Synthesis of macrocyclic precursors of phomactins using [2,3]-Wittig rearrangements†

Graham McGowan and Eric J. Thomas*

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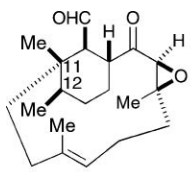
The combination of a [2,3]-Wittig rearrangement of a suitably substituted cyclohexenylmethyl propargyl ether with a subsequent conversion of the alkyne to a trisubstituted alkene and cyclisation *via* intramolecular sulfone alkylation has proved to be a useful stereoselective approach to advanced macrocyclic intermediates for a projected synthesis of phomactins. Thus Luche reduction of methyl (1*RS*,6*SR*)-2-(bromomethyl)-1,6-dimethyl-4-oxocyclohex-2-ene-1-carboxylate **24** gave methyl (1*RS*,4*RS*,6*SR*)-2-bromomethyl-4-hydroxy-1,6-dimethylcyclohex-2-ene-1-carboxylate **26** which was protected as its (2-trimethylsilylethoxy)methyl ether **27**. *O*-Alkylation of (*E*)-8-*tert*-butyldiphenylsilyloxy-7-methyloct-6-en-2-yn-1-ol **17** using this bromide gave the corresponding ether **28**. This was reduced and the resulting primary alcohol **29** converted into a phenylsulfonyl group by displacement of the corresponding mesylate by sodium thiophenoxide followed by oxidation. A [2,3]-Wittig rearrangement of the resulting propargylic ether **31** was stereoselective and gave predominantly (2*RS*,3*SR*,5*RS*,6*SR*)-2-[(1*RS*,6*E*)-8-*tert*-butyldiphenylsilyloxy-1-hydroxyoct-6-en-2-yn-1-yl)]-5,6-dimethyl-6-(phenylsulfonyl)methyl-3-(trimethylsilylethoxy)methoxy-1-methylenecyclohexane **37** together with its epimer at C(1′) **38**. Following protection as its 4-methoxybenzyl ether **39** with *O*-desilylation and conversion of the primary alcohol **40** into the corresponding bromide **41**, cyclisation by intramolecular allylation of the sulfone gave (1*SR*,2*RS*,11*SR*,12*RS*,14*SR*,7*E*)-10-phenylsulfonyl-8,11,12-trimethyl-15-methylene-2-(4-methoxybenzyl)-14-(2-trimethylsilylethoxy)methoxybicyclo-[9.3.1]pentadec-7-en-3-yne **42** and reductive desulfonylation and *O*-deprotection gave (1*RS*,2*RS*,11*SR*,12*RS*,14*SR*,7*E*)-8,11,12-trimethyl-15-methylene-14-(2-trimethylsilylethoxy)methoxybicyclo-[9.3.1]pentadec-7-en-3-yn-2-ol **44**. Analogous chemistry was carried out following protection of the Wittig rearrangement product as its tri-isopropylsilylether **45**. To prepare the corresponding (3*E*,7*E*)-3,7-dienol, the Wittig rearrangement products **37** and **38** were oxidised to the corresponding ketone **54**. Conjugate addition of thiophenol followed by substitution of the major phenylthio adduct **56** using lithium dimethylcuprate gave the corresponding (*E*)-conjugated enone **57** which was reduced using sodium borohydride and the resulting alcohol **58** converted into its benzyloxymethoxy ether **59**. This was taken through to give (1*RS*,2*RS*,11*SR*,12*RS*,14*SR*,3*E*,6*E*)-4,8,11,12-tetramethyl-15-methylene-14-(2-trimethylsilylethoxy)methoxybicyclo[9.3.1]pentadeca-3,7-dien-2-ol **63** which has the full carbon skeleton of the phomactins.

Introduction

The phomactins, *e.g.* **1–4**, are a group of diterpenes isolated from the marine fungus *Phoma* sp. which have interesting biological activities including platelet activating factor antagonism.[1] Structurally they are characterised by a bicyclo[9.3.1]pentadec-7-enyl framework with two *cis*-disposed methyl substituents at the 11- and 12-positions. In the case of phomactin A **2**, an ethereal group bridges the 4- and 14-positions to form a tetrahydropyranyl ring.

The phomactins have attracted considerable interest from synthetic organic chemists because of their novel structures and biological activities. Phomactin D **1** is the most active member of the series, and was the first naturally occurring phomactin to be prepared by total synthesis.[2] Since then two syntheses of the more complex phomactin A **2**,[3,4] and syntheses of phomactins G **3**[5] and B2 **4**,[6] have been described. In addition many other approaches to the synthesis of phomactins have been disclosed[7] and the



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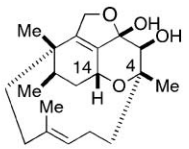

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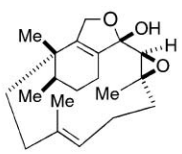

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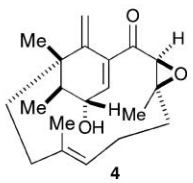

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The School of Chemistry, The University of Manchester, Manchester, M13 9PL, UK. E-mail: e.j.thomas@manchester.ac.uk

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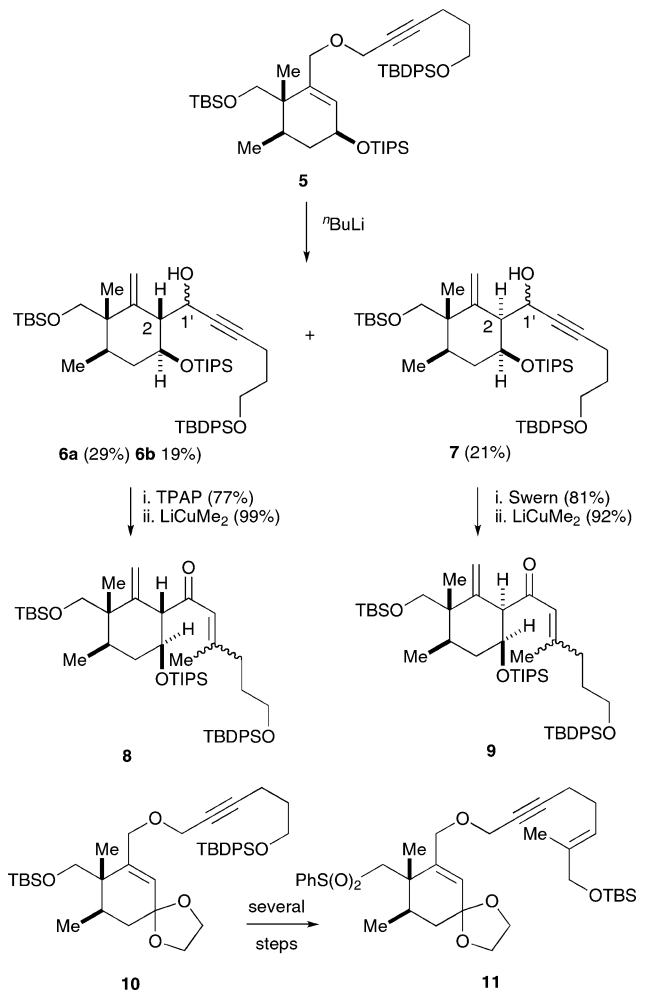
biogenesis of the phomactins and their structural homology to taxanes have been discussed.[8] The chemistry of phomactins has recently been reviewed.[8]

Preliminary studies have been carried out on a possible synthetic approach to phomactins using [2,3]-Wittig rearrangements to assemble methylenecyclohexanes suitably functionalised for subsequent formation of the bicyclo[9.3.1]pentadecenyl structure.[9] In particular, the propargylic ether **5** was found to rearrange on deprotonation using *n*-butyllithium to give a mixture of the alcohols **6a**,**b** and **7** which were taken through to mixtures of (*E*)- and (*Z*)-isomers of the conjugated enones **8** and **9** by oxidation and reaction with lithium dimethylcuprate (Scheme 1).[9b] The more advanced Wittig precursor **11** has also been prepared from the simpler propargylic ether **10**.[9b]



Scheme 1 Early studies of the synthesis of methylenecyclohexanes using [2,3]-Wittig rearrangements.

In this work, propargylic ethers were used to control the regioselectivity of the [2,3]-Wittig rearrangements with deprotonation taking place next to the alkyne, see Fig. 1.[9a] However, mixtures of stereoisomers at C(2) and C(1′), *e.g.* **6a**,**b** and **7**, were formed and mixtures of (*E*)- and (*Z*)-conjugated alkenes **8** and **9**, were obtained on addition of lithium dimethylcuprate to the ketones prepared by oxidation of the Wittig rearrangement products. The stereoselectivities of these reactions therefore needed to be improved and, as the synthesis of the more advanced Wittig precursor **11** was rather long, a better synthesis of analogous intermediates was required.

We now report the results of further investigations into this synthetic approach to phomactins, including stereoselective Wittig rearrangements of sulfones analogous to **11**, the development of an (*E*)-stereoselective synthesis of the required conjugated enones, and a synthesis of a bicyclic intermediate with the (3*E*,7*E*)-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-3,7-dienyl framework of the phomactins.[10]

Results and discussion

Hex-4-ynol **13** was prepared by alkylation of 3-*tert*-butyldimethylsilyloxypropyne **12** using oxetane,[11] see Scheme 2. Oxidation and an *in situ* Wittig reaction of the resulting aldehyde gave ester **14** which was converted to the alcohol **17** by reduction, further protection and selective removal of the *tert*-butyldimethylsilyl group.[12] Alkylation of alcohol **17** using the cyclohexenylmethyl bromide **18**[9b] gave the ether **19** which was reduced to the alcohol **20**. This was protected as its *tert*-butyldimethylsilyl ether **21** which was treated with *n*-butyllithium to effect a [2,3]-Wittig rearrangement. This gave an inseparable mixture of two diastereoisomers of the methylenecyclohexanes **22**, ratio 70:30, shown to be epimeric at C(2) as oxidation gave a mixture of the two ketones **23a**,**b** The formation of just two diastereoisomers of the methylenecyclohexane **22** is precedented in earlier studies.[9b]

Rather than take this mixture through the next stages of the synthesis, it was decided to convert alcohol **20** into the corresponding sulfone in anticipation of macrocyclisation by sulfone allylation. However, attempts to convert alcohol **20** into the corresponding thio-ether by displacement of its mesylate using sodium thiophenoxide were unsuccessful. Complex mixtures of products were obtained possibly because of neighbouring group participation involving the acetal as indicated in Fig. 2.

To avoid this neighbouring group participation the ketone **24** was reduced under Luche conditions.[13] At room temperature, mixtures of epimers **25** and **26** were formed, but at −78 °C only isomer **26** was isolated, the configuration shown being assigned on the basis of ^{1}H NMR data, *e.g.* a significant NOE enhancement of H(6) on irradiation of H(4) and *vice versa.* This alcohol was

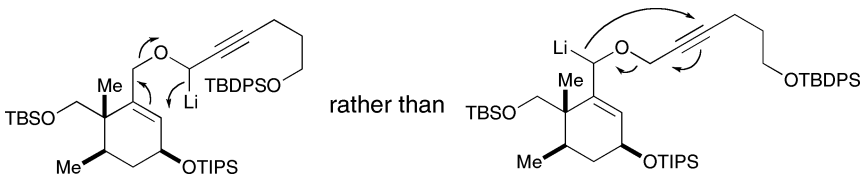
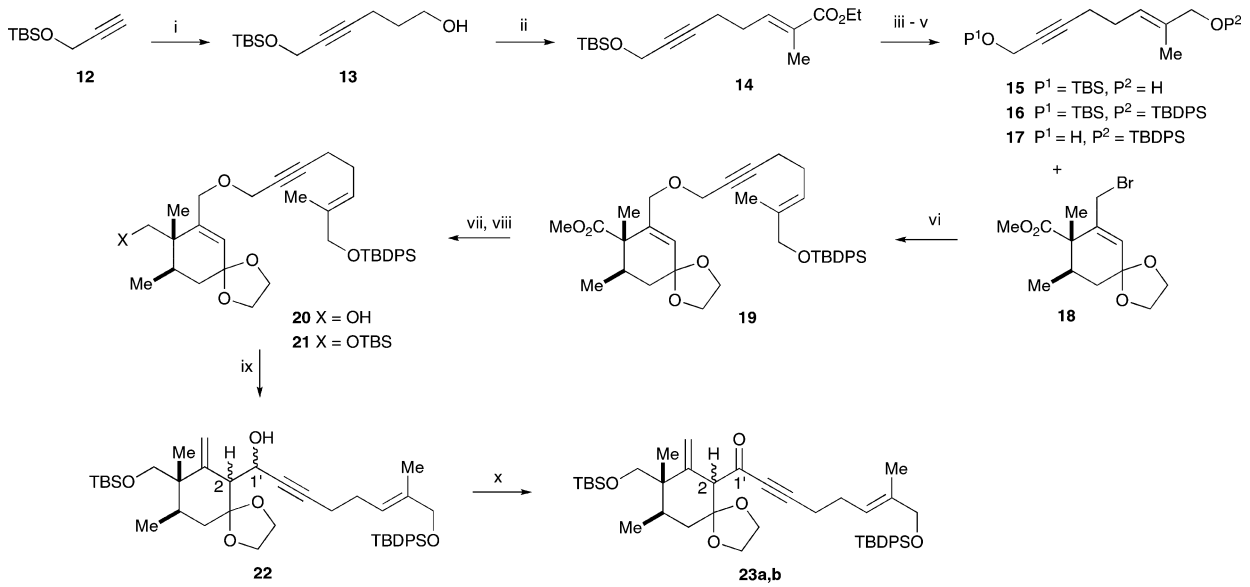


Fig. 1 Regioselectivity of the [2.3]-Wittig rearrangement of ether **5**.



Scheme 2 *Reagents and conditions*: i, ^{n}BuLi, oxetane, $BF_3.Et_2O$, THF, −78 °C, 2 h (85%); ii, DMSO, $(COCl)_2$, Et_3N, DCM, −78 °C to r.t., $Ph_3PC(CH_3)CO_2Et$, −78 °C-r.t., DCM, r.t., 16 h (90%); iii, $LiEt_3BH$, THF, −78 °C, 1 h (84%); iv, TBDPSCl, imid., DCM, 0 °C, 16 h (67%); v, MeOH, CCl_4, sonicated, 50 °C, 4 h (86%); vi, NaH, TBAI, 15-c-5, 5 min, add **18**, r.t., 16 h (42%); vii, $LiEt_3BH$, THF, 0 °C, 50 min (93%); viii, TBSOTf, Et_3N, DCM, r.t., 45 min (67%); ix, ^{n}BuLi, THF, −78 °C, 3 h (70:30, 83%); x, Dess–Martin periodinane, DCM, r.t., 30 min (**23a**, 33%; **23b**, 55%).

