Pheromone Synthesis, CXCIX[+]

Synthesis of All the Stereoisomers of 7-Methylheptadecane and 7,11-Dimethylheptadecane, the Female Sex Pheromone Components of the Spring Hemlock Looper and the Pitch Pine Looper

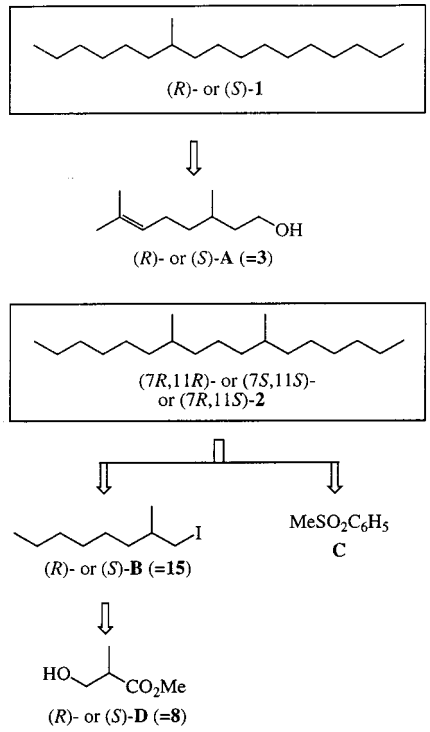
Yasuo Shirai,[a] Masanori Seki,[a] and Kenji Mori*[a]

Keywords: Alkanes / Chirality / *Lambdina athasaria* / *Lambdina pellucidaria* / Pheromones

All the stereoisomers of 7-methylheptadecane (**1**) and 7,11-dimethylheptadecane (**2**) were synthesized by starting from the enantiomers of citronellol (**3**) and methyl 3-hydroxy-2-methylpropanonate (**8**), respectively. A short synthesis of *meso*-7,11-dimethylheptadecane [(7*R*,11*S*)-**2**] was achieved starting from *meso*-2,6-dimethylheptanedioic acid [(2*R*,6*S*)-**21**]. A mixture of (*S*)-**1** and (7*R*,11*S*)-**2** is the pheromone of the spring hemlock looper moth (*Lambdina athasaria*) and the pitch pine looper moth (*L. pellucidaria*).

The spring hemlock looper (*Lambdina athasaria*) is a forest pest in northeastern America, and feeds primarily on hemlock (*Tsuga canadensis*). In 1994 Gries et al. identified 7-methylheptadecane (**1**) and 7,11-dimethylheptadecane (**2**) as the components of the female-produced sex pheromone of *L. athasaria*.[1] The same two methyl-branched alkanes **1** and **2** were also identified in 1998 as the female sex pheromone components of the pitch pine looper (*Lambdina pellucidaria*), which damages pitch pine (*Pinus rigida*) in northeastern America.[2] Although (±)-**1** and a mixture of (±)- and *meso*-**2** were synthesized and shown to be bioactive,[1] the absolute configurations of naturally occurring **1** and **2** remained unknown. This paper describes the synthesis of (*R*)- and (*S*)-**1**, and (7*R*,11*R*)-, (7*R*,11*S*)- and (7*S*,11*S*)-**2**. By testing our synthetic samples, Gries and co-workers have recently established that the bioactive pheromone components are (*S*)-**1** and (7*R*,11*S*)-**2** (*meso*-**2**).[3]

As shown in Scheme 1, both **1** and **2** can be synthesized from the readily available chiral and nonracemic building blocks **A** and **D**. The enantiomers of citronellol (**A**) give the enantiomers of **1**. The three stereoisomers of **2** can be prepared by connecting (*R*)- or (*S*)-**B** with **C**. The alkylating agent **B** is prepared from the (*R*)- or (*S*)-isomers of methyl 3-hydroxy-2-methylpropanoate (**D**).



Scheme 1. Structures of the pheromone components **1** and **2**, and their retrosynthetic analysis

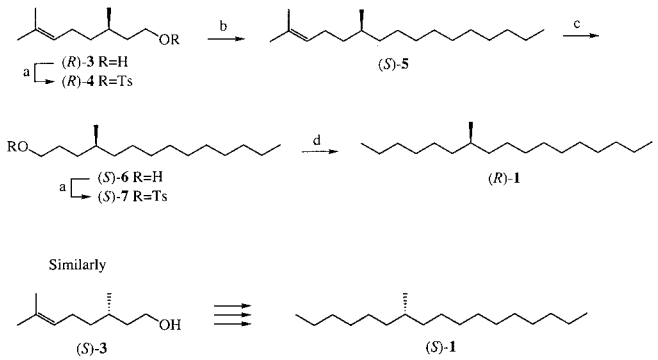
Scheme 2 summarizes the synthesis of (*R*)- and (*S*)-**1**. The tosylate **4** of (*R*)-citronellol (**3**, Takasago, 97% *ee*) was treated with octylmagnesium bromide in the presence of dilithium tetrachlorocuprate[4] to give (*S*)-**5**. Ozonolysis of (*S*)-**5** and reductive workup gave (*S*)-**6**, whose tosylate (*S*)-**7** was treated with *n*-propylmagnesium bromide under Schlosser conditions[4] to give the desired product (*R*)-**1**, $[\alpha]_D^{26} = -0.27$ (hexane) in 57% overall yield based on (*R*)-**3** (5 steps). Similarly, (*S*)-**3** (97% *ee*) was converted into (*S*)-**1**, $[\alpha]_D^{19} = +0.28$ (hexane), in 74% overall yield. Because there was no step which could cause racemization at C-7 of **1**, the enantiomers of **1** were assumed to retain the enantiomeric purity of **3**, i.e. 97% *ee*.

