Hosomi–Sakurai reactions of silacyclohexenes†

Nicholas J. Hughes,[a] Robert D. C. Pullin,[a] Mahesh J. Sanganee,[b] Jonathan D. Sellars,[a] Patrick. G. Steel*[a] and Michael J. Turner[a]

Received 19th June 2007, Accepted 10th July 2007
First published as an Advance Article on the web 31st July 2007
DOI: 10.1039/b709318g

Silacyclic allyl silanes, derived from silene–diene Diels–Alder reactions, combine with acetals in the presence of Lewis acids to afford, following oxidation of the intermediate fluorosilane, either butane-1,4-diols or tetrahydronaphthalenes containing four contiguous chiral centres with moderate to good diastereoselectivity.

Introduction

Originally considered to be objects of solely theoretical interest, silenes, compounds containing a silicon carbon double bond, have been demonstrated to be accessible species.[1–3] Although a number of silenes are isolable, Fig. 1,[4–11] most are highly reactive transient species that exhibit a unique reactivity profile, Fig. 2.

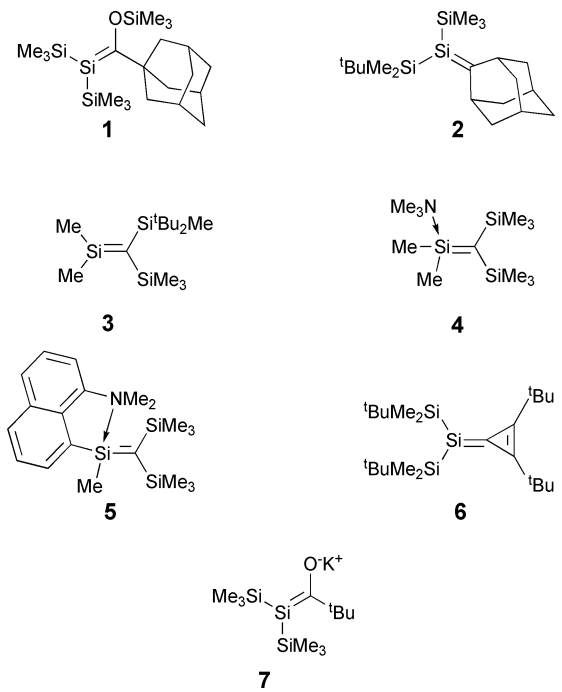


Fig. 1

Reflecting this, most research into the chemistry of silenes has focused on fundamental aspects of structure and reactivity with relatively little effort to explore these reagents in a more applied context.[12] With this in mind we have initiated a programme of work to study the use of silene cycloaddition chemistry to provide highly functionalised organosilanes suitable for further elaboration in a synthetic context.[13–16] We have previously shown that simple aryl and alkyl silenes, prepared through a sila modified Peterson reaction, combine with a range of simple alkyl dienes to afford silacyclohexenes with good levels of diastereoselectivity, Scheme 1. Following reduction of the double bond and conversion of the Si–Ph group to a Si–F unit, oxidative extrusion of the silicon centre afforded 1,4-diols and δ-lactones in good yield.[14] Alternatively, oxidation of the double bond provided access to the corresponding epoxide and diol respectively.[17] Both of these undergo facile acid mediated fragmentation, presumably through the intermediacy of a β-Si stabilised carbocation, to afford the allylic alcohol **15**.

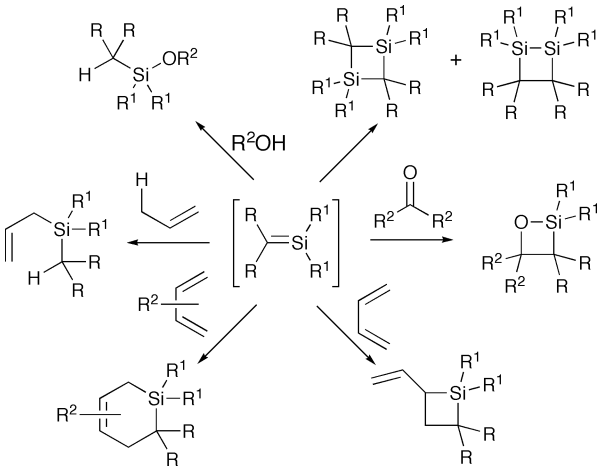
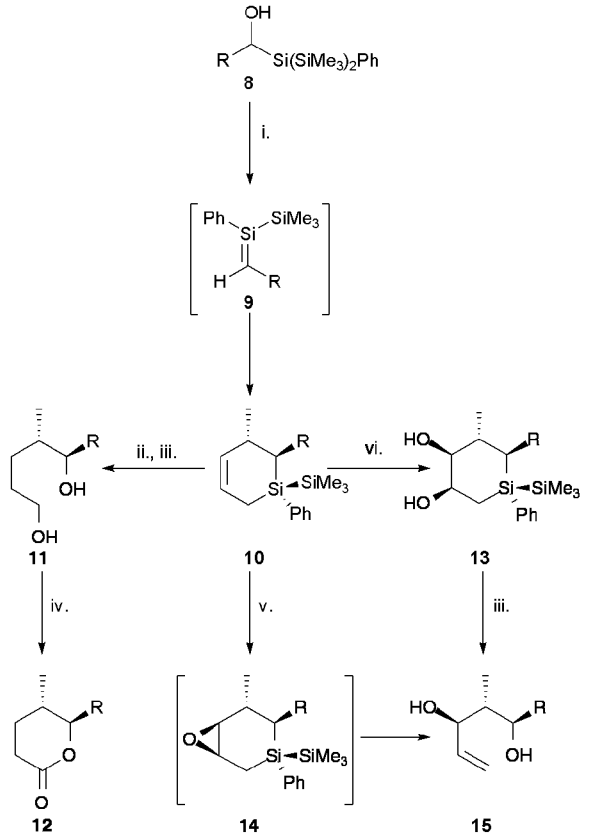


Fig. 2

This suggested that these silacyclohexenes could function as an allyl silane. Such species are widely used in organic chemistry and have been shown to undergo reactions involving both the silicon and olefinic moieties.[18] Probably the most common application in synthesis is the Hosomi–Sakurai reaction.[19–21] This transformation, which involves the Lewis acid promoted addition of allyl silanes to acetals and related electrophiles, is considered to follow a pathway involving addition of the carbon electrophile to the alkene leading to the formation of a carbocation intermediate stabilised by the presence of the β-silicon atom. Such a process requires efficient orbital overlap between the developing empty P_π orbital on the carbocation and a co-planar C–Si σ-bond, structure **16**, Fig. 3.

