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SYNTHESIS AND ABSOLUTE STEREOCHEMISTRY OF SERRICORNIN [(4*S*, 6*S*, 7*S*)-4,6-DIMETHYL-7-HYDROXY-3-NONANONE]

THE SEX PHEROMONE OF THE CIGARETTE BEETLE†

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Abstract—The absolute stereochemistry of serricornin (4,6-dimethyl-7-hydroxy-3-nonanone) was established as 4*S*, 6*S*, 7*S* by synthesizing both (4*S*, 6*S*, 7*S*)-isomer and its antipode. Only the natural enantiomer was bioactive.

Serricornin is the sex pheromone produced by the female cigarette beetle (*Lasioderma serricorne* F.), which is a serious pest of cured tobacco leaves.[1] The proposed structure, 4,6-dimethyl-7-hydroxy-3-nonanone **1a**, was proved by its synthesis as a diastereomeric mixture.[2,3] However, nothing was known about the absolute stereochemistry of its three chiral centers at the time of the structure proposal except that an acetate **1b** derived from the natural pheromone was levorotatory. Since the available amount of natural serricornin **1a** was quite limited (1.5 mg from 65,000 females), we decided to clarify its stereochemistry by stereoselectively synthesizing various stereoisomers of **1a** and comparing its physical and biological properties with those of the natural pheromone. Along this line we already published several stereoselective syntheses of stereoisomers of serricornin such as (4*RS*, 6*R*, 7*R*)-, (4*RS*, 6*R*, 7*S*)- and (4*S*, 6*R*, 7*R*)-**1a**.[4-6] Careful examination of the GLC, ^{13}C-NMR and chiroptical data of these synthetic stereoisomers suggested that the absolute stereochemistry of the natural pheromone **1a** is 4*S*, 6*S*, 7*S*.[6] Herein we report in detail the synthesis of the natural pheromone itself, (4*S*, 6*S*, 7*S*)-**1a**, and its antipode. A preliminary account of this work was briefly described in review articles by K. M.[7]

Our strategy was to first prepare an optically pure alkylating agent **A** starting from a readily available chiral compound and then to achieve the asymmetric alkylation of a diethyl ketone equivalent **B** with **A**. The starting material chosen for the synthesis of **A** was (2*R*, 3*R*)-*threo*-3-methylaspartic acid **2**, which finally yielded the natural serricornin. The known racemic acid (±)-**2**[8] was resolved with (*R*)-(+)-α-phenethylamine to give (2*R*, 3*R*)-3-methylaspartic acid **2**, $[\alpha]_D^{23}$ −13.3° (5N HCl).‡ Deamination of **2** with HNO_2 proceeded with retention of configuration to give a hydroxy acid (2*R*, 3*R*)-**3a**, $[\alpha]_D^{24}$ −5.3° (H_2O). The recorded procedure for the preparation of this acid was the resolution of (±)-**3a** obtained in three steps from ethyl propionate and diethyl oxalate.[12] The corresponding Me ester **3b** was obtained in 66.5% yield from **2** by treating **3a** with CH_2N_2. After protecting the OH group as THP ether, the ester **3c** was reduced with LAH to a diol (2*R*, 3*S*)-**4a**. Removal of the THP-protective group of **4a** with TsOH in MeOH yielded a triol **4b**, which was converted to the corresponding acetonide alcohol **4c** in the conventional manner in 86% yield from **3c**. Benzylation of **4c** was followed by the removal of the acetonide group to give **4e** *via* **4d**. The primary OH group in **4e** was selectively tosylated with 1 eq of TsCl in C_5H_5N to give **4f** in *ca.* 65% yield from **4c**. Upon treatment with KOH–MeOH, the monotosylate **4f** was smoothly converted to an epoxide (2*S*, 3*R*)-**5** in 73% yield. Cleavage of the epoxy ring with Me_2CuLi gave an alcohol (2*S*, 3*S*)-**6a** in 87% yield. After protecting the secondary OH group as THP ether **6b**, the benzyl group was removed by hydrogenolysis to give **6c**. This was tosylated to give **6d**. Treatment of **6d** with NaI in acetone yielded (2*R*, 3*S*)-**7a**. Since preliminary experiments on asymmetric alkylation of (*S*)-**9** with **7a** was not satisfactory,§ we decided to change the THP protective group of **7a** for 1-methyl-1-methoxyethyl protective group. Removal of the THP group of **7a** yielded **7b**. This gave **7c** when treated with 2-methoxypropene[13] and TsOH·C_5H_5N (PPTS). The overall yield of **7c** from **6d** was 29%. This completed the synthesis of the chiral

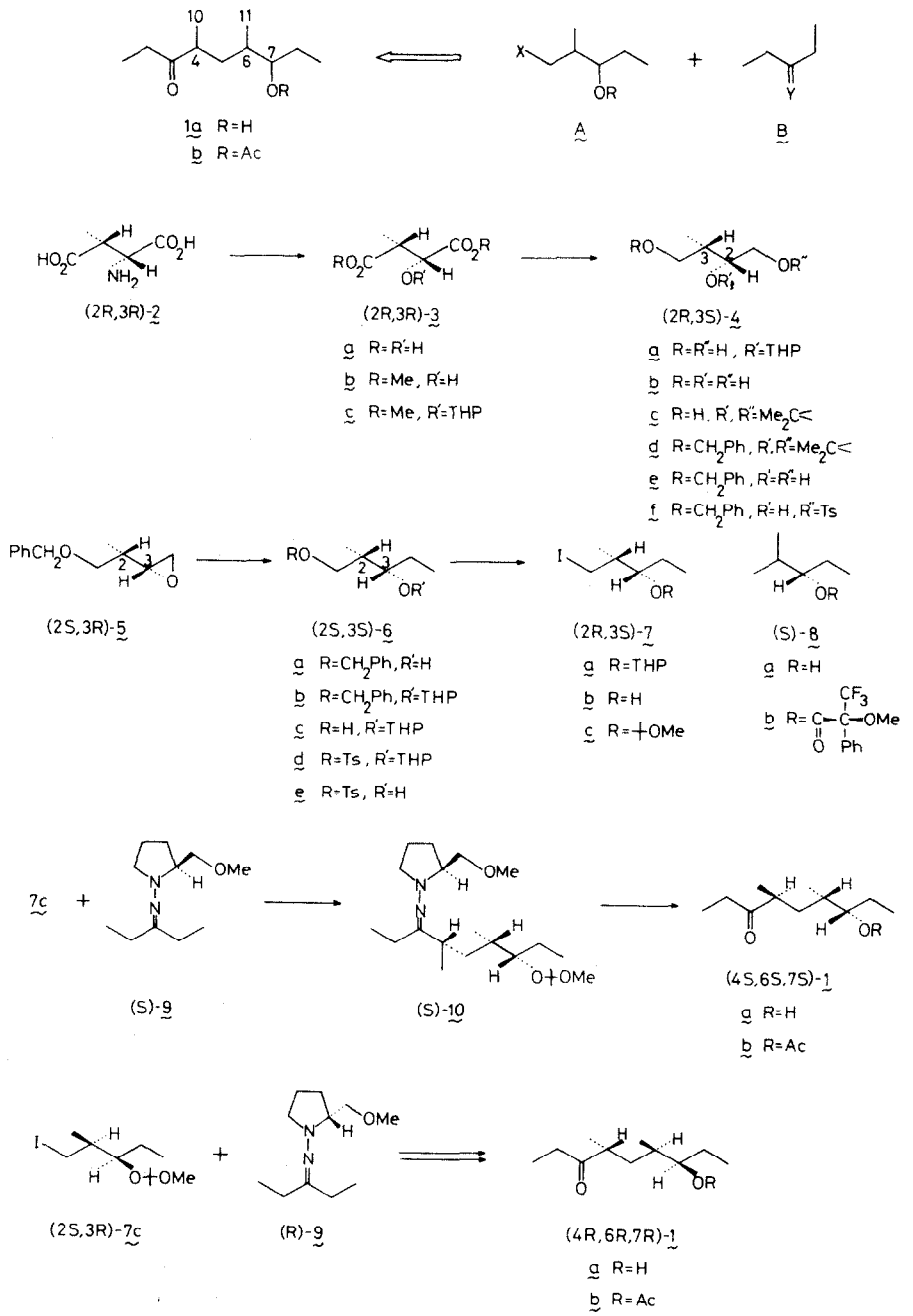
†Phermone Synthesis-53. Part 52, K. Mori, S. Kuwahara, H. Z. Levinson and A. R. Levinson. *Tetrahedron* **38**, 2291 (1982). This work was presented by K. M. at "Symposium International sur les Médiateurs Chimiques Agissant sur le Comportement des Insectes", Versailles, November 1981. The experimental part of this work was taken from the doctoral dissertation of H. N. (1983).

