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Enantioselective synthesis of three stereoisomers of 5,9-dimethylpentadecane, sex pheromone component of *Leucoptera coffeella*, from (−)-isopulegol

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Abstract—The coffee leaf miner, *Leucoptera coffeella*, is an economically important pest of coffee trees in Brazil. It has been demonstrated that the main sex pheromone component of this species is 5,9-dimethylpentadecane, however the stereochemistry of the natural pheromone remains unknown. We describe herein an enantioselective synthesis of three stereoisomers of 5,9-dimethylpentadecane from commercial (−)-isopulegol.

1. Introduction

The coffee leaf miner moth, *Leucoptera coffeella*, is an important pest of coffee trees in Brazil. The female-produced sex pheromone of this leaf miner moth has been proposed by Francke et al. to consist of 5,9-dimethylpentadecane and 5,9-dimethylhexadecane as the major and minor components, respectively.[1] Although it was identified in 1988, the stereochemistry of the natural pheromone remains unknown.

Compounds having stereochemically defined alkyl-branched hydrocarbon chains are widespread in nature. This fact is particularly important when enantiomerically active pheromones are considered.[2] Several insect pheromones present the 1,5-dimethyl skeleton.[3] It is evident from the facts discussed above that it is necessary to develop new synthetic methodologies for the preparation of this class of compound.

Kuwahara et al. have prepared all four 5,9-dimethylpentadecane isomers using a convergent approach in 15 steps.[4] The methyl esters of (*S*)- and (*R*)-3-hydroxy-2-methylpropanoic acid were used as chiral sources, following the procedure reported by Mori et al.[5]

In this paper we present the enantioselective synthesis of (5*S*,9*S*)-5,9-dimethylpentadecane **1** and its diastereoisomers (5*R*,9*S*)- and (5*S*,9*R*)-**1** starting from commercially available (−)-isopulegol. Our synthetic strategy was based on a methodology developed by Ferreira et al. and applied for the synthesis of two isomers of methyl 2,6,10-trimethyldodecanoate, male-produced pheromone of stink bugs *Euschistus* sp.,[6] and of (2*R*,3*R*,7*S*)-diprionol, sex pheromone component of the pine sawfly, *Neodiprion sertifer*.[7]

2. Results and discussion

Scheme 1 shows the retrosynthetic route to prepare three of the four possible stereoisomers of 5,9-dimethylpentadecane. (5*S*,9*S*)-**1** was obtained directly from (−)-isopulegol **2** following the synthetic route described in the Scheme 2, while (5*R*,9*S*)- and (5*S*,9*R*)-**1** were obtained from (+)-neoisopulegol **2a**, prepared from **2** in 72% yield in two steps using Bohlmann's conditions (Scheme 3).[8]

In the key step, the stereogenic center at C-5 of (5*S*,9*S*)-**1** was established through a stereoselective hydroboration of (−)-isopulegol **2**, with a diastereoisomeric ratio of 7:1 (measured by chiral GC).[9] The two stereoisomers of diol **4** formed were readily separated by flash column chromatography followed by recrystallization, affording pure (1*R*,3*R*,4*S*,8*R*)-diol **4** in 84% yield.

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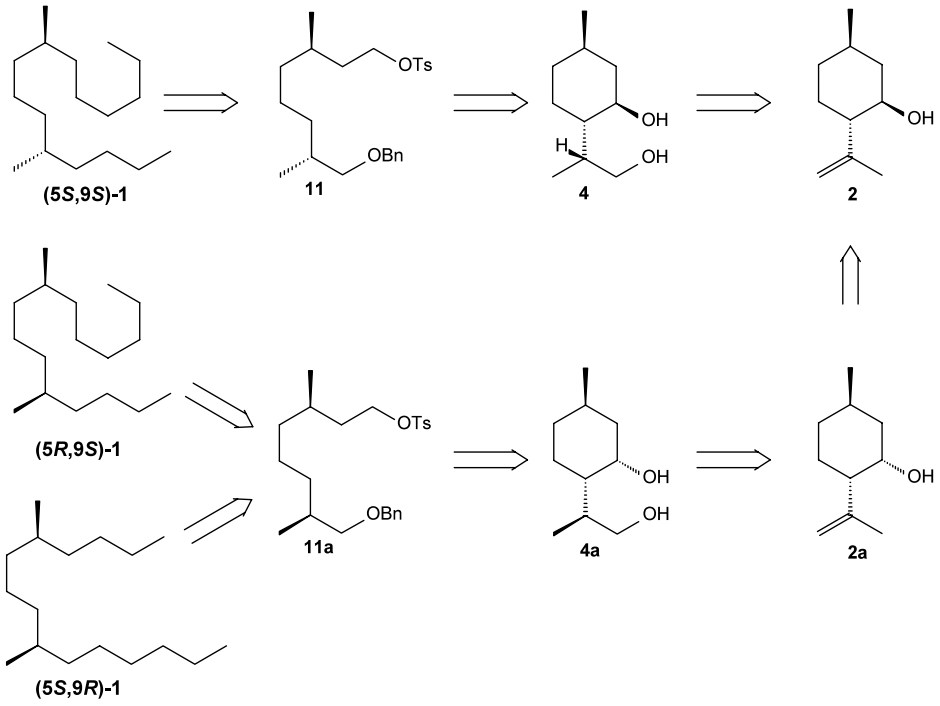
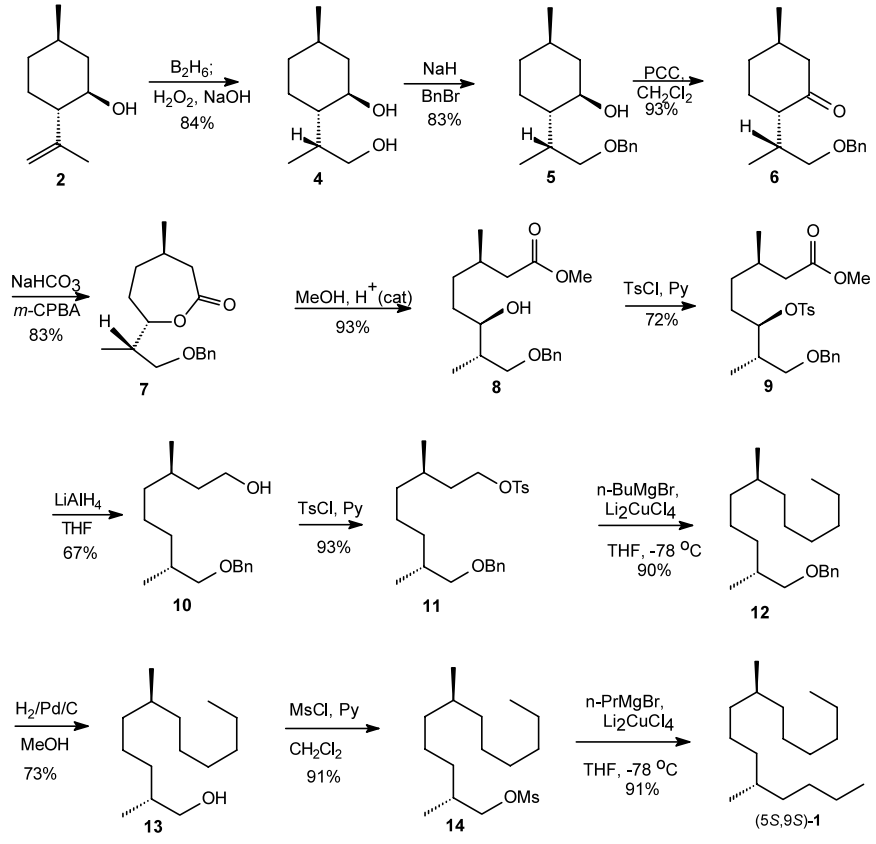
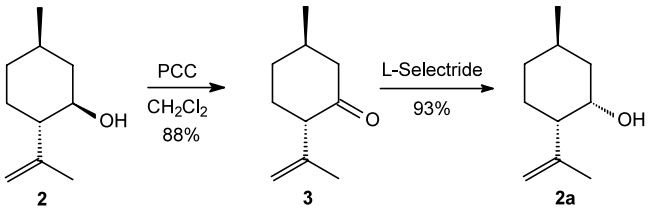


Scheme 1. Retrosynthetic analysis.



