Total synthesis of 7-

DOI:

[10.1039/c7ob02129a](https://doi.org/10.1039/c7ob02129a)

Document Version

Accepted author manuscript

[Link to publication record in Manchester Research Explorer](#)

Citation for published version (APA):

Green, A. P., Hardy, S., Lee, A. T. L., & Thomas, E. J. (2017). Total synthesis of 7-: Des-O -pivaloyl-7- O -benzylbryostatin 10. *Organic and Biomolecular Chemistry*, 15(44), 9497-9526. <https://doi.org/10.1039/c7ob02129a>

Published in:

Organic and Biomolecular Chemistry

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Total synthesis of 7-*des*-O-pivaloyl-7-O-benzylbryostatin 10

Anthony P. Green,^a Simon Hardy,^a Alan T. L. Lee^a and Eric J. Thomas^{a*}

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

The first total synthesis of a 20-deoxybryostatin, namely 7-*des*-O-pivaloyl-7-O-benzylbryostatin 10 is described. Preliminary studies demonstrated that the modified Julia reactions of 2-benzothiazolylsulfones, corresponding to the C17-C27 fragment, with aldehydes, corresponding to the C1-C16 fragment, provide an efficient and stereoselective assembly of advanced intermediates with the (*E*)-16,17-double-bond. The synthesis of the C1-C16 fragment was then modified so that the C1 acid was present as its allyl ester before the Julia coupling. A more efficient synthesis of the C17-C27 sulfone was developed in which a key step was the bismuth mediated coupling of an allylic bromide with an aldehyde in the presence of an acrylate moiety in the allylic bromide. A scaleable synthesis of an advanced macrolide was completed using the modified Julia reaction followed by selective deprotection and macrolactonisation. The final stages of the synthesis required selective hydroxyl deprotection and the introduction of the sensitive C19-C21 unsaturated keto-ester functionality. Unexpected selectivities were observed during studies of the hydroxyl group deprotections. In particular, cleavage of tri-isopropylsilyl ethers of the exocyclic primary allylic alcohols was observed in the presence of the triethylsilyl ether of the secondary alcohol at C19. Model studies helped in the design of the methods used to introduce the C19-C21 keto-ester functionality and led to the completion of a total synthesis of close analogue of bryostatin 10 in which a benzyloxy group rather than the pivaloyloxy group was present at C7.

Introduction

The total synthesis of bryostatins has been of considerable interest because of the biological activities of these macrolides and the difficulties of harvesting them from natural sources.^{1,2} The first total synthesis of a bryostatin was based on a convergent strategy that involved the assembly of the macrolide using a classical Julia reaction to prepare the 16,17-double-bond followed by macrolactonisation and led to a synthesis of bryostatin 7, see Figure 1.³ Subsequently improved syntheses of the two fragments were developed so completing a formal synthesis.⁴ This strategy was also applied to a total synthesis of bryostatin 3 that provided *ca.* 25 mg for biological studies.⁵ The Julia reaction was a key reaction in the total synthesis of bryostatin 2, in this case for the preparation of the C10-C27 fragment.⁶ Bryostatin 16 was prepared using an imaginative palladium catalysed diyne coupling to assemble the macrolide.⁷ A convergent synthesis of bryostatin 1 has been completed that uses a pyran annulation to synthesize the B-ring followed by macrocyclisation.⁸ A similar strategy was employed later in a

Figure 1 The structures of representative bryostatins prepared by total synthesis

^a The School of Chemistry, The University of Manchester, Manchester M13 9PL, UK

* Corresponding author; tel: +44 (0)161 275 4613; e-mail: e.j.thomas@manchester.ac.uk

Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Figure 2 Bryostatin 10, a naturally occurring 20-deoxybryostatin, showing the disconnections into the C1-C16 and C17-C27 fragments.

particularly efficient synthesis of bryostatin 7 which featured hydrogenative C-C coupling.⁹ In a synthesis of bryostatin 9, see Figure 1, an intramolecular Prins reaction was employed to form the B-ring with the advantage that only three steps were required to complete the synthesis after the assembly steps.¹⁰ These syntheses constitute seminal achievements in the context of the total synthesis of natural products and cancer chemotherapy. Moreover, synthetic analogues have been prepared that have either tumour suppressing, bryostatin-like, activity, or tumour promoting, phorbol-like, activity.^{11,12}

The 20-deoxybryostatins, e.g. bryostatin 10, see Figure 2, constitute a subset of bryostatins that have not been widely studied by synthetic chemists even though they retain most of the biological activities of their more oxygenated congeners.¹³ Therefore we identified the 20-deoxybryostatins as attractive targets for total synthesis.

We have reported syntheses of C1-C16 and C17-C27 fragments that could be used in either Julia or ring-closing metathesis based syntheses of bryostatin 10.^{14,15} However, the classical Julia reaction is difficult to optimise for a convergent synthesis because several steps have to be deferred until after the assembly steps,^{3,5,6} and ring closing metathesis was not useful for the synthesis of bryostatins with the geminal methyl groups at C18^{16,17} although it may be useful for synthesis of the recently isolated 18-monomethylbryostatins.^{1e}

For these reasons, a modified approach to bryostatin 10 was investigated that was based on an assembly using C1-C10 and C11-C27 fragments.¹⁸ During the course of this work, the modified Julia reaction¹⁹ was found to be significantly more useful than the classical Julia reaction for the synthesis of the C11-C19 intermediate **4** from the aldehyde **1**, see Figure 3. The construction of the C16-C17 bond of bryostatins using Julia reactions involving 17-sulfones is known to be sensitive to steric and structural effects with lower yields being observed for more advanced intermediates.⁶ Nevertheless, it was decided to investigate the viability of a synthesis of 20-deoxybryostatins using the modified Julia reaction for a convergent late-stage assembly from C1-C16 and C17-C27 fragments. The results of these investigations are reported herein.^{20,21}

Figure 3 Modified and conventional Julia reactions used for the synthesis of a bryostatin intermediate.¹⁸

Results and discussion

Preliminary studies to confirm the viability of the approach

The C1-C16 fragment **16** was prepared as outlined in Scheme 1 using chemistry developed earlier¹⁴ but with different protecting groups. The alcohol **5** was available in two steps from the 4-methoxybenzyl ether of (*S*)-glycidol and was protected as its triethylsilyl ether **6**. Following ester reduction to the alcohol **7**, silylation gave the tri-isopropylsilyl ether **8** that was converted into the aldehyde **10** by selective hydroxylation using AD-mix β and cleavage of the ensuing diol **9** using lead(IV) acetate. A Wadsworth-Emmons-Horner reaction with the ketophosphonate **11**¹⁴ using barium hydroxide as the base gave the α,β -unsaturated ketone **12**. Selective removal of the triethylsilyl ether then gave the alcohol **13** that was cyclised stereoselectively by treatment with potassium *tert*-butoxide to give the *cis*-2,6-disubstituted tetrahydropyran **14**. This was taken through to the methoxyacetal **15** using trimethyl orthoformate and pyridinium toluene *p*-sulfonate in methanol and protection gave the *tert*-butyldimethylsilyl ether **16**.

This bicyclic acetal corresponds to the C1-C16 fragment of the bryostatins with the longest sequence from (*R*)-pantolactone¹⁴ being 18 linear steps. Structures were assigned to the intermediates in this synthesis by analogy with earlier work¹⁴ and were consistent with spectroscopic data.

It was now necessary to check that the modified Julia reaction was reliable for the introduction of the 16,17-(*E*)-double-bond using C1-C16 aldehydes. The PMB-ether **16** was deprotected using DDQ to give the alcohol **17** with little hydrolysis of the methoxyacetal being observed in this case even though no phosphate buffer was used.¹⁴ A Dess Martin oxidation then gave the aldehyde **18** and a modified Julia reaction of this aldehyde with the sulfone **19**¹⁸ gave the alkene **20** in a reasonable yield, albeit as a mixture of (*E*)- and (*Z*)-isomers, ratio 2:1, see Scheme 2.

Scheme 1 Synthesis of the C1-C16 fragment Reagents and conditions i, imid., TESCl, DCM, rt, 16 h (77%); ii, DIBAL-H, heptanes, THF, -78°C , 4 h; iii, imid., TIPSCl, DCM, rt, 16 h (91% from **6**); iv, AD-mix β , OsO_4 , $t\text{BuOH}$, H_2O , 0°C , 24 h (77%; 3:2); v, $\text{Pb}(\text{OAc})_4$, py., DCM, rt, 1 h; vi, **11**, $\text{Ba}(\text{OH})_2 \cdot 0.8\text{H}_2\text{O}$, THF, rt, 2 h, add **10**, THF, H_2O , rt, 16 h (73% from **9**); vii, HF.py., py., THF, rt, 30 min; viii, $t\text{BuOK}$, THF, rt, 5 min (74% from **12**); ix, $\text{HC}(\text{OMe})_3$, DCM, MeOH, PPTS, rt, 16 h (88%); x, TBSOTf, 2,6-lut., DCM, -78°C , 2 h (86%).

Scheme 2 A modified Julia reaction of the C1-C16 aldehyde **18** Reagents and conditions i, DDQ, DCM, methanol, rt, 2 h (70%); ii, TPAP, NMO, 4 Å sieves, rt, 2 h; iii, **19**, -78°C , LiHMDS, 30 min, add **18**, THF, rt 16 h [78%; (*E*):(*Z*) = 2:1].

The (*E*)-stereoselectivity of the Julia reaction of sulfone **19** with aldehyde **18** was lower than expected from previous work using sulfone **19**¹⁸ but it was not optimised. Moreover, as the 20-deoxybryostatins remained our prime objectives, base promoted reactions of the dithiane **20** with aldehydes¹⁸ for a synthesis of 20-oxygenated bryostatins were not studied at this stage. Instead it was decided to investigate the modified Julia reaction of aldehyde **18** with a fully developed C17-C27 sulfone to assess the viability of the modified Julia reaction for a fully convergent synthesis of bryostatins.²² To expediate this work, rather than develop a completely new synthesis of a sulfone, it was decided to make use of the C20-C27 alcohol **21** that was available from earlier studies¹⁵ in multigram quantities, see Scheme 3.

The alcohol **21** was protected as its *tert*-butyldimethylsilyl ether **22** and debenzoylation using lithium naphthalenide gave

Scheme 3 Synthesis of the sulfone **32** Reagents and conditions i, TBSOTf, 2,6-lut., DCM, 0°C , 1 h (89%); ii, Li, naphthalene, THF, rt, 2 h, add to **22**, THF, -20°C (88%); iii, Ph_3P , CBr_4 , DCM, 0°C , 10 min (92%); iv, NaCN , DMF, 0°C , 3.5 h (**25**, 71%; recovered **24**, 24%); v, DIBAL-H, heptanes, THF, -78°C , 45 min, aq. NH_4Cl , EtOAc, rt, 30 min; vi, $\text{Me}_2\text{CHCO}_2\text{Me}$, LDA, THF, -78°C , 70 min, add **26**, THF, -78°C , 30 min, rt, 30 min (52% from **25**); vii, TESCl, imid., DMF, rt, 16 h (76%); viii, DIBAL-H, heptane, toluene, -78°C , 1.5 h (80%); ix, 2-BTSH, THF, Ph_3P , DIAD, rt, 24 h (93%); x, $t\text{PrOH}$, EtOH, $\text{Mo}_7\text{O}_{24}(\text{NH}_4)_6 \cdot 4\text{H}_2\text{O}$, 30% w/w H_2O_2 , rt, 72 h (**31**, 50%; **32**, 41%).

the primary alcohol **23** that was converted into the bromide **24**. Displacement of the bromide using sodium cyanide in *N,N*-dimethylformamide²³ gave the nitrile **25**. This reaction was clean if allowed to proceed to 70% completion, but attempts to drive it further led to decomposition. Reduction of the nitrile **25** with *in situ* hydrolysis gave the β,γ -unsaturated aldehyde **26** that was found to be unstable to chromatography and so was reacted immediately with lithiated methyl 2-methylpropanoate.²⁴ The aldol adduct **27** was isolated from this reaction in yields of ca. 50–60% from the nitrile **25** as a 50:50 mixture of epimers, and was protected as its triethylsilyl ether **28**. The ester was then reduced to the alcohol **29** that was converted into the 2-benzothiazolyl sulfide **30** using a Mitsunobu reaction. Oxidation to the required sulfone **32** was carried out in a mixture of isopropanol and ethanol to ensure that the sulfide **30** and the ammonium molybdate were in solution, but was found to be very slow and gave mixtures of the diastereoisomeric sulfoxides **31** and the sulfone **32** although the sulfoxides could be converted into the sulfone on further oxidation, see Scheme 3.

The reactivity of the sulfone **32** with aldehydes was first evaluated using butanal. With lithium hexamethyldisilazide as the base and an excess of butanal, an excellent yield of the (*E*)-diene **33** was obtained, see Scheme 4. The (*Z*)-isomer was detected as just a minor product from this reaction.

For the Julia reaction between aldehyde **18** and sulfone **32**, two equivalents of the sulfone were used and lithium hexamethyldisilazide as the base. The alkene **34** was obtained in

a yield of 60% based on the aldehyde **18**, with excellent (*E*)-stereoselectivity, as a 2:1 mixture of 19-epimers. The excess of the sulfone was recovered, see experimental. The formation of a 2:1 mixture of epimers of the alkene **34** from the 1:1 mixture of epimers of the sulfone **32**, indicated that some kinetic resolution had accompanied the Julia reaction. That the two products were epimers was established by selective cleavage of the triethylsilyl ether using pyridinium toluene *p*-sulfonate in methanol-trimethyl orthoformate, conditions that were known to retain the methoxy acetal,²⁵ to give the alcohol **35**, still a 2:1 mixture of epimers. Oxidation of this mixture using the Dess Martin reagent, buffered using solid sodium hydrogen carbonate to avoid enolisation of the skipped enone, gave the ketone **36**, now as a single compound, see Scheme 4.

This preparation of the alkene **34** confirmed that the modified Julia reaction can be used to prepare advanced intermediates for a convergent synthesis of a 20-deoxybryostatin. However, the alkene **34** was difficult to synthesise on a sufficiently large scale to enable a total synthesis of a 20-deoxybryostatin to be completed. In particular, a shorter and more efficient synthesis of the sulfone **32** was required. The introduction of an ester at C1 in the C1–C16 aldehyde would also reduce the number of steps required after the Julia reaction making the synthesis more convergent overall.

Development of a scaleable synthesis of the core of a 20-deoxybryostatin

To prepare a C1–C16 aldehyde with an ester at C1, the ketophosphonate **11** was desilylated to give the primary alcohol **37**. A Horner-Wadsworth-Emmons reaction of this ketophosphonate with the aldehyde **10** under the usual conditions gave the α,β -unsaturated ketone **38** that was selectively deprotected to give the diol **39**. However, on attempted purification of this diol by chromatography cyclisation occurred, and the 2,6-*trans*-disubstituted tetrahydropyran **40** was isolated, the 2,6-*trans*-configuration being established by ¹H NMR. Such a facile cyclisation had not been observed for enones that had been prepared previously in which the primary hydroxyl group had been silylated.¹⁴ These enones only cyclised on treatment with potassium *tert*-butoxide in THF^{14,26} and then gave 2,6-*cis*-disubstituted tetrahydropyrans. Indeed, treatment of the crude diol **39** with potassium *tert*-butoxide gave the required 2,6-*cis*-disubstituted tetrahydropyran **41**, *cf.* the base promoted cyclisation of the crude enone **13** as shown in Scheme 1. The 2,6-*trans*-isomer **40** is believed to be the kinetic product of the oxy-Michael addition of diol **39** whereas the *cis*-isomer **41** is the thermodynamic product,^{14,26} see Scheme 5.

The next step in the synthesis was the transacetalisation of the *cis*-2,6-disubstituted tetrahydropyran **41** using trimethyl orthoformate under mildly acidic conditions in methanol.¹⁴ However, the only products isolated from this reaction were the epimeric ortho-esters **42a,b** in which the hydroxyl groups at C1 and C3 had been trapped by the trimethyl orthoformate. If the orthoformate was omitted from this reaction, the required diol

Scheme 4 Assembly of the bryostatin core using a modified Julia reaction Reagents and conditions i, **32**, LiHMDS, toluene, THF, -78°C , to -60°C , 30 min, add butanal, THF, -78°C to rt, 1 h (85% based on **32**); ii, **32** (2 equiv.), LiHMDS, -78°C to -60°C , 30 min, add **18**, THF, -78°C , 20 min, rt, 30 min (**34**, 64%, 2:1 mixture of epimers; recovered **32**, 44%); iii, $\text{HC}(\text{OMe})_3$, PPTS, MeOH, THF, rt, 3 d (65%, 2:1 mixture of epimers); iv, Dess Martin periodinane, NaHCO_3 , DCM, rt, 45 min (85%).

Scheme 5 Attempted synthesis of a C1-C16 fragment using intermediates with a free alcohol at C1. Reagents and conditions: i, TBAF, THF, rt, 16 h (*ca.* 100%); ii, **37**, Ba(OH)₂·0.8H₂O, rt, 30 min, add **10**, rt, 16 h; iii, HF.py., THF, 0 °C, 25 min then chromatography; iv, KO^tBu, THF, rt, 5 min (**41**, 49% from **37**); v, HC(OMe)₃, PPTS, DCM, MeOH, rt, 16 h (**42a,b**, 1:1, 32%); vi, PPTS, MeOH, DCM, rt, 16 h (**43**, 41%; **44**, 20%).

43 was obtained but was accompanied by substantial amounts of the acetone **44**, see Scheme 5.

These results had shown that the primary alcohol at C1 was compatible with the Horner-Wadsworth-Emmons and oxy-Michael reactions but it complicated attempts to prepare the methoxyacetal **43**. To avoid this difficulty, the hydroxyl group of the 2,6-*cis*-disubstituted tetrahydropyran **41** was oxidised *via* the aldehyde to the carboxylic acid **45**. Conversion to the allyl ester **46** was then achieved using allyl bromide under basic conditions. The transacetalisation using trimethyl orthoformate now gave the required methoxyacetal **47** and silylation of the 3-hydroxyl group gave the *tert*-butyldimethylsilyl ether **48**. Oxidative cleavage gave the C1-C16 fragment **49** with the free hydroxyl group at C16 and the allyl ester at C1, Scheme 6.

It would improve the synthesis of sulfone **32** significantly if the sulfonyl moiety could be carried through most of the synthesis to avoid a late-stage sulfide to sulfone oxidation in the presence of the trisubstituted double bond. The alcohol **50** was therefore identified as a possible intermediate for a synthesis of the required sulfone **32** as esterification, ring-closing metathesis and reduction,¹⁸ could be used to introduce the trisubstituted alkene, see Figure 4.

Scheme 6 Completion of a synthesis of the C1-C16 fragment **49**. Reagents and conditions: i, (a) Dess Martin periodinane, py., DCM, rt, 1 h (b) NaClO₂, NaH₂PO₄·2H₂O, 2-methylbut-2-ene, ^tBuOH, rt, 1 h; ii, NaHCO₃, CH₂=CHCH₂Br, DMF, 70 °C, 16 h (70% from **41**); iii, HC(OMe)₃, PPTS, MeOH, rt, 16 h (66%); iv, TBSOTf, 2,6-lut., DCM, -78 °C, 1 h (84%); v, DDQ, DCM, MeOH, rt, 2 h (72%).

Figure 4 Outline of a modified approach to the sulfone **32**.

The addition of an organometallic reagent derived from the bromide **51** to the known aldehyde **52**¹⁸ followed by a protecting group exchange was seen as a possible synthesis of intermediate **50**. However, one concern with this approach was that the alkoxide formed during this addition step could react with the 2-benzothiazolyl sulfone and lead to decomposition. Nevertheless, this synthesis of sulfone **32** was investigated.

The alcohol **53** was available on a multigramme scale in six steps from methyl (*E*)-pent-3-enoate¹⁸ and was protected as its triethylsilyl ether **54** before the reductive removal of the benzyl ether to give the alcohol **55**. This was converted into the bromide **56** under Appel conditions.²⁷ Preliminary studies into the use of indium powder in DMF/water/THF²⁸ for the coupling

of bromide **56** with a model aldehyde, pivaldehyde, were unsuccessful and gave returned bromide. However, under Nozaki-Hiyama-Kishi conditions,²⁹ the required alcohol **57** was obtained as a mixture of epimers using the bromide **56** and an excess of the aldehyde **52**.¹⁸ Oxidation of this mixture of epimers **57** gave the ketone **58**. This β,γ -unsaturated ketone was unstable to chromatography, even using base-washed silica, but was characterised after rigorous washing. After protection of the alcohol **57** as the *tert*-butyldimethylsilyl ether **59**, selective removal of the triethylsilyl ether gave the alcohol **60** that was esterified to give the acrylate **61**. Ring-closing metathesis^{18,30} now gave the lactone **62** and reduction under Luche conditions gave the diol **63**. This reduction was rather slow and required hourly addition of aliquots of sodium borohydride and cerium(III) chloride to drive it to completion, but gave the diol **63** in a yield of 83%, see Scheme 7.

Scheme 7 Synthesis of the C17-C27 diol **63** Reagents and conditions i, TESCl, imid., DCM, rt, 1 h (98%); ii, Li, naphthalene, THF, rt, 2 h, add to **54**, THF, -25°C (97%); iii, Ph_3P , CBr_4 , Et_3N , DCM, 0°C , 20 min (95%); iv, **56**, **52**, CrCl_2 , THF, rt, 15 h (**57**, 63%); v, Dess-Martin periodinane, NaHCO_3 , DCM, rt, 1 h (ca. 100%); vi, TBSOTf, 2,6-lut., DCM, 0°C to rt, 2.5 h (86%); vii, PPTS, MeOH, THF, rt, 24 h (73%); viii, $\text{CH}_2=\text{CH.C}(\text{O})\text{Cl}$, $i\text{-Pr}_2\text{NEt}$, DCM, 0°C to rt, 1 h (ca. 100%); ix, Grubbs' II cat., DCE, reflux, 8 h (**62**, 52%; **61**, 39%); x, $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, NaBH_4 , MeOH, THF, rt, 10 h (83%).

This synthesis had shown that the reactions of allylic organometallics with the aldehyde **52** can be carried out without participation of the benzothiazolyl sulfone and that the product can be taken through the RCM sequence. However, to shorten the synthesis, the addition of an allylic organometallic reagent with the aldehyde **52** in the presence of an acrylate in organometallic reagent was investigated. This was a risky approach since the organometallic reactant could react intramolecularly with the acrylate, a reactive electrophile, even before the addition of the aldehyde. Nevertheless, the TES-protected bromide was deprotected to give the alcohol **64** that was converted into its acrylate **65**, see Scheme 8. However, indium mediated reactions of this bromide with the aldehyde **52** gave mixtures of products.

In a separate programme,³¹ bismuth(0) mediated reactions of 5-alkoxy-2-enyl bromides with aldehydes have been found to proceed with useful levels of 1,5-stereocontrol. Promotion of the reaction of the bromide **65** with the aldehyde **52** by bismuth(III) iodide and zinc dust was therefore investigated. This reaction did not proceed with remote stereocontrol but was successful in that a reasonable yield of a mixture of the epimers of the required alcohol **66** was obtained.

Scheme 8 Synthesis of the C17-C27 sulfone **32** Reagents and conditions i, PPTS, $\text{HC}(\text{OMe})_3$, MeOH, THF, rt, 3 h (95%); ii, $\text{CH}_2=\text{CH.C}(\text{O})\text{Cl}$, $i\text{-Pr}_2\text{NEt}$, DCM, 0°C , 40 min (97%); iii, BiI_3 , zinc powder, THF, rt, 75 min, add NaHCO_3 , **52** and **65**, heat under reflux, 4.5 h; iv, TESCl, imid., DCM, rt, 1.5 h (61% from **65**; 55:45); v, Grubbs' II cat., DCE, heat under reflux, 20 h (90%); vi, $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, NaBH_4 , MeOH, THF, 0°C to rt, 1.5 h (75%); vii, TIPSCl, imid., DCM, rt, 12 h (86%); viii, TBSOTf, 2,6-lut., DCM, rt, 2 h (93%).

The formation of this mixture of epimers was not surprising because of the relative complexity of bromide **65** for remote stereochemical control.³¹ Nevertheless this coupling had given the required product in the presence of the reactive acrylate.

The alcohol **66** was not purified but was immediately converted into its triethylsilyl ether **67** that was isolated in a *ca.* 60% yield based on the bromide **65**. Ring-closing metathesis using the Grubbs' II catalyst³⁰ gave the lactone **68** and reduction of the lactone under Luche's conditions gave the diol **69** that had the required (*E*)-trisubstituted double bond and more labile triethylsilyl group protecting the alcohol due to become the 19-ketone. Protection of the more accessible primary alcohol then provided the tri-isopropyl silyl ether **70** and further silylation gave the required C17-C27 sulfone **32**, Scheme 8.

The structures assigned to the products in this sequence were consistent with spectroscopic data. The C17-C27 sulfone **32** was now available on a multigram scale. The stage was therefore set for the crucial assembly phase of the synthesis.

Oxidation of the alcohol **49** gave the aldehyde **71**. The modified Julia reaction of this aldehyde with the sulfone **32** mediated with lithium hexamethyldisilazide was very efficient and gave the (*E*)-alkene **72** in an 80% yield, Scheme 9. However, attempts to cleave the 2-trimethylsilylethoxymethyl (SEM) ether selectively using magnesium bromide diethyl etherate and *n*-butanethiol prior to macrocyclisation, conditions that were known to be compatible with the other silyl protecting groups,^{15,32} were complicated by substitution of the methoxy group of the acetal by a thiobutyl substituent. Rather than attempt to use the thioacetal so formed or modify the reaction

Scheme 9 Modified Julia assembly using aldehyde **71** Reagents and conditions i, $\text{SO}_3\cdot\text{py.}$, DMSO, Pr_2NET , DCM, rt, 1 h (60%); ii, **32**, LiHMDS, THF, -78°C to -60°C , 30 min, add **71**, THF, -78°C , 1 h, rt, 20 min (80%).

conditions, it was decided to replace the SEM-ether by a more labile protecting group before the Julia step.

The 2-trimethylsilylethoxymethyl protecting group was removed from the sulfone **32** to give the alcohol **73**, Scheme 10. An attempted Julia reaction of this sulfone with the aldehyde **71** gave an intractable mixture of products and so the alcohol **73** was converted into its trimethylsilyl ether **74**. The modified Julia reaction of this sulfone **74** with the aldehyde **71** was carried out

Scheme 10 Synthesis of the advanced macrocyclic intermediate **78** Reagents and conditions i, K_2CO_3 , $n\text{BuSH}$, $\text{MgBr}_2\cdot\text{Et}_2\text{O}$, rt, 1 h (96%); ii, TMSCl , Et_3N , DCM, 0°C to rt, 3 h (*ca.* 100%); iii, **74**, LiHMDS, THF, -78°C to -60°C , 30 min, add **71**, -78°C , 1 h, rt, 20 min; iv, PPTS , HC(OMe)_3 , MeOH, DCM, rt, 1 h (60% from alcohol **49**); v, $\text{Pd(PPh}_3)_4$, morpholine, THF, rt, 16 h; vi, Et_3N , THF, 0°C , add 2,4,6- $\text{Cl}_3\text{C}_6\text{H}_2\text{(O)Cl}$, THF, rt, 16 h, added in toluene/THF slowly to DMAP in toluene at 40°C over 12 h (85% from **76**).

using an excess of the sulfone and gave a mixture of the (*E*)-alkene **75** together with the recovered sulfone. This mixture was immediately desilylated using pyridinium toluene *p*-sulfonate in the presence of trimethyl orthoformate, conditions that retained the methoxycetal, to provide the alcohol **76** in a 60% overall yield from the alcohol **49**. The allyl ester was now cleaved using a palladium(0) catalyst to give the seco-acid **77** and cyclisation using a modified Yamaguchi reaction gave the macrolide **78** in an excellent yield, see Scheme 10. The macrolide **78** was now available on the two hundred milligramme scale and so its conversion into a bryostatin could be investigated.

Preliminary studies of deprotection and selective oxidation

The 20-deoxybryostatins differ from the other members of the series in having a methylene group at C20 rather than an acyloxy group. This minor structural change affects the chemistry of the C18-C27 fragment. For example, attempts to protect the ketone at C19 as a methoxyacetal are complicated by dehydration.¹⁵ This is why the oxygenated substituents at C19 and C23 had to be carried through the synthesis as distinguishable silyl-ether protected alcohols as in the macrolide **78**. Such subtle differences meant that the final steps of the total syntheses of the other bryostatins, although of interest, could not be applied directly to complete a synthesis of a 20-deoxybryostatin.

Amongst the issues that had to be addressed was the choice of the final step used to introduce the C18-C27 fragment, *cf.* the unsaturated ester **79**. At the onset of our work, it was not clear whether this sensitive combination of functional groups would be better accessed by deprotection of a C23 silyl ether in which the unsaturated keto-ester component was already present, *e.g.* the ketoester **80**, or whether the selective oxidation of an allylic alcohol **81**, leading to the methoxycarbonylmethylene group in the presence of the 23-hydroxyl group, would be more efficient. In both cases, possible difficulties could be the subsequent dehydration of the hemiacetal leading to the enol ether **82**, which is preceded in the proposed biosynthesis³³ of the bryostatins, or migration of the double bond into conjugation with the ketone leading to the unwanted 20,21-alkene **83**, see Figure 5.

The silyl ether protecting groups present in the macrolide **78** had been chosen on the basis that the triethylsilyl ether would be the most labile allowing for the selective deprotection and oxidation of the 19-hydroxy group. The usually more resilient tri-isopropylsilyl groups had been chosen for the exocyclic allyl alcohols since the *tert*-butyldimethylsilyl ethers of these primary alcohols had proved to be rather labile during the development of the synthesis.¹⁴ It was thought that oxidation of the allylic alcohols would be possible in the presence of the unactivated secondary alcohols.

Following the procedure developed earlier, selective removal of the triethylsilyl ether from the macrolide **78** was

Figure 5 Options for the introduction of functionality into the C18-C27 fragment **5** with possible complications.

achieved using pyridinium toluene 4-sulfonate and trimethyl orthoformate in methanol/dichloromethane to give the 19-alcohol **84** although the reaction was rather slow taking 48 h to reach completion. Oxidation using TPAP then gave the required 19-ketone **85** but reactions of this ketone with aqueous hydrogen fluoride gave mixtures of polar products and the fully deprotected polyol **88** was not isolated.

Attempts at selective desilylation of the macrolide **78** using the HF.pyridine complex, aqueous hydrogen fluoride or TBAF gave mixtures of products that were not separated or characterised. However, rather unexpectedly, deprotection using tetra-*n*-butyl ammonium fluoride/acetic acid was selective for the allylic tri-isopropylsilyl ether attached to C13 rather than for the triethylsilyl ether and gave the primary alcohol **86** as the dominant product. The regioselectivity of this desilylation was established by oxidation of the alcohol **86** to give the methyl ester **87** using manganese dioxide and sodium cyanide in methanol/THF heated under reflux, see Scheme 11. This cleavage of the allylic tri-isopropylsilyl ether attached to C13 was highly regioselective. Significant removal of the tri-isopropylsilyl ether attached to C21 was not observed for the macrolide **78** using tetra-*n*-butyl ammonium fluoride/acetic acid even with prolonged reaction times.

Both the mono and bis-desilylated products **89** and **90** were isolated from the reaction of the 19-ketone **85** with TBAF/acetic acid. It would appear that the ketone at C19 slightly activates the allylic silyl ether attached to C21 towards desilylation. However, oxidation of the hydroxyketones **89** and **90** using manganese dioxide and sodium cyanide in methanol/THF gave complex mixtures of products, see Scheme 11.

Scheme 11 Selective deprotection and oxidation. Reagents and conditions i, PPTS, $\text{HC}(\text{OMe})_3$, DCM, MeOH, rt, 48 h (54%); ii, TPAP, NMO, DCM, rt, 6 h (50%); iii, TBAF, AcOH, THF, rt, 16 h (50%); iv, MnO_2 , NaCN, MeOH, THF, heat under reflux, 16 h (49%); v, TBAF-AcOH, THF, rt, 16 h (**89**, 28%; **90**, 32%).

These preliminary studies of the selective deprotection of the macrolide **78** and oxidation of the products had been promising in that conditions for the introduction of the ketone at C19 and the methoxycarbonylmethylene group at C13 had been successful. However, the desilylation and oxidation of the allylic ether at C21 had not been achieved and intermediates with the unsaturated keto-ester fragment at C19-C21 had not been prepared. At this stage, it was decided to study model systems to learn more about the likely chemistry of this fragment before using more of the valuable macrolide **78**.

Preliminary studies of simpler analogues of the C19-C27 fragment of a 20-deoxybryostatin

The benzothiazolyl sulfone **69** prepared earlier was silylated to give the tris-*tert*-butyldimethylsilyl ether **91** and a modified Julia reaction of this silylated sulfone with 2-methylpropanal gave the (*E*)-alkene **92** with good stereoselectivity. Treatment with pyridinium toluene 4-sulfonate now removed the triethylsilyl and allylic *tert*-butyldimethylsilyl ethers to give the diol **93** and selective oxidation via the corresponding aldehyde gave the acid **94** that was esterified using trimethylsilyl diazomethane to give the methyl ester **95**. Oxidation of this alcohol gave the unsaturated ketoester **96**. This corresponds to the key intermediate **80** considered during the planning stages of this work, see Figure 5, but attempts to desilylate this ketoester using the hydrogen fluoride pyridine complex were disappointing in that a hemi-acetal corresponding to the C19-C23 fragment of the 20-deoxybryostatins, *cf.* **79**, was not obtained, see Scheme 12. Instead a mixture of the (*E*)- and (*Z*)-enol ethers **97** together with a small amount of the lactone **98** were isolated, albeit in an excellent yield, see Scheme 12. When

Scheme 12 Model studies based on deprotection of the unsaturated ketoester **96**. Reagents and conditions i, TBSOTf, 2,6-lutidine, DCM, -78°C , 2 h (96%); ii, LiHMDS, THF, -78°C to -60°C 30 min, add 2-methylpropanal, -78°C , 1 h, rt, 20 min (52%); iii, PPTS, DCM, MeOH, rt, 16 h (50%); iv, (a) MnO_2 , DCM, rt, 4 h (b) NaClO_2 , $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$, $t\text{-BuOH}$, 2-methylbut-2-ene, H_2O , rt, 2 h; v, $\text{Me}_3\text{SiCHN}_2$, MeOH, toluene, 0°C , 1 h (77% from **93**); vi, Dess Martin periodinane, py., DCM, rt, 2 h (81%); vii, HF.py., THF, py., rt, 72 h (**97**, 93%; **98**, 6%).

this reaction was monitored by TLC, several intermediates were detected that were converted into the enol ethers **97**. However, attempts to isolate any of these were not successful.

An alternative approach to the C19-C23 fragment of the 20-deoxybryostatins was also briefly investigated. Monosilylation of the diol **93** gave the secondary alcohol **99** that was oxidised to the ketone **100**. However, attempts to remove the *tert*-butyldimethylsilyl ether protecting groups using aqueous HF, HF.pyridine, HF.triethylamine and TBAF gave complex mixtures

Scheme 13 Conjugated diene formation. Reagents and conditions i, TBSCl, imid., DCM, rt, 16 h (87%); ii, Dess Martin periodinane, NaHCO₃, DCM, rt, 2 h (90%); iii, TBAF, THF, rt, 16 h (**101** and **102**, each 35-40%).

Scheme 14 Completion of a synthesis of 7-des-O-pivaloyl-7-O-benzylbryostatatin 10 (**106**). Reagents and conditions i, TBAF, AcOH, THF, rt, 40 h (53%); ii, (a) MnO₂, DCM, rt, 1 h (b) NaClO₂, NaH₂PO₄·2H₂O, 2-methylbut-2-ene, ^tBuOH, THF, rt, 1 h (c) Me₃SiCHN₂, MeOH, tol., rt, 1 h (40% from **103**); iii, Dess Martin periodinane, py., DCM, rt, 2 h; iv, HF.py., THF, py., 0 °C to rt, 24 h, aq. HF, py., rt, 24 h (50% from **104**).

of products. The use of TBAF buffered with ammonium chloride gave the (*E*)- and (*Z*)-conjugated dihydroxydienes **101** and **102** as the major products, see Scheme 13.

Completion of a synthesis of 7-des-O-pivaloyl-7-O-benzylbryostatatin 10

Despite the difficulties encountered during attempts to prepare a simpler hemi-acetal corresponding to the C19-C23 fragment of a 20-deoxybryostatins, it was decided to study further the chemistry of the alcohol **84** to attempt to access a ketoester analogous to the proposed intermediate **79**.

Prolonged treatment of the alcohol **84** with TBAF-acetic acid gave the triol **103** by selective cleavage of the primary tri-isopropylsilyl ethers over the secondary *tert*-butyldimethylsilyl ethers. Oxidation of the allylic alcohols using manganese dioxide then gave the corresponding bis-aldehyde that was oxidised to the bis-acid under Pinnick conditions. Esterification using trimethylsilyl diazomethane gave the bis-methyl ester **104**. Oxidation of the remaining hydroxyl group using the Dess-Martin periodinane in the presence of pyridine gave the required ketoester **105**. Unlike the model system **96**, this was found to be unstable to chromatography, and so was immediately reacted with hydrogen fluoride.pyridine in tetrahydrofuran containing an excess of pyridine followed by further treatment with buffered aqueous hydrogen fluoride. This rather slow but carefully monitored deprotection gave 7-des-O-pivaloyl-7-O-benzylbryostatatin 10 (**106**), Scheme 14, as the

only isolatable product. Perhaps in the macrocyclic environment, the 19-hydroxy group is stabilised with respect to dehydration by hydrogen bonding to the 3-hydroxyl group. Such hydrogen bonding has been elucidated for bryostatin 10.^{13c}

The structure **106** was assigned to the final product in this synthesis using extensive ¹H and ¹³C NMR investigations including ¹H – ¹³C correlation spectroscopy to assign all the peaks in the ¹³C spectrum.³³ Selected ¹H and ¹³C peaks for the synthetic bryostatin **106** are compared with analogous peaks reported for bryostatin 10^{13c} and bryostatin 16 in Figure 6. All three compounds have a ¹³C peak at about δ 102 assigned to the anomeric carbon C9. However, for the bryostatin 16, C19 is seen at δ 151 whereas for the bryostatin 10 and **106**, C19 is also at ca. δ 102. No peak was observed in the ¹³C NMR spectrum of the synthetic compound **106** near to δ 150. This confirms that no oxygen-substituted double bond is present in the synthetic compound **106**. In their ¹H NMR spectra, the methylene protons at C20 for the 20-deoxybryostatins **106** and bryostatin 10 were observed at δ 2.1–2.35, whereas the single C20 vinylic proton observed for bryostatin 16 was reported at δ 5.50. Finally, the 19-hydroxyl protons for the synthetic compound **106** and bryostatin 10 are sharp singlets at δ 5.44 and δ 5.91, respectively, whereas no equivalent proton is seen for bryostatin 16 (for full NMR data see Table 1).

Figure 6 Comparison of selected ¹H and ¹³C NMR chemical shifts for the synthetic compound **106** with bryostatins 10 and 16.

Summary and conclusions

This paper reports the first synthesis of a 20-deoxybryostatin, namely 7-*des-O*-pivaloyl-7-*O*-benzylbryostatin 10 (**106**). One of the more difficult steps in the synthesis was the deprotection of the 23-hydroxyl group in the presence of the 19,21-unsaturated ketoester. This had to be carried out without concomitant dehydration or double bond migration if a 20-deoxybryostatin was to be prepared. This deprotection was achieved under very mild, albeit prolonged, reaction conditions that were carefully monitored by TLC. Interestingly, in model studies, the analogous deprotection was accompanied by dehydration and gave the isomeric enol ethers **97**.

Dehydration of a 20-deoxybryostatins to the corresponding 19,20-dehydrobryostatins, e.g. bryostatin 16, is believed to be a key step in bryostatin biosynthesis³⁴ with the subsequent hydroxylation of the 19,20-dehydrobryostatins leading to bryostatins that have an acyloxy group at C20. Such hydroxylation, albeit leading to the 20-epimer of bryostatin 7, has been exemplified using bryostatin 16.⁷ The enol ether containing bryostatins are therefore useful intermediates for the synthesis of several sub-sets of bryostatins. However they are significantly less biologically active than their hemiacetal analogues and so our initial objective had been to synthesise a 20-deoxybryostatin directly without any competing dehydration. In completing a synthesis of 7-*des-O*-pivaloyl-7-*O*-benzylbryostatin 10 (**106**) this had been achieved albeit not of a natural product because of the benzyl protection of the 7-hydroxyl group.

Perhaps the most significant result from this synthesis is the introduction of the modified Julia reaction using benzothiazolyl sulfones for an efficient and (*E*)-stereoselective assembly of the core structure of the 20-deoxybryostatins from advanced C1–C16 and C17–C27 components. This represents an improvement over the use of the classical Julia reaction for this transformation²² and may provide convergent access to bryostatins in general. Also of note is the bismuth(0) mediated reaction of the allylic bromide **65** with the aldehyde **52**³¹ that provided the secondary alcohol **66** with no involvement of either the acrylate functionality or the benzothiazolyl sulfone. Macrocyclisation of the selectively deprotected Julia product **77** was particularly efficient as has been observed in other bryostatin syntheses.

