# *Exaltone*® (= Cyclopentadecanone) from *Isomuscone*® (= Cyclohexadecanone), a One-C-Atom Ring-Contraction Methodology *via* a Stereospecific *Favorskii* Rearrangement: Regioselective Application to (−)-(*R*)-Muscone

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Lately dedicated to Prof. *J. Jurczak* on the occasion of his 70th birthday[1])

Treatment of cyclohexadecanone (**1g**; with $I_2$ (2.2 mol-euqiv.) and KOH in MeOH) furnished the unsaturated (*Z*)-ester **2g** in 83% yield, *via* a stereospecific *Favorskii* rearrangement (*Scheme 1*). Further treatment with 3-chloroperbenzoic acid (*m*-CPBA) afforded the unreported epoxy ester **3g** (88% yield), which was cleaved in 33% yield to *Exaltone*® (= cyclopentadecanone; **1f**) with NaOH in MeOH/$H_2O$ and then HCl at 65°. This methodology was similarly extended to higher ($C_{17}$) and lower ($C_{15}$ to $C_{11}$) cyclic ketone analogues, as well as regioselectively to (−)-(*R*)-muscone (**5c**) and homomuscone (**5f**) (*Scheme 2*). Olfactive properties of the corresponding macrocyclic 1-oxaspiro[2,*n*]alkanes and -alkenes **4** and **8**, resulting from a *Corey–Chaykovsky* oxiranylation, are also presented.

**Introduction.** – Among the historical nitro and polycyclic aromatic musks[2]) and a new class of musk-like aliphatic esters, more recently explored [2] by modifying *BASF's Cyclomusk*®[3]) [3], macrocyclic musks occupy a preponderant place[4]). The synthesis of these macrocyclic ketones or lactones relies principally on two distinctive methodologies, namely ring expansion or contraction, and macrocyclization. The latter are exemplified by macrolactonization [5][5]) or various reactions leading to C–C bond formation, such as intramolecular variants of the *Dieckmann* condensation [9], alkylation [10], either *McMurry* [11], *Wittig* [12], or metathesis reactions [13][9e], ketene dimerization [14], as well as *Ramberg–Bäcklund* rearrangement

[1]) In early 2011. For patent reasons, this manuscript (2008) was kept for several years prior to submission.
[2]) For a recent review, see [1].
[3]) 3-(5-Isopropenyl-2-methyl-cyclopent-1-en-1-yl)-2,2-dimethylpropyl propanoate.
[4]) For a specific review, see [4].
[5]) For supported conditions, see, *e.g.*, [6]; for enzymatic lactonization, see, *e.g.*, [7]; for a recent review, see [8].

[15][6]) or radical cyclizations [21]. Besides the heterogeneous acyloin condensation [22], the *Story* synthesis [23], *Carothers*' depolymerization reaction [24], or *Collaud*'s macrolactonization [25], almost all these approaches face the same entropic drawback, which necessitates high-dilution conditions to favor intra- *vs.* intermolecular reactions. This aspect massively reduces their industrial interest due to poor productivity and large quantities of solvent to recycle[7]). For this reason, the first strategy is by far the most economical, and in contrast to *Baeyer–Villiger* oxidation [29] or ring expansion [30], the macrocycle contraction methodology has been much less studied [31][8]). We thus present here our results, combining and extending methodologies previously reported for aliphatic linear ketones [34a] and for $C_{12}$ or $C_{11}$ medium-sized-ring ketones [35].

**Results and Discussion.** – First of all, starting from helvetone (=cyclododecanone; **1c**), we repeated the initial work of *Schank* and *Eistert* [35b][35c] by performing, according to *Wohllebe* and *Garbisch* [35d–f], the *Favorskii* rearrangement in MeOH rather than in $H_2O$, and by using the one-pot $I_2$ procedure of *Zacuto* and *Cai* [34a], instead of isolating the $Br_2$ adduct (*Scheme 1*). We thus directly obtained in 61% yield the known $\alpha,\beta$-unsaturated methyl ester **2c** [36] possessing the (*Z*)-configuration[9]) as shown by $^1$H-NMR analyses of the olefinic H-atom[10]). This result is noteworthy, since

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6) Treatment of the known 1,3-dioxolane-2,2-dioctanol (**Ia**) [16] with $CBr_4$ and $Ph_3P$ (see *Scheme 3* in the *Exper. Part*) afforded the unreported corresponding dibromide **Ib** (yield 65%), which was then cyclized ($Na_2S$, EtOH [17]) to the new cyclic thioether **IIa** (61%), prior to oxidation ($H_2O_2$, $NaHCO_3$, $MnSO_4$, MeCN [18]) to sulfone **IIb** (95%). When treated under *Ramberg–Bäcklund* conditions (KOH, $Al_2O_3$, EtOH, $CCl_4$ or $CBr_2F_2$, 60° [19]), this sulfone **IIb** afforded, in 70–82% yield, a 3:7 (*E*)/(*Z*) mixture of unsaturated macrocyclic acetal **III**, a known precursor in the synthesis of civetone (**IVa**) by *Stoll* and co-workers [20]. Similarly, hydrolysis of acetals **IIa** or **IIb** (HCl, THF/$H_2O$) furnished the corresponding macroheterocyclic ketones **Va** or **Vb** (58–60%) respectively, both devoid of olfactive character. Acylation of **Ia** (AcCl, DMAP, $Et_3N$, $CH_2Cl_2$) afforded diacetate **Ic** (60%). Quantitative hydrolysis of acetals **I** to ketones **VI** (HCl, THF/$H_2O$) allowed to access 9-hydroxynonanoic acid (**VIIb**), after *Bayer–Villiger* oxidation of **VIc** 3-chloroperbenzoic acid (*m*-CPBA), $CHCl_3$, 50°; yield 85%) and saponification (NaOH, EtOH, 78°; yield 89%).

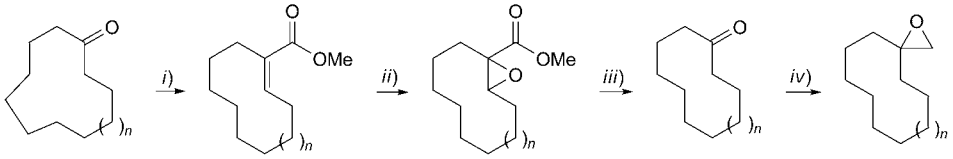
7) In this context, the vapor phase is technically by far the most economical, with, *e.g.*, intramolecular acid salt variants of the *Piria* reaction [26] or *Dieckmann* condensation [27]. For an example of high-dilution loop techniques, see [28].

8) This is understandable, as the starting material is already a macrocycle, and only the ones with an even number of C-atoms are efficiently accessible by dimeric metathesis of a medium-sized unsaturated ring [32] or by buta-1,3-diene *Wilke* catalytic trimerization [33].

9) For the stereospecific *Favorskii* rearrangement of diastereoisomeric cyclic $\alpha,\alpha'$-dibromo ketones, see [35e]. *Merck* chemists reported the alkoxide-promoted isomerization of $\alpha,\alpha$-diiodo ketones to their $\alpha,\alpha'$-isomers, and their observed (*Z*)-configuration was rationalized on the basis of an alkoxide-promoted disrotatory electrocyclic cyclopropanone opening, with concerted expulsion of iodide [34a]. For a recent theoretical study of this mechanism, see [34b]. Ester **2c** was also obtained as a 5:1 (*Z*)/(*E*) isomer mixture in 91% yield from the $\alpha,\alpha'$-dibromo ketone, according to [35f].

10) The $\delta$(H) of the olefinic H-atom of the (*E*)-isomers are at lower field (by *ca.* 0.6 ppm) than those of the (*Z*)-isomers. This is in agreement with empirical observations [36][37a]. This distinction may also be made on the basis of a comparison of the allylic methylene H-atoms [37b]. We unambiguously attributed the (*Z*)-configuration on the basis of NOESY experiments.

*Scheme 1*

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|---|---|---|---|---|
| *n* = 1: **1b** | **2b** 57% | **3b** 63% | **1a** 47% | **4a** 74% |
| *n* = 2: **1c** | **2c** 61% | **3c** 70% | **1b** 32% | **4b** 74% |
| *n* = 3: **1d** | **2d** 56% | **3d** 65% | **1c** 34% | **4c** 85% |
| *n* = 4: **1e** | **2e** 2% | **3e** 47%[a]) | **1d** 44%[a]) | **4d** 84% |
| *n* = 5: **1f** | **2f** 83% | **3f** 53% | **1e** 52% | **4e** 70% |
| *n* = 6: **1g** | **2g** 83% | **3g** 88% | **1f** 33% | **4f** 72% |
| *n* = 7: **1h** | **2h** 50% | **3h** 53% | **1g** 52% | **4g** 86% |

*i*) $I_2$ (2.2 mol-equiv.), KOH, MeOH, 0°. *ii*) *m*-CPBA, $CH_2Cl_2$. *iii*) NaOH, MeOH/$H_2O$, then HCl, 65°. *iv*) $Me_3S(O)I$, $^t$BuOH, $^t$BuOK, 50°.

[a]) GC Yield.

*Merck* chemists obtained $\alpha$-hydroxy ketals when they applied their $I_2$/KOH/MeOH conditions to small-ring ketones [34a]. Previous degradations of **2c** to **1b** made use of the *Curtius* rearrangement [35], which is industrially not acceptable due to both the high toxicity and instability of hydrazoic acid. We thus preferred to apply the known 3-chloroperbenzoic acid (*m*-CPBA) oxidation to afford epoxy ester **3c** [38] in 70% yield. Saponification with NaOH in refluxing MeOH/$H_2O$, followed by acidification with HCl [39], afforded undecanone **1b** in 32% yield[11]). Encouraged by these preliminary results, we applied our sequence to cyclotridecanone (**1d**). The corresponding unsaturated methyl ester (*Z*)-**2d**[12]) was isolated in 56% yield, and its glycidic acid ester or ester **3d** in 65% yield. Subsequent de(methoxycarbonyl)ation furnished cyclododecanone **1c** in 34% yield. As the efficiency of the *Favorskii* rearrangement may strongly depend on the ring size [35i], we were very interested to pursue our approach with larger macrocyclic ketones. Thus, cyclotetradecanone (**1e**) afforded methyl ester **2e** in only 2%. This illustrates the cyclic strain of the cyclotetradecane system, reluctant to form the transient intermediate [42][13]). When *Exaltone*® (**1f**) was submitted to the original *Favorskii* conditions, we isolated **2f** in 83% yield, and epoxy ester **3f** (53%

[11]) For an alternative $LiAlH_4$, then $NaIO_4$ sequence, see [38a]. For an unexpected regioselectivity in the cleavage of a glycidic acid ester (= oxiranecarboxylate), see [39b]. Thus, reduction of **3d**, resulting in 1-(hydroxymethyl)cyclododecan-1-ol [40], potentially gives access to the olfactory interesting 1-oxaspiro[2.11]tetradecane **4c** [30v], possessing cashmeran, musky, camphoraceous, woody, earthy, and mouldy notes [40b]. Alternatively, the other unreported oxaspiro compounds **4** were obtained by a direct *Corey–Chaykovsky* oxiranylation of ketones **1** [30v].

[12]) For (*E*)-**2d**, with an olefinic H-atom at $\delta$(H) 6.72, see [41].

[13]) Preliminary calculations at the B3LYP/6-31G** level [43] suggest a much higher transition state for the formation of the transient trisubstituted cyclopropanone derived from ketone **1e**, as compared to **1b**, **1c**, **1d**, **1f**, **1g**, and **1h**. This drawback precludes the preparative synthesis of either **3e** (47% GC yield) or **1d** (44% GC yield).

yield) afforded the cyclotetradecanone (**1e**) in 52% yield[14]). Potentially of highest interest, treatment of *Isomuscone*® (**1g**) furnished the unsaturated ester **2g**[15]) in 83% yield. Treatment with *m*-CPBA led to the unreported epoxy ester **3g** (88%), which afforded, in 33% yield, *Exaltone*® (**1f**). Finally, cycloheptadecanone (**1h**) gave **2h** in 50% yield. This latter was epoxidized (53%) to afford *Isomuscone*® (**1g**) in 52% yield after saponification and acidic decarboxylation.

We then extended this methodology to nonsymmetric macrocyclic ketones[16]) and were pleased to observe, with (−)-(*R*)-muscone (**5c**) (*Scheme* 2), a complete regioselectivity in favor of **6c** (56%)[17])[18]). Similarly, starting from the musky (−)-(*R*)-homomuscone (**5f**) [45], we only isolated **6f** (48%)[19])[20])[21]).

**Conclusion.** – For the preparation of either odd- or even-numbered macrocyclic ketones of olfactive interest, we combined a one-pot *Favorskii* process, reported to produce (*Z*)-prop-2-enoates from linear ketones, with a one-C-atom ring-contraction methodology, earlier applied to the preparation of medium-sized-ring ketones[22]). Most of the intermediate (*Z*)-unsaturated or epoxy methyl esters are new. This approach uses very simple scalable conditions and avoids high-dilution techniques, and may be regioselectively extended to $\beta$-substituted analogues. With either $C_{14}$, or $\alpha$-

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[14]) For alternative industrial conditions (maleic anhydride, $H_2O_2$), see [39b].

[15]) Ester **2g** of undefined configuration was independently obtained by an earlier method [44].

[16]) When 2-methylcyclopentadecanone [29b] was treated under the present *Favorskii* conditions, we isolated mainly 2-methoxy-2-methylcyclopentadecanone. IR: 2925, 2853, 1713, 1459, 1400, 1370, 1194, 1167, 1120, 1068, 903, 715. $^1$H-NMR: 3.22 (*s*, 3 H); 2.94–2.87 (*m*, 1 H); 2.31–2.23 (*m*, 1 H); 1.74–1.61 (*m*, 2 H); 1.39–1.29 (*m*, 14 H); 1.29–1.19 (*m*, 8 H); 1.24 (*s*, 3 H). $^{13}$C-NMR: 215.2 (*s*); 85.0 (*s*); 51.9 (*q*); 37.8 (*t*); 36.1 (*t*); 27.6 (2*t*); 27.2 (*t*); 26.8 (*t*); 26.7 (*t*); 26.4 (*t*); 26.3 (*t*); 26.1 (*t*); 25.9 (*t*); 22.6 (*t*); 22.1 (*t*); 18.9 (*q*). MS: 268 (5, $M^{+\bullet}$), 240 (12), 141 (7), 85 (100), 72 (60), 55 (17).

[17]) The intermediate cyclopropanone with the halide at the C-atom bearing the unsubstituted side chain is the more easily formed (see *Footnote 9*).

[18]) Further epoxidation (*m*-CPBA, $CH_2Cl_2$; → **7c** (82%)) followed by de(methoxycarbonyl)ation (NaOH, MeOH/$H_2O$, then HCl, 65°), furnished the musky (*R*)-normuscone (**5a**; 8%), besides the main (+)-(2*R*)-2-methyl cyclotetradecanone (55%, $[\alpha]_D^{20} = +7.5$ ($c = 1.6$, MeOH)). $^{13}$C-NMR: 215.5 (*s*); 45.6 (*d*); 38.4 (*t*); 33.0 (*t*); 26.3 (2*t*); 26.1 (*t*); 25.5 (*t*); 25.3 (*t*); 24.9 (*t*); 24.8 (*t*); 24.7 (*t*); 24.5 (*t*); 21.7 (*t*); 17.2 (*q*)), both already described as racemates [29b][30f][30v] (see *Footnote 11*).

