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SYNTHESIS OF BOTH THE ENANTIOMERS OF THE HETEROCYCLIC PHEROMONES ISOLATED FROM THE MALE SWIFT MOTH HEPIALUS HECTA L.†

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Abstract -- Both the enantiomers of the following three main components of the pheromone blend of the male swift moth Hepialus hecta L. were synthesized in highly optically pure state starting from chiral building blocks of microbial origin: (i) 6-ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one, (ii) 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one and (iii) 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene.

In 1985 Francke and his coworkers identified the three main components of the pheromone blend of the male swift moth Hepialus hecta L. as 6-ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one **1**, 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one **2** and 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene **3**.[1,2] Following Prof. Francke's suggestion, we undertook a project to synthesize both the enantiomers of these three compounds in highly optically pure state. The synthetic enantiomers of **1**, **2** and **3** would serve as reference

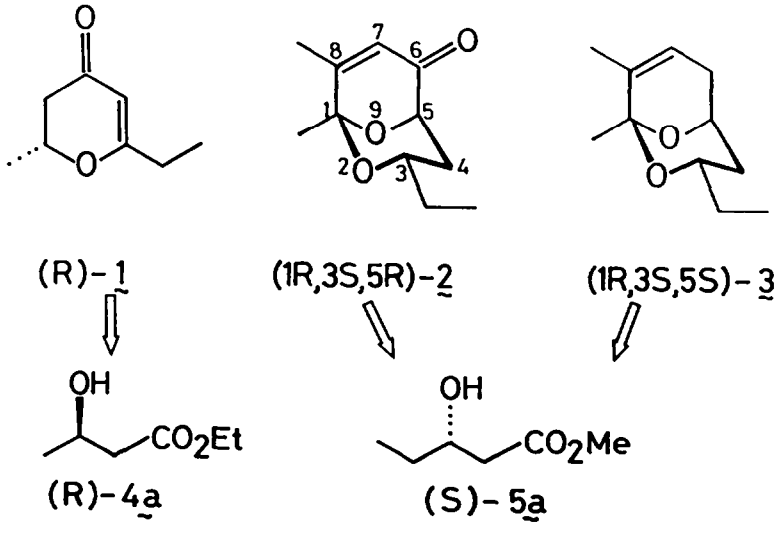

Fig. 1. Structures of the target molecules and their synthetic plan.

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samples in determining the absolute configuration of the natural products.[3] This paper describes in detail our synthesis of both the enantiomers of these oxygen heterocycles. After the completion of our work, a preliminary communication was published, in which DeShong et al. reported a synthesis of (1R,3S,5R)-2.[4]

Our synthetic plan as shown in Fig. 1 is to utilize chiral building blocks of microbial origin as starting materials. For the synthesis of both the enantiomers of **1**, ethyl (R)-3-hydroxybutanoate **4a**[5,6] and (S)-**4a'**[5,7] are the ideal starting materials. Both the enantiomers of 2 and 3 are derivable from methyl (R)-3-hydroxypentanoate **5a'**[8] and (S)-5a.[9] The above plan was put into practice as follows.

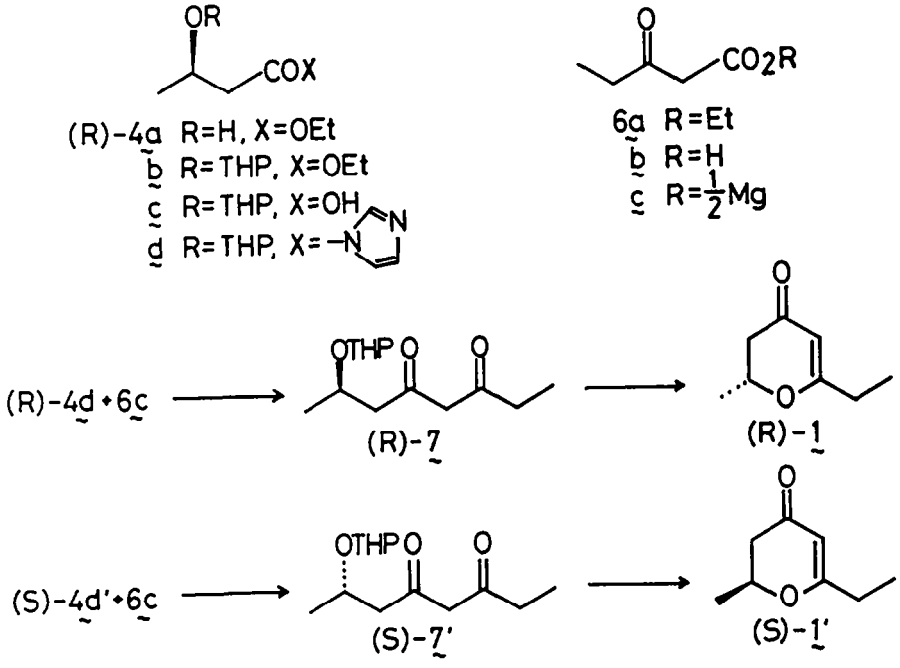

Fig. 2. Synthesis of both the enantiomers of 1.

Synthesis of both the enantiomers of 6-ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one (1 and 1').

Our synthetic route leading to **1** and **1'** is shown in Fig. 2. The strategy was to acylate the Mg salt **6c** of 3-oxopentanoic acid with the imidazolide **4d** of 3-tetrahydropyranyloxybutanoic acid. Optically pure (R)-**4a** was prepared from Zoogloea ramigera cells by the known method.[5,6] The corresponding THP ether **4b** was prepared as described previously.[6] This was hydrolyzed with KOH in aq MeOH to give **4c**, which was employed for the key acylation step. Another building block for **1** was ethyl 3-oxopentanoate **6a**. This was hydrolyzed to give **6b**. So as to connect **4c** with **6b**, Ohta's method for the preparation of 1,3-diketones was employed.[10] Treatment of **6b** with $Mg(OMe)_2$ in MeOH gave **6c**. In our hands, use of $Mg(OMe)_2$ gave better result than that could be achieved by the use of $Mg(OEt)_2$ in the original method.[10] The acylating agent **4d** was prepared from **4c** and N,N'-carbonyldiimidazole in DMF. The generated **4d** was treated in situ with **6c** to give (R)-**7** in 61 % yield. Removal of the THP protective group of 7 and subsequent cyclization of the resulting diketo alcohol was effected by stirring a soln of **7** in MeOH in the presence of a trace amount of p-TsOH. The cyclization was sluggish at 0°, while at the reflux temp partial racemization of the product was observed. The racemization presumably took place

by the retro-Michael-Michael process. At room temp, however, the cyclization of (R)-**7** proceeded smoothly to give (R)-**1**, $[\alpha]_D^{22}$ +195° (n-pentane), in 33 % overall yield in five steps from (R)-**4a**. The MS of (R)-**1** was in accord with the published data for the natural product.

For the synthesis of (S)-**1'**, (S)-**4a'** was prepared by the reduction of ethyl acetoacetate with Saccharomyces bailii KI 0116.[5] Further purification of the crude (S)-**4a'** (96 % e.e.) via its crystalline 3,5-dinitrobenzoate furnished (S)-**4a'** of 100 % e.e.[11] Conversion of (S)-**4a'** to (S)-**1'** was carried out as in the preparation of (R)-**1** to give (S)-**1'**, $[\alpha]_D^{22}$ -193° (n-pentane), in 27 % overall yield. The enantiomeric purity of both (R)-**1** and (S)-**1'** was estimated to be 100 % by measuring their 400 MHz ^{1}H NMR spectra in the presence of a chiral shift reagent tris[3-heptafluorobutanoyl-d-camphorato]europium (III) [Eu(hfc)$_3$] (see Experimental).

Synthesis of both the enantiomers of 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (2 and 2').

Construction of the 2,9-dioxabicyclo[3.3.1]non-7-en-6-one ring system was recently studied by Ziegler et al.[12] and by DeShong et al.[13,14] in connection with the synthesis of tirandamycin antibiotics. Ziegler et al. was the first to recognize the usefulness of a furan precursor in this problem.[12] Later DeShong et al. also adopted that approach,[13] and synthesized (±)-tirandamycin A by employing a furan precursor.[14] Our synthesis as shown in Fig. 3 also employed the furan precursor **10** and **10'** to prepare **2** and **2'**, respectively.

