From Vetiver to Patchouli: Discovery of a New High-Impact Spirocyclic Patchouli Odorant

Philip Kraft,*[a] Walter Eichenberger,[a] and David Frech[a]

Dedicated with respect and admiration to Dr. Roman Kaiser on the occasion of his 60th birthday

Keywords: Fragrances / Olfactory properties / Patchouli / Spiro compounds / Structure–activity relationships

In the course of synthetic work on new vetiver odorants, a new, potent patchouli odorant was discovered. Its structure was elucidated as 1-hydroxy-1,4,7,7,9-pentamethylspiro-[4.5]decan-2-one (**15/16**), and both diastereoisomers were synthesized from the previously reported 4,7,7,9-tetramethyl-1-methylenespiro[4.5]decan-2-one by epoxidation with *m*-chloroperoxybenzoic acid, reduction with lithium aluminum hydride, and subsequent oxidation with pyridinium chlorochromate or Dess–Martin periodinane. The 1,4-*unlike*-isomer **15** was found to be the diastereoisomer with the most powerful odor, and its excellent odor threshold of 0.067 ng/L air triggered the synthesis of the derivatives **19**, **22**, **23**, and **26** possessing a different methyl substitution pattern or ring size. Glycol cleavage in the oxidation step was circumvented by Swern oxidation. Three further 4-*demethylated* derivatives, **32**, **33**, and **34**, were prepared by a short sequence consisting of Diels–Alder reaction with 4-methylene-5-oxohexanenitrile (**28**), reductive radical cyclization mediated by the titanocene(III) complex $Cp_2Ti(Ph)(iPr)$, and standard hydrogenation. Finally, the enantiomers of **15** were separated by forming their SAMP hydrazones, which were subsequently cleaved by ozonolysis. The odor of the racemate **15** was shown to be exclusively due to the (+)-(1*S*,4*R*,5*R*,9*S*)-configured enantiomer **38**, the stereocenters of which superimpose well with those of (–)-patchoulol (**3**), the odorous principle of patchouli oil.

Introduction

"Interminably, Jamila twirled, lifting and lowering the aquamarine veil with which she covered her breast and abdomen. Suddenly the drum beat picked up [...], Jamila dropped her veil, revealing full breasts [...], and her odor of sweat and patchouli came to us."
Harold Nebenzal, *'Cafe Berlin'* [1]

Patchouli, which is said to be the most powerful and fixative of all scents of the flora, is the sensual fragrant allegory for India and the Middle East. With its woody–balsamic odor and well-balanced herbaceous, earthy, camphoraceous and floral facets, it is indispensable for the creation of sensuous oriental fragrances. Together with bergamot oil and oakmoss, and a floral heart of jasmine and rose, it also constitutes a key element of chypre perfumes, and in the prototype of the gourmand family "Angel" (T. Mugler, 1992) by Olivier Cresp and Yves de Chiris, patchouli oil is essential to balance and contrast the sugary accord of chocolate and toffee apple. The main constituent of patchouli oil is (–)-patchoulol, which makes up 35–40% of the oil, and upon standing, especially under arid conditions, often crystallizes out. This was long known by perfumers, who hence termed it *patchouli camphor*. Gal first investigated *patchouli camphor* in 1869,[2] but only 80 years later did Treibs propose[3] patchoulol to be the guaiane sesquiterpene alcohol **1** (Figure 1). Already a few years later, however, Büchi et al.[4] proved Treibs's structure **1** wrong, and proposed structure **2**. This was even proven by a total synthesis[5] starting from homocamphor. Thus, there was considerable astonishment when the X-ray crystal structure[6] of the chromate of (–)-patchoulol (**3**) was not in agreement with structure **2**: A Wagner–Meerwein rearrangement in the course of the peracid oxidation had led to the correct structure of (–)-patchoulol (**3**) without having been noticed in the synthetic work. Thus, (–)-patchoulol (**3**) was first synthesized unintentionally and unnoticed in an attempt to confirm the proposed structure **2**, which turned out to be wrong.

In addition, there was also confusion concerning the olfactory properties of (–)-patchoulol (**3**), which Gadamer[7] had reported in 1903 to be odorless, whereas Treibs and chemists at Schimmel & Co. saw in it the odorous principle of patchouli oil.[3] The controversy continued in 1974, when Teisseire et al.[8] claimed that perfectly pure (–)-patchoulol (**3**) was "*totally odorless*". According to them, the typical odor of patchouli oil was predominantly due to (+)-*nor*-

[a] Givaudan Schweiz AG, Fragrance Research,
Überlandstrasse 138, 8600 Dübendorf, Switzerland
Fax: +41-44-824-29-26
E-mail: philip.kraft@givaudan.com

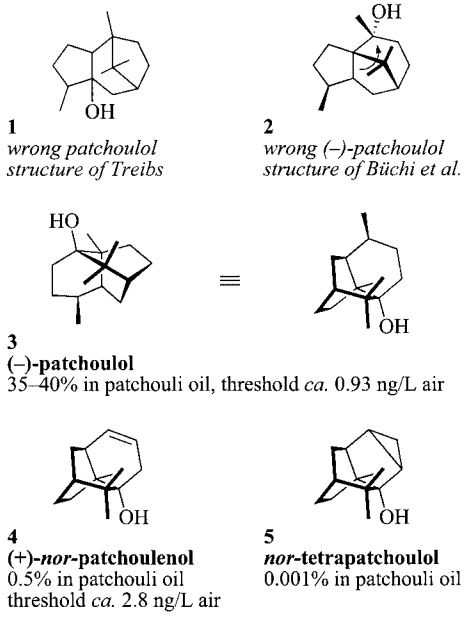
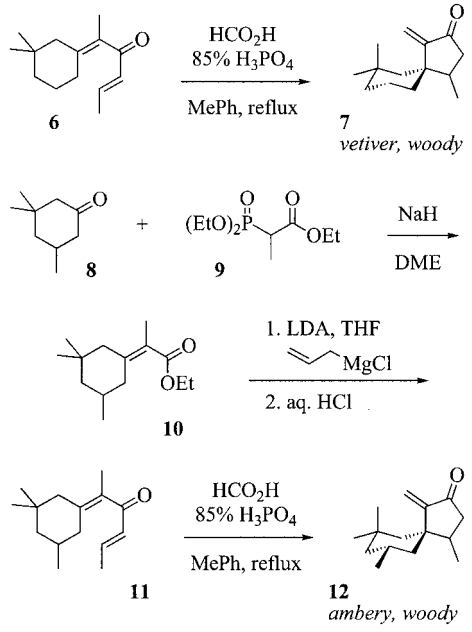


Figure 1. The naturally occurring patchouli odorants (–)-patchoulol (**3**), (+)-*nor*-patchoulenol (**4**), and *nor*-tetrapatchoulol (**5**).

patchoulenol (**4**), with around 0.5% rather a minor constituent that previously had not been reported to occur in nature. This immediately met the opposition of Kastner from Firmenich,[9] who stated that (–)-patchoulol (**3**) was recognized by all their perfumers unanimously as the prime odorant of patchouli oil, exhibiting a "*strong, typical patchouli scent with an earthy, slightly camphoraceous, powdery cellar note*".[10] (+)-*nor*-Patchoulenol (**4**), on the contrary, was seen by them only as a nuanceur, possessing an "*intense rooty, cellar note reminiscent of potatoes*".[9] Though (+)-*nor*-patchoulenol (**4**) was for Mookherjee et al.[11] a typical patchouli odorant, they agreed it to be clearly overshadowed by (–)-patchoulol (**3**) in natural patchouli oil. Even in pure form, (–)-patchoulol (**3**) was found to be stronger than (+)-*nor*-patchoulenol (**4**) in the dry-down.[11] In addition, they reported a new constituent with a *warm, woody, earthy–camphoraceous smell: nor*-Tetrapatchoulol (**5**, Figure 1). With a concentration of only 0.001%, however, it did not contribute much to the overall odor impression of the essential oil, as in the dry-down, **5** was comparable in strength to **3**.[11] The dispute was finally resolved by a stereoselective synthesis of **3**, which proved it to possess a typical patchouli note.[10,12] Nevertheless, we still find assessments like "*the odor of patchouli oil owes little to its major components*" in the recent literature,[13] perhaps because a great number of people possess partial anosmias, or at least very different sensitivities towards patchouli odorants. This complicates the determination of odor thresholds, but tentatively we determined threshold concentrations of about 0.93 ng/L air for **3** and about 2.8 ng/L air for **4**. Overall, compounds **3**–**5** are all patchouli odorants with threshold values in the range of a few nanograms per liter air. Therefore, we were very excited when we discovered a new odorant which possessed a typical patchouli odor profile and an odor threshold of 0.067 ng/L air without much individual variation among panelists − all the more as, despite many attempts, no synthetic patchouli odorant is yet commercially available.[14]

Results and Discussion

In the course of synthetic work on dienones, an intense vetiver odorant of structure **7** was discovered.[15] A direct route was developed by Nazarov cyclization of **6** (Scheme 1), and several new analogs were synthesized to study the structure–odor relationship of these spirocyclic vetiver odorants by superposition with khusimone.[15] In accordance with this superposition analysis, an additional 9-methyl substituent was found to extinguish the *vetiver* character, and **12** was only *ambery–woody*, but not *vetiver-like* in smell. This methylene spiroketone had been synthesized from 3,3,5-trimethylcyclohexanone (**8**) by Wadsworth–Horner–Emmons reaction with triethyl 2-phosphonopropionate (**9**), subsequent Grignard reaction of **10** with allylmagnesium chloride under in situ conversion to the lithium trienolate, and quenching with aqueous hydrochloric acid under isomerization of the terminal double bond. Nazarov cyclization of the resulting dienone **11** with formic and phosphoric acid in refluxing toluene afforded the *ambery–woody* odorant **12**. However, when we prepared additional material of **12**, some batches possessed a patchouli-like twist in the odor character, and by GC–olfactometry this patchouli odor could be attributed to a tiny peak that eluted some few minutes after **12** on a polar column (Stabilwax, 30 m × 0.32 mm ID, ft = 0.25 μm @ 1.4 mL He/min; **12**:

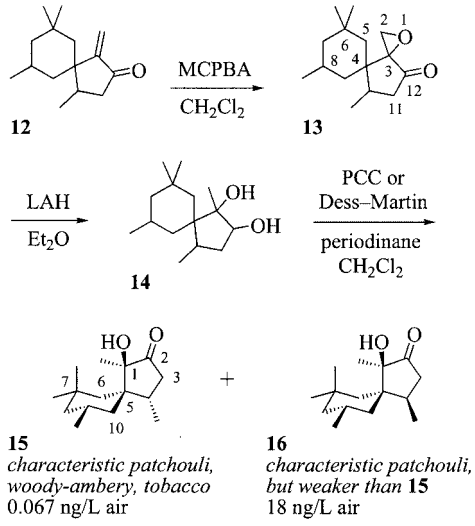


Scheme 1. Our synthetic route to novel spirocyclic vetiver odorants by Nazarov cyclization on the example of 4,7,7,9-tetramethyl-1-methylenespiro[4.5]decan-2-one (**12**) and 4,7,7-trimethyl-1-methylenespiro[4.5]decan-2-one (**7**), the most typical vetiver odorant synthesized.

29.50 min; patchouli-type impurity: 32.20 min). The content of the powerful patchouli-like smelling impurity varied with the conditions of the Nazarov reaction and also the work-up, and in some cases it was not detectable at all. Since it was usually formed in around 0.15–0.9% yield only, some batches were pooled and the powerful compound enriched up to a few percent by classical chromatography. Preparative GC with this enriched material finally afforded a sample of about 100 μg, for which the structure of 1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**15/16**) was proposed on the basis of NMR spectra.

Bifunctional odorants with a proton-donor–proton-acceptor unit are rather uncommon, especially if nonaromatic. The few prominent examples comprise lily-of-the-valley odorants such as hydroxycitronellal and Lyral® [4-(4-hydroxy-4-methylpentyl)cyclohex-3-enecarbaldehyde], the strawberry-like-smelling Furaneol® (2,5-dimethyl-4-hydroxy-2*H*-furan-3-one), and caramel-type flavor materials such as maltol and sotolone (4,5-dimethyl-2(5*H*)-furanone). In the musky, ambery and woody families, no intense bifunctional odorants are known, and that holds all the more true for vetiver and patchouli notes, which are far less common anyway. Therefore, the proposed structure for the new high-impact patchouli odorant was rather unusual, and required proof by a directed synthesis – and it was also desirable to evaluate its olfactory properties.

The synthesis of 1-hydroxy-1,4,7,7,9-pentamethylspiro-[4.5]decan-2-one (**15/16**) started from the methylene spiroketone **12** as outlined in Scheme 2. Epoxidation of the α,β-unsaturated double bond of **12** with *m*-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 furnished the epoxy ketone **13** in 61% yield after purification by flash chromatography (FC). This epoxy ketone **13** was reduced to the corresponding diol **14** by means of lithium aluminum hydride (LAH) in almost quantitative yield as indicated by GC. Without further purification, **14** was then oxidized to the target structure **15/16** employing pyridinium chlorochromate (PCC) on Celite®. Since the oxidative glycol cleavage of **14** was the main reaction, the yield in the ketols **15/16** was poor. Nevertheless, it proved possible to isolate the diastereoisomer **15** with the most powerful odor by simple FC, and thereby to obtain 30 mg of **15** (5%) in the form of colorless crystals that even allowed its structure and relative stereochemistry to be confirmed by X-ray crystallography.



Scheme 2. Synthesis of the new high-impact patchouli odorant (1*R**,4*S**,5*S**,9*R**)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**15**) by epoxidation/LAH reduction and subsequent oxidation of 4,7,7,9-tetramethyl-1-methylenespiro[4.5]decan-2-one (**12**).