[a]*Department of Chemistry, University of Durham, Science Laboratories, South Road, Durham, DH1 3LE, UK. E-mail: p.g.steel@durham.ac.uk*
[b]*GlaxoSmithKline, Gunnels Wood Road, Stevenage, Herts, SG1 2NY, UK*

† Electronic supplementary information (ESI) available: Characterisation data for silacycloadducts **10c** and **10d**, and Sakurai products **36–39**, **41–44**, **46** and **48–60**. See DOI: 10.1039/b709318g



Scheme 1 *Reagents:* i. *n*BuLi, LiBr, 1,3-pentadiene, THF, −20 °C; ii. H_2, Pd–C; iii. $BF_3{\cdot}2AcOH$ then H_2O_2, $KHCO_3$, THF, MeOH; iv. TPAP, NMO, DCM; v. DMDO, acetone, DCM then SiO_2; vi. OsO_4, NMO, acetone, H_2O.

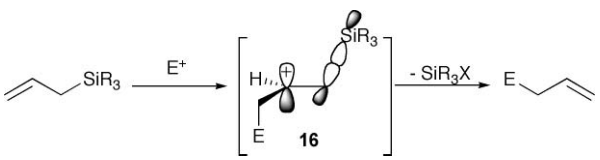
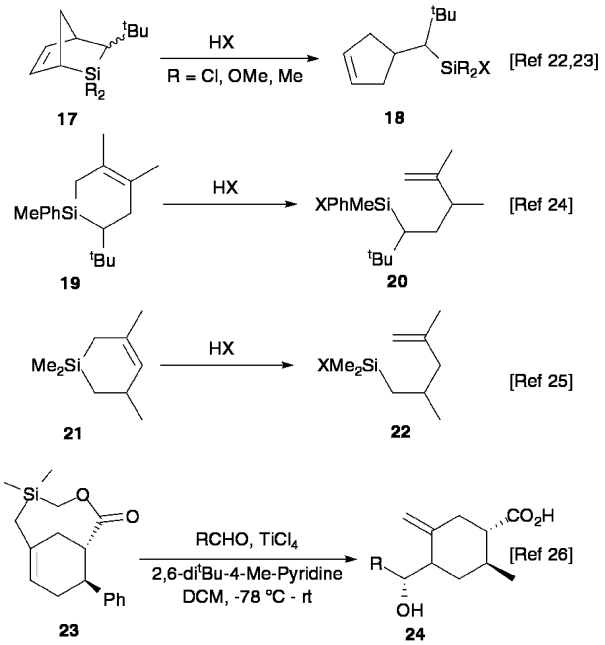


Fig. 3

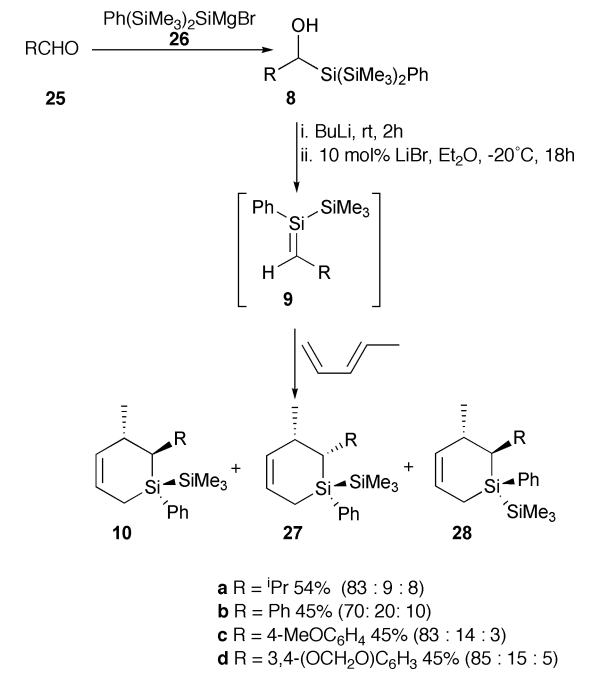
Whilst such an alignment is trivial in acyclic systems this is not the case for cyclic substrates. Although reactions of various related silacyclic substrates with simple electrophiles (H^+) have been described *e.g.* Scheme 2,[22–25] there is only one example of an analogous reaction involving a carbon centred electrophile. This involves the unique rigid bridgehead allylsilane **23**, described by Shea *et al.*, in which the silicon atom is held at an angle of 78° to the C=C plane, thus enforcing the required orbital overlap.[26] In this report we describe the full details of our studies on the use of silacyclic allyl silanes derived from silene-diene Diels–Alder reactions in the Hosomi–Sakurai reaction to provide access to either butane-1,4-diols or tetrahydronaphthols with 4 contiguous chiral centres.[27]

Results and discussion

Following the precedents established in our earlier work, each of the silacyclic allylsilanes used in this study was prepared in a standard way, Scheme 3. The appropriate aldehyde **25a–d** was



Scheme 2



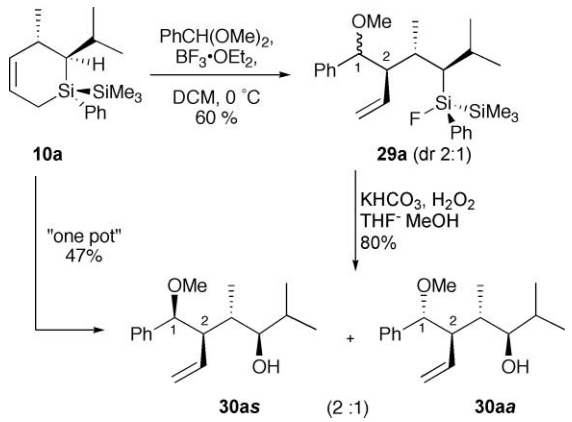
Scheme 3

combined with $Ph(SiMe_3)_2SiMgBr$ **26**, prepared by treatment of $PhSi(SiMe_3)_3$ with KO^{t}Bu followed by transmetallation with $MgBr_2$, to afford the silyl alcohols **8**. These on treatment with ^{n}BuLi and LiBr in the presence of the appropriate diene at −20 °C afforded the silacyclohexenes as an inseparable mixture of diastereoisomers. In all cases the major diastereoisomer obtained **10**, was consistent with a pathway proceeding *via* the preferential formation of a *Z*(Si) silene and subsequent [4 + 2] reaction with the diene through an *endo* Si–Ph transition state.[14]

