Further Explorations into the Synthesis of Dehydro-*Hedione*®

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Dedicated to the memory of Professor *J. Weber* (University of Geneva)

Dehydrohedione (DHH) **1** may be obtained in 20% overall yield by a *Reformatsky* reaction with enone methyl ether **3b**, followed by acidic workup of the crude reaction mixture. Alternatively, epoxidation (3-chloroperbenzoic acid, CH_2Cl_2, 84% yield) of the tertiary allyl alcohol derivative **4** affords a 1:2 mixture of **8a** and **8b**. The latter epoxy ester **8b** may also be obtained stereoselectively either from **4** (^{t}BuO$_2$H, [Mo(CO)$_6$], 1,2-dichloroethane, 70°, 62% yield; or ^{t}BuO$_2$H, [VO(acac)$_2$], decane, 20°, 92% yield), or from **5** (AcOMe, LiN(SiMe$_3$)$_2$, THF, −78°, 84–87%). $BF_3 \cdot Et_2O$-Catalyzed cascade rearrangement and OH elimination of **8a** afford selectively DHH **1** in 88% yield. The *cis* disposition of the side chains of the weakly odoriferous hedione-like analogues **2b** and **2c** was maintained by means of either an epoxy or a cyclopropane moiety.

Introduction. – The didehydro derivative **1** of *Hedione*®, called dehydrohedione (DHH) [1], is a key intermediate for both racemic and asymmetric industrial hydrogenations, directed towards either racemic *cis-Hedione*® **2a** [2a–2c], or its olfactively more precious enantiomer (+)-(1*R*,2*S*)-*Paradisone*® **2a** [2d–2j][2]). DHH **1** was earlier prepared from racemic **2a** (*ca.* 90:10 *trans*/*cis*-stereoisomers) by either bromination–elimination [1a] (< 80%), direct HIO_3 oxidation [1b] (65%), or by anodic [1c] (69%), or peracetic [1d] (63%) oxidation of the corresponding enol acetate. Several approaches to **1** were also reported starting from the industrially available cyclopentenone **3a** [1c][9], like the unselective direct addition of methyl diazoacetate [1e] (25%), or *via* either the CrO_3 oxidation of **4** [1f][1g] (87%)[3]), or *via* a *Horner–Wittig* reaction of the epoxycyclopentanone **5** [12], and rearrangement of the corresponding epoxy ester **6** [1h] (80%). Moreover, the desired compound **1** was also obtained by electroreductive intramolecular coupling of a keto nitrile [1i][1j] (10%), or

[1]) Deceased on 21st June 2009. Work performed in 1997.

[2]) (−)-*trans*-(1*R*,2*R*)-*Hedione*® (*ca.* 94:6 *trans*/*cis*) was discovered in 1957 by hydrogenation of (−)-methyl jasmonate, isolated from the Mediterranean *Jasminum grandiflorum* L. Its structure and use were protected in 1960 [3], and published two years later [4]. It was then found in tea flavor [5], in the nonacidic, intensely sweet, Brazilian Lima orange [6], as well as in several other plants [6], and its *trans*- and *cis*-racemate, as well as the optically active *Paradisone*® (*ca.* 93:7 *cis*/*trans* mixture), became ubiquitous bulk building blocks in perfumery [7], thus rendering their natural occurrence more difficult to put into evidence, due to possible artefacts. For reviews and historical discussions of methyl jasmonate and *Hedione*®, see [8].

[3]) As alternative to either pyridinium dichromate in CH_2Cl_2 at 0° [10], or TEMPO, iodosylbenzene in CH_2Cl_2 in the presence of cat. Bi(OTf)$_3$ and 4-Å molecular sieves [11].

more efficiently, *via* a *Baylis–Hillman* reaction from simple cyclopent-2-en-1-one [13], followed by a cascade orthoester *Claisen* rearrangement, with double-bond isomerization [1b] (60%). Finally, the correct state of oxidation may also be reached by 1,4-addition of dimethyl malonate either to the reported 3-methoxy-2-pentylcyclopent-2-en-1-one **3b** [1k][2a] (48%)[4]), or to the doubly unsaturated known cyclopentenone **7** [14] (45%) [1l], followed by de(methoxycarbonylation). We would like here to present alternative approaches, starting from either intermediates **3b**, **4**, or **5** (*Scheme*).

Results and Discussion. – Epoxidation of the tertiary allyl alcohol derivative **4**[5]) (3-chloroperbenzoic acid (MCPBA), CH_2Cl_2) afforded a 1:2 mixture of epoxy esters **8a**/**8b** in 84% yield[6]). They could be separated by column chromatography (CC; SiO_2). Alternatively, **8b** could also be obtained stereoselectively, either in 87% yield by addition of the $LiN(SiMe_3)_2$ generated methyl acetate enolate to the epoxy ketone **5**[7]), or by applying the anhydrous conditions reported by *Fehr* [18]. Thus, when hydroxy ester **4** was treated either with $^t BuO_2H$, $[Mo(CO)_6]$, and Na_2HPO_4 in 1,2-dichloroethane at 70°, or with $^t BuO_2H$ and $[VO(acac)_2]$ in decane at 20°, pure **8b** could be isolated in 62 and 92% yield, respectively[8]). The pure *cis* isomer **8b** (*cis* of OH and epoxy) was then treated with $BF_3 \cdot Et_2O$ in toluene at 20° to afford a 66:34 mixture of DHH **1** and dihydroxylactone **9b**, isolated by CC (SiO_2) in 52 and 31% yield, respectively[9]).

We anticipated that the *trans*-diastereoisomer **8a** (*trans* of OH and epoxy) would react more selectively during the catalyzed cascade rearrangement and OH elimination, since the CH_2COOMe moiety is not *trans* with respect to the epoxy moiety, and thus less prone to ring closure forming the lactone **9a**. Indeed, we were pleased to observe the formation of a 97:3 mixture of DHH **1** and dihydroxylactone **9a** after treatment with $BF_3 \cdot Et_2O$ in toluene (91% yield). This latter diol was oxidized to

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4) No chemical yield was reported in [2a].

5) Hydroxy ester **4** was obtained from **3a**, either by addition of $BrCH_2CO_2Me$ in the presence of Zn in toluene (60% yield) [1f] or of AcOMe in the presence of $LiN(SiMe_3)_2$ in THF at −78° (84% yield) [1g], as an alternative to the AcOMe, addition in the presence of lithium diisopropylamide (LDA) and CeF_3 in THF at −60° [15a]. An excess of base should be avoided since **3a** readily self-condenses into **I**. Furthermore, a nonacidic workup is imperative, otherwise **4** dehydrates into a 2:1 mixture of the uncharacterized (*E*)-ester **II** [16], and its unreported isomer **III** (see *Fig. 1*).

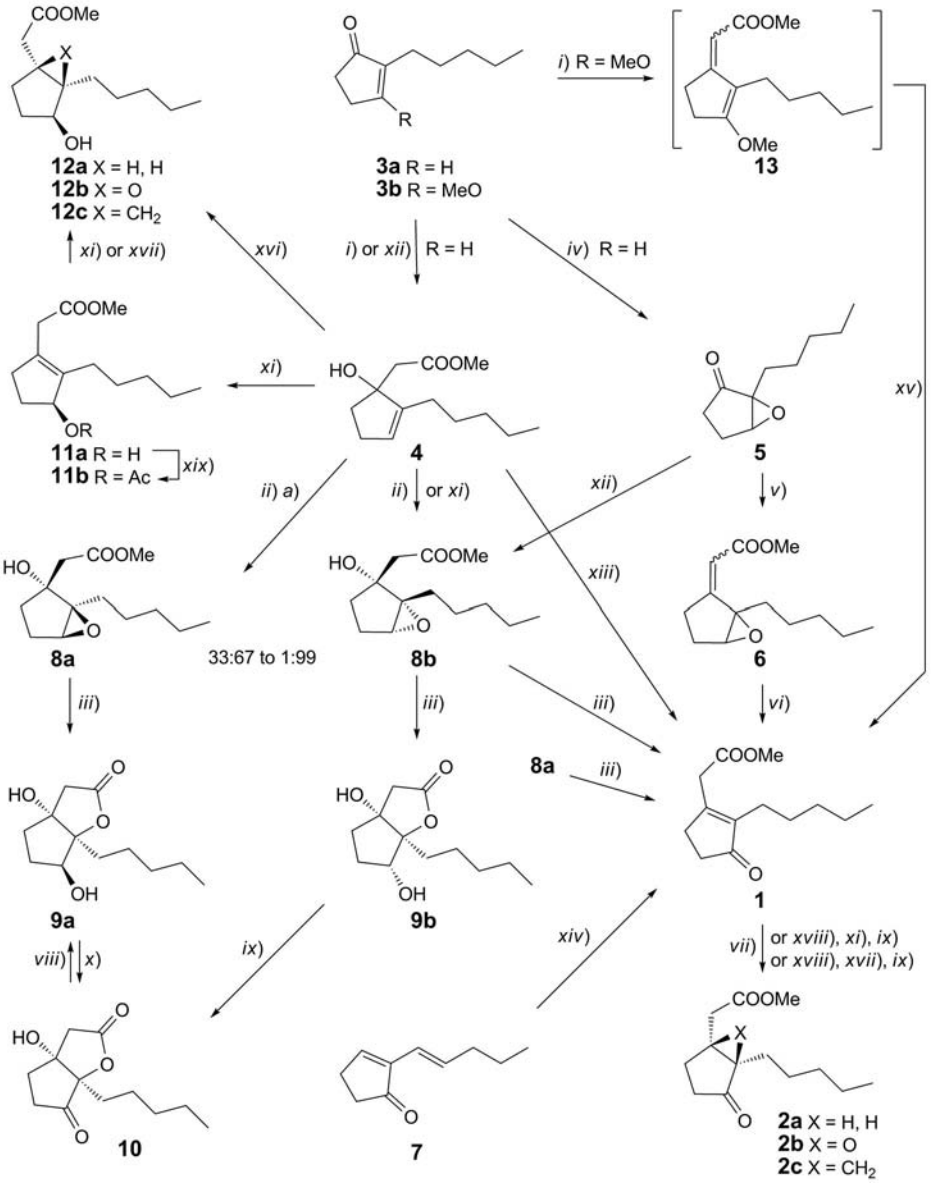
6) For an analogous 1:10 *anti*/*syn* epoxidation with MCPBA of identical diastereoselectivity directed by the OH function, see [17]. The worse diastereoselectivity observed in our case may be rationalized by H-bond complexation of the methoxycarbonyl group with either the hydroxy group or the peracid.