The X-ray crystal structure of the (1*R**,4*S**,5*S**,9*R**)-configured spiroketol **15** is depicted in Figure 2 with thermal ellipsoids drawn at the 50% probability level. Remarkable are the short interatomic distances of 3.4 Å between 1-OH and 7-Me_{ax}, and of 3.6 Å between 1-Me and 7-Me_{ax}, which imply considerable steric crowding. Inversion of the cyclohexyl chair, however, would bring both the 9-Me_{ax} and the 7-Me_{ax} substituent into the close proximity of 4-Me, which is energetically even more unfavorable, though only by 0.1 kcal/mol (PM3). In diastereoisomer **16**, the corresponding conformation becomes more distinctly favored, that is, by around 5.4 kcal/mol (PM3). It was isolated in an attempt to optimize the oxidation of **14** by employing Dess–Martin periodinane instead of PCC on Celite® (Scheme 2), but the glycol cleavage of **14** still prevailed vastly. Nevertheless, it was possible to obtain 60 mg (15%) diastereoisomerically pure **16**, the (1*R**,4*R**,5*S**,9*R**)-configuration of which was unambiguously proven by a NOESY experiment. Cross peaks between 1-Me and 4-H established the *like*-relationship of the stereocenters C-1 and C-4, while the cyclohexyl chair conformation was determined to correspond to that delineated in Figure 2 by cross peaks between 1-OH and 7-Me_{ax}, 1-Me and 7-Me_{ax}, as well as 9-H_{ax} and 1-OH. Diastereoisomer **16** also possessed a characteristic patchouli note, but was far weaker than the 1,4-*unlike*-isomer **15**, for which we determined an odor threshold of 0.067 ng/L air, in comparison with 18 ng/L air for **16**. Moreover, the odor character of the 1,4-*unlike*-isomer **15** was preferred over that of the 1,4-*like*-isomer **16**. On a blot-

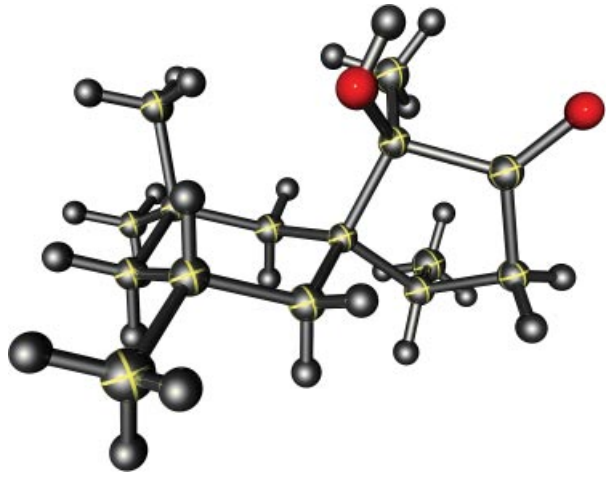


Figure 2. X-ray crystal structure of (1*R**,4*S**,5*S**,9*R**)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**15**) with thermal ellipsoids at the 50% probability level.

ter, **15** was described by perfumers as *strong, powerful, and characteristic of natural patchouli oil, with rich woody–ambery and tobacco-like facets.*

This interesting odor description prompted the synthesis of further derivatives of **15**, which are compiled in Figure 3. To further increase the steric bulk, we first desired to introduce an additional methyl substituent at C-9. A synthesis of 4,7,7,9,9-pentamethyl-1-methylenespiro[4.5]decan-2-one was already at hand,[15] and we thus decided to follow essentially the same route as we had for the synthesis of **15/16**, except for making use of a Swern oxidation in the last step to avoid glycol cleavage. Probably because of steric effects, the epoxidation of 4,7,7,9,9-pentamethyl-1-methylenespiro[4.5]decan-2-one was sluggish but diastereoselective, and **17** (Figure 3) was obtained in a moderate 29% yield. Standard LAH reduction of **17** furnished the diol **18** in 84% yield, and again only one diastereoisomer was isolated, the relative stereochemistry of which was unambiguously established by a NOESY experiment. Swern oxidation of **18** went as expected without glycol cleavage and provided the (1*R**,9*R**)-configured target molecule **19** in 65% yield. Although this was an acceptable chemical yield, the product **19** was difficult to purify for olfactory evaluation. Sulfurous off-notes were formed from trace impurities upon standing, and this observation called for additional chromatographic purification. The odor of **19** was also found to be patchouli-like, with some pronounced woody inflection; yet, with an odor threshold of 51 ng/L air, it turned out to be significantly weaker than even the corresponding 1,4-*like*-isomer **16** of the lead structure.

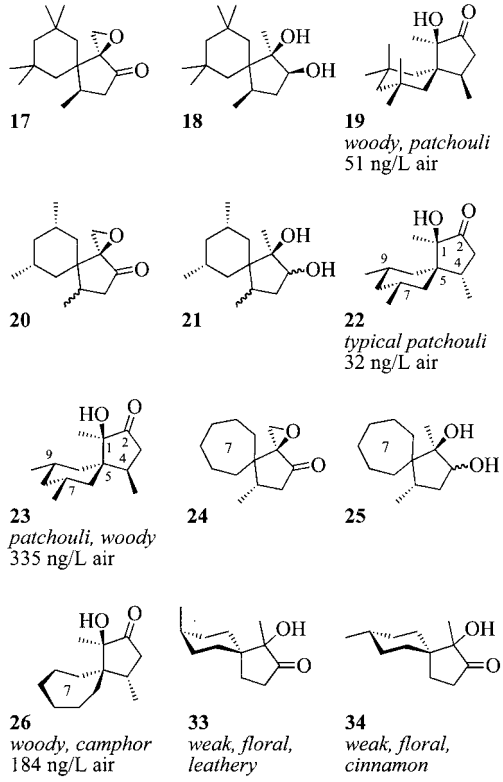


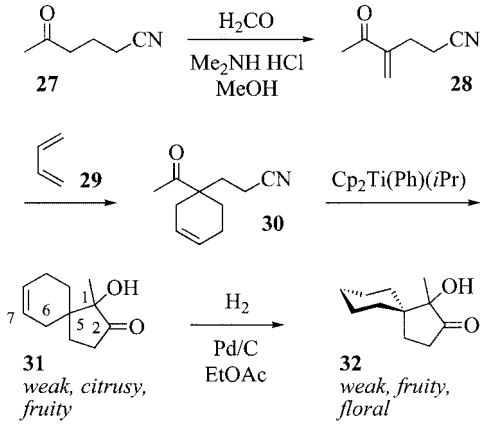
Figure 3. Overview of the structures of the synthesized analogous ketols **19**, **22**, **23**, **26**, **33**, and **34** with the respective intermediates **17**, **18**, **20**, **21**, **24**, and **25**.

Apparently, **19** was already sterically too crowded. So, instead of increasing the steric bulk, we planned to remove the axial 7-methyl group of the lead compound. The conformer with the diequatorially substituted cyclohexyl chair should now energetically be strongly favored over the diaxially configured one (by about 7.2 kcal/mol), thus stabilizing the conformation depicted in Figure 2 for **15**. Again, the starting material (5*r**,7*R**,9*R**)-4,7,9-trimethyl-1-methylenespiro[4.5]decan-2-one was prepared as described in earlier synthetic work on vetiver odorants.[15] Epoxidation with MCPBA in CH_2Cl_2 afforded the isomeric mixture **20**, which was reduced with LAH to the corresponding diol mixture **21** in 88% yield. Standard Swern oxidation of **21** then provided the isomeric spiroketols **22** and **23** (in 84% yield), which were separated by chromatography. Both emanated typical patchouli notes, the 1,4-*like*-isomer **23** possessing again a more woody inflection. As for the lead compounds **15/16**, the 1,4-*unlike*-isomer **22** was preferred for its more pronounced patchouli character and its better odor threshold of 32 ng/L air relative to 335 ng/L air for the 1,4-*like*-isomer **23**. Still the lead structure **15** was by far preferred over **22** in terms of both odor and intensity.

As it had been found in earlier work on vetiver odorants[15] that a cycloheptyl or cyclooctyl ring could replace a methylated cyclohexyl ring without much shift in the odor character, we wanted to see if this was also true for our new patchouli odorants. Consequently, 4-methyl-1-methylenespiro[4,6]undecan-2-one[15] was treated with MCPBA, and the *like*-epoxide **24** which led to the preferred *unlike*-configured spiroketol **26** was isolated by chromatography. Reduction with LAH provided in 76% yield the corresponding diol **25**, which was oxidized to the target compound **26** by employing PCC on Celite® to avoid the sulfurous-smelling impurities of Swern oxidation. However, glycol cleavage competed severely, and only 21 mg (4%) of the *unlike*-spiroketol **26** was isolated, nevertheless a sufficient quantity to establish the relative stereochemistry by a NOESY experiment and to characterize **26** as smelling woody, herbaceous, and reminiscent of camphor with a weak odor threshold of 184 ng/L air. Since only pronounced earthy aspects were missing, **26** could still be considered a patchouli odorant, but apparently the lower molecular boundaries for a patchouli scent in terms of volume and molecular weight had been reached, a fact that was supported by the subsequent findings.

Nevertheless, there was also interest in the parent core structure **32** (Scheme 3) of the high-impact patchouli odorant **15**. As the 2-hydroxy-2-methylcyclopentanone ring of **32** could be formed by a reductive radical cyclization of a cyanoketone, mediated by either Zn–TMSCl–lutidine[16] or $Cp_2Ti(Ph)(iPr)$,[17] a Diels–Alder transformation retrosynthetically revealed 4-methylene-5-oxohexanenitrile (**28**) as a suitable starting material. This was synthesized following the procedure of Szabó et al.[18] by methylenation of 5-oxohexanenitrile (**27**) with formaldehyde in the presence of dimethylamine hydrochloride. Diels–Alder reaction of **28**

with butadiene (**29**) in the presence of $AlCl_3$ and 2-nitropropane furnished the corresponding adduct **30** in 81% yield after chromatographic purification. Reductive radical cyclization of **30** was carried out according to Itoh and coworkers[17] in the presence of $Cp_2Ti(Ph)(iPr)$, for which better yields were reported than for the Zn–TMSCl–lutidine reagent system of Corey and Pyne.[16] For the cyclization of 3-(1′-acetylcyclohex-3′-enyl)propionitrile (**30**) to 1-hydroxy-1-methylspiro[4.5]dec-7-en-2-one (**31**), a disappointingly low 7% yield was obtained. The odor of **31** was described by perfumers as *weak, citrusy and fruity*, devoid of any patchouli-type descriptor. Hydrogenation of **31** in the presence of palladium on charcoal concluded the short sequence and provided the target molecule **32** in 70% yield. Compound **32** was likewise by no means reminiscent of patchouli oil and emanated only a *weak, fruity–floral odor* with a relatively bad odor threshold of 63.5 ng/L air.



Scheme 3. Synthesis of the parent ketol 1-hydroxy-1-methylspiro[4.5]decan-2-one (**32**) by reductive intramolecular cyclization with the titanocene(III) complex $Cp_2Ti(Ph)(iPr)$.

Figure 4 delineates the X-ray crystal structure of 1-hydroxy-1-methylspiro[4.5]decan-2-one (**32**), the parent core structure of the high-impact patchouli odorant **15**. In comparison with the crystal structure of the latter, the cyclohexyl chair of **32** is inverted and folded away from the substituents on C-1 in order to minimize steric interactions. So the importance of the 4-Me group in 'pushing' the cyclohexyl ring up to the C-1 substituents can be seen clearly. This might explain the importance of the 4-Me group for the patchouli character of **15** and its derivatives. The significance of the 4-methyl substitution was also confirmed by the synthesis of the 1-hydroxy-1,8-dimethylspiro[4.5]decan-2-ones **33** and **34** (Figure 3), both of which possessed *weak, floral odors, either with leathery or cinnamon nuances,* but clearly no patchouli-like facets. The Diels–Alder reaction of 4-methylene-5-oxohexanenitrile (**28**) with isoprene went smoothly (84% yield), but again the $Cp_2Ti(Ph)(iPr)$-mediated radical cyclization gave only 7% of the desired product. After hydrogenation, the stereoisomers **33** and **34** were separated by flash chromatography, and discriminated by their deviating ^{13}C-shifts caused by different γ-effects.

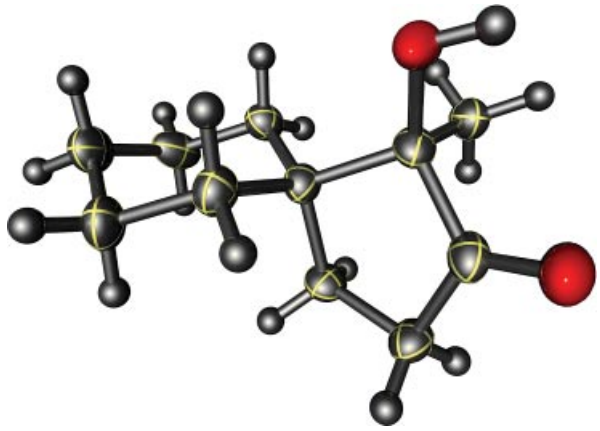
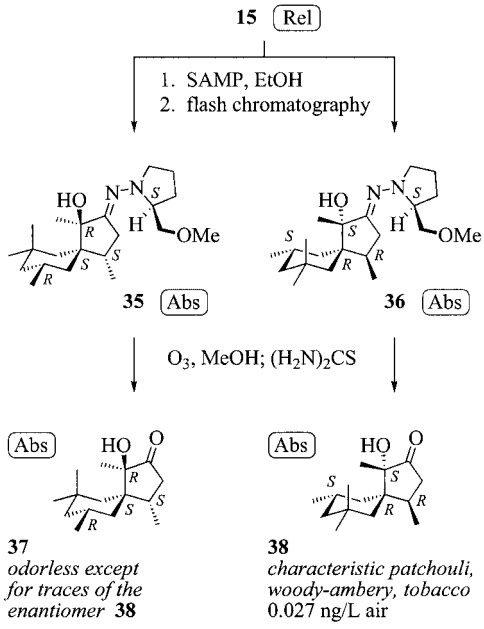


Figure 4. X-ray crystal structure of 1-hydroxy-1-methylspiro[4.5]-decan-2-one (**32**) with thermal ellipsoids at the 50% probability level.

