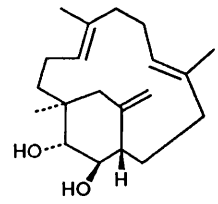
Synthesis of Secotrinervitanes, Unique Bicyclic Diterpenes from Termites

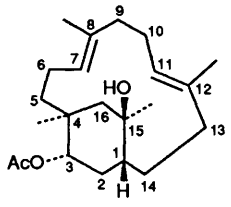
Toshifumi Hirukawa, Toshiyuki Shudo and Tadahiro Kato*
Department of Chemistry, Faculty of Science, Science University of Tokyo, 1–3, Kagurazaka, Shinjuku-ku, Tokyo 162, Japan

The synthesis of (±)-3α-acetoxy-7,16-secotrinervita-7,11-dien-15β-ol **2**, a defence substance of the termite *Nastitermes princeps*, is fully described. The key step is an intramolecular Dieckmann condensation of substrates **4** and **17**, in which an unusually low acidity of the methine proton alpha to the ester carbonyl is observed.

The defence chemicals of termite soldiers are a rich source of natural products.[1] Unusual bioactive terpenoids have been isolated, and their roles clarified in termite society, by several groups.[2] Of these terpenoids bicyclic diterpenes such as **1** and **2** possess the interesting cembrene skeleton. Compounds **1** and **2**, known as secotrinervitanes, are proposed intermediates in the biosynthesis of other polycyclic diterpenes such as trinervitanes and kempanes from cembrene.[2]



1



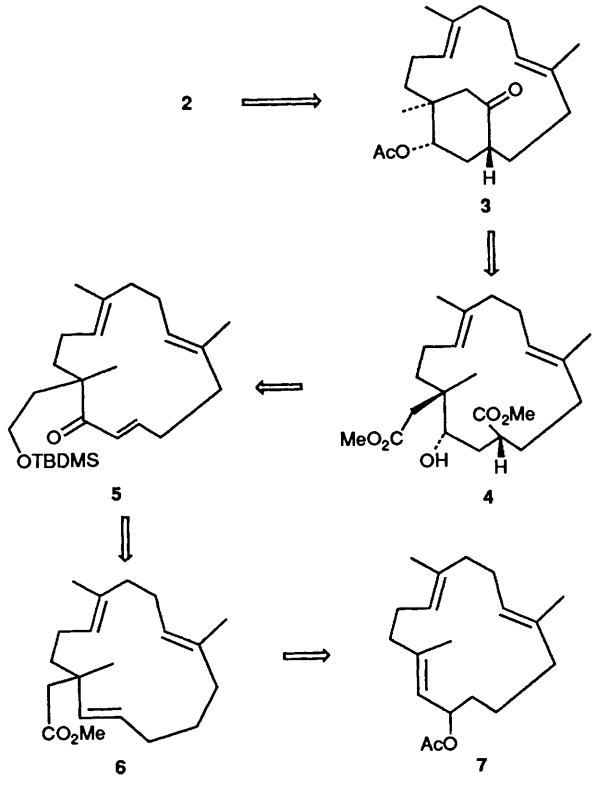
2

Because of these interesting features, the synthesis of these compounds has attracted interest.[3] We have achieved the total synthesis of (±)-**1** by a biomimetic route involving the stereospecific cyclization of a cembrene derivative.[4] In a preliminary publication we have also reported the synthesis of (±)-**2**.[5] We now describe details of the latter synthesis and note some unusual features of the secotrinervitane skeleton.

Results and Discussion

Our retro-synthesis is shown in Scheme 1. Despite a lack of information on the chemistry of both the macrocyclic ring **5** and the bicyclo[10.2.2] system **3** it was hoped that the acetoxy ketone **3** would be a convenient intermediate. Even if the desired stereoisomer was not obtained prior to the conversion into precursor **3**, the transformation of the stereochemistry at C-1 and C-3 in the cyclohexane portion could be expected to be carried out.† The proposed starting material was the allylic acetate **7** which we have previously synthesized by a method convenient for large-scale preparation.[6] Conversion into diester **4** would give an intermediate with the essential 14-membered ring and the requisite functionality for Dieckmann cyclization to form the cyclohexane ring.

The allyl acetate **7** was prepared and subjected to Ireland-type Claisen rearrangement.[7] Treatment of the lithium enolate of **7** with *tert*-butylchlorodimethylsilane (TBDMSCl) in tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) at −78 °C gave a ketene silyl acetal, which was smoothly rearranged into the desired γ,δ-unsaturated carboxylic acid by gradually warming to room temperature over a period of 15 h

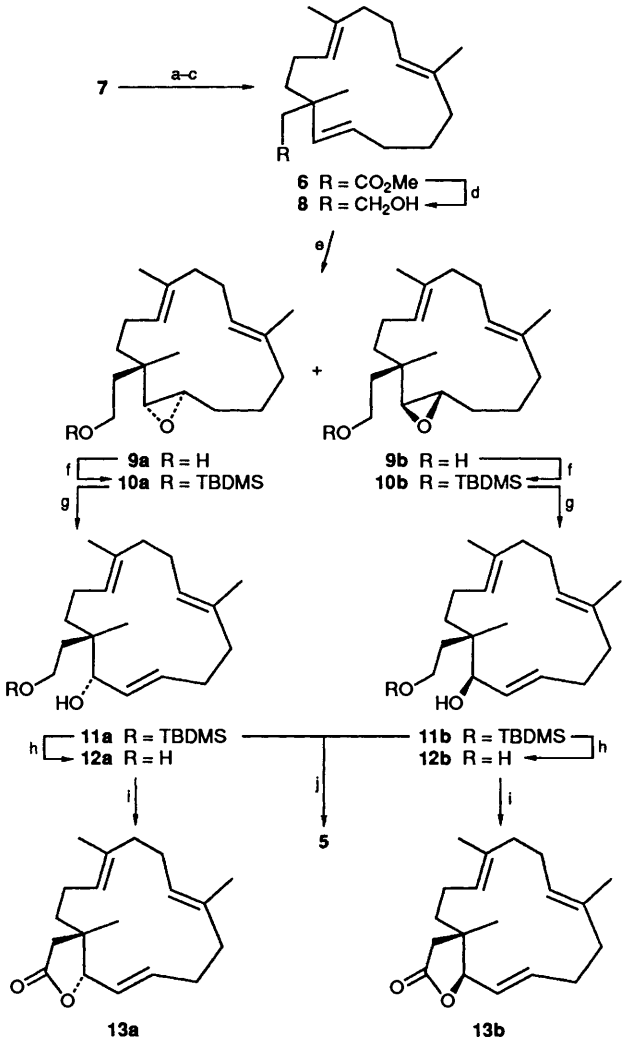


Scheme 1

(Scheme 2). Desilylation with 2 mol dm^{-3} HCl, followed by esterification with diazomethane, gave methyl ester **6** in 55% yield from **7**. The *trans* (*E*) configuration of the newly formed double bond was determined by the coupling constant ($J_{2,3}$ 15.6 Hz) observed in its ^{1}H NMR spectrum. The methyl ester **6** was reduced to the alcohol **8** by lithium aluminium hydride.

Regioselective oxidation of the disubstituted double bond of triene **8** occurred only when Sharpless oxidation, using vanadyl acetylacetonate and *tert*-butyl hydroperoxide, was employed in refluxing benzene.[8] The desired epoxide was produced in 72% yield as a ~1:1 mixture of diastereoisomers, accompanied by 11% of recovered alcohol **8**. At room temperature, the formation of a complete mixture of oxidized products was observed. The resultant mixture of desired epoxides was separated by column chromatography on silica gel to yield epoxides **9a** and **9b**. The stereochemistry was not determined at this stage. The hydroxy group of each epoxide was protected as the TBDMS ether (**10a** and **10b**) in high yield by conventional procedure. Ring opening of each epoxide was achieved by treatment with lithium diisopropylamide (LDA) in refluxing THF. The yield of the alcohol **11a** from epoxide **10a** was 89% and that of **11b** from **10b**

† Numbering is based on that of the secotrinervitane skeleton; see ref. 2(*b*).



Scheme 2 *Reagents and conditions:* (a) LDA, HMPA, THF, −80 to 0 °C; TBDMSCl, −80 °C to room temp.; (b) HCl; (c) CH_2N_2; (d) $LiAlH_4$, Et_2O; (e) Bu^{t}OOH, $VO(acac)_2$, benzene, reflux; (f) TBDMSCl, imidazole, DMF; (g) LDA, THF, reflux; (h) AcOH, aq. THF; (i) CrO_3, H_2SO_4, acetone, −15 °C; (j) $CrO_3(pyr)_2$.

was 88%. The newly formed double bond in both isomers was presumed to be *trans* (*E*) by the coupling patterns in the respective ^{1}H NMR spectra. The conversion of both isomers into enone **5** was achieved by Collins oxidation.

In order to determine the relative stereochemistry of the secotrinervitane C-3 position in alcohols **11a** and **11b**, both were converted into the conformationally fixed γ-lactones (**13a** and **13b**) by deprotection of the TBDMS ether groups with acetic acid followed by oxidation with Jones' reagent in 38% yield of **13a** from **11a** and in 77% yield of **13b** from **11b**. In the NMR spectra, a positive NOE (3%) was detected between 3-H (δ 4.56) and 4-Me (δ 1.17) in compound **13a** while no NOE was observed between these protons in the isomer **13b**. These facts clearly demonstrate the *cis* and *trans* relationship between 3-H and 4-Me in compounds **13a** and **13b**, respectively.

The next step was the construction of an appropriate intermediate **4**. Treatment of enone **5** with diethylaluminium cyanide in toluene at 0 °C gave the cyanide **14** in 82% yield as a ~1:1 mixture of diastereoisomers.[9] The mixture was separated by HPLC using a silica gel column. After deprotection of the TBDMS ether groups of nitriles **14a** and **14b**, the resultant primary alcohols were converted into the corresponding methyl esters **15a** and **15b** with Jones' reagent at −5 °C, followed by methylation with diazomethane without epimerization at the C-1 position (Scheme 3).

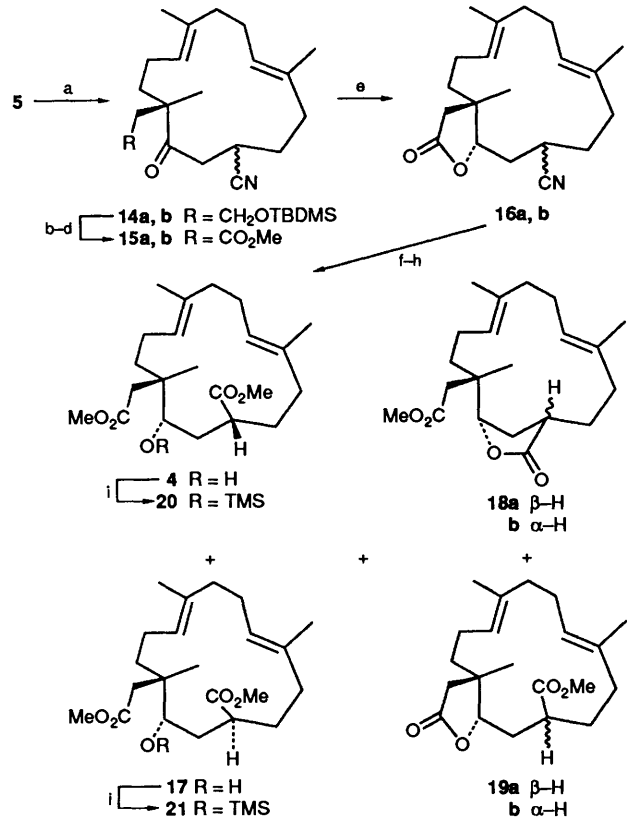
To our surprise, hydride reduction of the carbonyl group of both isomers **15a** and **15b** using lithium tri(*tert*-butoxy)-aluminium hydride and sodium borohydride proceeded with high stereoselectivity to produce the cyano lactones **16a** and **16b**, each as a single isomer in high yield. The stereochemistry of the resulting γ-lactone system of both products **16a** and **16b** was deduced from the positive NOE (1%) between 3-H (δ 4.37) and 4-Me (δ 1.24) in compound **16b** and the similarity of the chemical shifts of these protons showed there to be a 3,4-*cis* configuration. This deduction was borne out subsequently by their interconversion at a later stage.

