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New Musk Odorants: (3*E*)-4-(2′-Alkyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-ones and (3*E*)-1-Acetyl-3-alkylidene-4,4-dimethylcyclohexenes

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Dedicated to Dr. Charles S. Sell on the occasion of his 60th birthday

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Four new representatives, **18**, **23**, **29**, and **32**, of the young family of dienone musks were synthesized by two general routes. The first five-step synthetic route leading to (3*E*)-4-(2′-alkyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-ones commenced with the enolate alkylation of 2,2-dimethylcyclopentanone (**13**), either directly with an alkyl halide or through the Reetz *tert*-alkylation. Subsequent cerium(III)-mediated butynol Grignard reaction, dehydration with sulfuric acid, (*E*)-selective partial reduction of the triple bond with lithium aluminum hydride, and concluding pyridinium chlorochromate oxidation complemented this route. The second four-step route leading to (3*E*)-1-acetyl-3-alkylidene-4,4-dimethylcycloalk-1-enes commenced with the Woods–Grignard modification on the vinylogous ester 3-ethoxycyclohex-2-enone (**24**) employing ethylmagnesium bromide. The product **25** was then *gem*-6,6-dimethylated by its lithium enolate to provide **26**, which was subjected to a Schlosser–Wittig reaction to introduce the 3-alkylidene substituent. Dirhodium(II) caprolactamate-catalyzed allylic oxidation with *tert*-butyl hydroperoxide completed the second general synthetic scheme. The four target compounds, **18**, **23**, **29**, and **32**, were designed as *diseco* derivatives of a carotol lead, and they all constitute musk odorants with floral-fruity side notes. A *tert*-butyl group at the C-6 position of the (*E*)-hexa-3,5-dien-2-one skeleton was found to intensify the musk odor, and (*E*)-4-(2′-*tert*-butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one (**23**) was found the most intense and interesting odorant of the series, with a very uncommon undertone of beetroot and dried fruits.

Introduction

"À peine était-elle entrée qu'une hôtesse [...] lui proposait de l'asperger généreusement de la dernière senteur à la mode, Canary Wharf. Zofia déclina courtoisement d'un sourire effacé et lui demanda où trouver le parfum Habit Rouge. [...] la vendeuse vaporisa dans son dos deux pschitt de fumet jaune: « Les autres aussi ont le droit d'exister ! »"

Marc Levy, Sept jours pour une éternité...[1]

With currently over 500 perfume launches a year, it is increasingly difficult to create a bestselling fragrance that has a lasting impact on the market. A unique *sillage*, the scented wake a perfume wearer leaves behind, is however indisputably an indispensable ingredient of market success – and musk odorants are the lifeblood of the *sillage* of a perfume. A unique *sillage*, therefore, should ideally feature new musk odorants of uncommon tonality and character. For *Habit Rouge*, composed in 1963 with the intention to capture the sweet dusty, animalic-leathery aura of an equestrian,[2] Jean-Paul Guerlain did not have a huge palette of musk odorants at hand, and so the nitro musk Musk ketone (**1**, Figure 1), discovered by Bauer in 1894, was incorporated in the balsamic myrrh–labdanum–orris–vanilla fond that contrasts the bergamot–rosewood–verbena top. In 1966, Galaxolide (**2**), which had been discovered four years earlier by Heeringa and Beets,[3] appeared on the market and became the dominant musk for the next three decades, for which *Ysatis* (Givenchy, 1984) by Dominique Ropion and *Trésor* (Lancôme, 1990) by Sophia Grojsman are prime examples. Nature-identical macrocyclic musks such as Exaltolide/Thibetolide (**3**), and new nature-like derivatives such as Habanolide/Globalide,[4] Velvione/Ambretone, Muscenone and Nirvanolide took over the lead in the late 1990s, when biodegradability issues restricted the use of polycyclic musks (PCMs) such as **2**. With the discovery of a fourth family of musks, that of linear musks such as Helvetolide (**4**), Romandolide (**5**) and Serenolide (**6**),[5] the new trend of so-called "white-musk" accords began, in which fruity linear musks **4**–**6** are combined with metallic macrocyclic musks to give a "cotton and linen" effect such as in

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Emporio White for Her (Armani, 2001), created by Alberto Morillas employing 9% of Helvetolide (**4**). Other examples include *Flower* (Kenzo, 2000) with 4% of **4**, as well created by Alberto Morillas, and *Unforgivable Woman* (Sean John, 2008) by David Apel with 6% of Serenolide (**6**).

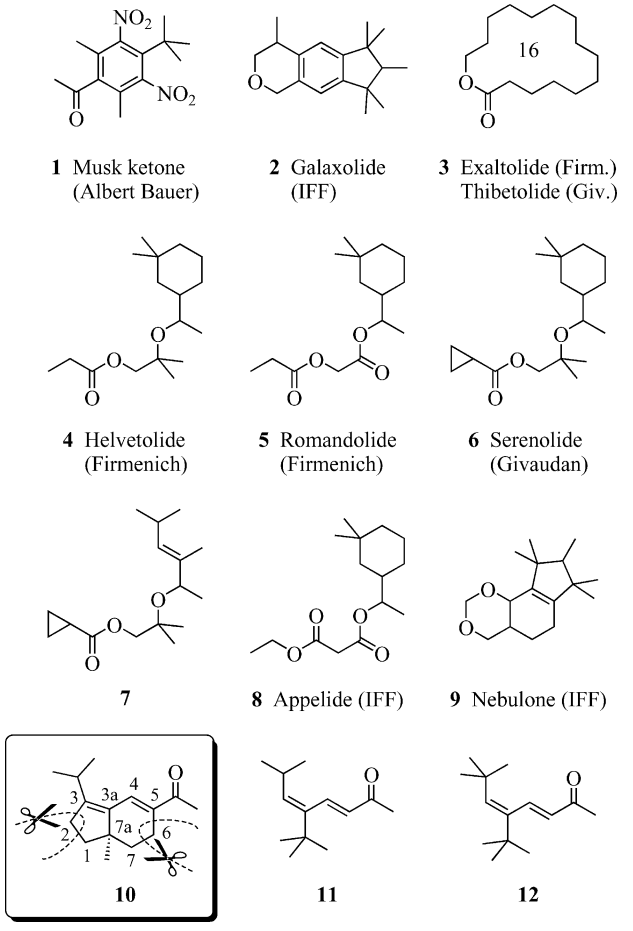


Figure 1. The different musk families with representative benchmark odorants.

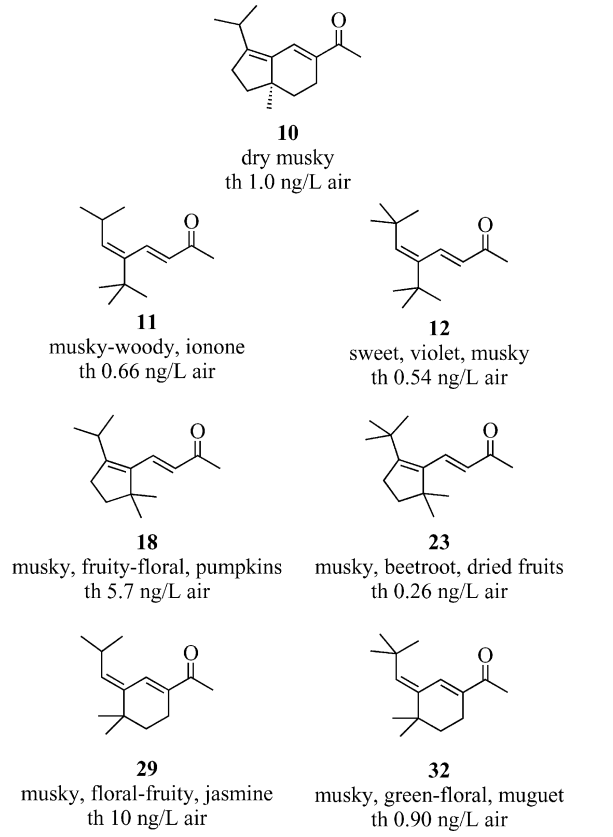


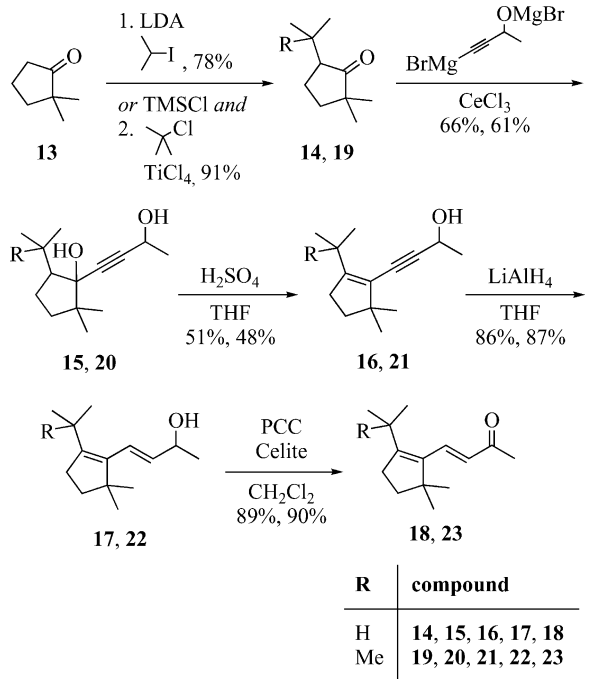
Figure 2. Overview over the olfactory properties of the dienone musk odorants investigated.

