Tetrahedron Vol 46, Nos 13/14, pp 4473–4486, 1990
Printed in Great Britain

0040–4020/90 $3 00 + 00

A NEW SYNTHESIS OF THE FOUR STEREOISOMERS OF 3,11-DIMETHYL-2-NONACOSANONE, THE FEMALE-PRODUCED SEX PHEROMONE OF THE GERMAN COCKROACH†

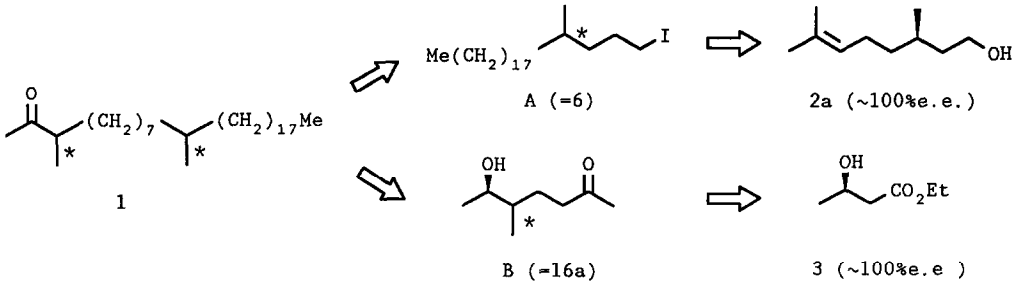
KENJI MORI* and HIROSATO TAKIKAWA

Department of Agricultural Chemistry, The University of Tokyo,
Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan

(*Received in UK 15 December* 1989)

Abstract — The pure four stereoisomers of 3,11-dimethyl-2-nonacosanone (**1**), the female-produced sex pheromone of the German cockroach, were synthesized starting from (*R*)-citronellol (**2a**) and ethyl (*R*)-3-hydroxybutanoate (**3**). The key step was the chromatographic separation of (5*RS*,6*R*)-6-hydroxy-5-methyl-2-heptanone (**16a**) to give pure (5*R*,6*R*)- and (5*S*,6*R*)-isomers. All of the four stereoisomers of **1** were bioactive.

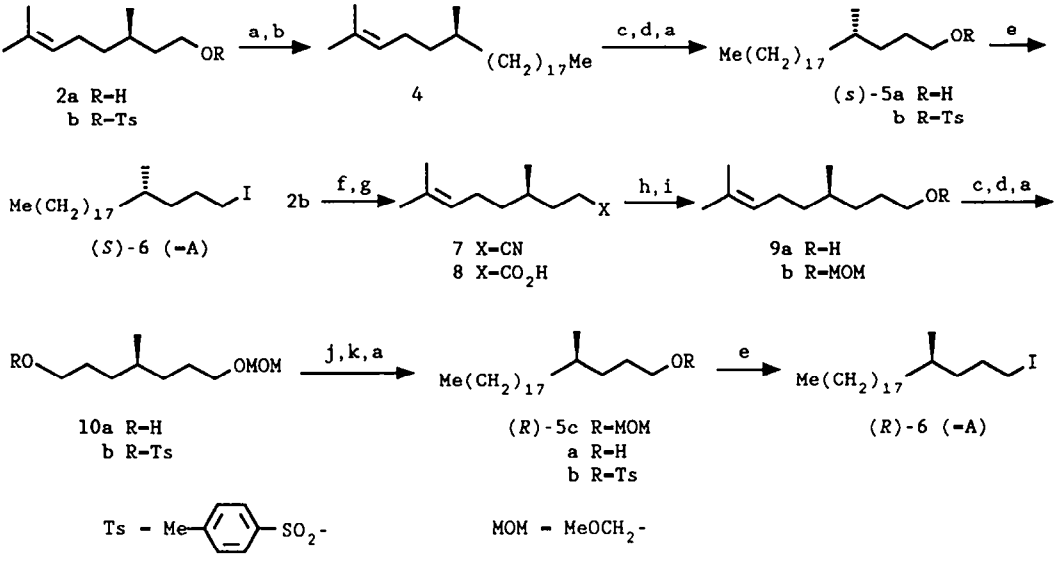
3,11-Dimethyl-2-nonacosanone (**1**) was isolated by Nishida *et al* in 1975 as the female-produced sex pheromone of the German cockroach, *Blattella germanica*.[1] Upon contact with antennae, it elicits wing-raising and direction-turning response from the male adults.[1,2] Our synthesis of its four stereoisomers in 1978 enabled us to assign (3*S*,11*S*)-stereochemistry to the natural pheromone.[3,4] Bioassay of these four stereoisomers of **1** showed them to be equally bioactive.[2] In our previous synthesis of **1**, however, the enantiomeric purity of the starting (*R*)-citronellic acid was only 92% e.e.[4] Although the stereoisomers of **1** could be purified by recrystallization, they might have been enantiomerically impure. In order to obtain conclusive evidence with regard to the non-stereoselective nature of the pheromone perception by male German cockroach, we undertook a project to synthesize all of the four stereoisomers of **1** in highly pure state. In our new synthetic plan as shown in Scheme 1, (*R*)-citronellol (**2a**) and ethyl (*R*)-3-hydroxybutanoate (**3**) are chosen as our starting materials, because both of them are available as enantiomerically pure compounds.[5] These two chiral building blocks (**2a** and **3**) will give all of the four stereoisomers of the target molecule **1** via intermediates **A** and **B**. Thus the enantiomers of iodide **A** and the diastereomers of hydroxy ketone **B** will separately be coupled to give the isomers of **1**. Separation of the two diastereomers of **B** will be the key to the success of synthesis. This plan was realized as detailed below.



Scheme 1. Retrosynthetic analysis of 1.

† Dedicated to Professor W. D. Ollis on the occasion of his 65th birthday. Pheromone synthesis, Part 119. Part 118, K. Mori and P Puapoomchareon, *Liebigs Ann. Chem.*, in press. The experimental part of this work was taken from the M.Sc. thesis of H. T. (March 1990).

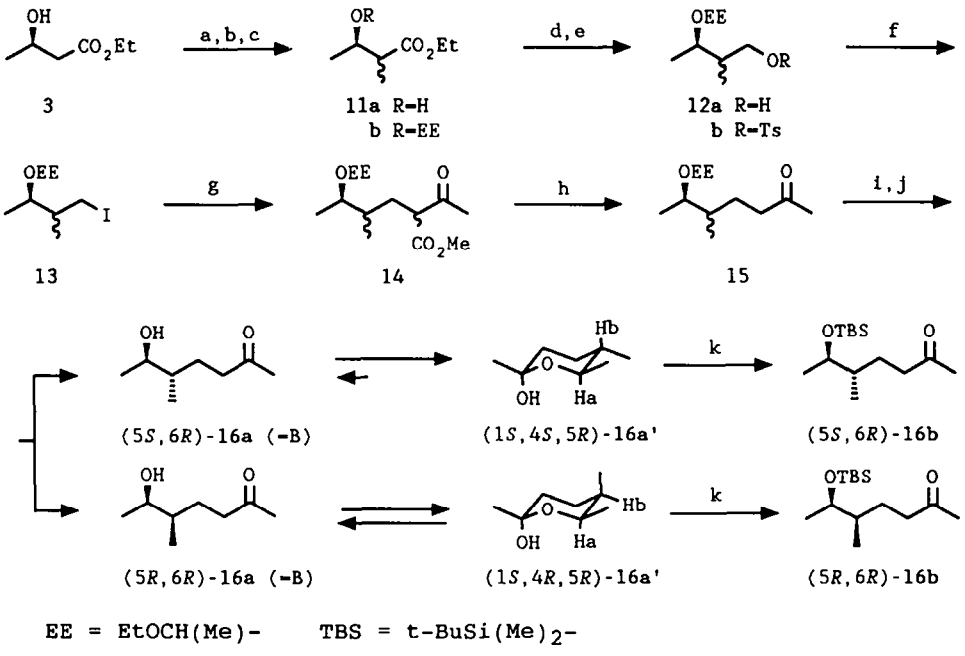
Scheme 2 illustrates our endeavor to prepare the enantiomers of **A** (=**6**). (*R*)-Citronellol (**2a**) of ~100% e.e. was prepared in the conventional manner from (*R*)-pulegone,[5] and converted to the corresponding tosylate **2b**. Treatment of **2b** with hexadecylmagnesium bromide in the presence of lithium tetrachlorocuprate[6] yielded **4**, ozonization of which was followed by reductive workup with sodium borohydride to give (*S*)-**5a**. The alcohol (*S*)-**5a** gave the desired crystalline iodide (*S*)-**6**, $[\alpha]_D^{19}$ +2.21°($CHCl_3$), via tosylate (*S*)-**5b** in the standard manner in 72% overall yield in 6 steps from **2a**. The synthesis of (*R*)-**6** was also straightforward, just reversing the direction of the chain-extension. Treatment of (*R*)-citronellyl tosylate (**2b**) with sodium cyanide gave nitrile **7**. Alkaline hydrolysis of **7** to **8** was followed by its reduction with lithium aluminum hydride to furnish alcohol **9a**. After protecting the hydroxyl group of **9a** as methoxymethyl (MOM) ether, the resulting **9b** was ozonized. Reductive workup of the ozonide with sodium borohydride yielded diol mono MOM ether **10a**. The corresponding tosylate **10b** was coupled with pentadecylmagnesium bromide under the Schlosser condition[6] to give (*R*)-**5c**. After removing the MOM protective group of **5c** with dilute acid, the resulting alcohol (*R*)-**5a** was converted to the crystalline iodide (*R*)-**6**, $[\alpha]_D^{18}$ -2.25°($CHCl_3$), via (*R*)-**5b** in 44% overall yield from **2a** in 12 steps.



Scheme 2. Synthesis of the enantiomers of **6**.

Reagents: (a)TsCl/C_5H_5N; (b)$Me(CH_2)_{15}MgBr$, Li_2CuCl_4/THF; (c)O_3; (d)$NaBH_4$; (e)NaI/Me_2CO; (f)NaCN/DMSO; (g)NaOH/aq EtOH; (h)$LiAlH_4$/Et_2O; (i)MOMCl, $(i\text{-}Pr)_2NEt/CH_2Cl_2$; (j)$Me(CH_2)_{14}MgBr$, Li_2CuCl_4/THF; (k)dil HCl.

