Cyclizations *versus* rearrangements in the reactions of some epoxyolefins with Lewis acids †

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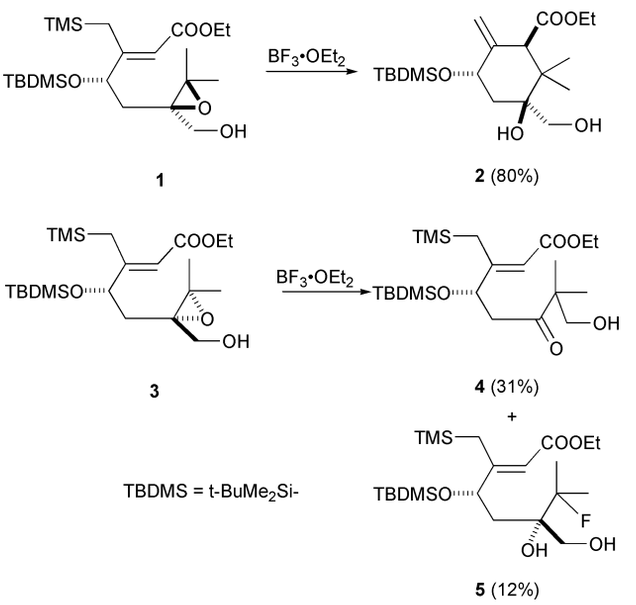
Treatment of various substituted epoxyolefins **A** with $BF_3{\cdot}OEt_2$ and other reagents that could be expected to induce carbocyclization to give cyclohexanes was investigated. It turned out that the general reaction of these systems was the epoxide to ketone rearrangement, while the carbocyclization was only a rare event. Only substrates carrying the allylsilane grouping underwent carbocyclization and in addition the protecting groups and the stereochemistry of the system had a decisive influence on whether ring closure or rearrangement were to take place.

Introduction

Electrophilic olefin cyclizations as formalised in Fig. 1(a) have been studied for over 40 years and have been employed in many biomimetic syntheses of carbocyclic compounds.[1–9] The initiating electrophilic center may be formed by the action of Lewis acids on a variety of structural units (starter groups) such as double bonds, epoxides, alcohols, acetals, *etc*. and the cyclization can be terminated by nucleophilic trapping or loss of a cationic species. In the latter case an olefin is formed. As a terminating group the 3-silylpropenyl group [allylic silane, Fig. 1 (b) and (c)] is very attractive due to its mild nucleophilicity and the controlled way in which the silyl moiety is eliminated.[10–20]

During our previous work with the synthesis of taxol A-ring building units we noticed that the diastereomeric epoxyallylsilanes **1** and **3** gave completely different products on treatment with $BF_3{\cdot}OEt_2$.[21,22] While **1** gave the cyclohexane derivative **2** (Scheme 1), compound **3** with the other configuration at the epoxide unit produced the rearranged product **4** and fluorohydrin **5** (Scheme 1). Related examples of diastereoselective ring closure of substituted epoxyallylsilane have been reported.[14,23–25]

Even though electrophilic carbocyclizations,[4–6,26–29] and rearrangements of epoxide to carbonyl compounds[7,30–33] and allylic alcohols[31,34,35] are well known synthetic transformations, the examples presented here seem to be the first cases where tetra-substituted epoxides have been used as starter units for the electrophile formation, and where electrophilic olefin cyclization could be expected to compete with epoxide rearrangements. A comparative investigation seemed appropriate and in this paper we report the reactions of several different substituted epoxyolefins **A** (Fig. 2) on treatment with $BF_3{\cdot}OEt_2$ and other reagents that were intended to induce carbocyclization. The epoxyolefins used (**A**) can be broadly divided into two categories; those carrying and those not carrying the allylic TMS-group *i.e.* R = TMS and H, respectively.



Scheme 1

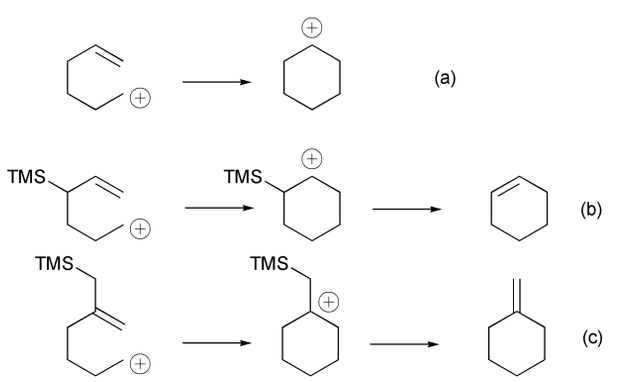


Fig. 1

Results

Our first attempts at ring closure of the epoxyolefins were made using the compounds lacking the allylic TMS group. This was reasonable since there were several such examples in the literature.[29,30] Thus, the bis-TBDMS protected epoxyolefin **6** was subjected to $BF_3{\cdot}OEt_2$ at rt, which, however, resulted in the

† ^{13}C NMR and elemental analysis data for compounds **6**–**40** and full experimental details for compounds **42**–**65** are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p1/b0/b010101j/

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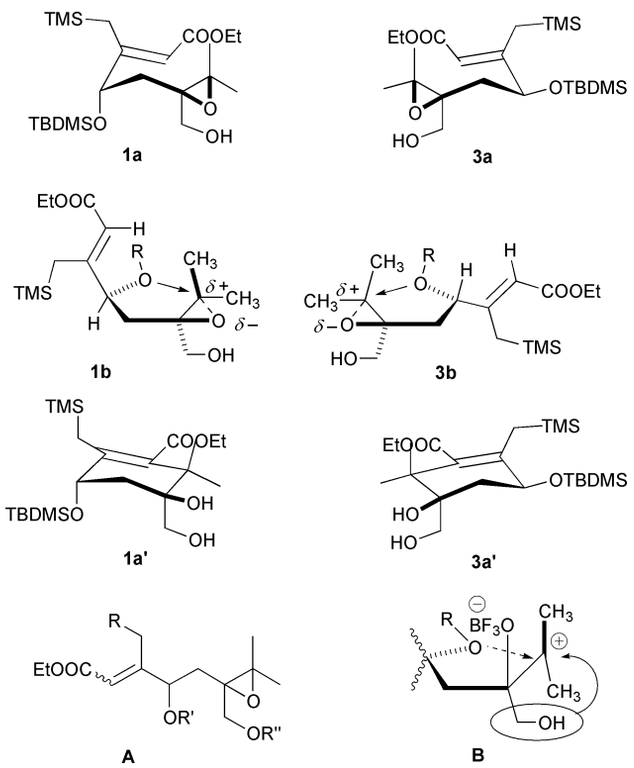
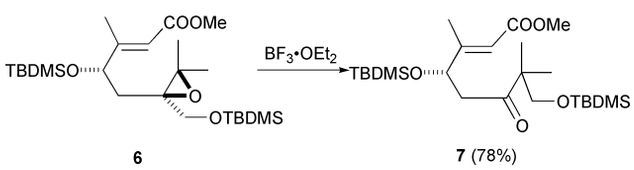


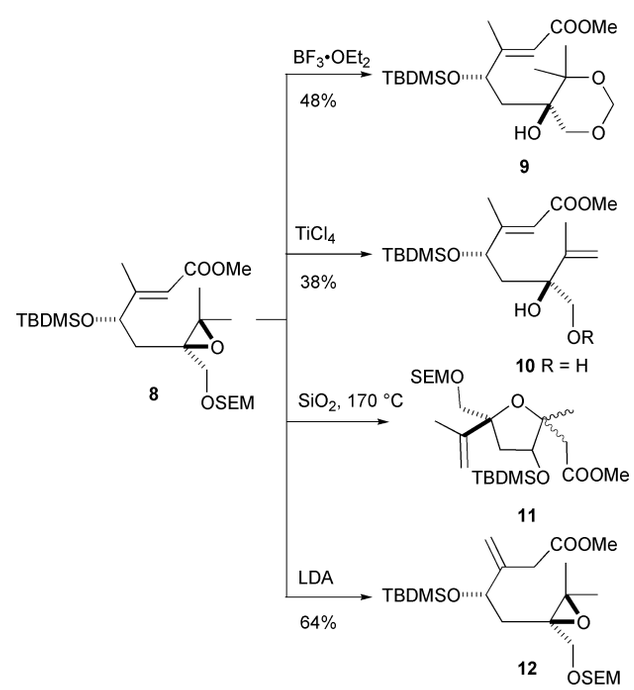
Fig. 2



Scheme 2

rearranged product **7** in good yield (Scheme 2). No ring-closed product could be identified.

In order to see if the migratory aptitude of the oxymethylene grouping could be reduced in favour of ring closure we instead tried the trimethylsilylethoxymethyl (SEM) protected **8** as substrate (Scheme 3). When reacting **8** with $BF_3{\cdot}OEt_2$ no

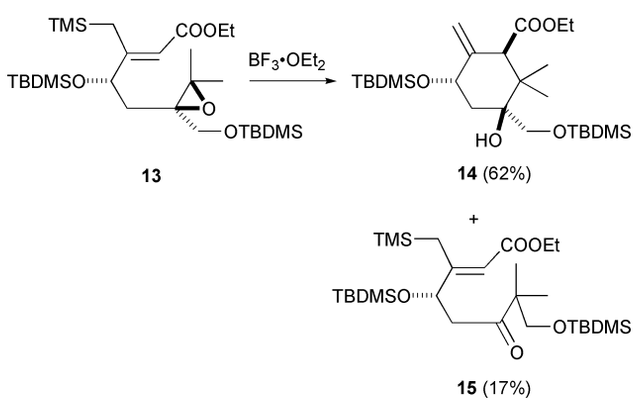


Scheme 3

rearrangement was observed but the oxirane ring was opened by the nucleophilic CH_2O moiety, presumably formed during desilylation of the SEM-group, to give **9**. The six-membered structure of the cyclic acetal **9** was indicated by the coupling constant of the geminal acetal protons, $J_{gem} = 6.3$ Hz. In the alternative five-membered acetal the corresponding coupling constant was expected to be *ca.* 0 Hz.[36] The epoxide to allylic alcohol rearrangement[31,34,35] occurred to give the SEM-deprotected allylic alcohol **10** when **8** was treated with $TiCl_4$ at 0 °C. Compound **10** was most likely an intermediate in the reaction when **8** was adsorbed and heated at 170 °C on silica gel, although **10** now cyclized to give **11** as a 1 : 5 mixture of diastereomers *via* an intramolecular Michael addition. A similar reaction has been described by Bartlett.[37] However, the yield of **11** was difficult to reproduce and an analytically pure sample could not be obtained.

Anionic nucleophilic cyclization of epoxy ester enolates was examined as an alternative, since it has been shown that such reactions may be useful for ring-constructions.[31,38] However, attempted carbocyclization *via* the enolate ion of **8**, generated by LDA treatment, resulted solely in deconjugation to give the β,γ-unsaturated ester **12**.

As was earlier shown by Fleming *et al.*[10] and extended by Armstrong and Weiler[14,15] ring-closure of epoxyolefins was greatly enhanced if the olefin part was in the form of an allylic silane. Indeed, subjected to $BF_3{\cdot}OEt_2$ the bis-OTBDMS protected allylic silane **13** (Scheme 4) cyclized to give **14** as the



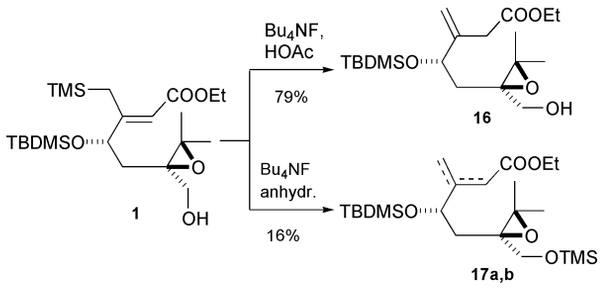
Scheme 4

major reaction, although some rearrangement also took place to give **15**.

As we noticed earlier, the migration was not observed when the primary TBS protection was absent as for **1**. This substrate gave a quite high yield of the desired cyclohexane derivative **2** (Scheme 1) without any traces of the rearranged product.[21,22] We assume that in this case the hydroxy did not react with $BF_3{\cdot}OEt_2$ to give a borate but perhaps only gave a coordination complex. Thus, the BF_3-coordinated $HOCH_2$-group ($BF_3{\cdot}HOCH_2$–) seemed to be less prone to migrate than $TBDMSOCH_2$–. Migration of the $TBDMSOCH_2$-group has been observed also in other compounds.[39,40]

Acidic conditions combined with fluoride ion attack on the allylic silane was a logical experiment in order to achieve ring closure. However, in contrast to the facile cyclization of **1** under $BF_3{\cdot}OEt_2$-conditions (Scheme 1) the use of $Bu_4NF{\cdot}3H_2O$ in the presence of HOAc in THF at 0 °C resulted in the exclusive formation of the deconjugated ester **16** (Scheme 5). The fluoride ion attack on the TMS-group probably facilitated the protiodesilylation, but it should be noted that the TBDMS-group was not removed nor was the epoxide ring cleaved.