New developments in the linear musk family comprise the more volatile allyloxyethyl ester **7**,[6] and Appelide (**8**),[7] the malonate analog of Romandolide (**5**, Figure 1). But even polycyclic musks such as Nebulone (**9**)[8] are still being developed. In 2002, the group of Kula discovered the unusual bicyclic musk **10**,[9] which is devoid of a pentamethyl hydroindene motive. Instead it features a dienone function, which was utilized as skeleton for a new family of musks exemplified by the 1(2),2(3),5(6),6(7)-*tetraseco* derivative **11** that possessed a woody-musky, ionone odor with a threshold of 0.66 ng/L air.[10] The ionone facets of **11** are not too surprising, since this fifth family of musks, that features a (*E*)-hexa-3,5-dien-2-one backbone with two bulky groups at C-5 and C-6, also structurally resembles *seco*-ionones, the first of which were reported already in 1962 by Sestanj.[11] Both the musk and the violet character is intensified in the di-*tert*-butyl derivative **12**, for which an odor threshold of 0.54 ng/L air was measured (Figure 2). As the parent bicyclic enone **10** has no floral-fruity facets, it was highly interesting to study *seco* derivatives of **10**, in which either C-2 or C-6 was cut out, and to investigate the effect of the C-3 substituent, the terminal group of the hexadienone backbone, on the odor. The aim was to intensify the characteristic floral-fruity character, and thereby to generate very characteristic new musk odorants. But of course, the dependence of the odor threshold and the musk intensity on the substitution pattern was also of interest.

Results and Discussions

The 5(6),6(7)-*diseco* derivatives **18** and **23** (Scheme 1) structurally resemble ionones more closely, and could be constructed by analogy with the synthesis of **11** and **12**[10] from a 5-substituted 2,2-dimethylcyclopentanone. Standard lithium diisopropylamide (LDA)-mediated alkylation of 2,2-dimethylcyclopentanone (**13**) with isopropyl iodide afforded the alkylation product **14** in 78% yield. This was then reacted with the Grignard reagent of but-3-yn-2-ol in the presence of stoichiometric amounts of anhydrous cerium(III) chloride[12] at 50 °C to afford the alkynediol **15** in 66% yield. The dehydration of **15** turned out to be more tricky than anticipated, and the cleanest conversion was observed with a mixture of 20% aqueous sulfuric acid and THF. The cyclopentenylbutynol **16** was thus obtained in 51% yield, and then subjected to (*E*)-selective partial re-

duction of the triple bond by means of lithium aluminum hydride (LAH)[13] to afford the cyclopentenylbutenol **17** in 86% yield after chromatographic purification. Concluding pyridinium chlorochromate (PCC) oxidation was straightforward and furnished the first dienone target **18** in 89% yield. Set against an elegant woody background, the first target structure **18** indeed possesses a powerful musk odor of characteristic fruity-floral tonality that is reminiscent of violets and orris as projected, but also has damascone-like aspects of dried apples that overall rather surprisingly conjures the special smell of pumpkins. With an odor threshold of 5.7 ng/L air, the dienone **18** is, however, less potent than the *tetraseco*-structures **11** and **12**.

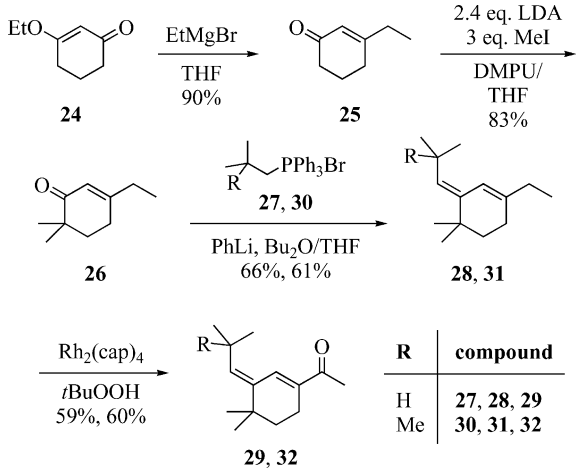


Scheme 1. Synthesis of the (3*E*)-4-(2′-alkyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one target structures **18** and **23**.

In analogy to the di-*tert*-butyl-substituted hexadienone **12**, it was however hoped that the threshold would improve by substituting the 2′-isopropyl group on the 5′,5′-dimethylcyclopentenyl ring by a *tert*-butyl moiety. The required starting material, 5-*tert*-butyl-2,2-dimethylcyclopentanone (**19**), was synthesized by Reetz *tert*-alkylation[14] of the silyl enol ether of 2,2-dimethyl cyclopentanone (**13**, Scheme 1). In the presence of titanium(IV) chloride, the *tert*-alkylation with 2-chloro-2-methylpropane provided 5-*tert*-butyl-2,2-dimethylcyclopentanone (**19**) in 91% yield after chromatographic purification. The subsequent steps were carried out in exactly the same way as in the synthesis of the first target structure **18**, affording the alkynediol **20** in 91% yield by Ce^{III}-mediated Grignard reaction, the corresponding cyclopentenyl butynol **21** in 48% yield by dehydration of **20** with a 1:1 mixture of 20% aqueous sulfuric acid and THF, and the (*E*)-butenol **22** by selective partial reduction of **21** with LAH in 87% yield by chromatographic isolation. The concluding oxidation of **22** with PCC on Celite® suspended in CH_2Cl_2 was also straightforward, and the second target compound, the (*E*)-4-(2′-*tert*-butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one (**23**), was obtained in 90% yield after work-up and chromatographic purification. Gratifyingly, the threshold of the *tert*-butyl-substituted target structure **23** indeed improves significantly to 0.26 ng/L air, which is better than that of Exaltolide/Thibetolide (**3**; 2.1 ng/L air[4]), or Galaxolide (**2**; 0.9 ng/L air[4]), and almost in the range of nitro musks such as Musk ketone (**1**; 0.1 ng/L air[4]). The odor of **23** is not far from that of the isopropyl derivative **18**, but with a more distinct musk character, no significant woody background, and a somewhat more pronounced damascone aspect of dried fruits. However, most characteristic is a special pleasant beetroot tonality that conveys on the *tert*-butyl derivative **23** a unique *sillage*, which for instance would ideally suit the oriental, ambery, sweet dusty *Habit Rouge*, but which could in combination with woody-ambery odorants and patchouli oil also help construct fragrances that satisfy the classical Chypre concept without containing any oakmoss absolute. Thus, the *tert*-butyl substituent is indeed of crucial importance for the improved olfactory properties of **23**.

The preparation of the 1(2),2(3)-*diseco* derivatives **29** and **32** (Scheme 2) was less apparent, and a new synthetic strategy had to be devised, especially with respect to the vinylic acetyl function on the six-membered ring. Yet, potentially the carbonylic oxygen could be introduced by allylic oxidation of a diene precursor at the only sterically accessible side. Dirhodium(II) caprolactamate, a bench-stable blue solid that can easily be prepared from caprolactam and rhodium(II) acetate in a Soxhlet extractor,[15] had recently been reported by Doyle and co-workers[16] to be an exceptional catalyst for the allylic oxidation of olefins with *tert*-butyl hydroperoxide. Classically, the allylic oxidation of alkenes to alkenones involved rather harsh conditions such as selenium dioxide in refluxing dioxane or generation of chromium(VI) oxide species. So the new protocol of Doyle et al.[16] made the allylic oxidation of a diene precursor appear a very attractive strategy for the synthesis of the remaining two target molecules **29** and **32**.

