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Synthesis of all the six components of the female-produced contact sex pheromone of the German cockroach, *Blattella germanica* (L.)☆

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Abstract

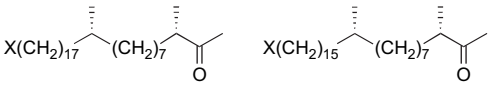
All of the following six components of the female sex pheromone of the German cockroach, *Blattella germanica* (L.) were synthesized: (3*S*,11*S*)-3,11-dimethyl-2-nonacosanone (**1**), its 29-hydroxy derivative **2**, its 29-oxo derivative **3**, (3*S*,11*S*)-3,11-dimethyl-2-heptacosanone (**4**), its 27-hydroxy derivative **5**, and its 27-oxo derivative **6**. Both the enantiomers of citronellal were employed as the chiral sources and Wacker oxidation was employed for the introduction of the carbonyl group at C-2.

1. Introduction

In 1974 Nishida et al. isolated and identified 3,11-dimethyl-2-nonacosanone (**1**, Fig. 1) as the major component of the female-produced contact sex pheromone of the German cockroach, *Blattella germanica* (L.).[2] Subsequent studies by Nishida et al. clarified the presence of two additional components, 29-hydroxy-3,11-dimethyl-2-nonacosanone (**2**) and 3,11-dimethyl-29-oxo-2-nonacosanone (**3**).[3–5] The amount of these components as isolated by them was 239 mg of **1**, 1.7 mg of **2**, and 20 μg of **3**.[5] The biological activities of the pheromone components as expressed by the concentration for 50% biological response were 3.7×10^{-6} M for **1**, 3.9×10^{-7} M for **2**, and 1.9×10^{-6} M for **3**.[5] In other words, **2** was about ten times more active than **1**, while **3** was about twice as active as **1**. Synthesis of all the four stereoisomers of **1** as well as those of **2** by Mori et al. in 1978 established the absolute configuration of **1** and **2** as 3*S*,11*S* after careful comparison of the physical properties of the natural and synthetic **1** and **2** including IR spectrum, mp, and specific rotation.[5–7] Both NMR and chromatographic analyses were proved to be useless in comparing the stereoisomers of these molecules **1** and **2** with two stereogenic centers separated by seven methylene groups.

In 1989 Jurenka et al. identified by mass spectrometry 3,11-dimethyl-2-heptacosanone (**4**) in the cuticular hydrocarbons of the female *B. germanica*.[8] The ketone **4** was subsequently reported to be the fourth component of the female sex pheromone of *B. germanica*.[9] We synthesized (3*S*,11*S*)-**4** in 1997,[10] and its pheromone activity was confirmed by Eliyahu et al.[11] They also found an interesting fact that the natural pheromone (3*S*,11*S*)-**1** is the least active one among the four stereoisomers of **1**.[11] At a discriminating dose of 1 ng, about 10% of the male *B. germanica* exhibited sexual responses to (3*S*,11*S*)-**1**, while 40–60% of the males responded to other stereoisomers.[11] At a dose of 2 ng, (3*R*,11*R*)-**1** was twice as bioactive as (3*S*,11*S*)-**1**.[11] The bioassay works of Eliyahu et al. employed highly pure stereoisomers of **1** synthesized by us in 1990.[12]

In 2007 Schal and his co-workers discovered two additional pheromone components **5** and **6** in the epicuticle of the



1 X = Me (470 ng)
2 X = CH_2OH (25.6 ng)
3 X = CHO (0.5 ng)

4 X = Me (97 ng)
5 X = CH_2OH (5.3 ng)
6 X = CHO (0.15 ng)

Figure 1. Structures of the six components **1**–**6** of the female-produced contact sex pheromone of the German cockroach, *B. germanica* (L). Figures in the parentheses indicate the amounts of the components on the cuticular surface of an adult female of *B. germanica* (L.) as estimated by GC analysis.[13]

☆ Pheromone synthesis, Part 235. For Part 234, see Ref. 1.

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German cockroach.[13] The contact sex pheromone of the female German cockroach thus consists of six biosynthetically related components **1**–**6** as depicted in Figure 1, in which the amounts of the components on the cuticular surface of an adult female *B. germanica* are also shown on the basis of GC analysis of the cuticular hydrocarbons.[13]

Schal's identification of **5** and **6** was made possible by direct comparison of the natural isolates with the synthetics as supplied by Mori.[13] After having prepared **5** and **6** as requested by Schal, I thought it better to synthesize all the other pheromone components, too, by a new route employing common intermediates. Because it is cumbersome and tedious to synthesize compounds such as **1**–**6** with two stereogenic centers separated by seven methylene units, there are only four publications, one by Katsuki and Yamaguchi[14] and three by ourselves,[7,10,12] reporting the synthesis of (3*S*,11*S*)-3,11-dimethyl-2-nonacosanone (**1**) and related compounds **2** and **4**. This paper describes the synthesis of **1**–**6** by a new synthetic route. Compounds **3**, **5**, and **6** were synthesized for the first time.

Our new synthetic plan is based on the idea that the enantiomers of citronellal can be used as the starting materials, because they are now commercially available in high ee of 97%.[15] In our 1978 synthesis, (*R*)-citronellic acid of 92% ee was the only available chiral source. In our second synthesis in 1990, highly pure four stereoisomers of **1** could be synthesized from (*R*)-citronellal and ethyl (*R*)-3-hydroxybutanoate.[12] However, the synthetic route in this 1990 synthesis was more complicated than that of our 1978 synthesis.

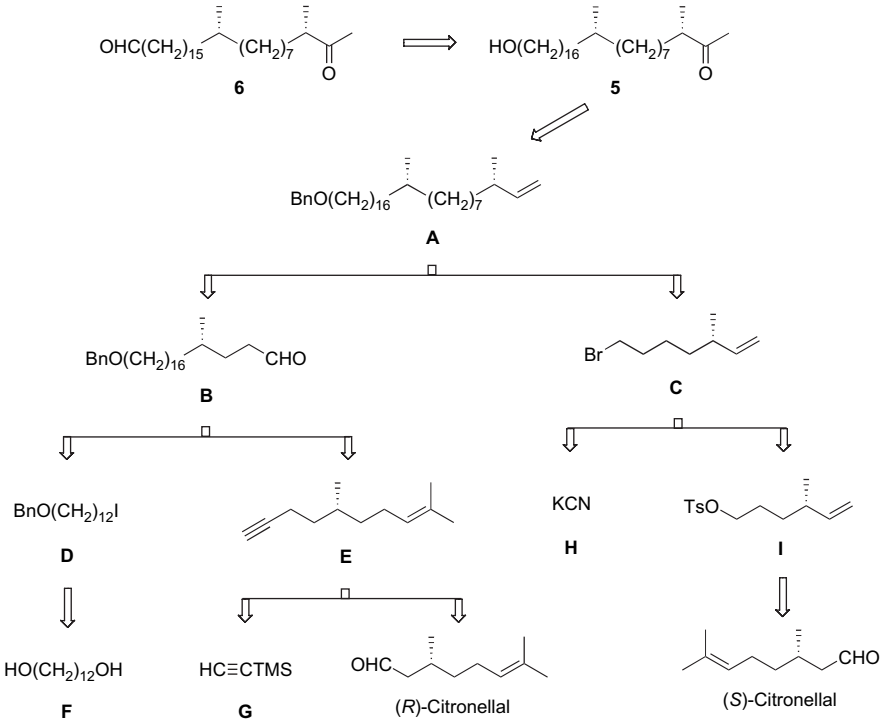
Our present retrosynthetic analysis of Schal's new pheromone components **5** and **6** is shown in Scheme 1. Aldehyde **6** can be derived from alcohol **5** by mild oxidation. Ketone **5** is to be prepared from alkene **A** by Pd^{2+}-catalyzed Wacker oxidation followed by hydrogenolytic debenzylation. In our 1978 synthesis, this conversion was executed by Hg^{2+}-catalyzed hydration of **A** followed by oxidation. Alkene **A** can be prepared by coupling **B** and **C** via Grignard reaction. Alkylation of acetylene **E** with iodide **D** followed by several steps including carbon-chain shortening gives aldehyde **B**. Iodide **D** can be prepared from commercially available 1,12-dodecanediol **F**, while acetylene **E** is to be synthesized from trimethylsilyl(TMS)acetylene **G** and (*R*)-citronellal. Another intermediate **C** can be prepared from (*S*)-citronellal via tosylate **I** and potassium cyanide **H**. All of the six pheromone components **1**–**6** were synthesized along this line.

2. Results and discussion

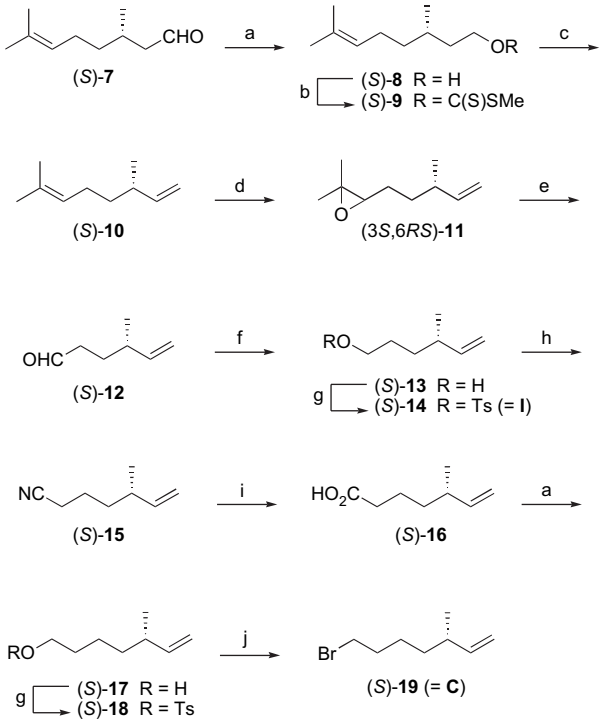
2.1. Synthesis of the key building block (*S*)-19 (=C)