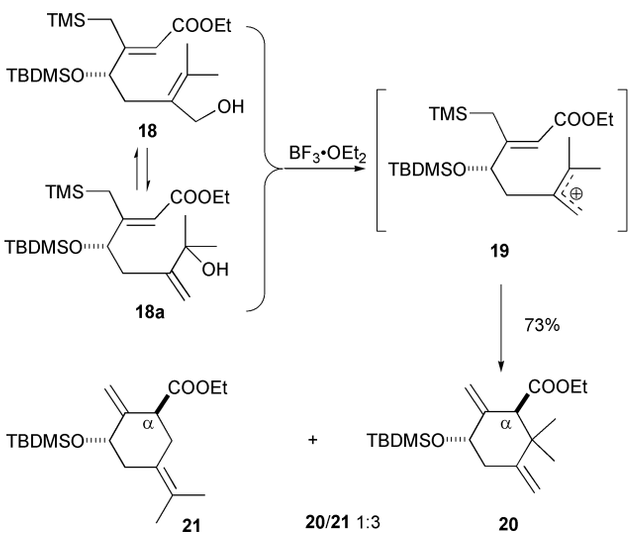
Aprotic fluoride ion conditions, which may result in ring closure *via* the enolate ion of **16**,[41] gave only a low yield of a mixture of the conjugated and the deconjugated *trans*-silylated esters **17a**,**b**. The primary TMS-ether was probably formed



Scheme 5

by intra- or intermolecular transfer of the TMS-group from the starting material. Thus, fluoride ion-induced cyclizations were not successful with **1**.

Since **18**,[22] carrying an allylic alcohol moiety as an alternative starter group, was the starting material for **1** it was natural to test **18** for cyclization (Scheme 6). Being a primary allylic

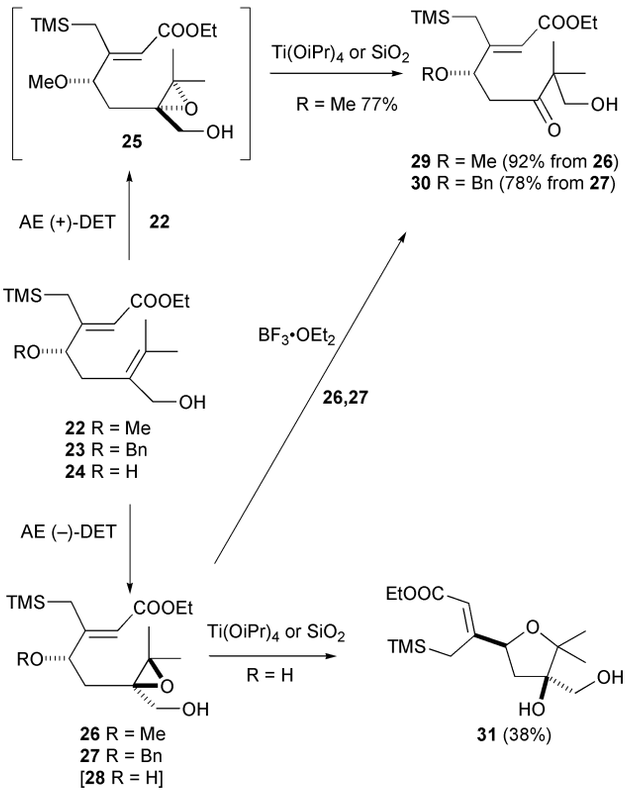


Scheme 6

alcohol it would have a tendency to rearrange to the tertiary allylic alcohol **18a** possibly *via* cation **19** or an equivalent species. This seemed to be the case since on treatment of **18** with $BF_3{\cdot}OEt_2$ a small amount of **18a** was detected by NMR spectroscopy and to judge from TLC analysis the cyclization was slow and occurred at least partly *via* **18a** to give a 3 : 1 mixture of **20** and **21**. Obviously the regiochemistry of the attack on the electrophilic allylic cation moiety was not dominated by the steric hindrance of the gem-dimethyl group. No diastereomeric compounds were detected and the configuration at the α-C was assumed to be the same as in **2**.

A rather unexpected influence of the protecting groups at O-4 was observed for **26** and **27** (Scheme 7). Instead of ring closure in parallel to **1**, only the hydroxymethyl migration took place to give the keto-alcohols **29** and **30**, respectively, in high yields. In fact, epoxides **26** and **27**, prepared *via* Sharpless epoxidation[42,43] of the corresponding allylic alcohols **22** and **23** using (−)-DET, could not be obtained pure by chromatography on silica gel due to this rearrangement. Moreover, according to NMR analysis of the crude product, a small amount (6%) of an allylic alcohol with a tentative structure similar to **10** (Scheme 3) was also formed.

An even more rearrangement-prone situation was found when **22** was epoxidized using (+)-DET, which would lead to **25**, the epoxide portion with the opposite configuration as compared with **26**. To judge from TLC analysis, the reaction mixture contained approximately equal amounts of epoxide and ketone. However, the epoxide **25** could not be isolated since it was totally rearranged upon chromatography on silica gel

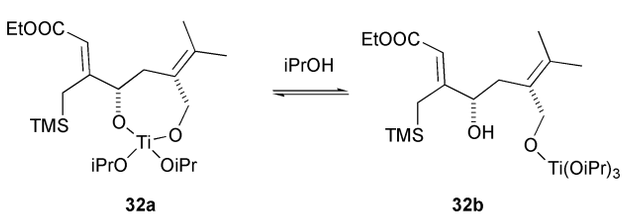


Scheme 7

to give keto-alcohol **29** in 77% isolated yield. Whether the rearrangement took place solely on silica gel, or if it was induced by the Ti-catalyst during epoxidation as well, was not possible to decide, since the reaction was monitored by silica gel TLC.

Interestingly, compound **28** having a free alcohol group at C-4 could not be isolated or even detected on Sharpless epoxidation of the corresponding allylic alcohol **24**. The reaction was slow and resulted in the formation of the tetrahydrofuran derivative **31** as the only isolable product. This compound may have been formed *via* **28**, which under the Lewis acidic reaction conditions ($Ti(OiPr)_4$) gave **31**, by attack of O-4 at the epoxide gem-dimethyl carbon. Similar acid catalyzed ring closures of hydroxy-epoxides have been developed previously for the syntheses of a variety of 5- and 6-membered heterocycles present as substructures in natural products.[44,45]

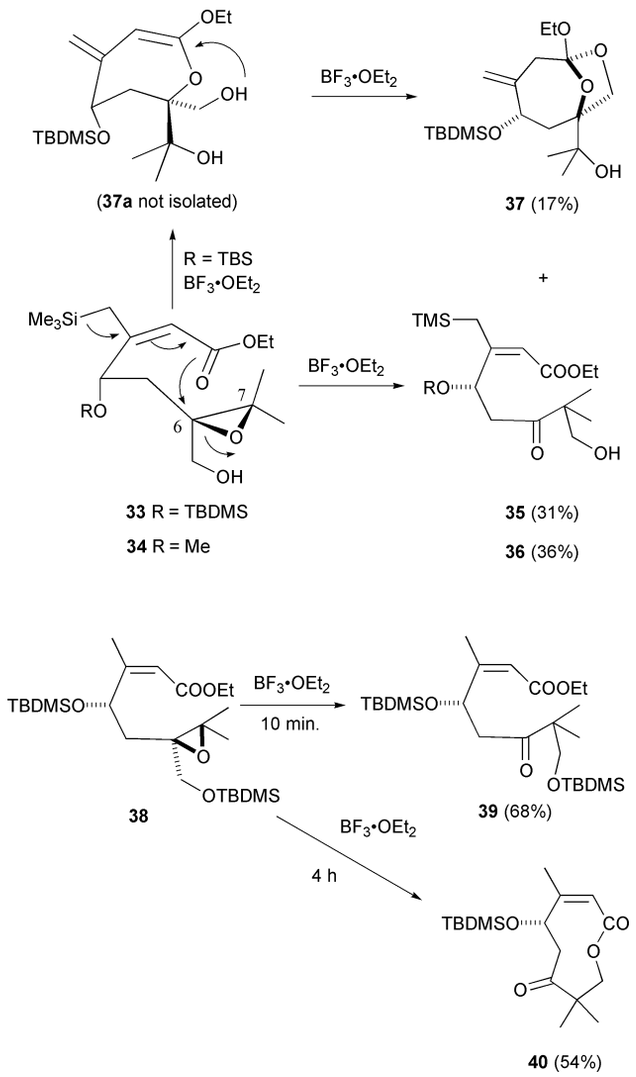
Since the reaction was very slow it was quenched before completion, hence the low yield of **31**. Titanate formation, **32a/32b** (Scheme 8) between the diol precursor **24** and the



Scheme 8

Ti-catalyst may have caused the slow reaction already at the epoxidation stage.[46] Alternatively, the formation of the tetrahydrofuran derivative may have occurred from **28** in contact with the silica gel used both in monitoring the reaction (TLC) and in the isolation of **31**. Further details were not investigated.

The compounds having *cis*-configuration at the α,β-unsaturated ester moiety rearranged to some extent but also underwent other reactions. However, no carbocyclization was observed. Thus, compound **33** (Scheme 9) gave, besides the rearrange-



Scheme 9

ment product **35**, the [4.2.1]bicyclic orthoester **37**, the carbon skeleton of which was not rearranged. The alternative [4.2.2]-bicyclo compound (epoxide-opening at C-7) was ruled out on spectroscopic grounds. The coupling constant of the geminal protons in the smaller ring of **37**, J_{gem} = 7.1 Hz, indicated that this ring was five-membered.[46,47] The ^{13}C NMR-signal of the quaternary orthoester carbon appeared as a singlet at 122.4 ppm, which was consistent with reported values for similar structures.[47–50] An attempted acetylation using standard acetylation conditions of **37** failed, which again indicated that the free hydroxy was tertiary and not primary.

Also in the case of **34**, with a methoxy instead of a TBDMSO-grouping at C-13, rearrangement took place to give **36**, which was formed in a small amount directly during epoxidation of the precursor allylic alcohol as well. Two compounds of unknown structures were also formed (*ca*. 25%). Thus, despite the presence of the allylic TMS-moiety no carbocyclization was observed for the *cis*-olefins.

The rearrangement of the "des-TMS" derivative **38** gave **39**, which lactonized to give the 9-membered lactone **40** after extended reaction time. Formation of 9-membered lactones is generally not a feasible process, but in this particular case the combination of the *syn*-geometry of the reacting terminals of **39** and the gem-dimethyl effect[51] may have contributed to this lactonization.

Discussion

The results presented show that compounds possessing the structural features as in **A** (Fig. 2) undergo three major reactions under BF_3-acidic conditions; epoxide rearrangement, carbocyclization and tetrahydrofuran ring closure.

Epoxide rearrangement by migration of the hydroxymethyl and $TBDMSOCH_2$-groups seems to be the generally preferred reaction. The high migratory aptitude of the $TBDMSOCH_2$-group was demonstrated by Maruoka *et al*. for rearrangement of TBDMS-protected epoxyalcohols to TBDMS-protected β-hydroxyaldehydes using methylaluminium bis(4-bromo-2,6-di-*tert*-butylphenoxide).[40] However, these authors pointed out that this rearrangement could not easily be accomplished with conventional Lewis acids such as $BF_3{\cdot}OEt_2$. Our results show that it obviously can, provided that the substrate has the appropriate structure. One should note that the substrates used by Maruoka *et al*. did not have the oxy-function at C-4, as was the case in all of our substrates.

Migration of the hydroxymethyl group was not unexpected but there are cases reported in the literature where hydroxyalkyl groups do not migrate, but instead, an alkyl group or an aryl group positioned at the same carbon as the hydroxy group migrates, in analogy with the pinacol rearrangement.[52–54] In the reaction with $BF_3{\cdot}OEt_2$ it seems likely that the epoxide oxygen of substrate **A** acts as the Lewis basic centre. Polarisation of the oxirane O–C bond would then result in the build-up of positive charge at C-6 and C-7. A five-membered arrangement involving C-7 as in **1b** and **3b** (Fig. 2) would therefore be favoured, leading to oxolanes as has been demonstrated in many similar cases[31,44,55] and also occurred with **A** when O-4 carried a proton as leaving group (Scheme 7, **31**). The corresponding MeO and BnO-derivatives **25**–**27** did not form the corresponding oxolane derivatives; instead the migration dominated to give **29** and **30**, respectively.

On the other hand, the bulky TBDMSO-group may prevent the oxygen atom from coming close to the C-7 cationic centre, which makes it possible for carbocyclization to compete, possibly *via* transition state **1a**. In addition to this steric effect, the complexing ability of the oxygen lone-pair electrons in silyl ethers is reduced by the p-accepting character of the empty d-orbitals of silicon.[56,57] Hence, the observed diminished ability to stabilise a positive charge by co-ordination for silyloxy-groups as compared to alkoxy-groups.

It is also worth mentioning that all ketones isolated were formed by migration of the hydroxymethyl grouping, and not by migration of the carbon chain residue (C-6 migration). If we assume that **1b** and **3b** are contributing to the stabilisation of the developing positive charge at C-7, the C-6 migration would have to be *syn*-periplanar with respect to the co-ordinating C-4 oxygen. However, the hydroxymethyl moiety can migrate in an *anti*-periplanar fashion, which seems more favourable. Interestingly, it was recently shown by computational methods, that the boron alcoholate moiety resulting in the opening of the epoxide ring was positioned in the same plane as the carbon frame work in the BF_3-induced hydride migration of methylpropene oxide to the corresponding aldehyde.[58] These results, transferred to our case, would give a conformation as shown in **B** (Fig. 2) and seems reasonable to explain the preferred migration of the hydroxymethyl group as depicted.