With the silacycles in hand, attention then turned to the Sakurai reaction. Initial attempts to generate the oxonium ion from an

 This journal is © The Royal Society of Chemistry 2007

acetal prior to addition of the cycloadducts were unsuccessful leading to an intractable mixture of products. However, addition of $BF_3{\cdot}OEt_2$ to a precooled (0 °C) mixture of the silacyclohexene **10a** and benzaldehyde dimethyl acetal in DCM afforded, after aqueous workup and purification by flash column chromatography, the anticipated silyl fluoride **29a** in 60% yield, as a 1.6 : 1 mixture of stereoisomers (Scheme 4) as ascertained by ^{19}F NMR spectroscopy [$\delta_F = -184.72$ (d, $J = 15.8$ Hz); $\delta_F = -185.57$ (d, $J = 17.8$ Hz)], Fig. 4.



Scheme 4

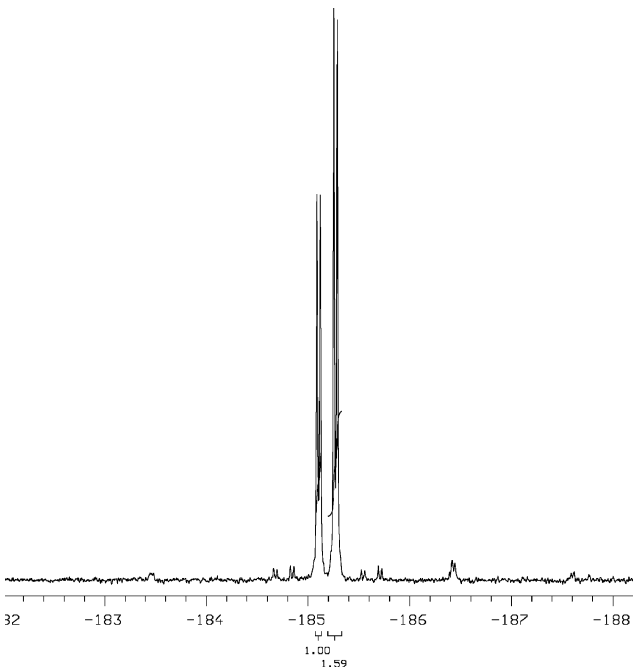
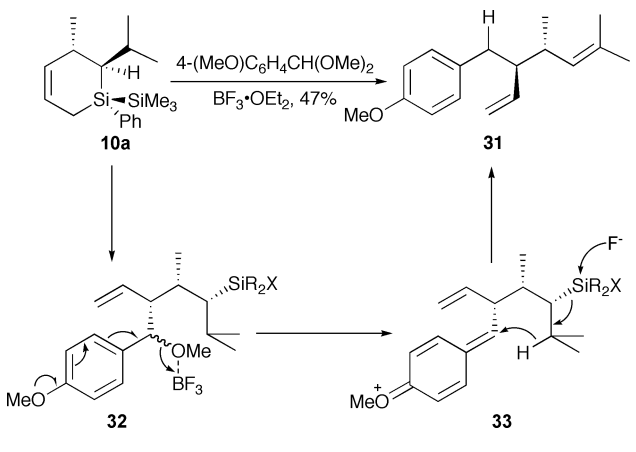


Fig. 4 ^{19}F NMR spectrum (376 MHz, $CDCl_3$) of silyl fluoride **29a**.

The regiochemistry is consistent with electrophilic addition to the allyl silane to form a carbocation intermediate stabilised by a β-silicon substituent followed by fluoride promoted fragmentation. At this stage it was not possible to determine the relative stereochemistry of either component and the mixture of isomers was oxidised by treatment with 35% w/w H_2O_2 in the presence of $KHCO_3$ to yield the monoprotected 1,4-diol (**30a**) in 80% yield. Importantly, this compound was also produced as a 1.6 : 1 mixture of diastereoisomers. Given that the Tamao oxidation is known to proceed with retention of configuration at carbon,[28] this suggested that the silyl fluoride was formed as a single Si stereoisomer and the mixture of isomers reflects the relative configurations at C-1 and C-2. Whilst the silyl fluoride proved to be a stable species, amenable to chromatography, it is possible to combine the two stages. After complete consumption of the silacyclohexene and a simple aqueous work-up, the crude reaction product is directly subjected to the oxidation process to afford the same product mixture in comparable yields.

A second experiment using 4-methoxybenzaldehyde dimethyl acetal was then undertaken. However, in this case, the addition of $BF_3{\cdot}OEt_2$ to the mixture of silacyclohexene **10a** and acetal led directly to the formation of the non-conjugated diene **31** in 47% yield. We account for this product, Scheme 5, through a sequence of steps involving initial addition of the oxonium ion to the silacycle followed by generation of a vinylogous oxacarbenium ion (*p*-quinone methide) **33**. Intramolecular hydride transfer to afford a silicon stabilised carbocation which undergoes rapid fluoride promoted desilylation to generate the second alkene. Importantly, in this case, the product was formed as a single diastereoisomer suggesting that the initial addition of the oxonium ion to the silacycle occurs stereoselectively to the face *syn* to the trimethylsilyl group of the starting silacyclohexene and the mixture of isomers observed with benzaldehyde dimethyl acetal reflects alternative configurations at the methoxy bearing carbon centre (C-1). Ultimately the relative stereochemistry of the major isomer from this reaction **30as** was established as the 1,2-*syn*, 2,3-*anti*, 3,4-*anti* configuration by single crystal X-ray diffraction, Fig. 5a.



