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Synthetic approaches to phomactins: on the stereoselectivity of some [2,3]-Wittig rearrangements

Timothy J. Blackburn, Michael J. Kilner, Eric J. Thomas *

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

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ABSTRACT

On treatment with *n*-butyllithium, 4-alkoxy- and 4-silyloxy-2-(tributylstannylmethoxymethyl)-1,6-dimethyl-1-(phenylsulfonylmethyl)cyclohex-2-enes undergo tin–lithium exchange followed by [2,3]-Wittig rearrangements to give 3-alkoxy- and 3-silyloxy-2-hydroxymethyl-5,6-dimethyl-1-methylene-6-(phenylsulfonylmethyl)cyclohexanes in which the 2-hydroxymethyl and 6-phenylsulfonylmethyl residues are *cis*-disposed about the six-membered ring. In contrast, the corresponding 1-(phenylsulfanylmethyl) cyclohexenes give mainly methylenecyclohexanes with the 2-hydroxymethyl and 6-phenylsulfanylmethyl groups *trans*-disposed about the six-membered ring. This stereoselectivity is independent of the nature of the alkoxy- or silyloxy-substituent and configuration at C4. The 3-*tert*-butyldiphenylsilyloxy-1-methylene-6-(phenylsulfonylmethyl)cyclohexane was converted into a macrocyclic precursor of the phomactins.

1. Introduction

The phomactins are diterpenes with distinctive structures and interesting biological activities that have provided challenging targets for synthetic organic chemists.[1] Several total syntheses, including syntheses of phomactin A **1**,[2] together with other novel synthetic approaches,[3] have been developed to date. Aspects of this chemistry have been reviewed.[4]

In our approach to the phomactins,[5] a key step was the [2,3]-Wittig rearrangement of the alkynylmethyl ether **2**. This gave a mixture of the epimeric alcohols **3** in which the side-chain at C2 was *cis*-disposed to the phenylsulfonylmethyl substituent at C6 for both epimers.[5b] This stereoselectivity had not been observed in earlier analogous [2,3]-Wittig rearrangements.[5a] The mixture of epimers was then converted into the bis-(*E*)-triene **4** that was taken through to the bicyclic triene **5**, a promising macrocyclic intermediate for the synthesis of phomactins.[5b]

In this work, the alkynylmethyl ether **2** was used rather than the bis(alkenylmethyl) ether **6**, as preliminary studies had indicated it would be difficult to direct the regioselectivity of deprotonation of the bis(alkenylmethyl) ether.[6] However, several steps were required to convert the alkyne **3** into the (*E*)-alkene **4** and this restricted the amount of material that could conveniently be taken through the synthesis. We now report a modified approach based on the Still [2,3]-Wittig rearrangement,[7] together with further studies of the stereoselectivity of the [2,3]-Wittig process (Fig. 1).[5c]

2. Results and discussion

2.1. Preliminary investigations of alternative approaches

The racemic keto-ester **7**, as a 75: 25 mixture of epimers at C6,[5a] was converted into the 2-(hydroxmethyl)cyclohexene **17** and the corresponding 2-(bromomethyl)cyclohexene **18**, see Scheme 1. O-Silylation of the ketoester **7** gave the dienyl enol ether **8** and this was oxidized using methyl(trifluoromethyl)dioxirane[8] generated in situ to give the 2-(hydroxymethyl)cyclohexenone **9** after desilylation during work-up, still as a mixture of C6 epimers, see Scheme 1. This mixture was protected as its *tert*-butyldimethylsilyl ether **10** that was reduced under Luche's conditions to give the C6 epimeric alcohols **11** and **13** that now could be separated. The configuration of the major product **11** at C4 was established by NOE studies and was confirmed later by X-ray diffraction. This structure was consistent with pseudo-axial attack on the preferred conformation of the major enone, away from the axial 1-methyl substituent. The structure of the minor alcohol **13** was assigned by analogy.

Following protection of the alcohol **11** as its trimethylsilylethoxymethyl (SEM) ether **12**, reduction of the ester using Super-Hydride™ gave the alcohol **14**. This was converted into the analogous phenylthioether **15** via the corresponding methanesulfonate, and selective oxidation on sulfur[9] gave the sulfone **16**. Desilylation

* Corresponding author. Tel.: +44 (0) 161 275 4613; e-mail address: e.j.thomas@manchester.ac.uk (E.J. Thomas).

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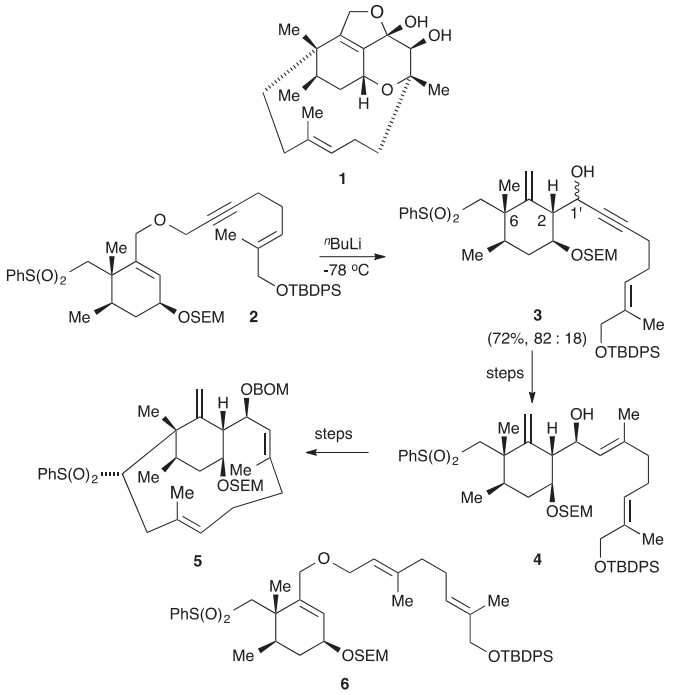
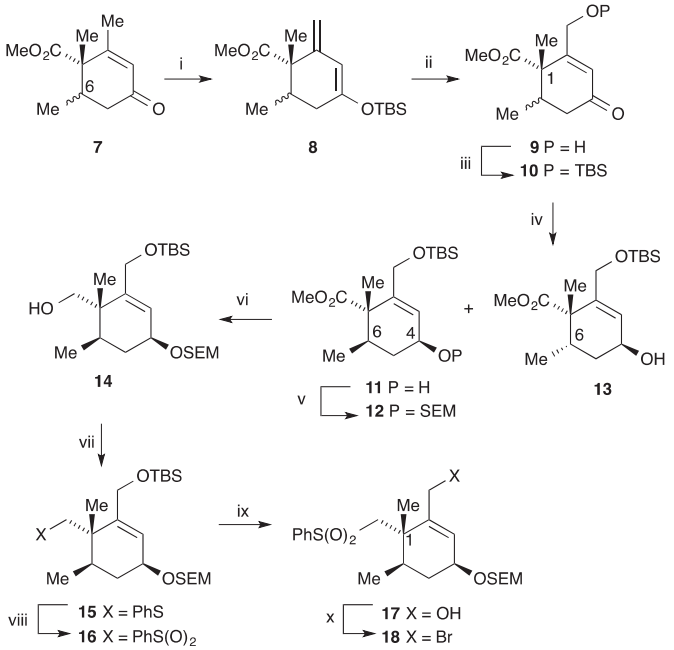


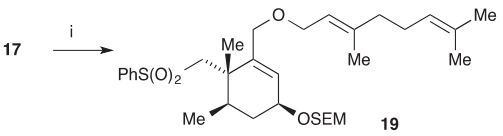
Fig. 1. The earlier [2,3]-Wittig rearrangement based synthesis of the phomactin core **5**.



Scheme 1. Synthesis of the 1-(phenylsulfonylmethyl)-2-(hydroxymethyl)cyclohex-2-ene **17** Reagents and conditions. i, Et_3N, $^tBuMe_2SiOTf$, DCM, 0 °C, 20 h (65%); ii, Na_2EDTA, CF_3COCH_3, oxone™, $NaHCO_3$, −10 °C, 1.5 h (68%); iii, $^tBuMe_2SiCl$, imid., DCM, rt, 24 h (92%); iv, $CeCl_3.7H_2O$, $NaBH_4$, −78 °C, 2 h (**11**, 63%; **13**, 18%); v, $^iPr_2NEt$, SEMCl, DCM, 0 °C to rt, 20 h (80%); vi, $LiEt_3BH$, THF, 0 °C to rt, 4 h (82%); vii, (a) Et_3N, MsCl, DCM, 0 °C, 2 h; (b) NaH, PhSH, DMF, 0 °C, 20 min, add mesylate, heat under reflux, 20 h (73%); viii, $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h (71%); ix, TBAF, THF, rt, 16 h (85%); x, MsCl, Et_3N, THF, 0 °C, 45 min, LiBr, THF, 0 °C, 1 h (86%).

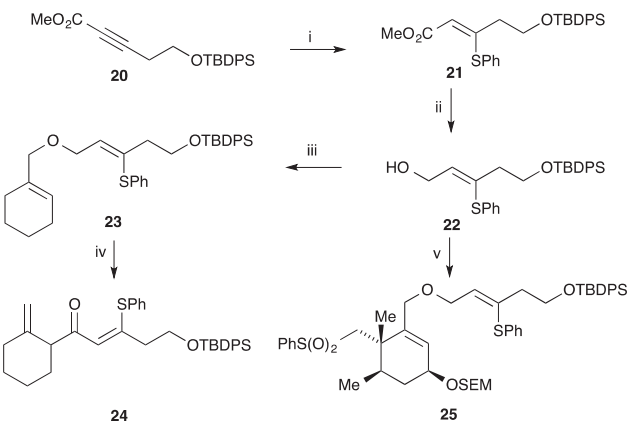
gave the primary alcohol **17** and this was converted into the bromide **18**, see Scheme 1.

[2,3]-Wittig rearrangements of bis(alkenylmethyl) ethers usually proceed with deprotonation of the more acidic methylene group next to the ethereal oxygen.[6] To check whether this preference could be overturned in the present case, e.g. by using bulky bases to remove the less hindered, albeit less acidic, proton at C1′, the alcohol **17** was alkylated using geranyl bromide to give the bis(alkenylmethyl) ether **19**, see Scheme 2. However, initial attempts to effect a [2,3]-Wittig rearrangement on this substrate using various bases, e.g., *sec*-butyllithium, gave either unchanged starting material or complex mixtures of products.



Scheme 2. Preparation of the model bis(alkenylmethyl) ether **19** Reagents and conditions. i, NaH, $^nBu_4NI$, THF, 0 °C, 20 min, 15-*c*-5, geranyl bromide, rt, 16 h (80%).

It has been shown that carbanion stabilising groups can control the deprotonation of bis(alkenylmethyl) ethers leading to regioselective [2,3]-Wittig rearrangements.[6,10] Since the stereoselective introduction of a vinylic methyl group by substitution of a phenylthio substituent had proved useful in earlier studies,[5b] the control of the regioselectivity of the Wittig rearrangement by a phenylthio group was briefly evaluated. The stereoselective addition[11] of thiophenol to the pentynyl ester **20** gave the thioether **21** that was reduced to the alcohol **22**. Alkylation of this using 1-(bromomethyl) cyclohexene gave the bis(alkenylmethyl) ether **23** that on treatment with *n*-butyllithium underwent a regioselective Wittig rearrangement to give the ketone **24** after oxidation of the intermediate alcohols. However, despite this promising model study, preliminary studies of the [2,3]-Wittig rearrangement of the more complex ether **25**, prepared by alkylation of the alcohol **22** using the bromide **18**, were unsuccessful in that either unchanged starting materials or complex mixtures of products were obtained, see Scheme 3.



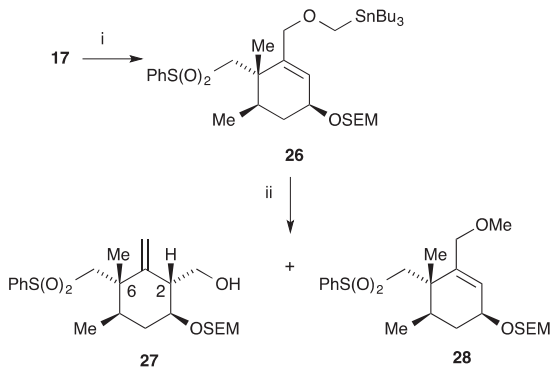
Scheme 3. Synthesis and rearrangement of phenylthio-substituted alkenyl ethers Reagents and conditions. i, NaOMe, PhSH, MeOH, rt, 16 h (85%); ii, DIBAL-H, THF, −78 °C, 3 h (88%); iii, **22**, NaH, $^nBu_4NI$, 0 °C, 20 min, 15-*c*-5, 1-(bromomethyl)cyclohexene, THF, rt, 24 h (93%); iv, (a) ^nBuLi, THF, −60 °C, 0.5 h; (b) IBX, DMSO, rt, 3 h (72%); v, NaH, $^nBu_4NI$, THF, 0 °C, 20 min, 15-*c*-5, **18**, THF, rt, 16 h (71%).

2.2. Use of the Still [2,3]-Wittig rearrangement

Although further studies into the [2,3]-Wittig rearrangement of the substituted bis(alkenylmethyl) ether **25** could have been carried out, it was decided instead to look at the simpler [2,3]-Still process[7] since an efficient incorporation of the products into the macrocyclisation precursor **4** could be envisaged.

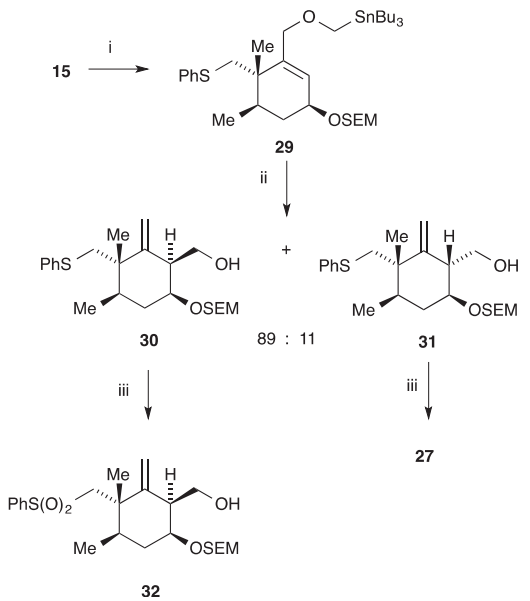
Alkylation of the alcohol **17** using iodomethyl(tributyl)stannane gave the ether **26**. On treatment with 2 equiv of *n*-butyllithium at −50 °C, this was converted into the [2,3]-Wittig product **27** that was isolated in a modest yield of 35%, together with the methyl ether **28**, presumably formed by protonation of the intermediate from the

tin–lithium exchange. The use of more vigorous conditions led to the formation of additional side-products that were not fully characterised and when only 1 equiv of *n*-butyllithium was used, 90% of unchanged starting material was obtained, see Scheme 4.



Scheme 4. Preparation and [2,3]-rearrangement of the sulfone **26** Reagents and conditions i, NaH, THF, rt, 5 min, $^{n}Bu_3SnCH_2I$, rt, 24 h (78%); ii, $^{n}BuLi$ (2 equiv), THF, −78 °C to−50 °C, 24 h (**27**, 35%; **28**, 60%).

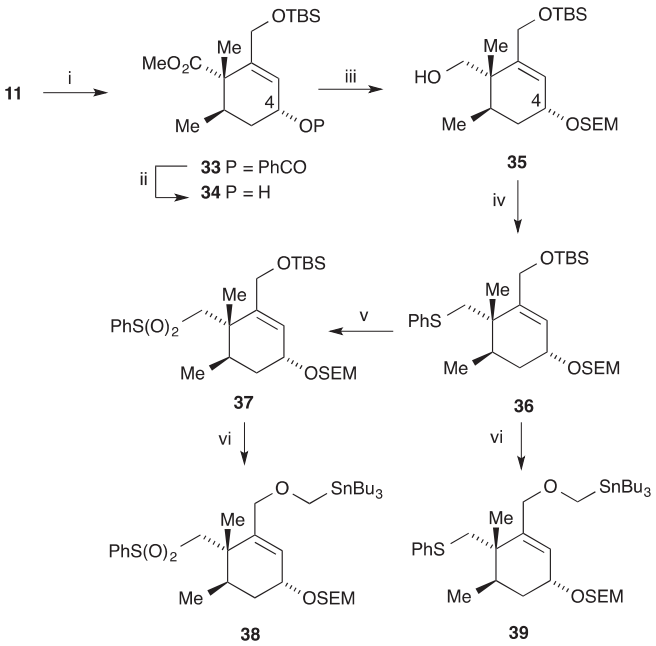
The 35% yield of the [2,3]-Wittig product **27** was disappointing but it was formed essentially as a single diastereoisomer. This was identified as having the 2-(hydroxymethyl) and 6-(phenylsulfonylmethyl) substituents *cis*-disposed about the six-membered ring on the basis of a significant NOE between 2-H and the 6-methyl substituent. As 2 equiv of base were required for the rearrangement, it was inferred that deprotonation of the phenylsulfonylmethylene group was taking place under the reaction conditions. To check whether this was influencing the [2,3]-Wittig reaction, it was decided to check the behaviour of the analogous, but less acidic, sulfide **29**. This was prepared by desilylating the *tert*-butyldimethylsilyl ether **15** followed by alkylation of the resulting alcohol and was found to rearrange efficiently on treatment with 1 equiv of *n*-butyllithium. Two diastereoisomeric rearrangement products **30** and **31** were isolated, ratio 89: 11, in which the major product **30** had the 2-(hydroxymethyl) and 6-(phenylsulfanylmethyl) groups *trans*-disposed about the six-membered ring. The structures of these products were established by



Scheme 5. Preparation and [2,3]-rearrangement of the sulfide **29** Reagents and conditions i, (a) TBAF, THF, rt, 16 h; (b) NaH, THF, rt, 5 min, $^{n}Bu_3SnCH_2I$, rt, 24 h (69%); ii, $^{n}BuLi$, THF, −78 °C to−50 °C, 24 h (**30**, 81%; **31**, 10%); iii, $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h (**32**, 86%; **27**, 86%).

correlation with the rearranged sulfone **27**, the minor rearrangement product **31** from the sulfide **29** giving the sulfone **27** on oxidation, whereas the major rearrangement product gave a new sulfone **32**, see Scheme 5.

The contrasting stereoselectivities observed for the Wittig rearrangements of the sulfone **26** and sulfide **29** were interesting and so it was decided to study the [2,3]-rearrangements of some analogous substrates. The epimeric substrates were prepared starting with alcohol **11**. Inversion to the epimeric alcohol **34** was carried out using a Mitsunobu reaction followed by hydrolysis of the intermediate ester **33**. After the SEM-protection, reduction of the ester gave the primary alcohol **35** that was converted into the thioether **36**. Oxidation gave the sulfone **37** and desilylation and O-alkylation of the sulfone **37** and sulfide **36** gave the [2,3]-rearrangement precursors **38** and **39**, see Scheme 6.



Scheme 6. Preparation of the rearrangement precursors **38** and **39** Reagents and conditions i, Ph_3P, DIAD, $PhCO_2H$, THF, 0 °C, 4 h; ii, NaOH, MeOH, rt, 30 min (94% two steps); iii, (a) $^{i}Pr_2NEt$, SEMCl, DCM, 0 °C to rt, 2 d; (b) $LiEt_3BH$, THF, 0 °C to rt, 4 h (74%); iv, (a) Et_3N, MsCl, DCM, 0 °C, 2 h; (b) NaH, PhSH, DMF, 0 °C, 20 min, add mesylate, heat under reflux, 4 h (75%); v, $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h (73%); vi, (a) TBAF, THF, rt, 18 h; (b) NaH, THF, 5 min, $^{n}Bu_3SnCH_2I$, rt, 24 h (**38**, 76%; **39**, 74%).

The Wittig rearrangements of the substrates **38** and **39** followed the pattern set by their epimers **26** and **29**. The rearrangement of the sulfone **38** was highly stereoselective in favour of the unsaturated alcohol **40** in which the 2-(hydroxymethyl) and 6-(phenylsulfonylmethyl) groups were *cis* to each other with respect to the six-membered ring albeit only a 37% yield was obtained. The rearrangement of the sulfide **39** was more efficient but gave a mixture of epimeric products **41** and **42**, ratio 92:8, in which the major product had the 2-(hydroxymethyl) and 6-(phenylsulfanylmethyl) groups *trans*-disposed with respect to the six-membered ring. The structures of these products were confirmed later but products from these reactions were correlated with each other in that oxidation of the minor product **42** from rearrangement of the sulfide **39** gave the product **40** obtained by rearrangement of the sulfone **38** whereas oxidation of the major product **41** from the rearrangement of the sulfide **39** gave a different sulfone **43**, see Scheme 7.

