Pheromone Synthesis, CCIV[‡]

Synthesis of the Enantiomers of *anti*-2,6-Dimethylheptane-1,7-diol Monotetrahydropyranyl Ether and Their Conversion into the Enantiomers of the Sex Pheromone Components of the Apple Leafminer, *Lyonetia prunifoliella*

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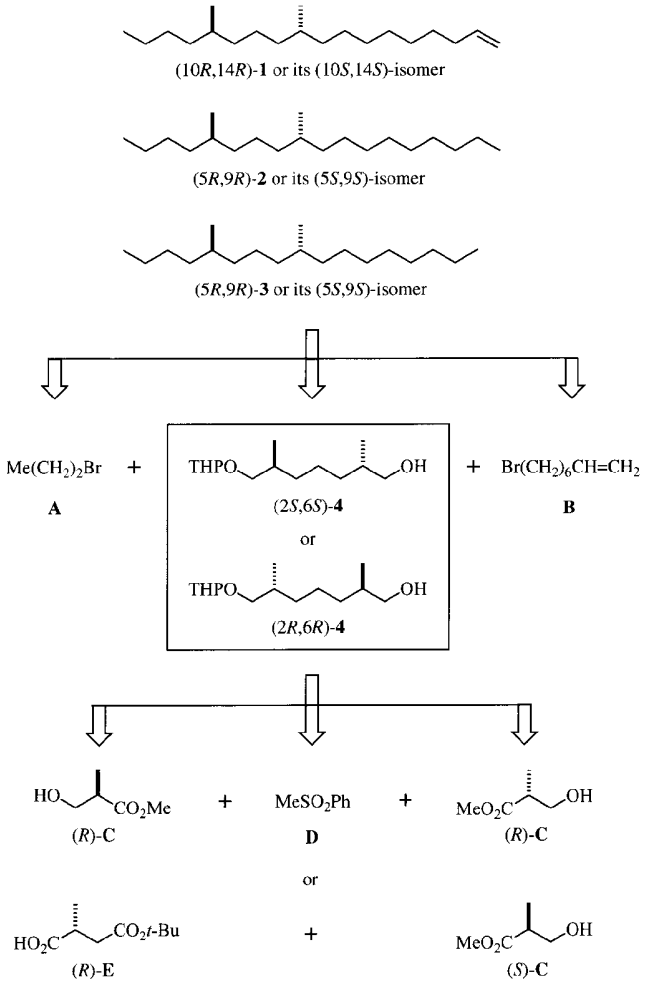
Both (2*R*,6*R*)- and (2*S*,6*S*)-isomers of 2,6-dimethylheptane-1,7-diol monotetrahydropyranyl ether (**4**) were synthesized, and converted into the enantiomers of *anti*-10,14-dimethyl-1-octadecene (**1**), *anti*-5,9-dimethyloctadecane (**2**) and *anti*-5,9-dimethylheptadecane (**3**), the sex pheromone components of the apple leafminer (*Lyonetia prunifoliella*).

Introduction

In 1997 Gries et al. identified three methyl-branched hydrocarbons, 10,14-dimethyl-1-octadecene (**1**, Scheme 1), 5,9-dimethyloctadecane (**2**) and 5,9-dimethylheptadecane (**3**), as the synergistic female-produced pheromone components of the apple leafminer (*Lyonetia prunifoliella*), which is a pest in apple orchards in eastern North America.[1] In field trapping experiments, **1**, **2** and **3** (each as a stereoisomeric mixture) singly were unattractive to males, but as a ternary mixture attracted numerous males. No attraction of males to the pheromone lure was observed without **1**, indicating the importance of **1** in the pheromone communication.[1]

In 1999 Mori and co-workers synthesized all of the possible stereoisomers of **1**, **2** and **3** by starting from the enantiomers of citronellol and methyl 3-hydroxy-2-methylpropanoate.[2] The synthetic samples were first bioassayed in Canada, and (10*R*,14*R*)-**1** elicited strong responses from male *L. prunifoliella* antennae in electrophysiological recordings.[3] Subsequent field trapping trials against *L. prunifoliella* in Korea, however, revealed (10*S*,14*S*)-**1** to be far more attractive than its stereoisomers.[4] These two contradictory results forced us to attempt a new synthesis of each enantiomer of *anti*-configured 1,5-dimethylated hydrocarbons **1**, **2** and **3** for further testing.

In our 1999 synthesis, the stereoisomers of **1** were prepared in a stepwise manner from two commercially available chiral building blocks (vide supra), and the synthesis was lengthy and cumbersome. It occurred to us that a chiral and nonracemic building block such as (2*R*,6*R*)- or (2*S*,6*S*)-**4** could also serve as the central part of the *anti*-1,5-dimethylated hydrocarbons **1**, **2** and **3**. Indeed, a similar building block with 1,5-*syn*-dimethyl groups was recently



Scheme 1. Sex pheromone components of *Lyonetia prunifoliella* and their retrosynthetic analysis

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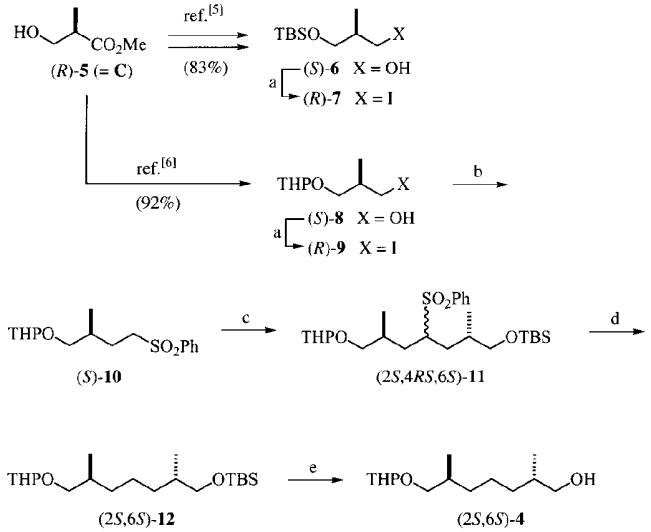
used by us successfully in our synthetic work on pine sawfly pheromones,[5] locust secretions[6] and others.[7] For the synthesis of **1**, the three building blocks **4**, **A** and **B** should be connected. Accordingly, the pheromone components **1**, **2** and **3** and, indeed, any compound with *anti*-1,5-dimethylated carbon skeleton can be prepared from **4**. The building block **4** will therefore serve as a widely useful building block in organic synthesis. The building block (2*S*,6*S*)-**4** would be prepared from (*R*)-**C** and **D**, while (2*R*,6*R*)-**4** would be obtainable from (*S*)-**C** and (*R*)-**E**. The enantiomers of methyl 3-hydroxy-2-methylpropanoate (**C**) and (*R*)-3-*tert*-butoxycarbonyl-2-methylpropanoic acid (**E**) are commercially available.

Results and Discussion

Synthesis of the Enantiomers of the Building Block 4

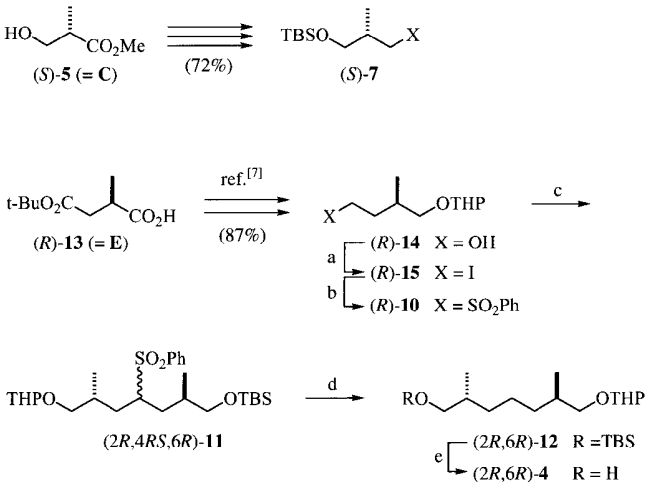
Scheme 2 summarizes the synthesis of the building block (2*S*,6*S*)-**4**. The strategy was to connect (*R*)-**7** with (*R*)-**9** by employing methyl phenyl sulfone (=**D**) as the linchpin. The iodide (*R*)-**7** was prepared from methyl (*R*)-3-hydroxy-2-methylpropanoate (**5**, ≈100% *ee*) via (*S*)-**6** according to Thomas and Whitehead,[8] while another iodide (*R*)-**9** was prepared from (*R*)-**5** via (*S*)-**8** according to Mori.[9]