Each of the cyanides **16a** and **16b** was hydrolysed with potassium hydroxide in refluxing aqueous ethanol. The resulting alkaline solution was carefully acidified with 0.1 mol dm^{-3} oxalic acid, and then methylated with diazomethane. Both cyanides afforded the same mixture of esters **4** and **17** and four kinds of γ-lactones (**18a**, **b** and **19a**, **b**) in approximate proportions **4**:**17**:**18** + **19**, 2:2:1. Both of the hydroxy diesters **4** and **17** were unstable in acidic or basic medium and slowly cyclized even in neutral medium to form the γ-lactones. The reaction mixtures were therefore treated with chlorotrimethylsilane (TMSCl) in weakly basic conditions to convert them into the corresponding TMS ether (**20** and **21**) in high yield. The TMS ethers were separated from the γ-lactones by simple column chromatography on silica gel. By independent treatment with potassium hydroxide under the same conditions, each of the hydroxy esters **4** and **17** and γ-lactones (**18** and **19**) give a mixture of **4**, **17** and γ-lactones in the same proportion. This operation provided silyl ethers **20** and **21** in greater than 90% total yield after several cycles. Since the exact stereochemistry at the C-1 position of hydroxy diesters **4** and **17** remained unclarified at this stage, each isomer was subjected to a separate intramolecular Dieckmann condensation.

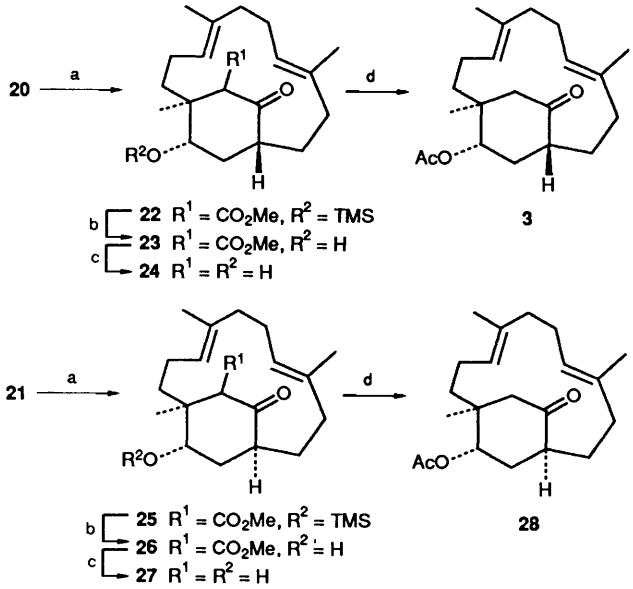
Diester **20**, upon treatment with a large excess of potassium *tert*-butoxide in refluxing diethyl ether, produced keto ester **22** possessing a 6-membered ring (Scheme 4). Similar treatment of the isomer **21** afforded the stereoisomeric keto ester **25**. These Dieckmann condensations proceeded in high yield without any epimerization at C-1. This unusual low acidity of the methine proton at C-1 in both diesters might be explained by stereochemical factors in which the C-1 proton is concealed inside the macrocycle; in stable conformations the hydrophilic groups tend to be directed toward the outside of the macrocycle. We could, however, not obtain spectroscopic evidence, such as NOE data, in the corresponding ^{1}H NMR spectra.

Demethoxycarbonylation of both isomers was carried out next. After deprotection of the TMS ether groups of keto esters **22** and **25**, each of the hydroxy keto esters (**23** and **26**) was treated with sodium chloride in refluxing dimethyl sulfoxide (DMSO) to yield the corresponding ketones (**24** from **22** and **27** from **25**), respectively.[10] The stereochemistries of the C-1 positions were determined after acetylation. The stereochemistry around the cyclohexanone ring of the acetates **3** and **28** were determined from the 500 MHz ^{1}H NMR spectra and NOESY experiments. The results are shown in Fig. 1. From coupling constants and NOE experiments, it was confirmed that the cyclohexane ring in compound **28** has a chair form possessing axial junction proton and acetoxy groups, an equatorial junction methyl group, and a 1,4-*cis* bridged system. In addition, a positive NOE between the C-2 axial proton and the C-13 proton on the macrocycle indicated the macrocycle was subtended on the upper face of the cyclohexanone ring as shown in Fig. 1. On the other hand, coupling constants suggested that ketone **3** had the desired 1,4-*trans* diequatorial bridged system possessing an equatorial acetoxy and an axial junction methyl group.

The final step in the synthesis of the racemic natural product



Scheme 3 *Reagents and conditions:* (a) Et_2AlCN, toluene, 0 °C; (b) AcOH, aq. THF; (c) CrO_3, H_2SO_4, acetone, −5 °C; (d) CH_2N_2; (e) Li $(Bu^tO)_3AlH$, Et_2O, 0 °C; (f) KOH, aq. EtOH, reflux; (g) HCl, $(CO_2H)_2$; (h) CH_2N_2; (i) TMSCl, Et_3N, DMAP, CH_2Cl_2



Scheme 4 *Reagents and conditions:* (a) Bu^tOK, Et_2O, reflux; (b) HCl; (c) NaCl, aq. DMSO, reflux; (d) Ac_2O, pyr., DMAP

2 is the introduction of a methyl group at the C-15 position of the desired 1,4-*trans*-bridged ketone **3**. Treatment of ketone **3** with methyllithium at −78 °C gave compound **29** in 91% yield as a single product, which was not identical with natural product **2** (Scheme 5). Compound **29** corresponds to the C-15 epimer of our target compound **2**. This high β-face selectivity is probably due to steric hindrance at the α-face of the carbonyl

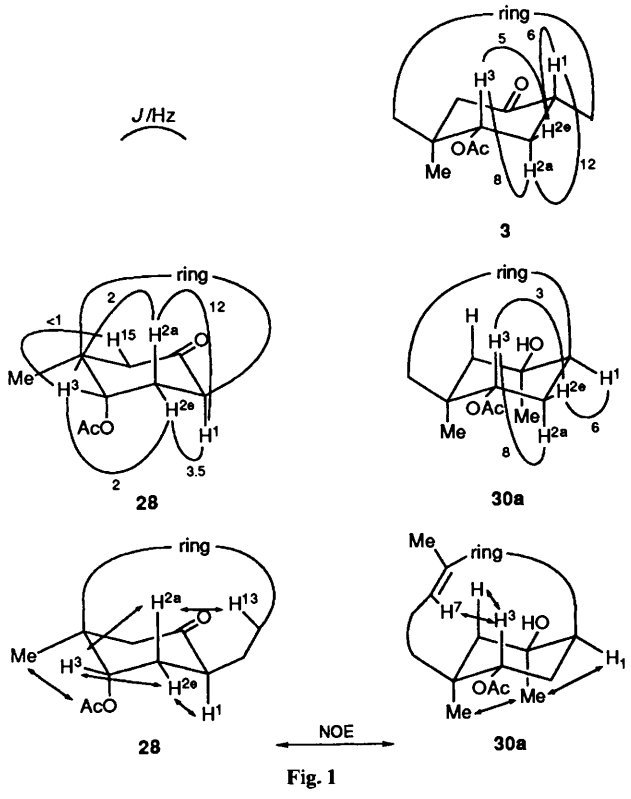
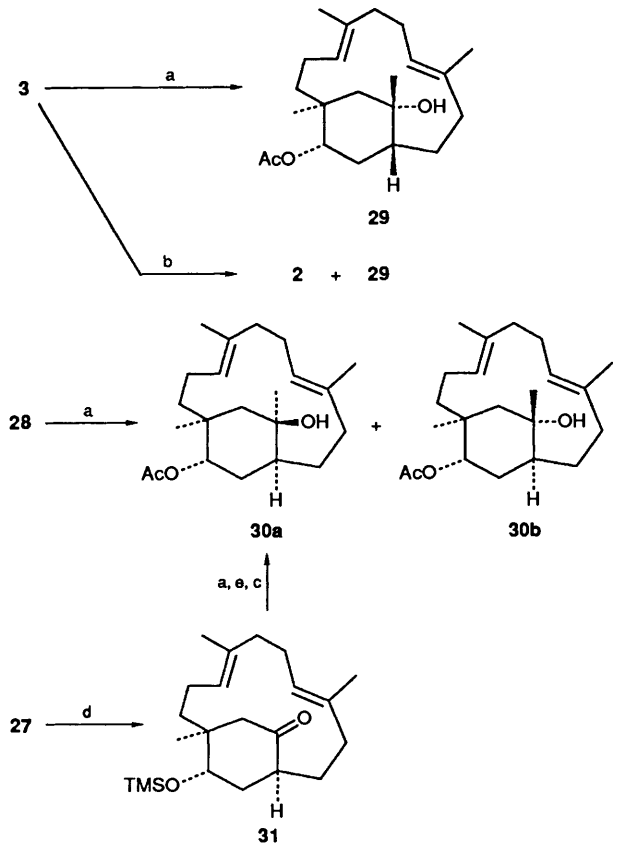


Fig. 1

group caused by the C-4 axial methyl. The macrocycle ring might be oriented above the acetoxy group rather than the C-15 carbonyl face. In order to reverse the facial selectivity, Yamamoto's bulky Lewis acid was applied to shield the less hindered β-side during nucleophilic addition.[11] A mixture of ketone **3** and 1 mol equiv. methylaluminium bis-(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) was treated with 4 mol equiv. of methyllithium at −78 °C for 4 h giving a mixture of the desired secotrinervitane **2** and its epimer **29** in a ~3:1 ratio in 30% yield together with 51% of recovered hydroxy ketone **24**. The synthetic compound **2** was identical with the natural 3α-acetoxy-7,16-secotrinervita-7,11-dien-15β-ol in its 200 MHz ^1H NMR, IR and mass spectroscopy.

