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Synthesis of medium-ring lactones via tandem methylenation/ Claisen rearrangement of cyclic carbonates

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Abstract—The conversion of vinyl-substituted 6- and 7-membered cyclic carbonates into 8- and 9-membered medium-ring lactones has been achieved in good yield using dimethyltitanocene in toluene at reflux. The reaction proceeds by initial formation of a ketene acetal which undergoes subsequent in situ Claisen rearrangement to provide the corresponding lactones. The preparation of the cyclic carbonates is carried out under basic conditions and hence this methodology complements our existing selenium-based methodology for the synthesis of medium-ring lactones. © 2002 Published by Elsevier Science Ltd.

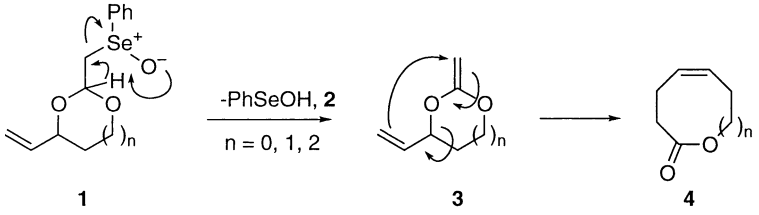
1. Introduction

Medium-ring oxacycles form the core of many biologically and structurally interesting natural products such as the brevetoxins,[1,2] obtusenyne[3,4] and (+)-laurencin[5] and an efficient route towards these systems is a desirable aim. In recent years we have developed an approach towards medium-ring oxacycles via the ring-expansion Claisen rearrangement of a vinyl-substituted ketene acetal **3**, generated in situ from the thermal elimination of benzeneselenenic acid **2** from the corresponding selenoxides **1** (Scheme 1).[6–8]

Whilst this methodology provides efficient access to medium-ring lactones **4** (which can be readily converted into medium-ring ethers)[5] several limitations became evident during the course of our investigations into the total synthesis of octalactins A and B.[9] In addition to the toxicity associated with selenium reagents,[10] the formation of the selenoacetal (precursor to the selenoxide **1**) from a 1,3- or a 1,4-diol requires acidic conditions (PPTS, refluxing toluene). This can be a problem in cases where the allylic hydroxyl group of the diol is prone to β-elimination. Exposure of **5** to our standard reaction conditions (phenylselanylacetaldehyde diethylacetal, PPTS, toluene, reflux) provided the selenoacetal **6** in low yield (46%) as well as varying amounts of the α-β-unsaturated aldehyde **7** (Scheme 2).

A further limitation of the selenium route to medium-ring lactones is that benzeneselenenic acid **2**, the product of selenoxide elimination, has been shown to disproportionate to benzeneseleninic acid and diphenyl diselenide under the reaction conditions.[10] The latter may be able to act as a reducing agent, converting the selenoxide (ketene acetal precursor) back into the selenoacetal (Scheme 3).

The disproportionation of benzeneselenenic acid **2** can be



1 **3** **4**

Scheme 1.

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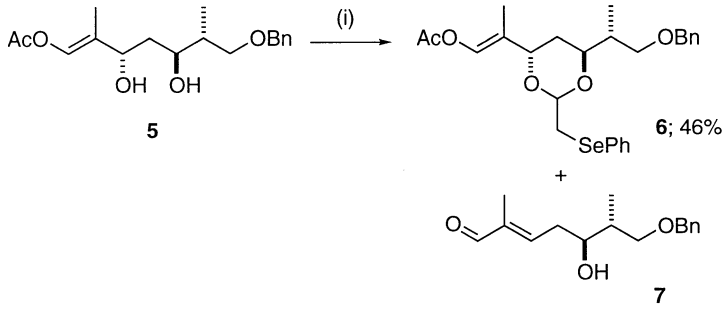
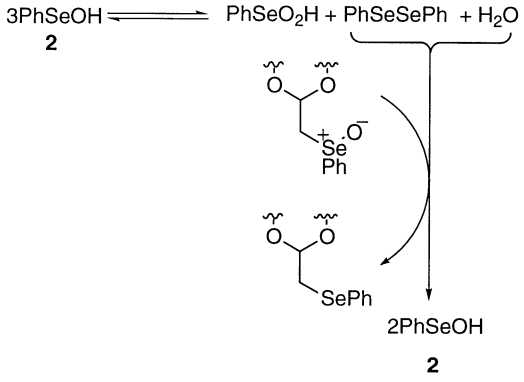


Scheme 2. (i) $PhSeCH_2(OEt)_2$, PPTS, toluene reflux.

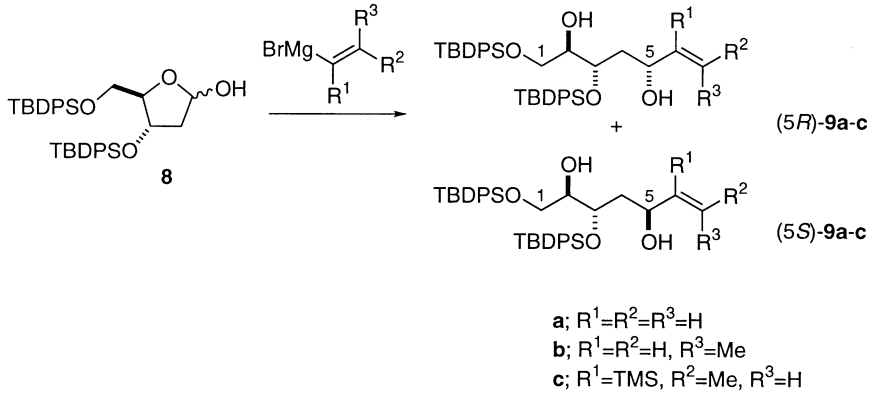


Scheme 3.

suppressed by the use of non-nucleophilic bases and the addition of a nucleophilic silyl ketene acetal as a selenium scavenger.[11] Even under these optimal conditions, oxygen transfer from the selenoxide to produce the selenoacetal can still be a significant side reaction which may lead to the recovery of large amounts of the selenide. Finally, selenoxide elimination towards oxygen and subsequent Claisen rearrangement require high temperatures (sealed tube, up to 185°C). These conditions and the need for high dilution (which also reduces the amount of disproportionation leading to recovered selenide) could make large scale preparations more troublesome. Here we report the synthesis of a series of 8- and 9-membered lactones via the methylenation of cyclic carbonates derived from allylic 1,3- and 1,4-diols using dimethyltitanocene,[12–14] and the subsequent in situ Claisen rearrangement of the presumed ketene acetal intermediates. Some of this work has been reported in a preliminary communication.[15]

2. Preparation of the 1,4-diols

Preparation of the allylic 1,4-diols **9a–c** could be achieved in three steps from 2-deoxy-D-ribose (Scheme 4, Table 1). Treatment of the lactols **8** (1:1 mixture of diastereomers derived from 2-deoxy-D-ribose according to our previously

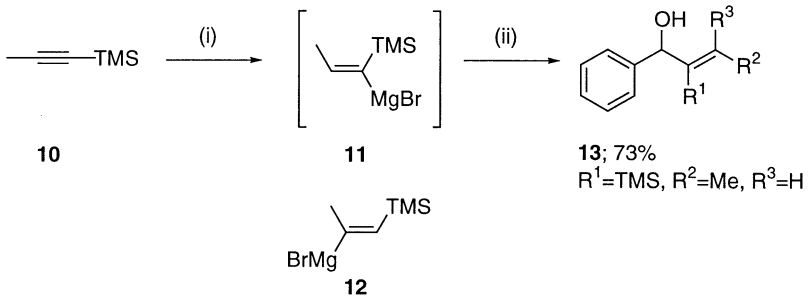


Scheme 4. Conditions—see Table 1.

Table 1. Addition of vinyl Grignard reagents to the lactols **8**, **19** or benzaldehyde

Entry	Compound	R^1	R^2	R^3	Conditions[a]	Yield (%)	d.r. (5*R*)/(5*S*)
1	**9a**	H	H	H	THF, 2 h	75	1:1
2	**9b**	H	H	Me	THF, 2.2 h	77	Nd
3[b]	**13**	TMS	Me	H	Ether, 30 min	73	–
4	**9c**	TMS	Me	H	Ether, 4 h[c]	53	1:1.65
5	**21**	H	H	H	THF, 1.5 h	78	–

[a] All reactions conducted at 0°C.
[b] Reaction with benzaldehyde.
[c] Grignard reagent prepared at 40°C from TMS-propyne, *i*-BuMgBr and Cp_2TiMe_2 (10 mol%) in ether.



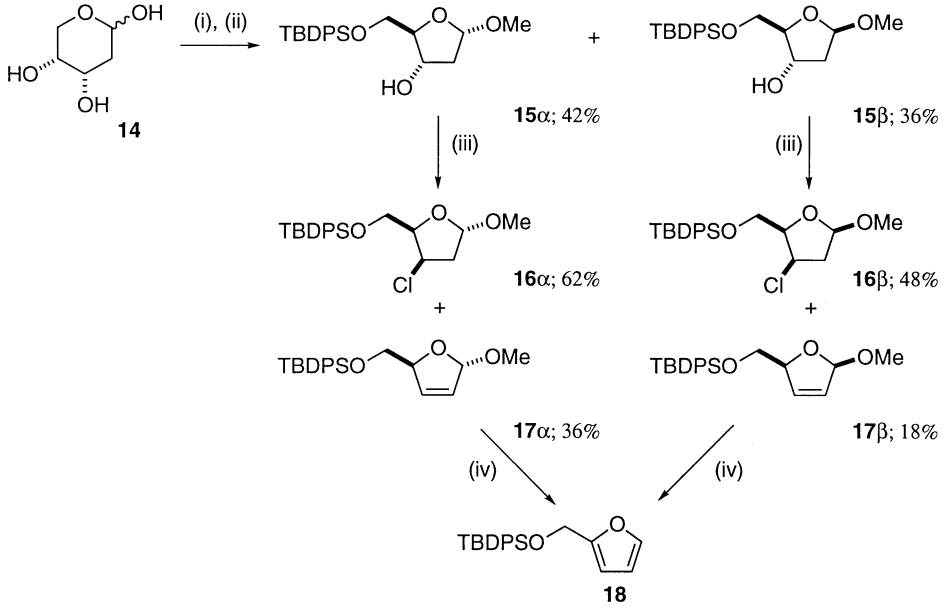
Scheme 5. (i) *i*-BuMgBr, Cp_2TiCl_2 (10 mol%), ether, reflux, 6 h; (ii) PhCHO, 0°C.

reported route)[16] with vinylmagnesium bromide provided the diols (5*R*)-**9a** and (5*S*)-**9a** as a 1:1 mixture of separable diastereomers (Table 1, entry 1, 75%). Similarly, reaction of the Grignard reagent derived from *cis*-1-bromoprop-1-ene[17] with the lactols **8** provided the diols (5*R*)-**9b** and (5*S*)-**9b** in 77% yield, again as a mixture of separable diastereomers (Table 1, entry 2). The stereochemistry of the diols was assigned on the basis of ^{1}H NMR nOe experiments on the corresponding carbonates (vide infra).

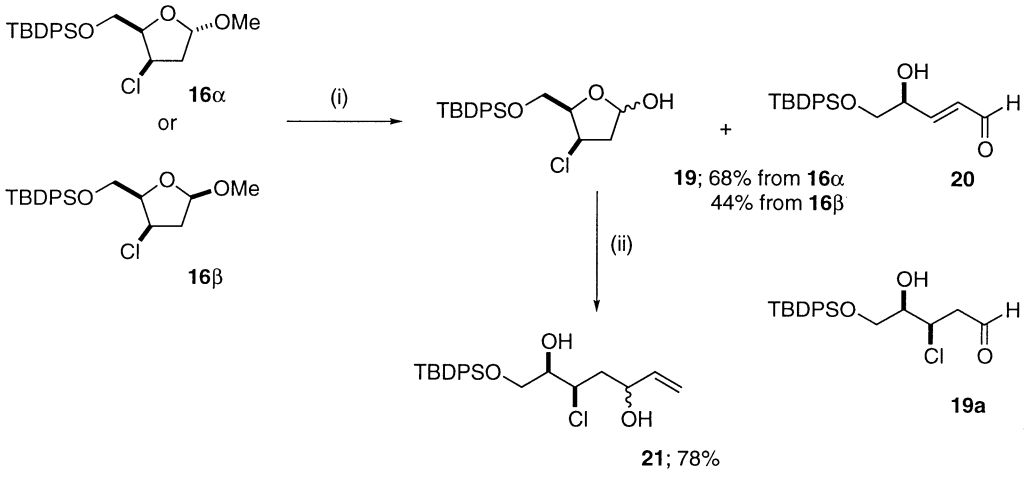
In an effort to extend the range of functionality introduced into the lactone target, the trisubstituted vinyl derivative **9c** was also prepared. Use of the titanocene dichloride catalysed alkyne hydromagnesiation methodology developed by Sato[18–20] allowed the preparation of what was presumed to be (*Z*)-1-trimethylsilyl-prop-1-enyl-1-magnesium bromide **11** from 1-trimethylsilyl-1-propyne **10**. Initial attempts to form this vinyl Grignard reagent **11** were conducted at 0°C or room temperature. Under these conditions a complex (1:1:1:1) mixture of isomeric products was obtained corresponding to the addition of a 1:1 mixture of (*Z*)-1-trimethylsilyl-prop-1-enyl-1-magnesium bromide **11** and (*E*)-1-trimethylsilyl-prop-1-enyl-2-magnesium bromide **12** to the lactols **8**, from which only the diol (5*S*)-**9c** could be isolated, in pure form (11% yield). Alternative routes to the desired vinyl anion using hydrozirconation[21–23] or hydroalumination[24] resulted in decomposition upon addition of the organometallic reagent to the lactols **8**. In the light of the failure of these routes, further investigation of the hydrotitanation/magnesiation strategy was carried out. The effect of the reaction temperature on the regioselectivity of hydrotitanation proved crucial, and preparation of the Grignard reagent **11** at 40°C (ether, reflux, **6** h) followed by addition to benzaldehyde at 0°C provided the corresponding addition product **13** as a single regioisomer in good yield (73%, Table 1, entry 3, Scheme 5).

Repetition of this experiment using the lactols **8** as the electrophilic substrates led to the formation of a 1.65:1 mixture of the separable diastereomers (5*S*)-**9c** and (5*R*)-**9c**, in 53% overall yield (Table 1, entry 4, Scheme 4), with no detection of the undesired isomers arising from addition of (*E*)-1-trimethylsilyl-prop-1-enyl-2-magnesium bromide **12** to the lactols **8**.

Our continued efforts towards the synthesis of the halogenated marine natural product obtusenyne[4] required the synthesis of a chlorinated 9-membered lactone which was made from 2-deoxy-D-ribose as outlined below. Thus exposure of 2-deoxy-D-ribose to acidic methanol followed



Scheme 6. (i) HCl, MeOH, ether, rt, 0.5 h; (ii) TBDPSCl, pyridine, RT, 18 h; (iii) $Me_2N^+{=}CCl_2Cl^-$, pyridine, CH_2Cl_2; (iv) SiO_2.



Scheme 7. (i) $BCl_3{\cdot}SMe_2$, ether, 10 min then THF, $NaHCO_3$ (aq) 1 h; (ii) vinylmagnesium bromide, THF 0°C.

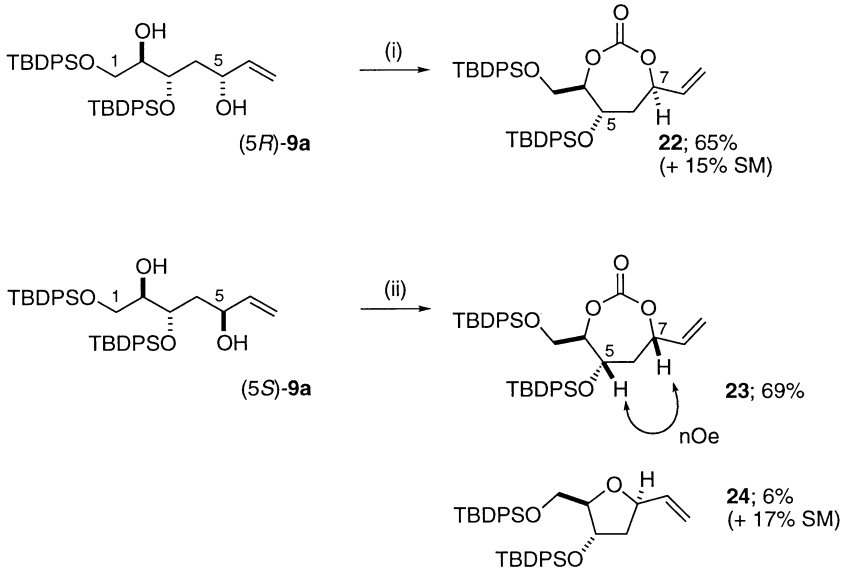
by the addition of pyridine and TBDPSCl provided the silylated methyl glycosides **15**α and **15**β in good yield as a 1.2:1 mixture of α- and β-anomers (Scheme 6).

Chlorination of the separated anomers **15** was achieved according to a modified literature procedure.[25] Exposure of **15** to phosgene iminium chloride and pyridine in dichloromethane provided the chlorinated furanosides **16**α and **16**β. These reactions also produced the corresponding dihydrofurans **17**α and **17**β which arise from a competing elimination reaction. The dihydrofurans are both acid sensitive and readily lose methanol to form the furan **18**[26] on flash chromatography on silica gel; purification of the dihydrofurans **17** can be achieved by column chromatography on silica gel made basic with triethylamine. The methyl glycosides **16** were readily deprotected on exposure to boron trichloride-methyl sulfide complex which provided the corresponding lactols **19** in good yield (Scheme 7); this reaction also produced a small quantity of the α-β-unsaturated aldehyde **20** which arises from elimination of HCl from the open-chain aldehyde **19a**. The ^{1}H NMR spectrum of the lactols **19** indicated that they were in equilibrium with the open-chain aldehyde **19a**.

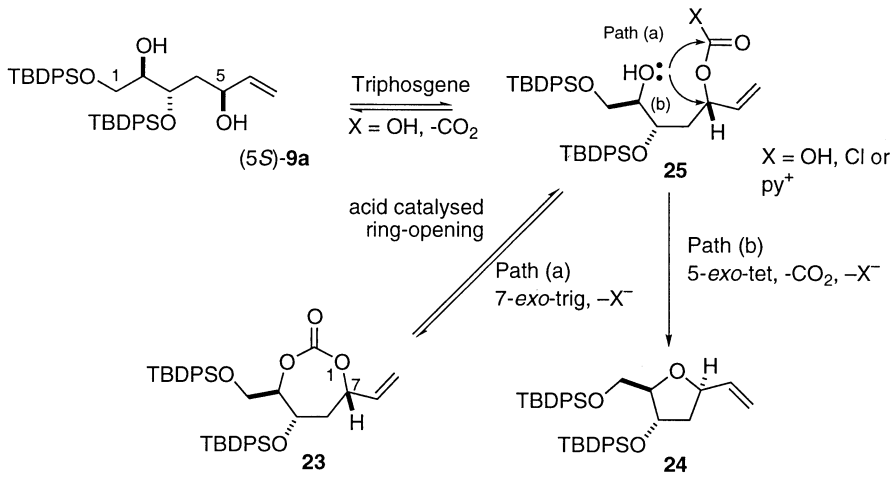
Addition of vinylmagnesium bromide to the lactols **19** provided the corresponding allylic alcohols **21** as white crystalline solids in good yield (Table 1, entry 5); the relative stereochemistry at C-5 of the diols **21** has not been established.

3. Preparation of the 7-membered carbonates

Our initial approach towards the carbonate Claisen rearrangement precursors was based on the work of Burk and Roof, who reported the synthesis of cyclic carbonates derived from 1,2- and 1,3-diols on treatment with triphosgene and pyridine.[27] Exposure of the diol (5*R*)-**9a** to 0.5 equiv. of triphosgene and 6 equiv. of pyridine in dichloromethane at −78°C provided the carbonate **22** as the sole product in 65% yield, together with 15% of recovered starting material (Scheme 8).



Scheme 8. (i) Triphosgene (0.5 equiv.), py (6 equiv.), CH_2Cl_2, −78°C, 105 min; (ii) as (i) reaction time 15 min.



Scheme 9. Possible mechanism for formation of the carbonate **23** and the THF **24**.

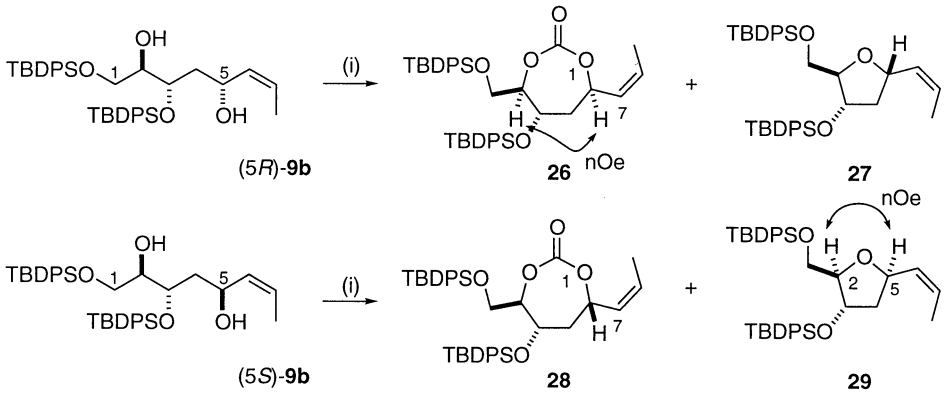
In contrast, reaction of the diol (5*S*)-**9a** under the same conditions led to the isolation of two products—the desired carbonate **23** (69%), a small amount of the tetrahydrofuran derivative **24** (6%), and 17% recovered starting material (Scheme 8). The stereochemistry at C-7 of the carbonate **23** [C-5 of the diol (5*S*)-**9a**] was assigned on the basis of ^{1}H NMR nOe experiments. Reciprocal nOes were observed between H-7 and H-5 in the carbonate **23** indicating that these two protons were on the same face of the molecule and that the carbonate **23** and the diol (5*S*)-**9a** had the (*S*) configuration at C-7 and C-5, respectively. By inference the stereochemistry at C-7 of the carbonate **22** and C-5 of the diol (5*R*)-**9a** has the opposite (*R*)-configuration.

The formation of the tetrahydrofuran by-product **24** can be rationalised by the initial acylation at the less hindered alcohol with the formation of an intermediate such as **25** [Scheme 9, shown for the diol (5*S*)-**9a**], which has a choice of two ring-closing pathways; 7-*exo*-trig cyclisation leads to the desired carbonate **23**, whereas 5-*exo*-tet ring closure (via an S_N2 type pathway) provides the tetrahydrofuran by-product **24** with inversion of configuration at the reacting centre.

The stereochemistry of the furan **24** was assigned by comparison with the stereochemistry of the furan **29** (vide infra) implying that the reaction occurred by an S_N2-like mechanism. Tetrahydrofuran formation may also be possible if nucleophilic ring-opening of the carbonate occurs to provide **25**. This process may be catalysed by pyridinium hydrochloride generated under the reaction conditions or may occur during purification. The intermediate **25** could subsequently cyclise to the undesired tetrahydrofuran product **24** or indeed may revert to the diol starting material.

The promising yields of the desired carbonates **22** and **23** prompted us to attempt carbonate formation from the methyl-substituted allylic diols (5*R*)-**9b** and (5*S*)-**9b**. In the event, treatment of the diols **9b** with triphosgene and pyridine led to the predominant formation of the tetrahydrofurans **27** and **29** (Scheme 10, Table 2, entries 1 and 2) as well as some of the desired carbonates **26** and **28**. The stereochemistry of the carbonate **26** [and hence that of the precursor diol (5*R*)-**9b**] was determined from ^{1}H NMR nOe studies. Mutual nOe enhancements were observed between H-7 and H-4 (carbonate numbering, Scheme 10); by inference the stereochemistry of the carbonate **26** and the diol (5*R*)-**9b** is as shown. Similarly, the stereochemistry of the tetrahydrofuran **29** arising from the diol (5*S*)-**9b** could be assigned from mutual nOe enhancements observed between H-2 and H-5 (tetrahydrofuran numbering) and, by inference, the stereochemistry at C-5 of the tetrahydrofuran **27** is (*S*). These stereochemical assignments indicate that tetrahydrofuran formation is occurring in a stereospecific manner via an S_N2-like mechanism with inversion of configuration at C-5 (diol numbering).

The low isolated yields of the carbonates **26** and **28** may be a consequence of the acid sensitivity of the carbonates to purification by flash chromatography (which may be reduced by the use of a basic solvent system) or an increased tendency of the diols **9b** to form tetrahydrofuran by-products under the reaction conditions. It is likely that the activation energy for the S_N2 reaction which leads to the tetrahydrofurans **27** and **29** is lower in energy than the corresponding transition state for the formation of **24** due to the greater electron releasing power of a 2-propenyl group compared with a vinyl group[28] and hence the tetrahydrofurans **27** and **29** form more readily than the tetrahydrofuran **24**. Whilst the use of pyridine is probably necessary to promote carbonate formation through pyridine-assisted activation of the triphosgene, the pyridinium hydrochloride formed in situ may also be sufficiently acidic (pK_a 5.23) to protonate the carbonate product to some extent, leading to eventual tetrahydrofuran formation by the mechanism discussed earlier. This hypothesis was tested by the addition of triethylamine (pK_a 10.75) into the reaction mixture. The use of 6 equiv. each of pyridine and triethylamine (Table 2, entry 3), followed by chromatography in the presence of triethylamine, led to suppression of tetrahydrofuran formation from the reaction of the diol (5*S*)-**9b**, and the desired carbonate **28** was formed in 77% yield. It was subsequently found that the inclusion of powdered 4 Å molecular sieves into the reaction mixture further increased consumption of starting material and improved the isolated yields of the carbonates **26** and **28** (Table 2, entries 4 and 5), although the diol (5*S*)-**9b** still showed some tendency towards formation of the tetrahydrofuran **29** compared with the diol



Scheme 10. (i) Triphosgene (0.5 equiv.), see Table 2.