The required diene precursor was synthesized starting by the Grignard reaction of the vinylogous ester **24** with ethylmagnesium bromide, according to the method of Woods and co-workers.[17,14b] After acidic hydrolysis and chromatographic purification, the 3-ethylcyclohex-2-enone (**25**) was obtained in 90% yield. Due to both inductive and field effects that diminish with distance, the α-hydrogen atoms at C-6 of the enone **25** are significantly more acidic than the conjugated γ-hydrogen atoms at C-4 and C-1′. 3-Ethylcyclohex-2-enone (**25**) was therefore subjected to direct lithium enolate alkylation under kinetic control employing 2.4 equiv. of LDA in 1:1 admixture with *N*,*N*′-dimethylpropylene urea (DMPU), and 3 equiv. of methyl iodide between –20 °C and room temperature. The desired *gem*-6,6-dimethylated product **26** was isolated in 83% yield after quenching with saturated aqueous ammonium chloride and flash chromatography (FC).



Scheme 2. Synthesis of the (3*E*)-1-acetyl-3-alkylidene-4,4-dimethylcycloalk-1-ene target compounds **29** and **32**.

The stage was now set for the introduction of the isobutylidene group, which had to be achieved with complete (*E*)-selectivity in order to assure seamless superposition on **10**–**12**, **18** and **23**. This, however, should be guaranteed by the Schlosser modification[18] of the classical Wittig reaction with non-stabilized phosphorus ylides. Commercially available isobutyl triphenylphosphonium bromide (**27**) was thus transformed into its deep-red ylide with one equivalent of phenyllithium in dibutyl ether/THF and then reacted with ethyl dimethyl cyclohexenone **26** at –70 °C. The resulting lithio betaine species was then deprotonated[18b,18c] by another equivalent of phenyllithium at –20 °C, and after 1 h of stirring quenched by addition of methanol. Standard work-up provided the desired isobutylidene cyclohexene **28** in 66%, exclusively in (3*E*)-configuration (Scheme 2).

All that was missing now for the completion of the target structure was the selective allylic oxidation at the ethyl substituent. According to the rules of Guillemonat[19a] with the expansion of Trachtenberg,[19b] methylene units are oxidized faster than CH_3 or $CHMe_2$ groups, which would give the right side selectivity on the diene system. On the other hand, these rules[19] also predicted that the allylic oxidation of 1-alkylcyclohexenes would occur in the ring rather than on the side chain, which would lead to the unwanted 6-oxo product. Yet the transfer of the *tert*-butyl peroxy ligand from the dirhodium complex[16] to the 6-position in the cyclohexene **28** should be sterically blocked by the *gem*-4,4-dimethyl moiety, which should finally favor the formation of the desired acetyl isobutylidene cyclohexene **29**. However, the degree of the selectivity of this radical reaction remained questionable, and it was thus all the more exciting to subject **28** to the allylic oxidation protocol elaborated by Doyle and co-workers.[16] The required blue dirhodium(II) caprolactamate catalyst was prepared from caprolactam and rhodium(II) acetate,[15] and added at 1 mol-% to a suspension of cyclohexene **28** with half an equivalent of potassium carbonate in dichloromethane. Upon addition of 5 equiv. of a 5 M *tert*-butyl hydroperoxide solution in decane at 0 °C, the reaction set in with vigorous evolution of oxygen and a color change from blue to deep red. After 1 h at 0 °C and 4 h at room temp., work-up and chromatographic purification afforded in 59% yield the desired acetyl isobutylidene cyclohexene **29**. The acetyl function was already apparent from the characteristic chemical shifts of the singlet at δ = 2.05 ppm (3 H, 2-H_3) in the ^{1}H NMR and the quartet at δ = 25.2 ppm (C-2) in the ^{13}C spectrum, but we unambiguously assigned also the remainder of the molecule by 2D NMR spectroscopy. In the ^{1}H,^{1}H NOESY spectrum, distinct crosspeaks between 2′-H of the cyclohexene double bond and 2′′-H of the isobutylidene branching as well as between the 1′′-H and the *gem*-4,4-dimethyl group corroborated the (3*E*)-configuration of the exocyclic double bond. Even the olfactory properties turned out as had been hoped for, and the first (3*E*)-1-acetyl-3-alkylidene-4,4-dimethylcycloalk-1-ene target structure **29** is a musk odorant as well, with a special floral-fruity character of jasmine tonality set against a woody, earthy background. With an odor threshold of 10 ng/L air, **29** is, however, the weakest member of the dienone musk family so far (Figure 2).

It was therefore interesting to investigate if the *tert*-butyl analog of **29** would display a lower threshold and an improved musk character, as was the case for **12** and **23** in comparison with their isopropyl analogs **11** and **18**. As the intermediate **26** was already at hand, only the non-commercial neopentyl triphenylphosphonium bromide **30** needed to be prepared, which went smoothly with 76% yield in refluxing xylene (see Exp. Sect.). The Schlosser–Wittig reaction[18] with **30** on the ethyl dimethyl cyclohexenone **26** was not much affected by the increased steric bulk of the ylide, and the desired (3*E*)-configured neopentylidene cyclohexene **31** was isolated as single isomer in 61% yield.

The dirhodium(II) caprolactamate-catalyzed allylic oxidation of the diene **31** according to the protocol Doyle et al.[16] was also straightforward and proceeded regioselectively on the ethyl side chain to provide the final target structure (3′*E*)-1-[3′-(2′′,2′′-dimethylpropylidene)-4′,4′-dimethylcyclohex-1′-enyl]ethanone (**32**) in 60% yield as colorless, odoriferous liquid. The acetyl group was apparent from the ^{1}H singlet at δ = 2.05 ppm (3 H, 2-H_3) and the ^{13}C quartet at δ = 25.1 ppm (C-2), almost identical to the chemical shifts in the isobutylidene analog **29**. But independent from **29**, all signals were unambiguously assigned by 2D NMR experiments, and the (3*E*)-configuration was established by the NOE correlation between 2′-H of the cyclohexene double bond and 2′′-Me of the neopentylidene substituent, in combination with those between 1′′-H and the *gem*-4,4-dimethyl group. Indeed, in comparison with the isobutylidene analog **29**, the musk note intensified, and the threshold was lowered by more than a factor of 10 to a value of 0.90 ng/L air. As was the case for **29**, the musk note of **32** is accompanied by floral facets, but this time not in a jasmine-fruity but in a green, lily-of-the-valley (muguet) direction, set against a woody background.

Olfactory Comparison and Conclusions

The olfactory properties of the seven dienone musks known to date, including odor thresholds as determined by

GC-olfactometry, are summarized in Figure 2. The young family around the parent bicyclic dienone **10** is still very small, so the four new members **18**, **23**, **29** and **32** reported in this paper significantly extend on their structure–odor correlations. In a previous work,[10] it was already suspected that a *tert*-butyl group on C-5 of the (*E*)-hexa-3,5-dien-2-one skeleton is responsible for the musk odor of compounds **11** and **12**. The new members of the family, **18**, **23**, **29** and **32**, demonstrate that the methyl-substituted, quaternary C-atom can also be incorporated in a ring, thereby confirming the importance of this structural element for the musk odor of the compounds. Another *tert*-butyl group or a related motif at position C-6 of the (*E*)-hexa-3,5-dien-2-one skeleton is not essential, but indeed improves the musk intensity significantly, and lowers the odor threshold impressively (Figure 2). While the bicyclic parent compound displays a dry musky note devoid of floral facets, the 1(2),2(3),5(6),6(7)-*tetraseco* derivatives **11** and **12** has a distinct sweet ionone, violet-orris-type inflection. One could have expected this ionone character to increase in the 5(6),6(7)-*diseco* derivatives **18** and **23**, because at first sight they seem structurally to resemble ionones more closely. However, instead the ionone character of **18** and **23** is less pronounced, and the floral-fruity, almost vegetal note that accompanies the main musk theme is reminiscent of pumpkins, beetroot and dried fruits, leading to a most unusual and typical musk signature. The floralcy again increases in the 1(2),2(3)-*diseco* derivatives **29** and **32**, which have, however, no violet but instead fruity, jasmine and green, muguet (lily of the valley) inclinations, respectively. With an odor threshold of 10 ng/L air, (3′*E*)-1-[4′,4′-dimethyl-3′-(2′′-methylpropylidene)cyclohex-1′-enyl]ethanone (**29**) is by far the weakest odorant of this new musk family, while (*E*)-4-(2′-*tert*-butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one (**23**) is with 0.26 ng/L the strongest odorant discovered within the family. The *tert*-butyl cyclopentenyl alkenone **23** is not only the most intense, but also the aesthetically most preferred musk with its most unusual but pleasant beetroot tonality.