Based on the Stork–Eschenmoser hypothesis for the electrophilic ring-closure of olefins[59,60] and previous discussions of the transition state for carbocyclization of epoxy-allylsilanes by Armstrong and Weiler[14] it seems necessary to achieve the correct alignment of the electrophilic centre, the double bond and the TMS-group as depicted in **1a** and **3a** (Fig. 2). The C–Si bond should be perpendicular to the plane of the double bond and also *anti*-periplanar to the epoxide C–C bond. When comparing **1** with **3** in their chair-like conformations **1a** and **3a** there was no obvious reason for their different behaviour, except that the steric bulk of the TBDMS-group may prevent the allylic TMS-group from aligning properly for carbocyclization to occur. This has been discussed by Prestwich *et al*.[23] for a similar

substrate and our experimental results are quite in line with their arguments. However, preliminary molecular mechanics calculations of the steric energies of a number of geometries of **1** and **3** do not point strongly in this direction. For example, **1a** and **3a** had essentially the same steric energies in the lowest energy conformations hitherto found. Also very similar energies were found for the ring closed forms **1a′** and **3a′**, which may be taken as gross approximations of possible transition state models. Moreover, there was no indication that the alignment of the C–Si bond would be disturbed in **3a** as compared to the situation for **1a**, an almost perfect 90 degree angle between the C–Si bond and the plane of the double bond was found for both arrangements. This was also found for the cyclohexene models **1a′** and **3a′**. The computations did indicate that the chair-like arrangements were of lower energies than the corresponding boat conformations but only by 1–2 kcal mol^{-1}. Obviously, more sophisticated and detailed computational work will be necessary in order to understand the choice of the competitive pathways of carbocyclization and epoxide rearrangement for compounds such as **A** and related derivatives. But at present it seems uncertain that the buttressing effect on the C–Si alignment of the allylic silane moiety by large neighbouring groups is a major factor.

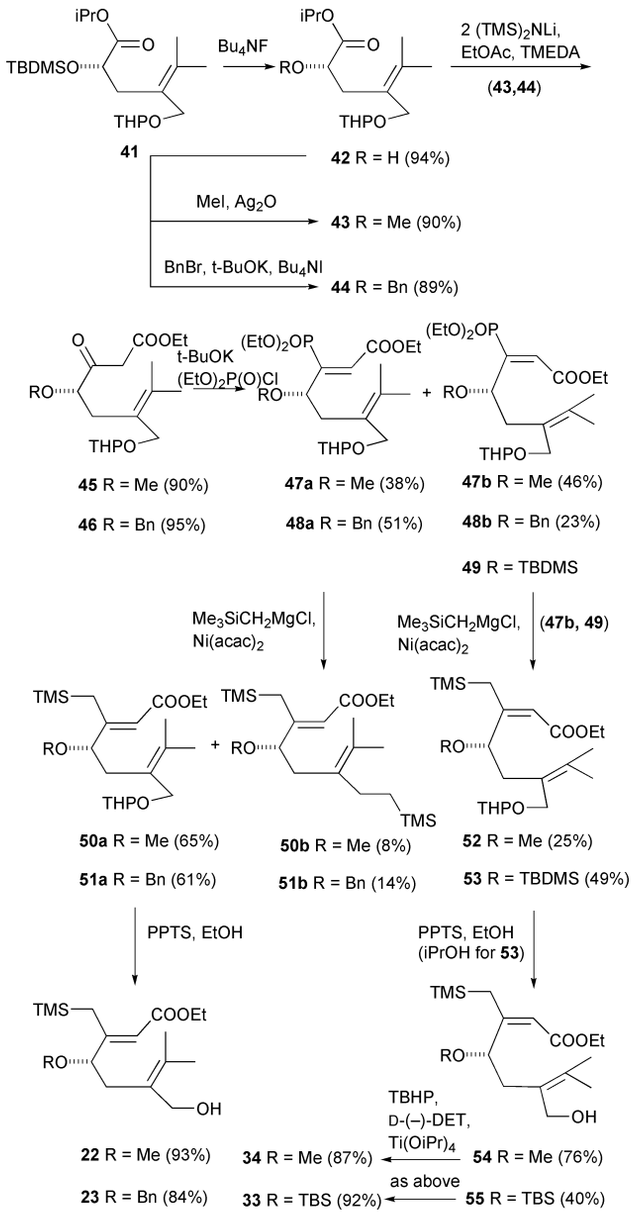
The first step in the orthoester formation (**37**, Scheme 9) resembles the cyclization of an epoxy allylsilane. One may speculate that a seven-membered transition state and a nucleophilic attack by oxygen as in **37a** was a consequence of steric congestion between the carboxylate group and the hydroxymethyl group as shown in **33** (Scheme 9), making a 6-membered carbocycle formation impossible.

A mechanistic possibility of fluorohydrins being general intermediates can not be ruled out. Formation of fluorohydrins in epoxyolefin cyclizations, when $BF_3{\cdot}OEt_2$ was used as reagent, was reported to be favoured in Et_2O as opposed to benzene, and in Et_2O further reaction of the fluorohydrins to give ketones occurred.[61] In our experiments CH_2Cl_2 was routinely used as solvent so no direct comparisons can be made. However, minor amounts of fluorohydrins were probably formed in most of our experiments since they were tentatively identified by TLC and NMR spectroscopy of crude reaction products. In one case a fluorohydrin **5** was isolated.

Syntheses of the starting materials

The common starting material for the allylsilanes was the earlier described doubly protected isopropyl ester **41**[22] (Scheme 10). After selective removal of the TBDMS-protection to give **42** the methyl- and benzyl-protecting groups were introduced by simple alkylation. Thus, methylation (MeI and Ag_2O in DMF)[62,63] and benzylation (BnBr, t-BuOK and Bu_4NI in THF)[62] of **42** gave **43** and **44**, respectively. These compounds were transformed into *Z*,*E*-mixtures of enolphosphates (**47a**,**b** and **48a**,**b**) *via* enolate trapping with dimethylphosphoric chloride of the corresponding β-ketoesters **45** and **46**, in their turn obtained by treatment of **43** and **44** with the lithium enolate of ethyl acetate. The *Z*- and *E*-isomers **47** and **48** were separated by column chromatography. Interestingly the *Z* : *E* ratio was dependent on the protecting group at O-4. While the methyl ether **45** gave a 45 : 55 *Z* : *E* ratio the more bulky benzyl ether **46** gave 7 : 3 and the even more bulky TBDMS-ether[22] gave a 9 : 1 ratio.

In the Ni-catalyzed coupling of **47a** and **48a** with $TMSCH_2$-MgCl both compounds gave, in addition to the expected allylic silanes **50a** and **51a**, respectively, the corresponding minor coupling products **50b** (8%) and **51b** (14%), resulting from coupling at the allylic THP ether site (Felkin-type coupling[64]). Since the desired coupling reaction was favoured by the use of an excess of the Grignard reagent a compromise was to use 2 equivalents of this reagent, which, still gave some Felkin-coupling. After separation of the Felkin products by column



Scheme 10

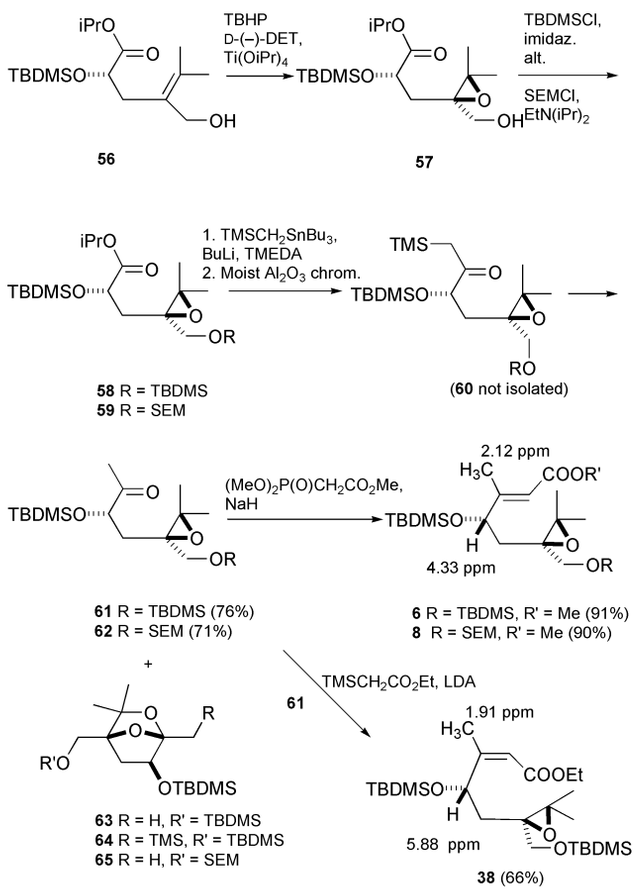
chromatography and removal of the THP protection using PPTS in EtOH, the resulting allylic alcohols **22** and **23** were epoxidized by the Sharpless asymmetric epoxidation conditions[42] using D-(−)-DET as ligand to give the epoxides **26** and **27** in 71 and 77% yield, respectively. Minor amounts of the rearrangement products, ketones **29** and **30** (Scheme 7) as well as the allylic alcohols corresponding to **10**, were also formed. These contaminants could not be removed from the main product by chromatography on silica gel since the silica gel itself induced the rearrangements. Thus, both **26** and **27** were used in their slightly contaminated forms in the $BF_3{\cdot}OEt_2$ treatments.

Ni-catalyzed cross-coupling of Me_3SiCH_2MgCl with the *E*-enolphosphates **49**[22] and **47b** (**48b** was not further transformed) gave lower yields of allylsilanes than the analogous *Z*-enolphosphates. Furthermore, Felkin coupling of the THP-protected allyl alcohol moieties in the *E*-enolphosphates was not observed. Isomerization of the double bond of the α,β-unsaturated ester in the reaction of **49** to give **53** (*E* : *Z* 6 : 1 according to NMR analysis) was noticed and for the further transformation the *Z*-isomer was removed by chromatography.

Removal of the THP protection of **52** was performed by using PPTS in EtOH to give **54**. The TBDMS-protected derivative **53** was, however, reacted in propan-2-ol to suppress solvolysis of the silylether. This gave **55** in 40% yield. Epoxid-

ation of **55** provided the epoxy allylsilane **33** in high yield. The epimeric epoxide was not prepared and the diastereomeric excess of the epoxidation was not determined with precision but was estimated to be 90–95% by ^{1}H NMR analysis. The epoxidation of **54** to give **34** was accompanied by rearrangement to ketone **36** (8%), which could not be separated from **34** by column chromatography. The rearrangement was caused by the silica gel, or by the reaction conditions in the epoxidation *e.g.* $Ti(OiPr)_4$.

The synthesis of the des-TMS derivatives **6**, **8** and **38** is outlined in Scheme 11. Epoxidation using the Sharpless AE



Scheme 11

conditions (D-(−)-DET) of the known allylic alcohol **56**[22] provided epoxy alcohol **57** (92%, 92% de). Short reaction times should be used since stirring the reaction mixture at rt overnight resulted in epoxide-opening and lactonization. After protecting the epoxy alcohol as the TBDMS-ether[65,66] and as the trimethylsilylethoxymethyl(SEM)-ether[67] to give **58** and **59**, respectively, we originally had in mind to synthesise allylic silanes similar to **1** and therefore sought methods to attach a $TMSCH_2$-group at C-1 of these compounds. Thus, isopropyl esters **58** and **59** were treated with an excess of Me_3SiCH_2Li, formed *in situ* from $Me_3SiCH_2SnBu_3$ and n-BuLi[68,69] (lithium–halogen exchange of Me_3SiCH_2Cl with Li was not effective), in the presence of TMEDA. The use of the Li-reagent, in favour of the more easily prepared Grignard-reagent, was indicated by the reported examples of bis-addition of the Grignard-reagent to esters.[11] We reasoned that the Li-reagent was probably capable of deprotonating the expected silylketone **60** at the α-position adjacent to silicon, thus protecting the carbonyl group from further addition.[70] However, silylketone **60** (R = TBDMS) was not detected (its presence was only indicated by the TMS-moiety in **64**). Instead, the desilylated ketone **61** together with the bicyclic acetals **63** and **64** were formed. These compounds could have been formed *via* two different reactions of the presumed silylketone **60**: a direct protiodesilylation or, alternatively, by C–O rearrangement of the α-TMS group to give the corresponding silylenol ether, which after hydrolytic work-up or during chromatography resulted in methylketone **61**.[71]

The other reaction, the intramolecular acetalization leading to the bicyclic acetals **63** and **64**, took place on silica gel and on dry neutral alumina. The isolation and purification of **61** therefore had to be conducted on wet alumina (10% water). During NMR analysis it was found that **61** could be quantitatively converted into acetal **63** by standing in dry $CDCl_3$ (most likely containing small amounts of DCl). Thus, the acetalization did not proceed *via* a diol obtained by hydrolysis of the epoxide but rather directly *via* a keto-epoxide to acetal conversion.[72] The SEM-protected **59** behaved analogously on treatment with the $TMSCH_2Li$ reagent and gave **62** together with **65**. Interestingly, the acetals **63**–**65** were diastereomerically pure, but we do not know the configurations of the bridgehead carbons, *i.e.* we do not know which of the two epoxide carbons was attacked by the carbonyl oxygen.

The *trans*-α,β-unsaturated esters **6** and **8** were prepared in good yields from **61** and **62**, respectively, by the reaction with the sodium salt of $(MeO)_2P(O)CH_2CO_2Me$ in 1,2-dimethoxyethane (DME).[73] Reaction of **61** with the lithium-salt of $Me_3SiCH_2CO_2Et$[74,75] provided the *cis*-ester **38**. Small amounts of the *trans*-isomer (detected by TLC) were probably formed in this reaction, but the purification of **38** was quite easy due to the large difference in R_f values on silica gel.

The stereochemistry of the double bond at the α,β-unsaturated ester was determined by ^{1}H NMR spectroscopy. A difference of 0.21 ppm was noticed for 3-CH_3 in **38** and **6/8** (1.91 ppm and 2.12 ppm, respectively) while a much larger effect (a difference of 1.55 ppm) was noticed for H-4. In **38** (5.88 ppm), this proton is probably forced to be in close proximity to the deshielding sector of the ester carbonyl[76,77] by the bulky TBDMSO-group and by the carbon-chain. This method of determining the stereochemistry of α,β-unsaturated esters was used for all similar derivatives in this work.