[19]) Further epoxidation (*m*-CPBA, $CH_2Cl_2$; → **7f** (79%)) followed by de(methoxycarbonyl)ation (NaOH, MeOH/$H_2O$, then HCl, 65°), furnished (−)-(*R*)-muscone (**5c**; 12%), besides the main (+)-(2*R*)-2-methylcyclopentadecanone (66%) [46] (see *Footnote 11*).

[20]) To determine their olfactive properties, we also prepared, by *Corey–Chaykovsky* reaction, the unreported oxaspiro compounds **8a**–**8j**.

[21]) Finally, even the unsaturated (+)-(*R*)-muscenone (**5d**) was prone to regioselective *Favorskii* reaction and afforded **6d**, albeit in a poor 3% yield. Addition of $I_2$ across the C=C bond was not exploited to regenerate a cycloalkynyl functionality. Similarly, a potential access to (3*R*,5*Z*)-configured **5b** ($LiAlH_4$, THF; [$VO(acac)_2$], $^t$BuOOH, toluene; $LiAlH_4$, THF; $NaIO_4$, THF/$H_2O$) was not attempted.

[22]) In this series, the methyl ester **2b** is the smallest reported medium-sized ring with a (*Z*)-configuration [35e]. Epoxidation with *m*-CPBA afforded directly **3b** (63%), and de(methoxycarbonyl)ation gave cyclodecanone **1a** in 47% yield. Further ring contraction was unsuccessfully attempted (for the (*E*)-isomer of cyclonon-1-ene-1-carboxylic acid methyl ester, with the signal of an olefinic H-atom at $\delta$(H) 6.85, see [36]).

substituted, or unsaturated macrocyclic ketones, the isolated yields become deceiving[23]).

We are indebted to Dr. *J.-Y. De Saint Laumer* for B3LYP/6-31G** preliminary calculations.

## Experimental Part

*General*. See [52]. Starting cyclic ketones[24]) were purchased from *Aldrich* (**1b**, **1c**, **1d**, and **1f**) and *Pfaltz–Bauer* (**1h**). Ketones **1e** and **1g** were obtained from **1f** and **1h**, resp., by the methodology described herein. The other unsaturated or methylated ketones **5b** (*Givaudan SA*), **5c** ($[\alpha]_D^{20} = -7.4$ ($c = 2.8$, MeOH); *Firmenich SA*), **5d** ($[\alpha]_D^{20} = +6.3$ ($c = 4.0$ MeOH); *Firmenich SA*), **5e** (*Firmenich SA*), **5f** ($[\alpha]_D^{20} = -6.9$ ($c = 1.0$ MeOH); [45]), **5g** (*Symrise GmbH*), **5h** (*Symrise GmbH*), **5i** (*BASF GmbH*), **5j** (*BASF GmbH*), and **IVa** (*Firmenich SA*) are industrially available.

*Transformations of* **1** → **2** *and* **5** → **6**: *General Procedure A* (*G.P.A*). The macrocyclic ketone **1** or **5** (1.0 mol-equiv.) was added dropwise/portionwise to a soln. of $I_2$ (2.2 mol-equiv.) in MeOH (3.9 ml/mmol) at $-5°$, and after 15 min, a soln. of KOH (5.0 mol-equiv.) in MeOH (3.6 ml/mmol) was added dropwise at 0°. After 1 h at 0°, the mixture was concentrated, diluted with $Et_2O$, washed with 15% aq. $NaHSO_3$ soln., dried ($Na_2SO_4$), and concentrated and the residue purified.

*Methyl (1Z)-Cyclodec-1-ene-1-carboxylate* (**2b**). According to *G.P.A*. After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 57%. IR: 2927, 2860, 1708, 1638, 1461, 1440, 1378, 1247, 1231, 1195, 1146, 1123, 1104, 1032, 897, 806, 774, 708. $^1$H-NMR: 6.25 (*t*, $J = 8$, 1 H); 3.76 (*s*, 3 H); 2.54 (br. *q*, $J = 7$, 2 H); 2.36 (*t*, $J = 6$, 2 H); 1.64–1.58 (*m*, 2 H); 1.56–1.51 (*m*, 2 H); 1.46–1.40 (*m*, 2 H); 1.32–1.26 (*m*, 3 H); 1.25–1.18 (*m*, 3 H). $^{13}$C-NMR: 168.5 (*s*); 145.7 (*d*); 129.8 (*s*); 51.1 (*q*); 34.7 (*t*); 29.4(*t*); 27.9 (*t*); 26.3 (*t*); 24.7 (*t*); 24.5 (*t*); 24.0 (*t*); 23.0 (*t*). MS: 196 (77, $M^+$), 165 (18), 153 (77), 137 (21), 135 (22), 125 (19), 95 (72), 81 (100), 79 (42), 67 (56), 55 (45), 53 (30), 41 (54).

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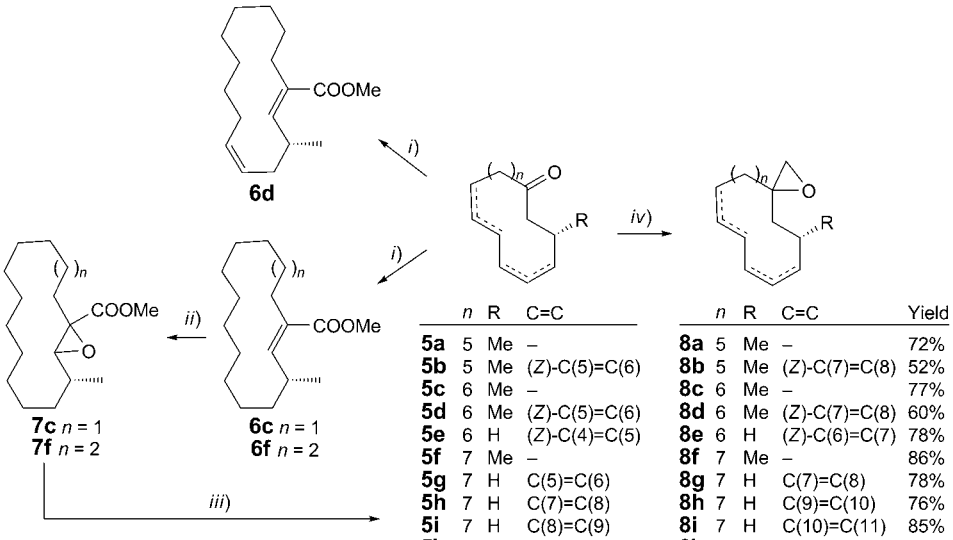
23) When these conditions were applied to the commercially available heptane-3,5-dione, we isolated the already reported 2-methyl-4-oxohexanoic acid methyl ester [47] in 48% yield ($^{13}$C-NMR: 209.5 (*s*); 176.5 (*s*); 51.7 (*q*); 45.4 (*t*); 36.3 (*t*); 34.8 (*d*); 17.3 (*q*); 7.7 (*q*). MS: 158 (1, $M^+$), 129(47), 127 (15), 101 (14), 59 (100), 57 (94), 41 (29), 29 (58), 27 (30)). For an analogous multi-step sequence *via* a $C_s$-symmetric monohalide, see [48] as a single example. Similarly, treatment of cycloheptane-1,3-dione afforded, after chromatographic purification ($SiO_2$, cyclohexane/AcOEt 97:3 → 60:40), *a*) the commercially available 3-oxocyclohexanecarboxylic acid methyl ester (4% yield), *b*) hexanedioic acid dimethyl ester (2% yield), *c*) the reported 3-oxocyclohex-1-ene-1-carboxylic acid methyl ester (11% yield) [49], *d*) 2-iodo-3-oxocyclohex-1-ene-1-carboxylic acid methyl ester (5% yield. IR: 2951, 1730, 1687, 1607, 1434, 1288, 1250, 1224, 1176, 1132, 1098, 1040, 977, 910, 800, 727, 647. $^1$H-NMR: 3.90 (*s*, 3 H); 2.70 (*t*, $J = 6.2$, 2 H); 2.67 (*t*, $J = 6.2$, 2 H); 2.14 (*quint.*, $J = 6.2$, 2 H). $^{13}$C-NMR: 197.6 (*s*); 167.2 (*s*); 156.8 (*s*); 94.2 (*s*); 52.3 (*q*); 36.8 (*t*); 25.6 (*t*); 21.1 (*t*). MS: 280 (100, $M^+$), 252 (19), 249 (11), 224 (12), 221 (7), 165 (16), 121 (8), 93 (12), 66 (48), 55 (23)), *e*) 2,4-diodo-3-methoxycyclohexa-1,3-diene-1-carboxylic acid methyl ester (14% yield. IR: 2947, 2830, 1717, 1602, 1546, 1432, 1362, 1278, 1241, 1191, 1155, 1135, 1078, 999, 977, 911, 866, 808, 793, 763, 728, 627. $^1$H-NMR: 3.82 (*s*, 3 H); 3.62 (*s*, 3 H); 2.75 (*dd*, $J = 7$, 9.8, 2 H); 2.59 (*dd*, $J = 7$, 9.8, 2 H). $^{13}$C-NMR: 167.0 (*s*); 153.6 (*s*); 136.8 (*s*); 97.4 (*s*); 85.9 (*s*); 60.0 (*q*); 52.1 (*q*); 35.9 (*t*); 29.1 (*t*). MS: 420 (0, $M^+$), 389 (10), 278 (8), 261 (19), 234 (62), 219 (27), 203 (8), 191 (18), 181 (9), 166 (100), 151 (12), 135 (35), 127 (10), 123 (17), 107 (20), 95 (18), 92 (23), 77 (41), 64 (29), 59 (32), 51 (16)), and *f*) the known cyclopent-2-ene-1,2-dicarboxylic acid dimethyl ester [50] (16% yield. $^{13}$C-NMR: 173.4 (*s*); 165.2 (*s*); 139.7 (*d*); 138.7 (*s*); 52.2 (*q*); 51.7 (*q*); 51.0 (*d*); 31.1 (*t*); 26.6 (*t*)). We are actually extending and exploring in more detail this particularly rare version of the *Favorskii* rearrangement to other substrates [51], with only 1.0 mol-equiv. of $I_2$.

24) Most of them are naturally occurring in musk rat (**1d**, **1f**, **1g**, and **1h** [53]), civet cat (**1e**, **1f**, **1g**, **1h**, and **IVa** [54][9b]), and musk deer (tincture of Tonkin musk, **1e**, and **5c** [55]).

*Scheme 2*




| | n | R | C=C |
|---|---|---|---|
| **5a** | 5 | Me | – |
| **5b** | 5 | Me | (*Z*)-C(5)=C(6) |
| **5c** | 6 | Me | – |
| **5d** | 6 | Me | (*Z*)-C(5)=C(6) |
| **5e** | 6 | H | (*Z*)-C(4)=C(5) |
| **5f** | 7 | Me | – |
| **5g** | 7 | H | C(5)=C(6) |
| **5h** | 7 | H | C(7)=C(8) |
| **5i** | 7 | H | C(8)=C(9) |
| **5j** | 3 | H | C(4)=C(5), C(8)=C(9) |

| | n | R | C=C | Yield |
|---|---|---|---|---|
| **8a** | 5 | Me | – | 72% |
| **8b** | 5 | Me | (*Z*)-C(7)=C(8) | 52% |
| **8c** | 6 | Me | – | 77% |
| **8d** | 6 | Me | (*Z*)-C(7)=C(8) | 60% |
| **8e** | 6 | H | (*Z*)-C(6)=C(7) | 78% |
| **8f** | 7 | Me | – | 86% |
| **8g** | 7 | H | C(7)=C(8) | 78% |
| **8h** | 7 | H | C(9)=C(10) | 76% |
| **8i** | 7 | H | C(10)=C(11) | 85% |
| **8j** | 3 | H | C(6)=C(7), C(10)=C(11) | 84% |

*i*) $I_2$ (2.2 mol-equiv.), KOH, MeOH, 0°. *ii*) *m*-CPBA, $CH_2Cl_2$. *iii*) NaOH, MeOH/$H_2O$, then HCl, 65°. *iv*) $Me_3S(O)I$, $^t$BuOH, $^t$BuOK, 50°.

*Methyl (1Z)-Cycloundec-1-ene-1-carboxylate* (**2c**). According to *G.P.A*. After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 61%. IR: 2927, 2858, 1714, 1639, 1463, 1437, 1376, 1345, 1323, 1231, 1191, 1163, 1115, 1054, 1031, 1010, 989, 939, 909, 882, 866, 838, 807, 788, 762, 736, 722. $^1$H-NMR: 6.10 (*t*, *J* = 10, 1 H); 3.76 (*s*, 3 H); 2.53 (*dt*, *J* = 5, 8, 2 H); 2.32 (*t*, *J* = 5.5, 2 H); 1.61–1.51 (*m*, 4 H); 1.43–1.34 (*m*, 4 H); 1.34–1.25 (*m*, 4 H); 1.23–1.18 (*m*, 2 H). $^{13}$C-NMR: 169.0 (*s*); 143.6 (*d*); 131.7 (*s*); 51.2 (*q*); 35.7 (*t*); 29.9 (*t*); 27.0 (*t*); 26.3 (*t*); 25.9 (2*t*); 25.8 (*t*); 25.6 (*t*); 25.2 (*t*). MS: 210 (100, $M^+$), 179 (20), 167 (18), 153 (96), 149 (22), 109 (24), 95 (69), 81 (62); 67 (48), 55 (33), 41 (42). Weak, very vaguely woody, cedar.

*Methyl (1Z)-Cyclododec-1-ene-1-carboxylate* (**2d**). According to *G.P.A*. After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 56%[25]). IR: 2926, 2859, 1715, 1637, 1461, 1439, 1377, 1231, 1193, 1152, 1121, 1106, 1057, 1004, 942, 918, 894, 852, 818, 730, 700. $^1$H-NMR: 6.11 (*t*, *J* = 8, 1 H); 3.75 (*s*, 3 H); 2.48 (*dt*, *J* = 5, 8, 2 H); 2.35 (*t*, *J* = 6.5, 2 H); 1.68–1.62 (*m*, 2 H); 1.54–1.50 (*m*, 2 H); 1.48–1.42 (*m*, 2 H); 1.39–1.23 (*m*, 10 H). $^{13}$C-NMR: 168.4 (*s*); 145.0 (*d*); 130.3 (*s*); 51.1 (*q*); 33.8 (*t*); 29.6 (*t*); 27.3 (*t*); 26.6 (*t*); 26.1 (*t*); 25.7 (*t*); 25.2 (*t*); 24.4 (*t*); 24.1 (*t*); 23.7 (*t*). MS: 224 (100, $M^+$), 193 (35), 167 (31), 153 (50), 109 (52), 95 (78), 81 (88), 67 (62), 55 (60), 41 (62).