The elaborated synthetic routes presented in Scheme 1 and Scheme 2, consisting of either enolate alkylation, butynol Grignard reaction, dehydration, partial LAH reduction of the triple bond and PCC oxidation of the hydroxy function, or Woods–Grignard on a vinylogous ester, enolate dialkylation, Schlosser–Wittig reaction and allylic oxidation for instance with the dirhodium(II) caprolactamate catalyst, make accessible a full panoply of structurally new and interesting compounds with potentially interesting odors.

Experimental Section

General: IR: Bruker VECTOR 22/Harrick SplitPea micro ATR, Si. NMR: Bruker Avance DPX-400, Bruker Avance 500 (TCI), TMS int. (= 0 ppm); multiplicity selection of ^{13}C peaks with Distortionless Enhancement by Polarization Transfer (DEPT) from ^{1}H nuclei using $\theta_y = 90°$ and $\theta_y = 135°$ pulse sequences. MS: Finnigan MAT 95 (EI: 70 eV), HP Chemstation 6890 GC/5973 Mass Sensitive Detector. FC (flash chromatography): Brunschwig Silica 100726 (32–63 μm, 60 Å). TLC: Merck Kieselgel 60 F_{254} (particle size 5–20 μm, layer thickness 250 μm on glass, 10 cm × 10 cm); visualization reagent: phosphomolybdic acid spray (Merck no. 1.00480.0100). Melting points: Büchi Melting Point B545 (uncorr.). Elemental analyses: Mikroanalytisches Laboratorium Ilse Beetz, 96301 Kronach, Germany. Unless otherwise stated, all reactions were performed under N_2. Starting materials, reagents and solvents were used without further purification: SAFC or Acros.

Odor thresholds were determined by GC-olfactometry: Different dilutions of the sample substance were injected into a gas chromatograph in descending order of concentration until the panelist failed to detect the respective substance at the sniffing port. The panelist smelled in blind and pressed a button on perceiving an odor. If the recorded time matched the retention time, the concentration was halved. The last concentration detected at the correct retention time is the individual odor threshold. The reported threshold values are the geometrical means of the individual odor thresholds of different panelists.

5-Isopropyl-2,2-dimethylcyclopentanone (14): At –70 °C, a solution of *N*,*N*′-dimethylpropylene urea (DMPU, 9.86 g, 77.0 mmol) in THF (100 mL) was added within 5 min to a stirred solution of lithium diisopropylamide (2 M in THF, 38.5 mL, 77.0 mmol). After 10 min of stirring at –70 °C, a solution of 2,2-dimethylcyclopentanone (**13**, 7.80 g, 70.0 mmol) in THF (50 mL) was added over a period of 30 min. The reaction mixture was warmed to –20 °C, and treated dropwise with 2-iodopropane (18.7 g, 105 mmol) prior to removal of the cooling bath. After stirring at room temp. overnight, the reaction was quenched by addition of satd. aq. NH_4Cl (300 mL). The product was extracted with Et_2O (3 × 300 mL), the combined organic extracts were dried (Na_2SO_4) and concentrated under the reduced pressure. The resulting residue was purified by silica gel FC (pentane/Et_2O, 98:2, R_f 0.25) to furnish the title compound **14** (8.42 g, 78%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1731 (s, $\nu_{C=O}$), 1462 [m, $\delta_{as}(CH_3)$], 1367 [m, $\delta_s(CH_3)$] cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.80/0.99 (2d, J = 7.0 Hz, 6 H, 1′-Me_2), 0.94/1.06 (2s, 6 H, 2-Me_2), 1.62–1.69 (m, 2 H, 3-, 4-H_b), 1.76–1.81 (m, 1 H, 5-H), 1.89–1.94 (m, 1 H, 1′-H), 2.11–2.17 (m, 2 H, 3-, 4-H_a) . ^{13}C NMR ($CDCl_3$): δ = 18.4/21.1 (2q, 1′-Me_2), 20.6 (t, C-4), 23.1/24.7 (2q, 2-Me_2), 27.4 (d, C-1′), 36.4 (t, C-3), 45.3 (s, C-2), 224.1 (s, C-1) ppm. MS (EI): *m*/*z* (%) = 154 (15) $[M]^+$, 139 (7) $[M - CH_3]^+$, 112 (36) $[M - C_3H_6]^+$, 97 (18) $[M - C_4H_9]^+$, 56 (100) $[C_3H_4O]^+$.

1-(3′-Hydroxybut-1′-ynyl)-5-isopropyl-2,2-dimethylcyclopentanol (15): A solution of 3-butyn-2-ol (3.72 g, 53.0 mmol) in THF (80 mL) was added dropwise within 20 min. to a stirred solution of ethylmagnesium bromide (3 M in Et_2O, 35.3 mL, 106 mmol), and the reaction mixture was refluxed for 2 h. In a separate 2-neck round-bottom flask, a solution of **14** (7.40 g, 48.0 mmol) in THF (100 mL) was added at 0 °C in one dash to anhydrous cerium(III) chloride (11.8 g, 48.0 mmol). After stirring for 4 h at room temp., the resulting viscous slurry was added dropwise at ambient temp. to the freshly prepared Grignard reagent, whereupon the temp. did not rise. The reaction mixture was stirred for 2 d at 50 °C, cooled to room temp., quenched with satd. aq. NH_4Cl solution (300 mL), and extracted with Et_2O (3 × 400 mL). The combined organic extracts were dried (Na_2SO_4) and the solvents evaporated. Purification of the resulting residue by silica gel FC (pentane/Et_2O, 6:4, R_f = 0.23) furnished the title compound **15** (7.12 g, 66%) as slightly yellowish oil. IR (neat): $\tilde{\nu}$ = 3297 (m, ν_{O-H}), 1467 [m, $\delta_{as}(CH_3)$], 1365 [m, $\delta_s(CH_3)$], 1061 (s, ν_{C-O}) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.91/1.04 (2d, J = 6.5 Hz, 6 H, 1′′-Me_2), 0.98/1.08 (2s, 6 H, 2-Me_2), 1.26–1.45 (m, 2 H, 3-, 4-H_b), 1.45/1.47 (2d, J = 6.5 Hz, 3 H, 4′-

H_3), 1.54–1.62 (m, 1 H, 5-H), 1.69–1.84 (m, 2 H, 3-, 4-H_a), 1.82 (br. s, 2 H, OH), 1.85–1.94 (m, 1 H, 1′′-H), 4.59/4.60 (2q, J = 6.5 Hz, 1 H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.6/21.7 (2q, 1′′-Me_2), 22.2/22.4 (2q, 2-Me_2), 24.3/24.5 (2q, C-4′), 25.4/26.8 (2t, C-4), 30.1/32.3 (2d, C-1′′), 35.4/35.7 (2t, C-3), 46.1/48.3 (2s, C-2), 54.0/54.1 (2d, C-5), 58.3/58.4 (2d, C-3′), 80.1/82.0 (2s, C-1), 84.3/86.4 (s, C-1′), 87.8/89.6 (2s, C-2′) ppm. MS (EI): *m/z* (%) = 224 (2) $[M]^+$, 209 (3) $[M - CH_3]^+$, 206 (10) $[M - H_2O]^+$, 191 (61) $[M - C_2H_5O]^+$, 45 (12) $[C_2H_5O]^+$.

