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Application of silacyclic allylsilanes to the synthesis of β-hydroxy-δ-lactones: synthesis of Prelactone B

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ABSTRACT

Silacyclic allylsilanes generated through a silene–diene Diels–Alder cycloaddition represent versatile bifunctional reagents for organic synthesis. This is demonstrated in a short stereocontrolled synthesis of (±)-Prelactone B.

1. Introduction

Allylsilanes are valuable and versatile intermediates for organic synthesis that enable a multitude of transformations notably the allylation of aldehydes, ketones and acetals.[1] Whilst the presence of the weakly polar C–Si bond is essential for this chemistry, this functionality is commonly lost during the reaction. In contrast, with cyclic allylsilanes the C–Si bond is retained in the product for further elaboration and thus these represent simple bifunctional reagents that permit two directional synthetic strategies to be developed.

As a component of a project exploring new silicon mediated synthetic methodology we have been exploring the chemistry of silacyclic allylsilanes generated through the cycloaddition of a transient silene.[2] As with acyclic allylsilanes these undergo allylation reactions to produce homoallylic alcohols but with the silicon functionality retained. This can subsequently be elaborated to provide an additional oxygen functionality and we have exploited this to produce butane-1,4-diols and aryltetralols.[3–5] Alternatively, electrophilic addition to the alkene enables functionalisation of the silacycle prior to activation and oxidation of the silicon unit. We first demonstrated this in the preparation of δ-lactones[6] and in this paper present the full details of the extension of this approach to produce β-hydroxy-δ-lactones.[7] This structural motif is found in a wide range of natural products, Figure 1. In this exemplification of our new methodology we focused on the relatively simple subgroup of β-hydroxy-δ-lactone natural products represented by the prelactones and in particular Prelactone B. Isolated from *Streptomyces griseus*, by Bindseil and Zeeck in 1993,[8] Prelactone B **1** is a shunt product of the biosynthetic pathway to macrolide bafilomycin. As with all the prelactones it has become a popular synthetic target to highlight new methodologies and a number of other synthetic routes have been reported.[9–25]

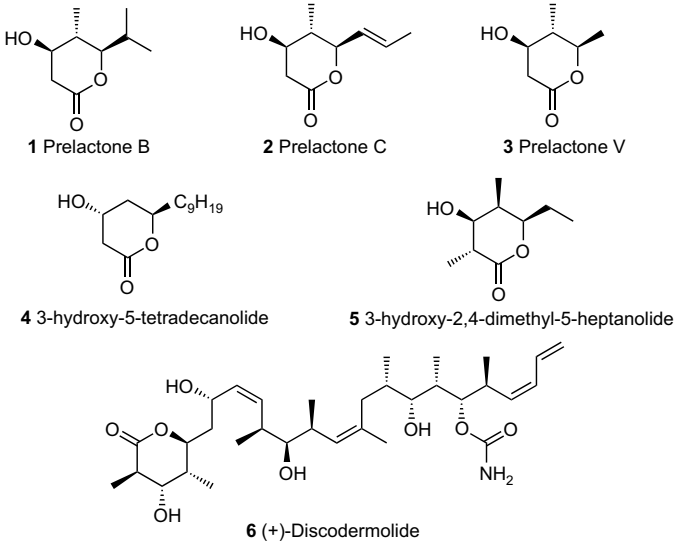

Figure 1. Selected examples of naturally occurring β-hydroxy-δ-lactones.

2. Results and discussion

Our initial retrosynthetic analysis of β-hydroxy-δ-lactones is shown in Scheme 1. The key intermediate was the silacyclohexene **10**, which would be generated through the Diels–Alder reaction of a suitably substituted butadiene and a transient silene. The latter could be generated in situ through the modified Peterson reaction of the 'silyl alcohol' **13**. At the outset of the project we envisaged

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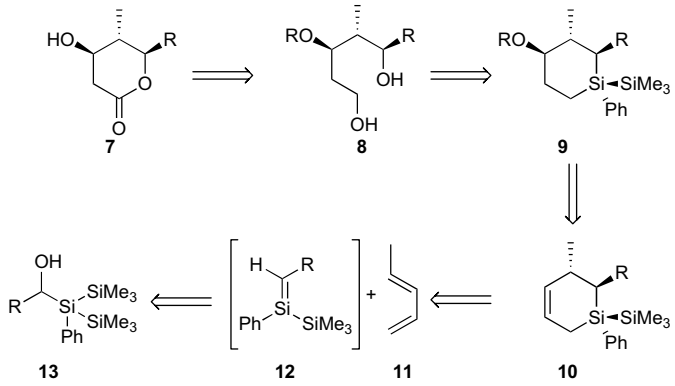
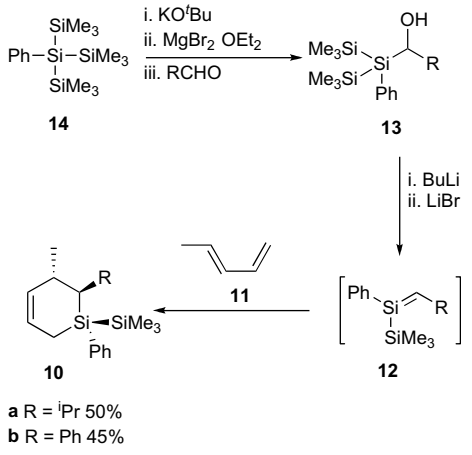


Scheme 1.

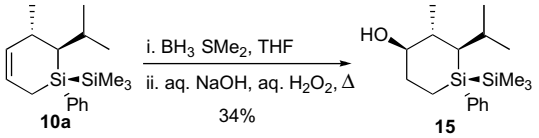
that the desired β-hydroxy group could be introduced by simple hydroboration directed by the presence of the silicon atom.[26] Following this, simple activation of the silyl centre and subsequent two-step oxidation, following the precedents of our earlier studies, would afford the desired lactone. With this in mind we commenced our studies by preparing the requisite silacycles.

Condensation of the hypersilyl magnesium reagent, generated from phenyltris(trimethylsilyl)silane **14**[27] by reaction with KO*t*Bu in THF followed by transmetallation with freshly prepared magnesium bromide in ether, with isobutyraldehyde or benzaldehyde afforded the silyl alcohols **13a** and **13b**, respectively. Treatment of a mixture of the silyl alcohol and excess 1,3-pentadiene with BuLi followed by the addition of LiBr afforded the key silacyclohexenes as an inseparable mixture of stereoisomers (ds 70:20:10) favouring the desired *endo* product **10** as ascertained by a combination of ^{1}H, ^{29}Si NMR, GC–MS analysis and subsequent chemical conversions, Scheme 2.[28]



Scheme 2.

With these silacyclic allylsilanes in hand attention then turned to the hydroboration sequence. Following precedents established by Soderquist, who had previously demonstrated that silacycles could be employed in these transformations with no significant side reactions at silicon,[29] **10a** was treated with borane–dimethylsulfide complex to afford after oxidation the desired alcohol in a modest 34% yield, accompanied by a significant amount of the putative alternative regioisomer (≤20%), Scheme 3. Attempts to enhance this process through the use of alternative borane sources or oxidation conditions proved to be unsuccessful. Moreover, all attempts to oxidise the C–Si bonds, either directly or following protection of the newly formed hydroxyl group, failed to provide the expected triol and alternative strategies for the elaboration of the silacycle were considered.



Scheme 3.

White had previously reported that epoxidation of silacyclohexene **16** could be efficiently achieved using classical Payne conditions, Figure 2.[30] Our intention was to utilise this, or other epoxidation methods, to provide access to the silacyclic oxirane **18**, which, when subjected to the Fleming–Tamao oxidation conditions, would undergo a regioselective fragmentation reaction, directed by the silicon atom, to produce the diol **21**, Scheme 4.

