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Synthesis of chiral methyl-branched linear pheromones starting from (+)-aromadendrene. Part 7

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Abstract—Ethyl (7*S*)-10-hydroxy-7-methyldecanoate (**4**), a linear methyl-branched intermediate with its chiral center at C7, and with two different functional groups at the ends of the chain, has been synthesized from (+)-aromadendrene in nine steps. A Baeyer–Villiger oxidation and a Grob fragmentation are the key reactions in this transformation. Intermediate **4** has been applied in the synthesis of three linear methyl-branched pheromones, (i) (*R*)-10-methyl-2-tridecanone, the active pheromone of the southern corn rootworm *Diabrotica undecimpunctata* howardi Barber, (ii) (*S*)-9-methylnonadecane, one of the sex pheromones of the cotton leafworm *Alabama argillacea*, and (iii) (*meso*)-13,23-dimethylpentatriacontane, the sex pheromone of the tse tse fly *Glossina pallidipes*.

1. Introduction

(+)-Aromadendrene (**1**) is a cheap and abundantly available chiral starting material[1] for organic syntheses. It has been shown by our laboratory that many other useful intermediates and natural products can be obtained from aromadendrene.[2–8] In most of these products, the basic structural features of the aromadendrene skeleton have been retained, although it was also shown that the monocyclic humulane skeleton could be obtained in an easy way.[6] Complex polycyclic sesquiterpenoids like (+)-aromadendrene have seldom been used for the preparation of chiral linear compounds. Mostly monoterpenoids like citronellol and pulegone have served as starting material for syntheses of, for instance, linear pheromones branched with one methyl group.[9,10] It will be shown here, that the linear methyl-branched ethyl (7*S*)-10-hydroxy-7-methyldecanoate (**4**), with its chiral center four carbon atoms from the end of the chain, can be derived from (+)-aromadendrene in a limited number of steps. A Baeyer–Villiger oxidation and a Grob fragmentation are the key reactions in this transformation. Compound **4** can be a versatile intermediate for the synthesis of several methyl-branched linear pheromones because it has two different functionalities at the ends of the chain. The chain can be elongated or shortened at will at either side, and pheromones with varying chain length and different positions of the chiral center become accessible. Here, we report on the synthesis of **4** and its application in the synthesis of three linear methyl-branched pheromones, (i) (*R*)-10-methyl-2-tridecanone, the active pheromone of the southern corn rootworm *Diabrotica undecimpunctata* howardi Barber, (ii) (*S*)-9-methylnonadecane, one of the sex pheromones of the cotton leafworm *Alabama argillacea*, and (iii) (*meso*)-13,23-dimethylpentatriacontane, the sex pheromone of the tse tse fly *Glossina pallidipes*.

2. Results and discussion

Two approaches have been investigated for the transformation of (+)-aromadendrene (**1**) to ethyl (7*S*)-10-hydroxy-7-methyldecanoate (**4**) (Scheme 1). In the first approach (+)-aromadendrene should be converted to apoaromadendrone (**6**), which in turn should undergo a Baeyer–Villiger oxidation to lactone **2**. Opening of the cyclopropane ring and the introduction of a good leaving group, then should give lactone **3**. This lactone should be subjected to a Grob fragmentation, and subsequent hydrogenation should finally lead to **4**.

In the second approach, (+)-aromadendrene (**1**) is first converted to the known alcohol **5** in four steps.[2] Conversion of the hydroxyl group in **5** to a good leaving group, followed by Baeyer–Villiger oxidation or the other way round, again should lead to lactone **3** and after Grob fragmentation and hydrogenation, **4** should be obtained.

In both approaches to lactone **3** the Baeyer–Villiger oxidation is a key step and for this reaction a carbonyl

Keywords: (+)-aromadendrene; Baeyer–Villiger oxidation; Grob fragmentation; linear methyl-branched pheromones.
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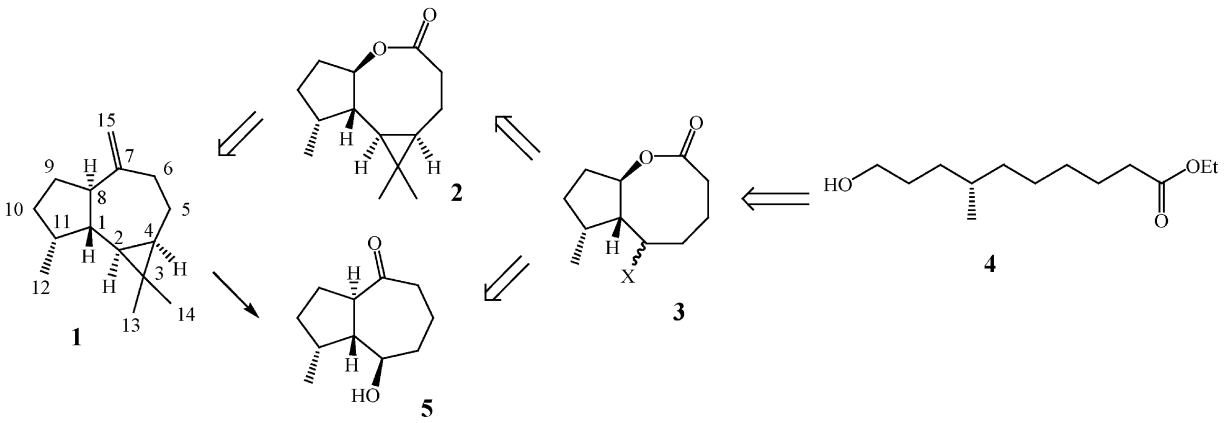


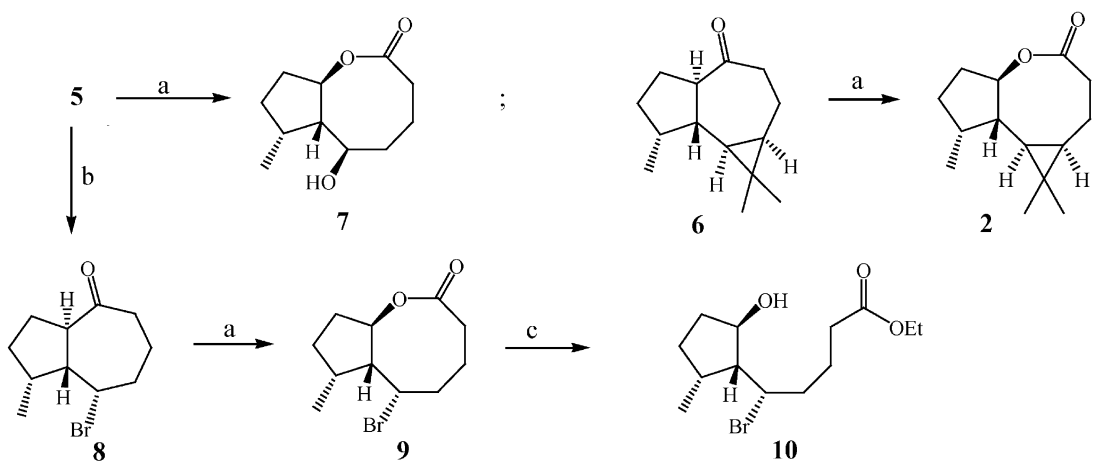
Scheme 1.

group is required at C7.[11] These ketones can be prepared from the distillation residue of the oil of *Eucalyptus globulus*[12] as shown by Gijsen et al.[2] The Baeyer–Villiger reaction of apoaromadendrone (**6**) went very well and lactone **2** was obtained in nearly quantitative yield (Scheme 2). However, attempts to open the cyclopropane ring with concentrated HCl in EtOH only led to opening of the lactone ring. When **2** was treated with TMSOTf in $CHCl_3$, opening of the cyclopropane ring to an unstable lactone did take place in a moderate yield, but further conversion of this lactone to a suitable substrate for the Grob fragmentation appeared to be problematic. This prompted us to investigate the second route for the synthesis of lactone **3**.