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[25]) If the reaction time and/or the temperature exceeded the prescription, methyl (1*Z*)-2-iodocyclododec-1-ene-1-carboxylate was also isolated as a by-product. $^1$H-NMR: 3.80 (*s*, 3 H); 2.58 (*t*, *J* = 7, 2 H); 2.45 (*t*, *J* = 6, 2 H); 1.68 (*quint.*, *J* = 6, 2 H); 1.49 (*quint.*, *J* = 7, 2 H); 1.41–1.30 (*m*, 12 H). $^{13}$C-NMR: 170.3 (*s*); 142.3 (*s*); 106.0 (*s*); 52.0 (*q*); 36.7 (*t*); 28.7 (*t*); 27.2 (*t*); 25.6 (*t*); 24.3 (*t*); 24.2 (2*t*); 24.1 (*t*); 22.9 (*t*); 22.3 (*t*). MS: 350 (40, $M^+$), 319 (10), 223 (23), 163 (63), 121 (28), 107 (21), 95 (55), 81 (100), 67 (47).

*Methyl (1Z)-Cyclotridec-1-ene-1-carboxylate* (**2e**). According to *G.P.A.* After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 2%[26]). IR (GC): 2925, 2858, 1715, 1638, 1460, 1440, 1375, 1233, 1195, 1153, 1124, 1106, 1057. $^1$H-NMR: 5.89 (*t*, *J* = 7.7, 1 H); 3.74 (*s*, 3 H); 2.44 (*dt*, *J* = 5, 6.3, 2 H); 2.35 (*t*, *J* = 7.5, 2 H); 1.68–1.23 (*m*, 18 H). $^{13}$C-NMR (deduced from impurities): 168.7 (*s*); 141.3 (*d*); 131.3 (*s*); 51.1 (*q*); 33.3 (*t*); 28.9 (*t*); 27.9 (*t*); 27.0 (*t*); 26.6 (*t*); 26.4 (*t*); 25.6 (*t*); 25.4 (*t*); 24.7 (*t*); 24.4 (*t*); 23.7 (*t*). MS: 238 (57, $M^+$), 207 (5); 178 (9), 164 (15), 153 (21), 149 (17), 141 (16), 135 (24), 127 (20), 125 (27), 123 (22), 121 (24); 113 (35), 111 (32), 109 (43), 107 (23), 101 (23), 97 (50), 95 (79), 87 (37), 81 (100), 69 (40), 67 (85), 55 (89), 41 (96).

*Methyl (1Z)-Cyclotetradec-1-ene-1-carboxylate* (**2f**). According to *G.P.A.* After distillation, yield 83%[27]). B.p. 120°/0.2 mbar. IR: 2925, 2856, 1715, 1640, 1457, 1440, 1373, 1349, 1321, 1234, 1196, 1169, 1154, 1138, 1125, 1105, 1057, 1025, 997, 948, 904, 805, 768, 748, 716. $^1$H-NMR: 5.82 (*t*, *J* = 7.5, 1 H); 3.73 (*s*, 3 H); 2.47 (*dt*, *J* = 5, 7, 2 H); 2.31 (*t*, *J* = 7, 2 H); 1.49–1.42 (*m*, 2 H); 1.40–1.22 (*m*, 18 H). $^{13}$C-NMR: 168.8 (*s*); 143.2 (*d*); 131.7 (*s*); 51.1 (*q*); 33.6 (*t*); 28.5 (*t*); 27.7 (*t*); 27.0 (*t*); 26.8 (*t*); 26.0 (*t*); 25.6 (*t*); 25.4 (*t*); 24.8 (*t*); 24.5 (*t*); 23.8 (*t*); 23.7 (*t*). MS: 252 (88, $M^+$), 221 (21), 113 (25), 109 (38), 95 (69), 81 (85), 67 (78), 55 (91), 41 (100).

*Methyl (1Z)-Cyclopentadec-1-ene-1-carboxylate* (**2g**). According to *G.P.A.* After CC ($SiO_2$, cyclohexane/$Et_2O$ 97:3 to 1:1), yield 83%. B.p. 180°/0.1 mbar. IR: 2924, 2855, 1716, 1640, 1458, 1437, 1375, 1323, 1195, 1154, 1028, 1000, 903, 809, 718. $^1$H-NMR: 5.86 (*t*, *J* = 6, 1 H); 3.73 (*s*, 3 H); 2.47 (*dt*, *J* = 5, 7, 2 H); 2.32 (*t*, *J* = 6, 2 H); 1.52–1.43 (*m*, 4 H); 1.38–1.22 (*m*, 18 H). $^{13}$C-NMR: 168.7 (*s*); 143.6 (*d*); 131.7 (*s*); 51.2 (*q*); 33.9 (*t*); 28.9 (*t*); 28.6 (*t*); 27.5 (*t*); 27.3 (*t*); 27.2 (*t*); 27.1 (2*t*); 26.9 (*t*); 26.8 (2*t*); 26.6 (*t*); 25.6 (*t*). MS: 266 (100, $M^+$), 235 (18), 109 (18), 95 (32), 81 (38), 67 (29), 55 (34), 41 (30).

*Methyl (1Z)-Cyclohexadec-1-ene-1-carboxylate* (**2h**). According to *G.P.A.* After CC ($SiO_2$, cyclohexane/$Et_2O$ 97:3), yield 50%. B.p. 200°/0.1 mbar. IR: 2923, 2854, 1717, 1640, 1459, 1435, 1376, 1325, 1192, 1154, 1029, 1003, 901, 811, 720. $^1$H-NMR: 5.85 (*t*, *J* = 6, 1 H); 3.73 (*s*, 3 H); 2.46 (*dt*, *J* = 5, 7, 2 H); 2.30 (*t*, *J* = 6, 2 H); 1.48–1.41 (*m*, 4 H); 1.35–1.24 (*m*, 20 H). $^{13}$C-NMR: 168.7 (*s*); 143.0 (*d*); 131.5 (*s*); 51.1 (*q*); 34.3 (*t*); 29.0 (*t*); 28.9 (*t*); 27.9 (*t*); 27.7 (*t*); 27.6 (*t*); 27.4 (*t*); 27.2 (2*t*); 27.1 (*t*); 26.7 (*t*); 25.9 (*t*); 25.7 (*t*); 25.4 (*t*). MS: 280 (100, $M^+$); 249 (12); 109 (18); 95 (30); 81 (32); 67 (24); 55 (27); 41 (25).

*Epoxidation to* **3** *or* **8**: *General Procedure B (G.P.B)*. A mixture of unsaturated ester **2** or **6** (1.0 mol-equiv.) and *m*-CPBA (1.0 mol-equiv.) in $CH_2Cl_2$ (2.7 ml/mmol) was stirred at 20° for 24 h. The mixture was diluted, extracted with 15% aq. $NaHSO_3$ soln., washed with sat. aq. $NaHCO_3$ soln. and brine, dried ($Na_2SO_4$), and concentrated and the residue purified.

*Methyl* cis-*11-Oxabicyclo[8.1.0]undecane-1-carboxylate* (**3b**). According to *G.P.B.* After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 63%. IR: 2935, 2871, 1749, 1448, 1278, 1193, 1129, 1006. $^1$H-NMR: 3.80 (*s*, 3 H); 3.43 (*dd*, *J* = 4, 10, 1 H); 2.56–2.50 (*m*, 1 H); 2.13–2.07 (*m*, 1 H); 1.83–1.76 (*m*, 1 H); 1.73–1.66 (*m*, 2 H); 1.62–1.44 (*m*, 9 H); 1.36–1.25 (*m*, 2 H). $^{13}$C-NMR: 173.8 (*s*); 64.6 (*d*); 64.6 (*s*); 52.3 (*q*); 34.1 (*t*); 27.5 (*t*); 26.8 (*t*); 26.0 (*t*); 24.4 (2*t*); 23.4 (*t*); 24.3 (*t*). MS: 212 (0, $M^+$), 153 (12), 135 (100), 109 (18), 95 (23), 93 (27), 81 (35), 71 (39), 69 (45), 67 (52), 55 (70), 41 (47).

*Methyl* cis-*12-Oxabicyclo[9.1.0]dodecane-1-carboxylate* (**3c**). According to *G.P.B.* After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 70%. IR: 2937, 2870, 1745, 1447, 1352, 1268, 1199, 1164, 1134, 999, 854,

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[26]) The main by-product was methyl (1*Z*)-2-iodocyclotridec-1-ene-1-carboxylate (64%): IR: 2937, 2867, 1746, 1437, 1267, 1155, 1121, 1027. $^1$H-NMR: 3.79 (*s*, 3 H); 2.60 (*t*, *J* = 7.5, 2 H); 2.37 (*t*, *J* = 7.5, 2 H); 1.70–1.64 (*m*, 2 H); 1.57–1.49 (*m*, 2 H); 1.43–1.32 (*m*, 12 H); 1.30–1.23 (*m*, 2 H). $^{13}$C-NMR: 170.1 (*s*); 144.4 (*s*); 106.1 (*s*); 52.1 (*q*); 39.4 (*t*); 29.9 (*t*); 26.5 (*t*); 26.1 (*t*); 26.0 (*t*); 25.9 (*t*); 25.8 (2*t*); 25.6 (2*t*); 25.5 (*t*). MS: 364 (18, $M^{+\bullet}$), 333 (6), 237 (28), 177 (22), 135 (18), 121 (23), 109 (21), 95 (100), 81 (67), 67 (42), 55 (35), 41 (35).

[27]) Methyl (1*Z*)-2-iodocyclotetradec-1-ene-1-carboxylate was also isolated in 14% yield. IR: 2926, 2856, 1727, 1627, 1460, 1443, 1431, 1350, 1270, 1248, 1206, 1190, 1168, 1145, 1124, 1103, 1062, 1043, 1031, 831, 806, 775, 750, 717. $^1$H-NMR: 3.79 (*s*, 3 H); 2.56 (*t*, *J* = 9, 2 H); 2.35 (*t*, *J* = 7, 2 H); 1.61 (*quint.*, *J* = 7.5, 2 H); 1.46–1.40 (*m*, 2 H); 1.38–1.30 (*m*, 16 H). $^{13}$C-NMR: 170.3 (*s*); 141.4 (*s*); 105.2 (*s*); 52.1 (*q*); 39.8 (*t*); 30.9 (*t*); 27.2 (*t*); 26.5 (*t*); 26.3 (*t*); 26.2 (*t*); 25.6 (*t*); 25.2 (*t*); 25.1 (*t*); 24.9 (*t*); 23.9 (*t*); 23.8 (*t*). MS: 378 (33, $M^{+\bullet}$), 347 (11), 251 (52), 191 (38), 135 (25), 109 (82), 95 (100), 81 (68), 67 (67), 55 (58), 41 (70).

771. $^1$H-NMR: 3.79 (*s*, 3 H); 3.38 (*dd*, *J* = 2, 9, 1 H); 2.50–2.43 (*m*, 1 H); 2.09–2.01 (*m*, 1 H); 1.83–1.73 (*m*, 1 H); 1.69–1.58 (*m*, 2 H); 1.55–1.23 (*m*, 13 H). $^{13}$C-NMR: 170.8 (*s*); 63.6 (*d*); 62.6 (*s*); 52.2 (*q*); 34.4 (*t*); 28.9 (*t*); 26.8 (*t*); 26.5 (*t*); 26.3 (*t*); 25.8 (*t*); 23.7 (*t*); 23.0 (*t*); 22.0 (*t*). MS: 226 (1, $M^+$), 210 (12), 167 (13), 149 (100), 95 (43), 81 (79), 71 (54), 67 (69), 55 (83), 41 (53).

*Methyl* cis-*13-Oxabicyclo[10.1.0]tridecane-1-carboxylate* (**3d**). According to *G.P.B.* After CC ($SiO_2$, cyclohexane/AcOEt 98:2), yield 65%. IR: 2926, 2860, 2842, 1740, 1471, 1433, 1326, 1308, 1289, 1257, 1243, 1217, 1197, 1135, 1102, 1059, 1034, 1004, 978, 962, 918, 877, 816, 753, 720, 703. $^1$H-NMR: 3.77 (*s*, 3 H); 3.22 (*dd*, *J* = 3, 10, 1 H); 2.47–2.40 (*m*, 1 H); 2.11–2.05 (*m*, 1 H): 1.90–1.86 (*m*, 1 H); 1.61–1.58 (*m*, 1 H); 1.53–1.24 (*m*, 16 H). $^{13}$C-NMR: 170.6 (*s*); 64.0 (*d*); 62.0 (*s*); 52.2 (*q*); 33.1 (*t*); 28.0 (*t*); 27.0 (*t*); 26.9 (*t*); 25.1 (*t*); 25.0 (*t*); 24.6 (*t*); 24.0 (*t*); 23.2 (*t*); 23.1 (*t*). MS: 240 (1, $M^+$), 181 (15), 163 (42), 121 (23), 109 (27), 95 (83), 81 (92), 71 (77), 67 (62), 55 (100), 41 (67).

*Methyl* cis-*14-Oxabicyclo[11.1.0]tetradecane-1-carboxylate* (**3e**). According to *G.P.B.* After CC ($SiO_2$, cyclohexane/AcOEt 98:2), GC yield 47%. IR (GC): 2937, 2868, 1745, 1448, 1351, 1263, 1198, 1159, 1132. $^1$H-NMR: 3.77 (*s*, 3 H); 3.18 (*dd*, *J* = 3.5, 10.2, 1 H); 2.44–2.39 (*m*, 1 H); 2.06–1.98 (*m*, 1 H); 1.72–1.65 (*m*, 1 H); 1.52–1.46 (*m*, 2 H); 1.44–1.20 (*m*, 17 H). $^{13}$C-NMR (deduced from impurities): 170.4 (*s*); 63.1 (*d*); 62.6 (*s*); 52.1 (*q*); 33.5 (*t*); 28.2 (*t*); 27.0 (*t*); 26.3 (*t*); 26.1(*t*); 25.0 (*t*); 24.9 (*t*); 24.7 (*t*); 24.17 (*t*); 23.9 (*t*); 23.0 (*t*). MS: 254 (3, $M^+$), 239 (4), 195 (9), 177 (6), 166 (6), 138 (8), 135 (12), 123 (11), 121 (13), 109 (27), 95 (64), 82 (68), 71 (79), 69 (44), 67 (53), 55 (100), 43 (28), 41 (75), 28 (50).

*Methyl* cis-*15-Oxabicyclo[12.1.0]pentadecane-1-carboxylate* (**3f**). According to *G.P.B.* After distillation, yield 53%. Bp. 150°/0.2 mbar. IR: 2926, 2858, 1733, 1458, 1440, 1349, 1323, 1250, 1195, 1152, 1129, 1076, 1016, 989, 923, 862, 757, 716. $^1$H-NMR: 3.77 (*s*, 3 H); 3.06 (*dd*, *J* = 3.8, 8.9, 1 H); 2.38–2.32 (*m*, 1 H); 1.97–1.91 (*m*, 1 H); 1.63–1.56 (*m*, 1 H); 1.52–1.46 (*m*, 2 H); 1.44–1.26 (*m*, 19 H). $^{13}$C-NMR: 170.3 (*s*); 62.8 (*d*); 62.8 (*s*); 52.1 (*q*); 32.1 (*t*); 27.7 (*t*); 26.9 (*t*); 26.5 (2*t*); 26.0 (*t*); 25.8 (*t*); 25.4 (*t*); 25.0 (*t*); 24.3 (2*t*); 24.0 (*t*). MS: 268 (5, $M^+$), 252 (31), 221 (10), 209 (13), 109 (40), 95 (62), 82 (72), 71 (62), 67 (58), 55 (100), 41 (70).