Scheme 2. Synthetic route for the preparation of (5*S*,9*S*)-dimethylpentadecane **1**.

Selective protection of the primary alcohol with benzyl bromide furnished alcohol **5**, which was oxidized with PCC to produce ketone **6**. Bayer–Villiger oxidation of this ketone with *m*-CPBA gave lactone **7**. Methanolysis of this lactone furnished hydroxyester **8**. To remove the oxygen function at C-3, the tosylate **9** was prepared.



Scheme 3. Preparation of neoisopulegol.

Reduction of both tosylate and methyl ester groups with $LiAlH_4$ gave alcohol **10**. In this step, initially, we obtained a 4:1 mixture of the desired product **10** and an olefin, resulting from an elimination of the tosyl group. To overcome this problem, the reaction mixture was cooled to 0°C.

Alcohol **10** was converted into its corresponding tosylate **11** and then coupled with n-butyl magnesium bromide, using Li_2CuCl_4 as catalyst,[10] affording **12**. Catalytic hydrogenation of the benzyl group furnished alcohol **13**. In our first attempt to prepare (5*S*,9*S*)-**1**, alcohol **13** was converted into its corresponding tosylate and then coupled with *n*-propyl magnesium bromide, following the same procedure described to prepare **12**, but the desired product was not obtained. Several experiments were carried out, changing the ratio of the Grignard reagent/ROTs, catalyst amount and temperature, but we just obtained the starting material and a by-product resulting from substitution of the tosyl group by bromine. Finally, alcohol **13** was converted into its corresponding mesylate which was successfully coupled with *n*-propyl magnesium bromide affording the desired alkane (5*S*,9*S*)-**1** in 91% yield.

In the same manner as described above, (+)-neoisopulegol **2a** was transformed into tosylate (3*R*,7*S*)-**11**, which was then converted to (5*R*,9*S*)-**1** and (5*S*,9*R*)-**1** only changing the alkylation sequence, as shown in the Scheme 4.

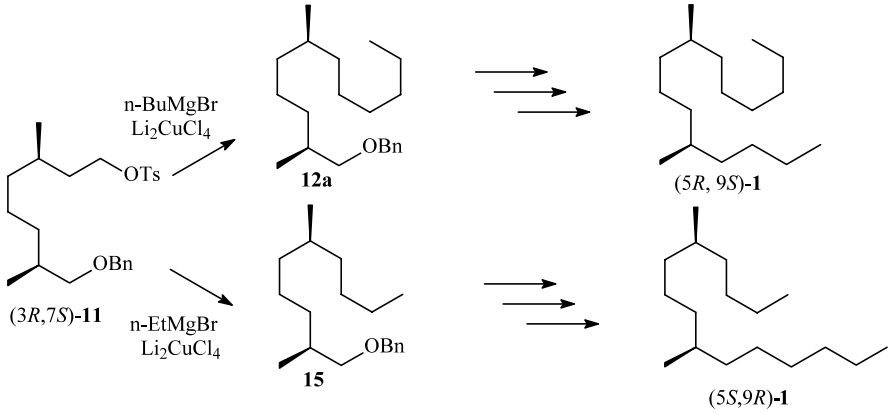
In conclusion, we have prepared three stereoisomers of (5*S*,9*S*)-5,9-dimethylpentadecane **1** in 12 steps and 16% overall yield, and its diastereoisomers (5*R*,9*S*)- and (5*S*,9*R*)-**1** in 14 steps, 7.2 and 6.5% overall yield, respectively, using commercially available (–)-isopulegol as starting material. The remaining stereoisomer (5*R*,9*R*)-**1** can be prepared employing the same methodology from commercial (+)-isopulegol. Since no chiroptical data of the natural pheromone are available, we have to rely on the careful comparison of pheromone activity of the stereoisomers of **1** in order to deduce the absolute configuration of the natural product. The biological study is in progress and will be published elsewhere in due course.

3. Experimental

Unless otherwise noted, all commercially available reagents were purchased from Aldrich Chemical Co. Reagents and solvents were purified when necessary according to the usual procedures described in the literature. The IR spectra refer to films and were measured on a Bomem M102 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker ARX-200 (200 and 50 MHz, respectively) and DRX-400 (400 and 100 MHz, respectively). Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Mass Spectra were recorded on a Shimadzu GCMS-QP5000. HRMS were obtained by direct injection in a VG-Autospec. Analytical thin-layer chromatography was performed on a 0.25 μm film of silica gel containing fluorescent indicator UV_{254} supported on an aluminum sheet (Sigma-Aldrich). Flash column chromatography was performed using silica gel (Kieselgel 60, 230–400 mesh, E. Merck). Gas chromatography was performed in a Shimadzu GC-17A with H_2 as carrier and using a DB-5 column. Chiral GC was performed in a HP 5890 with H_2 as carrier (14 psi) and using an heptakis(2,6-di-*O*-methyl-3-*O*-phenyl)-β-cyclodextrin column (20% in OV 1701, w/w, 25 m, 0.25 mm i.d.). Elemental analyses were performed on a Fisons EA 1108 CHNS-O.

3.1. Isopulegone 3

(–)-Isopulegol **2** (7.50 g; 48.7 mmol) was added to a suspension of PCC (15.75 g; 73.0 mmol) in dry CH_2Cl_2 (230 mL) at room temperature. After 3 h, dry ether (230 mL) was added and the mixture was filtered



Scheme 4. Synthesis of (5*R*,9*S*)- and (5*S*,9*R*)-**1**.

through three layer column containing Celite, silica gel and charcoal and then concentrated and distilled under vacuum yielding ketone **3** (6.53 g, 88.2% yield) as a colorless oil. $[\alpha]_D^{25}=-7.25$ (*c* 6.20, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3073, 2953, 2928, 3870, 1712, 1647. ^1H NMR (200 MHz, $CDCl_3$) δ 1.04 (d, *J* 6.0 Hz, 3H), 1.39–1.50 (m, 1H), 1.75 (dd, *J* 0.8 and 1.4 Hz, 3H), 1.80–2.12 (m, 5H), 2.41 (ddd, *J* 2.2, 3.2 and 12.8 Hz, 1H), 2.96 (dd, *J* 5.2, and 12.8 Hz, 1H), 4.70–4.75 (m, 1H), 4.91–4.96 (m, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.26, 22.25, 31.11, 33.78, 35.24, 50.48, 57.64, 112.76, 143.42, 210.18.