‡This was previously obtained by enzymatic resolution or by microbial synthesis.[9-11] In our hands enzymatic resolution of the racemic N-acetate of **2** with *Aspergillus* aminoacylase was less successful than the conventional resolution with α-phenethylamine.

§Removal of the THP group after the alkylation could not be effected under the condition mild enough to avoid racemization at C-4.

alkylating agent **A**. The optical purity of the iodide **7c** was estimated as follows. As detailed above, (2*R*, 3*S*)-**7c** was derived from pure (±)-*threo*-3-methylaspartic acid. GLC analysis of (2*R*, 3*R*)-**3b** proved its chemical purity as 100% *threo*-configuration. Therefore, instead of estimating the optical purity of (2*R*, 3*S*)-**7c** with two chiral centers, we determined the optical purity of (*S*)-**8a** with only one asymmetric carbon atom. This alcohol **8a** was derived from (2*S*, 3*S*)-**6e** by LAH reduction. The (*S*)-(−)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA)[14] ester (*S*)-**8b** was analyzed by capillary GLC to give two peaks of diastereomers in 96.5:3.5 ratio. This means the optical purity of 93% for (*S*)-**8a** and also for (2*R*, 3*S*)-**7c**.

The desired asymmetric alkylation of **B** with **A** was achieved by the method recently developed by Enders.[15,16] A hydrazone (*S*)-**9** was prepared from diethyl ketone and (*S*)-1-amino-2-methoxymethylpyrrolidine (SAMP).[15,16] This was metallated with lithium diisopropylamide (LDA) in ether and alkylated with (2*R*, 3*S*)-**7c** at −110 ~ −115°. The resulting hydrazone (*S*)-**10** was converted to its N-methiodide, which was hydrolyzed with dil HCl to yield **1a**. On the basis of Enders' work,[15,16] this asymmetric alkylation was thought to give the desired stereoisomer, (4*S*, 6*S*, 7*S*)-**1a**, on the assumption that the two chiral centers and two ether O atoms in the alkylating agent **7c** did not cause any disturbing effect against the desired asymmetric in-



duction. For the purpose of comparison with the authentic serricornin acetate, the synthetic product was converted to the corresponding acetate, (4*S*, 6*S*, 7*S*)-**1b**. This was purified by preparative GLC to give 12.2 mg of a pure sample. Its capillary GLC analysis revealed it to be highly pure with only 6% contamination with the C-4 epimer, (4*R*, 6*S*, 7*S*)-**1b**. This result means that the O-functions in the alkylating agent **7c** did not cause any appreciable effect against the normal course of asymmetric alkylation. Since the optical purity of (2*R*, 3*S*)-**7c** was 93%, the enantioselectivity of the alkylation was calculated to be $(96.5 \times 94 - 3.5 \times 6)/93 = 97.3\%$. These two figures allowed us to calculate the % composition of our synthetic **1b** to be 93.9% of (4*S*, 6*S*, 7*S*)-**1b**, 0.1% of (4*R*, 6*R*, 7*R*)-**1b**, 3.4% of (4*S*, 6*R*, 7*R*)-**1b** and 2.6% of (4*R*, 6*S*, 7*S*)-**1b**. The optical purity of our (4*S*, 6*S*, 7*S*)-**1b** was therefore calculated to be $(93.8/94.0) \times 100 = 99.8\%$. The synthetic (4*S*, 6*S*, 7*S*)-serricornin acetate **1b** was levorotatory, $[\alpha]_D^{23}$ −16.7° (*n*-hexane). The specific rotation of the acetate derived from natural serricornin was $[\alpha]_D^{23}$ −17.7° (*n*-hexane).† The identity of our (4*S*, 6*S*, 7*S*)-serricornin acetate **1b** with the natural one was confirmed by their indistinguishable IR, ^{1}H-NMR, ^{13}C-NMR, MS and GLC data. This unambiguously established the absolute stereochemistry of serricornin to be 4*S*, 6*S*, 7*S*.

In order to know whether the antipode of the natural serricornin is bioactive or not, we also synthesized (4*R*, 6*R*, 7*R*)-**1a** starting from (2*S*, 3*S*)-**2** obtained by resolution of the racemate with (*S*)-(−)-α-phenethylamine.‡ The optical purity of (2*S*, 3*R*)-**7c** was estimated to be 92% in the same manner as described for (2*R*, 3*S*)-**7c**. Alkylation of the hydrazone (*R*)-**9** derived from diethyl ketone and (*R*)-1-amino-2-methoxymethylpyrrolidine (RAMP) with (2*S*, 3*R*)-**7c** yielded crude (4*R*, 6*R*, 7*R*)-**1a**, whose purification by preparative GLC gave 7.2 mg of pure (4*R*, 6*R*, 7*R*)-**1b**, $[\alpha]_D^{23}$ +19.5° (*n*-hexane). Its spectral (IR, ^{1}H-NMR, ^{13}C-NMR and MS) data were identical with those reported for the natural isomer. In this case the sample was contaminated with 12% of the C-4 epimer as revealed by GLC.§ Therefore the enantioselectivity of this alkylation step was calculated to be 91% and our (4*R*, 6*R*, 7*R*)-**1b** was estimated to be 99% optically pure.