The influence of the protecting group of the allylic alcohol on the stereoselectivity of the [2,3]-rearrangement was investigated by protecting the hydroxy-ester **11** as its bulky *tert*-butyldiphenylsilyl

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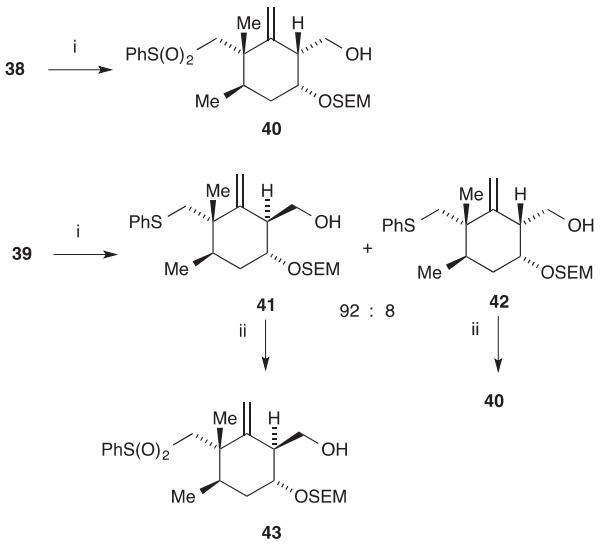
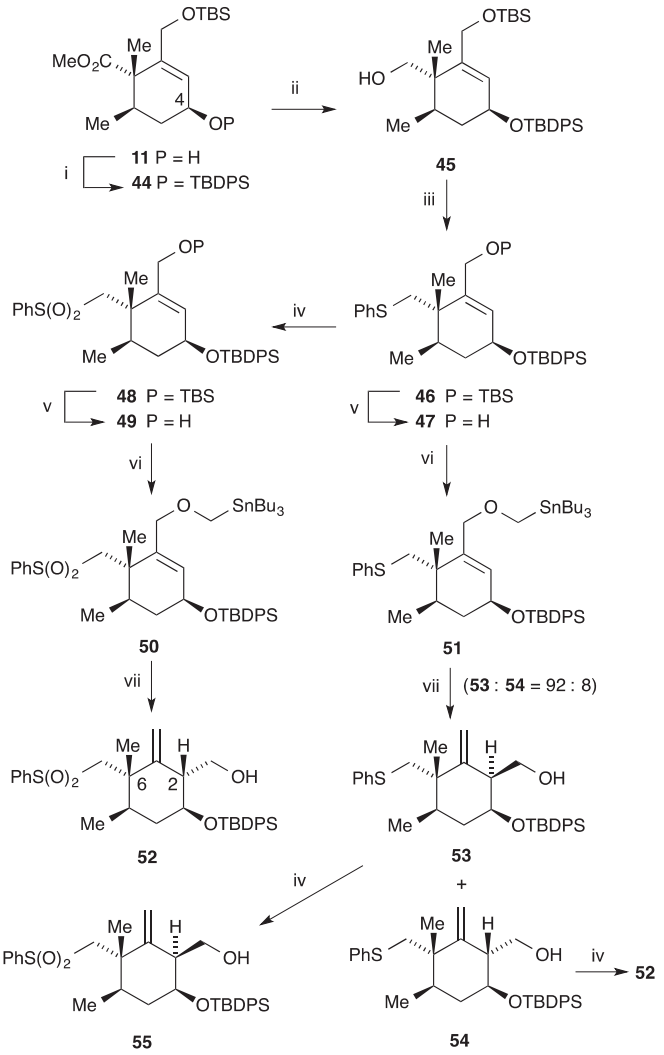


Scheme 7. [2,3]-Rearrangements of the sulfone **38** and sulfide **39** Reagents and conditions i, ^{n}BuLi, THF, −78 °C to −50 °C, 24 h (**40**, 37% using 2 equiv ^{n}BuLi; **41**, 81%; **42**, 7%); ii, $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h (**40**, 88%; **43**, 84%).

ether **44**. Reduction of the ester gave the alcohol **45** that was converted into the phenylthioether **46** via the corresponding mesylate. Oxidation of the thioether gave the sulfone **48**. The thioether **46** and sulfone **48** were selectively monodesilylated and the primary alcohols **47** and **49** so formed were alkylated using iodomethyl (tributyl)stannane to give the stannylmethyl ethers **51** and **50**, respectively. These were subjected to the [2,3]-Wittig rearrangements under the usual conditions. The rearrangement of the sulfone **50** was highly stereoselective and gave the homoallylic alcohol **52** in which the 2-(hydroxymethyl) and 6-(phenylsulfonylmethyl) groups were *cis*-disposed about the six-membered ring in an improved yield of 65%. As before, rearrangement of the thioether **51** was more efficient but again gave two products **53** and **54**, ratio 92:8. The major product was shown to be the epimer **53** in which the 2-(hydroxymethyl) and 6-(phenylsulfanylmethyl) groups are *trans*-disposed about the six-membered ring because oxidation gave a new sulfone **55**. Oxidation of the minor sulfide rearrangement product **54** gave sulfone **52**, see Scheme 8.

The structures of the [2,3]-rearrangements products prepared in this work had been established by oxidation of the products obtained from the sulfides into the sulfones and by ^{1}H NMR studies. However, the homoallylic alcohol **52**, prepared by rearrangement of the sulfone **50**, was crystalline. Its structure was confirmed unambiguously by X-ray diffraction, see Fig. 2.[12]

As the structure of the rearranged sulfone **52** was now secure, it was possible to confirm the structures assigned to the products in the other series. Deprotection of the crystalline sulfone **52** gave the diol **56** in which the 2-(hydroxymethyl) and 6-(phenylsulfonylmethyl) substituents must be *cis* to each other across the six-membered ring. The same diol was prepared by deprotection of the product **27** from rearrangement of the SEM-protected sulfone **26** so confirming the structure of this product as shown. S-Oxidation and deprotection of the major product **53** from rearrangement of the sulfide **51** gave diol **57** that was distinguishable from its epimer **56** by NMR. Oxidation of the major product **41** from rearrangement of the SEM-protected sulfide **39** had given the sulfone **43** that was benzoylated to give the benzoate **58**. Deprotection gave the alcohol **59** and inversion of the configuration at C3 via a Mitsunobu reaction with a final saponification of both esters, also gave the diol **57**, see Scheme 9. This sequence confirmed the stereochemistry assigned to the rearrangement product **41**. The oxidations of the sulfides had related the structures of the sulfides and sulfones within the series and so the structures of all products were now confirmed. It would appear that the 4-alkoxy- and



Scheme 8. Preparation and [2,3]-rearrangement of *tert*-butyldiphenylsilyloxysubstituted stannanes **50** and **51** Reagents and conditions i, *tert*-butyldiphenylsilyl chloride, imid., DCM, 0 °C to rt, 24 h (96%); ii, $LiEt_3BH$, THF, 0 °C to rt, 4 h (88%); iii, (a) Et_3N, MsCl, DCM, 0 °C, 2 h; (b) NaH, PhSH, DMF, 0 °C, 20 min, add mesylate, heat under reflux, 4 h (81%); iv, $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h (**48**, 88%; **52**, 86% from **54**; **55**, 86% from **53**); v, conc. aq HCl, EtOH, rt, 1 h (**47**, 95%; **49**, 95%); vi, NaH, THF, 5 min, $^{n}Bu_3SnCH_2I$, rt, 24 h (**50**, 83%; **51**, 83%); vii, ^{n}BuLi, THF, −78 °C to −50 °C, 24 h (**52**, 65% using 2 equiv ^{n}BuLi; **53**, 86%; **54**, 7%).

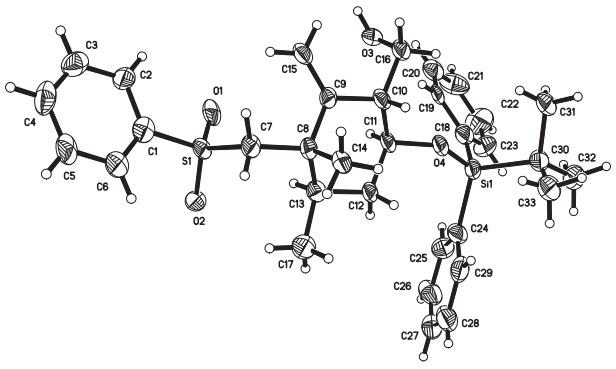
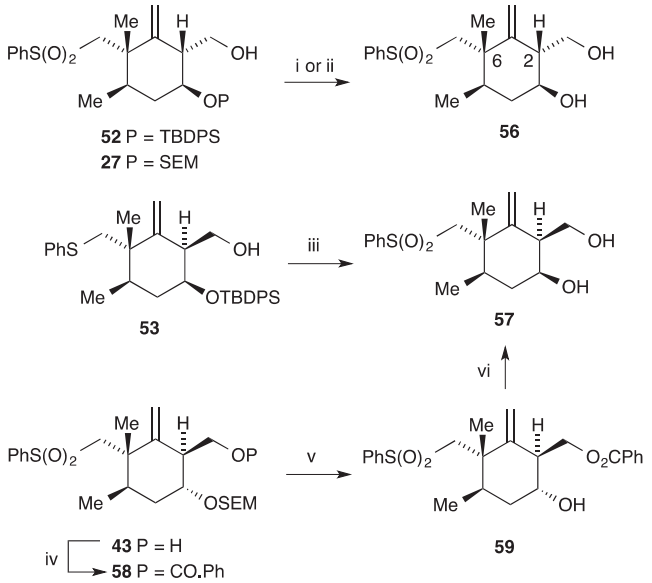


Fig. 2. An ORTEP projection of the [2,3]-rearrangement product **52** as established by X-ray diffraction.[12]

4-silyloxy-2-(tributylstannylmethoxymethyl)-1,6-dimethyl-1-(phenylsulfonylmethyl)cyclohexenes had rearranged to give the products with the 6-(phenylsulfonylmethyl) and 2-(hydroxymethyl) substituents *cis*-disposed about the six-membered ring irrespective of



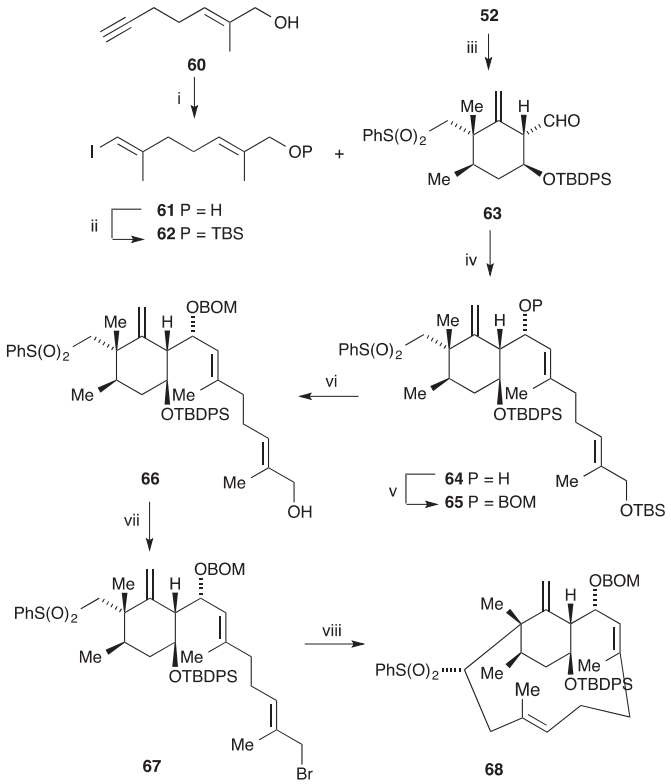
Scheme 9. Correlation of the products in the different series via the diols **56** and **57** Reagents and conditions i, TBAF, THF, rt, 24 h (83% from **52**); ii, $MgBr_2$, Et_2O, nitromethane, rt, 1 h (76% from **27**); iii, (a) $(NH_4)_2MoO_4$, H_2O_2, EtOH, 0 °C to rt, 24 h; (b) TBAF, THF, rt, 24 h (69%); iv, PhCOCl, DMAP, py, rt, 3 h; v, $MgBr_2$, Et_2O, nitromethane, rt, 1 h; vi, (a) Ph_3P, DIAD, THF, $PhCO_2H$, 0 °C, 4 h; (b) NaOH, MeOH, rt, 30 min (40% of **57** from **41**).

the nature of the substituent or the configuration at C4. Moreover, the analogous sulfides rearranged with the opposite stereoselectivity.

2.3. Synthesis of the core of the phomactins

The *tert*-butyldiphenylsilyl protected diol **52** was selected for incorporation into a synthesis of a macrocyclic precursor of phomactin A **1** and was oxidized to the corresponding aldehyde **63**. The hydroxyheptadienyl iodide **61** was prepared from the alkyne **60**[13] using Negishi conditions[14] and protected as its *tert*-butyldimethylsilyl ether **62**. The addition of organometallic reagents generated from the vinyl iodide **62** to the aldehyde **63** was then investigated. Initial studies with the vinyllithium reagent generated from the iodide **62** using *tert*-butyllithium to effect the iodide-lithium exchange, gave only modest yields of the adduct **64**. Slightly better yields were obtained if equimolar amounts of vinylic iodide and *tert*-butyllithium were employed but any excess of *tert*-butyllithium over the iodide resulted in a lower yield. The use of three molar equivalents each of iodide **62** and *tert*-butyllithum gave an optimised yield of 48%. These difficulties were attributed to the sensitivity to base of the βγ-unsaturated aldehyde **63**. Slightly improved yields were obtained when cerium(III) chloride[15] or anhydrous zinc(II) bromide[16] was added to the vinyllithium reagent before addition to the aldehyde, but the best yield, 85%, was achieved using ytterbium(III) triflate,[17,18] when a single adduct was isolated that was subsequently shown to be the alcohol **64**, see Scheme 10. The stereoselectivity of this reaction may be due to the organometallic reagent approaching the less hindered face of the co-ordinated aldehyde away from the bulky *tert*-butyldiphenylsilyloxy substituent, see Fig. 3.

Following protection of the alcohol **64** as its benzyloxymethyl (BOM) ether **65**, selective removal of the *tert*-butyldimethylsilyl group using acetic acid gave the alcohol **66**. This was converted into the bromide **67** via its mesylate, and an efficient cyclisation of the bromide using sodium hexamethyldisilazide as base gave the macrocycle **68** as a single epimer at C10. This was crystalline and its structure was confirmed by X-ray diffraction, see Fig. 4.[12] This X-ray structure confirmed the stereoselectivity of the addition of the vinylic organometallic reagent to the aldehyde **63** and established



Scheme 10. Synthesis of a macrocyclic precursor of the phomactins Reagents and conditions i, Cl_2ZrCp_2, $AlMe_3$, DCM, rt, 2 d, 0 °C, I_2, THF, rt, 5 h (62%); ii, $^tBuMe_2SiCl$, imid., rt, 24 h (96%); iii, $^iPr_2NEt$, py.SO_3, DMSO, DCM, 0 °C, 15 min (91%); iv, **62**, ^{t}BuLi, THF, pentane, −78 °C, 1 h, then add to $Yb(OTf)_3$, THF, −78 °C, 30 min, add to **63** in THF, −78 °C, 3 h (85%); v, BOMCl, $^iPr_2NEt$, $^nBu_4NI$, THF, rt, 16 h (82%); vi, AcOH, water, THF, rt, 2 d (91%); vii, Et_3N, MsCl, THF, 0 °C, 45 min, LiBr, THF, 0 °C, 1 h (86%); viii, NaHMDS, THF, 0 °C, add via a syringe pump over 40 min, 0 °C, 30 min (72%).

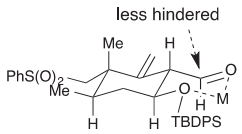


Fig. 3. Stereoselectivity of addition to the aldehyde **63.**

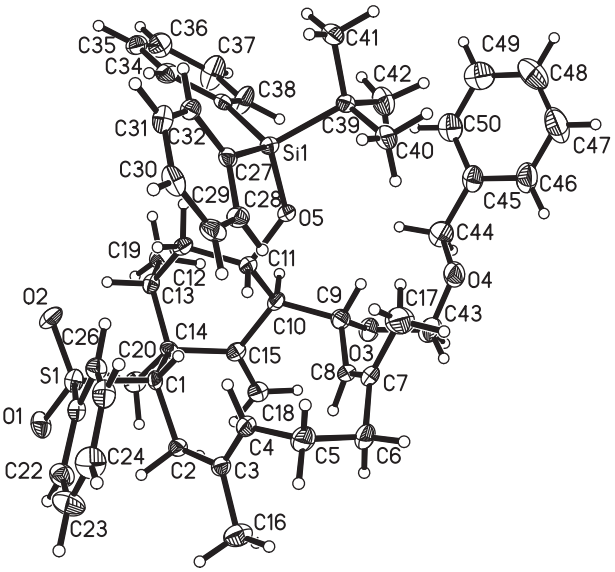


Fig. 4. An ORTEP projection of the macrocyclic compound **68** as determined by X-ray diffraction.[12]

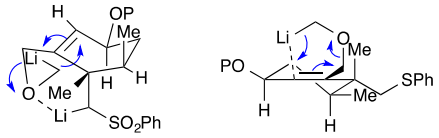
the configuration of the sulfone bearing stereogenic centre at C10, see Scheme 10.

3. Summary and conclusions

Macrocycle **68** has a structure that corresponds to the bicyclic core structure of the phomactins. Indeed it corresponds to the intermediate **5** prepared earlier, apart from the protecting group at C14 and the configuration at C2 (phomactin numbering), but is more accessible as the chemistry outlined in Scheme 10 is amenable to scale-up.

In the present work, it is of interest that the sulfones **26**, **38** and **50**, all rearranged with excellent stereoselectivity to give the products **27**, **40**, and **52**, in which the 2-(hydroxymethyl) groups were *cis*-disposed about the six-membered ring relative to the 6-(phenylsulfonylmethyl) substituents as had been observed earlier for the rearrangement of the phenylsulfonyl substituted alkynylmethyl ether **2**.[5b] In contrast the corresponding sulfides **29**, **39** and **51** rearranged to give predominantly [2,3]-rearrangement products in which the 2-(hydroxymethyl) and 6-(phenylsulfanylmethyl) substituents were *trans*-disposed about the six-membered ring. This remote substituent effect involving a reversal of the stereoselectivity of these rearrangement processes dependent on the oxidation state of the sulfur-containing substituent was not expected.

The stereoselectivity of the rearrangement of the sulfone **2** had been explained in terms of deprotonation of the sulfone to give a bis-lithiated intermediate following tin–lithium exchange. It was suggested that in this intermediate the migrating alkoxy group is coordinated to the lithiated sulfone and so is directed to the same face of the six-membered ring as the phenylsulfonylmethyl group. It would appear that this process is also taking place during the rearrangements of the phenylsulfones **26**, **38** and **50**, possibly via transition structure **69**, see Fig. 5. This explanation is consistent with the need for 2 equiv of *n*-butyllithium for these rearrangements



69 70

Fig. 5. Possible transition structures for the [2,3]-Wittig rearrangements.

For the sulfides, the rearrangements need just 1 equiv of *n*-butyllithium and so deprotonation of the methylene group next to the sulfide is not competing with tin–lithium exchange. The stereoselectivities of these rearrangements are consistent with the participation of transition structures analogous to **70**, see Fig. 5, in which the new carbon–carbon bond formation is taking place by axial attack on the carbon–carbon double-bond in the preferred conformation of the six-membered ring in which most of the substituents are equatorial. Analogous stereoselectivity has been observed in other systems.[19] In the case of sulfide **39**, it may be that steric hindrance due to the bulk of the protected 3-OH is also involved as implicated in earlier cases.[5c] Solvent effects on the stereoselectivities of these rearrangements were not investigated.

Further work is concerned with developing the chemistry of the macrocycle **68** to complete a synthesis of phomactin A **1**.[5c,20]

4. Experimental

4.1. General experimental procedures

^{1}H and ^{13}C NMR spectra were recorded on Varian Unity 500, Varian Unity Inova 400 and Varian Unity Inova 300 spectrometers with residual non-deuterated solvent as the internal standard. Only distinguishable peaks are reported for minor isomers in isomeric mixtures. IR spectra were recorded on an ATI Mattson Genesis FTIR as thin films produced by evaporation of a dichloromethane solution on sodium chloride plates unless otherwise stated. Mass spectra were recorded on Fison VG Trio 2000 and Kratos Concept spectrometers. For compounds containing tin only peaks corresponding to ^{120}Sn are reported and for bromine containing compounds ^{79}Br. Chemical ionisation (CI) was performed using ammonia. Chromatography refers to flash column chromatography using Merck silica gel 60H (230–300 mesh). Tetrahydrofuran (THF) was dried and distilled from sodium metal using benzophenone as an indicator under an atmosphere of nitrogen. Dichloromethane was dried and distilled from calcium hydride under an atmosphere of nitrogen. Ether refers to diethyl ether, which was dried and distilled from sodium metal using benzophenone as an indicator under an atmosphere of nitrogen. Light petroleum refers to the fraction that distilled between 40 and 60 °C. Benzene and hexane were dried over sodium metal. Butyllithium (1.6 M in hexanes) was titrated against a solution of propan-2-ol in xylene with 2,2′-bipyridine as an indicator. Triethylamine and di-isopropylamine were dried over potassium hydroxide pellets. Brine refers to saturated aqueous sodium chloride.

4.2. Experimental procedures

*4.2.1. Methyl 4-tert-butyldimethylsilyloxy-1,6-dimethyl-2-methylenecyclohex-3-ene-1-carboxylate (**8**).* Triethylamine (1.56 mL, 11.19 mmol) followed by *tert*-butyldimethylsilyl trifluoromethanesulphonate (2.49 mL, 10.84 mmol) were added at 0 °C to the enone **7**[5a] as a 75:25 mixture of epimers at C6 (1.42 g, 7.24 mmol) in dichloromethane (7 mL). After 20 h, dichloromethane (20 mL) was added and the mixture washed with saturated aqueous sodium bicarbonate (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was dissolved in ether, separated from the insoluble triethylammonium trifluoromethanesulphonate and the solution concentrated under reduced pressure. Chromatography of the residue on silica using 2% ether in light petroleum as eluent gave the *title compound* **8** (1.45 g, 65%) as a colourless oil, a 75: 25 mixture of diastereoisomers, R_f=0.7 (10% ether in light petroleum) (Found: M^+ Na, 333.1843. $C_{17}H_{30}O_3NaSi$ requires *M*, 333.1856); ν_{max}/cm^{-1} 2955, 2931, 2858, 1732, 1643, 1461, 1372, 1254, 1194, 1105, 1000, 890, 839 and 781; δ_H (300 MHz, $CDCl_3$) major epimer 5.47 (1H, s, 3-H), 4.71 and 4.49 (each 1H, s, 2-CH), 3.73 (3H, s, OCH_3), 2.48 (1H, m, 6-H), 2.20 (1H, m, 5-H), 1.88 (1H, m, 5-H′), 1.22 (3H, s, 1-CH_3), 0.95 [9H, s, $Si(CH_3)_3$], 0.88 (3H, d, *J* 7.0, 6-CH_3) and 0.19 (6H, s, 2×$SiCH_3$); minor epimer 5.53 (1H, s, 3-H), 4.87 and 4.81 (each 1H, s, 2-CH), 3.65 (3H, s, 1-OCH_3), 1.44 (3H, s, 1-CH_3) and 1.05 (3H, d, *J* 7.0, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 176.9, 174.8, 153.8, 153.2, 147.8, 146.6, 109.6, 108.4, 107.0, 106.2, 52.2, 51.8, 51.4, 48.8, 37.5, 37.0, 35.6, 34.7, 25.9, 25.9, 25.8, 22.4, 18.3, 17.8, 17.1, 16.3, −3.9, −4.0, −4.1 and −4.1; *m/z* (ES+) 333 (M^++123, 100%).