On the basis of these conformational considerations, the original lead compound **15** seemed to possess an ideal substitution pattern, and the excellent odor threshold of 0.067 ng/L air seemed difficult to improve on. By GC–olfactometry of **15** on a chiral phase (Supelco B-DEX110), it however surprisingly looked as if the odor were due to only one enantiomer. To find out which one, we decided to make use of Enders's SAMP-/RAMP-hydrazone methodology,[19] which has also been used occasionally for the separation of racemic ketones or aldehydes by chromatography.[20] The (–)-(*S*)-1-amino-2-methoxymethylpyrrolidine auxiliary was introduced simply by refluxing **15** with SAMP in EtOH. The resulting hydrazones were separable by silica-gel FC, and **35** and **36** (Scheme 4) were isolated in 34% and 39% yield, respectively. An X-ray structure analysis of the



Scheme 4. Separation of the enantiomers of (1*R**,4*S**,5*S**,9*R**)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**15**) via their SAMP hydrazones **35** and **36**.

crystalline hydrazone **36** (Figure 5) established its (1*S*,4*R*,5*R*,9*S*,2′*S*)-configuration, so all that remained to do was cleave the two hydrazones **35** and **36** to the corresponding ketol enantiomers **37** and **38**. This, however, turned out to be more difficult than anticipated, as all the acidic or reductive methods attempted for the cleavage of hydrazones[21] led to decomposition. Fortunately, ozonolysis with reductive work-up employing thiourea went smoothly, and the (–)-(1*R*,4*S*,5*S*,9*R*)-configured **37** as well as the (+)-(1*S*,4*R*,5*R*,9*S*)-configured enantiomer **38** were isolated in 40% and 34% yield, respectively.

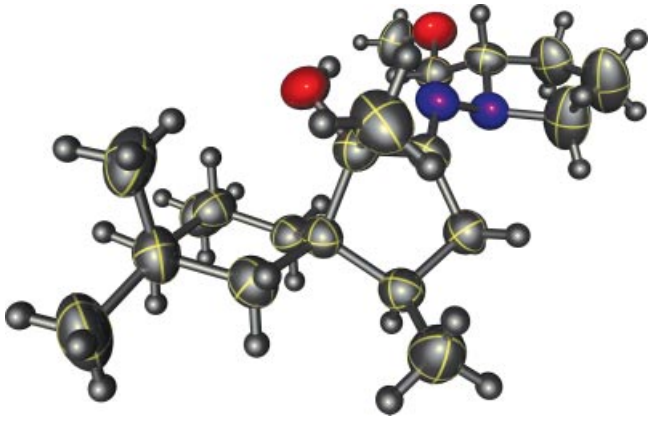


Figure 5. X-ray crystal structure of (+)-(1*S*,4*R*,5*R*,9*S*,2′*S*)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one 1′-amino-2′-methoxymethylpyrrolidine hydrazone (**36**) with thermal ellipsoids at the 50% probability level.

Having the pure enantiomers **37** and **38** at hand, it was indeed proven that only one enantiomer of **15** had an odor. Only the (+)-(1*S*,4*R*,5*R*,9*S*)-configured **38** emanated a strong, powerful, and characteristic patchouli note with rich woody–ambery and tobacco-like facets. And its odor threshold of 0.027 ng/L air was half that of **15**, within experimental error. By GC–olfactometry on the chiral phase, it was proven that the faint odor that **37** had on the blotter was indeed due only to traces of its enantiomer. As it is also known that only the naturally occurring (–)-enantiomer **3** of patchoulol[12] is responsible for the odor of the racemate,[10] it was questioned whether the stereochemistry of **3** and **38** would match. Figure 6 details the overlay of the structures **3** and **38**, and indeed their stereocenters superimpose well. Interestingly however, the 7-Me_2 and 9-Me groups, which were found crucial for the patchouli odor of **38**, lie outside the overlapping areas.

Unfortunately, patchouli oil is a rather inexpensive perfumery raw material, making it difficult to introduce a synthetic patchouli odorant, even if it is very powerful, as are **15** or **38**. The syntheses presented herein are obviously not suited for industrial production, and even on the smaller scale are not yet satisfactory in terms of the number of steps and yields. Nevertheless, the new high-impact spirocyclic patchouli odorant **38** and its racemate **15** are structurally interesting, and together with the presented derivatives provide new insight into the structure–odor correlation of patchouli odorants that indeed seems linked to some extent with that of vetiver materials like **7**.[15]

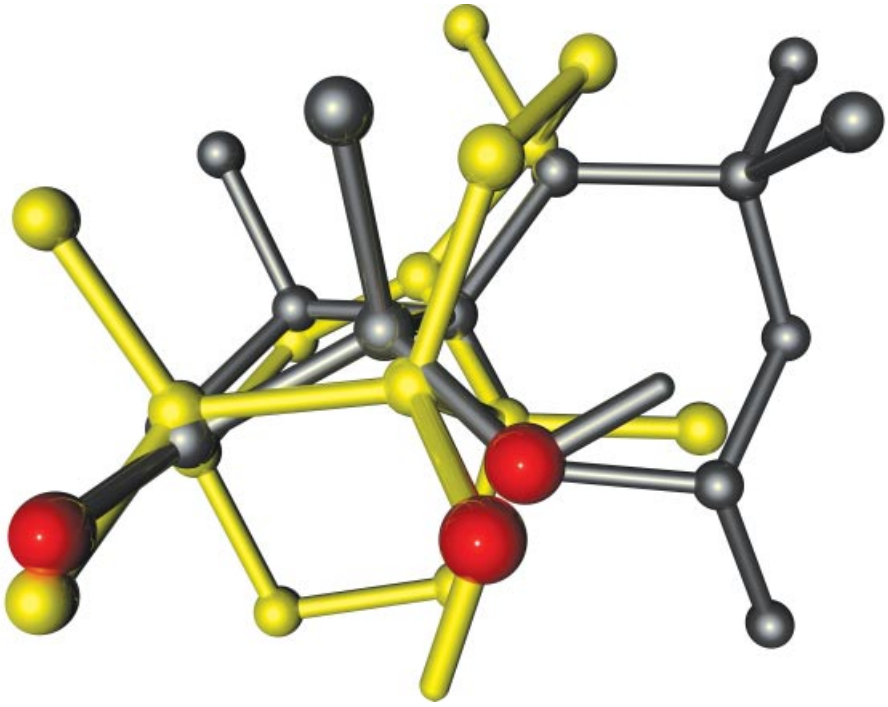


Figure 6. Superposition analysis of (+)-(1*S*,4*R*,5*R*,9*S*)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**38,** silver) and (–)-patchoulol (**3**, gold).

Experimental Section

IR: Bruker VECTOR 22/Harrick SplitPea micro ATR, Si. NMR: Bruker AVANCE DPX-400, Bruker AVANCE 500 (TCI), Bruker AVANCE 600, TMS int. (δ = 0 ppm). MS: Finnigan MAT 95 (EI: 70 eV), HP Chemstation 6890 GC/5973 Mass Sensitive Detector. FC: Merck Kieselgel 60 (40–63 μm). TLC: Merck Kieselgel 60 F_{254} (particle size 5–20 μm, layer thickness 250 μm on glass, 5 cm × 10 cm); visualization reagent: phosphomolybdic acid spray and plunge solution (Fluka 02553). Melting points: Büchi Melting Point B545 (uncorrected). Elemental analyses: Mikroanalytisches Laboratorium Ilse Beetz, D-96301 Kronach, Germany. X-ray: Hoffmann-La Roche, CH-4070 Basel, Switzerland; Stoe IPDS I diffractometer (Image Plate Diffraction System); SHELX-97. Unless otherwise stated, all reactions were performed under N_2 with reagents and solvents *(puriss.* or *purum)* from Fluka, used without further purification.

The odor thresholds were determined by GC–olfactometry: Different dilutions of the sample substance are injected into a gas chromatograph in descending order of concentration until the panelist fails to detect the respective substance at the sniffing port. The panelist smells in blind and presses a button on perceiving an odor. If the recorded time matches the retention time, the sample is further diluted. 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 the different panelists. The chemical purity of the compounds prepared for olfactory evaluation exceeds 99.9% (GC), and the olfactory purity has in addition been validated by the GC-sniffing technique prior to threshold determination.

CCDC-256512 (**15**), CCDC-256513 (**32**) and CCDC-256514 (**36**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

6,6,8,10-Tetramethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (13): At 0 °C, a solution of 4,7,7,9-tetramethyl-1-methylenespiro[4.5]decan-2-one (1.43 g, 6.49 mmol), prepared according to ref.[15] in CH_2Cl_2 (10 mL), was added dropwise within 45 min to a stirred solution of 3-chloroperbenzoic acid (70%, 1.76 g, 7.14 mmol) in CH_2Cl_2 (20 mL). After further stirring at 0 °C for 1 h, the cooling bath was removed, and the reaction mixture was stirred for 3 d, two additional portions of 3-chloroperbenzoic acid (70%, 1.76 g, 7.14 mmol) being added after the first and the second day. The insoluble material was removed by vacuum filtration and washed with CH_2Cl_2. The combined organic solutions were washed with aq. $NaHSO_3$ (20%), half-saturated $NaHCO_3$, and water (50 mL); the aqueous washings were again extracted with CH_2Cl_2 (50 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in a rotary evaporator. The residue was purified by silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.11) to provide the title compound (930 mg, 61%). IR (ATR): $\tilde{\nu}$ = 1753 (s, νC=O), 1457 (m, δH–C–H), 854 (m, δC–O–C, epoxide), 1196 (νC–O–C, epoxide) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.68/0.72 (2t, J = 12.5 Hz, 1 H, 7-H_{ax}), 0.83/0.84 (2d, J = 6.5 Hz, 3 H, 8-Me), 0.94–1.04 (m, 1 H, 9-H_{ax}), 0.91/0.93 (2s, 3 H, 6-Me_{eq}), 0.95/0.96 (2s, 3 H, 6-Me_{ax}), 1.02/1.10 (2d, J = 6.5 Hz, 3 H, 10-Me), 1.16–1.23 (m, 1 H, 5-H_{ax}), 1.31–1.98 (m, 5 H, 5-, 7-, 9-H_{eq}, 8-, 10-H), 1.99/2.07 (dd, J = 18.5, 12.5 Hz, 1 H, 11-H_b), 2.46/2.76 (dd, J = 18.5, 7.0 Hz, 1 H, 11-H_a), 2.63/2.74/2.93/2.96 (4d, J = 6.5 Hz, 2 H, 2-H_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.7/17.2 (2q, 10-Me), 22.9/23.0 (2q, 8-Me_{ax}), 24.4/25.2 (2d, C-8), 26.0/26.1 (2q, 6-Me_{eq}), 31.1/34.9 (2s, C-6), 35.0/35.0 (2q, 6-Me_{ax}), 35.4/40.7 (2t, C-11), 36.7/40.9 (2d, C-10), 41.2/41.6 (2s, C-4), 41.8/42.3/42.5/44.6 (4t, C-5, –9), 48.2/48.7 (2t, C-2), 50.1/50.2 (2t, C-7), 67.1/70.0 (2s, C-3), 213.7/214.9 (2s, C-12) ppm. MS (70 eV): m/z (%) = 236 (2) [M^+], 220 (28) [$M^+ - CH_3$], 205 (73) [$C_{14}H_{21}O^+$], 178 (36) [$M^+ - CH_3 - C_2H_2O$], 163 (24) [$M^+ - C_2H_2O - 2CH_3$], 150 [$C_{11}H_{18}^+$], 135 (68) [$C_{11}H_{18}^+ - CH_3$], 121 (59) [$C_{11}H_{18}^+ - C_2H_5$], 107 (89) [$C_{11}H_{18}^+ - C_3H_7$], 83 (80) [$C_6H_{11}^+$], 55 (88) [$C_4H_7^+$], 41 (100) [$C_3H_5^+$].