Scheme 2 summarizes the synthesis of the key building block (*S*)-**19** (=**C**), which constitutes the C-1 to C-7 portion of the pheromone components **1**–**6**. Tosylate (*S*)-**14** was previously prepared from (−)-isopulegol via (*R*)-citronellic acid and served as an intermediate for the synthesis of **1** and **2**.[7]

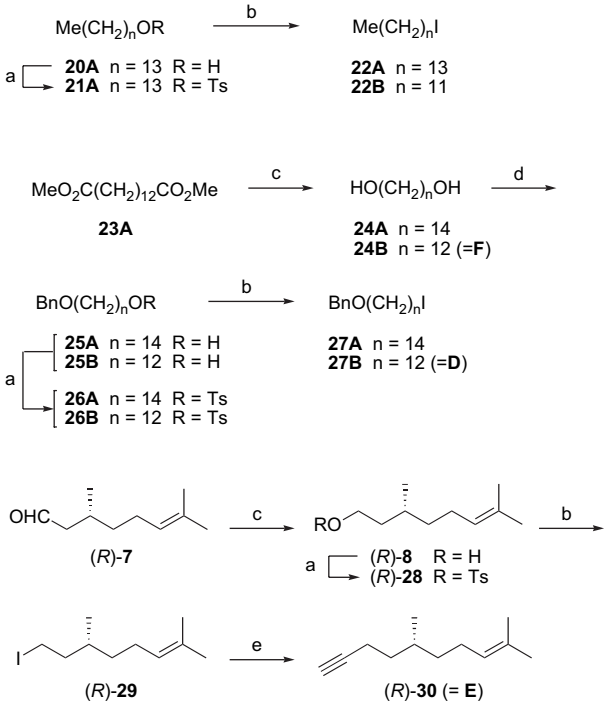
(*S*)-Citronellal (**7**, Takasago, 97% ee) was reduced to (*S*)-citronellol (**8**), whose methyl xanthate **9** was pyrolyzed to give (*S*)-**10**.[16] The corresponding monoepoxide **11**[16] was cleaved with periodic acid to afford aldehyde **12**, which was reduced to alcohol **13**. Tosylation of **13** yielded the known tosylate **14** (=**I**),[7] which was treated with potassium cyanide and sodium iodide in dimethyl sulfoxide (DMSO) to furnish nitrile



Scheme 1. Retrosynthetic analysis of the new components **5** and **6** of the female-produced contact sex pheromone of the German cockroach, *B. germanica* (L.).



Scheme 2. Synthesis of (*S*)-**19**. Reagents and conditions: (a) $LiAlH_4$, Et_2O [90% for **8**, quant. for **17** based on (*S*)-**15** (2 steps)]; (b) NaH, CS_2, MeI, THF; (c) heat, 240–270 °C (53–54%, 2 steps); (d) MCPBA, CH_2Cl_2 (quant.); (e) $HIO_4 \cdot 2H_2O$, THF, Et_2O; (f) $LiAlH_4$, Et_2O (65%, 2 steps); (g) TsCl, C_5H_5N (quant.); (h) KCN, NaI, DMSO (78%); (i) NaOH, EtOH, H_2O, then dil HCl; (j) LiBr, DMF (82%).



Scheme 3. Synthesis of **22A**, **27A**, **27B**, and (*R*)-**30**. Reagents and conditions: (a) TsCl, C_5H_5N (89%-quant.); (b) NaI, DMF (85% for **22A**; 96% for **27A**; 95% for **27B**); (c) $LiAlH_4$ THF [89% for **24A**; 90% for (*R*)-**8**]; (d) *t*-BuOK, BnCl, DMSO (30–35%); (e) (i) TMSC≡CH, *n*-BuLi, THF, HMPA; (ii) K_2CO_3, MeOH (71%).

15. Alkaline hydrolysis of **15** gave acid **16** after acidification. Reduction of **16** with lithium aluminum hydride provided alcohol **17**. The corresponding tosylate **18** was treated with lithium bromide in *N*,*N*-dimethylformamide (DMF) to give bromide (*S*)-**19** (=**C**). The overall yield of (*S*)-**19** was 16.5% (12 steps) based on citronellal (*S*)-**7**.

2.2. Synthesis of the iodides 22A, 27A, 27B (=D), and acetylene (R)-30 (=E)

Scheme 3 shows the synthesis of the iodides **22A**, **27A**, **27B** (=**D**), and acetylene (*R*)-**30** (=**E**). The former iodides serve as the left part (C-16 to C-27 or C-16 to C-29 portion), and the latter acetylene serves as the middle part (C-8 to C-15 portion) of the pheromone components **1**–**6**.

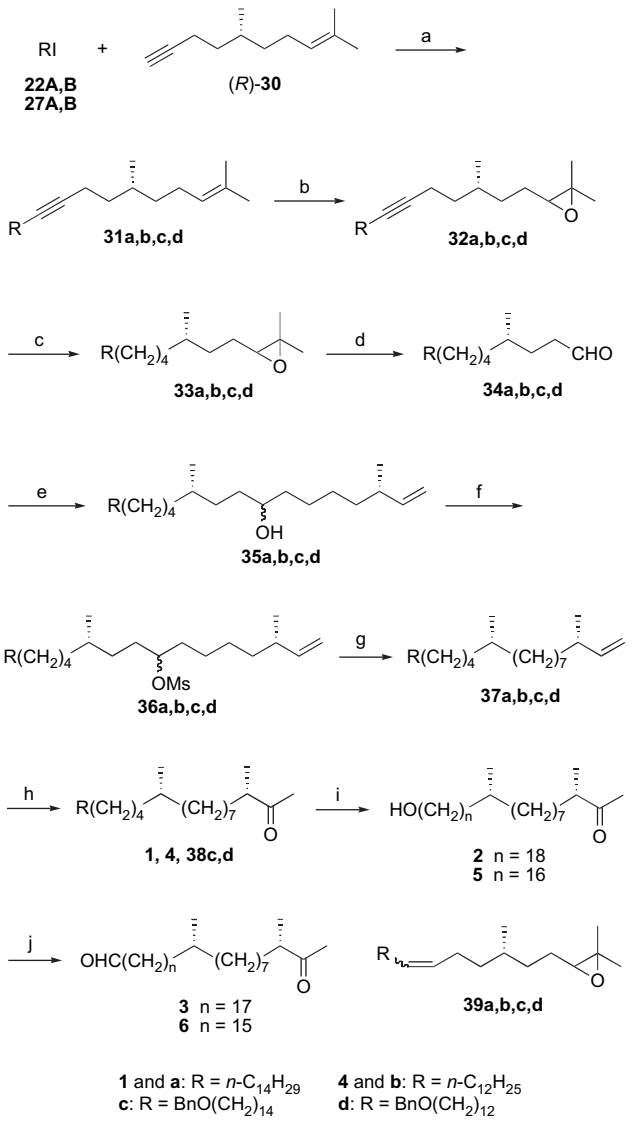
1-Iodotetradecane (**22A**) was prepared in 85% yield (2 steps) from commercially available 1-tetradecanol (**20A**) via the corresponding tosylate **21A**. 1-Iodododecane (**22B**) was commercially available. 14-Benzyloxytetradecyl iodide (**27A**)[7] was prepared from commercially available dimethyl tetradecanedioate (**23A**) by successive reduction to **24A**, monobenzylation to **25A**, tosylation to **26A**, and iodide formation by Finkelstein reaction to give **27A** in 27% overall yield based on **23A** (4 steps). As to monobenzylation of diol **24A** with benzyl chloride, use of potassium *tert*-butoxide in DMSO as the base was found to be operationally simple, because the desired product **25A** could readily be separated from the recovered diol **24A** and the unwanted dibenzyl ether by SiO_2 chromatography. Similarly, commercially available 1,12-dodecanediol **24B** (=**F**) was converted to iodide **27B** (=**D**) via **25B** and **26B** in 22% overall yield based on **24B** (3 steps).

Preparation of the known acetylene (*R*)-**30** (=**E**)[7] was facilitated by using commercially available TMS acetylene as one of the starting materials. (*R*)-Citronellal (**7**, Takasago, 97% ee) was reduced to (*R*)-citronellol (**8**), whose tosylate **28** was treated with sodium iodide in DMF to give iodide (*R*)-**29**. Alkylation of the lithiated TMS acetylene (LiC≡CTMS) with **29** was followed by removal of the TMS group with potassium carbonate in methanol to give (*R*)-**30**. The overall yield of (*R*)-**30** was 61% based on (*R*)-**7** (4 steps).

2.3. Synthesis of the six components 1–6 of the female sex pheromone of the German cockroach

Scheme 4 summarizes the coupling of the three building blocks **C** [=(*S*)-**19**], **D** [=**22A**,**B** and **27A**,**B**], and **E**[(*R*)-**30**] to construct the intermediates with the carbon skeletons of the pheromone molecules and their further conversion to the six components **1**–**6** of the German cockroach pheromone. Synthesis of (3*S*,11*S*)-29-hydroxy-3,11-dimethyl-2-nonacosanone (**2**) and the corresponding aldehyde **3** will be described in detail.

Alkylation of the lithiated acetylene (*R*)-**30** in THF/HMPA with 14-benzyloxytetradecyl iodide (**27A**) gave crude **31c**, which was immediately epoxidized with *m*-chloroperbenzoic



Scheme 4. Synthesis of the six components **1**–**6** of the female-produced contact sex pheromone of the German cockroach, *B. germanica* (L.). Reagents and conditions: (a) (*R*)-**30**, *n*-BuLi, THF, HMPA (quant.); (b) MCPBA, CH_2Cl_2 (43–79%); (c) H_2, Pd/C, EtOAc, Et_3N (82%-quant.); (d) $HIO_4{\cdot}2H_2O$, THF, Et_2O (88–98%); (e) (*S*)-**19**, Mg, THF, then **34** (65–98%); (f) MsCl, C_5H_5N, (quant.); (g) $LiAlH_4$, THF (47–64%); (h) $PdCl_2$, $Cu(OAc)_2{\cdot}H_2O$, O_2, DMA, H_2O (51–57%); (i) H_2, Pd/C, EtOAc, AcOH [45% for **2** (2 steps); 65% for **5** (2 steps)]; (j) Dess–Martin periodinane, CH_2Cl_2 (69% for **3**; 56% for **6**).

acid (MCPBA) in dichloromethane to give **32c** after SiO_2 chromatography. The triple bond of **32c** was then hydrogenated over Pd/C in ethyl acetate to give epoxide **33c**. Hydrogenolysis of the benzyl protective group as well as the possible hydrogenolysis of the epoxy group could be prevented by adding a small amount of Et_3N to the hydrogenation mixture. In some occasions, however, the presence of Et_3N retarded the complete hydrogenation of the triple bond, having allowed to leave a double bond intact to give **39c** instead of the desired **33c** as revealed by ^1H NMR analysis. Treatment of the epoxide **33c** with periodic acid in THF/ether afforded aldehyde **34c**.

