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1,5-Stereocontrol in reactions of 2,4-disubstituted alk-2-enylstannanes with aldehydes; an approach to the stereoselective synthesis of branched triols☆

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ABSTRACT

2-(*tert*-Butyldimethylsilyloxymethyl)-4-(methoxymethoxy)pent-2-enyl(tributyl)stannane is transmetallated by tin(IV) chloride stereoselectively to give a pent-1-en-3-yltin trichloride that reacts with aldehydes with excellent (*E*)-1,5-*syn*-stereocontrol, e.g. (3*E*)-1,5-*syn*-3-(*tert*-butyldimethylsilyloxymethyl)-5-(methoxymethoxy)-1-phenylhex-3-en-1-ol was the dominant product with benzaldehyde. The products from these reactions were taken through to more complex 2-substituted alk-2-enyl(tributyl)stannanes but only very low yields of the expected products were obtained from tin(IV) chloride mediated reactions of these stannanes and aldehydes. Nevertheless a stereoselective synthesis of 2-substituted 4-[(*E*)-2-alkoxypropylidene]tetrahydrofurans was developed.

1. Introduction

Lewis acid mediated reactions of alk-2-enyl(trialkyl)stannanes with aldehydes have been widely investigated [1]. Reactions of 4-, 5- and 6-alkoxy-alk-2-enyl(tributyl)stannanes with aldehydes when promoted by transmetallation using tin(IV) halides proceed with effective 1,5-, 1,6- and 1,7-(*Z*)-stereocontrol [2]. For example, 4-benzyloxypent-2-enyl(tributyl)stannane (**1**) reacts with aldehydes to give the (*Z*)-alkenols **2** with excellent 1,5-*syn*-stereoselectivity following stereoselective transmetallation with tin(IV) chloride, see Scheme 1.

It was decided to study the scope of this chemistry using more complex allylstannanes. In this context, the branched differentially protected triols **3** were identified as challenging targets for stereoselective synthesis since they could be useful as novel molecular scaffolds. They should be accessible by hydrogenation of the alkenes **4** which were expected to be available from tin(IV) halide mediated reactions of allylstannanes **5** with aldehydes. The allylstannanes **5** would be prepared from the homoallylic alcohols **6**, products from *syn*-selective reactions between allylstannanes **7** and aldehydes mediated by tin(IV) halides, see Scheme 2.

In this synthesis, the protecting group (P) in the allylstannanes **5** and **7** will be selected so that it will co-ordinate to the tin in the reactive allyltin trihalide intermediates, so directing stereoselective reactions with aldehydes to give 1,5-*syn*-5-alkoxyalk-3-enols **4** and **6** as the major products, *cf.* the example shown in Scheme 1 [3]. The trialkylsilyloxy groups should not participate in these reactions since they should not compete as ligands for the tin [4]. It is known that the (*E*,*Z*)-geometry of the 4-alkoxyalk-2-enylstannanes does not affect the (*Z*)-1,5-stereoselectivity of their reactions with aldehydes [2] and so mixtures of the geometrical isomers of stannanes **5** and **7** may be used. All of the stereogenic centres in the final alkene **4** should be 1,5-*syn*-disposed due to the expected 1,5-*syn*-stereoselectivities of the reactions of stannanes **5** and **7** with aldehydes. Therefore, racemic stannanes can be used in this work to deliver racemic products diastereoselectively.

The central tertiary carbon of the target compounds **3** is stereogenic and hydrogenation of the alkenol **4** could give rise to two diastereoisomers. However, the free hydroxyl group may influence the stereoselectivity of this process. As an aside, the central tertiary carbon in triols prepared by deprotection of the final products **3** will not be stereogenic if any two of the alkyl groups R^1, R^2 or R^3 are identical.

☆ This paper is dedicated to Stephen G. Davies in recognition of his outstanding contributions to organic chemistry.

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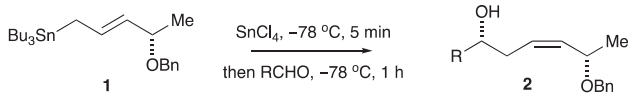
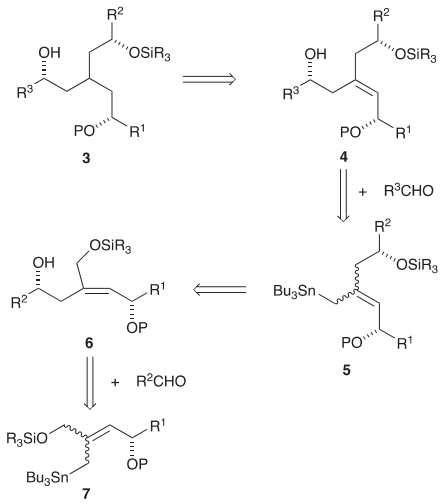


Scheme 1. 1,5-*syn*-(*Z*)-Stereoselectivity in the reactions of 4-alkoxypent-2-enylstannanes and aldehydes.



Scheme 2. Proposed stereoselective synthesis of derivatives of branched triols using complex allylstannanes.

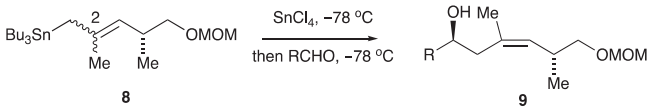
Apart from hoping that this work would lead to the potentially interesting products **3**, the initial objective was to see whether the stereoselectivity of the tin(IV) halide mediated reactions of 4-alkoxyalk-2-enylstannanes was compatible with substituents at the 2-position. At the onset of the work, (*Z*)-1,5-*anti*-selectivity had been shown for reactions of the 5-(methoxymethoxy)-2,4-dimethylpent-2-enyl(tributyl)stannanes **8** with aldehydes, see Scheme 3.[2a,5] However, in these reactions the 2-substituent in the stannane is an unfunctionalised methyl group and so it was not clear whether or not the stereoselectivity of the reaction would tolerate a more bulky, functionalised, alkyl group at this site.

It was therefore decided to prepare a 4-alkoxy-2-(trialkylsilyloxymethyl)pent-2-enyl(tributyl)stannane **7** ($R^1 = Me$), and to study its reactions with aldehydes mediated by tin(IV) chloride. If successful, the products would be used to prepare more complex allylstannanes, *cf.* **5**, and the reactivities of these would be investigated. The results of this study are reported herein [6].

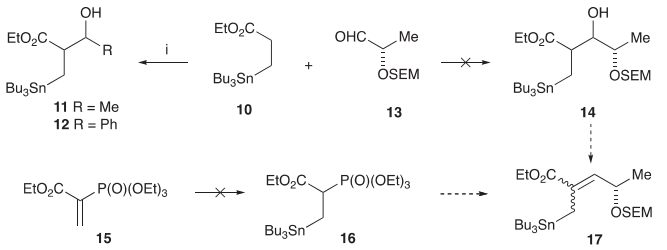
2. Results and discussion

Preliminary studies of the aldol reactions of ethyl 3-tributyltinpropanoate **10** [7] with acetaldehyde and benzaldehyde gave modest yields of the expected adducts **11** and **12**, but the analogous reaction with 2-(trimethylsilylethoxymethoxy)propanal **13** gave only unreacted starting material, see Scheme 4.

Attempts to effect a conjugate addition of tributyltin hydride to the 2-substituted acrylate **15** [8] under basic and free-radical



Scheme 3. (*Z*)-1,5-*anti*-stereoselective reactions of aldehydes with 2,4-dimethyl-5-(methoxymethoxy)pent-2-enylstannane **8**.



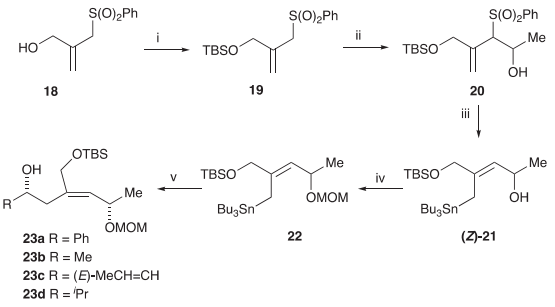
Scheme 4. Reagents and conditions: i, LDA, THF, −78 °C, 45 min, then RCHO, −78 °C, 10 min (R = Me, 45%; R = Ph, 23%).

conditions were also unsuccessful and so dehydration of the aldol adduct **14** or a Wadsworth-Emmons-Horner reaction of phosphonate **16** could not be investigated for the synthesis of the allylstannane **17** *en route* to the SEM-analogue of the target stannane **7** ($R^1 = Me$) see Scheme 4.

In previous work, the allylic displacement of a phenylsulfonyl group by a tributyltin moiety under free-radical conditions has proved to be a useful procedure for the synthesis of substituted allylstannanes [9]. 2-(Hydroxymethyl)propenyl phenyl sulfone (**18**) [10] was therefore protected as its *tert*-butyldimethylsilyl ether **19**. Addition of the lithiated sulfone **19** to freshly distilled acetaldehyde gave the adduct **20** as a mixture of diastereoisomers. A little surprisingly, the free-radical mediated allylic displacement of the mixture of sulfones **20** using tributyltin hydride in the presence of a sub-stoichiometric amount of azo-bis-*iso*butyronitrile (AIBN) gave the pent-2-enylstannane **21** predominantly as its (*Z*)-diastereoisomer, (*Z*) : (*E*) = 90 : 10 (^{1}H NMR), see Scheme 5.

The (*Z*)-geometry of the major allylstannane **21** was established by nOe studies. It has been suggested that the free-radical displacement of an allylic sulfone by a tributyltin radical is a concerted process in which allylic 1,3-strain is minimised [11]. In the present case, the formation of the major isomer (*Z*)-**21** by this mechanism is consistent with the transition structure **24**, see Fig. 1, being preferred over the alternative **25**. A non-concerted process with the tributyltin group of an intermediate tributyltin radical adduct co-ordinated to the hydroxyl group, see structure **26**, is also consistent with the observed stereoselectivity, but hydroxyl groups do not usually co-ordinate to tetralkylstannanes [12], see Fig. 1.

The 4-hydroxypent-2-enyl(tributyl)stannane **21** was alkylated using methoxymethyl chloride to give the required 4-alkoxypent-2-enylstannane **22**. Transmetallation of this allylstannane with tin(IV) chloride at −78 °C generated an allyltin trichloride that reacted with aldehydes highly stereoselectively to give major



Scheme 5. Synthesis and reactions with aldehydes of the 4-alkoxypent-2-enyl(tributyl)stannane **22**. Reagents and conditions: i, TBSCl, imid., CH_2Cl_2, 0 °C to rt, 15 h (73%); ii, LDA, −78 °C, 45 min, MeCHO, −78 °C, 30 min (68%, 55:45 mixture of diastereoisomers); iii, Bu_3SnH, AIBN (cat.), benzene, reflux, 2 h [69%, (*Z*) : (*E*) = 90 :10]; iv, MOMCl. $^i Pr_2NEt$, CH_2Cl_2, 0 °C to rt, 15 h (82%); v, $SnCl_4$, CH_2Cl_2, −78 °C, 5 min, add RCHO, −78 °C, 30 min (**23a**, 69%; **23b**, 57%; **23c**, 62%; **23d**, 59%).

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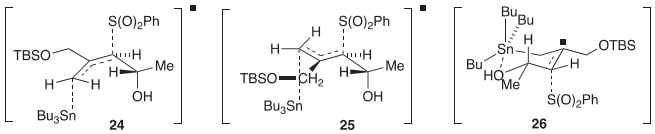
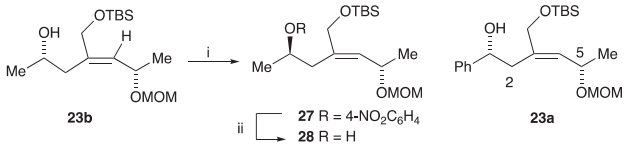


Fig. 1. Possible transition structures for the selective formation of the (*Z*)-4-hydroxypent-2-enylstannane (*Z*)-**21**.

products identified as the (*E*)-1,5-*syn*-isomers **23** [3], see Scheme 5. Less than 3% of any other diastereoisomer was detected in the product mixtures from these reactions.

Structures were assigned to the products **23** on the basis of precedent and spectroscopic data. To show that the 1,5-*syn*- and 1,5-*anti*-diastereoisomers could be distinguished by NMR, the major reaction product **23b** was converted into the inverted 4-nitrobenzoate **27** using a Mitsunobu reaction, and saponification gave the 1,5-*anti*-epimer **28**, Scheme 6. The *syn*- and *anti*-isomers **23b** and **28** were clearly distinguished by ^{1}H NMR, see experimental. The (*E*)-configuration [3] of the alkenol **23a** was confirmed by ^{1}H nOe. For example, irradiation of the 2-H_2 and 3-CH_2 caused significant enhancements of H-5 and H-4, respectively.

Following confirmation of the high (*E*)-stereoselectivity in the formation of the major product **23a**, the 1,5-*syn*-configuration was assigned on the basis of well precedented mechanistic considerations, see Fig. 2. Transmetallation of 4-alkoxyalk-2-enylstannanes has been shown to be highly stereoselective for the formation of allyltin trichloride intermediates in which the adjacent vinyl and methyl substituents are in a *trans*-relationship with respect to the four-membered oxastannane ring [2,4]. In the case of the MOM-protected stannane **22**, the expected transmetallation intermediate would be the epimer **31** formed *via* transition structure **29**. This stereoselectivity would be expected irrespective of which oxygen of the MOM-group was co-ordinated to the trichlorotin group [13,14]. Reaction of this intermediate allyltin trichloride with an aldehyde *via* the six-membered transition structure **32** that would introduce the (*E*)-double-bond into the product, would then give rise to the



Scheme 6. Conversion of the 1,5-*syn*-alkenol **23b** into its 1,5-*anti*-epimer **28**. Reagents and conditions: i, Ph_3P, 4-$NO_2C_6H_4CO_2H$, DEAD, THF, rt, 2 h (79%); ii, NaOH, MeOH, rt, 2 h (66%).