In order to gain insight into the conformation and steric effects of the macrocycle ring above the cyclohexanone, the methylation of 1,4-*cis*-bridged ketone **28** was also investigated with methyllithium at −78 °C. The *cis*-bridged ketone **28** yielded an inseparable mixture of acetoxycyclohexanols **30a** and **30b** in ~9:1 ratio. The major isomer **30a** was obtained exclusively when the corresponding TMS ether **31** was methylated under the same conditions. The single product was converted into the major isomer **30a** by deprotection of the TMS group with acid followed by acetylation. The structure of product **30a** was deduced from 500 MHz ^1H NMR, COSY and NOESY spectra as shown in Fig. 1. The local conformation around the cyclohexanol moiety was different from that of the starting ketone **28**. As a result of inversion of the cyclohexane ring, compound **30a** possesses an axial junction methyl and an equatorial junction proton. Thus, the methyl addition of 1,4-*cis* ketone **27** was found to occur predominantly from the α-side of both the acetate **28** and the silyl ether **31**. This differs from the case of the 1,4-*trans*-bridged ketone **3**.

These opposite face selectivities for epimers **3** and **28** may be due to steric factors around the cyclohexanone ring. In both isomers, methyllithium attacks from the equatorial side. This takes advantage of the steric hindrance with the axial group at C-4, such as the methyl group of compound **3**, and the axial macrocycle bridge of its epimer **28**. The role of the macrocycle



Scheme 5 *Reagents and conditions:* (a) MeLi, Et_2O, −78 °C; (b) MeLi, MAD, Et_2O– toluene, −78 °C; (c) Ac_2O, pyr., DMAP; (d) TMSCl, Et_3N; (e) HCl

surrounding the cyclohexanone ring is completely obscure in terms of steric factors. The macrocycle may act as a determinant of the conformation of the cyclohexanone ring in the secotrinervitane skeleton.

Experimental

Diethyl ether and THF were freshly distilled from Na/benzophenone ketyl. CH_2Cl_2 was distilled from P_2O_5 and kept over 4Å molecular sieves. Diisopropylamine was distilled from CaH_2. Column chromatography was performed on silica gel 60 (Merck). TLC was performed on precoated TLC plates, silica gel $60F_{254}$ (Merck). NMR spectra were taken for samples in $CDCl_3$, on JEOL JNM-FX-90Q, JNM-FX-200 or JNM-GSX-500 spectrometers; *J*-values are given in Hz. All electron-impact mass and HRMS data were measured at 70 eV on a Hitachi M-80 mass spectrometer. IR spectra were measured on a Hitachi 270-30 infrared spectrometer. M.p.s were measured on a Yanaco MP-40 melting point apparatus and are uncorrected.

Methyl 2-[(E,E,E)-1,7,11-*Trimethylcyclotetradeca*-2,7,11-*trienyl*]*acetate* **6**.—To a solution of diisopropylamine (0.31 cm^3, 2.2 mmol) in dry THF (2 cm^3) at −80 °C was added dropwise a solution of butyllithium in hexane (1.33 cm^3, 2.0 mmol) under Ar, and the mixture was stirred at the same temperature for 30 min and then at 0 °C for 10 min. HMPA (0.34 cm^3, 2.0 mmol) was added and the mixture was cooled to −80 °C, and then acetate **7** (291 mg, 1.0 mmol) was added dropwise. A solution of TBDMSCl (290 mg, 1.2 mmol) in THF (2 cm^3) was added and the stirred solution was gradually warmed to ambient temperature 20 h, quenched with 2 mol dm^{-3} hydrochloric acid (20 cm^3), and extracted with diethyl ether (25 cm^3 × 3). The combined organic layers were washed with brine and dried over Na_2SO_4. A solution of diazomethane in diethyl ether (10 cm^3) was added, and the solvent was removed under reduced pressure. Purification by column chromatography (EtOAc–hexane 1:20) gave methyl ester **6** (158 mg, 55%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2930, 1740 and 1440; δ_H(90 MHz) 5.49 (1 H, dt, *J* 15.6 and 1.0), 5.08 (1 H, dt, *J* 15.6 and 6.0), 5.0 (2 H, m), 3.55 (3 H, s), 2.21 (3 H, s), 1.56 (3 H, s), 1.52 (3 H, s) and 1.08 (3 H, s); δ_C(22.5 MHz) 172.0 (s), 137.8 (d), 131.8 (s × 2), 128.4 (d), 125.7 (d), 125.3 (d), 50.8 (q), 45.1 (t), 40.6 (t), 39.2 (t), 38.7 (s), 36.5 (t), 29.2 (t), 25.2 (q), 24.1 (t), 23.9 (t), 23.2 (t) and 14.8 (q × 2); *m/z* 304 (M^+, 8%), 289, 230 and 121 (100) (Found: M^+ 304.2420. $C_{20}H_{32}O_2$ requires *M*, 304.2404).

2-[(E,E,E)-1,7,11-*Trimethylcyclotetradeca*-2,7,11-*trienyl*]-*ethanol* **8**.—To a solution of the methyl ester **6** (1.27 g, 4.2 mmol) in diethyl ether (10 cm^3) at 0 °C was added $LiAlH_4$ (251 mg, 4.2 mmol), and the mixture was stirred at the same temperature for 30 min before being quenched with ethyl acetate (2 cm^3) and saturated aq. NH_4Cl and filtered through silica gel. Evaporation under reduced pressure gave the alcohol **8** (1.15 g, 99%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 3550, 3300, 2940 and 1420; δ_H(90 MHz) 5.47 (1 H, d, *J* 15.5), 5.07 (1 H, dt, *J* 15.5 and 6.0), 5.0 (2 H, m), 3.51 (2 H, t, *J* 7.2), 1.57 (3 H, t, *J* 0.6), 1.53 (3 H, d, *J* 0.7) and 0.99 (3 H, s); δ_C(22.5 MHz) 138.8 (d), 131.7 (s), 131.6 (s), 128.6 (d), 125.6 (d), 125.2 (d), 59.4 (t), 43.3 (t), 42.0 (t), 39.1 (t), 38.0 (s), 36.5 (t), 29.1 (t), 24.8 (q), 24.1 (t), 23.8 (t), 22.8 (t) and 14.8 (q × 2); *m/z* 276 (M^+, 2%), 231, 141 and 81 (100) (Found: M^+, 276.2457. $C_{19}H_{32}O$ requires *M*, 276.2455).

(1′SR,4′E,8′E,13RS,14RS)- *and* (1′SR,4′E,8′E,13′SR,14′SR)-2-(13′,14′-*Epoxy*-1′,5′,9′-*trimethylcyclotetradeca*-4′,8′-*dienyl*)-*ethanol* **9a** *and* **9b**.—To a refluxing solution of the alcohol **8** (1.15 g, 4.2 mmol) in benzene (60 cm^3) were added vanadyl acetylacetonate (22 mg, 0.084 mmol) and 70% aq. *tert*-butyl hydroperoxide (0.86 cm^3, 6.3 mmol), and the mixture was stirred under reflux for 30 min. Water (80 cm^3) and saturated aq. $Na_2S_2O_3$ (20 cm^3) were added to the solution, and the organic layer was separated. The water layer was extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:4) to elute, first, recovered alcohol **8** (196 mg, 11%); second, the epoxide **9a** (438 mg, 36%) as an oil; and last, epoxide **9b** (434 mg, 36%) as another oil. Compound **9a**; $\nu_{max}(CCl_4)/cm^{-1}$ 3550, 3300, 2940 and 1400; δ_H(90 MHz) 5.0 (2 H, m), 3.53 (2 H, t, *J* 6.5), 2.80 (1 H, dt, *J* 7.1 and 2.6), 2.40 (1 H, d, *J* 2.6), 1.56 (3 H, d, *J* 1.7), 1.54 (3 H, s) and 0.93 (3 H, s); δ_C(22.5 MHz) 133.8 (s), 132.6 (s), 126.6 (d), 126.3 (d), 65.5 (d), 58.7 (t), 55.4 (d), 39.9 (t), 38.4 (t), 37.6 (s), 36.6 (t), 36.2 (t), 28.2 (t), 24.3 (t), 24.1 (q), 23.5 (t), 21.3 (t), 14.9 (q) and 14.8 (q); *m/z* 292 (M^+, 19%), 274, 229, 151, 147, 121 and 81 (100) (Found: M^+, 292.2408. $C_{19}H_{32}O_2$ requires *M*, 292.2404).

Compound **9b**; $\nu_{max}(CCl_4)/cm^{-1}$ 3550, 3300, 2920 and 1405; δ_H(90 MHz) 5.0 (2 H, m), 3.59 (2 H, dt, *J* 2.6 and 6.2), 2.77 (1 H, dt, *J* 7.5 and 2.7), 2.49 (1 H, d, *J* 2.7), 1.56 (6 H, s) and 0.72 (3 H, s); δ_C(22.5 MHz) 133.5 (s), 132.3 (s), 126.5 (d), 125.9 (d), 64.3 (d), 58.6 (t), 54.7 (d), 45.2 (t), 39.8 (t), 38.0 (t), 36.2 (t), 35.8 (s), 27.9 (t), 24.2 (t), 23.5 (t), 21.2 (t), 17.9 (q), 14.7 (q) and 14.6 (q); *m/z* 292 (M^+, 9%), 247, 191, 149, 135, 107 and 81 (100) (Found: M^+, 292.2404).

(1E,5E,9SR,10RS,11RS)-9-[2-(tert-*Butyldimethylsiloxy*)-*ethyl*]-10,11-*epoxy*-1,5,9-*trimethylcyclotetradeca*-1,5-*diene* **10a**.—To a solution of the epoxy alcohol **9a** (1.62 g, 5.6 mmol) in dimethylformamide (DMF) (16 cm^3) were added imidazole (0.85 g, 12 mmol) and TBDMSCl (0.94 g, 6.0 mmol), and the

mixture was stirred at room temperature overnight. To the solution was added water (100 cm^3) and the mixture was extracted with diethyl ether (50 cm^3 × 3). The combined organic layers were washed successively with saturated aq. NH_4Cl and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:20) to give silyl ether **10a** (1.97 g, 86%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2950, 1260, 1100 and 845; δ_H(90 MHz) 5.1 (2 H, m), 3.64 (1 H, t, *J* 7.5), 2.65 (1 H, dt, *J* 6.9 and 2.4), 2.38 (1 H, d, *J* 2.4), 1.59 (3 H, s), 1.54 (3 H, d, *J* 1.3), 0.91 (9 H, s), 0.88 (3 H, s) and 0.07 (6 H, s); δ_C(22.5 MHz) 133.2 (s), 132.6 (s), 127.2 (d), 126.2 (d), 64.3 (d), 59.7 (t), 54.7 (d), 39.9 (t), 36.9 (t), 36.8 (t), 36.6 (t), 35.7 (s), 28.4 (t), 26.0 (q × 3), 24.2 (t), 23.8 (t), 23.3 (q), 21.4 (t), 18.3 (s), 14.8 (q × 2) and −5.2 (q × 2); *m/z* 406 (M^+, 1%), 349, 331, 257, 229, 201, 175, 161, 107 and 81 (100) (Found: M^+, 406.3290. $C_{25}H_{46}O_2Si$ requires *M*, 406.3269).