We then turned our attention to the preparation of another building block **B**. The strategy as shown in Scheme 3 enabled us to secure both (5*S*,6*R*)- and (5*R*,6*R*)-**16b** starting from **3**. The hydroxyl group of **3** was used as the handle to separate the diastereoisomeric mixture of **16a**. Ethyl (*R*)-β-hydroxybutanoate **3** (~100% e.e.) can readily be prepared by ethanolysis of poly-β-hydroxybutyrate (PHB) produced by *Zoogloea ramigera* I-16-M.[7] Alkylation of **3** with methyl iodide and 2 equivalents of lithium diisopropylamide (LDA) according to Fráter[8] yielded (2*R*,3*R*)-**11a** as the major product (*syn*:*anti* = 6:94). This isomer would lead to (5*S*,6*R*)-**16b**. However, because we also required (5*R*,6*R*)-**16b**, equilibration of (2*R*,3*R*)-**11a** was achieved by treating it with 2 equivalents of LDA followed by quenching with aqueous ammonium chloride. The resulting equilibration product was a mixture of (2*R*,3*R*)- and (2*S*,3*R*)-**11a** (*syn*:*anti* = 45:55). After protecting the hydroxyl group of **11a** as ethoxyethyl ether (EE), **11b** was reduced with lithium aluminum hydride to give **12a**. The alcohol **12a** furnished iodide **13** in the usual manner via tosylate **12b**. Chain-elongation of **13** with methyl acetoacetate was executed employing potassium carbonate as the base to give **14**. Hydrolysis of **14** with concomitant decarboxylation of the resulting acid furnished **15**, which was treated with dilute acetic acid to give a mixture of (5*S*,6*R*)- and (5*R*,6*R*)-**16a**.



Scheme 3. Synthesis of the isomeric ketones **16b**.

Reagents: (a)2eq LDA, MeI/THF-HMPA; (b)i)2eq LDA/THF, ii)NH_4Claq; (c)EtOCH=CH_2, TsOH; (d)$LiAlH_4/Et_2O$; (e)$TsCl/C_5H_5N$; (f)NaI, $NaHCO_3/Me_2CO$; (g)$MeCOCH_2CO_2Me$, K_2CO_3/Me_2CO-DMF; (h)KOH/aqMeOH; (i)aqAcOH/THF; (j)SiO_2 chromatog.; (k)TBSCl, imidazole/DMF.

Separation of the two isomers was achieved by silica gel chromatography due to such a large difference in their ease of cyclic hemiacetal formation as in the case of serricornin (7-hydroxy-4,6-dimethyl-3-nonanone, the cigarette beetle pheromone) stereoisomers.[9] The less polar *anti*-isomer (5*S*,6*R*)-**16a** readily formed the corresponding cyclic hemiacetal (1*S*,4*S*,5*R*)-**16a'** as crystals, while the more polar *syn*-isomer (5*R*,6*R*)-**16a** was obtained as an oily mixture of both the acyclic and cyclic forms. The yield of (5*S*,6*R*)- and (5*R*,6*R*)-**16a** was 25 and 40%, respectively, after purification. In Figure 1 are shown the 300 MHz ^1H NMR spectra of both (5*S*,6*R*)- and (5*R*,6*R*)-**16a** as benzene-d_6 solution. It is evident that the (5*S*,6*R*)-isomer exists as the cyclic hemiacetal form (1*S*,4*S*,5*R*)-**16a'** with the depicted conformation, because its J_{ab} was observed to be 9.7 Hz. In the case of (5*R*,6*R*)-**16a**, on the other hand, it exists as a roughly 1:1 mixture of the acyclic and cyclic hemiacetal forms. The conformation of the latter must be as depicted, because its J_{ab} was 2.5 Hz. Silylation of the hydroxy ketones **16a** with *t*-butyldimethylsilyl (TBS) chloride to (5*S*,6*R*)- and (5*R*,6*R*)-**16b** concluded the preparation of the key intermediates. These two isomers of **16b** were proved to be diastereoisomerically pure by GLC analysis. The overall yield of (5*S*,6*R*)-**16b** was 5.0% in 10 steps from **3**, while that of (5*R*,6*R*)-**16b** was 9.7%.

The final stage of the synthesis was the coupling of two intermediates and derivation of the coupling products to the German cockroach pheromone and its stereoisomers. At first, several attempts were made to directly alkylate **16b** with **6** under various conditions. However, none of them gave satisfactory results. Accordingly, we developed the route as shown in Scheme 4. The terminal carbon of the methyl ketone (5*S*,6*R*)-**16b** was activated by converting it to β-keto ester (6*S*,7*R*)-**17**. At this methoxycarbonylation step, a few % of the reaction took place at the undesired methylene position as revealed by the presence of a small signal due to $COC\underline{H}_3$ in the ^1H NMR spectrum of (6*S*,7*R*)-**17**. Alkylation of **17** with (*S*)-**6** was achieved by employing potassium carbonate as a base to give (2*R*,3*S*,7*RS*,11*S*)-**18**. The use of sodium hydride as a base gave inferior results. Saponification and decarboxylation of **18** yielded (2*R*,3*S*,11*S*)-**19**. In the ^1H NMR spectrum of **19**, a signal due to $COC\underline{H}_3$ was

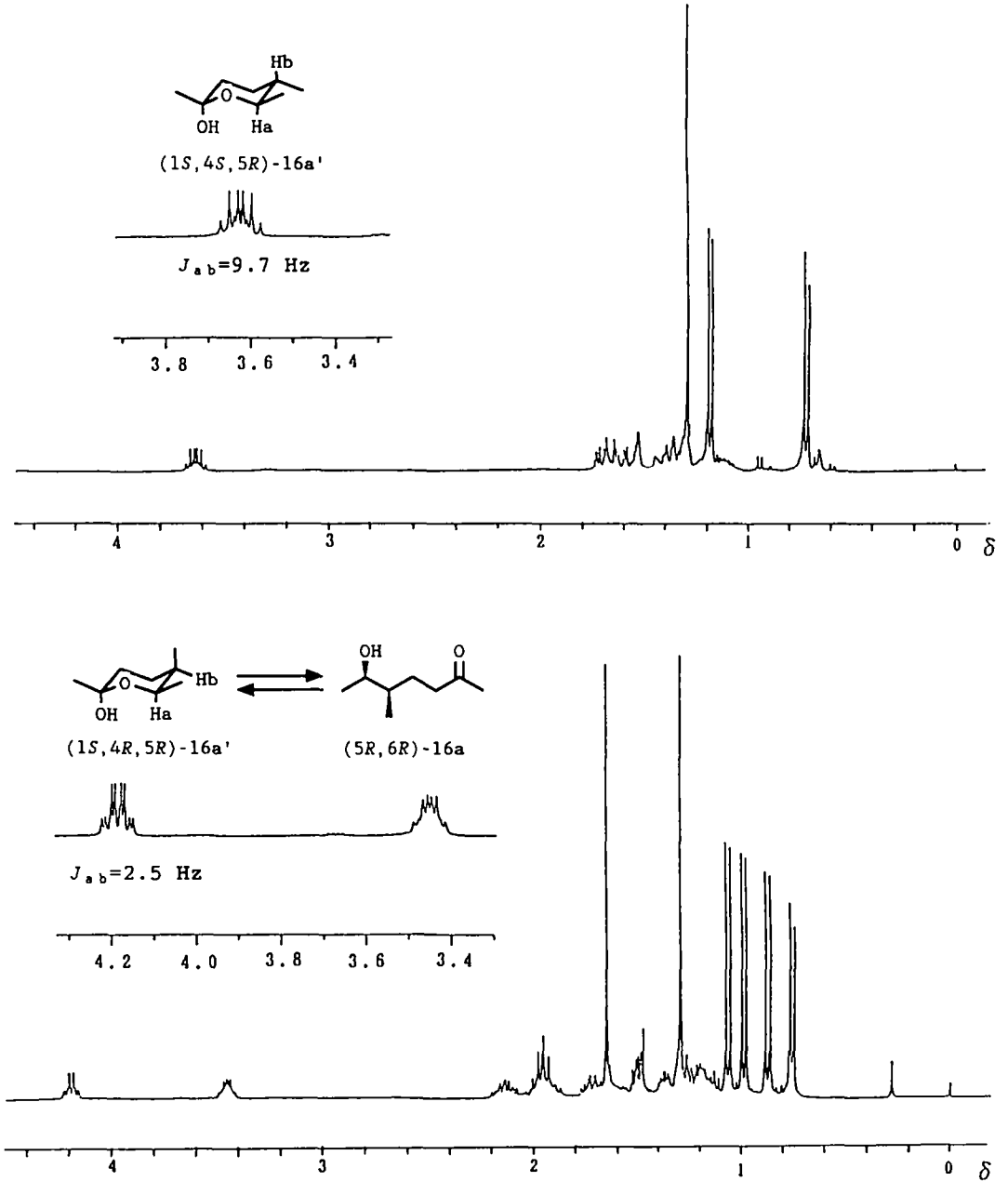
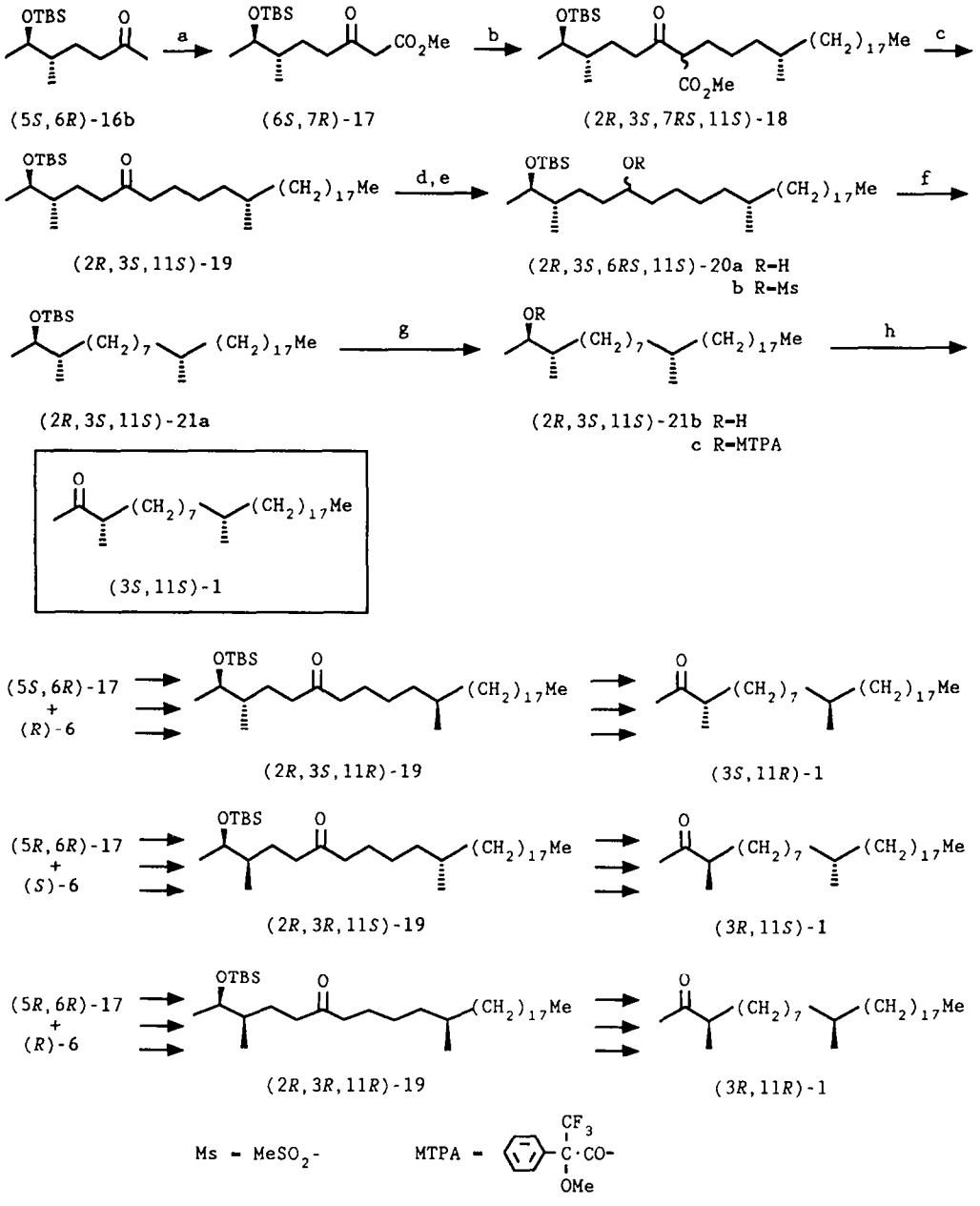