*4.2.2. Methyl 2-hydroxymethyl-1,6-dimethyl-4-oxocyclohex-2-ene-1-carboxylate (**9**).* Aqueous Na_2EDTA (95 mL, 0.0004 M) was added to the silyl ether **8** (5.94 g, 19 mmol) in acetonitrile (140 mL) and the solution cooled to −10 °C. Trifluoroacetone (19.1 mL, 213 mmol) was added using a pre-cooled syringe followed by a mixture of oxone® (58.6 g, 95.3 mmol) and sodium bicarbonate (12.4 g, 147 mmol) over a period of 1 h. The suspension was stirred at −10 °C for 1.5 h then filtered, and the filtrate was extracted with dichloromethane (4×100 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 30–90% ether in light petroleum gave the *title compound* **9**

(2.62 g, 68%) as a colourless oil, a 75:25 mixture of diastereoisomers, R_f=0.1 (30% ether in light petroleum) (Found: M^++NH_4, 230.1384. $C_{11}H_{20}NO_4$ requires *M*, 230.1387); ν_{max}/cm^{-1} 3437br, 2954, 2883, 1730, 1666, 1454, 1252, 1193, 1122 and 1070; δ_H (300 MHz, $CDCl_3$) major epimer 6.16 (1H, s, 3-H), 4.18 (2H, s, 2-CH_2), 3.69 (3H, s, OCH_3), 2.67 (1H, m, 6-H), 2.36 (1H, dd, *J* 15.5, 4.5, 5-H), 2.20 (1H, dd, *J* 15.5, 10.0, 5-H′), 1.27 (3H, s, 1-CH_3) and 0.88 (3H, d, *J* 7.0, 6-CH_3); minor epimer 3.66 (3H, s, OCH_3), 1.38 (3H, s, 1-CH_3) and 0.96 (3H, d, *J* 7.0, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 199.6, 198.7, 175.0, 173.0, 165.7, 163.1, 125.7, 124.0, 63.1, 62.1, 52.9, 52.6, 50.4, 49.8, 42.4, 41.8, 39.0, 36.9, 20.9, 16.9, 16.3 and 16.0; *m/z* (CI) 230 (M^++18, 100%) and 213 (80).

*4.2.3. Methyl 2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-oxocyclohex-2-ene-1-carboxylate (**10**).* Imidazole (6.3 g, 92 mmol) followed by *tert*-butyldimethylsilyl chloride (10.4 g, 69 mmol) were added to the alcohol **9** (9.77 g, 46 mmol) in DCM (340 mL) at 0 °C and the solution stirred at room temperature for 24 h. Saturated aqueous ammonium chloride (340 mL) was added and the mixture extracted into DCM (2×130 mL). The organic extracts were washed with brine (200 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using 1–30 % ether in light petroleum as eluent gave the *title compound* **10** (13.81 g, 92%) as a colourless oil, a 75: 25 mixture of diastereoisomers, R_f=0.46 (40% ether in light petroleum) (Found: M^++H, 327.1989. $C_{17}H_{31}O_4Si$ requires *M*, 327.1986); ν_{max}/cm^{-1} 2953, 2857, 1735, 1674, 1631, 1461, 1253, 1139, 1088, 838 and 780; δ_H (300 MHz, $CDCl_3$) major epimer 6.21 (1H, t, *J* 1.6, 3-H), 4.28 and 4.17 (each 1H, dd, *J* 17.0, 1.9, 2-CH), 3.74 (3H, s, OCH_3), 2.72 (1H, m, 6-H), 2.44 (1H, dd, *J* 16.0, 4.0, 5-H), 2.29 (1H, dd, *J* 16.0, 10.0, 5-H′), 1.33 (3H, s, 1-CH_3), 0.94 (3H, d, *J* 7.0, 6-CH_3), 0.92 [9H, s, $SiC(CH_3)_3$], 0.07 (6H, s, 2×$SiCH_3$); minor epimer 6.24 (1H, m, 3-H), 4.33 and 4.22 (each 1H, dd, *J* 17.0, 1.6, 2-CH), 3.70 (3H, s, OCH_3), 1.42 (3H, s, 1-CH_3) and 1.01 (3H, d, *J* 6.9, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 199.3, 198.3, 174.8, 172.5, 165.3, 162.4, 125.5, 123.7, 63.4, 62.3, 52.6, 52.4, 50.2, 49.6, 42.6, 41.9, 39.1, 36.9, 26.0, 25.9, 21.0, 18.6, 16.9, 16.2, 16.0, −3.3 and −5.3; *m/z* (ES+) 327 (M^++1, 100).

*4.2.4. Methyl (1SR,4SR,6RS)- and (1SR,4SR,6SR)-2-(tert-butyldimethylsilyloxymethyl)-4-hydroxy-1,6-dimethylcyclohex-2-ene-1-carboxylates (**11**) and (**13**).* Cerium(III) chloride heptahydrate (14.63 g, 39 mmol) was added to the enone **10** (11.55 g, 35 mmol) in methanol (345 mL) at room temperature and the suspension stirred until the solid had dissolved. The solution was cooled to −78 °C, sodium borohydride (1.93 g, 51 mmol) was added portionwise and the solution was stirred for 2 h. The reaction mixture was allowed to warm to room temperature and concentrated under reduced pressure. DCM (50 mL) and silica powder were added to the gelatinous residue until saturation of the solution occurred and the mixture was concentrated under reduced pressure then loaded directly onto silica gel. Chromatography using 40% ether in light petroleum as eluent gave the *title compound* **11** (7.35 g, 63%) as a colourless oil R_f=0.26 (30% ether in light petroleum) (Found: M^+, 328.2057. $C_{17}H_{32}O_4Si$ requires *M*, 328.2064); ν_{max}/cm^{-1} 3415, 2952, 2859, 1731, 1464, 1383, 1253, 1140, 1109, 1033, 839 and 778; δ_H (300 MHz, $CDCl_3$) 5.84 (1H, s, 3-H), 4.34 (1H, m, 4-H), 4.05 and 3.96 (each 1H, dt, *J* 14.0, 1.0, 2-CH), 3.63 (3H, s, OCH_3), 2.41 (1H, br s, OH), 2.22 (1H, m, 6-H), 1.86 (1H, ddd, *J* 12.9, 6.5, 2.6, 5-H), 1.40 (1H, td, *J* 12.9, 10.3, 5-H′), 1.18 (3H, s, 1-CH_3), 0.86 [9H, s, $SiC(CH_3)_3$], 0.82 (3H, d, *J* 6.9, 6-CH_3), 0.02 (6H, s, 2×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 176.6, 141.9, 126.2, 67.5, 63.1, 52.1, 49.6, 36.4, 35.4, 26.1, 18.6, 16.8, 16.5, −5.2 and −5.3; *m/z* (CI) 329 (M^++1, 80%), 312 (10), 311 (42), 271 (18), 197 (100) and 90 (20). The second fraction was the *title compound* **13** (2.1 g, 18%) as colourless oil, R_f=0.19 (30% ether in light petroleum) (Found: M^+, 328.2058. $C_{17}H_{32}O_4Si$ requires *M*, 328.2064); ν_{max}/cm^{-1} 3445, 2952, 2857, 1730, 1462, 1375, 1251, 1141, 1088, 1048, 836 and 778; δ_H (300 MHz, $CDCl_3$) 5.82 (1H, s, 3-H), 4.21 (1H, m, 4-H), 4.04 (2H, s, 2-CH_2), 3.62 (3H, s, OCH_3), 2.58 (1H, br s, OH), 1.71–1.67 (3H, m, 6-H and 5-H_2), 1.25 (3H, s, 1-CH_3), 0.82 (3H, d, *J* 6.9, 6-CH_3), 0.86 [9H, s, $SiC(CH_3)_3$], 0.02 (6H, s, 2×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 174.9, 140.3, 128.9, 67.3, 64.4, 51.8, 48.2, 38.2, 37.2, 26.1, 21.4, 18.6, 17.0 and −5.3; *m/z* (CI) 346 (M^++18, 10%), 329 (3) and 311 (100).

*4.2.5. Methyl (1SR,4SR,6RS)-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene-1-carboxylate (**12**).* *N*,*N*-Di-*iso*propylethylamine (9.48 mL, 54.4 mmol) and (2-trimethylsilylethoxy)methyl chloride (4.82 mL, 27 mmol) were added to the alcohol **11** (5.96 g, 18 mmol) in DCM (200 mL) at 0 °C. The solution was allowed to warm to room temperature and was stirred for 20 h. Water (100 mL) was added and the aqueous phase extracted with EtOAc (4×200 mL). The organic extracts were washed with brine (100 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica gel using 1–40% ether in light petroleum gave the *title compound* **12** (6.7 g, 80%) as a clear oil, R_f=0.66 (30% ether in light petroleum) (Found: M^++NH_4, 476.3228. $C_{23}H_{50}O_5Si_2N$ requires *M*, 476.3232); ν_{max}/cm^{-1} 2944, 2867, 1735, 1462, 1249 and 1058; δ_H (300 MHz, $CDCl_3$) 5.84 (1H, br s, 3-H), 4.78 and 4.75 (each 1H, d, *J* 7.1, OHC*H*O), 4.36 (1H, m, 4-H), 4.10 (1H, dt, *J* 14.0, 1.8, 2-CH), 3.95 (1H, ddd, *J* 14.0, 2.5, 1.8, 2-CH), 3.69 (3H, s, OCH_3), 3.66 (2H, m, OCH_2), 2.27 (1H, m, 6-H), 1.90 (1H, m, 5-H), 1.42 (1H, td, *J* 13.0, 10.0, 5-H′), 1.23 (3H, s, 1-CH_3), 0.97 (2H, m, CH_2Si), 0.91 [9H, s, $SiC(CH_3)_3$], 0.86 (3H, d, *J* 7.0, 6-CH_3), 0.05 (6H, s, 2×$SiCH_3$) and 0.03 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 176.5, 142.5, 124.1, 93.5, 72.5, 65.2, 63.3, 52.2, 49.7, 35.3, 33.6, 26.2, 18.7, 18.3, 17.0, 16.5, −1.2 and −5.2; *m/z* (CI) 476 (M^++18, 8%), 459 (M^++1, 7%), 328 (10), 312 (22), 311 (100) and 90 (17).

*4.2.6. (1SR,4SR,6RS)-1-Hydroxymethyl-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**14**); general procedure for ester reduction.* Lithium triethylborohydride (1.0 M in THF, 45 mL, 45 mmol) was added to the ester **12** (8.20 g, 18 mmol) in THF (140 mL) at 0 °C and the solution allowed to warm to room temperature and stirred for 4 h. Saturated aqueous ammonium chloride (70 mL) was added and the mixture diluted with EtOAc (50 mL). The aqueous phase was extracted with ether (4×50 mL) and the organic extracts were washed with water (70 mL) and brine (70 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica with 10–50% ether in light petroleum as eluent gave the *title compound* **14** (7.7 g, 82%), as a clear, viscous oil, R_f=0.42 (30% ether in light petroleum) (Found: M^++H, 431.3011. $C_{22}H_{47}O_4Si_2$ requires *M*, 431.3015); ν_{max}/cm^{-1} 3515br, 2944, 2866, 1659, 1464, 1382, 1250, 1054 and 836; δ_H (300 MHz, $CDCl_3$) 5.85 (1H, s, 3-H), 4.82 and 4.77 (each 1H, d, *J* 7.0, OHC*H*O), 4.30 (1H, d, *J* 10.6, 2-CH), 4.28 (1H, m, 4-H), 3.93 (1H, d, *J* 10.6, 2-CH′), 3.70–3.65 (2H, m, OCH_2), 3.58 and 3.41 (each 1H, d, *J* 12.0, 1-CH), 3.27 (1H, br s, OH), 2.20 (1H, m, 6-H), 1.94 (1H, m, 5-H), 1.48 (1H, td, *J* 12.3, 10.5, 5-H′), 0.88–1.00 [14H, m, CH_2Si, 6-CH_3 and $SiC(CH_3)_3$], 0.80 (3H, s, 1-CH_3), 0.16 and 0.14 (each 3H, s, 2×$SiCH_3$) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 143.6, 126.0, 93.4, 72.6, 69.1, 65.2, 63.6, 41.5, 34.1, 26.3, 25.8, 18.4, 18.0, 18.2, 15.8, −1.1 and −5.0.

*4.2.7. (1SR,4SR,6RS)-1-(Phenylsulfanylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**15**); general procedure for thioether synthesis.* Triethylamine (3.62 mL, 26.0 mmol) and methanesulfonyl chloride (1.45 mL, 14.86 mmol) were added to the alcohol **14** (3.2 g, 7.43 mmol) in DCM (130 mL) at 0 °C and the solution stirred at 0 °C for 2 h. When complete consumption of the starting material was observed by TLC, the solution was diluted with EtOAc

(130 mL) and saturated aqueous sodium bicarbonate (70 mL). The aqueous phase was extracted with EtOAc (4×40 mL) and the organic extracts were washed with saturated aqueous sodium bicarbonate (70 mL) and brine (70 mL), then dried ($MgSO_4$) and concentrated under reduced pressure to afford the mesylate as a pale orange oil. Benzenethiol (3.50 mL, 34 mmol) was added to sodium hydride (60% dispersion in mineral oil, 1.36 g, 34 mmol) in DMF (120 mL), at 0 °C. The solution was stirred for 20 min at 0 °C and the mesylate in DMF (100 mL) was added via a cannula. The solution was heated under reflux for 20 h, allowed to cool to room temperature, diluted with EtOAc (60 mL) and washed with aqueous sodium hydroxide (60 mL). The aqueous phase was extracted with EtOAc (3×50 mL) and the organic extracts were washed with water (60 mL) and brine (60 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using 1–20% ether in light petroleum as eluent gave the *title compound* **15** (2.84 g, 73%) as a pale yellow, viscous oil, R_f=0.25 (15% ether in light petroleum) (Found: M^+, 522.3003. $C_{28}H_{50}O_3SSi_2$ requires *M*, 522.3003); ν_{max}/cm^{-1} 2954, 2932, 2883, 2860, 1470, 1252, 1150, 1101, 1035, 859, 838 and 776; δ_H (300 MHz, $CDCl_3$) 7.16–7.40 (5H, m, ArH), 5.92 (1H, s, 3-H), 4.82 (2H, s, 4-OCH_2O), 4.20–4.38 (3H, m, 4-H and 2-CH_2), 3.70 (2H, m, OCH_2), 3.14 and 3.08 (each 1H, d, *J* 12.2, 1-CH), 2.18 (1H, m, 6-H), 1.91 and 1.51 (each 1H, m, 5-H), 1.16 (3H, s, 1-CH_3), 0.84–1.02 [14H, m, CH_2Si, 6-CH_3 and $SiC(CH_3)_3$] and 0.08 (15H, m, 5×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 143.6, 137.94, 129.4, 129.1, 126.2, 126.0, 93.4, 72.6, 65.2, 63.6, 41.5, 41.2, 34.1, 33.3, 26.3, 21.4, 18.4, 15.8, −1.1 and −5.0; *m/z* (CI) 522 (M^+, 2%) and 73 (100).

*4.2.8. (1SR,4SR,6RS)-1-(Phenylsulfonylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**16**); general procedure for sulfide oxidation.* Hydrogen peroxide (30% in water, 14.25 mL) was added to the sulfide **15** (2.50 g, 4.78 mmol) and ammonium molybdate (8.86 g, 7.17 mmol) in ethanol (500 mL) at 0 °C over a period of 5 min. The suspension was stirred for a further 5 min at 0 °C and at room temperature for 24 h. Water (100 mL) was added and the aqueous phase extracted into ether (6×100 mL). The organic extracts were washed with aqueous $FeSO_4$ (100 mL) and brine (100 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 5–30% ether in light petroleum as eluent gave the *title compound* **16** (1.88 g, 71%) as a clear, viscous oil, R_f=0.25 (20% ether in light petroleum); ν_{max}/cm^{-1} 2952, 2886, 2861, 1727, 1466, 1364, 1315, 1252, 1150, 1087, 1035, 838 and 776; δ_H (300 MHz, $CDCl_3$) 7.93 (2H, m, ArH), 7.54–7.70 (3H, m, ArH), 5.79 (1H, s, 3-H), 4.82 and 4.78 (each 1H, d, *J* 7.0, OHC*H*O), 4.45 (1H, d, *J* 12.0, 2-CH), 4.33 (1H, m, 4-H), 4.29 (1H, d, *J* 12.0, 2-CH′), 3.68 (2H, m, OCH_2), 3.51 and 3.35 (each 1H, d, *J* 14.8, 1-CH), 2.67 (1H, m, 6-H), 1.99 and 1.61 (each 1H, m, 5-H), 1.20 (3H, s, 1-CH_3), 0.98 (5H, m, CH_2Si and 6-CH_3), 0.88 [9H, s, $SiC(CH_3)_3$], 0.07 (15H, s, 5×CH_3); δ_C (75 MHz, $CDCl_3$) 142.8, 142.2, 133.7, 129.5, 127.6, 126.6, 93.5, 71.9, 65.9, 65.2, 61.0, 42.1, 33.8, 33.5, 26.2, 22.2, 18.5, 18.3, 16.3, −1.1 and −5.1; *m/z* (CI) 572 (M^++18, 3%) and 90 (100).

*4.2.9. (1SR,4SR,6RS)-1-(Phenylsulfonylmethyl)-2-hydroxymethyl-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**17**); general procedure for silyl ether deprotection using fluoride.* Tetra-*n*-butylammonium fluoride (1.0 M in THF, 1.59 mL, 1.59 mmol) was added to the *tert*-butyldimethylsilyl ether **16** (200 mg, 0.36 mmol) in THF (10.5 mL) at room temperature and the solution was stirred for 16 h. The reaction mixture was concentrated under reduced pressure and the residue added directly to silica. Elution with 20–80% ether in light petroleum gave the *title compound* **17** (135 mg, 85%), R_f=0.10 (40% ether in light petroleum) (Found: M^++NH_4, 458.2402. $C_{22}H_{40}O_5NSSi$ requires *M*, 458.2396); ν_{max}/cm^{-1} 3469, 2950, 2882, 1583, 1449, 1309, 1247, 1148, 1093, 1029, 838 and 749; δ_H (300 MHz, $CDCl_3$) 7.93 (2H, m, ArH), 7.54–7.69 (3H, m, ArH), 5.95 (1H, s, 3-H), 4.81 and 4.78 (each 1H, d, *J* 7.0, OHC*H*O), 4.40 (1H, m, 4-H), 4.28 and 4.20 (each 1H, d, *J* 12.7, 2-CH), 3.75–3.60 (3H, m, 1-CH and OCH_2), 3.26 (1H, d, *J* 14.4, 1-CH′), 2.74 (1H, m, 6-H), 1.96 (1H, m, 5-H), 1.48 (1H, td, *J* 12.7, 10.3, 5-H′), 1.05–0.95 (8H, m, 1-CH_3, $SiCH_2$ and 6-CH_3) and 0.06 [9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 143.3, 141.6, 133.9, 130.9, 129.6, 127.8, 93.6, 72.3, 65.3, 64.8, 60.9, 42.1, 34.2, 33.2, 21.7, 18.3, 16.2 and −1.1; *m/z* (CI) 458 (M^++18, 100%).

*4.2.10. (1SR,4SR,6RS)-2-Bromomethyl-1,6-dimethyl-1-(phenylsulfonylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**18**).* Triethylamine (0.25 mL, 1.82 mmol) and methanesulfonyl chloride (0.1 mL, 1.1 mmol) were added to the alcohol **17** (400 mg, 0.91 mmol) in THF (5 mL) at 0 °C and the solution was stirred at 0 °C for 45 min. Lithium bromide (325 mg, 3.7 mmol) in THF (3 mL) was added and the mixture stirred at 0 °C for 1 h. The mixture was partitioned between pentane (15 mL) and ice-cold water (10 mL). The organic phase was extracted with pentane (2×15 mL) and the organic extracts washed with saturated aqueous sodium bicarbonate (5 mL) and brine (5 mL) then dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 20% ether in light petroleum as eluent gave the *title compound* **18** (392 mg, 86%) as a clear oil, R_f=0.25 (20% ether in light petroleum); ν_{max}/cm^{-1} 2952, 2883, 1580, 1440, 1311, 1245, 1139, 1099, 1029, 838 and 749; δ_H (300 MHz, $CDCl_3$) 7.93 (2H, d, *J* 7.0, ArH), 7.69–7.61 (3H, m, ArH), 6.37 (1H, s, 3-H), 4.82 and 4.79 (each 1H, d, *J* 7.0, OHC*H*O), 4.37 (1H, br t, *J* 8.0, 4-H), 4.12 and 4.25 (each 1H, d, *J* 11.4, 2-CH), 3.70 (2H, m, OCH_2), 3.43 and 3.30 (each 1H, d, *J* 14.9, 1-CH), 2.65 (1H, m, 6-H), 1.98 (1H, ddd, *J* 12.5, 7.0, 1.7, 5-H), 1.57 (1H, td, *J* 12.5, 9.3, 5-H′), 1.29 (3H, s, 1-CH_3), 1.02 (5H, m, CH_2Si and 6-CH_3), 0.04 (9H, s, 3×$Si(CH_3)$; *m/z* (CI) 520 (M^++18, 4%) and 90 (100).

