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Total synthesis of (+)-phorboxazole A, a potent cytostatic agent from the sponge *Phorbas* sp.

Gerald Pattenden,* Miguel A. González, Paul B. Little, David S. Millan, Alleyn T. Plowright, James A. Tornos and Tao Ye

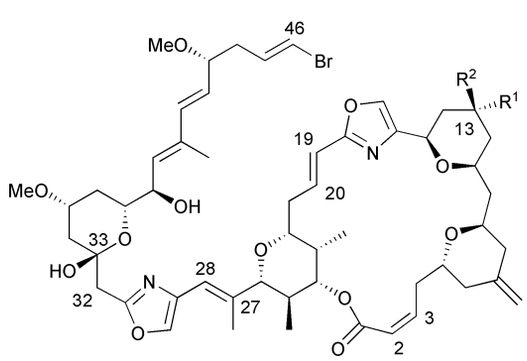
School of Chemistry, The University of Nottingham, University Park, Nottingham, UK NG7 2RD. E-mail: gp@nottingham.ac.uk; Fax: +44(0)115 951 3535; Tel: +44(0)115 951 3530

Received 22nd July 2003, Accepted 29th August 2003
First published as an Advance Article on the web 16th October 2003

A convergent total synthesis of phorboxazole A (**1a**), from the C(3–19), C(20–27) and C(33–46) fragments **5**, **4** and **91**, respectively, concentrating on stereocontrolled formation of the bonds at C(2–3), C(19–20) and C(27–28), is described. Although a coupling reaction between a macrolide ketone and the side chain substituted sulfone, at C(27–28) was not successful, a Wadsworth–Emmons olefination involving the oxane methyl ketone **4** and an oxazole produced the oxane **90** which was next coupled to **91** leading to the C(20–46) unit **100**. A further coupling of **100** to **71c** at C(19–20) then led to **105**, ultimately, and the synthesis was completed by a macrocyclisation reaction from **105**, at the C(2–3) alkene bond, followed by deprotection of **106**.

Introduction

Phorboxazole A (**1**) and its C-13 epimer phorboxazole B(**2**) are unique oxane–oxazole-based macrolides isolated from a species of Indian Ocean sponge of the genus *Phorbas* sp.[1] The compounds exhibit extraordinary cytotoxic activity (GI_{50} <8 × 10^{-10} M) against the entire panel of human tumour cell lines held at the National Cancer Institute. Together with the spongiastatins[2] the phorboxazoles are therefore the most potent naturally occurring cytotoxic agents yet discovered. Although their mechanism of action remains to be established, phorboxazole A has been shown to arrest the cell cycle in the S phase, whilst not inhibiting tubulin polymerisation or interfering with the integrity of microtubules, thereby suggesting a possibly unique mechanism.[1b] Their novel structure and potent biological activity have combined to make the scarcely available phorboxazoles attractive synthetic targets within the chemistry community.[3] Forsyth *et al.*[4] published the first total synthesis of phorboxazole A (**1**) in 1998, and this was followed by a description of a synthesis of phorboxazole B (**2**) by Evans *et al.* in 2000.[5] During 2001 Smith and his collaborators[6] described a second synthesis of phorboxazole A, and two new syntheses of this compound were reported contemporaneously in 2003 by Williams *et al.*[7] and from our own laboratory.[8] Several other research groups have described synthetic approaches to the natural phorboxazoles,[3] and a number of structure–activity studies have been carried out.[9] We now provide a full account of our own total synthesis of (+)-phorboxazole A (**1**).



1, R^1= OH, R^2= H
2, R^1= H, R^2= OH

Synthetic strategy

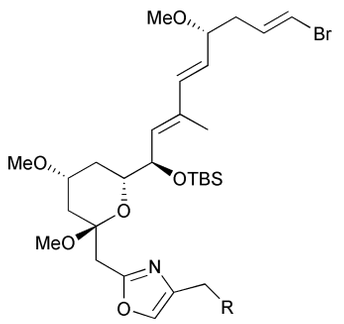
The structure of phorboxazole A (**1**) is based on a 21-membered macrolactone core, which accommodates a *trans*-fused oxane, two *cis*-fused oxanes and an oxazole linked by one *E*- and one *Z*-alkene bonds. A side chain is attached to the most substituted *cis*-oxane in the macrolactone by an *E*-trisubstituted alkene linked to a second oxazole, an oxane hemiacetal, an *E*,*E*-1,3-diene unit, and terminating in an *E*-vinyl bromide. With the three alkene bonds at C(2–3), C(19–20) and C(27–28) separating three structural units of comparable complexity, it was clear from the outset of our studies that the ordered, stereocontrolled formation of these alkenes would play a crucial role in any successful total synthesis of phorboxazole A (**1**). In our synthetic design we planned to synthesise the key units **3**,[10] **4**[11] and **5**,[12] and then to examine the coupling between **4** and **5** at C(19–20) using an *E*-selective Wittig reaction, followed by an intramolecular *Z*-selective Wadsworth–Emmons olefination reaction at C(2–3) leading to the macrolactone core in phorboxazole A. We then felt we would be able to complete a synthesis of phorboxazole using a Julia olefination with **3** (R = SO_2Ar) producing the C(27–28) *E*-alkene bond in the target. We recognised, of course, that having the key units **3**, **4** and **5**, and their synthetic precursors, available in quantity would provide us with the necessary flexibility to assemble them in a number of ways in order to achieve our objective. We therefore first describe syntheses of the key units **3**, **4**, and **5**, and then summarise strategies for their assembly, leading ultimately to phorboxazole A (**1**).

The C(28–46) polyene oxane–hemiacetal oxazole side chain 3

Our synthetic approach to the C(28–46) side chain portion **3** in phorboxazole A was based on using an *E*-selective Julia benzothiazole sulfone olefination reaction[13] between the sulfone **6** and the α,β-unsaturated aldehyde **7**, as a key step.[10] We then planned to elaborate the substituted 1,3-diene product **8**, from **6** and **7** to the C(31–46) fragment **9** as a prelude to conversion into the substituted oxazole target **3**.[14] Both the sulfone **6** and the α,β-unsaturated aldehyde **7** were easily synthesised from the chiral pool compounds D-malic acid and D-xylose respectively, as summarised in Schemes 1 and 2.

Thus, D-malic acid was first converted into the PMB ether **11** *via* the known dioxolaneethanol **10**,[15] and then into the differentially protected triol **13a** using three straightforward synthetic

DOI: 10.1039/b308305e



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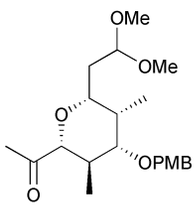

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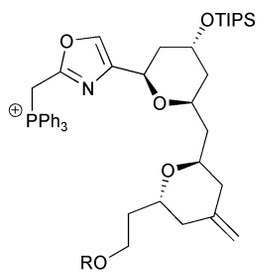

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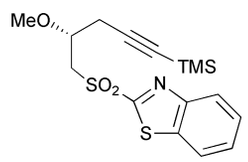

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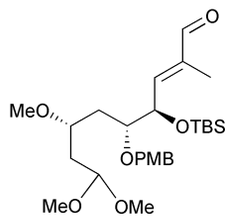

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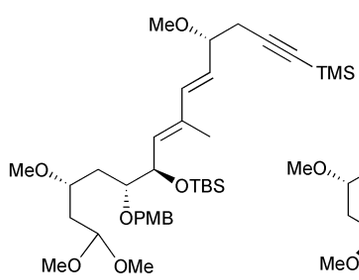

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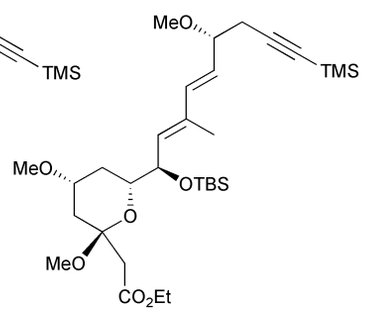

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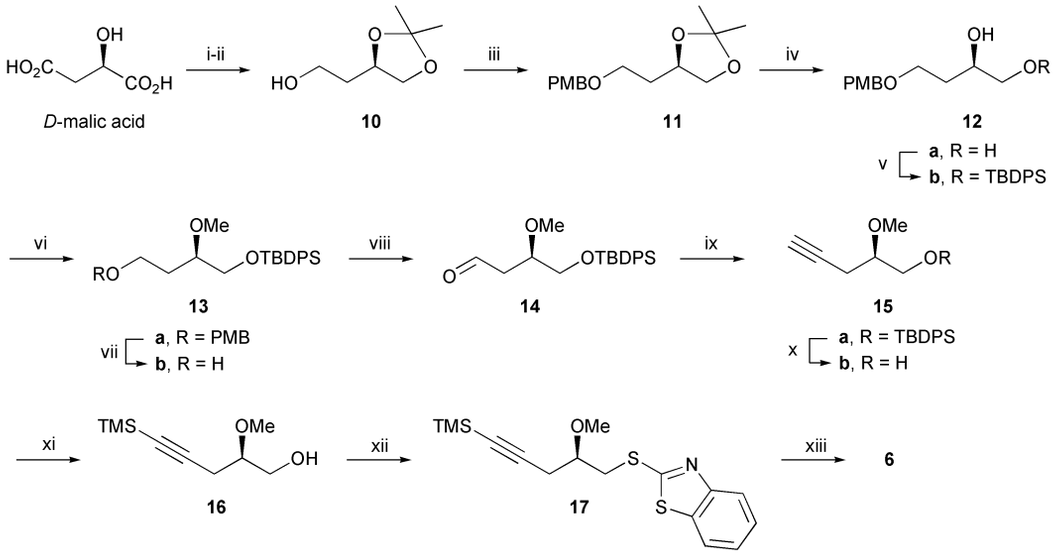
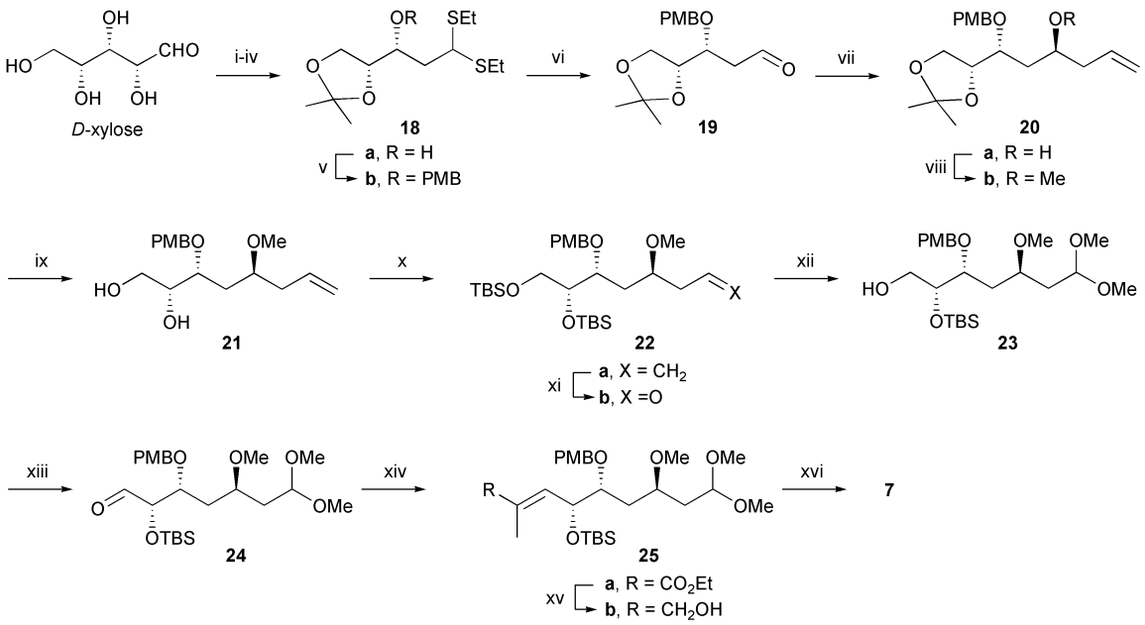
steps. Deprotection of the PMB ether group in **13a**, followed by oxidation of the resulting alcohol **13b** and treatment of the corresponding aldehyde **14** with Seyferth's reagent[16] next led to the terminal acetylene **15a** (Scheme 1). The acetylene **15a** was then elaborated to the alcohol **16**, which, on treatment with 2-mercaptobenzothiazole[17] gave the sulfide **17**. Oxidation of **17** using MCPBA then gave the benzothiazole sulfone intermediate **6** as a stable crystalline solid.

The α,β-unsaturated aldehyde **7** required for a Julia olefination reaction with the sulfone **6** was prepared from D-xylose as outlined in Scheme 2. Thus, using literature precedent,[18] D-xylose was first converted into the known dithioacetal **18a** in four straightforward steps. Protection of the alcohol group in **18a** as its PMB ether, followed by hydrolysis of the dithioacetal next gave the aldehyde **19**. Allylboration of **19**, using allyl diisopinocamphenylborane,[19] followed by oxidation with H_2O_2–NaOH led to the homoallylic alcohol **20a** which, on methylation and deprotection of the acetonide was then converted into the 1,2-diol **21**. After protection of the 1,2-diol functionality in **21**, oxidative cleavage of the terminal double bond gave the corresponding aldehyde **22b**, which on treatment with camphorsulfonic acid in methanol led directly to the dimethyl acetal **23**. Oxidation of **23**, using Dess–Martin periodinane,[20] followed by a Wittig reaction between the resulting aldehyde **24** and (carbethoxyethylidene)triphenylphosphorane then led exclusively to the *E*-unsaturated ester **25a**. Finally, reduction of **25a** using DIBAL, and oxidation of the alcohol product **25b** with Dess–Martin periodinane gave the *E*-αβ-unsaturated aldehyde **7**.

Deprotonation of the sulfone **6** using NaHMDS in THF at −78 °C in the presence of the unsaturated aldehyde **7** led smoothly to the *E*,*E*-1,3-diene **26** in 74% yield (<6% of the corresponding *Z*-olefination product was produced concurrently) (Scheme 3). Deprotection of the dimethyl acetal group in **26**, followed by treatment of the resulting aldehyde **27** with ethyl diazoacetate, in the presence of $Sn(II)Cl_2$,[21] next led to the β-keto ester **28**. Removal of the PMB protecting group in **28**, using DDQ,[22] resulted in spontaneous cyclisation of the intermediate δ-hydroxy ketone producing a single diastereoisomer of the cyclic hemiacetal **29a** in 90% yield. Protection of **29a** as its methyl ether **29b**, and deprotection of the terminal acetylene



Scheme 1 *Reagents and conditions*: i, $BH_3{\cdot}SMe_2$, $B(OEt)_3$; ii, Me_2CO, pTSA, $Cu(II)SO_4$, 77% (2 steps); iii, PMBCl, KO^{t}Bu, NBu_4I; iv, pTSA, MeOH, 69% (2 steps); v, TBDPSCl, Et_3N, DMAP, 94%; vi, NaH, MeI, 87%; vii, DDQ, 95%; viii, $(COCl)_2$, DMSO, Et_3N, 90%; ix, $(MeO)_2PCHN_2$, KO^{t}Bu, 75%; x, TBAF, 96%; xi, TMSCl, BuLi, 70%; xii, 2-mercaptobenzothiazole, PPh_3, DEAD, 94%; xiii, MCPBA, $NaHCO_3$, 85%.



Scheme 2 *Reagents and conditions*: i, EtSH, HCl; ii, Me_2CO, H_2SO_4; iii, KOBu^t, DMSO, 35%, three steps; iv, $LiAlH_4$, 90%; v, KOBu^t, PMBBr, 98%; vi $Hg(ClO_4)_2$, $CaCO_3$, 91%; vii, a) (−)-β-allyl diisopinocampheylborane, b), H_2O_2, NaOH, 82%; viii, KBuO^t, MeI, 97%; ix, pTSA, MeOH, 88%; x, TBSOTf, Et_3N, 98%; xi, OsO_4, NMO, $NaIO_4$, 94% (two steps); xii, CSA, MeOH–DCM, 89%; xiii, Dess–Martin periodinane, 95%; xiv, $CH_3C(PPh_3)CO_2Et$, 94%; xv, DIBALH, −78 °C, 89%; xvi, Dess–Martin periodinane, 94%.

unit next led to **30**, which on hydrostannylation and treatment of the resulting vinylstannane with NBS[23] in CH_3CN at 0 °C then gave the C(31–46) side chain portion **31** in the phorboxazoles.[10] The methyl ester corresponding to **31** was synthesised contemporaneously, but using a different route, by Ahmed and Forsyth.[24] Saponification of the ester group in **31**, followed by coupling the resulting carboxylic acid with serine in the presence of EDC–HOBT next led to the amide **32** which, by stepwise cyclodehydration, to **33**, and oxidation led to the substituted oxazole ester **34**.[25] The synthesis of the sulfone **36** was then completed following reduction of the ester **34** to the corresponding alcohol **35a**, mesylation to **35b**, displacement of the mesylate using the sodium salt of 2-mercaptobenzothiazole and, finally, oxidation of the resulting sulfide with H_2O_2 in the presence of ammonium molybdate (Scheme 3).

The C(20–26) pentasubstituted oxane unit 4

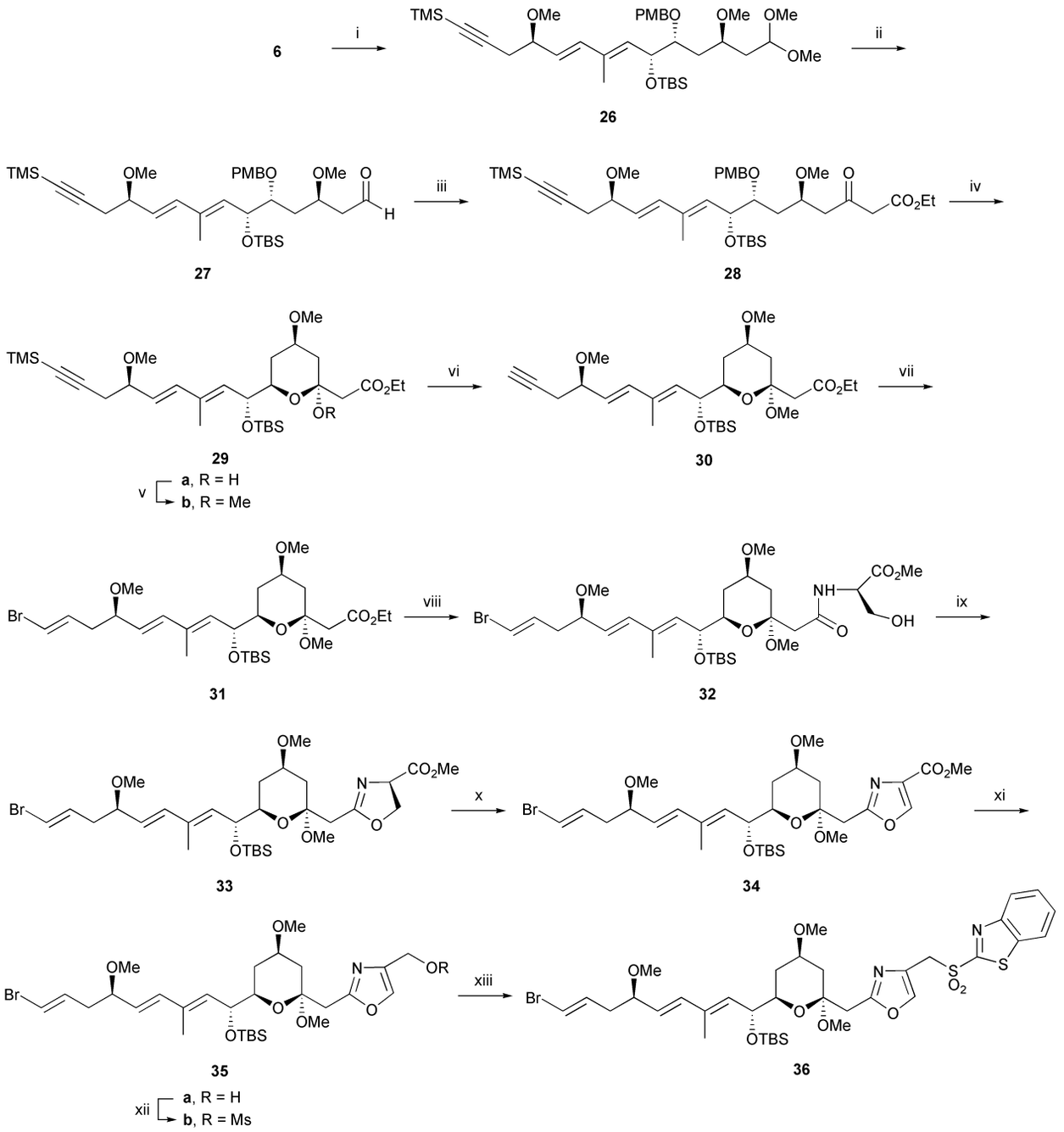
The 2,6-*cis* oxane unit **4** in the phorboxazoles contains five of the fifteen asymmetric centres in the natural products. Several solutions to the synthesis of this oxane have now been developed.[26] Our own synthesis, which is summarised in Scheme 4, started with the chiral pool ester **37**, and proceeded *via* the protected 1,3,5-triol **42** and the epoxide **48** as key intermediates.[11] Thus, following the conversion of methyl (*S*)-3-hydroxy-2-methylpropionate **37**[27] into the known aldehyde **38**,[28] a crotylboration reaction using (−)-methoxydiisopinocampheyborane and *E*-2-butene[29] next led to the substituted secondary alcohol **39** with 98% diastereoselectivity and in 76% yield. The protecting groups in **39** were then interchanged and the resulting alkene **40b** was cleaved oxidatively producing the corresponding aldehyde **41**. Allylation of **41** in a substrate-controlled manner, using allyltributyltin and $BF_3{\cdot}OEt_2$ catalysis[30] next gave rise to the homoallylic alcohol **42** in 94% yield and with 96% diastereoselectivity. A series of functional group manipulations was then used to convert the secondary alcohol **42** into the primary alcohol **43b** and then to the aldehyde **44**. A Wadsworth–Emmons olefination with **44** next produced the *E*-αβ-unsaturated ester **45** which on reduction using DIBAL at −78 °C led to the allylic alcohol **46**. Epoxidation of **46** under Sharpless conditions[31] using (+)-diethyl tartrate then gave rise to the key epoxide intermediate **47** in excellent yield and with excellent diastereoselectivity. Deprotection of the silyl ether group in **47**, followed by treatment of the resulting epoxy-alcohol **48** with titanium tetraisopropoxide in refluxing benzene,[32] gave the 2,6-*cis* oxane **49** with the absolute stereochemistry shown.[33]

The vicinal diol unit in **49** was next converted into the corresponding terminal epoxide **50**, which was then elaborated to the protected secondary alcohol **51b** in two steps. Oxidative cleavage of the alkene bond in **51b**, followed by protection of the resulting aldehyde **52** as its dimethyl acetal and deprotection of the silyl ether group led to **53** which on oxidation using Dess–Martin periodinane finally gave the methyl ketone **4**.

The C(3–19) bis-oxane oxazole unit 5

A number of alternative, but complementary, methods for the synthesis of the *cis*,*trans* bis-oxane portion and the corresponding C(3–19) bis-oxane oxazole unit **5** in phorboxazole A, have been published over the period 1997–2003.[34] These strategies have been based largely on use of the Williamson ether synthesis and the hetero Diels–Alder reaction,[3] but also some interesting catalytic asymmetric aldol methodology[5] and exploitation of the Petasis–Ferrier rearrangement.[6] Our own synthesis of the bis-oxane oxazole unit **5** was based on an oxy-anion intramolecular Michael reaction[35] of **60** leading to the *cis*-oxane intermediate **61**, followed by conversion of the oxazolidine unit in **61** to the corresponding oxazole **63**, and completed by an intramolecular (Williamson) cyclisation of **69** to give the *trans*-oxane ring in **70** (Scheme 5).[12]

Thus, allylboration of Garner's aldehyde **54**[36] first gave the homoallylic alcohol **55a** in 80% yield and with 92% diastereoselectivity. Ozonolysis of the protected alcohol **55b**, followed by a second allylboration[19] of the resulting aldehyde **56** next gave the corresponding homoallylic alcohol **57a** which was protected as its TIPS ether **57b**. Oxidative cleavage of the double bond in **57**, by ozonolysis, then gave the aldehyde **58**, which was converted into the *E*-unsaturated ester **59** using a Wittig reaction with (carboethoxymethylene)triphenylphosphorane. Deprotection of the TES group in **59** then revealed the 7-hydroxy unsaturated ester **60** which underwent a smooth and selective intramolecular oxy anion Michael reaction[35] in the presence of NaHMDS at −78 °C leading to the *cis*-oxane **61** in 88% yield. A small amount (<10%) of the corresponding *trans*-oxane was produced concurrently and was easily separated by routine chromatography. The oxazole ring in the next key intermediate *en route* to **5** was elaborated from the oxazolidine

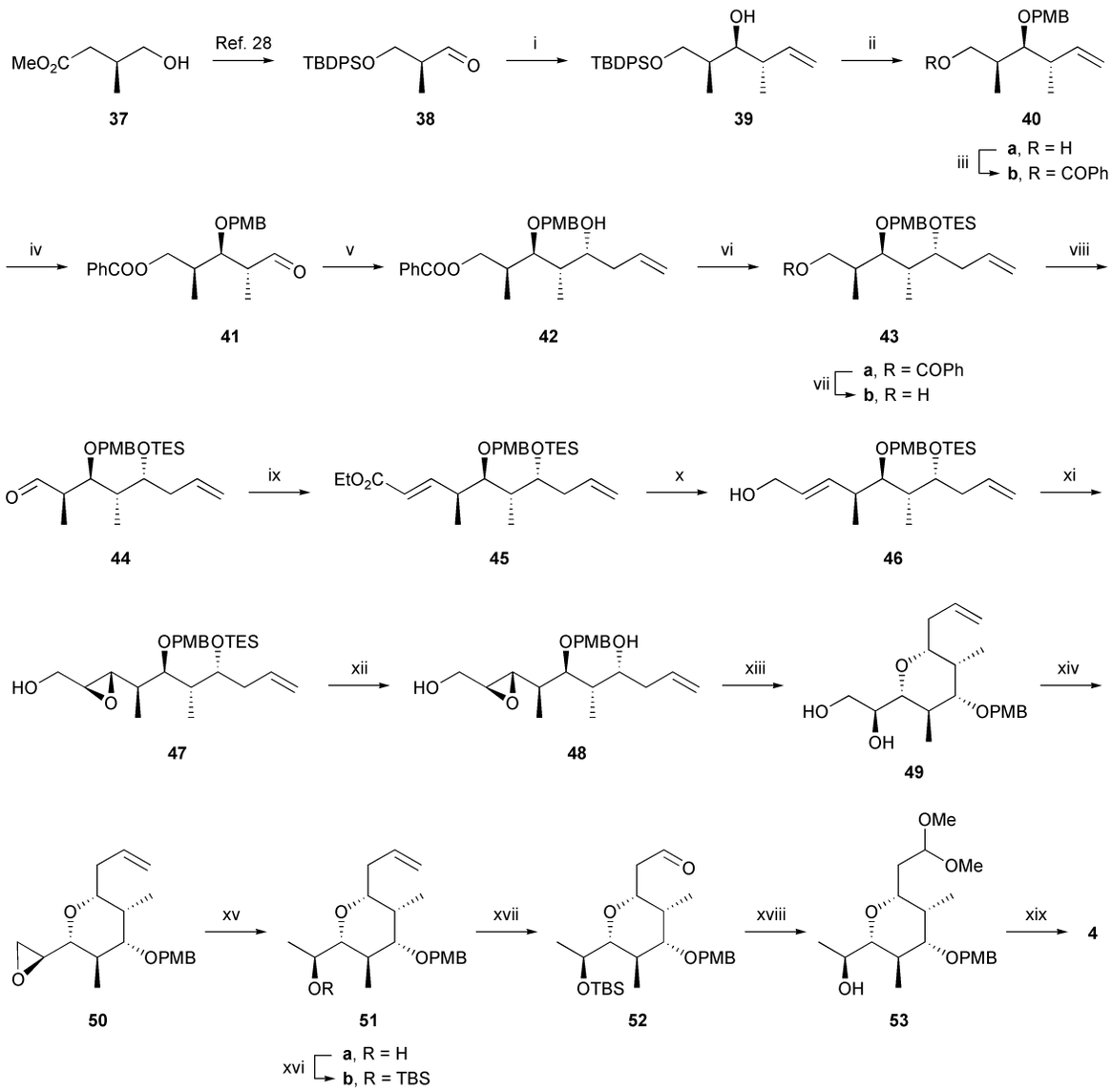


Scheme 3 *Reagents and conditions*: i, NaHMDS, −78 °C, then **7**, 74%; ii, Me_2BBr, −78 °C, 95%; iii, EtO_2CCHN_2, $SnCl_2$, 74%; iv, DDQ, 96%; v, PPTS, MeOH, 59%; vi, $AgNO_3$, KCN, 75%; vii, a) Bu_3SnH, AIBN, PhH, Δ, b) NBS, 60%, two steps; viii, a) LiOH, MeOH, b) Et_3N, serine, EDC, HOBT, 91%; ix, DAST, −78 °C, 98%; x, $BrCCl_3$, DBU, 66%; xi, DIBAL-H, −78 °C, 98%; xii, Et_3N, MsCl, xiii, a) NaHMDS, 2-mercaptobenzothiazole, 38%; b), $(NH_4)_6Mo_7O_{24}$, 30% H_2O_2, MeOH, 60%.

61, following deprotection and conversion of the resulting β-hydroxyamine to the amide **62a**, oxidation to the corresponding aldehyde **62b** and cyclisation to **63** using literature conditions.[37] NOE studies with the oxazole *cis*-oxane **63** confirmed the geometry of this intermediate.

An alternative synthesis of the oxazole *cis*-oxane **63** was developed later, which was more amenable to producing multigram quantities of this key intermediate. In this sequence the oxazole aldehyde **72** was first prepared starting from ethyl bromopyruvate and cinnamamide.[38] When the aldehyde **72** was next treated with Corey's allylborane[39] derived from 1,2-diphenylethane-1,2-diamine in methylene chloride at −78 °C an excellent yield of the corresponding alcohol **73** was produced in >95% ee. Using the same sequence of reactions we had used in converting the homoallylic alcohol **55a** to **61**, the alcohol **73** was then elaborated to **63** in nine straightforward steps.

In our preliminary publication,[12] we showed that the second, *trans*-oxane ring in **5** could be introduced *via* the epoxide **66** derived from **63**, following sequential conversion to the aldehyde **64a**, the alkene **64b**, the vicinal diol **65**[40] and cyclisation of the tosylate derived from **65**. Unfortunately, we observed no diastereoselectivity during the conversion of **64b** into **66**. Not withstanding this disappointment, we decided to press on with our synthesis of the penultimate precursor **69** to the bis-oxane **70**, and examine the reaction of the epoxide **66** with the cuprate intermediate derived from the vinyl iodide **67**. The iodide **67** was produced from (L)-malic acid **74** as shown in Scheme 6. Thus, exhaustive reduction of **74** first led to the corresponding 1,2,4-triol which was then protected as the pivaloyl acetonide **75**. Deprotection of the acetonide unit in **75** next gave the 1,2-diol **76** which was then converted into the epoxide **77**, using a three-step sequence developed by Kolb and Sharpless.[41] Treatment of **77** with the anion derived from trimethyl-

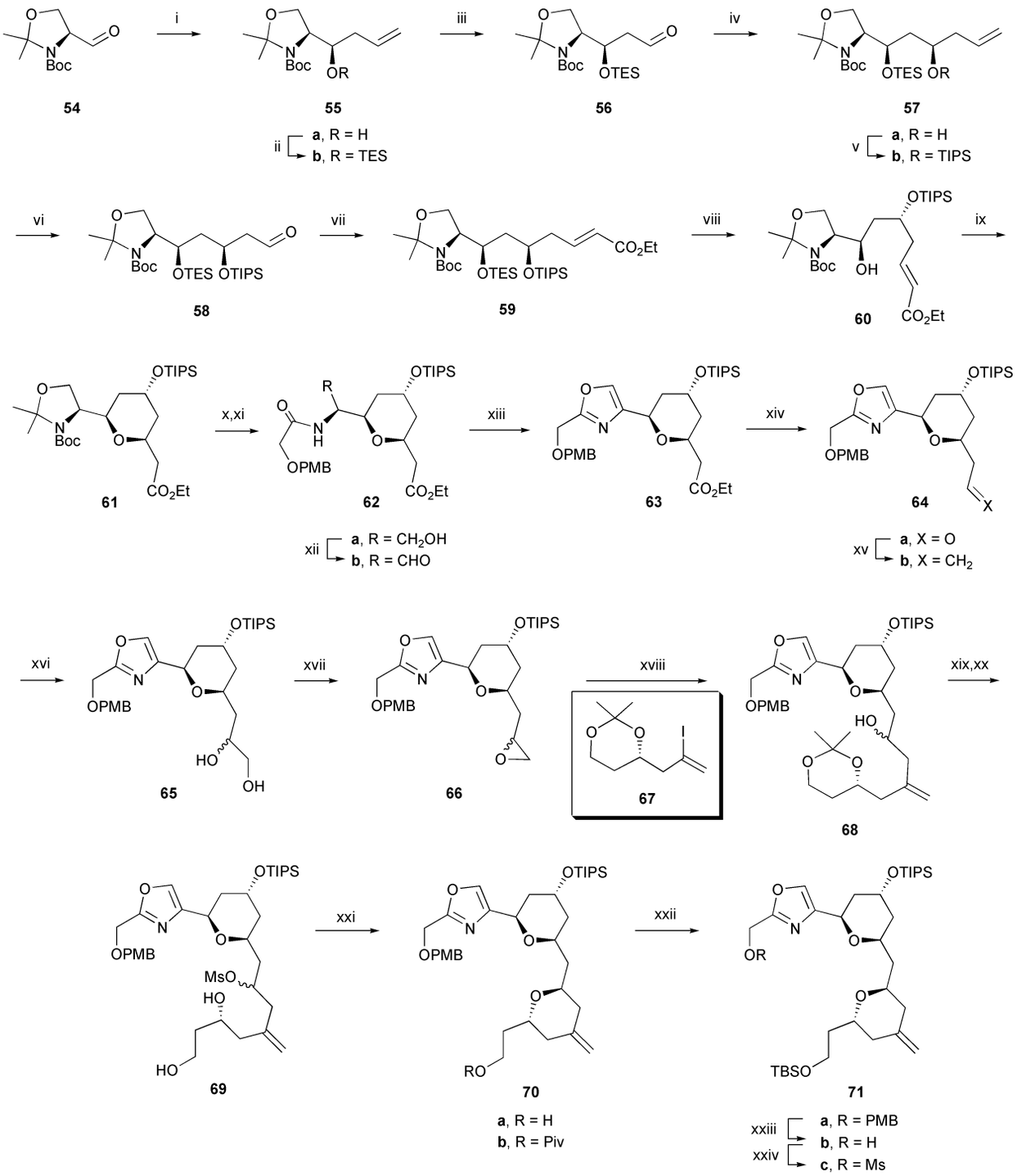


Scheme 4 *Reagents and conditions*: i, ^{n}BuLi, KO^{t}Bu, *trans*-2-butene, (−)-methoxydiisopinocampheylborane, −78 °C, $BF_3{\cdot}Et_2O$, then **38**, NaOH, 30% H_2O_2, 76%; ii, a) CF_3SO_3H, 4-methoxybenzyl 2,2,2-trichloroacetimidate; b) TBAF, 54%; iii, BzCl, pyridine, DMAP, 91%; iv, a) OsO_4, NMO; b) $NaIO_4$, pH = 7 buffer, 87%; v, $BF_3{\cdot}Et_2O$, $Bu_3SnCH_2CH{=}CH_2$, −78 °C, 94%; vi, 2,6-lutidine, TESOTf, −50 °C; vii, DIBAL-H, −78 °C, 82% (two steps); viii, $(COCl)_2$, DMSO, < −60 °C, then **43b**, Et_3N; ix, NaHMDS, $EtO_2CCH_2P(O)(OEt)_2$, −78 °C, 63% (two steps); x, DIBAL-H, −78 °C, 89%; xi, L-(+)-diethyl tartrate, $Ti(iOPr)_4$, ^{t}BuOOH, 4 Å sieves, −25 °C, 98%; xii, TBAF, 0 °C, 86%; xiii, $Ti(O^{i}Pr)_4$, PhH, 76%; xiv, Ts-imidazole, NaH, Et_2O, −78 °C to 0 °C, 60%; xv, $LiAlH_4$, Et_2O, 75%; xvi, TBSOTf, 2,6-lutidine, DCM, −78 °C to rt, 95%; xvii, a) OsO_4, NMO, acetone–water; b) $NaIO_4$ on silica, DCM, 88%; xviii, CSA, MeOH–DCM; xix, Dess–Martin periodinane, 2,6-lutidine, DCM, 72% (two steps).

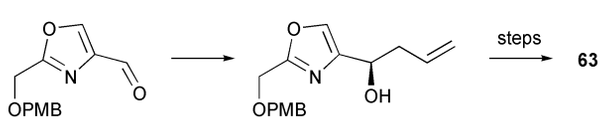
silylacetylene gave the secondary alcohol **78a** which was then elaborated to the monosubstituted acetylene **79**, *via* **78b**. Hydroiodination of **79**, using 9-iodo-9-borabicyclo[3.3.1]-nonane, under the conditions of Suzuki *et al.*,[42] next led to the vinyl iodide **80a** which was then deprotected to **81**, *via* **80b**, and finally elaborated to the vinyl iodide **67**. When the epoxide **66** was treated with the cuprate intermediate derived from the vinyl iodide **67**, a mixture of epimeric alcohols **68** was produced. The alcohol was converted into the mesylate diol **69** which then underwent oxane ring formation in the presence of Et_3N producing a 1:1 mixture of *trans*- **70a** and *cis* oxanes in 78% yield. The diastereoisomeric oxanes were separated cleanly by chromatography to afford the required oxazole bis-oxane **70a** in a 37% yield. The same oxazole bis-oxane unit **70**, but with different protecting groups, was synthesised independently by Forsyth, Evans, Smith and Williams and their respective collaborators during the course of our studies.[4–7] Indeed, we found that the strategy developed by Williams *et al.*[43] for the synthesis of the pivaloate **70b** from the aldehyde **64a** produced from the ester **63** was superior to our own route for producing gram quantities of the oxazole bis-oxane **71**. In this sequence, asymmetric allylation of the aldehyde **64a** using the reagent derived from the allylstannane **82** and (*S*,*S*)-1,2-diamino-1,2-diphenylethane bis-sulfonamide–BBr_3 leads first to the differentially protected polyol **83**. Mesylation of **83**, followed by deprotection of the TBS ether and cyclisation of the resulting alcohol then gave rise to the pivaloyl ester **84**. Protection of **84** as its TIPS ether **70b**,[43] and saponification of the resulting pivaloate finally gave the oxazole bis-oxane **70a**, which was identical with the same material we had synthesised earlier.

The C(1–27) macrolide 89

With the three sub-units **3**, **4** and **5** in phorboxazole A now synthesised, we examined their assembly to the natural product focusing on the stereocontrolled formation of the alkene bonds at C(2–3), C(19–20) and C(27–28). Our first strategy was to link the units **4** and **5** at C(19–20), and then to elaborate the macrolide **89** using an intramolecular Wadsworth–Emmons reaction at C(2–3) which had been highlighted in the first synthesis of phorboxazole A by Forsyth *et al.*[4] We then planned to complete the synthesis of **1a** by linking **89** to **3** (R=SO_2Ar) using a stereoselective Julia reaction.[13]

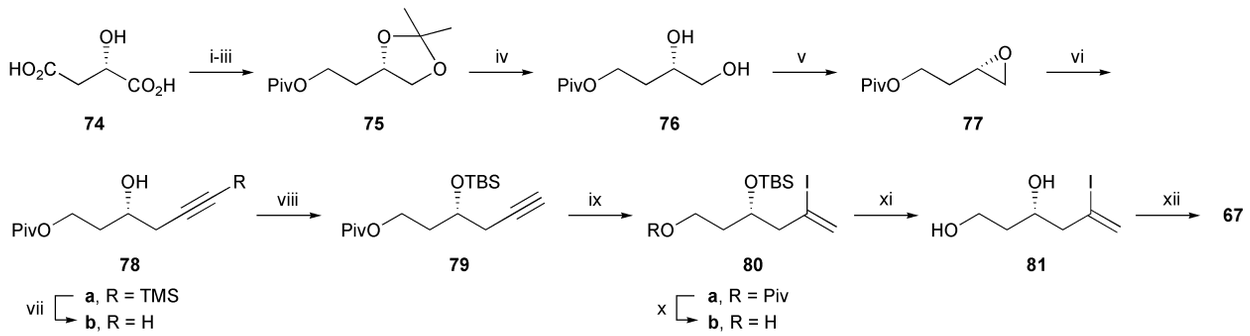


Scheme 5 *Reagents and conditions*: i, a) (+)-α-allyl diisopinocampheylborane, b) Et_3N, H_2O_2, 80%; ii, TESCl, Et_3N, DMAP, 90%; iii, a) O_3, $NaHCO_3$, b) PPh_3, 92%; iv, (+)-α-allyl diisopinocampheylborane, b) Et_3N, H_2O_2, 76%; v, TIPSOTf, 2,6-lutidine, 92%; vi, a) O_3, $NaHCO_3$, b) PPh_3, 95%; vii, Ph_3PCHCO_2Et, 87%; viii, PPTS, 84%; ix, NaHMDS, −78 °C, 88%; x, 4 M HCl, dioxane; xi, $PMBOCH_2CO_2H$, EDC, HOBt, Et_3N, 75% (2 steps); xii, Dess–Martin periodinane; xiii, a) 2,6-di-^{t}butylpyridine, PPh_3, $C_2Br_2Cl_4$, b) DBU, 73% (2 steps); xiv, DIBALH, 87%; xv, Ph_3PCH_3Br, ^{n}BuLi, 60%; xvi, $(DHQD)_2PYR$, $K_2OsO_2(OH)_4$, $K_3Fe(CN)_6$, K_2CO_3, 95% (based on recovered SM); xvii, NaH, *N*-tosylimidazole, 76%; xviii, ^{t}BuLi, 2-Th-CuCNLi, 60% (based on recovered SM); xix, MsCl, Et_3N; xx, CSA, MeOH, 60% (2 steps); xxi, Et_3N, MeCN, heat, 78%; xxii, TBSOTf, Et_3N, DCM, 0 °C, 90%; xxiii, DDQ, 50 : 1 DCM–H_2O, 0 °C–rt, 66%; xxiv, MsCl, $^i Pr_2NEt$, DCM, −5 °C, 76%.

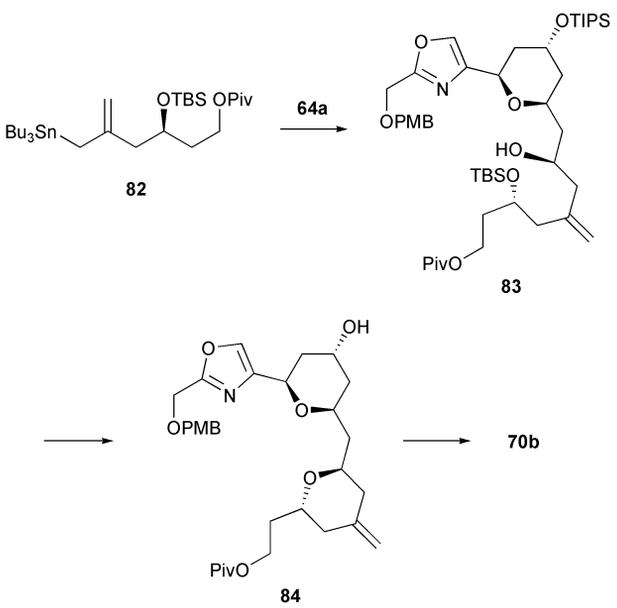


In pursuit of this goal, an *E*-selective Wittig reaction between the oxane–aldehyde **52** and the phosphonium salt derived from **70b** *via* the oxazole bis-oxane mesylate **85**, in the presence of DBU[44] first gave the oxazole tris-oxane **86a** (Scheme 7). Manipulation of the protecting groups in **86a** next gave the secondary alcohol **87a**, which was then converted into the bis-(2,2,2-trifluoroethyl)phosphonate ester **87b**.[4] Finally, deprotection of the two TBS groups in **87b**, using camphorsulfonic acid, and oxidation of the resulting diol using Dess–Martin periodinane[20] gave the aldehyde phosphonate intermediate **88**. Treatment of **88** under the conditions of Still and Gennari[45] (K_2CO_3 in the presence of 18-crown-6) then gave the α,β-unsaturated macrolide **89**, but as a disappointing 3 : 2 mixture of *Z*- and *E*- isomers.

In spite of model studies,[46] whereby we showed that the oxane methyl ketone **4** and oxazole methyl sulfones underwent



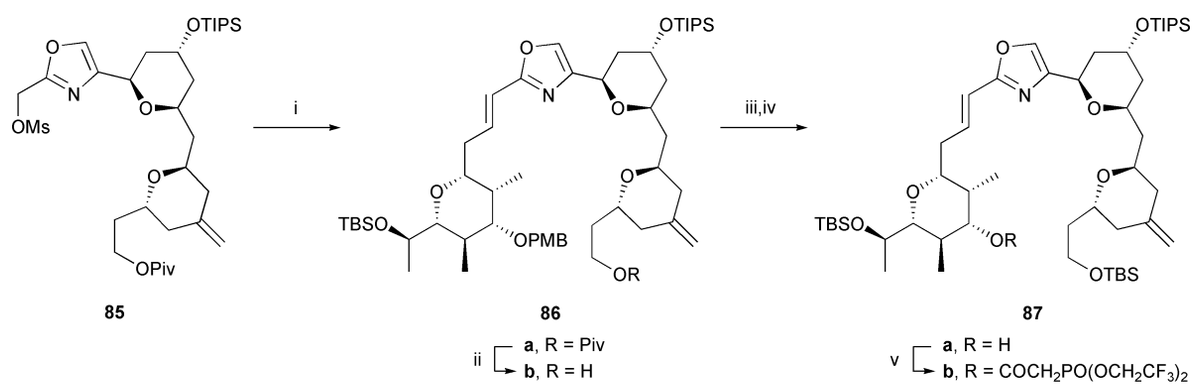
Scheme 6 *Reagents and conditions*: i, BH_3·SMe_2, $B(OEt)_3$, THF; ii, Me_2CO, pTSA, Cu(II)SO_4, 74% (2 steps); iii, PivCl, Et_3N, DMAP, CH_2Cl_2, 96%; iv, pTSA, MeOH, 83%; v, a) $MeC(OMe)_3$, PPTS, CH_2Cl_2; b) CH_3COBr, CH_2Cl_2; c) K_2CO_3, MeOH, 75%; vi,CH_3SiCCH, BuLi, BF_3OEt_2, THF, 99%; vii, TBAF, THF, 93%; viii, TBSOTf, 2,6-lutidine, CH_2Cl_2, 99%; ix, a) *B*-I-9BBN, pentane, b) AcOH, c) H_2O_2, NaOH; x, DIBALH, $PhCH_3$, 91%; xi, HF·py, THF, 96%; xii, CSA, 2,2-dimethoxypropane, 84%.

