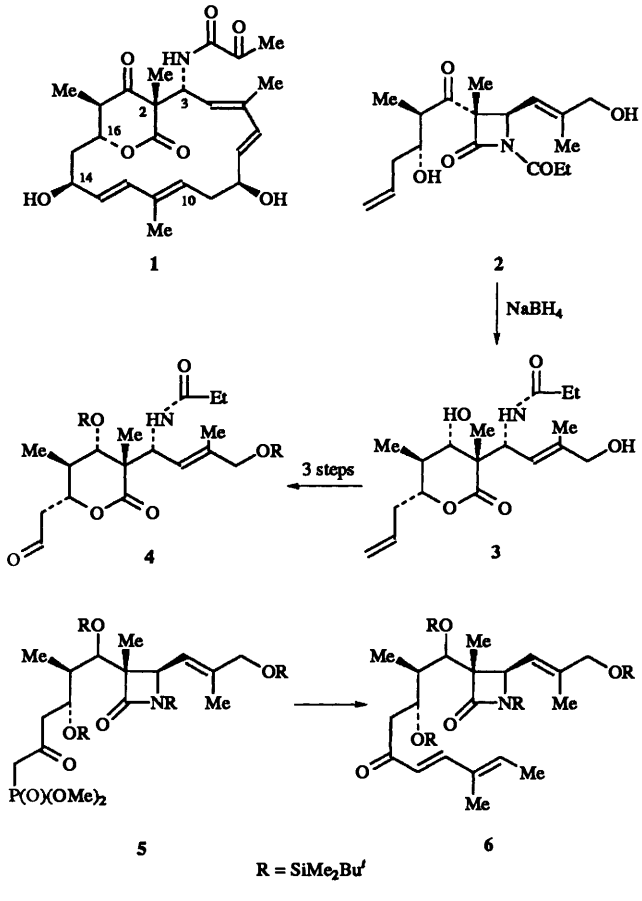
Development of a synthesis of lankacidins: an investigation into 17-membered ring formation

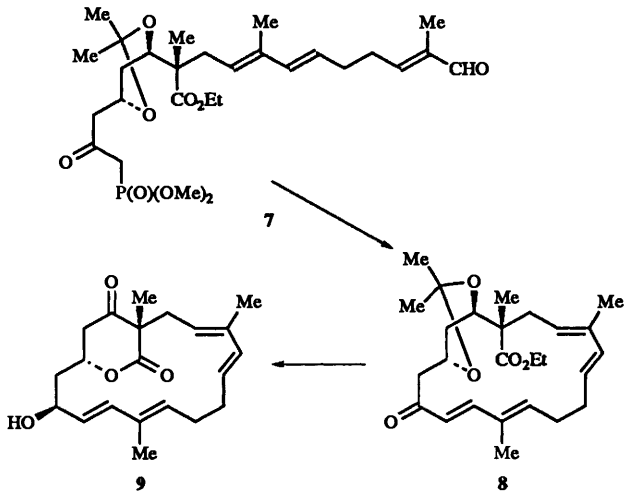
Ernesto G. Mata and Eric J. Thomas *
The Department of Chemistry, The University of Manchester, Oxford Road, Manchester M13 9PL, UK

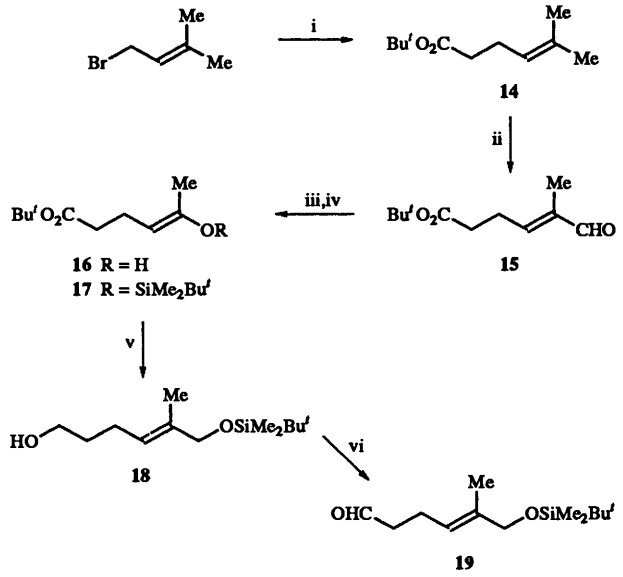
Studies are reported concerning the synthesis of macrocyclic analogues of the lankacidins. The long-chain trienylphosphonate **33** has been synthesized as a mixture of epimers at C(7), by a convergent route which involved alkylation of ethyl 2-methyl-3-oxobutanoate **10** by the 10-(*tert*-butyldimethylsilyloxy)-3,9-dimethyldeca-2,4,8-trienyl chloride **11** to give **27** followed by an aldol addition to the aldehyde **12**. Stereoselective reduction then gave the 1,3-*syn*-diol **35** which was protected as its acetonide **36**. However, it did not prove possible to hydrolyse the 1,3-dioxolane ring in **36** to reveal the keto phosphonate grouping and leave the acetonide component intact. To avoid this problem, acrolein was added to the alkylated keto ester **27** to give the aldol product **40** as a mixture of diastereoisomers. Stereoselective reduction gave the 1,3-*syn*-diols **41** and **42**, in a ratio of 75:25, which were separated and taken through to the δ-lactones **47** and **48**. The lactone **47** corresponds to the C(14)–C(12) fragment of the lankacidins, and the diol **41** is an advanced intermediate for a synthesis of a 17-membered macrocyclic analogue of the lankacidins. The diols **41** and **42** were protected as their acetonides **43** and **44** and these were taken through to the 16-formyl-2-oxophosphonates **7** and **57**. Cyclisations into the cycloheptadeca-2,4,8,10-tetraenones **8** and **58** were carried out using potassium carbonate in the presence of 18-crown-6 in toluene at 100 °C. Alternative conditions for the cyclisations were less successful as were attempts to cyclise the halogeno sulfones **62** and **63** although the 17-acetoxy sulfone **64** was cyclised using tetrakis(triphenylphosphine)palladium(0) and 1,3-bis(triphenylphosphino)propane, but only in a modest yield (18%). Deprotection and reduction of the cyclised products have been briefly investigated.

The lankacidins, exemplified by lankacidin C **1**, are an interesting group of natural products which exhibit both antibacterial and antitumour activity.[1] An approach to the synthesis of the lankacidins based on ring-opening of 3-(3'-hydroxyalkyl)azetidinones to provide the 3-[1'-(acylamino)-alkyl]-δ-lactone component has been developed independently in both our and Kende's laboratories,[2–4] and Kende has recently reported the first total synthesis of a lankacidin using this strategy.[5] During the course of our work we found that reduction of the 3-(1'-oxoalkyl)azetidinone **2** using sodium borohydride in ethanol is accompanied by azetidinone cleavage to give the δ-lactone **3**.[3] This has the stereochemistry and functionality required for incorporation into a synthesis of a lankacidin, and was taken through to the aldehyde **4** in order to investigate procedures for the introduction of the C(10)–C(14) dienyl fragment. However, the aldehyde **4** was found to be unstable under basic conditions, showing a tendency to undergo opening of the δ-lactone leading to the formation of αβ-unsaturated aldehydes.[3] It would appear prudent to avoid having intermediates which contain both the δ-lactone and a carbonyl substituent at C(14) (lankacidin numbering), at least before formation of the macrocycle. If, for example, a keto phosphonate–aldehyde condensation is to be used to introduce the C(10)–C(14) diene, it would seem necessary to carry out this reaction at the azetidinone stage, before the rearrangement to the δ-lactone. This option was shown to be viable by preparation of the 3-(6'-dimethoxyphosphinoyl-5'-oxohexyl)acetidinone **5** which was condensed efficiently with 2-methylbut-2-enal (tiglic aldehyde) to give the dienyl ketone **6**.[3]

The next stage in our work was to devise a procedure for the formation of the 17-membered macrocyclic ring of the lankacidins. As keto phosphonate–aldehyde reactions have been used to prepare macrocyclic compounds[6] it was decided to investigate an intramolecular keto phosphonate reaction, analogous to that which had been used to prepare **6**, for the preparation of the macrocyclic ring of the lankacidins. We now report on the synthesis of the 17-(dimethoxyphosphinoyl)-







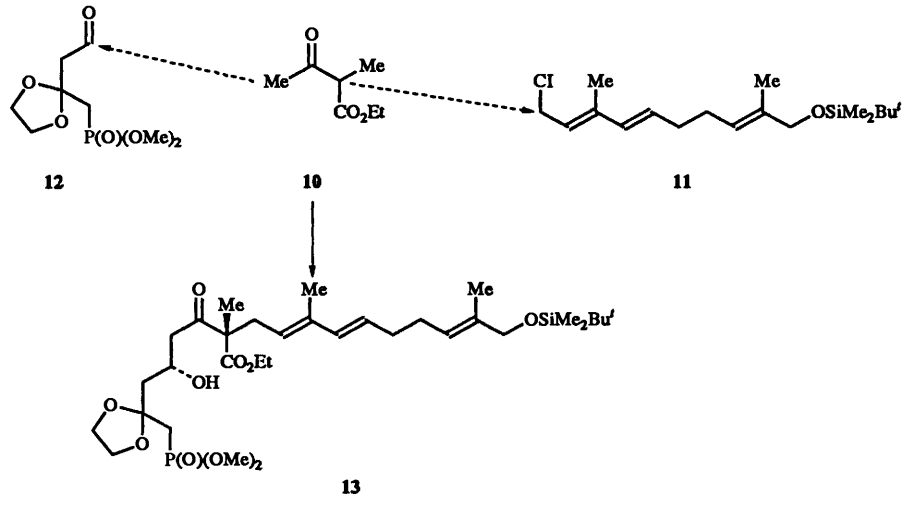
Scheme 1 *Reagents:* i, $LiCH_2CO_2Bu^t$, tetrahydrofuran, DMPU (97%); ii, selenium dioxide, ethanol; iii, sodium borohydride, ethanol (75% from **14**); iv, *tert*-butyldimethylsilyl chloride, triethylamine, 4-(dimethylamino)pyridine (90%); v, lithium aluminium hydride (97%); vi, chromium trioxide, pyridine, dichloromethane (87%)

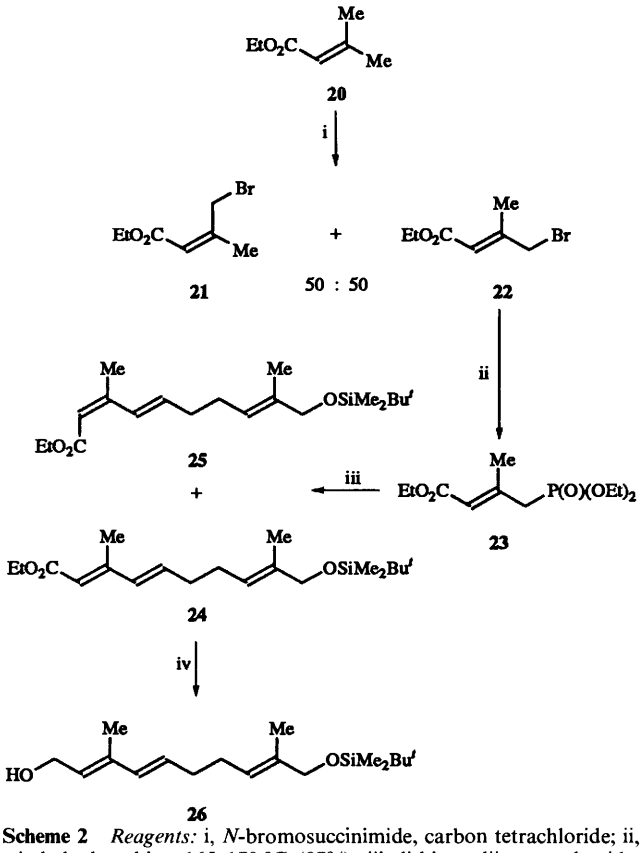
heptadecatrienal **7**, and its cyclisation to the 17-membered carbocycle **8**, a macrocyclic precursor of the lankacidin analogue **9**. A convergent synthesis of the heptatrienal **7** was envisaged based on the alkylation of ethyl 2-methyl-3-oxobutanoate **10** using (2*E*,4*E*,8*E*)-10-(*tert*-butyldimethylsilyloxy)-3,9-dimethyldeca-2,4,8-trienyl chloride **11** followed by an aldol condensation with 4-(dimethoxyphosphinoyl)-3,3-(ethylenedioxy)butanal **12** to give the heptadecatriene **13**, a possible precursor of the aldehyde **7**.

Results and discussion

(2*E*,4*E*,8*E*)-10-(*tert*-Butyldimethylsilyloxy)-3,9-dimethyldeca-2,4,8-trien-1-ol **26** was prepared as outlined in Schemes 1 and 2. Alkylation of *tert*-butyl acetate using 3-methylbut-2-enyl bromide gave ethyl 5-methylhex-4-enoate **14** which was oxidised stereoselectively using selenium dioxide in ethanol to give the aldehyde **15**.[7] This was reduced to the alcohol **16** using sodium borohydride (75% overall yield), and after protection of the hydroxyl group as its *tert*-butyldimethylsilyl ether, the ester **17** was reduced using lithium aluminium hydride and the alcohol **18** so obtained oxidised using Collin's reagent[8] to give the aldehyde **19**. This was found to decompose substantially on attempted silica gel chromatography, but could be used in the next step without purification.

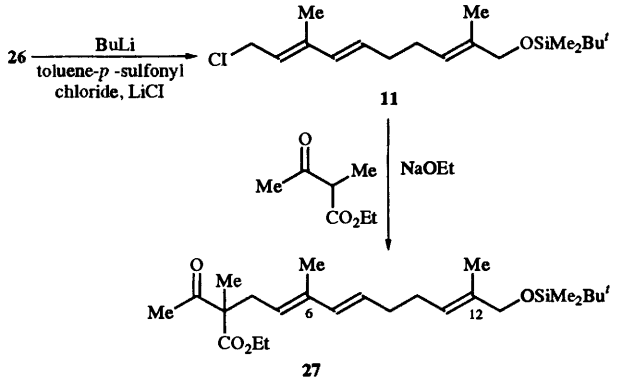
Free-radical bromination of ethyl 3-methylbut-2-enoate **20** gave a mixture of the (*Z*)- and (*E*)-4-bromobutenoates **21** and **22** which were separated by flash chromatography. Conversion of the (*E*)-isomer **22** into the diethyl phosphonate **23** was carried out with no isomerisation of the double-bond *via* an Arbusov reaction[9] using triethyl phosphite (87%). The Wadsworth Emmons Horner condensation of the phosphonate **23** with the aldehyde **19** was investigated under a variety of conditions. Initial reactions using lithium diisopropylamide as the base in tetrahydrofuran–1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one (DMPU)[10] were non-stereoselective and gave the (*E*)- and (*Z*)-alkenes **24** and **25** in an approximately 50:50 ratio, the lack of stereoselectivity being attributed to isomerisation of the lithiated phosphonate. Subsequently it was found that by carrying out the deprotonation of the phosphonate at −90 °C, with addition of the aldehyde within 1 min, the *E*:*Z* ratio could be improved to 93:7 with a combined yield of 84%. Reduction of the *E*-isomer **24** using lithium aluminium hydride–aluminium chloride[11] then gave the allylic alcohol **26** in a 95% yield. The geometry of the 4,5-double-bond in the trienol **26** was apparent from the coupling constant of 15 Hz between 4-H and 5-H in its ^1H NMR spectrum. The geometry of the 2,3-double-bond was confirmed by NOE studies later in the synthesis.





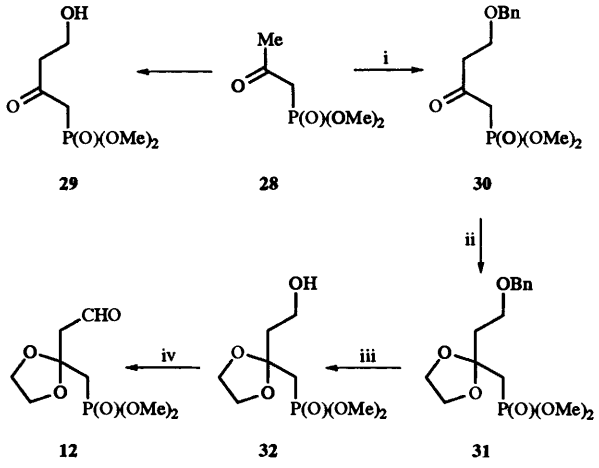
Scheme 2 *Reagents:* i, *N*-bromosuccinimide, carbon tetrachloride; ii, triethyl phosphite, 165–170 °C (87%); iii, lithium diisopropylamide, −90 °C, < 1 min, then add **19** (**24**, 78%; **25**, 6%); iv, lithium aluminium hydride, aluminium chloride (97%)

The conversion of the alcohol **26** into the corresponding allylic bromide or chloride was found to be complicated by the instability of the product. The best procedure in our hands was found to involve the use of butyllithium, toluene-*p*-sulfonyl chloride and lithium chloride as reported for dienyl alcohols by Stork which gave the chloride **11** which was used immediately without purification.[12] The long-chain keto ester **27** was then prepared by alkylation of ethyl 2-methyl-3-oxobutanoate using the crude allylic chloride **11** in an acceptable overall yield (57%).



The stereochemistry assigned to the trienyl keto ester **27** was confirmed by NOE studies. Irradiation of the 6-Me peak at δ 1.72 resulted in enhancement of the multiplets at δ 2.62 and 5.58 assigned to 4-H_2 and 8-H, respectively, but no enhancement of the peaks due to 5- or 7-H. Irradiation of the 12-Me peak at δ 1.59 caused an increase in the multiplet at δ 2.1 assigned to 10-H_2, but not for the multiplet at δ 5.39 due to 11-H.

The dimethyl phosphonate **12** was prepared as outlined in Scheme 3. Dilithiation of the ketophosphonate **28** and addition to formaldehyde[13] was inefficient in our hands giving only a 7% yield of the hydroxy ketone **29**. However, alkylation using benzyl chloromethyl ether gave an acceptable, 62%, yield of 4-benzyloxy-1-(dimethoxyphosphinoyl)butan-2-one **30** which, after protection of the ketone as its 1,3-dioxolane using ethylene glycol, was hydrogenolysed to give the alcohol **32**. Oxidation of the alcohol using tetrapropylammonium perruthenate[14] gave the aldehyde **12** (70%).