3.2. (+)-Neoisopulegol 2a

A solution of L-Selectride in THF (1.0 M, 64.0 mL, 64.0 mmol) was added dropwise at −78°C to a previously prepared solution of isopulegone **3** (6.50 g, 42.7 mmol) in dry THF (130 mL). The reaction temperature was raised slowly at rt (2 h). After stirring for 14 h, the mixture was cooled to 0°C, H_2O_2 (22 mL, 30 wt.% solution in water) was slowly added, followed by aqueous NaOH (15 mL, 15%), and stirred for an additional 30 min at room temperature. The organic layer was washed with brine (100 mL), dried over $MgSO_4$, filtered, and then concentrated and distilled under vacuum yielding compound **2a** (6.11 g, 92.7% yield) as a colorless oil. $[\alpha]_D^{25}=+28.7$ (*c* 17.2, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3457, 3085, 2947, 2925, 2868, 1643, 1450. ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (d, *J* 6.4 Hz, 3H), 0.92–1.16 (m, 2H), 1.40–1.52 (m, 2H), 1.65–1.77 (m, 3H), 1.79 (s, 3H), 1.92–2.00 (m, 2H), 4.00 (br s, 1H), 4.79 (s, 1H), 4.95 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.20, 22.79, 23.94, 25.81, 34.77, 40.92, 48.42, 66.28, 111.28, 147. 34. Anal. calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.75, H, 11.64.

3.3. (−)-(1*R*,3*R*,4*S*,8*R*)-*p*-Menthane-3,9-diol 4

$BF_3{\cdot}Et_2O$ (2.8 mL, 22.2 mmol) was added dropwise to a stirred suspension of $NaBH_4$ (0.74 g, 19.6 mmol) in diglyme (13 mL) at room temperature under nitrogen. The generated diborane was transferred via a cannula into a solution of (−)-isopulegol **2** (2.00 g, 13.0 mmol) in dry THF (52 mL) under nitrogen at 0°C. After stirring for 3 h, H_2O (2.0 mL) was slowly added, followed by H_2O_2 (3.0 mL, 30 wt% solution in water) and aqueous NaOH (3.0 mL, 30%), and stirred for an additional 30 min at room temperature. The reaction mixture was extracted with ether (3×40 mL) and the separated organic layer was washed with brine (30 mL) and dried over $MgSO_4$. The oil obtained was purified by column chromatography (hexane/ethyl acetate, 1:2) followed by recrystallization (cyclohexane:CH_2Cl_2, 2:1) to afford 1.88 g of diol **4** (84% yield) as colorless crystals. $[\alpha]_D^{25}=-18.5$ (*c* 5.00, $CHCl_3$), lit.[6] $[\alpha]_D^{25}=-18.6$ (*c* 10.0, $CHCl_3$). IR ($\nu_{max.}$ film, cm^{-1}): 3234, 2961, 2945, 2912, 1451, 1037. ^1H NMR (400 MHz, $CDCl_3$) δ 0.83–1.02 (m, 2H), 0.92 (d, *J* 6.5 Hz, 3H), 0.96 (d, *J* 7.3 Hz, 3H), 1.24 (dq, *J* 3.5 and 12.8 Hz, 1H), 1.35 (ddd, *J* 2.0, 3.2 and 9.8 Hz, 1H), 1.38–1.46 (m, 1H), 1.56 (dq, *J* 3.2 and 13.0 Hz, 1H), 1.64 (dqui, *J* 3.0 and 12.5 Hz, 1H), 1.78 (br s, 1H), 1.80–1.88 (m, 1H), 1.96 (ddd, *J* 1.8, 3.9 and 12.1 Hz, 1H), 3.36 (br s, 1H), 3.45 (td, *J* 4.3 and 10.6 Hz, 1H), 3.56 (dd, *J* 3.4 and 10.7 Hz, 1H), 3.65 (dd, *J* 5.5 and 10.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.92, 22.07, 29.48, 31.44, 34.56, 38.58, 44.60, 48.48, 67.18, 70.16. MS (rel. intensity) *m*/*z* 172 (M^+, 0.55), 154 (4.79), 139 (8.81), 112 (19.90), 95 (36.57), 81 (96.38), 71 (42.75), 55 (100).

3.4. (+)-(1*R*,3*S*,4*S*,8*S*)-*p*-Menthane-3,9-diol 4a

Similarly, (+)-neoisopulegol **2a** (6.10 g, 39.6 mmol) gave **4a**/**4b** (5.90 g) with a diastereoisomeric ratio of 3:1 in 87.6% overall yield. The oil obtained was purified by column chromatography (hexane/ethyl acetate, 1:2) affording pure (1*R*,3*R*,4*S*,8*R*)-diol **4a** (1.60 g). $[\alpha]_D^{25}=+17.2$ (*c* 4.00, $CHCl_3$), lit.:[6] $[\alpha]_D^{20}=+17.0$ (*c* 10.0, $CHCl_3$). IR ($\nu_{max.}$, film, cm^{-1}): 3317, 2947, 2920, 2869, 2843, 1455, 1036. ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (d, *J* 6.2 Hz, 3H), 0.99 (d, *J* 7.0 Hz, 3H), 1.07–1.32 (m, 2H), 1.41–1.91 (m, 7H), 3.45–3.70 (m, 3H), 3.66 (dd, *J* 2.8 and 10.8 Hz, 1H), 4.12 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.93, 22.44, 25.48, 26.17, 35.40, 38.17, 42.27, 46.04, 64.80, 66.34. Anal. calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.50, H, 11.42.

3.5. (−)-(1*R*,3*R*,4*S*,8*R*)-9-Benzyloxy-p-menthan-3-ol 5

Diol **4** (1.60 g, 9.3 mmol) was added dropwise to a stirred suspension of NaH (0.41 g, 10.2 mmol, 50% in mineral oil) in dry DMF (32 mL) under N_2 at 0°C. The resulting solution was cooled at −10°C and stirred for 1.5 h. The mixture was cooled at −60°C and a solution of benzyl bromide (1.10 mL, 9.3 mmol) in DMF (6.0 mL) was slowly added. The mixture was stirred at −60°C for 2 h, then the reaction temperature was raised to room temperature, and stirred for an additional 12 h. Saturated aqueous NH_4Cl (30 mL) was added, and the resulting mixture was extracted with ethyl acetate (3×40 mL). The organic layer was washed with brine (30 mL) and dried over Na_2SO_4, concentrated and the oil obtained was purified by column chromatographic (hexane:ethyl acetate, 5:1) to afford 2.01 g of the compound **5** (83% yield) as a colorless oil. $[\alpha]_D^{25}=-13.1$ (*c* 1.88, $CHCl_3$), lit.[6] $[\alpha]_D^{25}=-12.4$ (*c* 14.6, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3423, 3963, 3030, 2940, 2919, 1454, 1096. ^1H NMR (200 MHz, $CDCl_3$) δ 0.84–0.89 (m, 1H), 0.91 (d, *J* 6.4 Hz, 3H), 0.96 (d, *J* 7.4 Hz, 3H), 1.14 (dd, *J* 3.4 and 12 Hz, 1H), 1.22–1.80 (m, 5H), 1.85–2.15 (m, 2H), 3.36–3.55 (m, 3H), 3.62 (br s, 1H), 4.48 (d, *J* 12.0 Hz, 1H), 4.56 (d, *J* 12.0 Hz, 1H), 7.26–7.55 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.56, 22.19, 27.91, 31.48, 34.74, 35.51, 43.98, 48.99, 70.47, 73.36, 74.37, 127.72, 128.45, 137.57. MS (rel intensity) *m*/*z* 171 (2.67), 153 (15.52), 138 (14.54), 123 (6.62), 107 (14.34), 95 (30.17), 91 (100), 81 (34.28), 55 (34.26), 41 (44.06).