Table 2. Preparation of the carbonates **26** and **28** from the diols (5*R*)- and (5*S*)-**9b**

Entry	Diol	Py (equiv.)	Et_3N (equiv.)	Conditions	Carbonate (yield, %)	THF (yield, %)
1	(5*R*)-**9b**	6.2	–	−78°C, 20 min[a]	**26** (33)	**27** (57)
2	(5*S*)-**9b**	6	–	−78°C, 20 min[a]	**28** (4)	**29** (78)
3	(5*S*)-**9b**	6	6	−78°C, 20 min[b]	**28** (77)	**29** (trace)
4	(5*R*)-**9b**	6	6	4 Å MS, 15 min at −78°C then 10 min→rt[c]	**26** (99)	**27** (trace)
5	(5*S*)-**9b**	6	6	4 Å MS, 15 min at −78°C then 10 min→rt[c]	**28** (81)	**29** (12)
6	(5*R*)-**9b**	6[d]	–	4 Å MS, 15 min at −78°C then 10 min→rt	**26/27**, 1:1.5[e]	**26/27**, 1:1.5[e]
7	(5*S*)-**9b**	6[d]	–	4 Å MS, 15 min at −78°C then 10 min→rt	**28/29**, 1:2.5[e]	**28/29**, 1:2.5[e]

[a] Purification by flash chromatography (on silica; hexane/ether, 10:1).
[b] Purification by flash chromatography (on silica; hexane/ether, 4:1+2% Et_3N).
[c] Purification by flash chromatography (on silica; hexane/ether, 4:1+5% Et_3N).
[d] DMAP used instead of pyridine.
[e] Ratios determined by ^1H NMR; yield not determined.

(5*R*)-**9b**. Replacement of pyridine with the more nucleophilic DMAP (Table 2, entries 6 and 7) led to a greater proportion of tetrahydrofuran formation from both diols.

The effect of reaction temperature on the ratio of carbonate and tetrahydrofuran products was also investigated. Carbonate formation from the diol (5*S*)-**9b** was studied at a range of temperatures from −70°C to ambient temperature. An increased proportion of the tetrahydrofuran **29** was produced at higher temperatures (Table 3); this result illustrated the need to maintain the reaction temperature at −78°C during carbonate formation.

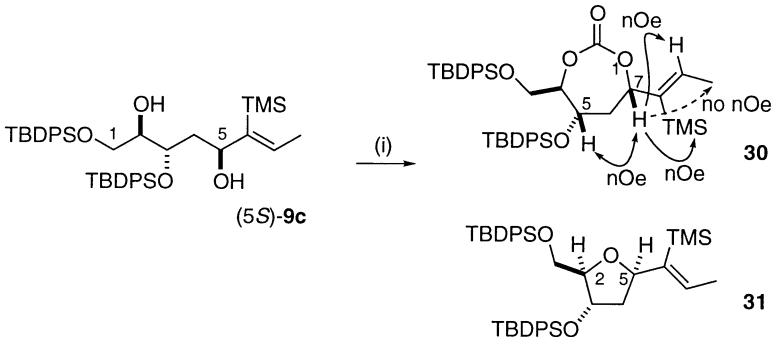
Table 3. Formation of the carbonate **28** and the tetrahydrofuran **29** from the diol (5*S*)-**9b**

Entry	Temperature (°C)	Product ratio[a,b] (carbonate **28**/THF **29**)
1	−70	9:1
2	−45	9:1
3	−25	5.1:1
4	0	1:1
5	25	0.35:1

[a] *Conditions*: Pyridine (6 equiv.), triethylamine (6 equiv.), CH_2Cl_2, 15–30 min.
[b] Determined by ^1H NMR.

Conversion of the diol (5*S*)-**9c** into the corresponding carbonate **30**, the potential Claisen rearrangement precursor to a tetrasubstituted lactone, could also be accomplished. Gratifyingly, treatment of the diol (5*S*)-**9c** with triphosgene in the presence of 4 Å molecular sieves, triethylamine and pyridine in dichloromethane at −78°C, according to our optimised procedure, led to the formation of the desired carbonate **30** and a small amount of what was presumed to be the tetrahydrofuran **31** in a 10.8:1 ratio (99% yield, Scheme 11). The stereochemistry of the carbonate **30** [and hence the diol (5*S*)-**9c**] was again assigned through ^1H NMR nOe experiments; mutual nOe enhancements were observed between H-5 and H-7 in **30**, indicating these two protons to be on the same face of the carbonate ring. ^1H NMR nOes from H-7 to the TMS group and the vinyl proton (but not to the vinyl methyl group) suggested the geometry of the olefin to be (*Z*) as expected.

Treatment of the diols **21** under our optimised conditions for carbonate formation, provided the corresponding carbonates **32** in moderate to good yields (50 and 77%, respectively;



Scheme 11. (i) Triphosgene (0.5 equiv.), py (6 equiv.), triethylamine (6 equiv.), 4 Å MS, CH_2Cl_2, −78°C, 25 min, 99% (**30/31**, 10.8:1).

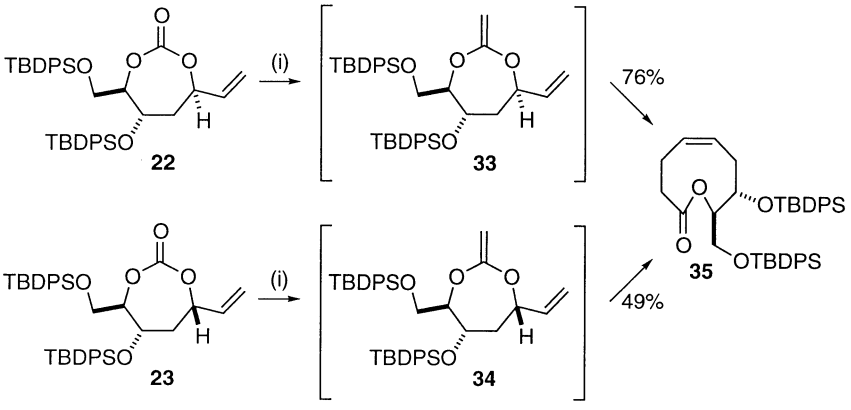
Scheme 12. (i) Triphosgene, pyridine, triethylamine, 4 Å MS, CH_2Cl_2.

Scheme 12). The carbonates were very unstable on storage and hence full characterisation was not possible.

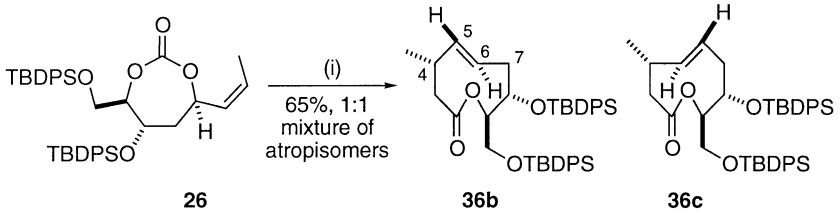
4. Conversion of the 7-membered carbonates to 9-membered lactones

With a range of 7-membered cyclic carbonates in hand, methylenation to the presumed ketene acetal intermediates and subsequent in situ Claisen rearrangement was investigated. Dimethyltitanocene was conveniently prepared according to the reported procedure and could be stored for several months in the freezer with no loss of activity.[29] Treatment of the diastereomeric carbonates **22** and **23** with dimethyltitanocene afforded the 9-membered lactone **35** in 76 and 49%, yields, respectively (Scheme 13); the lactone **35** was formed in 85% yield using the alternative selenium based methodology.[16]

The overall success of this transformation was encouraging and our attention was turned to the more heavily substituted vinyl carbonates **26**, **28**, **30** and the chloro-substituted vinyl carbonate **32**. Exposure of the carbonate **26** to 1.25 equiv. of dimethyltitanocene in toluene at reflux led to the formation



Scheme 13. (i) Cp_2TiMe_2 (1.25 equiv.), toluene, reflux, dark, 2 h.



Scheme 14. (i) Cp_2TiMe_2 (1.25 equiv.), toluene, reflux, 0.5 h, dark.

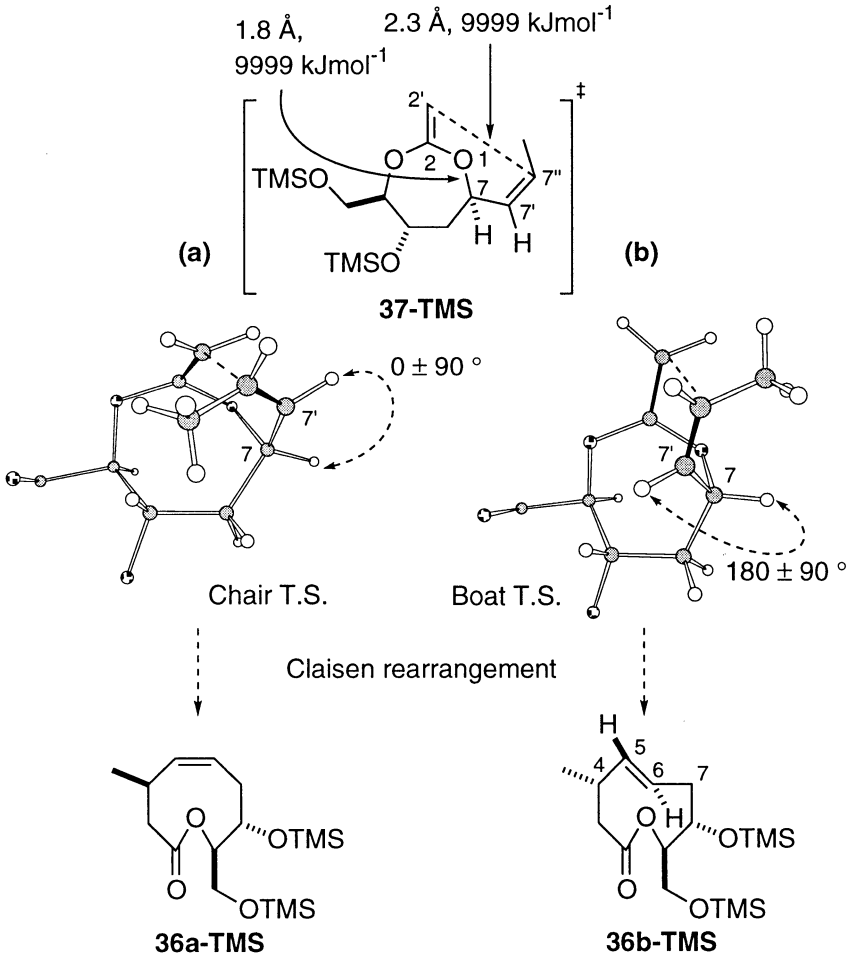


Figure 1. Lowest energy conformations for the constrained ketene acetal **37**-TMS filtered by the H-7–C-7–C-8–H-8 torsion angle: (a) 0±90° and (b) 180±90°. The oxygen lone pairs and TMS groups have been removed for clarity. Constrained bonds are indicated. Molecular modelling was carried out with in vacuo simulation.

of a single less polar compound by thin layer chromatography (TLC) (Scheme 14). Analysis of the purified product revealed that a 1:1 mixture of atropisomeric lactones **36b** and **36c** had been produced in 65% yield, as evidenced by the presence of two distinct methyl peaks in the ^{1}H NMR spectrum [δ_H ($CDCl_3$, 500 MHz) 1.13 (d, 3H, J=7.0 Hz), 1.18 (d, 3H, J=7.0 Hz)].

In an effort to identify and rationalise this mixture of products, a Monte Carlo conformational search[30] using the MM2 forcefield[31] implemented in Macromodel® version 5.5[32] was carried out for the analogous TMS-protected presumed ketene acetal intermediate **37**-TMS. The interatomic distance between C-2′ and C-7″ (forming bond) was constrained at 2.3 Å, whilst the C-7–O-1 (breaking bond) was set at 1.8 Å, in a crude transition state model.[†] All structures corresponding to unique energy minima were then filtered by the torsion angle H-7–C-7–C-7′–H-7′ into two sets, with angles 0±90 and 180±90°. These filtered sets correspond to chair- and boat-like Claisen rearrangement transition states, respectively; the lowest energy conformation of each set is illustrated (Fig. 1). Boltzmann distributions were calculated for each filtered set (at 384 K, with a global minimum of −11.866 kJ mol^{-1}, corresponding to a boat transition state), which predicted a transition state ratio of 1191:1, boat/chair. The large preference for a boat-like transition state predicted by molecular modelling [leading to an (*E*)-olefin, **36b**] can be rationalised by examination of the two transition state structures (Fig. 1). The *cis*-propenyl methyl group clearly leads to large unfavourable transannular interactions in the chair-like transition state [leading to a (*Z*)-olefin, **36a**] which are relieved in the alternative boat conformation, where the methyl group adopts an *exo*-orientation relative to the 7-membered ring.

The experimentally observed ratio of (*E*)-alkene isomers (1:1) does not seem to be supported by the molecular modelling calculations which would predict the formation of solely the lactone **36b** containing an (*E*)-olefin. One possible explanation for the formation of two atropisomeric lactones **36b** and **36c** is that the initially formed lactone **36b** undergoes rotation around the C-4–C-5 and C-6–C-7 bonds (atropisomerisation) under the reaction conditions to provide the lactone **36c**. The 1:1 ratio of **36b/36c** would therefore correspond to the thermodynamic ratio (Scheme 14). A Monte Carlo conformational search[30] using the

[†] The bond-making and bond-breaking distances were taken from an ab initio calculation (3-21G and 3-21G*) of the transition state for the Claisen rearrangement of a simple vinyl-substituted ketene acetal.

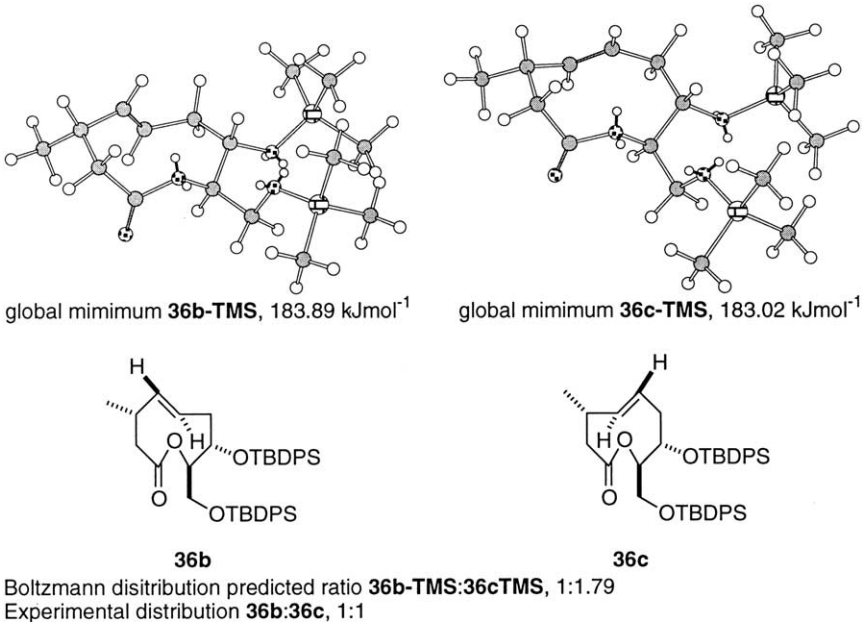
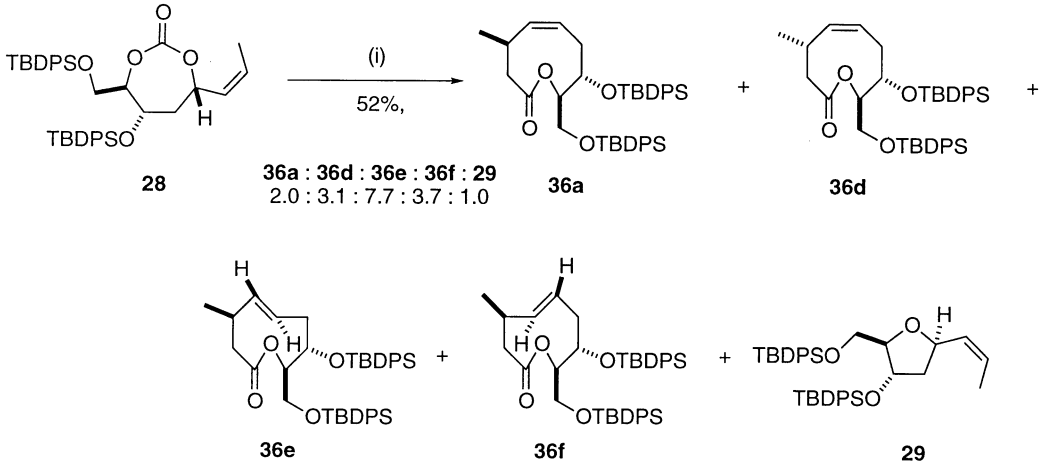


Figure 2. Lowest energy conformations for the atropisomers **36b**-TMS and **36c**-TMS and calculated and experimental ratios for **36b**-TMS, **36c**-TMS, **36b** and **36c**. Molecular modelling was carried out with in vacuo simulation.

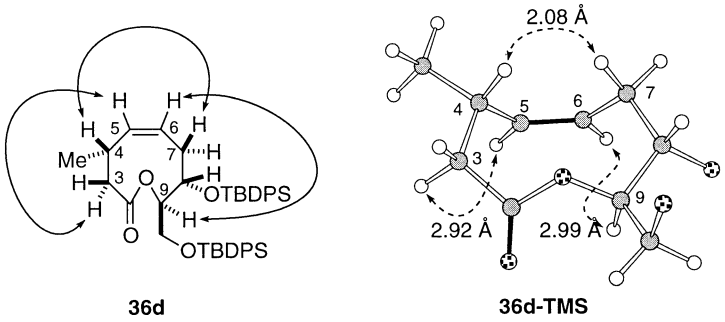
MM2 forcefield[31] in Macromodel® version 5.5[32] was carried out for the TMS-substituted (*E*)-olefin lactone isomer **36b**-TMS. The resultant set of unique energy minima were filtered by the H-4–C-4–C-5–H-5 torsion angle into two sets, with angles 0±90 and 180±90°, corresponding to the two atropisomers **36b** and **36c**, respectively (Fig. 2).

The Boltzmann distributions calculated for each set predicted a thermodynamic ratio of 1:1.79, **36b**-TMS/**36c**-TMS at 298 K (1:1.73 at 384 K). Although this calculation does not make any prediction with regard to the activation energy for atropisomerisation, the theoretical ratio of atropisomers is in reasonable agreement with the experimentally observed distribution of isomeric lactone products (**36b/36c**, 1:1), formed from equilibration of the initially formed atropisomer **36b**. The formation of atropisomeric 9-membered lactones following ring-expansion Claisen rearrangement of a ketene acetal has been reported by Pearson.[33] In this study a mixture of *cis*- and *trans*-9-membered lactones was observed and it was shown that the initially formed *trans*-9-membered lactone underwent atropisomerism on prolonged heating in toluene.

The diastereomeric carbonate **28** was also subjected to methylenation/Claisen rearrangement conditions (Scheme 15). A complex mixture of products was obtained in 52% yield; a ^{1}H NMR COSY experiment enabled identification of four separate lactone products. In addition, each lactone gave rise to at least one distinct peak in the ^{1}H NMR spectrum, unobscured by other lactone signals (as assigned through COSY analysis). Due to the complete connectivity of the ^{1}H spin systems, it was realised that this complex mixture of inseparable products could be conveniently analysed through a series of 1-D TOCSY experiments.[34–36] Irradiation of each of the distinct signals would lead to enhancements only at those protons within the same spin system; in other words, the ^{1}H NMR spectrum of each isomer would be resolved. After this study was complete the concept of analysing complex mixtures using 1-D TOCSY experiments was independently published by



Scheme 15. (i) Cp_2TiMe_2 (1.35 equiv.), toluene, reflux, 0.5 h, dark.



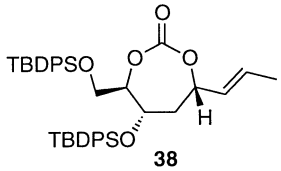
36d **36d-TMS**

Figure 3. Observed 1H NOESY crosspeaks for the lactone **36d** and calculated global minimum for the lactone **36d**-TMS. The oxygen lone pairs and TMS protecting groups have been removed for clarity. Distances were measured on the computer using Macromodel®. Molecular modelling was carried out with in vacuo simulation.

Sharman.[37] Examination of the resultant TOCSY spectra showed that the products could be assigned as **36a**, **36d**, **36e**, **36f** and **29** in a ratio of 2.0:3.1:7.7:3.7:1.0 (determined through integration of the ^{1}H NMR spectrum).

The geometry of the olefin in the unsaturated lactones **36a** and **36d** was assigned as (*Z*) on the basis of the coupling constant analysis [**36a**, δ_H ($CDCl_3$, 500 MHz) 4.79–4.89 (m, 1H, H-6), 5.01 (apparent ddm, 1H, H-5, J=11.0, 7.5 Hz); **36d**, δ_H ($CDCl_3$, 500 MHz) 5.35 (t, 1H, H-5, J=10.5 Hz), 5.71 (td, 1H, H-6, J=10.5, 5.5 Hz)]. A 2-D NOESY experiment on **36d** (prepared by $RhCl_3$ mediated isomerisation of a 1:1 mixture of **36b**,**c**) allowed assignment of the stereochemistry at C-4 as (*S*), and thus by inference the stereochemistry at C-4 of **36a** as (*R*). In the ^{1}H NMR NOESY spectrum of **36d** strong cross peaks were observed between H-3 and H-5, H-4 and H-7, H-9 and H-6. A Monte Carlo conformational search[30] using the MM2 forcefield[31] in Marcomodel® version 5.5[32] was conducted for the lactone **36d**-TMS. The global minimum conformation provided strong support for the proposed structure; the calculated interatomic distances were in good agreement with the observed NOESY crosspeaks (Fig. 3).

The unexpected formation of the isomer **36a** could be rationalised by close examination of the carbonate starting material which revealed a small amount of the *trans*-propenyl substituted carbonate **38**. The origin of this impurity was traced to the commercially purchased propenyl bromide (Aldrich stated purity, 97%) used for preparation of the corresponding Grignard reagent for coupling with the lactols **8**.



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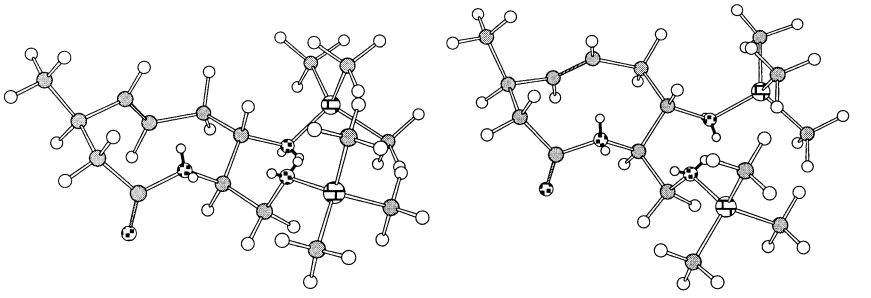
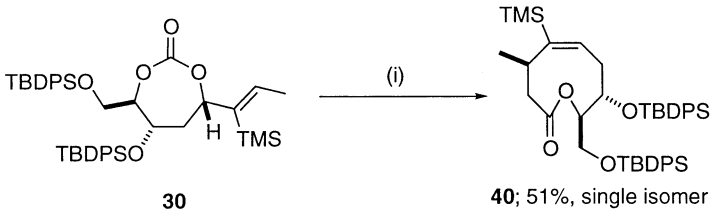


global mimimum **36e-TMS**, 178.58kJmol^{-1} global mimimum **36f-TMS**, 180.86 kJmol^{-1}

36e **36f**

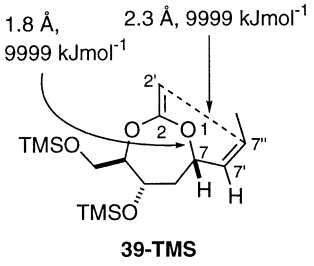
Boltzmann disitribution predicted ratio **36e-TMS**:**36fTMS**, 2.25:1
Experimental distribution **36e**:**36f**, 2.08:1

Figure 4. Lowest energy conformations for the atropisomers **36e**-TMS and **36f**-TMS and calculated and experimetental ratios for **36e**-TMS, **36f**-TMS, **36e** and **36f**. Molecular modelling was carried out with in vacuo simulation.



Scheme 16. (i) Cp_2TiMe_2 (1.15 equiv.), toluene, reflux, 0.5 h, dark.

Similarly, the double bond geometry of the atropisomeric lactones **36e** and **36f** were assigned (*E*) on the basis of coupling constant analysis; [**36e**, δ_H ($CDCl_3$, 500 MHz) 5.26 (ddd, 1H, H-6, *J*=16.5, 11.7, 3.2 Hz), 5.48 (1H, ddd, *J*=16.5, 7, 1 Hz); **36f**, δ_H ($CDCl_3$, 500 MHz) 5.05 (dd, 1H, H-5, *J*=16.5, 9.5 Hz), 5.43 (ddd, 1H, H-6, *J*=16.5, 8.8, 6.5 Hz)]. Assignment of the stereochemistry of the atropisomers **36e** and **36f** was made on the basis of the molecular modelling prediction of the product distributions. A Monte Carlo conformational search[30] using the MM2 forcefield[31] in Macromodel® version 5.5[32] was carried out for the analogous TMS-protected presumed ketene acetal intermediate **39**-TMS. The interatomic distance between C-2′and C-7″ (forming bond) was again constrained at 2.3 Å, whilst the C-7–O-1 (breaking bond) was set at 1.8 Å.



The structures corresponding to unique energy minima were then filtered by the torsion angle H-7–C-7–C-7′–H-7′ into two sets, with angles 0±90 and 180±90°. Boltzmann distributions were calculated for each filtered set (at 384 K, with a global minimum of -0.83847 kJ mol^{-1}, corresponding to a boat transition state), leading to a predicted transition state ratio (and corresponding *E*/*Z*, **36e**/**36d**, lactone olefin ratio) of 97:1 (boat/chair). Although this ratio is rather more in favour of the *E*-olefin isomer **36e**,**f** than the observed values (3.1:1), qualitative agreement between the experimental and theoretical ratios had been obtained. As before, a Monte Carlo conformational search[30] using the MM2 forcefield[31] in Macromodel® version 5.5[32] was carried out for the TMS-substituted *E*-olefin lactone isomer **36e**-TMS. Again, the resultant set of unique energy minima was filtered by the H-4–C-4–C-5–H-5 torsion angle into two sets, with angles 0±90 and 180±90°, corresponding to the two atropisomers **36e** and **36f**, respectively (Fig. 4). The Boltzmann distributions calculated for each set predicted a thermodynamic ratio of 2.68:1, **36e**-TMS/**36f**-TMS at 298 K (2.25:1 at 384 K). These ratios compared well with the experimentally observed ratio of 2.08:1 between the lactones assigned as **36e** and **36f**. The small amount of the tetrahydrofuran by-product **29** observed in the product mixture may have arisen from degradation of any remaining carbonate starting material during reaction or purification.

Attention was turned to the TMS-substituted propenyl carbonate **30**. The *trans*-stereochemistry of the methyl group relative to the carbonate ring in this compound was not expected to lead to the problematic mixture of products observed for the *cis*-propenyl derivatives **26** and **28**, as the proposed chair-like transition state for the Claisen rearrangement (with the methyl group in a pseudo-equatorial position) ought not lead to unfavourable transannular interactions in this instance. In the event, exposure of the carbonate **30** to dimethyltitanocene afforded solely the lactone **40** as a single isomer, in a satisfactory 51% yield (Scheme 16).