*Methyl* cis-*16-Oxabicyclo[13.1.0]hexadecane-1-carboxylate* (**3g**). According to *G.P.B.* After distillation, yield 88%. B.p. 130°/0.1 mbar. IR: 2925, 2857, 1733, 1458, 1440, 1350, 1325, 1254, 1195, 1150, 1129, 988, 924, 758, 716. $^1$H-NMR: 3.77 (*s*, 3 H); 3.05 (*dd*, *J* = 3.5, 8, 1 H); 2.29 (*dt*, *J* = 13, 7, 1 H); 1.91–1.84 (*m*, 1 H); 1.55 (*quint.*, *J* = 7, 2 H); 1.49–1.29 (*m*, 22 H). $^{13}$C-NMR: 170.5 (*s*); 62.7 (*s*); 62.2 (*d*); 52.1 (*q*); 32.7 (*t*); 28.0 (*t*); 27.7 (*t*); 27.3 (*t*); 27.0 (*t*); 26.9 (*t*); 26.8 (*t*); 26.6 (*t*); 26.5 (*t*); 26.4 (*t*); 26.1 (*t*); 25.3 (*t*); 24.9 (*t*). MS: 282 (10, $M^+$), 266 (10), 223 (22), 123 (27), 109 (34), 96 (58), 82 (88), 71 (81), 67 (53), 55 (100), 41 (68).

*Methyl* cis-*17-Oxabicyclo[14.1.0]heptadecane-1-carboxylate* (**3h**). According to *G.P.B.* After distillation, yield 53%. B.p. 150°/0.1 mbar. IR: 2924, 2855, 1733, 1458, 1439, 1352, 1328, 1260, 1194, 1149, 1130, 988, 925, 784, 759, 717. $^1$H-NMR: 3.77 (*s*, 3 H); 3.00 (*dd*, *J* = 4, 9, 1 H); 2.24 (*dt*, *J* = 13, 6, 1 H); 1.92–1.85 (*m*, 1 H); 1.56–1.44 (*m*, 4 H); 1.42–1.28 (*m*, 22 H). $^{13}$C-NMR: 170.3 (*s*); 63.0 (*s*); 62.5 (*d*); 52.1 (*q*); 32.8 (*t*); 27.8 (*t*); 27.5 (*t*); 27.4 (2*t*); 27.1 (*t*); 27.0 (*t*); 26.9 (*t*); 26.4 (*t*); 26.2 (2*t*); 26.1 (*t*); 25.3 (*t*); 24.2 (*t*). MS: 296 (10, $M^+$), 280 (85), 249 (15), 237 (19), 123 (21), 109 (35), 95 (68), 81 (75), 71 (58), 67 (62), 55 (100), 41 (70).

*Hydrolytic Decarboxylation of* **3** *to* **1** *or* **7** *to* **5**: *General Procedure C (G.P.C)*. A mixture of epoxy ester **3** or **7** (1.0 mol-equiv.), NaOH (2.1 mol-equiv.), and MeOH/$H_2O$ 1:1 (5.6 ml/mmol) was heated under reflux for 5 h. The cold mixture was then acidified with a soln. of 10N HCl (0.25 ml/mmol) in MeOH/$H_2O$ 1:1 (2.1 ml/mmol) and then heated under reflux. After 1 h, the cold mixture was poured into sat. aq. $NaHCO_3$ soln. and extracted with $Et_2O$. The org. phase was washed with brine, dried ($Na_2SO_4$), and concentrated and the residue purified by distillation: pure ketone **1** or **5** in the yields reported in *Schemes 1* and *2*.

*Oxiranylation to* **4** *or* **8**: *General Procedure D (G.P.D)*. To a suspension of $^t$BuOK (2.8g, 25 mmol) and trimethylsulfoxonium iodide (5.5 g, 25 mmol) in $^t$BuOH (42 ml) at 50°, the macrocyclic ketone **1** or **5** (21 mmol) was added dropwise, and the mixture was kept at 50° for 6 to 18 h. After completion, the cold soln. was diluted. with $Et_2O$ and washed twice with sat. aq. $NaHCO_3$ soln., then to neutrality with brine. The org. phase was dried ($MgSO_4$) and concentrated and the residue purified by CC ($SiO_2$, cyclohexane/AcOEt 9:1).

*1-Oxaspiro[2.9]dodecane* (**4a**). According to *G.P.D.* Yield 74%. IR: 2920, 2870, 1475, 1443, 1353, 1309, 1183, 1148, 1098, 1030, 988, 904, 851, 784, 763, 731. $^1$H-NMR: 1.6–1.5 (*m*, 14 H); 1.75–1.65 (*m*, 2 H); 1.85 (*t*, *J* = 5.8, 1 H); 1.88 (*t*, *J* = 7.8, 1 H); 2.61 (*s*, 2 H). $^{13}$C-NMR: 59.5 (*s*); 54.9 (*t*); 32.9 (2*t*); 25.1

(2*t*); 24.8 (*t*); 24.2 (2*t*); 22.6 (2*t*). MS: 168 (7, $M^+$), 139 (27), 125 (100), 111 (97), 97 (50), 95 (60), 85 (45), 83 (46), 81 (65), 72 (57), 69 (38), 67 (67), 55 (82), 41 (65). Metallic, naphthalenic. Citrus, lime, green and mango flavor.

*1-Oxaspiro[2.10]tridecane* (**4b**). According to *G.P.D.* Yield 74%. IR: 3028, 2918, 2862, 1473, 1443, 1393, 1346, 1276, 1231, 1211, 1187, 1153, 1106, 1081, 1029, 973, 957, 921, 895, 878, 842, 796, 767, 723, 702, 661. $^1$H-NMR: 2.61 (*s*, 2 H); 1.85–1.78 (*m*, 2 H); 1.64–1.40 (*m*, 18 H). $^{13}$C-NMR: 60.1 (*s*); 54.2 (*t*); 33.7 (2*t*); 26.7 (2*t*); 26.2 (2*t*); 25.6 (2*t*); 23.1 (2*t*). MS: 182 (2, $M^+$), 139 (70), 125 (100), 111 (43), 97 (45), 95 (30), 85 (62), 81 (33), 72 (72), 67 (52), 55 (64), 41 (65). Woody, grapefruit, moos, earthy.

*1-Oxaspiro[2.12]pentadecane* (**4d**). According to *G.P.D.* Yield 84%. IR: 3030, 2917, 2849, 1462, 1445, 1395, 1347, 1269, 1176, 1147, 1104, 1052, 975, 934, 898, 872, 822, 802, 753, 727, 711. $^1$H-NMR: 2.57 (*s*, 2 H); 1.69–1.61 (*m*, 2 H); 1.55–1.46 (*m*, 4 H); 1.41–1.36 (*m*, 18 H). $^{13}$C-NMR: 59.6 (*s*); 53.5 (*t*); 33.0 (2*t*); 27.0 (2*t*); 26.2 (2*t*); 25.7 (2*t*); 25.4 (2*t*); 22.8 (2*t*). MS: 210 (3, $M^+$), 195 (6), 125 (17), 111 (22), 97 (50), 85 (91), 72 (100), 55 (49), 41 (51). Fatty, costus with slightly pine aspects[28]).

*1-Oxaspiro[2.13]hexadecane* (**4e**). According to *G.P.D.* Yield 70%. IR: 3030, 2925, 2856, 1460, 1395, 1146, 1102, 900, 710. $^1$H-NMR: 2.56 (*s*, 2 H); 1.62–1.54 (*m*, 2 H); 1.48–1.42 (*m*, 2 H); 1.42–1.24 (*m*, 22 H). $^{13}$C-NMR: 59.6 (*s*); 53.8 (*t*); 32.7 (2*t*); 29.8 (2*t*); 26.3 (2*t*); 25.7 (2*t*); 24.7 (*t*); 23.9 (2*t*); 21.8 (2*t*). MS: 224 (4, $M^+$), 209 (9), 125 (14), 111 (22), 97 (48), 85 (93), 72 (100), 69 (21), 67 (30), 55 (54), 41 (50).

*1-Oxaspiro[2.14]heptadecane* (**4f**). According to *G.P.D.* Yield 72%. IR: 3030, 2924, 2855, 1458, 1396, 1349, 1287, 1145, 1099, 1064, 933, 901, 805, 746, 709. $^1$H-NMR: 2.57 (*s*, 2 H); 1.64–1.56 (*m*, 2 H); 1.52–1.43 (*m*, 4 H); 1.40–1.32 (*m*, 22 H). $^{13}$C-NMR: 59.8 (*s*); 53.8 (*t*); 33.8 (2*t*); 27.5 (2*t*); 26.8 (2*t*); 26.7 (2*t*); 26.6 (2*t*); 26.5 (2*t*); 23.5 (2*t*). MS: 238 (4, $M^+$), 223 (6), 125 (11), 111 (22), 97 (40), 85 (93), 72 (100), 67 (25), 55 (52), 41 (51). Vaguely woody, fruity, pear, ambrette, weak.

*1-Oxaspiro[2.15]octadecane* (**4g**). According to *G.P.D.* Yield 86%. IR: 3030, 2924, 2855, 1459, 1397, 1350, 1291, 1163, 1140, 1103, 939, 903, 808, 711. $^1$H-NMR: 2.56 (*s*, 2 H); 1.63–1.56 (*m*, 2 H); 1.52–1.46 (*q*, $J = 7$, 2 H); 1.45–1.40 (*m*, 4 H); 1.38–1.30 (*m*, 22 H). $^{13}$C-NMR: 59.6 (*s*); 53.7 (*t*); 33.7 (2*t*); 27.4 (2*t*); 27.1 (2*t*); 26.7 (2*t*); 26.5 (4*t*); 26.4 (*t*); 23.5 (2*t*). MS: 252 (5, $M^+$), 237 (7), 141 (8), 125 (9), 111 (19), 97 (34), 85 (92), 72 (100), 67 (24), 55 (52), 41 (51). Vaguely musky, heavy, weak.

*1-Oxaspiro[2.16]nonadecane* (**4h**). According to *G.P.D.* Yield 91%. Alternatively, a soln. of (11*Z*)-1-oxaspiro[2.16]nonadec-11-ene (**IVb**; 132 mg, 0.5 mmol) in AcOEt (3 ml) was hydrogenated in the presence of 5% Pd/C (13 mg). After absorption of 1.0 equiv. of $H_2$, the mixture was filtered, the filtrate concentrated, and the residue bulb-to bulb distilled: **4h** (58 %)[29]). IR: 2922, 2853, 1458, 1396, 1350, 1295, 1144, 1100, 1033, 933, 904, 803, 734, 718. $^1$H-NMR: 2.57 (*s*, 2 H); 1.63–1.57 (*m*, 2 H); 1.51–1.45 (*q*, $J = 7$, 2 H); 1.45–1.40 (*m*, 4 H); 1.40–1.27 (*m*, 24 H). $^{13}$C-NMR: 59.9 (*s*); 53.8 (*t*); 34.0 (2*t*); 28.2 (2*t*); 27.8 (2*t*); 27.7 (2*t*); 27.5 (2*t*); 27.1 (2*t*); 27.0 (2*t*); 23.9 (2*t*). MS: 266 (2, $M^+$), 135 (6), 121 (8), 111 (13), 97 (28), 83 (31), 69 (41), 55 (95), 41 (100), 29 (36). Woody, sawdust, weak.

*(+)-(1Z,3*R*)-Methyl 3-Methylcyclotetradec-1-ene-1-carboxylate* (**6c**). According to *G.P.A.* After bulb-to-bulb distillation, yield 56%. B.p. 100°/0.21 mbar. $[\alpha]_D^{20} = +24.5$ ($c = 3.0$, $CCl_4$). IR: 2926, 2857, 1715, 1640, 1456, 1440, 1370, 1228, 1192, 1171, 1126, 1099, 1067, 1031, 1002, 905, 820, 765, 718. $^1$H-NMR: 5.51 (*d*, $J = 7.5$, 1 H); 3.72 (*s*, 3 H); 3.11–3.03 (*m*, 1 H); 2.68–2.62 (*m*, 1 H); 1.91 (*dt*, $J = 2.8$, 12.0, 1 H); 1.52–1.32 (*m*, 9 H); 1.28–1.18 (*m*, 8 H); 1.14–1.05 (*m*, 3 H); 0.96 (*d*, $J = 7$, 3 H). $^{13}$C-NMR: 168.9 (*s*); 148.7 (*d*); 130.4 (*s*); 51.1 (*q*); 37.0 (*t*); 34.1 (*t*); 33.7 (*d*); 27.1 (*t*); 26.8 (*t*); 26.0 (*t*); 25.6 (2*t*); 24.5 (*t*); 24.4 (*t*); 23.4 (2*t*); 21.4 (*q*). MS : 266 (77, $M^+$), 235 (29), 141 (40), 128 (43), 109 (55), 95 (100), 81 (87), 67 (82), 55 (91), 41 (86).

*(+)-(1Z,3*R*,5Z)-Methyl 3-Methylcyclotetradeca-1,5-diene-1-carboxylate* (**6d**). According to *G.P.A.* After CC ($SiO_2$, cyclohexane/AcOEt 95:5), yield 3%. B.p. 100°/0.22 mbar. $[\alpha]_D^{20} = +47.4$ ($c = 1.9$, $CHCl_3$). IR: 3009, 2927, 2857, 1712, 1643, 1456, 1435, 1378, 1239, 1195, 1157, 1123, 1105, 1058, 1007, 831,

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[28]) Compound **4d** was already submitted to our perfumers in 1975 by *W. K. Giersch* (*Firmenich SA*).

[29]) In EtOH, over reduction produced methylcycloheptadecane in 38% yield. IR: 2921, 2852, 1458, 1375, 1350, 1294, 1110, 1066, 727. $^1$H-NMR: 1.46–1.42 (*m*, 1 H); 1.36–1.26 (*m*, 28 H); 1.19–1.11 (*m*, 4 H); 0.85 (*d*, $J = 7$, 3 H). $^{13}$C-NMR: 35.3 (2*t*); 31.3 (*d*); 28.2 (2*t*); 27.9 (2*t*); 27.6 (6*t*); 27.3 (2*t*); 25.5 (2*t*); 20.9 (*q*). MS: 252 (10, $M^{+\cdot}$), 125 (11), 111 (24), 97 (48), 83 (59), 69 (61), 57 (51), 55 (97), 43 (65), 41 (100), 29 (33).

756, 721. $^1$H-NMR: 5.56 (*d*, *J* = 8.5, 1 H); 5.53–5.37 (*m*, 2 H); 3.74 (*s*, 3 H); 3.28–3.20 (*m*, 1 H); 2.55–2.48 (*m*, 1 H); 2.24–2.02 (*m*, 4 H); 1.95–1.86 (*m*, 2 H); 1.57–1.48 (*m*, 1 H); 1.42–1.21 (*m*, 8 H); 1.17–1.09 (*m*, 2 H); 1.02 (*d*, *J* = 7, 3 H). $^{13}$C-NMR: 168.9 (*s*); 147.0 (*d*); 130.5 (*d*); 129.8 (*s*); 128.0 (*d*); 51.1 (*q*); 34.8 (*t*); 33.6 (*d*); 32.4 (*t*); 27.8 (*t*); 26.8 (*t*); 26.2 (*t*); 25.9 (*t*); 25.2 (*t*); 24.9 (*t*); 24.0 (*t*); 21.0 (*q*). MS: 264 (74, $M^+$), 233 (21), 205 (41), 175 (16), 149 (18), 135 (20), 126 (54), 95 (93), 81 (70), 67 (100), 55 (53), 41 (63).