Of general interest in this work are the relative reactivities of different *O*-silyl ethers. Triethylsilyl ethers are usually more reactive than their more hindered congeners, and indeed the triethylsilyl ether of the secondary 19-hydroxyl group was

removed selectively using pyridinium toluene 4-sulfonate and trimethyl orthoformate. However, rather surprisingly, the tri-isopropylsilyl ethers of the primary allylic alcohols were found to be more labile towards tetra-*n*-butylammonium fluoride in the presence of acetic acid than the triethylsilyl ether of the secondary alcohol at C19.

The later steps in the synthesis were not optimised and the synthesis is less efficient in terms of the number of steps and overall yield than other recent syntheses of bryostatins. Nevertheless, it is the first synthesis of a 20-deoxybryostatin. Conversion of the final product **106** into bryostatin 10 by selective hydrogenolysis of benzyl ether was not attempted because of the limited amount of material that was available. To prepare a naturally occurring 20-deoxybryostatin, e.g. bryostatin 10, it would be necessary to repeat the synthesis using a different protecting group, possibly a 4-methoxybenzyl ether, for the hydroxyl group at C7. However, it was decided that it would be more useful if the knowledge gained during the course of this work was used to prepare unnatural analogues for biological evaluation rather than a natural product. To this end, studies were initiated directed towards the synthesis of bryostatin analogues with fluorine substituents at C20.³⁵ Further details of these studies will be described in the final paper in this series.

Experimental

General experimental details

Flash column chromatography was performed using Merck silica gel (60H; 40–60 μ , 230–240 mesh). Light petroleum refers to the fraction boiling between 40 and 60 °C and was redistilled. Tetrahydrofuran was dried over sodium-benzophenone and was distilled under nitrogen. Dichloromethane was dried over CaH₂ and was distilled. Ether refers to diethyl ether. Reactions under non-aqueous conditions were carried out under an atmosphere of nitrogen or argon.

Mass spectra used electron impact ionisation (EI⁺), chemical ionisation using ammonia (CI⁺), electrospray ionisation in the positive mode (ES⁺), atmospheric pressure chemical ionisation in the positive mode (APCI⁺) and time of flight MS with electrospray ionisation (TOF ES⁺). Low resolution and high resolution mass spectra were recorded using a Micromass Trio 200 and a Kratos Concept IS spectrometer, respectively. Infra-red spectra were measured using a Genesis FTIR spectrometer on NaBr plates, either neat or as evaporated films. Nuclear magnetic resonance spectra were recorded using Varian Unity 500 (500 MHz), Varian INOVA 400 (400 MHz) and Varian Unity 300 (300 MHz) spectrometers. Coupling constants (*J*) are given in Hertz (Hz) and chemical shifts are relative to tetramethylsilane. Residual non-deuteriated solvent was used as the internal standard.

(2Z)-Methyl 3-[(2R)-3-(4-methoxybenzyloxy)-2-triethylsilyloxypropyl]hexa-2,5-dienoate (**6**).

Imidazole (8.29 g, 121.7 mmol) and triethylsilyl chloride (8.17 mL, 48.69 mmol) were added to the alcohol **5** (13 g) in DCM

(216 mL) and the solution was stirred at rt for 16 h before the addition of DCM (200 mL) and water (200 mL). The aqueous phase was extracted with DCM (2 × 200 mL) and the organic extracts were dried (MgSO₄), filtered and concentrated under reduced pressure. Chromatography (light petroleum to 1:10 EtOAc:light petroleum) afforded the *title compound 6* (13.5 g, 77%) as a pale oil, *R*_f 0.37 (1:5 ether:light petroleum), [α]_D²⁵ +53.3 (c 2.25, CHCl₃) (Found: M⁺ + Na, 457.2390. C₂₄H₃₈O₅NaSi requires M, 457.2381); ν_{max} /cm⁻¹ 2951, 2910, 2876, 1717, 1644, 1613, 1514, 1246, 1192, 1180, 1144, 1101, 1037, 1004 and 744; δ_{H} (400 MHz, CDCl₃) 0.49 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.83 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 2.52 (1 H, dd, *J* 12.4, 8.6, 1'-H), 2.87 (1 H, ddq, *J* 16.4, 7.1, 1.0, 4-H), 2.91–2.98 (2 H, m, 4-H', 1'-H'), 3.32 (2 H, d, *J* 5.0, 3'-H₂), 3.59 (3 H, s, CO₂CH₃), 3.73 (3 H, s, ArOCH₃), 4.08 (1 H, m, 2'-H), 4.38 and 4.41 (each 1 H, d, *J* 11.9, ArHCH), 5.01 (1 H, d, *J* 17.2, 6-H), 5.05 (1 H, d, *J* 10.1, 6-H'), 5.65 (1 H, s, 2-H), 5.69 (1 H, ddt, *J* 17.2, 10.3, 6.8, 5-H) and 6.79 and 7.19 (each 2 H, d, *J* 8.6, Ar-H); δ_{C} (100 MHz, CDCl₃) 4.9, 6.9, 37.4, 44.1, 50.9, 55.3, 71.6, 72.9, 74.8, 113.6, 116.9, 118.0, 129.3, 130.5, 134.4, 159.1, 160.4 and 166.8; *m/z* (ES⁺) 457.7 (M⁺ + 23, 100%).

(5R,2Z)-6-(4-Methoxybenzyloxy)-3-prop-2-enyl-5-triethylsilyloxy-1-tri-isopropylsilyloxyhex-2-ene (**8**).

Di-isobutylaluminium hydride (1 M in heptanes, 78 mL, 77.65 mmol) was added to the ester **6** (13.5 g, 31.06 mmol) in THF (109 mL) at –78 °C and the mixture was stirred at this temperature for 4 h. Methanol (10 mL) and aqueous sodium potassium tartrate (10%, 200 mL) were added and the reaction mixture was allowed to warm to rt before the addition of ether (200 mL). The aqueous phase was extracted with ether (2 × 200 mL) and the organic extracts were dried (Na₂SO₄), filtered and concentrated under reduced pressure to afford the alcohol **7**, as a pale oil (12.6 g) which was used directly in the next step.

Imidazole (5.27 g, 77.47 mmol) and tri-isopropylsilyl chloride (8.0 mL, 37.27 mmol) were added to the alcohol **7** (12.6 g, 31.06 mmol) in DCM (239 mL) and the solution was stirred at r.t. for 16 h. Water (250 mL) was added and the aqueous phase extracted with DCM (2 × 250 mL). The organic extracts were dried (MgSO₄), filtered and concentrated under reduced pressure. Chromatography (light petroleum to 1:50 EtOAc:light petroleum) afforded the *title compound 8* (15.9 g, 91%) as a pale oil, *R*_f 0.67 (1:20 ether:light petroleum), [α]_D²⁵ +3.89 (c 2.26, CHCl₃) (Found: (M⁺ + NH₄), 580.4206. C₃₂H₆₂O₄NSi₂ requires M, 580.4212); ν_{max} /cm⁻¹ 2946, 2868, 1614, 1514, 1463, 1248, 1102, 1008, 883 and 744; δ_{H} (500 MHz, CDCl₃) 0.50 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.85 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 0.93–1.06 [21 H, m, 3 × SiCH(CH₃)₂], 2.08 (1 H, dd, *J* 13.6, 7.3, 4-H), 2.25 (1 H, dd, *J* 13.5, 5.9, 4-H'), 2.68–2.72 (2 H, m, 1'-H₂), 3.24 (2 H, d, *J* 5.3, 6-H₂), 3.73 (3 H, s, OCH₃), 3.81 (1 H, m, 5-H), 4.17 (1 H, dd, *J* 13.1, 5.8, 1-H), 4.23 (1 H, dd, *J* 13.1, 6.3, 1-H'), 4.36 and 4.39 (each 1 H, d, *J* 11.6, ArHCH), 4.93–5.00 (2 H, m, 3'-H₂), 5.37 (1 H, t, *J* 6.1, 2-H), 5.71 (1 H, m, 2'-H) and 6.79 and 7.19 (each 2 H, d, *J* 8.6, ArH); δ_{C} (100 MHz, CDCl₃) 4.9, 6.9, 12.0, 18.0, 36.1, 42.1, 55.3, 60.5, 70.6, 73.0, 74.1, 113.7, 116.3, 128.9, 129.2, 130.5, 135.3, 136.5 and 159.1; *m/z* (ES⁺) 621.4 (M⁺ + 59, 100%), 585.9 (M⁺ + 23, 37) and 580.6 (M⁺ + 18, 95).

(2*RS*,6*R*)-7-(4-Methoxybenzyloxy)-6-triethylsilyloxy-4-[(*Z*)-2-triisopropylsilyloxyethylidene]heptane-1,2-diol (9**).**

AD-mix β (23.78 g, 28.30 mmol) was added portionwise to a well-stirred mixture of *t*-BuOH (75 mL) and H₂O (75 mL). After 10 min, the mixture was cooled to 0 °C and the diene **8** (15.93 g, 28.30 mmol) in *t*-BuOH (30 mL) was added. A solution of OsO₄ (360 mg, 1.41 mmol) in *t*-BuOH/H₂O (3:1, 60 mL) was added dropwise over 8 h by syringe pump and this process was repeated. The reaction mixture was then warmed to r.t. and aqueous Na₂SO₃ (48 g in 240 mL H₂O) was added. The mixture was stirred for 30 min before EtOAc (250 mL) was added and the aqueous phase was extracted with EtOAc (3 $\times$ 250 mL). After drying (MgSO₄), concentration under reduced pressure and chromatography (1:20 to 1:3 EtOAc:light petroleum) of the residue gave recovered diene **8** (1.5 g, 10%) followed by the *title compound* **9** as a pale oil (13.0 g, 77%), a 3:2 mixture of diastereoisomers, *R*_f 0.19 (1:3 EtOAc:light petroleum), $[\alpha]_D^{25} +2.7$ (c 1.86, CHCl₃) (Found: *M*⁺ + Na, 619.3823. C₃₂H₆₀O₆NaSi₂ requires *M*, 619.3821; $\nu_{\max}/\text{cm}^{-1}$ 3418, 2946, 2867, 1614, 1514, 1464, 1248, 1087, 1040, 1013, 883 and 745; δ_{H} (500 MHz, CDCl₃) 0.43–0.53 (6 H, m, 3 $\times$ SiCH₂), 0.84 (9 H, t, *J* 7.9, 3 $\times$ SiCH₂CH₃), 0.95–1.05 [21 H, m, 3 $\times$ SiCH(CH₃)₂], 2.03–2.12 (1.4 H, m, 3-H, 5-H), 2.13–2.24 (2.2 H, m, 3-H', 5-H₂), 2.27 (1 H, br. s, 1-OH), 2.36 (0.4 H, dd, *J* 13.9, 5.0, 5-H'), 2.53 (0.6 H, br. s, 2-OH), 2.65 (0.4 H, br. s, 2-OH), 3.23 and 3.27 (each 1 H, m, 7-H), 3.38 and 3.56 (each 1 H, m, 1-H), 3.73 (3 H, s, OCH₃), 3.74 (1 H, m, 2-H), 3.80 (1 H, m, 6-H), 4.15 (0.6 H, dd, *J* 12.9, 5.4, 2'-H), 4.20 (0.8 H, d, *J* 6.0, 2'-H₂), 4.25 (0.6 H, dd, *J* 12.9, 6.9, 2'-H), 4.35 and 4.38 (each 1 H, d, *J* 11.9, ArHCH), 5.45 (0.4 H, t, *J* 6.0, 1'-H), 5.45 (0.6 H, t, *J* 6.0, 1'-H) and 6.79 and 7.16 (each 2 H, d, *J* 8.5, ArH); δ_{C} (125 MHz, CDCl₃) 4.9, 6.8, 12.0, 18.0, 35.8, 36.1, 41.4, 41.9, 55.2, 55.3, 60.2(2), 66.5(2), 69.8, 70.2, 70.7, 71.2, 73.0, 73.8, 74.0, 113.7, 129.2, 130.2, 131.1, 131.6, 133.4, 133.9 and 159.2; *m/z* (ES⁺) 619.6 (*M*⁺ + 23, 100%).

(2*R*,6*E*,10*S*,12*R*,14*S*)-10-Benzyloxy-16-*tert*-butyldiphenylsilyloxy-4-[(*Z*)-2-triisopropylsilyloxyethylidene]-1-(4-methylbenzyloxy)-9,9-dimethyl-2-triethylsilyloxy-12,14-di-*O*-isopropylidenehexadec-6-en-8-one (12**).**

A solution of Pb(OAc)₄ (3.48 g, 7.84 mmol) and pyridine (3.9 mL) in DCM (87.1 mL) was added to the diol **9** (3.9 g, 6.53 mmol) in DCM (42 mL) and the mixture was stirred for 1 h at rt. After filtration through Celite[®], saturated aqueous NaHCO₃ (100 mL) was added to the filtrate and the aqueous phase was extracted with DCM (2 $\times$ 100 mL). The organic extracts were washed with brine, dried (MgSO₄), and concentrated under reduced pressure to afford the aldehyde **10** as a pale oil (3.7 g), used immediately in the next step, *R*_f 0.85 (1:3 EtOAc:light petroleum); δ_{H} (500 MHz, CDCl₃) 0.49 (6 H, q, *J* 7.9, 3 $\times$ SiCH₂), 0.84 (9 H, t, *J* 7.9, 3 $\times$ SiCH₂CH₃), 0.95–1.05 [21 H, m, 3 $\times$ SiCH(CH₃)₂], 2.19 (1 H, dd, *J* 13.6, 6.9, 4-H), 2.28 (1 H, dd, *J* 13.9, 5.0, 4-H'), 3.03–3.07 (2 H, m, 2-H₂), 3.21 (1 H, dd, *J* 9.5, 5.7, 6-H), 3.26 (1 H, dd, *J* 9.5, 4.7, 6-H'), 3.74 (3 H, s, OCH₃), 3.81 (1 H, m, 5-H), 4.21 (1 H, dd, *J* 13.2, 5.4, 2'-H), 4.27 (1 H, dd, *J* 13.2, 6.3, 2'-H'), 4.36 (2 H, s, ArCH₂), 5.51 (1 H, t, *J* 5.9, 1'-H), 6.80 and 7.16 (each 2 H, d, *J* 8.5, ArH) and 9.55 (1 H, t, *J* 1.0, 1-H).

Phosphonate **11** (955 mg, 1.32 mmol) in THF (11.22 mL) was added to a suspension of Ba(OH)₂·0.8 H₂O [275 mg, 1.45 mmol; prepared by heating Ba(OH)₂·8H₂O at 200 °C for 2 h] in THF (6.24 mL). The mixture was stirred for 2 h at rt before the aldehyde **10** (815 mg, 1.45 mmol) in THF/H₂O (40:1, 18 mL) was added dropwise over 10 min. After being stirred for 16 h, the mixture was filtered through Celite[®] and the solid residue washed with DCM (25 mL). The filtrate was washed with saturated aqueous NaHCO₃ (50 mL) and the aqueous phase extracted with DCM (2 $\times$ 50 mL). The organic extracts were washed with brine (100 mL), dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (1:20 to 1:10 ether:light petroleum) gave the *title compound* **12** as a pale oil (1.10 g, 73%), *R*_f 0.58 (1:5 EtOAc:light petroleum), $[\alpha]_D^{25} +0.53$ (c 2.25, CHCl₃); $\nu_{\max}/\text{cm}^{-1}$ 2946, 2867, 1690, 1617, 1514, 1465, 1428, 1381, 1248, 1225, 1173, 1109, 1039, 1011, 883, 823, 739 and 703; δ_{H} (500 MHz, CDCl₃) 0.48 (6 H, q, *J* 7.9, 3 $\times$ SiCH₂), 0.84 (9 H, t, *J* 7.9, 3 $\times$ SiCH₂CH₃), 0.91–1.02 [30 H, m, 3 $\times$ SiCH(CH₃)₂, SiC(CH₃)₃], 1.06 and 1.13 (each 3 H, s, 9-CH₃), 1.27 (6 H, s, 2 $\times$ CH₃), 1.37–1.54 (4 H, m, 11-H₂, 13-H₂), 1.54–1.71 (2 H, m, 15-H₂), 2.08 (1 H, dd, *J* 13.6, 7.3, 3-H), 2.23 (1 H, dd, *J* 13.6, 5.3, 3-H'), 2.85 (2 H, d, *J* 6.9, 5-H₂), 3.20 (1 H, dd, *J* 9.5, 5.4, 1-H), 3.24 (1 H, dd, *J*, 9.5, 5.0, 1-H'), 3.60 and 3.70 (each 1 H, m, 16-H), 3.71 (3 H, s, OCH₃), 3.78 (1 H, m, 2-H), 3.85 (1 H, m, 10-H), 3.92–4.03 (2 H, m, 12-H, 14-H), 4.14 (1 H, dd, *J* 12.9, 5.7, 2'-H), 4.21 (1 H, dd, *J* 12.9, 6.3, 2'-H'), 4.35 (2 H, s, ArCH₂), 4.48 and 4.52 (each 1 H, d, *J* 11.0, PhHCH), 5.37 (1 H, t, *J* 6.0, 1'-H), 6.51 (1 H, d, *J* 15.1, 7-H), 6.78 (2 H, d, *J* 8.5, ArH), 6.83 (1 H, dt, *J* 15.3, 7.7, 6-H), 7.13–7.18 (3 H, m, ArH), 7.18–7.25 (4 H, m, ArH), 7.26–7.37 (6 H, m, ArH) and 7.58 (4 H, t, *J* 6.5, ArH); δ_{C} (125 MHz, CDCl₃) 3.9, 5.8, 11.0, 17.0, 18.2, 19.5, 20.1, 24.2, 24.4, 25.8, 35.2, 37.7, 37.8(2), 39.6, 50.3, 54.2, 59.0, 59.3, 62.2, 62.3, 69.8, 71.9, 72.9, 73.7, 79.4, 99.2, 112.6, 126.0, 126.2, 126.4, 126.6(3), 127.3, 128.1, 128.5, 129.1, 129.3, 132.8, 132.9, 133.0, 134.5, 137.7, 143.6, 158.1 and 202.2; *m/z* (ES⁺) 1186.2 (*M*⁺ + 23, 100%).

(4*S*,6*R*,8*S*)-4-Benzyloxy-10-*tert*-butyldiphenylsilyloxy-1-[(2*S*,6*R*)-4-[(*Z*)-2-triisopropylsilyloxyethylidene]-6-(4-methoxybenzyloxymethyl)tetrahydropyran-2-yl]-6,8-di-*O*-isopropylidene-3,3-dimethyldecan-2-one (14**).**

Pyridine (2.53 mL) was added to the triethylsilyl ether **12** (1.37 g, 1.18 mmol) in THF (26 mL). After cooling to 0 °C, HF-pyridine complex (70:30, 1.27 mL) was added and the solution was stirred for 30 min. Saturated aqueous NaHCO₃ (100 mL) was added and the mixture warmed to rt before ether (100 mL) was added. The aqueous phase was extracted with ether (2 $\times$ 100 mL) and the organic extracts were washed with brine, dried (Na₂SO₄) and concentrated under reduced pressure to afford the alcohol **13** as a pale yellow oil that was used immediately without further purification, *R*_f 0.23 (1:5 EtOAc:light petroleum); δ_{H} (500 MHz, CDCl₃) 0.95–1.05 [30 H, m, 3 $\times$ SiCH(CH₃)₂, SiC(CH₃)₃], 1.06 and 1.13 (each 3 H, s, 9-CH₃), 1.27 (6 H, s, 2 $\times$ CH₃), 1.39–1.53 (4 H, m, 11-H₂, 13-H₂), 1.56–1.69 (2 H, m, 15-H₂), 2.10 (1 H, dd, *J* 13.9, 4.7, 3-H), 2.23 (1 H, dd, *J* 13.9, 8.8, 3-H'), 2.72 (1 H, d, *J* 3.5, OH), 2.86 (2 H, d, *J* 6.9, 5-H₂), 3.28 (1 H, dd, *J* 9.5, 6.3, 1-H), 3.32 (1 H, dd, *J* 9.5, 4.4, 1-H'), 3.59 (1 H, dt, *J* 10.4, 5.4, 16-H), 3.70 (1 H, m, 16-H'), 3.72 (3 H, s, OCH₃), 3.76 (1 H, m, 2-H), 3.83 (1 H, m, 10-H),

3.91-4.03 (2 H, m, 12-H, 14-H), 4.08 (1 H, dd, J 12.6, 6.6, 2'-H), 4.15 (1 H, dd, J 11.7, 6.6, 2'-H'), 4.39 (2 H, s, ArCH₂), 4.47 and 4.53 (each 1 H, d, J 11.0, PhHCH), 5.50 (1 H, t, J 6.6, 1'-H), 6.54 (1 H, d, J 15.1, 7-H), 6.80 (2 H, d, J 8.5, ArH), 6.81 (1 H, m, 6-H), 7.14-7.25 (7 H, m, ArH), 7.27-7.37 (6 H, m, ArH), and 7.58 (4 H, tt, J 6.5, 1.6, ArH).

Potassium *tert*-butoxide in THF (1 M, 2.17 mL, 0.217 mmol) was added to this alcohol **13** in THF (5 mL) at rt and the solution stirred for 5 min. Saturated aqueous NH₄Cl (20 mL) and ether (20 mL) were added and the aqueous phase was extracted with ether (2 × 20 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:10 to 1:5 ether:light petroleum) afforded the *title compound 14* as a pale oil (1.1 g, 74%), R_f 0.63 (1:5 EtOAc:light petroleum); δ_H (500 MHz, CDCl₃) 0.93-1.05 [33 H, m, 3 × SiCH(CH₃)₂, SiC(CH₃)₂, 3-CH₃], 1.15 (3 H, s, 3-CH₃'), 1.26 and 1.27 (each 3 H, s, CH₃), 1.39-1.69 (6 H, m, 5-H₂, 7-H₂, 9-H₂), 1.73 (1-H, t, J 12.7, 5'-H_{ax}), 1.82 (1-H, t, J 12.2, 3'-H_{ax}), 2.12 (1-H, d, J 13.2, 3'-H_{eq}), 2.37 (1 H, d, J 13.6, 5'-H_{eq}), 2.50 (1 H, dd, J 17.7, 6.3, 1-H), 2.93 (1-H, dd, J 17.7, 5.7, 1-H'), 3.32 (1 H, dd, J 10.4, 4.4, 6'-CH), 3.36 (1 H, m, 6'-CH'), 3.42 (1 H, m, 6'-H), 3.59 and 3.69 (each 1 H, dt, J 10.3, 5.4, 10-H), 3.72 (3 H, s, OCH₃), 3.79 (1 H, m, 2'-H), 3.85-4.01 (3 H, m, 4-H, 6-H and 8-H), 4.17 (2 H, d, J 6.3, 2'-H₂), 4.39 (2 H, s, ArCH₂), 4.49 and 4.57 (each 1 H, d, J 11.4, PhHCH), 5.33 (1 H, t, J 6.0, 1'-CH), 6.79 (2 H, d, J 8.6, ArH), 7.14-7.26 (7 H, m, ArH), 7.27-7.37 (6 H, m, ArH) and 7.58 (4 H, t, J 6.4, ArH).

(3S,5R,7S,9S,11S,15R)-7-Benzoyloxy-1-*tert*-butyldiphenylsilyloxy-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecan-3-ol (15).

Pyridinium toluene 4-sulfonate (18 mg, 0.0073 mmol) was added to the acetonide **14** (763 g, 0.073 mmol) and trimethyl orthoformate (1.6 mL) in DCM/methanol (1:1, 11 mL) and the solution was stirred at rt for 16 h. Ether (30 mL) and saturated aqueous NaHCO₃ (30 mL) were added and the aqueous phase was extracted with Et₂O (2 × 30 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:10 to 1:5 EtOAc:light petroleum) afforded the *title compound 15* as a pale oil (640 mg, 88%), R_f 0.34 (1:3 EtOAc:light petroleum), $[\alpha]_D^{25}$ +26.3 (c 3.30, CHCl₃); ν_{max}/cm^{-1} 3502, 3071, 2942, 2864, 1614, 1588, 1514, 1473, 1463, 1428, 1383, 1362, 1248, 1111, 882, 822, 738 and 702; δ_H (400 MHz, CDCl₃) 0.89-1.03 [36 H, m, 2 × 8-CH₃, 3 × SiCH(CH₃)₂, SiC(CH₃)₃], 1.39 (1 H, q, J 12.1, 6-H_{ax}), 1.46-1.79 (7 H, m, 2-H₂, 4-H₂, 6-H_{eq}, 10-H, 14-H_{ax}), 1.92 (1 H, t, J 12.5, 12-H_{ax}), 2.00 (1 H, dd, J 15.9, 5.3, 10-H'), 2.21 (1 H, d, J 12.9, 12-H_{eq}), 2.36 (1 H, d, J 13.6, 14-H_{eq}), 3.15 (3 H, s, 9-OCH₃), 3.35 (1 H, m, 15-H), 3.38 (1 H, m, 16-H), 3.44 (1 H, dd, J 10.1, 5.0, 16-H'), 3.51 (1 H, m, 11-H), 3.53 (1 H, d, J 2.5, OH), 3.64 (1 H, dd, J 11.4, 4.5, 7-H), 3.71 (3 H, s, ArOCH₃), 3.79 (2 H, m, 1-H₂), 3.80 (1 H, m, 5-H), 4.12 (1 H, m, 3-H), 4.16 (2 H, d, J 6.3, 2'-H₂), 4.37 (1 H, d, J 11.9, PhHCH), 4.41 (2 H, s, ArCH₂), 4.52 (1 H, d, J 11.9, PhHCH), 5.25 (1 H, t, J 6.3, 1'-H), 6.77 (2 H, d, J 8.6, ArH), 7.13-7.21 (3 H, m, ArH), 7.22-7.38 (10 H, m, ArH) and 7.60 (4 H, d, J 6.9, ArH); δ_C (100

MHz, CDCl₃) 12.0, 16.9, 18.0, 18.1, 19.0, 20.9, 26.6, 26.9, 31.6, 32.6, 39.1, 39.2, 43.0, 43.3, 48.2, 55.3, 59.5, 63.1, 65.5, 67.7, 71.6, 73.0, 75.2, 76.6, 78.8, 104.0, 113.7, 123.9, 127.3, 127.4, 127.8, 128.3, 129.2, 129.7, 129.8, 130.6, 133.1, 133.2, 134.8, 135.2, 135.6, 135.7, 139.4 and 159.1; m/z (ES⁺) 1081.9 (M⁺ + 59, 95%) and 1045.9 (M⁺ + 23, 100).

(3S,5S,7S,9S,11S,15R)-7-Benzoyloxy-3-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane (16).

tert-Butyldimethylsilyl trifluoromethanesulfonate (255 μ L, 1.11 mmol) and 2,6-lutidine (646 mL, 5.55 mmol) in DCM (4.6 mL) were added to the alcohol **15** (568 mg, 0.555 mmol) and 2,6-lutidine (646 μ L, 5.55 mmol) in DCM (26 mL) at -78 °C and the solution was stirred at -78 °C for 2 h. Dichloromethane (25 mL) and saturated aqueous NaHCO₃ (25 mL) were added and the aqueous phase was extracted with DCM (2 × 25 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:10 ether:light petroleum) afforded the *title compound 16* as a pale oil (550 mg, 86%), R_f 0.40 (1:10 EtOAc:light petroleum), $[\alpha]_D^{25}$ +17.8 (c 3.1, CHCl₃); ν_{max}/cm^{-1} 2944, 2863, 1613, 1587, 1513, 1471, 1463, 1428, 1382, 1361, 1250, 1172, 1104, 1039, 882, 835, 823, 774, 737 and 701; δ_H (400 MHz, CDCl₃) -0.06 and -0.03 (each 3 H, s, SiCH₃), 0.77 [9 H, s, SiC(CH₃)₃], 0.93 (3 H, s, 8-CH₃), 0.95-1.05 (33 H, m, 8-CH₃', 3 × SiCH(CH₃)₂, SiC(CH₃)₃), 1.27 (1 H, q, J 12.1, 6-H_{ax}), 1.47-1.63 (2 H, m, 2-H, 4-H), 1.64-1.83 (5 H, m, 2-H', 4-H', 6'-H_{eq}, 10-H, 14-H_{ax}), 1.89 (1 H, t, J 12.4, 12-H_{ax}), 1.96 (1 H, dd, J 15.9, 4.9, 10-H'), 2.24 (1 H, d, J 13.4, 12-H_{eq}), 2.38 (1 H, d, J 13.4, 14-H_{eq}), 3.09 (3 H, s, 9-OCH₃), 3.30-3.54 (5 H, m, 5-H, 11-H, 15-H, 16-H₂), 3.59 (1 H, dd, J 11.6, 4.5, 7-H), 3.62-3.70 (2 H, m, 1-H₂), 3.72 (3 H, s, ArOCH₃), 3.94 (1 H, m, 3-H), 4.18 (2 H, d, J 6.1, 2'-H₂), 4.35 (1 H, d, J 11.6, PhHCH), 4.44 (2 H, s, ArCH₂), 4.52 (1 H, d, J 11.6, PhHCH), 5.30 (1 H, t, J 6.1, 1'-H), 6.79 (2 H, d, J 8.6, ArH), 7.15-7.21 (3 H, m, ArH), 7.21-7.26 (4 H, m, ArH), 7.27-7.35 (6 H, m, ArH) and 7.56-7.61 (4 H, m, ArH); δ_C (100 MHz, CDCl₃) -5.3, -5.1, 11.0, 15.8, 17.0, 18.1, 19.9, 24.9, 25.9, 30.5, 32.2, 38.0, 39.5, 42.1, 42.4, 43.5, 47.1, 54.2, 58.4, 59.4, 65.0, 66.3, 70.6, 71.9, 72.0, 74.2, 75.6, 78.1, 103.1, 112.7, 122.9, 126.2, 126.3, 126.6(2), 127.2, 128.1, 128.5(2), 129.5, 132.8, 134.5(2), 134.7, 138.3 and 158.0; m/z (ES⁺) 1160 (M⁺ + 23, 7%). Traces of an impurity (<5%) were detected by ¹H and ¹³C NMR in the acetal **16** but were not removed or characterised.

(3S,5S,7S,9S,11S,15R)-7-Benzoyloxy-3-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxyhexadecan-16-ol (17).

Dichlorodicyanoquinone (9 mg, 0.041 mmol) was added to the PMB ether **16** (31 mg, 0.027 mmol) in DCM/methanol (9:1, 110 mL) at rt and the resulting black slurry stirred at for 2 h before the addition of saturated aqueous Na₂S₂O₃ (5 mL) and saturated aqueous NaHCO₃ (5 mL). After stirring for an additional 10 min, DCM (10 mL) was added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were washed with a

mixture of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 (1:1, 20 mL) and brine, then dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (1:20 to 1:10 EtOAc:light petroleum) afforded the *title compound 17* as a pale oil (20 mg, 70%), R_f 0.18 (1:10 EtOAc:light petroleum), $[\alpha]_D^{25} +18.0$ (c 1.6, CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ 3460, 2942, 2889, 2861, 1471, 1463, 1428, 1383, 1361, 1257, 1104, 1093, 882, 835, 774, 738 and 701; δ_{H} (500 MHz, CDCl_3) -0.06 and -0.03 (each 3 H, s, SiCH_3), 0.77 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.93 (3 H, s, 8- CH_3), 0.95-1.05 [30 H, m, 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$, $\text{SiC}(\text{CH}_3)_3$], 1.01 (3 H, s, 8- CH_3 '), 1.26 (1 H, q, J 12.2, 6- H_{ax}), 1.51 (1 H, dt, J 14.0, 5.8, 4-H), 1.57-1.75 (5 H, m, 14- H_{ax} , 10-H, 4-H', 2- H_2), 1.77 (1 H, m, 6- H_{eq}), 1.88 (1 H, t, J 12.4, 12- H_{ax}), 1.95 (1 H, dd, J 16.1, 7.4, 10-H'), 2.13 (1 H, dd, J 9.0, 3.0, OH), 2.17 (1 H, d, J 13.6, 12- H_{eq}), 2.28 (1 H, d, J 13.2, 14- H_{eq}), 3.09 (3 H, s, 9- OCH_3), 3.27 (1 H, m, 15-H), 3.44 (1 H, m, 16-H), 3.46-3.54 (2 H, m, 16-H', 5-H), 3.56 (1 H, m, 11-H), 3.58 (1 H, dd, J 11.7, 4.4, 7-H), 3.62-3.72 (2 H, m, 1- H_2), 3.95 (1 H, m, 3-H), 4.13-4.22 (2 H, m, 2'- H_2), 4.35 and 4.52 (each 1 H, d, J 11.7, PhHCH), 5.33 (1 H, t, J 6.1, 1'-H), 7.18 (1 H, m, ArH), 7.22-7.27 (4 H, m, ArH), 7.27-7.37 (6 H, m, ArH) and 7.56-7.61 (4 H, m, ArH); δ_{C} (125 MHz, CDCl_3) -5.2 , -5.1 , 11.0, 15.9, 17.0(2), 18.2, 20.0, 24.9, 25.9, 29.4, 32.2, 37.7, 39.6, 41.9, 42.1, 43.5, 47.1, 58.4, 59.5, 64.9, 65.1, 66.3, 70.7, 73.9, 76.3, 78.2, 103.0, 123.5, 126.2, 126.3, 126.6, 127.2, 128.5, 132.9(2), 133.9, 134.5(2) and 138.2; m/z (ES^+) 1040 (M^+ + 23, 4%).

(3S,5S,7S,9S,11S,15R)-7-Benzoyloxy-3-tert-butylidimethylsilyloxy-1-tert-butylidiphenylsilyloxy-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxyhexadecan-16-al (18).

Tetrapropylammonium perruthenate (0.35 mg, 0.00098 mmol) was added to the alcohol **17** (20 mg, 0.020 mmol), NMO (4.6 mg, 0.039 mmol) and powdered 4 Å molecular sieves (45 mg) in DCM (447 μL) at rt and the mixture stirred for 1 h. More NMO (4.6 mg, 0.039 mmol) was added and, after stirring for 1 h, the mixture was filtered through Celite®. A mixture of saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 (1:1, 10 mL) and Et_2O (10 mL) were added and the aqueous phase was extracted with Et_2O (2 $\times$ 20 mL). The organic extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure to leave the *title compound 18* that was used immediately without further purification, R_f 0.26 (1:10 EtOAc:light petroleum); $\nu_{\text{max}}/\text{cm}^{-1}$ 2929, 2860, 1741, 1472, 1463, 1428, 1382, 1361, 1258, 1106, 882, 835, 803, 774, 738 and 700; δ_{H} (500 MHz, C_6D_6) 0.00 and 0.02 (each 3 H, s, SiCH_3), 0.86 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.92-1.04 [21 H, m, 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$], 1.08 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 1.12 and 1.20 (each 3 H, s, 8- CH_3), 1.39 (1 H, q, J 12.2, 6- H_{ax}), 1.57-1.67 (2 H, m, 14- H_{ax} , 4-H), 1.68-1.89 (6 H, m, 12- H_{ax} , 10-H, 6- H_{eq} , 4-H', 2- H_2), 2.15-2.22 (2 H, m, 10-H', 14- H_{eq}), 2.60 (1 H, d, J 12.9, 12- H_{eq}), 3.10 (3 H, s, 9- OCH_3), 3.36 (1 H, dd, J 12.0, 2.8, 15-H), 3.59-3.70 (2 H, m, 11-H, 5-H), 3.71-3.85 (3 H, m, 7-H, 1- H_2), 4.07-4.22 (3 H, m, 2'- H_2 , 3-H), 4.18 and 4.39 (each 1 H, d, J 12.0, PhHCH), 5.46 (1 H, t, J 6.1, 1'-H), 6.97 (1 H, t, J 7.3 ArH), 7.06 (2 H, t, J 7.5, ArH), 7.10-7.18 (6 H, m, ArH), 7.21 (2 H, d, J 7.6, ArH), 7.66-7.72 (4 H, m, ArH) and 9.45 (1 H, s, 16-H); δ_{C} (100 MHz, C_6D_6) -5.3 , 10.9, 15.8, 16.9, 18.1, 19.9, 24.8, 25.8, 28.2, 32.3, 38.0, 39.9, 42.1, 42.2, 43.8, 47.0, 58.3, 59.5, 65.2, 66.6, 70.4,

74.6, 77.7, 80.0, 103.0, 124.4, 126.3(2), 126.7, 126.9, 128.7, 132.5, 132.8, 134.6, 138.4 and 199.0; m/z (ES^+) 1070 (100%) and 1038 (M^+ + 23, 45).

(3S,5S,7S,9S,11S,15R,16EZ)-7-Benzoyloxy-3-tert-butylidimethylsilyloxy-1-tert-butylidiphenylsilyloxy-18-(1,3-dithian-2-yl)-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8,18,18-tetramethyl-9-methoxyoctadec-16-ene (20).

Lithium hexamethyldisilazide (1.0 M in THF, 20 μL , 0.024 mmol) was added to the sulfone **19**¹⁸ (9 mg, 0.024 mmol) in THF (241 μL) at -78°C and the solution stirred for 30 min at -78°C . The aldehyde **18** (15 mg, 0.015 mmol) in THF (0.2 mL) was added in one portion and the solution was allowed to warm to rt and stirred for 16 h. The reaction mixture was partitioned between ether (10 mL) and saturated aqueous NaHCO_3 (10 mL) and the aqueous phase was extracted with ether (2 $\times$ 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:25 ether:light petroleum with 1% Et_3N) afforded the *title compound 20* as a pale oil (13.5 mg, 78%), (*E*):(*Z*) = 2:1 (^1H NMR), R_f 0.65, 0.74 [(*Z*)- and (*E*)-isomers, 1:3 ether:light petroleum]; $\nu_{\text{max}}/\text{cm}^{-1}$ 2956, 2928, 2858, 1742, 1471, 1463, 1428, 1385, 1361, 1259, 1104, 1091, 882, 835, 802, 775 and 700. Repeated chromatography gave the (*E*)-isomer; δ_{H} (500 MHz, CDCl_3) -0.06 and -0.03 (each 3 H, s, SiCH_3), 0.77 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.94 (3 H, s, 8- CH_3), 0.94-1.07 [33 H, m, 8- CH_3 ', 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$, $\text{SiC}(\text{CH}_3)_3$], 1.14 and 1.15 (each 3 H, s, 18- CH_3), 1.27 (1 H, q, J 12.2, 6- H_{ax}), 1.49-1.63 (2 H, m, 2-H, 4-H), 1.65-1.75 (5 H, m, 2-H', 4-H', 10-H, 14- H_{ax} , 5''-H), 1.90 (1 H, m, 12- H_{ax}), 1.95-2.05 (2 H, m, 10-H', 5''-H'), 2.24 (1 H, d, J 12.9, 14- H_{eq}), 2.43 (1 H, d, J 13.6, 12- H_{eq}), 2.72-2.82 (4 H, m, 4''- H_2 , 6''- H_2), 3.10 (3 H, s, 9- OCH_3), 3.44-3.53 (2 H, m, 5-H, 11-H), 3.59 (1 H, dd, J 11.5, 4.4, 7-H), 3.62-3.71 (3 H, m, 1- H_2 , 15-H), 3.93 (1 H, s, 2''-H), 3.94 (1 H, m, 3-H), 4.16-4.24 (2 H, m, 2'- H_2), 4.35 and 4.52 (each 1 H, d, J 11.7, PhHCH), 5.30 (1 H, t, J 6.2, 1'-H), 5.42 (1 H, dd, J 15.8, 5.7, 16-H), 5.70 (1 H, d, J 15.8, 17-H), 7.18 (1 H, m, ArH), 7.22-7.26 (4 H, m, ArH), 7.26-7.37 (6 H, m, ArH) and 7.56-7.61 (4 H, m, ArH); (*Z*)-isomer: 3.06 (3 H, s, 9- OCH_3), 3.99 (1 H, s, 2''-H), 5.33 (1 H, dd, J 12.3, 9.1, 16-H) and 5.51 (1 H, d, J 12.3, 17-H); m/z (ES^+) 1196 (M^+ + 23, 27%).

(5S,7R,8R,2E)-5,8-Bis-tert-butylidimethylsilyloxy-3-benzoyloxymethyl-1-triisopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (22).

