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ARTICLE

Synthetic approaches to the C11-C27 fragments of bryostatins

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The modified Julia reaction and acyl carbanion chemistry, especially reactions of 2-lithiated dithianes, have been investigated for the synthesis of intermediates that are the synthetic equivalents of the C11-C27 fragments of bryostatins. The modified Julia reaction using 2-benzothiazolylsulfones was found to be more useful for the formation of the C16-C17 double-bond than the classical Julia reaction using phenylsulfones, and bulky sulfones gave very good (*E*)-stereoselectivity. The alkylation of a dithiane monoxide that corresponded to a C19-acyl carbanion using (*E*)-1-bromobut-2-ene was efficient but the use of a more complex allylic bromide corresponding to the C20-C27 fragment of the bryostatins was unsuccessful, possibly due to competing elimination reactions. This meant that the use of C19 dithianes for the synthesis of 20-deoxybryostatins would have to involve the stepwise assembly of the C20-C27 fragment from simpler precursors. However, lithiated C19 dithianes gave good yields of adducts with aldehydes and conditions were developed for the stereoselective conversion of the major adducts into methoxyacetals that corresponded to the C17-C27 fragment of 20-oxygenated bryostatins. A convergent synthesis of the C11-C27 fragment of a 20-deoxybryostatin was subsequently achieved using a 2-benzothiazolylsulfone corresponding to the intact C17-C27 fragment.

Introduction

The synthesis of the bryostatins, as exemplified by bryostatins 1 (**1**) and 10 (**2**), see Figure 1, is of interest because of their biological activities and relative inaccessibility from natural sources.[1,2] Several outstanding total syntheses have been reported[3] and synthetic analogues have been discovered that have tumour suppressing bryostatin-like activity or tumour promoting phorbol-like activity.[4,5] This work has been a significant contribution to natural product synthesis and to cancer chemotherapy.

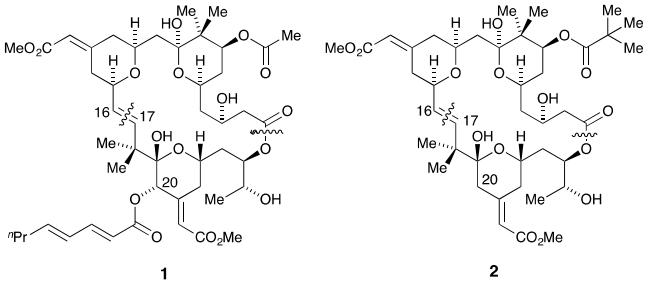

Figure 1 Representative bryostatins showing disconnections into C1-C16 and C17-C27 fragments

It was soon recognised that assembly of bryostatins by formation of the C16-C17 double-bond and C20 ester formation would lead to convergent syntheses and two early total syntheses were based on this strategy using Julia reactions to form the alkene followed by macrolactonisation.[3a,c] This work led to seminal syntheses, but the reaction conditions necessary for conventional Julia reactions meant that several steps had to be deferred until after the Julia reaction and this undermined the convergency of these approaches. Formation of the C16-C17 double bond by ring closing metathesis (RCM) has been investigated[6,7] but has not yet proved effective for the synthesis of naturally occurring bryostatins with the geminal methyl groups at C18, although it can be used for analogue synthesis.

Our work has been primarily concerned with the synthesis of bryostatins that do not have an acyloxy group at C20, e.g. bryostatin 10 (**2**).[8] These 20-deoxybryostatins are a subset of bryostatins that have not been synthesised even though they have biological activities reminiscent of their more highly oxygenated congeners. Our early studies were concerned with syntheses of the C(1)-C(16) and C(17)-C(27) fragments in anticipation of developing a convergent synthesis.[9,10] However, following our difficulties encountered in using RCM for the synthesis of 20-deoxybryostatins,[6] a new strategy had to be devised for their assembly. In any new approach, we intended to use as much of the chemistry that we had already developed as possible. Indeed, this had always been part of our philosophy. With this consideration in mind, an alternative assembly of the C20-deoxybryostatins predicated on an early introduction of the 16,17-double-bond,[3b,11] was investigated, see Figure 2.

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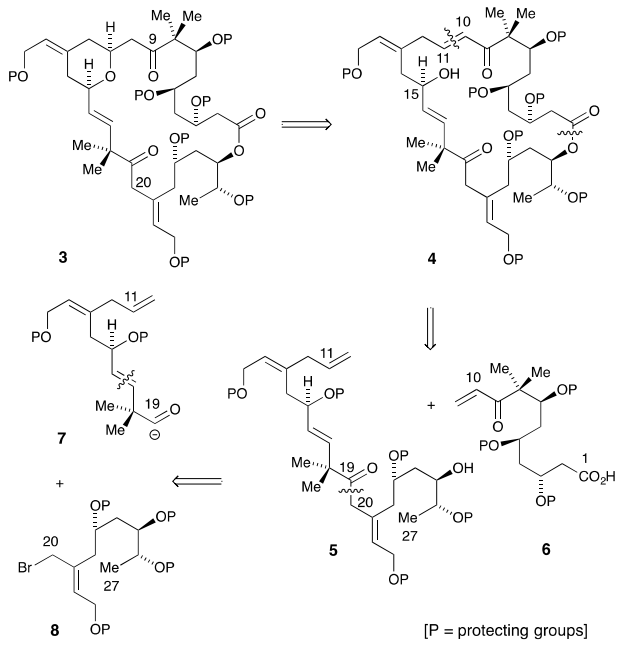


Figure 2 An alternative approach to 20-deoxybryostatins

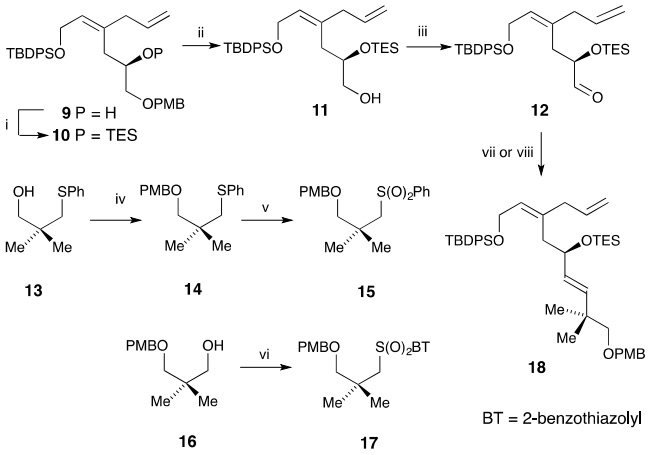
Intramolecular stereoselective oxy-Michael reactions of intermediates with hydroxyl groups at C15 (bryostatin numbering) with enones have been used to prepare C10-C16 fragments of bryostatins.[9] Enones **4** should therefore be useful for the preparation of the advanced intermediates **3**. However, the presence of the 10,11-double-bond in the enones **4** now provides considerable flexibility in planning their synthesis including the option of a RCM-based sequence from the ester derived from the C11-C27-alcohol **5** and the C1-C10-acid **6**. Intermediates that are equivalent to the acids **6** have already been prepared.[9] We now describe studies concerned with the synthesis of the C11-C27 ketones **5** using synthetic equivalents of the C19 acyl carbanions **7** and allylic halides **8**. During the course of this work, intermediates were also prepared that could be used for alternative procedures to form the 10,11-double bond, and to access bryostatins with acyloxy groups at C20.[12,13]

Results and discussion

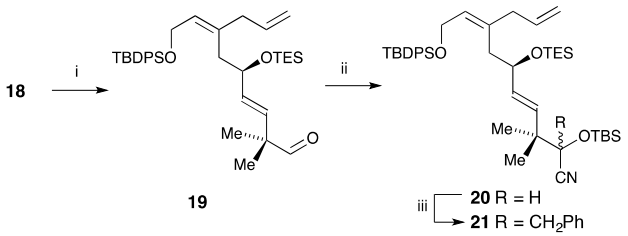
Syntheses and alkylation of synthetic equivalents of C19 acyl carbanions 7

Following the early syntheses of bryostatins, Julia reactions were investigated for the synthesis of synthetic equivalents of the acyl carbanions **7**. The aldehyde **12** was prepared from the known alcohol **9**[9] by *O*-silylation, PMB-deprotection and oxidation of the primary alcohol **11**. However, initial studies into the Julia reaction of this aldehyde with the phenylsulfone **15** that had been prepared from the sulfide **13**[14] via its PMB-ether **14**, see Scheme 1, were disappointing. The addition of the deprotonated sulfone to the aldehyde gave a mixture of four diastereoisomeric hydroxysulfones but these proved difficult to acetylate completely for the reductive elimination step. Moreover, reductive elimination of the hydroxysulfones themselves using freshly prepared samarium iodide,[15] gave only low yields of the required alkene **18**. Mixtures of side products including alcohols formed by the reductive removal of the phenylsulfonyl group were isolated from these reactions. In contrast, a modified Julia reaction[16] using the crystalline benzothiazolylsulfone **17**, prepared in two steps from the alcohol **16**,[17] was more successful and gave a 65% yield of the alkene **18** when lithium hexamethyldisilazide was used as the base. However, the (*E*):(*Z*) stereoselectivity of this reaction was capricious. Better results, up to 80:20 in favour of the (*E*)-isomer, were obtained when the aldehyde was added quickly to the deprotonated sulfone at –78 °C, followed by rapid warming to ambient temperature, see Scheme 1. Lithium hexamethyldisilazide was preferred over sodium or potassium hexamethyldilazide for these reactions. In our hands no improvement in stereoselectivity was observed using the analogous *N*-phenyltetrazolylsulfone.[3b,18]

The *O*-silylated cyanohydrin **20** was selected as the first C19 acyl carbanion equivalent.[19] Thus the alkene **18** was deprotected selectively and the resulting alcohol oxidised to the aldehyde **19** that was converted into a mixture of the epimeric *O*-silylated cyanohydrins **20**, see Scheme 2. However, alkylation of these hindered cyanohydrins proved to be difficult. Good yields of the benzylated cyanohydrin **21** were obtained using lithium di-isopropylamide as the base if HMPA was present during the deprotonation and alkylation steps. However, an excess of



Scheme 1 Synthesis of the alkene **18** Reagents and conditions i, imid., TESCl, DCM, 0 °C to rt, 2 h (*ca*. 100%); ii, DDQ, DCM, aq. pH 7 phosphate buffer, rt, 20 min (84%); iii, Dess-Martin periodinane, DCM, py., rt, 3 h; iv, TBAI, NaH, PMBCl, DMF, rt, 16 h (86%); v, Oxone, MeOH, THF, water, 0 °C to rt, 8 h (*ca*. 90%); vi, (a) 2-BTSH, Ph_3P, DIAD, THF, 0 °C to rt, 2.5 h (b) $Mo_7O_{24}(NH_4)_6.4H_2O$, 30% H_2O_2, EtOH, 0 °C to rt (80% from **16**); vii, (a) **15**, ^{n}BuLi, THF, –78 °C, 10 min, add **12**, –78 °C, 10 min (*ca*. 60%) (b) SmI_2, HMPA, THF, rt, 1 h (15% from **12**); viii, **17**, LiHMDS, –78 °C, 20 min, add **12**, warm to rt, 1.5 h [65%, (*E*) : (*Z*) = 80 : 20].

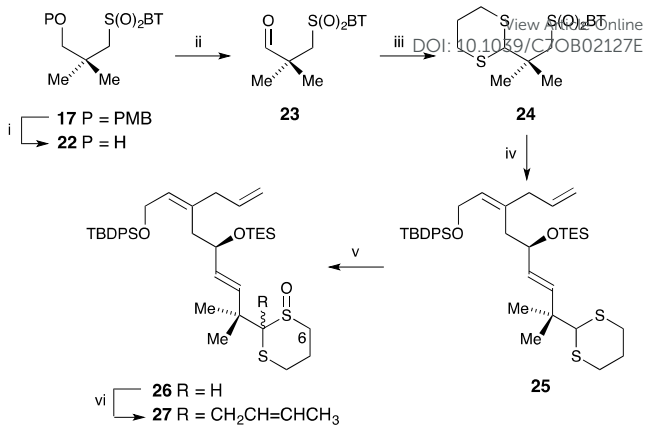


Scheme 2 Alkylation of the silylated cyanohydrin **20** Reagents and conditions i, (a) DDQ, DCM, aq. pH7 phospate buffer, rt, 20 min (b) Dess-Martin periodinane, py., DCM, rt, 1.5 h (80% from **18**); ii, TBSCN, ZnI_2, DCM, rt (65%); iii, HMPA, LDA, –78 °C, THF, 1 h, BnBr, –78 °C to rt, 1 h (83%, 55:45 mixture of epimers).

benzyl bromide was necessary and lower yields were obtained using allylic halides. As fairly complex allylic halides **8** would be required for a synthesis of the C11-C27 fragment **5**, allylation of the *O*-silylated cyanohydrin **20** was not taken any further.

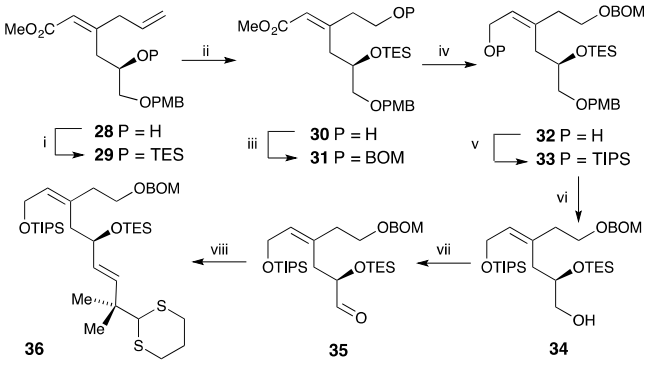
1,3-Dithianes have often been used as acyl carbanion equivalents.[20] Indeed alkylation of hindered neopentylic dithianes has been used for formation of the C9-C10 bond of bryostatins.[20b] The 2-(benzothiazolylsulfonylethyl)dithiane **24** was therefore prepared from the 3-*p*-methoxybenzyl ether **17** by deprotection, oxidation and reaction of the resulting aldehyde **23** with propane-1,3-dithiol. The modified Julia reaction of this sulfone with the aldehyde **12** was found to be more stereoselective than Julia reactions with sulfone **17**, and gave the (*E*)-alkene **25** together with only traces of its (*Z*)-isomer, see Scheme 3. However, attempts to alkylate this 1,3-dithiane using (*E*)-1-bromobut-2-ene, even using *tert*-butyllithium in tetrahydrofuran containing HMPA, conditions that had been used successfully with similar systems,[20b] gave either unchanged starting materials or complex mixtures of products. It appeared that base-promoted elimination reactions of the skipped diene **25** were taking place with loss of the *tert*-butyldiphenylsilyloxy group under the strongly basic reaction conditions required to deprotonate the neopentylic 1,3-dithiane. The allylic bromide was also unstable under the basic reaction conditions.

1,3-Dithiane monoxides require less basic reaction conditions for deprotonation than their parent 1,3-dithianes.[21-23] The dithiane **25** was therefore oxidised to the monosulfoxide **26** using *m*-chloroperbenzoic acid, Scheme 3. This was isolated as a mixture of the four diastereoisomers in a 1 : 1 : 9 : 9 ratio as determined by integration of the singlets assigned to the 1'-methyl groups. Peaks in the δ3.2-3.5 region were assigned to the equatorial protons at C6 in the major *trans*-dithiane monoxides.[22] Deprotonation could now be achieved with lithium di-isopropylamide and preliminary studies of the alkylation of the lithiated dithiane monoxide using an excess of (*E*)-1-bromobut-2-ene gave the alkylated product **27**. However, this was still a mixture of diastereoisomers and attempts to reduce it to the corresponding dithiane using diphosphorus tetraiodide[21,23] gave complex mixtures of products. The reasons for the difficulties in the reduction of the dithane monoxide **27** were not clear.



Scheme 3 Synthesis and alkylation of dithiane monoxide **26** Reagents and conditions i, DDQ, aq. pH7 phosphate buffer, DCM, rt, 30 min (*ca*. 100%); ii, $(COCl)_2$, DMSO, DCM, –78 °C, 1 h, **22**, –78 °C, 1 h, Et_3N, –78 °C to rt (93%); iii, propane-1,3-dithiol, $BF_3.Et_2O$, 0 °C to rt, *ca*. 1 h (77%); iv, LiHMDS, tol., THF, –78 °C, 20 min, add **12**, warm to rt, 1.5 h (55%); v, *m*CPBA, DCM, 0 °C to rt (78%; 1:1:9:9 mixture of diastereoisomers); vi, LDA, THF, HMPA, –78 °C, 1 h, (*E*)-$CH_3CH=CHCH_2Br$, –78 °C, 30 min, rt, 1 h (**27**, 50%; recovered **26**, 40%).

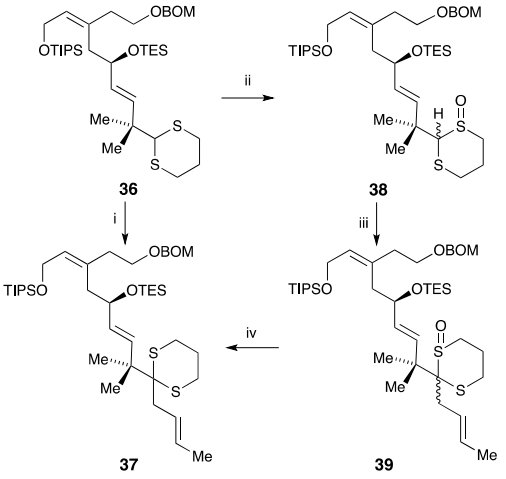
It was decided to study a related system that didn't have the base-sensitive skipped diene. The hydroxyester **28**[9] was *O*-silylated and the resulting ester **29** taken through to the primary alcohol **30** by hydroxylation and periodate cleavage of the diol with a reductive work-up.[9] Protection of the primary alcohol as its benzyloxymethyl derivative **31**, reduction of the ester and protection of the allylic alcohol **32** as its tri-isopropylsilyl ether **33**, gave the aldehyde **35** after removal of the *p*-methoxybenzyl ether and oxidation. The modified Julia reaction of this aldehyde with sulfone **24** then gave the (*E*)-alkene **36** in an excellent yield, 87%, and (*E*)-stereoselectivity, Scheme 4.



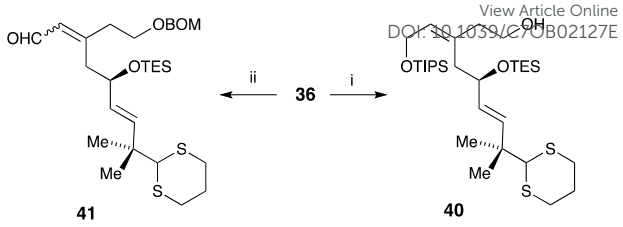
Scheme 4 Synthesis of 1,3-dithiane **36** Reagents and conditions i, imid., TESCl, DCM, rt, 2 h (82%); ii, (a) NMO, OsO_4 (cat.), ^tBuOH, acetone, water, rt, 4 h (98%) (b) $NaIO_4$, methanol, THF, 0 °C, 45 min, $NaBH_4$, 0 °C, 1 h (71% from **29**); iii, BOMCl, $^iPr_2NEt$, TBAI, THF, 0 °C to rt, 14 h (92%); iv, DIBAL-H, heptanes, THF, –78 °C, 1.5 h (91%); v, TIPSCl, imid., DCM, rt, 14 h (95%); vi, DDQ, aq. pH 7 phosphate buffer, DCM, 0 °C to rt, 1.5 h (65%); vii, Dess-Martin periodinane, py., DCM, rt, 45 min; viii, **24**, LiHMDS, tol., THF, –78 °C, 30 min., add **35**, rt, 1 h (87% from **34**).

Allowing 15 min. for the deprotonation, the direct allylation of the 1,3-dithiane **36** with (*E*)-1-bromobut-2-ene using *tert*-butyllithium and HMPA gave a modest, 35%, yield of the product **37** together with 20% of unchanged starting material and a mixture of side-products. Deprotonation for shorter periods gave more unchanged starting material **36** and longer deprotonation times gave more decomposition. However, oxidation of the dithiane **36** with careful monitoring of the oxidation by TLC, gave an excellent yield, *ca.* 95%, of the monosulfoxides **38**. The stereoselectivity in favour of the trans-sulfoxides was *ca*. 3:1 as indicated by NMR[22] although no attempt was made to separate the four diastereoisomers. Alkylation of this mixture of monosulfoxide diastereoisomers at –60 °C using (*E*)-1-bromobut-2-ene now gave a 79% yield of the alkylated product **39** and reduction using diphosphorus tetraiodide[23] under triethylamine buffered conditions gave the alkylated dithiane **37** (70%). This three-step conversion of dithiane **36** into the 2,2-disubstituted dithiane **37** was significantly more efficient than the direct alkylation and was considered to be a viable transformation, Scheme 5.