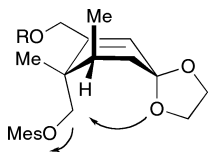
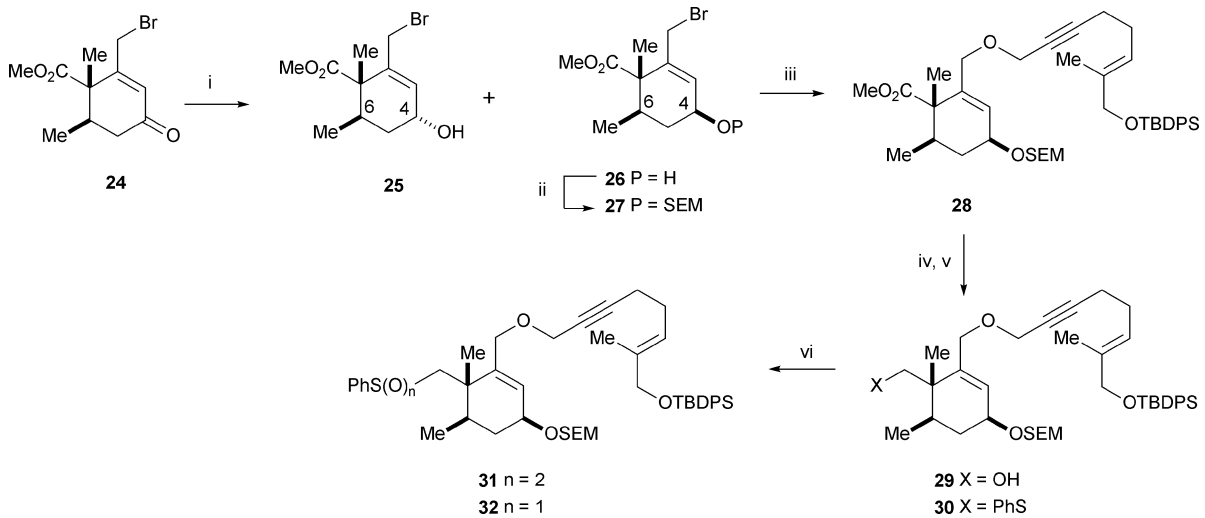


Fig. 2 Possible neighbouring group participation leading to loss of the mesylate derived from alcohol **20**.

converted into its (trimethylsilylethoxy)methyl ether **27** which was treated with the sodium salt of alcohol **17** to give the ether **28**. This was reduced using lithium triethylborohydride to the alcohol **29**. The direct conversion of alcohol **29** into thio-ether **30** using diphenyl disulfide and tributylphosphine[14] was difficult to scale up. However, substitution of the corresponding mesylate using sodium thiophenoxide gave a good yield, 85%, of the required thio-ether **30**. Initial attempts to oxidise thio-ether **30** to its sulfone using 3-chloroperoxybenzoic acid or OXONE® gave appreciable amounts of the epimeric sulfoxides **32** as well as the required sulfone, and the use of magnesium monoperoxyphthalate was accompanied by partial epoxidation of the side-chain double-bond. However, the use of hydrogen peroxide in the presence of ammonium molybdate[15] gave a 65% yield of the sulfone **31** together with small amounts of the sulfoxides **32**, which could be oxidised separately to the sulfone, see Scheme 3.



Scheme 3 *Reagents and conditions*: i, $NaBH_4$, $CeCl_3.7H_2O$, MeOH, −78 °C, 1.5 h (**26**, 91%); ii, $^{i}Pr_2NEt$, SEMCl, DCM, r.t., 16 h (80%); iii, TBAI, NaH, **17**, 0 °C, 20 min, add 15-c-5 and **27**, r.t., 16 h (65%); iv, $LiEt_3BH$, THF, 0 °C to r.t. (88%); v, (a) MesCl, Et_3N, DCM, 0 °C, 30 min (b) PhSH, NaH, DMF, 0 °C, 20 min, add the mesylate of **29**, heat under reflux, 16 h (85%); vi, ammonium molybdate, H_2O_2, EtOH, −10 °C, 5 min then r.t., 24 h (**31**, 65%)

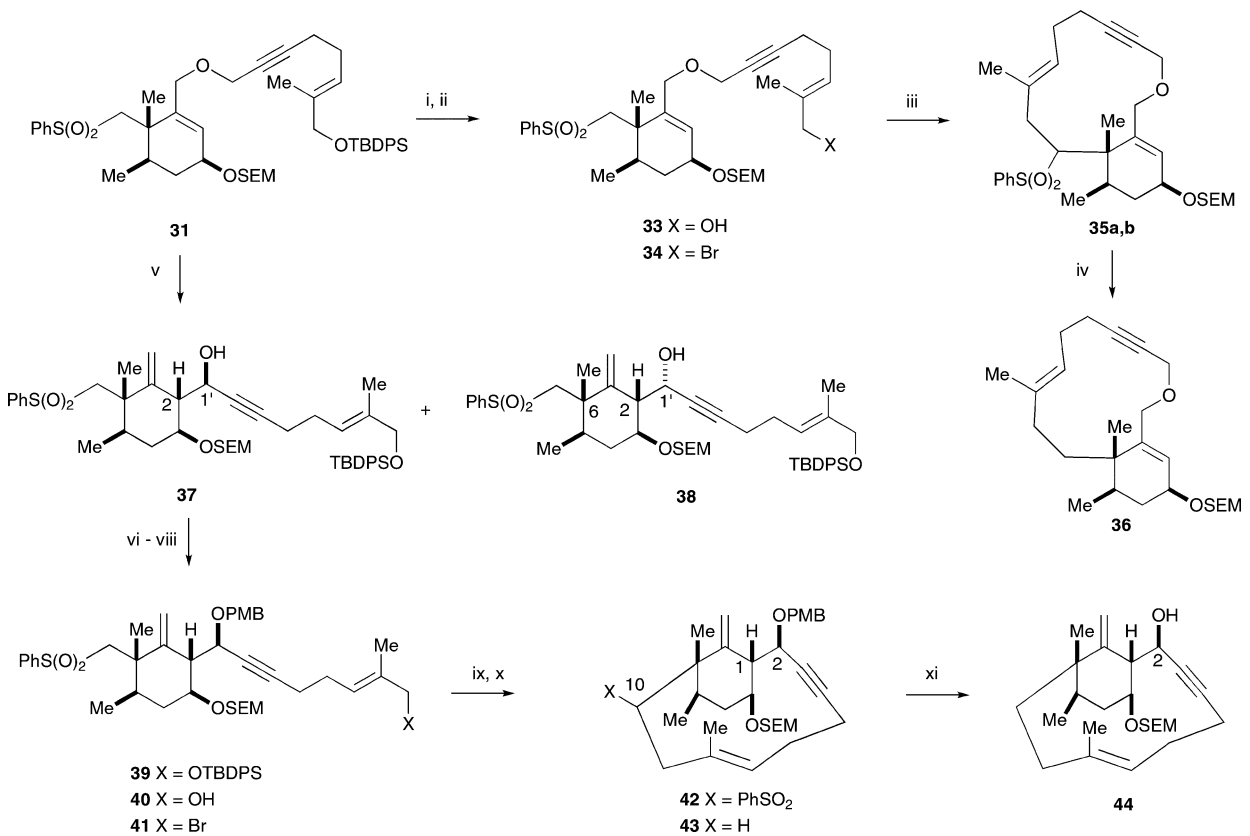
Sulfone **31** is suitably substituted for a [2,3]-Wittig rearrangement to form a methylenecyclohexane which could be incorporated into a synthesis of a phomactin. However, the option of carrying out the rearrangement on a macrocyclic ether, *i.e.* **36**, was investigated at this point since it was thought that steric constraints introduced by the bicyclic system could direct the facial selectivity of the Wittig rearrangement and hence control the configuration of the product at C(2). Moreover, such a rearrangement would lead directly to the bicyclo[9.3.1]pentadecenyl system present in the phomactins.

Selective removal of the *tert*-butyldiphenylsilyl ether from **31** gave the primary alcohol **33** which was converted into the bromide **34** by mesylation and substitution using lithium bromide, see Scheme 4. Macrocyclisation of this bromide using sodium hexamethyldisilazide was more efficient after chromatographic purification of the bromide and gave a mixture of the epimeric sulfones **35a**,**b**. Reductive removal of the phenylsulfonyl group to give the macrocyclic ether **36** was then achieved using sodium amalgam.[16] However, all attempts to effect a [2,3]-Wittig rearrangement of the macrocyclic propargylic ether **36** using *n*-butyllithium or amide bases at various temperatures using different solvents were unsuccessful. In all cases complex mixtures of ill-defined products were obtained. The [2,3]-Wittig rearrangement of the sulfone **31** was therefore investigated and, somewhat unexpectedly, was found to be stereoselective with respect to C(2). Two methylenecyclohexanes **37** and **38** were isolated in isolated yields of 59% and 13%, respectively, and were found to have the same configuration at C(2).

The C(2) configurations of the rearrangement products **37** and **38** were assigned on the basis of ^{1}H NMR data. For isomer **37** the diaxial coupling of 10 Hz observed between H(2) and H(3) established this configuration and for isomer **38**, a significant NOE enhancement of H(2) was observed on irradiation of 6-CH_3. That these compounds had the same configuration at C(2) was also confirmed later in the synthesis when they both gave the same ketone on oxidation, *vide infra.*

The stereoselectivity at C(2) observed in the formation of epimers **37** and **38** in this Wittig rearrangement contrasted with the lack of stereoselectivity with respect to C(2) which had been observed earlier.[9b] As the rearrangement of sulfone **31** required two equivalents of base, it may be that the facial selectivity with respect to the six-membered ring leading to the configuration shown at C(2) is due to lithiation α to the sulfone and co-ordination of the lithiated sulfone with the oxygen of the propargylic ether, see Fig. 3.

The configurations at C(1′) were not formally confirmed at this stage, but were assigned on the basis that the alkynyl moiety would prefer to adopt the less hindered outside position during the rearrangement leading to isomer **37** as the major product.[9b] ^{1}H NMR studies later in the synthesis confirmed these assignments.



Scheme 4 *Reagents and conditions*: i, TBAF, THF, r.t., 2 h (88%); ii, E_3N, MesCl, DCM, r.t., 30 min, LiBr, acetone, r.t., 30 min (83%); iii, NaHMDS, THF, 0 °C, 2 h (**35a**, 26%; **35b**, 49%); iv, Na-Hg, Na_2HPO_4, THF, MeOH, r.t., 1 h (62%); v, ^{n}BuLi, THF, −78 °C, 2.5 h (**37**, 59%; **38**, 13%); vi, NaH, DMF, r.t., 30 min, 4-$MeOC_6H_4CH_2Cl$, r.t., 16 h (58%); vii, TBAF, THF, r.t., 1.5 h (87%); viii, E_3N, MesCl, DCM, r.t., 30 min, LiBr, acetone, r.t., 30 min (92%); ix, NaHMDS, THF, r.t., 30 min (68%); x, $NaHPO_4$, THF, MeOH, Na-Hg, 0 °C to r.t., 1.5 h (93%); xi, DDQ, pH 7 phosphate buffer, DCM, 0 °C, 10 min (72%).

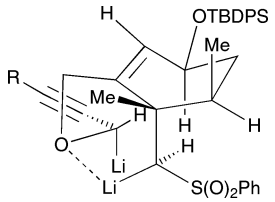


Fig. 3 Influence of the lithiated sulfone on the facial selectivity of the [2,3]-Wittig rearrangement of propargylic ether **31**.

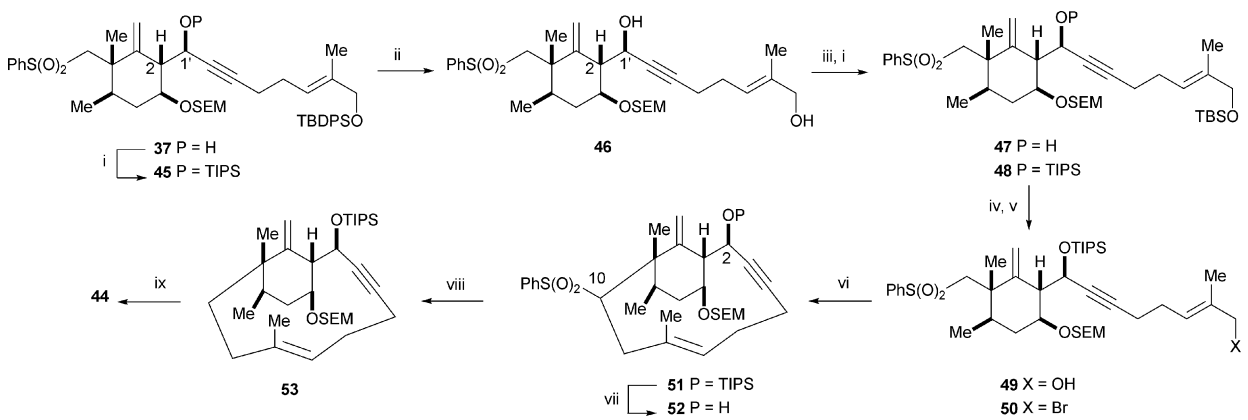
At this point it was necessary to protect the free hydroxyl group before attempting macrocyclisation and so the major rearrangement product **37** was converted into its *p*-methoxybenzyl ether **39** albeit in only a modest, 58%, yield. Following selective deprotection to give the primary alcohol **40** and conversion into the bromide **41**, macrocyclisation was achieved using sodium hexamethyldisilylazide to give the bicyclic sulfone **42** essentially as a single epimer at C(10). The configuration at C(2) was now established as shown on the basis of the small H(1)-H(2) coupling constant of *ca.* 4 Hz, and a strong NOE enhancement of H(2) on irradiation of H(1). The configuration of the sulfonyl bearing stereogenic centre, C(10), was not established.[17]

To complete a synthesis of a potential macrocyclic precursor of phomactins, the sulfone **42** was subjected to reductive sulfonylation using sodium-amalgam to give the macrocyclic alkyne **43** and the *p*-methoxybenzyl group removed using DDQ under buffered conditions[19] to give the alcohol **44**, see Scheme 4.

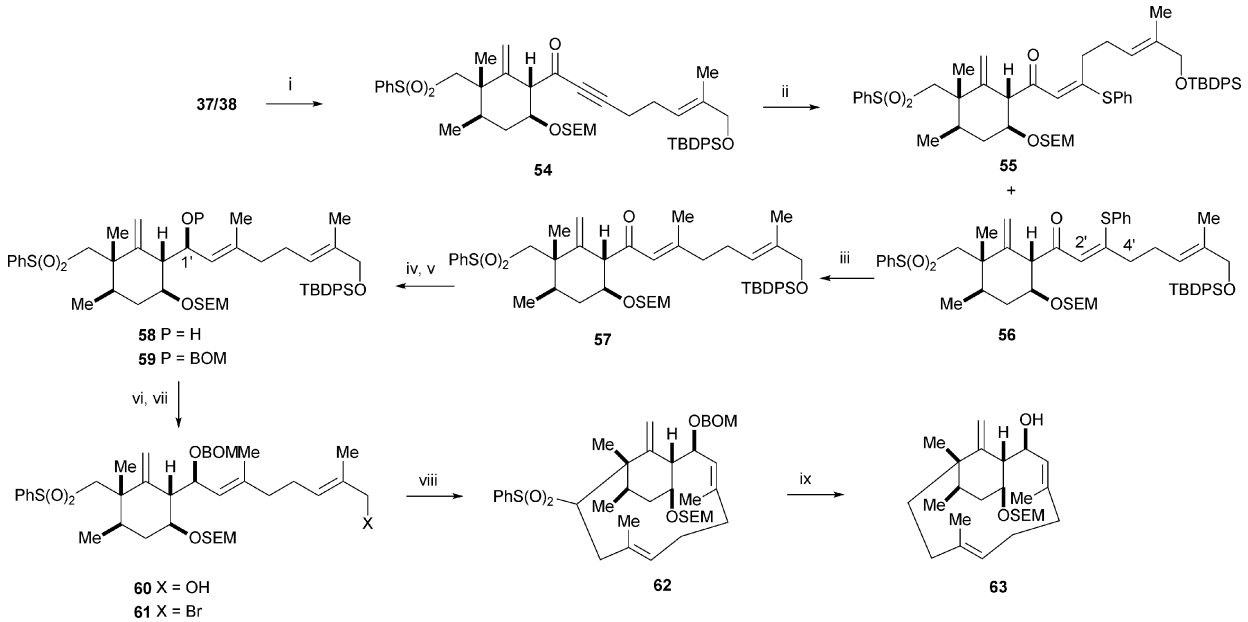
As the protection of the alcohol **37** as its 4-methoxybenzyl ether had not been particularly efficient, the use of silyl protecting groups was investigated. Alcohol **37** was converted into its tri-isopropylsilyl ether **45**[20] (Scheme 5) but attempts to remove selectively the *tert*-butyldiphenylsilyl group using 5% sodium hydroxide in ethanol gave only a 54% yield of the corresponding primary alcohol. Both silyl protecting groups were therefore cleaved using tetra-*n*-butylammonium fluoride to give the diol **46** which was silylated selectively on the primary alcohol using *tert*-butyldimethylsilyl chloride to give the monosilyl ether **47** and further silylated using tri-isopropylsilyl triflate to give the bis-silyl ether **48**. Selective removal of the *tert*-butyldimethyl silyl group was now possible using acetic acid in aqueous tetrahydrofuran to give the primary alcohol **49**. This sequence showed that it would be better to use the *tert*-butyldimethylsilyl analogue of the *tert*-butyldiphenylsilyl ether **17** in the synthesis since rearrangement of the corresponding propargyl ether would lead to the alcohol **47** directly. However, this option has not yet been investigated although the primary alcohol **49** was converted into the bromide **50** *via* its mesylate and cyclisation of the bromide using sodium hexamethyldisilazide gave the bicyclic alkyne **51** as a single epimer at C(10). Removal of the tri-isopropylsilyl group using tetra-*n*-butylammonium fluoride then gave the alcohol **52** and reductive removal of the sulfone group from **51** gave the bicyclic phomactin precursor **53** which was deprotected to give the alcohol **44**.