Scheme 5

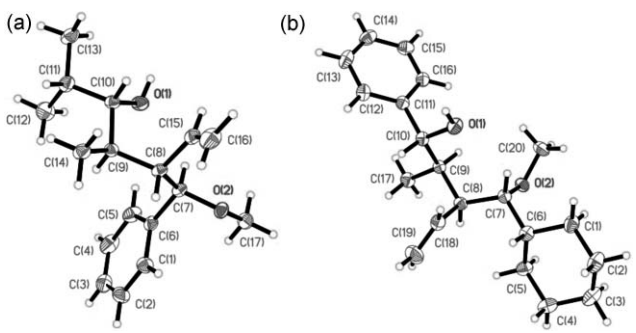
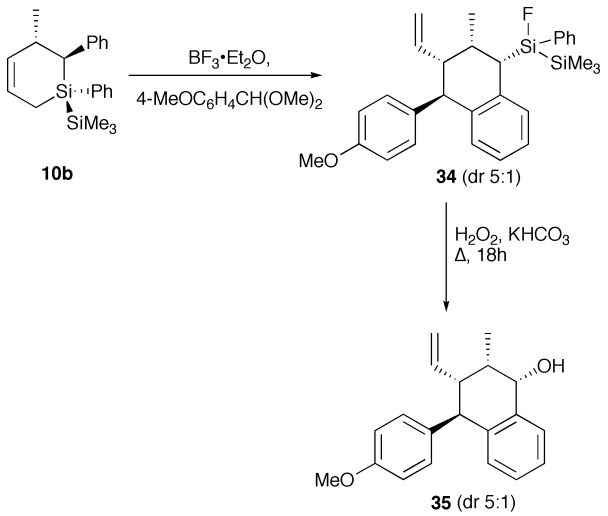


Fig. 5 (a) ORTEP structure of **30as** (co-crystalline phenol omitted for clarity; ellipsoids at 50% probability level). (b) ORTEP structure of **45** (ellipsoids at 50% probability level).

Formation of the non-conjugated diene through trapping of the benzylic oxonium ion by hydride migration suggested that further carbon–carbon bond formation could be combined with the Sakurai reaction if a suitable nucleophile could be incorporated into the silene precursor. Gratifyingly, reaction of a phenyl substituted silacycle with 4-methoxybenzaldehyde dimethyl acetal in the presence of $BF_3{\cdot}OEt_2$ at 0 °C afforded, after Tamao oxidation, the tetralol **35** in moderate yield as a 5 : 1 mixture of stereoisomers, Scheme 6. As before the intermediate silyl fluoride **34** can be isolated but there appears to be no material advantage in doing so. Moreover the diastereomeric ratio is unchanged on oxidation of the silyl fluoride to tetralol indicating that as before the silicon centre is a single stereoisomer and the mixture of diastereoisomers reflects alternative configurations at the benzylic carbon, C-1. The relative stereochemistry of the major isomer was assigned on the basis of ^{1}H NMR coupling constants and NOESY experiments, Fig. 6.



Scheme 6

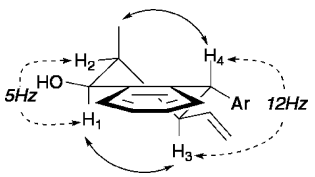
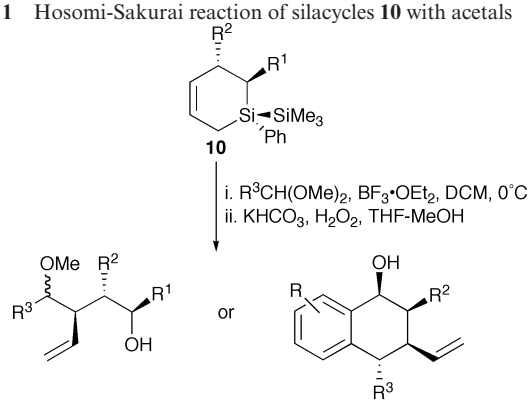


Fig. 6 Selected NOESY correlations (——) and coupling constants (---) for **35**.

Using the "single pot" process a range of acetals have been explored, Table 1 entries 1–13. With alkyl substituted silacycles (*e.g.* **10a**) both aromatic and alkyl acetals react to form butane diols although somewhat lower yields are observed with alkyl acetals. In general, more reactive electron deficient oxonium ions react more efficiently, Table 1 entry 8 and 10, although with these small amounts of an as yet unidentified third stereoisomer can be observed in the product mixture. In contrast, the use of acetals that can form very stable oxonium ions lead to extensive decomposition with no evidence for any Sakurai type products (entries 14–16). Attempts to use aldehydes as the electrophile either with $BF_3{\cdot}OEt_2$ or using fluoride anion initiation were equally unproductive. The use of other Lewis acids ($TiCl_4$, TMSOTf, $Sc(OTf)_3$) is viable and leads to similar isomer ratios although in somewhat reduced yields. This possibly reflects the benefits of forming a strong Si–F bond. Consistent with the need for a fluorine atom (nucleophile) to promote the fragmentation, attempts to use sub-stoichiometric amounts of $BF_3{\cdot}OEt_2$ led to diminished yields. In most cases the major diastereoisomer produced had the *syn*, *anti*, *anti* stereochemistry although use of cyclohexyl dimethyl acetal afforded the alternative *anti*, *anti anti* product **45** as the major isomer, Fig. 5b. Reaction of C-2 substituted aryl silacycles (**10b**,**c**,**d**) with aryl acetals which can promote the formation of

Table 1 Hosomi-Sakurai reaction of silacycles **10** with acetals



a R = ^{i}Pr; **b** R = Ph; **c** R = 4-$MeOC_6H_4$; **d** R = 3,4-$(OCH_2O)C_6H_3$