4-(2′-Isopropyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-yn-2-ol (16): At 0 °C, a solution of **15** (4.82 g, 21.5 mmol) in THF (20 mL) was added within 5 min to a mixture of 20% aq. H_2SO_4 (150 mL) and THF (150 mL). After stirring for 2 h at 0 °C, the reaction mixture was extracted with Et_2O (3 × 200 mL), and the combined organic extracts were washed with satd. aq. $NaHCO_3$ solution (2 × 200 mL) and brine (2 × 100 mL). After drying (Na_2SO_4), the solvent was evaporated on a rotary evaporator, and the resulting residue was purified by silica gel FC (pentane/Et_2O, 95:5, R_f = 0.14) to provide the title compound **16** (2.27 g, 51%) as colorless oil. IR (neat): $\tilde{\nu}$ = 3331 (m, ν_{O-H}), 2150 (w, $\delta_{C\equiv C-C}$), 1455 [m, $\delta_{as}(CH_3)$], 1360 [m, $\delta_s(CH_3)$], 1093 (s, ν_{C-O}) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.00 (d, J = 7.0 Hz, 6 H, 1′′-Me_2), 1.06 (s, 6 H, 5′-Me_2), 1.50 (d, J = 6.5 Hz, 3 H, 1-H_3), 1.66 (t, J = 7.0 Hz, 2 H, 4′-H_2), 1.95 (br. s, 1 H, OH), 2.30 (d, J = 7.0 Hz, 2 H, 3′-H_2), 2.87 (sept, J = 7.0 Hz, 1 H, 1′′-H), 4.71 (q, J = 6.5 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8 (q, 1′′-Me_2), 24.8 (q, C-1), 27.0/27.1 (2q 5′-Me_2), 28.7 (t, C-3′), 29.1 (d, C-1′′), 38.3 (t, C-4′), 46.6 (s, C-5′), 59.1 (d, C-2), 79.5 (s, C-3), 95.9 (s, C-4), 125.2 (s, C-1′), 155.2 (s, C-2′) ppm. MS (EI): *m/z* (%) = 206 (63) $[M]^+$, 191 (88) $[M - CH_3]^+$, 173 (23) $[M - CH_4O]^+$, 163 (46) $[M - C_3H_7]^+$, 45 (10) $[C_2H_5O]^+$, 43 (100) $[C_3H_7]^+$.

(*E*)-4-(2′-Isopropyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-ol (17): At room temp., a solution of **16** (1.91 g, 9.25 mmol) in THF (20 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (351 mg, 9.25 mmol) in THF (5.0 mL). The resulting reaction mixture was stirred for 4 h at room temp., prior to quenching with cooling in an ice bath by dropwise addition of water (0.35 mL), followed by 15% aq. NaOH (0.35 mL) and again water (1.05 mL). After stirring for further 30 min at room temp., the formed precipitate was filtered off by suction with the aid of a sintered funnel, and the filter cake washed with Et_2O (30 mL). The combined filtrates were evaporated under reduced pressure, and the resulting residue was purified by silica gel FC (pentane/Et_2O, 9:1, R_f = 0.21) to provide the title compound **17** (1.66 g, 86%) as colorless oil. IR (neat): $\tilde{\nu}$ = 3318 (m, ν_{O-H}), 1455 [m, $\delta_{as}(CH_3)$], 1361 [m, $\delta_s(CH_3)$], 1029 (s, ν_{C-O}), 964 (s, $\delta_{C=C-H}$) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.99 (d, J = 7.0 Hz, 6 H, 1′′-Me_2), 1.10/1.11 (2s, 6 H, 5′-Me_2), 1.31 (d, J = 6.5 Hz, 3-H, 1-H_3), 1.60 (t, J = 7.5 Hz, 2 H, 4′-H_2), 2.24 (t, J = 7.5 Hz, 2 H, 3′-H_2), 2.84 (sept, J = 7.0 Hz, 1 H, 1′′-H), 4.34 (quint, J = 6.5 Hz, 1 H, 2-H), 5.73 (dd, J = 16.0, 6.5 Hz, 1 H, 3-H), 6.18 (d, J = 16.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.3 (q, 1′′-Me_2), 24.5 (q, C-1), 27.0 (d, C-1′′), 27.1/27.2 (2q, 5′-Me_2), 27.8 (t, C-3′), 40.1 (t, C-4′), 46.5 (s, C-5′), 70.0 (d, C-2), 123.1 (d, C-3), 133.0 (d, C-4), 138.3 (s, C-1′), 146.8 (s, C-2′) ppm. MS (EI): *m/z* (%) = 208 (10) $[M]^+$, 193 (14) $[M - CH_3]^+$, 175 (40) $[M - CH_4O]^+$, 135 (100) $[C_{10}H_{15}]^+$, 45 (11) $[C_2H_5O]^+$, 43 (49) $[C_3H_7]^+$.

(*E*)-4-(2′-Isopropyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one (18): At room temp., pyridinium chlorochromate (1.97 g, 9.15 mmol) was added portionwise to a stirred suspension of **17** (1.27 g, 6.10 mmol) and Celite® (5.00 g) in CH_2Cl_2 (40 mL). After stirring for 5 h at room temp., the insoluble materials were filtered off over a pad of Celite®, and washed with Et_2O (50 mL). The combined filtrates were evaporated on a rotary evaporator, and the resulting residue was purified by silica gel FC (pentane/Et_2O, 98:2, R_f = 0.12) to provide the odoriferous title compound **18** (1.12 g, 89%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1688 (s, $\nu_{C=O}$, conj.), 1458 [m, $\delta_{as}(CH_3)$], 1360 [m, $\delta_s(CH_3)$], 1252 (s, $\nu_{C=C-C=O}$), 973 (m, $\delta_{C=C-H}$) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.04 (d, J = 7.0 Hz, 6 H, 1′′-Me_2), 1.18 (s, 6 H, 5′-Me_2), 1.67 (t, J = 7.5 Hz, 2 H, 4′-H_2), 2.29 (s, 3 H, 1-H_3), 2.34 (d, J = 7.5 Hz, 2 H, 3′-H_2), 2.99 (sept, J = 7.0 Hz, 1 H, 1′′-H), 6.28 (d, J = 16.5 Hz, 1 H, 3-H), 7.37 (d, J = 16.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.2 (q, 1′′-Me_2), 26.9 (q, 5′-Me_2), 27.3 (d, C-1′′), 27.6 (q, C-1), 28.7 (t, C-3′), 40.2 (t, C-4′), 46.3 (s, C-5′), 125.7 (d, C-3), 136.4 (d, C-4), 138.3 (s, C-1′), 159.0 (s, C-2′), 199.0 (s, C-2) ppm. MS (EI): *m/z* (%) = 206 (6) $[M]^+$, 191 (5) $[M - CH_3]^+$, 163 (100) $[M - C_2H_3O]^+$, 43 (38) $[C_3H_7]^+$. $C_{14}H_{22}O$ (206.3): calcd. C 81.50, H 10.75; found C 81.43, H 10.70. Odor: Powerful musk note with a special fruity-floral character recalling pumpkins, dried apples, violets and orris, in front of an elegant woody background. Odor threshold: 5.7 ng/L air.

5-*tert*-Butyl-2,2-dimethylcyclopentanone (19): At –70 °C, a solution of 2,2-dimethylcyclopentanone (10.1 g, 90.0 mmol) in THF (200 mL) was added within 30 min. to a stirred solution of lithium diisopropylamide (2 M in THF, 45.0 mL, 90.0 mmol). After 15 min of stirring at –70 °C, chlorotrimethylsilane (19.6 g, 180 mmol) was added dropwise over a period of 10 min, and the reaction mixture was warmed to 0 °C, stirred for 1 h at this temp., and then 2 h at room temp. The formed precipitate was filtered off by suction with the aid of a sintered funnel, and the filter cake was washed with Et_2O (100 mL). The combined filtrates were concentrated under reduced pressure to furnish the crude silyl enol ether (16.8 g, 88.9 mmol), which was taken up in CH_2Cl_2 (200 mL). At –60 °C, 2-chloro-2-methylpropane (8.80 g, 95.0 mmol) was added, followed by slow injection of a solution of $TiCl_4$ (17.1 g, 90 mmol) in CH_2Cl_2 (30 mL) within 10 min. Stirring was continued at –60 °C for further 30 min, before the reaction mixture was warmed to 0 °C. After quenching by slow addition of water (500 mL), the product was extracted with Et_2O (3 × 400 mL), and the combined organic extracts were washed with 10% aq. $NaHCO_3$ (2 × 150 mL) and brine (2 × 100 mL). After drying (Na_2SO_4), and evaporation of the solvent on a rotary evaporator, the resulting residue was purified by silica gel FC (pentane/Et_2O, 98:2, R_f = 0.27) to provide the title compound **19** (13.8 g, 91%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1722 (s, $\nu_{C=O}$), 1463 [m, $\delta_{as}(CH_3)$], 1361 [m, $\delta_s(CH_3)$] cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.92/1.05 (2s, 6 H, 2-Me_2), 0.99 (s, 9 H, 1′-Me_3), 1.51–1.59 (m, 1 H, 5-H), 1.64–1.80 (m, 2 H, 3-, 4-H_b), 1.92–2.15 (m, 2 H, 3-, 4-H_a) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.3 (t, C-4), 23.0/24.8 (2q, 2-Me_2), 27.8 (q, 1′-Me_3), 32.3 (s, C-1′), 35.8 (t, C-3), 45.7 (s, C-2), 223.5 (s, C-1) ppm. MS (EI): *m/z* (%) = 168 (24) $[M]^+$, 153 (11) $[M - CH_3]^+$, 112 (100) $[M - C_4H_8]^+$, 111 (52) $[M - C_4H_9]^+$, 57 (45) $[C_4H_9]^+$.

