Synthesis and Enantioselective Gas Chromatography of Stereoisomers of 7,11-Dimethylheptadecane − A Pheromone Component of *Lambdina* Species

Sharon Chow,[a] Wilfried A. Koenig,[b] and William Kitching*[a]

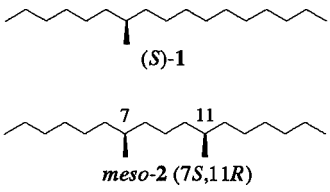
Keywords: Enantioselective gas chromatography / *Lambdina athasaria* / *Lambdina pellucidaria* / Pheromones / Hydrocarbons

The stereoisomers of 7,11-dimethylheptadecane exhibit a useful level of separation under enantioselective gas chromatographic conditions, using a modified cyclodextrin phase. Synthesis of the (7*R*,11*R*) isomer and coinjection studies establish the order of elution as (7*S*,11*S*), (7*R*,11*R*), and finally the *meso* form, the latter being a sex-pheromone component of *Lambdina* species. Enantiomeric assays of natural samples containing this hydrocarbon system will now be possible.

Introduction

Hydrocarbons are considered to have diverse roles in the life-cycles of insects, and cuticular hydrocarbons have been studied in considerable detail.[1] Recognition and pheromonal functions have been assigned to hydrocarbon components[2] and any chirality therein is usually, but not always,[3] associated with methyl branching. Although there is a perception, sometimes unwarranted, that insect hydrocarbons are unchallenging synthetically, this is certainly not the case for stereochemical determinations. With respect to absolute stereochemistry, enantiomer separation on chiral phases (GC or HPLC) is generally difficult[4] and bioassays of synthesised stereoisomers are then required.[5]

The hydrocarbons 7-methylheptadecane (**1**) and 7,11-dimethylheptadecane (**2**) have been identified as constituents of the female-generated sex pheromone of the spring hemlock looper (*Lambdina athasaria*) and the pitch pine looper (*L. pellucidaria*).[6,7] Subsequently, bioassays confirmed that (*S*)-**1** and *meso*-**2**, that is (7*S*,11*R*), were the bioactive stereoisomers.[8] A number of syntheses of these components have been described, with comments that stereoisomers of **1** and **2** are not amenable to separation on chiral stationary phases.[9−11] An additional problem for comparisons of *ee* values was the very low specific rotations for enantiomers of **1** and **2**. For example, for (7*R*,11*R*)-**2**, values of −1.26±0.04[9] and −1.48[11] have been reported as well as for (7*S*,11*S*)-**2**, +1.77±0.04,[9] +1.74,[11] and +1.63.[10] For the enantiomers of **1**, $[\alpha]_D$ values are reported to be between 0.26 and 0.29.[9−11]



Results and Discussion

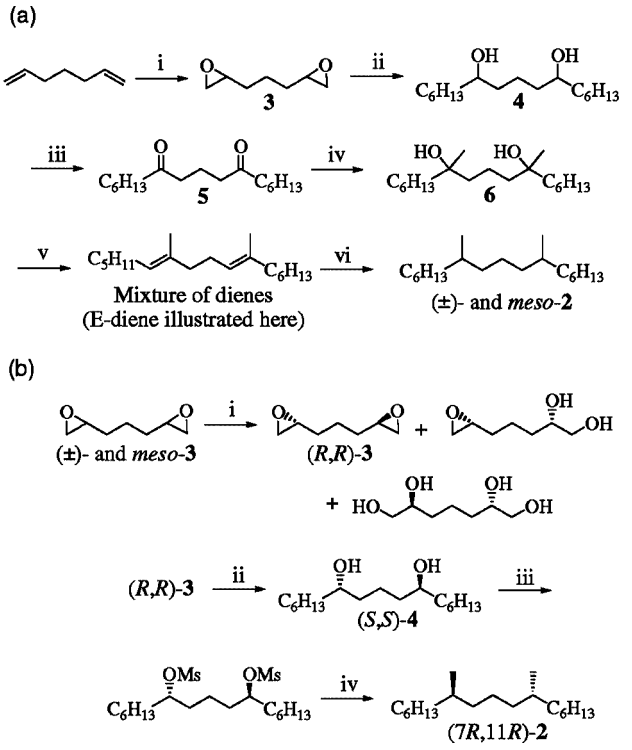
Recently, we demonstrated that hydrolytic kinetic resolution (HKR) of terminal bis(epoxides) delivered the enantiomerically enriched epoxides, epoxydiols, and tetrols, which served as useful intermediates for a range of oxygenated insect sex pheromones.[12] We have further developed this approach and now describe the conversion of racemic 1,3-bis(oxiranyl)propane to stereoisomers of 7,11-dimethylheptadecane and demonstrate for the first time that the three stereoisomers are separable on a cyclodextrin-based phase.