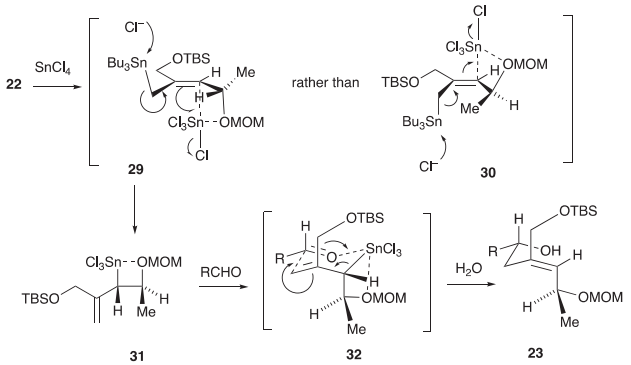


Fig. 2. Participation of the allyltin trichloride **31** in the stereoselective formation of the homoallylic alcohols **23**.

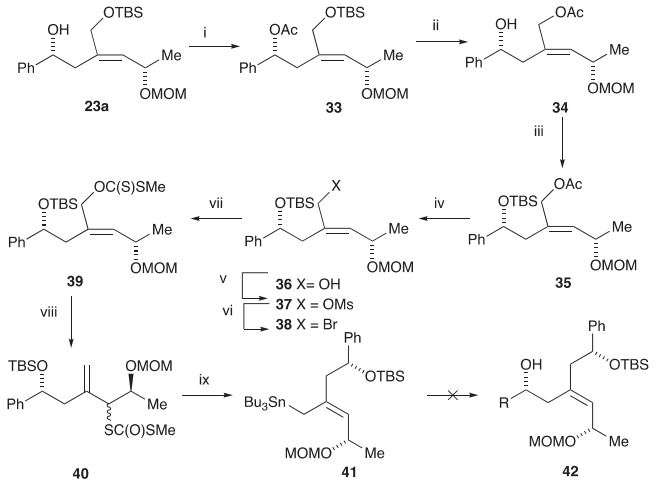
1,5-*syn*-products **23**, see Fig. 2.

The products **23** correspond to the intermediates **6** in the proposed synthesis of the branched triol derivatives **3**. The next stage was to convert these into the alkenylstannanes **5**. To effect this transformation, the hydroxyl group would need protection as a trialkylsilyl ether, and the *tert*-butyldimethylsilyloxy group converted into a tributylstannane.

As interim protection, the alcohol **23a** was converted into its acetate **33**, but removal of the *tert*-butyldimethylsilyl group was accompanied by migration of the acetate to give the hydroxyacetate **34**, migration of the acetate being confirmed by ^{1}H NMR, see experimental. Procedures are known for the conversion of primary allylic acetates into allylstannanes [15] and so the alcohol **34** was reprotected as its *tert*-butyldimethylsilyl ether **35**, Scheme 7. However, attempts to convert this allylic acetate into the corresponding tributylstannane were unsuccessful and mixtures of products were obtained. Saponification of the acetate gave the primary alcohol **36** which was converted into the mesylate **37** and hence into the bromide **38**, but treatment of these with tributyltin lithium or bis(tributyltin) oxide, 1,2-dibromoethane and magnesium, respectively, under published conditions [16] for the preparation of allylstannanes gave mixtures of products including elimination products. The conversion of alcohols into allylstannanes *via* their xanthates and rearranged dithiocarbonates is another well recognised procedure [2] and so the alcohol **36** was converted into the rearranged dithiocarbonate **40** *via* its xanthate **39**. In this case, reaction of the dithiocarbonate with tributyltin hydride under free-radical conditions gave the required allylstannane **41** in an acceptable yield of 58%, as a 94 : 6 mixture of geometrical isomers, Scheme 7. Again the major allylstannane **41** was shown to have the (*Z*)-configuration by nOe possibly due to some co-ordination of the tributyltin moiety by the MOM-group in free-radical intermediates, cf. Fig. 1.

This chemistry had led to the synthesis of the complex 2-substituted alk-2-enylstannane **41**, but attempts to effect tin(IV) chloride promoted reactions of this with aldehydes, including benzaldehyde and acetaldehyde, were unsuccessful and polymeric materials were the only products isolated.

It was decided to prepare a second allylstannane corresponding



Scheme 7. Synthesis and preliminary studies of the pent-2-enyl(tributyl)stannane **41**. Reagents and conditions: i, Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 1 h (94%); ii, TBAF, THF, rt, 1 h (60%); iii, TBSOTf, Et_3N, CH_2Cl_2, 0 °C to rt, 90 min (85%); iv, NaOH, MeOH, rt, 1 h (96%); v, mesyl anhydride, Et_3N, CH_2Cl_2, 0 °C to rt, 3 h (89%); vi, NaBr, DMF, rt, 6 h (85%); vii, NaH, tol., 0 °C to rt, 90 min, cooled to 0 °C, CS_2, 0 °C to rt, 3 h, MeI, rt, 18 h (63%); viii, tol., reflux, 6 h (ca. 100%); ix, Bu_3SnH, AIBN (cat.), tol., reflux, 90 min [58%, (*Z*) : (*E*) = 94:6].

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to intermediate **5** to investigate further the proposed stereoselective synthesis of the branched target compounds **3**. It wasn't clear why the reactions of the stannane **41** with aldehydes had not been successful but it was decided to use the acetaldehyde-derived product **23b** to prepare the next allylstannane and the more hindered *tert*-butyldiphenylsilyl ether for protection of the non-participating hydroxyl group.

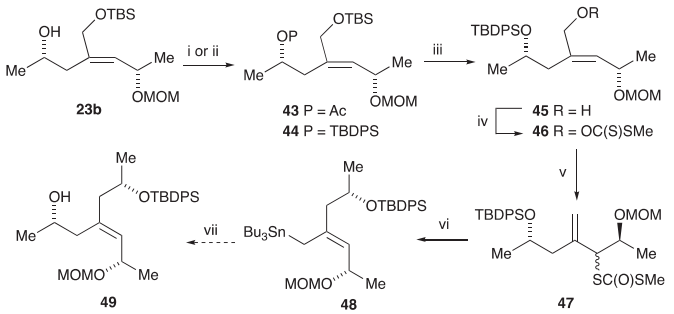
Acetylation of the homoallylic alcohol **23b** gave the acetate **43** but on desilylation only partial migration of the acetate group was observed and attempts to drive it to completion using base were unsuccessful. However, protection of the alcohol **23b** using *tert*-butyldiphenylsilyl chloride gave the bis-silylated diol **44** and selective removal of the *tert*-butyldimethylsilyl group using pyridinium toluene *p*-sulfonate [17] gave the required primary alcohol **45**. This was converted into its xanthate **46** that on heating in toluene rearranged to give the dithiocarbonate **47** as a mixture of epimers. The reaction with tributyltin hydride under free-radical conditions then gave the required allylstannane **48**, see Scheme 8. The geometry of the double-bond in this alkenylstannane was not confirmed but is shown as the (*Z*)-isomer by analogy with the stereoselectivity observed during the formation of the stannanes **22** and **41**.

Studies of the tin(IV) chloride mediated reactions of the stannane **48** with aldehydes were not encouraging. Generally polymeric materials were the main products, and only the attempted reaction with acetaldehyde gave a very low yield of the alcohol **49**. This product was provisionally identified on the basis of its ^{1}H NMR spectrum and MS data and by analogy with the earlier work, but the relative configurations of the stereogenic centres and the geometry of the double-bond were not formally established, see Scheme 8.

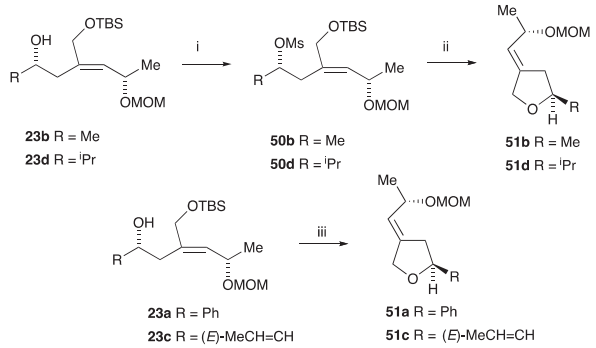
Notwithstanding the difficulties in using the complex stannanes **41** and **48** in reactions with aldehydes, aspects of the chemistry of the homoallylic alcohols **23** prepared from the earlier allylstannane **22** were briefly investigated. In particular, the alcohols **23b** and **23d** were converted into their mesylates **50b** and **50d**. On desilylation these gave the tetrahydrofurans **51b** and **51d**, respectively. The mesylates from the benzylic and allylic alcohols **23a** and **23c** were unstable. In these cases the mesylation, desilylation and cyclisation were carried out in one pot over a period of 18 h, see Scheme 9.

3. Summary and conclusions

The 2-substituted 4-alkoxypent-2-enyl(tributyl)stannanes **22**, **41** and **48** have been synthesised and their reactions with aldehydes that were promoted by tin(IV) chloride have been investigated. During their syntheses, the free-radical mediated allylic displacements of sulfur-based leaving groups by the tributyltin moiety were surprisingly stereoselective for formation of (*Z*)-pent-2-enyl(tributyl)stannanes. The 2-(*tert*-butyldimethylsilyloxymethyl)pent-2-enylstannane **22** reacted with aldehydes with excellent stereoselectivity in favour of formation of (*E*)-1,5-*syn*-alkenols **23** on transmetallation with tin(IV) chloride [3]. However, the analogous reactions using the 2-(2-*tert*-butyldimethyl- and 2-(2-*tert*-butyldiphenyl-silyloxyalkyl)pent-2-enylstannanes **41** and **48** were unsuccessful and unidentifiable polymeric products were isolated. Only a trace of the required product **49** was isolated in just one case.



Scheme 8. Synthesis and preliminary study of the pent-2-enyl(tributyl)stannane **48**. Reagents and conditions: i, Ac_2O, Et_3N, DMAP, CH_2Cl_2, 0 °C to rt, 1 h (76%); ii, TBDPSCl, imid., CH_2Cl_2, rt, 18 h (83%); iii, PPTS, EtOH, rt, 40 °C, 4 h (72%); iv, NaH, THF, rt, 90 min, CS_2, 2 h, MeI, rt, 18 h (70%); v, tol., reflux, 2 h (ca. 100%, 55 : 45 mixture of diastereoisomers), vi, Bu_3SnH, AIBN (cat.), benzene, reflux 1 h (77%, 70 : 30 mixture of geometrical isomers); vii, $SnCl_4$, CH_2Cl_2, −78 °C, 5 min, MeCHO, CH_2Cl_2, −78 °C, 45 min (1–2%).



Scheme 9. Synthesis of tetrahydrofurans **51**. Reagents and conditions: i, mesyl anhydride, Et_3N, CH_2Cl_2, 0 °C to rt, 2 h (**50b**, 91%; **50d**, 37%); ii, TBAF, THF, rt, 15 min (**51b**, 36%; **51d**, 43%); iii, mesyl anhydride, Et_3N, CH_2Cl_2, 0 °C to rt, 18 h (**51a**, 33%; **51c**, 24%).

The different behaviour of these stannanes is difficult to rationalise. Steric hindrance may be a factor. Another consideration may be the additional co-ordination of the electron deficient tin in the trichlorotin intermediates generated by transmetallation of these stannanes, see Fig. 3. If the tin trichloride is hexa-co-ordinated it will be unable to co-ordinate to an aldehyde and so unable to react to give the required products. It is conceivable that the equilibrium of penta- and hexa-co-ordinated tin trichlorides is biased towards hexaco-ordination for the allyltin trichlorides **52** but less so for the allyltin trichloride **31** perhaps because the co-ordination by the silyloxy groups would involve a five-membered co-ordinated species in the latter intermediate. If this is the case, then it is the position of the silyloxy group that determines the usefulness of the reactions of the stannanes **22**, **41** and **48** with aldehydes [18].

Clearly further work is required to resolve this dichotomy. Alternative protecting groups will need to be investigated for the non-participating hydroxyl groups. Perhaps other reaction

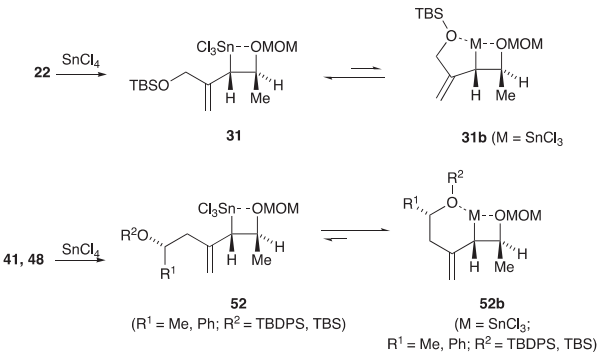


Fig. 3. Organotin trichlorides from transmetallation of pent-2-enylstannanes **22**, **41** and **48**.

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conditions will also be investigated, e.g. transmetallation using tin(IV) bromide. However, the reactions with aldehydes of the stannane **22** have led to the stereoselective synthesis of the useful products **23** with control of the geometry of trisubstituted double-bonds as illustrated in the subsequent syntheses of the 2-substituted 4-(2-alkoxyalkylidene)tetrahydrofurans **51**.

4. Experimental

4.1. General experimental details

Chromatography refers to flash column chromatography using Merck silica gel 60H (40–63 μ, 230–300 mesh). Light petroleum refers to the fraction boiling between 40 and 60 °C and was redistilled before use. THF was dried over sodium-benzophenone and distilled under nitrogen prior to use. CH_2Cl_2 was dried over CaH_2 and distilled before use. Ether refers to diethyl ether. Reactions under non-aqueous conditions were carried out under an atmosphere of nitrogen or argon. Low resolution electron impact (EI^+) and chemical ionisation mass spectra using ammonia (CI^+) were recorded using a Micromass Trio 2010 quadrupole mass spectrometer. Low resolution electrospray (ES) mass spectra were recorded on a Micromass Platform mass spectrometer. High solution mass spectra were recorded on a Kratos Concept-IS spectrometer. For organostannanes, peaks corresponding to the ^{120}Sn isotope are given. Infra-red spectra were measured using an ATI Mattson Genesis FTIR spectrometer on NaCl plates, either neat or in nujol. Nuclear magnetic resonance spectra were recorded using Varian Unity 500 (500 MHz) and Varian INOVA 300 (300 MHz) spectrometers. Coupling constants (*J*) are given in Hertz (Hz) and chemical shifts are relative to tetramethylsilane. Residual non-deuterated solvent was used as the internal standard.