5-*tert*-Butyl-1-(3′-hydroxybut-1′-ynyl)-2,2-dimethylcyclopentanol (20): As described for the preparation of **15**, from **19** (12.3 g, 73.0 mmol), 3-butyn-2-ol (5.61 g, 80 mmol) and cerium(III) chloride (18.0 g, 73.0 mmol) in THF (250 mL). The title compound **20** was obtained after standard workup and purification by silica gel FC (pentane/Et_2O, 6:4, R_f = 0.26) as slightly yellowish oil. Yield 61% (10.6 g). IR (neat): $\tilde{\nu}$ = 3301 (m, ν_{O-H}), 1465 [m, $\delta_{as}(CH_3)$], 1366 [m, $\delta_s(CH_3)$], 1078 (s, ν_{C-O}) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.01/1.03 (2s, 6 H, 2-Me_2), 1.07 (s, 9 H, 1′′-Me_3), 1.44 (d, J = 6.5 Hz, 3 H, 4′-H_3), 1.65–1.70 (m, 2 H, 3-, 4-H_b), 1.72–1.78 (m, 2 H, 3-, 4-H_a), 2.10–2.14 (m, 1 H, 5-H), 2.16 (br. s, 2 H, OH), 4.56 (q, J = 6.5 Hz, 1 H, 3′-H), ppm. ^{13}C NMR ($CDCl_3$): δ = 21.5/26.9 (2q, 2-Me_2),

22.9/23.0 (2t, C-4), 24.3/24.4 (2q, C-4′), 29.5/29.5 (2q, 1′′-Me_3), 33.7/33.7 (2s, C-1′′), 35.7/35.7 (2t, C-3), 48.4/48.5 (2s, C-2), 55.6/55.7 (2d, C-5), 58.4/58.4 (2d, C-3′), 81.5/81.5 (2s, C-1), 86.7/86.8 (s, C-1′), 87.8/87.8 (2s, C-2′) ppm. MS (EI): *m/z* (%) = 223 (2) $[M - CH_3]^+$, 205 (15) $[M - CH_3 - H_2O]^+$, 187 (2) $[M - CH_3 - H_2O - H_2O]^+$, 181 (12) $[M - C_4H_9]^+$, 164 (59) $[M - H_2O - C_4H_8]^+$, 149 (51) $[M - H_2O - C_5H_{11}]^+$, 121 (40)/107 (71)/93 (24)/79 (36) $[C_nH_{(2n-5)}]^+$, 57 (95) $[C_4H_9O]^+$, 45 (8) $[C_2H_5O]^+$, 43 (100) $[C_2H_3O]^+$.

4-(2′-*tert*-Butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-yn-2-ol (21): As described for the preparation of **16**, from **20** (6.20 g, 26.0 mmol) and 20% aq. H_2SO_4 solution (200 mL) in THF (200 mL). The title compound **21** was obtained after standard workup and purification by silica gel FC (pentane/Et_2O, 95:5, R_f = 0.16) as colorless oil. Yield 48% (2.75 g). IR (neat): $\tilde{\nu}$ = 3321 (m, ν_{O-H}), 2150 (w, $\delta_{C\equiv C-C}$), 1457 [m, $\delta_{as}(CH_3)$], 1360 [m, $\delta_s(CH_3)$] 1087 (s, ν_{C-O}) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.04 (s, 6 H, 5′-Me_2), 1.19 (s, 9 H, 1′′-Me_3), 1.49 (d, J = 6.5 Hz, 3 H, 1-H_3), 1.61 (t, J = 7.5 Hz, 2 H, 4′-H_2), 1.93 (br. s, 1 H, OH), 2.40 (d, J = 7.0 Hz, 2 H, 3′-H_2), 4.70 (q, J = 6.5 Hz, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.4 (q, C-1), 26.8/26.9 (2q, 5′-Me_2), 29.4 (q, 1′′-Me_3), 31.8 (t, C-3′), 34.0 (s, C-1′′), 38.0 (t, C-4′), 47.0 (s, C-5′), 59.1 (d, C-2), 81.3 (s, C-3), 96.9 (s, C-4), 124.6 (s, C-1′), 156.1 (s, C-2′) ppm. MS (EI): *m/z* (%) = 220 (53) $[M]^+$, 205 (87) $[M - CH_3]^+$, 187 (36) $[M - CH_4O]^+$, 163 (28) $[M - C_4H_9]^+$, 57 (34) $[C_4H_6]^+$, 43 (100) $[C_3H_7O]^+$.

(*E*)-4-(2′-*tert*-Butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-ol (22): As described for the preparation of **17**, from **21** (2.20 g, 10.0 mmol) and $LiAlH_4$ (350 mg, 9.22 mmol) in THF (25 mL). The title compound **22** was obtained after standard workup and purification by silica gel FC (pentane/Et_2O, 9:1, R_f = 0.22) as colorless oil. Yield 87% (1.94 g). IR (neat): $\tilde{\nu}$ = 3331 (m, ν_{O-H}), 1457 [m, $\delta_{as}(CH_3)$], 1360 [m, $\delta_s(CH_3)$], 1065 (s, ν_{C-O}), 968 (s, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.02/1.03 (2s, 6 H, 5′-Me_2), 1.11 (s, 9 H, 1′′-Me_3), 1.31 (d, J = 6.5 Hz, 3-H, 1-H_3), 1.56 (t, J = 7.0 Hz, 2 H, 4′-H_2), 2.32 (t, J = 7.0 Hz, 2 H, 3′-H_2), 4.33–4.35 (m, 1 H, 2-H), 5.54 (dd, J = 16.0, 6.5 Hz, 1 H, 3-H), 6.30 (d, J = 16.0 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.2 (q, C-1), 27.2 (q, 5′-Me_2), 30.7 (q, 1′′-Me_3), 31.4 (t, C-3′), 33.7 (s, C-1′′), 39.8 (t, C-4′), 47.9 (s, C-5′), 69.7 (d, C-2), 126.1 (d, C-3), 134.3 (d, C-4), 139.0 (s, C-1′), 146.1 (s, C-2′) ppm. MS (EI): *m/z* (%) = 222 (15) $[M]^+$, 207 (38) $[M - CH_3]^+$, 189 (83) $[M - CH_4O]^+$, 165 (8) $[M - C_4H_9]^+$, 133 (100) $[C_{12}H_{15}]^+$, 57 (87) $[C_4H_9]^+$, 45 (19) $[C_2H_5O]^+$, 43 (90) $[C_2H_3O]^+$.

(*E*)-4-(2′-*tert*-Butyl-5′,5′-dimethylcyclopent-1′-enyl)but-3-en-2-one (23): As described for the preparation of **18**, from **22** (1.50 g, 6.75 mmol) and pyridinium chlorochromate (2.18 g, 10.1 mmol) in CH_2Cl_2 (40 mL). The odoriferous title compound **23** was obtained after standard workup and purification by silica gel FC (pentane/Et_2O, 98:2, R_f = 0.15) as colorless liquid. Yield 90% (1.34 g). IR (neat): $\tilde{\nu}$ = 1664 (s, $\nu_{C=O}$, conj.), 1459 [m, $\delta_{as}(CH_3)$], 1360 [m, $\delta_s(CH_3)$], 1252 (s, $\nu_{C=C-C=O}$), 981 (m, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.14 (s, 6 H, 5′-Me_2), 1.20 (s, 9 H, 1′′-Me_3), 1.61 (t, J = 7.0 Hz, 2 H, 4′-H_2), 2.28 (s, 3 H, 1-H_3), 2.43 (d, J = 7.0 Hz, 2 H, 3′-H_2), 6.16 (d, J = 16.5 Hz, 1 H, 3-H), 7.37 (d, J = 16.5 Hz, 1 H, 4-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 26.9 (q, C-1), 27.0 (q, 5′-Me_2), 30.9 (q, 1′′-Me_3), 32.5 (t, C-3′), 34.4 (s, C-1′′), 40.3 (t, C-4′), 47.6 (s, C-5′), 126.6 (d, C-3), 138.7 (s, C-1′), 140.0 (d, C-4), 158.0 (s, C-2′), 199.1 (s, C-2) ppm. MS (EI): *m/z* (%) = 220 (6) $[M]^+$, 205 (15) $[M - CH_3]^+$, 163 (100) $[M - C_4H_9]^+$, 57 (10) $[C_4H_9]^+$, 43 (41) $[C_2H_3O]^+$. $C_{15}H_{24}O$ (220.4): calcd. C 81.76, H 10.98; found C 81.77, H 11.04. Odor: Powerful musk note with a special character recalling pumpkins, beetroot, dried fruits and violets. Odor threshold: 0.26 ng/L air.