Scheme 2. Synthesis of the building block (2*S*,6*S*)-**4**; reagents: (a) i) *p*-TsCl, C_5H_5N; ii) NaI, $NaHCO_3$, Me_2CO (94% for **7**; 93% for **9**); (b) $MeSO_2Ph$ (= **D**), *n*BuLi, THF/HMPA (74%); (c) *n*BuLi, (*R*)-**7**, THF/HMPA (88%); (d) Na-Hg, EtOH (87%); (e) $(n\text{Bu})_4\text{NF}$, THF (99%)

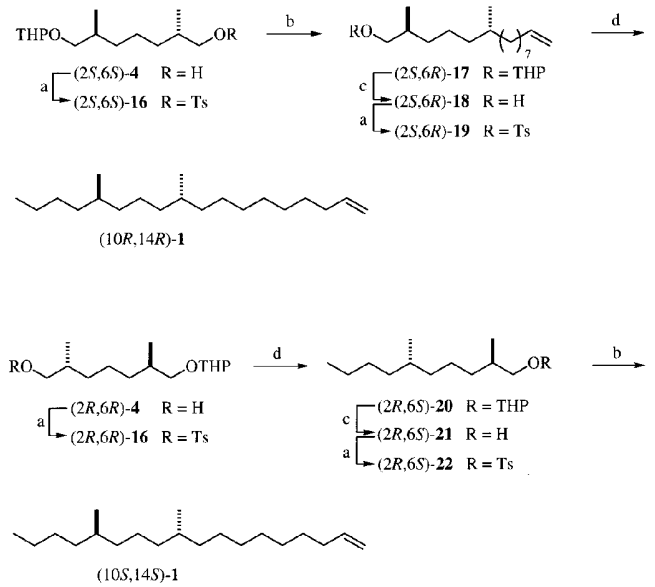
Alkylation of the anion derived from methyl phenyl sulfone with (*R*)-**9** gave (*S*)-**10**, which was further alkylated with (*R*)-**7** to furnish (2*S*,4*RS*,6*S*)-**11**. Removal of the phenylsulfonyl group of **11** with sodium-amalgam yielded (2*S*,6*S*)-**12**, whose *tert*-butyldimethylsilyl (TBS) group was removed by treatment with tetra(*n*-butyl)ammonium fluoride to afford (2*S*,6*S*)-**4** in 48% overall yield based on (*R*)-**5** (8 steps).

The synthesis of (2*R*,6*R*)-**4** is outlined in Scheme 3. The starting material (*S*)-**5** (99.8% *ee*) was converted into the iodide (*S*)-**7** in the conventional manner. The phenylsulfone (*R*)-**10**, another key intermediate, was prepared from the half ester (*R*)-**13** (>99.6% *ee*).[10]



Scheme 3. Synthesis of the building block (2*R*,6*R*)-**4**; reagents: (a) i) *p*-TsCl, C_5H_5N; ii) NaI, $NaHCO_3$, Me_2CO (93%); (b) $PhSO_2Na$, DMF (85%); (c) *n*BuLi, (*S*)-**7**, THF/HMPA (91%); (d) Na-Hg, EtOH (82%) or Mg, MeOH (69%); (e) $(n\text{Bu})_4\text{NF}$, THF (99%)

Conversion of (*R*)-**13** to (*R*)-**10** was executed via the known alcohol (*R*)-**14**[11] and the iodide (*R*)-**15**. Further steps from (*R*)-**10** to the building block (2*R*,6*R*)-**4** followed those employed for the preparation of (2*S*,6*S*)-**4**. Accordingly, (*R*)-**10** was alkylated with (*S*)-**7** to give (2*R*,4*RS*,6*R*)-**11**, which was reduced with sodium-amalgam or dissolving magnesium in methanol[12] to furnish (2*R*,6*R*)-**12**. Finally, removal of the TBS protective group of (2*R*,6*R*)-**12** afforded (2*R*,6*R*)-**4** in 51% overall yield based on (*R*)-**13** (9 steps).



Scheme 4. Synthesis of (10*R*,14*R*)- and (10*S*,14*S*)-**1**; reagents: (a) *p*-TsCl, C_5H_5N (quant.); (b) $CH_2{=}CH(CH_2)_6MgBr$, Li_2CuCl_4, THF (88% for **17**; 87% for **1**); (c) *p*-TsOH, EtOH (96% for **18**; 89% for **22**); (d) $Me(CH_2)_2MgBr$, Li_2CuCl_4, THF (94% for **1**; 92% for **20**)

Synthesis of the Sex Pheromone Components 1, 2 and 3 of the Apple Leafminer

Scheme 4 summarizes the synthesis of (10*R*,14*R*)- and (10*S*,14*S*)-10,14-dimethyl-1-octadecene (**1**), the most important component of the sex pheromone of the apple leafminer. Tosylation of the building block (2*S*,6*S*)-**4** gave the corresponding tosylate (2*S*,6*S*)-**16**, whose chain-elongation with 7-octenylmagnesium bromide under Schlosser conditions[13] furnished (2*S*,6*R*)-**17**.

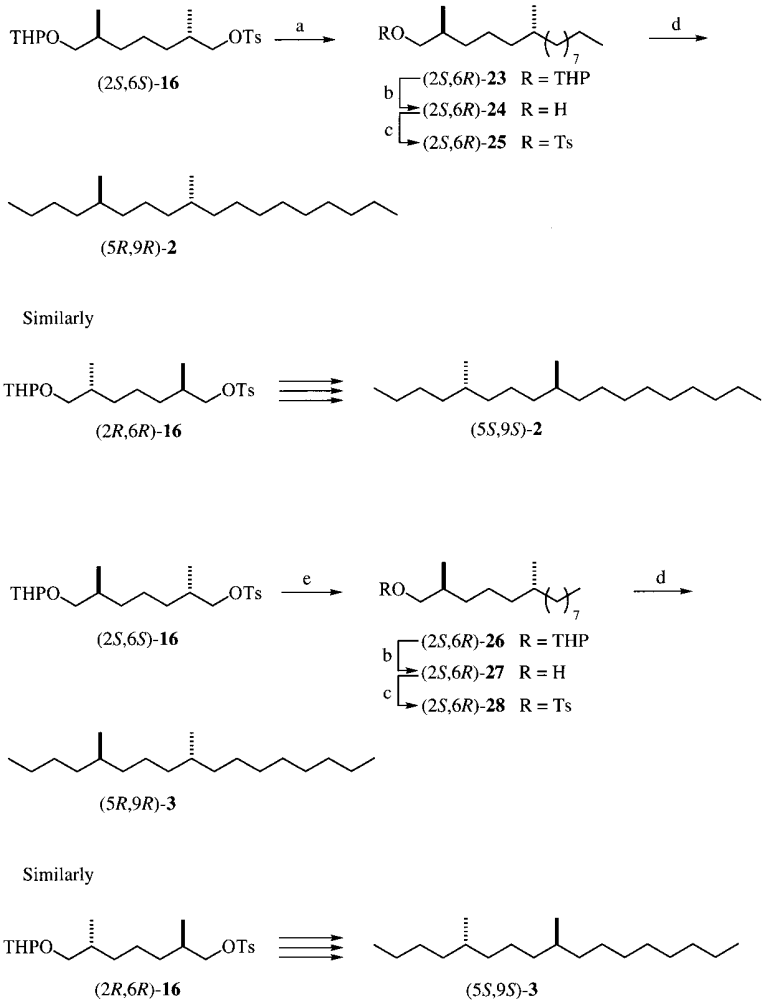
Removal of the tetrahydropyranyl (THP) protective group of **17** was followed by tosylation of the resulting alcohol (2*S*,6*R*)-**18** to give the tosylate (2*S*,6*R*)-**19**. A second chain-elongation under Schlosser conditions[13] converted (2*S*,6*R*)-**19** to the pheromone component (10*R*,14*R*)-**1**. The overall yield of (10*R*,14*R*)-**1** was 79% based on (2*S*,6*S*)-**4** (5 steps) or 38% based on (*R*)-**5** (13 steps).

A different route was employed for the synthesis of (10*S*,14*S*)-**1**. The tosylate (2*R*,6*R*)-**16** derived from (2*R*,6*R*)-**4** was treated with propylmagnesium bromide under Schlosser conditions[13] to give (2*R*,6*S*)-**20**. After the removal of the THP protective group of (2*R*,6*S*)-**20**, the resulting alcohol (2*R*,6*S*)-**21** was tosylated to furnish (2*R*,6*S*)-**22**. Its chain-elongation with 7-octenylmagnesium bromide in the presence of dilithium tetrachlorocuprate[13] gave (10*S*,14*S*)-**1** in 71% overall yield based on (2*R*,6*R*)-**4** (5 steps) or 36% based on (*R*)-**13** (14 steps).