Figure 1. 300 MHz ^{1}H NMR Spectra of the isomers of **16a**.



Scheme 4. Synthesis of the four stereoisomers of 1.

Reagents: (a) $CO(OMe)_2$, NaH/dioxan; (b) (*S*)-**6**, K_2CO_3/MeCOEt; (c) KOH, $(n\text{-}Bu)_4NOH$/aqTHF; (d)$NaBH_4$/*i*-PrOH; (e)MsCl, DMAP/C_5H_5N-CH_2Cl_2; (f)$LiEt_3BH$/THF; (g)aqHF/DME; (h)CrO_3/Et_2O.

absent. Apparently, the regioisomer of **17** generated by methoxycarbonylation at C-3 of **16b** could not be alkylated by such a bulky reagent as (*S*)-**6**. Pure **19** could thus be obtained after chromatographic purification.

The next problem was how to reduce the carbonyl group of **19** to methylene. Because our attempts to reduce (2*R*,3*S*,11*S*)-**19** by the Wolff-Kishner reduction were unsuccessful, we reduced **19** with sodium borohydride to give alcohol (2*R*,3*S*,6*RS*,11*S*)-**20a**. Mesylation of **20a** was followed by reduction of the mesylate **20b** with lithium triethylborohydride to give (2*R*,3*S*,11*S*)-**21a**. Desilylation of **21a** with hydrofluoric acid in 1,2-dimethoxyethane yielded crystalline alcohol **21b**. Finally oxidation of **21b** in ether with chromic acid[10] gave the natural pheromone (3*S*,11*S*)-**1**, which was recrystallized twice from ethanol to give pure (3*S*,11*S*)-**1**, m.p. 47.0-47.5°C, $[\alpha]_D^{19}$ +5.52°(*n*-hexane). The overall yield of (3*S*,11*S*)-**1** was 39% in 13 steps from (*R*)-citronellol (**2**) or 2.6% in 18 steps from ethyl (*R*)-3-hydroxybutanoate (**3**). By alkylating (5*S*,6*R*)-**17** with (*R*)-**6**, (3*S*,11*R*)-**1**, m.p. 40.5-41.0°C, $[\alpha]_D^{19}$ +5.51°(*n*-hexane), was synthesized in 23% overall yield from **2** or 2.6% overall yield from **3**. Similarly, (3*R*,11*S*)-**1**, m.p. 40.5-41.0°C, $[\alpha]_D^{19}$ -5.31°(*n*-hexane), and (3*R*,11*R*)-**1**, m.p. 47.0-47.5°C, $[\alpha]_D^{19}$ -5.44°(*n*-hexane), were prepared in 40% and 26% overall yield from **2**, respectively. Even at 500 MHz, ^{1}H NMR spectrum of (3*S*,11*S*)-**1** was indistinguishable from that of (3*S*,11*R*)-**1**. The 125 MHz ^{13}C NMR spectrum of (3*R*,11*R*)-**1** was also virtually identical with that of (3*R*,11*S*)-**1**. However, the IR spectrum (KBr disc) of (3*S*,11*S*)-**1** was clearly different from that of (3*S*,11*R*)-**1** (see Experimental).

The diastereoisomeric as well as enantiomeric purity of the stereoisomers of **21b** was checked by HPLC analysis of the corresponding (*R*)- and (*S*)-α-methoxy-α-trifluoromethylphenylacetates (MTPA esters)[11] **21c**. The isomeric pairs at C-11 of **21c** could not be separated by HPLC. We were confident, however, of >99% enantiomeric purity at C-11 of **21c**, because it was derived from the C-3 of the enantiomerically pure (*R*)-citronellol (**2**) without recourse to reactions with possible racemization at the chiral center. As to C-3, MTPA esters of (3*R*)-**21b** could be separated from those of (3*S*)-**21b**. We therefore reduced the pure isomers of **1** with diisobutyl aluminum hydride to give the corresponding isomeric mixtures at C-2 of **21b**, which were separately converted to the corresponding MTPA esters **21c**, and analyzed by HPLC to confirm the high stereochemical purity of the parent ketone **1**. Our four synthetic ketones **1** were therefore of >99% d.e. and ~100% e.e.

Preliminary behavioral bioassay of the four isomers of **1** was carried out against the male German cockroaches, and all of them were proved to be bioactive. Our previous results were thus confirmed. More detailed bioassays are now being carried out by Drs. Brossut (University of Bourgogne) and Dickens (U.S.D.A.), and the results will be reported in due course.

In summary, highly pure four stereoisomers of the German cockroach pheromone were synthesized, and found to be bioactive.

EXPERIMENTAL

All m.ps and b.ps were uncorrected. IR spectra were measured as films for oils and KBr disks or solns (in CCl_4) for solids on a Jasco IRA-102 spectrometer. 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 FX-100 spectrometer unless otherwise stated. Optical rotations were measured on a Jasco DIP-140 polarimeter. HPLC analyses were performed on a Shimadzu LC-6A chromatograph.

(R)-Citronellyl tosylate **2b**

p-TsCl (2.02 g, 10.6 mmol) was added to a stirred and ice-cooled solution of **2a** (1.10 g, 7.05 mmol) in dry pyridine (10 ml). The mixture was stirred overnight at 4°C. After quenching with water, it was then poured into dil HCl aq and extracted with ether. The ether soln was washed with dil HCl aq, water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 2.38 g (quant) of crude **2b**, IR νmax (film) 2910 (s), 1600 (m), 1360 (s), 1180 (s) cm^{-1}. This was employed for the next step without further purification.

(S)-2,6-Dimethyl-2-tetracosene **4**

To a stirred and cooled soln of **2b** (2.31 g, 10.6 mmol) in dry THF (20 ml) at -60°C under Ar was added dropwise a soln of $Me(CH_2)_{15}MgBr$ in THF (0.29 M, 75 ml, 22 mmol), followed by a soln of Li_2CuCl_4 in THF (0.1 M, 0.4 ml, 0.04 mmol). The resulting mixture was allowed to warm to room temp with stirring overnight. It was then poured into sat NH_4Cl aq and extracted with *n*-pentane. The organic layer was washed with water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo*.

The residue was chromatographed over SiO_2. Elution with *n*-hexane gave 6.80 g of waxy solid containing **4**. This was employed for the next step without further purification.

(S)-(-)-4-Methyl-1-docosanol (*S*)-**5a**

Ozone was bubbled into a stirred and cooled mixture of crude **4** (6.80 g) and $NaHCO_3$ (1.0 g, 12 mmol) in MeOH, CH_2Cl_2 and *n*-hexane (200 ml, respectively) below -50°C until saturation. After flashing off the excess O_3 with N_2 gas, $NaBH_4$ (2.8 g, 75 mmol) was added portionwise. The mixture was allowed to warm to room temp with stirring overnight. It was then concentrated *in vacuo* to remove the most part of the solvents, diluted with water, acidified with dil HCl aq, and extracted with ether. The ether soln was washed with water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 1.98 g (85% from **2a**) of (*S*)-**5a**. This was recrystallized from *n*-hexane to give 1.42 g of pure (*S*)-**5a** as colorless needles, m.p. 50.5-51.0°C; $[\alpha]_D^{19}$ -1.03° (c=2.11, $CHCl_3$); IR νmax (CCl_4) 3650 (m), 2955 (vs), 1470 (m), 1380 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.75-1.10 (6H, m), 1.24 (38H, br), 3.55 (2H, t, *J*=6 Hz). (Calc for $C_{23}H_{48}O$: C, 81.10; H, 14.20. Found: C, 80.96; H, 14.00%.)