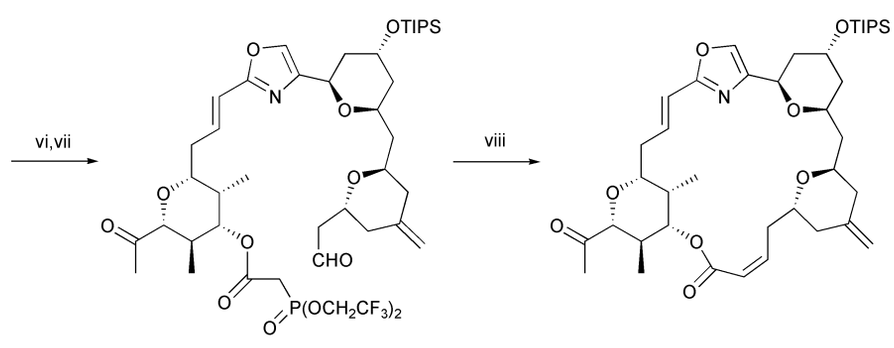


Julia olefination in the presence of NaHMDS at −78 °C, leading to the corresponding *E*-alkenes, much to our chagrin we were not able to realise a similar coupling reaction between the macrolide methyl ketone **89** and the side-chain substituted sulfone **36**, and complete a synthesis of phorboxazole A using this strategy.

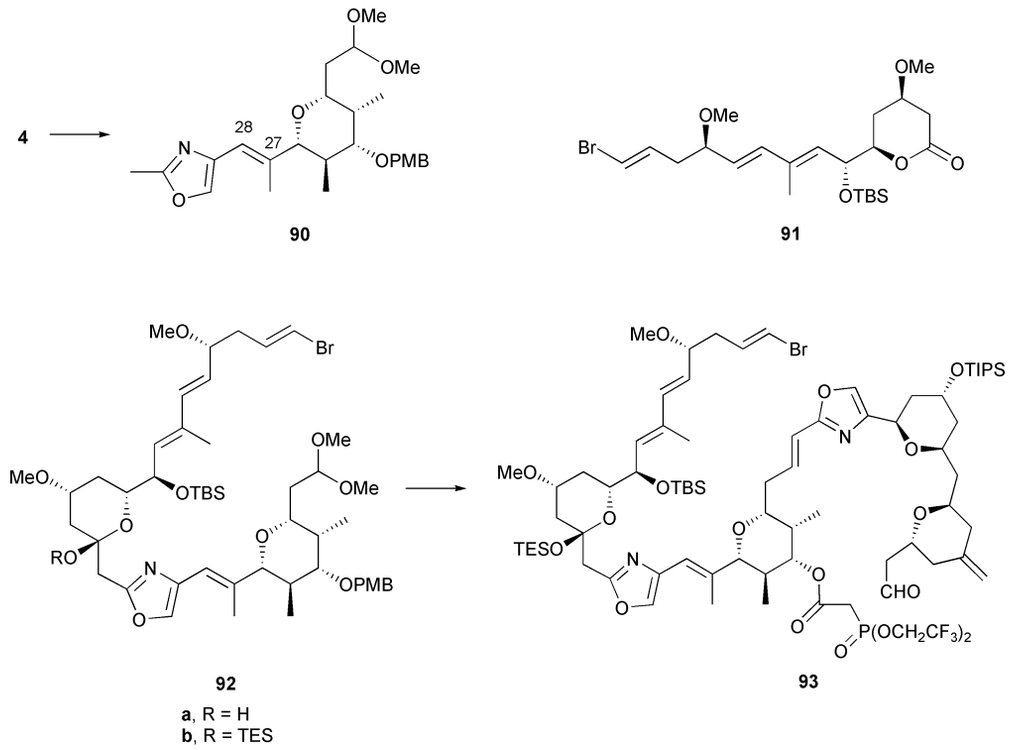
Side chain attachment to C(20–27) oxane 4

Following the disappointing outcome of our attempts to directly link the macrolide portion **89** to the side chain residue **36** in phorboxazole, we decided to follow a new strategy to the natural product. This strategy was based on first attaching the oxane methyl ketone **4** to the side chain oxazole at C(27–28) leading to the oxane–oxazole **90**. Encouraged by precedent established by Evans *et al.*[5b] and others,[47] we next planned to couple the side chain lactone **91** to the methyloxazole **90** using metallation chemistry, leading to the cyclic hemiacetal **92**. Manipulation of the functionality in **92** followed by addition of the oxazole bis-oxane **5**, at C(19–20), was then expected to lead to a precursor, *viz* **93**, for macrolide formation at C(2–3) and phorboxazole A itself (Scheme 8).

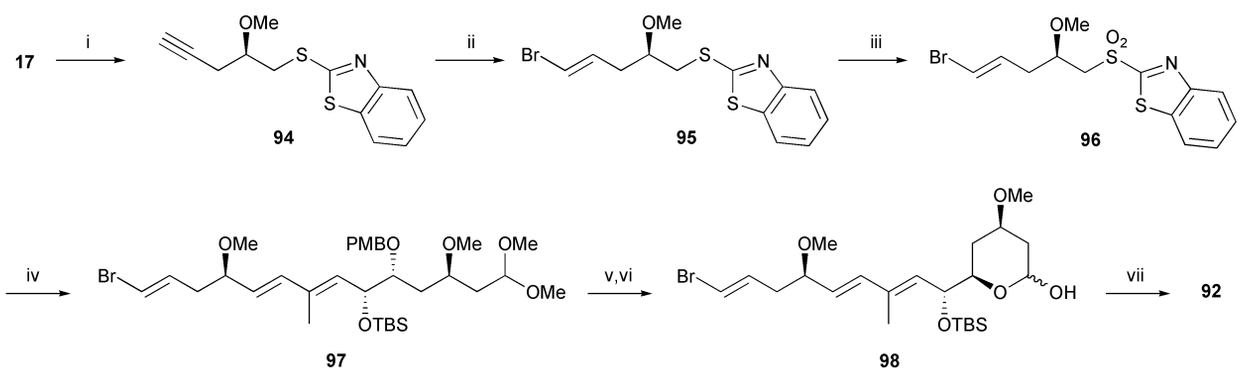




Scheme 7 *Reagents and conditions*: i, Bu_3P–DMF, then **52**, DBU; 99% ii, LiOH, THF–MeOH–H_2O; 96% iii, DDQ, DCM, pH = 7 buffer; 86% iv, TBSCl, imid., DMF; 73% v, $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, $PhCH_3$; 60% vi, CSA, MeOH–DCM; 93% vii, Dess–Martin periodinane, DCM; 92% viii, K_2CO_3, 18-crown-6, $PhCH_3$; 3 : 2 mixture of *Z*/*E*-somers; 77%.



Scheme 8



Scheme 9 *Reagents and conditions*: i, TBAF, 92%; ii, a) $Cp_2Zr(H)Cl$, DCM, b) NBS, 88% (2 steps); iii, $(NH_4)_6Mo_7O_{24}$, 30% H_2O_2, THF–MeOH, 95%; iv, NaHMDS, then **7**, THF, −78 °C to rt, 93%; v, Me_2BBr, Et_2O, −78 °C, 98%; vi, DDQ, 10 : 1 DCM–H_2O, 0 °C, 85%; vii, TPAP, NMO, powdered 4 Å sieves, DCM, 82%.

With this end-game in focus, the δ-lactone **91** was first prepared starting from the previously prepared aldehyde **7**, and the vinyl bromide sulfone **96** which was elaborated in three straightforward steps *via* **94** and **95** from the acetylene precursor **17** (Scheme 9). A Julia reaction[13] between **7** and **96** in the presence of NaHMDS at −78 °C gave the all-*E* triene **97** exclusively and in 93% yield. Sequential deprotection of the dimethylacetal and PMB groups in **97**, using dimethylboron bromide[48] and DDQ respectively, next gave the cyclic hemiacetal **98** which, on oxidation with TPAP–NMO, then led to the δ-lactone **91**.

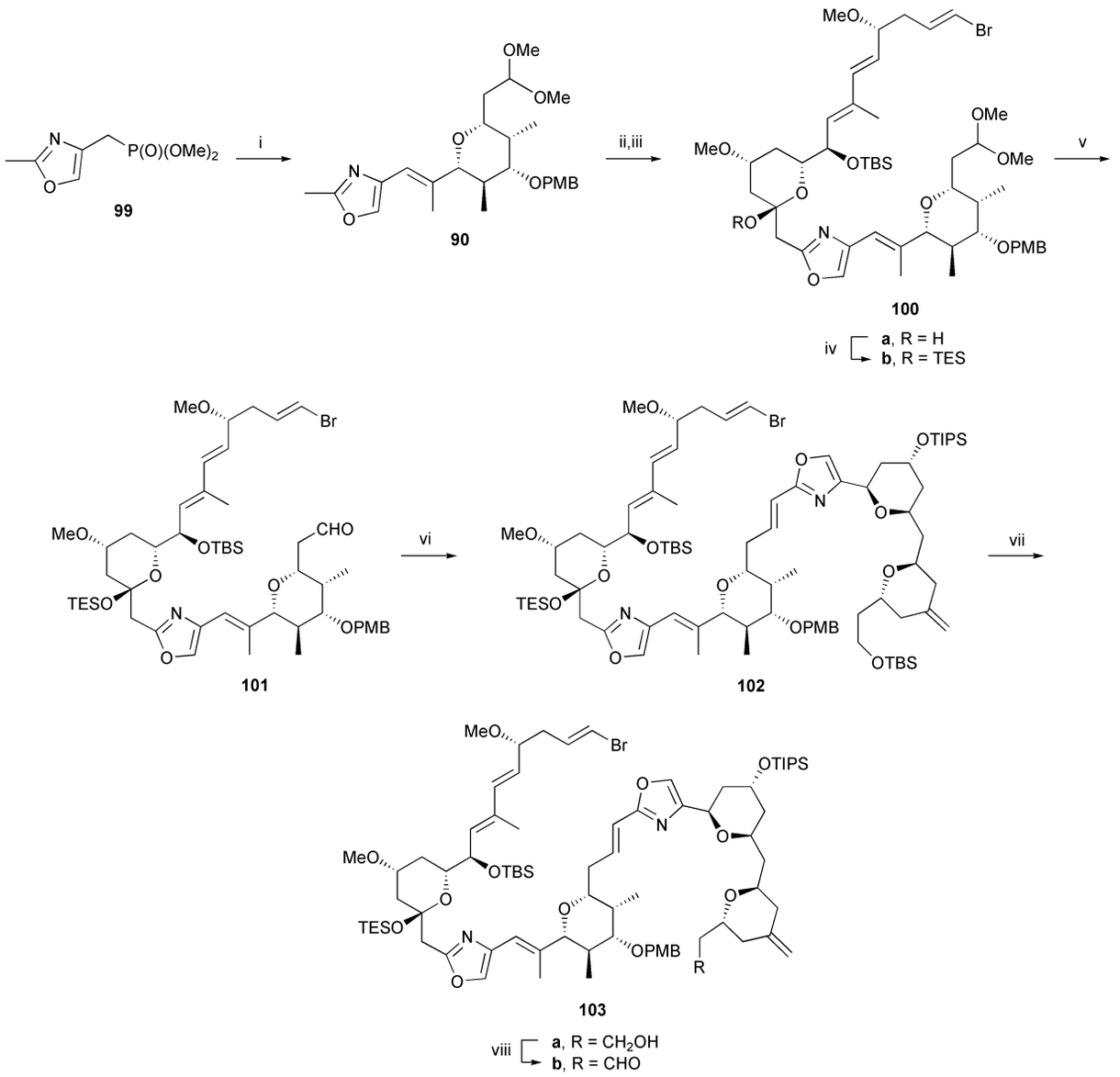
A Wadsworth–Emmons reaction between the oxazole phosphonate ester **99** and the oxane methyl ketone **4**, under optimized conditions, in the presence of LDA at −78 °C gave exclusively the *E*-alkene **90**. When the substituted 2-methyloxazole **90** was deprotonated with LDA, generated *in situ*, at −78 °C and then treated with the lactone **91** the desired cyclic hemiketal **100a** was obtained next in high yield and was immediately protected as its corresponding triethylsilylketal **100b** in 66% overall yield (Scheme 10).

Introduction of the oxazole bis-oxane unit 5

The next major step towards phorboxazole A required introduction of the oxazole bis-oxane unit **5**, leading to an intermediate whose functionality could be manipulated to the penultimate precursor **93** for macrolide construction and the natural product itself. In the total syntheses of the phorboxazoles described by Evans, Smith and Williams, and their respective collaborators, the oxazole bis-oxane unit **5** was attached to the pentasubstituted oxane residue **4** using an *E*-selective Wittig reaction at C(19–20) involving the phosphonium salt derived from **71c** and an appropriately substituted oxane aldehyde. We also used this strategy. Thus, selective cleavage of the dimethylacetal unit in **100b**, using dimethylboron bromide, first gave the corresponding oxane aldehyde **101** in excellent yield. Treatment of the mesylate **71c** with tributylphosphine led to the corresponding phosphonium salt which, *in situ*, was treated with the aldehyde **101**, followed by DBU, leading to the *E*-alkene **102** in 87% overall yield.

Completion of phorboxazole A (1)

With the three key units **3**, **4**, and **5** linked together in the shape of **102** we were now poised to construct the macrolide portion in phorboxazole A and complete its total synthesis. Accordingly, selective cleavage of the primary TBS ether in **102**, with



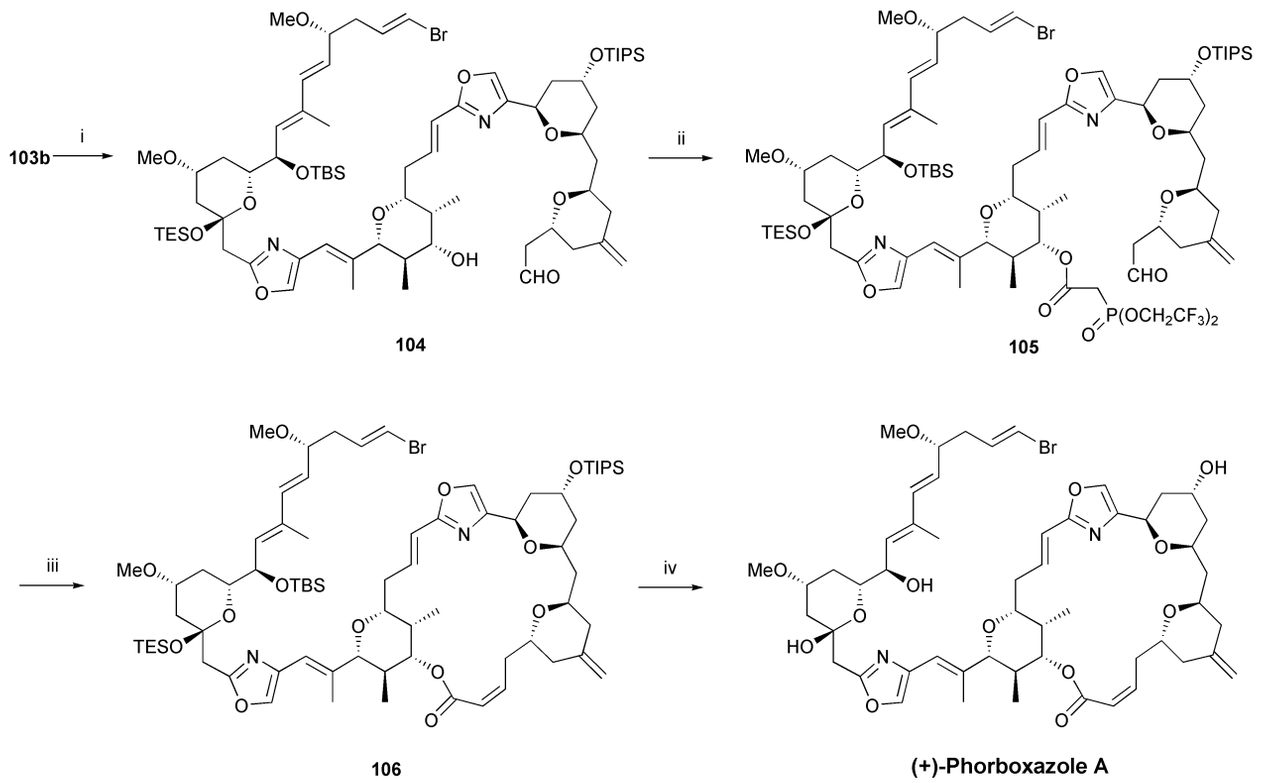
Scheme 10 *Reagents and conditions*: i, LDA, −78 °C, 30 min, then **4**, 89% (49% conversion); ii, Et_2NH, ^nBuLi,THF, −78 °C, then **91**; iv, TESOTf, py, 10 : 1 MeCN–Et_2O, −47 °C, 36 h, 74% (66% conversion, two steps); v, Me_2BBr, Et_2O, −78 °C, 85%; vi, **71c**, Bu_3P, DMF, then **101** and DBU, rt to 0 °C, 87%; vii, HF·pyr, pyr, THF, 0 °C to rt, 65–70%; viii, Dess–Martin periodinane, py, DCM, 94%.

HF·pyridine[5a] at 0 °C proceeded smoothly to give the alcohol **103a**, which was then oxidised to the corresponding aldehyde **103b** using Dess–Martin periodinane.[20] Removal of the PMB protecting group in **103b** with DDQ in CH_2Cl_2 at room temperature next led to the secondary alcohol **104** (Scheme 11), which was converted into the corresponding fluorophosphonate **105** by acylation with bis(2,2,2-trifluoroethyl)phosphonoacetic acid in the presence of EDC and HOBT.[4] Finally, intramolecular cyclisation of the aldehyde-phosphonate **105**, under the conditions of Still and Gennari,[45] gave the *Z*-αβ-unsaturated macrolide **106**, which was found to contain 20–25% of the corresponding *E*-isomer. The proportion of the *E*-isomer in the mixture followed from examination of the absorptions associated with the *E*-(δ 6.90 and 5.85 ppm) and *Z*-(δ 5.92 ppm) olefinic H-atoms in the ^{1}H NMR spectrum of mixtures; similar *Z* : *E*-ratios were observed by Forsyth *et al.*,[4] Smith *et al.*[6] and by Williams *et al.*[7] during their contemporaneous studies of this macrocyclisation approach to phorboxazole A. Removal of the three silyl ether protecting groups in **106** with tetrabutylammonium fluoride in THF at 0 °C followed by purification by reversed phase HPLC then gave phorboxazole A (**1a**) whose ^{1}H and ^{13}C NMR spectra, together with HRMS and optical rotation data corresponded to those reported for the natural product.[1a]

Experimental

General details

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were recorded in spectroscopic grade chloroform or dichloromethane on a Jasco DIP-370 polarimeter at ambient temperature. $[\alpha]_D$ values are recorded in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were obtained using a Perkin-Elmer 1600 series FT-IR instrument or a Nicolet Magna 550 instrument either as liquid films or as dilute solutions in spectroscopic grade chloroform. Proton (^{1}H) NMR spectra were recorded on either a Bruker WM 250 (250 MHz), a Bruker DPX 360 (360 MHz), a Bruker AM 400 (400 MHz), a Bruker DRX 500 (500 MHz), a Varian Unity 300 (300 MHz), a Varian Inova 400 (400 MHz) or a Jeol EX 270 (270 MHz) spectrometer as dilute solutions in deuterochloroform, unless otherwise stated. The chemical shifts are quoted in parts per million (ppm) relative to residual chloroform as internal standard (δ 7.27) and the multiplicity of each signal is designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; qu, quintet; b, broad; m, multiplet; app, apparent. The axial and equatorial protons that are found in six-membered rings are abbreviated as: ax, axial; eq, equatorial. All coupling constants are quoted in hertz. Carbon-13 (^{13}C)



Scheme 11 *Reagents and conditions*: i, DDQ, DCM–pH = 7 buffer, 85%; ii, EDCl·MeI, HOBT, $HO_2CCH_2PO(OCH_2CF_3)_2$, DCM, >80%; iii, K_2CO_3, 18-crown-6, $PhCH_3$, rt, 3 : 1 mixture of *Z*/*E*-isomers, 82%; iv, TBAF, THF, 0 °C–rt, 75%; RP-HPLC purification.

NMR spectra were recorded on either a Bruker DPX 360 (at 90.6 MHz), a Bruker DRX 500 (at 125.8 MHz) or a Jeol EX-270 (at 67.8 MHz) instrument as dilute solutions in deuterochloroform, unless otherwise stated. Chemical shifts are reported relative to internal chloroform standard (δ 77.0) on a broad band decoupled mode, and the multiplicities determined using a DEPT sequence. Where required, ^{1}H–^{1}H COSY and NOE spectra were recorded on a Bruker DPX 360 (360 MHz) or a Bruker DRX 500 (500 MHz) instrument using standard Bruker software with no modifications. Mass spectra were recorded on a VG Autospec, a MM-701CF, a VG Micromass 7070E or a Micromass LCT spectrometer using electron ionisation (EI), fast atom bombardment (FAB), chemical ionisation (CI) or electrospray ionisation (ESI) techniques. Microanalytical data were obtained on a Perkin-Elmer 240B elemental analyser.

Flash chromatography was performed on Merck silica gel 60 as the stationary phase and the solvents employed were either of analytical grade or were distilled before use. All reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F_{254} precoated aluminium backed plates which were visualised with ultraviolet light and then with either acidic alcoholic vanillin solution, basic potassium permanganate solution, or acidic anisaldehyde solution.

Routinely, dry organic solvents were stored under nitrogen and/or over sodium wire. Other organic solvents were dried by distillation from the following: THF and benzene (potassium benzophenone ketyl), dichloromethane (calcium hydride) and methanol (magnesium methoxide). Other organic solvents and reagents were purified by the accepted literature procedures. Dess–Martin periodinane was prepared according to the modified procedure of Ireland and Liu.[49] Dimethyl α-diazomethylphosphonate was prepared by the procedure of Seyferth.[16] All organic extracts were dried as stated. Solvent was removed on a Büchi rotary evaporator. Where necessary, reactions requiring anhydrous conditions were performed in a flame or oven dried apparatus under a nitrogen or argon atmosphere as stated.

(4*R*)-2′-(2,2-Dimethyl-[1,3]-dioxolan-4-yl)-ethanol (10). Borane–methyl sulfide complex (26 ml, 0.27 mol) was added dropwise over 50 min to a stirred solution of (D)-(+)-malic acid (12 g, 89 mmol) and trimethyl borate (41 g, 0.39 mol) in THF (120 ml) at 0 °C under a nitrogen atmosphere. The mixture was warmed to room temperature, then stirred at this temperature for 44 h before it was quenched, at 0 °C, by the slow dropwise addition of methanol (100 ml). The mixture was stirred at room temperature for 30 min and then concentrated *in vacuo*. Methanol (2 × 100 ml) was added to the residue and then removed *in vacuo* to leave 1,3-dihydroxybutanol as an opaque oil which was used without further purification.

Anhydrous copper(II) sulfate (11.2 g, 45 mmol) and *para*-toluenesulfonic acid monohydrate (0.34 g, 1.8 mmol) were added separately, each in one portion, to a stirred solution of the crude dihydroxybutanol in acetone (300 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 48 h, then solid sodium hydrogencarbonate (0.8 g) was added in one portion and the mixture was stirred for 20 min. The mixture was filtered and the filtrate was concentrated *in vacuo* to leave a light blue oil. Purification by flash chromatography, using 40% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the acetonide[15] (10.1 g, 77%) as a colourless oil; $[\alpha]_D^{21}$ +3.1 (*c* 0.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3534, 2946, 1372, 1152, 981; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.22–4.32 (1H, m, *H*-4), 4.09 (1H, dd, *J* 8.1, 6.0, *H*-5), 3.79 (2H, dd, *J* 10.8, 5.5, *H*-1′), 3.59 (1H, dd, *J* 8.1, 7.4, *H*-5), 2.36 (1H, bt, *J* 4.9, O*H*), 1.84–1.79 (2H, m, *H*-2′), 1.42 (3H, s, CCH_3), 1.36 (3H, s, CCH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 109.3 (s), 75.1 (d), 69.7 (t), 60.5 (t), 36.0 (t), 27.1 (q), 25.9 (q); *m*/*z* (EI) Found 131.0706 ([M − CH_3]$^+$ $C_6H_{11}O_3$ requires 131.0708).

(4*R*)-4-[2′-(4-Methoxybenzyloxy)-ethyl]-2,2-dimethyl-[1,3]-dioxolane (11). Potassium *tert*-butoxide (11.6 g, 104 mmol) was added in three portions over 10 min to a stirred solution of the alcohol (**10**) (10.1 g, 69.1 mmol) in THF (250 ml) at 0 °C under a nitrogen atmosphere. The yellow solution was stirred at 0 °C for 15 min and then 4-methoxybenzyl chloride (13.0 g, 10.5 ml,

76.0 mmol) was added dropwise over 20 min followed by tetrabutylammonium iodide (2.55 g, 6.91 mmol) in one portion. The mixture was stirred at room temperature for 12 h and then quenched by addition of a saturated aqueous solution of sodium hydrogencarbonate (80 ml). The separated aqueous layer was extracted with ethyl acetate (3 × 200 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 12% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *benzyloxy derivative* (15.1 g, 82%) as a light yellow oil; $[a]_D^{21}$ −1.0 (*c* 1.6 in $CHCl_3$) (Found: C, 67.2; H, 8.4. $C_{15}H_{22}O_4$ requires C, 67.6; H, 8.3%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2838, 1613, 1099; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.45 (2H, s, CH_2Ar), 4.16–4.26 (1H, m, *H*-4), 4.06 (1H, dd, *J* 8.0, 5.9, *H*-5), 3.82 (3H, s, OCH_3), 3.59–3.53 (3H, m, *H*-5, *H*-1′), 1.95–1.89 (1H, m, *H*-2′), 1.87–1.81 (1H, m, *H*-2′), 1.41 (3H, s, CCH_3), 1.36 (3H, s, CCH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 159.1 (s), 130.4 (s), 129.2 (d), 113.7 (d), 108.5 (s), 73.9 (d), 72.7 (t), 69.6 (t), 66.7 (t), 55.2 (q), 33.8 (t), 26.9 (q), 25.7 (q); *m*/*z* (EI) Found 266.1510 (M^+ $C_{15}H_{22}O_4$ requires 266.1518).

(2*R*)-4-(4-Methoxybenzyloxy)-butane-1,2-diol (12a). *para*-Toluenesulfonic acid (2.6 g, 13.6 mmol) was added in one portion to a stirred solution of the acetonide (**11**) (18.1 g, 68.0 mmol) in methanol (360 ml) at 0 °C under a nitrogen atmosphere. The mixture was warmed to room temperature and stirred at this temperature for 12 h before it was quenched with a saturated aqueous solution of sodium hydrogencarbonate (120 ml). The methanol was removed *in vacuo* and the remaining aqueous layer was then extracted with ethyl acetate (3 × 250 ml, 1 × 100 ml). The combined organic extracts was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 80% ethyl acetate–petroleum ether (bp 40–60 °C), increasing to ethyl acetate as eluent, gave the *diol* (12.6 g, 84%) as a light yellow oil; $[a]_D^{21}$ −7.7 (*c* 1.0 in $CHCl_3$) (Found: C, 63.9; H, 8.7. $C_{12}H_{18}O_4$ requires C, 63.7; H, 8.0%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3478, 2864, 1613, 1097; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.46 (2H, s, CH_2Ar), 3.91–3.87 (1H, m, *H*-2), 3.81 (3H, s, OCH_3), 3.68–3.58 (3H, m, *H*-1, *H*-4), 3.50 (1H, dd, *J* 11.3, 5.3, *H*-1), 3.26 (1H, d, *J* 3.5, O*H*), 2.54 (1H, t, *J* 6.2, O*H*), 1.84–1.77 (1H, m, *H*-3), 1.76–1.69 (1H, m, *H*-3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 159.2 (s), 129.8 (s), 129.3 (d), 113.8 (d), 72.9 (t), 71.2 (d), 67.7 (t), 66.5 (t), 55.2 (q), 32.7 (t); *m*/*z* (FAB) Found 227.1278 ($[MH]^+$ $C_{12}H_{19}O_4$ requires 227.1283).

(2*R*)-1-(*tert*-Butyldiphenylsilanyloxy)-4-(4-methoxybenzyloxy)-butan-2-ol (12b). *tert*-Butylchlorodiphenylsilane (12.4 g, 11.8 ml, 45 mmol) and 4-(dimethylamino)-pyridine (540 mg, 4.6 mmol) were added separately, each in one portion, to a stirred solution of the diol (**12a**) (10.0 g, 44 mmol) in dichloromethane (300 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 0 °C for 15 min and then triethylamine (12.3 ml, 88 mmol) was added dropwise over 5 min. The mixture was warmed to room temperature and stirred at this temperature for 12 h before it was quenched with a saturated aqueous solution of ammonium chloride (300 ml). The separated aqueous layer was extracted with dichloromethane (2 × 300 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave an opaque residue. Purification by flash chromatography, using 15% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *silyl ether* (19.2 g, 94%) as a colourless oil; $[a]_D^{21}$ −1.9 (*c* 1.5 in $CHCl_3$) (Found: C, 72.6; H, 8.0. $C_{28}H_{36}O_4Si$ requires C, 72.4; H, 7.8%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3572, 2860, 1613, 1089; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.69–7.66 (4H, m, C*H*, SiAr), 7.47–7.37 (6H, m, C*H*, SiAr), 7.23 (2H, d, *J* 8.7, C*H*, Ar), 6.87 (2H, d, *J* 8.7, C*H*, Ar), 4.43 (2H, s, CH_2Ar), 3.94–3.91 (1H, m, *H*-2), 3.81 (3H, s, OCH_3), 3.68–3.56 (4H, m, *H*-1, *H*-4), 2.88 (1H, d, *J* 3.5, O*H*), 1.7–1.83 (2H, m, *H*-3), 1.08 (9H, s, $C(CH_3)_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 159.1 (s), 135.5 (d), 133.2 (s), 130.2 (s), 129.7 (d), 129.2 (d), 127.7 (d), 113.7 (d), 72.8 (t), 70.4 (d), 67.7 (t), 67.5 (t), 55.2 (q), 32.9 (t), 26.8 (q), 19.2 (s); *m*/*z* (FAB) Found 463.2312 ($[M - H]^+$ $C_{28}H_{35}O_4Si$ requires 463.2305).

(2*R*)-*tert*-Butyl-[2-methoxy-4-(4-methoxybenzyloxy)-butoxy]-diphenylsilane (13a). A solution of the alcohol (**12b**) (21.3 g, 45.9 mmol) in THF (80 ml) was added dropwise over 30 min to a stirred suspension of sodium hydride (60% dispersion in mineral oil, 5.5 g, 138 mmol) in THF (320 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 0 °C for 45 min and then methyl iodide (32.5 g, 14.3 ml, 229 mmol) was added dropwise over 30 min. The mixture was warmed to room temperature and stirred at this temperature for 15 h before it was quenched with a saturated aqueous solution of ammonium chloride (100 ml). The mixture was concentrated *in vacuo* to leave an aqueous residue, which was taken up in ethyl acetate (200 ml). The separated aqueous layer was extracted with ethyl acetate (3 × 200 ml), and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 8% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *methyl ether* (19.0 g, 87%) as a colourless oil; $[a]_D^{20}$ +14.1 (*c* 1.1 in $CHCl_3$) (Found: C, 72.5; H, 8.1. $C_{29}H_{38}O_4Si$ requires C, 72.8; H, 8.0%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2859, 1613, 1090; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.71–7.68 (4H, m, C*H*, SiAr), 7.46–7.37 (6H, m, C*H*, SiAr), 7.26 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.43 (2H, d, *J* 2.7, CH_2Ar), 3.82 (3H, s, $ArOCH_3$), 3.67 (2H, d, *J* 4.9, *H*-1), 3.58–3.52 (2H, m, *H*-4), 3.43–3.47 (1H, m, *H*-2), 3.38 (3H, s, OCH_3), 1.89–1.85 (1H, m, *H*-3), 1.79–1.75 (1H, m, *H*-3), 1.07 (9H, s, $C(CH_3)_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 159.0 (s), 135.6 (d), 133.5 (s), 130.6 (s), 129.6 (d), 129.2 (d), 127.6 (d), 113.7 (d), 78.9 (d), 72.5 (t), 66.5 (t), 65.6 (t), 58.1 (q), 55.2 (q), 31.8 (t), 26.8 (q), 19.2 (s); *m*/*z* (FAB) Found 421.1832 ($[M - C_4H_9]^+$ $C_{25}H_{29}O_4Si$ requires 421.1835).

(3*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-3-methoxy-butan-1-ol (13b). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (2.8 g, 12.6 mmol) was added in one portion to a stirred solution of the differentially protected triol (**13a**) (4.0 g, 8.4 mmol) in dichloromethane (80 ml) and water (4 ml) at room temperature. The mixture was stirred at room temperature for 3 h, before it was quenched with a saturated aqueous solution of sodium hydrogencarbonate (20 ml). The mixture was filtered through celite and the filtrate was concentrated *in vacuo* to leave a red oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (2.8 g, 95%) as a colourless oil; $[a]_D^{21}$ +14.8 (*c* 0.5 in $CHCl_3$) (Found: C, 69.9; H, 8.7. $C_{21}H_{30}O_3Si$ requires C, 70.3; H, 8.4%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3494, 2931, 1112; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.72–7.67 (4H, m, C*H*, SiAr), 7.48–7.38 (6H, m, C*H*, SiAr), 3.78 (2H, app t, *J* ~5.6, *H*-1), 3.75 (1H, dd, *J* 10.8, 5.0, *H*-4), 3.66 (1H, dd, *J* 10.8, 5.2, *H*-4), 3.49 (1H, dddd, *J* 7.5, 5.2, 5.0, 5.0, *H*-3), 3.38 (3H, s, OCH_3), 2.63 (1H, b s, O*H*), 1.88–1.76 (2H, m, *H*-2), 1.08 (9H, s, $C(CH_3)_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 135.6 (d), 133.3 (s), 133.2(s), 129.7 (d), 127.7 (d), 81.4 (d), 65.1 (t), 60.7 (t), 57.9 (q), 33.9 (t), 26.8 (q), 19.2 (s); *m*/*z* (FAB) Found 359.2061 ($[MH]^+$ $C_{21}H_{31}O_3Si$ requires 359.2042).

(3*R*)-4-(*tert*-Butyldiphenylsilanyloxy)-3-methoxy-butyraldehyde (14). A solution of dimethyl sulfoxide (1.5 g, 1.38 ml, 19.4 mmol) in dichloromethane (16 ml) was added dropwise, *via* cannula, over 10 min to a stirred solution of oxalyl chloride (1.64 g, 1.13 ml, 12.9 mmol) in dichloromethane (30 ml) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 15 min and then a solution of the alcohol (**13b**)

(2.32 g, 6.47 mmol) in dichloromethane (24 ml) was added dropwise, *via* cannula, over 10 min. The mixture was stirred at −78 °C for 1 h and then diisopropylethylamine (3.34 g, 4.51 ml, 25.9 mmol) was added dropwise over 8 min. The mixture was warmed to −10 °C over 3.5 h, then quenched with a saturated aqueous solution of potassium hydrogensulfate (60 ml) and warmed to room temperature. The separated aqueous layer was extracted with dichloromethane (2 × 60 ml), and the combined organic extracts was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *aldehyde* (2.1 g, 90%) as a colourless oil; $[\alpha]_D^{21}$ +16.1 (*c* 1.1 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2931, 2858, 1715, 1112; ^1H NMR (360 MHz, $CDCl_3$) δ 9.83 (1H, t, *J* 2.0, *H*-1), 7.69–7.66 (4H, m, C*H*, SiAr), 7.46–7.38 (6H, m, C*H*, SiAr), 3.80–3.72 (2H, m, *H*-3, *H*-4), 3.66 (1H, dd, *J* 10.5, 5.4, *H*-4), 3.34 (3H, s, OCH_3), 2.70–2.67 (2H, m, *H*-2), 1.07 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.1 (d), 135.5 (d), 133.0 (s), 129.8 (d), 127.7 (d), 76.8 (d), 64.5 (t), 57.7 (q), 46.0 (t), 26.7 (q), 19.1 (s); *m*/*z* (EI) Found 299.1109 ([M − C_4H_9]$^+$ $C_{17}H_{19}O_3Si$ requires 299.1104).

(2*R*)-*tert*-Butyl-(2-methoxy-pent-4-ynyloxy)-diphenylsilane (15a). A solution of potassium *tert*-butoxide (1 M in THF, 0.86 g, 7.7 ml, 7.7 mmol) in THF (10 ml) was added dropwise over 8 min to a stirred solution of dimethyl α-diazomethylphosphonate (1.24 g, 8.2 mmol) in THF (30 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 25 min and then a solution of the aldehyde (**14**) (2.08 g, 5.9 mmol) in THF (15 ml) at −78 °C was added dropwise, *via* cannula, over 10 min. The mixture was stirred at −78 °C for 1 h 20 min, then quenched with water (40 ml) and allowed to warm to room temperature. The separated aqueous layer was extracted with ethyl acetate (3 × 50 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 8% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alkyne* (1.53 g, 75%) as a colourless oil; $[\alpha]_D^{21}$ + 5.9 (*c* 1.5 in $CHCl_3$) (Found: C, 75.1; H, 8.2. $C_{22}H_{28}O_2Si$ requires C, 75.0; H, 8.0%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3307, 2931, 1112, 1078; ^1H NMR (360 MHz, $CDCl_3$) δ 7.72–7.68 (4H, m, C*H*, SiAr), 7.44–7.37 (6H, m, C*H*, SiAr), 3.76 (2H, d, *J* 5.3, *H*-1), 3.4–3.5 (1H, m, *H*-2), 3.41 (3H, s, OCH_3), 2.59 (1H, ddd, *J* 17.1, 5.6, 2.7, *H*-3), 2.48 (1H, ddd, *J* 17.1, 5.6, 2.7, *H*-3), 1.97 (1H, t, *J* 2.7, *H*-5), 1.07 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 135.6 (d), 133.4 (s), 129.7 (d), 127.7 (d), 81.0 (d), 79.9 (d), 69.6 (s), 64.0 (t), 57.8 (q), 26.8 (q), 20.9 (t), 19.2 (s); *m*/*z* (FAB) Found 295.1179 ([M − C_4H_9]$^+$ $C_{18}H_{19}O_2Si$ requires 295.1154).

(2*R*)-2-Methoxy-pent-4-yn-1-ol (15b). Tetrabutylammonium fluoride (1 M in THF, 23.2 ml, 23.2 mmol) was added dropwise over 2 min to a stirred solution of the alkyne (**15a**) (6.8 g, 19.2 mmol) in THF (200 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h 45 min and then quenched with a saturated aqueous solution of ammonium chloride (200 ml). The separated aqueous layer was extracted with ethyl acetate (3 × 200 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave a red oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alkyne* (2.1 g, 96%) as a volatile colourless oil; $[\alpha]_D^{21}$ −38.9 (*c* 0.6 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3589, 3307, 2934, 2121, 1111; ^1H NMR (360 MHz, $CDCl_3$) δ 3.78 (1H, dd, *J* 11.7, 3.6, *H*-1), 3.64 (1H, dd, *J* 11.7, 6.0, *H*-1), 3.48–3.42 (4H, m, *H*-2, OCH_3), 2.48 (1H, ddd, *J* 16.9, 5.2, 2.7, *H*-3), 2.41 (1H, ddd, *J* 16.9, 7.1, 2.7, *H*-3), 2.13 (1H, b s, O*H*), 2.01 (1H, t, *J* 2.7, *H*-5); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 80.2 (d), 79.6 (d), 70.3 (s), 63.3 (t), 57.4 (q), 19.9 (t); *m*/*z* (ESI) Found 137.0584 ([M + Na]$^+$ $C_6H_{10}O_2Na$ requires 137.0578).

(2*R*)-2-Methoxy-5-(trimethylsilanyl)-pent-4-yn-1-ol (16). *n*-Butyllithium (1.6 M in hexanes, 16.2 ml, 25.8 mmol) was added dropwise over 10 min to a stirred solution of the alkyne (**15b**) (1.41 g, 12.3 mmol) in THF (120 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 1 h and then chlorotrimethylsilane (3.45 ml, 27.2 mmol) was added dropwise over 10 min. The mixture was stirred at −78 °C for 30 min and then warmed to room temperature and stirred at this temperature for a further 1 h 30 min. The mixture was quenched with a saturated aqueous solution of ammonium chloride (120 ml) and then concentrated *in vacuo* to leave an aqueous residue. The residue was extracted with diethyl ether (2 × 120 ml) and the combined extracts were stirred with 1 M hydrochloric acid (120 ml) for 45 min. The separated aqueous layer was extracted with diethyl ether (1 × 180 ml) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 30% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *silyl alkyne* (1.62 g, 70%) as a colourless oil; $[\alpha]_D^{21}$ −36.3 (*c* 1.8 in $CHCl_3$) (Found: C, 58.1; H, 10.2. $C_9H_{18}O_2Si$ requires C, 58.0; H, 9.8%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3589, 2934, 2174, 1265, 1112, 863; ^1H NMR (360 MHz, $CDCl_3$) δ 3.80 (1H, dd, *J* 11.6, 3.4, *H*-1), 3.62 (1H, dd, *J* 11.6, 6.1, *H*-1), 3.48–3.42 (4H, m, *H*-2, OCH_3), 2.55 (1H, dd, *J* 16.9, 5.0, *H*-3), 2.38 (1H, dd, *J* 16.9, 7.9, *H*-3), 2.05 (1H, b s, O*H*), 0.15 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 102.7 (s), 87.0 (s), 80.0 (d), 63.8 (t), 57.6 (q), 21.5 (t), 0.0 (q); *m*/*z* (CI) Found 187.1175 ([MH]$^+$ $C_9H_{19}O_2Si$ requires 187.1154).

(2*R*)-2′-[2-Methoxy-5-(trimethylsilanyl)-pent-4-ynylsulfanyl]-benzothiazole (17). A solution of the alcohol (**16**) (500 mg, 2.7 mmol) in THF (20 ml) was added dropwise over 2 min to a stirred solution of 2-mercaptobenzothiazole (0.9 g, 5.4 mmol) and triphenylphosphine (1.1 g, 4.0 mmol) in THF (20 ml) at 0 °C under a nitrogen atmosphere. Diethyl azodicarboxylate (0.8 ml, 5.1 mmol) was added dropwise over 2 min and the mixture was stirred for 1 h 30 min whilst it warmed to room temperature. The mixture was diluted with diethyl ether (40 ml), then water (40 ml) and brine (40 ml) were added. The separated aqueous layer was extracted with ethyl acetate (2 × 10 ml), and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave a white solid. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *thioether* (850 mg, 94%) as a colourless oil; $[\alpha]_D^{21}$ −8.4 (*c* 2.3 in $CHCl_3$) (Found: C, 57.5; H, 6.5; N, 4.1; S, 19.1. $C_{16}H_{21}ONS_2Si$ requires C, 57.3; H, 6.3; N, 4.2; S, 19.1%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2959, 2175, 1457, 1103, 996; ^1H NMR (360 MHz, $CDCl_3$) δ 7.86 (1H, ddd, *J* 8.4, 1.0, 0.5, C*H*, Ar), 7.76 (1H, ddd, *J* 8.1, 1.2, 0.5, C*H*, Ar), 7.42 (1H, ddd, *J* 8.4, 7.2, 1.2, C*H*, Ar), 7.30 (1H, ddd, *J* 8.1, 7.2, 1.0, C*H*, Ar), 3.78–3.73 (1H, m, *H*-2), 3.73 (1H, dd, *J* 16.5, 4.8, *H*-1), 3.61–3.54 (1H, m, *H*-1), 3.49 (3H, s, OCH_3), 2.68 (1H, dd, *J* 16.9, 5.4, *H*-3), 2.60 (1H, dd, *J* 16.9, 6.2, *H*-3), 0.18 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 167.5 (s), 153.1 (s), 135.0 (s), 126.0 (d), 124.2 (d), 121.5 (d), 120.9 (d), 102.3 (s), 88.0 (s), 78.2 (d), 58.0 (q), 36.7 (t), 24.5 (t), 0.0 (q); *m*/*z* (EI) Found 335.0849 (M$^+$ $C_{16}H_{21}ONS_2Si$ requires 335.0854).

(2*R*)-2′-[2-Methoxy-5-(trimethylsilanyl)-pent-4-yn-1-ylsulfonyl]-benzothiazole (6). A solution of *meta*-chloroperbenzoic acid (0.44 g, 2.6 mmol) in dichloromethane (10 ml) was added dropwise over 2 min to a stirred solution of the thioether (**13**) (368 mg, 1.08 mmol) and sodium hydrogencarbonate (0.48 g, 5.48 mmol) in dichloromethane (10 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 15 h and then was quenched with a saturated aqueous solution of sodium thiosulfate (10 ml). The separated aqueous layer was extracted with dichloromethane (2 × 40 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave a white solid. Purification by

flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *sulfone* (344 mg, 85%) which crystallized from petroleum ether as colourless crystals, mp 101–103 °C; $[\alpha]_D^{21}$ −35.7 (*c* 1.9 in $CHCl_3$) (Found: C, 52.3; H, 5.7; N, 3.6; S, 17.4. $C_{16}H_{21}O_3NS_2Si$ requires C, 52.3; H, 5.8; N, 3.8; S, 17.5%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2959, 2176, 1327, 1144, 1108; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.24–8.21 (1H, m, C*H*, Ar), 8.03–8.00 (1H, m, C*H*, Ar), 7.66–7.57 (2H, m, C*H*, Ar), 4.07–4.02 (1H, m, *H*-2), 3.94 (1H, dd, *J* 14.8, 8.9, *H*-1), 3.81 (1H, dd, *J* 14.8, 3.0, *H*-1), 3.25 (3H, s, OCH_3), 2.66 (1H, dd, *J* 17.0, 4.6, *H*-3), 2.46 (1H, dd, *J* 17.0, 7.4, *H*-3), 0.15 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 166.8 (s), 152.6 (s), 136.8 (s), 127.9 (d), 127.5 (d), 125.5 (d), 122.2 (d), 100.6 (s), 88.7 (s), 74.5 (d), 58.7 (t), 57.5 (q), 24.1 (t), −0.1 (q); *m*/*z* (FAB) Found 368.0798 ($[MH]^+$ $C_{16}H_{22}O_3NS_2Si$ requires 368.0810).