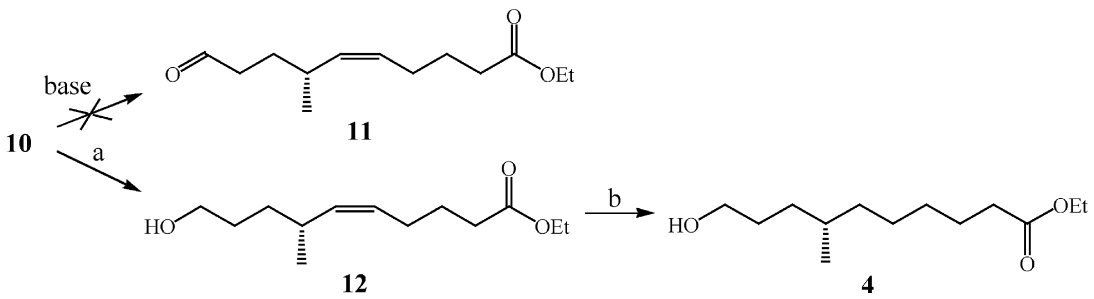
The Baeyer–Villiger reaction of **5**[2] with *m*CPBA in CH_2Cl_2 also proceeded well when $MgSO_4$ was added to the reaction mixture, and lactone **7** was isolated in 69% yield[13] (Scheme 2). For the Grob fragmentation, a good leaving group at C2 is necessary, but attempts to synthesize a lactone with a mesylate group as leaving group were not successful. The formation of a mesylate from alcohol **5** proceeded in a good yield, but when this β-mesylate was treated under Baeyer–Villiger conditions, the product decomposed before isolation. Also the mesylation of lactone **7** only led to a mixture of products. Finally, it was found that the α-bromide **8**, prepared by reaction of **5** with CBr_4 and PPh_3, gave a smooth Baeyer–Villiger reaction to lactone **9**, which was converted to the more stable ester **10** in a one-pot reaction with EtOH in the presence of TsOH.

The instability of lactones having a β-oriented mesylate at C2, might be caused by through-bond orbital interactions (TBI)[14] between the oxygen atom at C8 and the mesylate group. Because of the antiperiplanar relationship between the central C1–C8 bond and the β-orientated C2–OMs bond, TBI can be transmitted efficiently, through which the lactone function becomes very prone to nucleophilic attack with all its consequences. A similar TBI-induced instability has been observed for sulfonated silyl ethers.[15] The lactones **2** and **7** are stable because of the absence of a good leaving group at C2. In lactone **9** there is a bromide available at C2 as a good leaving group, but through its α-orientation there is no antiperiplanar relationship between the C1–C8 and the C2–Br bond as a result of which TBI is less efficient. Although bromo lactone **9** is not very stable, its stability is sufficient to allow further transformation to the more stable open ester **10**.

Several bases, like KO*t*Bu and NaOEt were tested for the Grob fragmentation of hydroxy bromide **10**, but the desired aldehyde **11** could never be isolated in an acceptable yield. Under the strongly basic conditions of the Grob fragmentation, this aldehyde appeared to be unstable and decomposed easily to a mixture of products (Scheme 3).



Scheme 2. (a) *m*CPBA, $MgSO_4$, CH_2Cl_2 (70–90%); (b) CBr_4, PPh_3, CH_2Cl_2 (78%); (c) TsOH, EtOH (69%).



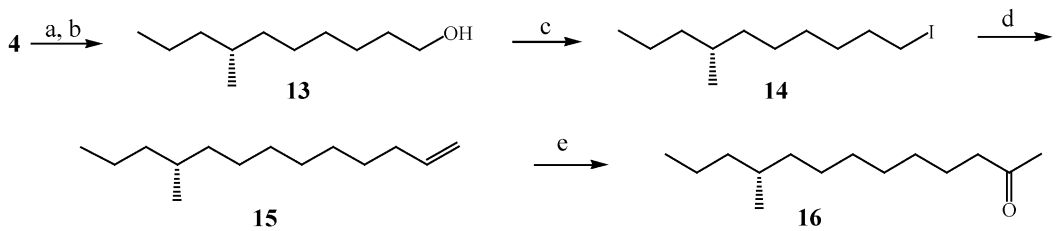
Scheme 3. (a) NaOEt, $NaBH_4$, EtOH (77%); (b) H_2, Pd (C), EtOAc (83%).

This problem could be solved by adding a reducing agent to the reaction mixture, and when the Grob fragmentation was carried out with NaOEt in EtOH in the presence of 5 equiv. of $NaBH_4$, alcohol **12** could be obtained in 80% yield.

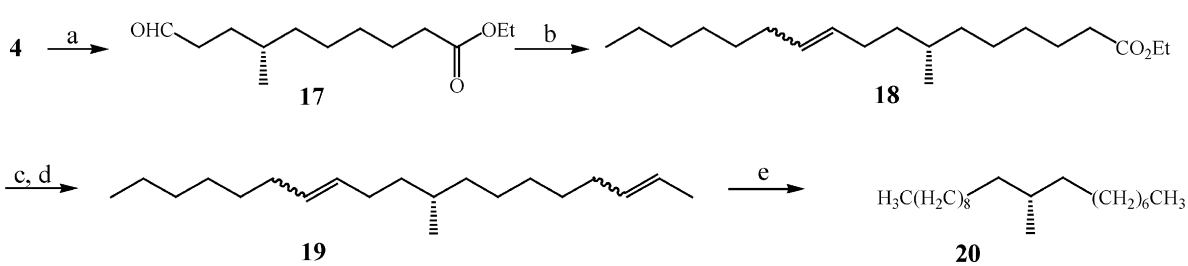
The reduction of the double bond in **12** with H_2 in the presence of Pd(C) went well and gave **4** in 85% yield. Sometimes partial racemization of allylic chiral centers may take place in catalytic reductions of double bonds. However, Larcheveque et al.[16] have shown that this is not a serious problem in reductions with Pd(C) as catalyst. Diimide reduction of **12** did not give satisfactory results. Attempts were made to establish the optical purity of **4**, but the preparation of diastereomeric esters of **4** with a chiral acid did not lead to a crystalline product, and no crystal structure could be determined.[17]

Ethyl (7*S*)-10-hydroxy-7-methyldecanoate (**4**) has been used for the synthesis of three linear methyl-branched pheromones. (*R*)-10-Methyl-2-tridecanone (**16**) is the active pheromone of the southern corn rootworm, *D. undecimpunctata* howardi Barber.[18] This pheromone has been synthesized before[19–25] and in our hands it was obtained from **4** in five steps with an overall yield of 57% (Scheme 4). At the left side of **4** the hydroxy group has to be removed and at the right side, the chain has to be elongated with a three-carbon fragment. For that reason the hydroxy group was converted to a tosylate group by reaction of **4** with TsCl in pyridine, followed by reduction of both the tosylate and the ester group to give the alcohol **13** in an overall yield of 75%. Replacement of the hydroxy group in **13** by iodide resulted in the formation of **14** in 91% yield.[26] Coupling of an allyl group to **14** and oxidation of the double bond[23] finally gave pheromone **16** in 83% yield.

