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Stereochemistry of the reaction of Si–phenyl silenes with butadienes: elaboration of the silacycloadducts to provide a novel route to substituted lactones†

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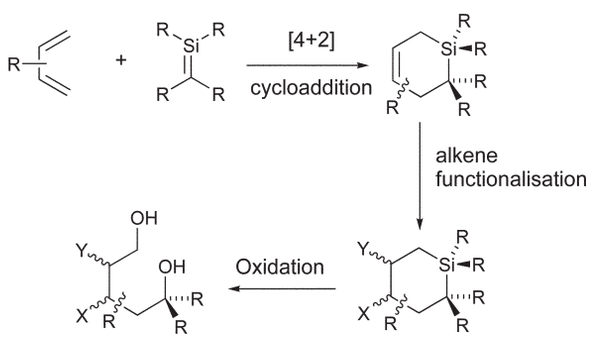
Received 22nd March 2004, Accepted 22nd June 2004
First published as an Advance Article on the web 29th July 2004

Silenes generated through a silyl-modified Peterson olefination procedure can be trapped with a range of alkyl butadienes *via* a [4 + 2] cycloaddition pathway to afford silacycles accompanied by variable amounts of competing ene, [2 + 2] and silene dimer by-products. The silacycles are formed with good chemo- and stereo-selectivity and provide access to diols and lactones *via* a phenyl-triggered Fleming–Tamao oxidation.

Introduction

Owing to their transient existence, silenes – compounds containing a silicon–carbon double bond – have primarily been the subject of research into fundamental aspects of structure and reactivity.[1] Although combining with a diverse set of functional groups there has been little effort to exploit the unique reactivity of these species in organic synthesis. With this objective in mind we have initiated a programme to explore this aspect of silene chemistry. In particular, we have undertaken a study of silene cycloaddition chemistry coupled with recently developed silicon oxidation methods to provide a novel strategy for the functionalisation of dienes, Scheme 1. In the accompanying paper we have described a robust and reliable method for the generation of silenes.[2] In this article we report how the product mixtures may be deconvoluted and how the major silacyclohexene products can be manipulated to provide a novel route to substituted lactones.[3]

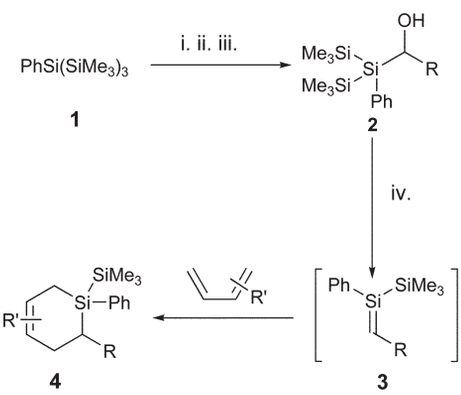


Scheme 1

Results and discussion

Our first attempts to generate synthetically useful silenes employed acylpolysilanes derived from tetrakis(trimethylsilyl)-silane *via* the Gilman reagent, $(Me_3Si)_3SiLi{\cdot}3THF$.[4,5] However, we were unable to activate the resultant trisilane unit for Fleming–Tamao oxidative extrusion of the silicon unit. Consequently, we modified the approach to generate the silyl alcohols **2** through addition of phenylbis(trimethylsilyl)silylmagnesium bromide to a range of aldehydes, Scheme 2. Deprotonation, with either MeLi, or more reproducibly, using our newly optimised conditions for the silyl-modified Peterson olefination, involving treatment of a mixture of the silyl alcohol and diene in Et_2O with

† Electronic supplementary information (ESI) available: standard protocols for the reduction of silacyclohexenes and for the oxidations of silacyclohexanes to diols. See http://www.rsc.org/suppdata/ob/b4/b404175e/



Scheme 2 *Reagents and conditions*: i. KO^{t}Bu, THF, 2 h; ii. $MgBr_2$, Et_2O; iii. RCHO, Et_2O; iv. ^{n}BuLi, Et_2O, rt, diene, 2 h then LiBr, −20 °C, 20 h or MeLi, Et_2O, rt, diene, −78 °C to 200 °C, 20 h.

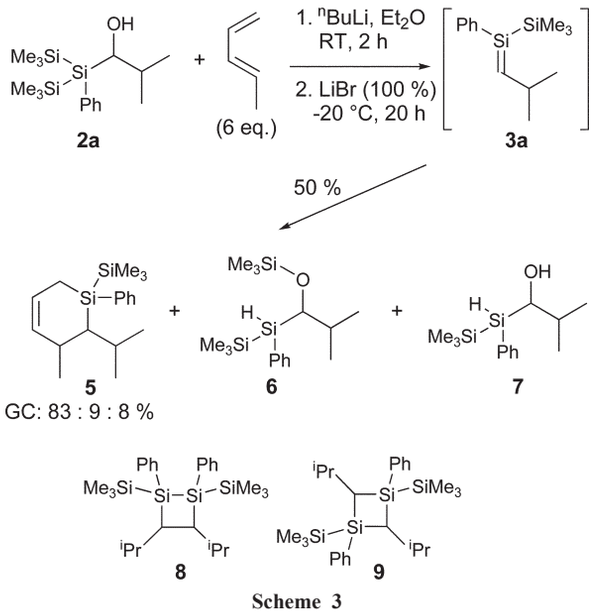
^{n}BuLi at room temperature followed by addition of LiBr, afforded the desired silacycles **4**.

In all cases, the [4 + 2] adducts were formed as the dominant component of a mixture containing variable quantities of products arising from ene and [2 + 2] reaction pathways as well as trace amounts of silene dimers. At this stage, although possible to determine that the stereoselectivity in the silene generation and consequent [4 + 2] reaction was good, it was not possible to determine the exact stereochemistry of the major isomer nor the identity of the minor components in the product mixture. A major problem in this was the difficulty in separation of the products owing to their common and highly non-polar nature. Consequently, we undertook the oxidation of each adduct using the Fleming variation for the oxidation of silicon centres containing an aryl substituent.[6]

Our first attempts focused on the use of the ^{i}Pr-substituted silene as this group provided a clear resolvable signal in the ^{1}H NMR spectra of the products. Treatment of the silyl alcohol **2a**, in the presence of an excess of 1,3-pentadiene, with ^{n}BuLi and LiBr, as described above, gave the desired silacyclohexene **5** in 50% yield as an 83 : 8 : 9 mixture as determined by simple (and uncorrected) integration of the GC trace, Scheme 3. Analysis of the mixture by GCMS suggested that these products were stereoisomers of the [4 + 2] pathway as opposed to alternative ene-type or [2 + 2] reaction products. Accompanying this mixture were small quantities of the silanes **6** and **7** arising from the modified Peterson reaction pathway and a mixture of products (*ca.* 5%) tentatively identified as silene dimers **8** and/or **9**.

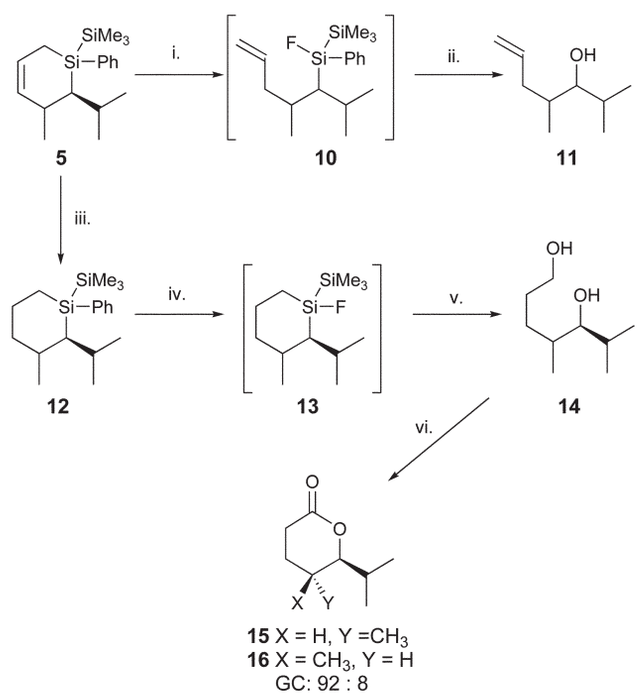
As anticipated, the silyl phenyl group allowed a relatively simple two-step Fleming–Tamao oxidation. Initial protodesilylation of the aryl ring with $BF_3{\cdot}2AcOH$ afforded the silyl fluoride **10**. This

DOI: 10.1039/b404175e



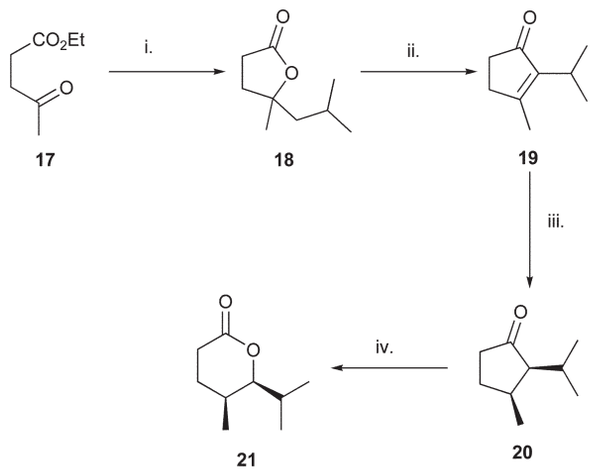
Scheme 3

could be isolated but was normally used directly in the oxidation stage involving treatment with H_2O_2, KF and $KHCO_3$ to give the bishomoallylic alcohol **11** in 43%, Scheme 4.[7,8] Alternatively, catalytic hydrogenation over Pd/C gave the corresponding silacyclohexanes **12** which could be oxidised by the same two-step method, albeit requiring slightly more forcing conditions, to yield the diol **14**. Although these steps removed many of the by-products from the reaction it was still not possible to unequivocally assign the stereochemistry.



Scheme 4 *Reagents and conditions*: i. $BF_3{\cdot}2AcOH$, $CHCl_3$, rt, 0.5 h; ii. H_2O_2, KF, $KHCO_3$, THF/MeOH, Δ, 18 h, 43% (2 steps); iii. H_2, Pd/C, toluene, 6 h, 74%; iv. $BF_3{\cdot}2AcOH$, $CHCl_3$, Δ, 18 h; v. H_2O_2, KF, $KHCO_3$, THF/MeOH, Δ, 18 h, 85% (2 steps); vi. TPAP, NMO, 4 Å sieves, DCM, rt, 16 h, 76%.

Attempts to prepare crystalline ester derivatives were not fruitful so diol **14** was converted to the cyclic lactones **15** and **16** by oxidation with TPAP, NMO.[9,10] At this point the ratio of diastereoisomers was 92 : 8, suggesting that one of the minor silacyclohexene components was due to a different configuration at the silicon centre and the other to the relative configuration at C-2 and C-3. NOESY experiments could not clearly distinguish between these so we prepared an authentic sample of the *cis*-lactone **21** following the literature procedures of Helquist and Kazmierczak,[11] Scheme 5. NMR studies clearly indicated that lactone **21** was different to the major isomer from the silene sequence allowing us to unambiguously assign the latter as the *trans*-lactone **15**.