Addition of the Grignard reagent prepared from (*S*)-**19** and Mg in THF to the aldehyde **34c** furnished alcohol **35c**, which could be purified by SiO_2 chromatography. Mesylation of **35c** with methanesulfonyl chloride (mesyl chloride, MsCl) in pyridine provided mesylate **36c**, which was reduced with lithium aluminum hydride to give alkene **37c**. Palladium^{2+}-catalyzed Wacker oxidation of the alkene **37c** with $PdCl_2$ and $Cu(OAc)_2$ in wet *N*,*N*-dimethylacetamide (DMA) under O_2[17–19] yielded methyl ketone **38c** in about 45% yield (72% based on the consumed **37c**) after 3 days at room temperature. Hydrogenolytic removal of the benzyl group of **37c** with H_2 and Pd/C in EtOAc containing a small amount of AcOH gave (3*S*,11*S*)-29-hydroxy-3,11-dimethyl-2-nonacosanone (**2**) as needle-like waxy solids, mp 38–39 °C, $[\alpha]_D^{25}$ +3.62 (hexane), in 45% yield based on **37c** (2 steps). Finally, oxidation of **2** with Dess–Martin periodinane[20] afforded (3*S*,11*S*)-3,11-dimethyl-29-oxo-2-nonacosanone (**3**) as a low melting solid, mp 27–29 °C, $[\alpha]_D^{23}$ +3.47 (hexane), in 69% yield. The overall yield of **3** was 2.1% based on (*S*)-citronellal (18 steps) or 5.6% based on (*R*)-citronellal (14 steps). Similarly, other four pheromone components were synthesized: (3*S*,11*S*)-3,11-dimethyl-2-nonacosanone (**1**), mp 38–40 °C, $[\alpha]_D^{25}$ +4.35 (hexane), (3*S*,11*S*)-3,11-dimethyl-2-heptacosanone (**4**), mp 37–39 °C, $[\alpha]_D^{27}$ +5.44 (hexane), (3*S*,11*S*)-27-hydroxy-3,11-dimethyl-2-heptacosanone (**5**), mp 30–32 °C, $[\alpha]_D^{23}$ +3.27 (hexane), and (3*S*,11*S*)-3,11-dimethyl-27-oxo-2-heptacosanone (**6**), mp 25 °C, $[\alpha]_D^{23}$ +3.47 (hexane).

3. Conclusion

All the six components **1**–**6** of the female-produced contact sex pheromone of the German cockroach, *B. germanica* (L.), were synthesized from the enantiomers of citronellal. Bioassay of these components indicates that both the hydroxy ketones **2** and **5** are about 10-fold more active than the respective parent ketones **1** and **4** of the same chain length.[5,11,13] Each of the six pheromone components can independently elicit the complete repertoire of sex response with no synergism among others.[13] The readily available enantiomers of citronellal will continue to serve as useful chiral sources in pheromone synthesis.[15,21]

4. Experimental

4.1. General

Boiling and melting points are uncorrected values. Refractive indices (n_D) were measured on an Atago DMT-1 refractometer. Optical rotations were measured on a Jasco P-1020 polarimeter. IR spectra were measured on a Jasco FT/IR-410 spectrometer. ^1H NMR spectra (400 MHz, TMS at δ=0.00 as internal standard) and ^{13}C NMR spectra (100 MHz, $CDCl_3$ at δ=77.0 as internal standard) were recorded on a Jeol JNM-AL 400 spectrometer. HRMS were recorded on a Jeol JMS-SX 102A. Column chromatography was carried out on Merck Kieselgel 60 Art 1.07734.

4.2. (*S*)-3,7-Dimethyl-6-octen-1-ol (citronellol) 8

A solution of (*S*)-**7** (Takasago, 97% ee; 57.6 g, 374 mmol) in dry Et_2O (50 mL) was added dropwise to a stirred and

ice-cooled suspension of $LiAlH_4$ (8.0 g, 210 mmol) in dry Et_2O (300 mL) at 5–15 °C. The mixture was stirred for 2 h at 10–15 °C and carefully poured onto ice–dil HCl portionwise. Subsequent work-up and distillation gave **8** (52.5 g, 90%) as a colorless oil, bp 96–97 °C/6 Torr; ν_{max} (film): 3330 (s, OH), 1672 (w, C=C), 1059 (s, C–O).

4.3. (S)-3,7-Dimethyl-1,6-octadiene (citronellene) *10*

Conversion of (*S*)-**8** to (*S*)-**10** was carried out via (*S*)-**9** according to Cernigliaro and Kocienski[16] to give (*S*)-**10** in 53–54% yield, bp 70–75 °C/35–40 Torr; ν_{max} (film): 3078 (w, C=CH_2), 1641 (m, C=C), 995 (m), 910 (s).

4.4. (3S,6RS)-6,7-Epoxy-3,7-dimethyl-1-octene *11*

Oxidation of (*S*)-**10** with 1.1 equiv of MCPBA in dichloromethane yielded (3*S*,6*RS*)-**11** (quant.) as an oil, which was used immediately in the next step. ν_{max} (film): 3078 (w, C=CH_2), 1641 (m, C=C), 1122 (m, C–O), 995 (m), 910 (s).

4.5. (S)-4-Methyl-5-hexenal *12*

Cleavage of the epoxide **11** with $HIO_4 \cdot 2H_2O$ in THF gave (*S*)-**12** as an odoriferous oil, which was used in the next step without distillation. ν_{max} (film): 3078 (w, C=CH_2), 2719 (w, O=C–H), 1726 (s, C=O), 1641 (w, C=C), 997 (m), 914 (s).

4.6. (S)-4-Methyl-5-hexen-1-ol *13*

Reduction of (*S*)-**12** with excess $LiAlH_4$ in ether gave the known (*S*)-**13** (62–65% based on **10**).[7] ν_{max} (film): 3327 (s, OH), 3078 (w, C=CH_2), 1641 (w, C=C), 1059 (s, C–O), 910 (s).

4.7. (S)-4-Methyl-5-hexenyl tosylate *14*

Tosylation of (*S*)-**13** in the standard manner afforded (*S*)-**14** (quant.) as an oil.[7] ν_{max} (film): 3074 (w, C=CH_2), 1641 (w, C=C), 1599 (m, arom. C=C), 1188 (s), 1178 (s), 1097 (m), 966 (s), 918 (s), 816 (s), 663 (s), 555 (s).

4.8. (S)-5-Methyl-6-hexenenitrile *15*

Crude (*S*)-**14** [29.4 g (110 mmol); prepared from 14.8 g of (*S*)-**13**] was dissolved in DMSO (80 mL). To the stirred solution was added KCN (9.6 g, 148 mmol) and NaI (0.5 g), and the mixture was stirred and heated at 100 °C for 2 h. After cooling, the mixture was diluted with water and extracted with ether. The ether extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give (*S*)-**15** (12.5 g, 78%) as an oil, bp 112–114 °C/54 Torr, n_D^{21}=1.4366; $[\alpha]_D^{23}$ +14.6 (*c* 5.12, hexane); ν_{max} (film): 3078 (m, C=CH_2), 2247 (m, C≡N), 1641 (m, C=C), 997 (m), 914 (s); δ_H ($CDCl_3$): 1.02 (3H, d, *J* 6.8, CHCH_3), 1.21 (2H, m), 1.65 (2H, m), 2.15 (1H, m), 2.33 (2H, t, *J* 6.8, CH_2CN), 4.95–5.00 (2H, m, CH=CH_2), 5.63 (1H, m, C*H*=CH_2). HRMS calcd for $C_8H_{13}N$: 123. 1048, found: 123. 1063.

4.9. (S)-5-Methyl-6-hexenoic acid *16*

A solution of (*S*)-**15** (12.5 g, 102 mmol) and NaOH (16 g, 400 mmol) in 95% EtOH (60 mL) and water (40 mL) was stirred and heated under reflux for 8 h. After dilution with water, the mixture was extracted with hexane to remove neutral impurities. The aqueous layer was acidified with dil HCl and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 14.4 g of crude (*S*)-**16**. A portion of it was distilled to give an analytical sample, bp 108–109 °C/6 Torr, n_D^{18}=1.4420; $[\alpha]_D^{23}$ +14.8 (*c* 3.48, hexane); ν_{max} (film): ca. 3200–2700 (m, CO_2H), 1711 (s, C=O), 1641 (w, C=C), 1292 (m), 995 (m), 912 (s); δ_H ($CDCl_3$): 0.99 (3H, d, *J* 6.8, CHCH_3), 1.33 (2H, m), 1.63 (2H, m), 2.13 (1H, m), 2.34 (2H, t, *J* 7.2, CH_2CO), 4.72–4.99 (2H, m, CH=CH_2), 5.67 (1H, m, C*H*=CH_2). HRMS calcd for $C_8H_{14}O_2$: 142.0994, found: 142.0993.