The biological activity of the both enantiomers of **1a** was tested on male cigarette beetles. Only the natural (4*S*, 6*S*, 7*S*)-serricornin **1a** was biologically active upon behavioral and EAG tests.

In conclusion the absolute stereochemistry of the natural serricornin was definitely proved to be 4*S*, 6*S*, 7*S*.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. IR spectra were determined as Nujol mulls (solid) or as film (liquid) on a Jasco-A-102 or a Jasco-IRA-1 spectrometer. NMR spectra were recorded at 60 MHz as CCl_4 soln with TMS as an internal standard on a Hitachi R-24A spectrometer unless otherwise stated. Optical rotations were measured on a Jasco DIP-140 or a Jasco DIP-181 polarimeter. GLC analyses were performed on a JEOL JGC-20K, a Yanaco G-180 or a Shimadzu Mini-1 (capillary GLC). GLC–MS was measured on a Hitachi 80M 002P.

†The previously reported value, $[\alpha]_D^{23}$ −26.7° (*c* = 0.075, *n*-hexane),[1] was in error.

‡For the complicated stereochemistry-pheromone activity relationship among insect pheromones see Ref. 17.

§This might be due to the partial racemization at C-4 during the hydrolysis of the N-methiodide.

(±)-threo-3-*Methylaspartic acid* (±)-**2**

A soln of diethyl acetaminomalonate (32.5 g) in EtOH (40 ml) was added to a stirred and ice-cooled soln of NaOEt (from 3.47 g of Na) in EtOH (75 ml). To this was added ethyl α-bromopropionate (30.04 g) and the mixture was stirred and heated under reflux for 7 hr. EtOH was removed *in vacuo*. The residue was diluted with water and extracted with ether. The ether soln was concentrated *in vacuo*. The resulting crude ester was mixed with conc HCl (72 ml) and water (24 ml). The mixture was stirred and heated under reflux for 20 hr. Then it was concentrated *in vacuo*. Addition of water to the residue and concentration *in vacuo* of the resulting soln were repeated to remove HCl. The residue was dissolved in EtOH (75 ml). The pH of the soln was adjusted to 3.1 by the addition of Et_3N. The precipitated amino acid (±)-**2** (10.06 g, 46%) was collected on a filter and recrystallized from water to give pure (±)-**2** (8.0 g), m.p. 272–276° (dec.) (lit.[8] m.p. 274–275°), ν_{max} 3150 (s), 1730 (br, m), 1615 (s), 1500 (s), 1465 (s), 1165 (s), 1090 (s) cm^{-1}. (Found: C, 40.44; H, 6.07; N, 9.45. Calc. for $C_9H_9O_4N$: C, 40.81; H, 6.17; N, 9.52%).

Optical resolution of (±)-**2**

(a) (2R, 3R)-(−)-**2**. (*R*)-(+)-α-Phenethylamine (46.35 g) was added to a soln of (±)-**2** in acetone (58 ml), MeOH (49 ml) and water (46 ml). Separated crystals (43 g, m.p. 250–256°) were collected on a filter. The second crop (15.7 g) of the salt (m.p. 258–263°) was also obtained. Several recrystallization of the salt from acetone–MeOH–water yielded 13.2 g of the pure salt, m.p. 262–264°, $[\alpha]_D^{22}$ +16.37° (*c* = 0.934, water). (Found: C, 57.93; H, 7.42; N, 10.39. Calc. for $C_{13}H_{20}O_4N_2$: C, 58.19; H, 7.51; N, 10.44%). This salt (4.54 g) was dissolved in water (25 ml) and adjusted to pH 3 by the addition of 3N HCl (8 ml) and EtOH (25 ml) to give (2*R*, 3*R*)-(−)-**2** (2.78 g), m.p. 259–262° (dec), $[\alpha]_D^{23}$ −13.3° (*c* = 0.949, 5N HCl); ν_{max} 3080 (m), ~2600 (br, m), 1680 (s), 1640 (s), 1615 (s), 1515 (sh, s), 1500 (s) cm^{-1} (Found: C, 40.66; H, 6.11; N, 9.44. Calc. for $C_5H_9O_4N$: C, 40.81; H, 6.17; N, 9.52%). The reported $[\alpha]_D$ value for this acid is: −13.3° ± 0.3° (*c* = 3, 5N HCl)[9], −13.9° (*c* = 1, 5N HCl)[10] and −13.1° ± 0.3° (*c* = 3.24, N HCl).[11] Our product therefore seems to be of high optical purity (≥95% e.e.).

(b) (2S, 3S)-(+)-**2**. In the same manner as described above (*S*)-(−)-α-phenethylamine salt of (2*S*, 3*S*)-(+)-**2** was obtained, m.p. 267–273°, $[\alpha]_D^{20}$ −16.35° (*c* = 1.012, H_2O); (Found: C, 58.37; H, 7.46; N, 10.56. Calc. for $C_{13}H_{20}O_4N_2$: C, 58.19; H, 7.51; N, 10.44%). The salt (2.53 g) was dissolved in water (10 ml) and the soln was adjusted to pH 3 by the addition of 3N HCl (2.8 ml) and 95% EtOH (10 ml). The precipitated crystals were collected on a filter to give 1.24 g of (2*S*, 3*S*)-(+)-**2**, $[\alpha]_D^{22}$ +12.8° (*c* = 0.995, 5N HCl). In other cases, (2*S*, 3*S*)-(+)-**2** with $[\alpha]_D^{23}$ +14.5° (*c* = 1.105, 5N HCl) and $[\alpha]_D^{23}$ +12.95° (*c* = 0.701, 5N HCl) was also obtained. The purified (2*S*, 3*S*)-(+)-**2** melted at 259–262° (dec). (Found: C, 40.93; H, 6.16; N, 9.56. Calc. for $C_5H_9O_4N$: C, 40.81; H, 6.17; N, 9.52%). The IR spectrum was identical with that of (2*R*, 3*R*)-(−)-**2**.

threo-3-*Methylmalic acid* **3a**

(a) (2R, 3R)-(−)-*Isomer*. A soln of $NaNO_2$ (1.76 g) in water (7.5 ml) was added during 45 min to a stirred and ice-cooled soln of (2*R*, 3*R*)-**2** (2.50 g) in N-H_2SO_4 (26.4 ml) at 0–5°. After stirring for 30 min at this temp, the mixture was stirred overnight at room temp. Then it was extracted with EtOAc. The aq layer was concentrated *in vacuo* after destroying H_2SO_4 with $NaNO_2$. The solid residue was washed with EtOAc. The combined EtOAc soln was dried (Na_2SO_4) and concentrated *in vacuo*. Recrystallization of the remaining solid from EtOAc–pet. ether gave 1.25 g (50%) of (2*R*, 3*R*)-(−)-**3a**, m.p. 95–97°, $[\alpha]_D^{24}$ −5.3° (*c* = 0.675, H_2O) (lit.[12] $[\alpha]_D$ −5.3° (*c* = 3.2, H_2O)), ν_{max} ~3200 (br. s), 2600 (m), 1720 (s), 1210 (s) cm^{-1}. (Found: C, 40.24; H, 5.48. Calc. for $C_5H_8O_5$: C, 40.54; H, 5.44%).