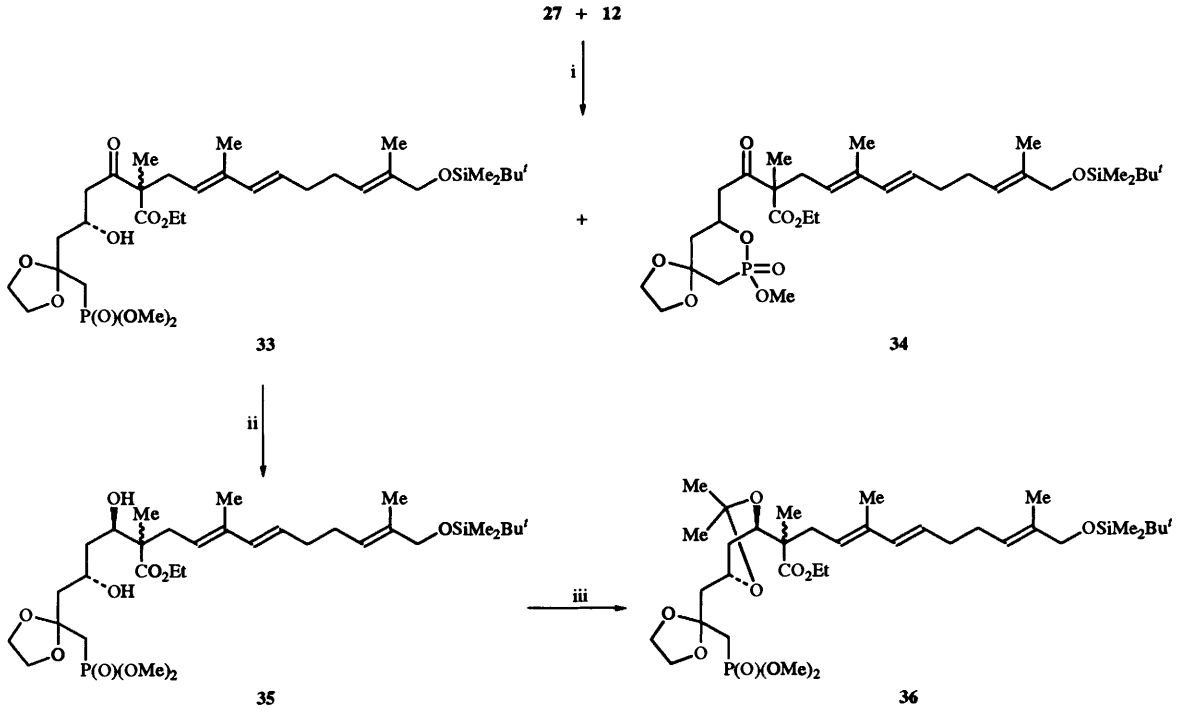


Scheme 3 *Reagents:* i, sodium hydride, butyllithium, benzyl chloromethyl ether (62%); ii, ethylene glycol, toluene-*p*-sulfonic acid (cat.), benzene, heat under reflux (78%); iii, hydrogen, 10% palladium-on-charcoal (95%); iv, tetrapropylammonium perruthenate, *N*-methylmorpholine *N*-oxide (70%)

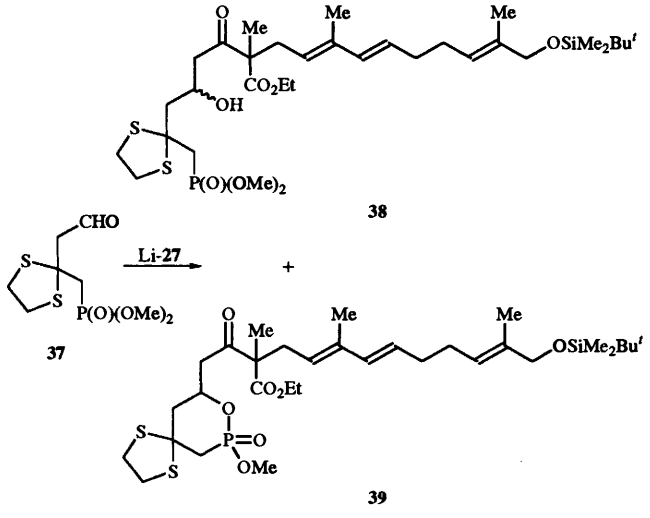
The aldol reaction between the keto ester **27** and the aldehyde **12** gave a 60% yield of the adduct **33** together with a minor side-product identified as the oxaphosphorinane **34** (see Scheme 4). Although the aldol product **33** comprised a mixture of two diastereoisomers, no attempt was made at this stage to separate them or to control the stereoselectivity of the aldol process. However, a stereoselective procedure was chosen to reduce the ketone carbonyl group in order to avoid increasing the number of diastereoisomers present. Reduction using sodium borohydride and dimethylmethoxyborane, a procedure which is known to reduce 3-hydroxy ketones stereoselectively to give *syn*-1,3-diols,[15] gave the diol **35** as a mixture of epimers at the quaternary centre, and these were protected as the acetonide **36**. However, all attempts to hydrolyse the 1,3-dioxolane ring selectively without hydrolysis of the acetonide were unsuccessful. For example the use of aqueous acidic tetrahydrofuran[16] cleaved the acetonide selectively and gave the starting diol **35** together with some triol corresponding to cleavage of the *tert*-butyldimethylsilyl ether. Similar results were obtained using pyridinium toluene-*p*-sulfonate in acetone–water, and oxalic acid in acetone[17] gave rise to the formation of complex mixtures of products.

Preliminary studies were carried out into the use of a 1,3-dithiolane as a ketone protecting group which it was hoped would be removed selectively in the presence of the acetonide. However, the aldol reaction between the dithiolane-protected formyl ketone **37** and the keto ester **27** was very inefficient, giving the aldol product **38** as only a minor component of a mixture with the 1,2-oxaphosphorinane **39**. Since preliminary attempts to methanolyse this to give more of the dimethoxyphosphonate **38** were unsuccessful, this approach was discontinued in favour of an alternative sequence in which this selective deprotection was avoided.

The aldol reaction between the keto ester **27** and acrolein gave the adduct **40** as an inseparable mixture of diastereoisomers (see Scheme 5). Reduction of this mixture using sodium borohydride and dimethylmethoxyborane[15] gave the *syn*-1,3-diols **41** and **42**, ratio 70:30, respectively, which were separated



Scheme 4 *Reagents:* i, lithium diisopropylamide (**33**, 60%; **34**, 8%); ii, dimethylmethoxyborane, sodium borohydride (86%); iii, dimethoxypropane, acetyl chloride (80%)



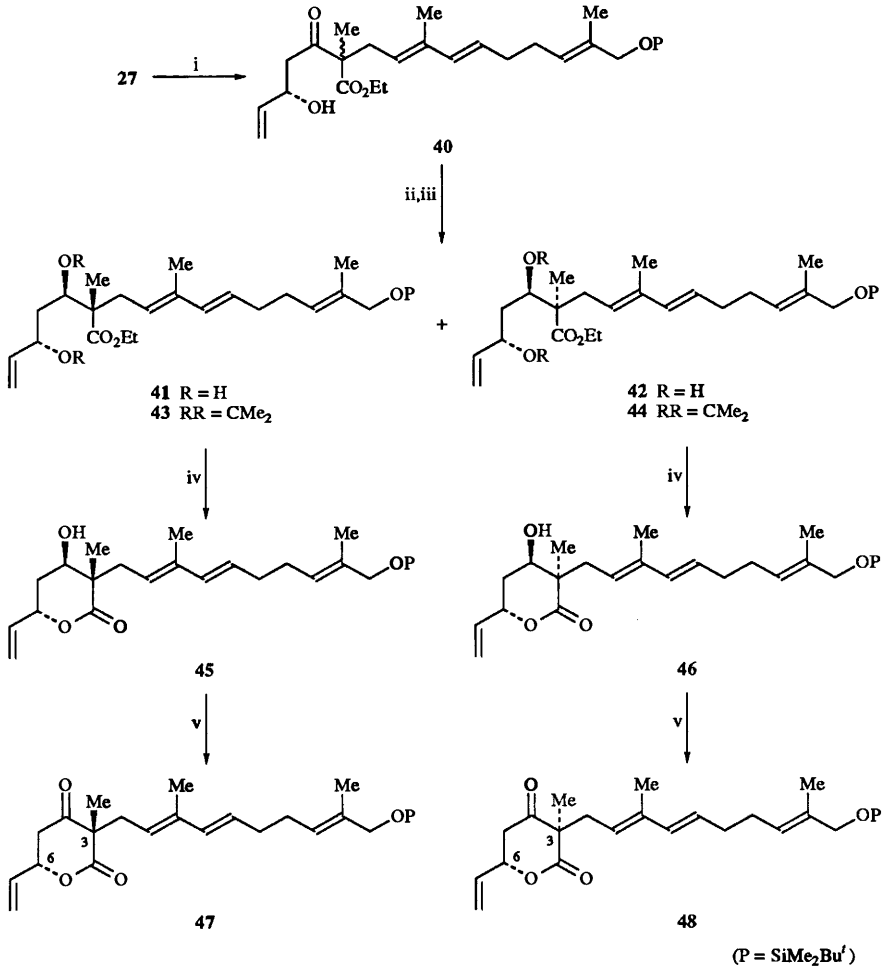
by flash chromatography. Protection of the separated diols using dimethoxypropane[18] gave the acetonides **43** and **44** the ^{13}C NMR spectra of which confirmed the *syn*-1,3-relationship between the hydroxyl groups.[19]

To establish the identity of each diol, they were separately taken through to the δ-hydroxy lactones **45** and **46** which were oxidised to the keto lactones **47** and **48**. These were studied by ^1H NOE difference spectroscopy. Irradiation of the singlet due to 3-Me in the ^1H NMR of the ketone prepared by oxidation of the major hydroxy lactone caused a 10% NOE enhancement of the multiplet assigned to 6-H, and *vice versa*, whereas no such NOE enhancement was observed for the keto lactone prepared from the minor diol. Analogous, although less pronounced effects were observed during ^1H NMR studies of the hydroxy lactones **45** and **46**. The major diol was, therefore, identified as diastereoisomer **41**, the derived hydroxy- and keto-lactones being identified as **45** and **47**. The minor diol was correspondingly identified as the diastereoisomer **42**, with the minor hydroxy- and keto-lactones being identified as **46** and **48**.

It is perhaps fortuitous that the stereochemistry of the major diol **41** and the lactones **45** and **47** corresponds to that found in the lankacidins. Indeed the lactone **47** possesses the structure of the C(14)–C(12) fragment of the lankacidins, missing only the 17-Me, the 3-acylamino-, and the 8-OH substituents. It was now necessary to develop the chemistry of the terminal double-bond of the acetonides **43** and **44** to prepare intermediates for macrocyclisation studies.

The major acetonide **43**, which has stereochemistry corresponding to the lankacidins, was converted into the 16-formyl keto phosphonate **7** as shown in Scheme 6. Regioselective hydroboration of the terminal double-bond using 9-borabicyclononane followed by oxidation gave the alcohol **49** which was oxidised using pyridinium chlorochromate[20] to the aldehyde **50**. This was found to be rather unstable and, after rapid flash chromatography, was treated with lithiated dimethyl methylphosphonate to give a mixture of the epimeric hydroxy phosphonates **51**. After selective removal of the *tert*-butyldimethylsilyloxy protecting group, oxidation of both of the hydroxyl substituents was carried out using tetrapropylammonium perruthenate to give the 16-formyl-2-oxo phosphonate **7**. The minor acetonide **44**, with stereochemistry corresponding to the unnatural configuration at C(3) in the lankacidins, was similarly taken through to the epimeric 16-formylketophosphonate **57** (Scheme 7).

Cyclisation of the formyl keto phosphonate **7** was studied under a wide variety of conditions. Diazabicycloundecane and lithium chloride in acetonitrile at 40 °C led to a complex mixture of products,[21] lithium hexamethyldisilazide in tetrahydrofuran–DMPU returned unchanged starting material,[22] and sodium hydride and 18-crown-6 in dimethoxyethane[23] gave only low yields of the required macrocycle together with complex mixtures of other products which were not separated or identified. Finally, the use of potassium carbonate in toluene at 100 °C in the presence of 18-crown-6 was found to give the cycloheptadecatetraenone **8** in yields of 35–40%. The epimeric phosphonate **57** was similarly cyclised to give the cycloheptadecatetraenone **58**, the geometry of the 2,3-double-bond of these products being assigned as *E* on the basis



Scheme 5 *Reagents:* i, lithium diisopropylamide, −78 °C, 30 min, then add acrolein (72%); ii, dimethylmethoxyborane, sodium borohydride (95%); iii, 2,2-dimethoxypropane, acetyl chloride (cat.) (90–98%); iv, sodium hydroxide acidified and heated under reflux in benzene (**45**, 92%; **46**, 85%); v, tetrapropylammonium perruthenate, *N*-methylmorpholine *N*-oxide (**47**, 77%; **48**, 69%)

of 16 Hz coupling between 2-H and 3-H in their ^{1}H NMR spectra.

Alternative macrocyclisation procedures were briefly investigated. The 17-bromo- and 17-iodo sulfones **62** and **63** were prepared as summarised in Scheme 8, but attempts to cyclise them under basic conditions, *e.g.* using potassium hexamethyldisilazide–18-crown-6 or lithium diisopropylamide,[24] gave complex mixtures of products perhaps due to interference by the ethyl ester. The corresponding 17-acetoxy-3-oxo sulfone **64** was converted into its enol trimethylsilyl ether using *O*,*N*-bis(trimethylsilyl)acetonide, and this was cyclised to the cycloheptadecatrienone **65**, albeit in rather a low yield, 18%, by addition to a mixture of tetrakis(triphenylphosphine)-palladium(0) and 1,3-bis(diphenylphosphino)propane in tetrahydrofuran heated under reflux.[25]

Having prepared the macrocycles **8** and **58**, aspects of their chemistry were briefly investigated. Reduction of the enone **8** using diisobutylaluminium hydride gave a mixture of epimeric alcohols in a ratio of 75:25 whereas sodium borohydride–cerium(III) chloride[26] was more stereoselective and gave the same alcohols in a ratio of 87:13. The configurations of these alcohols were not formally established, but simple modelling studies suggested that attack on the less hindered face of the enone **8** would give rise to the 14-β-isomer **66**. Reduction of the epimeric ketone **58** similarly gave two alcohols identified as **69** and **70**, the major diastereoisomer also being provisionally identified as the 14-β-epimer **69**. Attempts to hydrolyse the acetonide group in the alcohol **69** using acidic methanol gave mixtures of products in which the dienyl alcohol fragment appeared to have rearranged. Similarly attempts to deprotect the *p*-methoxybenzyloxy- or acetoxy-acetonides **68** and **71** using acidic methanol gave complex mixtures of products. However, a preliminary study of the hydrolysis of the benzoyloxyacetonide **72** indicated formation of the diol **73** as the major product although proper characterisation of these advanced intermediates was not possible because of lack of material.

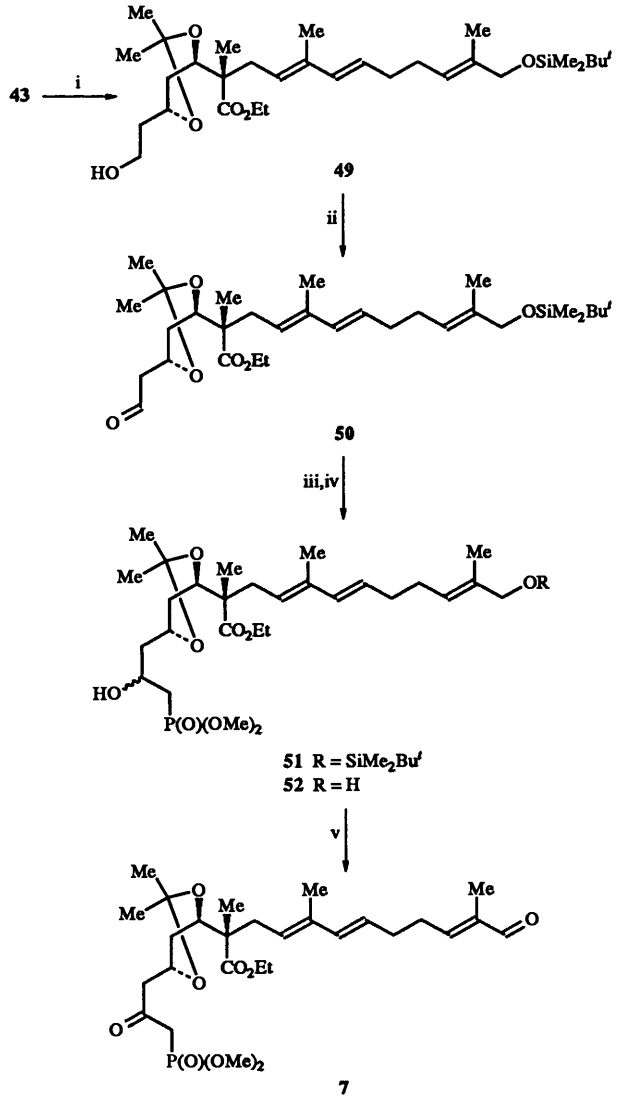
The work described in this paper establishes the viability of assembling the 17-membered carbocyclic ring of the lankacidins using a keto phosphonate–aldehyde cyclisation. The yields of the cyclisation step are, however, only modest, perhaps due to base-induced elimination of the 3,5-isopropylidenedioxy group from the keto phosphonate. Present work is concerned with applying the strategy reported here, and in the preceding papers,[2,3] to complete a total synthesis of lankacidin C **1**.[27]

Experimental

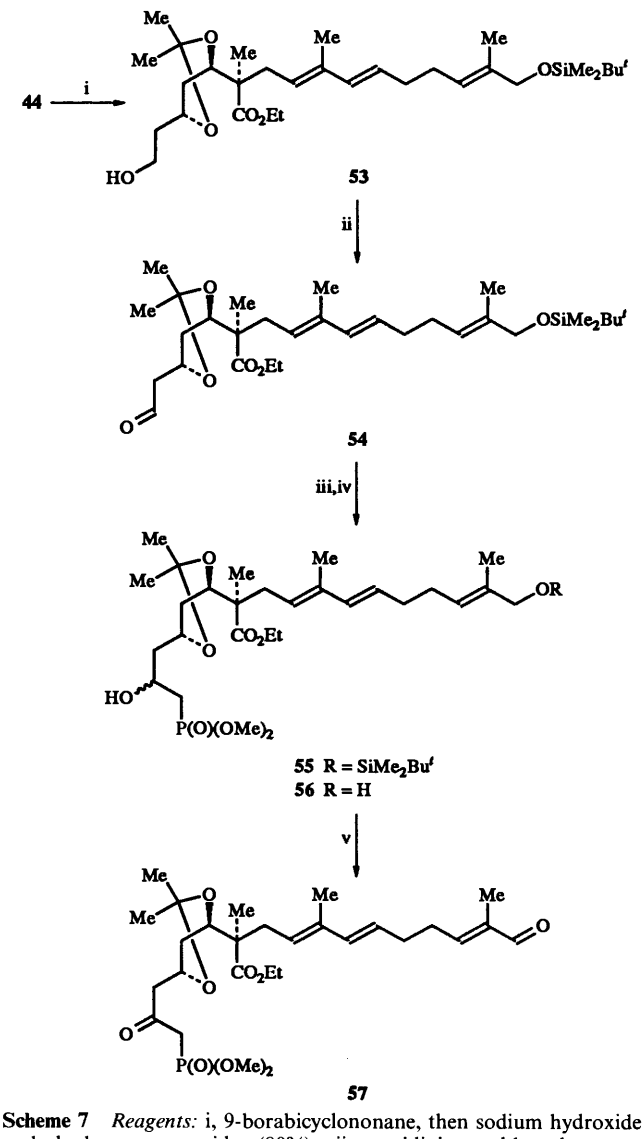
For general experimental details see the first full paper in this series.[2]

tert-Butyl 5-methylhex-4-enoate 14

Butyllithium (1.6 mol dm^{-3} in hexane; 6.6 cm^3, 10.57 mmol) was added to diisopropylamine (1.64 cm^3, 11.7 mol) in tetrahydrofuran (THF; 14 cm^3) at −78 °C. After 50 min, a solution of *tert*-butyl acetate (1.5 cm^3, 11.13 mmol) in THF (4 cm^3) was added dropwise over a period of 5 min to the reaction mixture.