*(+)-(1Z,3R)-Methyl 3-Methylcyclopentadec-1-ene-1-carboxylate* (**6f**). According to *G.P.A*. After bulb-to-bulb distillation, yield 48%. B.p. 110°/0.20 mbar. $[\alpha]_D^{20} = +9.8$ (*c* = 1.8, $CCl_4$). IR: 2923, 2852, 1717, 1640, 1449, 1440, 1371, 1350, 1192, 1163, 1106, 903, 861, 830, 761, 719. $^1$H-NMR: 5.57 (*d*, *J* = 8.5, 1 H); 3.73 (*s*, 3 H); 3.08–3.00 (*m*, 1 H); 2.65–2.59 (*m*, 1 H); 2.03–1.96 (*m*, 1 H); 1.49–1.40 (*m*, 9 H); 1.43–1.13 (*m*, 13 H); 0.95 (*d*, *J* = 7, 3 H). $^{13}$C-NMR: 169.0 (*s*); 148.1 (*d*); 130.6 (*s*); 51.1 (*q*); 38.1 (*t*); 34.2 (*t*); 33.6 (*d*); 27.8 (*t*); 27.7 (*t*); 27.5 (*t*); 27.2 (*t*); 27.1 (*t*); 27.0 (*t*); 26.9 (*t*); 26.7 (*t*); 26.4 (*t*); 25.8 (*t*); 21.8 (*q*). MS: 280 (18, $M^+$), 249 (9), 141 (16), 128 (14), 125 (14), 121 (11), 111 (18), 109 (26), 95 (49), 81 (49), 79 (32), 69 (43), 67 (54), 55 (85), 43 (40), 41 (100), 29 (35).

*(1R,13R,14R)/(1S,13R,14S)-Methyl 13-Methyl-15-oxabicyclo[12.1.0]pentadecane-1-carboxylate* (**7c**). According to *G.P.B*. After CC ($SiO_2$, cyclohexane/AcOEt 95:5), yield 82%; 8:2 mixture of stereoisomers. $[\alpha]_D^{20} = +8.43$ (*c* = 3.0, $CCl_4$). IR: 2926, 2858, 1734, 1458, 1441, 1349, 1322, 1251, 1195, 1156, 1136, 1104, 1047, 981, 956, 917, 794, 764, 718. $^1$H-NMR: 3.77 (*s*, 3 H); 2.77 (*d*, *J* = 9.5, 1 H); 2.44–2.37 (*m*, 1 H); 1.63–1.55 (*m*, 1 H); 1.50–1.34 (*m*, 18 H); 1.29–1.22 (*m*, 3 H); 1.10 (*d*, *J* = 7, 3 H). $^{13}$C-NMR: 170.4 (*s*); 68.4 (*d*); 63.7 (*s*); 52.0 (*q*); 34.6 (*t*); 33.2 (*d*); 32.4 (*t*); 26.8 (*t*); 26.7 (*t*); 26.4 (*t*); 26.3 (*t*); 25.8 (*t*); 24.4 (*t*); 24.0 (*t*); 23.7 (*t*); 23.6 (*t*); 18.6 (*q*). MS: major 282 (9, $M^+$), 254 (15), 223 (21), 149 (23), 123 (17), 109 (29), 95 (45), 85 (47), 82 (49), 69 (76), 55 (100), 41 (62); minor 282 (10, $M^+$), 254 (15), 223 (21), 149 (24), 123 (18), 109 (29), 95 (45), 85 (52), 82 (51), 69 (74), 55 (100), 41 (61).

*(1R,14R,15R)/(1S,14R,15S)-Methyl 14-Methyl-16-oxabicyclo[13.1.0]hexadecane-1-carboxylate* (**7f**). According to *G.P.B*. After CC ($SiO_2$, cyclohexane/AcOEt 97:3 → 95:5), yield 59%; 78:22 mixture of stereoisomers. $[\alpha]_D^{20} = +5.8$ (*c* = 2.5, $CCl_4$). IR: 2925, 2855, 1732, 1458, 1440, 1350, 1260, 1194, 1155, 1106, 1032, 790, 765, 729. $^1$H-NMR: major: 3.77 (*s*, 3 H); 2.75 (*d*, *J* = 9.5, 1 H); 2.37–2.28 (*m*, 1 H); 1.72–1.49 (*m*, 4 H); 1.45–1.16 (*m*, 20 H); 1.10 (*d*, *J* = 6.5, 3 H); minor: 3.75 (*s*, 3 H); 2.93 (*d*, *J* = 8, 1 H); 2.45–2.36 (*m*, 1 H); 1.72–1.49 (*m*, 4 H); 1.45–1.16 (*m*, 20 H); 0.93 (*d*, *J* = 6.5, 3 H). $^{13}$C-NMR (deduced from the mixture): 170.7 (*s*); 67.7 (*d*); 63.6 (*s*); 52.2 (*q*); 34.2 (*t*); 33.7 (*d*); 32.8 (*t*); 28.1 (*t*); 27.7 (*t*); 27.0 (*t*); 26.9 (*t*); 26.8 (*t*); 26.4 (*t*); 26.1 (*t*); 25.9 (*t*); 25.5 (*t*); 24.9 (*t*); 18.1 (*q*). MS: major: 296 (13, $M^+$), 280 (12), 268 (22), 237 (29), 181 (9), 163 (18), 127 (15), 123 (19), 109 (28), 95 (52), 81 (52), 69 (71), 55 (100), 41 (68); minor 296 (13, $M^+$), 280 (14), 268 (18), 237 (22), 181 (9), 163 (17), 127 (15), 123 (19), 109 (28), 95 (51), 85 (42), 82 (50), 81 (49), 69 (70), 55 (100), 41 (63).

rac-*5-Methyl-1-oxaspiro[2.13]hexadecane* (**8a**). According to *C.P.D*. After bulb-to-bulb distillation, 72% yield; 75:25 mixture of stereoisomers. B.p. 125°/0.1 mbar. IR: 2925, 2858, 1461, 1395, 1378, 1277, 1136, 943, 897, 800, 715. $^1$H-NMR: 2.60–2.53 (*m*, 1 H); 2.44–2.42 (*m*, 1 H); 2.03–1.95 (*m*, 2 H); 1.85–1.78 (*m*, 1 H); 1.5–1.34 (*m*, 16 H); 1.29–1.21 (*m*, 3 H); 1.19–1.10 (*m*, 3 H); 0.97 (*d*, *J* = 7, 2.25 H); 0.89 (*d*, *J* = 7, 0.75 H). $^{13}$C-NMR: major: 58.9 (*s*); 52.2 (*t*); 40.9 (*t*); 34.6 (*t*); 32.7 (*t*); 26.6 (*d*); 26.4 (*t*); 26.2 (*t*); 25.5 (*t*); 24.7 (*t*); 24.6 (*t*); 24.4 (*t*); 24.2 (*t*); 23.6 (*t*); 22.4 (*t*); 20.0 (*q*); minor: 58.8 (*s*); 54.8 (*t*); 40.2 (*t*); 35.2 (*t*); 32.8 (*t*); 27.1 (*d*); 26.3 (*t*); 23.7 (*t*); 24.8 (*t*); 24.6 (*t*); 24.3 (*t*); 24.2 (*t*); 24.0 (*t*); 23.6 (*t*); 21.1 (*t*); 19.9 (*q*). MS: major: 238 (6, $M^+$), 223 (36), 195 (12), 139 (22), 125 (18), 111 (100), 99 (41), 85 (51), 83 (33), 81 (31), 72 (55), 69 (38), 67 (30), 57 (22), 55 (68), 43 (27), 41 (58); minor: 238 (6, $M^+$), 223 (32), 195 (13), 139 (22), 125 (18), 111 (100), 99 (41), 85 (51), 83 (35), 81 (33), 72 (55), 69 (40), 67 (30), 57 (23), 55 (74), 43 (27), 41 (60). Woody, ambery, cedar, musky.

rac-*(7Z)-5-Methyl-1-oxaspiro[2.13]hexadec-7-ene* (**8b**). According to *G.P.D*. After bulb-to-bulb distillation, yield 52%; 80:20 mixture of stereoisomers. B.p. 120°/0.12 mbar. IR: 3028, 2926, 2851, 1456, 1396, 969, 937, 892, 837, 782, 706. $^1$H-NMR: 5.45–5.36 (*m*, 1 H); 5.25–5.20 (*m*, 1 H); 2.45 (*s*, 2 H); 2.16–2.07 (*m*, 4 H); 1.68–1.58 (*m*, 2 H); 1.52–1.33 (*m*, 11 H); 1.29–1.10 (*m*, 4 H); 1.06 (*d*, *J* = 7, 3 H). $^{13}$C-NMR: 132.0 (*d*); 130.9 (*d*); 58.5 (*s*); 53.4 (*t*); 41.6 (*t*); 37.8 (*t*); 33.3 (*t*); 30.5 (*d*); 30.2 (*t*); 27.7 (*t*); 27.1 (*t*); 24.7 (*t*); 24.1 (*t*); 23.4 (*t*); 23.2 (*t*); 21.6 (*q*). MS: 236 (32, $M^+$), 221 (10), 151 (12), 135 (16), 123 (30), 109 (46), 97 (72), 95 (74), 81 (94), 67 (87), 55 (100), 41 (87). Waxy, candle, musky, nitromusk, animal, woody, good.

*(5R)-5-Methyl-1-oxaspiro[2.14]heptadecane* (**8c**). According to *G.P.D*. After bulb-to-bulb distillation, yield 77%; 67:33 mixture of stereoisomers. B.p. 120°/0.1 mbar. $[\alpha]_D^{20} = +12.2$ (*c* = 1.7, $CHCl_3$). IR:

3029, 2923, 2855, 1458, 1395, 1377, 1350, 1284, 1138, 1102, 951, 897, 796, 710. $^1$H-NMR (deduced from the mixture): major: 2.54 (*d*, *J* = 4, 1 H); 2.46 (*d*, *J* = 4, 1 H); 1.96 – 1.60 (*m*, 9 H); 1.44 – 1.04 (*m*, 18 H); 0.96 (*d*, *J* = 7, 3 H); minor: 2.60 (*s*, 2 H); 2.12 – 1.60 (*m*, 9 H); 1.44 – 1.04 (*m*, 18 H); 0.90 (*d*, *J* = 7, 3 H). $^{13}$C-NMR: 58.9 (*s*); 52.8 (*t*); 41.5 (*t*); 35.7 (*t*); 33.8 (*t*); 28.2 (*d*); 27.5 (*t*); 27.0 (*t*); 26.8 (2*t*); 26.7 (2*t*); 26.5 (*t*); 26.2 (*t*); 25.1 (*t*); 23.9 (*t*); 20.6 (*q*). MS: major: 252 (10, $M^+$), 237 (22), 209 (11), 139 (12), 135 (12), 125 (15), 111 (63), 97 (55), 83 (63), 69 (67), 55 (100), 41 (73); minor: 252 (10, $M^+$), 237 (22), 209 (10), 139 (12), 135 (13), 125 (15), 111 (60), 97 (54), 83 (63), 69 (67), 55 (100), 41 (72). Rancid, oily, vaguely musky, candle, weak.

*(+)-(5*R*,7*Z*)-5-Methyl-1-oxaspiro[2.14]heptadec-7-ene* (**8d**). According to *G.P.D.* After bulb-to-bulb distillation, yield 60%; 60 : 40 mixture of stereoisomers. B.p. 120°/0.14 mbar. $[\alpha]_D^{20} = +15.1$ (neat). IR: 3008, 2924, 2855, 1458, 1395, 1376, 1349, 962, 897, 791, 721. $^1$H-NMR: (deduced from the mixture): major: 5.57 – 5.41 (*m*, 2 H); 2.55 (*d*, *J* = 4.5, 1 H); 2.50 (*d*, *J* = 4.5, 1 H); 2.26 – 2.12 (*m*, 2 H); 1.97 – 1.88 (*m*, 1 H); 1.75 – 1.62 (*m*, 2 H); 1.49 – 1.26 (*m*, 18 H); 1.00 (*d*, *J* = 7, 3 H); minor: 5.57 – 5.41 (*m*, 2 H); 2.58 (*s*, 2 H); 2.26 – 2.12 (*m*, 2 H); 1.97 – 1.88 (*m*, 1 H); 1.75 – 1.62 (*m*, 2 H); 1.49 – 1.26 (*m*, 18 H); 0.96 (*d*, *J* = 7, 3 H). $^{13}$C-NMR (deduced from the mixture): major: 131.6 (*d*); 128.0 (*d*); 58.6 (*s*); 53.1 (*t*); 41.8 (*t*); 34.5 (*t*); 33.4 (*t*); 32.0 (*d*); 28.0 (*t*); 27.2 (*t*); 27.0 (*t*); 26.6 (*t*); 26.3 (2*t*); 26.0 (2*t*); 22.8 (*t*); 20.1 (*q*); minor: 131.8 (*d*); 128.0 (*d*); 58.7 (*s*); 53.9 (*t*); 41.8 (*t*); 34.9 (*t*); 33.4 (*t*); 32.2 (*d*); 28.1 (*t*); 27.3 (*t*); 27.0 (*t*); 26.7 (*t*); 26.2 (*t*); 26.1 (*t*); 26.0 (*t*); 25.6 (*t*); 22.3 (*t*); 19.8 (*q*). MS: major: 250 (19, $M^+$), 235 (9), 193 (8), 147 (11), 135 (17), 123 (23), 111 (41), 109 (42), 97 (51), 95 (78), 81 (100), 67 (84), 55 (94), 41 (82); minor: 250 (20, $M^+$), 235 (10), 193 (9), 147 (10), 135 (17), 123 (23), 111 (43), 109 (41), 97 (54), 95 (76), 81 (100), 67 (84), 55 (96), 41 (84). Musky, animal, nitromusk, weak.

rac-*(6*Z*)-1-Oxaspiro[2.14]heptadec-6-ene* (**8e**). According to *G.P.D.* After bulb-to-bulb distillation, yield 78%. B.p. 120°/0.21 mbar. IR: 3005, 2924, 2855, 1457, 1397, 1349, 1036, 964, 903, 818, 768, 712. $^1$H-NMR: 5.46 – 5.33 (*m*, 2 H); 2.60 (*d*, *J* = 5, 1 H); 2.57 (*d*, *J* = 5, 1 H); 2.21 – 2.14 (*m*, 2 H); 2.09 – 1.97 (*m*, 2 H); 1.70 – 1.57 (*m*, 2 H); 1.48 – 1.33 (*m*, 18 H). $^{13}$C-NMR: 130.6 (*d*); 128.9 (*d*); 59.4 (*s*); 53.8 (*t*); 35.0 (*t*); 33.5 (*t*); 28.1 (*t*); 27.2 (*t*); 27.0 (*t*); 26.8 (*t*); 26.5 (*t*); 26.4 (2*t*); 26.2 (*t*); 23.4 (*t*); 23.2 (*t*). MS: 236 (11, $M^+$), 207 (10), 135 (12), 123 (26), 109 (50), 95 (77), 81 (89), 67 (100), 55 (88), 41 (83). Waxy, candle, musky, nitromusk, weak.

