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SYNTHESIS OF THE OPTICALLY ACTIVE FORMS OF 2,6-DIMETHYL-1,5-HEPTADIEN-3-OL ACETATE, THE PHEROMONE OF THE COMSTOCK MEALYBUG†

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Abstract—Both the enantiomers of 2,6-dimethyl-1,5-heptadien-3-ol acetate, the pheromone of *Pseudococcus comstocki*, were synthesized. The natural and dextrorotatory pheromone was proved to be the (*R*)-enantiomer.

In 1980 the structure of the pheromone of the comstock mealybug was shown to be 2,6-dimethyl-1,5-heptadien-3-ol acetate **1b** by two independent research groups.[1,2] The synthetic racemate **1b** was highly active as the pheromone.[2,3] However, the absolute configuration of the naturally occurring dextrorotatory pheromone **1b**, $[\alpha]_D$ +6.2° (hexane),[2] remained unknown. This paper describes a synthesis of the both enantiomers of **1b**, establishing the *R*-configuration at C-3 of the natural product.

The present synthesis is based on the application of the asymmetric epoxidation reaction recently reported by Sharpless.[4] A dienol **5** was the key intermediate, which was prepared according to the general procedure of Evans for the synthesis of allylic alcohols.[5]

Alkylation of β-methallyl 2-pyridyl sulfide **2** with isoprenyl bromide gave the alkylated sulfide **3** in 85% yield. This was oxidized with *m*-chloroperbenzoic acid to a sulfoxide **4**. Subsequent treatment of **4** with excess Et_2NH in MeOH yielded desired alcohol **5** in 46% yield from **3** after chromatographic purification and distillation.

Asymmetric epoxidation of the allylic alcohol **5** was carried out with Bu'OOH and $Ti(OPr^i)_4$ in the presence of diethyl *D*-(−)-tartrate as described by Sharpless[4] to give (2*R*, 3*R*)-epoxy alcohol **6a**, $[\alpha]_D^{22.5}$ +12.6° ($CHCl_3$), in 59% yield. In the similar manner, but using diethyl *L*-(+)-tartrate instead of the *D*-(−)-isomer, (2*S*, 3*S*)-epoxy alcohol **6a**, $[\alpha]_D^{22.5}$ −12.2° ($CHCl_3$), was obtained in

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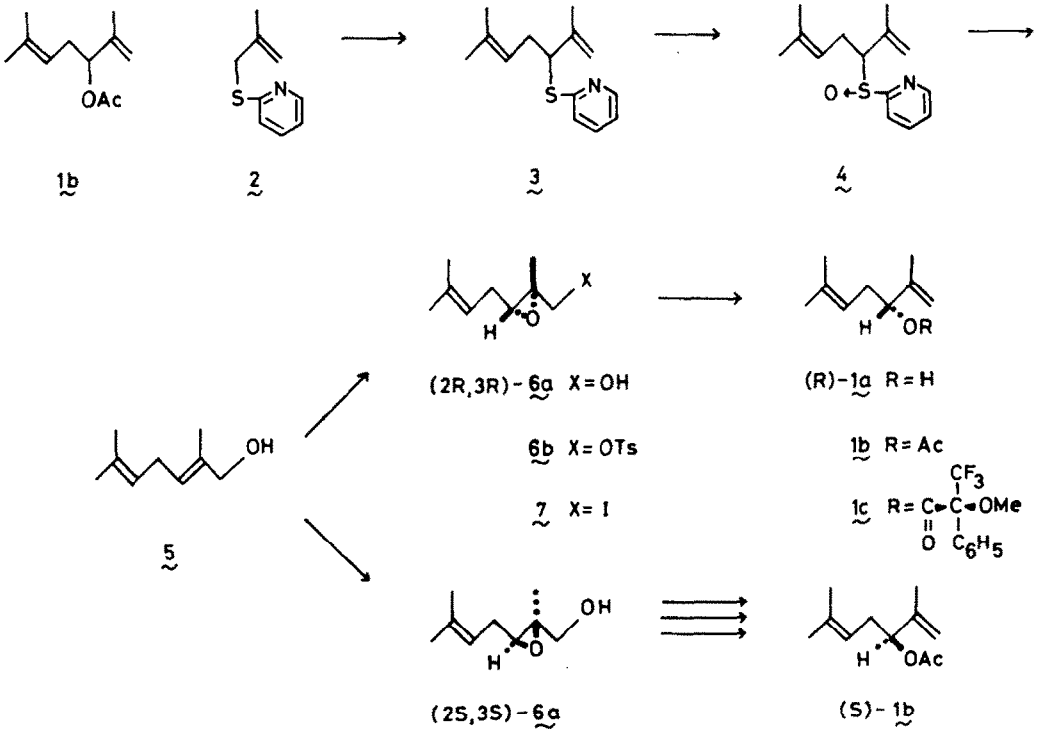