Scheme 6 *Reagents:* i, 9-borabicyclononane, then sodium hydroxide and hydrogen peroxide (81%); ii, pyridinium chlorochromate, dichloromethane (73%); iii, $LiCH_2P(O)(OMe)_2$ (77%); iv, anhydrous *tert*-butylammonium fluoride, tetrahydrofuran (95%); v, *N*-methylmorpholine *N*-oxide, tetrapropylammonium perruthenate (69%)



Scheme 7 *Reagents:* i, 9-borabicyclononane, then sodium hydroxide and hydrogen peroxide (80%); ii, pyridinium chlorochromate, dichloromethane (77%); iii, $LiCH_2P(O)(OMe)_2$ (76%); iv, anhydrous *tert*-butylammonium fluoride, tetrahydrofuran (89%); v, *N*-methylmorpholine *N*-oxide, tetrapropylammonium perruthenate (68%)

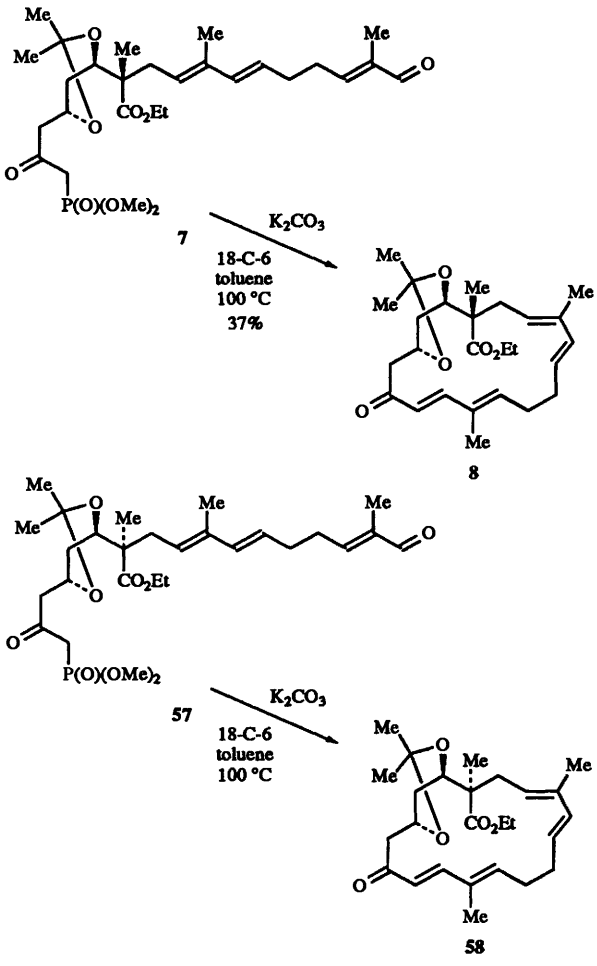
After being maintained at −78 °C for 40 min, the reaction mixture was transferred in portions to a solution of 3-methylbut-2-enyl bromide (0.7 cm^3, 6 mmol) in THF (11 cm^3) and DMPU (2 cm^3) at −78 °C. The mixture was stirred for a further 30 min, after which saturated aqueous ammonium chloride (20 cm^3) was added to it and the whole allowed to warm to room temperature. The mixture was extracted with ether (3 × 140 cm^3) and the extracts were washed with brine (3 × 90 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Flash column chromatography of the residue on silica gel with light petroleum–ether (99:1) as eluent, gave the *title compound* **14** as a colourless liquid (1.07 g, 97%); ν_{max}/cm^{-1} 1733, 1455, 1368, 1257, 1118, 1040, 850 and 755; δ_H 1.40 [9 H, s, $C(CH_3)_3$], 1.58 and 1.64 (each 3 H, s, CH_3), 2.19 (4 H, m, 2-H_2 and 3-H_2) and 5.03 (1 H, m, 4-H); δ_C 172.95, 132.69, 122.85, 80.05, 35.87, 28.20, 23.97, 25.77 and 17.78.

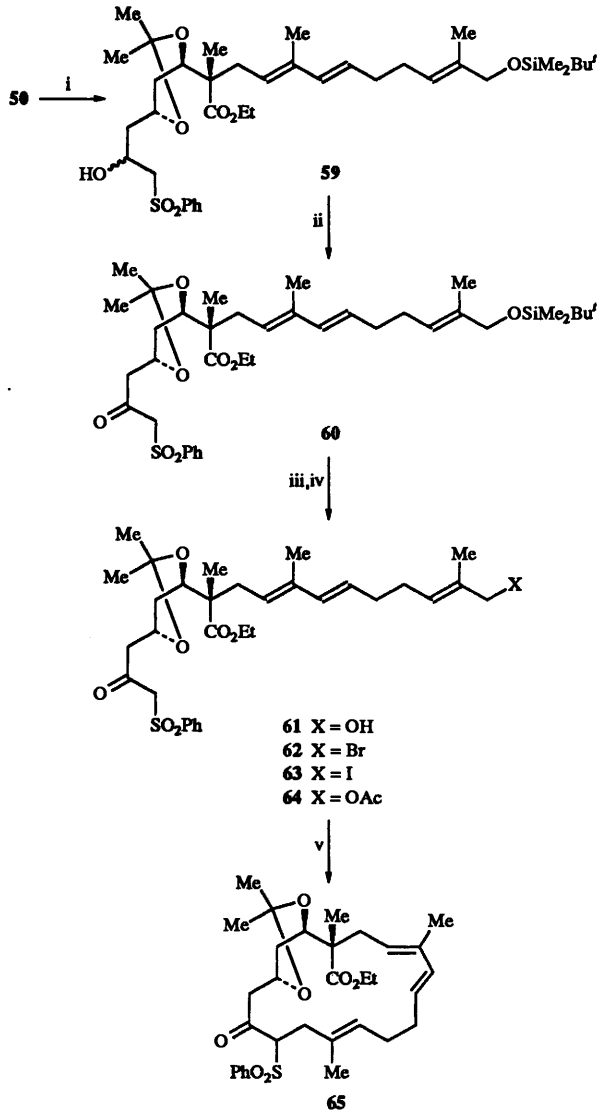
***tert*-Butyl (*E*)-5-formylhex-4-enoate 15**

A mixture of *tert*-butyl 5-methylhex-4-enoate **14** (1.39 g, 7.6 mmol) and selenium dioxide (1.175 g, 10.6 mmol) in aqueous ethanol (100 cm^3, 95% ethanol) was stirred under reflux for 16 h and then concentrated under reduced pressure. The residue was dissolved in ethyl acetate–hexane (1:1; 100 cm^3), and the solution washed with saturated aqueous sodium hydrogencarbonate (20 cm^3). The aqueous phase was back-extracted with additional ethyl acetate–hexane (2 × 10 cm^3), and the combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the crude aldehyde **15** which was used without further purification. A small sample was purified by flash column chromatography, light petroleum–ether (3:1) to give the *title compound* **15** (Found: M^+ + H, 199.1335. $C_{11}H_{19}O_3$ requires *M*, 199.1334); ν_{max}/cm^{-1} 2712, 1729, 1688, 1646, 1458, 1393, 1368, 1256, 1153, 1030, 848 and 754; δ_H 1.39 [9 H, s, $C(CH_3)_3$], 1.72 (3 H, s, CH_3), 2.43–2.47 (4 H, m, 2-H_2 and 3-H_2), 6.4 (1 H, t, *J* 6, 4-H) and 9.35 (1 H, s, CHO); δ_C 196.89, 173.97, 154.22, 141.92, 82.81, 35.96, 30.10, 26.51 and 11.28; *m/z* (CI) 216 (M^+ + NH_4, 55%), 199 (M^+ + H, 54%) and 160 (100).

***tert*-Butyl (*E*)-6-hydroxy-5-methylhex-4-enoate 16**

Sodium borohydride (152 mg, 4 mmol) was added in small portions to the aldehyde **15** (1.45 g, 7.3 mmol) in ethanol (25 cm^3) at 0 °C. Dilute aqueous hydrochloric acid was added to the reaction mixture which was then concentrated under



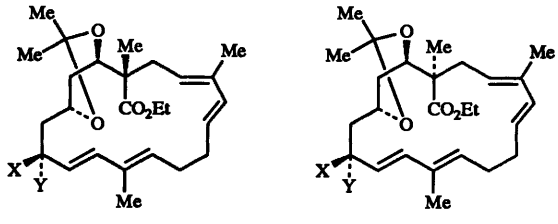


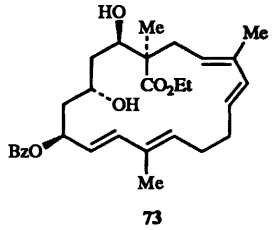
Scheme 8 *Reagents:* i, $LiCH_2SO_2Ph$ (90%); ii, oxalyl chloride, dimethyl sulfoxide (41%); iii, tetrabutylammonium fluoride, tetrahydrofuran (80%); iv, acetic anhydride, 4-dimethylaminopyridine (cat.), pyridine, dichloromethane (80%); v, *O*,*N*-bis(trimethylsilyl)acetamide then $Pd(PPh_3)_4$, $Ph_2PCH_2CH_2CH_2PPh_2$ (18%)

reduced pressure and diluted with ether. The organic and aqueous phases were separated, and the aqueous phase extracted with ether (3 × 20 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure and flash column chromatography of the residue on silica gel with light petroleum–ether (3:2) as eluent, gave the *title compound* **16** (1.14 g, 75%) (Found: $M^+ - CH_3$, 185.1173. $C_{10}H_{17}O_3$ requires *M*, 185.1178); ν_{max}/cm^{-1} 3436, 1729, 1457, 1393, 1368, 1257, 1148, 1011, 849 and 754; δ_H 1.39 [9 H, s, $C(CH_3)_3$], 1.63 (3 H, s, 5-CH_3), 1.7 (1 H, s, OH), 2.25 (4 H, m, 2-H_2 and 3-H_2), 3.94 (2 H, s, 6-H_2) and 5.35 (1 H, m, 4-H); δ_C 174.64, 137.94, 125.94, 82.29, 70.64, 37.42, 30.18, 25.42 and 15.78; *m*/*z* (CI) 218 ($M^+ + NH_4$, 4%).

tert-Butyl (*E*)-6-(*tert*-butyldimethylsilyloxy)-5-methyl-hex-4-enoate 17

Triethylamine (0.975 cm^3, 7 mmol), 4-(dimethylamino)pyridine (28.5 mg, 0.233 mmol) and *tert*-butyldimethylsilyl chloride (844 mg, 5.6 mmol) were added to a solution of alcohol **16** (933 mg, 4.665 mol) in dichloromethane (17 cm^3) and the mixture was stirred for 2 h. Water (2 cm^3) was then added to the mixture and the aqueous and organic phases were separated. The aqueous phase was extracted with dichloromethane (3 × 2 cm^3) and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography of the residue with light petroleum–ether (97:3), gave the *title compound* **17** (1.49 g, 90%) as a colourless oil (Found: $M^+ + NH_4$, 332.2621. $C_{17}H_{38}NO_3Si$ requires *M*, 332.2621); ν_{max}/cm^{-1} 1733, 1473, 1368, 1255, 1147, 1111, 1072, 838 and 777; δ_H −0.03 [6 H, s, $Si(CH_3)_2$], 0.82 [9 H, s, $SiC(CH_3)_3$], 1.35 [9 H, s, $C(CH_3)_3$], 1.52 (3 H, s, 5-CH_3), 2.19 (4 H, m, 2-H_2 and 3-H_2), 3.91 (2 H, s, 6-H_2) and 5.29 (1 H, m, 4-H); δ_C 172.57,





135.46, 122.43, 79.94, 66.29, 35.39, 28.06, 25.92, 23.23, 18.35, 13.37 and −5.32; *m/z* (EI) 257 ($M^+ - C_4H_9$, 2.2%), 201 (60) and 183 (100).

(*E*)-6-(*tert*-Butyldimethylsilyloxy)-5-methylhex-4-en-1-ol 18

A solution of the ester **17** (753 mg, 2.4 mmol) in THF (5 cm^3) was added dropwise to a suspension of lithium aluminium hydride (91 mg, 2.4 mmol) in dry THF (4 cm^3) at 0 °C. The mixture was stirred at 0 °C for 1 h and then quenched by the sequential dropwise addition of water (0.1 cm^3), aqueous sodium hydroxide (15% w/v; 0.1 cm^3), and water (0.3 cm^3). The resulting white suspension was stirred at room temperature for a further 30 min and then filtered through Celite which was then washed with THF (5 × 8 cm^3). The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to yield the *title compound* **18** (568 mg, 97%) (Found: $M^+ + H$, 245.1946. $C_{13}H_{29}O_2Si$ requires *M*, 245.1936); ν_{max}/cm^{-1} 3349, 1473, 1463, 1390, 1362, 1255, 1114, 1072, 939, 839 and 775; δ_H 0.08 [6 H, s, $Si(CH_3)_2$], 0.91 [9 H, s, $SiC(CH_3)_3$], 1.6 (1 H, br s, OH), 1.62 (3 H, s, 5-CH_3), 1.65 (2 H, m, 2-H_2), 2.12 (2 H, m, 3-H_2), 3.66 (2 H, t, *J* 7, 1-H_2), 4.02 (2 H, s, 6-H_2) and 5.5 (1 H, m, 4-H); δ_C 135.16, 123.84, 68.68, 62.86, 32.74, 26.19, 24.07, 18.68 and −4.99; *m/z* (CI) 245 ($M^+ + 1$, 8%) and 227 (87).

(*E*)-6-(*tert*-Butyldimethylsilyloxy)-5-methylhex-4-enal 19

Chromium trioxide (8.92 g, 89 mmol) was added to a solution of pyridine (14.32 cm^3, 178 mmol) in dichloromethane (212 cm^3) at 0 °C and the mixture was stirred at room temperature for 15 min. A solution of the alcohol **18** (3.34 g, 13.7 mmol) in dichloromethane (20 cm^3) was then added rapidly to it. After being stirred for 15 min the mixture was diluted with ether, washed with aqueous sodium hydroxide (5%), aqueous hydrochloric acid (5%), water, and saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and concentrated under reduced pressure to yield the aldehyde **19** (2.88 g, 87%) (Found: $M^+ - H$, 241.1630. $C_{13}H_{25}O_2Si$ requires *M*, 241.1624); ν_{max}/cm^{-1} 1728, 1473, 1463, 1390, 1362, 1253, 1114, 1073, 1007, 839 and 776; δ_H 0.12 [6 H, s, $Si(CH_3)_2$], 0.91 [9 H, s, $SiC(CH_3)_3$], 1.62 (3 H, s, 5-CH_3), 2.34 (4 H, m, 2-H_2 and 3-H_2), 3.99 (2 H, s, 6-H_2), 5.38 (1 H, m, 4-H) and 9.77 (1 H, t, *J* 1, CHO); δ_C 202.33, 136.12, 121.87, 68.33, 43.89, 26.14, 20.57, 18.63, 13.64 and −5.05; *m/z* (CI) 260 ($M^+ + NH_4$, 9%), 243 ($M^+ + 1$, 4.5), 185 (40) and 111 (100).

Ethyl (*E*)-4-bromo-3-methylbut-2-enoate 22

N-Bromosuccinimide (7.5 g, 42.5 mmol) and a catalytic amount of azoisobutyronitrile (0.01 g) were added to a solution of ethyl 3-methylbut-2-enoate (5 g, 39 mmol) in carbon tetrachloride (64 cm^3) and the mixture was heated under reflux for 3 h. It was then cooled and filtered, and the precipitate was washed with chloroform. The combined organic phases were washed with saturated aqueous sodium sulfite and brine, dried ($MgSO_4$), and concentrated under reduced pressure to give the (*E*)- and (*Z*)-4-bromo-3-methylbut-2-enoates **21** and **22** which were separated by flash column chromatography, light petroleum–ether (98.5:1.5), to give the *title compound* **22** as a pale yellow oil (Found: M^+, 205.9939. $C_7H_{11}{}^{79}BrO_2$ requires *M*, 205.9942); ν_{max}/cm^{-1} 1719, 1651, 1445, 1369, 1282, 1231, 1157, 1042, 891, 863 and 736; δ_H 1.22 (3 H, t, *J* 7, OCH_2CH_3), 2.21 (3 H, d, *J* 1.1, 3-CH_3), 3.89 (2 H, s, 4-H_2), 4.15 (2 H, q, *J* 7, OCH_2CH_3) and 5.9 (1 H, s, 2-H); δ_C 167.75, 154.26, 121.44, 62.09, 40.36, 19.23 and 16.31; *m/z* (EI) 208 (M^+, 45%), 206 (M^+, 48%), 180 (43), 178 (44), 163 (76) and 161 (77).