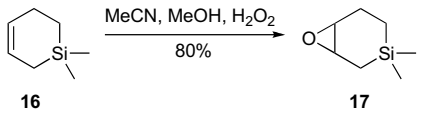
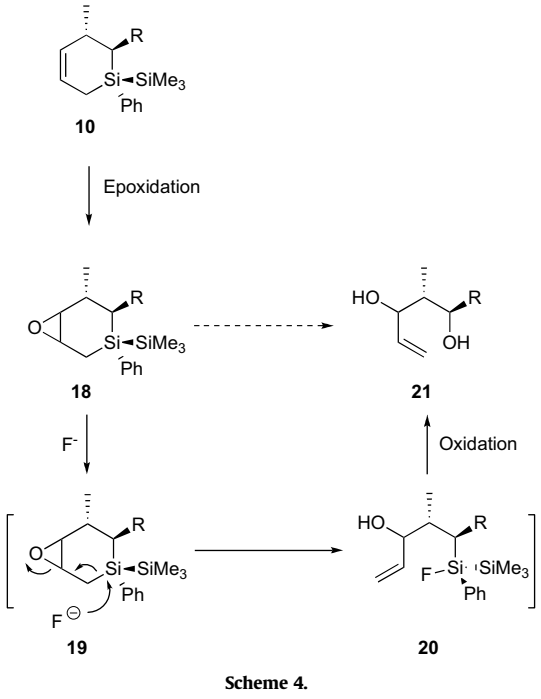
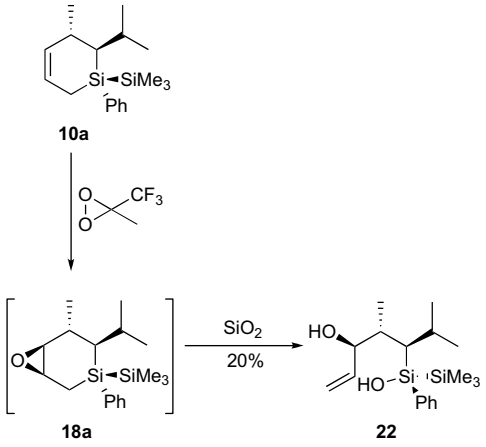


Figure 2.



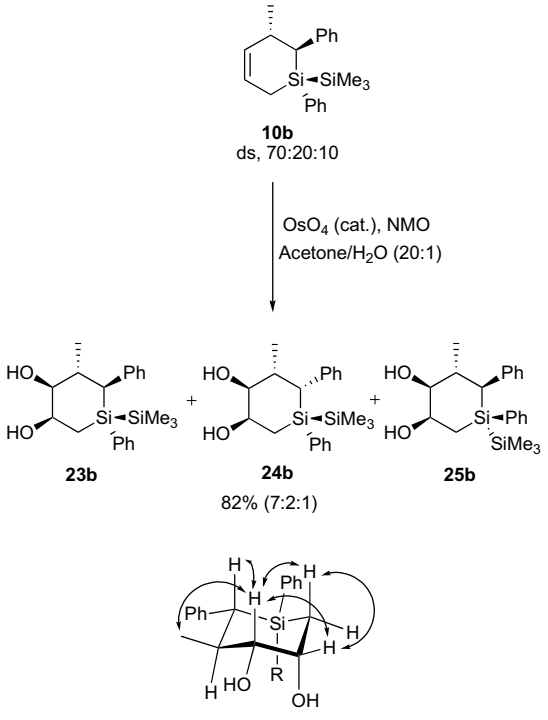
Scheme 4.

Whilst many epoxidation reagents either failed to react or led to extensive loss of material, successful epoxidation was ultimately realised through the use of (methyl)trifluoromethyldioxirane, albeit at low levels of conversion (~25%). This epoxide proved to be highly labile undergoing silicon induced ring fragmentation on passage through silica gel, Scheme 5. Interestingly this afforded a single diastereoisomer of the silanol **22** indicating that both epoxidation and nucleophilic attack at the silicon centre were highly stereoselective events. Whilst the stereochemistry at the latter position could not be unambiguously assigned we speculate that it is as shown in Scheme 5 reflecting inversion on substitution at silicon. Whilst the yield was disappointing, the selectivity of the reaction was promising and attention turned to dihydroxylation as this would also lead to intermediate **21** on silicon mediated ring fragmentation. Although the dihydroxylation of allylsilanes including silacyclic allylsilanes is well documented in the literature,[31–33] the dihydroxylation of silacyclohex-4-enes has not been



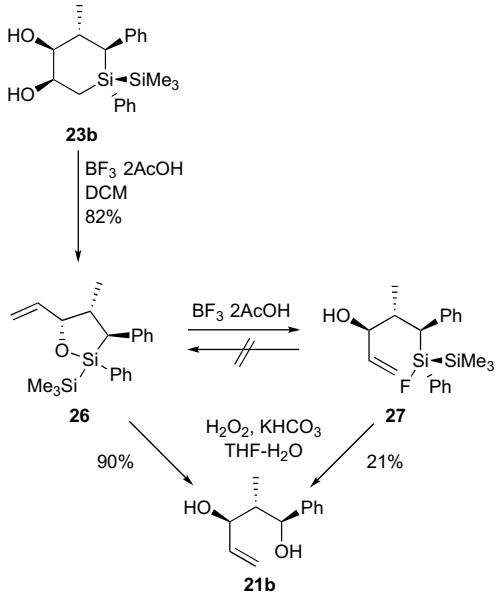
Scheme 5.

described. Despite this, treatment of silacycle **10b** using the classical Upjohn conditions (cat. OsO_4, NMO, acetone/H_2O 20:1) afforded the corresponding diols **23b**–**25b** in a combined 82% yield in a ratio of isomers reflecting that found in the starting material. Flash chromatography enabled the major diastereoisomer **23b** to be separated with subsequent NOESY experiments showing correlations consistent with the 4-hydroxy group being *trans* to the methyl group, Scheme 6.



Scheme 6.

Having developed an efficient oxidation protocol it was then necessary to promote ring fragmentation. Treatment of the diol **23b** with $BF_3{\cdot}2AcOH$ complex afforded a 1:1 mixture of diastereoisomers that showed a complete absence of a fluorine signal as ascertained by ^1H and ^{19}F NMR spectroscopy, respectively. ESMS analysis suggested a molecular ion of m/z=352, which coupled with a characteristic siloxane peak at δ=−21 ppm in the ^{29}Si NMR spectrum suggested this intermediate to be the cyclic siloxane **26**. Importantly, in the context of prelactone synthesis, direct oxidation

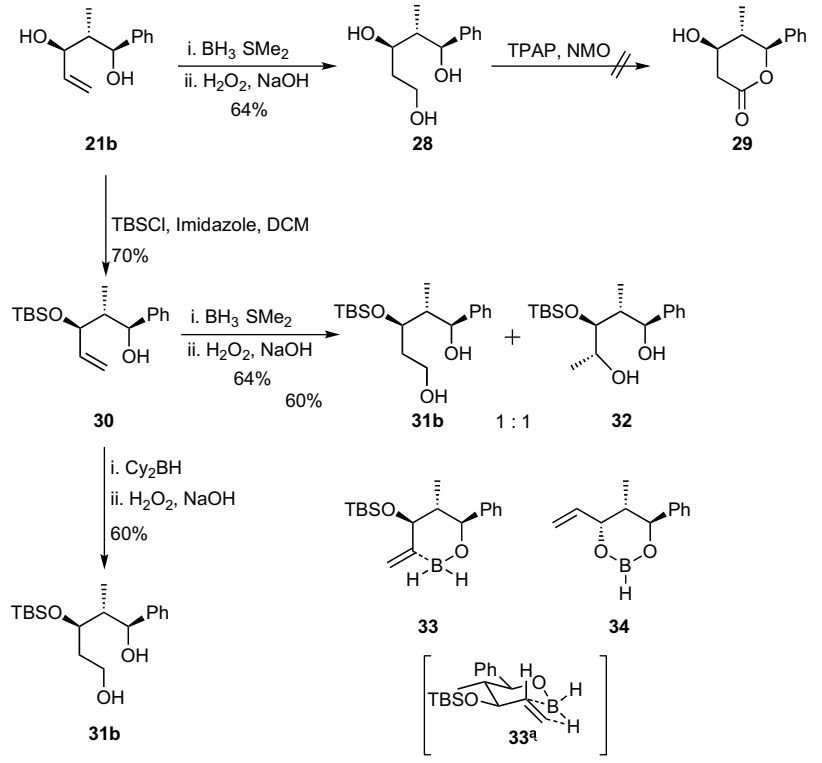


Scheme 7.