A mixture of *rac*- and *meso*-**3**, from peracid epoxidation of hepta-1,6-diene, was treated with *n*-pentylmagnesium bromide and CuI (in diethyl ether) to provide 7,11-heptadecanediol (**4**), as an isomeric mixture. Oxidation of this diol with Jones reagent provided the 7,11-diketone **5**, which was treated with an excess of MeMgI to furnish the tertiary alcohol **6**. Heating of diol **6** in DMSO generated a mixture of dienes which was immediately hydrogenated to a mixture of the (±)- and *meso*-7,11-dimethylheptadecanes. A diastereomeric mixture of bis(epoxide) **3** was subjected to HKR[12] with 1.4 % equiv. of [(*R*,*R*)-(salen)Co(OAc)] complex and 1.0 equiv. of H_2O to furnish epoxide enantiomer (*R*,*R*)-**3**, which was "scrubbed" with additional (*R*,*R*) catalyst and H_2O to ensure complete enantiomeric integrity.

[a] Department of Chemistry, School of Molecular and Microbial Science, The University of Queensland, Brisbane 4072, Australia
Email: w.kitching@mailbox.uq.edu.au
[b] Institut fur Organische Chemie, Universitat Hamburg, 20146 Hamburg, Germany

  DOI: 10.1002/ejoc.200300643

This bis(epoxide) was converted through the crystalline diol, (*S*,*S*)-**4** and then bis(mesylate), to (*R*,*R*)-7,11-dimethylheptadecane, $[\alpha]_D^{20} = -1.44$ ($CHCl_3$), exhibiting a mass spectrum identical with those reported with consistent ^1H and ^{13}C NMR spectra.[9] The displacement of the mesylate groups by Me_2CuLi [step iv, Scheme 1 (b)] affords, in addition to the desired (7*R*,11*R*)-**2**, monomethyl and alkenyl by-products which were separated by ozonolysis and then flash chromatography. These side-reactions resulted in a low yield of (7*R*,11*R*)-**2**. These procedures are summarised in Scheme 1 (a) and (b).



Scheme 1. (a) Synthesis of racemic 7,11-dimethylheptane, (±)- and *meso*-**2**: (i) *m*-CPBA, DCM; (ii) *n*-pentylMgBr, CuI, diethyl ether; (iii) Jones reagent; (iv) MeMgI, diethyl ether; (v) DMSO; (vi) H_2, Pd/C; (b) synthesis of (*R*,*R*)-**2**: (i) [(*R*,*R*)-salenCo^{III}OAc], H_2O; (ii) *n*-pentylMgBr, CuI; (iii) MsCl, Et_3N; (iv) Me_2CuLi, diethyl ether

Attention was then directed to the gas-chromatographic separation of the three stereoisomers, (7*R*,11*R*)-, (7*S*,11*S*)-, and *meso*-7,11-dimethylheptadecane. It was pleasing that useful separation was achievable, using a 25 m heptakis(6-*O*-TBDMS-2,3-di-*O*-methyl)-β-cyclodextrin phase (50 % in polysiloxane PS 086) at 115 °C. This is shown in Figure 1 (a). The synthesised (7*R*,11*R*) isomer provided a single peak, with no detectable presence of the (7*S*,11*S*) or *meso* forms [Figure 1 (b)]. Coinjection of this (7*R*,11*R*) isomer with the (±) and *meso* isomers [Figure 1 (c)] established that the order of elution was (7*S*,11*S*) then (7*R*,11*R*) followed by the *meso* isomer. It will now be possible to determine directly, with reasonable precision, the enantiomeric composition of samples of 7,11-dimethylheptadecane from natural sources.