The starting material (S)-**5a** was prepared from (S)-**5b**, which in turn was obtained by reducing n-octyl 3-oxopentanoate with baker's yeast.[9] The crude (S)-**5a** (96 % e.e.) was purified via its crystalline 3,5-dinitrobenzoate to afford pure (S)-**5a** (100 % e.e.).[cf.15] The OH group of (S)-**5a** was protected as a t-butyldimethylsilyl (TBDMS) ether[16] to give (S)-**5c** in 93 % yield. Reduction of (S)-**5c** with $LiBH_4$ according to Brooks et al.[17] furnished (S)-**8** in 82 % yield. Use of LAH instead of $LiBH_4$ was deteriorative. Oxidation of (S)-**8** with pyridinium chlorochromate (PCC) in CH_2Cl_2 in the presence of NaOAc and Molecular Sieves 3Å[18] gave (S)-**9** in 87 % yield. This was coupled with 2,3-dimethylfuran prepared by the known methods.[19,20] Addition of t-BuLi in n-pentane to 2,3-dimethylfuran in dry ether generated the lithiate.[cf.21] To this was added (S)-**9** to give a mixture of (1'R,3'S)-**10** and (1'S,3'S)-**11** in a ratio of ca. 1:1. These were separated by SiO_2 chromatography to give **10** (99.1 % diastereomeric purity; 30 % yield) and **11** (98.0 % diastereomeric purity; 32 % yield). The stereochemistries **10** and **11** assigned to them were based on their later conversion to (1R,3S,5R)-**2** and (1S,3S,5S)-**14a**, respectively. Separation of these two diastereomers could be achieved by employing the TBDMS group for the protection of the OH group at C-3'. The presence of a THP group instead of the TBDMS group complicated the situation owing to the presence of an extra chiral center in the THP group.

Oxidation of the furan ring of (1'R,3'S)-**10** with m-chloroperbenzoic acid (MCPBA)[14,22] gave in 88 % yield a crystalline hemiacetal **12**. Finally, treatment of **12** with aq HF in MeCN brought about deprotection of the TBDMS group followed by the intramolecular acetalization to give the desired product (1R,3S,5R)-**2**, $[\alpha]_D^{22}$ +370° ($CHCl_3$), in 80 % yield. Its ^{1}H and ^{13}C NMR spectral data were in very good accord with those reported for the natural pheromone.[2] The overall yield of **2** from **5a** was 14 % in six steps. The enantiomeric purity of (1R,3S,5R)-**2** was 100 % as determined by the 400 MHz ^{1}H NMR analysis in the presence of Eu(hfc)$_3$.

The diastereomeric furan precursor (1'S,3'S)-**11** was also oxidized with MCPBA to give another crystalline hemiacetal **13** in 93 % yield. When this was treated with BF_3 Et_2O in CH_2Cl_2 at low temp,[23] a small amount (8.5 % yield) of an isomeric acetal was obtained, to which was assigned the structure (1S,3S,5S)-**14a**. The structure assignment as **14a** was based on its IR spectrum (ν 1680, 1600 cm^{-1}), ^{1}H and ^{13}C NMR spectra (see Experimental) and the molecular formula $C_{11}H_{16}O_3$ as determined by MS. The alternative chair conformer

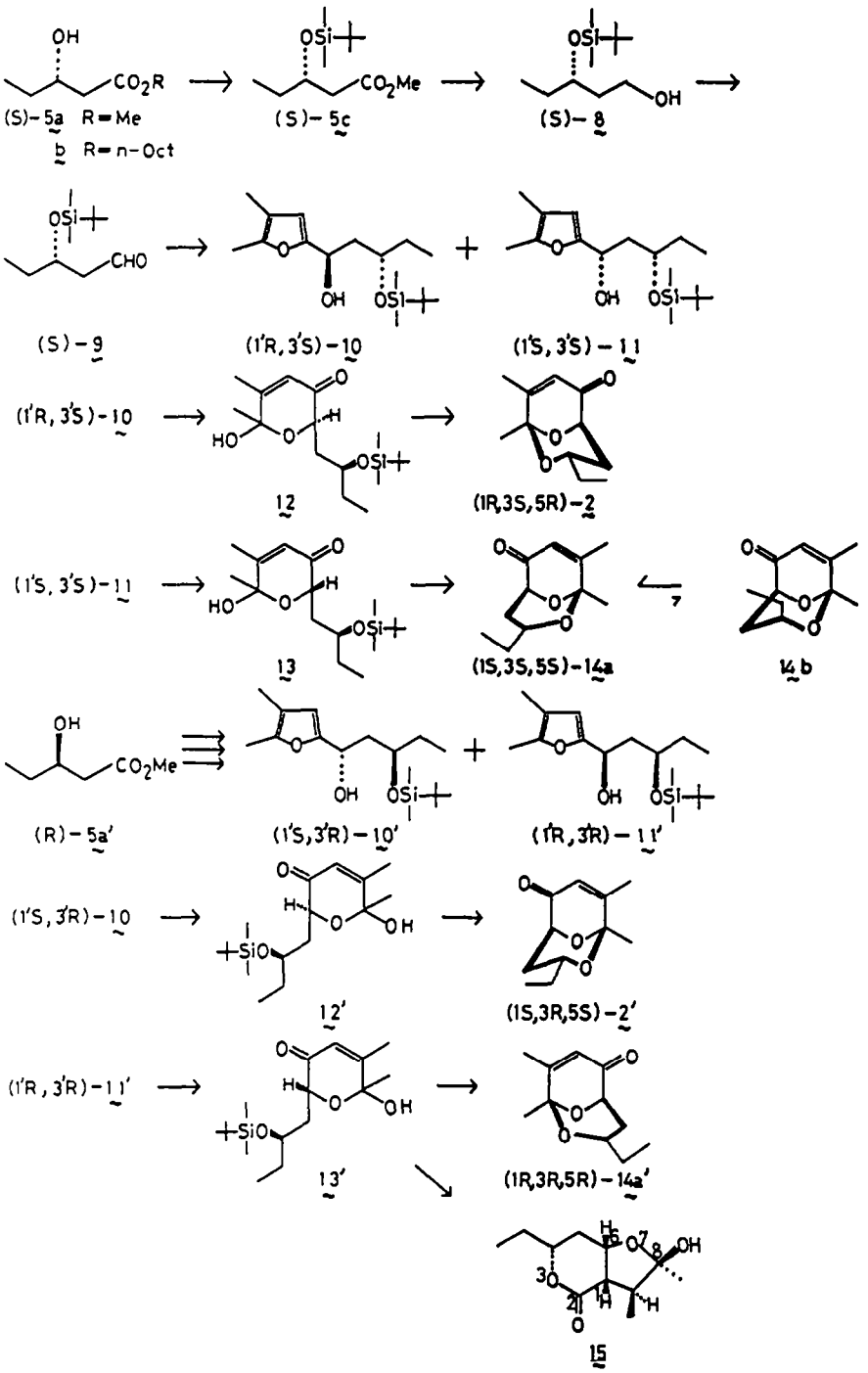

Fig. 3. Synthesis of both the enantiomers of 2.

14b must be too unstable to exist due to the severe 1,3-diaxial interaction caused by the ax Et group at C-3.

For the synthesis of (1S,3R,5S)-**2'**, we started from (R)-**5a'**. This was prepared from pentanoic acid by microbial β-oxidation employing Candida rugosa IFO 0750 followed by esterification.[8] The crude (R)-**5a'** (93 % e.e.) kindly given to us by Dr. J. Hasegawa was purified via its crystalline 3,5-dinitrobenzoate to give (R)-**5a'** of 100 % e.e.[15] Conversion of (R)-**5a'** to the furan precursors (1'S,3'R)-**10'** and (1'R,3'R)-**11'** was carried out as in the case of (S)-**5a**. Oxidation of **10'** with MCPBA gave crystalline **12'**, which was treated with aq HF in MeCN to give (1S,3R,5S)-**2'**, $[\alpha]_D^{22}$ -373° ($CHCl_3$) in 14 % overall yield in six steps from (R)-**5a'**. The enantiomeric purity of **2'** was estimated to be 100 % by the 400 MHz ^1H NMR analysis in the presence of $Eu(hfc)_3$. Comparison of the $[\alpha]_D$ values of our **2** and **2'** (+370° and -373°) with that of DeShong's **2** (+346.4°)[4] confirmed the high enantiomeric purity of our **2** and **2'**. DeShong et al. employed (S)-**5a** without purification via its 3,5-dinitrobenzoate and therefore their (S)-**5a** was presumably not of 100 % e.e.

When (1'R,3'R)-**11'** was oxidized with MCPBA, another crystalline hemiacetal **13'** was obtained in 86 % yield. Treatment of **13'** with BF_3 Et_2O at low temp gave (1R,3R,5R)-**14a'** in 16 % yield. Unlike in the case of (1S,3S,5S)-**14a**, (1R,3R,5R)-**14a'** was obtained in an amount sufficient for purification by distillation, and therefore its specific rotation could be measured accurately: $[\alpha]_D^{23.5}$ +349° ($CHCl_3$). When **13'** was treated with aq HF in MeCN, a crystalline compound, m.p. 102~104°, was generated in 52 % yield. Its IR and ^1H NMR spectra were identical with DeShong's data for the antipode of **15**.[4] Thus in accord with DeShong's result,[4] **13'** was quite different from **12'** in its behavior toward aq HF.

Synthesis of both the enantiomers of 1,8-dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (3 and 3').