4.10. (S)-5-Methyl-6-hexen-1-ol *17*

A solution of (*S*)-**16** (14.4 g, 80.3 mmol) in dry Et_2O (10 mL) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (4.8 g, 126 mmol) in dry Et_2O (200 mL) at 5–15 °C. The mixture was stirred overnight at room temperature, and the excess $LiAlH_4$ was destroyed by dropwise addition of water to the stirred and ice-cooled mixture. It was then acidified with dil HCl, and extracted with Et_2O. The extract was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give (*S*)-**17** (10.7 g, 82% based on **15**; 2 steps) as a colorless oil, bp 100–103 °C/37 Torr, n_D^{21}=1.4408; $[\alpha]_D^{23}$ +16.0 (*c* 4.68, hexane); ν_{max} (film): 3334 (s, OH), 3078 (m, C=CH_2), 1639 (m, C=C), 1051 (s, C–O), 993 (m), 910 (s); δ_H ($CDCl_3$): 0.99 (3H, d, *J* 6.8, CHCH_3), 1.32 (4H, m), 1.41 (1H, s), 1.54 (2H, m), 2.12 (1H, m), 3.63 (2H, t, *J* 6.8, CH_2OH), 4.90–4.97 (2H, m, CH=CH_2), 5.64–5.73 (1H, m, C*H*=CH_2). HRMS calcd for $C_8H_{16}O$: 128.1201, found: 128.1200.

4.11. (S)-5-Methyl-6-hexenyl tosylate *18*

Powdered tosyl chloride (6.0 g, 31 mmol) was added portionwise to a stirred and ice-cooled solution of (*S*)-**17** (3.3 g, 26 mmol) in dry pyridine (15 mL) at 5–10 °C. The mixture was left to stand overnight in a refrigerator (0–5 °C). It was then diluted with water and extracted with ether. The extract was washed with dil HCl, water, $NaHCO_3$ solution, and brine, dried ($MgSO_4$), and concentrated in vacuo to give (*S*)-**18** (7.3 g, quant.) as an oil. ν_{max} (film): 3072 (w, C=CH_2), 1639 (w, C=C), 1599 (m, arom. C=C), 1176 (s), 935 (s), 816 (s), 663 (s); δ_H ($CDCl_3$): 0.94 (3H, d, *J* 6.8, CHCH_3), 1.20–1.29 (4H, m), 1.59–1.64 (2H, m), 2.04 (1H, m), 2.45 (3H, s, $C_6H_4CH_3$), 4.01 (2H, t, *J* 6.8, CH_2OTs), 4.87–4.93

(2H, m, CH=CH_2), 5.57–5.66 (1H, m, CH=CH$_2$), 7.34 (2H, d, J 8.8, arom. H), 7.79 (2H, d, J 8.8, arom. H). This was employed for the next step without further purification.

4.12. (S)-5-Methyl-6-hexenyl bromide **19**

Powdered LiBr (7.0 g, 80 mmol) was added to a stirred solution of (*S*)-**18** (7.3 g, 26 mmol) in DMF (50 mL). After the exothermic reaction, the mixture was stirred at room temperature for 1 h, poured into ice-water, and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give (*S*)-**19** (4.1 g, 82%) as an oil, bp 86–90 °C/28 Torr, n_D^{18}=1.4651; $[\alpha]_D^{24}$ +10.9 (*c* 4.49, hexane); ν_{max} (film): 3078 (m, C=CH_2), 1641 (m, C=C), 995 (s), 912 (s); δ_H ($CDCl_3$): 0.99 (3H, d, J 6.8, CHCH_3), 1.27–1.33 (2H, m), 1.42 (2H, m), 1.85 (2H, m), 2.12 (1H, m), 3.40 (2H, t, J 6.8, CH_2Br), 4.91–4.98 (2H, m, CH=CH_2), 5.63–5.72 (1H, m, CH=CH$_2$). HRMS calcd for $C_8H_{15}Br$: 190.0357, found: 190.0359.

4.13. 1-Iodotetradecane **22A**

1-Tetradecanol (**20A**, 25 g, 117 mmol) was treated with tosyl chloride (24.5 g, 129 mmol) in dry pyridine (100 mL) to give **21A** (43 g, quant.), which was stirred and heated at 80 °C for 1 h with NaI (45 g, 300 mmol) in DMF (250 mL). After standard work-up and distillation 32.2 g (85%) of **22A** was obtained, bp 160–165 °C/7 Torr; ν_{max} (film): 2922 (s), 2854 (s), 1466 (m), 1178 (w), 721 (w), 602 (w); δ_H ($CDCl_3$): 0.88 (3H, t, J 6.8, CH_3), 1.26 (20H, br s), 1.38 (2H, m), 1.82 (2H, m), 3.19 (2H, t, J 7.1).

4.14. 1,14-Tetradecanediol **24A**

Reduction of **23A** (25 g, 87.4 mmol) with $LiAlH_4$ (7.0 g, 184 mmol) in dry THF (400 mL) at reflux (1 h) gave **24A** (17.8 g, 89%), mp 87–89 °C; ν_{max} (Nujol): 3351 (s, OH), 1051 (m, C–O), 1016 (m, C–O), 997 (w), 972 (w), 729 (w), 615 (w); δ_H ($CDCl_3$): 1.26 (24H, br s), 1.56 (2H, m), 3.64 (4H, t, J 6.8, CH_2OH).

4.15. 14-Benzyloxy-1-tetradecanol **25A**

Potassium *tert*-butoxide (11.2 g, 100 mmol) and **24A** (20.5 g, 89 mmol) were mixed in dry DMSO (100 mL) to give voluminous precipitates of the potassium salt of **24A**. Benzyl chloride (16.5 g, 130 mmol) was added to the mixture, which was heated on a water bath at 80 °C with swirling (later stirring) to dissolve the solid. After stirring for 1.5 h at 80 °C, the mixture was left to stand for 3 days. It was poured into ice-water and extracted with ether. The ether extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was triturated with hexane to recover 7.8 g of **24A**. The residue was chromatographed on SiO_2 (150 g). Elution with hexane gave 12.5 g of dibenzyl ether. Further elution with hexane/EtOAc (3:1) gave the known **25A** (10.0 g, 35%).[7] Elution with hexane/EtOAc (2:1) gave 2.4 g of **24A**. Total amount of the recovered **24A** was 10.2 g. Accordingly, the yield of **25A** based on the consumed **24A** was 70%. The monobenzyl ether **25A** showed the following spectral properties: ν_{max} (film): 3370 (s, OH), 1117 (m), 1061 (m), 735 (m), 696 (m); δ_H ($CDCl_3$): 1.26 (20H, br s), 1.58 (4H, m), 3.46 (2H, t, J 6.8, CH_2OBn), 3.63 (2H, t, J 6.8, CH_2OH), 4.50 (2H, s, $C_6H_5CH_2$), 7.26–7.37 (5H, m, C_6H_5).

4.16. 12-Benzyloxy-1-dodecanol **25B**

In the same manner as described above for the preparation of **25A**, **24B** (20.2 g, 100 mmol), *t*-BuOK (11.2 g, 100 mmol), BnCl (15 g, 120 mmol) in dry DMSO (100 mL) yielded 7.8 g (26%) of **25B**; n_D^{21}=1.4912; ν_{max} (film): 3375 (s, OH), 1103 (s, C–O), 735 (s), 698 (s); δ_H ($CDCl_3$): 1.27 (16H, br s), 1.54–1.63 (4H, m), 3.46 (2H, t, J 6.8, CH_2OBn), 3.63 (2H, t, J 6.8, CH_2OH), 4.50 (2H, s, $C_6H_5CH_2$), 7.26–7.35 (5H, m, C_6H_5). HRMS calcd for $C_{19}H_{32}O_2$: 292.2402, found: 292.2401.

4.17. 14-Benzyloxytetradecyl tosylate **26A**

In the same manner as described for the preparation of **18**, tosylation of **25A** (7.9 g, 25 mmol) with tosyl chloride (5.5 g, 29 mmol) in dry pyridine (50 mL) afforded 10.4 g (89%) of **26A**. ν_{max} (film): 3030 (w, arom. C–H), 1599 (w, arom. C=C), 1186 (s), 1171 (s), 949 (s), 733 (s); δ_H ($CDCl_3$): 1.15–1.40 (20H, m), 1.52–1.68 (4H, m), 2.45 (3H, s, $C_6H_4CH_3$), 3.46 (2H, t, J 6.8, BnOCH_2), 4.01 (2H, t, J 6.8, TsOCH_2), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.28 (2H, C_6H_4), 7.33–7.34 (5H, C_6H_5), 7.78 (2H, d, J 8.0, C_6H_4).

4.18. 12-Benzyloxydodecyl tosylate **26B**

In the same manner under the standard tosylation conditions, **25B** (7.8 g, 26 mmol) was treated with tosyl chloride (6.0 g, 32 mmol) in dry pyridine (50 mL) to give 10.5 g (90%) of **26B**. ν_{max} (film): 3030 (m, arom. C–H), 1599 (m, arom. C=C), 1171 (s), 1107 (s), 945 (s), 733 (s); δ_H ($CDCl_3$): 1.15–1.40 (16H, m), 1.55–1.70 (4H, m), 2.44 (3H, s, $C_6H_4CH_3$), 3.46 (2H, t, J 6.4, CH_2OBn), 4.01 (2H, t, J 6.4, CH_2OTs), 7.25–7.27 (2H, m, C_6H_4), 7.33–7.34 (5H, m, C_6H_5), 7.78 (2H, d, J 8.0, C_6H_4).

4.19. 14-Benzyloxytetradecyl iodide **27A**

Powdered NaI (7.5 g, 50 mmol) was added to a solution of **26A** (10.4 g, 22 mmol) in DMF (50 mL). The mixture was stirred and heated at 50 °C for 4 h, then diluted with water and extracted with hexane. The hexane solution was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 9.0 g (96%) of **27A** as an oil, n_D^{25}=1.5116; ν_{max} (film): 1103 (s, C–O), 735 (s), 696 (s); δ_H ($CDCl_3$) 1.26 (20H, m), 1.59 (2H, m), 1.80 (2H, m), 3.18 (2H, t, J 6.8, CH_2I), 3.46 (2H, t, J 6.8, BnOCH_2), 4.50 (2H, s, $C_6H_5CH_2$),

7.26–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{21}H_{35}IO$: 430.1733, found: 430.1729.