Synthesis of other two pheromone components **2** and **3** is summarized in Scheme 5. Chain-elongation of the tosylate (2*S*,6*S*)-**16** with octylmagnesium bromide gave (2*S*,6*R*)-**23**, which was converted into the tosylate (2*S*,6*R*)-**25** via the alcohol (2*S*,6*R*)-**24**. Further chain-elongation of (2*S*,6*R*)-**25** with propylmagnesium bromide afforded (5*R*,9*R*)-5,9-dimethyloctadecane (**2**).

The overall yield of (5*R*,9*R*)-**2** was 68% based on (2*S*,6*S*)-**4** (5 steps) or 33% based on (*R*)-**5** (13 steps). Similarly, (5*S*,9*S*)-**2** was synthesized from (2*R*,6*R*)-**4**.

The third pheromone component (5*R*,9*R*)-5,9-dimethylheptadecane (**3**) was prepared from (2*S*,6*S*)-**16** in a similar manner via (2*S*,6*R*)-**26**, (2*S*,6*R*)-**27** and (2*S*,6*R*)-**28**. The overall yield of (5*R*,9*R*)-**3** was 81% based on (2*S*,6*S*)-**4** (5 steps) or 39% based on (*R*)-**5** (13 steps). The opposite enantiomer (5*S*,9*S*)-**3** was synthesized from (2*R*,6*R*)-**16** in the same manner.



Scheme 5. Synthesis of (5*R*,9*R*)-**2** and (5*R*,9*R*)-**3** and their enantiomers; reagents: (a) $Me(CH_2)_7MgBr$, Li_2CuCl_4, THF (82% for **23**); (b) *p*-TsOH, EtOH (95% for **24**; 96% for **27**); (c) *p*-TsCl, C_5H_5N (quant.); (d) $Me(CH_2)_2MgBr$, Li_2CuCl_4, THF (86% for **2**; 92% for **3**); (e) $Me(CH_2)_6MgBr$, Li_2CuCl_4, THF (87% for **26**)

Conclusion

The usefulness of (2*R*,6*R*)- or (2*S*,6*S*)-2,6-dimethylheptane-1,7-diol mono THP ether (**4**) as a building block for the synthesis of enantiopure *anti*-1,5-dimethylated aliphatic compounds was successfully illustrated by the present work on the synthesis of **1**, **2** and **3**, the pheromone components of *Lyonetia prunifoliella*. Because sufficient amounts of pheromone samples have been secured, the future biological works will hopefully clarify the chirality problem in the chemical communication system of *L. prunifoliella*.

Experimental Section

General: IR: Jasco A-102. − ^{1}H NMR: Jeol JNM-EX 90A (90 MHz), Jeol JNM-LA400 (400 MHz) and Jeol JNM-LA500 (500 MHz) (TMS at δ = 0.00 or $CHCl_3$ at δ = 7.26 as an internal standard). − ^{13}C NMR: Jeol JNM-LA500 (125 MHz) ($CDCl_3$ at δ = 77.0 as an internal standard). − Optical rotation: Jasco DIP-1000. − Column chromatography: Merck Kieselgel 60 Art 1.07734. − TLC: 0.25 mm Merck silica gel plates (60F-254).

(*R*)-3-*tert*-Butyldimethylsilyloxy-2-methylpropyl Iodide [(*R*)-7]: i) To a solution of (*S*)-**6**[5] (5.91 g, 28.9 mmol) in dry pyridine (30 mL) was added *p*-toluenesulfonyl chloride (8.26 g, 43.4 mmol) at 0 °C. After stirring at 0 °C for 12 h, the mixture was poured into ice and 1 M hydrochloric acid and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 10.8 g (quant.) of crude tosylate of (*S*)-**6**. This was employed in the next step without further purification.
ii) To a solution of the tosylate (10.8 g) in dry acetone (115 mL) was added sodium iodide (6.51 g, 43.4 mmol) and $NaHCO_3$ (12.1 g, 144 mmol) at room temperature. After stirring for 4 h under reflux, the mixture was concentrated in vacuo. The residue was diluted with water and extracted with diethyl ether. The organic phase was washed with 10% aqueous sodium thiosulfate, water, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (100 g, hexane/ethyl acetate, 100:1) to give 8.55 g (94%) of (*R*)-**7** as a colorless oil; n_D^{26} = 1.4741. − $[\alpha]_D^{21}$ = −10.0 (*c* = 1.03, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1260 cm^{-1} (s, Si−CH_3), 1200 (m, CH_2I), 1105 (s, Si−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.06 (s, 6 H, Si−CH_3), 0.90, (s, 9 H, *t*Bu), 0.94 (d, *J*= 8.0 Hz, 3 H, 2-CH_3), 1.40−1.80 (m, 1 H, 2-H), 3.27 (d, *J* = 5.5 Hz, 1 H, 1-H_a), 3.28 (d, *J* = 5.2 Hz, 1 H, 1-H_b), 3.38 (dd, *J* = 6.4, 10.0 Hz, 1 H, 3-H_a), 3.54 (dd, *J* = 5.2, 10.0 Hz, 1 H, 3-H_b). − $C_{10}H_{23}IOSi$ (314.3): calcd. C 38.22, H 7.38; found C 37.72, H 7.07.

(*S*)-3-*tert*-Butyldimethylsilyloxy-2-methylpropyl Iodide [(*S*)-7]: In the same manner as described above, (*R*)-**6**[5] (7.47 g, 36.6 mmol) was converted into 10.5 g (92%) of (*S*)-**7** (as a colorless oil); n_D^{22} = 1.4733. − $[\alpha]_D^{21}$ = +10.1 (*c* = 1.10, $CHCl_3$) {ref.[14] $[\alpha]_D^{23}$ = +10.4 ($CHCl_3$)}. Its IR and NMR spectra were identical with those of (*R*)-**7**. − $C_{10}H_{23}IOSi$ (314.3): calcd. C 38.22, H 7.38; found C 38.27, H 6.98.

(*R*)-2-Methyl-3-tetrahydropyranyloxypropyl Iodide [(*R*)-9]: i) To a solution of (*S*)-**8**[6] (6.97 g, 40.0 mmol) in dry pyridine (40 mL) was added *p*-toluenesulfonyl chloride (9.53 g, 50.0 mmol) at 0 °C. After stirring at 0 °C for 14 h, the mixture was poured into ice and 1 M hydrochloric acid and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 13.5 g (quant.) of crude tosylate of (*S*)-**8**. This was employed in the next step without further purification.
ii) To a solution of the tosylate (13.5 g) in dry acetone (160 mL) was added sodium iodide (9.0 g, 60.0 mmol) and $NaHCO_3$ (16.8 g, 0.20 mol) at room temperature. After stirring for 4 h under reflux, the mixture was concentrated in vacuo. The residue was diluted with water and extracted with diethyl ether. The organic phase was washed with 10% aqueous sodium thiosulfate, water, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (150 g, hexane/ethyl acetate, 100:1) to give 10.6 g (93%) of (*R*)-**9** as a colorless oil; n_D^{25} = 1.5069. − $[\alpha]_D^{22}$ = −11.0 (*c* = 1.16, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1205 cm^{-1} (m, CH_2I), 1120 (s, C−O), 1030 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.99, 1.01 (each d, *J* = 6.7 Hz, total 3 H, 2-CH_3), 1.20−2.00 (m, 7 H, 2-H, 3′−5′-H_2), 3.09−4.00 (m, 6 H, 1-, 3-, 6′-H_2), 4.60 (br, 1 H, 2′-H). − $C_9H_{17}IO_2$ (284.0): calcd. C 38.04, H 6.04; found C 37.85, H 6.21.

(*R*)-3-Methyl-4-tetrahydropyranyloxybutyl Iodide [(*R*)-15]: i) To a solution of (*R*)-**14**[7] (7.50 g, 39.8 mmol) in dry pyridine (40 mL) was added *p*-toluenesulfonyl chloride (11.4 g, 60.0 mmol) at 0 °C. After stirring at 0 °C for 12 h, the mixture was poured into ice and 1 M hydrochloric acid and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 13.9 g (quant.) of crude tosylate of (*R*)-**14**. This was employed in the next step without further purification.
ii) To a solution of the tosylate (13.9 g) in dry acetone (160 mL) was added sodium iodide (9.0 g, 60.0 mmol) and $NaHCO_3$ (16.8 g, 0.20 mol) at room temperature. After stirring for 4 h under reflux, the mixture was concentrated in vacuo. The residue was diluted with water and extracted with diethyl ether. The organic phase was washed with 10% aqueous sodium thiosulfate, water, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (150 g, hexane/ethyl acetate, 100:1) to give 11.1 g (93%) of (*R*)-**15** as a colorless oil; n_D^{25} = 1.5073. − $[\alpha]_D^{22}$ = +10.1 (*c* = 1.17, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1200 cm^{-1} (s, CH_2I), 1120 (s, C−O), 1040 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.93, (d, *J* = 5.7 Hz, 3 H, 3-CH_3), 1.20−2.18 (m, 9 H, 3-H, 2-, 3′−5′-H_2), 3.11−3.96 (m, 6 H, 1-, 4-, 6′-H_2), 4.54 (br, 1 H, 2′-H). − $C_{10}H_{19}IO_2$ (298.2): calcd. C 40.28, H 6.42; found C 40.24, H 6.45.