(1E,5E,9SR,10SR,11SR)-9-[2-(tert-*Butyldimethylsiloxy*)-*ethyl*]-10,11-*epoxy*-1,5,9-*trimethylcyclotetradeca*-1,5-*diene* **10b**.—The silyl ether **10b** was prepared from the alcohol **9b** in 89% yield as an oil in a manner similar to that given previously for its isomer **10a**. Compound **10b**; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 1090 and 835; δ_H(90 MHz) 5.1 (2 H, m), 3.71 (2 H, dt, *J* 1.2 and 7.2), 2.67 (1 H, dt, *J* 7.4 and 2.1), 2.40 (1 H, d, *J* 2.1), 1.59 (6 H, s), 0.92 (9 H, s), 0.74 (3 H, s) and 0.08 (6 H, s); δ_C(22.5 MHz) 133.6 (s), 132.6 (s), 126.8 (d), 126.1 (d), 64.5 (d), 59.7 (t), 53.7 (d), 44.9 (t), 39.9 (t), 37.5 (t), 36.4 (t), 35.8 (s), 28.2 (t), 26.0 (q × 3) 24.3 (t), 23.6 (t), 21.4 (t), 18.3 (q), 18.2 (s) and 14.9 (q × 2); *m/z* 349 (M − Bu^t, 4%), 175, 161, 149, 147, 121, 109, 107, 95 and 81 (100) (Found: M^+ 406.3280).

(1SR,2E,6E,10E,14SR)-14-[2-(tert-*Butyldimethylsiloxy*)-*ethyl*]-6,10,14-*trimethylcyclotetradeca*-2,6,10-*trienol* **11a**.—To a solution of diisopropylamine (0.98 cm^3, 7.0 mmol) in dry THF (11 cm^3) at −80 °C was added dropwise a solution of butyllithium in hexane (4.65 cm^3, 7.0 mmol) under Ar, and the mixture was stirred at the same temperature for 30 min, and then the mixture was warmed to room temperature. To the mixture was added a solution of the epoxy silyl ether **10a** (1.89 g, 4.6 mmol) in THF (3.5 cm^3), and the mixture was refluxed for 2 h. After the mixture had been cooled to room temperature, saturated aq. NH_4Cl (20 cm^3) and water (50 cm^3) were added. The mixture was extracted with diethyl ether (50 cm^3 × 3) and the combined organic layers were washed successively with saturated aq. NH_4Cl and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and then the residue was purified by column chromatography (EtOAc–hexane 1:10) to give the alcohol **11a** (1.68 g, 89%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 3600, 3400, 2950, 1090 and 845; δ_H(90 MHz) 5.3 (2 H, m), 5.0 (2 H, m), 3.8 (3 H, m), 1.60 (3 H, s), 1.51 (3 H, s), 0.94 (12 H, s) and 0.10 (6 H, s); δ_C(22.5 MHz) 132.3 (s × 2), 131.9 (d), 130.4 (d), 126.8 (d), 126.0 (d), 77.4 (d), 59.9 (t), 40.0 (t × 2), 39.8 (t), 39.7 (s), 38.5 (t), 29.3 (t), 25.9 (q × 3), 24.6 (t), 21.7 (t), 20.0 (q), 18.3 (s), 15.1 (q), 14.5 (q), −5.4 (q) and −5.5 (q); *m/z* 407 and 406 (M^+, 2%), 389, 332, 275, 232, 230, 162, 153, 150 (100), 136, 125 and 108 (Found: M^+, 406.3281. $C_{25}H_{46}O_2Si$ requires *M*, 406.3269).

(1RS,2E,6E,10E,14SR)-14-[2-(tert-*Butyldimethylsiloxy*)-*ethyl*]-6,10,14-*trimethylcyclotetradeca*-2,6,10-*trienol* **11b**.—The alcohol **11b** was prepared from epoxide **10b** in 88% yield as an oil in a manner similar to that given previously for its epimer **11a**. Compound **11b**; $\nu_{max}(CCl_4)/cm^{-1}$ 3630, 3400, 2940, 1260 and 840; δ_H(90 MHz) 5.3 (2 H, m), 4.9 (2 H, m), 3.87 (1 H, br d, *J* 6.9), 3.71 (2 H, t, *J* 6.3), 2.60 (1 H, br s), 1.61 (3 H, s), 1.51 (3 H, s), 0.95 (9 H, s), 0.85 (3 H, s) and 0.11 (6 H, s); δ_C(22.5 MHz) 132.6 (d), 132.4 (s × 2), 130.4 (d), 126.8 (d), 126.0 (d), 77.4 (d), 59.9 (t), 40.5 (t), 40.1 (t), 40.0 (t), 39.9 (s), 38.5 (t), 29.5 (t), 25.9 (q × 3), 24.7 (t), 21.2 (t), 18.9 (q), 18.2 (s), 15.1 (q), 14.4 (q) and −5.5 (q × 2); *m/z* 406 (M^+, 1%), 388, 331, 231, 191, 189, 161, 149, 147 (100), 121 and 107 (Found: M^+, 406.3280).

(1SR,2E,6E,10E,14SR)-2-(2-*Hydroxyethyl*)-6,10,14-*trimethylcyclotetradeca*-2,6,10-*trienol* **12a**.—To a solution of the alcohol **11a** (113 mg, 0.28 mmol) in THF (1 cm^3) were added acetic acid (2 cm^3) and water (0.5 cm^3), and then the mixture was stirred at room temperature overnight. To the mixture was added water (25 cm^3), and the mixture was extracted with diethyl ether (10 cm^3 × 3). The combined organic layers were washed successively with saturated aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:2) to give diol **12a** (90 mg, 90%) as needles, m.p. 103.5–104 °C (from hexane–benzene 1:10); $\nu_{max}(CCl_4)/cm^{-1}$ 3600, 3210, 2928, 1438, 1384, 1078, 1020 and 972; δ_H(90 MHz) 5.5 (2 H, m), 4.9 (2 H, m), 3.98 (1 H, d, *J* 10.8), 3.71 (2 H, m), 2.9 (2 H, m), 1.59 (3 H, s), 1.50 (3 H, s) and 1.02 (3 H, s); δ_C(22.5 MHz) 133.0 (d), 132.4 (s), 132.2 (s), 129.9 (d), 126.6 (d), 126.2 (d), 77.7 (d), 58.7 (t), 40.6 (t), 40.0 (t × 2), 39.9 (s), 38.5 (t), 29.2 (t), 24.6 (t), 21.8 (t), 19.7 (q), 15.1 (q) and 14.4 (q); *m/z* 292 (M^+, 4%), 274, 192, 149, 137, 109, 107, 95, 81, 70 (100) and 41 (Found: M^+, 292.2400. $C_{19}H_{32}O_2$ requires *M*, 292.2404).

(1RS,2E,6E,10E,14SR)-14-(2-*Hydroxyethyl*)-6,10,14-*trimethylcyclotetradeca*-2,6,10-*trienol* **12b**.—The diol **12b** was prepared from the siloxy **11b** in 88% yield as prisms in a manner similar to that given previously for its epimer **12a**. Compound **12b**; m.p. 129.5–130 °C (from benzene); $\nu_{max}(KBr)/cm^{-1}$ 3396, 2912, 1450, 1042, 1004 and 974; δ_H(90 MHz) 5.40 (2 H, m), 4.9 (2 H, m), 4.04 (1 H, d, *J* 6.0), 3.72 (2 H, t, *J* 6.3), 2.95 (2 H, m), 1.59 (3 H, s), 1.49 (3 H, s) and 0.88 (3 H, s); δ_C(22.5 MHz) 133.7 (d), 132.6 (s), 132.3 (s), 130.1 (d), 126.6 (d), 126.3 (d), 78.0 (d), 58.9 (t), 40.9 (t), 40.6 (t), 40.0 (t), 39.7 (s), 38.5 (t), 29.5 (t), 24.8 (t), 21.2 (t), 18.9 (q), 15.3 (q) and 14.5 (q); *m/z* 292 (M^+, 2%), 274, 192, 149, 142, 137, 107, 95, 81 and 70 (100) (Found: M^+, 292.2410).

(3aSR,6E,10E,15aSR)-3a,4,5,8,9,12,13,15a-*Octahydro*-3a,7,11-*trimethylcyclotetradeca*[b]*furan*-2(3H)-*one* **13a**.—To a solution of the diol **12a** (90 mg, 0.31 mmol) in acetone (2 cm^3) was added dropwise Jones' reagent (0.5 cm^3; 2.7 mol dm^{-3}) at −15 °C, and the mixture was stirred at the same temperature for 1 h before being quenched with propan-2-ol (1 cm^3) and water (20 cm^3) and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:15) to give lactone **13a** (35 mg, 42%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2928, 1784, 1440, 1386, 1238, 1156 and 964; δ_H(90 MHz) 5.5 (2 H, m), 5.0 (2 H, m), 4.56 (1 H, d, *J* 5.6), 1.58 (3 H, s), 1.52 (3 H, s) and 1.17 (3 H, s); δ_C(22.5 MHz) 176.4 (s), 135.5 (d), 134.3 (s), 133.1 (s), 125.3 (d), 124.6 (d), 123.2 (d), 89.0 (d), 42.6 (s), 41.5 (t), 38.8 (t), 38.4 (t), 36.2 (t), 28.9 (t), 25.1 (t), 23.9 (q), 22.6 (t), 15.5 (q) and 15.1 (q); *m/z* 288 (M^+, 100%), 273, 228, 147, 133, 121 and 108 (Found: M^+, 288.2086. $C_{19}H_{28}O_2$ requires *M*, 288.2090).

(3aSR,6E,10E,14E,15aRS)-3a,4,5,8,9,12,13,15a-*Octahydro*-3a,7,11-*trimethylcyclotetradeca*[b]*furan*-2(3H)-*one* **13b**.—The lactone **13b** was prepared from the diol **12b** in 88% yield as an oil in a manner similar to that given previously for epimer **13a**. Compound **13b**; $\nu_{max}(CCl_4)/cm^{-1}$ 2928, 1788, 1384 and 1200; δ_H(90 MHz) 5.6 (2 H, m), 5.1 (2 H, m), 4.65 (1 H, d, *J* 7.6), 1.57 (6 H, s) and 1.00 (3 H, s); δ_C(22.5 MHz) 173.1 (s),

138.2 (d), 134.0 (s), 132.5 (s), 126.2 (d × 2), 122.6 (d), 86.6 (d), 43.9 (s), 41.8 (t), 40.0 (t), 39.1 (t), 36.4 (t), 28.3 (t), 24.9 (t), 22.0 (t), 21.8 (q), 15.2 (q) and 14.7 (q); *m/z* 288 (M^+, 33%), 229, 205, 180, 166, 120, 109 (100) and 94 (Found: M^+ 288.2092).