4.20. 12-Benzyloxydodecyl iodide *27B*

In the same manner as described above for **27A**, **26B** (10.5 g, 24 mmol) was treated with NaI (10 g, 67 mmol) in DMF (80 mL) to give 9.5 g (95%) of **27B** as an oil. ν_{max} (film): 1103 (s, C–O), 735 (s), 696 (s); δ_H ($CDCl_3$): 1.26 (16H, m), 1.61 (2H, m), 1.81 (2H, m), 3.18 (2H, t, *J* 6.8, CH_2I), 3.46 (2H, t, *J* 6.8, $BnOCH_2$), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{19}H_{31}IO$: 402.1420, found: 402.1415.

4.21. (R)-5,9-Dimethyl-8-decen-1-yne *30*

(*R*)-3,7-Dimethyl-6-octenyl iodide (**29**) was prepared from (*R*)-citronellal (**7**, Takasago, 97% ee) via (*R*)-**8** and **28** as reported previously.[7] A solution of *n*-BuLi (1.6 M in hexane, 100 mL, 160 mmol) was slowly added to a stirred and cooled solution of TMSC≡CH (15.7 g, 160 mmol) in dry THF (150 mL) and HMPA (10 mL) at −70 to −30 °C under Ar. The mixture was warmed to −10 °C and then cooled again to −70 °C. A solution of (*R*)-**29** (36.3 g, 136 mmol) in THF (10 mL) was added dropwise to the stirred and cooled solution at −70 to −30 °C. After having left to stand for 2 days at room temperature, the mixture was diluted with water and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated to give ca. 36 g of crude 1-trimethylsilylated **30**. ν_{max} (film): 2175 (m, C≡C), 1249 (s), 845 (s), 760 (s). This was dissolved in MeOH (300 mL), and K_2CO_3 (15 g) and water (20 mL) were added to the solution. The mixture was stirred at 50 °C for 1 h, diluted with water, and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 16.0 g (71%) of the known (*R*)-**30** as a colorless oil, bp 110–120 °C/38 Torr, $[\alpha]_D^{21}$ +2.64 (*c* 4.22, hexane); [Ref.7: $[\alpha]_D^{21}$ +3.8 (neat, *l*=1 dm)]; ν_{max} (film): 3311 (m, C≡C–H), 2119 (w, C≡C), 629 (s); δ_H ($CDCl_3$): 0.89 (3H, d, *J* 6, $CHCH_3$), 1.10–1.21 (1H, m), 1.30–1.40 (2H, m), 1.52–1.62 (2H, m), 1.60 (3H, s, C=CCH_3), 1.68 (3H, s, C=CCH_3), 1.92 (1H, t, *J* 1.2, C≡CH), 1.94–2.06 (2H, m), 2.10–2.28 (2H, m), 5.09 (1H, br t, C=CH).

4.22. (R)-1-Benzyloxy-17,21-dimethyl-20-docosen-13-yne *31d*

A solution of *n*-BuLi in hexane (1.6 M, 14 mL, 22 mmol) was added dropwise to a stirred and cooled solution of (*R*)-**30** (3.3 g, 20 mmol) in dry THF (20 mL) and HMPA (2 mL) at −70 °C under Ar. The mixture was warmed to −10 °C and then cooled again at −70 °C. A solution of **27B** (9.0 g, 22 mmol) in dry THF (10 mL) was added to the stirred and cooled mixture at −70 to −30 °C, and it was left to stand at room temperature for 3 days. Subsequently the mixture was diluted with water and extracted with hexane. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo to give 10.0 g (quant.) of crude **31d**. ν_{max} (film): 1103 (m), 735 (m), 696 (m); δ_H ($CDCl_3$): 1.59 (3H, s, C=CCH_3), 1.63 (3H, s, C=CCH_3), 5.10 (1H, br, C=CH). This was employed for the next step without further purification.

4.23. (R)-2,6-Dimethyl-2-tetracosen-9-yne *31a*

In the same manner as described above for **31d**, (*R*)-**30** (2.5 g, 15 mmol) was alkylated with **22A** (5.2 g, 16 mmol) and *n*-BuLi in hexane (1.6 M, 10 ml, 16 mmol) in THF (19 mL) and HMPA (1.5 mL) to give 6.54 g (quant.) of crude **31a**, whose ^{1}H NMR spectrum showed the presence of $CH{=}CMe_2$.

4.24. (R)-2,6-Dimethyl-2-docosen-9-yne *31b*

In the same manner as described above for **31d**, (*R*)-**30** (2.5 g, 15 mmol) was alkylated with **22B** (4.6 g, 15.5 mmol) and *n*-BuLi in hexane (1.6 M, 10 mL, 16 mmol) in THF (19 mL) and HMPA (1.5 mL) to give 6.3 g (quant.) of crude **31b**, whose ^{1}H NMR spectrum showed the presence of $CH{=}CMe_2$.

4.25. (R)-1-Benzyloxy-19,23-dimethyl-22-tetracosen-15-yne *31c*

In the same manner as described above for **31d**, (*R*)-**30** (1.6 g, 10 mmol) was alkylated with **27A** (4.2 g, 9.8 mmol) and *n*-BuLi in hexane (1.6 M, 7 mL, 11 mmol) in THF (13 mL) and HMPA (1 mL) to give 5.1 g (quant.) of crude **31c**, whose ^{1}H NMR spectrum showed the presence of $CH{=}CMe_2$.

4.26. (17S,20RS)-1-Benzyloxy-20,21-epoxy-17,21-dimethyl-13-docosyne *32d*

MCPBA (77% purity, 4.9 g, 22 mmol) was added portionwise to a stirred and ice-cooled solution of crude **31d** (10.0 g) in dry CH_2Cl_2 (100 mL) at 0–5 °C. After 1.5 h, the mixture was diluted with hexane and filtered to remove solid MCBA. The filtrate was washed with dil K_2CO_3 solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (10.6 g) was chromatographed over SiO_2 (70 g). After elution of less polar materials (3.16 g) with hexane/EtOAc=50:1, elution with hexane/EtOAc=50:1–20:1 gave 4.06 g [43% based on (*R*)-**30**, 2 steps] of **32d** as an oil, n_D^{25}=1.4892; ν_{max} (film): 1250 (w), 1205 (w), 1103 (s), 735 (m), 698 (m); δ_H ($CDCl_3$): 0.89 (3H, d, *J* 6.8, $CHCH_3$), 1.27 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.20–1.60 (27H, m), 2.13 (4H, m), 2.67 (1H, m, epoxide H), 3.46 (2H, t, *J* 6.8, CH_2O), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.35 (5H, m, C_6H_5). HRMS calcd for $C_{31}H_{50}O_2$: 454.3811, found: 454.3810.

4.27. (3RS,6S)-2,3-Epoxy-2,6-dimethyl-9-tetracosyne *32a*

In the same manner as described above for **32d**, (*R*)-**31a** (6.6 g, 15 mmol) in CH_2Cl_2 (70 mL) was epoxidized with

MCPBA (3.8 g, 17 mmol) at 0–5 °C for 1.5 h. Subsequent work-up was followed by chromatography of crude **32a** (7.0 g) over SiO_2 (70 g). Elution with hexane gave 1.63 g of less polar materials. Then elution with hexane/EtOAc=50:1 gave 3.0 g [53% based on (*R*)-**30**, 2 steps] of **32a** as an oil. ν_{max} (film): 1290 (w), 1255 (m), 1122 (w), 750 (w); δ_H ($CDCl_3$): 0.86–0.92 (6H, m, $CHCH_3$ and CH_2CH_3), 1.20–1.60 (34H, m), 1.31 (3H, s, CH_3), 2.10–2.24 (4H, m), 2.69 (1H, t, *J* 6.8, epoxide H).

4.28. (3RS,6S)-2,3-Epoxy-2,6-dimethyl-9-docosyne **32b**

In the same manner as described above for **32d**, (*R*)-**31b** (6.3 g, 15 mmol) in CH_2Cl_2 (70 mL) was epoxidized with MCPBA (3.8 g, 17 mmol) at 0–5 °C for 1 h. Subsequent work-up was followed by chromatography of crude **32b** (6.2 g) over SiO_2 (50 g). Elution with hexane gave 1.3 g of less polar materials. Then elution with hexane/EtOAc=50:3 gave 4.1 g [77% based on (*R*)-**30**, 2 steps] of **32b** as an oil. ν_{max} (film): 1290 (w), 1255 (m), 1122 (w), 750 (w); δ_H ($CDCl_3$): 0.86–0.92 (6H, m, $CHCH_3$ and CH_2CH_3), 1.20–1.62 (30H, m), 1.31 (3H, s, CH_3), 2.10–2.22 (4H, m), 2.70 (1H, m, epoxide H); δ_C ($CDCl_3$): 79.95 and 80.30 (C≡C).

4.29. (19S,22RS)-1-Benzyloxy-22,23-epoxy-19,23-dimethyl-15-tetracosyne **32c**

In the same manner as described above for **32d**, (*R*)-**31c** (5.1 g, 11 mmol) in CH_2Cl_2 (50 mL) was epoxidized with MCPBA (2.7 g, 12 mmol) at 0–10 °C for 1 h. Subsequent work-up was followed by chromatography over SiO_2 (50 g). Elution with hexane/EtOAc=50:3 gave 3.8 g [79% based on (*R*)-**30**, 2 steps] of **32c** as an oil. ν_{max} (film): 1255 (m), 1103 (s), 735 (m), 696 (m); δ_H ($CDCl_3$): 0.89 (3H, d, *J* 6.8, $CHCH_3$), 1.26 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.20–1.65 (31H, m), 2.10–2.22 (4H, m), 2.67 (1H, t-like, epoxide H), 3.46 (2H, t, *J* 6.8, CH_2O), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.35 (5H, m, C_6H_5).

4.30. (17S,20RS)-1-Benzyloxy-20,21-epoxy-17,21-dimethyldocosane **33d**

Palladium–charcoal (10%, 700 mg) was added to a solution of **32d** (4.0 g, 8.6 mmol) in EtOAc (40 mL) and Et_3N (0.4 mL). The mixture was stirred under H_2 (balloon) for 22 h at room temperature. The catalyst was filtered off through Celite and washed with EtOAc. The filtrate was concentrated in vacuo and the residue was chromatographed over SiO_2 (20 g). Elution with hexane/EtOAc=50:3 gave 4.0 g (quant.) of **33d** as an oil. ν_{max} (film): 1254 (m), 1103 (s), 735 (s), 696 (s); δ_H ($CDCl_3$): 0.87 (3H, d, *J* 6.4, $CHCH_3$), 1.22–1.65 (34H, m), 1.30 (3H, s, CH_3), 2.69 (1H, t, *J* 6.4, epoxide H), 3.46 (2H, t, *J* 6.8, CH_2O), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.40 (5H, m, C_6H_5).