Entry	Silacycle	Acetal (R^3)	Product	Yield (dr)[a]
1	**10a**	C_6H_5	**30**	50% (2 : 1)
2	**10a**	4-$MeOC_6H_4$	**31**	47% (1 : 0)
3	**10a**	4-$CF_3C_6H_4$	**36**	23% (2 : 1)[b]
4	**10a**	4-BrC_6H_4	**37**	23% (2 : 1)
5	**10a**	CH_3	**38**	21% (2 : 1)[b]
6	**10b**	C_6H_5	**39**	55% (2 : 1)[b]
7	**10b**	C_6H_5[c]	**40**[c]	8% (2 : 1)
8	**10b**	4-$CF_3C_6H_4$	**41**	50% (8 : 3 : 2)
9	**10b**	4-BrC_6H_4	**42**	46% (3 : 1)
10	**10b**	4-$NO_2C_6H_4$	**43**	63% (7 : 4 : 2)
11	**10b**	CH_3	**44**	32% (2 : 1)
12	**10b**	c-C_6H_{11}	**45**	36% (1 : 2)
13	**10b**	C_6H_{13}	**46**	22% (1 : 1)
14	**10b**	4-$NMe_2C_6H_4$	nr	—
15	**10b**	2,4-$(MeO)_2C_6H_3$	nr	—
16	**10b**	2-Furyl	nr	—
17	**10b**	2-Thienyl	**47**	<5% (nd)
18	**10b**	4-$MeOC_6H_4$	**35**	27% (5 : 1)[b]
19	**10b**	$C_6H_4CH{=}CH$	**48**	44% (7 : 2)
20	**10b**	4-MeC_6H_4	**49**	23% (2 : 1)[d]
21	**10b**	2,4-$Me_2C_6H_3$	**50**	34% (2 : 1)
22	**10b**	2-Me-4-$MeOC_6H_3$	**51**	16% (9 : 1)
23	**10b**	3,4-$(MeO)_2C_6H_3$	**52**	17% (9 : 1)
24	**10b**	3,4-(OCH_2O) C_6H_3	**53**	11% (9 : 1)
25	**10b**	3,4,5-$(MeO)_3C_6H_2$	**54**	32% (1 : 0)
26	**10d**	3,4,5-$(MeO)_3C_6H_2$	**55**	28% (1 : 0)
27	**10d**	3,4-$(MeO)_2C_6H_3$	**56**	20% (1 : 0)
28	**10d**	4 -$MeOC_6H_4$	**57**	15% (13 : 1)
29	**10d**	2,4-$Me_2C_6H_3$	**58**	20% (3 : 1)
30	**10c**	4-$MeOC_6H_4$	**59**	18% (1 : 0)
31	**10c**	2,4-$Me_2C_6H_3$	**60**	15% (3 : 1)

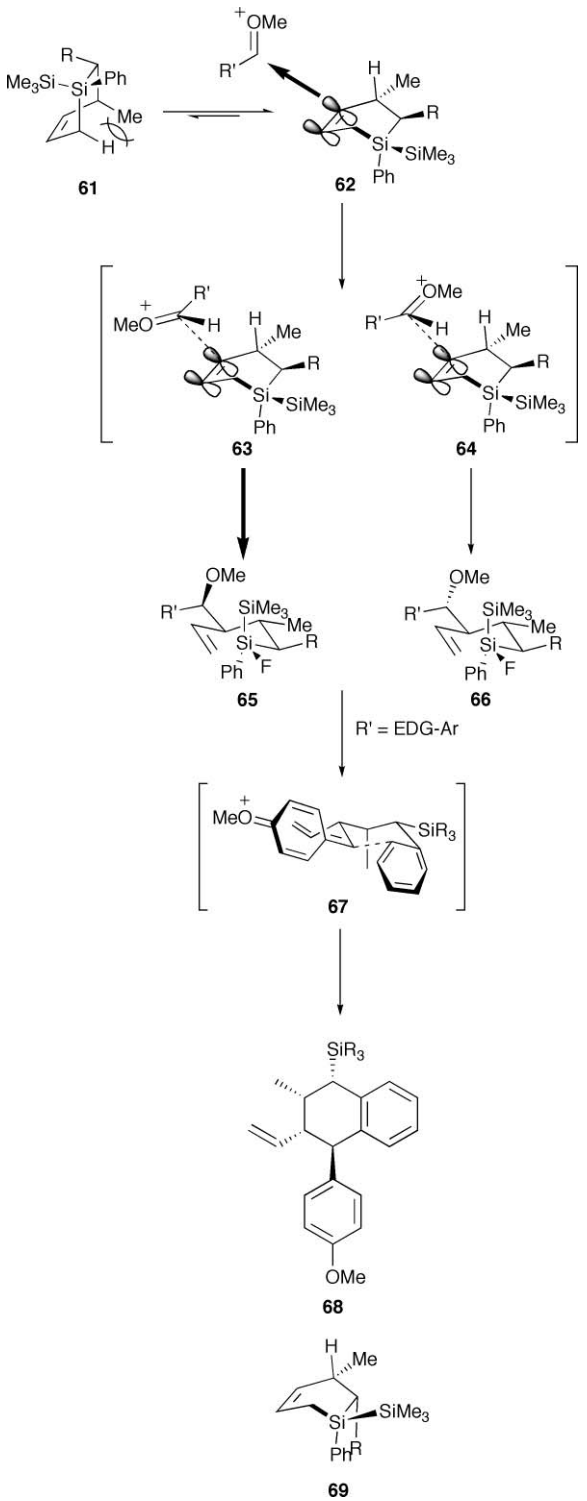
[a] dr determined from NMR of crude reaction mixture. [b] Yield for a two stage conversion involving isolation of intermediate silyl fluoride. [c] 2-Phenyl dioxane used—product **40** is 1,4-diphenyl-3-ethenyl-4-(3′-hydroxypropoxy)-2-methylbutan-1-ol (stereochemistry not determined). [d] Final reaction temperature = 25 °C.

This journal is © The Royal Society of Chemistry 2007

a benzylic carbocation affords tetralols *via* secondary cationic cyclisation, Table 1, entries 17–31. The limitation for this process is, as noted above, that if the first oxonium ion is too stable then the initial Sakurai reaction is not competitive with decomposition of the silacycle. The somewhat lower yields for this two step process are probably due to difficulties in achieving efficient conversion in this first step with the more electron rich (less reactive) substrates required to promote the formation of the second oxonium ion. However, the diastereoselectivity increases with electron donating ability of the acetal suggesting that in this series the major isomer reflects thermodynamic control. Consistent with this observation use of tolyldimethylacetal at 0 °C affords a mixture of the butane diol and tetralol **49** whilst allowing the reaction to warm to room temperature for a prolonged period (6 h) affords the tetralol as the exclusive product.