7) Nucleophilic 1,2-*Grignard* additions to a keto group at such skeletons were earlier reported as stereoselectively approaching *anti* to the epoxy moiety [17d].

8) For OH *syn* directing epoxidation using $^t BuO_2H$, see [19]. Alternatively, *Sharpless* conditions using *rac*-DET or *rac*-BINOL gave no reaction [20].

9) When pure **8b** was treated for 3 h at 200° with neutral Alox (50% by weight), a 87:13 mixture of DHH **1** and **9b** was obtained, and **1** could be isolated in 40% yield by CC SiO_2. Alternatively, when treated with 0.25 mol-equiv. of TsOH in refluxing cyclohexane for 6 h, a 72:28 mixture of **1** and **9b** was isolated. Concurrent formation of lactone **9b** is consistent with the *anti*-stereochemistry of the carbomethoxy functionality in **8b**. In some instances, under anhydrous conditions, alcohol **IV** could be isolated as intermediate towards DHH **1** (see *Fig. 1*).

Scheme



i) $BrCH_2CO_2Me$, Zn, toluene; 26–60%. *ii*) *a*) MCPBA, CH_2Cl_2; 84%, 1:2; or *b*) $^tBuO_2H$, $[Mo(CO)_6]$, Na_2HPO_4, 1,2-dichloroethane; 62%. *iii*) $BF_3 \cdot Et_2O$, toluene, 20°; 52–91%. *iv*) 70% H_2O_2, KOH, K_2CO_3, MeOH; 61%. *v*) $(MeO)_2P(O)CH_2CO_2Me$, MeONa, pentane; 91%. *vi*) H_2SO_4, Et_2O, 4°, or $SnCl_4$, toluene; 95%. *vii*) H_2, 5% Pd/C, cyclohexane, 0°; 98%. *viii*) $NaBH_4$, ^iPrOH; 60%. *ix*) PCC, CH_2Cl_2, 54%. *x*) *Jones* reagent, acetone; 77%. *xi*) $^tBuO_2H$, $[VO(acac)_2]$, H_2O/cyclohexane or anh. decane/toluene, 20–80°; 10–92%. *xii*) AcOMe, $LiN(SiMe_3)_2$, THF, −78°; 84–87%. *xiii*) CrO_3, dioxane, H_2SO_4; 87%. *xiv*) 1. MeONa, MeOH, dimethyl malonate; 45%; 2. NaCl, 1-methylpyrrolidin-2-one (NMP), 180°; 98%; *xv*) 10% aq. HCl, 20% from **3b**. *xvi*) H_2O_2, $(CF_3CO)_2O$, Na_2CO_3, CH_2Cl_2; 56%. *xvii*) Et_2Zn, CH_2I_2, CH_2Cl_2, 40°; 87%. *xviii*) 10 mol-% of (*R*)-methyloxazaborolidine, $BH_3 \cdot SMe_2$, THF; 92% ee, 92%. *xix*) Ac_2O, Py; >98%.

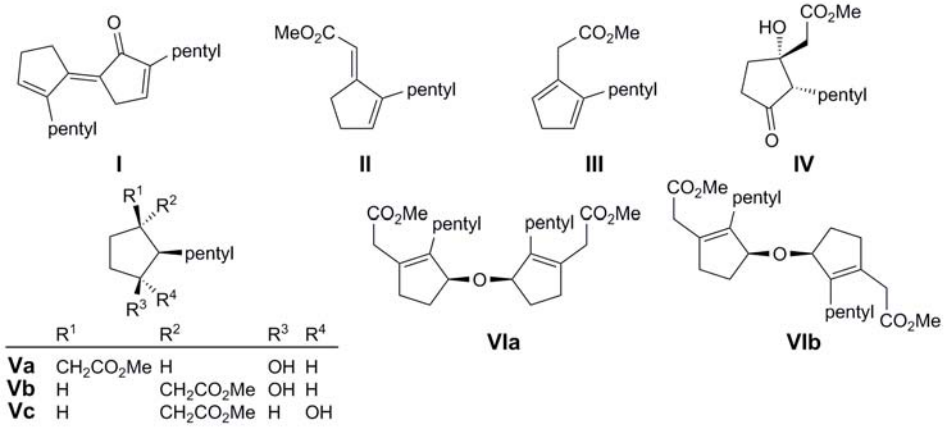


Fig. 1. *Isolated by-products*

ketone **10** (*Jones* reagent, acetone, 77% yield), and was recovered from **10**, *via* probable assistance of the free carbinol OH group, by stereoselective reduction with $NaBH_4$ in ^{i}PrOH (60% yield). Alternatively, oxidation of **9b** (pyridinium chlorochromate (PCC), CH_2Cl_2) also afforded ketone **10** in 54% yield. To reverse the diastereoselectivity during the epoxidation[10]) [22], attempts to protect the tertiary alcohol moiety as directing functionality with either a sterically demanding group (Me_3SiCl, 1*H*-imidazole, CH_2Cl_2, 20°; or $Me_3SiOSO_2CF_3$, Et_3N, CH_2Cl_2, −78°, or 0° [23]), or as a simpler methyl ether (NaH, MeI, THF), or acetate (AcCl, AgCN, toluene, 55°) failed, and essentially resulted in exocyclic elimination.

The junction of two five-membered rings in lactones **9** (*Fig. 2*) implies a *cis* relationship between the pentyl substituent and the tertiary-alcohol function. We initially unsuccessfully tried to ascertain the configuration of **9** based on the *Overhauser* effects. Indeed, for **9a**, irradiation of the pseudoaxial H–C(6) at the secondary-alcohol centre resulted in enhancement of the signals of $CH_2(1')$ and $CH_2(2')$ of the pentyl side chain, as well as of those of $CH_2(4)$. For **9b** the same irradiation on the pseudoequatorial H–C(6) resulted in enhancement of the $CH_2(2')$ signals of the pentyl

[10]) Treatment of **4** with 70% aq. ^{t}BuO$_2$H and [VO(acac)$_2$] in cyclohexane at 80° [15] resulted in 10% rearrangement into the corresponding unreported secondary-alcohol derivative **11a**, as the transient intermediate in the oxidation of **4** to **1** [1f][1g]. Hydroxy ester **11a** was also earlier obtained by *V. Rautenstrauch via* reduction of **1** (1992). Its octanoyl ester was used as a slow-release perfuming ingredient after washing textile in the presence of a lipase-containing detergent [21]. Treatment of **4** with AcO_2H in toluene furnished only the starting material **4** accompanied by a multitude of nonisolated by-products. Exocyclic elimination towards **II** occurred when **4** was treated with 35% H_2O_2 and maleic anhydride in CH_2Cl_2 at 20° for 24 h (53% yield). Treatment of **4** with CF_3CO_3H in CH_2Cl_2 also afforded **II** (38% yield), besides epoxy ester **12b** (56% yield). Alternatively, **12b** was also obtained in 47% yield by treatment of the allyl alcohol derivative **11a** with anh. ^{t}BuO$_2$H, [VO(acac)$_2$] in toluene at 20°. Further oxidation of **12b** (PCC, CH_2Cl_2, 79–94 % yield) afforded epoxy ester **2b**. The alternative cyclopropanation of **11a** (Et_2Zn, CH_2I_2, CH_2Cl_2, 40°; 87% yield) afforded, after PCC oxidation of **12c** (37–85% yield), the analogue **2c**. The more volatile nor analogue of **2c** carrying a butyl instead of a pentyl side chain shall be reported in due course.

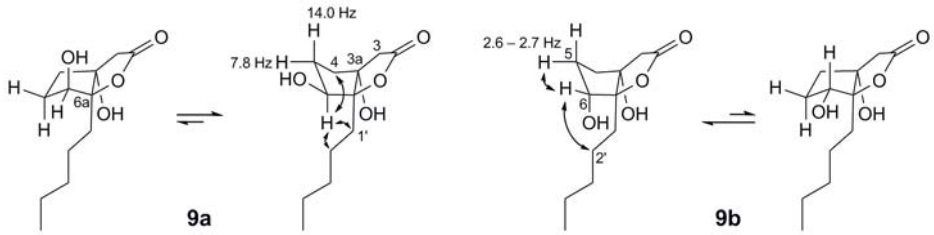


Fig. 2. *Attributions* via ^{1}*H-NMR and conformational analyses of* **9a** *and* **9b**

side chain, as well as of the $CH_2(5)$ signals. The problem is that the $CH_2(4)$ and $CH_2(5)$ signals are superimposed, and this precludes any confirmation of the configuration. We thus decided to compare the theoretical and experimental coupling constants of H–C(6). The B3LYP/6-31G** [24] conformational analysis of **9a** suggests that the pseudoequatorial secondary-alcohol derivative is 1.5 kcal/mol more stable than the conformation with this OH substituent in the pseudoaxial position. As a consequence, large coupling constants (calculated 6.1 and 10.3 Hz) are expected and compare well with the observed data ($^3J(6,5) = 7.8$ and 14.0 Hz). Alternatively, the *cis*-diol derivative **9b** prefers to orientate its secondary-alcohol function in the pseudoaxial position as compared to the 3.0 kcal/mol less stable pseudoequatorial conformer. Consequently, this diastereoisomer should exhibit smaller coupling constants (calculated 2.0 and 3.7 Hz) as experimentally observed ($^3J(6,5) = 2.6$ and 2.7 Hz). These considerations allowed definitive attributions.

Finally, treatment of cyclopentenone **3b** with Zn and $BrCH_2CO_2Me$ in toluene (26% yield) afforded directly the conjugated ester **13**[11]) as a 87:13 (*E*)/(*Z*) mixture. This latter does not need to be isolated since a subsequent hydrolytic treatment (10% aq. HCl) furnished DHH **1**[12]) in 20% global yield from **3b**.

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[11]) Ester **13** was also earlier obtained by *V. Rautenstrauch via O*-alkylation of the enolate derived from DHH **1** (1994).