2,6-Lutidine (0.52 mL, 4.46 mmol) was added to the alcohol **21** (1.0 g, 1.41 mmol) in DCM (12 mL) and the solution cooled to 0°C . *tert*-Butylidimethylsilyl trifluoromethylsulfonate (0.52 mL, 2.26 mmol) was added and the mixture stirred for 1 h. Water (10 mL) was added dropwise and the mixture allowed to warm to rt. Water (30 mL) and DCM (30 mL) were added and the aqueous layer was extracted with DCM (2 $\times$ 30 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 20:1 light petroleum:ether) gave the *title compound 22* as a clear, colourless oil (1.03 g, 89%), R_f = 0.60 (20:1 light petroleum:ether), $[\alpha]_D^{22} -13.6$ (c 6.1, CHCl_3) (Found: M^+ + Na,

847.5542. $C_{44}H_{88}O_6NaSi_4$ requires M, 847.5550; ν_{max}/cm^{-1} 3066, 3031, 2953, 2893, 2863, 1464, 1381, 1252, 1102, 1059, 937 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 (9 H, s, $3 \times SiCH_3$), 0.04 (9 H, s, $3 \times SiCH_3$), 0.04 (3 H, s, $SiCH_3$), 0.81-0.97 (2 H, m, $SiCH_2$), 0.86 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 1.01 (3 H, d, J 6.3, 9-H₃), 1.03-1.16 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.39 (1 H, ddd, J 13.5, 10.2, 2.5, 6-H), 1.58 (1 H, m, 6-H'), 2.22 (1 H, dd, J 13.4, 8.4, 4-H), 2.36 (1 H, dd, J 13.4, 5.2, 4-H'), 3.44 (1 H, m, $SiCH_2CH$), 3.502 (1 H, m, 7-H), 3.67 (1 H, m, $SiCH_2CH$), 3.88-4.05 (4 H, m, 3-CH₂, 5-H, 8-H), 4.34 (2 H, d, J 5.7, 1-H₂), 4.45 (2 H, s, $PhCH_2$), 4.65 (2 H, s, OCH_2O), 5.69 (1 H, t, J 5.7, 2-H) and 7.23-7.35 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) -3.3(2), -3.1, -2.4, 0.0, 13.4, 18.6, 19.4, 19.5, 19.6, 27.3, 27.4, 37.0, 39.2, 61.7, 66.6, 69.7, 70.4, 73.1, 75.7, 81.7, 97.5, 128.9, 129.2, 129.7, 132.3, 134.9 and 139.9; m/z (ES^+) 884.0 (75%) and 847.5 ($M^+ + 23$, 100).

(4S,6R,7R)-4,7-Bis-tert-butyl dimethylsilyloxy-2-[(E)-2-triisopropylsilyloxyethylidene]-6-(2-trimethylsilylethoxymethoxy)octan-1-ol (23).

Finely chopped lithium wire (53 mg, 7.6 mmol) was added to naphthalene (1.75 g, 13.7 mmol) in THF (10 mL) and the resulting deep green mixture was stirred at rt for 2 h. An aliquot of this solution (5 mL) was added over 1 h to the benzyl ether **22** (0.90 g, 1.09 mmol) in THF (32 mL) at -20 °C. At this point the starting material had reacted (TLC) and solid NH_4Cl was added slowly with stirring until the brown colour of the solution had disappeared. The mixture was allowed to warm to rt over 20 min and ether (200 mL) and saturated aqueous $NaHCO_3$ were added. The aqueous layer was extracted with ether (100 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (20:1 then 10:1 light petroleum:ether) afforded the *title compound* **23** as a clear, colourless oil (0.705 g, 88%), R_f = 0.15 (10:1 light petroleum:ether) [α_D^{34} +8.1 (c 6.4, $CHCl_3$) (Found: $M^+ + Na$, 757.5076. $C_{37}H_{82}O_6NaSi_4$ requires M, 757.5081); ν_{max}/cm^{-1} 3442, 2954, 2893, 2864, 1463, 1381, 1252, 1102, 1058, 937, 882 and 833; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.08 and 0.09 (each 3 H, s, $SiCH_3$), 0.77-0.99 [20 H, m, $2 \times SiC(CH_3)_3$, $SiCH_2$], 0.99-1.13 [24 H, m, $3 \times SiCH(CH_3)_2$, 8-H₃], 1.42 (1 H, ddd, J 14.2, 10.1, 4.1, 5-H), 1.62 (1 H, ddd, J 14.2, 7.6, 1.0, 5-H'), 2.26 (1 H, dd, J 13.8, 6.3, 3-H), 2.40 (1 H, dd, J 13.8, 5.0, 3-H'), 2.56 (1 H, br. t, J 6.0, OH), 3.45-3.55 (2 H, m, 6-H, $HCHCH_2Si$), 3.65 (1 H, ddd, J 10.1, 9.8, 5.7, $HCHCH_2Si$), 3.93-4.06 (4 H, m, 1-H₂, 4-H, 7-H), 4.28 (1 H, dd, J 13.2, 5.6, 2'-H), 4.32 (1 H, dd, J 13.2, 6.4, 2'-H'), 4.67 and 4.70 (each 1 H, d, J 6.9, OHCHO) and 5.69 (1 H, m, 1'-H); δ_C (125 MHz, $CDCl_3$) -3.3(2), -3.1, -2.6, 0.0, 13.4, 18.7, 19.5, 19.6, 27.3, 27.4, 37.0, 39.5, 61.7, 66.8, 69.3, 70.4, 70.9, 81.8, 97.3, 131.5 and 137.8; m/z (ES^+) 753.2 ($M^+ + 18$, 100%) and 735.7 ($M^+ + 1$, 83).

(5S,7R,8R,2E)-3-Bromomethyl-5,8-bis-tert-butyl dimethylsilyloxy-1-triisopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (24).

Carbon tetrabromide (2.83 g, 8.54 mmol) was added to triphenylphosphine (2.24 g, 8.54 mmol) in dry DCM (94 mL) at 0 °C. The solution was stirred for 1 min then transferred to a solution of the alcohol **23** (1.57 g, 2.13 mmol) in dry DCM (47

mL) at 0 °C. The mixture was stirred at 0 °C for 10 min and DCM (50 mL) and saturated aqueous $NaHCO_3$ (50 mL) were added. The aqueous layer was extracted with DCM (2×50 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (100:1 to 50:1 light petroleum:ether) gave the *title compound* **24** as a pale yellow oil (1.56 g, 92%), R_f = 0.23 (50:1 light petroleum:ether), [α_D^{34} -2.1 (c 13.6, $CHCl_3$) (Found: $M^+ + Na$, 819.4237. $C_{37}H_{81}O_5^{79}BrNaSi_4$ requires M, 819.4237); ν_{max}/cm^{-1} 2954, 2893, 2863, 1464, 1381, 1252, 1102, 1057, 937 and 833; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.07 and 0.10 (each 3 H, s, $SiCH_3$), 0.80-0.98 (2 H, m, $SiCH_2$), 0.86 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 0.98-1.14 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.01 (3 H, d, J 6.3, 9-H₃), 1.34 (1 H, ddd, J 13.9, 10.1, 3.2, 6-H), 1.59 (1 H, ddd, J 13.9, 8.5, 1.0, 6-H'), 2.33 (1 H, dd, J 13.9, 7.9, 4-H), 2.45 (1 H, dd, J 13.9, 5.5, 4-H'), 3.44-3.54 (2 H, m, 7-H, $HCHCH_2Si$), 3.66 (1 H, ddd, J 11.4, 9.8, 5.4, $HCHCH_2Si$), 3.94 (1 H, m, 5-H), 3.98-4.06 (3 H, m, 3-CH₂, 8-H), 4.27 (1 H, dd, J 13.9, 5.4, 1-H), 4.30 (1 H, dd, J 13.9, 5.8, 1 H'), 4.68 and 4.71 (each 1 H, d, J 7.0, OHCHO) and 5.80 (1 H, m, 2-H); δ_C (125 MHz, $CDCl_3$) -3.3(2), -3.1, -2.5, 0.0, 13.4, 18.6, 19.4(2), 19.5, 19.6, 27.3, 27.4, 37.2, 38.6, 40.6, 61.9, 66.8, 69.6, 70.3, 81.7, 97.5, 134.7 and 135.5; m/z (ES^+) 857.8 (100%), 855.8 (90), 821.2 ($M^+ + 23$, 33) and 819.4 ($M^+ + 23$, 20).

(5S,7R,8R)-5,8-Bis-tert-butyl dimethylsilyloxy-3-[(Z)-2-triisopropylsilyloxyethylidene]-7-(2-trimethylsilylethoxymethoxy)nonanenitrile (25).

Sodium cyanide (124 mg, 2.54 mmol) was added to the bromide **24** (1.56 g, 1.95 mmol) in DMF (20 mL) at 0 °C and the mixture was stirred at 0 °C for 3.5 h. Ether (250 mL) and water (150 mL) were added and the aqueous layer was extracted with ether (100 mL). The organic extracts were washed with water (2×50 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 20:1 light petroleum:ether) gave recovered bromide **24** (0.37 g, 24%) followed by the *title compound* **25** as a clear, colourless oil (1.03 g, 71%), R_f = 0.23 (10:1 light petroleum:ether), [α_D^{32} -5.5 (c 2.9, $CHCl_3$) (Found: $M^+ + Na$, 766.5096. $C_{38}H_{81}O_5NNaSi_4$ requires M, 766.5084); ν_{max}/cm^{-1} 2954, 2929, 2862, 2361, 2252, 1463, 1381, 1252, 1103, 1058, 937 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02, 0.03, 0.06 and 0.07 (each 3 H, s, $SiCH_3$), 0.83-0.98 (2 H, m, CH_2Si), 0.85 and 0.87 [each 9 H, s, $SiC(CH_3)_3$], 1.01 (3 H, d, J 6.3, 9-H₃), 1.02-1.12 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.34 (1 H, ddd, J 14.2, 10.1, 4.1, 6-H), 1.62 (1 H, ddd, J 14.2, 7.6, 1.9, 6-H'), 2.32 (2 H, d, J 6.0, 4-H₂), 3.15 (2 H, s, 2-H₂), 3.43-3.52 (2 H, m, 7-H, $HCHCH_2Si$), 3.66 (1 H, ddd, J 11.4, 9.5, 5.4, $HCHCH_2Si$), 3.93 (1 H, m, 5-H), 4.02 (1 H, dq, J 6.3, 5.7, 8-H) 4.27 (1 H, dd, J 13.2, 5.4, 2'-H), 4.30 (1 H, dd, J 13.2, 6.6, 2'-H'), 4.66 and 4.69 (each 1 H, d, J 7.0, OHCHO) and 5.78 (1 H, m, 1'-H); δ_C (125 MHz, $CDCl_3$) -3.3(2), -3.1, -2.6, 0.0, 13.4, 18.5, 19.2, 19.4, 19.5, 19.6, 27.3, 27.4(2), 36.9, 40.4, 61.6, 66.9, 70.2, 81.8, 97.4, 119.0, 128.1 and 133.7; m/z (ES^+) 802.3 (29%), 766.9 ($M^+ + 23$, 39) and 761.6 ($M^+ + 18$, 100).

Methyl (3RS,7S,9R,10R)-7,10-Bis-tert-butyl dimethylsilyloxy-3-hydroxy-2,2-dimethyl-5-[(Z)-2-triisopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecanoate (27).

Di-isobutylaluminium hydride (1 M in heptane, 1.64 mL, 1.64 mmol) was added to the nitrile **25** (1.06 g, 1.42 mmol) in DCM (17.5 mL) at -78°C and the mixture was stirred for 45 min before the dropwise addition of ethanol (7.3 mL). After stirring for 30 min, saturated aqueous NH_4Cl (100 mL) and ethyl acetate (100 mL) were added and the mixture stirred vigorously for 30 min before addition of saturated aqueous Rochelle's salt (100 mL) and further stirring for 2 h. The aqueous layer was extracted with ethyl acetate (2×100 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to leave the aldehyde **26** as a viscous, yellow oil (1.10 g) that was used directly in the next step, $R_f = 0.23$ (10:1 light petroleum:ether): δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.03, 0.04 and 0.05(2) (each 3 H, s, SiCH_3), 0.80-0.95 (2 H, m, CH_2Si), 0.86 [18 H, s, $2 \times \text{SiC}(\text{CH}_3)_3$], 1.04 (3 H, d, J 7.0, 9-H₃), 0.98-1.15 [21 H, m, $3 \times \text{SiCH}(\text{CH}_3)_2$], 1.38 (1 H, m, 6-H), 1.57 (1 H, dd, J 15.0, 7.9, 6-H'), 2.26 (2 H, d, J 8.0, 4-H₂), 3.09 (2 H, br. s, 2-H₂), 3.49 (1 H, m, HCHCH_2Si), 3.50 (1 H, m, 7-H), 3.65 (1 H, m, HCHCH_2Si), 3.90 (1 H, m, 5-H), 4.01 (1 H, pent, J 6.0, 8-H) 4.32 (2 H, d, J 7.0, 2'-H₂), 4.66 and 4.69 (each 1 H, d, J 7.0, OHCHO), 5.56 (1 H, t, J 7.0, 1'-H) and 9.61 (1 H, t, J 1.5, 1-H).

Lithium di-isopropylamide (1.7 M in THF, heptane, ethylbenzene, 0.92 mL, 1.56 mmol) was added to methyl 2-methylpropanoate (0.18 mL, 1.56 mmol) in THF (5.8 mL) at -78°C and the mixture stirred for 70 min at -78°C . A cooled solution of the aldehyde **26** (1.10 g, from 1.42 mmol nitrile **25**) in THF (5.83 mL) was added over 1 min and the mixture was stirred for 30 min, warmed to r.t. and stirred for a further 30 min. Ether and saturated aqueous NaHCO_3 (50 mL) were added and the aqueous layer was extracted with ether (2×50 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 10:1 light petroleum:ether) gave the *title compound* **27** as a pale yellow oil (0.63 g, 52% from nitrile **25**), as a 1:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.17$ and 0.20 (10:1 light petroleum:ether), $[\alpha]_{\text{D}}^{27} -10.2$ (c 11.8, CHCl_3) (Found: $\text{M}^+ + \text{NH}_4$, 866.6214. $\text{C}_{43}\text{H}_{96}\text{O}_8\text{NSi}_4$ requires M , 866.6208); $\nu_{\text{max}}/\text{cm}^{-1}$ 3509, 2953, 2864, 1728, 1463, 1381, 1250, 1186, 1099, 1058, 936 and 835; δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.03, 0.04 and 0.06 (each 3 H, s, SiCH_3), 0.07 and 0.08 (each 1.5 H, s, SiCH_3), 0.86(2) and 0.87(2) [each 4.5 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.88-0.98 (2 H, m, SiCH_2), 0.98-1.13 [24 H, m, $3 \times \text{SiCH}(\text{CH}_3)_2$, 11-H₃], 1.16, 1.17, 1.19 and 1.20 (each 1.5 H, s, 2-CH₃), 1.43 and 1.56 (each 1 H, m, 8-H), 1.89 (0.5 H, dd, J 13.7, 11.0, 4-H), 1.98 (0.5 H, dd, J 13.6, 10.6, 4-H), 2.11-2.46 (4 H, m, 4-H', 6-H₂, OH), 3.44 (1 H, ddd, J 11.0, 9.7, 6.1, HCHCH_2Si), 3.53 (1 H, m, 9-H), 3.69 (1 H, m, HCHCH_2Si), 3.68(2) (each 1.5 H, s, CO_2CH_3), 3.79-3.93 (2 H, m, 3-H, 7-H), 4.05 (1 H, m, 10-H), 4.28 (1 H, dd, J 13.1, 5.7, 2'-H), 4.30 (1 H, dd, J 13.1, 6.2, 2'-H'), 4.67, 4.68, 4.69 and 4.71 (each 0.5 H, d, J 7.0 OHCHO) and 5.49 and 5.51 (each 0.5 H, t, J 5.7, 1'-H); δ_{C} (125 MHz, CDCl_3) -3.3(2), -3.0, -2.3(2), 0.0, 13.5, 18.5(2), 19.5(2), 19.6, 21.8, 22.2, 22.6, 23.1, 27.3, 27.4(2), 36.8, 36.9, 40.6, 41.1, 41.7, 41.9, 48.4, 48.5, 53.3, 61.7, 61.9, 66.7(2), 70.0, 70.2(2), 70.5, 74.9, 75.5, 81.8, 81.9, 97.6(2), 133.0, 133.1, 135.5, 135.7, 178.9 and 179.0; m/z (ES^+) 907.2 (100%) and 866.3 ($\text{M}^+ + 18$, 31).

Methyl (3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-3-triethylsilyloxy-2,2-dimethyl-5-[(*E*)-2-triisopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecanoate (28).

Imidazole (0.387 g, 5.69 mmol) and triethylsilyl chloride (0.65 mL, 3.88 mmol) were added to the alcohol **27** (0.525 g, 0.618 mmol) in DMF (14 mL) and the solution stirred at rt for 16 h. Ether (150 mL) and saturated aqueous NaHCO_3 (100 mL) were added and the organic layer was washed with water (2×100 mL) and brine (50 mL), dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (100:1 then 10:1 light petroleum:ether) gave the *title compound* **28** as a pale yellow oil (0.452 g, 76%), a 1:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.58$ and 0.60 (10:1 light petroleum:ether), $[\alpha]_{\text{D}}^{26} -13.3$ (c 5.2, CHCl_3) (Found: $\text{M}^+ + \text{NH}_4$, 980.7081. $\text{C}_{49}\text{H}_{110}\text{O}_8\text{NSi}_5$ requires M , 980.7072); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2866, 1742, 1729, 1471, 1463, 1386, 1361, 1251, 1190, 1103, 1058, 937, 835 and 774; δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.03 (6 H, s, $2 \times \text{SiCH}_3$), 0.05(2), 0.07 and 0.09 (each 1.5 H, s, SiCH_3), 0.52 and 0.55 (each 3 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.81-0.95 (2 H, m, SiCH_2), 0.86(2), 0.87 and 0.88 [each 4.5 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.90 and 0.91 (each 4.5 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 1.01 (3 H, d, J 6.2, 11-H₃), 1.03-1.14 [21 H, m, $3 \times \text{SiCH}(\text{CH}_3)_2$], 1.09(2), 1.16, 1.17 (each 1.5 H, s, 2-CH₃), 1.39 and 1.42 (each 0.5 H, ddd, J 13.6, 10.5, 2.8, 8-H), 1.52 (1 H, m, 8-H'), 1.89-2.35 (4 H, m, 4-H₂, 6-H₂), 3.42 (1 H, td, J 10.4, 6.0, OHCHCH_2Si), 3.54 (1 H, m, 9-H), 3.64 (3 H, s, CO_2CH_3), 3.70 (1 H, td, J 10.4, 5.3, OHCHCH_2Si), 3.81 (1 H, m, 7-H), 4.07 (1 H, m, 10-H), 4.10 (0.5 H, dd, J 8.4, 3.3, 3-H), 4.13 (0.5 H, dd, J 8.9, 2.1, 3-H), 4.27 and 4.30 (each 1 H, dd, J 12.9, 5.7, 2'-H), 4.67 and 4.68 (each 0.5 H, d, J 7.6, OHCHO), 4.69 (1 H, s, OCH_2O) and 5.42 and 5.44 (each 0.5 H, t, J 5.7, 1'-H); δ_{C} (125 MHz, CDCl_3) -3.4, -3.3, -3.0(2), -2.3, -2.2, 0.0, 6.8, 6.9, 8.5, 13.4, 18.4(2), 19.5(2), 21.0, 22.3, 23.6, 27.3, 27.4, 36.7, 36.9, 41.0, 42.2, 42.8, 43.2, 49.9(2), 53.0, 53.1, 62.0, 62.1, 66.5, 66.6, 70.0, 70.1, 70.2, 70.3, 76.4, 76.9, 81.7, 81.8, 97.7, 132.4, 132.8, 134.6, 134.7 and 178.9; m/z (ES^+) 986.1 ($\text{M}^+ + 23$, 86%) and 981.5 ($\text{M}^+ + 18$, 100).

(3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-triisopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecan-1-ol (29).

Di-isobutylaluminium hydride (1 M in heptane, 0.80 mL, 0.80 mmol) was added to methyl ester **28** (0.308 g, 0.320 mmol) in dry toluene (6 mL) at -78°C and the solution stirred for 1.5 h before the addition of saturated aqueous Rochelle's salt. The mixture was allowed to warm to rt then stirred vigorously for 24 h. Ether (50 mL) and saturated aqueous Rochelle's salt (30 mL) were added and the aqueous layer extracted with ether (2×50 mL). The organic extracts were washed with water (20 mL) and brine (20 mL), dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (15:1 then 10:1 light petroleum:ether) gave the *title compound* **29** as a clear, colourless oil (0.24 g, 80%), a 1:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.19$ (10:1 light petroleum:ether), $[\alpha]_{\text{D}}^{30} -16.2$ (c 4.2, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 957.6673. $\text{C}_{48}\text{H}_{106}\text{O}_7\text{NaSi}_5$ requires M , 957.6677); $\nu_{\text{max}}/\text{cm}^{-1}$ 3504, 2956, 2866, 1464, 1380, 1251, 1100, 1058, 1014, 937, 859, 835 and 774; δ_{H} (500 MHz, CDCl_3) 0.00(2)

[each 4.5 H, s, Si(CH₃)₃], 0.03 (6 H, s, 2 × SiCH₃), 0.04 and 0.05 (each 1.5 H, s, SiCH₃), 0.07 (3 H, s, SiCH₃), 0.58 and 0.60 (each 3 H, q, *J* 8.0, 3 × SiCH₂), 0.81–0.97 (2 H, m, SiCH₂), 0.86(2) and 0.87(2) [each 4.5 H, s, SiC(CH₃)₃], 0.93 (9 H, t, *J* 8.0, 3 × SiCH₂CH₃), 0.97–1.17 [30 H, m, 3 × SiCH(CH₃)₂, 2 × 2-CH₃, 11-H₃], 1.42 and 1.53 (each 1 H, m, 8-H), 1.98–2.41 (4 H, m, 4-H₂, 6-H₂), 3.00 (1 H, br. s, OH), 3.25 and 3.26 (each 0.5 H, d, *J* 10.8, 1-H), 3.43 (1 H, m, OHCHCH₂Si), 3.53 (1 H, m, 9-H), 3.65–3.75 (3 H, m, 1-H', 3-H, OHCHCH₂Si), 3.65 (1 H, m, 7-H), 4.04 (1 H, m, 10-H), 4.28 (1 H, dd, *J* 12.8, 6.1, 2'-H), 4.30 (1 H, dd, *J* 12.8, 5.3, 2'-H'), 4.64–4.71 (2 H, m, OCH₂O) and 5.45 (1 H, m, 1'-H); δ_c (125 MHz, CDCl₃) –3.4(2), –3.3(2), –2.9, –2.3, –2.2, 0.0, 6.7, 6.8, 8.5, 13.4, 18.4, 18.5, 19.5(3), 23.3, 23.5, 24.8, 25.0, 27.3, 27.4(2), 36.5, 37.0, 40.8, 40.9, 41.0, 42.3, 42.4, 42.8, 62.0(2), 66.6, 69.9, 70.1, 70.2(2), 71.6, 71.7, 80.2, 80.9, 81.5, 81.6, 97.6, 131.8, 132.6, 135.0 and 135.2; *m/z* (ES⁺) 958.2 (M⁺ + 23, 100%).

(3*RS*,7*S*,9*R*,10*R*)-1-(Benzothiazol-2-ylsulfanyl)-7,10-bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecane (30).

2-Mercaptobenzothiazole (0.128 g, 0.763 mmol) and triphenylphosphine (0.198 g, 0.755 mmol) were added to the alcohol **29** (0.24 g, 0.254 mmol) in THF (3.6 mL) and the mixture stirred until homogeneous. Di-isopropyl azodicarboxylate (0.15 mL, 0.76 mmol) was added and the mixture stirred at rt for 24 h then concentrated under reduced pressure. The mixture was dissolved in the minimum of DCM and chromatography (100:1 then 50:1 light petroleum:ether) gave the *title compound* **30** as a viscous, clear, colourless oil (0.26 g, 93%), a 1:1 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.57 and 0.60 (15:1 light petroleum:ether), [α]_D²² –8.4 (c 4.3, CHCl₃); ν_{max}/cm^{–1} 2955, 2866, 1463, 1429, 1385, 1250, 1100, 1058, 993, 937, 835, 774 and 754; δ_H (500 MHz, CDCl₃) –0.01 and 0.00 [each 4.5 H, s, Si(CH₃)₃], 0.02 and 0.04 (each 3 H, s, SiCH₃), 0.06, 0.07, 0.09 and 0.11 (each 1.5 H, s, SiCH₃), 0.61 and 0.62 (each 3 H, q, *J* 7.9, 3 × SiCH₂), 0.80–0.98 (2 H, m, SiCH₂), 0.85, 0.87, 0.88 and 0.89 [each 4.5 H, s, SiC(CH₃)₃], 0.95 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 1.02 and 1.03 (each 1.5 H, d, *J* 6.3, 11-H₃), 1.03–1.15 [27 H, m, 3 × SiCH(CH₃)₂, 2 × 2-CH₃], 1.45 and 1.54 (each 1 H, m, 8-H), 1.97 and 2.03 (each 0.5 H, dd, *J* 14.1, 9.3, 4-H), 2.13 (0.5 H, dd, *J* 13.1, 8.6, 6-H), 2.24 (1 H, m, 6-H₂), 2.29–2.40 (1.5 H, m, 4-H', 6-H'), 3.42 (1 H, m, OHCHCH₂Si), 3.45 and 3.48 (each 1 H, s, 1-H₂), 3.54 (1 H, m, 9-H), 3.69 (1 H, m, OHCHCH₂Si), 3.75 (1 H, m, 3-H), 3.87 (1 H, m, 7-H), 4.06 (1 H, m, 10-H), 4.30 (1 H, dd, *J* 12.6, 5.6, 2'-H), 4.32 (1 H, dd, *J* 12.6, 6.3, 2'-H'), 4.66 (1 H, s, OCH₂O), 4.68 and 4.70 (each 0.5 H, d, *J* 7.0, OHCHO), 5.48 (1 H, m, 1'-H), 7.28 and 7.40 (each 1 H, m, ArH) and 7.74 and 7.84 (each 1 H, d, *J* 8.1, ArH); δ_c (125 MHz, CDCl₃) –3.4, –3.3(3), –2.2, –2.1, 0.0, 6.9, 7.1, 8.7(2), 13.4, 18.4, 18.5, 19.4, 19.5(2), 24.0, 24.1, 25.3, 25.5, 27.3, 27.4(2), 36.5, 36.9, 41.0, 41.8(2), 42.1, 42.3, 42.9, 44.6, 62.0, 62.1, 66.6, 69.8, 70.0, 70.2, 70.3, 79.1, 81.6, 81.7, 97.6, 97.7, 122.3, 122.8, 125.5, 127.4, 132.0, 132.9, 134.9, 135.2, 136.5, 154.6 and 169.8; *m/z* (ES⁺) 1143.7 (81%), 1107.4 (M⁺ + 23, 100) and 1085.9 (M⁺ + 1, 67).

(3*RS*,7*S*,9*R*,10*R*)-1-(Benzothiazol-2-ylsulfanyl)-7,10-bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-(2-trimethylsilylethoxymethoxy)undecane (32).

A portion (0.47 mL) of a freshly prepared solution of ammonium molybdate tetrahydrate (0.364 g) in aqueous H₂O₂ (30%, 1.60 mL) was added to the sulfide **30** (0.246 g, 0.226 mmol) in propan-2-ol (0.33 mL) and ethanol (0.50 mL) and the yellow mixture was stirred rapidly at rt. After 24 and 48 h, further aliquots (0.47 mL) of the catalyst and oxidant mixture were added. After 3 d, ether (50 mL) and saturated aqueous Na₂S₂O₃ (50 mL) were added and the aqueous layer was extracted with ether (2 × 50 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (25:1 then 15:1 light petroleum:ether) gave the *title compound* **32** as a viscous, colourless oil (0.103 g, 41%), a 1:1 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.13 (15:1 light petroleum:ether), [α]_D²⁸ –17.8 (c 14.2, CHCl₃); ν_{max}/cm^{–1} 2955, 2866, 1471, 1381, 1332, 1253, 1151, 1100, 1061, 937, 835 and 775; δ_H (500 MHz, C₆D₆) 0.00, 0.01 [each 4.5 H, s, Si(CH₃)₃], 0.13, 0.15, 0.17, 0.19, 0.23, 0.24, 0.26 and 0.27 (each 1.5 H, s, SiCH₃), 0.70 and 0.72 (each 3 H, q, *J* 7.7, 3 × SiCH₂), 0.88–0.98 (2 H, m, SiCH₂), 0.98–1.08 [27 H, m, 3 × SiCH₂CH₃, 2 × SiC(CH₃)₃], 1.10–1.23 [21 H, m, 3 × SiCH(CH₃)₂], 1.26–1.38 (9 H, m, 11-H₃, 2 × 2-CH₃), 1.76–1.99 (2.5 H, m, 8-H₂, 4-H), 2.07 (0.5 H, dd, *J* 14.2, 8.6, 4-H), 2.41–2.56 (2.5 H, m, 6-H, 6-H', 4-H'), 2.60 (0.5 H, dd, *J* 13.1, 5.8, 6-H'), 3.51 and 3.52 (each 0.5 H, dt, *J* 15.6, 9.6, OHCHCH₂Si), 3.64 and 3.73 (each 0.5 H, d, *J* 14.4, 1-H), 3.79–3.91 (2 H, m, OHCHCH₂Si, 9-H), 3.95 (1 H, m, 3-H), 3.96 and 4.05 (each 0.5 H, d, *J* 14.4, 1-H'), 4.20 (1 H, m, 7-H), 4.37 (1 H, m, 10-H), 4.46–4.60 (2 H, m, 2'-H₂), 4.83, 4.87, 4.89 and 4.93 (each 0.5 H, d, *J* 6.8, OHCHO), 5.65 and 5.70 (each 0.5 H, t, *J* 5.7, 1'-H), 6.90 (1 H, m, ArH), 7.02–7.12 (2 H, m, ArH) and 7.95 (1 H, m, ArH); δ_c (125 MHz, C₆D₆) –3.2(3), –2.7(2), –2.1, –2.0, –0.02, 0.0, 2.7, 7.3, 7.4, 8.8, 13.4, 13.7(2), 18.6, 18.7, 19.6, 19.7(2), 24.9, 25.1, 27.5, 27.6(2), 31.5, 36.8, 37.5, 41.3, 41.8, 42.0, 42.2(2), 43.2, 62.1, 62.3, 62.4, 62.5, 66.9, 67.0, 70.1, 70.6, 70.7, 79.7, 80.4, 81.9, 82.0, 98.0, 98.1, 123.7, 126.5, 126.6, 128.6, 128.8, 132.5, 133.6, 135.1, 135.6, 138.2(2) and 154.3; *m/z* (ES⁺) 1138.5 (M⁺ + 23, 100%) and 1133.6 (M⁺ + 18, 54). The second fraction was the sulfoxide **31** as a viscous, colourless oil (0.125 g, 50%), a mixture of diastereoisomers, *R*_f = 0.07 (15:1 light petroleum:ether), [α]_D²⁸ –5.3 (c 4.5, CHCl₃); ν_{max}/cm^{–1} 2949, 2927, 2863, 1470, 1462, 1427, 1384, 1255, 1250, 1094, 1056, 935, 858, 833, 806, 774 and 755; *m/z* (ES⁺) 1123.0 (M⁺ + 23, 100%) and 1117.8 (M⁺ + 18, 70). This sulfoxide **31** was oxidised as above and gave the sulfone **32** (56 mg, 36%) and recovered sulfoxide **31** (62 mg, 41%).

2,6-Lutidine (23 μL, 0.196 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (22 μL, 0.098 mmol) were added to the undecanol **70** (49 mg, 0.049 mmol) in DCM (0.5 mL) and the solution was stirred at rt for 2 h. Ether (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with ether (3 × 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (20:1 light petroleum:ether) of the residue

afforded the *title compound* **32** (51 mg, 93%), as a colourless oil, a 58:42 mixture of epimers (^1H NMR).

(7*RS*,11*S*,13*R*,14*R*,4*E*)-11,14-Bis-*tert*-butyldimethylsilyloxy-6,6-dimethyl-7-triethylsilyloxy-9-[(*E*)-2-tri-isopropylsilyloxyethylidene]-13-(2-trimethylsilylethoxymethoxy)pentadec-4-ene (33**).**

Lithium hexamethyldisilazide (1.05 M in toluene, 26 μL , 0.027 mmol) was added to the sulfone **32** (azeotroped twice with benzene, 28 mg, 0.0247 mmol) in THF (0.25 mL) at -78°C and the bright yellow solution was warmed to -60°C , stirred for 30 min then cooled to -78°C . A portion (0.16 mL, 0.124 mmol) of a solution of butanal (freshly distilled from calcium chloride, 0.11 mL) in THF (1.60 mL) was added dropwise and the solution was immediately allowed to warm to rt then stirred for 1 h. Ether (10 mL) and saturated aqueous NaHCO_3 (10 mL) were added and the aqueous layer was extracted with ether (2 $\times$ 5 mL). The organic extracts were diluted (to 50 mL) with ether then washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (100:1 light petroleum:ether) gave the *title compound* **33** as a clear, colourless oil (21 mg, 85%), as a 1:1 mixture of epimers (^1H and ^{13}C NMR), a 4:1 mixture of (*4E*)- and (*4Z*)-isomers, $R_f = 0.73$ (30:1 light petroleum:ether) (Found: $\text{M}^+ + \text{NH}_4$, 990.7644. $\text{C}_{52}\text{H}_{116}\text{O}_6\text{NSi}_5$ requires M , 990.7643); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2927, 2863, 1471, 1463, 1382, 1360, 1250, 1098, 1058, 938, 882, 858, 835, 806, 773 and 737; δ_{H} (500 MHz, CDCl_3) (*4E*)-isomer: 0.00(2) [each 4.5 H, s, $\text{Si}(\text{CH}_3)_3$] 0.03 (6 H, s, 2 $\times$ SiCH_3), 0.04 (3 H, s, SiCH_3), 0.06 and 0.07 (each 1.5 H, s, SiCH_3), 0.50–0.61 (6 H, m, 3 $\times$ SiCH_2), 0.81–0.98 (11 H, m, 1- H_3 , SiCH_2 2 $\times$ 6- CH_3), 0.86(2), 0.87 and 0.88 [each 4.5 H, s, $\text{Si}(\text{CH}_3)_3$], 0.92 (9 H, t, J 7.9, 3 $\times$ SiCH_2CH_3), 1.01 and 1.02 (each 1.5 H, d, J 6.3, 15- H_3), 1.03–1.15 [21 H, m, 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$], 1.36 (2 H, pent, J 7.3, 2- H_2), 1.40–1.56 (2 H, m, 12- H_2), 1.82 (0.5 H, dd, J 13.8, 9.1, 8- H), 1.85 (0.5 H, dd, J 13.9, 8.8, 8- H), 1.93–2.00 (2 H, m, 3- H_2), 2.04 (0.5 H, dd, J 13.1, 8.5, 10- H), 2.10–2.24 (2 H, m, 8- H' , 10- H , 10- H'), 2.27 (0.5 H, dd, J 13.2, 5.4, 10- H'), 3.42 (1 H, m, OHCHCH_2Si), 3.49–3.56 (2 H, m, 7- H , 13- H), 3.70(2) (each 0.5 H, ddd, J 11.1, 9.7, 5.5, OHCHCH_2Si), 3.81 (1 H, m, 11- H), 4.04 (1 H, m, 14- H), 4.23–4.33 (2 H, m, 2'- H_2), 4.66(2), 4.67 and 4.68 (each 0.5 H, d, J 6.9, OHCHO), 5.31 (1 H, dt, J 15.7, 6.7, 4- H), 5.39 (1 H, t, J 5.5, 1'- H) and 5.44 (1 H, dd, J 15.7, 1.4, 5- H); m/z (ES^+) 995.6 ($\text{M}^+ + \text{Na}$, 100%) and 917.8 (62).

(3*S*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-25-(2-trimethylsilylethoxymethoxy)-21-[(*E*)-2-tri-isopropylsilyloxyethylidene]-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-ene (34**).**

Lithium hexamethyldisilazide (1.05 M in toluene, 45 μL , 0.046 mmol) was added to the sulfone **32** (azeotroped twice with benzene, 47 mg, 0.042 mmol) in THF (0.42 mL) at -78°C and the bright yellow solution was warmed to -60°C and stirred for 30 min then cooled to -78°C . The aldehyde **18** (19 mg, 0.019 mmol) in THF (0.24 mL) at -78°C was added dropwise with rinsing using THF (0.20 mL). The solution was stirred at -78°C

for 20 min, allowed to warm to r.t. and stirred for 30 min. Ether (20 mL) and saturated aqueous NaHCO_3 (10 mL) were added and the aqueous layer was extracted with ether (2 $\times$ 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica (100:1 to 20:1 light petroleum:ether) gave the *title compound* **34** as a colourless gum (23 mg, 64%), as a 2:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.76$ (9:1 light petroleum:ether); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2863, 1464, 1383, 1362, 1253, 1102, 1060, 882 and 835; δ_{H} (500 MHz, C_6D_6) 0.00 [3 H, s, $\text{Si}(\text{CH}_3)_3$], 0.00 [6 H, s, $\text{Si}(\text{CH}_3)_3$], 0.10, 0.12 and 0.14 (each 3 H, s, SiCH_3), 0.17, 0.25, 0.28 (each 2 H, s, 3 $\times$ SiCH_3), 0.18, 0.24 and 0.27 (each 1 H, s, 3 $\times$ SiCH_3), 0.71–0.80 (6 H, m, 3 $\times$ SiCH_2), 0.90–1.06 (2 H, m, SiCH_2), 0.96 and 1.04 [each 9 H, s, $\text{Si}(\text{CH}_3)_3$], 1.00 [6 H, s, $\text{Si}(\text{CH}_3)_3$], 1.01 [3 H, s, $\text{Si}(\text{CH}_3)_3$], 1.06–1.17 [60 H, m, $\text{Si}(\text{CH}_3)_3$, 6 $\times$ $\text{Si}(\text{CH}(\text{CH}_3)_2$, 3 $\times$ SiCH_2CH_3], 1.17–1.30 (15 H, m, 2 $\times$ 8- CH_3 , 2 $\times$ 18- CH_3 , 26- H_3), 1.50 (1 H, m, 6- H), 1.68–2.72 (17 H, m, 2- H_2 , 4- H_2 , 6- H' , 10- H_2 , 12- H_2 , 14- H_2 , 20- H_2 , 22- H_2 , 24- H_2), 3.27 (2 H, s, 9- OCH_3), 3.28 (1 H, s, 9- OCH_3), 3.50 (1 H, m, OHCHCH_2Si), 3.71–3.98 (9 H, m, OHCHCH_2Si , 1- H_2 , 5- H , 7- H , 11- H , 15- H , 19- H , 25- H), 4.16–4.26 (2 H, m, 3- H , 23- H), 4.29 (1 H, d, J 11.7, PhHCH), 4.31–4.45 (3 H, m, SiOCH_2CH , 26- H) 4.47 (1 H, d, J 11.7, PhHCH), 4.50–4.61 (2 H, m, SiOCH_2CH), 4.81 (0.3 H, d, J 6.9, OHCHO), 4.83 (0.7 H, d, J 6.9, OHCHO), 4.89 (0.3 H, d, J 6.9, OHCHO), 4.90 (0.7 H, d, J 6.9, OHCHO), 5.58–5.69 (2 H, m, SiOCH_2CH , 16- H), 5.71 (1 H, m, SiOCH_2CH), 6.03 (0.7 H, d, J 16.0, 17- H), 6.11 (0.3 H, d, J 16.0, 17- H), 6.94–7.19 (3 H, m, ArH), 7.19–7.33 (8 H, m, ArH), and 7.76–7.83 (4 H, m, ArH); m/z (APCI^+) 1973.9 (50%), 1939.1 ($\text{M}^+ + 23$, 90) and 1884.8 (100). The second fraction was recovered sulfone **32** (21 mg, 44%).

