5,6,7-Trimethylocta-2,5-dien-4-one − A Suspected Odorant with Surprising Olfactory Properties

Philip Kraft,*[a] Caroline Denis,[a] and Walter Eichenberger[a]

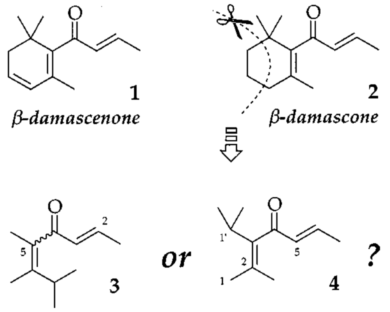
Keywords: Alkynes / Fragrances / Grignard reactions / Ketones / Odor−structure correlation

5,6,7-Trimethylocta-2,5-dien-4-one (**3**) was suspected of being a trace component smelling of damascone in a crude complex reaction product. Although this trace component eventually turned out to be the constitutional isomer 2-methyl-3-isopropylhepta-2,5-dien-4-one (**4**), the title compound **3** was found to possess even superior fruity, rosy odor characteristics, reminiscent of apples, plums, raisins and other dried fruits, and these odor characteristics are, surprisingly, due mainly to its (5*Z*)-isomer. The synthesis of **3** commenced with the preparation of 1-ethoxyprop-1-yne (**11**) from 2-chloro-1,1-diethoxyethane (**9**). Borontrifluoride-catalyzed addition of methyl isopropyl ketone (**10**) to **11** provided ethyl 2,3,4-trimethylpent-2-enoate (**8**), which was transformed into the target molecule **3** by Grignard reaction with propen-1-ylmagnesium bromide and in situ enolization. Further derivatives **13**–**16** provide more insight into the structure–odor correlation of damascone-type odorants, and the use of **3** in perfumery is illustrated by a composition formula of a demonstration perfume.

Introduction

Prior to the isolation,[1] structure elucidation,[2,3] synthesis,[4] and industrial production[5−7] of β-damascenone (**1**) and β-damascone (**2**), a true perfumistic reconstitution of Bulgarian rose oil (*Rosa damascena* Miller) was simply impossible.[2,3] Compounds **1**, **2**, and their commercial double bond isomers[6] not only revolutionized rose accords, but they also conferred volume, freshness, and naturalness to numerous floral and fruity perfumes, and overdoses of damascones also inspired completely new trends in perfumery.[8,9] The commercial importance of the damascones available on the market, ranging from 500 CHF/kg (for α-damascone) to 1700 CHF/kg (for **1**), is also documented in the elaboration of industrially feasible enantioselective syntheses of (*S*)-(−)-α-damascone.[10]

Therefore, we were very curious when, with the aid of GC−olfactometry analysis, we found a trace component (ca. 1.1%) with a very pleasant, damascone-like smell in a very complex, crude reaction product. No reasonable structure could be proposed on the basis of the chemistry involved or its GC/MS spectrum: m/z = 166 (34) [M^+], 151 (100) [$M^+ - CH_3$], 123 (32) [$M^+ - C_3H_7$], 109 (50), 97 (16), 81 (21), 69 (88), 55 (56), 41 (63). The intense m/z = 69 [$C_4H_5O^+$] fragment just indicated a but-2-en-1-one substructure and, assuming no further oxygen atoms, we proposed an empirical formula of $C_{11}H_{18}O$, which means 3 double bond equivalents − but this information was rather inadequate. A ca. 370 µg sample of the odoriferous trace component was thus isolated by preparative multidimensional GC, and HMBC and NOESY NMR spectra allowed two possible structures **3** and **4** to be proposed, as shown in Scheme 1.



Scheme 1. Damascones isolated from rose oil, and structures **3** and **4** proposed for the isolated trace constituent of a crude complex reaction product

While there was no doubt about a hepta-2,5-dien-4-one skeleton with one tetrasubstituted double bond bearing a methyl group and an isopropyl group, the relative position of the latter two could not be assigned. Both methyl groups on the tetrasubstituted double bond showed NOE crosspeaks with each other and with the methyl signals of the isopropyl moiety, and a NOE crosspeak between the vinylic proton at δ = 6.75 and the methyl hydrogens (doublet) of the isopropyl moiety at δ = 1.01 was also of little diagnostic value, as was the NOE between the methine proton and the downfield methyl hydrogens (singlet) at δ = 1.74. In the $^1H/^{13}C$ HMBC spectrum, the crosspeaks between the carbonyl carbon and the methine hydrogen atom were as strong as the signals between the carbonyl carbon and the methyl groups, also allowing no discrimination between the proposed structures **3** and **4**. Obviously, nothing could be said about the configuration of Δ^5 in case of **3**; however, the (*E*)-configuration of the disubstituted double bond was apparent from the ^3J = 15.6 Hz coupling constant of the vinylic protons.

---

[a] Givaudan Dübendorf AG,
Überlandstrasse 138, 8600 Dübendorf, Switzerland
Fax: (internat.) +41 (0)1/824 29 26
E-mail: philip.kraft@givaudan.com

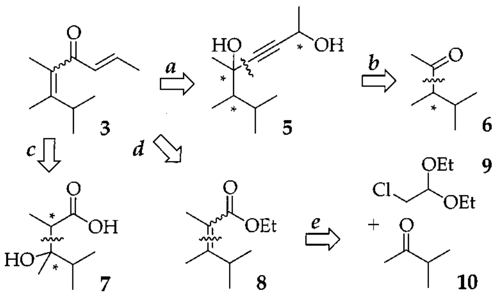
1434−193X/01/0612−2363 $ 17.50+.50/0

As is illustrated in Scheme 1, 2-methyl-3-isopropylhepta-2,5-dien-4-one (**4**) can be regarded as 2(3),4(5)-*diseco*-β-damascone, and so, with the work of Sestanj[9,11] on *seco*-ionones in mind, one might have expected damascone-like odor characteristics for this compound. Actually, we found 2-methyl-3-isopropylhepta-2,5-dien-4-one (**4**) was already covered by a patent of Takasago,[12] and that it was indeed claimed to possess a *sweet, natural, rosy* odor. Following the procedures disclosed in that patent,[12] we prepared a sample of **4**, and by comparison of its spectroscopic data and coinjection with the isolated sample, we proved that the isolated compound possessed structure **4**.

With the assignment of structure **4** to the trace component, our problem was – in principle – solved. Nevertheless, we also synthesized 5,6,7-trimethylocta-2,5-dien-4-one (**3**), and as it turned out this possessed surprising olfactory properties, superior to those of **4**. Here we report its synthesis and olfactory characterization.