These results can be rationalised by a unified pathway involving initial generation of the oxonium ion from the acetal followed by Sakurai reaction with the silacyclohexene. This requires co-planarity of the C–Si and alkene π-orbital which can only be efficiently achieved when the silacycle adopts a pseudo boat structure **62**, Scheme 7. Whilst this is possible for the major silacycle isomer the alternative diastereoisomer **69** is inhibited from adopting such a conformation by eclipsing interactions between the Si–Ph and C-2 substituent. Consistent with such a proposal when the less reactive acetals are used at lower temperatures it is possible to re-isolate small quantities of the starting silacycle that are enriched in the minor isomers whilst the use of more reactive oxonium ions (acetals) can lead to reaction *via* other less favourable conformers. The observed selectivity is then a matter of approach of the electrophile to the least hindered (convex) face of the conformation of the major isomer **62**, *i.e.* that which avoids prow interactions between the C-3 methyl group and a C-6 hydrogen. This generates the observed 2,3-*anti*, 3,4-*anti* configuration. The C-1 configuration is then a matter of synclinal **63** or antiperiplanar **64** alignment of the oxonium ion with the allylsilane such that the aryl group is orientated in an "*exo*" fashion. The formation of the observed products suggests the former is of lower energy although reasons for the reversal of selectivity with cyclohexane carboxaldehyde dimethyl acetal are not obvious. The preferential formation of the 1,2 *anti* configuration in the cationic cyclisation to give the tetralol skeleton has considerable precedent in the lignan synthesis literature.[29–32] Such an outcome is consistent with cyclisation proceeding through a chair-like transition state with all substituents occupying an equatorial position **67**. However, as suggested above, thermodynamic control cannot be excluded particularly with acetals containing more electron donating substituents as these enhance the reversibility of the process.

In conclusion, this work has demonstrated that silacyclohex-4-enes, derived from silene–diene cycloadditions are viable substrates for the Hosomi–Sakurai reaction with both aryl and alkyl acetals. Following Tamao oxidation of the resultant silyl fluoride mono-protected cyclobutane diols can be obtained in moderate yield and diastereoselectivity. Moreover, when aryl acetals containing *ortho* or *para* electron-donating substituents are combined with silacyclohexenes containing a C-2 aryl substituent a further cyclisation occurs to afford the tetralol skeleton found in many lignan natural products. Future work will focus on enhancing the stereochemical control observed in each step of this cascade and applying the methodology to the synthesis of target structures. Results of these studies will be reported in due course.



Scheme 7

Experimental

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. Lithium bromide was dried by heating at 100 °C at 0.06 mmHg for 3 h. Magnesium bromide was synthesised by addition of 1,2-dibromoethane to an equivalent amount of magnesium in 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.[33] Yields refer to isolated yields of products of greater than 95% purity as determined by $^{1}H + ^{13}C$ 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 using a Diamond ATR (attenuated total reflection) accessory (Golden Gate) or as a solution in chloroform *via* transmission IR cells 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 (ppm) (number of protons, multiplicity, coupling constant J (Hz), assignment). Residual protic solvent $CHCl_3$ ($\delta_H = 7.26$) was used as the internal reference. ^{13}C NMR spectra were recorded at 63 MHz or 126 MHz, using the central resonance of $CDCl_3$ ($\delta_C = 77.0$ ppm) as the internal reference. ^{29}Si NMR spectra were recorded at 99 MHz on Varian Inova-500. ^{19}F NMR spectra were recorded at 376 MHz or 282 MHz on Varian VXR-400 or Varian Unity-300 respectively. All chemical shifts are quoted in parts per million relative to tetramethylsilane ($\delta_H = 0.00$ 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 and NOESY experiments.

Gas chromatography-mass spectra (GCMS, EI or CI) were obtained using a Thermo TRACE mass spectrometer. Electrospray mass spectra (ES) 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. Detailed experimental procedures describing the formation and characterisation of the silene silacycloadducts **10a** and **10b** and the X-ray crystallography for **30as** has previously been reported.[13,14,27] Characterisation data for silacycloadducts **10c** and **10d**, and Sakurai products **36–39**, **41–44**, **46** and **48–60** can be found in the ESI.†

Standard procedure for the Hosomi–Sakurai reaction of silacycles 10

Stage 1. A solution of silacycle (0.3 mmol) in dichloromethane (5 ml) was treated with the appropriate acetal (0.6 mmol) and cooled to 0 °C. The solution was then treated with $BF_3{\cdot}Et_2O$ ([0.5 M] in DCM, 0.3 mmol) and stirred at 0 °C for 6 h. The reaction mixture was then poured into aq. NH_4Cl and extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The concentrated organic material could then be utilised directly in the next stage or purified by flash chromatography to afford the silyl fluoride species.

Stage 2. The crude organic material from stage 1 or purified silyl fluoride species was dissolved in methanol : THF (5 ml, 1 : 1) and treated with $KHCO_3$ (1.0 mmol) and a 35% w/w solution of H_2O_2 (4.0 mmol) at room temperature. The reaction mixture was then heated under reflux for 5 h and then poured into $Na_2S_2O_3$ and extracted with EtOAc (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography (petrol, ether [95 : 5], [9 : 1], [4 : 1]) afforded the desired mono-protected 1,4-diols or tetralol.

(1*RS**,2*R**,3*S**,4*R**,(Si)*R**)-3,5-Dimethyl-2-ethenyl-4-(1′-fluoro-2′,2′,2′-trimethyl-1′-phenyldisilyl)-1-methoxy-1-phenylhexane 29a

Silacycle **10a** (0.35 g, 1.1 mmol) was combined with benzaldehyde dimethylacetal to give the title silyl fluoride **29a** as a pale yellow oil as a (2 : 1) mixture of diastereoisomers (0.3 g, 60%); R_f 0.6 (petrol–ether 95 : 5). ν_{max} (thin film) 2926, 2918, 1675, 1651, 1536, 1454, 1428, 1359, 1245, 1189, 1105, 916, 836, 800, 735, 729, 699, 543 cm^{-1}; NMR data given for major isomer δ_H (500 MHz, $CDCl_3$) 7.50–7.49 (2H, m, Ar-*H*), 7.35–7.33 (2H, m, Ar-*H*), 7.32–7.30 (4H, m, Ar-*H*), 7.19–7.17 (2H, m, Ar-*H*), 5.70 (1H, dt, *J* 17, 10, =C*H*), 4.95 (1H, d, *J* 10, =CH*H*), 4.51 (1H, bs, 1-*H*), 4.44 (1H, d, *J* 17, =C*H*H), 3.29 (3H, s, OCH_3), 2.56 (1H, m, 3-*H*), 2.20 (1H, bt, *J* 10, 2-*H*), 1.97 (1H, m, 5-*H*), 1.35 (3H, d, *J* 7, 3-CH_3), 1.03 (3H, 5-CH_3), 0.62 (3H, d, *J* 7, 6-H_3), 0.13 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 141.5 (Ar-*C*), 137.3 (=*C*H), 137.0 (Ar-*C*), 132.7 (Ar-*C*), 132.6 (Ar-*C*), 129.0 (Ar-*C*), 127.7 (Ar-*C*), 127.2 (Ar-*C*), 126.8 (Ar-*C*), 118.5 (=CH_2), 65.86 (C-1), 57.44 (OCH_3), 57.42 (C-2), 38.8 (C-4), 35.7 (C-3), 26.2 (C-5), 25.9 (5-CH_3), 24.0 (C-6), 16.6 (3-CH_3), −2.1 (Si(CH_3)$_3$); δ_F (300 MHz, $CDCl_3$) −185.6 (1F, d, *J* 18, Si-*F*); *m/z* (CI) 460 (MNH_4^+, 100%), 428 (35%), 411 (M^+ − (OCH_3), 40%); HRMS (ES^+) Found MNH_4^+, 460.2863, $C_{26}H_{39}FOSi_2NH_4$ requires M^+ 460.2862.