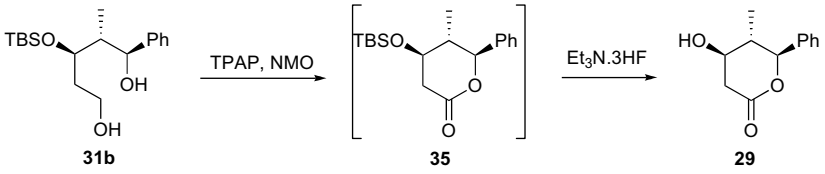
of this intermediate with hydrogen peroxide afforded the desired diol **21b** in 72% yield as a single diastereoisomer, Scheme 7.

On the basis of our earlier studies exploring the Hosomi Sakurai reaction in which the formation of a single silyl fluoride diastereoisomer could be observed,[3] the generation of a 1:1 isomeric mixture was unusual and merited further investigation. Whilst two possible reaction pathways could account for the formation of the cyclic siloxane neither is fully consistent with the production of a 1:1 isomeric mixture. Whilst a formal intramolecular S_N2 reaction of the allylic alcohol with silyl fluoride **27** leads to the observed product this might be expected to afford a single stereoisomer. Although scrambling of stereochemistry during substitution at silicon is possible via Berry pseudorotation the cyclic nature of this substrate might be expected to inhibit such a process. Similarly, whilst the observed product mixture could arise through a dissociative S_N1 type process the requirement for a 'silyl cation' renders this less likely. Consequently, in order to probe this transformation, further experiments were undertaken. Since both pathways require the intermediacy of the acyclic silyl fluoride **27**, the cyclic siloxane **26** was treated with $BF_3{\cdot}2AcOH$ complex. This afforded a new highly labile species, which resisted purification but on oxidation using hydrogen peroxide allowed isolation of the diol **21b**, albeit in a low (21%) yield. Curiously, ^1H and ^{19}F NMR analyses revealed it to be a single diastereoisomeric species possessing one fluorine atom. This was proposed to be the silyl fluoride **27** based on a characteristic doublet (δ=−140.8) observed in the ^{19}F NMR spectrum. Attempts to reverse the ring opening with base were not successful, leading to extensive decomposition, suggesting that the silyl fluoride is possibly not the original product of the fragmentation in these processes.

Returning to the synthesis of the prelactones, having identified an efficient method for the generation of diol **21b**, it remained to oxidise the alkene to a carboxylic acid and cyclise to form the lactone ring. Initial attempts to achieve this directly via hydroboration with in-situ oxidation proved not to be viable. Whilst simple hydroboration–oxidation did afford the desired triol **28** attempts to oxidise this proved not to be selective resulting in complex mixtures of products. Since the oxidative cyclisation of 1,6-diols to give lactones had been achieved using similar conditions in our earlier studies it was felt that protection of the allylic alcohol was required. Fortunately, this could be achieved by simple treatment with TBSCl and imidazole. Confirmation of the desired regiochemistry was

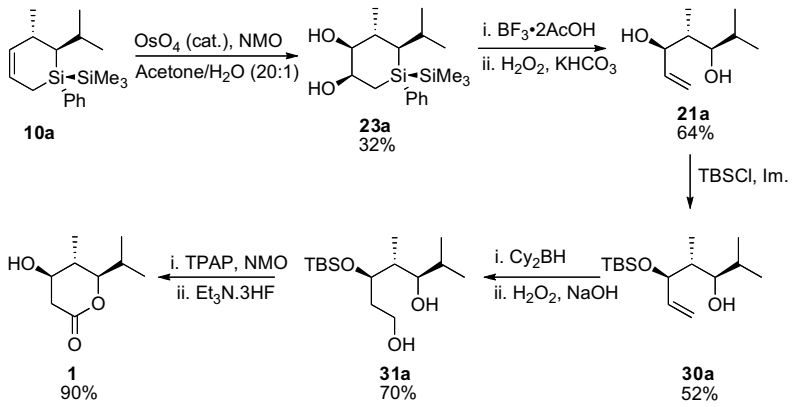


Scheme 8.



Scheme 9.

obtained through NOESY studies of the resultant silyl ether **30**, which revealed correlations between the methyl group of the TBS unit and the allylic, rather than the benzylic methine, hydrogen. Whilst, with the interfering alcohol now masked, alkene hydroboration using $BH_3 \cdot SMe_2$ complex followed by hydrogen peroxide oxidation proceeded smoothly this led to a 1:1 regioisomeric mixture of diols **31b** and **32** in 60% yield. This result differed to that obtained previously for the hydroboration of diol **21b** suggesting that the TBS group forces the allyl group in **30** into close proximity with a coordinated borane molecule leading to an intramolecular delivery of borane to the alkene. In contrast, with **21b** the borane reagent can coordinate both hydroxyl groups, locking the molecule and enabling selective hydroboration at the least hindered position, cf. structures **33** and **34**. In support of such a proposal diol **32** was isolated as a single, albeit unconfirmed, diastereoisomer consistent with a cyclic 6-membered ring transition state structure **33**‡ in which all substituents occupy pseudoequatorial positions. Based on this analysis we turned to more hindered boranes and explored the use of dicyclohexylborane. To our satisfaction, when treated with an excess of freshly prepared dicyclohexylborane and oxidised



Scheme 10.

under standard conditions, the desired diol **31b** was generated as the sole product in 60% yield. None of the regioisomeric product was present by TLC or ^{1}H NMR analysis of the crude material, Scheme 8.

With an efficient synthetic strategy in place to gain access to the 1,5-diols, attention turned to the final oxidation. Lactonisation of diol **31b** was undertaken with TPAP and NMO. Pleasingly, the lactone product **35b** was generated efficiently and on mild silicon deprotection utilising $Et_3N{\cdot}3HF$ in THF provided the β-hydroxy-δ-lactone **29** in quantitative yield from diol **31b**, Scheme 9.

Simple repetition of this sequence starting with the isopropyl substituted silacycle **10a** then afforded Prelactone B **1** in comparable yields, Scheme 10. The spectroscopic data for Prelactone B proved to be identical with those previously reported in the literature.

3. Conclusions

We have described a concise and flexible approach to the synthesis of the prelactones. This chemistry relies on the bifunctional nature of the cyclic allylsilanes that can be conveniently generated through a silene–diene cycloaddition. The modular nature of the approach will facilitate its future application to more highly substituted β-hydroxy-δ-lactones and work in this regard is in progress and will be reported in due course.

4. Experimental

4.1. General procedures

All air and/or moisture sensitive reactions were carried out under an argon atmosphere. Solvents were purified and dried following established protocols. Petrol refers to petroleum spirit boiling in the 40–60 °C range. Ether refers to diethyl ether. Aldehydes and dienes were distilled, immediately prior to use, from anhydrous calcium sulfate and sodium borohydride, respectively. All other commercially available reagents were used as received unless otherwise stated. Flash column chromatography was performed according to the method of Still et al. using 200–400 mesh silica gel.[34] Yields refer to isolated yields of products of greater than 95% purity as determined by ^{1}H+^{13}C NMR spectroscopy. Melting points were determined using Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded using a Diamond ATR (attenuated total reflection) accessory (Golden Gate) on a Perkin–Elmer FT-IR 1600 spectrometer. Unless otherwise stated ^{1}H NMR spectra were recorded in $CDCl_3$ on Varian Mercury 200, Varian Unity-300, Varian VXR-400 or Varian Inova-500 and are reported as follows; chemical shift δ (parts per million) (number of protons, multiplicity, coupling constant J (Hz), assignment). Residual protic solvent $CHCl_3$ (δ_H=7.26) was used as the internal reference. ^{13}C NMR spectra were recorded at 63 MHz or 126 MHz, using the central resonance of $CDCl_3$ (δ_C=77.0 ppm) as the internal reference. ^{29}Si NMR spectra were recorded at 99 MHz on Varian Inova-500. All chemical shifts are quoted in parts per million relative to tetramethylsilane (δ_H=0.00 ppm) and coupling constants are given in hertz. All ^{13}C spectra were proton decoupled. Assignment of spectra was carried out using DEPT, COSY, HSQC, HMBC and NOESY experiments.

