Pheromone Synthesis. Part 166.[1] Synthesis of (2*E*,5*R*,6*E*,8*E*)-5,7-Dimethyldeca-2,6,8-trien-4-one, the Major Component of the Sex Pheromone of the Israeli Pine Bast Scale, and Its Antipode

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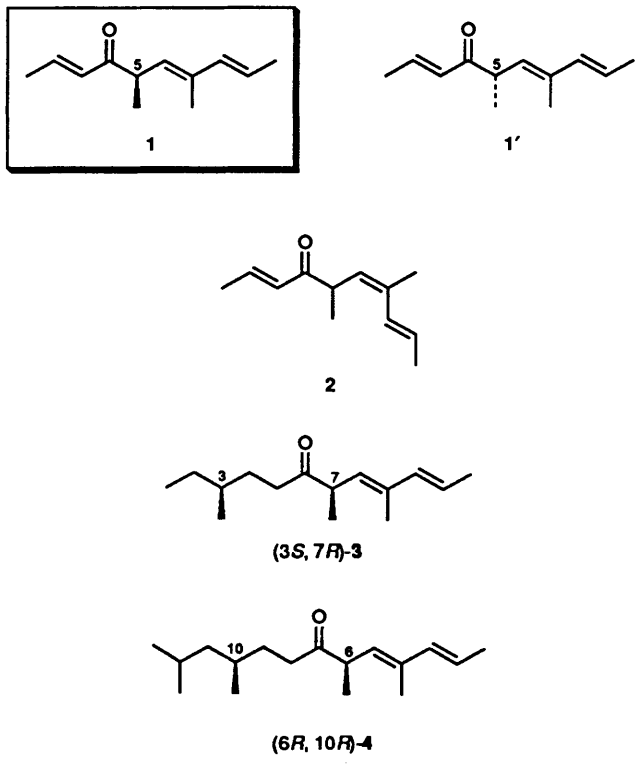
Both the enantiomers (**1** and **1'**) of (2*E*,6*E*,8*E*)-5,7-dimethyldeca-2,6,8-trien-4-one, the major component of the female-produced sex pheromone of the Israeli pine bast scale (*Matsucoccus josephi*) have been synthesized by starting from (2*S*,3*R*)-4-acetoxy-2,3-epoxybutan-1-ol **5**, which was obtained by enzymatic asymmetric hydrolysis of the corresponding *meso*-diacetate **E**. Bioassay of the pheromone enantiomers showed that the (*R*)-isomer **1** is the natural pheromone.

The Israeli pine bast scale, *Matsucoccus josephi*, is a major pest of pine trees in Israel. To monitor the population density of this pest, pheromone traps are extremely useful. In 1993, Dunkelblum *et al.* isolated 5–7 μg of the sex pheromone of *M. josephi* produced by 10 000 virgin females.[2] The pheromone was a 75:25 mixture of (2*E*,6*E*,8*E*)-5,7-dimethyldeca-2,6,8-trien-4-one (Scheme 1, **1** or **1'**) and its (2*E*,6*Z*,8*E*)-isomer **2**.‡[2] Soon afterwards in 1993, Zegelman *et al.* reported a synthesis of the racemates of both **1** and **2**.[3] Their bioassay revealed that the pheromone activity was due mainly to (±)-**1**, while the minor (2*E*,6*Z*,8*E*)-isomer (±)-**2** was of low activity.[3] We became interested in synthesizing both **1** and **1'** so as to clarify the absolute configuration of the major component of the naturally occurring pheromone. Our experience in the synthesis of related pine scale pheromones such as the pheromone of *M. feytaudi* (3*S*,7*R*)-**3**[4] and the pheromone of *M. matsumurae* (6*R*,10*R*)-**4** (matsuone)[5] suggested that the pheromone of *M. josephi* might also possess the *R*-configuration at C-5. Accordingly, the synthesis of **1** was first attempted.[6]



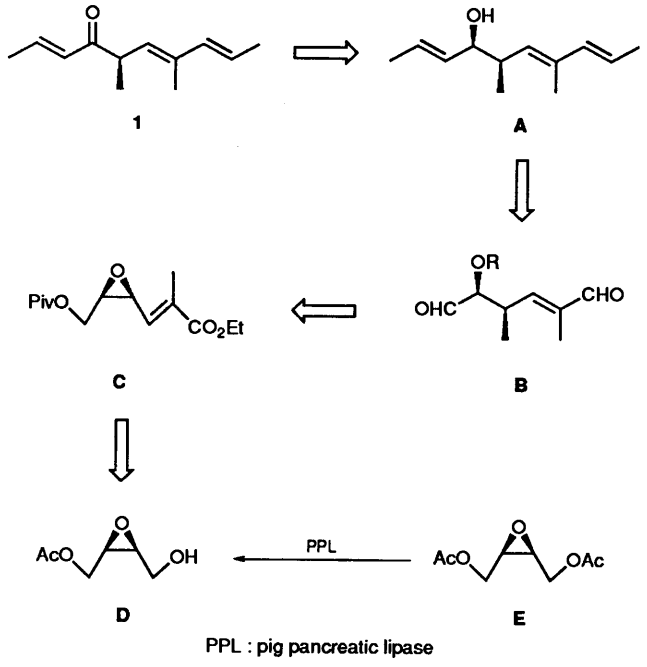
Scheme 1 Structures of the pheromones of the pine bast scale

Results and Discussion

Scheme 2 shows our synthetic plan. The target molecule **1** must be readily racemizable, because the chiral centre at C-5 is doubly activated by the carbonyl group at C-4 and the double bond at C-6. It is, therefore, natural to employ alcohol **A** as the immediate precursor to **1**. The trienol **A** may be prepared by chain-elongation at both ends of dialdehyde **B**. Because the target compound **1** is a ketone, the defined stereochemistry of the hydroxy (or alkoxy) group of **A** and **B** is not necessarily required. It may, however, facilitate their purification and analysis. Methylative cleavage of the epoxy ring of **C** will put the methyl group of **B** at the desired position with the desired absolute configuration. The epoxy unsaturated ester **C** can be prepared from the optically active epoxy alcohol **D**. The building block **D** was previously obtaind by the asymmetric hydrolysis of the *meso*-diacetate **E** with pig pancreatic lipase (PLE).[7] The versatile use of the optically active building block **D** in organic synthesis has already been discussed.[6,8]

The synthesis of the *R*-enantiomer of the pheromone **1** is summarized in Scheme 3. The enantiomerically pure starting material **6** was prepared from the monoacetate **5** (=**D**) as described previously.[7] Protection of the free hydroxy group of **6** as a pivaloyl (Piv) ester yielded **7**, the *tert*-butyldiphenylsilyl (TBDPS) group of which was removed by treatment with hydrofluoric acid–tetrabutylammonium fluoride mixture in aqueous THF to give **8**. The enantiomeric purity of **8** was checked by a 500 MHz ^{1}H NMR measurement of the corresponding (*R*)-α-methoxy-α-trifluoromethylphenylacetate (MTPA ester) **9**, and shown to be >98% e.e. It should be mentioned that the use of tetrabutylammonium fluoride alone for the deprotection of **7** generated (±)-**8** due to ester exchange. Swern oxidation of **8** furnished **10**, which was immediately treated with α-ethoxycarbonylethylidenephosphorane in THF to give the epoxy ester **11** (=**C**). Methylative cleavage of the epoxy ring of **11** was achieved with trimethylaluminium in the presence of a small amount of water[9] to afford **12** (97% purity as checked by GLC) in 92% yield. After protection of the secondary hydroxy group of **12** as a *tert*-butyldimethylsilyl (TBS) ether, the resulting compound **13** was reduced with diisobutylaluminium hydride to give the diol **14**. This diol was oxidized under the Swern conditions to give the dialdehyde **15** (=**B**).

† Research fellow on leave from T. Hasegawa Co., Ltd. (1991–1994).
‡ The nomenclature of compounds **1** and **2** in references 2 and 3 is incorrect.