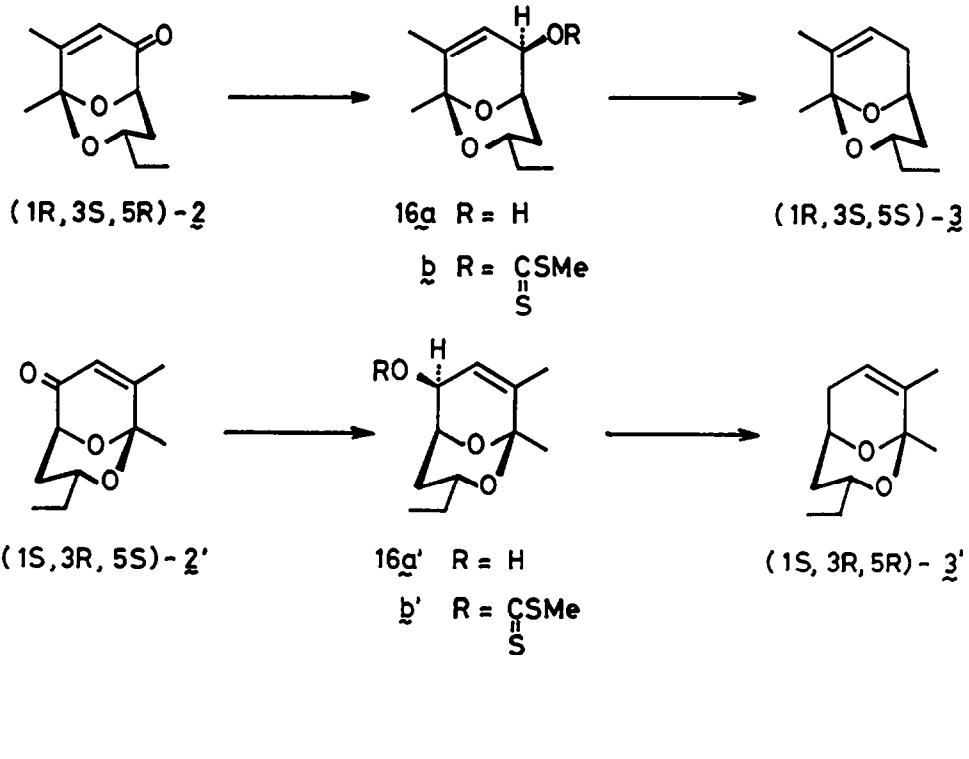

Fig. 4. Synthesis of both the enantiomers of 3.

In Fig. 4 is shown our synthesis of **3** and **3'**. The obvious precursors for **3** and **3'** were **2** and **2'**, respectively. Our plan was to employ Barton's radical-type deoxygenation procedure using $(n\text{-Bu})_3SnH$[24] as the key-step (**16b** → **3**). Reduction of (1R,3S,5R)-**2** with $NaBH_4$ in the presence of $CeCl_3$[25] gave **16a** in 94 % yield. The reduction was quite stereoselective to give only **16a** by the hydride attack from the convex side of **2**. When **16a** was processed to furnish **16b** according to Barton's procedure using NaH as the base,[24] **16b** was obtained only in poor yield. However, by employing n-BuLi as the base, the highly hindered OH group of **16a** was smoothly converted to the dithiocarbonate **16b** in 92 % yield. Tretment of **16b** with $(n\text{-Bu})_3SnH$ in toluene under reflux furnished (1R,3S,5S)-**3**, $[\alpha]_D^{23.5}$ +109° ($CHCl_3$), in 53 % yield. Its ^1H and ^{13}C NMR spectra were in very good accord with those published for the natural pheromone.[2] The overall yield of (1R,3S,5S)-**3** from (1R,3S,5R)-**2** was 46 % in three steps. Similarly, (1S,3R,5S)-**2'** afforded (1S,3R,5R)-**3'**, $[\alpha]_D^{24}$ -110° ($CHCl_3$), via **16a'** and **16b'**. The overall yield of **3'** was 40 % in three steps from **2'**. Although we tried the estimation of enantiomeric purity of **3** and **3'** by the ^1H NMR analysis in the presence of $Eu(hfc)_3$, no separation of the signals due to the enantiotopic protons of **3** and **3'** was observed after the addition of $Eu(hfc)_3$. Therefore the enantiomeric purity of **3** and **3'** could not be detemined by the NMR method. Schurig's complexation GLC method,[26] however, revealed all of our synthetic enantiomers (**1**, **1'**, **2**, **2'**, **3** and **3'**) to be of high enantiomeric purity. The results of the GLC analysis will be reported by Prof. Schurig in due course.

In conclusion, all of the three main components of the pheromone blend of the male swift moth were synthesized. By comparing the GLC behaviors of our synthetic enantiomers with those of the natural products, Schurig, Francke and their coworkers were able to determine the absolute configuration of the natural products to be as shown in Fig. 1. Details will be published elsewhere by Prof. W. Francke.[27]

EXPERIMENTAL

All b.ps and m.ps were uncorrected. UV sprctra were measured on a Hitachi 200-20 spectrophotometer. IR spectra were measured as films for oils or as nujol mulls for solids on a Jasco IRA-102 spectrometer. ^1H NMR spectra were recorded with TMS as an internal standard at 60 MHz on a Hitachi R-24A spectrometer or at 100 MHz on a JEOL JMN FX-100 spectrometer or at 400 MHz on a JEOL JMN GX-400 spectrometer. ^{13}C NMR spectra were measured at 100 MHz with TMS as an internal standard as $CDCl_3$ solution on a JEOL JMN GX-400 spectrometer. Optical rotations were measured on a Jasco DIP 140 polarimeter. CD spectra were measured on a Jasco J-20C spectropolarimeter. Mass spectra were recorded on a JEOL DX-303 spectrometer at 70 eV. Merck Kieselgel 60 (particle size 0.063~0.200 mm) was used for SiO_2 column chromatography. MPLC separation were performed on a Merck Lobar® column (Groesse B or C). HPLC analyses were performed on Nucleosil® 50-5 (25 cm x 4.6 mm) as a column.

3-Oxopentanoic acid **6b**. Ethyl 3-oxopentanoate **6a** (5.00 g, 34.7 mmol) was added to N-NaOH aq soln (35 ml) and the mixture was stirred for 24 h at room temp. After the mixture was washed with Et_2O (20 ml x 2), the aq layer was acidified with conc HCl aq at 0° and the mixture was extracted with Et_2O (20 ml x 3). The Et_2O soln was dried ($MgSO_4$) and concentrated in vacuo at 20~25° to give crude **6b** (2.20 g, 55 %) as a solid, m.p. 62~63°; (lit.[28] m.p. 64~66°); νmax 3000 (m,br), 2690 (w), 2600 (w), 1725 (s), 1695 (s), 920 (m) cm^{-1}; δ ($CDCl_3$) 1.09 (3H, t, J=6.9 Hz), 2.59 (2H, q, J=6.9 Hz), 3.50 (2H, s), 10.9 (1H, s). This was employed in the next step without further purification.

Magnesium 3-oxopentanoate **6c**. A mixture of Mg (0.152 g, 6.26 mmol), I_2 (trace amount) and dry MeOH (5 ml) was stirred and heated under reflux for 1 h under Ar. After Mg disappeared, the mixture was cooled to room temp. To the stirred mixture was added dropwise a soln of **6b** (1.60 g, 13.8 mmol) in dry MeOH (5 ml) over 5 min under Ar and the mixture was stirred and heated under reflux for 12 h. After cooling, the mixture was concentrated in vacuo. The residue was washed with dry Et_2O (50 ml x 2) and dried in vacuo to give **6c** (1.40 g, 88 %) as a white powder, m.p. >300°; νmax 3400 (s,br), 1710 (s), 1600 (s,br), 1430 (s,br), 1120 (m) cm^{-1}. This was employed in the next step without further purification.

(S)-3-Tetrahydropyranyloxybutanoic acid (S)-**4c'** (S)-**4b'** [b.p. 83~85°/1.5 Torr, 97 % from (S)-**4a'** (lit.[29] b.p. 85~90°/1.5 Torr)] was prepared according to the reported procedure[29]. To a stirred mixture of KOH (1.12 g), MeOH (5 ml) and water (3 ml) was added dropwise a soln of (S)-**4b'** (1.44 g, 6.65 mmol) in MeOH (10 ml) at 5~10° over 30 min. The mixture was stirred for 24 h at room temp. After MeOH was removed in vacuo, the residue was saturated with NaCl and washed with Et_2O (10 ml x 2). The aq layer was acidified to pH 4~5 by the addition of AcOH. The mixture was extracted with Et_2O (20 ml x 4). The Et_2O soln was dried ($MgSO_4$) and concentrated in vacuo to give crude (S)-**4c'** (1.05 g, 84 %), $n_D^{23.5}$ 1.4460; $[\alpha]_D^{23.5}$ +20.0° (c=1.08, 99.5 % EtOH); νmax 3000 (s,br), 2700 (m,br), 1710 (s) cm^{-1}; δ ($CDCl_3$) 1.27 (3H, m), 1.4~2.0 (6H, m), 2.4~2.8 (2H, m), 3.3~4.5 (3H, m), 4.6~4.9 (1H, m), 9.93 (1H, br). This was employed in the next step without further purification.