Results and Discussion

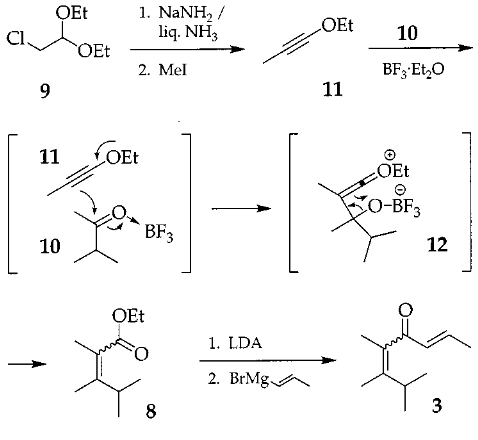
Scheme 2 details the retrosynthetic analysis of the target molecule **3**. The compound can be obtained from 5,6,7-trimethyloct-3-yne-2,5-diol (**5**) by Rupe alkynecarbinol rearrangement with subsequent dehydration of the α-hydroxy ketone produced (*transformation **a***). The intermediate **5** can be synthesized by means of a Grignard reaction between 3,4-dimethylpentan-2-one (**6**) and μ-(3-butyn-2-olato)bis-(magnesium bromide), the Grignard reagent of but-3-yn-2-ol (*dissection **b***). Ketone **6** should in turn be accessible from *n*-pentane by Nenitzescu reaction with acetyl chloride. However, Nenitzescu and Chicos reported no yields in their original publication,[14] and following their procedure we obtained a mere 4% of 3,4-dimethylpentan-2-one (**6**), based on the aluminum chloride used. Another problem was that the Nazarov cyclization of the final product **3** was competing with the acid-catalyzed Rupe rearrangement of **5**, making this route less attractive. Of course, a Reformatsky reaction of ethyl 2-bromopropionate with methyl isopropyl ketone (**10**) or the direct condensation of methyl isopropyl ketone (**10**) with lithium 2-lithiopropionate, leading to **7** (*route **c***), constitute alternatives for the construction of the target molecule **3**. However, the dehydration of **7** resulted in numerous double bond isomers, which we were unable to separate. Isomerization of the double bond into conjugation also failed utterly, and the Wittig dissection seemed problematic due to steric hindrance. We still wanted to introduce the propenyl moiety by a Grignard-type reaction through ethyl 2,3,4-trimethylpent-2-enoate **8** (*route **d***),[7] but planned instead to make use of an addition reaction of ketones to alkoxy alkynes, yielding esters.[15] This sequence (*dissection **e***), as also shown in Scheme 2, produces methyl isopropyl ketone (**10**) and 2-chloro-1,1-diethoxyethane (**9**), a starting material for the synthesis of 1-ethoxyprop-1-yne (**11**).[16]



Scheme 2. Retrosynthetic analysis of suspected odorant **3**

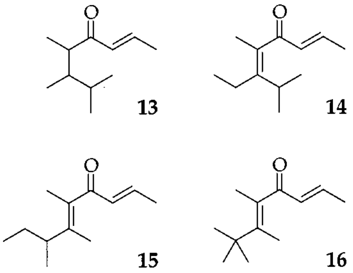
In the synthesis of 1-ethoxyprop-1-yne (**11**), we at first closely followed the procedure of Stalick, Hazlett, and Morris,[16] but later modified the workup when we found that crude **11** was sufficiently pure to be used in the intended addition reaction(s). Thus, 2-chloro-1,1-diethoxyethane (**9**) was treated with sodium amide in liquid ammonia, and the resulting sodium acetylide alkylated with iodomethane. After quenching, evaporation of the ammonia, and ether extraction, a ca. 2 M solution was obtained in 51% yield, and could be used without further purification in the subsequent reactions. The exact concentration of **11** could easily be determined by direct titration with an ethanolic bromine solution: at room temperature, **11** readily adds one mol of bromine to give 1,2-dibromo-1-ethoxypropene, and the end point is apparent from the color of excess bromine.

In the next step of the synthetic sequence, methyl isopropyl ketone (**10**) was treated with the prepared ethereal solution of **11** in the presence of boron trifluoride diethyl etherate.[15] What seems mechanistically to begin like a Mukaiyama aldol reaction (Scheme 3), probably produces the dipolar ketene intermediate **12**, which rearranges to the α,β-unsaturated ester **8**. In principal, this reaction is equivalent to a Wittig reaction between an α-bromopropionate and **10**; however, it is actually less sensitive to steric effects, as was apparent from the synthesis of more hindered derivatives (see Exp. Section). With methyl isopropyl ketone (**10**), and employing the crude ethereal solution of **11**, we isolated ethyl 2,3,4-trimethylpent-2-enoate (**8**) in 59% yield by flash chromatography.



Scheme 3. Synthesis of the target molecule **3**

The last step of our short synthetic sequence was a Grignard reaction between **8** and prop-1-en-1-ylmagnesium bromide with conversion in situ of the produced dienone **3** into its enolate,[7] in an attempt to avoid any further reaction to the corresponding carbinol. Nevertheless, we were only able to attain a 25% yield of olfactorily pure (2*E*,5*E*/*Z*)-5,6,7-trimethylocta-2,5-dien-4-one (**3**), the olfactory characteristics of which, however, made up for the fairly bad yield. To study the structure–odor correlation of this substance class, we also prepared the derivatives **13**, **14**, **15**, and **16** (Scheme 4) following the same sequence, but employing prop-1-enyllithium in a Gilman–Van-Ess coupling[17] in the final step. On a small scale, this reaction was easier to perform than the modified Grignard reaction, although yields were also low, in the range of 8–39%, based on olfactorily pure material.



Scheme 4. Further derivatives of compound **3**

Olfactory Properties

(2*E*,5*E*/*Z*)-5,6,7-Trimethylocta-2,5-dien-4-one (**3**) possesses a very powerful, fruity-rosy, β-damascone-like odor, reminiscent of apples, plums, raisins, and other dried fruits. In the top note, some slight aspects of maple, rum, and caramel join in the otherwise linear scent. In applications, **3** is very diffusive, and much more intense than **4**. Even more astonishingly, the odor of **3** is closer to that of β-damascone (**2**) than is the odor of the *seco*-β-damascone **4**, which is also fruity, damascone-like, and reminiscent of dried fruits, but with camphoraceous, turpentine- and cork-like notes in the top, and aspects of saffron, tobacco, and ionones in the dry down.

However, what was really surprising was that it was found by GC–olfactometry that the interesting odor characteristics of **3** were mainly due to the *cis* isomer (2*E*,5*Z*)-**3**, while (2*E*,5*E*)-**3** was barely detectable for some people. The *cis* isomer (2*E*,5*Z*)-**3** could be isolated by repeated FC on silica gel, and was identified by the ^5J = 1.0 Hz coupling constant between its methyl group groups at C-5 and C-6. This long-range coupling was about ^5J = 1.5 Hz in (2*E*,5*E*)-**3**. In addition, the *cis* isomer (2*E*,5*Z*)-**3** showed a pure-phase NOE between 5-Me and 6-Me, while a coupling artefact (*"COSY-type crosspeak"*) of mixed phase between 5-Me and 6-Me resulted in the NOESY spectrum of the *trans* isomer (2*E*,5*E*)-**3**. These recognition characteristics were also used for the Δ^5-double bond assignment of compounds **14**–**16**, while the (2*E*)-configuration of the second double bond was apparent for all compounds from the *vicinal* coupling of ^3J = 15.6 Hz.