14-[2-(tert-*Butyldimethylsiloxy)ethyl*]-6,10,14-*trimethylcyclotetradeca*-2,6,10-*trienone* **5**.—To a solution of Collins' reagent (14.1 g, 55 mmol) in CH_2Cl_2 (210 cm^3) was added a solution of the alcohol **11a** (2.78 g, 6.9 mmol) in CH_2Cl_2 (15 cm^3) and the mixture was stirred at room temperature for 15 min. To the mixture was added diethyl ether (200 cm^3), and the resulting suspension was filtered through silica gel. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:20) to give the ketone **5** (2.42 g, 87%). From the alcohol **11b** the ketone **5** was prepared similarly in 86% yield as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 1685, 1630 and 840; δ_H(90 MHz) 6.59 (1 H, dt, *J* 15.2 and 6.0), 6.24 (1 H, d, *J* 15.2), 4.9 (2 H, m), 3.50 (2 H, ddd, *J* 8.0, 6.3 and 1.8), 1.60 (3 H, s), 1.53 (3 H, s), 1.10 (3 H, s), 0.89 (9 H, s) and 0.03 (6 H, s); δ_C(22.5 MHz) 203.1 (s), 145.1 (d), 134.6 (s), 131.5 (s), 126.0 (d × 2), 124.7 (d), 59.5 (t), 48.4 (s), 41.8 (t), 40.2 (t), 39.0 (t), 36.8 (t), 29.1 (t), 25.9 (q), 25.0 (t), 22.9 (t), 19.8 (q), 18.3 (s), 16.3 (q), 15.3 (q) and −5.4 (q × 2); *m/z* 405 and 404 (M^+, 11%), 347, 272, 229, 197, 149 (100) and 75 (Found: M^+, 404.3109. $C_{25}H_{44}O_2Si$ requires *M*, 404.3112).

12-[2-(tert-*Butyldimethylsiloxy)ethyl*]-4,8,12-*trimethyl*-13-*oxocyclotetradeca*-4,8-*dienecarbonitrile* **14a** *and* **14b**.—To a solution of the enone **5** (1.07 g, 2.6 mmol) in toluene (35 cm^3) at −20 °C under Ar was added a 1.0 mol dm^{-3} solution of diethylaluminium cyanide in toluene (7.9 cm^3, 7.9 mmol). The stirred reaction mixture was warmed gradually to 0 °C during 1 h, quenched with 10% aq. KOH (30 cm^3), and poured into water. The mixture was extracted with diethyl ether (50 cm^3 × 3), washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane 1:10) to give a mixture of the cyanides **14a** and **14b** as an oil. Separation of the mixture was achieved by HPLC on silica gel (Lichrosolv SI-100; EtOAc–hexane 1:20) to elute, first, the cyanide **14a** (445 mg, 39%) and then its epimer **14b**. The low-polarity isomer **14a** was obtained as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 2245, 1705, 1095 and 835; δ_H(90 MHz) 4.9 (2 H, m), 3.57 (2 H, t), 2.7 (3 H, m), 1.55 (3 H, s), 1.50 (3 H, s), 1.17 (3 H, s), 0.84 (9 H, s) and 0.02 (6 H, s); δ_C(22.5 MHz) 211.4 (s), 134.7 (s), 131.2 (s), 127.5 (d), 125.3 (d), 122.6 (s), 59.5 (t), 49.0 (s), 41.7 (t), 39.6 (t), 39.4 (t), 38.0 (t), 36.0 (t), 27.7 (t), 26.0 (q × 3), 24.3 (t), 23.0 (t), 21.1 (q), 18.3 (s), 14.8 (t), 14.6 (t) and −5.4 (q × 2); *m/z* 431 (M^+, 11%), 376, 375 (100), 286, 149, 145, 95, 81 and 75 (Found: M^+, 431.3228. $C_{26}H_{45}NO_2Si$ requires *M*, 431.3222).

The high-polarity isomer **14b** was obtained as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2945, 2250, 1705, 1100 and 840; δ_H(90 MHz) 4.9 (2 H, m), 3.62 (2 H, dt, *J* 1.2 and 7.1), 2.77 (3 H, m), 1.58 (3 H, s), 1.50 (3 H, s), 1.12 (3 H, s), 0.91 (9 H, s) and 0.06 (6 H, s); δ_C(22.5 MHz) 210.8 (s), 134.9 (s), 131.2 (s), 127.2 (d), 124.9 (d), 122.5 (s), 59.2 (t), 49.5 (s), 42.4 (t), 40.3 (t), 39.3 (t), 37.4 (t), 35.7 (t), 28.4 (t), 25.9 (q × 3), 24.0 (t), 22.5 (t) 18.9 (q), 18.3 (s), 14.8 (q × 2) and −5.4 (q × 2); *m/z* 431 (M^+, 17%), 416, 374 (100), 344, 286, 149, 95, 81 and 75 (Found: M^+, 431.3226).

Methyl 2-(12-*Cyano*-1,5,9-*trimethyl*-14-*oxocyclotetradeca*-4,8-*dienyl)acetate* **15a**.—To a solution of the ketone **14a** (1.04 g, 2.4 mmol) in THF (4 cm^3) were added acetic acid (8 cm^3) and water (2 cm^3), and the solution was stirred at room temperature overnight, poured into water (200 cm^3), and extracted with diethyl ether (50 cm^3 × 3). The combined organic layers were washed successively with saturated aq. $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation under reduced pressure gave the hydroxy ketone as a pale yellow oil, which was used directly.

To a stirred solution of the previous material in acetone (25 cm^3) was added Jones' reagent (8.5 cm^3, 6.8 mmol) at −5 °C. After 1 h, the reaction mixture was quenched with propan-2-ol (1 cm^3), poured into water (200 cm^3), and extracted with diethyl ether (50 cm^3 × 3). The combined organic layers were washed with brine, and dried over Na_2SO_4. To the organic layer was added a solution of diazomethane in diethyl ether (20 cm^3), and then the solvent was removed under reduced pressure. The residue was purified by chromatography (EtOAc–hexane 1:6) to give methyl ester **15a** (598 mg; 72%) as needles, m.p. 86–87 °C (from hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 2930, 2250, 1735, 1710 and 880; δ_H(90 MHz) 5.04 (1 H, m), 4.81 (1 H, m), 3.76 (3 H, s), 2.9 (4 H, m), 1.60 (3 H, s), 1.55 (3 H, s) and 1.36 (3 H, s); δ_C(22.5 MHz) 210.8 (s), 171.8 (s), 135.4 (s), 131.1 (s), 127.3 (d), 124.8 (d), 121.0 (s), 51.7 (q), 48.3 (s), 43.6 (t), 40.0 (t), 39.6 (t), 39.2 (t), 35.9 (t), 28.1 (t), 24.3 (t), 22.6 (t), 21.5 (q), 14.9 (q) and 14.6 (q); *m/z* 345 (M^+, 47%), 287, 265, 217, 184, 136, 122, 113, 111, 108 (100) and 81 (Found: C, 72.4; H, 9.0; N, 4.1. $C_{21}H_{31}NO_3$ requires C, 73.00; H, 9.89; N, 4.05%).

Methyl 2-(12-*Cyano*-1,5,9-*trimethyl*-14-*oxocyclotetradeca*-4,8-*dienyl)acetate* **15b** (*Epimer of* **15a**).—The methyl ester **15b** was prepared similarly from the ketone **14b** in 71% yield as needles, m.p. 78–79 °C; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 2250, 1740, 1710 and 850; δ_H(90 MHz) 5.0 (2 H, m), 3.68 (3 H, s), 2.85 (4 H, m), 1.65 (3 H, s), 1.57 (3 H, s) and 1.25 (3 H, s); δ_C(22.5 MHz) 209.7 (s), 171.2 (s), 135.4 (s), 131.4 (s), 127.5 (d), 124.6 (d), 122.4 (s), 51.8 (q), 49.0 (s), 45.0 (t), 40.1 (t), 39.1 (t), 37.4 (t), 35.8 (t), 27.7 (t), 24.2 (t), 22.6 (t), 19.8 (q) and 14.8 (q × 2); *m/z* 346 and 345 (M^+, 100%), 286, 264, 216, 183, 135, 110, 107, 95 and 81 (Found: C, 72.9; H, 9.3; N, 3.7%).

(3aSR,6E,10E,15aSR)-14-*Cyano*-3a,4,5,8,9,12,13,14,15,15a-*decahydro*-3a,7,11-*trimethylcyclotetradeca*[b]*furan*-2(3H)-*one* **16a**.—To a solution of the methyl ester **15a** (863 mg, 2.5 mmol) in dry diethyl ether (30 cm^3) at 0 °C was added lithium tri (*tert*-butoxy)aluminium hydride (1.25 g, 5.0 mmol), and the mixture was stirred at the same temperature for 5 h. The reaction mixture was then quenched with saturated aq. NH_4Cl (1 cm^3), filtrated through silica gel, and evaporated under reduced pressure. The residue was purified by column chromatography (EtOAc–hexane 1:6) to give lactone **16a** (697 mg, 90%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2935, 2250, 1790 and 1085; δ_H(90 MHz) 5.1 (2 H, m), 4.33 (1 H, dd, *J* 11.2 and 2.1), 1.68 (3 H, s), 1.63 (3 H, s) and 1.23 (3 H, s); δ_C(22.5 MHz) 175.2 (s), 135.8 (s), 131.6 (s), 128.7 (d), 124.2 (d), 121.1 (s), 86.1 (d), 42.7 (t), 42.2 (s), 38.8 (t), 36.2 (t), 34.4 (t), 31.2 (t), 26.7 (t), 26.4 (d), 24.7 (q), 24.3 (t), 23.1 (t), 15.2 (q) and 15.0 (q); *m/z* 315 (M^+, 48%), 299, 256, 202, 188, 174, 147, 135, 121, 107, 95 and 81 (100) (Found: M^+, 315.2205. $C_{20}H_{29}NO_2$ requires *M*, 315.2200).

Sodium Borohydride Reduction of Keto Ester **15a**.—To a solution of the methyl ester **15a** (90 mg, 0.3 mmol) in methanol (2 cm^3) at 0 °C was added $NaBH_4$ (16 mg, 0.5 mmol) and the mixture was stirred at the same temperature for 1 h before being poured into water and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography (EtOAc–hexane 1:6) to give the lactone **16a** (61 mg, 81%).

(3aSR,6E,10E,15aSR)-14-*Cyano*-3a,4,5,8,9,12,13,14,15,15a-*decahydro*-3a,7,11-*trimethylcyclotetradeca*[b]*furan*-2(3H)-*one* **16b** (*Epimer of* **16a**).—The lactone **16b** was prepared similarly from the methyl ester **15b** in 90% yield as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2935, 2250, 1785 and 1100; δ_H(90 MHz) 5.1 (2 H, m) 4.37 (1 H,

dd, *J* 7.8 and 5.7), 1.62 (3 H, s), 1.54 (3 H, s) and 1.24 (3 H, s); δ_C(22.5 MHz) 175.0 (s), 136.3 (s), 132.5 (s), 127.1 (d), 124.8 (d), 120.0 (s), 85.5 (d), 42.3 (s), 42.2 (t), 38.2 (t), 36.5 (t), 34.3 (t), 33.5 (t), 29.9 (t), 26.6 (d), 24.8 (t), 24.3 (q), 22.7 (t), 15.9 (q) and 15.7 (q); *m/z* 315 (M^+, 42%), 299, 256, 187, 134, 121, 109, 93 and 81 (Found: M^+, 315.2210).