(S)-2-Tetrahydropyranyloxyoctane-4,6-dione (S)-**7'**. To a stirred soln of N,N'-carbonyldiimidazole (0.78 g, 4.8 mmol) in dry DMF (5 ml) was added dropwise a soln of (S)-**4c'** (0.82 g, 4.4 mmol) in dry DMF (5 ml) at room temp under N_2 and the mixture was stirred for 1 h. To this was added **6c** (0.61 g, 4.8 mmol), and the mixture was stirred for 15 h at room temp. Then the mixture was poured into sat NH_4Cl soln (30 ml) and the mixture was extracted with n-pentane (20 ml x 3). The extract was

washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with n-pentane-Et_2O (5:1) gave (S)-**7'** (0.50 g, 47 %), n_D^{24} 1.4703; $[\alpha]_D^{24}$ +22.5° (c=1.02, $CHCl_3$); νmax 1735 (m), 1715 (m), 1615 (s) cm^{-1}; δ ($CDCl_3$) 1.25 (6H, m), 1.3~1.8 (6H, m), 2.1~2.7 (4H, m), 3.2~4.3 (3.1H, m), 4.6 (1H, m), 5.38 (~0.4H, s), 5.46 (~0.3H, s). This was employed in the next step without further purification.

(S)-6-Ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one (S)-**1'**. To a stirred soln of (S)-**7'** (0.71 g, 2.9 mmol) in MeOH (10 ml) was added p-TsOH H_2O (0.04 g, 0.2 mmol) at room temp. The mixture was stirred for 3 h. To this was added sat $NaHCO_3$ soln (20 ml) and the mixture was extracted with Et_2O (30 ml x 3). The Et_2O soln was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by MPLC. Elution with n-pentane-Et_2O (5:1) gave (S)-**1'** (0.29 g, 71 %). This was distilled to give pure (S)-**1'** (0.24 g), b.p. 104~105°/20 Torr; n_D^{22} 1.4815; $[\alpha]_D^{22}$ -193° (c=1.46, n-pentane); CD (c=0.071, EtOH) Δε -1.5 (316 nm), CD spectrum of π→π* region could not be measured because of its perturbation. UV (c=5.1 x 10^{-5}M/L, 99.5 % EtOH) ε 1.4 x10^4 (262 nm); νmax 3010 (s), 2960 (s), 2900 (m), 1730 (w), 1670 (s), 1610 (s), 1460 (m), 1390 (s,br), 1340 (s), 1305 (m), 1275 (m), 1240 (m), 1205 (m), 1160 (m), 1110 (m), 1080 (m), 1040 (s), 1005 (m), 960 (m), 930 (m), 900 (m), 870 (m), 820 (m) cm^{-1}; δ (400 MHz, $CDCl_3$) 1.13 (3H, t, J=7.6 Hz), 1.45 (3H, d, J=6.4 Hz), 2.27 (2H, q, J=7.6 Hz), 2.38 (1H, dd, J=11.0, 16.0 Hz), 2.42 (1H, ddd, J=0.3, 6.0, 16.0 Hz), 4.49 (1H, ddq, J=11.0, 6.0, 6.4 Hz), 5.33 (1H, br.d, J=0.3 Hz). ^1H NMR study of (S)-**1'** in the presence of a chiral shift reagent [**1** or **1'** (5.0 mg) with $Eu(hfc)_3$ (51.0 mg) in C_6D_6 (0.4 ml)], C-5 olefinic proton signal; (S)-**1'** (δ 16.31, 100 %), (R)-**1** (δ 16.13), (S)-**1'** without $Eu(hfc)_3$ (δ 5.34). ^{13}C NMR δ 10.58, 20.37, 27.90, 42.67, 75.57, 102.92, 178.93, 193.16. GLC (Yanaco G-180; Column, Yanagimoto Silicon OV-101, 50 m x 0.25 mm at 120°; Carrier gas, N_2, 50 ml/min) Rt 21.7 min (100 %). MS m/z 140 (41 %), 111 (8 %), 99 (100 %), 74 (22 %), 69 (54 %), 59 (24 %), 57 (42 %), 45 (14 %), 43 (21 %). (Found MS: m/z 140.0804 (M^+). Calc for $C_8H_{12}O_2$, 140.0837). The fragmentation pattern of its mass spectrum was almost identical with that reported for the natural product.[1] (S)-**1'** was so volatile that correct combustion analytical data could not be obtained.

(R)-3-Tetrahydropyranyloxybutanoic acid (R)-**4c**. (R)-**4b** [b.p. 86~89°/1.6~2.1 Torr, 96 % from (R)-**4a** (lit.[25] b.p. 85~89°/2 Torr] was prepared in the same manner as described for (S)-**4b'**. In the same manner as described for the preparation of (S)-**4c'**, (R)-**4b** (5.00 g, 23.1 mmol) yielded (R)-**4c** (4.14 g, 95 %), n_D^{23} 1.4472, $[\alpha]_D^{23.5}$ -18.5° (c=1.11, 99.5 % EtOH). Its IR and NMR spectra were identical with those of (S)-**4c'**.

(R)-2-Tetrahydropyranyloxyoctane-4,6-dione (R)-**7**. In the same manner as described for the prepartion of (S)-**7'**, (R)-**4c** (1.88 g, 10 mmol) yielded (R)-**7** (1.47 g, 61 %), n_D^{22} 1.4717; $[\alpha]_D^{22}$ -22.3° (c=1.02, $CHCl_3$). Its IR and NMR spectra were identical with those of (S)-**7'**.

(R)-6-Ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one (R)-**1**. In the same manner as described for the preparation of (S)-**1'**, (R)-**7** (2.00 g, 8.25 mmol) yielded (R)-**1** (0.70 g, 60 %). This was distilled to give an analytical sample, b.p. 103~105°/20 Torr; n_D^{22} 1.4818; $[\alpha]_D^{22}$ +195° (c=2.17, n-pentane); CD (c=0.071, EtOH) Δε +1.7 (316 nm). CD spectrum of π→π* region could not be measured because of its perturbation. ^1H NMR study of (R)-**1** in the presence of a chiral shift reagent [**1** or **1'** (5.0 mg) with $Eu(hfc)_3$ (51.0 mg) in C_6D_6 (0.4 ml)], C-5 olefinic proton signal; (R)-**1** (δ 16.13, 100 %), (S)-**1'** (δ 16.31), (R)-**1** without $Eu(hfc)_3$ (δ 5.34). GLC (Yanaco G-180; Column, Yanagimoto Silicon OV-101, 50 m x 0.25 mm at 120°; Carrier gas, N_2, 50 ml/min) Rt 18.5 min (100 %). (Found MS: m/z 140.0899 (M^+). Calc for $C_8H_{12}O_2$, 140.0837). Its UV, IR and NMR spectra were identical with those of (S)-**1'**. The fragmentation pattern was identical with that of (S)-**1'**. Correct elemental analytical data could not be obtained due to the high volatility of (R)-**1**.

Methyl (S)-3-t-butyldimethylsilyloxypentanoate (S)-**5c**. To a mixture of TBDMS-Cl (3.28 g, 21.8 mmol) and imidazole (3.09 g, 45.4 mmol) was added a soln of (S)-**5a** (100 % e.e., 2.40 g, 18.2 mmol) in dry DMF (8 ml) at room temp under Ar, and the mixture was stirred for 20 h. Then the mixture was poured into ice-water (50 ml), and extracted with Et_2O (40 ml x 2). The extract was washed with water (30 ml x 3), dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (100 g). Elution with n-pentane-Et_2O (20:1) followed by distillation gave pure (S)-**5c** (4.19 g, 93 %), b.p. 73~74°/2.0 Torr; n_D^{23} 1.4251; $[\alpha]_D^{23}$ +23.4° (c=1.08, $CHCl_3$); νmax 1750 (s), 1255 (s), 1080 (s), 1040 (s), 1020 (s), 840 (s), 780 (s) cm^{-1}; δ ($CDCl_3$) 0.05 (3H, s), 0.06 (3H, s), 0.7~1.0 (3H, m), 0.87 (9H, s), 1.45 (2H, m), 2.42 (2H, d, J=6 Hz), 3.62 (3H, s), 4.05 (1H, m). GLC (Hitachi 163; Column, 3 % OV-17, 1.5 m x 3 mm at 100°; Carrier gas, N_2, 1.0 kg/cm^2) Rt 6.4 min (98.6 %). (Found: C, 58.33; H, 10.65. Calc for $C_{12}H_{26}O_3Si$: C, 58.49; H, 10.63 %).