3-Ethylcyclohex-2-enone (25): Between 10 and 12 °C, a solution of 3-ethoxycyclohex-2-enone (**24**, 63.1 g, 450 mmol) in THF (500 mL) was added over a period of 2 h to a stirred solution of ethylmagnesium bromide (3 M in Et_2O, 180 mL, 540 mmol). The mixture was stirred for further 3 h at room temp., prior to quenching by dropwise addition of aq. 3 M HCl solution (800 mL) under cooling in an ice-bath. After stirring at 0 °C for additional 6 h, the product was extracted with Et_2O (3 × 500 mL), and the combined organic extracts were washed with satd. aq. $NaHCO_3$ (2 × 200 mL) and brine (2 × 200 mL). After drying (Na_2SO_4) and evaporation of the solvent on a rotary evaporator, the resulting residue was purified by silica gel FC (pentane/Et_2O, 9:1, R_f = 0.12) to provide the title compound **25** (50.3 g, 90%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1662 (s, $\nu_{C=O}$, conj.), 1456 [m, $\delta_{as}(CH_3)$], 1348 [m, $\delta_s(CH_3)$], 886 (m, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.11 (t, J = 7.5 Hz, 3 H, 2′-H_3), 1.99 (quint, J = 7.0 Hz, 2 H, 5-H_2), 2.25 (q, J = 7.5 Hz, 2 H, 1′-H_2), 2.31 (t, J = 7.0 Hz, 2 H, 4-H_2), 2.36 (t, J = 7.0 Hz, 2 H, 6-H_2), 5.87 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.2 (q, C-2′), 22.7 (t, C-5), 29.6 (t, C-1′), 30.8 (t, C-4), 37.4 (t, C-6), 124.5 (d, C-2), 167.8 (s, C-3), 199.9 (s, C-1) ppm. MS (EI): *m/z* (%) = 124 (62) $[M]^+$, 109 (2) $[M - CH_3]^+$, 96 (100) $[M - C_2H_4]^+$, 67 (49) $[M - C_3H_5O]^+$.

3-Ethyl-6,6-dimethylcyclohex-2-enone (26): At –70 °C, a solution of DMPU (122 g, 950 mmol) in THF (300 mL) was added within 30 min to a stirred solution of LDA (2 M in THF, 475 mL, 950 mmol). After 20 min. of stirring at this temp., a solution of **25** (49.2 g, 396 mmol) in THF (400 mL) was added over a period of 1 h, and stirring was continued at –70 °C for an additional 30 min. The reaction mixture was warmed to –20 °C, and treated dropwise with MeI (169 g, 1.19 mol). The cooling bath was removed, and stirring was continued at room temp. overnight. After quenching by dropwise addition of satd. aq. NH_4Cl (700 mL), the product was extracted with Et_2O (3 × 400 mL). The combined organic extracts were dried (Na_2SO_4), and concentrated under reduced pressure. The resulting residue was purified by silica gel FC (pentane/Et_2O, 95:5, R_f = 0.15) to furnish the title compound **26** (50.7 g, 83%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1665 (s, $\nu_{C=O}$, conj.), 1452 [m, $\delta_{as}(CH_3)$], 1347 [m, $\delta_s(CH_3)$], 878 (m, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.10 (t, J = 7.5 Hz, 3 H, 2′-H_3), 1.81 (t, J = 7.0 Hz, 2 H, 5-H_2), 2.21 (q, J = 7.5 Hz, 2 H, 1′-H_2), 2.32 (t, J = 7.0 Hz, 2 H, 4-H_2), 5.77 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.3 (q, C-2′), 24.4 (s, 6-Me_2), 27.0 (t, C-1′), 30.4 (t, C-4), 36.3 (t, C-5), 40.4 (s, C-6), 122.9 (d, C-2), 165.4 (s, C-3), 204.5 (s, C-1) ppm. MS (EI): *m/z* (%) = 152 (18) $[M]^+$, 137 (3) $[M - CH_3]^+$, 124 (6) $[M - CO]^+$, 96 (100) $[M - C_4H_8]^+$, 67 (22) $[M - C_5H_9O]^+$.

(3*E*)-1-Ethyl-4,4-dimethyl-3-(2′′-methylpropylidene)cyclohexene (28): A phenyllithium solution in dibutyl ether (1.9 M, 41.0 mL, 78.2 mol) was added at room temp. dropwise within 15 min. to a stirred suspension of commercially available isobutyl triphenylphosphonium bromide (**27**, 31.2 g, 78.2 mmol) in THF (300 mL). The resulting deep-red solution was cooled to –70 °C, and a solution of **26** (11.3 g, 74.3 mmol) in dry Et_2O (100 mL) was added over a period of 10 min. After 15 min of stirring at –70 °C, the reaction mixture was warmed to –20 °C and treated dropwise with additional phenyllithium solution in dibutyl ether (1.9 M, 41.0 mL, 78.2 mol). After 1 h of stirring at –20 °C, MeOH (12 mL) was added dropwise, whereupon triphenylphosphane oxide precipitated. The resulting suspension was stirred for additional 2 h at room temp., then poured into water (200 mL), and extracted with Et_2O (3 × 300 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by silica gel FC (pentane, R_f = 0.45) to furnish the title compound **28** (9.43 g, 66%) as colorless liquid. IR (neat):

$\tilde{\nu}$ = 1460 [m, $\delta_{as}(CH_3)$], 1364 [m, $\delta_s(CH_3)$], 877 (m, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.96 (d, J = 6.5 Hz, 6 H, 2′′-Me_2), 1.00 (s, 6 H, 4-Me_2), 1.05 (t, J = 7.5 Hz, 3 H, 2′-H_3), 1.45 (t, J = 6.5 Hz, 2 H, 5-H_2), 2.07 (q, J = 7.5 Hz, 2 H, 1′-H_2), 2.09 (t, J = 6.5 Hz, 2 H, 6-H_2), 2.73 (dsept, J = 9.0, 6.5 Hz, 1 H, 2′′-H), 5.02 (d, J = 9.0 Hz, 1 H, 1′′-H), 6.12 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.4 (q, C-2′), 23.5 (q, 2′′-Me_2), 25.8 (d, C-2′′), 26.1 (t, C-6), 28.0 (q, 4-Me_2), 30.7 (t, C-1′), 33.2 (s, C-4), 37.2 (t, C-5), 117.6 (d, C-2), 128.7 (d, C-1′′), 139.9 (s, C-1), 141.0 (s, C-3) ppm. MS (EI): m/z (%) = 192 (30) $[M]^+$, 177 (26) $[M - CH_3]^+$, 121 (100) $[M - C_5H_{11}]^+$, 107 (78) $[C_8H_{11}]^+$, 43 (11) $[C_3H_7]^+$.