Gas chromatography-mass spectra (GC–MS, EI or CI) were obtained using a Thermo TRACE mass spectrometer. Electrospray (ES) mass spectra were obtained on a Micromass LCT mass spectrometer. High-resolution mass spectra were obtained using a Thermo LTQ mass spectrometer (ES) at the University of Durham, or performed by the EPSRC National Mass Spectrometry Service Centre, University of Wales, Swansea. Methods for the preparation of and associated characterisation data for silacyclohexenes **10a** and **10b** have previously been reported.[28]

4.1.1. *(1SR,2RS,3SR,4RS/SR) 1-Phenyl-1-trimethylsilyl-2-(isopropyl)-3-methyl-4-hydroxysilacyclohexane* ***15***

Borane–dimethylsulfide complex (0.060 ml, 0.70 mmol) in THF (4 ml) was cooled to 0 °C and treated with a solution of silacyclohex-4-ene **10a** (200 mg, 0.70 mmol) in THF (4 ml). The reaction was stirred for 2 h at 0 °C, then for 1 h at room temperature and treated with water (0.40 ml) (H_2 gas evolved), followed by 3 M NaOH (0.20 ml, 0.70 mmol) and a 35% w/w solution of H_2O_2 in water (0.20 ml, 2.2 mmol). The mixture was refluxed at 65 °C for 4 h after which time $Na_2S_2O_3$ (10 ml) was added. The aqueous layer was separated and extracted with EtOAc (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether, pet. ether/ether [14:1], [9:1], [4:1], [2:1]) afforded the title compound as a white solid (0.070 g, 34%); mp 118–120 °C; R_f 0.3 (pet. ether/ether 3:2); ν_{max} (ATR) 3368 (broad-OH), 3067, 2922, 2872, 1726, 1462, 1427, 1244, 1102, 1048, 1019, 852, 833, 735, 700 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.55–7.51 (2H, m, Ar-*H*), 7.32–7.29 (3H, m, Ar-*H*), 3.26 (1H, td, *J* 11, 3, 4-*H*), 2.18 (1H, m, 3-*H*), 2.05 (1H, m, 2-C*H*(CH_3)$_2$), 1.65 (2H, m, 6-H_2), 1.45 (1H, m, 2-*H*), 1.26 (2H, m, 5-H_2), 1.14 (3H, d, *J* 7, 2-CH(CH_3)$_2$), 1.00 (3H, d, *J* 7, 3-CH_3), 0.75 (3H, d, *J* 7, 2-CH(CH_3)$_2$), 0.29 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 139.9 (*ipso*-Ar-*C*), 134.5 (Ar-*C*), 128.5 (Ar-*C*), 127.9 (Ar-*C*), 77.8 (4-*C*), 41.9 (3-*C*), 38.6 (2-*C*), 35.2 (2-*C*H(CH_3)$_2$), 33.5 (5-*C*), 23.5 (2-CH(CH_3)$_2$), 22.1 (2-CH(CH_3)$_2$), 18.4 (3-*C*H_3), 9.6 (6-*C*), 0.3 (Si(CH_3)$_3$); *m*/*z* (ES$^+$) 343 (MNa$^+$), 303 (M$^+$−H_2O).

4.1.2. *(3RS,4SR,5RS,(Si)RS/SR) 3-(1-Hydroxy-2,2,2-trimethyl-1-phenyldisilanyl)-5-hydroxy-2,4-dimethylhept-6-ene* ***22***

A solution of silacyclohex-4-ene **10a** (100 mg, 0.30 mmol) in acetonitrile (2.5 ml) was cooled to 0 °C and treated with EDTA disodium salt (1.7 ml, 0.40 mM) and trifluoroacetone (0.30 ml, 3.7 mmol). This solution was then treated with a mixture of $NaHCO_3$ (0.20 g, 2.6 mmol) and oxone (1.0 g, 1.7 mmol) over a period of 1 h and reacted for a further 3 h, after which time the reaction was poured into water and extracted with DCM (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether, pet. ether [99:1], [98:2]) afforded the title silanol as a colourless oil (25 mg, 22%); R_f 0.6 (pet. ether/ether 9:1); ν_{max} (thin film) 3068 (broad-OH), 2956, 2928, 2892, 2870, 1718, 1427, 1244, 1103, 1004, 855, 835, 699 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.58–7.55 (2H, m, Ar-*H*), 7.35–7.34 (3H, m, Ar-*H*), 5.75 (1H, ddd, *J* 17, 10, 7, 6-*H*), 5.21 (1H, d, *J* 17, 7-*H*H), 5.08 (1H, d, *J* 10, 7-H*H*), 4.53 (1H, t, *J* 7, 5-*H*), 2.28 (1H, m, 4-*H*), 1.99 (1H, septet, *J* 6, 2-*H*), 1.26 (1H, m, 3-*H*), 1.09 (3H, d, *J* 6, 1-*H*), 1.07 (3H, d, *J* 6, 2-CH_3), 0.86 (3H, d, *J* 6, 4-CH_3), 0.17 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 139.6 (*ipso*-Ar-C), 137.5 (6-*C*), 133.7 (Ar-*C*), 128.9 (Ar-*C*), 127.8 (Ar-*C*), 116.4 (7-*C*), 84.3 (5-*C*), 44.5 (3-*C*), 40.7 (4-*C*), 27.5 (2-*C*), 25.2 (1-*C*), 23.4 (2-CH_3), 16.6 (4-CH_3), −1.4 (Si(CH_3)$_3$); *m*/*z* (ES$^+$) 359 (MNa$^+$); HRMS (ES$^+$). Found MNa$^+$, 359.1837 ($C_{18}H_{32}O_2Si_2Na$ requires 359.1833).

4.1.3. *(1SR,2SR,3SR,4SR,5SR) 4,5-Dihydroxy-3-methyl-1,2-diphenyl-1-(trimethylsilyl)silacyclohexane* ***23b***

A solution of silacyclohex-4-ene **10b** (50 mg, 0.15 mmol) in acetone/water (2.1 ml, 20:1) was treated with NMO (35 mg, 0.30 mmol), cooled to 0 °C and treated with a catalytic amount of osmium tetroxide (1.9 mg, 0.0070 mmol). After stirring for 45 min the reaction mixture was treated with aq $Na_2S_2O_3$ and extracted with EtOAc (3×5 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo gave the crude diols as a 7:2:1 mixture of diastereoisomers. Flash chromatography (pet. ether/ether [1:1], [1:2]) afforded the title dihydroxyl silacycle

23b as a colourless gum (30 mg, 56%); R_f 0.3 (pet. ether/ether 1:1); ν_{max} (thin film) 3631–3579 (broad-OH), 3069, 3026, 2955, 2925, 2895, 2871, 1598, 1426, 1256, 1242, 1049, 1021, 896, 835, 781 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.31–7.21 (5H, m, Ar-*H*), 7.18–7.12 (3H, m, Ar-*H*), 7.08–7.06 (2H, m, Ar-*H*), 4.48 (1H, m, 5-*H*), 3.38 (1H, dd, *J* 10, 3, 4-*H*), 2.57 (1H, m, 3-*H*), 2.15 (1H, d, *J* 12, 2-*H*), 1.63 (1H, dd, *J* 15.5, 6, 6-*H*H), 1.34 (1H, dd, *J* 15.5, 6, 6-H*H*), 0.95 (3H, d, *J* 7, 3-CH_3), 0.03 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 143.2 (*ipso*-Ar-*C*), 137.2 (*ipso*-Ar-*C*), 134.9 (Ar-*C*), 128.9 (Ar-*C*), 128.8 (Ar-*C*), 128.6 (Ar-*C*), 127.7 (Ar-*C*), 125.1 (Ar-*C*), 79.8 (4-*C*), 72.2 (5-*C*), 41.0 (2-*C*), 36.1 (3-*C*), 18.1 (3-CH_3), 17.5 (6-*C*), -0.7 (Si(CH_3)$_3$); δ_{Si} (100 MHz, $CDCl_3$) −18.72, −21.22; *m*/*z* (ES^+) 393 (MNa^+), 425 (MNa+$MeOH^+$), 763 ($2MNa^+$); HRMS (ES^+) Found MNa^+, 393.1676 ($C_{21}H_{30}O_2Si_2Na$ requires 393.1677). Further elution afforded an inseparable mixture of diols **24b** and **25b** (24%); key ^1H NMR signals (500 MHz, $CDCl_3$) 4.49 (1H, m, 5-*H*), 4.37 (1H, m, 5-*H*), −0.04 (9H, s, Si(CH_3)$_3$), −0.11 (9H, s, Si(CH_3)$_3$).