64% yield. Conventional tosylation of **6a** yielded the corresponding tosylate **6b**. This was converted into an iodide **7** by treatment with NaI in acetone. Reduction of **7** with Zn–AcOH gave an alcohol **1a**. The (*R*)-enantiomer of **1a** was obtained in 65% yield from (2*R*, 3*R*)-**6a**, which was acetylated to give the (*R*)-pheromone **1b**, $[\alpha]_D^{23}$ +5.68° (*n*-hexane). The (*S*)-enantiomer of **1a** gave, after acetylation, the (*S*)-pheromone **1b**, $[\alpha]_D^{23}$ −5.72° (*n*-hexane). The spectral data of our synthetic enantiomers (*R*)- and (*S*)-**1b** coincided with those of the natural product[1] or the synthetic racemate.[3]

As the natural pheromone was dextrorotatory, its absolute configuration at C-3 was assigned to be *R*. This was further supported by an independent synthesis of (*R*)-(+)-**1b** starting from (*S*)-phenylalanine.[6] The optical purities of the synthetic alcohols (*R*)- and (*S*)-**1a** were determined to be 90 and 91%, respectively, by converting them to the corresponding (*S*)-(−)-MTPA (α-methoxy-α-trifluoromethylphenylacetic acid)-esters (*R*)- and (*S*)-**1c** in the usual manner[7] and analyzing the diastereomeric ratio by glc. The pheromone enantiomers (*R*)- and (*S*)-**1b** were therefore of ~90% optical purities. This estimation was in good accord with the optical purity deduced by the comparison of the specific rotations of the natural and the synthetic pheromones [(5.68/6.2) × 100 = 92%].

The bioassay of the pheromone enantiomers was kindly carried out by Dr. T. Negishi, Otsuka Pharmaceutical Co., Ltd. The natural enantiomer (*R*)-(+)-**1b** was definitely more active than its antipode by a laboratory assay at 10μg dose. The average numbers of the trapped male insects were 15.3 for (*R*)-(+)-**1b**, 3.0 for (*S*)-(−)-**1b** and 2.0 for the blank. At 100 μg dose, (*S*)-(−)-**1b** was slightly active: the average catches of the insects by (*S*)-(−)-**1b** were 14.8, while those by (*R*)-(+)-**1b** were 36.4 with the blank catches of 10.3. This could be explained by the small contamination (~5%) with the natural (*R*)-enantiomer in our sample of (*S*)-(−)-**1b**. Details of the bioassay will be published elsewhere by Dr. T. Negishi.

EXPERIMENTAL

All b.ps were uncorrected. IR spectra refer to films and were determined on a Jasco A-102 spectrometer. NMR spectra were recorded at 60 MHz with TMS as an internal standard on a Hitachi R-24A spectrometer unless otherwise stated. Optical rotations were measured on a Jasco DIP-4 polarimeter. Glc analyses were performed on a Yanaco GCG-550F gas chromatograph.

β-Methallyl 2-pyridyl sulfide **2**. 2-Pyridinethiol (15.0 g) was dissolved into a soln of NaOEt (from 3.1 g of Na) in abs EtOH (100 ml). Methallyl chloride (14 g) was added to this soln with ice-cooling and stirring. After stirring for 3 hr, the mixture was concentrated *in vacuo* to remove EtOH. The residue was diluted with water and extracted with ether. The ether soln was washed with 5% NaOH aq, water and sat NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 21.0 g (94%) of **2**, b.p. 90–92°/1 mm, n_D^{22} 1.5676; ν_{max} 3060 (w), 3040 (w), 2960 (w), 2900 (w), 1645 (w), 1578 (s), 1552 (m), 1450 (s), 1410 (s), 1120 (s), 890 (m), 750 (s), 720 (m) cm^{-1}; δ ($CDCl_3$) 1.80 (3H, s), 3.80 (2H, s), 4.80 (1H, s), 4.96 (1H, s), 6.70–7.55 (3H, m), 8.25–8.45 (1H, m). (Found: C, 65.17; H, 6.92; N, 8.28. Calcd. for $C_9H_{11}NS$: C, 65.41; H, 6.71; N, 8.48%).