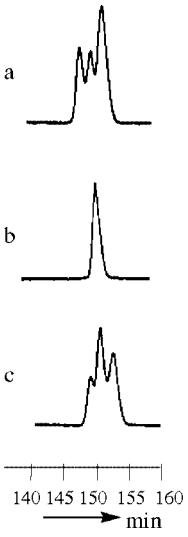


Figure 1. Enantioselective gas chromatography of 7,11-dimethylheptadecane: (a) a mixture of (±) and *meso* isomers; (b) (*R*,*R*)-isomer; (c) co-injection of isomeric mixture and the (*R*,*R*) isomer

The enantiomers of a few methyl-substituted alkanes have been separated under enantioselective gas chromatographic conditions[4] and these are shown below (Figure 2). Although 3-methylhexane responds well, separation is anticipated to be more difficult for longer chain 3-methylalkanes and bioassays would be necessary to establish the natural isomer.[5] These considerations apply also to *Lambdina* component **1**. Considerable variety is now being demonstrated in insect-derived methyl-branched hydrocarbons and establishing the absolute stereochemistry of such low-level hydrocarbons with multiple stereogenic centres is very demanding, for many of the reasons summarised in this report.

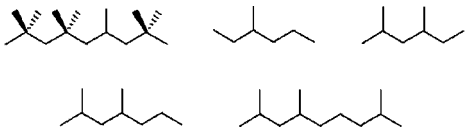


Figure 2. Examples of methylated alkanes whose enantiomers have been separated by enantioselective gas chromatography

Experimental Section

General: NMR spectra were obtained with a Bruker AV400 spectrometer and signals were referenced to the corresponding residual solvent signal, i.e. $\delta_H = 7.24$ and $\delta_C = 77.0$ ppm for $CDCl_3$. The mass spectra were recorded with either a Hewlett−Packard 5890A GC/Mass Detector at 70 eV or a Shimadzu QP5100 gas chromatography mass spectrometer both using a J & W Scientific DB-5 column. Flash chromatography was carried out using either Merck or Scharlau silica gel (230−400 mesh). Optical rotations were measured at 589 nm using a 1-dm cell with a Perkin−Elmer 241 MC polarimeter. Melting points were recorded with a Büchi

Schmelzpunktbestimmungs-Apparat and are uncorrected. Anhydrous diethyl ether and THF used in the moisture-sensitive reactions were freshly distilled from sodium wire and dry dichloromethane (DCM) was distilled from CaH_2.

1,3-Bis(oxiranyl)propane (3): Commercially available 1,6-heptadiene (3.0 g, 31.3 mmol) in DCM (60 mL) was cooled to 0 °C and *m*-chloroperbenzoic acid (50 %, 23.7 g, 68.7 mmol) was added portionwise followed by K_2CO_3 (0.70 g, 5.1 mmol). After stirring at 0 °C for 30 min and at room temperature for 4 h, the mixture was filtered and the precipitate was rinsed thoroughly with cold DCM (40 mL). The combined filtrates were washed successively with Na_2SO_3 (5 % solution, 30 mL), saturated $NaHCO_3$ (3 × 20 mL), and brine (30 mL). The organic layer was dried with $MgSO_4$, concentrated until solvent-free and purified by flash chromatography, eluting with 10% diethyl ether in petroleum spirit, to give 3.0 g of the titled bis(epoxide) in 75 % yield. EIMS: *m*/*z* (%) = 109 (1) [$M^+ - H_3O$], 97 (8), 83 (10), 79 (11), 69 (38), 54 (66), 43 (31), 41 (100). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 1.42−1.64 (m, 6 H, 1-, 2-, 3-H), 2.45 (dt, $^{2,3}J_{H,H}$ = 2.7, 5.2 Hz, 2 H, one of oxiranyl CH_2), 2.72 (dt, $^{2,3}J_{H,H}$ = 0.5, 4.5 Hz, 2 H, one of oxiranyl CH_2), 2.89 (m, 2 H, oxiranyl C*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 22.4, 22.5, 32.3, 46.91, 46.94, 52.00, 52.04 ppm. $C_7H_{12}O_2$ (128.02): calcd. C 65.60, H 9.44; found C 65.23, H 10.14.