(b) (2S, 3S)-(+)-*Isomer*. In the same manner as described for (2*R*, 3*R*)-(−)-**3a**, (2*S*, 3*S*)-**2** was deaminated to give crude (2*S*, 3*S*)-**3a**, which was directly used for the next step.

Dimethyl threo-3-*methylmalate* **3b**

(a) (2R, 3R)-(−)-*Isomer*. Methylation of (2*R*, 3*R*)-**3a** with ethereal CH_2N_2 yielded (2*R*, 3*R*)-**3b** in 66.5% yield from **2**, b.p.

107–110°/11 mm, $[\alpha]_D^{23}$ −5.19° (c = 1.535, Et_2O); ν_{max} 3500 (m), 1740 (s), 1260 (s), 1210 (s) cm^{-1}; δ 1.09 (3H, d, J = 7 Hz), 2.74 (1H, dt, J_1 = 4, J_2 = 7 Hz), 3.1 (1H, –OH), 3.61 (3H, s), 3.69 (3H, s), 4.37 (1H, d, J = 4 Hz). (Found: C, 47.43; H, 6.89; Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.87%). The $[\alpha]_D$ value of crude (−)-**3a** was only $[\alpha]_D^{24.5}$ −0.23° (Et_2O). Only after GLC purification, the specific rotation reported here was observed.

(b) (2S, 3S)-(+)-*Isomer.* In the same manner as described above (2*S*, 3*S*)-**3a** yielded (2*S*, 3*S*)-**3b**, b.p. 105–108°/10 mm, $[\alpha]_D^{23}$ +1.21° (c = 1.121, Et_2O). Its IR and NMR data were identical with those of (2*R*, 3*R*)-**3b**. This was not purified by preparative GLC. Therefore the $[\alpha]_D$ value was not reliable.

Dimethyl threo-3-*methylmalate THP ether* **3c**

(a) (2R, 3R)-*Isomer.* Dihydropyran (5.13 g) and *p*-TsOH (0.1 g) were added to a soln of (2*R*, 3*R*)-**3b** (9.40 g) in ether (72 ml). The mixture was stirred overnight at room temp, poured into ice-water and extracted with ether. The ether soln was washed with $NaHCO_3$ soln and brine, dired (K_2CO_3) and concentrated *in vacuo*. The residue (14.73 g, quantitative) was employed for the next step without further purification, ν_{max} 1740 (vs), 1205 (s), 1020 (s) cm^{-1}.

(b) (2S, 3S)-*Isomer.* In the same manner as described above, (2*S*, 3*S*)-**3b**(3.39 g) and dihydropyran (1.85 g) yielded 5.24 g (quantitative) of (2*S*, 3*S*)-**3c**. Its IR spectrum was identical with that of (2*R*, 3*R*)-**3c**.

threo-3-*Methylbutane*-1,2,4-*triol* 2-*THP ether* **4a**

(a) (2R, 3S)-*Isomer.* A soln of (2*R*, 3*R*)-**3c** (14.7 g) in ether (30 ml) was added dropwise to a stirred and ice-cooled suspension of LAH (3.05 g) in ether (90 ml). The mixture was stirred overnight and the excess LAH was destroyed by the addition of water (3 ml), 5% NaOH soln (6 ml) and water (3 ml). The mixture was filtered and the filter cake was washed with THF. The combined organic soln was dried (K_2CO_3) and concentrated *in vacuo* to give 10.35 g (95%) of (2*R*, 3*S*)-**4a**, ν_{max} 3400 (s), 1135 (s), 1075 (s), 1025 (s) cm^{-1}. This was employed for the next step without further purification.

(b) (2S, 3R)-*Isomer.* In the same manner as described above, (2*S*, 3*S*)-**3c** (5.41 g) was reduced with LAH (0.951 g) to give 3.64 g of crude (2*S*, 3*R*)-**4a**, whose IR spectrum was identical with that of (2*R*, 3*S*)-**4a**. This was directly employed for the next step.

threo-3-*Methylbutane*-1,2,4-*triol* **4b**

(a) (2R, 3S)-*Isomer.* *p*-TsOH (0.60 g) was added to a soln of (2*R*, 3*S*)-**4a** (10.34 g) in MeOH (80 ml). The mixture was stirred overnight at room temp. After neutralization with $NaHCO_3$, the mixture was filtered and the filtrate was concentrated *in vacuo* to give 7.38 g (quantitative) of (2*R*, 3*S*)-**4b**, ν_{max} 3350 (vs), 2950 (s), 2860 (m), 1460 (m), 1125 (m), 1075 (m), 1030 (s), 880 (w) cm^{-1}. This was employed for the next step without further purification.

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**4a** (3.64 g) yielded 2.28 g of (2*S*, 3*R*)-**4b**. Its IR spectrum was identical with that of the antipode. This was directly employed for the next step.

threo-3-*Methylbutane*-1,2,4-*triol* 1,2-*acetonide* **4c**

(a) (2R, 3S)-*Isomer.* *p*-TsOH (0.20 g) was added to a soln of (2*R*, 3*S*)-**4b** (7.38 g) in acetone (50 ml) and the mixture was stirred overnight at room temp. Then it was neutralized with $NaHCO_3$ and filtered. The filtrate was concentrated *in vacuo*. The residue was distilled to give 7.33 g (85.7% from **3b**) of (2*R*, 3*S*)-**4c**, b.p. 95–100°/11 mm, $[\alpha]_D^{22}$ +6.66° (c = 0.907, C_6H_6); ν_{max} 3400 (br. s), 1380 (s), 1370 (s), 1215 (s), 1060 (s), 1040 (s), 860 (s) cm^{-1}; δ 0.90 (3H, d, J = 7 Hz), 1.25 (3H, s), 1.30 (3H, s), 1.5–1.7 (1H, m), 2.4 (1H, br, –OH), 3.3–4.2 (5H, m). This was employed for the next step without further purification.