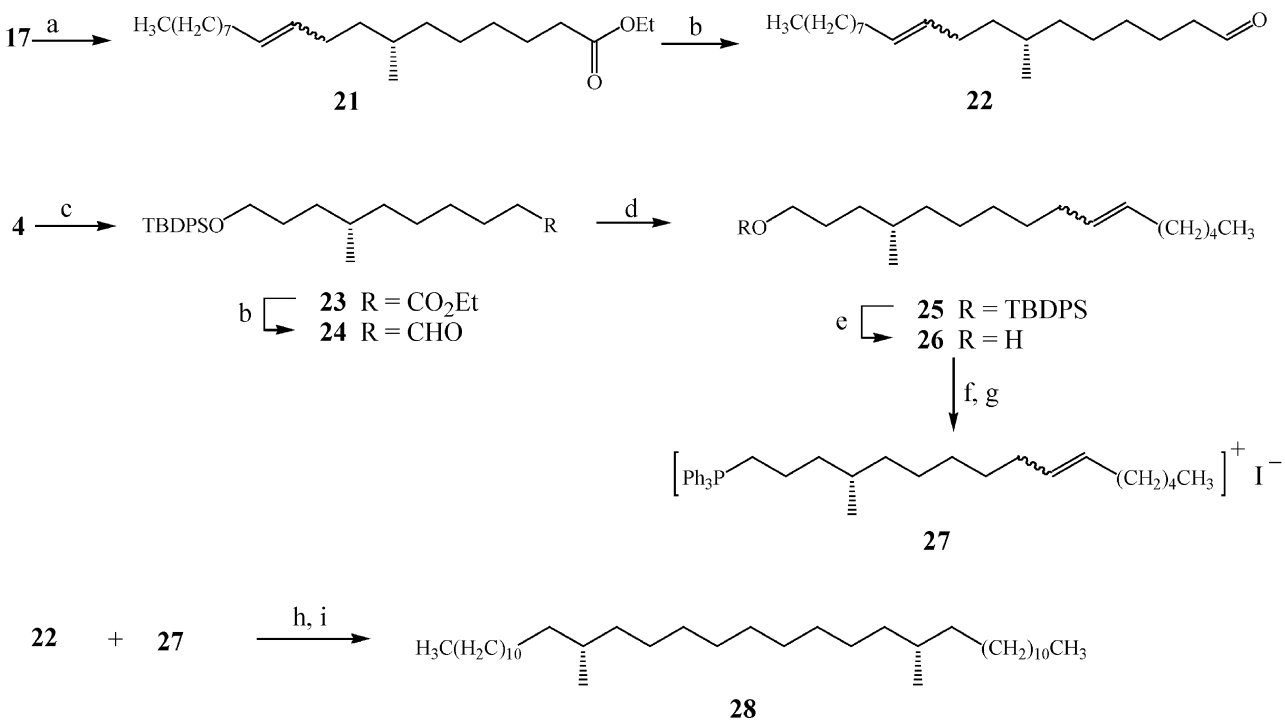
(*S*)-9-Methylnonadecane **20** has been identified as one of the sex pheromones of the cotton leafworm, *A. argillacea*.[27] The synthesis described below is the first synthesis of this pheromone (Scheme 5). For the synthesis of this pheromone from **4**, a seven-and a two-carbon fragment have to be added at the left and right side, respectively. For that reason the alcohol in **4** was oxidized first to afford aldehyde **17**, which in turn was elongated with a seven-carbon fragment via a Wittig reaction with heptyltriphenylphosphonium iodide. This reaction gave a mixture of the *Z* and *E* isomers of **18** in a ratio of 3:1 (according to GC-analysis) in 76% yield over two steps. Reduction of the ester group in compounds **18** with DIBAL-H[28] resulted in the formation of *Z* and *E* aldehydes in 86% yield, and a second Wittig reaction led to **19** as a mixture of four stereoisomers in 92% yield. The



Scheme 4. (a) TsCl, pyridine (79%); (b) $LiAlH_4$, THF (95%); (c) I_2, PPh_3, imidazole, CH_2Cl_2 (91%); (d) allylMgCl, THF (83%); (e) $PdCl_2$, CuCl, O_2, DMF (wet) (100%).



Scheme 5. (a) PCC, CH_2Cl_2 (78%); (b) $[C_7H_{15}PPh_3]^+I^-$, *n*BuLi, THF, −78°C (98%); (c) DIBAL-H, toluene, −78°C (86%); (d) $[C_2H_5PPh_3]^+I^-$, *n*BuLi, THF, −78°C (92%); H_2, Pd(C), EtOAc (95%).



Scheme 6. (a) $[C_9H_{19}PPh_3]^+Br^-$, *n*BuLi, THF, −78°C (89%); (b) DIBAL-H, toluene, −78°C (80%); (c) TBDPSCl, imidazole, DMAP, DMF (81%); (d) $[C_6H_{13}PPh_3]^+I^-$, *n*BuLi, THF, −78°C (61%); (e) TBAF, THF (94%); (f) I_2, PPh_3, imidazole, CH_3CN, Et_2O, 0°C to room temperature (87%); (g) PPh_3, toluene, reflux (80%); (h) *n*BuLi, THF, −78°C; (i) H_2, Pd(C) (99%).

formation of these stereoisomers was no problem, because hydrogenation of all double bonds led to a single product, pheromone **20**, in 95% yield. The synthesis of **20** from **4** took five steps and proceeded in an overall yield of 58%.

(*meso*)-13,23-Dimethylpentatriacontane (**28**) has been identified as the sex pheromone of the tse tse fly, *G. pallidipes*.[27] In this pheromone, the two chiral centers are separated from each other by nine carbon atoms, which makes it possible to use two units of **4**, coupled head to tail, to synthesize the central part of the chain. In our synthetic route, the left and right segments of the molecule are synthesized first. Both segments are then coupled to form the chain of 35 carbon atoms. The left segment consists of one molecule of **4** elongated at the left side with nine carbons whereas the right segment is built up from a second molecule of **4** elongated with a six-carbon segment (Scheme 6).

The left side of the molecule was synthesized via a Wittig reaction of aldehyde **17** (see Scheme 5) to give compound **21** in 89% yield. After reduction of **21** with DIBAL-H,[28] aldehyde **22** was obtained in 85% yield.

The first steps in the synthesis of the right side of the pheromone involved protection of the hydroxy group with a silyl group and reduction of the ester group to aldehyde **24** in 77% yield over two steps. Addition of a six-carbon fragment via a Wittig reaction (60% yield), followed by removal of the silyl group (94% yield), led to the formation of alcohol **26**. Replacement of the hydroxy group in **26** by iodide,[26] and subsequent reaction with PPh_3 gave phosphonium salt **27** in 86% yield over two steps. Then, the left and right parts of the pheromone (**22** and **27**) were coupled via a Wittig reaction (80% yield). In the final step, all the double bonds of the resulting triene were hydrogenated and pheromone **28** was obtained in 95% yield.

3. Conclusions

Ethyl (7*S*)-10-hydroxy-7-methyldecanoate (**4**), a linear methyl-branched intermediate with its chiral center at C7, and with two different functional groups at the ends of the chain, has been synthesized from (+)-aromadendrene in nine steps. A Baeyer–Villiger oxidation of keto-bromide **8** and a Grob fragmentation of hydroxy-bromide **10** are the key reactions in this transformation. Intermediate **4** has been applied in the synthesis of three linear methyl-branched pheromones, (i) (*R*)-10-methyl-2-tridecanone, the active pheromone of the southern corn rootworm *D. undecimpunctata* howardi Barber, (ii) (*S*)-9-methylnonadecane, one of the sex pheromones of the cotton leafworm *A. argillacea*, and (iii) (*meso*)-13,23-dimethylpentatriacontane, the sex pheromone of the tse tse fly *G. pallidipes*.