2-Deoxy-4,5-*O*-isopropylidene-D-*threo*-pentose diethyl dithioacetal (18a). Ethanethiol (50.0 ml, 0.676 mol) was added dropwise over 10 min to a stirred solution of (D)-xylose (50.0 g, 0.333mol) in 6 M hydrochloric acid (400 ml) at room temperature. The mixture was stirred at room temperature for 2 h and then neutralised with calcium carbonate (120 g) until pH 7 was attained. The precipitated inorganic residue was removed by filtration and washed with toluene (500 ml). The biphasic filtrate was concentrated *in vacuo* to leave a residue which was taken up in acetone (1 L), cooled to 0 °C and then treated with concentrated sulfuric acid (15 ml). The resulting solution was stirred for 16 h and then neutralised by the addition of calcium hydroxide (50 g). The precipitated solid was removed by filtration and washed with acetone (500 ml). The filtrate was concentrated *in vacuo* to leave a brown oil which was taken up in diethyl ether and washed with a saturated solution of sodium bicarbonate (600 ml), and then a saturated solution of brine (600 ml). The organic extract was dried and then evaporated *in vacuo* to leave the crude product (~70 g) as a yellow oil. An analytical sample was purified by chromatography on silica, eluting with 10% ethyl acetate in petroleum ether (bp 40–60 °C), to give 2,3:4,5-di-*O*-isopropylidene-D-xylose diethyl dithioacetal as a pale yellow oil; $[\alpha]_D^{21}$ −70.1 (*c* 2.6 in acetone) [lit.[50] −67.0 (*c* 2.8 in acetone)]; ν_{max} (soln: $CHCl_3$)/cm^{-1} 2982, 2931, 1381, 1372, 1070; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.34 (2H, m, *H-2, H-3*), 4.12 (1H, dd, *J* 7.4, 3.1, *H-4*), 4.04 (1H, dd, *J* 8.1, 6.7, *H-5*), 3.92 (1H, t, *J* 7.6, *H-5*), 3.89 (1H, d, *J* 5.2, *H-1*), 2.79–2.68 (4H, m, S(CH_2CH$_3$)$_2$), 1.45 (3H, s, CCH_3), 1.41 (6H, s, 2 × CCH_3), 1.36 (3H, s, CCH_3), 1.26 (3H, t, *J* 7.4, SCH$_2$CH_3), 1.25 (3H, t, *J* 7.4, SCH$_2$CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 110.0 (s), 109.4 (s), 80.0 (d), 78.6 (d), 75.2 (d), 65.8 (t), 53.0 (d), 27.3 (q), 27.1 (q), 26.1 (q), 25.5 (q), 25.3 (t), 24.9 (t), 14.3 (q), 14.2 (q); *m*/*z* (EI) Found: 336.1445 ($[M]^+$ $C_{15}H_{28}O_4S_2$ requires 336.1429).

A solution of the acetonide (70 g, 0.21 mol) in THF (300 ml) was added dropwise over 1 h to a solution of potassium *tert*-butoxide (30.4 g, 0.271mol) in THF (750 ml) and dimethyl sulfoxide (300 ml) at room temperature, under a nitrogen atmosphere. The mixture was stirred at room temperature for 1 h and then poured onto ice (500 g). The mixture was extracted with dichloromethane (3 × 400 ml) and the combined organic extracts were washed with water (500 ml) and dried (Na_2SO_4). The solution was concentrated *in vacuo* to leave a brown oil, which was purified by chromatography on silica, eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give 2-deoxy-4,5-*O*-isopropylidene-D-threo-pent-1-enose diethyl dithioacetal (32.8 g, 35%, 3 steps) as a pale yellow oil; $[\alpha]_D^{21}$ −54.4 (*c* 2.4 in $CHCl_3$) [lit.[18] −48.5 (*c* 2.4 in $CHCl_3$)] (Found: C, 52.0; H, 8.1%, Calc. for $C_{12}H_{22}O_3S_2$: C, 51.8; H, 8.0%); ν_{max}(soln: $CHCl_3$)/cm^{-1} 3566 (br), 1374, 1065; ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.85 (1H, d, *J* 8.6, *H-2*), 4.75–4.70 (1H, m, *H-3*), 4.03 (1H, app q, *J* 6.4, *H-4*), 3.91 (1H, dd, *J* 8.4, 6.4, *H-5*), 3.73 (1H, dd, *J* 8.4, 6.4, *H-5*), 2.86–2.66 (5H, m, S(CH_2CH$_3$)$_2$, O*H*), 1.42 (3H, s, CCH_3), 1.32 (3H, s, CCH_3), 1.21 (3H, t, *J* 7.4, SCH$_2$CH_3), 1.20 (3H, t, *J* 7.4, SCH$_2$CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 135.8 (s), 132.6 (d), 109.6 (s), 78.7 (d), 70.5 (d), 65.6 (t), 27.4 (t), 26.8 (t), 26.5 (q), 25.2 (q), 14.9 (q), 13.7 (q); *m*/*z* (EI) Found: 260.0908 ($[M - H_2O]^+$ $C_{12}H_{20}O_2S_2$ requires 260.0905).

A solution of the ketene dithioacetal (32.0 g, 0.115 mol) in THF (300 ml) was added dropwise over 2 h to a suspension of lithium aluminium hydride (10.0 g, 0.264 mol) in THF (800 ml) at room temperature, under a nitrogen atmosphere, and the mixture was then stirred for 3 h. The residual lithium aluminium hydride was quenched by dropwise sequential addition of water (10 ml), 2 M sodium hydroxide (10 ml) and water (20 ml) over a 1 h period. The resulting mixture was filtered through Celite, and the residual solid was washed with diethyl ether (500 ml). The filtrate was washed with brine (500 ml), then dried (Na_2SO_4) and concentrated *in vacuo* to leave the alcohol (29.1 g, 90%) as a colourless oil; $[\alpha]_D^{20}$ + 26.3 (*c* 3.9 in $CHCl_3$) [lit.[18] +25.6 (*c* 5.0 in $CHCl_3$)] (Found: C, 51.4; H, 8.9; S, 23.0%, Calc. for $C_{12}H_{24}O_3S_2$: C, 51.4; H, 8.6; S, 22.8%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3471(br), 1372, 1067; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.05 (1H, dd, *J* 10.4, 4.2, *H-1*), 4.01–3.95 (2H, m, *H-4, H-5*), 3.87 (1H, ddd, *J* 10.0, 4.5, 2.5, *H-3*), 3.73 (1H, dd, *J* 10.9, 9.5, *H-5*), 3.07 (1H, b s, O*H*), 2.72–2.51 (4H, m, S(CH_2CH$_3$)$_2$), 1.98 (1H, ddd, *J* 14.2, 7.8, 4.2, *H-2*), 1.67 (1H, ddd, *J* 14.2, 10.4, 2.5, *H-2*), 1.40 (3H, s, CCH_3), 1.33 (3H, s, CCH_3), 1.23 (6H, t, *J* 7.4, S(CH$_2$CH_3)$_2$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 109.4 (s), 78.5 (d), 69.5 (d), 65.8 (t), 47.5 (d), 40.1 (t), 26.4 (q), 25.1 (q), 24.2 (t), 23.9 (t), 14.4 (q), 14.3 (q); *m*/*z* (EI) Found: 280.1160 ($[M]^+$ $C_{12}H_{24}O_3S_2$ requires 280.1167).

3-*O*-(4′-Methoxy-benzyl)-2-deoxy-4,5-*O*-isopropylidene-D-*threo*-pentose diethyl dithioacetal (18b). Potassium *tert*-butoxide (2.21 g, 19.7 mmol) was added in one portion to a stirred solution of the alcohol (**18a**) (4.60 g, 16.4 mmol) in THF (100 ml) at −20 °C, under a nitrogen atmosphere. The solution was stirred at −20 °C for 1 h, and then tetrabutylammonium iodide (0.61 g, 1.6 mmol) followed by a solution of 4-methoxybenzyl bromide (4.62 g, 23.0 mmol) in THF (20 ml) were added. The suspension was allowed to warm to room temperature and stirring was continued for 15 h. Saturated ammonium chloride solution (50 ml) was added and the solvent was removed *in vacuo.* The residue was extracted with ethyl acetate (3 × 75 ml), the combined extracts were then dried and concentrated *in vacuo* to leave a yellow oil. The oil was purified by chromatography on silica, eluting with 10% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *4-methoxybenzyl ether* (6.41 g, 98%) as a colourless oil; $[\alpha]_D^{21}$ + 34.0 (*c* 2.4 in $CHCl_3$); ν_{max} (film)/cm^{-1} 1612, 854, 822; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* 8.8, Ar), 6.89 (2H, d, *J* 8.8, Ar), 4.75 (1H, d, *J* 11.2, OCH*H*Ar), 4.69 (1H, d, *J* 11.2, OC*H*HAr), 4.25 (1H, dd, *J* 13.2, 6.6, *H-4*), 4.00 (1H, dd, *J* 8.3, 6.6, *H-5*), 3.94 (1H, dd, *J* 10.6, 4.1, *H-1*), 3.94–3.88 (1H, m, *H-3*), 3.82 (3H, s, ArOCH_3), 3.74 (1H, dd, *J* 8.3, 7.1, *H-5*), 2.71–2.52 (4H, m, S(CH_2CH$_3$)$_2$), 2.00 (1H, ddd, *J* 14.2, 9.6, 4.1, *H-2*), 1.75 (1H, ddd, *J* 14.2, 10.6, 1.9, *H-2*), 1.47 (3H, s, CCH_3), 1.38 (3H, s, CCH_3) 1.24 (6H, t, *J* 7.4, S(CH$_2$CH_3)$_2$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.2 (s), 130.7 (s), 129.5 (d), 113.7 (d), 109.4 (s), 77.7 (d), 76.9 (d), 72.9 (t), 65.6 (t), 55.2 (q), 47.5 (d), 37.3 (t), 26.4 (q), 25.1 (q), 24.3 (t), 23.4 (t), 14.4 (q), 14.3 (q); *m*/*z* (EI) Found: 400.1751 (M^+ $C_{20}H_{32}O_4S_2$ requires 400.1742).

(3*R*,4′*R*)-3-(2′,2′-Dimethyl-[1′,3′]-dioxolan-4′-yl)-3-(4″-methoxy-benzyloxy)-propionaldehyde (19). Calcium carbonate (4.2 g, 42.8 mmol) and a solution of mercury(II) perchlorate hydrate (11.4 g, 28.5 mmol) in water (60 ml) were added successively to a solution of the dithioacetal (**18b**) (5.7 g, 14.2 mmol) in THF (375 ml). The mixture was stirred at room temperature for 3 h, then diethyl ether (600 ml) was added and the resulting suspension stirred for 15 min. The suspension was filtered through a short pad of silica and the filtrate was then dried

(Na_2SO_4) and evaporated *in vacuo* to leave a colourless oil. The residue was purified by chromatography on silica eluting with 50% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *aldehyde* (3.75 g, 91%) as a colourless oil; $[\alpha]_D^{21}$ + 28.5 (*c* 3.7 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2729, 1725; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.73 (t, *J* 1.7, 1H, *H-1′*), 7.24 (d, *J* 8.7, 2H, Ar), 6.88 (d, *J* 8.7, 2H, Ar), 4.59 (app q, *J* 11.3, 2H, CH_2Ar), 4.32–4.27 (m, 1H, *H-5′*), 4.14–4.09 (m, 1H, *H-3*), 4.00 (dd, *J* 8.6, 6.8, 1H, *H-4′*), 3.83–3.79 (m, 1H, *H-5′*), 3.80 (s, 3H, ArOCH_3), 2.61 (ddd, *J* 7.0, 1.7, 1.7, 2H, *H-2*), 1.44 (s, 3H, CCH_3), 1.36 (s, 3H, CCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 200.7 (d), 159.3 (s), 129.9 (s), 129.6 (d), 113.8 (d), 109.7 (s), 76.3 (d), 73.6 (d), 72.4 (t), 65.2 (t), 55.2 (q), 44.4 (t), 26.2 (q), 24.9 (q); *m/z* (EI) Found: 294.1460 ($[M]^+$ $C_{16}H_{22}O_5$ requires 294.1467).

(2′*R*,3*R*,5*S*)-1-(2′,2′-Dimethyl-[1′,3′]-dioxolan-4′-yl)-1-(4″-methoxy-benzyloxy)-hex-5-en-3-ol (20a). Allylmagnesium bromide (20.5 ml, 1.0 M in Et_2O, 20.5 mmol) was added dropwise over 15 min to a stirred solution of (−)-β-methoxydiisopinocampheylborane (7.0 g, 22.2 mmol)[19] in anhydrous diethyl ether (250 ml) at −78 °C under an argon atmosphere. The mixture was warmed to room temperature, stirred for 1 h and then recooled to −78 °C. A solution of the aldehyde (**19**) (5.1 g, 17.1 mmol) in diethyl ether (60 ml) was added dropwise over 15 min, and the suspension was stirred at −78 °C for 3 h before being quenched with methanol (4 ml). A solution of 2 M aqueous sodium hydroxide (100 ml) and then hydrogen peroxide (100 ml) were added, and the biphasic mixture was heated under reflux for 2 h. The mixture was then cooled and the organic layer was separated. The aqueous layer was extracted with ethyl acetate (3 × 100 ml) and the combined organic extracts were dried and concentrated *in vacuo* to leave a colourless oil. The oil was purified by chromatography on silica, eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *alcohol* (4.69 g, 82%) as a colourless oil; ν_{max} (film)/cm^{-1} 3474 (br), 1612; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.30 (2H, d, *J* 8.6, Ar), 6.90 (2H, d, *J* 8.6, Ar), 5.85–5.73 (1H, m, *H-5*), 5.13–5.08 (2H, m, *H-6*), 4.76 (1H, d, *J* 11.3, OCH*H*Ar), 4.61 (1H, d, *J* 11.3, OC*H*HAr), 4.26 (1H, ddd, *J* 7.2, 6.6, 6.6, *H-4′*), 4.07–3.97 (2H, m, *H-5′*), 3.93–3.86 (1H, m, *H-3*), 3.82 (3H, s, ArOCH_3), 3.67 (1H, dd, *J* 8.1, 7.6, *H-1*), 2.23–2.19 (2H, m, *H-4*), 1.65–1.45 (2H, m, *H-2*) 1.46 (3H, s, CCH_3), 1.40 (3H, s, CCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.3 (s), 134.4 (d), 130.3 (s), 129.8 (d), 118.0 (t), 113.9 (d), 109.6 (s), 78.4 (d), 76.5 (d), 72.8 (t), 68.0 (d), 65.9 (t), 55.3 (q), 42.0 (t), 37.0 (t), 26.5 (q), 25.4 (q); *m/z* (EI) Found: 336.1931 (M^+ $C_{19}H_{28}O_5$ requires 336.1937).

(2′*R*,3*R*,5*S*)-1-(2′,2′-Dimethyl-[1′,3′]-dioxolan-4′-yl)-1-(4″-methoxy-benzyloxy)-3-methoxy-5-hexene (20b). Potassium *tert*-butoxide (2.27 g, 20.2 mmol) was added in one portion to a stirred solution of the alcohol (**20a**) (3.40 g, 10.1 mmol) in THF (100 ml) at −20 °C, under a nitrogen atmosphere. The solution was stirred at −20 °C for 30 min and then methyl iodide (6.30 ml, 10.1 mmol) was added dropwise over 10 min. The mixture was allowed to warm to room temperature and then stirred for 6 h. Saturated ammonium chloride solution (50 ml) was added and the solvent was removed *in vacuo.* The residue was extracted with ethyl acetate (4 × 100 ml), and the combined organic extracts were dried and concentrated *in vacuo* to leave a yellow oil. The residue was purified by chromatography on silica, eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *methyl ether* (3.43 g, 97%) as a colourless oil; $[\alpha]_D^{20}$ + 63.7 (*c* 2.3 in $CHCl_3$) (Found: C, 68.7; H, 8.8%, $C_{20}H_{30}O_5$ requires C, 68.6; H, 8.6%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 1612; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.30 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 5.82–5.70 (1H, m, *H-5*), 5.11–5.05 (2H, m, *H-6*), 4.76 (1H, d, *J* 11.1, OCH_2Ar), 4.55 (1H, d, *J* 11.1, OCH_2Ar), 4.19 (1H, dd, *J* 13.9, 6.7, *H-5′*), 3.98 (1H, dd, *J* 8.2, 6.7, *H-4′*), 3.81 (3H, s, ArOCH_3), 3.73–3.66 (2H, m, *H-5′, H-1*), 3.48–3.42 (1H, m, *H-3*), 3.26 (3H, s, OCH_3), 2.30–2.26 (2H, m, *H-4*), 1.58–1.50 (1H, m, *H-2*), 1.46 (3H, s, CCH_3), 1.44–1.34 (1H, m, *H-2*), 1.38 (3H, s, CCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1 (s), 134.1 (d), 130.9 (s), 129.6 (d), 117.3 (t), 113.7 (d), 109.2 (s), 78.8 (d), 76.2 (d), 76.1 (d), 72.8 (t), 65.9 (t), 56.3 (q), 55.1 (q), 37.5 (t), 36.1 (t), 26.5 (q), 25.3 (q); *m/z* (EI) Found 350.2084 ($[M]^+$ $C_{20}H_{30}O_5$ requires 350.2093).

(2*R*,3*R*,5*S*)-5-Methoxy-3-(4′-methoxy-benzyloxy)-oct-7-ene-1,2-diol (21). 10-Camphorsulfonic acid (12.5 g, 53.9 mmol) was added to a solution of the acetonide (**20b**) (8.9 g, 25.4 mmol) in methanol (160 ml) at 0 °C, and the mixture was stirred for 6 h, whilst allowing it to warm to room temperature. Sodium bicarbonate (5 g) in water (10 ml) was added and the solvent was removed *in vacuo*. The aqueous residue was extracted with ethyl acetate (3 × 100 ml), and the combined organic extracts were dried (Na_2SO_4) and then concentrated *in vacuo* to leave an orange oil. The oil was purified by chromatography on silica eluting with ethyl acetate to give the *diol* (6.93 g, 88%) as a colourless oil; $[\alpha]_D^{21}$ + 3.7 (*c* 1.4 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3574 (br), 1613; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* 8.7, Ar*H*), 6.91 (2H, d, *J* 8.7, Ar*H*), 5.84–5.74 (1H, m, *H-7*), 5.14–5.10 (2H, m, *H-8*), 4.55 (2H, app q, *J* 11.1, OCH_2Ar), 3.82 (3H, s, ArOCH_3), 3.72–3.62 (4H, m, *H-1, H-2, H-3*), 3.46–3.39 (1H, m, *H-5*), 3.35 (3H, s, OCH_3), 3.05 (1H, d, *J* 3.9, CHO*H*), 2.77 (1H, b s, CH_2O*H*), 2.36–2.29 (2H, m, *H-6*), 1.75–1.71 (2H, m, *H-4*); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.3 (s), 133.8 (d), 130.2 (s), 129.5 (d), 117.6 (t), 113.8 (d), 76.9 (d), 76.6 (d), 73.7 (d), 72.7 (t), 63.8 (t), 56.0 (q), 55.2 (q), 37.3 (t), 35.9 (t); *m/z* (EI) Found: 310.1780 (M^+ $C_{17}H_{26}O_5$ requires 310.1780).

(4*S*,6*R*,7*R*)-7,8-Bis-(*tert*-butyl-dimethyl-silanyloxy)-4-methoxy-6-(4′-methoxy-benzyloxy)-oct-1-ene (22a). Triethylamine (10.9 ml, 77.4 mmol) was added in one portion to a solution of the diol (**21**) (6.0 g, 19.2 mmol) in dichloromethane (120 ml) at 0 °C, under a nitrogen atmosphere, and the solution was stirred at 0 °C for 5 min. *tert*-Butyldimethylsilyl triflate (10.7 ml, 46.4 mmol) was added dropwise over 1 min and the mixture was stirred for a further 1 h whilst allowing to warm to room temperature. Saturated ammonium chloride solution (240 ml) was added and the organic layer was separated. The aqueous phase was extracted with dichloromethane (3 × 300 ml) and the combined organic extracts were dried and then concentrated *in vacuo* to leave a yellow oil. The oil was purified by chromatography on silica eluting with 10% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *silyl ether* (10.3 g, 98%) as a colourless oil; $[\alpha]_D^{20}$ + 33.8 (*c* 3.0 in $CHCl_3$) (Found: C, 64.9; H, 10.3%, $C_{29}H_{54}O_5Si_2$ requires C, 64.6; H, 10.1%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 1612, 1086; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.28 (2H, d, *J* 8.7, Ar*H*), 6.89 (2H, d, *J* 8.7, Ar*H*), 5.86–5.74 (1H, m, *H-2*), 5.10–5.02 (2H, m, *H-1*), 4.61 (1H, d, *J* 11.3, OCH*H*Ar), 4.48 (1H, d, *J* 11.3, OC*H*HAr), 3.84–3.77 (2H, m, *H-7*, *H-8*), 3.81 (3H, s, ArOCH_3), 3.69 (1H, ddd, *J* 10.5, 3.8, 2.2, *H-6*), 3.52 (1H, dd, *J* 11.1, 7.9, *H-8*), 3.42–3.35 (1H, m, *H-4*), 3.26 (3H, s, OCH_3), 2.30–2.23 (2H, m, *H-3*), 1.72 (1H, ddd, *J* 14.4, 9.8, 2.2, *H-5*), 1.49 (1H, ddd, *J* 14.4, 10.5, 3.0, *H-5*), 0.91 (9H, s, SiC(CH_3)$_3$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.08 (3H, s, SiCH_3), 0.06 (9H, 3 × s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1 (s), 134.7 (d), 131.1 (s), 129.5 (d), 116.9 (t), 113.7 (d), 76.9 (d), 76.8 (d), 74.6 (d), 72.3 (t), 64.4 (t), 56.0 (q), 55.3 (q), 38.0 (t), 34.7 (t), 26.0 (q), 25.9 (q), 18.4 (s), 18.1 (s), −4.3 (q), −4.8 (q), −5.3 (q), −5.4 (q); *m/z* (EI) Found: 481.2794 ([M − ^{t}Bu]$^+$; $C_{25}H_{45}O_5Si_2$ requires 481.2816.

(3*R*,5*R*,6*R*)-6,7-Bis-(*tert*-butyl-dimethyl-silanyloxy)-3-methoxy-5-(4′-methoxy-benzyloxy)-heptanal (22b). 4-Methylmorpholine *N*-oxide (4.28 g, 36.6 mmol), and osmium tetroxide (110 mg, 0.43 mmol) were added sequentially to a solution of the silyl ether (**22a**) (6.6 g, 12.2 mmol) in acetone (88 ml) and water (4.4 ml). The mixture was stirred at room temperature for

12 h and then a saturated solution of sodium thiosulfate (30 ml) was added. The solvent was removed *in vacuo* and the aqueous residue was extracted with ethyl acetate (3 × 160 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo* to leave a colourless oil, which was used immediately without purification. The crude diol in dichloromethane (30 ml) was added dropwise over 2 min to an aqueous solution of 0.65 M sodium periodate (30 ml, 19.5 mmol,) and a stirred suspension of silica (35 g) in dichloromethane (160 ml) and the mixture was stirred at room temperature for 3 h. The suspension was filtered and the residue was washed with dichloromethane (500 ml). The combined organic extracts were evaporated to leave a colourless oil which was purified by chromatography on silica, eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *aldehyde* (6.2 g, 94%) as a colourless oil; $[\alpha]_D^{21}$ +37.7 (*c* 2.5 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2737, 1723; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.77 (1H, t, *J* 2.4, *H-1*), 7.26 (2H, d, *J* 8.6, Ar), 6.88 (2H, d, *J* 8.6, Ar), 4.61 (1H, d, *J* 11.2, OCH*H*Ar), 4.44 (1H, d, *J* 11.2, OC*H*HAr), 3.88–3.84 (1H, m, *H-3*), 3.81 (3H, s, ArOCH_3), 3.82–3.77 (2H, m, *H-6, H-7*), 3.63 (1H, ddd, *J* 10.4, 4.2, 1.8, *H-5*), 3.51 (1H, dd, *J* 10.3, 7.1, *H-7*), 3.25 (3H, s, OCH_3), 2.58 (2H, dd, *J* 5.7, 2.4, *H-2*), 1.97 (1H, ddd, *J* 14.4, 8.7, 1.8, *H-4*), 1.46 (1H, ddd, *J* 14.4, 10.4, 4.2, *H-4*), 0.91 (9H, s, SiC(CH_3)$_3$), 0.90 (9H, s, SiC(CH_3)$_3$), 0.09 (3H, s, SiCH_3), 0.07 (3H, s, SiCH_3), 0.06 (6H, 2 × s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.4 (d), 159.2 (s), 130.6 (s), 129.5 (d), 113.8 (d), 77.0 (d), 73.8 (d), 73.7 (d), 72.1 (t), 64.2 (t), 56.4 (q), 55.2 (q), 48.4 (t), 34.7 (t), 26.0 (q), 25.8 (q), 18.3 (s), 18.1 (s), −4.3 (q), −4.9 (q), −5.3 (q), −5.4 (q); *m*/*z* (CI, NH_3): Found 539.3219 ([M − H] $C_{28}H_{51}O_6Si_2$ requires 539.3224).

(2*R*,3*R*,5*R*)-2-(*tert*-Butyl-dimethyl-silanyloxy)-5,7,7-trimethoxy-3-(4′-methoxy-benzyloxy)-heptan-1-ol (23). 10-Camphorsulfonic acid (1.15 g, 5 mmol) was added in one portion to a stirred solution of the aldehyde (**22b**) (5.5 g, 10.2 mmol) in methanol (160 ml) and dichloromethane (160 ml) under a nitrogen atmosphere, and the mixture was stirred at room temperature for 1 h. Saturated sodium bicarbonate solution (15 ml) was added and the solvent was removed *in vacuo*. The aqueous residue was extracted with ethyl acetate (3 × 300 ml), and the combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo* to leave a colourless oil. The oil was purified by chromatography on silica eluting with 30% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *alcohol* (4.3 g, 89%) as a colourless oil; $[\alpha]_D^{21}$ + 26.0 (*c* 2.1 in $CHCl_3$); Found: C, 61.0; H, 9.7%, $C_{24}H_{44}O_7Si$ requires C, 61.0; H, 9.4%; ν_{max} (soln: $CHCl_3$)/cm^{-1} 3494, 2930, 1612, 1082; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (2H, d, *J* 8.6, Ar), 6.89 (2H, d, *J* 8.6, Ar), 4.60–4.49 (3H, m, OCH_2Ar, *H-7*), 3.94 (1H, ddd, *J* 5.5, 5.5, 4.9, *H-2*), 3.81 (3H, s, ArOCH_3), 3.79–3.68 (2H, m, *H-1, H-3*), 3.60–3.55 (1H, m, *H-1*), 3.49–3.45 (1H, m, *H-5*), 3.33 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 2.25 (1H, t, *J* 6.2, O*H*), 1.89–1.82 (2H, m, *H-4, H-6*), 1.77–1.71 (1H, m, *H-6*), 1.55 (1H, ddd, *J* 14.1, 10.3, 3.5, *H-4*), 0.90 (9H, s, SiC(CH_3)$_3$), 0.08 (6H, 2x s, SiCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (s), 130.5 (s), 129.6 (d), 113.8 (d), 102.1 (d), 77.8 (d), 74.6 (d), 72.3 (t), 71.2 (d), 63.5 (t), 59.2 (q), 55.3 (q), 52.8 (2x q), 37.5 (t), 34.3 (t), 25.8 (q), 18.0 (s), −4.7 (q), −4.8 (q); *m*/*z* (EI) Found: 351.1615 ([M − ^{t}Bu − 2MeOH]$^+$ $C_{18}H_{27}O_5Si$ requires 351.1628).

(2*S*,3*R*,5*R*)-2-(*tert*-Butyl-dimethyl-silanyloxy)-5,7,7-trimethoxy-3-(4′-methoxy-benzyloxy)-heptanal (24). 2,6-Di-*tert*-butylpyridine (5.0 ml, 21 mmol) and Dess–Martin periodinane (3.77 g, 8.89 mmol)[20] were added sequentially to a solution of the alcohol (**23**) (3.5 g, 7.41 mmol) in dichloromethane (30 ml) at room temperature, under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h, then diethyl ether (220 ml) was added and the resulting suspension was poured into a saturated solution of sodium thiosulfate and sodium bicarbonate (1 : 1, 220 ml) and stirred vigorously for 30 min. The organic layer was separated and the aqueous phase was extracted with ethyl acetate (3 × 200 ml). The combined organic extracts were dried (Na_2SO_4) and then evaporated *in vacuo* to leave a colourless oil, which was purified by chromatography on silica eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *aldehyde* (3.3 g, 95%) as a colourless oil; $[\alpha]_D^{21}$ + 35.0 (*c* 2.4 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 1732; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.71 (1H, d, *J* 1.3, *H-1*), 7.26 (2H, d, *J* 8.7, Ar), 6.88 (2H, d, *J* 8.7, Ar), 4.59–4.46 (3H, m, OCH_2Ar, *H-7*), 4.10 (1H, dd, *J* 4.6, 1.3, *H-2*), 3.93–3.86 (1H, m, *H-3*), 3.81 (3H, s, ArOCH_3), 3.50–3.45 (1H, m, *H-5*), 3.31 (6H, 2 × s, OCH_3), 3.26 (3H, s, OCH_3), 1.90–1.60 (4H, m, *H-4, H-6*), 0.92 (9H, s, SiC(CH_3)$_3$), 0.07 (3H, s, SiCH_3), 0.04 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 202.9 (d), 159.3 (s), 130.3 (s), 129.5 (d), 113.8 (d), 102.0 (d), 79.0 (d), 76.8 (d), 74.1 (d), 72.3 (t), 56.2 (q), 55.2 (q), 52.8 (q), 52.7 (q), 37.1 (t), 35.8 (t), 25.7 (q), 18.2 (s), −4.7 (q), −5.2 (q); *m*/*z* (EI) Found: 381.1740 ([M − ^{t}Bu − MeOH]$^+$ $C_{19}H_{29}O_6Si$ requires 381.1733).

(4*R*,5*R*,7*R*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-7,9,9-trimethoxy-5-(4′-methoxy-benzyloxy)-2-methyl-non-(2*E*)-enoic acid ethyl ester (25a). (Carbethoxyethylidene)triphenylphosphorane (94%, 9.35 g, 24.24 mmol) was added in one portion to a solution of the aldehyde (**24**) (3.8 g, 8.08 mmol) in dry benzene (115 ml) under a nitrogen atmosphere. The solution was heated at reflux for 2 days, then allowed to cool and concentrated *in vacuo*. The residue was purified by chromatography on silica eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *ester* (4.21 g, 94%) as a colourless oil; $[\alpha]_D^{21}$ + 45.0 (*c* 3.3 in $CHCl_3$); Found: C, 62.8; H, 9.4%, $C_{29}H_{50}O_8Si$ requires C, 62.8; H, 9.1%; ν_{max} (soln: $CHCl_3$)/cm^{-1} 1704, 1613; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* 8.7, Ar), 6.86 (2H, d, *J* 8.7, Ar), 6.65 (1H, d b q, *J* 9.1, 1.4, *H-3*), 4.70 (1H, d, *J* 11.0, OCH*H*Ar), 4.56–4.45 (3H, m, OC*H*HAr, *H-4, H-9*), 4.23–4.13 (2H, m, CH_3CH_2OCO), 3.78 (3H, s, ArOCH_3), 3.65 (1H, ddd, *J* 10.2, 5.4, 2.2, *H-5*), 3.50–3.44 (1H, m, *H-7*), 3.29 (6H, 2 × s, OCH_3), 3.22 (3H, s, OCH_3), 1.85 (3H, d, *J* 1.4, CH_3C=CH), 1.85–1.80 (1H, m, *H-8*), 1.76–1.66 (2H, m, *H-6, H-8*), 1.51 (1H, ddd, *J* 13.8, 10.2, 3.3, *H-6*), 1.28 (3H, t, *J* 7.1, CH_3CH_2OCO), 0.88 (9H, s, SiC(CH_3)$_3$), 0.04 (3H, s, SiCH_3), 0.00 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 167.6 (s), 159.1 (s), 140.8 (d), 130.7 (s), 129.5 (d), 128.6 (s), 113.7 (d), 101.9 (d), 79.2 (d), 74.2 (d), 73.1 (t), 71.5 (d), 60.6 (t), 55.9 (q), 55.1 (q), 52.7 (q), 52.5 (q), 37.1 (t), 35.5 (t), 25.7 (q), 18.0 (s), 14.1 (q), 13.3 (q), −4.6 (q), −4.9 (q); *m*/*z* (EI) Found: 433.2029 ([M − ^{t}Bu − 2MeOH]$^+$ $C_{23}H_{33}O_6Si$ requires 433.2046).

(4*R*,5*R*,7*R*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-7,9,9-trimethoxy-5-(4′-methoxy-benzyloxy)-2-methyl-non-(2*E*)-en-1-ol (25b). A solution of diisobutylaluminium hydride (11.3 ml, 1 M in hexane, 11.3 mmol) was added dropwise over 5 min to a stirred solution of the ester (**25a**) (2.5 g, 4.51 mmol) in dichloromethane (25 ml) at −78 °C, under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1 h, then allowed to warm to room temperature and stirred for a further 2 h. The mixture was quenched by the dropwise addition of methanol (1.5 ml), then poured into an aqueous solution of saturated potassium sodium tartrate (40 ml) and diluted with dichloromethane (100 ml), and stirred vigorously for 2 h. The separated aqueous layer was extracted with ethyl acetate (3 × 50 ml) and the combined organic extracts were then dried (Na_2SO_4), and evaporated *in vacuo* to leave a colourless oil. The oil was purified by chromatography on silica eluting first with 30% ethyl acetate in petrol ether and then with ethyl acetate to give the *alcohol* (2.05 g, 89%) as a colourless oil; $[\alpha]_D^{21}$ + 33.5 (*c* 1.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3613, 3455(br); ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.31 (2H, d, *J* 8.5, Ar), 6.89 (2H, d, *J* 8.5, Ar), 5.44 (1H, d b q, *J* 9.2, 1.2, *H-3*), 4.76 (1H, d, *J* 11.0, OCH*H*Ar),

4.55–4.48 (3H, m, OC*H*HAr, *H-4, H-9*), 4.00 (2H, s, *H-1*), 3.82 (3H, s, ArOCH_3), 3.59 (1H, ddd, *J* 9.7, 5.7, 1.9, *H-5*), 3.53–3.46 (1H, m, *H-7*), 3.33 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 1.97 (1H, b s, O*H*), 1.89–1.82 (1H, m, *H-8*), 1.76–1.69 (2H, m, *H-6, H-8*), 1.72 (3H, d, *J* 1.0, CH_3C=CH), 1.51 (1H, ddd, *J* 13.6, 10.0, 3.3, *H-6*), 0.91 (9H, s, SiC(CH_3)$_3$), 0.08 (3H, s, SiCH_3), 0.04 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1 (s), 136.9 (s), 131.0 (s), 129.5 (d), 125.7 (d), 113.7 (d), 101.9 (d), 79.6 (d), 74.5 (d), 73.0 (t), 71.3 (d), 68.2 (t), 56.1 (q), 55.2 (q), 52.7 (q), 52.5 (q), 37.2 (t), 35.7 (t), 25.8 (q), 18.1 (s), 14.5 (q), −4.3 (q), −4.7 (q); *m*/*z* (EI) Found: 391.1946 ([M − Bu − 2MeOH]$^+$ $C_{21}H_{31}O_5Si$ requires 391.1941).

(4*R*,5*R*,7*R*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-7,9,9-trimethoxy-5-(4′-methoxy-benzyloxy)-2-methyl-non-(2i)-enal (7). 2,6-Lutidine (0.16 ml, 1.4 mmol) and Dess–Martin periodinane (2 g, 4.7 mmol)[20] were added sequentially to a solution of the alcohol (**25b**) (800 mg, 1.6 mmol) in dichloromethane (50 ml) at room temperature, under a nitrogen atmosphere, and the mixture was then stirred for 1 h. Diethyl ether (200 ml) was added and the resulting suspension was poured into a saturated solution of sodium thiosulfate and sodium bicarbonate (1 : 1, 200 ml) and stirred vigorously for 30 min. The organic layer was separated and the aqueous phase was extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were dried (Na_2SO_4), and evaporated *in vacuo* to leave a colourless oil, which was purified by chromatography on silica eluting with 20% ethyl acetate in petroleum ether (bp 40–60 °C), to give the *aldehyde* (750 mg, 94%) as a colourless oil; $[\alpha]_D^{21}$ + 60.7 (*c* 1.3 in $CHCl_3$); λ_{max} (EtOH) 203 (ε 8500), 217 (10 100), 226 (9000), 232 (9000) nm; ν_{max} (soln: $CHCl_3$)/cm^{-1} 1688; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.42 (1H, s, *H-1*), 7.26 (2H, d, *J* 8.7, Ar), 6.87 (2H, d, *J* 8.7, Ar), 6.38 (1H, d b q, *J* 8.6, 2.3, *H-3*), 4.71 (1H, dd, *J* 8.6, 5.2, *H-4*), 4.67 (1H, d, *J* 11.1, OCH*H*Ar), 4.53 (1H, d, *J* 11.1, OC*H*HAr), 4.48 (1H, t, *J* 5.6, *H-9*), 3.80 (3H, s, ArOCH_3), 3.72 (1H, ddd, *J* 10.2, 5.2, 2.2, *H-5*), 3.51–3.45 (1H, m, *H-7*), 3.31 (3H, s, OCH_3), 3.30 (3H, s, OCH_3), 3.24 (3H, s, OCH_3), 1.86 (1H, ddd, *J* 14.2, 6.1, 5.6, *H-8*), 1.76–1.68 (2H, m, *H-6, H-8*), 1.77 (3H, d, *J* 2.3, CH_3C=CH), 1.54 (1H, ddd, *J* 13.6, 10.2, 3.2, *H-6*), 0.90 (9H, s, SiC(CH_3)$_3$), 0.07 (3H, s, SiCH_3), 0.00 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 195.1 (d), 159.3 (s), 152.5 (d), 139.2 (s), 130.5 (s), 129.6 (d), 113.8 (d), 101.9 (d), 79.0 (d), 74.2 (d), 73.1 (t), 71.0 (d), 56.1 (q), 55.3 (q), 52.8 (q), 52.6 (q), 37.1 (t), 35.6 (t), 25.8 (q), 18.1 (s), 10.1 (q), −4.6 (q), −4.8 (q); *m*/*z* (FAB) Found: 533.2911 ([M + Na]$^+$ $C_{27}H_{46}O_7NaSi$ requires 533.2911).

(4*R*,9*R*,10*R*,12*R*)-9-(*tert*-Butyldimethylsilanyloxy)-4,12,14,14-tetramethoxy-10-(4-methoxybenzyloxy)-7-methyl-1-(trimethylsilanyl)-tetradeca-di-(5*E*,7*E*)-en-1-yne (26). Sodium bis(trimethylsilyl)amide (1 M in THF, 780 µl, 800 µmol) was added dropwise over 5 min to a stirred solution of the sulfone (**6**) (250 mg, 700 µmol) and the aldehyde (**7**) (250 mg, 500 µmol) in THF at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 3 h and then warmed to room temperature over 1 h. The mixture was quenched with a saturated aqueous solution of ammonium chloride (50 ml) and the separated aqueous layer was extracted with ethyl acetate (4 × 50 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *1,3-diene* (240 mg, 74%) as a colourless oil; $[\alpha]_D^{20}$ + 41.3 (*c* 1.2 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2931, 2176, 1613, 1088; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 6.25 (1H, d, *J* 15.7, *H*-6), 5.54 (1H, dd, *J* 15.7, 7.8, *H*-5), 5.46 (1H, d, *J* 9.2, *H*-8), 4.76 (1H, d, *J* 11.0, CH_2Ar), 4.57 (1H, dd, *J* 9.2, 5.8, *H*-9), 4.51 (1H, d, *J* 11.0, CH_2Ar), 4.48 (1H, t, *J* 5.6, *H*-14), 3.81 (3H, s, ArOCH_3), 3.81–3.74 (1H, m, *H*-4), 3.60 (1H, ddd, *J* 10.0, 5.8, 1.9, *H*-10), 3.50–3.47 (1H, m, *H*-12), 3.30 (6H, s, 2 × OCH_3), 3.29 (3H, s, OCH_3), 3.23 (3H, s, OCH_3), 2.59 (1H, dd, *J* 16.7, 5.6, *H*-3), 2.46 (1H, dd, *J* 16.7, 7.1, *H*-3), 1.87–1.68 (3H, m, *H*-11, *H*-13), 1.79 (3H, s, CH_3C=), 1.48 (1H, ddd, *J* 14.0, 10.0, 3.3, *H*-11), 0.89 (9H, s, C(CH_3)$_3$), 0.14 (9H, s, Si(CH_3)$_3$), 0.05 (3H, s, SiCH_3), 0.00 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1 (s), 137.6 (d), 133.9 (s), 133.0 (d), 131.1 (s), 129.5 (d), 127.5 (d), 113.7 (d), 103.3 (s), 102.0 (d), 86.5 (s), 80.8 (d), 79.8 (d), 74.4 (d), 73.2 (t), 71.7 (d), 56.6 (q), 56.1 (q), 55.3 (q), 52.9 (q), 52.5 (q), 37.3 (t), 35.8 (t), 27.1 (t), 25.9 (q), 18.1 (s), 13.4 (q), 0.1 (q), −4.3 (q), −4.7 (q); *m*/*z* (FAB) Found 685.3972 ([MNa]$^+$ $C_{36}H_{62}O_7NaSi_2$ requires 685.3932).

(3*R*,5*R*,6*R*,11*R*)-6-(*tert*-Butyldimethylsilanyloxy)-3,11-dimethoxy-5-(4-methoxy-benzyloxy)-8-methyl-14-(trimethylsilanyl)-tetradeca-7,9-di-(7*E*,9*E*)-en-13-ynal (27). A solution of dimethylboron bromide[48] in dichloromethane (2.1 M, 0.92 ml, 1.9 mmol) was added in one portion to a stirred solution of the dimethyl acetal (**26**) (160 mg, 0.24 mmol) in diethyl ether (8 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 2.5 h and then transferred, *via* cannula, to a vigorously stirred suspension of THF (8 ml) and a saturated aqueous solution of sodium hydrogencarbonate (8 ml). The separated aqueous layer was extracted with diethyl ether (3 × 10 ml), and the combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to leave a colourless oil. Purification by flash chromatography, using 40% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *aldehyde* (142 mg, 95%) as a colourless oil; $[\alpha]_D^{20}$ + 50.4 (*c* 0.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2930, 2175, 1725, 1602, 1089; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.75 (1H, t, *J* 2.4, *H*-1), 7.27 (2H, d, *J* 8.6, C*H*, Ar), 6.89 (2H, d, *J* 8.6, C*H*, Ar), 6.25 (1H, d, *J* 15.7, *H*-9), 5.55 (1H, dd, *J* 15.7, 7.8, *H*-10), 5.44 (1H, d, *J* 9.2, *H*-7), 4.76 (1H, d, *J* 11.1, CH_2Ar), 4.62 (1H, dd, *J* 9.2, 5.6, *H*-6), 4.48 (1H, d, *J* 11.1, CH_2Ar), 3.86–3.75 (2H, m, *H*-3, *H*-11), 3.81 (3H, s, ArOCH_3), 3.63 (1H, ddd, *J* 10.4, 5.6, 2.0, *H*-5), 3.31 (3H, s, OCH_3), 3.23 (3H, s, OCH_3), 2.63–2.55 (3H, m, *H*-2, *H*-12), 2.44 (1H, dd, *J* 16.7, 7.2, *H*-12), 1.90–1.80 (1H, m, *H*-4), 1.80 (3H, s, CH_3C=), 1.47 (1H, ddd, *J* 14.4, 10.4, 3.8, *H*-4), 0.89 (9H, s, C(CH_3)$_3$), 0.14 (9H, s, Si(CH_3)$_3$), 0.06 (3H, s, SiCH_3), 0.01 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.4 (d), 159.3 (s), 137.4 (d), 134.3 (s), 132.4 (d), 130.6 (s), 129.6 (d), 127.7 (d), 113.8 (d), 103.3 (s), 86.5 (s), 80.7 (d), 79.5 (d), 73.2 (d), 73.1 (t), 70.9 (d), 56.7 (s), 56.3 (q), 55.3 (q), 48.3 (t), 35.6 (t), 27.1 (t), 25.8 (q), 18.1 (s), 13.4 (q), 0.1 (q), −4.3 (q), −4.8 (q).