The synthesis of the stereoisomers of **2** is summarized in Scheme 3. Methyl (*S*)-3-hydroxy-2-methylpropanoate (**8**, 99.8% *ee*) was converted into (*S*)-**11** via (*S*)-**9** and (*R*)-**10** as reported previously.[5] Treatment of (*S*)-**11** with *n*-pentyl-

[+] Part CXCVIII: Ref.[8]

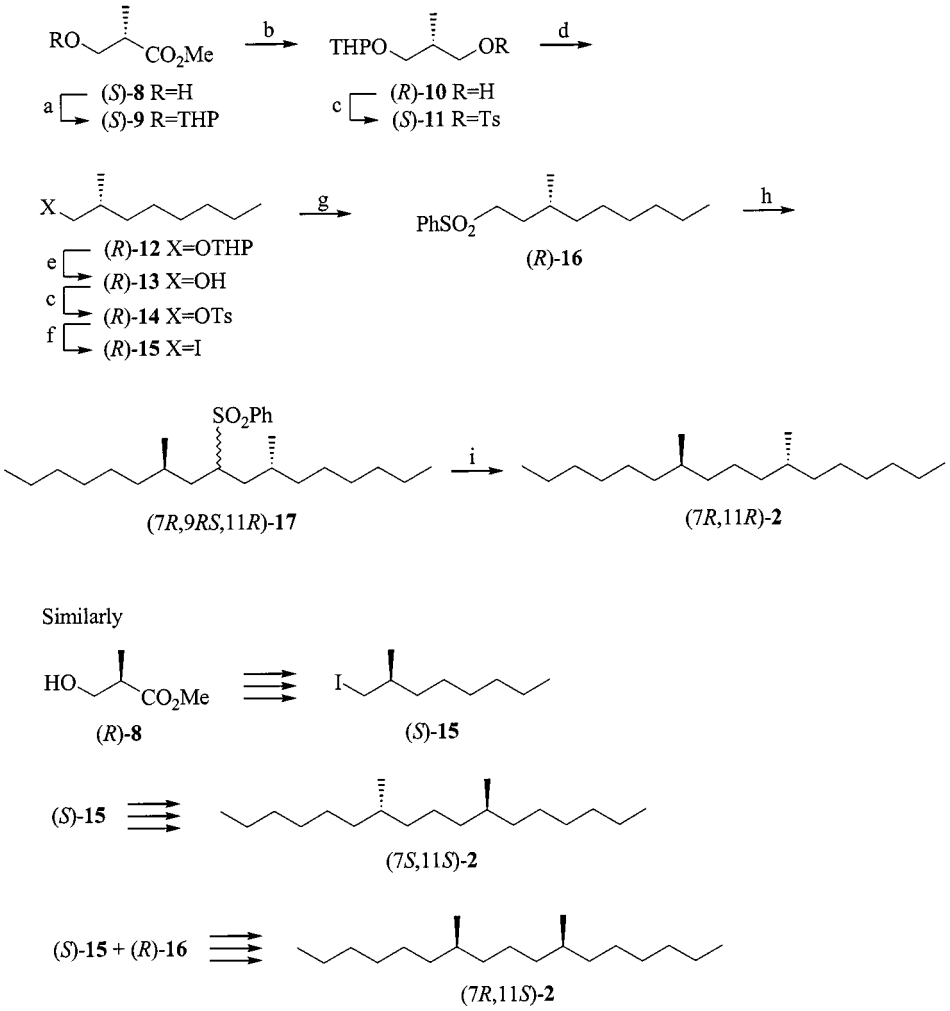
[a] Department of Chemistry, Faculty of Science, Science University of Tokyo,
Kagurazaka 1−3, Shinjuku-ku, Tokyo 162−8601, Japan
Fax: (internat.) + 81-3/3235-2214

  1434−193X/99/1111−3139 $ 17.50+.50/0

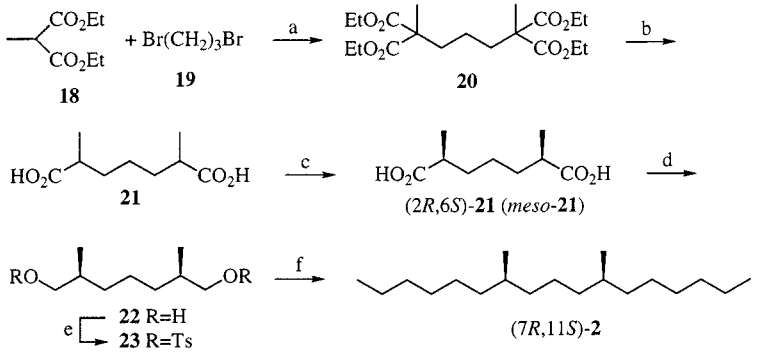


Scheme 2. Synthesis of (*R*)- and (*S*)-**1**; reagents: (a) *p*-TsCl, C_5H_5N [95% for (*S*)-**7**; 94% for (*R*)-**7**]; (b) $Me(CH_2)_7MgBr$, Li_2CuCl_4, THF; (c) (i) O_3, $MeOH/CH_2Cl_2$/hexane, (ii) $NaBH_4$ [72% of (*S*)-**6** from (*R*)-**3**; 79% of (*R*)-**6** from (*S*)-**3**]; (d) $Me(CH_2)_2MgBr$, Li_2CuCl_4, THF [83% for (*R*)-**1**; 99% for (*S*)-**1**]

magnesium bromide in the presence of dilithium tetrachlorocuprate[4] gave (*R*)-**12**, whose tetrahydropyranyl (THP) protective group was removed by acidic methanolysis to afford (*R*)-**13**. The corresponding tosylate (*R*)-**14** gave the iodide (*R*)-**15** upon Finkelstein displacement. Alkylation of the carbanion derived from methylphenylsulfone with (*R*)-**15** yielded (*R*)-**16**, which was further alkylated with (*R*)-**15** and *n*-butyllithium to furnish (7*R*,9*RS*,11*R*)-**17**. Removal of the phenylsulfonyl group of **17** with sodium amalgam gave the target molecule (7*R*,11*R*)-**2**, $[\alpha]_D^{22} = -1.26$ (hexane). It



Scheme 3. Synthesis of (7*R*,11*R*)-, (7*S*,11*S*)- and (7*R*,11*S*)-**2**; reagents: (a) DHP, *p*-TsOH, Et_2O; (b) $LiAlH_4$, Et_2O (80% based on **8**); (c) *p*-TsCl, C_5H_5N (quant.); (d) $Me(CH_2)_4MgBr$, Li_2CuCl_4, THF (90%); (e) *p*-TsOH, MeOH (90%); (f) NaI, Me_2CO (89%); (g) $MeSO_2C_6H_5$, BuLi, THF/HMPA (92%); (h) BuLi, THF/HMPA; (*R*)-**15** (80%); (i) (i) Na/Hg, Na_2HPO_4, EtOH; (ii) MCPBA, hexane; (iii) SiO_2 chromatog. (33%)



Scheme 4. Synthesis of (7*R*,11*S*)-**2**; reagents: (a) NaOEt, EtOH; (b) (i) KOH,MeOH/H_2O; (ii) HCl, H_2O, heat (43% based on **19**); (c) (i) a small amount of *meso*-**21** as seed crystals; (ii) two recrystallizations from hexane/Et_2O (2:1) (20%); (d) $LiAlH_4$, Et_2O (66%); (e) *p*-TsCl, C_5H_5N (94%); (f) $Me(CH_2)_4MgBr$, Li_2CuCl_4, THF (79%)

should be noted that a side reaction of the reduction gave a small amount of olefinic by-product(s) which could be removed by chromatographic purification of (7*R*,11*R*)-**2** after epoxidation of the olefinic by-product(s) with *m*-chloroperbenzoic acid (MCPBA). The overall yield of (7*R*,11*R*)-**2** was 16% based on (*S*)-**8** (11 steps). Since there was no step to cause racemization at the stereogenic centers, (7*R*,11*R*)-**2** was assumed to be highly pure [$(0.999)^2 \times 100 = 99.8\%$ purity]. Similarly, (*S*)-**15** was prepared from (*R*)-**8** (≈100% *ee*), and two other stereoisomers of **2** [(7*S*,11*S*)-**2**, $[\alpha]_D^{21} = +1.77$ (hexane); (7*R*,11*S*)-**2**, $[\alpha]_D^{22} = 0$ (hexane)] were synthesized in about 15% overall yield. These were also considered to be highly pure (>99.9% purity).