*4.2.11. (1SR,4SR,6RS)-2-[(2E)-3,7-Dimethylocta-2,6-dienyloxy]methyl-1,6-dimethyl-1-(phenylsulfonylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**19**).* A suspension of sodium hydride (60% dispersion in mineral oil, 13 mg, 0.32 mmol) and tetra-*n*-butylammonium iodide (45 mg, 0.12 mmol) in THF (0.15 mL) was cooled to 0 °C and the alcohol **17** (130 mg, 0.29 mmol) in THF (0.35 mL) was added. The suspension was stirred for 20 min prior to the dropwise addition of 15-crown-5 (0.06 mL, 0.29 mmol) and geranyl bromide (0.05 mL, 0.29 mmol) in THF (0.30 mL). The brown suspension was allowed to warm to room temperature and was stirred for 16 h. Saturated aqueous ammonium chloride (5 mL) was added and the aqueous phase extracted with EtOAc (4×10 mL). The organic extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ether in light petroleum as eluent gave the *title compound* **19** (150 mg, 80%) as a clear oil, R_f=0.41 (30% ether in light petroleum) (Found: M^++NH_4, 594.3656. $C_{32}H_{56}O_5NSSi$ requires *M*, 594.3648); ν_{max}/cm^{-1} 2930, 2877, 1667, 1448, 1376, 1315, 1249, 1150, 1093, 980, 838 and 748; δ_H (300 MHz, $CDCl_3$) 7.93 (2H, m, ArH), 7.54–7.68 (3H, m, ArH), 5.85 (1H, s, 3-H), 5.31 (1H, td, *J* 6.7, 1.2, 2′-H), 5.10 (1H, t, J 6.7, 6′-H), 4.81 and 4.78 (each 1H, d, *J* 7.0, OHC*H*O), 4.35 (1H, m, 4-H), 4.30 and 4.02 (each 1H, d, *J* 12.3, 2-CH), 3.97 (2H, m, 1′-H_2), 3.70 (2H, m, OCH_2), 3.52 and 3.34 (each 1H, d, *J* 14.8, 1-CH), 2.68 (1H, m, 6-H), 1.94–2.13 (5H, m, 4′-H_2, 5-H and 5′-H_2), 1.70 (3H, s, 3′-CH_3), 1.67 (3H, s, 7′-CH_3), 1.62 (3H, s, 8′-H_3), 1.58 (1H, m, 5-H′) 1.17 (3H, s, 1-CH_3), 1.02 (3H, d, *J* 6.7, 6-CH_3), 0.98 (2H, m, CH_2Si), 0.07 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.2, 140.5, 140.4, 133.7, 131.9, 130.3, 129.5, 127.7, 124.2, 121.0, 93.6, 72.9, 72.03, 66.7, 65.3, 60.9, 42.3, 39.9, 33.8, 33.4, 26.7, 25.9, 21.7, 18.3, 18.0, 16.8, 16.5 and −1.1; *m/z* (CI) 594 (M^++18, 10%) and 90 (100).

*4.2.12. Methyl (Z)-5-tert-butyldiphenylsilyloxy-3-phenylsulfanylpent-2-enoate (**21**).* Sodium methoxide (15 mg,

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0.27 mmol) was added to the alkynyl ester **20** (2.0 g, 5.5 mmol) and benzenethiol (720 mg, 6.5 mmol) in methanol (15 mL) at room temperature. The solution was stirred for 16 h, filtered through a silica pad and concentrated under reduced pressure. Chromatography of the residue on silica using 20% ether in light petroleum as eluent gave the *title compound* **21** (2.21 g, 85%) as a clear oil, R_f=0.32 (20% ether in light petroleum) (Found: M^++H, 477.1928. $C_{28}H_{33}O_3SSi$ requires *M*, 477.1920); ν_{max}/cm^{-1} 2951, 2858, 2253, 1697, 1711, 1581, 1474, 1216, 1110, 805 and 752; δ_H (300 MHz, $CDCl_3$) 7.61 (4H, m, ArH), 7.40 (11H, m, ArH), 5.99 (1H, s, 2-H), 3.80 (3H, s, OCH_3), 3.60 (2H, t, *J* 6.5, 5-H_2), 2.41 (2H, t, *J* 6.5, 4-H_2) and 1.01 [9H, s, $SiC(CH_3)_3$]; *m/z* (CI) 494 (M^++18, 31%), 477 (M^++1, 100%).

*4.2.13. (Z)-5-tert-Butyldiphenylsilyloxy-3-phenylsulfanylpent-2-en-1-ol (**22**).* Di-*iso*butylaluminium hydride (1.0 M in THF, 10.5 mmol, 10.5 mL) was added dropwise to the ester **21** (2.0 g, 4.2 mmol) in THF (40 mL) at −78 °C. After 3 h at −78 °C, saturated aqueous sodium potassium tartrate (40 mL) was added and the mixture extracted into ether (3×50 mL). The organic extracts were washed with water (30 mL) and brine (30 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica gel using 40% ether in light petroleum as eluent gave the *title compound* **22** (2.54 g, 88%) as a clear oil, R_f=0.30 (45% ether in light petroleum); ν_{max}/cm^{-1} 3425, 2951, 2858, 2253, 1637, 1473, 1383, 1217, 1110, 805 and 752; δ_H (300 MHz, $CDCl_3$) 7.70 (4H, m, ArH), 7.20–7.50 (11H, m, ArH), 6.20 (1H, t, *J* 6.3, 2-H), 4.43 (2H, d, *J* 6.3, 1-H_2), 3.85 (2H, t, *J* 6.4, 5-H_2), 2.49 (2H, t, *J* 6.4, 4-H_2), 1.81 (1H, br s, OH) and 1.10 [9H, s, $SiC(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 136.4, 135.9, 134.6, 134.1, 133.5, 130.3, 129.9, 129.3, 127.9, 126.8, 62.4, 61.0, 40.5, 27.1 and 19.5; *m/z* (CI) 466 (M^++18, 32%), 431 (44), 193 (68), 175 (100).

*4.2.14. Cyclohex-1-enylmethyl (Z)-5-tert-butyldiphenylsilyloxy-3-phenylsulfanylpent-2-enyl ether (**23**).* A suspension of sodium hydride (60% dispersion in mineral oil, 110 mg, 2.6 mmol) and tetra-*n*-butylammonium iodide (330 mg, 0.89 mmol) in THF (1 mL) was cooled to 0 °C. The alcohol **22** (1.00 g, 2.2 mmol) in THF (2 mL) was added the suspension was stirred for 20 min prior to the dropwise addition of 15-crown-5 (0.53 mL, 2.68 mmol) and 1-bromomethylcyclohex-1-ene (585 mg, 3.3 mmol) in THF (1.5 mL). The brown suspension was allowed to warm to room temperature and was stirred for 24 h. Saturated aqueous ammonium chloride (5 mL) was added and the aqueous phase extracted with EtOAc (4×5 mL). The organic extracts were washed with water (5 mL) and brine (5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica with 10% ether in light petroleum as eluent gave the *title compound* **23** (1.12 g, 9.1 mmol 93%) as a clear oil, R_f=0.25 (10% ether in light petroleum) (Found: M^++NH_4, 560.3023. $C_{34}H_{46}O_2NSSi$ requires *M*, 560.3018); ν_{max}/cm^{-1} 2951, 2858, 2253, 1650, 1470, 1381, 1210, 1110, 1060, 804 and 750; δ_H (300 MHz, $CDCl_3$) 7.65 (4H, m, ArH), 7.20–7.47 (11H, m, ArH), 6.18 (1H, t, *J* 6.0, 2′-H), 5.77 (1H, m, 2-H), 4.30 (2H, d, *J* 6.0, 1′-H_2), 3.91 (2H, s, 1-CH_2), 3.84 (2H, t, *J* 6.5, 5′-H_2), 2.49 (2H, t, *J* 6.5, 4′-H_2), 2.08 (4H, m, 3-H_2 and 6-H_2), 1.63 (4H, m, 4-H_2 and 5-H_2) and 1.10 [9H, s, $SiC(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 138.1, 137.2, 135.1, 134.0, 132.5, 130.4, 129.4, 129.3, 128.8, 125.6, 122.0, 111.0, 79.1, 67.4, 59.5, 43.2, 27.1, 26.3, 26.1, 23.2 and 19.5; *m/z* (CI) 560 (M^++18, 51%), 431 (50) and 175 (100).

*4.2.15. (Z)-5-tert-Butyldiphenylsilyloxy-1-(2-methylenecyclohexyl)-3-phenylsulfanylpent-2-en-1-one (**24**).* *n*-Butyllithium (1.6 M in THF, 0.56 mL, 0.92 mmol) was added to the diallyl ether **23** (200 mg, 0.37 mmol) in THF (2 mL) at −60 °C dropwise over 10 min and the yellow solution stirred at −60 °C for 0.5 h. Saturated aqueous ammonium chloride (1 mL) was added and, after being allowed to warm to room temperature, the mixture was diluted with water (5 mL) and extracted with EtOAc (10 mL). The aqueous phase was extracted with EtOAc (3×10 mL) and the organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. IBX (310 mg, 1.1 mmol) was added to the residue in DMSO (1 mL) and, after 3 h at room temperature, the reaction mixture was diluted with water (5 mL), filtered through Celite® and extracted into ether (3×15 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 20% ether in light petroleum as eluent gave the *title compound* **24** (143 mg, 72%) as a clear oil, R_f=0.20 (15% ether in light petroleum) (Found: M^++H, 541.2515. $C_{34}H_{41}O_2SSi$ requires *M*, 541.2518); δ_H (300 MHz, $CDCl_3$) 7.79 (4H, m, ArH), 7.37–7.50 (11H, m, ArH), 5.85 (1H, s, 2-H), 4.67 and 4.40 (each 1H, s, 2′-CH), 4.00 (2H, t, *J* 6.6, 5-H_2), 3.24 (2H, m, 4-H_2), 2.92 (1H, t, *J* 4.7, 1′-H), 2.01 (2H, m, 3′-H_2), 1.28–1.70 (6H, m, 4′-H_2, 5′-H_2 and 6′-H_2) and 1.12 [9H, s, $SiC(CH_3)_3$]; *m/z* (CI) 541 (M^++1, 40%), 448 (52) and 137 (100).

*4.2.16. (1SR,4SR,6RS)-2-[(Z)-5-tert-Butyldiphenylsilyloxy-3-phenylsulfanylpent-2-enyloxy]methyl-1,6-dimethyl-1-(phenylsulfonylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**25**).* The alcohol **22** (265 mg, 0.59 mmol) in THF (0.50 mL) was added to sodium hydride (60% dispersion in mineral oil, 24 mg, 0.59 mmol), tetra-*n*-butylammonium iodide (82 mg, 0.22 mmol) and THF (0.4 mL) at 0 °C and the suspension was stirred for 20 min. 15-Crown-5 (0.12 mL, 0.59 mmol) and the bromide **18** (245 mg, 0.49 mmol) in THF (0.40 mL) were added and the suspension was allowed to warm to room temperature and was stirred for 16 h. Saturated aqueous ammonium chloride (5 mL) and ethyl acetate (5 mL) were added and the aqueous phase extracted with EtOAc (4×5 mL). The organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using ether in light petroleum gave the *title compound* **25** (301 mg, 0.35 mmol 71%) as a clear oil, R_f=0.22 (25% ether in light petroleum) (Found: M^++Na, 893.3744. $C_{49}H_{66}O_6NaS_2Si_2$ requires *M*, 893.3732); ν_{max}/cm^{-1} 3064, 2947, 2864, 1471, 1442, 1380, 1313, 1248, 1148, 1102, 1034, 934, 834 and 743; δ_H (300 MHz, $CDCl_3$) 7.90 (2H, d, *J* 8.2, ArH), 7.20–7.72 (18H, m, ArH), 6.09 (1H, t, *J* 6.0, 2′-H), 5.88 (1H, s, 3-H), 4.82 and 4.75 (each 1H, d, *J* 7.0, OHC*H*O), 4.39 (1H, m, 4-H), 4.38 (1H, d, *J* 12.0, 2-CH), 4.27 (2H, d, *J* 6.0, 1′-H_2), 4.07 (1H, d, *J* 12.0, 2-CH′), 3.79 (2H, t, *J* 6.3, 5′-H_2), 3.69 (2H, m, OCH_2), 3.50 and 3.32 (1H, d, *J* 14.7, 1-CH), 2.70 (1H, m, 6-H), 2.25 (2H, t, *J* 6.3, 4′-H_2), 2.00 and 1.62 (each 1H, m, 5-H), 1.15 (3H, s, 1-CH_3), 0.92–1.10 [14H, m, 6-CH_3, CH_2Si, $SiC(CH_3)_3$] and 0.08 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.1, 140.4, 135.8, 134.3, 134.0, 133.8, 133.7, 130.4, 130.3, 129.9, 129.5, 129.3, 128.6, 127.9, 127.7, 126.8, 93.5, 73.4, 72.0, 68.1, 65.3, 62.4, 60.9, 42.3, 40.4, 33.9, 33.5, 27.1, 21.9, 19.5, 18.4, 16.5 and −1.1; *m/z* (ES+) 893 (M^++23, 100%).

*4.2.17. (1SR,4SR,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfonylmethyl)-4-(2-(trimethylsilylethoxy)methoxycyclohex-2-ene (**26**); general procedure for stannane synthesis.* Sodium hydride (60% dispersion in mineral oil, 52 mg, 1.29 mmol) was added to the alcohol **17** (406 mg, 0.92 mmol) in THF (7.5 mL) and the suspension stirred 5 min. Iodomethyl(tributyl) stannane (0.38 mL, 1.29 mmol) was added and the mixture stirred for 24 h. Water (10 mL) was added and the mixture extracted with ether (4×10 mL). The organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica with 20% ether in light petroleum as eluent gave the *title compound* **26** (534 mg, 0.72 mmol, 78%) as a clear oil, R_f=0.32 (20% ether in light petroleum); ν_{max}/cm^{-1} 2954, 2921, 2872, 1459, 1374, 1245, 1092, 1035, 855 and 834; δ_H (300 MHz, $CDCl_3$) 7.95 (2H, d, *J* 6.9, ArH) 7.60 (3H, m, ArH), 5.79 (1H, s, 3-H), 4.82 and 4.78 (1H, d, *J* 7.0, OHC*H*O), 4.35

(1H, m, 4-H), 4.30 and 3.87 (each 1H, d, *J* 12.3, 2-CH), 3.71 (1H, *J* 10.2, OHC*H*Sn), 3.70 (2H, m, OCH_2), 3.58 (1H, d, *J* 10.2, OHC*H*′Sn), 3.51 and 3.29 (each 1H, d, *J* 14.8, 1-CH), 2.65 (1H, m, 6-H), 1.98 (1H, ddd, *J* 12.9, 5.4, 2.2, 5-H), 1.60 (1H, m, 5-H′), 1.43 (6H, m, 3×$SnCH_2CH_2$), 1.29 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.17 (3H, s, 1-CH_3), 1.00–1.80 (20H, m, CH_2Si, 3×$SnCH_2$, 3×CH_3 and 6-CH_3) and 0.05 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.2, 140.7, 133.6, 129.4, 129.3, 127.6, 93.5, 79.2, 71.9, 65.2, 61.7, 60.9, 42.3, 33.8, 33.4, 29.3, 27.5, 21.8, 18.3, 16.4, 13.9, 9.1 and −1.2.

*4.2.18. (2RS,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**27**); general procedure for sulfone rearrangement.* *n*-Butyllithium (1.6 M in THF, 0.19 mL, 0.30 mmol) was added to the sulfone **26** (107 mg, 0.14 mmol) in THF (2.0 mL) at −78 °C dropwise over 10 min and the solution allowed to warm to −50 °C and stirred at this temperature for 24 h. Saturated methanolic ammonium chloride (0.5 mL) was added and, after being allowed to warm to room temperature, the mixture was diluted with water (10 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (4×10 mL) and the organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica with 50% ether in light petroleum as eluent gave the methyl ether **28** (39 mg, 60%), as a colourless oil, δ_H (300 MHz, $CDCl_3$) 7.94 (2H, d, *J* 7.0, ArH), 7.72–7.54 (3H, m, ArH), 5.85 (1H, s, 3-H), 4.81 and 4.79 (each 1H, d, *J* 6.9, OHC*H*O), 4.37 (1H, m, 4-H), 4.25 and 3.97 (each 1H, d, *J* 12.0, 2-CH), 3.68 (2H, m, OCH_2), 3.49 and 3.35 (each 1H, d, *J* 15.0, 1-CH), 3.31 (3H, s, OCH_3), 2.69 (1H, m, 6-H), 1.96 and 1.60 (each 1H, m, 5-H), 1.14 (3H, s, 1-CH_3), 1.05–0.90 (5H, m, CH_2Si and 6-CH_3) and 0.08 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.1, 140.1, 133.7, 130.5, 129.5, 127.7, 93.6, 75.3, 72.1, 65.3, 60.9, 58.1, 42.3, 33.9, 33.4, 21.7, 18.3, 16.4 and −1.1. The second fraction was the *title compound* **27** (23 mg, 35%) as a pale yellow oil, R_f=0.14 (40% ether in light petroleum) (Found: M^++NH_4, 472.2545. $C_{23}H_{42}O_5NSSi$ requires *M*, 472.2547); ν_{max}/cm^{-1} 3512, 2951, 2890, 1639, 1447, 1380, 1313, 1249, 1150, 1029, 935, 859, 837 and 749; δ_H (300 MHz, $CDCl_3$) 7.95 (2H, d, *J* 7.0, ArH), 7.60–7.55 (3H, m, ArH), 5.33 and 5.11 (each 1H, s, 1-CH), 4.81 and 4.72 (each 1H, d, *J* 6.9, OHC*H*O), 4.01 (1H, dd, *J* 11.3, 4.3, 2-CH), 3.96 (1H, dd, *J* 11.3, 5.0, 2-CH′), 3.71–3.54 (3H, m, 3-H and OCH_2), 3.54 and 3.45 (each 1H, d, *J* 15.0, 6-CH), 2.50 (1H, ddd, *J* 9.5, 5.0, 4.3, 2-H), 2.05–1.85 (2H, m, 4-H and 5-H), 1.51 (1H, q, *J* 11.7, 4-H′), 1.23 (3H, s, 6-CH_3), 0.93 (5H, m, CH_2Si and 5-CH_3) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 149.3, 142.8, 133.7, 129.6, 127.6, 110.3, 93.9, 78.9, 65.9, 63.5, 63.1, 47.2, 45.6, 36.5, 36.4, 19.7, 18.3, 16.9 and −1.2; *m/z* (CI) 472 (M^++18, 22%), 354 (36), 337 (66) and 294 (100).

Following the general procedure (4.2.8), the sulfide **31** (23 mg, 0.05 mmol), ammonium molybdate (11 mg, 0.008 mmol) and hydrogen peroxide (30% in water, 0.19 mL), after chromatography on silica with 50% ether in light petroleum, gave the title compound **27** (21 mg, 0.046 mmol, 86%) as a colourless oil, with spectroscopic data identical to those of the sample prepared from the stannane **26**.

*4.2.19. (1SR,4SR,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfanylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**29**).* Tetra-*n*-butylammonium fluoride (1.0 M in THF, 4.71 mL, 4.71 mmol) was added to the silyl ether **15** (559 mg, 1.07 mmol) in THF (30.0 mL) at room temperature and the solution stirred 16 h. Ethyl acetate (30 mL) and water (30 mL) were added and the aqueous phase extracted with ethyl acetate (3×10 mL). The organic extracts were washed with water (20 mL) and brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure to give the corresponding alcohol as a pale yellow oil used without further purification. Following the general procedure (4.2.7), this alcohol in THF (8.5 mL), sodium hydride (60% dispersion in mineral oil, 60 mg, 1.47 mmol) and iodomethyl(tributyl)stannane (0.44 mL, 1.47 mmol), after chromatography on silica using 15% ether in light petroleum, afforded the *title compound* **29** (525 mg, 0.74 mmol, 69%), as a clear oil, R_f=0.28 (15% ether in light petroleum); ν_{max}/cm^{-1} 2954, 2921, 2872, 1461, 1374, 1246, 1092, 1035, 859 and 836; δ_H (300 MHz, $CDCl_3$) 7.16–7.40 (5H, m, ArH), 5.93 (1H, s, 3-H), 4.82 (2H, s, OCH_2O), 4.21–4.35 (3H, m, 4-H and 2-CH_2), 3.71 (1H, d, *J* 10.0, OHC*H*Sn), 3.70 (2H, m, OCH_2), 3.57 (1H, d, *J* 10.0, OHC*H*′Sn), 3.13 and 3.08 (each 1H, d, *J* 12.1, 1-CH), 2.18 (1H, m, 6-H), 1.90 and 1.53 (each 1H, m, 5-H), 1.43 (6H, m, 3×$SnCH_2CH_2$), 1.28 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.16 (3H, s, 1-CH_3), 0.90 (20H, m, 3×CH_2Sn, CH_2Si, 3×CH_3 and 6-CH_3) and 0.05 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 144.6, 138.4, 128.7, 128.6, 126.7, 125.5, 93.8, 77.9, 69.3, 65.2, 61.6, 41.7, 41.4, 33.2, 30.6, 29.6, 27.6, 20.3, 18.4, 15.6, 14.0, 9.3 and −1.1.