Methyl (1RS,4E,8E,12SR,13SR)- *and* (1SR,4E,8E,12SR,-13SR)-13-*Hydroxy*-12-(*methoxycarbonylmethyl*)-4,8,12-*trimethylcyclotetradeca*-4,8-*dienecarboxylate* **4** *and* **17**.—To a solution of a 1:1 mixture of the cyano lactones **16a** and **16b** (540 mg, 1.7 mmol) in ethanol (4 cm^3) was added 50% aq. KOH (1 cm^3), and the mixture was refluxed under N_2 overnight. The reaction mixture was cooled to room temperature, acidified to pH ~4 by 2 mol dm^{-3} hydrochloric acid and 0.1 mol dm^{-3} aq. oxalic acid, and extracted with diethyl ether (50 cm^3 × 3). The combined organic layers were washed with brine, and dried over Na_2SO_4. A solution of diazomethane in diethyl ether (10 cm^3) was added to the solution, then the solvent was removed under reduced pressure. The residue was first purified by column chromatography (EtOAc–hexane 1:5) to elute: (a) the γ-lactone **18b** (30 mg, 5%) as prisms, (b) a mixture of the diester **4** and the γ-lactones **18a** and **19a** (305 mg ~47%), (c) the γ-lactone **19b** (25 mg, 4%) as needles, and (d) the diester **17** (230 mg, 36%) as an oil, which was contaminated by small amounts of lactones **18b** and **19b**. This contaminated diester **17** and the mixture of compounds **4**, **18a** and **19a** was used directly for the next synthetic step. Compound **18b**; m.p. 104–105 °C (from hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 1790 and 1740; δ_H(90 MHz) 5.1 (2 H, m), 3.83 (1 H, dd, *J* 11.4 and 3.6), 3.56 (3 H, s), 1.58 (3 H, s) and 1.23 (3 H, s); δ_C(22.5 MHz) 178.7 (s), 172.7 (s), 134.8 (s), 133.0 (s), 128.4 (d), 127.2 (d), 85.1 (d), 51.5 (q), 41.9 (d), 40.2 (s), 40.1 (t), 38.3 (t), 37.5 (t), 36.4 (t), 31.2 (t), 24.6 (t), 23.7 (t), 22.6 (q), 21.7 (t), 15.0 (q) and 14.7 (q); *m/z* 348 (M^+, 100), 317, 274, 249, 221, 147, 135, 121 and 107 (Found: C, 72.1; H, 9.3. $C_{21}H_{32}O_4$ requires C, 72.38; H, 9.26%).

Compound **19b**; m.p. 81–81.5 °C (from hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 2950, 1795 and 1740; δ_H(90 MHz) 4.95 (2 H, m), 3.94 (1 H, dd, *J* 7.4 and 6.2), 3.60 (3 H, s), 1.60 (6 H, s) and 1.14 (3 H, s); δ_H(22.5 MHz) 176.4 (s), 175.3 (s), 135.3 (s), 132.8 (s), 126.7 (d), 123.5 (d), 87.2 (d), 52.0 (q), 42.4 (t), 42.2 (d), 42.1 (s), 38.9 (t), 38.1 (t), 33.4 (t), 32.2 (t), 29.0 (t), 24.6 (t), 23.3 (t), 23.7 (q), 15.8 (q) and 15.1 (q); *m/z* 348 (M^+, 100%), 317, 288, 206, 151, 136, 122 and 108 (Found: C, 72.0; H, 9.3%).

Separation of a mixture of compounds **4**, **18a** *and* **19a**. Final purification of the mixture of compounds **4**, **18a** and **19a** was achieved by HPLC on silica gel (Lichrosolv SI-100; EtOAc–hexane 1:10) to elute (a) the γ-lactone **18a** (45 mg, 8%) as an oil, (b) the γ-lactone **19a** (43 mg, 7%) as an oil, and (c) the diester **4** (207 mg, 32%) as an oil which was contaminated by small amounts of lactones **18a** and **19a**. Compound **18a**; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 1780 and 1745; δ_H(90 MHz) 5.0 (2 H, m), 4.40 (1 H, dd, *J* 8.4 and 6.6), 3.60 (3 H, s), 2.21 (2 H, s), 1.63 (3 H, s), 1.57 (3 H, s) and 1.07 (3 H, s); δ_C(22.5 MHz) 179.8 (s), 172.1 (s), 134.6 (s), 134.3 (s), 125.9 (d), 125.7 (d), 83.4 (d), 51.5 (q), 40.3 (t), 40.0 (s), 39.3 (d), 38.6 (t), 36.6 (t), 35.4 (t), 26.8 (t), 26.4 (t), 24.5 (t), 21.7 (q), 15.8 (q) and 15.7 (q); *m/z* 348 (M^+, 98%), 317, 274 and 81 (100) (Found: M^+, 348.2309. $C_{21}H_{32}O_4$ requires *M*, 348.2302).

Compound **19a**; $\nu_{max}(CCl_4)/cm^{-1}$ 2940, 1785 and 1735; δ_H(90 MHz) 5.0 (2 H, m), 4.11 (1 H, dd, *J* 10.1 and 2.9), 3.59 (3 H, s), 1.59 (3 H, s), 1.52 (3 H, s) and 1.16 (3 H, s); δ_C(22.5 MHz) 176.2 (s), 175.6 (s), 135.0 (s), 132.5 (s), 127.4 (d), 125.1 (d), 87.0 (d), 51.5 (q), 42.6 (t), 42.2 (s), 39.7 (d), 38.6 (t), 36.8 (t), 34.9 (t), 30.3 (t), 28.4 (t), 25.3 (q), 24.6 (t), 22.9 (t), 15.5 (q) and 14.8 (q); *m/z* 348 (M^+, 100%), 317, 288 and 81 (Found: M^+, 348.2320).

Methyl (1RS,4E,8E,12SR,13SR)-12-(*Methoxycarbonylmethyl*)-4,8,12-*trimethyl*-13-(*trimethylsiloxy*)*cyclotetradeca*-4,8-*dienecarboxylate* **20**.—To a solution of the diester **4** (370 mg, 0.98 mmol), which was contaminated with small amounts of lactones **18a** and **19a**, in dichloromethane (3 cm^3) were added triethylamine (0.4 cm^3, 2.8 mmol), chlorotrimethylsilane (0.2 cm^3, 1.4 mmol) and 4-(dimethylamino)pyridine (DMAP) (1 mg). The mixture was stirred at room temperature overnight, poured into water, and extracted with diethyl ether (25 cm^3 × 3). The combined organic layers were washed successively with saturated aq. NH_4Cl and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:6) to elute, first, the silyl ether **20** (365 mg, 82%) as an oil, then a mixture of lactones **18a** and **19a** (49 mg, 17%). Compound **20** had $\nu_{max}(CCl_4)/cm^{-1}$ 2960, 1740 and 1260; δ_H(90 MHz) 5.29 (1 H, br t, *J* 7.0), 5.0 (1 H, m), 3.65 (3 H, s), 3.61 (3 H, s), 3.6 (1 H, m), 2.29 (2 H, s), 1.59 (6 H, s), 0.96 (3 H, s) and 0.13 (9 H, s); δ_C(22.5 MHz) 176.6 (s), 173.2 (s), 133.0 (s), 132.7 (s), 127.9 (d), 127.0 (d), 77.4 (d), 51.3 (q), 51.1 (q), 41.6 (s), 41.2 (d + t), 38.8 (t), 37.4 (t), 35.5 (t), 33.5 (t), 29.4 (t), 25.1 (t), 23.8 (q), 22.2 (t), 16.0 (q), 15.2 (q) and 0.6 (q × 3); *m/z* 362 (M − TMSOH, 37%), 330, 249, 217, 189, 187, 159, 147, 135, 133, 121 and 94 (100).

Methyl (1SR,4E,8E,12SR,13SR)-12-(*Methoxycarbonylmethyl*)-4,8,12-*trimethyl*-13-(*trimethylsiloxy*)*cyclotetradeca*-4,8-*dienecarboxylate* **21**.—The silyl ether **21** was prepared from hydroxy compound **17** in 70% yield as an oil contaminated with a mixture of lactones **18b** and **19b** (28%) in a manner similar to that given previously for compound **20**. Compound **21**; $\nu_{max}(CCl_4)/cm^{-1}$ 2960, 1740 and 1260; δ_H(90 MHz) 4.95 (2 H, m), 3.68 (3 H, s), 3.6 (1 H, m), 3.59 (3 H, s), 1.57 (6 H, s), 1.00 (3 H, s) and 0.10 (9 H, s); δ_C(22.5 MHz) 176.0 (s), 173.0 (s), 133.7 (s), 133.1 (s), 126.0 (d), 125.4 (d), 75.3 (d), 50.9 (q), 50.7 (q), 41.6 (s), 41.1 (d), 39.3 (t), 37.7 (t), 37.4 (t), 36.5 (t), 36.3 (t), 30.5 (t), 24.5 (t), 22.1 (q), 21.3 (t), 15.9 (q), 15.6 (q) and 0.2 (q × 3); *m/z* 452 (M^+, 1%), 362, 330, 249, 201, 187, 159, 121, 93 and 73 (100) (Found: M^+, 452.2952. $C_{25}H_{44}O_5Si$ requires *M*, 452.2959).

Methyl (1RS,4E,8E,12SR)-4,8,12-*Trimethyl*-14-*oxo*-16-(*trimethylsiloxy*)*bicyclo*[10.2.2]*hexadeca*-4,8-*diene*-13-*carboxylate* **22**.—To a suspension of potassium *tert*-butoxide (117 mg, 1.0 mmol) in dry diethyl ether (8 cm^3) was added a solution of the diester **20** (79 mg, 0.17 mmol) in dry diethyl ether (2 cm^3), and the mixture was refluxed under N_2 for 15 min, quenched with saturated aq. NH_4Cl, poured into water, and extracted with diethyl ether (25 cm^3 × 3). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:20) to give the keto ester **22** (59 mg, 81%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2956, 1740, 1716, 1250, 1072 and 896; δ_H(90 MHz) 5.4 (1 H, m), 4.95 (1 H, m), 4.91 (1 H, dd, *J* 6.9 and 3.6), 3.77 (1 H, s), 3.70 (3 H, s), 1.55 (6 H, s), 1.07 (3 H, s) and 0.10 (9 H, s); δ_C(22.5 MHz) 209.6 (s), 171.0 (s), 136.6 (s), 133.1 (s), 127.9 (d), 126.8 (d), 70.2 (d), 62.1 (d), 51.6 (q), 42.9 (s), 40.6 (d), 39.8 (t), 36.9 (t), 36.1 (t), 35.8 (t), 25.4 (t), 25.3 (t), 23.6 (q), 21.1 (t), 15.7 (q), 14.5 (q) and 0.3 (q × 3); *m/z* 388 (M − MeOH, 10%), 360, 298, 279, 217, 182, 147, 93 and 73 (100).

Methyl (1SR,4E,8E,12SR,16SR)-4,8,12-*Trimethyl*-14-*oxo*-16-(*trimethylsiloxy*)*bicyclo*[10.2.2]*hexadeca*-4,8-*diene*-13-*carboxylate* **25**.—The keto ester **25** was prepared from diester **21** in 86% yield as an oil in a manner similar to that given previously for its epimer **22**. Compound **25**; $\nu_{max}(CCl_4)/cm^{-1}$ 2952, 1748, 1712, 1252, 1200, 1070, 874 and 840; δ_H(90 MHz) 5.24 (1 H, m), 4.95 (1 H, m), 3.94 (1 H, m), 3.75 (1 H, s), 3.66 (3 H, s), 1.59 (3 H,

s), 1.50 (3 H, s), 0.99 (3 H, s) and 0.21 (9 H, s); δ_C(22.5 MHz) 206.7 (s), 169.0 (s), 135.4 (s), 132.1 (s), 128.0 (d), 124.8 (d), 71.3 (d), 61.4 (d), 51.2 (q), 46.5 (s), 43.9 (d), 39.1 (t), 35.7 (t), 34.7 (t), 33.2 (t), 24.5 (t), 22.6 (t), 20.8 (q), 19.9 (t), 14.6 (q), 14.2 (q) and 0.3 (q × 3); *m/z* 420 (M^+, 3%), 388, 370, 360, 298, 279, 229, 182, 147, 121 and 73 (100) (Found: M^+, 420.2691. $C_{24}H_{40}O_4Si$ requires *M*, 420.2697).