4.31. (3RS,6S)-2,3-Epoxy-2,6-dimethyltetracosane **33a**

In the same manner as described above for **33d**, **32a** (2.9 g, 7.7 mmol) was hydrogenated over 10% Pd/C (500 mg) in EtOAc (30 mL) and Et_3N (0.1 mL) to give 2.7 g (93%) of **33a** after SiO_2 chromatography (20 g SiO_2 and elution with hexane/EtOAc=50:3). ν_{max} (film): 1254 (m), 1122 (m), 899 (w), 750 (w); δ_H ($CDCl_3$): 0.87 (6H, m, CH_2CH_3 and $CHCH_3$), 1.20–1.60 (34H, m), 1.31 (3H, s, CH_3), 2.70 (1H, t-like, epoxide H).

4.32. (3RS,6S)-2,3-Epoxy-2,6-dimethyldocosane **33b**

In the same manner as described above for **33d**, **32b** (2.2 g, 6.3 mmol) was hydrogenated over 10% Pd/C (500 mg) in EtOAc (25 mL) and Et_3N (1 mL) to give 1.8 g (82%) of **33b** after SiO_2 chromatography (20 g SiO_2 and elution with hexane/EtOAc=100:3). ν_{max} (film): 1254 (m), 1122 (m), 871 (w), 750 (w); δ_H ($CDCl_3$): 0.86–0.90 (6H, m, CH_2CH_3 and $CHCH_3$), 1.20–1.60 (30H, m), 1.31 (3H, s, CH_3), 2.70 (1H, t-like, epoxide H).

4.33. (19S,22RS)-1-Benzyloxy-22,23-epoxy-19,23-dimethyltetracosane **33c**

In the same manner as described above for **33d**, **32c** (3.8 g, 7.6 mmol) was hydrogenated over 10% Pd/C (700 mg) in EtOAc (35 mL) and Et_3N (0.5 mL) to give 3.5 g (92%) of **33c** after SiO_2 chromatography (20 g SiO_2 and elution with hexane/EtOAc=50:3). ν_{max} (film): 1254 (m), 1103 (s), 735 (m), 696 (m); δ_H ($CDCl_3$): 0.87 (3H, d, *J* 7.2, $CHCH_3$), 1.22–1.65 (38H, m), 1.31 (3H, s, CH_3), 2.09 (1H, t-like, epoxide H), 3.46 (2H, t, *J* 6.8, CH_2O), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.40 (5H, m, C_6H_5). In these hydrogenation experiments, the triple bond could not be reduced to the single bond, giving **39a–d** as evidenced by the presence of a signal at δ=5.38 due to olefinic protons, if too much Et_3N was added or too short time was allowed for hydrogenation. Contamination of olefins at this stage necessitated another hydrogenation at the final step (**37a→1**).

4.34. (S)-20-Benzyloxy-4-methylicosanal **34d**

A solution of **33d** (3.8 g, 8.3 mmol) in ether (20 mL) was added to a stirred and ice-cooled solution of $HIO_4 \cdot 2H_2O$ (2.3 g, 10 mmol) in THF (40 mL) at 0–5 °C. The mixture soon became turbid and white solid (HIO_3) precipitated. The stirring was continued for 1 h at 0–5 °C. Subsequently, the mixture was diluted with water, and extracted with ether. The extract was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo to give 3.38 g (98%) of **34d** as an oil, n_D^{25}=1.4852; $[\alpha]_D^{25}$ −0.70 (*c* 3.60, hexane); ν_{max} (film): 2713 (w, O=C–H), 1726 (s, C=O), 1103 (m), 735 (m), 698 (m); δ_H ($CDCl_3$): 0.87 (3H, d, *J* 6.8, $CHCH_3$), 1.20–1.50 (27H, m), 1.58–1.80 (4H, m), 1.97 (2H, m), 2.40 (2H, m), 3.46 (2H, t, *J* 6.8, OCH_2), 4.50 (2H, s, $C_6H_5CH_2$), 7.25–7.40 (5H, m, C_6H_5), 9.76 (1H,

CHO). HRMS calcd for $C_{28}H_{48}O_2$: 416.3654, found: 416.3655.

4.35. (S)-4-Methyldocosanal **34a**

In the same manner as described above for **34d**, **33a** (2.7 g, 7.2 mmol) was treated with $HIO_4 \cdot 2H_2O$ (2.1 g, 9 mmol) in THF (30 mL) and ether (10 mL) at 0–5 °C for 1 h. Subsequent work-up and chromatographic purification over SiO_2 (20 g; elution with hexne/EtOAc=10:1) gave 2.2 g (91%) of **34a** as an oil, n_D^{25}=1.4598; $[\alpha]_D^{25}$ −0.23 (*c* 2.68, hexane); ν_{max} (film): 2711 (w, O=C−H), 1728 (s, C=O), 1255 (m), 750 (m); δ_H ($CDCl_3$): 0.86–0.90 (6H, m, CHC*H*$_3$, CH_2CH_3), 1.20–1.43 (33H, m), 1.92–2.03 (2H, m), 2.40–2.45 (2H, m), 9.77 (1H, CHO). HRMS calcd for $C_{23}H_{46}O$: 338.3545, found: 338.3538.

4.36. (S)-4-Methylicosanal **34b**

In the same manner as described above for **34d**, **33b** (1.8 g, 5.1 mmol) was treated with $HIO_4 \cdot 2H_2O$ (1.4 g, 6 mmol) in THF (25 mL) and ether (5 mL) at 0–5 °C for 1 h. Subsequent work-up and chromatographic purification gave 1.4 g (88%) of **34b** as an oil, n_D^{25}=1.4582; $[\alpha]_D^{25}$ −0.32 (*c* 2.78, hexane); ν_{max} (film): 2711 (w, O=C−H), 1728 (s, C=O), 1257 (m), 968 (m); δ_H ($CDCl_3$): 0.85–0.90 (6H, m, CHC*H*$_3$, CH_2CH_3), 1.20–1.45 (31H, m), 1.90–2.10 (2H, m), 2.40–2.44 (2H, m), 9.77 (1H, CHO). HRMS calcd for $C_{21}H_{42}O$: 310.3236, found: 310.3233.

4.37. (S)-22-Benzyloxy-4-methyldocosanal **34c**

In the same manner as described above for **34d**, **33c** (3.5 g, 7 mmol) was treated with $HIO_4 \cdot 2H_2O$ (1.8 g, 8 mmol) in THF (30 mL) and ether (10 mL) at 0–5 °C for 1 h. Subsequent work-up gave 3.1 g (97%) of **34c** as an oil, n_D^{25}=1.4860; $[\alpha]_D^{25}$ −0.26 (*c* 2.88, hexane); ν_{max} (film): 2713 (w, O=C−H), 1726 (s, C=O), 1103 (s), 1072 (s), 735 (m), 698 (m); δ_H ($CDCl_3$): 0.88 (3H, d-like, CHC*H*$_3$), 1.20–1.42 (31H, m), 1.58–1.70 (4H, m), 1.90–2.05 (2H, m), 2.38–2.42 (2H, m), 3.46 (2H, t, *J* 6.8, OCH_2), 4.50 (2H, s, $C_6H_5CH_2$), 9.77 (1H, CHO). HRMS calcd for $C_{30}H_{52}O_2$: 444.3967, found: 444.3968.

4.38. (3S,8RS,11S)-27-Benzyloxy-3,11-dimethyl-1-heptacosen-8-ol **35d**

Grignard reagent was prepared from bromide (*S*)-**19** (1.9 g, 10 mmol) and Mg (300 mg, 12.5 mmol) in dry THF (6 mL) by initiating the reaction with a trace amount of I_2, with stirring and heating under reflux under Ar. A solution of **34d** (3.1 g, 7.5 mmol) in dry THF (3 mL) was added dropwise to the stirred and ice-cooled Grignard reagent. After 2 h at room temperature, the mixture was quenched with NH_4Cl solution and ice. Then the mixture was extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (4.8 g) was chromatographed over SiO_2 (30 g). Elution with hexane/EtOAc=4:1 gave 2.9 g (74%) of **35d** as an oil, n_D^{24}=1.4841; $[\alpha]_D^{25}$ +2.97 (*c* 3.65, hexane); ν_{max} (film): 3394 (m, OH), 3066 (w), 3030 (w), 1639 (w, C=C), 1101 (s), 908 (m), 733 (m), 696 (m); δ_H ($CDCl_3$): 0.87 (3H, d, *J* 6.0, 11-CH_3), 0.98 (3H, d, *J* 60, 3-CH_3), 1.20–1.50 (38H, m), 1.57–1.70 (4H, m), 1.92–2.05 (2H, m), 2.11 (1H, m), 3.46 (2H, t, *J* 6.8, CH_2O), 3.55 (1H, m, C*H*OH), 4.50 (2H, s, $C_6H_5CH_2$), 4.85–5.00 (2H, m, CH=CH_2), 5.64–5.70 (1H, m, C*H*=CH_2), 7.25–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{36}H_{62}O$ (M^+-H_2O): 510.4801, found: 510.4801.

4.39. (3S,8RS,11S)-3,11-Dimethyl-1-nonacosen-8-ol **35a**

In the same manner as described above for **35d**, **34a** (1.9 g, 5.6 mmol) in THF (3 mL) was added to the Grignard reagent prepared from (*S*)-**19** (1.6 g, 8.3 mmol) and Mg (240 mg, 10 mmol) in THF (5 mL). Subsequent work-up and chromatographic purification over SiO_2 (25 g; elution with hexane/EtOAc=4:1) gave 2.5 g (98%) of **35a** as an oil, n_D^{25}=1.4632; $[\alpha]_D^{25}$ +3.35 (*c* 4.80, hexane); ν_{max} (film): 3361 (m), 3076 (w C=C−H), 1639 (w, C=C), 1255 (s), 910 (s); δ_H ($CDCl_3$): 0.86–0.90 (6H, m, CHC*H*$_3$, CH_2CH_3), 0.98 (3H, d, *J* 6.8, 3-CH_3), 1.20–1.60 (49H, m), 3.55 (1H, m C*H*OH), 4.85–5.00 (2H, m, CH=CH_2), 5.64–5.73 (1H, m, C*H*=CH_2). HRMS calcd for $C_{31}H_{60}$ (M^+-H_2O): 432.4695, found: 432.4698.