(*S*)-2-Methyl-4-phenylsulfonyl-1-tetrahydropyranyloxybutane [(*S*)-10]: Under argon atmosphere, to a stirred and cooled solution of methyl phenyl sulfone (2.06 g, 13.2 mmol) in dry THF (36 mL) and dry hexamethylphosphoric triamide (12 mL) was added dropwise a solution of *n*-butyllithium in hexane (1.50 M, 10.6 mL, 15.9 mmol) at −78 °C. After the addition, the mixture was kept at −30 °C for 0.5 h and again cooled to −78 °C. Then a solution of (*R*)-**9** (4.49 g, 15.8 mmol) in dry THF (10 mL) was added dropwise to the mixture at −78 °C with stirring. The mixture was stirred at ambient temperature for 9 h, then poured into ice and saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (50 g, hexane/ethyl acetate, 10:1) to give 3.06 g (74%) of (*S*)-**10** as a colorless oil; n_D^{26} = 1.5179. − $[\alpha]_D^{22}$ = −7.80 (*c* = 1.16, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1590 cm^{-1} (w, aromatic), 1310 (s, SO_2), 1150 (s, SO_2), 1030 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.90, (d, *J* = 6.4 Hz, 3 H, 2-CH_3), 1.05−2.00 (m, 9 H, 2-H, 3-, 3′−5′-H_2), 2.95−3.95 (m, 6 H, 1-, 4-, 6′-H_2), 4.50 (br, 1 H, 2′-H), 7.54−7.63 (m, 3 H, Ar-H), 7.87−7.97 (m, 2 H, Ar-H). − $C_{16}H_{24}O_4S$ (312.4): calcd. C 61.51, H 7.74; found C 61.28, H 7.67.

(*R*)-2-Methyl-4-phenylsulfonyl-1-tetrahydropyranyloxybutane [(*R*)-10]: To a stirred solution of (*R*)-**15** (5.07 g, 17.0 mmol) in dry DMF (50 mL) was added sodium benzenesulfinate dihydrate (5.10 g, 25.5 mmol). After stirring for 12 h at room temperature, the mixture was diluted with water and extracted with diethyl ether. The organic phase was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (100 g, hexane/ethyl acetate, 10:1) to give 4.51 g (85%) of (*R*)-**10** as a colorless oil; $n_D^{26} = 1.5180$. − $[\alpha]_D^{23} = +7.1$ ($c = 0.98$, $CHCl_3$). Its IR and NMR spectra were identical with those of (*S*)-**10**. − $C_{16}H_{24}IO_4S$ (312.4): calcd. C 61.51, H 7.74; found C 61.28, H 7.89.

(2*S*,4*RS*,6*S*)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyl-4-phenylsulfonyl-7-tetrahydropyranyloxyheptane [(2*S*,4*RS*,6*S*)-11]: Under argon atmosphere, to a stirred and cooled solution of (*S*)-**10** (2.65 g, 8.48 mmol) in dry THF (50 mL) and dry hexamethylphosphoric triamide (17 mL) was added dropwise a solution of *n*-butyllithium in hexane (1.50 M, 6.9 mL, 10.4 mmol) at −78 °C. After the addition, the mixture was kept at −30 °C for 1 h and again cooled to −78 °C. Then a solution of (*R*)-**7** (3.27 g, 10.4 mmol) in dry THF (12 mL) was added dropwise to the mixture at −78 °C with stirring. The mixture was stirred at ambient temperature for 10 h, then poured into ice and saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (70 g, hexane/ethyl acetate, 15:1) to give 3.73 g (88%) of (2*S*,4*RS*,6*S*)-**11** as a colorless oil; $n_D^{22} = 1.4980$. − IR (film): $\tilde{\nu}_{max} = 1590\ cm^{-1}$ (w, aromatic), 1310 (s, SO_2), 1250 (s, SO_2), 1090 (s, Si−O), 1035 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.00, 0.01 (each s, total 6 H, Si−CH_3), 0.84, 0.87 (each s, total 9 H, *t*Bu), 0.65−1.06 (m, 6 H, 2-, 6-CH_3), 1.07−2.20 (m, 12 H, 2-, 6-H, 3-, 5-, 3′−5′-H_2), 2.95−3.95 (m, 7 H, 4-H, 1-, 7-, 6′-H_2), 4.50 (br, 1 H, 2′-H), 7.52−7.60 (m, 3 H, Ar-H), 7.84−7.93 (m, 2 H, Ar-H). This was employed in the next step without further purification.

(2*R*,4*RS*,6*R*)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyl-4-phenylsulfonyl-7-tetrahydropyranyloxyheptane [(2*R*,4*RS*,6*R*)-11]: In the same manner as described above, (*R*)-**10** (1.95 g, 6.24 mmol) was converted into 2.84 g (91%) of (2*R*,4*RS*,6*R*)-**11** (as a colorless oil); $n_D^{26} = 1.4971$. Its IR and NMR spectra were identical with those of (2*S*,4*RS*,6*S*)-**11**. This was employed in the next step without further purification.

(2*S*,6*S*)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyl-7-tetrahydropyranyloxyheptane [(2*S*,6*S*)-12]: Under an argon atmosphere, a solution of (2*S*,4*RS*,6*S*)-**11** (909 mg, 1.82 mmol) in dry ethanol (50 mL) was added dropwise to 5% sodium amalgam (23.3 g, sodium 1.17 g, 50.6 mmol) at 0 °C. The mixture was stirred vigorously at room temperature for 26 h. It was then filtered thought Celite, and the filter cake was washed several times with diethyl ether. The combined filtrate and washings were concentrated in vacuo to give crude (2*S*,6*S*)-**12**. This crude material contained a few percent of olefinic compounds formed by elimination of the phenylsulfonyl group from (2*S*,4*RS*,6*S*)-**11**. The crude (2*S*,6*S*)-**12** was dissolved in hexane (50 mL), and *m*-CPBA (70%, 0.15 g, 0.61 mmol) was added at 0 °C. The mixture was stirred at room temperature for 4 h, then a saturated aqueous sodium thiosulfate and saturated aqueous $NaHCO_3$ were added, and extracted with hexane. The organic phase was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel to remove the contaminating epoxide (15 g, hexane/ethyl acetate, 150:1) to give 568 mg (87%) of (2*S*,6*S*)-**12** as a colorless oil; $n_D^{22} = 1.4484$. − $[\alpha]_D^{22} = -2.98$ ($c = 1.20$, hexane). − IR (film): $\tilde{\nu}_{max} = 1255\ cm^{-1}$ (s, Si−CH_3), 1110 (s, Si−O), 1030 (s, C−O). − ^1H NMR (400 MHz, $CDCl_3$): δ = 0.03 (s, 6 H, Si−CH_3), 0.86 (d, $J = 6.4$ Hz, 3 H, 2-CH_3), 0.89 (s, 9 H, *t*Bu), 0.91, 0.93 (each d, $J = 7.1$ Hz, total 3 H, 6-CH_3), 1.02−1.87 (m, 14 H, 2-, 6-H, 3−5-, 3′−5′-H_2), 3.14, 3.23 (each dd, $J = 6.8$, 9.3 Hz and $J = 5.9$, 9.8 Hz, total 1 H, 7-H_a), 3.35 (dd, $J = 6.8$, 9.8 Hz, 1 H, 1-H_a), 3.43 (dd, $J = 5.9$, 9.8 Hz, 1 H, 1-H_b), 3.47−3.52 (m, 1 H, 6′-H_a), 3.50, 3.60 (each dd, $J = 7.3$, 9.3 Hz and $J = 6.3$, 9.8 Hz, total 1 H, 7-H_b), 3.83−3.88 (m, 1 H, 6′-H_b), 4.55−4.58 (m, 1 H, 2′-H). − $C_{20}H_{42}O_3Si$ (358.6): calcd. C 66.98, H 11.80; found C 66.93, H 11.41.