Ethyl (*E*)-4-(diethoxyphosphinoyl)-3-methylbut-2-enoate 23

The bromo ester **22** (779 mg, 4.02 mmol) was added to freshly distilled triethyl phosphite (0.7 cm^3, 4.07 mmol) and the mixture was sitrred and heated to 165–170 °C for 5 min. The resulting material was fractionally distilled to provide the *title compound* **23** (922 mg, 87%) as a colourless liquid, bp 180 °C/1 mmHg (Found: M^+, 264.1135. $C_{11}H_{21}O_5P$ requires *M*, 264.1127); ν_{max}/cm^{-1} 1718, 1647, 1445, 1392, 1353, 1213, 1147, 1098, 1029, 965, 854 and 780; δ_H 1.25 (9 H, overlapping t, 3 × CH_3CH_2O), 2.25 (3 H, dd, *J* 3.5, 1.4, 3-CH_3), 2.62 (2 H, d, *J* 23, 4-H_2), 4.08 (6 H, m, 3 × CH_3CH_2O) and 5.72 (1 H, m, 2-H); δ_C 167.56 (d, *J* 3.5), 151.74 (d, *J* 11.9), 121.74 (d, *J* 11.2), 63.98 (d, *J* 7.3), 61.42, 40.29 (d, *J* 135), 21.81 (d, *J* 2.7), 18.25 (d, *J* 6.4) and 16.23; *m/z* (EI) 264 (M^+, 37%), 219 (55), 218 (100), 190 (95) and 162 (72).

Ethyl (2*E*,4*E*,8*E*)-10-(*tert*-butyldimethylsilyloxy)-3,9-dimethyldeca-2,4,8-trienoate 24

Butyllithium (1.6 mol dm^{-3} in hexane; 24.8 cm^3, 39.6 mmol) was added to a stirred solution of diisopropylamine (5.55 cm^3, 39.6 mmol) in dry THF (120 cm^3) at −78 °C. After 50 min DMPU (60 cm^3) was added to the reaction mixture which was then cooled to −90 °C. The phosphonate **23** (10.45 g, 39.6 mmol) dissolved in the minimum amount of THF was added rapidly to the reaction mixture and followed, within 1 min, by a solution of the aldehyde **19** (5.25 g, 21.7 mmol) also in the minimum amount of THF. The reaction mixture was stirred at −90 °C for 2 h and allowed to warm slowly to −10 °C when saturated aqueous ammonium chloride (63 cm^3) was added to it. The aqueous and organic phases were separated and the former was extracted with ether (3 × 25 cm^3). The combined organic extracts were washed with brine (3 × 40 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography of the residue with light petroleum–ether (93:7), gave the *title compound* **24** (5.92 g, 78%) (Found: $M^+ + H$, 353.2524. $C_{20}H_{37}O_3Si$ requires *M*, 353.2512); ν_{max}/cm^{-1} 1714, 1638, 1614, 1463, 1389, 1353, 1239, 1153, 1112, 1068, 1007, 966, 838 and 777; δ_H 0.02 [6 H, s, $Si(CH_3)_2$], 0.88 [9 H, s, $SiC(CH_3)_3$], 1.23 (3 H, t, *J* 7, OCH_2CH_3), 1.56 (3 H, s, 9-CH_3), 2.18 (4 H, m, 6-H_2 and 7-H_2), 2.22 (3 H, s, 3-CH_3), 3.98 (2 H, s, 10-H_2), 4.12 (2 H, q, *J* 7, OCH_2CH_2), 5.35 (1 H, m, 8-H), 5.64 (1 H, s, 2-H), 6.09 (2 H, m, 4-H and 5-H); δ_C 167.2, 152.47, 136.72, 134.09, 123.15, 117.94, 68.44, 59.56, 33.03, 27.11, 25.99, 18.44, 14.40, 13.82, 13.53 and −5.23; *m/z* (CI) 370 ($M^+ + NH_4$, 4.5%), 353 ($M^+ + 1$, 10.3), 295 (19.4) and 221 (100). The (2*Z*,4*E*,8*E*)-isomer **25** (0.4 g, 6%) was also isolated.

(2*E*,4*E*,8*E*)-10-(*tert*-Butyldimethylsilyloxy)-3,9-dimethyldeca-2,4,8-trien-1-ol 26

Aluminium trichloride (235 mg, 1.74 mmol) was added to a solution of lithium aluminium hydride (215 mg, 5.7 mmol) in ether (4 cm^3) at 0 °C and the mixture stirred at this temperature for 1 h. A solution of the ester **24** (1 g, 2.84 mmol) in ether was then added dropwise to the mixture which was then stirred at 0 °C for 30 min. Aqueous sodium hydroxide (2 mol dm^{-3}) was then added cautiously to the reaction mixture from which the resulting solid was filtered off and washed with ether. The combined organic fractions were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography with light petroleum–ether (7:3), gave the *title compound* **26** (797 mg, 97%) as an oil (Found: $M^+ + NH_4$, 328.2680. $C_{18}H_{38}NO_2Si$ requires *M*, 328.2672); ν_{max}/cm^{-1} 3344, 1463, 1389, 1253, 1071, 1006, 965, 838 and 776; δ_H 0.06 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.5 (1 H, br s, OH), 1.59 (3 H, s, 3-CH_3), 1.77 (3 H, s, 9-CH_3), 2.15 (4 H, m, 6-H_2 and 7-H_2), 4.0 (2 H, s, 10-H_2), 4.26 (2 H, d, *J* 7, 1-H_2), 5.39 (1 H, m, 8-H), 5.55 (1 H, t, *J* 7, 2-H), 5.66 (1 H, dt, *J* 15, 6.5, 5-H) and 6.07 (1 H, d, *J* 15, 4-H); δ_C 136.53, 134.91, 134.31, 130.05, 127.99, 123.78, 68.69, 59.49, 33.0, 27.73, 26.16, 18.64, 13.72, 12.8 and −5.01; *m/z* (CI) 328 ($M^+ + NH_4$, 4%) and 161 (100).

(5*E*,7*E*,11*E*)-13-(*tert*-Butyldimethylsilyloxy)-3-ethoxycarbonyl-3,6,12-trimethyltrideca-5,7,11-trien-2-one 27

Butyllithium (1.6 mol dm^{-3} in hexane; 0.88 cm^3, 1.41 mmol) was added dropwise to a stirred solution of the alcohol **26** (430 mg, 1.39 mmol) in THF (2.8 cm^3) at 0 °C followed by DMPU (1 cm^3) and toluene-*p*-sulfonyl chloride (319 mg, 1.67 mmol) in THF (1.8 cm^3). After 30 min, a solution of lithium chloride (176 mg, 4.14 mmol) in DMPU and *N*,*N*-dimethylformamide (3.2 cm^3, 60:40) was added dropwise to the mixture and the stirring continued at 0 °C for a further 45 min. Saturated aqueous sodium hydrogen carbonate (6 cm^3) was added to the mixture and the aqueous and organic phases were separated. The organic phase was extracted with ether (2 × 4 cm^3) and the combined extracts were washed with water (2 × 3 cm^3) and brine (3 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure at 0 °C to give the chloride **11** which was used immediately.

Ethyl 2-methyl-3-oxobutanoate **10** (0.268 cm^3, 1.86 mmol) was added dropwise to a solution of sodium ethoxide (106 mg, 1.53 mmol) in ethanol (9 cm^3) at 0 °C and this was followed by the chloride **11** in ethanol (5.6 cm^3). After 2.5 h at room temperature the reaction mixture was concentrated under reduced pressure and the residue taken up in ether (10 cm^3). The ethereal solution was washed with brine (2 cm^3) and the aqueous phase then back-extracted with ether (3 × 1 cm^3). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure and the residue was subjected to flash chromatography on silica gel with light petroleum–ether (92.5:7.5) to give the *title compound* **27** (360 mg, 59% from alcohol **26**) as a colourless oil (Found: $M^+ + NH_4$, 454.3336. $C_{25}H_{48}NO_4Si$ requires M, 454.3352); ν_{max}/cm^{-1} 1717, 1463, 1360, 1285, 1251, 1185, 1111, 964, 838 and 777; δ_H 0.06 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.25 (3 H, t, *J* 7, OCH_2CH_3), 1.32 (3 H, s, 3-CH_3), 1.59 (3 H, s, 12-CH_3), 1.72 (3 H, s, 6-CH_3), 2.05 (4 H, m, 9-H_2 and 10-H_2), 2.1 (3 H, s, 1-H_3), 2.62 and 2.7 (each 1 H, dd, *J* 7.5, 15, 4-H), 4.0 (2 H, s, 13-H_2), 4.18 (2 H, q, *J* 7, OCH_2CH_3), 5.18 (1 H, t, *J* 7, 5-H), 5.39 (1 H, m, 11-H), 5.58 (1 H, dt, *J* 15.7, 8-H) and 6.03 (1 H, d, *J* 15, 7-H); δ_C 205.0, 172.72, 136.96, 134.82, 134.72, 128.43, 123.89, 123.45, 68.69, 61.51, 59.97, 33.59, 32.97, 27.79, 26.4, 26.15, 19.15, 18.63, 14.26, 13.69, 12.89 and −5.02; *m*/*z* (CI) 454 ($M^+ + NH_4$, 5%), 437 ($M^+ + 1$, 0.5) and 305 (9).

4-Benzyloxy-1-dimethylphosphinoylbutan-2-one 30

A solution of dimethylphosphinoylpropanone (1.66 cm^3, 12 mmol) in THF (4.5 cm^3) was added slowly to a suspension of sodium hydride (612 mg, 26 mmol) in THF (30 cm^3) at 0 °C. After 1 h, butyllithium (1.6 mol dm^{-3} in hexane; 7.88 cm^3, 12.6 mmol) was added dropwise to the mixture which was then stirred for 1 h. After this the solution was cooled to −78 °C and benzyl chloromethyl ether (1.66 cm^3, 12 mmol) in THF (6 cm^3) was slowly added to it. The resulting mixture was stirred at 0 °C for 1 h and then poured into brine (30 cm^3). The mixture was acidified with aqueous hydrochloric acid (1 mol dm^{-3}) to pH ~2 and the organic phase separated. The aqueous solution was extracted with ether (2 × 15 cm^3) and the combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography of the residue on silica gel with light petroleum–ethyl acetate–methanol (12:4:1), gave the *title compound* **30** (2.12 g, 62%) (Found: $M^+ + H$, 287.1047. $C_{13}H_{20}O_5P$ requires *M*, 287.1048); ν_{max}/cm^{-1} 1718, 1497, 1455, 1369, 1256, 1186, 1029, 822 and 742; δ_H 2.84 (2 H, t, *J* 6.4, 3-H_2), 3.10 (2 H, d, *J* 23, 1-H_2), 3.68 (2 H, t, *J* 6.4, 4-H_2), 3.7 [6 H, d, *J* 11.6, $P(OCH_3)_2$], 4.44 (2 H, s, CH_2Ph), 7.26 (5 H, s, ArH); δ_C 202.27 (d, *J* 6.4), 139.92, 130.36, 129.67, 75.21, 66.93, 55.1 (d, *J* 6.4), 46.15 and 43.72 (d, *J* 128); *m*/*z* (CI) 287 ($M^+ + 1$, 93%) and 186 (100).

4-Benzyloxy-1-dimethylphosphinoyl-2,2-(ethylenedioxy)butane 31

The keto phosphonate **30** (2.7 g, 9.46 mmol), ethylene glycol (3.81 cm^3, 37.8 mmol) and toluene-*p*-sulfonic acid (20 mg) were dissolved in benzene (150 cm^3) and the solution heated at reflux using a Dean-Stark trap for 1.5 h. The reaction mixture was poured into ether (70 cm^3), and the ether solution washed with saturated aqueous sodium carbonate (40 cm^3). The aqueous and organic phases were separated and the aqueous solution was extracted with ether (2 × 20 cm^3). The combined organic extracts were washed with brine (2 × 20 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give a residue which was chromatographed on silica gel with light petroleum–ethyl acetate–methanol (12:4:1) as eluent to yield the *title compound* **31** (2.41 g, 78%) as a colourless oil (Found: $M^+ + H$, 331.1290. $C_{15}H_{24}O_6P$ requires *M*, 331.1310); ν_{max}/cm^{-1} 1455, 1370, 1251, 1034, 951, 848 and 738; δ_H 2.18 (2 H, t, *J* 6.6, 3-H_2), 2.32 (2 H, *J* 19, 1-H_2), 3.6 (2 H, t, *J* 6.6, 4-H_2), 3.7 [6 H, d, *J* 11, $P(OCH_3)_2$], 3.98 (4 H, m, OCH_2CH_2O), 4.49 (2 H, s, CH_2Ph) and 7.3 (5 H, s, ArH); δ_C 140.3, 130.29, 129.65, 129.49, 109.85 (d, *J* 2.7), 75.02, 67.91, 66.95, 54.36 (d, *J* 6.4), 40.26 and 36.89 (d, *J* 130 Hz); *m*/*z* (CI) 331 ($M^+ + 1$, 79%) and 211 (100).

4-Dimethoxyphosphinoyl-3,3-(ethylenedioxy)butan-1-ol 32

A solution of the benzyl ether **31** (2.56 g, 7.76 mmol) in methanol (35 cm^3) was added to a suspension of palladium-on-charcoal (10% w/w; 195 mg) in methanol (40 cm^3). The reaction mixture was stirred overnight at room temperature under an atmosphere of hydrogen and then filtered through Celite and concentrated under reduced pressure. Flash column chromatography of the residue with light petroleum–ethyl acetate–methanol (12:4:1), gave the *title compound* **32** (1.77 g, 95%) as a colourless oil (Found: $M^+ + 1$, 241.0840. $C_8H_{18}O_6P$ requires *M*, 241.0841); ν_{max}/cm^{-1} 3405, 1475, 1247, 1039, 961 and 865; $\delta_H(CD_2Cl_2)$ 2.1 (2 H, t, *J* 6.5, 2-H_2), 2.28 (2 H, d, *J* 20, 4-H_2), 2.65 (1 H, br s, OH), 3.18 (2 H, t, *J* 6.5, 1-H_2), 3.18 [6 H, d, *J* 11, $P(OCH_3)_2$] and 3.99 (4 H, m, OCH_2CH_2O); δ_C 110.73, 66.81, 60.32, 54.69 (d, *J* 6.3), 42.18 and 36.34 (d, *J* 138); *m*/*z* (CI) 241 ($M^+ + 1$, 100%).

4-Dimethylphosphinoyl-2,2-(ethylenedioxy)butanal 12

The alcohol **32** (100 mg, 0.42 mmol) was dissolved in dichloromethane (4 cm^3) containing powdered 4 Å molecular sieves (50 mg) and *N*-methylmorpholine *N*-oxide (74 mg, 0.63 mmol). Solid tetrapropylammonium perruthenate (8 mg, 0.021 mmol) was added to the mixture which was then stirred at room temperature for 2 h. Flash chromatography with light petroleum–ethyl acetate–methanol (12:4:0.8), gave the *title compound* **12** (70 mg, 70%) as a colourless oil; ν_{max}/cm^{-1} 1724, 1465, 1401, 1246, 1034, 951, 797 and 734; δ_H 2.34 (2 H, d, *J* 20, 4-H_2), 3.02 (2 H, d, *J* 2.5, 2-H_2), 3.72 [6 H, d, *J* 11, $P(OCH_3)_2$], 4.03 (4 H, m, OCH_2CH_2O) and 9.7 (1 H, t, *J* 2.5, CHO); δ_C 201.52, 108.67, 67.30, 54.8 (d, *J* 6.4), 53.28 and 36.88 (d, *J* 138); *m*/*z* (FAB) 255 ($M^+ + 17$, 100%) and 195 (90).

(9*E*,11*E*,15*E*)-17-(*tert*-Butyldimethylsilyloxy)-1-dimethylphosphinoyl-7-ethoxycarbonyl-2,2-(ethylenedioxy)-4-hydroxy-7,10,16-trimethylheptadeca-9,11,15-trien-6-one 33

Butyllithium (1.6 mol dm^{-3} in hexane; 0.168 cm^3, 0.268 mmol) was added to a stirred solution of diisopropylamine (0.038 cm^3, 0.268 mmol) in THF (1.5 cm^3) at 0 °C followed, after 20 min at 0 °C, by the keto ester **27** (106 mg, 0.244 mmol) in THF (1 cm^3). After the solution had been stirred for 30 min and cooled to −78 °C, the aldehyde **12** (58 mg, 0.244 mmol) in THF (1 cm^3) was added to it. After the mixture had been stored for 1.5 h at −78 °C, saturated aqueous ammonium chloride (1 cm^3) was added to it and the whole was allowed to attain room

temperature. The organic and aqueous phases were separated and the latter was extracted with ether (4 × 1 cm^3). The combined organic extracts were washed with brine (1 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Chromatography of the residue with light petroleum–ethyl acetate–methanol (14:8:0.8) as eluent gave the *oxaphosphorinane* **34** (12 mg, 8%); ν_{max}/cm^{-1} 1715, 1463, 1389, 1279, 1252, 1088, 1035, 991, 963, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.26 and 1.27 (each 1.5 H, t, *J* 7, OCH_2CH_3), 1.31 and 1.33 (each 1.5 H, s, 7-CH_3), 1.58 (3 H, s, 16-CH_3), 1.71 (3 H, s, 10-CH_3), 1.69–1.88 (2 H, m, 5-H_2), 2.0–2.4 (6 H, m), 2.5–2.8 (3 H, m, 3-H and 8-H_2), 3.0 (1 H, ddd, *J* 17, 7, 2.5, 3-H′), 3.8 and 3.81 (each 1.5 H, d, *J* 11, OCH_3), 3.92–4.10 (4 H, m, OCH_2CH_2O), 4.0 (2 H, s, 17-H_2), 4.19 (2 H, m, OCH_2CH_3), 4.79 (1 H, m, 4-H), 5.16 (1 H, m, 9-H), 5.39 (1 H, m, 15-H), 5.6 (1 H, dt, *J* 10, 4.5, 12-H) and 6.02 and 6.03 (each 0.5 H, d, *J* 16, 11-H); *m/z* (FAB) 665 (M^+ + 23, 0.4%) and 643 (M^+ + 1, 1%); followed by the *title compound* **33** (98 mg, 60%) (Found: M^+ + H, 675.3713. $C_{33}H_{60}O_{10}PSi$ requires *M*, 675.3693); ν_{max}/cm^{-1} 3393, 1713, 1462, 1251, 1035, 963, 838 and 778; δ_H 0.01 [6 H, s, $Si(CH_3)_2$], 0.92 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, t, *J* 7, OCH_2CH_3), 1.12 and 1.13 (each 1.5 H, s, 7-CH_3), 1.54 (3 H, s, 16-CH_3), 1.68 (3 H, s, 10-CH_3), 2.0 (2 H, m, 5-H_2), 2.08 (4 H, m, 13-H_2 and 14-H_2), 2.22–2.73 (6 H, m), 3.21 (1 H, br s, OH), 3.7 [6 H, d, *J* 11, $P(OCH_3)_2$], 3.96 (2 H, s, 17-H_2), 4.00–4.06 (4 H, m, OCH_2CH_2O), 4.14 (2 H, q, *J* 7, OCH_2CH_3), 4.35 (1 H, m, 4-H), 5.18 (1 H, t, *J* 8, 9-H), 5.38 (1 H, m, 15-H), 5.55 (1 H, dt, *J* 16, 6, 12-H) and 5.98 (1 H, d, *J* 16, 11-H); *m/z* (FAB) 697 (M^+ + 23, 2%) and 675 (M^+ + 1, 1.5).