*(5*R*)-5-Methyl-1-oxaspiro[2.15]octadecane* (**8f**). According to *G.P.D.* After bulb-to-bulb distillation, yield 86%; 69 : 31 mixture of stereoisomers. B.p. 120°/0.1 mbar. $[\alpha]_D^{20} = +2.7$ (*c* = 1.5, $CCl_4$). IR: 3034, 2934, 2865, 1460, 1382, 1354, 953, 745. $^1$H-NMR (deduced from the mixture): major: 2.54 (*d*, *J* = 4.7, 1 H); 2.45 (*dd*, *J* = 4.7, 1.5, 1 H); 1.96 – 1.70 (*m*, 9 H); 1.43 – 1.05 (*m*, 20 H); 0.96 (*d*, *J* = 6.3, 3 H); minor: 2.59 (*s*, 2 H); 2.12 – 1.70 (*m*, 9 H); 1.43 – 1.05 (*m*, 20 H); 0.90 (*d*, *J* = 6.3, 3 H). $^{13}$C-NMR: 58.9 (*s*); 52.7 (*t*); 41.6 (*t*); 35.6 (*t*); 33.7 (*t*); 28.6 (*d*); 27.5 (2*t*); 27.2 (*t*); 27.1 (*t*); 26.7 (*t*); 26.5 (*t*); 26.2 (2*t*); 26.0 (*t*); 25.5 (*t*); 24.1 (*t*); 20.4 (*q*). MS: major: 266 (10, $M^+$), 251 (19), 223 (8), 208 (7), 149 (8), 139 (10), 135 (12), 125 (17), 121 (11), 111 (51), 97 (55), 95 (49), 83 (60), 81 (48), 69 (67), 67 (38), 57 (55), 55 (100), 43 (42), 41 (78); minor: 266 (11, $M^+$), 251 (12), 248 (8), 223 (6), 208 (5), 166 (5), 149 (9), 139 (9), 135 (12), 125 (13), 121 (12), 111 (43), 97 (52), 95 (44), 83 (61), 81 (46), 69 (67), 67 (38), 57 (60), 55 (100), 43 (42), 41 (71).

rac-*1-Oxaspiro[2.15]octadec-7-ene* (**8g**). According to *G.P.D.* After bulb-to-bulb distillation, yield 78%; 60 : 40 (*E*)/(*Z*) mixture. B.p. 100°/0.09 mbar. IR: 3028, 2925, 2854, 1458, 1442, 1397, 1368, 1349, 1289, 966, 935, 903, 810, 727, 711. $^1$H-NMR: major (*E*): 5.38 – 5.32 (*m*, 2 H); 2.61 (*d*, *J* = 5, 1 H); 2.52 (*d*, *J* = 5, 1 H); 2.07 – 2.01 (*m*, 4 H); 1.62 – 1.55 (*m*, 2 H); 1.46 – 1.28 (*m*, 20 H); minor (*Z*): 5.47 – 5.37 (*m*, 2 H); 2.58 (*d*, *J* = 5, 1 H); 2.54 (*d*, *J* = 5, 1 H); 2.07 – 2.01 (*m*, 4 H); 1.62 – 1.55 (*m*, 2 H); 1.46 – 1.28 (*m*, 20 H). $^{13}$C-NMR: (deduced from the mixture): major (*E*): 131.6 (*d*); 130.6 (*d*); 59.6 (*s*); 53.2 (*t*); 34.5 (*t*); 33.7 (*t*); 32.1 (*t*); 31.9 (*t*); 28.1 (*t*); 27.6 (*t*); 27.2 (*t*); 27.1 (*t*); 26.5 (*t*); 26.4 (*t*); 25.4 (*t*); 24.6 (*t*); 23.1 (*t*); minor (*Z*): 130.3 (*d*); 129.4 (*d*); 59.6 (*s*); 53.7 (*t*); 34.5 (*t*); 32.1 (*t*); 31.9 (*t*); 28.6 (*t*); 27.8 (*t*); 28.0 (*t*); 27.6 (*t*); 27.0 (*t*); 26.7 (*t*); 26.3 (*t*); 25.8 (*t*); 25.0 (*t*); 22.2 (*t*). MS: major (*E*): 250 (28, $M^+$), 232 (11), 137 (13), 135 (15), 123 (23), 121 (21), 109 (43), 98 (58), 95 (79), 81 (83), 67 (94), 55 (100), 41 (87); minor (*Z*): 250 (30, $M^+$), 232 (11), 137 (11), 135 (17), 123 (21), 121 (23), 109 (41), 98 (50), 95 (77), 81 (83), 67 (90), 55 (100), 41 (87). Slightly musky, waxy, candle.

rac-*1-Oxaspiro[2.15]octadec-9-ene* (**8h**). According to *G.P.D.* After CC ($SiO_2$, cyclohexane/AcOEt 9 : 1), yield 76%; 57 : 43 (*E*)/(*Z*) mixture. IR: 3030, 2985, 2934, 2864, 1456, 1443, 967, 894, 795, 720. $^1$H-NMR: 5.37 – 5.33 (*m*, 2 H); 2.58 – 2.54 (*m*, 2 H); 2.08 – 2.03 (*m*, 4 H); 1.60 – 1.27 (*m*, 22 H). $^{13}$C-NMR

(deduced from the mixture): major: (*E*): 131.1 (*d*); 130.5 (*d*); 59.3 (*s*); 53.4 (*t*); 34.8 (*t*); 33.9 (*t*); 33.7 (*t*); 31.7 (*t*); 31.3 (*t*); 28.8 (*t*); 28.3 (*t*); 28.0 (*t*); 27.3 (*t*); 27.1 (*t*); 26.3 (*t*); 24.0 (*t*); 23.7 (*t*); minor: (*Z*): 131.1 (*d*); 130.9 (*d*); 59.6 (*s*); 53.7 (*t*); 34.5 (*t*); 33.3 (*t*); 32.3 (*t*); 32.1 (*t*); 32.0 (*t*); 31.5 (*t*); 29.3 (*t*); 27.2 (*t*); 27.1 (*t*); 26.7 (*t*); 26.1 (*t*); 24.1 (*t*); 22.6 (*t*). MS: major (*E*): 250 (35, $M^+$), 232 (9), 175 (6), 161 (7), 147 (10), 135 (20), 121 (26), 109 (38), 95 (77), 81 (87), 67 (93), 55 (100), 41 (89); (*Z*) 250 (33, $M^+$), 232 (9), 175 (5), 161 (7), 147 (11), 135 (18), 121 (24), 109 (36), 95 (76), 81 (84), 67 (94), 55 (100), 41 (90). Musky, nitromusk, animal, powdery.

rac-*1-Oxaspiro[2.15]octadec-10-ene* (**8i**). According to *G.P.D.* After CC ($SiO_2$, cyclohexane/AcOEt 9:1), yield 85%; 65:35 (*E*)/(*Z*) mixture. IR: 3028, 2985, 2924, 2852, 1459, 1442, 965, 895, 797, 719. $^1$H-NMR (deduced from the mixture): major: (*E*) 5.34–5.29 (*m*, 2 H); 2.55 (*d*, *J* = 5, 1 H); 2.51 (*d*, *J* = 5, 1 H); 2.08–2.03 (*m*, 4 H); 1.60–1.27 (*m*, 22 H); minor (*Z*): 5.41–5.37 (*m*, 2 H); 2.55 (*d*, *J* = 5, 1 H); 2.52 (*d*, *J* = 5, 1 H); 2.08–2.03 (*m*, 4 H); 1.60–1.27 (*m*, 22 H). $^{13}$C-NMR (deduced from the mixture): major (*E*): 131.5 (*d*); 130.0 (*d*); 59.4 (*s*); 53.8 (*t*); 33.6 (*t*); 32.5 (*t*); 32.3 (*t*); 29.0 (*t*); 28.4 (*t*); 28.1 (*t*); 28.0 (*t*); 27.8 (2*t*); 27.5 (*t*); 26.9 (*t*); 24.4 (*t*); 23.4 (*t*); minor (*Z*): 131.0 (*d*); 130.0 (*d*); 59.4 (*s*); 53.9 (*t*); 33.8 (*t*); 32.4 (*t*); 32.2 (*t*); 28.8 (*t*); 28.7 (*t*); 28.0 (*t*); 27.8 (2*t*); 27.6 (*t*); 27.5 (*t*); 27.1 (*t*); 23.4 (*t*); 23.3 (*t*). MS: major (*E*): 250 (13, $M^+$), 135 (20), 121 (25), 109 (32), 97 (43), 95 (66), 81 (81), 67 (100), 55 (86), 41 (91). minor (*Z*): 250 (13, $M^+$), 135 (16) 121 (22), 109 (28), 97 (43), 95 (62), 81 (82), 67 (100), 55 (85), 41 (88). Vaguely musky, candel, very weak.

rac-*1-Oxaspiro[2.11]tetradeca-6,10-diene* (**8j**). According to *G.P.D.* After CC ($SiO_2$, cyclohexane/AcOEt 9:1), yield 84%; 1:2 (6*E*,10*Z*)/(6*Z*,10*E*) mixture. IR: 3029, 2985, 2930, 2865, 1458, 1443, 966, 894, 795, 720. $^1$H-NMR: 5.6–5.2 (*m*, 4 H); 2.5–2.65 (*m*, 1 H); 2.52–2.49 (*m*, 1 H); 2.3–2.0 (*m*, 6 H); 1.8–1.55 (*m*, 4 H); 1.5–1.3 (*m*, 2 H). $^{13}$C-NMR (deduced from the mixture): major: 132.4 (*d*); 131.8 (*d*); 131.3 (*d*); 128.1 (*d*); 59.7 (*s*); 52.7 (*t*); 35.5 (*t*); 31.6 (*t*); 29.7 (*t*); 28.2 (*t*); 28.1 (*t*); 23.3 (*t*); 21.3 (*t*); minor: 130.3 (*d*); 129.6 (*d*); 129.4 (*d*); 129.3 (*d*); 59.2 (*s*); 52.6 (*t*); 34.1 (*t*); 30.9 (*t*); 30.8 (*t*); 29.1 (*t*); 28.0 (*t*); 25.7 (*t*) ; 23.0 (*t*). MS: major: 192 (2, $M^+$), 161 (20), 145 (15), 131 (22), 119 (26), 109 (28), 107 (31), 105 (44), 93 (49), 91 (67), 81 (52), 79 (100), 67 (91), 55 (29), 54 (27), 41 (30); minor: 192 (2, $M^+$), 161 (20), 145 (17), 131 (22), 119 (20), 109 (24), 107 (26), 105 (34), 93 (42), 91 (57), 81 (48), 79 (100), 67 (88), 55 (32), 54 (35), 41 (35). Cedar, eucalyptus, woody, pine.

*2,2-Bis(8-bromooctyl)-1,3-dioxolane* (**Ib**; *Scheme 3*). A mixture of diol **Ia** [16][30]) (108.5 g, 330 mmol), $CBr_4$ (217 g, 660 mmol), and $Ph_3P$ (190 g, 720 mmol) was heated at 30°. The strong exothermic reaction was then equilibrated at 30° for 6 h, before dilution with $Et_2O$. The $Ph_3P(O)$ was filtered and washed with $Et_2O$, the filtrate concentrated, and the residue purified by CC ($SiO_2$, cyclohexane/AcOEt 98:2); **Ib** (65%).

Alternatively, a soln. of 1,17-dibromoheptadecan-9-one (**VIb**; 1.0 g, 2.43 mmol) in cyclohexane (60 ml) was heated under reflux in the presence of TsOH (20 mg) and ethylene glycol (=ethane-1,2-diol; 3.0 g, 65.2 mmol). After 24 h and collection of the formed $H_2O$ with a *Dean–Stark* apparatus, the cold mixture was concentrated and the residue extracted with $Et_2O$. The org. phase was washed to neutrality with 15% aq. $NaHCO_3$ soln., then brine, dried ($Na_2SO_4$), and concentrated: pure **Ib** (quant.). IR: 2926, 2854, 1495, 1462, 1438, 1371, 1250, 1177, 1077, 1043, 947, 913, 729, 694, 666, 644. $^1$H-NMR: 3.92 (*s*, 4 H); 3.40 (*t*, *J* = 6, 4 H); 1.84 (*quint.*, *J* = 5, 4 H); 1.61–1.54 (*m*, 4 H); 1.45–1.40 (*m*, 4 H); 1.36–1.26 (*m*, 16 H). $^{13}$C-NMR: 111.8 (*s*); 64.9 (2*t*); 37.1 (2*t*); 34.0 (2*t*); 32.8 (2*t*); 29.8 (2*t*); 29.4 (2*t*); 28.7 (2*t*); 28.1 (2*t*); 23.8 (2*t*). MS: 454 (0, $M^+$), 265 (97), 263 (100), 183 (10), 99 (11), 69 (10), 55 (12).