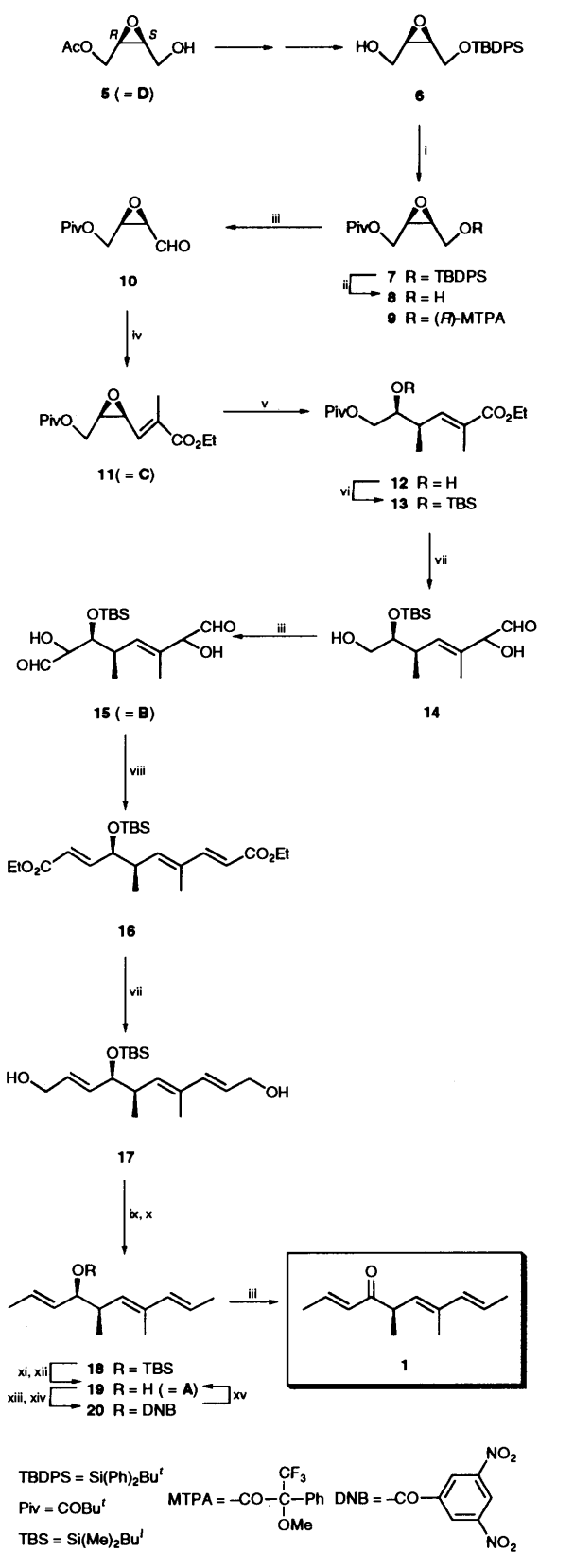


Scheme 2 Retrosynthetic analysis of **1**

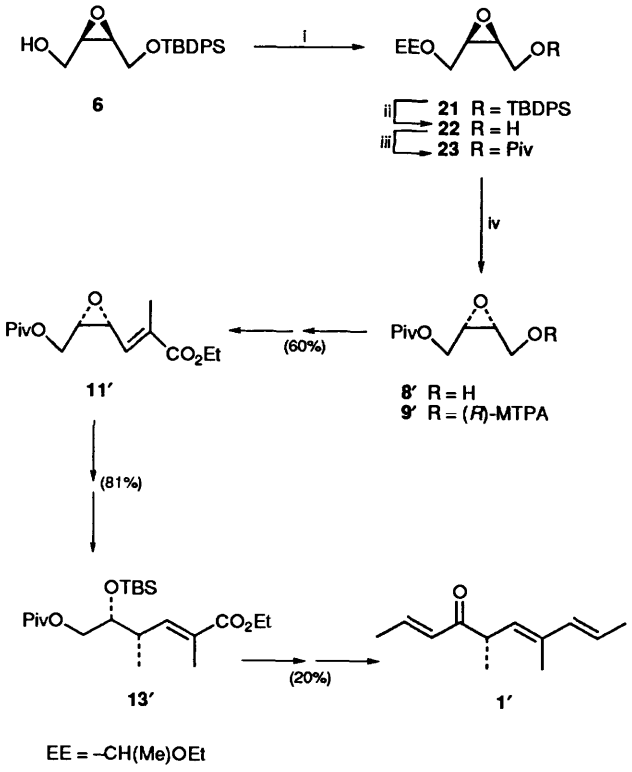
Chain-elongation of the dialdehyde **15** was executed by recourse to the Horner-type Wittig reaction at both ends of the molecule to give **16** in 61% yield. Reduction of **16** with diisobutylaluminium hydride furnished the diol **17**. Reductive deoxygenation of **17** at both ends of the molecule *via* its dimesylate furnished **18**. The TBS protective group of **18** was removed under standard conditions and the resulting alcohol **19** was purified by chromatography followed by recrystallization of the corresponding 3,5-dinitrobenzoate **20**, m.p. 106–107 °C. Removal of the 3,5-dinitrobenzoyl group of **20** gave the pure alcohol **19**, the Swern oxidation of which afforded (2*E*,5*R*, 6*E*,8*E*)-5,7-dimethyldeca-2,6,8-dien-4-one **1**, $[\alpha]_D^{26}$ −466 (*c* 1.16, pentane). Its IR, ^{1}H NMR and mass spectra were in good accord with those reported.[2,3] The overall yield of **1** was 6.5% based on **6** (15 steps). The enantiomeric purity of **1** was estimated by GC analysis using heptakis(2,6-di-*O*-methyl-3-*O*-pentyl)-β-cyclodextrin (DMPBCD-TH column) as the chiral stationary phase, and shown to be 96.6% e.e.

For the synthesis of the (*S*)-isomer **1′**, we prepared **8′** (the antipode of **8**) as shown in Scheme 4. Protection of the free hydroxy group of **6** as an ethoxyethyl (EE) ether gave **21**. The TBDPS protective group of **21** was then removed under the standard conditions to yield **22**. Esterification of **22** with pivaloyl chloride furnished **23**. Treatment of **23** with pyridinium-toluene-*p*-sulfonate (PPTS) in methanol afforded **8′**, the antipode of **8**. The enantiomeric purity of **8′** was estimated as 94% e.e. by 500 MHz ^{1}H NMR measurement of the corresponding (*R*)-MTPA ester **9′**. The epoxy alcohol **8′** was converted into **1′** *via* **11′** and **13′** in entirely the same manner as employed for the synthesis of **1**. The resulting compound **1′**, $[\alpha]_D^{23}$ +473 (*c* 1.21, pentane), had IR, ^{1}H NMR and mass spectra identical with those of compound **1**. Its enantiomeric purity as estimated by GC analysis was 99.0% e.e. The overall yield of **1′** was 7.1% based on **6** (17 steps).

Bioassay of compounds **1** and **1′** in Israel by Dr. Mendel showed the high degree of attractiveness of the (*R*)-isomer **1** for *M. josephi*, in contrast to the (*S*)-isomer **1′** which was almost inactive in this respect. The identity of **1** with the natural pheromone was confirmed by Dr. Dunkelblum by GC comparison on a chiral stationary phase. We therefore conclude that the natural pheromone is the (*R*)-isomer **1**. The biological results will be published separately by Drs. Dunkelblum and Mendel.



Scheme 3 *Synthesis of* **1**. *Reagents, conditions and yields:* i, PivCl, C_5H_5N/CH_2Cl_2 (93%); ii, Bu_4NF, HF, H_2O/THF (95%); iii, $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2 (92% for **1**); iv, $Ph_3P{=}C(Me)CO_2Et$, THF (63% based on **8**); v, Me_3Al (10 equiv.), H_2O (6 equiv.), CH_2Cl_2 (89%); vi, TBSCl, imidazole, DMF (91%); vii, $Bu^i{}_2AlH$, Et_2O (88% for **14**; 98% for **17**); viii, $(EtO)_2P(O)CH_2CO_2Et$, BuLi, THF (61% based on **14**); ix BuLi, $(MeSO_2)_2O$, THF; x, $LiHBEt_3$, THF; xi, Bu_4NF, THF; xii, TLC ($AgNO_3$–SiO_2) sepn. (50% based on **17**); xiii DNBCl, C_5H_5N; xiv, recryst'n (60%); xv, K_2CO_3, MeOH/THF (quant.)