4.2. Experimental procedures

4.2.1. Ethyl 3-hydroxy-2-(tri-n-butylstannylmethyl)butanoate (*11*)

n-Butyllithium (1.4 M in hexanes, 1.0 mL, 1.4 mmol) was added to di-isopropylamine (0.2 mL, 1.4 mmol) in THF (5 mL) at 0 °C and the mixture stirred for 30 min. The mixture was cooled to −78 °C, the β-stannyl ester **10** (0.5 g, 1.28 mmol) in THF (2 mL) was added, and the mixture was stirred for 45 min at −78 °C. Freshly distilled acetaldehyde (79 μL, 1.41 mmol) in THF (2 mL) was added at −78 °C and the mixture stirred for 10 min. Methanol (1 mL) followed by saturated aqueous ammonium chloride (2 mL) were added, and the mixture allowed to warm to rt. The mixture was poured into water (20 mL) and extracted with ether (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 10), gave the *title compound* **11** (250 mg, 45%, a 60 : 40 mixture of diastereoisomers) as a colourless oil; major diastereoisomer: R_F [ether-light petroleum (1 : 10)] 0.33 (Found: $M^+ - C_4H_9$, 379.1291. $C_{15}H_{31}O_3^{120}Sn$ requires *M*, 379.1294); ν_{max} (neat)/cm^{-1} 3442, 1730, 1462, 1374, 1253, 1184, 1105 and 1037; δ_H (300 MHz; $CDCl_3$) 4.19 (2H, m, CO_2CH_2), 3.97 (1H, m, 3-H), 2.63 (1H, dt, *J* 10.6, 4.8, 2-H), 2.42 (1H, d, *J* 5.6, OH), 1.49 (6H, m, 3 × $SnCH_2CH_2$), 1.33 (9H, m, 3 × $SnCH_2CH_2CH_2$ and $CO_2CH_2CH_3$), 1.22 (3H, d, *J* 6.5, 4-H_3) and 0.92 (17H, m, 3 × $SnCH_2CH_2CH_2CH_3$ and 2-CH_2); δ_C (75 MHz; $CDCl_3$) 175.9, 70.2, 60.6, 49.5, 29.0, 27.3, 19.7, 14.1, 13.6, 9.3 and 5.6; *m/z* (CI) 379 ($M^+ - 57$, 100%) and 308 (13); minor diastereoisomer: R_F [ether-light petroleum (1 : 10)] 0.30 (Found: $M^+ - C_4H_9$, 379.1293. $C_{15}H_{31}O_3^{120}Sn$ requires *M*, 379.1294); ν_{max} (neat)/cm^{-1} 3438, 1730, 1462, 1376, 1260, 1184, 1136, 1112, 1070 and 1040; δ_H (300 MHz; $CDCl_3$) 4.09 (2H, m, CO_2CH_2), 3.72 (1H, m, 3-H), 2.56 (1H, d, *J* 6.9, OH), 2.47 (1H, ddd, *J* 8.4, 7.1, 5.9, 2-H), 1.39 (6H, m, 3 × $SnCH_2CH_2$), 1.23 (9H, m, 3 × $SnCH_2CH_2CH_2$ and $CO_2CH_2CH_3$), 1.16 (3H, d, *J* 6.5, 4-H_3) and 1.00–0.66 (17H, m, 3 × $SnCH_2CH_2CH_2CH_3$ and 2-CH_2); δ_C (75 MHz; $CDCl_3$) 176.3, 71.0, 60.6, 50.0, 29.0, 27.3, 21.2, 14.1, 13.6, 9.2 and 8.5; *m/z* (CI) 437 ($M^+ + 1$, 8%), 379 ($M^+ - 57$, 100) and 308 (33).

4.2.2. Ethyl 3-hydroxy-3-phenyl-2-(tri-n-butylstannylmethyl) propanoate (*12*)

Following the procedure given for the preparation of **11**, *n*-butyllithium (1.4 M in hexanes, 1.0 mL, 1.4 mmol), di-isopropylamine (0.2 mL, 1.4 mmol), the β-stannyl ester **10** (0.5 g, 1.28 mmol) and benzaldehyde (0.14 mL, 1.4 mmol) gave the *title compound* **12** (147 mg, 23%, a 60 : 40 mixture of diastereoisomers) as a colourless oil; major diastereoisomer: R_F [ether-light petroleum (1 : 10)] 0.2 (Found: $M^+ - C_4H_9$, 441.1455. $C_{20}H_{33}O_3^{120}Sn$ requires *M*, 441.1451); ν_{max} (neat)/cm^{-1} 3468, 1720, 1455, 1374, 1339, 1250, 1183, 1156, 1040, 1027 and 699; δ_H (300 MHz; $CDCl_3$) 7.34 (5H, m, ArH), 4.97 (1H, dd, *J* 5.0, 3.2, 3-H), 4.07 (2H, m, CO_2CH_2), 2.91 (1H, m, 2-H), 2.74 (1H, d, *J* 3.2, OH), 1.44 (6H, m, 3 × $SnCH_2CH_2$), 1.29 (6H, m, 3 × $SnCH_2CH_2CH_2$), 1.17 (3H, t, *J* 7.1, $CO_2CH_2CH_3$) and 1.16–0.68 (17H, m, 3 × $SnCH_2CH_2CH_2CH_3$ and 2-CH_2); δ_C (75 MHz; $CDCl_3$) 175.7, 141.7, 128.1, 127.5, 126.1, 75.9, 60.6, 50.5, 29.0, 27.3, 13.9, 13.6, 9.3 and 5.4; *m/z* (CI) 499 ($M^+ + 1$, 25%), 481 ($M^+ - 17$, 53), 441 ($M^+ - 57$, 100), 335 (75) and 308 (93); minor diastereoisomer: R_F [ether-light petroleum (1 : 10)] 0.1 (Found: $M^+ - C_4H_9$, 441.1444. $C_{20}H_{33}O_3^{120}Sn$ requires *M*, 441.1451); ν_{max} (neat)/cm^{-1} 3443, 1731, 1455, 1375, 1250, 1180, 1160, 1040 and 700; δ_H (300 MHz; $CDCl_3$) 7.36 (5H, m, ArH), 4.72 (1H, dd, *J* 7.3, 5.6, 3-H), 4.15 (2H, m, CO_2CH_2), 3.08 (1H, d, *J* 5.6, OH), 2.93 (1H, ddd, *J* 10.6, 7.3, 5.0, 2-H), 1.43 (6H, m, 3 × $SnCH_2CH_2$), 1.28 (9H, m, 3 × $SnCH_2CH_2CH_2$ and $CO_2CH_2CH_3$) and 1.06–0.68 (17H, m, 3 × $SnCH_2CH_2CH_2CH_3$ and 2-CH_2); δ_C (75 MHz; $CDCl_3$) 176.2, 142.1, 128.3, 127.7, 126.5, 77.9, 60.7, 50.3, 28.9, 27.3, 14.0, 13.6, 9.1 and 8.6; *m/z* (CI) 481 ($M^+ - 17$, 46%), 441 ($M^+ - 57$, 31) and 308 (100).

4.2.3. (S)-2-(2-Trimethylsilylethoxymethoxy)propanal (*13*)

Powdered activated 4 Å molecular sieves (450 mg), *N*-methylmorpholine *N*-oxide (222 mg, 1.89 mmol) and TPAP (33 mg, 0.095 mmol) were added to (*S*)-2-(2-trimethylsilylethoxymethoxy) propan-1-ol (0.3 g, 1.46 mmol) in CH_2Cl_2 (5 mL) at rt. After 2 h, the mixture was filtered through a pad of Celite®, the pad thoroughly washed with CH_2Cl_2, and the filtrate concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 3), gave the *title compound* **13** (184 mg, 60%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.4; $[\alpha]_D^{20}$ −18.6 (*c* 1.4, CH_2Cl_2); ν_{max} (neat)/cm^{-1} 1737, 1378, 1250, 1109, 1061, 1033, 860 and 836; δ_H (300 MHz; $CDCl_3$) 9.61 (1H, d, *J* 1.5, CHO), 4.77 and 4,74 (each 1H, d, *J* 7.1, OC*H*HO), 4.01 (1H, qd, *J* 7.0, 1.5, 2-H), 3.66 (2H, m, $OCH_2CH_2SiMe_3$), 1.29 (3H, d, *J* 7.0, 3-H_3), 0.91 (2H, m, CH_2Si) and 0.00 (9H, s, 3 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 202.6, 94.3, 78.0, 65.7, 17.9, 15.2 and −1.6.

4.2.4. 2-(tert-Butyldimethylsilyloxymethyl)-1-(phenylsulfonyl) prop-2-ene (*19*)

Imidazole (8.1 g, 0.12 mol) and *tert*-butyldimethylsilyl chloride (14.4 g, 95 mmol) were added to 2-(phenylsulfonylmethyl)prop-2-en-1-ol **18** (16.8 g, 79 mmol) in CH_2Cl_2 (200 mL) at 0 °C. The mixture was allowed to warm to rt and left to stir for *ca.* 15 h. It was poured into water (200 mL) and the aqueous layer extracted with CH_2Cl_2 (1 × 200 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate-light petroleum (1 : 10), gave the *title compound* **19** (18.8 g, 73%) as a colourless oil (Found: $M^+ + H$, 327.1446. $C_{16}H_{27}O_3SSi$ requires *M*, 327.1450); ν_{max} (neat)/cm^{-1} 1652, 1586, 1471, 1463, 1447, 1320, 1310, 1255, 1156, 1129, 1103, 1085, 838, 778 and 689; δ_H (300 MHz; $CDCl_3$) 7.82 (2H, m, ArH), 7.59 (1H,

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m, ArH), 7.49 (2H, m, ArH), 5.28 and 4.82 (each 1H, s, 3-H), 4.09 (2H, s, 2-CH_2), 3.77 (2H, s, 1-H_2), 0.83 [9H, s, SiC$(CH_3)_3$] and 0.00 (6H, s, $2 \times SiCH_3$); δ_C (75 MHz; $CDCl_3$) 138.3, 136.4, 133.6, 128.9, 128.4, 119.1, 64.9, 59.4, 25.8, 18.2 and −5.5; *m/z* (CI) 344 ($M^+ + 18$, 65%) and 327 ($M^+ + 1$, 100).

4.2.5. 4-(tert-Butyldimethylsilyloxymethyl)-3-(phenylsulfonyl) pent-4-en-2-ol (**20**)

n-Butyllithium (1.65 M in hexanes, 7.0 mL, 11.5 mmol) was added to di-isopropylamine (1.6 mL, 11.5 mmol) in THF (20 mL) at 0 °C and the mixture stirred for 30 min. The mixture was cooled to −78 °C and the sulfone **19** (3.12 g, 9.6 mmol) in THF (30 mL) was added. After 45 min at −78 °C, freshly distilled acetaldehyde (5.4 mL, 96 mmol) was added dropwise. After stirring for 30 min, methanol (5 mL) was added and the reaction mixture allowed to warm to rt. The mixture was diluted with water (50 mL) and ether (50 mL), the aqueous layer was extracted with ether (2×20 mL), and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ethyl acetate-light petroleum (1 : 5), gave the *title compound* **20** (2.42 g, 68%, an inseparable 55 : 45 mixture of diastereoisomers) as a colourless viscous oil which solidified slowly on standing, R_F [ethyl acetate-light petroleum (1 : 5)] 0.3 (Found: $M^+ + H$, 371.1715. $C_{18}H_{31}O_4SSi$ requires *M*, 371.1712); ν_{max} (nujol)/cm^{-1} 3488, 1639, 1461, 1377, 1304, 1283, 1253, 1145, 1111, 1083, 858, 838, 776 and 686; δ_H (500 MHz; $CDCl_3$; major diastereoisomer) 7.87 (2H, m, ArH), 7.67 (1H, m, ArH), 7.56 (2H, m, ArH), 5.38 and 4.97 (each 1H, s, 5-H), 4.53 (1H, m, 2-H), 4.07 (1H, br s, OH), 3.86 and 3.81 (each 1H, br d, *J* 14.3, 4-C*H*H), 3.63 (1H, d, *J* 2.0, 3-H), 1.26 (3H, d, *J* 6.2, 1-H_3), 0.87 [9H, s, SiC$(CH_3)_3$] and 0.00 and −0.01 (each 3H, s, $SiCH_3$); δ_H (500 MHz; $CDCl_3$; minor diastereoisomer) 7.87 (2H, m, ArH), 7.67 (1H, m, ArH), 7.56 (2H, m, ArH), 5.49 (2H, $2 \times$ s, each 5-H), 4.62 (1H, m, 2-H), 4.12 and 3.93 (each 1H, d, *J* 13.5, 4-C*H*H), 3.64 (1H, d, *J* 3.5, 3-H), 3.50 (1H, d, *J* 3.5, OH), 1.29 (3H, d, *J* 6.5, 1-H_3), 0.88 [9H, s, SiC$(CH_3)_3$] and 0.04 (6H, $2 \times$ s, each $SiCH_3$); δ_C (75 MHz; $CDCl_3$; mixture of diastereoisomers) 139.3, 138.1, 137.1, 133.9, 133.8, 129.3, 129.0, 128.9, 128.8, 121.4, 118.0, 73.0, 72.1, 66.9, 65.9, 65.7, 65.0, 25.8, 21.0, 20.9, 18.2, −5.5 and −5.6; *m/z* (CI) 388 ($M^+ + 18$, 72%), 371 ($M^+ + 1$, 100), 213 (100) and 132 (52).