Because the bioactive stereoisomers of **2** turned out to be the *meso*-isomer or (7*R*,11*S*)-**2**, a much simpler synthesis was performed as summarized in Scheme 4. This strategy used *meso*-2,6-dimethylheptanedioic acid (**21**), which has been known since 1895,[6] as the starting material. A stereoisomeric mixture of the diacid **21** was prepared by malonic ester synthesis via **20**, starting from diethyl methylmalonate (**18**) and 1,3-dibromopropane (**19**). Addition of a very small amount of crystalline *meso*-**21** to the crude and oily **21** caused separation of a crystalline mass in 50% yield, which was found to be a mixture of *meso*-**21** and (±)-**21** (3:1). This was recrystallized from hexane/diethyl ether (2:1) to give purer *meso*-**21** (88% *de*) which, after a further recrystallization from the same solvent mixture, gave *meso*-**21** with 96.7% *de*. The diastereomeric purity of **21** could be estimated by HPLC analysis of the *bis*-amide of **21** obtained by its derivatization with (*S*)-1-(1-naphthyl)ethylamine. Reduction of *meso*-**21** with lithium aluminum hydride gave **22**. This *meso*-diol **22** was recently used as the prochiral building block to give its optically active monoacetate by lipase-catalyzed asymmetric acetylation.[7][8] The diol **22** was then tosylated to give the corresponding ditosylate **23**, which was treated with *n*-pentylmagnesium bromide under Schlosser conditions[4] to give the *meso*-alkane (7*R*,11*S*)-**2**. The overall yield of *meso*-**2** by this route was 49% based on *meso*-**21** (3 steps).

In conclusion we have synthesized all the possible stereoisomers of **1** and **2**. Our synthetic samples were bioassayed by Professer G. Gries in Canada, and the moths *Lambdina athasaria* and *L. pellucidaria* were found to use (*S*)-**1** and *meso*-**2** as pheromone components.

Experimental Section

General: All boiling points and melting points: uncorrected values. − IR: Jasco A-102 and Perkin−Elmer 1600. − ^1H NMR: Hitachi R-24B (60 MHz), Jeol JNM-EX90A (90 MHz) and Jeol JNM-XL270 (270 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-EX90A (90 MHz) and Jeol JNM-XL270 (270 MHz) and Jeol JNM-LA500 (125 MHz) (TMS at δ = 0.00 or $CHCl_3$ at δ = 77.0 as an internal standard). − Optical rotation: Jasco DIP-181. − GC MS: Shimadzu GC-MS QP 2000A spectrometer (70 eV). − GC: Shimadzu GC-14A gas chromatograph. − M.P.: Yanaco MP-S3. − Column chromatography: Merck Kieselgel 60 Art 1.07734. − TLC: 0.25 mm Merck silica gel plates (60F−254).

(*R*)-3,7-Dimethyl-6-octenyl Tosylate [(*R*)-4]: To a solution of (*R*)-citronellol (**3**, 2.00 g, 12.8 mmol) in dry pyridine (12 mL) was added *p*-toluenesulfonyl chloride (3.38 g, 16.8 mmol) at 0°C. The mixture was stirred at 0°C for 12 h. It was then poured into a mixture of ice and dilute HCl, and extracted with diethyl ether. The organic phase was washed with dilute HCl, water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo to give 3.76 g (95%) of crude (*R*)-**4**. This was employed in the next step without further purification. − IR (film): $\tilde{\nu}_{max} = 1600\ cm^{-1}$ (m, aromatic), 1455 (m), 1360 (s, sulfonate), 1175 (s, sulfonate), 815 (s, aromatic), 665 (s, C−S).

(*S*)-3,7-Dimethyl-6-octenyl Tosylate [(*S*)-4]: In the same manner as described above (*S*)-citronellol (**3**, 1.93 g, 12.4 mmol) was converted into 4.29 g (quant.) of (*S*)-**4**. The IR spectrum was identical to that of (*R*)-**4**.

(*S*)-2,6-Dimethyl-2-hexadecene [(*S*)-5]: To a stirred and cooled solution of (*R*)-**4** (3.76 g, 11.9 mmol) in dry THF (40 mL) at −78°C under argon was added dropwise a solution of *n*-octylmagnesium bromide in dry THF (30 mL), previously prepared from Mg (1.57 g, 64.5 mmol) and *n*-octyl bromide (7.73 g, 47.7 mmol), followed by a solution of dilithium tetrachlorocuprate (0.1 M in THF, 1 mL, 0.1 mmol). The resulting mixture was allowed to warm to 0°C with stirring for 12 h. The mixture was then poured into saturated aqueous NH_4Cl 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 (150 g, hexane) to give 3.24 g (quant.) of (*S*)-**5** as a colorless

oil. − n_D^{22} = 1.4449. − $[\alpha]_D^{27}$ = −1.82 (*c* = 4.76, hexane). − IR (film): $\tilde{\nu}_{max}$ = 2925 cm^{-1} (s), 2855 (s). − ^1H NMR (60 MHz, $CDCl_3$): δ = 0.80−1.00 (m, 6 H, 6-, 16-Me), 1.00−2.00 (m, 29 H, 1,2-Me, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-H), 5.05 (t, *J* = 6.0 Hz, 1 H, 3-H). − $C_{18}H_{36}$ (252.5): calcd. C 85.63, H 14.37; found C 85.24, H 14.21.

(*R*)-2,6-Dimethyl-2-hexadecene [(*R*)-5]: In the same manner as described above (*R*)-**4** (4.10 g, 12.4 mmol) was converted into 3.66 g (quant.) of (*R*)-**5**. − n_D^{22} = 1.4438. − $[\alpha]_D^{26}$ = +1.75 (*c* = 4.71, hexane). − $C_{18}H_{36}$ (252.5): calcd. C 85.63, H 14.37; found C 85.44, H 14.34. The IR and NMR spectra were identical to those of (*S*)-**5**.