[12]) Reduction of **1** to (3*S*)-**11a** catalyzed by 10 mol-% of (*R*)-methyloxazaborolidine was performed analogously to [16] (92% ee, 92% yield). The ee of (3*S*)-**11a** was measured by chiral GLC analysis (*Chirasil-Dex-CB* column (25 m × 0.25 mm), He, 1.2 ml/min, 150°) of the corresponding base-line separated acetate (3*S*)-**11b**: t_R (minor) 22.33 and t_R (major) 23.24 min, order of elution consistent with [16]. The absolute configuration was tentatively ascertained by hydrogenation of (3*S*)-**11a** (H_2, 2.5%/(*w*/*w*) *Adams* catalyst, AcOEt [25a]) to (1*S*,2*R*,3*S*)-**Va** [2g] (87% ee after PCC/CH_2Cl_2 oxidation to (−)-*cis*-(1*S*,2*R*)-*Paradisone*®), separated by CC/(SiO_2) from a 7:3 *trans*/*cis* mixture (42% ee) of (+)-(1*S*,2*S*)/(−)-(1*S*,2*R*)-*Paradisone*® resulting from competing double bond isomerization, as well as from (1*R*,2*R*,3*S*)-**Vb** (see *Fig.* 1; 82% ee after PCC/CH_2Cl_2 oxidation to (−)-*trans*-(1*R*,2*R*)-*Paradisone*®). In the presence of 2.5%/(*w*/*w*) of *Crabtree*'s catalyst in CH_2Cl_2 [25b], (3*S*)-**11a** gave (1*R*,2*S*,3*S*)-**12a** [2i] in 85% yield. Finally, this hydrogenation was unsuccessful with *Raney*-Ni in MeOH under normal pressure. In 1995, *V. Rautenstrauch* showed that DHH **1**, treated with D_2 and 5% Pd/C in cyclohexane, incorporates some D in all positions of the cyclopentanone moiety, as well as in the first ring-attached CH_2 group of each of its substituents (*cf.* [8d]). For the sake of completeness, stereoisomer (1*R*,2*R*,3*R*)-**Vc** [2h] was obtained by $NaBH_4$ reduction of (−)-(1*R*,2*R*)-*Paradisone*® [2d]. Interestingly, when treated with *Crabtree*'s catalyst, racemic **11a** afforded essentially a *ca.* 1:1 mixture of **VIa**/**VIb** separated by CC/(SiO_2) [26] (see *Fig. 1*).

Conclusion. – The *trans*-epoxy-hydroxy ester **8a** (*trans* of OH and epoxy) is required for efficient cascade rearrangement and OH elimination towards DHH **1** (88% yield). This latter may also be obtained directly from **3b** *via* a *Reformatsky* reaction, followed by an acidic workup. The nonepimerizable *cis*-disposition of the side chains in **2b** and **2c**, obtained by introduction of either an epoxy or a cyclopropane moiety [27], led to less volatile and much weaker hedione-like analogues.

We are indebted to Mrs. *S. Gallo-Fluckiger*, as well as to our apprentices *H. Belloto*, *L. Gachet*, and *M. Crétignier* for their experimental skill.

Experimental Part

General. See [28].

Methyl 3-Oxo-2-pentylcyclopent-1-ene-1-acetate (**1**). To a soln. of hydroxy ester **8a** (120 mg, 0.5 mmol) in toluene (5 ml) at 20°, was added $BF_3 \cdot Et_2O$ (0.05 ml, 0.4 mmol). After 20 h at 20°, the mixture was diluted with Et_2O (20 ml), washed with sat. aq. $NaHCO_3$ soln., dried (Na_2SO_4), and concentrated: **1**/**9a** 97:3 (91%).

Alternatively, to a stirred soln. of hydroxy ester **8b** (1200 mg, 5 mmol) in toluene (30 ml) at 0° was added $BF_3 \cdot Et_2O$ (1.24 ml, 10 mmol). After 40 h at 20°, the mixture was worked up as described above: **1**/**9b** 67:33 (95%). A bulb-to-bulb distillation afforded pure **1** (52%) as well as pure **9b** (37%). In this latter case and in some instances, under anh. conditions, intermediate **IV** (see below) could be isolated in traces for anal. purposes, by CC (SiO_2).

DHH **1** was also obtained in 20% global yield from **3b**, after bulb-to-bulb distillation, when the workup of **13** was performed with 10% aq. HCl soln. B.p. 175°/0.3 mbar. For analyses, see [1].

*Methyl (1*RS,*5*SR*)-4-Oxo-5-pentyl-6-oxabicyclo[3.1.0]hexane-1-acetate* (**2b**). A mixture of **12b** (20 mg, 0.078 mmol), PCC (25.6 mg, 0.116 mmol), and *Celite*® (530 mg) in CH_2Cl_2 (20 ml) was stirred for 2.5 h at 20°. The mixture was filtered, the filtrate concentrated, and the residue purified by CC (SiO_2, cyclohexane/AcOEt 9:1): **2b** (79%). Very weak hedione-like, metallic scent. IR: 2954, 2929, 2870, 2858, 1739, 1456, 1436, 1350, 1326, 1270, 1199, 1177, 1144, 1111, 1054, 1007, 989, 863, 726, 703, 684. ^{1}H-NMR: 0.89 (*t*, *J* = 6.5, 3 H); 1.29–1.33 (*m*, 4 H); 1.44–1.51 (*m*, 2 H); 1.64 (br. *s*, 1 OH); 1.67–1.73 (*m*, 2 H); 2.05–2.16 (*m*, 2 H); 2.32–2.41 (*m*, 2 H); 2.75 (*d*, *J* = 17, 1 H); 2.87 (*d*, *J* = 17, 1 H); 3.75 (*s*, 3 H). ^{13}C-NMR: 210.8 (*s*); 169.7 (*s*); 68.8 (*s*); 67.0 (*s*); 52.2 (*q*); 36.5 (*t*); 32.1 (*t*); 31.8 (*t*); 25.7 (*t*); 24.4 (*t*); 23.6 (*t*); 22.4 (*t*); 13.9 (*q*). MS: 240 (3, M^+), 194 (7), 183 (21), 167 (54), 151 (29), 153 (50), 141 (67), 137 (25), 129 (87), 123 (65), 111 (100), 99 (51), 97 (29), 95 (34), 83 (97), 81 (38), 71 (43), 69 (35), 59 (45), 55 (84), 53 (33), 43 (78), 41 (48), 28 (41).

*Methyl (1*S,*5*R*)-4-Oxo-5-pentyl-6-oxabicyclo[3.1.0]hexane-1-acetate* ((1*S*,5*R*)-**2b**). As described for **2b**: (1*S*,5*R*)-**2b** (94%). $[\alpha]_D^{20} = +38.0$ ($c = 0.034$, $CHCl_3$). Without olfactive character, similar to **2b**.

*Methyl (1*RS,*5*SR*)-4-Oxo-5-pentylbicyclo[3.1.0]hexane-1-acetate* (**2c**). As described for **2b**, from **12c**: **2c** (37%). Very weak hedione-like scent, without character. IR: 3064, 2963, 2938, 2880, 1744, 1439, 1331, 1174, 1063, 1024. ^{1}H-NMR: 0.88 (*t*, *J* = 7.1, 3 H); 0.96 (*d*, *J* = 5, 1 H); 1.19 (*d*, *J* = 5, 1 H); 1.23–1.33 (*m*, 5 H); 1.34–1.46 (*m*, 3 H); 1.91–1.98 (*m*, 1 H); 2.09–2.12 (*m*, 2 H); 2.17–2.22 (*m*, 1 H); 2.43 (*d*, *J* = 15, 1 H); 2.65 (*d*, *J* = 15, 1 H); 3.73 (*s*, 3 H). ^{13}C-NMR: 215.0 (*s*); 171.9 (*s*); 51.8 (*q*); 41.2 (*s*); 38.4 (*t*); 34.3 (*s*); 32.6 (*t*); 32.2 (*t*); 27.3 (*t*); 27.1 (*t*); 26.8 (*t*); 24.2 (*t*); 22.6 (*t*); 14.0 (*q*). MS: 238 (21, M^+), 179 (30), 164 (100), 136 (44), 121 (37), 109 (63), 107 (60), 95 (37), 93 (43), 81 (34), 79 (55), 77 (33), 74 (24), 65 (25), 55 (38), 41 (29).

*Methyl (1*S,*5*R*)-4-Oxo-5-pentylbicyclo[3.1.0]hexane-1-acetate* ((1*S*,5*R*)-**2c**). As described for **2b**, from (1*S*,4*S*,5*R*)-**12c**: (1*S*,5*R*)-**2c** (85%). Weakly hedione-like, slightly mushroom. $[\alpha]_D^{20} = +30.0$ ($c = 0.04$, $CHCl_3$).

*Methyl (1*RS,*2*SR,*5*RS*)-2-Hydroxy-1-pentyl-6-oxabicyclo[3.1.0]hexane-2-acetate* (**8a**). As described for **8b**. IR: 3473, 2953, 2932, 2861, 1735, 1437, 1339, 1312, 1204, 1164, 1109, 1045, 1008, 957, 909, 886, 833, 729, 669. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H); 1.24–1.33 (*m*, 6 H); 1.49–1.58 (*m*, 1 H); 1.64–1.75 (*m*, 2 H);

1.87–1.94 (*m*, 2 H); 1.97–2.06 (*m*, 1 H); 2.57 (*d*, *J* = 16, 1 H); 2.74 (*d*, *J* = 16, 1 H); 3.47 (*s*, 1 H); 3.64 (*s*, 10 H); 3.72 (*s*, 3 H). ^{13}C-NMR: 174.0 (*s*); 78.7 (*s*); 68.8 (*s*); 61.8 (*d*); 51.9 (*q*); 39.4 (*t*); 34.6 (*t*); 32.1 (*t*); 24.9 (*t*); 24.1 (*t*); 24.0 (*t*); 22.6 (*t*); 14.0 (*q*). MS: 242 (1, M^+), 224 (16), 183 (10), 167 (60), 153 (62), 130 (50), 116 (31), 111 (45), 99 (40), 83 (35), 71 (36), 69 (40), 55 (85), 43 (100).

*Methyl (1*RS*,2*RS*,5*RS*)-2-Hydroxy-1-pentyl-6-oxabicyclo[3.1.0]hexane-2-acetate* (**8b**). To a soln. of hydroxy ester **4** (820 mg, 3.6 mmol) in CH_2Cl_2 (20 ml) at 0° was added portionwise 50% MCPBA (1720 mg, 5.0 mmol). After 3 h at 20°, the mixture was washed with 10% aq. NaOH soln., 5% aq. NaOH soln., and sat. aq. $NaHCO_3$ soln., the org. phase dried (Na_2SO_4) and concentrated, and the residue (0.78 g) bulb-to-bulb distilled: **8a**/**8b** 1:2 (84%). Pure **8a** (23%) and **8b** (24%) were obtained after CC (SiO_2, toluene/AcOEt 4:1). Alternatively, 1M of $LiN(SiMe_3)_2$ in THF (25 ml, 25 mmol) at −78° was added to AcOMe (2.0 ml, 25 mmol), and after 15 min at −78°, epoxy ketone **5** (3.36g, 20 mmol) was added dropwise. After 30 min at −78°, pentane (10 ml) was added, then 10% aq. HCl soln. (15 ml), and the mixture was allowed to reach 0° before dilution with Et_2O (10 ml). The mixture was washed with H_2O, sat. aq. $NaHCO_3$ soln., and brine, the org. phase dried (Na_2SO_4) and concentrated, and the reddish oil (4.9 g, **8a**/**8b** 4:96) purified by bulb-to-bulb distillation: pure **8b** (87%; **8a**/**8b** 1:99).