(3*R**,4*S**,5*R**,6*S**)-2,4-Dimethyl-5-ethenyl-6-methoxy-6-phenylhexan-3-ol 30

Oxidation of fluorosilane **29** (0.3 g, 0.6 mmol) afforded the title alcohol **30** as a colourless oil as a (2 : 1) mixture of diastereoisomers (0.1 g, 80%); R_f 0.4 (petrol–ether 9 : 1). ν_{max} (thin film) 3326 (broad, OH), 2958, 2874, 2834, 1605, 1594, 1498, 1471, 1454, 1363, 1233, 1066, 992, 918, 752, 691 cm^{-1}; NMR data given for the major isomer **30as** δ_H (500 MHz, $CDCl_3$) 7.34–7.31 (2H, m, Ar-*H*), 7.27–7.23 (3H, m, Ar-*H*), 6.04 (1H, ddd, *J* 17, 10, 10, 5-C*H*=), 5.09 (1H, dd, *J* 10, 2, =CH*H*), 4.76 (1H, dd, *J* 17, 2, =C*H*H), 4.48 (1H, d, *J* 4, 6-*H*), 3.76 (1H, d, *J* 3, O*H*), 3.28 (1H, m, 3-*H*), 3.23 (3H, s, OCH_3), 2.26 (1H, m, 5-*H*), 1.82 (1H, m, 4-*H*), 1.74 (1H, m, 2-*H*), 1.00 (3H, d, *J* 7, 2-CH_3), 0.86 (3H, d, *J* 7, 4-CH_3), 0.81 (3H, d, *J* 7, 1-H_3); δ_C (126 MHz, $CDCl_3$) 140.7 (*ipso*-Ar-*C*), 134.3 (*C*H=), 128.0 (Ar-*C*), 127.4 (Ar-*C*), 127.3 (Ar-*C*), 118.8 (=CH_2), 86.9 (*C*-6), 76.9 (*C*-3), 57.8 (*C*-5), 57.0 (OCH_3), 40.9 (*C*-4), 29.6 (*C*-2), 20.7 (2-CH_3), 17.4 (4-CH_3), 13.6 (*C*-1); *m/z* (ES^+) 285 (MNa^+); HRMS (ES^+) MNa^+ Found 285.1825, $C_{17}H_{26}O_2Na$ requires M^+ 285.1825.

This journal is © The Royal Society of Chemistry 2007

(2′*R,3′*S**)-1-(3′,5′-Dimethyl-2′-ethenylhex-4′-enyl)-4-methoxybenzene 31**

A solution of silacycle **10a** (0.05 g, 0.2 mmol) in dichloromethane (5 ml) was cooled to −78 °C and treated with 4-methoxybenzaldehyde dimethylacetal (0.1 ml, 0.3 mmol), then $BF_3{\cdot}Et_2O$ (0.03 ml, 0.2 mmol) and the reaction mixture stirred at room temperature for 12 h. The reaction was poured into NH_4Cl and extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried *in vacuo*. Flash chromatography (petrol–ether [98 : 2], [95 : 5], [9 : 1]) afforded the title compound as a colourless oil (0.02 g, 47%); R_f 0.7 (pet. ether–ether 9 : 1); ν_{max} (thin film) 2955, 2927, 2871, 2833, 2362, 2337, 1510, 1440, 1299, 1243, 1175, 1038, 910, 834 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.02 (2H, d, *J* 9, Ar-*H*), 6.80 (2H, d, *J* 9, Ar-*H*), 5.68 (1H, ddd, *J* 17, 11, 10, 2′-C*H*=), 5.00 (1H, d, *J* 11, 4′-*H*), 4.85 (1H, d, *J* 11, =C*H*H), 4.82 (1H, d, *J* 17, =CH*H*), 3.78 (3H, s, -OCH_3), 2.55 (2H, dd, *J* 14, 6, 1-H_2), 2.44 (1H, m, 2′-*H*), 2.24 (1H, m, 3′-*H*), 1.73 (3H, s, 6′-H_3), 1.57 (3H, s, 5′-CH_3), 0.92 (3H, d, *J* 7, 3′-CH_3); δ_C (126 MHz, $CDCl_3$) 157.5 (*C*-4), 139.4 (2′-*C*H=), 133.2 (*C*-1), 131.2 (*C*-5′), 130.0 (Ar-*C*), 127.3 (*C*-4′), 115.9 (=*C*H_2), 113.4 (Ar-*C*), 55.2 (O*C*H_3), 51.9 (*C*-2′), 38.2 (*C*-1′), 35.3 (*C*-3′), 26.0 (*C*-6′), 19.5 (3′-*C*H_3), 18.1 (5′-*C*H_3); *m/z* (CI, NH_3) 262 (MNH_4^+, 15%), 245 (M^+, 65%), 161 (10%), 121 (100%); HRMS (ES$^+$) Found M^+ 245.1896, $C_{17}H_{24}O$ requires M^+ 245.1900.