However, contrary to what might have been expected, the characteristic fruity-rosy odor character of **3** is not lost completely in the partially hydrogenated compound **13**, although **13** is without doubt much weaker than **3**. In addition, it shows a quite strong raspberry inflection that is especially present in the top. What was found for the odor strength of the Δ^5-isomers of **3** also holds true for the 6-ethyl derivative **14**, though the difference is not so pronounced. Both are fruity-rosy, but (2*E*,5*Z*)-**14** is more intense, more diffusive, more agrestic, and more raspberry-like than (2*E*,5*E*)-**14**, which on the other hand is more reminiscent of fresh apples. It seems that when the larger C-6 substituent becomes more bulky, the strength of the (5*E*)-isomers increases. Thus, the (5*E*)-configured compounds **15** and **16** are also powerful odorants, though both clearly weaker than **3**. Compound **15**, however, is more long-lasting than **3**, while also possessing a fruity-rosy odor, reminiscent of apples and dried fruits. The 6-*tert*-butyl derivative **16** is still reminiscent of dried fruits with a distinct apple note, but the odor has already shifted to a rather celery- and jasmone-like tonality with additional agrestic aspects.

In conclusion, 5,6,7-trimethylocta-2,5-dien-4-one (**3**), erroneously suspected of being the damascone-like smelling trace component, serendipitously turned out to be the most superior damascone odorant of all investigated derivatives. Surprisingly, **3** is stronger and closer to β-damascone (**2**) than the *seco*-β-damascone **4** is, and because the odor of **3** is mainly due to its (2*E*,5*Z*)-isomer, it should not be considered as a *seco*-damascone derivative, but as a completely new structure with surprising olfactory properties. A floral-fruity feminine fragrance (see end of Exp. Section) demonstrates the use of **3** in perfumery. In comparison with damascones like **2**, compound **3** conveys more lift and diffusivity to the composition, blends well with the rose accord, but brings also out the fruity and agrestic aspects.

Experimental Section

IR: Bruker VECTOR 22/Harrick SplitPea micro ATR, Si. – NMR: Bruker AVANCE DPX 400, TMS int. – MS: Finnigan MAT 95; HP Chemstation 6890 GC/5973 Mass Sensitive Detector. – FC: Merck Kieselgel 60 (particle size 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: PMA spray soln. for TLC, Merck 1.00480.0100. – Melting points: Büchi Melting Point B545 (uncorrected). – Elemental analysis: F. Hoffmann-La Roche, Basel, PRPI-S. – All reactions were performed under nitrogen using reagents and solvents (puriss. or purum) from Fluka without further purification.

3-Isopropyl-2-methylhepta-2,5-dien-4-one (4): Prepared according to ref.,[12] but purified by silica gel FC (pentane/Et_2O, 19:1, R_f = 0.49). – IR (film): $\tilde{\nu}$ = 1648/1676 (s, ν C=O, unsatd.), 1618 (m, ν C=C), 974 (m, δ C=C–H oop.), 1376 (m, δ CH_3). – ^1H NMR ($CDCl_3$): δ = 1.00 (d, *J* = 6.8 Hz, 6 H, 1′-Me_2), 1.57 (s, 3 H, 2*Z*-Me), 1.74 (s, 3 H, 2*E*-Me), 1.92 (dd, *J* = 6.8, 1.6 Hz, 3 H, 7-H_3), 2.82 (sept, *J* = 6.8 Hz, 1 H, 1′-H), 6.14 (dq, *J* = 15.6, 1.6 Hz, 1 H, 5-H), 6.74

(dq, J = 15.6, 6.8 Hz, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$): δ = 18.2 (q, C-7), 19.0 (q, 2E-Me), 21.4 (2q, 1′-Me_2), 22.4 (q, 2Z-Me), 29.0 (d, C-1′), 128.4 (s, C-2), 134.6 (d, C-5), 139.9 (s, C-3), 146.1 (d, C-6), 202.1 (s, C-4). − MS (70 eV): m/z = 166 (34) [M^+], 151 (100) [$M^+ - CH_3$], 123 (32) [$M^+ - C_3H_7$], 109 (50) [$M^+ - C_4H_9$], 97 (16) [$M^+ - C_4H_5O$], 81 (21) [$C_6H_9^+$], 69 (88) [$C_4H_5O^+$], 55 (56) [$C_4H_7^+$], 41 (63) [$C_3H_5^+$]. − These spectroscopic data were identical to those reported in ref.,[12] as far as specified therein. − Odor: Fruity, damascone- and tobacco-like, with aspects of saffron, ionones, and camphor.

1-Ethoxyprop-1-yne (11): Anhydrous NH_3 (900 mL) was condensed at −70 °C in a reaction flask, and crushed $Fe(NO_3)_3 \cdot 9\ H_2O$ (750 mg, 1.86 mmol) was added with slow stirring. Chunks of freshly cut Na (56.2 g, 2.45 mol) were added at −60 to −40 °C over 1 h, and the reaction was allowed to reflux at −30 °C for 2 h. 2-Chloro-1,1-diethoxyethane (**9**, 114 mL, 750 mmol) was then added dropwise at this temp., with stirring, over a period of 30 min. Stirring was continued at −30 °C for 1 h, prior to dropwise addition of MeI (70.0 mL, 1.13 mol) over 30 min. The reaction mixture was stirred vigorously for 90 min at this temp., and then cautiously quenched by dropwise addition of a cooled satd. aq. NH_4Cl solution (90 mL), followed by pentane (120 mL) and additional satd. aq. NH_4Cl (500 mL). The cooling bath was removed, and the reaction mixture was allowed to warm to room temp. overnight, with evaporation of the NH_3. Water (150 mL) was added, and the organic layer was separated and washed with water (150 mL) and satd. aq. NaCl (50 mL). The combined aqueous solutions were extracted with Et_2O (3× 50 mL), and the organic extracts were combined with the separated organic layer to provide, after drying with Na_2SO_4, a 2.1 M ethereal solution of **11** (183 mL, 51%), sufficiently pure for subsequent reactions. The concentration of the solution of **11** was determined by titration with an ethanolic Br_2 solution, giving 1,2-dibromo-1-ethoxyprop-1-ene. A small sample of **11** was purified by distillation, and, in agreement with ref.,[16] showed the following spectroscopic data. − IR (film): $\tilde{\nu}$ = 2282 (m, ν C≡C). − ^{1}H NMR ($CDCl_3$): δ = 1.34 (t, J = 7.1 Hz, 3 H, 2′-H_3), 1.73 (s, 3 H, 3-H_3), 4.00 (q, J = 7.1 Hz, 2 H, 1′-H_2). − ^{13}C NMR ($CDCl_3$): δ = 1.45 (q, C-3), 14.2 (q, C-2′), 34.0 (t, C-2), 73.5 (t, C-1′), 87.9 (s, C-1). − MS (70 eV): m/z = 27 (41) [$C_2H_3^+$], 56 (100) [$M^+ - C_2H_4$], 69 (8) [$M^+ - CH_3$], 84 (75) [M^+].