*4.2.20. (2SR,3SR,5RS,6SR)- and (2RS,3SR,5RS,6SR)-5,6-dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfanylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**30**) and (**31**); general procedure for sulfide rearrangement.* *n*-Butyllithium (1.6 M in THF, 0.39 mL, 0.62 mmol) was added to the sulphide **29** (400 mg, 0.56 mmol) in THF (8.0 mL) at −78 °C dropwise over 10 min and the solution allowed to warmed to −50 °C and stirred at this temperature for 24 h. Saturated methanolic ammonium chloride (0.5 mL) was added and, after being allowed to warm to room temperature, the mixture was diluted with water (10 mL) and EtOAc (10 mL). The aqueous phase was extracted with EtOAc (4×10 mL) and the organic extracts washed with brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 30% ether in light petroleum as eluent gave the *title compound* **31** (23 mg, 0.056 mmol, 10%) as a pale yellow oil, R_f=0.23 (30% ether in light petroleum); ν_{max}/cm^{-1} 3482br, 3470, 2951, 2885, 1635, 1537, 1479, 1379, 1266, 1095, 1054, 1025, 940, 836 and 738; δ_H (300 MHz, $CDCl_3$) 7.39 and 7.31 (each 2H, m, ArH), 7.21 (1H, t, *J* 7.4, ArH), 5.18 and 4.98 (each 1H, s, 1-CH), 4.85 and 4.74 (each 1H, d, *J* 6.7, OHC*H*O), 3.99 (2H, m, 2-CH and 3-H), 3.80–3.50 (3H, m, 2-CH′ and OCH_2), 3.28 (1H, d, *J* 12.1, 6-CH), 3.19 (1H, br s, OH), 3.10 (1H, d, *J* 12.1, 6-CH′), 2.49 (1H, m, 2-H), 2.10–1.85 (2H, m, 4-H, 5-H), 1.52 (1H, m, 4-H′), 1.12 (3H, s, 6-CH_3), 0.95–0.80 (5H, m, CH_2Si and 5-CH_3) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 150.7, 138.6, 129.6, 129.2, 126.1, 108.7, 93.8, 80.0, 66.0, 63.2, 46.7, 44.7, 43.4, 36.8, 35.4, 20.5, 18.3, 16.2 and −1.2; *m/z* (ES) 445 (M^++23, 100%). The second fraction was the *title compound* **30** (192 mg, 0.45 mmol, 81%) as a pale yellow oil, R_f=0.22 (30% ether in light petroleum); ν_{max}/cm^{-1} 3483br, 3472, 2951, 2881, 1634, 1537, 1479, 1379, 1249, 1095, 1054, 1025, 936, 836 and 738; δ_H (300 MHz, $CDCl_3$) 7.39 (2H, m, ArH), 7.30 (3H, m, ArH), 5.09 and 5.00 (each 1H, s, 1-CH), 4.74 and 4.68 (each 1H, d, *J* 6.7, OHC*H*O), 4.10 (1H, q, *J* 4.6, 3-H), 4.00 (1H, m, 2-CH), 3.69 (3H, m, 2-CH′ and OCH_2), 3.29 and 3.12 (each 1H, d, *J* 12.1, 6-CH), 2.77 (1H, t, *J* 6.9, OH), 2.63 (1H, m, 2-H), 1.97 (2H, m, 4-H, 5-H), 1.71 (1H, m, 4-H′), 1.19 (3H, s, 6-CH_3), 0.93 (5H, m, CH_2Si and 5-CH_3) and 0.05 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 148.4, 138.1, 130.0, 129.1, 126.2, 122.3, 93.9, 75.5, 66.0, 62.5, 46.4, 44.7, 44.3, 36.4, 32.6, 22.8, 18.4, 17.5 and −1.2; *m/z* (ES) 445 (M^++23, 100%).

*4.2.21. (2SR,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**32**).* Following the general procedure (4.2.8), the sulfide **30** (43 mg, 0.10 mmol), ammonium molybdate (20 mg, 0.015 mmol) in ethanol (1.0 mL) and hydrogen peroxide (30% solution in water, 0.35 mL), after chromatography on silica using 50% ether in light petroleum as eluent, gave the *title compound* **32** (40 mg, 0.087 mmol, 86%) as a clear, viscous oil, R_f=0.17 (40% ether in light petroleum) (Found: M^++NH_4, 472.2545. $C_{23}H_{42}O_5NSSi$ requires *M*, 472.2547); δ_H (300 MHz, $CDCl_3$) 7.92 (2H, d, *J* 7.0, ArH),

7.62 (3H, m, ArH), 5.17 and 4.98 (each 1H, s, 1-CH), 4.69 and 4.61 (each 1H, d, *J* 6.7, OHC*H*O), 4.09 (1H, q, *J* 3.7, 3-H), 3.82 (1H, dd, *J* 10.7, 8.1, 2-CH), 3.55–3.73 (3H, m, 2-CH′ and OCH_2), 3.53 and 3.22 (each 1H, d, *J* 14.5, 6-CH), 2.77 (1H, br s, OH), 2.47 (1H, m, 2-H), 2.09 (1H, m, 5-H), 1.92 and 1.72 (each 1H, dt, *J* 15.2, 3.7, 4-H), 1.42 (3H, s, 6-CH_3), 0.98 (5H, m, CH_2Si and 5-CH_3) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 149.0, 141.9, 133.7, 130.2, 127.6, 109.7, 93.6, 79.3, 66.6, 63.8, 62.3, 47.6, 44.6, 36.4, 35.9, 20.5, 18.8, 17.8 and −1.2; *m/z* (CI) 472 (M^++18, 2%), 354 (4), 337 (6), 294 (8) and 90 (100).

*4.2.22. Methyl (1SR,4RS,6RS)-2-(tert-butyldimethylsilyloxymethyl)-4-hydroxy-1,6-dimethylcyclohex-2-ene-1-carboxylate (**34**).* The alcohol **11** (2.32 g, 7.07 mmol) and triphenylphosphine (2.78 g, 10.60 mmol) in THF (10 mL) were added to a solution of DIAD (2.09 mL, 10.6 mmol) and benzoic acid (1.29 g, 10.60 mmol) in THF (10 mL) at 0 °C and the mixture stirred for 4 h at 0 °C. After concentration under reduced pressure, chromatography of the residue on silica using 15% ether in light petroleum as eluent afforded benzoate **33** as a colourless oil; δ_H (300 MHz, $CDCl_3$) 8.10 (2H, d, *J* 7.1, ArH), 7.58 (1H, t, *J* 7.1, ArH), 7.46 (2H, t, *J* 7.1, ArH), 6.05 (1H, d, m, 3-H), 5.56 (1H, m, 4-H), 4.21 and 4.06 (each 1H, dt, *J* 15.0, 1.0, 2-CH), 3.76 (3H, s, OCH_3), 2.60 (1H, m, 6-H), 1.87 (2H, m, 5-H_2), 1.23 (3H, s, 1-CH_3), 0.92 [12H, s, 6-CH_3 and $SiC(CH_3)_3$] and 0.08 (6H, s, 2×$SiCH_3$). The benzoate was taken up into methanol containing sodium hydroxide (5% NaOH, 8.0 mL) and the mixture stirred for 30 min. After concentration under reduced pressure, the residue was dissolved in ether (100 mL) and the ethereal solution washed with water (20 mL) and brine (20 mL) then dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography of the residue on silica using 35% ether in light petroleum as eluent gave the *title compound* **34** (2.18 g, 94%) as a clear oil, R_f=0.25 (30% ether in light petroleum) (Found: M^+, 328.2058. $C_{17}H_{32}O_4Si$ requires *M*, 328.2064); ν_{max}/cm^{-1} 3410, 2953, 2934, 2859, 1731, 1464, 1384, 1253, 1139, 1102, 1034, 839 and 779; δ_H (300 MHz, $CDCl_3$) 5.96 (1H, br d, *J* 5.4, 3-H), 4.20 (1H, m, 4-H), 4.12 and 3.95 (each 1H, d, *J* 14.4, 2-CH), 3.68 (3H, s, OCH_3), 2.42 (1H, m, 6-H), 1.79 (1H, br s, OH), 1.68 (2H, m, 5-H_2), 1.13 (3H, s, 1-CH_3), 0.90 [9H, s, $SiC(CH_3)_3$], 0.86 (3H, d, *J* 6.9, 6-CH_3) and 0.05 (6H, s, 2×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 174.2, 141.5, 128.5, 66.1, 64.4, 51.1, 46.1, 38.2, 36.3, 25.0, 21.2, 19.0, 17.0 and −5.2; *m/z* (CI) 346 (M^++18, 10%) and 311 (100).

*4.2.23. (1SR,4RS,6RS)-1-Hydroxymethyl-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**35**).* *N*,*N*-Di-*iso*propylethylamine (2.28 mL, 13.10 mmol) and SEM-chloride (1.27 mL, 7.18 mmol) were added to the alcohol **34** (2.15 g, 6.54 mmol) in DCM (30 mL) at 0 °C and the reaction mixture was allowed to warm to room temperature then stirred for 2 d. Water (50 mL) was added and the aqueous phase was extracted with EtOAc (2×100 mL). The organic extracts were washed with water (60 mL), brine (60 mL) and dried ($MgSO_4$) then concentrated under reduced pressure. Lithium triethylborohydride (1.0 M in THF, 19.62 mL, 19.62 mmol) was added to the SEM-ether in THF (20 mL) at 0 °C and the solution allowed to warm to room temperature then stirred for 4 h. Saturated aqueous ammonium chloride (20 mL) was added, and the mixture was diluted with EtOAc (40 mL) then stirred at room temperature for 1 h. The aqueous phase was extracted into ether (440 mL) and the organic extracts were washed with water (70 mL) and brine (70 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using 25% ether in light petroleum gave the *title compound* **35** (2.09 g, 4.85 mmol, 74%) as a clear, viscous oil, R_f=0.40 (30% ether in light petroleum); ν_{max}/cm^{-1} 3515br, 2943, 2866, 1464, 1382, 1249, 1096, 1052 and 834; δ_H (300 MHz, $CDCl_3$) 5.89 (1H, br d, *J* 4.2, 3-H), 4.81 and 4.74 (each 1H, d, *J* 7.4, OHC*H*O), 4.30 (1H, d, *J* 10.9, 2-CH), 4.10 (1H, m, 4-H), 3.95 (1H, d, *J* 10.9, 2-CH′), 3.68 (2H, m, OCH_2), 3.58 and 3.35 (each 1H, d, *J* 13.2, 1-CH), 2.99 (1H, br s, OH), 2.27 (1H, m, 6-H), 1.78 (2H, m, 5-H_2), 0.90 [14H, m, CH_2Si, 6-CH_3 and $SiC(CH_3)_3$], 0.75 (3H, s, 1-CH_3), 0.14 (6H, s, 2×$SiCH_3$) and 0.05 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 143.1, 127.1, 92.9, 72.6, 68.7, 65.1, 63.1, 42.4, 34.9, 26.5, 24.2, 18.4, 18.0, 18.2, 16.4, −1.1 and −5.1; *m/z* (CI) 432 (M^++1, 2%), 300 (8), 283 (7), 168 (79) and 151 (100).

*4.2.24. (1SR,4RS,6RS)-1-(Phenylsulfanylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**36**).* Following the general procedure (4.2.7), the alcohol **35** (2.0 g, 4.64 mmol) in DCM (80 mL), triethylamine (2.26 mL, 16.31 mmol) and methanesulfonyl chloride (0.91 mL, 9.29 mmol) gave the mesylate as a pale orange oil. This was converted into the thioether **36** following the general procedure using sodium hydride (850 mg, 21.25 mmol) in DMF (75 mL) and benzenethiol (2.19 mL, 21.25 mmol) with the mesylate added in DMF (60 mL). After heating the reaction mixture under reflux for 4 h, chromatography on silica using 1–20% ether in light petroleum as eluent gave the *title compound* **36** (1.82, g, 3.48 mmol, 75%) as a pale yellow, viscous oil, R_f=0.21 (15% ether in light petroleum) (Found: M^++NH_4, 540.3355: $C_{28}H_{54}O_3NSSi_2$ requires *M*, 540.3357); ν_{max}/cm^{-1} 2953, 2930, 2886, 2859, 1618, 1583, 1474, 1359, 1251, 1152, 1097, 1030, 932, 837, 776 and 738; δ_H (300 MHz, $CDCl_3$) 7.52 (2H, d, *J* 7.0, ArH), 7.18–7.20 (3H, m, ArH), 5.98 (1H, br d, *J* 4.6, 3-H), 4.81 (2H, s, OCH_2O), 4.32 and 4.27 (each 1H, d, *J* 13.8, 2-CH), 4.17 (1H, m, 4-H), 3.75–3.65 (2H, m, OCH_2), 3.20 and 3.12 (1H, d, *J* 12.0, 1-CH), 2.18 (1H, m, 6-H), 1.85-1.65 (2H, m, 5-H_2), 1.10 (3H, s, 1-CH_3), 1.02 (2H, m, CH_2Si), 0.93 [9H, s, $SiC(CH_3)_3$], 0.91 (3H, d, *J* 6.3, 6-CH_3), 0.09 (3H, s, $SiCH_3$) and 0.07 (12H, s, 4×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 145.6, 138.2, 129.3, 129.1, 125.9, 123.3, 93.3, 68.8, 65.1, 63.8, 41.8, 41.2, 33.2, 30.7, 26.2, 20.3, 18.6, 18.4, 15.4, −1.1, −5.0 and −5.2; *m/z* (CI) 540 (M^++18, 6%) and 375 (100).

*4.2.25. (1SR,4RS,6RS)-1-(Phenylsulfonylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**37**).* Following the general procedure (4.2.8), the sulfide **36** (887 mg, 1.70 mmol), ammonium molybdate (3.14 mg, 2.54 mmol) in ethanol (175 mL) and hydrogen peroxide (30% solution in water, 5.06 mL), after chromatography on silica using 5–30% ether in light petroleum as eluent, gave the *title compound* **37** (687 mg, 1.24 mmol, 73%) as a clear, viscous oil, R_f=0.25 (20% ether in light petroleum) (Found: M^++NH_4, 572.3264. $C_{28}H_{54}O_5NSSi_2$ requires *M*, 572.3256); ν_{max}/cm^{-1} 2952, 2931, 2887, 2859, 1616, 1467, 1448, 1315, 1251, 1150, 1033, 837, 776 and 745; δ_H (300 MHz, $CDCl_3$) 7.91 (2H, d, *J* 7.0, ArH), 7.33-7.75 (3H, m, ArH), 5.74 (1H, br d, *J* 2.9, 3-H), 4.78 (2H, s, OCH_2O), 4.26 (1H, d, *J* 12.7, 2-CH), 4.22 (1H, m, 4-H), 4.08 (1H, d, *J* 12.7, 2-CH′), 3.64 (2H, m, OCH_2), 3.62 and 3.44 (each 1H, d, *J* 14.5, 1-CH), 2.92 (1H, m, 6-H), 1.91 (2H, m, 5-H_2), 1.39 (3H, s, 1-CH_3), 0.98 (2H, t, *J* 8.5, CH_2Si), 0.97 (3H, d, *J* 7.0, 6-CH_3), 0.82 [9H, s, $SiC(CH_3)_3$], 0.05 (12H, s, 4×$SiCH_3$) and 0.02 (3H, s, $SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.4, 136.8, 133.5, 129.4, 127.7, 125.7, 93.6, 69.6, 65.7, 65.3, 63.5, 41.8, 33.4, 33.2, 26.1, 21.1, 18.4, 15.7, −1.1 and −5.2; *m/z* (CI) 572 (M^++18, 30%), 407 (68) and 268 (100).

*4.2.26. (1SR,4RS,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfonylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**38**).* Following the general procedure (4.2.9), desilylation of the silyl ether **37** (654 mg, 1.18 mmol) in THF (30 mL) using tetra-*n*-butylammonium fluoride (1.0 M in THF, 5.16 mL, 5.16 mmol) gave the corresponding alcohol that was dissolved in THF (10 mL). O-Alkylation was ahieved following the general procedure (4.2.17) using sodium hydride (66 mg, 1.65 mmol, 60% dispersion in mineral oil) and iodomethyl(tributyl)stannane (0.48 mL, 1.61 mmol) to give, after chromatography on silica using 15% ether in light petroleum as eluent, the *title compound* **38** (669 mg, 0.90 mmol, 76%) as a clear oil, R_f=0.20 (40% ether in light

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petroleum); ν_{max}/cm^{-1} 2955, 2918, 2872, 1460, 1374, 1241, 1096, 1035, 855 and 834; δ_H (300 MHz, $CDCl_3$) 7.95 (2H, d, *J* 6.9, ArH), 7.65–7.52 (3H, m, ArH), 5.78 (1H, d, *J* 3.2, 3-H), 4.79 (2H, s, OCH_2O), 4.21 (1H, m, 4-H), 3.90 (2H, s, 2-CH_2), 3.68 (2H, t, *J* 8.5, OCH_2), 3.65 and 3.59 (each 1H, d, *J* 10.2, OHC*H*Sn), 3.46 and 3.44 (each 1H, d, *J* 15.0, 1-CH), 2.92 (1H, m, 6-H), 1.90 (2H, m, 5-H_2), 1.60–1.35 (6H, m, 3×$SnCH_2CH_2$), 1.40–1.20 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.30 (3H, s, 1-CH_3), 0.81–1.05 (20H, m, 3×CH_2Sn, CH_2Si, 3×CH_3 and 6-CH_3) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 142.4, 141.3, 133.5, 129.4, 127.8, 127.5, 93.5, 78.8, 69.3, 63.0, 62.0, 42.0, 33.2, 32.8, 29.4, 29.1, 27.5, 21.1, 18.4, 14.0, 10.9, 9.1 and −1.1.

*4.2.27. (1SR,4RS,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfanylmethyl)-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene (**39**).* Following the general procedure (4.2.9), desilylation of the silyl ether **36** (900 mg, 1.72 mmol) in THF (50 mL) using tetra-*n*-butylammonium fluoride (1.0 M in THF, 7.58 mL, 7.58 mmol) gave the corresponding alcohol as a pale yellow oil; δ_H (300 MHz, $CDCl_3$) 7.40–7.15 (5H, m, ArH), 6.04 (1H, d, *J* 4.7, 3-H), 4.81 (2H, s, OCH_2O), 4.30 (1H, dd, *J* 13.6, 5.4, 2-CH), 4.22 (1H, d, *J* 13.6, 6.6, 2-CH′), 4.15 (1H, m, 4-H), 3.65 (2H, m, OCH_2), 3.21 and 3.15 (each 1H, d, *J* 11.9, 1-CH), 2.58 (1H, br s, OH), 2.39 (1H, m, 6-H), 1.85–1.60 (2H, m, 5-H_2), 1.10 (3H, s, 1-CH_3), 0.98 (2H, m, CH_2Si), 0.91 (3H, d, *J* 6.9, 6-CH_3) and 0.06 (9H, s, 3×$SiCH_3$). This was dissolved in THF (15 mL) and O-alkylation was achieved following the general procedure (4.2.17) using sodium hydride (97 mg, 2.37 mmol, 60% dispersion in mineral oil) and iodomethyl(tributyl)stannane (0.71 mL, 2.37 mmol) to give, after chromatography on silica using 15% ether in light petroleum as eluent, the *title compound* **39** (905 mg, 1.27 mmol, 74%), as a clear oil, R_f=0.26 (15% ether in light petroleum) (Found: M^++Na, 735.3260. $C_{35}H_{64}O_3NaSSi^{120}Sn$ requires *M*, 735.3265); ν_{max}/cm^{-1} 2954, 2921, 2872, 1461, 1374, 1247, 1035, 859 and 836; δ_H (300 MHz, $CDCl_3$) 7.13–7.40 (5H, m, ArH), 5.91 (1H, d, *J* 4.4, 3-H), 4.80 (2H, s, OCH_2O), 4.17 (1H, m, 4-H), 4.13 and 3.85 (each 1H, d, *J* 12.6, 2-CH), 3.61–3.79 (4H, m, OCH_2Sn and OCH_2), 3.18 (2H, s, 1-CH_2), 2.35 (1H, m, 6-H), 1.75 (2H, m, 5-H_2), 1.50 (6H, m, 3×$SnCH_2CH_2$), 1.31 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.10 (3H, s, 1-CH_3), 0.81–1.05 (20H, m, 3×CH_2Sn, CH_2Si, 3×CH_3 and 6-CH_3) and 0.04 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 143.6, 138.3, 129.2, 129.0, 126.4, 125.8, 93.5, 77.7, 69.0, 65.2, 61.9, 41.7, 41.4, 33.2, 30.6, 29.4, 27.6, 20.3, 18.4, 15.6, 14.0, 9.3 and −1.1; *m/e* (ES) 735 (M^++23, 48%) and 565 (100).

*4.2.28. (2RS,3RS,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**40**).* Following the general procedure (4.2.18), the sulfone **38** (353 mg, 0.475 mmol) in THF (8 mL) and *n*-butyllithium (1.6 M in THF, 0.64 mL, 1.02 mmol), after chromatography on silica using 50% ether in light petroleum as eluent, gave the *title compound* **40** (80 mg, 0.18 mmol, 37%) as a pale yellow oil, R_f=0.17 (40% ether in light petroleum) (Found: M^++NH_4, 472.2545. $C_{23}H_{42}O_5NSSi$ requires *M*, 472.2547); ν_{max}/cm^{-1} 3512, 2951, 2890, 1639, 1447, 1380, 1313, 1249, 1150, 1029, 935, 859, 837 and 749; δ_H (300 MHz, $CDCl_3$) 7.97 (2H, d, *J* 6.9, ArH), 7.64 (3H, m, ArH), 5.31 and 5.01 (each 1H, s, 1-CH), 4.70 (2H, s, OCH_2O), 4.09 (1H, m, 3-H), 3.94 (1H, dd, *J* 11.0, 8.1, 2-CH), 3.79 (1H, dd, *J* 11.0, 6.0, 2-CH′), 3.75-3.50 (2H, m, OCH_2), 3.49 (2H, s, 6-CH_2), 2.72 (1H, m, 2-H), 2.18 (1H, m, 5-H), 1.89 (1H, ddd, *J* 14.4, 6.2, 4.4, 4-H), 1.62 (1H, ddd, *J* 14.4, 9.6, 3.6, 4-H′), 1.37 (3H, s, 6-CH_3), 0.99 (2H, t, *J* 8.5, CH_2Si), 0.93 (3H, d, *J* 6.7, 5-CH_3), 0.05 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 149.0, 142.5, 133.3, 129.9, 127.9, 109.9, 93.6, 79.1, 66.0, 63.5, 62.9, 47.5, 45.0, 36.0, 35.9, 20.2, 18.5, 17.3 and −0.7; *m/z* (CI) 472 (M^++18, 2%), 354 (4), 337 (6), 294 (4) and 90 (100).