Alternatively, a mixture of $[Mo(CO)_6]$ (10.6 mg, 0.04 mmol), 1,2-dichloroethane (5 ml), and 5.5M ^{t}BuO$_2$H in decane (0.66 ml, 3.63 mmol) was heated at 70° for 0.5 h and then introduced within 0.25 h into a stirred mixture of **4** (510 mg, 2.14 mmol), Na_2HPO_4 (11 mg, 0.076 mmol), and 1,2-dichloroethane (10 ml) at 70°. After 3.5 h, the mixture was cooled and worked up as above: **8b** (62%) after CC (SiO_2, cyclohexane/AcOEt 9:1 → 85:15).

Alternatively, 5.5M ^{t}BuO$_2$H in decane (0.211 ml, 1.16 mmol) was added dropwise to a soln. of **4** (200 mg, 0.773 mmol) and $[VO(acac)_2]$ (6 mg, 0.023 mmol) in toluene (15 ml) at 20°. After 6h at 20°, the red mixture was poured onto sat. aq. $NaHCO_3$ soln., and diluted with Et_2O. The org. phase was washed with 20% aq. Na_2SO_3 soln. and H_2O, dried (Na_2SO_4), and concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 8:2): pure **8b** (92%). B.p. 120°/0.3 mbar; 125°/0.5 mbar. IR: 3476, 3021, 2953, 2933, 2861, 1735, 1437, 1340, 1312, 1203, 1164, 1108, 1009, 958, 909, 886, 669. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H); 1.24–1.34 (*m*, 4 H); 1.42–1.50 (*m*, 1 H); 1.57–1.70 (*m*, 4 H); 1.85–1.93 (*m*, 1 H); 1.96–2.08 (*m*, 2 H); 2.47 (*d*, *J* = 14.7, 1 H); 2.70 (*d*, *J* = 14.7, 1 H); 2.99 (*s*, 10 H); 3.37 (*s*, 1 H); 3.73 (*s*, 3 H). ^{13}C-NMR: 171.8 (*s*); 79.3 (*s*); 69.0 (*s*); 61.0 (*d*); 51.9 (*q*); 40.4 (*t*); 33.4 (*t*); 32.2 (*t*); 25.4 (*t*); 25.3 (*t*); 23.8 (*t*); 22.5 (*t*); 14.0 (*q*). MS: 242 (1, M^+), 224 (17), 183 (10), 167 (60), 153 (60), 130 (47), 116 (32), 111 (47), 99 (42), 83 (36), 71 (37), 69 (39), 55 (85), 43 (100).

*(3a*RS*,6*RS*,6a*SR*)-Hexahydro-3a,6-dihydroxy-6a-pentyl-2*H*-cyclopenta[*b*]furan-2-one* (**9a**). To a soln. of keto lactone **10** (250 mg, 1.1 mmol) in ^{i}PrOH (5 ml) at 0° was added $NaBH_4$ (50 mg, 1.3 mol). The mixture was allowed to reach 20°, and after 1 h, the mixture was diluted with Et_2O (20 ml) and washed twice with brine (10 ml), the org. phase dried (Na_2SO_4) and concentrated and the residue bulb-to-bulb distilled: pure **9a** (60%). B.p. 175°/0.2 mbar. IR: 3396, 2955, 2931, 2872, 1749, 1456, 1408, 1379, 1312, 1255, 1237, 1207, 1161, 1091, 1043, 987, 952, 899, 816. ^{1}H-NMR: 0.90 (*t*, *J* = 7, 3 H); 1.30–1.36 (*m*, 4 H); 1.45–1.55 (*m*, 3 H); 1.69–1.73 (*m*, 1 H); 1.73–1.80 (*m*, 2 H); 2.06–2.13 (*m*, 2 H); 2.77 (*d*, *J* = 19.5, 1 H); 2.86 (br. *s*, 1 OH); 2.91 (*d*, *J* = 19.5, 1 H); 3.13 (br. *s*, 1 OH); 3.94 (*dd*, *J* = 14, 7.8, 1 H). ^{13}C-NMR: 175.5 (*s*); 95.7 (*s*); 81.5 (*s*); 75.9 (*d*); 45.0 (*t*); 37.1 (*t*); 32.4 (*t*); 32.3 (*t*); 29.9 (*t*); 22.8 (*t*); 22.5 (*t*); 14.0 (*q*). MS: 228 (1, M^+), 129 (100), 111 (34), 101 (40), 99 (45), 83 (70), 71 (23), 55 (41), 43 (52).

*(3a*RS*,6*RS*,6a*RS*)-Hexahydro-3a,6-dihydroxy-6a-pentyl-2*H*-cyclopenta[*b*]furan-2-one* (**9b**). See procedure for **1**. IR: 3440, 2955, 2931, 2871, 1748, 1459, 1448, 1412, 1375, 1312, 1256, 1239, 1215, 1161, 1137, 1118, 1096, 1040, 1023, 999, 950, 904, 882, 729, 634. ^{1}H-NMR: 0.91 (*t*, *J* = 7, 3 H); 1.31–1.37 (*m*, 4 H); 1.38–1.47 (*m*, 1 H); 1.52–1.68 (*m*, 2 H); 1.77–1.84 (*m*, 2 H); 1.86–1.95 (*m*, 1 H); 2.11–2.18 (*m*, 1 H); 2.20–2.30 (*m*, 1 H); 2.71 (*d*, *J* = 18, 1 H); 2.92 (*dd*, *J* = 3, 18, 1 H); 2.95 (br. *s*, 1 OH); 3.07 (br. *s*, 1 OH); 4.23 (*dd*, *J* = 2.6, 2.7, 1 H). ^{13}C-NMR: 174.6 (*s*); 98.1 (*s*); 82.7 (*s*); 75.5 (*d*); 43.5 (*t*); 40.4 (*t*); 32.4 (*t*); 30.3 (*t*); 29.4 (*t*); 23.1 (*t*); 22.6 (*t*); 14.0 (*q*). MS: 228 (1, M^+), 129 (100), 111 (32), 101 (35), 99 (40), 83 (59), 71 (18), 55 (35), 43 (48).

(*3a*RS*,6a*RS*)-Tetrahydro-3a-hydroxy-6a-pentyl-2*H*-cyclopenta[*b*]furan-2,6(3*H*)-dione* (**10**). To a suspension of PCC (860 mg, 4.0 mmol) in CH_2Cl_2 (10 ml) was added a soln. of **9b** (460 mg, 2 mmol) in CH_2Cl_2 (5 ml), and the mixture was stirred at 20° for 50 h. The mixture was diluted with Et_2O (20 ml) and filtered over *Florisil*, the filtrate concentrated, and the residue bulb-to-bulb distilled: pure **10** (54%).

Alternatively, to a soln. of **9a** (400 mg, 1.7 mmol) in acetone (10 ml) at 20° was added 2.1N *Jones* reagent (1 ml, 2.1 mmol), and the mixture was stirred at 20° for 1 h. After dilution with Et_2O, the mixture was washed with sat. aq. $NaHCO_3$ soln. and brine, the org. phase dried (Na_2SO_4) and concentrated, and the residue purified by bulb-to-bulb distillation: pure **10** (77%). B.p. 150°/0.2 mbar. IR: 3638, 2965, 2880, 1818, 1774, 1460, 1425, 1176, 1125, 1019, 955, 728. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.28–1.35 (*m*, 4 H); 1.35–1.42 (*m*, 1 H); 1.44–1.54 (*m*, 1 H); 1.76–1.93 (*m*, 2 H); 2.13–2.22 (*m*, 1 H); 2.28–2.36 (*m*, 1 H); 2.42–2.52 (*m*, 1 H); 2.60–2.70 (*m*, 1 H); 2.73 (*d*, *J* = 18.6, 1 H); 2.81 (*d*, *J* = 18.6, 1 H); 3.67 (br. *s*, 1 OH). ^{13}C-NMR: 211.9 (*s*); 174.5 (*s*); 91.8 (*s*); 80.6 (*s*); 42.3 (*t*); 35.1 (*t*); 32.2 (*t*); 30.7 (*t*); 29.1 (*t*); 22.3 (*t*); 22.2 (*t*); 14.0 (*q*). MS : 226 (0, M^+), 208 (8), 184 (18), 170 (41), 127 (10), 99 (100), 86 (18), 71 (19), 55 (14), 43 (38).

*Methyl (3*RS*)-3-Hydroxy-2-pentylcyclopent-1-ene-1-acetate* (**11a**). By-product isolated in 10% yield by CC (SiO_2) after treatment of **4** with 70% aq. ^{t}BuO$_2$H soln. (1.0 equiv.) and [VO(acac)$_2$] (0.015 equiv.) in refluxing cyclohexane for 7 h.

By analogy to [27], $NaBH_4$ (0.39 g, 10.31 mmol) was added portionwise at 20° to a mixture of DHH **1** (0.5 g, 2.05 mmol) and anh. $CeCl_3$ (518 mg, 2.08 mmol) in MeOH (15 ml). After 1.25 h at 20°, the mixture was poured onto ice/aq. sat. $NaHCO_3$ soln. and then extracted with Et_2O. The org. phase was washed with aq. sat. $NaHCO_3$ soln., dried (Na_2SO_4), and concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 8 :2): **11a** (42%). IR: 3417, 2954, 2929, 2856, 1738, 1455, 1435, 1323, 1263, 1195, 1170, 1044, 972, 730, 662. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.21–1.40 (*m*, 6 H); 1.45–1.51 (*m*, 1 H); 1.59 (br. *s*, 1 OH); 1.63–1.71 (*m*, 2 H); 2.10–2.18 (*m*, 2 H); 2.24–2.33 (*m*, 2 H); 2.43–2.53 (*m*, 1 H); 3.12 (*dd*, *J* = 5, 16, 1 H); 3.68 (*s*, 3 H). ^{13}C-NMR: 171.6 (*s*); 142.2 (*s*); 132.0 (*s*); 79.1 (*d*); 51.8 (*q*); 34.5 (*t*); 33.4 (*t*); 32.8 (*t*); 31.9 (*t*); 27.8 (*t*); 25.7 (*t*); 22.6 (*t*); 14.0 (*q*). MS: 226 (0, M^+), 208 (11), 165 (8), 152 (50), 134 (31), 119 (32), 109 (19), 107 (17), 105 (50), 91 (100), 79 (47), 77 (35), 67 (15).