Scheme 5 *Reagents and conditions*: i. $(CH_3)_2CHCH_2MgBr$, THF, 0 °C, 15 min, 51%; ii. H_3PO_4, P_2O_5, solvent, 98 °C, 72%; iii. H_2, Ph/C, 25 psi, 22 h, 50%; iv. mCPBA, $NaHCO_3$, hexane/DCM, 0 °C, 74 h, 41%.

Having established the relative stereochemistry between silene and the diene 1-substituent we then turned to examine the geometry of the silene formed in the silyl-modified Peterson reaction. Retaining the ^{i}Pr substituent we explored the reaction with 2,3-dimethylbutadiene as this should only afford isomers arising from differing silene geometries. Reaction of silene **3a**, derived from alcohol **2a** by deprotonation with MeLi, with 2,3-dimethylbutadiene yielded silacycle **22** as the major product in an inseparable mixture (83 : 9 : 8) of isomers (m/z = 316) which also included trace amounts of a fourth component tentatively identified as a silene–diene [2 + 2] adduct, Scheme 6. On the basis of the GCMS fragmentation pattern, the 9% component was hypothesised to be the other diastereoisomer of the major [4 + 2] cycloadduct. The presence of olefinic peaks in the NMR spectrum (see Experimental section for details) and the loss of fragments with m/z = 57 and 81 in the GCMS trace implied that the 8% component of the mixture was silyldiene **23**, the result of an ene reaction between 2,3-dimethylbutadiene and the silene. The stereochemistry of the major isomer **22a** was determined by NMR studies. Notably, the coupling constant between 2-H and 3-H_{ax}, J = 11.0 Hz, is consistent with coupling between two axially orientated protons. This latter signal exhibits a NOE correlation to both the ^{i}Pr group and the transannular 6-H, Fig. 1. Since previous studies have demonstrated that silenes are configurationally stable with no rotation about a Si=C double bond,[12] this stereochemistry indicated the preferential formation of the *cis*-silene (see below).

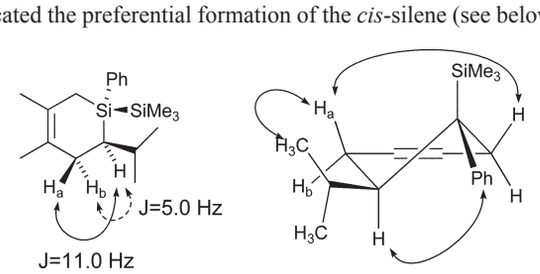


Fig. 1 Selected coupling constants and NOESY correlations for **22a**.

Having established the preferred silene stereochemistry we then turned to deconvolution of the remainder of the reaction pathway. Hydrogenation of the crude reaction mixture using a Pd/C catalyst was unsuccessful and alternative sets of reaction conditions were screened. Ultimately, apart from some competitive reduction of the phenyl group, success was attained using PtO_2 in EtOH.[13–15] However, under these conditions, an inseparable mixture of saturated silanes **24**–**28** was obtained resulting from scrambling of stereochemistry at the β-silyl centre prior to reduction from the face opposite the bulkier phenyl substituent. Such scrambling is

well documented in the literature and is ascribed to migration of the double bond.[15–17] As described below, the composition of this mixture was ultimately ascertained by two sets of experiments involving excision of the silyl unit and benzoylation or oxidation of the resulting diols.

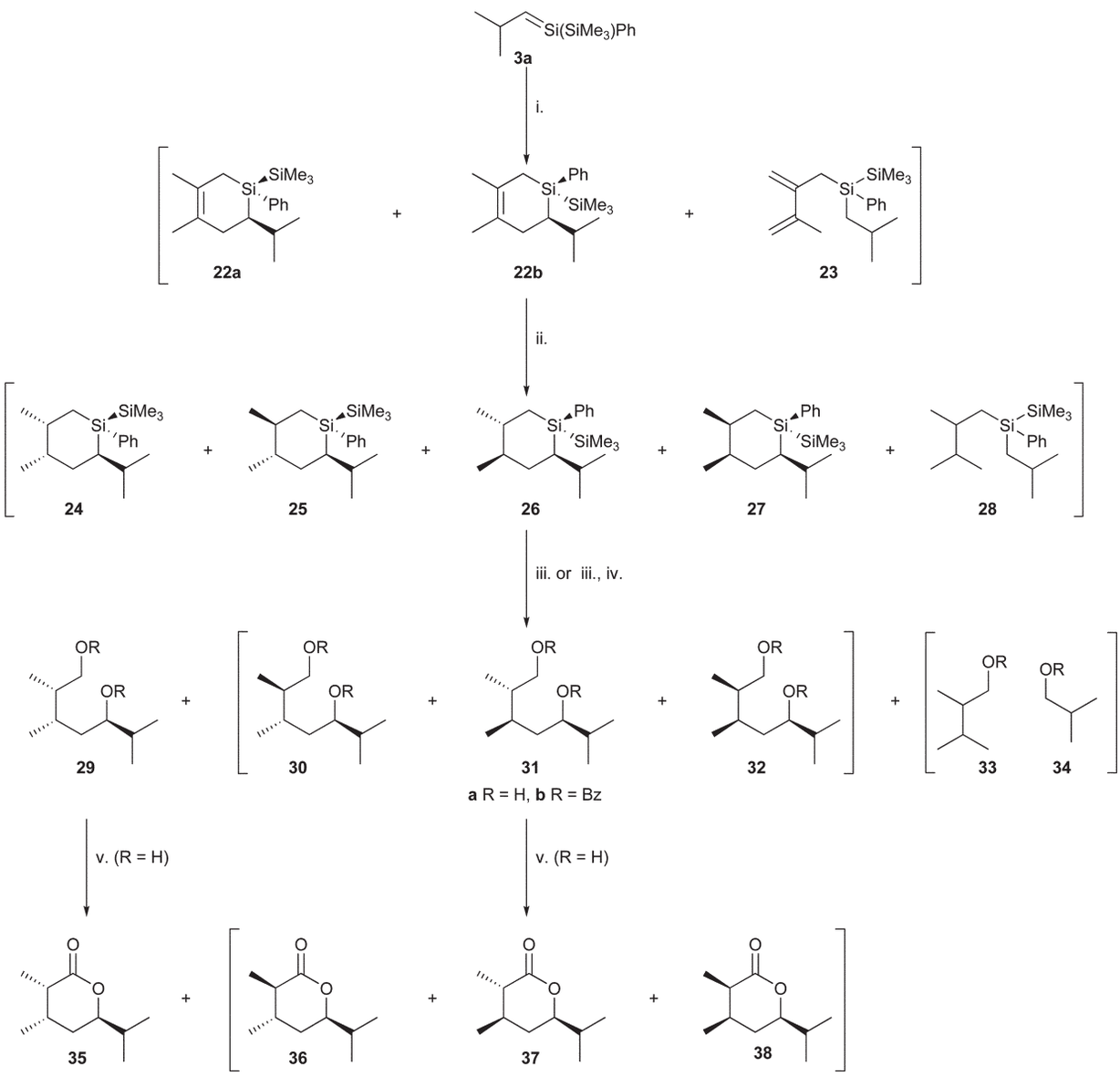
Fleming–Tamao oxidation of mixture **24**–**28** produced a crude mixture of all possible alcohols **29a**–**34a**. This mixture was divided, with half being purified by chromatography to afford pure diol **29** and an inseparable mixture of diols **30a**–**32a** in 39 and 24% yield, respectively. The remaining half of the crude mixture was treated with benzoyl chloride to trap the volatile alcohols **33a** and **34a**, providing additional evidence for the formation of ene product **23**. Identification of all of the benzoylated products in the GCMS trace of this mixture was aided by synthesis of the benzoyl esters **29b**–**32b** from the separated purified diols. Finally, oxidation of the two sets of diols afforded the corresponding lactones **35**–**38**, from which NOESY experiments allowed assignment of the stereochemistry as shown in Scheme 6.

Combination of these two studies, involving 1,3-pentadiene and 2,3-dimethylbutadiene, established that the ^{i}Pr silene was generated with a preference for the *Z*-stereochemistry and combined with simple butadienes with a preference for the Si–phenyl substituent to occupy an *endo* position in the Diels–Alder transition state.

Similar studies with other alkyl butadienes, Table 1, revealed that this was a common pathway. Other similar trends identified were that the presence of a terminal substituent on the diene appeared to favour the [4 + 2] pathway over the ene pathway (entries **a**, **d** and **e** *vs.* entries **b** and **c**), whilst attempted hydrogenolysis and oxidation of silacyclohexenes with alkene substituents are complicated by olefin scrambling and decomposition, respectively.[18]

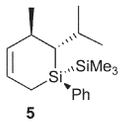
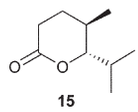
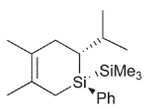
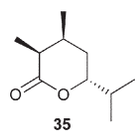
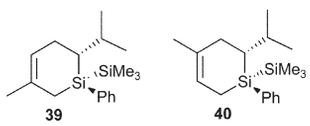
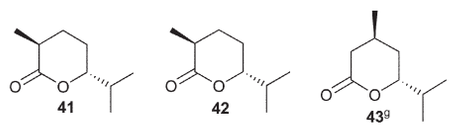
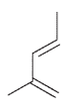
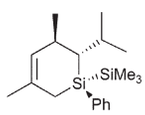
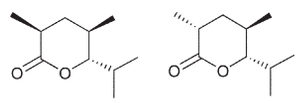
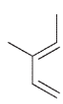
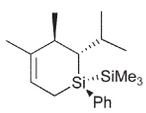
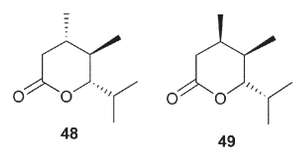
Finally, to investigate the effect of the silene substituent on the outcome of this sequence we explored the use of the Me **2b**, ^{n}Pr **2c**, ^{t}Bu **2d**, and phenyl **2e** substituted silyl alcohol analogues, Table 2. The methyl, ^{n}Pr and phenyl derivatives combined with 1,3-pentadiene to produce the equivalent *trans*-adduct as obtained with the ^{i}Pr analogue, whereas the ^{t}Bu silene (entry **c**) produced the corresponding *cis*-lactone **55** as the major product after the reduction and oxidation sequence. In each case the stereochemistry was established by either comparison with literature data or through the use of NOESY experiments (see Table 2, and Figs. 2 and 3 contained therein).