Methyl (1RS,4E,8E,12SR,16SR)-16-*Hydroxy*-4,8,12-*trimethyl*-14-*oxobicyclo*[10.2.2]*hexadeca*-4,8-*diene*-13-*carboxylate* **23**.—To a solution of the keto ester **22** (110 mg, 0.26 mmol) in methanol (1 cm^3) was added 2 mol dm^{-3} hydrochloric acid (0.1 cm^3), and the mixture was swirled for a few minutes before being poured into water and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent gave hydroxy ester **23** (91 mg, quant.) as an oil, which was used directly for the next step; $\nu_{max}(CCl_4)/cm^{-1}$ 3640, 3400, 2936, 1754, 1714, 1436, 1206, 1132 and 908; δ_H(90 MHz) 5.37 (1 H, m), 4.95 (1 H, m), 4.02 (1 H, dd, *J* 7.3 and 3.6), 3.80 (1 H, s), 3.73 (3 H, s), 1.55 (6 H, s) and 1.18 (3 H, s); δ_H(22.5 MHz) 209.5 (s), 171.3 (s), 136.8 (s), 133.0 (s), 127.9 (d), 126.6 (d), 69.6 (d), 61.9 (d), 51.8 (q), 42.5 (s), 40.5 (d), 39.8 (t), 37.2 (t), 36.0 (t), 35.2 (t), 25.4 (t), 25.1 (t), 23.1 (q), 21.1 (t), 15.7 (q) and 14.5 (q); *m/z* 348 (M^+, 10%), 330, 316, 288, 229, 189, 147, 117, 91 and 81 (100) (Found: M^+, 348.2299. $C_{21}H_{32}O_4$ requires *M*, 348.2302).

Methyl (1SR,4E,8E,12SR,16SR)-16-*Hydroxy*-4,8,12-*trimethyl*-14-*oxobicyclo*[10.2.2]*hexadeca*-4,8-*diene*-13-*carboxylate* **26**.—Compound **26** was prepared from silyl ester **25** in quantitative yield as an oil in a manner similar to that given previously for the epimer **23**. Compound **26** had $\nu_{max}(CCl_4)/cm^{-1}$ 3640, 3300, 2942, 1752, 1716, 1436, 1206 and 908; δ_H(90 MHz) 5.19 (1 H, m), 4.98 (1 H, m), 4.06 (1 H, m), 3.99 (1 H, s), 3.71 (3 H, s), 1.59 (3 H, s), 1.49 (3 H, s) and 1.10 (3 H, s); δ_C(22.5 MHz) 207.0 (s), 169.7 (s), 135.6 (s), 132.6 (s), 127.9 (d), 124.8 (d), 70.4 (d), 61.2 (d), 51.4 (q), 46.2 (s), 44.0 (d), 39.1 (t), 35.7 (t), 35.2 (t), 32.8 (t), 24.6 (t), 22.5 (q), 20.5 (t), 14.6 (q) and 14.4 (q); *m/z* 348 (M^+, 7%), 330, 316, 298, 288, 229, 207, 147, 119, 117 and 81 (100) (Found: M^+, 348.2291).

(1SR,4E,8E,12RS,15SR)-15-*Hydroxy*-1,5,9-*trimethylbicyclo*-[10.2.2]*hexadeca*-4,8-*dien*-13-*one* **24**.—To a solution of the keto ester **23** (91 mg, 0.26 mmol) in DMSO (5 cm^3) were added NaCl (152 mg, 2.6 mmol) and water (0.05 cm^3), and the mixture was refluxed under N_2 for 30 min, cooled to room temperature, poured into water, and extracted with diethyl ether (10 cm^3 × 3). The combined organic layers were washed with brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc–hexane 1:4) to give ketone **24** (66 mg, 83%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 3640, 3450, 2940, 1705, 1440 and 1054; δ_H(90 MHz) 5.31 (1 H, m), 4.80 (1 H, m), 3.99 (1 H, dd, *J* 6.5 and 5.8), 1.61 (3 H, s), 1.56 (3 H, s) and 1.01 (3 H, s); δ_C(22.5 MHz) 210.4 (s), 136.4 (s), 133.0 (s), 127.9 (d), 126.3 (d), 69.3 (d), 47.7 (t), 40.5 (s), 40.3 (d), 39.8 (t), 37.8 (t), 36.2 (t), 33.2 (t), 25.4 (t), 24.1 (t), 23.9 (q), 22.1 (t), 15.1 (q) and 14.8 (q); *m/z* 290 (M^+, 1%), 272, 249, 189, 121 and 81 (100) Found: M^+ 290.2240. $C_{19}H_{30}O_2$ requires *M*, 290.2247).

(1SR,4E,8E,12SR,15SR)-15-*Hydroxy*-1,5,9-*trimethylbicyclo*-[10.2.2]*hexadeca*-4,8-*dien*-13-*one* **27**.—Compound **27** was prepared from keto ester **26** in 86% yield as an oil in a manner similar to that given previously for the epimer **24**. Compound **27** showed $\nu_{max}(CCl_4)/cm^{-1}$ 3650, 3500, 2950, 1705 and 1056; δ_H(90 MHz) 5.10 (1 H, m), 4.89 (1 H, m), 4.04 (1 H, br t, *J* 3.3), 1.62 (3 H, s), 1.51 (3 H, s) and 1.01 (3 H, s); δ_C(22.5 MHz) 211.0 (s), 135.9 (s), 132.9 (s), 127.6 (d), 124.8 (d), 71.4 (d), 49.1 (t), 44.0 (d), 42.2 (s), 39.8 (t), 39.1 (t), 35.2 (t), 32.5 (t), 24.3 (t), 22.6 (q), 20.5 (t), 14.7 (q) and 14.4 (q); *m/z* 290 (M^+, 2%), 272, 262, 121 and 81 (100) (Found: M^+, 290.2253).

(1SR,4E,8E,12RS,15SR)-15-*Acetoxy*-1,5,9-*trimethylbicyclo*-[10.2.2]*hexadeca*-4,8-*dien*-13-*one* **3**.—To a solution of the alcohol **24** (66 mg, 0.23 mmol) in pyridine (1 cm^3) were added acetic anhydride (0.5 cm^3) and DMAP (cat.), and the mixture was stirred at room temperature overnight before being quenched with methanol (1 cm^3), poured into water, and extracted with diethyl ether (10 cm^3 × 3). The combined organic layers were successively washed with 5 mol dm^{-3} aq. $CuSO_4$, water and brine. The solution was dried over Na_2SO_4, then evaporated under reduced pressure, and the residue was purified by column chromatography (AcOEt–hexane 1:10) to give the acetate **3** (70 mg, 96%) as an oil, $\nu_{max}(CCl_4)/cm^{-1}$ 2924, 1738, 1722, 1450, 1384 and 1240; δ_H(500 MHz) 5.32 (1 H, br t, *J* 7.0), 5.16 (1 H, dd, *J* 7.4 and 5.6), 4.82 (1 H, br t, *J* 7.0), 2.62 (1 H, d, *J* 16.7), 2.52 (1 H, ddt, *J* 12.3, 5.4 and 7.2), 2.33 (1 H, ddd, *J* 13.9, 7.1 and 5.6), 2.15 (3 H, m), 2.11 (1 H, d, *J* 16.7), 2.05 (3 H, s), 1.99 (1 H, m), 1.91 (1 H, m), 1.71 (1 H, ddd, *J* 14.5, 7.5 and 2.3), 1.60 (3 H, s), 1.54 (3 H, s), 1.45 (1 H, ddd, *J* 13.9, 12.3 and 7.4), 1.09 (1 H, dddd, *J* 13.7, 9.7, 5.4 and 4.3) and 0.96 (3 H, s); δ_C(50 MHz) 212.3 (s), 170.6 (2), 135.8 (s), 133.2 (s), 127.8 (d), 126.0 (d), 73.6 (d), 48.9 (t), 41.0 (d), 40.2 (s), 39.2 (t), 37.9 (t), 36.5 (t), 33.6 (t), 25.1 (t), 24.9 (q), 24.1 (t), 23.2 (t), 21.2 (q) and 15.1 (q × 2); *m/z* 272 (M − AcOH, 100%), 189, 176, 161, 134, 121, 109 and 81.

(1SR,4E,8E,12SR,15SR)-15-*Acetoxy*-1,5,9-*trimethylbicyclo*-[10.2.2]*hexadeca*-4,8-*dien*-5-*one* **28**.—Compound **28** was prepared from the hydroxy ketone **27** in 83% yield as an oil in a manner similar to that given previously for the epimer **3**. Compound **28** showed $\nu_{max}(CCl_4)/cm^{-1}$ 2936, 1768, 1710, 1244 and 1022; $\delta_H(C_6D_6$, 500 MHz) 5.32 (1 H, t, *J* 2), 5.12 (1 H, br dd, *J* 6.5 and 9), 4.92 (1 H, br dd, *J* 4 and 9.5), 2.47 (1 H, ddd, *J* 14, 11 and 2.5), 2.39 (1 H, dd, *J* 13 and 2.5), 2.35 (1 H, dd, *J* 13 and 3.5), 2.31 (1 H, d, *J* 14), 2.21 (1 H, m), 2.15 (2 H, m), 2.13 (1 H, dd, *J* 14 and 1), 1.98 (1 H, m), 1.95 (1 H, m), 1.92 (1 H, m), 1.78 (2 H, m), 1.71 (3 H, s), 1.45 (3 H, br s), 1.40 (3 H, br s), 1.35 (1 H, m), 1.28 (1 H, m), 1.03 (1 H, dt, *J* 14 and 5.5) and 0.75 (3 H, s); δ_C(50 MHz) 211.4 (s), 170.6 (s), 136.3 (s), 133.4 (s), 127.5 (d), 124.6 (d), 72.9 (d) 50.5 (t), 44.6 (d), 41.5 (s), 40.2 (t), 39.1 (t), 35.8 (t), 30.1 (t), 24.6 (t), 23.7 (t), 22.8 (q), 21.3 (q), 20.8 (t), 14.8 (q) and 14.4 (q); *m/z* 272 (M − AcOH, 11%), 189, 135, 121, 117, 109, 95 and 81 (100).