4.40. (3S,8RS,11S)-3,11-Dimethyl-1-heptacosen-8-ol **35b**

In the same manner as described above for **35d**, **34b** (1.4 g, 4.5 mmol) in THF (3 mL) was added to the Grignard reagent prepared from (*S*)-**19** (1.4 g, 7.3 mmol) and Mg (240 mg, 10 mmol) in THF (5 mL). Subsequent work-up and chromatographic purification over SiO_2 (20 g; elution with hexane/EtOAc=10:1) gave 1.8 g (95%) of **35b** as an oil, n_D^{26}= 1.4652; $[\alpha]_D^{25}$ +4.16 (*c* 3.07, hexane); ν_{max} (film): 3356 (s, OH), 3076 (w, C=C−H), 1639 (w, C=C), 910 (m); δ_H ($CDCl_3$): 0.86–0.90 (6H, m, CHC*H*$_3$, CH_2CH_3), 0.98 (3H, d, *J* 6.8, 3-CH_3), 1.20–1.60 (45H, m), 3.55 (1H, m, C*H*OH), 4.85–5.00 (2H, m, CH=CH_2), 5.64–5.73 (1H, m, C*H*=CH_2). HRMS calcd for $C_{29}H_{56}$ (M^+-H_2O): 404.4436, found: 404.4442.

4.41. (3S,8RS,11S)-29-Benzyloxy-3,11-dimethyl-1-nonacosen-8-ol **35c**

In the same manner as described above for **35d**, **34c** (2.8 g, 6.2 mmol) in THF (3 mL) was added to the Grignard reagent prepared from (*S*)-**19** (1.5 g, 8 mmol) and Mg (240 mg, 10 mmol) in THF (5 mL). Subsequent work-up and chromatographic purification over SiO_2 (30 g; elution with hexane/EtOAc=10:1) gave 2.2 g (65%) of **35c** as an oil, n_D^{25}= 1.4836; $[\alpha]_D^{25}$ +3.00 (*c* 2.68, hexane); ν_{max} (film): 3384 (s, OH), 3066 (w), 3030 (w), 1639 (w, C=C), 1101 (s), 910 (s), 733 (m), 696 (m); δ_H ($CDCl_3$): 0.87 (3H, d, *J* 6, 11-CH_3), 0.98 (3H, d, *J* 6, 3-CH_3), 1.20–1.50 (42H, m), 1.57–1.70 (4H, m), 1.92–2.05 (2H, m), 2.11 (1H, m), 3.46 (2H, t, *J* 6.8, CH_2O), 3.55 (1H, m, C*H*OH), 4.50 (2H, s, $C_6H_5CH_2$), 4.85–5.00 (2H, m, CH=CH_2), 5.64–5.71 (1H, m,

C*H*=CH_2), 7.25–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{38}H_{66}O$ (M^+-H_2O): 538.5113, found: 538.5115.

4.42. (3S,11S)-27-Benzyloxy-3,11-dimethyl-1-heptacosene *37d*

Methanesulfonyl chloride (1.0 mL, ca. 1.5 g, 13 mmol) was added to a stirred and ice-cooled solution of **35d** (2.9 g, 5.5 mmol) in CH_2Cl_2 (5 mL) and C_5H_5N (5 mL) at 0–5 °C. The mixture was left to stand overnight in a refrigerator (5 °C), poured into ice-water, and extracted with ether. The ether extract was washed with dil HCl, $NaHCO_3$ solution, and brine, dried ($MgSO_4$), and concentrated in vacuo to give 2.1 g of crude **36d**. ν_{max} (film): 3066 (w), 3030 (w), 1639 (w, C=C), 1358 (s), 1176 (s), 906 (s); δ_H ($CDCl_3$): 3.00 (3H, s, SO_2CH_3). A solution of crude **36d** (2.1 g) in dry THF (10 mL) was added dropwise to a stirred and ice-cooled suspension of $LiALH_4$ (0.6 g, 15.8 mmol) in dry THF (15 mL). The mixture was then stirred and heated under reflux for 1 h. After cooling, the mixture was carefully acidified with ice and dil HCl, and extracted with ether. The extract was washed with water, $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (1.7 g) was chromatographed over SiO_2 (20 g). Elution with hexane gave 0.28 g of less polar impurities. Further elution with hexane/EtOAc=20:1 afforded 1.37 g (49% based on **35d**; 2 steps) of **37d**, n_D^{24}=1.4822; $[\alpha]_D^{25}$ +2.47 (*c* 3.11, hexane); ν_{max} (film): 3066 (w), 3030 (w), 1639 (w, C=C), 1103 (s), 908 (m), 733 (m), 696 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.8, CHC*H*$_3$), 0.97 (3H, d, *J* 6.8, CHC*H*$_3$), 1.10–1.40 (41H, br s), 1.55–1.65 (3H, m), 1.90–2.10 (2H, m), 3.46 (2H, t, *J* 6.4, OCH_2), 4.50 (2H, s, $C_6H_5CH_2$), 4.88–5.00 (2H, m, CH=C*H*$_2$), 5.64–5.74 (1H, m, C*H*=CH_2), 7.25–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{36}H_{64}O$: 512.4957, found: 512.4939.

4.43. (3S,11S)-3,11-Dimethyl-1-nonacosene *37a*

In the same manner as described above for **37d**, **35a** (2.2 g, 4.9 mmol) was mesylated with MsCl (1.0 mL, 13 mmol) in CH_2Cl_2 (5 mL) and C_5H_5N (5 mL) to give 2.3 g of crude **36a**. Reduction of **36a** with $LiAlH_4$ (0.6 g, 15.8 mmol) in THF (25 mL) furnished 1.01 g (47% based on **35a**; 2 steps) of **37a** after chromatographic purification [SiO_2 (20 g); elution with hexane] as an oil, n_D^{24}=1.4523; $[\alpha]_D^{24}$ +4.19 (*c* 3.48, hexane); ν_{max} (film): 3078 (w, C=C–H), 1639 (w, C=C), 993 (m), 966 (w), 910 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 0.97 (3H, d, *J* 6.4, 3-CH_3), 1.00–1.15 (2H), 1.20–1.50 (45H, m), 1.90–2.04 (2H), 2.05–2.15 (1H), 4.88–4.96 (2H, m, CH=C*H*$_2$), 5.64–5.74 (1H, m, C*H*=CH_2). HRMS calcd for $C_{31}H_{62}$: 434.4852, found: 434.4851.

4.44. (3S,11S)-3,11-Dimethyl-1-heptacosene *37b*

In the same manner as described above for **37d**, **35b** (1.7 g, 4.0 mmol) was mesylated with MsCl (1.2 mL, 16 mmol) in CH_2Cl_2 (5 mL) and C_5H_5N (5 mL) to give 1.53 g of crude **36b**. Reduction of **36b** with $LiAlH_4$ (0.6 g, 15.8 mmol) in THF (20 mL) furnished 0.89 g (54% based on **35b**, 2 steps) of **37b** after chromatographic purification [SiO_2 (20 g); elution with hexane] as an oil, n_D^{26}=1.4562; $[\alpha]_D^{25}$ +4.51 (*c* 2.95, hexane); ν_{max} (film): 3078 (w, C=C–H), 1639 (w, C=C), 993 (w), 966 (w), 910 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 0.97 (3H, d, *J* 6.8, 3-CH_3), 1.00–1.18 (2H), 1.20–1.45 (41H, m), 1.90–2.05 (2H), 2.05–2.15 (1H), 4.88–4.96 (2H, m, CH=C*H*$_2$), 5.64–5.74 (1H, m, C*H*=CH_2). HRMS calcd for $C_{29}H_{58}$: 406.4539, found: 406.4546.

4.45. (3S,11S)-29-Benzyloxy-3,11-dimethyl-1-nonacosene *37c*

In the same manner as described above for **37d**, **35c** (2.2 g, 4.0 mmol) was mesylated with MsCl (1.0 mL, 13 mmol) in CH_2Cl_2 (10 mL) and C_5H_5N (10 mL) to give 2.1 g of crude **36c**. Reduction of **36c** with $LiAlH_4$ (0.6 g, 15.8 mmol) in THF (25 mL) furnished 1.37 g (64% based on **35c**; 2 steps) of **37c** as an oil, n_D^{25}=1.4840; $[\alpha]_D^{25}$ +2.02 (*c* 3.38, hexane); ν_{max} (film): 3064 (w), 3030 (w), 1639 (w, C=C), 1103 (s), 908 (m), 733 (s), 696 (s); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 0.97 (3H, d, *J* 6.8, 3-CH_3), 1.05–1.15 (2H), 1.15–1.45 (45H, m), 1.55–1.65 (3H, m), 1.90–2.10 (2H, m), 3.46 (2H, t, *J* 6.4, OCH_2), 4.50 (2H, s, $C_6H_5CH_2$), 4.88–4.96 (2H, m, CH=C*H*$_2$), 5.64–5.74 (1H, m, C*H*=CH_2), 7.25–7.34 (5H, m, C_6H_5). HRMS calcd for $C_{38}H_{68}O$: 540.5270, found: 540.5264.