(1*R,4*S**,5*S**,9*R**)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (15):** A solution of 6,6,8,10-tetramethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (**13**, 580 mg, 2.45 mmol) in Et_2O (1.5 mL) was added dropwise with stirring at room temp. to a suspension of lithium aluminum hydride (280 mg, 7.36 mmol) in Et_2O (3.0 mL). After stirring at this temp. for 30 min, the reaction was quenched by the careful addition of water (5.0 mL) followed by aq. HCl (5 N, 5.0 mL) at 0 °C. The organic layer was separated, and the aqueous one extracted with Et_2O (2 × 25 mL). The combined organic extracts were washed with water (25 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated in a rotary evaporator under reduced pressure to provide the corresponding crude diol (630 mg). A solution of pyridinium chlorochromate (1.06 g, 4.90 mmol) in CH_2Cl_2 (4.0 mL) was added at room temp. in one dash to a vigorously stirred suspension of Celite® (1.00 g) in CH_2Cl_2 (8.0 mL). Stirring was continued at this temp. for 10 min, prior to the addition of the crude diol (630 mg) dissolved in CH_2Cl_2 (4.0 mL). After stirring for an additional 30 min, the insoluble material was removed by vacuum filtration through a pad of Celite® with thorough washing with CH_2Cl_2. The organic extracts were concentrated under reduced pressure, and the resulting residue was purified by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.46) to afford, as the most intensely smelling fraction, the title compound **15** (30 mg, 5%) in the form of colorless crystals, mp. 73–74 °C. IR (ATR): $\tilde{\nu}$ = 1738 (s, νC=O), 1098 (s, νC–O), 3456 (s, νO–H), 1382 (m, δCH_3) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.31 (dd, J = 12.0, 12.0 Hz, 1 H, 10-H_{ax}), 0.62 (dd, J = 12.0, 12.0 Hz, 1 H, 8-H_{ax}), 0.66 (d, J = 7.5 Hz, 3 H, 4-Me), 0.79 (dt, J = 14.5, 2.5 Hz, 1 H, 6-H_{ax}), 0.81 (d, J = 6.5 Hz, 3 H, 9-Me_{eq}), 0.95 (s, 3 H, 7-Me_{eq}), 1.00 (s, 3 H, 1-Me), 1.22 (s, 3 H, 7-Me_{ax}), 1.35 (m_c, 1 H, 4-H_{ax}), 1.36 (ddt, J = 12.0, 6.0, 2.5 Hz, 1 H, 8-H_{eq}), 1.50 (dt, J = 14.5, 2.5 Hz, 1 H, 6-H_{eq}), 1.57 (ddt, J = 12.0, 6.0, 2.5 Hz, 1 H, 10-H_{eq}), 1.62 (dd, J = 20.0, 3.0 Hz, 1 H, 3-H_{eq}), 2.27 (dd, J = 20.0, 9.5 Hz, 1 H, 3-H_{ax}), 2.34 (m_c, 1 H, 9-H), 2.90 (s, 1 H, O-H) ppm. $^1H,^1H$ NOESY: 1-Me × 4-Me, 1-Me × 6-H_{eq}, 4-Me × 6-H_{ax}, 4-Me × 6-H_{eq}, 7-Me_{ax} × 9-H_{ax}. ^{13}C NMR (C_6D_6): δ = 18.4 (q, 4-Me), 23.6 (q, 9-Me), 24.1 (q, 1-Me), 26.4 (d, C-9), 26.5 (q, 7-Me_{ax}), 31.6 (s, C-7), 35.2 (q, 7-Me_{eq}), 39.6 (t, C-3), 40.6 (d, C-4), 42.0 (t, C-6), 46.0 (s, C-5), 47.8 (t, C-10), 49.2 (t, C-8), 81.3 (s, C-1), 221.2 (s, C-2) ppm. MS (70 eV): m/z (%) = 238 (4) [M^+], 220 (1) [$M^+ - H_2O$], 205 (1) [$M^+ - H_2O - CH_3$], 168 (4) [$C_{11}H_{20}O^+$], 152 (39) [$C_{11}H_{20}^+$], 137 (11) [$C_{11}H_{20}^+ - CH_3$], 123 (25) / 109 (22) / 95 (15) [$C_nH_{(2n-3)}^+$], 83 (100) [$M^+ - C_9H_{15}O_2$], 69 (13) [$C_5H_9^+$], 55 (22) [$C_4H_7^+$], 43 (36) [$C_3H_7^+$]. Crystal data and structure refinement: Empirical formula $C_{15}H_{26}O_2$, molecular mass 238.36, crystal dimensions 0.5 × 0.4 × 0.01 mm, temperature 150 K, wavelength 0.71073 Å, triclinic crystal system, space group $P\bar{1}$, unit cell dimensions a = 9.6129(19) Å, b = 13.368(3) Å, c = 13.402(3) Å, α = 112.17(3)°, β = 104.57(3)°, γ = 103.52(3)°, V = 1436.1(5) $Å^3$, Z = 4, ρ = 1.102 $Mg \cdot m^{-3}$, μ(Mo-K_α) = 0.071 mm^{-1}, F(000) 528, θ range 2.35–26.00°, limiting indices $-11 \le h \le 11$, $-16 \le k \le 16$, $-15 \le l \le 16$, total reflections collected 10964, symmetry-independent reflections 5162, R_{int} = 0.0283, refinement full-matrix least-squares on F^2, data 5162, parameters 319, goodness-of-fit on F^2 0.877, final R indices [$I > 2\sigma(I)$], R_1 = 0.0392, wR_2 = 0.0861, R indices (all data) R_1 = 0.0711, wR_2 = 0.0945, $\Delta\rho$ (max, min) = 0.265, –0.124 e $Å^{-3}$. CCDC

256512. $C_{15}H_{26}O_2$ (238.4): calcd. C 75.58, H 10.99; found C 75.56, H 10.99. Odor: Strong, powerful and characteristic of natural patchouli oil, with rich woody–ambery and tobacco-like facets. Odor threshold: 0.067 ng/L air.

(1*R,4*R**,5*S**,9*R**)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (16):** A solution of Dess–Martin periodinane (780 mg, 1.84 mmol) in CH_2Cl_2 (20 mL) was added in one dash to a stirred solution of 1,4,7,7,9-pentamethylspiro[4.5]decan-1,2-diol (**14**, 400 mg, 1.66 mmol) in CH_2Cl_2 (15 mL). Stirring was continued at room temp. for 6 h prior to quenching by dropwise addition of a solution of $Na_2S_2O_3$ (950 mg, 6.00 mmol) in satd. aq. $NaHCO_3$ (40 mL). After stirring for 30 min, water (50 mL) was added, the organic layer was separated, and the aqueous one extracted with CH_2Cl_2 (50 mL). The combined organic extracts were washed with water (50 mL), dried (Na_2SO_4), vacuum-filtered over a pad of Celite®, and concentrated in a rotary evaporator. The resulting residue (430 mg) was separated by repeated silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.48) to finally provide the weaker, less polar (1*R**,4*R**,5*S**,9*R**)-configured diastereoisomer of 1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one **16** (60 mg, 15%) in pure form as colorless crystals, mp. 72–73 °C. IR (ATR): $\tilde{\nu}$ = 1743 (s, νC=O), 1106/1081 (s, νC–O), 3470 (s, νO–H), 1385 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.64 (t, J = 12.0 Hz, 1 H, 8-H_{ax}), 0.72 (t, J = 12.5 Hz, 1 H, 10-H_{ax}), 0.78 (d, J = 7.0 Hz, 3 H, 9-Me), 0.94 (s, 3 H, 7-Me_{eq}), 1.00 (d, J = 6.5 Hz, 3 H, 4-Me), 1.02 (d, J = 12.5 Hz, 1 H, 10-H_{eq}), 1.14 (s, 3 H, 3 H, 7-Me_{ax}), 1.17 (s, 3 H, 1-Me), 1.20 (d, J = 14.5 Hz, 1 H, 6-H_{ax}), 1.35 (d, J = 12.0 Hz, 1 H, 8-H_{eq}), 1.45 (d, J = 14.5 Hz, 1 H, 6-H_{eq}), 1.82 (dd, J = 16.5, 11.0 Hz, 1 H, 3-H_b), 1.87 (m_c, 1 H, 4 H), 2.16 (m_c, 1 H, 9-H), 2.54 (dd, J = 16.5, 6.5 Hz, 1 H, 3-H_a), 2.84 (s, 1 H, OH) ppm. ^1H,^1H NOESY: 1-Me × 4-H, 1-Me × 7-Me_{ax}, 1-OH × 7-Me_{ax}, 1-OH × 9-H_{ax}, 7-Me_{ax} × 9-H_{ax}. ^{13}C NMR ($CDCl_3$): δ = 14.5 (q, 4-Me), 21.4 (q, 1-Me), 23.3 (q, 9-Me), 25.3 (d, C-9), 26.3 (q, 7-Me_{ax}), 31.2 (s, C-7), 34.8 (q, 7-Me_{eq}), 34.8 (t, C-10), 35.8 (d, C-4), 38.5 (t, C-3), 40.9 (t, C-6), 47.0 (s, C-5), 49.0 (t, C-8), 83.9 (s, C-1), 221.6 (s, C-2) ppm. MS (70 eV): m/z (%) = 238 (7) [M^+], 220 (1) [$M^+ - H_2O$], 205 (1) [$M^+ - H_2O - CH_3$], 168 (2) [$C_{11}H_{20}O^+$], 152 (40) [$C_{11}H_{20}^+$], 137 (12) [$C_{11}H_{20}^+ - CH_3$], 123 (26) / 109 (22) / 95 (15) [$C_nH_{(2n-3)}^+$], 83 (100) [$M^+ - C_9H_{15}O_2$], 67 (12) [$C_5H_7^+$], 55 (24) [$C_4H_7^+$], 43 (37) [$C_3H_7^+$]. Odor: Nice, pleasant and characteristic of natural patchouli oil, but weaker than the (1*R**,4*S**,5*S**,9*R**)-isomer. Odor threshold: 18 ng/L air.

(3*R,10*S**)-6,6,8,8,10-Pentamethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (17):** A solution of 4,7,7,9,9-pentamethyl-1-methylenespiro[4.5]decan-2-one[15] (19.0 g, 81.1 mmol) in CH_2Cl_2 (250 mL) was added dropwise at 0 °C during 2 h to a stirred solution of 3-chloroperbenzoic acid (70%, 40.0 g, 162 mmol) in CH_2Cl_2 (500 mL). The cooling bath was removed after stirring for 2 h at 0 °C, and the stirring was continued for 5 d at room temp., two additional portions of 3-chloroperbenzoic acid (70%, 40.0 g, 162 mmol) being added after the second and fourth day. The reaction mixture was then vacuum filtered through a pad of Celite®, and poured into ice-cold aq. $NaHSO_3$ (20%, 1 L). The precipitate formed was removed by vacuum filtration through Celite® and washed thoroughly with CH_2Cl_2. Water (200 mL) was added to the filtrate and the pH was adjusted to 8 by addition of satd. aq. Na_2CO_3 (ca. 200 mL). The organic layer was separated and washed with water (500 mL), the aqueous layer was extracted with CH_2Cl_2 (500 mL). The combined organic extracts were dried (Na_2SO_4), and the solvent was removed in a rotary evaporator. The resulting residue (18.8 g) was purified by silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.11) to provide **17** (5.89 g, 29%). IR (ATR): $\tilde{\nu}$ = 1751 (s, νC=O), 1367 (s, δCH_3), 852 (m, δC–O–C, epoxide), 1458 (m, δH–C–H) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.60 (d, J = 15.0 Hz, 1 H, 11-H_{ax}), 0.92/0.96 (2s, 6 H, 6-,8-Me_{ax}), 1.00 (d, J = 14.0 Hz, 1 H, 5-H_{ax}), 1.08 (d, J = 7.0 Hz, 3 H, 10-Me), 1.10 (d, J = 14.0 Hz, 1 H, 7-H_{ax}), 1.14/1.17 (2s, 6 H, 6-,8-Me_{eq}), 1.34 (dt, J = 14.0, 1.5 Hz, 1 H, 7-H_{eq}), 1.59 (dt, J = 15.0, 1.5 Hz, 1 H, 11-H_{eq}), 1.69 (dt, J = 14.0, 1.5 Hz, 1 H, 5-H_{eq}), 2.11 (dd, J = 18.5, 2.0, 1 H, 9-H_{ax}), 2.70 (d, J = 5.5 Hz, 1 H, 2-H_b), 2.77 (dd, J = 18.5, 7.0, 1 H, 9-H_{eq}), 2.84 (quint. d, J = 7.0, 2.0 Hz, 1 H, 10-H), 3.00 (d, J = 5.5 Hz, 1 H, 2-H_a) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.8 (q, 10-Me), 29.7 (2q, 6-,8-Me_{eq}), 30.7/31.5 (2s, C-6,-8), 35.3 (d, C-10), 35.7 (2q, 6-,8-Me_{ax}), 36.5 (t, C-11), 42.6 (s, C-4), 43.4/45.1 (2t, C-5,-9), 47.1 (t, C-2), 51.7 (t, C-7), 66.7 (s, C-3), 215.1 (s, C-12) ppm. MS (70 eV): m/z (%) = 250 (2) [M^+], 234 (11) [$M^+ - O$], 219 (100) [$M^+ - O - CH_3$], 208 (6) [$M^+ - C_3H_6$], 205 (7) [$M^+ - O - C_2H_5$], 193 (29) [$M^+ - O - C_3H_5$], 164 (22) [$C_{11}H_{16}O^+$], 149 (52) [$C_{11}H_{16}O^+ - CH_3$], 121 (50) [$C_{11}H_{16}O^+ - C_3H_7$], 91 (54) [$C_7H_7^+$], 79 (50) [$C_6H_7^+$], 55 (48) [$C_4H_7^+$], 41 (60) [$C_3H_5^+$].

(1*R,2*S**,4*R**)-1,4,7,7,9,9-Hexamethylspiro[4.5]decane-1,2-diol (18):** A solution of (3*R**,10*S**)-6,6,8,8,10-pentamethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (**17**, 5.65 g, 22.6 mmol) in Et_2O (10 mL) was added dropwise within 20 min to a stirred suspension of lithium aluminum hydride (1.29 g, 33.8 mmol) in Et_2O (25 mL). The reaction mixture was refluxed for 3 h, and then stirred at room temp. overnight, prior to being quenched at 0 °C by addition of water (20 mL), followed by aq. HCl (5 N, 20 mL). The organic layer was separated, and the aqueous one extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with water (50 mL) and brine (25 mL), dried (Na_2SO_4), and concentrated in a rotary evaporator. The resulting residue was purified by silica-gel FC (pentane/Et_2O, 4:1, R_f = 0.10) to provide **18** (4.82 g, 84%). IR (ATR): $\tilde{\nu}$ = 1098/1075 (s, νC–O), 1366 (m, δCH_3), 3411 (m, νO–H) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.91/0.97 (s, 6 H, 7-,9-Me_{ax}), 0.93 (m_c, 2 H, 6-H_2), 0.94 (s, 3 H, 1-Me), 1.02 (d, 13.0 Hz, 1 H, 8-H_{ax}), 1.03/1.07 (s, 6 H, 7-,9-Me_{ax}), 1.09 (d, J = 15.0 Hz, 1 H, 10-H_{ax}), 1.17 (d, J = 13.0 Hz, 1 H, 8-H_{eq}), 1.19 (ddd, J = 14.0, 6.0, 4.5 Hz, 1 H, 3-H_b), 1.24 (d, J = 7.5 Hz, 3 H, 4-Me), 1.44 (d, J = 6.5 Hz, 1 H, 2-OH), 1.78 (d, J = 15.0 Hz, 1 H, 10-H_{eq}), 1.81 (s, 1 H, 1-OH), 2.11 (m_c, 1 H, 4-H), 2.31 (dt, J = 14.0, 9.0 Hz, 1 H, 3-H_a), 3.59 (dt, J = 9.0, 6.5 Hz, 1 H, 2-H) ppm. ^1H,^1H NOESY: 1-OH × 10-H_{ax}, 1-OH × 4-Me, 4-Me × 10-H_{eq}, 1-Me × 2-H, 2-H × 6-H_{eq}, 1-OH × 3-H_b, 3-H_a × 6-H_{eq}, 6-H_{eq} × 4-H. ^{13}C NMR (C_6D_6): δ = 21.4 (q, 4-Me), 21.7 (q, 1-Me), 30.2/30.6 (2q, 7-,9-Me_{ax}), 36.3/43.5 (2t, C-6,-10), 36.6/37.0 (2q, 7-,9-Me_{eq}), 38.3 (d, C-4), 40.7 (t, C-3), 49.7 (s, C-5), 51.8 (t, C-8), 77.0 (d, C-2), 84.0 (s, C-1) ppm. MS (70 eV): m/z (%) = 254 (32) [M^+], 236 (2) [$M^+ - H_2O$], 221 (8) [$M^+ - H_2O - CH_3$], 203 (11) [$M^+ - 2H_2O - CH_3$], 191 (22) [$C_{14}H_{23}^+$], 166 (46) [$C_{12}H_{22}^+$], 151 (28) [$C_{12}H_{22}^+ - CH_3$], 137 (54) / 123 (39) / 109 (61) [$C_nH_{(2n-3)}^+$], 97 (90) [$C_7H_{13}^+$], 87 (31) [$C_4H_7O_2^+$], 69 (63) [$C_5H_9^+$], 55 (68) [$C_4H_7^+$], 43 (100) [$C_3H_7^+$].