We rationalise these observations through the preferential formation of a *Z*-silene geometry for most substituents *via* fast equilibration and *anti* elimination from the silyl anion to give the least hindered silene, Eq. 1 in Scheme 7. The exception occurs with the ^{t}Bu silene **3d** which appears to be formed as the alternative *E*-silene isomer **3d(*E*)**. We speculate that in this case 1,3-TMS group migration occurs from the more accessible eclipsed conformation **60**. Interconversion of this silyl anion is restricted by the steric bulk of the ^{t}Bu group (*A*-values: ^{i}Pr, 9.25; Ph, 11.71; Me_3Si, 10.5; ^{t}Bu, 19.7 kJ mol^{-1})[19] and the



Scheme 6 *Reagents and conditions*: i. ^{n}BuLi, Et_2O, rt, 2 h then LiBr (10 mol%), Et_2O, 2,3-dimethylbutadiene, −20 °C, 20 h, 48% (**22a**:**22b**:**23** 83:9:8); ii. H_2, $PtO_2{\cdot}H_2O$, EtOH, 21 h, 64% (**51**:**25**:**26**:**27**:**28** 51:30:6:5:8); iii. $BF_3{\cdot}2AcOH$, $CHCl_3$, ^{2}, 17 h, then H_2O_2, KF, $KHCO_3$, THF/MeOH, ^{2}, 21 h, **29a** (64%), **30a**–**32a** (24%); iv. BzCl, Et_3N, DMAP, DCM, **29b** (32%), **30b**–**32b** (82:12:6, 24%); v. TPAP, NMO, DCM, **35** (63%), **36**–**38** (64%).

Table 1 Silacyles and lactones generated from the reaction of **3a** with alkyl-substituted butadienes

	Dienes	[4 + 2] Silacycloadducts[a,b]	Lactones
a		 **5** 46% (92 : 8)[c]	 **15** (92 : 8)[b]
b		 **22** 42%[d] (83 : 17)[c]	 **35** (93 : 7)[b] **36** (95 : 5)[b]
c		 **39** **40** 36%[e] (86 : 14)[f]	 **41** **42** **43**[g] (66 : 34)
d		 **44** 43%[h] (80 : 14 : 4)[c]	 **45** **46** (79 : 11 : 8 : 2)[b]
e		 **47** 38% (86 : 9 : 4 : 1)[c]	 **48** **49** (87 : 10 : 3)[b,i]

[a] Silene generated using [n]BuLi/LiBr (method B) – combined yield of [4+2] silacycloadducts shown. [b] Major stereoisomer only indicated. [c] Ratio of diastereoisomers. [d] Ene product formed in 6% yield. [e] Ene product formed in 5% yield. [f] Ratio of regioisomers. [g] Only diastereoisomer detected. [h] Ene product formed in 1% yield. [i] Hydrogenation of **47**/**48** required use of H_2, Ir(P-c-Hx_3)(cod)pyr·PF_6, DCM, 8 d (81% conversion) – minor regioisomer not detected.

only accessible *anti* conformation **62** available for elimination leads to the *E*-silene, Eq. 2 in Scheme 7. All the silenes then react with the Si–phenyl group adopting an *endo* orientation in the transition state. This latter observation can be attributed to favourable interactions between the aromatic nucleus and the diene.

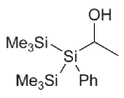
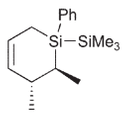
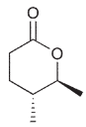
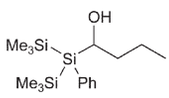
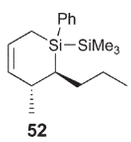
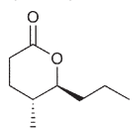
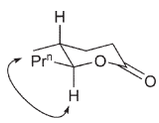
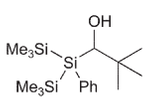
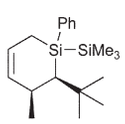
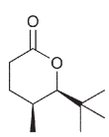
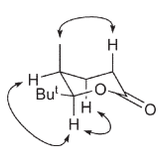
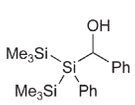
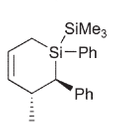
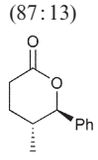
In conclusion, silenes generated through a silyl-modified Peterson olefination are formed with good levels of stereocontrol that can be rationalised on the basis of simple steric interactions. These are highly reactive species which combine *in situ* with a range of alkyl butadienes. The predominant pathway is a [4 + 2] cycloaddition to afford silacyclohexenes accompanied by variable amounts of competing ene, [2 + 2] and silene dimer by-products. The formation of these by-products is very dependent on the nature of the diene substituent with terminal alkyl substituents promoting the [4 + 2] pathway. The silacycles are formed with good chemo- and stereoselectivity and provide access to diols and lactones *via* a phenyl-triggered Fleming–Tamao oxidation. Overall this represents a novel 1,4-functionalisation of the diene. Alternative modes of silacycle functionalisation through addition of electrophiles to the allylsilane component can be envisaged. Work exploring these transformations is in progress and results will be reported in due course.

Experimental

All air- and or moisture-sensitive reactions were carried out under an argon atmosphere. Solvents were purified following established protocols. Petrol refers to petroleum spirit boiling in the 40–60 °C range. Ether refers to diethyl ether. Commercially available reagents were used as received unless otherwise stated. Flash column chromatography was performed according to the method of Still *et al.*[20] using 200–400 mesh silica gel. Yields refer to isolated yields of products of greater than 95% purity as determined by ^{1}H and ^{13}C NMR spectroscopy or elemental analysis (Durham University Microanalytical Laboratory).

Melting points were determined using Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded as thin films between KBr plates (liquids) or as compression-formed discs made using KBr (solids) on a Perkin-Elmer FT-IR 1600 spectrometer. Unless otherwise stated, ^{1}H NMR spectra were recorded in $CDCl_3$ on Varian Mercury 200, Bruker AM-250, Varian Unity-300, Varian VXR-400 or Varian Inova-500 spectrometers and are reported as follows: chemical shift δ (ppm) [number of protons, multiplicity, coupling constant J (Hz), assignment]. Residual protic solvent $CHCl_3$ (δ_H = 7.26 ppm) was used as the internal reference. ^{13}C NMR spectra were recorded at 63 MHz, 101 MHz or 126 MHz on Bruker AM-250, Varian VXR-400 or Varian Inova-500 instruments, respectively, 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 a Varian Inova-500 spectrometer. ^{19}F NMR spectra were recorded at 376 MHz or 282 MHz on Varian VXR-400 or Varian Unity-300 spectrometers, respectively. All chemical shifts are quoted in parts per million relative to tetramethylsilane (δ_H = 0.00 ppm) and coupling constants are given in Hertz to the nearest 0.3 Hz. All ^{13}C spectra were proton decoupled. Assignment of spectra was carried out using DEPT, COSY, HSQC and NOESY experiments. Low-resolution mass spectra (EI or CI) were obtained on a Micromass Autospec Mass Spectrometer. Gas chromatography–mass spectra (GCMS, EI or CI) were taken using a Hewlett Packard 5890 Series II gas chromatograph, equipped with a 25 m 5% diphenyl-/95% dimethyl-polysiloxane column and flame ionisation detection, connected to a VG

Table 2 Silacyles and lactones generated from the reaction of silenes **3b**–**3e** with *E*-1,3-pentadiene

	Silyl alcohol	[4 + 2] Silacycloadducts[a,b]	Lactones[b,c]	NOESY – ref. no.
a	 **2b**	 **50**	 **51**	25
		28% (89 : 7 : 4)[c]	(89 : 11)	
b	 **2c**	 **52**	 **53**	 Figure 2
		12% (81 : 12 : 7)	(72 : 28)	
c	 **2d**	 **54**	 **55**	 Figure 3
		35% (85 : 5 : 5 : 5)	(87 : 13)	
d	 **2e**	 **56**	 **57**	26
		45% (74 : 20 : 6)		

[a] Silene generated using [n]BuLi/LiBr (method B) – combined yield of [4+2] silacycloadducts shown. [b] Major stereoisomer only indicated. [c] Ratio of isomers shown in parentheses.

Trio-1000 mass spectrometer. Electrospray mass spectra (ES) were obtained on a Micromass LCT Mass Spectrometer. High-resolution mass spectra were performed by the EPSRC service at the University of Swansea or on a Micromass Autospec Mass Spectrometer in Durham. Detailed experimental procedures describing the formation and characterisation of silyl alcohols,[2] the silene cycloadducts[2] and compounds **18**–**21** [11] have been previously reported. Characterisation data for the intermediate silanes and diols produced in the conversion of silacycloadducts **39**, **40**, **44**, **47**, **50**, **52**, **54** and **56** to the corresponding lactones can be found in the ESI.†

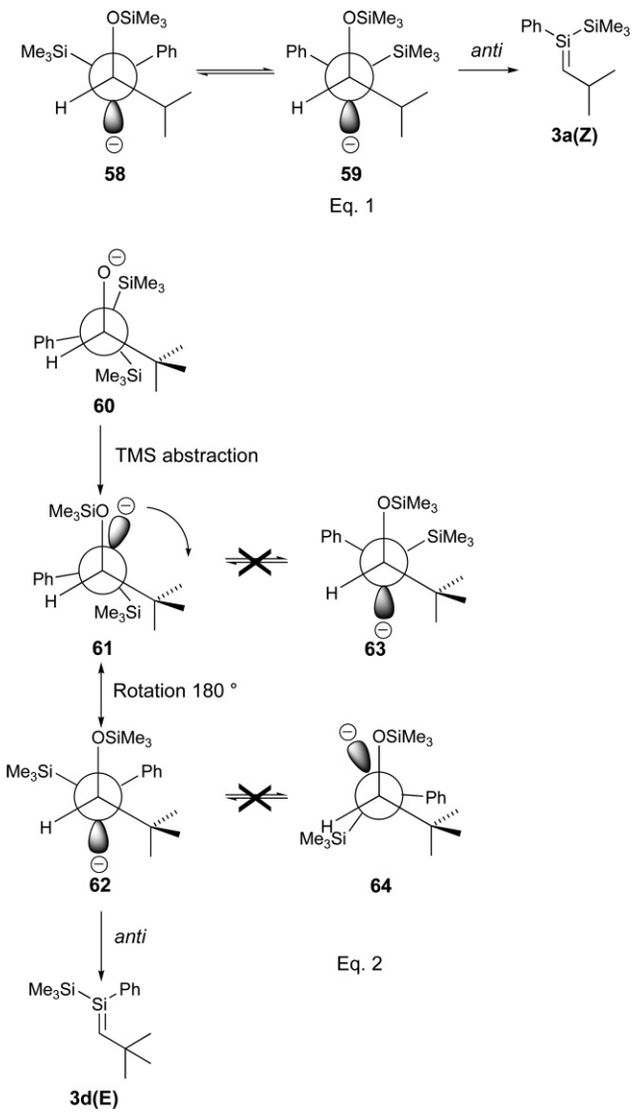
1-Phenyl-1-trimethylsilyl-2-(prop-2′-yl)-3-methylsilacyclohex-4-ene 5

Method A. Methyllithium (1.6 M solution in ether, 13.0 ml, 20.9 mmol) was added to a stirred solution of silyl alcohol **2a** (6.76 g, 20.9 mmol) and 1,3-pentadiene (mixture of *cis*- and *trans*-isomers, 12.5 ml, 125.2 mmol) in ether (300 ml) at −78 °C. The mixture was allowed to warm to −30 °C and stirred for 22 h, then to 0 °C and stirred for 8 h. Saturated ammonium chloride solution (200 ml) was added and the mixture allowed to reach RT. The aqueous layer was separated and extracted with ether (3 × 200 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash column chromatography (hexane) gave the title compound as a mixture of diastereoisomers (3.25 g, 52%).