*1,3-Dioxolan-2,2-dioctanol Diacetate* (**Ic**). AcCl (95 g, 1.2 mol) was added dropwise in 1 h at < 30° to a soln. of **Ia** (90.0 g, 0.27 mol) and DMAP (11.4 g, 0.09 mol) in $Et_3N$ (200 ml) and $CH_2Cl_2$ (500 ml). After 3 h, the mixture was poured onto ice, and extracted with $Et_2O$. The org. phase was washed to neutrality with brine, dried ($Na_2SO_4$), and concentrated. The residue was subjected to CC ($SiO_2$, cyclohexane/AcOEt 7:3): **Ic** (60%). IR: 2929, 2855, 1737, 1465, 1387, 1365, 1233, 1144, 1116, 1080, 1038, 948, 897, 859, 724, 634, 606. $^1$H-NMR: 4.05 (*t*, *J* = 7, 4 H); 3.92 (*s*, 4 H); 2.04 (*s*, 6 H); 1.64–1.56 (*m*, 8 H); 1.37–1.25 (*m*,

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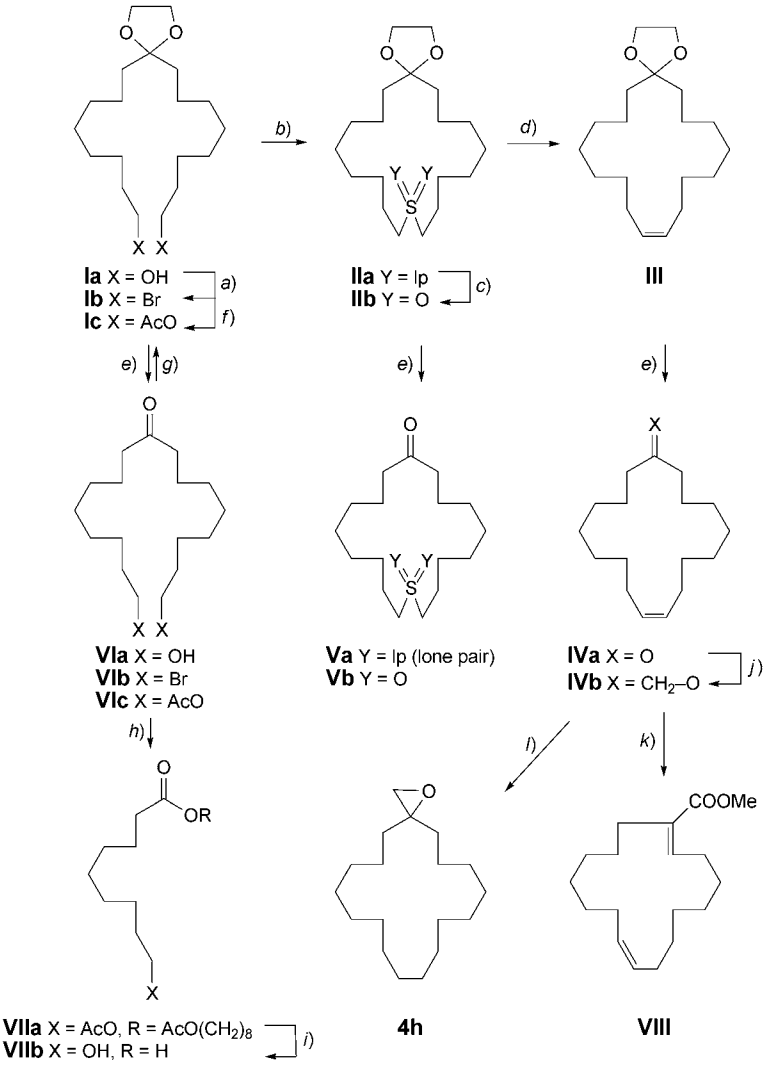
30) IR: 3346, 2925, 2853, 1464, 1372, 1348, 1316, 1209, 1136, 1051, 948, 902, 787, 723, 621. $^1$H-NMR: 3.92 (*s*, 4 H); 3.62 (*t*, *J* = 7, 4 H); 1.84 (br. *s*, 2 H); 1.61–1.52 (*m*, 8 H); 1.36–1.25 (*m*, 20 H). $^{13}$C-NMR: 111.9 (*s*); 64.9 (2*t*); 62.9 (2*t*); 37.1 (2*t*); 32.8 (2*t*); 29.8 (2*t*); 29.5 (2*t*); 29.3 (2*t*); 25.7 (2*t*); 23.8 (2*t*). MS: 330 (0, $M^{+\bullet}$), 269 (1), 201 (100), 99 (9), 69 (7), 55 (9).

*Scheme 3*




*a*) $CBr_4$, $PPh_3$. *b*) $Na_2S$, EtOH. *c*) $H_2O_2$, $NaHCO_3$, $MnSO_4$, MeCN. *d*) KOH $Al_2O_3$, EtOH, $CBr_2F_2$, 60°. *e*) HCl, $H_2O$/THF. *f*) AcCl, *N*,*N*-dimethylpyridin-4-amine (DMAP), $Et_3N$, $CH_2Cl_2$. *g*) Ethylene glycol, TsOH, cyclohexane, 85°. *h*) *m*-CPBA, $CHCl_3$, 50°. *i*) NaOH, EtOH/$H_2O$, 78°. *j*) $Me_3S(O)$, $^t$BuOK, $^t$BuOH, 50°. *k*) $I_2$ (2.2 mol-equiv.), KOH, MeOH. *l*) $H_2$, Pd/C, AcOEt.

20 H). $^{13}$C-NMR; 171.2 (2*s*); 111.8 (*s*); 64.9 (2*t*); 64.6 (2*t*); 37.1 (2*t*); 29.8 (2*t*); 29.5 (2*t*); 29.2 (2*t*); 28.6 (2*t*); 25.9 (2*t*); 23.8 (2*t*); 21.0 (2*q*). MS: 414 (0, $M^+$), 243 (100), 99 (9), 87 (8), 43 (7).

*1,4-Dioxa-14-thiaspiro[4.17]docosane* (**IIa**). To refluxing EtOH (1.0 l) were added simultaneously a soln. of dibromide **Ib** (8.0 g, 17 mmol) in EtOH (150 ml) and $Na_2S$ (2.7 g, 35 mmol) in EtOH (150 ml). After 1.5 h, the solvent was evaporated and the mixture diluted with pentane, before extraction with $H_2O$. The residue of the concentrated org. phase was purified by CC ($SiO_2$, hexane/$CH_2Cl_2$ 9:1 → 1:1) and

recrystallization from EtOH: pure **IIa** (61%). M.p. 44–45.5°. IR: 2919, 2851, 1471, 1415, 1379, 1226, 719, 648. $^1$H-NMR: 3.91 (*s*, 4 H); 2.48 (*t*, *J* = 8, 4 H); 1.64–1.56 (*m*, 8 H); 1.43–1.31 (*m*, 20 H). $^{13}$C-NMR: 112.1 (*s*); 64.4 (2*t*); 35.4 (2*t*); 30.1 (2*t*); 28.7 (2*t*); 28.5 (2*t*); 27.8 (4*t*); 27.4 (2*t*) ; 23.3 (2*t*). MS: 328 (25, $M^+$), 285 (17), 283 (19), 267 (13), 215 (62), 183 (78), 155 (20), 141 (18), 99 (100), 86 (21), 55 (25).

*1,4-Dioxa-14-thiaspiro[4.17]docosane 14,14-Dioxide* (**IIb**). A mixture of 30% aq. $H_2O_2$ soln. (3 ml) and 0.2M aq. $NaHCO_3$ (103 ml) was added dropwise at 20° to a soln. of **IIa** (2.0 g, 1.5 mmol) and $MnSO_4 \cdot H_2O$ (12 mg) in MeCN (138 ml). After 0.5 h, sat. aq. NaCl soln. (50 ml) was added, the mixture extracted with AcOEt, and the extract concentrated: **IIb** (95%). IR: 2920, 2855, 1461, 1415, 1371, 1350, 1315, 1290, 1270, 1218, 1184, 1152, 1125, 1077, 1050, 1033, 952, 906, 825, 719. $^1$H-NMR: 3.92 (*s*, 4 H); 2.81 (*sept.*, *J* = 8, 2 H); 2.75 (*sept.*, *J* = 8, 2 H); 1.71 (*quint.*, *J* = 8, 4 H); 1.61–1.55 (*m*, 4 H); 1.52–1.46 (*m*, 4 H); 1.38–1.32 (*m*, 16 H). $^{13}$C-NMR: 112.0 (*s*); 64.5 (2*t*); 49.6 (2*t*); 35.4 (2*t*); 28.2 (2*t*); 27.5 (2*t*); 27.4 (2*t*); 27.0 (2*t*); 23.2 (2*t*); 20.7 (2*t*). MS : 360 (5, $M^+$), 317 (35), 183 (85), 155 (20), 141 (19), 99 (100), 86 (21), 55 (16).

*(13Z)-1,4-Dioxaspiro[4.16]henicos-13-ene* (**III**). A suspension of KOH/$Al_2O_3$ 1:3 (by wt.; 2.7 g) in EtOH (10 ml) was heated at 60°, and **IIb** (100 mg, 0.2 mmol) was added, followed by dropwise addition of $CBr_2F_2$ (2 ml). After 6 h the solvent was evaporated and the residue dissolved in $CH_2Cl_2$. The org. phase was washed with brine, dried ($Na_2SO_4$), and concentrated and the residue purified by CC ($SiO_2$, hexane/AcOEt 2:1): pure **III** (82%); 3:7 mixture of (*E*)/(*Z*) isomers. Both the (*E*)/(*Z*) ratio and the chemical yield depend on the source of halogen (KOH/$Al_2O_3$, EtOH, $CCl_4$: (*E*)/(*Z*) 3:7, 70%), the solvent (KOH/$Al_2O_3$, $^t$BuOH, $CBr_2F_2$: (*E*)/(*Z*) 6:4, 91%), and the base (NaOH, $^t$BuOH, $CBr_2F_2$: (*E*)/(*Z*) 45:55, 75%; $^t$BuOK, THF, $CBr_2F_2$: (*E*)/(*Z*) 9:1, 86%). IR: 3000, 2923, 2853, 1495, 1458, 1353, 1292, 1210, 1189, 1178, 1073, 945, 915, 728, 694. $^1$H-NMR: 5.33 (*t*, *J* = 5, 2 H); 3.90 (*s*, 4 H); 2.04 (*dt*, *J* = 5, 7, 4 H); 1.60–1.50 (*m*, 4 H); 1.40–1.21 (*m*, 20 H). $^{13}$C-NMR: 130.1 (2*d*); 112.2 (*s*); 64.3 (2*t*); 35.8 (2*t*); 32.4 (2*t*); 29.2 (2*t*); 28.7 (2*t*), 27.8 (2*t*); 27.1 (2*t*), 22.9 (2*t*). MS: 294 (3, $M^+$), 251 (5), 155 (32), 142 (11), 99 (100), 86 (14), 67 (10), 55 (19).

For the hydrolysis of **III** to civetone (**IVa**), see [20][31]).

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[31]) When civetone (**IVa**; (*E*)/(*Z*) < 5:95 ) was treated under *Favorskii* conditions, we isolated the macrocyclic methoxycarbonyl derivative **VIII** (7%). Furthermore, when civetone **IVa** was treated under *Corey–Chaykovsky* conditions, (11*Z*)-1-oxaspiro[2.16]nonadec-11-ene (**IVb**) was isolated in 94% yield (*Scheme 3*). Its hydrogenation afforded the corresponding saturated 1-oxaspiro compound **4h**. Earlier treatment of **3c** with $BF_3 \cdot Et_2O$ afforded, after a three-step sequence, a complex mixture of the conjugated/deconjugated cycloundecenones [38a]. (2*E*)-Cyclopentadec-2-en-1-one (**IXa**; *Scheme 4*) may be readily obtained from cyclopentadecanone (**1f**), either in a single step according to *Nicolaou*'s protocol [56a–c] (*o*-iodoxybenzoic acid, PhF, DMSO, 65°, yield 83%), or in a two-step low-temperature lithium diisopropylamide (LDA) deprotonation with $Me_3SiCl$ quenching, followed by oxidation with stoichiometric [Pd(OAc)$_2$] according to either *Schäfer* and co-workers [57a] (yield 80%) or *Rüedi* and *Hansen* [57b] (yield 85%), or *via* an efficient four-step sequence (*Scheme 4*) comprising acetalization to **Xa** [58] (ethylene glycol, cyclohexane, TsOH, yield 98%), bromination to **XIa** [58b][58c] ($PhMe_3N^+Br_3^-$, THF, yield 98%; $^{13}$C-NMR: 22.2 (*t*); 25.9 (*t*); 26.4 (2*t*); 26.5 (2*t*); 26.6 (*t*); 26.8 (2*t*); 26.9 (*t*); 27.4 (*t*); 32.3 (*t*); 35.4 (*t*); 61.1 (*d*); 65.6 (*t*); 66.1 (*t*); 111.0 (*s*)), elimination to **XIIa** (MeOK (see [58d] for MeONa as base), DMSO, yield 99%; $^{13}$C-NMR: 23.4 (*t*); 25.9 (*t*); 26.8 (*t*); 26.9 (2*t*); 27.1 (2*t*); 27.2 (*t*); 28.0 (*t*); 28.3 (*t*); 31.1 (*t*); 38.7 (*t*); 64.2 (2*t*); 109.6 (*s*); 130.1 (*d*); 132.5 (*d*)), and deprotection to **IXa** [58] (10% aq. HCl soln., acetone, yield 90%), by analogy with *Mookherjee*'s report [58b]. For alternative syntheses, see [59]. We applied this sequence also to cyclohexadecanone (**1g**), *via* the uncharacterized acetal **Xb** [60] and its unreported intermediates **XIb** and **XIIb**, for the preparation of the musk-like (2*E*)-cyclohexadecenone **IXb** [44][61] (m.p. 30–32°, $^{13}$C-NMR: 25.1 (*t*); 26.2 (*t*); 26.4 (*t*); 26.5 (*t*); 26.7 (*t*); 26.9 (*t*); 27.0 (*t*); 27.1 (*t*); 27.3 (*t*); 27.4 (2*t*); 31.6 (*t*); 38.9 (*t*); 131.3 (*d*); 148.2 (*d*); 201.7 (*s*); MS: 236 (79, $M^{+\bullet}$), 178 (15), 137 (18), 135 (17), 123 (20), 121 (18), 109 (82), 96 (100), 81 (91), 68 (48), 55 (87), 41 (56)). (–)-(*R*)-**5f** was obtained in 35% yield (62% ee) from **IXb**, after 24 h at 20°, by analogy with [62]. (2*E*,14*E*)-Cyclopentadeca-2,14-dien-1-one was isolated in only 12% yield from **1f**, under $HIO_3$/DMSO/cyclohexene conditions [56d].

*(11Z)-1-Oxaspiro[2.16]nonadec-11-ene* (**IVb**). According to *G.P.D.* Yield 94%. IR: 3000, 2920, 2853, 1459, 1398, 1367, 990, 903, 715. $^1$H-NMR: 5.34 (*t*, *J* = 5, 2 H); 2.55 (*s*, 2 H); 2.10–2.03 (*m*, 4 H); 1.65–1.56 (*m*, 2 H); 1.46–1.27 (*m*, 22 H). $^{13}$C-NMR: 130.2 (2*d*); 59.4 (*s*); 53.8 (*t*); 34.5 (2*t*); 29.3 (2*t*); 28.8 (2*t*); 28.2 (2*t*); 27.8 (2*t*); 27.0 (2*t*); 24.0 (2*t*). MS: 264 (20, $M^+$), 246 (10), 149 (12), 135 (28), 121 (35), 109 (42), 95 (81), 81 (93), 67 (94), 55 (100), 41 (83). Fruity, marmalade, green, geranium leaf, weak.

*Thiacyclooctadecan-10-one* (**Va**). A soln. of acetal **IIa** (1.0 g, 3.04 mmol) in THF (5 ml) and $H_2O$ (5 ml) was hydrolyzed at 20° for 18 h in the presence of conc. HCl soln. (1 ml). The mixture was diluted with $Et_2O$, neutralized with sat. $NaHCO_3$ soln., and then extracted 3 times with $Et_2O$. The org. phase was washed with $H_2O$, dried ($Na_2SO_4$), and concentrated. Recrystallization from EtOH afforded **Va** (58%). M.p. 72–73.5°. IR: 2918, 2850, 1700, 1471, 1415, 1379, 1310, 1256, 1226, 1112, 1064, 966, 718, 680, 646. $^1$H-NMR: 2.51 (*t*, *J* = 7.7, 4 H); 2.41 (*t*, *J* = 6, 4 H); 1.63 (*quint.*, *J* = 8, 4 H); 1.58 (*quint.*, *J* = 7, 4 H); 1.42 (*quint.*, *J* = 6.7, 4 H); 1.35–1.28 (*m*, 12 H). $^{13}$C-NMR: 212.3 (*s*); 42.1 (2*t*); 31.4 (2*t*); 28.8 (2*t*); 28.2 (2*t*); 28.1 (2*t*); 28.0 (2*t*); 27.3 (2*t*); 23.8 (2*t*). MS: 284 (28, $M^+$), 201 (8), 153 (11), 129 (35), 96 (21), 87 (43), 81 (24), 69 (44), 55 (100), 41 (74).