(3*S*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-5,9-epoxy-11,15-epoxy-25-(2-trimethylsilylethoxymethoxy)-13,21-bis-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-en-19-ol (35**).**

Trimethylsilyl trifluoromethanesulfonate (33 μL , 0.30 mmol) was added to the triethylsilyl ether **34** (18 mg, 0.0094 mmol) in THF (0.21 mL) and methanol (0.32 mL) followed by a portion (20 μL , 5.1 μmol) of a solution of pyridinium toluene *p*-sulfonate (0.29 g, 1.03 mmol) in methanol (4 mL). The mixture was stirred for r.t. for 3 d and then ether (20 mL) and saturated aqueous NaHCO_3 (10 mL) were added. The aqueous phase was extracted with ether (20 mL) and the organic extracts were washed with water (2 $\times$ 5 mL) and brine (5 mL), then dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica (pentane to 20:1 pentane:ether) gave recovered triethylsilyl ether **34** (2.5 mg, 14%) followed by the *title compound* **35** as a clear, colourless gum (11 mg, 65%), as a 2:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.36$ (9:1 light petroleum:ether); $\nu_{\text{max}}/\text{cm}^{-1}$ 3539, 2955, 2862, 1465, 1429, 1383, 1362, 1256, 1103, 1061, 938, 882, 835, 807 and 775; δ_{H} (500 MHz, C_6D_6) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.10, 0.22 and 0.23 (each 1 H, s, SiCH_3), 0.10 and 0.25(2) (each 2 H, s, SiCH_3), 0.13 (6 H, s, 2 $\times$ SiCH_3), 0.17 (3 H, s, SCH_3), 0.88–1.07 (2 H, m, SiCH_2Si), 0.96 and 1.00 [each 9 H, s, $\text{Si}(\text{CH}_3)_3$], 1.03 [3 H, s, $\text{Si}(\text{CH}_3)_3$], 1.04 [6 H, s,

SiC(CH₃)₃, 1.06–1.16 [42 H, m, 6 × SiCH(CH₃)₂], 1.19 [9 H, s, SiC(CH₃)₃], 1.16–1.36 [15 H, m, 2 × 8-CH₃, 2 × 18-CH₃, 27-H₃], 1.50 (1 H, q, *J* 12.5, 6-H_{ax}), 1.67–2.72 (18 H, m, 2-H₂, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24-H₂, OH), 3.29 (3 H, s, 9-OCH₃), 3.46–3.60 (2 H, m, OHCHCH₂Si, 19-H), 3.70–3.99 (8 H, m, OHCHCH₂Si, 1-H₂, 5-H, 7-H, 11-H, 15-H, 25-H), 4.18–4.55 (7 H, m, 3-H, 23-H, 2 × SiOCH₂CH, 26-H), 4.29 and 4.48 (each 1 H, d, *J* 11.7, PhHCH), 4.81 and 4.87 (each 1 H, d, *J* 6.9, OHCHO), 5.56–5.79 (3 H, m, 2 × SiOCH₂CH, 16-H), 5.97 (0.7 H, d, *J* 16.0, 17-H), 6.06 (0.3 H, d, *J* 16.0, 17-H), 7.02–7.19 (3 H, m, ArH), 7.19–7.33 (8 H, m, ArH) and 7.76–7.83 (4 H, m, ArH); *m/z* (APCI⁺) 1825 (M⁺ + 23, 55%), 1772 (100), 1597 (74) and 1422 (39).

(3S,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-5,9-epoxy-11,15-epoxy-25-(2-trimethylsilylethoxymethoxy)-21-[(E)-2-triisopropylsilyloxyethylidene]-13-[(Z)-2-triisopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-en-19-one (36).

Sodium hydrogen carbonate (4 mg, 0.044 mmol) and the Dess-Martin periodinane (3.5 mg, 0.008 mmol) were added to the alcohol **35** (10 mg, 0.0058 mmol) in DCM (0.20 mL) and the mixture was stirred for 45 min at rt. A mixture of saturated aqueous NaHCO₃ and saturated aqueous Na₂S₂O₃ (1:1, 2 mL) was added and the mixture was extracted with ether (3 × 4 mL). The organic extracts were washed with water (5 mL) and brine (5 mL), then dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue on base-washed silica (30:1 to 20:1 pentane:ether) gave the *title compound* **36** as a colourless gum (8.5 mg, 85%), *R*_f = 0.57 (9:1 light petroleum:ether), [α]_D²⁵ +4.8 (*c* 4.4, CH₂Cl₂); ν_{max}/cm⁻¹ 2958, 2861, 1714, 1667, 1470, 1464, 1385, 1362, 1259, 1104, 939, 835, 775 and 702; δ_H (400 MHz, C₆D₆) 0.00 [9 H, s, Si(CH₃)₃], 0.09, 0.12, 0.13, 0.17, 0.25 and 0.26 (each 3 H, s, SiCH₃), 0.89–1.05 (2 H, m, SiCH₂), 0.95, 0.99 and 1.03 [each 9 H, s, SiC(CH₃)₃], 1.05–1.16 [42 H, m, 6 × SiCH(CH₃)₂], 1.18 [9 H, s, SiC(CH₃)₃], 1.19–1.34 (15 H, m, 2 × 8-CH₃, 2 × 18-CH₃, 27-H₃), 1.50 (1 H, q, *J* 12.1, 6-H_{ax}), 1.70–2.10 (10 H, m, 2-H₂, 4-H₂, 6-H', 10-H, 12-H, 14-H, 24-H₂), 2.30–2.68 (3 H, m, 10-H', 12-H', 14-H'), 2.63 (1 H, dd, *J* 13.7, 8.1, 22-H), 2.72 (1 H, dd, *J* 13.7, 5.7, 22-H') 3.27 (3 H, s, 9-OCH₃), 3.27 and 3.35 (each 1 H, d, *J* 16.1, 20-H), 3.51 (1 H, td, *J* 9.7, 6.5, OHCHCH₂Si), 3.70–3.97 (8 H, m, OHCHCH₂Si, 1-H₂, 5-H, 7-H, 11-H, 15-H, 25-H), 4.17–4.55 (9 H, m, PhCH₂, 3-H, 23-H, 26-H, 2 × SiOCH₂CH), 4.81 and 4.89 (each 1 H, d, *J* 7.0, OHCHO), 5.57–5.70 (3 H, m, 16-H, 2 × SiOCH₂CH), 5.98 (1 H, d, *J* 15.9, 17-H), 7.00–7.34 (11 H, m, ArH) and 7.73–7.84 (4 H, m, ArH); δ_C (100 MHz, C₆D₆) –4.7(2), –4.3, –4.1, –4.0, –3.6, –1.5, 12.2, 12.3, 17.0, 17.3, 18.2(3), 18.3, 19.3, 21.1, 22.5, 24.2, 24.3, 26.0, 26.2, 27.0, 30.0, 32.3, 33.6, 35.5, 36.0, 39.5, 39.9, 41.1, 43.2, 43.5, 43.8, 45.0, 46.0, 48.2, 50.2, 59.6, 60.7, 60.8, 65.4, 66.3, 67.8, 69.0, 69.3, 71.6, 75.4, 72.5, 79.0, 80.6, 96.6, 104.4, 124.3, 129.8(2), 130.9, 132.1, 132.3, 134.1, 134.9, 135.8(2), 136.2, 139.7 and 209.0; *m/z* (APCI⁺) 1822 (M⁺ + 23, 100%), 1791 (49), 1770 (89), 1594 (83), 1509 (33), 1464 (43) and 1421 (58).

Dimethyl (4S)-4-benzoyloxy-5-[(4R,6S)-6-(2-hydroxyethyl)-2,2-dimethyl-1,3-dioxan-4-yl]-3,3-dimethyl-2-oxopentylphosphonate (37).

Tetra-*n*-butylammonium fluoride (1 M in THF, 12.87 mL, 12.87 mmol) was added to the *tert*-butyldiphenylsilyloxyphosphonate **11** (7.8 g, 10.73 mmol) in THF (300 mL) and the mixture was stirred for 16 h. Ethyl acetate (300 mL) and saturated aqueous NaHCO₃ (300 mL) were added and the aqueous phase was extracted with EtOAc (2 × 100 mL). The organic extracts were washed with brine (200 mL), dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:1 EtOAc:light petroleum to EtOAc with 1% Et₃N) afforded the *title compound* **37** as a colourless oil (5.4 g, 100%), *R*_f = 0.14 (EtOAc), [α]_D²⁵ –4.9 (*c* 1.87, CH₂Cl₂) (Found: M⁺ + Na, 509.2276. C₂₄H₃₉O₈NaP requires M, 509.2275); ν_{max}/cm⁻¹ 3419, 2982, 2955, 1703, 1455, 1380, 1259, 1223, 1096, 1029 and 805; δ_H (500 MHz, C₆D₆) 1.26 and 1.29 (each 3 H, s, 3-CH₃), 1.39 (1 H, m, 5'-H), 1.40 and 1.46 (each 3 H, s, 2'-CH₃), 1.51 (1 H, m, 5'-H'), 1.60 (1 H, m, 1''-H), 1.64–1.73 (2 H, m, 5-H₂), 1.81 (1 H, m, 1''-H'), 2.77 (1 H, br. s, OH), 3.23 and 3.38 (each 1 H, dd, *J* 21.5, 15.5, 1-H), 3.58 and 3.62 (each 3 H, d, *J* 11, OCH₃), 3.76 and 3.82 (each 1 H, m, 2''-H), 4.01 (1 H, m, 4-H), 4.07 (1 H, m, 6'-H), 4.17 (1 H, m, 4'-H), 4.67 and 4.78 (each 1 H, d, *J* 11.4, PhHCH), 7.21 (1 H, m, ArH), 7.27–7.32 (2 H, m, ArH) and 7.45 (2 H, d, *J* 7.6, ArH); δ_C (125 MHz, C₆D₆) 19.5, 19.8, 24.0, 24.2, 36.6 (d, ¹J_{C-P} 136.2), 37.3(2), 38.0, 51.0 and 51.1 (each d, ²J_{C-P} 6.4), 52.4 (d, ³J_{C-P} 3.6), 58.7, 62.5, 64.2, 73.9, 80.1, 99.0, 126.1, 126.4, 127.3, 137.8, 205.2 (d, ²J_{C-P} 7.0); *m/z* (ES⁺) 509 (M⁺ + 23, 100%).

(2R,6E,10S,12R,14S)-10-Benzoyloxy-16-hydroxy-4-[(Z)-2-triisopropylsilyloxyethylidene]-1-(4-methylbenzyloxy)-9,9-dimethyl-2-triethylsilyloxy-12,14-di-*O*-isopropylidenehexadec-6-en-8-one (38).

The phosphonate **37** (2.9 g, 5.96 mmol) in THF (50.7 mL) was added to a suspension of Ba(OH)₂·0.8H₂O [886 mg, 4.77 mmol, prepared by heating Ba(OH)₂·8H₂O at 200 °C for 2 h] in THF (20.5 mL) and the mixture was stirred for 30 min before the aldehyde **10** (3.7 g, 6.56 mmol) in THF/H₂O (40:1, 81.3 mL) was added over 10 min. After 16 h, the mixture was filtered through a pad of Celite[®] and the precipitate washed with DCM (25 mL). The filtrate was washed with saturated aqueous NaHCO₃ (150 mL) and the aqueous phase extracted with DCM (2 × 100 mL). The organic extracts were washed with brine (100 mL), dried (Na₂SO₄) and concentrated under reduced pressure to afford the *title compound* **38** as a pale yellow oil that was used immediately, *R*_f 0.24 (1:3 EtOAc:light petroleum) (Found: M⁺ + Na, 947.5851. C₅₃H₈₈O₉NaSi₂ requires M, 947.5859); δ_H (400 MHz, CHCl₃) 0.48 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.84 (9 H, t, *J* 7.8, 3 × SiCH₂CH₃), 0.93–1.02 [21 H, m, 3 × SiCH(CH₃)₂], 1.06 and 1.13 (each 3 H, s, 9-CH₃), 1.29 and 1.31 (each 3 H, s, CH₃), 1.40–1.51 (3 H, m, 11-H₂, 15-H), 1.56–1.72 (4 H, m, 13-H₂, 15-H', OH), 2.08 (1 H, dd, *J* 13.6, 7.3, 3-H), 2.23 (1 H, dd, *J* 13.4, 5.3, 3-H'), 2.85 (2 H, d, *J* 7.1, 5-H₂), 3.20 (1 H, dd, *J* 9.6, 5.6, 1-H), 3.25 (1 H, dd, *J* 9.6, 5.2, 1-H'), 3.62–3.70 (2 H, m, 16-H₂), 3.72 (3 H, s, OCH₃), 3.78 (1 H, m, 2-H), 3.85 (1 H, m, 10-H), 3.92–4.02 (2 H, m, 12-H, 14-H), 4.14 (1 H, dd, *J* 13.1, 5.6, 2'-H), 4.21 (1 H, dd, *J* 12.9, 6.4, 2'-H'), 4.36 (2 H, s, ArCH₂), 4.51 (2 H, s, PhCH₂), 5.36 (1 H, t, *J* 6.0, 1'-H), 6.50 (1 H, d, *J* 15.1, 7-H), 6.76–6.87

(3 H, m, 6-H, ArH) and 7.13–7.28 (7 H, m, ArH); m/z (ES^+) 947.6 ($M^+ + 23$, 100%) and 942.8 ($M^+ + 18$, 70).

(4S,6R,8S)-4-Benzoyloxy-10-hydroxy-1-[(2S,6R)-4-[(Z)-2-triisopropylsilyloxyethylidene]-6-(4-methoxybenzyloxymethyl)tetrahydropyran-2-yl]-6,8-di-O-isopropylidene-3,3-dimethyldecan-2-one (41).

Pyridine (14.04 mL) was added to the enone **38** (prepared from phosphonate **37**, 2.9 g, 5.96 mmol) in THF (144 mL) and, after cooling to 0 °C, HF-pyridine complex (7.08 mL) was added rapidly. The mixture was stirred for 25 min and saturated aqueous $NaHCO_3$ (200 mL) was added quickly. After warming to rt, ether (200 mL) was added and aqueous phase was extracted with ether (2 × 100 mL). The organic extracts were washed with brine (200 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford the diol **39** as a pale, yellow oil.

Potassium *tert*-butoxide in THF (1 M, 16.37 mL, 1.64 mmol) was added rapidly to this diol **39** in THF (37.5 mL) at rt and the mixture stirred for 5 min. Saturated aqueous NH_4Cl (100 mL) and ether (100 mL) were added and the aqueous phase was extracted with ether (2 × 100 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (1:10 to 1:3 EtOAc:light petroleum) afforded the *title compound 41* as a pale, yellow oil (2.37 g, 49% from phosphonate **37**), R_f 0.13 (1:3 EtOAc:light petroleum), $[\alpha]_D^{25} +5.6$ (c 2.35, $CHCl_3$) (Found: $M^+ + Na$, 833.4989. $C_{47}H_{74}O_9NaSi$ requires M , 833.4994); ν_{max}/cm^{-1} 3476, 2942, 2865, 1704, 1613, 1587, 1514, 1464, 1381, 1366, 1248, 1224, 1172, 1099, 1063, 1039, 883, 821 and 735; δ_H (400 MHz, $CDCl_3$) 0.95–1.03 [24 H, m, 3 × $SiCH(CH_3)_2$, 3- CH_3 '], 1.15 (3 H, s, 3- CH_3 '), 1.29 and 1.30 (each 3 H, s, CH_3), 1.30–1.55 (4 H, m, 5- H_2 , 7- H_2), 1.56–1.68 (2 H, m, 9- H_2), 1.73 (1 H, t, J 12.6, 5'- H_{ax}), 1.82 (1 H, t, J 12.2, 3'- H_{ax}), 2.12 (1 H, d, J 13.1, 3'- H_{eq}), 2.37 (1 H, d, J 13.8, 5'- H_{eq}), 2.40 (1 H, br. s, OH), 2.50 (1 H, dd, J 17.6, 6.5, 1-H), 2.93 (1 H, dd, J 17.6, 5.8, 1-H'), 3.30–3.38 (2 H, m, 6'- CH_2), 3.41 (1 H, m, 6'-H), 3.67 (2 H, m, 10- H_2), 3.73 (3 H, s, OCH_3), 3.79 (1 H, m, 2'-H), 3.87 (1 H, dd, J 9.8, 1.0, 4-H), 3.90–4.00 (2 H, m, 6-H, 8-H), 4.18 (2 H, d, J 6.3, 2''- H_2), 4.39 (2 H, s, $ArCH_2$), 4.51 and 4.57 (each 1 H, d, J 11.3, $PhHCH$), 5.33 (1 H, t, J 6.2, 1''-H), 6.79 (2 H, d, J 8.6, ArH) and 7.17–7.29 (7 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 11.0, 17.0, 19.2, 19.9, 24.2(2), 30.4, 36.5, 37.5, 38.0, 40.3, 44.0, 51.8, 54.2, 58.4, 60.3, 62.5, 65.9, 71.7, 71.9, 73.4, 73.9, 75.6, 79.4, 99.5, 112.7, 123.5, 126.1, 126.5, 127.4, 128.3, 129.3, 133.6, 137.6, 158.1 and 211.6; m/z (ES^+) 833.5 ($M^+ + 23$, 100%) and 828.5 ($M^+ + 18$, 17).

Attempted chromatography of the diol **39** (1:10 to 1:3 EtOAc:light petroleum with 1% Et_3N) provided the 2,6-*trans*-disubstituted tetrahydropyran **40** as a colourless oil, R_f 0.13 (1:3 EtOAc:light petroleum) (Found: $M^+ + Na$, 833.4979. $C_{47}H_{74}O_9NaSi$ requires M , 833.4994); δ_H (400 MHz, $CDCl_3$) 0.94–1.01 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.02 and 1.12 (each 3 H, s, 3- CH_3), 1.28 and 1.30 (each 3 H, s, CH_3), 1.33–1.51 (2 H, m, 5- H_2), 1.56–1.71 (4 H, m, 7- H_2 , 9- H_2), 1.87 (1 H, dd, J 13.3, 5.8, 3'-H), 2.06 (1 H, dd, J 13.6, 7.3, 5'-H), 2.27 (1 H, dd, J 13.4, 3.8, 5'-H'), 2.33 (1 H, dd, J 13.0, 4.3, 3'-H'), 2.45 (1 H, br. s, OH), 2.69 (1 H, dd, J 17.7, 5.0, 1-H), 2.77 (1 H, dd, J 17.7, 7.9, 1-H'), 3.34 and 3.41 (each 1 H, dd, J 9.8, 5.8, 6'-CH), 3.64–3.70 (2 H, m, 10- H_2), 3.73 (1 H, s, OCH_3), 3.79 (1 H, m, 6'-H),

3.84 (1 H, dd, J 9.4, 2.0, 4-H), 3.95 (2 H, m, 6-H, 8-H), 4.12 and 4.18 (each 1 H, dd, J 12.6, 6.1, 2''-H), 4.30 (1 H, m, 2'-H), 4.36 and 4.14 (each 1 H, d, J 11.7, $ArHCH$), 4.51 and 4.56 (each 1 H, d, J 11.1, $PhHCH$), 5.34 (1 H, t, J 6.1, 1''-H), 6.79 (2 H, d, J 8.5, ArH) and 7.15–7.27 (7 H, m, ArH); m/z (ES^+) 833.6 ($M^+ + 23$, 100%) and 828.7 ($M^+ + 18$, 48).

(3S,5R,7S,9S,11S,15R)-7-Benzoyloxy-13-[(Z)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane-1,3-diyl methyl orthoformate (42a,b).

Pyridinium toluene *p*-sulfonate (1 mg, 0.0038 mmol) was added to the hydroxyacetone **41** (31 mg, 0.038 mmol) and trimethyl orthoformate (83 μ L) in DCM (291 μ L) and methanol (291 μ L) and the solution was stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:25 EtOAc:light petroleum) afforded the less polar epimer of the *title compound 42a* as a pale oil (5 mg, 16%), R_f 0.62 (1:3 EtOAc:light petroleum) (Found: $M^+ + Na$, 849.4953. $C_{47}H_{74}O_{10}NaSi$ requires M , 849.4943); δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, 8- CH_3 '), 0.95–1.07 [24 H, m, 3 × $SiCH(CH_3)_2$, 8- CH_3 '], 1.26 (1 H, m, 2- H_{ax}), 1.38 (1 H, m, 6- H_{ax}), 1.42–1.54 (2 H, m, 4- H_2), 1.61–1.83 (3 H, m, 14- H_{ax} , 10-H, 2- H_{eq}), 1.92 (1 H, t, J 12.2, 12- H_{ax}), 2.01 (1 H, dd, J 15.9, 4.3, 10-H'), 2.33–2.41 (2 H, m, 12- H_{eq} , 14- H_{eq}), 3.12 (3 H, s, 9- OCH_3), 3.22 (3 H, s, OCH_3), 3.36–3.46 (3 H, m, 15-H, 16- H_2), 3.50 (1 H, m, 11-H), 3.58–3.71 (2 H, m, 5-H, 1- H_{ax}), 3.63 (1 H, dd, J 11.6, 4.5, 7-H), 3.73 (3 H, s, $ArOCH_3$), 4.06 (1 H, m, 1- H_{eq}), 4.20 (2 H, m, 2'- H_2), 4.37 (1 H, d, J 11.7, $PhHCH$), 4.40 (1 H, m, 3-H), 4.45 (2 H, s, $ArCH_2$), 4.52 (1 H, d, J 11.7, $PhHCH$), 5.27 (1 H, s, $MeOCHO_2$), 5.31 (1 H, t, J 6.1, 1'-H), 6.80 (2 H, d, J 8.6, ArH), 7.16–7.22 (4 H, m, ArH) and 7.26 (3 H, d, J 4.3, ArH); δ_C (100 MHz, $CDCl_3$) 11.0, 15.6, 17.0, 19.8, 30.6, 32.1, 37.8, 41.8, 42.4, 47.0, 51.8, 54.2, 57.1, 58.5, 62.8, 63.6, 70.6, 71.9, 72.0, 74.4, 75.7, 77.7, 102.8, 108.1, 112.7, 122.8, 126.2, 126.3, 127.2, 128.2, 129.5, 134.8, 138.3 and 158.1; m/z (ES^+) 849.6 ($M^+ + 23$, 100%) and 844.7 ($M^+ + 18$, 39). Further elution (1:25 to 1:10 EtOAc:light petroleum) afforded the more polar epimer of the *title compound 42b* as a pale, yellow oil (5 mg, 16%), R_f 0.48 (1:3 EtOAc:light petroleum) (Found: $M^+ + Na$, 849.4957. $C_{47}H_{74}O_{10}NaSi$ requires M , 849.4943); δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, 8- CH_3 '), 0.95–1.07 [24 H, m, 3 × $SiCH(CH_3)_2$, 8- CH_3 '], 1.18 (1 H, m, 6- H_{ax}), 1.28 (1 H, m, 2- H_{ax}), 1.52–1.63 (3 H, m, 4- H_2 , 2- H_{eq}), 1.67–1.80 (3 H, m, 14- H_{ax} , 10-H, 6- H_{eq}), 1.95 (1 H, t, J 12.1, 12- H_{ax}), 2.00 (1 H, dd, J 16.0, 4.3, 10-H'), 2.27 (1 H, d, J 13.4, 12- H_{eq}), 2.36 (1 H, d, J 13.6, 14- H_{eq}), 3.10 (3 H, s, 9- OCH_3), 3.33–3.46 (3 H, m, 15-H, 16- H_2), 3.39 (3 H, s, OCH_3), 3.48 (1 H, m, 11-H), 3.62 (1 H, dd, J 11.6, 4.5, 7-H), 3.73 (3 H, s, $ArOCH_3$), 3.77 (1 H, t, J 11.6, 1- H_{ax}), 4.00 (1 H, m, 3-H), 4.06 (1 H, m, 1- H_{eq}), 4.17 (1 H, dd, J 12.9, 6.1, 2'-H), 4.22 (1 H, dd, J 12.6, 6.3, 2'-H'), 4.38 (1 H, d, J 11.7, $PhHCH$), 4.45 (2 H, s, $ArCH_2$), 4.52 (1 H, d, J 11.7, $PhHCH$), 5.04 (1 H, s, $MeOCHO_2$), 5.26 (1 H, t, J 6.3, 1'-H), 6.80 (2 H, d, J 8.8, ArH), 7.16–7.23 (4 H, m, ArH) and 7.26 (3 H, d, J 4.3, ArH); δ_C (100 MHz, $CDCl_3$) 11.0, 15.7, 17.0, 19.9, 29.6, 30.5, 31.8, 38.0, 41.1, 42.3, 42.5, 46.8, 52.1, 54.2, 58.4, 62.5, 63.8, 70.6, 71.9,

72.0, 74.4, 75.7, 77.7, 102.9, 111.2, 112.7, 123.0, 126.3, 126.4, 127.2, 128.2, 129.4, 134.6, 138.2 and 158.1; m/z (E^+) 849.7 ($M^+ + 23$, 100%), 844.5 ($M^+ + 18$, 19).

(3*S*,5*R*,7*S*,9*S*,11*S*,15*R*)-7-Benzoyloxy-13-[(*Z*)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane-1,3-diol (43) and (3*S*,5*R*,7*S*,9*S*,11*S*,15*R*)-7-Benzoyloxy-13-[(*Z*)-2-triisopropylsilyloxyethylidene]-5,9-epoxy-11,15-epoxy-1,3-di-*O*-isopropylidene-8,8-dimethyl-9-methoxy-16-(4-methoxybenzyloxy)hexadecane (44).

Pyridinium toluene *p*-sulfonate (0.15 mg, 0.0006 mmol) was added to the hydroxyacetone **41** (5 mg, 0.0062 mmol) in DCM (47 μ L) and methanol (47 μ L) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous NaHCO_3 (10 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:10 EtOAc:light petroleum) afforded the *title compound 44* as a colourless oil (1 mg, 20%), R_f 0.84 (1:3 EtOAc:light petroleum) (Found: $M^+ + \text{Na}$, 847.5158. $\text{C}_{48}\text{H}_{76}\text{O}_9\text{NaSi}$ requires M , 847.5151); $\nu_{\text{max}}/\text{cm}^{-1}$ 2959, 2864, 1612, 1514, 1463, 1455, 1379, 1367, 1260, 1171, 1099, 970, 882, 870 and 803; δ_{H} (400 MHz, CDCl_3) 0.93 (3 H, s, 8- CH_3), 0.95-1.05 [21 H, m, 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$], 1.15 (3 H, s, 8- CH_3'), 1.22 (1 H, m, 6- H_{ax}), 1.29 (3 H, s, CCH_3), 1.32 (1 H, m, 2- H_{ax}), 1.35 (3 H, s, CCH_3'), 1.43-1.56 (3 H, m, 4- H_2 , 2- H_{eq}), 1.67-1.79 (3 H, m, 14- H_{ax} , 10- H , 6- H_{eq}), 1.93 (1 H, t, J 12.4, 12- H_{ax}), 1.99 (1 H, dd, J 15.4, 4.2, 10- H'), 2.35 (2 H, m, 12- H_{eq} , 14- H_{eq}), 3.09 (3 H, s, 9- OCH_3), 3.34-3.45 (3 H, m, 15- H , 16- H_2), 3.48 (1 H, m, 11- H), 3.62 (1 H, dd, J 11.4, 4.3, 7- H), 3.69 (1 H, m, 5- H), 3.73 (3 H, s, ArOCH_3), 3.75 (1 H, m, 1- H_{ax}), 3.92 (1 H, td, J 11.7, 2.4, 1- H_{eq}), 4.13 (1 H, t, J 9.9, 3- H), 4.20 (2 H, m, 2'- H_2), 4.37 (1 H, d, J 11.7, PhHCH), 4.45 (2 H, s, ArCH_2), 4.52 (1 H, d, J 11.7, PhHCH), 5.27 (1 H, t, J 6.4, 1'- H), 6.80 (2 H, d, J 8.6, ArH), 7.16-7.22 (4 H, m, ArH), and 7.26 (3 H, d, J 4.5, ArH); m/z (E^+) 847 ($M^+ + 23$, 100%). Further elution (1:10 to 1:5 EtOAc:light petroleum) afforded the *title compound 43* as a pale oil (2 mg, 41%), R_f 0.27 (30% EtOAc/light petroleum) (Found: $M^+ + \text{Na}$, 807.4838. $\text{C}_{45}\text{H}_{72}\text{O}_9\text{NaSi}$ requires M , 807.4838); $\nu_{\text{max}}/\text{cm}^{-1}$ 3436, 2959, 2864, 1612, 1586, 1514, 1463, 1455, 1379, 1367, 1260, 1171, 1099, 882, 870 and 803; δ_{H} (400 MHz, CDCl_3) 0.91-1.08 [27 H, m, 2 $\times$ 8- CH_3 , 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$], 1.43-1.59 (2 H, m, 6- H_{ax} , 2- H), 1.59-1.72 (5 H, m, 2- H' , 4- H_2 , 6- H_{eq} , 10- H), 1.77 (1 H, dd, J 13.5, 12.5, 14- H_{ax}), 1.95 (1 H, t, J 12.2, 12- H_{ax}), 2.05 (1 H, dd, J 15.7, 7.0, 10- H'), 2.14 (1 H, d, J 13.6, 12- H_{eq}), 2.37 (1 H, d, J 13.9, 14- H_{eq}), 2.82 (1 H, t, J 4.8, 1- OH), 3.13 (3 H, s, 9- OCH_3), 3.37 (1 H, m, 15- H), 3.41 (1 H, dd, J 9.8, 4.1, 16- H), 3.46 (1 H, dd, J 10.1, 4.8, 16- H'), 3.50 (1 H, br. s, 3- OH), 3.59 (1 H, m, 11- H), 3.67 (1 H, dd, J 11.5, 4.8, 7- H), 3.7-3.77 (2 H, m, 1- H_2), 3.73 (3 H, s, ArOCH_3), 3.82 (1 H, m, 5- H), 4.16 (1 H, m, 3- H), 4.19 (2 H, d, J 6.1, 2'- H_2), 4.40 (1 H, d, J 11.8, PhHCH), 4.44 (2 H, s, ArCH_2), 4.54 (1 H, d, J 11.8, PhHCH), 5.32 (1 H, t, J 6.1, 1'- H), 6.80 (2 H, d, J 8.6, ArH), 7.16-7.22 (4 H, m, ArH), and 7.27 (3 H, d, J 4.3, ArH); m/z (E^+) 807 ($M^+ + 23$, 100%).

Prop-2-enyl (3*R*,5*R*,7*S*)-7-Benzoyloxy-10-[(2*S*,6*R*)-4-[(*Z*)-2-triisopropylsilyloxyethylidene]-6-(4-

methoxybenzyloxymethyl)tetrahydropyran-2-yl]-3,5-di-*O*-isopropylidene-8,8-dimethyl-9-oxodecanoate (46).

The alcohol **41** (1.5 g, 1.85 mmol) in DCM (27.8 mL) was added to the Dess-Martin periodinane (1.18 g, 2.77 mmol) and pyridine (2.24 mL, 27.74 mmol) in DCM (42.6 mL) and the mixture stirred for 1 h at rt. Ether (100 mL), saturated aqueous NaHCO_3 (50 mL) and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL) were added and the aqueous phase was extracted with ether (2 $\times$ 20 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give a pale yellow oil that was azeotroped with toluene to leave the corresponding aldehyde, R_f 0.84 (1:3 EtOAc:light petroleum).

Sodium chlorite (1.01 g, 11.12 mmol) and $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ (2.89 g, 18.54 mmol) in H_2O (14.8 mL) were added to a solution of this aldehyde and 2-methyl-2-butene (2 M in THF, 18.5 mL) in *t*-butanol (27.8 mL) at rt and the mixture stirred for 1 h. Brine (100 mL) and EtOAc (100 mL) were added and the aqueous phase extracted with EtOAc (2 $\times$ 100 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the carboxylic acid **45** as a pale, yellow oil, R_f 0.27 (1:3 EtOAc:light petroleum) (Found: $M^+ + \text{Na}$, 847.4784. $\text{C}_{47}\text{H}_{72}\text{O}_{10}\text{NaSi}$ requires M , 847.4792); m/z (E^+) 843.0 ($M^+ + 18$, 100%).

1-Bromoprop-2-ene (0.48 mL, 5.56 mmol) was added to this acid **45** and NaHCO_3 (312 mg, 3.71 mmol) in DMF (5.5 mL) and the reaction mixture was stirred at 70 $^\circ\text{C}$ for 16 h. Saturated aqueous NH_4Cl (100 mL) and ether (100 mL) were added and the aqueous phase extracted with ether (2 $\times$ 100 mL). The organic extracts were washed with brine (100 mL) and concentrated under reduced pressure. Chromatography of the residue (1:20 to 1:7 EtOAc:light petroleum with 1% Et_3N) gave the *title compound 46* as a pale, yellow oil (1.1 g, 70% from the alcohol **41**), R_f 0.40 (1:3 EtOAc:light petroleum), $[\alpha]_{\text{D}}^{25} +2.2$ (c 2.44, CHCl_3) (Found: $M^+ + \text{Na}$, 887.5094. $\text{C}_{50}\text{H}_{76}\text{O}_{10}\text{NaSi}$ requires M , 887.5100); $\nu_{\text{max}}/\text{cm}^{-1}$ 2942, 2866, 1740, 1706, 1613, 1514, 1464, 1381, 1367, 1248, 1224, 1171, 1101, 1066, 1038, 993, 882 and 820; δ_{H} (400 MHz, CDCl_3) 0.95-1.03 [24 H, m, 3 $\times$ $\text{SiCH}(\text{CH}_3)_2$, 8- CH_3], 1.14 (3 H, s, 8- CH_3'), 1.27 and 1.28 (each 3 H, s, CCH_3), 1.37 (1 H, ddd, J 14.6, 10.6, 1.5, 6- H), 1.42-1.61 (3 H, m, 6- H' , 4- H_2), 1.73 (1 H, t, J 12.3, 5'- H_{ax}), 1.82 (1 H, t, J 12.3, 3'- H_{ax}), 2.11 (1 H, d, J 12.3, 3'- H_{eq}), 2.36 (1 H, dd, J 15.4, 5.3, 2- H), 2.37 (1 H, m, 5'- H_{eq}), 2.47 (1 H, dd, J 15.4, 8.3, 2- H'), 2.50 (1 H, dd, J 17.6, 6.6, 10- H), 2.93 (1 H, dd, J 17.6, 5.8, 10- H'), 3.29-3.38 (2 H, m, 6'- CH_2), 3.41 (1 H, m, 6'- H), 3.73 (3 H, s, OCH_3), 3.78 (1 H, m, 2'- H), 3.88 (1 H, dd, J 9.8, 1.4, 7- H), 3.95 (1 H, m, 5- H), 4.18 (2 H, d, J 6.1, 2''- H_2), 4.19 (1 H, m, 3- H), 4.39 (2 H, s, ArCH_2), 4.48-4.54 (3 H, m, PhHCH , CO_2CH_2), 4.56 (1 H, d, J 11.4, PhHCH), 5.15 (1 H, dq, J 10.4, 1.3, $\text{HC}=\text{CHH}$), 5.24 (1 H, dq, J 17.2, 1.5, $\text{HC}=\text{CHH}$), 5.33 (1 H, t, J 6.3, 1''- H), 5.83 (1 H, ddt, J 17.2, 10.6, 5.8, $\text{HC}=\text{CH}_2$), 6.79 (2 H, d, J 8.6, ArH), 7.17 (2 H, d, J 8.6, ArH) and 7.18-7.28 (5 H, m, ArH); δ_{C} (100 MHz, CDCl_3) 11.0, 17.0, 19.4, 19.7, 24.0, 24.1, 30.5, 37.1, 37.9, 39.7, 40.3, 44.0, 51.7, 54.2, 58.4, 62.3, 64.1, 71.8, 71.9, 73.4, 73.8, 75.6, 79.4, 99.6, 112.7, 117.2, 123.5, 126.0, 126.4, 127.3, 128.3, 129.3, 131.0, 133.7, 137.7, 158.1, 169.5 and 211.6; m/z (E^+) 903.9 ($M^+ + 39$, 100%) and 888.0 ($M^+ + 23$, 38).

Prop-2-enyl (3R,5R,7S,9S,11S,15R)-7-benzyloxy-5,9-epoxy-11,15-epoxy-3-hydroxy-13-[(Z)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-16-(4-methoxybenzyloxy)-8,8-dimethylhexadecanoate (47).

Pyridinium toluene *p*-sulfonate (32 mg, 0.127 mmol) was added to the ester **46** (1.1 g, 0.042 mmol) and trimethyl orthoformate (2.8 mL) in DCM (9.8 mL) and methanol (9.8 mL). The solution was stirred at rt for 1 h before EtOAc (50 mL) and saturated aqueous NaHCO₃ (50 mL) were added. The aqueous phase was extracted with EtOAc (2 × 50 mL) and the organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:10 to 1:7 EtOAc:light petroleum) afforded the *title compound* **47** (700 mg, 66%) as a pale yellow oil, *R*_f 0.70 (1:3 EtOAc:light petroleum), [α]_D²⁵ +33.1 (c 2.56, CHCl₃) (Found: M⁺ + Na, 861.4940. C₄₈H₇₄O₁₀NaSi requires M, 861.4943; ν_{max}/cm⁻¹ 3494, 2945, 2863, 1737, 1733, 1615, 1514, 1463, 1454, 1362, 1259, 1171, 1096, 883 and 802; δ_H (400 MHz, CDCl₃) 0.94 (3 H, s, 8-CH₃), 0.95-1.08 [24 H, m, 8-CH₃'], 3 × SiCH(CH₃)₂, 1.41 (1 H, q, *J* 12.1, 6-H_{ax}), 1.48-1.58 (2 H, m, 4-H₂), 1.64-1.72 (2 H, m, 10-H, 6-H_{eq}), 1.74 (1 H, t, *J* 12.4, 14-H_{ax}), 1.93 (1 H, t, *J* 12.5, 12-H_{ax}), 2.00 (1 H, dd, *J* 16.1, 6.1, 10-H'), 2.16 (1 H, d, *J* 13.1, 12-H_{eq}), 2.38 (1 H, d, *J* 13.4, 14-H_{eq}), 2.37-2.48 (2 H, m, 2-H₂), 3.14 (3 H, s, 9-OCH₃), 3.31 (1 H, d, *J* 3.8, OH), 3.31-3.42 (2 H, m, 15-H, 16-H), 3.46 (1 H, dd, *J* 10.2, 5.0, 16-H'), 3.53 (1 H, m, 11-H), 3.64 (1 H, dd, *J* 11.4, 4.8, 7-H), 3.73 (3 H, s, OCH₃), 3.80 (1 H, m, 5-H), 4.18 (2 H, d, *J* 6.1, 13-CHCH₂), 4.28 (1 H, m, 3-H), 4.38 (1 H, d, *J* 11.6, PhHCH), 4.44 (2 H, s, ArCH₂), 4.48-4.59 (3 H, m, 1'-H₂, PhHCH), 5.17 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.25 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.29 (1 H, t, *J* 6.3, 13-CH), 5.84 (1 H, ddt, *J* 17.2, 10.6, 5.8, 2'-H), 6.80 (2 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH) and 7.24-7.28 (3 H, m, ArH); δ_C (100 MHz, CDCl₃) 11.0, 15.9, 17.0(2), 19.8, 30.5, 31.3, 38.3, 40.8(2), 42.0, 42.2, 47.4, 54.2, 58.4, 63.7, 64.2, 64.4, 70.6, 71.9(2), 73.9, 75.5, 77.7, 103.1, 112.7, 117.4, 122.9, 126.3(2), 127.2, 128.1, 129.6, 130.9, 134.6, 138.3, 158.0 and 171.2; *m/z* (ES⁺) 861.6 (M⁺ + 23, 100%).

Prop-2-enyl (3R,5S,7S,9S,11S,15R)-7-benzyloxy-3-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-13-[(Z)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-16-(4-methoxybenzyloxy)-8,8-dimethylhexadecanoate (48).

tert-Butylidimethylsilyl trifluoromethanesulfonate (411 μL, 1.79 mmol) and 2,6-lutidine (1.04 mL, 8.94 mmol) in DCM (7.4 mL) were added to the 3-hydroxyhexadecanoate **47** (700 mg, 0.894 mmol) and 2,6-lutidine (1.04 mL, 8.94 mmol) in DCM (41.1 mL) at -78 °C and the solution stirred at -78 °C for 1 h. Ether (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with ether (3 × 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (light petroleum to 1:20 EtOAc:light petroleum) of the residue afforded the *title compound* **48** as a pale oil (666 mg, 84%), *R*_f 0.65 (1:10 EtOAc:light petroleum), [α]_D²⁴ +25.7 (c 2.13, CH₂Cl₂) (Found: M⁺ + NH₄, 970.6257. C₅₄H₉₂O₁₀NSi₂ requires M, 970.6254; ν_{max}/cm⁻¹ 2946, 2864, 1738, 1613, 1514, 1464, 1382, 1362, 1249, 1171, 1096, 883, 835 and 776; δ_H (400 MHz, CDCl₃) -0.03 and 0.00 (each 3 H, s, SiCH₃), 0.79 [9 H, s, SiC(CH₃)₃], 0.93 (3 H, s, 8-CH₃), 0.95-1.05 [24 H, m, 8-CH₃'], 3 × SiCH(CH₃)₂, 1.30 (1 H, q, *J* 12.1, 6-

H_{ax}), 1.57 (1 H, dt, *J* 14.2, 4.9, 4-H), 1.65-1.79 (4 H, m, 4-H', 6-H_{eq}, 10-H, 14-H_{ax}), 1.87-1.98 (2 H, m, 10-H', 12-H_{ax}), 2.20 (1 H, d, *J* 13.4, 12-H_{eq}), 2.37 (1 H, d, *J* 13.6, 14-H_{eq}), 2.41 (1 H, dd, *J* 14.9, 7.8, 2-H), 2.58 (1 H, dd, *J* 14.9, 4.3, 2-H'), 3.11 (3 H, s, 9-OCH₃), 3.31-3.46 (3 H, m, 15-H, 16-H₂), 3.46-3.55 (2 H, m, 5-H, 11-H), 3.59 (1 H, dd, *J* 11.6, 4.8, 7-H), 3.73 (3 H, s, OCH₃), 4.19 (2 H, d, *J* 6.1, 13-CHCH₂), 4.19 (1 H, m, 3-H), 4.38 (1 H, d, *J* 11.9, PhHCH), 4.44 (2 H, s, ArCH₂), 4.49 (2 H, m, 1'-H₂), 4.54 (1 H, d, *J* 11.9, PhHCH), 5.15 (1 H, dq, *J* 10.3, 1.3, 3'-H), 5.24 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.31 (1 H, t, *J* 6.1, 13-CH), 5.84 (1 H, ddt, *J* 17.2, 10.3, 5.8, 2'-H), 6.80 (2 H, d, *J* 8.6, ArH), 7.16-7.22 (4 H, m, ArH) and 7.23-7.29 (3 H, m, ArH); δ_C (100 MHz, CDCl₃) -5.5, -5.3, 11.0, 15.8, 16.9, 17.0(2), 19.9, 24.8, 30.5, 32.3, 38.1, 42.1, 42.3, 42.5, 43.5, 47.3, 54.2, 58.4, 65.1, 67.1, 70.7, 71.9, 72.0, 74.0, 75.6, 77.8, 103.2, 112.7, 117.2, 122.9, 126.3(2), 127.2, 128.1, 129.5, 131.1, 134.6, 138.3, 158.1 and 170.2; *m/z* (ES⁺) 976.2 (M⁺ + 23, 64%) and 971.2 (M⁺ + 18, 100%).