(5*R*,7*R*,8*R*,13*R*)-8-(*tert*-Butyldimethylsilanyloxy)-5,13-dimethoxy-7-(4-methoxy-benzyloxy)-10-methyl-3-oxo-16-trimethylsilanyl)-hexadeca-di-(9*E*,11*E*)-en-15-ynoic acid ethyl ester (28). Ethyl diazoacetate (28 mg, 26 µl, 250 µmol) was added in one portion to a stirred suspension of tin(II) chloride (4 mg, 20 µmol) in dichloromethane (10 ml) at room temperature under a nitrogen atmosphere. A solution of the aldehyde (**27**) (140 mg, 23 µmol) in dichloromethane (10 ml) was added dropwise, *via* cannula, over 2 min, and the reaction mixture was stirred for 2 h before being concentrated *in vacuo* to leave a yellow residue. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *β-keto ester* (120 mg, 74%) as a colourless oil; $[\alpha]_D^{20}$ + 39.5 (*c* 1.2 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2930, 2175, 1740, 1716, 1088; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 6.25 (1H, d, *J* 15.7, *H*-11), 5.54 (1H, dd, *J* 15.7, 7.8, *H*-12), 5.43 (1H, d, *J* 9.2, *H*-9), 4.75 (1H, d, *J* 11.0, CH_2Ar), 4.60 (1H, dd, *J* 9.2, 5.6, *H*-8), 4.48 (1H, d, *J* 11.0, CH_2Ar), 4.18 (2H, q, *J* 7.1, CO_2CH_2), 3.86–3.74 (2H, m, *H*-5, *H*-13), 3.81 (3H, s, ArOCH_3), 3.58 (1H, ddd, *J* 10.2, 5.6, 1.8, *H*-7), 3.42 (2H, s, *H*-2), 3.31 (3H, s, OCH_3), 3.21 (3H, s, OCH_3), 2.74 (1H, dd, *J* 16.1, 7.1, *H*-4), 2.63 (1H, dd, *J* 16.1, 4.7, *H*-4), 2.59 (1H, dd, *J* 16.7, 5.6, *H*-14), 2.44 (1H, dd, *J* 16.7, 7.1, *H*-14), 1.81–1.73 (1H, m, *H*-6), 1.79 (3H, d, *J* 1.0, CH_3C=), 1.44 (1H, ddd, *J* 14.5, 10.2, 4.3, *H*-6), 1.27 (3H, t, *J* 7.1,

$CO_2CH_2CH_3$), 0.88 (9H, s, $C(CH_3)_3$), 0.14 (9H, s, $Si(CH_3)_3$), 0.05 (3H, s, $SiCH_3$), 0.00 (3H, s, $SiCH_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.4 (s), 167.0 (s), 159.2 (s), 137.5 (d), 134.2 (s), 132.5 (d), 130.7 (s), 129.6 (d), 127.6 (d), 113.8 (d), 103.3 (s), 86.5 (s), 80.7 (d), 79.8 (d), 74.2 (d), 72.9 (t), 71.0 (d), 61.3 (t), 56.6 (2 × q), 55.3 (q), 50.0 (t), 48.1 (t), 35.3 (t), 27.1 (t), 25.8 (q), 18.1 (s), 14.9 (q), 13.4 (q), 0.1 (q), −4.3 (q), −4.8 (q); *m*/*z* (FAB) Found 725.3815 ($[MNa]^+$ $C_{38}H_{62}O_8NaSi_2$ requires 725.3881).

(2*R*,4*R*,6*R*,1′*R*,6′*R*)-{6-[1′-(*tert*-Butyldimethylsilanyloxy)-6′-methoxy-3′-methyl-9′-(trimethylsilanyl)-nona-di-(2′*E*,4′*E*)-en-8′-ynyl]-2-hydroxy-4-methoxy-tetrahydro-pyran-2-yl}-acetic acid ethyl ester (29a). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (40 mg, 170 μmol) was added in one portion to a stirred solution of the β-keto ester (**28**) (80 mg, 110 μmol) in dichloromethane (4 ml) and water (4 drops) at room temperature. The mixture was stirred at room temperature for 1 h, then diluted with dichloromethane (10 ml) and quenched with a saturated aqueous solution of sodium hydrogencarbonate (4 ml). The suspension was filtered through celite and washed with dichloromethane (100 ml), and the filtrate was then concentrated *in vacuo* to leave a red oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *cyclic hemiketal* (64 mg, 96%) as a colourless oil; $[\alpha]_D^{20}$ + 3.4 (*c* 0.6 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3466, 2930, 2175, 1714, 1086; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.26 (1H, d, *J* 15.7, *H*-4′), 5.54 (1H, dd, *J* 15.7, 7.8, *H*-5′), 5.40 (1H, d, *J* 9.0, *H*-2′), 5.10 (1H, d, *J* 2.4, O*H*), 4.45 (1H, dd, *J* 9.0, 6.0, *H*-1′), 4.24–4.15 (2H, m, CO_2CH_2), 3.89 (1H, ddd, *J* 12.0, 6.0, 2.0, *H*-6), 3.81–3.76 (1H, m, *H*-6′), 3.72–3.67 (1H, m, *H*-4), 3.35 (3H, s, OCH_3), 3.33 (3H, s, OCH_3), 2.65–2.56 (3H, m, CH_2CO_2Et, *H*-7′), 2.45 (1H, dd, *J* 16.8, 7.2, *H*-7′), 2.20 (1H, m, *H*-3*eq*), 2.03 (1H, m, *H*-5*eq*), 1.75 (3H, d, *J* 1.0, CH_3C=), 1.29 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.16 (1H, ddd, *J* 16.9, 11.9, 2.4, *H*-3*ax*), 1.05 (1H, app q, *J* ~12.0, *H*-5*ax*), 0.85 (9H, s, $C(CH_3)_3$), 0.14 (9H, s, $Si(CH_3)_3$), 0.02 (3H, s, $SiCH_3$), −0.01 (3H, s, $SiCH_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 172.1 (s), 137.6 (d), 134.1 (s), 132.6 (d), 127.3 (d), 103.3 (s), 96.5 (s), 86.5 (s), 80.5 (d), 73.2 (d), 73.1 (d), 71.4 (d), 60.8 (t), 56.6 (q), 55.6 (q), 44.5 (t), 40.7 (t), 32.1 (t), 26.9 (t), 25.8 (q), 18.2 (s), 14.0 (q), 13.3 (q), 0.1 (q), −4.5 (q), −4.8 (q); *m*/*z* (FAB) Found 605.3347 ($[MNa]^+$ $C_{30}H_{54}O_7NaSi_2$ requires 605.3330).

(2*R*,4*R*,6*R*,1′*R*,6′*R*)-{6-[1′-(*tert*-Butyldimethylsilanyloxy)-6′-methoxy-3′-methyl-9′-(trimethylsilanyl)-nona-di-(2′*E*,4′*E*)-en-8′-ynyl]-2,4-dimethoxy-tetrahydropyran-2-yl}-acetic acid ethyl ester (29b). Pyridinium *para*-toluenesulfonate (35 mg, 136 μmol) was added in one portion to a stirred solution of the *cyclic hemi*-ketal (**29a**) (80 mg, 136 μmol) in methanol (8 ml) and dichloromethane (5.5 ml) at room temperature under a nitrogen atmosphere. The solution was stirred at room temperature for 66 h and then quenched with a saturated aqueous solution of sodium hydrogencarbonate (15 ml). The mixture was extracted with ethyl acetate (3 × 10 ml), and the combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to leave a colourless oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *methyl ketal* (48 mg, 59%) as a colourless oil; $[\alpha]_D^{20}$ −30.6 (*c* 0.2 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2931, 2176, 1729, 1089; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.25 (1H, d, *J* 15.7, *H*-4′), 5.56 (1H, dd, *J* 15.7, 7.6, *H*-5′), 5.39 (1H, d, *J* 9.2, *H*-2′), 4.42 (1H, dd, *J* 9.2, 7.0, *H*-1′), 4.20–4.12 (2H, m, CO_2CH_2), 3.78 (1H, app q, *J* ~7.6, *H*-6′), 3.59 (1H, dddd, *J* 11.0, 11.0, 4.5, 4.5, *H*-4), 3.47 (1H, ddd, *J* 12.0, 7.0, 1.9, *H*-6), 3.33 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 2.83 (1H, d, *J* 14.0, CH_2CO_2Et), 2.60 (1H, dd, *J* 17.0, 5.6, *H*-7′), 2.57 (1H, d, *J* 14.0, CH_2CO_2Et), 2.44 (1H, dd, *J* 17.0, 7.3, *H*-7′), 2.45–2.42 (1H, m, *H*-3*eq*), 1.93–1.88 (1H, m, *H*-5*eq*), 1.80 (3H, d, *J* 1.1, CH_3C=), 1.44 (1H, dd, *J* 15.7, 11.0, *H*-3*ax*), 1.28 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.04 (1H, app q, *J* ~12.0, *H*-5*ax*), 0.87 (9H, s, $C(CH_3)_3$), 0.14 (9H, s, $Si(CH_3)_3$), 0.07 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 169.1 (s), 137.3 (d), 134.2 (s), 132.2 (d), 127.8 (d), 103.2 (s), 99.4 (s), 86.6 (s), 80.7 (d), 73.4 (2xd), 72.1 (d), 60.5 (t), 56.6 (q), 55.6 (q), 47.9 (q), 42.0 (t), 39.3 (t), 32.6 (t), 27.0 (t), 25.8 (q), 18.2 (s), 14.2 (q), 13.4 (q), 0.1 (q), −4.6 (q), −4.7 (q); *m*/*z* (FAB) Found 595.3467 ($[M - H]^+$ $C_{31}H_{55}O_7Si_2$ requires 595.3486).

(2*R*,4*R*,6*R*,1′*R*,6′*R*)-{6-[1′-(*tert*-Butyldimethylsilanyloxy)-6′-methoxy-3′-methyl-nona-di-(2′*E*,4′*E*)-en-8′-ynyl]-2,4-dimethoxy-tetrahydropyran-2-yl}-acetic acid ethyl ester (30). A solution of silver nitrate (43 mg, 250 μmol) in a 1 : 1 mixture of ethanol and water (350 μl of each) was added dropwise over 1 min to a stirred solution of the trimethylsilyl acetylene (**29b**) (38 mg, 64 μmol) in THF (1.0 ml) and ethanol (600 μl) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 20 min, then a solution of potassium cyanide (30 mg, 450 μmol) in water (500 μl) was added dropwise over 1 min. The mixture was stirred at room temperature for a further 2 h, and then diluted with ethyl acetate (50 ml) and water (20 ml). The separated aqueous layer was extracted with ethyl acetate (2 × 50 ml), and the combined organic extracts was dried (Na_2SO_4) and concentrated *in vacuo* to leave an opaque oil. Purification by flash chromatography, using 12% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alkyne* (25 mg, 75%) as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.26 (1H, d, *J* 15.7, *H*-4′), 5.59 (1H, dd, *J* 15.7, 7.8, *H*-5′), 5.40 (1H, d, *J* 9.3, *H*-2′), 4.42 (1H, dd, *J* 9.3, 7.0, *H*-1′), 4.19–4.12 (2H, m, CO_2CH_2), 3.80 (1H, app q, *J* ~6.5, *H*-6′), 3.60 (1H, dddd, *J* 11.5, 11.5, 4.5, 4.5, *H*-4), 3.46 (1H, ddd, *J* 11.5, 7.0, 1.9, *H*-6), 3.33 (6H, s, 2xOCH_3), 3.26 (3H, s, OCH_3), 2.83 (1H, d, *J* 14.0, CH_2CO_2Et), 2.57 (1H, d, *J* 14.0, CH_2CO_2Et), 2.50 (2H, ddd, *J* 6.0, 6.0, 2.6, *H*-7′), 2.46–2.40 (1H, m, *H*-3*eq*), 2.02 (1H, t, *J* 2.6, *H*-9π), 1.92–1.88 (1H, m, *H*-5*eq*), 1.80 (3H, d, *J* 1.0, CH_3C=), 1.44 (1H, dd, *J* 12.6, 11.5, *H*-3*ax*), 1.28 (3H, td, *J* 7.1, 1.1, $CO_2CH_2CH_3$), 1.05 (1H, ddd, *J* 11.5, 11.5, 11.5, *H*-5*ax*), 0.87 (9H, s, $C(CH_3)_3$), 0.06 (3H, s, $SiCH_3$), 0.01 (3H, s, $SiCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1 (s), 137.5 (d), 134.1 (s), 132.5 (d), 127.4 (d), 99.4 (s), 80.6 (d), 80.3 (d), 73.4 (d), 73.3 (d), 72.1 (d), 69.9 (s), 60.5 (t), 56.6 (q), 55.6 (q), 47.9 (q), 42.0 (t), 39.3 (t), 32.5 (t), 25.8 (t), 25.8 (q), 18.2 (s), 14.2 (q), 13.4 (q), −4.7 (q), −4.7 (q); *m*/*z* (ESI) Found 547.3104 ($[MNa]^+$ $C_{28}H_{48}O_7SiNa$ requires 547.3067).

(2*R*,4*R*,6*R*,1′*R*,6′*R*)-{6-[9′-Bromo-1′-(*tert*-butyldimethylsilanyloxy)-6′-methoxy-3′-methyl-nona-tri-(2′*E*,4′*E*,8′*E*)-enyl]-2,4-dimethoxy-tetrahydropyran-2-yl}-acetic acid ethyl ester (31). Tributyltin hydride (21 mg, 71 μmol) and azo bis(isobutyronitrile) (catalytic) were added separately, each in one portion, to a stirred solution of the alkyne (**30**) (25 mg, 48 μmol) in benzene (2 ml) at room temperature under a nitrogen atmosphere. The mixture was heated at reflux for 1 h 30 min and then concentrated *in vacuo* to leave the crude *vinyl stannane* as an opaque residue.

N-Bromosuccinimide (15 mg, 71 μmol) was added in one portion to a stirred solution of the vinyl stannane in acetonitrile (2 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 15 min and then concentrated *in vacuo* to leave an opaque residue. Purification by flash chromatography, using 15% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *vinyl bromide* (17 mg, 60% over two steps) as a colourless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.19 (1H, d, *J* 15.7, *H*-4′), 6.21–6.17 (1H, m, *H*-8′), 6.10 (1H, d, *J* 13.6, *H*-9′), 5.45 (1H, dd, *J* 15.7, 7.9, *H*-5′), 5.39 (1H, d, *J* 9.2, *H*-2′), 4.42 (1H, dd, *J* 9.2, 7.0, *H*-1′), 4.18–4.13 (2H, m, CO_2CH_2), 3.67–3.56 (2H, m, *H*-4, *H*-6′), 3.48 (1H, ddd, *J* 12.0, 7.0, 1.7, *H*-6), 3.33 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 2.83 (1H, d, *J* 14.0, CH_2CO_2Et), 2.57 (1H, d, *J* 14.0, CH_2CO_2Et), 2.45–2.41 (1H, m, *H*-3*eq*), 2.37–2.23 (2H, m, *H*-7′), 1.92–1.89 (1H, m, *H*-5*eq*), 1.78 (3H, s, CH_3C=), 1.44 (1H,

dd, *J* 12.7, 11.1, *H*-3*ax*), 1.28 (3H, t, *J* 7.2, CH_2CH_3), 1.05 (1H, ddd, *J* 12.0, 12.0, 12.0, *H*-5*ax*), 0.88 (9H, s, $C(CH_3)_3$), 0.07 (3H, s, $SiCH_3$), 0.02 (3H, s, $SiCH_3$); *m*/*z* (ESI) Found 627.2308 ($[MNa]^+$ $C_{28}H_{49}O_7SiBrNa$ requires 627.2329).

Tetrahydropyranyl amide alcohol (32). Aqueous lithium hydroxide (257 µl; 0.26 mmol) was added to a solution of the ester (**31**) (15.5 mg; 0.03 mmol) in methanol (0.5 ml) and THF (0.5 ml), and the mixture was stirred at room temperature for 22 h. The mixture was neutralized at 0 °C with 10% citric acid solution, and then extracted with ethyl acetate (3 × 5 ml). The separated organic layer was washed with brine (2 ml), dried (Na_2SO_4) and the solvent was then evaporated to leave a pale orange oil. The oil was purified by eluting through a short plug of silica with ethyl acetate to afford the corresponding carboxylic acid as a pale yellow oil (15 mg) which was used without further purification. Triethylamine (15 µl; 0.11 mmol) was added to a solution of serine (5 mg; 0.03 mmol) in THF (1 ml), at 0 °C, and the mixture was stirred at 0 °C for 15 min. A solution of the crude carboxylic acid (15 mg; 0.03 mmol) in THF (1.5 ml) was added *via* cannula, followed by EDC (6.2 mg; 0.03 mmol), and HOBT (4 mg; 0.03 mmol), and the mixture was allowed to warm to room temperature overnight. The mixture was quenched with saturated ammonium chloride solution (1 ml), diluted with water (1 ml) and extracted with ethyl acetate (4 × 5 ml). The separated organic extracts were dried (Na_2SO_4) and the solvent was then evaporated to leave a pale yellow oil. The oil was purified by chromatography on silica, eluting with ethyl acetate, to give the *amide* (15.8 mg; 91%) as a colourless oil; ^{1}HNMR (360 MHz, $CDCl_3$) δ 6.50–6.06 (3H, m, H-4′, H-8′, H-9′), 5.50 (1H, dd, *J* 15.7, 7.5, H-5′), 5.44 (1H, d, *J* 8.4, H-2′), 4.70–4.55 (2H, m, $CHCO_2Me$, CH_2OH), 4.0–3.88 (1H, m, CH_2OH), 3.78 (3H, s, CO_2Me, 3.70–3.53 (H, m, H-4, H-6′), 3.52–3.43 (1H, m, H-6), 3.32 (3H, s, OCH_3), 3.28 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 2.83 (1H, d, *J* 14.8, CH_2OX), 2.54 (1H, d, *J* 14.8, CH_2OX), 2.40–2.23 (3H, m, H-3_{eq}, H-7′), 1.95–1.83 (1H, m, H-5_{eq}), 1.81 (3H, s, CH_3C=, H-5_{ax} + H-3_{ax} not observed (hidden under impurities), 0.90 (9H, s, $C(CH_3)_3$), 0.08 (3H, s, CH_3), 0.03 (3H, s, CH_3); *m*/*z* (ESI) Found 700.2547 ($[M + Na]^+$ $C_{30}H_{52}O_9NSi^{79}BrNa$ requires 700.2492).

Tetrahydropyranyl oxazolidine (33). DAST (4.3 µl; 0.03 mmol) was added to a solution of the amide alcohol (**32**) (15.8 mg; 0.02 mmol) in dichloromethane (0.5 ml) at −78 °C and the mixture was stirred at −78 °C for 1 h, then quenched with saturated sodium bicarbonate solution (1 ml) and allowed to warm to room temperature. The mixture was diluted with water (2 ml) and extracted with ethyl acetate (4 × 5 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated to leave a pale yellow oil. The oil was eluted through a short plug of silica with ethyl acetate to give the *oxazoline* (15 mg; 98%) as a pale yellow oil, which was used without further purification; ^{1}HNMR (360 MHz, $CDCl_3$) δ 6.25–6.15 (2H, m, H-4′, H-8′), 6.09 (1H, d, *J* 13.6, H-9′), 5.44 (1H, dd, *J* 15.7, 7.8, H-5′), 5.38 (1H, d, *J* 8.8, H-2′), 4.75 (1H, dd, *J* 10.4, 8.0, CH_2OH), 4.50 (1H, t, *J* 8.3, $CHCO_2Me$), 4.46–4.38 (2H, m, H-1′, CH_2OH), 3.78 (3H, s, CO_2Me), 3.68–3.52 (2H, m, H-4, H-6′), 3.51–3.45 (1H, m, H-6), 3.32 (3H, s, OCH_3), 3.28 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 3.02 (1H, d, *J* 14.4Hz, CH_2OX), 2.53 (1H, d, *J* 14.4Hz, CH_2OX), 2.47–2.39 (1H, m, H-3_{eq}), 2.36–2.24 (2H, m, H-7′), 1.92–1.85 (1H, m, H-5_{eq}), 1.77 (3H, d, *J* 1HZ, CH_3C=), 1.46 (1H, dd, *J* 12.7, H-3_{ax}), 1.03 (1H, dd, *J* 23.5, 11.9Hz, H-5_{ax}), 0.86 (9H, s, $C(CH_3)_3$), 0.05 (3H, s, CH_3), 0.01 (3H, s, CH_3); *m*/*z* (ESI) Found 682. 2416 ($[M+Na]^+$ $C_{30}H_{50}O_8NSi^{79}BrNa$ requires 682.2387).

Tetrahydropyranyl oxazole ester (34). Bromotrichloromethane (9 µl; 0.09 mmol), followed by DBU (14 µl; 0.09 mmol), were added to a solution of the oxazoline (**33**) (15 mg; 0.022 mmol) in dichloromethane (0.5 ml) at 0 °C and the mixture was then stirred overnight at room temperature. Analysis by TLC showed the presence of remaining starting material, and so further portions of bromotrichloromethane and DBU were added and the mixture was again stirred for 24 h. The mixture was evaporated *in vacuo* and the residue was purified by chromtography on silica, eluting with 50% ethyl acetate–petrol, to give the *oxazole* (9.9 mg; 66%) as a pale yellow oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.26–6.15 (2H, m, H-4′, H-8′), 6.10 (1H, d, *J* 13.6, H-9′), 5.45 (1H, dd, *J* 15.7, 7.8, H-5′), 5.38 (1H, d, *J* 9.2, H-2′), 4.42 (1H, dd, *J* 9.1, 6.8, H-1′), 3.91 (3H, s, CO_2CH_3), 3.69–3.60 (1H, m, H-6′), 3.59–3.42 (2H, m, H-4, H-6), CH_2OX not observed (under OCH_3 resonances), 3.33 (3H, s, OCH_3), 3.29 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 3.09 (1H, d, *J* 14.7, CH_2OX), 2.39–2.20 (3H, m, H-3_{eq}, H-7′), 1.92–18.5 (1H, m, H-5_{eq}), 1.78 (3H, d, *J* 11.1, CH_3C=), 1.41–1.36 (1H, m, H-3_{ax}), 1.03 (1H, dd, *J* 23.6, 11.7, H-5_{ax}), 0.87 (9H, s, $C(CH_3)_3$), 0.06 (3H, s, CH_3), 0.01 (3H, s, CH_3); *m*/*z* (ESI) Found 680.2191 ($[M + Na]^+$ $C_{30}H_{48}O_8NSi^{79}BrNa$ requires 680.2230).

Tetrahydropyranyl oxazole methylsulfone (36). Diisobutylaluminium hydride (1.5 M solution; 36 µl; 0.04 mmol) was added over 5 min to a stirred solution of the ester (**34**) (9.5 mg; 0.014 mmol) in dichloromethane (0.5 ml) at −78 °C and the mixture was allowed to warm to 0° over 2 h. The mixture was quenched with saturated ammonium chloride solution (2 drops), stirred for 15 min, and then eluted through a short column of silica with ethyl acetate to give the corresponding *alcohol* (**35a**) (8.9 mg; 98%) as a pale yellow oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.52 (1H, s, CH), 6.26–6.16 (2H, m, H-4′, H-8′), 6.1 (1H, d, *J* 13.1, H-9′), 5.45 (1H, dd, *J* 15.6, 7.7Hz, H-5′), 5.39 (1H, d, *J* 9.9, H-2′), 4.58 (2H, s, CH_2), 4.4 3(1H, dd, *J* 9.11, 6.8, H-1′), 3.58–3.42 (3H, m, H-6′, H-4, H-6), 3.33 (3H, s, OCH_3), 3.30 (3H, s, OCH_3), 3.27 (3H, s, OCH), CH_2OX not observed (under methyl resonances), 3.00 (1H, d, *J* 15.0, CH_2OX, 2.37–2.23 (3H, m, H-3_{eq}, H-7′), 1.95–1.87 (1H, m, H-5_{eq}), 1.78 (3H, s, CH_3C=), 1.41–1.35 (1H, m, H-3_{ax}), 1.04 (1H, dd, *J* 23.6, 12.0, H-5_{ax}), 0.88 (9H, s, $C(CH_3)_3$), 0.07 (3H, s, CH_3), 0.01 (3H, s, CH_3); *m*/*z* (ESI) Found 652.2291 ($[M + Na]^+$ $C_{29}H_{48}O_7NSi^{79}BrNa$ requires 652.2281).

Triethylamine (13 µl; 0.09 mmol), followed by methanesulfonyl chloride (3.6 µl; 0.05 mmol) were added to a solution of the obtained alcohol (8.9 mg; 0.0137 mmol) in dichloromethane (0.5 ml) at room temperature and the mixture was stirred at room temperature for 1 h. The mixture was quenched with saturated sodium bicarbonate solution (2 drops) and the solvents were then evaporated to dryness. The residue was eluted through a short column of silica with ethyl acetate to give the *mesylate* (**35b**) (10 mg) as a pale yellow oil.

A solution of 1 M NaHMDS (28 µl; 0.03 mmol) was added to a solution of 2-mercaptobenzothiazole (4.7 mg; 0.03 mmol) in THF (0.1 ml) and the solution was stirred at room temperature for 10 min and then added *via* cannula to a solution of the crude mesylate (10 mg; 0.02 mmol) in THF (0.2 ml) at 0 °C. The mixture was stirred at room temperature for 2 h, and then evaporated *in vacuo*. The residue was purified by chromatography on silica, eluting with 10% ethyl acetate–petrol to give the *sulfide* (4.2 mg; 38%) as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.89 (1H, d, *J* 8.1, ArH, 7.75 (1H, d, *J* 8.1, ArH), 7.47–7.36 (1H, m, ArH), 7.34–7.23 (1H, m, ArH), 6.23–6.15 (2H, m, H-4′, H-8′), 6.09 (1H, d, *J* 13.5, H-9′), 5.38 (1H, dd, *J* 15.5, 7.9, H-5′), 5.38 (1H, d, *J* 8.4, H-2′), 4.48 (2H, d, *J* 3.5, CH_2S), 4.42 (1H, dd, *J* 9.3, 7.0, H-1′), 3.69–3.61 (1H, m, H-6), 3.60–3.41 (2H, m, H-6′, H-4, 3.32 (3H, s, OCH_3), 3.29 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 2.97 (1H, d, *J* 14.9, CH_2OX), 2.40–2.20 (3H, m, H-3_{eq}, H-7′), 1.98–1.83 (1H, m, H-5_{eq}), 1.77 (3H, s, CH_3C=), 1.38 (1H, dd, *J* 12.8, 11.7, H-3_{ax}), 1.03 (1H, dd, *J* 23.7, 12.2, H-5_{ax}), 0.87 (9H, s, $C(CH_3)_3$), 0.07 (3H, s, CH_3), 0.01 (3H, s, CH_3); *m*/*z* (ESI) Found 801.1987 ($[M + Na]^+$ $C_{36}H_{51}{}^{79}BrN_2O_6S_2SiNa$ requires 801.2039).

Ammonium molybdate (3.6 mg; 2.9 μmol), followed by 30% hydrogen peroxide solution (65 μl; 57.8 μmol) were added successively to a solution of the sulfide (4.5 mg; 5.2 μmol) in methanol (0.5 ml) at room temperature, and the mixture was then stirred at room temperature for 3 days. The solvent was evaporated and the residue was purified by chromatography on silica eluting with 20% ethyl acetate–petrol to give the *sulfone* (2.6 mg; 60%) as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.25 (1H, d, *J* 8.3, ArH), 7.99 (1H, d, *J* 8.3, ArH), 7.67–7.57 (2H, m, ArH), 7.65 (1H, s, CH), 6.26–6.15 (2H, m, H-4′, H-8′), 6.09 (1H, d, *J* 13.6, H-9), 5.61–5.41 (1H, m, H-5′), 5.37–5.35 (1H, m, H-2′), 4.75 (2H, s, CH_2SO_2Ar), 4.39 (1H, dd, *J* 8.7, 7.4, H-1′), 3.82–3.62 (1H, m, H-6), 3.54–3.38 (2H, m, H-6′, H-4), 3.27 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 3.17 (3H, s, OCH_3), 2.88 (1H, d, *J* 14.9, CH_2OX), 2.51–2.45 (1H, m, H-3_{eq}), 2.37–2.24 (1H, m, H-7′), 2.1–2.07 (1H, m, H-7′), 1.90–1.82 (1H, m, H-5_{eq}), 1.77 (3H, d, *J* 4.6, CH_3C=), 1.22 (1H, dd, *J* 14.1, 11.5, H-3_{ax}), 0.99 (1H, dd, *J* 23.4, 12.3, H-5_{ax}), 0.85 (9H, s, $C(CH_3)_3$), 0.04 (3H, s, CH_3), −0.1 (3H, s, CH_3); *m*/*z* (ESI) Found 833.1938 ([M + Na]$^+$ $C_{36}H_{51}{}^{79}BrN_2O_8S_2SiNa$ requires 833.1937).

1-(*tert*-Butyl-diphenyl-silanyloxy)-2,4-dimethyl-hex-5-en-3-ol (39). *n*-Butyllithium in THF (1.6 M, 25 mmol) was added over 10 min, to a stirred mixture of potassium *tert*-butoxide (2.8 g, 25 mmol, dried at 80 °C/0.5 mm for 8 h), THF (7 ml), and *trans*-2-butene (4.5 ml, 50 mmol), at −78 °C. The mixture was stirred at −45 °C for 10 min, recooled to −78 °C, and then treated dropwise over 10 min with a solution of (−)-methoxydiisopinocampheylborane in ether (1 M, 30 mmol). The mixture was stirred at −78 °C for 30 min, and then boron trifluoride etherate (4 ml, 33.5 mmol) was added dropwise over 10.5 min, followed by (*S*)-3-(tert-butyldiphenylsilanyloxy-2-methylpropanal (**38**)[28] (8.2 g, 25 mmol) over 30 min at −78 °C. The mixture was stirred at −78 °C for 3 h, then treated with 3 M NaOH (18 ml) and 30% H_2O_2 (7.5 ml), and stirred overnight. The separated organic layer was washed with water (30 ml) and brine (30 ml), then dried over anhydrous $MgSO_4$ and evaporated to dryness. The residue was purified by flash chromatography on silica gel eluting with 10–30% ether–petrol to give the *homoallylic alcohol* (7.3 g, 76% yield, 92% de by NMR analysis), as a colourless oil; $[\alpha]_D^{22}$ +15.2 (*c* 0.4 in $CHCl_3$); ν_{max}(NaCl)/cm^{-1} 3550–3300, 3068, 2955, 2927, 2851, 1590, 1471, 1427, 1261, 1112; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.6–7.7 (4H, m, Ph), 7.2–7.4 (6H, m, Ph), 5.82–5.9 (1H, m, C*H*=CH_2), 5.10 (1H, d, *J* 6.9, CH=CH_2), 5.08 (1H, s, CH=CH_2), 3.70 (2H, d, *J* 5.2, CH_2O), 3.58 (1H, d, *J* 8.5, C*H*OH), 2.40 (1H, b s, OH), 2.2–2.3 (1H, m, CH), 1.8–1.85 (1H, m, CH), 1.06 (9H, s, Bu^t), 0.94 (3H, d, *J* 6.8, CH_3) and 0.93 (3H, d, *J* 6.4, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 141.9(d), 135.6(d), 133.3(s), 129.7(d), 127.7(d), 115.3(t), 76.1(d), 68.4(t), 41.7(d), 36.7(d), 26.7(q), 19.2(s), 16.7(q), 9.6(q); *m*/*z* (FAB) Found 383.2408 ([M + H]$^+$ $C_{24}H_{34}O_2Si$ requires 383.2406).

3-(4-Methoxy-benzyloxy)-2,4-dimethyl-hex-5-en-1-ol (40a). Trifluoromethanesulfonic acid (12 ml, 0.13 mmol) was added to a stirred mixture of the alcohol (**39**) (1.0 g, 2.6 mmol) and 4-methoxybenzyl 2,2,2-trichloroacetimidate (1.5 g, 5.2 mmol) in ether (26 ml) at 0 °C. The mixture was stirred at 0 °C for 10 min, then allowed to warm to room temperature and treated with saturated $NaHCO_3$ solution (30 ml). The organic layer was separated and the aqeous layer was extracted with ether (3 × 50 ml). The combined organic extracts were washed with water (50 ml) and brine (50 ml), then dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (5–10% ether-petrol as eluant) to give the corresponding PMB ether as a colourless oil, which was used in the next step.

TBAF (1 M solution, 3.9 ml) was added dropwise over 5 mins to a stirred solution of the PMB ether in THF (20 ml) at 0 °C. The mixture was stirred at room temperature for 1 hour and then poured into aqueous NH_4Cl solution (50 ml). The separated aqueous layer was extracted with ethyl acetate (3 × 30 ml), and the combined organic extracts were washed with brine (50 ml), dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (20–30% ethyl acetate–petrol as eluant) to give the primary *alcohol* (371 mg, 54%) as a colourless oil; $[\alpha]_D^{22}$ +6.5 (*c* 1.7 in $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3517, 2930, 2854, 1612, 1588, 1463, 1112; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (2H, d, *J* 7.0, ArH), 6.88 (2H, d, *J* 7.0, ArH), 5.8–5.9 (1H, m, C*H*=CH_2), 5.11 (1H, d, *J* 17.2, CH=CH_2), 5.05 (1H, d, *J* 10.0, CH=CH_2), 4.58 (1H, d, *J* 10.6, $ArCH_2O$), 4.45 (1H, d, *J* 10.6, $ArCH_2O$), 3.81 (3H, s, CH_3O), 3.6–3.65 (1H, m, CH_2O), 3.35–3.4 (1H, m, C*H*OH), 3.5–3.55 (1H, m, CH_3CH), 1.90 (1H, b s, OH), 1.04 (3H, d, *J* 6.1, CH_3) and 0.95 (3H, d, *J* CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.1 (s), 141.8 (d), 130.8 (s), 129.4 (d), 114.4 (t), 113.7 (d), 83.8 (d), 73.7(t), 66.1 (t), 55.2 (q), 40.8 (d), 17.4 (q), 11.2 (q); *m*/*z* (FAB) Found 263.1640 ([M − H]$^+$ $C_{16}H_{23}O_3$ requires 263.1647).

Benzoic acid 3-(4-methoxy-benzyloxy)-2,4-dimethyl-hex-5-enyl ester (40b). Benzoyl chloride (2.1 g, 15 mmol) was added dropwise over 10 min to a stirred mixture of the alcohol (**40a**) (2.64 g, 10 mmol) in pyridine (10 ml), and DMAP (5 mg) at 0 °C. The mixture was stirred at 25 °C for 3 h and then poured into aqueous 0.5 M HCl (50 ml) at 0 °C, and extracted with ethyl acetate (3 × 70 ml). The combined organic extracts were washed with water (50 ml) and brine (50 ml), then dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was purified by flash chromatography on silica gel eluting with 10% ether–petrol to give the *ester* (3.4 g, 91% yield), as a colourless oil; $[\alpha]_D^{22}$ +33.0 (*c* 0.2 in $CHCl_3$); ν_{max}(NaCl)/cm^{-1} 2926, 1719, 1612, 1513, 1452, 1273, 1111; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.05 (2H, d, *J* 7.0, ArH), 7.55 (1H, d, *J* 7.4, ArH), 7.45 (2H, dd, *J* 7.0, 7.4, ArH), 7.26 (2H, d, *J* 8.6, ArH), 6.87 (2H, d, *J* 8.6, ArH), 5.8–5.9 (1H, m, C*H*=CH_2), 5.10 (1H, d, *J* 16.2, CH=CH_2), 5.07 (1H, d, *J* 11.7, CH=CH_2), 4.57 (1H, d, *J* 10.6, CH_2O), 4.44 (1H, d, *J* 10.6, CH_2O), 4.2–4.3 (2H, m, OCH_2), 3.80 (3H, s, CH_3O), 3.37 (1H, dd, *J* 4.0, 6.7, OCH), 2.5–2.6 (1H, m, CH_3CH), 2.18–2.26 (1H, m, CH_3CH), 1.07 (3H, d, *J* 6.9, CH_3) and 1.06 (3H, d, *J* 6.9, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.6(s), 159.1(s), 141.5(d), 132.8(d), 130.9(s), 130.5(s), 129.5(d), 129.5(d), 129.3(d), 128.3(d), 114.6(s), 113.7(d), 82.7(d), 74.1(t), 67.1(t), 55.2(q), 40.9(d), 35.1(d), 17.1(q) and 11.4(q); *m*/*z* (ESI) Found 391.2036 ([M + Na]$^+$ $C_{23}H_{28}O_4Na$ requires 391.1885).

Benzoic acid 3-(4-methoxy-benzyloxy)-2,4-dimethyl-5-oxo-pentyl ester (41). Osmium tetroxide (20 mg) was added to a stirred mixture of the alkene (**40b**) (3.2 g, 8.7 mmol) and NMO (1.5 g, 13.1 mmol) in acetone–water (9 : 1) (50 ml) at 0 °C. The mixture was stirred at room temperature for 12 h, and then aqueous $Na_2S_2O_3$ (1 M, 20 mol) was added. The mixture was evaporated to leave an aqueous layer, which was extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were washed with sodium bicarbonate and brine, dried (Na_2SO_4), and then evaporated. The residue was filtered through a pad of silica gel with 30–50% ethyl acetate–petrol to give the corresponding 1,2-diol as a colourless oil.

Sodium periodate (2.8 g, 13.1 mmol) was added to a stirred solution of the 1,2-diol in THF–pH7 buffer (3 : 1, 50 ml) at 0 °C. The reaction was monitored by TLC until the starting material was consumed. The mixture was evaporated to leave an aqueous layer which was extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were washed with water and brine, dried (Na_2SO_4), and then evaporated. The residue was purified by flash chromatography on silica gel eluting with 10–20% ether–petrol to give the *aldehyde* (3.2 g, 87% over two steps), as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.80 (1H, d, *J* 2.3, C*H*O), 8.02–8.05 (2H, m, ArH), 7.50–7.56 (1H, m, ArH), 7.38–7.45 (2H, m, ArH), 7.21 (2H, d, *J* 8.7, ArH),

6.82 (2H, d, *J* 8.7, ArH), 4.50 (2H, dd, *J* 10.8, 13.3, C*H*$_2$O), 4.28 (2H, d, *J* 7.1, C*H*$_2$O), 3.83 (1H, dd, *J* 3.1, 7.8, CHOCH$_2$), 3.71 (3H, s, C*H*$_3$O), 2.7–2.8 (1H, m, CH$_3$CH), 2.18–2.27 (1H, m, CH$_3$CH), 1.06 (3H, d, *J* 7.0, CH$_3$) and 1.05 (3H, d, *J* 6.9, CH$_3$); ^{13}C NMR (90 MHz, CDCl$_3$) δ 203.9 (d), 158.9 (s), 132.8 (d), 129.7 (s), 129.2 (d), 129.2 (d), 128.2 (d), 113.5 (d), 79.3 (d), 73.7 (t), 66.5 (t), 54.8 (q), 48.9 (d), 35.0 (d), 11.0 (q), 10.5 (q).

Benzoic acid 5-hydroxy-3-(4-methoxy-benzyloxy)-2,4-dimethyl-oct-7-enyl ester (42). Boron trifluoride diethyerate (123 ml, 1 mmol) was added dropwise over 5 min to a stirred solution of allyltributyltin (341 ml, 1.1 mmol) and the aldehyde (**41**) (370 mg, 1 mmol) in CH_2Cl_2 (10 ml) at −78 °C, and the mixture was stirred at −78 °C for 2 h, then quenched with saturated aqueous $NaHCO_3$ (10 ml) and warmed to ambient temperature. The mixture was diluted with CH_2Cl_2 (50 ml) and washed with saturated aqueous $NaHCO_3$ (50 ml). The aqueous layer was extracted with CH_2Cl_2 (30 ml) and the combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness *in vacuo*. The residue was purified by flash chromatograpy on silica gel eluting with 10% ethyl acetate–petrol to give the *homoallylic alcohol* (388 mg, 94% yield, 96% de), as a colourless oil; $[\alpha]_D^{22}$ +7.1 (*c* 0.2 in $CHCl_3$); ν_{max}(NaCl)/cm^{-1} 3600–3350, 2922, 1718, 1605, 1513, 1454, 1273, 1112; ^{1}H NMR (360 MHz, $CDCl_3$) δ 8.0–8.1 (2H, m, Ph), 7.49–7.57 (1H, m, Ph), 7.36–7.46 (2H, m, ArH), 7.26 (2H, d, *J* 8.7, ArH), 6.84 (2H, d, *J* 8.7, ArH), 5.72–5.9 (1H, m, C*H*=CH$_2$), 5.10 (1H, d, *J* 15.3, CH=C*H*$_2$), 5.06 (1H, d, *J* 10.0, CH=C*H*$_2$) 4.58 (2H, s, CHOCH$_2$), 4.22–4.32 (2H, m), 4.03–4.9 (1H, m, C*H*OH), 3.78 (3H, s, CH$_3$O), 3.64 (1H, dd, *J* 4.3, 8.0, C*H*OCH$_2$), 2.73 (1H, br. s, OH), 2.2–2.38 (2H, m, C*H*$_2$CHOH), 2.1–2.2 (1H, m, C*H*CH$_3$), 1.75–1.83 (1H, m, C*H*CH$_3$), 1.07 (3H, d, *J* 6.9, CH$_3$) and 0.96 (3H, d, *J* 7.0, CH$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.2(s), 159.0(s), 135.2(d), 132.8(d), 130.1 (s), 129.9(s), 129.3(d), 129.2(d), 128.2(d), 117.1(t), 113.6(d), 82.5(d), 74.9(t), 69.5(d), 67.3(t), 54.9(q), 39.5(d), 38.8(d), 35.2(d), 11.5(q), 10.3(q); *m*/*z* (FAB) Found 413.2349 ([M + H]$^+$ $C_{25}H_{33}O_5$ requires 413.2328).

3-(4-Methoxy-benzyloxy)-2,4-dimethyl-5-(triethyl-silanyl-oxy)-oct-7-en-1-ol (43b). 2,6-Lutidine (140.0 ml 1.1 mmol) was added dropwise over 15 min to a stirred mixture of the ester (**42**) (412.5 mg, 1 mmol) and TESOTf (162.0 ml, 1.1 mmol) in CH_2Cl_2 (10 ml) at −50 °C. The reaction was monitored by TLC until the starting material was consumed. The mixture was diluted with CH_2Cl_2 (50 ml) and the separated organic extract was washed with saturated aqeous $NaHCO_3$ (50 ml). The aqueous extract was extracted with CH_2Cl_2 (30 ml) and the combined organic extracts were then washed with water and brine, dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography on silica gel eluting with 10% ether–petrol to give the corresponding silyl ether (**43a**) as a colourless oil.

DIBALH (1.67 ml of a 1.5 M solution in toluene, 2.5 mmol) was added dropwise over 15 min to a stirred solution of the silyl ether in hexane (50 ml) at −78 °C under an argon atmosphere and the mixture was stirred for 2 h and then quenched with saturated aqueous ammonium chloride solution (1 ml) and allowed to warm to room temperature. The suspension was diluted with ether (50 ml), dried over Na_2SO_4 and the solid inorganic materials were then removed by filtration through Florisil. The filtrate was evaporated to dryness and the residue was purified by chromatography on silica gel (30% ethyl acetate–petrol) to give the *alcohol* (347 mg, 82% over two steps), as a colourless oil; $[\alpha]_D^{22}$ +6.7 (*c* 0.7 in $CHCl_3$); ν_{max}(NaCl)/cm^{-1} 3550–3300, 2955, 2872, 1611, 1514, 1458, 1248, 1036; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.50 (2H, d, *J* 8.6, ArH), 6.86 (2H, d, *J* 8.6, ArH), 5.60–5.80 (1H, m, C*H*=CH$_2$), 5.07 (1H, d, *J* 17.4, CH=C*H*$_2$), 5.02 (1H, d, *J* 8.2, CH=C*H*$_2$), 4.60 (1H, d, *J* 11.0, OCH$_2$), 4.49 (1H, d, *J* 11.0, OCH$_2$), 4.1–4.2 (1H, m, OCH), 3.77 (3H, s, CH$_3$O), 3.64 (1H, dd, *J* 2.0, 9.3, OCH), 3.51–3.61 (2H, m, OCH$_2$), 2.3–2.4 (2H, m, OCHC*H*$_2$), 2.27 (1H, br. s, OH), 1.86–1.93 (1H, m, C*H*CH$_3$), 1.78–1.85 (1H, m, C*H*CH$_3$), 0.97 (9H, t, *J* 7.8, 3 × SiCH$_2$C*H*$_3$), 0.87 (3H, d, *J* 6.9, CH$_3$), 0.82 (3H, d, *J* 7.0, CH$_3$) and 0.63 (6H, q, *J* 7.8, 3 × SiC*H*$_2$CH$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 158.8(s), 134.8(d), 131.1(s), 128.7(d), 116.7(t), 113.6(d), 80.0(d), 73.4(t), 71.3(d), 66.4(t), 55.0(q), 40.2(t), 39.0(d), 37.4(d), 10.0(q), 9.1(q), 7.00(q), 5.7(t); *m*/*z* (ESI) Found 445.2902 ([M + Na]$^+$ $C_{24}H_{42}O_4SiNa$ requires 445.2750).

5-(4-Methoxy-benzyloxy)-4,6-dimethyl-7-(triethyl-silanyoxy)-deca-2,9-dienoic acid ethyl ester (45). A solution of dry DMSO (157 ml, 2.2 mmol) in dichloromethane (2 ml) was added dropwise over 30 min, at a rate sufficient to maintain the internal temperature < −60 °C, to a stirred solution of freshly distilled oxalyl chloride (96 ml, 1.1 mmol) in dichloromethane (10 ml) under a nitrogen atmosphere. The mixture was stirred at −70 °C for 10 min, and then a solution of the alcohol (**43b**) (423 mg, 1 mmol) in dichloromethane (2 ml) was added dropwise over 15 min. Triethylamine (307 ml, 2.2 mmol) was added to the mixture at −70 °C, and it was then allowed to warm to −30 °C over 1.5 h. The mixture was poured into iced 1 M HCl (2.5 ml) and then saturated with NaCl. The separated organic layer was washed with sodium bicarbonate and brine, dried (Na_2SO_4), and then evaporated to dryness. The residue was purified by flash chromatography on silica gel eluting with 5–10% ether–petrol to give the corresponding aldehyde (**44**) as a colourless oil.

NaHMDS (1 M solution, 2 ml) was added over 10 min to a stirred solution of triethyl phosphonoacetate (595 ml, 3 mmol) in THF (10 ml) at 0 °C under an argon atmosphere and the mixture was stirred at 0 °C for 10 min, and then cooled at −78 °C. A solution of the aldehyde in THF (2 ml) was added dropwise at −78 °C, and after 1 h at −78 °C, the mixture was allowed to warm gradually to 0 °C, where it was quenched with saturated aqueous ammonium chloride solution (1 ml). The mixture was evaporated and the aqueous residue was extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were washed with water and brine, then dried (Na_2SO_4), and evaporated to dryness. The residue was purified by flash chromatography on silica gel eluting with 10–20% ether-petrol to give the *α,β-unsaturated ester* (309 mg, 63% over two steps), as a colourless oil; $[\alpha]_D^{22}$ +29.1 (*c* 0.7 in $CHCl_3$); ν_{max}(NaCl)/cm^{-1} 2921, 1718, 1593, 1510, 1248, 1115, 1038; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.22 (2H, d, *J* 8.6, ArH), 7.15 (1H, dd, *J* 15.8, 7.0, OCCH=C*H*), 6.86 (2H, d, *J*, ArH), 5.86 (1H, d, *J* 15.8, OCC*H*=CH), 5.6–5.8 (1H, m, C*H*=CH$_2$), 5.06 (1H, d, *J* 17.9, CH=C*H*$_2$), 5.02 (1H, d, *J* 10.2, CH=C*H*$_2$), 4.42 (2H, dd, *J* 16.4, 10.6, CH$_2$O), 4.20 (2H, q, *J* 7.0, CH$_2$O), 4.1–4.2 (1H, m, OCH), 3.80 (3H, s, CH$_3$O), 3.45 (1H, dd, *J* 2.7, 8.9, OCH), 2.55–2.65 (1H, m, CH$_3$C*H*), 2.2–2.4 (2H, m, C*H*$_2$CHO), 1.7–1.8 (1H, m, C*H*CH$_3$), 1.30 (3H, t, *J* 7.0, C*H*$_3$CH$_2$O), 1.06 (3H, d, *J* 6.8, CH$_3$), 0.96 (9H, t, *J* 7.9, 3 × C*H*$_3$CH$_2$Si), 0.83 (3H, d, *J* 6.9, CH$_3$) and 0.59 (6H, q, *J* 7.9, 3 × CH$_3$C*H*$_2$Si); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.8(s), 159.0(s), 153.6(d), 134.8(d), 130.9(s), 129.0(d), 120.1(d), 116.9(t), 113.6(d), 83.0(d), 78.7(t), 71.0(d), 60.2(t), 55.2(q), 40.3(t), 39.7(d), 38.5(d), 14.2(q), 12.0(q), 9.1(q), 7.1(q), 5.7(t); *m*/*z* (ESI) Found 513.3120 ([M + Na]$^+$ $C_{28}H_{46}O_5SiNa$ requires 513.3012).