It was decided to check that the BOM-protecting group could be removed in the presence of a dithiane. Treatment of the BOM-protected dithiane **36** with sodium in liquid ammonia and ethanol, gave only a modest yield of the alcohol **40** together with unchanged starting material. Better yields, >70%, were obtained using lithium naphthalenide in THF although the product **40** was contaminated with 2-phenylethanol.[24] More complex dithianes would have different polarities from the simpler system **40** and should be separable from any phenylethanol. No reaction was observed on attempted hydrogenolysis of the BOM-protected dithiane **36** using Perlman's catalyst and an attempted oxidative deprotection using DDQ gave the aldehyde **41** as a 3:1 mixture of geometrical isomers consistent with preferred allylic oxidation,[25] Scheme 6.



Scheme 5 Alkylation of the dithiane **36** Reagents and conditions i, ^{t}BuLi, HMPA, THF, –78 °C, 15 min, (*E*)-$CH_3CH{=}CHCH_2Br$, –78 °C, 30 min (**37**, 35%; **36**, 20%); ii, *m*CPBA, DCM, 0 °C (95%); iii, LDA, HMPA, THF, –78 °C to –60 °C, 30 min, (*E*)-$CH_3CH{=}CHCH_2Br$, –78 °C, 20 min (79%); iv, P_2I_4, Et_3N, DCM, rt, 40 min (70%).



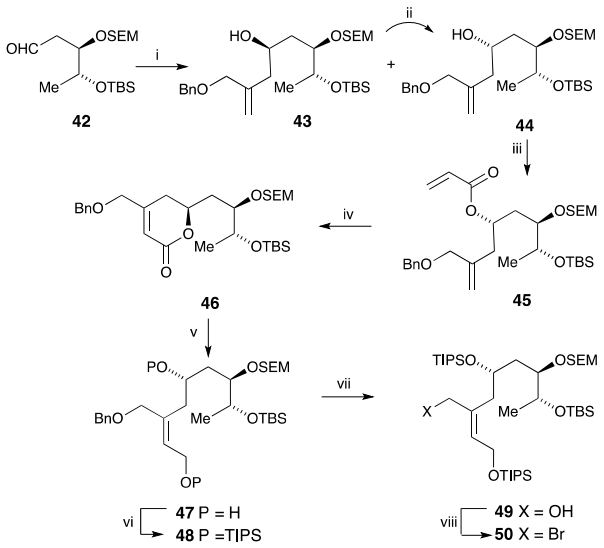
Scheme 6 Removal of the BOM-protecting group Reagents and conditions i, (a) NH_3, EtOH, THF, –78 °C, 5 min (49%) or (b) lithium naphthalenide, THF, –20 °C (71% with 2-phenylethanol); ii, DDQ, pH 7 phosphate buffer, DCM, rt, 1 h (**41**, 43%; **36**, 38%).

Having shown that the dithiane monoxide **38** can be used as the synthetic equivalent of a C19 acyl carbanion, it was now necessary to prepare an allylic halide corresponding to the C20-C27 fragment **8**. Our earlier routes to this fragment had been based on stereoselective conjugate addition reactions of alkynyl esters.[10] However, a new route was envisaged in which the geometry of the trisubstituted double-bond would be controlled by a ring-closing metathesis, see Scheme 7.

The indium-mediated addition of 2-benzyloxymethyl-1-bromopropene to the aldehyde **42** gave a *ca*. 50 : 50 mixture of the alcohols **43** and **44** in keeping with other reactions of this aldehyde.[10] However these isomers were relatively easy to separate and the less polar epimer was shown to have the required (4*S*)-configuration by comparison of the relative ^{1}H NMR chemical shifts of its (*R*)- and (*S*)-*O*-acetyl mandelates.[26] The more polar (4*R*)-epimer **43** was converted into the less polar (4*S*)-isomer **44** by a Mitsunobu reaction followed by saponification of the resulting nitrobenzoate making the required (4*S*)-epimer **44** available in an overall yield of *ca*. 75% from the aldehyde **42**. In our hands this indium-mediated procedure was more efficient than addition of the analogous Grignard reagent to the aldehyde.

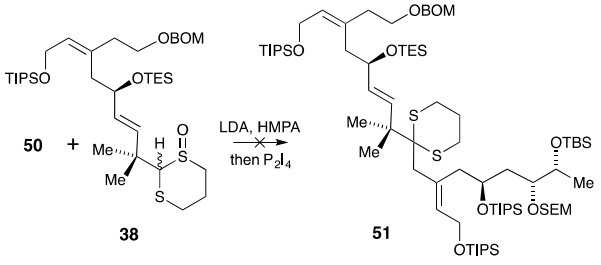
The alcohol **44** was converted into its acrylate **45** and a ring-closing metathesis[27,28] of this ester gave the lactone **46**. This reaction introduced the required trisubstituted double bond with complete stereochemical control. A Luche reduction of the lactone **46** now gave the diol **47** that was protected as its bis-tri-isopropylsilyl ether **48**. Removal of the benzyl ether was carried out using lithium naphthalenide and the resulting allylic alcohol **49** was converted into the bromide **50** using mesyl chloride and lithium bromide, see Scheme 7.

However, attempts to alkylate the dithiane monoxide **38** using the allylic bromide **50** under the conditions that had been successful for (*E*)-1-bromobut-2-ene gave complex mixtures of products, see Scheme 8. Attempts to reduce the number of diastereoisomeric products by reduction of the crude mixtures did not lead to the dithiane **51**, a synthetic equivalent of the C11-C27 fragment **5**. The use of higher reaction temperatures or nucleophilic catalysts did not facilitate the allylation step. It would appear that the alkylation of the hindered dithiane monoxide **38** is difficult with bulky, base-sensitive, allylic halides.



Scheme 7 Synthesis of the allylic bromide **50** Reagents and conditions i, $BnOCH_2C(=CH_2)CH_2Br$, In, THF, H_2O, rt, 45 min (**43**, 43%; **44**, 45%); ii, (a) 4-nitrobenzoic acid, Ph_3P, DIAD, THF, 0 °C to rt, 12 h (92%) (b) K_2CO_3, MeOH, 0 °C, 3 h (90%); iii, $^iPr_2NEt$, CH_2=CHC(O)Cl, DCM, 0 °C, 5 h (97%); iv, Grubbs II, DCE, heat under reflux, 26 h (80%); v, $CeCl_3.7H_2O$, $NaBH_4$, MeOH, 0 °C (98%); vi, 2,6-lut., $^iPr_3SiOTf$, DCM, 0 °C to rt, 2 h (82%); vii, Li, naph., THF, rt, 1 h, add to **48**, THF, –30 °C (77%); viii, Et_3N, MsCl, THF, 0 °C, 1 h, LiBr, THF, 0 °C, 1 h (93%).

Other procedures can be envisaged for the conversion of the dithiane monoxide **38** into the C11-C27 fragment of the 20-deoxybryostatins **51**, for example by using a less complex allylic bromide with further modification after the alkylation step. However, as reactions of lithiated dithianes with aldehydes are very well known, it was also of interest to see whether reactions of lithiated C19 dithianes with aldehydes could be used to prepare intermediates that correspond to the C11-C27 fragments of bryostatins, e.g. bryostatin 1 (**1**), with an acyloxy group at C20. A synthesis of an intermediate that corresponds to the C11-C27 fragment **51** of a 20-deoxybryostatin was subsequently developed that did not use dithiane chemistry. This is presented in the summary and is outlined in Scheme 14.



Scheme 8 Unsuccessful synthesis of dithiane **51**

Reactions of lithated dithianes with aldehydes for the synthesis of the C11-C27 fragment of 20-oxygenated bryostatins

It was decided to study the reactions of lithiated dithianes with aldehydes before investigating the modified Julia reaction for an approach to the C11-C27 fragment **52** of a 20-oxygenated bryostatin, see Figure 3. The C17-C27 fragment **53** was to be prepared using the base-promoted reaction between the simple dithiane **54** and the C20-C27 aldehyde **55** albeit control of the configuration at C20 was expected to be an issue. The subsequent introduction of the benzothiazolylsulfonyl group and modified Julia reaction would complete the synthesis.

The diol **47** was converted into the aldehyde **59** by protection of the primary allylic alcohol as its tri-isopropylsilyl ether **56** followed by conversion of the secondary alcohol into the more labile triethylsilyl ether **57**. These conversions were in anticipation of selective deprotection of the secondary alcohol later in the synthesis. The benzyl group was then removed using lithium naphthalenide and the resulting alcohol **58** was oxidised to give the aldehyde **59**, see Scheme 9.

Deprotonation of the dithiane **60**, prepared from 3-benzyloxy-2,2-dimethylpropanal (see experimental), was achieved using *n*-butyllithium, and the lithiated dithiane found to react with the aldehyde **59** to give a *ca*. 2 : 1 mixture of the epimeric alcohols **61** and **62**. These were separated and then desilylated to give the diols **63** and **64**, see Scheme 9. The configurations of the alcohols **61** and **62** and the diols **63** and **64** at C4 were confirmed by nOe studies later in the synthesis. It transpired that the configuration at C4 of the major epimers **61** and **63** corresponded to that required at C20 in the bryostatins although the stereoselectivity was only modest. Procedures to improve this stereochemical control were not investigated.

Protection of the ketone at C19 in derivatives of 20-oxygenated bryostatins as methoxyacetals is well known.[3] It was therefore of interest to convert the dithianes **63** and **64** into methoxyacetals reminiscent of the C17-C27 fragments of bryostatins and to study the introduction of the 2-benzothiazolylsulfonyl moiety and the modified Julia reaction.

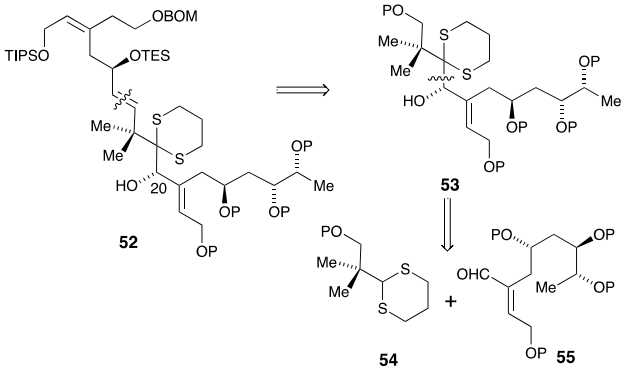


Figure 3 Proposed dithiane – aldehyde synthesis of the C11-C27 and C17-C27 intermediates **52** and **53**.

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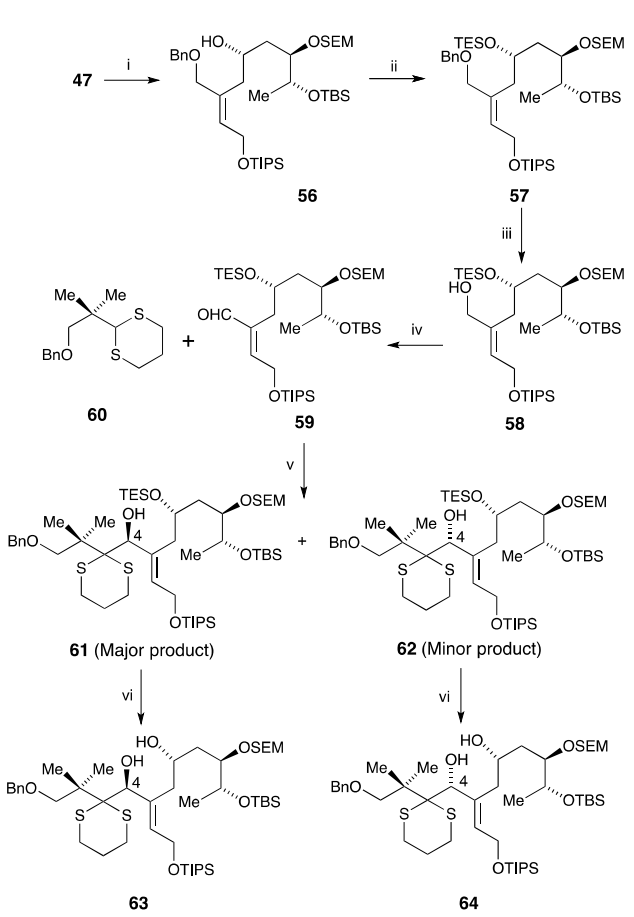
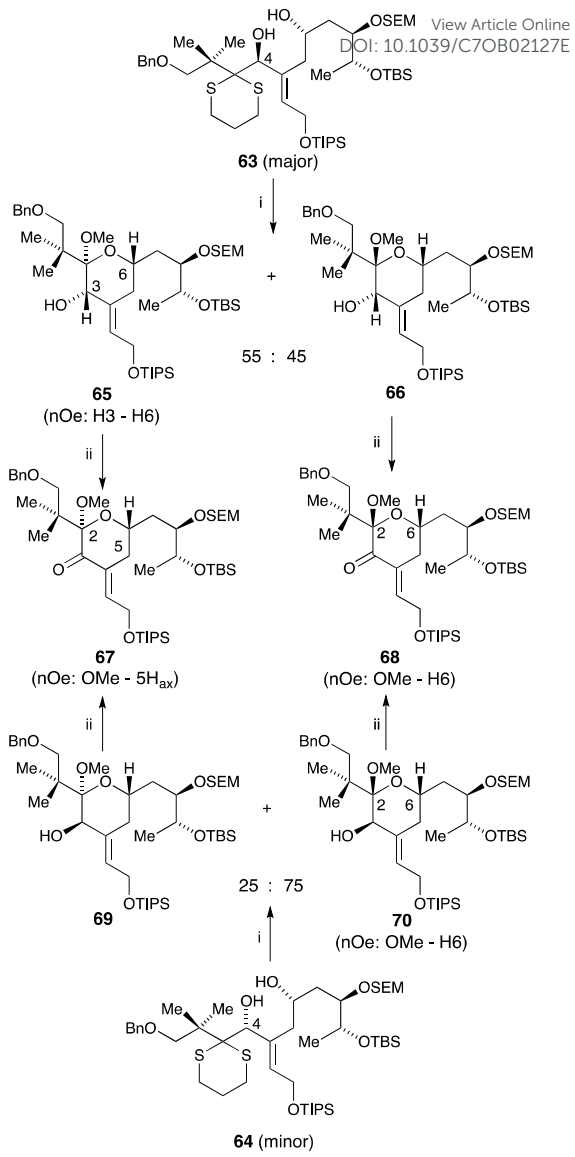


Scheme 9 Assembly of the C17-C27 fragment Reagents and conditions i, $^{i}Pr_3SiCl$, imid., DCM, rt, 2 h (90%); ii, Et_3SiCl, imid., DCM, rt, 90 min (92%); iii, Li, naph., THF, rt, 1 h, add to **57**, –30 °C (81%); iv, Dess-Martin periodinane, py., rt, 1 h (95%); v, **60**, $^{n}BuLi$, THF, rt, 5 min, –78 °C, add **59**, –78 °C, 15 min (**61**, 53%; **62**, 26%); vi, $HC(OMe)_3$, MeOH, THF, PPTS, rt, 1 h (**63**, 92%; **64**, 90%).

Treatment of the major dihydroxydithiane **63** with mercury(II) perchlorate in methanol[29] gave the two methoxyacetals **65** and **66** that were epimers at the anomeric position, in isolated yields of 37% and 25%, respectively, Scheme 10. The corresponding transacetalisation of the minor dithiane **64** gave a mixture of the two methoxyacetals **69** and **70**, ratio *ca*. 1 : 3, in a combined yield of 60%, although small samples of each were obtained on repeated chromatography.

Interestingly, oxidation of the major methoxyacetal **65** from the major dithiane **63**, gave the ketone **67** that was also obtained by oxidation of the minor methoxyacetal **69** prepared from the minor dithiane **64**. Correspondingly the minor methoxyacetal **66** from the major dithiane **63** gave ketone **68** that was also obtained by oxidation of the major methoxyacetal **70** from the minor dithiane **64**, see Scheme 10.

The configurations of the epimeric dithianes **63** and **64** at C4, the ketones **67** and **68** at C2 and the methoxyacetals **65**, **66**, **69** and **70** at C2 and C3 were confirmed by extensive nOe studies.

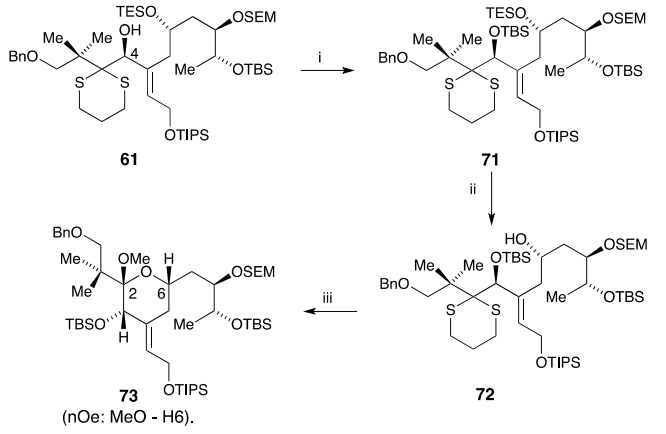


Scheme 10 Preparation of C17-C27 methoxyacetals from dithianes **63** and **64** Reagents and conditions i, $Hg(ClO_4)_2.3H_2O$, THF, MeOH, 2,6-lut., –5 °C, 30 min (**65**, 37%; **66**, 25%; **69** and **70**, 60%, 1:3); ii, Dess-Martin periodinane, py., DCM, rt, 1 h (**67**, 55% from **65**, 51% from **69**; **68**, 63% from **66**, 61% from **70**).

For the major methoxyacetal obtained from the minor dithiane, and the corresponding ketone, significant nOes were observed between the anomeric methoxy goup and H6 consistent with these groups being *cis* to each other as shown in structures **70** and **68**. For the major methoxyacetal obtained from the major dithiane, significant nOes were observed between H3 and H6 showing that these hydrogens are *cis* to each other as shown in structure **65**. Moreover, for the ketone prepared by oxidation of this methoxyacetal, a significant nOe was observed between the methoxy group at C2 and the axial hydrogen at C5 consistent with the structure **67**, see Scheme 10.

The non-stereoselective acetal formation from the dithianes **63** and **64** was unexpected since it would appear that anomeric effects were not dominating the stereoselectivity. Attempts to equilibrate the epimeric acetals **65** and **66** under acidic conditions led to extensive decomposition. The major methoxyacetals **65** and **70** formed in the transacetalisation processses had the 3-hydroxyl groups *cis* disposed to the anomeric methoxy groups. It may be that the acetal formation is under kinetic control and is being influenced by intramolecular hydrogen bonding involving the 3-hydroxyl and anomeric methoxy groups. However, this suggestion is only speculative.

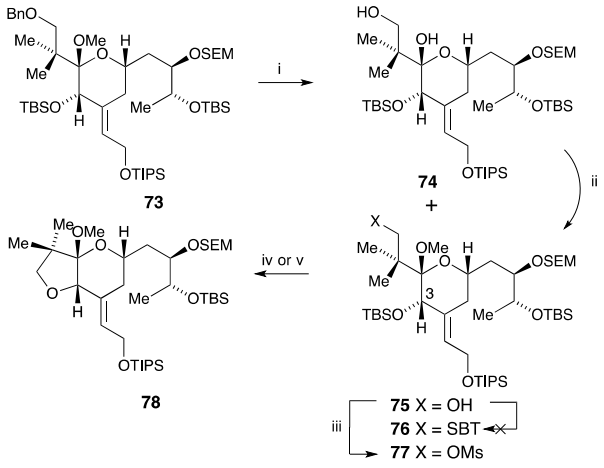
Nevertheless, the formation of two methoxyacetals from each of the dithianes would lead to complications if these products were to be taken further in the synthesis and a more stereoselective acetal formation was really required. With the hydrogen bonding explanation in mind for the formation of the unexpected methoxyacetal **65** as the major product from diol **63**, it was decided to see if protection of the C4 hydroxyl group had any effect on the stereoselectivity of the transacetalisation. The major alcohol **61** from the dithiane addition reaction was therefore protected as its *tert*-butyldimethylsilyl ether **71** using an excess of *tert*-butyldimethylsilyl triflate to drive the silyation of this hindered alcohol to completion. Following a selective removal of the triethylsilyl group, the transacetalisation of the resulting alcohol **72** was examined. This was found to be much slower than the transacetalisations of the diols **63** and **64** that were complete within 30 min at –30 °C. Indeed the transacetalisation of the alcohol **72** was only complete after 8 h at room temperature. However, a single diastereoisomer was isolated in an excellent yield, 88%, and was identified as the expected anomer **73** on the basis of significant nOes between the anomeric methoxy group and H6, see Scheme 11. Because of the relatively vigorous conditions required, the stereoselectivity of this transacetalisation may be due to thermodynamic rather than kinetic control.