(1*R,4*R**)-1-Hydroxy-1,4,7,7,9,9-hexamethylspiro[4.5]decan-2-one (19):** With rigorous exclusion of moisture, a solution of dimethyl sulfoxide (340 mg, 4.40 mmol) in CH_2Cl_2 (1 mL) was injected with a syringe at –70 °C within 5 min into a stirred oxalyl chloride solution in CH_2Cl_2 (2 M, 1.10 mL, 2.20 mmol) diluted with CH_2Cl_2 (5 mL). After stirring at this temp. for 5 min, (1*R**,2*S**,4*R**)-1,4,7,7,9,9-hexamethylspiro[4.5]decan-1,2-diol (510 mg, 2.00 mmol) dissolved in CH_2Cl_2 (1 mL) was injected during 5 min dropwise with a syringe. Stirring was continued at –70 °C for 30 min, prior to injection of Et_3N (1.01 g, 10.0 mmol). The cooling bath was removed, and the reaction mixture was allowed to warm to room temp., prior to being poured into water (50 mL). The organic layer was separated, and the aqueous one extracted with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed

with water (50 mL), dried (Na_2SO_4), and concentrated in a rotary evaporator. Purification of the resulting residue by two silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.17) furnished **19** (330 mg, 65%). IR (ATR): $\tilde{\nu}$ = 1741 (s, νC=O), 1362/1381 (m, δCH_3), 1066/1164/1128 (s, νC–O), 3468 (s, νO–H) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.96–1.18 (m, 3 H, 8-H_{ax},10-H_2), 0.91/0.99 (2s, 6 H, 7-,9-Me_{eq}), 1.02/1.11 (2s, 6 H, 7-,9-Me_{ax}), 1.07 (d, J = 6.5 Hz, 3 H, 4-Me), 1.21 (s, 3 H, 1-Me), 1.33 (d, J = 13.0 Hz, 1 H, 8-H_{eq}), 1.35 (d, J = 14.5 Hz, 1 H, 6-H_{ax}), 1.55 (d, J = 14.5 Hz, 1 H, 6-H_{eq}), 1.82 (dd, J = 19.5, 10.0 Hz, 1 H, 3-H_b), 2.04 (m_c, 1 H, 4-H), 2.48 (dd, J = 19.5, 9.0 Hz, 1 H, 3-H_a), 2.86 (s, 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.7 (q, 4-Me), 20.3 (q, 1-Me), 29.6/31.1 (2s, C-7,-9), 31.6/32.7/34.1/34.4 (4q, 7-,9-Me_2), 33.6/37.5/38.8 (3t, C-3,-6,-10), 35.8 (d, C-4), 47.6 (s, C-5), 49.2 (t, C-8), 83.9 (s, C-1), 220.6 (s, C-2) ppm. MS (70 eV): m/z (%) = 252 (7) [M^+], 237 (1) [$M^+ - CH_3$], 219 (1) [$M^+ - CH_3 - H_2O$], 191 (3) [$C_{14}H_{23}^+$], 182 (4) [$C_{12}H_{22}O^+$], 166 (66) [$C_{12}H_{22}^+$], 151 (39) [$C_{12}H_{22}^+ - CH_3$], 137 (40) / 123 (23) / 109 (37) [$C_nH_{(2n-3)}^+$], 97 (100) [$C_7H_{13}^+$], 55 (41) [$C_4H_7^+$], 43 (72) [$C_3H_7^+$]. $C_{16}H_{28}O_2$ (252.4): calcd. C 76.14, H 11.18; found C 76.18, H 11.13. Odor: Woody, patchouli. Odor threshold: 51 ng/L air.

6,8,10-Trimethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (20): As described above for the preparation of (3*R**,10*S**)-6,6,8,8,10-pentamethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (**17**), (5*r**,7*R**,9*S**)-4,7,9-trimethyl-1-methylenespiro[4.5]decan-2-one[15] (5.21 g, 25.3 mmol) was treated with 70% 3-chloroperbenzoic acid (2×8.72 g, 2×50.5 mmol) in CH_2Cl_2 (75 mL + 150 mL) at room temp. for 4 d. Work-up with aq. $NaHSO_3$ (20%, 200 mL) and purification by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.22) provided **20** (2.12 g, 38%). IR (ATR): $\tilde{\nu}$ = 1751 (s, νC=O), 1456 (s, δH–C–H), 865 (m, δC–O–C, epoxide), 1367 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.41/0.44 (2 pseudo q, J = 12.5 Hz, 1 H, 11-H_{ax}), 0.83/0.85/0.86/0.87 (4d, J = 9.0, 6 H, 6-,8-Me), 0.90–2.13 (m, 8 H, 6-,8-,9-H_{ax}, 5-,7-H_2, 11-H_{eq}), 1.04/1.09 (2d, J = 7.0 Hz, 3 H, 10-Me), 2.70/2.74 (2dd, J = 18.5, 9.0 Hz, 1 H, 9-H_{eq}), 2.77–2.95 (m, 1 H, 10-H), 2.82/2.82 (2d, J = 6.5 Hz, 1 H, 2-H_b), 2.96/2.97 (2d, J = 6.5 Hz, 1 H, 2-H_a) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.8/16.9 (q, 10-Me), 22.8/22.9/22.9/23.0 (4q, 6-,8-Me), 27.4/27.5/27.6/28.3 (4d, C-6,-8), 35.5/38.6/40.7/41.0/42.2/43.2 (6t, C-5,-9,-11), 43.5/43.7 (2t, C-7), 36.7/38.6 (d, C-10), 40.6/40.8 (2s, C-4), 48.6/49.1 (t, C-2), 66.9/69.7 (2s, C-3), 213.8/214.9 (2s, C-12) ppm. MS (70 eV): m/z (%) = 222 (4) [M^+], 207 (7) [$M^+ - CH_3$], 189 (33) [$M^+ - CH_3 - H_2O$], 165 (38) [$C_{11}H_{17}O^+$], 149 (23) [$C_{11}H_{17}^+$], 136 (39) [$C_{10}H_{16}^+$], 121 (38) [$C_9H_{13}^+$], 107 (71) [$C_8H_{11}^+$], 95 (71) [$C_7H_{11}^+$], 79 (70) [$C_6H_7^+$], 55 (80) [$C_4H_7^+$], 41 (100) [$C_3H_5^+$].

1,4,7,9-Tetramethylspiro[4.5]decan-1,2-diol (21): As described above for the preparation of (1*R**,2*S**,4*R**)-1,4,7,7,9,9-hexamethylspiro-[4.5]decane-1,2-diol (**18**), 6,8,10-trimethyl-1-oxadispiro[2.0.5.3]-dodecan-12-one (**20**, 2.11 g, 9.49 mmol) was reduced with lithium aluminum hydride (530 mg, 14.2 mmol) in refluxing Et_2O (5 mL + 10 mL) for 90 min. Quenching with water (10 mL) and aq. HCl (5 N, 10 mL), usual extraction and purification by silica-gel FC (pentane/Et_2O, 2:1, R_f = 0.20) furnished **21** (1.88 g, 88%). IR (ATR): $\tilde{\nu}$ = 1455 (s, δH–C–H), 1074/1049 (s, νC–O), 1374 (m, δCH_3), 3397 (m, νO–H) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.40/0.40/0.43 (3dd, J = 12.0, 12.0 Hz, 1 H, 10-H_b), 0.62–1.43 (m, 14 H, 3-H_b, 6-,8-H_2, 4-,7-,9-Me), 1.13/1.23/1.33 (3s, 3 H, 1-Me), 1.62–2.23 (m, 6 H, 2-OH, 4-,7-,9-H, 3-,10-H_a), 2.74 (br. s, 1 H, 1-OH), 3.95/3.97/3.60 (3dd, J = 8.0, 6.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR (C_6D_6): δ = 14.5/15.2/15.8 (3q, 4-Me), 21.4/23.1/23.3 (3q, 1-Me), 23.4/23.4/23.5/23.6/25.3/25.4 (6q, 7-,9-Me), 28.2/28.7/28.8/28.9/29.0/29.1 (6d, C-7,-9), 34.9/35.1/38.4/38.6/38.8/39.1 (6t, C-6,-10), 39.2/39.9/40.3 (3d, C-4), 41.3/43.5/43.9/44.1/44.4/65.8 (6t, C-3,-8), 46.7/47.5/49.0 (3s, C-5), 77.4/77.5/79.1 (3d, C-2), 81.3/81.8/84.0 (3s, C-1) ppm. MS (70 eV): m/z (%) = 226 (13) [M^+], 208 (5) [$M^+ - H_2O$], 193 (2) [$M^+ - H_2O - CH_3$], 175 (3) [$M^+ - 2H_2O - CH_3$], 150 (10) [$M^+ - 2H_2O - 2CH_3$], 138 (47) [$C_{10}H_{18}^+$], 109 (100) [$C_8H_{13}^+$], 95 (37) [$C_7H_{11}^+$], 81 (37) [$C_6H_9^+$], 55 (48) [$C_4H_7^+$], 43 (61) [$C_3H_7^+$].

(1*R,4*S**,5*r**,7*R**,9*S**)-1-Hydroxy-1,4,7,9-tetramethylspiro[4.5]decan-2-one (22):** With rigorous exclusion of moisture, a solution of dimethyl sulfoxide (680 mg, 8.80 mmol) in CH_2Cl_2 (2 mL) was injected at –75 °C within 5 min into a stirred oxalyl chloride solution in CH_2Cl_2 (2 M, 2.20 mL, 4.40 mmol) diluted with CH_2Cl_2 (10 mL). After being stirred at this temperature for 5 min, (4*R**,5*r**,7*R**,9*S**)-1,4,7,9-tetramethylspiro[4.5]decan-1,2-diol (**21**, 910 mg, 4.00 mmol) dissolved in CH_2Cl_2 (2 mL) was injected dropwise during 5 min with a syringe. Stirring was continued at –70 °C for 15 min, prior to quenching with Et_3N (2.02 g, 20.0 mmol). The reaction mixture was allowed to warm to room temp. and poured into water (50 mL). The organic layer was separated, and the aqueous one extracted with CH_2Cl_2 (2×50 mL). The combined organic extracts were washed with water (50 mL) and dried (Na_2SO_4). After removal of the solvent in a rotary evaporator, the resulting residue was purified by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.12) to provide **22** (530 mg, 59%). IR (ATR): $\tilde{\nu}$ = 1732 (s, νC=O), 3428 (s, νO–H), 1063/1089 (s, νC–O), 1359 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.46 (pseudo q, J = 12.0 Hz, 1 H, 8-H_{ax}), 0.74 (dq, J = 13.5, 12.5 Hz, 1 H, 6-H_{ax}), 0.83/0.88 (2d, J = 6.5 Hz, 6 H, 7-,9-Me), 0.91 (dd, J = 13.5, 13.5 Hz, 1 H, 10-H_{ax}), 1.05 (d, J = 7.5 Hz, 3 H, 4-Me), 1.29 (s, 3 H, 1-Me), 1.41 (dq, 13.5, 2.0 Hz, 1 H, 10-H_{eq}), 1.67 (m_c, 1 H, 9-H_{ax}), 1.69 (dq, 12.0, 2.0 Hz, 1 H, 8-H_{eq}), 1.82 (dq, J = 11.5, 2.0 Hz, 1 H, 6-H_{eq}), 1.91 (m_c, 1 H, 7-H_{ax}), 1.96 (dd, J = 19.0, 8.0 Hz, 1 H, 3-H_b), 2.09 (ddq, J = 7.5, 7.5, 7.5 Hz, 1 H, 4-H), 2.26 (s, 1 H, O-H), 2.57 (dd, J = 19.0, 9.0 Hz, 1 H, 3-H_a) ppm. ^1H,^1H NOESY: 1-Me×4-Me, 1-Me×10-H_{ax}, 1-Me×10-H_{eq}, 1-Me×9-H_{ax}, 4-H×6-H_{ax}. ^{13}C NMR ($CDCl_3$): δ = 15.8 (q, 4-Me), 22.7 (q, 1-Me), 23.2/23.3 (2q, 7-,9-Me), 28.4 (d, C-9), 29.0 (d, C-7), 35.8 (t, C-10), 37.4 (d, C-4), 40.5 (t, C-3), 41.1 (t, C-6), 43.8 (t, C-8), 46.7 (s, C-5), 81.2 (s, C-1), 219.6 (s, C-2) ppm. MS (70 eV): m/z (%) = 224 (14) [M^+], 206 (3) [$M^+ - H_2O$], 191 (2) [$M^+ - H_2O - CH_3$], 154 (12) [$C_{10}H_{18}O^+$], 138 (60) [$C_{10}H_{18}^+$], 123 (19) / 109 (100) / 95 (27) [$C_nH_{(2n-3)}^+$], 81 (29) [$C_6H_9^+$], 69 (21) [$C_5H_9^+$], 55 (29) [$C_4H_7^+$], 43 (51) [$C_3H_7^+$]. Odor: Typical patchouli odor. Odor threshold: 32 ng/L air.