Scheme 4 *Synthesis of* **1'**. *Reagents, conditions and yields:* i, CH_2=CHOEt, TsOH, Et_2O (93%); ii, Bu_4NF, THF; iii, PivCl, C_5H_5N/CH_2Cl_2 (87% based on **21**); iv, PPTS, MeOH (92%)

Experimental

All m.p.s were measured on Yanaco micro melting point apparatus and are uncorrected. IR spectra were measured as films for oils or as KBr disks for solids on a JASCO IRA-102 spectrometer. ^{1}H NMR spectra were recorded at 90 MHz on a JEOL JNM EX-90 spectrometer, at 300 MHz on a Bruker AC-300 spectrometer or at 500 MHz on a JEOL GSX-500 spectrometer. The peak for $SiMe_4$ or solvent ($CHCl_3$: δ_H 7.26) was used for the internal standard. *J* Values are given in Hz. ^{13}C NMR spectra were recorded at 75 MHz on a Bruker AC-300 spectrometer. Solvent peak ($CDCl_3$: δ_C 77.0) was used for the internal standard. Optical rotations, measured on a JASCO DIP-371 polarimeter, are recorded in units of 10^{-1} deg cm^2 g^{-1}. GC analyses were performed on a Shimadzu GC-14A with a flame-ionization detector. HPLC analyses were performed on a Shimadzu LC-6A as a pump and an SPD-6A as a detector. Mass spectra were recorded on a HITACHI M-80B mass spectrometer or a JEOL JMS DX-303 mass spectrometer at 70 eV. Refractive indexes were measured on an ATAGO Abbe refractometer 1_T.

(2R,3S)-4-tert-*Butyldiphenylsilyloxy*-2,3-*epoxybutyl Pivalate* **7**.—To a stirred and ice-cooled solution of the alcohol **6** (11.0 g, 32.2 mmol) and pyridine (15.6 cm^3, 193 mmol) in dry dichloromethane (156 cm^3) was added dropwise pivaloyl chloride (4.65 g, 38.6 mmol) at 0–5 °C under Ar. After being stirred for 7 h at room temperature, the mixture was poured into water and extracted with diethyl ether. The extract was washed successively with 1 mol dm^{-3} hydrochloric acid, brine, saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *ester* **7** (12.7 g, 93%) as a colourless oil, n_D^{23} 1.5232 (Found: C, 70.4; H, 8.0. $C_{25}H_{34}O_4Si$ requires C, 70.38; H, 8.03%); $[\alpha]_D^{24}$ −4.41 (*c* 1.27, Et_2O); ν_{max}(film)/cm^{-1} 3080m (aromatic C–H), 3060m (aromatic C–H), 1735s (C=O), 1655w (aromatic C–H), 1595w (aromatic C–C), 1430m (Si–C), 1365m (C–O), 1285m (CO–O), 1160s (CO–O), 1115s (Si–O), 745m (aromatic C–H) and 710s (aromatic C–H); δ_H(90 MHz; $CDCl_3$) 1.07 (9 H, s, Bu^{t}Si), 1.19 (9 H, s, Bu^{t}C=O), 3.12–3.37 (2 H, m, 2- and 3-H), 3.80 (2 H, br d, *J* 4.8, 4-H), 3.94 (1 H, dd, *J* 6.6 and 12.3, 1-H), 4.24 (1 H, dd, *J* 3.5 and 12.3, 1-H), 7.28–7.55 (6 H, m, *m*- and *p*-C_6H_5) and 7.55–7.79 (4 H, m, *o*-C_6H_5).

(2R,3S)-4-*Hydroxy*-2,3-*epoxybutyl Pivalate* **8**.—A mixture of tetrabutylammonium fluoride (1.0 mol dm^{-3} in THF; 54.1 cm^3, 54.1 mmol) and water (5.4 cm^3) was acidified to pH 4 (universal indicator) by addition of 46% hydrofluoric acid. The mixture was added dropwise to a stirred and ice-cooled solution of the ester **7** (19.2 g, 45.1 mmol) in THF (380 cm^3) at 2–3 °C. Stirring was continued for 2 h at this temperature. The mixture was poured into saturated aqueous ammonium sulfate and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *hydroxy ester* **8** (8.06 g, 95%) as a colourless oil, n_D^{23} 1.4441 (Found: C, 57.3; H, 8.6. $C_9H_{16}O_4$ requires C, 57.43; H, 8.57%); $[\alpha]_D^{24}$ +19.3 (*c* 2.15, MeOH); ν_{max}(film)/cm^{-1} 3460s (OH), 1735s (C=O), 1370m (C–O), 1290s (CO–O), 1160s (CO–O) and 1040s (C–O); δ_H(90 MHz; $CDCl_3$) 1.23 (9 H, s, Bu^t), 2.18–2.68 (1 H, m, OH), 3.06–3.38 (2 H, m, 2- and 3-H), 3.82 (2 H, br d, *J* 5.2, 4-H), 4.19 (1 H, dd, *J* 5.5, 12.3, 1-H) and 4.28 (1 H, dd, *J* 5.5, 12.3, 1-H).

For determination of the enantiomeric purity, the hydroxy ester **8** was converted into the corresponding (*R*)-α-methoxy-α-trifluoromethylphenylacetate (MTPA ester) **9**. A comparison of signal areas due to the protons of MTPA ester **9** by 500 MHz ^{1}H NMR measurement reveals that the (2*R*,3*S*)-isomer seems to exist as a single enantiomer (> 98% e.e.).

3-*Formyl*-2,3-*epoxypropyl Pivalate*, (2R,3R)-*Isomer* **10** *and* (2S,3S)-*Isomer* **10'**.—(1) (2R,3R)-*Isomer*. A solution of dimethyl sulfoxide (6.0 cm^3, 85 mmol) in dry dichloromethane (15 cm^3) was added dropwise to a stirred and cooled solution of oxalyl chloride (8.1 g, 64 mmol) in dry dichloromethane (200 cm^3) at < −70 °C under Ar. After the mixture had been stirred for 1 h at this temperature, a solution of the hydroxy ester **8** (8.00 g, 42.6 mmol) in dry dichloromethane (25 cm^3) was added dropwise to it at < −70 °C. Stirring was continued at this temperature for 1.5 h, after which the mixture was treated with triethylamine (24 cm^3, 0.17 mol) and subsequently warmed to room temperature. The mixture was then poured into saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed successively with brine, saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the formyl ester **10** (6.8 g) as a yellow oil; ν_{max}(film)/cm^{-1} 1735s (C=O), 1370m (C–O), 1290m (CO–O), 1160s (CO–O) and 1040m (C–O); δ_H(90 MHz; $CDCl_3$) 1.22 (9 H, s, Bu^t), 3.37–3.70 (2 H, m, 2- and 3-H), 4.33 (2 H, d, *J* 5.3, 1-H) and 9.50 (1 H, d, *J* 5.3, CHO). This oil was immediately used for the next step without further purification.

(2) (2S,3S)-*Isomer*. In the same manner as described above, the alcohol **8'** (11.2 g, 59.6 mmol) was oxidized to give the formyl ester **10'** (8.1 g). The IR and NMR spectral data were identical with those of **10**. This was immediately used for the next step without further purification.