Method B. *n*-Butyllithium (1.6 M solution in hexane, 0.58 ml, 0.92 mmol) was added to a stirred solution of silyl alcohol **2a** (0.29 g, 0.88 mmol) and 1,3-pentadiene (mixture of *cis*- and *trans*-isomers, 0.53 ml, 5.28 mmol) in dry ether (10 ml) at RT. The mixture was stirred for 2 h after which time TLC showed complete consumption of starting material. The solution was cooled to −20 °C and an anhydrous suspension of LiBr in ether (1.75 M, 0.5 ml, 0.88 mmol) was added and seen to go into solution. The mixture was stirred at −20 °C for 19.5 h after which time saturated ammonium chloride solution (10 ml) was added and the mixture allowed to reach RT. The aqueous layer was separated and extracted with ether (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash column chromatography (petroleum ether) gave the title compound (0.133 g, 50%) as a mixture of diastereoisomers in a ratio of 83 : 9 : 8% (ratio of product peak integrals by GC); R_f (hexane) 0.71; ν_{max} (thin film) 3067, 2997, 2958, 2872, 1461, 1396, 1246, 1108, 855, 838, 736, 702 cm^{-1}; NMR data for major isomer **5**: δ_H (200 MHz; $CDCl_3$) 7.51–7.48 (2H, m, Ar–*H*), 7.31–7.28 (3H, m, Ar–*H*), 5.82 (1H, dtd, *J* = 10.5, 5.2, 1.8 Hz, 5-*H*), 5.54 (1H, ddt, *J* = 10.5, 4.4, 1.8 Hz, 4-*H*), 2.36 (1H, m, 3-*H*), 2.10 [1H, septet, d, *J* = 6.8, 3.3 Hz, C*H*$(CH_3)_2$], 1.68 (1H, ddt, *J* = 17.2, 5.2, 1.8 Hz, 6-*H*H), 1.47 (1H, ddt, *J* = 17.2, 5.2, 1.8 Hz, 6-H*H*), 1.20 (1H, dd, *J* = 6.5, 3.3 Hz, 2-*H*), 1.03 [3H, d, *J* = 6.8 Hz, CH$(CH_3)_2$], 0.93 (3H, d, *J* = 7.2 Hz, 7-H_3), 0.88 [3H, d, *J* = 6.8 Hz, CH$(CH_3)_2$], 0.14 [9H, s, Si$(CH_3)_3$]; δ_C (126 MHz; $CDCl_3$) 139.36 (*ipso*-*Ar*), 137.41 (4-*C*), 134.48 (*Ar*), 128.19 (*Ar*), 127.66 (*Ar*), 123.56 (5-*C*), 38.21 (2-*C*), 32.77 (3-*C*), 30.02 (2′-*C*), 23.56 (7-*C*), 22.99 (1′-*C*), 22.45 (1′-*C*), 9.74 (6-*C*), −0.55 [Si$(CH_3)_3$]; *m*/*z* (EI) 302 (M^+, 7%), 259 ($M^+ - {}^iPr$, 4%), 229 ($M^+ - SiMe_3$, 56%), 218 (27), 203 (47), 185 (11), 173 (29), 161 (100), 145 (31), 135 (82), 121 (69).

(±)-(4*R**,5*S**)-4,6-Dimethylhept-1-en-5-ol 11 [21]

To a solution of silacycle **5** (1.65 g, 5.46 mmol) in dry chloroform (130 ml) was added the trifluoroborane–acetic acid complex (1.7 ml, 12.2 mmol). The mixture was stirred at RT for 30 min, after which time saturated sodium hydrogen carbonate solution (60 ml) was added. The aqueous layer was separated and extracted with DCM (3 × 60 ml). The combined organic extracts were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo* to give a clear oil. Potassium hydrogen carbonate (1.05 g, 10.53 mmol) and potassium fluoride (0.63 g, 10.86 mmol) were then added and the



Scheme 7

mixture dissolved in THF/MeOH solution (1 : 1, 37 ml). Hydrogen peroxide (35% w/w solution in water, 6.3 ml, 65.1 mmol) was then added and the mixture was heated to reflux and stirred for 18 h. The mixture was then allowed to cool to RT and saturated sodium thiosulfate solution (35 ml) was added together with ethyl acetate (40 ml). The aqueous layer was separated and extracted with ethyl acetate (3 × 40 ml). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated. Flash column chromatography (petroleum ether/ethyl acetate [9 : 1]) gave the title compound **11** (0.34 g, 43%) along with a trace amount of the (4*S**,5*S**)-diastereoisomer; R_f (petroleum ether/ethyl acetate [9 : 1]) 0.64; ν_{max} (thin film) 3406 (broad, O–H), 3075, 2961, 2874, 1640 (C=C), 1463, 992, 909, 741 cm^{-1}; NMR data for major isomer: δ_H (500 MHz; $CDCl_3$) 5.82 (1H, m, 2-*H*), 5.00 (1H, d, J = 17.5 Hz, 1-*H*, *cis*), 4.99 (1H, d, J = 10.5 Hz, 1-*H*, *trans*), 3.09 (1H, dd, J = 7.0, 5.0 Hz, 5-*H*), 2.36 (1H, dm, J = 14.0 Hz, 3-*H*H), 1.91 (1H, ddd, J = 14.0, 9.0, 9.0 Hz, 3-H*H*), 1.80 (1H, m, 6-*H*), 1.66 (1H, m, 4-*H*), 0.93 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.88 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.87 (3H, d, J = 7.0 Hz, 8-H_3); δ_C (126 MHz; $CDCl_3$) 137.66 (2-*C*), 115.89 (1-*C*), 80.59 (5-*C*), 36.44 (3-*C*), 35.79 (4-*C*), 30.01 (6-*C*), 20.00 [CH(CH_3)$_2$], 16.16 (8-*C*), 15.87 [CH(CH_3)$_2$]; *m*/*z* (EI) 124 ($M^+ - H_2O$, 11%), 123 (5), 110 (5), 109 ($M^+ - H_2O$ − Me, 46%), 100 (24), 99 ($M^+ - {}^iPr$, 100%), 98 (32).

1-Phenyl-1-trimethylsilyl-2-(prop-2′-yl)-3-methylsilacyclohexane 12

A mixture of silacycle **5** (1.00 g, 3.32 mmol) and Pd on carbon (10% Pd, *ca.* 0.01 g) in dry toluene (20 ml) was repeatedly evacuated and flushed with hydrogen from a balloon. The mixture was then stirred under the hydrogen atmosphere for 6 h. It was then filtered through a Celite pad and washed through with ether. The filtrate was concentrated and dried *in vacuo*. Flash column chromatography (hexane) gave the title compound as a mixture of diastereoisomers (0.745 g, 74%); R_f (hexane) 0.94; ν_{max} (thin film) 3067, 2953, 2907, 2870, 1463, 1427, 1259, 1244, 1099, 853, 833, 755, 734, 699 cm^{-1}; NMR data for major isomer **12**: δ_H (500 MHz; $CDCl_3$) 7.57–7.55 (2H, m, Ar–*H*), 7.33–7.30 (3H, m, Ar–*H*), 2.16 [1H, septet, d, J = 7.0, 3.8 Hz, C*H*(CH_3)$_2$], 1.95 (1H, dm, J = 13.0 Hz, 5-H*H*), 1.81 (1H, m, 3-*H*), 1.74 (1H, dm, J = 13.5 Hz, 4-H*H*), 1.50 (1H, qt, J = 13.0, 3.0 Hz, 5-*H*H), 1.19 (1H, m, 4-*H*H), 1.11 (1H, dd, J = 10.0, 3.8 Hz, 2-*H*), 1.07 (1H, m, 6-H*H*), 1.02 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.97 (3H, d, J = 6.5 Hz, 7-H_3), 0.79 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.27 [9H, s, Si(CH_3)$_3$]; δ_C (126 MHz; $CDCl_3$) 140.62 (*ipso*-*Ar*), 134.53 (*Ar*), 128.10 (*Ar*), 127.61 (*Ar*), 40.54 (2-*C*), 39.03 (4-*C*), 34.16 (3-*C*), 28.73 (2′-*C*), 23.59 (7-*C*), 23.38 (5-*C*), 23.18 (1′-*C*), 22.53 (1′-*C*), 13.01 (6-*C*), 0.20 [Si(CH_3)$_3$]; *m*/*z* (EI) 304 (M^+, 37%), 289 (M^+ − Me, 6%), 231 (M^+ − $SiMe_3$, 100%), 203 (5), 187 (10), 175 (25), 161 (33), 147 (19), 135 (49), 121 (65), 107 (28), 105 (37).

Standard procedure for oxidations of silacyclohexane mixtures as applied to (±)-(4*R**,5*S**)-4,6-dimethylheptane-1,5-diol 14 [22]

Stage 1. To a solution of silacycle **12** (0.75 g, 2.45 mmol) in dry chloroform (28 ml) was added the trifluoroborane–acetic acid complex (6.8 ml, 49.0 mmol). The mixture was then heated to reflux and stirred for 18 h. The solution was then allowed to cool to RT and saturated sodium hydrogen carbonate solution (40 ml) was added. The aqueous layer was separated and extracted with DCM (3 × 40 ml). The combined organic layers were then dried over $MgSO_4$, filtered, concentrated and dried *in vacuo* to give a dark orange oil which was used immediately in stage 2.

Stage 2. To the dark orange oil was added potassium hydrogen carbonate (0.94 g, 9.43 mmol) and potassium fluoride (0.57 g, 9.75 mmol). The mixture was dissolved in THF/MeOH solution (1 : 1, 19 ml) and hydrogen peroxide (35% w/w solution in water, 5.8 ml, 58.4 mmol) was added. The mixture was heated to reflux and stirred for 19 h. The mixture was then allowed to cool to RT and saturated sodium thiosulfate solution (19 ml) was added together with ethyl acetate (30 ml). The aqueous layer was separated and extracted with ethyl acetate (3 × 30 ml). The combined organic extracts were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash column chromatography (petroleum ether/ethyl acetate [1 : 1]) gave the title compound **14** as a colourless oil (0.332 g, 85%); R_f (petroleum ether/ethyl acetate [1 : 1]) 0.23; ν_{max} (thin film) 3346 (broad, O–H), 2959, 2932, 2872, 1465, 1054, 989, 971 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 3.65 (2H, t, J = 5.5 Hz, 1-H_2), 3.09 (1H, t, J = 6.5 Hz, 5-*H*), 1.82 (1H, octet, J = 6.5 Hz, 6-*H*), 1.69 (2H, m, 3-H*H* and 2-H*H*), 1.60 (1H, m, 4-*H*), 1.50 (1H, m, 2-*H*H), 1.18 (1H, q, J = 8.5 Hz, 3-*H*H), 0.93 [3H, d, J = 6.5 Hz, CH(CH_3)$_2$], 0.90 (3H, d, J = 6.5 Hz, 8-H_3), 0.89 [3H, d, J = 6.5 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 80.96 (5-*C*), 63.23 (1-*C*), 35.51 (4-*C*), 30.86 (2-*C*), 30.00 (6-*C*), 27.41 (3-*C*), 20.05 [CH(*C*H_3)$_2$], 16.41 (8-*C*), 16.00 [CH(*C*H_3)$_2$]; *m*/*z* (ES^+) 333 (M_2Na^+, 4%), 183 (M + Na^+, 100%); HRMS (CI) Found MNH_4^+ 178.1813; $C_9H_{24}NO_2$ requires MNH_4^+, 178.1807.