Following the general procedure (4.2.8), the sulfide **42** (23 mg, 0.05 mmol), ammonium molybdate (11 mg, 0.008 mmol) and hydrogen peroxide (30% in water, 0.19 mL), after chromatography on silica with 50% ether in light petroleum, gave the title compound **40** (21 mg, 0.046 mmol, 86%) as a colourless oil, with spectroscopic data identical to those of the sample prepared from the stannane **38**.

*4.2.29. (2SR,3RS,5RS,6SR)- and (2RS,3RS,5RS,6SR)-5,6-dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfanylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**41**) and (**42**).* Following the general procedure (4.2.20), the sulphide **39** (524 mg, 0.73 mmol) in THF (10 mL) and *n*-butyllithium (1.6 M in THF, 0.51 mL, 0.81 mmol), after chromatography on silica using 30% ether in light petroleum as eluent gave the *title compound* **42** (23 mg, 0.051 mmol, 7%) as a pale yellow oil, R_f=0.25 (30% ether in light petroleum) (Found: M^++Na, 445.2203. $C_{23}H_{38}O_3NaSSi$ requires *M*, 445.2203); ν_{max}/cm^{-1} 3470, 2951, 2881, 1634, 1479, 1535, 1375, 1249, 1095, 1054, 1025, 936, 836 and 738; δ_H (300 MHz, $CDCl_3$) 7.38 (2H, d, *J* 6.9, ArH), 7.28 (3H, m, ArH), 5.10 and 4.99 (each 1H, s, 1-CH), 4.85 and 4.69 (each 1H, d, *J* 6.9, OHC*H*O), 3.90–3.60 (5H, m, 2-CH_2, 3-H and OCH_2), 3.40 and 3.09 (each 1H, d, *J* 11.9, 6-CH), 2.80 (1H, br s, OH), 2.20 (1H, dt, *J* 10.3, 4.1, 2-H), 2.00 (3H, m, 4-H_2 and 5-H), 1.20 (3H, s, 6-CH_3), 0.99 (2H, t, *J* 8.2, CH_2Si), 0.80 (3H, d, *J* 7.2, 5-CH_3), 0.06 (9H, s, 3×$SiCH_3$); *m/z* (ES) 445 (M^++23, 100%). The second fraction was the *title compound* **41** (281 mg, 0.62 mmol, 81%) as a pale yellow oil, R_f=0.22 (30% ether in light petroleum) (Found: M^++Na, 445.2203. $C_{23}H_{38}O_3NaSSi$ requires *M*, 445.2203); ν_{max}/cm^{-1} 3483br, 2951, 2882, 1635, 1584, 1480, 1438, 1380, 1249, 1095, 1054, 1025, 836 and 738; δ_H (300 MHz, $CDCl_3$) 7.38 (2H, d, *J* 6.9, ArH), 7.24 (3H, m, ArH), 5.15 and 5.04 (each 1H, s, 1-CH), 4.75 and 4.69 (each 1H, d, *J* 6.9, OHC*H*O), 3.99 (1H, dd, *J* 11.4, 4.3, 2-CH), 3.91 (1H, dd, *J* 11.4, 4.4, 2-CH′), 3.75–3.55 (3H, m, 3-H and OCH_2), 3.43 and 3.09 (each 1H, d, *J* 11.9, 6-CH), 2.82 (1H, br s, OH), 2.39 (1H, dt, *J* 10.3, 4.1, 2-H), 2.04 (1H, m, 5-H), 1.95 (1H, m, 4-H), 1.84 (1H, ddd, *J* 13.2, 5.0, 3.0, 4-H′), 1.22 (3H, s, 6-CH_3), 0.99 (1H, t, *J* 8.5, CH_2Si), 0.92 (3H, d, *J* 7.2, 5-CH_3) and 0.06 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 147.7, 137.8, 130.0, 129.0, 126.2, 111.9, 94.0, 76.4, 66.0, 62.3, 47.0, 44.8, 44.3, 37.1, 35.5, 22.9, 18.5, 16.6 and −1.2; *m/z* (ES) 445 (M^++23, 100%).

*4.2.30. (2SR,3RS,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-(2-trimethylsilylethoxy)methoxycyclohexane (**43**).* Following the standard procedure (4.2.8), the sulfide **41** (214 mg, 0.50 mmol), ammonium molybdate (100 mg, 0.075 mmol) in ethanol (5 mL) and hydrogen peroxide (30% solution in water, 1.74 mL) after chromatography on silica using 50% ether in light petroleum as eluent gave the *title compound* **43** (208 mg, 0.46 mmol, 84%) as a clear, viscous oil, R_f=0.20 (40% ether in light petroleum); δ_H (300 MHz, $CDCl_3$) 7.87 (2H, d, *J* 7.5, ArH), 7.63 (1H, t, *J* 7.5, ArH), 7.52 (2H, t, *J* 7.5, ArH), 5.12 and 5.07 (each 1H, s, 1-CH), 4.70 and 4.62 (each 1H, d, *J* 6.9, OHC*H*O), 3.80 (2H, m, 2-CH_2), 3.70–3.45 (3H, m, 3-H and OCH_2), 3.57 and 3.28 (each 1H, d, *J* 14.4, 6-CH), 2.91 (1H, br t, *J* 5.9, OH), 2.25 (1H, m, 2-H), 2.10 (1H, m, 5-H), 1.82 (2H, m, 4-H_2), 1.42 (3H, s, 6-CH_3), 0.94 (1H, t, *J* 8.5, CH_2Si), 0.86 (3H, d, *J* 7.2, 5-CH_3) and 0.01 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 145.9, 141.6, 133.8, 129.5, 128.1, 113.0, 94.1, 75.8, 66.0, 63.9, 61.5, 47.3, 44.0, 37.7, 35.7, 22.7, 18.3, 15.9 and −1.2.

*4.2.31. Methyl (1SR,4SR,6RS)-2-(tert-butyldimethylsilyloxymethyl)-4-tert-butyldiphenylsilyloxy-1,6-dimethylcyclohex-2-ene-1-carboxylate (**44**).* Imidazole (15.62 g, 228 mmol), *tert*-butyldiphenylsilyl chloride (47.46 mL, 182 mmol) and DMAP (7.21 g, 59 mmol) were added to the alcohol **11** (30.00 g, 91 mmol) in DCM (600 mL) at 0 °C and the solution stirred at room temperature for 24 h. Saturated aqueous ammonium chloride (300 mL) was added and the mixture extracted into DCM (2×150 mL). The organic extracts were washed with water (200 mL) and brine (200 mL), then dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the

residue on silica using 10% ether in light petroleum as eluent gave the *title compound* **44** (49.90 g, 88 mmol, 96%) as a colourless oil, R_f=0.65 (20% ether in light petroleum) (Found: M^++Na, 589.3136. $C_{33}H_{50}O_4Si_2Na$ requires *M*, 589.3140); ν_{max}/cm^{-1} 2937, 2857, 1732, 1665, 1590, 1465, 1431, 1251, 1106, 1057, 838 and 778; δ_H (300 MHz, $CDCl_3$) 7.74 (4H, m, ArH), 7.42 (6H, m, ArH), 5.87 (1H, br s, 3-H), 4.46 (1H, m, 4-H), 4.10 and 3.92 (each 1H, dt, *J* 14.1, 1.8, 2-CH), 3.66 (3H, s, OCH_3), 2.10 (1H, m, 6-H), 1.70–1.50 (2H, m, 5-H_2), 1.22 (3H, s, 1-CH_3), 1.12 and 0.96 [each 9H, s, $SiC(CH_3)_3$], 0.79 (3H, d, *J* 6.9, 6-CH_3) and 0.04 (6H, s, $SiCH_3$); δ_C (75 MHz, $CDCl_3$) 176.7, 140.8, 136.1, 134.8, 129.8, 127.8, 126.8, 69.2, 63.0, 52.1, 49.6, 36.5, 35.3, 27.3, 26.2, 19.5, 18.7, 16.9, 16.5 and −5.2; *m/z* (ES+) 589 (M^++23, 100%).

*4.2.32. (1SR,4SR,6RS)-1-Hydroxymethyl-2-(tert-butyldimethylsilyloxymethyl)-4-tert-butyldiphenylsilyloxy-1,6-dimethylcyclohex-2-ene (**45**).* Following the general procedure (4.2.6), reduction of the ester **44** (49.90 g, 88 mmol) in THF (600 mL) using lithium triethylborohydride (1.0 M in THF, 220 mL, 220 mmol), after chromatography silica using 10–50% ether in light petroleum as eluent gave the *title compound* **45** (41.57 g, 77 mmol, 88%) as a clear, viscous oil, R_f=0.51 (30% ether in light petroleum) (Found: M^++Na, 562.3261. $C_{32}H_{51}O_3Si_2Na$ requires *M*, 562.3269); ν_{max}/cm^{-1} 3464, 2955, 2931, 2857, 1467, 1254, 1108, 1051, 837 and 777; δ_H (300 MHz, $CDCl_3$) 7.67 (4H, m, ArH), 7.42 (6H, m, ArH), 5.78 (1H, br s, 3-H), 4.41 (1H, br dd, *J* 6.5, 6.3, 4-H), 4.26 and 3.86 (each 1H, d, *J* 10.8, 2-CH), 3.52 and 3.34 (each 1H, d, *J* 11.9, 1-CH), 2.00 (1H, m, 6-H), 1.70–1.45 (2H, m, 5-H_2), 1.11 and 0.93 [each 9H, s, $SiC(CH_3)_3$], 0.93 (3H, d, *J* 7.0, 6-CH_3), 0.81 (3H, s, 1-CH_3) and 0.11 and 0.10 (each 3H, s, $OSiCH_3$); δ_C (75 MHz, $CDCl_3$) 141.9, 137.3, 136.1, 134.7, 129.8, 127.8, 69.3, 65.5, 43.4, 37.0, 30.9, 27.3, 26.1, 19.5, 18.5, 16.6, 16.0 and −5.1; *m/z* (ES+) 562 (M^++23, 60%) and 561 (100).

*4.2.33. (1SR,4SR,6RS)-1-(Phenylsulfanylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-4-tert-butyldiphenylsilyloxy-1,6-dimethylcyclohex-2-ene (**46**).* Following the general procedure (4.2.7), the alcohol **45** (20.79 g, 39 mmol) in DCM (400 mL), triethylamine (18.74 mL, 135 mmol) and methanesulfonyl chloride (7.50 mL, 77 mmol) gave the mesylate as a pale orange oil. This was converted into the thioether following the general procedure using sodium hydride (60% dispersion in mineral oil, 7.70 g, 193 mmol) in DMF (500 mL), and benzenethiol (19.76 mL, 193 mmol) with the mesylate added in DMF (300 mL). After heating the reaction mixture under reflux, for 4 h, chromatography on silica using 1–20% ether in light petroleum as eluent gave the *title compound* **46** (19.68 g, 31 mmol, 81%) as a pale yellow, viscous oil, R_f=0.37 (15% ether in light petroleum) (Found: M^++NH_4, 648.3745. $C_{38}H_{58}O_2NSSi_2$ requires *M*, 648.3721); ν_{max}/cm^{-1} 3069, 2955, 2932, 2857, 1584, 1470, 1431, 1254, 1107, 1057, 838, 776 and 739; δ_H (300 MHz, $CDCl_3$) 7.77 (4H, m, ArH), 7.45 (6H, m, ArH), 7.30 (4H, m, ArH), 7.20 (1H, m, ArH), 5.95 (1H, br s, 3-H), 4.45 (1H, m, 4-H), 4.30 and 4.23 (each 1H, d, *J* 13.8, 2-CH), 3.10 and 3.02 (each 1H, d, *J* 12.0, 1-CH), 2.01 (1H, m, 6-H), 1.65 (2H, m, 5-H_2), 1.19 (3H, s, 1-CH_3), 1.17 and 0.99 [each 9H, s, $SiC(CH_3)_3$], 0.85 (3H, d, *J* 7.0, 6-CH_3) and 0.12 and 0.10 (each 3H, s, $OSiCH_3$); δ_C (75 MHz, $CDCl_3$) 137.9, 136.1(2), 131.0, 129.7, 129.3(2), 129.1, 127.8, 127.7, 127.4, 125.9, 69.2, 63.2, 41.2, 37.0, 33.4, 27.3, 26.3, 22.9, 21.3, 19.5, 18.7, 15.7 and −5.0; *m/z* (ES+) 653 (M^++23, 100%).

*4.2.34. (1SR,4SR,6RS)-1-(Phenylsulfanylmethyl)-2-hydroxymethyl-1,6-dimethyl-4-tert-butyldiphenylsilyloxycyclohex-2-ene (**47**); general procedure for silyl deprotection using acid.* Concentrated aqueous hydrogen chloride (12 M, 131 μl, 1.57 mmol) was added dropwise to the silyl ether **46** (497 mg, 0.78 mmol) in ethanol (12.5 mL) at room temperature and the solution was stirred for 1 h. Saturated aqueous sodium hydrogen carbonate (15 mL) was added and the aqueous phase extracted with EtOAc (5×15 mL). The organic extracts were washed with saturated aqueous sodium hydrogen carbonate (20 mL) and brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using 40% ether in light petroleum as eluent gave the *title compound* **47** (771 mg, 1.49 mmol, 95%) as a clear oil, R_f=0.24 (40% ether in light petroleum) (Found: M^++NH_4, 534.2841. $C_{32}H_{44}O_2SSiN$ requires *M*, 534.2857); δ_H (300 MHz, $CDCl_3$) 7.75 (4H, m, ArH), 7.45 (6H, m, ArH), 7.28 (4H, m, ArH), 7.20 (1H, m, ArH), 5.88 (1H, br s, 3-H), 4.45 (1H, m, 4-H), 4.12 (2H, br s, 2-CH_2), 3.12 and 3.07 (each 1H, d, *J* 11.9, 1-CH), 1.99 (1H, m, 6-H), 1.70–1.60 (3H, m, OH and 5-H_2), 1.12 [9H, s, $SiC(CH_3)_3$], 1.10 (3H, s, 1-CH_3) and 0.85 (3H, d, *J* 6.9, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 143.0, 137.1, 136.2, 136.1, 134.8, 134.7, 132.1, 129.9(2), 129.6, 129.2, 127.(2), 126.3, 69.3, 63.8, 41.5, 41.4, 37.0, 33.2, 27.3, 21.3, 19.5 and 15.8; *m/z* (CI) 534 (M^++18, 4%) and 261 (100).

*4.2.35. (1SR,4SR,6RS)-1-(Phenylsulfonylmethyl)-2-(tert-butyldimethylsilyloxymethyl)-4-tert-butyldiphenylsilyloxy-1,6-dimethylcyclohex-2-ene (**48**).* Following the general procedure (4.2.8), the sulfide **46** (19.56 g, 31 mmol) was oxidised using ammonium molybdate (57.46 g, 47 mmol) in ethanol (500 mL) and hydrogen peroxide (30% solution in water, 14.25 mL) to give, after chromatography on silica using 5–30% ether in light petroleum as eluent, the *title compound* **48** (17.90 g, 27 mmol, 88%) as a clear, viscous oil, R_f=0.30 (20% ether in light petroleum) (Found: M^++Na, 685.3188. $C_{38}H_{54}O_4NaSSi_2$ requires *M*, 685.3174); ν_{max}/cm^{-1} 3069, 2953, 2933, 2857, 1665, 1588, 1467, 1312, 1253, 1149, 1107, 837, 777 and 742; δ_H (300 MHz, $CDCl_3$) 7.40–7.86 (15H, m, ArH), 5.72 (1H, br s, 3-H), 4.20 (1H, m, 4-H), 4.29 and 4.22 (each 1H, d, *J* 13.1, 2-CH), 3.37 and 3.29 (each 1H, d, *J* 14.8, 1-CH), 2.48 (1H, m, 6-H), 1.65 (2H, m, 5-H_2), 1.21 (3H, s, 1-CH_3), 1.11 [9H, s, $SiC(CH_3)_3$], 0.95 (3H, d, *J* 6.7, 6-CH_3), 0.90 [9H, s, $SiC(CH_3)_3$] and 0.09 and 0.07 (each 3H, s, $OSiCH_3$); δ_C (75 MHz, $CDCl_3$) 141.7, 140.7, 135.9, 134.5, 134.3, 133.4, 129.6, 129.2, 128.8, 127.6(2), 127.4, 67.9, 65.0, 61.0, 41.7, 36.3, 33.1, 27.0, 25.9, 21.8, 19.2, 18.2, 16.1, −5.3 and −5.5; *m/z* (ES) 685 (M^++23, 100%).

*4.2.36. (1SR,4SR,6RS)-1-(Phenylsulfonylmethyl)-2-hydroxymethyl-1,6-dimethyl-4-tert-butyldiphenylsilyloxycyclohex-2-ene (**49**).* Following the general procedure (4.2.34), the silyl ether **48** (11.60 g, 17.4 mmol) in ethanol (290 mL) with concentrated aqueous hydrogen chloride (12 M, 3.0 mL, 36.0 mmol), after chromatography on silica using 45% ether in light petroleum, gave the *title compound* **49** (9.17 g, 16.7 mmol, 95%) as a clear oil, R_f=0.18 (40% ether in light petroleum) (Found: M^++Na, 571.2316. $C_{32}H_{40}O_4NaSSi$ requires *M*, 571.2309); ν_{max}/cm^{-1} 3503, 3069, 2958, 2934, 2858, 1588, 1468, 1447, 1427, 1307, 1147, 1109, 1077, 822 and 743; δ_H (300 MHz, $CDCl_3$) 7.89 (2H, d, *J* 7.3, ArH), 7.72 (4H, d, *J* 7.6, ArH), 7.40–7.70 (9H, m, ArH), 5.92 (1H, br s, 3-H), 4.50 (1H, br t, *J* 7.2, 4-H), 4.21 and 4.12 (each 1H, d, *J* 12.5, 2-CH), 3.64 and 3.22 (each 1H, d, *J* 14.5, 1-CH), 2.53 (1H, br s, OH), 2.50 (1H, m, 6-H), 1.65–1.40 (2H, m, 5-H_2), 1.12 [9H, s, $SiC(CH_3)_3$], 1.04 (3H, s, 1-CH_3) and 0.95 (3H, d, *J* 6.7, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 141.7, 136.1, 134.7, 134.4, 133.8, 130.0, 129.9, 129.5, 127.9, 127.8, 68.9, 65.2, 61.1, 42.0, 37.0, 33.2, 27.3, 21.8, 19.5, and 16.2; *m/z* (ES+) 571 (M^++23, 100%).

*4.2.37. (1SR,4SR,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfonylmethyl)-4-tert-butyldiphenylsilyloxycyclohex-2-ene (**50**).* Following the general procedure (4.2.17), sodium hydride (60% dispersion in mineral oil, 515 mg, 12.88 mmol), the alcohol **49** (5.00 g, 9.11 mmol) in dry THF (75 mL) and iodomethyl(tributyl)stannane (3.76 mL, 12.78 mmol), after chromatography on silica using 25% ether in light petroleum as eluent gave the *title compound* **50** (6.44 g, 7.56 mmol, 83%) as a clear oil, R_f=0.41 (20% ether in light petroleum) (Found: M^++Na, 875.3518. $C_{45}H_{68}O_4NaSSi^{120}Sn$ requires *M*, 875.3527); ν_{max}/cm^{-1} 3067, 2956, 2927, 2856, 1588, 1460, 1316, 1149, 1108, 1060, 821 and

742; δ_H (300 MHz, $CDCl_3$) 7.89 (2H, d, *J* 7.2, ArH), 7.75 (4H, d, *J* 7.4, ArH), 7.40–7.68 (9H, m, ArH), 5.70 (1H, br s, 3-H), 4.41 (1H, br t, *J* 7.3, 4-H), 4.19 and 3.79 (each 1H, d, *J* 12.0, 2-CH), 3.72 and 3.59 (each 1H, d, *J* 10.2, OHC*H*Sn), 3.44 and 3.25 (each 1H, d, *J* 14.7, 1-CH), 2.49 (1H, m, 6-H), 1.63 (2H, m, 5-H_2), 1.46 (6H, m, 3×$SnCH_2CH_2$), 1.31 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.18 (3H, s, 1-CH_3), 1.12 [9H, s, $SiC(CH_3)_3$] and 0.85–1.00 (18H, m, 3×$SnCH_2$, 3×CH_3 and 6-CH_3); δ_C (75 MHz, $CDCl_3$) 142.1, 139.0, 136.1, 134.7, 134.6, 133.6, 132.2, 129.9, 129.4, 127.8, 79.2, 68.4, 61.7, 61.2, 42.3, 33.4, 29.4, 27.6, 27.3, 22.9, 21.9, 19.5, 16.5, 14.0 and 9.2; *m/z* (ES+) 876 (100%).