Conclusions

To the best of our knowledge this is the first time a series of tetra-substituted epoxides have been investigated under conditions where carbocyclizations of epoxyolefins to give 6-membered rings could be expected. Our experiments showed that a particularly facile reaction for these kinds of compounds was the 1,2-rearrangement of the $–CH_2OH$ and $–CH_2$-OTBDMS moieties to give 1,3-hydroxyketones. Other competing reactions were the epoxide to allylic alcohol rearrangement and the formation of THF-derivatives. The SEM-protecting group makes other reaction paths possible and is obviously a rather reactive protecting group under Lewis acidic conditions.[78,79]

It could be concluded that the epoxyolefins lacking the allylic TMS-group were unable to form carbocyclic products. Thus, the allylsilane moiety was crucial for the epoxyolefin carbocyclization in these cases. However, the structural tolerance is very narrow and the presence of the allylic silane moiety is not enough to achieve carbocyclization. A further feature beneficial for the carbocyclization was the low nucleophilicity of the 4-OTBDMS oxygen combined with the large bulk of the TBDMS-group, which prevented the cation stabilizing effect of the 4-O coordination, thus allowing a folding of the carbon chain leading to carbocyclization. Substrates with a more electron rich 4-O in combination with a smaller oxygen substituent probably folded in a fashion favouring a five-membered arrangement, which prevented carbocyclization. In these cases the 1,2-rearrangement of the $–CH_2OH$ and $–CH_2OTBDMS$ moieties or oxolane formation occurred.

Experimental

Column chromatography separations were performed using Merck SiO_2 60 (0.040–0.063 mm) silica gel. TLC analyses were done on Merck SiO_2 60 F254 precoated aluminium sheets and the spots were visualized by charring with 10% aqueous H_2SO_4 or by Merck molybdophosphoric acid spray reagent. The chromatographic eluents were heptane–ethyl acetate (H–E) mixtures throughout and the ratios are given in parentheses in this order. Melting points were determined with a Reichert microscope and are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 polarimeter. Mass spectra were recorded on a Finnigan 4021 spectrometer (electron impact mode at 70 eV). NMR spectra were recorded at 23 °C with a Varian XL-300 spectrometer using $CDCl_3$ as solvent and $CHCl_3$ as internal standard if not otherwise stated (δ (^{1}H) 7.26 ppm). The following abbreviations are used: br (broad), s (singlet), d (doublet), t (triplet), q (quartet), sept (septet), m (multiplet or complex signal). Heptane and EtOAc were distilled before use. Dry CH_2Cl_2 and DMF were purified by distillation and stored over molecular sieves (4 Å). Dry toluene, Et_2O, THF and DME were prepared by drying the commercial solvents (*p.a.* grade) over molecular sieves (4 Å). The molecular sieves were activated at 170 °C under vacuum. All other reagents were used as delivered. Organic extracts were dried using either Na_2SO_4 or $MgSO_4$ throughout. ^{13}C NMR data for all compounds are available as Supplementary material together with full details of the syntheses of compounds **42**–**65**.†

Methyl (4*S*,6*R*,2*E*)-4-(*tert*-butyldimethylsilyloxy)-6-[(*tert*-butyldimethylsilyloxy)methyl]-6,7-epoxy-3,7-dimethyloct-2-enoate (6)

Trimethyl phosphonoacetate (0.159 mL, 1.1 mmol) was added to a slurry of NaH (38 mg, *ca.* 1.0 mmol, *ca.* 63% in mineral oil) in dry DME (3.0 mL) under nitrogen. The slurry was stirred for 30 min at rt and then a solution of **61** (159 mg, 0.382 mmol) in dry DME (1.0 mL) was added. The temperature was raised to 90 °C and stirring was continued for 3 h. After cooling, ether (100 mL) was added and the solution was washed with water, dried and the solvent was evaporated at reduced pressure. Column chromatography (H–E, 50 : 1) gave **6** (oil, 164 mg, 91%): R_f (10 : 1) 0.33; $[\alpha]_D^{20}$ −25 (*c* 1.23, $CDCl_3$); δ_H −0.01, 0.06, 0.07, 0.08 (4s, 12H, –Si(CH_3)$_2$–), 0.90, 0.91 (2s, 18H, t-Bu), 1.31, 1.35 (2s, 6H, >C(CH_3)$_2$), 1.77 (dd, 1H, J_{AB} = 14.2 Hz, J = 10.0 Hz, H-5), 2.02 (dd, 1H, J_{AB} = 14.2 Hz, J = 3.0 Hz, H-5), 2.12 (d, 3H, J = 1.6 Hz, –C(CH_3)=CH–), 3.70 (s, 3H, –OCH_3), 3.78, 3.80 (2d, 2H, J_{AB} = 11.1 Hz, –CH_2O–), 4.33 (dd, 1H, J = 10.0 Hz, 3.0 Hz, H-4), 5.87 (m, 1H, vinyl) (Found: C, 61.13; H, 10.31. $C_{24}H_{48}O_5Si_2$ requires C, 60.97; H, 10.23%).

Methyl (4*S*,2*E*)-4,8-bis(*tert*-butyldimethylsilyloxy)-3,7,7-trimethyl-6-oxooct-2-enoate (7)

The experiment was performed as described for **14** using **6** (116 mg, 0.245 mmol) as starting material. Column chromatography (H–E, 50 : 1) gave **7** (oil, 90 mg, 78%): R_f (10 : 1) 0.42; $[\alpha]_D^{20}$ −32 (*c* 1.16, $CDCl_3$); δ_H 0.01 (s, 3H, –Si(CH_3)$_2$–), 0.02 (s, 6H, –Si(CH_3)$_2$–), 0.03 (s, 3H, –Si(CH_3)$_2$–), 0.85, 0.85 (2s, 18H, t-Bu), 1.06 (s, 6H, –C(CH_3)$_2$–), 2.08 (d, 3H, J = 1.3 Hz, –C(CH_3)=CH–), 2.43 (dd, 1H, J_{AB} = 17.3 Hz, J = 3.1 Hz, H-5), 2.90 (dd, 1H, J_{AB} = 17.3 Hz, J = 8.3 Hz, H-5), 3.50, 3.59 (2d, 2H, J_{AB} = 9.9 Hz, –CH_2O–), 3.70 (s, 3H, –OCH_3), 4.68 (ddd, 1H, J = 3.1 Hz, 8.3 Hz, 0.9 Hz, H-4), 5.96 (m, 1H, vinyl) (Found: C, 61.29; H, 10.29. $C_{24}H_{48}O_5Si_2$ requires C, 60.97; H, 10.23%).

Methyl (4*S*,6*R*,2*E*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-3,7-dimethyl-6-[(2-trimethylsilylethoxy)methoxymethyl]oct-2-enoate (8)

The experiment was performed as described for **6** using **62** (402 mg, 0.929 mmol) as starting material. Column chromatography (H–E, 10 : 1) gave **8** (oil, 410 mg, 90%): R_f (1 : 1) 0.68; $[\alpha]_D^{20}$ −33 (*c* 0.92, $CDCl_3$); δ_H 0.00 (s, 3H, –Si(CH_3)$_2$–), 0.02 (s, 9H, TMS), 0.08 (s, 3H, –Si(CH_3)$_2$–), 0.90 (s, 9H, t-Bu), 0.95 (m, 2H, –CH_2–TMS), 1.35 (s, 6H, >C(CH_3)$_2$), 1.84 (dd, 1H, J_{AB} = 14.2 Hz, J = 9.5 Hz, H-5), 1.94 (dd, 1H, J_{AB} = 14.2 Hz, J = 3.1 Hz, H-5), 2.12 (d, 3H, J = 1.6 Hz, –C(CH_3)=CH–), 3.64 (m, 2H, –C$H_2$$CH_2$–TMS), 3.68 (d, 1H, J_{AB} = 10.4 Hz, –CH_2-OSEM), 3.70 (s, 3H, –OCH_3), 3.78 (d, 1H, J_{AB} = 10.4 Hz, –CH_2-OSEM), 4.32 (dd, 1H, J = 9.5, 3.1 Hz, H-4), 4.70 (s, 2H, –OCH_2O–), 5.88 (m, 1H, vinyl) (Found: C, 58.94; H, 9.96. $C_{24}H_{48}O_6Si_2$ requires C, 58.97; H, 9.90%).

(5*R*,2′*S*,3′*E*)-5-Hydroxy-4,4-dimethyl-5-(4′-methoxycarbonyl-3′-methyl-2′-*tert*-butyldimethylsilyloxybut-3′-enyl)-1,3-dioxane (9)

The experiment was performed as described for **14** using **8** (50 mg, 0.10 mmol) as starting material. Column chromatography (H–E, 10 : 1) gave **9** (oil, 19 mg, 48%): R_f (1 : 1) 0.53; $[\alpha]_D^{20}$ −41 (*c* 0.55, $CDCl_3$); δ_H −0.03, 0.11 (2s, 6H, –Si(CH_3)$_2$–), 0.91 (s, 9H, t-Bu), 1.20, 1.33 (2s, 6H, >C(CH_3)$_2$), 1.40 (ddd, 1H, J_{AB} = 14.4 Hz, J = 8.8 Hz, 1.9 Hz, H-5), 1.53 (dd, 1H, J_{AB} = 14.4 Hz, J = 2.0 Hz, H-5), 2.11 (d, 3H, J = 1.1 Hz, –C(CH_3)=CH–), 3.23 (d, 1H, J = 1.9 Hz, –OH), 3.70 (s, 3H, –OCH_3), 3.83 (d, 1H, J_{AB} = 12.3 Hz, –CH_2O–), 4.05 (dd, 1H, J_{AB} = 12.3, 1.0 Hz, –CH_2O–), 4.52 (ddd, 1H, J = 8.8, 2.0, 0.8 Hz, H-4), 4.80 (dd, 1H, J_{AB} = 6.3 Hz, J = 1.0 Hz, acetal), 4.95 (d, 1H, J_{AB} = 6.3 Hz, acetal), 5.91 (dq, 1H, J = 0.8 Hz, 1.1 Hz, vinyl) (Found: C, 58.68; H, 9.30. $C_{19}H_{36}O_6Si$ requires C, 58.73; H, 9.34%).

Methyl (4*S*,6*S*,2*E*)-4-(*tert*-butyldimethylsilyloxy)-6-hydroxy-6-hydroxymethyl-3,7-dimethylocta-2,7-dienoate (10)

$TiCl_4$ (0.102 mL, 0.10 mmol, 1.0 M in CH_2Cl_2) was added to a solution of **8** (50 mg, 0.10 mmol) in dry CH_2Cl_2 (0.5 mL) under nitrogen at 0 °C. The reaction mixture was stirred for 15 min and $NaHCO_3$ (sat., 0.5 mL) was then added followed by tartaric acid (10% aq., 0.5 mL) and ether (10 mL). The organic phase was washed with water, dried and the solvent was evaporated at reduced pressure to give crude **10** which was slightly decomposed when standing at rt overnight. Column chromatography (H–E, 3 : 1) gave **10** (oil, 14 mg, 38%): R_f (1 : 1) 0.43; $[\alpha]_D^{20}$ −5 (*c* 0.35, $CDCl_3$); δ_H −0.01, 0.08 (2s, 6H, –Si(CH_3)$_2$–), 0.92 (s, 9H, t-Bu), 1.69 (dd, 1H, J_{AB} = 14.9 Hz, J = 1.7 Hz, H-5), 1.75 (dd, 3H, J = 1.7, 0.7 Hz, H-8), 2.07 (dd, 1H, J_{AB} = 14.9 Hz, J = 10.7 Hz, H-5), 2.13 (d, 3H, J = 1.1 Hz, –C(CH_3)=CH–), 3.43 (s, 2H, –CH_2OH), 3.71 (s, 3H, –OCH_3), 4.32 (ddd, 1H, J = 1.7, 10.7, 0.7 Hz, H-4), 4.38 (s, 1H, –OH), 5.11 (dq, 1H, J = 2.0, 1.7 Hz, =CH_2), 5.25 (dq, 1H, J = 2.0, 0.7 Hz, =CH_2), 5.82 (dq, 1H, J = 0.7, 1.1 Hz, H-2) (Found: C, 60.39; H, 9.54. $C_{18}H_{34}O_5Si$ requires C, 60.30; H, 9.56%).

Methyl 2-[2-methyl-3-*tert*-butyldimethylsilyloxy-5-(propen-2-yl)-5-(trimethylsilylethoxymethoxymethyl)tetrahydrofuran-2-yl]acetate (11)

Silica gel (Merck SiO_2 60, 660 mg) was added to a solution of **8** (22 mg) in ether (*ca.* 2 mL). The solvent was removed at reduced pressure and the residue was then heated under nitrogen at 170 °C for 45 min. After cooling, EtOAc (5 mL) was added and the slurry was stirred for 2 min. Filtration and evaporation of the solvent at reduced pressure was followed by column chromatography (H–E, 20 : 1) to give **11** (oil, 9 mg, 41%) as a diastereomeric mixture (1 : 5). The reaction gave variable yields on repeated experiments and analytically pure samples could not be obtained.

For **11a** (major isomer): δ_H 0.01 (s, 9H, TMS), 0.06, 0.06 (2s, 6H, –Si(CH_3)$_2$–), 0.87 (s, 9H, t-Bu), 0.92 (m, 2H, –CH_2–TMS), 1.22 (s, 3H, >C(CH_3)O–), 1.75 (d, 3H, J = 0.8 Hz, –C(CH_3)=CH_2), 1.95, 2.77 (2dd, 2H, J_{AB} = 12.9 Hz, J = 6.6 Hz,

–CH_2–), 2.52, 2.58 (2d, 2H, J_{AB} = 13.9 Hz, –CH_2-CO_2–), 3.41, 3.43 (2d, 2H, J_{AB} = 10.5 Hz, –CH_2-OSEM), 3.62 (m, 2H, –CH_2CH_2–TMS), 3.65 (s, 3H, –OCH_3), 4.48 (t, 1H, J = 6.6 Hz, –CH(OTBDMS)–), 4.66 (s, 2H, –OCH_2O–), 4.84, 5.09 (2m, 2H, =CH_2).