(1*R,4*R**,5*r**,7*R**,9*S**)-1-Hydroxy-1,4,7,9-tetramethylspiro[4.5]decan-2-one (23):** In addition to (1*R**,4*S**,5*r**,7*R**,9*S**)-1-hydroxy-1,4,7,9-tetramethylspiro[4.5]decan-2-one (**22**), the silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.27) also furnished **23** (220 mg, 25%). IR (ATR): $\tilde{\nu}$ = 1744 (s, νC=O), 1095/1119 (m, νC–O), 1371 (m, δCH_3), 3487 (m, νO–H) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.41 (pseudo q, J = 12.0 Hz, 1 H, 8-H_{ax}), 0.79/0.88 (2d, J = 6.5 Hz, 6 H, 7-,9-Me), 0.81 (dd, J = 13.5, 13.5 Hz, 1 H, 6-H_{ax}), 0.98 (dd, J = 13.5, 13.5 Hz, 1 H, 10-H_{ax}), 1.01 (d, J = 7.0 Hz, 3 H, 4-Me), 1.08 (dq, J = 15.5, 2.0 Hz, 1 H, 6-H_{eq}), 1.17 (s, 3 H, 1-Me), 1.55 (dq, J = 13.5, 2.0 Hz, 1 H, 10-H_{eq}), 1.68 (dq, J = 12.0, 2.0 Hz, 1 H, 8-H_{eq}), 1.77 (m_c, 1 H, 9-H_{ax}), 1.85 (dd, J = 19.0, 11.0 Hz, 1 H, 3-H_b), 1.93 (m_c, 1 H, 4-H), 2.23 (m_c, 1 H, 7-H_{ax}), 2.53 (dd, J = 19.0, 8.5 Hz, 1 H, 3-H_a), 2.76 (s, 1 H, 1 O-H) ppm. ^1H,^1H NOESY: 4-Me×3-H, 1-Me×4-Me, 1-Me×6-H_{eq}, 4-Me×10-H_{ax}. ^{13}C NMR ($CDCl_3$): δ = 14.3 (q, 4-Me), 21.3 (q, 1-Me), 22.9/23.4 (2q, 7-,9-Me), 28.0 (d, C-9), 28.5 (d, C-7), 34.8 (t, C-6), 35.3 (d, C-4), 38.7 (t, C-10), 38.9 (t, C-3), 44.1 (t, C-8), 47.1 (s, C-5), 84.5 (s, C-1), 221.1 (s, C-2) ppm. MS (70 eV): m/z (%) = 224 (15) [M^+], 206 (2) [$M^+ - H_2O$], 191 (1) [$M^+ - H_2O - CH_3$], 154 (10) [$C_{10}H_{18}O^+$], 138 (60) [$C_{10}H_{18}^+$], 123 (19) / 109 (100) / 95 (26) [$C_nH_{(2n-3)}^+$], 81 (29) [$C_6H_9^+$], 67 (22) [$C_5H_7^+$], 55 (28) [$C_4H_7^+$], 43 (53) [$C_3H_7^+$]. Odor: Patchouli-like, woody odor. Odor threshold: 335 ng/L air.

(3*R,11*R**)-11-Methyl-1-oxadispiro[2.0.6.3]tridecan-13-one (24):** As described above for the preparation of (3*R**,10*S**)-6,6,8,8,10-pentamethyl-1-oxadispiro[2.0.5.3]dodecan-12-one (**17**), 4-methyl-1-methylenespiro[4.6]undecan-2-one[15] (5.29 g, 27.5 mmol) was treated with 3-chloroperbenzoic acid (70%, 13.6 g, 55.0 mmol) in CH_2Cl_2 (75 mL + 150 mL) at room temp. for 4 d, three additional portions of 3-chloroperbenzoic acid (70%, 7.00 g, 28.4 mmol) being added after every day. Work-up with aq. $NaHSO_3$ (20%, 250 mL) and purification by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.19) provided **24** (1.01 g, 18%), in addition to the (3*R**,11*S**)-diastereomer (R_f = 0.14, 820 mg, 14%). IR (ATR): $\tilde{\nu}$ = 1749 (s, νC=O), 1460 (s, δH–C–H), 830 (m, δC–O–C, epoxide), 1381 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.05 (d, J = 7.0 Hz, 3 H, 11-Me), 1.35–1.66 (m, 12 H, 5-H_2–10-H_2), 1.99 (dd, J = 19.0, 3.0 Hz, 1 H, 12-H_b), 2.37 (dqd, J = 7.5, 7.0, 3.0 Hz, 1 H, 11-H), 2.63 (dd, J = 19.0, 7.5 Hz, 1 H, 12-H_a), 2.93 (d, J = 6.5 Hz, 1 H, 2-H_b), 2.98 (d, J = 6.5 Hz, 1 H, 2-H_a) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.5 (q, 11-Me), 22.7/23.0 (2t, C-6,-9), 30.1/30.6/31.2/35.8 (4t, C-5,-7,-8,-10), 35.5 (d, C-11), 43.1 (s, C-4), 51.6 (t, C-2), 67.5 (s, C-3), 215.3 (s, C-13) ppm. MS (70 eV): *m*/*z* (%) = 208 (2) [M^+], 192 (10) [$C_{13}H_{20}O^+$], 177 (9) [$C_{13}H_{20}O^+ - CH_3$], 164 (17) [$C_{13}H_{20}O^+ - CO$], 150 (24) [$C_{11}H_{18}^+$], 135 (17) [$C_{11}H_{18}^+ - CH_3$], 122 (51) [$C_{11}H_{18}^+ - C_2H_4$], 107 (46) [$C_8H_{11}^+$], 93 (65) [$C_7H_9^+$], 79 (100) [$C_6H_7^+$], 67 (41) [$C_5H_7^+$], 41 (50) [$C_3H_5^+$].

(1*R,2*R**,4*S**)-/(1*R**,2*S**,4*S**)-1,4-Dimethylspiro[4.6]undecane-1,2-diol (25):** As described above for the preparation of (1*R**,2*S**,4*R**)-1,4,7,7,9,9-hexamethylspiro[4.5]decane-1,2-diol (**18**), (3*R**,11*S**)-11-methyl-1-oxadispiro[2.0.6.3]tridecan-13-one (**24**, 800 mg, 3.84 mmol) was reduced with lithium aluminum hydride (440 mg, 11.5 mmol) in Et_2O (2 mL + 4 mL) at ambient temp. for 16 h. Quenching with water (5 mL) and aq. HCl (5 N, 5 mL), usual extraction and purification by silica-gel FC (pentane/Et_2O, 2:1, R_f = 0.16) furnished **25** (620 mg, 76%). IR (ATR): $\tilde{\nu}$ = 1076/1049 (s, νC–O), 1455/1474/1444 (s, δH–C–H), 1377 (m, δCH_3), 3388 (m, νO–H) cm^{-1}. ^1H NMR (C_6D_6): δ = 0.84/0.91 (2d, J = 7.0 Hz, 3 H, 4-Me), 1.06/1.09 (2s, 3 H, 1-Me), 1.07–2.15 (m, 16 H, 1-,2-OH, 3-H_2, 6-H_2–11-H_2), 1.94/2.29 (2m_c, 1 H, 4-H), 3.58 (dt, J = 10.0, 5.0 Hz)/3.60 (t, J = 7.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR (C_6D_6): δ = 15.7/16.3 (2q, 4-Me), 20.1/21.2 (2q, 1-Me), 24.8/25.0/25.1/25.2 (4t, C-7,-10), 29.1/30.0/32.5/32.8/32.9/33.0/33.2/35.7 (8t, C-6,-8,-9,-11), 39.5/40.5 (2t, C-3), 41.0/41.3 (2d, C-4), 50.0/51.4 (2s, C-5), 75.9/79.8 (2d, C-2), 82.9/84.9 (2s, C-1) ppm. MS (70 eV): *m*/*z* (%) = 212 (12) [M^+], 194 (4) [$M^+ - H_2O$], 192 (2) [$M^+ - H_2O - H_2$], 179 (4) [$M^+ - H_2O - CH_3$], 167 (5) [$M^+ - C_2H_5O$], 149 (22) [$C_{11}H_{17}^+$], 136 (17) [$C_{10}H_{16}^+$], 124 (92) [$C_9H_{16}^+$], 109 (20) [$C_9H_{16}^+ - CH_3$], 107 (28) [$C_{10}H_{16}^+ - C_2H_5$], 95 (100) [$C_7H_{11}^+$], 87 (36) [$C_4H_7O_2^+$], 81 (96) [$C_6H_9^+$], 74 (49) [$C_3H_6O_2^+$], 67 (79) [$C_5H_7^+$], 55 (92) [$C_4H_7^+$], 43 (100) [$C_3H_7^+$].

(1*R,4*S**)-1-Hydroxy-1,4-dimethylspiro[4.6]undecan-2-one (26):** As described above for the preparation of (1*R**,4*S**,5*S**,9*R**)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (**15**), (1*R**,2*R**,4*S**)-/(1*R**,2*S**,4*S**)-1,4-dimethylspiro[4.6]undecane-1,2-diol (**25**, 570 mg, 2.69 mmol) was oxidized with pyridinium chlorochromate (630 mg, 2.95 mmol) on Celite® (630 mg) in CH_2Cl_2 (10 + 12 mL) at room temp. for 12 h. Standard work-up by vacuum filtration through a pad of Celite® furnished after purification by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.10) **26** (21 mg, 4%). IR (ATR): $\tilde{\nu}$ = 1733 (s, νC=O), 1100/1059 (s, νC–O), 3429 (s, νO–H), 1382 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.14 (d, J = 7.0 Hz, 3 H, 4-Me), 1.24 (s, 3 H, 1-Me), 1.26–1.65 (m, 12 H, 6-H_2–11-H_2), 1.93 (dd, J = 19.5, 8.0 Hz, 1 H, 3-H_b), 2.08 (s, 1 H, O-H), 2.32 (ddq, J = 9.5, 8.0, 7.0 Hz, 1 H, 4-H), 2.54 (dd, J = 19.5, 9.5 Hz, 1 H, 3-H_a) ppm. ^1H,^1H NOESY: 1-Me × 4-Me, 3-H_b × 4-Me, 1-Me × 3-H_b. ^{13}C NMR ($CDCl_3$): δ = 16.9 (q, 4-Me), 20.5 (q, 1-Me), 23.9/24.3 (2t, C-7,-10), 29.0/31.8/31.9/35.2 (4t, C-6,-8,-9,-11), 37.0 (d, C-4), 40.7 (t, C-3), 48.6 (s, C-5), 82.3 (s, C-1), 219.1 (s, C-2) ppm. MS (70 eV): *m*/*z* (%) = 210 (16) [M^+], 192 (3) [$M^+ - H_2O$], 177 (3) [$M^+ - H_2O - CH_3$], 124 (99) [$C_9H_{16}^+$], 109 (13) [$C_8H_{13}^+$], 95 (100) [$C_7H_{11}^+$], 81 (66) [$C_6H_9^+$], 67 (55) [$C_5H_7^+$], 55 (45) [$C_4H_7^+$], 43 (77) [$C_3H_7^+$]. Odor: Woody, herbaceous, camphoraceous. Odor threshold: 184 ng/L air.

3-(1′-Acetylcyclohex-3′-enyl)propionitrile (30): At 0 °C, 2-nitropropane (920 mg, 10.3 mmol) was added to a stirred suspension of $AlCl_3$ (1.38 g, 10.3 mmol) in CH_2Cl_2 (10 mL). Next, a solution of 4-methylene-5-oxohexanenitrile[18] (**28**, 12.8 g, 104 mmol) in CH_2Cl_2 (10 mL) was added dropwise at this temp., and after stirring for 5 min butadiene (**29**, 11.3 g, 209 mmol) was introduced. The cooling bath was removed, and stirring was continued at room temp. for 16 h prior to pouring the reaction mixture into water (500 mL). The organic layer was separated, and the aqueous one extracted with Et_2O (2 × 500 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in a rotary evaporator. Kugelrohr distillation at 150 °C/0.1 mbar provided **30** (14.9 g, 81%) as a colorless oil. IR (ATR): $\tilde{\nu}$ = 1698 (s, νC=O), 653 (s, νH–C=C–H oop), 1362 (m, δCH_3), 1439 (m, δH–C–H), 2247 (m, νCN) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.65 (dt, J = 13.0, 6.5 Hz, 1 H, 6′-H_{ax}), 1.89–2.07 (m, 6 H, 3-H_2, 2′-H_{ax}, 5′-H_2, 6′-H_{eq}), 2.18 (s, 3 H, 2′′-H_3), 2.20–2.24 (m, 2 H, 2-H_2), 2.46 (d, J = 17.0 Hz, 1 H, 2′-H_{eq}), 5.67 (pseudo t, J = 12.5 Hz, 2 H, 3′-,4′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 12.4 (t, C-2), 22.2 (t, C-5′), 25.2 (q, C-2′′), 28.3 (t, C-3), 31.6/31.7 (2t, C-2′,-6′), 49.3 (s, C-1′), 119.5 (s, C-1), 124.0/126.6 (2d, C-3′,-4′), 211.5 (s, C-1′′) ppm. MS (70 eV): *m*/*z* (%) = 177 (1) [M^+], 176 (2) [$M^+ - H$], 162 (2) [$M^+ - CH_3$], 148 (2) [$M^+ - C_2H_5$], 134 (57) [$M^+ - C_3H_7$], 123 (15) [$C_7H_9ON^+$], 93 (35) [$C_7H_9^+$], 77 (15) [$C_6H_5^+$], 54 (10) [$C_4H_6^+$], 43 (100) [$C_3H_7^+$].