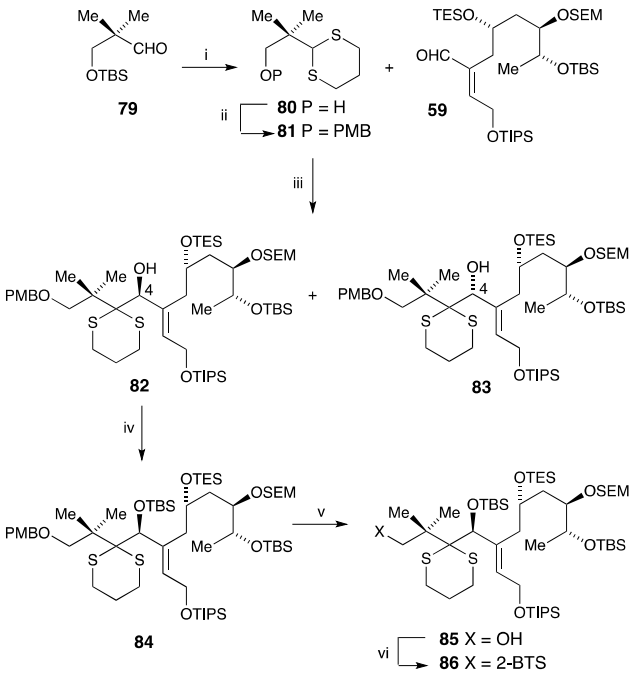
Scheme 11 Stereoselective transacetalisation Reagents and conditions: i, TBSOTf, 2,6-lut., DCM, rt, 14 h (92%); ii, $HC(OMe)_3$, MeOH, THF, PPTS, rt, 12 h (92%); iii, $Hg(ClO_4)_2.3H_2O$, 0 °C to rt, 8 h (88%).

The methoxyacetal **73** corresponds to the C17-C27 fragment of a 20-oxygenated bryostatin. It remained to convert the benzyloxy group into a 2-benzothiazolylsulfonyl moiety ready for assembly of the C11-C27 fragment by a modified Julia reaction. Hydrogenolysis of the benzyl ether **73** gave a mixture of the methoxy acetal **75** and the hemiacetal **74** but the hemiacetal could be converted into the methoxyacetal **75** using trimethyl orthoformate and pyridinium toluene *p*-sulfonate. However, attempts to convert the primary alcohol **75** into the correponding sulfide **76** using 2-mercaptobenzothiazole under Mitsunobu conditions were unsuccessful. The only product isolated was the tetrahydrofuran **78**. The same product **78** was also formed during attempts to convert the primary mesylate **77** into the sulfide **76** using 2-mercaptobenzothiazole. Hale's double Thorpe-Ingold effect[1d] would appear to be facilitating an intramolecular displacement involving the *tert*-butyldimethylsilyloxy group at C3 leading to the cyclised product **78** after desilylation. This process competed with the required S_N2 reactions of derivatives of the hindered neopentylic alcohol **75** with external nucleophiles, Scheme 12.

It was thought that the introduction of the primary benzothiazolyl group before the conversion of the dithiane into a methoxyacetal might avoid the formation of tetrahydrofuran **78**. However, attempts to remove the benzyl group from dithiane **71** using Birch conditions or lithium naphthalenide led to decomposition and another protecting group was required for the primary alcohol. The 4-methoxybenzyloxy group was considered an option, but it was recognised that lithiation of the corresponding dithiane could be complicated by competing lithiation ortho to the aromatic methoxy group.[30] Nevertheless the 4-methoxbenzyl ether **81** was prepared from the corresponding alcohol **80**[32] that had been prepared from 3-*tert*-butyldimethylsilyloxy-2,2-dimethylpropanal **79** and the regioselectivity of its lithiation was investigated, see Scheme 13.



Scheme 12 An unexpected cyclisation Reagents and conditions i, H_2, Pd/C, EtOAc, MeOH, 1 bar, 25 °C (**75**, 50%; **74**, 40%); ii, $HC(OMe)_3$, PPTS, MeOH, THF (74%); iii, MsCl, Et_3N, DCM, 0 °C, 1 h; iv, **75**, 2-BTSH, PPh_3, DIAD, rt, 3 h (79%); v, 2-BTSH, DMF, NaH, 0 °C, 20 min, add **77**, 120 °C, 12 h (72% from **75**).



Scheme 13 Introduction of the 2-benzothiazolylsulfanyl group Reagents and conditions i, propane-1,3-dithiol, $BF_3.Et_2O$, DCM, 0 °C to rt, 16 h (82%); ii, NaH, DMF, 0 °C, 30 min, add PMBCl, TBAI (cat.), 0 °C to rt, 1 h (65%); iii, **81**, ^{n}BuLi, ^{t}BuOMe, rt, 5 min, –78 °C, add **59**, –78 °C, 15 min (**82**, 34%; **83**, 21%); iv, TBSOTf, 2,6-lut., DCM, rt, 3 h (90%); v, DDQ, pH7.2 phosphate buffer, DCM, rt, 30 min (81%); vi, 2-BTSH, Ph_3P, THF, DIAD, 0 °C to rt, 4 h (78%).

Deprotonation of the dithiane **81** using the conditions that had been used previously, i.e. *n*-butyllithium in THF for 5 min, followed by quenching with D_2O, showed that some deprotonation had occurred ortho to the methoxy group as well as at C2 of the dithiane.[30] Using ether as the solvent, selective dithiane deuteriation was observed but was incomplete after allowing 5 min for the lithiation. Longer lithiation times led to precipitation of a white solid that if taken up in D_2O gave 52% deuterium incorporation at C-2 of the dithiane. The precipitation of the lithiated intermediate was avoided by using *tert*-butyl methyl ether as the solvent and led to >70% deuteriation of the dithiane after lithiation for 8 min and quenching with D_2O.

Lithiation of the dithiane **81** under these optimised conditions followed by the addition of the aldehyde **59** gave a mixture of the epimeric alcohols **82** and **83**. The configurations of these alcohols at C4 were assigned by comparision of their ^{1}H NMR spectra with those of the analogous benzyl ethers **61** and **62**. Silylation of the major epimer **82** gave the *tert*-butyldimethylsilyl ether **84** that was converted into the primary alcohol **85** by oxidative removal of the 4-methoxybenzyloxy moiety. Finally this alcohol was converted into the corresponding thioether **86** using 2-mercaptobenzothiazole under Mitsunobu conditions, see Scheme 13. No side-product analogous to the tetrahydrofuran **78** was isolated from this reaction.

Summary and conclusions

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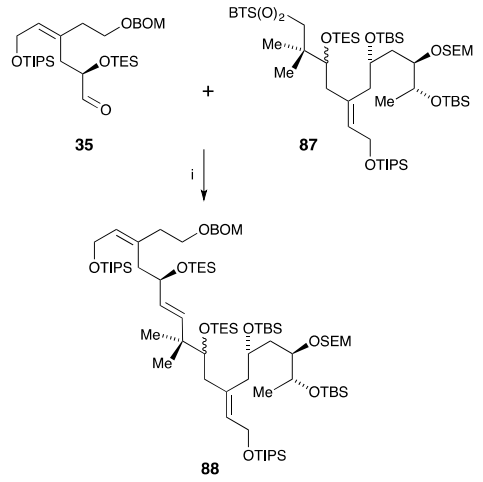
The modified Julia reaction and acyl carbanion chemistry, especially the reactions of 2-lithiated dithianes, have been investigated for the synthesis of intermediates that are synthetic equivalents of C11-C27 fragments of bryostatins. The modified Julia reaction using 2-benzothiazolylsulfones was found to be more useful for the formation of the 16,17-double-bond than the classical Julia reaction using phenylsulfones, and the bulky sulfone **24** gave very good (*E*)-stereoselectivity. Conditions were developed for the alkylation of the neopentylic dithiane monoxide **38** that corresponded to a C19-acyl carbanion, using (*E*)-1-bromobut-2-ene, but the use of the more complex allylic bromide **50** was unsuccessful perhaps because of competing elimination reactions under the basic reaction conditions. This meant that the use of dithianes for the synthesis of 20-deoxybryostatins would have to involve the stepwise assembly of the C20-C27 fragment from simpler precursors. However, dithiane **60** gave a good yield of adducts with the aldehyde **59**, and conditions were developed for the conversion of the major adduct **61** into the methoxyacetal **73** that corresponds to the C17-C27 fragment of 20-oxygenated bryostatins.

It would appear that the use of dithianes as acyl carbanion equivalents was being pushed to its limits during the course of this work. Of interest in this respect were the better yields obtained with dithiane **36** and its monoxide **38** than those obtained using the dithiane **25** and monoxide **26**. This was attributed to the presence of a skipped diene in the latter compounds that made these intermediates unstable to the strongly basic conditions used for dithiane deprotonation. The stereoselective syntheses of C20-C27 intermediates, e.g. the bromide **50** and the aldehyde **59** based on the use of ring-closing metathesis to introduce the trisubstituted double-bond *via* the six-membered lactone **46**, were also of interest.[28] The kinetic and thermodynamic control observed in the conversions of the dithianes **63**, **64** and **72**, into methoxyacetals was of note, with the transacetalisation of dithiane **72** providing the required C17-C27 fragment **73** with excellent stereoselectivity. The *tert*-butyldimethylsilyloxy group at C-3 may be influencing the stereoselectivity of this conversion. The formation of the tetrahydrofuran **78** from the 3-*tert*-butyldimethylsilyl ether **75** and mesylate **77** was unexpected[1d] and competed with the required substitution reactions with external nucleophiles. Finally the role of the solvent in influencing the regioselectivity of lithiation of the 2-(2-*p*-methoxybenzyloxyethyl)dithiane **81** was useful.

The benzothiazolylsulfide **86** would appear to be a useful intermediate for the further elaboration of the C11-C27 fragment **52** of 20-oxygenated bryostatins. However, our prime concern remained with the synthesis of 20-deoxybryostatins, e.g. bryostatin 10 (**2**), because these bryostatins had not been the subject of many investigations by synthetic chemists. Therefore, rather than continue with studies of the sulfone **86**, it was decided, as our next objective, to study the use of the modified Julia reaction using more complex substrates for the synthesis of a 20-deoxybryostatin. Since the complexity and

steric hindrance of the substrates will affect the efficiency of this assembly process,[3b,11] it was not clear, at this stage, whether a properly convergent synthesis could be developed. In the event, this work led to the first synthesis of a 20-deoxybryostatin and is described in full in the following paper.[33] During the course of these studies, the C17-C27 benzothiazolylsulfone **87** was prepared and was found to undergo a modified Julia reaction with the aldehyde **35** to give the (*E*)-alkene **88** with excellent stereoselectivity, see Scheme 14. This alkene corresponds to the target C11-C27 fragment **5** of a 20-deoxybryostatin, see Figure 2, and could be incorporated into a total synthesis as outlined in Figure 2, although this option has not yet been investigated.[33]



Scheme 14 Synthesis of a C11-C27 fragment Reagents and conditions i, **87**, LiHMDS, THF, –78 °C to –60 °C, 30 min, add **35**, –78 °C, 20 min, rt (53%).

Experimental

General experimental details

Flash column chromatography was performed using Merck silica gel (60H; 40-60μ, 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 CaH_2 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^+) and atmospheric pressure chemical ionisation in the positive or negative mode ($APCI^+$ or $APCI^-$). Low 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.

(1*RS*,2*RS*)-2-{(2*E*,4*R*)-6-[(*Z*)-2-*tert*-Butyldiphenylsilyloxyethylidene]-1,1-dimethyl-4-triethylsilyloxynona-2,8-dien-1-yl}-1,3-dithiane-1-oxide (26). An aliquot (0.85 mL, 0.12 mmol) of a solution of *m*-chloroperoxybenzoic acid (70% w/w, 83 mg, 0.34 mmol) in DCM (2.5 mL) was added to the dithiane **25** (84 mg, 0.13 mmol) in DCM (1 mL) at 0 °C and the mixture warmed to r.t. before DCM (10 mL) and saturated aqueous sodium bisulfite (10 mL) were added. The aqueous layer was extracted with DCM (2 × 10 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (gradient elution 8.5:1 light petroleum:ether to ethyl acetate) gave the *title compound* **26** as a viscous, colourless oil (67 mg, 78%) as four diastereoisomers, ratio 9:9:1:1, R_f = 0.43 (ethyl acetate), $[\alpha]_D^{28}$ +0.4 (*c* 15.8, $CHCl_3$) (Found: M^+ + Na, 719.3412. $C_{39}H_{60}O_3Na_1S_2Si_2$ requires M, 719.3415); ν_{max}/cm^{-1} 3064, 2952, 2924, 2868, 1469, 1460, 1427, 1236, 1108, 1049, 1041, 1007, 973, 912, 820 and 738; δ_H (400 MHz, $CDCl_3$) major epimers 0.42 (6 H, q, *J* 8.0, 3 × $SiCH_2$), 0.79(2) (each 4.5 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 0.97 [9 H, s, $SiC(CH_3)_3$], 1.19, 1.20, 1.21, 1.23 (each 1.5 H, s, 1′-CH_3), 1.91 and 1.92 (each 0.5 H, dd, *J* 13.4, 6.3, 5′-H), 2.03 (1 H, dd, *J* 13.4, 6.9, 5′-H′), 2.06 and 2.27 (each 1 H, m, 5-H), 2.33-2.50 (2 H, m, 4-H_2), 2.57 (1 H, m, 6-H), 2.68 (2 H, d, *J* 6.7, 7′-H_2), 3.27 (1 H, m, 6-H′), 3.38 (1 H, s, 2-H), 4.00 (1 H, m, 4′-H), 4.17 (2 H, d, *J* 6.1, 2′′-H_2), 4.96 (1 H, d, *J* 16.8, 9′-H), 4.97 (1 H, d, *J* 10.4, 9′-H′), 5.23 and 5.26 (each 0.5 H, dd, *J* 15.7, 6.7, 3′-H), 5.41 (1 H, t, *J* 6.1, 1′′-H), 5.53 and 5.56 (each 0.5 H, d, *J* 15.7, 2′-H), 5.69 (1 H, m, 8′-H), 7.25-7.38 (6 H, m, ArH) and 7.57-7.65 (4 H, m, ArH); δ_C (100 MHz, $CDCl_3$) major epimers 3.7(2), 5.8, 18.1, 23.8, 24.1, 25.8, 26.7, 27.0, 28.8, 29.0, 29.4(2), 38.8, 39.7, 41.4, 54.6(2), 60.2, 71.4, 71.5, 75.3, 75.4, 115.3, 126.6, 127.0, 128.5, 130.6, 130.7, 132.9(2), 133.7, 134.0, 134.5, 134.6 and 135.4; *m/z* (ES^+) 719.2 (M^+ + 23, 100%), 714.2 (M^+ + 1, 44) and 565.1 (13). The second fraction was mixture of the corresponding diastereoisomeric dithiane-1,3-dioxides (8 mg, 10%), R_f = 0.20 (ethyl acetate), $[\alpha]_D^{28}$ 0.0 (*c* 7.5, $CHCl_3$) (Found: M^+ + Na, 735.3384. $C_{39}H_{60}O_4NaS_2Si_2$ requires M, 735.3369); ν_{max}/cm^{-1} 3067, 2954, 2927, 2873, 1470, 1462, 1427, 1387, 1360, 1110, 1046, 823, 739 and 702; *m/z* (ES^+) 736 (M^+ + 23, 100%), 730 (M^+ + 18, 25) and 621 (56).

(1*RS*,2*RS*)-2-[(2*E*)-But-2-enyl]-2-{(2*E*,4*R*)-6-[(*Z*)-2-*tert*-butyldiphenylsilyloxyethylidene]-1,1-dimethyl-4-triethylsilyloxynona-2,8-dienyl}-1,3-dithiane-1-oxide (27). Lithium di-isopropylamide (1.8 M in THF/heptanes/ethylbenzene, 0.061 mL, 0.11 mmol)) was added to the dithiane-1-oxide **26** (64 mg, 0.092 mmol) in THF (0.61 mL) and HMPA (43 μL, 0.18 mmol) at –78 °C and the solution stirred at –78 °C for 1 h. (*E*)-1-Bromobut-2-ene (85% w/w, 14 μL, 0.14 mmol) was added and the mixture was stirred at –78 °C for 30 min and at rt for 1 h. Ethyl acetate (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The

organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue gave the *title compound* **27** a viscous, pale yellow oil (35 mg, 50%) as a mixture of diastereoisomers (^{1}H NMR), R_f = 0.57 (ethyl acetate) (Found: M^+ + Na, 773.3891. $C_{43}H_{66}O_3NaS_2Si_2$ requires M, 773.3884); ν_{max}/cm^{-1} 2954, 2927, 2873, 1426, 1388, 1360, 1237, 1111, 1053, 1005, 973, 823, 739 and 702; δ_H (400 MHz, $CDCl_3$) 0.41 and 0.42 (each 3 H, q, *J* 7.9, 3 × $SiCH_2$), 0.79(2) (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.97 [9 H, s, $SiC(CH_3)_3$], 1.13 and 1.24 (each 3 H, s, 1′-CH_3), 1.55-1.70 (3 H, m, 4′′-H_3), 1.84-2.09 (3 H, m, 5′-H_2, 5-H), 2.10-2.29 (2 H, m, 4-H, 5-H′), 2.35-3.06 (7 H, m, 6-H_2, 4-H′, 1′′-H_2, 7′-H_2), 3.99 (1 H, m, 4′-H), 4.12-4.28 (2 H, m, 2′′′-H_2), 4.92-5.03 (2 H, m, 9′-H_2), 5.20 and 5.24 (each 0.5 H, dd, *J* 15.7, 6.8, 3′-H), 5.40 (1 H, m, 1′′′-H), 5.44-5.84 (4 H, m, 2′-H, 2′′-H, 3′′-H, 8′-H), 7.25-7.38 (6 H, m, ArH) and 7.57-7.65 (4 H, m, ArH); *m/z* (ES^+) 773.6 (M^+ + 23, 100%). The starting dithiane monoxide **26** (26 mg, 40%) was also isolated.

Methyl (2*Z*,5*R*)-3-prop-2-enyl-6-(4-methoxybenzyloxy)-5-triethylsilyloxyhex-2-enoate (29).

Imidazole (260 mg, 3.85 mmol) and triethylsilyl chloride (0.26 mL, 1.55 mmol) were added to the hydroxyester **28** (410 mg, 1.44 mmol) in DCM (6.8 mL) and the solution stirred for 2 h at rt. Water (30 mL) and DCM (30 mL) were added and the aqueous phase extracted with DCM (2 × 30 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the *title compound* **29** (510 mg, 82%) as a colourless oil, R_f = 0.63 (1:1 light petroleum:ether), $[\alpha]_D^{27}$ +66 (*c* 1.2, $CHCl_3$) (Found: M^+ + Na, 457.2376. $C_{24}H_{38}O_5NaSi$ requires M, 457.2381); ν_{max}/cm^{-1} 2952, 2908, 2875, 1718, 1644, 1613, 1513, 1248, 1192, 1180, 1143, 1099, 1035, 1004 and 742; δ_H (500 MHz, $CDCl_3$) 0.54 (6 H, q, m, 3 × $SiCH_2$), 0.89 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 2.58 (1 H, dd, *J* 12.5, 8.5, 4-H), 2.94 (1 H, dd, *J* 16.4, 6.9, 1′-H), 2.97-3.03 (2 H, m, 4-H′, 1′-H′), 3.37 (2 H, d, *J* 5.0, 6-H_2), 3.64 and 3.78 (each 3 H, s, OCH_3), 4.14 (1 H, m, 5-H), 4.44 and 4.45 (each 1 H, d, *J* 11.6, Ar*H*CH), 5.06 (1 H, d, *J* 17.0, 3′-H), 5.10 (1 H, d, *J* 10.1, 3′-H′), 5.70 (1 H, s, 2-H), 5.74 (1 H, ddt, *J* 17.0, 10.2, 6.9, 2′-H) and 6.85 and 7.24 (each 2 H, d, *J* 7.1, ArH); δ_C (125 MHz, $CDCl_3$) 4.9, 6.9, 37.4, 44.2, 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 (M^+ + 23, 100%) and 377 (14).

Methyl (2*Z*,5*R*)-3-(2-hydroxyethyl)-6-(4-methoxybenzyloxy)-5-triethylsilyloxyhex-2-enoate (30).