3.6. (+)-(1*R*,3*S*,4*S*,8*S*)-9-Benzyloxy-*p*-menthan-3-ol 5a

Similarly, **4a** (1.55 g, 9.0 mmol) gave **5a** (2.10 g, 89.4%) as a colorless oil. $[\alpha]_D^{25}=+3.6$ (*c* 5.60, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3428, 2945, 2916, 2867, 1453. ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, *J* 6.2 Hz, 3H), 0.97 (d, *J* 7.0 Hz, 3H), 1.05–1.19 (m, 2H), 1.40–1.93 (m, 7H), 3.28

(dd, *J* 1.4 and 2.9 Hz, 1H), 3.40 (dd, *J* 6.6 and 9.2 Hz, 1H), 3.48 (dd, *J* 3.0 and 9.2 Hz, 1H), 4.02 (br s, 1H), 4.51 (s, 2H), 7.22–7.36 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.49, 22.46, 25.38, 26.16, 35.38, 36.17, 41.90, 46.64, 66.63, 73.47, 74.16, 127.77, 128.46, 137.68. Anal. calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.59, H, 9.65.

3.7. (–)-(1*R*,4*S*,8*R*)-9-Benzyloxy-*p*-menthan-3-one 6

Alcohol **5** (3.38 g; 12.9 mmol) was added to a suspension of PCC (4.20 g, 19.3 mmol) in dry CH_2Cl_2 (105 mL) at room temperature. After 3 h, dry ether (100 mL) was added and the mixture was filtered through a three layer column containing Celite, silica gel and charcoal and then concentrated. The oil was purified by column chromatography (hexane:ethyl acetate, 5:1) to afford 3.11 g of the ketone **6** (93% yield). $[\alpha]_D^{25} = -10.8$ (*c* 1.30, $CHCl_3$), lit.[6] $[\alpha]_D^{25} = -10.5$ (*c* 36.8, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3088, 3063, 3030, 2953, 2926, 2869, 1708, 1454, 1099. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.00 (d, *J* 6.3 Hz, 3H), 1.01 (d, *J* 6.9 Hz, 3H), 1.32–1.44 (m, 1H), 1.70–1.78 (m, 1H), 1.79–1.89 (m, 2H), 1.90–2.00 (m, 1H), 2.01–2.08 (m, 1H), 2.09–2.20 (m, 1H), 2.31–2.37 (m, 2H), 3.38 (dd, *J* 6.0 and 9.1 Hz, 1H), 3.48 (dd, *J* 5.4 and 9.1 Hz, 1H), 4.46 (d, *J* 15.2 Hz, 1H), 4.49 (d, *J* 15.2 Hz, 1H), 7.24–7.27 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.48, 22.30, 29.47, 32.65, 34.09, 35.48, 50.97, 52.20, 72.92, 73.02, 127.48, 128.25, 138.73, 212.01. MS (rel. intensity) *m*/*z* 260 (M^+, 1.18), 202 (21.40), 169 (24.92), 139 (24.95), 112 (80.75), 91 (100), 69.15 (53.15), 55 (61.17).

3.8. (–)-(1*R*,4*S*,8*S*)-9-Benzyloxy-*p*-menthan-3-one 6a

Similarly, **5a** (2.05 g, 7.8 mmol) gave **6a** (1.93 g, 94.4%) as a colorless oil. $[\alpha]_D^{25} = -7.7$ (*c* 0.7, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3086, 3064, 3030, 2953, 2926, 2969, 1707, 1454, 1204, 737, 698. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.85 (d, *J* 6.8 Hz, 3H), 1.01 (d, *J* 6.0 Hz, 3H), 1.16–1.48 (m, 2H), 1.70–2.10 (m, 4H), 2.30–2.60 (m, 3H), 3.30 (dd, *J* 6.9 and 9.4 Hz, 1H), 3.36 (dd, *J* 6.0 and 9.4 Hz), 4.44 (d, *J* 12.1 Hz, 1H), 4.51 (d, *J* 12.1 Hz, 1H), 7.10–7.40 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.22, 22.35, 26.78, 30.94, 33.84, 35.20, 50.14, 50.74, 72.81, 73.20, 127.51, 127.57 (2C), 128.34 (2C), 138.68. 212.11. Anal. calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.12, H, 9.00.

3.9. (+)-(3*R*,6*S*)-3-Methyl-6-[(1′*S*)-1′-methyl-2-benzil-oxymethyl]-ε-caprolactone 7

Ketone **6** (3.07 g, 11.8 mmol) was added to a stirred solution of *m*-CPBA (40%, 6.04 g, 15.3 mmol) in CH_2Cl_2 (80 mL) containing a suspension of $NaHCO_3$ (6.00 g, 71 mmol). After stirring for 20 h at room temperature, aqueous KI (24 mL, 40%) and aqueous $NaHSO_3$ (40%, 24 mL) were added to reduce the excess of oxidant. The resulting two phase system was stirred for 10 min. After separation the organic phase was washed with brine (20 mL), dried over Na_2SO_4, concentrated and the residue was purified by column chromatography (hexane/ethyl acetate, 5:1) to afford 2.45 g of lactone **7** (75% yield). $[\alpha]_D^{25} = +2.5$ (*c* 0.85, $CHCl_3$), IR ($\nu_{max.}$, film cm^{-1}): 3033, 2959, 2928, 2871, 1729, 1454, 1102. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (d, *J* 7.0 Hz, 3H), 1.04 (d, *J* 6.7 Hz, 3H), 1.29–1.38 (m, 1H), 1.66–1.78 (m, 2H), 1.78–1.88 (m, 1H), 1.88–1.98 (m, 2H), 2.45 (dt, *J* 1.8 and 13.4 Hz, 1H), 2.54 (dd, *J* 11.5 and 13.4 Hz, 1H), 3.36 (dd, *J* 5.3 and 9.2 Hz, 1H), 3.49 (t, *J* 9.0 Hz, 1H), 4.49 (s, 2H), 4.49–4.52 (m, 1H), 7.26–7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.23, 23.96, 30.29, 32.11, 37.29, 39.39, 42.47, 71.79, 73.16, 79.03, 127.65, 128.38, 138.28, 174.96. MS (rel intensity) *m*/*z* 276 (M^+, 3.43), 230 (1.22), 170 (1.60), 152 (9.75), 128 (10.09), 11 (71.66), 91 (100), 69 (51.01), 55 (65.54).

3.10. (–)-(3*R*,6*S*)-3-Methyl-6-[(1′*R*)-1′-methyl-2-benzyl-oxymethyl]-ε-caprolactone 7a

Similarly, **6a** (1.92 g, 7.4 mmol) gave **7a** (1.55 g, 76.0%) as a white solid. $[\alpha]_D^{25} = -7.3$ (*c* 1.05, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3063, 3030, 2961, 1927, 2871, 1729, 1454, 1292, 1102, 739. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.99 (d, *J* 7.0 Hz, 3H), 1.04 (d, *J* 6.6 Hz, 3H), 1.10–1.40 (m, 1H), 1.40–1.70 (m, 1H), 1.70–2.00 (m, 3H), 2.14 (hept, *J* 7.0 Hz, 1H), 2.40–2.70 (m, 2H), 3.42 (dd, *J* 6.6 and 9.4 Hz, 1H), 3.48 (dd, *J* 5.8 and *J* = 9.0 Hz, 1H), 4.35 (dd, *J* 5.1 and 9.0 Hz, 1H), 4.45 (d, *J* 12.2 Hz, 1H), 4.52 (d, *J* 12.2 Hz, 1H), 7.10–7.50 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.18, 24.31, 30.20, 30.68, 37.68, 38.81, 42.75, 71.80, 73.45, 81.65, 127.93, 127.98 (2C), 128.74 (2C), 138.67, 175.26. Anal. calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.67, H, 8.56.