(2*E*/*Z*)-Ethyl 2,3,4-Trimethylpent-2-enoate (8): A $BF_3 \cdot Et_2O$ solution in Et_2O (48%, 19.9 mL, 76.0 mmol) was added at −15 °C under N_2, over a period of 15 min, to a stirred solution of methyl isopropyl ketone (**10**, 6.60 g, 76.6 mmol) in Et_2O (76 mL). Stirring was continued at this temp. for 10 min, prior to the dropwise addition of a solution of **11** (1.9 M, 40 mL, 76 mmol) over 20 min, during which time the temp. was kept below 0 °C. After further stirring at 0 °C for 1 h, the reaction mixture was poured into ice/water (1:1, 100 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (2× 100 mL), and the combined organic extracts were washed with water (100 mL) and satd. aq. NaCl solution (50 mL), and dried with Na_2SO_4. Evaporation of the solvent in a rotary evaporator, and purification of the resulting residue (12.5 g) by silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.63) provided **8** (7.60 g, 59%) as a colorless liquid mixture of 2E/Z isomers, the spectroscopic data of which were in agreement with those reported in ref.,[15] as far as detailed therein. − IR (film): $\tilde{\nu}$ = 1219 (s, ν_{as} C−CO−O), 1713 (s, ν C=O), 1104 (s, ν_{as} O−C−C). − ^{1}H NMR ($CDCl_3$): δ = 0.99/1.00 (2d, J = 6.8 Hz, 6 H, 4-Me_2), 1.29/1.30 (2t, J = 7.2 Hz, 3 H, 2′-H_3), 1.63 (s, 3 H, 3E-Me), 1.87 (s, 3 H, 3Z-Me), 1.81/1.82 (2s, 3 H, 2-Me), 2.88/3.13 (2sept., J = 6.8 Hz, 1 H, 4-H), 4.17/4.18 (2q, J = 7.2 Hz, 2 H, 1′-H_2). − ^{13}C NMR ($CDCl_3$): δ = 12.8/14.08/14.13/14.2/14.6/15.7 (6q, 2-,3-Me, C-2′), 19.7/20.5 (4q, 4-Me_2), 30.7/31.9 (2d, C-4), 59.88/59.91 (2t, C-1′), 121.5/121.9 (2s, C-2), 148.0/149.3 (2s, C-3), 170.5 (2s, C-1). − MS (70 eV): m/z = 55 (92) [$C_4H_7^+$], 81 (61) [$C_6H_9^+$], 97 (52) [$M^+ - C_3H_5O_2$], 109 (90) [$M^+ - C_2H_5O_2$], 125 (97) [$M^+ - C_2H_5O$], 127 (90) [$M^+ - CH_3 - C_2H_4$], 155 (100) [$M^+ - CH_3$], 170 (46) [M^+].

(2*E*,5*E*/*Z*)-5,6,7-Trimethylocta-2,5-dien-4-one (3): A Grignard solution was prepared under N_2, by addition, in small portions, of a solution of 1-bromoprop-1-ene (6.30 mL, 73.9 mmol) in anhydrous THF (60 mL) to Mg turnings (1.80 g, 73.9 mmol), while occasionally heating with a heat gun. In a separate flask, an LDA solution was prepared by dropwise addition, at −70 °C under N_2, of a solution of *n*BuLi in hexanes (10 M, 4.3 mL, 43 mmol) to a stirred solution of *i*Pr_2NH (6.20 mL, 43.0 mmol) in anhydrous THF (22 mL). After stirring for 10 min at this temp., the prepared Grignard solution was added dropwise at room temp. to this reaction mixture over 20 min, followed by dropwise addition at 35 °C of a solution of (2E/Z)-ethyl 2,3,4-trimethylpent-2-enoate (7.30 g, 42.9 mmol) in dry THF (90 mL), over 20 min. Stirring was continued at this temp. for 2 h, and the mixture was then refluxed for 1 h. After the reaction mixture had cooled to room temp., it was poured into water and extracted with Et_2O. The combined organic extracts were washed with water and satd. aq. NaCl solution, dried with Na_2SO_4, and concentrated in a rotary evaporator. Silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.22) on the resulting residue afforded **3** (1.80 g, 25%) as a colorless, odoriferous liquid. − IR (film): $\tilde{\nu}$ = 1653 (s, ν C=O, unsatd.), 1620 (s, ν C=C), 973 (m, δ C=C−H oop.), 1377 (m, δ CH_3). − ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, J = 6.6 Hz, 6 H, 7-Me_2, 5E), 1.01 (d, J = 6.8 Hz, 6 H, 7-Me_2, 5Z), 1.54 (q, ^5J = 1.5 Hz, 3 H, 6-Me, 2E, 5Z), 1.61 (q, ^5J = 1.0 Hz, 3 H, 6-Me, 2E, 5E), 1.74 (q, ^5J = 1.0 Hz, 3 H, 5-Me, 2E, 5E), 1.79 (q, ^5J = 1.5 Hz, 3 H, 5-Me, 2E, 5Z), 1.91−1.94 (m, 6 H, 1-H_3, 5E+5Z), 2.57 (sept, J = 6.6 Hz, 1 H, 7-H, 5E), 2.86 (sept, J = 6.8 Hz, 1 H, 7-H, 5Z), 6.11 (dq, J = 15.9, 2.0 Hz, 1 H, 3-H, 2E, 5Z), 6.12 (dq, J = 15.6, 1.6 Hz, 1 H, 3-H, 2E, 5E), 6.74 (dq, J = 15.9, 9.2 Hz, 1 H, 2-H, 2E, 5Z), 6.77 (dq, J = 15.6, 6.8 Hz, 1 H, 2-H, 2E, 5E). − ^{13}C NMR ($CDCl_3$): δ = 11.2/13.8 (2q, 5-Me), 15.0/15.9 (2q, 6-Me), 18.1/18.2 (2q, C-1), 20.0/20.4 (4q, 7-Me_2), 29.5/32.4 (2d, C-7), 128.7/128.8 (2s, C-5), 132.0/132.4 (2d, C-3), 140.3/140.5 (2s, C-6), 145.1/145.3 (2d, C-2), 201.6/201.8 (2s, C-4). − MS (70 eV): m/z = 41 (43) [C_3H_5], 55 (30) [C_4H_7], 69 (32) [C_4H_5O], 123 (20) [$M^+ - C_3H_7$], 136 (31) [$M^+ - 2\ CH_3$], 151 (100) [$M^+ - CH_3$], 166 (11) [M^+]. − $C_{11}H_{18}O$ (166.26): calcd. C 79.46, H 10.91; found C 79.23, H 11.13. − Odor: Linear, very intense and very diffusive, fruity-rosy, reminiscent of apples, plums, raisins, and other dried fruits; slightly rum- and caramel-like in the top note.