(4*RS*,6*SR*,9*E*,11*E*,15*E*)-17-(*tert*-Butyldimethylsilyloxy)-1-dimethylphosphinoyl-7-ethoxycarbonyl-2,2-ethylenedioxy-7,10,16-trimethylheptadeca-9,11,15-triene-4,6-diol 35

Dimethylmethoxyborane THF (0.144 cm^3, 0.144 mmol) was added to a solution of the hydroxy ketone **33** (87 mg, 0.129 mmol) in THF–methanol (5:1; 1.5 cm^3) at −78 °C. After 15 min, sodium borohydride (6 mg, 0.15 mmol) was added to the mixture which was then stirred at −78 °C for 5 h. After this, acetic acid (0.14 cm^3) was added to the reaction mixture at −78 °C and the whole poured into saturated aqueous sodium hydrogen carbonate (4 cm^3) and extracted with ethyl acetate (3 × 4 cm^3). The combined extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was taken up in methanol (4 cm^3) and the solvent removed under reduced pressure. This procedure was repeated 10 times. Flash chromatography with light petroleum–ethyl acetate–methanol (14:8:1), of the residue gave the *title compound* **35** (75 mg, 86%) as an inseparable mixture of diastereoisomers (Found: M^+ + H, 677.3844. $C_{33}H_{62}O_{10}PSi$ requires *M*, 677.3850); ν_{max}/cm^{-1} 3413, 1724, 1463, 1251, 1187, 1035, 964, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.15 (3 H, s, 7-CH_3), 1.23 (3 H, t, *J* 7, OCH_2CH_3), 1.58 (3 H, s, 16-CH_3), 1.7 (3 H, s, 10-CH_3), 1.95–2.6 (6 H, m, 3-H_2, 5-H_2, 8-H_2), 2.12 (4 H, m, 13-H_2, 14-H_2), 2.3 (2 H, d, *J* 18, 1-H_2), 3.72 [6 H, d, *J* 11, $P(OCH_3)_2$], 4.0 (2 H, s, 17-H_2), 4.1 (4 H, m, OCH_2CH_2O), 4.1–4.25 (4 H, m, OCH_2CH_3, 4-H and 6-H), 5.3 (1 H, t, *J* 8, 9-H), 5.4 (1 H, m, 15-H), 5.55 (1 H, dt, *J* 15, 6, 12-H) and 6.05 (1 H, d, *J* 15, 11-H); *m/z* (FAB) 699 (M^+ + 23, 2.5%).

(4*RS*,6*SR*,9*E*,11*E*,15*E*)-17-(*tert*-Butyldimethylsilyloxy)-1-dimethylphosphinoyl-7-ethoxycarbonyl-2,2-ethylenedioxy-4,6-isopropylidenedioxy-7,10,16-trimethylheptadeca-9,11,15-triene 36

2,2-Dimethoxypropane (0.07 cm^3, 0.56 mmol) and acetyl chloride (0.2 mm^3) were added to a solution of the diol **35** (38 mg, 0.056 mmol) in dichloromethane (1 cm^3) at 0 °C and, after 25 min, followed by saturated aqueous sodium hydrogen carbonate. The phases were separated and aqueous phase was extracted with dichloromethane (2 × 0.4 cm^3). The combined organic extracts were washed with brine (0.4 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography of the residue gave the *title compound* **36** (32 mg, 80%) as a colourless oil (Found: M^+ + H, 717.4176. $C_{36}H_{66}O_{10}SiP$ requires *M*, 717.4163); ν_{max}/cm^{-1} 1724, 1463, 1381, 1256, 1201, 1107, 1035, 965, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, s, 7-CH_3), 1.2 (3 H, m, OCH_2CH_3), 1.29 and 1.32 (each 1.5 H, s, CH_3), 1.38 (3 H, s, CH_3), 1.57 (3 H, s, 16-CH_3), 1.67 (3 H, s, 10-CH_3), 1.7–1.9 (4 H, m), 2.1 (4 H, m, 13-H_2 and 14-H_2), 2.3–2.5 (2 H, m, 8-H_2), 2.35 and 2.45 (each 1 H, d, *J* 18, 1-H), 3.7 [6 H, d, *J* 11, $P(OCH_3)_2$], 4.0 (2 H, s, 17-H_2), 3.9–4.2 (8 H, m, 4-H, 6-H, OCH_2CH_3, OCH_2CH_2O), 5.2 (1 H, t, *J* 7.5, 9-H), 5.35 (1 H, m, 15-H), 5.55 (1 H, dt, *J* 15, 6, 12-H) and 6.0 (1 H, d, *J* 15, 11-H); *m/z* (CI) 734 (M^+ + NH_4, 5.7%), 717 (M^+ + 1, 3.4%) and 195 (100).

(8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-3-hydroxy-6,9,15-trimethylhexadeca-1,8,10,14-tetraen-5-one 40

Butyllithium (1.6 mol dm^{-3} in hexane; 3.1 cm^3, 4.96 mmol) was added to a solution of diisopropylamine (0.7 cm^3, 4.96 mmol) in THF (13 cm^3) at 0 °C. After 20 min at 0 °C, the keto ester **27** (1.19 g, 2.73 mmol) in THF (6 cm^3) was added to the mixture which was then stirred for 30 min before being cooled to −78 °C. Acrolein (0.35 cm^3, 5.24 mmol) was added to the mixture which was then stirred for 1.5 h at −78 °C before the addition of saturated aqueous ammonium chloride (10 cm^3) and warming to room temperature. The organic and aqueous phases were separated and the latter was extracted with ether (4 × 10 cm^3). The combined extracts were washed with brine (7 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography of the residue with light petroleum–ether (80:20) gave the *title compound* **40** (1.01 g, 72%) (Found: M^+ + Na, 515.3165. $C_{28}H_{48}NaO_5Si$ requires *M*, 515.3169); ν_{max}/cm^{-1} 3527, 1713, 1463, 1378, 1252, 1110, 1068, 964, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.26 (3 H, t, *J* 7, OCH_2CH_3), 1.32 and 1.34 (each 1.5 H, s, 6-CH_3), 1.61 (3 H, s, 15-CH_3), 1.71 (3 H, s, 9-CH_3), 2.1 (4 H, m, 12-H_2 and 13-H_2), 2.64 (4 H, m, 4-H_2 and 7-H_2), 3.0 (1 H, br s, OH), 4.02 (2 H, s, 16-H_2), 4.17 (2 H, q, *J* 7, OCH_2CH_3), 4.55 (1 H, m, 3-H), 5.11 (1 H, d, *J* 10, 1-H), 5.16 (1 H, t, *J* 7.5, 8-H), 5.28 (1 H, dd, *J* 17, 1.5, 1-H′), 5.39 (1 H, m, 14-H), 5.58 (1 H, dt, *J* 15.5, 6.5, 11-H), 5.82 (1 H, ddd, *J* 17, 10, 5.5, 2-H), 6.03 (1 H, d, *J* 15.5, 10-H); *m/z* (FAB) 515 (M^+ + 23, 0.1%) and 493 (M^+ + 1, 0.26).

(3*SR*,5*RS*,6*SR*)- and (3*SR*,5*RS*,6*RS*)-(8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-6,9,15-trimethylhexadeca-1,8,10,14-tetraene-3,5-diols 41 and 42

Following the procedure outlined above for the synthesis of **35**, the hydroxy ketone **40** (0.95 g, 1.9 mmol) was reduced using sodium borohydride and dimethylmethoxyborane to give the diols **41** and **42** (0.9 g, 95%). Flash chromatography with light petroleum–ethyl acetate (85:15), gave the (3SR,5RS,6SR)-*isomer* **41** (Found: M^+ + Na, 517.3345. $C_{28}H_{50}NaO_5Si$ requires *M*, 517.3325); ν_{max}/cm^{-1} 3415, 1723, 1463, 1253, 1189, 964, 926, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.15 (3 H, s, 6-CH_3), 1.25 (3 H, t, *J* 7, OCH_2CH_3), 1.58 (3 H, s, 15-CH_3), 1.6 (2 H, m, 4-H_2), 1.72 (3 H, s, 9-CH_3), 2.12 (4 H, m, 12-H_2 and 13-H_2), 2.41 and 2.58 (each 1 H, dd, *J* 8, 14.5, 7-H), 2.9 (2 H, br s, 2 × OH), 4.02 (2 H, s, 16-H_2), 4.05 (1 H, m, 5-H), 4.14 (2 H, m, OCH_2CH_3), 4.38 (1 H, m, 3-H), 5.1 (1 H, d, *J* 10, 1-H), 5.27 (1 H, d, *J* 17, 1-H′), 5.32 (1 H, t, *J* 8, 8-H), 5.4 (1 H, m, 14-H), 5.6 (1 H, dt, *J* 15, 7, 11-H), 5.86 (1 H, ddd, *J* 17, 10, 6, 2-H) and 6.05 (1 H, d, *J* 15, 10-H); δ_C 176.8, 141, 136.5, 135.8, 135.7, 128.8, 125.3, 124.3, 115.4, 76.8, 74, 69.2, 61.6, 51.7, 38.8, 34.7, 33.6, 28.1, 26.2, 18.7, 17.8, 14.9, 14.1, 13.5 and

−5.02; *m/z* (FAB) 517 (M^+ + 23, 0.4%) and 495 (M^+ + 1, 0.2%); followed by the (3SR,5RS,6RS)-*isomer* **42** (Found: M^+ + H, 495.3525. $C_{28}H_{51}O_5Si$ requires *M*, 495.3506); ν_{max}/cm^{-1} 3430, 1723, 1252, 1191, 1110, 1071, 964, 925, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.18 (3 H, s, 6-CH_3), 1.27 (3 H, t, *J* 7, OCH_2CH_3), 1.54 (2 H, m, 4-H_2), 1.6 (3 H, s, 15-CH_3), 1.7 (3 H, s, 9-CH_3), 2.1 (4 H, m, 12-H_2 and 13-H_2), 2.42 and 2.48 (each 1 H, dd, *J* 7.5, 15, 7-H), 3.0 (2 H, br s, 2 × OH), 3.98 (1 H, m, 5-H), 4.02 (2 H, s, 16-H_2), 4.18 (2 H, q, *J* 7, OCH_2CH_3), 4.37 (1 H, m, 3-H), 5.12 (1 H, d, *J* 10, 1-H), 5.25 (1 H, m, 8-H), 5.3 (1 H, d, *J* 17, 1-H′), 5.4 (1 H, m, 14-H), 5.6 (1 H, dt, *J* 15, 7, 11-H), 5.85 (1 H, ddd, *J* 17, 10, 6, 2-H) and 6.05 (1 H, d, *J* 15, 10-H); δ_C 177.16, 140.9, 136.80, 135.22, 128.76, 124.39, 124.29, 115.14, 76.41, 73.87, 69.02, 61.46, 51.48, 37.91, 35.24, 33.28, 28.11, 26.43, 18.7, 17.89, 14.68, 13.97, 13.15 and −4.7; *m/z* (CI) 495 (M^+ + 1, 30%), 364 (54), 363 (100) and 345 (42).

(3*SR*,5*RS*,6*SR*,8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-3,5-isopropylidenedioxy-6,9,15-trimethylhexadeca-1,8,10,14-tetraene 43

Following the procedure outlined above for the synthesis of the acetonide **36**, the diol **41** (576 mg, 1.17 mmol) gave, after flash chromatography with light petroleum–ether (90:10) as eluent, the *title compound* **43** (612 mg, 98%) as an oil (Found: M^+ − C_4H_9, 477.3026. $C_{27}H_{45}O_5Si$ requires *M*, 477.3036); ν_{max}/cm^{-1} 1724, 1463, 1388, 1256, 1201, 1094, 990, 964, 923, 838 and 776; δ_H 0.08 [6 H, s, $Si(CH_3)_2$], 0.91 [9 H, s, $SiC(CH_3)_3$], 1.12 (3 H, s, 6-CH_3), 1.23 (3 H, t, *J* 7, OCH_2CH_3), 1.39 (2 H, m, 4-H_2), 1.4 and 1.44 (each 3 H, s, CH_3), 1.59 (3 H, s, 15-CH_3), 1.7 (3 H, s, 9-CH_3), 2.12 (4 H, m, 12-H_2 and 13-H_2), 2.39 and 2.52 (each 1 H, dd, *J* 7.5, 14.5, 7-H), 4.0 (2 H, s, 16-H_2), 4.1 (1 H, m, 5-H), 4.12 (2 H, q, *J* 7, OCH_2CH_3), 4.35 (1 H, m, 3-H), 5.11 (1 H, d, *J* 10, 1-H), 5.25 (1 H, d, *J* 17, 1-H′), 5.28 (1 H, t, *J* 8, 8-H), 5.4 (1 H, m, 14-H), 5.56 (1 H, dt, *J* 15.5, 7, 11-H), 5.8 (1 H, ddd, *J* 17, 10, 6, 2-H) and 6.04 (1 H, d, *J* 15, 10-H); δ_H 175.44, 139.15, 136.17, 135.56, 135.05, 128.06, 125.74, 124.39, 115.86, 99.32, 72.31, 70.75, 69.05, 60.88, 50.6, 35.34, 33.29, 32.08, 30.58, 28.18, 26.44, 20.14, 18.5, 16.74, 14.74, 13.96, 13.13 and −4.76; *m/z* (FAB) 519 (M^+ − 15, 0.3%) and 477 (M^+ − 57, 2.5).

(3*SR*,5*RS*,6*RS*,8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-3,5-isopropylidenedioxy-6,9,15-trimethylhexadeca-1,8,10,14-tetraene 44

Following the procedure outlined above for the synthesis of the acetonide **36**, the diol **42** gave the *title compound* **44** (Found: M^+ − C_4H_9, 477.3023. $C_{27}H_{45}SiO_5$ requires *M*, 477.3036); ν_{max}/cm^{-1} 1724, 1463, 1380, 1258, 1202, 1109, 1072, 990, 964, 924, 838 and 776; δ_H 0.07 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.13 (3 H, s, 6-CH_3), 1.23 (3 H, t, *J* 7, OCH_2CH_3), 1.37 (3 H, s, CH_3), 1.42 (2 H, m, 4-H_2), 1.43 (3 H, s, CH_3), 1.58 (3 H, s, 15-CH_3), 1.69 (3 H, s, 9-CH_3), 2.13 (4 H, m, 12-H_2 and 13-H_2), 2.22 and 2.4 (each 1 H, dd, *J* 14, 7, 7-H), 4.0 (2 H, s, 16-H_2), 4.1 (2 H, m, OCH_2CH_3), 4.15 (1 H, m, 5-H), 4.35 (1 H, m, 3-H), 5.12 (1 H, d, *J* 10, 1-H), 5.25 (1 H, m, 8-H), 5.26 (1 H, d, *J* 17, 1-H′), 5.39 (1 H, m, 14-H), 5.57 (1 H, dt, *J* 15, 7, 11-H), 5.84 (1 H, ddd, *J* 17, 10, 6, 2-H) and 6.04 (1 H, d, *J* 15, 10-H); δ_C 175.55, 139.18, 136.46, 135.37, 135.18, 128.35, 124.94, 124.36, 116.0, 99.26, 73.78, 70.88, 69.05, 60.82, 50.9, 34.23, 33.28, 31.40, 30.50, 28.14, 26.44, 20.03, 18.5, 16.18, 14.79, 13.97, 13.13 and −4.76; *m/z* (FAB) 519 (M^+ − 15, 2%) and 477 (M^+ − 57, 8).

(3*SR*,4*RS*,6*SR*)-3-[(2′*E*,4′*E*,8′*E*)-10′-(*tert*-Butyldimethylsilyloxy)-3′,9′-dimethyldeca-2′,4′,8′-trienyl]-4-hydroxy-3-methyl-6-vinyltetrahydropyran-2-one 45

Aqueous sodium hydroxide (0.5 mol dm^{-3}; 0.572 cm^3) was added to a solution of the dihydroxy ester **41** (120 mg, 0.243 mmol) in THF (2 cm^3) at 0 °C. After being stirred for 5 min at room temperature, the mixture was cooled at 0 °C and aqueous tartaric acid (12% w/v, 3.6 cm^3) was added to it. The organic and aqueous phases were separated and the latter was extracted with ethyl acetate (4 × 2 cm^3). The combined extracts were washed with brine (2 × 2 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure to give the dihydroxy acid. This was dissolved in benzene (10 cm^3) and the solution heated under reflux using a Dean-Stark trap for 16 h. Concentration under reduced pressure gave a residue which was flash chromatographed with light petroleum–ether (1:1) as eluent to give the *title compound* **45** (100 mg, 92%) (Found: M^+ + H, 449.3028. $C_{26}H_{45}O_4Si$ requires *M*, 449.3087); ν_{max}/cm^{-1} 3450, 1708, 1463, 1377, 1253, 1188, 1069, 1008, 964, 929, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.3 (3 H, s, 3-CH_3), 1.6 (3 H, s, 9′-CH_3), 1.72 (3 H, s, 3′-CH_3), 2.06 (2 H, m, 5-H_2), 2.10 (1 H, br s, OH), 2.14 (4 H, m, 6′-H_2 and 7′-H_2), 2.48 (2 H, d, *J* 7.5, 1′-H_2), 4.0 (3 H, m, 10′-H_2 and 4-H), 5.13 (1 H, q, *J* 6.5, 6-H), 5.23 (1 H, d, *J* 10, 2″-H), 5.35 (1 H, d, *J* 17, 2″-H′), 5.35 (1 H, m, 2′-H), 5.4 (1 H, m, 8′-H), 5.61 (1 H, dt, *J* 16, 6, 5′-H), 5.88 (1 H, ddd, *J* 17, 10, 5, 1″-H), 6.05 (1 H, d, *J* 16, 4′-H); *m/z* (FAB) 449 (M^+ + 1, 6%).