(2*R*,6*R*)-1-*tert*-Butyldimethylsilyloxy-2,6-dimethyl-7-tetrahydropyranyloxyheptane [(2*R*,6*R*)-12]: a) Reduction with sodium amalgam; In the same manner as described above, (2*R*,4*RS*,6*R*)-**11** (680 mg, 1.36 mmol) was converted into 401 mg (82%) of (2*R*,6*R*)-**12** (as a colorless oil); $n_D^{26} = 1.4498$. − $[\alpha]_D^{24} = +2.68$ ($c = 1.08$, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*S*)-**12**. − $C_{20}H_{42}O_3Si$ (358.6): calcd. C 66.98, H 11.80; found C 67.29, H 11.88.

b) Reduction with dissolving magnesium in methanol; Under an argon atmosphere, a solution of (2*R*,4*RS*,6*R*)-**11** (500 mg 1.00 mmol) in dry methanol (10 mL) was added dropwise to magnesium (243 mg, 10.0 mmol) at room temperature. After stirring at room temperature for 4 h, the mixture was diluted with diethyl ether and quenched by adding 3 M hydrochloric acid. The resulting mixture was stirred for 10 min, and extracted with diethyl ether. The organic phase was washed with water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give crude (2*R*,6*R*)-**12**. In the same manner as described above for the purification of crude (2*S*,6*S*)-**12**, crude (2*R*,6*R*)-**12** furnished 248 mg (69%) of (2*R*,6*R*)-**12**.

(2*S*,6*S*)-2,6-Dimethyl-7-tetrahydropyranyloxy-1-heptanol [(2*S*,6*S*)-4]: To a solution of (2*S*,6*S*)-**12** (510 mg, 1.42 mmol) in dry THF (15 mL) was added $(n\text{Bu})_4NF$ (1.0 M solution in dry THF, 1.85 mL, 1.85 mmol) at room temperature. After stirring at room temperature for 4 h, the mixture was poured into water and extracted with diethyl ether. The organic phase was washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (12 g, hexane/ethyl acetate, 15:1) to give 343 mg (99%) of (2*S*,6*S*)-**4**; $n_D^{26} = 1.4591$. − $[\alpha]_D^{24} = -3.27$ ($c = 1.17$, hexane). − IR (film): $\tilde{\nu}_{max} = 3420\ cm^{-1}$ (s, O−H), 1120 (s, C−O), 1030 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.91, 0.93 (each d, $J = 6.4$ Hz, total 6 H, 2-, 6-CH_3), 1.06−1.86 (m, 15 H, 2-, 6-H, 3−5-, 3′−5′-H_2, OH), 3.14, 3.23 (each dd, $J = 6.6$, 9.3 Hz and $J = 5.9$, 9.3 Hz, 1 H, 7-H_a), 3.42 (dd, $J = 6.5$, 10.4 Hz, 1 H, 1-H_a), 3.50 (dd, $J = 5.6$, 10.4 Hz, 1 H, 1-H_b), 3.47−3.61 (m, 2 H, 7-H_b, 6′-H_a), 3.83−3.88 (m, 1 H, 6′-H_b), 4.55−4.57 (m, 1 H, 2′-H). − $C_{14}H_{28}O_3$ (244.4): calcd. C 68.81, H 11.55; found C 68.96, H 11.81.

(2*R*,6*R*)-2,6-Dimethyl-7-tetrahydropyranyloxy-1-heptanol [(2*R*,6*R*)-4]: In the same manner as described above, (2*R*,6*R*)-**12** (722 mg, 2.01 mmol) was converted into 489 mg (99%) of (2*R*,6*R*)-**4** (as a colorless oil); $n_D^{26} = 1.4589$. − $[\alpha]_D^{24} = +3.13$ ($c = 1.26$, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*S*)-**4**. − $C_{14}H_{28}O_3$ (244.4): calcd. C 68.81, H 11.55; found C 68.56, H 11.53.

(2*S*,6*S*)-2,6-Dimethyl-7-tetrahydropyranyloxyheptyl Tosylate [(2*S*,6*S*)-16]: To a solution of (2*S*,6*S*)-**4** (225 mg, 0.92 mmol) in dry pyridine (3 mL) was added *p*-toluenesulfonyl chloride (262 mg, 1.37 mmol) at 0 °C. After stirring at 0 °C for 12 h, the mixture was poured into ice and water and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water,

saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 372 mg (quant.) of crude (2*S*,6*S*)-**16**. This was employed in the next step without further purification; IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1360 (s, SO_2), 1190 (s, SO_2), 1180 (s, SO_2), 1030 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.6 Hz, 6 H, 2-, 6-CH_3), 1.00−2.00 (m, 14 H, 2-, 6-H, 3−5-, 3′−5′-H_2), 2.45 (s, 3 H, Ar−CH_3), 3.03−3.98 (m, 6 H, 1-, 7-, 6′-H_a), 4.54 (br, 1 H, 2′-H), 7.34 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.79 (d, *J* = 8.2 Hz, 2 H, Ar-H).

(2*R*,6*R*)-2,6-Dimethyl-7-tetrahydropyranyloxyheptyl Tosylate [(2*R*,6*R*)-16]: In the same manner as described above, (2*R*,6*R*)-**16** (250 mg, 1.02 mmol) was converted into 415 mg (quant.) of (2*R*,6*R*)-**16**. This was employed in the next step without further purification. Its IR and NMR spectra were identical with those of (2*S*,6*S*)-**16**.

(2*S*,6*R*)-2,6-Dimethyl-1-tetrahydropyranyloxy-14-pentadecene [(2*S*,6*R*)-17]: Magnesium (167 mg, 6.87 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of 7-octenyl bromide (875 mg, 4.58 mmol) in dry THF (8 mL), and the mixture was stirred at 45 °C for 1 h. The resulting solution was used immediately. Under argon atmosphere, to a solution of (2*S*,6*S*)-**16** (372 mg, ca. 0.92 mmol) in dry THF (5 mL) were added the above Grignard reagent and a solution (0.32 M, 0.1 mL, 0.032 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 2 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 15 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (10 g, hexane/ethyl acetate = 500:1) to give 274 mg (88%) of (2*S*,6*R*)-**17** as a colorless oil; n_D^{26} = 1.4599. − $[\alpha]_D^{24}$ = −1.89 (*c* = 1.03, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3100 cm^{-1} (w, C=C−H), 1650 (w, C=C), 1130 (m, C−O), 1040 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.2 Hz, 3 H, 6-CH_3), 0.91, 0.93 (each d, *J* = 6.4 Hz, total 3 H, 2-CH_3), 1.00−2.20 (m, 28 H, 2-, 6-H, 3−5-, 7−13-, 3′−5′-H_2), 3.12−4.00 (m, 4 H, 1-, 6′-H_2), 4.56 (br, 1 H, 2′-H), 4.87−5.09 (m, 2 H, 15-H_2), 5.61−6.05 (m, 1 H, 14-H). − $C_{20}H_{42}O_2$ (338.3): calcd. C 78.05, H 12.50; found C 77.98, H 12.64.

(2*S*,6*R*)-2,6-Dimethyl-14-pentadecen-1-ol [(2*S*,6*R*)-18]: To a solution of (2*S*,6*R*)-**17** (218 mg, 0.64 mmol) in 95% EtOH (8 mL) was added *p*-toluenesulfonic acid monohydrate (10.0 mg, 0.06 mmol) and the mixture was stirred for 3 h under reflux. After neutralization with K_2CO_3, the mixture was poured into brine and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (4 g, hexane/ethyl acetate, 50:1) to give 157 mg (96%) of (2*S*,6*R*)-**18** as a colorless oil; n_D^{21} = 1.4580. − $[\alpha]_D^{24}$ = −7.8 (*c* = 0.67, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3340 cm^{-1} (s, O−H), 3100 (w, C=C−H), 1640 (m, C=C), 1040 (s, C−O). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.7 Hz, 3 H, 6-CH_3), 0.92 (d, *J* = 6.7 Hz, 3 H, 2-CH_3), 1.03−1.60 (m, 20 H, 6-H, 3−5-, 7−12-H_2, OH), 1.62 (octet like, *J* = 6.5 Hz, 1 H, 2-H), 2.04 (q like, *J* = 7.1 Hz, 2 H, 13-H_2), 3.42 (dd, *J* = 6.7, 10.4 Hz, 1 H, 1-H_a), 3.51 (dd, *J* = 5.8, 10.4 Hz, 1 H, 1-H_b), 4.93 (ddt, *J* = 1.1, 2.0, 10.4 Hz, 1 H, 15-H_{cis}), 4.99 (ddt, *J* = 1.8, 2.0, 17.1 Hz, 1 H, 15-H_{trans}), 5.82 (ddt, *J* = 6.7, 10.4, 17.1 Hz, 1 H, 14-H). − $C_{17}H_{34}O$ (254.3): calcd. C 80.24, H 13.47; found C 80.48, H 13.74.