N-Methylmorpholine-*N*-oxide (3.79 g, 32.4 mmol) was added to the alkene **29** (12.9 g, 29.7 mmol) in acetone (360 mL) and water (51 mL) and the mixture stirred until homogeneous. Osmium tetraoxide (0.60 g, 2.35 mmol) in water (35 mL) and *tert*-butanol (35 mL) were added and the mixture was stirred for 4 h. Saturated aqueous sodium bisulfite (750 mL) was added and the mixture stirred for 20 min. The aqueous layer was extracted with ethyl acetate (5 × 500 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (4:1 then 8:1 light petroleum:ether) of the residue gave methyl (2*Z*,5*RS*)-3-[(2*R*)-3-(4-methoxybenzyloxy)-2-triethylsilyloxypropyl]-5,6-dihydroxyhex-2-enoate as a pale yellow oil (10.6 g, 76%), as a mixture of epimers, R_f = 0.10 (1:2 light petroleum:ether), $[\alpha]_D^{27}$ +21 (*c* 9.9, $CHCl_3$) (Found: M^+ + Na, 491.2444. $C_{24}H_{40}O_7NaSi$ requires M, 491.2436); ν_{max}/cm^{-1} 3421, 2952, 2879, 1717, 1644, 1613, 1514, 1458, 1434, 1248, 1197, 1179, 1148, 1096, 1037, 1008, 820 and 743; δ_H (400 MHz, $CDCl_3$) 0.48 and 0.49 (each 3 H, q, *J* 7.9, 3 × $SiCH_2$), 0.82 and 0.83 (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 2.17-2.37 (2 H, m, 1′-H_2), 2.51 (0.5 H, dd, *J* 12.7, 8.9, 4-H), 2.78 (0.5 H, dd, *J* 12.7, 8.1, 4-H), 2.86 (0.5 H, dd, *J* 12.7, 4.8, 4-H′), 3.08 (0.5 H, dd, *J* 12.7, 3.9, 4-H′), 3.30-3.42 (3 H, m, 3′-H_2, 6-H), 3.53 (1 H, m, 6-H′), 3.59 and 3.60 (each 1.5 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 3.83 (1 H, m, 5-H), 4.09 and 4.18 (each 0.5 H, m, 2′-H), 4.37 (1 H, s, $ArCH_2$), 4.38 and 4.39 (each 0.5 H, d, *J* 11.6, Ar*H*CH), 5.75 (1 H, m, 2-H), 6.79 (2 H, d, *J* 8.7, ArH) and 7.15-7.20 (2 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 4.8(2), 6.8(2), 15.3, 29.2, 37.0, 37.3, 43.6, 44.4, 51.0, 55.3, 66.4, 66.5, 69.8, 70.3, 71.4, 71.7, 73.0(2), 74.5, 74.7, 113.7, 119.1, 119.2, 129.4, 130.3, 157.4, 158.5, 159.1 and 166.4; *m/z* (ES^+) 491.3 (M^+ + 23, 100%), 289.2 (14), 271.3 (15) and 145.3 (52).

Sodium periodate (10.3 g, 48.1 mmol) was added to a mixture of these diols (5.02 g, 10.7 mmol) in THF (140 mL), methanol (140 mL) and water (175 mL) at 0 °C and the mixture was stirred at 0 °C for 1 h. Sodium borohydride (1.21 g, 32.0 mmol) was added with cooling to maintain the reaction temperature < 10 °C. After 1 h, brine (300 mL) was added and the mixture was allowed to warm to rt then extracted with ether (4 × 500 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (2:1 then 1:1 light petroleum:ether) afforded the *title compound* **30** as a clear, colourless oil (3.55 g, 76%), R_f = 0.48 (1:2 light petroleum:ether), $[\alpha]_D^{27}$ +46 (*c* 5.4, $CHCl_3$) (Found: M^+ + Na, 461.2331. $C_{23}H_{38}O_6NaSi$ requires M, 461.2330); ν_{max}/cm^{-1} 3447, 2951, 2879, 1713, 1644, 1613, 1514, 1434, 1248, 1194, 1179, 1145, 1104, 1037, 1008 and 820; δ_H (400 MHz, $CDCl_3$) 0.49 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.83 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.89 (1 H, br. s, 2′-OH), 2.41 (2 H, td, *J* 6.2, 0.9, 1′-H_2), 2.59 (1 H, dd, *J* 12.6, 8.5, 4-H), 2.97 (1 H, ddd, *J* 12.6, 4.4, 0.8, 4-H′), 3.33 (2 H, d, *J* 5.0, 6-H_2), 3.60 (3 H, s, OCH_3), 3.64-3.72 (2 H, m, 2′-H_2), 3.73 (3 H, s, OCH_3), 4.14 (1 H, m, 5-H), 4.38 and 4.39 (each 1 H, d, *J* 11.6, Ar*H*CH), 5.72 (1 H, m, 2-H) and 6.79 and 7.18 (each 2 H, d, *J* 8.7, ArH); δ_C (100 MHz, $CDCl_3$) 4.9, 6.8, 37.1, 43.2, 50.9, 55.2, 60.5, 71.5, 72.9, 74.7, 113.7, 118.4, 129.4, 130.4, 158.6, 159.1 and 166.4; *m/z* (ES^+) 461.4 (M^+ + 23, 100%), 179.1 (43) and 145.3 (25).

Methyl (2*Z*,5*R*)-3-(2-Benzyloxymethoxyethyl)-6-(4-methoxybenzyloxy)-5-triethylsilyloxyhex-2-enoate (31).

Di-isopropylethylamine (10 mL, 57 mmol) was added to the alcohol **30** (5.70 g, 13.0 mmol) in THF (29 mL) and the solution cooled to 0 °C. Benzyloxymethyl chloride (approx 60% w/w, 4.50 mL, 19.4 mmol) was added and the mixture was stirred at rt for 16 h. Ether (100 mL) and saturated aqueous sodium bicarbonate (100 mL) were added and the aqueous layer was extracted with ether (2 × 100 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (10:1 to 3:1 light petroleum:ether) gave the *title compound* **31** as a clear, colourless oil (6.68 g, 93%), R_f = 0.52

(2:1 light petroleum:ether), $[\alpha]_D^{27}$ +36 (*c* 20.6, $CHCl_3$) (Found: M^+ + Na, 581.2905, $C_{31}H_{46}O_7NaSi$ requires M, 581.2905); ν_{max}/cm^{-1} 2951, 2879, 1717, 1644, 1613, 1514, 1456, 1434, 1367, 1248, 1194, 1150, 1111, 1042, 820 and 740; δ_H (400 MHz, $CDCl_3$) 0.48 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.82 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 2.43-2.49 (2 H, m, 1′-H_2), 2.58 (1 H, dd, *J* 12.5, 8.5, 4-H), 2.95 (1 H, dd, *J* 12.5, 4.4, 4-H′), 3.31 (2 H, d, *J* 5.0, 6-H_2), 3.58 (3 H, s, OCH_3), 3.62-3.65 (2 H, m, 2′-H_2), 3.71 (3 H, s, OCH_3), 4.07 (1 H, m, 5-H), 4.38 and 4.39 (each 1 H, d, *J* 11.7, Ar*H*CH), 4.50 (2 H, s, $PhCH_2$), 4.65 (2 H, s, OCH_2O), 5.70 (1 H, m, 2-H), 6.78 and 7.18 (each 2 H, d, *J* 8.7, ArH) and 7.15-7.29 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 4.9, 6.9, 37.2, 39.8, 50.9, 55.2, 65.6, 69.5, 71.7, 72.9, 74.8, 94.5, 113.6, 117.7, 127.7, 127.9, 128.4, 129.3, 130.5, 137.8, 158.8, 159.1 and 166.6; *m/z* (ES^+) 581.4 (M^+ + 23, 100%), 197.2 (13) and 151.3 (18).

(2*Z*,5*R*)-3-(2-Benzyloxymethoxyethyl)-6-(4-methoxybenzyloxy)-5-triethylsilyloxyhex-2-en-1-ol (32).

Di-isobutylaluminium hydride (1.0 M in heptanes, 25 mL, 25 mmol) was added to the ester **31** (6.40 g, 11.5 mmol) in toluene (100 mL) at –78 °C and the mixture stirred at –78 °C for 45 min. Methanol (1.5 g, 47 mmol) in toluene (20 mL) was added and the mixture stirred for 10 min then allowed to warm to 0 °C. Saturated aqueous Rochelle's salt (100 mL) was added and the mixture was allowed to warm to rt, with vigorous stirring over 1 h. More saturated aqueous Rochelle's salt (400 mL) and DCM (400 mL) were added and the aqueous layer was extracted with DCM (2 × 400 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (3:1 then 1:1 light petroleum:ether) of the residue gave the *title compound* **32** as a clear, colourless oil (5.38 g, 89%), R_f = 0.19 (1:1 light petroleum:ether), $[\alpha]_D^{27}$ +4.7 (*c* 1.7, $CHCl_3$) (Found: M^+ + Na, 553.2957. $C_{30}H_{46}O_6NaSi$ requires M, 553.2956); ν_{max}/cm^{-1} 3452, 2951, 2875, 1613, 1513, 1460, 1248, 1168, 1106, 1037, 1008, 820 and 737; δ_H (400 MHz, $CDCl_3$) 0.50 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.84 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 2.23-2.38 (4 H, m, 4-H_2, 1′-H_2), 2.36 (1 H, br. s, OH), 3.26 (1 H, dd, *J* 9.7, 5.9, 6-H), 3.33 (1 H, dd, *J* 9.7, 4.8, 6-H′), 3.61 (2 H, t, *J* 6.9, 2′-H_2), 3.72 (3 H, s, OCH_3), 3.84 (1 H, m, 5-H), 3.92 (1 H, dd, *J* 12.3, 7.3, 1-H), 4.02 (1 H, dd, *J* 12.3, 7.0, 1-H′), 4.38 and 4.39 (each 1 H, d, *J* 10.5, ArHC*H*), 4.50 (2 H, s, $PhCH_2$), 4.66 (2 H, s, OCH_2O), 5.66 (1 H, m, 2-H), 6.79 and 7.17 (each 2 H, d, *J* 8.7, ArH) and 7.18-7.29 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 4.8, 6.8, 35.5, 36.7, 55.3, 58.1, 66.5, 69.4, 69.6, 73.1, 73.9, 94.6, 113.7, 127.7, 127.8, 128.4(2), 129.4, 130.1, 137.9(2) and 159.2; *m/z* (ES^+) 553.7 (M^+ + 23, 100%), 289.2 (15), 243.2 (19), 153.3 (17) and 145.3 (36).

(4*Z*,2*R*)-4-(2-Benzyloxymethoxyethyl)-1-(4-methoxybenzyloxy)-2-triethylsilyloxy-6-tri-isopropylsilyloxyhex-4-ene (33).

Imidazole (1.88 g, 27.6 mmol) was added to the alcohol **32** (5.04 g, 9.53 mmol) in DCM (55 mL) and the mixture was cooled to 0 °C before the dropwise addition of tri-isopropylsilyl chloride (2.70 mL, 12.6 mmol). The mixture was stirred at rt for 16 h and DCM (50 mL) and water (50 mL) were added. The aqueous layer was extracted with DCM (2 × 100 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (9:1 light petroleum:ether) of the residue gave the *title compound* **33** as a clear, colourless oil (6.42 g, 98%), R_f = 0.32 (5:1 light petroleum:ether), $[\alpha]_D^{27}$ +0.4 (*c* 14.0, $CHCl_3$) (Found: M^+ + NH_4, 704.4747. $C_{39}H_{70}O_6NSi_2$ requires M, 704.4736); ν_{max}/cm^{-1} 2941, 2866, 1613, 1514, 1460, 1248, 1171, 1106, 1083, 1039, 1011, 884 and 739; δ_H (400 MHz, $CDCl_3$) 0.50 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.85 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.94-1.05 [21 H, m, 3 × $SiCH(CH_3)_2$], 2.11 (1 H, dd, *J* 13.6, 7.2, 3-H), 2.23-2.32 (3 H, m, 3-H′, 1′-H_2), 3.24 and 3.25 (each 1 H, dd, *J* 9.7, 5.2, 1-H), 3.61 (2 H, t, *J* 7.1, 2′-H_2), 3.72 (3 H, s, OCH_3), 3.81 (1 H, m, 2-H), 4.18 (1 H, dd, *J* 13.1, 5.8, 6-H), 4.22 (1 H, dd, *J* 13.1, 6.4, 6-H′), 4.36 and 4.37 (each 1 H, d, *J* 12.3, Ar*H*CH), 4.52 (2 H, s, $PhCH_2$), 4.67 (2 H, s, OCH_2O), 5.37-5.43 (1 H, m, 5-H), 6.79 and 7.17 (each 2 H, d, *J* 8.7, ArH) and 7.19-7.30 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 4.9, 6.9, 12.0, 18.0, 36.4, 37.4, 55.2, 60.4, 66.8, 69.3, 70.8, 72.9, 74.0, 94.6, 113.7, 127.6, 127.9, 128.4, 129.1, 129.5, 130.5, 133.7, 138.0 and 159.1; *m/z* (ES^+) 704.6 (M^+ + 18, 100%), 662.5 (5), 214.2 (12) and 151.2 (15).

(4*Z*,2*R*)-4-(2-Benzyloxymethoxyethyl)-2-triethylsilyloxy-6-tri-isopropylsilyloxyhex-4-en-1-ol (34).

An aqueous pH7 phosphate buffer (5.10 mL) was added to the PMB-ether **33** (4.88 g, 7.10 mmol) in DCM (97 mL) and the mixture cooled to 0 °C. Dichlorodicyanoquinone (1.71 g, 7.53 mmol) was added in one portion with rapid stirring and the mixture was stirred vigorously for 1 h at 0 °C then at 10 °C for 2 h. Dichloromethane (250 mL) and saturated aqueous sodium bicarbonate (250 mL) were added and the aqueous layer was extracted with DCM (2 × 250 mL). The organic extracts were washed with saturated aqueous sodium bisulfite (250 mL) and saturated aqueous sodium bicarbonate (250 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in methanol (150 mL) and the solution cooled to 0 °C. Sodium borohydride (0.41 g, 10.8 mmol) was added to reduce the 4-methoxybenzaldehyde side-product and the mixture stirred at 0 °C for 20 min. After concentrating under reduced pressure (to *ca*. 20 mL), ether (100 mL) and water (100 mL) were added and the aqueous layer was extracted with ether (2 × 100 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (10:1 then 4:1 light petroleum:ether) of the residue gave the *title compound* **34** as a clear, colourless oil (2.56 g, 64%), R_f = 0.40 (2:1 light petroleum:ether);, $[\alpha]_D^{27}$ –7.1 (*c* 14.0, $CHCl_3$) (Found: M^+ + Na, 589.3715. $C_{31}H_{58}O_5NaSi_2$ requires M, 589.3715); ν_{max}/cm^{-1} 3468, 2944, 2867, 1463, 1383, 1241, 1166, 1109, 1058, 883 and 744; δ_H (500 MHz, $CDCl_3$) 0.41 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.75 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.83-0.94 [21 H, m, 3 × $SiCH(CH_3)_2$], 2.05-2.23 (4 H, m, 3-H_2, 1′-H_2), 2.42 (1 H, m, OH), 3.21 (1 H, ddd, *J* 11.5, 7.4, 4.3, 1-H), 3.31 (1 H, dt, *J* 11.5, 5.9, 1-H′), 3.49 (2 H, t, *J* 6.9, 2′-H_2), 3.65 (1 H, m, 2-H), 4.04 and 4.06 (each 1 H, dd, *J* 12.5, 6.7, 6-H), 4.39 (2 H, s, $PhCH_2$), 4.54 (2 H, s, OCH_2O), 5.34 (1 H, t, *J* 6.7, 5-H) and 7.05-7.17 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) 4.9, 6.9, 12.0, 18.0, 35.1, 37.4, 59.8, 65.3, 66.7, 69.4, 71.4, 94.6, 127.7, 127.9, 128.4, 128.6, 135.3 and 137.9; *m/z* (ES^+) 589.4 (M^+ + 23, 100%) and 584.3 (M^+ + 18, 14).

2-[(2*E*,6*Z*,4*R*)-6-(2-Benzyloxymethoxyethyl)-1,1-dimethyl-4-triethylsilyloxy-8-tri-isopropylsilyloxyocta-2,6-dienyl]-1,3-dithiane (36).

Pyridine (0.18 ml, 2.22 mmol) and the Dess-Martin periodinane (0.167 g, 0.394 mmol) were added to the alcohol **34** (0.107 g, 0.189 mmol) in DCM (1.3 mL) and the mixture was stirred for 3 h at rt. Ether (10 mL) and a mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium bisulfite (1:1, 10 mL) were added and the aqueous layer was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the aldehyde **35**, a a yellow oil (0.13 g) that was used directly in the next step.

Lithium hexamethyldisilazide (1.0 M in toluene, 0.20 mL) was added to the sulfone **24** (73 mg, 0.20 mmol) in THF (1.9 mL) at −78 °C and the solution stirred for 20 min. The aldehyde **35** (0.13 g, from 0.189 mmol of the alcohol **34**) in THF (1.2 mL) was added rapidly and the mixture was immediately allowed to warm to rt. After stirring for 1 h, ether (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added and the aqueous layer extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (100:1 then 50:1 light petroleum:ether) of the residue gave the *title compound* **36** as a pale yellow oil (71 mg, 52%), R_f = 0.43 (5:1 light petroleum:ether), $[\alpha]_D^{27}$ –2.2 (*c* 10.6, $CHCl_3$) (Found: M^+ + Na, 745.4127. $C_{39}H_{70}O_4NaS_2Si_2$ requires M, 745.4146); ν_{max}/cm^{-1} 2943, 2868, 1463, 1421, 1385, 1365, 1243, 1166, 1106, 1063, 882 and 743; δ_H (400 MHz, $CDCl_3$) 0.48 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.83 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.92-1.05 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.08 and 1.10 (each 3 H, s, 1′-CH_3), 1.67 and 1.95 (each 1 H, m, 5-H), 2.09 (1 H, dd, *J* 13.4, 6.4, 5′-H), 2.22 (1 H, dd, *J* 13.4, 7.0, 5′-H′), 2.26 (2 H, t, *J* 7.0, 1′′-H_2), 2.70-2.80 (4 H, m, 2-H_2, 4-H_2), 3.59 (2 H, t, *J* 7.1, 2′′-H_2), 3.89 (1 H, s, 2-H), 4.07 (1 H, m, 4′-H), 4.13-4.24 (2 H, m, 8′-H_2), 4.50 (2 H, s, $PhCH_2$), 4.65 (2 H, s, OCH_2O), 5.30 (1 H, dd, *J* 15.6, 7.0, 3′-H), 5.36 (1 H, t, *J* 6.1, 7′-H), 5.57 (1 H, dd, *J* 15.6, 0.8, 2′-H) and 7.16-7.28 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 4.9, 6.9, 12.0, 18.0, 25.0, 25.4, 26.0, 31.2, 37.6, 40.4, 40.5, 60.5, 60.8, 66.8, 69.3, 73.1, 94.6, 127.6, 127.9, 128.4, 129.3, 130.8, 133.5, 136.9 and 138.0; *m/z* (ES^+) 745.8 (M^+ + 23, 100%), 553.2 (10), 197.3 (17) and 151.3 (38).

(1*RS*,2*RS*)-2-[(2*E*,6*Z*,4*R*)-6-(2-Benzyloxymethoxyethyl)-1,1-dimethyl-4-triethylsilyloxy-8-tri-isopropylsilyloxyocta-2,6-dien-1-yl]-1,3-dithiane-1-oxide (38).

An aliquot (1.08 mL) of a solution of *m*-chloroperoxybenzoic acid (70% w/w, 101 mg, 0.410 mmol) in DCM (2.0 mL) was added to the dithiane **36** (151 mg, 0.207 mmol) in DCM (1.7 mL) at 0 °C with monitoring the consumption of starting material by TLC during the addition. After warming the reaction mixture to rt, DCM (10 mL) and saturated aqueous sodium bisulfite (10 mL) were added the aqueous layer was extracted with DCM (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (gradient elution ether to ethyl acetate) of the residue gave the *title compound* **38** as a mixture of diastereoisomers, ratio 3:3:1:1, as a clear, colourless oil (146 mg, 95%), R_f = 0.53 (ethyl acetate), $[\alpha]_D^{28}$ –2.4 (*c* 8.5, $CHCl_3$) (Found: M^+ + Na, 761.4104. $C_{39}H_{70}O_5NaS_2Si_2$ requires M, 761.4095); ν_{max}/cm^{-1} 2944, 2865, 1464, 1425, 1386, 1366, 1238, 1166, 1105, 1051, 1042, 974 and 822; δ_H (400 MHz, $CDCl_3$) major diastereoisomers 0.51 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.86 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.95-1.07 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.27, 1.28 and 1.31(2) (each 1.5 H, s, 1′-CH_3), 2.03-2.18 (2 H, m, 5-H, 5′-H), 2.19-2.36 (4 H, m, 1′′-H_2, 5-H′, 5′-H′), 2.41-2.53 (2 H, m, 4-H_2), 2.60 (0.5 H, td, *J* 13.0, 3.2, 6-H), 2.61 (0.5 H, td, *J* 13.2, 3.3, 6-H), 3.23-3.32 (1 H, m, 6-H′), 3.43 (1 H, s, 2-H), 3.62 (2 H, t, *J* 7.1, 2′′-H_2), 4.12 (1 H, m, 4′-H), 4.16-4.27 (2 H, m, 8′-H_2), 4.52 (2 H, s, $PhCH_2$), 4.68 (2 H, s, OCH_2O), 5.34-5.48 (2 H, m, 3′-H, 7′-H), 5.63(2) (each 0.5 H, dd, *J* 15.6, 0.8, 2′-H) and 7.17-7.33 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) major diastereoisomers 3.8, 3.9(2), 11.0, 17.0, 23.9, 24.3, 26.6, 27.1, 28.9(2), 29.5(2), 36.6, 39.3(2), 39.8, 54.6, 54.7, 59.5, 65.7(2), 71.8(2), 75.3, 75.4, 93.5, 126.6, 126.8, 127.4, 128.4, 130.7, 130.9, 132.4, 134.0, 134.2 and 136.9; *m/z* (ES^+) 761.5 (M^+ + 23, 100%), 397.6 (39), 389.6 (38) and 211.1 (21).