Ethyl (E)-2-*Methyl*-6-*pivaloyloxy*-4,5-*epoxyhex*-2-*enoate*, (4S,5R)-*Isomer* **11** *and* (4R,5S)-*Isomer* **11'**.—(1) (4S,5R)-*Isomer*. A mixture of the formyl ester **10** (6.8 g, 37 mmol) and α-ethoxycarbonylethylidenephosphorane (27 g, 74 mmol) in dry THF (530 cm^3) was stirred at room temperature under Ar for 15 h after which it was concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *ester* **11** (7.25 g, 63% based on hydroxy ester **8**) as a pale yellow oil, n_D^{23}

1.4609 (Found: C, 62.0; H, 8.2. $C_{14}H_{22}O_5$ requires C, 62.20; H, 8.20%); $[\alpha]_D^{22}$ +34.7 (*c* 1.48, Et_2O); ν_{max}(film)/cm^{-1} 1735s [C=O (Piv)], 1715s [C=O (CO_2Et)], 1650m (C=C), 1285s (CO–O), 1245s (CO–O), 1155s (CO–O), 1035m (C–O) and 750m; δ_H(90 MHz; $CDCl_3$) 1.22 (9 H, s, Bu^t), 1.30 (3 H, t, *J* 7.0, OCH_2CH_3), 2.00 (3 H, d, *J* 1.3, 2-Me), 3.45 (1 H, dt, *J* 6.2 and 3.9, 5-H), 3.75 (1 H, dd, *J* 3.9 and 7.4, 4-H), 4.08 (1 H, dd, *J* 6.2 and 12.3, 6-H), 4.21 (2 H, q, *J* 7.0, OCH_2Me), 4.28 (1 H, dd, *J* 3.9 and 12.3, 6-H) and 6.49 (1 H, dq, *J* 7.4 and 1.3, 3-H). GC analysis revealed the ester to be a mixture of the (*E*)- and (*Z*)-isomers in a ratio of 98:2 (column: HR-20M, 0.25 mm × 50 m at 70–230 °C +3 °C min^{-1}; carrier gas: He, 1.0 kg cm^{-2}): t_R = 55.8 min [(*E*)-isomer (97.7%)], t_R = 57.8 min [(*Z*)-isomer (2.3%)].

(2) (4R,5S)-*Isomer*. In the same manner as described above, the formyl ester **10'** (8.1 g, 44 mmol) was converted into the *ester* **11'** (9.71 g, 60% based on the alcohol **8'**) as a yellow oil n_D^{27} 1.4597 (Found: C, 61.8; H, 8.2. $C_{14}H_{22}O_5$ requires C, 62.20; H, 8.20%); $[\alpha]_D^{26}$ −31.4 (*c* 1.87, Et_2O). The IR and NMR spectral data were identical with those of the ester **11**. GC analysis revealed that the ester was a mixture of the (*E*)- and (*Z*)-isomers in a ratio of 95:5 (under the same conditions as described above): t_R = 56.7 min [(*E*)-isomer (95.3%)], t_R = 58.6 min [(*Z*)-isomer (4.7%)].

Ethyl (E)-5-*Hydroxy*-2,4-*dimethyl*-6-*pivaloyloxyhex*-2-*enoate*, (4R,5S)-*Isomer* **12** *and* (4S,5R)-*Isomer* **12'**.—(1) (4R,5S)-*Isomer*. To a stirred and cooled mixture of water (2.88 g, 160 mmol) and dichloromethane (524 cm^3) was added dropwise trimethylaluminium (1.02 mol dm^{-3} in hexane; 262 cm^3, 267 mmol) at −45 to −40 °C. Stirring was continued at this temperature for 30 min, after which a solution of the ester **11** (7.21 g, 26.7 mmol) in dichloromethane (50 cm^3) was added dropwise to the reaction mixture at −45 to −40 °C. After being stirred for 1 h at this temperature, the reaction mixture was poured into 1 mol dm^{-3} hydrochloric acid and extracted with diethyl ether. The extract was washed successively with brine, saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *hydroxy ester* **12** (6.81 g, 89%) as a pale yellow oil, n_D^{22} 1.4618 (Found: C, 62.45; H, 9.2. $C_{15}H_{26}O_5$ requires C, 62.91; H, 9.15%); $[\alpha]_D^{22}$ +32.7 (*c* 1.12, Et_2O); ν_{max}(film)/cm^{-1} 3520m (OH), 1730s [C=O (Piv)], 1715s [C=O (CO_2Et)], 1650m (C=C), 1285s (CO–O), 1165s (CO–O), 1100m (C–O), 1035m (C–O) and 755m; δ_H(90 MHz; $CDCl_3$) 1.16 (3 H, t, *J* 6.6, OCH_2CH_3), 1.22 (9 H, s, Bu^t), 1.26 (3 H, d, *J* 7.1, 4-Me), 1.86 (3 H, d, *J* 1.3, 2-Me), 2.16 (1 H, br s, OH), 2.68 (1 H, ddq, *J* 7.0, 10.1 and 7.1, 4-H), 3.71 (1 H, ddd, *J* 3.5, 6.2 and 7.0, 5-H), 3.95 (1 H, dd, *J* 6.2 and 11.4, 6-H), 4.15 (1 H, dd, *J* 3.5 and 11.4, 6-H), 4.19 (2 H, q, *J* 6.6, OCH_2Me) and 6.59 (1 H, dq, *J* 10.1 and 1.3, 3-H). GC analysis revealed that the hydroxy ester was 97.0% pure (under the same conditions as described for the ester **11**): t_R = 65.3 min (97.0%), t_R = 66.8 and 67.6 min [unidentified impurities (1.3 and 1.7%)].

(2) (4S,5R)-*Isomer*. In the same manner as described above, the epoxy ester **11'** (9.65 g, 35.7 mmol) was converted into the *hydroxy ester* **12'** (8.84 g, 87%) as a pale yellow oil, n_D^{19} 1.4642 (Found: C, 62.7; H, 9.15. $C_{15}H_{26}O_5$ requires C, 62.91; H, 9.15%); $[\alpha]_D^{22}$ −31.1 (*c* 1.27, Et_2O). The IR and NMR spectral data were identical with those of the hydroxy ester **12**. GC analysis revealed that the hydroxy ester was 98.0% pure (under the same conditions as described for the ester **11**): t_R = 65.6 min (98.0%), t_R = 67.0 and 67.7 min [unidentified impurities (0.8 and 1.3%)].

Ethyl (E)-5-(tert-*Butyldimethylsilyloxy*)-2,4-*dimethyl*-6-*pivaloyloxyhex*-2-*enoate*, (4R,5S)-*Isomer* **13** *and* (4S,5R)-*Isomer* **13'**.—(1) (4R,5S)-*Isomer*. Imidazole (4.83 g, 70.9 mmol) was added to a stirred and ice-cooled solution of the hydroxy ester **12** (6.76 g, 23.6 mmol) and *tert*-butyldimethylsilyl chloride (5.34 g, 35.5 mmol) in dry DMF (70 cm^3). The mixture was stirred at room temperature under Ar for 15 h and then poured into water and extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *ester* **13** (8.60 g, 91%) as a colourless oil, n_D^{22} 1.4544 (Found: C, 63.0; H, 10.0. $C_{21}H_{40}O_5Si$ requires C, 62.96; H, 10.06%); $[\alpha]_D^{22}$ +19.0 (*c* 1.36, Et_2O); ν_{max}(film)/cm^{-1} 1735s [C=O (Piv)], 1715s [C=O (CO_2Et)], 1650m (C=C), 1285s (CO–O), 1255s (Si–CH_3), 1155s (CO–O), 1040m (C–O), 840s (olefinic C–H), 780s and 755m; δ_H(90 MHz; $CDCl_3$) 0.07 (6 H, s, $SiMe_2$), 0.89 (9 H, s, Bu^{t}Si), 1.03 (3 H, d, *J* 7.1, 4-Me), 1.20 (9 H, s, Bu^{t}C=O), 1.28 (3 H, t, *J* 7.1, OCH_2CH_3), 1.84 (3 H, d, *J* 1.3, 2-Me), 2.48–2.92 (1 H, m, 4-H), 3.61–3.85 (1 H, m, 5-H), 3.86 (1 H, dd, *J* 4.4 and 11.4, 6-H), 4.05 (1 H, dd, *J* 6.2 and 11.4, 6-H), 4.18 (2 H, q, *J* 7.1, OCH_2Me) and 6.66 (1 H, dq, *J* 10.1 and 1.3, 3-H).

(2) (4S,5R)-*Isomer*. In the same manner as described above, the hydroxy ester **12'** (8.74 g, 30.6 mmol) was converted into the *ester* **13'** (11.3 g, 93%) as a colourless oil, n_D^{23} 1.4538 (Found: C, 62.7; H, 10.1. $C_{21}H_{40}O_5Si$ requires C, 62.96; H, 10.06%); $[\alpha]_D^{25}$ −18.3 (*c* 1.29, Et_2O). The IR and NMR spectral data were identical with those of the ester **13**.