(S)-3-t-Butyldimethylsilyloxypentan-1-ol (S)-**8**. To a stirred suspension of $LiBH_4$ (0.31 g, 14 mmol) in dry THF (10 ml) was added dropwise a soln of (S)-**5c** (3.50 g, 14.2 mmol) in dry THF (10 ml) at room temp over 5 min, and the mixture was stirred and heated under reflux for 2 h. The mixture was then diluted with Et_2O (30 ml) at 0°, and sat NH_4Cl soln (1 ml) was added dropwise to it over 10 min at 0°. The mixture was stirred for 30 min at 0°, then dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with n-pentane-Et_2O (5:1) followed by distillation gave pure (S)-**8** (2.55 g, 82 %), b.p. 76~78°/1.1 Torr; n_D^{22} 1.4358; $[\alpha]_D^{22}$ +16.8° (c=1.13, $CHCl_3$); νmax 3350 (s), 1260 (s), 1040 (s), 1010 (s), 840 (s), 780 (s) cm^{-1}; δ ($CDCl_3$) 0.08 (6H, s), 0.7~1.0 (3H, m), 0.88 (9H, s), 1.3~1.9 (4H, m), 2.3 (1H, br.s), 3.6~4.0 (3H, m). GLC (Hitachi 163; Column, 3 % OV-17, 1.5 m x 3 mm at 100°; Carrier gas, N_2, 1.0 kg/cm^2) Rt 5.9 min (100 %). (Found: C, 60.46; H, 11.91. Calc for $C_{11}H_{26}O_2Si$: C, 60.19; H, 12.00 %). The optical purity of (S)-**8** was determined by the HPLC analysis of the corresponding (R)-MTPA ester.cf.[30] HPLC: [n-hexane-THF (200:1), 1.0 ml/min; detected at 254 nm] Rt 14.2 min (100 %). Its diastereomer [(R)-MTPA ester of (R)-**8**] was eluted at Rt 13.5 min.

(S)-3-t-Butyldimethylsilyloxypentanal (S)-**9**. To a suspension of PCC (2.55 g, 11.8 mmol), powdered NaOAc (0.68 g, 8.3 mmol) and powdered MS 3A (5.9 g) in dry CH_2Cl_2 (30 ml) was added a soln of (S)-**8** (2.58 g, 11.8 mmol) in dry CH_2Cl_2 (20 ml) at room temp under Ar, and the mixture was stirred for 3 h at room temp. Then the mixture was filtered through Florisil (60~100 mesh, 100 g). The filter-cake was washed with CH_2Cl_2 (500 ml). The combined filtrate and washings were concentrated in vacuo at <25° to give crude (S)-**9** (2.21 g, 87 %), νmax 2720 (w), 1725 (s), 1040 (s), 1020 (s) cm^{-1}. GLC (Hitachi 163; Column, 3 % OV-17, 1.5 m x 3 mm at 100°; Carrier gas, N_2, 1.0 kg/cm^2) Rt 4.4 min (94.7 %), 6.9 min [5.3 %, unreacted (S)-**8**]. This was employed in the next step without further purification.

(1'R,3'S)-5-(3'-t-Butyldimethylsilyloxy-1'-hydroxypentyl)-2,3-dimethylfuran (1'R,3'S)-**10** and (1'S,3'S)-**11**. To a stirred soln of 2,3-dimethylfuran (purity, 93.4 %; 0.471 g, 4.58 mmol) in dry Et_2O (10 ml) was added dropwise t-BuLi (2.3 M in n-pentane, 1.99 ml, 4.58 mmol) at 4~5° over 10 min under Ar, and the mixture was stirred for 2 h. To this was added a soln of (S)-**9** (0.425 g, 1.96 mmol) in dry Et_2O (5 ml) at -77° over 10 min and the mixture was stirred for 1 h at -77° then warmed to room temp and stirred for 15 h. The mixture was poured into crushed ice (50 g). The mixture was saturated with NaCl, stirred for 10 min and extracted with Et_2O (30 ml x 3). The extract was washed with brine, dried ($MgSO_4$) and concentrated in vacuo to give a crude mixture (0.707 g) of (1'R,3'S)-**10** and (1'S,3'S)-**11**. The ratio of the diastereomers was 45~50:55~50 based upon the HPLC analysis of the mixture. HPLC: [n-hexane-THF (20:1), 0.8 ml/min; detected at 230 nm] Rt 11.7 min (**10**, 45~50 %), 14.6 min (**11**, 50~55 %). This mixture was purified by MPLC. Elution with n-pentane-Et_2O (20:1) gave less polar (1'R,3'S)-**10** as an oil (diastereomeric purity: 99.1 %; 0.181 g, 30 %), νmax 3450 (m), 1250 (s), 1220 (s), 1040 (s) cm^{-1}. Further elution with the same solvent gave more polar (1'S,3'S)-**11** as an oil (diastereomeric purity: 98.0 %; 0.195 g, 32 %). The IR spectrum of (1'S,3'S)-**11** was almost identical with that of (1'R,3'S)-**10**.

(2R,6RS,2'S)-2-(2'-t-Butyldimethylsilyloxybutyl)-5,6-dimethyl-6-hydroxy-2H-pyran-3(6H)-one (2R,6RS,2'S)-**12**. To a stirred soln of (1'R,3'S)-**10** (0.181 g, 0.58 mmol) in dry CH_2Cl_2 (20 ml) was added MCPBA (80 %, 0.125 g, 0.58 mmol) at 0°, and the mixture was stirred for 1 h. Then the mixture was poured into ice-cooled sat $NaHCO_3$ soln (20 ml) and stirred for 5 min at 0°. The organic layer was separated, washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over SiO_2 (40 g). Elution with n-pentane-Et_2O (3:1) followed by recrystallization from n-pentane gave (2R,6RS,2'S)-**12** (0.168 g, 88 %), m.p. 69~71°; νmax 1685 (s), 1250 (s), 1120 (s), 1050 (s), 835 (s), 775 (s) cm^{-1}; δ ($CDCl_3$) 0.10 (6H, s), 0.8~1.0 (3H, m), 0.90 (9H, s), 1.5~1.7 (2H, m), 1.62 (3H, s), 1.8~2.1 (2H, m), 2.03 (3H, m), 3.3~3.6 (1H, m), 3.8~4.0 (1H, m), 4.4~4.7 (1H, m), 5.85 (1H, br.s).

(1R,3S,5R)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (1R,3S,5R)-**2**. To a stirred soln of (2R,6RS,2'S)-**12** (0.265 g, 0.81 mmol) in MeCN (18 ml) was added dropwise 46 % HF aq soln (2.5 ml, 58 mmol) at 0° over 2 min, and the mixture was stirred at room temp for 1 h. To this was added slowly sat K_2CO_3 soln (20 ml) at 0° over 5 min with stirring. The organic layer was separated and the aq layer was extracted with Et_2O (50 ml x 2). The combined organic soln was washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over SiO_2 (20 g). Elution with n-pentane-Et_2O (20:1) followed by distillation in the presence of MgO gave pure (1R,3S,5R)-**2** (0.126 g, 80 %), b.p. 85°(bath temp)/0.2 Torr; n_D^{22} 1.4821; $[\alpha]_D^{22}$ +370° (c=1.23, $CHCl_3$); CD (c=0.023, EtOH) Δε +21.6 (214 nm), -8.3 (242 nm), +3.9 (352 nm); UV (c=4.7 x 10^{-5}M/L, 99.5 % EtOH) ε 1.1 x10^4 (226 nm); νmax 2990 (s), 2940 (s), 2900 (m), 1690 (s), 1630 (m), 1435 (s), 1380 (s), 1340 (m), 1300 (m), 1280 (s), 1250 (m), 1230 (s), 1200 (w), 1190 (m), 1140 (s), 1115 (s), 1050 (m), 1035 (m), 1030 (m), 985 (m), 965 (s), 940 (w), 920 (m), 880 (s), 840 (m) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.88 (3H, t, J=7.6 Hz), 1.46 (1H, ddq, J=14.0, 6.7, 7.6 Hz), 1.53 (3H, s), 1.57 (1H, ddq, J=14.0, 6.7, 7.6 Hz), 1.59 (1H, ddd, J=14.0, 3.5, 1.8 Hz), 1.87 (1H, ddd, J=14.0, 12.5, 6.2 Hz), 1.95 (3H, d, J=1.6 Hz), 3.64 (1H, dddd, J=12.5, 6.7, 6.7, 3.5 Hz), 4.32 (1H, ddd, J=6.2, 1.8, 1.6 Hz), 6.15 (1H, dq, J=1.6, 1.6 Hz). ^1H NMR study of (1R,3S,5R)-**2** in the presence of a chiral shift reagent [**2** or **2'** (5.0 mg) with $Eu(hfc)_3$ (12.1 mg) in C_6D_6 (0.4 ml), C-7 olefinic proton signal; (1R,3S,5R)-**2** (δ 10.34, 100 %), (1S,3R,5S)-**2'** (δ 9.81), (1R,3S,5R)-**2** without $Eu(hfc)_3$ (δ 5.96). ^{13}C NMR δ 9.05, 19.35, 24.73, 29.01, 32.11, 69.27, 75.04, 95.99, 126.84, 156.89, 197.31. GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 130°; Carrier gas, N_2, 50 ml/min, 1.0 kg/cm^2) Rt 22.1 min (100 %). MS: m/z 196 (M^+, 14 %), 167 (16 %), 154 (7 %), 138 (8 %), 123 (10 %), 112 (100 %), 97 (12 %), 95 (10 %), 85 (25 %), 81 (5 %), 74 (36 %), 69 (43 %), 67 (14 %), 59 (53 %). (Found MS: m/z 196.1103 (M^+). Calc for $C_{11}H_{16}O_3$: 196.1099). Its ^1H and ^{13}C NMR spectra were identical with those of the natural product. MS of (1R,3S,5R)-**2** was almost identical with the reported spectrum of the natural product.[2] Due to the high volatility of (1R,3S,5R)-**2**, its correct combustion analytical data could not be obtained.