4.2.6. (E)- and (Z)-5-tert-Butyldimethylsilyloxy-4-(tri-n-butylstannylmethyl)pent-3-en-2-ol (**21**)

Pentenol **20** (3.76 g, 10.16 mmol), tri-*n*-butyltin hydride (5.5 mL, 20.32 mmol) and azo*bis*isobutyronitrile (83 mg, 0.51 mmol) were taken up benzene (80 mL). The mixture was degassed for 15 min using argon and then heated under reflux for 2 h under argon. After being allowed to cool to rt, the mixture was concentrated under reduced pressure and chromatography of the residue, eluting with ether-light petroleum-triethylamine (25 : 125: 3), gave the *title compound* **21** [3.63 g, 69%, (*Z*) : (*E*) = 90 : 10] as a colourless oil, R_F [ether-light petroleum (1 : 5)] 0.4 (Found: M^+, 520.2768. $C_{24}H_{52}O_2Si^{120}Sn$ requires *M*, 520.2757); ν_{max} (neat)/cm^{-1} 3358, 1653, 1463, 1376, 1362, 1253, 1117, 1082, 1050, 1005, 858, 838, 777 and 668; δ_H [300 MHz; $CDCl_3$; (*Z*)-isomer] 5.17 (1H, br d, *J* 8.7, 3-H), 4.46 (1H, m, 2-H), 3.87 (2H, m, 5-H_2), 1.76 and 1.61 (each 1H, d, *J* 11.7, 4-CH*H*), 1.41 (6H, m, $3 \times SnCH_2CH_2$), 1.23 (9H, m, $3 \times SnCH_2CH_2CH_2$ and 1-H_3), 0.82 [24H, m, $3 \times SnCH_2CH_2CH_2CH_3$ and SiC$(CH_3)_3$] and 0.00 (6H, s, $2 \times SiCH_3$); δ_C [75 MHz; $CDCl_3$; (*Z*)-isomer] 141.7, 122.4, 67.5, 64.5, 29.0, 27.3, 25.9, 23.4, 18.4, 13.6, 10.5, 9.7 and −5.3; *m/z* (CI) 366 (32%), 213 (100) and 132 (35).

4.2.7. (E)- and (Z)-5-tert-Butyldimethylsilyloxy-2-methoxymethoxy-4-(tri-n-butylstannylmethyl)pent-3-ene (**22**)

Di-isopropylethylamine (1.88 mL, 10.8 mmol) and chloromethyl methyl ether (0.61 mL, 8.1 mmol) were added to the allylstannane **21** (2.8 g, 5.4 mmol) in CH_2Cl_2 (60 mL) at 0 °C. The mixture was allowed to warm to rt and stirred for 15 h. Saturated aqueous ammonium chloride (5 mL) was added and the mixture stirred for 15 min then diluted with water (50 mL). The aqueous layer was extracted with CH_2Cl_2 (1×50 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum-triethylamine (1 : 30 : 0.3), gave the *title compound* **22** [2.5 g, 82%, (*Z*) : (*E*) = 90 : 10] as a colourless oil (Found: $M^+ + H$, 565.3096. $C_{26}H_{57}O_3Si^{120}Sn$ requires *M*, 565.3098); ν_{max} (neat)/cm^{-1} 1657, 1463, 1376, 1252, 1158, 1097, 1031, 838, 777 and 667; δ_H [300 MHz; $CDCl_3$; (*Z*)-isomer]] 5.01 (1H, br d, *J* 9.1, 3-H), 4.62 and 4.43 (each 1H, d, *J* 6.6, OC*H*HO), 4.40 (1H, dq, *J* 9.1, 6.5, 2-H), 3.89 (2H, m, 5-H_2), 3.31 (3H, s, OCH_3), 1.92 and 1.51 (each 1H, d, *J* 11.8, 4-CH*H*), 1.42 (6H, m, $3 \times SnCH_2CH_2$), 1.25 (6H, sextet, *J* 7.5, $3 \times SnCH_2CH_2CH_2$), 1.18 (3H, d, *J* 6.5, 1-H_3), 0.82 [24H, m, SiC$(CH_3)_3$ and $3 \times SnCH_2CH_2CH_2CH_3$] and 0.00 (6H, s, $2 \times SiCH_3$); δ_C [75 MHz; $CDCl_3$; major (*Z*)-isomer] 143.1, 119.6, 93.1, 67.6, 67.3, 54.9, 29.0, 27.3, 25.9, 21.4, 18.3, 13.6, 10.2, 9.7 and −5.3; *m/z* (EI) 445 (2%), 265 (33), 155 (54), 75 (97) and 49 (100).

4.2.8. (3E,1RS,5SR)-3-(tert-Butyldimethylsilyloxymethyl)-5-methoxymethoxy-1-phenylhex-3-en-1-ol (**23a**)

Tin(IV) chloride (1.0 M in CH_2Cl_2, 2.8 mL, 2.8 mmol) was added to the allylstannane **22** (1.32 g, 2.35 mmol) in CH_2Cl_2 (25 mL) at −78 °C and the mixture stirred for 5 min. Benzaldehyde (0.29 mL 2.8 mmol) in CH_2Cl_2 (5 mL) was added at −78 °C and the mixture stirred for 30 min. Saturated aqueous sodium hydrogen carbonate (2 mL) was added, and the mixture allowed to warm to rt then diluted with water (30 mL). The aqueous layer was extracted with CH_2Cl_2 (1×30 mL) and the organic extracts dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum-triethylamine (25 : 75: 1), gave the *title compound* **23a** (618 mg, 69%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.3 (Found: $M^+ - CH_2OCH_3$, 336.2129. $C_{19}H_{31}O_3Si$ requires *M*, 336.2121); ν_{max} (neat)/cm^{-1} 3427, 1673, 1603, 1471, 1463, 1453, 1255, 1156, 1098, 1029, 837, 777 and 700; δ_H (300 MHz; $CDCl_3$) 7.20 (5H, m, ArH), 5.36 (1H, br d, *J* 9.1, 4-H), 4.64 (1H, dm, *J* 9.8, 1-H), 4.58 and 4.44 (each 1H, d, *J* 6.8, OCH*H*O), 4.40 (1H, dq, *J* 9.1, 6.3, 5-H), 4.10 and 4.00 (each 1H, dd, *J* 12.5, 1.0, 3-C*H*H), 3.84 (1H, br d, *J* 3.5, OH), 3.26 (3H, s, OCH_3), 2.50 (1H, br dd, *J* 14.1, 3.5, 2-H), 2.36 (1H, dd, *J* 14.1, 9.8, 2-H′), 1.12 (3H, d, *J* 6.3, 6-H_3), 0.83 [9H, s, SiC$(CH_3)_3$] and 0.01 and 0.00 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 144.9, 138.4, 130.5, 128.3, 127.1, 125.4, 93.6, 72.8, 67.6(2), 55.1, 39.7, 25.9, 21.3, 18.3 and −5.4(2); *m/z* (CI) 336 ($M^+ - 45$, 26%), 213 (60) and 187 (100).

4.2.9. (3E,2SR,6SR)-4-(tert-Butyldimethylsilyloxymethyl)-2-methoxymethoxyhept-3-en-6-ol (**23b**)

Following the procedure given for the synthesis of **23a**, the allylstannane **22** (0.5 g, 0.89 mmol), tin(IV) chloride (1.0 M in CH_2Cl_2, 1.06 mL, 1.06 mmol) and freshly distilled acetaldehyde (75 μL, 1.33 mmol) gave the *title compound* **23b** (160 mg, 57%) as a colourless oil, R_F [ether-light petroleum (1 : 2)] 0.2 (Found: $M^+ - CH_3OCH_2O$, 257.1941. $C_{14}H_{29}O_2Si$ requires *M*, 257.1937); ν_{max} (neat)/cm^{-1} 3450, 1672, 1463, 1372, 1255, 1157, 1100, 1030, 838, 777 and 670; δ_H (300 MHz; $CDCl_3$) 5.45 (1H, dm, *J* 9.5, 3-H), 4.66 and 4.55 (each 1H, d, *J* 6.8, OCH*H*O), 4.49 (1H, dq, *J* 9.5, 6.3, 2-H), 4.13 and 4.06 (each 1H, dd, *J* 12.5, 1.0, 4-C*H*H), 3.82 (1H, m, 6-H), 3.54 (1H, br d, *J* 3.6, OH), 3.36 (3H, s, OCH_3), 2.33 (1H, dd, *J* 14.1, 2.7, 5-H), 2.18 (1H, dd, *J* 14.1, 9.5, 5-H′), 1.26 (3H, d, *J* 6.3, 1-H_3), 1.21 (3H, d, *J* 6.0, 7-H_3), 0.91 [9H, s, SiC$(CH_3)_3$] and 0.09 and 0.08 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 138.5, 130.2, 93.5, 67.7, 67.6, 66.6, 55.0, 38.9, 25.7, 23.7, 21.2, 18.1, −5.5 and −5.6; *m/z* (CI) 274 (9%) and 125 (100).

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*4.2.10. (3E,7E,2SR,6RS)-4-(tert-Butyldimethylsilyloxymethyl)-2-methoxymethoxynona-3,7-dien-6-ol (**23c**)*

Following the procedure given for the synthesis of **23a**, the allylstannane **22** (250 mg, 0.45 mmol), tin(IV) chloride (1.0 M in CH_2Cl_2, 0.53 mL, 0.53 mmol) and (*E*)-crotonaldehyde (44 μL, 0.53 mmol) gave the *title compound* **23c** (94 mg, 62%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.2 (Found: $M^+ + H$, 345.2467. $C_{18}H_{37}O_4Si$ requires *M*, 345.2461); ν_{max} (neat)/cm^{-1} 3443, 1672, 1463, 1449, 1388, 1372, 1362, 1254, 1156, 1098, 1030, 836, 776 and 666; δ_H (300 MHz; $CDCl_3$) 5.69 (1H, dq, *J* 15.3, 6.5, 8-H), 5.50 (1H, dd, *J* 15.3, 1.2, 7-H), 5.44 (1H, d, *J* 9.4, 3-H), 4.67 and 4.53 (each 1H, d, *J* 6.9, OCH*H*O), 4.49 (1H, dq, *J* 9.4, 6.3, 2-H), 4.14 (1H, d, *J* 12.5, 4-C*H*H), 4.07 (1H, m, 6-H), 4.07 (1H, d, *J* 12.5, 4-CH*H*), 3.36 (3H, s, OCH_3), 2.38 (1H, dd, *J* 13.9, 3.8, 5-H), 2.25 (1H, dd, *J* 13.9, 9.3, 5-H′), 1.69 (3H, d, *J* 6.5, 9-H_3), 1.26 (3H, d, *J* 6.3, 1-H_3), 0.91 [9H, s, $SiC(CH_3)_3$] and 0.08 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 138.2, 134.0, 130.1, 125.9, 93.6, 71.3, 67.7, 67.5, 55.1, 37.4, 25.8, 21.3, 18.3, 17.6, −5.4 and −5.5; *m/z* (CI) 362 ($M^+ + 18$, 1%), 345 ($M^+ + 1$, 1), 327 ($M^+ - 17$, 1) and 151 (100).

*4.2.11. (5E,3SR,7RS)-5-(tert-Butyldimethylsilyloxymethyl)-7-methoxymethoxy-2-methyloct-5-en-3-ol (**23d**)*

Following the procedure given for the synthesis of **23a**, the allylstannane **22** (250 mg, 0.44 mmol), tin(IV) chloride (1.0 M CH_2Cl_2, 0.53 mL, 0.53 mmol) and 2-methylpropanal (48 μL, 0.53 mmol) gave the *title compound* **23d** (90 mg, 59%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.3 (Found: $M^+ - CH_3OCH_2O$, 285.2250. $C_{16}H_{33}O_2Si$ requires *M*, 285.2250); ν_{max} (neat)/cm^{-1} 3469, 1672, 1466, 1386, 1364, 1255, 1156, 1099, 1031, 838, 777 and 670; δ_H (300 MHz; $CDCl_3$) 5.42 (1H, dm, *J* 9.5, 6-H), 4.70 and 4.54 (each 1H, d, *J* 6.7, OCH*H*O), 4.49 (1H, dq, *J* 9.5, 6.4, 7-H), 4.17 and 4.07 (each 1H, dd, *J* 12.5, 1.0, 5-CH*H*), 3.41 (2H, m, 3-H and OH), 3.36 (3H, s, OCH_3), 2.36 and 2.15 (each 1H, m, 4-H), 1.70 (1H, m, 2-H), 1.28 (3H, d, *J* 6.4, 8-H_3), 0.96 and 0.95 (each 3H, d, *J* 6.8, either 1-H_3 or 2-CH_3), 0.91 [9H, s, $SiC(CH_3)_3$] and 0.09 (6H, 2 × s, each $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 139.6, 129.4, 93.4, 75.0, 67.5(2), 55.0, 34.2, 33.2, 25.8, 21.3, 18.3, 18.2, 17.6, −5.4 and −5.5; *m/z* (CI) 302 (7%) and 153 (100).

*4.2.12. (3E,2SR,6RS)-4-(tert-Butyldimethylsilyloxymethyl)-2-methoxymethoxy-6-(4-nitrophenylcarbonyloxy)hept-3-ene (**27**)*

Triphenylphosphine (62 mg, 0.27 mmol) and the alcohol **23b** (50 mg, 0.16 mmol) in THF (2 mL) were added to 4-nitrobenzoic acid (29 mg, 0.17 mmol) and diethyl azodicarboxylate (37 μL, 0.24 mmol) in THF (2 mL) at rt. The mixture was stirred for 2 h then poured into water (10 mL) and extracted with ether (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 3), gave the *title compound* **27** (58 mg, 79%) as a yellow oil, R_F [ether-light petroleum (1 : 2)] 0.5 (Found: $M^+ + NH_4$, 485.2677. $C_{23}H_{41}N_2O_7Si$ requires *M*, 485.2683); ν_{max} (neat)/cm^{-1} 1780, 1724, 1607, 1530, 1463, 1349, 1274, 1101, 1030, 919, 838, 779 and 720; δ_H (300 MHz; $CDCl_3$) 8.27 and 8.16 (each 2H, m, ArH), 5.41 (1H, br d, *J* 9.6, 3-H), 5.36 (1H, m, 6-H), 4.62 (1H, d, *J* 6.9, OC*H*HO), 4.58 (1H, dq, *J* 9.6, 6.5, 2-H), 4.50 (1H, d, *J* 6.9, OCH*H*O), 4.17 and 4.10 (each 1H, dd, *J* 13.5, 1.5, 4-CH*H*), 3.37 (3H, s, OCH_3), 2.71 (1H, dd, *J* 14.1, 8.3, 5-H), 2.37 (1H, dd, *J* 14.1, 5.1, 5-H′), 1.38 (3H, d, *J* 6.3, 7-H_3), 1.10 (3H, d, *J* 6.5, 1-H_3), 0.89 [9H, s, $SiC(CH_3)_3$] 0.04 (6H, 2 × s, each $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 163.7, 150.3, 137.5, 135.8, 130.4, 128.6, 123.3, 93.0, 71.1, 66.5, 66.1, 55.0, 34.2, 25.6, 21.3, 20.1, 18.1, −5.56 and −5.59; *m/z* (CI) 485 ($M^+ + 18$, 37%), 406 ($M^+ - 61$, 60) and 376 (100).