Prop-2-enyl (3R,5S,7S,9S,11S,15R)-7-benzyloxy-3-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-16-hydroxy-13-[(Z)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8-dimethylhexadecanoate (49).

Dichlorodicyanoquinone (107 mg, 0.472 mmol) was added to the PMB-ether **48** (300 mg, 0.315 mmol) in DCM/methanol (9:1, 12.6 mL) at rt and the black slurry stirred at for 2 h. Saturated aqueous Na₂S₂O₃ (50 mL) and saturated aqueous NaHCO₃ (50 mL) were added and the mixture stirred for 10 min. Dichloromethane (100 mL) was added and the aqueous phase was extracted with DCM (2 × 50 mL). The organic extracts were washed with a mixture of saturated aqueous Na₂S₂O₃ and saturated aqueous NaHCO₃ (1:1, 100 mL) and brine (100 mL), then dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (1:20 to 1:10 EtOAc:light petroleum) of the residue afforded the *title compound* **49** as a pale, yellow oil (190 mg, 72%), *R*_f 0.46 (1:10 EtOAc:light petroleum), [α]_D²⁴ +29.3 (c 2.06, CH₂Cl₂) (Found: M⁺ + Na, 855.5219. C₄₆H₈₀O₉NaSi₂ requires M, 855.5233; ν_{max}/cm⁻¹ 3471, 2944, 2865, 1738, 1463, 1382, 1361, 1256, 1170, 1096, 882, 836 and 776; δ_H (400 MHz, C₆D₆) 0.03(2) (each 3 H, s, SiCH₃), 0.86 [9 H, s, SiC(CH₃)₃], 0.95-1.03 [21 H, m, 3 × SiCH(CH₃)₂], 1.05 and 1.15 (each 3 H, s, 8-CH₃), 1.28 (1 H, q, *J* 12.1, 6-H_{ax}), 1.50-1.68 (4 H, m, 4-H, 6-H_{eq}, 12-H_{ax}, 14-H_{ax}), 1.68-1.82 (2 H, m, 4-H', 10-H), 1.95-2.09 (3 H, m, 10-H', 12-H_{eq}, OH), 2.17 (1 H, d, *J* 13.4, 14-H_{eq}), 2.50 (1 H, dd, *J* 15.1, 7.8, 2-H), 2.61 (1 H, dd, *J* 15.1, 4.0, 2-H'), 3.05 (3 H, s, 9-OCH₃), 3.22 (1 H, m, 15-H), 3.31-3.43 (2 H, m, 16-H₂), 3.57-3.69 (3 H, m, 5-H, 7-H, 11-H), 4.12 (1 H, d, *J* 11.9, PhHCH), 4.14 (1 H, m, 13-CHCHH), 4.19 (1 H, dd, *J* 12.6, 6.3, 13-CHCHH), 4.40 (1 H, d, *J* 11.9, PhHCH), 4.33-4.44 (3 H, m, 1'-H₂, 3-H), 4.87 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.03 (1 H, dq, *J* 17.2, 1.6, 3'-H'), 5.46 (1 H, t, *J* 6.1, 13-CH), 5.65 (1 H, ddt, *J* 17.2, 10.3, 5.8, 2'-H), 6.97 (1 H, t, *J* 7.3, ArH), 7.02-7.09 (2 H, m, ArH) and 7.18 (2 H, d, *J* 7.3, ArH); δ_C (100 MHz, C₆D₆) -5.4, 11.0, 15.8, 16.9(2), 19.9, 24.7, 29.5, 32.3, 38.0, 42.0(2), 42.6, 43.8, 47.1, 58.4, 63.7, 64.8, 65.0, 67.2, 70.3, 73.8, 76.6, 77.6, 103.1, 116.5, 123.4, 126.1, 126.2, 127.1, 131.4, 134.2, 138.5 and 169.6; *m/z* (ES⁺) 856.0 (M⁺ + 23, 56%), 851.3 (M⁺ + 18, 20) and 257.1 (100%).

(4S,6R,7R)-2-Benzoyloxymethyl-7-tert-butyldimethylsilyloxy-4-triethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)oct-1-ene (54).

Imidazole (86 mg, 1.26 mmol) and triethylsilyl chloride (0.106 mL, 0.62 mmol) were added to the alcohol **53** (250 mg, 0.48 mmol) in DCM (3.4 mL) and the solution stirred at rt for 60 min. Dichloromethane (30 mL) and saturated aqueous NaHCO₃ (30 mL) were added and the aqueous phase was extracted with DCM (2 × 30 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (35:1 light petroleum:ether) afforded the *title compound* **54** (298 mg, 98%) as a colourless oil, *R*_f = 0.55 (19:1 light petroleum:ether) (Found: M⁺ + Na, 661.4116. C₃₄H₆₆O₅Si₃Na requires M, 661.4116); ν_{max}/cm⁻¹ 2954, 2929, 2876, 2858, 1649, 1462, 1377, 1250, 1102, 1071, 1057, 1033, 1017, 859, 835, 774 and 740; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.04 (6 H, s, 2 × SiCH₃), 0.58 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.83–0.99 (2 H, m, SiCH₂), 0.87 [9 H, s, SiC(CH₃)₃], 0.93 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 1.05 (3 H, d, *J* 6.3, 8-H₃), 1.53 (1 H, ddd, *J* 14.2, 9.1, 3.5, 5-H), 1.59 (1 H, ddd, *J* 14.3, 8.1, 2.5, 5-H'), 2.22 (1 H, dd, *J* 13.9, 7.8, 3-H), 2.38 (1 H, dd, *J* 13.9, 4.8, 3-H'), 3.48 (1 H, ddd, *J* 11.1, 9.6, 6.1, OHCHCH₂Si), 3.56 (1 H, ddd, *J* 9.1, 4.5, 2.8, 6-H), 3.67 (1 H, ddd, *J* 11.4, 9.6, 5.6, OHCHCH₂Si), 3.93 (1 H, d, *J* 12.6, 2-CH), 3.96–4.04 (3 H, m, 2-CH', 4-H, 7-H), 4.47 (2 H, s, PhCH₂), 4.68 (2 H, s, OCH₂O), 4.97 and 5.11 (each 1 H, s, 1-H) and 7.22–7.35 (5 H, m, Ar-H); δ_C (125 MHz, CDCl₃) –3.3, –3.2, 0.0, 6.7, 8.5, 18.8, 19.6(2), 27.3, 37.4, 43.8, 66.7, 69.6, 70.8, 73.4, 74.8, 81.5, 97.4, 115.6, 128.9, 129.1, 129.7, 139.9 and 144.4; *m/z* (ES⁺) 661.9 (M⁺ + 23, 100) and 656.6 (M⁺ + 18, 32).

(4S,6R,7R)-7-tert-Butyldimethylsilyloxy-2-methylene-4-triethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)octan-1-ol (55).

Lithium (864 mg, 123.2 mmol) was added to naphthalene (28.0 g, 218.4 mmol) in THF (160 mL) and the mixture stirred vigorously at rt for 2 h. The resulting dark green solution was added dropwise to the benzyl ether **54** (6.14 g, 9.62 mmol) in THF (276 mL) at –25 °C until consumption of the starting material was observed by TLC. Water was added dropwise and the mixture partitioned between ether (300 mL) and saturated aqueous NaHCO₃ (400 mL). The aqueous phase was extracted with ether (2 × 300 mL) and the organic extracts were dried (MgSO₄) then concentrated under reduced pressure. Chromatography (7:1 light petroleum:ether) of the residue afforded the *title compound* **55** (5.13 g, 97%) as a colourless oil, *R*_f = 0.21 (4:1 light petroleum:ether), [α]_D²⁹ +6.9 (c 2.0, CHCl₃) (Found: M⁺ + Na, 571.3632. C₂₇H₆₀O₅Si₃Na requires M, 571.3646); ν_{max}/cm⁻¹ 3444, 3072, 2954, 2928, 2878, 2858, 1651, 1472, 1463, 1414, 1378, 1250, 1148, 1102, 1057, 1034, 938, 899, 860, 835, 775 and 744; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.04 (6 H, s, 2 × SiCH₃), 0.62 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.83–0.99 (2 H, m, SiCH₂), 0.87 [9 H, s, SiC(CH₃)₃], 0.95 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 1.06 (3 H, d, *J* 6.3, 8-H₃), 1.59 (1 H, ddd, *J* 14.3, 8.6, 5.4, 5-H), 1.66 (1 H, ddd, *J* 14.4, 7.1, 3.8, 5-H'), 2.32 (1 H, dd, *J* 13.9, 5.8, 3-H), 2.39 (1 H, dd, *J* 14.0, 4.5, 3-H'), 3.01 (1 H, t, *J* 6.1, OH), 3.47–3.55 (2 H, m, OHCHCH₂Si, 6-H), 3.64 (1 H, ddd, *J* 11.3, 9.6, 5.8, OHCHCH₂Si), 3.98 (1 H, qd, *J* 6.3, 4.5, 7-H), 4.02

(2 H, d, *J* 6.1, 1-H₂), 4.06 (1 H, m, 4-H), 4.69 (2 H, s, OCH₂O), 4.91 and 5.09 (each 1 H, s, 2-CH); δ_C (75 MHz, CDCl₃) –3.3, –3.2, 0.0, 6.5, 8.4, 18.9, 19.5, 19.6, 27.3, 37.2, 44.1, 66.8, 68.1, 70.6, 71.0, 81.1, 96.9, 115.9 and 147.1; *m/z* (ES⁺) 608.5 (68%), 571.5 (M⁺ + 23, 42), 549.5 (M⁺ + 1, 100) and 431.2 (19).

(4S,6R,7R)-2-Bromomethyl-7-tert-butyldimethylsilyloxy-4-triethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)oct-1-ene (56).

Carbon tetrabromide (909 mg, 2.74 mmol) was added to the alcohol **55** (503 mg, 0.91 mmol), triphenylphosphine (759 mg, 2.90 mmol) and triethylamine (1.30 mL, 9.36 mmol) in DCM (35.0 mL) at 0 °C and the solution stirred at this temperature for 20 min. Dichloromethane (30 mL), saturated aqueous NaHCO₃ (30 mL) and saturated aqueous Na₂S₂O₃ (30 mL) were added and the aqueous phase was extracted with DCM (2 × 40 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (40:1 light petroleum:ether) of the residue afforded the *title compound* **56** (526 mg, 95%) as a colourless oil, *R*_f = 0.15 (60:1 light petroleum:ether), [α]_D²⁴ +0.8, (c 2.0, CHCl₃) (Found: M⁺ + Na, 633.2802. C₂₇H₅₉O₄⁷⁹BrSi₃Na requires M, 633.2802); ν_{max}/cm⁻¹ 3082, 2954, 2877, 1639, 1472, 1463, 1377, 1250, 1148, 1102, 1057, 1034, 938, 910, 859, 835, 775, 745 and 726; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.04 (6 H, s, 2 × SiCH₃), 0.61 (6 H, q, *J* 7.8, 3 × SiCH₂), 0.83–0.99 (2 H, m, SiCH₂), 0.86 [9 H, s, SiC(CH₃)₃], 0.95 (9 H, t, *J* 7.9, 3 × SiCH₂CH₃), 1.04 (3 H, d, *J* 6.3, 8-H₃), 1.47 (1 H, ddd, *J* 14.2, 9.6, 4.0, 5-H), 1.61 (1 H, ddd, *J* 14.4, 8.3, 2.5, 5-H'), 2.38 (1 H, dd, *J* 14.1, 7.3, 3-H), 2.49 (1 H, dd, *J* 14.1, 4.8, 3-H'), 3.50 (1 H, ddd, *J* 11.1, 9.6, 5.8, OHCHCH₂Si), 3.54 (1 H, ddd, *J* 9.6, 4.5, 2.5, 6-H), 3.66 (1 H, ddd, *J* 11.4, 9.6, 5.5, OHCHCH₂Si), 3.96–4.03 (2 H, m, 4-H, 7-H), 3.98 and 4.02 (each 1 H, d, *J* 9.8, 2-CH), 4.71 (2 H, s, OCH₂O) and 4.99 and 5.21 (each 1 H, s, 1-H); δ_C (100 MHz, CDCl₃) –3.3, –3.2, 0.0, 6.6, 8.5, 18.8, 19.5, 19.6, 27.3, 37.4, 38.9, 43.3, 66.8, 69.6, 70.7, 81.4, 97.3, 119.4 and 144.1; *m/z* (ES⁺) 635.1 (M⁺ + 23, 87%) and 633.3 (M⁺ + 23, 100).

(3R,5S,9R,10R)-1-(2-Benzothiazolylsulfonyl)-10-tert-butyldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecan-3-ol (57).

Chromium(II) chloride (95 mg, 0.77 mmol) was heated to 180 °C under reduced pressure in a round bottomed flask for 45 min. The flask was purged with N₂ and allowed to cool to r.t. Tetrahydrofuran (90 µL) was added followed by the bromide **56** (42 mg, 0.069 mmol) and the aldehyde **52**¹⁸ (74 mg, 0.26 mmol) in THF (0.16 mL). The resulting dark red mixture was stirred at r.t. for 15 h, diluted with ether (5 mL) and filtered through a short pad of silica, washing the silica thoroughly with ether (10 mL). Water and saturated aqueous sodium bisulfite (1:1) were added and aqueous phase was extracted with ether (2 × 5 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 5:1 light petroleum:ether) gave recovered bromide **56** (4 mg, 10%) followed by the *title compound* **57** (34 mg, 63%) as a colourless, viscous oil, a 1:1 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.48 and 0.52 (1:1 light petroleum:ether),

$[\alpha]_D^{31} -4.5$ (c 14.2, CHCl_3) (Found: $\text{M}^+ + \text{NH}_4$, 833.4469. $\text{C}_{39}\text{H}_{77}\text{O}_7\text{N}_2\text{S}_2\text{Si}_3$ requires M , 833.4475); $\nu_{\text{max}}/\text{cm}^{-1}$ 3564, 2954, 2927, 2873, 1645, 1557, 1471, 1377, 1330, 1250, 1149, 1103, 1056, 1032, 833 and 760; δ_{H} (400 MHz, CDCl_3) 0.00(2) [each 4.5 H, s, $\text{Si}(\text{CH}_3)_3$], 0.04 (1.5 H, s, SiCH_3), 0.05 (4.5 H, s, $2 \times \text{SiCH}_3$), 0.59 and 0.60 (each 3 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.81–0.98 (2 H, m, SiCH_2), 0.87(2) [each 4.5 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.94 and 0.95 (each 4.5 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 1.05 and 1.06 (each 1.5 H, d, J 6.3, 11- H_3), 1.19(2), 1.35 and 1.36 (each 1.5 H, s, 2- CH_3), 1.50–1.70 (2 H, m, 8- H_2), 1.95 (0.5 H, dd, J 13.7, 11.0, 4-H), 2.00 (0.5 H, dd, J 13.7, 10.9, 4-H), 2.19–2.39 (3 H, m, 4- H' , 6- H_2), 2.41 and 2.55 (each 0.5 H, d, J 3.0, OH), 3.43–3.63 (3 H, m, OHCHCH_2Si , 1-H, 9-H), 3.63–3.75 (2 H, m, OHCHCH_2Si , 3-H), 3.80 and 3.81 (each 0.5 H, d, J 14.2, 1- H'), 3.93–4.06 (2 H, m, 7-H, 10-H), 4.67–4.75 (2 H, m, OCH_2O), 4.92 (0.5 H, s, 5-CH), 4.94–4.99 (1.5 H, m, 5- CH' , 5- CH_2), 7.58, 7.63, 8.01 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl_3) –3.3 –3.2, 0.0, 6.7, 6.8, 8.5(2), 18.7, 19.5, 19.6(2), 23.8, 25.6, 27.3, 37.2, 37.3, 39.8, 40.2, 41.3, 41.4, 45.8, 45.9, 63.2, 66.7, 66.8, 70.0, 70.7, 76.0, 76.2, 81.4, 81.5, 97.2, 97.3, 117.6, 123.8, 126.9, 129.0, 129.4, 138.2, 145.0, 145.2, 154.1 and 169.3; m/z (ES^+) 838.6 ($\text{M}^+ + 23$, 100%) and 834.0 ($\text{M}^+ + 18$, 4). Unreacted aldehyde **52** (16 mg, 22%) was also recovered.

(7S,9R,10R)-1-(2-Benzothiazolylsulfonyl)-10-tert-butylldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecan-3-one (58).

Sodium hydrogen carbonate (21 mg, 0.25 mmol) and Dess Martin periodinane (30 mg, 0.070 mmol) were added to the alcohol **57** (13 mg, 0.015 mmol) in DCM (1 mL) and the suspension stirred at rt for 1 h. Ether (10 mL) was added and the solution washed with saturated aqueous sodium bisulfite (2×10 mL), saturated aqueous sodium hydrogen carbonate (2×10 mL), water (10 mL) and brine (10 mL). The organic layer was dried (MgSO_4) and concentrated under reduced pressure to yield the *title compound* **58** as a pale yellow, viscous oil (13 mg, ca. 100%), $R_f = 0.50$ (1:1 light petroleum:ether), $[\alpha]_D^{30} -8.8$ (c 5.0, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 836.3863. $\text{C}_{39}\text{H}_{71}\text{O}_7\text{N}_2\text{S}_2\text{Si}_3$ requires M , 836.3872); $\nu_{\text{max}}/\text{cm}^{-1}$ 2955, 2932, 2876, 1713, 1471, 1375, 1332, 1250, 1151, 1101, 1054 and 835; δ_{H} (400 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.04(2) (each 3 H, s, SiCH_3), 0.58 (6 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.82–0.99 (2 H, m, SiCH_2), 0.87 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.93 (9 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 1.05 (3 H, d, J 6.3, 11- H_3), 1.46 and 1.47 (each 3 H, s, 2- CH_3), 1.50–1.64 (2 H, m, 8- H_2), 2.21 (1 H, dd, J 14.2, 7.5, 6-H), 2.35 (1 H, dd, J 14.2, 5.1, 6- H'), 3.37 (2 H, s, 4- H_2), 3.47 (1 H, ddd, J 11.1, 9.6, 6.0, OHCHCH_2Si), 3.54 (1 H, ddd, J 9.3, 4.3, 2.6, 9-H), 3.68 (1 H, ddd, J 11.3, 9.6, 5.6, OHCHCH_2Si), 3.92–4.05 (2 H, m, 7-H, 10-H), 3.93 and 3.94 (each 1 H, d, J 14.4, 1-H), 4.70 and 4.71 (each 1 H, d, J 7.1, OHCHO), 4.87 and 5.00 (each 1 H, s, 5-CH), 7.58 and 7.62 (each 1 H, m, ArH) and 8.00 and 8.20 (each 1 H, d, J 8.0, ArH); δ_{C} (100 MHz, CDCl_3) –3.3(2), 0.0, 6.7, 8.5, 18.8, 19.5, 19.6, 26.2, 26.4, 27.3, 37.4, 45.9, 46.2, 48.7, 63.8, 66.7, 70.0, 70.7, 81.5, 97.4, 118.6, 123.8, 126.9, 129.0, 129.4, 138.2, 141.2, 153.9, 168.9 and 210.8; m/z (ES^+) 836.3 ($\text{M}^+ + 23$, 100%) and 832.2 ($\text{M}^+ + 18$, 50).

2-[(3RS,7S,9R,10R)-3,10-Bis-tert-butylldimethylsilyloxy-2,2-dimethyl-5-methylene-7-triethylsilyloxy-9-(2-trimethylsilylethoxymethoxy)undecanyl-1-sulfonyl]benzothiazole (59).

2,6-Lutidine (45 μL , 0.386 mmol) was added to the alcohol **57** (98 mg, 0.120 mmol) in DCM (1 mL) and the solution cooled to 0 °C. *tert*-Butylldimethylsilyl triflate (44 μL , 0.192 mmol) was added and the solution stirred for 2 h at rt. Additional 2,6-lutidine (45 μL , 0.386 mmol) and *tert*-butylldimethylsilyl triflate (44 μL , 0.192 mmol) were added and the mixture stirred for a further 30 min. The mixture was partitioned between DCM (10 mL) and water (10 mL) and the aqueous phase was extracted with DCM (2×10 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (20:1 light petroleum:ether) gave the *title compound* **59** as a clear, colourless oil (93 mg, 86%), a 1:1 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.68$ (2:1 light petroleum:ether), $[\alpha]_D^{31} -3.1$ (c 15.6, CHCl_3) (Found: $\text{M}^+ + \text{NH}_4$, 947.5349. $\text{C}_{45}\text{H}_{91}\text{O}_7\text{N}_2\text{S}_2\text{Si}_4$ requires M , 947.5339); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2927, 2876, 2857, 1645, 1471, 1377, 1331, 1250, 1150, 1102, 1072, 938, 835 and 775; δ_{H} (400 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.01–0.06 (12 H, overlapping s, $4 \times \text{SiCH}_3$), 0.58 (6 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.81–0.98 (2 H, m, SiCH_2), 0.86(3) and 0.87 [each 4.5 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.93 and 0.94 (each 4.5 H, t, J 7.9, $3 \times \text{SiCH}_2\text{CH}_3$), 1.03 and 1.04 (each 1.5 H, d, J 6.3, 11'- H_3), 1.22, 1.23, 1.24 and 1.26 (each 1.5 H, s, 2'- CH_3), 1.45–1.61 (2 H, m, 8'- H_2), 1.97 (0.5 H, dd, J 12.5, 7.3, 4'-H), 2.00 (0.5 H, dd, J 11.8, 6.6, 4'-H), 2.11 (0.5 H, dd, J 8.2, 2.8, 6'-H), 2.15 (0.5 H, dd, J 8.4, 3.0, 6'-H), 2.26–2.42 (2 H, m, 4'- H' , 6'- H'), 3.46 (1 H, m, OHCHCH_2Si), 3.52–3.73 (3.5 H, m, OHCHCH_2Si , 1'-H, 3'-H, 9'-H), 3.77 and 3.78 (each 0.5 H, d J 14.4, 1'-H or 1'- H'), 3.78 (0.5 H, d, J 14.4, 1'- H'), 3.95 (1 H, m, 7'-H), 4.04 (1 H, m, 10'-H), 4.65–4.70 (1.5 H, m, OCH_2O), 4.71 (0.5 H, d, J 7.0, OHCHO), 4.85–4.90 (1.5 H, m, 5'- CH_2 , 5'-CH), 4.91 (0.5 H, s, 5'- CH') and 7.56, 7.62, 8.00 and 8.19 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl_3) –3.3 –3.2, –2.9, –2.7, –1.8, –1.7, 0.0, 6.8, 6.9, 8.5, 18.6, 18.7, 19.5(2), 19.6, 19.7, 19.8, 24.4, 24.5, 26.1, 26.3, 27.3, 27.6(2), 37.0, 37.3, 41.8, 42.1, 42.2, 46.8, 47.3, 62.2, 62.3, 66.7, 69.7, 70.0, 70.6(2), 79.3, 79.5, 81.4, 97.4, 97.5, 116.4, 117.0, 123.8, 126.9, 128.9, 129.3, 138.1, 144.3, 144.6, 154.1 and 169.5(2); m/z (ES^+) 990.3 (22%), 952.7 ($\text{M}^+ + 23$, 100) and 948.2 ($\text{M}^+ + 18$, 19).

(2R,3R,5S,9RS)-11-(2-Benzothiazolylsulfonyl)-2,9-bis-tert-butylldimethylsilyloxy-10,10-dimethyl-7-methylene-3-(2-trimethylsilylethoxymethoxy)undecan-5-ol (60).

An aliquot (20 μL , 0.0056 mmol) of a solution of PPTS (0.28 g, 1.11 mmol) in methanol (4 mL) was added to the triethylsilyl ether **59** (74 mg, 0.082 mmol) in THF-methanol (2:3, 0.52 mL). The mixture was stirred at r.t. for 24 h then partitioned between ether (5 mL) and saturated aqueous sodium hydrogen carbonate (5 mL). The aqueous layer was extracted with ether (2×5 mL) and the organic extracts were washed with brine (5 mL), dried (MgSO_4) and concentrated under reduced pressure. Chromatography of the residue (10:1 to 2:1 light petroleum:ether) gave recovered silyl ether **59** (8 mg, 11%) followed by the *title compound* **60** as a clear, colourless oil (49 mg, 73%), $R_f = 0.39$ (2:1 light petroleum:ether), $[\alpha]_D^{30} +14.5$ (c

6.6, CHCl₃) (Found: M⁺ + Na, 838.4040. C₃₉H₇₃O₇NNa₂Si₃ requires M, 838.4028); $\nu_{\max}/\text{cm}^{-1}$ 3463, 3068, 2953, 2928, 2893, 2856, 1645, 1472, 1388, 1329, 1250, 1150, 1085, 1057, 1023, 938, 835 and 775; δ_{H} (400 MHz, CDCl₃) 0.00–0.04 [15 H, m, Si(CH₃)₃, 2 × SiCH₃], 0.06 and 0.07(3) (each 1.5 H, s, SiCH₃), 0.82–0.99 (2 H, m, SiCH₂), 0.86(2) and 0.88(2) [each 4.5 H, s, SiC(CH₃)₃], 1.10 (3 H, d, *J* 6.3, 1-H₃), 1.23, 1.24 and 1.25(2) (each 1.5 H, s, 10-CH₃), 1.50–1.62 (2 H, m, 4-H₂), 1.99–2.34 (3 H, m, 6-H₂, 8-H), 2.45 (0.5 H, dd, *J* 10.6, 3.8, 8-H'), 2.49 (0.5 H, dd, *J* 10.1, 3.5, 8-H'), 3.51–3.70 (5 H, m, 3-H, OH, OCH₂CH₂Si, 11-H), 3.74 (1 H, m, 9-H), 3.77(2) (each 0.5 H, d, *J* 14.5, 11-H'), 3.82–3.95 (2 H, m, 2-H, 5-H), 4.70(2) (each 0.5 H, d, *J* 6.7, OHCHO), 4.75 (1 H, d, *J* 6.7, OHCHO), 4.89–4.93 (1.5 H, m, 7-CH, 7-CH₂), 4.94 (0.5 H, s, 7-CH') and 7.58, 7.63, 8.01 and 8.20 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl₃) -3.3(2), -2.8, -2.7, -1.7(2), 0.0, 19.5, 19.6, 19.7, 20.0, 20.1, 24.6, 24.7, 26.1, 27.3(2), 27.6, 39.1(2), 41.7, 41.8, 42.3(2), 45.7(2), 62.3, 62.4, 67.2(2), 67.3, 67.6, 68.0, 72.3(2), 79.2(2), 81.5, 97.5, 97.6, 116.4, 116.5, 123.8, 126.9, 129.0, 129.3, 138.2, 145.1, 145.3, 154.1 and 169.5; *m/z* (ES⁺) 838.3 (M⁺ + 23, 100%), 833.7 (M⁺ + 18, 43), 748.6 (22), 533.5 (39) and 435.6 (50).

(2R,3R,5S,9RS)-11-(2-Benzothiazolylsulfonyl)-2,9-bis-tert-butylidimethylsilyloxy-10,10-dimethyl-7-methylene-3-(2-trimethylsilylethoxymethoxy)undecan-5-yl acrylate (61).

Di-isopropylethylamine (0.11 ml, 0.63 mmol) was added to the alcohol **60** (49 mg, 0.06 mmol) in DCM (1.1 mL) and the solution cooled to 0 °C. Acryloyl chloride (25 μ L, 0.31 mmol) was added dropwise, and the mixture stirred at rt for 1 h then partitioned between DCM (5 mL) and brine (5 mL). The aqueous layer was extracted with DCM (2 × 5 mL) and the organic extracts were washed with saturated aqueous sodium hydrogen carbonate (10 mL), dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue (10:1 to 2:1 light petroleum:ether) gave the *title compound* **61** as a clear, colourless gum (52 mg, 100%), a 1:1 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.50 (2:1 light petroleum:ether), [α]_D²⁸ -13 (c 9.7, CHCl₃) (Found: M⁺ + Na, 892.4126. C₄₂H₇₅O₈NNa₂Si₃ requires M, 892.4134); $\nu_{\max}/\text{cm}^{-1}$ 2951, 2925, 2853, 1716, 1636, 1470, 1328, 1248, 1197, 1171, 1148, 1101, 1055, 1024 and 835; δ_{H} (400 MHz, CDCl₃) -0.03 to 0.05 [21 H, m, Si(CH₃)₃, 4 × CH₃], 0.78–0.97 (2 H, m, SiCH₂), 0.86(2) and 0.87(2) [each 4.5 H, s, SiC(CH₃)₃], 1.06 (3 H, d, *J* 6.3, 1'-H₃), 1.23, 1.24, 1.26 and 1.27 (each 1.5 H, s, 10'-CH₃), 1.56 and 1.59 (each 0.5 H, ddd, *J* 14.8, 4.4, 2.0, 4'-H), 1.84 (0.5 H, ddd, *J* 14.8, 10.8, 1.2, 4'-H'), 1.89 (0.5 H, ddd, *J* 14.6, 10.5, 1.3, 4'-H'), 2.00 (0.5 H, dd, *J* 15.1, 7.3, 8'-H), 2.05 (0.5 H, dd, *J* 15.1, 7.0, 8'-H), 2.21 (0.5 H, dd, *J* 13.1, 7.2, 6'-H), 2.27 (0.5 H, dd, *J* 14.1, 5.4, 6'-H), 2.37 (0.5 H, dd, *J* 14.1, 7.8, 6'-H'), 2.41–2.51 (1.5 H, m, 6'-H', 8'-H'), 3.36 (1 H, m, 3'-H), 3.45 (1 H, m, OHCHCH₂Si), 3.57–3.70 (2.5 H, m, OHCHCH₂Si, 11'-H, 9'-H), 3.71–3.82 (1.5 H, m, 11'-H', 9'-H), 4.03 (1 H, m, 2'-H), 4.55, 4.59 and 4.67(2) (each 0.5 H, d, *J* 7.1, OHCHO), 4.88 (0.5 H, s, 7'-CH), 4.90 (1.5 H, s, 7'-CH, 7'-CH'), 5.16 and 5.25 (each 0.5 H, m, 5'-H), 5.77 and 5.78 (each 0.5 H, dd, *J* 10.4, 1.5, 3-H), 6.04(2) (each 0.5 H, dd, *J* 17.3, 10.4, 2-H), 6.33 and 6.34 (each 0.5 H, d, *J* 17.3, 1.5, 3-H') and 7.57, 7.63, 8.01 and 8.20 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl₃) -3.4, -3.2, -2.7, -1.7(2), 0.0, 18.3, 19.5, 19.7, 19.8, 24.6(2), 26.1, 26.2, 27.3, 27.6(2), 34.0, 34.6, 40.9, 41.3, 42.3(2),

43.6(2), 62.3, 66.6, 66.7, 70.0, 70.8, 70.9, 79.2, 79.3, 80.1, 80.4, 97.6, 97.7, 117.7, 118.0, 123.8, 126.9, 128.9, 129.3, 130.1, 132.0(2), 138.2(2), 143.3, 143.4, 154.1, 167.1 and 169.5(2); *m/z* (ES⁺) 892.6 (M⁺ + 23, 100%).

(6S)-4-[(2RS)-4-(2-Benzothiazolylsulfonyl)-2-tert-butylidimethylsilyloxy-3,3-dimethylbutyl]-6-[(2R,3R)-3-tert-butylidimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-5,6-dihydropyran-2-one (62).

An aliquot (60 μ L, 0.0028 mmol, 6 mol%) of a solution of Grubbs II catalyst (8 mg, 0.0094 mmol) in DCE (0.20 mL) was added to the acrylate **61** (42 mg, 0.048 mmol) in DCE (0.36 mL) and the solution degassed (freeze-thaw × 3) then heated under reflux. Four further aliquots of the Grubbs II solution (30 μ L, 0.0014 mmol, 3 mol%) were added every 2 h, and the reaction mixture was then stirred under reflux for 16 h. After cooling to rt, the mixture was concentrated under reduced pressure and chromatography of the residue (20:1 to 2:1 light petroleum:ether) gave unreacted acrylate **61** (16 mg, 39%) followed by the *title compound* **62** as a clear, pale brown gum (20 mg, 52%), a 1:1 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.33 (2:1 light petroleum:ether), [α]_D²⁸ -27.2 (c 6.9, CHCl₃) (Found: M⁺ + NH₄, 859.4267. C₄₀H₇₅O₈N₂Si₃ requires M, 859.4267); $\nu_{\max}/\text{cm}^{-1}$ 2953, 2924, 2853, 1718, 1472, 1387, 1328, 1250, 1148, 1103, 1056, 1027, 937, 857 and 836; δ_{H} (400 MHz, CDCl₃) 0.00(2) [each 4.5 H, s, Si(CH₃)₃], 0.01 and 0.04 (each 1.5 H, s, SiCH₃), 0.07 (6 H, s, 2 × SiCH₃), 0.09 and 0.11 (each 1.5 H, s, SiCH₃), 0.82–0.98 (2 H, m, SiCH₂), 0.88(2) and 0.89(2) [each 4.5 H, s, SiC(CH₃)₃], 1.10(2) (each 1.5 H, d, *J* 6.3, 4''-H₃), 1.21–1.27 (6 H, overlapping s, 2 × 3'-CH₃), 1.64 and 2.07 (each 1 H, m, 1''-H), 2.26–2.48 (3 H, 1'-H, 5-H₂), 2.65 (1 H, m, 1'-H'), 3.51 (1 H, m, OHCHCH₂Si), 3.59–3.68 (2 H, m, OHCHCH₂Si, 4'-H), 3.70 and 3.71 (each 0.5 H, d, *J* 14.6, 4'-H'), 3.78 (1 H, m, 2''-H), 3.96 (0.5 H, dd, *J* 6.3, 4.1, 2'-H), 3.99–4.09 (1.5 H, m, 2'-H, 3''-H), 4.60 (1 H, m, 6-H), 4.70 and 4.71 (each 0.5 H, d, *J* 7.0, OHCHO), 4.72 (1 H, s, OCH₂O), 5.88 (1 H, s, 3-H) and 7.59, 7.66, 8.03 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl₃) -3.3, -2.8(2), -1.9, 0.0, 18.7, 18.8, 19.5(2), 19.6, 19.7, 24.7, 25.0, 25.7(2), 27.3, 27.4(2), 31.1, 35.7, 35.9, 36.0, 37.0, 42.5, 42.6, 42.9, 62.2, 66.9, 67.3, 70.3, 70.4, 75.4, 75.6, 77.0(2), 79.2, 97.4(2), 119.5, 120.2, 123.8, 126.9, 129.0, 129.1, 129.5, 129.9, 138.1, 154.0, 158.8, 159.0, 165.9, 166.0, 169.0 and 169.1; *m/z* (ES⁺) 864.5 (M⁺ + 23, 100%) and 859.3 (M⁺ + 18, 2).

(2E)-(5S,7R,8R)-3-[(2RS)-4-(2-Benzothiazolylsulfonyl)-2-tert-butylidimethylsilyloxy-3,3-dimethylbutyl]-8-tert-butylidimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene-1,5-diol (63).

Cerium(III) chloride heptahydrate (44 mg, 0.12 mmol) was added to the lactone **62** (20 mg, 0.0233 mmol) in methanol (0.29 mL) and THF (0.09 mL) at 0 °C. After the solid had dissolved, sodium borohydride (4 mg, 0.11 mmol) was added and the solution was stirred at rt for 2 h. Five further portions of cerium trichloride and sodium borohydride were then added every 2 h. Dichloromethane was added the mixture added to silica gel with chromatography (20:1 to 1:2 light petroleum:ether) giving the *title compound* **63** as a colourless

gum (16 mg, 83%), a 1:1 mixture of epimers (^1H and ^{13}C NMR), R_f = 0.42 and 0.45 (1:2 light petroleum:ether), $[\alpha]_D^{25}$ -1.6 (c 8.8, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 868.4113. $\text{C}_{40}\text{H}_{75}\text{O}_8\text{NNaSi}_2\text{Si}_3$ requires M , 868.4134); $\nu_{\text{max}}/\text{cm}^{-1}$ 3420, 2951, 2928, 2857, 1472, 1328, 1250, 1149, 1084, 1058, 1024, 937, 856, 835 and 775; δ_{H} (400 MHz, CDCl_3) -0.09 and -0.03 (each 1.5 H, s, SiCH_3), 0.00(2) [each 4.5 H, s, $\text{Si}(\text{CH}_3)_3$], 0.01 and 0.04 (each 1.5 H, s, SiCH_3), 0.07 (3 H, s, SiCH_3), 0.07 and 0.08 (each 1.5 H, s, SiCH_3), 0.83-0.94 (2 H, m, SiCH_2), 0.86 and 0.87 [each 4.5 H, s, $\text{Si}(\text{CH}_3)_3$], 0.88 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 1.11(2) (each 1.5 H, d, J 6.3, 9- H_3), 1.23, 1.24(2), 1.27 (each 1.5 H, s, 3'- CH_3), 1.50-1.73 (2 H, m, 6- H_2), 1.95-2.10 (2 H, m, 1'-H, 4-H), 2.40-2.58 (2 H, m, 1'-H', 4-H'), 2.79 (2 H, br. s, 2 $\times$ OH), 3.46-3.91 (9 H, m, 1-H, 5-H, 7-H, 8-H, 2'-H, $\text{OCH}_2\text{CH}_2\text{Si}$, 4'- H_2), 4.15 (1 H, m, 1-H'), 4.70(2) (each 0.5 H, d, J 6.5, OHCHO), 4.75 (1 H, d, J 6.5, OHCHO), 5.82 (1 H, m, 2-H), 7.58, 7.64, 8.02 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl_3) -3.3(2), -2.7, -2.3, -1.9, -1.6, 0.0, 16.7, 19.5, 19.7, 19.8, 20.2, 20.3, 23.8, 25.1, 25.5, 25.9, 26.2, 27.3, 27.6(2), 38.5, 40.0, 40.1, 40.7, 41.8, 42.3(2), 58.8, 59.0, 62.5, 62.6, 66.1, 66.4, 67.3, 72.6, 72.7, 80.1, 81.7, 81.9, 97.6, 97.7, 123.8, 126.9, 129.0, 129.4, 129.9, 130.4, 132.0, 138.1, 139.4, 141.1, 154.1(2), 169.4 and 169.5; m/z (ES^+) 869.0 ($\text{M}^+ + 23$, 100%) and 846.0 ($\text{M}^+ + 1$, 5).

(4S,6R,7R)-2-Bromomethyl-7-tert-butyldimethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)oct-1-en-4-ol (64).

Pyridinium toluene *p*-sulfonate (21 mg, 0.082 mmol) was added to the triethylsilyl ether **56** (526 mg, 0.860 mmol) in a mixture of THF (14.0 mL), methanol (14.0 mL) and trimethyl orthoformate (1.4 mL, 12.8 mmol) and the solution stirred at rt for 3 h. Ether (60 mL) and saturated aqueous NaHCO_3 (60 mL) were added and the aqueous phase was extracted with ether (3 $\times$ 50 mL). The organic extracts were dried (MgSO_4) and then concentrated under reduced pressure. Chromatography (5:1 light petroleum:ether) of the residue afforded the *title compound* **64** (405 mg, 95%) as a colourless oil, R_f = 0.28 (4:1 light petroleum:ether), $[\alpha]_D^{26}$ +34.7 (c 1.2, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 519.1927. $\text{C}_{21}\text{H}_{45}\text{O}_4^{79}\text{BrSi}_2\text{Na}$ requires M , 519.1937); $\nu_{\text{max}}/\text{cm}^{-1}$ 3467, 3080, 2953, 2929, 2896, 2857, 1641, 1472, 1463, 1377, 1250, 1210, 1151, 1102, 1056, 1031, 938, 860, 832 and 775; δ_{H} (400 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.06 and 0.07 (each 3 H, s, SiCH_3), 0.88 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.93 (2 H, m, SiCH_2), 1.10 (3 H, d, J 6.3, 8- H_3), 1.54 (1 H, ddd, J 14.4, 8.6, 3.3, 5-H), 1.60 (1 H, ddd, J 14.4, 9.1, 5.0, 5-H'), 2.33-2.43 (2 H, m, 3- H_2), 3.55 (1 H, td, J 9.5, 8.0, OHCHCH_2Si), 3.59 (1 H, dt, J 8.7, 5.4, 6-H), 3.69 (1 H, td, J 9.6, 7.8, OHCHCH_2Si), 3.73 (1 H, d, J 3.2, OH), 3.83 (1 H, pent, J 6.0, 7-H), 3.97 (1 H, m, 4-H), 4.04 and 4.05 (each 1 H, dd, J 10.1, 0.8, 2-CH), 4.70 and 4.76 (each 1 H, d, J 6.8, OHCHO) and 5.05 and 5.24 (each 1 H, m, 1-H); δ_{C} (100 MHz, CDCl_3) -3.3, 0.0, 19.5, 19.6, 20.3, 27.3, 38.5, 39.4, 42.6, 67.5(2), 72.5, 81.7, 97.7, 118.8 and 144.7; m/z (ES^+) 558.5 (25%), 556.4 (30), 521.3 ($\text{M}^+ + 23$, 75), 519.2 ($\text{M}^+ + 23$, 100), 499.2 ($\text{M}^+ + 1$, 22) and 497.4 ($\text{M}^+ + 1$, 23).