The stereochemistry of the lactone **40** was assigned through a ^1H NMR NOESY experiment. Strong crosspeaks were observed between H-4 and H-7α, and between H-7α and H-9, all of which are proposed to be on the lower face of the lactone ring (as drawn). A strong enhancement was also seen between H-6 and the TMS group, confirming the stereochemistry of the double bond to be *cis* with respect to the lactone ring. A Monte Carlo conformational search[30] using the MM2 forcefield[31] in Macromodel® version 5.5[32] was carried out for the lactone **40**-TMS. The global minimum conformation provided strong support for the assigned structure as the calculated interatomic distances were in good agreement with the observed NOESY crosspeaks (Fig. 5).

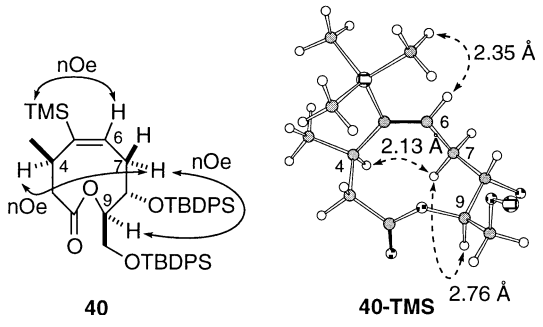
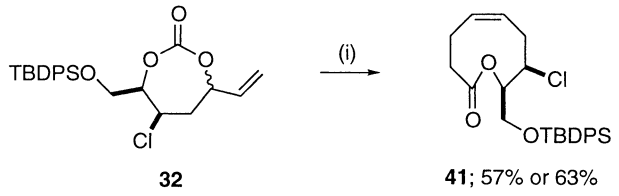


Figure 5. Observed 1H NOESY crosspeaks for the lactone **40** and calculated global minimum for the lactone **40**-TMS. The oxygen lone pairs and TMS protecting groups have been removed for clarity. Distances were measured on the computer using Macromodel®. Molecular modelling was carried out with in vacuo simulation.

The final 7-membered carbonates to be studied in this series were the chlorinated compounds **32**. On exposure to dimethyltitanocene in toluene at reflux the separated carbonates **32** provided the 9-membered lactone **41** in 55 and 63% yields (Scheme 17). This transformation indicates that it is possible to use reducible functional groups (i.e. alkyl halides) in the presence of dimethyltitanocene. Furthermore, when the formation of the lactone **41** was attempted from



32 **41**; 57% or 63%

Scheme 17. (i) Cp_2TiMe_2, toluene, reflux.

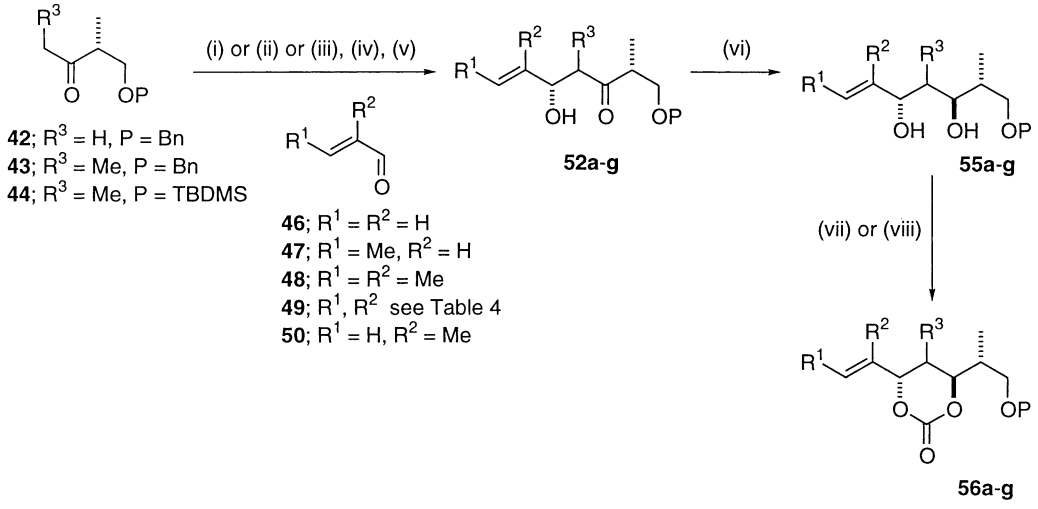
the corresponding selenoxide using our standard Claisen rearrangement conditions (toluene, DBU, reflux, 18 h) the lactone **41** was isolated in very poor yield and was of a low purity.

The effect of the substitution pattern of the carbonates subjected to the methylenation/Claisen rearrangement reaction clearly has a strong influence on the product distributions in the case of 9-membered lactones. The application of the carbonate/Claisen rearrangement methodology to a range of 8-membered lactones was also investigated.

5. Preparation of the 1,3-diols

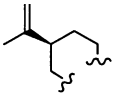
The synthesis of a range of representative 1,3-diols (for subsequent conversion to 8-membered lactones)[8] was readily achieved using the boron-mediated aldol methodology developed by Paterson.[38–40] A (+)-Ipc-boron mediated aldol reaction between the enolate derived from the ketone **42** [readily prepared in three steps from (*R*)-(+)-methyl-3-hydroxy-2-methylpropionate][39] and a range of commercially available acyclic aldehydes **46**–**48** and the cyclohexenyl-substituted (−)-perillaldehyde **49** provided the *syn*-hydroxyketone products **52a**–**d** in 80–95% yields as single diastereomers as judged by ^{1}H NMR (Scheme 18, Table 4).

The absolute configuration of the product **52a** was

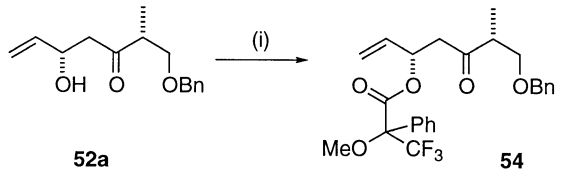


Scheme 18. (i) (+)-Ipc_2BCl, Et_3N, ether, 0°C, 2 h; (ii) (−)-Ipc_2BOTf, *i*-Pr_2NEt_2, CH_2Cl_2, 25°C, 3 h; (iii) Cy_2BCl, Et_3N, ether, −78°C, 3 h; (iv) RCHO (**46**–**50**), ether, −78°C; (v) H_2O_2, pH 7 buffer, MeOH, rt, 1 h; (vi) $Me_4NBH(OAc)_3$, MeCN, AcOH, see Table 4; (vii) carbonyldiimidazole, toluene, reflux; (viii) triphosgene, py, Et_3N, 4 Å MS, CH_2Cl_2, −78°C.

Table 4. Preparation of the hydroxyketones **52a**–**g**, the diols **55a**–**g** and the carbonates **56a**–**g**

Ketone	P	R^1	R^2	R^3	Hydroxyketone	Yield **52a**–**h** (%)	Yield **55a**–**g** (%)	*t* (h)	*T* (°C)	Yield **56a**–**g** (%)	*t* (h)
42	Bn	H	H	H	**52a**	81[a]	91	18	−40	66,[b] 45[c,d]	48, 0.25
42	Bn	Me	H	H	**52b**	95[a]	91	18	−35	77[c]	0.5
42	Bn	Me	Me	H	**52c**	–[a]	66[e]	18	−35	32,[b] 46[c]	25, 1.0
42	Bn			H	**52d**	–[a]	51[e]	18	−35	28[b]	24
43	Bn	H	Me	Me	**52e** C-4-(*S*)[f]	90[g]	72	18	−35	100[b]	20
43	Bn	H	Me	Me	**52f** C-4-(*R*)[f]	72[h]	72	48	−30	91[b]	23
44	TBDMS	H	Me	Me	**52g** C-4-(*R*)[f]	73[h]	77	72	−30	78[b]	20

[a] *Conditions*: Scheme 18 (i), (iv), (v).
[b] *Conditions*: Scheme 18 (vii).
[c] *Conditions*: Scheme 18 (viii).
[d] 33% Recovered **55a**.
[e] Yield over 2 steps.
[f] The configurations at C-4 in **52e**–**g** only apply to the hydroxyketones **52e**–**g** and not to the diols **55e**–**g** or the carbonates **56e**–**g**.
[g] *Conditions*: Scheme 18 (ii), (iv), (v).
[h] *Conditions*: Scheme 18 (iii), (iv), (v).

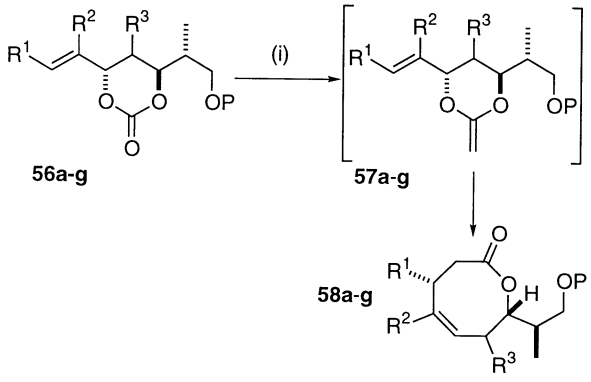


Scheme 19. (i) (*R*)- or (*S*)-MTPA, DCC, DMAP, CH_2Cl_2, rt.

established by 500 MHz ^{1}H NMR analysis following conversion of the free hydroxy group to the (*R*)-(+)- and (*S*)-(−)-phenylmethoxy(trifluoromethyl) acetate (MTPA) **53** derivatives according to the method of Kawisawa (Scheme 19; see Section 9).[41]

The aldols **52a** and **52b** were readily purified by flash chromatography, however, **52c** and **52d** could not be completely separated from isopinocampheol (an oxidative side product) and were used in partially purified form.

In a similar manner, the ethyl ketone **43** (prepared in by an analogous route to the methyl ketone **42**) could be combined with methacrolein **50** using a boron-mediated aldol reaction. Formation of the (*Z*)-enolate of the ketone **43** using (−)-di-isopinocampheylboron triflate followed by addition of methacrolein **50** afforded the *syn*-aldol product **52e** in 90% yield (Scheme 11, Table 4), containing an (*S*)-methyl substituent on the carbon backbone.[40] In contrast, the (*E*)-enolate of the ethyl ketone **43** was formed on treatment with dicyclohexylboron chloride, which provided the *anti*-aldol product **52f**, containing an (*R*)-methyl group, after reaction with the aldehyde **50**.[40] The analogous TBDMS protected hydroxyketone **52g** was prepared using identical methodology from the ethyl ketone **44** and aldehyde **50**, for comparison of the effect of the protecting group on the Claisen rearrangement.



Scheme 20. (i) Cp_2TiMe_2, toluene, reflux, dark; P=Bn (**56a–f**); P=TBDMS (**56g**).

Anti-reduction of the hydroxyketones **52a–g** was achieved on treatment with tetramethylammonium triacetoxyborohydride[42] at −35°C for at least 18 h (Scheme 18, Table 4); moderate to good yields of the corresponding *anti*-diols **55a–g** were obtained with excellent diastereoselectivity (generally single diastereomers by ^{1}H NMR). Conversion of these diols to the desired 6-membered cyclic carbonate derivatives **56a–g** proved less problematic than the 7-membered cases. Either the triphosgene or carbonyldiimidazole (CDI) methodology could be used to effect this transformation (Table 4).

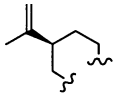
6. Conversion of the 6-membered carbonates to 8-membered lactones

With a range of carbonate substrates in hand, the tandem methylenation/Claisen rearrangements were carried out (Scheme 20, Table 5). Treatment of the carbonates **56a–g** with dimethyltitanocene in toluene at reflux provided the 8-membered lactone Claisen rearrangement products **58a–g** as single diastereomers (by ^{1}H NMR analysis) in reasonable to good yields. Carbonates with a greater degree of substitution around the Claisen rearrangement skeleton (**56c** and **56d**) were both more difficult to synthesise, and required longer reaction times with lower overall yields for the Claisen rearrangement step. The nature of the side-chain protecting group (**56f**, Bn; and **56g**, TBDMS) did not seem to greatly affect the overall yield of the Claisen rearrangement. Gratifyingly, the overall yield for the two-step procedure (carbonate formation then Claisen rearrangement) was found to be comparable, and in several cases superior, to the alternative selenium route to the same lactones.[8]

7. Discussion

The synthesis of both 8- and 9-membered lactones from 6- and 7-membered carbonates has been achieved in moderate to good yields. The ring-expansion reaction proceeds via initial methylenation of the carbonate with dimethyltitanocene followed by in situ Claisen rearrangement of the derived ketene acetals which provides the corresponding medium-ring lactones. If the rate of the methylenation of the carbonates is faster than the rate of the Claisen rearrangement of the corresponding ketene-acetals, then the

Table 5. Preparation of the 8-membered lactones **58a–g**

Carbonate	R^1	R^2	R^3	Yield **58a–g** (%)	*t* (h)
56a	H	H	H	52	3.5
56b	Me	H	H	52	2.5
56c	Me	Me	H	34	4.5
56d			H	25	24
56e	H	Me	Me	48; C-7-(*S*)	3.0
56f	H	Me	Me	63; C-7-(*R*)	16
56g	H	Me	Me	67; C-7-(*R*)	20

ketene-acetal will build up as an intermediate and most of the dimethyltitanocene reagent will be consumed before the conversion of the ketene-acetals into the corresponding medium-ring lactones. However, if the Claisen rearrangement of the ketene-acetals is rapid compared with methylenation of the carbonate, then the lactone products will be formed in the presence of dimethyltitanocene and so may be subject to methylenation. In many of the reactions extra dimethyltitanocene was added to the reaction mixture when TLC analysis indicated that the reaction had not gone to completion. In these cases the lactones were still isolated as the major component from the reaction mixture thus indicating that methylenation of a carbonate carbonyl group is faster than methylenation of a medium ring lactone carbonyl group. The reason for the selective methylenation of a carbonate in the presence of a lactone is unclear.[43]

8. Conclusion

An alternative ring-expansion route to 8- and 9-membered lactones by tandem methylenation/Claisen rearrangement, which avoids the problems associated with toxic selenium reagents, has been developed. Comparable, and in certain cases superior, yields to the selenium route were obtained for the lactonisation processes. The formation of the chlorolactone **41** was achieved in good yield utilising this carbonate methodology but was formed in very poor yield using our selenium based methodology. The formation of the carbonates occurs under basic conditions and hence complements our alternative selenoacetal methodology in which the key selenoacetal is synthesised under acidic conditions. We can now prepare both acid and base sensitive medium-ring lactones (and precursors) using these complementary methodologies.

The chemistry reported above should enable the synthesis of a range of previously inaccessible medium-ring oxacyclic natural products.

9. Experimental

9.1. General

^{1}H NMR spectra were recorded on Bruker DPX-250 (250 MHz), WM-400 (400 MHz), AM-400 (400 MHz), DRX-500 (500 MHz) and DRX-800 (800 MHz) spectrometers. Chemical shifts are quoted in ppm relative to tetramethylsilane (δ=0 ppm) and referenced to the solvent residual. For convenience, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet; dd, doublet of doublets; etc. Where useful, the FID was zero-filled (128 K) and sine-bell shifted (SSB=30) prior to Fourier Transformation in order to provide baseline resolved multiplets and, as a result, easily identifiable and measurable coupling constants.

All two-dimensional (2D) spectra were recorded on a Bruker DRX-500 spectrometer, fitted with gradient coils. Double Quantum Filtered (DQF) and magnitude COSY spectra were typically acquired with 256 slices in F_1 and 2048 points in F_2 (acquisition time approximately 20 min). NOESY spectra were typically acquired with 640 slices in F_1 and 2048 points in F using a mixing time (τ_m) of 1.6 s (acquisition time typically 8 h).

^{13}C NMR spectra were recorded on Bruker DPX-250 (62.5 MHz), AM-400 (100 MHz), WM-400 (100 MHz) and WM-200 (50 MHz) spectrometers in the solvent indicated and with proton decoupling. Chemical shifts are quoted relative to tetramethylsilane (δ=0 ppm). The attached proton tests (APT) and DEPT-135 experiments were used to assign signals in particular cases.

Infrared spectra were recorded on a Perkin–Elmer 1600 FT IR spectrophotometer. The sample was prepared as a thin liquid film, a KBr disc or as a solution in the solvent indicated. Calibration was relative to polystyrene at 1603 cm^{-1}.

Mass Spectra were carried out at the EPSRC Mass Spectrometry Service Centre, University of Swansea or at the Cambridge University Chemical Laboratory. In Swansea, Electron Impact (EI) and Chemical Ionisation (CI) low-resolution spectra were carried out on a VG model 12-253 under ACE conditions. Accurate mass measurements for EI and CI were performed on a +VG ZAB-E instrument. In Cambridge EI and CI, low resolution and accurate mass, spectra were performed on a KRATOS MS-890. Electrospray spectra were determined with an ES Bruker FTICR. All CI measurements were performed with NH_3 as the carrier gas.

Optical rotations were measured using a Perkin–Elmer 241 polarimeter, in a cell of 1 dm path length. The concentration (c) is expressed in g/100 mL (equivalent to g/0.1 dm^3). Specific rotations denoted as $[\alpha]_D^T$, imply units of dm^2 g^{-1} (T=temperature (°C)).

Microanalyses were carried out by the staff of the Cambridge University Chemical Laboratory Microanalytical Department.

Melting points (mp) were determined using a Kofler block or a Büchi 510 melting point apparatus and are uncorrected.

Analytical TLC was carried out on Merck pre-coated 0.25 mm thick plates of Kieselgel 60 F_{254}. Preparative layer chromatography was carried out on 1 mm thick plates (18 cm×20 cm) of Merck Kieselgel PF_{254}. Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh).

Non-aqueous reactions were carried out under an atmosphere of dry argon unless indicated to the contrary.

Dry THF was distilled from potassium in a recycling still using benzophenone ketyl as indicator. Other dry solvents were purified by standard techniques.[44]

Ether refers to diethyl ether. Light petroleum refers to the fraction boiling between 40 and 60°C. Brine refers to a saturated solution of sodium chloride in water.

9.1.1. (2*R*,3*R*,5*R*)-2,5-Dihydroxy-1,3-bis-[*tert*-butyldiphenylsilyloxy]-hept-6-ene (5*R*)-9a and (2*R*,3*R*,5*S*)-2,5-dihydroxy-1,3-bis[*tert*-butyldiphenylsilyloxy]-hept-6-ene (5*S*)-9b. The lactols **8**[16] were dissolved in benzene, the

resulting solution was heated at reflux for 2 h under Dean–Stark conditions and the solvent was then removed in vacuo. To a stirred solution of the lactols **8** (dried as above, 13.81 g, 22.6 mmol) in THF (100 mL) at 0°C was slowly added a solution of vinylmagnesium bromide (52 mL of a 1.0 M solution in THF, 52 mmol). After addition was complete stirring was continued for 2 h at 0°C whereupon the reaction was quenched by careful addition of a saturated aqueous solution of ammonium chloride (20 mL) followed by water (20 mL). The mixture was extracted with ether (4×100 mL), the combined organic extracts were washed with brine (100 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and purification by flash chromatography (hexane/ether, 2:1) provided the diols **9a** as a 1:1 mixture of a colourless oil and a slowly crystallising white solid (10.81 g, 75%). The diastereomeric diols **9a** could be separated by flash chromatography (hexane/ether, 4:1) for the purposes of characterisation.

Data for (5*R*)-**9a**: R_F 0.23 (hexane/ether, 2:1); $[\alpha]_D^{25}=+5.5$ (*c* 1.87 in $CHCl_3$); ν_{max} ($CHCl_3$) 3415 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.98 [s, 9H, C(CH_3)$_3$], 1.02 [s, 9H, C(CH_3)$_3$], 1.69–1.75 (m, 2H, H-4), 2.85–3.30 (br d, 2H, OH), 3.48 (dd, 1H, H-1, *J*=10, 7 Hz), 3.71 (dd, 1H, H-1, *J*=10, 5 Hz), 3.84–4.02 (m, 2H, H-2, H-3), 4.43 (br q, 1H, H-5, *J*=5.5 Hz), 4.97 (dt, 1H, H-7$_{cis}$, *J*=10, 1.5 Hz), 5.10 (dt, 1H, H-7$_{trans}$, *J*=17, 1.5 Hz), 5.62 (ddd, 1H, H-6, *J*=17, 10, 5.5 Hz), 7.25–7.47 (m, 12H, ArH); MS (CI, NH_3) *m/z*: 639.333 [(M+H)$^+$. $C_{39}H_{51}O_4Si_2$ requires 639.3326], 639 (1%), 274 (100). Found: C, 73.5; H, 7.9; $C_{39}H_{50}O_4Si_2$ requires C, 73.3, H, 7.9%.

Data for (5*S*)-**9a**: R_F 0.27 (hexane/ether, 2:1); $[\alpha]_D^{25}=+7.5$ (*c* 0.65 in $CHCl_3$); δ_H ($CDCl_3$, 250 MHz) 0.97 [s, 9H, C(CH_3)$_3$], 1.03 [s, 9H, C(CH_3)$_3$], 1.58–1.70 (m, 1H, H-4), 1.78 (ddd, 1H, H-4, *J*=15, 5.9, 2.4 Hz), 2.52 (br d, 1H, OH), 2.69 (br s, 1H, OH), 3.43 (dd, 1H, H-1, *J*=10, 8 Hz), 3.75 (dd, 1H, H-1, *J*=10, 4 Hz), 3.82–3.91 (br m, 1H), 3.95 (q, 1H, *J*=4.5 Hz), 4.03–4.14 (br m, 1H, H-5), 4.96 (dt, 1H, H-7$_{cis}$, *J*=10, 1.5 Hz), 5.07 (dt, 1H, H-7$_{trans}$, *J*=17, 1.5 Hz), 5.66 (ddd, 1H, H-6, *J*=17, 10, 5.5 Hz), 7.28–7.48 (m, 12H, ArH); MS (CI, NH_3) *m/z*: 639.334 [(M+H)$^+$. $C_{39}H_{51}O_4Si_2$ requires 639.3326], 639 (1%), 274 (100). Found: C, 73.5; H, 7.9; $C_{39}H_{50}O_4Si_2$ requires C, 73.3, H, 7.9%.

9.1.2. (*Z*)-(2*R*,3*S*,5*S*)-1,3-Bis-(*tert*-butyldiphenylsilyloxy)-oct-6-ene-2,5-diol (5*S*)-9b and (*Z*)-(2*R*,3*S*,5*R*)-1,3-bis-(*tert*-butyldiphenylsilyloxy)-oct-6-ene-2,5-diol (5*R*)-9b. *cis*-Propenylmagnesium bromide[17] (4.4 mL of a 0.75 M solution in THF, 3.25 mmol) was added over 5 min to a stirred solution of the lactols **8** in THF (10 mL) at 0°C. After 2 h 10 min, the reaction mixture was allowed to warm to ambient temperature over 20 min. The reaction was quenched by careful addition of a saturated aqueous solution of ammonium chloride (1 mL) followed by water (5 mL), and the layers were then separated. The aqueous phase was extracted with ether (2×15 mL), the organic extracts were combined, washed with brine (15 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether, 2:1) provided the diol (5*S*)-**9b** (127 mg, 0.194 mmol, 14%, containing a trace amount of the lactols **8**) as a clear and colourless oil. Further elution of the column provided a mixture of the diols (5*S*)-**9b** and (5*R*)-**9b** (308 mg, 0.470 mmol, 33%) as a clear and colourless oil and a slow-crystallising white solid (Found: C, 73.5; H, 8.0; $C_{40}H_{52}O_4Si_2$ requires C, 73.6; H, 8.0%). Further elution of the column provided the diol (5*R*)-**9b** [315 mg, 0.482 mmol, 34%, containing a trace amount of the diol (5*S*)-**9b**]. Further purification by preparative TLC (hexane/ether, 1:1) provided the analytically pure diols.

The diol (5*S*)-**9b** was isolated as a clear and colourless oil; R_F 0.20 (hexane/ether, 1:1); $[\alpha]_D^{20}=-5.6$ (*c* 1.43 in $CHCl_3$); ν_{max} ($CHCl_3$) 3586 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 1.00 [s, 9H, C(CH_3)$_3$], 1.02 [s, 9H, C(CH_3)$_3$], 1.49 (dd, 3H, H-8, *J*=6.9, 1.7 Hz), 1.68–1.72 (m, 2H, H-4), 2.26 (br s, 1H, OH), 2.66 (br s, 1H, OH), 3.42 (dd, 1H, H-1, *J*=10.2, 8.1 Hz), 3.73 (dd, 1H, H-1, *J*=10.2, 5.0 Hz), 3.89 (dt, 1H, H-2, *J*=8.1, 5.0 Hz), 3.96 (q, 1H, H-3, *J*=5.0 Hz), 4.50–4.56 (m, 1H, H-5), 5.26 (ddq, 1H, H-6, *J*=10.9, 8.4, 1.7 Hz), 5.40 (dqd, 1H, H-7, *J*=10.9, 6.9, 1.0 Hz), 7.27–7.46 (m, 12H, ArH), 7.55–7.65 (m, 8H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.1, 19.1, 19.4, 26.8, 27.0, 40.4, 64.3, 65.4, 72.4, 74.6, 125.3, 127.8, 129.8, 133.2, 133.3, 133.5, 135.5, 135.9, 136.0; MS (ES$^+$) *m/z*: 675.3320 [(M+H)$^+$. $C_{40}H_{52}O_4Si_2$ requires 675.3302].

The diol (5*S*)-**9a** was isolated as a clear and colourless oil which slowly solidified to a white micro-crystalline solid; mp 91–100°C; R_F 0.15 (hexane/ether, 1:1); $[\alpha]_D^{20}=+20.5$ (*c* 0.92 in $CHCl_3$); ν_{max} ($CHCl_3$) 3564, 3412 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.98 [s, 9H, C(CH_3)$_3$], 1.02 [s, 9H, C(CH_3)$_3$], 1.59 (dd, 3H, H-8, *J*=6.9, 1.7 Hz), 1.66 (ddd, 1H, H-4, *J*=14.9, 6.1, 2.8 Hz), 1.80 (1H, H-4, ddd, *J*=14.9, 9.0, 3.6 Hz), 3.05 (br s, 2H, OH), 3.46 (dd, 1H, H-1, *J*=10.3, 7.6 Hz), 3.67 (dd, 1H, H-1, *J*=10.3, 5.3 Hz), 3.88 (dt, 1H, H-2, *J*=7.6, 5.3 Hz), 4.03–3.97 (m, 1H, H-3), 4.82 (td, 1H, H-5, *J*=9.0, 2.5 Hz), 5.33 (ddq, 1H, H-6, *J*=10.9, 8.8, 1.7 Hz), 5.45 (dqd, 1H, H-7, *J*=10.9, 6.9, 0.9 Hz), 7.28–7.44 (m, 12H, ArH), 7.52–7.65 (m, 8H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.2 (C-8), 19.3, 19.1, 26.8, 27.0, 40.3, 62.9, 65.1, 71.8, 74.4, 125.5, 127.6, 127.7, 129.8, 133.3, 133.5, 135.5, 135.9; MS (ES$^+$) *m/z*: 675.3345 [(M+H)$^+$. $C_{40}H_{52}O_4Si_2$ requires 675.3302].