(E)-5-(tert-*Butyldimethylsilyloxy*)-2,4-*dimethylhex*-2-*ene*-1,6-*diol*, (4R,5S)-*Isomer* **14** *and* (4S,5R)-*Isomer* **14'**.—(1) (4R,5S)-*Isomer*. To a stirred and cooled solution of the ester **13** (8.53 g, 21.3 mmol) in dry diethyl ether (100 cm^3) was added dropwise a solution of diisobutylaluminium hydride (1.0 mol dm^{-3} in hexane; 93.8 cm^3, 93.8 mmol) at −70 to −68 °C under Ar. After being stirred for 1 h at this temperature, the reaction mixture was poured into saturated aqueous potassium sodium tartrate and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *diol* **14** (5.12 g, 88%) as a colourless oil, n_D^{22} 1.4714 (Found: C, 60.9; H, 11.0. $C_{14}H_{30}O_3Si$ requires C, 61.26; H, 11.02%); $[\alpha]_D^{23}$ −3.91 (*c* 2.94, MeOH); ν_{max}(film)/cm^{-1} 3340s, (OH), 1655w (C=C), 1255s (Si–CH_3), 1120s (C–O), 1050s (C–O), 1010s, 835s (olefinic (C–H) and 775s; δ_H(90 MHz; $CDCl_3$) 0.09 (6 H, s, $SiMe_2$), 0.92 (9 H, s, Bu^t), 0.97 (3 H, d, *J* 7.0, 4-H), 1.62 (2 H, br s, OH), 1.69 (3 H, d, *J* 1.3, 2-Me), 2.44–2.92 (1 H, m, 4-H), 3.26–3.61 (3 H, m, 5- and 6-H), 4.00 (2 H, br s, 1-H) and 5.22 (1 H, dq, *J* 9.7 and 1.3, 3-H).

(2) (4S,5R)-*Isomer*. In the same manner as described above, the ester **13'** (11.2 g, 28.0 mmol) was converted into the *diol* **14'** (6.87 g, 90%) as a colourless oil, n_D^{23} 1.4701 (Found: C, 60.8; H, 11.05. $C_{14}H_{30}O_3Si$ requires C, 61.26; H, 11.02%); $[\alpha]_D^{25}$ +3.65 (*c* 2.77, MeOH). The IR and NMR spectral data were identical with those of the diol **14**.

(E)-5-(tert-*Butyldimethylsilyloxy*)-2,4-*dimethylhex*-2-*ene*-1,6-*dial* (4R,5S)-*Isomer* **15** *and* (4S,5R)-*Isomer* **15'**.—(1) (4R,5S)-*Isomer*. A solution of dimethyl sulfoxide (5.23 cm^3, 73.7 mmol) in dry dichloromethane (20 cm^3) was added dropwise to a stirred and cooled solution of oxalyl chloride (7.02 g, 55.3 mmol) in dry dichloromethane (170 cm^3) at < −70 °C under Ar. After the mixture had been stirred for 30 min at this temperature, a solution of the diol **14** (5.05 g, 18.4 mmol) in dry dichloromethane (25 cm^3) was added dropwise to it at < −70 °C. Stirring was continued at this temperature for 1 h, after which triethylamine (20.6 cm^3, 147 mmol) was added to the mixture which was subsequently warmed to room temperature. The mixture was poured into saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the crude *dialdehyde* **15** (5.35 g) as a yellow oil,

ν_{max}(film)/cm^{-1} 2830m (CHO), 2730w (CHO), 1740s [C=O (6-C)], 1695s [C=O (1-C)], 1645m (C=C), 1255s (Si–CH_3), 1125s (C–O), 1030s (C–O), 845s (olefinic C–H) and 785s; δ_H(90 MHz; $CDCl_3$) 0.07 (3 H, s, SiMe), 0.08 (3 H, s, SiMe), 0.94 (9 H, s, Bu^t), 1.12 (3 H, d, *J* 7.0, 4-Me), 1.77 (3 H, d, *J* 1.3, 2-Me), 2.92–3.40 (1 H, m, 4-H), 3.93 (1 H, dd, *J* 1.3 and 4.8, 5-H), 6.38 (1 H, dq, *J* 10.1 and 1.3, 3-H), 9.40 (1 H, s, 1-H), 9.62 (1 H, d, *J* 1.3, 6-H). This was immediately used for the next step without further purification.

(2) (4S,5R)-*Isomer*. In the same manner as described above, the diol **14** (5.00 g, 18.2 mmol) was oxidized to give the crude dialdehyde **15** (5.16 g) as a yellow oil. The IR and NMR spectral data for this were identical with those of the dialdehyde **15**. This was immediately used for the next step without further purification.

Diethyl (2E,4E,8E)-7-(tert-*Butyldimethylsilyloxy*)-4,6-*dimethyldeca*-2,4,8-*triene*-1,10-*dioate*, (6R,7S)-*Isomer* **16** *and* (6S,7R)-*Isomer* **16′**.—(1) (6R,7S)-*Isomer*. A solution of butyllithium (1.66 mol dm^{-3} in hexane; 49.8 cm^3, 82.6 mmol) was added to a stirred and ice-cooled solution of ethyl (diethoxyphosphoryl)acetate (20.4 g, 90.6 mmol) in dry THF (300 cm^3) at 4–7 °C under Ar. After the mixture had been stirred for 30 min at this temperature, a solution of the crude dialdehyde **15** (5.31 g, 19.7 mmol) in dry THF (50 cm^3) was added to it at 3–6 °C, and stirring was continued at this temperature for 14 h. The mixture was poured into saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *diester* **16** (4.57 g, 61% based on diol **14**) as a colourless oil, n_D^{27} 1.4911 (Found: C, 64.2; H, 9.3. $C_{22}H_{38}O_5Si$ requires C, 64.35; H, 9.33%); $[\alpha]_D^{27}$ +22.4 (*c* 1.06, Et_2O); ν_{max}(film)/cm^{-1} 1720s (C=O), 1660m (C=C), 1625m (C=C), 1370m, 1305s, 1270s, (CO–O), 1170s (CO–O), 1120m (C–O), 1035m (C–O), 985m (olefinic C–H) and 835s (olefinic C–H); δ_H(90 MHz; $CDCl_3$) 0.00 (3 H, s, SiMe), 0.03 (3 H, s, SiMe), 0.91 (9 H, s, Bu^t), 1.01 (3 H, d, *J* 6.5, 6-Me), 1.30 (6 H, t, *J* 7.0, 2 × OCH_2CH_3), 1.76 (3 H, d, *J* 0.9, 4-Me), 2.44–2.96 (1 H, m, 6-H), 3.82–4.14 (1 H, m, 7-H), 4.20 (2 H, q, *J* 7.0, OCH_2Me), 4.21 (2 H, q, *J* 7.0, OCH_2Me), 5.72 (1 H, dq, *J* 10.6 and 0.9, 5-H), 5.80 (1 H, d, *J* 15.4, 2-H), 5.95 (1 H, dd, *J* 1.3 and 15.4, 9-H), 6.89 (1 H, dd, *J* 4.8 and 15.4, 8-H) and 7.28 (1 H, d, *J* 15.4, 3-H).

(2) (6S,7R)-*Isomer*. In the same manner as described above, the crude dialdehyde **15′** (5.08 g, 18.8 mmol) was converted into the *diester* **16′** (4.62 g, 62% based on diol **14′**) as a colourless oil, n_D^{24} 1.4919 (Found: C, 64.3; H, 9.3. $C_{22}H_{38}O_5Si$ requires C, 64.35; H, 9.33%); $[\alpha]_D^{26}$ −22.0 (*c* 1.28, Et_2O). The IR and NMR spectral data were identical with those of the diester **16**.