5-(4-Methoxy-benzyloxy)-4,6-dimethyl-7-(triethyl-silanyloxy)-deca-2,9,-dien-1-ol (46). A solution of diisobutylaluminium hydride (1.5 M) in toluene (0.73 ml, 1.1 mmol) was added dropwise over 10 min to a solution of the ester (**45**) (246 mg, 0.5 mmol) in hexane (5 ml) at −78 °C under an argon atmosphere. The mixture was stirred at −78 °C for 2 h, then quenched with saturated aqueous ammonium chloride solution (2 ml) and allowed to warm to room temperature. The suspension was diluted with ether (20 ml) and dried over Na_2SO_4. The solid

inorganic materials were removed by filtration through Florisil and the filtrate was evaporated to dryness. The residue was purified by flash chromatography of the residue on silica gel (20–30% ether–petrol) gave the *alcohol* (200 mg, 89%), as a colourless oil, $[\alpha]_D^{21}$ +12.7 (*c* 0.85 in $CHCl_3$); ν_{max} (film)/cm^{-1} 4600–3300, 2955, 1514, 1248, 1037; ^1H NMR (360 MHz, $CDCl_3$) δ 7.23 (2H, d, *J* 8.6, ArH), 6.85 (2H, d, *J* 8.6, ArH), 5.78 (1H, dd, *J* 7.1, 15.8, CH=CHC*H*(CH_3)), 5.7–5.8 (1H, m, C*H*=CH_2), 5.64 (1H, dt. *J* 5.8, 15.6, C*H*=CHCH(CH_3)), 5.06 (1H, d, *J* 17.1, CH=CH_2), 5.02 (1H, d, *J* 9.3, CH=CH_2) 4.48 (2H, dd, *J* 10.5, 10.5, CH_2O), 4.12–4.18 (1H, m, OCH), 4.05 (2H, d, *J* 5.7, OCH_2), 3.78 (3H, s, CH_3O, 3.37 (1H, dd, *J* 2.9, 9.7, OCH), 2.4–2.5 (1H, m, CH_3CH), 2.24–2.37 (2H, m, CH_2CHO), 1.69–1.78 (1H, m, C*H*CH_3), 1.01 (3H, d, *J* 6.9, CH_3), 0.97 (9H, t, *J* 8.0, 3 × CH_3CH_2Si), 0.83 (3H, d, *J* 6.9, CH_3) and 0.61 (6H, q, *J* 8.0, 3 × CH_3CH_2Si); ^{13}C NMR (90 MHz, $CDCl_3$) δ 158.9(s), 137.4(d), 135.0(d), 131.4(s), 128.8(d), 127.7(d), 116.7(t), 113.6(d), 83.8(d), 73.6(t), 71.2(d), 63.7(t), 55.2(q), 40.4(t), 39.7(d), 38.2(d), 13.1(q), 9.4(q), 7.0(q), and 5.7(t); *m*/*z* (FAB) Found 449.3062 ($[M + H]^+$ $C_{26}H_{46}O_4Si$ requires 449.3087).

(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-5-(4-Methoxybenzyloxy)-4,6-dimethyl-2,3-epoxy-7-triethylsilanyloxy-9-decene-1-ol (47). A solution of L-(+)-diethyl tartrate (115 µl, 0.67 mmol), titanium tetraisopropoxide (167 µl, 0.60 mmol, and 5 M *tert*-butylhydroperoxide in decane (448 µl, 2.24 mmol) was added to a stirred mixture containing 4 Å molecular sieves (500 mg) under dichloromethane (10 ml) at −25 °C. The solution was stirred at −25 °C for 15 min, and then a solution of the allyl alcohol (**46**) (501 mg; 1.12 mmol) in dichloromethane (5 ml) was added dropwise over 0.5 h *via* cannula. The solution was stirred at −25 °C for 30 min and then stored at −20 °C for 14 h. The mixture was quenched with 0.5 M tartaric acid solution (1.5 ml), then stirred for 10 min, and extracted with ethyl acetate (3 × 15 ml). The separated organic extracts were washed with brine (10 ml), dried and evaporated to leave a colourless oil. The oil was purified by chromatography, on silica, eluting with 20% ethyl acetate–petrol, to give the *epoxide* (507 mg; 98%) as a colourless oil; $[\alpha]_D^{21}$ + 3.7 (*c* 0.98 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3441, 2954, 1514, 1248, 1087, 1036, 742; ^1H NMR (360 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* 8.5, ArH), 6.87 (2H, d, *J* 8.6, ArH), 5.77–5.66 (1H, m, C*H*=CH_2), 5.08–5.01 (2H, m, CH=CH_2), 4.51 (2H, dd, *J* 10.7, 10.7, CH_2Ar), 4.20–4.15 (1H, m, C*H*OPMB), 3.90–3.86 (1H, m, C*H*O), 3.80 (3H, s, OCH_3), 3.63–3.57 (1H, m, C*H*O), 3.48 (1H, dd, *J* 9.2, 1.7, CHOTES), 3.03–2.99 (2H, m, CH_2OH), 2.38–2.25 (2H, m, CH_2CH=CH_2), 1.94 (1H, t, *J* 6.1, OH), 1.78–1.73 (1H, m, C*H*CH_3), 1.56–1.52 (1H, m, C*H*CH_3), 1.05 (3H, d, *J* 6.9, CH_3), 0.97 (9H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.77 (3H, d, *J* 6.9, CH_3), 0.62 (6H, q, *J* 7.7, 3 × $SiCH_2CH_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.0(s), 134.7(d), 130.9(s), 128.9(d), 116.9 (t), 113.7 (d), 81.9(d), 73.5(t), 71.0(d), 61.6(t), 60.05(d), 58.0(d), 55.2(q), 40.3(t), 39.2(d), 38.4(d), 10.4(q), 9.1 (q), 7.1(q), 5.8(t); *m*/*z* (FAB) Found 465.3005 ($[M + H]^+$ $C_{26}H_{45}O_5Si$ requires 465.3036).

(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-5-(4-Methoxybenzyloxy)-4,6-dimethyl-2,3-epoxy-9-decene-1,7-diol (48). *n*-Tetrabutylammonium fluoride (241 mg; 0.76 mmol) was added portionwise over 2 min to a stirred solution of the silyl ether (**47**) (236 mg; 0.51 mmol) in THF (5 ml) at 0 °C. The solution was stirred at 0 °C for 90 min and then quenched with saturated ammonium chloride solution (5 ml). The mixture was extracted with ethyl acetate (3 × 10 ml), and the separated organic extracts were washed with brine (10 ml), dried (Na_2SO_4) and evaporated to leave a colourless oil. The oil was purified by chromatography on silica, eluting with 50% ethyl acetate–petrol, to give the *1,7-diol* (153 mg; 86%) as a colourless oil; $[\alpha]_D^{21}$ −14.2 (*c* 0.36 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3427, 2974, 1514, 1249, 1082, 1035; ^1H NMR (360 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* 9.9, ArH), 6.87 (2H, d, *J* 8.7, ArH), 5.84–5.73 (1H, m, C*H*=CH_2), 5.14–5.06 (2H, m, CH=CH_2), 4.55 (2H, dd, *J* 10.5, 10.5, C*H*CH_2OAr), 4.04–4.00 (1H, m, C*H*OPMB) 3.87–3.84 (1H, m, CH_2OH), 3.79 (3H, s, OCH_3), 3.62–3.59 (1H, m, CH_2OH), 3.45 (1H, t, *J* 5.5, OC*H*), 3.02–2.99 (1H, m, C*H*OH), 2.93 (1H, d, *J* 2.3, O*H*), 2.88 (1H, dd, *J* 7.7, 2.2, C*H*O), 2.36–2.26 (2H, m, OH, CH_2CH=CH_2), 2.17–2.10 (1H, m, CH_2CH=CH_2), 1.80–1.68 (2H, m, 2 × C*H*CH_3), 1.12 (3H, d, *J* 6.8, CH_3), 0.97 (3H, d, *J* 7.1, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.3(s), 135.2(d), 129.9(s), 129.5(d), 117.35(t), 113.9(d), 85.8(d), 75.0(t), 69.8(d), 61.2(t), 58.6(d), 55.2(q), 39.4(t), 38.6(d), 38.25(d), 12.4(q), 10.9(q); *m*/*z* (FAB) Found 351.2162 ($[M + H]^+$ $C_{20}H_{31}O_5$ requires 351.2171).

1-[6-Allyl-4-(4-methoxy-benzyl)-3,5-dimethyl-tetrahydroyran-2-yl]-ethane-1,2-diol (49). Titanium tetraisopropoxide (60 ml, 1.1 mmol) was added to a solution of the epoxy-alcohol (**48**) (350 mg, 1.0 mmol) in dry benzene (20 ml), at room temperature under an argon atmosphere. The mixture was heated under reflux for 2 h, then cooled to room temperature and quenched with saturated NH_4Cl solution (50 ml). The mixture was diluted with ethyl acetate (200 ml) and the separated aqueous layer was extracted with ethyl acetate (100 ml). The combined organic extracts were washed with brine (200 ml), dried, and evaporated to dryness. The residue was purified by chromatography on silica gel (30–50% ethyl acetate–petrol as eluant) to give the *pyran* (270 mg, 76%) as a colourless oil, $[\alpha]_D^{21}$ + 48.0 (*c* 0.5 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3418, 2973, 1514, 1248, 1072; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* 8.4, ArH), 6.88 (2H, d, *J* 8.4, ArH), 5.68–5.88 (1H, m, C*H*=CH_2), 5.10 (1H, d, *J* 10.7, CH=CH_2), 5.07 (1H, d, *J* 11.0, CH=CH_2), 4.56 (1H, d, *J* 11.0, CH_2O), 4.27 (1H, d, *J* 11.0, CH_2O), 3.78–3.85 (1H, m, OCH), 3.80 (3H, s, CH_3O), 3.70–3.76 (1H, m, OCH_2), 3.61–3.70 (1H, m, OCH_2), 3.35–3.40 (1H, m, OCH), 3.28–3.36 (1H, m, OCH), 3.1–3.18 (1H, m, OCH), 2.86 (1H, b s, OH), 2.58 (1H, b d, *J* 8.0, OH), 2.3–2.44 (1H, m, $OCHCH_2$), 2.18–2.2 (1H, m, $OCHCH_2$), 2.1–2.15 (1H, m, CH_3CH), 1.6–1.68 (1H, m, CH_3CH), 0.94 (3H, d, *J* 6.4, CH_3) and 0.89 (3H, d, *J* 6.4, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2(s), 134.3(d), 130.3(s), 129.3(d), 117.2(d), 113.8(d), 85.0(d), 82.8(d), 78.4(d), 70.3(d), 69.7(t), 62.4(t), 55.2(q), 37.2(t), 33.6(d), 32.7(d), 12.7(q) and 5.6(q); *m*/*z* (FAB) Found: 351.2163 ($[M + H]^+$ $C_{20}H_{31}O_5$ requires 351.2171).

The corresponding acetonide derivative (DMP, PPTSA, 92%) showed ^1HNMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* 8.2), 6.87 (2H, d, *J* 8.2), 5.75–5.83 (1H, m), 5.09 (1H, d, *J* 17.2), 5.04 (1H, d, *J* 9.8), 4.56 (1H, d, *J* 11.0), 4.26 (1H, d, *J* 11.0), 4.17 (1H, m), 3.99 (2H, app d, *J* 7.0), 3.80 (3H, s), 3.35–3.38 (1H, m), 3.15(1H, dd, *J* 10.4, 4.3), 3.12 (1H, dd, *J* 8.8, 4.6), 2.37–2.42 (1H, m), 2.13–2.16 (1H, m), 2.08–2.12 (1H, m), 1.48–1.53(1H, m), 1.40(3H, s), 1.36 (3H, s), 1.01 (3H, d, *J* 6.3), 0.88 (3H, d, *J* 6.8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.19(s), 135.0(d), 130.58(s), 129.31(d), 116.69(t), 113.80(d), 109.20(s), 83.20(d), 80.99(d), 77.77(d), 77.30(d), 69.68(t), 65.51(t), 55.27(s), 37.26(t), 34.54(d), 33.48(d), 26.23(q), 25.97(q), 13.38(q), 5.71(q).

(2*R*,3*R*,4*R*,5*R*,6*S*)-2-Allyl-6-((*S*)-oxiranyl)-4-(4-methoxy-benzyloxy)-3,5-dimethyltetrahydropyran (50). 60% Sodium hydride (110 mg; 2.73 mmol) was added to a solution of the vicinal diol (**49**) (319 mg; 0.91 mmol) in THF (5 ml) at −78 °C and the mixture was stirred at −78 °C for 20 min. *N*-Tosylimidazole (223 mg; 1.00 mmol) was added and the mixture was allowed to warm to room temperature over 4 h. The mixture was quenched with saturated ammonium chloride solution and then extracted with ethyl acetate. The separated organic extract was washed with brine (2 × 5 ml), dried, and evaporated to leave a pale orange oil. The oil was purified by chromatography on silica, eluting with 30% ethyl acetate-petrol, to give the *epoxide* (181 mg; 60%; d.e. 86%) as a colourless oil; $[\alpha]_D^{21}$ + 88.0 (*c* 0.6 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3073, 2976, 1642, 1613,

1513, 1249, 1106; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.28 (2H, d, *J* 8.7, ArH), 6.88 (2H, d, *J* 8.7, ArH), 5.83–5.72 (1H, m, C*H*=CH_2), 5.14–5.04 (2H, m, CH=CH_2), 4.57 (1H, d, *J* 11.1, CH_2Ar), 4.28 (1H, d, *J* 11.1, CH_2Ar), 3.80 (3H, s, OCH_3), 3.35 (1H, ddd, *J* 1.9, 7.1, 7.1, CHOCH_2), 3.14 (1H, dd, *J* 10.4, 4.7, epox-C*H*O), 2.97–2.94 (1H, m, C*H*CH_2CH=CH_2), 2.75 (1H, dd, *J* 5.3, 4.0, C*H*OPMB), 2.71–2.64 (2H, m, CHOCH_2), 2.44–2.36 (1H, m, CH_2CH=CH_2), 2.21–2.06 (2H, m, CH_2-CH=CH_2, C*H*CH_3), 1.85–1.76 (1H, m, C*H*CH_3), 1.06 (3H, d, *J* 6.5Hz, CH_3), 0.92 (3H, d, *J* 6.9, CH_3); ^{13} C NMR (90 MHz, $CDCl_3$) δ 159.1(s), 134.5(d), 130.5(s), 129.2(d), 116.8(t), 113.8(d), 82.7(d), 82.4(d), 78.1(d), 69.6(t), 55.2(q), 53.1(d), 44.3(t), 37.0(t), 35.8(d), 33.2(d), 12.8(q), 5.5(q); *m*/*z* (ESI) Found 355.1919 ([M + Na]$^+$ $C_{20}H_{28}O_4Na$ requires 355.1885).

(2*R*,3*R*,4*R*,5*R*,6*S*)-2-Allyl-6-((*S*)-1-hydroxyethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydropyran (51a). A solution of the epoxide (**50**) (175 mg; 0.53 mmol) in ether (2.5 ml) was added dropwise over 15 min to a slurry of lithium aluminium hydride (22 mg; 0.58 mmol) in ether (2.5 ml), and the mixture was stirred at room temperature for 1 h, and then heated under reflux for 1 h. The mixture was quenched with saturated ammonium chloride (0.2 ml) and filtered through a pad of celite. The filtrate was evaporated to leave a colourless oil, which was purified by chromatography on silica, eluting with 20% ethyl acetate–petrol, to give the *alcohol* (132 mg; 75%) as a colourless oil; $[\alpha]_D^{21}$ + 81.1 (*c* 0.75 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3450, 3075, 2972, 1514, 1463; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* 8.7, ArH), 6.88 (2H, d, *J* 8.7, ArH), 5.85–5.73 (1H, m, C*H*=CH_2), 5.14–5.04 (2H, m, CH=CH_2), 4.57 (1H, d, *J* 11.0, CH_2Ar), 4.27 (1H, d, *J* 11.0, CH_2Ar), 3.87–3.81 (1H, m, C*H*OH), 3.81 (3H, s, OCH_3), 3.42–3.37 (1H, m, C*H*OPMB), 3.17–3.12 (2H, m), 2.45 (1H, d, *J* 10.7, C*H*CHOH), 2.42–2.36 (1H, m, CH_2CH=CH_2), 2.21–2.09 (2H, m, CH_2CH=CH_2, C*H*CH_3), 1.62–1.55 (1H, m, C*H*CH_3), 1.15 (3H, d, *J* 6.5, CH_3), 0.90 (3H, d, *J* 6.8, CH_3), 0.88 (3H, d, *J* 6.2, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.2(s), 134.8(d), 130.5(s), 129.35(d), 116.9(t), 113.8(d), 83.95(d), 83.15(d), 77.75(d), 69.7(t), 67.3(d), 55.3(q), 37.2(t), 33.8(d), 32.7(d), 16.2(q), 12.4(q), 5.6(q); *m*/*z* (ESI) Found 357.2034 ([M + Na]$^+$ $C_{20}H_{30}O_4Na$ requires 357.2042).

(2*R*,3*R*,4*R*,5*R*,6*S*)-2-Allyl-6-((*S*)-1-*tert*-butyldimethylsilanyloxyethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydropyran (51b). 2,6-Lutidine (136 µl; 1.17 mmol) was added to a stirred solution of the alcohol (**51a**) (130 mg; 0.389 mmol) in dichloromethane (5 ml) at −78 °C, followed by *tert*-butyldimethylsilyl triflate (136 µl; 1.17 mmol) and the mixture was then allowed to warm to room temperature over 6 h. The mixture was quenched with saturated ammonium chloride solution (1 ml) and extracted with ether (3 × 10 ml). The separated ether extracts were washed with brine (2 × 2 ml), dried, and then evaporated to leave a colourless oil. The oil was purified by chromatography on silica, eluting with 20% ethyl acetate–petrol, to give the *silyl ether* (165 mg; 95%) as a colourless oil; $[\alpha]_D^{21}$ + 68.0 (*c* 0.6 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3075, 2931, 1643, 1614, 1587, 1514, 1463, 1248, 1089, 834; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.29 (2H, d, *J* 9.0, ArH), 6.89 (2H, d, *J* 9.0, ArH), 5.90–5.79 (1H, m, C*H*=CH_2), 5.14–5.03 (2H, m, CH=CH_2), 4.58 (1H, d, *J* 11.1, CH_2Ar), 4.27 (1H, d, *J* 11.1, CH_2Ar), 4.02–3.95 (1H, m, C*H*OH), 3.82 (3H, s, OCH_3), 3.31 (1H, ddd, *J* 1.7, 7.1, 7.1m, C*H*CH_2CH=CH_2), 3.11 (1H, dd, *J* 10.4, 4.7, C*H*OPMB), 2.98 (1H, dd, *J* 10.4, 2.3, C*H*CHOTBS), 2.48–2.41 (1H, m, CH_2CH=CH_2), 2.21–2.13 (1H, m, CH_2CH=CH_2), 2.10–2.06 (1H, m, C*H*CH_3), 1.64–1.58 (1H, m, C*H*CH_3), 1.16 (3H, d, *J* 6.5, CH_3), 0.94 (3H, d, *J* 6.4, CH_3), 0.90 (3H, d, *J* 6.9, CH_3), 0.89 (9H, s, Bu^t), 0.08 (3H, s, CH_3), 0.06 (3H, s, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1(s), 135.4(d), 130.7(s), 129.4(d), 116.3(t) 113.8(d), 85.8(d), 83.5(d), 77.8(d), 69.5(t), 69.2(d), 55.3(q), 37.2(t), 33.4(d), 32.9(d), 25.9(q), 18.2(s), 17.6(q), 13.4(q), 5.6(q), 1.0(q), −4.5(q); *m*/*z* (ESI) Found 471.2905 ([M + Na]$^+$ $C_{26}H_{44}O_4SiNa$ requires 471.2907).

(2*R*,3*R*,4*R*,5*R*,6*S*)-2-(2-Oxoethyl)-6-((*S*)-1-*tert*-butyldimethylsilanyloxyethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydropyran (52). Osmium tetroxide (2.5 wt% in ^{t}BuOH, 500 µl) and *N*-methylmorpholine *N*-oxide (94 mg, 0.8 mmol) were added to a solution of the alkene (**51b**) (113 mg, 0.27 mmol) in acetone (26 ml) and water (2 ml). The mixture was stirred at room temperature for 24 h and then saturated aqueous sodium thiosulfate (2 ml) was added. The acetone was evaporated off *in vacuo* and the residue was filtered through a short column of silica, eluting with ethyl acetate. The filtrate was evaporated to leave a colourless oil which was taken up in dichloromethane and treated with sodium periodate–silica (0.7 g). The mixture was stirred for 1.5 h, then the solvent was removed *in vacuo*, and the residue was purified by chromatography on silica, using 10% ethyl acetate in petrol as eluant to give the *aldehyde* (90 mg, 88%) as a colourless oil;^{1}H NMR (360 MHz, $CDCl_3$) δ 9.80 (1H, t, *J* 1.91, CHO), 7.28 (2H, d, *J* 8.7, ArH), 6.89 (2H, d, *J* 8.7, ArH), 4.57 (1H, d, *J* 11.0, OCH_2Ar), 4.29 (1H, d, *J* 11.0, OCH_2Ar), 3.95 (1H, dq, *J* 6.4, 2.1), 3.87 (1H, ddd, *J* 9.2, 4.2, 2.0), 3.82 (3H, s, OMe), 3.18 (1H, dd, *J* 10.4, 4.7), 3.05(1H, dd, *J* 10.4, 2.1), 2.78 (1H, ddd, *J* 16.4, 9.2, 1.8), 2.36 (1H, ddd, *J* 16.4, 3.9, 2.4), 2.05–2.15 (1H, m), 1.57–1.68 (1H, m), 1.15 (3H, d, *J* 6.5, Me), 0.94 (3H, d, *J* 6.4, Me), 0.91 (3H, d, *J* 6.9), 0.88 (9H, s, Me_3), 0.04 (6H, s, 2 × Me); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.7(d), 159.2(s), 130.4(s), 129.3(d), 2 × 113.8(d), 86.0(d), 82.8(d), 73.3(d), 69.7(t), 68.8(d), 55.2(q), 46.8(t), 34.1(d), 32.6(d), 3 × 25.8(q), 18.1(s), 17.5(q), 13.2(q), 6.0(q), −4.6(q), −4.7(q); *m*/*z* (ESI) Found 473.2725 ([M + Na]$^+$ $C_{26}H_{44}O_4SiNa$ requires 473.2700).

(2*R*,3*R*,4*R*,5*R*,6*R*)-2-(2-Dimethoxyethylacetal)-6-(1-oxoethyl)-4-(4-methoxybenzyloxy)-3,5-dimethyltetrahydropyran (4). 10-Camphorsulfonic acid (11 mg, 0.047 mmol) was added to a solution of the aldehyde (**52**) (135 mg, 0.3 mmol) in dichloromethane (4 ml) and methanol (4 ml), and the mixture was stirred at room temperature for 3 h. The mixture was filtered through a short column of silica using ethyl acetate as eluant to give the dimethyl acetal secondary alcohol intermediate (**53**) (138 mg) as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.27(2H, d, *J* 8.5, ArH), 6.88 (2H, d, *J* 8.5, ArH), 4.56 (1H, d, *J* 11.0, CH_2Ar), 4.51 (1H, dd, *J* 7.6, 4.0, H-20), 4.28 (2H, d, *J* 11, CH_2), 3.83 (1H, m), 3.81 (3H, s, OMe), 3.51 (1H, ddd, *J* 9.3, 2.3, 2.3), 3.36 (3H, s, OMe), 3.34 (3H, s, OMe), 3.20–3.11 (2H, m), 2.0–2.8 (1H, m), 1.9–1.98 (1H, m), 1.6–1.7 (1H, m), 1.57–1.63(1H, m), 1.15 (3H, d, *J* 6.5), 0.91 (3H, d, *J* 6.9), 0.84 (3H, d, *J* 6.3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.2(s), 130.4(s), 129.4 × 2 (d), 113.8 × 2 (d), 102.5(d), 84.0(d), 82.9(d), 74.8(d), 69.8(t), 67.3(d), 55.3(q), 53.9(q), 52.5(), 36.5(t), 34.8(d), 32.7(d), 16.2(q), 12.4(q), 5.9(q). The crude product was used in the next step without further purification.

Dess–Martin periodinane (254 mg, 0.6 mmol) was added to a stirred solution of the secondary alcohol (**53**) in dichloromethane (2 ml) and 2,6-lutidine (200 µl, 1.7 mmol) at 0 °C, and the mixture was stirred and allowed to warm to room temperature over 18 h. The mixture was diluted with diethyl ether, then quenched with saturated $Na_2S_2O_3$ solution (2 ml) and saturated $NaHCO_3$ solution (2 ml), and diluted with ethyl acetate.

The separated organic extract was washed with brine and saturated $NaHCO_3$ solution, then dried, and evaporated to dryness. The residue was purified by careful chromatography on silica eluting with 10% ethyl acetate–petroleum ether to give the methyl ketone (89 mg, 78%; two steps) as a colourless oil; $[\alpha]^{21}$ + 112.0 (*c* 1.4 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2967, 2935, 1717, 1613, 1514, 1248, 820; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (2H, d, *J* 8.6, ArH), 6.88 (2H, d, *J* 8.6, ArH), 4.56 (1H, d, *J* 11.1, OCH_2Ar), 4.52 (1H, dd, *J* 8.2, 3.3, $(MeO)_2$ CH), 4.29 (1H, d,

J 11.1, OCH_2 Ar), 3.80 (3H, s, OMe), 3.53 (1H, ddd, *J* 9.6, 3.0, 2.0), 3.37 (1H, d, *J* 10.8), 3.35 (3H, s, OMe), 3.33 (3H, s, OMe), 3.29 (1H, dd, *J* 10.4, 4.7), 2.16 (3H, s, Me), 2.06 (1H, m), 1.93 (1H, m), 1.77 (1H, m), 1.66 (1H, m), 0.97 (3H, d, *J* 6.9, Me), 0.89 (3H, d, *J* 6.4, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.21(s), 159.2(s), 130.3(s), 2 × 129.3(d), 2 × 113.8(d), 102.2(d), 87.7(d), 82.7(d), 74.7(d), 69.7(t), 55.3(q), 53.9(q), 52.8(q), 36.6(t), 34.5(d), 32.3(d), 25.3(q), 12.8(q), 6.0(q); *m*/*z* (ESI) Found 403.2128 ($[M + Na]^+$ $C_{21}H_{32}O_6$ requires 403.2096).

(4*S*,1′*R*)-4-(1′-Hydroxybut-3′-enyl)-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (55a).[29]. A solution of allylmagnesium bromide (1 M) in diethyl ether (35 ml, 350 mmol) was added dropwise over 5 min to a stirred solution of (+)-β-methoxydiisopinocampheylborane (12.1 g, 38.2 mmol) in diethyl ether (200 ml) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 30 min and then it was warmed to room temperature and stirred for 1 h. The mixture was cooled to −78 °C and the Garner's aldehyde (**54**)[36] (7.3 g, 31.2 mmol) in diethyl ether (120 ml) was added dropwise, *via* cannula, over 5 min under a nitrogen atmosphere. The mixture was stirred at −78 °C for 2 h before it was quenched by the dropwise addition of methanol (120 ml). Triethylamine (9 ml) and hydrogen peroxide (30 ml) were then added successively, each in one portion, and the mixture was allowed to warm to room temperature and stirred for 12 h. A saturated aqueous solution of sodium thiosulfate (30 ml) was added to the mixture and then it was concentrated *in vacuo* to leave an opaque residue. The residue was diluted with water (20 ml) and then extracted with ethyl acetate (3 × 50 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave a light yellow oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (6.9 g, 80%) as a colourless oil; $[a]_D^{20}$ −17.6 (*c* 3.4 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3368, 2934, 1692, 1455; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) δ 5.93–5.86 (1H, m, *H*-3′), 5.07–4.98 (2H, m, *H*-4′), 3.90–3.84 (3H, bm, *H*-4, *H*-5, *H*-1′), 3.62 (1H, dd, *J* 9.0, 6.8, *H*-5), 2.19 (2H, app t, *J* ~6.4, *H*-2′), 1.59 (3H, s, CCH_3), 1.44 (3H, s, CCH_3), 1.36 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) δ 153.4 (s), 135.9 (d), 117.1 (t), 94.5 (s), 80.2 (s), 72.2 (d), 64.6 (t), 62.2 (d), 38.9 (t), 28.5 (q), 27.1 (q), 24.3 (q); *m*/*z* (EI) Found 256.1544 ($[M - CH_3]^+$ $C_{13}H_{22}O_4N$ requires 256.1549).

(4*S*,1′*R*)-2,2-Dimethyl-4-[1′-(triethylsilanyloxy)-but-3′-enyl]-oxazolidine-3-carboxylic acid *tert*-butyl ester (55b). Chlorotriethylsilane (2.67 g, 2.97 ml, 17.7 mmol) and 4-(dimethylamino)pyridine (1.47 mmol, 0.18 g) were added separately, each in one portion, to a solution of the alcohol (**55a**) (4.00 g, 14.7 mmol) in dichloromethane (150 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 15 min and then triethylamine (2.98 g, 4.11 ml, 29.5 mmol) was added dropwise over 5 min. The mixture was warmed to room temperature and stirred for 12 h before it was quenched with a saturated aqueous solution of ammonium chloride (100 ml). The two layers were separated and the aqueous layer was extracted with dichloromethane (2 × 100 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave an opaque residue. Purification by flash chromatography, using 5% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *protected alkene* (5.10 g, 90%) as a colourless oil; $[a]_D^{20}$ −42.9 (*c* 2.5 in $CHCl_3$) (Found: C, 62.3; H, 10.4; N, 3.4. $C_{20}H_{39}O_4NSi$ requires C, 62.3; H, 10.2; N, 3.6%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2877, 1682, 1456; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) δ 5.86 (1H, dddd, *J* 17.2, 10.1, 7.1, 7.1, *H*-3′), 5.05–4.95 (2H, m, *H*-4′), 4.42 (1H, b s, *H*-1′), 4.11 (1H, dd, *J* 8.4, 3.9, *H*-5), 3.91 (1H, b s, *H*-4), 3.72 (1H, dd, *J* 8.4, 7.1, *H*-5), 2.35–2.27 (1H, m, *H*-2′), 2.20–2.12 (1H, m, *H*-2′), 1.67 (3H, s, CCH_3), 1.52 (3H, s, CCH_3), 1.42 (9H, s, C(CH_3)$_3$), 1.01 (9H, t, *J* 7.9, Si(CH$_2$CH_3)$_3$), 0.65 (6H, q, *J* 7.9, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) δ 153.0 (s), 135.3 (d), 117.2 (t), 94.6 (s), 79.7 (s), 71.5 (d), 63.5 (t), 61.6 (d), 40.7 (t), 28.7 (q), 27.2 (q), 25.2 (q), 7.3 (q), 6.0 (t); *m*/*z* (EI) Found 385.2646 ($[M]^+$ $C_{20}H_{39}O_4NSi$ requires 385.2648).

(4*S*,1′*R*)-2,2-Dimethyl-4-[3′-oxo-1′-(triethylsilanyloxy)-propyl]-oxazolidine-3-carboxylic acid *tert*-butyl ester (56). Ozone was bubbled through a stirred solution of the alkene (**55b**) (4.00 g, 10.4 mmol) and sodium hydrogencarbonate (1.74 g, 20.8 mmol) in dichloromethane (110 ml) at −78 °C. The solution was stirred at −78 °C for 1 h, at which time the solution became blue, and then oxygen was bubbled through the solution until it became colourless. Triphenylphosphine (2.72 g, 10.4 mmol) was then added to the stirred solution at −78 °C and then it was allowed to warm to room temperature over 14 h under a nitrogen atmosphere. The solution was filtered and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 7% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *aldehyde* (3.68 g, 92%) as a colourless oil; $[a]_D^{21}$ −23.4 (*c* 1.6 in $CHCl_3$) (Found: C, 59.2; H, 9.8; N, 3.6. $C_{19}H_{37}O_5NSi$ requires C, 58.9; H, 9.6; N, 3.6%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2878, 2733, 1722, 1692, 1368; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) δ 9.68 (1H, b s, *H*-3′), 4.46 (1H, app q, *J* ~5.9, *H*-1′), 3.99 (1H, dd, *J* 8.8, 2.0, *H*-5), 3.89 (1H, b s, *H*-4), 3.61 (1H, dd, *J* 8.8, 6.0, *H*-5), 2.58–2.49 (1H, m, *H*-2′), 2.44 (1H, ddd, *J* 16.5, 5.0, 1.6, *H*-2′), 1.59 (3H, s, CCH_3), 1.45 (3H, s, CCH_3), 1.38 (9H, s, C(CH_3)$_3$), 0.93 (9H, t, *J* 7.9, Si(CH$_2$CH_3)$_3$), 0.58 (6H, q, *J* 7.9, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) δ 199.1 (d), 153.1 (s), 94.7 (s), 80.3 (s), 68.7 (d), 64.6 (t), 62.2 (d), 49.5 (t), 28.5 (q), 27.6 (q), 24.5 (q), 7.0 (q), 5.7 (t); *m*/*z* (FAB) Found 388.2543 ($[M + H]^+$ $C_{19}H_{38}O_5NSi$ requires 388.2519).

(4*S*,1′*R*,3′*R*)-4-[3′-Hydroxy-1′-(triethylsilanyloxy)-hex-5′-enyl]-2,2-dimethyl-oxazolidine-3-carboxylic acid *tert*-butyl ester (57a). Allylmagnesium bromide (1 M in diethyl ether, 11.8 ml, 11.8 mmol) was added dropwise over 15 min to a stirred solution of (+)-β-methoxydiisopinocampheylborane (4.08 g, 12.9 mmol) in diethyl ether (75 ml) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 30 min and then it was warmed to room temperature and stirred for 1 h. The mixture was cooled to −78 °C and the aldehyde (**56**) (4.16 g, 10.7 mmol) in diethyl ether (30 ml) was added dropwise, *via* cannula, over 10 min under a nitrogen atmosphere. The mixture was stirred at −78 °C for 2 h 15 min and then it was quenched by the dropwise addition of methanol (15 ml). Triethylamine (3 ml) and hydrogen peroxide (12 ml) were then added successively, each in one portion, and the mixture was allowed to warm to room temperature and stirred for 12 h. A saturated aqueous solution of sodium thiosulfate (80 ml) was added to the mixture, which was then concentrated *in vacuo* to leave an opaque residue. The residue was diluted with water (20 ml) and extracted with ethyl acetate (3 × 100 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (3.51 g, 76%) as a colourless oil; $[a]_D^{21}$ −50.0 (*c* 2.6 in $CHCl_3$) (Found: C, 61.3; H, 10.1; N, 3.2. $C_{22}H_{43}O_5NSi$ requires C, 61.5; H, 10.1; N, 3.3%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3400, 2877, 1668, 1394; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) δ 5.87 (1H, b s, *H*-5′), 5.07–5.01 (2H, m, *H*-6′), 4.46 (1H, ddd, *J* 7.6, 3.8, 3.8, *H*-1′), 4.18 (1H, dd, *J* 8.5, 3.1, *H*-5), 4.12 (1H, b s, *H*-3′), 3.84 (1H, b s, *H*-4), 3.68 (1H, app t, *J* ~7.7, *H*-5), 2.21 (2H, b s, *H*-4′), 1.74 (1H, ddd, *J* 14.0, 9.7, 3.8, *H*-2′), 1.65 (3H, s, CC*H*′), 1.57 (1H, ddd, *J* 14.0, 8.8, 3.8, *H*-2′), 1.47 (3H, s, CCH_3), 1.39 (9H, s, C(CH_3)$_3$), 1.03 (9H, t, *J* 7.9, Si(CH$_2$CH_3)$_3$), 0.69 (6H, q, *J* 7.9, Si(CH_2CH$_3$)$_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) δ 153.5 (s), 135.2 (d), 117.0

(t), 93.8 (s), 80.7 (s), 69.0 (d), 67.1 (d), 63.4 (t), 60.1 (d), 43.0 (t), 40.4 (t), 28.3 (q), 27.1 (q), 24.6 (q), 6.9 (q), 5.0 (t); *m/z* (EI) Found 414.2689 ([M − CH_3]$^+$ $C_{21}H_{40}O_5NSi$ requires 414.2676).

(4*S*,1′*R*,3′*R*)-2,2-Dimethyl-4-[1′-(triethylsilanyloxy)-3′-(triisopropylsilanyloxy)-hex-5′-enyl]-oxazolidine-3-carboxylic acid *tert*-butyl ester (57b). 2,6-Lutidine (1.2 g, 1.3 ml, 11.2 mmol) and triisopropylsilyl trifluoromethane-sulfonate (1.7 g, 0.15 ml, 5.6 mmol) were added separately, each in one portion, to a stirred solution of the alcohol (**57a**) (2.0 g, 4.7 mmol) in dichloromethane (50 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 1 h 15 min and then it was quenched with a saturated aqueous solution of ammonium chloride (40 ml). The layers were separated and the aqueous layer was extracted with dichloromethane (2 × 100 ml). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to leave a colourless oil. Purification by flash chromatography, using 5% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *protected olefin* (2.5 g, 92%) as a colourless oil; $[\alpha]_D^{21}$ −32.2 (*c* 2.8 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2868, 1688, 1640, 1090; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) *δ* 5.93 (1H, dddd, *J* 17.2, 10.2, 7.0, 7.0, *H*-5′), 5.18 (1H, dd, *J* 17.2, 1.4, *H*-6′), 5.08 (1H, dd, *J* 10.2, 1.4, *H*-6′), 4.52 (1H, b s, *H*-1′), 4.18–4.11 (2H, m, *H*-5, *H*-3′), 4.06 (1H, b s, *H*-4), 3.84 (1H, app t, *J* ~7.7, *H*-5), 2.67–2.59 (1H, m, *H*-4′), 2.42–2.35 (1H, m, *H*-4′), 1.87 (1H, ddd, *J* 13.8, 7.0, 4.8, *H*-2′), 1.76 (1H, ddd, *J* 13.8, 6.7, 6.7, *H*-2′), 1.68 (3H, s, CCH_3), 1.50 (3H, s, CCH_3), 1.43 (9H, s, $OC(CH_3)_3$), 1.13 (21H, s, $Si(CH(CH_3)_2)_3$), 1.05 (9H, t, *J* 7.9, $Si(CH_2CH_3)_3$), 0.72 (6H, q, *J* 7.9, $Si(CH_2CH_3)_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) *δ* 153.4 (s), 135.0 (s), 117.8 (t), 94.7 (s), 79.8 (s), 70.2 (d), 69.1 (d), 63.7 (t), 62.5 (d), 43.0 (t), 41.4 (t), 28.7 (q), 27.3 (q), 25.3 (q), 18.7 (q), 13.4 (d), 7.4 (q), 6.3 (t); *m/z* (ESI) Found 608.4172 ([M + Na]$^+$ $C_{31}H_{63}O_5NSi_2$ requires 608.4143).

(4*S*,1′*R*,3′*S*)-2,2-Dimethyl-4-[5′-oxo-1′-(triethylsilanyloxy)-3′-(triisopropylsilanyl-oxy)-pentyl]-oxazolidine-3-carboxylic acid *tert*-butyl ester (58). Ozone was bubbled through a stirred solution of the alkene (**57b**) (4.50 g, 7.68 mmol) and sodium hydrogencarbonate (1.29 g, 15.4 mmol) in dichloromethane (70 ml) at −78 °C. The solution was stirred at −78 °C for 30 min, at which time the solution had become blue, and then oxygen was bubbled through the solution until it became colourless. Triphenylphosphine (2.12 g, 8.06 mmol) was added to the stirred solution at −78 °C and then it was stirred at room temperature for 14 h under a nitrogen atmosphere. The solution was filtered and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *aldehyde* (4.30 g, 95%) as a colourless oil; $[\alpha]_D^{21}$ −21.9 (*c* 3.1 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2864, 2730, 1721, 1688; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) *δ* 9.71 (1H, b s, *H*-5′), 4.50 (1H, app qu, *J* ~5.8, *H*-3′), 4.37 (1H, b s, *H*-1′), 4.11 (1H, dd, *J* 8.4, 3.6, *H*-5), 4.04 (1H, b s, *H*-4), 3.83 (1H, app t, *J* ~7.6, *H*-5), 2.76 (1H, app dd, *J* ~16.2, 5.5, *H*-4′), 2.47 (1H, ddd, *J* 16.2, 5.1, 2.2, *H*-4′), 2.03–1.96 (1H, m, *H*-2′), 1.74 (1H, ddd, *J* 14.0, 6.9, 6.9, *H*-2′), 1.65 (3H, s, CCH_3), 1.46 (3H, s, CCH_3), 1.41 (9H, s, $OC(CH_3)_3$), 1.06 (21H, s, $Si(CH(CH_3)_2)_3$), 1.01 (9H, t, *J* 7.9, $Si(CH_2CH_3)_3$), 0.68 (6H, q, *J* 7.9, $Si(CH_2CH_3)_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) *δ* 199.9 (d), 153.5 (s), 94.7 (s), 79.9 (s), 69.3 (d), 67.0 (d), 63.7 (t), 62.5 (d), 50.6 (t), 43.9 (t), 28.7 (q), 27.4 (q), 25.0 (q), 18.6 (q), 13.2 (d), 7.4 (q), 6.2 (t); *m/z* (ESI) Found 610.3981 ([M + Na]$^+$ $C_{30}H_{61}O_6NSi_2$ requires 610.3935).

(4*S*,1′*R*,3′*R*)-4-[6′-Ethoxycarbonyl-1′-(triethylsilanyloxy)-3′-(triisopropylsilanyl-oxy)-hex-(5′*E*)-enyl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (59). (Carboethoxymethylene)triphenylphosphorane (2.68 g, 7.68 mmol) was added in one portion to a stirred solution of the aldehyde (**58**) (4.30 g, 7.31 mmol) in dichloromethane (70 ml) at 0 °C under a nitrogen atmosphere. The solution was warmed to room temperature and stirred for 14 h, and then it was concentrated *in vacuo* to leave a white solid. Purification by flash chromatography, using 2% ethyl acetate–petroleum ether (bp 40–60 °C) to 8% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *α,β-unsaturated ester* (4.20 g, 87%) as a colourless oil; $[\alpha]_D^{21}$ −24.5 (*c* 2.6 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2868, 1689, 1367; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) *δ* 7.20 (1H, ddd, *J* 15.7, 7.3, 7.3, *H*-5′), 6.10 (1H, d, *J* 15.7, *H*-6′), 4.49 (1H, b s, *H*-1′), 4.21–4.14 (1H, m, *H*-3′), 4.16 (1H, dd, *J* 8.5, 3.8, *H*-5), 4.08–4.00 (1H, b s, *H*-4), 4.05 (2H, q, *J* 7.1, CO_2CH_2), 3.85 (1H, app t, *J* ~7.7, *H*-5), 2.78–2.70 (1H, m, *H*-4′), 2.45–2.38 (1H, m, *H*-4′), 1.89 (1H, ddd, *J* 11.6, 7.2, 4.5, *H*-2′), 1.77–1.70 (1H, m, *H*-2′), 1.68 (3H, s, CCH_3), 1.49 (3H, s, CCH_3), 1.43 (9H, s, $C(CH_3)_3$), 1.12–1.00 (33H, m, $CO_2CH_2CH_3$, $Si(CH_2CH_3)_3$, $Si(CH(CH_3)_2)_3$), 0.71 (6H, q, *J* 7.9, $Si(CH_2CH_3)_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) *δ* 165.9 (s), 153.5 (s), 144.6 (d), 128.9 (d), 125.1 (d), 94.7 (s), 79.9 (s), 69.7 (d), 63.6 (t), 62.5 (d), 60.1 (t), 43.3 (t), 39.5 (t), 28.7 (q), 27.4 (q), 25.0 (q), 18.6 (q), 14.5 (q), 13.2 (d), 7.4 (q), 6.3 (t); *m/z* (ESI) Found 680.4327 ([M + Na]$^+$ $C_{34}H_{67}O_7NSi_2Na$ requires 680.4354).

(4*S*,1′*R*,3′*R*)-4-[6′-Ethoxycarbonyl-1′-hydroxy-3′-(triisopropylsilanyloxy)-hex-(5′*E*)-enyl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (60). Pyridinium *para*-toluenesulfonate (2.1 g, 8 mmol) was added in one portion to a stirred solution of the alkene (**59**) (5 g, 7.6 mmol) in dichloromethane (80 ml) at room temperature under a nitrogen atmosphere. The solution was stirred for 4 h and then it was quenched with a saturated aqueous solution of sodium hydrogencarbonate (400 ml). The mixture was diluted with ethyl acetate (500 ml) and the layers were separated. The aqueous layer was extracted with ethyl acetate (2 × 200 ml) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave an opaque oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (3.5 g, 84%) as a colourless oil; $[\alpha]_D^{21}$ −22.7 (*c* 6.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3366, 2867, 1704, 1657, 1368; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) *δ* 7.24 (1H, ddd, *J* 15.7, 7.3, 7.3, *H*-5′), 5.97 (1H, d, *J* 15.7, *H*-6′), 4.38 (1H, dddd, *J* 9.2, 4.9, 4.9, 4.9, *H*-3′), 4.03 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 3.86 (1H, b s, *H*-1′), 3.73 (1H, b s, *H*-5), 3.65 (2H, bm, *H*-4, *H*-5), 2.59–2.52 (1H, m, *H*-4′), 2.38–2.31 (1H, m, *H*-4′), 1.77 (1H, m, *H*-2′), 1.70–1.63 (1H, m, *H*-2′), 1.56 (3H, s, CCH_3), 1.38 (12H, s, CCH_3, $C(CH_3)_3$), 1.09 (21H, s, $Si(CH(CH_3)_2)_3$), 1.02 (3H, t, *J* 7.1, $CO_2CH_2CH_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) *δ* 166.0 (s), 154.3 (s), 145.4 (d), 124.7 (d), 94.9 (s), 80.8 (s), 70.7 (d), 70.2 (d), 65.4 (t), 63.4 (d), 60.1 (t), 40.7 (t), 39.6 (t), 28.6 (q), 26.9 (q), 24.3 (q), 18.6 (q), 14.5 (q), 13.2 (d); *m/z* (ESI) Found 566.3522 ([M + Na]$^+$ $C_{28}H_{53}O_7NSiNa$ requires 566.3489).