(*S*)-4-Methyl-1-tetradecanol [(*S*)-6]: Ozonized oxygen was passed through a solution of (*S*)-**5** (3.01 g, 11.9 mmol) in MeOH (150 mL), CH_2Cl_2 (150 mL) and hexane (80 mL) at −78°C. Completion of the reaction was indicated by the appearance of the characteristic blue color of ozone. The excess ozone was removed with a stream of oxygen and sodium borohydride (1.98 g, 49.9 mmol) added. The solution was stirred at −78°C for 0.5 h, then saturated aqueous NH_4Cl was added. The mixture was stirred at 0°C for 2 h. The solvent was removed in vacuo and water was added. The aqueous phase was extracted with diethyl ether. The combined organic phases were washed with water, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (50 g, hexane/ethyl acetate 50:1) to give 2.12 g [72% from (*R*)-**3**] of (*S*)-**6** as a colorless oil. − n_D^{23} = 1.4471. − $[\alpha]_D^{27}$ = −1.27 (*c* = 1.81, hexane). − IR (film): $\tilde{\nu}_{max}$ = 3300 cm^{-1} (br, OH) 1465 (m), 1375 (m) 1060 (w, C−O). − ^1H NMR (60 MHz, $CDCl_3$): δ = 0.75−1.00 (m, 6 H, 4-, 14-Me), 1.20 (s, 22 H, 2-, 3-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-H), 1.45−1.70 (m, 2 H, OH, 4-H), 3.40−3.70 (m, 2 H, 1-H). − $C_{15}H_{32}O$ (228.4): calcd. C 78.87, H 14.12; found C 79.12, H 13.78.

(*R*)-4-Methyl-1-tetradecanol [(*R*)-6]: In the same manner as described above (*R*)-**5** (3.44 g, 68.4 mmol) was converted into 2.23 g [79% from (*S*)-**3**] of (*R*)-**6**. − n_D^{23} = 1.4468. − $[\alpha]_D^{26}$ = +1.50 (*c* = 1.78, hexane). The IR and NMR spectra were identical to those of (*S*)-**5**. − $C_{15}H_{32}O$ (228.4): calcd. C 78.87, H 14.12; found C 78.46, H 14.27.

(*S*)-4-Methyltetradecyl Tosylate [(*S*)-7]: The alcohol (*S*)-**6** (2.05 g, 8.97 mmol) was converted into (*S*)-**7** (3.26 g, 95%) in the usual manner. − IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1465 (m), 1365 (vs, sulfonate), 1190 (vs, sulfonate), 815 (s, aromatic). − ^1H NMR (60 MHz, $CDCl_3$): δ = 0.60−0.90 (m, 6 H, 4-, 14-CH_3), 1.20 (s, 22 H, 2-, 3-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-H), 1.35−1.50 (m, 1 H, 4-H), 2.45 (s, 3 H, *p*-CH_3), 3.80 (t, *J* = 6.0 Hz, 2 H, 1-H), 7.00 (d, *J* = 8.0 Hz, 2 H, aromatic), 7.40 (d, *J* = 8.0 Hz, 2 H, aromatic).

(*R*)-4-Methyltetradecyl Tosylate [(*R*)-7]: The alcohol (*R*)-**6** (0.98 g, 4.23 mmol) was converted into (*R*)-**7** (1.55 g, 94%) in the same manner. The IR and NMR spectra were identical to those of (*S*)-**7**.

(*R*)-7-Methylheptadecane [(*R*)-1]: To a stirred and cooled solution of (*S*)-**7** (3.22 g, 8.42 mmol) in dry THF (30 mL) at −78°C under argon was added dropwise a solution of *n*-propylmagnesium bromide in dry THF (35 mL), previously prepared from Mg (1.05 g, 43.2 mmol) and *n*-propyl bromide (4.20 g, 34.1 mmol), followed by a solution of dilithium tetrachlorocuprate (0.1 M in THF, 0.6 mL, 0.06 mmol). The resulting mixture was allowed to warm to 0°C whilst stirring for 12 h. The mixture was then poured into saturated aqueous NH_4Cl 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 (230 g, hexane) to give 1.77 g (83%) of (*R*)-**1** as a colorless oil. − n_D^{23} = 1.4378. − $[\alpha]_D^{26}$ = −0.266±0.002 (*c* = 5.045, hexane). − GC (column: Nihon chromato works, Ltd. Rascot NC−17, 0.25 mm × 30 m, 100°C + 3.0°C/min; carrier gas: He, press 1.0 kg/cm^2, t_R = 29.9 min (98%). − GC-MS (70 eV); *m*/*z* (%): 254 (0.1) [M^+], 239 (0.4), 225 (0.3), 211 (0.8), 197 (0.9), 168 (3.7), 155 (7.7), 140 (1.3), 127 (1.6), 112 (10.6), 99 (5.8), 85 (19.9), 71 (63.4), 57 (100), 43 (78.4). − IR (film): $\tilde{\nu}_{max}$ = 2955 cm^{-1} (s), 2925 (vs), 2855 (s), 1465 (m), 1375 (m). − ^1H NMR (270 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.3 Hz, 3 H, 7-Me), 0.89 (t, *J* = 6.7 Hz, 6 H, 1,17-Me), 1.00−1.40 (m, 29 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-H). − ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 14.1, 19.7, 22.7, 27.1, 29.4, 29.7, 29.8, 30.1, 31.97, 32.00, 32.8, 37.1. − $C_{18}H_{38}$ (254.5): calcd. C 84.95, H 15.05; found C 84.71, H 15.10.

(*S*)-7-Methylheptadecane [(*S*)-1]: In the same manner as described above (*R*)-**7** (1.51 g, 3.94 mmol) was converted into 0.99 g (99%) of (*S*)-**1** as a colorless oil. − n_D^{27} = 1.4371. − $[\alpha]_D^{26}$ = +0.275 ± 0.001 (*c* = 5.025, hexane). − GC (column: Nihon chromato works, Ltd. Rascot NC−17, 0.25 mm × 30 m, 100°C + 3.0°C/min; carrier gas: He, press 1.0 kg/cm^2, t_R = 32.7 min (99%). − $C_{18}H_{38}$ (254.5): calcd. C 84.95, H 15.05; found C 84.86, H 14.91. Its spectral data were identical to those of (*R*)-**1**.