*4.2.13. (3E,2SR,6RS)-4-(tert-Butyldimethylsilyloxymethyl)-2-methoxymethoxyhept-3-en-6-ol (**28**)*

Sodium hydroxide (4 mg, 0.1 mmol) in methanol (0.4 mL) was added to the 4-nitrobenzoate **27** (40 mg, 0.086 mmol) in methanol (2 mL) at rt and the mixture stirred for 2 h then concentrated under reduced pressure. The residue was partitioned between water (10 mL) and ether (10 mL) and the aqueous layer was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 2), gave the *title compound* **28** (18 mg, 66%) as a colourless oil, R_F [ether-light petroleum (1 : 2)] 0.1 (Found: $M^+ + H$, 319.2305. $C_{16}H_{35}O_4Si$ requires *M*, 319.2304); ν_{max} (neat)/cm^{-1} 3450, 1671, 1463, 1371, 1255, 1157, 1100, 1030, 838, 777 and 669; δ_H (300 MHz; $CDCl_3$) 5.45 (1H, br d, *J* 9.3, 3-H), 4.61 and 4.51 (each 1H, d, *J* 6.8, OCH*H*O), 4.51 (1H, dq, *J* 9.3, 6.3, 2-H), 4.09 (2H, br. s, 4-CH_2), 3.94 (1H, m, 6-H), 3.35 (3H, s, OCH_3), 2.95 (1H, br d, *J* 3.6, OH), 2.28 (2H, d, *J* 6.0, 5-H_2), 1.25 and 1.20 (each 3H, d, *J* 6.3, either 1-H_3 or 7-H_3), 0.90 [9H, s, $SiC(CH_3)_3$] and 0.08 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 138.1, 130.8, 93.1, 67.9, 67.1, 66.1, 54.9, 38.7, 25.7, 23.1, 21.1, 18.1 and −5.6; *m/z* (CI) 319 ($M^+ + 1$, 3%) and 125 (100).

*4.2.14. (3E,1RS,5SR)-1-Acetoxy-3-(tert-butyldimethylsilyloxymethyl)-5-methoxymethoxy-1-phenylhex-3-ene (**33**)*

Acetic anhydride (0.47 mL, 4.97 mmol) was added to the homoallylic alcohol **23a** (894 mg, 2.35 mmol), triethylamine (2.08 mL, 14.9 mmol) and 4-dimethylaminopyridine (30 mg, 0.25 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The mixture was allowed to warm to rt, stirred for 1 h, and then poured into saturated aqueous sodium hydrogen carbonate (20 mL). The aqueous layer was extracted with CH_2Cl_2 (1 × 20 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 4), gave the *title compound* **33** (936 mg, 94%) as a colourless oil, R_F [ether-light petroleum (1 : 4)] 0.3 (Found: $M^+ + NH_4$, 440.2850. $C_{23}H_{42}NO_5Si$ requires *M*, 440.2832); ν_{max} (neat)/cm^{-1} 1742, 1470, 1463, 1454, 1371, 1234, 1156, 1098, 1029, 838, 777 and 700; δ_H (500 MHz; $CDCl_3$) 7.31 (5H, m, ArH), 5.86 (1H, t, *J* 7.5, 1-H), 5.39 (1H, br d, *J* 9.5, 4-H), 4.65 and 4.51 (each 1H, d, *J* 7.0, OCH*H*O), 4.38 (1H, dq, *J* 9.5, 6.1, 5-H), 4.07 and 3.96 (each 1H, dd, *J* 13.8, 1.3, 3-CH*H*), 3.38 (3H, s, OCH_3), 2.65 (2H, d, *J* 7.5, 2-H_2), 2.07 (3H, s, $COCH_3$), 0.97 (3H, d, *J* 6.1, 6-H_3), 0.91 [9H, s, $SiC(CH_3)_3$] and 0.06 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 170.0, 140.2, 136.7, 129.0, 128.4, 128.0, 126.5, 93.3, 74.7, 67.1, 66.3, 55.0, 35.3, 25.9, 21.2, 21.0, 18.3 and −5.4; *m/z* (CI) 440 ($M^+ + 18$, 33%), 361 ($M^+ - 61$, 18) and 301 (100).

*4.2.15. (3E,1RS,5SR)-3-Acetoxymethyl-5-methoxymethoxy-1-phenylhex-3-en-1-ol (**34**)*

Tetra-*n*-butylammonium fluoride (1.0 M in THF, 4.4 mL, 4.4 mmol) was added to the acetate **33** (936 mg, 2.22 mmol) in THF (20 mL) at rt and the mixture stirred for 1 h then poured into water (20 mL). The mixture was extracted with ether (3 × 20 mL) and the organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 1), gave the *title compound* **34** (414 mg, 60%) as a colourless oil, R_F [ether-light petroleum (1 : 1)] 0.2 (Found: $M^+ + NH_4$, 326.1960. $C_{17}H_{28}NO_5$ requires *M*, 326.1967); ν_{max} (neat)/cm^{-1} 3437, 1736, 1674, 1452, 1372, 1231, 1156, 1094, 1028, 917, 758 and 703; δ_H (300 MHz; $CDCl_3$) 7.29 (5H, m, ArH), 5.50 (1H, br d, *J* 9.3, 4-H), 4.80 (1H, dt, *J* 9.5, 4.5, 1-H), 4.71 (1H, d, *J* 7.1, OC*H*HO), 4.66 (1H, dd, *J* 13.1, 1.1, 3-C*H*H), 4.57 (1H, d, *J* 7.1, OCH*H*O), 4.53 (1H, dd, *J* 13.1, 1.1, 3-CH*H*), 4.45 (1H, dq, *J* 9.3, 6.3, 5-H), 3.36 (3H, s, OCH_3), 3.21 (1H, br d, *J* 4.5, OH), 2.59 (1H, dd, *J* 14.4, 9.5, 2-H),

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2.44 (1H, dd, *J* 14.4, 4.5, 2-H′), 2.08 (3H, s, $OCOCH_3$) and 1.12 (3H, d, *J* 6.3, 6-H_3); δ_C (75 MHz; $CDCl_3$) 170.7, 144.4, 133.6, 133.2, 128.4, 127.5, 125.4, 93.9, 72.0, 67.9, 67.4, 55.2, 39.0, 21.1 and 20.9; *m/z* (CI) 326 ($M^+ + 18$, 26%), 264 (40) and 141 (100).

4.2.16. (3E,1RS,5SR)-3-Acetoxymethyl-1-tert-butyldimethylsilyloxy-5-methoxymethoxy-1-phenylhex-3-ene (**35**)

Triethylamine (0.56 mL, 4.03 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.46 mL, 2.02 mmol) were added to the alcohol **34** (414 mg, 1.34 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the mixture was allowed to warm to rt and stirred for 90 min. Saturated aqueous ammonium chloride (2 mL), water (20 mL) and CH_2Cl_2 (20 mL) were added and the aqueous layer extracted with CH_2Cl_2 (1 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 4), gave the *title compound* **35** (483 mg, 85%) as a colourless viscous oil, R_F [ether-light petroleum (1 : 1)] 0.6 (Found: $M^+ + NH_4$, 440.2846. $C_{23}H_{42}NO_5Si$ requires *M*, 440.2832); ν_{max} (neat)/cm^{-1} 1744, 1673, 1471, 1453, 1370, 1250, 1227, 1156, 1094, 1067, 1029, 836, 777 and 701; δ_H (300 MHz; $CDCl_3$) 7.26 (5H, m, ArH), 5.33 (1H, br d, *J* 9.3, 4-H), 4.76 (1H, t, *J* 7.0, 1-H), 4.57 (1H, d, *J* 6.7, OC*H*HO), 4.43 (3H, m, 3-CH_2 and OCH*H*O), 4.29 (1H, dq, *J* 9.3, 6.3, 5-H), 3.33 (3H, s, OCH_3), 2.62 and 2.45 (each 1H, dd, *J* 13.7, 7.0, 2-H), 2.09 (3H, s, $COCH_3$), 0.92 (3H, d, *J* 6.3, 6-H_3), 0.84 [9H, s, $SiC(CH_3)_3$], 0.00 and −0.15 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 170.5, 144.3, 133.8, 131.6, 128.1, 127.3, 125.9, 93.3, 74.5, 67.9, 66.9, 55.0, 39.9, 25.7, 20.9, 20.8, 18.1, −4.8 and −5.2; *m/z* (CI) 440 ($M^+ + 18$, 46%) and 221 (100).

4.2.17. (3E,1RS,5SR)-1-tert-Butyldimethylsilyloxy-3-hydroxymethyl-5-methoxymethoxy-1-phenylhex-3-ene (**36**)

Sodium hydroxide (44 mg, 1.1 mmol) in methanol (4.4 mL) was added to the allylic acetate **35** (380 mg, 0.9 mmol) in methanol (10 mL) at rt and the solution stirred for 60 min then concentrated under reduced pressure. Water (20 mL) and ether (20 mL) were added, the aqueous layer was extracted with ether (2 × 20 mL) and the organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 1), gave the *title compound* **36** (330 mg, 96%) as a colourless oil, R_F [ether-light petroleum (1 : 1)] 0.3 (Found: $M^+ + H$, 381.2465. $C_{21}H_{37}O_4Si$ requires *M*, 381.2461); ν_{max} (neat)/cm^{-1} 3447, 1671, 1471, 1453, 1371, 1255, 1156, 1092, 1066, 1030, 919, 836, 777 and 701; δ_H (300 MHz; $CDCl_3$) 7.30 (5H, m, ArH), 5.36 (1H, br d, *J* 9.4, 4-H), 4.75 (1H, dd, *J* 7.7, 5.6, 1-H), 4.54 and 4.45 (each 1H, d, *J* 6.7, OCH*H*O), 4.40 (1H, dq, *J* 9.4, 6.3, 5-H), 4.02 and 3.95 (each 1H, dd, *J* 14.0, 6.0, 3-CH*H*), 3.28 (3H, s, OCH_3), 2.64 (1H, dd, *J* 13.9, 5.6, 2-H), 2.50 (1H, dd, *J* 13.9, 7.7, 2-H′), 2.29 (1H, t, *J* 6.0, OH), 1.12 (3H, d, *J* 6.3, 6-H_3), 0.87 [9H, s, $SiC(CH_3)_3$] and 0.00 and −0.16 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 144.4, 139.1, 129.1, 128.1, 127.4, 125.9, 93.3, 75.7, 67.3, 67.1, 55.0, 39.7, 25.7, 21.1, 18.1, −4.7 and −5.1; *m/z* (CI) 381 ($M^+ + 1$, 1%), 319 ($M^+ - 61$, 1) and 187 (100).

4.2.18. (3E,1RS,5SR)-1-tert-Butyldimethylsilyloxy-3-methanesulfonyloxymethyl-5-methoxymethoxy-1-phenylhex-3-ene (**37**)

Methanesulfonic anhydride (188 mg, 1.08 mmol) was added to the allylic alcohol **36** (205 mg, 0.54 mmol) and triethylamine (0.4 mL, 2.70 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The mixture was allowed to warm to rt, stirred for 3 h, then poured into saturated aqueous sodium hydrogen carbonate (20 mL) and extracted with CH_2Cl_2 (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **37** (220 mg, 89%) as a brown oil which was used without further purification (Found: $M^+ + NH_4$, 476.2499. $C_{22}H_{42}NO_6SSi$ requires *M*, 476.2502); ν_{max} (neat)/cm^{-1} 1672, 1604, 1471, 1454, 1359, 1256, 1176, 1157, 1094, 1067, 1031, 936, 919, 836, 778 and 702; δ_H (300 MHz; $CDCl_3$) 7.27 (5H, m, ArH), 5.51 (1H, br d, *J* 9.3, 4-H), 4.79 (1H, t, *J* 6.6, 1-H), 4.58 and 4.48 (each 1H, d, *J* 6.9, OCH*H*O), 4.47 and 4.41 (each 1H, dd, *J* 11.7, 1.1, 3-CH*H*), 4.39 (1H, dq, *J* 9.3, 6.5, 5-H), 3.34 (3H, s, OCH_3), 2.95 (3H, s, SO_2CH_3), 2.60 and 2.50 (each 1H, dd, *J* 13.8, 6.6, 2-H), 1.07 (3H, d, *J* 6.5, 6-H_3), 0.86 [9H, s, $SiC(CH_3)_3$] and 0.00 and −0.16 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 144.1, 135.1, 132.1, 128.3, 127.5, 125.9, 93.5, 74.7, 73.7, 67.0, 55.2, 39.1, 37.7, 25.8, 20.8, 18.1, −4.8 and −5.1; *m/z* (CI) 476 ($M^+ + 18$, 14%) and 221 (100).

4.2.19. (3E,1RS,5SR)-3-Bromomethyl-1-tert-butyldimethylsilyloxy-5-methoxymethoxy-1-phenylhex-3-ene (**38**)

Sodium bromide (40 mg, 0.59 mmol) was added in one portion to the allylic mesylate **37** (67 mg, 0.15 mmol) in *N*,*N*-dimethylformamide (3 mL) at rt and the reaction mixture stirred for 6 h then being poured into water (30 mL) and extracted with ether (3 × 20 mL). The organic extracts were washed with water (2 × 20 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give the *title compound* **38** (55 mg, 85%) as a colourless oil which was used without further purification (Found: $M^+ + NH_4$, 460.1889. $C_{21}H_{39}NO_3^{79}BrSi$ requires *M*, 460.1883); ν_{max} (neat)/cm^{-1} 1472, 1463, 1453, 1371, 1255, 1205, 1156, 1094, 1066, 1030, 918, 836, 777 and 701; δ_H (300 MHz; $CDCl_3$) 7.28 (5H, m, ArH), 5.51 (1H, d, *J* 9.3, 4-H), 4.80 (1H, t, *J* 6.7, 1-H), 4.60 and 4.47 (each 1H, d, *J* 6.7, OCH*H*O), 4.35 (1H, dq, *J* 9.3, 6.3, 5-H), 3.88 and 3.77 (each 1H, d, *J* 9.6, 3-CH*H*), 3.35 (3H, s, OCH_3), 2.67 (2H, d, *J* 6.7, 2-H_2), 1.06 (3H, d, *J* 6.3, 6-H_3), 0.87 [9H, s, $SiC(CH_3)_3$] and 0.02 and −0.14 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 144.3, 136.1, 134.6, 128.1, 127.3, 125.9, 93.4, 74.7, 67.1, 55.1, 39.5, 39.1, 25.7, 20.7, 18.1, −4.8 and −5.1; *m/z* (CI) 462 ($M^+ + 18$, 9%), 460 ($M^+ + 18$, 9) and 221 (100).