(2E,4E,8E)-7-(tert-*Butyldimethylsilyloxy*)-4,6-*dimethyldeca*-2,4,8-*triene*-1,10-*diol* (6R,7S)-*Isomer* **17** *and* (6S,7R)-*Isomer* **17′**.—(1) (6R,7S)-*Isomer*. To a stirred and cooled solution of the diester **16** (4.13 g, 10.1 mmol) in dry diethyl ether (50 cm^3) was added dropwise a solution of diisobutylaluminium hydride (1.0 mol dm^{-3} in hexane; 50.4 cm^3, 50.4 mmol) at −74 to −70 °C under Ar. After being stirred for 2.5 h at this temperature, the reaction mixture was poured into saturated aqueous potassium sodium tartrate and extracted with ethyl acetate. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *diol* **17** (3.22 g, 98%) as a colourless oil, n_D^{20} 1.5001 (Found: C, 65.7; H, 10.0. $C_{18}H_{34}O_3Si$ requires C, 66.21; H, 10.50%); $[\alpha]_D^{23}$ −12.7 (*c* 1.07, MeOH); ν_{max}(film)/cm^{-1} 3330s (OH), 3040w (olefinic C–H), 1645w (C=C), 1250s (Si–CH_3), 1090s (C–O), 1060s, 1025s, 1000s, 965s (olefinic C–H), 835s (olefinic C–H) and 775s; δ_H(90 MHz; $CDCl_3$) 0.00 (3 H, s, SiMe), 0.03 (3 H, s, SiMe), 0.90 (9 H, s, Bu^t), 0.97 (3 H, d, *J* 6.6, 6-Me), 1.44, (2 H, br s, 2 × OH), 1.74 (3 H, d, *J* 0.9, 4-Me), 2.35–2.81 (1 H, m, 6-H), 3.83–4.12 (1 H, m, 7-H), 4.11 (2 H, br d, *J* 3.9, 10-H), 4.20 (2 H, br d, *J* 6.2, 1-H), 5.33 (1 H, dq, *J* 10.1 and 0.9, 5-H), 5.45–5.97 (3 H, m, 2-, 8- and 9-H) and 6.24 (1 H, br d, *J* 15.4, 3-H).

(2) (6S,7R)-*Isomer*. In the same manner as described above, the diester **16′** (4.88 g, 11.9 mmol) was converted into the *diol* **17′** (3.75 g, 97%) as a colourless oil, n_D^{19} 1.5010 (Found: C, 65.8; H, 10.5. $C_{18}H_{34}O_3Si$ requires C, 66.21; H, 10.50%); $[\alpha]_D^{23}$ +12.8 (*c* 1.44, MeOH). The IR and NMR spectral data were identical with those of the diol **17**.

(2E,4E,8E)-7-(tert-*Butyldimethylsilyloxy*)-4,6-*dimethyldeca*-2,4,8-*triene*, (6R,7S)-*Isomer* **18** *and* (6S,7R)-*Isomer* **18′**.—(1) (6R,7S)-*Isomer*. To a stirred and cooled solution of the diol **17** (1.63 g, 5.00 mmol) in dry THF (50 cm^3) was added dropwise a solution of butyllithium (1.63 mol dm^{-3} in hexane; 7.36 cm^3, 12.0 mmol) at −70 to −65 °C under Ar. After the mixture had been stirred for 30 min at this temperature, a solution of methanesulfonic anhydride (2.61 g, 15.0 mmol) in dry THF (10 cm^3) was added dropwise to it at −70 to −65 °C. Stirring was continued for 1.5 h at this temperature, after which Super-Hydride® (lithium triethylborohydride; 1.0 mol dm^{-3} in THF; 45.0 cm^3, 45.0 mmol) was added dropwise to the mixture at −71 to −68 °C. Stirring was continued for 1 h at this temperature, after which the mixture was allowed to rise to room temperature. It was then poured into saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the crude triene **18** (1.08 g) as a pale yellow oil, ν_{max}(film)/cm^{-1} 3040w (olefinic C–H), 1670w (C=C), 1630w (C=C), 1250s (Si–CH_3), 1090s (C–O), 1050s, 965s (olefinic C–H), 840s (olefinic C–H) and 775s; δ_H(90 MHz; $CDCl_3$) −0.01 (3 H, s, SiMe), 0.02 (3 H, s, SiMe), 0.89 (9 H, s, Bu^t), 0.94 (3 H, d, *J* 7.0, 6-Me), 1.66 (3 H, d, *J* 5.7, 10-H), 1.70 (3 H, d, *J* 1.3, 4-Me), 1.75 (3 H, d, *J* 6.2, 1-H), 2.33–2.77 (1 H, m, 6-H), 3.73–3.95 (1 H, m, 7-H), 5.18 (1 H, dq, *J* 9.7 and 1.3, 5-H), 5.32–5.78 (3 H, m, 2-, 8- and 9-H) and 6.05 (1 H, br d, *J* 14.9, 3-H). It seemed that this was a mixture of inseparable diastereoisomeric impurities; GC analysis showed that the triene **18** was 79.3% pure (under the same conditions as described for the ester **11**): t_R = 30.6 min (79.3%). This was employed for the next step without further purification.

(2) (6S,7R)-*Isomer*. In the same manner as described above, the diol **17′** (1.04 g, 3.19 mmol) was converted into the crude triene **18′** (727 mg) as a pale yellow oil. The IR and NMR spectral data were identical with those of the triene **18**. GC analysis showed that the triene **18′** was 92.0% pure (under the same conditions as described for the ester **11**): t_R = 30.7 min (92.0%). This was employed for the next step without further purification.

(2E,6E,8E)-5,7-*Dimethyldeca*-2,6,8-*trien*-4-*ol* (4S,5R)-*Isomer* **19** *and* (4R,5S)-*Isomer* (*in an Impure State*).—(1) (4S,5R)-*Isomer*. To a stirred and ice-cooled solution of the crude triene **18** (1.07 g, 3.64 mmol) in THF (90 cm^3) was added a solution of tetrabutylammonium fluoride (1.0 mol dm^{-3} in THF; 18.2 cm^3, 18.2 mmol) at < 10 °C. After being stirred for 2 h at room temperature, the mixture was poured into water and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 and purified by preparative TLC ($AgNO_3$-coated SiO_2) to give the crude trienol **19** (448 mg, 50% based on the diol **17**) as a pale yellow oil. GC analysis showed that the trienol was 94.0% pure (under the same conditions as described for ester **11**): t_R = 40.0 min (94.0%). The

physical and spectral data for the trienol **19** are described below for a pure sample.

(2) (4R,5S)-*Isomers*. In the same manner as described above, the crude triene **18'** (708 mg, 2.41 mmol) was converted into the crude trienol **19'** (329 mg, 59% based on the diol **17'**) as a pale yellow oil. GC analysis showed that the trienol was 98.8% pure (under the same conditions as described for the ester **11**): t_R = 39.9 min (98.8%). The physical and spectral data for the trienol **19'** are described below for a pure sample.

Purification of Trienol **19** *and* **19'** *via the corresponding DNB Ester* **20** *and* **20'**.—(1'E,3E,5E)-2,4-*Dimethyl*-1-(*prop*-1'-*enyl*)-*hepta*-3,5-*dienyl* 3,5-*Dinitrobenzoate* (1S,2R)-*Isomer* **20** *and* (1R,2S)-*Isomer* **20'**.—(1) (1S,2R)-*Isomer*. 3.5-Dinitrobenzoyl chloride (1.11 g, 4.83 mmol) was added to a stirred and ice-cooled solution of the trienol **19** (435 mg, 2.42 mmol) in dry pyridine (13 cm^3) at 0–5 °C under Ar. After being stirred for 1 h at this temperature, the mixture was poured into water and extracted with diethyl ether. The extract was washed successively with 1 mol dm^{-3} hydrochloric acid (×3), brine, saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the crude DNB ester **20** (962 mg, 98%). This was repeatedly recrystallized from hexane–diethyl ether to give the pure *DNB ester* **20** (581 mg, 60%) as yellow needles, m.p. 106–107 °C (Found: C, 60.75; H, 5.9; N, 7.45. $C_{19}H_{22}N_2O_6$ requires C, 60.95; H, 5.92; N, 7.48%); $[\alpha]_D^{26}$ −20.1 (*c* 1.41, Et_2O); ν_{max}(film)/cm^{-1} 3120m (aromatic C–H), 3050w (olefinic C–H), 1720s (C=O), 1675w (C=C), 1630m (C=C), 1550s (N=O), 1455m, 1345s (N=O), 1275s (CO–O), 1170s (CO-O), 1075m (C–O), 970s (olefinic C–H), 950s, 925s, 910s, 835m (olefinic C–H), 735s and 725s; δ_H(90 MHz; $CDCl_3$) 1.06 (3 H, d, *J* 6.6, 2-Me), 1.62–1.93 (9 H, m, 3'- and 7-H and 4-Me), 2.82–3.23 (1 H, m, 2-H), 5.20 (1 H, dq, *J* 10.1 and 1.3, 3-H), 5.32–5.97 (4 H, m, 1-, 1'-, 2'- and 6-H), 6.10 (1 H, dq, *J* 15.8 and 0.9, 5-H), 9.13 (2 H, d, *J* 1.8, *o*-arom) and 9.19 (1 H, t, *J* 1.8, *p*-arom). HPLC analysis showed that the DNB ester was 97.6% e.e. [column, Daicel Chiralcel OJ® (0.46 cm × 25 cm); solvent, hexane–propan-2-ol (10:1), 0.5 cm^3 min^{-1}; detected at 254 nm] t_R = 19.5 min [(1*R*,2*S*)-isomer (1.21%)] and t_R = 24.9 min [(1*S*,2*R*)-isomer (98.6%)].