(1*RS*,2*RS*)-2-[(2*E*,6*Z*,4*R*)-6-(2-Benzyloxymethoxyethyl)-1,1-dimethyl-4-triethylsilyloxy-8-tri-isopropylsilyloxyocta-2,6-dien-1-yl]-2-[(2*E*)-but-2-enyl]-1,3-dithiane-1-oxide (39).

Lithium di-isopropylamide (1.8 M in THF/heptanes/ethylbenzene, 0.13 mL, 0.23 mmol) was added dropwise to the dithiane-1-oxide **38** (0.146 g, 0.197 mmol) in THF (1.3 mL) and hexamethyl phosphoric triamide (70 µL, 0.39 mmol) at −78 °C and the solution was stirred for 30 min at −78 °C. (2*E*)-1-Bromobut-2-ene (85% w/w, 30 µL, 0.25 mmol) was added and the solution stirred at −78 °C for 30 min and at rt 30 min. Ethyl acetate (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The organic extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (gradient elution ether to ethyl acetate) gave the *title compound* **39** as a viscous, colourless oil (0.11 g, 71%), a mixture of diastereoisomers, R_f = 0.70 (ethyl acetate), $[\alpha]_D^{29}$ –8.6 (*c* 7.4, $CHCl_3$) (Found: M^+ + Na, 815.4558. $C_{43}H_{76}O_5NaS_2Si_2$ requires M, 815.4565); ν_{max}/cm^{-1} 2942, 2865, 1460, 1385, 1362, 1236, 1161, 1105, 1054, 1038, 971, 882 and 741; δ_H (400 MHz, $CDCl_3$) major diastereoisomers 0.46-0.55 (6 H, m, 3 × $SiCH_2$), 0.86 and 0.87 (each 4.5 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.96-1.08 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.20(2) (each 1.5 H, s, 1′-CH_3), 1.32 (3 H, s, 1′-CH_3′), 1.55-1.74 (3 H, m, 4′′-H_3), 1.95-3.08 (12 H, m, 4-H_2, 5-H_2, 6-H_2, 5′-H_2, 1′′-H_2, 1′′′-H_2), 3.62 and 3.63 (each 1 H, t, *J* 7.1, 2′′′-H_2), 4.12 (1 H, m, 4′-H), 4.16-4.29 (2 H, m, 8′-H_2), 4.53 (2 H, s, CH_2Ph), 4.68 (2 H, s, OCH_2O), 5.29-5.45 (2 H, m, 3′-H, 7′-H), 5.47-5.81 (2 H, m, 2′′-H, 3′′-H), 5.86 (1 H, m, 2′-H) and 7.18-7.33 (5 H, m, ArH); *m/z* (ES^+) 815.6 (M^+ + 23, 100%), 761.5 (21), 424.4 (86) and 416.4 (36). Some unreacted starting material **38** (20 mg, 13%) was also isolated.

2-[(2*E*,6*Z*,4*R*)-6-(2-Benzyloxymethoxyethyl)-1,1-dimethyl-4-triethylsilyloxy-8-tri-isopropylsilyloxyocta-2,6-dien-1-yl]-2-[(2*E*)-but-2-enyl]-1,3-dithiane (37).

Hexamethyl phosphoric triamide (0.22 mL) was added to the dithiane **36** (0.191 g, 0.264 mmol) in THF (2.6 mL) and the solution cooled to −78 °C. *tert*-Butyllithium (1.6 M in pentane,

0.26 mL, 0.42 mmol) was added and the solution was stirred for 15 min, before the dropwise addition of (2*E*)-1-bromobut-2-ene (85% w/w, 0.11 mL, 9.09 mmol). The solution was stirred for 30 min at −78 °C, methanol (0.1 mL) was added and the solution was allowed to warm to rt over 10 min. Ether (10 mL) and saturated aqueous sodium bicarbonate (10 mL) were added and the aqueous layer was extracted with ether (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (20:1 then 10:1 light petroleum:ether) of the residue gave the title compound **37** as a pale yellow oil (72 mg, 35%), followed by unreacted starting material **36** (39 mg, 20%).

P_2I_4 (38 mg, 0.067 mmol) was added to a foil-wrapped round-bottomed flask under N_2 followed by DCM (1.8 mL) and Et_3N (40 μL, 0.29 mmol). The dithiane-1-oxide **39** (93 mg, 0.118 mmol) in DCM (1.8 mL) was added and the mixture was stirred at rt for 40 min. DCM (10 mL) and saturated aqueous sodium bisulfite (6 mL) were added and the aqueous layer was extracted with DCM (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (20:1 to 5:1 light petroleum:ether) of the residue gave the *title compound* **37** as a clear, colourless oil (64 mg, 70%), R_f = 0.50 (5:1 light petroleum:ether), $[\alpha]_D^{29}$ −1.6 (*c* 8.8, $CHCl_3$) (Found: M^+ + Na, 799.4619. $C_{43}H_{76}O_4NaS_2Si_2$ requires M, 799.4616); ν_{max}/cm^{-1} 2941, 2866, 1463, 1455, 1383, 1252, 1164, 1105, 1064, 973, 882 and 743; δ_H (400 MHz, $CDCl_3$) 0.51 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.86 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.96-1.07 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.16 and 1.18 (each 3 H, s, 1′-CH_3), 1.58-1.64 (3 H, m, 4′′-H_3), 1.71 and 1.88 (each 1 H, m, 5-H), 2.12 (1 H, dd, *J* 13.4, 6.1, 5′-H), 2.24 (1 H, dd, *J* 13.4, 7.1, 5′-H′), 2.29 (2 H, t, *J* 7.2, 1′′′-H), 2.61 (2 H, dt, *J* 14.4, 5.0, 4-H, 6-H), 2.68 (1 H, m, 1′′-H), 2.71-2.88 (3 H, m, 4-H′, 6-H′, 1′′-H′), 3.62 (2 H, t, *J* 7.2, 2′′′-H_2), 4.10 (1 H, m, 4′-H), 4.17-4.29 (2 H, m, 8′-H_2), 4.53 (2 H, s, $PhCH_2$), 4.68 (2 H, s, OCH_2O), 5.31 (1 H, dd, *J* 15.7, 7.1, 3′-H), 5.38 (1 H, t, *J* 6.0, 7′-H), 5.42 (1 H, m, 3′′-H), 5.62 (1 H, dtq, *J* 15.3, 6.8, 1.4, 2′′-H), 5.89 (1 H, d, *J* 15.7, 2′-H) and 7.18-7.32 (5 H, m, ArH); δ_C (100 MHz), 3.9, 5.9, 11.0, 17.0, 17.1, 22.6, 23.1, 25.7, 36.6, 39.3, 39.9, 45.0, 59.5, 61.0, 65.7, 68.3, 72.3, 93.5, 125.5, 126.6, 126.9, 127.4, 128.1, 128.3, 130.1, 132.5, 135.0 and 136.9; *m/z* (ES^+) 799.5 (M^+ + 23, 100%) and 408.5 (25).

(2*E*)-(5*S*,7*R*,8*R*)-3-Benzyloxymethyl-8-*tert*-butyldimethylsilyloxy-1-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-en-5-ol (56).

Imidazole (59 mg, 0.87 mmol) and tri-isopropylsilyl chloride (0.092 mL, 0.43 mmol) were added to the diol **47** (200 mg, 0.36 mmol) in DCM (2.5 mL) and the solution stirred at rt for 2 h. Dichloromethane (20 mL) and saturated aqueous $NaHCO_3$ (20 mL) were added the aqueous phase was extracted with DCM (2 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (9:1 light petroleum:ether) gave the *title compound* **56** (231 mg, 90%) as a colourless oil, R_f = 0.16 (9:1 light petroleum:ether), $[\alpha]_D^{28}$ +8.0, (*c* 1.1, $CHCl_3$) (Found: M^+ + H, 711.4862. $C_{38}H_{75}O_6Si_3$ requires M, 711.4866); ν_{max}/cm^{-1} 3468, 2950, 2893, 2865, 1463, 1381, 1251, 1104, 1058, 1030, 883, 859, 835 and 776; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.06 and 0.07 (each 3 H, s, $SiCH_3$), 0.86-0.95 (2 H, m, CH_2Si), 0.88 [9 H, s, $SiC(CH_3)_3$], 1.02-1.16 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.09 (3 H, d, *J* 6.2, 9-H_3), 1.49 (1 H, ddd, *J* 14.1, 9.3, 2.8, 6-H), 1.57 (1 H, ddd, *J* 14.0, 9.8, 3.8, 6-H'), 2.26 (1 H, dd, *J* 13.6, 4.8, 4-H), 2.33 (1 H, dd, *J* 13.6, 7.8, 4-H'), 3.54-3.66 (3 H, m, OCH_2CH_2Si, 7-H), 3.68 (1 H, d, *J* 3.8, 5-OH), 3.83-3.92 (2 H, m, 5-H, 8-H), 3.96 and 4.01 (each 1 H, d, *J* 11.9, 3-CH), 4.32 and 4.35 (each 1 H, dd, *J* 13.1, 6.1, 1-H), 4.48 and 4.49 (each 1 H, d, *J* 11.9, PhHC*H*), 4.70 and 4.73 (each 1 H, d, *J* 6.8, OHC*H*O), 5.77 (1 H, t, *J* 6.1, 2-H) and 7.24-7.35 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3, 0.0, 13.5, 19.5(2) 19.9, 27.3, 38.6, 39.0, 61.4, 67.0, 67.9, 72.0, 73.3, 76.0, 81.4, 97.7, 129.0, 129.2, 129.8, 132.7, 136.0 and 139.7; *m/z* (ES^+) 770.5 (19%), 733.4 (M^+ + 23, 100), 711.5 (M^+ + 1, 17), 593.4 (19) and 419.2 (30).

(2*E*)-(5*S*,7*R*,8*R*)-3-Benzyloxymethyl-8-*tert*-butyldimethylsilyloxy-5-triethylsilyloxy-1-tri-isopropylsilyloxy-7-(2-trimethylsilylethoxymethoxy)non-2-ene (57).

Imidazole (25 mg, 0.37 mmol) and triethylsilyl chloride (0.031 mL, 0.18 mmol) were added to the alcohol **56** (100 mg, 0.14 mmol) in DCM (1.0 mL) and the solution stirred at rt for 90 min before the addition of DCM (10 mL) and water (10 mL). The aqueous phase was extracted with DCM (2 × 10 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (40:1 light petroleum:ether) gave the *title compound* **57** (107 mg, 92%) as a colourless oil, R_f = 0.44 (19:1 light petroleum:ether); $[\alpha]_D^{27}$ −9.3 (*c* 0.9, $CHCl_3$) (Found: M^+ + Na, 847.5583. $C_{44}H_{88}O_6Si_4Na$ requires M, 847.5550); ν_{max}/cm^{-1} 2952, 2867, 1462, 1414, 1380, 1250, 1148, 1103, 1059, 1015, 882, 860 and 835; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 × $SiCH_3$) , 0.57 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.92 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.93 (1 H, m, HC*H*Si), 1.02 (3 H, d, *J* 6.3, 9-H_3), 1.04-1.14 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.40 (1 H, ddd, *J* 13.7, 9.8, 3.2, 6-H), 1.55 (1 H, ddd, *J* 14.0, 8.8, 1.3, 6-H'), 2.23 (1 H, dd, *J* 13.3, 8.2, 4-H), 2.36 (1 H, dd, *J* 13.5, 5.4, 4-H'), 3.43 (1 H, ddd, *J* 11.1, 9.7, 6.0, OHC*H*CH_2Si), 3.53 (1 H, ddd, *J* 9.9, 4.4, 1.4, 7-H), 3.67 (1 H, ddd, *J* 11.4, 9.6, 5.4, $OHCHCH_2Si$), 3.91 (1 H, d, *J* 12.3, 3-CH), 3.95 (1 H, m, 5-H), 3.99 (1 H, d, *J* 12.1, 3-CH'), 4.02 (1 H, qd, *J* 6.3, 4.6, 8-H), 4.34 (2 H, d, *J* 5.1, 1-H_2), 4.45 (2 H, s, $PhCH_2$), 4.66 (2 H, s, OCH_2O), 5.69 (1 H, t, *J* 5.1, 2-H) and 7.24-7.34 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −3.3(2), 0.0, 6.7, 8.5, 13.5, 18.6, 19.5, 19.6, 27.3, 37.2, 39.2, 61.8, 66.6, 69.9, 70.5, 73.1, 75.7, 81.7, 97.6, 128.9, 129.2, 129.7, 132.4, 134.9 and 140.0; *m/z* (ES^+) 884.0 (85%), 847.8 (M^+ + 23, 100) and 842.9 (M^+ + 18, 33).

(4*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-4-triethylsilyloxy-2-[(*E*)-2-tri-isopropylsilyloxyethylidene]-6-(2-trimethylsilylethoxymethoxy)octan-1-ol (58).

Lithium (183 mg, 26.2 mmol) was added to naphthalene (5.03 g, 39.3 mmol) in THF (67 mL) and the mixture stirred vigorously at rt for 1 h then added dropwise to the benzyl ether **57** (3.20 g, 3.96 mmol) in THF (33 mL) at −30 °C until the reaction was complete (TLC). Water, ether (150 mL) and saturated aqueous $NaHCO_3$ (150 mL) were added and the aqueous phase was extracted with ether (2 × 150 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure.

Chromatography of the residue (9:1 light petroleum:ether) gave the *title compound* **58** (2.32 g, 81%) as a colourless oil, R_f = 0.54 (3:1 light petroleum:ether), $[\alpha]_D^{25}$ +3.3 *(c* 1.1, $CHCl_3$) (Found: M^+ + H, 735.5285. $C_{37}H_{83}O_6Si_4$ requires M, 735.5261); ν_{max}/cm^{-1} 3436, 2953, 2868, 1462, 1380, 1250, 1102, 1057, 1010, 882, 859, 835, 775 and 742; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03(2) (each 3 H, s, $SiCH_3$), 0.62 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.83-0.97 (2 H, m, CH_2Si), 0.86 [9 H, s, $SiC(CH_3)_3$], 0.95 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 1.02 (3 H, d, *J* 6.3, 8-H_3), 1.03-1.12 [21 H, m, 3 × $Si(CH(CH_3)_2]$, 1.43 (1 H, ddd, *J* 14.5, 10.1, 4.7, *5*-H), 1.66 (1 H, ddd, *J* 14.3, 6.9, 1.9, 5-H'), 2.29 (1 H, dd, *J* 13.9, 6.0, 3-H), 2.40 (1 H, dd, *J* 13.9, 5.7, 3-H'), 2.80 (1 H, t, *J* 6.2, OH), 3.46-3.52 (2 H, m, OHC*H*CH_2Si, 6-H), 3.65 (1 H, ddd, *J* 11.4, 9.8, 5.7, OHC*H*CH_2Si), 3.94-4.02 (4 H, m, 1-H_2, 4-H, 7-H), 4.27 (1 H, dd, *J* 13.2, 5.5, 2'-H), 4.31 (1 H, dd, *J* 13.0, 6.3, 2'-H'), 4.67 and 4.70 (each 1 H, d, *J* 6.9, OHC*H*O) and 5.69 (1 H, t, *J* 6.0, 1′-H); δ_C (125 MHz, $CDCl_3$) −3.3, −3.2, 0.0, 6.5, 8.4, 13.5, 18.7, 19.5, 19.6, 27.3, 37.1, 39.6, 61.7, 66.9, 69.5, 70.5, 71.2, 82.0, 97.3, 131.7 and 137.8; *mlz* (ES^+) 793.4 (68%) and 736.1 (M^+ + 1, 100).

(4*S*,6*R*,7*R*)-7-*tert*-Butyldimethylsilyloxy-4-triethylsilyloxy-2-[(*E*)-2-tri-isopropylsilyloxyethylidenel-6-(2-trimethylsilylethoxymethoxy)octanal (59).

Pyridine (0.19 mL, 2.35 mmol) and the Dess-Martin periodinane (177 mg, 0.42 mmol) were added to the alcohol **58** (150 mg, 0.20 mmol) in DCM (1.45 mL) and the solution stirred for 1 h at rt. Ether (30 mL), saturated aqueous $NaHCO_3$ (15 mL) and saturated aqueous $Na_2S_2O_3$ (15 mL) were added and the aqueous phase was extracted with ether (2 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (15:1 light petroleum:ether) gave the *title compound* **59** (142 mg, 95%) as a colourless oil, R_f = 0.34 (15:1 light petroleum:ether), $[\alpha]_D^{21}$ −9.0 *(c* 1.7, $CHCl_3$) (Found: $M^+ + NH_4$, 750.5369. $C_{37}H_{84}O_6Si_4N$ requires M, 750.5370); ν_{max}/cm^{-1} 2953, 2869, 1693, 1463, 1379, 1250, 1102, 1055, 1006, 881, 860, 835 and 776; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 × $SiCH_3$), 0.58 (6 H, q, *J* 7.8, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (1 H, m, OHC*H*Si), 0.93 (9 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 1.02 (3 H, d, *J* 6.3, 8-H_3), 1.05-1.13 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.30 (1 H, ddd, *J* 14.4, 9.7, 5.0, *5*-H), 1.65 (1 H, ddd, *J* 14.2, 7.4, 1.7, 5-H'), 2.36 and 2.42 (each 1 H, dd, *J* 13.0, 6.7, 3-H), 3.44 (1 H, ddd, *J* 11.2, 9.6, 6.0, OHC*H*CH_2Si), 3.51 (1 H, ddd, *J* 9.6, 4.4, 1.7, 6-H), 3.67 (1 H, ddd, *J* 11.5, 9.5, 5.3, OHC*H*CH_2Si), 3.84 (1 H, qd, *J* 6.8, 5.0, 4-H), 4.03 (1 H, qd, *J* 6.3, 4.5, 7-H), 4.60 (2 H, d, *J* 5.3, 2'-H_2), 4.69 and 4.71 (each 1 H, d, *J* 7.0, OHC*H*O), 6.62 (1 H, t, *J* 5.3, 1'-H) and 9.40 (1 H, s, 1-H); δ_C (125 MHz, $CDCl_3$) −3.3(2), 0.0, 6.6, 8.5, 13.4, 18.5, 19.4, 19.5, 19.6, 27.3, 35.6, 37.8, 62.5, 66.7, 70.4, 70.5, 81.8, 97.6, 140.4, 157.6 and 195.9; *mlz* (ES^+) 792.0 (44%) and 756.1 (M^+ + 23, 100).

2-(2-Benzyloxy-1,1-dimethylethyl)-[1,3]dithiane (60).

Boron trifluoride diethyletherate (5.63 mL, 45.6 mmol) was added to 3-benzyloxy-2,2-dimethylpropanal (15.0 mmol) and 1,3-propanedithiol (2.75 mL, 27.4 mmol) in DCM (180 mL) at 0 °C and the reaction mixture stirred at rt for 16 h. Dichloromethane (100 mL) and water (100 mL) were added and the aqueous phase was extracted with DCM (100 mL). The organic extracts were washed with aqueous NaOH (1 M, 2 × 100 mL) and water (100 mL) then dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (15:1 light petroleum:ether) gave the *title compound* **60** (3.7 g, 85%) as a colourless oil, R_f = 0.23 (20:1 light petroleum:ether) (Found: M^+ + Na, 305.1013. $C_{15}H_{22}OS_2Na$ requires M, 305.1004); ν_{max}/cm^{-1} 3061, 3027, 2962, 2929, 2893, 1495, 1470, 1452, 1421, 1382, 1364, 1275, 1099, 1028, 904, 776, 736 and 697; δ_H (400 MHz, $CDCl_3$) 1.04 (6 H, s, 2 × CH_3), 1.74 and 2.00 (each 1 H, m, 5-H), 2.76-2.88 (4 H, m, 4-H_2, 6-H_2), 3.31 (2 H, s, 2'-H_2), 4.25 (1 H, s, 2-H), 4.46 (2 H, s, $PhCH_2$) and 7.18-7.29 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 22.9, 26.2, 31.4, 39.9, 57.8, 73.3, 76.8, 127.5, 128.3 and 138.8; *mlz* (ES^+) 305 (M^+ + 23, 100%).