(S)-4-Methyl-1-docosyl tosylate (*S*)-**5b**

In the same manner as described for the preparation of **2b**, (*S*)-**5a** (3.00 g, 8.81 mmol) gave 4.02 g (93%) of crude (*S*)-**5b**, IR νmax (film) 2945 (vs), 2870 (s), 1600 (w), 1190 (m), 1170 (m) cm^{-1}. This was employed for the next step without further purification.

(S)-(+)-4-Methyl-1-docosyl iodide (*S*)-**6**

A mixture of (*S*)-**5b** (4.00 g, 8.08 mmol) and NaI (1.8 g, 12 mmol) in dry acetone (50 ml) was stirred and heated under reflux for 5 hr. After cooling, it was poured into water and extracted with *n*-hexane. The organic layer was washed with sat $Na_2S_2O_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 3.38 g (85% from (*S*)-**5a**) of (*S*)-**6**. An analytical sample was obtained by recrystallization from *i*-PrOH as colorless needles, m.p. 36.5-37.0°C; $[\alpha]_D^{19}$ +2.21° (c=6.71, $CHCl_3$); IR νmax (CCl_4) 2945 (vs), 2860 (s), 1460 (s), 1380 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.70-1.00 (6H, m), 1.23 (41H, br), 3.01 (2H, t, *J*=7 Hz). (Calc for $C_{23}H_{47}I$: C, 61.32; H, 10.52. Found: C, 61.45; H, 10.45%.)

(R)-Citronellyl cyanide **7**

A mixture of **2b** (59.0 g, 190 mmol) and NaCN (12.1 g, 247 mmol) in DMSO (150 ml) was stirred overnight at room temp. The reaction mixture was poured into ice-water and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 followed by distillation to give 29.0 g (88% from **2a**) of **7**, b.p. 100-101°C/6 Torr; IR νmax (film) 2250 (m), 1450 (m), 1380 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.93 (3H, d, *J*=6 Hz), 1.60 (3H, s), 1.67 (3H, s), 1.00-2.50 (9H, m), 5.05 (1H, t, *J*=6 Hz). This was employed for the next step without further purification.

(R)-4,8-Dimethyl-7-nonenoic acid **8**

A mixture of **7** (28.5 g, 173 mmol) and NaOH (138 g, 3.45 mol) in 60% aq EtOH (400 ml) was stirred and heated under reflux for 38 hr. It was then concentrated *in vacuo* to remove EtOH, diluted with water, acidified with conc HCl aq, and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was distilled to give 30.0 g (94%) of **8**, b.p. 129-132°C/2 Torr; IR νmax (film) 2700 (m), 1710 (s), 1280 (m), 940 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.90 (3H, d, *J*=5 Hz), 1.58 (3H, s), 1.66 (3H, s), 1.00-2.50 (9H, m), 5.05 (1H, t, *J*=6 Hz), 12.06 (1H, s). This was employed for the next step without further purification.

(R)-(+)-4,8-Dimethyl-7-nonen-1-ol **9a**

A soln of **8** (29.5 g, 160 mmol) in dry ether (50 ml) was added dropwise to a stirred and ice-cooled suspension of LAH (9.2 g, 0.24 mmol) in dry ether (200 ml). The mixture was stirred for 1 hr at room temp. It was then ice-cooled and the excess LAH was destroyed by the successive addition of water (9.2 ml), 15% NaOH aq (9.2 ml) and water (27.6 ml). After stirring for 30 min at room temp, $MgSO_4$ was added to the mixture and it was then filtered. The filtrate was concentrated *in vacuo*. The residue was distilled to give 26.7 g (98%) of **9a**, b.p. 79-80°C/0.6 Torr; n_D^{21} 1.4522; $[\alpha]_D^{21}$ +5.07° (neat, d=0.848); IR νmax (film) 3350 (s), 1060

(m) cm^{-1}; δ (60 MHz, CCl_4) 0.85 (3H, d, J=5 Hz), 1.55 (3H, s), 1.62 (3H, s), 1.00-2.20 (9H, m), 2.55 (1H, br), 3.44 (2H, t, J=6 Hz), 4.99 (1H, t, J=6 Hz). (Calc for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.20; H, 12.81%.)

(R)-(-)-1-Methoxymethoxy-4,8-dimethyl-7-nonene **9b**

To a stirred and ice-cooled mixture of **9a** (15.0 g, 88.1 mmol) and $(i\text{-Pr})_2NEt$ (30.7 ml, 176 mmol) in dry CH_2Cl_2 (75 ml), MOMCl (10.1 ml, 133 mmol) was added dropwise under Ar. The mixture was stirred for 15 min at 0°C and then for 1.5 hr at room temp. It was then poured into sat $NaHCO_3$ aq and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 18.0 g (95%) of **9b**. An analytical sample was obtained by distillation as a colorless oil, b.p. 82-83°C/0.25 Torr; n_D^{19} 1.4352; $[\alpha]_D^{19}$ -1.51° (c=1.92, $CHCl_3$); IR νmax (film) 1140 (m), 1110 (s), 1040 (s), 920 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.85 (3H, d, J=5 Hz), 1.55 (3H, s), 1.62 (3H, s), 1.00-2.20 (9H, m), 3.22 (3H, s), 3.55 (2H, t, J=6 Hz), 4.44 (2H, s), 4.99 (1H, t, J=6 Hz). (Calc for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23. Found: C, 72.98; H,12.21%.)

(R)-(-)-7-Methoxymethoxy-4-methyl-1-heptanol **10a**

Ozone was bubbled into a stirred and cooled mixture of **9b** (11.5 g, 53.7 mmol) and $NaHCO_3$ (2.2 g, 0.26 mol) in MeOH (120 ml) at -78°C until saturation. After flashing off the excess O_3 with N_2 gas, $NaBH_4$ (4.07 g, 107 mmol) was added portionwise. The mixture was allowed to warm to room temp with stirring overnight. It was then concentrated *in vacuo* to remove MeOH, poured into water, neutralized with dil HCl aq, and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 9.60 g (94%) of **10a**. An analytical sample was obtained by distillation as a colorless oil, b.p. 92°C/0.5 Torr; n_D^{22} 1.4332; $[\alpha]_D^{19}$ -1.46° (c=1.85, $CHCl_3$); IR νmax (film) 3400 (s), 1110 (s), 1040 (s), 920 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.87 (3H, d, J=5 Hz), 1.00-1.80 (9H, m), 2.32 (1H, br), 3.28 (3H, s), ~3.65 (4H, m), 4.48 (2H, s). (Calc for $C_{10}H_{22}O_3$: C, 63.12; H, 11.65. Found: C, 62.80; H, 11.66%.)

(S)-7-Methoxymethoxy-4-methylheptyl tosylate **10b**

p-TsCl (5.72 g, 30.0 mmol) was added to a stirred and cooled soln of **10a** (3.80 g, 22.0 mmol) in dry pyridine (20 ml). The mixture was stirred overnight at 4°C. After quenching with water, it was poured into water and extracted with ether. The ether soln was washed with water, sat $CuSO_4$ aq, water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 5.80 g (84%) of **10b**, IR νmax (film) 1600 (s), 1360 (s) cm^{-1}. This was employed for the next step without further purification.

(R)-(+)-1-Methoxymethoxy-4-methyldocosane **5c**

To a stirred and cooled soln of **10b** (5.36 g, 15.6 mmol) in dry THF (50 ml) below -40°C under Ar was added dropwise a soln of $Me(CH_2)_{14}MgBr$ in THF (0.3 N, 150 ml, 45 mmol), followed by a soln of Li_2CuCl_4 in THF (0.1 N, 0.8 ml, 0.08 mmol). The resulting mixture was allowed to warm to room temp with stirring overnight. To the mixture, sat NH_4Cl aq was added and it was then concentrated *in vacuo* to remove THF. The residue was diluted with water and extracted with *n*-pentane. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 5.80 g (82% from **10b**) of **5c**, n_D^{22} 1.4415; $[\alpha]_D^{25}$ +0.1° (c=12.0, $CHCl_3$); IR νmax (film) 2940 (vs), 1460 (s), 1380 (s), 1215 (m), 1150 (m), 1115 (s), 1045 (s), 920 (s), 720 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.85 (6H, m), 1.24 (39H, br), 3.20 (3H, s), ~3.50 (2H, m), 4.40 (2H, s). (Calc for $C_{25}H_{52}O_2$: C, 78.05; H, 13.63. Found: C, 78.22; H, 13.69%.)

(R)-(+)-4-Methyl-1-docosanol (R)-**5a**

To a soln of (*R*)-**5c** (5.72 g, 14.9 mmol) in THF (60 ml), 6 N HCl aq (10 ml) was added and the mixture was stirred for 3 days at 50°C. It was then poured into brine and extracted with ether. The ether soln was washed with sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 4.53 g (89%) of (*R*)-**5a**. This was recrystallized from *n*-hexane to give 3.78 g of pure (*R*)-**5a** as colorless needles, m.p. 50.5-51.0°C; $[\alpha]_D^{18}$ +1.08° (c=1.76, $CHCl_3$); Its IR and ^1H NMR spectra were identical with those of (*S*)-**5a**. (Calc for $C_{23}H_{48}O$: C, 81.10; H, 14.20. Found: C, 80.96; H, 14.35%.)

(R)-(-)-4-Methyl-1-docosyl iodide (R)-6

In the same manner as described for the preparation of (*S*)-**6** from (*S*)-**5a**, (*R*)-**5a** (2.75 g, 6.07 mmol) was converted to 2.98 g (82% from (*R*)-**5a**) of (*R*)-**6**. An analytical sample was obtained by recrystallization from *i*-PrOH as colorless needles, m.p. 36.5-37.0°C; $[\alpha]_D^{18}$ -2.25° (c = 5.60, $CHCl_3$); Its IR and ^1H NMR spectra were identical with those of (*S*)-**6**. (Calc for $C_{23}H_{47}I$: C, 61.32; H, 10.52. Found: C, 61.15, H, 10.42%.)