1-Isopropenyl-4-methyl-3-pentenyl 2-pyridyl sulfide **3**. A soln of *n*-BuLi in *n*-hexane (1.5 N, 60 ml) was added dropwise to a stirred and cooled soln of **2** (14.0 g) in dry THF (150 ml) from −50 to −30° under Ar. The soln turned wine red. To this a soln of isoprenyl bromide (13.5 g) in dry THF (50 ml) was added dropwise with stirring from −70 to −60°. The deep-red color of the soln faded rapidly. The mixture was stirred for 1 hr from −70 to −50°. Then the temp was raised gradually to room temp during 1 hr. The reaction was quenched with sat NH_4Cl aq and the organic layer was separated. The aq layer was extracted with ether. The combined organic layer was dried (K_2CO_3) and concentrated *in vacuo*. The residue was distilled to give 16.8 g (85%) of **3**, b.p. 110–120°/1 mm. An analytical sample boiled at 115–120°/1 mm, n_D^{22} 1.5549; ν_{max} 3060 (w), 3040 (w), 2970 (m), 2920 (m), 2850 (w), 1640 (w), 1580 (s), 1555 (m), 1450 (s), 1415 (s), 1375 (m), 1120 (s), 890 (m), 755 (s), 720 (m) cm^{-1}; δ ($CDCl_3$) 1.62 (6H, br. s), 1.80 (3H, s), 2.50 (2H, t, J = 7Hz), 4.40 (1H, t, J = 7Hz), 4.81 (1H, t, J = 2Hz), 4.98 (1H, s), 5.15 (1H, t, J = 6Hz), 6.75–7.60 (3H, m), 8.30–8.50 (1H, m). (Found: C, 71.91; H, 8.17; N, 6.02. Calcd. for $C_{14}H_{19}NS$: C, 72.05; H, 8.21; N, 6.00%).

1-Isopropenyl-4-methyl-3-pentenyl 2-pyridyl sulfoxide **4**. A soln of *m*-chloroperbenzoic acid (85% purity, 15.7 g) in CH_2Cl_2 (250 ml) was added dropwise during 1 hr to a stirred and cooled soln of **3** (17.2 g) in CH_2Cl_2 (200 ml) from −30 to −20° under Ar. After 30 min m-chlorobenzoic acid began to precipitate. The temp was raised during 2 hr to 10°. The mixture was then washed with Na_2CO_3 aq. The CH_2Cl_2 soln was dried ($MgSO_4$) and concentrated *in vacuo* to give 19.0 g (quantitative) of crude oily **4**, ν_{max} 3050 (w), 2970 (m), 2910 (m), 2850 (m), 1640 (w), 1578 (s), 1560 (m), 1450 (s), 1420 (s), 1378 (m), 1082 (m), 1050 (s), 1030 (s), 985 (m), 895 (m), 770 (s), 735 (m) cm^{-1}; δ ($CDCl_3$) ~1.2–~1.9 (9H, m, 1.40, 1.50, 1.68, 1.86), ~2.0–~2.8 (2H, m), ~3.3–~3.7 (1H, m), ~4.4–~5.2 (3H, m), ~7.2–~7.5 (1H, m), ~7.8–~8.1 (2H, m), ~8.5–~8.7 (1H, m). This was employed for the next step without further purification.

(E)-2, 6-Dimethyl-2, 5-heptadien-1-ol **5**. Et_2NH (80 ml) was added to a soln of **4** (19.0 g) in MeOH(80 ml) and the resulting mixture was stirred overnight at room temp. Then it was concentrated *in vacuo*. The residue was diluted with water and extracted with ether. The ether soln was washed with dil HCl aq, $NaHCO_3$ aq and sat NaCl aq, dried (K_2CO_3) and concentrated *in vacuo* to give a crude oily **5**. This was purified by chromatography over Merck Kieselgel 60 (Art 7734) to give 6.31 g (46%) of pure **5**, b.p. 97–99°/9 mm, n_D^{22} 1.4715; ν_{max} 3320 (s), 3040 (w), 2980 (s), 2920 (s), 2860 (s), 2730 (w), 1670 (w), 1450 (m), 1378 (m), 1010 (s) cm^{-1}; δ (100MHz, CCl_4) 1.63 (6H, s), 1.67 (3H, s), 2.68 (2H, t, J = 7Hz), 3.17 (1H, br. s), 3.86 (2H, s), 5.05 (1H, t, J = 7Hz), 5.29 (1H, t, J = 7Hz); glc (Column, Thermon 1000, 30 m × 0.2 mm at 100° + 8°/min; Carrier gas, N_2, 1.2 kg/cm²) Rt 12.15 min (2.3%, (*Z*)-isomer ?), 12.42 min (97.7%, (*E*)-isomer). (Found: C, 76.35; H, 11.62. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50%).