3.11. (–)-Methyl (3*R*,6*S*,7*S*)-8-benzyloxy-6-hydroxy-3,7-dimethyl-octanoate 8

Concentrated H_2SO_4 (five drops) was added to a solution of lactone **7** (2.30 g, 8.3 mmol) in MeOH (25 mL), and the mixture was refluxed for 30 min. After cooling, saturated aqueous $NaHCO_3$ (10 mL) was added, most of the MeOH was evaporated and the residue was extracted with ether (3×25 mL). The organic phase was washed with brine (20 mL), dried over Na_2SO_4, concentrated and the residue was purified by column chromatography (hexane/ethyl acetate, 5:2) to afford 2.39 g of the desired hydroxy ester **8** (93% yield). $[\alpha]_D^{25} = -1.7$ (*c* 2.88, $CHCl_3$), lit.[6] $[\alpha]_D^{25} = -1.1$ (*c* 3.6, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3491, 3063, 3030, 2954, 2672, 1725, 1454, 1099, 1010. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, *J* 7.0 Hz, 3H), 0.94 (d, *J* 6.6 Hz, 3H), 1.12–1.23 (m, 1H), 1.38–1.47 (m, 2H), 1.48–1.58 (m, 1H), 1.84–2.03 (m, 2H), 2.12 (dd, *J* 8.2 and 14.8 Hz, 1H), 2.32 (dd, *J* 5.9 and 14.8 Hz, 1H), 2.57 (sl, 1H), 3.52 (d, *J* 6.0 Hz, 1H), 3.52 (d, *J* 5.0 Hz, 1H), 3.65 (s, 3H), 3.72 (td, *J* 2.5 and 6.7 Hz, 1H), 4.48 (d, *J* 11.7 Hz, 1H), 4.52 (d, *J* 11.7 Hz, 1H), 7.26–7.37 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.59, 19.72, 30.39, 31.19, 33.22, 37.67, 41.43, 51.32, 73.34, 74.14, 74.66, 127.63, 128.36, 137.93, 173.63. MS (rel. intensity) *m*/*z* 276 (1.84), 230 (0.76), 184 (0.76), 152 (6.62), 127 (6.56), 110 (40.99), 91 (100), 81 (20.38), 69 (30.81), 55 (37.04).

3.12. (−)-Methyl (3*R*,6*S*,7*R*)-8-benzyloxy-6-hydroxy-3,7-dimethyl-octanoate 8a

Similarly, **7a** (1.53 g, 5.0 mmol) gave **8a** (1.58 g, 91.3%) as a colorless oil. $[\alpha]_D^{25} = -14.1$ (*c* 3.97, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3494, 3088, 3063, 2955, 2873, 1736, 1454, 1096, 737, 699. ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (d, $J=7.0$ Hz, 3H), 0.95 (d, $J=6.5$ Hz, 3H), 1.15–1.60 (m, 4H), 1.60–1.70 (m, 1H), 1.70–2.00 (m, 1H), 2.11 (dd, *J* 8.2 Hz and 14.5 Hz, 1H), 2.34 (dd, *J* 5.6 and 14.5 Hz, 1H), 3.36 (br s, 1H), 3.46 (dd, *J* 7.3 and 9.2 Hz, 1H), 3.61 (dd, *J* 4.3 and 9.2 Hz, 1H), 3.66 (s, 3H), 4.51 (s, 2H), 7.20–7.40 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.96, 19.86, 30.49, 32.12, 32.23, 38.08, 41.35, 51.32, 73.42, 75.03, 76.20, 127. 61 (2C), 127.73, 128.40 (2C), 137.65, 173.71. Anal. calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.10, H, 9.15.

3.13. (+)-Methyl (3*R*,6*S*,7*S*)-8-benzyloxy-3,7-dimethyl-6-*p*-toluenesulfonyloxyoctanoate 9

Tosyl chloride (2.61 g, 13.6 mmol) was added in small portions (1 h) to ester **8** (2.10 g, 6.8 mmol) in dry pyridine (1.61 g, 20.4 mmol), DMAP (20 mg) and chloroform (10 mL), with magnetic stirring at 0°C. After 12 h, ethyl ether (15 mL) was added and the solution was thoroughly washed with aqueous HCl (10%, 10 mL) and saturated solution of $NaHCO_3$ (10 mL). The organic layer was dried over Na_2SO_4, concentrated and the oil obtained was purified by column chromatographic (hexane:ethyl acetate, 9:1) to afford 2.26 g of **9** as a colorless oil (72% yield). $[\alpha]_D^{25} = +5.6$ (*c* 1.54, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3063, 3030, 2955, 2873, 1736, 1362, 1175, 903. ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, *J* 6.6 Hz, 3H), 0.89 (d, *J* 7.0 Hz, 3H), 1.01–1.36 (m, 2 H), 1.58–1.70 (m, 2H), 1.78–1.96 (m, 1H), 1.97–2.10 (m, 2 H), 2.19 (dd, *J* 6.2 and 15.0 Hz, 1H), 2.42 (s, 3H), 3.25 (d, *J* 6.6 Hz, 2H), 3.64 (s, 3H), 4.31 (d, *J* 11.8 Hz, 1H), 4.41 (d, *J* 11.8 Hz, 1H), 4.79 (td, *J* 3.0 and 7.0 Hz, 1H), 7.26–7.35 (m 7H), 7.77 (d, *J* 8.0 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 11.00, 19.48, 21.60, 29.40, 30.05, 31.98, 36.55, 41.29, 51.42, 71.71, 72.97, 84.48, 127.57 (3C), 127.71 (2C), 128.35 (2C), 129.66 (2C), 134.73, 138.38, 144.38, 173.31.

3.14. (−)-Methyl (3*R*,6*S*,7*R*)-8-benzyloxy-3,7-dimethyl-6-*p*-toluene-sulfonyloxyoctanoate 9a

Similarly, **8a** (1.50 g, 4.9 mmol) gave **9a** (1.82 g, 80.5%) as a colorless oil. $[\alpha]_D^{25} = -0.75$ (*c* 2.55, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3088, 3063, 3031, 2955, 2872, 1735, 1495, 1454, 1361, 1306, 1290. ^1H NMR (200 MHz, $CDCl_3$) δ 0.83 (d, *J* 6.6 Hz, 3H), 0.88 (d, *J* 7.0 Hz, 3H), 0.90–1.35 (m, 2H), 1.40–1.65 (m, 2H), 1.65–1.90 (m, 1H), 1.90–2.21 (m, 2H), 2.01 (dd, *J* 8.0 and 14.7 Hz, 1H), 2.42 (s, 3H), 3.25 (dd, *J* 5.9 and 9.6 Hz, 1H), 3.35 (dd, *J* 6.7 and 9.6 Hz, 1H), 3.64 (s, 3H), 4.36 (d, *J* 12.0 Hz, 1H), 4.45 (d, *J* 12.0 Hz, 1H), 4.68 (td, *J* 4.8 and 6.9 Hz, 1H), 7.20–7.40 (m 7H), 7.77 (d, *J* 8.3 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.31, 19.63, 21.58, 27.62, 30.14, 31.58, 36.74, 41.18, 51.36, 71.55, 72.90, 85.51, 127.50 (2C), 127.56, 127.79 (2C), 128.35 (2C), 129.67 (2C), 134.69, 138.38, 144.42, 173.30. Anal. calcd for $C_{25}H_{34}O_6S$: C, 64.91; H, 7.41; S, 6.93. Found: C, 64.66, H, 7.24; S, 6.90.