*Methyl (3*S*)-3-Hydroxy-2-pentylcyclopent-1-ene-1-acetate* ((3*S*)-**11a**). (3*S*)-**11a** (92%), 92% ee. As described in [16]. $[\alpha]_D^{20} = -24.1$ ($c = 0.03$, $CHCl_3$).

*Methyl (3*S*)-3-(Acetyloxy)-2-pentylcyclopent-1-ene-1-acetate* ((3*S*)-**11b**). Ac_2O (1 ml) was added at 0° to a soln. of (3*S*)-**11a** (42 mg, 0.186 mmol) in pyridine (1 ml). After 1 h at 20°, the mixture was poured onto ice/10% aq. HCl soln. and then extracted with Et_2O. The org. phase was washed to neutral with H_2O, dried (Na_2SO_4), and concentrated and the residue purified by bulb-to-bulb distillation: (3*S*)-**11b** (> 98%). $[\alpha]_D^{20} = -2.7$ ($c = 0.56$, $CHCl_3$). IR: 2953, 2925, 2855, 1735, 1457, 1435, 1371, 1237, 1195, 1169, 1023, 963. ^{1}H-NMR: 0.88 (*t*, *J* = 7.3, 3 H); 1.10–1.43 (*m*, 6 H); 1.68–1.74 (*m*, 1 H); 1.98–2.14 (*m*, 2 H); 2.05 (*s*, 3 H); 2.28–2.39 (*m*, 2 H); 2.49–2.55 (*m*, 1 H); 3.11 (*d*, *J* = 16.5, 1 H); 3.20 (*d*, *J* = 16.5, 1 H); 3.68 (*s*, 3 H); 5.74 (br. *t*, *J* = 5.3, 1 H). ^{13}C-NMR: 171.2 (*s*); 171.1 (*s*); 138.2 (*s*); 135.0 (*s*); 81.5 (*d*); 51.9 (*q*); 34.5 (*t*); 33.9 (*t*); 31.8 (*t*); 29.7 (*t*); 29.6 (*t*); 27.6 (*t*); 25.9 (*t*); 22.5 (*t*); 21.3 (*q*); 14.0 (*q*). MS: 268 (0, M^+), 208 (35), 152 (86), 149 (17), 134 (38), 119 (28), 105 (45), 91 (100), 79 (38), 77 (24), 43 (20).

*Methyl (1*R*,2*S*,3*S*)-3-Hydroxy-2-pentylcyclopentaneacetate* ((1*R*,2*S*,3*S*)-**12a**). A soln. of (3*S*)-**11a** (100 mg, 0.398 mmol) in CH_2Cl_2 (5 ml) was hydrogenated over [Ir(cod)Py(PCy_3)]PF_6 (cod = cycloocta-1,5-diene, Cy = cyclohexyl; 3 mg) for 22 h. The mixture was concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 8 :2): (1*R*,2*S*,3*S*)-**12a** (85%). R_f (cyclohexane/AcOEt 8 :2) 0.26. GLC: (*DB-1*, 15 m, 250 μm, 0.25 mm, 100°, 1 min; 15°/min → 220°): t_R 6.65 min. $[\alpha]_D^{20} = +13.6$ ($c = 0.035$, $CHCl_3$). IR: 3415, 2953, 2926, 2858, 1737, 1459, 1436, 1376, 1258, 1194, 1170, 1060, 1011, 967, 886, 845, 721. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.10–1.19 (*m*, 1 H); 1.22–1.36 (*m*, 7 H); 1.49–1.58 (*m*, 1 H); 1.76–1.83 (*m*, 2 H); 1.90–1.98 (*m*, 1 H); 2.01–2.10 (*m*, 2 H); 2.14 (*dd*, *J* = 10, 14.6, 1 H); 2.38 (*dd*, *J* = 6.1, 14.6, 1 H); 2.58–2.67 (*m*, 1 H); 3.67 (*s*, 3 H); 3.98 (*dt*, *J* = 4.4, 6.8, 1 H). ^{13}C-NMR: 173.9 (*s*); 77.5 (*d*); 51.5 (*q*); 50.8 (*d*); 36.8 (*d*); 35.1 (*t*); 32.8 (*t*); 32.2 (*t*); 28.3 (*t*); 27.8 (*t*); 27.4 (*t*); 22.6 (*t*); 14.1 (*q*). MS: 228 (1, M^+), 210 (8), 197 (13), 185 (28), 169 (15), 153 (25), 150 (22), 139 (30), 136 (60), 121 (11), 110 (33), 107 (18), 100 (20), 95 (41), 93 (21), 83 (40), 81 (41), 79 (30), 74 (100), 69 (37), 67 (34), 59 (18), 57 (20), 55 (42), 43 (26), 41 (31).

*Methyl (1*RS*,4*RS*,5*RS*)-4-Hydroxy-5-pentyl-6-oxabicyclo[3.1.0]hexane-1-acetate* (**12b**). At 0°, 35% aq. H_2O_2 soln. (0.265 g, 2.73 mmol) was added dropwise to a soln. of trifluoroacetic anhydride (1.25g, 5.9 mmol) in CH_2Cl_2 (15 ml). After 0.5 h at 0°, this mixture was added dropwise at −50° to a mixture of **4** (0.5 g, 2.1 mmol) and Na_2CO_3 (0.67g, 6.3 mmol) in CH_2Cl_2 (15 ml). After 1.5 h, the cold mixture was poured onto 10% aq. Na_2SO_3 soln. and extracted. The org. phase was washed with aq. sat. $NaHCO_3$ soln.

and brine, dried (Na_2SO_4), and concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 95:5 → 8:2): pure **12b** (56%), besides the diene resulting from exocyclic elimination (38%).

Alternatively, 5.5M $^tBuO_2H$ in decane (0.11 ml, 0.605 mmol) was added dropwise at 20° to a soln. of **11a** (110 mg, 0.433 mmol) and [$VO(acac)_2$] (2 mg, 0.0072 mmol) in toluene (10 ml). After 18 h at 20°, the mixture was quenched with H_2O, and extracted with toluene. The org. phase was dried ($MgSO_4$) and concentrated and the residue purified by CC as described above: pure **12b** (47%). IR: 3453, 2953, 2930, 2860, 1739, 1456, 1435, 1325, 1264, 1201, 1172, 1144, 1072, 990, 943, 926, 884, 850, 726, 615. ^{1}H-NMR: 0.90 (*t*, *J* = 7, 3 H); 1.21–1.35 (*m*, 5 H); 1.39–1.47 (*m*, 2 H); 1.50–1.58 (*m*, 1 H); 1.66–1.76 (*m*, 2 H); 1.94–2.01 (*m*, 2 H); 2.10 (*dd*, *J* = 9, 14, 1 H); 2.61 (*d*, *J* = 16, 1 H); 2.72 (*d*, *J* = 16, 1 H); 3.72 (*s*, 3 H); 4.20 (br. *q*, *J* = 6.5, 1 H). ^{13}C-NMR: 170.4 (*s*); 74.0 (*d*); 71.3 (*s*); 66.8 (*s*); 51.9 (*q*); 36.3 (*t*); 32.2 (*t*); 28.3 (*t*); 28.2 (*t*); 27.4 (*t*); 24.8 (*t*); 22.5 (*t*); 14.0 (*q*). MS: 242 (2, M^+), 223 (28), 167 (43), 153 (84), 151 (65), 139 (13), 129 (53), 127 (42), 125 (31), 116 (51), 111 (100), 107 (21), 101 (22), 99 (55), 97 (35), 95 (28), 83 (42), 71 (38), 69 (130), 59 (38), 55 (62), 43 (68).

Methyl (1S,4S,5S)-4-Hydroxy-5-pentyl-6-oxabicyclo[3.1.0]hexane-1-acetate ((1*S*,4*S*,5*S*)-**12b**). As described for **12b**: (1*S*,4*S*,5*S*)-**12b** (63%). $[\alpha]_D^{20} = +1.5$ (*c* = 0.033, $CHCl_3$).

*Methyl (1*RS,*4*RS,*5*SR*)-4-Hydroxy-5-pentylbicyclo[3.1.0]hexane-1-acetate* (**12c**). Diiodomethane (126 mg, 0.47 mmol) was added dropwise at 20° to a soln. of 1M Et_2Zn (2 ml, 2.0 mmol) in CH_2Cl_2 (15 ml) and 1,2-dimethoxyethane (0.21 ml) in the presence of 4 Å molecular sieves. The mixture was heated at 40°, and a soln. of **11a** (107 mg, 0.426 mmol) in CH_2Cl_2 (5 ml) was added dropwise. After 7 h, the mixture was quenched at 20° by addition of NH_4Cl and then extracted with Et_2O. The org. phase was washed with 15% NaOH soln., then 10% HCl soln., and brine to neutrality, dried (Na_2SO_4), and concentrated and the residue purified by CC (SiO_2, cyclohehane/AcOEt 8:2): pure **12c** (87%). IR: 3416, 2953, 2927, 2859, 1737, 1452, 1435, 1322, 1261, 1245, 1216, 1200, 1166, 1057, 1013, 976. ^{1}H-NMR: 0.17 (*d*, *J* = 5.3, 1 H); 0.89 (*t*, *J* = 7.3, 3 H); 0.91 (*d*, *J* = 5.3, 1 H); 0.99–1.10 (*m*, 1 H); 1.23–1.68 (*m*, 9 H); 1.70 (br. *s*, 1 OH); 1.85–1.96 (*m*, 2 H); 2.27 (*d*, *J* = 15.5, 1 H); 2.43 (*d*, *J* = 15.5, 1 H); 3.68 (*s*, 3 H); 4.38 (*t*, *J* = 8.3, 1 H). ^{13}C-NMR: 173.0 (*s*); 77.0 (*d*); 51.5 (*q*); 38.3 (*t*); 36.1 (*s*); 32.4 (*t*); 31.2 (*t*); 29.8 (*t*); 29.7 (*t*); 29.0 (*s*); 27.0 (*t*); 22.7 (*t*); 15.5 (*t*) ; 14.1 (*q*). MS: 240 (3, M^+), 222 (7), 183 (12), 166 (70), 151 (24), 134 (18), 123 (19), 119 (12), 109 (41), 105 (47), 95 (39), 93 (34), 91 (100), 81 (29), 74 (59), 67 (23), 55 (35), 43 (29), 41 (30).