9.1.3. (*Z*)-(*R*,*S*)-1-Phenyl-2-trimethylsilylbut-2-en-1-ol 13. To a stirred solution of titanocene dichloride (75 mg, 0.3 mmol) in ether (3 mL) at reflux was added a solution of isobutylmagnesium bromide (1.5 mL of a 2.0 M solution in ether, 3 mmol). The solution was heated at reflux for 30 min, then 1-(trimethylsilyl)-1-propyne (443 μL, 336 mg, 3 mmol) was added. The mixture was stirred at 40°C for 6 h, and then cooled to 0°C. Benzaldehyde (203 μL, 211 mg, 2 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched at 0°C by the addition of a saturated aqueous solution of ammonium chloride (10 mL). The layers were separated, and the aqueous phase was extracted with ether (3×15 mL). The combined organic extracts were washed with brine (15 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography (hexane/EtOAc, 9:1) provided the alcohol **13** (320 mg, 1.45 mmol, 73%) as a colourless oil; R_F 0.4 (hexane/EtOAc, 9:1); ν_{max} ($CDCl_3$) 3604 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.05 [s, 9H, $(CH_3)_3Si$], 1.85 (m, 1H, OH), 1.91 (dd, 3H, CH_3, *J*=0.7, 7.0 Hz), 5.29 (m, 1H,

H-1), 6.40 (qd, 1H, H-3, J=1.2, 7.0 Hz), 7.23–7.34 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 0.3, 17.5, 78.8, 126.9, 127.2, 128.1, 138.2, 142.4, 143.3.

9.1.4. (*Z*)-(2*R*,3*S*,5*S*)-1,3-Bis-(*tert*-butyldiphenylsilyloxy)-6-trimethylsilyl-oct-6-ene-2,5-diol (5*S*)-9c and (*Z*)-(2*R*, 3*S*,5*R*)-1,3-bis-(*tert*-butyldiphenylsilyloxy)-6-trimethylsilyl-oct-6-ene-2,5-diol (5*R*)-9c. To a stirred solution of titanocene dichloride (75 mg, 0.3 mmol) in ether (3 mL) at reflux was added a solution of isobutylmagnesium bromide (1.5 mL of a 2.0 M solution in ether, 3.0 mmol). The solution was heated at reflux for 30 min then 1-(trimethylsilyl)-1-propyne (443 μL, 336 mg, 3 mmol) was added. The mixture was stirred at 40°C for 6 h, and then cooled to 0°C. A solution of the lactols **8** (650 mg, 1.07 mmol) in ether (2 mL) was added. The reaction was stirred for 16 h at 0°C, then quenched by the addition of a saturated aqueous solution of ammonium chloride (10 mL). The layers were separated, and the aqueous phase was extracted with ether (2×15 mL). The combined organic extracts were washed with brine (15 mL) and dried ($MgSO_4$), and then they were concentrated. ^{1}H NMR analysis of the crude product showed a 13:5 mixture of isomers (5*S*)-**9c** and (5*R*)-**9c**. Purification by flash chromatography (hexane/ether, 9:1) yielded the diastereomer (5*S*)-**9c** (237 mg, 33%) as a colourless oil; R_F 0.25 (hexane/ether, 9:1); $[\alpha]_D^{28}=-1.2$ (c 2.34 in $CHCl_3$); ν_{max} ($CDCl_3$) 3584 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.09 [s, 9H, $(CH_3)_3Si$], 0.99 [s, 9H, $(CH_3)_3C$], 1.01 [s, 9H, $(CH_3)_3C$], 1.57–1.65 (m, 1H, H-4), 1.73 (d, 3H, H-8, J= 7.0 Hz), 1.76–1.81 (m, 1H, H-4), 2.37 (br s, 1H, OH), 2.68 (br s, 1H, OH), 3.37 (dd, 1H, H-1, J=10.1, 8.1 Hz), 3.70 (dd, 1H, H-1, J=10.1, 4.5 Hz), 3.85–3.98 (m, 2H, H-2, H-3), 4.24 (br d, 1H, H-5, J=10.0 Hz), 6.18 (qd, 1H, H-7, J= 7.0, 0.8 Hz), 7.26–7.44 (m, 8H, ArH), 7.54–7.63 (m, 8H, ArH); δ_C ($CDCl_3$, 100 MHz) 0.6, 17.4, 19.1, 19.4, 26.8, 27.0, 41.2, 65.4, 72.9, 73.0, 74.6, 127.6, 127.7, 127.7, 129.7, 129.8, 133.1, 133.1, 133.3, 133.4, 134.8, 135.5, 135.8, 135.9, 136.0, 143.5; MS (CI, NH_3) m/z: 725.410 $[(M-OH+NH_4)^+$. $C_{43}H_{63}NO_3Si_3$ requires 725.4116], 725 (5%), 373 (100).

Further elution of the column provided the diastereomer (5*R*)-**9c** (142 mg, 20%) as a colourless oil; R_F 0.15 (hexane/ether, 9:1); ν_{max} ($CDCl_3$) 3550 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.13 [s, 9H, $(CH_3)_3Si$], 0.98 [s, 9H, $(CH_3)_3C$], 1.02 [s, 9H, $(CH_3)_3C$], 1.60–1.66 (m, 1H, H-4), 1.72 (d, 3H, H-8, J=7.0 Hz), 1.80–1.87 (m, 1H, H-4), 2.82 (br s, 1H, OH), 2.95 (br s, 1H, OH), 3.44–3.49 (m, 1H, H-1), 3.64 (dd, 1H, H-1, J=10.3, 5.4 Hz), 3.82–4.06 (m, 2H, H-2, H-3), 4.46 (br d, 1H, H-5, J=8.3 Hz), 6.11 (q, 1H, H-7, J=7.0 Hz), 7.26–7.43 (m, 8H, ArH), 7.53–7.66 (m, 8H, ArH); δ_C ($CDCl_3$, 100 MHz) 0.9, 17.4, 19.1, 19.4, 26.8, 27.1, 39.9, 65.1, 72.5, 74.2, 74.3, 127.6, 127.7, 127.7, 129.7, 129.7, 129.7, 129.8, 133.1, 133.2, 133.6, 135.5, 135.9, 136.0, 137.0, 143.5.

9.1.5. 2(*R*),3(*R*),5(*S*)-2-*tert*-Butyldiphenylsilyloxymethyl-3-hydroxy-5-methoxy-tetrahydrofuran 15α and 2(*R*),3(*R*), 5(*R*)-2-*tert*-butyldiphenylsilyloxymethyl-3-hydroxy-5-methoxy-tetrahydrofuran 15β. To a stirring solution of 2-deoxy-D-ribose **14** (3.0 g, 22.4 mmol) in methanol (115 mL) was added a solution of hydrogen chloride (8.08 mL of a 1 M solution in ether, 8.08 mmol) and the resulting solution was stirred for 0.5 h whereupon pyridine (57 mL) was added. The solvent was removed in vacuo (high vacuum rotary evaporator) and the residue was co-evaporated with pyridine (50 mL). The residue was dried under high vacuum for 0.5 h and then pyridine (23 mL) and *tert*-butylchlorodiphenylsilane (5.86 mL, 6.19 g, 22.5 mmol) were added. The resulting solution was stirred for 18 h and then the solvent was removed in vacuo. To the residue was added water (100 mL) and ethyl acetate (100 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2×100 mL). The organic extracts were washed with saturated aqueous copper(II) sulfate (2×50 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether, 7:3) provided the title compounds as clear and colourless oils.

15α-less polar anomer (3.65 g, 9.46 mmol, 42%); R_F 0.2 (hexane/ether, 1:1);$[\alpha]_D^{19}=+67.3$ (c 1.48 in methanol); δ_H ($CDCl_3$, 250 MHz) 1.05 [s, 9H, $(CH_3)_3CSi$], 2.01 (bd, H-4, 1H, J=13.5 Hz), 2.26–2.31 (m, 1H, H-4), 2.81 (bd, 1H, OH, J=10.7 Hz), 3.38 (s, 3H, CH_3O), 3.61 (dd, 1H, C*H*HOSi, J=10.9, 4.9 Hz), 3.76 (dd, 1H, CH*H*OSi, J= 10.9, 3.6 Hz), 4.16 (m, 1H, H-3), 4.30 (bdd, 1H, H-3, J=10.1, 5.6 Hz), 5.11 (bd, 1H, H-5, J=4.5 Hz), 7.34–7.47 (m, 6H, ArH), 7.62–7.71 (m, 4H, ArH); δ_C ($CDCl_3$, 100 MHz) 19.2, 26.8, 41.1, 54.8, 64.4, 73.3, 87.7, 105.6, 127.7, 127.7, 129.7, 129.8, 133.1, 133.2, 135.6, 135.6; MS (CI, NH_3) m/z: 404.2249 $[(M+NH_4)^+$. $C_{22}H_{34}NO_4Si$ requires 404.2257], 404 (15%), 98 (100). Found: C, 68.4; H, 7.9; $C_{22}H_{30}O_4Si$; requires C, 68.36; H, 7.82%

15β-less polar anomer (3.07 g, 7.94 mmol, 36%); R_F 0.1 (hexane/ether, 1:1); $[\alpha]_D^{19}=-29.3$ (c 1.88 in methanol); δ_H ($CDCl_3$, 250 MHz) 1.08 [s, 9H, $(CH_3)_3CSi$], 1.80 (bd, 1H, OH, J=4.1 Hz), 2.00–2.12 (m, 1H, H-4), 2.21 (ddd, 1H, H-4, J=13.3, 6.9, 1.9 Hz), 3.27 (s, 3H, CH_3O), 3.66 (dd, 1H, C*H*HOSi, J=10.1, 7.5 Hz), 3.82 (dd, 1H, CH*H*OSi, J=10.1, 4.8 Hz), 3.94 (dt, 1H, H-3, J=7.5, 4.8 Hz), 4.57–4.47 (m, 1H, H-2), 5.05 (dd, 1H, H-5, J=5.1, 1.9 Hz), 7.34–7.46 (m, 6H, ArH), 7.65–7.72 (m, 4H, ArH); δ_C ($CDCl_3$, 100 MHz) 19.2, 26.8, 41.0, 55.0, 65.4, 73.3, 85.7, 105.0, 127.8, 129.8, 133.2, 135.5; MS (CI, NH_3) m/z: 404.2264 $[(M+NH_4)^+$. $C_{22}H_{34}NO_4Si$ requires 404.2257], 404 (25%), 372 (100). Found: C, 68.4; H, 7.9; $C_{22}H_{30}O_4Si$; requires C, 68.36; H, 7.82%.

9.1.6. 2(*R*),3(*R*),5(*S*)-2-*tert*-Butyldiphenylsilyloxymethyl-3-chloro-5-methoxy-tetrahydofuran 16α and 2(*R*),5(*S*)-2-*tert*-butyldimethylsilyloxymethyl-5-methoxy-2,5-dihydro-furan 17α. A Schlenk tube was charged with (dichloromethylene)dimethyl-ammonium chloride (1.22 g, 7.5 mmol) and was vacuum purged with argon (3 times). Dichloromethane (40 mL) and pyridine (0.9 mL, 880 mg, 11.1 mmol) were added. The reaction mixture was cooled to 0°C and the furanoside **15**α (861 mg, 2.23 mmol) was added via cannula as a solution in dichloromethane (6 mL, 2×2 mL rinse). The reaction mixture was allowed to come to ambient temperature, stirred for 1 h and then quenched by the addition of saturated aqueous $NaHCO_3$ (50 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (3×30 mL). The organic layers were washed with saturated aqueous copper(II) sulfate (50 mL) and dried ($MgSO_4$). Purification by flash

chromatography (hexane/ether/triethylamine, 200:10:1) provided the chlorofuranoside **16**α as a clear and colourless oil (555 mg, 1.37 mmol, 62%); R_F 0.4 (hexane/ether, 3:1); $[\alpha]_D^{18}=-40.5$ (*c* 0.385 in $CHCl_3$); δ_H ($CDCl_3$, 250 MHz) 1.08 [s, 9H, $(CH_3)_3CSi$], 2.38 (ddd, 1H, H-4, *J*=14.7, 6.0, 4.2 Hz), 2.57 (ddd, 1H, H-4, *J*=14.7, 5.3, 2.0 Hz), 3.40 (s, 3H, CH_3O), 3.93 (dd, 1H, C*H*HOSi, *J*=13.2, 10.3 Hz), 3.98 (dd, 1H, C*H*HOSi, *J*=13.2, 8.3 Hz), 4.23–4.24 (m, 1H, H-3), 4.54–4.62 (m, 1H, H-2), 5.23 (dd, 1H, H-5, *J*=5.3, 4.2 Hz), 7.35–7.50 (4H, m, ArH), 7.65–7.77 (6H, m, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.3, 26.8, 27.0, 44.2, 55.6, 59.7, 63.2, 80.4, 104.3, 127.7, 129.7, 133.4, 133.5, 135.6, 135.6, 135.9, 136.0; MS (CI, NH_3) *m/z*: 422.1919 [$(M+NH_4)^+$. $C_{22}H_{33}ClNO_3Si$ requires 422.1918], 422 [$(M+NH_4)^+$, 100%], 405 [$(M+H)^+$, 1]. Found: C, 65.41; H, 7.27; $C_{22}H_{29}ClO_3Si$ requires C, 65.24; H, 7.22%.

Further elution of the column provided dihydrofuran **17**α as a clear and colourless oil (300 mg, 0.81 mmol, 36%); R_F 0.3 (hexane/ether, 3:1); $[\alpha]_D^{14}=-70.9$ (*c* 1.075 in $CHCl_3$); δ_H ($CDCl_3$, 250 MHz) 1.06 [s, 9H, $(CH_3)_3CSi$], 3.39 (s, 3H, CH_3O) 3.68 (dd, 1H, C*H*HOSi, *J*=10.3, 5.6 Hz), 3.81 (dd, 1H, CH*H*OSi, *J*=10.3, 4.5 Hz), 5.00–4.99 (m, 1H), 5.80 (d, 1H, *J*=4.3 Hz), 5.85 (bd, 1H, *J*=6 Hz), 6.25 (d, 1H, *J*=6 Hz), 7.35–7.47 (m, 6H, ArH), 7.66–7.69 (m, 4H, ArH), δ_C ($CDCl_3$, 62.5 MHz) 19.3, 26.8, 53.8, 66.1, 86.0, 109.4, 127.1, 127.7, 129.7, 133.9, 135.6; MS (CI, NH_3) *m/z*: 386 [$(M+NH_4)^+$, 100%], 369 [$(M+H)^+$, 20]. Found: C, 71.73; H, 7.64; $C_{22}H_{28}O_3Si$ requires C, 71.70; H, 7.66%.

9.1.7. 2(*R*),3(*R*),5(*R*)-2-*tert*-Butyldiphenylsilyloxymethyl-3-chloro-2-methoxy-tetrahydofuran 16β and 2(*R*),5(*R*)-2-*tert*-butyldimethylsilyloxymethyl-5-methoxy-2,5-dihydro-furan 17β. A Schlenk tube was charged with (dichloroemethylene)dimethyl-ammonium chloride (784 g, 4.8 mmol) and was vacuum purged with argon (3 times). Dichloromethane (25 mL) and pyridine (0.57 mL, 562 mg, 11.1 mmol) were added. The reaction mixture was cooled to 0°C and the furanoside **15**β (548 mg, 1.42 mmol) was added via cannula as a solution in dichloromethane (4 mL, 2×1 mL rinse). The reaction mixture was allowed to come to ambient temperature, stirred for 1 h and then quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (3×30 mL). The organic layers were washed with saturated aqueous copper(II) sulfate (50 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether/triethylamine, 200:10:1) provided the dihydrofuran **17**β as a clear and colourless oil (93 mg, 0.25 mmol, 18%); R_F 0.4 (hexane/ether, 3:1); $[\alpha]_D^{15}=-88.2$ (*c* 0.27 in $CHCl_3$); δ_H ($CDCl_3$, 250 MHz) 1.07 [s, 9H, $(CH_3)_3CSi$], 3.36 (s, 3H, CH_3O) 3.66 (dd, 1H, C*H*HOSi, *J*=10.1, 6.2 Hz), 3.80 (dd, 1H, CH*H*OSi, *J*=10.1, 5.8 Hz), 4.86–4.78 (m, 1H, H-2), 5.73 (q, 1H, H-5, *J*=1.2 Hz), 5.84 (ddd, 1H, *J*=6.0, 2.1, 1.1 Hz), 6.26 (dt, 1H, *J*=6.0, 1.3 Hz), 7.33–7.46 (m, 6H, ArH), 7.64–7.73 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 26.8, 54.5, 67.3, 86.0, 109.4, 127.2, 127.7, 129.7, 133.6, 135.6, 135.6; MS (CI, NH_3) *m/z*: 386.2152 [$(M+NH_4)^+$. $C_{22}H_{33}ClNO_3Si$ requires 386.2151], 386 (100%), 369 [$(M+H)^+$, 17]. Found: C, 71.76; H, 7.67; $C_{22}H_{28}O_3Si$ requires C, 71.70; H, 7.66.

Further elution of the column provided chlorofuranoside **16**β as a clear and colourless oil (275 mg, 0.68 mmol, 48%); R_F 0.3 (hexane/ether, 3:1); $[\alpha]_D^{18}=-58.3$ (*c* 0.695 in $CHCl_3$); δ_H ($CDCl_3$, 250 MHz) 1.08 [s, 9H, $(CH_3)_3CSi$], 2.36 (dt, 1H, H-4, *J*=14.7, 1.8 Hz), 2.59 (dt, 1H, H-4, *J*=14.7, 6.3 Hz), 3.40 (s, 3H, CH_3O), 3.95 (dd, 1H, C*H*HOSi, *J*=10.4, 6.1 Hz), 4.03 (dd, 1H, *C*H*H*OSi, *J*=10.4, 6.2 Hz), 4.24 (dt, 1H, H-2, *J*=6.1, 4.6 Hz), 4.51 (ddd, 1H, H-2, *J*=6.6, 4.6, 2.0 Hz), 5.08 (dd, 1H, H-3, *J*=6.0, 2.6 Hz), 7.33–7.46 (4H, m, ArH), 7.74–7.69 (6H, m, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.3, 26.8, 42.8, 55.7, 57.2, 64.2, 82.6, 104.8, 127.7, 129.7, 129.7, 133.4, 133.6, 135.6, 135.6; MS (CI, NH_3) *m/z*: 422.1919 [$(M+NH_4)^+$. $C_{22}H_{33}ClNO_3Si$ requires 422.1918], 422 (100%), 405 [$(M+H)^+$, 1].

If purification of the dihydrofurans **17** was carried out by silica gel chromatography in the absence of triethylamine then the furan **18** was isolated instead of the respective dihydrofurans.

9.1.8. *tert*-Butyl-(furan-2-ylmethoxy)-diphenyl-silane 18.[26] δ_H ($CDCl_3$, 250 MHz) 1.07 [s, 9H, $(CH_3)_3Si$], 4.66 (s, 2H, CH_2O), 6.15 (1H, d, *J*=3.2 Hz), 6.30–6.32 (m, 1H), 7.35–7.50 (m, 7H, ArH, furan), 7.67–7.75 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.3, 26.8, 58.9, 107.3, 110.1, 127.7, 129.7, 133.4, 135.6, 142.0, 154.1.

9.1.9. 5(*R*,*S*),3(*R*),2(*R*)-2-*tert*-Butyldiphenylsilyloxymethyl-4-chloro-2-hydroxy-tetrahydrofuran 19. The furanosides were isolated as a mixture of diastereomers **19** in equilibrium with the open-chain form **19a**.

To a stirring solution of the chlorofuranoside **16**α (555 mg, 1.37 mmol) in ether (20 mL) was added boron trichloride–methyl sulfide complex (1.37 mL of a 2.0 M solution in dichloromethane, 2.74 mmol). The resulting solution was stirred for 10 min and then quenched by the addition of saturated aqueous sodium carbonate solution (20 mL) followed rapidly by the addition of THF (10 mL). The resulting biphasic mixture was stirred vigorously for 1 h. The phases were separated and the aqueous phase was extracted with ether (2×30 mL). The organic phases were washed with brine (50 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether, 2:1→1:1) provided the title compounds as a clear and colourless oil (365 mg, 0.94 mmol, 68%); ν_{max} ($CDCl_3$) 3506 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.09 [s, 9H, $(CH_3)_3C$, major furanoside], 1.11 [s, 9H, $(CH_3)_3C$, minor furanoside], 2.54–2.59 (m, 1H, major furanoside), 2.33–2.43 (m), 2.60–2.66 (m, 1H, minor furanoside), 3.02 (dd, *J*=6.7, 1.3 Hz), 3.47–3.56 (m), 3.90 (dd, 1H, C*H*HOSi, major furanoside, *J*=10.5, 6.2 Hz), 3.96 (dd, 1H, CH*H*OSi, major furanoside, *J*=10.5, 5.5 Hz), 4.02 (d, 2H, CH_2OSi, minor furanoside, *J*=5.6 Hz), 4.14–4.20 (m, 1H, minor furanoside), 4.57 (ddd, 1H, minor furanoside, *J*=6.0, 4.2, 2.3 Hz), 4.60–4.65 (m, 1H, major furanoside), 4.69 (m, 1H, open chain), 5.49 (dd, H-2, minor furanoside, 1H, *J*=9.6, 5.5 Hz), 5.77 (brm, 1H, H-2, major furanoside), 7.51–7.37 (m, 6H, ArH, all compounds), 7.66–7.77 (m, 4H, ArH, all compounds), 9.79 (bs, 1H, CHO); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 26.9, 26.9, 44.0, 44.8, 58.2, 59.8, 63.8, 80.7, 82.5, 97.9, 98.8, 127.7, 127.8, 127.9, 129.8, 129.9, 133.3, 133.4, 135.6, 135.7; MS (CI, NH_3) *m/z*: 408.1761 [$(M+NH_4)^+$. $C_{21}H_{31}ClNO_3Si$ requires 408.1762], 408 (30%), 390 [$(M+NH_4-H_2O)^+$, 15], 274 (100).

The lactols **19** were prepared in a similar manner in 44% yield starting from the β-glycoside **16**β

9.1.10. 3(*R*),5(*R*),6(*R*)-7-*tert*-Butyldiphenylsilyloxy-5-chloro-3,6-dihydroxy-hept-1-ene (3*R*)-21 and 3(*S*),5(*R*),6(*R*)-7-*tert*-butyldiphenylsilyloxy-5-chloro-3,6-dihydroxy-hept-1-ene(3*S*)-21. To a stirring solution of the lactols **19** (365 mg, 0.94 mmol), previously dried by azeotropic distillation with toluene (2×5 mL), in THF (15 mL) at 0°C was added vinylmagnesium bromide (2.15 mL, of a 1.0 M solution in THF, 2.15 mmol) and the resulting solution was stirred for 1.5 h before being quenched by the addition of saturated aqueous ammonium chloride (25 mL) and ether (25 mL). The aqueous phase was separated and extracted with ether (2×25 mL). The organic phases were washed with brine (25 mL) and dried ($MgSO_4$). Purification by flash chromatography (ether/hexane, 2:1) provided the title compounds **21** as white crystalline solids.

Less polar diastereomer **21**-LP: (122 mg, 0.29 mmol, 31%); mp 60–62°C (hexane/ether); R_F 0.3 (hexane/ether, 1:1); $[\alpha]_D^{18}=+3.6$ (*c* 1.35 in $CHCl_3$); ν_{max} ($CDCl_3$) 3606, 3564 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.10 [s, 9H, $(CH_3)_3CSi$], 1.82–2.00 (m, 2H), 2.09 (ddd, 1H, *J*=14.6, 10.4, 2.8 Hz), 2.48 (bd, 1H, OH), 3.74–3.95 (m, 3H), 4.53 (bdt, 1H, *J*=10.0, 3.0 Hz), 5.14 (d, 1H, H-1$_{cis}$, *J*=10.4 Hz), 5.30 (d, 1H, H-1$_{trans}$, *J*=17.2 Hz), 5.92 (ddd, 1H, H-2, *J*=17.2, 10.4, 5.7 Hz), 7.35–7.50 (m, 6H, ArH), 7.63–7.76 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 26.9, 42.0, 60.9, 65.0, 69.7, 74.2, 114.8, 127.8, 133.0, 133.1, 135.6, 135.6, 140.6; MS (CI, NH_3) *m/z*: 436.2073 $[(M+NH_4)^+$. $C_{23}H_{35}ClNO_3Si$ requires 436.2075], 436 (100%), 420 $[(M+H)^+$, 3]; Found: C, 65.9; H, 7.5; $C_{23}H_{31}ClO_3Si$ requires C, 65.93; H, 7.46%.

More polar diastereomer **21**-MP: (183 mg, 0.44 mmol); mp 74–75°C (hexane); R_F 0.2 (hexane/ether); $[\alpha]_D^{18}=-2.13$ (*c* 0.89 in $CHCl_3$); ν_{max} ($CDCl_3$) 3603 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.09 [s, 9H, $(CH_3)_3CSi$], 2.22–2.03 (m, 2H), 2.67 (br, 1H, OH), 2.97 (d, 1H, OH, *J*=6.4 Hz), 3.74 (dd, 1H, C*H*HOSi, *J*=10.0, 7.0 Hz), 3.79 (dd, 1H, CH*H*OSi, *J*=10.0, 5.6 Hz), 3.85–3.96 (m, 1H), 4.36–4.51 (m, 2H), 5.19 (d, H-1$_{cis}$, *J*=10.3 Hz), 5.33 (d, 1H, H-1$_{trans}$, *J*=17.2 Hz), 5.87 (ddd, 1H, H-2, *J*=17.2, 10.3, 6.5 Hz), 7.37–7.50 (m, 6H, ArH), 7.64–7.78 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.3, 26.9, 42.1, 60.7, 64.7, 70.3, 73.4, 116.1, 127.8, 127.9, 133.0, 133.1, 135.5, 135.6, 139.7; MS (CI, NH_3) *m/z*: 436.2071 $[(M+NH_4)^+$. $C_{23}H_{35}ClNO_3Si$ requires 436.2075], 436 (100%), 420 $[(M+H)^+$, 20]; Found: C, 65.9; H, 7.5; $C_{23}H_{31}ClO_3Si$ requires C, 65.93; H, 7.46%.