(2R, 3R)-(+)-2,3-Epoxy-2,6-dimethyl-5-hepten-1-ol (2*R*, 3*R*)-**6a**. $Ti(OPr^i)_4$ (2.12 ml) and diethyl D-(−)-tartrate (1.22 ml) were added to stirred and cooled (dry ice-CCl_4) dry CH_2Cl_2 (72 ml) at −23°. After 5 min **5** (1.00 g) and Bu^tOOH (3.64M soln in $ClCH_2CH_2Cl$, 3.92 ml) were added to the mixture. The resulting soln was left to stand overnight at −20°. Then the flask was cooled in a dry ice-CCl_4 bath. 10% Tartaric acid aq (18 ml) was added dropwise to the stirred and cooled soln. The mixture was stirred at −23° for 30 min. Then the cooling bath was removed and the temp was raised to room temp. After stirring for 1 hr the organic layer was separated, washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in ether (50 ml). 10% NaOH aq (20 ml) was added to the stirred and ice-cooled ether soln and the mixture was stirred for 30 min at 0–5°. The ether layer was separated, washed with sat NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 1.32 g of crude **6a**. This was purified by chromatography over Merck Kieselgel 60 (Art 7734) to give 0.66 g (59%) of pure (2*R*, 3*R*)-**6a**, b.p. 83–84°/0.7 mm, $n_D^{22.5}$ 1.4591; $[\alpha]_D^{22.5}$ +12.6° (*c* = 2.13, $CHCl_3$); ν_{max} 3450 (s), 2980 (s), 2930 (s), 2860 (s), 1660 (w), 1450 (m), 1380 (m), 1080 (m), 1040 (s), 890 (w), 860 (m), 835(w) cm^{-1}; δ (CCl_4) 1.22 (3H, s), 1.60 (3H, s), 1.68 (3H, s), 1.95–2.35 (2H, m), 2.82 (1H, t, J = 7Hz), 3.21 (1H, br. s), 3.19–3.58 (2H, m), 5.05 (1H, t, J = 7Hz). (Found: C, 68.81; H, 10.44. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%).

(2S, 3S)-(−)-2,3-Epoxy-2,6-dimethyl-5-hepten-1-ol (2*S*, 3*S*)-**6a**. In the same manner as described above, **5** (2.00 g) yielded 1.42 g (64%) of (2*S*, 3*S*)-**6a**, b.p. 91–93°/1.0 mm, n_D^{22} 1.4588; $[\alpha]_D^{22.5}$ −12.2° (*c* = 1.56, $CHCl_3$). (Found: C, 69.05; H, 10.50. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32%). The spectral data were same as those of (2*R*, 3*R*)-**6a**.

(2*R*, 3*R*)-2, 3-*Epoxy*-2, 6-*dimethyl*-5-*hepten*-1-*ol tosylate* (2*R*, 3*R*)-**6b**. TsCl (1.44 g) was added portionwise to a stirred and ice-cooled soln of (2*R*, 3*R*)-**6a** (1.00 g) in dry C_5H_5N (11 ml). The mixture was left to stand overnight at 0–5°, then poured into ice-water and extracted with ether. The ether extract was washed with water, $CuSO_4$ aq, $NaHCO_3$ aq and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 1.83 g (92%) of curde (2*R*, 3*R*)-**6b**, ν_{max} 2980 (m), 2930 (m), 1600 (m), 1500 (w), 1450 (m), 1362 (s), 1310 (w), 1290 (w), 1210 (w), 1190 (s), 1180 (s), 1100 (m), 970 (s), 835 (m), 815 (m), 785 (m) cm^{-1}; δ (CCl_4) 1.23 (3H, s), 1.59 (3H, s), 1.67 (3H, s), 1.92–2.32 (2H, m), 2.39 (3H, s), 2.63 (1H, t, J = 7 Hz), 3.80 (2H, s), 5.03 (1H, t, J = 7Hz), 7.24 (2H, d, J = 8Hz), 7.66 (2H, d, J = 8Hz). This was employed for the next step without further purification.