(4S,6R,7R)-2-Bromomethyl-7-tert-butyldimethylsilyloxy-6-(2-trimethylsilylethoxymethoxy)oct-1-en-4-yl acrylate (65).

N,N-Di-isopropylethylamine (0.51 mL, 2.87 mmol) and acryloyl chloride (0.116 mL, 1.39 mmol) were added to the alcohol **64**

(405 mg, 0.82 mmol) in DCM (5.5 mL) at 0 °C and the solution stirred at this temperature for 40 min. Dichloromethane (40 mL) and saturated aqueous NaHCO_3 (400 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 40 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (10:1 light petroleum:ether) of the residue afforded the *title compound* **65** (435 mg, 97%) as a colourless oil, R_f = 0.68 (4:1 light petroleum:ether), $[\alpha]_D^{27}$ -0.7 (c 1.2, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 573.2053. $\text{C}_{24}\text{H}_{47}\text{O}_5^{79}\text{BrSi}_2\text{Na}$ requires M , 573.2038); $\nu_{\text{max}}/\text{cm}^{-1}$ 2953, 2928, 2858, 2893, 1724, 1638, 1405, 1296, 1250, 1192, 1103, 1056, 985, 860, 835, 809 and 776; δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.02 and 0.03 (each 3 H, s, SiCH_3), 0.84 (1 H, ddd, J 13.6, 11.4, 5.0, SiHCH), 0.86 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.95 (1 H, ddd, J 13.9, 12.0, 6.0, SiHCH), 1.06 (3 H, d, J 6.3, 8'- H_3), 1.58 (1 H, ddd, J 14.2, 10.4, 1.9, 5'-H), 1.92 (1 H, dd, J 14.2, 10.4, 5'-H'), 2.46 (1 H, dd, J 14.5, 8.2, 3'-H), 2.58 (1 H, dd, J 14.5, 4.7, 3'-H'), 3.36 (1 H, dd, J 10.1, 4.4, 6'-H), 3.49 (1 H, ddd, J 11.3, 10.1, 5.9, OHCHCH_2Si), 3.66 (1 H, ddd, J 11.7, 9.8, 5.4, OHCHCH_2Si), 3.95 (1 H, d, J 10.4, 2'-CH), 4.01 (1 H, qd, J 6.2, 4.7, 7'-H), 4.07 (1 H, d, J 10.4, 2'-CH'), 4.60 and 4.70 (each 1 H, d, J 7.1, OHCHO), 4.99 and 5.20 (each 1 H, s, 1'-H), 5.27 (1 H, m, 4'-H), 5.79 (1 H, d, J 10.5, 3-H), 6.05 (1 H, dd, J 17.3, 10.4, 2-H) and 6.35 (1 H, d, J 17.3, 3-H'); δ_{C} (125 MHz, CDCl_3) -3.4, -3.2, 0.0, 18.3, 19.5, 27.3, 34.7, 37.9, 40.8, 66.8, 70.0, 70.5, 80.3, 97.6, 119.8, 130.0, 132.2, 143.0 and 167.2; m/z (ES^+) 575.2 ($\text{M}^+ + 23$, 84%), 573.3 ($\text{M}^+ + 23$, 100), 570.2 ($\text{M}^+ + 18$, 68) and 568.3 ($\text{M}^+ + 18$, 61).

(2R,3R,5S,9RS)-11-Benzothiazol-2-ylsulfonfyl-2-tert-butyldimethylsilyloxy-10,10-dimethyl-7-methylene-9-triethylsilyloxy-3-(2-trimethylsilylethoxymethoxy)undecan-5-yl acrylate (67).

Activated zinc powder (11 mg, 0.172 mmol) was added to a vigorously stirred solution of bismuth(III) iodide (89 mg, 0.151 mmol) in THF (0.5 mL) and the resulting orange/grey suspension stirred vigorously at rt for 75 min resulting in the formation of a black suspension. Solid NaHCO_3 (38 mg, 0.455 mmol) was added in one portion, followed by the bromide **65** (50 mg, 0.091 mmol) and aldehyde **52** (80 mg, 0.282 mmol) in THF (0.35 mL). The mixture was heated under reflux for 4.5 h before being diluted with ether (5 mL) and filtered through celite. The filter cake was washed with ether (2 $\times$ 5 mL) and saturated aqueous NaHCO_3 (5 mL). Water (10 mL) was added to the washings and the aqueous phase was extracted with ether (3 $\times$ 10 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (3:1 light petroleum:ether) of the residue afforded the alcohol **66** as a mixture of epimers together with the excess of the aldehyde **52**. This mixture was used without purification, R_f = 0.25 (3:1 light petroleum:ether).

Imidazole (60 mg, 0.88 mmol) and triethylsilyl chloride (0.067 mL, 0.40 mmol) were added to the alcohol **66** in DCM (0.5 mL) and the solution stirred at rt for 90 min. Ether (10 mL) and saturated aqueous NaHCO_3 (10 mL) were added and the aqueous phase was extracted with ether (3 $\times$ 10 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (9:1 light petroleum:ether) of the residue afforded the *title compound* **67** (48 mg, 61% from

bromide **65**), a colourless oil, a 55:45 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.19$ (9:1 light petroleum:ether), $[\alpha]_D^{28} -10.1$ (c 1.0, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 892.4117. $\text{C}_{42}\text{H}_{75}\text{O}_8\text{NS}_2\text{Si}_3\text{Na}$ requires M , 892.4140); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2924, 2874, 1722, 1471, 1404, 1330, 1250, 1195, 1150, 1102, 1055, 1023, 856, 835, 761 and 729; δ_{H} (400 MHz, CDCl_3) 0.00 [4.95 H, s, $\text{Si}(\text{CH}_3)_3$], 0.00 [4.05 H, s, $\text{Si}(\text{CH}_3)_3$], 0.02 and 0.04 (each 1.35 H, s, SiCH_3), 0.03 and 0.04 (each 1.65 H, s, SiCH_3), 0.55 (3.3 H, q, J 8.1, $3 \times \text{SiCH}_2$), 0.56 (2.7 H, q, J 8.0, $3 \times \text{SiCH}_2$), 0.78-0.98 (2 H, m, SiCH_2), 0.87 [4.05 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.87 [4.95 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.90 (4.95 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 0.91 (4.05 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 1.06 (1.65 H, d, J 6.3, $1'\text{-H}_3$), 1.07 (1.35 H, d, J 6.3, $1'\text{-H}_3$), 1.23 (1.35 H, s, $10'\text{-CH}_3$), 1.27 (3 H, s, $10'\text{-CH}_3$), 1.29 (1.65 H, s, $10'\text{-CH}_3$), 1.59 (1 H, m, $4'\text{-H}$), 1.80-2.01 (2 H, m, $4'\text{-H}'$, $8'\text{-H}$), 2.18-2.48 (3 H, m, $6'\text{-H}_2$, $8'\text{-H}'$), 3.35 (0.45 H, ddd, J 10.9, 4.3, 1.1, $3'\text{-H}$), 3.38 (0.55 H, ddd, 10.9, 4.5, 1.0, $3'\text{-H}$), 3.45 (1 H, m, OHCHCH_2Si), 3.57 (1 H, d, J 14.1, $11'\text{-H}$), 3.60-3.72 (2 H, m, OHCHCH_2Si , $9'\text{-H}$), 3.75 (0.45 H, d, J 14.4, $11'\text{-H}'$), 3.77 (0.55 H, d, J 14.4, $11'\text{-H}'$), 4.02 (1 H, qd, J 6.3, 4.5, $2'\text{-H}$), 4.55 (0.55 H, d, J 7.1, OHCHO), 4.60 (0.45 H, d, J 7.1, OHCHO), 4.67 (0.55 H, d, J 7.1, OHCHO), 4.67 (0.45 H, d, J 7.1, OHCHO), 4.88 (1.45 H, s, $7'\text{-CH}_2$, $7'\text{-CH}$), 4.90 (0.55 H, s, $7'\text{-CH}'$), 5.15 (0.55 H, m, $5'\text{-H}$), 5.25 (0.45 H, m, $5'\text{-H}$), 5.77 (0.45 H, dd, J 10.3, 1.5, 3-H), 5.78 (0.55 H, dd, J 10.5, 1.5, 3-H), 6.04 (0.45 H, dd, J 17.4, 10.3, 2-H), 6.04 (0.55 H, dd, J 17.2, 10.3, 2-H), 6.34 (1 H, dd, J 17.4, 1.5, $3\text{-H}'$), 7.55-7.65 (2 H, m, ArH) and 8.00 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz) -3.4, -3.2, 0.0, 7.0, 8.6, 18.3, 19.5, 24.7(2), 26.1, 27.3, 33.9, 34.7, 40.7, 41.0, 42.1(2), 43.3, 43.4, 62.1, 66.6, 66.7, 70.0(2), 70.7, 70.9, 80.0, 80.1, 80.2, 80.4, 97.6, 97.7, 117.7, 118.0, 123.8, 126.9, 129.0(2), 129.3, 130.1(2), 132.0, 138.2(2), 143.0, 143.3, 154.1, 167.1 and 169.5(2); m/z (ES^+) 887.8 ($\text{M}^+ + 18$, 50%).

(6S)-4-[(2RS)-4-Benzothiazol-2-ylsulfonfyl-3,3-dimethyl-2-triethylsilyloxybutyl]-6-[(2R,3R)-3-tert-butylidimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-5,6-dihydropyran-2-one (68).

A de-gassed solution of Grubbs' 2nd generation catalyst (2.6 mg, 3.1 μmol) was added *via* a syringe pump over 20 h to a de-gassed solution of the acrylate **67** (50 mg, 0.058 mmol) in DCE (0.45 mL) heated under reflux. The reaction mixture was then allowed to cool to rt and was concentrated under reduced pressure. Chromatography (3:1 light petroleum:ether) of the residue afforded the *title compound* **68** (44 mg, 90%), as a pale red oil, a 55:45 mixture of epimers (^1H and ^{13}C NMR), $R_f = 0.13$ (3:1 light petroleum:ether), $[\alpha]_D^{28} -28.2$ (c 1.0, CHCl_3) (Found: $\text{M}^+ + \text{NH}_4$, 864.3814. $\text{C}_{40}\text{H}_{71}\text{O}_8\text{NS}_2\text{Si}_3\text{Na}$ requires M , 864.3827); $\nu_{\text{max}}/\text{cm}^{-1}$ 2954, 2935, 2879, 1716, 1643, 1471, 1390, 1328, 1250, 1150, 1101, 1056, 1029, 939, 858, 836, 761 and 730; δ_{H} (400 MHz, CDCl_3) 0.00 [4.05 H, s, $\text{Si}(\text{CH}_3)_3$], 0.00 [4.95 H, s, $\text{Si}(\text{CH}_3)_3$], 0.07 (6 H, s, $2 \times \text{SiCH}_3$), 0.53-0.67 (6 H, m, $3 \times \text{SiCH}_2$), 0.82-0.99 (2 H, m, SiCH_2), 0.87 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.94 (4.05 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 0.94 (4.95 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 1.09 (1.65 H, d, J 6.3, $4''\text{-H}_3$), 1.10 (1.35 H, d, J 6.3, $4''\text{-H}_3$), 1.24 (4.35 H, s, $3'\text{-CH}_3$, $3'\text{-CH}_3'$), 1.26 (1.65 H, s, $3'\text{-CH}_3'$), 1.63 (1 H, m, $1''\text{-H}$), 2.05 (0.55 H, ddd, J 9.3, 7.1, 2.3, $1''\text{-H}'$), 2.08 (0.45 H, ddd, J 9.6, 7.1, 2.3, $1''\text{-H}'$), 2.24-2.46 (3 H, m, $1'\text{-H}$, 5-H_2), 2.59 (1 H, m, $1'\text{-H}'$), 3.50 (1 H, m, OHCHCH_2Si), 3.58 (0.45 H, d, J 14.4, $4'\text{-H}$), 3.59 (0.55 H, d, J

14.4, $4'\text{-H}$), 3.65 (1 H, m, OHCHCH_2Si), 3.70 (0.45 H, d, J 14.4, $4'\text{-H}'$), 3.71 (0.55 H, d, J 14.4, $4'\text{-H}'$), 3.77 (1 H, m, $2''\text{-H}$), 3.96 (0.45 H, dd, J 7.6, 3.3, $2'\text{-H}$), 4.00 (0.55 H, dd, J 7.1, 4.0, $2'\text{-H}$), 4.04 (1 H, qd, J 6.3, 4.8, $3''\text{-H}$), 4.59 (1 H, m, 6-H), 4.71 (2 H, s, OCH_2O), 5.86 (1 H, s, 3-H), 7.57-7.67 (2 H, m, ArH) and 8.02 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl_3) -3.3, -3.3, 0.0, 7.0, 8.5, 8.6, 18.7, 18.8, 19.5(2), 25.0, 25.1, 25.7, 27.3, 31.7, 35.7, 35.9(2), 42.2, 42.4, 42.5, 42.7, 62.2, 66.8(2), 70.2, 70.3, 75.5(2), 77.6, 77.9, 79.2, 79.3, 97.4, 97.4, 119.6, 120.1, 123.8, 126.9, 129.1, 129.5, 138.1, 154.0, 158.8, 159.0, 165.8, 166.0 and 169.0(2); m/z (ES^+) 1297.7 (35%), 1283.4 (23), 901.8 (69), 864.6 ($\text{M}^+ + 23$, 100) and 859.7 ($\text{M}^+ + 18$, 81), 454.0 (23) and 440.9 (37).

(E)-(5S,7R,8R)-3-[(RS)-4-Benzothiazol-2-ylsulfonfyl-3,3-dimethyl-2-triethylsilyloxybutyl]-8-tert-butylidimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene-1,5-diol (69).

Cerium(III) chloride heptahydrate (44 mg, 0.12 mmol) was added to the lactone **68** (20 mg, 0.0233 mmol) in methanol (0.29 mL) and THF (0.09 mL) at 0 °C. After the solid had dissolved, sodium borohydride (4 mg, 0.11 mmol) was added and the mixture was stirred at rt for 7.5 h with further portions of cerium(III) chloride heptahydrate and sodium borohydride added every 1.5 h. The reaction mixture was then partitioned between ether (10 mL) and water (10 mL), and the aqueous phase was extracted with ether (2 $\times$ 10 mL). The organic extracts were dried (MgSO_4) and concentrated under reduced pressure. Chromatography (2:1 to 1:1 light petroleum:ether) of the residue gave unreacted lactone **68** (5 mg, 25%) followed by the *title compound* **69** (15 mg, 75%) as a colourless oil, a 58:42 mixture of diastereoisomers (^1H and ^{13}C NMR), $R_f = 0.24$ (1:1 light petroleum:ether), $[\alpha]_D^{28} +27.9$ (c 0.9, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 868.4146. $\text{C}_{40}\text{H}_{75}\text{O}_8\text{NS}_2\text{Si}_3\text{Na}$ requires M , 868.4140); $\nu_{\text{max}}/\text{cm}^{-1}$ 3391, 2953, 2925, 2873, 1472, 1329, 1250, 1150, 1097, 1055, 1009, 856, 832, 761 and 729; δ_{H} (400 MHz, CDCl_3) 0.00 [3.78 H, s, $\text{Si}(\text{CH}_3)_3$], 0.00 [5.22 H, s, $\text{Si}(\text{CH}_3)_3$], 0.07 (3 H, s, SiCH_3), 0.07 (1.26 H, s, SiCH_3), 0.08 (1.74 H, s, SiCH_3), 0.47-0.59 (6 H, m, $3 \times \text{SiCH}_2$), 0.82-0.95 (2 H, m, SiCH_2), 0.88 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.91 (3.78 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 0.92 (5.22 H, t, J 8.1, $3 \times \text{SiCH}_2\text{CH}_3$), 1.11 (3 H, d, J 6.3, 9-H_3), 1.24 (1.26 H, s, $3'\text{-CH}_3$), 1.24 (1.74 H, s, $3'\text{-CH}_3$), 1.26 (3 H, s, $3'\text{-CH}_3'$), 1.55 and 1.67 (each 1 H, m, 6-H), 1.91-2.09 (2 H, m, $1'\text{-H}$, 4-H), 2.35-2.59 (2 H, m, $1'\text{-H}'$, $4\text{-H}'$), 3.45-3.91 (9 H, m, 1-H , 5-H , 7-H , 8-H , $2'\text{-H}$, $\text{OCH}_2\text{CH}_2\text{Si}$, $4'\text{-H}_2$), 3.95 (2 H, br. s, $2 \times \text{OH}$), 4.15 (1 H, m, $1\text{-H}'$), 4.70 (1 H, d, J 6.6, OHCHO), 4.75 (0.58 H, d, J 6.6, OHCHO), 4.75 (0.42 H, d, J 6.6, OHCHO), 5.81 (1 H, t, J 7.8, 2-H), 7.56-7.66 (2 H, m, ArH) and 8.01 and 8.21 (each 1 H, m, ArH); δ_{C} (100 MHz, CDCl_3) -3.3, -3.3, 0.0, 6.9, 7.1, 8.6, 19.4, 19.5, 20.2, 20.3, 25.0, 25.3, 25.9, 26.0, 27.3, 38.4, 39.9, 40.2, 40.6, 41.6, 42.2(2), 59.0, 62.4, 62.5, 66.1, 66.6, 67.3, 67.4, 72.6, 72.7, 79.4, 80.9, 81.8, 82.0, 97.7, 97.8, 123.8, 126.9, 129.1, 129.4, 130.3, 132.0, 138.2, 139.4, 141.0, 154.1 and 169.5; m/z (ES^+) 868.6 ($\text{M}^+ + 23$, 100%), 863.6 ($\text{M}^+ + 18$, 10) and 846.7 ($\text{M}^+ + 1$, 8).

(2R,3R,5S,9RS)-11-Benzothiazol-2-ylsulfonfyl-2-tert-butylidimethylsilyloxy-10,10-dimethyl-9-triethylsilyloxy-7-[(E)-2-tri-isopropylsilyloxyethylidene]-3-(2-trimethylsilylethoxymethoxy)undecan-5-ol (70).

Imidazole (18 mg, 0.26 mmol) and tri-isopropylsilyl chloride (0.026 mL, 0.12 mmol) were added to the diol **69** (50 mg, 0.059 mmol) in DCM (0.5 mL) and the solution was stirred at rt for 12 h. Ether (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with ether (3 × 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (6:1 light petroleum:ether) of the residue afforded the *title compound* **70** (51 mg, 86%), as a colourless oil, a 58:42 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.33 (4:1 light petroleum:ether), [α]_D²⁸ +1.5 (c 0.8, CHCl₃) (Found: M⁺ + Na, 1024.5477. C₄₉H₉₅O₈NS₂Si₄Na requires M, 1024.5474); ν_{max}/cm⁻¹ 3468, 2951, 2868, 1471, 1331, 1250, 1150, 1098, 1057, 1013, 856, 835, 776, 762 and 730; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.06 (1.74 H, s, SiCH₃), 0.06 (1.26 H, s, SiCH₃), 0.07 (3 H, s, SiCH₃), 0.56 (2.52 H, q, J 7.9, 3 × SiCH₂), 0.56 (3.48 H, q, J 7.9, 3 × SiCH₂), 0.85–0.97 (2 H, m, SiCH₂), 0.88 [5.22 H, s, SiC(CH₃)₃], 0.88 [3.78 H, s, SiC(CH₃)₃], 0.91 (9 H, t, J 7.9, 3 × SiCH₂CH₃), 1.02–1.13 [24 H, m, 1-H₃, 3 × SiCH(CH₃)₂], 1.24 and 1.27 (each 1.26 H, s, 10-CH₃), 1.25 and 1.27 (each 1.74 H, s, 10-CH₃), 1.44–1.62 (2 H, m, 4-H₂), 1.91 (0.58 H, dd, J 13.9, 8.5, 8-H), 1.95 (0.42 H, dd, J 14.1, 8.5, 8-H), 2.07 (0.42 H, dd, J 13.6, 4.4, 6-H), 2.19 (0.58 H, dd, J 13.6, 6.0, 6-H), 2.25 (0.58 H, dd, J 13.6, 7.3, 6-H'), 2.35 (0.42 H, dd, J 13.6, 8.2, 6-H'), 2.43 (0.42 H, d, J 14.2, 8-H'), 2.48 (0.58 H, d, J 13.9, 8-H'), 3.49–3.76 (6 H, m, 3-H, 5-OH, 9-H, 11-H, OCH₂CH₂Si), 3.75 (1 H, d, J 14.2, 11-H'), 3.80 (1 H, m, 5-H), 3.86 (0.58 H, pent, J 6, 2-H), 3.90 (0.42 H, pent, J 6, 2-H), 4.18–4.30 (2 H, m, 2'-H₂), 4.69 (0.58 H, d, J 6.8, OHCHO), 4.70 (0.42 H, d, J 6.6, OHCHO), 4.72 (0.42 H, d, J 6.6, OHCHO), 4.73 (0.58 H, d, J 6.6, OHCHO), 5.51 (0.58 H, t, J 6.2, 1'-H), 5.56 (0.42 H, t, J 6.3, 1'-H), 7.58 and 7.63 (each 1 H, t, J 6.7, ArH) and 8.00 and 8.21 (each 1 H, d, J 6.7, ArH); δ_C (125 MHz, CDCl₃) -3.3, 0.0, 7.0, 8.6, 13.4, 19.5, 19.8, 20.0, 24.8, 26.1, 26.2, 27.3(2), 38.9, 39.0, 40.1, 41.9, 42.0, 42.1(2), 61.3, 61.5, 62.3, 66.9, 67.1, 67.5, 68.1, 72.0, 72.2, 80.2, 80.4, 81.4(2), 97.6, 123.8, 126.9, 129.0, 129.3, 131.8, 132.0, 136.7, 136.8, 138.2, 154.1 and 169.5; *m/z* (TOF ES⁺) 1024.7 (M⁺ + 23, 100%), 710.4 (38), 578.3 (78), 466.2 (23), 446 (29) and 398.2 (55).

Prop-2-enyl (3R,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-benzyloxy-3,23,26-tris-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-9-methoxy-19-triethylsilyloxy-21-[(E)-2-tri-isopropylsilyloxyethylidene]-13-[(Z)-2-tri-isopropylsilyloxyethylidene]-25-(2-trimethylsilylethoxymethoxy)-8,8,18,18-tetramethylheptacos-16-enoate (72).

Lithium hexamethyldisilazide (1.0 M in THF, 14 μL, 0.014 mmol) was added dropwise to the sulfone **32** (16 mg, 0.014 mmol) in THF (147 μL) at -78 °C and the yellow solution stirred at -60 °C for 30 min then cooled to -78 °C. The aldehyde **71** (8 mg, 0.010 mmol; for its preparation see experimental for alkene **76**) in THF (98 μL) was added and the solution was stirred for 1 h at -78 °C, allowed to warm to rt, and stirred for 20 min. Ethyl acetate (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with EtOAc (2 × 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (3% Et₂O/light petroleum with 1% Et₃N) afforded the *title compound*

72 as a pale, yellow oil (10 mg, 60%), a 60:40 mixture of epimers (¹H NMR), *R*_f 0.68 (15% EtOAc/light petroleum), [α]_D²⁵ +6.8 (c 1.0, CH₂Cl₂); ν_{max}/cm⁻¹ 2951, 2863, 1742, 1738, 1471, 1463, 1382, 1361, 1259, 1094, 834, 808, 776 and 667; δ_H (400 MHz, C₆D₆) -0.03 to 0.29 (27 H, overlapping s, 9 × SiCH₃), 0.60–1.20 [86 H, m, SiCH₂, 3 × SiCH₂CH₃, 3 × SiC(CH₃)₃, 6 × SiCH(CH₃)₂], 1.23–1.35 (15 H, m, 27-H₃, 2 × 8-CH₃, 2 × 18-CH₃), 1.45 (1 H, m, 6-H_{ax}), 1.70–2.75 (17 H, m, 2-H₂, 4-H₂, 6-H_{eq}, 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24-H₂), 3.22 (0.6 H, s, 9-OCH₃), 3.23 (0.4 H, s, 9-OCH₃), 3.48 (1 H, m, OHCHCH₂Si), 3.68–3.89 (6 H, m, 5-H, 7-H, 11-H, 19-H, 25-H, OHCHCH₂Si), 3.94 (1 H, m, 15-H), 4.20 (1 H, m, 23-H), 4.25 (1 H, d, J 11.9, PhHCH), 4.31–4.59 (9 H, m, 1'-H₂, 3-H, 26-H, PhHCH, 13-CHCH₂, 21-CHCH₂), 4.82 and 4.90 (each 1 H, m, OHCHO), 5.01 (1 H, dq, J 10.4, 1.1, 3'-H), 5.16 (1 H, dq, J 17.2, 1.5, 3'-H'), 5.59–5.76 (3 H, m, 16-H, 13-CH, 21-CH), 5.80 (1 H, ddt, J 17.2, 10.6, 5.6, 2'-H), 6.03 (0.6 H, d, J 15.9, 17-H), 6.11 (0.4 H, d, J 15.9, 17-H), 7.03–7.19 (3 H, m, ArH) and 7.26–7.33 (2 H, m, ArH); *m/z* (ES⁺) 1755.2 (100%) and 1754.2 (M⁺ + 23, 75).

(2R,3R,5S,9RS)-11-(Benzothiazol-2-ylsulfonyl)-2,5-bis-(tert-butylidimethylsilyloxy)-10,10-dimethyl-9-triethylsilyloxy-7-[(E)-2-tri-isopropylsilyloxyethylidene]undecan-3-ol (73).

Potassium carbonate (155 mg, 1.12 mmol), *n*-butanethiol (0.102 mL, 0.95 mmol) and MgBr₂·OEt₂ (243 mg, 0.85 mmol) were added to the SEM-ether **32** (125 mg, 0.112 mmol) in Et₂O (2.5 mL) and the mixture stirred vigorously at rt for 1 h. Ether (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase was extracted with ether (2 × 20 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography (50:1 then 9:1 light petroleum:ethyl acetate) of the residue afforded the *title compound* **73** (106 mg, 96%), as a colourless oil, a 50:50 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.31 (4:1 light petroleum:ethyl acetate), [α]_D²⁴ +4.2 (c 2.1, CHCl₃) (Found: M⁺ + Na, 1008.5555. C₄₉H₉₅O₇NS₂Si₄Na requires M, 1008.5519); ν_{max}/cm⁻¹ 3565, 2946, 2864, 1471, 1463, 1331, 1257, 1151, 1084, 1006, 836, 776 and 729; δ_H (500 MHz, C₆D₆) 0.00, 0.02, 0.03, 0.04, 0.26(3) and 0.28 (each 1.5 H, s, SiCH₃), 0.69–0.77 (6 H, m, 3 × SiCH₂), 0.90, 0.91, 1.02 and 1.05 [each 4.5 H, s, SiC(CH₃)₃], 1.06 (9 H, t, J 7.9, 3 × SiCH₂CH₃), 1.10–1.19 [24 H, m, 3 × SiCH(CH₃)₂, 1-H₃], 1.33(2), 1.35 and 1.44 (each 1.5 H, s, 10-CH₃), 1.55 and 1.77 (1 H, m, 4-H), 1.93 (0.5 H, dd, J 13.9, 9.5, 8-H), 2.10 (0.5 H, dd, J 13.9, 8.8, 8-H), 2.45–2.55 (2.5 H, m, 6-H, 8-H', 3-OH), 2.56 (0.5 H, dd, J 13.6, 6.0, 6-H), 2.60 (0.5 H, dd, J 13.6, 8.8, 6-H'), 2.69 (0.5 H, dd, J 13.2, 6.3, 6-H'), 3.57 (1 H, m, 2-H), 3.68 and 3.73 (each 0.5 H, d, J 14.2, 11-H), 3.77 (1 H, m, 3-H), 3.92 (0.5 H, d, J 14.2, 11-H'), 3.99 (1 H, m, 9-H), 4.07 (0.5 H, d, J 14.2, 11-H'), 4.39 (1 H, m, 5-H), 4.49 (0.5 H, dd, J 12.6, 5.4, 2'-H), 4.54 (1 H, m, 2 × 2'-H), 4.60 (0.5 H, dd, J 12.6, 6.3, 2'-H'), 5.68 (0.5 H, t, J 5.8, 1'-H), 5.73 (0.5 H, t, J 5.8, 1'-H), 6.88 (1 H, m, ArH), 7.01–7.08 (2 H, m, ArH) and 7.98 (1 H, m, ArH); δ_C (100 MHz, CDCl₃) -5.8, -5.7, -5.2, -5.2, -5.1, 4.4, 4.5, 6.2, 11.0, 16.6, 17.0, 18.9, 22.3(2), 23.6, 23.8, 24.8, 24.9, 38.1, 39.0, 39.3, 39.4(2), 39.6(2), 59.4(2), 59.8(2), 67.7, 67.8, 70.9, 71.1, 78.0, 78.3, 121.3, 124.4, 126.5, 126.8, 130.0, 130.4, 132.3, 132.4, 135.7, 151.6 and 167.0(2); *m/z* (ES⁺) 1008 (M⁺ + 23, 100%).

2-[(3*RS*,7*S*,9*R*,10*R*)-7,10-Bis-*tert*-butyldimethylsilyloxy-2,2-dimethyl-3-triethylsilyloxy-5-[(*E*)-2-triisopropylsilyloxyethylidene]-9-trimethylsilyloxyundecan-1-ylsulfonyl]benzothiazole (74).

Triethylamine (0.30 mL, 2.15 mmol) and trimethylsilyl chloride (0.068 mL, 0.537 mmol) were added to the alcohol **73** (106 mg, 0.107 mmol) in DCM (2.14 mL) at 0 °C and the stirred at rt for 3 h. Ethyl acetate (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase was extracted with ethyl acetate (2 × 20 mL). The organic extracts were dried (MgSO₄) and then concentrated under reduced pressure. Chromatography (light petroleum with 1% Et₃N) of the residue afforded the *title compound* **74** (115 mg, 100%), as a colourless oil, a 50:50 mixture of epimers (¹H and ¹³C NMR), *R*_f = 0.45 (4:1 light petroleum:ethyl acetate), [α]_D²⁴ +8.7 (c 2.4, CHCl₃) (Found: M⁺ + Na, 1080.5933. C₅₂H₁₀₃O₇NS₂Si₅Na requires M, 1080.5915); ν_{max}/cm⁻¹ 2956, 2865, 1473, 1464, 1331, 1251, 1151, 1093, 1062, 1006, 837 and 775; δ_H (500 MHz, C₆D₆) -0.02, 0.00, 0.02, 0.04, 0.12, 0.13, 0.14 and 0.15 (each 1.5 H, s, SiCH₃), 0.10 and 0.12 [each 4.5 H, s, Si(CH₃)₃], 0.61 (6 H, q, *J* 7.9, 3 × SiCH₂), 0.88, 0.91 and 0.93(2) [each 4.5 H, s, SiC(CH₃)₃], 0.94 and 0.95 (each 4.5 H, t, *J* 7.9, 3 × SiCH₂CH₃), 1.02-1.10 [22.5 H, m, 3 × SiCH(CH₃)₂, 11'-H₃], 1.12 (1.5 H, d, *J* 6.3, 11'-H₃), 1.22, 1.24, 1.27 and 1.37 (each 1.5 H, s, 2'-CH₃), 1.54-1.82 (2.5 H, m, 8'-H₂, 4'-H), 1.93 (0.5 H, dd, *J* 14.2, 8.5, 4'-H), 2.31 (0.5 H, dd, *J* 12.9, 8.8, 6'-H), 2.35 (1 H, m, 4'-H'), 2.42 (1 H, d, *J* 7.3, 6'-H₂), 2.49 (0.5 H, dd, *J* 12.9, 5.5, 6'-H'), 3.56 and 3.66 (each 0.5 H, d, *J* 14.5, 1'-H), 3.77 (0.5 H, dd, *J* 8.5, 2.5, 3'-H), 3.79-3.98 (3.5 H, m, 1'-H', 3'-H, 9'-H, 10'-H), 4.00 and 4.05 (each 0.5 H, m, 7'-H), 4.37-4.51 (2 H, m, 2''-H₂), 5.52 and 5.58 (each 0.5 H, t, *J* 5.7, 1''-H), 6.81 (1 H, m, ArH), 6.93-7.00 (2 H, m, ArH) and 7.85 (1 H, m, ArH); δ_C (100 MHz, C₆D₆) -5.5(2), -4.8, -4.2, -4.1, 0.0, 0.1, 4.9, 5.0, 6.5, 11.3, 15.6, 16.0, 16.9, 17.2, 17.3(2), 22.4, 22.7, 23.6, 24.0, 25.0, 25.2(2), 36.1, 37.0, 39.1, 39.5, 39.7, 39.8(2), 40.9, 59.7, 59.9, 60.1(2), 68.1, 68.5, 69.8, 70.0, 71.8, 72.0, 77.4, 78.0, 121.3, 124.1, 124.2, 126.2, 126.4, 130.2, 131.2, 132.7, 132.8, 135.8(2), 152.0 and 168.5(2); *m/z* (ES⁺) 1080 (M⁺ + 23, 100%).

Prop-2-enyl (3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-benzyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-25-hydroxy-21-[(*E*)-2-triisopropylsilyloxyethylidene]-13-[(*Z*)-2-triisopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enoate (76).

The sulfur trioxide-pyridine complex (146 mg, 0.912 mmol) was added to the alcohol **49** (190 mg, 0.228 mmol), DMSO (162 μL, 2.28 mmol) and DIPEA (278 μL, 1.60 mmol) in DCM (2.28 mL) at rt and the mixture stirred for 1 h. Saturated aqueous NaHCO₃ (20 mL) and DCM (20 mL) were added and the aqueous phase was extracted with DCM (2 × 20 mL). The organic extracts were washed with brine (20 mL), dried (Na₂SO₄) and concentrated under reduced pressure. The residue was passed through a short silica column (1:5 EtOAc:light petroleum with 1% Et₃N) to afford the aldehyde **71** (190 mg) as a pale, yellow oil, *R*_f 0.50 (with streaking, 1:3 EtOAc:light petroleum); δ_H (400 MHz, C₆D₆) 0.27 (6 H, s, 2 × SiCH₃), 1.11 [9 H, s, SiC(CH₃)₃], 1.17-1.30 [21 H, m, 3 × SiCH(CH₃)₂], 1.32 and 1.40 (each 3 H, s, 8-CH₃), 1.57 (1 H,

q, *J* 12.1, 6-H_{ax}), 1.78-2.04 (6 H, m, 4-H₂, 6-H_{eq}, 10-H, 12-H_{ax}, 14-H_{ax}), 2.30-2.40 (2 H, m, 10-H', 12-H_{eq}), 2.72 (1 H, dd, *J* 15.1, 7.3, 2-H), 2.78 (1 H, dd, *J* 15.1, 4.8, 2-H'), 2.87 (1 H, d, *J* 12.9, 14-H_{eq}), 3.28 (3 H, s, 9-OCH₃), 3.69 (1 H, dd, *J* 11.9, 2.8, 7-H), 3.82-3.91 (2 H, m, 5-H, 11-H), 3.92 (1 H, dd, *J* 11.6, 4.5, 15-H), 4.32-4.45 (3 H, m, PhHCH, 13-CHCH₂), 4.57 (1 H, d, *J* 11.6, PhHCH), 4.60-4.68 (3 H, m, 1'-H₂, 3-H), 5.13 (1 H, dq, *J* 10.4, 1.2, 3'-H), 5.28 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.73 (1 H, t, *J* 6.3, 13-CH), 5.90 (1 H, ddt, *J* 17.2, 10.5, 5.7, 2'-H), 7.22 (1 H, m, ArH), 7.28-7.33 (2 H, m, ArH), 7.44 (2 H, d, *J* 7.3, ArH) and 9.71 (1 H, s, 16-H).

Lithium hexamethyldisilazide (1.0 M in THF, 343 μL, 0.343 mmol) was added dropwise to the sulfone **74** (363 mg, 0.343 mmol) in THF (3.5 mL) at -78 °C and the yellow solution stirred at -60 °C for 30 min. The reaction mixture was then cooled to -78 °C and the aldehyde **71** (190 mg, 0.229 mmol) in THF (2.34 mL) was added. The reaction mixture was stirred for 1 h, allowed to warm to rt and stirred for a further 20 min. Ethyl acetate (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase was extracted with EtOAc (2 × 20 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure to give the alkene **75** containing traces of sulfone **74** (combined mass 390 mg); δ_H (400 MHz, C₆D₆) alkene **75**: 0.00 and 0.04 (each 3 H, s, SiCH₃), 0.07 (6 H, s, 2 × SiCH₃), 0.13 and 0.15 (each 3 H, s, SiCH₃), 0.29-0.32 (9 H, overlapping s, 3 × SiCH₃), 0.75-0.85 (6 H, m, 3 × SiCH₂), 1.02-1.03 [18 H, overlapping s, 2 × SiC(CH₃)₃], 1.08 [9 H, s, SiC(CH₃)₃], 1.11-1.38 [66 H, m, 27-H₃, 2 × 8-CH₃, 2 × 18-CH₃, 3 × SiCH₂CH₃, 6 × SiCH(CH₃)₂], 1.49 (1 H, q, *J* 12.3, 6-H_{ax}), 1.70-2.80 (17 H, m, 2-H₂, 4-H₂, 6-H_{eq}, 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24-H₂), 3.15 (3 H, s, 9-OCH₃), 3.60-3.78 (4 H, m, 5-H, 7-H, 11-H, 25-H), 3.80-3.89 (2 H, m, 15-H, 26-H), 3.94 (1 H, dd, *J* 9.6, 3.9, 19-H), 4.05 (1 H, m, 23-H), 4.17 (1 H, d, *J* 11.6, PhHCH), 4.26-4.53 (8 H, m, 1'-H₂, 3-H, PhHCH, 13-CHCH₂, 21-CHCH₂), 4.93 (1 H, dq, *J* 10.4, 1.3, 3'-H), 5.09 (1 H, dq, *J* 17.2, 1.5, 3'-H'), 5.58 (1 H, dd, *J* 16.0, 5.4, 16-H), 5.58-5.65 (2 H, m, 13-CH, 21-CH), 5.72 (1 H, ddt, *J* 17.2, 10.6, 5.7, 2'-H), 5.96 (0.6 H, d, *J* 16.0, 17-H), 6.05 (0.4 H, d, *J* 16.0, 17-H), 6.99 (1 H, t, *J* 7.3, ArH) and 7.04-7.10 and 7.19-7.25 (each 2 H, m, ArH).