4.2.20. (3E,1RS,5SR)-1-tert-Butyldimethylsilyloxy-5-methoxymethoxy-3-(methyldithiocarbonyloxy)methyl-1-phenylhex-3-ene (**39**)

The allylic alcohol **36** (394 mg, 1.04 mmol) in toluene (5 mL) was added to a vigorously stirred suspension of sodium hydride (60% dispersion in mineral oil, 62 mg dispersion, 1.56 mmol) in toluene (5 mL) at 0 °C. The mixture was allowed to warm to rt, stirred for 90 min, and then cooled to 0 °C. Carbon disulfide (0.25 mL, 4.15 mmol) was added and the mixture allowed to warm to rt then stirred for 3 h. Iodomethane (0.26 mL, 4.15 mmol) was added, the mixture was stirred for *ca*. 18 h and then water (2 mL) was added cautiously. Water (50 mL) and CH_2Cl_2 (50 mL) were added and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 10), gave the *title compound* **39** (306 mg, 63%) as a pale yellow oil, R_F [ether-light petroleum (1 : 10)] 0.4 (Found: $M^+ + NH_4$, 488.2319). $C_{23}H_{42}NO_4S_2Si$ requires *M*, 488.2324); ν_{max} (neat)/cm^{-1} 1492, 1471, 1453, 1254, 1200, 1156, 1094, 1064, 1031, 836, 777 and 701; δ_H (300 MHz; $CDCl_3$) 7.27 (5H, m, ArH), 5.41 (1H, d, *J* 9.3, 4-H), 5.00 and 4.92 (each 1H, d, *J* 12.6, 3-CH*H*), 4.78 (1H, t, *J* 6.8, 1-H), 4.57 and 4.45 (each 1H, d, *J* 6.7, OCH*H*O), 4.30 (1H, dq, *J* 9.3, 6.3, 5-H), 3.34 (3H, s, OCH_3), 2.67 (1H, dd, *J* 13.7, 6.8, 2-H), 2.58 (3H, s, SCH_3), 2.50 (1H, dd, *J* 13.7, 6.8, 2-H′), 0.93 (3H, d, *J* 6.3, 6-H_3), 0.86 ([9H, s, $SiC(CH_3)_3$] and 0.00 and −0.15 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 215.3, 144.2, 133.7, 133.0, 128.1, 127.3, 126.0, 93.4, 77.4, 74.5, 66.8, 55.1, 40.0, 25.8, 20.7, 19.0, 18.1, −4.8 and −5.1; *m/z* (CI) 488 ($M^+ + 18$, 2%), 409 ($M^+ - 61$, 6) and 221 (100).

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*4.2.21. (1RS,5SR)-1-tert-Butyldimethylsilyloxy-5-methoxymethoxy-3-methylene-4-(methylthiocarbonyl)thio-1-phenylhexane (**40**)*

The allylic xanthate **39** (70 mg, 0.15 mmol) in toluene (2 mL) was heated under reflux for 6 h and the solution then allowed to cool to rt and concentrated under reduced pressure to give the *title compound* **40** (70 mg, *ca.* 100%, a 55 : 45 mixture of diastereoisomers) as a pale yellow oil used without further purification (Found: $M^+ + NH_4$, 488.2330. $C_{23}H_{42}NO_4S_2Si$ requires *M*, 488.2324); ν_{max} (neat)/cm^{-1} 1730, 1644, 1471, 1453, 1375, 1361, 1255, 1151, 1089, 1068, 1035, 863, 837, 777 and 701; δ_H (300 MHz; $CDCl_3$; major diastereoisomer) 7.27 (5H, m, ArH), 5.16 and 5.00 (each 1H, br s, 3-CH*H*), 4.84 (1H, m, 1-H), 4.63 (2H, m, OCH_2O), 4.42 (1H, d, *J* 4.7, 4-H), 3.98 (1H, qd, *J* 6.3, 4.7, 5-H), 3.38 (3H, s, OCH_3), 2.56 (1H, m, 2-H), 2.43 (3H, s, SCH_3), 2.42 (1H, m, 2-H′), 1.20 (3H, d, *J* 6.3, 6-H_3), 0.86 [9H, s, $SiC(CH_3)_3$] and 0.03 and −0.21 (each 3H, s, $SiCH_3$); δ_H (300 MHz; $CDCl_3$; minor diastereoisomer) 7.27 (5H, m, ArH), 5.09 and 4.97 (each 1H, br s, 3-CH*H*), 4.84 (1H, m, 1-H), 4.63 (2H, m, OCH_2O), 4.24 (1H, d, *J* 5.8, 4-H), 3.90 (1H, quin, *J* 5.8, 5-H), 3.36 (3H, s, OCH_3), 2.56 (1H, m, 2-H), 2.44 (3H, s, SCH_3), 2.42 (1H, m, 2-H′), 1.17 (3H, d, *J* 5.8, 6-H_3), 0.85 [9H, s, $SiC(CH_3)_3$] and 0.01 and −0.21 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$; mixture of diastereoisomers) 189.1, 188.9, 145.1, 144.8, 142.1, 141.3, 128.0, 127.9, 127.1, 127.0, 126.21, 126.18, 117.9, 117.1, 95.3(2), 74.2, 74.0, 73.8, 55.7, 55.6, 55.3, 46.7, 46.2, 25.8, 18.4, 18.1, 17.9, 13.1, −4.6, −4.7, −5.0 and −5.1; *m/z* (CI) 488 ($M^+ + 18$, 1%), 339 (40) and 221 (100).

*4.2.22. (3E,1RS,5SR)- and (3Z,1RS,5SR)-1-tert-Butyldimethylsilyloxy-5-methoxymethoxy-1-phenyl-3-(tri-n-butylstannylmethyl)hex-3-ene (**41**)*

A solution of the dithiocarbonate **40** (150 mg, 0.319 mmol), tri-*n*-butyltin hydride (129 μL, 0.479 mmol) and azo*bis*isobutyronitrile (2.6 mg, 0.016 mmol) in toluene (2 mL) was degassed for 15 min using argon then heated under reflux for 90 min under nitrogen. After being allowed to cool to rt, the mixture was concentrated under reduced pressure and chromatography of the residue, eluting with ether-light petroleum-triethylamine (1 : 50: 0.5), gave the *title compound* **41** [120 mg, 58%, (*Z*): (*E*) = 94 : 6] as a colourless oil, R_F [ether-light petroleum (1 : 30)] 0.2; ν_{max} (neat)/cm^{-1} 1642, 1463, 1375, 1362, 1251, 1156, 1096, 1070, 1031, 836, 776, 699 and 664; δ_H [500 MHz; C_6D_6; (*Z*)-isomer] 7.33 and 7.15 (each 2H, m, ArH), 7.03 (1H, m, ArH), 4.92 (1H, d, *J* 8.9, 4-H), 4.88 (1H, t, *J* 6.5, 1-H), 4.66 (1H, d, *J* 6.6, OC*H*HO), 4.59 (1H, dq, *J* 8.9, 6.5, 5-H), 4.41 (1H, d, *J* 6.6, OCH*H*O), 3.22 (3H, s, OCH_3), 2.55 and 2.36 (each 1H, m, 2-H), 2.10 and 1.90 (each 1H, d, *J* 11.6, 3-CH*H*), 1.56 (6H, m, 3 × $SnCH_2CH_2$), 1.35 (9H, m, 3 × $SnCH_2CH_2CH_2$ and 6-H_3], 0.96 [9H, s, $SiC(CH_3)_3$], 0.95 (6H, m, 3 × $SnCH_2$), 0.93 (9H, t, *J* 7.2, 3 × $SnCH_2CH_2CH_2CH_3$) and 0.09 and −0.12 (each 3H, s, $SiCH_3$); δ_C [75 MHz; C_6D_6; (*Z*)-isomer] 145.1, 139.8, 127.8, 126.9, 125.9, 125.0, 92.7, 75.3, 67.1, 54.3, 51.0, 29.0, 27.3, 25.6, 21.4, 17.8, 14.5, 13.3, 9.5, −4.9 and −5.3; *m/z* (ES+) 693 (M^+ + K, 7%) and 111 (100).

*4.2.23. (3E,2SR,6SR)-6-Acetoxy-4-tert-butyldimethylsilyloxymethyl-2-methoxymethoxyhept-3-ene (**43**)*

Acetic anhydride (73 μL, 0.77 mmol) was added to the homoallylic alcohol **23b** (120 mg, 0.38 mmol), triethylamine (0.27 mL, 1.9 mmol) and 4-dimethylaminopyridine (5 mg, 0.04 mmol) in CH_2Cl_2 (2 mL) at 0 °C and the mixture was allowed to warm to rt and stirred for 1 h. Saturated aqueous sodium hydrogen carbonate (10 mL) was added and the mixture extracted with CH_2Cl_2 (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 4), gave the *title compound* **43** (105 mg, 76%) as a colourless oil, R_F [ether-light petroleum (1 : 4)] 0.3 (Found: $M^+ + NH_4$, 378.2679. $C_{18}H_{40}NO_5Si$ requires *M*, 378.2676); ν_{max} (neat)/cm^{-1} 1739, 1463, 1372, 1241, 1158, 1098, 1032, 838 and 777; δ_H (300 MHz; $CDCl_3$) 5.44 (1H, br d, *J* 9.3, 3-H), 5.01 (1H, sextet, *J* 6.3, 6-H), 4.62 (1H, d, *J* 6.6, OC*H*HO), 4.54 (1H, dq, *J* 9.3, 6.3, 2-H), 4.49 (1H, d, *J* 6.6, OCH*H*O), 4.12 and 4.04 (each 1H, dd, *J* 14.0, 1.5, 4-CH*H*), 3.36 (3H, s, OCH_3), 2.33 (2H, m, 5-H_2), 2.01 (3H, s, CH_3CO), 1.26 (3H, d, *J* 6.3, 1-H_3), 1.20 (3H, d, *J* 6.3, 7-H_3), 0.89 [9H, s, $SiC(CH_3)_3$] and 0.05 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 170.3, 137.5, 128.2, 93.1, 69.6, 67.0, 66.1, 54.9, 34.2, 25.7, 21.2, 21.1, 19.8, 18.1 and −5.6(2); *m/z* (CI) 378 ($M^+ + 18$, 21%) and 299 ($M^+ - 61$, 100).

*4.2.24. (3E,2SR,6SR)-4-tert-Butyldimethylsilyloxymethyl-6-tert-butyldiphenylsilyloxy-2-methoxymethoxyhept-3-ene (**44**)*

Imidazole (51 mg, 0.76 mmol) and *tert*-butyldiphenylsilyl chloride (0.17 mL, 0.65 mmol) were added to the homoallylic alcohol **23b** (160 mg, 0.5 mmol) in CH_2Cl_2 (5 mL) at rt and the mixture stirred for 18 h before being poured into water (20 mL) and extracted with CH_2Cl_2 (2 × 20 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 10), gave the *title compound* **44** (230 mg, 83%) as a colourless oil, R_F [ether-light petroleum (1 : 10)] 0.4 (Found: $M^+ + NH_4$, 574.3743. $C_{32}H_{56}NO_4Si_2$ requires *M*, 574.3748); ν_{max} (neat)/cm^{-1} 1589, 1471, 1463, 1428, 1376, 1362, 1254, 1157, 1104, 1031, 837 and 703; δ_H (300 MHz; $CDCl_3$) 7.68 (4H, m, ArH), 7.39 (6H, m, ArH), 5.38 (1H, br d, *J* 9.5, 3-H), 4.56 and 4.42 (each 1H, d, *J* 6.6, OCH*H*O), 4.39 (1H, dq, *J* 9.5, 6.1, 2-H), 3.94 (1H, m, 6-H), 3.83 (2H, m, 4-CH_2), 3.31 (3H, s, OCH_3), 2.29 (1H, dd, *J* 13.5, 8.3, 5-H), 2.12 (1H, dd, *J* 13.5, 5.1, 5-H′), 1.16 (3H, d, *J* 6.1, 1-H_3), 1.06 [9H, s, $SiPh_2C(CH_3)_3$], 1.02 (3H, d, *J* 6.1, 7-H_3), 0.86 [9H, s, $SiMe_2C(CH_3)_3$] and −0.01 and −0.02 (each 3H, s, $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 138.5, 135.7, 134.3, 134.0, 129.4, 129.3, 127.3(2), 126.6, 93.0, 68.5, 67.0, 65.9, 54.8, 38.2, 26.8, 25.7, 22.7, 21.2, 18.9, 18.1 and −5.6; *m/z* (CI) 574 ($M^+ + 18$, 27%), 495 ($M^+ - 61$, 38) and 239 (100).