(2*S*, 3*S*)-2, 3-*Epoxy*-2, 6-*dimethyl*-5-*hepten*-1-*ol tosylate* (2*S*, 3*S*)- **6b**. In the same manner as described above, (2*S*, 3*S*)-**6a**(1.10g) yielded 2.01g (92%) of crude (2*S*, 3*S*)-**6b**. This was directly employed for the next step.

(2*R*, 3*R*)-2, 3-*Epoxy*-2, 6-*dimethyl*-5-*heptenyl iodide* (2*R*, 3*R*)-**7**. NaI (3.23g) was added to a soln of (2*R*, 3*R*)-**6b** (1.82g) in acetone (30 ml) and the mixture was stirred and heated under reflux for 1.5 hr. Then it was concentrated *in vacuo*, diluted with water and extracted with ether. The ether soln was washed with water, $Na_2S_2O_3$ aq, $NaHCO_3$ aq and sat NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (Mallinckrodt CC-7) to give 1.39g (89%) of (2*R*, 3*R*)-**7**, $n_D^{22.5}$ 1.5110; ν_{max} 2970 (s), 2930 (s), 2860 (m), 1670 (w), 1450 (m), 1385 (s), 1255 (m), 1175 (m), 1135 (w), 1065 (m), 865 (m) cm^{-1}; δ (CCl_4) 1.40 (3H, s), 1.62 (3H, s), 1.71 (3H, s), 1.92–2.33 (2H, m), 2.69 (1H, t, J = 7Hz), 2.91 (1H, d, J = 10Hz), 3.16 (1H, d, J = 10 Hz), 5.06 (1H, t, J = 7Hz). This was directly used for the next step.

(2*S*, 3*S*)-2,3-*Epoxy*-2,6-*dimethyl*-5-*heptenyl iodide* (2*S*, 3*S*)-**7**. In the same manner as described above, (2*S*, 3*S*)-**6b** (1.96g) yielded 1.54g (92%) of (2*S*, 3*S*)-**7**, $n_D^{22.5}$ 1.5136. This was used for the next step without further purification.

(*R*)-(+)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol* (*R*)-**1a**. Zn dust (1.20g) was added portionwise to a stirred and ice-cooled soln of (2*R*, 3*R*)-**7** (1.21g) in AcOH (7 ml). The mixture was stirred for 30 min after the addition at room temp. Then it was diluted with ether and filtered through Celite, The ether soln was washed with water, $Na_2S_2O_3$ aq, $NaHCO_3$ aq and sat NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 0.50g (79%) of (*R*)-**1a**, b.p. 82–83°/15 mm, n_D^{23} 1.4606; $[\alpha]_D^{23}$ + 26.4° (*c* = 5.11, *n*-hexane); ν_{max} 3400 (m), 3080 (w), 2980 (s), 2930 (s), 1650 (w), 1445 (m), 1375 (m), 1305 (w), 1240 (w), 1160 (w), 1110 (w), 1050 (m), 1025 (m), 895 (s), 830 (w) cm^{-1}; δ (CCl_4) 1.59 (3H, s), 1.66 (6H, s), 2.14 (2H, t, J = 7Hz), 2.48 (1H, s), 3.87 (1H, t, J = 7Hz), 4.67 (1H, br. s), 4.80 (1H, br. s), 5.00 (1H, t, J = 7Hz). (Found: C, 77.61; H, 12.16. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50%).

(*S*)-(−)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol* (*S*)-**1a**. In the same manner as described above, (2*S*, 3*S*)-**7** (1.41 *g*) yielded 0.54g (73%) of (*S*)-**1a**, b.p. 64–65°/5 mm, n_D^{23} 1.4591; $[\alpha]_D^{23}$ − 26.5° (*c* = 6.11, *n*-hexane). (Found: C, 76.23; H, 11.70. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50%).