(*R*)-2-Methyl-1-octanol Tetrahydropyranyl Ether [(*R*)-12]: To a stirred and cooled solution of (*S*)-**11** (43.9 g, 153 mmol) in dry THF (300 mL) at −78°C under argon was added dropwise a solution of *n*-pentylmagnesium bromide in dry THF (300 mL), previously prepared from Mg (18.0 g, 740 mmol) and *n*-pentyl bromide (92.0 g, 609 mmol), followed by a solution of dilithium tetrachlorocuprate (0.1 M in THF, 15 mL, 1.5 mmol). The resulting mixture was allowed to warm to 0°C whilst stirring for 38 h. The mixture was then poured into saturated aqueous NH_4Cl 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 (610 g, hexane/ethyl acetate 100:1) to give 30.5 g [90% from (*R*)-**10**] of (*R*)-**12** as a colorless oil. − n_D^{27} = 1.4408. − $[\alpha]_D^{24}$ = +0.39 (*c* = 1.63, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1120 cm^{-1} (m), 1035 (m). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.85−0.95 (m, 6 H, 2-Me, 8-H), 1.10−1.85 (m, 17 H, 2-, 3-, 4-, 5-, 6-, 7-, 3′, 4′, 5′-H), 3.00−4.00 (m, 4 H, 1-, 6′-H), 4.56 (br, 1 H, 2′-H). − $C_{14}H_{28}O_2$ (228.4): calcd. C 73.63, H 12.36; found C 73.40, H 12.47.

(*S*)-2-Methyl-1-octanol Tetrahydropyranyl Ether [(*S*)-12]: In the same manner as described above (*R*)-**11** (30.3 g, 92.6 mmol) was converted into 17.4 g [85% from (*S*)-**10**] of (*S*)-**12**. − n_D^{23} = 1.4418. − $[\alpha]_D^{23}$ = +0.63 (*c* = 1.60, $CHCl_3$). − $C_{14}H_{28}O_2$ (228.4): calcd. C 73.63, H 12.36; found C 74.20, H 12.83. The IR and NMR spectra of (*S*)-**12** were identical to those of (*R*)-**12**.

(*R*)-2-Methyl-1-octanol [(*R*)-13]: A mixture of **12** (30.1 g, 132 mmol) and *p*-TsOH·H_2O (0.1 g, 0.05 mmol) in MeOH (700 mL) was stirred for 3 h at 70°C. After this time it was cooled to 0°C, neutralized with K_2CO_3, 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 distilled to give 17.2 g (91%) of (*R*)-**13**. − b.p. 75−77°C/3 Torr. − n_D^{25} = 1.4310. − $[\alpha]_D^{25}$ = +13.2 (*c* = 1.63, EtOH). − IR (film): $\tilde{\nu}_{max}$ = 3300 cm^{-1} (s, O−H), 1305 (s, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.80−1.05 (m, 6 H, 2-Me, 8-H), 1.10−1.80 (m, 12 H, 2-, 3-, 4-, 5-, 6-, 7-H, OH), 3.39 (dd, *J* = 10.5, 6.1 Hz, 1 H, 1-H), 3.54 (dd, *J* = 10.5, 5.6 Hz, 1 H, 1-H). − HRMS [$C_9H_{20}O^+$]: calcd. 144.1515; found. 144.1534. Due to the volatility of **13**, correct combustion analytical data could not be obtained.

(*S*)-2-Methyl-1-octanol [(*S*)-13]: In the same manner as described above (*S*)-**12** (15.0 g, 65.7 mmol) was converted into 8.64 g (91%) of (*S*)-**13**. − b.p. 68−69°C/2 Torr. − n_D^{24} = 1.4302. − $[\alpha]_D^{25}$ =

−13.1 (*c* = 1.63, EtOH). − HRMS [$C_9H_{20}O^+$]: calcd. 144.1515; found. 144.1520. The IR and NMR spectra of (*S*)-**13** were identical to those of (*R*)-**13**.

(*R*)-2-Methyloctyl Tosylate [(*R*)-14]: The alcohol (*R*)-**13** (14.6 g, 101 mmol) was converted into (*R*)-**14** (30.7 g, quant.) in the usual manner. This was employed in the next step without further purification. − IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (m, aromatic), 1360 (s,sulfonate), 1175 (s, sulfonate), 815 (s, aromatic), 665 (s, C−S).

(*S*)-2-Methyloctyl Tosylate [(*S*)-14]: In the same manner as described above (*S*)-**13** (7.43 g, 51.5 mmol) was converted into 14.9 g (quant.) of (*S*)-**14**. This was employed in the next step without further purification. The IR spectrum of (*S*)-**14** was identical to that of (*R*)-**14**.

(*R*)-2-Methyloctyl Iodide [(*R*)-15]: A mixture of (*R*)-**14** (30.7 g, 103 mmol) and sodium iodide (20.3 g, 140 mmol) in dry acetone (500 mL) was stirred and heated under reflux for 20 h. After cooling, the mixture was poured into ice water and extracted with hexane. The organic phase was washed with water, saturated aqueous $NaHCO_3$, and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was distilled to give 22.9 g [89% from (*R*)-**13**] of (*R*)-**15**. − b.p. 72−73°C/3 Torr. − n_D^{25} = 1.4865. − $[\alpha]_D^{25}$ = −2.77 (*c* = 2.36, hexane). − IR (film): $\tilde{\nu}_{max}$ = 1195 cm^{-1} (s). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.80−1.05 (m, 6 H, 2-Me, 8-H), 1.10−1.60 (m, 12 H, 2-, 3-, 4-, 5-, 6-, 7-H), 3.12 (dd, *J* = 9.7, 5.1 Hz, 1 H, 1-H), 3.27 (dd, *J* = 9.7, 4.4 Hz, 1 H, 1-H). − $C_9H_{19}I$ (254.2): calcd. C 42.53, H 7.54; found C 42.61, H 7.54.

(*S*)-2-Methyloctyl Iodide [(*S*)-15]: In the same manner as described above (*S*)-**14** (14.9 g, 49.9 mmol) was converted into 11.7 g [90% from (*S*)-**13**] of (*S*)-**15**. − b.p. 68−70°C/2 Torr. − n_D^{23} = 1.4882. − $[\alpha]_D^{27}$ = +3.28 (*c* = 2.22, hexane). The spectral data of (*S*)-**15** were identical to those of (*R*)-**15**.