4.1.4. (1SR,2RS,3SR,4SR,5SR) 4,5-Dihydroxy-1-phenyl-1-trimethylsilyl-2-(isopropyl)-3-methylsilacyclohexane **23a**

Following the same procedure as described for diol **10b**, silacyclohex-4-ene **10a** (170 mg, 0.56 mmol) was transformed into the title compound, which was isolated as a yellow oil (60 mg, 32%); R_f 0.3 (pet. ether/ether 1:1); ν_{max} (thin film) 3498–3211 (broad-OH), 2950, 2932, 2898, 2864, 1426, 1096, 1022, 992, 832, 731, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.53–7.51 (2H, m, Ar-*H*), 7.31–7.30 (3H, m, Ar-*H*), 4.20 (1H, m, 5-*H*), 3.49 (1H, m, 4-*H*), 2.25 (1H, m, 3-*H*), 2.14 (1H, m, 2-C*H*(CH_3)$_2$), 1.36 (1H, dd, *J* 14, 9, 6-*H*H), 1.18 (1H, m, 6-H*H*), 1.08 (1H, dd, *J* 9, 6, 2-*H*), 1.04 (3H, d, *J* 7, 2-CH(CH_3)$_2$), 0.97 (3H, d, *J* 7, 3-CH_3), 0.91 (3H, d, *J* 7, 2-CH(CH_3)$_2$), 0.21 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 140.2 (*ipso*-Ar-*C*), 134.4 (Ar-*C*), 128.5 (Ar-*C*), 128.0 (Ar-*C*), 78.8 (4-*C*), 70.2 (5-*C*), 36.8 (2-*C*), 35.8 (3-*C*), 29.1 (2-*C*H(CH$_3$)$_2$), 23.8 (2-CH(*C*H$_3$)$_2$), 19.4 (3-CH$_3$), 16.5 (6-*C*), −0.4 (Si(*C*H$_3$)$_3$); δ_{Si} (100 MHz, $CDCl_3$) −17.90, −23.36; *m*/*z* (ES^+) 359 (MNa^+); HRMS (ES^+). Found MNa^+, 359.1834 ($C_{18}H_{32}Si_2O_2Na$ requires 359.1833). Further elution afforded an inseparable mixture of diols **24a** and **25a**; key ^1H NMR signals (300 MHz, $CDCl_3$) 4.15 (1H, m, 5-*H*), 3.83 (1H, m, 5-*H*), 0.23 (9H, s, Si(CH_3)$_3$), 0.05 (9H, s, Si(CH_3)$_3$).

4.1.5. (3RS,4RS,5RS) 4,6-Dimethylhept-1-ene-3,5-diol **21a**

To a solution of silacyclic diol **23a** (60 mg, 0.18 mmol) in dry DCM (4 ml) was added trifluoroborane–acetic acid complex (0.049 ml, 0.36 mmol). The solution was stirred for 15 min at room temperature then mixed with saturated $NaHCO_3$ solution (5 ml) and extracted with DCM (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo to give a colourless oil, which was used immediately without further purification.

To the colourless oil was added $KHCO_3$ (50 mg, 0.54 mmol) and KF (21 mg, 0.36 mmol). The mixture was dissolved in methanol/THF solution (1:1, 4 ml) and a 35% w/w solution of H_2O_2 in water (0.21 ml, 2.1 mmol) then added. The mixture was heated to reflux and stirred for 1 h. The mixture was then allowed to cool to room temperature and saturated $Na_2S_2O_3$ solution (5 ml) was added together with EtOAc (10 ml). The aqueous layer was separated and extracted with EtOAc (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether/ether [9:1], [4:1], [3:2], [1:1], [1:2]) afforded the desired diol **21a** as a colourless oil (18 mg, 64%); R_f 0.3 (pet. ether/ether 1:1); ν_{max} (thin film) 3525–3134 (broad-OH), 2962, 2870, 1459, 1427, 1118, 1081, 974, 919, 844, 697, 639 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 5.94 (1H, ddd, *J* 16, 10, 5, 2-*H*), 5.29 (1H, d, *J* 16, 1-*H*H), 5.19 (1H, d, *J* 10, 1-H*H*), 4.41 (1H, s, 3-*H*), 3.39 (1H, m, 5-*H*), 3.11 (1H, br s, –O*H*), 2.53 (1H, br s, –O*H*), 1.89 (1H, qd, *J* 7, 3, 4-*H*), 1.82 (1H, m, 6-*H*), 0.94 (3H, d, *J* 8, 7-CH_3), 0.92 (3H, d, *J* 8, 6-CH_3), 0.87 (3H, d, *J* 7, 4-CH_3); δ_C (126 MHz, $CDCl_3$) 138.9 (2-*C*), 115.4 (1-*C*), 79.8 (5-*C*), 75.1 (3-*C*), 39.6 (4-*C*), 30.6 (6-*C*), 20.0 (7-CH_3), 16.0 (6-CH_3), 12.2 (4-CH_3); *m*/*z* (ES^+) 181 (MNa^+); HRMS (ES^+). Found MNa^+, 181.1199 ($C_9H_{18}O_2Na$ requires 181.1199).

4.1.6. (1SR,2SR,3RS) 2-Methyl-1-phenylpent-4-ene-1,3-diol **21b**

Following the same procedure outlined above, silacyclic diol **23b** (120 mg, 0.32 mmol) was transformed into the title compound **21b**, which was isolated as a colourless oil (45 mg, 72%); R_f 0.3 (pet. ether/ether 1:1); ν_{max} (thin film) 3502–3214 (broad-OH), 3064, 2974, 2886, 1721, 1711, 1690, 1601, 1512, 1450, 1332, 1216, 1128, 1080 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.38–7.36 (4H, m, Ar-*H*), 7.33–7.28 (1H, m, Ar-*H*), 6.00 (1H, ddd, *J* 16, 10, 5, 4-*H*), 5.33 (1H, d, *J* 16, 5-*H*H), 5.26 (1H, d, *J* 10, 5-H*H*), 4.69 (1H, d, *J* 9, 1-*H*), 4.40 (1H, m, 3-*H*), 2.95 (1H, br s, –O*H*), 2.11 (1H, qd, *J* 9, 3, 2-*H*), 0.82 (3H, d, *J* 9, 2-CH_3); δ_C (126 MHz, $CDCl_3$) 143.7 (*ipso*-Ar-*C*), 138.5 (4-*C*), 128.7 (Ar-*C*), 128.0 (Ar-*C*), 126.8 (Ar-*C*), 115.8 (5-*C*), 78.3 (1-*C*), 74.9 (3-*C*), 44.3 (2-*C*), 12.5 (2-CH_3); *m*/*z* (ES^+) 215 (MNa^+); HRMS (ES^+). Found MNa^+, 215.1043 ($C_{12}H_{16}O_2Na$ requires 215.1043).

4.1.7. (2SR/RS,3SR,4SR,5SR) 4-Methyl-2,3-diphenyl-2-(trimethylsilyl)-5-vinyl-1,2-oxasilolane **26**

