9 (s, C-1), 207.7 (s, C-2).

MS: *m*/*z* (%) = 41 (74) $[C_2HO]^+$, 79 (100) $[C_9H_{13} - C_3H_6]^+$, 93 (65) $[C_9H_{13} - C_2H_4]^+$, 107 (50) $[C_7H_7O]^+$, 121 (53) $[C_9H_{13}]^+$, 135 (33) $[C_{11}H_{15}O - C_2H_4]^+$, 149 (31) $[M - C_4H_9]^+$, 163 (57) $[C_{11}H_{15}O]^+$, 178 (31) $[M - C_2H_4]^+$, 191 (12) $[M - CH_3]^+$, 206 (22) $[M]^+$.

HRMS: $C_{14}H_{22}O$: *m*/*z* Calcd. 206.1671. Found 206.1670 (41%). $C_{12}H_{18}O$: *m*/*z* Calcd 178.1358. Found 178.1362 (50%).

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