Standard protocol for TPAP oxidation of diols to lactones as applied to (±)-(4*R**,5*S**)-4-methyl-5-prop-2′-yl-δ-valerolactone 15 [23]

To a solution of diol **14** (0.05 g, 0.32 mmol) in dry DCM (4 ml) was added powdered molecular sieves (4 Å, *ca.* 0.1 g), NMO (0.15 g, 1.25 mmol) and TPAP (0.03 g, 0.08 mmol). The mixture was stirred at RT for 16 h. It was then diluted with ether (8 ml), filtered through silica and washed through with more ether. The filtrate was concentrated under reduced pressure. Flash column chromatography (petroleum ether/ether [1 : 1]) gave the title compound along with a

small amount of the (4*S**,5*S**)-diastereoisomer **16** in a ratio of 92 : 8% (ratio of product peak integrals by GC) (0.04 g, 76%); R_f (hexane/ether [1 : 1]) 0.41; ν_{max} (thin film) 2966, 2940, 2884, 1738 (C=O), 1468, 1254, 1218, 1007 cm^{-1}; NMR data for the major isomer **15**: δ_H (500 MHz; $CDCl_3$) 3.80 (1H, dd, J = 10.0, 2.5 Hz, 6-*H*), 2.59 (1H, ddd, J = 17.5, 7.0, 4.0 Hz, 3-*H*H), 2.43 (1H, ddd, J = 17.5, 10.0, 7.0 Hz, 3-H*H*), 1.93 (1H, septet, d, J = 7.0, 2.5 Hz, 7-*H*), 1.86 (1H, ddt, J = 13.5, 7.0, 4.0 Hz, 4eq-*H*), 1.79 (1H, m, 5-*H*), 1.51 (1H, dtd, J = 13.5, 10.0, 7.0 Hz, 4ax-*H*), 1.05 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.96 (3H, d, J = 7.0 Hz, 9-H_3), 0.88 [3H, d, J = 7.0, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 172.13 (C=O), 89.72 (6-*C*), 29.94 (5-*C*), 29.47 (3-*C*), 29.18 (7-*C*), 19.75 [CH(*C*H_3)$_2$], 17.13 (9-*C*), 14.18 [CH(*C*H_3)$_2$]; *m/z* (EI) 156 (M^+, 24%), 128 (43), 114 (29), 113 (100), 95 (15), 86 (22), 85 (81), 84 (75), 71 (33), 69 (38), 67 (64).

4,5-Dimethyl-1-phenyl-2-(prop-2′-yl)-1-(trimethylsilyl)-silacyclohex-4-ene 22; and 1-phenyl-1-(2′-methylpropyl)-2,2,2-trimethyl-1-(3′-methyl-2′-methylene-but-3′-enyl)-disilane 23

Following method A, reaction of alcohol **2a** with 2,3-dimethylbutadiene afforded following chromatography (petroleum ether) the title compounds as a colourless oil (45%) as a mixture composed of two diastereoisomers of the title silacycle **22** and ene product **23** in a ratio of 83 : 8 : 7% (ratio of product peak integrals by GC) whilst method B gave the same compounds (48%) in a ratio of 73 : 15 : 12%; R_f (petroleum ether) 0.70; ν_{max} (thin film) 3067, 3049, 2953, 2925, 2866, 1464, 1443, 1430, 1390, 1246, 1121, 1108, 853, 838, 732, 706 cm^{-1}; **22a**: δ_H (200 MHz; $CDCl_3$) 7.48–7.47 (2H, m, Ar–*H*), 7.30–7.29 (3H, m, Ar–*H*), 2.23 (1H, dd, J = 15.0, 5.0 Hz, 3a-*H*), 1.98 (1H, dd, J = 15.0, 11.0 Hz, 3b-*H*), 1.83 [1H, m, C*H*(CH_3)$_2$], 1.74 (3H, s, 8-H_3), 1.69 (3H, s, 7-H_3), 1.58 (2H, s, 6-H_2), 1.09 (1H, ddd, J = 11.0, 8.5, 5.0 Hz, 2-*H*), 0.99 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.98 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.11 [18H, s, Si(Si(CH_3)$_3$]$_2$); δ_C (126 MHz; $CDCl_3$) 139.51 (*ipso-Ar*), 134.52 (*Ar*), 128.68 (4 or 5-*C*), 128.26 (*Ar*), 127.66 (*Ar*), 125.33 (4 or 5-*C*), 35.33 (3-*C*), 34.47 (2-*C*), 30.30 (2′-*C*), 24.89 (1′-*C*), 22.61 (8-*C*), 22.20 (1′-*C*), 20.74 (7-*C*), 18.92 (6-*C*), −0.33 [Si(Si(*C*H_3)$_3$)$_2$]; *m/z* (GCMS, CI) 317 (M + H^+, 100%), 316 (M^+, 65%), 315 (M^+ − H, 15%), 303 (25), 301 (M^+ − Me, 60%), 273 (M^+ − ^{i}Pr, 1%), 243 (M^+ − $SiMe_3$, 79%), 245 (13), 239 (M^+ − Ph, 23%), 187 (24), 161 (21), 135 (17); **23**: δ_H (200 MHz) (discernable peaks) 5.08 (1H, s, =CH_2), 5.06 (1H, s, =CH_2), 4.98 (1H, s, =CH_2) and 4.86 (1H, s, =CH_2); *m/z* (GCMS, EI) 316 (M^+, 13%), 259 [M^+ − (CH_3)$_2$CHCH_2, 9%], 245 (10), 243 (M^+ − $SiMe_3$, 9%), 235 [M^+ − CH_3CH(CH_2)CH(CH_2)CH_2, 8%], 187 (72), 180 (55), 179 (100), 177 (22), 159 (20), 145 (29), 135 (84), 121 (40).

4,5-Dimethyl-1-phenyl-2-(prop-2′-yl)-1-(trimethylsilyl)-silacyclohexane 24–27; and 1-(2′,3′-dimethylbut-1′-yl)-1-(2′-methylpropyl)-2,2,2-trimethyl-1-phenyldisilane 28

A mixture of silanes **22** and **23** (0.57 g, 1.79 mmol) and platinum dioxide monohydrate (*ca.* 0.01 g, 0.04 mmol) in absolute ethanol (8 ml) was repeatedly evacuated and flushed with hydrogen from a balloon. The mixture was then stirred under the hydrogen atmosphere for 21 h. It was then filtered through a Celite pad and washed through with ether (15 ml). The filtrate was concentrated and dried *in vacuo*. Flash column chromatography (petroleum ether) gave two separate mixtures.

The first fraction (0.03 g, 6%); R_f (petroleum ether) 0.97; consisted of isomers of: 1-cyclohexyl-4,5-dimethyl-2-(prop-2′-yl)-1-(trimethylsilyl)silacyclohexane; *m/z* (GCMS, EI) 324 (M^+, 11%), 251 (M^+ − $SiMe_3$, 79%), 241 (M^+ − cyclohexyl, 12%), 209 (9), 195 (24), 181 (32), 169 (58), 127 (45); and 1-cyclohexyl-4,5-dimethyl-2-(prop-2′-yl)-1-(trimethylsilyl)silacyclohex-4-ene; *m/z* (GCMS, EI) 322 (M^+, 9%), 249 (M^+ − $SiMe_3$, 50%), 239 (M^+ − cyclohexyl, 11%), 193 (48), 181 (23), 169 (26), 167 (27); in a 15 : 62 : 11 : 12% ratio (ratio of product peak integrals by GC).

The second fraction (0.37 g, 64%); R_f (petroleum ether) 0.87; consisted of the title compounds in the ratio 51 : 30 : 6 : 5 : 8 (ratio of product peak integrals by GC), consisting of: four diastereoisomers **24**–**27** of the silacycle; *m/z* (GCMS, EI) 318 (M^+, 22%), 245 (M^+ − $SiMe_3$, 100%), 203 (34), 189 (50), 175 (82), 161 (44), 147 (28), 135 (70), 121 (28), 111 (70); and disilane **28**; *m/z* (GCMS, EI) 320 (M^+, 7%), 247 (M^+ − $SiMe_3$, 38%), 235 [M^+ − (CH_3)$_2$CHCH(CH_3)CH_2, 3%], 221 (4), 191 (73), 179 (66), 163 (39), 135 (71), 121 (100), 107 (82), 105 (51), 85 [(CH_3)$_2$CHCH(CH_3)CH_2^+, 33%].

(±)-(2*R**,3*S**,5*R**) 2,3,6-Trimethylheptane-1,5-diol 29a

A solution of silacycle mixture **24**–**27** was oxidised following the standard protocol as described above to afford the title compound as a viscous colourless oil (39%); R_f (petroleum ether/ethyl acetate [1 : 1]) 0.56; ν_{max} (thin film) 3354 (broad, O–H), 2958, 2931, 2876, 1464, 1383, 1103, 1024, 948, 935 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 3.57 (1H, dd, J = 7.0, 11.0 Hz, 1-*H*H), 3.49 (1H, dt, J = 8.0, 5.0 Hz, 5-*H*), 3.46 (1H, dd, J = 10.5, 7.0 Hz, 1-H*H*), 1.82 (1H, m, 3-*H*), 1.71 (1H, m, 2-*H*), 1.66 (1H, m, 6-*H*), 1.57 (1H, ddd, J = 14.0, 6.5, 5.0 Hz, 4-*H*H), 1.21 (1H, ddd, J = 14.0, 8.0, 7.0 Hz, 4-H*H*), 0.94 (3H, d, J = 7.0 Hz, 9-H_3), 0.92 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.88 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.87 (3H, d, J = 7.0 Hz, 8-H_3); δ_C (126 MHz; $CDCl_3$) 75.39 (5-*C*), 65.34 (1-*C*), 39.88 (2-*C*), 37.05 (4-*C*), 32.98 (6-*C*), 30.69 (3-*C*), 19.09 [CH(*C*H_3)$_2$], 18.43 (9-*C*), 16.54 [CH(*C*H_3)$_2$], 13.12 (8-*C*); *m/z* (ES^+) 197 (M + Na^+, 100%); HRMS (ES^+) Found M^+, 175.1697; $C_{10}H_{23}O_2$ requires M, 175.1698. Further elution gave a mixture of other diastereoisomers of 2,3,6-trimethylheptane-1,5-diol **30a**–**33a** as a white amorphous solid (24%); R_f (petroleum ether/ethyl acetate [1 : 1]) 0.29; mp 42.0–43.5 °C; ν_{max} (thin film) 3264 (broad, O–H), 2953, 2909, 2872, 1470, 1381, 1355, 1146, 1025, 989, 857 cm^{-1}; NMR data for major isomer 289: δ_H (500 MHz; $CDCl_3$) 3.54–3.39 (3H, m, 1-H_2 and 5-*H*), 1.93 (1H, m, 3-*H*), 1.79 (1H, m, 2-*H*), 1.63 (1H, m, 6-*H*), 1.47 (1H, ddd, J = 14.0, 9.0, 3.5 Hz, 4-*H*H), 1.28 (1H, ddd, J = 14.0, 9.0, 5.0 Hz, 4-H*H*), 0.92 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.90 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.82 (3H, d, J = 7.0 Hz, 9-H_3), 0.76 (3H, d, J = 7.0 Hz, 8-H_3); δ_C (126 MHz; $CDCl_3$) 73.92 (5-*C*), 66.70 (1-*C*), 38.91 (4-*C*), 37.36 (2-*C*), 33.72 (6-*C*), 29.11 (3-*C*), 18.80 [CH(*C*H_3)$_2$], 17.09 [CH(*C*H_3)$_2$], 15.00 (9-*C*), 10.59 (8-*C*); *m/z* (ES^+) 197 (M + Na^+); Found C, 69.08; H, 12.85; $C_{10}H_{23}O_2$ requires C, 68.92; H, 12.72%.