*Methyl (1*S,*4*S,*5*R*)-4-Hydroxy-5-pentylbicyclo[3.1.0]hexane-1-acetate* ((1*S*,4*S*,5*R*)-**12c**). As described for **12c**: (1*S*,4*S*,5*R*)-**12c** (47%). $[\alpha]_D^{20} = -22.5$ (*c* = 0.02, $CHCl_3$).

*Methyl (2*E*)-2-(3-Methoxy-2-pentylcyclopent-2-en-1-ylidene)acetate* ((*E*)-**13**). According to the *Reformatsky* procedure described for its analogue **3a** [1f]. Workup with H_2O and purification by CC (SiO_2, cyclohexane/AcOEt 8:2) gave (*E*)-**13** (26%), *i.e.*, 87:13 (*E*)/(*Z*) mixture. IR: 2930, 2857, 1699, 1584, 1459, 1433, 1373, 1324, 1251, 1242, 1154, 1123, 1026, 925, 831. ^{1}H-NMR: 0.88 (*t*, *J* = 7, 3 H); 1.20–1.40 (*m*, 6 H); 2.11 (*t*, *J* = 7, 2 H); 2.67 (*t*, *J* = 4, 2 H); 3.09 (*dt*, *J* = 4, 2, 2 H); 3.68 (*s*, 3 H); 3.82 (*s*, 3 H); 5.46 (*t*, *J* = 2, 1 H). ^{13}C-NMR: 171.4 (*s*); 168.7 (*s*); 168.2 (*s*); 119.7 (*s*); 100.0 (*d*); 56.9 (*q*); 50.4 (*q*); 31.9 (*t*); 28.3 (*t*); 27.9 (*t*); 27.4 (*t*); 22.5 (2*t*); 14.1 (*q*). MS: 238 (18, M^+), 207 (17), 182 (17), 165 (100), 149 (14), 135 (13), 123 (35), 121 (16), 109 (7), 91 (15), 79 (8), 77 (11).

*(5*E*)-2-Pentyl-5-(2-pentylcyclopent-2-en-1-ylidene)cyclopent-2-en-1-one* (**I**). When the procedures reported in [1f] for deprotonation of AcOMe were not respected, by using an excess of $LiN(SiMe_3)_2$ (1.2 to 1.5 instead of 1.0 mol.-equiv.), self-condensation of **3a** occurred, and **I** was isolated in 8–18% yield by CC (SiO_2, cyclohexane/AcOEt 98:2 → 8:2). IR: 2954, 2926, 2858, 1687, 1645, 1625, 1590, 1458, 1377, 1342, 1260, 1241, 1162, 1105, 1033, 956, 918, 876, 850, 818, 787, 730. ^{1}H-NMR: 0.90 (*t*, *J* = 7, 3 H); 0.92 (*t*, *J* = 7, 3 H); 1.30–1.37 (*m*, 8 H); 1.52 (*t*, *J* = 7, 2 H); 1.54 (*t*, *J* = 7, 2 H); 2.25 (*t*, *J* = 7, 2 H); 2.38 (*t*, *J* = 7, 2 H); 2.48–2.52 (*m*, 2 H); 3.24–3.28 (*m*, 2 H); 3.37 (*s*, 2 H); 6.46 (*s*, 1 H); 7.05 (*s*, 1 H). ^{13}C-NMR: 198.4 (*s*); 157.6 (*s*); 148.6 (*s*); 146.5 (*s*); 146.4 (*d*); 145.9 (*d*); 122.4 (*s*); 32.1 (*t*); 31.9 (*t*); 31.8 (*t*); 31.7 (*t*); 31.4 (*t*); 29.4 (*t*); 28.8 (*t*); 27.4 (*t*); 25.4 (*t*); 22.6 (*t*); 22.5 (*t*); 14.1 (*q*); 14.0 (*q*). MS: 286 (100, M^+), 243 (17), 229 (80), 216 (10), 173 (17); 159 (12); 145 (10), 131 (10), 129 (12), 117 (12), 105 (10), 91 (20), 79 (11), 41 (12).

*Methyl (2*E*)-2-(2-Pentylcyclopent-2-en-1-ylidene)acetate* (**II**). For the preparation, see [16] or **III**. Fatty, paper, weak odor. IR: 2952, 2926, 2858, 1709, 1611, 1432, 1350, 1291, 1214, 1157, 1030, 929, 906, 848, 727. ^{1}H-NMR: 0.90 (*t*, *J* = 7, 3 H); 1.23–1.36 (*m*, 4 H); 1.56–1.48 (*m*, 2 H); 2.16 (*t*, *J* = 8.5, 2 H); 2.51 (*m*,

2 H); 3.08 (*m*, 2 H); 3.72 (*s*, 3 H); 5.68 (br. *s*, 1 H); 6.35 (br. *s*, 1 H). ^{13}C-NMR: 168.5 (*s*); 168.3 (*s*); 145.4 (*s*); 143.4 (*d*); 105.5 (*d*); 50.8 (*q*); 31.8 (*t*); 31.2 (*t*); 31.4 (*t*); 27.4 (*t*); 26.9 (*t*); 22.5 (*t*); 14.0 (*q*). MS: 208 (38, M^+), 179 (15), 177 (28), 151 (21), 134 (90), 119 (81), 105 (66), 93 (60), 91 (100), 79 (48), 77 (42), 65 (23), 43 (35), 41 (53).

Methyl 5-Pentylcyclopenta-1,4-diene-1-acetate (**III**). A soln. of crude **4** [1f][1g] (2260 mg, 10 mmol) in THF (50 ml) was treated at 20° with 10% aq. HCl soln. (50 ml). After 10 min, the org. phase was washed to neutral with brine, dried (Na_2SO_4), and concentrated: **II/III** 2:1 (quant.). Purification by CC (SiO_2, cyclohexane/AcOEt 98:2 → 9:1) afforded pure **II** (43%) and pure **III** (16%). **III**: IR: 2953, 2930, 2858, 1736, 1436, 1331, 1200, 1167, 1045, 730, 665. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.25–1.35 (*m*, 4 H); 1.46–1.51 (*m*, 2 H); 2.29 (*t*, *J* = 7.4, 2 H); 3.04 (br. *s*, 2 H); 3.36 (*s*, 2 H); 3.67 (*s*, 3 H); 6.31 (*dt*, *J* = 1.6, 5.5, 1 H); 6.39 (*dt*, *J* = 1.6, 5.5, 1 H). ^{13}C-NMR: 172.2 (*s*); 143.1 (*s*); 134.9 (*d*); 131.6 (*d*); 131.1 (*s*); 51.8 (*q*); 44.3 (*t*); 33.7 (*t*); 31.7 (*t*); 28.9 (*t*); 27.3 (*t*); 22.6 (*t*); 14.0 (*q*). MS: 208 (28, M^+), 152 (43), 149 (12), 134 (24), 119 (19), 105 (35), 91 (100), 79 (29), 77 (21), 28 (24).

*Methyl (1*RS,*2*SR*)-1-Hydroxy-3-oxo-2-pentylcyclopentaneacetate* (**IV**). Isolated in < 5% yield during the purification of **1/9b** by CC (SiO_2, cyclohexane/AcOEt 97:3 → 8:2). IR: 3505, 2954, 2929, 2859, 1731, 1438, 1405, 1379, 1345, 1268, 1195, 1174, 1093, 1036, 987, 632. ^{1}H-NMR: 0.89 (*t*, *J* = 7.1, 3 H); 1.39–1.25 (*m*, 5 H); 1.48–1.41 (*m*, 1 H); 1.60–1.54 (*m*, 1 H); 1.7–1.62 (*m*, 1 H); 1.9–1.83 (*m*, 2 H); 2.23 (*ddd*, *J* = 1.8, 9, 13, 1 H); 2.29 (*ddt*, *J* = 1.5, 9, 19, 1 H); 2.44 (*ddd*, *J* = 9, 11, 19, 1 H); 2.56 (*d*, *J* = 16, 1 H); 2.89 (*d*, *J* = 16, 1 H); 3.38 (*d*, *J* = 1.5, 1 OH); 3.76 (*s*, 3 H). ^{13}C-NMR: 217.4 (*s*); 172.9 (*s*); 76.8 (*s*); 58.6 (*d*); 52.0 (*q*); 42.8 (*t*); 34.6 (*t*); 34.0 (*t*); 32.1 (*t*); 28.4 (*t*); 23.5 (*t*); 22.5 (*t*); 14.1 (*q*). MS: 242 (12, M^+), 224 (9), 210 (9), 169 (22), 167 (17), 154 (29), 153 (48), 151 (13), 140 (16), 129 (21), 111 (70), 99 (100), 97 (22), 83 (16), 69 (15), 55 (44), 43 (22).

*Methyl (1*S,*2*R,*3*S*)-3-Hydroxy-2-pentylcyclopentaneacetate* ((1*S*,2*R*,3*S*)-**Va**). A soln. of (3*S*)-**11a** (100 mg, 0.44 mmol) in AcOEt (4 ml) was hydrogenated over PtO_2 (2.5 mg) for 18 h. The mixture was concentrated and the residue purified by CC (SiO_2, cyclohexane/AcOEt 98:2 → 8:2): (1*S*,2*R*,3*S*)-**Va** (44%), then a 7:3 *trans*/*cis* mixture (+)-((1*S*,2*S*)/(−)-(1*S*,2*R*)-*Paradisone*® (31%), and then the more polar (1*R*,2*R*,3*S*)-**Vb** (20%). For analyses, see [2g], for optical purities, see *Footnote 12*. (1*S*,2*R*,3*S*)-**Va**: R_f (cyclohexane/AcOEt 8:2) 0.44. GLC (*DB-1*, 15 m, 250 μm, 0.25 mm, 100°, 1 min; 15°/min → 220°): t_R 6.72 min. $[\alpha]_D^{20} = -28.0$ (*c* = 0.34, $CHCl_3$).