(2*S*,6*R*)-2,6-Dimethyl-14-pentadecenyl Tosylate [(2*S*,6*R*)-19]: To a solution of (2*S*,6*R*)-**18** (125 mg, 0.49 mmol) in dry pyridine (2 mL) was added *p*-toluenesulfonyl chloride (140 mg, 0.74 mmol) at 0 °C. After stirring at 0 °C for 12 h, the mixture was poured into ice and water and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 214 mg (quant.) of crude (2*S*,6*R*)-**19**. This was employed in the next step without further purification; IR (film): $\tilde{\nu}_{max}$ = 1640 cm^{-1} (w, C=C), 1600 (w, aromatic), 1360 (s, SO_2), 1190 (s, SO_2), 1180 (s, SO_2). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.81 (d, *J* = 6.0 Hz, 3 H, 6-CH_3), 0.88 (d, *J* = 6.6 Hz, 3 H, 2-CH_3), 1.00−2.20 (m, 22 H, 2-, 6-H, 3−5-, 7−13-H_2), 2.45 (s, 3 H, Ar−CH_3), 3.78 (dd, *J* = 6.2, 9.2 Hz, 1 H, 1-H_a), 3.91 (dd, *J* = 5.9, 9.2 Hz, 1 H, 1-H_b), 4.84−5.09 (m, 2 H, 15-H_2), 5.61−6.05 (m, 1 H, 14-H), 7.34 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.79 (d, *J* = 8.2 Hz, 2 H, Ar-H).

(10*R*,14*R*)-10,14-Dimethyl-1-octadecene [(10*R*,14*R*)-1]: Magnesium (91 mg, 3.75 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of *n*-propyl bromide (307 mg, 2.5 mmol) in dry THF (5 mL), and the mixture was stirred at room temperature for 1 h. The resulting solution was used immediately. Under an argon atmosphere, to a solution of (2*S*,6*R*)-**19** (214 mg, ca. 0.49 mmol) in dry THF (4 mL) were added the above Grignard reagent and a solution (0.32 M, 0.08 mL, 0.026 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 2 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 24 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (10 g, pentane) to give 129 mg (94%) of (10*R*,14*R*)-**1** as a colorless oil; n_D^{24} = 1.4435. − $[\alpha]_D^{25}$ = −1.83 (*c* = 1.33, $CHCl_3$) {ref.[2] $[\alpha]_D^{21}$ = −1.70 (*c* = 1.27, $CHCl_3$)}. − IR (film): $\tilde{\nu}_{max}$ = 3060 cm^{-1} (w, C=C−H), 2980 (s, C−H), 2950 (s, C−H), 2880 (s, C−H), 1640 (m, C=C), 1460 (s, C−H), 1380 (m, C−H), 990 (m), 910 (s), 725 (w). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.840, 0.843 (each d, *J* = 6.7, 6.4 Hz, total 6 H, 10-, 14-CH_3), 0.89 (t, *J* = 6.9 Hz, 3 H, 18-H_3), 1.03−1.43 (m, 26 H, 10-, 14-H, 4−9-, 11−13-, 15−17-H_2), 2.04 (q like, *J* = 7.1 Hz, 2 H, 3-H_2), 4.93 (ddt, *J* = 1.2, 2.1, 10.1 Hz, 1 H, 1-H_{cis}), 4.99 (ddt, *J* = 1.8, 2.1, 17.1 Hz, 1 H, 1-H_{trans}), 5.82 (ddt, *J* = 6.7, 10.1, 17.1 Hz, 1 H, 2-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 19.7, 23.0, 24.5, 27.1, 29.0, 29.2, 29.3, 29.5, 30.0, 32.72, 32.74, 33.8, 36.8, 37.1, 37.4, 114.1, 139.3. − $C_{20}H_{40}$ (280.5): calcd. C 85.63, H 14.37; found C 85.57, H 14.39. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 27.1 min. (99.0%)

(2*R*,6*S*)-2,6-Dimethyl-1-tetrahydropyranyloxydecane [(2*R*,6*S*)-20]: Magnesium (124 mg, 5.1 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of *n*-propyl bromide (492 mg, 4.0 mmol) in dry THF (7 mL), and the mixture was stirred at room temperature for 1 h. The resulting solution was used immediately. Under an argon atmosphere, to a solution of (2*R*,6*R*)-**16** (415 mg, ca. 1.02 mmol) in dry THF (5 mL) were added the above Grignard reagent and a solution (0.32 M, 0.10 mL, 0.032 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 1 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 20 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (10 g, hexane/ethyl acetate = 500:1) to give 254 mg (92%) of (2*R*,6*S*)-**20** as a colorless oil; n_D^{26} = 1.4510. − $[\alpha]_D^{23}$ = +3.99 (*c* = 1.09, hexane). − IR (film): $\tilde{\nu}_{max}$ = 1130 cm^{-1} (s, C−O), 1040 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.84, (d, *J* = 6.0 Hz, 3 H, 6-CH_3), 0.88 (t, *J* = 6.3 Hz, 3 H, 10-H_3), 0.91, 0.93 (each d, *J* = 6.7 Hz, total 3 H, 2-CH_3), 1.00−2.00 (m, 20 H, 2-, 6-H, 3−5-, 6−8-, 3′−5′-H_2),

3.04−4.01 (m, 4 H, 1-, 6′-H_2), 4.56 (br, 1 H, 2′-H). − $C_{17}H_{34}O_2$ (270.5): calcd. C 75.50, H 12.67; found C 75.28, H 12.88.

(2*R*,6*S*)-2,6-Dimethyl-1-decanol [(2*R*,6*S*)-21]: To a solution of (2*R*,6*S*)-**20** (246 mg, 0.91 mmol) in 95% EtOH (7 mL) was added *p*-toluenesulfonic acid monohydrate (5.0 mg, 0.03 mmol) and the mixture was stirred for 4 h under reflux. After neutralization with K_2CO_3, the mixture was poured into brine and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (4 g, hexane/ethyl acetate, 50:1) to give 150 mg (89%) of (2*R*,6*S*)-**21** as a colorless oil; n_D^{25} = 1.4421. − $[\alpha]_D^{24}$ = +13.3 (*c* = 1.04, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3450 cm^{-1} (s, O−H), 1040 (s, C−O). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.7 Hz, 3 H, 6-CH_3), 0.89 (t, *J* = 6.9 Hz, 3 H, 10-H_3), 0.92 (d, *J* = 6.7 Hz, 3 H, 2-CH_3), 1.06−1.38 (m, 14 H, 6-H, 3−5-, 7−9-H_2, OH), 1.62 (octet like, *J* = 6.5 Hz, 1H, 2-H), 3.42 (dd, *J* = 6.7, 10.4 Hz, 1 H, 1-H_a), 3.51 (dd, *J* = 5.8, 10.4 Hz, 1 H, 1-H_b). − $C_{12}H_{26}O$ (186.3): calcd. C 77.35, H 14.06; found C 76.97, H 14.30.

(2*R*,6*S*)-2,6-Dimethyldecyl Tosylate [(2*R*,6*S*)-22]: To a solution of (2*R*,6*S*)-**21** (95 mg, 0.51 mmol) in dry pyridine (2 mL) was added *p*-toluenesulfonyl chloride (153 mg, 0.81 mmol) at 0 °C. After stirring at 0 °C for 14 h, the mixture was poured into ice and water and extracted with diethyl ether. The organic phase was washed with saturated aqueous $CuSO_4$, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 180 mg (quant.) of crude (2*R*,6*S*)-**22**. This was employed in the next step without further purification; IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1360 (s, SO_2), 1190 (s, SO_2), 1180 (s, SO_2). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.77−0.92 (m, 6 H, 6-CH_3, 10-H_3), 0.88 (d, *J* = 6.6 Hz, 3 H, 2-CH_3), 1.00−2.00 (m, 14 H, 2-, 6-H, 3−5-, 7−9-H_2), 2.45 (s, 3 H, Ar−CH_3), 3.78 (dd, *J* = 6.2, 9.4 Hz, 1 H, 1-H_a), 3.91 (dd, *J* = 5.9, 9.4 Hz, 1 H, 1-H_b), 7.34 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.79 (d, *J* = 8.2 Hz, 2 H, Ar-H).