(4*S*,2′*R*,4′*R*,6′*S*)-4-[6′-Ethoxycarbonylmethyl-4′-(triisopropylsilanyloxy)-tetrahydropyran-2′-yl]-2,2-dimethyloxazolidine-3-carboxylic acid *tert*-butyl ester (61). A solution of sodium bis(trimethylsilyl)amide (1 M) in THF (3.26 ml, 3.26 mmol) was added dropwise over 2 min to a stirred solution of the alcohol (**60**) (1.61 g, 2.96 mmol) in THF (30 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 1 h and then it was quenched with a saturated aqueous solution of ammonium chloride (30 ml). The mixture was warmed to room temperature and then concentrated *in vacuo* to leave the aqueous residue. The aqueous residue was extracted with ethyl acetate (3 × 50 ml) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a colourless oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *tetrahydropyran* (1.40 g, 87%) as a colourless oil; ν_{max} (soln: $CHCl_3$)/cm^{-1} 2867, 1729, 1688, 1367; ^{1}H NMR (360 MHz, C_6D_6, *T* = 340 K) *δ* 4.47–4.39 (1H, m, *H*-6′), 4.24 (1H, b d, *J* ~8.5, *H*-5), 4.19 (1H, b s, *H*-4′), 4.13 (1H, ddd, *J* 10.8, 8.3, 2.0, *H*-2′), 4.02–3.93 (1H,

m, *H*-4), 3.98 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 3.68 (1H, dd, *J* 8.6, 5.5, *H*-5), 2.51 (1H, dd, *J* 15.0, 7.3, *H*-1″), 2.25 (1H, dd, *J* 15.0, 6.1, *H*-1″), 1.90–1.84 (1H, m, *H*-3′eq), 1.75–1.68 (4H, m, CCH_3, *H*-5′eq), 1.61–1.53 (4H, m, *H*-3′ax, CCH_3), 1.44 (9H, s, $OC(CH_3)_3$), 1.30 (1H, ddd, *J* 13.6, 11.6, 2.5, *H*-5′ax), 1.17–1.03 (21H, m, $Si(CH(CH_3)_2)_3$), 1.00 (3H, t, *J* 7.1, $CO_2CH_2CH_3$); ^{13}C NMR (90 MHz, C_6D_6, *T* = 340 K) δ 170.5 (s), 152.9 (s), 94.4 (s), 79.6 (s), 73.2 (d), 69.6 (d), 65.8 (d), 65.4 (t), 61.4 (d), 60.2 (t), 42.0 (t), 39.7 (t), 37.5 (t), 28.7 (q), 27.9 (q), 24.6 (q), 18.5 (q), 14.4 (q), 12.9 (d); *m*/*z* (FAB) Found 544.3668 ($[M + H]^+$ $C_{28}H_{54}O_7NSi$ requires 544.3670).

(1*S*,2′*S*,4′*R*,6′*R*)-[6′-{2-Hydroxy-1-[2-(4-methoxybenzyloxy)-acetylamino]-ethyl}-4′-(triisopropylsilanyloxy)-tetrahydropyran-2′-yl]-acetic acid ethyl ester (62a). A solution of hydrochloric acid (4 M) in dioxane (30 ml) was added in one portion to the tetrahydropyran (**61**) (1.60 g, 29.4 mmol) at room temperature under a nitrogen atmosphere. The solution was stirred for 1 h 20 min and then toluene (50 ml) was added and the solution was concentrated *in vacuo*. Two subsequent additions of toluene (2 × 30 ml) followed by concentration *in vacuo* left the crude hydrochloride salt of the amino-alcohol as a yellow residue, which was used without further purification.

Triethylamine (1.20 g, 1.66 ml, 11.9 mmol) was added in one portion to a stirred solution of the crude amino-alcohol in THF (30 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 15 min and then (4-methoxybenzyloxy)-acetic acid (0.82 g, 4.16 mmol), 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (0.80 g, 4.16 mmol) and 1-hydroxybenzotriazole (0.52 g, 3.87 mmol) were added separately, each in one portion. The mixture was stirred at 0 °C for 45 min and then at room temperature for 20 h before it was quenched with a saturated aqueous solution of ammonium chloride (40 ml). The mixture was extracted with ethyl acetate (3 × 50 ml) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a brown oil. Purification by flash chromatography, using 50% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *hydroxy-amide* (1.34 g, 75% over 2 steps) as a colourless oil; ν_{max} (soln: $CHCl_3$)/cm^{-1} 3506, 3407, 2866, 1730, 1667; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.27 (2H, d, *J* 8.6, C*H*, Ar), 6.90 (2H, d, *J* 8.6, C*H*, Ar), 4.52 (2H, s, $ArCH_2$), 4.35 (1H, app qu, *J* ~2.6, *H*-4′), 4.30–4.22 (1H, m, *H*-2′), 4.13 (2H, q, *J* 7.1, $CO_2CH_2CH_3$), 4.04 (1H, ddd, *J* 11.5, 5.4, 1.8, *H*-6′), 3.95 (2H, s, $PMBOCH_2$), 3.97–3.88 (2H, m, *H*-1), 3.82 (3H, s, $ArOCH_3$), 3.60 (1H, b d, *J* ~12.2, *H*-2), 3.02 (1H, b s, O*H*), 2.47 (1H, dd, *J* 15.2, 8.0, *H*-1″), 2.41 (1H, dd, *J* 15.2, 5.1, *H*-1″), 1.74–1.67 (2H, m, *H*-3′eq, *H*-5′eq), 1.59 (1H, ddd, *J* 13.2, 11.5, 2.6, *H*-3′ax), 1.49 (1H, ddd, *J* 13.7, 11.5, 2.6, *H*-5′ax), 1.25 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.09–1.01 (21H, m, $Si(CH(CH_3)_2)_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 171.1 (s), 169.6 (s), 159.6 (s), 129.6 (d), 128.9 (s), 113.9 (d), 73.9 (d), 73.2 (t), 69.4 (d), 69.0 (t), 64.5 (d), 62.5 (t), 60.6 (t), 55.3 (q), 52.8 (d), 40.9 (t), 38.7 (t), 36.1 (t), 18.1 (q), 14.1 (q), 12.1 (d); *m*/*z* (ESI) Found 604.3289 ($[M + Na]^+$ $C_{30}H_{51}O_8NSiNa$ requires 604.3282).

(2′*S*,4′*R*,6′*R*)-[6′-{2-(4-Methoxybenzyloxymethyl)-oxazol-4-yl}-4′-(triisopropyl-silanyloxy)-tetrahydropyran-2′-yl]-acetic acid ethyl ester (63). Dess–Martin periodinane (2.35 g, 5.52 mmol) was added in one portion to a stirred solution of the alcohol (**62a**) (1.10 g, 1.84 mmol) in dichloromethane (18 ml) at room temperature under a nitrogen atmosphere. The solution was stirred for 2 h and then it was diluted with dichloromethane (10 ml). The solution was poured onto a stirred solution of saturated aqueous sodium hydrogencarbonate (15 ml) and saturated aqueous sodium thiosulfate (15 ml) and stirred for 30 min. The layers were separated and the aqueous layer was extracted with dichloromethane (2 × 50 ml). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to provide the crude *aldehyde* (**62b**) as a pink oil, which was used without further purification.

Triphenylphosphine (2.42 g, 9.23 mmol), 2,6-di-*tert*-butylpyridine (3.53 g, 4.13 ml, 18.5 mmol) and dibromotetrachloroethane (3.00 g, 9.23 mmol) were added successively, each in one portion, to a stirred solution of the crude aldehyde (1.10 g, 1.85 mmol) in dichloromethane (18 ml) at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 3 h and then 1,8-diazabicyclo[5.4.0]undec-7-ene (7.03 g, 6.90 ml, 46.2 mmol) in acetonitrile (10 ml) was added dropwise, *via* cannula, over 10 min. The mixture was stirred at room temperature for 1 h and then it was concentrated *in vacuo* to leave a black residue. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *oxazole* (0.65 g, 73% over 2 steps) as a colourless oil; ν_{max} (soln: $CHCl_3$)/cm^{-1} 2944, 1729, 1100; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.56 (1H, s, C*H*, ox), 7.29 (2H, d, *J* 8.4, C*H*, Ar), 6.88 (2H, d, *J* 8.4, C*H*, Ar), 4.97 (1H, dd, *J* 11.5, 2.0, *H*-6′), 4.56 (2H, s, $ArCH_2$), 4.55 (2H, s, $PMBOCH_2$), 4.47 (1H, dddd, *J* 13.4, 6.7, 6.7, 1.8, *H*-2′), 4.42–4.40 (1H, m, *H*-4′), 4.17–4.11 (2H, m, $CO_2CH_2CH_3$), 3.81 (3H, s, $ArOCH_3$), 2.67 (1H, dd, *J* 14.9, 6.7, *H*-1″), 2.42 (1H, dd, *J* 14.9, 6.7, *H*-1″), 1.98–1.95 (1H, m, *H*-5′eq), 1.91–1.86 (1H, m, *H*-5′ax), 1.84–1.81 (1H, m, *H*-3′eq), 1.60–1.54 (1H, m, *H*-3′ax), 1.25 (3H, t, *J* 7.1, $CO_2CH_2CH_3$), 1.14–1.06 (21H, m, $Si(CH(CH_3)_2)_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 171.0 (s), 160.9 (s), 159.5 (s), 142.1 (s), 135.8 (d), 129.8 (d), 129.3 (s), 113.9 (d), 72.7 (t), 69.1 (d), 67.4 (d), 64.7 (d), 63.7 (t), 60.4 (t), 55.3 (q), 41.6 (t), 38.8 (t), 38.1 (t), 18.1 (q), 14.2 (q), 12.2 (d); *m*/*z* (ESI) Found 584.2977 ($[M + Na]^+$ $C_{30}H_{47}O_7NSiNa$ requires 584.3020).

(2′*R*,4′*R*,6′*R*)-4-(6′-Allyl-4′-triisopropylsilanyloxy-tetrahydropyran-2′-yl)-2-(4-methoxybenzyloxymethyl)-oxazole (64b). A solution of diisobutylaluminium hydride (1.5 M) in toluene (0.75 ml, 1.1 mmol) was added dropwise over 5 min to a stirred solution of the ester (**63**) (0.60 g, 1.1 mmol) in toluene (9 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 2 h 30 min and then it was quenched by the dropwise addition of methanol (1.5 ml) and warmed to room temperature. The mixture was added, *via* cannula, to a saturated aqueous solution of potassium sodium tartrate (30 ml) and stirred vigorously for 3 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (4 × 50 ml). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 25% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave (2′*S*,4′*R*,6′*R*)-[6′-{2-(4-methoxybenzyloxymethyl)-oxazol-4-yl}-4′-(triisopropyl-silanyloxy)-tetrahydropyran-2′-yl]-acetaldehyde (**64a**) (0.48 g, 87%) as a colourless oil; ν_{max} (soln: $CHCl_3$)/cm^{-1} 2866, 1725, 1103; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.81 (1H, app t, *J* 2.3, *H*-2″), 7.55 (1H, d, *J* 0.5, C*H*, ox), 7.28 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 4.98 (1H, dd, *J* 11.2, 2.6, *H*-6′), 4.61–4.56 (1H, m, *H*-2′), 4.55 (2H, s, $ArCH_2$), 4.54 (2H, s, $PMBOCH_2$), 4.43–4.40 (1H, m, *H*-4′), 3.80 (3H, s, $ArOCH_3$), 2.66 (1H, ddd, *J* 16.3, 7.8, 2.3, *H*-1″), 2.49 (1H, ddd, *J* 16.3, 5.0, 2.3, *H*-1″), 1.98 (1H, ddd, *J* 13.5, 5.0, 2.6, *H*-5′eq), 1.90 (1H, ddd, *J* 13.5, 11.2, 2.4, *H*-5′ax), 1.80–1.73 (1H, m, *H*-3′eq), 1.60 (1H, ddd, *J* 13.5, 11.6, 2.2, *H*-3′ax), 1.11–1.05 (21H, m, $Si(CH(CH_3)_2)_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 201.2 (d), 160.9 (s), 159.4 (s), 141.8 (s), 135.7 (d), 129.7 (d), 129.1 (s), 113.8 (d), 72.6 (t), 67.8 (d), 67.3 (d), 64.5 (d), 63.5 (t), 55.2 (q), 49.5 (t), 38.9 (t), 37.8 (t), 18.0 (q), 12.1 (d); *m*/*z* (FAB) Found 518.2986 ($[M + H]^+$ $C_{28}H_{44}O_6NSi$ requires 518.2938).

n-Butyllithium (2.5 M in hexane, 0.42 ml, 1.1 mmol) was added dropwise over 2 min to a stirred solution of methyltriphenylphosphonium bromide (0.39 g, 1.1 mmol) in THF (3 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 1 h and then it was cooled to −78 °C. The above aldehyde (0.45 g, 0.90 mmol) in THF (4.5 ml) was added

dropwise, *via* cannula, over 5 min and the solution was warmed to room temperature over 16 h. The solution was quenched with ammonium chloride (15 ml) and extracted with ethyl acetate (3 × 25 ml). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *terminal olefin* (270 mg, 59%) as a colourless oil and as a single diastereoisomer; $[\alpha]_D^{21}$ + 3.3 (*c* 0.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2944, 2866, 1045; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.57 (1H, d, *J* 0.7, C*H*, ox), 7.28 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 5.84 (1H, dddd, *J* 17.1, 10.2, 7.1, 7.1, *H*-2″), 5.11–5.03 (2H, m, *H*-3″), 4.94 (1H, dd, *J* 11.4, 2.4, *H*-2′), 4.56 (2H, s, ArCH_2), 4.54 (2H, s, PMBOCH_2), 4.41–4.39 (1H, m, *H*-4′), 4.10–4.02 (1H, m, *H*-6′), 3.81 (3H, s, ArOCH_3), 2.44–2.37 (1H, m, *H*-1″), 2.25–2.17 (1H, m, *H*-1″), 1.96 (1H, ddd, *J* 13.4, 5.0, 2.4, *H*-3′eq), 1.87 (1H, ddd, *J* 13.4, 11.4, 2.5, *H*-3′ax), 1.78–1.73 (1H, m, *H*-5′eq), 1.49 (1H, ddd, *J* 13.6, 11.4, 2.4, *H*-5′ax), 1.07 (21H, s, Si(C*H*(CH_3)$_2$)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 160.8 (s), 159.4 (s), 142.3 (s), 135.7 (d), 134.7 (d), 129.7 (d), 129.2 (s), 116.7 (t), 113.8 (d), 72.6 (t), 71.7 (d), 67.2 (d), 64.8 (d), 63.6 (t), 55.2 (q), 40.5 (t), 38.5 (t), 38.1 (t), 18.1 (q), 12.2 (d); *m*/*z* (FAB) Found 516.3144 ([M + H]$^+$ $C_{29}H_{45}O_5NSi$ requires 516.3145).

(2′*R*,4*R*,6′*R*)-3″-{6′-[2-(4-Methoxybenzyloxymethyl)-oxazol-4-yl]-4′-triisopropyl-silanyloxy-tetrahydropyran-2′-yl}-propane-1″,2″-diol (65). A solution of the terminal alkene (**64b**) (56 mg, 0.11 mmol) in *tert*-butanol (0.3 ml) was added dropwise over 2 min to a vigorously stirred solution of commercial AD-mix β (0.15 g, 1.4 g per mmol) in *tert*-butanol (0.2 ml) and water (0.5 ml) at 0 °C and the solution was stirred at 0 °C for 18 h. Thin layer chromatography showed that starting material was still present, therefore methanesulfonamide (10 mg, 0.11 mmol) was added in one portion and the solution was stirred for a further 48 h. Sodium sulfite (0.14 g, 0.87 mmol) was added in one portion and the mixture was stirred for 30 min before it was diluted with water (2 ml). The mixture was extracted with ethyl acetate (4 × 5 ml) and the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 65% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *diol* (30 mg, 50%) as a colourless oil (along with the olefin starting material (28 mg, 50%)); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3464, 2867, 1047; ^{1}H NMR (360 MHz, $CDCl_3$) major isomer δ 7.55 (1H, s, C*H*, ox), 7.29 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 4.99 (1H, dd, *J* 10.9, 2.7, *H*-6′), 4.55 (2H, s, ArCH_2), 4.54 (2H, s, PMBOCH_2), 4.42–4.31 (2H, m, *H*-4′, *H*-2″), 4.03–3.98 (1H, m, *H*-2′), 3.81 (3H, s, ArOCH_3), 3.63 (1H, dd, *J* 11.2, 3.8, *H*-1″), 3.48 (1H, dd, *J* 11.2, 5.5, *H*-1″), 1.98–1.85 (2H, m), 1.82–1.55 (4H, m), 1.14–1.07 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); ^{1}H NMR (360 MHz, $CDCl_3$) minor isomer δ 7.55 (1H, s, C*H*, ox), 7.29 (2H, d, *J* 8.6, C*H*, Ar), 6.88 (2H, d, *J* 8.6, C*H*, Ar), 4.93 (1H, dd, *J* 11.2, 2.3, *H*-6′), 4.55 (2H, s, ArCH_2), 4.54 (2H, s, PMBOCH_2), 4.42–4.31 (2H, m, *H*-4′, *H*-2″), 4.03–3.98 (1H, m, *H*-2′), 3.81 (3H, s, ArOCH_3), 3.62 (1H, dd, *J* 11.2, 3.8, *H*-1″), 3.52 (1H, dd, *J* 11.2, 6.7, *H*-1″), 1.98–1.85 (2H, m), 1.82–1.55 (4H, m), 1.14–1.07 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) major isomer δ 161.1 (s), 159.4 (s), 141.8 (s), 135.4 (d), 129.7 (d), 129.2 (s), 113.9 (d), 72.6 (t), 72.0 (d), 69.3 (d), 67.2 (d), 66.6 (t), 64.4 (d), 63.5 (t), 55.3 (q), 39.6 (t), 38.7 (t), 37.7 (t), 18.1 (q), 12.2 (d); ^{13}C NMR (90 MHz, $CDCl_3$) minor isomer δ 161.1 (s), 159.4 (s), 141.9 (s), 135.5 (d), 129.7 (d), 129.2 (s), 113.9 (d), 73.0 (d), 72.6 (t), 69.9 (d), 67.2 (d), 66.8 (t), 64.7 (d), 63.5 (t), 55.3 (q), 39.0 (t), 38.6 (t), 37.8 (t), 18.1 (q), 12.2 (d); *m*/*z* (ESI) Found 572.3048 ([M + Na]$^+$ $C_{29}H_{47}O_7NSiNa$ requires 572.3020).

(2′*R*,4′*R*,6′*R*)-2-(4-Methoxybenzyloxymethyl)-4-(6′-oxiranyl-methyl-4′-triiso-propylsilanyloxy-tetrahydropyran-2′-yl)-oxazole (66). Sodium hydride (60% dispersion in mineral oil, 7.1 mg, 0.18 mmol) was added in one portion to a stirred solution of the diol (**65**) (45 mg, 71 μmol) in THF (1 ml) at 0 °C under a nitrogen atmosphere. The solution was warmed to room temperature and stirred for 1 h and then it was cooled to 0 °C and *N*-tosylimidazole (15.9 mg, 71 μmol) was added in one portion. The stirred solution was warmed to room temperature over 3 h and then it was quenched with saturated aqueous ammonium chloride (3 ml). Ethyl acetate (10 ml) was added and the layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 10 ml). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the epoxide (30 mg, 76%) as a colourless oil; ν_{max} (soln: $CHCl_3$)/cm^{-1} 2944, 1101; ^{1}H NMR (360 MHz, $CDCl_3$) major isomer δ 7.56 (1H, d, *J* 0.7, C*H*, ox), 7.29 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.94 (1H, dd, *J* 15.2, 2.8, *H*-2′), 4.56 (2H, s, ArCH_2), 4.55 (2H, s, PMBOCH_2), 4.43–4.40 (1H, m, *H*-4′), 4.30–4.16 (1H, m, *H*-6′), 3.80 (3H, s, ArOCH_3), 3.13–3.07 (1H, m, *H*-2″), 2.77 (1H, app t, *J* ~4.9, *H*-3″), 2.48 (1H, app dd, *J* ~4.9, ~2.8, *H*-3″), 1.99–1.83 (3H, m), 1.81–1.65 (2H, m), 1.62–1.46 (1H, m), 1.14–1.05 (21H, s, Si(C*H*(CH_3)$_2$)$_3$); ^{1}H NMR (360 MHz, $CDCl_3$) minor isomer δ 7.57 (1H, d, *J* 0.8, C*H*, ox), 7.29 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.97 (1H, dd, *J* 14.9, 2.7, *H*-2′), 4.56 (2H, s, ArCH_2), 4.55 (2H, s, PMBOCH_2), 4.43–4.40 (1H, m, *H*-4′), 4.30–4.16 (1H, m, *H*-6′), 3.80 (3H, s, ArOCH_3), 3.13–3.07 (1H, m, *H*-2″), 2.76 (1H, app t, *J* ~4.6, *H*-3″), 2.50 (1H, app dd, *J* ~4.6, ~2.8, *H*-3″), 1.99–1.83 (3H, m), 1.81–1.65 (2H, m), 1.62–1.46 (1H, m), 1.14–1.05 (21H, s, Si(C*H*(CH_3)$_2$)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) major isomer δ 160.9 (s), 159.4 (s), 142.2 (s), 135.7 (d), 129.7 (d), 129.2 (s), 113.8 (d), 72.6 (t), 70.1 (d), 67.1 (d), 64.7 (d), 63.6 (t), 55.2 (q), 49.6 (d), 47.0 (t), 39.4 (t), 38.7 (t), 38.1 (t), 18.1 (q), 12.2 (d); ^{13}C NMR (90 MHz, $CDCl_3$) minor isomer δ 160.9 (s), 159.4 (s), 142.2 (s), 135.7 (d), 129.7 (d), 129.2 (s), 113.8 (d), 72.6 (t), 69.7 (d), 67.2 (d), 64.7 (d), 63.6 (t), 55.2 (q), 49.3 (d), 46.7 (t), 39.4 (t), 38.9 (t), 38.0 (t), 18.1 (q), 12.2 (d); *m*/*z* (ESI) Found 554.2968 ([M + Na]$^+$ $C_{29}H_{45}O_6NSiNa$ requires 554.2914).

4*S*)-2″,2″-Dimethyl-propionic acid 2-(2,2-dimethyl-[1,3]-dioxolan-4-yl)-ethyl ester (75). Trimethylacetyl chloride (0.54 g, 0.55 ml, 4.45 mmol) and 4-(dimethylamino)pyridine (42 mg, 0.34 mmol) were added, each in one portion, to a stirred solution of the enantiomer of (**10**) (0.50 g, 3.42 mmol) in dichloromethane (20 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 20 min and then triethylamine (0.87 g, 1.19 ml, 8.55 mmol) was added in one portion. The solution was warmed to room temperature over 12 h and then quenched with saturated aqueous ammonium chloride (10 ml). The separated aqueous layer was extracted with dichloromethane (2 × 20 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to leave an opaque residue. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *pivaloate* (0.75 g, 95%) as a colourless oil; $[\alpha]_D^{21}$ −4.8 (*c* 1.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2975, 1722, 1060; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.25–4.10 (3H, m, *H*-1′, *H*-4), 4.08 (1H, dd, *J* 7.9, 5.9, *H*-5), 3.58 (1H, dd, *J* 7.9, 7.2, *H*-5), 2.00–1.82 (2H, m, *H*-2′), 1.41 (3H, s, CCH_3), 1.35 (3H, s, CCH_3), 1.20 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 178.4 (s), 108.8 (s), 73.4 (d), 69.4 (t), 61.3 (t), 38.7 (s), 32.8 (t), 27.1 (q), 26.9 (q), 25.7 (q); *m*/*z* (EI) Found 215.1288 ([M − CH_3]$^+$ $C_{11}H_{19}O_4$ requires 215.1283).

(3*S*)-2′,2′-Dimethyl-propionic acid 3,4-dihydroxy-butyl ester (76). *para*-Toluenesulfonic acid (0.48 g, 2.54 mmol) was added in one portion to a stirred solution of the acetonide (**75**) (1.17 g, 5.01 mmol) in methanol (30 ml) at 0 °C under a nitrogen atmosphere. The mixture was warmed to room temperature and stirred at this temperature for 12 h before it was quenched with a saturated aqueous solution of sodium hydrogencarbonate

(30 ml). The mixture was concentrated *in vacuo* to leave the aqueous layer which was extracted with ethyl acetate (3 × 40 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 70% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *diol* (0.80 g, 83%) as a colourless oil; $[\alpha]_D^{22}$ −8.8 (*c* 2.3 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3617, 2969, 1721, 1054; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.36 (1H, ddd, *J* 11.2, 8.5, 5.3, *H*-1), 4.15 (1H, ddd, *J* 11.2, 5.5, 5.5, *H*-1), 3.80–3.73 (1H, m, *H*-3), 3.66 (1H, dd, *J* 11.2, 3.2, *H*-4), 3.49 (1H, dd, *J* 11.2, 7.3, *H*-4), 2.59 (2H, b s, 2 × O*H*), 1.82–1.73 (2H, m, *H*-2), 1.20 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 179.1 (s), 69.0 (d), 66.4 (t), 61.1 (t), 38.7 (s), 32.2 (t), 27.1 (q); *m*/*z* (ES) Found 191.1330 ($[MH]^+$ $C_9H_{19}O_4$ requires 191.1283).

(3*S*)-2′,2′-Dimethyl-propionic acid 2-oxiranyl-ethyl ester (77). Trimethyl orthoacetate (0.15 g, 0.16 ml, 1.26 mmol) was added in one portion to a stirred solution of the diol (**76**) (0.20 g, 1.05 mmol) and pyridinium *para*-toluenesulfonate (2.0 mg, 11 μmol) in dichloromethane (8 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred for 30 min and then concentrated *in vacuo* to leave the crude cyclic orthoester as a colourless oil, which was used without further purification.

Acetyl bromide (0.16 g, 0.10 ml, 1.26 mmol) was added dropwise over 2 min to a stirred solution of the cyclic orthoester in dichloromethane (8 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 45 min and then concentrated *in vacuo* to leave the crude acetoxy bromide as a colourless oil, which was used without further purification.

Potassium carbonate (0.20 g, 1.47 mmol) was added in one portion to a stirred solution of the acetoxy bromide in methanol (8 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 2 h 30 min, then quenched with saturated aqueous ammonium chloride (20 ml) and extracted with dichloromethane (3 × 20 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a residue which was purified by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, to give the *epoxide* (0.14 g, 75%) as a colourless oil; $[\alpha]_D^{21}$ −12.5 (*c* 0.9 in $CHCl_3$); (Found: C, 62.7; H, 9.4. $C_9H_{16}O_3$ requires C, 62.8; H, 9.4%); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2972, 1722, 1288, 900; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.20 (2H, app t, *J* ~6.3, *H*-1), 3.02–2.97 (1H, m, *H*-3), 2.78 (1H, dd, *J* 5.0, 4.3, *H*-4), 2.50 (1H, dd, *J* 5.0, 2.7, *H*-4), 1.93–1.76 (2H, m, *H*-2), 1.19 (9H, s, C(CH_3)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 178.3 (s), 61.2 (t), 49.5 (d), 46.8 (t), 38.6 (s), 31.9 (t), 27.1 (q).

(3*R*)-2′,2′-Dimethyl-propionic acid 3-hydroxy-6-trimethylsilanyl-hex-5-ynyl ester (78a). *n*-Butyllithium (2.5 M in hexanes, 2.10 ml, 5.23 mmol) was added dropwise over 5 min to a stirred solution of trimethylsilylacetylene (0.51 g, 0.74 ml, 5.23 mmol) in THF (25 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 10 min, then boron trifluoride diethyl etherate (0.46 ml, 3.74 mmol) was added dropwise over 2 min and the mixture was stirred at −78 °C for 10 min. A solution of the epoxide (**77**) (0.60 g, 3.48 mmol) in THF (10 ml) was added dropwise over 5 min and the mixture was stirred at −78 °C for 30 min, then quenched with a saturated aqueous solution of ammonium chloride (20 ml) and allowed to warm to room temperature. The mixture was concentrated *in vacuo* to leave the aqueous residue which was extracted with ethyl acetate (4 × 20 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a residue which was purified by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, to give the *alcohol* (0.93 g, 99%) as a colourless oil; $[\alpha]_D^{21}$ −4.0 (*c* 2.1 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3591, 2960, 2173, 1721; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.29 (1H, ddd, *J* 11.2, 8.6, 4.9, *H*-1), 4.17 (1H, ddd, *J* 11.2, 5.5, 5.5, *H*-1), 3.85–3.78 (1H, m, *H*-3), 2.51–2.39 (2H, m, *H*-4), 1.97–1.88 (1H, m, *H*-2), 1.83–1.73 (2H, m, *H*-2), 1.20 (9H, s, C(CH_3)$_3$), 0.15 (9H, s, Si(CH_3)$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 178.7 (s), 102.6 (s), 87.8 (s), 67.0 (d), 61.2 (t), 38.7 (s), 35.2 (t), 28.8 (t), 27.2 (q), 0.00 (q); *m*/*z* (FAB) Found 271.1730 ($[MH]^+$ $C_{14}H_{27}O_3Si$ requires 271.1729).

(3*R*)-2′,2′-Dimethyl-propionic acid 3-hydroxy-hex-5-ynyl ester (78b). Tetrabutylammonium fluoride trihydrate (1.25 g, 3.98 mmol) was added in one portion to a stirred solution of the alcohol (**78a**) (0.90 g, 3.31 mmol) in THF (40 ml) at 0 °C under a nitrogen atmosphere. The solution was warmed to room temperature, then stirred at this temperature for 1 h 15 min, and quenched with saturated aqueous ammonium chloride (20 ml). The mixture was concentrated *in vacuo* to leave an aqueous residue which was extracted with ethyl acetate (3 × 40 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a residue which was purified by flash chromatography, using 15% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, to give the monosubstituted *alkyne* (0.66 g, 93%) as a colourless oil; $[\alpha]_D^{21}$ −9.9 (*c* 1.3 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3592, 3307, 2971, 2120, 1721; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.27 (1H, ddd, *J* 11.2, 8.5, 5.3, *H*-1), 4.15 (1H, ddd, *J* 11.2, 5.3, 5.3, *H*-1), 3.86–3.79 (1H, m, *H*-3), 2.63 (1H, b s, O*H*), 2.43 (1H, ddd, *J* 16.7, 5.6, 2.6, *H*-4), 2.36 (1H, ddd, *J* 16.7, 6.1, 2.6, *H*-4), 2.05 (1H, t, *J* 2.6, *H*-6), 1.91 (1H, dddd, *J* 14.3, 8.5, 5.3, 3.7, *H*-2), 1.79 (1H, dddd, *J* 14.3, 9.0, 5.3, 5.3, *H*-2), 1.17 (9H, s, C(CH_3)$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 178.8 (s), 80.4 (d), 70.9 (s), 66.8 (d), 61.2 (t), 38.7 (s), 35.1 (t), 27.2 (t), 27.1 (q); *m*/*z* (EI) Found 180.1157 ($[M - H_2O]^+$ $C_{11}H_{16}O_2$ requires 180.1150).

(3*R*)-2′,2′-Dimethyl-propionic acid 3-(*tert*-butyldimethylsilanyloxy)-hex-5-ynyl ester (79). 2,6-Lutidine (0.47 g, 0.51 ml, 4.34 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.57 g, 0.50 ml, 2.17 mmol) were added, each in one portion, to a stirred solution of the alcohol (**78b**) (0.29 g, 1.45 mmol) in dichloromethane (14 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 1 h and then quenched with a saturated aqueous solution of ammonium chloride (10 ml). The separated aqueous layer was extracted with dichloromethane (2 × 20 ml), and the combined organic extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 5% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *TBS ether* (0.45 g, 100%) as a colourless oil; $[\alpha]_D^{22}$ −32.6 (*c* 1.4 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3308, 2931, 2120, 1721, 1101; ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.23 (1H, ddd, *J* 11.0, 5.3, 5.3, *H*-1), 4.08 (1H, ddd, *J* 11.0, 8.5, 5.3, *H*-1), 3.97–3.90 (1H, m, *H*-3), 2.39 (1H, ddd, *J* 16.6, 5.2, 2.7, *H*-4), 2.33 (1H, ddd, *J* 16.6, 7.0, 2.7, *H*-4), 1.99 (1H, t, *J* 2.7, *H*-6), 2.04–1.95 (1H, m, *H*-2), 1.80 (1H, dddd, *J* 13.4, 8.0, 5.3, 5.3, *H*-2), 1.20 (9H, s, C(CH_3)$_3$), 0.89 (9H, s, SiC(CH_3)$_3$), 0.09 (3H, s, SiCH_3), 0.07 (3H, s, SiCH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 178.4 (s), 80.9 (d), 70.4 (s), 67.7 (d), 60.9 (t), 38.7 (s), 35.4 (t), 27.7 (t), 27.2 (q), 25.7 (q), 18.0 (s), −4.5 (q), −4.9 (q); *m*/*z* (EI) Found 255.1415 ($[M - C_4H_9]^+$ $C_{13}H_{23}O_3Si$ requires 255.1417).

(3*S*)-2′,2′-Dimethyl-propionicacid3-(*tert*-butyldimethylsilanyloxy)-5-iodo-hex-5-enyl ester (80a). A solution of the alkyne (**79**) (0.45 g, 1.44 mmol) in pentane (6 ml) was added dropwise, *via* cannula, over 5 min to a stirred solution of 9-iodo-9-borabicyclo[3.3.1]nonane (1 M in hexane, 1.58 ml, 1.58 mmol) in pentane (10 ml) at −20 °C under a nitrogen atmosphere. The mixture was stirred at −20 °C for 1 h 30 min, then glacial acetic acid (0.9 ml) was added in one portion and the solution was stirred at −20 °C for 1 h. An aqueous solution of sodium hydroxide (3 M, 11 ml) and hydrogen peroxide (1.8 ml) were added, each in one portion, and the mixture was stirred at room temperature for 1 h 30 min. The mixture was diluted with ethyl

acetate (10 ml) and water (5 ml) and the separated aqueous layer was extracted with ethyl acetate (2 × 30 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a residue which was purified by flash chromatography, using petroleum ether (bp 40–60 °C) and increasing to 3% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, to give the *vinyl iodide* (0.60 g, 95%) as an orange oil; $[a]_D^{21}$ −12.6 (*c* 2.3 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2930, 1720, 1618, 901; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.09 (1H, d, *J* 1.1, *H*-6), 5.75 (1H, d, *J* 1.1, *H*-6), 4.22 (1H, ddd, *J* 11.2, 5.6, 5.6, *H*-1), 4.11–4.04 (2H, m, *H*-1, *H*-3), 2.61 (1H, app dd, *J* ~13.9, ~5.5, *H*-4), 2.47 (1H, ddd, *J* 13.9, 6.7, 0.7, *H*-4), 1.86 (1H, dddd, *J* 14.2, 9.9, 5.6, 4.2, *H*-2), 1.69–1.61 (1H, m, *H*-2), 1.22 (9H, s, C(C*H*$_3$)$_3$), 0.89 (9H, s, SiC(C*H*$_3$)$_3$), 0.11 (3H, s, SiC*H*$_3$), 0.10 (3H, s, SiC*H*$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 178.4 (s), 128.2 (t), 107.4 (s), 67.8 (d), 60.7 (t), 53.1 (t), 38.7 (s), 35.2 (t), 27.3 (q), 25.8 (q), 18.0 (s), −4.1 (q), −4.7 (q); *m*/*z* (ES) Found 463.1152 ([MNa]$^+$ $C_{17}H_{33}O_3SiINa$ requires 463.1141).

(3*S*)-3-(*tert*-Butyldimethylsilanyloxy)-5-iodo-hex-5-en-1-ol (80b). Diisobutylaluminium hydride (1.5 M in toluene, 1.82 ml, 2.72 mmol) was added dropwise over 5 min to a stirred solution of the ester (**80a**) (0.48 g, 1.09 mmol) in toluene (11 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 1 h and then quenched by the dropwise addition of methanol (3 ml). The mixture was added, *via* cannula, to a saturated aqueous solution of potassium sodium tartrate (25 ml) and the resulting mixture was then stirred vigorously for 3 h. The separated aqueous layer was extracted with ethyl acetate (3 × 50 ml), and the combined extracts were then dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (0.35 g, 91%) as a colourless oil; $[a]_D^{21}$ −2.0 (*c* 1.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3517, 2930, 1618, 1060; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.09 (1H, d, *J* 1.1, *H*-6), 5.75 (1H, d, *J* 1.1, *H*-6), 4.19–4.12 (1H, m, *H*-3), 3.81 (1H, ddd, *J* 11.0, 8.2, 4.5, *H*-1), 3.73 (1H, ddd, *J* 11.0, 5.6, 5.6, *H*-1), 2.64 (1H, app dd, *J* ~14.0, ~5.7, *H*-4), 2.53 (1H, app dd, *J* ~14.0, ~7.2, *H*-4), 2.46 (1H, b s, O*H*), 1.87 (1H, dddd, *J* 14.3, 8.2, 5.6, 4.5, *H*-2), 1.62 (1H, app dq, *J* ~14.3, ~5.6, *H*-2), 0.88 (9H, s, SiC(C*H*$_3$)$_3$), 0.13 (3H, s, SiC*H*$_3$), 0.12 (3H, s, SiC*H*$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 128.2 (t), 107.0 (s), 70.2 (d), 59.7 (t), 52.3 (t), 37.2 (t), 25.8 (q), 17.9 (s), −4.3 (q), −4.7 (q); *m*/*z* (EI) Found 298.9964 ([M − C_4H_9]$^+$ $C_8H_{16}O_2SiI$ requires 298.9964).

(3*S*)-5-Iodo-hex-5-ene-1,3-diol (81). Hydrogen fluoride–pyridine (0.4 ml) was added in one portion to a stirred solution of the alcohol (**80b**) (0.15 g, 0.41 mmol) in THF (4 ml) at room temperature under a nitrogen atmosphere. The solution was stirred at room temperature for 3 h, then a second portion of hydrogen fluoride–pyridine (0.4 ml) was added and the mixture was stirred for a further 2 h. The mixture was quenched by the dropwise addition of sodium hydrogencarbonate (5 ml) and then it was stirred for 30 min. Ethyl acetate (10 ml) was added and the separated aqueous layer was extracted with ethyl acetate (2 × 10 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a residue which was purified by flash chromatography, using 70% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent to give the *diol* (95 mg, 96%) as a colourless oil; $[a]_D^{21}$ +4.9 (*c*2.9 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 3626, 3511, 1617, 1068; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.17 (1H, d, *J* 1.2, *H*-6), 5.83 (1H, d, *J* 1.2, *H*-6), 4.16–4.09 (1H, m, *H*-3), 3.91–3.80 (2H, m, *H*-1), 3.13 (2H, b s, 2 × O*H*), 2.60–2.49 (2H, m, *H*-4), 1.78–1.67 (2H, m, *H*-2); ^{13}C NMR (90 MHz, $CDCl_3$) δ 128.6 (t), 107.0 (s), 69.8 (d), 61.2 (t), 52.8 (t), 37.1 (t).

(4*S*)-4-(2′-Iodo-allyl)-2,2-dimethyl-[1,3]-dioxane (67). 10-Camphorsulfonic acid (18 mg, 78 μmol) was added in one portion to a stirred solution of the diol (**81**) (95 mg, 0.39 mmol) in 2,2-dimethoxypropane (3 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 6.5 h, then diluted with ethyl acetate (10 ml) and quenched with a saturated aqueous solution of sodium hydrogencarbonate (3 ml). The separated aqueous layer was extracted with ethyl acetate (2 × 10 ml) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 10% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *vinyl iodide* (93 mg, 84%) as a colourless oil; $[a]_D^{21}$ +9.1 (*c*3.2 in $CHCl_3$); ν_{max} (soln: $CHCl_3$)/cm^{-1} 2951, 1620, 1098; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.12 (1H, q, *J* 1.3, *H*-3′), 5.79 (1H, d, *J* 1.3, *H*-3′), 4.18–4.10 (1H, m, *H*-4), 4.00 (1H, ddd, *J* 11.9, 11.9, 3.1, *H*-6), 3.84 (1H, ddd, *J* 11.9, 5.4, 1.7, *H*-6), 2.60 (1H, dd, *J* 14.3, 6.9, *H*-1′), 2.42 (1H, dd, *J* 14.3, 5.8, *H*-1′), 1.57 (1H, dddd, *J* 11.9, 11.9, 11.9, 5.4, *H*-5), 1.50 (3H, s, C*H*$_3$), 1.47–1.44 (1H, m, *H*-5), 1.38 (3H, s, C*H*$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 128.0 (t), 106.0 (s), 98.5 (s), 67.6 (d), 59.8 (t), 51.3 (t), 30.1 (t), 29.8 (q), 19.2 (q); *m*/*z* (EI) Found 266.9880 ([M − CH_3]$^+$ $C_8H_{12}O_2I$ requires 266.9882).

(2′*R*,4′*R*,6′*R*,4″*R*)-4-(2″,2″-Dimethyl-[1″,3″]-dioxan-4″-ylmethyl)-1-{6′-[2-(4-methoxybenzyloxymethyl)-oxazol-4-yl]-4′-triisopropylsilanyloxy-tetrahydro-pyran-2′-yl}-pent-4-en-2-ol (68). *tert*-Butyllithium (1.5 M in pentane, 0.24 ml, 0.40 mmol) was added dropwise over 2 min to a stirred solution of the vinyl iodide (**67**) (56 mg, 200 μmol) in THF (0.8 ml) at −78 °C under an argon atmosphere. The solution was stirred at −78 °C for 30 min and then a freshly prepared solution of lithium 2-thienylcyanocuprate (0.3 M in THF, 0.66 ml, 200 μmol) was added dropwise over 2 min. The mixture was stirred at −40 °C for 1 h and then cooled to −78 °C. A solution of the epoxide (**13**) (50 mg, 0.30 mmol) in THF (1.2 ml) was added dropwise, *via* cannula, over 2 min and the resulting solution was warmed to 0 °C over 1 h. The solution was stirred at 0 °C for 23 h and then it was quenched with a mixture of saturated aqueous ammonium chloride and concentrated ammonium hydroxide (10 : 1 v/v, 4 ml). The mixture was poured onto water (4 ml) and extracted with ethyl acetate (3 × 20 ml). The combined organic layer was washed with brine (20 ml), dried (Na_2SO_4) and concentrated *in vacuo* to leave a brown oil. Purification by flash chromatography, using 20% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the *alcohol* (16 mg, 20%) and the starting *epoxide* (26 mg, 41%), both as colourless oils; ^{1}H NMR (360 MHz, $CDCl_3$) major isomer δ 7.55 (1H, s, C*H*, ox), 7.29 (2H, d, *J* 8.6, C*H*, Ar), 6.89 (2H, d, *J* 8.6, C*H*, Ar), 4.97 (1H, app dd, *J* ~11.5, ~1.8, *H*-6′), 4.91 (1H, s, *H*-5), 4.90 (1H, s, *H*-5), 4.54 (2H, s, CH_2Ar), 4.53 (2H, s, CH_2Ar), 4.39–4.37 (1H, m, *H*-4′), 4.30–4.25 (1H, m, *H*-2), 4.10–4.02 (2H, m, *H*-2′, *H*-4″), 3.96 (1H, ddd, *J* 12.1, 12.1, 2.9, *H*-6″), 3.85–3.83 (1H, m, *H*-6″), 3.81 (3H, s, OCH_3), 2.32–2.13 (4H, m, *H*-3, *H*-1″), 1.95–1.93 (1H, m), 1.91–1.85 (1H, m), 1.72–1.52 (6H, m), 1.46 (3H, s, C*H*$_3$), 1.38 (3H, s, C*H*$_3$), 1.12–1.04 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); *m*/*z* (ESI) Found 710.4082 ([M + Na]$^+$ $C_{38}H_{61}O_8NSiNa$ requires 710.4064).

(2′*S*,4′*R*,6′*R*,5*R*)-Methanesulfonic acid 5,7-dihydroxy-1-{6′2-(4-methoxy-benzyloxymethyl)-oxazol-4-yl]-4′triisopropylsilanyloxy-tetrahydropyran-2′yl-methyl}-3-methyleneheptyl ester (69). Triethylamine (59 mg, 81 μl, 580 μmol) and methanesulfonyl chloride (33 mg, 22 μl, 290 μmol) were added, each in one portion, to a stirred solution of the alcohol (**68**) (40 mg, 58 μmol) in dichloromethane (2 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at 0 °C for 45 min and then it was quenched with a saturated aqueous solution of sodium hydrogencarbonate (30 ml). The mixture was extracted with dichloromethane (3 × 50 ml) and the combined organic layer was dried (Na_2SO_4). Concentration *in vacuo* left the *mesylate* as a light yellow oil, which was used without further purification.

10-Camphorsulfonic acid (6 mg, 24 μmol) was added in one portion to a stirred solution of the mesylate (45 mg, 59 μmol) in methanol (2 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 1 h 30 min and then it was quenched with a saturated aqueous solution of sodium hydrogencarbonate (30 ml). The mixture was extracted with ethyl acetate (3 × 50 ml) and then the combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 60% ethyl acetate–petroleum ether (bp 40–60 °C) and increasing to ethyl acetate as eluent, gave the *diol* (25 mg, 60% over 2 steps) as a colourless oil; ^{1}H NMR (360 MHz, $CDCl_3$) major isomer δ 7.57 (1H, s, C*H*, ox), 7.30 (2H, d, *J* 8.5, C*H*, Ar), 6.90 (2H, d, *J* 8.5, C*H*, Ar), 5.13–5.04 (1H, m, *H*-1), 5.02 (1H, s, C=C*H*), 4.98 (1H, s, C=C*H*), 4.84 (1H, app dd, *J* ~10.9, ~2.4, *H*-6′), 4.57 (2H, s, CH_2Ar), 4.56 (2H, s, CH_2Ar), 4.43–4.40 (1H, m, *H*-4′4.21–4.00 (2H, m, *H*-5, *H*-2′3.85–3.73 (2H, m, *H*-7), 3.82 (3H, s, OCH_3), 2.94 (3H, s, SO_2CH_3), 2.76 (1H, app dd, *J* ~14.4, ~3.9, *H*-2), 2.44 (1H, dd, *J* 14.4, 8.4, *H*-2), 2.43–2.38 (1H, m), 2.32–2.17 (2H, m), 2.13–2.05 (1H, m), 1.95–1.80 (4H, m), 1.77–1.51 (2H, m), 1.14–1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); *m*/*z* (ESI) Found 748.3510 ([M + Na]$^+$ $C_{36}H_{59}O_{10}NSSiNa$ requires 748.3527).