9.1.11. (4*R*,5*S*,7*R*)-5-*tert*-Butyldiphenylsilyloxy-4-*tert*-butyldiphenylsilyloxymethyl-7-vinyl-[1,3]-dioxepan-2-one 22. A solution of triphosgene (11.7 mg, 0.039 mmol) in dichloromethane (1 mL) was added via cannula over 5 min to a stirred solution of the diol (5*R*)-**9a**[16] (50.0 mg, 0.078 mmol) and anhydrous pyridine (38 μL, 37 mg, 0.47 mmol) in dichloromethane (4 mL) at −78°C. After 1 h 45 min at −78°C the reaction was quenched by addition of a saturated solution of aqueous ammonium chloride (5 mL) and water (2 mL), followed by the addition of further dichloromethane (2 mL). The mixture was allowed to warm to 15°C and the organic phase was separated. The aqueous phase was extracted with dichloromethane (3×5 mL), then the organic extracts were combined. The organic extracts were washed with 1 M hydrochloric acid (5 mL), a saturated aqueous solution of sodium bicarbonate (10 mL), brine (10 mL), were dried (Na_2SO_4) and concentrated. Purification by flash chromatography (hexane/ether, 3:1) provided the carbonate **22** (34.0 mg, 0.051 mmol, 65%) as a clear and colourless oil; R_F 0.37 (hexane/ether, 2:1); $[\alpha]_D^{21}=-0.26$ (*c* 1.55 in $CHCl_3$); ν_{max} ($CHCl_3$) 1748 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.97 [s, 9H, $C(CH_3)_3$], 1.05 [s, 9H, $C(CH_3)_3$], 1.74–1.83 (m, 1H, H-6), 1.89 (ddd, 1H, H-6, *J*=15.5, 10.6, 3.0 Hz), 3.74 (dd, 1H, C*H*HOSi, *J*=11.0, 5.5 Hz), 3.80 (dd, 1H, CH*H*OSi, *J*=11.0, 5.5 Hz), 4.16–4.18 (m, 1H, H-5), 4.42 (q, 1H, H-4, *J*=5 Hz), 5.18 (dd, 1H, CH=CHH_{cis}, *J*=10.6, 0.9 Hz,), 5.26 (dd, 1H, H-7, *J*=10.6, 6.0 Hz), 5.32 (d, 1H, CH=CHH_{trans}, *J*=17.0 Hz), 5.73 (ddd, 1H, C*H*=CH_2, *J*=17.0, 10.6, 5.9 Hz), 7.30–7.45 (m, 12H, ArH), 7.55–7.63 (m, 8H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.1, 19.2, 26.7, 26.9, 37.7, 62.3, 67.2, 76.5, 83.1, 116.9, 127.8, 127.9, 127.9, 129.8, 129.8, 130.1, 132.7, 132.7, 133.0, 135.5, 135.7, 135.7, 152.1; MS (FIB) *m/z*: (FIB) 665.31250 $[(M+H)^+$. $C_{40}H_{49}O_5Si_2$ requires 665.31183].

Further elution of the column provided the starting diol (5*R*)-**9a** as a clear and colourless oil (7.7 mg, 0.012 mmol, 15%).

9.1.12. (4*R*,5*S*,7*S*)-5-*tert*-Butyldiphenylsilyloxy-4-*tert*-butyldiphenylsilyloxymethyl-7-vinyl[1,3]dioxepan-2-one 23 and (2*R*,3*S*,5*R*)-3-*tert*-butyldiphenylsilyl-2-*tert*-butyldiphenylsilyloxymethyl-5-vinyl-tetrahydrofuran 24. A solution of triphosgene (30.4 mg, 0.102 mmol) in dichloromethane (1 mL) was added via cannula over 5 min to a stirred solution of the diol (5*S*)-**9a**[16] (130.8 mg, 0.205 mmol) and anhydrous pyridine (100 μL, 98 mg, 1.23 mmol) in dichloromethane (9 mL) at −78°C. After 15 min at −78°C the reaction was quenched by addition of a saturated aqueous solution of ammonium chloride (5 mL) followed by water (2 mL). The mixture was allowed to warm to 5°C and the organic phase was separated. The aqueous phase was extracted with dichloromethane (3×15 mL), then the organic extracts were combined, washed with brine (30 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography (hexane/ether, 10:1→2:1) provided the tetrahydrofuran **24** as a clear and colourless oil; R_F 0.59 (hexane/ether, 2:1); $[\alpha]_D^{19}=+40.3$ (*c* 0.30 in $CHCl_3$); ν_{max} ($CHCl_3$) 3072, 3011, 2932, 2859, 1589 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.93 [s, 9H, $C(CH_3)_3$], 1.08 [s, 9H, $C(CH_3)_3$], 1.64 (ddd, 1H, H-4, *J*=12.7, 10.8 Hz, *J*=5.2 Hz), 1.94 (dd, 1H, H-4, *J*=12.7, 5.5 Hz), 3.29 (dd, 1H, C*H*HOSi, *J*=10.9, 3.7 Hz), 3.39 (dd, 1H, CH*H*OSi, *J*=10.9, 4.3 Hz), 3.99–4.06 (m, 1H, H-3), 4.48 (d, 1H, H-2, *J*=4.9 Hz), 4.62–4.75 (m, 1H, H-5), 5.10 (br d, 1H, CH=CHH_{cis}, *J*=10.3 Hz), 5.30 (br d, 1H, CH=CHH_{trans}, *J*=17.2 Hz), 5.82 (ddd, 1H, C*H*=CH_2, *J*=17.2, 10.3, 6.8 Hz), 7.24–7.44 (m, 12H, ArH), 7.48–7.68 (m, 8H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.1, 26.7, 27.0, 42.1, 64.4, 75.7, 79.9, 88.0, 116.0, 127.6, 127.7, 129.5, 129.7, 133.3, 133.3, 133.8, 134.0, 134.8, 135.6, 135.6, 135.8, 138.6; MS (CI, NH_3) *m/z* 638.349 $[(M+NH_4)^+$. $C_{39}H_{52}NO_3Si_2$ requires 638.3485], 638 (15%), 109 (100).

Further elution of the column provided the carbonate **23** (93.4 mg, 0.140 mmol, 69%) as a clear and colourless oil; R_F 0.40 (hexane/ether, 2:1); $[\alpha]_D^{18}$=+12.2 (*c* 1.88 in $CHCl_3$); ν_{max} ($CHCl_3$) 1762 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.99 [9H, s, $C(CH_3)_3$], 1.08 [9H, s, $C(CH_3)_3$], 1.76–1.84 (m, 1H, H-6), 1.89 (ddd, 1H, H-6, *J*=14.7, 4.9, 2.1 Hz), 3.85 (dd, 1H, C*H*HOSi, *J*=11.3, 5.9 Hz), 4.04 (td, 1H, H-5, *J*=8.7, 4.9 Hz), 4.12 (dd, 1H, CH*H*OSi, *J*=11.3, 2.9 Hz), 4.24 (ddd, 1H, H-4, *J*=8.7, 5.9, 2.9 Hz), 4.51–4.55 (m, 1H, H-7), 5.10–5.16 (m, 2H, CH=CH_2), 5.71 (ddd, 1H, C*H*=CH_2, *J*=17.2, 10.6, 5.6 Hz), 7.30–7.46 (m, 12H, ArH), 7.60–7.63 (m, 4H, ArH), 7.72–7.68 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 19.3, 26.9, 40.9, 63.3, 69.0, 77.2, 85.2, 116.9, 127.7, 127.9, 129.7, 129.8, 130.0, 130.1, 132.5, 133.2, 133.4, 135.1, 135.8, 153.0; MS (CI, NH_3) *m/z* 682.338 $[(M+NH_4)^+$. $C_{40}H_{52}NO_5Si_2$ requires 682.3382], 682 (2%), 638 (13), 467 (26), 411 (23), 349 (78), 323 (40), 316 (69), 309 (100), 295 (51), 289 (57) and 287 (100). Found: C, 72.3; H, 7.4; $C_{40}H_{48}O_5Si_2$ requires: C, 72.3; H, 7.3%.

9.2. Representative procedure for the formation of the carbonates 26, 28 and 30

9.2.1. (4*R*,5*S*,7*R*)-5-*tert*-Butyldiphenylsilyloxy-4-*tert*-butyldiphenylsilyloxymethyl-7-[(*Z*)-prop-1-enyl][1,3]-dioxepan-2-one 26 and (2*R*,3*S*,5*S*)-3-*tert*-butyldiphenylsilyl-2-*tert*-butyldiphenylsilyloxymethyl-5-[(*Z*)-prop-1-enyl]-tetrahydrofuran 27. A solution of triphosgene (7.3 mg, 0.025 mmol) in dichloromethane (0.6 mL) was added over 10 min to a stirred solution of the diol (5*R*)-**9b** (32.1 mg, 0.049 mmol), pyridine (24 μL, 0.29 mmol), triethylamine (40 μL, 30 mg, 0.29 mmol) and powdered 4 Å molecular sieves (spatula tip) in dichloromethane (0.6 mL) at −78°C. The reaction mixture became pink/peach coloured, and after 5 min was allowed to warm to ambient temperature. After 10 min of warming, the reaction was quenched by the addition of a saturated aqueous solution of ammonium chloride (1 mL) and water (1 mL). The layers were separated, and the aqueous phase was extracted with dichloromethane (2×2 mL). The organic phases were combined, washed with brine (5 mL), then they were dried (Na_2SO_4) and concentrated. Purification by flash chromatography (hexane/ether/triethylamine, 80:20:5) provided the tetrahydrofuran **27** and the carbonate **26** (30.3 mg, 48 μmol, 98%) as a 1:8 mixture.

The THF **27** was isolated from a number of experiments as a clear and colourless oil; R_F 0.61 (hexane/ether, 2:1); δ_H ($CDCl_3$, 500 MHz) 0.98 [9H, s, $C(CH_3)_3$], 1.10 [9H, s, $C(CH_3)_3$], 1.64 (dd, 3H, *J*=7.9, 1.7 Hz, CH=CHCH_3), 1.73–1.84 (m, 2H, H-4), 3.44 (dd, C*H*HOSi, 1H, *J*=11.0, 3.5 Hz), 3.60 (dd, 1H, CH*H*OSi, *J*=11.0, 3.5 Hz), 4.12 (q, 1H, H-2, *J*=3.5 Hz), 4.59–4.64 (m, 1H, H-3), 4.90 (q, 1H, H-5, *J*=7.5 Hz), 5.56–5.64 (m, 1H, C*H*=CH), 5.72–5.77 (m, 1H, CH=C*H*), 7.30–7.45 (m, 12H, ArH), 7.56–7.58 (m, 2H, ArH), 7.63–7.70 (m, 6H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.1, 19.2, 26.8, 27.0, 42.1, 64.7, 74.3, 75.1, 86.5, 126.0, 127.6, 127.7, 127.7, 129.5, 129.7, 132.5, 133.4, 133.8, 133.9, 135.6, 135.8, 135.9; MS (FIB) *m/z*: 633.31980 $[(M-H)^+$. $C_{40}H_{49}O_3Si_2$ requires 633.32202].

The carbonate **26** was isolated as a clear and colourless oil; R_F 0.39 (hexane/ether, 2:1); $[\alpha]_D^{25}$=+4.6 (*c* 0.68 in $CHCl_3$); ν_{max} ($CDCl_3$) 1743 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.93 [9H, s, $C(CH_3)_3$], 1.03 [9H, s, $C(CH_3)_3$], 1.70 (dd, 3H, CH=CHCH_3, *J*=3.6, 0.9 Hz,), 1.70–1.75 (m, 1H, H-6), 1.95 (ddd, 1H, H-6, *J*=7.9, 5.4, 1.5 Hz), 3.68 (dd, 1H, C*H*HOSi, *J*=5.6, 2.7 Hz), 3.75 (dd, 1H, CH*H*OSi, *J*=5.6, 2.7 Hz), 4.12–4.15 (m, 1H, H-5), 4.39 (q, 1H, *J*=2.7 Hz, H-4), 5.39–5.45 (m, 1H, H-7), 5.59–5.66 (m, 2H, C*H*=C*H*), 7.31–7.37 (m, 8H, ArH), 7.39–7.46 (m, 4H, ArH), 7.52–7.65 (m, 8H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.3, 19.1, 19.2, 26.7, 26.9, 38.3, 62.3, 67.5, 72.1, 83.2, 127.7, 127.8, 127.9, 127.9, 128.0, 128.5, 129.8, 129.8, 130.1, 132.6, 132.9, 135.5, 135.6, 135.7, 135.7, 152.6; MS (CI, NH_3) *m/z*: 696.3540 $[(M+NH_4)^+$. $C_{41}H_{54}NO_5Si_2$ requires 696.3540].

9.2.2. (4*R*,5*S*,7*S*)-5-*tert*-Butyldiphenylsilyloxy-4-*tert*-butyldiphenylsilyloxymethyl-7-[(*Z*)-prop-1-enyl][1,3]dioxepan-2-one 28 and (2*R*,3*S*,5*R*)-3-*tert*-butyldiphenylsilyl-2-*tert*-butyldiphenylsilyloxymethyl-5-[(*Z*)-prop-1-enyl]-tetrahydrofuran 29. Triphosgene (7.1 mg, 24 μmol) was added to a solution of the diol (5*S*)-**9b** (31.4 mg, 0.048 mmol), pyridine (23 μL, 22 mg, 0.28 mmol), triethylamine (40 μL, 29 mg, 0.29 mmol) and powdered 4 Å molecular sieves (spatula tip) according to the standard procedure. Purification by flash chromatography (hexane/ether/triethylamine, 80:20:5) provided the carbonate **28** (33.2 mg, 0.049 mmol, 99%) containing a trace of the THF **29**.

The THF **28** was isolated from a number of experiments as a clear and colourless oil; R_F 0.60 (hexane/ether, 2:1); $[\alpha]_D^{20}$=+7.4 (*c* 0.35 in $CHCl_3$); ν_{max} ($CHCl_3$) 2931, 2859 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.97 [s, 9H, $C(CH_3)_3$], 1.12 [s, 9H, $C(CH_3)_3$], 1.55–1.65 (m, 1H, H-4), 1.76 (dd, 3H, CH=CHCH_3, *J*=7.0, 1.7 Hz), 1.92 (dd, 1H, H-4, *J*=12.7, 4.9 Hz), 3.37 (dd, 1H, C*H*HOSi, *J*=10.9, 3.7 Hz), 3.42 (dd, 1H, CH*H*OSi, *J*=10.9, 4.6 Hz), 4.05–4.07 (m, 1H, H-2), 4.54 (d, 1H, *J*=5.0 Hz, H-3), 5.08–5.15 (m, 1H, H-5), 5.38–5.43 (m, 1H, C*H*=CHCH$_3$), 5.57–5.65 (m, 1H, CH=C*H*CH$_3$), 7.31–7.44 (m, 12H, ArH), 7.55–7.57 (m, 2H, ArH), 7.60–7.62 (m, 2H, ArH), 7.66–7.70 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.4, 19.2, 26.8, 27.0, 42.1, 64.5, 74.1, 76.1, 87.8, 127.1, 127.6, 127.7, 127.7, 129.5, 129.6, 129.7, 131.1, 133.4, 133.9, 134.1, 135.6, 135.6, 135.8; MS (CI, NH_3) *m/z*: 652.3640 $[(M+NH_4)^+$. $C_{40}H_{54}NO_3Si_2$ requires 652.3642].

The carbonate **28** was isolated as a clear and colourless oil which contained traces of the tetrahydrofuran **29**; R_F 0.41 (hexane/ether, 2:1); $[\alpha]_D^{20}$=+7.4 (*c* 0.35 in $CHCl_3$); ν_{max} ($CHCl_3$) 1760 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.95 [9H, s, $C(CH_3)_3$], 1.06 [9 H, s, $C(CH_3)_3$], 1.38 (dd, 3H, CH=CHCH_3, *J*=7.0, 1.7 Hz), 1.72 (ddd, 1H, H-6, *J*=14.7, 4.7, 1.7 Hz), 1.80–1.88 (m, 1H, H-6), 3.84 (dd, 1H, C*H*HOSi, *J*=11.3, 6.0 Hz), 4.00 (td, 1H, H-5, *J*=9.0, 4.7 Hz), 4.11 (dd, 1H, CH*H*OSi, *J*=11.3, 2.9 Hz), 4.20 (ddd, 1H, H-4, *J*=9.0, 6.0, 2.9 Hz), 4.78 (t, 1H, H-7, *J*=9.3 Hz), 5.36–5.40 (m, 1H, C*H*=CH), 5.45–5.52 (m, 1H, CH=C*H*), 7.28–7.44 (m, 12H, ArH), 7.58–7.60 (m, 2H, ArH), 7.66–7.70 (m, 2H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.1, 19.2, 19.3, 26.8, 26.8, 41.6, 63.4, 69.0, 73.5, 85.2, 127.7, 127.9, 129.6, 129.7, 130.0, 130.1, 132.3, 133.1, 133.2, 133.3, 135.6, 135.8, 153.4; MS (ES^+)

m/z: 701.30778 [(M+Na)$^+$. $C_{41}H_{50}NaO_5Si_2$ requires 701.30944].

9.2.3. (4*R*,5*S*,7*S*)-5-*tert*-Butyldiphenylsilyloxy-4-*tert*-butyldiphenylsilyloxymethyl-7-[(*Z*)-1-trimethylsilyl-prop-1-enyl]-[1,3]dioxepan-2-one 30. Triphosgene (5.1 mg, 0.017 mmol) was added to a solution of the diol (5*S*)-**9c** (24.9 mg, 0.034 mmol), pyridine (18 μL, 17 mg, 0.21 mmol), triethylamine (29 μL, 21 mg, 0.21 mmol) and powdered 4 Å molecular sieves (spatula tip) according to the standard procedure. Purification by flash chromatography (hexane/ether:triethylamine, 85:15:5) yielded a mixture of the carbonate **30** (25.5 mg, 99%, containing a small amount of the presumed THF **31**, 10.8:1 ratio) as a clear and colourless oil. Further purification of the mixture by flash chromatography (hexane/ether/triethylamine, 90:10:5) provided a pure sample of **30**; R_F 0.51 (hexane/ether, 2:1); $[\alpha]_D^{25}$=+8.5 (*c* 0.69 in $CHCl_3$); ν_{max} ($CHCl_3$) 1756 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) −0.04 [s, 9H, $(CH_3)_3Si$], 0.93 [s, 9H, $(CH_3)_3C$], 1.07 [s, 9H, $(CH_3)_3C$], 1.70 (dd, 3H, CH=CHC*H*$_3$, *J*=7.1, 0.7 Hz,), 1.72–1.82 (m, 2H, H-6), 3.84–3.89 (m, 1H, C*H*HOSi), 3.98 (td, 1H, H-5, *J*=9.4, 5.3 Hz), 4.11–4.17 (m, 2H, H-4, CH*H*OSi), 4.44 (d, 1H, H-7, *J*=9.5 Hz), 6.18–6.24 (m, 1H, CH=C*H*CH_3), 7.26–7.45 (m, 12H, ArH), 7.57–7.61 (m, 4H, ArH), 7.68–7.72 (m, 4H, ArH); δ_C ($CDCl_3$; 62.5 MHz) −0.1, 17.4, 19.2, 19.3, 26.8, 26.8, 43.4, 63.5, 69.0, 80.9, 85.2, 127.6, 127.7, 127.7, 127.9, 129.6, 129.7, 129.9, 130.1, 132.5, 133.3, 133.5, 135.7, 135.8, 137.8, 138.2, 153.6.

9.2.4. 4(*R*),5(*R*)-4-*tert*-Butyldiphenylsilyloxymethyl-5-chloro-7-vinyl-[1,3]-dioxepan-2-one 32. To a stirring solution of the more polar diol **21**-MP (30 mg, 70 μmol), pyridine (33 μL, 33 mg, 0.42 mmol), triethylamine (97 μL, 70 mg, 0.7 mmol) and 4 Å molecular sieves in dichloromethane (2 mL) at −78°C was added triphosgene (20 mg, 70 μmol) as a solution in dichloromethane (0.5 mL, 0.5 mL rinse) via cannula. The resulting orange reaction mixture was stirred for 10 min at −78°C and then for 0.5 h at ambient temperature before being quenched by the addition of saturated aqueous ammonium chloride (5 mL) and ether (5 mL). The aqueous phase was separated and the organic phase was extracted with ether (2×5 mL). The organic phases were washed with saturated aqueous copper(II) sulfate solution (10 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether, 3:1) provided the title compound **32** as a clear and colourless oil (24 mg, 54 μmol, 77%); R_F 0.8 (ether/hexane, 1:1); $[\alpha]_D^{24}$=−18.8 (*c* 0.33 in $CHCl_3$); ν_{max} ($CDCl_3$) 1763 cm^{-1}; δ_H ($CDCl_3$, 400 MHz), 1.06 [s, 9H, $(CH_3)_3CSi$], 2.29 (1H, ddd, *J*=16, 3.6, 1.0 Hz), 2.36 (ddd, 1H, *J*=16, 3.2, 1.8 Hz), 3.83 (dd, 1H, C*H*HOSi, *J*=10, 9 Hz), 3.86 (dd, 1H, CH*H*OSi, *J*=10.0, 6.0 Hz), 4.41 (dd, 1H, *J*=8.0, 6.0 Hz), 4.72 (t, 1H, *J*=3.5 Hz), 5.10–5.16 (m, 1H), 5.29 (d, 1H, C=C*H*H$_{trans}$, *J*=10.2 Hz), 5.44 (d, 1H, C=CH*H*$_{trans}$ *J*=16.0 Hz), 5.88 (1H, ddd, C*H*=CH_2, *J*=16.0, 10.2, 5.6 Hz), 7.36–7.50 (m, 6H, ArH), 7.60–7.70 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 26.8, 41.8, 55.3, 62.2, 76.3, 79.9, 227.8, 127.9, 127.9, 130.1, 130.1, 132.5, 132.6, 134.5, 135.5, 135.5, 152.3;

9.2.5. 4(*R*),5(*R*)-4-*tert*-Butyldiphenylsilyloxymethyl-5-chloro-7-vinyl-[1,3]-dioxepan-2-one 32. To a stirring solution of the less polar diol **21**-LP (53 mg, 0.126 mmol), pyridine (61 μL, 60 mg, 0.76 mmol), triethylamine (0.175 mL, 127 mg, 126 mmol) and 4 Å molecular sieves in dichloromethane (4 mL) at −78°C was added triphosgene (37.6 mg, 126 mmol) as a solution in dichloromethane (2.0 mL) via cannula. The resulting orange reaction mixture was stirred for 10 min at −78°C and then for 0.5 h at 0°C before being quenched by the addition of saturated aqueous ammonium chloride (3 mL). The aqueous phase was separated and the organic phases was extracted with dichloromethane (2×5 mL). The organic phases were washed with saturated aqueous copper(II) sulfate solution (10 mL) and dried ($MgSO_4$). Purification by flash chromatography (hexane/ether, 1:1) provided the title compound **32** as a clear and colourless oil (28 mg, 63 μmol, 50%); R_F 0.2 (ether/hexane, 1:1); $[\alpha]_D^{18}$=−21.0 (*c* 1.6 in $CHCl_3$); ν_{max} ($CDCl_3$) 1757 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.08 [s, 9H, $(CH_3)_3CSi$], 2.45 (1H, ddd, H-6, *J*=15.5, 9.6, 8.3 Hz), 2.57 (ddd, 1H, H-6, *J*=15.5, 6.3, 2.8 Hz), 3.97 (dd, 1H, C*H*HOSi, *J*=11.1, 6.4 Hz), 4.02 (dd, 1H, CH*H*OSi, *J*=11.1, 5.9 Hz), 4.51 (ddd, 1H, *J*=9.2, 6.3, 3.0 Hz), 4.61 (ddd, 1H, *J*=6.2, 3.0 Hz), 4.83–4.90 (m, 1H), 5.31 (dt, 1H, C=C*H*H$_{cis}$, *J*=10.5, 1.0 Hz), 5.46 (dt, 1H, C=CH*H*$_{trans}$, *J*=17.1, 1.0 Hz), 5.97 (ddd, 1H, C*H*=CH_2, *J*=17.1, 10.5, 6.1 Hz), 7.38–7.50 (m, 6H, ArH), 7.66–7.71 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 26.8, 39.9, 54.8, 62.1, 79.4, 79.5, 118.4, 127.9, 130.0, 132.5, 132.6, 134.4, 135.6, 135.6, 150.7.

9.3. Representative procedure for tandem methylenation/Claisen rearrangement of the carbonates 22, 23 and 26

9.3.1. (*Z*)-(8*S*,9*R*)-8-*tert*-Butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 35. *Preparation from the carbonate* **22**. Dimethyltitanocene (0.12 mL of a 0.24 M solution in toluene, 28 μmol) was added to a stirred solution of carbonate **22** (14.5 mg, 22 μmol) in toluene (3 mL). The resulting solution was heated at reflux for 70 min in the absence of light, after which time, starting material remained. Further dimethyltitanocene (0.05 mL of a 0.24 M solution in toluene, 12 μmol) was added. After a further 25 min reflux the reaction mixture was allowed to cool and was evaporated onto silica. Purification by flash chromatography (hexane/ether, 4:1) provided the lactone **35** (11.0 mg, 17 μmol, 76%) as a pale yellow oil identical to previously prepared; $[\alpha]_D^{25}$=−8.8 (*c* 1.77 in $CHCl_3$); {lit.[16] $[\alpha]_D^{18}$=−10.8 (*c* 0.87 in MeOH)}; δ_H ($CDCl_3$, 500 MHz) 1.00 [s, 9H, or 9H′, $C(CH_3)_3$], 1.03 [s, 9H, or 9H′, $C(CH_3)_3$], 2.11–2.33 (m, 5H, H-3, H-4, H-7), 2.39–2.45 (m, 1H), 3.74–3.81 (m, 2H, CH_2OSi), 4.13–4.17 (m, 1H, H-8), 4.98–5.01 (m, 1H, H-9), 5.31–5.37 (m, 1H, H-6), 5.46–5.52 (m, 1H, H-5), 7.30–7.43 (m, 12H, ArH), 7.56–7.60 (m, 4H, ArH), 7.63–7.66 (m, 4H, ArH); *m/z*: (CI; NH_3) 663.333 [(M+H)$^+$. $C_{41}H_{51}O_4Si_2$ requires 663.3326].

Preparation from the carbonate **23**. Dimethyltitanocene (0.28 mL of a 0.24 M solution in toluene, 67 μmol) and the carbonate **23** (34.9 mg, 52 μmol) were used according to the standard procedure; reaction time 2 h at reflux. Purification by PLC (hexane/ether, 2:1) provided the lactone **35** (17.0 mg, 26 μmol, 49%) as a clear and colourless oil; data identical to previous values.