(4*S*,7*S*,9*R*,10*R*)- and (4*R*,7*S*,9*R*,10*R*)-1-Benzyloxy-10-*tert*-butyldimethylsilyloxy-7-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecan-4-ols (61) and (62).

n-Butyllithium (1.60 M in hexanes, 1.20 mL, 1.92 mmol) was added to the dithiane **60** (617 mg, 2.18 mmol) in THF (12 mL) at rt and the solution stirred for 5 min before cooling to −78 °C. The aldehyde **59** (1.06 g, 1.45 mmol) in THF (8.4 mL) was added and the solution stirred at −78 °C for 15 min. Methanol (1.0 mL) was added and the mixture allowed to warm to rt then partitioned between ether (60 mL) and saturated aqueous $NaHCO_3$ (60 mL). The aqueous phase was extracted with ether (2 × 50 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 15:1 light petroleum:ether) gave the (4*R*)-epimer of the *title compound* **62** as a pale, yellow oil (385 mg, 26%), R_f = 0.53 (9:1 light petroleum:ether), $[\alpha]_D^{21}$ −9.6 *(c* 0.9, $CHCl_3$); ν_{max}/cm^{-1} 3375, 2949, 2863, 1460, 1376, 1247, 1099, 1056, 858, 833, 772 and 742; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 × $SiCH_3$), 0.59 (6 H, q, *J* 7.9, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.92 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.93 (1 H, m, HC*H*Si), 1.01-1.11 [24 H, m, 11-H_3, 3 × $Si(CH(CH_3)_2]$, 1.23 and 1.31 (each 3 H, s, 2-CH_3), 1.55 (1 H, ddd, *J* 14.6, 9.6, 5.3, 8-H), 1.70-1.82 (2 H, m, 8-H', SCH_2HCH), 1.87 (1 H, m, SCH_2HCH), 2.43 (1 H, ddd, *J* 14.1, 6.1, 3.5, S*H*CH), 2.53 (1 H, dd, *J* 13.6, 6.1, 6-H), 2.70 (1 H, ddd, *J* 13.3, 7.3, 5.5, SHC*H*), 2.83-2.94 (2 H, m, 6-H', SHC*H*), 3.01 (1 H, ddd, *J* 14.7, 10.5, 5.4, SHC*H*), 3.41 (1 H, ddd, *J* 11.1, 9.6, 6.0, OHC*H*CH_2Si), 3.48-3.54 (2 H, m, 1-H, 9-H), 3.71 (1 H, ddd, *J* 11.4, 9.5, 5.3, OHC*H*CH_2Si), 3.79 (1 H, m, 7-H), 3.83 (1 H, d, *J* 9.3, 1-H'), 4.06 (1 H, qd, *J* 6.3, 4.3, 10-H), 4.28 (1 H, dd, *J* 12.6, 5.3, 2'-H), 4.39 (1 H, dd, *J* 12.5, 7.2, 2'-H'), 4.50 and 4.51 (each 1 H, d, *J* 12.4, PhHC*H*), 4.54 (1 H, s, 4-H), 4.57 (1 H, br. s, OH), 4.69 (2 H, s, OCH_2O), 6.05 (1 H, m, 1′-H) and 7.22-7.32 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3(2), 0.0, 6.7, 8.4, 13.4, 18.5, 19.5(2), 19.6, 22.9(2), 24.3, 24.5, 27.3, 27.9, 28.4, 37.3, 48.6, 61.7, 66.5, 68.0, 70.5, 72.8, 74.8, 77.9, 78.8, 82.2, 97.7, 128.8, 128.9, 129.7, 133.5, 139.2 and 139.8; *m/z* (ES^+) 1075.3 (62%), 1037.9 (M^+ + 23, 100) and 1033.9 (M^+ + 18, 30). The second fraction was the (4*S*)-epimer of the *title compound* **61** (784 mg, 53%) as a colourless oil, R_f = 0.49 (9:1 light petroleum:ether), $[\alpha]_D^{20}$ −42.8 *(c* 1.3, $CHCl_3$); ν_{max}/cm^{-1} 3419,

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2953, 2870, 1462, 1375, 1250, 1102, 1057, 835 and 775; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 × $SiCH_3$), 0.54-0.66 (6 H, m, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (1 H, m, HC*H*Si), 0.94 (9 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 1.03 (3 H, d, *J* 6.4, 11-H_3), 1.04-1.12 [21 H, m, 3 × $SiCH(CH_3)_2$] 1.26 and 1.32 (each 3 H, s, 2-CH_3), 1.49 (1 H, ddd, *J* 14.2, 9.7, 4.5, 8-H), 1.62 (1 H, ddd, *J* 14.4, 7.3, 1.3, 8-H′), 1.80 and 1.90 (each 1 H, m, SCH_2HCH), 2.44 (1 H, ddd, *J* 14.1, 5.3, 3.8, SHC*H*), 2.57 (1 H, dd, *J* 13.6, 6.6, 6-H), 2.66 (1 H, ddd, *J* 14.0, 6.7, 5.2, SHC*H*), 2.83 (1 H, dd, *J* 13.5, 6.5, 6-H'), 2.98-3.06 (2 H, m, 2 × SHC*H*), 3.42 (1 H, ddd, *J* 10.9, 9.7, 6.1, OHC*H*CH_2Si), 3.50 (1 H, d, *J* 9.5, 1-H), 3.54 (1 H, ddd, *J* 9.4, 4.2, 1.5, 9-H), 3.69 (1 H, ddd, *J* 11.4, 9.8, 5.4, OHC*H*CH_2Si), 3.83 (1 H, d, *J* 9.5, 1-H'), 3.96 (1 H, qd, *J* 6.6, 4.7, 7-H), 4.04 (1 H, qd, *J* 6.3, 4.5, 10-H), 4.25 (1 H, br. s, OH), 4.30 (1 H, dd, *J* 12.5, 5.2, 2'-H), 4.39 (1 H, dd, *J* 12.5, 7.6, 2'-H'), 4.49 and 4.52 (each 1 H, d, *J* 12.2, PhHC*H*), 4.60 (1 H, br. s, 4-H), 4.67 and 4.70 (each 1 H, d, *J* 6.9, OHC*H*O), 6.21 (1 H, t, *J* 6.3, 1'-H) and 7.23-7.33 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −3.3, 0.0, 6.7, 8.5, 13.5, 18.7, 19.5, 19.6, 23.2, 24.4, 24.7, 27.3, 27.8, 28.3, 37.5, 42.2, 48.5, 61.9, 66.5, 67.8, 70.6, 70.7, 72.3, 74.8, 77.9, 82.0, 97.5, 128.8, 128.9, 129.7, 132.9, 139.7 and 140.4; *mlz* (ES^+) 1037.6 (M^+ + 23, 100%), 1032.6 (M^+ + 18, 65) and 997.7 (43).

(4*S*,7*S*,9*R*,10*R*)-1-Benzyloxy-10-*tert*-butyldimethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecane-4,7-diol (63).

Pyridinium toluene 4-sulfonate (1.2 mg, 4.7 μmol) was added to the triethylsilyl ether **61** (43 mg, 0.042 mmol) in THF (0.50 mL), methanol (1.45 mL) and trimethyl orthoformate (0.15 mL, 1.37 mmol) and the solution stirred at rt for 1 h. Ether (15 mL) and saturated aqueous $NaHCO_3$ (15 mL) were added and the aqueous phase was extracted with ether (3 × 15 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (7:1 light petroleum:ether) gave the *title compound* **63** (35 mg, 92%) as a viscous colourless oil, R_f = 0.46 (3:1 light petroleum:ether), $[\alpha]_D^{30}$ −9.1 (*c* 0.8, $CHCl_3$) (Found: M^+ + Na, 923.5186. $C_{46}H_{88}O_7S_2Si_3Na$ requires M, 923.5171); ν_{max}/cm^{-1} 3436, 2943, 2928, 2865, 1730, 1463, 1379, 1250, 1102, 1058, 835 and 776; δ_H (500 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.06(2) (each 3 H, s, $SiCH_3$), 0.87-0.97 (2 H, m, CH_2Si), 0.88 [9 H, s, $SiC(CH_3)_3$], 1.03-1.13 [21 H, m, 3 × $SiCH(CH_3)_2$] 1.08 (3 H, d, *J* 6.3, 11-H_3), 1.25 and 1.31 (each 3 H, s, 2-CH_3), 1.51 (1 H, ddd, *J* 13.9, 9.1, 2.5, 8-H), 1.58 (1 H, ddd, *J* 13.9, 10.1, 4.1, 5-H'), 1.81 and 1.91 (each 1 H, m, SCH_2HCH), 2.47 (1 H, ddd, *J* 14.2, 5.6, 4.1, SHC*H*), 2.66 (1 H, dd, *J* 13.9, 7.6, 6-H), 2.68-2.79 (2 H, m, 6-H', SHC*H*), 2.96 (1 H, m, SHC*H*), 3.03 (1 H, ddd, *J* 15.1, 10.7, 5.4, SHC*H*), 3.46 (1 H, d, *J* 9.8, 1-H), 3.54-3.66 (3 H, m, 9-H, OC*H*$_2$$CH_2$Si), 3.72 (1 H, br. s, OH), 3.85 (1 H, d, *J* 9.4, 1-H'), 3.87 (1 H, quin, *J* 6.2, 10-H), 3.93 (1 H, m, 7-H), 4.29 (1 H, dd, *J* 12.6, 5.7, 2'-H), 4.37 (1 H, dd, *J* 12.6, 6.9, 2'-H'), 4.49 and 4.53 (each 1 H, d, *J* 12.1, PhHC*H*), 4.59 (1 H, br. s, OH), 4.71 (1 H, d, *J* 6.9, OHC*H*O), 4.72 (1 H, s, 4-H), 4.74 (1 H, d, *J* 6.9, OHC*H*O), 6.14 (1 H, t, *J* 6.3, 1'-H) and 7.24-7.35 (5 H, m, ArH); δ_C (125 MHz, $CDCl_3$) −3.3, 0.0, 13.4, 19.5(3), 20.1, 23.1, 24.6, 24.7, 27.3, 28.0, 28.5, 38.8, 40.5, 48.4, 61.6, 67.1, 68.1, 69.7, 72.2, 74.8, 77.8, 81.8, 97.8, 128.9(2), 129.8, 133.3, 139.6 and 140.4; *mlz* (ES^+) 923.9 (M^+ + 23, 100%).

(4*R*,7*S*,9*R*,10*R*)-1-Benzyloxy-10-*tert*-butyldimethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecane-4,7-diol (64).

The same procedure using pyridinium toluene 4-sulfonate (2.0 mg, 7.7 μmol) and triethylsilyl ether **62** (70 mg, 0.068 mmol) in THF (0.81 mL), methanol (2.4 mL) and trimethyl orthoformate (0.24 mL, 2.23 mmol), after chromatography (7:1 light petroleum:ether), gave the *title compound* **64** (56 mg, 90%) as a viscous colourless oil, R_f = 0.41 (3:1 light petroleum:ether), $[\alpha]_D^{29}$ −23.6 (*c* 0.6, $CHCl_3$) (Found: M^+ + Na, 923.5181. $C_{46}H_{88}O_7S_2Si_3Na$ requires M, 923.5171); ν_{max}/cm^{-1} 3371, 2945, 2925, 2889, 2863, 1462, 1377, 1250, 1101, 1056, 883, 858, 834 and 773; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.07(2) (each 3 H, s, $SiCH_3$), 0.85-0.95 (2 H, m, CH_2Si), 0.88 [9 H, s, $SiC(CH_3)_3$], 1.02-1.13 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.10 (3 H, d, *J* 6.3, 11-H_3), 1.25 and 1.32 (each 3 H, s, 2-CH_3), 1.55 (1 H, ddd, *J* 13.8, 9.4, 2.5, 8-H), 1.65 (1 H, ddd, *J* 14.0, 10.1, 4.0, 8-H'), 1.78-1.93 (2 H, m, SCH_2CH_2), 2.43 (1 H, d, *J* 14.1, 6-H), 2.49 (1 H, ddd, *J* 14.1, 5.8, 4.3, SHC*H*), 2.75 (1 H, ddd, *J* 13.7, 7.6, 5.8, SHC*H*), 2.85 (1 H, dt, *J* 14.4, 5.8, SHC*H*), 2.93 (1 H, ddd, *J* 14.6, 9.6, S.8, SHC*H*), 3.05 (1 H, t, *J* 11.9, 6-H'), 3.54-3.64 (4 H, m, 1-H, 9-H, OC$H_2$$CH_2$Si), 3.71 (1 H, m, 7-H), 3.8S (1 H, d, *J* 9.3, 1-H'), 3.87 (1 H, pent, *J* 6.0, 10-H), 4.31 (2 H, d, *J* 6.1, 2'-H_2), 4.50 (1 H, br. s, OH), 4.50 and 4.53 (each 1 H, d, *J* 12.1, PhHC*H*), 4.58 (1 H, s, 4-H), 4.71 and 4.73 (each 1 H, d, *J* 6.7, OHC*H*O), 5.48 (1 H, br. s, OH), 5.93 (1 H, br. t, *J* 5.8, 1'-H) and 7.23-7.35 (5 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3, 0.0, 13.4, 19.4, 19.5, 20.0, 23.0, 24.4(2), 27.3, 28.0, 28.8, 39.0, 39.4, 48.9, 61.4, 67.1, 68.0, 70.0, 72.3, 74.8, 77.8, 80.6, 81.7, 97.8, 128.9(2), 129.8, 134.4, 139.8 and 140.2; *mlz* (ES^+) 923 (M^+ + 23, 100%).

(2*R*,3*S*,6*S*)- and (2*S*,3*S*,6*S*)-2-(2-Benzyloxy-1,1-dimethylethyl)-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2 (trimethylsilylethoxymethoxy)butyl]-2-methoxy-4-[(*E*)-2-tri-isopropylsilyloxyethylidene]tetrahydropyran-3-ols (65) and (66).

2,6-Lutidine (73 μL, 0.63 mmol) and $Hg(ClO_4)_2.2H_2O$ (96 mg, 0.23 mmol) was added to the diol **63** (100 mg, 0.11 mmol) in THF (1.3 mL) and MeOH (1.3 mL) at −5 °C and the white suspension was stirred at −5 °C for 30 min then filtered through celite with copious ether washings. The organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL) and the aqueous phase extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using base-washed silica (20:1 to 12:1 light petroleum:ether) gave first the *title compound* **65** (34 mg, 37%) as a colourless oil, R_f = 0.33 (9:1 light petroleum:ether), $[\alpha]_D^{22}$ −25.1 (*c* 0.7, DCM) (Found: M^+ + Na, 847.5334. $C_{44}H_{84}O_8Si_3Na$ requires M, 847.5372); ν_{max}/cm^{-1} 3382, 2952, 2893, 2866, 1463, 1381, 1250, 1201, 1096, 1057, 938, 920, 883, 860, 836, 811, 776 and 736; δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.14 and 0.18 (each 3 H, s, $SiCH_3$), 0.93 (1 H, ddd, *J* 13.9, 9.8, 5.7, HC*H*Si), 1.00 (1 H, m, HC*H*Si), 1.00 [9 H, s, $SiC(CH_3)_3$], 1.08-1.16 [21 H, m, 3 × $Si(CH(CH_3)_2$], 1.25 and 1.26

(each 3 H, s, 1'-CH_3), 1.28 (3 H, d, *J* 6.3, 4'"-H_3), 1.57 (1 H, ddd, *J* 14.2, 10.2, 2.5, 1'"-H), 2.02 (1 H, ddd, *J* 14.2, 9.5, 1.3, 1'"-H'), 2.25-2.38 (2 H, m, 5-H_2), 3.18 (1 H, d, *J* 9.1, 2'-H), 3.39 (3 H, s, 2-OCH_3), 3.49 (1 H, td, *J* 9.8, 6.3, OHC*H*CH_2Si), 3.81 (1 H, td, *J* 9.9, 5.8, OHC*H*CH_2Si), 3.87 (1 H, d, *J* 9.1, 2'-H'), 3.99 (1 H, ddd, *J* 10.1, 4.4, 1.5, 2'"-H), 4.12 (1 H, m, 6-H), 4.13 (1 H, d, *J* 6.6, OH), 4.23 (1 H, d, *J* 12.0, PhHC*H*), 4.29-4.40 (4 H, m, 3'"-H, PhHC*H*, 2"-H_2), 4.71 (1 H, m, 3-H), 4.75 and 4.86 (each 1 H, d, *J* 6.9, OHC*H*O), 6.40 (1 H, m, 1"-H), 7.05 (1 H, m, ArH) and 7.13 and 7.24 (each 2 H, m, ArH); δ_C (100 MHz, C_6D_6) −4.8, −4.7, −1.5, 12.3, 17.0, 18.2, 18.3, 21.4, 21.5, 26.0, 34.4, 35.9, 46.6, 50.5, 60.7, 65.5, 67.1, 67.5, 69.1, 73.5, 76.9, 80.0, 96.7, 102.7, 123.8, 127.7(2), 128.5, 135.5 and 138.4; *mlz* (ES^+) 885 (25%), 848 (M^+ + 23, 100), 619 (23) and 469 (11). The second fraction was the *title compound* (**66**) (23 mg, 25%), R_f = 0.21 (4:1 light petroleum:ether), $[\alpha]_D^{23}$ −20.4 (*c* 1.4, DCM) (Found: M^+ + Na, 847.5345. $C_{44}H_{84}O_8Si_3Na$ requires M, 847.5372); ν_{max}/cm^{-1} 3355, 2955, 2894, 2866, 1463, 1381, 1362, 1250, 1105, 1060, 937, 920, 883, 860, 835, 811 and 776; δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.17 and 0.21 (each 3 H, s, $SiCH_3$), 0.90-1.03 (2 H, m, CH_2Si), 1.03 [9 H, s, $SiC(CH_3)_3$], 1.09-1.15 [21 H, m, 3 × $Si(CH(CH_3)_2]$, 1.19 (3 H, s, 1'-CH_3), 1.28 (3 H, d, *J* 6.3, 4'"-H_3), 1.29 (3 H, s, 1'-CH_3), 1.64 (1 H, ddd, *J* 13.9, 10.4, 2.5, 1'"-H), 2.11 (1 H, ddd, *J* 14.1, 10.1, 1.6, 1'"-H'), 2.31 (1 H, dd, *J* 14.5, 2.8, 5-H), 2.50 (1 H, t, *J* 13.3, 5-H'), 3.33 (3 H, s, 2-OCH_3), 3.45-3.54 (3 H, m, 2'-H_2, OHC*H*CH_2Si), 3.81 (1 H, td, *J* 10.0, 5.9, OHC*H*CH_2Si), 4.01 (1 H, ddd, *J* 10.4, 4.4, 1.6, 2'"-H), 4.22 (1 H, m, 6-H), 4.26-4.41 (5 H, m, 3'"-H, $PhCH_2$, 2"-H_2), 4.39 (1 H, d, *J* 4.7, 3-H), 4.74 (1 H, d, *J* 6.9, OHC*H*O), 4.81 (1 H, d, *J* 4.1, OH), 4.87 (1 H, d, *J* 6.9, OHC*H*O), 5.90 (1 H, t, *J* 6.0, 1'-H), 7.06 (1 H, m, ArH) and 7.15 and 7.26 (each 2 H, m, ArH); δ_C (100 MHz, C_6D_6) −3.2, −3.1, 0.0, 13.7, 18.7, 19.7, 23.7, 24.0, 27.6, 33.1, 37.3, 47.1, 52.9, 61.4, 66.8, 69.8, 71.0, 73.7, 75.0, 78.5, 81.1, 98.1, 105.3, 126.7, 129.2, 129.5, 130.0, 138.6 and 139.3; *m/z* (ES^+) 885 (13%), 848 (M^+ + 23, 100), 619 (11) and 469 (13).