(10*S*,14*S*)-10,14-Dimethyl-1-octadecene [(10*S*,14*S*)-1]: Magnesium (91 mg, 3.75 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of 7-octenyl bromide (516 mg, 2.7 mmol) in dry THF (6 mL), and the mixture was stirred at 45 °C for 1 h. The resulting solution was used immediately. Under an argon atmosphere, to a solution of (2*R*,6*S*)-**22** (180 mg, ca. 0.51 mmol) in dry THF (4 mL) were added the above Grignard reagent and a solution (0.32 M, 0.08 mL, 0.026 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 1 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 24 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (50 g, pentane) to give 125 mg (87%) of (10*S*,14*S*)-**1** as a colorless oil; n_D^{25} = 1.4431. − $[\alpha]_D^{25}$ = +1.78 (*c* = 1.31, $CHCl_3$) {ref.[2] $[\alpha]_D^{21}$ = +1.92 (*c* = 1.06, $CHCl_3$)}. Its IR and NMR spectra were identical with those of (10*R*,14*R*)-**1**. − $C_{20}H_{40}$ (280.5): calcd. C 85.63, H 14.37; found C 85.40, H 14.51. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 27.3 min. (98.1%).

(2*S*,6*R*)-2,6-Dimethyl-1-tetrahydropyranyloxypentadecane [(2*S*,6*R*)-23]: Magnesium (175 mg, 7.2 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of *n*-octyl bromide (0.93 g, 4.8 mmol) in dry THF (7 mL), and the mixture was stirred at 45 °C for 1 h. The resulting solution was used immediately. Under argon atmosphere, to a solution of (2*S*,6*S*)-**16** (392 mg, ca. 0.96 mmol) in dry THF (5 mL) were added the above Grignard reagent and a solution (0.32 M, 0.15 mL, 0.048 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 3 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 12 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (12 g, hexane/ethyl acetate = 500:1) to give 270 mg (82%) of (2*S*,6*R*)-**23** as a colorless oil; n_D^{24} = 1.4519. − $[\alpha]_D^{21}$ = −2.56 (*c* = 1.20, hexane). − IR (film): $\tilde{\nu}_{max}$ = 1130 cm^{-1} (s, C−O), 1040 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.84, (d, *J* = 6.0 Hz, 3 H, 6-CH_3), 0.89 (t, *J* = 7.0 Hz, 3 H, 15-CH_3), 0.91, 0.93 (each d, *J* = 6.6 Hz, total 3 H, 2-CH_3), 1.00−2.00 (m, 30 H, 2-, 6-H, 3−5-, 7−14-, 3′−5′-H_2), 2.95−4.05 (m, 4 H, 1-, 6′-H_2), 4.56 (br, 1 H, 2′-H). − $C_{22}H_{44}O_2$ (340.6): calcd. C 77.58, H 13.02; found C 77.70, H 12.92.

(2*R*,6*S*)-2,6-Dimethyl-1-tetrahydropyranyloxypentadecane [(2*R*,6*S*)-23]: In the same manner as described above, (2*R*,6*R*)-**16** (240 mg, ca. 0.59 mmol) was converted into 162 mg (81%) of (2*R*,6*S*)-**23** (as a colorless oil); n_D^{25} = 1.4524. − $[\alpha]_D^{21}$ = +2.4 (*c* = 0.90, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**23**. − $C_{22}H_{44}O_2$ (340.6): calcd. C 77.58, H 13.02; found C 77.74, H 12.94.

(2*S*,6*R*)-2,6-Dimethyl-1-pentadecanol [(2*S*,6*R*)-24]: In the same manner as described above for the preparation of (2*S*,6*R*)-**18**, (2*S*,6*R*)-**23** (228 mg, 0.67 mmol) was converted into 163 mg (95%) of (2*S*,6*R*)-**24** (as a colorless oil); n_D^{24} = 1.4494. − $[\alpha]_D^{20}$ = −7.7 (*c* = 0.82, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3340 cm^{-1} (s, O−H), 1040 (s, C−O). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.7 Hz, 3 H, 6-CH_3), 0.88 (t, *J* = 7.0 Hz, 3 H, 15-H_3), 0.92 (d, *J* = 6.7 Hz, 3 H, 2-CH_3), 1.03−1.39 (m, 24 H, 6-H, 3−5-, 7−14-H_2, OH), 1.62 (octet like, *J* = 6.5 Hz, 1 H, 2-H), 3.42 (dd, *J* = 6.7, 10.4 Hz, 1 H, 1-H_a), 3.51 (dd, *J* = 5.8, 10.4 Hz, 1 H, 1-H_b). − $C_{17}H_{36}O$ (256.5): calcd. C 79.61, H 14.15; found C 79.51, H 14.08.

(2*R*,6*S*)-2,6-Dimethyl-1-pentadecanol [(2*R*,6*S*)-24]: In the same manner as described above for the preparation of (2*S*,6*R*)-**18**, (2*R*,6*S*)-**23** (150 mg, ca. 0.44 mmol) was converted into 108 mg (96%) of (2*R*,6*S*)-**24** (as a colorless oil); n_D^{24} = 1.4483. − $[\alpha]_D^{21}$ = +7.9 (*c* = 0.97, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**24**. − $C_{17}H_{36}O$ (256.5): calcd. C 79.61, H 14.15; found C 79.37, H 14.41.

(2*S*,6*R*)-2,6-Dimethylpentadecyl Tosylate [(2*S*,6*R*)-25] In the same manner as described above for the preparation of (2*S*,6*R*)-**19**, (2*S*,6*R*)-**24** (123 mg, ca. 0.48 mmol) was converted into 200 mg (quant.) of crude (2*S*,6*R*)-**25**. This was employed in the next step without further purification; IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1360 (s, SO_2), 1190 (s, SO_2), 1180 (s, SO_2). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.77−0.91 (m, 6 H, 6-CH_3, 15-H_3), 0.88 (d, *J* = 6.8 Hz, 3 H, 2-CH_3), 1.00−1.80 (m, 24 H, 2-, 6-H, 3−5-, 7−14-H_2), 2.45 (s, 3 H, Ar−CH_3), 3.78 (dd, *J* = 6.2, 9.2 Hz, 1 H, 1-H_a), 3.91 (dd, *J* = 5.9, 9.2 Hz, 1 H, 1-H_b), 7.34 (d, *J* = 8.2 Hz, 2 H, Ar-H), 7.79 (d, *J* = 8.2 Hz, 2 H, Ar-H).

(2*R*,6*S*)-2,6-Dimethylpentadecyl Tosylate [(2*R*,6*S*)-25]: In the same manner as described above for the preparation of (2*S*,6*R*)-**19**, (2*R*,6*S*)-**24** (93 mg, ca. 0.36 mmol) was converted into 154 mg (quant.) of (2*R*,6*S*)-**25**. This was employed in the next step without further purification. Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**25**.

(5*R*,9*R*)-5,9-Dimethyloctadecane [(5*R*,9*R*)-2]: In the same manner as described above for the preparation of (10*R*,14*R*)-**1**, (2*S*,6*R*)-**25** (200 mg, ca. 0.48 mmol) was converted into 118 mg (87%) of (5*R*,9*R*)-**2** (as a colorless oil); n_D^{24} = 1.4418. − $[\alpha]_D^{25}$ = −1.88 (*c* =

2.56, hexane). − IR (film): $\tilde{\nu}_{max}$ = 2980 cm^{-1} (s, C−H), 2950 (s, C−H), 2880 (s, C−H), 1465 (s, C−H), 1380 (m, C−H), 725 (w). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.839, 0.842 (each d, *J* = 6.7, 6.4 Hz, total 6 H, 5-, 9-CH_3), 0.88, 0.89 (each t, *J* = 6.9 Hz, total 6 H, 1-, 18-H_3),1.03−1.32 (m, 28 H, 2−4-, 6−8-, 10−17-H_2), 1.33−1.42 (m, 2 H, 5-, 9-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 22.7, 23.0, 24.5, 27.1, 29.36, 29.37, 29.67, 29.74, 30.0, 31.9, 32.73, 32.75, 36.8, 37.2, 37.4. − $C_{20}H_{42}$ (282.6): calcd. C 85.02, H 14.98; found C 84.75, H 15.12. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 27.1 min. (98.5%).

(5*S*,9*S*)-5,9-Dimethyloctadecane [(5*S*,9*S*)-2]: In the same manner as described above for the preparation of (10*R*,14*R*)-**1**, (2*R*,6*S*)-**25** (154 mg, ca. 0.36 mmol) was converted into 88 mg (86%) of (5*S*,9*S*)-**2** (as a colorless oil); n_D^{24} = 1.4412. − $[\alpha]_D^{25}$ = +1.86 (*c* = 2.32, hexane). Its IR and NMR spectra were identical with those of (5*R*,9*R*)-**2**. − $C_{20}H_{42}$ (282.6): calcd. C 85.02, H 14.98; found C 85.25, H 14.86. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 26.9 min. (99.2%).