(2′*R*,4′*R*,6′*R*,2*R*,6*R*)-2″-{6′2-(4-Methoxybenzyloxymethyl)-oxazol-4-yl]-4′tri-isopropylsilanyloxy-tetrahydropyran-2′yl-methyl}-4-methylene-tetrahydro-pyran-2-yl)-ethanol (70a). Triethylamine (150 mg, 210 μl, 1.5 mmol) was added in one portion to a stirred solution of the diol (**69**) (25 mg, 34 μmol) in acetonitrile (3 ml) at room temperature under a nitrogen atmosphere. The solution was heated at reflux for 44 h and then it was cooled to room temperature and diluted with ethyl acetate (30 ml), brine (15 ml) and water (15 ml). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 50 ml). The combined organic layer was dried (Na_2SO_4) and concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography, using 25% ethyl acetate–petroleum ether (bp 40–60 °C) as eluent, gave the required *trans-pyran* (8 mg, 37%) and the *cis-pyran* (9 mg, 41%), both as colourless oils; *trans*-pyran: $[\alpha]_D^{24}$ −78.8 (*c* 2.8 in $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.57 (1H, d, *J* 0.8, C*H*, ox), 7.27 (2H, d, *J* 8.7, C*H*, Ar), 6.89 (2H, d, *J* 8.7, C*H*, Ar), 4.91 (1H, dd, *J* 11.2, 3.2, *H*-6′), 4.77 (1H, s, C=C*H*), 4.72 (1H, s, C=C*H*), 4.56 (2H, s, CH_2Ar), 4.55 (2H, s, CH_2Ar), 4.41–4.39 (1H, m, *H*-4′), 4.18–4.04 (2H, m, *H*-2, *H*-2′), 4.01–3.95 (1H, m, *H*-6), 3.81 (3H, s, OCH_3), 3.74–3.71 (2H, m, *H*-1″), 2.76 (1H, b s, O*H*), 2.41 (1H, dd, *J* 13.2, 4.8), 2.28 (1H, dd, *J* 13.2, 3.7), 2.08 (1H, b d, *J* ~14.0), 2.06 (1H, b d, *J* ~13.2), 1.98–1.80 (4H, m), 1.74–1.70 (2H, m), 1.66–1.60 (2H, m), 1.17–1.04 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); ^{13}C NMR (90 MHz, $CDCl_3$) δ 161.0 (s), 159.8 (s), 142.2 (s), 141.8 (s), 135.9 (d), 129.8 (d), 129.3 (s), 113.9 (d), 110.5 (t), 72.7 (t), 71.0 (d), 70.0 (d), 69.8 (d), 67.2 (d), 65.0 (d), 63.7 (t), 60.7 (t), 55.4 (q), 40.2 (t), 39.5 (t), 39.0 (t), 38.6 (t), 38.2 (t), 37.1 (t), 18.2 (d), 12.3 (q); *cis*-pyran: ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.57 (1H, d, *J* 0.7, C*H*, ox), 7.27 (2H, d, *J* 8.7, C*H*, Ar), 6.88 (2H, d, *J* 8.7, C*H*, Ar), 4.90 (1H, dd, *J* 11.1, 2.7, *H*-6′), 4.71–4.69 (2H, m, C=CH_2), 4.56 (2H, s, CH_2Ar), 4.54 (2H, s, CH_2Ar), 4.43–4.41 (1H, m, *H*-4′), 4.30–4.24 (1H, m, *H*-2′), 3.94–3.88 (1H, m), 3.81 (3H, s, OCH_3), 3.76–3.70 (1H, m), 3.60–3.54 (2H, m, *H*-1″), 2.36 (2H, app t, *J* ~7.3), 2.23–2.17 (2H, m), 2.08–1.85 (4H, m), 1.80–1.63 (4H, m), 1.14–1.06 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); *m*/*z* (ESI) Found 652.3633 ([M + Na]$^+$ $C_{35}H_{55}O_7NSiNa$ requires 652.3646).

The same oxazole *cis*, *trans* bis-pyran (**70a**) was obtained by saponification of the corresponding pivaloate (**70b**) prepared by the procedure described by Williams *et al.*[43]

Oxazole bis-oxane PMB ether (71a). *tert*-Butyldimethylsilyl chloride (30 μl, 0.126 mmol) was added dropwise over 10 min to a solution of the alcohol (**70a**) (66.0 mg, 0.105 mmol) and triethylamine (23 μl, 0.21 mmol) and dichloromethane (1.2 ml) at 0 °C, and the mixture was stirred for 30 min at 0 °C and then quenched with saturated aqueous ammonium chloride and diluted with diethyl ether. The separated ether extract was washed with brine, then dried (Na_2SO_4) and evaporated to dryness *in vacuo*. The residue was purified by chromatography, eluting with 30% ethyl acetate in petrol ether to give the *silyl ether* (70.0 mg, 90%) as a yellow oil; $[\alpha]_D^{25}$ −11.1 (*c* 2.8 in $CHCl_3$); ^{1}H NMR (360 MHz) δ 7.56 (1H, s, oxC*H*); 7.29 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 4.90 (1H, b d, *J* 9.6), 4.75 (1H, b s, =CH_2), 4.72 (1H, b s, =CH_2), 4.55 (2H, s, PMBOCH_2), 4.54 (2H, s, PMBOCH_2), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.10–4.00 (2H, m), 3.91 (1H, m), 3.81 (3H, s, OCH_3), 3.66 (2H, t, *J* 6.5, CH_2OTBS), 2.36 (2H, m), 2.06–1.50 (10H, m), 1.15–1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.89 (9H, s, SiC(*CH*$_3$)$_3$), 0.05 (6H, s, Si(*CH*$_3$)$_2$); ^{13}C NMR (90 MHz) δ 160.7(s), 159.4(s), 142.5(s), 142.3(s), 135.6(s), 2 × 129.7(d), 129.3(s), 2 × 113.8(d), 110.1(t), 72.6(t), 69.1(d), 69.0(d), 68.9(d), 67.3(d), 64.9(d), 63.6(t), 59.8(t), 55.3(q), 39.9(t), 39.3(t), 39.3(t), 39.1(t), 38.4(t), 37.0(t), 3 × 26.0(q), 3 × 18.2(q), 18.1(s), 6 × 12.3(d), 2 × −5.2(q); *m*/*z* (FAB) Found: 744.4734 ([M + Na]$^+$ $C_{41}H_{70}NO_7Si_2$ requires 744.4691).

Oxazole bis-oxane methanol (71b). Dichlorodicyanoquinone (36.0 mg, 0.16 mmol) was added to a stirred solution of the PMB-ether (**71a**) (56.0 mg, 0.078 mmol) in methylene chloride (0.8 ml) and water (80 μl) at room temperature, and the mixture was stirred vigorously for 2 h, and then saturated aqueous sodium bicarbonate (0.2 ml) was added. The mixture was added to a short column of silica, and eluted with 30% ethyl acetate in petrol ether. The solvents were removed *in vacuo* to leave the *alcohol* (43.0 mg, 90%) as a pale orange oil; $[\alpha]_D^{22}$ −10.0 (*c* 2.2 in $CHCl_3$); ^{1}H NMR (360 MHz) δ 7.54 (1H, d, *J* 0.7, oxC*H*), 4.89 (1H, dd, *J* 8.6, 2.4), 4.75 (1H, b s, =CH_2), 4.72 (1H, b s, =CH_2), 4.70 (2H, s, CH_2OH), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.10–3.95 (2H, m), 3.90 (1H, m), 3.66 (2H, t, *J* 6.5, CH_2OTBS), 2.36 (2H, m), 2.08–1.50 (10H, m), 1.15–1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$) 0.89 (9H, s, SiC(*CH*$_3$)$_3$), 0.05 (6H, s, Si(*CH*$_3$)$_2$); ^{13}C NMR (90 MHz) δ 163.0(s), 142.3(s), 135.4(d), 135.4(s), 110.2(t), 69.3(d), 69.1(d), 69.0(d), 67.2(d), 64.9(d), 59.9(t), 57.6(t), 39.9(t), 39.3(t), 39.3(t), 39.2(t), 38.4(t), 37.0(t), 3 × 26.0(q), 6 × 18.3(q), 18.1 (s), 3 × 12.0(d), 2 × −5.3(q); *m*/*z* (FAB) Found: 624.4114 ([M + H]$^+$ $C_{33}H_{62}NO_6Si_2$ requires 624.4116).

Oxazole bis-oxane mesylate (71c). *N*,*N*-Diisopropylethylamine (30 μl, 0.176 mmol) and methanesulfonyl chloride (8 μl, 0.105 mmol) were added to a stirred solution of the alcohol (**71b**) (55.0 mg, 0.088 mmol) in methylene chloride (1 ml) at −5 °C. The mixture was stirred at room temperature for 30 min, then loaded onto a short column of silica, which was eluted with 20% ethyl acetate in petrol ether. The solvents were removed *in vacuo* to leave the *mesylate* (47 mg, 76%) as a colourless oil; $[\alpha]_D^{23}$ −11.5 (*c* 1.6 in $CHCl_3$); ^{1}H NMR (360 MHz) δ 7.62 (1H, d, *J* 0.8, oxC*H*), 5.27 (2H, s, $CH_3SO_2OCH_2$), 4.90 (1H, b d, *J* 10.1), 4.75 (1H, b s, =CH_2), 4.73 (1H, b s, =CH_2), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.15–3.95 (2H, m), 3.90(1H, m), 3.66 (2H, t, *J* 6.4, CH_2OTBS), 3.11 (3H, s, CH_3SO_2), 2.36 (2H, m), 2.06–1.87 (4H, m), 1.83–1.74 (2H, m), 1.68–1.48 (4H, m), 1.15–1.00 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.89 (9H, s, SiC(*CH*$_3$)$_3$), 0.05 (6H, s, Si(*CH*$_3$)$_2$); ^{13}C NMR (90 MHz) δ 156.5(s), 143.7(s), 142.3(s), 136.8(d), 110.2(t), 69.3(d), 69.1(d), 68.9(d), 67.3(d), 64.8(d), 62.1(t), 59.9(t), 39.8(t), 39.4(t), 39.3(t), 39.2(t), 38.6(t), 38.5(q), 37.0(t), 3 × 26.0(q), 6 × 18.2(q), 17.8(s), 3 × 12.3(d), 2 × −5.3(q); *m*/*z* (FAB) Nominal mass Found: 725 ([M + H + Na]$^+$ $C_{34}H_{64}NO_8Si_2S$ requires 725).

Oxazole tris-oxane alcohol 87a. Tributylphosphine (10 μl, 36 μmol) was added to a stirred solution of the mesylate (**85**) (6 mg, 9 μmol) in dimethylformamide (2 ml) and the mixture

was stirred at room temperature for 24 h. A solution of the aldehyde (**52**) (4.1 mg, 9 μmol) in dimethylformamide (1 ml) was added *via* canula followed by DBU (3.3 μl, 21 μmol), and the mixture was stirred at room temperature for 30 min. The solvents were removed *in vacuo* [0.2mm Hg, 30 °C] and the residue was purified by chromatography on silica using ethyl acetate in petrol (3 : 7) as eluant to give the *E-olefin* (**86a**) (9 mg, 99%) as a colourless oil; ^{1}HNMR (500 MHz) δ 7.45 (1H, s, oxC*H*), 7.28 (2H, d, *J* 8.7, Ar*H*), 6.88 (2H, d, *J* 8.7, Ar*H*), 6.70 (1H, ddd, *J* 16.0, 8.7, 6.0, H-20), 6.35 (1H, d, *J* 16.0, H-19), 4.89 (1H, b d, *J* 8.9, H-15), 4.77 (1H, s, =CH_2), 4.73 (1H, s, =CH_2), 4.56 (1H, d, *J* 11.0, OCH_2Ar), 4.40 (1H, b app s, H-13), 4.30–4.28 (1H, m, H-5), 4.25 (1H, d, *J* 11.0, OCH_2Ar), 4.18–4.05 (5H, m, CH_2OPiv, H-11, H-22), 3.96 (1H, dq, *J* 6.4, 2.0, C*H*OTBS), 3.92–3.85 (1H, m, H-9), 3.81 (3H, s, OMe), 3.39–3.36 (1H, m, H-26), 3.11 (1H, dd, *J* 10.4, 5.7, H-24), 2.94–3.0 (1H, m), 2.61–2.58 (1H, m), 2.28–2.45 (2H, m), 1.5–2.1 (6H, m), 1.05–1.15 (21H, m, OTIPS), 0.85 (9H, s, $SiCMe_3$).

Lithium hydroxide (13 mg, 540 μmol) was added to a stirred solution of the ester (**86a**) (18 mg, 18 μmol) in methanol (0.5 ml), tetrahydrofuran (0.5 ml) and water (0.05 ml) and the mixture was stirred at room temperature for 16 h. Water (5 ml) and ethyl acetate (5 ml) were added and the separated aqueous layer was then extracted with ethyl acetate (5 × 5 ml). The combined organic extracts were dried and evaporated to leave the *alcohol* (**86b**) (16 mg, 96%) as a colourless oil; ^{1}HNMR (500 MHz) δ 7.46 (1H, s, oxC*H*), 7.29 (2H, d, *J* 8.0, Ar*H*), 6.89 (2H, d, *J* 8.0, Ar*H*), 6.71 (1H, ddd, *J* 16.0, 8.6, 5.9, H-20), 6.35 (1H, d, *J* 16.0, H-19), 4.89 (1H, dd, *J* 7.8, 6.1, H-15), 4.76 (1H, s, =CH_2), 4.72 (1H, s, =CH_2), 4.56 (1H, d, *J* 10.9, OCH_2Ar), 4.40 (1H, b app s, H-13), 4.25 (1H, d, *J* 10.9, OCH_2Ar), 4.18–3.92 (5H, m), 3.82 (3H, s, OMe), 3.75 (2H, t, *J* 5.6, CH_2OH), 3.38 (1H, dd, *J* 7.6, 5.9, H-24), 3.13 (1H, dd, *J* 9.5, 4.8, H-26), 2.98 (1H, dd, *J* 10.4, 2.2, H-21), 2.34–2.56 (1H, m, H-21), 2.41–2.27 (2H, m), 2.07–1.54 (12H, m), 1.15 (3H, d, *J* 6.5, CH_3), 1.10 (21H, s, OTIPS), 0.93 (3H, d, *J* 6.5, CH_3), 0.91 (3H, d, *J* 5.4, CH_3), 0.87 (9H, s, ^{t}*Bu*(Me)$_2$Si), 0.04 (6H, s, ^{t}Bu(*Me*)$_2$Si).

Dichlorodicyanoquinone (10 mg, 43 μmol) was added to a solution of the alcohol (**86b**) (16 mg, 17.2 μmol) in dichloromethane (0.5 ml) and water (0.05 ml) and the solution was stirred at room temperature for 15 h, and then saturated aqueous sodium bicarbonate (0.1 ml) was added. The mixture was added to a short pad of celite and eluted with dichloromethane (50 ml). The filtrate was evaporated to dryness *in vacuo* [0.2 mmHg, 48 h], to leave the corresponding C3, C24 *diol* (12 mg, 86%) as a orange oil; ^{1}HNMR (500 MHz) δ 7.44 (1H, s, oxC*H*), 6.67 (1H, ddd, *J* 16.0, 7.5, 6.1, H-20), 6.34 (1H, d, *J* 16.0, H-19), 4.88 (1H, dd, *J* 8.5, 5.1, H-15), 4.77 (1H, s, =CH_2), 4.72 (1H, s, =CH_2), 4.40 (1H, b app s, H-13), 4.37–4.23 (2H, m, H-11 and H-5), 4.16–4.10 (1H, m, H-9), 4.10–3.93 (1H, m, H-26), 3.75 (2H, dd, *J* 5.9, 5.7, CH_2OH), 3.46–3.38 (1H, m, H-24), 2.98 (1H, dd, *J* 10.2, 2.1, H-21), 2.62–2.52 (1H, m, H-21), 2.46–2.18 (2H, m), 2.15–1.48 (10H, m), 1.17 (3H, d, *J* 6.5, CH_3), 1.08 (21H, s, OTIPS), 0.98 (3H, d, *J* 6.1, CH_3), 0.88 (9H, s, ^{t}*Bu*(Me)$_2$Si), 0.06 (6H, s, ^{t}Bu(*Me*)$_2$Si).

Chloro-*tert*-butyldimethylsilane (30 mg, 20 μmol) and imidazole (2.7 mg, 40 μmol) were added to a solution of the aforementioned diol (12 mg, 14.9 μmol) in dimethylformamide (0.1 ml), and the mixture was then stirred at room temperature for 30 min. Water (1 ml), followed by ethyl acetate (5 ml), were added and the separated aqueous phase was then extracted with ethyl acetate (5 × 5 ml). The combined organic extracts were dried and evaporated, and the residue was then purified by chromatography using ethyl acetate in petrol (3 : 7) as eluent to give the *alcohol* (10 mg, 73%) as a colourless oil; ^{1}HNMR (500 MHz) δ 7.43 (1H, s, oxC*H*), 6.68 (1H, ddd, *J* 16.2, 8.4, 6.1, H-20), 6.34 (1H, d, *J* 16.2, H-19), 4.88 (1H, d, *J* 9.4, H-15), 4.75 (1H, s, =CH_2), 4.72 (1H, s, =CH_2), 4.42–4.39 (1H, b app s, H-13), 4.08–3.98 (2H, m, H-11and H-5), 3.96–3.85 (1H, m, H-5), 3.66 (2H, dd, *J* 6.5, 6.4, CH_2OTBS), 3.45–3.41 (2H,m), 2.99 (1H, dd, *J* 16.1, 4.1, H-21), 2.61–2.54 (1H, m, H-21), 2.41–2.28 (3H, m), 2.06–1.74 (8H, m), 1.68–1.48 (4H, m), 1.27 (3H, d, *J* 7.1, CH_3), 1.19 (21H, s, OTIPS), 1.01 (3H, d, *J* 5.5, CH_3), 0.89 (18H, s, 2 × ^{t}*Bu*(Me)$_2$Si), 0.06 (12H, s, 2 × ^{t}Bu(*Me*)$_2$Si); *m*/*z* (ESI) Found 920.6312; $C_{50}H_{94}NO_8Si_3$ requires 920.6287.

Oxazole tris-oxane phosphonate 87b. Bis-(2,2,2-trifluoroethyl) [methoxy carbonylmethyl] phosphonate (3.8 μl, 20 μmol) and *N*,*N*-dimethylaminopyridine (2.4 mg, 20 μmol) were added to a solution of the alcohol (**87a**) (10 mg, 11 μmol) in toluene (1 ml), and the mixture was then heated to 120 °C for 30 h. The cooled solution was evaporated and the residue was purified by chromatography on a short column of silica, eluting with ethyl acetate to give the *phosphonate ester* (8 mg, 60%) as a colourless oil; ^{1}HNMR (500 MHz) δ 7.43 (1H, s, oxC*H*), 6.64 (1H, ddd, *J* 16.1, 8.4, 6.3, H-20), 6.33 (1H, d, *J* 16.1, H-19), 4.88 (1H, d, *J* 9.0, H-15), 4.75 (1H, s, =CH_2), 4.72 (1H, s, =CH_2), 4.52–4.44 (4H, m, 2 × CF_3, CH_2O), 4.39 (1H, b app s, H-13), 4.08–3.97 (2H, m, H-11 and H-5), 3.91–3.88 (1H, m, H-9), 3.66 (2H, dd, *J* 6.6, 6.4, CH_2OTBS), 3.49 (1H, dd, *J* 6.1, 6.0, H-22), 3.23 (1H, s, CH_2P), 3.17 (1H, s, CH_2P), 3.03 (1H, dd, *J* 10.3, 1.9, H-26), 2.59–2.51 (1H, m), 2.41–2.18 (3H, m), 2.06–1.74 (10H, m), 1.18 (3H, d, *J* 6.5, CH_3), 1.09–0.97 (24H, m, OTIPS and CH_3), 0.92–0.87 (21H, m, 2 × ^{t}*Bu*(Me)$_2$ Si and CH_3), 0.06 (12H, 2 × ^{t}Bu(*Me*)$_2$Si); *m*/*z* (ESI) Found 1206.616 (M + H)$^+$; $C_{56}H_{99}NO_{12}Si_3F_6P$ requires 1206.612.

Macrolide 89. 10-Camphorsulfonic acid (5 mg, 22 μmol) was added to a solution of the phosphonate (**87b**) (8 mg, 6.6. μmol) in methanol (0.1 ml) and dichloromethane (0.5 ml). The solution was stirred at room temperature for 1 h and then added to a short column of silica, which was eluted with ethyl acetate in petrol (3 : 7) to give the corresponding C-3, C-27 *diol* (6 mg, 93%) as a colourless oil; ^{1}HNMR (500 MHz) δ 7.45 (1H, s, oxC*H*), 6.67 (1H, ddd, *J* 16.0, 6.8, 5.5, H-20), 6.33 (1H, d, *J* 16.0, H-19), 4.87 (1H, dd, *J* 9.3, 7.5, H-15), 4.75 (1H, s, =CH_2), 4.72 (1H, s, =CH_2), 4.51–4.42 (4H, m, 2 × CF_3 CH_2O), 4.40 (1H, b app s, H-13), 4.16–3.97 (3H, m, H-11, H-5 and H-24), 3.89–3.86 (1H, m, H-9), 3.76 (1H, dd, *J* 5.9, 5.6, CH_2OH), 3.61–3.52 (1H, m, H-22), 3.26 (1H, dd, *J* 10.3, 2.4, H-26), 3.23 (1H, s, CH_2P), 3.17 (1H, s, CH_2P), 2.62–2.52 (1H, m), 2.38–2.33 (3H, m), 2.18–1.51 (10H, m), 1.19 (3H, d, *J* 6.4, CH_3), 1.08 (21H, s, OTIPS), 0.92 (3H, d, *J* 6.9, CH_3), 0.83 (3H, d, *J* 6.5, H50); *m*/*z* (ESI) Found 978.4387. (M + H)$^+$; $C_{44}H_{71}NO_{12}SiPF_6$ requires 978.4390.

A solution of Dess–Martin periodinane (15% wt/vol) in dichloromethane (1 ml) was added to a solution of the C-3, C-27 diol (6 mg, 6 μmol) in dichloromethane (0.1 ml) containing *tert*-butanol (15 ml) and sodium bicarbonate (20 mg). The mixture was stirred at room temperature for 1 h and then added to a short column of silica, which was eluted with ethyl acetate in petrol (3:7) to give the *aldehyde* (**88**) (5.5 mg, 92%) as a oil; ^{1}HNMR (500 MHz) δ 9.75 (1H, t, *J* 1.2, C*H*O), 7.47 (1H, s, oxC*H*), 6.59 (1H, ddd, *J* 16.0, 8.1, 7.8, H-20), 6.35 (1H, d, *J* 16.0, H-19), 4.88 (1H, dd, 10.5, 3.6, H-15), 4.80 (1H, s, =CH_2), 4.77 (1H, s, =CH_2), 4.76 (1H, m), 4.51–4.42 (4H, m, 2 × $CF_3C$$H_2$O), 4.40 (1H, b app s, H-13), 4.37–4.28 (1H, m, H-24), 4.08–4.05 (2H, m, H-11 and H-5), 3.64–3.59 (1H, m, H-22), 3.48 (1H, d, *J* 10.7, H-26), 3.23 (1H, s, CH_2P), 3.17 (1H, s, CH_2P), 2.67–2.46 (3H, m), 2.44–2.28 (3H, m), 2.23 (3H, s, CH_3), 2.18–2.13 (1H, m), 2.08–1.84 (7H, m), 1.08 (21H, s, OTIPS), 1.01 (3H, d, *J* 6.8, CH_3), 0.86 (3H, d, *J* 6.4, CH_3).

Anhydrous potassium carbonate (3.25 mg, 23 μmol) was added to a stirred solution of 18-crown-6 (12.5 mg, 47 μmol) in toluene (2 ml) at room temperature. The mixture was stirred for 3 h, then cooled to −40 °C and a solution of the aldehyde (**88**) (5.5 mg, 5.6 μmol) in toluene (1 ml) was then added *via* cannula. The mixture was allowed to warm to room temperature overnight and was then purified by chromatography on a short column of silica, eluting with ethyl acetate in petrol (3 : 7) to

give the *macrolide* (2 mg, 77% based on recovered aldehyde), as an oily 3 : 2 mixture of *Z*/*E*-isomers; ^{1}HMNR (500 MHz) δ 7.46 (1H, s, oxC*H*), 6.74 (1H, ddd, *J* 16.0, 9.4, 3.6, H-20), 6.35 (1H, d, *J* 16.0, H-19), 6.32–6.29 (1H, m, H-2), 6.01–5.92 (1H, m, H-3), 5.03 (1H, s, =CH_2), 4.83 (1H, d, *J* 6.7, H-15), 4.66 (1H, s, =CH_2), 4.51 (1H, dd, *J* 11.4, 4.1, H-24), 4.42 (1H, b app s, H-13), 4.19–4.01 (2H, m, H-11 and H-5), 3.79–3.65 (1H, m, H-9), 3.60–3.40 (3H, m, H-26, H-22 and H-4), 2.74 (1H, b d, *J* 11.8, H-8), 2.63–2.35 (5H, m), 2.27 (3H, s, Me), 2.10–1.40 (9H, m), 1.10 (21H, s, OTIPS), 1.00 (3H, b d, *J* 6.9, CH_3), 0.88 (3H, b d, *J* 6.3, CH_3); *m*/*z* (ESI) Found 712.425. $C_{40}H_{61}O_5NSi$ requires 712.425.

2-(*R*)-2-Methoxypent-4-ynylsulfanyl)benzothiazole (94). Tetrabutylammonium fluoride (1.17 g, 3.7 mmol) was added in one portion to a stirred solution of the silyl alkyne (**17**) (1.4 g, 3.1 mmol) in THF (20 ml) at 0 °C. The mixture was stirred at 0 °C for 2 h, then quenched with saturated aqueous ammonium chloride (5 ml), and extracted with ethyl acetate (3 × 20 ml). The combined organic extracts were washed with brine (5 ml), then dried and evaporated to dryness *in vacuo* to leave a brown oil. Chromatography, using 10% ethyl acetate–petroleum ether as eluant gave the *alkyne* (0.75 g, 92%) as a colourless oil, $[\alpha]_D^{21}$ −8.4 (*c* 1.0 in $CHCl_3$); ν_{max} (film)/cm^{-1} 3292, 3062, 2932, 2120, 1445, 1428, 1104, 996; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.85 (1H, dd, *J* 8.1, 0.5, ArH), 7.75 (1H, dd, *J* 8.0, 0.6, ArH), 7.38–7.46 (1H, m, ArH), 7.25–7.35 (1H, m, ArH), 3.72–3.82 (1H, m, C*H* OMe)Me), 3.62–3.66 (2H, m, CH_2 S), 3.50 (3H, s, OMe), 2.62 (2H, dd, *J* 5.3, 2.7, CH_2C≡CH), 2.08 (1H, t, *J* 2.7, C≡CH); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.4 (s), 153.1 (s), 135.3 (s), 126.0 (d), 124.3 (d), 121.5 (d), 121.0 (d), 79.8 (d), 77.8 (d), 70.8 (d), 57.8 (q), 36.1 (t), 23.0 (t); m/z (FAB) Found 254.0521 ([M + H]$^+$ $C_{13}H_{14}NOS_2$ requires 264.0521).

2-((R)-(*E*)-5-Bromo-2-methoxypent-4-enylsulfanyl)benzothiazole (95). Freshly prepared Cp_2ZrHCl (Schwartz reagent)[23] (584 mg 2.3 mmol) was added in three portions to a solution of the alkyne (**94**) (400 mg, 1.52 mmol) in DCM (6 ml) at room temperature and the mixture was stirred at this temperature for 3 h. The resulting yellow slurry was treated with NBS (812 mg, 4.56 mmol) and it quickly became dark red coloured. The mixture was stirred for 15 min, then saturated aqueous $Na_2S_2O_3$ (10 ml) was added, followed by ethyl acetate. The separated organic layer was washed with brine, then dried and evaporated to dryness *in vacuo*. The oily residue was purified by chromatography eluting with ethyl acetate-petroleum ether (5:95 to 2:4) to give the *E-vinyl bromide* (460 mg, 88%) as a colourless oil, $[\alpha]_D^{20}$ −29.5 (*c* 1.1 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2929, 1622, 1456, 1428, 1101; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.86 (1H, dd, *J* 8.1, 0.5, ArH), 7.75 (1H, dd, *J* 8.1, 0.5, ArH), 7.38–7.46 (1H, m, ArH), 7.28.7.32 (1H, m, ArH), 6.2–6.3 (1H, m, C*H*=CH Br), 6.12–6.19 (1H, d, *J* 13.6, CH=C*H* Br), 3.6–3.64 (1H, m, C*H* OMe), 3.47–3.55 (2H, m, CH_2S), 3.46 (3H, s, OMe), 2.36–48 (2H, m, CH_2 CHOMe); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.3(s), 153.0 (s), 135.3 (s), 133.1 (d), 126.0 (d), 124.3 (d), 121.5 (d), 121.0 (d), 107.2 (d), 78.6 (d), 57.6 (q), 36.5 (t), 36.0 (t); *m*/*z* (FAB) Found 343.9795 ([M + H]$^+$ $C_{13}H_{15}{}^{79}BrN\,OS_2$ requires 343.9778).

When the same transformation was effected using Bu_3SnH–AIBN, instead of Schwartz reagent, followed by quenching with NBS, a 9 : 2 mixture of *E*- and *Z*- vinyl bromides was obtained.

2-((*R*)-*E*-5-Bromo-2-methoxypent-2-ene-1-sulfonyl)benzothiazole (96). A solution of ammonium molybdate (3.25 g, 2.62 mmol) in 30% hydrogen peroxide (7.7 ml) was added dropwise *via* pipette over 5 min to a stirred solution of the sulfide (**95**) (0.9 g, 2.6 mmol) in THF–MeOH (1 : 1, 40 ml) at 0 °C. The mixture was stirred at 0 °C for 26 h, then diluted with water and extracted with dichloromethane. The combined organic extracts were washed with brine and then evaporated to dryness *in vacuo*. The residue was purified by chromatography on silica using ethyl–petroleum ether as eluant (2 : 8 to 3 : 7) to give the *sulfone* (940 mg, 95%) as a colourless crystalline solid, mp 96–98 °C (EtOAc), $[\alpha]_D$ −20.5 (*c* 0.8 in $CHCl_3$); ν_{max} (film)/cm^{-1} 2928, 1622, 1327, 1147, 761. ′H NMR (360 MHz, $CDCl_3$) δ 8.23 (1H, d, *J* 8, ArH), 8.02 (1H, d, *J* 8, ArH), 7.55–7.70 (2H, m, ArH), 6.1 −6.22 (2H, m), 3.93–4.05 (1H, m, CHOMe), 3.84 (1H, dd, *J* 14.7, 7.6, CH_2SO_2Ar), 3.53 (1H, dd, *J* 14.7, 4.2, CH_2SO_2Ar), 3.27 (3H, s, OMe), 2.4–2.6 (2H, m, CH_2CH_2-C*H*OMe); ^{13}C NMR (90 MHz, $CDCl_3$) δ 166.5 (s), 152.5 (s), 136.7(s), 131.6(d), 128.0(d), 127.6(d), 125.4(d), 122.3(d), 108.4(d), 74.3(d), 58.2(t), 57.3(q), 36.3(t); m/z (ESI) Found: 397.9495 ([M + Na]$^+$ $C_{13}H_{14}{}^{79}BrNO_3S_2Na$ requires 397.9496).

(1*R*,4*R*,10*R*,12*R*)-1*E*,5*E*,7*E*)-1-Bromo-9-(*tert*-butyldimethylsilanyloxy)-10-(4-methoxybenzyloxy)-7-methyl-4–12,12,14-tetramethoxytetradeca-1,5,7-triene (97). Sodium bis(trimethylsilyl)amide (2 M in THF, 650 μL; 1.30 mmol) was added dropwise *via* syringe over 5 min to a stirred solution of the sulfone (**96**) (420 mg; 1.117 mmol) and the aldehyde (**7**) (660 mg; 1.30 mmol) in THF (12 ml) at −78 °C under a nitrogen atmosphere. The resulting orange coloured solution was allowed to warm to room temperature over 5 h, then quenched with saturated ammonium chloride solution (20 ml), diluted with ethyl acetate (150 ml) and phases separated. The aqueous phase was extracted with ethyl acetate and the combined organic extracts were washed with brine, then dried and concentrated *in vacuo*. The residue was dissolved in petroleum ether and the solution was stored overnight in a fridge at 0 °C. The petrol was decanted and the solid residue was then washed with additional petrol ether. The combined organic extracts were evaporated to leave a residue which was purified by flash chromatography using 20% ethyl acetate–petroleum ether as eluant to give the *E-olefin* (696 mg, 93% as a colourless oil; $[\alpha]_D^{21}$ + 44.4 (*c* 1.08 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2934, 1614, 1514, 1250, 1096; ^{1}H NMR (360 MHz, $CHCl_3$) δ 7.28 (2H, d, *J* 8.7, ArH), 6.87 (2H, d, *J* 8.7, ArH), 6.21–6.15 (2H, m, CH-9, H-13), 6.09 (1H, d, *J* 13.6, H-14), 5.45 (1H, d, *J* 8.4, H-1) 5.42 (1H, dd, *J* 15.4, 7.7, H-10), 4.75(1H, d, *J* 11.1, OCH_2Ar), 4.55 (1H, dd, *J* 9.2, 5.8, H-1), 4.51 (1H, d, *J* 11.1, OCH_2Ar), 4.46 (1H, dd, *J* 5.3, 5.3, H-6), 3.81 (3H, s, OMe), 3.70–3.55 (2H, m, H-5, H-1), 3.49 (1H, m, H-3), 3.30 (3H, s, OMe), 3.29 (3H, s, OMe), 3.26 (3H, s, OMe), 3.23 (1H, s, OMe), 2.40–2.20 (2H, m, H-2), 1.85–1.65 (3H, m, H-4, H-12), 1.77 (3H, s, Me), 1.47 (1H, m, H-4), 0.89 (9H, s, Me_3), 0.05 (3H, s, Me), 0.01 (3H, s, Me); ^{13}C NMR (90 MHz, $CDCl_3$) δ 159.1 (s), 137.6 (d), 133.9 (d), 133.7 (s), 133.1 (d), 131.0 (s), 2 × 129.5 (d), 127.7 (d), 2 × 133.7 (d), 106.2 (d), 101.9 (d), 81.2 (d), 79.7 (d), 74.3 (d), 73.1 (t), 71.8 (d), 56.3 (q), 56.1 (q), 55.2 (q), 52.9(q), 52.5 (q), 39.2 (t), 37.2 (t), 35.8 (t), 3 × 25.8 (q), 18.1 (s), 13.4 (q), −4.4 (q), −4.7(q); *m*/*z* (ESI) Found 693.2796 ([M + Na]$^+$ $C_{33}H_{55}{}^{79}BrO_7SiNa$ requires 693.2798).

(4*R*,6*R*)-6-[(1*R*,6*R*)-(2*E*,4*E*,8*E*)-9-Bromo-1-(*tert*-butyldimethylsilanyloxy)-6-methoxy-3-methylnona-2,4,8-trienyl]-4-methoxytetrahydropyran-2-one (91). A solution of freshly prepared dimethylboron bromide[47] in dichloromethane (1.7 M, 7.4 ml, 12.5 mmol) was added in one portion to a stirred solution of the dimethyl acetal (**97**) (1.4 g 2.09 mmol) in dimethyl ether (60 ml) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1.5 h, and then transferred *via* cannula to a vigorously stirred suspension of THF (40 ml) and saturated aqueous sodium hydrogencarbonate solution (40 ml). The separated aqueous layer was extracted with ethyl acetate (3 × 20 ml) and the combined organic extracts were then washed with brine (5 ml), dried and evaporated to dryness *in vacuo*. The residue was filtered through a short pad of silica eluting with ethyl acetate–petroleum ether (1:4 to 3:7) to give the corresponding *aldehyde* (1.3 g, 98%) as a pale yellow oil; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.73 (1H, t, *J* 2.4, CHO),

7.26 (2H, d, *J* 8.6 ArH), 6.87 (2H, d, *J* 8.6, ArH), 6.25–6.10 (2H, m), 6.09 (1H, d, *J* 13.6), 5.44 (1H, dd, *J* 15.6, 7.9), 5.41 (1H, d, *J* 8.0), 4.74 (1H, d, *J* 11.1, OCH_2 Ar), 4.59 (1H, dd, *J* 9.2, 5.6), 4.47 (1H, d, *J* 11.1, OCH_2Ar), 3.82–3.84 (1H, m), 3.80 (3H, s, OMe), 3.70–3.60 (2H, m), 3.26 (3H, s, OMe), 3.22 (3H, s, OMe), 2.5–2.6 (2H, m), 2.26–2.34 (2H, m), 1.84 (1H, m), 1.77 (3H, s, Me), 1.47 (1H, ddd, *J* 14.2, 10.4, 3.7), 0.88 (9H, s, Me_3), 0.05 (3H, s, Me), 0.00 (3H, s, Me); ^{13}C NMR (90 MHz) δ 201.5 (d), 159.3 (s), 137.5 (d), 134.3 (s), 134.0 (d), 132.6 (d), 130.7 (s), 129.7 (d), 128.1 (d), 113.9 (d), 106.4 (d), 81.3 (d), 79.5 (d), 73.2 (d), 73.2 (t), 71.1 (d), 56.5(q), 56.4 (q), 55.4 (q), 48.3 (t), 39.3 (t), 35.6 (t), 3 × 25.9 (q), 18.2 (s), 13.5 (q), −4.3 (q), −4.7 (q).

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (665 mg 2.87 mmol) was added in one portion to a solution of the aldehyde (1.28 g, 2.05 mmol) in dichloromethane (50 ml) and water (5 ml) at 0 °C. The mixture was stirred at 0 °C for 1 h, then quenched with saturated aqueous sodium hydrogencarbonate (10 ml). The suspension was filtered through celite, eluting with dichloromethane, and the filtrate was then concentrated *in vacuo*. The residue was purified by flash chromatography, using 20% ethyl acetate in petroleum ether as eluant to give the cyclic hemiketal (**98**) (880 mg, 85%) as an oily 3 : 2 mixture of two anomers.

TPAP (55 mg, 0.146 mmol) was added to a stirred solution of the hemiketal (736 mg 1.45 mmol) and *N*-methylmorpholine *N*-oxide (268 mg, 2.27 mmol) in dichloromethane (8 ml) containing powdered 4 Å molecular sieves (783 mg). The mixture was stirred at room temperature for 24 h, then filtered through a pad of silica eluting with ethyl acetate, and evaporated to dryness *in vacuo*. The residue was purified by flash chromatography using petroleum ether and then 10–30% ethyl acetate in petroleum ether as eluant to give the *lactone* (600 mg, 82%) as a colourless oil, $[a]_D^{21}$ −4.9 (*c* 2.4 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2930, 1746, 1254, 1096; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (1H, d, *J* 15.6, H-9), 6.08 (1H, d, *J* 13.6, H-14), 6.16 (1H, dd, *J* 13.6, 7.2, H-13), 5.48 (1H, dd, *J* 15.6, 7.8, H-10), 5.46 (1H, *J* 9, H-7), 4.6 (1H, dd, *J* 9, 4.8, H-6), 4.16 (1H, ddd, *J* 12, 4.8, 3.2, H-5), 3.65–3.73 (1H, m, H-3), 3.34 (3H, s, OMe), 3.25 (3H, s, OMe), 2.86 (1H, ddd, *J* 17.2, 5.7, 11.3, H-2), 2.42 (1H, ddd, *J* 17.2, 8.1, H-2), 3.64 (1H, dd, *J* 13.2, 6.4, H-11), 2.37–2.22 (3H, m, H-4, H-12), 1.80 (3H, s, Me), 1.53–1.63 (1H, m, H-4), 0.86 (9H, s, Me_3), 0.06 (3H, s, Me), 0.02 (3H, s, Me); ^{13}C NMR (125 MHz) δ 169.8 (s), 136.9 (d), 135.3 (s), 133.8 (d), 130.5 (d), 128.8 (d), 106.3 (d), 81.1 (d), 80.0 (d), 72.4 (d), 70.3 (d), 56.4 (q), 56.0 (q), 39.1 (t), 36.7 (t), 30.1 (t), 25.7(q), 18.1 (s), 13.4 (q), −4.5 (q), −4.9 (q); *m*/*z* (FAB) Found 525.1628 ([M + Na]$^+$ $C_{23}H_{39}BrO_3SiNa$ requires 525.1648).

Dimethyl 4-(2-methyloxazole)-methylphosphonate (99). Carbon tetrabromide (2.75 g, 8.3 mmol), followed by triphenylphosphine (2.6 g, 9.95 mmol) were added to a stirred solution of 4-hydroxymethyl-2-methyloxazole (0.75 g, 6.64 mmol)[51] in dichloromethane (18 ml) at 0 °C, and the mixture was allowed to warm to room temperature where it was stirred for 4 h. The mixture was evaporated to dryness *in vacuo* and the residue was purified by chromatography on silica using 1 : 1 ethyl acetate in petroleum ether as eluant to give the corresponding oxazole-methyl bromide (0.9 g, 76%) as a pale yellow oil; ^{1}H NMR (360 Mz) δ 7.54 (1H, s, CH), 4.35 (2H, s, CH_2), 2.46 (3H, s, Me); ^{13}C NMR (90 MHz) δ 162.9(s), 136.9(s), 135.5(d), 22.9(t), 13.7(q); *m*/*z* (ESI) Found 174.9640 ([M]$^+$ C_5H_6BrNO requires 174.9633).

Trimethyl phosphite (7 ml, 5.68 mmol) was added to a solution of the bromide (1.0 g, 5.68 mmol) in benzene (20 ml) and the mixture was heated undre reflux for 24 h and then evaporated *in vacuo*. The residue was distilled under reduced pressure to give the phosphonate (0.7 g, 60%) as a pale yellow oil; bp 40–50 °C at 0.5 mmHg; ν_{max} (film)/cm^{-1} 2957, 1580, 1332, 1255, 1030; ^{1}H NMR (360 Mz) δ 7.48(1H, d, *J*, 3,5, CH), 3.77 (3H, s, OMe), 3.74 (3H, s, OMe), 3.07 (2H, d, *J* 20.8, CH_2), 2.42 (3H, s, Me); ^{13}C NMR (90 MHz) δ 161.1(s), 135.7(d), 130.7(s), 52.6(q), 52.5(q), 23.5(t, CH_2), 13.5(q); *m*/*z* (ESI) 206.0227 ([M + H]$^+$ $C_7H_{12}NPO_4$ requires 206.0242).

Oxane–oxazole (90). A solution of lithium diisopropylamide (0.6 M, 0.79 mmol) in THF (1.32 ml) was added over 5 min *via* syringe to a stirred solution of the oxazole phosphonate (**99**) (162.0 mg, 79 mmol) in tetrahydrofuran (1.2 ml) at −78 °C under a nitrogen atmosphere. The resulting orange solution was stirred at −78 °C for 30 min and then a solution of the ketone (**4**) (60.0 mg, 0.158 mmol) in tetrahydrofuran (1.8 ml) was added *via* cannula. The mixture was allowed to warm slowly to room temperature over 5 h, stirred overnight, and then quenched with saturated aqueous ammonium chloride (1.6 ml) and diluted with ethyl acetate. The organic extract was washed with brine, then dried and evaporated to dryness. The residue was purified by chromatography eluting with ethyl acetate in petrol (3 : 7) to give the *alkene* (35.0 mg, 49%; 89% based on recovered starting material) as a colourless oil; $[a]_D^{20}$ + 47.6 (*c* 0.8 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2931, 1720, 1613, 1586, 1514, 1248, 1109, 1035; ^{1}H NMR (500 MHz) δ 7.49 (1H, s, oxC*H*), 7.27 (2H, d, *J* 8.5, Ar*H*), 6.88 (2H, d, *J* 8.5, Ar*H*), 6.17 (1H, s, oxC=C*H*), 4.57 (1H, d, *J* 11.1, OCH_2Ar), 4.51 (1H, dd, *J* 8.0, 3.6, C*H*$(OCH_3)_2$), 4.30 (1H, d, *J* 11.1, OCH_2Ar), 3.80 (3H, s, ArOCH_3), 3.53 (1H, b d, *J* 7.9, OC*H*), 3.43 (1H, d, *J* 10.2, OC*H*), 3.35 (3H, s, OCH_3), 3.32 (3H, s, OCH_3), 3.21 (1H, dd, *J* 10.5, 4.7, PMBOC*H*), 2.44 (3H, s, oxCH_3), 2.06 (1H, m, C*H*CH_3), 1.92 (1H, m, OCHCH_2), 1.89 (3H, s, CH=CCH_3), 1.83–1.88 (1H, m, C*H*CH_3), 1.6–1.7 (1H, m, OCHCH_2), 0.97 (3H, d, *J* 6.9, CHCH_3), 0.81 (3H, d, *J* 6.3, CHCH_3); ^{13}C NMR (90 MHz) δ 160.7(s), 159.2(s), 138.3(s), 137.8(s), 135.6(d), 130.7(s), 2 × 129.4(d), 118.6(d), 2 × 113.9(d), 102.6(d), 88.9(d), 83.1(d), 74.4(d), 69.7(t), 55.4(q), 54.0(q), 53.1(q), 36.8(t), 34.6(d), 33.2(d), 14.2(q), 13.9(q), 13.8 (q), 6.2(q); *m*/*z* (ESI) Found 482.2750 ([M + Na]$^+$ $C_{26}H_{37}O_6NNa$ requires 482.2518).