(±)- and *meso*-Heptadecane-7,11-diol (4): Under an inert gas, a few drops of neat *n*-pentyl bromide (0.58 mL, 4.7 mmol) was added to predried Mg turnings (0.15 g, 6.2 mmol) in anhydrous diethyl ether (2 mL) to initiate the formation of the organometallic species. The remaining bromide was diluted with diethyl ether (3 mL) and added dropwise to the Mg mixture to maintain gentle reflux. Upon completion of addition, the Grignard solution was stirred for another 40 min before cannulating it into a suspension of CuI (17 mg, 89.3μmol) in diethyl ether (0.5 mL) at −40 °C. After 10 min of stirring, a mixture of (±)- and *meso*-**3** (0.10 g, 0.78 mmol) in diethyl ether (1 mL) was added dropwise to the above and the dark blue solution was stirred overnight while gradually warming to room temperature. The reaction mixture was recooled to 0 °C and carefully quenched with saturated NH_4Cl (10 mL). The separated aqueous layer was re-extracted with diethyl ether (3 × 8 mL) and the combined extracts were washed with brine (10 mL), dried ($MgSO_4$), and concentrated. A diastereomeric mixture of diol **4** was obtained as a white solid (0.18 g) in 81 % yield after flash chromatography (DCM, then 5% MeOH in DCM). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.86 (t, $^3J_{H,H}$ = 6.6 Hz, 6 H, 1-, 17-H), 1.27−1.42 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 8-, 9-, 10-, 12-, 13-, 14-, 15-, 16-H), 3.59 (m, 2 H, 7-, 11-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.1, 21.6, 22.6, 25.6, 29.3, 31.8, 37.4, 37.5, 71.9 ppm. M.p. 82.0 −86.0 °C. The spectroscopic data are in agreement with those reported.[6]

Heptadecane-7,11-dione (5): To a solution of a diastereomeric mixture of the diol **4** (0.15 g, 0.55 mmol) in acetone (5 mL) was slowly added Jones reagent (8 M in H_2O/H_2SO_4, 1.0 mL) at 0 °C. The reaction mixture was stirred overnight and allowed to warm to room temperature. After consuming the excess oxidising reagent with 2-propanol (1 mL), the mixture was filtered through Celite, where the precipitate was washed thoroughly with diethyl ether (20 mL). After concentrating under reduced pressure, saturated $NaHCO_3$ (10 mL) was carefully added, followed by extraction with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried ($MgSO_4$). After solvent removal, diketone **5** was revealed as a white paste (0.13 g, 87 %). EIMS: *m*/*z* (%) = 268 (2) [M^+], 211 (4), 198 (22), 183 (15), 155 (55), 141 (39), 128 (100), 113 (62), 95 (25), 85 (52), 71 (39), 55 (61). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.85 (t, $^3J_{H,H}$ = 6.7 Hz, 6 H, 1-, 17-H), 1.22−1.29 (m, 12 H, 2-, 3-, 4-, 14-, 15-, 16-H), 1.50 (m, 4 H, 5-, 13-H), 1.80 (p, $^3J_{H,H}$ = 7.1 Hz, 2 H, 9-H), 2.35 (t, $^3J_{H,H}$ = 7.4 Hz, 4 H, 6-, 12-H), 2.40 (t, $^3J_{H,H}$ = 7.1 Hz, 4 H, 8-, 10-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.0, 17.8, 22.5, 23.8, 28.9, 31.6, 41.5, 42.8, 210.9 ppm. The spectroscopic data agree with those reported.[6]

(±)- and *meso*-7,11-Dimethylheptadecane-7,11-diol (6): Diketone **5** (0.13 g, 0.48 mmol) in dry diethyl ether (3 mL) was slowly added to MeMgI (1.2 M in diethyl ether, 2.5 mL) at 0 °C under an inert gas. After 1.5 h of stirring, the reaction mixture (at 20 °C) was diluted with diethyl ether (15 mL) and quenched by cautious addition of saturated NH_4Cl (8 mL). The standard reaction workup yielded diol **6** as an oil (0.11 g, 85 %) after column purification (30% DCM in hexane). EIMS: *m*/*z* (%) = 249 (3) [$M^+ - (CH_3, H_2O)$], 197 (47), 179 (57), 154 (9), 138 (13), 129 (84), 109 (50), 95 (64), 84 (54), 69 (100), 55 (82). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.83 (t, $^3J_{H,H}$ = 6.6 Hz, 6 H, 1-, 17-H), 1.09 (s, 6 H, 7-, 11-H), 1.23−1.38 (m, 26 H, 2-, 3-, 4-, 5-, 6-, 8-, 9-, 10-, 12-, 13-, 14-, 15-, 16-H), 1.69 (br. s, 2 H, O*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.0, 18.1, 22.5, 23.8, 26.8, 29.8, 31.8, 42.0, 42.2, 72.7 ppm.