(*R*)-3-Methyl-1-(phenylsulfonyl)nonane [(*R*)-16]: *n*BuLi (1.56 M 1.9 mL, 3.0 mmol) was added dropwise to a solution of methylphenylsulfone (1.00 g, 6.4 mmol) in dry THF (20 mL) and dry hexamethylphosphoric triamide (HMPA, 1.5 mL) at −78°C under argon, and the mixture was stirred and warmed up to −30°C. After this, the solution was re-cooled to −78°C and treated dropwise with a solution of (*R*)-**15** (765 mg, 2.56 mmol) in dry THF (20 mL). This reaction mixture was allowed to warm to room temperature whilst stirring for 24 h. After this time it was quenched with saturated aqueous NH_4Cl and then extracted with diethyl ether. The extract was washed with water and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (20 g, hexane/ethyl acetate 25:1) to give 0.66 g (92%) of (*R*)-**16**. − n_D^{23} = 1.5049. − $[\alpha]_D^{23}$ = −5.49 (*c* = 1.49, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1585 cm^{-1} (w, aromatic), 1445 (s), 1305 (s, sulfonate), 1150 (vs, sulfonate), 740 (s, aromatic), 690 (s, C−S). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.78−0.96 (m, 6 H, 3-Me, 9-H), 1.10−1.70 (m, 13 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-H), 2.99−3.17 (m, 2 H, 1-H), 7.54−7.67 (m, 3 H, aromatic), 7.86−7.97 (m, 2 H, aromatic). − $C_{16}H_{26}O_2S$ (282.5): calcd. C 68.04, H 9.28; found C 67.83, H 9.11.

(*S*)-3-Methyl-1-(phenylsulfonyl)nonane [(*S*)-16]: In the same manner as described above (*S*)-**15** (949 mg, 3.18 mmol) was converted into 683 mg (76%) of (*S*)-**16**. − n_D^{23} = 1.5048. − $[\alpha]_D^{23}$ = +5.48 (*c* = 1.58, $CHCl_3$). − $C_{16}H_{26}O_2S$ (282.5): calcd. C 68.04, H 9.28; found C 68.20, H 9.38. The IR and ^{1}H NMR spectra of (*S*)-**16** were identical to those of (*R*)-**16**.

(7*R*,9*RS*,11*R*)-7,11-Dimethyl-9-phenylsulfonylheptadecane [(7*R*,9*RS*,11*R*)-17]: *n*-Butyllithium (1.68 M, 0.95 mL, 1.6 mmol) was added dropwise to a solution of (*R*)-**16** (427 mg, 1.51 mmol) and dry hexamethylphosphoric triamide (HMPA, 1.5 mL) in dry THF (6 mL) at −78°C under argon. To the resulting mixture was added a solution of (*R*)-**15** (500 mg, 1.68 mmol) in dry THF (6 mL) at −78°C. It was allowed to warm to room temperature whilst stirring for 2 h, then poured into saturated aqueous NH_4Cl, and extracted with diethyl ether. The ethereal extract 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 100:1) to give 494 mg (80%) of (7*R*,9*RS*,11*R*)-**17**. − n_D^{21} = 1.4935. − $[\alpha]_D^{23}$ = −17.4 (*c* = 1.36, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1585 cm^{-1} (vw, aromatic), 1445 (m), 1305 (s, sulfonate), 1145 (vs, sulfonate), 735 (s, aromatic), 690 (s, C−S). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.75−1.05 (m, 12 H, 1-, 17-H, 7-, 11-Me), 1.05−1.80 (m, 26 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H), 2.90−3.10 (m, 1 H, 9-H), 7.50−7.70 (m, 3 H, aromatic), 7.70−8.00 (m, 2 H, aromatic). − $C_{25}H_{44}O_2S$ (408.7): calcd. C 73.47, H 10.85; found C 73.68, H 11.23.

(7*R*,9*RS*,11*S*)-7,11-Dimethyl-9-phenylsulfonylheptadecane [(7*R*,9*RS*,11*S*)-17]: In the same manner as described above (*R*)-**16** (663 mg, 2.35 mmol) and (*S*)-**15** (700 mg, 2.34 mmol) were converted into 814 mg (85%) of (7*R*,9*RS*,11*S*)-**17**. − n_D^{22} = 1.4930. − $[\alpha]_D^{22}$ = 0 (*c* = 1.49, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1585 cm^{-1} (vw, aromatic), 1445 (m, aromatic), 1305 (s, sulfonate), 1145 (vs, sulfonate), 735 (s, aromatic), 690 (s, C−S). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.72−0.97 (m, 12 H, 1-, 17-H, 7-, 11-Me), 1.02−1.80 (m, 26 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H), 2.90−3.20 (m, 1 H, 9-H), 7.53−7.67 (m, 3 H, aromatic), 7.80−7.94 (m, 2 H, aromatic). − $C_{25}H_{44}O_2S$ (408.7): calcd. C 73.47, H 10.85; found C 73.56, H 10.71.

(7*S*,9*RS*,11*S*)-7,11-Dimethyl-9-phenylsulfonylheptadecane [(7*S*,9*RS*,11*S*)-17]: In the same manner as described above (*S*)-**16** (640 mg, 2.27 mmol) and (*S*)-**15** (700 mg, 2.34 mmol) were converted into 757 mg (82%) of (7*S*,9*RS*,11*S*)-**17**. − n_D^{23} = 1.4935. − $[\alpha]_D^{23}$ = +17.7 (*c* = 1.46, $CHCl_3$). The IR and ^{1}H NMR spectra of (7*S*,9*RS*,11*S*)-**17** were identical to those of (7*R*,9*RS*,11*R*)-**17**. − $C_{25}H_{44}O_2S$ (408.7): calcd. C 73.47, H 10.85; found C 73.28, H 10.58.

(7*R*,11*R*)-7,11-Dimethylheptadecane [(7*R*,11*R*)-2]: Sodium amalgam was prepared from Hg (13 g) and Na (750 mg, 35 mmol) under argon in the usual manner. A solution of (7*R*,9*RS*,11*R*)-**17** (417 mg, 1.02 mmol) in EtOH (8 mL) was added dropwise to the prepared sodium amalgam under argon. The reaction mixture was stirred for 6 h at room temperature and then diluted with hexane. The mixture was filtered through a pad of Celite, and the filtrate was washed with water and brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (4 g, hexane) to give a mixture of (7*R*,11*R*)-**2** and inseparable by-product(s). To a solution of this mixture in hexane (15 mL) was added *m*-chloroperbenzoic acid (MCPBA, 80%, 500 mg, 2.29 mmol) at 0°C. The resulting mixture was stirred for 12 h at room temperature. Subsequently, aqueous $Na_2S_2O_3$ was added to the reaction mixture to destroy the unreacted MCPBA. It was then stirred for 1 h and extracted with hexane. The organic phase was washed with aqueous $Na_2S_2O_3$, water, saturated aqueous $NaHCO_3$ and brine, dried with Na_2SO_4, and concentrated in vacuo. The residue was chromatographed on silica gel (4 g, hexane) and distilled to give 79 mg (33%) of (7*R*,11*R*)-**2**. − b.p. 121−123°C/4 Torr. − n_D^{23} = 1.4408. − $[\alpha]_D^{22}$ = −1.26 ± 0.04 (*c* = 1.38, hexane). − GC (column: Neutrabond−5 (5% phenyl-, 95% methylpolysiloxane), 0.25 mm × 30 m, 100°C + 3.0°C/min; carrier gas: He, press 0.6 kg/cm^2, t_R = 29.1 min (97%). − GC-MS (70 eV); *m*/*z* (%): 268 (2.6) [M^+], 253 (2.8), 239 (1.6), 225 (1.2), 211 (0.8), 197 (0.9), 183 (20.9), 169 (1.3), 155 (7.7), 141 (4.0), 127 (10.9), 112 (55.4), 99 (31.6), 85