9.3.2. (*E*)-(4*S*,8*S*,9*R*)-8-*tert*-Butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-4-methyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 36b/c. Dimethyltitanocene (0.46 mL of a 0.24 M solution in toluene, 0.110 mmol) and the carbonate **26** (60.4 mg, 89 μmol) in toluene (5.5 mL) were used according to the standard procedure; reaction time 0.5 h at reflux. Purification by flash chromatography (hexane/ether, 20:1) afforded the lactone **36b/c** (39.4 mg, 58 μmol, 65%) as a clear and colourless oil (1:1 mixture of atropisomers); R_F 0.58 (hexane/ether, 2:1); ν_{max} ($CHCl_3$) 1730 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.95 [s, 9H or 9H′, C(CH_3)$_3$], 0.97 [s, 9H, or 9H′, C(CH_3)$_3$], 1.02 [s, 9H, or 9H′, C(CH_3)$_3$], 1.06 [s, 9H, or 9H′, C(CH_3)$_3$], 1.13 (d, 3H, CH_3CH, *J*=6.8 Hz,), 1.18 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.92 (dd, 1H, H-3, *J*=11.0, 2.3 Hz), 1.99–2.20 (m, 3H, H-7, H-3′, H-7′), 2.29–2.45 (m, 4H, H-3, H-7, H-7′), 2.49–2.75 (m, 2H, H-4, H-4′), 3.56 (dd, 1H, C*H*′H′OSi, *J*=11.1, 7.1 Hz), 3.87 (dd, 1H, CH′*H*′OSi, *J*=11.1, 3.4 Hz), 3.94–4.06 (m, 4H, H-8, C*H*HOSi, CH*H*OSi, H-8′), 4.70–4.75 (m, 1H, H-9), 4.97–5.07 (m, 3H, H-5, H-6, H-9′), 5.53–5.57 (m, 2H, H-5′, H-6′), 7.27–7.45 (m, 24H, ArH, ArH′), 7.50–7.68 (m, 16H, ArH, ArH′); δ_C ($CDCl_3$, 62.5 MHz) 15.1, 19.3, 21.4, 26.8, 26.9, 32.2, 37.4, 42.2, 43.2, 44.2, 64.0, 64.5, 71.3, 73.6, 79.5, 121.5, 127.5, 127.7, 127.8, 129.5, 129.6, 129.6, 129.8, 133.5, 133.7, 133.8, 134.1, 135.7, 135.8, 135.8, 135.9, 136.0, 138.4, 171.8, 172.7; MS (CI, NH_3) *m/z*: 677.3480 [(M+H)$^+$. $C_{42}H_{53}O_4Si_2$ requires 677.3482].

9.3.3. (*Z*)-(4*R*,8*S*,9*R*)-8-*tert*-Butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-4-methyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 36a, (*Z*)-(4*S*,8*S*,9*R*)-8-*tert*-butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-4-methyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 36d and (*E*)-(4*R*,8*S*,9*R*)-8-*tert*-butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-4-methyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 36e/f. Dimethyltitanocene (50 μL of a 0.24 M solution in toluene, 12 μmol) was added to a stirred solution of the carbonate **28** (25.5 mg, 38 μmol) in dry toluene (5 mL). The solution was heated to reflux for 35 min in the absence of light, then it was allowed to cool to room temperature and diluted with light petroleum (8 mL). After 5 min the solution was filtered and concentrated. Purification by flash chromatography (hexane/ether, 15:1) afforded an inseparable 1:2.5:1.2 mixture (as judged by ^{1}H NMR) of the lactones **36d/36e/36f** (13.1 mg, 0.019 mmol, 52%) (containing a small amount of the lactone **36a**, due to small amounts of the corresponding *trans*-propenyl substituted carbonate, and the tetrahydrofuran **29**, due to degradation of the remaining carbonate during purification) as a clear and colourless oi1; δ_C ($CDCl_3$, 62.5 MHz) 18.3, 19.1, 19.2, 19.3, 19.7, 20.2, 22.5, 26.8, 26.8, 26.9, 27.0, 29.4, 29.7, 31.0, 31.8, 32.0, 35.5, 37.2, 38.3, 42.0, 42.4, 42.6, 45.1, 45.8, 63.5, 63.9, 64.0, 64.5, 71.5, 72.4, 73.8, 76.0, 77.2, 78.3, 79.3, 79.5, 79.8, 80.0, 124.2, 127.5, 127.5, 127.5, 127.7, 127.8, 129.5, 129.5, 129.7, 129.8, 133.2, 133.5, 133.7, 133.7, 134.0, 135.6, 135.7, 135.8, 135.9, 135.9, 139.2, 172.7, 173.2, 173.6, 174.0; *m/z*: (FIB) 677.34170 [(M+H)$^+$. $C_{42}H_{53}O_4Si_2$ requires 677.34827]. ^{1}H NMR spectra of the individual lactones were obtained from standard Bruker 1-D selective TOCSY experiments,[34–36] with a Gaussian selective pulse (1% truncation). The pulse was for a duration of 50 ms (power=56 dB) and had a typical excitation bandwidth of 100 Hz. Signals were assigned on the basis of a COSY experiment run on the mixture. The signals for the protecting group protons were not seen in the 1-D TOCSY experiment as they were not part of the spin system which was irradiated.

Data for **36a**: δ_H ($CDCl_3$, 500 MHz; pulsed at δ_H 4.86) 1.07 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.88 (t, 1H, *J*=11.0 Hz, H-3), 1.89–1.95 (m, 1H, H-7), 2.18–2.28 (m, 2H, H-3, H-7), 2.58–2.66 (m, 1H, H-4), 3.87–3.90 (m, 2H, CH_2OSi), 3.93 (t, 1H, H-8, *J*=9.0 Hz), 4.79–4.89 (m, 1H, H-9), 5.01 (apparent ddm, 1H, *J*=11.0, 7.5 Hz), 5.18–5.24 (m, 1H, H-6).

Data for **36d**: δ_H ($CDCl_3$, 500 MHz; pulsed at δ_H 5.73) 1.03 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.93 (dd, 1H, H-3, *J*=13.9, 11.2 Hz), 1.96–2.02 (m, 1H, H-7), 2.47–2.54 (m, 1H, H-7), 2.57 (dd, 1H, H-3, *J*=13.9, 6.5 Hz), 2.98–3.06 (m, 1H, H-4), 3.60 (dd, 1H, C*H*HOSi, *J*=11.5, 4.3 Hz), 3.64 (dd, 1H, CH*H*OSi, *J*=11.5, 2.5 Hz), 4.36–4.40 (m, 1H, H-8), 4.69–4.74 (m, 1H, H-9), 5.35 (t, 1H, H-5 *J*=10.5 Hz), 5.71 (td, 1H, H-6, *J*=10.5, 5.5 Hz).

Data for **36e**: δ_H ($CDCl_3$, 500 MHz; pulsed at δ_H 4.69) 1.08 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.80 (dd, 1H, H-3, *J*=10.5, 8.5 Hz), 2.04 (q, 1H, H-7, *J*=11.0 Hz), 2.39–2.48 (m, 2H, H-3, H-7), 2.53–2.60 (m, 1H, H-4), 4.00–4.07 (m, 3H, H-8, CH_2OSi), 4.67 (dt, 1H, H-9, *J*=9.3, 4.0 Hz), 5.26 (ddd, 1H, H-6, *J*=16.5, 11.7, 3.2 Hz), 5.48 (ddd, 1H, H-5, *J*=16.5, 7.0, 1.0 Hz).

Data for **36f**: δ_H ($CDCl_3$, 500 MHz; pulsed at δ_H 3.97) 1.06 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.85 (t, 1H, H-3, *J*=11.0 Hz), 2.02–2.08 (m, 1H, H-7), 2.25–2.32 (m, 1H, H-7), 2.36 (dd, 1H, H-3, *J*=11.0, 5.0 Hz), 2.48–2.56 (m, 1H, H-4), 3.62 (dd, 1H, C*H*HOSi, *J*=11.0, 7.0 Hz), 3.89–3.98 (m, 2H, H-8, CH*H*OSi), 4.98 (td, 1H, H-9, *J*=7.0, 3.0 Hz), 5.05 (dd, 1H, H-5, *J*=16.5, 9.5 Hz), 5.43 (ddd, 1H, H-6, *J*=16.5, 8.8, 6.5 Hz).

9.3.4. (*E*)-(4*R*,8*S*,9*R*)-8-*tert*-Butyldiphenylsilyloxy-9-*tert*-butyldiphenylsilyloxymethyl-4-methyl-5-trimethylsilyl-2,3,4,7,8,9-hexahydro-oxonin-2-one 40. To the carbonate **30** (20.6 mg, 27 μmol, 10.8:1 mixture with the tetrahydrofuran **31**) in toluene (5 mL) was added a solution of dimethyltitanocene (130 μL of a 50 mg/mL solution in toluene, 0.031 mmol). The resultant solution was heated at reflux, in the dark, for 30 min. The reaction mixture was allowed to cool to ambient temperature, and was then diluted with light petroleum (7 mL). After 5 min, the resultant suspension was filtered through a small plug of silica and the mixture was concentrated. Purification by flash chromatography (hexane/ether, 30:1) provided the lactone **40** (10.5 mg, 14 μmol, 51%) as a clear and colourless oil; R_F 0.38 (hexane/ether, 30:1); $[\alpha]_D^{25}=-5.7$ (*c* 0.39 in $CHCl_3$); ν_{max} ($CHCl_3$) 1721 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) −0.01 [s, 9H, (CH_3)$_3$Si], 0.99 [s, 9H, (CH_3)$_3$C], 1.02 [s, 9H, (CH_3)$_3$C], 1.23 (d, 3H, CH_3CH, *J*=7.3 Hz), 1.87–1.98 (m, 1H, H-7), 2.02 (t, 1H, H-3, *J*=11.0 Hz), 2.14 (d, 1H, H-3, *J*=11.0 Hz), 2.33–2.42 (m, 1H, H-7), 2.87–2.95 (m, 1H, H-4), 3.84 (dd, 1H, C*H*HOSi, *J*=11.5, 1.9 Hz), 4.00–4.08 (m, 2H, H-8, CH*H*OSi), 5.10–5.16 (m, 2H, H-6, H-9), 7.28–

7.45 (m, 12H, ArH), 7.58–7.62 (m, 4H, ArH), 7.64–7.70 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 1.0, 19.2, 19.3, 22.5, 26.8, 26.8, 35.2, 36.2, 42.6, 62.9, 71.2, 79.7, 127.5, 127.8, 129.5, 129.6, 129.9, 133.0, 133.1, 133.8, 134.0, 135.5, 135.8, 135.9, 138.9, 142.3, 174.5; MS (CI, NH_3) *m/z*: 749.388 [$(M+H)^+$. $C_{45}H_{61}O_4Si_3$ requires 749.3877], 766 [$(M+NH_4)^+$, 5%], 749 [$(M+H)^+$, 5], 691 (2), 671 (2), 274 (13), 196 (10), 98 (55), 90 (100), 78 (50). Found: C, 71.2; H, 8.2; $C_{45}H_{60}O_4Si_3$ requires C, 71.22; H, 8.34%.

The reaction mixture also contained what is believed to be tetrahydrofuran by-products (^{1}H NMR analysis).

9.3.5. 8(*R*),9(*R*)-*tert*-Butyldiphenylsilyloxymethyl-8-chloro-4,7,8,9-tetrahydro-(3*H*)-oxonin-2-one 41. To a stirred solution of the carbonate **32** (prepared from **21**-MP) (24 mg, 54 μmol) in toluene (4 mL) was added dimethyltitanocene (0.17 mL, of a 87 mg/mL solution in toluene, 70 μmol) and the resulting solution was heated under reflux for 2 h. The solvent was removed in vacuo and purification by flash chromatography (hexane/dichloromethane, 3:2) provided the lactone **41** as a clear and colourless oil (13.5 mg, 29 μmol, 55%); $[\alpha]_D^{17}=-61.2$ (*c* 0.94 in $CHCl_3$); ν_{max} ($CHCl_3$) 1742 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.07 [s, 9H, $(CH_3)_3C$)Si], 2.08–2.20 (m, 1H) 2.32 (ddd, 1H, *J*=13.3, 10.9, 4.9 Hz), 2.46–2.61 (m, 2H), 2.72–2.88 (m, 1H), 2.94–3.07 (m, 1H), 3.89–4.01 (m, 2H, CH_2OSi), 4.52 (dd, 1H, H-8, *J*=9.9, 4.3 Hz), 4.90–4.97 (m, 1H, H-9), 5.67 (m, 2H, H-5, H-6), 7.35–7.47 (m, 6H, ArH), 7.66–7.74 (m, 4H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 19.2, 23.7, 26.7, 33.2, 34.1, 60.2, 62.8, 76.1, 127.7, 128.3, 129.7, 129.8, 130.5, 133.1, 135.5, 135.7, 174.3; MS (CI, NH_3) *m/z*: 460.2084 [$(M+NH_4)^+$. $C_{25}H_{35}ClO_3NSi$ requires 460.2084], 460 (100%), 443 [$(M+H)^+$, (70). Found: C, 67.76; H, 7.06; $C_{25}H_{31}ClO_3Si$ requires C, 67.77; H, 7.05%.

The lactone **41** could be prepared from the carbonate **32**, derived from the diol **21**-LP, in 63% yield.

9.4. Representative procedure for the preparation of the 3-hydroxyketones 52a–d

9.4.1. (2*R*,5*S*)-1-Benzyloxy-5-hydroxy-2-methyl-hept-6-en-3-one 52a. To a cooled (0°C) solution of (+)-Ipc_2BCl (2.6 g, 8.1 mmol) in dry ether (60 mL) was added Et_3N (1.2 mL, 871 mg, 8.6 mmol) via syringe followed by a solution of the ketone **42** (1.00 g, 5.2 mmol) in ether (10 mL) via cannula. The white suspension was stirred for 2 h and then cooled to −78°C. A solution of acrolein **46** (0.7 mL, 587 mg, 10.5 mmol) in ether (10 mL) was added dropwise via syringe. The reaction mixture was stirred at −78°C until TLC analysis (hexane/EtOAc, 4:1) of an aliquot (quenched with water, methanol and a 30% aqueous solution of hydrogen peroxide, followed by extraction with EtOAc) showed consumption of the ketone **46**. After 2.5 h, the reaction was quenched with a mixture of methanol (130 mL), pH 7 buffer (45 mL) and an aqueous solution of hydrogen peroxide (30%, 15 mL). The biphasic system was stirred vigorously at ambient temperature for at least 1 h. The mixture was poured into water (100 mL) and was extracted with EtOAc/hexane (1:1, 400 mL; emulsions tended to form if EtOAc was used). The aqueous layer was saturated with sodium chloride and was extracted with EtOAc (2×250 mL). The organic extracts were washed with water (50 mL), brine (50 mL), were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (hexane/EtOAc, 17:3→4:1) yielded a mixture of the product **52a** and IpcOH. Further purification by flash chromatography (hexane/EtOAc, 9:1→17:3) yielded the pure hydroxyketone **52a** (1.045 g, 4.21 mmol, 81%) as a colourless oil; R_F 0.16 (light petroleum/EtOAc, 4:1); $[\alpha]_D^{28}=-33.8$ (*c* 2.36 in $CHCl_3$); ν_{max} ($CDCl_3$) 3543, 1707, 1658 cm^{-1}; δ_H ($CDCl_3$, 200 MHz) 1.08 (d, 3H, CH_3, *J*=7.0 Hz), 2.78 (m, 1H, H-4), 2.83 (m, 1H, H-4), 2.91–3.01 (m, 1H, H-2), 3.20 (br s, 1H, OH), 3.52 (dd, 1H, *J*=8.9, 5.1 Hz, H-1), 3.60 (dd, 1H, *J*=8.9, 8.2 Hz, H-1), 4.49 (s, 2H, CH_2Ph), 4.55–4.64 (m, 1H, H-5), 5.12 (dt, 1H, H-7, *J*=10.5, 1.0 Hz), 5.27 (dt, 1H, H-7, *J*=17.0, 1.0 Hz), 5.85 (ddd, 1H, H-6, *J*=17.0, 10.5, 5.0 Hz), 7.25–7.37 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.1, 46.9, 48.5, 68.4, 72.1, 73.3, 114.8, 127.7, 127.8, 128.4, 137.8, 139.1, 213.5; MS (ES^+) *m/z* 271 [$(M+Na)^+$, 82%], 249 [$(M+H)^+$, 40], 231 [$(M-H_2O+H)^+$, 100]. Found: C, 72.4; H, 8.0; $C_{15}H_{20}O_3$ requires C, 72.6; H, 8.1%.

9.4.2. (*E*)-(2*R*,5*S*)-1-Benzyloxy-5-hydroxy-2-methyl-oct-6-en-3-one 52b. (+)-Ipc_2BCl (11.34 g, 35.4 mmol), triethylamine (4.34 mL, 3.15 g, 31.2 mmol), the ketone **42** (4.0 g, 20.8 mmol), ether (240 mL) and crotonaldehyde **47** (3.45 mL, 2.92 g, 41.6 mmol) were used according to the standard procedure. Purification by flash chromatography (EtOAc/hexane, 4:1) afforded the hydroxyketone **52b** (5.20 g, 19.8 mmol, 95%) as a pale yellow oil; R_F 0.24 (hexane/EtOAc, 4:1); $[\alpha]_D^{22}=-35.1$ (*c* 1.03 in $CHCl_3$); ν_{max} ($CHCl_3$) 3603, 1705, 1602 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.07 (d, 3H, CH_3CHCO, *J*=7.0 Hz), 1.68 (ddd, 3H, H-8, *J*=6.5, 1.5, 1.5 Hz), 2.67–2.71 (m, 2H, H-4), 2.82–2.96 (m, 1H, H-2), 3.03 (d, 1H, *J*=3.5 Hz, OH), 3.49 (dd, 1H, H-1, *J*=9.0, 5.0 Hz), 3.62 (dd, 1H, H-1, *J*=9.0, 8.0 Hz), 4.48 (s, 2H, CH_2Ph), 4.48–4.59 (m, 1H, H-5), 5.47 (ddq, 1H, H-6, *J*=15.5, 6.5, 1.5 Hz), 5.68 (dqd, 1H, H-7, *J*=15.5, 6.5, 1.0 Hz), 7.26–7.35 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.1, 17.6, 46.9, 48.9, 68.4, 72.1, 73.3, 126.9, 127.6, 127.7, 128.4, 132.0, 137.9, 213.8; MS (FAB) *m/z*: 261.1491 [$(M-H)^+$. $C_{16}H_{21}O_3$ requires 261.1491]. Found: C, 72.6; H, 8.5; $C_{16}H_{22}O_3$ requires C, 73.3; H 8.5%.

9.4.3. (*E*)-(2*R*,5*S*)-1-Benzyloxy-5-hydroxy-2,6-dimethyl-oct-6-en-3-one 52c. (+)-Ipc_2BCl (4.0 g, 12.2 mmol), triethylamine (1.7 mL, 1.23 g, 12.2 mmol), the ketone **42** (1.5 g, 7.8 mmol), ether (90 mL) and *trans*-2-methylbut-2-enal **48** (tiglic aldehyde; 1.5 mL, 1.31 g, 15 mmol) were used according to the standard procedure. Purification by flash chromatography (hexane/EtOAc, 41:9) yielded the hydroxyketone **52c** as a mixture with IpcOH, the bulk of which was used without further purification. A small portion was rechromatographed to provide material for characterisation; R_F 0.13 (light petroleum/EtOAc, 4:1); $[\alpha]_D^{18}=-23.6$ (*c* 2.28 in $CHCl_3$); ν_{max} ($CHCl_3$) 3602, 1706, 1652 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.08 (d, 3H, CH_3CHCO, *J*=7.5 Hz), 1.59 (d, 3H, H-8, *J*=0.5 Hz,), 1.61 (s, 3H, CH_3C=CH), 2.77 (s, 1H, H-4), 2.71 (d, 1H, H-4, *J*=2.5 Hz), 2.93–3.00 (m, 1H, H-2), 3.01 (d, 1H, OH, *J*=2.0 Hz), 3.50 (dd, 1H, H-1, *J*=9.0, 5.0 Hz), 3.62 (t, 1H, H-1, *J*=9.0 Hz), 4.48–4.54 (m, 1H, H-5), 4.54 (s, 2H, CH_2Ph), 5.53 (m, 1H, H-7), 7.25–7.37 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 11.8, 13.0, 13.1, 46.9, 47.6, 72.2, 72.7,

73.2, 120.6, 127.6, 127.7, 128.4, 136.2, 137.9, 214.1; MS (ES^+) *m/z*: 276.1724 (M^+. $C_{17}H_{24}O_3$ requires 276.1725).

9.4.4. (2*R*,5*S*)-1-Benzyloxy-5-hydroxy-5-[(4*S*)-4-isopropenyl-cyclohex-1-enyl]-2-methyl-pentan-3-one 52d. (+)-Ipc_2BCl (2.5 g, 7.8 mmol), triethylamine (1.2 mL, 871 mg, 8.6 mmol), the ketone **42** (1.01 g, 5.3 mmol, 60 mL) and (−)-perillaldehyde **49** (1.7 mL, 1.64 g, 11 mmol) were used according to the standard procedure. Purification by flash 15% (hexane/EtOAc, 17:3) yielded some of the pure product **52d** as a colourless oil and predominantly the hydroxyketone **52d** mixed with IpcOH. This was used without further purification; R_F 0.19 (light petroleum/EtOAc, 4:1); $[\alpha]_D^{21}=-51.5$ (*c* 2.33 in $CHCl_3$); ν_{max} ($CHCl_3$) 1716, 1602 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.08 (d, 3H, C*H*$_3$CHCO, *J*=7.0 Hz), 1.41–1.51 (m, 2H, H-5′), 1.73 (s, 3H, C*H*$_3$CH=CH), 1.79–2.26 (5 H, m, H-3′, H-4′, H-6′), 2.78–2.83 (m, 2H, H-4), 2.87–2.11 (m, 1H, H-2), 3.09 (br s, 1H, OH), 3.49 (dd, 1H, H-1, *J*=9.0, 5.0 Hz), 3.62 (dd, 1H, H-1, *J*=9.0, 8.0 Hz), 4.44–4.49 (m, 1H, H-5), 4.49 (s, 2H, C*H*$_2$Ph), 4.70 (m, 2H, C=C*H*$_2$), 5.73 (m, 1H, H-2′), 7.17–7.41 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 13.0, 20.7, 24.9, 27.3, 30.2, 41.0, 46.8, 47.7, 70.9, 72.0, 73.2, 108.5, 109.2, 121.6, 127.6, 127.7, 128.3, 137.7, 149.6, 214; MS (CI) *m/z*: 360.2539 [$(M+NH_4)^+$. $C_{22}H_{34}NO_3$ requires 360.2539].

9.4.5. (*R*)-[Methoxy(trifluoromethyl)phenyl]-acetic acid, 2(*R*),5(*S*)-1-(4-benzyloxy-3-methyl-2-oxobutyl)-allyl ester (*R*)-54. A solution of the alcohol **52a** (4.0 mg, 16 μmol), (*R*)-(+)-MTPA (8 mg, 0.03 mmol), DCC (79 mg, 0.4 mmol) and a catalytic quantity of DMAP in dichloromethane (1.1 mL) was stirred overnight under nitrogen. The resultant suspension was filtered through a small pad of Celite™, washed with 2 M hydrochloric acid, saturated aqueous sodium bicarbonate, dried ($MgSO_4$) and concentrated. The ester (*R*)-**54** was purified by passage through a plug of silica; R_F 0.42 (light petroleum/EtOAc, 4:1); ν_{max} ($CDCl_3$) 1750, 1719 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 1.01 (d, 3H, C*H*$_3$CH, *J*=7 Hz), 2.85 (dd, 1H, C*H*HCHO, *J*=18, 4 Hz), 2.82 (m, 1H, C*H*CH$_3$), 3.00 (dd, 1H, CH*H*CHO, *J*=18, 9 Hz), 3.45–3.60 (m, 5H, C*H*$_2$OBn, C*H*$_3$O), 4.44 (d, 1H, C*H*HPh, *J*=12 Hz), 4.48 (d, 1H, CH*H*Ph, *J*=12 Hz), 5.24 (d, 1H, CH=CHH_{cis}, *J*=10.5 Hz), 5.29 (d, 1H, CH=CHH_{trans}, *J*=17 Hz), 5.75 (m, 1H, CH$_2$=C*H*), 5.94 (m, 1H, CHOCO), 7.10–7.72 (m, 10H, ArH).

9.4.6. (*S*)-[Methoxy(trifluoromethyl)phenyl]-acetic acid, 2(*R*),5(*S*)-1-(4-benzyloxy-3-methyl-2-oxobutyl)-allyl ester (*S*)-54. A solution of the alcohol **52a** (4.0 mg, 16 μmol), (*S*)-(−)-MTPA (41 mg, 0.18 mmol), DCC (8 mg, 40 μmol) and a catalytic quantity of DMAP in dichloromethane (1.1 mL) was stirred overnight under nitrogen. The resultant suspension was filtered through a small pad of Celite™, washed with 2 M hydrochloric acid, saturated aqueous sodium bicarbonate, dried ($MgSO_4$) and concentrated. The ester (*S*)-**54** was purified by passage through a plug of silica; R_F 0.40 (light petroleum/EtOAc, 4:1); ν_{max} ($CDCl_3$) 1750, 1720 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.81 (d, 3H, C*H*$_3$CH, *J*=7 Hz), 2.84 (m, 1H, C*H*HCHO), 2.91 (m, 1H, C*H*CH$_3$), 2.110 (dd, 1H, CH*H*CHO, *J*=18, 9 Hz), 3.40–3.55 (m, 5H, C*H*$_2$OBn, C*H*$_3$O), 4.42 (d, 1H, C*H*HPh, *J*=12 Hz), 4.46 (d, 1H, CH*H*Ph, *J*=12 Hz), 5.27 (d, 1H, CH=CHH_{cis}, *J*=10.5 Hz), 5.41 (d, 1H, CH=CHH_{trans}, *J*=17 Hz), 5.85 (m, 1H, CH$_2$=C*H*), 5.99 (m, 1H, CHOCO), 7.26–7.49 (m, 10H, ArH).