(3′*E*)-1-[4′,4′-Dimethyl-3′-(2′′-methylpropylidene)cyclohex-1′-enyl]-ethanone (29): According to the general procedure in ref.[16] a *tert*-butyl hydroperoxide solution in decane (5 M, 12.0 mL, 60 mmol) was added at 0 °C within 20 min. to a stirred suspension of **28** (2.31 g, 12.0 mmol), K_2CO_3 (829 mg, 6.00 mmol) and dirhodium(II) caprolactamate {$[Rh_2(cap)_4]$,[15] 78.5 mg, 0.12 mmol} in CH_2Cl_2 (60 mL), upon which a vigorous oxygen evolution was observed while the color turned from blue to deep red. The reaction mixture was stirred for an additional 1 h at 0 °C, and 4 h at room temp., prior to filtration through a pad of Celite® with washing the filter cake with CH_2Cl_2 (20 mL). The combined filtrates were evaporated on a rotary evaporator, and the resulting residue was purified by silica gel FC (pentane/Et_2O, 98:2, R_f 0.16) to provide the odoriferous title compound **29** (1.46 g, 59%) as colorless liquid. IR (neat): $\tilde{\nu}$ = 1661 (s, $\nu_{C=O}$, conj.), 1462 [m, $\delta_{as}(CH_3)$], 1355 [m, $\delta_s(CH_3)$], 1248 (s, $\nu_{C=C-C=O}$), 862 (w, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.90 (d, J = 6.5 Hz, 6 H, 2′′-Me_2), 0.94 (s, 6 H, 4′-Me_2), 1.25 (t, J = 6.5 Hz, 2 H, 5′-H_2), 2.05 (s, 3 H, 2-H_3), 2.41 (t, J = 6.5 Hz, 2 H, 6′-H_2), 2.70 (dsept, J = 9.0, 6.5 Hz, 1 H, 2′′-H), 5.48 (d, J = 9.0 Hz, 1 H, 1′′-H), 7.16 (s, 1 H, 2′-H) ppm. ^1H,^1H NOESY (C_6D_6): 2′-H × 2′′-H, 1′′-H × 4′-Me_2. ^{13}C NMR (C_6D_6): δ = 21.3 (t, C-6′), 23.3 (q, 2′′-Me_2), 25.2 (q, C-2), 26.8 (d, C-2′′), 28.0 (q, 4′-Me_2), 33.4 (s, C-4′), 36.6 (t, C-5′), 131.9 (d, C-2′), 137.8 (s, C-1′), 138.2 (d, C-1′′), 140.3 (s, C-3′), 197.3 (s, C-1) ppm. MS (EI): m/z (%) = 206 (44) $[M]^+$, 191 (15) $[M - CH_3]^+$, 163 (16) $[M - CO]^+$, 164 (3) $[M - C_3H_6]^+$, 135 (65) $[M - C_5H_{11}]^+$, 107 (59) $[C_8H_{11}]^+$, 43 (100) $[C_2H_3O]^+$. $C_{14}H_{22}O$ (206.3): calcd. C 81.50, H 10.75; found C 81.55, H 10.72. Odor: Musk note with a special floral-fruity character of jasmine tonality in front of a woody, earthy background. Odor threshold: 10 ng/L air.

Neopentyl Triphenylphosphonium Bromide (30): At room temp., neopentyl bromide (21.5 g, 142 mmol) was added dropwise to a stirred solution of triphenylphosphane (37.3 g, 142 mmol) in xylene (200 mL), and the reaction mixture was stirred at reflux for 2 d. The reaction mixture was cooled to room temp., and the formed precipitate was filtered off with suction with the aid of a sintered funnel, washed with xylene (200 mL) and dried to constant weight on a high vacuum pump to provide the title compound **30** (44.6 g, 76%) as a slightly yellowish solid. IR (neat): $\tilde{\nu}$ = 1435 [m, $\delta_{as}(CH_3)$], 1367 [m, $\delta_s(CH_3)$], 692 (s, ν_{C-Br}) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.02 (br. s, 9 H, 2-Me_3), 3.96 (d, $^2J_{HP}$ = 13.0 Hz, 1-H_2), 7.76–8.07 (m, 15 H, 2′-H–6′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 31.6/31.7 (2q, 2-Me_3), 32.9/33.0 (2s, C-2), 34.8/35.3 (2CH_2 by DEPT-135, C-1), 119.4/120.3 (2s, C-1′), 130.3/130.4 (2d, C-3′,-5′), 133.7/133.8 (2d, C-2′,-6′), 134.7/134.8 (2d, C-4′) ppm. MS (ESI): m/z (%) = 333 (100) $[M - Br]^+$.

(3*E*)-1-Ethyl-4,4-dimethyl-3-(2′′,2′′-dimethylpropylidene)cyclohexene (31): As described for the preparation of **28**, from **26** (3.73 g, 24.5 mmol) and **30** (10.6 g, 25.7 mmol) in THF (100 mL), with a phenyllithium solution in dibutyl ether (1.9 M, 27 mL, 51.3 mmol). The title compound **31** was obtained after standard workup and purification by silica gel FC (pentane, R_f = 0.46) as colorless liquid. Yield 61% (3.06 g). IR (neat): $\tilde{\nu}$ = 1461 [m, $\delta_{as}(CH_3)$], 1361 [m, $\delta_s(CH_3)$], 881 (m, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.99 (s, 9 H, 2′′-Me_3), 1.05 (t, J = 7.5 Hz, 3 H, 2′-H_3), 1.15 (s, 6 H, 4-Me_2), 1.46 (t, J = 6.5 Hz, 2 H, 5-H_2), 2.06 (q, J = 7.5 Hz, 2 H, 1′-H_2), 2.08 (t, J = 6.5 Hz, 2 H, 6-H_2), 5.22 (s, 1 H, 1′′-H), 6.34 (s, 1 H, 2-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 12.3 (q, C-2′), 26.2 (t, C-6), 28.3 (q, 4-Me_2), 30.7 (t, C-1′), 31.8 (s, C-2′′), 31.9 (q, 2′′-Me_3), 33.8 (s, C-4), 37.4 (t, C-5), 118.6 (d, C-2), 130.8 (d, C-1′′), 140.2 (s, C-1), 141.4 (s, C-3) ppm. MS (EI): m/z (%) = 206 (51) $[M]^+$, 191 (85) $[M - CH_3]^+$, 135 (100) $[M - C_5H_{11}]^+$, 107 (65) $[C_8H_{11}]^+$, 57 (16) $[C_4H_9]^+$.

(3′*E*)-1-[4′,4′-Dimethylcyclohex-1′-enyl-3′-(2′′,2′′-dimethylpropylidene)]ethanone (32): As described for preparation of **29**, from **31** (1.53 g, 7.42 mmol), K_2CO_3 (513 mg, 3.71 mmol), and $[Rh_2(cap)_4]$[15] (48.5 mg, 0.074 mmol) in CH_2Cl_2 (50 mL), with a *tert*-butyl hydroperoxide solution in decane (5 M, 7.42 mL, 37.1 mmol). The odoriferous title compound **32** was obtained after standard workup and purification by silica gel FC (pentane/Et_2O, 98:2, R_f = 0.17) as colorless liquid. Yield 60% (981 mg). IR (neat): $\tilde{\nu}$ = 1664 (s, $\nu_{C=O}$, conj.), 1464 [m, $\delta_{as}(CH_3)$], 1362 [m, $\delta_s(CH_3)$], 1245 (s, $\nu_{C=C-C=O}$), 846 (w, $\delta_{C=C-H}$) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.94 (s, 6 H, 4′-Me_2), 1.18 (s, 9 H, 2′′-Me_3), 1.26 (t, J = 6.5 Hz, 2 H, 5′-H_2), 2.05 (s, 3 H, 2-H_3), 2.38 (t, J = 6.5 Hz, 2 H, 6′-H_2), 5.47 (s, 1 H, 1′′-H), 7.65 (s, 1 H, 2′-H) ppm. ^1H,^1H NOESY (C_6D_6): 2′-H × 2′′-Me, 1′′-H × 4′-Me. ^{13}C NMR (C_6D_6): δ = 21.1 (t, C-6′), 25.1 (q, C-2), 28.2 (q, 4′-Me_2), 32.2 (q, 2′′-Me_3), 32.9 (s, C-2′′), 33.9 (s, C-4′), 36.7 (t, C-5′), 132.9 (d, C-2′), 137.2 (s, C-1′), 140.7 (s, C-3′), 141.5 (d, C-1′′), 197.3 (s, C-1) ppm. MS (EI): m/z (%) = 220 (31) $[M]^+$, 205 (18) $[M - CH_3]^+$, 177 (15) $[M - CO]^+$, 164 (11) $[M - C_4H_8]^+$, 149 (34) $[M - C_5H_{11}]^+$, 107 (59) $[C_8H_{11}]^+$, 43 (100) $[C_2H_3O]^+$. $C_{15}H_{24}O$ (220.4): calcd. C 81.76, H 10.98; found C 81.75, H 10.96. Odor: Musk note with a special fruity, green-floral character of muguet (lily of the valley) tonality in front of a woody background. Odor threshold: 0.90 ng/L air.

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