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**4b** (2.28 g) yielded (2*S*, 3*R*)-**4c** (2.157 g, 70% from **3b**), b.p. 73–74°/4 mm, $[\alpha]_D^{22}$ −7.55° (c = 1.043, C_6H_6). This exhibited the same IR and NMR spectra as those of (2*R*, 3*S*)-**4c**. Upon GLC analysis this was shown to be 81.2% pure. The $[\alpha]_D$ value was therefore not reliable.

threo-3-*Methylbutane*-1,2,4-*triol* 1,2-*acetonide* 4-*benzyl ether* **4d**

(a) (2R, 3S)-*Isomer.* A soln of (2*R*, 3*S*)-**4c** (4.86 g) in DMSO (3.7 ml) was added dropwise to a stirred soln of $NaCH_2SOMe$ (from 1.78 g of 50% NaH) in DMSO (17 ml) at room temp. After stirring for 1 hr, $PhCH_2Cl$ (4.67 g) was added to the mixture. The stirring was continued for 4 hr at room temp. Then the mixture was diluted with ice-water and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 9.75 g of crude (2*R*, 3*S*)-**4d**, ν_{max} 1215 (s), 1100 (s), 1060 (s) cm^{-1}; δ 0.95 (3H, d, J = 7 Hz), 1.25 (3H, s), 1.28 (3H, s), 1.6–1.9 (1H, m), 3.0–4.0 (6H, s), 4.40 (2H, s), 7.10 (5H, s). This was employed for the next step without further purification.

(b) (2S, 3R)-*Isomer.* In the same manner as described above, (2*S*, 3*R*)-**4c** (2.15 g) yielded 4.00 g of crude (2*S*, 3*R*)-**4d**, whose IR and NMR spectra were identical with those of (2*R*, 3*S*)-**4d**. This was employed for the next step without further purification.

threo-3-*Methylbutane*-1,2,4-*triol* 4-*benzyl ether* **4e**

(a) (2R, 3S)-*Isomer.* A mixture of N HCl–MeOH–water (1:6:2.4, 55 ml) was added to (2*R*, 3*S*)-**4d** (9.75 g). The resulting mixture was stirred and heated at 60° for 6.5 hr. Then it was neutralized with $NaHCO_3$ and extracted once with *n*-hexane. The aq layer was concentrated *in vacuo* and extracted thoroughly with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 4.17 g (65% from **4c**) of (2*R*, 3*S*)-**4e**, b.p. 148–150°/0.2 mm, $[\alpha]_D^{23}$ +4.36° (c = 1.583, C_6H_6); ν_{max} 3400 (br. s), 1600 (w), 1100 (s), 1060 (s), 1020 (s), 730 (s), 700 (s) cm^{-1}; δ 0.88 (3H, d, J = 6 Hz), 1.5–1.9 (1H, m), 3.30 (2H, d, J = 6 Hz), 3.38 (2H, d, J = 6 Hz), 3.4–3.6 (1H, m), 3.3–3.6 (2H, –OH), 4.33 (2H, s), 7.08 (5H, s). (Found: C, 68.32; H, 8.81. Calc. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63%).

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**4d** (from 2.15 g of **4c**) yielded 1.45 g (51% from **4c**) of (2*S*, 3*R*)-**4e**, b.p. 149–151°/0.15 mm, $[\alpha]_D^{22}$ −5.77° (c = 1.001, C_6H_6). This exhibited the identical IR and NMR spectra with those of (2*R*, 3*S*)-**4e**.

threo-3-*Methylbutane*-1,2,3-*triol* 4-*benzyl ether* 1-*tosylate* **4f**

(a) (2R, 3S)-*Isomer.* *p*-TsCl (3.93 g) was added to a stirred and ice-cooled soln of (2*R*, 3*S*)-**4e** (4.17 g) in C_5H_5N (8.7 ml). After stirring for a while at 0–5°, the mixture was left to stand overnight in a refrigerator. It was poured into ice-water and extracted with ether. The ether soln was washed with water, dil HCl, water, $CuSO_4$ soln, water, $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 6.80 g (94%) of (2*R*, 3*S*)-**4f**, ν_{max} 1595 (m), 1190 (s), 1180 (s), 1100 (s) cm^{-1}; δ 0.85 (3H, d, J = 6 Hz), 1.8–2.0 (1H, m), 2.37 (3H, s), 2.6–2.9 (1H, –OH), 3.33 (2H, d, J = 5 Hz), 3.82 (2H, s), 3.7–4.0 (1H, m), 4.32 (2H, s), 7.08 (5H, s), 7.10 (2H, d, J = 8 Hz), 7.55 (2H, d, J = 8 Hz). This was employed for the next step without further purification.

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*S*)-**4e** (1.55 g) yielded 2.47 g (92%) of (2*S*, 3*R*)-**4f**. This was employed directly for the next step.

3,4-*Epoxy*-2-*methyl*-1-*butanol benzyl ether* **5**

(a) (2S, 3R)-*Isomer.* A soln of (2*R*, 3*S*)-**4f** (3.64 g) in MeOH (3.3 ml) was added to a stirred and ice-cooled soln of KOH (0.69 g) in MeOH (10 ml). The mixture was stirred at 0–5° for 15 min and then at 17° for 20 min. MeOH was removed *in vacuo*. The residue was diluted with ice-water and extracted with ether. The ether soln was washed with dil HCl and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 1.40 g (73%) of (2*S*, 3*R*)-**5**, b.p. 99–100°/0.18 mm, $[\alpha]_D^{22}$ +9.67° (c = 0.947, C_6H_6); ν_{max} 1600 (w), 1100 (s), 740 (s), 700 (s) cm^{-1}; δ 0.97 (3H, d, J = 6Hz), 1.3–1.7 (1H, m), 2.3–2.7 (3H, m), 3.30 (2H, d, J = 6 Hz), 4.39 (2H, s), 7.15 (5H, s). (Found: C, 74.19; H, 8.39. Calc. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39%).

(b) (2R, 3S)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**4f** (2.47 g) gave 0.863 g (66%) of (2*R*, 3*S*)-**5**, b.p. 90–91°/0.12 mm, n_D^{22} 1.5005; $[\alpha]_D^{22}$ −11.4° (c = 1.08, C_6H_6); GLC (Column, 3% SE-30 at 135°; Carrier gas, N_2, 0.95 kg/cm^2): R_t 5.43 min (97.6%). (Found: 74.53; H, 8.54. Calc. for $C_{12}H_{16}O_2$: C, 74.97;

H, 8.39%). The IR and NMR spectral data of (2*R*, 3*S*)-**5** were identical with those of (2*S*, 3*R*)-**5**.

threo-2-*Methylpentane*-1,3-*diol* 1-*benzyl ether* **6a**

(a) (2S, 3S)-*Isomer.* A soln of MeLi in ether was prepared from MeBr (43.22 g) and Li (4.93 g) in ether (210 ml). A portion (90 ml) of this MeLi soln was added dropwise to a stirred and cooled suspension of CuI (6.95 g) in ether (15 ml) at −30° under Ar. To this Me_2CuLi soln was added dropwise with stirring and cooling a soln of (2*S*, 3*R*)-**5** (1.40 g) in ether (5 ml) at −53 ~ −55°. The temp was gradually raised to −20° during 4 hr. Then the mixture was left to stand overnight at −20°. The reaction was quenched by the addition of NH_4Cl soln under ice-cooling. The mixture was extracted with ether. The ether soln was washed with NH_4Cl soln and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 1.32 g (87%) of (2*S*, 3*S*)-**6a**, b.p. 112–113°/0.20 mm, $[\alpha]_D^{24}$ +3.52° (*c* = 0.997, C_6H_6); ν_{max} 3450 (br. s), 1605 (vw), 1100 (s), 1070 (s), 970 (s), 740 (s), 700 (s) cm^{-1}; δ 0.85 (3H, d, J = 6 Hz), 0.92 (3H, t, J = 6 Hz), 1.1–1.4 (2H, m), 1.5–1.8 (1H, m), 1.90 (1H, –OH), 3.37 (2H, d, J = 5 Hz), 3.42 (1H, m), 4.30 (2H, s), 7.12 (5H, s). (Found: C, 74.64; H, 9.74. Calc. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%).