(3*RS*,4*RS*,6*SR*)-3-[(2′*E*,4′*E*,8′*E*)-10′-(*tert*-Butyldimethylsilyloxy)-3′,9′-dimethyldeca-2′,4′,8′-trienyl]-4-hydroxy-3-methyl-6-vinyltetrahydropyran-2-one 46

Following the above procedure, the dihydroxy ester **42** (48 mg, 0.097 mmol) gave the *title compound* **46** (37 mg, 85%) as an oil (Found: M^+ + NH_4, 466.3356. $C_{26}H_{48}NO_4Si$ requires *M*, 466.3352); ν_{max}/cm^{-1} 3437, 1709, 1462, 1369, 1253, 1187, 1068, 1007, 965, 929, 838 and 777; δ_H 0.05 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.28 (3 H, s, 3-CH_3), 1.6 (3 H, s, 9′-CH_3), 1.79 (3 H, s, 3′-CH_3), 2.01 (2 H, m, 5-H_2), 2.15 (4 H, m, 6′-H_2 and 7′-H_2), 2.2 (1 H, br s, OH), 2.68 (1 H, dd, *J* 16, 9, 1′-H), 2.72 (1 H, dd, *J* 16, 7, 1′-H′), 3.95 (1 H, m, 4-H), 4.0 (2 H, s, 10′-H_2), 5.18 (1 H, t, *J* 8, 6-H), 5.21 (1 H, d, *J* 10.5, 2″-H), 5.35 (1 H, d, *J* 17, 2″-H′), 5.4–5.55 (2 H, m, 2′-H and 8′-H), 5.62 (1 H, dt, *J* 15, 6, 5′-H), 5.89 (1 H, ddd, *J* 17, 10.5, 6, 1″-H) and 6.09 (1 H, d, *J* 15, 4′-H); *m/z* (CI) 466 (M^+ + NH_4, 33%), 449 (7), 352 (15), 335 (49) and 319 (50).

(3*SR*,6*SR*)-3-[(2′*E*,4′*E*,8′*E*)-10′-*tert*-(Butyldimethylsilyloxy)-3′,9′-dimethyldeca-2′,4′,8′-trienyl]-3-methyl-6-vinyltetrahydropyran-2,4-dione 47

The hydroxy lactone **45** (30 mg, 0.067 mmol) was oxidised using tetrapropylammonium perruthenate and *N*-methylmorpholine *N*-oxide following the procedure outlined above for the synthesis of **12**, to give the *title compound* **47** (23 mg, 77%) (Found: M^+ + NH_4, 464.3186. $C_{26}H_{46}NO_4Si$ requires *M*, 464.3196); ν_{max}/cm^{-1} 1756, 1723, 1456, 1376, 1254, 1116, 1086, 965, 938, 838 and 777; δ_H 0.09 [6 H, s, $Si(CH_3)_2$], 0.92 [9 H, s, $SiC(CH_3)_3$], 1.51 (3 H, s, 3-CH_3), 1.62 (3 H, s, 9′-CH_3), 1.73 (3 H, s, 3′-CH_3), 2.13 (4 H, m, 6′-H_2 and 7′-H_2), 2.54 (1 H, dd, *J* 16, 10, 5-H), 2.8 (3 H, m, 5-H′ and 1′-H_2), 4.05 (2 H, s, 10′-H_2), 5.0 (1 H, m, 6-H), 5.18 (1 H, t, *J* 7, 2′-H), 5.38 (1 H, d, *J* 10, 2″-H), 5.4 (1 H, m, 8′-H), 5.45 (1 H, d, *J* 16, 2″-H′), 5.63 (1 H, dt, *J* 15, 6, 5′-H), 5.92 (1 H, ddd, *J* 16, 10, 6, 1″-H) and 6.0 (1 H, d, *J* 15, 4′-H); *m/z* (CI) 464 (M^+ + NH_4, 20%), 447 (2) and 315 (64).

(3*RS*,6*SR*)-3-[(2′*E*,4′*E*,8′*E*)-10′-(*tert*-Butyldimethylsilyloxy)-3′,9′-dimethyldeca-2′,4′,8′-trienyl]-3-methyl-6-vinyltetrahydropyran-2,4-dione 48

The hydroxy lactone **46** was oxidised using tetrapropylammonium perruthenate and *N*-methylmorpholine *N*-oxide as outlined above for the synthesis of **12**, to give the *title compound* **48** (69%) (Found: M^+ + NH_4, 464.3188. $C_{26}H_{46}NO_4Si$ requires *M*, 464.3196); ν_{max}/cm^{-1} 1752, 1719, 1462, 1374, 1308,

1251, 1072, 964, 938, 838 and 776; δ_H 0.1 [6 H, s, $Si(CH_3)_2$], 0.95 [9 H, s, $SiC(CH_3)_3$], 1.46 (3 H, s, 3-CH_3), 1.62 (3 H, s, 9′-CH_3), 1.72 (3 H, s, 3′-CH_3), 2.17 (4 H, m, 6′-H_2 and 7′-H_2), 2.65–2.9 (4 H, m, 5-H_2 and 1′-H_2), 4.04 (2 H, s, 10′-H_2), 5.05 (1 H, m, 6-H), 5.26 (1 H, t, *J* 8, 2′-H), 5.38 (1 H, d, *J* 11, 2″-H), 5.41 (1 H, m, 8′-H), 5.43 (1 H, d, *J* 17, 2″-H′), 5.7 (1 H, dt, *J* 16, 6, 5′-H), 5.92 (1 H, ddd, *J* 17, 11, 5.5, 1″-H), 6.06 (1 H, d, *J* 16, 4′-H); *m/z* (CI) 464 ($M^+ + NH_4$, 8%), 389 (3) and 315 (28).

(3*RS*,5*RS*,6*SR*,8*E*,10*E*,14*E*)- and (3*RS*,5*RS*,6*RS*,8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-3,5-isopropylidenedioxy-6,9,15-trimethylhexadeca-8,10,14-trien-1-ol 49 and 53

9-Borabicyclononane (0.5 mol dm^{-3} in tetrahydrofuran; 0.73 cm^3, 0.38 mmol) was added dropwise over a period of 50 min to a solution of the alkene **43** (135 mg, 0.253 mmol) in the minimum amount of tetrahydrofuran at 30 °C and the mixture heated under reflux for 3 h. Water (0.62 cm^3) was added dropwise at room temperature to the mixture which was then stirred for 10 min. After being cooled to 0 °C, the mixture was treated with aqueous sodium hydroxide (3 mol dm^{-3}; 0.65 cm^3) and aqueous hydrogen peroxide (30%; 0.65 cm^3), and then stirred at 50 °C for 1 h. After this, water (3.2 cm^3) was added at room temperature to the mixture and the aqueous and organic phases were separated; the latter was then extracted with ether (3 × 5 cm^3). The combined extracts were washed with brine (2 × 2 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure. Flash column chromatography of the residue with light petroleum–ether (40:60) as eluent gave the (3*RS*,5*RS*,6*SR*,8*E*,10*E*,14*E*)-diastereoisomer of the *title compound* **49** (119 mg, 81%) as a colourless oil; ν_{max}/cm^{-1} 3462, 1724, 1472, 1463, 1381, 1252, 1201, 1166, 1108, 964, 838 and 776; δ_H 0.08 [6 H, s, $Si(CH_3)_2$], 0.91 [9 H, s, $SiC(CH_3)_3$], 1.13 (3 H, s, 6-CH_3), 1.23 (3 H, t, *J* 7, OCH_2CH_3), 1.3–1.45 (2 H, m, 4-H_2), 1.36 and 1.43 (each 3 H, s, H_3CCCH_3), 1.59 (3 H, s, 15-CH_3), 1.69 (3 H, s, 9-CH_3), 1.69 (2 H, m, 2-H_2), 2.12 (4 H, m, 12-H_2 and 13-H_2), 2.39 and 2.49 (each 1 H, dd, *J* 14.5, 7.5, 7-H), 2.56 (1 H, br s, OH), 3.76 (2 H, m, 1-H_2), 4.0 (2 H, s, 16-H_2), 4.09 (2 H, m, 3-H and 5-H), 4.12 (2 H, q, *J* 7, OCH_2CH_3), 5.26 (1 H, t, *J* 7.5, 8-H), 5.39 (1 H, m, 14-H), 5.57 (1 H, dt, *J* 15, 7, 11-H) and 6.05 (1 H, d, *J* 15, 10-H); δ_C 175.48, 136.24, 135.49, 135.16, 128.17, 125.67, 124.41, 99.37, 72.58, 70.08, 69.07, 61.49, 60.94, 50.6, 38.56, 35.30, 33.29, 31.98, 30.6, 28.19, 26.41, 20.19, 18.5, 16.75, 14.74, 13.97, 13.14 and −4.76; *m/z* (CI) 570 ($M^+ + NH_4$, 1%), 537 ($M^+ - 15$, 3) and 495 ($M^+ - 57$, 100).

The (3*RS*,5*RS*,6*RS*,8*E*,10*E*,14*E*)-diastereoisomer of the *title compound* **53** was similarly prepared; ν_{max}/cm^{-1} 3457, 1724, 1463, 1381, 1255, 1202, 1109, 964, 838 and 777; δ_H 0.07 [6 H, s, $Si(CH_3)_2$], 0.89 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, s, 6-CH_3), 1.2 (3 H, t, *J* 7, OCH_2CH_3), 1.31 (3 H, s, H_3CCCH_3), 1.33–1.43 (2 H, m, 4-H_2), 1.4 (3 H, s, H_3CCCH_3), 1.57 (3 H, s, 15-CH_3), 1.67 (3 H, s, 9-CH_3), 1.67–1.77 (2 H, m, 2-H_2), 2.06 (1 H, br s, OH), 2.1 (4 H, m, 12-H_2 and 13-H_2), 2.19 and 2.37 (1 H, dd, *J* 14.5, 7, 7-H), 3.76 (2 H, t, *J* 5, 1-H_2), 3.99 (2 H, s, 16-H_2), 4.0–4.2 (4 H, m, OCH_2CH_3, 3-H and 5-H), 5.22 (1 H, t, *J* 7.5, 8-H), 5.38 (1 H, m, 14-H), 5.55 (1 H, dt, *J* 15, 7, 11-H) and 6.02 (1 H, d, *J* 15, 10-H); δ_C 175.5, 136.48, 135.34, 135.18, 128.39, 124.92, 124.35, 99.27, 73.97, 69.95, 69.04, 61.34, 60.85, 50.86, 38.73, 34.21, 33.28, 31.29, 30.52, 28.14, 26.44, 20.08, 18.5, 16.28, 14.79, 13.97, 13.14 and −4.76; *m/z* (FAB) 537 ($M^+ - 15$, 0.4%) and 495 ($M^+ - C_4H_9$, 2.5).

(3*SR*,5*RS*,6*SR*,8*E*,10*E*,14*E*)- and (3*SR*,5*RS*,6*RS*,8*E*,10*E*,14*E*)-16-(*tert*-Butyldimethylsilyloxy)-6-ethoxycarbonyl-3,5-isopropylidenedioxy-6,9,15-trimethylhexadeca-8,10,14-trienal 50 and 54

Pyridinium chlorochromate (104 mg, 0.49 mmol) and powdered 4 Å molecular sieves (150 mg) were added to a stirred solution of alcohol **49** (110 mg, 0.2 mmol) in dichloromethane (2 cm^3) at 0 °C. After 1 h, the reaction mixture was filtered through a pad of Celite which was then washed with dichloromethane. The filtrate was concentrated under reduced pressure and quickly chromatographed on silica with ether–light petroleum (85:15) as eluent to give the (3*SR*,5*RS*,6*SR*,8*E*,10*E*,14*E*)-diastereoisomer of the *title compound* **50** (80 mg, 73%) as an oil; ν_{max}/cm^{-1} 1729, 1463, 1381, 1255, 1201, 1108, 964, 838 and 776; δ_H 0.06 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, s, 6-CH_3), 1.24 (3 H, t, *J* 7, OCH_2CH_3), 1.33 (3 H, s, H_3CCCH_3), 1.4 (2 H, m, 4-H_2), 1.44 (3 H, s, H_3CCCH_3), 1.6 (3 H, s, 15-CH_3), 1.7 (3 H, s, 9-CH_3), 2.12 (4 H, m, 12-H_2 and 13-H_2), 2.3–2.7 (4 H, m, 2-H_2 and 7-H_2), 4.0 (2 H, s, 16-H_2), 4.1 (3 H, q, *J* 7, OCH_2CH_3 overlapping 5-H), 4.4 (1 H, m, 3-H), 5.26 (1 H, t, *J* 8, 8-H), 5.4 (1 H, m, 14-H), 5.56 (1 H, dt, *J* 15, 7, 11-H), 6.06 (1 H, d, *J* 15, 10-H) and 9.75 (1 H, t, *J* 1.5, CHO); δ_C 201.41, 175.36, 136.28, 135.47, 135.18, 128.22, 125.57, 124.40, 99.55, 72.47, 69.07, 65.27, 60.98, 50.57, 50.31, 35.28, 33.30, 31.95, 30.43, 28.20, 26.45, 20.06, 18.6, 16.81, 14.65, 13.97, 13.15 and −4.75.

The (3*SR*,5*RS*,6*RS*,8*E*,10*E*,14*E*)-diastereoisomer of the *title compound* **54** was similarly prepared; ν_{max}/cm^{-1} 1729, 1463, 1381, 1255, 1202, 1110, 1069, 964, 838 and 777; δ_H 0.08 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.1 (3 H, s, 6-CH_3), 1.22 (3 H, t, *J* 7, OCH_2CH_3), 1.3 (3 H, s, H_3CCCH_3), 1.4 (2 H, m, 4-H_2), 1.42 (3 H, s, H_3CCCH_3), 1.58 (3 H, s, 15-CH_3), 1.68 (3 H, s, 9-CH_3), 2.12 (4 H, m, 12-H_2 and 13-H_2), 2.1–2.7 (4 H, m), 4.0 (2 H, s, 16-H_2), 4.02–4.22 (3 H, m, OCH_2CH_3 and 5-H), 4.4 (1 H, m, 3-H), 5.23 (1 H, t, *J* 8, 8-H), 5.38 (1 H, m, 14-H), 5.55 (1 H, dt, *J* 15, 7, 11-H), 6.04 (1 H, d, *J* 15, 10-H) and 9.77 (1 H, t, *J* 2, 1-H).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)- and (4*SR*,6*RS*,7*RS*,9*E*,11*E*,15*E*)-17-(*tert*- Butyldimethylsilyloxy)-1-dimethylphosphinoyl-7-ethoxycarbonyl-4,6-isopropylidenedioxy-7,10,16-trimethylheptadeca-9,11,15-trien-2-ol 51 and 55

Butyllithium (1.6 mol dm^{-3} in hexane; 0.403 cm^3, 0.65 mmol) was added to a solution of dimethyl methylphosphonate (0.068 cm^3, 0.63 mmol) in tetrahydrofuran (2.5 cm^3) at −78 °C. The mixture was stirred at −78 °C for 1 h after which a cooled (−78 °C) solution of aldehyde **50** (289 mg, 0.525 mmol) in tetrahydrofuran (2.5 cm^3) was added to it. The resulting mixture was stirred at −78 °C for 1 h, after which it was treated with saturated aqueous ammonium chloride (2.5 cm^3) and allowed to warm to room temperature. The organic and aqueous phases were separated and the latter was extracted with ether (3 × 3 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure, and chromatography of the residue with light petroleum–ethyl acetate–methanol (14:8:0.8) as eluent gave the (4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-diastereoisomer of the *title compound* **51** (272 mg, 77%) as an inseparable mixture of epimers at C(2) (Found: $M^+ - C_4H_9$, 617.3283. $C_{30}H_{54}O_9PSi$ requires *M*, 617.3275); ν_{max}/cm^{-1} 3381, 1724, 1463, 1381, 1251, 1039, 964, 839 and 776; δ_H 0.02 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, $SiC(CH_3)_3$], 1.11 (3 H, s, 7-CH_3), 1.22 (3 H, t, *J* 7, OCH_2CH_3), 1.35 (2 H, m, 5-H_2), 1.37 (3 H, s, H_3CCCH_3), 1.42 and 1.44 (each 1.5 H, s, H_3CCCH_3), 1.6 (3 H, s, 16-CH_3), 1.69 (3 H, s, 10-CH_3), 1.88–2.06 (4 H, m, 1-H_2 and 3-H_2), 2.14 (4 H, m, 13-H_2 and 14-H_2), 2.3–2.58 (2 H, m, 8-H_2), 3.78 (6 H, d, *J* 10, OCH_3), 4.0 (2 H, s, 17-H_2), 4.1 (2 H, q, *J* 7, OCH_2CH_3), 4.05–4.3 (3 H, m, 2-H, 4-H and 6-H), 5.25 (1 H, t, *J* 7, 9-H), 5.4 (1 H, m, 15-H), 5.57 (1 H, dt, *J* 15, 7, 12-H) and 6.05 (1 H, d, *J* 15, 11-H); *m/z* (FAB) 697 ($M^+ + 23$, 10%), 675 ($M^+ + 1$, 5) and 617 ($M^+ - 57$, 20).