(2) (1R,2S)-*Isomer*. In the same manner as described above, the trienol **19'** (329 mg, 1.83 mmol) was converted into the pure *DNB ester* **20'** (509 mg, 69%) as yellow needles, m.p. 105–106 °C (Found: C, 60.9; H, 6.0; N, 7.4. $C_{19}H_{22}N_2O_6$ requires C, 60.95; H, 5.92; N, 7.48%); $[\alpha]_D^{23}$ +20.9 (*c* 1.14, Et_2O). The IR and NMR spectral data were identical with those of the DNB ester **20**. HPLC analysis showed that the DNB ester was *ca.* 100% e.e. (under the same conditions as described above) t_R = 19.1 min [(1*R*,2*S*)-isomer (99.6%)]. The peak of (1*S*,2*R*)-isomer was not detected.

(2E,6E,8E)-5,7-*Dimethyldeca*-2,6,8-*trien*-4-*ol*, (4S,5R)-*Isomer* **19** *and* (4R,5S)-*Isomer* **19'** (*in a Pure State*).—(1) (4S,5R)-*Isomer*. To a stirred and ice-cooled solution of the DNB ester **20** (328 mg, 0.808 mmol) in THF (5 cm^3) and methanol (10 cm^3) was added potassium carbonate (332 mg, 2.40 mmol). Stirring was continued for 40 min at 0–5 °C after which the mixture was poured into saturated aqueous ammonium chloride and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the pure *trienol* **19** (146 mg, quant.) as a pale yellow oil, n_D^{25} 1.5002 (Found: C, 79.6; H, 11.1. $C_{12}H_{20}O$ requires C, 79.94; H, 11.18%); $[\alpha]_D^{28}$ −12.1 (*c* 1.10, Et_2O); ν_{max}(film)/cm^{-1} 3380m (OH), 3030w (olefinic C–H), 1665w (C=C), 1625w (C=C), 1445m, 1375m, 1005m (C–O) and 965s (olefinic C–H); δ_H(90 MHz; $CDCl_3$) 0.98 (3 H, d, *J* 6.5, 5-Me), 1.51 (1 H, s, OH), 1.70 (3 H, d, *J* 4.8, 1-H), 1.76 (3 H, d, *J* 1.3, 7-Me), 1.76 (3 H, d, *J* 7.0, 10-H), 2.44–2.93 (1 H, m, 5-H), 3.92 (1 H, dd, *J* 5.7 and 6.2, 4-H), 5.19 (1 H, br d, *J* 9.7, 6-H), 5.28–5.87 (3 H, m, 2-, 3- and 9-H) and 6.09 (1 H, br d, *J* 15.8, 8-H). GC analysis showed that the trienol **19** was 98.7% pure (under the same conditions as described for the ester **11**): t_R = 40.1 min (98.7%).

(2) (4R,5S)-*Isomer*. In the same manner as described above, the DNB ester **20'** (328 mg, 0.808 mmol) was converted into the pure *trienol* **19'** (146 mg, quant.) as a pale yellow oil, n_D^{25} 1.5008 (Found: C, 79.5; H, 11.05. $C_{12}H_{20}O$ requires C, 79.94; H, 11.18%); $[\alpha]_D^{24}$ +12.8 (*c* 1.00, Et_2O). The IR and NMR spectral data were identical with those of the trienol **19**. GC analysis showed that the trienol **19'** was *ca.* 100% pure (under the same conditions as described for the ester **11**): t_R = 40.0 min (single peak).

(2E,6E,8E)-5,7-*Dimethyldeca*-2,6,8-*trien*-4-*one*, (R)-*Isomer* **1** *and* (S)-*Isomer* **1'**.—(1) (R)-*Isomer*. To a stirred and cooled solution of oxalyl chloride (0.119 cm^3, 1.36 mmol) in dry dichloromethane (6 cm^3) was added dropwise a solution of dimethyl sulfoxide (0.164 cm^3, 2.31 mmol) in dry dichloromethane (0.6 cm^3) at < −70 °C under Ar. After the mixture had been stirred for 1 h at this temperature, a solution of the trienol **19** (122 mg, 0.678 mmol) in dry dichloromethane (2.5 cm^3) was added dropwise to it at < −70 °C. Stirring was continued for 1 h at this temperature, after which triethylamine (0.607 cm^3, 4.35 mmol) was added to the mixture which was subsequently warmed to room temperature. The mixture was then poured into water and extracted with diethyl ether. The extract was washed successively with saturated aqueous ammonium chloride and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *trienone* **1** (111 mg, 92%) as a colourless oil, n_D^{27} 1.5068 (Found: C, 80.4; H, 10.25%. M^+, 178.1375. $C_{12}H_{18}O$ requires C, 80.85; H, 10.18%. *M*, 178.1357); $[\alpha]_D^{26}$ −466 (*c* 1.16, pentane); ν_{max}(film)/cm^{-1} 3040w (olefinic C–H), 2990m, 2940m, 2880w, 1695s (C=O), 1670s (C=C), 1630s (C=C), 1445s, 1390m, 1375m, 1325m, 1290m, 1215w, 1185m, 1140m, 1100w, 1040m, 1010w, 965s (olefinic C–H), 930m, 870w, 835w and 785m; δ_H(300 MHz; $CDCl_3$) 1.17 (3 H, d, *J* 6.9, 5-Me), 1.77 (3 H, dd, *J* 1.4 and 6.6, 10-H), 1.81 (3 H, d, *J* 1.1, 7-Me), 1.86 (3 H, dd, *J* 1.7 and 6.9, 1-H), 3.60 (1 H, dq, *J* 9.7 and 6.9, 5-H), 5.25 (1 H, br d, *J* 9.7, 6-H), 5.67 (1 H, dq, *J* 15.5 and 6.6, 9-H), 6.07 (1 H, dq, *J* 15.5 and 1.4, 8-H), 6.16 (1 H, dq, *J* 15.4 and 1.7, 3-H) and 6.89 (1 H, dq, *J* 15.4 and 6.9, 2-H); δ_C(75 MHz; $CDCl_3$) 12.9 (5-Me), 16.6 (7-Me), 18.2 (1- and 10-C), 44.6 (5-C), 124.0, 128.5, 129.8 (2-C), 135.5, 142.5 (3-C), 200.3 (4-C); *m/z* (GC-MS) 178 (M^+, 8), 161 (1), 109 (100), 91 (5), 81 (14), 79 (8), 77 (8), 69 (68), 67 (44), 55 (13), 53 (5), 43 (13), 41 (39) and 39 (17). The IR, ^1H NMR and GC-MS spectral data were identical with those reported.[2,3] GC analyses showed that the trienone was 98.4% pure (under the same conditions as described for the ester **11**): t_R = 38.4 min (98.4%) and 96.6% e.e. (column: DMPBCD-TH, 0.25 mm × 50 m at 70–140 °C +0.7 °C min^{-1}; carrier gas: He, 1.0 kg cm^{-2}): t_R = 92.8 min [(*R*)-isomer (98.3%)], t_R = 94.3 min [(*S*)-isomer (1.7%)] (resolution: 1.9).

(2) (S)-*Isomer*. In the same manner as described above, the trienol **19'** (140 mg, 0.778 mmol) was oxidized to the *trienone* **1'** (123 mg, 89%), a colourless oil, n_D^{18} 1.5106 (Found: C, 81.0; H, 10.1. $C_{12}H_{18}O$ requires C, 80.85; H, 10.18%); $[\alpha]_D^{23}$ +473 (*c* 1.21, pentane). The IR, NMR and GC-MS spectral data were identical with those of the trienone **1**. GC analysis showed that the trienone was *ca.* 100% pure (under the same conditions as described for the ester **11**): t_R = 38.1 min (single peak) and 99.0% e.e. (under the same conditions as described above): t_R = 92.9 min [(*R*)-isomer (0.5%)], t_R = 94.3 min [(*S*)-isomer (99.5%)] (resolution: 2.2).