Ethyl (3R)-3-hydroxy-2-methylbutanoate **11a**

(a) *Methylation of* **3**. A soln of LDA was prepared by the dropwise addition of *n*-BuLi soln (1.54 N in *n*-hexane, 216 ml, 333 mmol) to a stirred and cooled soln of $(i\text{-Pr})_2NH$ (33.7 g, 333 mmol) in dry THF (80 ml) below 0°C under Ar. The mixture was stirred for 1 hr below 0°C under cooling with an ice-salt bath. To the stirred and cooled soln of LDA was added dropwise a soln of **3** (20.0 g, 151 mmol) in dry THF (20 ml) at -60°C. After stirring for 30 min at -10°C, a soln of MeI (27.7 g, 182 mmol) in HMPA (42 ml) was added dropwise to the mixture at -40°C. It was allowed to warm to room temp with stirring during 3 hr, then poured into sat NH_4Cl aq, and extracted with ether. The ether soln was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 followed by distillation to give 16.7 g (75%) of (2*R*,3*R*)-**11a**, b.p. 88-89°C/23 Torr; n_D^{21} 1.4188; $[\alpha]_D^{21}$ -29.2° (c = 0.97, $CHCl_3$); IR νmax (film) 3450 (s), 3000 (s), 1730 (vs), 1460 (m), 1375 (m), 1260 (m), 1185 (s), 1115 (m), 925 (m), 860 (m) cm^{-1}; δ (60 MHz, CCl_4) 1.00-1.40 (9H, m), 2.30 (1H, m), ~2.70 (1H, br), 3.37 (1H, m), 4.08 (2H, q, *J* = 7 Hz); GLC (column, PEG-20M, 0.25 mmφ x 50 m at 80°C + 1°C/min; carrier gas, N_2, 1.1 kg/cm^2): *Rt* 14.3 min (**3**, 5.9%), 16.0 min ((2*R*,3*R*)-**11a**, 88.6%), 16.9 min ((2*S*,3*R*)-**11a**, 5.5%). This was employed for the next step without further purification.

(b) *Equilibration of* (2*R*,3*R*)-**11a**. In the same manner as described above, (2*R*,3*R*)-**11a** (17.9 g, 123 mmol) was converted to its dianion. Then it was quenched with sat NH_4Cl aq and extracted with ether. The ether soln was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was, after filtration over SiO_2, distilled to give 14.2 g (79%) of **11a**, b.p. 96-99°C/33 Torr; n_D^{21} 1.4187; $[\alpha]_D^{21}$ -18.7° (c = 1.15, $CHCl_3$); IR νmax (film) 3450 (s), 3000 (s), 1730 (vs) cm^{-1}; δ (60 MHz, CCl_4) 1.00-1.50 (9H, m), 2.10-2.60 (1H, m), 2.75 (1H, br), 3.50-4.00 (1H, m), 4.10 (2H, q, *J* = 7 Hz); GLC (column, PEG-20M, 0.25 mmφ x 50 m at 80°C + 1°C/min; carrier gas, N_2, 1.1 kg/cm^2): *Rt* 14.7 min (**3**, 6.5%), 16.4 min ((2*R*,3*R*)-**11a**, 51.2%), 17.3 min ((2*S*,3*R*)-**11a**, 42.3%). This was employed for the next step without further purification.

Ethyl (2RS,3R)-3-(1'-ethoxyethoxy)-2-methylbutanoate **11b**

To a stirred and ice-cooled soln of **11a** (13.5 g, 92.4 mmol) in ethyl vinyl ether (30 ml) was added *p*-TsOH (5 mg) and the stirring was continued for 1 hr at 0°C. Then, *p*-TsOH (about the same amount) was added to it and the mixture was further stirred for 1 hr. This procedure was repeated once more. Subsequently, the ice bath was removed, and the stirring was continued for 1 hr. The mixture was neutralized with $NaHCO_3$, diluted with ether, filtrated through Florisil, and concentrated *in vacuo*. The residue was chromatographed over SiO_2 followed by distillation to give 15.5 g (77%) of pure **11b**, b.p. 118-121°C/32 Torr; n_D^{21} 1.4130; $[\alpha]_D^{21}$ -11.5° (c = 1.10, $CHCl_3$); IR νmax (film) 3000 (s), 1735 (vs), 1450 (s), 1380 (s), 1340 (m), 1255 (m), 1195 (s), 1130 (s), 1180 (s), 960 (s), 860 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.90-1.50 (15H, m), 2.35 (1H, m), 3.20-4.00 (3H, m), 4.04 (2H, q, *J* = 7 Hz),

(2RS,3R)-3-(1'-Ethoxyethoxy)-2-methyl-1-butanol **12a**

A soln of **11b** (15.3 g, 70.1 mmol) in ether (100 ml) was added to a stirred and ice-cooled suspension of LAH (3.3 g, 87 mmol) in ether (200 ml). The mixture was stirred for 1 hr at room temp. After the usual basic workup, the residue was purified by SiO_2 chromatography to give 12.2 g (99%) of **12a**, n_D^{21} 1.4235; $[\alpha]_D^{21}$ -46.7° (c = 1.17, $CHCl_3$); IR νmax (film) 3450 (s), 3000 (s), 2950 (s), 1450 (m), 1380 (s), 1335 (m), 1130 (s), 1080 (s), 1055 (s), 960 (s), 855 (m), 785 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.60-1.30 (12H, m), ~1.90 (1H, m), 2.30-2.80 (1H, m), 3.20-3.90 (5H, m), 4.55 (1H, m). (Calc for $C_9H_{20}O_3$: C, 61.33; H, 11.44. Found: C, 61.02; H, 11.22%.)

(2RS,3R)-3-(1'-Ethoxyethoxy)-2-methylbutyl tosylate **12b**

In the same manner as described for the preparation of **10b**, **12a** (12.1 g, 68.7 mmol) was converted to 22.0 g (97%) of **12b**, IR νmax (film) 1600 (s), 1360 (s), 1180 (s), 665 (s) cm^{-1}. This was employed for the next step without further purification.

(2RS,3R)-3-(1'-Ethoxyethoxy)-2-methylbutyl iodide **13**

A mixture of **12b** (21.9 g, 66.3 mmol), NaI (14.9 g, 99.6 mmol), $NaHCO_3$ (15 g, 0.18 mol), dry DMF (10 ml) and dry acetone (150 ml) was stirred and heated under reflux for 15 hr under Ar. It was then poured into water and extracted with *n*-pentane. The organic layer was washed with sat $Na_2S_2O_3$ aq and brine, dried (K_2CO_3), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 18.3 g (93% from **12a**) of **13**, n_D^{21} 1.4735; $[\alpha]_D^{21}$ -21.6° (c = 1.03, $CHCl_3$); IR νmax (film) 3000 (s), 1380 (s), 960 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.80-1.30 (12H, m), ~1.90 (1H, m), 2.80-3.90 (5H, m), 4.62 (1H, m). This was employed for the next step without further purification.

(3RS,5RS,6R)-6-(1'-Ethoxyethoxy)-3-methoxycarbonyl-5-methyl-2-heptanone **14**

A mixture of **13** (18.2 g, 63.6 mmol), K_2CO_3 (32.6 g, 4.24 mol), methyl acetoacetate (9.0 ml, 83 mmol), dry DMF (9 ml) and dry acetone (180 ml) was stirred and heated under reflux for 14 hr under Ar. It was then poured into ice-water and extracted with CH_2Cl_2. The organic layer was washed with sat $Na_2S_2O_3$ aq, sat $NaHCO_3$ aq and brine, dried (K_2CO_3), and concentrated in vacuo. The residue was chromatographed over SiO_2 to give 13.8 g (79%) of 14, IR νmax (film) 1750 (s), 1720 (s) cm^{-1}; δ (60 MHz, CCl_4) 0.60-1.30 (12H, m), ~1.90 (3H, m), ~2.20 (1H, m), 2.13 (3H, s), 3.10-3.80 (3H, m), 3.66 (3H, s), 4.60 (1H, m). This was employed for the next step without further purification.

(5RS,6R)-6-(1'-Ethoxyethoxy)-5-methyl-2-heptanone **15**

A mixture of **14** (13.6 g, 46.9 mmol), 10% KOH aq (140 ml) and MeOH (140 ml) was stirred and heated under reflux for 2 hr. It was then poured into water and extracted with ether. The ether soln was washed with water and brine, dried (K_2CO_3), and concentrated *in vacuo*. The residue was distilled to give 7.84 g (73%) of **15**, b.p. 73-75°C/0.15 Torr; n_D^{21} 1.4255; $[\alpha]_D^{21}$ -7.35° (c = 1.36, $CHCl_3$); IR νmax (film) 1720 (vs), 1445 (m), 1380 (m), 1170 (s), 1130 (s), 1085 (s), 1060 (s), 960 (s), 855 (m) cm^{-1}; δ (60 MHz, CCl_4) 0.70-1.30 (12H, m), ~1.90 (3H, m), 2.06 (3H, s), 2.35 (2H, t, J = 7 Hz), 3.10-3.90 (3H, m), ~4.60 (1H, m). (Calc for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 66.64; H, 11.13%.)

(5S,6R)-6-Hydroxy-5-methyl-2-heptanone and its (5R,6R)-isomer **16a**

A soln of **15** (7.61 g, 35.2 mmol) in AcOH-H_2O-THF (1:2:2, 100 ml) was stirred overnight at room temp. The reaction mixture was then neutralized with 20% NaOH aq at 0°C. To this mixture $NaHCO_3$ was added, and the stirring was continued for 2 hr. It was then poured into water and extracted with ether. The ether soln was washed with water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give crude (5*RS*,6*R*)-**16a**. This was chromatographed over SiO_2 (500 g). Elution with *n*-hexane-ether (5:1) gave 1.29 g (25%) of (5*S*,6*R*)-**16a** as crystals. This was further purified by recrystallization from *n*-hexane to give 0.74 g of pure (5*S*,6*R*)-**16a** (This was a hemiacetal **16a'**.) as colorless needles, m.p. 63.5-64.5°C; $[\alpha]_D^{21}$ +82.9° (c = 0.79, *n*-pentane); IR νmax (CCl_4) 3640 (s), 3450 (w), 3000 (s), 2950 (s), 2900 (m), 1450 (m), 1380 (s), 1245 (m), 1225 (m), 1195 (m), 1170 (m), 1140 (s), 1095 (s), 1050 (s), 1025 (m), 995 (s), 960 (m), 910 (s), 855 (m) cm^{-1}; δ (300 MHz, C_6D_6) 0.66 (1H, br), 0.73 (3H, d, J = 6.6 Hz), 1.18 (3H, d, J = 6.2 Hz), 1.05-1.25 (1H, m), 1.29 (3H, s), 1.27-1.46 and 1.50-1.75 (4H, m), 3.63 (1H, dq, J = 3.5, 9.7 Hz); TLC (Merck Kieselgel 60 F_{254} Art. 5715, *n*-hexane-EtOAc 1:1) *Rf* 0.7 (Calc for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.30; H, 10.79%.)