3.15. (+)-(3*R*,7*R*)-8-Benzyloxy-3,7-dimethyloctan-1-ol 10

Tosylate **9** (2.20 g, 4.8 mmol) was dissolved in dry ether (200 mL) and then $LiAlH_4$ (1.63 g, 42.8 mmol) was added. After stirring at room temperature for 3 h, excess of the hydride was destroyed with addition of water (2.0 mL), aqueous solution of NaOH (15%, 2.0 mL) and water (8.0 mL) again. The suspension was filtered through Celite, dried over Na_2SO_4 and concentrated. The product obtained was purified by column chromatography (hexane:ethyl acetate, 5:1) affording 0.84 g of the alcohol **10** (67% yield). $[\alpha]_D^{25} = +3.3$ (*c* 1.70, $CHCl_3$), lit.[6] $[\alpha]_D^{25} = +3.6$ (*c* 2.80, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3374, 3064, 3030, 2953, 2928, 1454, 1100. ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (d, *J* 6.8 Hz, 3H), 0.92 (d, *J* 7.0 Hz, 3H), 1.00–1.19 (m, 2H), 1.25–1.43 (m, 6H), 1.53–1.61 (m, 2H), 1.67–1.80 (m, 1H), 3.24 (dd, *J* 6.6 and 9.0 Hz, 1H), 3.32 (dd, *J* 6.4 and 9.0 Hz, 1H), 3.50–3.60 (m, 2H), 4.50 (s, 2H), 7.26–7.35 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.12, 19.60, 24.24, 29.41, 33.44, 33.85, 37.30, 40.00, 61.19, 72.98, 76.04, 127.42, 127.54, 128.30, 138.80. MS (rel. intensity) m/z 264 (M^+, 3.04), 155 (2.00), 107 (34.01), 91 (100), 69 (26.44), 55 (43.18).

3.16. (+)-(3*R*,7*S*)-8-Benzyloxy-3,7-dimethyloctan-1-ol 10a

Similarly, **9a** (1.80 g, 3.5 mmol) gave **10a** (0.71 g, 69.2%) as a colorless oil. $[\alpha]_D^{25} = +2.5$ (*c* 0.70, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3379, 3064, 3031, 2953, 2928, 2857, 1454, 1363, 1100, 1072, 735. ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (d, *J* 6.5 Hz, 3H), 0.93 (d, *J* 6.7 Hz, 3H), 1.00–1.40 (m, 8H), 1.45–1.80 (m, 3H), 3.23 (dd, *J* 6.7 and 9.0 Hz, 1H), 3.33 (dd, *J* 6.1 and 9.0 Hz, 1H), 3.50–3.75 (m, 2H), 4.50 (s, 2H), 7.20–7.40 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.20, 19.67, 24.23, 29.49, 33.47, 33.91, 37.39, 39.89, 61.19, 72.97, 75.97, 127.41, 127.53 (2C), 128.30 (2C). 138.79. Anal. calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.00, H, 10.59.

3.17. (+)-(3*R*,7*R*)-8-Benzyloxy-3,7-dimethyloctyl-1-*p*-toluenesulfonylate 11

Tosyl chloride (1.17 g, 6.0 mmol) was added in small portions, during 1 h, to a solution containing alcohol **10** (0.80 g, 3.0 mmol), dry pyridine (0.8 mL, 9.0 mmol), DMAP (10 mg) and chloroform (10 mL), with magnetic stirring at 0°C. After 12 h, ethyl ether (10 mL) was added and the solution was thoroughly washed with aqueous HCl (10%, 5 mL), saturated solution of $NaHCO_3$ (5 mL), dried, concentrated and the oil obtained was purified by column chromatography (hexane:ethyl acetate, 9:1) to afford 1.19 g of tosylate **11** as a colorless oil (93% yield). $[\alpha]_D^{25} = +1.9$ (*c* 7.40, CH_2Cl_2). IR ($\nu_{max.}$, film cm^{-1}): 3063, 3031, 2956, 2928, 2857, 1454, 1362, 1177, 944. ^1H NMR (400 MHz, $CDCl_3$) δ 0.79 (d, *J* 6.5 Hz, 3H), 0.90 (d, *J* 6.7 Hz, 3H), 1.02–1.10

(m, 2H), 1.10–1.27 (m, 3H), 1.30–1.46 (m, 2H), 1.48–1.54 (m, 1H), 1.61–1.75 (m, 2H), 2.44 (s, 3H), 3.23 (dd, *J* 6.6 and 9.0 Hz, 1H), 3.29 (dd, *J* 6.2 and 9.2 Hz, 1H), 4.05 (dt, *J* 2.7 and 6.4 Hz, 2H), 4.78 (d, *J* 12.2 Hz, 1H), 4.51 (d, *J* 12.2 Hz, 1H), 7.25–7.34 (m, 7H), 7.79 (d, *J* 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.02, 19.02, 21.59, 24.02, 29.08, 33.36, 33.49, 35.68, 36.77, 69.03, 72.91, 75.89, 127.39, 127.49, 127.83, 128.06, 128.27, 129.77, 133.08, 138.70, 144.61. MS (rel. intensity) *m*/*z* 246 (0.83), 155 (2.38), 137 (7.29), 107 (9.47), 91 (100), 69 (29.57), 55 (52.43). Anal. calcd for $C_{24}H_{34}O_4S$: C, 68.87; H, 8.19; S, 7.66. Found: C, 68.83; H, 8.38; S, 7.93.

3.18. (+)-(3*R*,7*S*)-8-Benzyloxy-3,7-dimethyloctyl-1-*p*-toluenesulfonylate 11a

Similarly, **10a** (0.61 g, 2.3 mmol) gave **11a** (0.97 g, 96.8%) as a colorless oil. $[\alpha]_D^{25}=+1.9$ (*c* 1.45, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3063, 3031, 2956, 2928, 1598, 1454, 1361, 1188, 1177, 944, 890, 738. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.79 (d, *J* 6.2 Hz, 3H), 0.90 (d, *J* 6.7 Hz, 3H), 1.00–1.80 (m, 10H), 2.43 (s, 3H), 3.22 (dd, *J* 6.6 and 9.0 Hz, 1H), 3.30 (dd, *J* 6.1 and 9.0 Hz, 1H), 4.05 (t, *J* 6.5 Hz, 2H), 4.55 (s, 2H), 7.20–7.40 (m, 7H), 7.79 (d, *J* 8.3 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.16, 19.16, 21.62, 24.05, 29.18, 33.43, 33.79, 35.64, 36.89, 69.08, 72.97, 75.88, 127.43, 127.53 (2C), 127.86 (2C), 128.31 (2C), 129.80 (2C), 133.20, 138.77, 144.63. Anal. calcd for $C_{24}H_{34}O_4S$: C, 68.87; H, 8.19; S.7.66 Found: C, 68.68; H, 7.98; S, 7.43.