To a solution of silacyclic diol **23b** (40 mg, 0.11 mmol) in dry DCM (2 ml) was added trifluoroborane–acetic acid complex (0.030 ml, 0.22 mmol). The solution was stirred for 15 min at room temperature then mixed with saturated $NaHCO_3$ solution (5 ml) and extracted with DCM (3×5 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether, pet. ether/ether [98:2]) gave the title compound as an opaque oil (27 mg, 72%) as an inseparable 1:1 mixture of diastereoisomers; R_f 0.3 (pet. ether/ether 98:2); ν_{max} (thin film) 2956, 2923, 1650, 1555, 1427, 1244, 1107, 1003, 835, 698 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.62–7.59 (2H, m, Ar-*H*), 7.43–7.41 (3H, m, Ar-*H*), 7.34–7.30 (3H, m, Ar-*H*), 7.24–7.20 (2H, m, Ar-*H*), 7.17–7.03 (9H, m, Ar-*H*), 6.74 (1H, d, *J* 8, Ar-*H*{B}), 5.95 (1H, ddd, *J* 17, 9, 6, 5-C*H*=CH$_2${B}), 5.84 (1H, ddd, *J* 17, 11, 8, 5-C*H*=CH$_2${A}), 5.41 (1H, d, *J* 17, 5-CH=C*H*H{B}), 5.31 (1H, d, *J* 9, 5-CH=CH*H*{B}), 5.30 (1H, m, 5-CH=C*H*H{A}), 5.17 (1H, d, *J* 11, 5-CH=CH*H*{A}), 4.92 (1H, t, *J* 6, 5-*H*{B}), 4.80 (1H, t, *J* 7, 5-*H*{A}), 2.94 (1H, sept, *J* 7, 4-*H*{A}), 2.72 (1H, d, *J* 12, 3-*H*{A}), 2.69–2.63 (2H, m, 4-*H*, 3-*H*{B}), 0.95 (3H, d, *J* 7, 4-CH_3{A}), 0.91 (3H, d, *J* 6, 4-CH_3{B}), 0.21 (9H, s, Si(CH_3)$_3${B}), 0.11 (9H, s, Si(CH_3)$_3${A}); δ_C (126 MHz, $CDCl_3$) 140.9 (*ipso*-Ar-*C*), 139.4 (*ipso*-Ar-C), 138.8 (*ipso*-Ar-C), 137.2 (5-*C*H=CH$_2${B}), 136.7 (5-*C*H=CH$_2${A}), 135.7 (*ipso*-Ar-*C*), 133.9 (Ar-*C*), 133.0 (Ar-*C*), 129.3 (Ar-*C*), 129.0 (Ar-*C*), 128.3 (Ar-*C*), 128.0 (Ar-*C*), 127.7 (Ar-*C*), 127.4 (Ar-*C*), 126.8 (Ar-*C*), 124.7 (Ar-*C*), 124.4 (Ar-*C*), 116.7 (5-CH=*C*H$_2${B}), 116.4 (5-CH=*C*H$_2${A}), 84.6 (5-*C*{A}), 83.4 (5-*C*{B}), 41.7 (3-*C*{A}), 41.5 (4-*C*{A}), 40.27 (3-*C*{B}), 40.25 (4-*C*{B}), 15.3 (4-*C*H$_3${A}), 15.1 (4-*C*H$_3${B}),-2.1 (Si(*C*H$_3$)$_3${A}), −1.3 (Si(*C*H$_3$)$_3${B}); δ_{Si} (100 MHz, $CDCl_3$) 19.5, 14.5, −20.8, −21.0; *m*/*z* (ES^+) 353 (MH^+); HRMS (ES^+). Found MH^+, 353.1752 ($C_{21}H_{29}OSi_2$ requires 353.1752).

4.1.8. (1SR,2SR,3RS) 2-Methyl-1-phenylpentane-1,3,5-triol **28**

A solution of diol **21b** (20 mg, 0.10 mmol) in THF (1 ml) was treated with borane–dimethylsulfide complex (0.035 ml, 0.37 mmol) at 0 °C. The reaction was then warmed to room temperature and reacted for 1 h. The mixture was then treated successively with water (0.50 ml), NaOH (0.035 ml, 0.10 mmol) and H_2O_2 (0.13 ml, 1.3 mmol). The mixture was then refluxed for 1 h, at which point the mixture was cooled and poured into $Na_2S_2O_3$ and extracted with EtOAc (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (DCM/MeOH [98:2], [95:5], [9:1]) afforded the title triol as a colourless oil (15 mg, 64%); R_f 0.3 (DCM/MeOH 9:1); ν_{max} (thin film) 3348–3119 (broad-OH), 2962, 2924, 2360, 1684, 1437, 1338, 1223, 1077, 907, 730, 650 cm^{-1}; δ_H (500 MHz, $CDCl_3$)

7.36–7.34 (4H, m, Ar-*H*), 7.28 (1H, m, Ar-*H*), 4.68 (1H, d, *J* 8, 1-*H*), 4.08 (1H, d, *J* 11, 3-*H*), 3.89–3.82 (3H, m, 5-H_2, –O*H*), 1.98–1.93 (3H, m, 4-*H*H, 2-*H*, –O*H*), 1.55 (1H, d, *J* 11, 4-H*H*), 0.83 (3H, d, *J* 7, 2-CH_3); δ_C (126 MHz, $CDCl_3$) 143.8 (*ipso*-Ar-*C*), 128.7 (Ar-*C*), 127.9 (Ar-*C*), 126.7 (Ar-*C*), 78.5 (1-*C*), 74.7 (3-*C*), 63.0 (5-*C*), 44.4 (2-*C*), 34.4 (4-*C*), 12.8 (2-CH_3); *m*/*z* (ES^+) 233 (MNa^+); HRMS (ES^+). Found MNa^+, 233.1148 ($C_{12}H_{18}O_3Na$ requires 233.1148).

4.1.9. (3RS,4RS,5RS) 5-(tert-Butyldimethylsilyloxy)-2,4-dimethylhept-6-en-3-ol **30a**

To a solution of diol **21a** (18 mg, 0.11 mmol) in dry DCM (2 ml) were added imidazole (31 mg, 0.47 mmol) and *tert*-butylchlorodimethylsilane (21 mg, 0.14 mmol). The solution was stirred for 2 h at room temperature then diluted with EtOAc and washed with water (5 ml) and brine (5 ml). The organic layer was dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether/ether [95:5], [9:1]) afforded the desired the title silyl ether **30a** as a colourless oil (16 mg, 52%); R_f 0.3 (pet. ether/ether 95:5); ν_{max} (thin film) 3630–3130 (broad-OH), 2957, 2930, 2857, 1471, 1384, 1254, 1126, 1022, 996, 835, 776 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 5.93 (1H, ddd, *J* 17, 10, 6, 6-*H*), 5.22 (1H, d, *J* 17, 7-*H*H), 5.19 (1H, d, *J* 10, 7-H*H*), 4.30 (1H, m, 5-*H*), 3.95 (1H, br s, –O*H*), 3.41 (1H, d, *J* 9, 3-*H*), 1.82 (1H, m, 4-*H*), 1.68 (1H, qd, *J* 7, 2, 2-*H*), 0.99 (3H, d, *J* 7, 1-*H*), 0.91 (9H, s, SiC(CH_3)$_3$), 0.86 (3H, d, *J* 7, 2-CH_3), 0.77 (3H, d, *J* 7, 4-CH_3), 0.09 (3H, s, Si(CH_3)$_2$^{t}Bu), 0.06 (3H, s, Si(CH_3)$_2$^{t}Bu); δ_C (126 MHz, $CDCl_3$) 137.3 (6-*C*), 116.4 (7-*C*), 79.1 (5-*C*), 77.5 (3-*C*), 41.3 (4-*C*), 30.1 (2-*C*), 26.0 (SiC(CH_3)$_3$), 20.4 (1-*C*), 18.4 (Si*C*(CH_3)$_3$), 14.2 (2-CH_3), 13.1 (4-CH_3), −4.3 (Si(CH_3)$_2$^{t}Bu), −5.0 (Si(CH_3)$_2$^{t}Bu); *m*/*z* (ES^+) 295 (MNa^+); HRMS (ES^+) Found MH^+, 273.2245 ($C_{15}H_{33}O_2Si$ requires 273.2244).

4.1.10. (1SR,2RS,3RS) 3-(tert-Butyldimethylsilyloxy)-2-methyl-1-phenylpent-4-en-1-ol **30b**

Following the same procedure as described for **30a**, diol **21b** (20 mg, 0.10 mmol) was converted into the title ether, which was isolated as a colourless oil (22 mg, 70%); R_f 0.3 (pet. ether/ether 95:5); ν_{max} (thin film) 3572–3286 (broad-OH), 2960, 2932, 2894, 2852, 1468, 1368, 1256, 1026, 926, 832, 770 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.34–7.27 (5H, m, Ar-*H*), 6.05 (1H, ddd, *J* 17, 10, 7, 4-*H*), 5.33–5.27 (2H, dd, *J* 17, 10, 5-H_2), 4.54 (1H, d, *J* 9, 1-*H*), 4.45–4.43 (1H, m, 3-*H*), 2.04 (1H, sd, *J* 9, 3, 2-*H*), 0.99 (9H, s, SiC(CH_3)$_3$), 0.58 (3H, d, *J* 9, 2-CH_3), 0.17 (3H, s, Si(CH_3)$_2$^{t}Bu), 0.12 (3H, s, Si(CH_3)$_2$^{t}Bu); δ_C (126 MHz, $CDCl_3$) 143.9 (*ipso*-Ar-*C*), 137.2 (4-*C*), 128.4 (Ar-*C*), 127.7 (Ar-*C*), 127.3 (Ar-*C*), 116.7 (5-*C*), 78.3 (3-*C*), 77.6 (1-*C*), 45.7 (2-*C*), 26.1 (SiC(CH_3)$_3$), 18.3 (Si*C*(CH_3)$_3$), 13.4 (2-CH_3), −4.2 (Si(CH_3)$_2$^{t}Bu) −4.9 (Si(CH_3)$_2$^{t}Bu); *m*/*z* (ES^+) 329.3 (MNa^+), 635 ($2MNa^+$); HRMS (ES^+). Found MNa^+, 329.1907 ($C_{18}H_{30}O_2SiNa$ requires 329.1907).