(±)- and *meso*-7,11-Dimethylheptadecane (2): Racemic diol **6** (0.10 g, 0.33 mmol) in dry DMSO (0.4 mL) was heated to ca. 130 °C for 15 h. The chocolate-brown solution was poured into H_2O (40 mL) and extracted with hexane (3 × 15 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The product was purified by flash chromatography (hexane) to give a clear liquid (50 mg, 57 %). The diene mixture (36 mg, 0.13 mmol) was then taken up in hexane (1.5 mL) and stirred with a catalytic amount of Pd/C (10 % active, ca 5 mg) in the presence of H_2 (balloon) overnight. Upon filtration through Celite, removal of solvent under vacuum and flash chromatography (hexane) produced the required hydrocarbon as a mixture of diastereomers (35 mg) in quantitative yield based on the diene. EIMS: *m*/*z* (%) = 268 (< 1) [M^+], 253 (< 1), 183 (3), 155 (1), 127 (2), 113 (4), 99 (5), 85 (13), 71(44), 57 (100), 43 (91), 41 (53). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.821 (t, $^3J_{H,H}$ = 6.46 Hz, 3 H, 1-, 17-H or 7-, 11-Me), 0.822 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, 1- or 17-H or 7- or 11-Me), 0.87 (t, $^3J_{H,H}$ = 7.0 Hz, 3 H, 1- or 17-H or 7- or 11-Me), 1.01−1.38 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.1, 19.7, 19.8, 22.7, 24.5, 27.1, 29.7, 32.0, 32.74, 32.77, 37.1, 37.1, 37.37, 37.42 ppm. The spectroscopic data agree with those reported.[6]

(1*R*,3*R*)-Bis(oxiranyl)propane [(*R*,*R*)-3], (2*S*,5*R*)-5-Oxiranylpentane-1,2-diol and (2*S*,6*S*)-Heptane-1,2,6,7-tetrol: A diastereomeric mixture of bis(epoxide) **3** (2.9 g, 30.2 mmol) was stirred with Jacobsen catalyst [(*R*,*R*), 0.23 g, 0.32 mmol] and H_2O (0.55 mL, 30.6 mmol) for 3 d. The mixture was separated by flash chromatographies to give (*R*,*R*)-**3** (0.73 g, 14 %), (2*S*,5*R*)-5-oxiranylpentane-1,2-diol (1.7 g, 40 %) and (2*S*,6*S*)-heptane-1,2,6,7-tetrol (0.93 g, 18 %). To ensure a high enantiopurity of the chiral bis(epoxide), (*R*,*R*)-**3** was then stirred with additional (*R*,*R*) catalyst (20 mg, 28 μmol) and H_2O (80 μL, 4.4 μmol), followed by the same workup. **(*R*,*R*)-3:** EIMS: *m*/*z* (%) = 109 (1) [$M^+ - H_3O$], 97 (8), 83 (10), 79 (11), 69 (39), 54 (68), 43 (30), 41 (100). ^{1}H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 1.48−1.62 (m, 6 H, 1-, 2-, 3-H), 2.43 (dd, $^{2,3}J_{H,H}$ = 2.7, 5.0 Hz, 2 H, one of oxiranyl CH_2), 2.71 (t, $^{2,3}J_{H,H}$ = 4.9 Hz, 2 H, one of oxiranyl CH_2), 2.88 (m, 2 H, oxiranyl C*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 22.4, 32.0, 46.8, 51.9 ppm. The spectroscopic data agree with those of the mixture