4. Experimental

4.1. General

^1H NMR spectra (200 MHz) and ^{13}C NMR spectra (50 MHz) were recorded on a Bruker AC-E 200. $CDCl_3$ was used as solvent, unless stated otherwise, and chemical shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0). MS and HRMS data were obtained with a Finnigan Mat 95 spectrometer. MSD

spectra were recorded on a HP5973 spectrometer. Analytical data were obtained using a Carlo Erba Analyzer 1106. GC analyses were performed using a Fisons GC 8000 gas chromatograph with a flame ionization detector and a DB-17 fused silica capillary column (30 m×0.25 mm i.d., film thickness 0.25 μm). GC peak areas were integrated electronically with a Fisons integrator DP700 or the Lab Systems X-Chrom integrating system. For dry reactions, flasks were dried at 125°C, flushed with nitrogen just before use and kept under nitrogen atmosphere during the reaction. Column and flash chromatography were performed with ICN silica gel 60 (230–400 mesh), using mixtures of petroleum ether bp 40–60°C (PE) and ethyl acetate (EA) as eluents, unless reported otherwise.

Compounds **5** and **6** were prepared from the distillation tail of *E. globulus* as described by Gijsen et al.[2]

4.1.1. (1*R*,3a*R*,7a*R*,8a*R*,8b*S*)-1,8,8-Trimethyldecahydro-5*H*-cyclopenta[*b*]cyclopropa-[*d*]-oxocin-5-one (2). To a stirred solution of 13.4 g (65 mmol) of **6** in 300 mL of CH_2Cl_2, cooled to 0°C, was added 30.7 g (125–133 mmol) of 70–75% *m*CPBA and 21 g of $NaHCO_3$. After stirring for 1 h at room temperature, 100 mL of CH_2Cl_2 was added to the suspension, because stirring became increasingly difficult. After stirring for another 1.5 h, the reaction mixture was diluted with 300 mL of water and 100 mL of saturated aqueous $NaHCO_3$. After separation of the layers, the organic layer was washed successively with 300 mL of 10% aqueous $Na_2S_2O_3$, 400 mL of saturated aqueous $NaHCO_3$, and brine, and then dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, 14.9 g (99%) of **2** was obtained as a white solid.

IR (CCl_4) 2956, 2872, 1743, 1456, 1430, 1377, 1322, 1225, 1089, 1036 cm^{-1}; ^1H NMR δ 0.35–0.54 (m, 2H, 2× cyclopropane–H), 0.82 (d, J=7.2 Hz, 3H, CHMe), 0.90 (s, 3H, Me), 0.99 (s, 3H, Me), 1.0–1.7 (m, 4H), 1.86–2.07 (m, 4H), 2.27 (dt, J=4.7, 10.5 Hz, 1H), 2.56 (m, 1H), 4.89 (dt, J=1.9, 9.2 Hz, 1H, CHOC=O); ^{13}C NMR δ 15.0 (q), 18.0 (q), 19.2 (s), 21.5 (t), 25.4 (d), 27.0 (d), 28.6 (t), 28.8 (q), 30.7 (t), 31.9 (d), 35.9 (t), 47.8 (d), 84.8 (d), 179.2 (s); HRMS calcd for $C_{14}H_{22}O_2$ (M^+) 222.1620, found 222.1616.

4.1.2. (6*R*,6a*S*,7*R*,9a*R*)-6-Hydroxy-7-methyloctahydrocyclopenta[*b*]oxocin-2(3*H*)-one (7). To a stirred solution of 182 mg (1.0 mmol) of **5** in 10 mL of CH_2Cl_2, cooled to 0°C, were added 1.2 g (4.9–5.2 mmol) of 70–75% *m*CPBA and 1.2 g of $MgSO_4$. After stirring for 72 h at room temperature, the reaction mixture was washed with 10% aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 3:2) to yield 137 mg (69%) of **7** as white crystals: mp 99–100°C; $[\alpha]_D$=−100.7° (c=1.425, $CHCl_3$); IR (CCl_4) 3623, 3483, 2958, 2906, 2876, 1742, 1237, 1045 cm^{-1}; ^1H NMR δ 0.86 (d, J=7.2 Hz, 3H, CH*Me*), 1.32–2.66 (m, 13H), 4.07 (dt, J=4.6, 8.1 Hz, 1H, C*H*OH), 4.35 (dt, J=3.1, 9.7 Hz, 1H, C*H*OC=O); ^{13}C NMR δ 15.8 (q), 18.7 (t), 27.1 (t), 29.7 (t), 30.9 (t), 33.9 (t), 34.1 (d), 56.4 (d), 73.6 (d), 80.8 (d), 172.1 (s); MS *m*/*z* (r.i.) 180 (M^+-H_2O, 25), 154 (100), 99 (84), 95 (46), 82 (57), 81 (42), 71 (55), 67 (64), 55 (61), 43 (36), 41 (40); HRMS calcd for $C_{11}H_{16}O_2$ (M^+-H_2O) 180.1150, found 180.1150.

4.1.3. (1*R*,3a*R*,8*S*,8a*R*)-8-Bromo-1-methyloctahydro-4(1*H*)-azulenone (8). To a stirred solution of 1.5 g (8.2 mmol) of **5** and 3.0 g (9.0 mmol) of CBr_4 in 75 mL of CH_2Cl_2 was added 4.3 g (16.4 mmol) of PPh_3, in small portions over a period of 1 h. After stirring for 15 min. at room temperature, the reaction mixture was concentrated to a volume of approximately 10 mL and then column chromatographed (PE/EA 1:1) to yield 1.57 g (78%) of 8 as a light yellow oil. ^1H NMR δ 1.18 (d, J=6.7 Hz, 3H, CH*Me*), 1.37–2.57 (m, 12H), 3.62 (q, J=8.6 Hz, 1H, C*H*C=O), 4.79 (t, J=3.2 Hz, 1H, C*H*Br); ^{13}C NMR δ 13.9 (q), 18.9 (t), 25.8 (t), 33.6 (t), 37.6 (d), 40.7 (t), 42.5 (t), 47.8 (d), 53.7 (d), 59.7 (d), 213.1 (s); MS *m*/*z* (r.i.) 246 (M^+, ^{81}Br, 36), 244 (M^+, ^{79}Br, 36), 165 (100), 164 (32), 162 (31), 147 (24), 137 (22), 109 (51), 95 (41), 81 (64); HRMS calcd for $C_{11}H_{17}O^{79}Br$/$C_{11}H_{17}O^{81}Br$ 244.0463/246.0443, found 244.0470/246.0440.

4.1.4. Ethyl (5*S*)-5-bromo-5-[(1*R*,2*R*,5*R*)-2-hydroxy-5-methylcyclopentyl]pentanoate (10). To a stirred solution of 1.7 g (6.9 mmol) of **8** in 100 mL of CH_2Cl_2 was added 8.3 g (ca. 35 mmol) of 70–71% *m*CPBA. After stirring for 2 days at room temperature, 40 mL of EtOH and a catalytic amount of $TsOH{\cdot}H_2O$ were added. After stirring for another day, the reaction mixture was diluted with 200 mL of saturated aqueous $NaHCO_3$. The two-phase system was separated and the water layer extracted with two 100-mL portions of CH_2Cl_2. The combined organic layers were washed with 10% aqueous $Na_2S_2O_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was chromatographed (PE/EA 1:1) to give 0.16 g (10%) of starting material and 1.25 g (59%) of **10** as a colorless oil.

IR (CCl_4) 3577, 2962, 2874, 1736, 1459, 1376, 1245, 1187, 1041 cm^{-1}; ^1H NMR δ 0.75 (d, J=7.1 Hz, 3H, CH*Me*), 1.19 (t, J=7.1 Hz, 3H, OCH$_2$*Me*), 1.3–2.4 (m, 13H), 4.11 (q, J=7.1 Hz, 2H, OC*H*$_2$Me), 4.04–4.42 (m, 2H, C*H*OH and C*H*Br); ^{13}C NMR δ 14.3 (q), 14.5 (q), 22.5 (t), 31.8 (t), 31.8 (t), 33.4 (t), 37.0 (t), 37.1 (d), 59.0 (d), 60.5 (t), 60.6 (d), 77.3 (d), 173.2 (s); MS *m*/*z* (r.i.) 227 (M^+-Br, 28), 209 (88), 181 (100), 163 (98), 135 (81), 121 (61), 95 (70), 93 (60), 81 (92), 55 (87), 41 (56); HRMS calcd for $C_{13}H_{23}O_3$ (M^+-Br) 227.1647, found 227.1650.