This work has shown that the [2,3]-Wittig rearrangement can be used to prepare methylenecyclohexanes which can be taken through to bicyclo[9.3.1]pentadec-7-en-3-ynes reminiscent of phomactins with overall useful levels of stereoselectivity. To complete a synthesis of intermediates with the full carbon skeleton of phomactins it remained to convert the alkyne moiety into the corresponding methyl substituted (*E*)-alkene regio- and stereoselectively. Propargylic alcohols can be converted into the corresponding (*Z*)-3-iodoalkenes, possible precursors of (*E*)-3-methylalkenes, by reduction using lithium aluminium hydride or Red-Al followed by treatment with iodine.[21] However, in our hands, attempts to convert the propargylic alcohol **44** into the corresponding (*Z*)-vinyl iodide using these procedures were unsuccessful, unchanged starting material being recovered, and similar studies using the Wittig rearrangement product **37** gave a mixture of unstable products possibly formed by competing iodination α to the sulfone. Attention was therefore directed towards conjugate addition reactions of the ketone **54** prepared by oxidation of alcohols **37** and **38** using the Dess Martin periodinane.[22]

Preliminary studies of the conjugate addition of lithium dimethylcuprate to the alkynone **54** gave rise to a (*E*,*Z*)-mixture of conjugated alkenes which could not be separated and which did not appear to isomerise to the required (*E*)-isomer on treatment with thiols. However, reaction of ketone **54** with thiophenol under basic conditions[23,24] gave a mixture of the separable vinyl sulfides **55** and **56**, from which the (*Z*)-isomer **56** could be isolated in a 69% yield, and treatment of this with lithium dimethyl cuprate gave the required (*E*)-alkene **57** in a 97% yield (Scheme 6).[25] The geometries of the alkenes **55–57** were confirmed by ^{1}H NMR NOE



Scheme 5 *Reagents and conditions*: i, TIPSOTf, 2,6-lutidine, DCM, 0 °C, 30 min (**45**, 87%; **48**, 97%); ii, TBAF, THF, r.t., 1.5 h (93%); iii, TBSCl, imid., DCM, r.t., 30 min (89%); iv, AcOH, THF, H_2O, 0 °C, r.t., 24 h (82%); v, MesCl, Et_3N, DCM, r.t., 30 min, then LiBr, acetone, r.t., 30 min (86%); vi, NaHMDS, THF, 0 °C, 1 h (64%); vii, TBAF, THF, r.t., 1.5 h (73%); viii, Na-Hg, $NaHPO_4$, r.t., 2 h (69%); ix, TBAF, THF, r.t. (43% from **50**).



Scheme 6 *Reagents and conditions*: i, Dess–Martin periodinane, DCM, r.t., 30 min (89%); ii, PhSH, Et_3N, THF, –20 °C, 2 h (**55**, 26%; **56**, 69%); iii, CuI, MeLi, Et_2O, 0 °C, 30 min, then add to **56**, –78 °C, 30 min (97%); iv, $NaBH_4$, EtOH, r.t., 18 h (59%); v, $^iPr_2NEt$, BOMCl, TBAI, r.t., 16 h (85%); vi, TBAF, THF, r.t., 2 h (79%); vii, MesCl, Et_3N, DCM, 0 °C, 30 min, then LiBr, acetone, 0 °C, 30 min (69%); viii, NaHMDS, THF, 0 °C, syringe pump, 40 min, then 30 min; ix, Na, liq. NH_3, THF, EtOH, –60 °C (45% from **61**).

and chemical shift studies, *e.g.* the observation of an enhancement of 4′-H_2 on irradiation of 2′-H for the (*Z*)-isomer **56**. Since the enone **57** would be incompatible with the strongly basic conditions required for macrocyclisation, it was reduced to the alcohol **58** using sodium borohydride, the configuration of the alcohol at C(1′) being assigned by ^{1}H NMR studies later in the synthesis. Although this reduction was somewhat capricious, alternative procedures including the use of Luche conditions, gave unchanged starting material, and more reactive hydride reducing agents gave complex mixtures of products. Following protection of the alcohol **58** as its benzyloxymethyl (BOM) derivative **59**, desilylation gave the alcohol **60**. This taken through to the bromide **61** *via* its mesylate and cyclisation of the bromide was carried out under the usual conditions to give the macrocyclic sulfone **62**. This was immediately subjected to a Birch reduction[2,26] to remove both the BOM and phenylsulfonyl groups giving the 2-hydroxy-15-methylene-4,8,11,12-tetramethylbicyclo[9.3.1]pentadeca-3,7-diene **63** which has the full carbon skeleton of the phomactins.

Summary and conclusions

This work has achieved a synthesis of 15-methylenebicyclo[9.3.1]-pentadec-7-en-4-ynes and related dienes which have the bicyclic framework present in the phomactins. The [2,3]-Wittig rearrangement of cyclohexenyl propargylic ethers[7] has proved to be useful for the synthesis of methylenecyclohexanes and the effect of a phenylsulfonyl group on the stereoselectivity of these rearrangements is of interest. The macrocyclisation procedure involving an intramolecular allylation of a sulfone using an allylic bromide, which was used in the early synthesis of phomactin D,[1] has proved to be generally useful in this system and has delivered quite acceptable yields of macrocycles. Indeed the combination of a [2,3]-Wittig rearrangement and subsequent cyclisation would appear to provide useful stereoselective access to the phomactin system. The need for a propargylic ether for control of the regioselectivity of the Wittig rearrangements meant that a stereoselective procedure had to be developed to convert the 3-alkyne into an (*E*)-alkene later in the synthesis. Although a procedure was devised to achieve this, some improvements to this part of the synthesis are necessary. Further work is on-going to improve the overall synthesis and to bring through larger amounts of material to enable the completion of a synthesis of phomactin A **2**.[18]

Experimental

Methyl (1*SR*,4*SR*,6*RS*)-2-bromomethyl-4-hydroxy-1, 6-dimethylcyclohex-2-ene-1-carboxylate 26

Cerium(III) chloride heptahydrate (1.043 g, 2.805 mmol) was added to the enone **24** (7.0 g, 2.55 mmol) in methanol (210 cm^3) at room temperature and the resulting suspension was stirred until the solid had dissolved. The mixture was then cooled to –78 °C and sodium borohydride (1.16 g, 3.07 mmol) was added. The solution was stirred for 1.5 h then warmed to room temperature and concentrated under reduced pressure. Dichloromethane (30 cm^3) and silica powder were added and the dichloromethane removed under reduced pressure. The solid residue was dried under reduced pressure and loaded onto a silica gel column. Flash chromatography, with 5–40% ether in petrol as eluent, afforded the *title compound* **26** as an oil (6.4 g, 91%), R_f = 0.075 (50% ether in petrol) (Found; $M^+ + NH_4$, 294.0706. $C_{11}H_{21}O_3{}^{79}BrN$ requires *M*, 294.0705); ν_{max}/cm^{-1} 3424 (br), 2949, 2875, 1729, 1451, 1434 1384, 1254, 1118, 1022 and 967; δ_H (300 MHz, $CDCl_3$) 6.07 (1 H, s, 3-*H*), 4.42 (1 H, t, *J* 8, 4-*H*), 3.96 and 3.83 (each 1 H, d, *J* 11, 2-C*H*), 3.74 (3 H, s, 1-CO_2CH_3), 2.36 (1 H, dqd, *J* 13, 7, 2.5, 6-*H*),

2.01 (1 H, br s, O*H*), 1.93 (1 H, ddd, *J* 12.5, 2.5, 1, 5-*H*), 1.38 (1 H, m, 5-*H′*), 1.30 (3 H, s, 1-CH_3) and 0.91 (3 H, d, *J* 7, 6-CH_3); δ_C (75 MHz, $CDCl_3$) 175.5, 138.7, 135.0, 67.1, 52.3, 50.9, 35.3, 34.5, 31.6, 16.7 and 16.5; *m/z* (CI) 296 ($M^+ + 18$, 30%), 294 ($M^+ + 18$, 30), 261 (100) and 259 (95).

Methyl (1*SR*,4*SR*,6*RS*)-2-bromomethyl-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene-1-carboxylate 27

N,N-Di-isopropylethylamine (12.1 cm^3, 6.96 mmol) and 2-trimethylsilylethoxymethyl chloride (6.2 cm^3, 3.5 mmol) were added to the alcohol **26** (6.4 g, 2.32 mmol) in dichloromethane (20 cm^3) at 0 °C and the solution allowed to warm to room temperature. After 16 h, the solution was diluted with ethyl acetate (20 cm^3) and water (40 cm^3). The aqueous phase was extracted with ethyl acetate (4 × 20 cm^3) and the organic extracts washed with brine (40 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography of the residue on silica gel, eluted with 1–15% ether in petrol, afforded the *title compound* **27** as a clear oil (7.5 g, 80%), R_f = 0.75 (20% ether in petrol) (Found; $M^+ + NH_4$, 424.1519. $C_{17}H_{35}O_4BrSiN$ requires *M*, 424.1519); ν_{max}/cm^{-1} 2951, 2878, 1732, 1459, 1378, 1249, 1101, 1035, 860 and 836; δ_H (300 MHz, $CDCl_3$) 6.06 (1 H, s, 3-*H*), 4.83 and 4.78 (each 1 H, d, *J* 7, OCH*H*O), 4.37 (1 H, m, 4-*H*), 4.03 and 3.95 (each 1 H, d, *J* 11.5, 2-C*H*), 3.74 (3 H, s, CO_2CH_3), 3.68 (2 H, m, OCH_2CH_2Si), 2.35 (1 H, dqd, *J* 13, 7, 2, 6-*H*), 1.95 (1 H, ddd, *J* 13, 2.5, 1, 5-*H*), 1.47 (1 H, m, 5-*H′*), 1.29 (3 H, s, 1-CH_3), 0.98 (2 H, m, CH_2Si), 0.92 (3 H, d, *J* 7, 6-CH_3) and 0.01 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 175.5, 138.9, 131.4, 93.5, 72.2, 65.1, 52.2, 50.7, 44.4, 34.5, 32.7, 18.0, 16.8, 16.3 and −1.5; *m/z* (CI) 426 ($M^+ + 18$, 2%), 424 ($M^+ + 18$, 2), 380 (60), 232 (45), 215 (100) and 181 (34).

Methyl (1*SR*,4*SR*,6*RS*)-2-[(6*E*)-8-*tert*-butyldiphenylsilyloxy-7-methyloct-6-en-2-yn-1-yloxy]methyl-1,6-dimethyl-4-(2-trimethylsilylethoxy)methoxycyclohex-2-ene-1-carboxylate 28

Sodium hydride (60% dispersion in mineral oil, 1.49 g, 37.2 mmol) and *tetra*-*n*-butylammonium iodide (4.6 g, 21.4 mmol) were added to tetrahydrofuran (12.5 cm^3) and the suspension cooled to 0 °C. Alcohol **17** (13.4 g, 34.1 mmol) in tetrahydrofuran (25 cm^3) was added and the suspension stirred for 20 min before the addition of 15-crown-5 (7.4 cm^3) and bromide **27** (12.6 g, 31.0 mmol) in tetrahydrofuran (20 cm^3). The brown suspension was warmed to room temperature and stirred for 16 h. Saturated aqueous ammonium chloride (40 cm^3) was then added and the aqueous phase extracted into ethyl acetate (4 × 30 cm^3). The organic extracts were washed with brine (40 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography of the residue afforded the *title compound* **28** as a clear oil (14.5 g, 65%), R_f = 0.5 (20% ether in petrol) (Found; $M^+ + NH_4$, 736.4425; $C_{42}H_{66}O_6Si_2N$ requires *M*, 736.4428); ν_{max}/cm^{-1} 2951, 2857, 1732, 1461, 1428, 1249, 1110, 1055, 836 and 707; δ_H (300 MHz, $CDCl_3$) 7.73 (4 H, m, Ar-*H*), 7.41 (6 H, m, Ar-*H*), 5.88 (1 H, s, 3-*H*), 5.53 (1 H, m, *J* 5, 6′-*H*), 4.82 and 4.81 (each 1 H, d, *J* 7, OCH*H*O), 4.39 (1 H, m, 4-*H*), 4.10 (2 H, s, 8′-H_2), 4.07 (2 H, s, 1′-H_2), 4.01 and 3.93 (each 1 H, d, *J* 12.5, 2-C*H*), 3.67–3.72 (5 H, m, CO_2CH_3 and OCH_2CH_2Si), 2.38 (1 H, m, 6-*H*), 2.28 (4 H, m, 4′-H_2 and 5′-H_2), 1.97 (1 H, ddd, *J* 13.5, 6.5, 2, 5-*H*), 1.65 (3 H, s, 7′-CH_3), 1.47 (1 H, m, 5-*H′*), 1.26 (3 H, s, 1-CH_3), 1.11 [9 H, s, OSiC(CH_3)$_3$], 0.99 (2 H, m, CH_2Si), 0.91 (3 H, d, *J* 6.5, 6-CH_3) and 0.07 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 175.9, 139.2, 135.5, 135.3, 133.7, 129.5, 128.6, 127.5, 122.4, 93.3, 86.6, 75.8, 72.2, 69.8, 68.7, 65.0, 57.7, 52.0, 49.6, 35.3, 34.4, 33.0, 26.8, 19.2, 19.0, 18.0, 16.8, 16.0, 13.5 and −1.4; *m/z* (CI) 736 ($M^+ + 18$, 10%), 360 (12) and 90 (100).