(b) (2R, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*S*)-**5** (0.86 g) yielded 0.764 g (82%) of (2*R*, 3*R*)-**6a**, b.p. 104–105°/0.13 mm, n_D^{22} 1.4990; $[\alpha]_D^{23}$ −5.40° (*c* = 1.010, C_6H_6); GLC (Column 3% SE-30 at 140°; Carrier gas, N_2, 0.99 kg/cm^2): Rt 6.20 min (97.0%); (Found: C, 74.47; H, 9.75. Calc. for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%). Its IR and NMR spectra were identical with those of (2*S*, 3*S*)-**6a**.

threo-2-*Methylpentane*-1,3-*diol* 1-*benzyl ether* 3-*THP ether* **6b**

(a) (2S, 3S)-*Isomer.* Dihydropyran (0.93 g) and *p*-TsOH (0.10 g) were added to a soln of (2*S*, 3*S*)-**6a** (2.09 g) in ether (14 ml). The mixture was stirred overnight at room temp. Then it was poured into ice–water and extracted with ether. The ether soln was washed with water, $NaHCO_3$ soln and brine, dried (K_2CO_3) and concentrated *in vacuo* to give crude (2*S*, 3*S*)-**6b**, which was directly used for the next step, ν_{max} 1115 (s), 1080 (s), 1030 (s), 1000 (s), 740 (s), 700 (s) cm^{-1}; δ 0.88 (3H, d, J = 6 Hz), 0.90 (3H, t, J = 7Hz), 1.2–2.1 (~9H, m), 3.1–3.8 (5H, m), 4.37 (2H, s), 4.47 (1H, br), 7.13 (5H, s).

(b) (2R, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*R*)-**6a** (0.785 g) gave 1.08 g (98%) of (2*R*, 3*R*)-**6b**, whose IR and NMR spectra were same as those of (2*S*, 3*S*)-**6b**.

threo-2-*Methylpentane*-1,3-*diol* 3-*THP ether* **6c**

(a) (2S, 3S)-*Isomer.* 5% Pd–C (0.50 g) was added to a soln of (2*S*, 3*S*)-**6b** (3.09 g) in EtOH (45 ml). When the H_2 uptake ceased, the catalyst was filtered off and the filtrate was concentrated *in vacuo* to give 1.64 g of crude (2*S*, 3*S*)-**6c**. Judging from its NMR spectrum this was contaminated with (2*S*, 3*S*)-2-*methylpentane*-1,3-diol generated by removal of the THP protective group. A small amount of (2*S*, 3*S*)-**6b** was also detected in the crude product as revealed by the presence of a signal at δ 7.1. This was employed for the next step without further purification.

(b) (2R, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*R*)-**6b** (1.08 g) yielded 0.522 g (88%) of (2*R*, 3*R*)-**6c** as a crude mixture contaminated with (2*R*, 3*R*)-2-methylpentane-1,3-diol and (2*R*, 3*R*)-**6b**. This was directly employed for the next step.

threo-2-*Methylpentane*-1,3-*diol* 3-*THP ether* 1-*tosylate* **6d**.

(a) (2S, 3S)-*Isomer.* *p*-TsCl (1.60 g) was added to a stirred and ice-cooled soln of (2*S*, 3*S*)-**6c** (crude product, 1.64 g) in C_5H_5N (3.6 ml). The mixture was stirred for 8 hr, then diluted with ice–water and extracted with ether. The ether soln was washed with water, $CuSO_4$ soln, $NaHCO_3$ soln and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 2.46 g of an oil. This was dissolved in ether (7 ml) and mixed with dihydropyran (1.5 ml) and *p*-TsOH (0.05 g). The mixture was stirred overnight at room temp, washed with water, $NaHCO_3$ soln and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 3.03 g of (2*S*, 3*S*)-**6d**, ν_{max} 1600 (m), 1360 (s), 1190 (s), 1175 (s), 1030 (s), 965 (s) cm^{-1}; δ 0.87 (3H, d, J = 6 Hz), 0.87 (3H, t, J = 7 Hz), 1.4–2.0 (9H, m), 2.37 (3H, s), 3.3–3.9 (5H, m), 4.32 (1H, s), 7.14 (2H, d, J = 8 Hz), 7.57 (2H, d, J = 8 Hz). This was employed for the next step without further purification.

(b) (2R, 3R)-*Isomer.* In the same manner as described above 0.522 g of (2*R*, 3*R*)-**6c** yielded 0.858 g (84%) of an oil. A portion (0.693 g) of it was treated with dihydropyran and *p*-TsOH in ether to give 0.779 g (quantitative) of (2*R*, 3*R*)-**6d**.

threo-1-*Iodo*-2-*methyl*-3-*pentanol* 3-*THP ether* **7a**

(a) (2R, 3S)-*Isomer.* NaI (1.01 g) and K_2CO_3 (24.3 mg) were added to a soln of (2*S*, 3*S*)-**6d** (1.85 g) in acetone (9.6 ml). The mixture was stirred at room temp for 5 days. Then it was diluted with water and extracted with ether. The ether soln was washed with 5% $Na_2S_2O_3$ soln, water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 1.45 g (90%) of (2*R*, 3*S*)-**7a**. Major part of it (1.30 g) was chromatographed over SiO_2 (Mallinckrodt CC-7, 20 g, 39 cm × 1.5 cm). Elution with *n*-hexane–ether gave (2*R*, 3*S*)-**7a** (0.439 g), (2*R*, 3*S*)-**7b** (0.154 g), (2*S*, 3*S*)-**6a** (48 mg) and a mixture of **7a**, **7b** and an unidentified compound (0.303 g). The yield of the pure (2*R*, 3*S*)-**7a** was 48%, ν_{max} 1125 (s), 1075 (s), 1030 (s), 995 (s) cm^{-1}. This was used directly for the next step.