Pyridinium toluene *p*-sulfonate (7 mg, 0.027 mmol) was added to this mixture of alkene **75** and sulfone **74** (390 mg) together with trimethyl orthoformate (594 μL) in DCM/methanol (1:1, 4.18 mL) and the reaction mixture was stirred at rt for 1 h. Dichloromethane (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase was extracted with EtOAc (2 × 20 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (light petroleum to 1:50 EtOAc:light petroleum with 1% Et₃N) of the residue afforded the *title compound* **76** (220 mg, 60% (from the alcohol **49**), as a pale, yellow oil, a 3:2 mixture of epimers (¹H and ¹³C NMR), *R*_f 0.21 (1:15 EtOAc:light petroleum), [α]_D²⁴ +20.4 (c 2.05, CH₂Cl₂); ν_{max}/cm⁻¹ 3561, 2952, 2865, 1741, 1463, 1382, 1359, 1256, 1088, 1005, 882, 836, 776 and 735; δ_H (500 MHz, C₆D₆) -0.01, 0.00, 0.01 and 0.03 (each 1.5 H, s, SiCH₃), 0.14 (6 H, s, 2 × SiCH₃), 0.26 and 0.27 (each 3 H, s, SiCH₃), 0.70-0.79 (6 H, m, 3 × SiCH₂), 0.90, 0.97 and 1.03 [each 9 H, s, SiC(CH₃)₃], 1.05-1.36 [66 H, m, 27-H₃, 2 × 8-CH₃, 2 × 18-CH₃, 3 × SiCH₂CH₃, 6 × SiCH(CH₃)₂], 1.40-1.58 (2 H, m, 6-H_{ax}, 24-H),

1.67-2.74 (17 H, m, 2-H₂, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24-H', OH), 3.22 (1.8 H, s, OCH₃), 3.23 (1.2 H, s, OCH₃), 3.55 (1 H, m, 26-H), 3.67-3.85 (5 H, m, 5-H, 7-H, 11-H, 19-H, 25-H), 3.91 (1 H, m, 15-H), 4.25 (1 H, d, *J* 11.7, PhHCH), 4.31-4.58 (9 H, m, 1'-H₂, 3-H, PhHCH, 23-H, 13-CHCH₂, 21-CHCH₂), 5.01 (1 H, d, *J* 10.4, 0.6, 3'-H), 5.16 (1 H, dd, *J* 17.3, 1.3, 3'-H'), 5.57-5.74 (3 H, m, 16-H, 13-CH, 21-CH), 5.79 (1 H, m, 2'-H), 6.02 (0.6 H, d, *J* 15.8, 17-H), 6.07 (0.4, d, *J* 15.8, 17-H), 7.06 (1 H, m, ArH) and 7.12-7.18 (2 H, m, ArH) and 7.27 (2 H, d, *J* 7.6, ArH); δ_c (100 MHz, C₆D₆) -6.1(2), -5.8, -5.7, -5.5(3), -5.1, 4.7, 4.8, 6.3, 11.0, 11.1, 12.9, 15.6, 16.7, 16.8, 16.9, 17.0, 18.7, 18.8, 19.9, 21.3, 22.4, 22.6, 22.7, 22.9, 23.2, 24.6, 24.7, 24.9(2), 32.4, 34.4, 34.7, 37.8, 38.2, 38.6, 39.1, 39.3, 39.8, 40.0, 40.4(2), 40.5, 40.8, 42.3, 42.6, 42.7, 43.8, 47.0, 58.5, 59.6, 59.7, 63.7, 65.2, 67.3, 67.6, 67.9, 70.3, 70.9(2), 71.1, 71.3, 74.0, 76.8, 77.4, 77.6, 78.2, 103.3, 116.6, 122.8, 122.9, 126.1, 126.2, 127.1, 127.2, 127.3(2), 127.5, 127.6, 127.8, 129.1, 129.4, 129.7, 131.4, 133.8, 134.0, 135.2, 135.3, 136.7, 137.0, 138.5 and 169.5(2); *m/z* (ES⁺) 1625.9 (M⁺ + 23, 100%).

25-(3R,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-Benzoyloxy-3,23,26-tris-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-21-[(E)-2-tri-isopropylsilyloxyethylidene]-13-[(Z)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide (78).

Tetrakis(triphenylphosphine)palladium(0) (16 mg, 10 mol%) was added to the prop-2-enyl ester **76** (220 mg, 0.137 mmol) and morpholine (120 μ L, 1.37 mmol) in THF (3.43 mL) at rt and the mixture stirred for 16 h. An aqueous pH 4.6 acetate buffer (20 mL) and DCM (20 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 20 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure to leave the *seco*-lactone **77**, as a pale yellow oil, a 60:40 mixture of epimers (¹H NMR) with traces of triphenylphosphine derived impurities, *R*_f 0.11 (6% EtOAc/light petroleum); δ_H (400 MHz, C₆D₆) -0.02 to 0.05 (6 H, overlapping s, 2 $\times$ SiCH₃), 0.15 and 0.17 (each 3 H, s, SiCH₃), 0.24-0.30 (6 H, m, 2 $\times$ SiCH₃), 0.70-0.79 (6 H, m, 3 $\times$ SiCH₂), 0.90, 0.98 and 1.03 (each 9 H, s, SiC(CH₃)₃), 1.05-1.35 [66 H, m, 27-H₃, 2 $\times$ 8-CH₃, 2 $\times$ 18-CH₃, 3 $\times$ SiCH₂CH₃, 6 $\times$ SiCH(CH₃)₂], 1.40-1.55 (2 H, m, 6-H_{ax}, 24-H), 1.68-2.82 (17 H, m, 2-H₂, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24'-H, 25-OH), 3.18 (1.2 H, s, 9-OCH₃), 3.20 (1.8 H, s, 9-OCH₃), 3.31 (1 H, m, 19-H), 3.57 (1 H, m, 26-H), 3.71-3.87 (5 H, m, 5-H, 7-H, 11-H, 25-H), 3.98 (1 H, m, 15-H), 4.21 (1 H, d, *J* 11.6, PhHCH), 4.24-4.58 (7 H, m, 3-H, PhHCH, 23-H, 13-CHCH₂, 21-CHCH₂), 5.61-5.76 (3 H, m, 16-H, 13-CH, 21-CH), 6.05 (1 H, m, 17-H), 7.06 (1 H, m, ArH), 7.11-7.18 (2 H, m, ArH) and 7.27 (2 H, d, *J* 7.3, ArH).

Triethylamine in THF (0.1 M, 13.8 mL, 1.376 mmol) was added to this *seco*-lactone **77** in THF (3.45 mL) at 0 °C followed by 2,4,6-trichlorobenzoyl chloride in THF (0.1 M, 6.88 mL, 0.688 mmol). The reaction mixture was stirred at rt for 16 h then diluted with toluene/THF (3:1, 75 mL) and added *via* a syringe-pump to a stirred solution of DMAP (336 mg) in toluene (92 mL) at 40 °C over 12 h. The residual contents of the syringe were rinsed into the reaction flask with toluene (29 mL) and the stirring was continued for 2 h. The reaction mixture was cooled to rt and washed with saturated aqueous NaHCO₃ (2 $\times$ 50 mL)

and brine (100 mL). The organic phase was dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (light petroleum to 1:50 EtOAc:light petroleum) of the residue gave the *title compound* **78** (180 mg, 85%) as a pale yellow oil, a 65:35 mixture of epimers (¹H and ¹³C NMR), *R*_f 0.29 (1:15 EtOAc:light petroleum), $[\alpha]_D^{24}$ 20.2 (c 2.33, CH₂Cl₂); ν_{max}/cm^{-1} 2956, 2864, 1734, 1463, 1381, 1361, 1255, 1088, 1013, 1005, 882, 836, 775 and 736; δ_H (500 MHz, C₆D₆) 0.04, 0.05, 0.09 and 0.10 (each 1.5 H, s, SiCH₃), 0.13 and 0.14 (each 3 H, s, SiCH₃), 0.22, 0.23, 0.25 and 0.26 (each 1.5 H, s, SiCH₃), 0.63 (6 H, m, 3 $\times$ SiCH₂), 0.92 [18 H, s, 2 $\times$ SiC(CH₃)₃], 0.95-1.17 [75 H, m, 27-H₃, 2 $\times$ 8-CH₃, 2 $\times$ 18-CH₃, 3 $\times$ SiCH₂CH₃, SiC(CH₃)₃, 6 $\times$ SiCH(CH₃)₂], 1.36 (1 H, m, 6-H_{ax}), 1.56-2.46 (14 H, m, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H, 20-H₂, 22-H₂, 24-H₂), 2.52 (1 H, dd, *J* 16.1, 7.6, 2-H), 2.60 (1 H, d, *J*, 13.6, 14-H'), 2.78 (1 H, dd, *J* 16.1, 3.2, 2-H'), 3.19 (2.1 H, s, OCH₃), 3.20 (0.9 H, s, OCH₃), 3.64 (1 H, m, 19-H), 3.68-3.80 (4 H, m, 5-H, 7-H, 11-H, 15-H), 3.94 (1 H, m, 23-H), 4.07 (1 H, m, 26-H), 4.14 (1 H, d, *J* 12.0, PhHCH), 4.16-4.50 (6 H, m, 3-H, PhHCH, 13-CHCH₂, 21-CHCH₂), 5.12 (0.3 H, m, 25-H), 5.17 (0.7 H, m, 25-H), 5.47-5.60 (3 H, m, 16-H, 13-CH, 21-CH), 5.75 (0.3 H, d, *J* 15.9, 17-H), 5.92 (0.7 H, d, *J* 16.0, 17-H), 6.99 (1 H, m, ArH), 7.08 (2 H, t *J* 7.6, ArH) and 7.21 (2 H, d, *J* 7.3, ArH); δ_c (100 MHz, C₆D₆) -5.9, -5.8, -5.7, -5.6, -5.5(2), -5.3, -5.2, -5.1, 4.6(2), 4.7, 6.2, 9.8, 11.0, 11.1, 13.0(2), 16.5, 16.6, 16.7, 16.9, 17.0, 17.1, 19.7, 19.8, 21.7, 22.0, 22.8, 24.6, 24.8(2), 24.9, 25.0, 25.1, 26.0, 27.9, 28.8, 29.4, 32.6, 32.8, 33.8, 34.2, 34.6, 34.9, 37.8, 38.5, 39.0, 39.1, 39.2, 39.5, 40.3, 40.5, 41.1, 41.2, 42.0, 42.1, 42.6, 44.6, 44.8, 47.9, 48.0, 58.4, 59.7, 59.8, 65.2, 65.5, 66.6, 67.1(2), 67.2(2), 67.9, 68.1, 70.2, 70.3, 73.5, 73.6(2), 76.1, 76.2, 77.1, 78.3, 80.1, 102.8, 102.9, 123.1, 126.1, 126.2, 127.1(2), 127.3, 127.4, 127.5, 127.7, 128.3, 128.5, 129.9, 132.0, 132.7, 132.9, 133.5, 134.3, 134.9, 135.9, 137.0, 138.5, 169.6 and 169.7; *m/z* (ES⁺) 1566.8 (M⁺ + 23, 8%) and 413.3 (100).

25-(3R,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-Benzoyloxy-3,23,26-tris-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-13,21-bis-[(Z)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide (84).

Pyridinium toluene 4-sulfonate (0.65 mg, 10 mol%) in DCM/methanol [1:1, 394 μ L, taken from PPTS (6.5 mg) in DCM (1.97 mL) and methanol (1.97 mL) and trimethyl orthoformate (56 μ L) were added to the triethylsilyl ether **78** (40 mg, 0.026 mmol) and the solution stirred at rt for 48 h. Dichloromethane (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:50 to 1:15 EtOAc:light petroleum with 1% Et₃N) afforded the *title compound* **84** (20 mg, 54%) as a pale oil, a 50 : 50 mixture of epimers (¹H and ¹³C NMR), *R*_f 0.36 and 0.29 (1:10 EtOAc:light petroleum), $[\alpha]_D^{24}$ 26.7 (c 1.42, CH₂Cl₂); ν_{max}/cm^{-1} 3564, 2957, 2864, 1738, 1658, 1471, 1463, 1382, 1362, 1259, 1091, 882, 835, 806 and 776; δ_H (500 MHz, C₆D₆) 0.09 (3 H, s, SiCH₃), 0.12(2) (each 1.5 H, s, SiCH₃), 0.15-0.18 (9 H, overlapping s, 3 $\times$ SiCH₃), 0.21 and 0.24 (each 1.5 H, s, SiCH₃), 0.91-1.22 [84 H, m, 27-H₃, 2 $\times$ 8-CH₃, 2 $\times$ 18-CH₃, 3 $\times$ SiC(CH₃)₃, 6 $\times$ SiCH(CH₃)₂], 1.41 (1 H, m, 6-H_{ax}), 1.58-2.68 (17 H, m, 2-H, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂,

19-OH, 20-H₂, 22-H₂, 24-H₂), 2.81 (1 H, m, 2-H'), 3.19 and 3.21 (each 1.5 H, s, OCH₃), 3.31 and 3.38 (each 0.5 H, m, 19-H), 3.70-3.85 (4 H, m, 5-H, 7-H, 11-H, 15-H), 4.00 (1 H, m, 23-H), 4.07 and 4.11 (each 0.5 H, m, 26-H), 4.18 (1 H, d, *J* 11.7, PhHCH), 4.25-4.54 (6 H, m, 3-H, PhHCH, 13-CHCH₂, 21-CHCH₂), 5.14 (0.5 H, dd, *J* 9.4, 3.2, 25-H), 5.19 (0.5 H, dd, *J* 9.7, 3.7, 25-H), 5.49 (0.5 H, dd, *J* 15.8, 5.7, 16-H), 5.52 (1 H, m, 13-CH or 21-CH), 5.55 (0.5 H, dd, *J* 15.8, 5.0, 16-H), 5.63 (1 H, m, 13-CH or 21-CH), 5.86 (0.5 H, d, *J* 16.0, 17-H), 5.96 (0.5 H, d, *J* 15.8, 17-H), 7.02 (1 H, m, ArH), 7.11 (2 H, t, *J*, 7.5, ArH) and 7.24 (2 H, d, *J* 7.6, ArH); δ_{C} (100 MHz, C₆D₆) -6.0, -5.9(3), -5.6(2), -5.5, -5.3, -5.2, -5.1, -5.0, 11.0(4), 12.9, 16.5, 16.6, 16.7, 17.0, 19.7, 20.8, 21.3, 21.7, 22.1(2), 24.0, 24.7(2), 24.8(2), 24.9, 28.8, 32.8, 33.0, 34.1, 34.4(2), 34.7, 38.6, 39.1(3), 39.2(2), 39.3, 39.8, 41.1, 42.0, 42.4, 42.7, 44.9, 45.0, 47.9(2), 51.9, 58.3, 58.4, 59.3, 59.4, 64.9, 65.0, 66.7(2), 66.9, 67.0, 68.0(2), 68.3, 70.2, 72.8, 73.3, 73.4, 73.5, 74.7, 76.1, 76.2, 76.8, 77.1, 102.8(2), 123.1(2), 126.0(2), 126.1(2), 127.1, 127.3(2), 128.2, 128.6, 129.4, 129.9, 134.2, 134.4, 134.8, 135.0, 137.1, 137.3, 138.5, 169.7 and 169.9; *m/z* (ES⁺) 1453 (M⁺ + 23, 67%) and 413 (100).

25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-21-[(*E*)-2-tri-isopropylsilyloxyethylidene]-13-[(*Z*)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide (85).

Tetrapropylammonium perruthenate (TPAP) (0.25 mg, 5 mol%) was added to the alcohol **84** (20 mg, 0.014 mmol), *N*-methylmorpholine-*N*-oxide (NMO) (8 mg, 0.07 mmol) and 4 Å molecular sieves (32 mg) in DCM (322 µL). After stirring the mixture for 4 h, additional NMO (8 mg, 0.07 mmol) and TPAP (0.25 mg) were added and the mixture stirred for a further 2 h. Saturated aqueous Na₂S₂O₃ (5 mL) and saturated aqueous NaHCO₃ (5 mL) were added. After stirring for a further 10 min, DCM (10 mL) was added and the aqueous phase was extracted with more DCM (2 × 10 mL). The organic extracts were washed with brine (10 mL), dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (1:20 to 1:10 EtOAc:light petroleum) afforded the *title compound* **85** (10 mg, 50%) as a pale oil, *R*_f 48 (1:10 EtOAc/light petroleum), $[\alpha]_{\text{D}}^{24}$ 12.5 (c 1.60, CH₂Cl₂) (Found: M⁺ + NH₄⁺, 1445.0001. C₇₉H₁₅₀O₁₂NSi₅ requires *M*, 1444.9999; $\nu_{\text{max}}/\text{cm}^{-1}$ 2929, 2863, 1733, 1716, 1470, 1463, 1380, 1361, 1259, 1091, 881, 835, 807 and 776; δ_{H} (400 MHz, C₆D₆) 0.19 (6 H, s, 2 × SiCH₃), 0.26, 0.27, 0.30 and 0.33 (each 3 H, s, SiCH₃), 1.04, 1.05 and 1.09 [each 9 H, s, SiC(CH₃)₃], 1.00-1.38 [57 H, m, 27-H₃, 2 × 8-CH₃, 2 × 18-CH₃ and 6 × SiCH(CH₃)₂], 1.49 (1 H, q, *J* 12.1, 6-H_{ax}), 1.75-2.11 (8 H, m, 4-H₂, 6-H_{eq}, 10-H, 12-H_{ax}, 14-H_{ax}, 24-H₂), 2.15 (1 H, d, *J* 13.1, 12-H_{eq}), 2.26 (1 H, dd, *J* 16.5, 6.6, 10-H'), 2.55-2.70 (3 H, m, 2-H, 14-H_{eq}, 22-H), 2.81 (1 H, dd, *J* 13.5, 4.5, 22-H'), 2.94 (1 H, dd, *J* 15.6, 3.7, 2-H'), 3.25 (2 H, m, 20-H₂), 3.29 (3 H, s, OCH₃), 3.76-3.90 (4 H, m, 5-H, 7-H, 11-H, 15-H), 4.09 (1 H, m, 23-H), 4.23 (1 H, m, 26-H), 4.27 (1 H, d, *J* 11.9, PhHCH), 4.35-4.58 (6 H, m, 3-H, PhHCH, 13-CHCH₂, 21-CHCH₂), 5.29 (1 H, m, 25-H), 5.58-5.65 (3-H, m, 16-H, 13-CH, 21-CH), 6.03 (1 H, dd, *J* 15.9, 1.26, 17-H), 7.11 (1 H, t, *J* 7.3, ArH), 7.21 (2 H, t, *J* 7.6, ArH) and 7.34 (2 H, d, *J* 7.3, ArH); δ_{C} (100 MHz, C₆D₆) -5.9, -5.8, -5.7(2), -5.2(2), 11.0, 11.1, 16.5,

16.9(2), 17.0, 20.0, 22.8, 23.0, 24.8(2), 25.0, 30.1, 32.9, 34.0, 34.3, 39.1, 39.3, 41.1, 42.0, 42.6, 44.1, 44.8, 47.7, 48.9, 58.4, 59.4, 65.5, 66.9, 67.2, 67.3, 70.2, 73.2, 73.6, 75.7, 77.1, 102.9, 123.3, 126.1, 126.2, 127.1, 129.5, 130.1, 131.6, 134.1, 134.7, 138.5, 169.6 and 207.7; *m/z* (ES⁺) 1446 (M⁺ + 18, 100%).

25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-13-[(*Z*)-2-hydroxyethylidene]-21-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide (86).

Tetra-*n*-butylammonium fluoride-acetic acid [1:1, 65 µL, 0.0647 mmol from TBAF (1 M in THF, 1 mL) and glacial AcOH (57 µL)] was added to the bis-tri-isopropylsilyl ether **78** (5 mg, 0.00324 mmol) in THF (158 µL) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (pentane to 1:10 EtOAc:petroleum with 1% Et₃N) afforded the *title compound* **86** as a pale, yellow oil (2 mg, ca. 50%) as a 70:30 mixture of epimers (¹H NMR), *R*_f 0.10 (1:10 EtOAc:light petroleum); δ_{H} (500 MHz, C₆D₆) 0.05, 0.09, 0.12, 0.15, 0.22 and 0.25 (each 2 H, s, SiCH₃), 0.06, 0.08, 0.11, 0.14, 0.20 and 0.24 (each 1 H, s, SiCH₃), 0.59-0.70 (6 H, m, 3 × SiCH₂), 0.91 and 0.92 [each 9 H, s, SiC(CH₃)₃], 0.96-1.03 [18 H, m, 3 × SiCH₂CH₃, SiC(CH₃)₃], 1.03-1.26 [36 H, m, 2 × 8-CH₃, 2 × 18-CH₃, 27-H₃, 3 × SiCH(CH₃)₂], 1.36 (1 H, m, 6-H_{ax}), 1.59-2.57 (17 H, m, 2-H, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂, 20-H₂, 22-H₂, 24-H₂, OH), 2.71 (0.3 H, m, 2-H'), 2.75 (0.7 H, dd, *J* 16.2, 2.9, 2-H'), 3.19 (3 H, s, 9-OCH₃), 3.62-3.68 (2 H, m, 15-H, 19-H), 3.68-3.81 (3 H, m, 5-H, 7-H, 11-H), 3.82-3.98 (3 H, m, 23-H, 13- or 21-CHCH₂), 4.08 (1 H, m, 26-H), 4.16 (1 H, d, *J* 11.7, PhHCH), 4.33-4.51 (4 H, m, 3-H, PhHCH, 21- or 13-CHCH₂), 5.15 (1 H, m, 25-H), 5.28 (1 H, m, 13- or 21-CH), 5.47 (0.7 H, dd, *J* 15.9, 4.9, 16-H), 5.53 (0.3 H, dd, *J* 15.9, 4.9, 16-H), 5.58 (1 H, m, 21- or 13-CH), 5.70 (0.3 H, d, *J* 16.0, 17-H), 5.87 (0.7 H, d, *J* 16.0, 17-H), 6.99 (1 H, m, ArH), 7.08 (2 H, t, *J* 7.6, ArH) and 7.21 (2 H, d, *J* 7.6, ArH).

25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-triethylsilyloxy-13-[(*Z*)-methoxycarbonylmethylidene]-21-[(*E*)-2-tri-isopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide (87).

Methanol in THF [0.73 mL, from methanol (20 µL) in THF (1 mL)], sodium cyanide (3.6 mg, 0.0036 mmol) and manganese(IV) dioxide (94 mg, 0.054 mmol) were added to the alcohol **86** (2 mg, 0.0014 mmol) and the reaction mixture heated under reflux for 16 h then filtered through a pad of Celite and partitioned between DCM (10 mL) and saturated aqueous NaHCO₃ (10 mL). The aqueous phase was extracted with DCM (2 × 10 mL) and the organic extracts dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (pentane to 1:10 EtOAc:petroleum with 1% Et₃N) afforded the *title compound* **87** as a pale, yellow oil (1 mg, 49%), a 70:30 mixture of epimers (¹H NMR), *R*_f 0.38 (1:5 EtOAc:light petroleum); $\nu_{\text{max}}/\text{cm}^{-1}$ 2925, 2862, 1735, 1462, 1381, 1360, 1258, 1091, 882, 836, 776 and 736; δ_{H}

(500 MHz, C_6D_6) 0.04, 0.08, 0.12(2), 0.24 and 0.25 (each 2 H, s, $SiCH_3$), 0.05, 0.07, 0.09, 0.11, 0.13 and 0.14 (each 1 H, s, $SiCH_3$), 0.57–0.67 (6 H, m, $3 \times SiCH_2$), 0.88–1.26 [72 H, m, 27- H_3 , $2 \times 8-CH_3$, $2 \times 18-CH_3$, $3 \times SiC(CH_3)_3$, $3 \times SiCH_2CH_3$, $3 \times SiCH(CH_3)_2$], 1.33–2.45 (16 H, m, 4- H_2 , 6- H_2 , 10- H_2 , 12- H_2 , 14- H_2 , 20- H_2 , 22- H_2 , 24- H_2), 2.49 (1 H, dd, J 16.4, 7.6, 2-H), 2.63 (0.35 H, m, 2-H'), 2.72 (0.65 H, dd, J 16.4, 3.5, 2-H'), 3.08 (1.05 H, s, 9-OCH₃), 3.13 (1.95 H, s, 9-OCH₃), 3.32 (3 H, s, CO₂CH₃), 3.58–4.48 (12 H, m, 3-H, 5-H, 7-H, PhCH₂, 11-H, 15-H, 19-H, 23-H, 26-H, 21-CHCH₂), 5.14 (0.35 H, m, 25-H), 5.18 (0.65 H, m, 25-H), 5.47 (0.65 H, dd, J 16.1, 4.5, 16-H), 5.56 (1 H, t, J 6.0, 21-CH) 5.60 (0.35 H, m, 16-H), 5.63 (1 H, br. s, 13-CH), 5.77 (0.35 H, d, J 16.0, 17-H), 5.87 (0.65 H, d, J 16.0, 17-H), 6.99 (1 H, m, ArH), 7.08 (2 H, t, J 7.6, ArH) and 7.18–7.23 (2 H, m, ArH); m/z (TOF ES⁺) 1439.6 (M^+ + 23, 100%).

25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-13-[(*Z*)-2-hydroxyethylidene]-21-[(*E*)-2-triisopropylsilyloxyethylidene]-9-methoxy-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide (89) and 25-(3*R*,5*S*,7*S*,9*S*,11*S*,15*R*,19*RS*,23*S*,25*R*,26*R*,16*E*)-7-Benzoyloxy-3,23,26-tris-*tert*-butyldimethylsilyloxy-5,9-epoxy-11,15-epoxy-21-[(*E*)-2-hydroxyethylidene]-13-[(*Z*)-2-hydroxyethylidene]-9-methoxy-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide (90).

Tetra-*n*-butylammonium fluoride-acetic acid [1:1, 112 μ L, 0.112 mmol, from TBAF (1 M in THF, 1 mL) and glacial AcOH (57 μ L)] was added to the bis-tri-isopropylsilyl ether **85** (8 mg, 0.0056 mmol) in THF (273 μ L) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (pentane to 1:10 EtOAc:pentane with 1% Et₃N) afforded the *title compound* **89** as a pale, yellow oil (2 mg, 28%), R_f 0.04 (1:10 EtOAc:light petroleum); δ_H (500 MHz, C_6D_6) 0.05(2), 0.10, 0.13, 0.17 and 0.19 (each 3 H, s, $SiCH_3$), 0.89, 0.91 and 0.95 [each 9 H, s, $3 \times SiC(CH_3)_3$], 0.98–1.24 [36 H, m, 27- H_3 , $2 \times 8-CH_3$, $2 \times 18-CH_3$, $3 \times SiCH(CH_3)_2$], 1.36 (1 H, q, J 12.0, 6- H_{ax}), 1.55–1.99 (10 H, m, 4- H_2 , 6- H' , 10-H, 12- H_2 , 14-H, 24- H_2 , OH), 2.13 (1 H, dd, J 16.7, 6.9, 10-H'), 2.38 (1 H, d, J 14.8, 14-H'), 2.44 (1 H, dd, J 13.8, 10.5, 22-H), 2.50 (1 H, dd, J 16.5, 8.0, 2-H), 2.66 (1 H, dd, J 14.0, 4.9, 22-H'), 2.77 (1 H, dd, J 16.3, 3.4, 2-H'), 3.11 (2 H, s, 20- H_2), 3.16 (3 H, s, 9-OCH₃), 3.61 (1 H, m, 15-H), 3.64–3.72 (2 H, m, 5-H, 11-H), 3.75 (1 H, dd, J 12.2, 4.9, 7-H), 3.81–3.89 (2 H, m, 13- or 21-CHCH₂), 3.93 (1 H, m, 23-H), 4.09 (1 H, m, 26-H), 4.14 and 4.34 (each 1 H, d, J 12.0, PhHCH), 4.29–4.44 (3 H, m, 3-H, 21- or 13-CHCH₂), 5.15 (1 H, m, 25-H), 5.26 (1 H, m, 13- or 21-CH), 5.45 (1 H, dd, J 16.1, 5.0, 16-H), 5.49 (1 H, m, 21- or 13-CH), 5.84 (1 H, d, J 16.7, 17-H), 6.98 (1 H, t, J 7.3, ArH), 7.07 (2 H, t, J 7.6, ArH) and 7.20 (2 H, d, J 7.5, ArH); m/z (TOF ES⁺) 1294 (M^+ + 23, 80%) and 355 (100). Further elution (1:5 to 1:3 EtOAc:pentane with 1% Et₃N) afforded *title compound* **90** as a pale, yellow oil (2 mg, 32%), R_f 0.15 (2:5 EtOAc:light petroleum); ν_{max}/cm^{-1} 3452, 2961, 2925, 2855, 1735, 1711, 1470, 1361, 1260, 1091, 1018 and 799; δ_H (500 MHz, C_6D_6) 0.04 and 0.05 (each 3 H, s, $SiCH_3$), 0.09 (6 H, s, $2 \times SiCH_3$), 0.11 and 0.12 (each 3 H, s, $SiCH_3$), 0.88, 0.90 and

0.92 [each 9 H, s, $3 \times SiC(CH_3)_3$], 1.03, 1.07, 1.08 and 1.13 (each 3 H, s, 8- or 18- CH_3), 1.15 (3 H, d, J 6.3, 27- H_3), 1.33 (1 H, q, J 12.2, 6- H_{ax}), 1.60 (1 H, t, J 12.4, 14- H_{ax}), 1.61–1.79 (6 H, m, 4-H, 6-H', 10-H, 12- H_{ax} , 24-H, OH), 1.85–1.96 (2 H, m, 24-H', OH), 1.98 (1 H, d, J 13.2, 12-H'), 2.09 (1 H, dd, J 16.4, 6.3, 10-H'), 2.24 (1 H, dd, J 13.5, 8.3, 22-H), 2.35 (1 H, d, J 13.4, 14-H'), 2.49 (1 H, dd, J 16.1, 7.9, 2-H), 2.63 (1 H, dd, J 13.6, 5.4, 22-H'), 2.84 (1 H, dd, J 16.1, 3.5, 2-H'), 3.09 and 3.12 (each 1 H, d, J 17.3, 20-H), 3.18 (3 H, s, 9-OCH₃), 3.58 (1 H, m, 15-H), 3.61–3.70 (2 H, m, 5-H, 11-H), 3.71 (1 H, dd, J 11.7, 4.6, 7-H), 3.78–3.89 (2 H, m, 13- or 21-CHCH₂), 3.91–4.01 (3 H, m, 23-H, 21- or 13-CHCH₂), 4.04 (1 H, m, 26-H), 4.14 and 4.34 (each 1 H, d, J 11.7, PhHCH), 4.39 (1 H, m, 3-H), 5.02 (1 H, m, 25-H), 5.25 and 5.32 (each 1 H, t, J 6.8, 13- or 21-CH), 5.41 (1 H, dd, J 15.7, 5.0, 16-H), 5.81 (1 H, d, J 15.7, 17-H), 6.98 (1 H, t, J 7.4, ArH), 7.07 (2 H, t, J 7.5, ArH) and 7.20 (2 H, d, J 7.5, ArH); m/z (TOF ES⁺) 1138 (M^+ + 23, 100%).

(*E*)-(5*S*,7*R*,8*R*)-3-[(2*RS*)-4-(Benzothiazol-2-yl)sulfonyl-3,3-dimethyl-2-triethylsilyloxybutyl]-1,5,8-tris-*tert*-butyldimethylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (91).

tert-Butyldimethylsilyl trifluoromethanesulfonate (81 μ L, 0.354 mmol) was added to the diol **69** (100 mg, 0.118 mmol) and 2,6-lutidine (137 μ L, 1.18 mmol) in DCM (945 μ L) at $-78^\circ C$ and the solution stirred at $-78^\circ C$ for 2 h. Ether (20 mL) and saturated aqueous NaHCO₃ (20 mL) were added and the aqueous phase was extracted with ether (3 $\times$ 20 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:10 ether:light petroleum) afforded the *title compound* **91** as a colourless oil (120 mg, 96%), R_f 0.48 (1:10 ether:light petroleum), $[\alpha]_D^{25} -9.9$ (c 2.01, CHCl₃); ν_{max}/cm^{-1} 2929, 2956, 2882, 2857, 1472, 1463, 1331, 1251, 1151, 1101, 1058, 835, 775 and 729. δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02–0.06 (18 H, overlapping s, $6 \times SiCH_3$), 0.54 (2.8 H, q, J 7.8, $3 \times SiCH_2$), 0.56 (3.2 H, q, J 7.6, $3 \times SiCH_2$), 0.84–0.87 [27 H, overlapping s, $3 \times SiC(CH_3)_3$], 0.80–0.98 (2 H, m, $SiCH_2$), 0.98 (4.8 H, t, J 8.1, $3 \times SiCH_2CH_3$), 0.90 (4.2 H, t, J 8.1, $3 \times SiCH_2CH_3$), 1.01 (1.4 H, d, J 6.3, 9- H_3), 1.02 (1.6 H, d, J 6.3, 9- H_3), 1.22 and 1.26 (each 1.4 H, s, 3'-CH₃), 1.24 and 1.29 (each 1.6 H, s, 3'-CH₃), 1.41 and 1.54 (each 1 H, m, 6-H), 1.82 (0.53 H, dd, J 13.9, 9.3, 1'-H), 1.88 (0.47 H, dd, J 14.1, 8.6, 1'-H), 2.08 (0.47 H, dd, J 13.1, 8.1, 4-H), 2.14–2.36 (2.53 H, m, 1'-H', 4-H', 4-H₂), 3.42 (1 H, m, OHCHCH₂Si), 3.52 (1 H, m, 7-H), 3.53 (0.53 H, d, J 14.4, 4'-H), 3.56 (0.47 H, d, J 14.4, 4'-H), 3.60 (0.53, dd, J 9.3, 1.8, 2'-H), 3.64 (0.47, dd, J 8.6, 2.8, 2'-H), 3.70 (1 H, m, OHCHCH₂Si), 3.75 (0.53 H, d, J 14.4, 4'-H'), 3.75 (0.47 H, d, J 14.4, 4'-H'), 3.84 (1 H, m, 5-H), 4.05 (1 H, m, 8-H), 4.13–4.25 (2 H, m, 1-H₂), 4.63–4.71 (2 H, m, OCH₂O), 5.38 (0.53 H, t, J 6.1, 2-H), 5.40 (0.47 H, t, J 5.8, 2-H), 7.54–7.64 (2 H, m, ArH) and 8.00 and 8.19 (each 1 H, m, ArH); δ_C (100 MHz, CDCl₃) -3.9 , -3.4 , $-3.3(2)$, -2.9 , -2.3 , -2.2 , 0.0, 6.8, 6.9, 8.6, 18.4, 18.5, 19.4(2), 19.5, 19.7, 24.6, 24.7, 26.2, 26.3, 27.3, 27.4, 36.4, 37.1, 40.8, 41.6, 41.8, 42.0(2), 42.6, 61.6, 61.7, 62.1, 62.2, 66.6, 69.8, 70.1, 70.2(2), 78.6, 80.3, 80.9, 81.5, 81.7, 97.6(2), 123.8, 126.9, 128.9, 129.3, 132.0, 132.7, 134.9, 135.0, 138.2, 154.1 and 169.5(2); m/z (ES⁺) 1097 (M^+ + 23, 100%).

(6*RS*,10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*E*)-2-*tert*-butyldimethylsilyloxyethylidene]-6-triethylsilyloxy-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-ene (92).

Lithium hexamethyldisilazide (1.0 M in THF, 133 μ L, 0.134 mmol) was added to the sulfone **91** (120 mg, 0.112 mmol) in THF (5.7 mL) at -78°C and the yellow solution was stirred at -60°C for 30 min then cooled to -78°C . 2-Methylpropanal (42 μ L, 0.465 mmol) in THF (1.14 mL) was added and the solution was stirred for 1 h at -78°C and at rt for 20 min. Ether (20 mL) and saturated aqueous NaHCO_3 (20 mL) were added and the aqueous phase was extracted with Et_2O (2×20 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:20 ether:light petroleum) afforded the *title compound* **92** as a colourless oil (54 mg, 52%), R_f 0.24 (1:20 ether:light petroleum), $[\alpha]_{\text{D}}^{25} -14.8$ (c 2.69, CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ 2956, 2928, 2883, 2858, 1472, 1463, 1382, 1361, 1258, 1099, 1058, 938, 835, 808, 774 and 737; δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.03–0.07 (18 H, overlapping s, $6 \times \text{SiCH}_3$), 0.54 (2.82 H, q, J 7.9, $3 \times \text{SiCH}_2$), 0.55 (3.18 H, q, J 7.6, $3 \times \text{SiCH}_2$), 0.80–0.98 [50 H, m, 1- H_3 or 2- CH_3 , $2 \times 5\text{-CH}_3$, 14- H_3 , $3 \times \text{SiCH}_2\text{CH}_3$, $3 \times \text{SiC}(\text{CH}_3)_3$, SiCH_2], 1.02 (3 H, d, J 6.3, 1- H_3 or 2- CH_3), 1.42 and 1.51 (each 1 H, m, 11-H), 1.83 (1 H, m, 7-H), 2.04 (0.47 H, dd, J 12.9, 8.5, 9-H), 2.15–2.30 (2.5 H, m, 2-H, 9-H', 9-H₂), 3.42 (1 H, m, OHCHCH_2Si), 3.47–3.57 (2 H, m, 6-H, 12-H), 3.70 (1 H, m, OHCHCH_2Si), 3.81 (1 H, m, 10-H), 4.05 (1 H, m, 13-H), 4.15–4.24 (2 H, m, 2'- H_2), 4.64–4.70 (2 H, m, OCH_2O), 5.25 (0.47 H, dd, J 15.6, 7.0, 3-H), 5.27 (0.53 H, dd, J 15.6, 6.8, 3-H), 5.36 (1 H, m, 1'-H), 5.38 (0.53 H, d, J 15.8, 4-H) and 5.39 (0.47 H, d, J 15.8, 4-H); δ_{C} (100 MHz, CDCl_3) -3.9 , -3.4 , $-3.3(2)$, -3.0 , -2.9 , -2.3 , -2.2 , 0.0, 2.5, 6.9, 7.0, 8.7, 18.5, 18.6, 19.5(2), 19.8, 24.2, 24.3, 24.4, 24.5, 26.5, 26.7, 27.3(2), 27.4(2), 32.7, 32.8, 36.5, 37.0, 41.3, 42.5, 42.6, 42.7, 42.9, 61.8, 61.9, 66.5, 69.8, 70.1, 70.3, 70.4, 78.6, 79.8, 80.8, 81.7(2), 97.6, 97.7, 131.0, 131.6, 135.8(2), 135.9 and 136.2(2); m/z (ES^+) 954 ($\text{M}^+ + 23$, 100%).

(6*RS*,10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*Z*)-2-hydroxyethylidene]-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-en-6-ol (93).

Pyridinium toluene 4-sulfonate (1.5 mg, 0.027 mmol) was added to the alkene **92** (54 mg) in DCM/methanol (1:1, 884 μ L) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and saturated aqueous NaHCO_3 (10 mL) were added and the aqueous phase was extracted with EtOAc (2×10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (1:5 to 1:1 ether:light petroleum) afforded the *title compound* **93** as a pale oil (20 mg, 50%), R_f 0.33 (3:2 ether:light petroleum), $[\alpha]_{\text{D}}^{25} -9.6$ (c 2.03, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 725.5007. $\text{C}_{37}\text{H}_{78}\text{O}_6\text{NaSi}_3$ requires M , 725.4999); $\nu_{\text{max}}/\text{cm}^{-1}$ 3349, 2954, 2925, 2858, 1470, 1464, 1377, 1359, 1274, 1251, 1101, 1056, 1033, 835, 770 and 750; δ_{H} (500 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.04 and 0.05 (each 6 H, s, $2 \times \text{SiCH}_3$), 0.87 [18 H, s, $2 \times \text{SiC}(\text{CH}_3)_3$], 0.85–1.05 [2 H, m, SiCH_2], 0.97 (6 H, d, J 6.3, $2 \times \text{CHCH}_3$), 1.00 (6 H, s, $2 \times 5\text{-CH}_3$), 1.03 and 1.04 (each 1.5 H, d, J 5.5, 14- H_3), 1.42–1.92 (4 H, m, 7-H, 11- H_2 , OH), 2.15 (1 H, m, 9-H), 2.21–2.38 (3.45 H, m, 2-H,

7-H', 9-H', OH), 2.51 (0.55 H, m, 9-H'), 3.36 (1 H, m, 6-H), 3.42–3.57 (2 H, m, 12-H, OHCHCH_2Si), 3.68 (1 H, m, OHCHCH_2Si), 3.89 (1 H, m, 10-H), 4.01–4.09 (2 H, m, 2'-H, 13-H), 4.20 (1 H, m, 2'-H'), 4.65–4.71 (2 H, m, OCH_2O), 5.32–5.42 (2 H, m, 3-H, 4-H), 5.59 (0.45 H, t, J 6.9, 1'-H) and 5.63 (0.55 H, t, J 6.9, 1'-H); δ_{C} (100 MHz, CDCl_3) $-3.3(2)$, -3.0 , -2.9 , $-2.4(2)$, 0.0, 18.6, 19.5(2), 19.6, 24.3(2), 24.5, 24.7, 25.0, 25.1, 27.4(2), 32.8(2), 37.2, 37.3, 40.5, 40.7, 41.0, 41.6, 41.7, 60.3, 60.4, 66.8, 66.9, 70.3, 70.4(2), 70.8, 77.2, 77.7, 78.7, 81.6, 81.9, 97.2, 97.3, 130.2, 130.9, 135.0, 135.1, 137.7, 137.9, 140.1 and 140.2; m/z (ES^+) 726 ($\text{M}^+ + 23$, 100%) and 721 ($\text{M}^+ + 18$, 20).

Methyl (5*RS*,2*Z*,7*E*)-3-[(2*S*,4*R*,5*R*)-2,5-bis-*tert*-butyldimethylsilyloxy-4-(2-trimethylsilylethoxymethoxy)hexyl]-5-hydroxy-6,6,9-trimethyldeca-2,7-dienoate (95).

Manganese(IV) dioxide (74 mg, 0.854 mmol) was added to the diol **93** (20 mg, 0.0284 mmol) in DCM (568 μ L) and the mixture was stirred at rt for 4 h then filtered through Celite. The filter cake was washed with DCM (10 mL) and the filtrate was concentrated under reduced pressure to give the corresponding aldehyde as a pale oil, R_f 0.56 (1:1 ether:light petroleum); δ_{H} (500 MHz, CDCl_3) 5.3 (1 H, d, J 16.0, 7-H), 5.42 (1 H, dd, J 16.0, 6.3, 8-H), 6.0 (1 H, d, J 6.5, 2-H), and 9.99 (1 H, d, J 6.5, 1-H).