Further elution with *n*-hexane-ether (3:1~1:1) gave 2.16 g of (5*R*,6*R*)-**16a**. This was chromatographed over SiO_2 again to give 2.04 g (40%) of (5*R*,6*R*)-**16a** (This was a roughly 1:1 mixture of **16a** and **16a'** in C_6D_6.) as a colorless oil, n_D^{21} 1.4427; $[\alpha]_D^{21}$ +66.6° (c = 0.88, *n*-pentane); IR νmax (CCl_4) 3630 (m), 3350 (m), 3000 (s), 2950 (s), 2900 (s), 1720 (s), 1455 (m), 1385 (m), 1375 (m), 1240 (m), 1225 (m), 1090 (s), 1060 (s), 1005 (m), 960 (s), 905 (s), 860 (m), 840 (m) cm^{-1}; δ (300 MHz, C_6D_6) 0.76 (1.5H, d, J = 6.6 Hz), 0.88 (1.5H, d, J = 7.0 Hz), 0.99 (1.5H, d, J = 6.4 Hz), 1.07 (1.5H, d, J = 6.6 Hz), 1.18-1.42 (2.5H, m), 1.30 (1.5H, s), 1.47-1.53 (1H, m), 1.55-1.82 (1H, m), 1.64 (1.5H, s), 1.87-2.06 (2H, m), 2.06-2.22 (0.5H, m), 3.46 (0.5H, dq, J = 4.0, 6.3 Hz), 4.19 (0.5H, dq, J = 2.5, 6.6 Hz); TLC (Merck Kieselgel 60 F_{254} Art. 5715, *n*-hexane-EtOAc 1:1) *Rf* 0.3-0.6 (Calc for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.45; H, 10.97%.)

6-t-Butyldimethylsilyloxy-5-methyl-2-heptanone **16b**

(a) *(5S,6R)-Isomer.* A mixture of (5*S*,6*R*)-**16a** (0.57 g, 4.0 mmol), imidazole (1.62 g, 23.8 mmol),and TBSCl (1.79 g, 11.9 mmol) in dry DMF (12 ml) was stirred for 5 days at room temp under Ar. It was then poured into water and extracted with ether. The

ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 followed by distillation to give 0.82 g (81%) of (5*S*,6*R*)-**16b**, b.p. 112°C/5 Torr; n_D^{21} 1.4325; $[\alpha]_D^{21}$ -20.8° (c = 2.06, $CHCl_3$); IR νmax (film) 1720 (s), 1255 (s), 1105 (s), 1050 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.83 (3H, d, *J* = 6 Hz), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.15-1.90 (3H, m), 2.14 (3H, s), 2.30-2.60 (2H, m), 3.65 (1H, dq, *J* = 4, 6 Hz); GLC (column, PEG-20M, 0.25 mmφ x 60 m at 70°C +1°C/min; carrier gas, N_2, 1.5 kg/cm^2): *Rt* 74.9 min (99.7%, 100% d.e.). (Calc for $C_{14}H_{30}O_2Si$: C, 65.06; H, 11.70. Found: C, 64.98; H, 11.67%.)

(b) *(5R,6R)-Isomer.* A mixture of (5*R*,6*R*)-**16a** (1.88 g, 13.0 mmol), imidazole (5.33 g, 78.3 mmol), and TBSCl (5.90 g, 39.1 mmol) in dry DMF (38 ml) was stirred for 20 hr at room temp under Ar. It was then worked up in the same manner as described above to give 2.94 g (87%) of (5*R*,6*R*)-**16b**, b.p. 99-100°C/4 Torr; n_D^{21} 1.4336; $[\alpha]_D^{21}$ -0.85° (c = 2.24, $CHCl_3$); IR νmax (film) 1720 (s), 1255 (s), 1050 (m), 960 (m), 840 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.83 (3H, d, *J* = 6 Hz), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.20-1.60 (2H, m), 1.60-1.90 (1H, m), 2.14 (3H, s), 2.43 (2H, t, *J* = 7 Hz), 3.69 (1H, dq, *J* = 3, 6 Hz); GLC (column, PEG-20M, 0.25 mmφ x 60 m at 70°C +1°C/min; carrier gas, N_2, 1.5 kg/cm^2): *Rt* 74.3 min (99.4%, 100% d.e.). (Calc for $C_{14}H_{30}O_2Si$: C, 65.06; H, 11.70. Found: C, 64.83; H, 11.56%.)

Methyl 7-t-butyldimethylsilyloxy-6-methyl-3-oxooctanoate **17**

(a) *(6S,7R)-Isomer.* To a stirred and heated (under reflux) suspension of NaH (60%, 0.34 g, 8.5 mmol) in $(MeO)_2CO$ (1.4 ml, 17 mmol) and dry dioxan (3 ml), a soln of (5*S*,6*R*)-**16b** (891 mg, 3.45 mmol) in dry dioxan (1.5 ml)was added dropwise slowly under Ar. The mixture was stirred and heated under reflux for 2 hr and cooled. It was then quenched with water, neutralized with 1N HCl aq, diluted with water, and extracted with ether. The ether soln was washed with water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 993 mg (91%) of (6*S*,7*R*)-**17**. (A few % of the undesired regioisomer was detected by ^1H NMR.), n_D^{19} 1.4437; $[\alpha]_D^{19}$ -19.5° (c = 2.30, $CHCl_3$); IR νmax (film) 1750 (s), 1720 (s), 1650 (m), 1630 (m), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.83 (3H, d, *J* = 6 Hz), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.20-1.60 (2H, m), 1.60-1.90 (1H, m), ~2.30 (0.2H, m), 2.15 (0.1H, s, regioisomer), 2.40-2.70 (1.8H, m), 3.46 (1.8H, s), 3.65 (1H, dq, *J* = 4, 6 Hz), 3.74 (3H, s), 5.00 (0.1H, s), 12.10 (0.1H, s). From the ^1H NMR spectrum it was clear that (6*S*,7*R*)-**17** was a roughly 9:1 mixture of keto- and enol-forms in $CDCl_3$. (Calc for $C_{16}H_{32}O_4Si$: C, 60.72; H, 10.19. Found: C, 60.63; H, 10.20%.)

(b) *(6R,7R)-Isomer.* In the same manner as described above, (5*R*,6*R*)-**16b** (296 mg, 1.15 mmol) gave 349 mg (96%) of (6*R*,7*R*)-**17**, n_D^{25} 1.4425; $[\alpha]_D^{25}$ +0.92° (c = 1.95, $CHCl_3$); IR νmax (film) 1750 (s), 1720 (s), 1650 (m), 1625 (m), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.83 (3H, d, *J* = 6 Hz), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.20-1.90 (3H, m), ~2.30 (0.2H, m), 2.20 (0.1H, s, regioisomer), 2.56 (1.8H, t, *J* = 7 Hz), 3.45 (1.8H, s), 3.70 (1H, dq, *J* = 3, 6 Hz), 3.73 (3H, s), 4.98 (0.1H, s), 12.20 (0.1H, s). (Calc for $C_{16}H_{32}O_4Si$: C, 60.72; H, 10.19. Found: C, 60.61; H, 10.15%.)

2-t-Butyldimethylsilyloxy-3,11-dimethyl-6-nonacosanone **19**

(a) *(2R,3S,11S)-Isomer.* A mixture of (6*S*,7*R*)-**17** (450 mg, 1.42 mmol), K_2CO_3 (590 mg, 4.27 mmol) and (*S*)-**6** (671 mg, 1.49 mmol) in dry 2-butanone (9 ml) was stirred and heated under reflux for 20 hr under Ar. This mixture was then diluted with *n*-hexane, filtered through Celite, and concentrated *in vacuo*. The residue was filtered through SiO_2 to give 0.86 g of crude (2*R*,3*S*,11*S*)-**18**. This was dissolved in THF (9 ml). To this soln 15% NaOH aq (1.6 ml) and 10% $(n\text{-}Bu)_4NOH$ aq (1.2 ml) were added, and the stirring was continued for 24 hr at room temp. The mixture was then poured into water, acidified with dil HCl aq, and extracted with *n*-hexane. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 29 mg (8%) of (5*S*,6*R*)-**16b** and 505 mg (61%) of (2*R*,3*S*,11*S*)-**19**, n_D^{14} 1.4550; $[\alpha]_D^{14}$ -9.11° (c = 4.79, $CHCl_3$); IR νmax (film) 2950 (s), 2870 (s), 1715 (s), 1460 (s), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.27 (44H, br), 2.25-2.55 (4H, m), 3.55-3.80 (1H, m). (Calc for $C_{37}H_{76}O_2Si$: C, 76.48; H, 13.18. Found: C, 76.65; H, 13.33%.)

(b) *(2R,3S,11R)-Isomer.* In the same manner as described above, (6*S*,7*R*)-**17** (455 mg, 1.44 mmol) and (*R*)-**6** (671 mg, 1.49 mmol) gave 70 mg (19%) of (6*S*,7*R*)-**16b** and 493 mg (59%) of (2*R*,3*S*,11*R*)-**19**, n_D^{17} 1.4541; $[\alpha]_D^{19}$ -8.40° (c = 4.50, $CHCl_3$); IR νmax (film) 2950 (s), 2870 (s), 1715 (s), 1460 (s), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J* = 6 Hz), 1.27 (44H, br), 2.25-2.55 (4H, m), 3.55-3.80 (1H, m). (Calc for $C_{37}H_{76}O_2Si$: C, 76.48; H, 13.18. Found: C, 76.26; H, 13.30%.)