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*R*)-**6d** (0.779 g) yielded 0.673 g of an oil. A portion of it (0.354 g) was purified by prep TLC (developed with *n*-hexane–Et_2O 2:1) to give 0.244 g of pure (2*S*, 3*R*)-**7a** (R_f 0.40–0.69). This was employed for the next step without further purification.

threo-1-*Iodo*-2-*methyl*-3-*pentanol* **7b**

(a) (2R, 3S)-*Isomer.* *p*-TsOH (6.5 mg) was added to a soln of (2*R*, 3*S*)-**7a** (0.529 g) in MeOH (4 ml). The mixture was stirred overnight at room temp, then neutralized with $NaHCO_3$ and filtered. The filtrate was concentrated *in vacuo* to give 0.475 g of (2*R*, 3*S*)-**7b**, ν_{max} 3400 (br, s), 1195 (s), 970 (s), 960 (s) cm^{-1}; δ 0.96 (3H, t, J = 6 Hz), 1.00 (3H, d, J = 6 Hz), 1.25–1.75 (3H, m), 2.0 (1H, br. s), 3.01 (1H, dd, J_1 = 9, J_2 = 6 Hz), 3.20 (1H, dd, J_1 = 9, J_2 = 2 Hz), 3.4–3.55 (1H, m).

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**7a** (0.318 g) yielded 0.228 g (98%) of (2*S*, 3*R*)-**7b**. This was employed for the next step without further purification. The IR and NMR spectra were identical with those of (2*R*, 3*S*)-**7b**.

threo-1-*Iodo*-2-*methyl*-3-*pentanol* 3-(1′-*methoxy*-1′-*methyl*)*ethyl ether* **7c**

(a) (2R, 3S)-*Isomer.* A trace amount of TsOH–C_5H_5N (PPTS) was added to a soln of (2*R*, 3*S*)-**7b** (0.475 g) in 2-methoxypropene (7 ml) and the mixture was stirred overnight at room temp. Then it was poured into water and extracted with ether. The ether soln was washed with water, $NaHCO_3$ soln and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 0.304 g (60% from **7a**) of (2*R*, 3*S*)-**7c**, ν_{max} 1200 (s), 1180 (s), 1150 (s), 1120 (s), 1070 (s), 1040 (s), 1000 (s) cm^{-1}; δ 0.90 (3H, t, J = 6 Hz), 0.95 (3H, d, J = 5 Hz), 1.25 (3H, s), 1.30 (3H, s), 1.4–1.7 (3H, m), 3.18 (3H, s), 2.9–3.2 (3H, m); MS: *m*/*z* 211 (15%, M-89 = M-$OCMe_2OMe$) 169 (20%), 155 (9%), 73 (100%).

(b) (2S, 3R)-*Isomer.* In the same manner as described above (2*S*, 3*R*)-**7b** (0.228 g) yielded 0.248 g (83%) of (2*S*, 3*R*)-**7c**. This showed the IR, NMR and mass spectra identical with those of (2*R*, 3*S*)-**7c**.

threo-2-*Methylpentane*-1,3-*diol* 1-*tosylate* **6e**

(a) (2S, 3S)-*Isomer.* A trace amount of *p*-TsOH was added to a soln of (2*S*, 3*S*)-**6d** (0.393 g) in MeOH (1 ml). The soln was stirred overnight at room temp, neutralized with $NaHCO_3$ and filtered. The filtrate was concentrated *in vacuo* to give 0.315 g (quantitative) of (2*S*, 3*S*)-**6e**, ν_{max} 1190 (s), 1180 (s), 960 (s) cm^{-1}; δ 0.78 (3H, d, J = 7 Hz), 0.84 (3H, t, J = 6 Hz), 1.2–1.7 (3H, m), 2.27 (3H, s), 2.2 (1H, s, –OH), 3.2–4.2 (3H, m), 7.13 (2H, d, J = 8 Hz), 7.50 (2H, d, J = 8 Hz).

(b) (2R, 3R)-*Isomer.* In the same manner as described above (2*R*, 3*R*)-**6d** (0.143 g) yielded 0.133 g of crude (2*R*, 3*R*)-**6e**. The IR and NMR spectra were identical with those of (2*S*, 3*S*)-**6e**.

2-*Methyl*-3-*pentanol* **8a**

(a) (S)-*Isomer.* A soln of (2*S*, 3*S*)-**6e** (0.31 g) in ether (1 ml) was

added dropwise to a suspension of LAH (62 mg) in ether (2 ml). The mixture was stirred and heated under reflux for 12 hr. The excess LAH was destroyed by the addition of 20% KOH soln (0.1 ml) and water (0.1 ml). The mixture was diluted with ether and filtered. The ether soln was dried ($MgSO_4$) and concentrated under atm press to give 0.103 g of crude (*S*)-**8a**. A portion of it (32 mg) was used for the prepn of the MTPA ester and the rest of the material was purified by prep GLC (column, 10% FFAP, 2 m × 3 mm at 60°) to give 7.8 mg of pure (*S*)-**8a**, $[\alpha]_D^{23}$ −16.9° (*c* = 0.390, EtOH) (lit.[18] $[\alpha]_D$ +16.40° (*c* = 1.06, EtOH) for (*R*)-**8a**).

(b) (R)-*Isomer.* In the same manner as described above (2*R*, 3*R*)-**6e** (0.133 g) yielded 50 mg of crude (*R*)-**8a**.

2-*Methyl*-3-*pentanol* (S)-(−)-*MTPA ester* **8b**

(a) (S)-*Isomer.* MTPA ester was prepared in the conventional manner from (*S*)-MTPA Cl and (*S*)-**8a**.[14] Thus obtained (*S*)-**8b** showed the following properties: ν_{max} 1745 (s), 1270 (s), 1170 (s) cm^{-1}; δ 0.86 (3H, t, J = 6 Hz), 0.92 (6H, d, J = 6 Hz), 1.0–2.0 (3H, m), 3.46 (3H, s), 4.6–4.9 (1H, m), 7.0–7.5 (5H, m); GLC (Column, Carbowax 20M, 50 m × 0.28 mm at 150°; Carrier gas, He, 30 psi): R_t 21.31 min (3.5%). 21.71 min (96.5%). Optical purity of (*S*)-**8a** = 93% e.e.

(b) (R)-*Isomer.* In the same manner as described above, MTPA ester was prepared from (*S*)-MTPA Cl and (*R*)-**8a** (22.1 mg). Thus obtained (*R*)-**8b** showed IR and NMR spectra very similar to those of (*S*)-**8b**. GLC of (*R*)-**8b** (Column, Carbowax 20M, 50 m × 0.28 mm at 150°; Carrier gas, He, 30 psi): R_t 18.42 min (96.0%), 18.58 min (4.0%). Optical purity of (*R*)-**8a** = 92% e.e.