The (4*SR*,6*RS*,7*RS*,9*E*,11*E*,15*E*)-diastereoisomer of the *title compound* **55** was similarly prepared as a mixture of epimers at C(2); ν_{max}/cm^{-1} 3392, 1724, 1463, 1381, 1255, 1035, 839 and 777; δ_H 0.08 [6 H, s, $Si(CH_3)_2$], 0.9 [9 H, s, SiC-

$(CH)_3)_3$], 1.15 (3 H, s, 7-CH_3), 1.26 (3 H, t, *J* 7, OCH_2CH_3), 1.36 (3 H, s, H_3CCCH_3), 1.4 (2 H, m, 5-H_2), 1.4 and 1.46 (each 1.5 H, s, H_3CCCH_3), 1.63 (3 H, s, 16-CH_3), 1.72 (3 H, s, 10-CH_3), 1.75–2.15 (4 H, m, 1-H_2 and 3-H_2), 2.13 (4 H, m, 13-H_2 and 14-H_2), 2.23 and 2.43 (each 1 H, dd, *J* 14, 7.5, 8-H), 3.79 (6 H, d, *J* 10, OCH_3), 4.03 (2 H, s, 17-H_2), 4.05–4.30 (4 H, m, 2-H, 4-H and OCH_2CH_3), 5.27 (1 H, t, *J* 7, 9-H), 5.43 (1 H, m, 15-H), 5.61 (1 H, dt, 15, 6, 12-H) and 6.07 (1 H, d, *J* 15, 11-H).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)- and (4*SR*,6*RS*,7*RS*,9*E*,11*E*,15*E*)-1-Dimethylphosphinoyl-7-ethoxycarbonyl-4,6-isopropylidenedioxy-7,10,16-trimethylheptadeca-9,11,15-triene-2,17-diol 52 and 56

Anhydrous tetrabutylammonium fluoride (1 mol dm^{-3} in tetrahydrofuran; 0.184 cm^3, 0.184 mmol) was added dropwise to a solution of the phosphonate **51** (62 mg, 0.092 mmol) in tetrahydrofuran (1 cm^3) and the mixture stirred at room temperature for 2 h. After concentration under reduced pressure, chromatography of the residue with light petroleum–ethyl acetate–methanol (6:3:1) as eluent, gave the (4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-diastereoisomer of the *title compound* **52** (49 mg, 95%) (Found: M^+ + Na, 583.3012. $C_{28}H_{49}NaO_9P$ requires *M*, 583.3012); ν_{max}/cm^{-1} 3398, 1723, 1461, 1381, 1200, 1036 and 850; δ_H 1.1 (3 H, s, 7-CH_3), 1.25 (3 H, t, *J* 7, OCH_2CH_3), 1.3–1.45 (2 H, m, 5-H_2), 1.36 (3 H, s, H_3CCCH_3), 1.42 and 1.45 (each 1.5 H, s, H_3CCCH_3), 1.67 (3 H, s, 16-CH_3), 1.7 (3 H, s, 10-CH_3), 1.7–2.1 (4 H, m, 1-H_2 and 3-H_2), 2.15 (4 H, m, 13-H_2 and 14-H_2), 2.3–2.55 (2 H, m, 8-H_2), 3.75 (6 H, d, *J* 10, OCH_3), 3.99 (2 H, s, 17-H_2), 4.12 (2 H, q, *J* 7, OCH_2CH_3), 4.05–4.3 (3 H, m, 2-H, 4-H, 6-H), 5.28 (1 H, t, *J* 7, 9-H), 5.41 (1 H, m, 15-H), 5.55 (1 H, dt, *J* 16, 6.5, 12-H), 6.05 (1 H, d, *J* 15, 11-H); *m/z* (FAB) 583 (M^+ + 23, 9%), 561 (M^+ + 1, 2%) and 503 (16).

The (4*SR*,6*RS*,7*RS*,9*E*,11*E*,15*E*)-diastereoisomer of the *title compound* **56** was similarly prepared; ν_{max}/cm^{-1} 3397, 1724, 1426, 1381, 1202, 1036 and 846; δ_H 1.15 (3 H, s, 7-CH_3), 1.25 (3 H, t, *J* 7, OCH_2CH_3), 1.3–1.5 (2 H, m, 5-H_2), 1.34 (3 H, s, H_3CCCH_3), 1.42 and 1.44 (each 1.5 H, s, H_3CCCH_3), 1.69 (3 H, s, 16-CH_3), 1.72 (3 H, s, 10-CH_3), 1.75–2.1 (4 H, m, 1-H_2 and 3-H_2), 2.15 (4 H, m, 13-H_2 and 14-H_2), 2.2 (1 H, dd, *J* 14, 8, 8-H), 2.43 (1 H, dd, *J* 14, 7, 8-H), 3.65 (1 H, br s, OH), 3.78 (6 H, d, *J* 10, OCH_3), 3.9 (1 H, br s, OH), 4.01 (2 H, s, 17-H_2), 4.05–4.3 (5 H, overlapping m, OCH_2CH_3, 2-H, 4-H and 6-H), 5.28 (1 H, t, *J* 8, 9-H), 5.43 (1 H, m, 15-H), 5.58 (1 H, dt, *J* 16, 7, 12-H) and 6.05 (1 H, d, *J* 16, 11-H); *m/z* (FAB) 583 (M^+ + 23, 8%), 561 (M^+ + 1, 6), 503 (52) and 325 (100).

(4*SR*,6*RS*,7*SR*,2*E*,6*E*,8*E*)- and (4*SR*,6*RS*,7*RS*,2*E*,6*E*,8*E*)-17-Dimethylphosphinoyl-11-ethoxycarbonyl-12,14-isopropylidenedioxy-2,8,11-trimethyl-16-oxoheptadeca-2,6,8-trienal 7 and 57

The diol **52** (49 mg, 0.0875 mmol) was dissolved in dichloromethane (1.3 cm^3) containing powdered 4 Å molecular sieves (130 mg) and *N*-methylmorpholine *N*-oxide (39 mg, 0.33 mmol) and tetrapropylammonium perruthenate (5.4 mg, 0.014 mmol) were added to the mixture. After being stirred at room temperature for 45 min work-up and chromatography with light petroleum–ethyl acetate–methanol (6:3:1) as eluent gave the (4*SR*,6*RS*,7*SR*,2*E*,6*E*,8*E*)-diastereoisomer of the *title compound* **7** (33 mg, 69%) as a colourless oil (Found: M^+ + H, 557.2872. $C_{28}H_{46}O_9P$ requires *M*, 557.2879); ν_{max}/cm^{-1} 1719, 1687, 1644, 1448, 1381, 1261, 1191, 1098, 1034 and 976; $\delta_H(C_6D_6)$ 1.07 (3 H, t, *J* 7, OCH_2CH_3), 1.37 and 1.39 (each 3 H, s, H_3CCCH_3), 1.48 (3 H, s, 11-CH_3), 1.5–1.6 (2 H, m, 13-H_2), 1.7 (3 H, s, 2-CH_3), 1.82 (3 H, s, 8-CH_3), 2.03 (4 H, m, 4-H_2 and 5-H_2), 2.55–2.89 (4 H, m, 10-H_2 and 15-H_2), 2.88 (2 H, d, *J* 22, 17-H_2), 3.42 and 3.44 (each 3 H, d, *J* 11, OCH_3), 4.06 (2 H, q, *J* 7, OCH_2CH_3), 4.28 (1 H, dd, *J* 11, 3, 12-H), 4.43 (1 H, m, 14-H), 5.49 (1 H, dt, *J* 15, 6, 6-H), 5.71 (1 H, t, *J* 7.5, 9-H), 5.9 (1 H, m, 3-H), 6.2 (1 H, d, *J* 15, 7-H) and 9.3 (1 H, s, 1-H); δ_C 199 (d, *J* 5), 194.43, 174.83, 152.74, 140.04, 136.91, 136.13, 127.35, 126.61, 99.58, 73.26, 66.28, 60.88, 52.89, 52.77, 50.91, 50.77, 42.81 (d, *J* 131), 35.62, 32.13, 32.08, 30.6, 29.37, 19.97, 17.35, 14.75, 13.32 and 9.69; *m/z* (FAB) 579 (M^+ + 23, 12%), 557 (M^+ + 1, 22), 499 (50), 481 (45), 415 (39) and 305 (50).

The (4*SR*,6*RS*,7*RS*,2*E*,6*E*,8*E*)-diastereoisomer of the *title compound* **57** was similarly prepared (Found: M^+ + H, 557.2860. $C_{28}H_{46}O_9P$ requires *M*, 557.2880); ν_{max}/cm^{-1} 1719, 1686, 1644, 1463, 1382, 1262, 1202, 1109, 1034, 980, 874 and 810; δ_H 1.08 (3 H, s, 11-CH_3), 1.18 (3 H, t, *J* 7, OCH_2CH_3), 1.23 and 1.35 (each 3 H, s, H_3CCCH_3), 1.25–1.5 (2 H, m, 13-H_2), 1.64 (3 H, s, 2-CH_3), 1.69 (3 H, s, 8-CH_3), 2.1–2.45 (6 H, m, 4-H_2, 5-H_2 and 15-H_2), 2.63 (1 H, dd, *J* 17, 5, 10-H), 2.79 (1 H, dd, *J* 17, 7, 10-H), 3.1 (2 H, dd, *J* 23, 3, 17-H_2), 3.74 and 3.75 (each 3 H, d, *J* 11, OCH_3), 3.99–4.15 (3 H, m, OCH_2CH_3 and 12-H), 4.3 (1 H, m, 14-H), 5.24 (1 H, t, *J* 7, 9-H), 5.49 (1 H, dt, *J* 15, 7, 6-H), 6.0 (1 H, d, *J* 15, 7-H), 6.55 (1 H, t, *J* 7, 3-H) and 9.32 (1 H, s, 1-H); δ_C 200.49 (d, *J* 6), 195.71, 175.31, 154.31, 140.03, 136.38, 136.09, 126.49, 125.83, 99.32, 73.74, 66.12, 60.82, 53.55, 53.42, 50.78, 42.55 (d, *J* 127), 34.15, 31.90, 31.0, 30.38, 30.31, 29.43, 19.88, 16.19, 14.73, 13.09 and 9.72; *m/z* (CI) 574 (M^+ + 18, 10%), 557 (M^+ + 1, 22) and 499 (100).

(13*SR*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)- and (13*RS*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-13-Ethoxycarbonyl-14,16-isopropylidenedioxy-4,10,13-trimethylcycloheptadecatetra-2,4,8,10-en-1-one 8 and 58

The aldehyde phosphonate **7** (40 mg, 0.072 mmol) in toluene (4.5 cm^3) was added dropwise over 1 h to a stirred suspension of potassium carbonate (61 mg, 0.44 mmol) and 18-crown-6 (231 mg, 0.87 mmol) in toluene (48 cm^3) at 100 °C. After the mixture had been stirred for 15 h it was allowed to cool to room temperature, when saturated aqueous ammonium chloride (5 cm^3) was added to it. After separation of the phases, the aqueous phase was extracted with ether (3 × 5 cm^3). The combined extracts were washed with saturated aqueous potassium chloride (5 × 10 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (1:1) as eluent gave the (13*SR*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-diastereoisomer of the *title compound* **8** (11 mg, 37%) (Found: M^+ + H, 431.2783. $C_{26}H_{39}O_5$ requires *M*, 431.2797); ν_{max}/cm^{-1} 1729, 1687, 1649, 1626, 1460, 1379, 1239, 1201, 1165, 1095 and 972; $\delta_H(C_6D_6)$ 0.96 (3 H, s, 13-CH_3), 0.99 (3 H, t, *J* 7, OCH_2CH_3), 1.34 and 1.39 (each 3 H, s, H_3CCCH_3), 1.3–1.5 (2 H, m, 15-H_2), 1.51 (3 H, s, 4-CH_3), 1.63 (3 H, s, 10-CH_3), 1.82–2.06 (4 H, m, 6-H_2 and 7-H_2), 2.72 (1 H, dd, *J* 12, 4.5, 17-H), 2.72–2.76 (1 H, m, 12-H), 3.16 (1 H, dd, *J* 16, 7, 12-H), 3.22 (1 H, dd, *J* 12, 8.5, 17-H), 4.0 (2 H, m, OCH_2CH_3), 4.21 (1 H, dd, *J* 11.5, 2, 14-H), 4.27 (1 H, m, 16-H), 5.16 (1 H, dt, *J* 15, 7, 8-H), 5.4 (1 H, t, *J* 7, 5-H), 5.52 (1 H, t, *J* 8, 11-H), 5.75 (1 H, d, *J* 15, 9-H), 6.22 (1 H, d, *J* 16, 2-H) and 7.08 (1 H, d, *J* 16, 3-H); $\delta_C(C_6D_6)$, 198.8, 176.1, 150.27, 144.28, 139.67, 134.8, 134.2, 127.12, 123.60, 99.9, 74.64, 69.56, 60.93, 50.02, 45.15, 32.45, 31.11, 30.8, 27.86, 20.09, 14.69, 13.04 and 12.45; *m/z* (EI) 431 (M^+ + 1, 31%), 372 (26) and 308 (11).

The (13*RS*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-diastereoisomer of the *title compound* **58** was similarly prepared (Found: M^+ + H, 431.2795. $C_{26}H_{39}O_5$ requires *M*, 431.2797); ν_{max}/cm^{-1} 1733, 1682, 1651, 1625, 1591, 1445, 1380, 1241, 1201, 1171, 1097, 1032, 980 and 876; $\delta_H(C_6D_6)$ 1.06 (3 H, t, *J* 7, OCH_2CH_3), 1.4–1.62 (2 H, m, 15-H_2), 1.39 (3 H, s, 13-CH_3), 1.44 and 1.46 (each 3 H, s, H_3CCCH_3), 1.55 (3 H, s, 4-CH_3), 1.63 (3 H, s, 10-CH_3), 1.8–2.16 (4 H, m, 6-H_2 and 7-H_2), 2.54 (1 H, dd, *J* 16, 8, 12-H), 2.59 (1 H, dd, *J* 16, 6.5, 12-H), 2.88 (1 H, dd, *J* 12, 5, 17-H), 3.01 (1 H, dd, *J* 12, 9, 17-H), 4.06 (2 H, m, OCH_2CH_3), 4.36 (1 H, dd, *J* 11.5, 2, 14-H), 4.38 (1 H, m, 6-H), 5.25 (1 H, dt, *J* 16, 7.5, 8-H), 5.32 (1 H, br t, *J* 7, 11-H), 5.52 (1 H, br t, *J* 8, 5-H), 5.71 (1 H, d,

J 16, 9-H), 6.16 (1 H, d, *J* 16, 2-H) and 7.21 (1 H, d, *J* 16, 3-H); $\delta_C(C_6D_6)$ 197.93, 175.73, 148.69, 143.09, 139.07, 135.39, 134.70, 127.48, 126.24, 124.29, 99.63, 73.78, 68.65, 60.75, 51.13, 47.98, 35.03, 33.93, 30.82, 27.91, 20.07, 19.30, 14.69, 12.89 and 12.72; *m/z* (CI) 431 ($M^+ + 1$, 68%) and 373 (100).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-17-(*tert*-Butyldimethylsilyloxy)-7-ethoxycarbonyl-4,6-isopropylidenedioxy-7,9,15-trimethyl-1-phenylsulfonylheptadeca-9,11,15-trien-2-ol 59

Butyllithium (1.6 mol dm^{-3} in hexane; 0.074 cm^3, 0.12 mmol) was added to diisopropylamine (0.018 cm^3, 0.123 mmol) in anhydrous tetrahydrofuran (0.3 cm^3) at 0 °C. After 20 min the mixture was cooled to −78 °C when methyl phenyl sulfone (18 mg, 0.115 mmol) in tetrahydrofuran (0.1 cm^3) was added dropwise to it. After 1 h, a cooled (−78 °C) solution of the aldehyde **50** (48 mg, 0.087 mmol) in tetrahydrofuran (0.1 cm^3) was added followed, after a further 45 min, by saturated aqueous ammonium chloride (0.1 cm^3) the mixture was then allowed to attain room temperature. The aqueous and organic phases were separated and the aqueous phase was extracted with ether (3 × 0.1 cm^3). The combined extracts were washed with brine (0.1 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **59** (56 mg, 90%) as a mixture of epimers at C(2) (Found: $M^+ + Na$, 729.3850. $C_{38}H_{62}NaO_8SSi$ requires *M*, 729.3833); ν_{max}/cm^{-1} 3517, 1724, 1448, 1382, 1307, 1254, 1148, 1105, 965, 838 and 777; δ_H 0.1 [6 H, s, $Si(CH_3)_2$], 0.94 [9 H, s, $SiC(CH_3)_3$], 1.12 (3 H, s, 7-CH_3), 1.27 and 1.28 (each 1.5 H, t, *J* 7, $OCHCH_3$), 1.30 (2 H, m, 5-H_2), 1.32 and 1.41 (each 3 H, s, H_3CCCCH_3), 1.62 (3 H, s, 15-CH_3), 1.73 (3 H, s, 10-CH_3), 1.7–1.83 (2 H, m, 3-H_2), 2.17 (4 H, s, 13-H_2 and 14-H_2), 2.41 (1 H, dd, *J* 15, 8, 8-H), 2.50 (1 H, dd, *J* 15, 7.5, 8-H), 3.3 (2 H, m, 1-H_2), 3.78 (1 H, br s, OH), 4.05 (2 H, s, 17-H_2), 4.08–4.2 (4 H, m, OCH_2CH_3, 4-H and 6-H), 4.39 (1 H, m, 2-H), 5.29 (1 H, t, *J* 7, 9-H), 5.44 (1 H, m, 15-H), 5.62 (1 H, dt, *J* 15.5, 6.5, 12-H), 6.08 (1 H, d, *J* 15.5, 11-H), 7.58–7.75 (3 H, m, ArH) and 7.93–8.01 (2 H, m, ArH); *m/z* (FAB) 729 ($M^+ + Na$, 7%), 649 (8), 517 (12) and 449 (9).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-17-(*tert*-Butyldimethylsilyloxy)-7-ethoxycarbonyl-4,6-isopropylidenedioxy-7,9,15-trimethyl-1-phenylsulfonylheptadeca-9,11,15-trien-2-one 60

Dimethyl sulfoxide (32 mm^3) in dichloromethane (0.2 cm^3) was added to oxalyl chloride (19 mm^3) in dichloromethane (1 cm^3) at −70 °C followed by the alcohol **59** (133 mg, 0.19 mmol). After 1 h, diisopropylethylamine (167 cm^3) was added to the mixture which was then allowed to warm to room temperature. After water (1 cm^3) had been added to the mixture it was extracted with dichloromethane to give, after work-up and chromatography using light petroleum–ethyl acetate (4:1) as eluent, the *title compound* **60** (55 mg, 41%) (Found: $M^+ + Na$, 727.3663. $C_{38}H_{60}NaO_8SSi$ requires *M*, 727.3676); ν_{max}/cm^{-1} 1723, 1382, 1326, 1252, 1157, 1104, 965, 838 and 776; δ_H 0.01 [6 H, s, $Si(CH_3)_2$], 0.94 [9 H, s, $SiC(CH_3)_3$], 1.14 (3 H, s, 7-CH_3), 1.28 (3 H, t, *J* 7, OCH_2CH_3), 1.3–1.4 (2 H, m, 5-H_2), 1.35 and 1.39 (each 3 H, s, H_3CCCCH_3), 1.62 (3 H, s, 15-CH_3), 1.73 (3 H, s, 10-CH_3), 2.15 (4 H, s, 13-H_2 and 14-H_2), 2.41 and 2.52 (each 1 H, dd, *J* 14, 8, 8-H), 2.73 (1 H, dd, *J* 16, 4, 3-H), 2.89 (1 H, dd, *J* 16, 7.5, 3-H), 4.05 (2 H, s, 17-H_2), 4.13 (1 H, m, 6-H), 4.13 (2 H, q, *J* 7, OCH_2CH_3), 4.24 (2 H, s, 1-H_2), 4.3–4.38 (1 H, m, 4-H), 5.29 (1 H, t, *J* 7.5, 9-H), 5.43 (1 H, m, 15-H), 5.61 (1 H, dt, *J* 15, 6.5, 12-H), 6.07 (1 H, d, *J* 15, 11-H), 7.59–7.75 (3 H, m, ArH) and 7.9–7.95 (2 H, m, ArH); δ_C 197.08, 174.82, 136.28, 135.46, 134.74, 129.78, 128.80, 128.21, 125.54, 124.40, 99.52, 72.44, 69.08, 68.13, 66.40, 60.98, 50.67, 50.57, 35.24, 33.29, 31.66, 30.30, 28.20, 26.44, 19.99, 18.25, 16.78, 14.74, 13.89, 13.13 and −4.77; *m/z* (FAB) 727 ($M^+ + 23$, 1%), 689 (2), 647 (20) and 199 (100).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-7-Ethoxycarbonyl-17-hydroxy-4,6-isopropylidenedioxy-7,9,15-trimethyl-1-phenylsulfonylheptadeca-9,11,15-trien-2-one 61