*Thiacyclooctadecan-10-one 1,1-Dioxide* (**Vb**)[32]). As described for **Va**: **Vb** (60%). IR: 2920, 2855, 1702, 1461, 1289, 1270, 1125, 1077, 825. $^1$H-NMR: 2.96 (*t*, *J* = 8, 4 H); 2.41 (*t*, *J* = 6, 4 H); 1.81 (*quint.*, *J* = 7, 4 H); 1.62 (*quint.*, *J* = 7, 4 H); 1.48 (*quint.*, *J* = 6, 4 H); 1.39–1.27 (*m*, 12 H). $^{13}$C-NMR: 212.1 (*s*); 51.4 (2*t*); 42.1 (2*t*); 28.0 (2*t*); 27.9 (2*t*); 27.6 (2*t*); 27.2 (2*t*); 23.5 (2*t*); 21.8 (2*t*). MS: 316 (45, $M^+$), 259 (18), 229 (9), 163 (63), 155 (59), 111 (20), 97 (97), 69 (53), 55 (100), 41 (50).

*1,17-Dihydroxyheptadecan-9-one* (**VIa**). As described for **Va**: **VIa** (quant.). IR: 3259, 2916, 2883, 2849, 1704, 1487, 1472, 1461, 1407, 1379, 1343, 1323, 1285, 1270, 1243, 1202, 1119, 1060, 1030, 1012, 993, 967, 942, 922, 882, 848, 809, 762, 731, 719, 680. $^1$H-NMR : 3.63 (*t*, *J* = 6.5, 4 H); 2.38 (*t*, *J* = 7.7, 4 H); 1.62 (br. *s*, 2 H); 1.56 (*quint.*, *J* = 6.5, 8 H); 1.36–1.26 (*m*, 16 H). $^{13}$C-NMR: 211.9 (*s*); 63.0 (*t*); 42.8 (*t*); 32.8 (*t*); 29.3 (*t*); 29.2 (*t*); 29.1 (*t*); 25.7 (*t*); 23.8 (*t*). MS: 286 (5, $M^+$), 207 (14), 172 (46), 157 (14), 139 (20), 129 (19), 111 (28), 97 (39), 71 (41), 69 (87), 58 (37), 55 (100), 41 (41).

*1,17-Dibromoheptadecan-9-one* (**VIb**). As described for **Va**: **VIb** (quant.). IR: 2958, 2913, 2887, 2850, 1700, 1471, 1415, 1378, 1310, 1262, 1254, 1243, 1224, 1112, 1067, 1055, 998, 974, 967, 718, 645. $^1$H-NMR: 3.40 (*t*, *J* = 8, 4 H); 2.39 (*t*, *J* = 7, 4 H); 1.85 (*quint.*, *J* = 7, 4 H); 1.56 (*quint.*, *J* = 8, 4 H); 1.45–1.38 (*m*, 4 H); 1.33–1.26 (*m*, 12 H). $^{13}$C-NMR: 211.5 (*s*); 42.8 (2*t*); 34.0 (2*t*); 32.8 (2*t*); 29.2 (2*t*); 29.1 (2*t*); 28.6 (2*t*); 28.1 (2*t*); 23.8 (2*t*). MS: 412 (2, $M^+$), 333 (7), 331 (6), 249 (13), 247 (14), 236 (33), 234 (31), 221 (67), 219 (69), 176 (30), 155 (49), 137 (20), 69 (99), 55 (100), 41 (65).

*9-Oxoheptadecane-1,17-diyl Diacetate* (*=1,17-Bis(acetyloxy)heptadecan-9-one*; **VIc**). As described for **Va**: **VIc** (quant.). IR: 2947, 2926, 2912, 2850, 1731, 1702, 1479, 1462, 1418, 1396, 1371, 1295, 1243, 1122, 1053, 1023, 965, 892, 757, 729, 718, 682, 646, 608. $^1$H-NMR: 4.05 (*t*, *J* = 8, 4 H); 2.39 (*t*, *J* = 7, 4 H); 2.05 (*s*, 6 H); 1.63–1.54 (*m*, 8 H); 1.36–1.25 (*m*, 16 H). $^{13}$C-NMR: 211.5 (*s*); 171.2 (2*s*); 64.6 (2*t*); 42.8 (2*t*); 29.3 (2*t*); 29.2 (2*t*); 29.1 (2*t*); 28.6 (2*t*); 25.9 (2*t*); 23.8 (2*t*), 21.0 (2*q*). MS: 370 (1, $M^+$), 227 (15), 214 (75), 157 (62), 154 (36), 139 (66), 111 (41), 97 (100), 69 (71), 55 (84), 43 (80).

*8-(Acetyloxy)octyl 9-(Acetyloxy)nonanoate* (**VIIa**). A mixture of **VIc** (28.0 g, 63.4 mmol) and *m*-CPBA (70%; 35.0 g, 140 mmol) in $CHCl_3$ (200 ml) was heated at 50° for 48 h. The solvent was evaporated and replaced by $Et_2O$. The soln. was washed with $NaHSO_3$ soln., $H_2O$, 30% aq. $NaHCO_3$ soln., and brine to neutrality, dried ($Na_2SO_4$) and concentrated: pure **VIIa** (85%). IR: 2945, 2920, 2910, 1728, 1370, 730. $^1$H-NMR: 4.06 (*t*, *J* = 7, 2 H); 4.05 (*t*, *J* = 7, 2 H); 4.04 (*t*, *J* = 7, 2 H); 2.3 (*t*, *J* = 8, 2 H); 2.05 (*s*, 6 H); 1.66–1.59 (*m*, 8 H); 1.40–1.30 (*m*, 16 H). $^{13}$C-NMR: 173.9 (*s*); 171.2 (2*s*); 64.6 (2*t*); 64.3 (*t*); 34.4 (*t*); 29.1 (5*t*); 28.6 (3*t*); 25.9 (3*t*); 25.0 (*t*); 21.0 (2*q*). MS: 386 (0, $M^+$), 217 (10), 199 (100), 157 (60), 148 (32), 110 (50), 69 (50), 43 (48).

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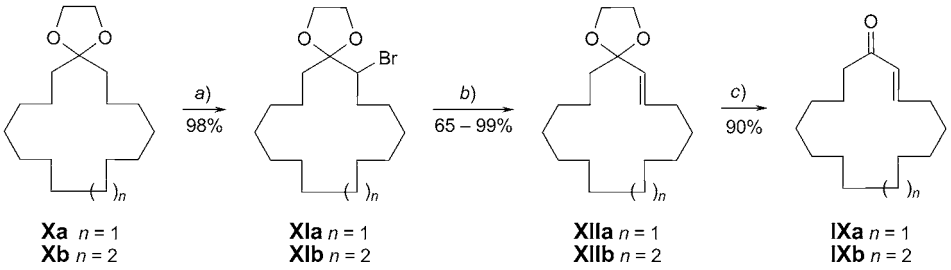
[32]) In some instances, a partial oxidation allowed the isolation of traces of the corresponding odorless thiacyclooctadecan-10-one 1-oxide: $^1$H-NMR: 2.74 (*t*, *J* = 6, 4 H); 2.48–2.34 (*m*, 4 H); 1.87–1.77 (*m*, 2 H); 1.77–1.66 (*m*, 2 H); 1.66–1.55 (*m*, 4 H); 1.48 (*quint.*, *J* = 7, 4 H); 1.37–1.25 (*m*, 12 H). $^{13}$C-NMR: 211.9 (*s*); 51.6 (*t*); 42.1 (*t*); 28.0 (*t*); 27.9 (*t*); 27.6 (*t*); 27.2 (*t*); 23.5 (*t*); 21.8 (*t*). MS: 300 (12, $M^{+\bullet}$), 255 (10), 251 (8), 217 (11), 183 (20), 143 (28), 139 (24), 111 (50), 94 (36), 69 (70), 55 (100), 41 (42).

*9-Hydroxynonanoic Acid* (**VIIb**). A soln. of **VIIa** (42.0 g, 109 mmol) and NaOH (17.2 g, 430 mmol) in EtOH (500 ml) was heated under reflux for 15 h. The solvent was evaporated and, replaced by $Et_2O$ and the soln. washed with $H_2O$. After acidification (pH 2) of the aq. phase with 15% HCl, and extraction with $Et_2O$, the org. phase was washed with brine to neutrality, dried ($Na_2SO_4$), and concentrated: pure **VIIb** (89%). IR: 3240; 2912, 1710, 728. $^1$H-NMR: 7.08 (br *s*, 2 H); 3.63 (*t*, *J* = 7, 2 H); 2.33 (*t*, *J* = 7, 2 H); 1.66 – 1.52 (*m*, 4 H); 1.36 – 1.29 (*m*, 8 H). $^{13}$C-NMR: 179.0 (*s*); 62.7 (*t*); 34.1 (*t*); 32.4 (*t*); 29.2 (*t*) ; 29.1 (*t*) ; 29.0 (*t*) ; 25.6 (*t*); 24.7 (*t*). MS: 174 (0, $M^+$), 144 (18), 110 (18), 97 (28), 84 (30), 73 (53), 69 (33), 60 (50), 55 (100), 41 (51).

*(1Z,9Z)-Methyl Cyclohexadeca-1,9-diene-1-carboxylate* **VIII**. According to *G.P.A.* Yield 7%. B.p. 130°/0.25 mbar. IR: 3000, 2924, 2854, 1717, 1641, 1459, 1434, 1376, 1348, 1191, 1162, 1030, 969, 907, 810, 776, 718. $^1$H-NMR: 5.86 (*t*, *J* = 7.8, 1 H); 5.45 – 5.30 (*m*, 2 H); 3.74 (*s*, 3 H); 2.5 – 2.44 (*m*, 2 H); 2.35 – 2.28 (*m*, 2 H); 2.07 – 1.97 (*m*, 4 H); 1.51 – 1.41 (*m*, 4 H); 1.39 – 1.24 (*m*, 12 H). $^{13}$C-NMR: 168.8 (*s*); 143.0 (*d*); 131.4 (*s*); 130.1 (*d*); 129.9 (*d*); 51.1 (*q*); 34.1 (*t*); 29.6 (*t*); 29.2 (2*t*); 28.9 (*t*); 27.8 (2*t*); 27.7 (*t*); 27.3 (*t*); 26.8 (*t*); 26.1 (*t*); 25.5 (*t*). MS: 278 (37, $M^+$), 247 (24), 219 (24), 161 (12), 149 (19), 135 (34), 121 (40), 109 (40), 95 (83), 81 (100), 67 (94), 55 (66), 41 (70).

*1,4-Dioxaspiro[4.15]icosane* (**Xb**; *Scheme 4*). In a *Dean–Stark* apparatus, a soln. of ketone **1g** (66.6 g, 280 mmol), ethylene glycol (25 g, 400 mmol), and TsOH (1 g, 9.8 mmol), in cyclohexane (600 ml) was heated under reflux for 48 h, and $H_2O$ was collected. The cold soln. was extracted with $H_2O/Et_2O$, washed with $NaHCO_3$ soln. and then brine to neutrality, dried ($Na_2SO_4$), and concentrated and the residue distilled through a *Vigreux* column: **Xb** (91%). B.p. 125 – 127°/0.1 mbar. M.p. 35 – 36°. IR: 2924, 2855, 1459, 1348, 1287, 1188, 1146, 1069, 945, 892, 831, 711. $^1$H-NMR: 3.91 (*s*, 4 H); 1.61 – 1.57 (*t*, *J* = 10.9, 4 H); 1.4 – 1.25 (*m*, 26 H). $^{13}$C-NMR: 112.2 (*s*); 64.3 (2*t*); 35.4 (2*t*); 27.2 (2*t*); 26.9 (2*t*); 26.6 (2*t*); 26.3 (*t*); 26.3 (2*t*); 25.8 (2*t*); 22.7 (2*t*). MS: 282 (18, $M^+$), 239 (29), 155 (29), 99 (100), 86 (16), 55 (23), 41 (22). Without character.

*Scheme 4*




*a*) $PhMe_3N^+Br_3^-$, THF. *b*) MeOK, DMSO. *c*) 10% aq. HCl soln., acetone.

*6-Bromo-1,4-dioxaspiro[4.15]icosane* (**XIb**). $PhMe_3NBr_3$ (10.2 g, 270 mmol) was added portionwise to a soln. of **Xb** (70 g, 250 mmol) in THF (2 l) at 0°. After 3 h at 0°, sat. $NaHCO_3$ soln. (500 ml) was added, and the solvent was evaporated. The aq. soln. was extracted with $Et_2O$, and the org. phase was washed with $NaHCO_3$ soln. and then brine to neutrality, dried ($Na_2SO_4$), and concentrated: **XIb** (quant.). IR: 2924, 2854, 1105, 710. $^1$H-NMR: 4.24 – 4.14 (*m*, 1 H); 4.01 – 3.96 (*m*, 1 H); 3.76 – 3.73 (*m*, 2 H); 3.46 (*t*, *J* = 8, 1 H); 2.0 – 1.92 (*m*, 2 H); 1.88 – 1.83 (*m*, 2 H); 1.77 – 1.69 (*m*, 4 H); 1.55 – 1.2 (*m*, 20 H). $^{13}$C-NMR: 111.0 (*s*); 68.0 (*t*); 65.7 (*t*); 60.9 (*d*); 35.4 (*t*); 32.7 (*t*); 29.2 (*t*); 27.3 (*t*); 26.8 (*t*); 26.7 (*t*); 26.6 (2*t*); 26.4 (2*t*); 26.3 (*t*); 26.1 (*t*); 25.8 (*t*); 22.3 (*t*). MS: 362 (4), 360 (4, $M^+$), 319 (10), 317 (10), 281 (49), 155 (23), 99 (100), 55 (16).

*(6*E*)-1,4-Dioxaspiro[4.15]icos-6-ene* (**XIIb**). MeOK (53 g, 760 mmol) was added in one portion to a soln. of **XIb** (98 g, 250 mmol) in DMSO (360 ml). After 3 h at 20°, the mixture was poured onto brine and extracted with pentane, the extract dried ($Na_2SO_4$) and concentrated, and the residue distilled through a *Vigreux* column: pure **XIIb** (65%). B.p. 120 – 128°/0.2 mbar. IR: 2923, 2854, 1459, 1337, 1257, 1184, 1121,

1045, 973, 945, 909, 805, 723. $^1$H-NMR: 5.71 (*dt*, *J* = 9, 19.2, 1 H); 5.3 (*d*, *J* = 19.2, 1 H); 3.95–3.85 (*m*, 4 H); 2.11 (*q*, *J* = 7.7, 2 H); 1.70–1.65 (*m*, 2 H); 1.4–1.2 (*m*, 22 H). $^{13}$C-NMR: 132.2 (*d*); 129.8 (*d*); 109.5 (*s*); 64.2 (2*t*); 38.9 (*t*); 31.7 (*t*); 28.4 (*t*); 28.0 (2*t*); 27.4 (*t*); 27.3 (2*t*); 26.2 (*t*); 25.8 (*t*); 25.2 (*t*); 25.0 (*t*); 23.7 (*t*); MS : 280 (12, $M^+$), 237 (22), 183 (27), 125 (100), 99 (40), 55 (15). Vaguely woody, very weak.

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