(2*E*,5*Z*)-5,6,7-Trimethylocta-2,5-dien-4-one [(5*Z*)-3]: Repeated FC (pentane/Et_2O, 9:1, R_f = 0.53) on the (2E,5E/Z)-**3** mixture resulted in the isolation of a pure sample of (2E,5Z)-5,6,7-trimethylocta-2,5-dien-4-one [(2E,5Z)-**3**], which possessed the following spectroscopic and olfactory characteristics. − IR (film): $\tilde{\nu}$ = 1653 (s, ν C=O, unsatd.), 1620 (s, ν C=C), 973 (m, δ C=C−H oop.), 1377 (m, δ CH_3). − ^{1}H NMR ($CDCl_3$): δ = 0.94 (d, J = 6.6 Hz, 6 H, 7-Me_2), 1.61 (q, ^5J = 1.0 Hz, 3 H, 6-Me, thus 5Z; the 5E isomer shows 1.5 Hz), 1.74 (q, ^5J = 1.0 Hz, 3 H, 5-Me, thus 5Z; the 5E isomer shows 1.5 Hz), 1.92 (dd, J = 6.8, 1.6 Hz, 3 H, 1-H_3), 2.57 (sept, J = 6.6 Hz, 1 H, 7-H), 6.12 (dq, J = 15.6, 1.6 Hz, 1 H, 3-H, thus 2E), 6.77 (dq, J = 15.6, 6.8 Hz, 1 H, 2-H, thus 2E). − NOESY (^{1}H/^{1}H): 3-H/7-Me, 5-Me/6-Me. − ^{13}C NMR ($CDCl_3$): δ = 11.3 (q, 5-Me), 16.0 (q, 6-Me), 18.2 (q, C-1), 20.5 (2q, 7-Me_2), 32.4 (d, C-7), 128.9 (s, C-5), 132.5 (d, C-3), 140.5 (s, C-6), 145.4 (d, C-2), 201.9 (s, C-4). − MS (70 eV): m/z = 41 (41) [C_3H_5], 55 (30) [C_4H_7], 69 (31) [C_4H_5O], 123 (20) [$M^+ - C_3H_7$], 136 (33) [$M^+ - 2CH_3$], 151 (100) [$M^+ - CH_3$], 166 (11) [M^+]. − Odor: Similar to **3**, but even more intense and radiant, possessing an odor threshold of 0.5 ng/L air.

(±)-(2*E*,5*RS*,6*RS*)-5,6,7-Trimethyloct-2-en-4-one (13): In the presence of 10% Pt/C (0.50 g, 0.26 mmol, 0.2 mol %), a vigorously stirred solution of (2*E*/*Z*)-ethyl 2,3,4-trimethylpent-2-enoate (**8**, 20.0 g, 117 mmol) in EtOAc (200 mL) was hydrogenated with 25 bar H_2 in an autoclave over 4 h at room temp. The catalyst was removed by vacuum filtration over a pad of Celite®, and the filtrate was concentrated in a rotary evaporator. Distillation of the resulting residue through a 10 cm Widmer column afforded (2*RS*,3*RS*)-ethyl 2,3,4-trimethylvalerate (16.9 g, 83%) as a colorless mixture of diastereoisomers at 105−108 °C/100 mbar. This mixture (98.1 mmol) was dissolved in EtOH/water (1:1, 150 mL), and treated with 86% KOH (9.60 g, 147 mmol). After 2 h at reflux, the reaction mixture was allowed to cool to room temp., diluted with water (500 mL), and acidified with HCl to pH 1. The product was extracted three times with Et_2O, and the ethereal extracts were combined, dried with Na_2SO_4, and concentrated in a rotary evaporator. The crude 2,3,4-trimethylvaleric acid (14.3 g) was taken up in anhydrous THF (250 mL). A solution of *n*BuLi (10 M, 9.8 mL, 98 mmol) in hexanes was added dropwise at −10 °C with stirring. Stirring was continued at this temp. for 40 min, prior to the dropwise addition of a propenyllithium solution in Et_2O (0.8 M, 123 mL, 98 mmol). After 4 h stirring at 30 °C, the reaction was again cooled down to −10 °C, and quenched by dropwise addition of Me_2CO (16 mL, 218 mmol). Stirring was continued at this temp. for a further 10 min, and satd. aq. NH_4Cl solution (200 mL) was added. The cooling bath was removed, and the quenched reaction mixture diluted with water (200 mL) and extracted three times with Et_2O. The combined organic extracts were dried with $MgSO_4$, the solvent was evaporated in a rotary evaporator, and **13** (6.50 g, 39%) isolated as a colorless, odoriferous mixture of diastereoisomers, after purification of the crude material by silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.24). − IR (film): $\tilde{\nu}$ = 1629 (s, ν C=C), 1695/1668 (s, ν C=O, unsatd.), 970 (m, δ C=C−H oop.), 1378 (m, δ CH_3). − ^1H NMR ($CDCl_3$): δ = 0.70/0.74/0.76/0.84 (4d, *J* = 6.8 Hz, 6 H, 7-Me_2), 0.92/0.93 (2d, *J* = 6.5 Hz, 3 H, 6-Me), 0.98/1.05 (2d, *J* = 6.8 Hz, 3 H, 5-Me), 1.49−1.71 (m, 1 H, 7-H), 1.85−1.93 (m, 4 H, 1-H_3, 6-H), 2.78 (quint, *J* = 6.8 Hz)/2.61 (dq, *J* = 9.6, 6.8 Hz) (1 H, 5-H), 6.21 (dq, *J* = 15.4, 1.6 Hz, 1 H, 3-H), 6.85−6.94 (m, 1 H, 2-H). − ^{13}C NMR ($CDCl_3$): δ = 11.0/11.7 (4q, 7-Me_2), 15.0/15.2 (2q, 5-Me), 18.1/18.2 (2q, C-1), 21.35/21.42 (2q, 6-Me), 27.1/30.3 (2d, C-7), 40.3/40.5 (2d, C-6), 46.7/47.7 (2d, C-5), 130.2/130.9 (2d, C-3), 141.8/142.2 (2d, C-2), 203.8/204.5 (2s, C-4). − MS (70 eV): *m*/*z* (%) = 69 (100) [$C_4H_5O^+$], 83 (16) [$M^+ - C_5H_{10} - CH_3$], 98 (58) [$M^+ - C_5H_{10}$, McLafferty fragmentation], 125 (2) [$M^+ - C_3H_7$], 168 (1) [M^+]. − Odor: Much weaker than **3**, but still very diffusive, fruity-rosy, reminiscent of raspberries and dried fruits.