4.1.11. (3RS,4RS,5RS) 3-(tert-Butyldimethylsilyloxy)-4,6-dimethylheptane-1,5-diol **31a**

A solution of alkene **30a** (16 mg, 0.060 mmol) in THF (2 ml) was treated with an excess of freshly prepared dicyclohexylborane at 0 °C. The reaction was then warmed to room temperature and reacted for 1 h. The reaction was then treated successively with water (0.50 ml), 3 M aq NaOH (0.050 ml, 0.15 mmol) and H_2O_2 (0.070 ml, 0.71 mmol). The mixture was then refluxed for 1 h, then cooled, poured into $Na_2S_2O_3$ and extracted with Et_2O (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether/ether [1:1], [2:3]) afforded the title diol as a colourless oil (12 mg, 70%); R_f 0.3 (pet. ether/ether 1:1); ν_{max} (thin film) 3562–3356 (broad-OH), 3005, 2949, 2931, 1713, 1417, 1360, 1223, 1089, 1051, 838, 530 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 4.00 (1H, m, 3-*H*), 3.79 (1H, m, 1-H*H*), 3.70 (1H, m, 1-*H*H), 3.51 (1H, dd, *J* 10, 2, 5-*H*), 1.90–1.83 (2H, m, 4-*H*, 2-*H*H), 1.78 (1H, m, 2-H*H*), 1.68 (1H, m, 6-*H*), 1.00 (3H, d, *J* 6, 7-CH_3), 0.90 (9H, s, SiC(CH_3)$_3$), 0.84 (3H, d, *J* 6, 6-CH_3), 0.76 (3H, d, *J* 7, 4-CH_3), 0.41 (3H, s, Si(CH_3)$_2$^{t}Bu), 0.11 (3H, s, Si(CH_3)$_2$^{t}Bu); δ_C (126 MHz, $CDCl_3$) 75.4 (3-*C*), 60.2 (1-*C*), 40.3 (4-*C*), 34.0 (2-*C*), 30.0 (6-*C*), 26.0 (SiC(CH_3)$_3$), 20.4 (7-CH_3), 18.4 (Si*C*(CH_3)$_3$), 13.83 (6-CH_3), 13.82 (4-CH_3), −4.1 (Si(CH_3)$_2$^{t}Bu), −4.7 (Si(CH_3)$_2$^{t}Bu); *m*/*z* (ES^+) 313 (MNa^+), 291 (MH^+); HRMS (ES^+) Found MH^+, 291.2349 ($C_{15}H_{35}O_3Si$ requires 291.2350).

4.1.12. (1SR,2RS,3RS) 3-(tert-Butyldimethylsilyloxy)-2-methyl-1-phenylpentane-1,5-diol **31b**

Following the identical procedure as outlined for compound **31a**, alkene **30b** (20 mg, 0.070 mmol) was transformed into the title diol **31b**, which was isolated as a colourless oil (12 mg, 60%); R_f 0.3 (pet. ether/ether 2:3); ν_{max} (thin film) 3490–3182 (broad-OH), 2956, 2932, 2886, 2860, 1684, 1676, 1560, 1437, 1259, 1202, 1075, 1050, 781 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.34–7.31 (5H, m, Ar-*H*), 4.58 (1H, d, *J* 10, 1-*H*), 4.14 (1H, dt, *J* 10, 3, 3-*H*), 3.85 (1H, m, 5-H*H*), 3.75 (1H, m, 5-*H*H), 2.07–1.96 (2H, m, 2-*H*, 4-*H*H), 1.89 (1H, m, 4-H*H*), 0.97 (9H, s, SiC(CH_3)$_3$), 0.57 (3H, d, *J* 7, 2-CH_3), 0.22 (3H, s, Si(CH_3)$_2$^{t}Bu), 0.16 (3H, s, Si(CH_3)$_2$^{t}Bu); δ_C (126 MHz, $CDCl_3$) 143.9 (*ipso*-Ar-*C*), 128.5 (Ar-*C*), 127.8 (Ar-*C*), 127.3 (Ar-*C*), 77.8 (1-*C*), 74.6 (3-*C*), 60.1 (5-*C*), 45.2 (2-*C*), 34.3 (4-*C*), 26.1 (SiC(CH_3)$_3$), 18.2 (Si*C*(CH_3)$_3$), 14.0 (2-CH_3), −4.1 (Si(CH_3)$_2$^{t}Bu), −4.6 (Si(CH_3)$_2$^{t}Bu); *m*/*z* (ES^+) 347 (MNa^+); HRMS (ES^+). Found MNa^+, 347.2014 ($C_{18}H_{32}O_3SiNa$ requires 347.2013).

4.1.13. (1SR,2RS,3SR,4RS) 3-(tert-Butyldimethylsilyloxy)-2-methyl-1-phenylpentane-1,4-diol **32**

A solution of mono-protected diol **30b** (22 mg, 0.070 mmol) in THF (1 ml) was treated with borane–dimethylsulfide complex (0.020 ml, 0.18 mmol) at 0 °C. The reaction was then warmed to room temperature and stirred for 1 h. The reaction was then treated successively with water (0.50 ml), NaOH (0.020 ml, 0.070 mmol) and H_2O_2 (0.090 ml, 0.86 mmol). The mixture was then refluxed for 1 h, at which point the mixture was cooled and poured into $Na_2S_2O_3$ and extracted with Et_2O (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (pet. ether, pet. ether/ether [9:1], [4:1], [1:1], [2:3]) afforded the title compound as a white solid (7 mg, 30%); R_f 0.4 (pet. ether/ether 2:3); mp 120–122 °C; ν_{max} (ATR) 3518–3190 (broad-OH), 3124, 3030, 2962, 2932, 2856, 1606, 1255, 1068, 1024, 896, 835, 716 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.38–7.31 (5H, m, Ar-*H*), 4.46 (1H, d, *J* 9, 1-*H*), 4.11 (1H, dd, *J* 5, 2, 3-*H*), 3.99 (1H, m, 4-*H*), 2.53 (1H, s, –O*H*), 2.19–2.06 (2H, m, 2-*H*, –O*H*), 1.26 (3H, d, *J* 8, 5-*H*), 0.99 (9H, s, SiC(CH_3)$_3$), 0.71 (3H, d, *J* 7, 2-CH_3), 0.22 (3H, s, Si(CH_3)$_2$^{t}Bu), 0.17 (3H, s, Si(CH_3)$_2$^{t}Bu); δ_C (126 MHz, $CDCl_3$) 143.9 (*ipso*-Ar-*C*), 128.4 (Ar-*C*), 127.7 (Ar-*C*), 126.9 (Ar-*C*), 76.7 (1-*C*), 75.4 (3-*C*), 70.3 (4-*C*), 41.8 (2-*C*), 25.9 (SiC(CH_3)$_3$), 19.1 (5-*C*), 18.3 (Si*C*(CH_3)$_3$), 12.0 (2-CH_3), −4.2 (Si(CH_3)$_2$^{t}Bu), −4.6 (Si(CH_3)$_2$^{t}Bu); *m*/*z* (ES^+) 347 (MNa^+); HRMS (ES^+). Found MNa^+, 347.2011 ($C_{18}H_{32}O_3SiNa$ requires 347.2013). Further elution afforded 3-(*tert*-butyldimethylsilyloxy)-2-methyl-1-phenylpentane-1,5-diol **31b** (7 mg, 30%) identical with that described above.