Methyl (R)-3-t-butyldimethylsilyloxypentanoate (R)-**5c'**. In the same manner as described for the preparation of (S)-**5c**, (R)-**5a'** (100 % e.e., 2.00 g, 15.1 mmol) yielded (R)-**5c'** (3.28 g, 88 %), b.p. 71~72°/1.85 Torr; n_D^{22} 1.4252; $[\alpha]_D^{22}$ -25.1° (c=1.09, $CHCl_3$). GLC [under the same condition for the analysis of (S)-**5c**] Rt 6.9 min (99.9 %). (Found: C, 58.40; H, 10.67. Calc for $C_{12}H_{26}O_3$: C, 58.49; H, 10.63 %). Its IR and NMR spectra were identical with those of (S)-**5c**.

(R)-3-t-Butyldimethylsilyloxypentan-1-ol (R)-**8'**. In the same manner as described for the preparation of (S)-**8**, (R)-**5c'** (3.28 g, 13.3 mmol) yielded (R)-**8'** (2.60 g, 90 %), b.p. 75~76°/1.1 Torr; n_D^{23} 1.4352; $[\alpha]_D^{23}$ -17.5° (c=1.03, $CHCl_3$). GLC [under the same condition for the analysis of (S)-**8**] Rt 5.9 min (99.9 %). (Found: C, 60.19; H, 11.89. Calc for $C_{11}H_{26}O_2Si$: C, 60.49; H, 12.00 %). Its IR and NMR spectra were identical with those of (S)-**8**. In the same manner as described for the determination of the optical purity of (S)-**8**, the optical purity of (R)-**8'** was determined by the HPLC analysis of the corresponding (R)-MTPA ester. The (R)-MTPA ester was eluted at 13.5 min (100 %).

(R)-3-t-Butyldimethylsilyloxypentanal (R)-**9'**. In the same manner as described for the preparation of (S)-**9**, (R)-**8'** (2.18 g, 10.0 mmol) yielded crude (R)-**9'** (2.21 g, quantitative). GLC (Hitachi 163; Column, 3 % OV-17, 1.5 m x 3 mm at 100°; Carrier gas, N_2, 1.0 kg/cm^2) Rt 3.8 min (98.1 %). Its IR spectrum was identical with that of (S)-**9**. This was employed in the next step without further purification.

(1'S,3'R)-5-(3'-t-Butyldimethylsilyloxy-1'-hydroxypentyl)-2,3-dimethylfuran (1'S,3'R)-**10'** and (1'R,3'R)-**11'**. In the same manner as described for the preparation of (1'R,3'S)-**10** and (1'S,3'S)-**11**, (R)-**9'** (2.16 g, 10.0 mmol) yielded crude mixture (3.73 g) of (1'S,3'R)-**10'** and (1'R,3'R)-**11'**. The ratio of the diastereomers was 51~52:49~48 based upon the HPLC analysis of the mixture under the same condition for the analysis of (1'R,3'S)-**10** and (1'S,3'S)-**11**. This mixture was purified by MPLC. Elution with n-pentane-Et_2O (20:1) gave less polar (1'S,3'R)-**10'** as an oil (diastereomeric purity: 99.4 %; 0.80 g, 26 %). Further elution with the same solvent gave more polar (1'R,3'R)-**11'** as an oil (diastereomeric purity: 98.2 %; 0.83 g, 27 %). The IR spectra of (1'S,3'R)-**10'** and (1'R,3'R)-**11'** were identical with those of (1'R,3'S)-**10** and (1'S,3'S)-**11**, respectively.

(2S,6RS,2'R)-2-(2'-t-Butyldimethylsilyloxybutyl)-5,6-dimethyl-6-hydroxy-2H-pyran-3(6H)-one (2S,6RS,2'R)-**12'**. In the same manner as described for the preparation of (2R,6RS,2'S)-**12**, (1'S,3'R)-**10'** (0.75 g, 2.4 mmol) yielded (2S,6RS,2'R)-**12'** (0.71 g, 90 %), m.p. 59~71°. (Found: C, 63.62; H, 9.65. Calc for $C_{17}H_{32}O_4Si$: C, 62.15; H, 9.82 %). Its IR and NMR spectra were almost identical with those of (2R,6RS,2'S)-**12**. This was employed in the next step without further purification.

(1S,3R,5S)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (1S,3R,5S)-**2'**. In the same manner as described for the preparation of (1R,3S,5R)-**2**, (2S,6RS,2'R)-**12'** (0.70 g, 2.1 mmol) yielded (1S,3R,5S)-**2'** (0.32 g, 77 %). Distillation in the presence of MgO gave an analytical sample, b.p. 85°(bath temp)/0.2 Torr; n_D^{22} 1.4821; $[\alpha]_D^{22}$ -373° (c=1.14, $CHCl_3$); CD (c=0.023, EtOH) Δε -22.4 (214 nm), +8.2 (242 nm), -4.0 (352 nm); ^1H NMR study of (1S,3R,5S)-**2'** in the presence of a chiral shift reagent [**2** or **2'** (5.0 mg) with $Eu(hfc)_3$ (12.1 mg) in C_6D_6 (0.4 ml), C-7 olefinic proton signal; (1S,3R,5S)-**2'** (δ 9.81, 100 %), (1R,3S,5R)-**2** (δ 10.34), (1S,3R,5S)-**2'** without $Eu(hfc)_3$ (δ 5.96). GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 130°; Carrier gas, N_2, 50 ml/min, 1.0 kg/cm^2) Rt 22.6 min (100 %). (Found MS: m/z 196.1124 (M^+). Calc for $C_{11}H_{16}O_3$: 196.1099). Its UV, IR, ^1H NMR, ^{13}C NMR spectra and the fragmentation pattern of the mass spectrum were identical with those of (1R,3S,5R)-**2**. Due to the high volatility of (1S,3R,5S)-**2'**, its correct combustion analytical data could not be obtained.

(2S,6RS,2'S)-2-(2'-t-Butyldimethylsilyloxybutyl)-5,6-dimethyl-6-hydroxy-2H-pyran-3(6H)-one (2S,6RS,2'S)-**13**. In the same manner as described for the preparation of (2R,6RS,2'S)-**12**, (1'S,3'S)-**11** (0.195 g, 0.62 mmol) yielded (2S,6RS,2'S)-**13** (0.191 g, 93 %), m.p. 77~79°; νmax 3300 (m), 1685 (s), 1255 (s), 1130 (s), 1105 (s), 1050 (s) cm^{-1}; δ ($CDCl_3$) 0.03 (6H, s), 0.8~1.1 (3H, m), 0.88 (9H, s), 1.2~1.8 (2H, m), 1.59 (3H, s), 1.9~2.2 (2H, m), 2.00 (3H, m), 3.3~3.6 (1H, m), 3.8~4.0 (1H, m), 4.4~4.7 (1H, m), 5.80 (1H, br.s). This was employed in the next step without further purification.

(1S,3S,5S)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (1S,3S,5S)-**14a**. To a stirred soln of (2S,6RS,2'S)-**13** (0.148 g, 0.45 mmol) in dry CH_2Cl_2 (20 ml) was added BF_3 Et_2O (56 μl, 0.45 mmol) at -60° under Ar, and the mixture was stirred for 4 h. To the mixture was added slowly sat $NaHCO_3$ soln (20 ml) at -60°. The mixture was warmed to room temp. The organic layer was separated from the mixture, washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by MPLC. Elution with n-pentane-Et_2O (20:1) gave (1S,3S,5S)-**14a** (7.5 mg, 8.5 %) as an oil, $[\alpha]_D^{25}$ -246° (c=0.10, $CHCl_3$); νmax ($CHCl_3$ soln) 2980 (s), 2950 (s), 2870 (m), 1680 (s), 1600 (w), 1480 (w), 1380 (m), 1190 (w), 1115

(s), 995 (w), 965 (w), 885 (w), 860 (w), 840 (w) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.88 (3H, t, J=7.6 Hz), 1.46 (1H, ddq, J=14.7, 6.7, 7.6 Hz), 1.49 (3H, s), 1.58 (1H, ddq, J=14.7, 6.7, 7.6 Hz), 1.59 (1H, ddd, J=14.0, 8.8, 5.0 Hz), 2.01 (3H, d, J=1.3 Hz), 2.32 (1H, ddd, J=14.0, 9.5, 5.5 Hz), 4.07 (1H, dddd, J=8.8, 6.7, 6.7, 5.5 Hz), 4.37 (1H, ddd, J=9.5, 5.0, 0.8 Hz), 5.73 (1H, dq, J=0.8, 1.3 Hz). ^{13}C NMR δ 9.67, 19.44, 23.95, 28.47, 30.57, 70.91, 72.55, 95.76, 121.18, 162.73, 198.51. GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 130°; Carrier gas, N_2, 50 ml/min, 1.05 kg/cm^2) Rt 22.6 min (99.0 %). Its diastereomer (1R,3S,5R)-**2** eluted Rt 20.0 min (1.0 %). MS: m/z 196 (M^+, 14 %), 167 (14 %), 154 (6 %), 147 (3 %), 139 (7 %), 123 (9 %), 112 (100 %), 111 (31 %), 85 (40 %), 74 (26 %), 69 (50 %), 59 (37 %), 57 (38 %). (Found MS: m/z 196.1169 (M^+) Calc for $C_{11}H_{16}O_3$: 196.1099). Due to the scarcity of the material, **14a** could not be distilled.