*4.2.25. (3E,2SR,6SR)-6-tert-Butyldiphenylsilyloxy-4-hydroxymethyl-2-methoxymethoxyhept-3-ene (**45**)*

Pyridinium toluene *p*-sulfonate (56 mg, 0.221 mmol) was added in one portion to the *bis*-silyl ether **44** (410 mg, 0.74 mmol) in absolute ethanol (5 mL) at rt and the mixture stirred at 40 °C for 4 h. After being allowed to cool to rt and concentrated under reduced pressure, water (10 mL) and ether (10 mL) were added, and the aqueous layer was extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (3 : 2), gave the *title compound* **45** (236 mg, 72%) as a colourless viscous oil, R_F [ether-light petroleum (3 : 2)] 0.4 (Found: $M^+ - CH_3OCH_2 + H$, 398.2283. $C_{24}H_{34}O_3Si$ requires *M*, 398.2277); ν_{max} (neat)/cm^{-1} 3415, 1671, 1590, 1473, 1428, 1376, 1157, 1104, 1032, 822 and 703; δ_H (300 MHz; $CDCl_3$) 7.69 (4H, m, ArH), 7.41 (6H, m, ArH), 5.38 (1H, br d, *J* 9.3, 3-H), 4.57 and 4.45 (each 1H, d, *J* 6.6, OCH*H*O), 4.38 (1H, dq, *J* 9.3, 6.3, 2-H), 3.96 (3H, m, 4-CH_2 and 6-H), 3.30 (3H, s, OCH_3), 2.36 (1H, dd, *J* 14.0, 6.5, 5-H), 2.26 (1H, dd, *J* 14.0, 5.9, 5-H′), 2.16 (1H, br s, OH), 1.17 (3H, d, *J* 6.3, 1-H_3), 1.06 [9H, s, $SiC(CH_3)_3$] and 1.04 (3H, d, *J* 6.3, 7-H_3); δ_C (75 MHz; $CDCl_3$) 138.8, 135.7, 133.9, 133.5, 129.6, 129.5, 129.1, 127.4(2), 93.1, 69.0, 66.9, 54.9, 37.9, 26.8, 22.6, 21.1 and 18.9; *m/z* (CI) 381 ($M^+ - 61$, 33%) and 125 (100).

*4.2.26. (3E,2SR,6SR)-6-tert-Butyldiphenylsilyloxy-2-methoxymethoxy-4-(methyldithiocarbonyloxy)methylhept-3-ene (**46**)*

Following the procedure outlined for the synthesis of xanthate **39**, the allylic alcohol **45** (236 mg, 0.534 mmol) in THF (2 mL),

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sodium hydride (60% dispersion in mineral oil, 32 mg dispersion, 0.8 mmol) in THF (2 mL), carbon disulfide (0.13 mL, 2.14 mmol) and iodomethane (0.13 mL, 2.14 mmol) with extraction using ether (3 × 15 mL) and chromatography, eluting with ether-light petroleum (1 : 5), gave the *title compound* **46** (200 mg, 70%) as a pale yellow oil, R_F [ether-light petroleum (1 : 5)] 0.4 (Found: $M^+ + NH_4$, 550.2483. $C_{28}H_{44}NO_4S_2Si$ requires *M*, 550.2481); ν_{max} (neat)/cm^{-1} 1589, 1471, 1449, 1427, 1376, 1212, 1192, 1103, 1077, 1060, 1031, 918, 822, 739 and 703; δ_H (300 MHz; $CDCl_3$) 7.68 (4H, m, ArH), 7.40 (6H, m, ArH), 5.45 (1H, br d, *J* 9.3, 3-H), 4.92 and 4.85 (each 1H, dd, *J* 12.8, 1.1, 4-CH*H*), 4.57 and 4.45 (each 1H, d, *J* 6.8, OCH*H*O), 4.41 (1H, dq, *J* 9.3, 6.3, 2-H), 4.00 (1H, m, 6-H), 3.32 (3H, s, OCH_3), 2.51 (3H, s, SCH_3), 2.41 (1H, dd, *J* 13.7, 7.8, 5-H), 2.28 (1H, dd, *J* 13.7, 5.7, 5-H′), 1.18 (3H, d, *J* 6.3, 1-H_3), 1.06 [9H, s, $SiC(CH_3)_3$] and 1.04 (3H, d, *J* 7.2, 7-H_3); δ_C (75 MHz; $CDCl_3$) 214.9, 135.7, 135.6, 134.1, 133.7, 133.2, 133.1, 129.5, 129.4, 127.4, 127.3, 93.3, 76.8, 68.3, 66.9, 55.0, 38.3, 26.8, 22.8, 20.9, 18.9 and 18.8; *m/z* (CI) 550 (M^+ + 18, 100%), 471 (M^+ − 61, 83), 425 (31) and 283 (76).

4.2.27. (2SR,3SR,6SR)- and (2SR,3RS,6SR)-6-tert-Butyldiphenylsilyloxy-2-methoxymethoxy-4-methylene-3-(methylthiocarbonyl)thioheptane (**47**)

The allylic xanthate **46** (200 mg, 0.38 mmol) in toluene (5 mL) was heated under reflux for 2 h and the solution allowed to cool to rt then concentrated under reduced pressure to give the *title compound* **47** (200 mg, *ca.* 100%, a 55 : 45 mixture of diastereoisomers) as a pale yellow oil that was used without further purification (Found: $M^+ + NH_4$, 550.2471. $C_{28}H_{44}NO_4S_2Si$ requires *M*, 550.2481); ν_{max} (neat)/cm^{-1} 1645, 1471, 1427, 1377, 1107, 1034, 917, 866, 822, 739 and 703; δ_H (500 MHz; $CDCl_3$; major diastereoisomer) 7.70 (4H, m, ArH), 7.41 (6H, m, ArH), 5.14 and 4.92 (each 1H, s, 4-CH*H*), 4.56 and 4.53 (each 1H, d, *J* 6.9, OCH*H*O), 4.21 (1H, d, *J* 4.9, 3-H), 4.12 (1H, m, 6-H), 3.84 (1H, m, 2-H), 3.33 (3H, s, OCH_3), 2.40 (3H, s, SCH_3), 2.40 and 2.21 (each 1H, m, 5-H), 1.13 (3H, d, *J* 6.4, 1-H_3), 1.11 (3H, d, *J* 6.0, 7-H_3) and 1.06 [9H, s, $SiC(CH_3)_3$]; δ_H (500 MHz; $CDCl_3$; minor diastereoisomer) 7.70 (4H, m, ArH), 7.41 (6H, m, ArH), 5.10 and 4.93 (each 1H, s, 4-CH*H*), 4.61 and 4.57 (each 1H, d, *J* 6.9, OCH*H*O), 4.19 (1H, d, *J* 6.0, 3-H), 4.07 (1H, m, 6-H), 3.84 (1H, m, 2-H), 3.35 (3H, s, OCH_3), 2.41 (3H, s, SCH_3), 2.40 (1H, m, 5-H), 2.21 (1H, m, 5-H′), 1.18 (3H, d, *J* 6.2, 1-H_3), 1.09 (3H, d, *J* 6.2, 7-H_3) and 1.06 [9H, s, $SiC(CH_3)_3$]; δ_C (75 MHz; $CDCl_3$; mixture of diastereoisomers) 188.9, 188.8, 142.8, 142.2, 135.8, 134.6(2), 134.3, 134.1, 129.5, 129.4, 129.0, 128.2, 127.5, 127.4, 125.2, 116.9, 116.6, 95.5, 74.3, 73.6, 68.4, 68.1, 56.0, 55.7, 55.6, 55.4, 45.2, 45.0, 27.0, 23.0, 22.9, 19.2, 18.7, 17.9 and 13.1; *m/z* (CI) 550 (M^+ + 18, 32%), 533 (M^+ + 1, 6) and 283 (100).

4.2.28. (3E,2SR,6SR)- and (3Z,2SR,6SR)-6-tert-Butyldiphenylsilyloxy-2-methoxymethoxy-4-(tri-n-butylstannylmethyl)hept-3-ene (**48**)

A solution of the dithiocarbonate **47** (58 mg, 0.11 mmol), tri-*n*-butyltin hydride (44 μL, 0.164 mmol) and azo*bis*isobutyronitrile (2 mg, 0.01 mmol) in benzene (2 mL) was degassed for 15 min using argon. The mixture was then heated under reflux for 1 h, allowed to cool to rt and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum-triethylamine (1 : 30: 0.3), gave the *title compound* **48** [60 mg, 77%, a 70 : 30 mixture of (*Z*) and (*E*)-isomers] as a colourless oil, R_F [ether-light petroleum (1 : 30)] 0.4; ν_{max} (neat)/cm^{-1} 1642, 1590, 1463, 1427, 1375, 1108, 1030, 998, 917, 822, 739 and 702; δ_H [300 MHz; C_6D_6; (*Z*)-isomer] 7.80 (4H, m, ArH), 7.20 (6H, m, ArH), 4.94 (1H, d, *J* 9.2, 3-H), 4.76 (1H, d, *J* 6.6, OC*H*HO), 4.57 (1H, dq, *J* 9.2, 6.3, 2-H), 4.43 (1H, d, *J* 6.6, OCH*H*O), 4.19 (1H, m, 6-H), 3.19 (3H, s, OCH_3), 2.42 (1H, m, 5-H), 2.14 (2H, m, 5-H′ and 4-C*H*H), 1.50 (7H, m, 3 × $SnCH_2CH_2CH_2$ and 4-CH*H*), 1.31 (9H, m, 3 × $SnCH_2CH_2CH_2$ and 1-H_3), 1.16 [12H, m, $SiC(CH_3)_3$ and 7-H_3] and 0.90 (15H, m, 3 × $SnCH_2CH_2CH_2CH_3$); δ_H [300 MHz; C_6D_6; (*E*)-isomer] 7.80 (4H, m, ArH), 7.20 (6H, m, ArH), 5.08 (1H, d, *J* 9.5, 3-H), 4.78 (1H, d, *J* 6.8, OC*H*HO), 4.48 (1H, dq, *J* 9.5, 6.3, 2-H), 4.44 (1H, d, *J* 6.8, OCH*H*O), 4.19 (1H, m, 6-H), 3.16 (3H, s, OCH_3), 2.42 and 2.14 (1H, m, 5-H), 1.79 and 1.72 (each 1H, d, *J* 11.6, 4-CH*H*), 1.50 (6H, m, 3 × $SnCH_2CH_2$), 1.31 (9H, m, 3 × $SnCH_2CH_2CH_2$ and 1-H_3), 1.16 [12H, m, $SiC(CH_3)_3$ and 7-H_3] and 0.90 (15H, m, 3 × $SnCH_2CH_2CH_2CH_3$); δ_C (75 MHz; C_6D_6; mixture of isomers) 141.2, 140.9, 136.3, 135.1, 134.7, 129.9, 127.9, 125.2, 124.8, 93.2, 93.1, 69.6, 69.2, 67.6, 67.5, 54.8, 50.4, 43.1, 29.6, 29.5, 27.3, 23.54, 23.50, 22.3, 22.0, 21.1, 19.5, 19.4, 14.6, 13.9, 10.0 and 9.8; *m/z* (ES+) 739 (M^+ + Na, 15%), 655 (24) and 332 (100).

4.2.29. (3E,2SR,2′SR,6SR)-4-[2-(tert-Butyldiphenylsilyloxy)propyl]-2-methoxymethoxyhept-3-en-6-ol (**49**)

Tin(IV) chloride (1.0 M in CH_2Cl_2, 0.17 mL, 0.17 mmol) was added to the allylstannane **48** (100 mg, 0.14 mmol) in CH_2Cl_2 (2 mL) at −78 °C and the mixture stirred for 5 min. Freshly distilled acetaldehyde (15 μL, 0.28 mmol) in CH_2Cl_2 (1 mL) was added at −78 °C and the mixture stirred for 45 min at −78 °C. Saturated aqueous sodium hydrogen carbonate (2 mL) was added, and the mixture allowed to warm to rt, poured into water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum-triethylamine (50 : 50: 1), gave the *title compound* **49** (ca. 1 mg, 1%) as a colourless gum, R_F [ether-light petroleum (1 : 1)] 0.2; δ_H (300 MHz; $CDCl_3$) 7.67 (4H, m, ArH), 7.40 (6H, m, ArH), 5.16 (1H, br d, *J* 9.0, 3-H), 4.69 and 4.54 (each 1H, d, *J* 6.9, OCH*H*O), 4.43 (1H, dq, *J* 9.0, 6.3, 2-H), 3.97 (1H, sextet, *J* 6.3, either 6-H or 2′-H), 3.60 (1H, m, either 6-H or 2′-H), 3.34 (3H, s, OCH_3), 2.19 (2H, m, either 5-H_2 or 1′-H_2), 2.11 (1H, dd, *J* 14.0, 9.1, either 5-H or 1′-H), 1.97 (1H, dd, *J* 14.0, 3.8, either 5-H′ or 1′-H′), 1.25 (1H, s, OH), 1.19 (3H, d, *J* 6.3, 1-H_3), 1.06 (6H, d, *J* 6.0, 7-H_3 and 3′-H_3) and 1.04 [9H, s, $SiC(CH_3)_3$]; *m/z* (ES+) 493 (M^+ + Na, 100%), 409 (16) and 283 (45).

4.2.30. (3E,2SR,6SR)-4-tert-Butyldimethylsilyloxymethyl-6-methanesulfonyloxy-2-methoxymethoxyhept-3-ene (**50b**)

Methanesulfonic anhydride (66 mg, 0.38 mmol) was added to the homoallylic alcohol **23b** (60 mg, 0.19 mmol) and triethylamine (0.13 mL, 0.95 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the mixture allowed to warm to rt then stirred for 2 h. After concentration under reduced pressure, saturated aqueous sodium hydrogen carbonate (10 mL) and ether (10 mL) were added and the aqueous layer extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford the *title compound* **50b** (68 mg, 91%) as a colourless oil that was used without further purification, R_F [ether-light petroleum (1 : 2)] 0.2 (Found: $M^+ + NH_4$, 414.2340. $C_{17}H_{40}NO_6SSi$ requires *M*, 414.2345); ν_{max} (neat)/cm^{-1} 1674, 1463, 1358, 1255, 1176, 1099, 1031, 920, 838, 779 and 671; δ_H (300 MHz; $CDCl_3$) 5.48 (1H, br d, *J* 9.1, 3-H), 4.96 (1H, m, 6-H), 4.63 and 4.51 (each 1H, d, *J* 6.9, OCH*H*O), 4.50 (1H, dq, *J* 9.1, 6.1, 2-H), 4.13 and 4.06 (each 1H, dd, *J* 13.3, 1.1, 4-CH*H*), 3.35 (3H, s, OCH_3), 2.98 (3H, s, SO_2CH_3), 2.53 (1H, dd, *J* 14.0, 7.6, 5-H), 2.40 (1H, dd, *J* 14.0, 6.6, 5-H′), 1.40 (3H, d, *J* 6.1, 1-H_3), 1.26 (3H, d, *J* 6.6, 7-H_3), 0.90 [9H, s, $SiC(CH_3)_3$] and 0.06 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 136.2, 130.1, 93.5, 78.5, 67.4, 66.8, 55.1, 38.3, 35.3, 25.8, 21.3, 18.2, −5.4 and −5.5; *m/z* (CI) 414 (M^+ + 18, 21%), 335 (M^+ − 61, 44) and 125 (100).