9.4.7. (2*R*,4*S*,5*S*)-1-Benzyloxy-5-hydroxy-2,4,6-trimethyl-hept-6-en-3-one 52e.[40] To a stirred solution of (−)-$(Ipc)_2BOTf$ (prepared according to the literature procedure,[45] 6.2 mL, 8.1 mmol, ca. 1.3 M in hexane) in dichloromethane (20 mL) at room temperature was added dropwise *N*,*N*-diisopropylethylamine (3.5 mL, 2.6 g, 20 mmol) and the solution decolourised. This was followed by the addition of a solution of the ketone **43** (1.03 g, 5.01 mmol) in dichloromethane (10 mL, 10 mL rinse) via cannula. The pale yellow solution was stirred at ambient temperature for 3 h and then cooled to 0°C. A solution of methacrolein **50** (1.3 mL, 1.10 g, 16 mmol) in dichloromethane (8 mL) was added dropwise via cannula and the reaction stirred at −5°C for 16 h. The reaction mixture was then partitioned between ether (3×250 mL) and pH 7 buffer (250 mL) and the combined organic extracts were concentrated. The residue was resuspended in methanol (50 mL) and pH 7 buffer (12 mL) and cooled to 0°C. An aqueous solution of hydrogen peroxide (30%, 25 mL) was added dropwise and stirring continued at ambient temperature for 1 h. The mixture was poured into water (100 mL) and extracted with dichloromethane (3×100 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium bicarbonate (75 mL) and brine (50 mL), then they were dried ($MgSO_4$) and concentrated. Flash chromatography (dichloromethane/ether, 9:1→light petroleum/EtOAc, 25:4) gave the product **52e** (1.24 g, 4.5 mmol, 90%) as a colourless oil; R_F 0.49 (dichloromethane/ether, 9:1); $[\alpha]_D^{27}=-38.4$ (*c* 2.5 in $CHCl_3$) {lit.[40] *ent*-**52e** $[\alpha]_D^{20}=+43.6$ (*c* 2.1 in $CHCl_3$)}; ν_{max} ($CHCl_3$) 3495 (br), 1698 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.02 (d, 3H, C*H*$_3$CHCH$_2$O, *J*=7.0 Hz), 1.07 (d, 3H, C*H*$_3$CHCOH, *J*=7.0 Hz), 1.63 (s, 3H, C*H*$_3$CH=CH), 2.87 (dq, H-4, 1H, *J*=7.0, 2.0 Hz), 3.13–3.21 (m, 2H, H-2, OH), 3.48 (dd, 1H, H-1, *J*=9.0, 5.0 Hz), 3.62 (t, 1H, H-1, *J*=9.0 Hz), 4.42–4.50 (m, 3H, H-5, C*H*$_2$Ph), 4.93 (d, 1H, H-7, *J*=1.5 Hz), 5.09 (apparent br s, 1H, H-7), 7.23–7.33 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 Hz) 8.3, 13.6, 19.6, 44.7, 48.4, 72.7, 73.2, 73.5, 111.4, 127.7, 127.8, 128.4, 137.5, 143.4, 218.0; MS (CI, NH_3) *m/z*: 294.2069 [$(M+NH_4)^+$. $C_{17}H_{28}NO_3$ requires 294.2069], 294 [$(M+NH_4)^+$, 15%], 224 (100). Found: C, 74.3; H, 8.8; $C_{17}H_{24}O_3$ requires C, 73.9; H 8.8%.

9.5. Procedure for the preparation of the hydroxyketones 52f and 52g

9.5.1. (2*R*,4*R*,5*S*)-1-Benzyloxy-5-hydroxy-2,4,6-trimethyl-hept-6-en-3-one 52f.[40] To a stirred solution of Cy_2BCl (prepared according to the literature procedure,[45] 1.4 mL, 1.36 g, 6.5 mmol) in ether (10 mL) at −78°C was added dropwise triethylamine (1.2 mL, 871 mg, 8.6 mmol). This was followed by addition of the ketone **43** (1.10 g, 5.36 mmol) in ether (3 mL, 3 mL rinse) via cannula. A white precipitate formed, and after 3 h at −78°C methacrolein **50** (0.89 mL, 754 mg, 10.8 mmol) was added dropwise. The reaction mixture was stirred for 3 h at −78°C and then allowed to warm to −20°C for 18 h. The solution was partitioned between ether (70 mL) and pH 7 buffer solution (70 mL), then extracted with ether (3×70 mL). The combined organic extracts were concentrated. The residue was

resuspended in methanol (25 mL) and pH 7 buffer (5 mL) at 0°C. An aqueous solution of hydrogen peroxide (30%, 10 mL) was added dropwise and the mixture was stirred at room temperature for 2 h. The mixture was then poured into water (70 mL) and extracted with dichloromethane (4× 70 mL). The combined organic extracts were washed with a saturated aqueous solution of sodium bicarbonate (50 mL) and brine (50 mL), then they were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (dichloromethane/ether, 9:1) provided the hydroxyketone **52f** (1.06 g, 3.84 mmol, 72%) as a colourless oil; R_F 0.53 (dichloromethane/ether, 9:1); $[\alpha]_D^{21}=-20.9$ (*c* 4.67 in $CHCl_3$); ν_{max} ($CHCl_3$) 3456 (br), 1707, 1649 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.98 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.06 (d, 3H, C*H*$_3$CHOH, *J*=7.0 Hz), 1.73 (br s, 3H, C*H*$_3$CH=CH), 2.10 (dq, 1H, H-4, *J*=16.0, 7.0 Hz), 3.05–3.11 (m, 1H, H-2), 3.45 (dd, 1H, 1-H, *J*=9.0, 5.0 Hz), 3.67 (t, 1H, H-1, *J*=9.0 Hz), 4.20 (dd, 1H, H-5, *J*=9.0, 4.0 Hz), 4.43 (d, 1H, C*H*$_2$Ph, *J*=12.0 Hz), 4.54 (d, 1H, C*H*$_2$Ph, *J*=12.0 Hz), 4.91 (q, 1H, C*H*=CH, *J*=1.5 Hz), 4.94 (br d, 1H, CH=C*H*, *J*=1.0 Hz), 7.26–7.34 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.4, 13.7, 16.9, 46.2, 49.1, 73.2, 73.4, 78.3, 113.9, 127.6, 127.6, 128.3, 137.8, 144.6, 217.2; MS (CI) *m/z*: 277.1804 [$(M+H)^+$. $C_{17}H_{25}O_3$ requires 277.1804], 294 [$(M+NH_4)^+$, 95%], 277 [$(M+H)^+$, 30], 224 (100).

9.5.2. (2*R*,4*R*,5*S*)-1-*tert*-Butyldimethylsilyloxy-5-hydroxy-2,4,6-trimethyl-hept-6-en-3-one 52g.[40] Cy_2BCl (5.9 mL, 5.72 g, 27.1 mmol), triethylamine (4.9 mL, 3.56 g, 35.2 mmol), the ketone **43** (5.0 g, 21.7 mmol) ether (45 mL) and methacrolein **50** (5.0 g, 21.7 mmol) were used according to the standard procedure. Purification by flash chromatography (hexane/ether, 17:3) provided the hydroxyketone **52g** (4.84 g, 15.9 mmol, 73%) as a colourless oil; R_F 0.17 (hexane/ether, 17:3); $[\alpha]_D^{21}=-25.5$ (*c* 4.6 in $CHCl_3$); ν_{max} ($CHCl_3$) 3606, 3435 (br), 1706, 1649 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.03 [2×s, 6H, $(CH_3)_2Si$], 0.86 [d, 9H, $(CH_3)_3C$, *J*=0.9 Hz], 0.97–1.01 (m, 6H, C*H*$_3$CH$_2$, C*H*$_3$CHOH), 1.73 (s, 3H, C*H*$_3$CH=CH), 2.61 (d, 1H, *J*=3.5 Hz, OH), 2.86–2.95 (m, 2H, H-2, H-4), 3.58 (dd, 1H, H-1, *J*=9.1, 4.4 Hz), 3.80 (t, 1H, H-1, *J*=9.1 Hz), 4.18 (dd, 1H, H-5, *J*=8.3, 3.5 Hz), 4.90 (d, 1H, C*H*=CH, *J*=1.2 Hz), 4.94 (br s, 1H, CH=C*H*, *J*=1.0 Hz); δ_C ($CDCl_3$, 100 MHz) −5.6, 12.9, 13.6, 18.3, 25.8, 48.8, 48.8, 65.4, 78.3, 113.8, 144.7, 217.6; MS (EI) *m/z*: 301.2193 [$(M+H)^+$. $C_{16}H_{33}O_3Si$ requires 301.2199].

9.6. Representative procedure for the preparation of the diols 55a–g

9.6.1. (3*S*,5*S*,6*R*)-7-Benzyloxy-6-methyl-hept-1-ene-3,5-diol 55a. To a stirred suspension of $Me_4NBH(OAc)_3$ (1.8 g, 6.8 mmol) in acetonitrile (25 mL) at ambient temperature was added acetic acid (6.5 mL). The colourless solution was cooled to −40°C and a solution of the hydroxyketone **52a** (0.488 g, 1.17 mmol) in acetonitrile (5 mL, 5 mL rinse) was added via cannula. The mixture was stirred at −40°C for 18 h and then allowed to warm to −20°C for 2 h after which time consumption of the starting material was complete. The reaction was quenched with a saturated aqueous solution of potassium sodium tartrate (28 mL), then was allowed to warm to ambient temperature and was stirred for 30 min. A white precipitate formed. The mixture was poured over ice, was neutralised with a saturated aqueous solution of sodium bicarbonate (100 mL) followed by portionwise additions of solid sodium bicarbonate, and was extracted with EtOAc (350 mL). The aqueous layer was saturated with solid sodium chloride and was extracted again with EtOAc (2×350 mL). The combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (200 mL), brine (150 mL), were dried ($MgSO_4$) and concentrated. Purification by flash chromatography (ether/hexane, 1:1→1:0) afforded the diol **55a** (0.450 g, 1.8 mmol, 91%) as a colourless oil; R_F 0.25 (hexane/EtOAc); $[\alpha]_D^{28}=-13.4$ (*c* 1.55 in $CHCl_3$); ν_{max} ($CHCl_3$) 3608, 3450 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.86 (d, 3H, CH_3, *J*=7.0 Hz), 1.69–1.75 (m, 2H, H-4), 1.88–2.04 (m, 1H, H-6), 3.48 (dd, 1H, H-7, *J*=9.0, 8.0 Hz), 3.64 (dd, 1H, H-7, *J*=9.0, 4.0 Hz), 3.00–3.70 (br s, 2H, 2×OH), 3.87 (dt, 1H, H-5, *J*=7.5, 4.0 Hz), 4.44–4.53 (m, 1H, H-3), 4.53 (s, 2H, C*H*$_2$Ph), 5.12 (dt, 1H, H-1$_{cis}$, *J*=10.5, 2.0 Hz), 5.30 (dt, 1H, H-1$_{trans}$, *J*=17.0, 2.0 Hz), 5.93 (ddd, 1H, H-2, *J*=17.0, 10.5, 5.0 Hz), 7.25–7.40 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 13.6, 36.2, 39.9, 70.1, 73.4, 74.0, 75.3, 113.9, 127.6, 127.8, 128.4, 137.5, 140.9; MS (CI) *m/z*: 251.1647 [$(M+H)^+$. $C_{15}H_{23}O_3$ requires 251.1647].

9.6.2. (*E*)-(4*S*,6*S*,7*R*)-8-Benzyloxy-7-methyl-oct-2-ene-4,6-diol 55b. $Me_4NBH(OAc)_3$ (3.5 g, 13 mmol), acetic acid (7 mL), acetonitrile (20 mL) and the hydroxyketone **52b** (0.874 g, 3.34 mmol) were used according to the standard procedure at −35°C for 18 h. Purification by flash chromatography (hexane/EtOAc, 4:1) afforded the diol **55b** (0.798 g, 3.02 mmol, 91%) as a colourless oil; R_F 0.32 (light petroleum/EtOAc, 1:1); $[\alpha]_D^{18}=-12.4$ (*c* 2.7 in $CHCl_3$); ν_{max} ($CHCl_3$) 3606, 3456 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.86 (d, 3H, C*H*$_3$CHOH, *J*=7.0 Hz), 1.69 (d, 3H, H-1, *J*=6.0 Hz), 1.87–2.04 (m, 1H, H-7), 3.20 (br s, 1H, OH), 3.48 (dd, 1H, H-8, *J*=9.0, 8.0 Hz), 3.61 (dd, 1H, H-8, *J*=9.0, 4.5 Hz), 3.85 (dd, 1H, H-6, *J*=13.0, 6.0 Hz), 3.97 (br s, 1H, OH), 4.40 (dd, 1H, H-4, *J*=11.5, 6.0 Hz), 4.52 (s, 2H, C*H*$_2$Ph), 5.55 (ddq, 1H, H-3, *J*=15.0, 7.0, 1.5 Hz), 5.69 (dqd, 1H, H-4, *J*=15.0, 6.0, 1.0 Hz), 7.22–7.39 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.6, 17.7, 38.2, 40.2, 70.0, 73.5, 74.1, 75.5, 125.8, 127.7, 127.8, 128.5, 134.0, 137.6; MS (CI) *m/z*: 265.1804 [$(M+H)^+$. $C_{16}H_{25}O_3$ requires 265.1804].

9.6.3. (*E*)-(4*S*,6*S*,7*R*)-8-Benzyloxy-2,7-dimethyl-oct-2-ene-4,6-diol 55c. $Me_4NBH(OAc)_3$ (5.8 g, 22 mmol), acetic acid (15 mL), acetonitrile (80 mL) and the crude hydroxyketone **52c** (7.1 mmol) were used according to the standard procedure at −35°C for 18 h. Purification by flash chromatography (hexane/EtOAc, 4:1) afforded the *diol***55c** (1.30 g, 4.65 mmol, 66% over two steps) as a colourless oil; R_F 0.1 (hexane/EtOAc, 10:3); $[\alpha]_D^{18}=-15.7$ (*c* 2.52 in $CHCl_3$); ν_{max} ($CHCl_3$) 3608, 3450 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.86 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.58–1.68 (m, 7H, C*H*$_3$C=CH, H-1, H-5), 1.80 (ddd, 1H, H-5, *J*=14.0, 18.5, 3.0 Hz), 1.94–2.03 (m, 1H, H-7), 3.49 (dd, 1H, H-8, *J*=9.0, 8.0 Hz), 3.63 (dd, 1H, H-8, *J*=9.0, 4.0 Hz), 3.80 (dt, 1H, H-6, *J*=8.0, 3.0 Hz), 4.32 (dd, 1H, H-4, *J*=8.5, 3.0 Hz), 4.53 (s, 2H, C*H*$_2$Ph), 5.57 (m, 1H, H-2), 7.29–7.39 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 13.0, 13.8, 21.1, 38.1, 38.6, 73.5, 74.0, 74.0, 75.2, 119.0, 127.7, 127.8, 128.5, 137.7, 138.0; MS (FAB) *m/z*: 279.1941 [$(M+H)^+$. $C_{17}H_{27}O_3$ requires

279.1960), 279 [(M+H)$^+$, 15%], 261 [(M−H_2O+H)$^+$, 20], 243 (100).

9.6.4. (1*S*,3*S*,4*R*)-5-Benzyloxy-1-[(4*S*)-4-isopropenylcyclohex-1-enyl]-4-methyl-pentane-1,3-diol 55d. $Me_4NBH(OAc)_3$ (5.6 g, 21 mmol), acetic acid (11 mL), acetonitrile (60 mL) and the crude ketone **52d** (4.6 mmol) were used according to the standard procedure at −35°C for 18 h. Purification by flash chromatography (hexane/EtOAc, 4:1) afforded the diol **55d** (0.810 g, 2.35 mmol, 51% over two steps) as a colourless oil; R_F 0.18 (light petroleum/EtOAc, 10:3); $[\alpha]_D^{18}$=−68.8 (*c* 1.96 in $CHCl_3$); ν_{max} ($CHCl_3$) 3606, 3462, 1643 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.87 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.74 (s, 3H, CH_3C=CH_2), 1.40–2.20 (m, 10 H, H-2, H-4, H-3′, H-4′, H-5′, H-6′), 3.48 (dd, 1H, H-5, *J*=9.0, 8.0 Hz), 3.63 (dd, 1H, H-5, *J*=9.0, 4.0 Hz), 3.82 (dt, 1H, H-3, *J*=8.0, 3.5 Hz), 3.98 (br s, 1H, OH), 4.3 (m, 1H, H-1), 4.53 (s, 2H, CH_2Ph), 4.72 (br s, 2H, C=CH_2), 5.80 (m, 1H, H-2′), 7.22–7.39 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 13.7, 20.7, 25.6, 27.5, 30.4, 38.0, 38.1, 41.4, 72.8, 73.5, 74.4, 75.5, 108.5, 120.7, 127.7, 128.5, 127.9, 137.5, 139.2, 150.0; MS (FAB) *m/z*: 345.2430 [(M+H)$^+$. $C_{22}H_{33}O_3$ requires 345.2430], 345 [(M+H)$^+$], 309 [(M−2H_2O+H)$^+$, 70], 154 (100).

9.6.5. (3*S*,4*R*,5*R*,6*R*)-7-Benzyloxy-2,4,6-trimethyl-hept-1-ene-3,5-diol 55e.[46] $Me_4NBH(OAc)_3$ (1.2 g, 4.6 mmol), acetic acid (6 mL), acetonitrile (18 mL) and the hydroxyketone **52e** (0.312 g, 1.13 mmol) were used according to the standard procedure at −35°C for 18 h. Purification by flash chromatography (hexane/EtOAc, 7:3) afforded the diol **55e** (0.226, 0.81 mmol, 72%) as a translucent low-melting solid; mp 30–32°C; R_F 0.28 (light petroleum/EtOAc, 10:3); $[\alpha]_D^{25}$=−13.1 (*c* 3.8 in $CHCl_3$); ν_{max} ($CHCl_3$) 3607, 3434, 1652 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.88 (d, 3H, CH_3CHCH_2O, *J*=7.0 Hz), 0.95 (d, 3H, CH_3CHOH, *J*=7.0 Hz), 1.67 (s, 3H, CH_3C=CH), 1.83–1.86 (m, 1H, H-6), 2.28–2.27 (m, 1H, H-4), 3.52 (t, 1H, H-7, *J*=9.0 Hz), 3.60–3.70 (m, 1H, H-7), 3.93 (s, 1H, H-5), 4.44 (d, 1H, H-3, *J*=2.0 Hz), 4.54 (s, 2H, CH_2Ph), 4.92 (d, 1H, H-1, *J*=1.0 Hz), 5.11 (br s, 1H, H-1), 7.26–7.40 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 10.4, 13.7, 19.9, 35.7, 35.9, 73.3, 73.7, 76.1, 81.7, 110.2, 127.7, 128.0, 128.6, 137.4, 145.2; MS (CI) *m/z*: 279.1960 [(M+H)$^+$. $C_{17}H_{27}O_3$ requires 279.1960], 279 [(M+H)$^+$, 65%], 106 (100).

9.6.6. (3*S*,4*S*,5*R*,6*R*)-7-Benzyloxy-2,4,6-trimethyl-hept-1-ene-3,5-diol 55f.[46] $Me_4NBH(OAc)_3$ (1.02 g, 3.88 mmol), acetic acid (5 mL), acetonitrile (15 mL) and the ketone **52f** (0.261 g, 0.944 mmol) were used according to the standard procedure at −30°C for 18 h. Purification by flash chromatography (hexane/EtOAc, 25:8) afforded the diol **55f** (0.226 g, 0.81 mmol, 72%) as a colourless oil; R_F 0.28 (light petroleum/EtOAc, 10:3); $[\alpha]_D^{23}$=−34.9 (*c* 5.45 in $CHCl_3$); ν_{max} ($CHCl_3$) 3604, 3452, 1650 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.75 (d, 3H, CH_3CHCH_2O, *J*=7.0 Hz), 1.02 (d, 3H, CH_3CHCHOH, *J*=7.0 Hz), 1.69 (s, 3H, CH_3C=CH), 1.80 (qn, 1H, H-4, *J*=7.0 Hz), 1.97–2.04 (m, 1H, H-6), 3.51 (t, 1H, H-7, *J*=9.0 Hz), 3.57 (dd, 1H, H-7, *J*=9.0, 4.0 Hz), 3.79 (d, 2H, H-5, *J*=9.0 Hz), 4.04–4.05 (m, 2H, H-3, OH), 4.50 (d, 1H, CH_2Ph, *J*=12.0 Hz), 4.54 (d, 1H, CH_2Ph, *J*=12.0 Hz), 4.95 (d, 1H, H-1, *J*=1.0 Hz), 5.12 (br s, 1H, 1-H), 7.25–7.36 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 10.1, 13.0, 18.8, 35.5, 35.8, 73.5, 76.1, 76.6, 79.3, 111.5, 127.6, 127.8, 128.4, 137.5, 146.0; MS (CI) *m/z*: 279.1960 [(M+H)$^+$. $C_{17}H_{27}O_3$ requires 279.1960], 279 (100%). Found: C, 73.6; H, 9.3; $C_{17}H_{26}O_3$ requires: C, 73.4; H, 9.4%.

9.6.7. (3*S*,4*S*,5*R*,6*R*)-7-*tert*-Butyldimethylsilyloxy-2,4,6-trimethyl-hept-1-ene-3,5-diol 55g. $Me_4NBH(OAc)_3$ (6.92 g, 26.3 mmol), acetic acid (20 mL), acetonitrile (100 mL) and the ketone **52g** (1.94 g, 6.37 mmol) were used according to the standard procedure at −50°C for 30 min then at −30°C for 48 h. Additional $Me_4NBH(OAc)_3$ (3.25 g, 12.4 mmol) was added and the mixture stirred for a further 24 h. Following the usual work-up, purification by flash chromatography (hexane/ether, 7:3→3:2) afforded the diol **55g** (1.51 g, 4.92 mmol, 77%) as a colourless oil; R_F 0.29 (hexane/ether, 1:1); $[\alpha]_D^{22}$=−18.6 (*c* 2.4 in $CHCl_3$); ν_{max} ($CHCl_3$) 3609, 3438 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.07 [s, 6H, $(CH_3)_2$Si], 0.69 (d, 3H, CH_3CHCH_2, *J*=6.9 Hz), 0.89 [s, 9H, $(CH_3)_3$C], 1.01 (d, 3H, CH_3CHCHOH, *J*=7.0 Hz), 1.69 (s, 3H, CH_3C=CH), 1.71–1.87 (m, 2H, H-4, H-6), 3.44 (d, 1H, OH, *J*=6.0 Hz), 3.58 (t, 1H, H-7, *J*=9.9 Hz), 3.72 (dd, 1H, H-7, *J*=9.9, 4.3 Hz), 3.80 (td, 1H, H-5, *J*=9.4, 1.5 Hz), 4.04 (d, 1H, H-3, *J*=6.0 Hz), 4.32 (s, 1H, OH), 4.93 (s, 1H, H-1), 5.10 (br s, 1H, H-1); δ_C ($CDCl_3$, 100 MHz) −5.6, 10.1, 12.6, 18.1, 18.7, 25.9, 35.8, 37.2, 69.9, 76.4, 79.3, 111.5, 146.4; MS (EI) *m/z*: 303.2350 [(M+H)$^+$. $C_{16}H_{35}O_3Si$ requires 303.2355].

9.7. Representative procedures for the preparation of the cyclic carbonates

9.7.1. (4*S*,6*S*)-4-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-6-vinyl-[1,3]dioxan-2-one 56a. *Preparation using carbonyldiimidazole*. A solution of the diol **55a** (26.8 mg, 0.107 mmol) and carbonyldiimidazole (20.5 mg, 0.126 mmol) in toluene (2 mL) was heated under reflux for 48 h. Further carbonyldiimidazole (2×10 mg) was added after 23 and 28 h, after which time no starting material remained. The reaction mixture was poured into water (5 mL) and extracted with ether (3×10 mL). The combined organic phases were washed with water (2×5 mL) and brine (5 mL), then they were dried (Na_2SO_4) and concentrated. Purification by flash chromatography (light petroleum/EtOAc, 7:3→1:0) gave the carbonate **56a** (19.5 mg, 0.071 mmol, 66%) as a colourless oil; R_F 0.34 (hexane/EtOAc, 1:1); $[\alpha]_D^{25}$=+56.0 (*c* 1.8 in $CHCl_3$); ν_{max} ($CHCl_3$) 1745 cm^{-1}; δ_H ($CDCl_3$, 360 MHz) 1.01 (d, 3H, CH_3, *J*=7.0 Hz), 1.94 (dt, 1H, H-5, *J*=14.0, 3.0 Hz), 2.10–2.42 (m, 2H, H-1′, H-5), 3.43–3.56 (m, 2H, H-2′), 4.42–4.57 (m, 3H, CH_2Ph, H-4), 5.04–5.07 (m, 1H, H-6), 5.36–5.43 (m, 2H, CH_2=CH), 5.85 (ddd, 1H, CH_2=CH, *J*=17.0, 11.0, 4.0 Hz), 7.24–7.37 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 12.5, 27.9, 37.6, 70.7, 73.2, 76.8, 112.6, 118.1, 127.6, 127.7, 128.4, 134.4, 138.2, 148.9; MS (CI) *m/z*: 277.1440 [(M+H)$^+$. $C_{16}H_{21}O_4$ requires 277.1440].

Preparation using triphosgene. To a solution of diol **55a** (37.6 mg, 0.15 mmol) in dichloromethane (0.75 mL) at −78°C was added dry pyridine (0.075 mL, 73 mg, 0.93 mmol). A solution of triphosgene (23 mg, 0.77 mmol) in dichloromethane (0.75 mL) was added dropwise via cannula. The mixture was stirred at −78°C for 15 min

and then quenched with a saturated aqueous solution of ammonium chloride (10 mL) before removing the cooling bath. The mixture was poured into ether (20 mL) and water (10 mL) and the organic phase separated. The organic layer was washed sequentially with saturated aqueous solutions of copper(II) sulphate (10 mL), sodium bicarbonate (10 mL) and brine (10 mL). The organic phase was dried ($MgSO_4$) and concentrated. Purification by flash chromatography (light petroleum/EtOAc, 4:1→0:1) gave the carbonate **56a** (18.5 mg, 0.067 mmol, 45%, data identical to previous values) and the starting diol **55a** (12.2 mg, 0.049 mmol, 33%).