4.1.5. Ethyl (5*Z*,7*R*)-10-hydroxy-7-methyl-5-decenoate (12). To a stirred solution of 0.60 g (1.95 mmol) of **10** in 70 mL of 0.5 M ethanolic NaOEt was added 0.38 g (10 mmol) of $NaBH_4$. After stirring for 2 h at room temperature, the reaction mixture was diluted with 100 mL of 1 M aqueous HCl and extracted with three 50-mL portions of CH_2Cl_2. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 1:1) to yield 0.26 g (77%) of **19** as a colorless oil. IR (film) 3410, 2936, 2870, 1736, 1457, 1374, 1096, 1058 cm^{-1}; ^1H NMR δ 0.87 (d, J=5.1 Hz, 3H, CH*Me*), 1.19 (t, J=7.1 Hz, 3H, OCH$_2$*Me*), 1.30–1.69 (m, 8H), 1.95–2.02 (m, 2H), 2.2–2.4 (m, 2H), 3.55 (t, J=6.5 Hz, 2H, CH_2OH), 4.06 (q, J=7.1 Hz, 2H, OC*H*$_2$Me), 5.04–5.29 (m, 2H, C*H*=C*H*); ^{13}C NMR δ

14.3 (q), 21.4 (q), 25.0 (t), 26.8 (t), 30.8 (t), 31.5 (d), 33.4 (t), 33.8 (t), 60.3 (t), 63.1 (t), 127.4 (d), 137.0 (d), 174 (s); MS *m/z* (r.i.) 210 (M^+-H_2O, 16), 185 (33), 152 (86), 123 (35), 99 (47), 95 (73), 81 (100), 69 (34), 67 (42), 55 (51), 41 (34); HRMS calcd for $C_{13}H_{22}O_2$ (M^+-H_2O) 210.1620, found 210.1616.

4.1.6. Ethyl (7*S*)-10-hydroxy-7-methyldecanoate (4). To a solution of 100 mg (0.44 mmol) of **12** in 5 mL of EtOAc was added 50 mg of 10% Pd(C). The solution was hydrogenated for 1 h in a Parr apparatus under 4 atm of H_2 and then filtered over hyflo. The hyflo was washed with CH_2Cl_2 and the filtrate was evaporated under reduced pressure. The residue was column chromatographed (PE/EA 2:1) to yield 84 mg (83%) of **4** as a colorless oil.

IR (film) 3373, 2932, 2859, 1737, 1464, 1375, 1181, 1057 cm^{-1}; ^1H NMR δ 0.86 (d, *J*=6.3 Hz, 3H, CH*Me*), 1.25 (t, *J*=7.1 Hz, 3H, OCH_2*Me*), 1.00–1.70 (m, 14H), 2.28 (t, *J*=7.5 Hz, 2H), 3.61 (t, *J*=6.6 Hz, 2H, CH_2OH), 4.12 (q, *J*=7.1 Hz, 2H, OCH_2Me); ^{13}C NMR δ 14.3 (q), 19.6 (q), 25.0 (t), 26.6 (t), 29.4 (t), 30.3 (t), 32.5 (d), 32.9 (t), 34.4 (t), 36.7 (t), 60.2 (t), 63.3 (t), 174.0 (s); HRMS calcd for $C_{12}H_{24}O_2$ (M^+-CH_2O) 200.1776, found 200.1778.

4.1.7. (7*R*)-7-Methyl-1-decanol (13). To a stirred solution of 0.22 g (0.96 mmol) of **4** in 20 mL of pyridine was added 0.91 g (4.8 mmol) of TsCl. After stirring for 4 h at room temperature, the reaction mixture was diluted with 100 mL of 1 M aqueous HCl and extracted with three 50-mL portions of EtOAc. The combined organic layers were washed with 1 M aqueous HCl and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 2:1) to yield 0.29 g (79%) of the corresponding tosylate as a colorless oil.

^1H NMR δ 0.79 (d, *J*=6.2 Hz, 3H, CH*Me*), 1.24 (t, *J*=7.1 Hz, 3H, OCH_2*Me*), 1.0–1.4 (m, 8H), 1.53–1.70 (m, 5H), 2.27 (t, *J*=7.5 Hz, 2H), 2.68 (s, 3H, Ar*Me*), 3.99 (t, *J*=6.5 Hz, 2H, CH_2OSO_2), 4.11 (q, *J*=7.1 Hz, 2H, OCH_2Me), 7.33 (d, *J*=8.2 Hz, 2H, 2×Ar–*H*), 7.78 (d, *J*=8.3 Hz, 2H, 2×Ar–*H*); ^{13}C NMR δ 14.3 (q), 19.4 (q), 21.7 (q), 25.0 (t), 26.5 (t), 26.6 (t), 29.4 (t), 32.2 (d), 32.5 (t), 34.4 (t), 36.5 (t), 60.2 (t), 71.1 (t), 127.9 (d, 2C), 129.8 (d, 2C), 133.2 (s), 144.7 (s), 173.9 (s).

To a stirred solution of 0.29 g (0.76 mmol) of this tosylate in 25 mL of dry THF was added 0.15 g (4.0 mmol) of $LiAlH_4$. After stirring for 1.5 h at room temperature, the reaction mixture was diluted with 100 mL of 1 M aqueous HCl and extracted with three 40-mL portions of CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 2:1) to yield 124 mg (95%) of **13** as a colorless oil.

^1H NMR δ 0.85 (d, *J*=6.3 Hz, 3H, CH*Me*), 0.88 (t, *J*=6.9 Hz, 3H, CH_2*Me*), 1.04–1.65 (m, 15H), 3.65 (t, *J*=6.5 Hz, 2H, CH_2OH); ^{13}C NMR δ 14.4 (q), 19.7 (q), 20.1 (t), 25.8 (t), 27.0 (t), 29.8 (t), 32.5 (d), 32.8 (t), 37.0 (t), 39.4 (t), 63.1 (t). The ^1H NMR spectrum of **13** corresponds to that of the racemic compound reported in literature.[29]

4.1.8. (7*R*)-1-Iodo-7-methyldecane (14). To a stirred solution of 106 mg (0.62 mmol) of **13** in 20 mL of CH_2Cl_2 were added 0.32 g (1.2 mmol) of PPh_3, 90 mg (1.3 mmol) of imidazole and 0.32 g (1.3 mmol) of I_2. After stirring for 40 min at room temperature, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and extracted three times with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed twice (PE/EA 5:1) to yield 158 mg (91%) of **14** as a colorless oil.

IR (film) 2956, 2927, 2855, 1464, 1378, 1200, 1169 cm^{-1}; ^1H NMR δ 0.83 (d, *J*=6.3 Hz, 3H, CH*Me*), 0.87 (t, *J*=6.9 Hz, 3H, CH_2*Me*), 1.04–1.37 (m, 13H), 1.75–1.89 (m, 2H), 3.18 (t, *J*=7.0 Hz, 2H, CH_2I); ^{13}C NMR δ 7.4 (t), 14.4 (q), 19.7 (q), 20.1 (t), 26.9 (t), 28.9 (t), 30.6 (t), 32.4 (d), 33.6 (t), 36.9 (t), 39.4 (t); MS *m/z* (r.i.) 282 (M^+, 8), 155 (35), 99 (12), 85 (47), 71 (69), 69 (17), 57 (100), 55 (35), 43 (92), 41 (41), 39 (9); HRMS calcd for $C_{11}H_{23}I$ (M^+) 282.0845, found 282.0838.