(88.4), 71 (100). − IR (film): $\tilde{\nu}_{max}$ = 2955 cm^{-1} (s), 2925 (vs), 2855 (s), 1465 (m), 1375 (m), 725 (w). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.80−1.02 (m, 12 H, 7-, 11-Me, 1-, 17-H), 1.02−1.52 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H). − ^{13}C NMR (22.4 MHz, $CDCl_3$): δ = 14.1, 19.7, 22.7, 24.5, 27.1, 29.7, 32.0, 32.8, 37.2, 37.4. − $C_{19}H_{40}$ (268.5): calcd. C 84.99, H 15.01; found C 85.23, H 15.12.

(7*R*,11*S*)-7,11-Dimethylheptadecane [(7*R*,11*S*)-2]: In the same manner as described above (7*R*,9*RS*,11*S*)-**17** (506 mg, 1.24 mmol) was converted into 103 mg (31%) of (7*R*,11*S*)-**2**. − b.p. 123−125°C/4 Torr. − n_D^{23} = 1.4402. − $[\alpha]_D^{22}$ = 0 (*c* = 1.53, hexane). − GC (column: Neutrabond−5 (5% phenyl-, 95% methylpolysiloxane), 0.25 mm × 30 m, 100°C + 3.0°C/min; carrier gas: He, press 0.6 kg/cm^2, t_R = 29.1 min (97%). − GC-MS (70 eV); *m*/*z* (%): 268 (3.8) [M^+], 253 (5.2), 239 (3.4), 225 (2.1), 211 (1.6), 197 (2.4), 183 (48.4), 169 (1.9), 155 (13.0), 141 (7.0), 127 (17.1), 112 (83.1), 99 (40.5), 85 (100), 71 (99.9). − IR (film): $\tilde{\nu}_{max}$ = 2955 cm^{-1} (s), 2925 (vs), 2855 (s), 1465 (m), 1375 (m), 725 (w). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.81−1.02 (m, 12 H, 7-, 11-Me, 1-, 17-H), 1.02−1.52 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H). − ^{13}C NMR (22.4 MHz, $CDCl_3$): δ = 14.1, 19.8, 22.7, 24.5, 27.1, 29.7, 32.0, 32.8, 37.1, 37.5. − $C_{19}H_{40}$ (268.5): calcd. C 84.99, H 15.01; found C 85.09, H 15.16.

(7*S*,11*S*)-7,11-Dimethylheptadecane [(7*S*,11*S*)-2]: In the same manner as described above (7*S*,9*RS*,11*S*)-**17** (460 mg, 1.13 mmol) was converted into 121 mg (40%) of (7*S*,11*S*)-**2**. − b.p. 128−130°C/4 Torr. − n_D^{23} = 1.4410. − $[\alpha]_D^{22}$ = +1.77±0.04 (*c* = 1.41, hexane). − GC (column: Neutrabond−5 (5% phenyl-, 95% methylpolysiloxane), 0.25 mm × 30 m, 100°C + 3.0°C/min; carrier gas: He, press 0.6 kg/cm^2, t_R = 28.8 min (98%). − GC-MS (70 eV); *m*/*z* (%): 268 (3.1) [M^+], 253 (6.8), 239 (3.8), 225 (1.9), 211 (1.3), 197 (2.4), 183 (48.3), 169 (2.4), 155 (17.9), 141 (8.1), 127 (20.7), 112 (99.9), 99 (49.7), 85 (99.9), 72 (100). − $C_{19}H_{40}$ (268.5): calcd. C 84.99, H 15.01; found C 84.77, H 15.42. The IR and NMR spectra of (7*S*,11*S*)-**2** were identical to those of (7*R*,11*R*)-**2**.

(2*R*,6*S*)-2,6-Dimethyl-1,7-heptanedioic Acid [(2*R*,6*S*)-21]: Diethyl methylmalonate (**18**, 525 g, 3.00 mol) was added to a stirred solution of NaOEt [from 66.7 g (2.90 mol) of Na] in abs. EtOH (1700 mL). To this mixture was added 1,3-dibromopropane (**19**, 250 g, 1.23 mol) whilst stirring at room temperature. It was then stirred and heated under reflux for 24 h. After cooling, saturated aqueous NH_4Cl was added, and the mixture was concentrated in vacuo. The residue was extracted with ethyl acetate and washed with water and brine, dried with $MgSO_4$ and concentrated in vacuo to give 540 g (quant.) of crude **20**. To a stirred solution of KOH (418 g, 7.44 mol) in H_2O (1000 mL) was added a solution of **20** in MeOH (500 mL), and the mixture was stirred and heated under reflux for 22 h. MeOH was removed in vacuo. It was then acidified with conc. HCl to pH <2 and the solution was stirred and heated under reflux for 80 h. After cooling, the mixture was extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried with $MgSO_4$ and concentrated in vacuo to give 101 g (43%) of **21**. A very small amount of crystalline (2*R*,6*S*)-**21** was added to the crude **21** and it was set aside at room temperature. The separated crystals of **21** {57 g, *meso*-**21**:(±)-**21** = 3:1} were collected on a filter and recrystallized from hexane/ether (2:1) to give (2*R*,6*S*)-**21** (14.7 g, 88.0% *de*). The crude (2*R*,6*S*)-**21** (88.0% *de*) was recrystallized from hexane/ether (2:1) to give (2*R*,6*S*)-**21** (5.47 g, 96.7% *de*). − m.p. 78−80°C (Ref.[6] m.p. 81−81.5°C). − IR (KBr): $\tilde{\nu}_{max}$ = ≈3200 cm^{-1} (br, CO_2 H), ≈ 2500 cm^{-1} (br, CO_2 H), 1700 (s, C=O), 1460 (s), 1235 (s, C−O), 945 (m). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.17 (d, *J* = 7.0 Hz, 6 H, 2-, 6-Me), 1.24−1.66 (m, 6 H, 3-, 4-, 5-H), 2.43−2.50 (m, 2 H, 2-, 6-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.3, 25.2, 34.0, 39.8, 183.6. − $C_9H_{16}O_4$ (188.2): calcd. C 57.43, H 8.57; found C 57.43, H 8.69.