Bis-oxane oxazole (100b). A solution of *n*-butyllithium (2.5 M) in hexanes (87 µl, 0.218 mmol) was added dropwise over 10 min to a stirred solution of the methyl oxazole (**90**) (77.0 mg, 0.168 mmol) and diethylamine (0.1 ml, 1.0 mmol) in tetrahydrofuran (1.1 ml) at −78 °C under a nitrogen atmosphere. The resulting light orange solution was stirred at −78 °C for 12 min and then a solution of the lactone (**91**) (95.0 mg, 0.189 mmol) in tetrahydrofuran (0.6 ml) was added dropwise over 15 min *via* cannula. The mixture was stirred at −78 °C for 30 min, then quenched with water (5 ml), and extracted with ethyl acetate (3 × 20 ml). The separated organic extract was dried and evaporated to dryness *in vacuo* to leave the crude cyclic *hemiketal* (**100a**) (170.0 mg) as a colourless oil; ν_{max} (NaCl)/cm^{-1} 3379, 2929, 1613, 1585, 1514, 1248, 1092, 1034; ^{1}H NMR (500 MHz) δ 7.50 (1H, s, oxC*H*), 7.27 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 6.25–6.05 (3H, m), 6.17 (1H, s, oxC=C*H*), 5.43 (1H, dd, *J* 15.8, 8.0, CH(OCH_3)C*H*=CH), 5.34 (1H, d, *J* 9.0, =C*H*CH(OTBS)), 5.32 (1H, d, *J* 2.0, OH), 4.58 (1H, d, *J* 11.1, OCH_2Ar), 4.51 (1H, dd, *J* 8.0, 3.5, C*H*$(OCH_3)_2$), 4.34 (1H, dd, *J* 9.0, 6.5, =CHC*H*(OTBS)), 4.30 (1H, d, *J* 11.1, OCH_2Ar), 3.85 (1H, ddd, *J* 11.7, 6.5, 1.5, CH(OTBS)C*H*OC=O), 3.80 (3H, s, ArOCH_3), 3.77–3.68 (1H, m, $CH_2CH(OCH_3)CH_2$), 3.63 (1H, dd, *J* 13.7, 7.0, $CH_2CH(OCH_3)CH_2$), 3.53 (1H, b d, *J* 7.7, OC*H*), 3.43 (1H, d, *J* 10.2, OC*H*), 3.35 (3H, s, CH$(OCH_3)_2$), 3.35 (3H, s, CH$(OCH_3)_2$), 3.32 (3H, s, OCH_3), 3.27 (3H, s, OCH_3), 3.21 (1H, dd, *J* 10.3, 4.5, PMBOC*H*), 3.08 (1H, d, *J* 15.4, C(OH)CH_2ox), 3.01 (1H, d, *J* 15.4, C(OH)CH_2ox), 2.38–2.22 (3H, m), 1.98–2.02 (1H, m, C*H*CH_3), 1.92–1.97 (1H, m, OCHCH_2), 1.91 (3H, s, CH=CCH_3), 1.78–1.84 (2H, m), 1.67 (3H, s, CH=CCH_3), 1.3–1.4 (1H, m, CH_2C(OH)), 1.0–1.04 (1H, m, OCHCH_2), 0.97 (3H, d, *J* 6.9, CHCH_3), 0.82 (3H, d, *J* 6.4, CHCH_3), 0.76 (9H, s, SiC$(CH_3)_3$), −0.08 (3H, s, Si$(CH_3)_2$), −0.13 (3H, s, Si$(CH_3)_2$); ^{13}C NMR (125 MHz) δ 160.2(s),

159.1(s), 138.6(s), 137.6(s), 137.5(d), 135.4(d), 134.0(s), 133.9(d), 132.6(d), 130.5(s), 2 × 129.3(d), 127.6(d), 117.8(d), 2 × 113.7(d), 106.2(d), 102.4(d), 96.4(s), 88.8(d), 83.1(d), 81.2(d), 74.4(d), 73.4(d), 73.2(d), 71.6(d), 69.6(t), 56.3(q), 55.6(q), 55.3(q), 53.8(q), 52.9(q), 40.6(t), 39.7(t), 39.1(t), 36.7(t), 34.5(d), 33.2(d), 32.4(t), 3 × 25.7(q), 18.1(s), 14.2(q), 13.7(q), 13.3(q), 6.1(q), −4.7(q), −4.9(q); *m/z* (ESI) Found 984.4288 ([M + Na]$^+$ $C_{49}H_{76}{}^{79}BrO_{11}$-NSiNa requires 984.4269).

A solution of the crude hemiketal (**100a**) (168 mg) in pyridine (0.27 ml, 0.168 mmol), acetonitrile (13 ml) and diethyl ether (1.3 ml) at −47 °C was treated with triethylsilyl trifluoromethanesulfonate (0.42 ml, 1.86 mmol), and the mixture was stirred at −47 °C for 36 h. The mixture was quenched with saturated aqueous sodium bicarbonate (16 ml) and extracted with ethyl acetate and dichloromethane. The combined organic extracts were dried, filtered, and concentrated *in vacuo*. The residue was purified by chromatography, using 20–50% ethyl acetate in petrol ether as eluent, on silica pre-treated with 20% ethyl acetate in petrol ether containing 1% of triethylamine to give the *TES-protected hemiketal* (119.0 mg, 66%; over two steps) as a colourless oil. ^{1}H NMR analysis showed the presence of 12% of the corresponding anomer; $[\alpha]_D^{25}$ −4.0 (*c* 2.5 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2955, 1726, 1614, 1514, 1248, 1090, 835; ^{1}H NMR (500 MHz) δ 7.44 (1H, s, oxC*H*), 7.28 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 6.24–6.15 (2H, m), 6.16 (1H, s, oxC=C*H*), 6.09 (1H, d, *J* 13.6, =C*H*Br), 5.43 (1H, dd, *J* 15.5, 8.0, CH(OCH$_3$)C*H*=CH), 5.40 (1H, d, *J* 8.9, =C*H*CH-(OTBS)), 4.58 (1H, d, *J* 11.1, OCH_2Ar), 4.52 (1H, dd, *J* 8.0, 3.5, C*H*(OCH$_3$)$_2$), 4.46 (1H, dd, *J* 8.9, 5.0, =CHC*H*(OTBS)), 4.31 (1H, d, *J* 11.1, OCH_2Ar), 3.81 (3H, s, ArOCH_3), 3.80–3.75 (1H, m), 3.62 (2H, m), 3.54 (1H, b d, *J* 7.7, OC*H*), 3.43 (1H, d, *J* 10.2, OC*H*), 3.36 (3H, s, CH(OCH_3)$_2$), 3.33 (6H, s, OCH_3 and CH(OCH_3)$_2$), 3.26 (3H, s, OCH_3), 3.22 (1H, dd, *J* 10.3, 4.6, PMBOC*H*), 3.16 (1H, d, *J* 14.2, C(OH)CH_2ox), 3.10 (1H, d, *J* 14.2, C(OH)CH_2ox), 2.26–2.34 (2H, m), 2.20 (1H, dd, *J* 12.3, 2.6), 2.05 (1H, dd, *J* 8.1, 8.1), 1.97 (1H, b d, *J* 12.3), 1.89 (3H, s, CH=CCH_3), 1.81 (1H, m), 1.77 (3H, s, CH=CCH_3), 1.6–1.68 (2H, m), 1.37 (1H, dd, *J* 11.5, 11.5), 1.05 (1H, ddd, *J* 12.0, 11.8, 11.8, OCHCH_2), 0.98 (9H, t, *J* 7.8, Si(CH$_2$CH_3)$_3$), 0.97 (3H, d, *J* 6.9, CHCH_3), 0.86 (9H, s, SiC(CH_3)$_3$), 0.82 (3H, d, *J* 6.5, CHCH_3), 0.69 (6H, q, *J* 7.8, Si(CH_2CH$_3$)$_3$), 0.04 (3H, s, Si(CH_3)$_2$), −0.01 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 159.6(s), 159.1(s), 138.1(s), 137.8(d), 137.7(s), 135.9(d), 134.0(d), 133.6(s), 132.9(d), 130.6(s), 2 × 129.3(d), 127.3(d), 118.5(d), 2 × 113.8(d), 106.2(d), 102.5(d), 99.0(s), 88.8(d), 83.1(d), 81.3(d), 74.3(d), 73.7(d), 73.5(d), 71.1(d), 69.6(t), 56.3(q), 55.5(q), 55.3(q), 54.0(q), 53.0(q), 41.9(t), 40.8(t), 39.2(t), 36.8(t), 34.5(d), 33.2(d), 31.8(t), 3 × 25.8(q), 18.1(s), 14.1(q), 13.7(q), 13.3(q), 3 × 7.0(q), 3 × 6.2(t), 6.1(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1098.5002 ([M + Na]$^+$ $C_{55}H_{90}{}^{79}$-BrO$_{11}$NSi$_2$Na requires 1098.5133).

Attempts to protect the hemiketal (**100a**) as its TBS group, under similar conditions, instead led to the TBS ether of the corresponding ring-opened tautomeric δ-hydroxy ketone.

Bis-oxane oxazole aldehyde (101). A solution of dimethylboron bromide[26] in dichloromethane (1.33 M, 275 µl; 0.364 mmol) was added in one portion to a stirred solution of the dimethyl acetal (**100b**) (98.0 mg; 0.091 mmol) in diethyl ether (3.5 ml) at −78 °C under a nitrogen atmosphere. The solution was stirred at −78 °C for 30 min before being transferred, *via* cannula, to a vigorously stirred suspension of THF (5 ml) and saturated aqueous sodium bicarbonate solution (5 ml). The mixture was diluted with ethyl acetate and the separated aqueous layer was then extracted with ethyl acetate (3 × 10 ml). The combined organic extracts were washed with brine, then dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography, using 20–40% ethyl acetate in petrol ether as eluent, on silica pre-treated with 20% ethyl acetate in petrol ether containing 1% of triethylamine to give the *aldehyde* (79.0 mg, 85%) as a pale yellow oil; $[\alpha]_D^{22}$ −1.7 (*c* 2.6 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2955, 1727, 1613, 1514, 1248, 1090, 836; ^{1}H NMR (500 MHz) δ 9.77 (1H, d, *J* 0.5, oxC*H*), 7.44 (1H, s, oxC*H*), 7.28 (2H, d, *J* 8.3, Ar*H*), 6.89 (2H, d, *J* 8.3, Ar*H*), 6.26–6.16 (2H, m), 6.17 (1H, s, oxC=C*H*), 6.10 (1H, dd, *J* 13.6, 0.7 =C*H*Br), 5.42 (1H, dd, *J* 15.3, 8.1, CH(OCH$_3$)C*H*=CH), 5.40 (1H, d, *J* 8.8, =C*H*CH(OTBS)), 4.58 (1H, d, *J* 11.1, OCH_2Ar), 4.46 (1H, dd, *J* 8.8, 4.8, =CHC*H*(OTBS)), 4.32 (1H, d, *J* 11.1, OCH_2Ar), 4.0–4.06 (1H, m), 3.82 (3H, s, ArOCH_3), 3.80–3.75 (1H, m), 3.68–3.58 (2H, m), 3.50 (1H, d, *J* 10.3, OC*H*), 3.33 (3H, s, OCH_3), 3.27 (1H, dd, *J* 10.4, 4.6, PMBOC*H*), 3.25 (3H, s, OCH_3), 3.16 (1H, d, *J* 14.2, C(OH)CH_2ox), 3.09 (1H, d, *J* 14.2, C(OH)CH_2ox), 2.77 (1H, dd, *J* 16.6, 8.6), 2.44 (1H, ddd, *J* 16.6, 4.5, 1.4), 2.31 (2H, m), 2.20 (1H, dd, *J* 12.1, 3.2), 2.12–2.18 (1H, m), 1.97 (1H, b d, *J* 11.9), 1.89 (3H, s, CH=CCH_3), 1.83 (1H, m), 1.76 (3H, s, CH=CCH_3), 1.38 (1H, dd, *J* 11.6, 11.6), 1.04 (1H, ddd, *J* 12.0, 11.9, 11.9, OCHCH_2), 0.98 (9H, t, *J* 7.8, Si(CH$_2$CH_3)$_3$), 0.97 (3H, d, *J* 6.9, CHCH_3), 0.86 (9H, s, SiC(CH_3)$_3$), 0.84 (3H, d, *J* 6.5, CHCH_3), 0.69 (6H, q, *J* 7.8, Si(CH_2CH$_3$)$_3$), 0.04 (3H, s, Si(CH_3)$_2$), −0.01 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 201.2(d), 159.5(s), 159.2(s), 137.8(d), 137.6(s), 137.4(s), 136.0(d), 134.0(d), 133.6(s), 132.9(d), 130.4(s), 2 × 129.3(d), 127.2(d), 118.9(d), 2 × 113.8(d), 106.2(d), 99.0(s), 89.1(d), 82.6(d), 81.3(d), 80.4(d), 73.7(d), 73.5(d), 73.2(d), 71.1(d), 69.7(t), 56.2(q), 55.4(q), 55.2(q), 47.0(t), 42.0(t), 40.7(t), 39.1(t), 34.2(d), 33.1(d), 31.7(t), 3 × 25.8(q), 18.1(s), 14.0(q), 13.6(q), 13.2(q), 3 × 7.0(q), 3 × 6.2(t), 6.1(q), −4.6(q), −4.9(q).

Tetra-oxane oxazole (102). Tributylphosphine (60 µl, 0.232 mmol) was added to a stirred solution of the mesylate (**71c**) (47.0 mg, 0.067 mmol) in dimethylformamide (4.5 ml), and the mixture was stirred at room temperature for 15 h. A solution of the aldehyde (**101**) (60.0 mg, 0.058 mmol) in dimethylformamide (2.4 ml) was added *via* cannula followed by DBU (20 µl, 0.128 mmol), and the mixture was then stirred at room temperature for 1 h. The solvents were removed *in vacuo* [0.2 mm Hg, 30 °C] and the orange residue was purified by chromatography on silica using ethyl acetate in petrol ether (5 : 95 to 2 : 8) as eluant to give the *E*-C(19–20) alkene (82.0 mg, 87%) as a pale yellow oil; $[\alpha]_D^{21}$ −3.5 (*c* 1.5 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2953, 1614, 1514, 1462, 1249, 1093, 836; ^{1}H NMR (500 MHz) δ 7.45 (1H, s, oxC*H*), 7.44 (1H, s, oxC*H*), 7.27 (2H, d, *J* 8.6, Ar*H*), 6.87 (2H, d, *J* 8.6, Ar*H*), 6.63 (1H, ddd, *J* 16.0, 8.4, 7.2, CH$_2$C*H*=CHox), 6.36 (1H, d, *J* 16.0, CH=C*H*ox), 6.22–6.15 (2H, m), 6.18 (1H, s, oxC=C*H*), 6.09 (1H, d, *J* 13.6, =C*H*Br), 5.41 (1H, dd, *J* 15.6, 8.0, CH(OCH$_3$)C*H*=CH), 5.40 (1H, d, *J* 8.9, =C*H*CH(OTBS)), 4.88 (1H, b d, *J* 9.6), 4.74 (1H, b s, =CH_2), 4.71 (1H, b s, =CH_2), 4.57 (1H, d, *J* 10.9, OCH_2Ar), 4.45 (1H, dd, *J* 8.9, 5.0, =CHC*H*(OTBS)), 4.39 (1H, b s, C*H*OSi(CH(CH$_3$)$_2$)$_3$), 4.27 (1H, d, *J* 10.9, OCH_2Ar), 4.10–4.00 (2H, m), 3.84–3.9 (1H, m), 3.80 (3H, s, ArOCH_3), 3.80–3.76 (1H, m), 3.66–3.57 (4H, m), 3.53 (1H, b d, *J* 7.1, OC*H*), 3.43 (1H, d, *J* 9.9, OC*H*), 3.32 (3H, s, OCH_3), 3.25 (3H, s, OCH_3), 3.19 (1H, dd, *J* 10.4, 4.5, PMBOC*H*), 3.16 (1H, d, *J* 14.4, C(OTES)-CH_2ox), 3.09 (1H, d, *J* 14.4, C(OTES)CH_2ox), 2.58 (1H, m), 1.90 (3H, s, CH=CCH_3), 1.76 (3H, s, CH=CCH_3), 1.36 (1H, dd, *J* 11.7, 11.7), 1.12–1.02 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.98 (3H, d, *J* 6.9, CHCH_3), 0.97 (9H, t, *J* 7.8, Si(CH$_2$CH_3)$_3$), 0.88 (9H, s, SiC(CH_3)$_3$), 0.86 (9H, s, SiC(CH_3)$_3$), 0.82 (3H, d, *J* 6.5, CHCH_3), 0.68 (6H, q, *J* 7.8, Si(CH_2CH$_3$)$_3$), 0.04 (9H, s, Si(CH_3)$_2$), −0.01 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 160.9(s), 159.5(s), 159.1(s), 143.1(s), 142.3(s), 137.8(d), 137.7(s), 137.7(s), 135.9(d), 135.4(d), 134.2(d), 133.9(d), 133.6(s), 132.9(d), 130.6(s), 2 × 129.3(d), 127.3(d), 118.8(d), 118.7(d), 2 × 113.8(d), 110.0(t), 106.2(d), 99.0(s), 89.1(d), 83.2(d), 81.3(d), 77.3(d), 73.7(d), 73.5(d), 71.1(d), 69.7(t), 69.1(d), 69.0(d), 68.9(d), 67.3(d), 64.9(d), 59.8(t), 56.2(q), 55.4(q), 55.3(q), 41.9(t), 40.7(t), 39.8(t), 39.1(t), 39.1(t), 38.3(t), 37.0(t), 36.3(t), 33.5(d), 33.2(d), 31.8(t), 3 × 25.9(q), 3 × 25.8(q),

18.2(s), 6 × 18.1(q), 17.7(s), 14.1(q), 13.7(q), 13.3(q), 3 × 12.2(d), 3 × 7.0(q), 3 × 6.2(t), 5.7(q), −4.5(q), −4.8(q), 2 × −5.3(q); *m/z* (ESI) Found 1641.8864 ([M + Na]$^+$ $C_{86}H_{143}{}^{79}BrO_{14}N_2Si_4Na$ requires 1641.8697).

Tetra-oxane oxazole alcohol (103a). A solution of pyridine-buffered pyridinium hydrofluoride, [prepared from 0.5 ml of Aldrich pyridinium hydrofluoride (0.5 ml), pyridine (1 ml) and tetrahydrofuran (4 ml)] was added to a solution of the silyl ether (**102**) (30.0 mg, 18.5 μmol) in tetrahydrofuran (3 ml) in a polyethylene reaction flask at 0 °C. The mixture was stirred at 0 °C for 5 min and then allowed to warm to room temperature, where it was stirred for a further 1 h 30 min. The mixture was cooled to 0 °C, and then quenching by careful addition of saturated aqueous sodium bicarbonate solution (5 ml). It was then diluted with diethyl ether and brine, and extracted with diethyl ether and dichloromethane. The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated *in vacuo*. The residue was purified by chromatography (Pasteur pipette) using 20–40% ethyl acetate in petrol ether as eluent to give the *alcohol* (18.1 mg, 65%) as a colourless foam; $[a]_D^{22}$ + 0.6 (*c* 1.4 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 3440, 2936, 1513, 1462, 1248, 1090, 1032; ^{1}H NMR (500 MHz) δ 7.46 (1H, s, oxC*H*), 7.45 (1H, s, oxC*H*), 7.28 (2H, d, *J* 8.6, Ar*H*), 6.88 (2H, d, *J* 8.6, Ar*H*), 6.65 (1H, ddd, *J* 16.0, 8.5, 6.2, CH_2C*H*=CHox), 6.36 (1H, d, *J* 16.0, CH=C*H*ox), 6.22–6.16 (2H, m), 6.18 (1H, s, oxC=C*H*), 6.10 (1H, d, *J* 13.6, =C*H*Br), 5.42 (1H, dd, *J* 15.7, 8.0, CH(OCH_3)C*H*=CH), 5.41 (1H, d, *J* 8.9, =C*H*CH(OTBS)), 4.89 (1H, dd, *J* 7.0, 7.0), 4.76 (1H, b s, =CH_2), 4.71 (1H, b s, =CH_2), 4.58 (1H, d, *J* 11.0, OCH_2Ar), 4.46 (1H, dd, *J* 8.9, 5.0, =CHC*H*(OTBS)), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.28 (1H, d, *J* 11.0, OCH_2Ar), 4.14–4.05 (2H, m), 3.99 (1H, m), 3.81 (3H, s, ArOCH_3), 3.75 (2H, dd, *J* 5.2, 5.2), 3.66–3.57 (2H, m), 3.53 (1H, b d, *J* 6.9, OC*H*), 3.47 (1H, d, *J* 10.2, OC*H*), 3.33 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 3.19 (1H, dd, *J* 10.4, 4.5, PMBOC*H*), 3.16 (1H, d, *J* 14.2, C(OTES)CH_2ox), 3.10 (1H, d, *J* 14.2, C(OTES)CH_2ox), 2.55–2.6 (1H, m), 1.91 (3H, s, CH=CCH_3), 1.77 (3H, s, CH=CCH_3), 1.36 (1H, dd, *J* 11.7, 11.7), 1.14–1.00 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.99 (3H, d, *J* 6.9, CHCH_3), 0.98 (9H, t, *J* 7.8, Si(CH_2CH_3)$_3$), 0.87 (9H, s, SiC(CH_3)$_3$), 0.83 (3H, d, *J* 6.5, CHCH_3), 0.69 (6H, q, *J* 7.8, Si(CH_2CH_3)$_3$), 0.05 (3H, s, Si(CH_3)$_2$), −0.005 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 161.1(s), 159.5(s), 159.1(s), 142.8(s), 141.8(s), 137.8(d), 137.8(s), 137.7(s), 136.0(d), 135.8(d), 134.3(d), 134.0(d), 133.7(s), 132.9(d), 130.6(s), 2 × 129.3(d), 127.3(d), 118.8(d), 118.6(d), 2 × 113.8(d), 110.4(t), 106.3(d), 99.0(s), 89.1(d), 83.2(d), 81.3(d), 77.2(d), 73.7(d), 73.5(d), 71.1(d), 70.6(d), 69.9(d), 69.9(d), 69.7(t), 67.1(d), 64.9(d), 60.2(t), 56.3(q), 55.4(q), 55.3(q), 42.0(t), 40.8(t), 40.1(t), 39.5(t), 39.2(t), 39.0(t), 38.7(t), 37.9(t), 36.3(t), 36.2(t), 33.5(d), 33.2(d), 31.8(t), 3 × 25.8(q), 6 × 18.1(q), 17.7(s), 14.1(q), 13.7(q), 13.3(q), 3 × 12.2(d), 3 × 7.1(q), 3 × 6.2(t), 5.7(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1527.5842 ([M + Na]$^+$ $C_{80}H_{129}{}^{79}BrO_{14}N_2Si_3Na$ requires 1527.7833).

Tetra-oxane oxazole aldehyde (103b). Dess–Martin periodinane (9.0 mg, 21.2 μmol) was added to a solution of the alcohol (**103a**) (16.0 mg, 10.6 μmol) and pyridine (5 μl, 62 μmol) in dichloromethane (1.2 ml) and the mixture was stirred for 1 h, then diluted with diethyl ether (2 ml) and saturated aqueous sodium bicarbonate solution (2 ml). The mixture was stirred vigorously for 5 min, and then poured into a separating funnel containing diethyl ether and a 1 : 1 mixture of saturated aqueous $NaHCO_3$–$Na_2S_2O_3$ (1 ml). The organic layer was separated and the aqueous phase was extracted with dichloromethane. The combined organic extracts were dried and concentrated *in vacuo*. The yellow residue was purified by chromatography (Pasteur pipette) eluting with 10–20% ethyl acetate in petrol ether to give the *aldehyde* (15.0 mg, 94%) as a colourless oil; $[a]_D^{22}$ + 2.8 (*c* 2.0 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2926, 1727, 1514, 1462, 1259, 1098, 1032; ^{1}H NMR (500 MHz) δ 9.75 (t, *J* 2.1, C*H*O), 7.47 (1H, s, oxC*H*), 7.45 (1H, s, oxC*H*), 7.28 (2H, d, *J* 8.5, Ar*H*), 6.88 (2H, d, *J* 8.5, Ar*H*), 6.65 (1H, ddd, *J* 15.9, 8.4, 6.0, CH_2C*H*=CHox), 6.36 (1H, d, *J* 15.9, CH=C*H*ox), 6.23–6.17 (2H, m), 6.18 (1H, s, oxC=C*H*), 6.10 (1H, d, *J* 13.6, =C*H*Br), 5.42 (1H, dd, *J* 15.8, 8.2, CH(OCH_3)C*H*=CH), 5.41 (1H, d, *J* 8.8, =C*H*CH(OTBS)), 4.89 (1H, dd, *J* 10.7, 3.0), 4.80 (1H, b s, =CH_2), 4.77 (1H, b s, =CH_2), 4.58 (1H, d, *J* 10.9, OCH_2Ar), 4.46 (1H, dd, *J* 8.8, 5.0, =CHC*H*(OTBS)), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.29 (1H, d, *J* 10.9, OCH_2Ar), 4.12–4.04 (2H, m), 3.81 (3H, s, ArOCH_3), 3.79 (1H, m), 3.66–3.56 (2H, m), 3.54 (1H, b d, *J* 7.4, OC*H*), 3.47 (1H, d, *J* 9.4, OC*H*), 3.33 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 3.19 (1H, dd, *J* 10.2, 4.3, PMBOC*H*), 3.16 (1H, d, *J* 14.5, C(OTES)CH_2ox), 3.10 (1H, d, *J* 14.5, C(OTES)CH_2ox), 1.91 (3H, s, CH=CCH_3), 1.77 (3H, s, CH=CCH_3), 1.12–1.00 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.99 (3H, d, *J* 6.6, CHCH_3), 0.98 (9H, t, *J* 7.8, Si(CH_2CH_3)$_3$), 0.87 (9H, s, SiC(CH_3)$_3$), 0.83 (3H, d, *J* 6.4, CHCH_3), 0.69 (6H, q, *J* 7.8, Si(CH_2CH_3)$_3$), 0.05 (3H, s, Si(CH_3)$_2$), −0.004 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 201.0(d), 161.0(s), 159.5(s), 159.2(s), 143.0(s), 141.0(s), 137.8(d), 137.8(s), 137.7(s), 136.0(d), 135.6(d), 134.3(d), 134.0(d), 133.7(s), 132.9(d), 130.6(s), 2 × 129.3(d), 127.3(d), 125.5(d), 118.8(d), 118.7(d), 2 × 113.8(d), 111.2(t), 106.3(d), 99.0(s), 89.1(d), 83.2(d), 81.3(d), 77.2(d), 73.7(d), 73.5(d), 71.1(d), 69.7(t), 69.1(d), 67.3(d), 67.1(d), 64.9(d), 56.3(q), 55.4(q), 55.3(q), 47.9(t), 42.0(t), 40.8(t), 39.7(t), 39.2(t), 39.2(t), 38.9(t), 38.2(t), 36.4(t), 33.5(d), 33.2(d), 31.9(t), 31.8(t), 3 × 25.8(q), 6 × 18.1(q), 17.7(s), 14.1(q), 13.8(q), 13.3(q), 3 × 12.2(d), 3 × 7.1(q), 3 × 6.2(t), 5.7(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1525.7427 ([M + Na]$^+$ $C_{80}H_{127}{}^{79}BrO_{14}N_2Si_3Na$ requires 1525.7676).

Tetra-oxane oxazole hydroxy aldehyde (104). Dichlorodicyanoquinone (6.0 mg, 24 μmol) was added to a stirred solution of the PMB-ether (**103b**) (15 mg, 10 μmol) in methylene chloride (1.8 ml) and pH = 7 buffer (180 μl) at room temperature, and the mixture was stirred vigorously for 2 h, then quenched with saturated aqueous sodium bicarbonate (3 ml). The mixture was diluted with dichloromethane and poured into saturated aqueous sodium bicarbonate–brine (6 ml). The separated aqueous phase was extracted with dichloromethane, and the combined organic extracts were dried and then evaporated to dryness *in vacuo*. The yellow residue was purified by chromatography (Pasteur pipette) eluting with 20–50% ethyl acetate in petrol ether to give the *alcohol* (11.7 mg, 85%) as a pale yellow oil; $[a]_D^{23}$ −4.1 (*c* 1.0 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 3404, 2928, 1726, 1462, 1249, 1102; ^{1}H NMR (500 MHz) δ 9.75 (t, *J* 1.9, C*H*O), 7.46 (1H, s, oxC*H*), 7.45 (1H, s, oxC*H*), 6.63 (1H, ddd, *J* 16.0, 8.4, 6.6, CH_2C*H*=CHox), 6.36 (1H, d, *J* 16.0, CH=C*H*ox), 6.23–6.16 (2H, m), 6.19 (1H, s, oxC=C*H*), 6.10 (1H, d, *J* 13.6, =C*H*Br), 5.42 (1H, dd, *J* 15.8, 8.2, CH(OCH_3)C*H*=CH), 5.41 (1H, d, *J* 8.7, =C*H*CH(OTBS)), 4.88 (1H, dd, *J* 10.9, 2.6), 4.80 (1H, b s, =CH_2), 4.77 (1H, b s, =CH_2), 4.46 (1H, dd, *J* 8.7, 5.0, =CHC*H*(OTBS)), 4.40 (1H, b s, C*H*OSi(CH(CH_3)$_2$)$_3$), 4.33 (1H, m), 4.12–4.04 (2H, m), 3.80 (1H, m), 3.66–3.56 (3H, m), 3.42–3.48 (2H, m), 3.33 (3H, s, OCH_3), 3.26 (3H, s, OCH_3), 3.17 (1H, d, *J* 14.3, C(OTES)CH_2ox), 3.10 (1H, d, *J* 14.3, C(OTES)CH_2ox), 1.93 (3H, s, CH=CCH_3), 1.77 (3H, s, CH=CCH_3), 1.12–1.00 (21H, m, Si(C*H*(CH_3)$_2$)$_3$), 0.99 (3H, d, *J* 6.6, CHCH_3), 0.98 (9H, t, *J* 7.8, Si(CH_2CH_3)$_3$), 0.87 (9H, s, SiC(CH_3)$_3$), 0.87 (3H, d, *J* 6.4, CHCH_3), 0.69 (6H, q, *J* 7.8, Si(CH_2CH_3)$_3$), 0.05 (3H, s, Si(CH_3)$_2$), −0.003 (3H, s, Si(CH_3)$_2$); ^{13}C NMR (125 MHz) δ 201.1(d), 159.9(s), 159.6(s), 143.0(s), 141.0(s), 137.8(d), 137.7(s), 137.5(s), 136.0(d), 135.4(d), 134.2(d), 133.9(d), 133.7(s), 132.9(d), 127.3(d), 118.8(d), 118.7(d), 111.2(t), 106.2(d), 99.0(s), 88.8(d), 81.3(d), 77.5(d), 76.7(d), 73.7(d), 73.5(d), 71.1(d), 69.7(t), 69.1(d), 67.3(d), 67.1(d), 64.9(d), 56.3(q), 55.4(q), 47.9(t), 42.0(t), 40.8(t), 39.7(t), 39.1(t), 39.1(t), 38.8(t), 38.8(t), 38.2(t), 37.8(d), 36.1(t), 34.6(d), 31.8(t), 3 × 25.8(q), 6 × 18.1(q), 17.7(s), 14.2(q),

13.4(q), 13.3(q), 3 × 12.2(d), 3 × 7.1(q), 3 × 6.2(t), 5.5(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1405.7173 ([M + Na]$^+$; $C_{72}H_{119}{}^{79}BrO_{13}N_2Si_3Na$ requires 1405.7101).

Tetra-oxane oxazole aldehyde phosphonate (105). A solution of bis(2,2,2-trifluoroethyl)phosphonoacetic acid (30.4 mg, 0.1 mmol) in methylene chloride (2 ml) was added to a stirred solution of the alcohol-aldehyde (**104**) (11.3 mg, 8.2 μmol) in methylene chloride (2 ml), followed by EDCl·MeI (24.7 mg, 83 μmol) and HOBT (0.34 mg, 2.5 μmol). The mixture was stirred at room temperature for 1 h 30 min and then filtered through a short pad of silica eluting with 50% ethyl acetate in petrol ether. The filtrate was evaporated to leave a yellow residue which was purified by chromatography (Pasteur pipette) eluting with 5–40% ethyl acetate in petrol ether to give the *aldehyde-phosphonate* (11.4 mg, 84%) as a yellow oil; $[a]_D^{20}$ −10.9 (*c* 1.8 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 3410, 2951, 1729, 1462, 1268, 1099; ^{1}H NMR (500 MHz) δ 9.74 (t, *J* 1.9, C*H*O), 7.47(1H, s, oxC*H*), 7.45 (1H, s, oxC*H*), 6.60 (1H, ddd, *J* 16.0, 8.4, 6.3, CH_2C*H*=CHox), 6.36 (1H, d, *J* 16.0, CH=C*H*ox), 6.23–6.16 (2H, m), 6.21(1H, s, oxC=C*H*), 6.10 (1H, d, *J* 13.6, =C*H*Br), 5.43 (1H, dd, *J* 15.5, 8.1, CH(OCH$_3$)C*H*=CH), 5.41 (1H, d, *J* 8.5, =C*H*CH(OTBS)), 4.8–4.85 (1H, dd, *J* 11.2, 2.7), 4.8–4.85 (1H, m), 4.79(1H, b s, =CH_2), 4.77 (1H, b s, =CH_2), 4.50–4.43 (6H, m), 4.40 (1H, b s, C*H*OSi(CH(CH$_3$)$_2$)$_3$), 4.33 (1H, m), 4.10–4.04 (2H, m), 3.81 (1H, m), 3.66–3.56 (3H, m), 3.54 (1H, d, *J* 10.2, OC*H*), 3.33 (3H, s, OC*H*$_3$), 3.26 (3H, s, OC*H*$_3$), 3.20 (2H, d, *J* 21.3, CH_2P=O), 3.17 (1H, d, *J* 14.1, C(OTES)CH_2ox), 3.11 (1H, d, *J* 14.1, C(OTES)CH_2ox), 2.65–2.55 (2H, m), 2.49 (1H, m), 2.21 (1H, m), 2.12 (1H, m), 1.92 (3H, s, CH=CCH_3), 1.77 (3H, s, CH=CCH_3), 1.56–1.50 (2H, m), 1.34 (1H, dd, *J* 11.5, 11.5), 1.12–1.00 (21H, m, Si(C*H*(CH$_3$)$_2$)$_3$), 0.99 (3H, d, *J* 6.6, CHC*H*$_3$), 0.98 (9H, t, *J* 7.8, Si(CH$_2$C*H*$_3$)$_3$), 0.87 (9H, s, SiC(C*H*$_3$)$_3$), 0.77 (3H, d, *J* 6.4, CHC*H*$_3$), 0.69 (6H, q, *J* 7.8, Si(CH_2CH$_3$)$_3$), 0.05 (3H, s, Si(C*H*$_3$)$_2$), −0.004 (3H, s, Si(C*H*$_3$)$_2$); ^{13}C NMR (125 MHz) δ 201.1(d), 164.0(s), 160.9(s), 159.9(s), 142.8(s), 140.9(s), 137.9(d), 137.3(s), 137.0(s), 136.2(d), 135.3(d), 134.3(d), 133.9(d), 133.7(s), 132.9(d), 127.3(d), 2 × 123.5(s, couple with F), 119.1(d), 118.7(d), 111.2(t), 106.3(d), 98.9(s), 88.6(d), 81.3(d), 81.0(d), 76.8(d), 73.7(d), 73.5(d), 71.1(d), 69.7(d), 69.1(d), 67.1(d), 67.1(d), 64.8(d), 2 × 62.7(t, coupled with F), 56.3(q), 55.4(q), 47.9(t), 41.8(t), 40.8(t), 39.7(t), 39.1(t), 39.1(t), 38.8(t), 38.8(t), 38.2(t), 35.9(t), 35.2(d), *C*H$_2$P=O (34.6, 34.4, 33.5, 33.2), 32.1(d), 31.7(t), 3 × 25.8(q), 6 × 18.1(q), 17.7(s), 14.1(q), 13.3(q), 13.2(q), 3 × 12.2(d), 3 × 7.0(q), 3 × 6.2(t), 6.0(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1691.2015 ([M + Na]$^+$ $C_{78}H_{124}{}^{79}BrO_{17}N_2F_6PSi_3Na$ requires 1691.6931).

Phorboxazole macrolide (106). A suspension of anhydrous K_2CO_3 (11.4 mg, 82.6 μmol) in 18-crown-6 (90 mg, 0.34 mmol) and toluene (5 ml) was stirred at room temperature for 5 h. A solution of the aldehyde-phosphonate (**105**) (10.0 mg, 6.0 μmol) in toluene (4 ml) was added over 15 min to the suspension *via* cannula, and the mixture was stirred at room temperature for 30 min and then poured into brine and extracted with ethyl acetate. The combined organic extracts were washed with brine, then dried and concentrated *in vacuo*. The oily residue was purified by chromatography (Pasteur pipette) on silica using 10–40% ethyl acetate in petrol ether as eluant to give the *macrolide* (6.9 mg, 82%); as an oily 3 : 1 mixture of *Z*/*E* isomers; $[a]_D^{20}$ −2.45 (*c* 0.5 in $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 2935, 2860, 1719, 1462, 1101, 1089; ^{1}H NMR (500 MHz) major isomer δ 7.47 (1H, s, oxC*H*), 7.42 (1H, s, oxC*H*), 6.71 (1H, ddd, *J* 16.1, 9.6, 6.2, CH_2C*H*=CHox), 6.30 (1H, d, *J* 16.1, CH=C*H*ox), 6.23 (1H, s, oxC=C*H*), 6.20 (1H, m), 6.18 (1H, d, *J* 15.5, CH=C*H*CCH$_3$), 6.11 (1H, d, *J* 13.6, =C*H*Br), 5.43 (1H, dd, *J* 15.7, 8.1, CH(OCH$_3$)C*H*=CH), 5.41 (1H, d, *J* 8.5, =C*H*CH(OTBS)), 5.00 (1H, b s, =CH_2), 4.64 (1H, b s, =CH_2), 4.53 (1H, dd, *J* 11.1, 4.2, (CH$_3$)CHC*H*CH(CH$_3$)), 4.46 (1H, dd, *J* 8.9, 5.0), 4.40 (1H, b s, C*H*OSi(CH(CH$_3$)$_2$)$_3$), 4.18 (1H, m), 3.95–4.12 (1H, m), 3.82–3.78 (2H, m), 3.58 (1H, d, *J* 10.2, OC*H*), 3.33 (3H, s, OC*H*$_3$), 3.27 (3H, s, OC*H*$_3$), 3.17 (1H, d, *J* 14.2, C(OTES)CH_2ox), 3.10 (1H, d, *J* 14.2, C(OTES)CH_2ox), 2.73 (1H, b d, *J* 12.4), 1.97 (3H, s, CH=CCH_3), 1.77 (3H, s, CH=CCH_3), 1.14–1.00 (21H, m, Si(C*H*(CH$_3$)$_2$)$_3$), 0.98 (9H, t, *J* 7.8, Si(CH$_2$C*H*$_3$)$_3$), 0.87 (9H, s, SiC(C*H*$_3$)$_3$), 0.78 (3H, d, *J* 6.4, CHC*H*$_3$), 0.69 (6H, q, *J* 8.0, Si(CH_2CH$_3$)$_3$), 0.05 (3H, s, Si(C*H*$_3$)$_2$), −0.003 (3H, s, Si(C*H*$_3$)$_2$); ^{13}C NMR (125 MHz) major isomer δ 165.6(s), 161.3(s), 159.6(s), 144.3(d), 142.3(s), 141.7(s), 137.8(d), 137.6(s), 136.9(s), 136.1(d), 134.1(d), 133.9(d), 133.7(d), 132.9(d), 127.3(d), 121.0(d), 119.3(d), 119.2(d), 110.1(t), 106.2(d), 99.0(s), 89.3(d), 81.3(d), 79.4(d), 77.9(d), 77.2(d), 73.7(d), 73.5(d), 71.1(d), 69.1(d), 68.7(d), 67.0(d), 65.8 (d), 64.9(d), 56.3(q), 55.4(q), 41.9(t), 41.3(t), 40.7(t), 40.1(t), 39.2(t), 38.9(t), 37.0(t), 35.8(t), 34.4(t), 32.5(d), 31.7(t), 30.4(t), 3 × 25.8(q), 6 × 18.1(q), 17.7(s), 14.1(q), 13.3(q), 13.3(q), 3 × 12.2(d), 3 × 7.0(q), 3 × 6.2(t), 6.0(q), −4.5(q), −4.8(q); *m/z* (ESI) Found 1429.7211 ([M + Na]$^+$ $C_{74}H_{119}{}^{79}BrO_{13}N_2F_6Si_3Na$ requires 1429.7101).

Phorboxazole A (1). A solution of tetrabutylammonium fluoride (1.0 M) in THF (4.5 μl) was added to a solution of the silyl-protected macrolide (**106**) (6.30 mg, 4.5 μmol) in THF (1.2 ml) at 0 °C, and the mixture was stirred at 0 °C for 30 min and then at room temperature for 50 min. A solution of fresh tetrabutylammonium fluoride (20 μmol, 1.0 M) in THF (20 μl) was added and the mixture was stirred at room temperature for a further 1.5 h. The mixture was quenched with saturated aqueous ammonium chloride (3 ml) and then poured into a mixture of methylene chloride–brine and extracted with methylene chloride and ethyl acetate. The combined organic extracts were dried, and then concentrated *in vacuo*. The residue was purified by chromatography (Pasteur pipette) on silica using 1 : 2 petrol ether in ethyl acetate as eluant, followed by 0–10% methanol in ethyl acetate, to give *macrolide* (3.5 mg, 75%; 3 : 1 *Z*/*E*) as a pale yellow, amorphous solid. The macrolide was further purified using a reverse phase Zorbax SB-C18 column (4.6 × 150 mm), eluting with 80 : 20 MeOH–H_2O at 0.6 ml min^{-1} to give pure *phorboxazole A* (2.3 mg) as an almost colourless amorphous solid: $[a]_D^{20}$ + 43.3 (*c* 0.12 in $CHCl_3$) (lit.[1a] + 44.8 (*c* 1.0 in MeOH) ν_{max} (neat/NaCl)/cm^{-1} 3378, 2925, 1715, 1376, 1188, 1154, 1089; ^{1}H NMR (500 MHz) δ 7.58 (1H, s, oxC*H*), 7.43 (1H, s, oxC*H*), 6.70 (1H, ddd, *J* 15.9, 9.7, 6.3, CH_2C*H*=CHox), 6.30 (1H, d, *J* 15.9, CH_2CH=C*H*ox), 6.25 (1H, s, oxC=C*H*), 6.20 (1H, d, *J* 15.8, =C*H*CCH$_3$), 6.14–6.18 (1H, m, C*H*=CHBr), 6.10 (1H, d, *J* 13.6, =C*H*Br), 5.92 (2H, m, C*H*=C*H*CO$_2$), 5.51 (1H, dd, *J* 15.7, 7.7, CH(OCH$_3$)C*H*=CH), 5.37 (1H, d, *J* 9.0, =C*H*CH(OTBS)), 5.31 (1H, d, *J* 2.4, OH), 5.00 (1H, b s, =CH_2), 4.75 (1H, dd, *J* 10.0, 3.6, OC*H*), 4.63 (1H, b s, =CH_2), 4.53 (1H, dd, *J* 11.2, 4.4, (CH$_3$)CHC*H*CH(CH$_3$)), 4.36–4.42 (1H, m), 4.32 (1H, dd, *J* 8.4, 8.4, =C*H*OH), 4.18 (1H, b ddd, *J* 12.5, 4.8, 4.8), 4.08 (1H, dddd, *J* 11.5, 11.5, 3.1, 3.1), 3.99 (1H, m), 3.81 (1H, ddd, *J* 12.0, 8.4, 2.0), 3.77 (1H, dddd, *J* 11.1, 11.1, 4.6, 4.6), 3.66 (1H, ddd, *J* 7.7, 6.5, 6.5), 3.59 (1H, d, *J* 10.2), 3.55 (1H, b dd, *J* 11.3, 5.6), 3.50 (1H, m), 3.37 (3H, s, OC*H*$_3$), 3.27 (3H, s, OC*H*$_3$), 3.16 (1H, d, *J* 15.5, C(OH)CH_2ox), 3.09 (1H, d, *J* 15.5, C(OH)CH_2ox), 2.72 (1H, b d, *J* 12.3), 2.54 (1H, ddd, *J* 12.5, 10.2, 5.2), 2.28 (1H, m), 2.07 (1H, b d, *J* 12.7), 1.99 (3H, s, CH=CCH_3), 1.86–1.90 (1H, m), 1.82 (3H, s, CH=CCH_3), 1.72 (1H, b d, *J* 13.6), 1.43–1.47 (1H, m), 1.37 (1H, dd, *J* 12.0, 12.0, 1.5), 1.12 (1H, ddd, *J* 12.0, 11.8, 11.8), 0.97 (3H, d, *J* 6.9, CHC*H3*), 0.77 (3H, d, *J* 6.5, CHC*H3*); ^{13}C NMR (125 MHz) δ 165.6 (s), 161.3 (s), 160.1 (s), 144.4 (d), 142.1 (s), 141.7 (s), 138.0 (s), 137.5 (s), 137.6 (s), 137.0 (d), 135.9 (d), 134.1 (d), 133.7 (d), 133.7 (d), 129.7 (d), 128.9 (d), 121.0 (d), 119.3 (d), 118.5 (d), 110.1 (t), 106.4 (d), 96.6 (s), 89.2 (d), 81.1 (d), 79.3 (d), 78.0 (d), 73.5 (d), 73.0 (d), 72.5 (d), 70.9 (d), 69.1 (d), 68.6 (d), 66.9 (d), 64.4 (d), 56.4 (q), 55.8 (q), 41.3 (t), 40.5 (t), 39.7 (t), 39.2 (t), 38.9 (t), 39.0 (t), 36.9 (t), 35.0 (t), 34.3 (t), 33.1 (t), 32.5 (d), 31.7 (d), 30.5 (t), 14.2 (q), 13.4 (q), 13.3 (q), 6.0 (q); *m/z* (ESI) Found 1045.4053 ([M + Na, ^{79}Br]$^+$ $C_{53}H_{71}N_2O_{13}{}^{79}BrNa$ requires 1045.4037).

Acknowledgements

We thank the EPSRC (Fellowships to DSM and TY) and the University of Nottingham (Fellowships to MAG and PBL) for support of this work. We also thank Merck, Sharp and Dohme, and Pfizer Ltd (Studentships to ATP and JAT) for their continued financial support, and Dr S Jayaprakash and D. J. Sinclair for their contributions to some of the experimental work.

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