(2*E*,5*Z*)-6-Ethyl-5,7-dimethylocta-2,5-dien-4-one (14): (2*E*/*Z*)-Ethyl 3-ethyl-2,4-dimethylpent-2-enoate (2.11 g, 11.4 mmol), prepared by addition of 2-methylpentan-3-one to 1-ethoxyprop-1-yne (**11**) in 16% yield in analogy with the synthesis of (2*E*/*Z*)-ethyl 2,3,4-trimethylpent-2-enoate (**8**), was dissolved in EtOH/water (1:1, 34 mL), and treated with 86% KOH (2.24 g, 34.3 mmol). After 22 h at reflux, the reaction mixture was poured into ice/water (1:1, 200 mL), and the aqueous solution was washed with Et_2O (2× 100 mL), adjusted to pH 1 with 2 N aq. HCl, and extracted with Et_2O (2× 100 mL). The ethereal extracts were washed with water (100 mL) and satd. aq. NaCl (25 mL), dried with Na_2SO_4, and concentrated using a rotary evaporator to provide crude (2*E*/*Z*)-3-ethyl-2,4-dimethylpent-2-enoic acid (1.56 g, 88%). A portion of this material (1.44 g, 9.22 mmol) was dissolved in anhydrous THF (23 mL), and prop-1-enyllithium solution in Et_2O (0.8 M, 23.0 mL, 18.4 mmol) was added dropwise at −10 °C under N_2 over a period of 20 min, with stirring. The cooling bath was removed, and the reaction mixture was stirred for 2 h at room temp., and for 1 h at 40 °C, prior to quenching with Me_2CO (5 mL) at −10 °C. Stirring was continued for 10 min at −10 °C, and satd. aq. NH_4Cl (30 mL) was added at that temp. The reaction mixture was allowed to warm to room temp. overnight, then poured into water (100 mL), and extracted with Et_2O (2× 100 mL). The ethereal extract was washed with water (100 mL) and satd. aq. NaCl (25 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The resulting residue (1.12 g) was purified by FC on silica gel (pentane/Et_2O, 98:2) to provide − besides (2*E*,5*E*)-**14** (107 mg, 6%, R_f = 0.31 in pentane/Et_2O, 19:1) − the title compound (2*E*,5*Z*)-**14** (72.2 mg, 4%). − IR (film): $\tilde{\nu}$ = 1651 (s, ν C=O, unsatd.), 972 (s, δ C=C−H oop.), 1621 (m, ν C=C), 1376 (w, δ CH_3). − ^1H NMR ($CDCl_3$): δ = 0.94 (d, *J* = 6.8 Hz, 6 H, 7-Me_2), 1.06 (t, *J* = 7.6 Hz, 3 H, CH_3, 6-Et), 1.77 (s, 3 H, 5-Me), 1.93 (dd, *J* = 6.8, 1.6 Hz, 3 H, 1-H_3), 2.07 (q, *J* = 7.6 Hz, 2 H, CH_2, 6-Et), 2.54 (sept, *J* = 6.8 Hz, 1 H, 7-H), 6.11 (dq, *J* = 15.7, 1.6 Hz, 1 H, 3-H, thus 2*E*), 6.77 (dq, *J* = 15.7, 6.8 Hz, 1 H, 2-H, thus 2*E*). − NOESY (^1H/^1H): 5-Me/CH_2CH_3. − ^{13}C NMR ($CDCl_3$): δ = 14.1 (q, 5-Me), 15.6 (q, CH_3, 6-Et), 18.2 (q, C-1), 19.3 (t, CH_2, 6-Et), 20.8 (2q, 7-Me_2), 32.9 (d, C-7), 129.4 (s, C-5), 132.6 (d, C-3), 145.4 (d, C-2), 145.6 (s, C-6), 202.3 (s, C-4). − MS (70 eV): *m*/*z* (%) = 41 (80) [C_3H_5], 55 (29) [C_4H_7], 69 (61) [C_5H_9], 81 (17)/95 (17)/109 (24)/123 (40)/137 (76)/151 (36)/165 (100) [$M^+ - C_nH_{2n+1}$], 180 (14) [M^+]. − Odor: Fruity-rosy, reminiscent of raspberries and dried fruits, more intense, more diffusive, but also more agrestic than the corresponding (2*E*,5*E*)-**14**, which is more reminiscent of fresh apples.

(2*E*,5*E*)-5,6,7-Trimethylnona-2,5-dien-4-one (15): (2*E*/*Z*)-Ethyl 2,3,4-trimethylhex-2-enoate (5.83 g, 31.7 mmol), prepared by addition of 3-methylpentan-2-one to 1-ethoxyprop-1-yne (**11**) in 46% yield in analogy with the synthesis of (2*E*/*Z*)-ethyl 2,3,4-trimethylpent-2-enoate (**8**), was dissolved in EtOH/water (1:1, 100 mL), and treated with 86% KOH (2.93 g, 44.4 mmol). After 3 h at reflux, another portion of 86% KOH (2.93, 44.4 mmol) was added to the stirred reaction mixture, and heating was continued for a further 3 h. After the reaction mixture had cooled down to room temp., water (300 mL) was added, and the aqueous solution was acidified with conc. H_3PO_4 and extracted with Et_2O (400 mL). The organic extract was dried, concentrated in a rotary evaporator, and purified by FC on silica gel (pentane/Et_2O, 4:1) to provide 2,3,4-trimethylhex-2-enoic acid (3.77 g, 76%), which was taken up in anhydrous THF (50 mL). A solution of *n*BuLi in THF (1.6 M, 15.1 mL, 24.2 mmol) was added dropwise at −10 °C under N_2, with stirring. Stirring was continued at this temp. for 15 min prior to the dropwise addition of a prop-1-enyllithium solution in Et_2O (0.8 M, 30 mL, 24.2 mmol). The cooling bath was removed, and the reaction mixture stirred at 30 °C for 1 h. The reaction mixture was then cooled to 0 °C, and quenched by addition of Me_2CO (4 mL), followed by satd. aq. NH_4Cl (50 mL). The cooling bath was removed and the reaction mixture diluted with water (200 mL), and extracted with Et_2O (3× 400 mL). The organic extracts were combined, dried, and concentrated using a rotary evaporator, the resulting residue purified by silica-gel FC (4 L pentane/Et_2O, 49:1, and 2 L pentane/Et_2O, 19:1) to provide **15** (0.67 g, 15%) as a colorless, odoriferous liquid. − IR (film): $\tilde{\nu}$ = 1652 (s, ν C=O, unsatd.), 972 (s, δ C=C−H oop.), 1620 (m, ν C=C), 1376 (m, δ CH_3). − ^1H NMR ($CDCl_3$): δ = 0.87 (t, *J* = 7.4 Hz, 3 H, 9-H_3), 0.99 (d,