(2S,3R)-1-(tert-*Butyldimethylsilyloxy*)-4-(1′-*ethoxyethoxy*)-2,3-*epoxybutane* **21**.—To a stirred and ice-cooled solution of the alcohol **6** (28.5 g, 83.3 mmol) and toluene-*p*-sulfonic acid monohydrate (0.57 g, 3.0 mmol) in diethyl ether (150 cm^3) was added dropwise a solution of ethyl vinyl ether (12.0 g, 167 mmol) in diethyl ether (30 cm^3) at 2–4 °C. After being stirred for 30 min at this temperature, the mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *ether* **21** (31.9 g, 93%) as a colourless oil, n_D^{20} 1.5241 (Found: C, 69.5; H, 8.3. $C_{24}H_{34}O_4Si$ requires C, 69.53; H, 8.27%); $[\alpha]_D^{24}$ −3.61 (*c* 1.48, Et_2O); ν_{max}(film)/cm^{-1} 3090m (aromatic C–H), 3070m (aromatic C–H), 1655w (aromatic C–H), 1590w (aromatic C–C), 1430s (Si–C), 1390m (C–O), 1135s (C–O), 1115s (Si–O), 745m (aromatic C–H) and 710s (aromatic C–H); δ_H(90 MHz; $CDCl_3$) 1.07 (9 H, s, Bu^t), 1.14 (3 H, t, *J* 7.1, OCH_2CH_3 of EE group), 1.26 and 1.27 (total 3 H, 2 × d, *J* 5.3, 2′-H), 3.08–3.76 (6 H, m, 2-, 3- and 4-H and OCH_2Me of EE group), 3.79 (2 H, d, *J* 4.8, 1-H), 4.69 (1 H, q, *J* 5.3, 1′-H), 7.30–7.51 (6 H, m, *m*- and *p*-C_6H_5) and 7.52–7.81 (4 H, m, *o*-C_6H_5).

(2S,3R)-4-(1′-*Ethoxyethoxy*)-2,3-*epoxybutan*-1-*ol* **22**.—To a stirred and ice-cooled solution of the ether **21** (31.8 g, 76.8 mmol) in THF (277 cm^3) was added dropwise a solution of tetrabutylammonium fluoride (1.0 mol dm^{-3} in THF; 92.2 cm^3, 92.2 mmol) at 3–5 °C. Stirring was continued at this temperature for 1 h after which the mixture was poured into saturated aqueous ammonium sulfate. The aqueous mixture was neutralized to pH 9 (universal indicator) by addition of ammonia (28% solution in water) and extracted with ethyl acetate. The extract was washed with saturated aqueous ammonium sulfate (neutralized by ammonia), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the crude alcohol **22** (13.6 g) as a pale yellow oil, ν_{max}(film)/cm^{-1} 3450m (OH), 1385m (C–O), 1135s (C–O) and 1050s (C–O); δ_H(90 MHz; $CDCl_3$) 1.21 (3 H, t, *J* 7.0, OCH_2CH_3 of EE group), 1.34 (3 H, d, *J* 5.3, 2′-H), 2.06–2.53 (1 H, m, OH), 3.12–3.38 (2 H, m, 2- and 3-H), 3.38–4.01 (6 H, m, 1- and 4-H and OCH_2Me of EE group) and 4.77 and 4.80 (total 1 H, 2 × q, *J* 5.3, 1′-H). This compound was employed for the next step without further purification.

(2R,3S)-4-(1′-*Ethoxyethoxy*)-2,3-*epoxybutyl Pivalate* **23**.—To a stirred and ice-cooled solution of the crude alcohol **22** (13.5 g, 76.7 mmol) and pyridine (37.2 cm^3, 460 mmol) in dry dichloromethane (370 cm^3) was added dropwise pivaloyl chloride (11.1 g, 92.0 mmol) at 5–10 °C under Ar. After being stirred for 11 h at room temperature, the mixture was poured into water and extracted with diethyl ether. The extract was washed successively with saturated aqueous sodium hydrogen carbonate and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *ester* **23** (17.2 g, 87% based on the ether **21**) as a colourless oil, n_D^{23} 1.4323 (Found: C, 59.75; H, 9.3. $C_{13}H_{24}O_5$ requires C, 59.98; H, 9.29%); $[\alpha]_D^{24}$ −6.47 (*c* 1.33, Et_2O); ν_{max}(film)/cm^{-1} 1735s (C=O), 1485m, 1385m (C–O), 1285m (CO–O), 1155s (CO–O), 1135s (C–O) and 1060m (C–O); δ_H(90 MHz; $CDCl_3$) 1.21 [3 H, t, *J* 7.0, 1′-(OCH_2CH_3)], 1.23 (9 H, s, Bu^t), 1.33 (3 H, d, *J* 5.6, 2′-H), 3.12–3.38 (2 H, m, 2- and 3-H), 3.38–3.79 (4 H, m, 4-H and OCH_2Me of EE group), 4.06 (1 H, dd, *J* 6.6 and 12.3, 1-H), 4.35 (1 H, dd, *J* 3.9 and 12.3, 1-H) and 4.77 (2 H, q, *J* 5.6, 1′-H).

(2S,3R)-4-*Hydroxy*-2,3-*epoxybutyl Pivalate* **8′**.—Pyridinium toluene-*p*-sulfonate (0.34 g, 1.4 mmol) was added to a solution of the ester **23** (17.1 g, 65.8 mmol) in methanol (340 cm^3) and the mixture was stirred for 3 h at room temperature. Sodium hydrogen carbonate (powder; 5.0 g) was added to the reaction mixture. After being stirred for a few minutes, the mixture was filtered through Florisil® and the filtrate was concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *hydroxy ester* **8′** (11.4 g, 92%) as a colourless oil, n_D^{26} 1.4442 (Found: C, 57.3; H, 8.6. $C_9H_{16}O_4$ requires C, 57.43; H, 8.57%); $[\alpha]_D^{27}$ −18.7 (*c* 2.06, MeOH). The IR and NMR spectral data were identical with those of the hydroxy ester **8**.

For determination of the enantiomeric purity, the hydroxy ester **8′** was converted into the corresponding (*R*)-α-methoxy-α-trifluoromethylphenylacetate (MTPA ester) **9′**. A comparison of the signal areas due to the protons of (*R*)-MTPA ester **9′** by 500 MHz ^1H NMR measurement showed that the (2*S*,3*R*)-isomer was 94% e.e.

Acknowledgements

We thank Drs. Ezra Dunkelblum and Zvi Mendel (Institute of Plant Protection, Volcani Center, Israel) for GC comparison and bioassay of compounds **1** and **1′**. Our thanks are also due to Ms. Y. Naito (the University of Tokyo) for elemental analyses. This work was financially supported by T. Hasegawa Co., Ltd. (Kawasaki, Japan).

References

1 Part 165, K. Mori, T. Furuuchi and H. Kiyota, *Liebigs Ann. Chem.*, in press.
2 E. Dunkelblum, Z. Mendel, F. Assael, M. Harel, L. Kerhoas and J. Einhorn, *Tetrahedron Lett.*, 1993, **34**, 2805.
3 L. Zegelman, A. Hassner, Z. Mendel and E. Dunkelblum, *Tetrahedron Lett.*, 1993, **34**, 5641.
4 K. Mori and S. Harashima, *Liebigs Ann. Chem.*, 1993, 391.
5 K. Mori and S. Harashima, *Liebigs Ann. Chem.*, 1993, 993.
6 Preliminary communication: K. Mori, *Pure Appl. Chem.*, in press.
7 J.-L. Brevet and K. Mori, *Synthesis*, 1992, 1007.
8 K. Mori, *Bull. Soc. Chim. Belg.*, 1992, **101**, 393.
9 M. Miyashita, M. Hoshino and A. Yoshikoshi, *J. Org. Chem.*, 1991, **56**, 6483.

Paper 4/03138E
Received 25*th May* 1994
Accepted 14*th June* 1994