9.7.2. (4*S*,6*S*)-4-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-6-[(*E*)-propenyl]-[1,3]dioxan-2-one 56b. The diol **55b** (3.35 g, 12.65 mmol), 4 Å molecular sieves (spatula tip), pyridine (6.14 mL, 6.0 g, 75.9 mmol), triethylamine (10.59 mL, 7.7 mL, 75.9 mmol), dichloromethane (75 mL) and triphosgene (1.88 g, 6.33 mmol) were used according to the standard procedure at −78°C for 30 min. Following work-up, the concentrate was passed through a silica plug (light petroleum/EtOAc, 3:1) to remove pyridine and then reconcentrated. Purification by flash chromatography (light petroleum/EtOAc, 3:1) yielded the carbonate **56b** as a pale yellow oil (2.81 g, 9.68 mmol, 77%); R_F 0.14 (light petroleum/EtOAc, 5:1); $[\alpha]_D^{25}$=+64.4 (*c* 5.52 in $CHCl_3$); ν_{max} ($CHCl_3$) 3019, 1737, 1674 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.00 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.76 (dt, 3H, CH_3C=C, *J*=6.5, 1.5 Hz), 1.90 (dt, 1H, H-5, *J*=14.5, 3.5 Hz), 2.05–2.18 (m, 2H, H-5, H-1′), 3.52 (m, 2H, H-2), 4.50 (dd, 2H, C*H*$_2$Ph, *J*=17.5, 12.0 Hz), 4.46–4.60 (m, 1H, H-4), 4.93–5.02 (m, 1H, H-6), 5.52 (ddq, 1H, MeCH=C*H*, *J*=15.5, 5.5, 1.5 Hz), 5.82 (ddq, 1H, Me*H*C=C, *J*=15.5, 6.5, 1.5 Hz), 7.22–7.36 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 12.4, 17.7, 28.3, 37.6, 70.8, 73.2, 76.8, 127.5, 127.5, 127.6, 128.4, 130.3, 138.2, 149.1; MS (CI) *m/z*: 308.1855 [(M+NH_4)$^+$. $C_{17}H_{26}O_4N$ requires 308.1862], 308 (84%), 229 (100). Found: C, 70.5; H, 7.66; $C_{17}H_{22}O_4$ requires C, 70.3; H, 7.64%.

9.7.3. (4*S*,6*S*)-6-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-4-[(*E*)-1-methyl-propenyl]-[1,3]dioxan-2-one 56c. The diol **55c** (54.4 mg, 0.195 mmol), toluene (4.2 mL) and carbonyldiimidazole (39 mg, 0.24 mmol) were used according to the standard procedure at reflux for 25 h. Further carbonyldiimidazole was added after 20 h (40 mg) and 23.5 h (5 mg). Purification by flash chromatography (dichloromethane/ether, 19:1) provided the carbonate **56c** (19.2 mg, 63 μmol, 32%) as a colourless oil; R_F 0.56 (hexane/ether, 9:1); $[\alpha]_D^{21}$=+10.2 (*c* 1.3 in $CHCl_3$); ν_{max} ($CHCl_3$) 1742 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.00 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.62 (dd, 3H, H-3″, *J*=11.0, 1.0 Hz), 1.71 (d, 3H, CH_3C=C, *J*=1.0 Hz,), 2.01–2.17 (m, 3H, H-1′, H-5), 3.52 (d, 1H, H-2′, *J*=5.0 Hz), 4.41–4.85 (m, 3H, C*H*$_2$Ph, H-4), 4.85 (br m, 1H, H-6), 5.53–5.57 (m, 1H, H-2″), 7.26–7.38 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 12.5, 12.7, 13.1, 26.4, 37.4, 70.9, 73.3, 76.9, 79.9, 122.6, 127.6, 127.7, 128.4, 131.4, 138.2, 149.4; MS (CI) *m/z*: 322.2018 [(M+NH_4)$^+$. $C_{18}H_{28}NO_4$ requires 322.2018], 322 (20%).

9.7.4. (4*S*,6*S*)-6-[(1*R*)-2-Benzyloxy-1-methyl-ethyl)-4-[(4*S*)-4-isopropenyl-cyclohex-1-enyl]-[1,3]-dioxan-2-one 56d. The diol **55d** (32.5 mg, 94.3 μmol), toluene (3 mL) and carbonyldiimidazole (18.1 mg, 110 μmol) were used according to the standard procedure at reflux for 24 h. Further carbonyldiimidazole was added after 16 h (19.6 mg) and 23 h (11.7 mg). Purification by flash chromatography (dichloromethane/ether, 19:1) gave the carbonate **56d** (9.6 mg, 26 μmol, 28%) as a colourless oil; R_F 0.58 (dichloromethane/ether, 9:1); $[\alpha]_D^{27}$=−16.7 (*c* 2.5 in $CHCl_3$); ν_{max} ($CHCl_3$)1739 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.00 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.25–2.41 (m, 13H, H-5, H-1′, H-3″, H-4″, H-5″, H-6″, C*H*$_3$C=CH$_2$), 3.45–3.59 (m, 2H, H-2′), 4.41–4.56 (m, 2H, C*H*$_2$Ph), 4.72 (dt, 1H, H-6, *J*=9, 2.5 Hz), 4.86 (br s, 1H, H-4), 5.29 (s, 2H, CH_2=C), 5.77–5.84 (m, 1H, H-2′), 7.18–7.38 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 12.3, 20.7, 25.3, 25.7, 27.0, 30.2, 37.2, 40.0, 70.7, 73.3, 78.7, 109.0, 124.1, 127.6, 127.7, 128.4, 132.9, 138.0, 149.1; MS (CI) *m/z*: 388.2488 [(M+NH_4)$^+$. $C_{23}H_{34}NO_4$ requires 388.2488], 388 (15%), 196 (100).

9.7.5. (4*S*,5*R*,6*R*)-6-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-5-methyl-4-isopropenyl-[1,3]dioxan-2-one 56e. The diol **55e** (38.5 mg, 0.138 mmol), toluene (3 mL) and carbonyldiimidazole (26.7 mg, 0.165 mmol) were used according to the standard procedure at reflux for 23 h. Further carbonyldiimidazole (2×13 mg) was added after 6.75 and 21.25 h. Purification by flash chromatography (dichloromethane/ether, 19:1) gave the carbonate **56e** as a colourless oil (42 mg, 0.138 mmol, 100%); R_F 0.64 (dichloromethane/ether, 9:1); $[\alpha]_D^{24}$=+23.3 (*c* 4.34 in $CHCl_3$); ν_{max} ($CHCl_3$) 1742 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.99 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.06 (d, 3H, C*H*$_3$CHCHO, *J*=7.0 Hz), 1.70 (s, 3H, CH_3C=C), 2.09–2.28 (dq, 1H, H-1′, *J*=7.0, 2.0 Hz), 2.27–2.37 (m, 1H, H-5), 3.56 (dd, 1H, H-2′, *J*=9.0, 3.0 Hz), 3.63 (dd, 1H, H-2′, *J*=9.0, 5.0 Hz), 4.20 (dd, 1H, H-6, *J*=8.0, 3.0 Hz), 4.51 (s, 2H, C*H*$_2$Ph), 4.79 (br s, 1H, H-4), 5.08 (d, 1H, *J*=1.0 Hz, C*H*H=CCH$_3$), 5.18 (br s, 1H, CH*H*=CH$_3$), 7.24–7.39 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 12.0, 14.0, 19.2, 29.2, 37.3, 71.0, 73.4, 79.3, 85.1, 113.3, 127.6, 127.6, 128.4, 138.2, 138.3, 148.9; MS (CI) *m/z*: 305.1753 [(M+H)$^+$. $C_{18}H_{25}O_4$ requires 305.1753], 322 [(M+NH_4)$^+$, 100%], 305 (20).

9.7.6. (4*S*,5*S*,6*R*)-6-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-5-methyl-4-isopropenyl-[1,3]dioxan-2-one 56f. The diol **55f** (71.9 mg, 0.258 mmol), toluene (5.5 mL) and carbonyldiimidazole (51 mg, 0.31 mmol) were used according to the standard procedure at reflux for 20 h. Further carbonyldiimidazole (50 mg) was added after 16.5 h. Purification by flash chromatography (dichloromethane/ether,1:0→19:1) gave the carbonate **56f** as a colourless oil (71.5 mg, 0.24 mmol, 91%); R_F 0.62 (light petroleum/ether, 9:1); $[\alpha]_D^{29}$=+61.7 (*c* 7.38 in $CHCl_3$); ν_{max} ($CHCl_3$) 1740 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 0.95 (d, 3H, C*H*$_3$CHCH$_2$, *J*=7.0 Hz), 1.14 (d, 3H, C*H*$_3$CHCHO, *J*=7.0 Hz), 1.73 (s, 3H, CH_3C=C), 1.90–2.05 (m, 1H, H-1′), 2.15 (dq, 1H, H-5, *J*=7.0, 1.0 Hz), 3.56 (dd, 1H, H-2′, *J*=9.0, 5.0 Hz), 3.60 (dd, H-1′, *J*=9.0, 7.0 Hz), 4.31 (dd, 1H, H-6, *J*=10.0, 2.5 Hz), 4.50 (s, 2H, C*H*$_2$Ph), 4.62 (br s, 1H, H-4), 5.03 (d, 1H, C*H*H=CCH$_3$, *J*=0.5 Hz), 5.11 (d, 1H, CH*H*=CCH$_3$, *J*=0.5 Hz), 7.25–7.33 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 11.0, 12.8, 19.1, 28.2, 35.0, 70.6, 73.2, 77.6, 85.9, 113.5, 127.5, 127.5, 128.3, 138.5, 140.6, 148.5; MS (CI) *m/z*: 305.1753 [(M+H)$^+$. $C_{18}H_{25}O_4$ requires 305.1753], 322 [(M+NH_4)$^+$, 100%], 305 (20).

9.7.7. (4*S*,5*S*,6*R*)-6-[(1*R*)-2-*tert*-Butyldimethylsilyloxy-1-methyl-ethyl]-5-methyl-4-isopropenyl-[1,3]dioxan-2-one 56g. The diol **55g** (1.45 g, 4.8 mmol), toluene (100 mL) and carbonyldiimidazole (0.9 g, 5.52 mmol) were used according to the standard procedure at reflux for 44 h. Further carbonyldiimidazole (0.9 g, 5.52 mmol) was added after 20 h. Purification by flash chromatography (hexane/ether, 4:1) gave the carbonate **56g** as white needle-like crystals (1.23 g, 3.74 mmol, 78%); mp 124–127°C; R_F 0.27 (hexane/EtOAc, 3:2); $[\alpha]_D^{22}=+45.2$ (*c* 1.89 in $CHCl_3$); ν_{max} ($CHCl_3$) 1739, 1653 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.02 [s, 6H, $(CH_3)_2Si$], 0.85 [s, 9H, $(CH_3)_3C$], 0.89 (d, 3H, CH_3CHCH_2, *J*=6.9 Hz), 1.14 (d, 3H, CH_3CHCHO, *J*=7.1 Hz), 1.73 (s, 3H, $CH_3C{=}C$), 1.77–1.85 (m, 1H, H-1′), 2.06–2.13 (m, 1H, H-5), 3.61 (dd, 1H, H-2′, *J*=9.8, 2.6 Hz), 3.79 (dd, 1H, H-1′, *J*=9.8, 4.4 Hz), 4.34 (dd, 1H, H-6, *J*=10.3, 2.4 Hz), 4.61 (br s, 1H, H-4), 5.03 (br s, 1H, $CHH{=}C$), 5.10 (br s, 1H, $CHH{=}C$); δ_C ($CDCl_3$, 100 MHz) −5.6, −5.5, 11.0, 12.3, 18.2, 19.0, 25.8, 28.1, 36.3, 62.9, 76.9, 85.9, 113.4, 140.8, 148.6; MS (CI, NH_3) *m/z* 329.2155 $[(M+H)^+$. $C_{17}H_{33}O_4Si$ requires 329.2148], 346 $[(M+NH_4)^+$, 20%], 329 (18), 83 (100). Found: C, 62.2; H, 9.9; $C_{17}H_{32}O_4Si$ requires: C, 62.2; H, 9.8%.

9.8. Representative procedure for tandem methylenation/Claisen rearrangement of the carbonates 56a–g

9.8.1. (8*S*)-8-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-3,4,7,8-tetrahydrooxocin-2-one 58a. A solution of the carbonate **56a** (40.5 mg, 0.147 mmol) and dimethyltitanocene (0.73 mL of a 50 mg/mL solution in toluene, 0.176 mmol) in toluene (5 mL) was heated at reflux in the absence of light for 3.5 h. The reaction mixture was allowed to cool, and was then concentrated. Purification by flash chromatography (light petroleum/EtOAc, 4:1) provided the lactone **58a** (20.9 mg, 0.076 mmol, 52%); R_F 0.23 (hexane/ether, 20:3); $[\alpha]_D^{27}=-3.9$ (*c* 3.65 in $CHCl_3$); ν_{max} ($CHCl_3$) 1740 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 1.04 (d, 3H, CH_3CH_2O, *J*=7.0 Hz), 1.96–2.26 (m, 3H, H-4, H-7, H-1′), 2.28–2.36 (ddd, 1H, H-3, *J*=16.0, 11.0, 6.0 Hz), 2.44–2.54 (ddd, 1H, H-7, *J*=11.0, 4.0, 2.0 Hz), 2.77–2.76 (m, 1H, H-3), 2.78–2.98 (m, 1H, H-4), 3.37 (dd, 1H, H-2′, *J*=9.0, 7.0 Hz), 3.58 (dd, 1H, H-2′, *J*=9.0, 5.0 Hz), 4.50 (s, 2H, CH_2Ph), 4.49–4.59 (m, 1H, H-8), 5.70–5.83 (m, 2H, H-5, H-6), 7.24–7.38 (5 H, m, ArH); δ_C ($CDCl_3$, 62.5 MHz) 14.1, 24.3, 31.4, 37.6, 37.9, 72.2, 73.2, 79.9, 127.5, 127.6, 128.3, 128.6, 132.7, 138.6, 177.0; MS (CI) *m/z*: 275.1647 $[(M+H)^+$. $C_{17}H_{23}O_3$ requires 275.1647]. Further elution of the column gave the carbonate **56a** (2.4 mg, 8.7 mmol, 6%).

9.8.2. (4*R*,8*S*)-8-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-4-methyl-3,4,7,8-tetrahydro-oxocin-2-one 58b. The carbonate **56b** (0.5 g, 1.72 mmol), toluene (70 mL) and dimethyltitanocene (9.3 mL of a 50 mg/mL solution in toluene, 2.23 mmol) were used according to the standard procedure for 3 h at reflux. The crude mixture was passed through a silica plug (light petroleum/EtOAc, 3:1) to remove baseline titanium residues. The filtrate was reconcentrated, and purification by flash chromatography (light petroleum/EtOAc, 17:3) provided the lactone **58b** as a pale yellow oil (0.255 g, 0.88 mmol, 52%); R_F 0.38 (light petroleum/EtOAc, 4:1); $[\alpha]_D^{24}=-38.6$ (*c* 1.07 in $CHCl_3$); ν_{max} ($CHCl_3$) 1719 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.05 (d, 3H, CH_3CH_2O, *J*=7.0 Hz), 1.14 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.94–2.07 (m, 1H, H-1′), 2.14–2.25 (m, 1H, H-7), 2.35 (dd, 1H, H-3, *J*=12.5, 11.0 Hz), 2.60 (dt, 1H, H-7, *J*=17.0, 5.0 Hz), 2.65 (dd, 1H, H-3, *J*=12.5, 5.5 Hz), 2.75–2.90 (m, 1H, H-4), 3.47–3.49 (m, 2H, H-2′), 4.49 (s, 2H, CH_2Ph), 4.70 (dt, 1H, H-8, *J*=9.0, 5.5 Hz), 5.56–5.59 (m, 2H, H-5, H-6), 7.25–7.37 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 14.0, 22.6, 30.2, 30.7, 37.1, 45.3, 71.8, 73.2, 76.0, 152.2, 127.5, 127.6, 128.3, 137.6, 138.6, 175.9; MS (CI) *m/z*: 289.1804 $[(M+H)^+$. $C_{18}H_{25}O_3$ requires 289.1804], 306 $[(M+NH_4)^+$, 45%], 289 (50). Found: C, 74.6; H, 8.4; $C_{18}H_{24}O_3$ requires C, 75.0; H, 8.4%.

9.8.3. (4*R*,8*S*)-8-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-4,5-dimethyl-3,4,7,8-tetrahydrooxocin-2-one 58c. The carbonate **56c** (18.6 mg, 61.1 μmol), toluene (2.6 mL) and dimethyltitanocene (0.32 mL of a 50 mg/mL solution in toluene, 76 μmol) were used according to the standard procedure at reflux for 4.5 h. Purification by flash chromatography (light petroleum/ether, 9:1→4:1) afforded the lactone **58c** (6.3 mg, 21 μmol, 34%) as a pale yellow oil; R_F 0.16 (hexane/EtOAc, 9:1); $[\alpha]_D^{25}=-17.9$ (*c* 0.7 in $CHCl_3$); ν_{max} ($CHCl_3$) 1722 cm^{-1}); δ_H ($CDCl_3$, 360 MHz) 1.03 (d, 3H, CH_3CH_2O, *J*=7.0 Hz), 1.10 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.70 (t, 3H, $CH_3C{=}C$, *J*=1.5 Hz), 1.94–2.01 (m, 1H, H-1′), 2.28 (dt, 1H, H-7, *J*=16.0, 9.0 Hz), 2.48 (dd, 1H, H-3, *J*=14.0, 11.0 Hz), 2.47–2.54 (m, 1H, H-7), 2.94 (dd, 1H, H-3, *J*=14.0, 7.0 Hz), 3.01–3.08 (m, 1H, H-4), 3.45 (dd, 1H, H-2′, *J*=9.0, 4.0 Hz), 3.53 (dd, 1H, H-2′, *J*=9.0, 5.0 Hz), 4.48 (s, 2H, CH_2Ph), 4.73 (dt, 1H, H-8, *J*=9.0, 5.0 Hz), 5.32 (dd, 1H, H-6, *J*=12.0, 5.0 Hz), 7.25–7.38 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 13.6, 18.8, 19.8, 31.0, 32.7, 38.7, 44.6, 71.7, 73.2, 77.6, 120.2, 127.8, 128.4, 138.4, 141.7, 174.4; MS (CI) *m/z*: 303.1960 $[(M+H)^+$. $C_{19}H_{27}O_3$ requires 303.1960].

9.8.4. (4*S*,9*S*,10a*R*)-4-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-9-isopropenyl-1,4,5,7,8,9,10,10a-octahydro-benzo[*d*]-oxocin-2-one 58d. The carbonate **56d** (15.1 mg, 40.8 μmol), toluene (1.3 mL) and dimethyltitanocene (0.22 mL of a 50 mg/mL solution in toluene, 53 μmol) were used according to the standard procedure at reflux for 24 h. The reaction mixture was diluted with light petroleum until the mixture became cloudy and filtered through a pad of silica. The mixture was then concentrated, and purification by flash chromatography (light petroleum/ether, 9:1→4:1) afforded the lactone **58d** (3.8 mg, 10 μmol, 25%) as a pale yellow oil; R_F 0.29 (hexane/ether, 5:1); $[\alpha]_D^{27}=+31.8$ (*c* 0.4 in $CHCl_3$); ν_{max} ($CHCl_3$) 1721 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 1.03 (d, 3H, CH_3CH_2O, *J*=7.0 Hz), 1.39–1.50 (m, 2H, H-4, H-7), 1.69 (s, 3H, $CH_3C{=}C$), 1.77 (m, 2H, H-4, H-7), 1.96–2.12 (m, 3H, H-5, H-6, H-1′), 2.23–2.37 (m, 2H, H-6, H-9), 2.47–2.56 (m, 2H, H-3, H-9), 2.66 (dd, 1H, H-3, *J*=12.0, 5.0 Hz), 2.84–2.80 (m, 1H, H-3a), 3.45 (dd, 1H, H-2′, *J*=9.0, 6.0 Hz), 3.51 (dd, 1H, H-2′, *J*=9.0, 4.0 Hz), 4.49 (s, 2H, CH_2Ph), 4.55 (dt, 1H, H-10, *J*=9.0, 6.0 Hz), 4.67 (br s, 2H, $C{=}CH_2$), 5.39 (t, 1H, H-8, *J*=7.0 Hz), 7.26–7.36 (m, 5H, ArH); δ_C ($CDCl_3$, 62.5 MHz) 14.0, 20.5, 29.8, 29.9, 32.1, 36.0, 37.4, 38.1, 41.6, 43.2, 71.9, 73.2, 76.9, 108.6, 118.2, 127.5, 127.6, 128.3, 138.0, 143.4, 149.4, 175.7; MS (CI) *m/z*: 369.2430 $[(M+H)^+$. $C_{24}H_{33}O_3$ requires 369.2430].

9.8.5. (7*S*,8*S*)-8-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-5,7-dimethyl-3,4,7,8-tetrahydrooxocin-2-one 58e. The carbonate **56e** (33.3 mg, 0.109 mmol), toluene (4 mL) and dimethyltitanocene (0.57 mL of a 0.24 M solution in toluene; 0.14 mmol) were used according to the standard procedure at reflux for 3 h. Purification by flash chromatography (hexane/ether, 9:1) afforded the lactone **58e** (15.8 mg, 0.052 mmol, 48%) as a pale yellow oil; R_F 0.33 (light petroleum/ether, 17:3); $[\alpha]_D^{25}=-48.1$ (*c* 1.1 in $CHCl_3$); ν_{max} ($CHCl_3$) 1737 cm^{-1}; δ_H ($CDCl_3$, 500 MHz) 0.97 (d, 3H, CH_3CH, *J*=7.0 Hz), 1.09 (d, 3H, CH_3CH$_2$O, *J*=7.0 Hz), 1.70 (s, 3H, CH_3CH$_2$), 1.85–1.89 (ddd, 1H, H-4, *J*=12.0, 5.0, 2.0 Hz), 2.00–2.24 (m, 1H, H-1′), 2.37–2.43 (dtm 1H, H-3, *J*=13.0, 5.0 Hz, 3-H), 2.68–2.83 (ddd, 1H, H-3, *J*=13.0, 6.0, 2.0), 2.78–2.84 (m, 1H, H-7), 2.91 (dt, 1H, H-4, *J*=12.0, 6.0 Hz), 3.30 (dd, 1H, H-2′, *J*=9.0, 8.0 Hz), 3.74 (dd, 1H, *J*=9.0, 6.0 Hz, H-2′), 4.27 (dd, 1H, H-8, *J*=10.0, 2.0 Hz), 4.53 (s, 2H, CH_2Ph), 5.07 (d, 1H, H-6, *J*=7.0 Hz), 7.26–7.36 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 16.2, 17.0, 24.1, 29.5, 33.9, 36.5, 36.6, 70.7, 73.1, 87.7, 127.4, 127.5, 128.3, 131.5, 138.0, 138.6, 176.4; MS (CI) *m/z*: 303.1960 [(M+H)$^+$. $C_{19}H_{27}O_3$ requires 303.1960], 320 [(M+NH_4)$^+$, 100%], 303 (20).

9.8.6. (7*R*,8*S*)-8-[(1*R*)-2-Benzyloxy-1-methyl-ethyl]-5,7-dimethyl-3,4,7,8-tetrahydrooxocin-2-one 58f. The carbonate **56f** (1.8 g, 5.9 mmol), and dimethyltitanocene (34.0 mL of a 50 mg/mL solution in toluene, 8.26 mmol) were used according to the standard procedure at reflux for 16 h. Purification by flash chromatography on silica (hexane/ether, 17:3) afforded the lactone **58f** (1.13 g, 3.73 mmol, 63%) as a pale yellow oil; R_F 0.28 (light petroleum/ether, 17:3); $[\alpha]_D^{20}=+5.38$ (*c* 5.7 in $CDCl_3$); ν_{max} ($CHCl_3$) 1735 cm^{-1}; δ_H ($CDCl_3$, 250 MHz) 1.01 (d, 3H, CH_3CHCH$_2$O, *J*=7.0 Hz), 1.15 (d, 3H, CH_3CHCH$_2$, *J*=6.0 Hz), 1.72 (s, 3H, CH_3CHCHO), 2.05–2.08 (m, 1H, H-1′), 2.12–2.18 (m, 1H, H-4), 2.46–2.53 (m, 2H, H-3, H-7), 2.63–2.71 (m, 2H, H-3, H-4), 3.38 (dd, 1H, H-2′, *J*=9.0, 7.0 Hz), 3.57 (dd, 1H, H-2′, *J*=9.0, 3.0 Hz), 4.48 (s, 2H, CH_2Ph), 4.61 (dd, H-8, 1H, *J*=9.0, 3.0 Hz), 5.41 (dd, 1H, H-6, *J*=8.0, 1.5 Hz), 7.24–7.33 (m, 5H, ArH); δ_C ($CDCl_3$, 100 MHz) 14.1, 14.4, 26.0, 30.0, 31.6, 34.8, 35.3, 36.2, 72.6, 73.2, 81.4, 127.4, 127.6, 128.3, 128.7, 137.6, 138.6, 176.6; MS (CI, NH_3) *m/z*: 303.1960 [(M+H)$^+$. $C_{19}H_{27}O_3$ requires 303.1960], 320 [(M+NH_4)$^+$, 40%], 303 (20), 106 (100). Found: C, 75.5; H, 8.6; $C_{19}H_{26}O_3$ requires C, 75.5; H, 8.7%.

9.8.7. (7*R*,8*S*)-8-[(1*R*)-2-*tert*-Butyldimethylsilyloxy-1-methyl-ethyl]-5,7-dimethyl-3,4,7,8-tetrahydrooxocin-2-one 58g. The carbonate **56g** (1.19 g, 3.62 mmol), toluene (100 mL) and dimethyltitanocene (21.0 mL of a 50 mg/mL solution in toluene; 5.05 mmol) were used according to the standard procedure at reflux for 20 h. Purification by flash chromatography (hexane/ether, 17:3) afforded the lactone **58g** (0.788 g, 2.41 mmol, 67%) as a yellow oil; R_F 0.48 (hexane/ether, 4:1); $[\alpha]_D^{22}=+8.0$ (*c* 1.5 in $CHCl_3$); ν_{max} ($CDCl_3$) 1739 cm^{-1}; δ_H ($CDCl_3$, 400 MHz) 0.03 [s, 6H, (CH_3)$_2$Si], 0.89 [s, 9H, (CH_3)$_3$C)], 0.94 (d, 3H, CH_3CHCH$_2$O, *J*=6.8 Hz), 1.15 (d, 3H, CH_3CHCHO, *J*=7.3 Hz), 1.73 (d, 3H, CH_3C=C, *J*=0.9 Hz), 1.84–1.94 (m, 1H, H-1′), 2.16–2.23 (m, 1H, H-4), 2.46–2.57 (m, 1H, H-7), 2.57–2.74 (m, 3H, H-3, H-4), 3.52 (dd, 1H, H-2′, *J*=9.7, 6.4 Hz), 3.66 (dd, 1H, H-2′, *J*=9.7, 3.2 Hz), 4.63 (dd, 1H, H-8, *J*=9.4, 3.2 Hz), 5.41 (dd, 1H, H-6, *J*=7.4, 0.9 Hz); δ_C ($CDCl_3$ 100 MHz) −5.4, 18.3, 26.0, 29.9, 35.4, 36.0, 36.7, 64.9, 80.9, 128.8, 137.5, 176.4; MS (CI, NH_3) *m/z*: 327.2381 [(M+H)$^+$. $C_{18}H_{35}O_3Si$ requires 327.2355], 344 [(M+NH_4)$^+$, 2%], 327 (40), 195 (100).

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