4.1.9. (10*R*)-10-Methyl-1-tridecene (15). To a stirred solution of 32 mg (0.11 mmol) of **14** in 2 mL of dry THF, cooled to 0°C, was added 0.22 mL of 1 M allylMgCl in THF. After stirring for 1 h at 0°C, the reaction mixture was diluted with 1 M aqueous HCl and extracted three times with Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 5:1) to yield 19 mg (83%) of **15** as a colorless oil.

^1H NMR δ 0.93–0.99 (m, 6H), 1.08–1.42 (m, 17H), 2.00–2.18 (m, 2H), 5.01–5.15 (m, 2H, CH=CH_2), 5.75–5.95 (m, 1H, CH=CH_2); ^{13}C NMR δ 14.4 (q), 19.6 (q), 20.3 (t), 27.3 (t), 29.1 (t), 29.3 (t), 29.7 (t), 30.2 (t), 32.7 (d), 34.0 (t), 37.3 (t), 39.5 (t), 114.3 (t), 139.0 (d). The ^1H NMR spectrum of **15** corresponds to that of the racemic compound reported in literature.[19]

4.1.10. (10*R*)-10-Methyl-2-tridecanone (16). A suspension of 7.8 mg (0.079 mmol) of CuCl and 1.4 mg (0.008 mmol) of $PdCl_2$ in 0.5 mL of DMF, containing one drop of water, was stirred for 2 h under oxygen atmosphere. Then, a solution of 15 mg (0.077 mmol) of **15** in 1 mL of DMF was added and the reaction mixture was stirred for 1 day. The mixture was diluted with 1 M aqueous HCl and extracted three times with Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 5:1) to yield 16 mg (100%) of **16** as a colorless oil. The ^1H and ^{13}C NMR spectra of **16** correspond to those reported in literature.[24]

4.1.11. Ethyl (7*S*)-7-methyl-10-oxodecanoate (17). To a stirred solution of 0.35 g (1.52 mmol) of **4** in 7 mL of CH_2Cl_2 were added 41 mg (0.5 mmol) of NaOAc and 0.49 g (2.25 mmol) of PCC. After stirring for 2.5 h at room temperature, the reaction mixture was loaded to a silica gel column. Elution with PE/EA 19:1 yielded 0.27 g (78%) of **17** as a colorless oil. $[\alpha]_D=-0.36°$ (*c*=1.4, $CHCl_3$); IR (film) 1735, 1720, 1179 cm^{-1}; ^1H NMR δ 0.83 (d,

J=6.7 Hz, 3H, CHMe), 1.23 (t, J=7.1 Hz, 3H, OCH$_2Me$), 1.10–1.66 (m, 11H), 2.27 (t, J=7.6 Hz, 2H), 2.39 (dt, J=1.8, 6.9 Hz, 2H), 4.10 (q, J=7.1 Hz, 2H, OCH_2Me), 9.75 (t, J=1.8 Hz, 1H, CH=O); ^{13}C NMR δ 14.3 (q), 19.3 (q), 24.9 (t), 26.6 (t), 28.8 (t), 29.3 (t), 32.3 (d), 34.3 (t), 36.5 (t), 41.7 (t), 60.2 (t), 173.9 (s), 203.1 (d); MS m/z (r.i.) 200 (M^+-CO, 21), 185 (92), 183 (40), 172 (37), 139 (75), 101 (78), 97 (45), 88 (100), 83 (34), 69 (42), 55 (62); HRMS calcd for $C_{12}H_{24}O_2$ (M^+-CO) 200.1776, found 200.1774.

4.1.12. Ethyl (7*S*)-7-methyl-10-heptadecenoate (18). To a stirred solution of 0.73 g (1.5 mmol) of $[H_{15}C_7PPh_3]^+I^-$ in 5 mL of dry THF, cooled to 0°C and under argon atmosphere, was added 0.94 mL (1.5 mmol) of 1.6 M *n*BuLi in hexane. After stirring for 2 h at 0°C, the solution was cooled to −78°C and a solution of 0.27 g (1.18 mmol) of **17** in 3 mL of THF was added dropwise. After stirring for 1 h at −78°C and 1 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 19:1) to yield 0.36 g (98%) of **18** as a mixture of *Z*/*E* isomers in a ratio of 3:1 (according to GC-analysis): ^{1}H NMR δ 0.85 (d, J=6.3 Hz, 3H, CHMe), 0.87 (t, J=5.9 Hz, 3H, CH$_2Me$), 1.24 (t, J=7.1 Hz, 3H, OCH$_2Me$), 1.03–1.65 (m, 19H), 2.00 (m, 4H), 2.28 (t, J=7.7 Hz, 2H), 4.11 (q, J=7.1 Hz, 2H, OCH_2Me), 5.25–5.39 (m, 2H, CH=CH); ^{13}C NMR δ 14.1 (q), 14.2 (q), 19.5 (q), 22.6 (t), 24.7 (t), 25.0 (t), 26.6 (t), 27.2 (t), 29.0 (t), 29.5 (t), 29.7 (t), 31.8 (t), 32.1 (d), 34.4 (t), 36.7 (t), 37.0 (t), 60.1 (t), 129.8 (d, *Z*), 130.0 (d, *Z*), 130.2 (d, *E*), 130.4 (d, *E*), 173.9 (s).

4.1.13. (9*S*)-9-Methyl-2,12-nonadecadiene (19). To a stirred solution of 0.34 g (1.1 mmol) of **18** in 30 mL of toluene, cooled to −78°C, was added slowly 0.77 mL (1.2 mmol) of 1.5 M DIBAL-H in toluene. After stirring for 1 h, 3 mL of 1 M aqueous AcOH was carefully added, while keeping the temperature below −65°C, and the reaction mixture was stirred for another 30 min. Then the reaction mixture was poured slowly into ice-cold 1 M aqueous HCl and extracted with three 30-mL portions of Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 97:3) to yield 0.25 (86%) of the corresponding aldehyde as a colorless oil, which was used immediately in the next reaction.

To a stirred solution of 0.46 g (1.2 mmol) of $[H_5C_2PPh_3]^+I^-$ in 4 mL of dry THF, cooled to 0°C and under argon atmosphere, was added 0.70 mL (1.1 mmol) of 1.6 M *n*BuLi in hexane. After stirring for 2 h at 0°C, the solution was cooled to −78°C and a solution of 0.25 g (0.94 mmol) of the aldehyde in 2 mL of THF was added dropwise. After stirring for 1 h at −78°C and 1 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE) to yield 0.24 g (92%) of **19** as a mixture of four stereoisomers.

^{1}H NMR δ 0.85 (d, J=6.5 Hz, 3H, CHMe), 0.85 (t, J=6.0 Hz, 3H, CH$_2Me$), 1.07–1.64 (m, 19H), 1.59 (d, J=5.4 Hz, 3H, =CHMe), 1.97–2.03 (m, 6H), 5.25–5.48 (m, 4H, CH$_2$CH=CHCH$_2$ and CH$_2$CH=CHMe); ^{13}C NMR δ 14.2 (q, 2C atoms), 19.6 (q), 22.7 (q), 24.8 (t), 26.9 (t), 27.2 (t), 29.0 (t), 29.6 (t, 2C atoms), 29.8 (t), 31.8 (t), 32.4 (d), 32.6 (t), 36.9 (t), 37.1 (t), 123.6, 124.5, 129.7, 130.1, 130.9, 131.7 (all d, 4C, *Z*/*E*); MS m/z (r.i.) 278 (M^+, 30), 109 (39), 97 (53), 96 (67), 95 (37), 83 (58), 81 (43), 69 (73), 68 (46), 55 (100), 41 (38); HRMS calcd for $C_{20}H_{38}$ (M^+) 278.2974, found 278.2971.