(c) *(2R,3R,11S)-Isomer.* In the same manner as described above, (6*R*,7*R*)-**17** (442 mg, 1.40 mmol) and (*S*)-**6** (660 mg, 1.47 mmol) gave 30 mg (7%) of (6*R*,7*R*)-**16b** and 510 mg (63%) of (2*R*,3*R*,11*S*)-**19**, n_D^{22} 1.4475; $[\alpha]_D^{22}$ +0.06° (c=5.11, $CHCl_3$); IR νmax (film) 2950 (s), 2870 (s), 1715 (s), 1460 (s), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (44H, br), 2.40 (4H, t-like, *J*=7 Hz), 3.70 (1H, t-like, *J*=5 Hz). (Calc for $C_{37}H_{76}O_2Si$: C, 76.48; H, 13.18. Found: C, 76.53; H, 13.09%.)

(d) *(2R,3R,11R)-Isomer.* In the same manner as described above, (6*R*,7*R*)-**17** (705 mg, 2.23 mmol) and (*R*)-**6** (1.05 g, 2.33 mmol) gave 56 mg (10%) of (6*R*,7*R*)-**16b** and 940 mg (73%) of (2*R*,3*R*,11*R*)-**19**, n_D^{19} 1.4502; $[\alpha]_D^{19}$ +0.56° (c=5.16, $CHCl_3$); IR νmax (film) 2950 (s), 2870 (s), 1715 (s), 1460 (s), 1250 (s), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (44H, br), 2.40 (2H, t, *J*=6 Hz), 2.40 (2H, t, *J*=7 Hz), 3.69 (1H, dq, *J*=4, 7 Hz). (Calc for $C_{37}H_{76}O_2Si$: C, 76.48; H, 13.18. Found: C, 76.43; H, 13.17%.)

2-t-Butyldimethylsilyloxy-3,11-dimethyl-6-nonacosanol **20a**

(a) *(2R,3S,6RS,11S)-Isomer.* To a stirred and ice-cooled soln of (2*R*,3*S*,11*S*)-**19** (467 mg, 0.82 mmol) in *i*-PrOH (9 ml), $NaBH_4$ (30 mg, 0 79 mmol) was added portionwise. The mixture was stirred overnight at room temp, then diluted with water, acidified with dil HCl aq (to pH 6), and extracted with *n*-hexane. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 414 mg (88%) of (2*R*,3*S*,6*RS*,11*S*)-**20a**, n_D^{16} 1.4528; $[\alpha]_D^{16}$ -7.80° (c=5.06, $CHCl_3$); IR νmax (film) 3350 (s), 2940 (s), 2870 (s), 1250 (s), 1110 (m), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (49H, br), 3.45-3.80 (2H, m). (Calc for $C_{37}H_{78}O_2Si$: C, 76.21; H, 13.48. Found: C, 76.40; H, 13.30%.)

(b) *(2R,3S,6RS,11R)-Isomer.* In the same manner as described above, (2*R*,3*S*,11*R*)-**19** (475 mg, 0.82 mmol) was converted to 396 mg (83%) of (2*R*,3*S*,6*RS*,11*R*)-**20a**, n_D^{19} 1.4550; $[\alpha]_D^{19}$ -8.40° (c=4.50, $CHCl_3$); IR νmax (film) 3350(s), 2940 (s), 2870 (s), 1250 (s), 1110 (m), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (49H, br), 3.45-3.80 (2H, m). (Calc for $C_{37}H_{78}O_2Si$: C, 76.21; H, 13.48. Found: C, 76.05; H, 13.31%.)

(c) *(2R,3R,6RS,11S)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*S*)-**19** (330 mg, 0.58 mmol) was converted to 308 mg (93%) of (2*R*,3*R*,6*RS*,11*S*)-**20a**, n_D^{23} 1.4533; $[\alpha]_D^{23}$ +1.07° (c=5.11, $CHCl_3$); IR νmax (film) 3350(s), 2940 (s), 2870 (s), 1250 (s), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (49H, br), 3.45-3.85 (2H, m). (Calc for $C_{37}H_{78}O_2Si$: C, 76.21; H, 13.48. Found: C, 76.11; H, 13.46%.)

(d) *(2R,3R,6RS,11R)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*R*)-**19** (820 mg, 1.41 mmol) was converted to 682 mg (82%) of (2*R*,3*R*,6*RS*,11*R*)-**20a**, n_D^{22} 1.4561; $[\alpha]_D^{16}$ +0.82° (c=6.34, $CHCl_3$); IR νmax (film) 3350(s), 2940 (s), 2870 (s), 1250 (s), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.06 (3H, d, *J*=6 Hz), 1.27 (49H, br), 3.45-3.85 (2H, m). (Calc for $C_{37}H_{78}O_2Si$: C, 76.21; H, 13.48. Found: C, 76.08; H, 13.25%.)

2-t-Butyldimethylsilyloxy-3,11-dimethylnonacosane **21a**

(a) *(2R,3S,11S)-Isomer.* To a stirred and ice-cooled soln of (2*R*,3*S*,6*RS*,11*S*)-**20a** (397 mg, 0.68 mmol), DMAP (8 mg, 0.07 mmol) and dry pyridine (340 μl, 4.2 mmol) in dry CH_2Cl_2 (6 ml), MsCl (106 μl, 1.37 mmol) was added and the stirring was continued overnight at 4°C. It was then quenched with water, diluted with water and extracted with *n*-hexane. The organic layer was washed with water, sat $CuSO_4$ aq, water, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 446 mg (96%) of crude (2*R*,3*S*,11*S*)-**20b**. This was dissolved in dry THF (3.4 ml). To this soln, $LiEt_3BH$ (1 N in THF, 3.4 ml, 3.4 mmol) was added dropwise at 0°C under Ar. After removal of the ice-bath, the stirring was continued for 2 hr. It was quenched with water, poured into water and extracted with *n*-hexane. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 361 mg (93% from **20a**) of (2*R*,3*S*,11*S*)-**21a**, n_D^{21} 1.4493; $[\alpha]_D^{21}$ -8.13° (c=5.04, $CHCl_3$); IR νmax (film) 2940 (s), 2860 (s), 1460 (s), 1375 (m), 1250 (s), 1105 (m), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.04 (3H, d, *J*=6 Hz), 1.27 (50H, br), 3.64 (1H, dq, *J*=4.5, 6 Hz). (Calc for $C_{37}H_{78}OSi$: C, 78.36; H, 13.86. Found: C, 78.37; H, 13.96%.)

(b) *(2R,3S,11R)-Isomer.* In the same manner as described above, (2*R*,3*S*,6*RS*,11*R*)-**20a** (387 mg, 0.66 mmol) was converted to 343 mg (91%) of (2*R*,3*S*,11*R*)-**21a**, n_D^{19} 1.4504; $[\alpha]_D^{19}$ -8.21° (c=5.05, $CHCl_3$); IR νmax (film) 2940 (s), 2860 (s), 1460 (s), 1375 (m), 1250 (s), 1105 (m), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.04 (3H, d, *J*=6 Hz), 1.27 (50H, br), 3.64 (1H, dq, *J*=4.5, 6 Hz). (Calc for $C_{37}H_{78}OSi$: C, 78.36; H, 13.86. Found: C, 78.18; H, 13.82%.)

(c) *(2R,3R,11S)-Isomer.* In the same manner as described above, (2*R*,3*R*,6*RS*,11*S*)-**20a** (305 mg, 0.52 mmol) was converted to 257 mg (87%) of (2*R*,3*R*,11*S*)-**21a**, n_D^{22} 1.4522; $[\alpha]_D^{22}$ +1.21° (c=4.15, $CHCl_3$); IR νmax (film) 2940 (s), 2860 (s), 1460 (s), 1375 (m), 1250 (s), 1050 (s), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.05 (3H, d, *J*=6 Hz), 1.27 (50H, br), 3.67 (1H, dq, *J*=4, 6 Hz). (Calc for $C_{37}H_{78}OSi$: C, 78.36; H, 13.86. Found: C, 78.43; H, 13.84%.)

(d) *(2R,3R,11R)-Isomer.* In the same manner as described above, (2*R*,3*R*,6*RS*,11*R*)-**20a** (656 mg, 1.13 mmol) was converted to 590 mg (92%) of (2*R*,3*R*,11*R*)-**21a**, n_D^{19} 1.4502; $[\alpha]_D^{19}$ +0.56° (c=5.16, $CHCl_3$); IR νmax (film) 2940 (s), 2860 (s), 1460 (s), 1375 (m), 1250 (s), 1050 (s), 955 (m), 835 (s), 775 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.03 (6H, s), 0.75-0.95 (9H, m), 0.88 (9H, s), 1.05 (3H, d, *J*=6 Hz), 1.27 (50H, br), 3.67 (1H, dq, *J*=4, 6 Hz). (Calc for $C_{37}H_{78}OSi$: C, 78.36; H, 13.86. Found: C, 78.35; H, 13.67%.)

3,11-Dimethyl-2-nonacosanol **21b**

(a) *(2R,3S,11S)-Isomer.* To a soln of (2*R*,3*S*,11*S*)-**21a** (351mg, 0.62 mmol) in DME (13 ml), 46% HF aq (0.5 ml) was added dropwise and the stirring was continued overnight at room temp. It was then neutralized with sat $NaHCO_3$ aq, diluted with water, and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 270 mg (96%) of (2*R*,3*S*,11*S*)-**21b**. This was further purified by recrystallization from MeOH to give 193 mg of pure **20b** as colorless needles, m.p. 46.0-46.5°C; $[\alpha]_D^{20}$ -7.95° (c=2.51, $CHCl_3$); IR νmax (CCl_4) 3640 (m), 2950 (s), 2870 (s), 1465 (s), 1375 (m), 1075 (m), 715 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.75-0.95 (9H, m), 1.12 (3H, d, *J*=6 Hz), 1.27 (51H, br), 3.66 (1H, dq, *J*=5, 7 Hz). (Calc for $C_{31}H_{64}O$: C, 82.22; H, 14.25. Found: C, 82.49; H, 14.10%.) The corresponding (*R*)- and (*S*)-MTPA esters **21c** were prepared as usual and analyzed by HPLC (column, Senshu pak-Silica 1251-N, 4.6 mmφ x 250 mm; solvent, *n*-hexane-1,2-dichloroethane (30:1); flow rate, 1.2 ml/min; detector, SPD-6A, 254 nm): *Rt* 29.1 min (0.5%, (*R*)-MTPA ester of (2*S*,3*R*)-**21c**), 32.8 min (99.5%, (*R*)-MTPA ester of (2*R*,3*S*)-**21c**). The stereochemical purity of (2*R*,3*S*,11*S*)-**21b** was ~100% e.e. and 99% d.e. The stereochemical purity of other isomers of **21b** was determined to ~100% e.e. and >99% d.e. by the same procedure.