(±)-(2*S**,3*R**,5*S**) 1,5-Bisbenzoyloxy-2,3,6-trimethylheptane 29b

To a solution of diol **29a** (0.03 g, 0.16 mmol) and DMAP (0.04 g, 0.30 mmol) in THF (6 ml) was added dropwise a solution of benzoyl chloride (0.19 ml, 1.60 mmol) and triethylamine (0.3 ml, 2.3 mmol) in THF (6 ml). The mixture was stirred at RT for 18 h. Water (10 ml) and ether (10 ml) were then added. The aqueous layer was separated and extracted with ether (3 × 10 ml). The combined organic extracts were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash column chromatography (hexane/ethyl acetate [9 : 1]) gave the pure title ester **29b** as a thick colourless oil (0.02 g, 32%); R_f (hexane/ethyl acetate [4 : 1]) 0.90; ν_{max} (thin film) 2964, 2907, 2878, 1714 (C=O), 1602, 1584, 1463, 1451, 1389, 1314, 1273, 1176, 1112, 1070, 1026, 971 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 8.05 (4H, m, Ar–*H*), 7.56 (2H, t, J = 7.5 Hz, Ar–*H*), 7.44 (4H, m, Ar–*H*), 5.18 (1H, m, 5-*H*), 4.29 (1H, dd, J = 11.0, 6.0z, 1-*H*H), 4.17 (1H, dd, J = 11.0, 7.0 Hz, 1-H*H*), 2.07 (1H, m, 2-*H*), 1.97 (1H, m, 6-*H*), 1.79 (1H, m, 4-*H*H), 1.73 (1H, m, 3-*H*), 1.59 (1H, dt, J = 13.5, 7.5 Hz, 4-H*H*), 1.00 (6H, d, J = 7.0 Hz, 8-H_3 and 9-H_3), 0.98 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.96 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 166.64 (C=O), 166.27 (C=O), 132.85 (*Ar*), 132.76 (*Ar*), 130.70 (*ipso-Ar*), 130.36 (*ipso-Ar*), 129.53 (*Ar*), 129.52 (*Ar*), 128.33 [*Ar*(×2)], 77.61 (5-*C*), 67.21 (1-*C*), 36.54 (2-*C*), 34.79 (4-*C*), 32.46 (3-*C*), 31.25 (6-*C*), 18.96 [CH(*C*H_3)$_2$], 16.90 (8- or 9-*C*), 16.72 [CH(*C*H_3)$_2$], 14.53 (8- or 9-*C*); *m/z* (CI) 400 (M + NH_4^+, 100%), 383 (M + H^+, 4%), 338 (8), 324 (4), 278 (M − PhCO + H^+, 38%), 261 (M^+ − $PhCO_2$, 70%), 218 (10), 200 (13), 183 (54), 156 (10); HRMS (CI) Found MNH_4^+, 400.2483; $C_{24}H_{33}NO_4$ requires MNH_4, 400.2488. Further elution gave 5-hydroxy-2,3,6-trimethylhept-1-yl benzoate (0.01 g, 19%); R_f (hexane/ethyl acetate [9 : 1]) 0.58; ν_{max} (thin film) 3423 (broad, O–H),

2960, 2929, 2875, 1720 (C=O), 1601, 1451, 1383, 1275, 1213, 1175, 1113, 1070, 1026, 987 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 8.04 (2H, d, J = 8.5 Hz, Ar–*H*), 7.55 (1H, m, Ar–*H*), 7.44 (2H, t, J = 7.5 Hz, Ar–*H*), 4.31 (1H, dd, J = 11.0, 6.5 Hz, 1-*H*H), 4.14 (1H, dd, J = 11.0, 7.5 Hz, 1-H*H*), 3.54 (1H, dt, J = 8.0, 4.5 Hz, 5-*H*), 2.04 (1H, m, 2-*H*), 1.81 (1H, m, 3-*H*), 1.69–1.60 (2H, m's, 4-*H*H and 6-*H*), 1.29 (1H, ddd, J = 14.5, 8.0, 7.5 Hz, 4-H*H*), 1.03 (3H, d, J = 7.0 Hz, 8-H_3), 1.01 (3H, d, J = 7.0 Hz, 9-H_3), 0.93 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.87 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 166.69 (C=O), 132.86 (*Ar*), 130.57 (*ipso-Ar*), 129.51 (*Ar*), 128.35 (*Ar*), 75.04 (5-*C*), 67.38 (1-*C*), 37.95 (4-*C*), 36.31 (2-*C*), 33.13 (6-*C*), 32.66 (3-*C*), 19.09 [CH(*C*H$_3$)$_2$], 17.31 (9-*C*), 16.08 [CH(*C*H$_3$)$_2$], 14.62 (8-*C*); *m/z* (ES^+) 579 (M_2Na^+, 3%), 301 (M + Na^+, 100%); HRMS (CI) Found MNa^+, 301.1779; $C_{17}H_{26}O_3Na$ requires MNa, 301.1780.

1,5-Bisbenzoyloxy-2,3,6-trimethylheptane 30b–32b

To a solution of diol mixture **30a**–**32a** (0.03 g, 0.18 mmol) and DMAP (0.04 g, 0.34 mmol) in THF (7 ml) was added dropwise a solution of benzoyl chloride (0.21 ml, 1.84 mmol) and triethylamine (0.37 ml, 2.68 mmol) in THF (7 ml). The mixture was stirred at RT for 19 h. Saturated sodium hydrogen carbonate solution (10 ml) and ether (10 ml) were then added. The aqueous layer was separated and extracted with ether (3 × 10 ml). The combined organic extracts were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash column chromatography (petroleum ether/ethyl acetate [9 : 1]) gave the title compounds (0.04 g, 60%) as a mixture in a ratio of 82 : 12 : 6 (ratio of product peak integrals by GC); R_f (hexane/ethyl acetate [4 : 1]) 0.85; data for the major diastereoisomer **30b**: ν_{max} (thin film) 2963, 2877, 1717 (C=O), 1601, 1584, 1491, 1465, 1451, 1388, 1370, 1314, 1275, 1176, 1112, 1069, 1026, 971, 711 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 8.04 (2H, dd, J = 7.5, 1.0 Hz, Ar–*H*), 7.93 (2H, dd, J = 7.5, 1.0 Hz, Ar–*H*), 7.55 (1H, tt, J = 7.5, 1.0 Hz, Ar–*H*), 7.49 (1H, tt, J = 7.5, 1.0 Hz, Ar–*H*), 7.42 (2H, t, J = 7.5 Hz, Ar–*H*), 7.30 (2H, t, J = 7.5 Hz, Ar–*H*), 5.17 (1H, dt, J = 9.0, 4.5 Hz, 5-*H*), 4.18 (1H, d, J = 7.5 Hz, 1-*H*H), 4.17 (1H, d, J = 6.5 Hz, 1-H*H*), 2.22 (1H, m, 2-*H*), 1.97 (1H, m, 6-*H*), 1.88 (1H, m, 3-*H*), 1.74–1.61 (2H, m, 4-H_2), 0.99 [3H, d, J = 5.0 Hz, CH(CH_3)$_2$], 0.98 [3H, d, J = 5.0 Hz, CH(CH_3)$_2$], 0.91 (3H, d, J = 7.0 Hz, 8-H_3), 0.90 (3H, d, J = 7.0 Hz, 9-H_3); δ_C (126 MHz; $CDCl_3$) 166.56 (C=O), 166.21 (C=O), 132.70 (*Ar*), 132.63 (*Ar*), 130.58 (*ipso-Ar*), 130.28 (*ipso-Ar*), 129.53 (*Ar*), 129.44 (*Ar*), 128.30 (*Ar*), 128.19 (*Ar*), 76.74 (5-*C*), 67.99 (1-*C*), 35.72 (4-*C*), 34.55 (2-*C*), 31.78 (6-*C*), 29.80 (3-*C*), 18.59 [CH(*C*H$_3$)$_2$], 17.33 [CH(*C*H$_3$)$_2$], 14.86 (9-*C*), 10.79 (8-*C*); *m/z* (GCMS, CI) 401 (M + NH_4 + H^+, 60%), 400 (M + NH_4^+, 100%), 383 (M + H^+, 44%), 278 (M^+ − PhCO, 51%), 261 (M^+ − $PhCO_2$, 90%), 156 (13), 139 (36), 122 (30), 105 (61), 95 (32). Further elution gave 5-hydroxy-2,3,6-trimethylheptyl benzoate as a clear oil (0.01 g, 26%); R_f (hexane/ethyl acetate [4 : 1]) 0.56; ν_{max} (thin film) 3493 (broad, O–H), 2960, 2927, 2876, 1721 (C=O), 1602, 1468, 1452, 1383, 1276, 1177, 1115, 1070, 1027, 985 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 8.04 (2H, d, J = 8.0 Hz, Ar–*H*), 7.55 (1H, m, Ar–*H*), 7.44 (2H, t, J = 8.0 Hz, Ar–*H*), 4.25 (1H, dd, J = 11.0, 4.0 Hz, 1-*H*H), 4.19 (1H, dd, J = 11.0, 7.0 Hz, 1-H*H*), 3.49 (1H, dt, J = 9.0, 4.5 Hz, 5-*H*), 2.11 (1H, m, 2-*H*), 1.97 (1H, m, 3-*H*), 1.65 (1H, m, 4-*H*H), 1.53 (1H, m, 6-*H*), 1.32 (1H, m, 4-H*H*), 0.94 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.91 (3H, d, J = 7.0 Hz, 8-H_3), 0.91 (3H, d, J = 7.0 Hz, 9-H_3), 0.90 [3H, d, J = 7.0, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 166.66 (C=O), 132.84 (*Ar*), 130.42 (*ipso-Ar*), 129.51 (*Ar*), 128.34 (*Ar*), 74.30 (5-*C*), 68.63 (1-*C*), 38.89 (4-*C*), 34.75 (2-*C*), 33.63 (6-*C*), 30.30 (3-*C*), 18.85 [CH(*C*H$_3$)$_2$], 16.71 [CH(*C*H$_3$)$_2$], 15.25 (8-*C*), 10.97 (9-*C*); *m/z* (ES^+) 579 (M_2Na^+, 3%), 301 (M + Na^+, 100%); HRMS (ES^+) Found M^+, 279.1963; $C_{17}H_{27}O_3$ requires M, 279.1960.