4.2.31. (3E,2SR,6RS)-4-tert-Butyldimethylsilyloxymethyl-6-methanesulfonyloxy-2-methoxymethoxy-7-methyloct-3-ene (**50d**)

Following the procedure outlined for the synthesis of mesylate

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50b, the homoallylic alcohol **23d** (76 mg, 0.22 mmol), methanesulfonic anhydride (77 mg, 0.44 mmol) and triethylamine (0.15 mL, 1.1 mmol) gave the *title compound* **50d** (34 mg, 37%) as a colourless oil, R_F [ether-light petroleum (1 : 2)] 0.4 (Found: $M^+ + NH_4$, 442.2650. $C_{19}H_{44}NO_6SSi$ requires *M*, 442.2658); ν_{max} (neat)/cm^{-1} 1673, 1471, 1359, 1255, 1175, 1098, 1031, 907, 838, 778 and 666; δ_H (300 MHz; $CDCl_3$) 5.48 (1H, br d, *J* 9.3, 3-H), 4.74 (1H, ddd, *J* 9.2, 5.6, 3.7, 6-H), 4.65 and 4.53 (each 1H, d, *J* 6.8, OCH*H*O), 4.50 (1H, dq, *J* 9.3, 6.3, 2-H), 4.16 and 4.07 (each 1H, dd, *J* 13.5, 1.2, 4-CH*H*), 3.35 (3H, s, OCH_3), 2.98 (3H, s, SO_2CH_3), 2.43 (2H, m, 5-H_2), 2.02 (1H, m, 7-H), 1.27 (3H, d, *J* 6.3, 1-H_3), 1.02 and 0.98 (each 3H, d, *J* 6.9, either 7-CH_3 or 8-H_3), 0.90 [9H, s, $SiC(CH_3)_3$] and 0.06 (6H, s, 2 × $SiCH_3$); δ_C (75 MHz; $CDCl_3$) 136.7, 129.8, 93.6, 86.7, 67.5, 66.6, 55.0, 38.4, 31.9, 29.3, 25.8, 21.3, 18.2, 17.7, 17.0 and −5.4; *m/z* (CI) 442 ($M^+ + 18$, 95%) and 363 ($M^+ - 61$, 100).

4.2.32. (2RS)-4-[(E,2SR)-2-Methoxymethoxypropylidene]-2-methyltetrahydrofuran (*51b*)

Tetra-*n*-butylammonium fluoride (1.0 M in THF, 0.18 mL, 0.18 mmol) was added to the homoallylic mesylate **50b** (60 mg, 0.15 mmol) in THF (2 mL) at rt, and the mixture stirred for 15 min, poured into water (10 mL) and extracted with ether (3 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 2), gave the *title compound* **51b** (10 mg, 36%) as a colourless oil, R_F [ether-light petroleum (1 : 2)] 0.4 (Found: $M^+ + NH_4$, 204.1604. $C_{10}H_{22}NO_3$ requires *M*, 204.1600); ν_{max} (neat)/cm^{-1} 1446, 1385, 1374, 1216, 1156, 1133, 1097, 1029, 917 and 833; δ_H (300 MHz; $CDCl_3$) 5.16 (1H, br d, *J* 9.1, 1′-H), 4.65 and 4.51 (each 1H, d, *J* 6.7, OCH*H*O), 4.38 (1H, br d, *J* 13.3, 5-H), 4.32 (1H, dq, *J* 9.1, 6.4, 2′-H), 4.25 (1H, br d, *J* 13.3, 5-H′), 4.02 (1H, m, 2-H), 3.36 (3H, s, OCH_3), 2.74 (1H, dd, *J* 16.0, 5.3, 3-H), 2.03 (1H, dd, *J* 16.0, 9.1, 3-H′), 1.29 (3H, d, *J* 5.9, 2-CH_3) and 1.25 (3H, d, *J* 6.4, 3′-H_3); δ_C (75 MHz; $CDCl_3$) 142.9, 120.2, 93.1, 75.7, 70.7, 69.4, 54.9, 36.7, 20.8 and 20.1; *m/z* (CI) 204 ($M^+ + 18$, 6%), 142 (27) and 125 (100).

4.2.33. (2SR)-4-[(E,2SR)-2-Methoxymethoxypropylidene]-2-prop-2-yltetrahydrofuran (*51d*)

Following the procedure outlined for the preparation of the tetrahydrofuran **51b**, the homoallylic mesylate **50d** (20 mg, 0.05 mmol) and tetra-*n*-butylammonium fluoride (1.0 M in THF, 50 μL 0.05 mmol) gave the *title compound* **51d** (4.5 mg, 43%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.3 (Found: $M^+ + NH_4$, 232.1911. $C_{12}H_{26}NO_3$ requires *M*, 232.1912); ν_{max} (neat)/cm^{-1} 1469, 1388, 1372, 1299, 1216, 1157, 1134, 1097, 1029, 918 and 838; δ_H (300 MHz; $CDCl_3$) 5.17 (1H, br d, *J* 9.0, 1′-H), 4.66 and 4.53 (each 1H, d, *J* 6.7, OCH*H*O), 4.37 (1H, br d, *J* 13.2, 5-H), 4.35 (1H, dq, *J* 9.0 6.3, 2′-H), 4.25 (1H, br d, *J* 13.2, 5-H′), 3.57 (1H, m, 2-H), 3.37 (3H, s, OCH_3), 2.66 (1H, dd, *J* 15.9, 5.8, 3-H), 2.11 (1H, dd, *J* 15.9, 9.3, 3-H′), 1.73 (1H, octet, *J* 6.8, 2-CH), 1.25 (3H, d, *J* 6.3, 3′-H_3) and 0.99 and 0.90 (each 3H, d, *J* 6.8, 2-CHCH_3); δ_C (75 MHz; $CDCl_3$) 142.7, 120.4, 93.3, 85.4, 71.0, 69.6, 55.1, 33.0, 32.9, 21.0, 19.1 and 18.5; *m/z* (CI) 232 ($M^+ + 18$, 5%), 202 (2), 170 (21) and 153 (100).

4.2.34. (2SR)-4-[(E,2SR)-2-Methoxymethoxypropylidene]-2-phenyltetrahydrofuran (*51a*)

Methanesulfonic anhydride (85 mg, 0.49 mmol) was added to the benzylic alcohol **23a** (93 mg, 0.25 mmol) and triethylamine (0.17 mL, 1.22 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the mixture allowed to warm to rt and stirred for 18 h. After concentration under reduced pressure, saturated aqueous sodium hydrogen carbonate (10 mL) and ether (10 mL) were added and the aqueous layer extracted with ether (2 × 10 mL). The organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue, eluting with ether-light petroleum (1 : 3), gave the *title compound* **51a** (20 mg, 33%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.4 (Found: $M^+ + NH_4$, 266.1751. $C_{15}H_{24}NO_3$ requires *M*, 266.1756); ν_{max} (neat)/cm^{-1} 1687, 1605, 1452, 1372, 1216, 1156, 1131, 1096, 1028, 917, 839, 755 and 699; δ_H (300 MHz; $CDCl_3$) 7.31 (5H, m, ArH), 5.25 (1H, br d, *J* 8.9, 1′-H), 4.95 (1H, dd, *J* 9.1, 6.3, 2-H), 4.71 (1H, d, *J* 6.7, OC*H*HO), 4.58 (1H, br d, *J* 13.1, 5-H), 4.55 (1H, d, *J* 6.7, OCH*H*O), 4.43 (1H, br d, *J* 13.1, 5-H′), 4.35 (1H, dq, *J* 8.9, 6.4, 2′-H), 3.37 (3H, s, OCH_3), 3.08 (1H, dd, *J* 15.8, 6.3, 3-H), 2.43 (1H, dd, *J* 15.8, 9.1, 3-H′) and 1.25 (3H, d, *J* 6.4, 3′-H_3); δ_C (75 MHz; $CDCl_3$) 142.1, 141.5, 128.3, 127.6, 125.8, 120.8, 93.3, 81.1, 71.3, 69.6, 55.1, 37.7 and 21.0; *m/z* (CI) 266 ($M^+ + 18$, 23%), 244 (99) and 187 (100).

4.2.35. (2SR)-4-[(E,2SR)-2-(Methoxymethoxypropylidene]-2-[(E)-prop-1-enyltetrahydrofuran (*51c*)

Following the procedure outlined for the preparation of the tetrahydrofuran **51a**, the allylic alcohol **23c** (70 mg, 0.20 mmol), methanesulfonic anhydride (71 mg, 0.41 mmol) and triethylamine (0.14 mL, 1.0 mmol) gave the *title compound* **51c** (11 mg, 24%) as a colourless oil, R_F [ether-light petroleum (1 : 3)] 0.4 (Found: $M^+ + NH_4$, 230.1737. $C_{12}H_{24}NO_3$ requires *M*, 230.1756); ν_{max} (neat)/cm^{-1} 1449, 1371, 1299, 1216, 1156, 1136, 1096, 1029, 966 and 917; δ_H (300 MHz; $CDCl_3$) 5.76 (1H, dqd, *J* 15.3, 6.6, 0.8, 2″-H), 5.52 (1H, ddq, *J* 15.3, 7.2, 1.5, 1″-H), 5.17 (1H, br d, *J* 9.0, 1′-H), 4.66 and 4.52 (each 1H, d, *J* 6.8, OCH*H*O), 4.39 (1H, br d, *J* 12.9, 5-H), 4.33 (2H, m, 2-H and 2′-H), 4.27 (1H, br d, *J* 12.9, 5-H′), 3.36 (3H, s, OCH_3), 2.76 (1H, dd, *J* 16.1, 5.9, 3-H), 2.20 (1H, dd, *J* 16.1, 8.9, 3-H′), 1.71 (3H, dd, *J* 6.6, 1.5, 3″-H_3) and 1.25 (3H, d, *J* 6.3, 3′-H_3); δ_C (75 MHz; $CDCl_3$) 142.3, 130.5, 128.8, 120.4, 93.1, 80.2, 70.5, 69.4, 55.0, 35.4, 20.8 and 17.5; *m/z* (CI) 230 ($M^+ + 18$, 6%) and 151 (100).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2019.130734.

References

[1] E.J. Thomas, Chem. Rec. 7 (2007) 115.
[2] (a) A.H. MacNeill, E.J. Thomas, Synthesis (1994) 322;
(b) J.S. Carey, S. MacCormick, S.J. Stanway, A. Teerawutgulrag, E.J. Thomas, Org. Biomol. Chem. 9 (2011) 3896;
(c) D.J. Hallett, N. Tanikkul, E.J. Thomas, Org. Biomol. Chem. 10 (2012) 6130;
(d) S.J. Stanway, E.J. Thomas, Tetrahedron 68 (2012) 5998.
[3] The double-bonds in the products **6** are assigned the (*E*)-configuration, even though the 1,5-*syn*-substituted hydroxy- and alkoxy-alkyl groups are *cis* to each other across the newly introduced double-bond, *cf.* the original products **2** where they are assigned the (*Z*)-configuration. This is a consequence of the IUPAC Priority Rules that give the trialkylsilyloxymethyl group a higher priority than a 2-hydroxyalkyl group.
[4] L.A. Hobson, E.J. Thomas, Org. Biomol. Chem. 10 (2012) 7510.
[5] A. Teerawutgulrag, E.J. Thomas, J. Chem. Soc. Perkin Trans. I (1993) 2863.
[6] Preliminary communication on part of this work see: E.J. Thomas, D.R. Tray Tetrahedron Lett. 52 (2011) 2065.
[7] M. Pereyre, G. Colin, J. Valade, Bull. Soc. Chim. Fr. (1968) 3358.
[8] W.A. Kleschick, C.H. Heathcock, J. Org. Chem. 43 (1978) 1256.
[9] Y. Ueno, S. Aoki, M. Okawara, J. Am. Chem. Soc. 101 (1979) 5414.
[10] P. Breuilles, D. Uguen, Tetrahedron Lett. 28 (1987) 6053.
[11] C.-S. Hau, C. Tindall, J.B. Sweeney, Synlett (1996) 749.
[12] D.C. Deka, E.J. Thomas, Tetrahedron 57 (2001) 10017.
[13] In transmetallation of 4-, 5- and 6-alkoxyalk-2-enyl(tributyl)stannanes with tin(IV) chloride, the substituent on the tin-bearing carbon is always *trans* to any substituent on the adjacent carbon in the oxastannane rings formed by co-ordination of the electron deficient tin by the alkoxy group, see ref. 4. This applies to 4-, 5- and 6-membered oxastannane rings.

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[14] It has not been confirmed which oxygen in MOMO- and SEMO substituted alkenyltin trichlorides co-ordinate preferentially to the tin. However, the (*Z*)-1,5-*syn*-stereoselectivity observed for the 4-benzyloxypent-2-enylstannane **1** has also been confirmed for analogous 4-(2-trimethylsilyloxymethoxy)pent-2-enylstannanes, see: K. Hoegenauer, E.J. Thomas Org. Biomol. Chem. 10 (2012) 6995.
[15] (a) B.M. Trost, J.W. Herndon, J. Am. Chem. Soc. 106 (1984) 6835;
(b) T. Tabuchi, J. Inanaga, M. Yamaguchi, Tetrahedron Lett. 28 (1987) 215.
[16] (a) S. Weigand, R. Bruckner, Synthesis (1996) 475;
(b) A.S.-Y. Lee, W.-C. Dai, Tetrahedron 53 (1997) 859.
[17] C. Prakash, S. Saleh, I.A. Blair, Tetrahedron Lett. 30 (1989) 19.
[18] This explanation is very tenuous. Primary 5-*tert*-butyldimethylsilyloxy groups can co-ordinate to allyltin trichlorides and so influence the stereoselectivities of their reactions with aldehydes. However, secondary 4-*tert*-butyldimethylsilyloxy groups can be less effective in this respect, see ref. 4. In Figure 3, it is a secondary *tert*-butyldimethylsilyloxy group that is involved but it may be that participation of co-ordination via the six-membered ring is important, see **52b** *cf*. **31b**.

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