(*R*)-(+)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol acetate* (*R*)-**1b**. Ac_2O (1 ml) was added to a stirred soln of (*R*)-**1a** (0.40g) in dry C_5H_5N (2 ml). The mixture was left to stand overnight at room temp. Then it was poured into ice-water and extracted with ether. The ether soln was washed with dil HCl aq, $NaHCO_3$aq, water and sat NaClaq, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 0.41g (80%) of (*R*)-**1b**, b.p. 65–67°/15 mm, $n_D^{22.5}$ 1.4426; $[\alpha]_D^{22}$ + 5.68° (*c* = 1.76, *n*-hexane); ν_{max} 3100 (w), 2980 (m), 2930 (m), 2860 (w), 1745 (s), 1655 (w), 1450 (m), 1370 (m), 1240 (s), 1180 (w), 1110 (w), 1045 (m), 1020 (m), 990 (w), 955 (w), 935 (w), 905 (m), 840 (w) cm^{-1}; δ (100 MHz, CCl_4) 1.61 (3H, s), 1.69 (6H, s), 1.96 (3H, s), 2.26 (2H, t, J = 7Hz), 4.75 – 5.17 (4H, m, 4.83, 4.90, 5.01, 5.08, 5.15); MS: *m/z* 182 (M^+, 1.8%), 140 (M^+–CH_2=C=O, 1.8%), 122 (M^+–AcOH, 52%), 113 (M^+–C_5H_9, 21%), 107 (M^+–AcOH–Me, 68%), 91 (18%), 79 (14%), 69 (57%), 43 (100%, base peak), 41 (63%); MS: *m/z* 122. 1085 ($C_9H_{14} = M^+$–AcOH); glc (Column, 5% FFAP, 1.5 m × 2 mm at 90°; Carrier gas, N_2, 1.0 kg/cm^2) Rt 3.6 min (4.3%), 6.3 min (2.7%), 7.3 min (93.0%, **1b**). (Found: C, 71.88; H, 9.95. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96%).

(*S*)-(−)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol acetate* (*S*)-**1b**. In the same manner as described above, (*S*)-**1a** (0.43g) yielded 0.45g (81%) of (*S*)-**1b**, b.p. 66°/15 mm, $n_D^{22.5}$ 1.4426; $[\alpha]_D^{22}$ − 5.72° (*c* = 1.96, *n*-hexane); glc (same conditions as above) Rt 3.6 min (2.9%), 6.3 min (2.6%), 7.3 min (94.4%, **1b**). (Found: C, 72.14; H, 10.13. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96%).

(*R*)-(+)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol* (*S*)-(−)-*MTPA ester* (*R*)-**1c**. (*S*)-MTPA-Cl (102 mg) was added to a soln of (*R*)-**1a** (53.9 mg) and DMAP (4-N, N-dimethylaminopyridine, 102 mg) in dry CH_2Cl_2 (0.5 ml) with stirring. The mixture was left to to stand overnight at room temp. Conventional work-up of the mixture gave 135 mg of (*R*)-**1c**, ν_{max} 1750 (s), 1270 (s), 1250 (s), 1185 (s), 1170 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.62 (3H, s), 1.63 (3H, s), 1.69 (3H, s), 2.16–2.62 (2H, m), 3.53 (3H, s), 4.88 (1H, br. s), 4.93 (1H, br. s), 5.06 (1H, t, J = 7Hz), 5.35 (1H, t, J = 7Hz), 7.12–7.60 (5H, m); glc (Column, Thermon 1000, 30 m × 0.2 mm at 100–200° (1°/min); Carrier gas, N_2, 1.0 kg/cm^2) Rt 60.23 min (5.0%), 61.28 min (95.0%). This glc analysis revealed that the optical purity of (*R*)-**1a** was 90%.

(*S*)-(−)-2, 6-*Dimethyl*-1, 5-*heptadien*-3-*ol* (*S*)-(−)-*MTPA ester* (*S*)-**1c**. In the same manner as described above, (*S*) − **1a** (55.5 mg) was converted into the corresponding (*S*)-(−)-MTPA ester (*S*)-**1c** (119 mg), ν_{max} 1750 (s), 1270 (s), 1250 (s), 1185 (s), 1170 (s), cm^{-1}; δ (100 MHz, $CDCl_3$) 1.55 (3H, s), 1.64 (3H, s), 1.75 (3H, s), 2.18–2.58 (2H, m), 3.54 (3H, s), 4.82–5.18 (3H, with two br. singlets at δ 4.98 and 5.08), 5.45 (1H, t, J = 7Hz), 7.26–7.70 (5H, m); glc (same conditions as above) Rt 60.35 min (95.5%), 60.77 min (4.5%). This glc analysis showed that the optical purity of (*S*)-**1a** was 91%. Bierl-Leonhardt *et al.* prepared (*R*)-(+)-MTPA Ester of (±)-**1a**. They found that the (*R*)-(+)-MTPA ester of the natural **1a** was a single diastereomer at the earlier retention time. Considering our glc data, this should be (*R*)-(+)-MTPA ester of (*R*)-**1a**. In our case (*S*)-(−)-MTPA ester of (*S*)-**1a** showed earlier retention time than that of (*R*)-**1a**. These glc data were in agreement with our assignment of *R*-configuration to natural (+)-**1b**.

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