(±)-(6*S**,3*S**,4*R**)3,4-Dimethyl-6-(prop-2′-yl)tetrahydropyran-2-one 35

A solution of diol **29a** (0.07 g, 0.43 mmol) was oxidised using standard TPAP conditions to give the title compound **35** (0.05 g, 63%); R_f (hexane/ether [1 : 1]) 0.73; ν_{max} (thin film) 2963, 2933, 2870, 1731 (C=O), 1457, 1387, 1181, 1133, 1088, 1032, 987 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 4.22 (1H, dt, J = 11.0, 5.0 Hz, 6-*H*), 2.49 (1H, qd, J = 7.0, 5.0 Hz, 3-*H*), 2.12 (1H, m, 4-*H*), 1.86–1.75 [2H, m, 5eq-*H* and C*H*(CH$_3$)$_2$], 1.70 (1H, dt, J = 14.0, 5.0 Hz, 5ax-*H*), 1.16 (3H, d, J = 7.0 Hz, 9-H_3), 0.97 (3H, d, J = 7.5 Hz, 10-H_3), 0.93 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.90 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (100 MHz; $CDCl_3$) 174.67 (C=O), 81.61 (6-*C*), 40.58 (3-*C*), 33.04 (7-*C*), 32.66 (5-*C*), 30.15 (4-*C*), 17.61 [CH(*C*H$_3$)$_2$], 17.52 [CH(*C*H$_3$)$_2$], 14.04 (10-*C*), 13.67 (9-*C*); *m/z* (EI) 170 (M^+, 32%), 128 (26), 127 (M^+ − ^{i}Pr, 56%), 100 (27), 99 (63), 56 (100); HRMS (EI) Found M^+, 170.1305; $C_{10}H_{18}O_2$ requires M, 170.1307.

3,4-Dimethyl-6-(prop-2′-yl)tetrahydropyran-2-one 36–38

A solution of diol mixture **30a**–**32a** (0.04 g, 0.25 mmol) was oxidised using standard TPAP conditions to give the title compounds **36**–**38** (0.03 g, 64%) as a mixture of diastereoisomers in a ratio of 84 : 12 : 4 (ratio of product peak integrals by GC); R_f (hexane/ether [1 : 1]) 0.57; ν_{max} (thin film) 2965, 2934, 2877, 1742 (C=O), 1456, 1373, 1358, 1259, 1237, 1199, 1138, 1097, 1049, 999 cm^{-1}; NMR data for the major isomer **36**: δ_H (500 MHz; $CDCl_3$) 4.00 (1H, ddd, J = 11.0, 6.0, 3.0 Hz, 6-*H*), 2.15 (1H, m, 3-*H*), 1.86 (1H, m, 5a-*H*), 1.81 [1H, m, C*H*(CH$_3$)$_2$], 1.70 (1H, m, 4-*H*), 1.48 (1H, dt, J = 14.0, 3.5 Hz, 5b-*H*), 1.21 (3H, d, J = 7.0 Hz, 9-H_3), 1.11 (3H, d, J = 6.5 Hz, 10-H_3), 0.98 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.93 [3H, d, J = 7.0 Hz, C*H*(CH$_3$)$_2$]; δ_C (126 MHz; $CDCl_3$) 176.44 (C=O), 80.18 (6-*C*), 40.46 (3-*C*), 32.81 (5-*C*), 32.11 [*C*H(CH$_3$)$_2$], 31.03 (4-*C*), 21.19 (10-*C*), 18.01 [CH(*C*H$_3$)$_2$], 17.85 [CH(*C*H$_3$)$_2$], 14.20 (9-*C*); *m/z* (EI) 170 (M^+, 8%), 128 (20), 127 (M^+ − ^{i}Pr, 100%), 99 (83), 83 (33), 81 (73), 71 (34), 70 (52), 69 (50).

(±)-(3*R**,6*S**) 3-Methyl-6-prop-2′-yl-tetrahydropyran-2-one 41; and (±)-(3*S**,6*S**) 3-methyl-6-prop-2′-yl-tetrahydropyran-2-one 42

Obtained following flash column chromatography as a mixture in a 66 : 34 ratio (35%) (GC and NMR); R_f (petroleum ether/ether [1 : 1]) 0.45; ν_{max} (thin film) 2965, 2936, 2877, 1737 and 1731 (C=O), 1462, 1377, 1243, 1186, 1119, 1093, 1012, 996, 931 cm^{-1}; *m/z* (EI) 156 (M^+, 18%), 114 (21), 113 (M^+ − ^{i}Pr, 56%), 84 (80). **41** δ_H (500 MHz; $CDCl_3$) 4.08 (1H, ddd, J = 11.0, 5.5, 3.0 Hz, 6-*H*), 4.01 2.40 (1H, m, 3-*H*), 2.02 (1H, m, 4-*H*H), 1.91–1.81 [3.2H, m, 5-*H*, C*H*(CH$_3$)$_2$], 1.68–1.46 (3.2H, m, 5-H*H*, 4-H*H*), 1.29 (3H, d, J = 7.0 Hz, 9-H_3), 0.97 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.95 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (100 MHz; $CDCl_3$) 174.66 (C=O), 86.41 (6-*C*), 36.21 (3-*C*), 32.92 [*C*H(CH$_3$)$_2$], 28.44 (4-*C*), 25.64 (5-*C*), 17.68 [CH(*C*H$_3$)$_2$], 17.61 [CH(*C*H$_3$)$_2$], 17.38 (9-*C*); **42** δ_H (500 MHz; $CDCl_3$) 4.01 (1H, ddd, J = 11.5, 6.5, 3.5 Hz, 6-*H*), 2.59 (1H, m, 3-*H*), 2.07 (1H, m, 4-*H*H), 1.91–1.81 [2H, m, 5-*H*H and C*H*(CH$_3$)$_2$], 1.68–1.46 (2H, m, 5-H*H* and 4-H*H*), 1.20 (3H, d, J = 6.5 Hz, 9-H_3), 0.99 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.94 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (100 MHz; $CDCl_3$) 176.65 (C=O), 82.70 (6-*C*), 32.98 (3-*C*), 32.32 [*C*H(CH$_3$)$_2$], 25.52 (4-*C*), 23.41 (5-*C*), 17.97 [CH(*C*H$_3$)$_2$], 17.61 [CH(*C*H$_3$)$_2$], 16.11 (9-*C*) accompanied on further elution by (±)-(4*S**,6*S**) 4-methyl-6-prop-2′-yl-tetrahydropyran-2-one **43** (15%); R_f (petroleum ether/ether [1 : 1]) 0.33; ν_{max} (thin film) 2961, 2930, 2875, 1740 (C=O), 1464, 1388, 1371, 1282, 1250, 1237, 1183, 1084, 1066, 1002 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 4.08 (1H, ddd, J = 10.5, 6.5, 4.0 Hz, 6-*H*), 2.55 (1H, dd, J = 9.0, 9.0 Hz, 3-*H*H), 2.18 (2H, m, 3-H*H* and 4-*H*), 1.87 [1H, oct, J = 6.5 Hz, C*H*(CH$_3$)$_2$], 1.83 (1H, ddd, J = 14.0, 10.5, 7.0 Hz, 5a-*H*), 1.52 (1H, ddd, J = 14.0, 5.5, 4.0 Hz, 5b-*H*), 1.10 (3H, d, J = 6.5 Hz, 9-H_3), 1.01 [3H, d, J = 6.5 Hz, CH(CH_3)$_2$], 0.95 [3H, d, J = 6.5 Hz, CH(CH_3)$_2$]; δ_C (101 MHz; $CDCl_3$) 172.91 (C=O), 81.61 (6-*C*), 37.28 (3-*C*), 32.43 [*C*H(CH$_3$)$_2$], 31.94 (5-*C*), 23.89 (4-*C*), 21.37 (9-*C*), 18.07 [CH(*C*H$_3$)$_2$], 18.02 [CH(*C*H$_3$)$_2$]; *m/z* (EI) 156 (M^+, 19%), 128 (15), 114 (24), 113 (M^+ − ^{i}Pr, 97%), 85 (100).

(±)-(6*S**,3*S**,5*R**) 3,5-Dimethyl-6-prop-2′-yl-tetrahydropyran-2-one 45 [24,25]

Obtained following flash column chromatography as a colourless oil (petroleum ether/ether [1 : 1]) (45%); R_f (petroleum ether/ether

[1 : 1]) 0.68; ν_{max} (thin film) 2965, 2935, 2877, 1731 (C=O), 1462, 1380, 1356, 1333, 1215, 1192, 1171, 1121, 1099, 1076, 1041, 996 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 3.83 (1H, dd, J = 10.5, 2.0 Hz, 6-*H*), 2.47 (1H, m, 3-*H*), 1.94 [1H, sept, d, J = 7.0, 2.0 Hz, C*H*$(CH_3)_2$], 1.92–1.82 (2H, m, 4b-H and 5-*H*), 1.46 (1H, q, J = 13.0 Hz, 4a-*H*), 1.27 (3H, d, J = 7.0 Hz, 9-H_3), 1.08 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.96 (3H, d, J = 7.0 Hz, 10-H_3), 0.89 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 174.92 (*C*=O), 90.95 (6-*C*), 37.66 (4-*C*), 36.25 (3-*C*), 31.14 [CH(*C*H_3)$_2$], 29.34 (5-*C*), 19.94 [CH(*C*H_3)$_2$], 17.30 (9-*C* and 10-*C*), 14.15 [CH(*C*H_3)$_2$]; *m*/*z* (EI) 170 (M^+, 8%), 127 ($M^+ - {}^iPr$, 80%), 100 (12), 99 (71).

(±)-(6*S**,3*R**,5*R**) 3,5-Dimethyl-6-(prop-2′-yl)tetrahydropyran-2-one 46

Obtained following flash column chromatography as a colourless oil (petroleum ether/ether [1 : 1]) as a mixture of isomers in a ratio of 79 : 11 : 8 : 2 (ratio of product peak integrals by GC); (26%); R_f (petroleum ether/ether [1 : 1]) 0.63; ν_{max} (thin film) 2966, 2934, 2875, 1743 (C=O), 1459, 1379, 1329, 1199, 1147, 1113, 1093, 1023, 997 cm^{-1}; NMR data for the major isomer **46**: δ_H (500 MHz; $CDCl_3$) 3.80 (1H, dd, J = 10.0, 2.5 Hz, 6-*H*), 2.62 (1H, pent, d, J = 8.5, 7.0 Hz, 3-*H*), 1.94 (1H, m, 5-*H*), 1.90 [1H, sept, d, J = 7.0, 2.5 Hz, C*H*$(CH_3)_2$], 1.68–1.64 (2H, m, 4-H_2), 1.20 (3H, d, J = 7.0 Hz, 9-H_3), 1.06 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.97 (3H, d, J = 7.0 Hz, 10-H_3), 0.92 [3H, d, J = 7.0 Hz, C*H*$(CH_3)_2$]; δ_C (126 MHz; $CDCl_3$) 176.75 (*C*=O), 87.24 (6-*C*), 35.17 (4-*C*), 32.40 (3-*C*), 28.97 [*C*H$(CH_3)_2$], 28.59 (5-*C*), 19.95 [CH(*C*H_3)$_2$], 17.67 (10-*C*), 16.45 (9-*C*), 14.28 [CH(*C*H_3)$_2$]; *m*/*z* (EI) 170 (M^+, 10%), 127 ($M^+ - {}^iPr$, 81%), 100 (15), 98 (76).