3.19. (−)-(2*R*,6*S*)-1-Benzyloxy-2,6-dimethyldodecane 12

Magnesium turnings (0.087 g, 3.6 mmol) were added to a solution of 1-bromobutane (0.49 g, 3.6 mmol) in dry ethyl ether (12 mL) at rt. After 6 h the solution containing the Grignard reagent was added dropwise at −78°C to a previously prepared solution of tosilate **11** (0.30 g, 0.7 mmol) in dry THF (12 mL). Then, a solution of Li_2CuCl_4 in THF (0.1 M, 0.15 mL, 0.015 mmol) was added to the mixture. The temperature was raised slowly until rt during 2 h and then stirred for 10 h. The reaction was quenched with saturated solution of NH_4Cl (20 mL) and the resulting mixture was extracted with ether (3×40 mL). The organic layer was washed with saturated $NaHCO_3$ solution (2×20 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and evaporated in vacuo. The residue was chromatographed over silica gel (hexane:ethyl acetate, 95:5) and 0.177 g of **12** was obtained (81% yield). $[\alpha]_D^{25}=-0.6$ (*c* 1.32, CH_2Cl_2). IR ($\nu_{max.}$, film cm^{-1}): 3087, 3064, 2955, 2926, 2855, 1376, 1363, 1100, 735, 697. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 5.0 Hz, 3H), 0.92 (d, *J* 6.7 Hz, 3H), 1.00–1.50 (m, 7H), 1.63–1.85 (m, 1H), 3.23 (dd, *J* 6.7 and 9.0 Hz, 1H), 3.33 (dd, *J* 6.1 and 9.0 Hz, 1H), 4.50 (s, 2H), 7.10–7.40 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.13, 17.15, 19.67, 22.71, 24.36, 27.08, 29.71, 31.98, 32.75, 33.49, 33.98, 37.17, 37.32, 72.97, 76.12, 127.39, 127.52 (2C), 128.30 (2C), 138.85. Anal. calcd for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.63; H, 11.88.

3.20. (+)-(2*S*,6*S*)-1-Benzyloxy-2,6-dimethyldodecane 12a

In the same manner as that described for the preparation of **11**, **10a** (0.150 g, 0.36 mmol) gave **11a** (0.099 g, 90.8%) as a colorless oil. $[\alpha]_D^{25}=+1.6$ (*c* 1.73, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3067, 3030, 2955, 2925, 2854, 1454, 1376, 1363, 1099, 733, 696. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 6.4 Hz, 3H), 0.93 (d, *J* 6.7 Hz, 3H), 1.00–1.50 (m, 17H), 1.60–1.90 (m, 1H), 3.23 (dd, *J* 6.7 and 9.0 Hz, 1H), 3.33 (dd, *J* 6.0 and 9.0 Hz, 1H), 4.50 (s, 2H), 7.10–7.50 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.10, 17.21, 19.72, 22.68, 24.36, 27.02, 29.67, 31.94, 32.74, 33.48, 34.00, 37.02, 37.34, 72.94, 76.04, 127.36, 127.49 (2C), 128.27 (2C), 138.86. Anal. calcd for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.82; H, 11.90.

3.21. (+)-(2*S*,6*S*)-1-Benzyloxy-2,6-dimethyldecane 15

In the same manner as that described for the preparation of **11**, **10a** (0.150 g, 0.36 mmol) gave **15** (0.088 g, 89%) as a colorless oil. $[\alpha]_D^{25}=+2.4$ (*c* 0.82, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3087, 3067, 3030, 2955, 2926, 2855, 1454, 1376, 1100, 696. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.83 (d, *J* 6.2 Hz, 3H), 0.88 (t, *J* 5.4 Hz, 3H), 0.92 (d, *J* 6.7 Hz, 3H), 1.00–1.50 (m, 13H), 1.62–1.85 (m, 1H), 3.22 (dd, *J* 6.8 and 9.1 Hz, 1H), 3.33 (dd, *J* 6.0 and 9.1 Hz, 1H), 4.50 (s, 2H), 7.10–7.40 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.17, 17.24, 19.76, 23.05, 24.39, 29.33, 32.74, 33.51, 34.03, 36.72, 37.36, 72.97, 76.07, 127.37 (2C), 128.60 (2C), 128.82. Anal. calcd for $C_{19}H_{32}O$: C, 82.55; H, 11.67. Found: C, 82.42; H, 11.51.

3.22. (+)-(2*R*,6*S*)-2,6-Dimethyldodecan-1-ol 13

A mixture of benzyl ether **12** (0.170 g, 0.5 mmol) and 10% Pd/C (0.020 g) in ethanol (5 mL) was hydrogenated at room temperature under hydrogen atmosphere for 12 h. The mixture was filtered through Celite, and the filtrate evaporated at reduced pressure to afford alcohol **12** (0.108 g) in 86% yield. $[\alpha]_D^{25}=+9.6$ (*c* 7.35, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3373, 2957, 2926, 2855, 1639, 1464, 1377, 1036, 724. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 6.2 Hz, 3H), 0.91 (d, *J* 6.7 Hz, 3H), 1.00–1.40 (m, 17H), 1.50–1.67 (m, 1H), 1.73 (br s, 1H), 3.40 (dd, *J* 6.6 and 10.5 Hz, 1H), 3.51 (dd, *J* 5.8 and 10.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.16, 16.59, 19.67, 22.73, 24.41, 27.10, 29.73, 31.99, 32.76, 33.47, 35.79, 37.19, 37.33, 68.43. Anal. calcd for $C_{14}H_{30}O$: C, 78.43; H, 14.10. Found: C, 78.42; H, 14.00.

3.23. (−)-(2*S*,6*S*)-2,6-Dimethyldodecan-1-ol 13a

Similarly, 1**2a** (0.090 g, 0.30 mmol) gave **13a** (0.052 g, 82.0%) as a colorless oil. $[\alpha]_D^{25}=-7.1$ (*c* 0.73, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3422, 2955, 2925, 2855, 1639, 1463, 1377, 1098, 1030, 733, 696. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 6.3 Hz, 3H), 0.92 (d, *J* 6.7 Hz, 3H), 0.95–1.40 (m, 17H), 1.45–1.70 (m, 1H), 3.41 (dd, *J* 6.5 and 10.5 Hz, 1H), 3.52 (dd, *J* 5.7 and 10.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ

14.08, 16.61, 19.70, 22.66, 24.38, 27.00, 29.66, 31.92, 32.71, 33.47, 35.77, 37.01, 37.32, 68.37. Anal. calcd for $C_{14}H_{30}O$: C, 78.43; H, 14.10. Found: C, 78.43, H, 14.10.

3.24. (−)-(2*S*,6*S*)-2,6-Dimethyldecan-1-ol 16

Similarly, **15** (0.080 g, 0.29 mmol) gave **16** (0.042 g, 78.0%) as a colorless oil. $[\alpha]_D^{25}=-7.95$ (*c* 1.85, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3423, 2956, 2926, 2856, 1639, 1463, 1030, 696. ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, *J* 6.2 Hz, 3H), 0.88 (t, *J* 6.6 Hz, 3H), 0.92 (d, *J* 6.7 Hz, 3H), 0.94–1.70 (m, 15H), 3.41 (dd, *J* 6.5 and 10.5 Hz, 1H), 3.52 (dd, *J* 5.7 and 10.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.13, 16.62, 19.71, 23.01, 24.40, 29.31, 32.71, 33.45, 35.78, 36.70, 37.34, 68.36. Anal. calcd for $C_{12}H_{26}O$: C, 77.35; H, 14.06. Found: C, 77.30, H, 14.00.