(2*R*,6*S*)-2,6-Dimethyl-1,7-heptanediol [(2*R*,6*S*)-22]: A solution of (2*R*,6*S*)-**21** (5.40 g, 29.0 mmol) in dry diethyl ether (70 mL) was added to a stirred, ice-cooled suspension of $LiAlH_4$ (9.20 g, 242 mmol) in dry diethyl ether (250 mL), and stirring was then continued for 2 h at room temperature. It was then ice-cooled, and the unreacted $LiAlH_4$ was destroyed by successive addition of water (9.2 mL), 15% aqueous NaOH (9.2 mL), and water (27.6 mL). After stirring for 1 h at room temperature, $MgSO_4$ was added to the mixture which was then filtered. The filtrate was concentrated in vacuo. The residue was distilled to give 3.04 g (66%) of (2*R*,6*S*)-**22**. − b.p. 122−125°C/2 Torr. − n_D^{21} = 1.4615. − IR (film): $\tilde{\nu}_{max}$ = 3335 cm^{-1} (s, O−H), 1030 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.82 (d, *J* = 6.4 Hz, 6 H, 2-, 6-Me), 1.10−1.75 (m, 10 H, 2-, 3-, 4-, 5-, 6-H, O−H), 3.40 (dd, *J* = 10.8, 6.3 Hz, 2 H, 1-, 7-H), 3.55 (dd, *J* = 10.8, 5.9 Hz, 2 H, 1-, 7-H). − $C_9H_{20}O_4$ (160.3): calcd. C 67.45, H 12.58; found C 67.44, H 12.51.

(2*R*,6*S*)-2,6-Dimethyl-1,7-ditosyloxyheptane [(2*R*,6*S*)-23]: The alcohol (2*R*,6*S*)-**22** (1.00 g, 6.24 mmol, 96.7% *de*) was converted into (2*R*,6*S*)-**23** (2.74 g, 94%) in the usual manner, which was used immediately in the next reaction. − IR (film): $\tilde{\nu}_{max}$ = 1600 cm^{-1} (w, aromatic), 1465 (m), 1360 (vs, sulfonate), 1175 (vs, sulfonate), 815 (s, aromatic), 665 (s, C−S).

(7*R*,11*S*)-7,11-Dimethylheptadecane [(7*R*,11*S*)-2]: To a stirred and cooled solution of (2*R*,6*S*)-**23** (2.66 g, 5.68 mmol) in dry THF (50 mL) at −78°C under argon was added dropwise a solution of *n*-pentylmagnesium bromide in dry THF (30 mL), previously prepared from Mg (2.70 g, 111 mmol) and *n*-pentyl bromide (9.06 g, 60.0 mmol), followed by a solution of dilithium tetrachlorocuprate (0.07 M in THF, 20 mL, 1.4 mmol). The resulting mixture was allowed to warm to 0°C with stirring for 40 h. The mixture was then poured into saturated aqueous NH_4Cl 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 (30 g, hexane) and distilled to give 1.20 g (79%) of (7*R*,11*S*)-**2**. − b.p. 118−120°C/2 Torr. − n_D^{23} = 1.4404. − IR (film): $\tilde{\nu}_{max}$ = 2955 cm^{-1} (s), 2925 (vs), 2855 (s), 1465 (m), 1375 (m), 725 (w). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.81−1.02 (m, 12 H, 7-, 11-Me, 1-, 17-H), 1.02−1.52 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H). − ^{13}C NMR (22.4 MHz, $CDCl_3$): δ = 14.1, 19.8, 22.7, 24.5, 27.1, 29.7, 32.0, 32.8, 37.1, 37.5. These spectral data coincided with those of (7*R*,11*S*)-**2** prepared previously.

Determination of the Diastereomeric Purity of (2*R*,6*S*)-21: A mixture of (2*R*,6*S*)-**21** (1 mg), an excess of (*S*)-1-(1-naphthyl)ethylamine (10 eq), DMAP (0.5 eq) and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (4 eq) in CH_2Cl_2 (0.5 mL) was stirred at room temperature. This mixture was diluted with CH_2Cl_2 and washed with dilute HCl, saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel ($CHCl_3$/MeOH 15:1) to give 3 mg (quant.) of the *bis*-amide of (2*R*,6*S*)-**21**. − HPLC analysis [column: PEGASIL Silica 60−5, 4.6 mm × 25 cm; solvent: hexane/CH_2Cl_2/THF, 6:4:1, flow rate: 0.1 mL/min; detection: 254 nm], t_R = 40.6 min [(2*R*,6*R*)-**21**, 0.89%], 55.3 min [(2*S*,6*S*)-**21**, 0.73%], 58.3 min [(2*R*,6*S*)-**21**, 98.4%]. The diastereomeric purity of (2*R*,6*S*)-**21** was 96.7% *de*.

Acknowledgments

We thank Mr. T. Tasaku for his contribution to the early phase of this work. Our thanks are due to Mitsubishi Chemical Co., Nissan Chemical Co. and Nitto Denko Co. for their financial support. This work was also supported by a Grant-in-Aid for Scientific Research (No.09680576), Japanese Ministry of Education, Science, Sports and Culture.

[1] R. Gries, G. Gries, J. Li, C. T. Maier, C. R. Lemmon, K. N. Slessor, *J. Chem. Ecol.* **1994**, *20*, 2501−2511.
[2] C. T. Maier, R. Gries, G. Gries, *J. Chem. Ecol.* **1998**, *24*, 491−500.
[3] C. M. Duff, G. Gries, K. Mori, Y. Shirai, M. Seki, H. Takikawa, T. Sheng, K. N. Slessor, R. Gries, C. T. Maier, *J. Chem. Ecol.* in press.
[4] C. Fouquet, M. Schlosser, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 82−83.
[5] K. Mori, H. Takikawa, *Liebigs Ann. Chem.* **1991**, 497−500.
[6] F. S. Kipping, *J. Chem. Soc.* **1895**, *67*, 143−155.
[7] R. Chênevert, M. Desjardins, *J. Org. Chem.* **1996**, *61*, 1219−1222.
[8] Y. Nakamura, K. Mori, *Eur. J. Org. Chem.* **1999**, 2175−2182.

Received May 14, 1999
[O99271]