Treatment of the *tert*-butyldimethylsilyl ether **60** (60 mg, 0.085 mmol) with tetrabutylammonium fluoride as outlined above for the synthesis of **52** gave, after chromatography using light petroleum–ethyl acetate (1:1) as eluent, the *title compound* **61** (40 mg, 80%); ν_{max}/cm^{-1} 3533, 1723, 1448, 1382, 1325, 1264, 1198, 1157, 1099, 975, 742 and 689; δ_H 1.14 (3 H, s, 7-CH_3), 1.28 (3 H, t, *J* 7, OCH_2CH_3), 1.35 (3 H, s, H_3CCCCH_3), 1.33–1.40 (2 H, m, 5-H_2), 1.39 (3 H, s, H_3CCCCH_3), 1.55 (1 H, br s, OH), 1.7 (3 H, s, 15-CH_3), 1.74 (3 H, s, 10-CH_3), 2.17 (4 H, m, 13-H_2 and 14-H_2), 2.43 and 2.52 (each 1 H, dd, *J* 14.5, 7.5, 8-H), 2.75 (1 H, dd, *J* 16, 4, 3-H), 2.88 (1 H, dd, *J* 16, 8, 3-H), 4.03 (2 H, br s, 17-H_2), 4.06–4.11 (1 H, m, 6-H), 4.16 (2 H, q, *J* 7, OCH_2CH_3), 4.25 (2 H, s, 1-H_2), 4.33 (1 H, m, 4-H), 5.31 (1 H, t, *J* 7, 9-H), 5.47 (1 H, m, 15-H), 5.6 (1 H, dt, *J* 15, 7, 12-H), 6.08 (1 H, d, *J* 15, 11-H), 7.6–7.76 (3 H, m, ArH) and 7.91–7.95 (2 H, m, ArH); δ_C 197.08, 175.29, 139.26, 136.2, 135.62, 134.76, 129.79, 128.80, 127.92, 126.0, 125.73, 99.52, 72.41, 69.36, 68.08, 66.36, 61.07, 50.66, 50.57, 35.22, 33.17, 31.63, 30.38, 28.24, 19.99, 16.83, 14.74, 14.23 and 13.15; *m/z* (FAB) 589 (M − 1, 15%), 565 (9), 549 (27) and 531 (100).

(4*SR*,6*RS*,7*SR*,9*E*,11*E*,15*E*)-17-Acetoxy-7-ethoxycarbonyl-4,6-isopropylidenedioxy-7,9,15-trimethyl-1-phenylsulfonylheptadeca-9,11,15-trien-2-one 64

Acetic anhydride (0.051 cm^3, 0.53 mmol) was added to a solution of the alcohol **61** (74 mg, 0.125 mmol), pyridine (0.03 cm^3, 0.37 mmol) and a catalytic amount of 4-dimethylaminopyridine in dichloromethane (2 cm^3) at −10 °C. After 15 min, the reaction mixture was poured into saturated aqueous ammonium chloride (0.5 cm^3). The aqueous phase was separated and extracted with dichloromethane (3 × 1 cm^3) and the combined organic extracts were washed with brine (2 × 1 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **64** (64 mg, 80%) as a colourless oil; ν_{max}/cm^{-1} 1728, 1448, 1381, 1326, 1240, 1157, 1025, 975 and 743; δ_H 1.13 (3 H, s, 7-CH_3), 1.28 (3 H, t, *J* 7, OCH_2CH_3), 1.36 (2 H, m, 5-H_2), 1.35 and 1.4 (each 3 H, s, H_3CCCCH_3), 1.69 (3 H, s, 15-CH_3), 1.73 (3 H, s, 10-CH_3), 2.11 (3 H, s, O_2CCH_3), 2.18 (4 H, m, 13-H_2 and 14-H_2), 2.41 and 2.53 (each 1 H, dd, *J* 15, 8, 8-H), 2.75 (1 H, dd, *J* 16, 4, 3-H), 2.98 (1 H, dd, *J* 16, 7.5, 3-H), 4.09 (1 H, m, 6-H), 4.15 (2 H, q, *J* 7, OCH_2CH_3), 4.25 (2 H, s, 1-H_2), 4.33 (1 H, m, 4-H), 4.48 (2 H, s, 17-H_2), 5.31 (1 H, t, *J* 7.5, 9-H), 5.52 (1 H, m, 15-H), 5.58 (1 H, m, 12-H), 6.08 (1 H, d, *J* 15, 11-H), 7.57–7.75 (3 H, m, ArH) and 7.9–7.95 (2 H, m, ArH); δ_C 197.07, 175.24, 171.24, 139.31, 136.16, 135.71, 134.73, 130.84, 129.77, 129.56, 128.78, 127.67, 125.81, 99.50, 72.41, 70.70, 68.03, 66.32, 60.98, 50.64, 50.55, 35.21, 32.91, 31.62, 30.37, 28.35, 21.49, 19.98, 16.79, 14.72, 14.48 and 13.12; *m/z* (FAB) 649 ($M^+ + 23$, 0.4%), 633 ($M^+ + 1$, 1.1), 591 (7) and 575 (6).

(13*SR*,14*RS*,16*SR*,4*E*,8*E*,10*E*)-13-Ethoxycarbonyl-14,16-isopropylidenedioxy-2-phenylsulfonyl-4,10,13-trimethylcycloheptadeca-4,8,10-trien-1-one 65

O,*N*-Bis(trimethylsilyl)acetamide (0.028 cm^3, 0.1 mmol) was added dropwise to the acetate **64** (35 mg, 0.055 mmol) under argon followed by degassed tetrahydrofuran (5.2 cm^3). The system was evacuated and re-filled with argon 6 times. The mixture was heated under reflux for 3 h and then cooled to room temperature. Degassed tetrahydrofuran (5.2 cm^3) was added to tetrakis(triphenylphosphine)palladium(0) (4 mg, 0.0034 mmol) and 1,3-bis(diphenylphosphine)propane (3 mg, 0.0073 mmol) under argon, after which the system was evacuated and re-filled with argon 6 times. The solution was heated under reflux for 1 h, after which the solution of the silylated acetate **64** was added to it. The mixture was heated

under reflux for 19 h, before being concentrated under reduced pressure. Chromatography of the residue using light petroleum–ether (7:3) as eluent, gave the *title compound* **65** (6 mg, 18%) (Found: $M^+ + H$, 573.2881. $C_{32}H_{45}O_7S$ requires *M*, 573.2886); ν_{max}/cm^{-1} 1724, 1448, 1381, 1310, 1240, 1198, 1151, 1110, 982, 966 and 733; δ_H 1.18 (3 H, s, 13-CH_3), 1.22 (3 H, t, *J* 7, OCH_2CH_3), 1.28 (2 H, m, 15-H_2), 1.28 and 1.34 (each 3 H, s, H_3CCCH_3), 1.53 (3 H, s, 4-CH_3), 1.7 (3 H, s, 10-CH_3), 1.96–2.3 (4 H, m, 6-H_2 and 7-H_2), 2.17 (1 H, m, 12-H), 2.24 (1 H, dd, *J* 19, 9, 17-H), 2.39 (1 H, dd, *J* 14, 10, 3-H), 2.5 (1 H, br d, *J* 14, 3-H), 2.98 (1 H, dd, *J* 14, 11, 12-H), 3.16 (1 H, dd, *J* 19, 3, 17-H), 4.01 (1 H, m, 16-H), 4.09 (2 H, m, OCH_2CH_3), 4.14 (1 H, br d, *J* 10, 2-H), 4.24 (1 H, dd, *J* 12, 2.3, 14-H), 4.89 (1 H, br t, *J* 5, 5-H), 5.31 (1 H, ddd, *J* 15, 9, 5, 8-H), 5.4 (1 H, dd, *J* 11, 4.5, 11-H), 5.89 (1 H, d, *J* 15, 9-H), 7.55 (2 H, t, *J* 7.5, ArH), 7.67 (1 H, t, *J* 7.5, ArH), 7.77 (2 H, d, *J* 8, ArH); δ_C 200.72, 177.21, 136.87, 136.31, 135.22, 134.79, 130.29, 129.46, 129.32, 128.43, 128.39, 127.23, 98.99, 73.59, 73.08, 65.65, 61.05, 54.14, 49.94, 37.43, 32.25, 31.04, 30.51, 29.88, 27.75, 19.96, 19.42, 16.74, 14.73 and 14.05; *m/z* (FAB) 573 ($M^+ + 1$, 26%), 557 (6), 515 (35) and 497 (36).

(1*SR*,13*SR*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)- and (1*SR*,13*RS*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-13-Ethoxycarbonyl-14,16-isopropylidenedioxy-4,10,13-trimethylcyclohepta-decatetra-2,4,8,10-en-1-ol 66 and 69

Cerium(III) chloride hydrate (16 mg, 0.042 mmol) was added to a solution of the ketone **8** (9 mg, 0.021 mmol) in methanol (0.4 cm^3) at −35 °C followed by sodium borohydride (2 mg, 0.042 mmol). After 10 min, saturated aqueous ammonium chloride (0.1 cm^3) was added to the mixture which was then concentrated under reduced pressure to give a residue which was taken up in ether (1 cm^3). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give a mixture of epimeric alcohols **66** and **67**, ratio 87:13. Chromatography of this mixture using light petroleum–ether (1:1) as eluent, gave the (1*SR*,13*SR*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-diastereoisomer of the *title compound* **66** (7 mg, 77%) (Found: $M^+ - CH_3$, 417.2638. $C_{25}H_{37}O_5$ requires *M*, 417.2641); ν_{max}/cm^{-1} 3442, 1723, 1380, 1240, 1201, 1166, 1137, 1095, 1034, 962 and 876; δ_H 1.18 (3 H, s, 13-CH_3), 1.24 (3 H, t, *J* 7, OCH_2CH_3), 1.3 (3 H, s, H_3CCCH_3), 1.28–1.56 (2 H, m, 15-H_2), 1.38 (3 H, s, H_3CCCH_3), 1.52 (3 H, s, 4-CH_3), 1.62 (3 H, s, 10-CH_3), 1.74 (1 H, ddd, *J* 14.5, 7.5, 1.5, 17-H), 1.86 (1 H, br s, OH), 1.98 (1 H, ddd, *J* 14.5, 6, 3, 17-H), 2.05 (1 H, m), 2.2 (4 H, m), 2.68 (1 H, dd, *J* 16, 6.5, 12-H), 3.82 (1 H, dd, *J* 14, 1.4, 14-H), 3.95 (1 H, m, 16-H), 4.14 (2 H, m, OCH_2CH_3), 4.57 (1 H, m, 1-H), 5.26 (1 H, t, *J* 6, 5-H), 5.31 (1 H, t, *J* 7, 11-H), 5.34 (1 H, ddd, *J* 15, 8, 6, 8-H), 5.42 (1 H, dd, *J* 15, 5, 2-H), 5.77 (1 H, d, *J* 15, 9-H) and 6.2 (1 H, d, *J* 15, 3-H); δ_C 175.94, 137.53, 135.98, 134.42, 133.91, 131.20, 129.42, 125.27, 99.54, 74.97, 69.55, 66.30, 60.93, 49.27, 43.79, 33.97, 33.10, 32.68, 30.63, 28.03, 20.98, 20.10, 14.82, 13.35 and 13.06; *m/z* (EI) 417 ($M^+ - 15$, 19%), 415 ($M^+ - 17$, 13), 374 (64) and 357 (100).

Reduction of the ketone **58** (40 mg, 0.093 mmol) following the same procedure gave the (1*SR*,13*SR*,14*RS*,16*SR*,2*E*,4*E*,8*E*,10*E*)-diastereoisomer of the *title compound* **69** (30 mg, 75%) (Found: $M^+ + H$, 433.2956. $C_{26}H_{41}O_5$ requires *M*, 433.2954); ν_{max}/cm^{-1} 3467, 1728, 1444, 1380, 1258, 1201, 1171, 1099, 964, 876 and 733; δ_H 1.13 (3 H, s, 13-CH_3), 1.22 (3 H, t, *J* 7, OCH_2CH_3), 1.25 (2 H, m, 15-H_2), 1.28 and 1.42 (each 3 H, s, H_3CCCH_3), 1.57 (3 H, s, 4-CH_3), 1.6 (3 H, s, 10-CH_3), 1.67 (1 H, ddd, *J* 15, 5, 2, 17-H), 1.98 (1 H, ddd, *J* 15, 6, 3.5, 17-H), 2.0–2.2 (4 H, m, 6-H_2 and 7-H_2), 2.14 (1 H, dd, *J* 16, 9, 12-H), 2.3 (1 H, br s, OH), 2.42 (1 H, dd, *J* 16, 6, 12-H), 3.98 (1 H, m, 16-H), 4.12 (2 H, m, OCH_2CH_3), 4.24 (1 H, dd, *J* 11.5, 2, 14-H), 4.52 (1 H, m, 1-H), 5.28–5.38 (3 H, overlapping m, 5-H, 8-H and 11-H), 5.41 (1 H, dd, *J* 16, 4.5, 2-H), 5.8 (1 H, d, *J* 16, 9-H) and 6.22 (1 H, d, *J* 16, 3-H); δ_C 176.2, 137.0, 135.8, 134.3, 134.1, 131.3, 128.9, 126.1, 124.9, 99.4, 72.2, 69.5, 65.6, 60.9, 49.3, 44.0, 35.7, 33.0, 32.9, 30.6, 27.7, 20.1, 17.5, 14.7, 13.5 and 12.9; *m/z* (CI) 433 ($M^+ + 1$, 6%), 431 ($M^+ - 1$, 5), 415 (20), 375 (24) and 357 (100).

Acknowledgements

We thank the SERC and CONICET (Argentina) for support (to E. G. M.).

References

1 M. Uramoto, N. Otake, L. Cary and M. Tanabe, *J. Am. Chem. Soc.*, 1978, **100**, 3616; K. Kakinuma, J. Uzawa and M. Uramoto, *Tetrahedron Lett.*, 1982, **23**, 5303; S. Harada, J. Okada, M. Takeda and T. Yamazi, *J. Antibiot.*, 1985, **38**, 877.
2 E. J. Thomas and A. C. Williams, *J. Chem. Soc., Chem. Commun.*, 1987, 992; E. J. Thomas and A. C. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1995, 351.
3 J. M. Roe and E. J. Thomas, *Synlett*, 1990, 727; J. M. Roe and E. J. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1995, 359.
4 A. S. Kende, M. J. Luzzio and K. Koch, in *Chemistry and Biotechnology of Biologically Active Natural Products, Proceedings of the Fourth International Conference*, ed. C. Szantay, Budapest, Hungary, 1987 (*Chem. Abstr.*, 1989, **111**, 214771m).
5 A. S. Kende, K. Koch, G. Dorey, I. Kaldor and K. Liu, *J. Am. Chem. Soc.*, 1993, **115**, 9842.
6 P. C. Astles and E. J. Thomas, *Synlett*, 1989, 43; K. C. Nicolaou, M. R. Pavia and S. P. Seitz, *J. Am. Chem. Soc.*, 1981, **103**, 1224.
7 R. W. Curley Jr. and C. J. Ticoras, *J. Org. Chem.*, 1986, **51**, 256.
8 J. C. Collins, W. W. Hess and F. J. Frank, *Tetrahedron Lett.*, 1968, 3363.
9 P. J. Van den Tempel and H. O. Huisman, *Tetrahedron*, 1966, **22**, 293.
10 A. Ichihara, H. Kawagishi, N. Tokugawa and S. Sakamura, *Tetrahedron Lett.*, 1986, **27**, 1347.
11 J. K. Gawronski and H. M. Walborsky, *J. Org. Chem.*, 1986, **51**, 2863.
12 G. Stork, P. A. Grieco and M. Gregson, *Tetrahedron Lett.*, 1969, 1393.
13 E. Wada, S. Kanemasa and O. Tsuge, *Bull. Chem. Soc. Japan.*, 1989, **62**, 860.
14 W. F. Griffith and S. V. Ley, *Aldrichimica Acta*, 1990, **23**, 13.
15 K. M. Chen, G. E. Hardtmann, K. Prasad, O. Repic and M. J. Shapiro, *Tetrahedron Lett.*, 1987, **28**, 155.
16 P. A. Grieco, Y. Yokoyama, G. P. Withers, F. J. Okuniewicz and C.-L. J. Wang, *J. Org. Chem.*, 1978, **43**, 4178.
17 E. J. Corey, P. Da Silva Jardine and J. C. Rohloff, *J. Am. Chem. Soc.*, 1988, **110**, 3672.
18 M. A. Tius and N. K. Reddy, *Tetrahedron Lett.*, 1991, **32**, 3605.
19 S. D. Rychnovsky and D. J. Skalitzky, *Tetrahedron Lett.*, 1990, **31**, 945; D. A. Evans, D. L. Rieger and J. R. Gage, *Tetrahedron Lett.*, 1990, **31**, 7099.
20 E. J. Corey and T. Suggs, *Tetrahedron Lett.*, 1975, 2647.
21 M. A. Blanchette, W. Choy, J. T. Davis, A. P. Essenfeld, S. Masamune, W. R. Roush and T. Sakai, *Tetrahedron Lett.*, 1984, **25**, 2183.
22 G. Stork and E. Nakamura, *J. Org. Chem.*, 1979, **44**, 4010.
23 M. Kodama, Y. Shiobara, H. Sumitomo, K. Fukuzumi, H. Minami and Y. Miyamoto, *J. Org. Chem.*, 1988, **53**, 1437.
24 H. Takayanagi, T. Uyehara and T. Kato, *J. Chem. Soc., Chem. Commun.*, 1978, 359.
25 B. M. Trost and S. J. Brickner, *J. Am. Chem. Soc.*, 1983, **105**, 568.
26 A. L. Gemal and J.-L. Luche, *J. Am. Chem. Soc.*, 1981, **103**, 5454.
27 C. Brain, A. Chen and E. J. Thomas, unpublished observations.

Paper 4/06851C
Received 9th *November* 1994
Accepted 8th *December* 1994