(±)-7,16-*Secotrinervita*-7,11-*diene*-3α,15α-*diol* 3-*Acetate* **29**.—To a solution of the ketone **3** (27 mg, 0.081 mmol) in diethyl ether (2 cm^3) at −78 °C under Ar was added a solution of methyllithium (1.4 mol dm^{-3}; 0.06 cm^3), and the mixture was stirred at the same temperature for 1 h. The reaction mixture was quenched with saturated aq. NH_4Cl, poured into water, and extracted with diethyl ether. The combined organic layers were washed with brine, and dried over Na_2SO_4. After evaporation under reduced pressure, the residual oil was purified by column chromatography (AcOEt–hexane 1:15) to give title compound **29** (26 mg, 91%) as needles; m.p. 145–147 °C (from hexane); ν_{max}(KBr)/cm^{-1} 3472, 2948, 1704, 1454, 1382, 1264, 1152, 1028 and 964; δ_H(200 MHz) 5.46 (1 H, dd, *J* 10.4 and 4.8), 5.31 (1 H, m), 5.15 (1 H, m), 2.5–2.3 (4 H, m), 2.08 (3 H, s), 1.56 (3 H, s), 1.54 (3 H, s), 1.14 (3 H, s) and 1.07 (3 H, s); δ_C(22.5 MHz) 170.8 (s), 133.1 (s), 132.6 (s), 128.8 (d), 127.2 (d), 75.4 (d), 72.4 (s), 48.7 (t), 39.9 (d), 39.4 (t), 37.2 (s), 36.7 (t), 36.5 (t), 29.4 (q), 26.2 (q), 25.4 (t), 24.9 (t), 24.5 (t), 22.5 (t), 21.4 (q), 15.2 (q) and 14.3 (q); *m/z* 288 (M − AcOH, 32%), 270, 189, 175, 161, 159, 154, 149, 147, 145, 138, 136, 135, 133, 121, 119, 109, 107, 95 (100), 81, 69 and 43 (Found: C. 75.9; H, 10.4. $C_{22}H_{36}O_3$ requires C, 75.82; H, 10.41%).

(±)-1-epi-7,16-*Secotrinervita*-7,11-*diene*-3α,15-*diol* 3-*Acetate as a Mixture of* C-15 *Epimers* **30a** *and* **30b**.—An inseparable mixture of the major isomer **30a** and the minor isomer **30b** in the ratio ~9:1 was prepared from ketone **28** in 90% yield as an oil in a manner similar to that given previously for the 1-epimer **29**. The diastereoisomer ratio of this mixture was determined as above by the ratio of intensities of the signal at δ 5.06 (dd, *J* 7.4 and 3.1, C*H*OAc) of **30a** and that at δ 4.99 (dd, *J* 7.2 and 3.2, C*H*OAc) of **30b** in the 500 MHz ^{1}H NMR spectrum.

(±)-7,16-*Secotrinervita*-7,11-*diene*-3α,15β-*diol* 3-*Acetate* **2**.—To a solution of 2,6-di-*tert*-butyl-4-methylphenol (119 mg, 0.54 mmol) in toluene (1 cm^3) was added a solution of trimethylaluminium in toluene (1.0 mol dm^{-3}; 0.27 cm^3) under Ar, and the mixture was stirred at room temperature for 1 h, then was cooled to −78 °C, and to this was added a solution of the ketone **3** (30 mg, 0.09 mmol) in diethyl ether (2 cm^3). To this cooled solution was slowly added a solution of methyllithium in diethyl ether (1.26 mol dm^{-3}; 0.36 cm^3), and this mixture was stirred at −78 °C for 3 h. The reaction mixture was then quenched with 2 mol dm^{-3} hydrochloric acid at −78 °C, warmed to room temperature, and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed successively with saturated aq. $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residual oil was purified by column chromatography (AcOEt–hexane 1:6) to elute, first, the hydroxy ketone **24** (51%); second, title compound (±)-**2** (22%) as a powder; and finally compound **29** (8%). Compound (±)-**2** had m.p. (from hexane) 113–114.5 °C; $\nu_{max}(CCl_4)$/cm^{-1} 2930, 1732, 1374, 1256 and 1024; δ_H(200 MHz) 5.48 (1 H, dd, *J* 11.2 and 5.3), 5.31 (1 H, m), 5.13 (1 H, m), 2.6–2.2 (5 H, m), 2.06 (3 H, s), 1.60 (3 H, br s), 1.57 (3 H, br s), 1.21 (3 H, s) and 0.97 (3 H, s); δ_C(22.5 MHz) 170.8 (s), 133.3 (s), 132.9 (s), 128.6 (d), 126.7 (d), 74.8 (d), 72.3 (s), 50.5 (t), 41.2 (d), 39.3 (t), 37.8 (s), 36.6 (t), 36.4 (t), 28.3 (q), 25.2 (t), 24.7 (t), 24.5 (t), 22.5 (t), 21.7 (q), 21.3 (q), 15.1 (q) and 14.5 (q); *m*/*z* 288 (M − AcOH, 1%), 270 (100), 255, 187, 173, 159, 146, 145, 133, 132, 121, 120, 119, 109, 107, 95 and 81 (Found: C, 75.8; H, 10.40. Calc. for $C_{22}H_{36}O_3$: C, 75.82; H, 10.41%).

(1SR,4E,8E,12SR,15SR)-1,5,9-*Trimethyl*-15-(*trimethylsiloxy*)*bicyclo*[10.2.2]*hexadeca*-4,8-*dien*-13-*one* **31**.—To a solution of the hydroxy ketone **27** (45 mg, 0.15 mmol) in CH_2Cl_2 were added triethylamine (0.10 cm^3) and TMSCl (0.060 cm^3), and the mixture was stirred at room temperature overnight, quenched with saturated aq. NH_4Cl, and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residual oil was purified by column chromatography (AcOEt–hexane 1:8) to give compound **31** (93%) as an oil, $\nu_{max}(CCl_4)$/cm^{-1} 2936, 1710, 1438, 1250, 1076 and 948; δ_H(90 MHz) 5.15 (1 H, br t, *J* 7.0), 4.97 (1 H, m), 3.87 (1 H, t, *J* 2.5), 1.57 (3 H, s), 1.47 (3 H, d, *J* 1.0), 0.88 (3 H, s) and 0.12 (9 H, s); δ_C(22.5 MHz) 212.5 (s), 136.3 (s), 132.6 (s), 128.0 (d), 124.4 (d), 71.0 (d), 50.1 (t), 43.8 (d), 42.9 (s), 40.1 (t), 39.1 (t), 35.9 (t), 33.4 (t), 24.6 (t), 23.5 (t), 23.2 (q), 20.7 (t), 14.8 (q), 14.3 (q), and 0.3 (q × 3); *m*/*z* 362 (M$^+$, 72%), 293, 279, 209, 189, 143, 121, 109, 81 and 73 (100) (Found: M$^+$, 362.2640. $C_{22}H_{38}O_2Si$ requires *M*, 362.2639).

(±)-1-epi-7,16-*Secotrinervita*-7,11-*diene*-3α,15β-*diol* 3-*Acetate* **30a**.—The methylation of ketone **31** (47 mg) with methyllithium was carried out in a similar manner to that described previously for reaction of compound **3**, and the product was submitted to further reaction without purification.

To a solution of the residual oil in methanol (1 cm^3) was added 2 mol dm^{-3} hydrochloric acid (0.1 cm^3), and the mixture was stirred for 5 min, poured into water, and extracted with diethyl ether (25 cm^3 × 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residual oil was used directly for the next acetylation.

To a solution of the previous oil in CH_2Cl_2 (2 cm^3) were added pyridine (0.2 cm^3), DMAP (cat.) and acetic anhydride (0.1 cm^3), and the mixture was stirred at room temperature overnight before being quenched with methanol (0.1 cm^3), poured into water, and extracted with diethyl ether (15 cm^3 × 2). The combined organic layers were washed successively with 5 mol dm^{-3} aq. $CuSO_4$, water and brine. The organic layer was dried over Na_2SO_4, and evaporated under reduced pressure. The residual oil was purified by column chromatography (AcOEt–hexane 1:6) to give compound **30a** (82%) as an oil, $\nu_{max}(CCl_4)$/cm^{-1} 3452, 2922, 1730, 1432, 1240 and 946; δ_H(500 MHz) 5.37 (1 H, m), 5.19 (1 H, m), 5.04 (1 H, dd, *J* 7.5 and 2.9), 2.47 (1 H, ddd, *J* 13.3, 5.5 and 2.9), 2.3–2.1 (8 H, m), 2.05 (3 H, s), 1.88 (1 H, m), 1.84 (1 H, m), 1.71 (1 H, m), 1.64 (3 H, s), 1.57 (3 H, s), 1.5–1.35 (7 H, m), 1.31 (3 H, s) and 0.88 (3 H, s); δ_C(100 MHz) 170.7 (s), 137.5 (s), 134.4 (s), 125.6 (d), 125.3 (d), 76.8 (d), 73.5 (s), 50.1 (t), 41.2 (d), 39.6 (t), 38.7 (t), 37.6 (t), 36.6 (s), 31.0 (t), 27.2 (q), 25.3 (t), 25.1 (t), 24.7 (t), 22.1 (q), 21.4 (q), 15.6 (q) and 14.7 (q); *m*/*z* 288 (M − AcOH, 2%), 270 (100), 187, 173, 159, 145, 133, 121, 119, 109, 107, 95 and 81.

Acknowledgements

We gratefully acknowledge Prof. J. C. Braeckman for sending copies of the ^{1}H NMR and IR spectra of the natural product.

References

1 S. H. Goh, C. H. Chuah, Y. P. Tho and G. D. Prestwich, *J. Chem. Ecol.*, 1984, **10**, 929.
2 (*a*) G. D. Prestwich, M. S. Tempesta and C. Turner, *Tetrahedron Lett.*, 1984, **25**, 1531; (*b*) J. C. Braeckman, D. Daloze, A. Dupont, J. Pasteels, B. Tursch, J. P. Declercq, G. Germain and M. van Meerssche, *Tetrahedron Lett.*, 1980, **21**, 2761; (*c*) R. Baer, A. J. Organ, K. Prout and R. Jones, *Tetrahedron Lett.*, 1984, **25**, 579.
3 W. Oppolzer and R. J. Devita, *J. Org. Chem.*, 1991, **56**, 6256; W. G. Dauben, I. Farkas, D. P. Bridon, C.P. Chuang and K. E. Henegar, *J. Am. Chem. Soc.*, 1991, **113**, 5256.
4 T. Kato, T. Hirukawa and Y. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 1987, 977; T. Hirukawa, A. Koarai and T. Kato, *J. Org. Chem.*, 1991, **56**, 4520.
5 T. Kato, T. Hirukawa, T. Uyehara and Y. Yamamoto, *Tetrahedron Lett.*, 1987, **28**, 1439.
6 M. Aoki, T. Uyehara and T. Kato, *Chem. Lett.*, 1984, 695.
7 R. E. Ireland, R. H. Mueller and A. F. Willard, *J. Am. Chem. Soc.*, 1976, **98**, 2868.
8 K. B. Sharpless and R. C. Michaelson *J. Am. Chem. Soc.*, 1973, **95**, 6136.
9 W. Nagata, M. Yoshioka and S. Hirai, *J. Am. Chem. Soc.*, 1972, **94**, 4635.
10 A. O. Rapcho and A. J. Lovey, *Tetrahedron Lett.*, 1973, 957.
11 K. Maruoka, T. Itoh and H. Yamamoto, *J. Am. Chem. Soc.*, 1985, **107**, 4573.

Paper 2/04904J
Received 14*th September* 1992
Accepted 21*st September* 1992