(2R,6RS,2'R)-2-(2'-t-Butyldimethylsilyloxybutyl)-5,6-dimethyl-6-hydroxy-2H-pyran-3(6H)-one (2R,6RS,2'R)-**13'**. In the same manner as described for the preparation of (2R,6RS,2'S)-**12**, (1'R,3'R)-**11'** (0.937 g, 3.11 mmol) yielded (2R,6RS,2'R)-**13'** (0.875 g, 86 %), m.p. 77~80°. Its IR and NMR spectra were identical with those of (2S,6RS,2'S)-**13**. This was employed in the next step without further purification.

(1S,4R,6S,8R,9S)-8,9-Dimethyl-4-ethyl-8-hydroxy-3,7-dioxabicyclo[4.3.0]nonan-2-one (1S,4R,6S,8R,9S)-**15**. To a stirred soln of (2R,6RS,2'R)-**13'** (0.708 g, 2.16 mmol) in MeCN (45 ml) was added 46 % HF aq soln (6.0 ml) at 0° over 2 min, and the mixture was stirred at room temp for 1 h. Then sat K_2CO_3 soln (50 ml) was added to the mixture at 0° over 5 min. The organic layer was separated and the aq layer was extracted with Et_2O (50 ml x 2). The combined organic soln was washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with Et_2O gave (1S,4R,6S,8R,9S)-**15** (0.239 g, 52 %) as colorless needles, m.p. 102~104°; $[\alpha]_D^{24}$ -36.8° (c=0.50, $CHCl_3$); νmax 3400 (s), 1695 (s), 1245 (s), 1190 (m), 1020 (m), 900 (m) cm^{-1}; νmax (CCl_4 soln) 3620 (w), 2990 (m), 1950 (m), 2900 (w), 1745 (s), 1380 (m), 1235 (m), 1210 (w), 1190 (w), 1160 (w), 1020 (m), 915 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.02 (3H, t, J=7 Hz), 1.29 (3H, d, J=7 Hz), 1.48 (3H, s), 1.57~1.82 (3H, m), 2.03~2.40 (3H, m), 2.90 (1H, t, J=10 Hz), 3.95~4.23 (1H, m), 4.57 (1H, ddd, J=11, 10, 7 Hz). (Found: C, 61.83; H, 8.35. Calc for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47 %). The IR and NMR spectra of (1S,4R,6S,8R,9S)-**15** were in good accord with those described for the antipode of **15**.[4]

(1R,3R,5R)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one (1R,3R,5R)-**14a'**. In the same manner as described for the preparation of (1S,3S,5S)-**14a**, (2R,6RS,2'R)-**13'** (0.540 g, 1.64 mmol) yielded (1R,3R,5R)-**14a'** (0.053 g, 16 %). The analytical sample was distilled in the presence of MgO, b.p. 80~100°(bath temp)/0.2 Torr; $n_D^{23.5}$ 1.4801; $[\alpha]_D^{23.5}$ +349° (c=0.29, $CHCl_3$); CD (c=0.025, EtOH) Δε -13.8 (230 nm), +10.9 (257 nm), +2.1 (352 nm). νmax 2980 (s), 2950 (s), 2900 (s), 1690 (s), 1630 (m), 1440 (m), 1380 (s), 1360 (w), 1340 (w), 1300 (m), 1280 (m), 1265 (m), 1210 (m), 1200 (s), 1110 (s), 1080 (m), 1050 (m), 1035 (m), 995 (m), 970 (m), 940 (w), 920 (m), 890 (m) cm^{-1}. GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 130°; Carrier gas, N_2, 50 ml/min, 1.0 kg/cm^2) Rt 25.5 min (99.4 %). (Found MS: m/z 196.1109 (M^+). Calc for $C_{11}H_{16}O_3$: 196.1099). Its ^1H NMR, ^{13}C NMR and mass spectra were identical with those of (1S,3S,5S)-**14a**.

(1R,3S,5R,6R)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-ol (1R,3S,5R,6R)-**16a**. To a stirred soln of (1R,3S,5R)-**2** (0.420 g, 2.14 mmol) and $CeCl_3$ $7H_2O$ (0.797 g, 2.14 mmol) in MeOH (20 ml) was added $NaBH_4$ (0.081 g, 2.1 mmol) at room temp, and the mixture was stirred for 10 min. The mixture was diluted with cooled H_2O (20 ml) and the pH of the mixture was adjusted to 7 by the addition of dil HCl. The mixture was extracted with Et_2O (50 ml x 4). The extract was washed with brine, dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with n-pentane-Et_2O (1:1) gave (1R,3S,5R,6R)-**16a** (0.398 g, 94 %), n_D^{23} 1.4793; $[\alpha]_D^{23}$ +45.7° (c=0.81, $CHCl_3$); νmax 3450 (s), 1340 (s), 1235 (s), 1195 (s), 1150 (s), 1105 (s), 1060 (s), 1030 (s), 880 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.91 (3H, t, J=7.0 Hz), 1.1~2.0 (5H, m), 1.43 (3H, s), 1.67 (3H, m), 3.5~3.9 (1H, m), 4.1~4.3 (1H, m), 4.5~4.7 (1H, br.m), 5.70 (1H, br.m). GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 130°; Carrier gas, N_2, 50 ml/min, 1.2 kg/cm^2) Rt 22.4 min (100 %). (Found MS: m/z 198.1149 (M^+). Calc for $C_{11}H_{18}O_3$: 198.1256).

(1R,3S,5R,6R)-O-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-yl S-methyl dithiocarbonate (1R,3S,5R,6R)-**16b**. To a stirred soln of (1R,3S,5R,6R)-**16a** (0.364 g, 1.84 mmol) in dry THF (30 ml) was added dropwise n-BuLi (1.5 M in n-hexane, 1.22 ml, 1.84 mmol) at -77° over 5 min under N_2, and the mixture was stirred at 0° for 1 h. To this was added a soln of CS_2 (0.280 g, 3.67 mmol) in dry THF (5 ml) at 0° over 5 min, and the mixture was stirred for 30 min. Then a soln of MeI (0.782 g, 5.51 mmol) in dry THF (5 ml) was added to it at 0° over 10 min and the mixture was stirred at 0° for 30 min. After stirring for 12 h at room temp, the mixture was poured into sat NH_4Cl soln (100 ml) and extracted with Et_2O (50 ml x 3). The organic soln was dried ($MgSO_4$) and concentrated in vacuo. The residue was chromatographed over SiO_2 (50 g). Elution with n-pentane-Et_2O (40:1) gave (1R,3S,5R,6R)-**16b** (0.489 g, 92 %), n_D^{24} 1.5429; $[\alpha]_D^{24}$ -36.1° (c=0.72, $CHCl_3$); νmax 1210 (s), 1155 (m), 1145 (m), 1110 (m), 1060 (s), 970 (m), 880 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.93 (3H, t, J=7.0 Hz), 1.3~1.9 (4H, m), 1.44 (3H, s), 1.71 (3H, m), 2.59 (3H, s), 3.6~4.0 (1H, m), 4.4~4.6 (1H, m), 5.78 (1H, br), 6.2~6.4 (1H, m). HPLC: [n-hexane-THF (200:1), 1.0 ml/min; detected at 254 nm] Rt 26.5 min (99.5 %). This was employed in the next step without further purification.