of diastereomers. $[\alpha]_D^{20} = +24.9$ ($c = 1.7$, $CHCl_3$). **(2*S*,5*R*)-5-Oxiranylpentane-1,2-diol:** ^1H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 1.42−1.62 (m, 8 H, 3-, 4-, 5-H, 2 O*H*), 2.43 (dd, $^{2,3}J_{H,H}$ = 2.8, 5.0 Hz, 1 H, one of oxiranyl CH_2), 2.71 (t, $^{2,3}J_{H,H}$ = 4.9 Hz, 1 H, one of oxiranyl CH_2), 2.87 (m, 1 H, oxiranyl C*H*), 3.36 [dd, $^{2,3}J_{H,H}$ = 7.5, 10.9 Hz, 1 H, one of CH_2(OH)CH], 3.54 [m, 2 H, one of CH_2(OH), C*H*(OH)] ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 22.0, 32.2, 32.6, 37.0, 52.3, 66.6, 71.9 ppm. Acetonide derivative: $[\alpha]_D^{20} = +21.7$ ($c = 0.6$, $CHCl_3$). $C_{10}H_{18}O_3$ (186.13): calcd. C 64.49, H 9.74; found C 64.40, H 9.89. **(2*S*,6*S*)-Heptane-1,2,6,7-tetrol:** This was converted into the bis(acetonide) derivative, by stirring with excess 2,2-dimethoxypropane and *p*-toluenesulfonic acid in DCM, for ease in data analyses. EIMS: *m*/*z* (%) = 229 (14) [$M^+ - CH_3$], 171 (3), 141 (< 1), 129 (< 1), 111 (12), 93 (13), 72 (25), 59 (10), 43 (100). ^1H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 1.32 (s, 6 H, Me), 1.37 (s, 6 H, Me), 1.42 (m, 2 H, CH_2), 1.51 (m, 2 H, CH_2), 1.63 (m, 2 H, CH_2), 3.48 (t, $^3J_{H,H}$ = 7.1 Hz, 2 H, CH_2O), 4.00 (d, $^3J_{H,H}$ = 12.3 Hz, 1 H, one of CH_2O), 4.01 (d, $^3J_{H,H}$ = 7.4 Hz, 1 H, one of CH_2O), 4.04 (ds, $^3J_{H,H}$ = 1.0, 6.9 Hz, 2 H, C*H*O) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 22.2, 25.7, 33.6, 69.4, 75.9, 108.7. $[\alpha]_D^{20} = +24.1$ ($c = 2.8$, $CHCl_3$).

(7*S*,11*S*)-Heptadecane-7,11-diol [(*S*,*S*)-4]: The preparation of (*S*,*S*)-**4** followed the procedure described for the racemate, listed above, but starting with the chiral bis(epoxide) (*R*,*R*)-**3**. EIMS: *m*/*z* (%) = 229 (2) [$M^+ - CH_3$], 187 (4), 169 (24), 151 (19), 115 (17), 95 (62), 83 (30), 79 (42), 55 (100), 43 (75). ^1H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.86 (t, $^3J_{H,H}$ = 6.6 Hz, 6 H, 1-, 17-H), 1.27−1.55 (m, 26 H, 2-, 3-, 4-, 5-, 6-, 8-, 9-, 10-, 12-, 13-, 14-, 15-, 16-H, 2O*H*), 3.57 (m, 2 H, 7-, 11-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.1, 21.8, 22.6, 25.6, 29.4, 31.8, 37.2, 37.6, 71.8 ppm. The spectroscopic data agree with those of the diastereomeric mixture. M.p. 85.0−86.0 °C. $[\alpha]_D^{20} = +2.4$ ($c = 0.5$, $CHCl_3$).