1-Hydroxy-1-methylspiro[4.5]dec-7-en-2-one (31): At ambient temp., a solution of *i*PrMgCl (17.0 g, 165 mmol) in Et_2O (330 mL) was added dropwise to a stirred solution of Cp_2TiCl_2 (37.3 g, 150 mmol) in MePh (300 mL). The reaction mixture was stirred for 30 min at this temp., and a solution of PhMgBr (30.0 g, 165 mmol) in Et_2O (300 mL) was then added within 5 min to the resulting green solution. After the mixture was stirred at room temp. for further 30 min, **30** (8.85 g, 49.9 mmol) was added with stirring to the dark-green Cp_2TiPh solution obtained. Stirring was continued at room temp. for 16 h prior to quenching by addition of aq. HCl (2 N, 500 mL). The resulting precipitate was filtered off, and the organic layer of the filtrate separated. The aqueous layer of the filtrate was extracted with Et_2O (1 L), and the combined organic extracts were washed with brine (500 mL), dried (Na_2SO_4), and concentrated in vacuo. Silica-gel FC (pentane/Et_2O, 5:1, R_f = 0.33) of the resulting residue provided **31** (600 mg, 7%). IR (ATR): $\tilde{\nu}$ = 1739 (s, νC=O), 1154/1031 (s, νC–O), 3441 (s, νO–H), 1369 (m, δCH_3) cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.15–2.43 (m, 11 H, 3-,4-,6-,9-,10-H_2, OH), 1.18 (s, 3 H, 1-Me), 5.61–5.68 (m, 2 H, 7-,8-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.1/19.2 (2q, 1-Me), 22.3/22.4 (2t, C-4), 24.1/25.7/26.5/26.6 (4t, C-9,-10), 29.1/30.6/30.9/31.5 (4t, C-3,-6), 42.2/42.6 (2s, C-5), 81.6/81.7 (2s, C-1), 124.8/125.0/126.2/126.3 (4d, C-7,-8), 220.5/220.7 (2s, C-2) ppm. MS (70 eV): *m*/*z* (%) = 180 (7) [M^+], 162 (6) [$M^+ - H_2O$], 152 (3) [$M^+ - CO$], 147 (4) [$M^+ - H_2O - CH_3$], 144 (6) [$M^+ - 2H_2O$], 134 (9) [$C_{10}H_{14}^+$], 124 (52) [$C_9H_{16}^+$], 94 (52) [$C_7H_{10}^+$], 79 (100) [$C_6H_7^+$], 43 (76) [$C_3H_7^+$]. $C_{11}H_{16}O_2$ (180.3): calcd. C 73.30, H 8.95; found C 73.30, H 8.94. Odor: Weak, citrusy, fruity.

1-Hydroxy-1-methylspiro[4.5]decan-2-one (32): A suspension of **31** (85 mg, 0.47 mmol) and Pd/C (10%, 25 mg, 0.024 mmol) in EtOAc

(1 mL) was evacuated and flushed with N_2 three times. After evacuating and flushing with H_2 three times, the reaction mixture was stirred under H_2 for 3 d. The catalyst was removed by vacuum filtration through a small pad of silica gel, washed with EtOAc (3 × 5 mL), and the combined organic filtrates were concentrated under reduced pressure. The resulting amorphous residue was crystallized from pentane to afford **32** (60 mg, 70%) as colorless crystals with only very faint odor. IR (ATR): $\tilde{\nu}$ = 1739 (s, νC=O), 3455 (s, νO–H), 1127/1140 (s, νC–O), 1369 (m, δCH_3) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 1.14 (s, 3 H, 1-Me), 1.15–1.68 (m, 11 H, 6-H_2–10-H_2, OH), 2.13–2.36 (m, 4 H, 3-,4-H_2) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.4 (q, 1-Me), 21.9/22.1 (2t, C-4,-9), 25.5/26.0 (2t, C-7,-10), 28.0 (t, C-8), 30.6/31.2 (2t, C-3,-6), 44.0 (s, C-5), 81.7 (s, C-1), 220.8 (s, C-2) ppm. MS (70 eV): *m*/*z* (%) = 182 (37) [M$^+$], 164 (3) [M$^+$ – H_2O], 154 (11) [M$^+$ – CO], 139 (5) [M$^+$ – CO – CH_3], 136 (7) [M$^+$ – CO – H_2O], 126 (46) [$C_7H_{10}O_2^+$], 121 (19) [M$^+$ – CO – CH_3 – H_2O], 111 (26) [$C_7H_{10}O_2^+$ – CH_3], 96 (89) [$C_7H_{12}^+$], 87 (41) [$C_4H_7O_2^+$], 81 (100) [$C_6H_9^+$], 43 (92) [$C_3H_7^+$]. Crystal data and structure refinement: Empirical formula $C_{11}H_{18}O_2$, molecular mass 182.25, crystal dimensions 0.8 × 0.2 × 0.03 mm, temperature 150 K, wavelength 0.71073 Å, triclinic crystal system, space group $P\bar{1}$, unit cell dimensions a = 6.3264(13) Å, b = 10.814(2) Å, c = 15.773(3) Å, α = 107.04(3)°, β = 91.40(3)°, γ = 90.78(3)°, V = 1031.2(4) Å^3, Z = 4, ρ = 1.174 Mg·m^{-3}, μ(Mo-K_α) = 0.079 mm^{-1}, F(000) 400, θ range 1.97–24.12°, limiting indices $-7 \le h \le 7$, $-12 \le k \le 12$, $-18 \le l \le 18$, total reflections collected 11034, symmetry-independent reflections 3086, refinement full-matrix least-squares on F^2, data 3086, parameters 235, goodness-of-fit on F^2 1.048, final R indices [$I > 2\sigma(I)$], R_1 = 0.0796, wR_2 = 0.2319, R indices (all data) R_1 = 0.1122, wR_2 = 0.2522, $\Delta\rho$(max, min) = 0.538, –0.264 e·Å^{-3}. CCDC 256513. $C_{11}H_{18}O_2$ (182.3): calcd. C 72.49, H 9.95; found C 72.44, H 9.96. Odor: Weak, fruity, floral. Odor threshold: 63.5 ng/L air.

1-Hydroxy-1,8-dimethylspiro[4.5]decan-2-one (33/34): To a stirred suspension of $AlCl_3$ (700 mg, 5.25 mmol) in 2-nitropropane (450 mg, 5.05 mmol) and CH_2Cl_2 (10 mL) was added at 0 °C a solution of 4-methylene-5-oxohexanenitrile[18] (**28**, 6.16 g, 50.0 mmol) in CH_2Cl_2 (10 mL). Isoprene (6.80 g, 99.8 mmol) was then added dropwise at this temp. within 20 min, and stirring was continued at 0 °C for 1 h prior to removal of the cooling bath. After being stirred further at room temp. for 1 h, the reaction mixture was poured into water (300 mL). The organic layer was separated, and the aqueous one extracted with Et_2O (2 × 250 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in a rotary evaporator. The resulting residue was purified by silica-gel FC (pentane/Et_2O, 1:1) to furnish 3-(1′-acetyl-4′-methylcyclohex-3′-enyl)propionitrile (8.00 g, 84%). At room temp., a solution of *i*PrMgCl (14.3 g, 139 mmol) in Et_2O (250 mL) was added dropwise with stirring to a solution of Cp_2TiCl_2 (31.3 g, 126 mmol) in MePh (400 mL). After stirring for 30 min, a solution of PhMgBr (25.2, 139 mmol) in Et_2O (220 mL) was added within 5 min, and stirring was continued for 1 h. Next, a solution of the prepared 3-(1′-acetyl-4′-methylcyclohex-3′-enyl)propionitrile (8.00 g, 42.0 mmol) in MePh (400 mL) was added during a period of 1 h dropwise with stirring, which was continued at room temp. for a further 16 h. After quenching by addition of aq. HCl (2 N, 500 mL), the organic layer was separated, and the aqueous one extracted with Et_2O (2 × 500 mL). The combined organic extracts were washed with brine (500 mL), dried (Na_2SO_4), and concentrated in a rotary evaporator. Silica-gel FC (pentane/Et_2O, 5:1) of the resulting residue provided 1-hydroxy-1,8-dimethylspiro[4.5]dec-7-en-2-one (600 mg, 7%). A suspension of Pd/C (10%, 30 mg, 0.029 mmol) and 1-hydroxy-1,8-dimethylspiro[4.5]dec-7-en-2-one (300 mg, 1.54 mmol) in EtOAc (3 mL) was evacuated and flushed with N_2 three times, and then evacuated and flushed with H_2 three times. After being stirred for 1 d at ambient temp. under a positive pressure of H_2, the catalyst was removed by vacuum filtration through a small pad of Celite®, and rinsed with EtOAc (3 × 5 mL). The organic filtrates were combined, the solvent was evaporated in a rotary evaporator, and the resulting residue purified by silica-gel FC (pentane/Et_2O, 100:1) to provide the two stereoisomers **33** (100 mg, 33%) and **34** (100 mg, 33%) in pure form.

***pseudo*-(5*s*,8*s*)-1-Hydroxy-1,8-dimethylspiro[4.5]decan-2-one (33):** IR (ATR): $\tilde{\nu}$ = 1742 (s, νC=O), 1093/1122/1055 (s, νC–O), 3476 (m, νO–H), 1366 (m, δCH_3) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, J = 7.0 Hz, 3 H, 8-Me), 1.15 (s, 3 H, 1-Me), 1.26–1.83 (m, 10 H, 6-,7-,9-,10-H_2, 4-H_b, 8-H), 2.23–2.34 (m, 4 H, 3-H_2, 4-H_a, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.0/20.5 (2q, 1-Me, 8-Me_{ax}), 29.4/29.7/30.1/30.2/30.2/30.6 (6t, C-3,-4,-6,-7,-9,-10), 29.9 (d, C-8), 43.3 (s, C-5), 82.7 (s, C-1), 221.6 (s, C-2) ppm. MS (70 eV): *m*/*z* (%) = 196 (37) [M$^+$], 178 (2) [M$^+$ – H_2O], 168 (6) [M$^+$ – CO], 150 (6) [M$^+$ – CO – H_2O], 140 (46) [$C_8H_{12}O_2^+$], 135 (14) [M$^+$ – CO – CH_3 – H_2O], 110 (48) [$C_8H_{14}^+$], 95 (85) [$C_7H_{11}^+$], 87 (37) [$C_4H_7O_2^+$], 81 (55) [$C_6H_9^+$], 74 (3) [$C_3H_6O_2^+$], 55 (54) [$C_4H_7^+$], 43 (100) [$C_3H_7^+$]. Odor: Weak, floral, leathery.

***pseudo*-(5*r*,8*r*)-1-Hydroxy-1,8-dimethylspiro[4.5]decan-2-one (34):** IR (ATR): $\tilde{\nu}$ = 1741 (s, νC=O), 971/1077/1123 (s, νC–O), 3469 (s, νO–H), 1367 (m, δCH_3) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.90 (d, J = 6.5 Hz, 3 H, 8-Me), 1.00–1.07 (m, 3 H, 6-,9-,10-H_{ax}), 1.15 (s, 3 H, 1-Me), 1.32 (m_c, 1 H, 8-H_{ax}), 1.48–1.61 (m, 6 H, 4-H_b, 7-H_2, 6-,9-,10-H_{eq}), 2.12–2.38 (m, 4 H, 3-H_2, 4-H_a, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.3 (q, 1-Me), 22.5 (q, 8-Me_{eq}), 25.1 (t, C-4), 27.6 (t, C-9), 30.5/30.7 (2t, C-6,-10), 30.6 (t, C-3), 31.0 (t, C-7), 32.4 (d, C-8), 43.6 (s, C-5), 81.6 (s, C-1), 220.9 (s, C-2) ppm. MS (70 eV): *m*/*z* (%) = 196 (36) [M$^+$], 178 (2) [M$^+$ – H_2O], 168 (6) [M$^+$ – CO], 150 (5) [M$^+$ – CO – H_2O], 140 (35) [$C_8H_{12}O_2^+$], 135 (14) [M$^+$ – CO – CH_3 – H_2O], 110 (48) [$C_8H_{14}^+$], 95 (84) [$C_7H_{11}^+$], 87 (40) [$C_4H_7O_2^+$], 81 (56) [$C_6H_9^+$], 74 (4) [$C_3H_6O_2^+$], 55 (53) [$C_4H_7^+$], 43 (100) [$C_3H_7^+$]. $C_{12}H_{20}O_2$ (196.3): calcd. C 73.43, H 10.27; found C 73.62, H 10.11. Odor: Weak, fruity, cinnamon.