For **11b** (minor isomer): δ_H 0.0 (s, 9H, TMS), 0.04, 0.05 (2s, 6H, –Si(CH_3)$_2$–), 0.86 (s, 9H, t-Bu), 0.90 (m, 2H, –CH_2–TMS), 1.43 (s, 3H, >C(CH_3)O–), 1.76 (s, 3H, –C(CH_3)=CH_2), 1.99 (dd, 2H, J_{AB} = 12.7 Hz, J = 6.8 Hz, –CH_2–), 2.30 (dd, 2H, J_{AB} = 12.7 Hz, J = 6.1 Hz, –CH_2–), 2.52, 2.64 (2d, 2H, J_{AB} = 15.6 Hz, –CH_2-CO_2–), 3.43 (s, 2H, –CH_2-OSEM), 3.61 (m, 2H, –CH_2CH_2–TMS), 3.64 (s, 3H, –OCH_3), 4.20 (dd, 1H, J = 6.1, 6.8 Hz, –CH(OTBDMS)–), 4.68 (s, 2H, –OCH_2O–), 4.85, 5.10 (2m, 2H, =CH_2).

Methyl (4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-7-methyl-3-methylene-6-[(2-trimethylsilylethoxy)methoxymethyl]-octanoate (12)

n-BuLi (0.100 mL, 0.15 mmol, 1.5 M in hexane) was added to a solution of diisopropylamine (0.028 mL, 0.20 mmol) in dry THF (0.2 mL) under nitrogen at 0 °C. After stirring for 10 min, a solution of **8** (50 mg, 0.10 mmol) in dry THF (0.1 mL) was added. After another 10 min stirring at 0 °C, ether (10 mL) and HCl (1.0 mL, 1.0 M) was added and the organic phase was washed with water, dried and the solvent was evaporated at reduced pressure. Column chromatography (H–E, 10 : 1) gave **12** (oil, 32 mg, 64%): R_f (1 : 1) 0.65; $[a]_D^{20}$ −18 (*c* 0.52, $CDCl_3$); δ_H 0.02 (s, 12H, TMS, –Si(CH_3)$_2$–), 0.08 (s, 3H, –Si(CH_3)$_2$–), 0.89 (s, 9H, t-Bu), 0.95 (m, 2H, –CH_2–TMS), 1.35, 1.35 (2s, 6H, >C(CH_3)$_2$), 1.85 (dd, 1H, J_{AB} = 14.4 Hz, J = 9.2 Hz, H-5), 1.94 (dd, 1H, J_{AB} = 14.4 Hz, J = 3.7 Hz, H-5), 3.08 (s, 2H, H-2), 3.56–3.71 (m, 2H, –CH_2CH_2–TMS), 3.67 (d, 1H, J_{AB} = 10.9 Hz, –CH_2-OSEM), 3.68 (s, 3H, –OCH_3), 3.77 (d, 1H, J_{AB} = 10.9 Hz, –CH_2-OSEM), 4.42 (dd, 1H, J = 9.2, 3.7 Hz, H-4), 4.70 (s, 2H, –OCH_2O–), 5.01 (m, 1H, vinyl), 5.18 (s, 1H, vinyl) (Found: C, 59.00; H, 9.96. $C_{24}H_{48}O_6Si_2$ requires C, 58.97; H, 9.90%).

Ethyl (4*S*,6*R*,2*Z*)-4-(*tert*-butyldimethylsilyloxy)-6-[*tert*-butyldimethylsilyloxymethyl]-6,7-epoxy-7-methyl-3-[(trimethylsilyl)-methyl]oct-2-enoate (13)

Compound **1** [22] (133 mg, 0.300 mmol) was added to a solution of TBDMSCl (54 mg, 0.360 mmol) and imidazole (51 mg, 0.75 mmol) in DMF (1 mL). The reaction mixture was stirred at rt for 1 h and then CH_2Cl_2 (5 mL) was added. The solution was washed with water, 1.0 M HCl, $NaHCO_3$ (sat.), again with water and dried. The solvent was evaporated at reduced pressure followed by column chromatography of the residue (H–E, 10 : 1) to give **13** (oil, 163 mg, 98%): R_f (3 : 1) 0.64; $[a]_D^{20}$ +53 (*c* 0.96, $CDCl_3$); δ_H 0.03 (s, 3H, –Si(CH_3)$_2$–), 0.08 (s, 6H, –Si(CH_3)$_2$–), 0.09 (s, 12H, –Si(CH_3)$_2$–, TMS), 0.91, 0.93 (2s, 18H, t-Bu), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.32, 1.35 (2s, 6H, >C(CH_3)$_2$), 1.67 (dd, 1H, J_{AB} = 14.2 Hz, J = 10.0 Hz, H-5), 1.75 (d, 1H, J_{AB} = 11.7 Hz, –C(H)H-TMS), 2.17 (dd, 1H, J_{AB} = 14.2 Hz, J = 2.2 Hz, H-5), 2.89 (dd, 1H, J_{AB} = 11.7 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.82 (s, 2H, –CH_2-OTBDMS), 4.11, 4.14 (2dq, 2H, J_{AB} = 10.6 Hz, J = 7.1 Hz, Et), 4.28 (ddd, 1H, J = 10.0, 2.2, 1.0 Hz, H-4), 5.85 (dd, 1H, J = 1.0 Hz, 1.0 Hz, vinyl) (Found: C, 60.20; H, 10.44. $C_{28}H_{58}O_5Si_3$ requires C, 60.16; H, 10.46%).

Ethyl (1*R*,3*S*,5*S*)-5-(*tert*-butyldimethylsilyloxy)-3-[(*tert*-butyldimethylsilyloxy)methyl]-3-hydroxy-2,2-dimethyl-6-methylenecyclohexanecarboxylate (14) and ethyl (4*S*,2*Z*)-4,8-bis(*tert*-butyldimethylsilyloxy)-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)-methyl]oct-2-enoate (15)

BF_3·OEt_2 (0.243 mL, 0.243 mmol, 1.0 M in CH_2Cl_2) was added to a solution of **13** (136 mg, 0.243 mmol) in dry CH_2Cl_2 (12 mL) under nitrogen at 0 °C. The reaction mixture was stirred for 10 min and $NaHCO_3$ (sat., 5 mL) was then added followed by ether (25 mL). The organic phase was washed with brine and dried ($MgSO_4$). Evaporation of the solvent at reduced pressure and column chromatography (H–E, 120 : 1 then 60 : 1) gave **14** (oil, 73 mg, 62%) and **15** (oil, 23 mg, 17%).

For **14**: R_f (40 : 1) 0.11; $[a]_D^{20}$ +48 (*c* 1.36, $CDCl_3$); δ_H 0.06, 0.06, 0.09, 0.10 (4s, 12H, –Si(CH_3)$_2$–), 0.89, 0.92 (2s, 18H, t-Bu), 1.00, 1.14 (2s, 6H, >C(CH_3)$_2$), 1.26 (t, 3H, J = 7.0 Hz, Et), 1.70 (dd, 1H, J_{AB} = 13.2 Hz, J = 10.8 Hz, H-4), 1.94 (dd, 1H, J_{AB} = 13.2 Hz, J = 5.4 Hz, H-4), 3.08 (s, 1H, H-1), 3.52, 3.55 (2d, 2H, J_{AB} = 10.0 Hz, –CH_2-OTBDMS), 4.13, 4.15 (2dq, 2H, J_{AB} = 10.9 Hz, J = 7.0 Hz, Et), 4.83 (dddd, 1H, J = 10.8, 5.4, 2.0, 1.7 Hz, H-5), 4.90 (dd, 1H, J = 2.0 Hz, 1.7 Hz, vinyl), 5.22 (dd, 1H, J = 2.0 Hz, 2.0 Hz, vinyl) (Found: C, 61.63; H, 10.39. $C_{25}H_{50}O_5Si_2$ requires C, 61.68; H, 10.35%).

For **15**: R_f (40 : 1) 0.23; $[a]_D^{20}$ +47 (*c* 0.30, $CDCl_3$); δ_H 0.02 (s, 6H, –Si(CH_3)$_2$–), 0.04, 0.06 (2s, 6H, –Si(CH_3)$_2$–), 0.08 (s, 9H, TMS), 0.86, 0.87 (2s, 18H, t-Bu), 1.08 (s, 6H, –C(CH_3)$_2$–), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.41 (d, 1H, J_{AB} = 11.3 Hz, –C(H)H-TMS), 2.57 (dd, 1H, J_{AB} = 17.8 Hz, J = 2.2 Hz, H-5), 2.83 (dd, 1H, J_{AB} = 17.8 Hz, J = 8.4 Hz, H-5), 2.97 (dd, 1H, J_{AB} = 11.3 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.51, 3.59 (2d, 2H, J_{AB} = 10.1 Hz, H-8), 4.13 (q, 2H, J = 7.1 Hz, Et), 4.66 (ddd, 1H, J = 8.4, 2.2, 1.0 Hz, H-4), 5.95 (dd, 1H, J = 1.0, 1.0 Hz, vinyl) (Found: C, 60.23; H, 10.50. $C_{28}H_{58}O_5Si_3$ requires C, 60.16; H, 10.46%).

Ethyl (4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-6-hydroxymethyl-7-methyl-3-methyleneoctanoate (16)

A solution of Bu_4NF·$(H_2O)_3$ (95 mg, 0.30 mmol) in dry THF (0.3 mL) was added to a solution of **1** (131 mg, 0.295 mmol) and HOAc (0.050 mL, 0.87 mmol) in dry THF (1.5 mL) under nitrogen at 0 °C. After stirring for 2 h, the reaction mixture was diluted with ether (20 mL) and washed with $NaHCO_3$ (sat.) and brine. The organic phase was dried and the solvent was evaporated at reduced pressure to give crude **16** (109 mg, 99%) which was pure on TLC (H–E, 3 : 1). Column chromatography (H–E, 5 : 1) gave **16** (oil, 87 mg, 79%): R_f (3 : 1) 0.13; $[a]_D^{20}$ −9 (*c* 1.41, $CDCl_3$); δ_H 0.05, 0.12 (2s, 6H, –Si(CH_3)$_2$–), 0.91 (s, 9H, t-Bu), 1.26 (t, 3H, J = 7.1 Hz, Et), 1.33 (s, 6H, >C(CH_3)$_2$), 1.94 (dd, 1H, J_{AB} = 14.6 Hz, J = 4.0 Hz, H-5), 1.99 (dd, 1H, J_{AB} = 14.6 Hz, J = 8.9 Hz, H-5), 3.07 (s, 2H, H-2), 3.67 (d, 1H, J_{AB} = 12.2 Hz, broad, –C(H)HOH), 3.80 (dd, 1H, J_{AB} = 12.2 Hz, J = 5.6 Hz, broad, –C(H)HOH), 4.15 (q, 2H, J = 7.1 Hz, Et), 4.39 (dd, 1H, J = 4.0 Hz, 8.9 Hz, H-4), 5.05 (d, 1H, J = 1.0 Hz, vinyl), 5.21 (s, 1H, vinyl) (Found: C, 61.19; H, 9.75. $C_{19}H_{36}O_5Si$ requires C, 61.25; H, 9.74%).

Ethyl (2*E*,4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-3,7-dimethyl-6-[(trimethylsilyloxy)methyl]oct-2-enoate (17a) and ethyl (4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-7-methyl-3-methylene-6-[(trimethylsilyloxy)methyl]octanoate (17b)

Anhydrous Bu_4NF (1.0 mL, 0.21 mmol, 0.21 M in dry THF) was added to a solution of **1** (93 mg, 0.21 mmol) in dry THF (4.0 mL) under nitrogen at 0 °C. TLC analysis (H–E, 3 : 1) of the reaction mixture directly after the addition showed mostly nonpolar products. After stirring for 15 min at the same temperature, ether (20 mL) was added and the solution was washed with water and dried ($MgSO_4$). The solvent was evaporated at reduced pressure to give 97 mg of crude product. Column chromatography (H–E, 50 : 1 then 20 : 1) gave **17a** (oil, 8 mg, 9%) containing *ca.* 7% of **17b**, and **17b** (oil, 6 mg, 7%) containing *ca.* 15% of **17a**. The low yields might be due to the instability of TMS-ethers on silica gel. The elemental analysis was carried out on a mixture of **17a** and **17b**.

For **17a**: R_f (10 : 1) 0.31; δ_H 0.00, 0.06 (2s, 6H, –Si(CH_3)$_2$–), 0.14 (s, 9H, TMS), 0.90 (s, 9H, t-Bu), 1.28 (t, 3H, J = 7.1 Hz, Et), 1.32, 1.35 (2s, 6H, >C(CH_3)$_2$), 1.76 (dd, 1H, J_{AB} = 14.2 Hz,

J = 9.8 Hz, H-5), 2.02 (dd, 1H, J_{AB} = 14.2 Hz, J = 3.1 Hz, H-5), 2.12 (d, 3H, J = 1.3 Hz, –C(CH_3)=CH–), 3.75, 3.78 (2d, 2H, J_{AB} = 11.2 Hz, –CH_2-OTMS), 4.16 (q, 2H, J = 7.1 Hz, Et), 4.33 (dd, 1H, J = 9.8, 3.1 Hz, H-4), 5.86 (m, 1H, vinyl).