(3*SR*,5*RS*,6*SR*)-1-[(6*E*)-8-*tert*-Butyldiphenylsilyloxy-7-methyloct-6-en-2-yn-1-yloxy]methyl-5,6-dimethyl-6-hydroxymethyl-3-(2-trimethylsilylethoxy)methoxycyclohex-1-ene 29

Lithium triethylborohydride (1.0 M in tetrahydrofuran, 14.5 cm^3, 14.6 mmol) was added to the ester **28** (4.17 g, 5.85 mmol) in tetrahydrofuran (47 cm^3) at 0 °C. The solution was stirred at room temperature for 3 h then cooled to 0 °C and more lithium triethylborohydride (1.0 M in THF, 5.85 cm^3, 5.85 mmol) was added. After 1 h, saturated aqueous ammonium chloride (30 cm^3) was added and the mixture diluted with ethyl acetate (20 cm^3) then stirred at room temperature for 1 h. The aqueous phase was extracted with ether (4 × 20 cm^3), and the organic extracts washed with water (30 cm^3) and brine (30 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue on silica gel, eluted with 1–40% ether in petrol, afforded the *title compound* **29** (3.57 g, 88%) as a clear, viscous oil, R_f = 0.15 (50% ether in petrol) (Found; $M^+ + NH_4$, 708.4487. $C_{41}H_{66}O_5Si_2N$ requires *M*, 708.4479); ν_{max}/cm^{-1} 3468 (br), 2954, 2862, 1465, 1428, 1375, 1249, 1106, 1055 and 835; δ_H (500 MHz, $CDCl_3$) 7.62 (4 H, dt, *J* 7, 1.5, Ar-*H*), 7.40 (6 H, m, Ar-*H*), 5.93 (1 H, s, 2-*H*), 5.40 (1 H, m, 6′-*H*), 4.79 and 4.74 (each 1 H, d, *J* 7, OCH*H*O), 4.27 (1 H, ddd, *J* 10, 5, 2, 3-*H*), 4.19 (1 H, d, *J* 15.5, 1′-C*H*), 4.16 (1 H, d, *J* 9.5, 1-C*H*), 4.11 (1 H, d, *J* 15.5, 1′-C*H′*), 4.06 (2 H, s, 8′-CH_2), 3.80 (1 H, d, *J* 10, 1-C*H′*), 3.65 (2 H, m, OCH_2CH_2Si), 3.56 (1 H, dd, *J* 12, 4.5, 6-C*H*), 3.38 (1 H, t, *J* 11.5, 6-CH′), 2.91 (1 H, dd, *J* 11, 4.5, OH), 2.64 (4 H, m, 4′-CH_2 and 5′-CH_2), 2.20 (1 H, dqd, *J* 14, 4, 2.5, 5-*H*), 1.91 (1 H, dd, *J* 11.5, 2, 4-*H*), 1.61 (3 H, s, 7′-CH_3), 1.47 (1 H, m, 4-*H′*), 1.07 [9 H, s, SiC(CH_3)$_3$], 0.95 (2 H, m, CH_2Si), 0.92 (3 H, d, *J* 7.5, 5-CH_3), 0.77 (3 H, s, 6-CH_3) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (100 MHz, $CDCl_3$) 140.9, 136.3, 135.5, 133.8, 129.5, 127.6, 122.2, 93.3, 87.6, 77.2, 75.1, 72.3, 71.1, 68.6, 65.0, 64.9, 58.4, 43.2, 33.7, 30.2, 26.8, 19.3, 19.0, 18.0, 16.4, 15.8, 13.5 and −1.4; *m/z* (CI) 708 ($M^+ + 18$, 5%), 410 (4), 167 (15), 151 (12), 123 (20) and 90 (100).

(3*SR*,5*RS*,6*SR*)-1-[(6*E*)-8-*tert*-Butyldiphenylsilyloxy-7-methyloct-6-en-2-yn-1-yloxy]methyl-5,6-dimethyl-6-phenylthiomethyl-3-(2-trimethylsilylethoxy)methoxycyclohex-1-ene 30

Triethylamine (2.54 cm^3, 18.2 mmol) and methanesulfonyl chloride (0.8 cm^3, 10.4 mmol) were added to the alcohol **29** (3.6 g, 5.21 mmol) in dichloromethane (90 cm^3) at 0 °C and the solution stirred at 0 °C for 0.5 h. Ethyl acetate (90 cm^3) and saturated aqueous sodium bicarbonate (50 cm^3) were added and the aqueous phase extracted with ethyl acetate (4 × 30 cm^3). The organic extracts were washed with saturated aqueous sodium bicarbonate (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and concentrated

under reduced pressure to afford the mesylate as a pale orange oil used without further purification.

Sodium hydride (1.04 g, 26 mmol) was added to anhydrous *N*,*N*-dimethylformamide (90 cm^3) and the suspension cooled to 0 °C. Benzenethiol (2.67 cm^3, 26 mmol) was added dropwise and the yellow solution stirred for 20 min at 0 °C. The mesylate in anhydrous *N*,*N*-dimethylformamide (80 cm^3) was added, and the solution heated under reflux for 16 h. After being allowed to cool to room temperature, the reaction mixture was diluted with ethyl acetate (50 cm^3) and washed with aqueous sodium hydroxide (50 cm^3). The aqueous phase was extracted with ethyl acetate (3 × 40 cm^3) and the organic extracts were washed with water (50 cm^3) and brine (50 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue using 0–25% ether in petrol as eluent afforded the *title compound* **30** (3.41 g, 85%) as a pale yellow, viscous oil, $R_f = 0.6$ (50% ether in petrol) (Found; $M^+ + NH_4$, 800.4555. $C_{47}H_{70}O_4Si_2SN$ requires *M*, 800.4563); ν_{max}/cm^{-1} 3070, 2954, 2857, 1471, 1428, 1361, 1249, 1109, 1056, 836, 740 and 707; δ_H (500 MHz, $CDCl_3$) 7.69 (4 H, d, *J* 6.5, Ar-*H*), 7.14–7.45 (10 H, m, Ar-*H*), 7.16 (1 H, t, *J* 7.5, Ar-*H*), 5.89 (1 H, s, 2-*H*), 5.47 (1 H, t, *J* 6, 6′-*H*), 4.79 and 4.77 (each 1 H, d, *J* 7, OCH*H*O), 4.29 (1 H, t, *J* 7.5, 3-*H*), 4.19 (1 H, d, *J* 12.5, 1-C*H*), 4.13 and 4.07 (each 1 H, d, *J* 15.5, 1′-C*H*), 4.06 (2 H, s, 8′-CH_2), 4.01 (1 H, d, *J* 12.5, 1-C*H*′), 3.66 (2 H, m, OCH_2CH_2), 3.15 and 3.09 (each 1 H, d, *J* 12, 6-C*H*), 2.14–2.24 (5 H, m, 5-*H*, 4′-H_2 and 5′-H_2), 1.88 (1 H, dd, *J* 11.5, 5.5, 4-*H*), 1.57 (3 H, s, 7′-CH_3), 1.51 (1 H, m, 4-*H*′), 1.11 (3 H, s, 6-CH_3), 1.06 [9 H, s, SiC(CH_3)$_3$], 0.96 (2 H, m, CH_2Si), 0.87 (3 H, d, *J* 7, 4-CH_3) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (91 MHz, $CDCl_3$) 142.3, 139.5, 137.4, 137.2, 135.7, 132.1, 131.4, 131.1, 130.7, 129.4, 127.6, 124.4, 95.1, 88.5, 77.9, 74.1, 72.1, 70.6, 66.8, 59.5, 43.4, 42.9, 35.5, 34.7, 28.8, 28.7, 22.8, 21.1, 20.9, 19.9, 17.5, 15.4 and 0.4; *m*/*z* (CI) 800 ($M^+ + 18$, 1%), 407 (20), 261 (30), 259 (30), 123 (45), 196 (25) and 90 (100).

(3*SR*,5*RS*,6*SR*)-1-[(6*E*)-8-*tert*-Butyldiphenylsilyloxy-7-methyloct-6-en-2-yn-1-yloxy]methyl-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxycyclohex-1-ene 31

Sulfide **30** (0.55 g, 0.0703 mmol) and ammonium molybdate (0.13 g, 0.105 mmol) in ethanol (7.4 cm^3) were cooled to −10 °C, and hydrogen peroxide (30% solution in water, 0.21 cm^3) was added over 5 min. The suspension was stirred at −10 °C for 5 min and at room temperature for 24 h then water (10 cm^3) was added. The solution was partitioned with ether and the aqueous phase was extracted with ether (6 × 10 cm^3). The organic extracts were washed with aqueous iron(II) sulfate (20 cm^3), brine (20 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue on silica gel, eluted with 1–30% ether in petrol, afforded the *title compound* **31** (0.372 g, 65%) as a clear, viscous oil, $R_f = 0.5$ (50% ether in petrol) (Found; $M^+ + NH_4$, 832.4455. $C_{47}H_{70}O_6Si_2SN$ requires *M*, 832.4462); ν_{max}/cm^{-1} 2955, 2894, 1727, 1447, 1308, 1249. 1149, 1109, 1056, 836 and 745; δ_H (500 MHz, $CDCl_3$) 7.92 (2 H, d, *J* 7, Ar-*H*), 7.73 (2 H, dd, 6, 1.5, Ar-*H*), 7.68 (3 H, dd, *J* 6.5, 1.5, Ar-*H*), 7.62 (1 H, t, *J* 7.5, Ar-*H*), 7.54 (2 H, t, *J* 7.5, Ar-*H*), 7.37–7.44 (5 H, m, Ar-*H*), 5.85 (1 H, s, 2-*H*), 5.47 (1 H, t, *J* 6, 6′-*H*), 4.78 and 4.75 (each 1 H, d, *J* 6.5, OCH*H*O), 4.33 (2 H, m, 3-*H* and 1-C*H*), 4.07–4.13 (3 H, m, 1-C*H*′ and 1′-CH_2), 4.05 (2 H, s, 8′-CH_2), 3.65 (2 H, m, CH_2CH_2Si), 3.50 and 3.29 (each 1 H, d, *J* 14.5, 6-C*H*), 2.66 (1 H, dqd, *J* 14, 6.5, 2, 5-*H*), 2.23 (4 H, m, 4′-H_2 and 5′-H_2), 1.95 (1 H, dd, *J* 11.5, 5.5, 4-*H*), 1.60 (3 H, s, 7′-CH_3), 1.55 (1 H, m, 4-*H*′), 1.11 (3 H, s, 6-CH_3), 1.07 [9 H, s, SiC(CH_3)$_3$], 0.99 (3 H, d, *J* 6.5, 5-CH_3), 0.95 (2 H, m, CH_2Si) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 141.8, 139.4, 135.5, 135.4, 133.7, 133.3, 130.95, 129.5, 129.1, 127.7, 127.5, 127.4, 122.3, 93.3, 86.7, 75.9, 71.8, 68.7, 65.0, 60.5, 57.4, 41.9, 33.6, 33.0, 26.9, 26.8, 21.5, 19.2, 19.0, 18.0, 16.1, 13.5 and −1.4; *m*/*z* (CI) 831 ($M^+ + 17$, 1%), 322 (26), 196 (62), 160 (62) and 90 (100).

(3*SR*,5*RS*,6*SR*)-5,6-Dimethyl-1-[(6*E*)-8-hydroxy-7-methyloct-6-en-2-yn-1-yloxy]methyl-6-phenylsulf-onylmethyl-3-(2-trimethylsilylethoxy)methoxycyclohex-1-ene 33

tetra-n-Butylammonium fluoride (1.0 M in tetrahydrofuran, 0.34 cm^3, 0.34 mmol) was added to the sulfone **31** (0.25 g, 0.31 mmol) in tetrahydrofuran (8 cm^3) at 0 °C and the pale orange solution stirred at room temperature for 2 h. After concentration under reduced pressure, column chromatography of the residue on silica gel, eluted with 10–50% ether in petrol, afforded the *title compound* **33** (0.157 g, 88%) as a clear, viscous oil, $R_f = 0.1$ (50% ether in petrol) (Found; $M^+ + NH_4$, 594.3290. $C_{31}H_{52}O_6SSiN$ requires *M*, 594.3284); ν_{max}/cm^{-1} 3468 (br), 2949, 2894, 2874, 1447, 1378, 1361, 1308, 1248, 1149, 1030, 836 and 748; δ_H (300 MHz, $CDCl_3$) 7.92 (2 H, d, *J* 8.5, Ar-*H*), 7.63 (1 H, m, Ar-*H*), 7.55 (2 H, m, Ar-*H*), 5.85 (1 H, s, 2-*H*), 5.47 (1 H, m, 6′-*H*), 4.79 and 4.75 (each 1 H, d, *J* 7, OCH*H*O), 4.32 (2 H, m, 1-C*H* and 3-*H*), 4.09 (3 H, m, 1-C*H*′ and 1′-H_2), 4.00 (2 H, s, 8′-H_2), 3.65 (2 H, m, CH_2CH_2Si), 3.50 and 3.30 (each 1 H, d, *J* 14.5, 6-C*H*), 2.64 (1 H, m, 5-*H*), 2.26 (4 H, m, 4′-H_2 and 5′-H_2), 1.94 (1 H, dd, *J* 11.5, 6.5, 4-*H*), 1.70 (1 H, br s, OH), 1.67 (3 H, s, 7′-CH_3), 1.54 (1 H, dt, 12.5, 9.5, 4-*H*′), 1.11 (3 H, s, 6-CH_3), 0.97 (3 H, d, *J* 7, 5-CH_3), 0.93 (2 H, m, CH_2Si) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 141.8, 139.4, 136.3, 133.3, 130.9, 129.1, 127.4, 123.5, 93.3, 86.6, 71.8, 71.5, 68.3, 65.0, 60.1, 57.3, 41.9, 33.5, 33.0, 29.6, 26.7, 21.4, 18.9, 18.0, 16.1, 13.7 and −1.5; *m*/*z* (CI) 594 ($M^+ + 18$, 3%), 456 (2), 293 (21), 170 (30), 137 (32) and 90 (100).

(3*SR*,5*RS*,6*SR*)-1-[(6*E*)-8-Bromo-7-methyloct-6-en-2-yn-1-yloxy]methyl-6-phenylsulfonylmethyl-5,6-dimethyl-3-(2-trimethylsilylethoxy)methoxycyclohex-1-ene 34

Triethylamine (0.06 cm^3, 0.417 mmol) then methanesulfonyl chloride (0.02 cm^3, 0.26 mmol) were added to alcohol **33** (0.06 g, 0.104 mmol) in dichloromethane (1.5 cm^3) at 0 °C and the pale orange solution was stirred at room temperature for 30 min. After cooling to 0 °C, lithium bromide (0.135 g, 1.56 mmol) in acetone (0.5 cm^3) was added and, after 30 min at ambient temperature, the suspension was filtered through a pad of celite, the filter cake was washed with dichloromethane and the filtrate concentrated under reduced pressure. The residue was taken up in ethyl acetate (5 cm^3) and washed with saturated aqueous sodium bicarbonate solution (5 cm^3). The aqueous phase was washed with ethyl acetate (3 × 5 cm^3) and the organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue on silica gel, eluted with 1–20% ether on petrol, afforded the *title compound* **34** (0.55 g, 83%) as a

clear, viscous oil, $R_f = 0.5$ (50% ether in petrol) (Found; $M^+ + NH_4$, 656.2435. $C_{31}H_{51}O_5SSi^{79}BrN$ requires M, 656.2441); ν_{max}/cm^{-1} 2948, 2878, 1446, 1361, 1313, 1248, 1149, 1087, 1053 1032, 837 and 748; δ_H (300 MHz, $CDCl_3$) 7.92 (2 H, d, J 7, Ar-H), 7.63 (1 H, t, J 7, Ar-H), 7.55 (2 H, t, J 7.5, Ar-H), 5.84 (1 H, s, 2-H), 5.56 (1 H, m, 6′-H), 4.79 and 4.75 (each 1 H, d, J 7, OCHHO), 4.32 (2 H, m, 3-H and 1′-H), 4.11–3.95 (5 H, m, 1-CH_2, 1′-$H′$ and 8′-H_2), 3.65 (2 H, m, CH_2CH$_2$Si), 3.50 and 3.30 (each 1 H, d, J 15, 6-CH), 2.65 (1 H, m, 5-H), 2.25 (4 H, br s, 4′-H_2 and 5′-H_2), 1.95 (1 H, dd, J 12, 6.5, 4-H), 1.75 (3 H, s, 7′-CH_3), 1.54 (1 H, td, J 13, 9.5, 4-$H′$), 1.12 (3 H, s, 6-CH_3), 0.98 (3 H, d, J 6.5, 5-CH_3), 0.93 (2 H, m, CH_2Si) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 142.2, 139.7, 133.7, 131.4, 129.5, 129.4, 128.9, 127.8, 93.6, 86.3, 72.1, 65.3, 60.8, 57.7, 42.3, 41.4, 33.9, 33.4, 27.8, 27.5, 21.8, 18.9, 18.8, 18.3, 16.4, 15.1 and −1.1; m/z (CI) 658 ($M^+ + 18$, 1.5%), 656 ($M^+ + 18$, 1.5%), 612 (2), 578 (1), 493 (2), 391 (35) and 90 (100).