*Methyl (1*R,*2*R,*3*S*)-3-Hydroxy-2-pentylcyclopentaneacetate* ((1*R*,2*R*,3*S*)-**Vb**). See procedure for ((1*S*,2*R*,3*S*)-**Va**). R_f (cyclohexane/AcOEt 8:2) 0.37. GLC (*DB-1*, 15 m, 250 μm, 0.25 mm, 100°, 1 min; 15°/min → 220°): t_R 6.52 min. $[\alpha]_D^{20} = +57.8$ (*c* = 0.5, $CHCl_3$). IR: 3659, 2962, 2934, 2871, 1757, 1441, 1169. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.25–1.45 (*m*, 6 H); 1.59 (br. *s*, 1 OH); 1.61–1.67 (*m*, 2 H); 1.83–1.91 (*m*, 2 H); 2.05–2.20 (*m*, 3 H); 2.32 (*dd*, *J* = 16, 9, 1 H); 2.48–2.55 (*m*, 2 H); 3.67 (*s*, 3 H); 4.23 (br. *t*, *J* = 4.3, 1 H). ^{13}C-NMR: 173.7 (*s*); 74.0 (*d*); 51.4 (*q*); 51.1 (*d*); 39.3 (*t*); 38.8 (*d*); 33.5 (*t*); 32.3 (*t*); 29.2 (*t*); 28.0 (*t*); 27.4 (*t*); 22.6 (*t*); 14.1 (*q*). MS: 228 (1, M^+), 210 (12), 196 (10), 185 (13), 169 (18), 153 (82), 136 (59), 110 (20), 97 (20), 95 (38), 83 (38), 81 (44), 74 (100), 67 (37), 55 (36), 43 (23), 41 (26).

*Methyl (1*R,*2*R,*3*R*)-3-Hydroxy-2-pentylcyclopentaneacetate* ((1*R*,2*R*,3*R*)-**Vc**). (−)-(1*R*,2*R*) *Paradisone*® (98% *trans*, 60% ee; 6.0 g, 26.5 mmol) was added at 0° to a mechanically stirred soln. of $NaBH_4$ (840 mg, 22 mmol) in MeOH (50 ml). The cooling bath was removed, and stirring was continued for 15 min at 20°. A soln. of conc. H_2SO_4 soln. (2.58 ml) in H_2O (22.5 ml) was then added at 0°. After concentration (60°/240 mbar), the product was extracted with Et_2O and the org. phase washed with H_2O, sat. aq. $NaHCO_3$, soln., and brine, dried (Na_2SO_4), and concentrated: (1*R*,2*R*,3*R*)-**Vc**/(1*R*,2*R*,3*S*)-**Vb** 60:40 (quant.). Separation by CC (SiO_2, cyclohexane/AcOEt 9:1) afforded pure (1*R*,2*R*,3*R*)-**Vc** (6%) as more polar stereoisomer. R_f (cyclohexane/AcOEt 8:2) 0.30. GLC (*DB-1*, 15 m, 250 μm, 0.25 mm, 100°, 1 min; 15°/min → 220°): t_R 6.35 min. $[\alpha]_D^{20} = +14.8$ (*c* = 0.04, $CHCl_3$). IR: 3417, 2953, 2925, 2857, 1737, 1457, 1436, 1376, 1333, 1255, 1199, 1170, 1146, 1094, 1071, 998, 879, 842, 724. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 3 H); 1.26–1.52 (*m*, 6 H); 1.59–1.68 (*m*, 2 H); 1.76–1.92 (*m*. 4 H); 2.04–2.18 (*m*, 2 H); 2.32 (*dd*, *J* = 9.1, 15.3, 1 H); 2.47–2.51 (*m*, 1 H); 2.53 (*dd*, *J* = 4.9, 15.3, 1 H); 3.67 (*s*, 3 H); 3.92 (*dt*, *J* = 4.0, 5.6, 1 H). ^{13}C-NMR: 173.8 (*s*); 53.8 (*d*); 51.4 (*q*); 40.9 (*d*); 39.9 (*t*); 34.2 (*t*); 33.4 (*t*); 32.2 (*t*); 29.5 (*t*); 27.5 (*t*); 22.6 (*t*); 14.1 (*q*). MS: 228 (0, M^+), 210 (8), 185 (27), 178 (12), 154 (21), 150 (30), 136 (100), 126 (13), 121 (11), 110 (38), 107 (15), 98 (25), 95 (32), 83 (48), 81 (50), 74 (79), 69 (30), 67 (40), 55 (43), 43 (23), 41 (36).

*Dimethyl (3*RS*,3′*RS*)-3,3′-Oxybis[2-pentylcyclopent-1-ene-1-acetate]* (**VIb**) *and Its* meso-*(3*RS*,3′*SR*)-Stereoisomer* **VIa**. After treatment of racemic-**11a** under the conditions described for (1*R*,2*S*,3*S*)-**12a**, the mixture **VIa**/**VIb** 1:1 was separated by CC (SiO_2, cyclohexane/AcOEt 9:1): less polar (35%) and more polar stereoisomer (30%), obviously formed before addition of H_2. Less polar stereoisomer: IR: 2952, 2926, 2853, 1738, 1434, 1314, 1262, 1193, 1167, 1142, 1081, 1046, 842, 727. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 6 H); 1.20–137 (*m*, 10 H); 1.42–1.52 (*m*, 2 H); 1.70–1.80 (*m*, 2 H); 2.07–2.18 (*m*, 6 H); 2.28–2.37 (*m*, 2 H); 2.42–2.50 (*m*, 2 H); 3.02 (*d*, *J* = 15.2, 2 H); 3.20 (*d*, *J* = 15.2, 2 H); 3.67 (*s*, 6 H); 4.47–4.51 (*m*, 2 H). ^{13}C-NMR: 171.6 (2*s*); 140.7 (2*s*); 132.2 (2*s*); 84.2 (2*d*); 51.7 (2*q*); 34.6 (2*t*); 33.6 (2*t*); 31.9 (2*t*); 29.7 (2*t*); 27.8 (2*t*); 25.8 (2*t*); 22.6 (2*t*); 14.1 (2*q*). MS: 450 (0, M^+), 356 (1), 225 (51), 209 (71), 177 (19), 165 (9), 152 (65), 149 (48), 135 (44), 119 (28), 107 (22), 105 (43), 93 (78), 91 (100), 79 (57), 77 (30), 41 (12). More polar stereoisomer: IR: 2953, 2927, 2853, 1739, 1455, 1434, 1317, 1261, 1193, 1167, 1142, 1081, 1046, 842, 727. ^{1}H-NMR: 0.89 (*t*, *J* = 7, 6 H); 1.20–137 (*m*, 10 H); 1.42–1.52 (*m*, 2 H); 1.73–1.82 (*m*, 2 H); 2.07–2.22 (*m*, 6 H); 2.27–2.35 (*m*, 2 H); 2.39–2.47 (*m*, 2 H); 3.03 (*d*, *J* = 15.2, 2 H); 3.19 (*d*, *J* = 15.2, 2 H); 3.66 (*s*, 6 H); 4.48–4.53 (*m*, 2 H). ^{13}C-NMR: 171.6 (2*s*); 141.1 (2*s*); 131.6 (2*s*); 86.9 (2*d*); 51.7 (2*q*); 34.6 (2*t*); 33.7 (2*t*); 32.0 (2*t*); 31.0 (2*t*); 27.9 (2*t*); 26.0 (2*t*); 22.7 (2*t*); 14.1 (2*q*). MS: 450 (0, M^+), 356 (1), 225 (39), 209 (96), 177 (24), 165 (8), 152 (68), 149 (53), 135 (51), 119 (27), 107 (25), 105 (44), 93 (82), 91 (100), 79 (61), 77 (28), 41 (12).

REFERENCES

[1] a) P. Dubs, R. Stüssi, *Helv. Chim. Acta* **1978**, *61*, 998; b) C. Chapuis, G. H. Büchi, H. Wüest, *Helv. Chim. Acta* **2005**, *88*, 3069; c) T. Shono, M. Okawa, I. Nishiguchi, *J. Am. Chem. Soc.* **1975**, *97*, 6144; d) K. Crawford, V. Rautenstrauch, A. Uijttewaal, *Synlett* **2001**, 1127; e) K. Sisido, S. Kurozumi, K. Utimoto, *Perfum. Essent. Oil Rec.* **1969**, *60*, 267); f) U. Ravid, R. Ikan, *J. Org. Chem.* **1974**, *39*, 2637; g) U. Ravid, R. Ikan, R. M. Sachs, *J. Agric. Food. Chem.* **1975**, *23*, 835; h) B. Winter, to *Firmenich SA*, US5302745, 12 Apr. 1994 (*Chem. Abstr.* **1994**, *120*, 269718); i) T. Shono, N. Kise, *Tetrahedron Lett.* **1990**, *31*, 1303; j) T. Shono, N. Kise, T. Fujimoto, N. Tominaga, H. Morita, *J. Org. Chem.* **1992**, *57*, 7175; k) D. Anderson, G. Frater, to *Givaudan-Roure SA*, EP953562, 03 Nov. 1999 (*Chem. Abstr.* **1999**, *131*, 324143); l) F. Näf, R. Decorzant, to *Firmenich SA*, US5760277, 2 Jun. 1998 (*Chem. Abstr.* **1997**, *126*, 143920).

[2] a) S. Katsuya, M. Fumio, to *Asahi Kasei Chem. Co.*, WO2007/4442, 11 Jan. 2007 (*Chem. Abstr.* **2007**, *146*, 142304); b) T. Yamada, H. Fujisawa, H. Tanaka, to *Nippon Zeon*, EP399788, 25 Aug. 1989 (*Chem. Abstr.* **1990**, *114*, 163600); c) P. Teisseire, M. Plattier, to *Roure-Bertrand & Dupont*, FR7046407, 23 Dec. 1970 (*Chem. Abstr.* **1972**, *78*, 3798); d) D. A. Dobbs, K. P. M. Vanhessche, E. Brazi, V. Rautenstrauch, J.-Y. Lenoir, J.-P. Genêt, J. Wiles, S. H. Bergens, *Angew. Chem., Int. Ed.* **2000**, *39*, 1992; e) V. Rautenstrauch, K. P. M. Vanhessche, J. P. Genêt, J. Y. Lenoir, to *Firmenich SA*, US5874600, 23 Feb. 1999 (*Chem. Abstr.* **1997**, *127*, 183071); f) D. Dobbs, K. P. M. Vanhessche, V. Rautenstrauch, to *Firmenich SA*, US6214763, 10 Apr. 2001 (*Chem. Abstr.* **1998**, *130*, 40076); g) T. Ebata, K. Matsumoto, H. Matsushita, *Heterocycles* **1994**, *38*, 2231; h) M. Hamberg, O. Miersch, G. Sembdner, *Lipids* **1988**, *23*, 521; i) O. Miersch, A. Preiss, G. Sembdner, K. Schreiber, *Phytochemistry* **1987**, *26*, 1037; j) R. K. Hill, A. G. Edwards, *Tetrahedron* **1965**, *21*, 1501.