J = 7.2 Hz, 3 H, 7-Me), 1.38 (qd, J = 7.4, 7.2 Hz, 2 H, 8-H_2), 1.50 (q, ^5J = 1.5 Hz, 3 H, 6-Me), 1.79 (q, ^5J = 1.5 Hz, 3 H, 5*E*-Me), 1.92 (dd, J = 6.8, 1.6 Hz, 3 H, 1-H_3), 2.60 (sext, J = 7.2 Hz, 1 H, 7-H), 6.11 (dq, J = 15.6, 1.6 Hz, 1 H, 3-H), 6.80 (dq, J = 15.6, 6.8 Hz, 1 H, 2*E*-H). − ^{13}C NMR ($CDCl_3$): δ = 12.2 (q, C-9), 13.6 (q, 5-Me), 15.4 (q, 6-Me), 18.16/18.23 (2q, C-1, 7-Me), 27.3 (t, C-8), 36.7 (d, C-7), 130.1 (s, C-5), 132.1 (d, C-3), 139.1 (s, C-6), 145.1 (d, C-2), 201.8 (s, C-4). − MS (70 eV): m/z (%) = 41 (73) $[C_3H_5]$, 55 (33) $[C_4H_7]$, 69 (62) $[C_4H_5O]$, 109 (43) $[M^+ - C_5H_{11}]$, 123 (43) $[M^+ - C_4H_9]$, 136 (17) $[M^+ - C_3H_8]$, 151 (100) $[M^+ - C_2H_5]$, 165 (26) $[M^+ - CH_3]$, 180 (13) $[M^+]$. − Odor: Linear, very intense and long-lasting, fruity-rosy, reminiscent of apples and dried fruits.

(2*E*,5*E*)-5,6,7,7-Tetramethylocta-2,5-dien-4-one (16): (2*E*/*Z*)-Ethyl 2,3,4,4-tetramethylpent-2-enoate (4.11 g, 22.3 mmol), prepared by addition of pinacolone to 1-ethoxyprop-1-yne (**11**) in 30% yield, in analogy with the synthesis of (2*E*/*Z*)-ethyl 2,3,4-trimethylpent-2-enoate (**8**), was dissolved in EtOH/water (1:1, 70 mL), and treated with 86% KOH (4.37 g, 66.9 mmol). After 24 h at reflux, the reaction mixture was poured into ice/water (1:1, 100 mL), and the aqueous solution was washed with Et_2O (2× 100 mL) and NaOH (2 N, 100 mL), acidified to pH 1 by addition of 2 N aq. HCl, and extracted with Et_2O (2 × 250 mL). The ethereal extract was washed with water (100 mL) and satd. aq. NaCl (25 mL), dried with Na_2SO_4 and concentrated in a rotary evaporator to provide crude (2*E*/*Z*)-2,3,4,4-tetramethylpent-2-enoic acid (2.43 g, 70%). A portion of this material (2.27 g, 14.5 mmol) was dissolved in anhydrous THF (38 mL), and a solution of prop-1-enyllithium in Et_2O (0.8 M, 36.3 mL, 29.0 mmol) was added dropwise at −10 °C under N_2 with stirring, over a period of 40 min. The cooling bath was removed, and the reaction mixture was stirred for 2 h at room temp., and for 1 h at 40 °C, prior to quenching with Me_2CO (5 mL) at −10 °C. Stirring was continued for 10 min at −10 °C, and satd. aq. NH_4Cl (35 mL) was added at that temp. The reaction mixture was allowed to warm to room temp. overnight, poured into water (100 mL), and extracted with Et_2O (2× 100 mL). The ethereal extract was washed with water (100 mL) and satd. aq. NaCl (25 mL), dried with Na_2SO_4, and concentrated under reduced pressure. The resulting residue (1.91 g) was purified by silica-gel FC (pentane/Et_2O, 19:1, R_f = 0.24) to afford **16** (216 mg, 8%). − IR (film): $\tilde{\nu}$ = 1653 (s, ν C=O, unsatd.), 972 (m, δ C=C−H oop.), 1621 (m, ν C=C), 1377 (w, δ CH_3). − ^1H NMR ($CDCl_3$): δ = 1.21 (s, 9 H, 7-Me_3), 1.57 (q, J = 1.5 Hz, 3 H, 6-Me, 5*E*), 1.88 (q, J = 1.5 Hz, 3 H, 5*E*-Me), 1.93 (dd, J = 7.0, 1.6 Hz, 3 H, 1-H_3), 6.04 (dq, J = 15.7, 1.6 Hz, 1 H, 3-H, 2*E*), 6.74 (dq, J = 15.7, 6.8 Hz, 1 H, 2*E*-H). − NOESY (^1H/^1H): 5-Me/7-Me_3, 6-Me/7-Me_3. − ^{13}C NMR ($CDCl_3$): δ = 17.8 (q, 5-Me), 18.3 (q, C-1), 19.1 (q, 6-Me), 29.8 (3q, 7-Me_3), 35.9 (s, C-7), 130.4 (s, C-5), 131.9 (d, C-3), 140.4 (s, C-6), 145.7 (d, C-2), 203.2 (s, C-4). − MS (EI): m/z (%) = 41 (81) $[C_3H_5]$, 57 (76) $[C_4H_9]$, 69 (65) $[C_5H_9]$, 109 (38) $[M^+ - C_5H_{11}]$, 124 (30) $[M^+ - C_4H_8]$, 137 (24) $[M^+ - C_3H_7]$, 150 (9) $[M^+ - 2CH_3]$, 165 (100) $[M^+ - CH_3]$, 180 (10) $[M^+]$. − Odor: Fruity, smelling intensely of apples, but also reminiscent of dried fruits, with a somewhat celery- and jasmon-like side, and additional agrestic aspects.