4.1.14. (9*S*)-9-Methylnonadecane (20). To a solution of 0.24 g (0.86 mmol) of **19** in 35 mL of EtOAc was added 80 mg of 10% Pd(C). The solution was hydrogenated for 1.5 h in a Parr apparatus under 4 atm of H_2 and then filtered over silica gel. The filtrate was evaporated under reduced pressure and the residue was flash chromatographed (PE) to yield 0.23 g (95%) of **20** as a colorless oil.

^{1}H NMR δ 0.86 (d, J=6.4 Hz, 3H, CHMe), 0.85 (t, J=8.2 Hz, 6H, 2×CH$_2Me$), 1.00–1.55 (m, 33H); ^{13}C NMR δ 14.1 (q, 2C), 19.7 (q), 22.7 (t, 2C), 27.1 (t, 2C), 29.4 (t, 3C), 29.7 (t, 3C), 30.0 (t, 2C), 31.9 (t, 2C), 32.7 (d), 37.1 (t, 2C); MS m/z (r.i.) 282 (M^+, 4), 168 (17), 141 (17), 140 (28), 85 (63), 71 (72), 57 (100), 56 (17), 55 (23), 43 (68), 41 (27); HRMS calcd for $C_{20}H_{42}$ (M^+) 282.3287, found 282.3287.

4.1.15. Ethyl (7*S*)-7-methyl-10-nonadecenoate (21). To a stirred solution of 0.70 g (1.5 mmol) of $[H_{19}C_9PPh_3]^+Br^-$ in 5 mL of dry THF, cooled to 0°C and under argon atmosphere, was added 0.60 mL (1.5 mmol) of 2.5 M *n*BuLi in hexane. After stirring for 2 h at 0°C, the solution was cooled to −78°C and a solution of 0.27 g (1.18 mmol) of **17** in 3 mL of THF was added dropwise. After stirring for 1 h at −78°C and 1 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 19:1) to yield 0.36 g (89%) of **21** as a 4:1 mixture of *Z*/*E* isomers.

IR (CCl_4) 2930, 2858, 1737, 1712, 1464, 1418, 1375, 1179 cm^{-1}; ^{1}H NMR δ 0.88 (d, J=6.4 Hz, 3H, CHMe), 0.87 (t, J=7.2 Hz, 3H, CH$_2Me$), 1.25 (t, J=7.1 Hz, 3H, OCH$_2Me$), 1.07–2.18 (m, 23H), 1.99–2.02 (m, 4H) 2.28 (t, J=7.3 Hz, 2H), 4.12 (q, J=7.1 Hz, 2H, OCH_2Me), 5.25–5.39 (m, 2H, CH=CH); ^{13}C NMR δ 14.1 (q), 14.2 (q), 19.5 (q), 22.7 (t), 24.7 (t), 25.0 (t), 26.7 (t), 27.2 (t), 29.3 (t, 2C), 29.5 (t, 2C), 29.7 (t), 31.9 (t), 32.3 (d), 34.4 (t), 36.7 (t), 37.0 (t), 60.1 (t), 129.8 (d, *Z*), 123.0 (d, *Z*), 130.2 (d, *E*), 130.4 (d, *E*), 173.9 (s); MS m/z (r.i.) 338 (M^+, 24), 209 (54), 138 (100), 97 (65), 91 (40), 83 (66), 69 (72), 57 (49), 55 (96), 43 (52), 41 (46); HRMS calcd for $C_{22}H_{42}O_2$ (M^+) 338.3185, found 338.3185.

4.1.16. (7*S*)-7-Methyl-10-nonadecenal (22). To a stirred solution of 0.29 g (0.85 mmol) of **21** in 25 mL of toluene, cooled to −78°C, was added slowly 0.60 mL (0.90 mmol) of 1.5 M DIBAL-H in toluene. After stirring for 1 h, 3 mL of 1 M aqueous AcOH was added carefully maintaining the

temperature below −65°C, and then stirring was continued for another 30 min. The reaction mixture was poured slowly into ice-cold 1 M aqueous HCl and extracted with three 30-mL portions of Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 97:3) to yield 0.20 g (80%) of **22** as a 4:1 mixture of *Z*/*E* isomers: ^{1}H NMR δ 0.85 (d, *J*=6.5 Hz, 3H, CH*Me*), 0.85 (t, *J*=6.1 Hz, 3H, CH_2*Me*), 1.08–1.30 (m, 21H), 1.5–1.66 (m, 2H), 1.90–2.05 (m, 4H), 2.42 (dt, *J*=1.9, 7.3 Hz, 2H), 5.25–5.39 (m, 2H, C*H*═C*H*), 9.76 (t, *J*=1.9 Hz, 1H, C*H*═O); ^{13}C NMR δ 14.2 (q), 19.5 (q), 22.1 (t), 22.7 (t), 24.8 (t), 26.8 (t), 27.2 (t), 29.2 (t), 29.3 (t), 29.5 (t), 29.7 (t), 29.8 (t), 31.9 (t), 32.3 (d), 36.7 (t), 36.9 (t), 43.9 (t), 129.8, 130.0, 130.4 (all d, 2C, *Z*/*E*), 203.0 (d); MS *m*/*z* (r.i.) 294 (M^+, 25), 135 (65), 126 (79), 109 (61), 97 (85), 83 (70), 81 (56), 69 (75), 57 (57), 55 (100), 43 (51); HRMS calcd for $C_{20}H_{38}O$ (M^+) 294.2923, found 294.2924.

4.1.17. Ethyl (7*S*)-10-{[*tert*-butyl(diphenyl)silyl]oxy}-7-methyldecanoate (23). To a stirred solution of 0.35 g (1.5 mmol) of **4**, 0.23 g (3.0 mmol) of imidazole and 30 mg of DMAP in 4 mL of DMF was added a solution of 0.42 g (1.55 mmol) of TBDPSCl in 1.5 mL of DMF. After stirring for 4 h at room temperature, the reaction mixture was diluted with 30 mL of water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 97:3) to yield 0.61 g (81%) of **23** as a colorless oil: ^{1}H NMR δ 0.82 (d, *J*=6.2 Hz, 3H, CH*Me*), 1.03 (s, 9H, C*Me*$_3$), 1.25 (t, *J*=7.2 Hz, 3H, OCH_2*Me*), 1.01–1.61 (m, 13H), 2.29 (t, *J*=7.3 Hz, 2H), 3. 64 (t, *J*=6.5 Hz, 2H), 4.12 (q, *J*=7.2 Hz, 2H), 7.33–7.43 (m, 6H, 6×Ar–*H*), 7.65–7.71 (m, 4H, 4×Ar–*H*).

4.1.18. (7*S*)-10-{[*tert*-Butyl(diphenyl)silyl]oxy}-7-methyldecanal (24). To a stirred solution of 0.61 g (1.3 mmol) of **23** in 35 mL of toluene, cooled to −78°C, was added slowly 0.92 mL (1.4 mmol) of 1.5 M DIBALH in toluene. After stirring for 1 h, 3 mL of 1 M aqueous AcOH was carefully added, while keeping the temperature below −65°C, and the reaction mixture was stirred for another 30 min. Then the reaction mixture was poured slowly into ice-cold 1 M aqueous HCl and extracted with three 30-mL portions of Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 97:3) to yield 0.49 g (89%) of **24** as a colorless oil: ^{1}H NMR δ 0.83 (d, *J*=6.2 Hz, 3H, CH*Me*), 1.05 (s, 9H, C*Me*$_3$), 1.03–1.66 (m, 13H), 2.41 (dt, *J*=1.8, 7.3 Hz, 2H), 3.64 (t, *J*=6.5 Hz, 2H, CH_2OSi), 7.33–7.46 (m, 6H, 6×Ar–*H*), 7.65–7.69 (m, 4H, 4×Ar–*H*), 9.76 (t, *J*=1.8 Hz, 1H, C*H*═O); ^{13}C NMR δ 19.2 (s), 19.7 (q), 22.1 (t), 26.8 (t), 26.9 (q, 3C), 29.5 (t), 30.1 (t), 32.5 (d), 32.9 (t), 36.7 (t), 44.0 (t), 64.3 (t), 127.6 (d, 4C), 129.5 (d, 2C), 134.2 (s, 2C), 135.6 (d, 4C), 203.0 (d).