Sodium chlorite (30 mg, 0.342 mmol) and $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ (88 mg, 0.568 mmol) in H_2O (554 μ L) were added to this aldehyde and 2-methyl-2-butene (2 M in THF, 568 μ L, 1.14 mmol) in *t*-butanol (426 μ L) and the mixture stirred at rt for 2 h. Brine (10 mL) and EtOAc (10 mL) were added and the aqueous phase extracted with EtOAc (2×10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the acid **94** as a pale oil, R_f 0.81 (1:1 ether:light petroleum).

A solution of the acid **94** in methanol (966 μ L) and toluene (484 μ L) was cooled to 0°C and (trimethylsilyl)diazomethane (2 M in hexanes, 42 μ L, 0.0854 mmol) was added dropwise. After stirring for 1 h at 0°C , acetic acid (2–3 drops) was added and the reaction mixture was partitioned between saturated aqueous NaHCO_3 (10 mL) and DCM (10 mL). The aqueous phase was extracted with DCM (2×10 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:20 ether:light petroleum) afforded the *title compound* **95** as a pale oil (16 mg, 77%), R_f 0.12 (1:10 ether:light petroleum), $[\alpha]_{\text{D}}^{25} -39.5$ (c 1.60, CHCl_3) (Found: $\text{M}^+ + \text{Na}$, 753.4930. $\text{C}_{38}\text{H}_{78}\text{O}_7\text{NaSi}_3$ requires M , 753.4948); $\nu_{\text{max}}/\text{cm}^{-1}$ 3487, 2955, 2928, 2856, 1719, 1641, 1663, 1470, 1463, 1432, 1378, 1359, 1250, 1101, 1056, 832 and 775; δ_{H} (400 MHz, CDCl_3) 0.00 [9 H, s, $\text{Si}(\text{CH}_3)_3$], 0.01–0.07 (12 H, overlapping s, $4 \times \text{SiCH}_3$), 0.81–0.99 [2 H, m, SiCH_2], 0.88 [18 H, s, $2 \times \text{SiC}(\text{CH}_3)_3$], 0.97 (6 H, d, J 6.3, 10- H_3 , 9- CH_3), 1.00 (6 H, s, $2 \times 6\text{-CH}_3$), 1.01–1.06 (3 H, m, 6'- H_3), 1.41 and 1.49 (each 0.5 H, m, 3'-H), 1.60–1.82 (2 H, m, OH, 3'-H'), 1.96 (0.55 H, dd, J 13.6, 10.6, 4-H), 2.06 (0.45 H, dd, J 13.9, 10.3, 4-H), 2.27 (1 H, m, 9-H), 2.33–2.43 (1 H, m, 1'-H and 4-H'), 2.50 (0.55 H, d, J 13.6, 4-H'), 2.84 (0.45, dd, J 12.4, 7.3, 1'-H), 2.97 (0.45, dd, J 12.4, 7.3, 1'-H'), 3.30 (0.55 H, dd, J 12.4, 6.1, 1'-H'), 3.40 (1 H, m, 5-H), 3.44 (1 H, m, OHCHCH_2Si), 3.56 (1 H, m, 4'-H), 3.65 (3 H, s,

CO₂CH₃), 3.69 (1 H, m, OHCHCH₂Si), 3.99–4.10 (2 H, m, 2'-H, 5'-H), 4.67–4.74 (1.54 H, m, OCH₂O, OHCHO), 4.78 (0.46 H, d, *J* 7.1, OHCHO), 5.33 (0.46 H, d, *J* 16.1, 7-H), 5.34 (0.54 H, d, *J* 15.9, 7-H), 5.34 (0.54 H, dd, *J* 15.9, 6.3, 8-H), 5.41 (0.46 H, dd, *J* 15.9, 6.3, 8-H) and 5.77 (1 H, s, 2-H). δ_c (100 MHz, CDCl₃) –3.3(2), –3.1, –3.0, –2.6, –2.3, 0.0, 18.5, 18.7, 19.4, 19.5(2), 19.6, 24.2, 24.3, 24.5, 24.8, 25.2, 27.4(3), 27.5, 32.8(2), 37.7, 38.0, 41.4, 41.8, 42.0, 42.5, 43.3, 43.8, 52.3, 66.6, 70.6, 71.0, 72.3, 77.4, 81.7, 82.0, 97.5, 97.7, 120.0, 120.3, 134.7(2), 138.4, 160.6, 161.4 and 167.7(2); *m/z* (ES⁺) 753 (M⁺ + 23, 100%) and 749 (M⁺ + 18, 93).

Methyl (2*E*,7*E*)-3-[(2*S*,4*R*,5*R*)-2,5-bis-*tert*-butyldimethylsilyloxy-4-(2-trimethylsilylethoxymethoxy)hexyl]-6,6,9-trimethyl-5-oxodeca-2,7-dienoate (96).

A solution of the Dess-Martin periodinane (50 mg, 0.118 mmol) and pyridine (95 μ L, 1.18 mmol) in DCM (5.21 mL) was stirred for 5 min. An aliquot (4.79 mL, 0.109 mmol) was added to the alcohol **95** (16 mg, 21.9 μ mol) and the solution stirred for 2 h at rt. Dichloromethane (10 mL), saturated aqueous NaHCO₃ (5 mL) and saturated aqueous Na₂S₂O₃ (5 mL) were added and the aqueous phase was extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of the residue (light petroleum to 1:30 ether:light petroleum) afforded the *title compound* **96** as a pale oil (13 mg, 81%), *R_f* 0.27 (1:10 ether:light petroleum), $[\alpha]_D^{25}$ –53.1 (c 1.40, CHCl₃) (Found: M⁺ + Na, 751.4801. C₃₈H₇₆O₇NaSi₃ requires M, 751.4792); $\nu_{\max}/\text{cm}^{-1}$ 2956, 2930, 2858, 1721, 1645, 1464, 1378, 1251, 1142, 1101, 1049, 937, 835 and 775; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.01 (3 H, s, SiCH₃), 0.04 (9 H, s, 3 $\times$ SiCH₃), 0.85 (1 H, m, HCHSi), 0.86 and 0.87 [each 9 H, s, SiC(CH₃)₃], 0.94 (1 H, m, HCHSi), 0.98 (6 H, d, *J* 6.9, 10-H₃, 9-CH₃), 1.03 (3 H, d, *J* 6.3, 6'-H₃), 1.18 and 1.19 (each 3 H, s, 6-CH₃), 1.37 (1 H, ddd, *J* 14.8, 9.5, 5.4, 3'-H), 1.74 (1 H, ddd, *J* 14.2, 6.9, 1.0, 3'-H'), 2.29 (1 H, oct, *J* 6.6, 9-H), 2.56 (1 H, dd, *J* 12.6, 7.3, 1'-H), 3.05 (1 H, dd, *J* 12.6, 5.7, 1'-H'), 3.26 (1 H, d, *J* 16.4, 4-H), 3.45 (1 H, m, OHCHCH₂Si), 3.48 (1 H, d, *J* 16.0, 4-H'), 3.54 (1 H, ddd, *J* 9.5, 4.1, 1.3, 4'-H), 3.65 (3 H, s, CO₂CH₃), 3.69 (1 H, ddd, *J* 11.4, 9.8, 5.4, OHCHCH₂Si), 3.99–4.08 (2 H, m, 2'-H, 5'-H), 4.69 and 4.75 (each 1 H, d, *J* 6.9, OHCHO), 5.40 (1 H, d, *J* 15.8, 7-H), 5.51 (1 H, dd, *J* 15.8, 6.6, 8-H) and 5.62 (1 H, s, 2-H); δ_c (100 MHz, CDCl₃) –3.3, –3.0, –2.6, 0.0, 18.5, 19.4, 19.6, 23.9, 25.4, 25.5, 27.4, 27.5, 32.7, 38.1, 42.1, 49.5, 51.7, 52.3, 66.6, 70.6, 72.2, 81.9, 97.7, 121.6, 132.2, 139.7, 156.9, 167.4 and 211.0; *m/z* (ES⁺) 751 (M⁺ + 23, 100%) and 746 (M⁺ + 18, 9).

(6*S*)-6-[(2*R*,3*R*)-3-Hydroxy-2-(2-trimethylsilylethoxymethoxy)butyl]-4-[(*EZ*)-methoxycarbonylmethylene]-2-[(*E*)-2,5-dimethylhex-3-en-2-yl]-5,6-dihydropyran (97).

Pyridine (64 μ L, 0.796 mmol) was added to the ketoester **96** (13 mg, 0.0179 mmol) in THF (284 μ L) and HF-pyridine (70:30, 23 μ L, 0.893 mmol) was added at 0 °C. The mixture was stirred at rt for 72 h and saturated aqueous NaHCO₃ (10 mL) and EtOAc (10 mL) were added. The aqueous phase was extracted with EtOAc (2 $\times$ 10 mL) and the organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography of

the residue (pentane to 1:20 EtOAc:pentane with 1% Et₃N) afforded the lactone **98** as a colourless oil (0.5 mg, 6%), *R_f* 0.72 (1:5 ether:light petroleum); $\nu_{\max}/\text{cm}^{-1}$ 3445, 2959, 2926, 1713, 1464, 1379, 1260, 1147, 1098, 1029, 978, 938, 861, 836 and 800; δ_H (500 MHz, CDCl₃) 0.00 [9 H, s, Si(CH₃)₃], 0.92 and 0.93 (each 3 H, d, *J* 6.3, 6'-CH₃ or 7'-H₃), 0.98 (2 H, m, SiCH₂), 1.05 and 1.06 (each 3 H, s, 3'-CH₃), 1.15 (3 H, d, *J* 6.3, 4''-H₃), 1.41 (1 H, m, 1''-H), 1.74 (1 H, ddd, *J* 14.2, 10.1, 2.2, 1''-H'), 1.85–1.94 (2 H, m, 5-H₂), 2.14 (1 H, oct, *J* 6.7, 6'-H), 2.80 and 2.86 (each 1 H, d, *J* 16.4, 1'-H), 3.39 (1 H, d, *J* 2.9, 3''-OH), 3.51 (1 H, dt, *J* 9.8, 6.9, OHCHCH₂Si), 3.68–3.75 (2 H, m, 3''-H, OHCHCH₂Si), 3.78 (1 H, m, 2''-H), 4.62 and 4.68 (each 1 H, d, *J* 6.9, OHCHO), 4.68 (1 H, m, 6-H), 5.25 (1 H, dd, *J* 15.8, 0.6, 4'-H), 5.37 (1 H, dd, *J* 15.8, 6.9, 5'-H) and 5.79 (1 H, s, 3-H); *m/z* (ES⁺) 491 (M⁺ + 23, 100%) and 486 (M⁺ + 18, 16). Further elution (1:20 to 1:10 EtOAc:pentane with 1% Et₃N) afforded the *title compound* **97** as a colourless oil (7 mg, 93%), (*E*):(*Z*) = 44:56 (¹H NMR), *R_f* 0.35 (1:5 ether:light petroleum), $[\alpha]_D^{25}$ 28.5 (c 0.70, CHCl₃) (Found: M⁺ + Na, 505.2955. C₂₆H₄₆O₆NaSi requires M, 505.2956); $\nu_{\max}/\text{cm}^{-1}$ 3462, 2960, 2926, 1708, 1609, 1434, 1376, 1317, 1261, 1213, 1153, 1095, 1056, 1023, 861, 836 and 801; δ_H (400 MHz, CDCl₃) 0.00 [9 H, s, 3 $\times$ Si(CH₃)₃], 0.91–0.99 (2 H, m, CH₂Si), 0.95–1.00 (6 H, m, 5'-CH₃, 6'-H₃), 1.14 and 1.15 (each 1.5 H, d, *J* 6.3, 4''-H₃), 1.17 and 1.21 (each 3 H, s, 1'-H₃, 2'-CH₃), 1.56 (0.5 H, ddd, *J* 14.4, 10.6, 2.0, 1''-H), 1.62 (0.5 H, ddd, *J* 14.6, 10.3, 2.0, 1''-H), 1.81 and 1.85 (each 0.5 H, m, 1''-H'), 2.20–2.50 (2.5 H, 5-H, 5-H', 5'-H), 3.50 (0.5 H, m, 5-H'), 3.50–3.58 (2 H, m, 2''-H, OHCHCH₂Si), 3.64 (1 H, m, 3''-H), 3.65 and 3.68 (each 1.5 H, s, CO₂CH₃), 3.77 (1 H, m, OHCHCH₂Si), 3.68 (1 H, br. d, *J* 6.6, OH), 4.07 and 4.18 (each 0.5 H, m, 6-H), 4.68(2), 4.79 and 4.80 (each 0.5 H, d, *J* 7.0, OHCHO), 5.20 (0.5 H, s, 3-H), 5.35–5.47 (2 H, m, 3'-H, 4'-H), 5.36 and 5.43 (each 0.5 H, s, 4-CH) and 6.79 (0.5 H, s, 3-H); δ_c (100 MHz, CDCl₃) 0.0, 19.6, 20.3, 24.1, 27.2, 27.4(2), 31.2, 32.6, 33.0, 38.1, 38.4, 38.6, 42.5, 42.6, 52.2, 67.6, 67.7, 71.6, 74.3, 74.4, 85.6, 98.1, 98.4, 102.1, 109.2, 109.6, 134.5, 134.6, 136.7, 136.8, 149.8, 151.8, 169.3, 171.3 and 171.8; *m/z* (ES⁺) 505 (M⁺ + 23, 100%).

(10*S*,12*R*,13*R*,3*E*)-10,13-Bis-*tert*-butyldimethylsilyloxy-8-[(*Z*)-(2-*tert*-butyldimethylsilyloxyethylidene)]-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)tetradec-3-en-6-one (100).

Imidazole (4 mg, 0.0626 mmol) and *tert*-butyldimethylsilyl chloride (5 mg, 0.0312 mmol) were added to the diol **93** (20 mg, 0.0284 mmol) in DCM (284 μ L) and the solution stirred at rt for 16 h. Dichloromethane (10 mL) and water (10 mL) were added and the aqueous phase extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue through a short plug of silica (1:10 ether:pentane) gave the alcohol **99** as a pale oil (20 mg, 87%); δ_H (400 MHz, C₆D₆) 0.00 [9 H, s, Si(CH₃)₃], 0.02–0.07 (18 H, m, 6 $\times$ SiCH₃), 0.80–0.98 [29 H, m, CH₂Si, 3 $\times$ SiC(CH₃)₃], 0.96 (6 H, d, *J* 6.8, 1-H₃, 2-CH₃), 0.98–1.01 (6 H, overlapping s, 2 $\times$ 5-CH₃), 1.02 and 1.02 (each 1.5 H, d, *J* 6.1, 14-H₃), 1.43 and 1.54 (each 1 H, m, 11-H), 1.73 (0.5 H, d, *J* 2.8, 6-OH), 1.79 (0.5 H, dd, *J* 13.9, 10.9, 7-H), 1.85 (0.5 H, d, *J* 3.3, 6-OH), 1.87 (0.5 H, dd, *J* 13.9, 10.9, 7-H), 2.10–2.40 (4 H, m, 2-H, 7-H', 9-H₂), 3.34 (1 H, dd, *J* 10.6, 2.0, 6-H), 3.44 (1 H, m,

OHCHCH₂Si), 3.52 (1 H, m, 12-H), 3.69 (1 H, m, OHCHCH₂Si), 3.85 (1 H, m, 10-H), 4.04 (1 H, m, 13-H), 4.19 (1 H, dd, *J* 12.9, 5.6, 8-CHCH), 4.24 (1 H, m, 8-CHCH), 4.65–4.71, m, OCH₂O), 5.32–5.41 (2 H, m, 3-H, 4-H) and 5.44 (1 H, t, *J* 6.1, 8-CH); *m/z* (ES⁺) 816 (M⁺, 100%).

The Dess-Martin periodinane (56 mg, 0.132 mmol) was added to the alcohol **99** (20 mg, 0.024 mmol) and NaHCO₃ (48 mg, 5.71 mmol) in DCM (4.8 mL) and the reaction mixture stirred for 2 h at rt. Dichloromethane (10 mL) and a mixture of saturated aqueous NaHCO₃ (5 mL) and saturated aqueous Na₂S₂O₃ (5 mL) were added and the aqueous phase extracted with DCM (2 × 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure to give a pale, yellow oil. Chromatography of the residue (light petroleum to 1:30 ether:light petroleum) afforded the *title compound 100* as a pale oil (18 mg, 90%), *R_f* 0.17 (1:20 EtOAc:light petroleum); δ_H (400 MHz, C₆D₆) 0.00 [9 H, s, Si(CH₃)₃], 0.11(2), 0.14, 0.18, 0.25 and 0.27 (each 3 H, s, SiCH₃), 0.92 (1 H, m, HCHSi), 0.94 (6 H, d, *J* 6.8, 1-H₃, 2-CH₃), 0.99, 1.00 and 1.04 [each 9 H, s, SiC(CH₃)₃], 1.16 and 1.17 (each 3 H, s, 5-CH₃), 1.23 (1 H, m, HCHSi), 1.28 (3 H, d, *J* 6.3, 14-H₃), 1.78 (1 H, ddd, *J* 13.6, 10.1, 3.0, 11-H), 1.92 (1 H, ddd, *J* 14.1, 8.8, 1.3, 11-H'), 2.18 (1 H, m, 2-H), 2.61 (1 H, dd, *J* 13.6, 8.1, 9-H), 2.73 (1 H, dd, *J* 13.6, 5.6, 9-H'), 3.23 and 3.28 (each 1 H, d, *J* 16.5, 7-H), 3.51 (1 H, dt, *J* 9.8, 6.3, OHCHCH₂Si), 3.78–3.91 (2 H, m, 12-H, OHCHCH₂Si), 4.24 (1 H, m, 10-H), 4.29–4.37 (2 H, m, 13-H, 8-CHCH), 4.40 (1 H, dd, *J* 12.9, 6.3, 8-CHCH), 4.81 and 4.89 (each 1 H, d, *J* 6.8, OHCHO), 5.39–5.47 (2 H, m, 3-H, 4-H) and 5.58 (1 H, t, *J* 6.1, 8-CH); δ_C (100 MHz, C₆D₆) –3.6, –3.2, –2.9, –2.2, 0.0, 2.7, 15.6, 18.8, 19.6, 19.7(2), 19.8, 23.9, 24.0, 25.7, 27.5(2), 27.6, 32.9, 37.5, 41.4, 47.2, 51.7, 61.8, 66.9, 70.5, 70.8, 82.1, 98.0, 129.5, 133.3, 134.1, 138.7 and 210.8; *m/z* (ES⁺) 839 (M⁺ + 23, 15%).

(10S,12R,13R,3E,7E)- and (10S,12R,13R,3E,7Z)-8-Ethenyl-10,13-dihydroxy-2,5,5-trimethyl-12-(2-trimethylsilylethoxymethoxy)-tetradeca-3,7-dien-6-one (101) and (102).

Tetra-*n*-butylammonium fluoride (1 M in THF, 18 μL, 0.018 mmol) was added to the ketone **100** (5 mg, 0.0061 mmol) in THF (515 μL) and the mixture was stirred at rt for 16 h. Ethyl acetate (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase extracted with EtOAc (2 × 10 mL). The organic extracts were washed with brine, dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (light petroleum to 1:10 EtOAc:light petroleum with 1% Et₃N) afforded the (7E)-isomer of the *title compound 101* as a colourless oil (1 mg, 37%), *R_f* 0.43 (1:3 EtOAc:light petroleum) (Found: M⁺ + Na, 477.3017. C₂₅H₄₆O₅NaSi requires M, 477.3007); ν_{max}/cm^{–1} 3444, 2956, 2920, 2855, 1716, 1608, 1463, 1379, 1260, 1096, 1055, 1029, 860, 836 and 802; δ_H (400 MHz, CDCl₃) –0.05 [9 H, s, Si(CH₃)₃], 0.86–0.97 (2 H, m, CH₂Si), 0.93 (6 H, d, *J* 6.8, 1-H₃, 2-CH₃), 1.04 and 1.06 (each 3 H, s, 5-CH₃), 1.09 (3 H, d, *J* 6.3, 14-H₃), 1.51 (1 H, m, 11-H), 1.56 (1 H, ddd, *J* 7.3, 4.0, 1.5, 11-H'), 2.06 (1 H, dt, *J* 16.7, 2.8, 9-H), 2.24 (1 H, m, 2-H), 2.33 (1 H, d, *J* 17.1, 9-H'), 3.44–3.62 (3 H, m, 12-H, 13-H, OHCHCH₂Si), 3.69 (1 H, m, OHCHCH₂Si), 4.44 (1 H, m, 10-H), 4.70 and 4.76 (each 1 H, d, *J* 6.8, OHCHO), 4.94 (1 H, d, *J* 10.6, 2'-H), 5.05 (1 H, d, *J* 17.4, 2'-H'), 5.44 (1 H, dd, *J* 16.1, 7.1, 3-H), 5.57 (1 H, s, 7-H), 5.57 (1 H,

d, *J* 16.0, 0.8, 4-H) and 6.30 (1 H, dd, *J* 17.5, 10.7, 1'-H); *m/z* (ES⁺) 477 (M⁺ + 23, 100%). Further elution (1:10 to 1:5 EtOAc:light petroleum with 1% Et₃N) afforded the (7Z)-isomer of the *title compound 102* as a colourless oil (1 mg, 37%), *R_f* 0.27 (1:3 EtOAc:light petroleum) (Found: M⁺ + Na, 477.2986. C₂₅H₄₆O₅NaSi requires M, 477.3007); ν_{max}/cm^{–1} 3400, 2960, 2916, 2848, 1681, 1571, 1462, 1378, 1260, 1096, 1055, 1021, 860, 835 and 799; δ_H (400 MHz, CDCl₃) –0.06 [9 H, s, Si(CH₃)₃], 0.72–0.94 (2 H, m, CH₂Si), 0.91 (6 H, d, *J* 6.6, 1-H₃, 2-CH₃), 1.08 (3 H, d, *J* 6.3, 14-H₃), 1.13 and 1.14 (each 3 H, s, 5-CH₃), 1.45–1.61 (2 H, m, 11-H₂), 2.22 (1 H, oct, *J* 6.6, 2-H), 2.33 (1 H, dd, *J* 13.6, 8.3, 9-H), 2.46 (1 H, dd, *J* 13.4, 4.3, 9-H'), 2.69 and 3.02 (each 1 H, br. s, OH), 3.49 (1 H, ddd, *J* 9.6, 6.6, 3.5, OHCHCH₂Si), 3.54–3.64 (3 H, m, 12-H, 13-H, OHCHCH₂Si), 3.87 (1 H, m, 10-H), 4.68 and 4.73 (each 1 H, d, *J* 6.9, OHCHO), 5.37 (1 H, d, *J* 15.7, 4-H), 5.37 (1 H, m, 2'-H), 5.44 (1 H, dd, *J* 15.7, 6.1, 3-H), 5.53 (1 H, d, *J* 17.7, 2'-H'), 6.23 (1 H, s, 7-H) and 7.49 (1 H, ddd, *J* 17.7, 11.1, 0.8, 1'-H); *m/z* (ES⁺) 477 (M⁺ + 23, 100%).

25-(3R,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-Benzoyloxy-3,23,26-tris-tert-butyltrimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-13,21-bis-[(Z)-2-hydroxyethylidene]-9-methoxy-8,8,18,18-tetramethylheptacos-16-enolide (103).

Tetra-*n*-butylammonium fluoride and acetic acid in THF [280 μL, 0.28 mmol; from TBAF in THF (1 M, 1 mL) and AcOH (57 μL)] was added to the bis-tri-isopropylsilyl ether **84** (20 mg, 0.014 mmol) in THF (0.68 mL) and the solution stirred at rt for 40 h. Dichloromethane (10 mL) and saturated aqueous NaHCO₃ (10 mL) were added and the aqueous phase was extracted with DCM (2 × 10 mL). The organic extracts were dried (Na₂SO₄) and concentrated under reduced pressure. Chromatography (pentane to 2:3 EtOAc:pentane with 1% Et₃N) of the residue afforded the *title compound 103* (8 mg, 53%) as a pale oil, a 55 : 45 mixture of epimers, *R_f* 0.24 and 0.17 (1:1 EtOAc:light petroleum), [α]_D²⁴ 33 (c 1.7, CH₂Cl₂) (Found: M⁺ + NH₄⁺, 1134.7533. C₆₁H₁₁₂NO₁₂Si₃ requires M, 1134.7487); ν_{max}/cm^{–1} 3401, 2955, 2929, 2856, 1737, 1732, 1471, 1463, 1380, 1361, 1258, 1091, 1005, 836, 810 and 776; δ_H (400 MHz, C₆D₆) 0.00–0.25 (18 H, overlapping s, 6 × SiCH₃), 0.87–1.28 [42 H, m, 27-H₃, 2 × 8-CH₃, 2 × 18-CH₃, 3 × SiC(CH₃)₃], 1.35 (1 H, m, 6-H_{ax}), 1.59–2.56 (17 H, m, 2-H, 4-H₂, 6-H', 10-H₂, 12-H₂, 14-H₂, 19-OH, 20-H₂, 22-H₂, 24-H₂), 2.80 (1 H, m, 2-H'), 3.17 (1.35 H, s, 9-OCH₃), 3.19 (1.65 H, s, 9-OCH₃), 3.24 (1 H, m, 19-H), 3.61–4.11 (10 H, m, 5-H, 7-H, 11-H, 15-H, 23-H, 26-H, 13-CHCH₂, 21-CHCH₂), 4.16 and 4.35 (each 0.45 H, d, *J* 11.7, PhHCH), 4.17 and 4.36 (each 0.55 H, d, *J* 11.7, PhHCH), 4.47 (0.55 H, m, 3-H), 4.53 (0.45 H, m, 3-H), 4.97 (0.55 H, m, 25-H), 5.10 (0.45 H, m, 25-H), 5.29 (1 H, t, *J* 6.7, 13- or 21-CH), 5.33–5.52 (2 H, m, 16-H, 13- or 21-CH), 5.80 (0.45 H, d, *J* 16.0, 17-H), 5.88 (0.55 H, d, *J* 16.0, 17-H), 7.00 (1 H, m, ArH), 7.08 (2 H, m, ArH) and 7.21 (2 H, m, ArH); *m/z* (TOF ES⁺) 1135 (M⁺ + 18, 100%).

25-(3R,5S,7S,9S,11S,15R,19RS,23S,25R,26R,16E)-7-Benzoyloxy-3,23,26-tris-tert-butyltrimethylsilyloxy-5,9-epoxy-11,15-epoxy-19-hydroxy-9-methoxy-13,21-bis-[(Z)-methoxycarbonylmethylidene]-8,8,18,18-tetramethylheptacos-16-enolide (104).

Manganese(IV) oxide (233 mg, 2.68 mmol) was added to the alcohol **103** (5 mg, 0.0045 mmol) in DCM (894 μ L) and the reaction mixture was stirred at r.t. for 1 h then filtered through a pad of Celite. The filter cake was washed with DCM (10 mL) and the filtrate was concentrated under reduced pressure to give the 13,21-bis-formylmethylidene lactone as a pale yellow oil, R_f 0.43 and 0.29 (1:4 EtOAc:light petroleum). Sodium chlorite (4.9 mg, 0.054 mmol) and $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ (14 mg, 0.090 mmol) in H_2O (72 μ L) were added to this bis-aldehyde and 2-methyl-2-butene (2 M in THF, 90 μ L, 0.180 mmol) in *t*-butanol (135 μ L) at r.t. After 1 h, the reaction mixture was partitioned between brine (10 mL) and EtOAc (10 mL) and the aqueous phase was extracted with EtOAc (2 $\times$ 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to leave the bis-acid as a pale oil, R_f 0.13 (1:4 EtOAc:light petroleum). A solution of this bis-acid in methanol (148 μ L) and toluene (74 μ L) was cooled to 0 $^\circ\text{C}$ and (trimethylsilyl)diazomethane (2 M in hexanes, 6.5 μ L, 0.0131 mmol) was added dropwise. After stirring for 1 h at 0 $^\circ\text{C}$, the reaction mixture was partitioned between saturated aqueous NaHCO_3 (10 mL) and DCM (10 mL). The aqueous phase was extracted with DCM (2 $\times$ 10 mL) and the organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue (pentane to 1:15 EtOAc:pentane with 1% Et_3N) afforded the *title compound* **104** (2 mg, 40%) as a pale yellow oil, a 70 : 30 mixture of epimers (^1H NMR), R_f 0.38 (1:4 EtOAc:light petroleum), $[\alpha]_{\text{D}}^{24}$ 31 (c 0.26, CH_2Cl_2); $\nu_{\text{max}}/\text{cm}^{-1}$ 3523, 2953, 2928, 2855, 1719, 1653, 1647, 1472, 1462, 1437, 1378, 1361, 1257, 1173, 1150, 1091, 836, 809 and 776; δ_{H} (500 MHz, C_6D_6) 0.17(2), 0.23, 0.26, 0.32 and 0.35 (each 2 H, s, SiCH_3), 0.18, 0.21, 0.24, 0.27, 0.31 and 0.35 (each 1 H, s, SiCH_3), 1.03, 1.04 and 1.09 [each 9 H, s, $\text{Si}(\text{CH}_3)_3$], 1.22–1.30 (15 H, m, 27- H_3 , 2 $\times$ 8- CH_3 , 2 $\times$ 18- CH_3), 1.48 (1 H, m, 6- H_{ax}), 1.65–2.40 (15 H, m, 4- H_2 , 6- H' , 10- H_2 , 12- H_2 , 14- H , 19-OH, 20- H_2 , 22- H_2 , 24- H_2), 2.56 (0.7 H, dd, J 16.4, 7.1, 2-H), 2.62 (0.3 H, dd, J 16.7, 7.8, 2-H), 2.79 (0.7 H, dd, J 16.4, 3.8, 2- H'), 2.88 (0.3 H, dd, J 16.7, 3.5, 2- H'), 3.07 (1 H, dd, J 12.3, 6.0, 14- H'), 3.23 (1 H, m, 19-H), 3.24 (2.1 H, s, 9-OCH₃), 3.29 (0.9 H, s, 9-OCH₃), 3.42–3.45 (6 H, overlapping s, 2 $\times$ CO₂CH₃), 3.58 (1 H, m), 3.71–3.90 (3 H, m), 4.15 (1 H, m, 26-H), 4.23–4.39 (2 H, m, 23-H, PhHCH), 4.46–4.59 (2 H, m, 3-H, PhHCH), 5.31 (0.7 H, m, 25-H), 5.36 (0.3 H, m, 25-H), 5.51 (1 H, dd, J 15.8, 5.5, 16-H), 5.77 (1 H, m, 13-CH or 21-CH), 5.81 (0.3 H, d, J 15.4, 17-H), 5.90 (0.7 H, d, J 15.9, 17-H), 5.95 (1 H, m, 13-CH or 21-CH), 7.12 (1 H, m, ArH), 7.21 (2 H, m, ArH) and 7.35 (2 H, m, ArH); δ_{C} (100 MHz, C_6D_6) –5.9, –5.7, –5.5, –5.2, –5.1, 12.9, 14.2, 16.5, 17.0, 17.2, 18.2, 19.4, 19.7, 21.0, 21.3, 21.7, 22.7, 24.8, 25.0, 26.6, 27.6, 28.2, 28.4(2), 28.6, 28.8, 30.9(2), 32.6, 32.7, 33.0, 34.9, 35.6, 39.2, 39.4, 40.1(2), 40.2, 40.4, 40.6, 41.5, 41.9, 42.4, 44.7, 47.8, 49.2, 64.5, 65.1, 66.8, 67.4, 68.8, 70.1, 73.2(2), 73.6, 75.3, 76.4, 76.6, 76.8, 77.0, 102.7, 113.5, 118.3, 136.8, 138.5, 156.3, 157.6, 164.9, 165.1 and 169.5; m/z (ES^+) 1196 ($\text{M}^+ + 23$, 18 %) and 343 ($\text{M}^+ + 39$, 100).

25-(3R,5S,7S,9S,11S,15R,19R,23S,25R,26R,16E)-7-Benzyl-oxo-3,23,26-tris-tert-butylidimethylsilyloxy-5,9-epoxy-11,15-epoxy-9-methoxy-21-[(E)-methoxycarbonylmethylidene]-13-[(Z)-

methoxycarbonylmethylidene]-8,8,18,18-tetramethyl-19-oxoheptacos-16-enolide (105).

A solution of the Dess-Martin periodinane (10 mg, 23.6 μ mol) and pyridine (19.2 μ L, 0.236 mmol) in DCM (1.04 mL) was stirred for 5 min. An aliquot (373 μ L, 8.5 μ mol) was added to alcohol **104** (2 mg, 1.70 μ mol). After stirring for 2 h at r.t., the reaction mixture was partitioned between DCM (10 mL) and a mixture of saturated aqueous NaHCO_3 (5 mL) and saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). After separation of the organic layer, the aqueous phase was extracted with DCM (2 $\times$ 10 mL). The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the *title compound* **105** (ca. 1.5 mg) as a pale oil that was azeotroped with toluene and used immediately (decomposed on attempted chromatography using 1:4 EtOAc:pentane with 1% Et_3N), R_f 0.60 (1:4 EtOAc:light petroleum) (Found: $\text{M}^+ + \text{Na}$, 1193.6759. $\text{C}_{63}\text{H}_{106}\text{O}_{14}\text{Si}_3\text{Na}$ requires M , 1193.6783; $\nu_{\text{max}}/\text{cm}^{-1}$ 2959, 2927, 2853, 1723, 1651, 1470, 1460, 1432, 1377, 1359, 1259, 1093, 1018 and 799; δ_{H} (400 MHz, C_6D_6) 0.12–0.25 (18 H, overlapping s, 6 $\times$ SiCH_3), 0.97, 0.98 and 1.00 [each 9 H, s, $\text{Si}(\text{CH}_3)_3$], 1.09–1.30 (15 H, m, 27- H_3 , 2 $\times$ 8- CH_3 , 2 $\times$ 18- CH_3), 1.40 (1 H, m, 6- H_{ax}), 1.60–2.25 (10 H, m, 4- H_2 , 6- H' , 10- H_2 , 12- H_2 , 22- H , 24- H_2), 2.60 (1 H, dd, J 16.1, 7.5, 2-H), 2.81–2.91 (2 H, m, 2-H, 14- H_{ax}), 3.15 (1-H, d, J 17.2, 20-H), 3.24 (3 H, s, 9-OCH₃), 3.31 and 3.38 (each 3 H, s, CO₂CH₃), 3.38 (1 H, d, J 17.2, 20-H'), 3.67–3.81 (5 H, m, 5-H, 7-H, 11-H, 15-H, 22-H'), 4.14 (1 H, m, 26-H), 4.18–4.30 (3 H, m, 14- H_{eq} , 23-H, PhHCH), 4.42 (1 H, d, J 11.9, PhHCH), 4.47 (1 H, m, 3-H), 5.24 (1 H, m, 25-H), 5.49 (1 H, dd, J 15.9, 4.8, 16-H), 5.72 and 5.78 (each 1 H, s, 13-CH or 21-CH), 5.86 (1 H, dd, J 15.7, 1.1, 17-H), 7.06 (1 H, m, ArH) and 7.16 and 7.29 (each 2 H, m, ArH); m/z (TOF ES^+) 1194.8 ($\text{M}^+ + 23$, 31%), 1188.8 ($\text{M}^+ + 18$, 80) and 610.2 (100).

25-(3R,5S,7S,9S,11S,15R,19R,23S,25R,26R,16E)-7-Benzyl-oxo-5,9-epoxy-11,15-epoxy-19,23-epoxy-3,9,19,26-tetrahydroxy-21-[(E)-methoxycarbonylmethylidene]-13-[(Z)-methoxycarbonylmethylidene]-8,8,18,18-tetramethylheptacos-16-enolide (106).

Pyridine (50 μ L, 0.618 mmol) was added to the keto bis-ester **105** (ca. 1.5 mg) in THF (376 μ L) and the mixture cooled to 0 $^\circ\text{C}$. HF-pyridine (70:30, 18 μ L, 0.693 mmol) was added and the mixture stirred at r.t. After 24 h, the mixture was cooled to 0 $^\circ\text{C}$ and pyridine (40 μ L, 0.497 mmol) was added followed by aqueous hydrogen fluoride (48 % in H_2O , 18 μ L, 0.497 mmol). The mixture was stirred for 24 h before partitioning between saturated aqueous NaHCO_3 (10 mL) and EtOAc (10 mL). After separation of the phases, the aqueous phase was extracted with EtOAc (2 $\times$ 10 mL), and the organic extracts were dried (Na_2SO_4) then concentrated under reduced pressure. Chromatography on silica (neutralised with aqueous potassium bicarbonate and oven dried; 1:5 to 1:1 EtOAc:pentane) afforded the *title compound* **106** (ca. 0.5 mg; 50% from **104**), as a white solid, R_f 0.73 (4:5 EtOAc:light petroleum) (Found: $\text{M}^+ + \text{Na}$, 837.4030. $\text{C}_{44}\text{H}_{62}\text{O}_{14}\text{Na}$ requires M , 837.4032; $\nu_{\text{max}}/\text{cm}^{-1}$ 3459, 3354, 2929, 2853, 1716, 1652, 1436, 1381, 1362, 1279, 1261, 1246, 1230, 1153, 1076, 858, 801, 736 and 700; δ_{H} (500 MHz, C_6D_6) see Table; δ_{C} (100 MHz, C_6D_6)³³ see Table; m/z (ES^+) 837 ($\text{M}^+ + 23$, 100%) and 833 ($\text{M}^+ + 18$, 25).

Table 1 NMR data for the 7-*des*-O-pivaloyl-7-O-benzylbryostatin 10 (**106**) in benzene-*d*₆.

Position	¹ H (500 MHz)	¹³ C (100 MHz)
1	-	172.91 ¹
2a	2.18 (1 H, dd, <i>J</i> 12.0, 1.6)	42.70
2b	2.43 (1 H, t, <i>J</i> 12.0)	-
3	4.10 (1 H, br. t, <i>J</i> 11.9)	68.85
3-OH	4.47 (1 H, d, <i>J</i> 12.3)	-
4a	0.99 (1 H, m)	40.52
4b	1.64 (1 H, m)	-
5	3.79 (1 H, m)	66.47
6 _{ax}	1.18 (1 H, q, <i>J</i> 12.5)	33.69
6 _{eq}	1.33 (1 H, m)	-
7	3.53 (1 H, dd, <i>J</i> 11.5, 4.5)	78.11
8	-	42.78
9	-	102.30
9-OH	2.14 (1 H, s)	-
10a	1.42 (1 H, d, <i>J</i> 15.1)	42.97
10b	2.10 (1 H, dd, <i>J</i> 15.1, 7.3)	-
11	3.76 (1 H, m)	72.09
12 _{eq}	1.62 (1 H, m)	44.69
12 _{ax}	1.88 (1 H, br. t, <i>J</i> 12.4)	-
13	-	157.06
14 _{ax}	2.05 (1 H, br. t, <i>J</i> 12.6)	37.65
14 _{eq}	4.21 (1 H, d, <i>J</i> 12.9)	-
15	4.55 (1 H, br. t, <i>J</i> 9.9)	80.09
16	5.63 (1 H, dd, <i>J</i> 15.9, 8.4)	131.23
17	6.24 (1 H, d, <i>J</i> 15.8)	139.11
18	-	45.39
19	-	101.97
19-OH	5.44 (1 H, s)	-
20	2.21 (2 H, br. s)	40.76
21	-	157.91
22 _{ax}	1.73 (1 H, m)	36.66
22 _{eq}	4.39 (1 H, m)	-
23	4.33 (1 H, br. t, <i>J</i> 11.5)	65.47
24a	1.55 (1 H, ddd, <i>J</i> 14.5, 11.0, 2.5)	36.56
24b	1.73 (1 H, m)	-
25	5.23 (1 H, ddd, <i>J</i> 11.8, 5.7, 2.5)	74.25
26	3.66 (1 H, m)	70.50
26-OH	1.77 (1 H, br. s)	-
27	1.00 (3 H, d, <i>J</i> 6.6)	20.02
28/29	0.99 (3 H, s)	17.12
29/28	1.10 (3 H, s)	24.92
30	5.76 (1 H, s)	115.31
31/35	-	166.75
32/33	1.09 (3 H, s)	20.81
33/32	1.11 (3 H, s)	21.88
34	5.90 (1 H, s)	116.73
35/31	-	167.19
36/37	3.32 (3 H, s)	51.05

37/36	3.36 (3 H, s)	50.76
1'a	4.17 (1 H, d, <i>J</i> 11.7)	71.70
1'b	4.38 (1 H, d, <i>J</i> 11.7)	-
2'	-	139.94
3'	7.30 (2 H, d, <i>J</i> 7.6)	127.87
4'	7.20 (2 H, t, <i>J</i> 7.6)	128.00
5'	7.12 (1 H, t, <i>J</i> 7.1)	128.91

¹HMBC correlation with 2b-H **Figure 7** The numbering system used in **Table 1** for the synthetic 20-deoxybryostatin **106**.^{13c}

Acknowledgements

We thank the EPSRC for a research grant (for A. T. L. L.) and studentships (to S. H. and A. P. G.).

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