(13*SR*,14*RS*,16*SR*,9*E*)-12-Phenylsulfonyl-10,13,14-trimethyl-16-(2-trimethylsilylethoxy)methoxy-3-oxabicyclo[11.4.0]heptadeca-9,17-dien-5-yne 35,a,b

Sodium hexamethylsilazide (1.0 M in tetrahydrofuran, 0.19 cm^3, 0.186 mmol) was added to the bromide **34** (39 mg, 0.0619 mmol) in tetrahydrofuran (1.24 cm^3) at 0 °C using a syringe pump over 1 h and the mixture stirred for 1 h. Saturated aqueous ammonium chloride (2 cm^3) and ethyl acetate (2 cm^3) were added and the aqueous phase extracted into ethyl acetate (3 × 5 cm^3). The organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 0–10% ether in petrol, gave the *title compound* **35a** (9 mg, 26%) as a clear oil, R_f = 0.52 (50% ether in petrol) (Found; $M^+ + NH_4$, 576.3196. $C_{31}H_{50}O_5SSiN$ requires M, 576.3179); ν_{max}/cm^{-1} 2925, 2857, 1719, 1670, 1449, 1310, 1246, 1149, 1085, 1029, 838 and 749; δ_H (300 MHz, $CDCl_3$) 7.88 (2 H, d, J 6.5, Ar-H), 7.45–7.57 (3 H, m, Ar-H), 6.04 (1 H, s, 17-H), 4.74 (2 H, s, OCH_2O), 4.20 (2 H, d, J 16, 2-H and 4-H), 4.15 (1 H, m, 9-H), 3.92 (1 H, m, 16-H), 3.86 (1 H, d, J 15, 4-$H′$), 3.68 (1 H, d, J 15.5, 2-$H′$), 3.50 (2 H, m, CH_2CH$_2$Si), 3.38 (1 H, t, J 4, 12-H), 2.65 (1 H, d, J 19.5, 11-H), 2.46 (1 H, m, 14-H), 2.19 (1 H, dd, J 19, 4, 11-$H′$), 2.12 (1 H, m, 15-H), 1.96–2.06 (4 H, m, J 9, 7-H_2 and 8-H_2), 1.54 (3 H, s, 10-CH_3), 1.44 (1 H, m, 15-$H′$), 1.33 (3 H, s, 13-CH_3), 1.27 (3 H, d, J 6.5, 14-CH_3), 0.92 (2 H, m, CH_2Si) and 0.00 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 141.2, 139.3, 133.6, 133.2, 129.0, 128.9, 126.0, 120.7, 93.1, 87.9, 78.3, 70.3, 70.1, 66.0, 65.0, 58.0, 47.9, 35.4, 35.1, 31.1, 25.9, 22.6, 19.7, 18.6, 18.4, 18.1 and −1.4; m/z (CI) 576 ($M^+ + 18$, 5%), 411 (100), 269 (50), 160 (35) and 90 (72). The second fraction was recovered starting material **34** (5 mg, 13%) followed by the *title compound* **35b** (17 mg, 49%) as a clear oil, R_f = 0.48 (50% ether in petrol) (Found; $M^+ + NH_4$, 576.3178; $C_{31}H_{50}O_5SSiN$ requires M, 576.3179); ν_{max}/cm^{-1} 2925, 2859, 2234, 1720, 1669, 1449, 1378, 1311, 1247, 1149, 1084, 1030, 936, 838 and 749; δ_H (500 MHz, $CDCl_3$) 8.05 (2 H, d, J 7, Ar-H), 7.61 (1 H, t, J 7.5, Ar-H), 7.54 (2 H, t, J 8, Ar-H), 5.92 (1 H, s, 17-H), 4.78 and 4.74 (each 1 H, d, J 7, OCHHO), 4.66 (1 H, t, J 6.5, 9-H), 4.42 (1 H, dd, J 10, 6, 16-H), 4.32 (1 H, d, J 16, 2-H), 4.28 (1 H, dd, J 6, 2, 12-H), 4.25 and 4.07 (each 1 H, d, J 10, 4-H), 4.03 (1 H, d, J 16, 2-$H′$), 3.64 (2 H, m, CH_2CH$_2$Si), 3.03 (1 H, dqd, J 12.5, 7, 2.5, 14-H), 2.68 (1 H, d, J 17, 11-H), 2.49 (1 H, dd, J 17, 6, 11-$H′$), 2.22 (1 H, m, 15-H), 2.00 (2 H, m), 1.85 (2 H, m), 1.56 (1 H, td, J 12.5, 10.5, 15-$H′$), 1.36 (3 H, s, 10-CH_3), 1.21 (3 H, d, J 7, 14-CH_3), 1.20 (3 H, s, 13-CH_3), 0.96 (2 H, m, CH_2Si) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 142.9, 140.5, 135.5, 134.0, 133.1, 129.2, 128.8, 124.8, 93.2, 86.6, 79.0, 72.2, 72.0, 70.5, 65.0, 58.4, 45.1, 35.3, 34.1, 33.8, 24.3, 19.9, 18.6, 18.2, 18.0 and −1.4; m/z (CI) 576 ($M^+ + 18$, 10%), 411 (40), 359 (12), 271 (42), 215 (30) and 90 (100).

(13*SR*,14*RS*,16*SR*,9*E*)-10,13,14-Trimethyl-16-(2-trimethylsilylethoxy)methoxy-3-oxabicyclo[11.4.0]-heptadeca-9,17-dien-5-yne 36

Sodium-mercury amalgam (10%, 0.12 g, 0.538 mmol) was added to a suspension of the sulfones **35a**,**b** (50 mg, 0.0896 mmol) and disodium hydrogen phosphate in tetrahydrofuran (0.3 cm^3) and anhydrous methanol (0.5 cm^3) at 0 °C and the suspension stirred at ambient temperature for 1 h. Saturated aqueous ammonium chloride (1.5 cm^3) and ethyl acetate (2 cm^3) were added and the mixture decanted from the residues which were washed with ethyl acetate (3 × 5 cm^3). The aqueous phase was extracted with ethyl acetate (3 × 2 cm^3) and the organic extracts washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 0–5% ether in petrol, afforded the *title compound* **36** (0.023 g, 62%) as a clear, viscous oil, R_f = 0.8 (50% ether in petrol) (Found; $M^+ + NH_4$, 436.3238. $C_{25}H_{46}O_3SiN$ requires M, 436.3247); ν_{max}/cm^{-1} 2924, 2855, 1735, 1459, 1376, 1147 and 1037; δ_H (300 MHz, $CDCl_3$) 5.86 (1 H, s, 17-H), 5.24 (1 H, m, 9-H), 4.78 (2 H, s, OCH_2O), 4.37 (1 H, dt, J 13, 2, 2-H), 4.26 (1 H, m, 16-H), 4.25 (1 H, dt, J 16, 2, 4-H), 4.04 (1 H, dt, J 16, 2, 4-$H′$), 3.87 (1 H, dt, J, 13, 2, 2-$H′$), 3.66 (2 H, m, CH_2CH$_2$Si), 2.37 (2 H, m, 7-H_2), 2.28 (1 H, m, 8-H), 2.13 (1 H, dd, J 12.5, 5.5, 8-$H′$), 2.04 and 1.80 (each 1 H, m, 11-H), 1.70 (2 H, m, 14-H and 15-H), 1.61 (3 H, s, 10-CH_3), 1.52 (1 H, m, 12-H), 1.26–1.36 (2 H, m, 15-$H′$ and 12-$H′$), 0.97 (3 H, s, 13-CH_3), 0.89 (3 H, d, J 7, 14-CH_3), 0.88 (2 H, m, CH_2Si) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 142.9, 137.6, 124.8, 123.5, 92.9, 87.7, 78.5, 72.5, 68.2, 64.8, 58.2, 40.9, 34.1, 33.8, 33.4, 32.3, 24.5, 21.7, 18.5, 18.0, 15.6, 15.3 and −1.5; m/z (CI) 436 ($M^+ + 18$, 1%), 288 (3), 271 (45), 178 (50) 161 (45) and 146 (100).

(1′*RS*)- and (1′*SR*)-(2*RS*,3*SR*,5*RS*,6*SR*)-2-[(6*E*)-8-*tert*-Butyldiphenylsilyloxy-1-hydroxy-7-methyloct-6-en-2-yn-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)-methoxy-1-methylenecyclohexanes 37 and 38

n-Butyllithium(1.6 M in tetrahydrofuran, 0.31 cm^3, 0.491 mmol) was added dropwise over 10 min to the sulfone **31** (0.16 g, 0.197 mmol) in tetrahydrofuran (3.9 cm^3) at −78 °C and the mixture stirred for 2.5 h before saturated aqueous ammonium chloride (4 cm^3) was added. After allowing to warm to room temperature, ethyl acetate (10 cm^3) was added, the aqueous phase was extracted with ethyl acetate (4 × 10 cm^3), and the organic extracts were washed with brine (15 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 0–30% ether in petrol, afforded the *title compound* **37** (94 mg, 59%) as a pale yellow oil, R_f = 0.45 (50% ether in petrol) (Found; $M^+ + NH_4$, 832.4485. $C_{47}H_{70}O_6Si_2SN$ requires M, 832.4462); ν_{max}/cm^{-1} 3493 (br), 3069, 2953, 2857, 1462, 1447, 1319, 1248, 1151, 1110, 1027, 859, 836, 743 and 707; δ_H (400 MHz,

$CDCl_3$) 7.93 (2 H, d, *J* 7, Ar-*H*), 7.68 (4 H, dd, *J* 7.5, 1.5, Ar-*H*), 7.64 (1 H, m, Ar-*H*), 7.57 (2 H, t, *J* 7.5, Ar-*H*), 7.36–7.42, (6 H, m, Ar-*H*), 5.46 (1 H, m, 6′-*H*), 5.33 and 5.17 (each 1 H, s, 1-C*H*), 4.84 and 4.80 (each 1 H, d, *J* 7, OCH*H*O), 4.62 (1 H, br d, *J* 9, 1′-*H*), 4.09 (1 H, d, *J* 10, O*H*), 4.05 (2 H, s, 8′-H_2), 3.89 (1 H, td, *J* 10, 5, 3-*H*), 3.74 (1 H, td, *J* 10, 5, OCH*H*CH_2Si), 3.57 (1 H, td, *J* 10, 6, OCH*H*′CH_2Si), 3.47 and 3.36 (each 1 H, d, *J* 15, 6-C*H*), 2.70 (1 H, dd, *J* 9, 2, 2-*H*), 2.27 (4 H, m, 4′-H_2 and 5′-H_2), 2.09 (1 H, dt, *J* 12.5, 4.5, 4-*H*), 1.84 (1 H, m, 5-*H*), 1.62 (3 H, s, 7′-CH_3), 1.56 (1 H, m, 4-*H*′), 1.27 (3 H, s, 6-CH_3), 1.06 [9 H, s, SiC(CH_3)$_3$], 0.95 (2 H, m, CH_2Si), 0.91 (3 H, d, *J* 7, 5-CH_3) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 147.5, 142.5, 135.5, 135.3, 133.7, 133.3, 129.5, 129.3, 127.5, 127.3, 122.5, 111.7, 94.6, 86.7, 79.5, 79.4, 68.7, 65.6, 64.4, 63.2, 51.0, 45.3, 36.7, 36.1, 30.2, 27.2, 26.8, 19.2, 19.1, 18.0, 16.5, 13.6 and –1.5; *m*/*z* (CI) 832 (M^+ + 18, 12%), 442 (12), 408 (73), 391 (32), 365 (26), 294 (46) and 277 (100). The second fraction was the *title compound* **38** (22 mg, 13%) as a pale yellow oil, R_f = 0.42 (50% ether in petrol) (Found; M^+ + NH_4, 832.4450. $C_{47}H_{70}O_6Si_2SN$ requires *M*, 832.4462); ν_{max}/cm^{-1} 3421 (br), 2953, 2929, 1719, 1695, 1560, 1318, 1150 and 1030; δ_H (300 MHz, $CDCl_3$) 7.93 (2 H, d, *J* 8, Ar-*H*), 7.68 (4 H, d, *J* 8, Ar-*H*), 7.62 (1 H, t, *J* 7, Ar-*H*), 7.55 (2 H, dd, *J* 8, 6.5, Ar-*H*), 7.39 (6 H, m, Ar-*H*), 5.49 and 5.44 (each 1 H, s, 1-C*H*), 5.38 (1 H, m, 6′-*H*), 4.82 (1 H, m, 1′-*H*), 4.73 (2 H, s, OCH_2O), 4.05 (2 H, s, 8′-H_2), 3.70 (1 H, m, 3-*H*), 3.66 (2 H, t, *J* 8.5, CH_2CH_2Si), 3.53 and 3.41 (each 1 H, d, *J* 15, 6-C*H*), 3.27 (1 H, d, *J* 7.5, O*H*), 2.76 (1 H, dd, *J* 7, 5.5, 2-*H*), 2.21 (4 H, m, 4′-H_2 and 5′-H_2), 1.96 (1 H, dt, *J* 13, 4, 4-*H*), 1.81 (1 H, m, 5-*H*), 1.60 (3 H, s, 7′-CH_3), 1.50 (1 H, m, 4-*H*′), 1.33 (3 H, s, 6-CH_3), 1.07 [9 H, s, SiC(CH_3)$_3$], 0.97 (2 H, m, CH_2Si), 0.90 (3 H, d, *J* 6.5, 5-CH_3) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 147.1, 142.9, 135.8, 135.7, 134.1, 133.6, 129.8, 129.5, 128.6, 127.8, 127.7, 122.9, 114.7, 94.3, 86.9, 80.8, 69.1, 65.8, 63.9, 63.4, 52.8, 44.9, 37.3, 36.2, 27.3, 27.1, 19.5, 19.4, 18.3, 16.9, 13.8 and –1.2; *m*/*z* (CI) 832 (M^+ + 18, 2%), 498 (2), 294 (36), 277 (100), 196 (32), 135 (28) and 90 (61).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*RS*,6*E*)-8-*tert*-Butyldiphenylsilyloxy-1-(4-methoxy)benzyloxy-7-methyloct-6-en-2-yn-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 39