4.46. (3S,11S)-3,11-Dimethyl-2-nonacosanone *1*

A suspension of $PdCl_2$ (492 mg, 2.8 mmol) and $Cu(OAc)_2\cdot H_2O$ (1.047 g, 5.2 mmol) in *N*,*N*-dimethylacetamide (DMA, 7 mL) and water (2 mL) was stirred vigorously under O_2 (balloon) for 0.5 h. Then a solution of **37a** (1.01 g, 2.3 mmol) in DMA (5 mL) was added to the mixture. The stirring was continued for 3 days at room temperature under O_2. Subsequently, the mixture was diluted with dil HCl and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue (1.1 g) was chromatographed over SiO_2 (10 g). Elution with hexane gave recovered **37a** (0.4 g, 39.6%). Further elution with hexane/EtOAc=20:1 gave 0.65 g of crude **1**. This was dissolved in EtOAc (20 mL) containing 1 drop of AcOH, and hydrogenated over 10% Pd/C (0.4 g) for 1.5 h under H_2. The catalyst was filtered off through Celite and the filtrate was concentrated in vacuo to give 600 mg (57%) of **1** as a solid. This was recrystallized from 99% EtOH to give 220 mg of **1** as needles, mp 38–40 °C (Ref.7: 44.0–44.5 °C); $[\alpha]_D^{25}$ +4.35 (*c*=1.17, hexane) {Ref.7: $[\alpha]_D^{21}$ +5.98±0.30 (*c* 0.90, hexane)}; ν_{max} (Nujol): 1709 (s, C=O), 1186 (w), 1149 (w), 955 (w), 719 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.05–1.40 (48H, m), 1.58–1.70 (1H, m), 2.13 (3H, s, $COCH_3$), 2.45–2.60 (1H, m, COCH); δ_C ($CDCl_3$): 14.1, 16.2, 19.7, 22.7, 27.02, 27.07, 27.09, 27.2, 27.9, 29.3, 29.48, 29.50, 29.63, 29.67, 29.71, 29.9, 30.0, 31.9, 32.7, 32.9,

37.1, 47.2, 212.8 (C=O). HRMS calcd for $C_{31}H_{62}O$: 450.4801, found: 450.4803.

4.47. (3S,11S)-3,11-Dimethyl-2-heptacosanone *4*

In the same manner as described above for **1**, **37b** (600 mg, 1.5 mmol) was oxidized with O_2, $PdCl_2$ (267 mg, 1.5 mmol) and $Cu(OAc)_2 \cdot H_2O$ (600 mg, 3 mmol) in DMA (7 mL) and water (1 mL) for 2 days at room temperature. The resulting oil (570 mg) was chromatographed over SiO_2 (10 g). Elution with hexane gave recovered **37b** (260 mg, 43%). Further elution with hexane/EtOAc=20:1 gave 320 mg (51%) of **4** as a solid. Recrystallization from 99% EtOH gave needles, mp 37–39 °C (Ref.10: mp 41.0–41.5 °C); $[\alpha]_D^{27}$ +5.44 (*c* 0.268, hexane) {Ref.10: $[\alpha]_D^{22}$ +5.84 (*c* 1.09, hexane)}; ν_{max} (Nujol): 1708 (s, C=O), 1180 (w), 1149 (w), 958 (w), 721 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 0.88 (3H, t, *J* 6.8, CH_2CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.05–1.40 (44H, m), 1.58–1.70 (1H, m), 2.13 (3H, s, $COCH_3$), 2.45–2.55 (1H, m, COCH); δ_C ($CDCl_3$): 14.1, 16.1, 19.7, 22.7, 27.06, 27.2, 27.9, 29.3, 29.46, 29.5, 29.62, 29.67, 29.7, 29.9, 30.0, 31.9, 32.7, 32.9, 37.0, 47.2, 212.8 (C=O). HRMS calcd for $C_{29}H_{58}O$: 422.4488, found: 422.4487.

4.48. (3S,11S)-29-Hydroxy-3,11-dimethyl-2-nonacosanone *2*

A suspension of $PdCl_2$ (302 mg, 1.7 mmol) and $Cu(OAc)_2 \cdot H_2O$ (605 mg, 3.0 mmol) in DMA (7 mL) and water (2 mL) was stirred vigorously under O_2 for 0.5 h. Then a solution of **37c** (990 mg, 1.9 mmol) in DMA (5 mL) was added to the mixture. The stirring was continued for 3 days at room temperature under O_2. Subsequent work-up and chromatography over SiO_2 (20 g) gave 390 mg (39%) of the recovered **37c** and 430 mg (45%) of **38c**. This was dissolved in EtOAc (15 mL) containing 3 drops of AcOH and hydrogenated over 10% Pd/C (0.4 g) for 2.5 h under H_2. The catalyst was filtered off through Celite and the filtrate was concentrated in vacuo to give 400 mg (45%) of **2** as a waxy solid. Recrystallization from pentane gave needle-like waxy solids, mp 38–39 °C (Ref.7: mp 41–42 °C); $[\alpha]_D^{25}$ +3.62 (*c* 1.06, hexane) {Ref.7: $[\alpha]_D^{20}$+6.1±0.7 (*c* 0.65, hexane)}; ν_{max} (Nujol): 3435 (s, OH), 1712 (s, C=O), 1240 (m), 1057 (m), 723 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.15–1.40 (47H, m), 1.52–1.68 (3H, m), 2.13 (3H, s, $COCH_3$), 2.45–2.60 (1H, m, COCH), 3.64 (2H, t, *J* 6.8, CH_2OH); δ_C ($CDCl_3$): 16.2, 19.7, 25.7, 27.02, 27.07, 27.09, 27.93, many signals around 29.2–30.0, 32.7, 32.8, 32.9, 37.03, 37.05, 42.8, 47.2, 63.0, 212.8 (C=O). HRMS calcd for $C_{31}H_{62}O_2$: 466.4750, found: 466.4749.

4.49. (3S,11S)-27-Hydroxy-3,11-dimethyl-2-heptacosanone *5*

In the same manner as described above for **2**, **37d** (900 mg, 1.8 mmol) was oxidized with O_2, $PdCl_2$ (662 mg, 3.7 mmol) and $Cu(OAc)_2 \cdot H_2O$ (1.196 g, 6.0 mmol) in DMA (11 mL) and water (2 mL) for 3 days at room temperature. Subsequent work-up gave 240 mg (27%) of the recovered **37d** and 660 mg (70%) of crude **38d**. This was dissolved in EtOAc (15 mL) containing 3 drops of AcOH and hydrogenated over 10% Pd/C (0.4 g) for 2 days at room temperature to give 500 mg (65%) of **5** as a waxy solid. Recrystallization from pentane gave 380 mg of **5** as waxy needles, mp 30–32 °C, $[\alpha]_D^{23}$ +3.27 (*c* 1.92, hexane); ν_{max} (Nujol): 3437 (s, OH), 1712 (s, C=O), 1059 (m), 723 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.4, 11-CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.15–1.40 (43H, m), 1.50–1.70 (3H, m), 2.13 (3H, s, $COCH_3$), 2.45–2.60 (1H, m, COCH), 3.64 (2H, t, *J* 6.8, CH_2OH); δ_C ($CDCl_3$): 16.2, 19.7, 25.7, 27.01, 27.06, 27.21, 27.93, many signals around 29.2–30.0, 32.7, 32.8, 32.9, 37.03, 37.06, 42.8, 47.2, 63.0, 212.8 (C=O). HRMS calcd for $C_{29}H_{58}O_2$: 438.4437, found: 438.4433.

4.50. (3S,11S)-3,11-Dimethyl-29-oxo-2-nonacosanone *3*

Dess–Martin periodinane (600 mg, 1.4 mmol) was added to a stirred and ice-cooled solution of **2** (160 mg, 0.4 mmol) in dry CH_2Cl_2 (10 mL). After the addition, the mixture was stirred for 45 min at room temperature. Then hexane (10 mL) and ca. 10 mL of dil $NaHCO_3$ and $Na_2S_2O_3$ solution were added to the mixture. After having stirred for 5 min, the mixture was extracted with hexane. The extract was washed with $NaHCO_3$ solution and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was chromatographed over SiO_2 (5 g). Elution with hexane/EtOAc (20:1) gave 110 mg (69%) of **3** as a waxy solid, mp 27–29 °C, $[\alpha]_D^{23}$ +3.47 (*c* 0.70, hexane); ν_{max} (Nujol): 2713 (w, O=C–H), 1718 (s, C=O), 1169 (w), 721 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.8, 11-CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.15–1.40 (45H, m), 1.50–1.70 (2H, m), 2.13 (3H, s, $COCH_3$), 2.32–2.43 (2H, m), 2.44–2.52 (1H, m, COCH), 9.76 (1H, CHO); δ_C ($CDCl_3$): 11.4, 14.1, 16.1, 19.2, 19.7, 22.1, 27.1, 27.2, 27.9, many signals around 29.1–30.0, 32.7, 32.9, 34.4, 36.6, 37.1, 42.8, 43.9, 47.2, 202.7 (C=O), 212.8 (C=O). HRMS calcd for $C_{31}H_{60}O_2$: 464.4593, found: 464.4589.

4.51. (3S,11S)-3,11-Dimethyl-27-oxo-2-heptacosanone *6*

In the same manner as described above for **3**, oxidation of **5** (214 mg, 0.49 mmol) with Dess–Martin perodinane (750 mg, 1.8 mmol) in CH_2Cl_2 (12 mL) gave 120.1 mg (56%) of **6** as a waxy solid melting around 25 °C, $[\alpha]_D^{22}$ +3.70 (*c* 0.49, hexane); ν_{max} (film): 2713 (w, O=C–H), 1722 (s, C=O), 1167 (m), 721 (m); δ_H ($CDCl_3$): 0.83 (3H, d, *J* 6.8, 11-CH_3), 1.07 (3H, d, *J* 6.8, 3-CH_3), 1.15–1.40 (41H, m), 1.50–1.70 (2H, m), 2.13 (3H, s, $COCH_3$), 2.32–2.43 (2H, m), 2.44–2.52 (1H, m, COCH), 9.76 (1H, CHO); δ_C ($CDCl_3$): 11.4, 16.2, 19.2, 19.7, 22.1, 27.1, 27.2, 27.9, many signals around 29.1–30.0, 32.6, 32.7, 34.4, 36.6, 37.1, 42.8, 43.9, 47.2, 202.7 (C=O), 212.8 (C=O). HRMS calcd for $C_{29}H_{56}O_2$: 436.4280, found: 436.4279.

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