[3] E. Demole E. Lederer, to *Firmenich SA*, CH382731, 25 Feb. 1960; E. Demole E. Lederer, to *Firmenich SA*, CH490313, 27 Jul. 1960 (*Chem. Abstr.* **1970**, *73*, 109368); A. Firmenich, R. Firmenich, G. Firmenich, R. E. Firmenich, to *Firmenich SA*, CH382731, 24 Feb. 1961 (*Chem. Abstr.* **1963**, *58*, 3038).

[4] E. Demole, E. Lederer, D. Mercier, *Helv. Chim. Acta* **1962**, *45*, 675; E. Demole, E. Lederer, D. Mercier, *Helv. Chim. Acta* **1962**, *45*, 685; E. Demole, M. Stoll, *Helv. Chim. Acta* **1962**, *45*, 692.

[5] W. Renold, R. Näf-Muller, U. Keller, B. Willhalm, G. Ohloff, *Helv. Chim. Acta* **1974**, *57*, 1301; L. G. Kharebava, A. G. Tsirgvava, *Chai. Kul'tura I Pr-vo, Tbilisi* **1979**, *2*, 26, (*Chem. Abstr.* **1979**, *92*, 162361); A. G. Sardzhveladze, I. A. Chernavina, L. G. Kharebava, *Subtrop. Kul't.* **1985**, *6*, 78, (*Chem. Abstr.* **1985**, *104*, 206166).

[6] P. Werkhoff, G. Krammer, S. Brennecke, M. Roloff, H.-J. Bertram, *Food Rev. Int.* **2002**, *18*, 103; R. Näf, in 'Citrus Oils, Composition, Advanced Analytical Techniques, Contaminants, and Biological Activity', Eds. G. Dugo, L. Mondello, CRC Press, London, 2011, p. 463.
[7] O. Cresp, J. Cavallier, P.-A. Blanc, A. Morillas, *Perfum. Flavor.* **2011**, *36(11)*, 24; A. Boix Camps, *Perfum. Flavor.* **2007**, *32(11)*, 40.
[8] a) E. Demole, 'Fragrance Chemistry, the Science of the Sense of Smell', Ed. E. T. Theimer, Academic Press, New York, 1982, p. 349; b) T. K. Sarkar, B. K. Ghorai, *J. Indian Chem. Soc.* **1999**, *76*, 693; c) C. Chapuis, *Perfum. Flavor.* **2011**, *36(12)*, 36; d) C. Chapuis, *Helv. Chim. Acta* **2012**, *95*, 1479.
[9] M. F. Ansell, J. W. Ducker, *J. Chem. Soc.* **1959**, 329; K. Oshima, H. Yamamoto, H. Nozaki, *J. Am. Chem. Soc.* **1973**, *95*, 4446; M. L. Roumestant, M. Malacria, J. Goré, J. Grimaldi, M. Bertrand, *Synthesis* **1976**, 755; V. Rautenstrauch, to *Firmenich SA*, US4499297, 12 Feb. 1985 (*Chem. Abstr.* **1984**, *101*, 170776).
[10] B. M. Trost, A. B. Pinkerton, *Org. Lett.* **2000**, *2*, 1601; B. M. Trost, A. B. Pinkerton, *J. Org. Chem.* **2001**, *66*, 7714; B. M. Trost, A. B. Pinkerton, *J. Am. Chem. Soc.* **2002**, *124*, 7376.
[11] J.-M. Vatèle, *Synlett.* **2008**, 1785; J.-M. Vatèle, *Tetrahedron*, **2010**, *66*, 904.
[12] A. Eschenmoser, US3939207, 17 Feb. 1976 (*Chem. Abstr.* **1971**, *75*, 484341); A. Barco, S. Benetti, G. P. Pollini, R. Taddia, *Synthesis* **1975**, 104; T. Punniyamurthy, B. Bhatia, M. M. Reddy, G. C. Madhava, J. Iqbal, *Tetrahedron* **1997**, *53*, 7649; E. Delort, A. Velluz, E. Frérot, M. Rubin, A. Jacquier, M. Rubin, S. Linder, K. F. Eidman, B. S. Mac Dougall, *J. Agric. Food. Chem.* **2011**, *59*, 11752.
[13] H. Baltz, B. Bierling, K. Kirschke, H. Oberender, M. Schultz, DD81650, 5 May 1971 (*Chem. Abstr.* **1973**, *78*, 99214); K. Blau, U. Müller, W. Pritzkow, W. Schmidt-Renner, Z. Sedshaw, *J. Prakt. Chem.* **1980**, *322*, 915; S. Uemur, S. R. Patil, *Tetrahedron Lett.* **1982**, *23*, 4353; S. Uemura, S. R. Patil, *Chem. Lett.* **1982**, *11*, 1743; anonymous, to *Jpn Kokai Tokkyo Koho*, JP 5872533, 30 Apr. 1983 (*Chem. Abstr.* **1983**, *99*, 87704); anonymous, to *Nippon Zeon*, JP 5980619, 10 May 1984 (*Chem. Abstr.* **1984**, *101*, 151487); M. Uyanik, M. Akakura, K. Ishihara, *J. Am. Chem. Soc.* **2009**, *131*, 251.
[14] E. Nakamura, J. Shimada, I. Kuwajima, *J. Chem. Soc., Chem. Commun.* **1983**, 498; I. Erden, N. Oecal, J. Song, C. Gleason, C. Gärtner, *Tetrahedron* **2006**, *62*, 10676.
[15] a) M. M. Kabat, L. M. Garofalo, A. R. Daniewski, S. D. Hutchings, W. Liu, M. Okabe, R. Radinov, Y. Zhou, *J. Org. Chem.* **2001**, *66*, 6141; b) B. M. Trost, P. Seoane, S. Mignani, M. Acemoglu, *J. Am. Chem. Soc.* **1989**, *111*, 7487.
[16] C. Fehr, J. Galindo, *Angew. Chem., Int. Ed.* **2000**, *39*, 569; *Angew. Chem.* **2000**, *112*, 581.
[17] a) K. Fujiwara, H. Sakai, T. Tanaka, M. Hiroma, *Chem. Lett.* **1994**, *23*, 457; b) S.-J. Jeon, P. J. Walsh, *J. Am. Chem. Soc.* **2003**, *125*, 9544; c) S.-J. Jeon, H. Li, C. Garcia, L. K. LaRochelle, P. J. Walsh, *J. Org. Chem.* **2005**, *70*, 448; d) T. J. Snape, *Org. Biomol. Chem.* **2006**, *4*, 4144. e) J. M. Carr, T. S. Snowden, *Tetrahedron* **2008**, *64*, 2897.
[18] C. Fehr, *Angew. Chem.* **1998**, *110*, 2509; *Angew. Chem., Int. Ed.* **1998**, *37*, 2407.
[19] J. Gon Kim, K. M. Waltz, I. F. Garcia, D. Kwiatkowski, P. J. Walsh, *J. Am. Chem. Soc.* **2004**, *126*, 12580; S.-J. Jeon, H. Li, P. J. Walsh, *J. Am. Chem. Soc.* **2005**, *127*, 16416; A. J. Wooten, J. G. Kim, P. J. Walsh, *Org. Lett.* **2007**, *9*, 381; Y.-M. Zao, P. Gu, H.-J. Zhang, Q.-W. Zhang, C.-A. Fan, Y.-Q. Tu, F.-M. Zhang, *J. Org. Chem.* **2009**, *74*, 3211.
[20] A. G. Myers, M. Hammond, Y. Wu, J.-N. Xiang, P. M. Harrington, E. Y. Kuo, *J. Am. Chem. Soc.* **1996**, *118*, 10006; A. G. Myers, R. Glatthar, M. Hammond, P. M. Harrington, E. Y. Kuo, J. Liang, S. E. Schaus, Y. Wu, J.-N. Xiang, *J. Am. Chem. Soc.* **2002**, *124*, 5380.
[21] W. Paget, D. Reichlin, E. C. Walborsky, R. L. Snowden, C. Vial, to *Firmenich SA*, US 5726345, 10 Mar. 1998 (*Chem. Abstr.* **1995**, *123*, 116298).
[22] D.-R. Ahn, M. Mosimann, C. J. Leumann, *Nucleosides, Nucleotides Nucleic Acids*, **2003**, *22*, 1207; D.-R. Ahn, M. Mosimann, C. J. Leumann, *J. Org. Chem.* **2003**, *68*, 7693; W.-K. Chan, P. Liu, W.-Y. Yu, M.-K. Wong, C.-M. Che, *Org. Lett.* **2004**, *6*, 1597; E. Elhalem, M. J. Comin, J. B. Rodriguez, *Eur. J. Org. Chem.* **2006**, 4473.
[23] A. B. Smith III, M. A. Guaciaro, S. R. Schow, P. M. Wovkulich, B. H. Toder, T. W. Hall, *J. Am. Chem. Soc.* **1981**, *103*, 219; A. G. Myers, P. M. Harrington, E. Y. Kuo, *J. Am. Chem. Soc.* **1991**, *113*, 694; T. Doi, T. Takahashi, *J. Org. Chem.* **1991**, *56*, 3465.

[24] Jaguar, version 7.8, Schrödinger, LLC, New York, NY, 2011; J. A. R. Luft, K. Meleson, K. N. Houk, *Org. Lett*. **2007**, *9*, 555.
[25] a) M. Ohba, T. Haneishi, T. Fujii, *Chem. Pharm. Bull*. **1996**, *44*, 525; b) R. H. Crabtree, M. W. Davis, *J. Org. Chem*. **1986**, *51*, 2655.
[26] M. Vincens, C. Dumont, M. Vidal, *Bull. Soc. Chim. Fr.* **1984**, II-59.
[27] H. Kiyota, S. Takigawa, S. Kuwahara, *Helv. Chim. Acta* **2004**, *87*, 1854; H.-K. Yim, Y. Liao, H. N. C. Wong, *Tetrahedron* **2003**, *59*, 1877.
[28] C. Chapuis, M. Barthe, J.-Y. de Saint Laumer, *Helv. Chim. Acta* **2001**, *84*, 230.

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