Sodium hydride (2.5 mg, 0.062 mmol) was suspended in anhydrous *N*,*N*-dimethylformamide (0.25 cm^3) and the suspension cooled to 0 °C. The alcohol **37** (42 mg, 0.052 mmol) in tetrahydrofuran (0.25 cm^3) was added and the resulting yellow solution was allowed to warm to room temperature and stirred for 30 min. The solution was cooled to 0 °C and 4-methoxybenzyl chloride (0.008 cm^3, 0.062 mmol) was added. After 16 h at room temperature, water (2 cm^3) and ethyl acetate (2 cm^3) were added and the aqueous phase extracted into ethyl acetate (3 × 3 cm^3). The organic extracts were washed with brine (5 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 1–10% ether in petrol, afforded the *title compound* **39** (28 mg, 58%) as a pale yellow oil, R_f = 0.65 (50% ether in petrol); ν_{max}/cm^{-1} 2952, 2932, 2859, 1612, 1513, 1465, 1317, 1249, 1150, 1108, 1108, 1052, 1034 and 833; δ_H (300 MHz, $CDCl_3$) 7.89 (2 H, d, *J* 8, Ar-*H*), 7.70 (4 H, d, *J* 7.5, Ar-*H*), 7.61 (1 H, t, *J* 8, Ar-*H*), 7.51 (2 H, t, *J* 7.5, Ar-*H*), 7.41 (6 H, m, Ar-*H*), 7.24 (2 H, d, *J* 8.5, Ar-*H*), 6.86 (2 H, d, *J* 8, Ar-*H*), 5.50 (2 H, br s, 1-C*H* and 6′-*H*), 5.34 (1 H, s, 1-C*H*′), 4.73 (1 H, d, *J* 11.5, CH*H*Ar), 4.66 and 4.59 (each 1 H, d, *J* 7, OCH*H*O), 4.54 (1 H, m, 1′-*H*), 4.35 (1 H, d, *J* 11, CH*H*′Ar), 4.08 (2 H, s, 8′-H_2), 3.82 (3 H, s, OCH_3), 3.70 (2 H, m, 3-*H* and OCH*H*CH_2Si), 3.55 (1 H, d, *J* 14.5, 6-C*H*), 3.48 (1 H, m, OCH*H*′CH_2Si), 3.34 (1 H, d, *J* 14.5, 6-C*H*′), 2.62 (1 H, dd, *J* 8, 4, 2-*H*), 2.29 (4 H, m, 4′-H_2 and 5′-H_2), 2.00 (1 H, dt, *J* 13, 5, 4-*H*), 1.91 (1 H, m, 5-*H*), 1.65 (3 H, s, 7′-CH_3), 1.52 (1 H, m, 4-*H*′), 1.32 (3 H, s, 6-CH_3), 1.08 [9 H, s, SiC(CH_3)$_3$], 0.94 (3 H, d, *J* 6.5, 5-CH_3), 0.90 (2 H, m, CH_2Si) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 146.6, 143.0, 142.3, 135.81, 135.80, 134.1, 133.4, 130.4, 129.8, 129.4, 127.9, 127.7, 123.0, 120.8, 114.7, 113.9, 103.6, 95.0, 91.7, 88.4, 78.2, 77.2, 70.3, 69.1, 69.0, 65.2, 63.9, 55.5, 52.1, 45.1, 36.4, 35.2, 27.5, 27.1, 19.5, 18.3, 17.2, 13.9 and –1.2.

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*RS*,6*E*)-8-Hydroxy-1-(4-methoxy)-benzyloxy-7-methyloct-6-en-2-ynyl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 40

tetra-*n*-Butylammonium fluoride (1.0 M solution in tetrahydrofuran, 0.0192 cm^3, 0.0192 mmol) was added to the silylether **39** (18 mg, 0.0192 mmol) in tetrahydrofuran (0.4 cm^3) at room temperature and the solution stirred for 1.5 h. After concentration under reduced pressure, chromatography of the residue, eluting with 5–50% ether in petrol, afforded the *title compound* **40** (0.012 g, 87%) as a clear oil, R_f = 0.1 (50% ether in petrol) ν_{max}/cm^{-1} 3509 (br), 2930, 1612, 1513, 1448, 1376, 1313, 1248, 1149, 1031 and 835; δ_H (300 MHz, C_6D_6) 7.84 (2 H, br d, *J* 8, Ar-*H*), 7.36 (2 H, d, *J* 8.5, Ar-*H*), 7.12 (1 H, m, Ar-*H*), 6.94 (2 H, m, Ar-*H*), 6.80 (2 H, m, Ar-*H*), 5.95 (1 H, s, 1-C*H*), 5.64 (2 H, m, 6′-*H* and 1-C*H*′), 4.99 (1 H, d, *J* 11, CH*H*Ar), 4.91 (1 H, d, *J* 4, 1′-*H*), 4.81 and 4.68 (each 1 H, d, *J* 7, OCH*H*O), 4.47 (1 H, d, *J* 11, CH*H*′Ar), 4.34 (1 H, br s, O*H*), 3.98 (1 H, m, 3-*H*), 3.94 (2 H, s, 8′-H_2), 3.80 and 3.59 (each 1 H, q, *J* 8.5, CH*H*CH_2Si), 3.43 (1 H, d, *J* 15, 6-C*H*), 3.29 (3 H, s, OCH_3), 3.24 (1 H, d, *J* 15, 6-C*H*′), 2.92 (1 H, dd, *J* 8, 4, 2-*H*), 2.21 (4 H, br s, 4-H_2 and 5-H_2), 2.10 (1 H, m, 4-*H*), 1.86 (1 H, m, 5-*H*), 1.55 (3 H, s, 7′-CH_3), 1.57 (1 H, m, 4-*H*′), 1.36 (3 H, s, 6-CH_3), 0.98 (2 H, m, CH_2Si), 0.78 (3 H, d, *J* 6.5, 5-CH_3) and 0.00 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 159.4, 147.1, 142.9, 136.7, 133.5, 130.4, 129.8, 129.5, 127.7, 123.6, 114.0, 95.0, 88.4, 78.4, 70.3, 69.2, 68.5, 65.2, 63.8, 55.5, 51.6, 45.3, 37.2, 37.1, 27.0, 19.3, 18.6, 18.2, 17.0, 4.1 and –1.2; *m*/*z* (ES^+) 719 (M^+ + 23, 47%) and 105 (100); ($APCI^-$) 731 (M^+ + 35, 100%), 712 (12) and 612 (21).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*RS*,6*E*)-8-Bromo-1-(4-methoxy) benzyloxy-7-methyloct-6-en-2-yn-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 41

Triethylamine (0.03 cm^3, 0.22 mmol) and methanesulfonyl chloride (0.01 cm^3) were added to the alcohol **40** (0.038 g, 0.0545 mmol) in dichloromethane (0.8 cm^3) at 0 °C and the solution allowed to warm to room temperature and stirred for 30 min. The mixture was cooled to 0 °C and lithium bromide (0.07 g, 0.88 mmol) in acetone (0.4 cm^3) was added. After 30 min at room temperature, the suspension was filtered through a pad of celite and the filter-cake washed with dichloromethane. The filtrate was concentrated under

reduced pressure and the residue was taken up in ethyl acetate (5 cm^3) and washed with saturated aqueous sodium bicarbonate (5 cm^3). The aqueous phase was extracted with ethyl acetate (3 × 5 cm^3), the organic extracts were washed with brine (5 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 1–10% ether in petrol, afforded the *title compound* **41** (0.035 g, 92%) as a clear oil, R_f = 0.5 (50% ether in petrol); ν_{max}/cm^{-1} 2950, 2837, 1612, 1513, 1446, 1316, 1248, 1149, 1032 and 835; δ_H (300 MHz, $CDCl_3$) 7.89 (2 H, d, *J* 7, Ar-*H*), 7.62 (1 H, t, *J* 7.5, Ar-*H*), 7.53 (2 H, t, *J* 7.5, Ar-*H*), 7.24 (2 H, d, *J* 8.5, Ar-*H*), 6.87 (2 H, d, *J*, 9, Ar-*H*), 5.69 (1 H, t, *J* 6.5, 6′-*H*), 5.51 and 5.36 (each 1 H, s, 1-C*H*), 4.73 (1 H, d, *J* 11, CH*H*Ar), 4.63 and 4.56 (each 1 H, d, *J* 7, OCH*H*O), 4.55 (1 H, m, 1′-*H*), 4.35 (1 H, d, *J* 11.5, CH*H*′Ar), 3.98 (2 H, s, 8′-H_2), 3.81 (3 H, s, OCH_3), 3.63–3.72 (2 H, m, 3-*H* and CH*H*CH_2Si), 3.53 (1 H, d, *J* 15, 6-C*H*), 3.45 (1 H, m, CH*H*′CH_2Si), 3.35 (1 H, d, *J* 15, 6-C*H*′), 2.60 (1 H, dd, *J* 9, 3.5, 2-*H*), 2.26–2.33 (4 H, m, 4′-H_2 and 5′-H_2), 1.98 (1 H, dt, *J* 13, 4.5, 4-*H*), 1.84 (1 H, m, 5-*H*), 1.77 (3 H, s, 7′-CH_3), 1.49 (1 H, m, 4-*H*′), 1.31 (3 H, s, 6-CH_3), 0.91 (3 H, d, *J* 6.5, 5-CH_3), 0.87 (2 H, m, CH_2Si) and 0.01 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 159.1, 146.2, 142.7, 133.2, 130.0, 129.5, 129.2, 128.3, 127.4, 114.1, 113.7, 94.8, 87.3, 78.5, 70.1, 68.3, 64.9, 63.6, 55.3, 51.5, 45.0, 41.3, 36.8, 36.4, 27.6, 18.7, 18.6, 18.0, 16.8, 14.9 and −1.5; *m*/*z* (ES^+) 783 (M^+ + 23, 71%), 767 (100), 765 (93), 737 (44) and 721 (94).

(1*SR*,2*RS*,11*SR*,12*RS*,14*SR*,7*E*)-10-Phenylsulfonyl-8,11,12-trimethyl-15-methylene-2-(4-methoxy)-benzyloxy-14-(2-trimethylsilylethoxy)methoxybicyclo[9.3.1]pentadec-7-en-3-yne 42

Sodium hexamethyldisilazide (1.0 M in tetrahydrofuran, 0.356 cm^3, 0.356 mmol) was added to the bromide **41** (0.09 g, 0.19 mmol) in tetrahydrofuran (1.5 cm^3) at 0 °C using a syringe pump over 1 h and the mixture stirred for 30 min before saturated ammonium chloride (2 cm^3) and ethyl acetate (5 cm^3) were added. The aqueous phase was extracted with ethyl acetate (3 × 5 cm^3) and the organic extracts were washed with brine (10 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 1–10% ether in petrol, afforded the *title compound* **42** (0.055 g, 68%) as a clear oil, R_f = 0.6 (50% ether in petrol) (Found; $M^+ + NH_4$, 696.3749. $C_{39}H_{58}O_6SSiN$ requires *M*, 696.3754); ν_{max}/cm^{-1} 2923, 2871, 1613, 1514, 1446, 1303, 1249, 1142, 1050, 1035, 923 and 836; δ_H (300 MHz, $CDCl_3$) 7.97 (2 H, d, *J* 7, Ar-*H*), 7.56–7.66 (3 H, m, Ar-*H*), 7.31 (2 H, d, *J* 8, Ar-*H*), 6.90 (2 H, d, *J* 8.5, Ar-*H*), 6.05 (1 H, s, 15-C*H*), 6.00 (1 H, s, 15-C*H*′), 5.53 (1 H, m, 7-*H*), 4.80 (1 H, d, *J* 11.5, CH*H*Ar), 4.65 and 4.55 (each 1 H, d, *J* 6.5, OCH*H*O), 4.54 (1 H, m, 2-*H*), 4.29 (1 H, d, *J* 11, CH*H*′Ar), 3.83 (3 H, s, OCH_3), 3.71 (2 H, m, 14-*H* and CH*H*CH_2Si), 3.59 (1 H, m, 10-*H*), 3.43 (1 H, td, *J* 10, 7, CH*H*′CH_2Si), 3.17 (1 H, t, *J* 13, 9-*H*), 2.91 (1 H, m, 12-*H*), 2.41 (1 H, dd, *J* 11, 4, 1-*H*), 2.29 (2 H, m), 2.06–2.19 (4 H, m), 1.44 (3 H, s, 8-CH_3), 1.25 (1 H, m, 13-*H*′), 1.09 (6 H, m, 11-CH_3 and 12-CH_3), 0.91 (2 H, m, CH_2Si) and 0.00 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 158.6, 145.4, 142.1, 133.1, 133.0, 130.2, 130.0, 129.0, 128.1, 115.6, 113.6, 95.1, 85.9, 82.2, 78.6, 72.3, 70.7, 67.8, 64.9, 55.2, 53.5, 52.9, 39.8, 39.2, 37.6, 29.6, 26.2, 22.4, 18.3, 18.1, 17.9, 17.3 and −1.5; *m*/*z* (CI) 690 (M^+ + 18, 0.3%), 154 (37), 177 (100) and 100 (49).

(1*SR*,2*RS*,7*E*,11*SR*,12*RS*,14*SR*)-2-(4-Methoxy)benzyloxy-15-methylene-8,11,12-trimethyl-14-(2-trimethylsilylethoxymethoxy)-bicyclo[9.3.1]pentadec-7-en-3-yne 43

Disodium hydrogen phosphate (23 mg, 0.16 mmol) was added to the sulfone **42** (10 mg, 0.016 mmol) in tetrahydrofuran (0.1 cm^3) and anhydrous methanol (0.4 cm^3) was added. The suspension was cooled to 0 °C, sodium-mercury amalgam (5%, 0.074 g, 0.16 mmol) was added portionwise, and the mixture allowed to warm to room temperature. After stirring for 1.5 h, saturated aqueous ammonium chloride (1 cm^3) was added, and the mixture diluted with ethyl acetate (3 cm^3) and decanted from the residue which was washed with ethyl acetate (2 × 2 cm^3). The aqueous phase was extracted into ethyl acetate (3 × 3 cm^3), and the organic extracts washed with brine (5 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 0–5% ether in petrol, afforded the *title compound* **43** (8 mg, 93%) as a clear oil, R_f = 0.6 (50% ether in petrol) (Found; $M^+ + NH_4$, 556.3821. $C_{33}H_{54}O_4NSi$ requires *M*, 556.3822); ν_{max}/cm^{-1} 2952, 2926, 1727, 1639, 1613, 1514, 1461, 1380, 1249, 1106, 1054, 1036 and 836; δ_H (300 MHz, $CDCl_3$) 7.30 and 6.89 (each 2 H, d, *J* 8.5, Ar-*H*), 5.45 (1 H, s, 15-C*H*), 5.02 (1 H, br d, *J* 7.5, 7-*H*), 4.92 (1 H, s, 15-C*H*′), 4.78 (1 H, d, *J* 11.5, CH*H*Ar), 4.67 and 4.56 (each 1 H, d, *J* 6.5, OCH*H*O), 4.45 (1 H, d, *J* 4, 2-*H*), 4.28 (1 H, d, *J* 11.5, CH*H*′Ar), 3.82 (3 H, s, OCH_3), 3.73 (1 H, td, *J* 10.5, 6, CH*H*CH_2Si), 3.60 (1 H, td, *J* 10.5, 6, 14-*H*), 3.42 (1 H, td, *J* 10, 6.5, CH*H*′CH_2Si), 2.64 (1 H, dd, *J* 10.5, 4, 1-*H*), 2.40–2.20 (4 H, m), 1.90–2.10 (4 H, m), 1.62 (3 H, s, 8-CH_3), 1.42–1.52 (2 H, m), 1.27 (1 H, m, 12-*H*), 1.04 (3 H, s, 11-CH_3), 0.89 (2 H, m, CH_2Si), 0.77 (3 H, d, *J* 6.5, 12-CH_3) and 0.00 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 158.8, 150.4, 135.9, 130.4, 129.1, 126.3, 113.5, 109.1, 95.1, 86.9, 81.4, 79.6, 70.5, 68.0, 64.7, 55.2, 51.8, 44.2, 42.9, 39.5, 35.2, 30.1, 29.6, 27.2, 18.7, 17.9, 16.3, 15.5 and −1.5; *m*/*z* (CI) 556 (M^+, 0.5%), 391 (6), 361 (5), 257 (4), 154 (43), 137 (29), 121 (100) and 90 (33).