*4.2.38. (1SR,4SR,6RS)-1,6-Dimethyl-2-(tributylstannylmethoxymethyl)-1-(phenylsulfanylmethyl)-4-tert-butyldiphenylsilyloxycyclohex-2-ene (**51**).* Following the general procedure (4.2.17), sodium hydride (60% dispersion in mineral oil, 515 mg, 12.88 mmol), the alcohol **47** (5.00 g, 9.11 mmol) in dry THF (75 mL) and iodomethyl(tributyl)stannane (3.76 mL, 12.78 mmol), after chromatography on silica using 25% ether in light petroleum as eluent gave the *title compound* **51** (6.44 g, 7.56 mmol, 83%) as a clear oil, R_f=0.59 (20% ether in light petroleum); ν_{max}/cm^{-1} 3099, 2950, 2925, 2855, 1460, 1374, 1246, 1092, 1035, 859 and 836; δ_H (300 MHz, $CDCl_3$) 7.75 (4H, m, ArH), 7.45 (6H, m, ArH), 7.28 (4H, m, ArH), 7.20 (1H, m, ArH), 5.64 (1H, br s, 3-H), 4.36 (1H, m, 4-H), 4.15 and 3.76 (each 1H, d, *J* 12.0, 2-CH), 3.71 and 3.57 (each 1H, d, *J* 10.1, OHC*H*Sn), 3.17 and 3.13 (each 1H, d, *J* 12.4, 1-CH), 2.04 (1H, m, 6-H), 1.58 (2H, m, 5-H_2), 1.44 (6H, m, 3×$SnCH_2CH_2$), 1.29 (6H, m, 3×$SnCH_2CH_2CH_2$), 1.15 (3H, s, 1-CH_3), 1.12 [9H, s, $SiC(CH_3)_3$] and 0.85–1.00 (18H, m, 3×$SnCH_2$, 3×CH_3 and 6-CH_3); δ_C (75 MHz, $CDCl_3$) 142.1, 137.2, 136.4, 133.6, 132.6, 130.1, 129.4, 129.0, 128.4, 126.8, 79.0, 68.0, 61.2, 40.8, 33.2, 29.0, 27.1, 27.0, 23.4, 22.9, 21.9, 18.0, 16.2, 13.6 and 9.0; *m/z* (ES+) 843 (M^++23, 100%).

*4.2.39. (2RS,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-tert-butyldiphenylsilyloxycyclohexane (**52**).* Following the general procedure (4.2.18), the sulfone **50** (6.40 g, 7.51 mmol) in THF (125 mL) and *n*-butyllithium (1.6 M in THF, 10.12 mL, 16.13 mmol), after chromatography on silica using 50% ether in light petroleum as eluent gave the *title compound* **52** (2.75 g, 4.88 mmol, 65%) as a white solid, mp 143–144 °C, R_f=0.18 (40% ether in light petroleum) (Found: M^++Na, 585.2465. $C_{33}H_{42}O_4NaSSi$ requires *M*, 585.2465); ν_{max}/cm^{-1} 3516, 3088, 2933, 2859, 1635, 1588, 1469, 1449, 1312, 1148, 1108, 739 and 703; δ_H (300 MHz, $CDCl_3$) 7.92 (2H, d, *J* 6.9, ArH), 7.77 (4H, d, *J* 7.2, ArH), 7.40–7.72 (9H, m, ArH), 5.35 and 5.08 (each 1H, s, 1-CH), 3.88 (2H, m, 2-CH_2), 3.75 (1H, m, 3-H), 3.44 and 3.37 (each 1H, d, *J* 14.8, 6-CH), 2.66 (1H, m, 2-H), 2.62 (3H, br s, OH), 1.71 (1H, m, 5-H), 1.59 (2H, m, 4-H_2), 1.30 (3H, s, 6-CH_3), 1.13 [9H, s, $SiC(CH_3)_3$] and 0.80 (1H, d, *J* 6.6, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 148.7, 142.6, 136.1(2), 134.4, 133.7, 133.6, 130.2, 130.0, 129.6, 128.0, 127.9, 127.6, 111.7, 74.4, 63.7, 63.2, 50.6, 45.0, 38.9, 36.2, 27.2, 20.5, 19.5 and 16.7; *m/z* (ES+) 585 (M^++23, 100%).

Following the general procedure (4.2.8), the sulfide **54** was oxidised to the title compound **52** with spectroscopic data identical to those of the sample prepared from the stannane **50**.

*4.2.40. (2SR,3SR,5RS,6SR)- and (2RS,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfanylmethyl)-3-tert-butyldiphenylsilyloxycyclohexane (**53**) and (**54**).* Following the general procedure (4.2.20), the sulphide **51** (989 mg, 1.21 mmol) in THF (17 mL) and *n*-butyllithium (1.6 M in THF, 0.87 mL, 1.33 mmol), after chromatography on silica gel using 30% ether in light petroleum as eluent, gave the *title compound* **54** (50 mg, 0.097 mmol, 8%) as a pale yellow oil, R_f=0.25 (30% ether in light petroleum); δ_H (300 MHz, $CDCl_3$) 7.60 (4H, m, ArH), 7.32 (6H, m, ArH), 7.10 (4H, m, ArH), 7.02 (1H, m, ArH), 5.00 and 4.75 (each 1H, s, 1-CH), 4.00 (2H, m, 2-CH and 3-H), 3.55 (1H, dd, *J* 10.6, 5.2, 2-CH′), 3.05 and 2.85 (each 1H, d, *J* 12.4, 6-CH), 2.44 (1H, m, 2-H), 1.90 (1H, br s, OH), 1.60 (2H, m, 4-H and 5-H), 1.39 (1H, m, 4-H′), 0.94 [9H, s, $SiC(CH_3)_3$], 0.90 (3H, s, 6-CH_3) and 0.59 (3H, d, *J* 6.9, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 134.9, 134.4, 133.8, 132.1, 129.7, 129.4, 125.2, 124.5, 112.2, 71.0, 63.1, 48.4, 42.7, 40.8, 37.5, 34.9, 27.5, 20.3, 18.2 and 17.5. The second fraction was the *title compound* **53** (575 mg, 1.11 mmol, 92%) as a pale yellow oil, R_f=0.21 (30% ether in light petroleum); δ_H (300 MHz, $CDCl_3$) 7.60 (4H, m, ArH), 7.32 (6H, m, ArH), 7.12 (4H, m, ArH), 7.02 (1H, m, ArH), 4.94 and 4.89 (each 1H, s, 1-CH), 4.04 (1H, td, *J* 8.7, 3.4, 3-H), 3.87 and 3.42 (each 1H, dd, *J* 10.6, 5.2, 2-CH), 3.20 and 2.92 (each 1H, d, *J* 12.5, 6-CH), 2.67 (1H, m, 2-H), 1.92 (1H, br s, OH), 1.60 (1H, m, 4-H and 5-H), 1.39 (2H, m, 4-H′) 0.94 [9H, s, $SiC(CH_3)_3$], 0.92 (3H, s, 6-CH_3) and 0.68 (3H, d, *J* 6.4, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 134.9, 134.7, 134.1, 133.8, 132.6, 130.0, 129.4, 125.0, 124.6, 112.2, 71.0, 63.1, 48.1, 43.1, 40.8, 37.5, 35.9, 27.1, 20.3, 18.2 and 17.5.

*4.2.41. (2SR,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)-3-tert-butyldiphenylsilylcyclohexane (**55**).* Following the general procedure (4.2.8) using the sulfide **53** (570 mg, 1.07 mmol), ammonium molybdate (214 mg, 0.16 mmol) in ethanol (11 mL) and hydrogen peroxide (30% solution in water, 3.72 mL) after chromatography on silica using 50% ether in light petroleum as eluent, gave the *title compound* **55** (518 mg, 0.92 mmol, 86%) as a clear, viscous oil, R_f=0.19 (40% ether in light petroleum) (Found: M^++Na, 585.2465. $C_{33}H_{42}O_4NaSSi$ requires *M*, 585.2465); ν_{max}/cm^{-1} 3516, 3067, 1469, 1448, 1428, 1385, 1312, 1148, 1108, 1084, 1039 and 739; δ_H (300 MHz, $CDCl_3$) 7.89 (2H, d, *J* 7.0, ArH), 7.40–7.78 (13H, m, ArH), 5.25 and 5.02 (each 1H, s, 1-CH), 4.29 (1H, m, 3-H), 3.60–3.40 (3H, m, 6-CH and 2-CH_2), 3.21 (1H, d, *J* 14.4, 6-CH′), 2.48 (1H, m, 2-H), 2.01 (1H, m, 5-H), 1.78 (2H, m, 4-H_2), 1.42 (3H, s, 6-CH_3), 1.10 [9H, s, $SiC(CH_3)_3$], 1.08 (3H, d, *J* 7.2, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 136.4, 136.1, 134.1, 133.7, 130.2, 130.0, 129.4, 128.0, 127.6, 113.0, 71.0, 64.3, 62.1, 48.1, 44.4, 37.9, 36.1, 27.4, 22.6, 19.7 and 17.6; *m/z* (ES) 585 (M^++23, 100%).

*4.2.42. (2RS,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)cyclohexan-3-ol (**56**).* Magnesium bromide (440 mg, 2.32 mmol) was dissolved in ether (1.5 mL) and nitromethane (265 μL, 4.68 mmol) and added to the SEM ether **27** (76 mg, 0.17 mmol) in ether (1.5 mL). The reaction mixture was stirred at room temperature for 1 h and then diluted with ether (50 mL), washed with water (10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue using ether as eluent gave the *title compound* **56** (43 mg, 0.13 mmol, 76%) as a pale yellow oil, R_f=0.18 (ether) (Found: M^++NH_4, 342.1737. $C_{17}H_{28}O_4NS$ requires *M*, 342.1734); ν_{max}/cm^{-1} 3430, 2928, 1637, 1447, 1409, 1306, 1144, 1085 and 742; δ_H (300 MHz, $CDCl_3$) 7.98 (2H, d, *J* 7.0, ArH), 7.72–7.58 (3H, m, ArH), 5.29 and 4.85 (each 1H, s, 1-CH), 4.15 (1H, dd, *J* 10.5, 3.7, 2-CH), 4.02 (1H, dd, *J* 10.5, 7.8, 2-CH′), 3.69 (1H, td, *J* 10.5, 4.6, 3-H), 3.58 and 3.44 (each 1H, d, *J* 15.0, 6-CH), 3.45 (2H, br s, 2×OH), 2.50 (1H, m, 2-H), 2.05–1.75 (2H, m, 4-H and 5-H), 1.59 (1H, q, *J* 10.5, 4-H′), 1.24 (3H, s, 6-CH_3) and 0.97 (3H, d, *J* 6.6, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 149.3, 142.8, 133.8, 129.7, 127.6, 109.2, 75.2, 65.5, 63.3, 46.7, 46.0, 39.7, 36.5, 19.5 and 16.8; *m/z* (CI) 342 (M^++18, 100%).

Following the general procedure (4.2.9) tetra-*n*-butylammonium fluoride (1.0 M in THF, 0.25 mL, 0.25 mmol) was added to the silyl ether **52** (90 mg, 0.16 mmol) in THF (0.80 mL) at room temperature and the solution was stirred for 24 h then concentrated under reduced pressure. Chromatography of the residue on silica using ether as the eluent gave the title compound **56** (43 mg, 0.13 mmol, 83%) with spectroscopic data identical to those obtained earlier.

*4.2.43. (2SR,3SR,5RS,6SR)-5,6-Dimethyl-2-hydroxymethyl-1-methylene-6-(phenylsulfonylmethyl)cyclohexan-3-ol (**57**).* Following

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the general procedure (4.2.8) the sulfone **55** was prepared from the sulfide **53** (80 mg, 0.15 mmol), ammonium molybdate (30 mg, 0.022 mmol) and hydrogen peroxide (30% in water, 0.52 mL). Without purification it was dissolved in THF (0.5 mL) and following the general procedure (4.2.9) tetra-*n*-butylammonium fluoride (1 M in THF, 0.65 mL, 0.65 mmol) was added. The reaction mixture was stirred for 24 h then concentrated under reduced presure. Chromatography of the residue on silica gel using ether as eluent gave the *title compound* **57** (57 mg, 0.10 mmol, 69%) as a pale yellow oil, R_f=0.20 (ether) (Found: M^++NH_4, 342.1724. $C_{17}H_{28}O_4NS$ requires *M*, 342.1734); ν_{max}/cm^{-1} 3436, 2925, 1636, 1448, 1305, 1143, 1085, 1021, 903 and 744; δ_H (300 MHz, $CDCl_3$) 7.90 (2H, d, *J* 8.5, ArH), 7.52–7.71 (3H, m, ArH), 5.20 and 5.10 (each 1H, s, 1-CH), 4.25 (1H, m, 3-H), 3.91 (1H, dd, *J* 10.7, 6.8, 2-CH), 3.80 (1H, dd, *J* 10.7, 5.3, 2-CH′), 3.60 and 3.20 (each 1H, d, *J* 14.4, 6-CH), 3.98 (1H, br s, OH), 2.57 (2H, m, 2-H and OH), 2.02 (2H, m, 4-H and 5-H), 1.62 (1H, m, 4-H′), 1.39 (3H, s, 6-CH_3) and 1.02 (3H, d, *J* 7.0, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 145.4, 141.6, 133.9, 129.6, 128.0, 113.4, 69.7, 64.4, 62.3, 45.6, 44.5, 37.7, 36.3, 22.6 and 17.8; *m/z* (CI) 342 (M^++18, 50%), 307 (69) and 147 (100).

Following the general procedure (4.2.8), sulfide **41** (55 mg, 0.13 mmol), ammonium molybdate (26 mg, 0.019 mmol) in ethanol (1.0 mL) and hydrogen peroxide (30% in water, 0.45 mL) gave the sulfone **43**. Without purification, this was dissolved in pyridine (0.5 mL) and benzoyl chloride (0.49 mL, 4.2 mmol) and DMAP (10 mg, cat.) were added. After 3 h, methanol (0.5 mL) was added and the mixture stirred for 10 min before being concentrated under reduced pressure. Chromatography of the residue on silica using 15% ether in light petroleum as eluent gave the benzoate **58** (70 mg, 0.14 mmol) as a colourless oil (Found: M^++Na, 581.2373. $C_{30}H_{42}O_6NaSSi$ requires *M*, 581.2364); ν_{max}/cm^{-1} 2949, 2882, 1717, 1313, 1275, 1146, 1112, 1031 and 836; δ_H (300 MHz, $CDCl_3$) 8.09 and 7.98 (each 2H, d, *J* 7.8, ArH), 7.70 (1H, t, *J* 7.3, ArH), 7.62 (3H, t, *J* 7.4, ArH), 7.50 (2H, t, *J* 7.6, ArH), 5.28 and 5.22 (each 1H, s, 1-CH), 4.81 and 4.64 (each 1H, d, *J* 7.3, OHC*H*O), 4.60 (2H, m, 2-CH_2), 3.85 (1H, td, *J* 10.7, 5.4, 3-H), 3.75–3.50 (2H, m, OCH_2), 3.61 and 3.45 (each 1H, d, *J* 14.4, 6-CH), 2.52 (1H, br d, *J* 10.7, 2-H), 2.30 (1H, m, 5-H), 2.10–1.90 (2H, m, 4-H_2), 1.58 (3H, s, 6-CH_3), 1.02 (3H, d, *J* 7.0, 5-CH_3), 0.94 (2H, m, CH_2Si) and 0.02 (9H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 166.7, 145.6, 141.8, 133.9, 133.3, 130.5, 129.9, 129.5, 128.7, 128.2, 113.7, 94.2, 72.8, 65.8, 63.9, 62.1, 45.0, 44.1, 37.4, 35.6, 23.2, 18.2, 16.0 and −1.2; *m/z* (ES+) 581 (M^++23, 95%). Magnesium bromide (24 mg, 1.75 mmol) in ether (0.5 mL) and nitromethane (50 μL) was added to the benzoate in ether (0.5 mL) and the mixture stirred for 1 h. Ether (30 mL) was added and the solution washed with water (5 mL) and brine (5 mL), then dried (Na_2SO_4), and concentrated under reduced pressure to give the alcohol **59** as a colourless oil (Found: M^++Na, 451.1559. $C_{24}H_{28}O_5NaS$ requires *M*, 451.1550); ν_{max}/cm^{-1} 3492br, 3055, 2928, 1715, 1584, 1476, 1434, 1277, 1145, 1088, 1027 and 744; δ_H (300 MHz, $CDCl_3$) 8.08 and 7.95 (each 2H, d, *J* 7.5, ArH), 7.70–7.40 (6H, m, ArH), 5.44 and 5.22 (each 1H, s, 1-CH), 5.02 (1H, dd, *J* 7.0, 3.0, 2-CH), 4.40 (1H, dd, *J* 7.0, 2.0, 2-CH′), 3.68 (1H, d, *J* 13.0, 6-CH), 3.64 (1H, m, 3-H), 3.42 (1H, br s, OH), 3.30 (1H, d, *J* 13.0, 6-CH′), 2.40 (1H, br d, *J* 7.5, 2-H), 2.11 (1H, m, 5-H), 2.00–1.80 (2H, m, 4-H_2), 1.52 (3H, s, 6-CH_3) and 0.89 (3H, d, *J* 7.0, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 167.8, 145.6, 141.8, 133.9, 133.7, 130.0, 129.9, 129.5, 128.8, 128.2, 113.7, 66.5, 63.9, 63.1, 48.0, 44.1, 38.0, 37.2, 23.2 and 15.9; *m/z* (ES+) 451 (M^++23, 50%). This was dissolved in THF (0.5 mL) with triphenylphosphine (52 mg, 0.20 mmol) and the solution added to DIAD (0.038 mL, 0.20 mmol) and benzoic acid (12 mg, 0.20 mmol) in THF (0.5 mL) at 0 °C. After 4 h at 0 °C, the mixture was concentrated under reduced pressure and chromatography of the residue on silica using 15% ether in light petroleum as eluent gave the inverted bis-benzoate as a colourless oil (Found: M^++Na, 555.1812. $C_{31}H_{32}O_6NaS$ requires *M*, 555.1812); ν_{max}/cm^{-1} 1715, 1450, 1276, 1146, 1112 and 1025; δ_H (300 MHz, $CDCl_3$) 8.15 and 7.95 (6H, m, ArH), 7.70–7.55 (5H, m, ArH), 7.50–7.40 (4H, m, Ar), 5.62 (1H, m, 3-H), 5.32 and 5.17 (each 1H, s, 1-CH), 4.51 (1H, dd, *J* 8.0, 5.4, 2-CH), 4.42 (1H, dd, *J* 8.0, 7.0, 2-CH′), 3.69 and 3.32 (each 1H, d, *J* 14.5, 6-CH), 2.99 (1H, m, 2-H), 2.30–2.10 (2H, m, 4-H and 5-H), 2.04 (2H, dt, *J* 15.0, 1.0, 4-H′), 1.55 (3H, s, 6-CH_3) and 1.02 (3H, d, *J* 7.5, 5-CH_3); δ_C (75 MHz, $CDCl_3$) 166.6, 165.8, 144.5, 141.7, 133.9, 133.4, 133.3, 130.4, 1303, 129.9, 129.8, 129.6, 128.7(2), 128.2, 113.3, 70.9, 64.3, 63.2, 44.4, 41.2, 37.6, 32.8, 23.0 and 17.5; *m/z* (ES+) 555 (M^++23, 100%). This was taken up in methanol containing sodium hydroxide (5%, 1.0 mL) and the solution stirred for 30 min. After concentration under reduced pressure, the residue was dissolved in ether (30 mL) and the solution washed with water (5 mL) and brine (5 mL), then dried Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica eluting with 35% ether in light petroleum gave the title compound **57** (17 mg, 0.055 mmol, 40%) with spectroscopic data identical to those obtained earlier.

*4.2.44. (2E,6E)-7-Iodo-2,6-dimethylhepta-2,6-dien-1-ol (**61**).* Trimethylaluminium (2.0 M in DCM, 63.3 mL, 126.6 mmol) was added to a suspension of Cl_2ZrCp_2 (24.7 g, 84.4 mmol) in DCM (40 mL) at room temperature and the reaction mixture stirred until all the solids had dissolved. The alkyne **60** (5.24 g, 42.2 mmol) in DCM (10 mL) was added and the reaction mixture stirred at room temperature for 2 d. After cooling to 0 °C, iodine (54.1 g, 211 mmol) in THF (50 mL) was added, and the mixture was allowed to warm to room temperature and was stirred until TLC indicated the complete consumption of the starting material (5 h). The mixture was cooled to 0 °C and then water (75 mL) was added. The organic phase was washed with saturated aqueous sodium sulfite (40 mL) and brine (40 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using ether as eluent gave the *title compound* **61** (6.96 g, 26.2 mmol, 62%) as a pale yellow oil, R_f=0.20 (40% ether in light petroleum) (Found; M^++NH_4, 284.0506; $C_9H_{19}ONI$ requires *M*, 284.0506); ν_{max}/cm^{-1} 3331br, 3057, 2914, 2856, 1619, 1443, 1376, 1268, 1141, 1000 and 768; δ_H (300 MHz, $CDCl_3$) 5.92 (1H, s, 7-H), 5.39 (1H, td, *J* 6.8, 1.2, 3-H), 4.02 (2H, s, 1-H_2), 2.35–2.08 (4H, m, 4-H_2 and 5-H_2), 1.88 and 1.69 (each 3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 147.8, 136.0, 124.7, 75.3, 68.9, 39.4, 26.1, 24.2 and 14.0; *m/z* (CI) 284 (M^++18, 100%).