Floral-Fruity Feminine Fragrance Featuring 3: 10 g of perfume oil was compounded from 30 mg of Adoxal® (*Givaudan*, 2,6,10-trimethylundec-9-enal), 150 mg of a 10% solution of Ambrofix® (*Givaudan*, 3a,6,6,9a-tetramethyldodecahydronaphtho[2,1-b]furan) in benzylbenzoate, 60 mg of benzyl acetate, 0.8 g of bergamot oil, 40 mg of Calone® 1951 [*CAL Pfizer*, 7-methyl-2H-1,5-benzodioxepin-3(4*H*)-one], 50 mg of cedryl methyl ether (*Kao*), 350 mg of citronellol, 150 mg of citronellyl acetate (3,7-dimethyloct-6-en-1-yl acetate), 20 mg of Dimetol® (*Givaudan*, 2,6-dimethylheptan-2-ol), 940 mg of DPG (dipropylene glycol), 10 mg of estragol (4-allylanisole), 350 mg of ethyl linalool (*Givaudan*, 3,7-dimethylnona-1,6-dien-3-ol), 30 mg of eugenol (4-allyl-2-methoxyphenol), 40 mg of a 10% solution of Floralozon® [*IFF*, 3-(4-ethylphenyl)-2,2-dimethylpropanal] in DPG, 30 mg of Floropal® (*H&R*, 2,4,6-trimethyl-4-phenyl-1,3-dioxan), 1.4 g of Galaxolide® 50 PHT (*IFF*, 4,6,6,7,8,8,-hexamethyl-1,3,4,6,7,8-hexahydrocyclopenta[*g*]benzopyran), 0.3 g of Gardenol® (*Rhodia*, 1-phenylethyl acetate), 1.2 g of Hedione® [*Firmenich*, (3-oxo-2-pentylcyclopentyl)acetic acid methyl ester], 170 mg of a 10% solution of (3*Z*)-hexenyl acetate in DPG, 90 mg of (3*Z*)-hexenyl salicylate, 0.6 g of Iso E Super® [*IFF*, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,8,8-tetramethylnaphthalen-2-yl)-ethan-1-one + 1-(1,2,3,5,6,7,8,8a-octahydro-1,2,8,8-tetramethylnaphthalen-2-yl)ethan-1-one], 350 mg of Isoraldein® 70 (*Givaudan*, isomeric 8-methylionones), 70 mg of lavender oil (French), 0.3 g of lemon oil (Italian), 0.9 g of Lilial® [*Givaudan*, 3-(4-*tert*-butylphenyl)-2-methylpropanal], 120 mg of a 10% solution of Melonal® (*Givaudan*, 2,6-dimethyl-5-hepten-1-al) in DPG, 60 mg of 3-(4-methoxyphenyl)-2-methylpropanal, 90 mg of 2-methyl-1-phenylprop-2-yl acetate, 150 mg of Sandalore® [*Givaudan*, 3-methyl-5-(2,2,3-trimethylcyclopent-3-en-1-yl)pentan-2-ol], 10 mg of Strawberry pure® (*Givaudan*, ethyl 3-methyl-3-phenylglycidate), 30 mg of taget oil, 0.1 g of α-terpineol (*p*-meth-1-en-8-ol), 0.5 g of a 10% solution of 5,6,7-trimethylocta-2,5-dien-4-one (**3**) in DPG, 480 mg of Tropional® [*Givaudan*, 2-methyl-3-(3,4-methylenedioxyphenyl)propanal], 10 mg of Viridine® (*H&R*, 1,1-dimethoxy-2-phenylethane), and 20 mg of ylang-ylang oil. This perfume oil was diluted with 90 mL of 90 vol.-% EtOH to provide a floral-fruity, aquatic composition with hesperidic-green top, floral heart note consisting of rose, lily-of-the-valley, and watermelon accords, and a fruity, musky-woody, dry down. Compound **3** blends very well with the rose accord, brings out the fruity aspects of this fragrance, and integrates the lavender note. In comparison with damascones, 5,6,7-trimethylocta-2,5-dien-4-one (**3**) conveys more lift to the hesperidic elements and confers more diffusivity to the composition.

Acknowledgments

We are grateful to U. Müller and R. Cadalbert for additional experimental work, to M. Jocher for the preparative multidimensional GC isolation of trace compound **4**, to N. Añorga, E. Senn, H. Koch, and A. Flückiger for GC-olfactometry analyses, to Dr. G. Brunner, J. Märki, and Dr. J. Schmid for spectroscopic data, and to Dr. R. Rueher, F. Hoffman-La Roche AG, CH-4070 Basel, for the elemental analysis.

---

[1] E. sz. Kováts, *J. Chromatogr.* **1987**, *406*, 185−222.

[2] D. Kastner, *Parfuem. Kosmet.* **1985**, *66*, 5−16.

[3] D. Kastner, *Parfuem. Kosmet.* **1994**, *75*, 170−181.

[4] E. Demol, P. Enggist, U. Säuberli, M. Stoll, E. sz. Kováts, *Helv. Chim. Acta* **1970**, *53*, 541−551.

[5] [5a] G. Ohloff, E. Demol, *J. Chromatogr.* **1987**, *406*, 181−183, and literature cited therein. − [5b] G. Ohloff, *Riechstoffe und Geruchssinn: Die molekulare Welt der Düfte*, Springer-Verlag, Berlin, **1990**, pp. 120−124. English edition: *Scent and Fragrances: The Fascination of Fragrances and their Chemical Perspectives*, Springer-Verlag, Berlin, **1994**, pp. 120−124, and further references cited therein.

[6] G. Fráter, J. A. Bajgrowicz, P. Kraft, *Tetrahedron* **1998**, *54*, 7633−7703.

[7] C. Fehr, J. Galindo, *Helv. Chim. Acta* **1986**, *69*, 228−235. Today, the industrial synthesis of **1**, **2**, and all their commercial derivatives at Firmenich SA, CH-1211 Geneva, is carried out

according to this route starting from methyl geraniate,[3] which in turn is produced from 6-methylhept-5-en-2-one.

[8] [8a] M. Gras, *Perfum. Flavor.* **1990**, *15*, 25–28. – [8b] M. Gras, *Perfum. Flavor.* **1992**, *17*, 1–12.

[9] P. Kraft, J. A. Bajgrowicz, C. Denis, G. Fráter, *Angew. Chem.* **2000**, *112*, 3106–3138; *Angew. Chem. Int. Ed.* **2000**, *39*, 2980–3010.

[10] [10a] C. Fehr, J. Galindo, *Angew. Chem.* **1994**, *106*, 1967–1969; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1888–1890. – [10b] C. Fehr, *Angew. Chem.* **1996**, *108*, 2726–2748; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2566–2587.

[11] [11a] K. Sestanj, *Croat. Chem. Acta* **1962**, *43*, 211–217. – [11b] P. Kraft, *Synthesis* **1999**, 695–703.

[12] Takasago Perfumery KK (T. Kobayashi, H. Sugiyama, H. Tsuruta, T. Yoshida), JP 1323532 (prior. August 15, 1978, JP 53-99202); *Chem. Abstr.* **1980**, *93*, 149797; AN 1980:549797; DW1985-32.

[14] C. D. Nenitzescu, I. Chicos, *Ber. Dtsch. Chem. Ges.* **1935**, *68*, 1584–1587.

[15] H. Vieregge, H. M. Schmidt, J. Renema, H. J. T. Bos, J. F. Arends, *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 929–951.

[16] W. M. Stalick, R. N. Hazlett, R. E. Morris, *Synthesis* **1988**, 287–290.

[17] [17a] H. Gilman, P. R. Van Ess, *J. Am. Chem. Soc.* **1933**, *55*, 1258–1261. – [17b] Recently, for example, employed in the synthesis of macrocycles by: L. Rodefeld, I. Heinemann, W. Tochtermann, *Tetrahedron* **1998**, *54*, 5265–5286.

Received December 8, 2000
[O00644]