For **17b**: R_f (10 : 1) 0.26; δ_H 0.03, 0.07 (2s, 6H, –Si(CH_3)$_2$–), 0.13 (s, 9H, TMS), 0.90 (s, 9H, t-Bu), 1.26 (t, 3H, J = 7.1 Hz, Et), 1.32, 1.35 (2s, 6H, >C(CH_3)$_2$), 1.79 (dd, 1H, J_{AB} = 14.2 Hz, J = 9.6 Hz, H-5), 1.99 (dd, 1H, J_{AB} = 14.2 Hz, J = 3.6 Hz, H-5), 3.06 (s, 2H, H-2), 3.72, 3.78 (2d, 2H, J_{AB} = 11.0 Hz, –CH_2-OTMS), 4.14 (q, 2H, J = 7.1 Hz, Et), 4.44 (dd, 1H, J = 9.6, 3.6 Hz, H-4), 5.01 (m, 1H, vinyl), 5.17 (s, 1H, broad, vinyl) (Found: C, 59.50; H, 10.10. $C_{24}H_{44}O_5Si_2$ requires (mixture of **17a** and **17b**) C, 59.41; H, 9.97%).

Ethyl (1*S*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-6,6-dimethyl-2,5-dimethylenecyclohexanecarboxylate (20) and ethyl (1*S*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-2-methylene-5-isopropylidenecyclohexanecarboxylate (21)

The experiment was performed as described for **14** using **18**[22] (107 mg, 0.250 mmol) as starting material. The reaction mixture was stirred at rt for 3 h. Column chromatography (H–E, 150 : 1) gave a mixture of **20** and **21** (3 : 1, oil, 62 mg, 73%) and **18a** (<2 mg). The proposal of structure **18a** was based on its NMR data: δ_H 1.30, 1.38 (2s, 6H, –C(CH_3)$_2$OH), 4.81, 4.89 (2m, 2H, =CH_2); δ_C 27.46, 28.79, 82.50 (–C(CH_3)$_2$OH), 103.96, 155.18 (>C=CH_2).

For **20**: R_f (3 : 1) 0.64; $[\alpha]_D^{20}$ +78 (*c* 0.86, $CDCl_3$); δ_H 0.08 (s, 6H, –Si(CH_3)$_2$–), 0.92 (s, 9H, t-Bu), 1.09, 1.14 (2s, 6H, >C(CH_3)$_2$), 1.23 (t, 3H, J = 7.0 Hz, Et), 2.33 (dd, 1H, J_{AB} = 12.9 Hz, J = 10.8 Hz, H-4), 2.53 (dddd, 1H, J_{AB} = 12.9 Hz, J = 5.9, 1.7, 1.7 Hz, H-4), 3.14 (s, 1H, H-1), 4.06, 4.10 (2dq, 2H, J_{AB} = 10.7 Hz, J = 7.0 Hz, Et), 4.67 (dddd, 1H, J = 10.8, 5.9, 2.0, 2.0 Hz, H-3), 4.76, 4.84, 4.96, 5.26 (4dd, 4H, J = 2 Hz, 2 Hz, vinyl).

For **21**: δ_H 0.10 (s, 6H, –Si(CH_3)$_2$–), 0.93 (s, 9H, t-Bu), 1.24 (t, 3H, J = 7.0 Hz, Et), 1.70 (s, 6H, broad, =C(CH_3)$_2$), 1.85–1.95, 2.06–2.15 (2m, 2H, H-4), 2.76 (dd, 1H, J_{AB} = 13.5 Hz, J = 5.1 Hz, H-6), 2.99 (dd, 1H, J_{AB} = 13.5 Hz, J = 4.1 Hz, H-6), 3.45 (dd, 1H, J = 5.1 Hz, 4.1 Hz, H-1), 4.02–4.20 (m, 2H, Et), 4.29 (dddd, 1H, J = 11, 4.9, 2, 2 Hz, H-3), 4.86, 5.19 (2dd, 2H, J = 2, 2 Hz, vinyl) (Found: C, 67.45; H, 10.16. $C_{19}H_{34}O_3Si$ (mixture of **20** and **21**) requires C, 67.41; H, 10.12%).

Ethyl (2*Z*,4*S*)-6-hydroxymethyl-4-methoxy-7-methyl-3-[(trimethylsilyl)methyl]octa-2,6-dienoate (22)

Pyridinium tosylate (19 mg, 0.075 mmol) was added to **50a** (297 mg, 0.720 mmol) dissolved in EtOH (absolute, 6.0 mL). The reaction mixture was stirred at 50 °C for 24 h and after cooling, ether (*ca.* 100 mL) was added. The solution was washed with $NaHCO_3$ (sat.) and brine, dried and the solvent was evaporated at reduced pressure. Column chromatography (H–E, 10 : 1) gave **22** (oil, 219 mg, 93%): R_f (3 : 1) 0.31; $[\alpha]_D^{20}$ +108 (*c* 1.10, $CDCl_3$); δ_H 0.10 (s, 9H, TMS), 1.29 (t, 3H, J = 7.0 Hz, Et), 1.65 (d, 1H, J_{AB} = 11.5 Hz, –C(H)H-TMS), 1.72, 1.77 (2s, 6H, =C(CH_3)$_2$), 2.13 (dd, 1H, J_{AB} = 14.7 Hz, J = 9.6 Hz, H-5), 2.65 (dd, 1H, J_{AB} = 14.7 Hz, broad, H-5), 3.05 (dd, 1H, J_{AB} = 11.5 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.28 (s, 3H, –OCH_3), 3.57 (dd, 1H, J = 9.6, 2.5 Hz, H-4), 3.89 (d, 1H, J_{AB} = 12.1 Hz, –C(H)HOH), 4.14 (q, 2H, J = 7.0 Hz, Et), 4.29 (d, 1H, J_{AB} = 12.1 Hz, –C(H)-HOH), 5.81 (s, 1H, broad, vinyl) (Found: C, 62.14; H, 9.85. $C_{17}H_{32}O_4Si$ requires C, 62.20; H, 9.82%).

Ethyl (2*Z*,4*S*)-4-benzyloxy-6-hydroxymethyl-7-methyl-3-[(trimethylsilyl)methyl]octa-2,6-dienoate (23)

The experiment was performed as described for **22** using **51a** (150 mg, 0.307 mmol) as starting material. Column chromatography (H–E, 10 : 1) gave **23** (oil, 104 mg, 84%): R_f (3 : 1) 0.33; $[\alpha]_D^{20}$ +18 (*c* 1.20, $CDCl_3$); δ_H 0.09 (s, 9H, TMS), 1.30 (t, 3H, J = 7.1 Hz, Et), 1.62 (s, 3H, =C(CH_3)CH_3), 1.69 (d, 1H, J_{AB} = 11.5 Hz, –C(H)H-TMS), 1.74 (s, 3H, =C(CH_3)CH_3), 2.24 (dd, 1H, J_{AB} = 14.5 Hz, J = 9.9 Hz, H-5), 2.65 (d, 1H, J_{AB} = 14.5 Hz, broad, H-5), 3.02 (s, 1H, broad, –OH), 3.06 (dd, 1H, J_{AB} = 11.5 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.82 (ddd, 1H, J = 9.9, 2.3, 0.7 Hz, H-4), 3.99 (d, 1H, J_{AB} = 12.1 Hz, –C(H)-HOH), 4.16 (q, 2H, J = 7.1 Hz, Et), 4.24 (d, 1H, J_{AB} = 11.7 Hz, benzyl), 4.28 (d, 1H, J_{AB} = 12.1 Hz, –C(H)HOH), 4.64 (d, 1H, J_{AB} = 11.7 Hz, benzyl), 5.95 (s, 1H, vinyl), 7.25–7.38 (m, 5H, –Ph) (Found: C, 68.30; H, 8.84. $C_{23}H_{36}O_4Si$ requires C, 68.27; H, 8.97%).

Ethyl (2*Z*,4*S*,6*R*)-6,7-epoxy-6-hydroxymethyl-4-methoxy-7-methyl-3-[(trimethylsilyl)methyl]oct-2-enoate (26)

D-(−)-Diethyl tartrate (20.6 mg, 0.100 mmol) and Ti(OiPr)$_4$ (0.025 mL, 0.084 mmol) were added to a mixture of **22** (100 mg, 0.305 mmol) and powdered molecular sieves (50 mg, 4 Å, activated at 170 °C *in vacuo*) in dry CH_2Cl_2 (2 mL) under nitrogen at −15 °C. The mixture was stirred for 10–15 min at −15 °C and the temperature was then lowered to −40 °C. At this temperature *tert*-butyl hydroperoxide (anhydrous, 0.16 mL, 0.48 mmol, 3.0 M in toluene) was slowly added. After 30 min stirring at this temperature a solution of $FeSO_4$ (150 mg) and tartaric acid (70 mg) in water (1 mL) was added followed by ether (5 mL). Stirring was continued at rt for 20 min and the organic phase was then washed with brine, dried and the solvent was evaporated at reduced pressure. Column chromatography (H–E, 5 : 1) gave **26** (oil, 103 mg, 98% recovery) contaminated by the epoxide rearranged allylic alcohol (4%) and by ketone **29** (23%) according to ^{1}H NMR analysis.

For **26** (contaminated): R_f (1 : 1) 0.40; $[\alpha]_D^{20}$ +77 (*c* 1.25, $CDCl_3$); δ_H 0.09 (s, 9H, TMS), 1.28 (t, 3H, J = 7.1 Hz, Et), 1.32, 1.36 (2s, 6H, >C(CH_3)$_2$), 1.54 (d, 1H, J_{AB} = 11.5 Hz, –C(H)H-TMS), 1.91 (dd, 1H, J_{AB} = 15.1 Hz, J = 2.9 Hz, H-5), 1.98 (dd, 1H, J_{AB} = 15.1 Hz, J = 9.0 Hz, H-5), 2.97 (dd, 1H, J_{AB} = 11.5 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.34 (s, 3H, –OCH_3), 3.67–3.76 (m, 3H, –CH_2OH, H-4), 4.14 (q, 2H, J = 7.1 Hz, Et), 5.85 (s, 1H, broad, vinyl) (Found: C, 59.23; H, 9.41. $C_{17}H_{32}O_5Si$ requires C, 59.27; H, 9.36%).

Ethyl (2*Z*,4*S*,6*R*)-4-benzyloxy-6,7-epoxy-6-hydroxymethyl-7-methyl-3-[(trimethylsilyl)methyl]oct-2-enoate (27)

The experiment was performed as described for **26** using **23** (96 mg, 0.237 mmol) as starting material. Column chromatography (H–E, 6 : 1) gave **27** (93 mg, 93%) as an oil which crystallized on standing. This product was contaminated by the epoxide rearranged allylic alcohol (6%) and by ketone **30** (10%).

For **27** (contaminated): R_f (3 : 1) 0.23; mp 53–70 °C; $[\alpha]_D^{20}$ +69 (*c* 0.45, $CDCl_3$); δ_H 0.12 (s, 9H, TMS), 1.30 (t, 3H, J = 7.1 Hz, Et), 1.33, 1.34 (2s, 6H, >C(CH_3)$_2$), 1.60 (d, 1H, J_{AB} = 11.5 Hz, –C(H)H-TMS), 1.96 (dd, 1H, J_{AB} = 14.9 Hz, J = 9.5 Hz, H-5), 2.04 (dd, 1H, J_{AB} = 14.9 Hz, J = 2.7 Hz, H-5), 2.71 (t, 1H, J = 6.2 Hz, broad, –OH), 3.03 (dd, 1H, J_{AB} = 11.5 Hz, J = 1.0 Hz, –C(H)H-TMS), 3.66 (d, 2H, J = 6.2 Hz, –CH_2OH), 3.99 (dd, 1H, J = 9.5, 2.7 Hz, H-4), 4.16 (q, 2H, J = 7.1 Hz, Et), 4.31, 4.59 (2d, 2H, J_{AB} = 10.7 Hz, benzyl), 5.99 (s, 1H, vinyl), 7.25–7.42 (m, 5H, –Ph) (Found: C, 65.60; H, 8.72. $C_{23}H_{36}O_5Si$ requires C, 65.68; H, 8.63%).

Ethyl (2*Z*,4*S*)-8-hydroxy-4-methoxy-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)methyl]oct-2-enoate (29)

The experiment was performed as described for **14** using **26** (60 mg, 0.175 mmol) as starting material. Column chromatography (H–E, 6 : 1) gave **29** (oil, 55 mg, 92%): R_f (1 : 1) 0.45; $[\alpha]_D^{20}$ +50 (*c* 0.72, $CDCl_3$); δ_H 0.11 (s, 9H, TMS), 1.11, 1.14 (2s, 6H, –C(CH_3)$_2$–), 1.29 (t, 3H, J = 7.0 Hz, Et), 1.53 (d, 1H, J_{AB} = 11.4 Hz, –C(H)H-TMS), 2.35 (dd, 1H, J_{AB} = 16.4 Hz, J = 2.2 Hz, H-5), 2.89 (dd, 1H, J_{AB} = 16.4 Hz, J = 9.7 Hz, H-5), 2.98 (dd, 1H, J_{AB} = 11.4 Hz, J = 0.9 Hz, –C(H)H-TMS), 3.25 (s,

3H, $-OCH_3$), 3.48, 3.71 (2d, 2H, J_{AB} = 11.5 Hz, H-8), 4.12 (m, 1H, H-4), 4.15 (q, 2H, J = 7.0 Hz, Et), 5.87 (s, 1H, vinyl) (Found: C, 59.22; H, 9.42. $C_{17}H_{32}O_5Si$ requires C, 59.27; H, 9.36%).