Asymmetric alkylation of **9** *with* **7c**

(a) *Alkylation of* (S)-**9** with (2R, 3S)-**7c**. A soln of LDA was prepared by the addition of *n*-BuLi (1.40 N in *n*-hexane, 6.8 ml) to a stirred and cooled soln of *i*-Pr_2NH (1.3 ml) in ether (26 ml) at −3 ~ −1° under Ar. After stirring for 15 min a soln of (*S*)-**9** (1.787 g) in ether (9.2 ml) was added dropwise to a cooled and stirred LDA soln at −7 ~ −4°. After stirring for 2 hr at this temp, the mixture was cooled to −110°. A soln of (2*R*, 3*S*)-**7c** (0.300 g) in ether (8 ml) was added dropwise to the stirred mixture at −110 ~ −115°. The mixture was kept at this temp for 1 hr, at −100 ~ −85° for 1 hr, at −85 ~ −68° for 1 hr, at ~ −43° for 2 hr and finally left to stand overnight at −20°. The mixture was diluted with ice–water and extracted with ether. The ether soln was washed with water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give 1.905 g of a mixture of (*S*)-**9** *and* (*S*)-**10**. This was directly employed for the next step.

(b) *Alkylation of* (R)-**9** *with* (2S, 3R)-**7c**. In the same manner as described above (*R*)-**9** (1.146 g) was alkylated with (2*S*, 3*R*)-**7c** (0.248 g) in the presence of LDA prepared from 1.60N *n*-BuLi (3.8 ml) and *i*-Pr_2NH (0.87 ml) in ether. The resultant mixture (1.26 g) of (*R*)-**9** and (*R*)-**10** was directly used for the next step.

Sericornin (4,6-*dimethyl*-7-*hydroxy*-3-*nonanone*) **1a**

(a) (4S, 6S, 7S)-*Isomer* (= *natural sericornin*). To the above mentioned mixture of (*S*)-**9** and (*S*)-**10** (1.905 g) was added MeI (0.87 ml). The mixture was heated under reflux at 60° for 16 hr. The excess MeI was removed *in vacuo*. 3N HCl (18 ml) was added to the residue. The mixture was stirred for 5 min at room temp. Then *n*-pentane was added and the stirring was continued for 30 min. The pentane layer was separated, washed with water and brine, dried (Na_2SO_4) and concentrated under atm press to give 0.124 g of crude (4*S*, 6*S*, 7*S*)-**1a**, ν_{max} 3500 (m), 2960 (s), 2920 (s), 2870 (s), 2850 (m), 1710 (s), 1460 (s), 1410 (m), 1380 (m), 1260 (w), 1230 (w), 1165 (m), 1150 (m), 1100 (s), 1040 (m), 1000 (m), 980 (s), 910 (w), 895 (w), 800 (w) cm^{-1}.

(b) (4R, 6R, 7R)-*Isomer.* In the same manner as described above the above mentioned mixture of (*R*)-**9** and (*R*)-**10** (1.26 g) was treated with MeI (1.4 ml) for 16 hr at 60° to give N-methiodide. This was hydrolyzed with 3N HCl (29 ml) in the presence of *n*-pentane (148 ml). Subsequent work-up gave 80 mg of crude (4*R*, 6*R*, 7*R*)-**1a** (52% yield from **7c**). This exhibited the IR spectrum identical with that of (4*S*, 6*S*, 7*S*)-**1a**.

Sericornin acetate (4,6-*dimethyl*-7-*acetoxy*-3-*nonanone*)**1b**

(a) (4S, 6S, 7S)-*Isomer* (= *natural sericornin acetate*). Ac_2O (0.4 ml) was added to an ice-cooled soln of (4*S*, 6*S*, 7*S*)-**1a** (96.6 mg) in C_5H_5N (0.4 ml). The mixture was stirred overnight at room temp. Then it was diluted with ice–water and extracted with *n*-pentane. The pentane soln was washed with water and brine, dried (Na_2SO_4) and concentrated to give 0.124 g of **1b**. This was purified by prep GLC. (Column, 10% OV-101, 2 m × 3 mm; Carrier gas, He, 40 ml/min) to give 12.2 mg of pure (4*S*, 6*S*, 7*S*)-**1b**, ν_{max} 2955 (s), 2930 (s), 2870 (m), 1730 (s), 1710 (s), 1460 (m), 1370 (m), 1240 (s), 1150 (w), 1100 (m), 1070 (w), 1020 (m), 960 (m), 920 (w), 890 (w), 800 (w), 705 (w) cm^{-1}; δ (100MHz, $CDCl_3$) 0.8–1.14 (12H, m), 1.3–1.7 (5H, m), 2.08 (3H, s), 2.4–2.8 (3H, m), 4.76 (1H, m); ^{13}C-NMR (25MHz, $CDCl_3$) δ 7.84 (C-1), 34.22 (C-2) 214.88 (C-3), 43.47 (C-4), 24.16 (C-5), 33.70 (C-6) 78.04 (C-7), 35.92 (C-8), 10.18 (C-9), 16.62 (C-10) 14.39 (C-11); MS: m/z 168 (14%), 157 (30%), 140 (3%), 139 (33%), 128 (8%), 127 (6%). 125 (4%), 117 (5%), 112 (6%), 111 (43%), 101 (3%), 99 (19%), 97 (3%), 91 (7%), 87 (9%), 86 (100%), 84 (6%), 83 (42%), 82 (5%), 70 (29%), 69 (49%), 57 (68%), 56 (4%), 55 (15%), 43 (44%). These IR, NMR and MS data were completely identical with those of the natural sericornin acetate. The capillary GLC analysis (Column, OV-101, 30 m × 0.25 mm at 80° + 2°/min upto 240°; Carrier gas, He, 1 ml/min) revealed 6% contamination with the C-4 epimer [(4*S*, 6*S*, 7*S*)-**1b**: (4R, 6S, 7S)-**1b** = 94:6]. The optical rotation data of this compound are shown in Table 1.

(b) (4R, 6R, 7R)-*Isomer.* Ac_2O (0.9 ml) was added to an ice-cooled soln of (4*R*, 6*R*, 7*R*)-**1a** (41 mg) in C_5H_5N (0.9 ml). The mixture was stirred overnight and worked up as described above. After prep GLC on OV-101, 7.2 mg of pure (4*R*, 6*R*, 7*R*)-**1b** was obtained. Its IR, NMR and MS data coincided with those of (4*S*, 6*S*, 7*S*)-**1b**. The capillary GLC analysis as for (4*S*, 6*S*, 7*S*)-**1b** revealed 12% contamination with the C-4 epimer [(4*R*, 6*R*, 7*R*)-**1b**: (4*S*, 6*R*, 7*R*)-**1b** = 88: 12]. The optical rotation data of this compound are shown in Table 1.

Table 1. Optical rotations of natural and synthetic sericornin acetate **1b** as measured in *n*-hexane at 23°

	Natural	Synthetic	
	1b	(4S,6S,7S)-**1b**	(4R,6R,7R)-**1b**
$[\alpha]_D$	−17.7° *	−16.7° †	+19.5° ‡
$[\alpha]_{577}$	———	−19.6°	+20.5°
$[\alpha]_{546}$	−19.7°	−22.0°	+23.0°
$[\alpha]_{435}$	−36.8°	−45.3°	+48.3°
$[\alpha]_{365}$	−70.3°	−92.0°	+92.1°

* c = 0.155. † c = 0.295. ‡ c = 0.220.

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