(1R,3S,5S)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (1R,3S,5S)-**3**. To a stirred soln of $(n\text{-Bu})_3SnH$ (97 %, 0.680 ml, 2.45 mmol) in dry toluene (50 ml) was added dropwise over 2.5 h a soln of (1R,3S,5R,6R)-**16b** (0.472 g, 1.64 mmol) in dry toluene (20 ml) with stirring and heating at reflux under Ar. The mixture was stirred and heated under reflux for 6 h. After cooling, the mixture was concentrated in vacuo. The residue was purified by MPLC. Elution with n-pentane-Et_2O (20:1) gave (1R,3S,5S)-**3** (0.157 g, 53 %). This was distilled to give an analytical sample, b.p. 75°(bath temp)/1.6 Torr; $n_D^{23.5}$ 1.4619; $[\alpha]_D^{23.5}$ +109° (c=0.67, $CHCl_3$); CD (c=0.044, EtOH), Δε -4.2 (202 nm); νmax 3050 (w), 2980 (s), 2950 (s), 2900 (s), 2850 (m), 1460 (m), 1435 (s), 1370 (s), 1360 (w), 1350 (m), 1335 (w), 1330 (w), 1315 (m), 1300 (w), 1270 (w), 1225 (s), 1200 (m), 1145 (s), 1135 (s), 1110 (s), 1100 (s), 1065 (s), 1050 (m), 1025 (m), 1010 (m), 995 (m), 975 (s), 965 (m), 950 (m), 915 (m), 900 (m), 875 (s), 865 (s), 810 (w), 790 (m), 765 (w) cm^{-1}; δ (400 MHz, $CDCl_3$) 0.89 (3H, t, J=7.6 Hz), 1.37 (1H, ddd, J=13.0, 3.5, 1.2 Hz), 1.38 (1H, ddq, J=13.3, 6.7, 7.6 Hz), 1.41 (3H, s), 1.54 (1H, ddq, J=13.3, 6.7, 7.6 Hz), 1.64 (3H, ddd, J=2.4, 1.8, 1.7 Hz), 1.82 (1H, ddd, J=13.0, 12.5, 5.3 Hz), 1.87 (1H, dddq, J=19.0, 5.2, 5.0, 1.7 Hz), 2.65 (1H, dddq, J=19.0, 6.7, 2.5, 1.8 Hz), 3.77 (1H, dddd, J=12.5, 6.7, 6.7, 3.5 Hz), 4.31 (1H, dddd, J=6.7, 5.3, 5.2, 1.2 Hz), 5.76 (1H, ddq, J=5.0, 2.5, 2.4 Hz). ^{13}C NMR δ 9.38, 18.53, 24.68, 29.39, 30.35, 36.13, 66.56, 68.97, 95.33, 123.35, 132.93. GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 110°; Carrier gas, N_2, 50 ml/min, 1.0 kg/cm^2) Rt 11.3 min (100 %). MS: m/z 182 (M^+, 46 %), 112 (25 %), 111 (38 %), 110 (40 %), 109 (100 %), 107 (20 %), 93 (36 %), 85 (74 %), 83 (22 %), 81 (37 %), 74 (22 %), 67 (27 %), 59 (32 %), 57 (43 %). (Found MS: m/z 182.1290 (M^+). Calc for $C_{11}H_{18}O_2$: 182.1307). Its ^1H and ^{13}C NMR spectra were identical with those of the natural product.[2] Its MS was also in accord with that of the natural product.[2] Due to the volatility of the material, the correct combustion analysis of (1R,3S,5S)-**3** could not be obtained.

(1S,3R,5S,6S)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-ol (1S,3R,5S,6S)-**16a'**. In the same manner as described for the preparation of (1R,3S,5R,6R)-**16a**, (1S,3R,5S)-**2'** (0.310 g, 1.58 mmol) yielded (1S,3R,5S,6S)-**16a'** (0.308 g, 98 %), n_D^{23} 1.4792; $[\alpha]_D^{23}$ -45.3° (c=1.20, $CHCl_3$). GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 160°; Carrier gas, N_2, 50 ml/min, 1.2 kg/cm^2) Rt 22.3 min (100 %). Its IR and NMR spectra were identical with those of (1R,3S,5R,6R)-**16a**.

(1S,3R,5S,6S)-O-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-yl S-methyl dithiocarbonate (1S,3R,5S,6S)-**16b'**. In the same manner as described for the preparation of (1R,3S,5R,6R)-**16b**, (1S,3R,5S,6S)-**16a'** (0.305 g, 1.54 mmol) yielded (1S,3R,5S,6S)-**16b'** (0.350 g, 79 %), n_D^{24} 1.5428; $[\alpha]_D^{24}$ +33.5° (c=0.65, $CHCl_3$); HPLC analysis [under the same condition for the analysis of (1R,3S,5R,6R)-**16b**] Rt 26.1 min (98.5 %). Its IR and NMR spectra were identical with those of (1R,3S,5R,6R)-**16b**.

(1S,3R,5R)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene (1S,3R,5R)-**3'**. In the same manner as described for the preparation of (1R,3S,5S)-**3**, (1S,3R,5S,6S)-**16b'** (0.323 g, 1.12 mmol) yielded (1S,3R,5R)-**3'** (0.105 g, 52 %). The analytical sample was distilled in the presence of MgO, b.p. 75°(bath temp)/1.6~1.7 Torr; n_D^{24} 1.4616; $[\alpha]_D^{24}$ -110° (c=0.66, $CHCl_3$); CD (c=0.044, EtOH) $\Delta\varepsilon$ +4.2 (202 nm). GLC (Yanaco G-180; Column, PEG-20M, 50 m x 0.25 mm at 110°; Carrier gas, N_2, 50 ml/min, 0.95 kg/cm^2) Rt 16.4 min (100 %). (Found MS: m/z 182.1313 (M^+). Calc for $C_{11}H_{18}O_2$: 182.1307). Its IR, NMR and mass spectra were identical with those of (1R,3S,5S)-**3**. Due to the volatility of the material, the correct combustion analysis of (1S,3R,5R)-**3'** could not be obtained.

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REFERENCES

1 W. Francke, W. Mackenroth, W. Schroeder, S. Schulz, J. Tengoe, E. Engels, W. Engels, R. Kittmann and D. Schneider, Z. Naturforsch. **40c**, 145 (1985).
2 V. Sinnwell, S. Schulz, W. Francke, R. Kittmann and D. Schneider, Tetrahedron Lett. **26**, 1707 (1985).
3 K. Mori, in Techniques in Pheromone Research (edit. by H. E. Hummel and T. A. Miller), pp. 323-370, Springer Verlag, New York (1984).
4 P. DeShong, M.-T. Lin and J. J. Perez, Tetrahedron Lett. **27**, 2091 (1986).
5 T. Sugai, M. Fujita and K. Mori, Nippon Kagaku Kaishi 1315 (1983).
6 K. Mori and H. Watanabe, Tetrahedron **40**, 299 (1984).
7 K. Mori, Tetrahedron **37**, 1341 (1981).
8 J. Hasegawa, S. Hamaguchi, M. Ogura and K. watanabe, J. Ferment. Technol. **59**, 257 (1981).
9 K. Mori, H. Mori and T. Sugai, Tetrahedron **41**, 919 (1985).
10 S. Ohta, A. Tsujimura and M. Okamoto, Chem. Pharm. Bull. **29**, 2762 (1981).
11 E. Hungerbuehler, D. Seebach and D. Wasmuth, Helv. Chim. Acta **64**, 1467 (1981).
12 F. E. Ziegler and J. K. Thottathil, Tetrahedron Lett. **22**, 4883 (1981).
13 P. DeShong, S. Ramesh, J. J. Perez and C. Bodish, Tetrahedron Lett. **23**, 2243 (1982).
14 P. DeShong, S. Ramesh, V. Elango and J. J. Perez, J. Am. Chem. Soc. **107**, 5219 (1985).
15 K. Mori and H. Watanabe, Tetrahedron **41**, 3423 (1985).
16 E. J. Corey and A. Venkateswarlu, J. Am. Chem. Soc. **94**, 6190 (1972).
17 D. W. Brooks and R. P. Kellogg, Tetrahedron Lett. **23**, 4991 (1982).
18 J. Herscovici and K. Antonakis, J. Chem. Soc. Chem. Commun. 561 (1980).
19 H. E. Winberg, F. S. Fawcett, W. E. Mochel and C. W. Theobald, J. Am. Chem. Soc. **82**, 1428 (1960).
20 K. C. Rice and J. R. Dyer, Jr., J. Heterocyclic Chem. **12**, 1325 (1975).
21 V. Ramanathan and R. Levine, J. Org. Chem. **27**, 1216 (1962).
22 Y. Lefebvre, Tetrahedron Lett. 133 (1972).
23 D. R. Kelly, S. M. Roberts and R. F. Newton, Synth. Commun. **9**, 295 (1979).
24 D. H. R. Barton and S. W. McCombie, J. Chem. Soc. Perkin I 1574 (1975).
25 A. L. Gemal and J.-L. Luche, J. Am. Chem. Soc. **103**, 5454 (1981).
26 V. Schurig, in Asymmetric Synthesis (edit. by J. D. Morrison) Vol. 1, p. 59, Academic Press, New York (1983).
27 W. Francke et al., to be submitted to J. Chem. Ecol.
28 H. Nishimura, T. Takabatake, K. Kaku, A. Seo and J. Mizutani, Agric. Biol. Chem. **45**, 1861 (1981).
29 K. Mori and K. Tanida, Tetrahedron **37**, 3221 (1981).
30 J. A. Dale and H. S. Mosher, J. Am. Chem. Soc. **95**, 512 (1973).