Ethyl (2*Z*,4*S*)-8-hydroxy-4-methoxy-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)methyl]oct-2-enoate (29) *via* (25)

The experiment was performed as described for **26** using **22** (85 mg, 0.26 mmol) as starting material and L-(+)-diethyl tartrate instead of D-(−)-diethyl tartrate. The reaction mixture was stirred for 2 h 40 min. The crude product contained approximately equal amounts of epoxide **25** and ketone **29** as judged from TLC (3 : 1). However, after column chromatography on silica gel (H–E, 10 : 1) the only product isolated was ketone **29** (69 mg, 77%). Recovered starting material (10 mg, 12%) was also isolated.

Ethyl (2*Z*,4*S*)-4-benzyloxy-8-hydroxy-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)methyl]oct-2-enoate (30)

The experiment was performed as described for **14** using **27** (40 mg, 0.095 mmol) as starting material. Column chromatography (H–E, 7 : 1) gave **30** (31 mg, 78%) as an oil which crystallized on standing: R_f (3 : 1) 0.24; mp 43–49 °C; $[\alpha]_D^{20}$ +33 (*c* 0.47, $CDCl_3$); δ_H 0.12 (s, 9H, TMS), 1.10, 1.12 (2s, 6H, $-C(CH_3)_2-$), 1.30 (t, 3H, J = 7.1 Hz, Et), 1.56 (d, 1H, J_{AB} = 11.5 Hz, –C(H)H-TMS), 2.39 (dd, 1H, J = 7.8, 6.3 Hz, –OH), 2.40 (dd, 1H, J_{AB} = 16.4 Hz, J = 2.2 Hz, H-5), 2.97 (dd, 1H, J_{AB} = 16.4 Hz, J = 10.0 Hz, H-5), 3.03 (dd, 1H, J_{AB} = 11.5 Hz, J = 0.9 Hz, –C(H)H-TMS), 3.45 (dd, 1H, J_{AB} = 11.5 Hz, J = 7.8 Hz, H-8), 3.64 (dd, 1H, J_{AB} = 11.5 Hz, J = 6.3 Hz, H-8), 4.16 (q, 2H, J = 7.1 Hz, Et), 4.28 (d, 1H, J_{AB} = 10.7 Hz, benzyl), 4.41 (dd, 1H, J = 2.2 Hz, 10.0 Hz, H-4), 4.52 (d, 1H, J_{AB} = 10.7 Hz, benzyl), 6.00 (s, 1H, vinyl), 7.25–7.38 (m, 5H, –Ph) (Found: C, 65.48; H, 8.69. $C_{23}H_{36}O_5Si$ requires C, 65.68; H, 8.63%).

Ethyl (2*Z*,2′*S*,4′*R*)-3-(5′,5′-dimethyl-4′-hydroxy-4′-hydroxymethyltetrahydrofuran-2′-yl)-4-trimethylsilylbut-2-enoate (31)

The experiment was performed as described for **26** using **24**[22] (100 mg, 0.318 mmol) as starting material. The reaction mixture was stirred at −40 °C for 30 min and then at −20 °C for 4 h. Column chromatography (H–E, 3 : 1 then 1 : 1) gave crystalline **31** (40 mg, 38%). Recovered starting material (58 mg, 58%) was also isolated.

For **31**: R_f (2 : 1) 0.11; mp 59–60 °C; $[\alpha]_D^{20}$ +110 (*c* 0.20, $CDCl_3$); δ_H 0.06 (s, 9H, TMS), 1.21 (s, 3H, $-C(CH_3)CH_3-$), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.37 (s, 3H, $-C(CH_3)CH_3-$), 1.57 (d, 1H, J_{AB} = 11.6 Hz, –C(H)H-TMS), 1.94 (dd, 1H, J_{AB} = 13.7 Hz, J = 5.1 Hz, $-CH_2-$), 2.52 (dd, 1H, J_{AB} = 13.7 Hz, J = 9.8 Hz, $-CH_2-$), 3.06 (dd, 1H, J_{AB} = 11.6 Hz, J = 0.8 Hz, –C(H)H-TMS), 3.63 (s, 2H, $-CH_2OH$), 4.11, 4.16 (2dq, 2H, J_{AB} = 10.9 Hz, J = 7.1 Hz, Et), 4.35 (ddd, 1H, J = 5.1, 9.8, 1.2 Hz, >CHO–), 6.03 (s, 1H, vinyl) (Found: C, 58.10; H, 9.18. $C_{16}H_{30}O_5Si$ requires C, 58.15; H, 9.15%).

Ethyl (2*E*,4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6,7-epoxy-6-hydroxymethyl-7-methyl-3-[(trimethylsilyl)methyl]oct-2-enoate (33)

The experiment was performed as for **26** using **55** (242 mg, 0.564 mmol) as starting material. Column chromatography (H–E, 6 : 1) of the crude product gave **33** (oil, 230 mg, 92%): R_f (3 : 1) 0.34; $[\alpha]_D^{20}$ +18 (*c* 1.43, $CDCl_3$); δ_H −0.01, 0.08 (2s, 6H, $-Si(CH_3)_2-$), 0.10 (s, 9H, TMS), 0.91 (s, 9H, t-Bu), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.33, 1.40 (2s, 6H, $>C(CH_3)_2$), 1.61 (dd, 1H, J_{AB} = 14.0 Hz, J = 1.7 Hz, –C(H)H-TMS), 1.67 (s, 1H, broad, –OH), 1.78 (dd, 1H, J_{AB} = 14.2 Hz, J = 10.9 Hz, H-5), 1.99 (dd, 1H, J_{AB} = 14.2 Hz, J = 2.3 Hz, H-5), 2.17 (d, 1H, J_{AB} = 14.0 Hz, –C(H)H-TMS), 3.56–3.73 (m, 2H, $-CH_2OH$), 4.09–4.20 (m, 2H, Et), 5.52 (s, 1H, broad, vinyl), 5.79 (dd, 1H, J = 10.9, 2.3, 1.0 Hz, H-4) (Found: C, 59.28; H, 9.93. $C_{22}H_{44}O_5Si_2$ requires C, 59.41; H, 9.97%).

Ethyl (2*E*,4*S*,6*R*)-6,7-epoxy-6-hydroxymethyl-4-methoxy-7-methyl-3-[(trimethylsilyl)methyl]oct-2-enoate (34)

The experiment was performed as described for **26** using **54** (78 mg, 0.24 mmol) as starting material. The reaction mixture was stirred for 1 h 20 min. Column chromatography (H–E, 10 : 1) gave **34** (oil, 71 mg, 87%) contaminated by ketone **36** (8%).

For **34** (contaminated with **36**): R_f (3 : 1) 0.18; $[\alpha]_D^{20}$ −40 (*c* 1.29, $CDCl_3$); δ_H 0.09 (s, 9H, TMS), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.35, 1.38 (2s, 6H, $>C(CH_3)_2$), 1.75 (dd, 1H, J_{AB} = 13.5 Hz, J = 1.3 Hz, $-CH_2-$TMS), 1.86 (d, 1H, J_{AB} = 13.5 Hz, $-CH_2-$TMS), 1.86–1.99 (m, 2H, H-5), 3.27 (s, 3H, $-OCH_3$), 3.68 (m, 1H, –C(H)OH, addition of D_2O gives δ at 3.66 ppm, J_{AB} = 12.4 Hz), 3.69 (s, 1H, –OH, disappears on addition of D_2O), 3.98 (m, 1H, –C(H)HOH, addition of D_2O gives δ at 3.97 ppm, J_{AB} = 12.4 Hz), 4.12, 4.15 (2dq, 2H, J_{AB} = 11.0 Hz, J = 7.1 Hz, Et), 5.22 (ddd, 1H, J = 9.3, 4.2, 1 Hz, H-4), 5.63 (m, 1H, vinyl) (Found: C, 59.25; H, 9.40. $C_{17}H_{32}O_5Si$ requires C, 59.27; H, 9.36%).

Ethyl (2*E*,4*R*)-4-(*tert*-butyldimethylsilyloxy)-8-hydroxy-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)methyl]oct-2-enoate (35) and (1*S*,4*S*,6*S*)-1-ethoxy-3-methylene-4-*tert*-butyldimethylsilyloxy-6-(2-hydroxypropan-2-yl)-8,9-dioxa[4.2.1]bicyclononane (37)

The experiment was performed as described for **14** using **33** (100 mg, 0.225 mmol) as starting material. Column chromatography (H–E, 10 : 1 then 7 : 1) gave **35** (oil, 31 mg, 31%) and **37** (28 mg, of *ca.* 80% purity as determined by ^1H NMR analysis) which was further purified by acetylation of the by-products (Ac_2O and 4-pyrrolidinopyridine in pyridine) followed by column chromatography (H–E, 10 : 1) to give **37** (oil, 14 mg, 17%).

For **35**: R_f (3 : 1) 0.24; $[\alpha]_D^{20}$ +33 (*c* 0.35, $CDCl_3$); δ_H 0.01, 0.05 (2s, 6H, $-Si(CH_3)_2-$), 0.12 (s, 9H, TMS), 0.85 (s, 9H, t-Bu), 1.11, 1.13 (2s, 6H, $-C(CH_3)_2-$), 1.26 (t, 3H, J = 7.1 Hz, Et), 1.61 (dd, 1H, J_{AB} = 13.5 Hz, J = 1.3 Hz, $-CH_2-$TMS), 2.24 (d, 1H, J_{AB} = 13.5 Hz, J = 1.2 Hz, $-CH_2-$TMS), 2.27 (dd, 1H, J_{AB} = 16.4 Hz, J = 2.2 Hz, H-5), 2.95 (dd, 1H, J_{AB} = 16.4 Hz, J = 9.3 Hz, H-5), 3.52, 3.55 (2d, 2H, J_{AB} = 11.4 Hz, H-8), 4.11, 4.14 (2dq, 2H, J_{AB} = 10.9 Hz, J = 7.1 Hz, Et), 5.50 (s, 1H, broad, vinyl), 6.02 (d, 1H, J = 9.3 Hz, broad, H-4) (Found: C, 59.50; H, 10.06. $C_{22}H_{44}O_5Si_2$ requires C, 59.41; H, 9.97%).

For **37**: R_f (3 : 1) 0.35; $[\alpha]_D^{20}$ −21 (*c* 0.74, $CDCl_3$); δ_H 0.02, 0.04 (2s, 6H, $-Si(CH_3)_2-$), 0.89 (s, 9H, t-Bu), 1.14 (s, 3H, $>C(CH_3)-CH_3$), 1.21 (t, 3H, J = 7.1 Hz, Et), 1.33 (s, 3H, $>C(CH_3)CH_3$), 1.56 (dd, 1H, J_{AB} = 13.4 Hz, J = 9.4 Hz, $-CH_2-$), 2.49 (dd, 1H, J_{AB} = 13.4 Hz, J = 5.9 Hz, $-CH_2-$), 2.59 (d, 1H, J_{AB} = 13.9 Hz, broad, $-CH_2C(O-)_3$), 2.76 (d, 1H, J_{AB} = 13.9 Hz, $-CH_2C(O-)_3$), 3.69, 3.78 (2dq, 2H, J_{AB} = 9.3 Hz, J = 7.1 Hz, Et), 3.80, 4.25 (2d, 2H, J_{AB} = 7.1 Hz, $-CH_2O-$), 4.34 (dd, 1H, J = 9.4 Hz, 5.9 Hz, broad, –CH(OTBDMS)–), 5.03, 5.34 (2m, 2H, vinyl) (Found: C, 61.07; H, 9.82. $C_{19}H_{36}O_5Si$ requires C, 61.25; H, 9.74%).

Ethyl (2*E*,4*S*)-8-hydroxy-4-methoxy-7,7-dimethyl-6-oxo-3-[(trimethylsilyl)methyl]oct-2-enoate (36)

The experiment was performed as described for **14** using **34** (45 mg, 0.13 mmol) as starting material. Column chromatography (H–E, 10 : 1 then 5 : 1) gave **36** (oil, 16 mg, 36%) and two other compounds with unknown structures.

For **36**: R_f (3 : 1) 0.15; $[\alpha]_D^{20}$ −5 (*c* 0.52, $CDCl_3$); δ_H 0.11 (s, 9H, TMS), 1.14, 1.14 (2s, 6H, $-C(CH_3)_2-$), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.75 (dd, 1H, J_{AB} = 13.1 Hz, J = 1.0 Hz, $-CH_2-$TMS), 1.90 (d, 1H, J_{AB} = 13.1 Hz, $-CH_2-$TMS), 2.39 (dd, 1H, J_{AB} = 16.4 Hz, J = 2.4 Hz, H-5), 2.95 (dd, 1H, J_{AB} = 16.4 Hz, J = 9.5 Hz, H-5), 3.25 (s, 3H, $-OCH_3$), 3.50, 3.64 (2d, 2H, J_{AB} = 11.5 Hz,

H-8), 4.13 (q, 2H, J = 7.1 Hz, Et), 5.42 (ddd, 1H, J = 2.4, 9.5, 1 Hz, H-4), 5.61 (m, 1H, vinyl) (Found: C, 59.31; H, 9.38. $C_{17}H_{32}O_5Si$ requires C, 59.27; H, 9.36%).