4.1.14. (±)-Prelactone B **1**

A solution of 1,6-diol **31a** (12 mg, 0.041 mmol) in DCM (2 ml) was treated with NMO (15 mg, 0.12 mmol) and 4 Å molecular sieves. The mixture was then treated with TPAP (0.70 mg, 0.0020 mmol) at room temperature. After 1 h at room temperature the mixture was filtered through a pad of silica gel (pet. ether/ether 2:3). The filtrate was concentrated and dried in vacuo to give a colourless oil, which was then redissolved in THF (2 ml) and treated with $Et_3N{\cdot}3HF$ (0.070 ml, 0.41 mmol) at room temperature. The reaction was left overnight and then mixed with water (2 ml) and extracted with DCM (3×10 ml). The combined organic layers

were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash chromatography (DCM/ether [9:1], [4:1], [7:3]) afforded the desired lactone as a white solid (5 mg, 90%); R_f 0.3 (DCM/ether 7:3); mp 90–92 °C (lit. mp 97–98 °C); [10]ν_{max} (ATR) 3516–3180 (broad-OH), 2967, 2929, 2876, 2260, 2245, 1731 (C=O), 1600, 1253, 1009, 896, 716, 650 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 3.78–3.76 (2H, m, 6-*H*, 4-*H*), 2.93 (1H, dd, *J* 17, 6, 3-*H*H), 2.48 (1H, dd, *J* 17, 6, 3-H*H*), 2.00 (1H, qd, *J* 7, 2, 6-C*H*$(CH_3)_2$), 1.74 (1H, m, 5-*H*), 1.10 (3H, d, *J* 7, 6-CH$(CH_3)_2$), 1.08 (3H, d, *J* 7, 5-CH_3), 0.92 (3H, d, *J* 7, 6-CH$(CH_3)_2$); δ_C (126 MHz, $CDCl_3$) 170.7 (*C*=O), 86.2 (6-*C*), 69.9 (4-*C*), 39.1 (5-*C*), 39.0 (3-*C*), 28.9 (6-*C*H$(CH_3)_2$), 20.0 (6-CH$(CH_3)_2$), 14.0 (5-CH_3), 13.5 (6-CH$(CH_3)_2$); *m*/*z* (ES^+) 195 (MNa^+), 227 (MNa+$MeOH^+$); HRMS (ES^+). Found MH^+, 173.1173 ($C_9H_{17}O_3$ requires 173.1172). All data agree with those reported in the literature.[10]

4.1.15. (4RS,5SR,6SR) 4-Hydroxy-5-methyl-6-phenyltetrahydro-2H-pyran-2-one ***29***

Following the same protocol as outlined above for Prelactone B, diol **31b** (12 mg, 0.037 mmol) was converted into the title lactone **29**, which was isolated as a white solid (8 mg, 100%); R_f 0.3 (DCM/ether 7:3); mp 118–120 °C; ν_{max} (ATR) 3530–3190 (broad-OH), 2922, 2852, 2359, 2339, 1736 (C=O), 1654, 1245, 1161, 1056, 1022, 894, 837 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.42–7.38 (3H, m, Ar-*H*), 7.34–7.27 (2H, m, Ar-*H*), 4.77 (1H, d, *J* 11, 6-*H*), 3.95 (1H, m, 4-*H*), 3.09 (1H, dd, *J* 18, 7, 3-*H*H), 2.69 (1H, dd, *J* 18, 7, 3-H*H*), 2.00 (1H, m, 5-*H*), 0.94 (3H, s, 5-CH_3); δ_C (126 MHz, $CDCl_3$) 170.1 (*C*=O), 137.6 (*ipso*-Ar-*C*), 129.2 (Ar-*C*), 128.9 (Ar-*C*), 127.7 (Ar-*C*), 85.2 (6-*C*), 70.1 (4-*C*), 43.5 (5-*C*), 39.5 (3-*C*), 13.9 (5-CH_3); *m*/*z* (ES^+) 261 (MNa+$MeOH^+$); HRMS (ES^+). Found MNa+$MeOH^+$, 261.1098 ($C_{13}H_{18}O_4Na$ requires 261.1097).

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References and notes

1. Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, 3173–3199.
2. Ottosson, H.; Steel, P. G. *Chem.—Eur. J.* **2006**, *12*, 1576–1585.
3. Sellars, J. D.; Steel, P. G.; Turner, M. J. *Chem. Commun.* **2006**, 2385–2387.
4. Pullin, R. D. C.; Sellars, J. D.; Steel, P. G. *Org. Biomol. Chem.* **2007**, *5*, 3201–3206.
5. Hughes, N. J.; Pullin, R. D. C.; Sanganee, M. J.; Sellars, J. D.; Steel, P. G.; Turner, M. J. *Org. Biomol. Chem.* **2007**, *5*, 2841–2848.
6. Sanganee, M. J.; Steel, P. G.; Whelligan, D. K. *Org. Biomol. Chem.* **2004**, *2*, 2393–2402.
7. Sellars, J. D.; Steel, P. G. *Org. Biomol. Chem.* **2006**, *4*, 3223–3224.
8. Bindseil, K. U.; Zeeck, A. *Helv. Chim. Acta* **1993**, *76*, 150–157.
9. Esumi, T.; Fukuyama, H.; Oribe, R.; Kawazoe, K.; Iwabuchi, Y.; Irie, H.; Hatakeyama, S. *Tetrahedron Lett.* **1997**, *38*, 4823–4826.
10. Hanefeld, U.; Hooper, A. M.; Staunton, J. *Synthesis* **1999**, 401–403.
11. Chakraborty, T. K.; Tapadar, S. *Tetrahedron Lett.* **2001**, *42*, 1375–1377.
12. Yamashita, Y.; Saito, S.; Ishitani, H.; Kobayashi, S. *Org. Lett.* **2002**, *4*, 1221–1223.
13. Chakraborty, T. K.; Tapadar, S. *Tetrahedron Lett.* **2003**, *44*, 2541–2543.
14. Csaky, A. G.; Mba, M.; Plumet, J. *Synlett* **2003**, 2092–2094.
15. Enders, D.; Haas, M. *Synlett* **2003**, 2182–2184.
16. Fournier, L.; Gaudel-Siri, A.; Kocienski, P. J.; Pons, J. M. *Synlett* **2003**, 107–111.
17. Pihko, P. M.; Erkkila, A. *Tetrahedron Lett.* **2003**, *44*, 7607–7609.
18. Yamashita, Y.; Saito, S.; Ishitani, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3793–3798.
19. Aggarwal, V. K.; Bae, I.; Lee, H. Y. *Tetrahedron* **2004**, *60*, 9725–9733.
20. Dias, L. C.; Steil, L. J.; Vasconcelos, V. D. *Tetrahedron: Asymmetry* **2004**, *15*, 147–150.
21. Yadav, J. S.; Reddy, K. B.; Sabitha, G. *Tetrahedron Lett.* **2004**, *45*, 6475–6476.
22. Salaskar, A. A.; Mayekar, N. V.; Sharma, A.; Nayak, S. K.; Chattopadhyaya, A.; Chattopadhyay, S. *Synthesis* **2005**, 2777–2781.
23. Yadav, J. S.; Reddy, M. S.; Prasad, A. R. *Tetrahedron Lett.* **2005**, *46*, 2133–2136.
24. Sabitha, G.; Padmaja, P.; Reddy, K. B.; Yadav, J. S. *Tetrahedron Lett.* **2008**, *49*, 919–922.
25. Srihari, P.; Ravindar, K.; Somaiah, R.; Yadav, J. S. *Synth. Commun.* **2008**, *38*, 1389–1397.
26. Soderquist, J. A.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3571.
27. Sanganee, M. J.; Steel, P. G.; Whelligan, D. K. *J. Org. Chem.* **2003**, *68*, 3337–3339.
28. Berry, M. B.; Griffiths, R. J.; Sanganee, M. J.; Steel, P. G.; Whelligan, D. K. *Org. Biomol. Chem.* **2004**, *2*, 2381–2392.
29. Soderquist, J. A.; Negron, A. *Tetrahedron Lett.* **1998**, *39*, 9397–9400.
30. Badali, F.; Karalis, A.; Tham, W. Y.; White, J. M. *Aust. J. Chem.* **1996**, *49*, 1293–1299.
31. Ward, R. A.; Procter, G. *Tetrahedron* **1995**, *51*, 12821–12836.
32. Fleming, I.; Lawrence, N. J.; Sarkar, A. K.; Thomas, A. P. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3303–3308.
33. Landais, Y.; Mahieux, C.; Schenk, K.; Surange, S. S. *J. Org. Chem.* **2003**, *68*, 2779–2789.
34. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.