4.1.19. *tert*-Butyl(diphenyl)silyl (4*S*)-4-methyl-10-hexadecenyl ether (25). To a stirred solution of 0.58 g (1.22 mmol) of $[H_{13}C_6PPh_3]^+I^-$ in 5 mL of dry THF, cooled to 0°C and under argon atmosphere, was added 0.75 mL (1.2 mmol) of 1.6 M *n*BuLi in hexane. After stirring for 2 h at 0°C, the solution was cooled to −78°C and a solution of 0.47 g (0.94 mmol) of **24** in 3 mL of THF was added dropwise. After stirring for 1 h at −78°C and 1 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE/EA 99:1) to yield 0.33 g (61%) of **25** as a colorless oil, which was used immediately in the next reaction.

4.1.20. (4*S*)-4-Methyl-10-hexadecen-1-ol (26). To a stirred solution of 0.33 g (0.67 mmol) of **25** in 5.5 mL of THF was added dropwise 0.8 mL of 1.1 M TBAF in THF. After stirring for 3 h at room temperature, the reaction mixture was diluted with water and extracted with four 20-mL portions of Et_2O. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was flash chromatographed (PE/EA 17:3) to yield 0.16 g (94%) of **26** as a mixture of *Z*/*E* isomers: ^{1}H NMR δ 0.85 (d, *J*=6.3 Hz, 3H, CH*Me*), 0.85 (t, *J*=6.1 Hz, 3H, CH_2*Me*), 1.03–1.68 (m, 20H), 1.96–2.04 (m, 4H), 3.62 (t, *J*=6.6 Hz, 2H, CH_2OH), 5.26–5.42 (m, 2H, C*H*═C*H*); ^{13}C NMR δ 14.1 (q), 19.6 (q), 22.6 (t), 26.9 (t), 27.2 (t), 29.4 (t), 29.6 (t), 29.7 (t), 30.3 (t), 31.5 (t), 32.6 (d), 32.6 (t), 32.9 (t), 36.9 (t), 63.4 (t), 129.8 (d, *Z*), 129.90 (d, *Z*), 130.3 (d, *E*), 130.4 (d, *E*).

4.1.21. (4*S*)-4-Methyl-10-hexadecenyltriphenylphosphonium iodide (27). To a stirred solution of 0.19 g (0.73 mmol) of PPh_3 and 57 mg (0.73 mmol) of imidazole in 3.5 mL of Et_2O/CH_3CN 5:2, cooled to 0°C, was added 0.18 g (0.72 mmol) of I_2. The resulting slurry was stirred for 30 min at room temperature and then cooled again to 0°C. A solution of 0.16 g (0.63 mmol) of **26** in 0.5 mL of Et_2O was added slowly and the reaction mixture was stirred for 2 h at room temperature. The mixture was flash chromatographed directly (PE/EA 99:1) to yield 0.20 g (87%) of the iodide as a mixture of *Z*/*E* isomers.

^{1}H NMR δ 0.85 (d, *J*=6.3 Hz, 3H), 0.88 (t, *J*=6.2 Hz, 3H), 1.06–1.87 (m, 19H), 1.97–2.20 (m, 4H), 3.16 (t, *J*=7.1 Hz, 2H), 5.27–5.40 (m, 2H, *Z*/*E*); ^{13}C NMR δ 14.1 (q), 19.6 (q), 22.6 (t), 26.9 (t), 27.2 (t, 2C), 29.5 (t), 29.6 (t), 29.8 (t), 31.3 (t), 31.6 (t), 32.1 (t), 32.6 (d), 36.8 (t), 37.9 (t), 129.8 (d, *Z*), 129.9 (d, *Z*), 130.3 (d, *E*), 130.5 (d, *E*).

Upon a 24 h-treatment with 1 equiv. of PPh_3 in toluene at reflux temperature, the iodide was converted quantitatively to its phosphonium salt **27**.[30]

4.1.22. (13*R*,23*S*)-13,23-Dimethylhexatriacontane (28). To a stirred solution of 255 mg (0.41 mmol) of **27** in 4 mL of dry THF, cooled to 0°C and under argon atmosphere, was added 0.25 mL (0.4 mmol) of 1.6 M *n*BuLi in hexane. After stirring for 2 h at 0°C, the solution was cooled to −78°C and a solution of 100 mg (0.34 mmol) of **22** in 2 mL of THF was added dropwise. After stirring for 1 h at −78°C and 1 h at room temperature, the reaction mixture was diluted with 20 mL of water and extracted with four 20 mL portions of Et_2O. The combined organic layers

were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure. The residue was column chromatographed (PE) to yield 140 mg (80%) of the triene as a mixture of stereoisomers.

^{1}H NMR δ 0.85 (d, J=6.6 Hz, 6H, 2×CH*Me*), 0.86 (t, J=6.1 Hz, 6H, 2×CH_2*Me*), 1.08–1.45 (m, 40H), 1.90–2.10 (m, 12H), 5.23–5.40 (m, 6H, 3×C*H*=C*H*); ^{13}C NMR δ 14.1 (q, 2C), 19.6 (q, 2C), 22.6 (t), 22.7 (t), 24.8 (t, 2C), 26.9 (t, 2C), 27.2 (t, 2C), 29.3, 29.5, 29.6, 29.7, 29.8 (all t, 7C), 30.2 (t), 31.4 (t), 31.6 (t), 31.9 (t), 32.3 (t), 32.4 (d, 2C), 32.6 (t), 36.9 (t, 2C), 37.1 (t, 2C), 129.8, 129.9, 129.9, 130.1, 130.4 (all d, 6C).

To a solution of 140 mg (0.27 mmol) of the triene from the previous reaction in 50 mL of EA was added 60 mg of 10% Pd(C). The solution was hydrogenated for 1.5 h in a Parr apparatus under 4 atm of H_2 and then filtered over silica gel. The filtrate was evaporated under reduced pressure and the residue was column chromatographed (PE) to yield 141 mg (99%) of **28** as a colorless oil, which solidified upon standing at room temperature: mp 33–34°C (lit. 29–30°C[29]); ^{1}H NMR δ 0.85 (d, J=6.4 Hz, 6H, 2×CH*Me*), 0.84 (t, J=6.1 Hz, 6H, 2×CH_2*Me*), 1.25 (m, 64H); ^{13}C NMR δ 14.1 (q, 2C), 19.7 (q, 2C), 22.7 (t, 2C), 27.1 (t, 4C), 29.4, 29.7, 30.0 (all t, 19C), 31.9 (t, 2C), 32.7 (d, 2C), 37.1 (t, 4C); MS m/z (r.i.) 520 (M^+, 4), 351 (71), 350 (41), 197 (46), 196 (100), 85 (53), 71 (69), 69 (25), 57 (90), 55 (22), 43 (43); HRMS calcd for $C_{37}H_{76}$ 520.5947, found 520.5941. The ^{1}H NMR spectrum of **28** corresponds to that reported in literature.[31]

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