Ethyl (2*Z*,4*S*,6*R*)-4-(*tert*-butyldimethylsilyloxy)-6-[(*tert*-butyldimethylsilyloxy)methyl]-6,7-epoxy-3,7-dimethyloct-2-enoate (38)

n-BuLi (2.0 mL, 3.0 mmol, 1.50 M in hexane) was added to a solution of diisopropylamine (0.434 mL, 3.1 mmol) in dry THF (1.5 mL) under nitrogen at 0 °C. After stirring for 10 min, $Me_3SiCH_2CO_2Et$ (481 mg, 3.0 mmol) was added and stirring was continued for another 10 min. A solution of **61** (300 mg, 0.720 mmol) in dry THF (0.5 mL) was then added and the reaction mixture was stirred for 30 min at 0 °C. Heptane (100 mL) was added and the solution was washed with water, 1.0 M HCl, $NaHCO_3$ (sat.) again with water and dried ($MgSO_4$). Evaporation of the solvent at reduced pressure was followed by column chromatography (H–E, 50 : 1) to give **38** (oil, 231 mg, 66%): R_f (10 : 1) 0.45; $[\alpha]_D^{20}$ −2 (*c* 1.17, $CDCl_3$); δ_H −0.02, 0.05 (2s, 6H, –Si(CH_3)$_2$–), 0.08 (s, 6H, –Si(CH_3)$_2$–), 0.88, 0.89 (2s, 18H, t-Bu), 1.26 (t, 3H, J = 7.1 Hz, Et), 1.32, 1.38 (2s, 6H, >C(CH_3)$_2$), 1.91 (d, 3H, J = 1.1 Hz, –C(CH_3)=CH–), 1.95, 1.95 (2d, 2H, J = 5.8, 7.5 Hz, H-5), 3.58, 3.91 (2d, 2H, J_{AB} = 10.6 Hz, –CH_2O–), 4.12 (q, 2H, J = 7.1 Hz, Et), 5.61 (m, 1H, vinyl), 5.88 (dd, 1H, J = 5.8, 7.5 Hz, broad, H-4) (Found: C, 61.59; H, 10.29. $C_{25}H_{50}O_5Si_2$ requires C, 61.68; H, 10.35%).

Ethyl (2*Z*,4*S*)-4,8-bis(*tert*-butyldimethylsilyloxy)-3,7,7-trimethyl-6-oxooct-2-enoate (39)

The experiment was performed as described for **14** using **38** (50.0 mg, 0.102 mmol) as starting material. Column chromatography (H–E, 50 : 1) gave **39** (oil, 34 mg, 68%): R_f (10 : 1) 0.45; $[\alpha]_D^{20}$ +3 (*c* 0.75, $CDCl_3$); δ_H 0.02 (s, 9H, –Si(CH_3)$_2$–), 0.06 (s, 3H, –Si(CH_3)$_2$–), 0.83, 0.86 (2s, 18H, t-Bu), 1.08 (s, 6H, –C(CH_3)$_2$–), 1.27 (t, 3H, J = 7.1 Hz, Et), 1.90 (d, 3H, J = 1.4 Hz, –C(CH_3)= CH–), 2.34 (dd, 1H, J_{AB} = 16.8 Hz, J = 3.0 Hz, H-5), 3.05 (dd, 1H, J_{AB} = 16.8 Hz, J = 8.9 Hz, H-5), 3.51, 3.58 (2d, 2H, J_{AB} = 9.8 Hz, –CH_2O–), 4.13, 4.16 (2dq, 2H, J_{AB} = 11.0 Hz, J = 7.1 Hz, Et), 5.60 (m, 1H, vinyl), 6.04 (ddd, 1H, J = 3.0, 8.9, 0.8 Hz, H-4) (Found: C, 61.84; H, 10.40. $C_{25}H_{50}O_5Si_2$ requires C, 61.68; H, 10.35%).

(2*Z*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)-3,7,7-trimethyl-6-oxooct-2-en-8-olide (40)

The experiment was performed as described for **14** using **38** (100 mg, 0.205 mmol) as starting material, except that the reaction mixture was stirred for 4 h. Column chromatography (H–E, 10 : 1 then 5 : 1) gave **40** (oil, 36 mg, 54%): R_f (1 : 1) 0.47; $[\alpha]_D^{20}$ +10 (*c* 0.64, $CDCl_3$); δ_H 0.03 (s, 6H, –Si(CH_3)$_2$–), 0.86 (s, 9H, t-Bu), 1.11, 1.12 (2s, 6H, –C(CH_3)$_2$–), 2.01 (dd, 3H, J = 1.5, 0.8 Hz, –C(CH_3)=CH–), 2.84 (dd, 1H, J_{AB} = 17.9 Hz, J = 5.6 Hz, H-5), 3.00 (dd, 1H, J_{AB} = 17.9 Hz, J = 6.7 Hz, H-5), 3.56, 3.58 (2d, 2H, J_{AB} = 9.9 Hz, –CH_2O–), 5.38 (dddd, 1H, J = 5.6, 6.7, 1.6, 0.8 Hz, H-4), 5.80 (dq, 1H, J = 1.6, 1.5 Hz, vinyl) (Found: C, 62.63; H, 9.27. $C_{17}H_{30}O_4Si$ requires C, 62.54; H, 9.26%).

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References

1 W. S. Johnson, *Acc. Chem. Res.*, 1968, **1**, 1.
2 W. S. Johnson, *Angew. Chem.*, 1976, **88**, 33.
3 W. S. Johnson, *Bioorg. Chem.*, 1976, **5**, 51.
4 P. A. Bartlett, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3, p. 341.
5 D. Goldsmith, *Fortschr. Chem. Org. Naturst.*, 1971, **29**, 363.
6 J. K. Sutherland, *Chem. Soc. Rev.*, 1980, 265.
7 N. Murase, K. Maruoka, T. Ooi and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1997, **70**, 707.
8 E. E. van Tamelen, *Acc. Chem. Res.*, 1968, **1**, 111.
9 J. K. Sutherland, in *Comprehensive Organic Synthesis: Polyene Cyclizations*, ed. B. Trost, I. Flemming and G. Pattenden, Pergamon Press, Oxford, 1991, vol. 3, p. 341.
10 I. Fleming, A. Pearce and R. L. Snowden, *J. Chem. Soc., Chem. Commun.*, 1976, 182.
11 I. Fleming and A. Pearce, *J. Chem. Soc., Perkin Trans. 1*, 1981, 251.
12 H. F. Chow and I. Fleming, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1815.
13 G. Majetich, in *Allylsilanes in Organic Synthesis*, ed. T. Hudlicky, JAI Press Inc., Greenwich, Connecticut, 1989, vol. 1, p. 175.
14 R. J. Armstrong and L. Weiler, *Can. J. Chem.*, 1983, **61**, 2530.
15 R. J. Armstrong, F. L. Harris and L. Weiler, *Can. J. Chem.*, 1982, **60**, 673.
16 W. S. Johnson, J. D. Elliott and G. J. Hanson, *J. Am. Chem. Soc.*, 1984, **106**, 1138.
17 R. J. Armstrong and L. Weiler, *Can. J. Chem.*, 1986, **64**, 584.
18 W. S. Johnson, S. D. Lindell and J. Steele, *J. Am. Chem. Soc.*, 1987, **109**, 5852.
19 D. Guay, W. S. Johnson and U. Schubert, *J. Org. Chem.*, 1989, **54**, 4731.
20 S. Hatakeyama, H. Numata, K. Osanai and S. Takano, *J. Chem. Soc., Chem. Commun.*, 1989, 1893.
21 L. Pettersson, T. Frejd and G. Magnusson, *Tetrahedron Lett.*, 1987, **28**, 2753.
22 L. Pettersson, T. Frejd and G. Magnusson, *Acta Chem. Scand.*, 1993, **47**, 196.
23 X. Xiao, S.-K. Park and G. D. Prestwich, *J. Org. Chem.*, 1988, **53**, 4869.
24 D. Serramedan, B. Delmond, G. Deleris, J. Dunogues, M. Pereyre and C. Filliatre, *J. Organomet. Chem.*, 1990, **398**, 79.
25 M. E. Jung, Y. M. Cho and Y. H. Jung, *Tetrahedron Lett.*, 1996, **37**, 3.
26 S. K. Taylor, S. A. May and E. S. Stansby, *J. Org. Chem.*, 1996, **61**, 2075.
27 T. Doi, J. Robertson, G. Stork and A. Yamashita, *Tetrahedron Lett.*, 1994, **35**, 1481.
28 N. K. Yee and R. M. Coates, *J. Org. Chem.*, 1992, **57**, 4598.
29 S. K. Taylor, *Org. Prep. Proced. Int.*, 1992, **24**, 245.
30 B. Rickborn, in *Comprehensive Organic Synthesis; Carbon-Carbon σ-Bond Formation*, ed. B. M. Trost, I. Fleming and G. Pattenden, Pergamon Press, Oxford, 1991, vol. 3, ch. 3.3.
31 A. S. Rao, S. K. Paknikar and J. G. Kirtane, *Tetrahedron*, 1983, **39**, 2323.
32 R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737.
33 B. C. Ranu and U. Jana, *J. Org. Chem.*, 1998, **63**, 8212.
34 H. Itokawa, H. Nakanishi and S. Mihashi, *Chem. Pharm. Bull. Jpn.*, 1983, **31**, 1991.
35 G. H. Magnusson, *Org. Prep. Proced. Int.*, 1990, **22**, 547.
36 Atta-ur-Rahman, *Nuclear Magnetic Resonance*, Springer-Verlag, New York, 1986.
37 P. A. Bartlett, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1984, vol. 3 (part B), p. 411.
38 G. Stork, L. D. Cama and D. R. Coulson, *J. Am. Chem. Soc.*, 1974, **96**, 5268.
39 S. P. Tanis, Y.-H. Chuang and D. B. Head, *J. Org. Chem.*, 1988, **53**, 4929.
40 K. Maruoka, T. Ooi and H. Yamamoto, *J. Am. Chem. Soc.*, 1989, **111**, 6431.
41 G. Majetich, A. Casares, D. Chapman and M. Behnke, *J. Org. Chem.*, 1986, **51**, 1745.
42 T. Katsuki and K. B. Sharpless, *J. Am. Chem. Soc.*, 1980, **102**, 5974.
43 R. M. Hanson and K. B. Sharpless, *J. Org. Chem.*, 1986, **51**, 1922.
44 K. C. Nicolaou, C. V. C. Prasad, P. K. Somers and C. K. Hwang, *J. Am. Chem. Soc.*, 1989, **111**, 5330.
45 P. G. Wuts, R. D'Costa and W. Butler, *J. Org. Chem.*, 1984, **49**, 2582.
46 M. G. Finn and K. B. Sharpless, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, Orlando, 1985, vol. 5, p. 247.
47 S. D. Jolad, J. J. Hoffmann, K. H. Schram, J. R. Cole, M. S. Tempesta and R. B. Bates, *J. Org. Chem.*, 1981, **46**, 641.
48 A. E. de Jesus, R. M. Horak, P. S. Steyn and R. Vleggaar, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2253.
49 E. Taskinen, *J. Org. Chem.*, 1978, **43**, 2773.
50 R. Radeglia, H. Schuetz, L. Haase and E. Klemm, *Z. Chem.*, 1985, **25**, 66.

51 C. Galli, G. Giovannelli, G. Illuminati and L. Mandolini, *J. Org. Chem.*, 1979, **44**, 1258.
52 S. W. Baldwin, P. Chen, N. Nikolic and D. C. Weinseimer, *Org. Lett.*, 2000, **2**, 1193.
53 M. Shimazaki, H. Hara, K. Suzuki and G. Tsuchihashi, *Tetrahedron Lett.*, 1987, **28**, 5891.
54 K. Maruoka, M. Hasegawa and H. Yamamoto, *J. Am. Chem. Soc.*, 1986, **108**, 3827.
55 A. M. Doherty and S. V. Ley, *Tetrahedron Lett.*, 1986, **27**, 107.
56 G. E. Keck and S. Castellino, *Tetrahedron Lett.*, 1987, **28**, 281.
57 S. D. Kahn, G. E. Keck and W. J. Hehre, *Tetrahedron Lett.*, 1987, **28**, 279.
58 J. M. Coxon, A. J. Thorpe and W. B. Smith, *J. Org. Chem.*, 1999, **64**, 9575.
59 A. Eschenmoser, L. Ruzicka, O. Jeger and D. Arigoni, *Helv. Chim. Acta*, 1955, **38**, 1890.
60 G. Stork and A. W. Burgstahler, *J. Am. Chem. Soc.*, 1955, **77**, 5068.
61 D. J. Goldsmith, *J. Am. Chem. Soc.*, 1962, **84**, 3913.
62 T. Purdie and J. C. Irvine, *J. Chem. Soc.*, 1903, **83**, 1021.
63 R. Kuhn, H. Trischmann and I. Löw, *Angew. Chem.*, 1955, **67**, 32.
64 A. Yamamoto, *Organotransition Metal Chemistry. Fundamental Concepts and Applications*, John Wiley & Sons, 1986, 391.
65 E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190.
66 G. van Look, *Silylating Agents*, Fluka Chemie, 1988.
67 B. H. Lipshutz and J. J. Pegram, *Tetrahedron Lett.*, 1980, **21**, 3343.
68 D. E. Seitz and A. Zapata, *Synthesis*, 1981, 557.
69 D. E. Seitz and A. Zapata, *Tetrahedron Lett.*, 1980, **21**, 3451.
70 M. Demuth, *Helv. Chim. Acta*, 1978, **61**, 3136.
71 G. L. Larson, D. Hernandez, I. Montes de Lopez-Cepero and L. E. Torres, *J. Org. Chem.*, 1985, **50**, 5260.
72 A. Meskens, *Synthesis*, 1981, 501.
73 W. S. Wadsworth and D. W. Emmons, *J. Am. Chem. Soc.*, 1961, **83**, 1733.
74 K. Shimoji, H. Taguchi, K. Oshima, H. Yamamoto and H. Nozaki, *J. Am. Chem. Soc.*, 1974, **96.**
75 H. Taguchi, K. Shimoji, H. Yamamoto and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 2529.
76 G. L. Larson, J. A. Preito and A. Hernandes, *Tetrahedron Lett.*, 1981, **22**, 1575.
77 L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 1960, 2886.
78 K. Jansson, T. Frejd, J. Kihlberg and G. Magnusson, *Tetrahedron Lett.*, 1986, **27**, 753.
79 K. Jansson, S. Ahlfors, T. Frejd, J. Kihlberg and G. Magnusson, *J. Org. Chem.*, 1988, **53**, 5629.