3.25. (+)-(2*R*,6*S*)-1-Methanesulfonate-2,6-dimethyldodecane 14

Methanesulfonyl chloride (0.07 mL, 0.94 mmol) was added in small portions during 1 h to a solution of alcohol **13** (0.100 g, 0.47 mmol) in dry pyridine (0.12 mL, 1.4 mmol) and CH_2Cl_2 (2 mL), with magnetic stirring at 0°C. After 5 h, ethyl ether (10 mL) was added and the solution was thoroughly washed with aqueous HCl (10%, 1 mL), saturated solution of $NaHCO_3$ (5 mL), brine (5 mL), dried, concentrated and the oil obtained was purified by column chromatography (hexane:ethyl acetate, 9:1) to afford 0.126 g of compound **14** (93% yield) as a colorless oil. $[\alpha]_D^{25}=+1.8$ (*c* 1.96, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3031, 2957, 2926, 2856, 1459, 1358, 1177, 958, 824, 529. ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 6.2 Hz, 3H), 0.99 (d, *J* 6.7 Hz, 3H), 1.05–1.50 (m, 17H), 1.70–2.00 (m, 1H), 3.01 (s, 3H), 4.00 (dd, *J* 6.6 and 9.4 Hz, 1H), 4.10 (dd, *J* 5.8 and 9.4 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.05, 16.36, 19.55, 22.63, 24.04, 26.98, 29.61, 31.89, 32.62, 32.97, 33.00, 37.03 (2C), 37.14, 74.68. Anal. calcd for $C_{15}H_{32}O_3S$: C, 61.60; H, 11.03; S, 10.96. Found: C, 61.61; H, 11.03; S, 10.93.

3.26. (−)-(2*S*,6*S*)-1-Methanesulfonate-2,6-dimethyldodecane 14a

Similarly, **13a** (0.040 g, 0.19 mmol) gave **14a** (0.051 g, 93.0%) as a colorless oil. $[\alpha]_D^{25}=-1.2$ (*c* 0.93, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3031, 2957, 2927, 2857, 1465, 1356, 1177, 989, 829, 750, 529. ^1H NMR (200 MHz, $CDCl_3$) δ 0.85 (d, *J* 6.3 Hz, 3H), 0.88 (t, *J* 6.1 Hz, 3H), 0.99 (d, *J* 6.7 Hz, 3H), 1.05–1.48 (m, 17H), 1.75–2.00 (m, 1H), 3.00 (s, 3H), 4.00 (dd, *J* 6.6 and 9.4 Hz, 1H). 4.10 (dd, *J* 5.7 and 9.4 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 16.47, 19.63, 22.64, 24.08, 26.97, 29.62, 31.90, 32.64, 33.00, 33.06, 36.95, 37.08, 37.16, 74.65. HRMS (*m*/*z*) Found: 292.2072: calcd for $C_{15}H_{32}O_3S$: 292.2072.

3.27. (−)-(2*S*,6*S*)-1-Methanesulfonate-2,6-dimethyldecane 17

Similarly, **16** (0.035 g, 0.19 mmol) gave **17** (0.044 g, 89.0%) as a colorless oil. $[\alpha]_D^{25}=-1.2$ (*c* 1.8, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 3030, 2957, 2927, 2857, 1464, 1356, 1177, 959, 819, 529. ^1H NMR (200 MHz, $CDCl_3$) δ 0.85 (d, *J* 6.2 Hz, 3H), 0.89 (t, *J* 5.9 Hz, 3H), 0.99 (d, *J* 6.7 Hz, 3H), 1.02–1.50 (m, 13H), 1.70–1.90 (m, 1H), 3.00 (s, 3H), 4.00 (dd, *J* 6.7 and 9.5 Hz, 1H). 4.10 (dd, *J* 5.7 and 9.5 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.12, 16.49, 19.66, 23.00, 24.09, 29.27, 32.64, 33.03, 33.08, 36.64, 37.09, 37.19, 74.65. Anal. calcd for $C_{13}H_{28}O_3S$: C, 59.05; H, 10.67; S.12.12 Found: C, 58.98; H, 11.03; S, 12.03.

3.28. (+)-(5*S*,9*S*)-5,9-Dimethylpentadecane 1

Magnesium turnings (0.102 g, 4.2 mmol) were added to a solution of 1-bromopropane (0.38 mL, 4.2 mmol) in dry ethyl ether (12 mL) at rt. After 6 h the solution containing the Grignard reagent (7.3 mL, 2.6 mmol) was added dropwise at −78°C to a previously prepared solution of mesilate **14** (0.050 g, 0.17 mmol) in dry THF (3 mL). Then, a solution of Li_2CuCl_4 in THF (0.1 M, 0.40 mL) was added to the mixture. The reaction temperature was raised slowly at rt (2 h) and stirred for 14 h. The reaction was quenched with saturated solution of NH_4Cl (5 mL) and the resulting mixture was extracted with ether (3×15 mL). The organic layer was washed with saturated $NaHCO_3$ solution (2×10 mL) and brine (30 mL), dried over $MgSO_4$, filtered, and evaporated in vacuo. The residue was chromatographed over silica gel (hexane:ethyl acetate, 95:5) and 0.037 g of (5*S*,9*S*)-**1** was obtained (90% yield). $[\alpha]_D^{25}=+4.2$ (*c* 0.98, $CHCl_3$). lit.[4] $[\alpha]_D^{25}=+6.2$ (*c* 1.30, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}):2957, 2925, 2857, 1464, 1377, 717. ^1H NMR (200 MHz, $CDCl_3$) δ 0.65–0.95 (m, 12H), 0.96–1.50 (m, 24H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.08, 14.13, 19.67 (2C), 22.67, 23.02, 24.44, 27.03, 29.33, 29.67, 31.94, 32.70, 32.72, 36.82, 37.14, 37.36 (2C). MS (rel. intensity) *m*/*z* 240 ($M^{+\cdot}$0.90), 225 (1.28), 211 (0.87), 183 (7.35), 155 (14.74), 141 (2.83), 127 (8.83), 113 (20.30), 99 (31.85), 85 (79.09), 71 (93.47), 57 (100).. HRMS (*m*/*z*). Found: 240.2817: calcd for $C_{17}H_{36}$: 240.2817.

3.29. (−)-(5*R*,9*S*)-5,9-Dimethylpentadecane 1

Similarly, **14a** (0.040 g, 0.14 mmol) gave (5*R*,9*S*)-**1** (0.029 g, 85.3%) as a colorless oil. $[\alpha]_D^{25}=-1.2$ (*c* 0.88, $CHCl_3$) lit.[4] $[\alpha]_D^{25}=-1.0$ (*c* 4.18, $CHCl_3$). IR ($\nu_{max.}$, film cm^{-1}): 2957, 2925, 2871, 2857, 1459, 1377, 722. ^1H NMR (200 MHz, $CDCl_3$) δ 0.63–0.95 (m, 12H), 0.95–1.50 (m, 24H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.12, 14.17, 19.77 (2C), 22.70, 23.06, 24.48, 27.05, 29.35, 29.71, 31.97, 32.77, 32.79, 36.76, 37.08, 37.45 (2C). MS (rel. intensity) *m*/*z* identical with those of (5*S*,9*S*)-**1**. HRMS (*m*/*z*) Found: 240.2817: calcd for $C_{17}H_{36}$: 240.2817.

3.30. (+)-(5*S*,9*R*)-5,9-Dimethylpentadecane 1

Similarly, **17** (0.020 g, 0.08 mmol) gave (5*S*,9*R*)-**1** (0.015 g, 82.5%) as a colorless oil. $[\alpha]_D^{25}=+1.4$ (*c* 1.10, $CHCl_3$) lit.[4] $[\alpha]_D^{25}=+1.1$ (*c* 3.81, $CHCl_3$). The IR, ^1H and ^{13}C NMR spectra were identical with those of (5*R*,9*S*)-**1**. HRMS (*m*/*z*) Found: 240.2817: calcd for $C_{17}H_{36}$: 240.2817.

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