(1*RS*,2*RS*,7*E*,11*SR*,12*RS*,14*SR*)-2-Hydroxy-15-methylene-8,11,12-trimethyl-14-(2-trimethylsilylethoxymethoxy)-bicyclo[9.3.1]pentadec-7-en-3-yne 44

An aqueous pH 7 phosphate buffer (0.054 cm^3) was added to a rapidly stirred solution of the ether **43** (32 mg, 0.0594 mmol) in dichloromethane (0.4 cm^3) and the mixture was cooled to 0 °C. Dichlorodicyanoquinone (0.015 g, 0.0654 mmol) was added and, after 10 min, dichloromethane (2 cm^3) and aqueous pH 7 buffer (5 cm^3) were added. The aqueous phase was extracted into dichloromethane (4 × 5 cm^3) and the organic extracts were washed with aqueous pH 7 buffer (2 × 5 cm^3), water (5 cm^3) and brine (5 cm^3), dried (Na_2SO_4), and concentrated under reduced pressure. Column chromatography of the residue, eluted with 1–15% ether in petrol, afforded the *title compound* **44** (18 mg, 72%) as a clear oil, R_f = 0.55 (50% ether in petrol) (Found; M^+ + H, 419.2973. $C_{25}H_{43}O_3Si$ requires *M*, 419.2981); ν_{max}/cm^{-1} 3454 (br), 2920, 2851, 1731, 1462, 1379, 129, 1054, 1037, 859 and 838; δ_H (400 MHz, $CDCl_3$) 5.50 (1 H, s, 15-C*H*), 4.98 (1 H, br d, *J* 9, 7-*H*), 4.91 (1 H, s, 15-C*H*′), 4.82 (1 H, br s, 2-*H*), 4.70 and 4.67 (each 1 H, d, *J* 6.5, OCH*H*O), 3.75 (2 H, m, O*H* and CH*H*CH_2Si), 3.51 (2 H, m, 14-*H* and CH*H*′CH_2Si), 2.52 (1 H, dd, *J* 11, 4, 1-*H*), 2.28–2.38 (3 H, m, 5-*H*, 6-*H* and 9-*H*), 2.23 (1 H, td, *J* 13, 2, 5-*H*′), 1.98

(2 H, m, 6-*H′* and 9-*H′*), 1.86 (1 H, m, 13-*H*), 1.61 (3 H, s, 8-CH_3), 1.46 (1 H, dt, *J* 14, 3.6, 10-*H*), 1.42 (1 H, m, 13-*H′*), 1.23–1.34 (2 H, m, 10-*H′*and 12-*H*), 1.02 (3 H, s, 11-CH_3), 0.97 (2 H, m, CH_2Si), 0.77 (3 H, d, *J* 7, 12-CH_3) and 0.02 [9 H, s, Si(CH_3)$_3$]; δ_C (100 MHz, $CDCl_3$) 150.6, 135.8, 126.5, 108.9, 95.3, 86.5, 81.4, 76.3, 65.9, 61.4, 52.0, 44.4, 42.9, 38.6, 35.1, 30.0, 27.1, 18.8, 18.0, 17.9, 16.5, 15.4 and −1.6; *m*/*z* (CI) 419 ($M^+ + 1$, 3%), 343 (12) and 271 (100).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(6*E*)-8-*tert*-Butyldiphenylsilyloxy-7-methyl-1-oxo-oct-6-en-2-yn-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 54

Dess–Martin periodinane (0.14 g, 0.33 mmol) was added to a mixture of the alcohols **37** and **38** (0.225 g, 0.277 mmol) in dichloromethane (15 cm^3) at room temperature and the suspension stirred for 30 min. Aqueous sodium hydroxide (1.6 M, 10 cm^3) and ether (20 cm^3) were added and the aqueous phase extracted with ether (4 × 10 cm^3). The organic extracts were washed with aqueous sodium hydroxide (1.6 M, 20 cm^3), brine (20 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 1–25% ether in petrol, afforded the *title compound* **54** (0.201 g, 89%) as a clear oil, R_f = 0.5 (50% ether in petrol) (Found; $M^+ + NH_4$, 830.4304. $C_{47}H_{68}O_6Si_2SN$ requires *M*, 830.4306); ν_{max}/cm^{-1} 3069, 2952, 2893, 2857, 2212, 1672, 1447, 1428, 1320, 1248, 1150, 1110, 1058, 1032, 835, 741 and 707; δ_H (400 MHz, C_6D_6), 7.45–7.81 (6 H, m, Ar-*H*), 7.26 (6 H, m, Ar-*H*), 6.91 (3 H, m, Ar-*H*), 5.39 (2 H, m, 6′-*H* and 1-C*H*), 5.30 (1 H, s, 1-C*H′*), 4.82 and 4.74 (each 1 H, d, *J* 7, OCH*H*O), 4.37 (1 H, td, *J* 10, 5, 3-*H*), 4.08 (2 H, s, 8′-CH_2), 3.78 (1 H, d, *J* 9.5, 2-*H*), 3.71 (2 H, m, CH_2CH$_2$Si), 3.18 and 3.01 (each 1 H, d, *J* 15, 6-C*H*), 2.18 (1 H, m, 5-*H*), 2.09 (3 H, m, 4′-H_2 and 4-*H*), 1.97 (2 H, t, *J* 7, 5′-H_2), 1.48 (3 H, s, 7-CH_3), 1.44 (1 H, m, 4-*H′*), 1.19 [9 H, s, SiC(CH_3)$_3$], 1.0 (3 H, s, 6-CH_3), 1.01 (2 H, m, CH_2Si), 0.76 (3 H, d, *J* 6.5, 5-CH_3) and 0.03 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 187.7, 146.1, 142.5, 136.2, 135.5, 133.7, 133.4, 129.5, 129.3, 128.3, 127.6, 127.3, 121.5, 113.1, 95.1, 94.5, 81.0, 76.0, 68.6, 65.2, 62.5, 61.6, 45.2, 35.6, 35.2, 26.8, 26.1, 19.9, 19.4, 19.2, 17.9, 16.7, 13.6, and −1.4; *m*/*z* (CI) 830 ($M^+ + 18$, 0.4%), 682 (1.3) and 90 (100).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(2*E*,6*E*)- and -2-[(2*Z*,6*E*)-8-*tert*-Butyldiphenylsilyloxy-7-methyl-3-phenylthio-1-oxo-oct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 55 and 56

Triethylamine (0.07 cm^3, 0.504 mmol) and thiophenol (0.5 M solution in methanol, 0.52 cm^3, 0.26 mmol) were added to the alkynone **53** (0.195 g, 0.24 mmol) in tetrahydrofuran (2.2 cm^3) at −20 °C and the solution stirred for 2 h. Saturated aqueous ammonium chloride (2.5 cm^3) was added and the mixture allowed to warm to room temperature. Ethyl acetate (3 cm^3) was added, the aqueous layer extracted with ethyl acetate (4 × 3 cm^3) and the organic extracts combined and washed with brine (5 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 0–25% ether in petrol, afforded the *title compound* **55** (0.058 g, 26%) as a pale yellow oil, R_f = 0.5 (50% ether in petrol); ν_{max}/cm^{-1} 3069, 2953, 2930, 2857, 1671, 1562, 1472, 1445, 1428, 1320, 1248, 1150, 1110, 1056, 1030, 859, 835, 745 and 705; δ_H (300 MHz, $CDCl_3$) 7.89 (2 H, d, *J* 6.5, Ar-*H*), 7.74 (4 H, dd, *J* 7.5, 2, Ar-*H*), 7.50 (4 H, m, Ar-*H*), 7.45 (4 H, m, Ar-*H*), 7.39 (6 H, m, Ar-*H*), 5.70 (1 H, s, 2′-*H*), 5.51 (1 H, t, *J* 7.5, 6′-*H*), 5.15 and 4.70 (each 1 H, s, 1-C*H*), 4.63 and 4.60 (each 1 H, d, *J* 7, OCH*H*O), 4.67 (2 H, br s, 8′-H_2), 3.92 (1 H, td, *J* 8, 6, 3-*H*), 3.65–3.45 (2 H, m, CH_2CH$_2$Si), 3.38 (1 H, d, *J* 14.5, 6-C*H*), 3.15 (1 H, d, *J* 8, 2-*H*), 3.05 (1 H, d, 6-C*H′*), 2.72 (2 H, m, 4′-H_2), 2.30 (2 H, m, 5′-H_2), 1.96 (1 H, m, 4-*H* and 5-*H*), 1.66 (3 H, s, 7′-CH_3), 1.43 (1 H, m, 4-*H′*), 1.25 (3 H, s, 6-CH_3), 1.08 [9 H, br s, SiC(CH_3)$_3$], 0.93 (2 H, m, CH_2Si), 0.88 (3 H, d, *J* 6.5, 5-CH_3) and 0.00 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 195.6, 165.8, 147.3, 142.8, 135.8, 135.5, 135.0, 134.1, 133.6, 130.0, 129.9, 129.6, 129.5, 127.9, 127.5, 123.2, 118.0, 114.4, 94.8, 75.6, 69.2, 65.3, 62.8, 61.3, 45.2, 36.1, 35.1, 34.2, 27.9, 27.2, 27.0, 26.8, 19.6, 18.2, 17.0, 13.8 and −1.2; *m*/*z* (ES+) 945 ($M^+ + 23$, 7%), 923 ($M^+ + 1$, 8), 517 (9) and 145 (100). The second fraction was the *title compound* **56** (0.152 g, 69%), as a pale yellow oil R_f = 0.4 (50% ether in petrol); ν_{max}/cm^{-1} 3068, 2925, 2855, 1735, 1664, 1543, 1446, 1318, 1149, 1109, 1030, 835 and 747; δ_H (400 MHz, C_6D_6) 7.83 (2 H, m, Ar-*H*), 7.74 (3 H, m, Ar-*H*), 7.45 (2 H, m, Ar-*H*), 7.22 (7 H, m, Ar-*H*), 6.92 (6 H, m, Ar-*H*), 6.62 (1 H, s, 2′-H), 5.39 and 5.26 (each 1 H, d, *J* 1, 1-C*H*), 5.18 (1 H, m, 6′-*H*), 4.84 and 4.73 (each 1 H, d, *J* 7, OCH*H*O), 4.45 (1 H, td, *J* 8.5, 4.5, 3-*H*), 3.97 (2 H, s, 8′-H_2), 3.75 (1 H, d, *J* 6.5, 2-*H*), 3.72 (2 H, m, CH_2CH$_2$Si), 3.29 and 3.10 (each 1 H, d, *J* 14.5, 6-C*H*), 2.17–2.07 (5 H, m, 4-H, 4′-H_2 and 5′-H_2), 1.98 (1 H, m, 5-*H*), 1.57 (1 H, td, *J* H 13.5, 5.5, 4-*H′*), 1.36 (3 H, s, 7′-CH_3),1.34 (3 H, s, 6-CH_3), 1.15 [9 H, s, SiC(CH_3)$_3$], 1.01 (2 H, m, CH_2Si), 0.80 (3 H, d, *J* 7, 5-CH_3) and 0.04 [9 H, s, Si(CH_3)$_3$]; δ_C (75 MHz, $CDCl_3$) 197.3, 162.3, 147.4, 142.5, 135.6, 135.4, 135.2, 133.7, 133.3, 131.0, 129.5, 129.2, 129.0, 127.5, 127.3, 121.8, 119.9, 114.0, 94.6, 75.7, 68.5, 65.0, 62.7, 59.8, 44.9, 36.5, 36.3, 35.3, 28.0, 26.8, 19.3, 19.2, 18.0, 16.7, 13.5, 13.3 and −1.4; *m*/*z* (ES+) 945 ($M^+ + 23$, 38%) and 923 ($M^+ + 1$, 53).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(2*E*,6*E*)-8-*tert*-Butyldiphenylsilyloxy-3,7-dimethyl-1-oxo-oct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 57

Methyllithium (1.6 M in ether, 0.26 cm^3, 0.428 mmol) was added to a suspension of copper(I) iodide (0.041 g, 0.214 mmol) in diethyl ether (0.75 cm^3) at 0 °C and the suspension stirred for 30 min. The solution was cooled to −78 °C and a precooled solution of the thioether **56** (0.152 g, 1.65 mmol) in diethyl ether (0.75 cm^3) was added using a cannula. After 30 min, saturated aqueous ammonium chloride and saturated aqueous ammonia (1:1, 2 cm^3) was added and the mixture allowed to warm to room temperature. Ether (5 cm^3) was added, the aqueous phase extracted with ether (4 × 5 cm^3) and the organic extracts combined and washed with brine (10 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 1–25% ether in petrol, afforded the *title compound* **57** (0.13 g, 97%) as a clear oil, R_f = 0.3 (50% ether in petrol) (Found; $M^+ + NH_4^+$, 846.4628. $C_{48}H_{72}O_6NSSi_2$ requires *M*, 846.4619); ν_{max}/cm^{-1} 3069, 2931, 2893, 2857, 1685, 1615, 1471, 1446, 1428, 1320, 1248, 1150, 1110, 1056, 1032, 859 and 835; δ_H (400 MHz, C_6D_6) 7.80 (6 H, m, Ar-*H*), 7.26 (6 H, m, Ar-*H*), 6.91 (3 H, m, Ar-*H*), 6.33

(1 H, s, 2′-*H*), 5.43 (1 H, t, *J* 6.5, 6′-*H*), 5.34 and 5.13 (each 1 H, s, 1-C*H*), 4.82 and 4.72 (each 1 H, d, *J* 7, OCH*H*O), 4.35 (1 H, td, *J* 9, 5, 3-*H*), 4.11 (2 H, s, 8′-H_2), 3.70 (2 H, m, CH_2CH_2Si), 3.62 (1 H, d, *J* 9, 2-*H*), 3.24 and 3.02 (each 1 H, d, *J* 15, 6-C*H*), 2.19 (3 H, s, 3′-CH_3), 2.15 (1 H, dt, *J* 13.5, 4.5, 4-*H*), 2.09 (2 H, t, *J* 7.5, 5′-H_2), 2.02 (1 H, m, 5-*H*), 1.94 (2 H, t, *J* 7.5, 4′-H_2), 1.55 (1 H, m, 4-*H*′), 1.52 (3 H, s, 7′-CH_3), 1.23 (3 H, s, 6-CH_3), 1.20 [9 H, s, $SiC(CH_3)_3$], 0.99 (2 H, m, CH_2Si), 0.77 (3 H, d, *J* 6.5, 5-CH_3) and 0.02 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 200.0, 158.9, 147.4, 142.5, 135.5, 135.0, 133.8, 133.3, 129.5, 129.2, 128.3, 127.6, 127.3, 123.8, 122.9, 113.2, 94.4, 75.7, 68.8, 65.0, 62.7, 60.3, 45.0, 41.1, 36.0, 35.5, 26.8, 25.8, 19.5, 19.3, 18.0, 16.7, 13.5 and −1.4; *m*/*z* (CI) 846 (M^+ + 18, 0.1%), 426 (3), 408 (3.5), 405 (3) and 90 (100).