(2*R*,3*R*,6*S*)- and (2*S*,3*R*,6*S*)-2-(2-Benzyloxy-1,1-dimethylethyl)-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(trimethylsilylethoxymethoxy)butyl]-2-methoxy-4-[(*E*)-2-tri-isopropylsilyloxyethylidene]tetrahydropyran-3-ols (69) and (70)

This procedure using 2,6-lutidine (73 µL, 0.63 mmol), $Hg(ClO_4)_2.2H_2O$ (96 mg, 0.23mmol) and diol **64** (100 mg, 0.11 mmol) in THF (1.3 mL) and MeOH (1.3 mL), after chromatography using base washed silica (12:1 light petroleum:ether), gave the *title compounds* **69** and **70** (55 mg, 60%) as a colourless oil, a 1:3 mixture of diastereoisomers that were difficult to separate by TLC, R_f = 0.17 (9:1 light petroleum:ether), $[\alpha]_D^{24}$ −13.7 (*c* 4.0, DCM) (Found: M^+ + Na, 847.5398. $C_{44}H_{84}O_8Si_3Na$ requires M, 847.5372); ν_{max}/cm^{-1} 3379, 2951, 2891, 2865, 1471, 1463, 1380, 1250, 1148, 1105, 1057, 882, 859, 835 and 775; δ_C (100 MHz, CD_2Cl_2) −3.3(2), −3.2(2), 0.0, 13.8(2), 18.4, 18.5, 19.6(2), 19.7(2), 19.8, 19.9, 22.9, 23.7, 24.0, 24.5, 27.4(2), 34.4, 36.3, 36.8, 37.2, 46.7, 47.7, 52.3, 53.4, 61.6, 61.7, 66.9, 67.0, 68.8, 69.9, 70.5, 70.7, 73.8, 75.2, 75.4, 76.6, 78.4(2), 81.0, 81.6, 98.0, 98.1, 104.1, 104.2, 123.4, 129.4(2), 129.7(2), 130.1, 130.2, 130.5, 136.0, 138.0, 139.3 and 140.0; *mlz* (ES^+) 958 (11%), 927 (17), 848 (M^+ + 23, 100), 843 (M^+ + 18, 22) and 133 (17). Repeated chromatography gave small samples of each diastereoisomer: δ_H (400 MHz, C_6D_6) (2*R*)-epimer **69** 0.00 [9 H, s, $Si(CH_3)_3$], 0.16 and 0.20 (each 3 H, s, $SiCH_3$), 0.95 (1 H, ddd, *J* 14.2, 10.4, 5.7, HC*H*Si), 1.01 [9 H, s, $SiC(CH_3)_3$], 1.04 (1 H, m, HC*H*Si), 1.09-1.14 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.17 (3 H, s, 1'-CH_3), 1.30 (3 H, d, *J* 6.3, 4'"-H_3), 1.35 (3 H, s, 1'-CH_3), 1.63 (1 H, ddd, *J* 14.1, 10.4, 1.9, l"'-H), 2.08 (1 H, dd, *J* 14.1, 10.0, 1'"-H'), 2.21 and 2.44 (each 1 H, m, 5-H), 3.29 (3 H, s, 2-OCH_3), 3.42 and 3.50 (each 1 H, d, *J* 9.1, 2'-H), 3.56 (1 H, td, *J* 10.1, 6.0, OHC*H*CH_2Si), 3.82 (1 H, ddd, *J* 10.7, 9.8, 5.7, OHC*H*CH_2Si), 4.07 (1 H, ddd, *J* 10.2, 4.5, 1.0, 2'"-H), 4.23 (1 H, d, *J* 11.7, PhHC*H*), 4.27-4.35 (5 H, m, 3-H, 3'"-H, PhHC*H*, 2"-H_2), 4.72 (1 H, d, 12.8, OH), 4.79 (1 H, d, *J* 6.9, OHC*H*O), 4.92 (1 H, m, 6-H), 4.92 (1 H, d, *J* 6.9, OHC*H*O), 5.91 (1 H, m, 1"-H), 7.05 (1 H, m, ArH) and 7.12 and 7.22 (each 2 H, m, ArH); (2*S*)-epimer **70** 0.00 [9 H, s, $Si(CH_3)_3$], 0.15 and 0.19 (each 3 H, s, $SiCH_3$), 0.89-1.01 (2 H, m, CH_2Si), 1.02 [9 H, s, $SiC(CH_3)_3$], 1.09-1.15 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.27 (3 H, d, *J* 6.3, 4'"-H_3), 1.28 and 1.31 (each 3 H, s, 1'-CH_3), 1.62 (1 H, ddd, *J* 14.2, 10.4, 2.2, 1'"-H), 1.78 (1 H, t, *J* 12.6, 5-H), 2.00 (1 H, ddd, *J* 13.9, 10.1, 1.3, 1'"-H'), 2.62 (1 H, dd, *J* 13.6, 2.2, 5-H'), 3.33 (1 H, d, *J* 9.1, 2'-H), 3.46 (3 H, s, 2-OCH_3), 3.47 (1 H, td, *J* 9.8, 6.6, OHC*H*CH_2Si), 3.65 (1 H, d, *J* 6.9, OH), 3.68 (1 H, d, J 9.0, 2'-H'), 3.82 (1 H, td, *J* 9.9, 5.8, OHC*H*CH_2Si), 3.93 (1 H, ddd, *J* 10.4, 4.4, 1.3, 2'"-H), 4.04 (1 H, m, 6-H), 4.29 (1 H, d, *J* 12.0, PhHC*H*), 4.31-4.41 (5 H, m, 3-H, 3'"-H, PhHC*H*, 2"-H_2), 4.73 and 4.83 (each 1 H, d, *J* 6.8, OHC*H*O), 6.26 (1 H, m, 1"-H), 7.07 (1 H, m, ArH) and 7.16 and 7.28 (each 2 H, m, ArH).

(2*R*,6*S*)-2-(2-Benzyloxy-1,1-dimethylethyl)-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-2-methoxy-4-[(*E*)-2-tri-isopropylsilyloxyethylidene)-5,6-dihydropyran-3-one (67).

Pyridine (13 µL, 0.161 mmol) and the Dess-Martin periodinane (11.6 mg, 0.027 mmol) were added to the alcohol **65** (11 mg, 0.013 mmol) in DCM (0.15 mL) and the solution stirred at rt for 1 h. Ether (10 mL), saturated aqueous $Na_2S_2O_3$ (5 mL) and saturated aqueous $NaHCO_3$ (5 mL) were added and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (12:1 light petroleum:ether) gave the *title compound* **67** (6 mg, 55%) as a colourless oil, R_f = 0.32 (9:1 light petroleum:ether), $[\alpha]_D^{23}$ −1.8 (*c* 0.7, DCM) (Found: M^+ + Na, 845.5217. $C_{44}H_{82}O_8Si_3Na$ requires M, 845.5215); ν_{max}/cm^{-1} 2952, 2866, 1703, 1627, 1463, 1380, 1250, 1104, 1055, 881, 860, 835 and 776; δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.16 and 0.20 (each 3 H, s, $SiCH_3$), 0.95 (1 H, ddd, *J* 13.9, 10.0, 5.8, HC*H*Si), 1.01 (1 H, m, HC*H*Si), 1.02 [9 H, s, $SiC(CH_3)_3$], 1.03-1.07 [21 H, m, 3 × $Si(CH(CH_3)_2]$, 1.31 (3 H, d, *J* 6.3, 4'"-H_3), 1.35 and 1.60 (each 3 H, s, 1'-CH_3), 1.61 (1 H, ddd, *J* 14.2, 10.4, 2.2, 1'"-H), 2.11 (1 H, ddd, *J* 14.2, 9.8, 1.1, 1'"-H'), 2.22 (1 H, m, 5-H), 2.52 (1 H, dd, *J* 15.5, 1.9, 5-H'), 3.21 (3 H, s, 2-OCH_3), 3.50 (1 H, td, *J* 9.8, 6.3, OHC*H*CH_2Si), 3.57 and 3.76 (each 1 H, d, *J* 9.0, 2'-H), 3.84 (1 H, ddd, *J* 10.2, 9.6, 5.8, OHC*H*CH_2Si), 4.07 (1 H, ddd, *J* 10.1, 4.4, 1.3, 2'"-H), 4.18 and 4.20 (each 1 H, ddd, *J* 15.5, 5.7, 1.9, 2"-H), 4.36-4.44 (4 H, m, 3'"-H, $PhCH_2$, 6-H), 4.77 and 4.90 (each 1 H, d, *J* 6.9, OHC*H*O), 7.00 (1 H, m, l"-H), 7.08 (1 H, m, ArH) and 7.17 and 7.28 (each 2 H, m, ArH); δ_C (100

MHz, CD_2Cl_2) –3.4, –3.2, 0.0, 13.7, 18.4, 19.5, 19.7, 19.9, 22.3, 23.2, 27.4, 35.2, 37.3, 47.9, 52.2, 62.3, 67.1, 70.5, 70.7, 74.8, 77.6, 81.2, 98.0, 105.4, 129.0, 129.1, 129.9, 134.9, 140.6, 140.7 and 198.0; *m/z* (ES^+) 883 (23%), 846 (M^+ + 23, 100) and 830 (51).

Using the same procedure, alcohol **69** (9 mg, 0.011 mmol) gave the ketone **67** (4.5 mg, 51%) as a colourless oil.

(2*S*,6*S*)-2-(2-Benzyloxy-1,1-dimethylethyl)-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-2-methoxy-4-[(*E*)-2-tri-isopropylsilyloxyethylidene)-5,6-dihydropyran-3-one (68).

Using the same procedure, alcohol **66** (6 mg, 0.0073 mmol) gave the *title compound* **68** (4 mg, 63%) as a colourless oil, R_f = 0.19 (15:1 light petroleum:ether), $[\alpha]_D^{23}$ –41.0 (*c* 0.8, DCM) (Found: M^+ + Na, 845.5215. $C_{44}H_{82}O_8Si_3Na$ requires M, 845.5215); ν_{max}/cm^{-1} 2953, 2892, 2865, 1703, 1627, 1471, 1463, 1379, 1362, 1250, 1101, 1058, 882, 860, 835 and 776; δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.16 and 0.20 (each 3 H, s, $SiCH_3$), 0.89-1.02 (2 H, m, CH_2Si), 1.02 [9 H, s, $SiC(CH_3)_3$], 1.04-1.11 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.31 (3 H, d, *J* 6.3, 4'''-H_3), 1.32 and 1.49 (each 3 H, s, 1'-CH_3), 1.64 (1 H, ddd, *J* 14.2, 10.4, 2.5, 1'''-H), 2.08 (1 H, ddd, *J* 14.2, 9.8, 1.6, 1'''-H'), 2.27-2.39 (2 H, m, 5-H_2), 3.34 (3 H, s, 2-OCH_3), 3.48 (1 H, td, *J* 9.8, 6.6, OHC*H*CH_2Si), 3.52 and 3.74 (each 1 H, d, *J* 8.8, 2'-H), 3.78 (1 H, td, *J* 9.6, 5.7, OHC*H*CH_2Si), 4.03 (1 H, ddd, *J* 10.1, 4.1, 1.6, 2'''-H), 4.09 and 4.23 (each 1 H, dd, *J* 15.6, 5.0, 2''-H), 4.28 (1 H, m, 6-H), 4.32 and 4.35 (each 1 H, d, *J* 12.3, PhHC*H*), 4.37 (1 H, m, 3'''-H), 4.70 and 4.84 (each 1 H, d, *J* 6.8, OHC*H*O), 7.04-7.09 (2 H, m, 1''-H, ArH) and 7.16 and 7.27 (each 2 H, m, ArH); δ_C (100 MHz, CD_2Cl_2) –5.1, –5.0, –1.8, 11.9, 16.7, 17.7, 17.9, 18.0, 19.8, 20.0, 25.6, 33.8, 35.1, 45.0, 52.2, 60.7, 65.2, 68.8, 69.6, 73.1, 75.5, 79.2, 96.1, 103.9, 127.2, 127.2, 128.1, 133.0, 139.0, 139.4 and 195.4; *mlz* (ES^+) 883 (25%), 846 (M^+ + 23, 100), 301 (11) and 229 (13).

Using the same procedure, alcohol **70** (4 mg, 0.005 mmol) gave the ketone **68** (2.5 mg, 61 %) as a colourless oil.

(2*S*,3*S*,6*S*)-2-(2-Hydroxy-1,1-dimethylethyl)-6-[(2*R*,3*R*)-3-*tert*-butyldimethylsilyloxy-2-(trimethylsilylethoxymethoxy)butyl]-3-*tert*-butyldimethylsilyloxy-2-methoxy-4-[(*E*)-2-tri-isopropylsilyloxyethylidene]tetrahydropyran (75).

A solution of benzyl ether **73** (80 mg, 0.085 mmol) in ethyl acetate (1.5 mL) and methanol (1.5 mL) was pumped through the H-cube™ flow hydrogenator fitted with a 10% Pd/C catalyst cartridge (previously saturated with hydrogen gas for 10 min) at 25 °C and 1 bar pressure with the full hydrogen option enabled. The flow rate was set at 1 mL/min. After concentration of the efluent under reduced presure, chromatography of the residue (15:1 to 4:1 light petroleum:ether) gave the *title compound* **75** (36 mg, 50%) as a viscous, colourless oil, R_f = 0.45 (4:1 light petroleum:ether), $[\alpha]_D^{25}$ –14.2 (*c* 0.7, DCM) (Found: M^+ + Na, 871.5755. $C_{43}H_{92}O_8Si_4Na$ requires M, 871.5761); ν_{max}/cm^{-1} 3525, 2955, 2934, 2892, 2864, 1463, 1381, 1251, 1100, 1056, 938, 882, 860, 836 and 775; δ_H (400 MHz, C_6D_6) 0.00 [9 H, s, $Si(CH_3)_3$], 0.13, 0.15, 0.18 and 0.26 (each 3 H, s, $SiCH_3$), 0.89-1.04 (2 H, m, CH_2Si), 1.01 and 1.03 [each 9 H, s, $SiC(CH_3)_3$], 1.06-1.14 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.24 and 1.26 (each 3 H, s, 1'-CH_3), 1.27 (3 H, d, *J* 6.4, 4'''-H_3), 1.67 (1 H, t, *J* 12.2, 1'''-H), 2.09 (1 H, dd, *J* 13.9, 10.6, 1'''-H'), 2.24 (1 H, dd, *J* 13.7, 3.2, 5-H), 2.32 (1 H, t, *J* 13.6, 5-H'), 3.02 (1 H, br. s, OH), 3.33 (3 H, s, 2-OCH_3), 3.50 (1 H, td, *J* 9.6, 6.6, OHC*H*CH_2Si), 3.71 (1 H, m, 2'-H), 3.78 (1 H, td, *J* 9.8, 6.1, OHC*H*CH_2Si), 3.95-4.04 (2 H, m, 2'-H', 2'''-H), 4.17 (1 H, m, 6-H), 4.22-4.41 (4 H, m, 3-H, 3'''-H, 2"-H_2), 4.75 and 4.85 (each 1 H, d, *J* 6.8, OHC*H*O) and 5.73 (1 H, m, 1''-H); δ_C (100 MHz, C_6D_6) –3.4, –3.1, 0.0, 13.7, 18.6, 19.6, 19.7, 19.9, 23.6, 23.9, 27.5, 27.6, 37.2, 46.7, 53.2, 61.1, 66.9, 70.1, 70.5, 72.3, 76.9, 81.2, 98.2, 106.6, 128.7 and 137.6; *mlz* (ES^+) 871.9 (M^+ + 23, 100%). The second fraction was the hemi-acetal **74** (28 mg, 40%), a viscous, colourless oil, R_f = 0.29 (4:1 light petroleum:ether), $[\alpha]_D^{29}$ –20.0 (*c* 2.6, $CHCl_3$) (Found: M^+ + Na, 857.5602. $C_{42}H_{90}O_8Si_4Na$ requires M, 857.5605); ν_{max}/cm^{-1} 3366, 2955, 2930, 2894, 2864, 1463, 1385, 1252, 1106, 1088, 1056, 861, 838 and 776; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (3 H, s, $SiCH_3$), 0.07 (6 H, s, $2 \times SiCH_3$), 0.10 (3 H, s, $SiCH_3$), 0.83-0.98 (2 H, m, CH_2Si), 0.88 and 0.89 [each 9 H, s, $SiC(CH_3)_3$], 1.01 (3 H, s, 1'-CH_3), 1.03-1.12 [21 H, m, $3 \times SiCH(CH_3)_2$], 1.10 (3 H, d, *J* 6.3, 4'''-H_3), 1.13 (3 H, s, 1'-CH_3'), 1.51 (1 H, ddd, *J* 13.5, 11.0, 2.1, 1'''-H), 1.79 (1 H, ddd, *J* 13.9, 11.0, 1.4, 1'''-H'), 2.18 (2 H, m, 5-H_2), 3.24 (1 H, dd, *J* 10.6, 5.8, 2'-H), 3.33 (1 H, t, *J* 5.2, 2'-OH), 3.58 (1 H, ddd, *J* 11.1, 9.8, 6.1, OHC*H*CH_2Si), 3.64 (1 H, ddd, *J* 11.4, 9.8, 6.0, OHC*H*CH_2Si), 3.78 (1 H, ddd, *J* 10.9, 5.0, 1.3, 2'''-H), 3.89 (1 H, qd, *J* 6.3, 5.0, 3'''-H), 3.95 (1 H, m, 6-H), 4.01 (1 H, s, 3-H), 4.07 (1 H, dd, *J* 10.6, 4.5, 2'-H'), 4.26 (1 H, dd, *J* 12.6, 5.6, 2"-H), 4.31 (1 H, dd, *J* 12.6, 6.7, 2"-H'), 4.38 (1 H, s, 2-OH), 4.69 and 4.77 (each 1 H, d, *J* 7.1, OHC*H*O) and 5.60 (1 H, t, *J* 6.1, 1"-H); (100 MHz, $CDCl_3$) –3.3(3), –2.3, 0.0, 13.4, 19.2, 19.5, 19.7, 22.0, 22.8, 27.3, 27.5, 32.3, 37.0, 43.6, 60.7, 67.2, 67.6, 71.1, 72.5, 78.0, 80.1, 97.8, 102.6, 129.7 and 138.0; *m/z* (ES^+) 858 (M^+ + 23, 100%).

(3a*S*,5*S*,7a*S*)-5-[(2*R*,3*R*)-3-*tert*-Butyldimethylsilyloxy-2-(2-trimethylsilylethoxymethoxy)butyl]-3a-methoxy-3,3-dimethyl-7-[(*E*)-2-tri-isopropylsilyloxyethylidene]hexahydrofuro[3,2-*b*]pyran (78).

Triethylamine (0.068 mL, 0.49 mmol) and methanesulfonyl chloride (0.019 mL, 0.24 mmol) were added to the alcohol **75** (42 mg, 0.049 mmol) in DCM (0.50 mL) at 0 °C and the solution stirred at 0 °C for 1 h. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with ether (2×10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the mesylate **77** (42 mg), R_f = 0.53 (4:1 light petroleum:ether), which was used without purification.

Sodium hydride (60% dispersion in mineral oil, 20 mg, 0.51 mmol) was added to 2-mercaptobenzothiazole (85 mg, 0.51 mmol) in DMF (0.30 mL) at 0 °C and the suspension stirred at 0 °C for 20 min then allowed to warm to rt. The mesylate **77** (42 mg, 0.045 mmol) in DMF (0.20 mL) was added and the reaction mixture stirred at 120 °C for 12 h. After allowing the mixture to cool to rt, ether (10 mL) and water (10 mL) were added and the aqueous phase extracted with ether (2×10 mL) The organic extracts were washed with water (2×20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (12:1 light petroleum:ether) gave the *title compound* **78** (23 mg, 72%) as a colourless oil, R_f = 0.34 (9:1,

light petroleum:ether); $[\alpha]_D^{29}$ −30.2 (*c* 0.5, DCM) (Found: M^+ + Na, 739.4800. $C_{37}H_{76}O_7Si_3Na$ requires M, 739.4791); ν_{max}/cm^{-1} 2956, 2931, 2866, 1464, 1380, 1250, 1160, 1108, 1059, 996, 883, 860, 835 and 775; δ_H (400 MHz, C_6D_6), 0.00 [9 H, s, $Si(CH_3)_3$], 0.16 and 0.18 (each 3 H, s, $SiCH_3$), 0.91-1.01 (2 H, m, CH_2Si), 1.02 [9 H, s, $SiC(CH_3)_3$], 1.04-1.12 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.12 (6 H, s, 2 × 3-CH_3), 1.28 (3 H, d, *J* 6.3, 4'-H_3), 1.66 (1 H, ddd, *J* 14.4, 10.1, 2.5, 1'-H), 2.15 (1 H, ddd, *J* 14.1, 9.6, 1.4, 1'-H'), 2.31 (1 H, td, *J* 13.6, 1.3, 6-H), 2.36 (1 H, dd, *J* 13.6, 3.0, 6-H'), 3.24 (3 H, s, 3a-OCH_3), 3.49 (1 H, td, *J* 9.8, 6.6, OHC*H*CH_2Si), 3.56 (1 H, d, *J* 7.6, 2-H), 3.79 (1 H, ddd, *J* 10.2, 9.6, 5.9, OHC*H*CH_2Si), 3.92 (1 H, d, *J* 7.4, 2-H'), 3.94 (1 H, m, 2'-H), 4.00 (1 H, m, 5-H), 4.27-4.36 (3 H, m, 3'-H, 2''-H_2), 4.37 (1 H, s, 7a-H), 4.74 and 4.78 (each 1 H, d, *J* 7.1, OHC*H*O) and 5.89 (1 H, td, *J* 6.1, 1.5, 1''-H); δ_C (100 MHz, C_6D_6) −4.7, −1.5, 12.2, 17.1, 18.1, 19.4, 23.1, 25.9, 30.0, 31.5, 35.6, 44.5, 49.3, 59.7, 65.4, 68.2, 69.3, 80.4, 81.0, 81.8, 96.6, 105.5, 130.6, 133.5; *mlz* (ES^+) 775.6 (23%), 739.7 (M^+ + 23, 100) and 734.4 (M^+ + 18, 13).

Di-isopropyl azodicarboxylate (8 µL, 0.014 mmol) was added to the alcohol **75** (12 mg, 0.014 mmol), PPh_3 (11 mg, 0.042 mmol) and 2-mercaptobenzothiazole (7 mg, 0.042 mmol) in THF (0.2 mL) and the solution stirred at rt for 3 h. After concentration under reduced pressure, chromatography of the residue (20:1 to 12:1 light petroleum:ether) gave the title compound **78** (8 mg, 79%) as a colourless oil.