(7*R*,11*R*)-7,11-Dimethylheptadecane [(*R*,*R*)-2]: To a solution of diol (*S*,*S*)-**4** (0.15 g, 0.55 mmol) in dry DCM (2 mL) was added Et_3N (0.79 mL, 5.4 mmol) under an inert gas. After stirring for 10 min, mesyl chloride (0.21 mL, 2.6 mmol) was added at 0 °C. The reaction mixture was stirred for a further 15 min and then at room temperature for 2 h. Diethyl ether (8 mL) was added and the precipitate was filtered off. The filtrate was washed with dilute $NaHCO_3$ (4 mL) and brine (4 mL), dried ($MgSO_4$), and solvent was removed in vacuo. In a separate flask, MeLi (1.4 M in diethyl ether, 4.0 mL) was added dropwise to a suspension of CuI (0.56 g, 2.9 mmol) in anhydrous diethyl ether (15 mL) at −10 °C under N_2. The initial bright orange colour faded upon the completion of addition. The resulting colourless solution was stirred for another 10 min before the crude bis(mesylate) in diethyl ether (2 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 5 h and worked up carefully by addition of saturated NH_4Cl (10 mL). After extraction of the aqueous layer with diethyl ether (3 × 10 mL), the combined ethereal extracts were then washed with brine (8 mL), dried ($MgSO_4$), and concentrated. Flash chromatography (hexane) provided a mixture of hydrocarbons (ca. 70 mg) including the desired alkane, plus the monomethylated alkene and diene. A portion of the mixture (20 mg) was treated with ozone to convert the alkenes into carbonyl compounds and thereby assist flash chromatography purification. Pure dimethyl alkane was obtained (13 mg, ca. 19 % from the diol). EIMS: *m*/*z* (%) = 268 (< 1) [M^+], 253 (< 1), 211 (< 1), 183 (3), 155 (2), 127 (2), 112 (9), 99 (5), 85 (16), 71 (49), 57 (100), 43 (76). ^1H NMR (400 MHz, $CDCl_3$, 28 °C): δ = 0.82 (d, $^3J_{H,H}$ = 6.5 Hz, 6 H, Me), 0.86 (t, $^3J_{H,H}$ = 6.6 Hz, 6 H, Me), 0.99−1.39 (m, 28 H, 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 12-, 13-, 14-, 15-, 16-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 28 °C): δ = 14.1, 19.7, 22.7, 24.5, 27.1, 29.7, 32.0, 32.7, 37.2, 37.4 ppm. The spectroscopic data agree with those of the mixture of diastereomers and those reported.[9] $[\alpha]_D^{20} = -1.44$ ($c = 0.9$, $CHCl_3$) or −1.22 ($c = 0.9$, hexane).

[1] [1a] T. L. Singer, *Am. Zool.* **1998**, *38*, 394. [1b] R. W. Howard, C. A. McDaniel, G. T. Blomquist, *J. Chem. Ecol.* **1978**, *4*, 233.
[2] W. Francke, *Pheromones in Comprehensive Natural Products Chemistry*, vol. 8 (Ed.: K. Mori), Elsevier, Oxford, **1999**, pp. 247−249.
[3] See, for example: M. J. McGrath, M. T. Fletcher, W. A. Konig, C. J. Moore, B. W. Cribb, P. G. Allsopp, W. Kitching, *J. Org. Chem.* **2003**, *68*, 3739.
[4] For some examples, see: W. A. Koenig, *Gas Chromatographic Enantiomer Separation with Modified Cyclodextrins*, Hüthig, Heidelberg, **1992**, especially pp. 27−29. Also see: U. J. Meierhenrish, M. Nguyen, B. Barbier, A. Brack, W. H. Thiemann, *Chirality* **2003**, *15*, S13−S16.
[5] For a summary, see: K. Marukawa, H. Takikawa, K. Mori, *Biosci. Biotechnol. Biochem.* **2001**, *65*, 305.
[6] R. Gries, G. Gries, J. Li, C. T. Maier, C. R. Lemmon, K. N. Slessor, *J. Chem. Ecol.* **1994**, *20*, 2501.
[7] C. T. Maier, R. Gries, G. Gries, *J. Chem. Ecol.* **1998**, *24*, 491.
[8] C. M. Duff, G. Gries, K. Mori, Y. Shirai, M. Seki, H. Takikawa, T. Sheng, K. N. Slessor, R. Gries, C. T. Maier, *J. Chem. Ecol.* **2001**, *27*, 431.
[9] Y. Shirai, M. Seki, K. Mori, *Eur. J. Org. Chem.* **1999**, 3139.
[10] D. D. Diaz, V. S. Martin, *J. Org. Chem.* **2000**, *65*, 7896.
[11] D. Enders, T. Schusseler, *Tetrahedron Lett.* **2002**, *43*, 3467.
[12] S. Chow, W. Kitching, *Tetrahedron: Asymmetry* **2002**, *13*, 779.

Received October 10, 2003