(+)-(1*R*,4*S*,5*S*,9*R*,2′*S*)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]-decan-2-one 1′-Amino-2′-methoxymethylpyrrolidine Hydrazone (35): (1*R**,4*S**,5*S**,9*R**)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]-decan-2-one (**15**, 500 mg, 2.10 mmol) and (–)-(*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP, 340 mg, 2.62 mmol) were refluxed in EtOH (10 mL) under N_2 for 44 h. The solvent was then evaporated, and the resulting residue taken up in Et_2O/water (1:1, 40 mL). The organic layer was separated, the aqueous one extracted with Et_2O (20 mL), and the combined organic extracts were washed with water (20 mL) and brine (20 mL), dried (Na_2SO_4), and concentrated to dryness in a rotary evaporator. The resulting residue (780 mg) was separated into both diastereoisomers by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.07 for **35**, and R_f = 0.17 for **36**) to afford **35** (250 mg, 34%) and **36** (290 mg, 39%) in isomerically pure form. Spectroscopic data for **35**: IR (ATR): $\tilde{\nu}$ = 1104/1128/1067 (s, νC–O), 1454 (s, δCH_2), 3427 (m, νO–H), 1633 (w, νC=N–N<) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 0.46 (dd, J = 11.5, 11.5 Hz, 1 H, 10-H_{ax}), 0.67 (dd, J = 12.0, 12.0 Hz, 1 H, 8-H_{ax}), 0.77 (d, J = 6.5 Hz, 3 H, 4-Me), 0.95 (s, 3 H, 7-Me_{eq}), 0.96 (d, J = 7.5 Hz, 3 H, 9-Me), 1.03 (d, J = 12.0 Hz, 1 H, 6-H_{ax}), 1.13 (s, 3 H, 1-Me), 1.18–2.18 (m, 11 H, 3-,3′-,4′-H_2, 4-,9-H, 6-,8-,10-H_{eq},), 1.33 (s, 3 H, 7-Me_{ax}), 2.70 (dd, J = 7.5, 7.0 Hz, 1 H, 5′-H_b), 2.81 (dd, J = 7.5, 7.5 Hz, 1 H, 5′-H_a), 2.94 (s, 1 H, O-H), 3.27–3.56 (m, 3 H, CH_2O, 2′-H), 3.36 (s, 3 H, O-Me) ppm. ^{13}C NMR ($CDCl_3$): δ = 18.4 (q, 4-Me), 22.3 (t, C-4′), 23.4 (q, 9-Me), 26.2 (q, 1-Me), 26.3 (t, C-3′), 26.5 (d, C-9), 27.4 (q, 7-Me_{ax}), 31.4 (s, C-7), 34.1 (t, C-3), 35.1 (q, 7-Me_{eq}),

41.7 (t, C-6), 44.6 (d, C-4), 47.2 (t, C-10), 47.5 (s, C-5), 49.2 (t, C-8), 53.6 (t, C-5′), 59.2 (q, O-Me), 66.4 (d, C-2′), 74.8 (t, CH_2O), 80.0 (s, C-1) ppm, C-2: N.R. MS (70 eV): *m/z* (%) = 350 (1) [M^+], 332 (7) [$M^+ - H_2O$], 317 (2) [$M^+ - H_2O - CH_3$], 305 (2) [$M^+ - C_2H_5O$], 287 (100) [$M^+ - C_2H_5O - H_2O$], 189 (2) [$M^+ - C_2H_5O - H_2O - C_7H_{14}$], 45 (11) [$C_2H_5O^+$]. Polarimetry (*c* 0.99 in EtOH): $[\alpha]_D^{22}$ = +133.3, $[\alpha]_{578}^{22}$ = +121.6, $[\alpha]_{546}^{22}$ = +151.0, $[\alpha]_{436}^{22}$ = +417.3.

(–)-(1*R*,4*S*,5*S*,9*R*)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (37): A stirred solution of (+)-(1*R*,4*S*,5*S*,9*R*,2′*S*)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one 1′-amino-2′-methoxymethylpyrrolidine hydrazone (80 mg, 0.23 mmol) in MeOH (5 mL) was ozonized at –78 °C for 10 min, prior to the addition of thiourea (200 mg, 1.11 mmol) at 0 °C. The solvent was evaporated in vacuo, and the resulting residue purified by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.46) to afford the (–)-(1*R*,4*S*,5*S*,9*R*)-configured **37** (22.0 mg, 40%), the spectroscopic data of which were identical to those of the racemate **15** (vide supra). Chiral GC (Supelco B-DEX110, 60 m × 0.25 mm ID, ft = 0.25 μm): 94.53%*ee*. Polarimetry (*c* 0.46 in EtOH): $[\alpha]_D^{22}$ = –38.7, $[\alpha]_{578}^{22}$ = –41.5, $[\alpha]_{546}^{22}$ = –50.5, $[\alpha]_{436}^{22}$ = –132.5, $[\alpha]_{365}^{22}$ = –421.8. Odor: Odorless on GC–olfactometry on the chiral phase; the odor on the smelling strip is therefore due to traces of the enantiomer **38**.

(+)-(1*S*,4*R*,5*R*,9*S*,2′*S*)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]-decan-2-one 1′-Amino-2′-methoxymethylpyrrolidine Hydrazone (36): For the preparation see **35** above; yield 290 mg (39%), R_f = 0.17 (pentane/Et_2O, 9:1), colorless crystals, mp. 71–75 °C (pentane/Et_2O). IR (ATR): $\tilde{\nu}$ = 1103/1128/1070 (s, *ν*C–O), 1457 (s, *δ*CH_2), 3427 (m, *ν*O–H), 1633 (w, *ν*C=N–N<) cm^{-1}. ^1H NMR ($CDCl_3$): *δ* = 0.35 (dd, *J* = 11.5, 11.5 Hz, 1 H, 10-H_{ax}), 0.64 (dd, *J* = 12.0, 12.0 Hz, 1 H, 8-H_{ax}), 0.73 (d, *J* = 6.5 Hz, 3 H, 4-Me), 0.95 (s, 3 H, 7-Me_{eq}), 1.03 (d, *J* = 12.0 Hz, 1 H, 6-H_{ax}), 1.05 (d, *J* = 7.5 Hz, 3 H, 9-Me), 1.16 (s, 3 H, 1-Me), 1.28 (s, 3 H, 7-Me_{ax}), 1.33–2.22 (m, 11 H, 3-,3′-,4′-H_2, 4-,9-H, 6-,8-,10-H_{eq}), 2.47 (dd, *J* = 7.5, 7.0 Hz, 1 H, 5′-H_b), 2.76 (dd, *J* = 7.5, 7.5 Hz, 1 H, 5′-H_a), 3.33–3.54 (m, 3 H, CH_2O, 2′-H), 3.37 (s, 3 H, O-Me), 3.83 (s, 1 H, O-H) ppm. ^{13}C NMR ($CDCl_3$): *δ* = 19.4 (q, 4-Me), 22.4 (t, C-4′), 23.4 (q, 9-Me), 26.2 (d, C-9), 26.3 (t, C-3′), 26.4 (q, 1-Me), 27.1 (q, 7-Me_{ax}), 31.4 (s, C-7), 33.4 (t, C-3), 35.2 (q, 7-Me_{eq}), 41.6 (t, C-6), 43.6 (d, C-4), 46.5 (t, C-5), 47.6 (t, C-10), 49.2 (t, C-8), 54.1 (t, C-5′), 59.2 (q, O-Me), 66.2 (d, C-2′), 75.3 (t, CH_2O), 79.9 (s, C-1) ppm, C-2: N.R. MS (70 eV): *m/z* (%) = 350 (1) [M^+], 332 (7) [$M^+ - H_2O$], 317 (2) [$M^+ - H_2O - CH_3$], 305 (2) [$M^+ - C_2H_5O$], 287 (100) [$M^+ - C_2H_5O - H_2O$], 189 (2) [$M^+ - C_2H_5O - H_2O - C_7H_{14}$], 45 (9) [$C_2H_5O^+$]. Crystal data and structure refinement: Empirical formula $C_{21}H_{38}N_2O_2$, molecular mass 350.53, crystal dimensions 0.4 × 0.3 × 0.1 mm, temperature 293 K, wavelength 0.71073 Å, orthorhombic crystal system, space group $P2_12_12_1$, unit cell dimensions *a* = 9.3720(19) Å, *b* = 13.955(3) Å, *c* = 16.782(3) Å, *α* = 90°, *β* = 90°, *γ* = 90°, *V* = 2194.8(8) $Å^3$, *Z* = 4, *ρ* = 1.061 $Mg·m^{-3}$, *μ*(Mo-K_α) = 0.067 mm^{-1}, *F*(000) 776, *θ* range 1.90–24.18°, limiting indices $-10 \le h \le 10$, $-16 \le k \le 16$, $-19 \le l \le 19$, total reflections collected 20042, symmetry-independent reflections 3471, R_{int} = 0.0534, refinement full-matrix least-squares on F^2, data 3471, parameters 233, goodness-of-fit on F^2 0.799, final *R* indices [$I > 2\sigma(I)$], R_1 = 0.0352, wR_2 = 0.0752, *R* indices (all data) R_1 = 0.0669, wR_2 = 0.0811, Δ*ρ*(max, min) = 0.116, –0.081 e·$Å^{-3}$. CCDC 256514. Polarimetry (*c* 1.00 in EtOH): $[\alpha]_D^{22}$ = +181.6, $[\alpha]_{578}^{22}$ = +194.1, $[\alpha]_{546}^{22}$ = +237.9, $[\alpha]_{436}^{22}$ = +610.0.

(+)-(1*S*,4*R*,5*R*,9*S*)-1-Hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one (38): A stirred solution of (+)-(1*S*,4*R*,5*R*,9*S*,2′*S*)-1-hydroxy-1,4,7,7,9-pentamethylspiro[4.5]decan-2-one 1′-amino-2′-methoxymethylpyrrolidine hydrazone (100 mg, 0.29 mmol) in MeOH (5 mL) was ozonized at –78 °C for 10 min prior to the addition of thiourea (200 mg, 1.11 mmol) at 0 °C. The solvent was evaporated in vacuo, and the resulting residue purified by silica-gel FC (pentane/Et_2O, 9:1, R_f = 0.46) to afford the (+)-(1*S*,4*R*,5*R*,9*S*)-configured **38** (22.8 mg, 34%), the spectroscopic data of which were identical to those of the racemate **15** (vide supra). Chiral GC (Supelco B-DEX110, 60 m × 0.25 mm ID, ft = 0.25 μm): 98.18%*ee*. Polarimetry (*c* 0.72 in EtOH): $[\alpha]_D^{22}$ = +35.2, $[\alpha]_{578}^{22}$ = +37.6, $[\alpha]_{546}^{22}$ = +45.9, $[\alpha]_{436}^{22}$ = +121.8, $[\alpha]_{365}^{22}$ = +399.2. Odor: Strong, powerful, and characteristic of natural patchouli oil, with rich woody–ambery and tobacco-like facets. Odor threshold: 0.027 ng/L air.

Acknowledgments

For the X-ray structure determinations we are indebted to André Alker, Dr. Armin Ruf and Dr. Michael Hennig of F. Hoffmann-La Roche AG, Basel. Thanks are also due to Dr. Roman Kaiser, Erwin Senn, Irene Hickel and Michael Rothaupt for preparative GC, to Marcel Redard and Samuel Jordi for additional experimental work, to Melanie Stang and Thomas Reinmann for the preparation of larger quantities for further olfactory evaluations, to Dr. Gerhard Brunner for multidimensional NMR experiments, to Katarina Grman and Adriana Flückiger for GC-threshold determinations, to Caroline Gaillardot for GC–olfactometry, and to Jean-Jacques Rouge for the odor descriptions. Careful proofreading of the manuscript by Dr. Samuel Derrer, Dr. Markus Gautschi and John Anthony M^{c}Stea is also acknowledged with gratitude.

[1] H. Nebenzal, *Cafe Berlin*, Overlook Press, Woodstock, **1992**, p. 9; German ed.: H. Nebenzal, *Café Berlin*, Haffmanns Verlag, Zürich, **1994**, pp. 16–17.
[2] H. Gal, *Justus Liebigs Ann. Chem.* **1869**, *150*, 374–376.
[3] W. Treibs, *Justus Liebigs Ann. Chem.* **1949**, *564*, 141–151.
[4] a) G. Büchi, E. R. Erickson, *J. Am. Chem. Soc.* **1956**, *78*, 1262–1263; b) G. Büchi, E. R. Erickson, N. Wakabayashi, *J. Am. Chem. Soc.* **1961**, *83*, 927–938.
[5] G. Büchi, W. D. MacLeod, *J. Am. Chem. Soc.* **1962**, *84*, 3205–3206.
[6] M. Dobler, J. D. Dunitz, B. Gubler, H. P. Weber, G. Büchi, O. J. Padilla, *Proc. Chem. Soc. London* **1963**, 383.
[7] J. Gadamer, T. Amenomiya, *Arch. Pharm.* **1903**, *241*, 22–47.
[8] a) P. Teisseire, P. Maupetit, B. Corbier, P. Rouillier, *Recherches (Paris)* **1974**, *19*, 36–61; b) W. E. Oberhänsli, P. Schönholzer, *Recherches (Paris)* **1974**, *19*, 62–68.
[9] D. Kastner, *Riechst. Aromen Kosmet.* **1977**, *27*, 79–80.
[10] F. Näf, R. Decorzant, W. Giersch, G. Ohloff, *Helv. Chim. Acta* **1981**, *64*, 1387–1397.
[11] B. D. Mookherjee, K. K. Light, I. D. Hill, in: *178th ACS National Meeting*, Washington D.C., Sept. 9–14, **1979**, Abstracts of papers, I, AGFD 55; and in: *Essential Oils* (Eds.: B. D. Mookherjee, C. J. Mussinan), Allured Publishing Coorp.,Wheaton, IL, **1981**, pp. 246–272.
[12] G. Ohloff, *Düfte – Signale der Gefühlswelt*, Verlag Helvetica Chimica Acta Zürich **2004**, pp. 52–53.
[13] C. Sell, *A Fragrant Introduction to Terpenoid Chemistry*, Royal Society of Chemistry, Cambridge, **2003**, p. 200.
[14] G. Fráter, J. A. Bajgrowicz, P. Kraft, *Tetrahedron* **1998**, *54*, 7633–7703.
[15] P. Kraft, R. Cadalbert, *Synthesis* **2002**, 2243–2253.
[16] E. J. Corey, S. G. Pyne, *Tetrahedron Lett.* **1983**, *24*, 2821–2824.
[17] a) Y. Yamamoto, D. Matsumi, K. Itoh, *Chem. Commun.* **1998**, 875–876; b) Y. Yamamoto, D. Matsumi, R. Hattori, K. Itoh, *J. Org. Chem.* **1999**, *64*, 3224–3229.

[18] L. Szabó, K. Honty, L. Töke, I. Tóth, C. Szántay, *Chem. Ber.* **1972**, *105*, 3215–3230.
[19] A. Job, C. F. Janeck, W. Bettray, R. Peters, D. Enders, *Tetrahedron* **2002**, *58*, 2253–2329.
[20] P. Herold, J. W. Herzig, P. Wenk, T. Leutert, P. Zbinden, W. Fuhrer, S. Stutz, K. Schenker, M. Meier, G. Rihs, *J. Med. Chem.* **1995**, *38*, 2946–2954.
[21] D. Enders, L. Wortmann, R. Peters, *Acc. Chem. Res.* **2000**, *33*, 157–169.

Received: February 1, 2005