(2*S*,6*R*)-2,6-Dimethyl-1-tetrahydropyranyloxytetradecane [(2*S*,6*R*)-26]: Magnesium (157 mg, 6.5 mmol) was added to an argon-purged flask. To the metal was added dropwise a solution of *n*-heptyl bromide (0.77 g, 4.3 mmol) in dry THF (8 mL), and the mixture was stirred at 45 °C for 1 h. The resulting solution was used immediately. Under argon atmosphere, to a solution of (2*S*,6*S*)-**16** (368 mg, ca. 0.88 mmol) in dry THF (5 mL) were added the above Grignard reagent and a solution (0.32 M, 0.13 mL, 0.041 mmol) of Li_2CuCl_4 in dry THF at −78 °C. After stirring at this temperature for 2 h, the mixture was warmed slowly to 0 °C, and stirred at 0 °C for 20 h. The mixture was quenched with saturated aqueous NH_4Cl, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (10 g, hexane/ethyl acetate = 500:1) to give 264 mg (92%) of (2*S*,6*R*)-**26** as a colorless oil; n_D^{22} = 1.4542. − $[\alpha]_D^{23}$ = −2.06 (*c* = 1.02, hexane). − IR (film): $\tilde{\nu}_{max}$ = 1120 cm^{-1} (s, C−O), 1030 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.84, (d, *J* = 6.2 Hz, 3 H, 6-CH_3), 0.89 (t, *J* = 6.2 Hz, 3 H, 14-H_3), 0.91, 0.93 (each d, *J* = 6.2 Hz, total 3 H, 2-CH_3), 1.00−1.90 (m, 28 H, 2-, 6-H, 3−5-, 7−13-, 3′−5′-H_2), 3.04−4.01 (m, 4 H, 1-, 6′-H_2), 4.56 (br, 1 H, 2′-H). − $C_{21}H_{42}O_2$ (326.6): calcd. C 77.24, H 12.96; found C 77.41, H 12.85.

(2*R*,6*S*)-2,6-Dimethyl-1-tetrahydropyranyloxytetraadecane [(2*R*,6*S*)-26]: In the same manner as described above, (2*R*,6*R*)-**16** (450 mg, ca. 1.11 mmol) was converted into 323 mg (89%) of (2*R*,6*S*)-**26** (as a colorless oil); n_D^{23} = 1.4531. − $[\alpha]_D^{24}$ = +1.98 (*c* = 1.11, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**26**. − $C_{21}H_{42}O_2$ (326.6): calcd. C 77.24, H 12.96; found C 77.11, H 12.83.

(2*S*,6*R*)-2,6-Dimethyl-1-tetradecanol [(2*S*,6*R*)-27]: In the same manner as described above for the preparation of (2*S*,6*R*)-**18**, (2*S*,6*R*)-**26** (230 mg, 0.70 mmol) was converted into 165 mg (96%) of (2*S*,6*R*)-**27** (as a colorless oil); n_D^{24} = 1.4483. − $[\alpha]_D^{24}$ = −8.48 (*c* = 1.02, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3340 cm^{-1} (s, O−H), 1040 (s, C−O). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.4 Hz, 3 H, 6-CH_3), 0.88 (t, *J* = 7.0 Hz, 3 H, 14-H_3), 0.92 (d, *J* = 6.7 Hz, 3 H, 2-CH_3), 1.03−1.43 (m, 22 H, 6-H, 3−5-, 7−13-H_2, OH), 1.62 (octet like, *J* = 6.5 Hz, 1 H, 2-H), 3.42 (dd, *J* = 6.7, 10.4 Hz, 1 H, 1-H_a), 3.51 (dd, *J* = 5.8, 10.4 Hz, 1 H, 1-H_b). − $C_{16}H_{34}O$ (242.4): calcd. C 79.27, H 14.14; found C 78.99, H 14.18.

(2*R*,6*S*)-2,6-Dimethyl-1-tetradecanol [(2*R*,6*S*)-27]: In the same manner as described above for the preparation of (2*S*,6*R*)-**18**, (2*R*,6*S*)-**26** (270 mg, ca. 0.83 mmol) was converted into 195 mg (97%) of (2*R*,6*S*)-**27** (as a colorless oil); n_D^{22} = 1.4474. − $[\alpha]_D^{20}$ = +8.74 (*c* = 1.10, hexane). Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**27**. − $C_{16}H_{34}O$ (242.4): calcd. C 79.27, H 14.14; found C 79.21, H 14.10.

(2*S*,6*R*)-2,6-Dimethyltetradecyl Tosylate [(2*S*,6*R*)-28]: In the same manner as described above for the preparation of (2*S*,6*R*)-**19**, (2*S*,6*R*)-**27** (124 mg, 0.51 mmol) was converted into 222 mg (quant.) of crude (2*S*,6*R*)-**28**. This was employed in the next step without further purification; IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1360 (s, SO_2), 1190 (s, SO_2), 1180 (s, SO_2). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.77−0.92 (m, 6 H, 6-CH_3, 14-H_3), 0.88 (d, *J* = 6.8 Hz, 3 H, 2-CH_3), 1.00−1.90 (m, 22 H, 2-, 6-H, 3−5-, 7−13-H_2), 2.45 (s, 3H, Ar−CH_3), 3.78 (dd, *J* = 6.2, 9.2 Hz, 1 H, 1-H_a), 3.91 (dd, *J* = 5.9, 9.2 Hz, 1 H, 1-H_b), 7.34 (d, *J* = 8.1 Hz, 2 H, Ar-H), 7.79 (d, *J* = 8.1 Hz, 2 H, Ar-H).

(2*R*,6*S*)-2,6-Dimethyltetradecyl Tosylate [(2*R*,6*S*)-28]: In the same manner as described above for the preparation of (2*S*,6*R*)-**19**, (2*R*,6*S*)-**27** (102 mg, 0.42 mmol) was converted into 170 mg (quant.) of (2*R*,6*S*)-**28**. This was employed in the next step without further purification. Its IR and NMR spectra were identical with those of (2*S*,6*R*)-**28**.

(5*R*,9*R*)-5,9-Dimethylheptadecane [(5*R*,9*R*)-3]: In the same manner as described above for the preparation of (10*R*,14*R*)-**1**, (2*S*,6*R*)-**28** (222 mg, ca. 0.51 mmol) was converted into 126 mg (92%) of (5*R*,9*R*)-**3** (as a colorless oil); n_D^{24} = 1.4392. − $[\alpha]_D^{25}$ = −2.00 (*c* = 2.60, hexane). − IR (film): $\tilde{\nu}_{max}$ = 2980 cm^{-1} (s, C−H), 2950 (s, C−H), 2880 (s, C−H), 1460 (s, C−H), 1380 (m, C−H), 720 (w). − ^1H NMR (500 MHz, $CDCl_3$): δ = 0.840, 0.842 (each d, *J* = 6.7, 6.4 Hz, total 6 H, 5-, 9-CH_3), 0.88, 0.89 (each t, *J* = 7.0, 6.9 Hz, total 6 H, 1-, 17-H_3), 1.03−1.32 (m, 26 H, 2−4-, 6−8-, 10−16-H_2), 1.33−1.42 (m, 2 H, 5-, 9-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 22.7, 23.1, 24.5, 27.1, 29.36, 29.37, 29.7, 30.0, 31.9, 32.75, 36.9, 37.2, 37.4. − $C_{19}H_{40}$ (268.5): calcd. C 84.99, H 15.01; found C 84.89, H 14.89. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 23.5 min. (98.9%).

(5*S*,9*S*)-5,9-Dimethylheptadecane [(5*S*,9*S*)-3]: In the same manner as described above for the preparation of (10*R*,14*R*)-**1**, (2*R*,6*S*)-**28** (170 mg, ca. 0.42 mmol) was converted into 92 mg (81%) of (5*S*,9*S*)-**3** (as a colorless oil); n_D^{25} =1.4403. − $[\alpha]_D^{25}$ = +2.03 (*c* = 2.59, hexane). Its IR and NMR spectra were identical with those of (5*R*,9*R*)-**3**. − $C_{19}H_{40}$ (268.5): calcd. C 84.99, H 15.01; found C 85.13, H 15.24. − GC [column: DB-5 (0.25 mm × 30 m), 120 to 250 °C/min., +3.0 °C/min.; carrier gas: He, pressure: 110 kPa]: t_R = 23.6 min. (98.7%).

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