*4.2.45. (2E,6E)-1-tert-Butyldimethylsilyloxy-7-iodo-2,6-dimethylhepta-2,6-diene (**62**).* Imidazole (3.59 g, 54.4 mmol) and *tert*-butyldimethylsilyl chloride (5.92 g, 39.3 mmol) were added to the alcohol **61** (6.96 g, 26.2 mmol) in DCM (200 mL) at 0 °C and the solution stirred at room temperature for 24 h. Saturated aqueous ammonium chloride (200 mL) was added and the mixture was extracted with DCM (2×75 mL). The organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue on silica using 1% ether in light petroleum as eluent gave the *title compound* **62** (9.56 g, 25.2 mmol, 96%) as a colourless oil, R_f=0.20 (1% ether in light petroleum) (Found: M^+, 380.1023. $C_{15}H_{29}OISi$ requires *M*, 380.1027); ν_{max}/cm^{-1} 2953, 2927, 2855, 1470, 1461, 1253, 1110, 1069, 836 and 774; δ_H (300 MHz, $CDCl_3$) 5.91 (1H, s, 7-H), 5.39 (1H, td, *J* 6.8, 1.2, 3-H), 4.02 (2H, s, 1-H_2), 2.35–2.20 (4H, m, 4-H_2 and 5-H_2), 1.88 and 1.62 (each 3H, s, CH_3), 0.94 [9H, s, $SiC(CH_3)_3$] and 0.09 (6H, s, 3×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 147.9, 135.6, 123.0, 75.2, 68.6, 39.5, 26.2, 26.1, 24.2, 18.7, 13.7 and −5.0; *m/z* (CI) 398 (M^++18, 18%), 381 (M^++1, 9%) and 121 (100).

*4.2.46. (1SR,3SR,4RS,6SR)-6-tert-Butyldiphenylsilyloxy-3,4-dimethyl-2-methylene-3-(phenylsulfonylmethyl)cyclohexane-1-carboxaldehyde (**63**).* Di-*iso*propylethylamine (2.48 mL, 13.0 mmol) was added to the alcohol **52** (1.66 g, 2.94 mmol) in DCM (12 mL) at room temperature and the solution cooled to 0 °C before the

addition of py.SO_3 (1.60 g, 8.85 mmol) in DMSO (13 mL). The reaction mixture was stirred at 0 °C for 15 min then poured into brine (20 mL), and the aqueous phase extracted with ethyl acetate (4×20 mL). The organic extracts were washed with saturated aqueous copper(II) sulfate (30 mL), water (30 mL) and brine (30 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on silica using 40% ether in light petroleum gave the *title compound* **63** (1.50 g, 91%) as a colourless oil, R_f=0.27 (40% ether in light petroleum) (Found: M^++Na, 583.2316. $C_{33}H_{40}O_4NaSSi$ requires *M*, 583.2309); ν_{max}/cm^{-1} 3069, 2959, 2934, 2859, 1728, 1634, 1587, 1468, 1448, 1428, 1315, 1149, 1109, 1042, 911, 824 and 740; δ_H (300 MHz, $CDCl_3$) 9.46 (1H, d, *J* 3.2, 1-CH), 7.88 (2H, d, *J* 7.9, ArH), 7.40–7.67 (13H, m, ArH), 5.37 and 4.93 (each 1H, s, 2-CH), 4.32 (1H, td, *J* 7.8, 4.4, 6-H), 3.32 and 3.22 (each 1H, d, *J* 14.8, 3-CH), 3.14 (1H, m, 1-H), 2.09 (1H, m, 4-H), 1.79 (1H, dt, *J* 13.8, 4.4, 5-H), 1.60 (1H, m, 5-H′), 1.29 (3H, s, 3-CH_3), 1.08 [9H, s, $SiC(CH_3)_3$] and 0.96 (1H, d, *J* 6.9, 4-CH_3); δ_C (75 MHz, $CDCl_3$) 202.7, 144.4, 142.4, 136.1(2), 134.2, 133.8, 133.6, 130.3, 130.1, 129.6, 128.1, 127.9, 127.6, 115.1, 69.6, 62.9, 62.6, 44.8, 36.9, 35.2, 27.2, 22.2, 19.4 and 17.1; *m/z* (ES) 583 (M^++23, 100%).

*4.2.47. (1SR,3SR,4RS,6SR)-1-[(1RS,2E,6E)-8-tert-Butyldimethylsilyloxy-1-hydroxy-3,7-dimethylocta-2,6-dien-1-yl]-6-tert-butyldiphenylsilyloxy-3,4-dimethyl-2-methylene-3-(phenylsulfonylmethyl)cyclohexane (**64**).* Ytterbium triflate (5.93 g, 9.57 mmol) was heated to 140 °C with stirring overnight under a high vacuum and then allowed to cool to room temperature under an atmosphere of nitrogen. *tert*-Butyllithium (1.7 M in pentane, 5.63 mL, 9.57 mmol) was added to the vinyl iodide **62** (3.63 g, 9.57 mmol) in THF (24 mL) at −78 °C. The solution was stirred for 1 h at −78 °C and then added to the ytterbium triflate in THF (210 mL). After being stirred at −78 °C for 30 min, a portion (81 mL) of the organoytterbium reagent was added to the aldehyde **63** (0.89 g, 1.6 mmol) in THF (9.4 mL) at −78 °C and the resulting solution stirred at −78 °C for 3 h. More organo-ytterbium reagent (40 mL) was added and the solution stirred at −78 °C for a further 1.5 h. Saturated methanolic ammonium chloride (48 mL) was added and the mixture allowed to warm to ambient temperature before the addition of saturated aqueous Rochelle's salt (48 mL). The aqueous phase was extracted with ethyl acetate (4×30 mL) and the organic extracts washed with brine (100 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 5–50% ether in light petroleum as eluent gave the *title compound* **64** (1.10 g, 85%) as a white solid, mp 97–98 °C, R_f=0.25 (40% ether in light petroleum) (Found: M^++Na, 837.4386; $C_{48}H_{70}O_5NaSSi_2$ requires *M*, 837.4375); ν_{max}/cm^{-1} 3511br, 3071, 2956, 2931, 2857, 1629, 1588, 1447, 1428, 1387, 1308, 1254, 1148, 1108, 1053, 837, 776, 741 and 704; δ_H (300 MHz, $CDCl_3$) 7.89 (2H, d, *J* 7.0, ArH), 7.76 (4H, m, ArH), 7.40–7.68 (9H, m, ArH), 5.35 (1H, br t, *J* 6.5, 6′-H), 5.23 (1H, s, 2-CH), 5.12 (1H, d, *J* 8.6, 2′-H), 4.95 (1H, s, 2-CH′), 4.42 (1H, m, 1′-H), 4.12 (1H, m, 6-H), 4.05 (2H, s, 8′-H_2), 3.37 and 3.07 (each 1H, d, *J* 14.6, 3-CH), 2.49 (2H, m, 1-H and OH), 2.10–1.90 (5H, m, 4-H, 4′-H_2, 5′-H_2), 1.66 (2H, m, 5-H_2), 1.65 (3H, s, 7′-CH_3), 1.50 (3H, s, 3′-CH_3), 1.21 (3H, s, 3-CH_3), 1.10 and 0.98 [each 9H, s, $SiC(CH_3)_3$], 0.91 (3H, d, *J* 6.9, 4-CH_3), and 0.11 (6H, s, 2×$SiCH_3$); δ_C (75 MHz, $CDCl_3$) 148.8, 142.8, 139.4, 136.3, 136.2, 135.0, 134.2, 133.9, 133.6, 130.1(2), 129.5, 127.9(2), 127.7, 126.7, 124.5, 115.2, 74.6, 69.6, 69.0, 63.7, 56.1, 44.8, 39.5, 37.2, 36.2, 27.2, 26.3, 21.1, 19.4, 18.7, 17.5, 16.5, 13.8 and −4.9; *m/z* (+ES) 837 (M^++23, 48%), 798 (100), 667 (66) and 409 (54).

*4.2.48. (1SR,3SR,4RS,6SR)-1-[(1RS,2E,6E)-1-(Benzyloxymethoxy)-8-tert-butyldimethylsilyloxy-3,7-dimethylocta-2,6-dien-1-yl]-6-tert-butyldiphenylsilyloxy-3,4-dimethyl-2-methylene-3-(phenylsulfonylmethyl)cyclohexane (**65**).* Di-*iso*propylethylamine (1.05 mL, 36.2 mmol), benzyloxymethyl chloride (0.75 mL, 5.2 mmol) and tetra-*n*-butylammonium iodide (35 mg, 0.085 mmol) were added to the alcohol **64** (700 mg, 0.85 mmol) in THF (1.5 mL) at room temperature. The reaction mixture was stirred for 16 h, methanol (0.4 mL) was added and the mixture stirred for 1 h. Ethyl acetate (10 mL) and water (10 mL) were added the aqueous phase extracted into ethyl acetate (4×5 mL). The organic extracts were washed with aqueous sodium bisulfite (0.5 N, 15 mL), an aqueous pH 7 buffer (15 mL) and brine (15 mL), then dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 30% ether in light petroleum as eluent gave the *title compound* **65** (652 mg, 82%) as a pale yellow oil, R_f=0.35 (40% ether in light petroleum) (Found: M^++Na, 957.4953. $C_{56}H_{78}O_6NaSSi_2$ requires *M*, 957.4950); ν_{max}/cm^{-1} 3069, 2930, 2856, 1666, 1628, 1588, 1461, 1385, 1318, 1257, 1150, 1105, 1039, 837, 776, 742 and 703; δ_H (300 MHz, $CDCl_3$) 7.84 (2H, d, *J* 7.2, ArH), 7.75 (4H, d, *J* 8.8, ArH), 7.30–7.65 (12H, m, ArH), 7.15 (2H, m, ArH), 5.29 (1H, t, *J* 7.0, 6′-H), 5.24 and 5.15 (each 1H, s, 2-CH), 4.89 (1H, d, *J* 8.8, 2′-H), 4.46 (1H, d, *J* 7.0, OHC*H*O), 4.38 (1H, m, 1′-H), 4.28 (1H, d, *J* 7.0, OHC*H*′O), 4.12 (1H, m, 6-H), 4.10 and 4.03 (each 1H, d, *J* 12.0, HC*H*Ph), 4.04 (2H, s, 8′-H_2), 3.32 (1H, d, *J* 14.3, 3-CH), 2.70 (1H, br d, *J* 8.8, 1-H), 2.65 (1H, d, *J* 14.3, 3-CH′), 2.59 (1H, m, 4-H), 1.80–2.00 (5H, m, 4′-H_2, 5′-H_2, 5-H), 1.63 (1H, m, 5-H′), 1.61 (3H, s, 7′-CH_3), 1.51 (3H, s, 3′-CH_3), 1.12 (3H, d, *J* 7.3, 4-CH_3), 1.09 [9H, s, $SiC(CH_3)_3$], 1.05 (3H, s, 3-CH_3), 0.98 [9H, s, $SiC(CH_3)_3$] and 0.10 (6H, s, 2×$SiCH_3$); δ_C (125 MHz, $CDCl_3$) 146.4, 141.3, 139.7, 137.1, 135.3, 135.2, 133.8, 133.3, 133.2, 132.3, 128.5(2), 128.2, 127.3, 126.5, 126.4, 126.3, 126.2, 122.8, 122.0, 117.0, 89.2, 70.0, 69.8, 68.3, 67.6, 62.7, 56.1, 42.7, 38.3, 32.6, 32.0, 28.7, 26.0, 25.0, 22.1, 18.1, 17.4, 14.7, 12.5 and −6.3; *m/z* (+ES) 958 (40%) and 515 (100).

*4.2.49. (1SR,3SR,4RS,6SR)-1-[(1RS,2E,6E)-1-(Benzyloxymethoxy)-8-hydroxy-3,7-dimethylocta-2,6-dien-1-yl]-6-tert-butyldiphenylsilyloxy-3,4-dimethyl-2-methylene-3-(phenylsulfonylmethyl)cyclohexane (**66**).* The silyl ether **65** (300 mg, 0.31 mmol) was dissolved in acetic acid: water: THF (3:1:1, 2 mL) and the solution stirred at room temperature for 2 d. Toluene (50 mL) was added and the solution dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 50% ether in light petroleum as eluent gave the *title compound* **66** (240 mg, 0.29 mmol, 91%) as a glassy white solid, R_f=0.21 (50% ether in light petroleum) (Found: M^++Na, 843.4074; $C_{50}H_{64}O_6NaSSi$ requires *M*, 843.4085); ν_{max}/cm^{-1} 3523, 3068, 2929, 2856, 1447, 1383, 1307, 1158, 1103, 1038 and 702; δ_H (300 MHz, $CDCl_3$) 7.80 (2H, d, *J* 8.1, ArH), 7.71 (4H, d, *J* 8.0, ArH), 7.57 (1H, m, ArH), 7.30–7.50 (11H, m, ArH), 7.11 (2H, m, ArH), 5.24 (1H, s, 2-CH), 5.24 (1H, t, *J* 6.6, 6′-H), 5.14 (1H, s, 2-CH′), 4.88 (1H, d, *J* 9.9, 2′-H), 4.42 (1H, d, *J* 7.0, OHC*H*O), 4.32 (1H, m, 1′-H), 4.25 (1H, d, *J* 7.0, OHC*H*′O), 4.02–4.20 (4H, m, OH, 6-H, OCH_2Ph), 4.01 (2H, s, 8′-H_2), 3.28 (1H, d, *J* 14.1, 3-CH), 2.70 (1H, br d, *J* 9.0, 1-H), 2.65 (1H, d, *J* 14.1, 3-CH′), 2.57 (1H, m, 4-H), 1.82–2.03 (5H, m, 4′-H_2, 5′-H_2 and 5-H), 1.80 (1H, m, 5-H′), 1.68 (3H, s, 7′-CH_3), 1.51 (3H, s, 3′-CH_3), 1.11 (3H, d, *J* 7.2, 4-CH_3), 1.07 [9H, s, $SiC(CH_3)_3$] and 0.98 (3H, s, 3-CH_3); δ_C (125 MHz, $CDCl_3$) 147.5, 142.3, 140.4, 138.1, 136.3, 136.2, 135.7, 134.3, 134.2, 133.5, 129.6, 129.4, 129.3, 128.4, 127.6, 127.5, 127.3, 127.2, 124.7, 123.5, 118.0, 90.2, 71.0, 69.4, 68.8, 63.5, 57.1, 43.7, 39.0, 33.6, 33.0, 27.0, 25.3, 23.0, 19.1, 18.5, 15.4 and 13.8; *m/z* (+ES) 843 (M^++23, 100%).

*4.2.50. (1SR,3SR,4RS,6SR)-1-[(1RS,2E,6E)-1-(Benzyloxymethoxy)-8-bromo-3,7-dimethylocta-2,6-dien-1-yl]-6-tert-butyldiphenylsilyloxy-3,4-dimethyl-2-methylene-3-(phenylsulfonylmethyl)cyclohexane (**67**).* Triethylamine (0.15 mL, 1.05 mmol) and methanesulfonyl chloride (0.06 mL, 0.63 mmol) were added to the alcohol **66** (432 mg, 0.54 mmol) in THF (3 mL) at 0 °C and the solution was stirred at 0 °C for 45 min. Lithium bromide (195 mg, 2.16 mmol) in THF (1 mL) was added and, after 1 h at 0 °C, pentane (15 mL) and ice-cold water (10 mL) were added. The aqueous phase was extracted with pentane (2×15 mL) and the organic extracts washed with saturated aqueous sodium bicarbonate (5 mL) and brine (5 mL),

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dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 20% ether in light petroleum as eluent gave the *title compound* **67** (411 mg, 86%) as a clear oil, R_f=0.32 (40% ether in light petroleum); ν_{max}/cm^{-1} 3070, 2931, 2857, 1663, 1628, 1588, 1447, 1428, 1385, 1318, 1308, 1149, 1104, 1038, 910, 742 and 702; δ_H (500 MHz, $CDCl_3$) 7.65 (2H, d, *J* 7.8, ArH), 7.65 (4H, d, *J* 7.8, ArH), 7.46 (1H, m, ArH), 7.20–7.40 (11H, m, ArH), 7.09 (2H, d, *J* 8.2, ArH), 5.37 (1H, t, *J* 6.3, 6′-H), 5.12 and 5.05 (each 1H, s, 2-CH), 4.89 (1H, d, *J* 9.0, 2′-H), 4.32 (1H, d, *J* 7.0, OHC*H*O), 4.25 (1H, m, 1′-H), 4.19 (1H, d, *J* 7.0, OHC*H*′O), 4.03 (1H, d, *J* 12.0, OHC*H*Ph), 4.01 (1H, m, 6-H), 3.92 (1H, d, *J* 12.0, OHC*H*′Ph), 3.87 (2H, s, 8′-H_2), 3.22 (1H, d, *J* 14.3, 3-CH), 2.60 (1H, br d, *J* 9.2, 1-H), 2.55 (1H, d, *J* 14.3, 3-CH′), 2.43 (1H, m, 4-H), 1.67–1.92 (5H, m, 4′-H_2, 5′-H_2 and 5-H), 1.62 (3H, s, 7′-CH_3), 1.45 (1H, m, 5-H′), 1.39 (3H, s, 3′-CH_3), 1.01 (3H, d, *J* 7.0, 4-CH_3), 0.96 [9H, s, SiC(CH_3)$_3$] and 0.95 (3H, s, 3-CH_3); δ_C (125 MHz, $CDCl_3$) 148.0, 142.6, 140.3, 138.4, 136.5, 136.4, 134.5(2), 133.6, 132.7, 130.5, 129.8, 129.6, 129.5, 128.6, 127.7, 127.5(2), 123.8, 118.1, 90.6, 71.3, 69.7, 64.0, 57.2, 44.0, 41.7, 38.9, 33.9, 33.6, 30.6, 27.3, 26.7, 19.4, 18.6, 16.0 and 15.0; *m/z* (ES+) 905 (M^++23, 100%).

*4.2.51. (1SR,2RS,10SR,11SR,12RS,14SR,3E,7E)-2-(Benzyloxymethoxy)-14-tert-butyldiphenylsilyloxy-15-methylene-4,8,11,12-tetramethyl-10-phenylsulfonylbicyclo[9.3.1]pentadeca-3,7-diene (**68**).* Sodium hexamethyldisilazide (1.0 M in THF, 0.98 mL, 0.98 mmol) was added to the bromide **67** (288 mg, 0.32 mmol) in THF (6.4 mL) at 0 °C via syringe pump over 40 min and the yellow solution was stirred for a further 30 min. Saturated aqueous ammonium chloride (5 mL) and ethyl acetate (5 mL) were added. The aqueous phase was extracted with ethyl acetate (4×5 mL) and the organic extracts were washed with brine (5 mL), dried (Na_2SO_4) and concentrated under reduced pressure. Chromatography of the residue on silica using 40% ether in light petroleum as eluent gave the *title compound* **68** (185 mg, 72%) as a white solid, mp 163–165 °C, R*f*=0.21 (50% ether in light petroleum) (Found: M^++Na, 825.3969. $C_{50}H_{62}O_5NaSSi$ requires *M*, 825.3979); ν_{max}/cm^{-1} 3066, 2933, 2885, 2856, 1588, 1446, 1428, 380, 1304, 1143, 1109, 1085, 1035, 910 and 823; δ_H (300 MHz, $CDCl_3$) 7.85 (4H, m, ArH), 7.27–7.58 (16H, m, ArH), 6.03 (1H, d, *J* 2.0, 15-CH), 5.24 (1H, d, *J* 10.2, 2-H), 5.12 (1H, d, *J* 2.2, 15-CH′), 4.89 (1H, d, *J* 10.2, 3-H), 4.80 (3H, m, OHC*H*Ph, OCH_2O), 4.66 (1H, d, *J* 12.4, OHC*H*′Ph), 3.89 (2H, m, 7-H and 14-H), 3.27 (1H, br d, *J* 11.7, 1-H), 2.99 (1H, br s, 10-H), 2.82 (1H, m, 12-H), 2.60 (1H, m, 13-H), 2.38 (2H, br s, 9-H_2), 1.70–1.93 (5H, m, 5-H_2, 6-H_2 and 13-H′), 1.50 (3H, s, 4-CH_3), 1.38 (3H, s, 8-CH_3), 1.17 (3H, s, 11-CH_3), 1.10 [9H, s, SiC(CH_3)$_3$] and 1.00 (3H, d, *J* 7.1, 12-CH_3); δ_C (75 MHz, $CDCl_3$) 146.4, 141.0, 138.5, 137.6, 136.4, 136.3, 135.6, 134.7, 133.2, 129.8, 129.7, 129.4, 128.9, 128.7, 128.5, 128.0, 127.8, 127.7, 127.6, 125.1, 120.7, 119.2, 92.1, 73.2, 69.6, 68.6, 62.0, 52.7, 49.6, 39.0, 37.3, 35.0, 34.9, 27.5, 22.8, 22.0, 21.1, 19.5, 17.3, and 17.2; *m/z* (+ES) 825 (M^++23, 100%) and 270 (99).

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12. Crystallographic data for sulfone 52: SG Cc, *a*=9.335(5) Å, *b*=38.229(5) Å, *c*=9.125(5) Å, α=90.000(5)o, β=107.509(5)o, γ=90.000(5)o, V=3106(2) A3, *T*=100(2)K, *Z*=4. Crystallographic data for compound 52 (CCDC-1044748) can be obtained free of charge from the CCDC via www.ccdc.cam.ac.uk/data_request/cif. Crystal data for sulfone 68: $C_{50}H_{62}O_5SSi$, MW 803.15, monoclinic, space group $P2_1/c$, *a*=22.478(2), *b*=10.2390(11), *c*=21.361(2) Å, β=115.739(2) °, V=4428.5(8) Å^3, *Z*=4, Dc=1.205 g cm^{-3}, μ(MoKα)=0.146 mm^{-1}, *F*(000=1728, *T*=100 K. Crystal dimensions were 0.4×0.07×0.02 mm 31,135 reflections measured, 7817 independent reflections (R_{int}=0.116), *R*1=0.039 for the 3559 reflections with $I>2\sigma(I)$, wR(F^2)=0.112 (all data). CCDC 712103.
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