(b) *(2R,3S,11R)-Isomer.* In the same manner as described above, (2*R*,3*S*,11*R*)-**21a** (332 mg, 0.56 mmol) was converted to 249 mg (94%) of (2*R*,3*S*,11*R*)-**21b**. This was further purified by recrystallization from MeOH to give 185 mg of pure **21b** as colorless needles, m.p. 43.5-44.0°C; $[\alpha]_D^{18}$ -7.80° (c=3.89, $CHCl_3$); IR νmax (CCl_4) 3640 (m), 2950 (s), 2870 (s), 1465 (s), 1375 (m), 1075 (m), 715 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.75-0.95 (9H, m), 1.12 (3H, d, *J*=6 Hz), 1.27 (51H, br), 3.66 (1H, dq, *J*=5, 7 Hz). (Calc for $C_{31}H_{64}O$: C, 82.22; H, 14.25. Found: C, 82.23; H, 14.14%.)

(c) *(2R,3R,11S)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*S*)-**21a** (247 mg, 0.44 mmol) was converted to 195 mg (99%) of (2*R*,3*R*,11*S*)-**21b**. This was further purified by recrystallization from EtOH to give 180 mg of pure **21b** as colorless needles, m.p. 37.5-38.0°C; $[\alpha]_D^{21}$ +7.52° (c=4.81, $CHCl_3$); IR νmax (CCl_4) 3640 (m), 2950 (s), 2870 (s), 1465 (s), 1375 (m), 1080 (m), 715 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.75-0.95 (9H, m), 1.16 (3H, d, *J*=6 Hz), 1.27 (51H, br), 3.70 (1H, dq, *J*=4, 7 Hz). (Calc for $C_{31}H_{64}O$: C, 82.22; H, 14.25. Found: C, 82.09; H, 14.21%.)

(d) *(2R,3R,11R)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*R*)-**21a** (565 mg, 1.00 mmol) was converted to 448 mg (99%) of (2*R*,3*R*,11*R*)-**21b**. This was further purified by recrystallization from MeOH to give 420 mg of pure **21b** as colorless needles, m.p. 52.0-52.5°C; [a]$_D^{16}$ +7.61° (c=4.67, $CHCl_3$); IR νmax (CCl_4) 3640 (m), 2950 (s), 2870 (s), 1465 (s), 1375 (m), 1080 (m), 715 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.75-0.95 (9H, m), 1.16 (3H, d, *J*=6 Hz), 1.27 (51H, br), 3.70 (1H, dq, *J*=4, 7 Hz). (Calc for $C_{31}H_{64}O$: C, 82.22; H, 14.25. Found: C, 82.13; H, 14.42%.)

3,11-Dimethyl-2-nonacosanone **1**

(a) *(3S,11S)-Isomer.* To a stirred and ice-cooled soln of (2*R*,3*S*,11*S*)-**21b** (185 mg, 0.41 mmol) in ether (19 ml), chromic acid aq[10] (0.4 N, 2.05 ml, 1.00 eq) was added dropwise. This mixture was stirred for 10 min at 0°C. After addition of a few drops of *i*-PrOH, the mixture was stirred 3 min, then poured into ice-water, and extracted with *n*-hexane. The organic layer was washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 to give 181 mg (99%) of (3*S*,11*S*)-**1**. This was further purified by recrystallization from EtOH to give 150 mg of pure **1** as colorless needles, m.p. 47.0-47.5°C; $[\alpha]_D^{19}$ +5.52° (c=0.92, *n*-hexane); IR νmax (KBr) 2990 (w), 2940 (s), 2870 (s), 1715 (s), 1475 (m), 1465 (s), 1420 (w), 1370 (m), 1295 (w), 1275 (w), 1245 (w), 1215 (w), 1210 (w), 1185 (m), 1150 (m), 1100 (w), 1085 (w), 1035 (w), 955 (m), 930 (w), 885 (w), 875 (w), 775 (w), 730 (s), 720 (s) cm^{-1}; δ (500 MHz, CCl_4) 0.833 (3H, d, *J*=6.5 Hz), 0.887 (3H, t, *J*=7 Hz), 1.134 (3H, d, *J*=7 Hz), 1.248 (50H, br), 1.603 (1H, sext-like, *J*=7 Hz), 2.035 (3H, s), 2.388 (1H, sext, *J*=7 Hz). (Calc for $C_{31}H_{62}O$: C, 82.59; H,

13.86. Found: C, 82.31; H, 14.06%.)

(b) *(3S,11R)-Isomer.* In the same manner as described above, (2*R*,3*S*,11*R*)-**21b** (101 mg, 0.22 mmol) was converted to 98 mg (97%) of (3*S*,11*R*)-**1**. This was further purified by recrystallization from EtOH to give 73 mg of pure **1** as colorless needles, m.p. 40.5-41.0°C; $[\alpha]_D^{19}$ +5.51° (c=2.05, *n*-hexane); IR νmax (KBr) 2980 (m), 2940 (s), 2870 (s), 1705 (s), 1475 (s), 1365 (m), 1295 (w), 1200 (w), 1185 (w), 1150 (m), 1135 (m), 955 (m), 930 (w), 890 (w), 725 (s) cm^{-1}; δ (500 MHz, CCl_4) 0.833 (3H, d, *J*=6.5 Hz), 0.887 (3H, t, *J*=7 Hz), 1.134 (3H, d, *J*=7 Hz), 1.248 (50H, br), 1.603 (1H, sext-like, *J*=7 Hz), 2.035 (3H, s), 2.388 (1H, sext, *J*=7 Hz). (Calc for $C_{31}H_{62}O$: C, 82.59; H, 13.86. Found: C, 82.64; H, 13.99%.)

(c) *(3R,11S)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*S*)-**21b** (140 mg, 0.31 mmol) was converted to 139 mg (100%) of (3*R*,11*S*)-**1**. This was further purified by recrystallization from EtOH to give 108 mg of pure **1** as colorless needles, m.p. 40.5-41.0°C; $[\alpha]_D^{21}$ -5.31° (c=4.03, *n*-hexane); Its IR and ^1H NMR spectra were identical with those of (3*S*,11*R*)-**1**. ^{13}C NMR (125 MHz, C_6D_6) δ 14.32, 16.25, 19.97, 23.09, 27.59, 29.79, 29.97, 30.17, 30.42, 30.51, 32.31, 33.22, 37.56, 47.06, 209.80. (Calc for $C_{31}H_{62}O$: C, 82.59; H, 13.86. Found: C, 82.60; H, 13.95%.)

(d) *(3R,11R)-Isomer.* In the same manner as described above, (2*R*,3*R*,11*R*)-**21b** (200 mg, 0.44 mmol) was converted to 198 mg (99%) of (3*R*,11*R*)-**1**. This was further purified by recrystallization from EtOH to give 146 mg of pure **1** as colorless needles, m.p. 47.0-47.5°C; $[\alpha]_D^{19}$ -5.44° (c=4.09, *n*-hexane); Its IR and ^1H NMR spectra were identical with those of (3*S*,11*S*)-**1**. ^{13}C NMR (125 MHz, C_6D_6) δ 14.32, 16.25, 19.97, 23.07, 27.59, 29.79, 29.97, 30.16, 30.42, 30.51, 32.31, 33.20, 37.56, 47.06, 209.78. (Calc for $C_{31}H_{62}O$: C, 82.59; H, 13.86. Found: C, 82.38; H, 14.01%.)

Determination of the stereochemical purity of **1**

(3*R*,11*R*)-**1** was reduced with DIBAL in *n*-hexane at -78°C in the usual manner. The resulting (2*RS*,3*R*,11*R*)-**21b** was converted to the corresponding MTPA esters **21c** and analyzed by HPLC under the same conditions as already described. HPLC: *Rt* 27.5 min (55.2%, (*R*)-MTPA ester of (2*S*,3*R*)-**21b**), 33.7 min (44.8%, (*R*)-MTPA ester of (2*R*,3*R*)-**21b**). The stereochemical purity of (3*R*,11*R*)-**1** was ~100% e.e. and >99% d.e.. The stereochemical purity of other isomers were ~100% e.e. and >99% d.e.

Acknowledgment — We thank Dr. Y. Nakazono and Miss H. Mizuno of Nitto Denko Co. (Osaka) for the bioassay of our materials. Generous financial support of this work by Nitto Denko Co. is acknowledged with thanks. This work was also supported by a Grant-in-Aid for Scientific Research from Japanese Ministry of Education, Science, and Culture.

REFERENCES

1 Nishida, R.; Fukami, H. and Ishii, S. *Appl. Entomol. Zool.* **1975**, *10*, 10.
2 Nishida, R. and Fukami, H. *Mem. Coll. Agric., Kyoto Univ.* **1983**, *No.112*, 1.
3 Mori, K.; Suguro, T. and Masuda, S. *Tetrahedron Lett.* **1978**, 3477.
4 Mori, K.; Masuda, S. and Suguro, T. *Tetrahedron* **1981**, *37*, 1329.
5 Review: Mori, K. *Tetrahedron* **1989**, *45*, 3233.
6 Fouquet, C. and Schlosser, M. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 83.
7 Mori, K. and Watanabe, H. *Tetrahedron* **1984**, *40*, 299.
8 Fráter, G. *Helv. Chim. Acta* **1979**, *62*, 2825.
9 Mori, K. and Watanabe, H. *Tetrahedron* **1985**, *41*, 3423.
10 Brown, H. C.; Garg, P. C. and Liu, K.-T. *J. Org. Chem.* **1971**, *36*, 387.
11 Dale, J. A. and Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *94*, 4184.