(2*RS*,3*SR*,5*RS*,6*SR*)-2-[(1*SR*,2*E*,6*E*)-8-*tert*-Butyldiphenylsilyloxy-3,7-dimethyl-1-hydroxyoct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 58

Sodium borohydride (20 mg, 0.504 mmol) was added to the ketone **57** (0.278 g, 0.34 mmol) in ethanol (1.67 cm^3) at room temperature and the solution stirred for 18 h. The mixture was concentrated under reduced pressure and column chromatography of the residue, eluting with 0–20% ether in petrol, afforded the *title compound* **58** (0.165 g, 59%) as a clear oil, R_f = 0.25 (50% ether in petrol); ν_{max}/cm^{-1} 3499 (br), 2954, 2930, 2858, 1626, 1448, 1428, 1382, 1312, 1250, 1149, 1108, 1055, 1027, 936, 859, 834, 743 and 709; δ_H (300 MHz, C_6D_6) 7.80 (6 H, m, Ar-*H*), 7.24 (6 H, m, Ar-*H*), 6.92 (3 H, m, Ar-*H*), 5.65 (1 H, d, *J* 8, 2′-*H*), 5.57 (1 H, t, *J* 7, 6′-*H*), 5.49 and 5.39 (each 1 H, s, 1-C*H*), 4.75 (1 H, td, *J* 8, 3.5, 1′-*H*), 4.61 and 4.57 (each 1 H, d, *J* 7, OCH*H*O), 4.14 (2 H, br s, 8′-H_2), 3.92 (1 H, m, 3-*H*), 3.85 (1 H, d, *J* 3.5, OH), 3.62 (2 H, m, CH_2CH_2Si), 3.19 and 3.12 (each 1 H, d, *J* 14, 6-C*H*), 2.82 (1 H, dd, *J* 8, 4, 2-*H*), 2.23–2.09 (4 H, m, 4′-H_2 and 5′-H_2), 2.00 (1 H, m, 5-*H*), 1.88 (1 H, dt, *J* 14, 5.5, 4-*H*), 1.70 (3 H, s, 3′-CH_3), 1.62 (3 H, s, 7′-CH_3), 1.53 (1 H, m, 4-*H*′), 1.25 (3 H, s, 6-CH_3), 1.17 [9 H, s, $SiC(CH_3)_3$], 0.95 (2 H, m, CH_2Si), 0.89 (3 H, d, *J* 6.5, 5-CH_3) and 0.00 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, C_6D_6) 147.2, 143.0, 138.9, 135.9, 134.5, 134.2, 132.9, 129.8, 129.1, 124.7, 117.6, 93.4, 74.6, 69.5, 67.9, 65.3, 64.2, 56.4, 43.7, 39.9, 34.9, 34.7, 27.0, 26.6, 22.7, 19.5, 18.2, 17.2, 16.7, 13.6, 1.3 and −1.4.

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*SR*,2*E*,6*E*)-8-*tert*-Butyldiphenylsilyloxy-3,7-dimethyl-1-benzyloxymethoxyoct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 59

Di-isopropylethylamine (0.16 cm^3), benzyloxymethyl chloride (0.11 cm^3) and tetra-*n*-butylammonium iodide (0.005 g, 0.0127 mmol) were added to the alcohol **58** (0.105 g, 0.127 mmol) in tetrahydrofuran (0.16 cm^3) at room temperature and the solution stirred for 16 h. Methanol (0.025 cm^3) and, after 1 h, ethyl acetate (10 cm^3) and water (10 cm^3) were added. The aqueous layer was extracted with ethyl acetate (4 × 5 cm^3) and the organic extracts were washed with aqueous sodium hydrogen sulfate (0.5 M, 15 cm^3), aqueous pH 7 buffer (15 cm^3) and brine (15 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 0–20% ether in petrol, gave the *title compound* **59** (0.104 g, 85%) as a pale yellow oil, R_f = 0.6 (50% ether in petrol); ν_{max}/cm^{-1} 2927, 2889, 2862, 1470, 1316, 1253, 1152, 1105, 1029 and 833; δ_H (300 MHz, $CDCl_3$) 7.90 (2 H, dd, *J* 7, 2, Ar-*H*), 7.71 (4 H, dd, *J* 7, 1.5, Ar-*H*), 7.60–7.20 (14 H, m, Ar-*H*), 5.42 (1 H, t, *J* 7, 6′-*H*), 5.34 and 5.23 (each 1 H, s, 1-C*H*), 5.20 (1 H, m, 2′-*H*), 4.73 (3 H, br s, OCH_2O and CH*H*Ar), 4.69 (1 H, m, 1′-*H*), 4.60 (1 H, d, *J* 12, OCH*H*O), 4.56 (1 H, d, *J* 7, CH*H*′Ar), 4.48 (1 H, d, *J* 12, OCH*H*′O), 4.06 (2 H, br s, 8′-H_2), 3.79 (1 H, m, 3-*H*), 3.76 (1 H, d, *J* 14.5, 6-C*H*), 3.63 (2 H, m, CH_2CH_2Si), 3.33 (1 H, d, *J* 14.5, 6-C*H*′), 2.54 (1 H, t, *J* 5, 2-*H*), 2.15–1.95 (6 H, m, 4′-H_2, 5′-H_2, 4-*H* and 5-*H*), 1.73 (3 H, s, 3′-CH_3), 1.63 (3 H, s, 7′-CH_3), 1.59 (1 H, m, 4-*H*′), 1.42 (3 H, s, 6-CH_3), 1.09 [9 H, s, $SiC(CH_3)_3$], 1.00 (3 H, d, *J* 7, 5-CH_3), 0.94 (2 H, m, CH_2Si) and 0.04 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 147.3, 140.7, 138.2, 135.8, 134.6, 134.1, 133.4, 129.8, 129.4, 128.8, 128.7, 127.9, 127.7, 127.3, 124.2, 123.7, 117.4, 94.1, 92.0, 73.5, 70.0, 69.3, 65.6, 65.3, 64.1, 55.7, 44.3, 41.1, 39.9, 35.9, 35.2, 27.1, 26.6, 24.1, 19.6, 18.3, 17.5, 17.0, 13.8 and −1.1; *m*/*z* (ES+) 973 (M^+ + 23, 100%), 933 (18), 827 (31), 372 (81), 341 (93) and 311 (73).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*SR*,2*E*,6*E*)-3,7-Dimethyl-1-benzyloxymethoxy-8-hydroxyoct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 60

tetra-n-Butylammonium fluoride (1.0 M in tetrahydrofuran, 0.16 cm^3) was added to the silyl ether **59** (0.15 g, 0.16 mmol) in tetrahydrofuran (1.5 cm^3) at room temperature and the solution stirred for 2 h. After concentration under reduced pressure, column chromatography of the residue, eluted with 10–50% ether in petrol, gave the *title compound* **60** (0.089 g, 79%) as a pale yellow oil, R_f = 0.05 (50% ether in petrol); ν_{max}/cm^{-1} 3443 (br), 2925, 2886, 1587, 1447, 1380, 1312, 1149, 1027 and 836; δ_H (300 MHz, C_6D_6) 7.89 (2 H, m, Ar-*H*), 7.35 (2 H, d, *J* 7.5, Ar-*H*), 7.19 and 7.09 (each 1 H, m, Ar-*H*), 6.92 (4 H, m, Ar-*H*), 5.57 (1 H, m, 2′-*H*), 5.53 and 5.51 (each 1 H, s, 1-C*H*), 5.37 (1 H, t, *J* 6.5, 6′-*H*), 4.97 (1 H, dd, *J* 9, 4.5, 1′-*H*), 4.80 (1 H, d, *J* 6.5, CH*H*Ar), 4.72 (2 H, br s, OCH_2O), 4.62 (1 H, d, *J* 12, OCH*H*O), 4.61 (1 H, d, *J* 6.5, CH*H*′Ar), 4.46 (1 H, d, *J* 12, OCH*H*′O), 4.01 (1 H, m, 3-*H*), 3.86 (2 H, br s, 8′-H_2), 3.69 (1 H, d, *J* 14.5, 6-C*H*), 3.63–3.71 (2 H, m, CH_2CH_2Si), 3.38 (1 H, d, *J* 14.5, 6-C*H*′), 2.78 (1 H, t, *J* 5, 2-*H*), 2.25–1.95 (6 H, m, 4-*H*, 5-*H*, 4′-H_2, 5′-H_2), 1.65 (3 H, s, 3′-CH_3), 1.61 (1 H, m, 4-*H*), 1.55 (3 H, s, 7′-CH_3), 1.50 (3 H, s, 6-CH_3), 0.95 (2 H, CH_2Si), 0.92 (3 H, d, *J* 7, 5-CH_3) and 0.00 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 147.4, 143.8, 139.5, 138.5, 135.8, 132.6, 129.0, 128.5, 127.7, 124.8, 124.3, 117.4, 94.1, 92.1, 76.9, 73.6, 69.8, 68.4, 65.1, 64.1, 54.1, 44.4, 39.5, 36.1, 35.4, 30.3, 25.7, 20.8, 18.2, 17.3, 16.4, 13.7, 1.3 and −1.4; *m*/*z* (ES+) 735 (M^+ + 23, 100%), 640 (23), 589 (23), 140 (42) and 126 (44).

(2*SR*,3*SR*,5*RS*,6*SR*)-2-[(1*SR*,2*E*,6*E*)-8-Bromo-3,7-dimethyl-1-benzyloxymethoxyoct-2,6-dien-1-yl]-5,6-dimethyl-6-phenylsulfonylmethyl-3-(2-trimethylsilylethoxy)methoxy-1-methylenecyclohexane 61

Triethylamine (0.016 cm^3, 0.112 mmol) and methanesulfonyl chloride (0.006 cm^3, 0.0702 mmol) were added to the alcohol **60** (20 mg, 0.028 mmol) in dichloromethane (0.41 cm^3) at 0 °C and the solution stirred at room temperature for 0.5 h. After

cooling to 0 °C, lithium bromide (0.036 g, 0.422 mmol) in acetone (0.3 cm^3) was added, and the mixture stirred at room temperature for 0.5 h then filtered through a pad of celite. The filter cake was washed with dichloromethane and the filtrate concentrated under reduced pressure. The residue was taken up in ethyl acetate (2 cm^3) and washed with saturated aqueous sodium bicarbonate (2 cm^3). The aqueous layer was extracted with ethyl acetate (4 × 2 cm^3) and the organic extracts were washed with brine (4 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluting with 0–15% ether in petrol, afforded the *title compound* **61** (0.015 g, 69%) as a clear oil, R_f = 0.5 (50% ether in petrol); ν_{max}/cm^{-1} 2926, 2892, 1663, 1633, 1449, 1381, 1315, 1251, 1150, 1093, 1030, 854 and 836; δ_H (300 MHz, $CDCl_3$) 7.91 (2 H, d, *J* 7.5, Ar-*H*), 7.74 (1 H, dd, *J* 7, 2, Ar-*H*), 7.56 (3 H, m, Ar-*H*), 7.37 (4 H, m, Ar-*H*), 5.57 (1 H, t, *J* 6, 6′-*H*), 5.37 (1 H, s, 1-C*H*), 5.30 (1 H, d, *J* 7.5, 2′-*H*), 5.25 (1 H, s, 1-C*H*′), 4.75–4.65 (4 H, m, OCH_2O, OCH*H*O and 1′-H), 4.60 (1 H, d, *J* 12, CH*H*Ar), 4.58 (1 H, d, *J* 6.5, OCH*H*′O), 4.50 (1 H, d, *J* 12, CH*H*′Ar), 3.96 (2 H, br s, 8′-H_2), 3.79 (1 H, m, 3-*H*), 3.71 (1 H, d, *J* 14.5, 6-C*H*), 3.62 (2 H, m, OCH_2CH_2Si), 3.35 (1 H, d, *J* 14.5, 6-C*H*′), 2.52 (1 H, t, *J* 5, 2-*H*), 2.17–2.00 (5 H, m, 4′-H_2, 5′-H_2 and 4-*H*), 1.97 (1 H, m, 5-*H*), 1.76 (3 H, s, 3′-CH_3), 1.70 (3 H, s, 7′-CH_3), 1.55 (1 H, m, 4-*H*′), 1.41 (3 H, s, 6-CH_3), 0.95 (5 H, m, CH_2Si and 5-CH_3) and 0.03 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 147.2, 143.0, 139.6, 138.1, 135.1, 133.4, 130.9, 129.9, 129.4, 128.7, 127.9, 127.6, 124.3, 117.1, 94.2, 92.2, 73.5, 70.0, 65.3, 64.0, 53.5, 44.4, 41.9, 39.1, 36.2, 35.3, 26.8, 24.1, 20.4, 18.3, 17.4, 16.8, 15.0 and −1.2; *m*/*z* (ES+) 799 (M^+ + 23, 100%), 797 (M^+ + 23, 80), 753 (22) and 652 (25).

(1*SR*,2*SR*,11*SR*,12*RS*,14*SR*,3*E*,7*E*)-4,8,11,12-Tetramethyl-15-methylene-14-(2-trimethylsilylethoxy)methoxybicyclo-[9.3.1]pentadec-3,7-dien-2-ol 63

Sodium hexamethyldisilazide (1.0 M in tetrahydrofuran, 0.248 mmol) was added over 40 min to the bromide **61** (0.064 g, 0.0826 mmol) in tetrahydrofuran (1.65 cm^3) at 0 °C using a syringe pump. The solution was stirred for 30 min then saturated aqueous ammonium chloride (5 cm^3) and ethyl acetate (5 cm^3) were added. The aqueous phase was extracted into ethyl acetate (4 × 5 cm^3) and the organic extracts washed with brine (5 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure.

The residue in tetrahydrofuran (1 cm^3) was added to liquid ammonia (1.5 cm^3) at −60 °C, followed by ethanol (0.007 cm^3). Finely chopped sodium was added until a dark blue colour persisted. Solid ammonium chloride was added until the solution was decolourised and the white residue was allowed to warm to room temperature and stirred for 30 min to allow evaporation of ammonia. Tetrahydrofuran (10 cm^3) was added and the mixture filtered through a pad of cotton-wool. The filtrate was concentrated under reduced pressure and the residue dissolved in water (10 cm^3). The aqueous phase was extracted with ethyl acetate (5 × 5 cm^3) and the organic extracts washed with brine (10 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography of the residue, eluted with 0–10% ether in petrol, afforded the *title compound* **63** (16 mg, 45% from **61**) as a clear oil, R_f = 0.6 (20% ether in petrol); ν_{max}/cm^{-1} 3483 (br), 2954, 2924, 2855, 1725, 1463, 1372, 1249, 1110, 1054, 1021, 857 and 836; δ_H (300 MHz, $CDCl_3$) 5.57 (2 H, s, 15-C*H* and 3-*H*), 4.93 (1 H, m, 15-C*H*′), 4.89 (2 H, m, 2-*H* and 7-*H*), 4.74 (2 H, s, OCH_2O), 3.90–3.50 (4 H, m, CH_2CH_2Si, O*H* and 14-*H*), 2.54 (1 H, dt, *J* 14, 7, 13-*H*), 2.42 (1 H, dd, *J* 11, 4.5, 1-*H*), 1.98–2.20 (6 H, m, 5-H_2, 6-H_2 and 9-H_2), 1.87 (1 H, m, 13-*H*′), 1.73 (2 H, m, 10-H_2), 1.57 (3 H, s, 4-CH_3), 1.54 (3 H, s, 8-CH_3), 1.34 (1 H, m, 12-*H*), 0.98 (2 H, m, CH_2Si), 0.84 (3 H, s, 11-CH_3), 0.75 (3 H, d, *J* 6.5, 12-CH_3) and 0.09 [9 H, s, $Si(CH_3)_3$]; δ_C (75 MHz, $CDCl_3$) 153.0, 133.6, 131.4, 130.7, 130.2, 109.8, 96.6, 82.6, 67.5, 66.2, 51.0, 47.3, 43.8, 39.2, 38.8, 35.4, 29.9, 25.5, 19.0, 18.2, 17.9, 17.3, 15.4 and −1.3; *m*/*z* (ES+) 458 (M^+ + 23, 81%), 419 (23), 391 (72), 359 (22), 272 (31) and 271 (44).

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