2-(1,1-Dimethyl-2-hydroxyethyl)-1,3-dithiane (80).[32]

Boron trifluoride diethyletherate (0.86 mL, 6.96 mmol) was added to the aldehyde **79** (2.29 mmol) and 1,3-propanedithiol (0.42 mL, 4.18 mmol) in DCM (27.5 mL) at 0 °C and the solution stirred at rt for 16 h. Dichloromethane (20 mL) and water (20 mL) were added and the aqueous phase extracted with DCM (20 mL). The organic extracts were washed with aqueous NaOH (1 M, 2 × 20 mL) and water (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (1:1 light petroleum:ether) gave the title compound **80** (360 mg, 82%) as a white solid, R_f = 0.38 (1:1 light petroleum:ether), m.p. 57.2-58.8 °C (lit.[32] 55.3-57.4 °C); ν_{max}/cm^{-1} 3337, 2967, 2938, 2901, 1466, 1411, 1363, 1273, 1194, 1037, 1003, 906 and 779; δ_H (400 MHz, $CDCl_3$) 1.01 (6 H, s, 2 × 1'-CH_3), 1.77 (1 H, m, 5-H), 2.02-2.11 (2 H, m, OH, 5-H'), 2.78-2.92 (4 H, m, 4-H_2, 6-H_2), 3.47 (2 H, d, *J* 5.1, 2'-H_2) and 4.16 (1 H, s, 2-H); δ_C (100 MHz) 22.5, 26.1, 31.4, 40.2, 57.7 and 69.9; *m/z* (ES^+) 215 (M^+ + 23, 100%).

2-[1,1-Dimethyl-2-(4-methyoxybenzyloxy)ethyl]-1,3-dithiane (81).

Sodium hydride (60% dispersion in mineral oil, 13.5 mg, 0.34 mmol) was added to the alcohol **80** (50 mg, 0.26 mmol) in DMF (0.4 mL) at 0 °C and the mixture stirred at 0 °C for 30 min. 4-Methoxybenzyl chloride (46 µL, 0.34 mmol) and TBAI (9.6 mg, 0.026 mmol) were added and the mixture stirred at rt for 1 h. Ether (10 mL) and water (10 mL) were added and the aqueous phase extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (15:1 light petroleum:ether) gave the *title compound* **81** (53 mg, 65%) as a pale yellow oil, R_f = 0.18 (15:1 light petroleum:ether) (Found: M^+ + Na, 335.1113. $C_{16}H_{24}O_2S_2Na$ requires M, 335.1110); ν_{max}/cm^{-1} 2960, 2931, 2895, 2855, 1612, 1585, 1512, 1465, 1247, 1172, 1096, 1036 and 820; δ_H (400 MHz, $CDCl_3$) 1.02 (6 H, s, 2 × 1'-CH_3), 1.73 and 2.00 (each 1 H, m, 5-H), 2.76-2.91 (4 H, m, 4-H_2, 6-H_2), 3.27 (2 H, s, 2'-H_2), 3.73 (3 H, s, OCH_3), 4.24 (1 H, s, 2-H), 4.39 (2 H, s, $ArCH_2$) and 6.80 and 7.20 (each 2 H, m, ArH); δ_C (100 MHz, $CDCl_3$) 22.9, 26.2, 31.4, 39.8, 55.3, 57.8, 72.9, 76.5, 113.7, 129.1, 130.8 and 159.0; *mlz* (ES^+) 335.0 (M^+ + 23, 100%), 330.0 (M^+ + 18, 44) and 313.0 (M^+ + 1, 38).

(4*S*,7*S*,9*R*,10*R*)- and (4*R*,7*S*,9*R*,10*R*)-10-*tert*-Butyldimethylsilyloxy-7-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-1-(4-methoxybenzyloxy)-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecan-4-ol (82) and (83).

n-Butyllithium (53 µL, 1.60 M in hexanes, 0.086 mmol) was added to the dithiane **81** (41 mg, 0.13 mmol) in *t*-BuOMe (0.5 mL) at rt and the solution stirred for 5 min before cooling to −78 °C. The aldehyde **59** (29 mg, 0.039 mmol) in *t*-BuOMe (0.5 mL) was added and the solution stirred at −78 °C for 15 min. Methanol (0.1 mL) was added and the mixture allowed to warm to rt. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (50:1 to 15:1 light petroleum:ether) gave the (4*R*)-epimer of the *title compound* **83** (8.5 mg, 21%) as a viscous colourless oil, R_f = 0.62 (5:1 light petroleum:ether), $[\alpha]_D^{29}$ −4.0 (*c* 1.0, DCM); ν_{max}/cm^{-1} 3380, 2946, 2863, 1612, 1513, 1462, 137, 1249, 1099, 1058, 882, 856, 835, 775 and 739; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 × $SiCH_3$), 0.60 (6 H, q, *J* 7.8, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (9 H, t, *J* 7.8, 3 × $SiCH_2CH_3$), 0.93 (1 H, m, HC*H*Si), 1.02-1.13 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.03 (3 H, d, *J* 6.3, 11-H_3), 1.21 and 1.29 (each 3 H, s, 2-CH_3), 1.55 (1 H, ddd, *J* 14.1, 9.6, 5.0, 8-H), 1.72 (1 H, ddd, *J* 13.9, 6.8, 1.3, 8-H'), 1.73-1.92 (2 H, m, SCH_2CH_2), 2.43 (1 H, ddd, *J* 13.9, 5.8, 3.3, SHC*H*), 2.53 (1 H, dd, *J* 13.9, 6.6, 6-H), 2.70 (1 H, ddd, *J* 13.1, 7.0, 5.3, SHC*H*), 2.82-2.93 (2 H, m, 6-H', SHC*H*), 3.02 (1 H, ddd, *J* 14.0, 10.5, 5.6, SHC*H*), 3.42 (1 H, ddd, *J* 11.1, 9.6, 6.1, OHC*H*CH_2Si), 3.46 (1 H, d, *J* 9.3, 1-H), 3.51 (1 H, ddd, *J* 9.5, 4.2, 1.5, 9-H), 3.71 (1 H, ddd, *J* 11.4, 9.6, 5.6, OHC*H*CH_2Si), 3.78 (3 H, s, $ArOCH_3$), 3.79 (1 H, m, 7-H), 3.80 (1 H, d, *J* 9.3, 1-H'), 4.06 (1 H, qd, *J* 6.3, 4.3, 10-H), 4.28 (1 H, dd, *J* 12.6, 5.3, 2'-H), 4.39 (1 H, dd, *J* 12.5, 7.1, 2'-H'), 4.42 and 4.44 (each 1 H, d, *J* 11.7, ArHC*H*), 4.53 (1 H, d, *J* 3.5, 4-H), 4.60 (1 H, br. s, OH), 4.69 (2 H, s, OCH_2O), 6.06 (1 H, m, 1'-H) and 6.84 and 7.23 (each 2 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3, 0.0, 6.7, 8.4, 13.4, 18.5, 19.5(2), 22.9, 24.5, 27.3, 27.9, 28.4, 37.3, 41.6, 48.6, 56.7, 61.7, 66.5, 68.1, 70.5, 72.7, 74.5, 77.5, 78.7, 82.2, 97.7, 115.1, 130.5, 131.9, 133.4, 139.2 and 160.5; *mlz* (ES^+) 1147.3 (22%), 1068.1 (M^+ + 23, 100) and 1063.2 (M^+ + 18, 17). The seond fraction was the *title compound* **82** (14 mg, 34%), a viscous colourless oil, R_f = 0.56 (5:1 light petroleum:ether), $[\alpha]_D^{29}$ −34.6 (*c* 1.4, DCM); ν_{max}/cm^{-1} 3396, 2952, 2863, 1615, 1514, 1463, 1379, 1249, 1099, 1057, 882, 858, 835, 807, 775 and 742; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 ×

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$SiCH_3$), 0.56-0.64 (6 H, m, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (1 H, m, HC*H*Si), 0.93 (9 H, t, *J* 7.8, 3 × $SiCH_2CH_3$), 1.02-1.13 [24 H, m, 11-H_3, 3 × $SiCH(CH_3)_2$], 1.23 and 1.30 (each 3 H, s, 2-CH_3), 1.49 (1 H, ddd, *J* 14.0, 9.6, 4.7, SCH_2HCH), 1.62 (1 H, ddd, *J* 14.1, 7.2, 1.5, SCH_2HCH), 1.80 and 1.90 (each 1 H, m, 8-H), 2.43 (1 H, ddd, *J* 14.1, 5.8, 3.5, SHC*H*), 2.57 (1 H, dd, *J* 13.6, 6.6, 6-H), 2.66 (1 H, ddd, *J* 13.9, 6.8, 5.0, SHC*H*), 2.82 (1 H, dd, *J* 13.6, 6.5, 6-H'), 2.95-3.07 (2 H, m, 2 × SHC*H*), 3.39-3.46 (2 H, m, OHC*H*CH_2Si, 1-H), 3.54 (1 H, ddd, *J* 9.3, 4.3, 1.8, 9-H), 3.70 (1 H, ddd, *J* 11.4, 9.6, 5.6, OHC*H*CH_2Si), 3.79 (3 H, s, $ArOCH_3$), 3.81 (1 H, d, *J 9.4,* 1-H'), 3.95 (1 H, qd, *J 6.8,* 4.8, 7-H), 4.04 (1 H, qd, *J 6.3,* 4.3, 10-H), 4.29 (1 H, dd, *J* 12.4, 5.3, 2'-H), 4.37 (1 H, br. s, OH), 4.39 (1 H, dd, *J* 12.5, 7.6, 2'-H'), 4.41 and 4.45 (each 1 H, d, *J* 11.8, ArHC*H*), 4.59 (1 H, d, *J* 4.8, 4-H), 4.68 and 4.71 (each 1 H, d, *J* 6.9, OHC*H*O), 6.20 (1 H, t, *J* 6.3, 1'-H) and 6.85 and 7.23 (each 2 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.3, 0.0, 6.7, 8.5, 13.4, 18.6, 19.5, 19.6, 23.1, 24.6, 27.3, 27.8, 28.3, 37.5, 42.3, 48.4, 56.7, 61.8, 66.5, 67.8, 70.6, 72.3, 74.5, 76.2, 77.5, 82.0, 97.5, 115.2, 130.5, 131.7, 132.9, 140.3 and 160.5; *m/z* (ES^+) 1068.2 (M^+ + 23, 51%), 1063.2 (M^+ + 18, 100) and 327.1 (19).

(4*S*,7*S*,9*R*,10*R*)-4,10-Bis-*tert*-butyldimethylsilyloxy-7-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-1-(4-methoxybenzyloxy)-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecane (84).

2,6-Lutidine (17 µL, 0.14 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (16 µL, 0.073 mmol) were added to the alcohol **82** (13 mg, 0.012 mmol) in DCM (0.20 mL) and the solution stirred at rt for 3 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 ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (55:1 light petroleum:ether) gave the *title compound* **84** (13 mg, 90%) as a viscous colourless oil, R_f = 0.50 (15:1 light petroleum:ether), $[\alpha]_D^{29}$ −15.3 (*c* 1.1, DCM); ν_{max}/cm^{-1} 2953, 2925, 2863, 1613, 1513, 1463, 1376, 1249, 1093, 1060, 885, 858, 836, 776 and 745; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.02 (3 H, s, $SiCH_3$), 0.04 (6 H, s, 2 × $SiCH_3$), 0.11 (3 H, s, $SiCH_3$), 0.56-0.67 (6 H, m, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 and 0.93 [each 9 H, s, $SiC(CH_3)_3$], 0.94 (1 H, m, HC*H*Si), 0.95 (9 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 0.99 (3 H, d, *J* 6.3, 11-H_3), 1.03-1.12 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.26 and 1.28 (each 3 H, s, 2-CH_3), 1.38-1.50 (2 H, m, SCH_2CH_2), 1.74-1.89 (2 H, m, 8-H_2), 2.36 (1 H, t, *J* 12.6, 6-H), 2.55-2.91 (4 H, m, 2 × SCH_2), 3.04 (1 H, d, *J* 12.6, 6-H'), 3.39 (1 H, ddd, *J* 11.0, 9.6, 6.1, OHC*H*CH_2Si), 3.62 (1 H, m, 9-H), 3.65 (1 H, d, *J* 8.8, 1-H), 3.70 (1 H, ddd, *J* 11.4, 9.6, 5.5, OHC*H*CH_2Si), 3.79 (3 H, s, $ArOCH_3$), 3.82 (1 H, d, *J* 8.6, 1-H'), 4.09 (1 H, m, 7-H), 4.13 (1 H, qd, *J* 6.3, 4.5, 10-H), 4.29 (1 H, dd, *J* 12.9, 5.3, 2'-H), 4.36 (1 H, dd, *J* 13.0, 6.6, 2'-H'), 4.39 and 4.46 (each 1 H, d, *J* 11.6, ArHC*H*), 4.56 (1 H, s, 4-H),4.66 and 4.70 (each 1 H, d, *J* 7.0, OHC*H*O), 6.14 (1 H, m, 1'-H) and 6.85 and 7.24 (each 2 H, m, ArH); δ_C (100 MHz, $CDCl_3$) −3.7, −3.4, −3.3, −0.7, 0.0, 7.1, 8.6, 13.4, 18.5, 19.5(2), 20.2, 23.8, 23.9, 27.3, 27.8, 28.3, 36.1, 43.1, 50.4, 56.7, 62.2, 66.5, 69.0, 69.9, 71.9, 74.5, 77.1, 77.9, 81.9, 97.9, 115.0, 130.1, 132.9, 134.1, 137.7 and 160.3; *mlz* (ES^+) 1263.8 (100%), 1182.5 (M^+ + 23, 100) and 1177.5 (M^+ + 18, 39).

(4*S*,7*S*,9*R*,10*R*)-4,10-Bis-*tert*-butyldimethylsilyloxy-7-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecan-1-ol (85).

Dichlorodicyanoquinone (3 mg, 0.013 mmol) was added to the 4-methoxybenzyl ether **84** (13 mg, 0.011 mmol) in DCM (0.25 mL) and an aqueous pH 7.2 phosphate buffer (0.05 mL) and the mixture stirred for 30 min. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with ether (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* **85** (9.5 mg, 81%) as a viscous colourless oil, R_f = 0.31 (7:1 light petroleum:ether), $[\alpha]_D^{29}$ −16.5 (*c* 0.8, DCM); ν_{max}/cm^{-1} 3438, 2952, 2925, 2866, 1470, 1464, 1377, 1250, 1093, 1055, 884, 861, 836 and 775; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.03 (6 H, s, 2 × $SiCH_3$), 0.05 and 0.15 (each 3 H, s, $SiCH_3$), 0.55-0.66 (6 H, m, 3 × $SiCH_2$), 0.84 (1 H, ddd, *J* 13.9, 11.1, 5.3, HC*H*Si), 0.87 and 0.95 [each 9 H, s, $SiC(CH_3)_3$], 0.93 (1 H, m, HC*H*Si), 0.95 (9 H, t, *J* 8.0, 3 × $SiCH_2CH_3$), 0.98 (3 H, d, *J* 6.3, 11-H_3), 1.03-1.12 [21 H, m, 3 × $SiCH(CH_3)_2$], 1.19 and 1.21 (each 3 H, s, 2-CH_3), 1.38-1.51 (2 H, m, 8-H_2), 1.79-1.92 (2 H, m, SCH_2CH_2), 2.38 (1 H, t, *J* 12.8, 6-H), 2.60-2.94 (4 H, m, 2 × SCH_2), 2.99 (1 H, d, *J* 13.0, 6-H'), 3.08 (1 H, br. s, OH), 3.39 (1 H, ddd, *J* 11.1, 9.6, 6.1, OHC*H*CH_2Si), 3.62 (1 H, ddd, *J* 9.6, 4.3, 2.8, 9-H), 3.70 (1 H, ddd, *J* 11.4, 9.6, 5.4, OHC*H*CH_2Si), 3.74 (2 H, br. s, 1-H_2), 4.09 (1 H, m, 7-H), 4.13 (1 H, qd, *J* 6.3, 4.5, 10-H), 4.29 (1 H, dd, *J* 12.9, 5.0, 2'-H), 4.37 (1 H, dd, *J* 12.9, 7.1, 2'-H'), 4.56 (1 H, s, 4-H), 4.66 and 4.69 (each 1 H, d, *J* 6.8, OHC*H*O) and 6.18 (1 H, m, 1'-H); δ_C (100 MHz) −3.7, −3.4, −3.3, −0.8, 0.0, 7.1, 8.6, 13.7, 18.5, 19.5(3), 20.2, 23.0, 23.7, 24.5, 27.2, 27.3, 27.8, 28.3, 36.1, 43.2, 48.8, 62.1, 66.6, 69.0, 69.9, 71.6, 72.5, 78.3, 81.8, 97.8, 134.5 and 137.4; *mlz* (ES^+) 1141.3 (100%), 1062.2 (M^+ + 23, 71) and 492.4 (24).

(4*S*,7*S*,9*R*,10*R*)-1-(Benzothiazol-2-ylsulfanyl)-4,10-bis-*tert*-butyldimethylsilyloxy-7-triethylsilyloxy-5-[(*E*)-2-tri-isopropylsilyloxyethylidene]-2,2-dimethyl-9-(2-trimethylsilylethoxymethoxy)-3,3-(1,3-dithiopropyl)undecane (86).

Di-isopropyl azodicarboxylate (0.54 M in THF, 50 µL, 0.027 mmol) was added to the alcohol **85** (9.5 mg, 0.009 mmol), PPh_3 (7 mg, 0.027 mmol) and 2-mercaptobenzothiazole (4.5 mg, 0.027 mmol) in THF (0.2 mL) at 0 °C and the mixture stirred at 0 °C for 1 h then at rt for 3 h. Ether (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added and the aqueous phase was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue (70:1 light petroleum:ether) gave the *title compound* **86** (8.5 mg, 78%) as a viscous colourless oil, R_f = 0.22 (40:1 light petroleum:ether), $[\alpha]_D^{29}$ −14.2 (*c* 0.9, DCM); ν_{max}/cm^{-1} 2946, 2865, 1463, 1428, 1382, 1361, 1250, 1145, 1096, 1058, 1017, 933, 886, 860, 835, 776, 754, 725 and 667; δ_H (400 MHz, $CDCl_3$) 0.00 [9 H, s, $Si(CH_3)_3$], 0.04 (6 H, s, 2 ×

$SiCH_3$), 0.07 and 0.20 (each 3 H, s, $SiCH_3$), 0.54-0.67 (6 H, m, 3 × $SiCH_2$), 0.85 (1 H, m, HC*H*Si), 0.87 [9 H, s, $SiC(CH_3)_3$], 0.93 (1 H, m, HC*H*Si), 0.93 (9 H, t, *J* 7.9, 3 × $SiCH_2CH_3$), 0.96 [9 H, s, $SiC(CH_3)_3$], 0.98-1.08 [24 H, m, 11-H_3, 3 × $SiCH(CH_3)_2$], 1.34 (6 H, s, 2 × 2-CH_3), 1.41-1.52 (2 H, m, 8-H_2), 1.78-1.95 (2 H, m, SCH_2CH_2), 2.42 (1 H, t, *J* 12.5, 6-H), 2.62-2.95 (4 H, m, 2 × SCH_2), 3.05 (1 H, d, *J* 12.6, 6-H'), 3 .40 (1 H, td, *J* 10.4, 6.0, OHC*H*CH_2Si), 3.62 (1 H, m, 9-H), 3.72 (1 H, ddd, *J* 11.4, 10.1, 5.4, OHC*H*CH_2Si), 3.93-4.00 (2 H, m, 1-H_2), 4.10-4.17 (2 H, m, 7-H, 10-H), 4.31 (1 H, dd, *J* 12.9, 5.4, 2'-H), 4.36 (1 H, dd, *J* 12.9, 6.6, 2'-H'), 4.65 (1 H, s, 4-H), 4 .68 and 4.72 (each 1 H, d, *J* 6.9, OHC*H*O), 6.18 (1 H, m, 1'-H), 7.25 and 7.36 (each 1 H, t, *J* 7.6, ArH), 7. 71 (1 H, d, *J* 7.8, ArH) and 7.82 (1 H, d, *J* 7.9, ArH); δ_C (100 MHz, $CDCl_3$) −3.7, −3.4, −3.3, −0.7, 0.0, 7.1, 8.6, 13.4, 18.5, 19.5, 19.6, 20.2, 23.7, 27.3, 27.6, 27.8, 28.6, 36.1, 43.1, 44.7, 50.1, 62.1, 66.6, 69.0, 69.9, 73.1, 78.1, 81.9, 97.9, 122.2, 122.9, 125.3, 127.3, 134.6, 136.6, 137.7, 154.8 and 170.2; *m/z* (ES^+) 1188.6 (M^+ + 23, 31%) and 540.7 (100).

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