(±)-(6*R**,4*R**,5*S**) 4,5-Dimethyl-6-(prop-2′-yl)tetrahydropyran-2-one 48

Obtained following column chromatography as a colourless oil (petroleum ether/ether [2 : 1]) (13%); R_f (petroleum ether/ether [1 : 1]) 0.35; ν_{max} (thin film) 2961, 2929, 2875, 2857, 1739 (C=O), 1462, 1378, 1247, 1197, 1114, 1013 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 3.83 (1H, dd, J = 10.0, 2.0 Hz, 6-*H*), 2.67 (1H, dd, J = 17.0, 6.0 Hz, 3eq-*H*), 2.12 (1H, dd, J = 17.0, 9.0 Hz, 3ax-*H*), 1.97 [1H, sept, d, J = 7.0, 2.0 Hz, C*H*$(CH_3)_2$], 1.69 (1H, m, 4-*H*), 1.38 (1H, m, 5-*H*), 1.09 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 1.02 (3H, d, J = 7.0 Hz, 9-H_3), 0.97 (3H, d, J = 7.0 Hz, 10-H_3), 0.89 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 172.31 (C=O), 88.88 (6-*C*), 37.65 [3 or *C*H$(CH_3)_2$], 37.50 [3 or *C*H$(CH_3)_2$], 32.84 (4-*C*), 29.07 (5-*C*), 20.10 [CH(*C*H_3)$_2$], 19.99 (9-*C*), 14.83 (10-*C*), 13.96 [CH(*C*H_3)$_2$]; *m*/*z* (EI) 170 (M^+, 6%), 152 (6), 142 (8), 128 (14), 127 ($M^+ - {}^iPr$, 100%), 109 (7), 99 (42), 98 (50).

(±)-(6*R**,4*S**,5*S**) 4,5-Dimethyl-6-(prop-2′-yl)tetrahydropyran-2-one 49

Obtained following column chromatography as a colourless oil (petroleum ether/ether [2 : 1]) as a mixture of isomers in the ratio 87 : 10 : 3% (ratio of product peak integrals by GC) (60%); R_f (petroleum ether/ether [1 : 1]) 0.44; ν_{max} (thin film) 2963, 2930, 2878, 1734 (C=O), 1456, 1389, 1237, 1216, 1110, 1085, 1022, 990 cm^{-1}; NMR data for major isomer **49**: δ_H (500 MHz; $CDCl_3$) 3.95 (1H, dd, J = 9.0, 4.0 Hz, 6-*H*), 2.55 (1H, dd, J = 17.5, 6.0 Hz, 3ax-*H*), 2.35 (1H, dd, J = 17.5, 5.0 Hz, 3eq-*H*), 2.08 (1H, m, 4-*H*), 1.95 (1H, m, 5-*H*), 1.88 [1H, sept, d, J = 7.0, 4.0 Hz, C*H*$(CH_3)_2$], 1.05 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$], 0.99 (3H, d, J = 7.0 Hz, 9-H_3), 0.96 (3H, d, J = 7.0 Hz, 10-H_3), 0.93 [3H, d, J = 7.0 Hz, CH(CH_3)$_2$]; δ_C (126 MHz; $CDCl_3$) 171.77 (C=O), 86.94 (6-*C*), 37.47 (3-*C*), 32.67 (5-*C*), 29.94 [*C*H$(CH_3)_2$], 29.49 (4-*C*), 19.83 [CH(*C*H_3)$_2$], 15.30 [CH(*C*H_3)$_2$], 14.83 (9-*C*), 14.21 (10-*C*); *m*/*z* (EI) 170 (M^+, 8%), 152 (9), 142 (14), 128 (21), 127 ($M^+ - {}^iPr$, 67%), 109 (9), 99 (48), 98 (49).

(±)-(6*R**,5*S**) 5,6-Dimethyltetrahydropyran-2-one 51 [26]

Obtained following flash column chromatography as a colourless oil (petroleum ether/ether [2 : 1]) along with the (6*S**,5*S**) diastereoisomer in a ratio of 89 : 11 (56%) (by GC and NMR); R_f (petroleum ether/ether [1 : 1]) 0.22; ν_{max} (thin film) 2959, 2924, 2886, 2852, 1734 (C=O), 1458, 1383, 1351, 1251, 1225, 1095, 1046 cm^{-1}; NMR data for the major isomer **51**: δ_H (500 MHz; $CDCl_3$) 4.05 (1H, dq, J = 9.5, 6.5 Hz, 6-*H*), 2.63 (1H, ddd, J = 17.5, 7.0, 4.0 Hz, 3a-*H*), 2.48 (1H, ddd, J = 17.5, 10.0, 7.5 Hz, 3b-*H*), 1.90 (1H, m, 4a-*H*), 1.65–1.51 (2H, m, 5-*H* and 4b-*H*), 1.36 (3H, d, J = 6.0 Hz, 7-H_3), 1.00 (3H, d, J = 6.5 Hz, 8-H_3); δ_C (126 MHz; $CDCl_3$) 171.71 (C=O), 82.48 (6-*C*), 34.61 (5-*C*), 29.65 (3-*C*), 27.85 (4-*C*), 19.97 (7-*C*), 17.34 (8-*C*); *m*/*z* (EI) 128 (M^+, 5%), 113 ($M^+ - Me$, 4%), 99 (1), 85 (10), 84 ($M^+ - {}^iPr$, 80%), 69 (8), 56 (100).

(±)-(5*R**,6*S**) 5-Methyl-6-prop-1′-yl-tetrahydropyran-2-one 53

Obtained following flash column chromatography as a colourless oil (petroleum ether/ether [2 : 1]) along with the (5*S**,6*S**) diastereoisomer in a ratio of 72 : 28 (29%) (ratio of product peak integrals by GC); ν_{max} (thin film) 2960, 2931, 2874, 1736 (C=O), 1463, 1383, 1251, 1212, 1116, 1097, 1068, 1033, 1000 cm^{-1}; NMR data for major isomer **53**: δ_H (500 MHz; $CDCl_3$) 3.94 (1H, td, J = 8.0, 3.0 Hz, 6-*H*), 2.61 (1H, ddd, J = 18.0, 7.0, 4.5 Hz, 3a-*H*), 2.46 (1H, ddd, J = 18.0, 10.0, 7.0 Hz, 3b-*H*), 1.90 (1H, ddt, J = 13.5, 7.0, 5.0 Hz, 4a-*H*), 1.73–1.65 (2H, m, 5-*H* and 7-*H*H), 1.60–1.51 (3H, m, 7-H*H*, 8-*H*H and 4b-*H*), 1.43 (1H, m, 8-H*H*), 1.00 (3H, d, J = 6.5 Hz, 10-H_3), 0.93 (3H, t, J = 7.5 Hz, 9-H_3); δ_C (126 MHz; $CDCl_3$) 171.92 (C=O), 85.67 (6-*C*), 35.54 (5-*C*), 32.23 (7-*C*), 29.52 (3-*C*), 27.78 (4-*C*), 17.72 (8-*C*), 17.44, (10-*C*), 13.90 (9-*C*); *m*/*z* (EI) 156 (M^+, 1%), 138 (1), 128 (6), 113 ($M^+ - {}^nPr$, 86%), 85 (49), 84 (78).

(±)-(5*S**6*S**) 6-*tert*-Butyl-5-methyltetrahydropyran-2-one 55 [27]

Obtained following flash column chromatography as a colourless oil (petroleum ether/ether [2 : 1]) along with the (5*S**,6*S**) diastereoisomer in a ratio of 87 : 13 (36%) (ratio of product peak integrals by GC); ν_{max} (thin film) 2959, 2930, 2873, 1742 (C=O), 1482, 1460, 1380, 1368, 1328, 1244, 1197, 1081, 1061, 1003 cm^{-1}; NMR data for major isomer **55**: δ_H (500 MHz; $CDCl_3$) 3.71 (1H, d, J = 7.0 Hz, 6-*H*), 2.46 (1H, ddd, J = 17.5, 8.5, 5.0 Hz, 3ax-*H*), 2.32 (1H, ddd, J = 17.5, 9.0, 5.0 Hz, 3eq-*H*), 2.01 (1H, m, 5-*H*), 1.85 (1H, m, 4ax-*H*), 1.57 (1H, m, 4eq-*H*), 1.11 (3H, d, J = 7.0 Hz, 9-H_3), 0.99 [9H, s, C(CH_3)$_3$]; δ_C (126 MHz; $CDCl_3$) 173.04 (C=O), 92.54 (6-*C*), 36.17 (3-*C*), 28.69 (4-*C*), 27.86 (5-*C*), 27.75 [*C*(CH$_3$)$_3$], 25.98 [C(*C*H$_3$)$_3$], 21.41 (9-*C*); *m*/*z* (EI) 170 (M^+, 1%), 155 ($M^+ - Me$, 1%), 142 (1), 127 (4), 114 (44), 113 ($M^+ - {}^tBu$, 100%), 99 (12), 85 (62); HRMS (EI) Found M^+, 170.1302; $C_{10}H_{18}O_2$ requires M, 170.1301.

(±)-(6*S**,5*R**) 6-Phenyl-5-methyltetrahydro-pyran-2-one 57 [27]

Obtained following column chromatography (petroleum ether/ether [2 : 1]) (71%); R_f (petroleum ether/ether [1 : 1]) 0.21; ν_{max} (thin film) 3066, 3030, 2966, 2932, 2880, 1731 (C=O), 1455, 1382, 1247, 1221, 1201, 1147, 1084, 1036, 1016, 755, 701 cm^{-1}; δ_H (500 MHz; $CDCl_3$) 7.39–7.34 (3H, m, Ar–*H*), 7.31–7.29 (2H, m, Ar–*H*), 4.85 (1H, d, J = 10.5 Hz, 6-*H*), 2.77 (1H, ddd, J = 17.5, 7.0, 4.0 Hz, 3a-*H*), 2.65 (1H, ddd, J = 17.5, 10.0, 6.5 Hz, 3b-*H*), 2.06–1.97 (2H, m, 4a-*H* and 5-*H*), 1.71 (1H, m, 4b-*H*), 0.85 (3H, d, J = 6.5 Hz, 7-*H*); δ_C (126 MHz; $CDCl_3$) 171.23 (C=O), 138.39 (*ipso-Ar*), 128.65 (*Ar*), 128.50 (*Ar*), 127.12 (*Ar*), 88.34 (6-*C*), 34.75 (5-*C*), 29.71 (3-*C*), 27.81 (4-*C*), 17.18 (7-*C*); *m*/*z* (EI) 190 (M^+, 69%), 162 (28), 148 (14), 128 (6), 120 (16), 118 (52), 117 (54), 105 (93), 91 (38), 84 (79), 77 (Ph^+, 70%).

Acknowledgements

We thank the EPSRC and GlaxoSmithKline for financial support of this work (CASE award to D. K. W.); The EPSRC Mass Spectrometry Service for accurate mass determinations, Dr A. M. Kenwright for assistance with NMR experiments and Dr M. Jones for mass spectra.

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