(1*R,2*R**,3*R**,4*S**,(Si)*R**)-1-(1′-Fluoro-2′,2′,2′-trimethyl-1′-phenyldisilyl)-4-(4″-methoxyphenyl)-2-methyl-3-ethenyl-1,2,3,4-tetrahydronaphthalene 34**

Silacycle **10b** (0.6 g, 1.8 mmol) was combined with 4-methoxybenzaldehyde dimethylacetal to give the title compound as a colourless gum (0.4 g, 44%); R_f 0.3 (petrol–ether 95 : 5) as a 5 : 1 mixture of diastereoisomers; ν_{max} (thin film) 1609, 1509, 1487, 1442, 1427, 1301, 1243, 1175, 1105, 1036, 912, 835 cm^{-1}; NMR data given for major isomer δ_H (500 MHz, $CDCl_3$) 7.66–7.64 (2H, m, Ar-*H*), 7.44–7.42 (3H, m, Ar-*H*), 7.38 (1H, m, Ar-*H*), 7.25 (1H, m, Ar-*H*), 6.98–6.96 (3H, m, Ar-*H*), 6.80–6.77 (3H, m, Ar-*H*), 5.71 (1H, m, 3-C*H*=), 4.87 (1H, d, *J* 10, =C*H*H), 4.76 (1H, d, *J* 17, =CH*H*), 3.87 (1H, d, *J* 11, 4-*H*), 3.78 (3H, s, OCH_3), 3.25 (1H, m, 1-*H*), 2.62 (1H, m, 3-*H*), 2.31 (1H, m, 2-*H*), 1.05 (3H, d, *J* 7, 2-CH_3), 0.14 (9H, s, Si(CH_3)$_3$); δ_C (126 MHz, $CDCl_3$) 157.8 (Ar-*C*), 140.2 (3-*C*H=), 139.9 (Ar-*C*), 138.0 (Ar-*C*), 135.2 (Ar-*C*), 136.8 (Ar-*C*), 136.4 (Ar-*C*), 133.2 (Ar-*C*), 130.9 (Ar-*C*), 130.4 (Ar-*C*), 129.7 (Ar-*C*), 128.2 (Ar-*C*), 125.9 (Ar-*C*), 125.5 (Ar-*C*), 116.0 (=*C*H_2), 113.5 (Ar-*C*), 55.1 (O*C*H_3), 52.7 (*C*-3), 46.3 (*C*-4), 38.7 (*C*-1), 34.4 (*C*-2), 12.8 (2-*C*H_3), −1.4 (Si(*C*H_3)$_3$); δ_F (300 MHz, $CDCl_3$) −183.5 (1F, d, *J* 7, Si-*F*); *m/z* (ES$^+$) 497 (MNa^+), 971 ($2M^+ - 2OCH_3$); HRMS (ES$^+$) Found MNa^+ 497.2107, $C_{29}H_{35}Si_2OFNa$ requires M^+ 497.2103).

(1*R,2*R**,3*R**,4*S**)-4-(4′-Methoxyphenyl)-2-methyl-3-ethenyl-1,2,3,4-tetrahydronaphthalen-1-ol 35**

Following stage 2 of the standard procedure fluorosilane **34** (0.37 g, 0.7 mmol) was oxidised to afford, following chromatography, the title tetralol as a white solid (0.085 g, 61%) as a 5 : 1 mixture of diastereoisomers; R_f 0.1 (petrol–ether 9 : 1); mp 122–124; Found C, 81.15%; H, 7.59%; required for $C_{20}H_{22}O_2$: C, 81.59%; H, 7.53%. ν_{max} (thin film) 3350 (broad, OH), 2961, 2907, 1611, 1511, 1451, 1301, 1261, 1245, 1177, 1115, 1026, 913 cm^{-1}; NMR data for major isomer δ_H (500 MHz, CD_3COCD_3) 7.68 (1H, d, *J* 10, 8-*H*), 7.20 (1H, m, 7-*H*), 7.09–7.04 (3H, m, 6-*H*, Ar-*H*), 6.86 (2H, d, *J* 11, Ar-*H*), 6.75 (1H, d, *J* 10, 5-*H*), 5.96 (1H, ddd, *J* 20, 11, 9, 3-C*H*=), 5.14 (1H, t, *J* 8, 5, 1-*H*), 4.91 (2H, m, =CH_2), 4.41 (1H, d, *J* 8, -O*H*), 3.99 (1H, d, *J* 12, 4-*H*), 3.79 (3H, s, OCH_3), 2.82 (1H, ddd, *J* 12, 3, 2, 3-*H*), 2.35 (1H, qdd, *J* 7, 5, 3, 2-*H*), 0.94 (3H, d, *J* 9, 2-CH_3); δ_C (126 MHz, CD_3COCD_3) 159.7 (Ar-*C*), 142.0 (3-*C*H=), 140.8 (Ar-*C*), 140.5 (Ar-*C*), 139.6 (Ar-*C*), 136.7 (Ar-*C*), 136.3 (Ar-*C*), 131.9 (Ar-*C*), 128.1 (*C*-8), 128.0 (*C*-7), 116.5 (3-CH=*C*H_2), 115.1 (Ar-*C*), 72.8 (*C*-1), 56.1 (O*C*H_3), 51.9 (*C*-3), 48.3 (*C*-4), 41.0 (*C*-2), 8.7 (2-*C*H_3); *m/z* (ES$^+$) 317 (MNa^+).

(1*S,2*S**,3*R**,4*R**)-4-Cyclohexyl-3-ethenyl-4-methoxy-2-methyl-1-phenylbutan-1-ol 45**

Reaction of silacycle **10b** and cyclohexanecarboxaldehyde dimethylacetal afforded, following column chromatography, the title alcohol **45** as a colourless oil as a 1 : 2 mixture of diastereoisomers (36%); mp 106–108; R_f 0.3 (petrol–ether 9 : 1); ν_{max} (thin film) 3324 (broad, OH), 3068, 3038, 2930, 2853, 2358, 2241, 1716, 1602, 1540, 1455, 1078, 1010, 834 cm^{-1}; δ_H (500 MHz, $CDCl_3$) major isomer 7.32–7.30 (5H, m, Ar-*H*), 6.10 (1H, ddd, *J* 17, 10, 10, 3-C*H*=), 5.19 (1H, d, *J* 10, =CH*H*), 5.10 (1H, d, *J* 17, =C*H*H), 4.32 (1H, d, *J* 10, 1-*H*), 3.58 (3H, s, OCH_3), 3.06 (1H, t, *J* 6, 4-*H*), 2.45 (1H, m, 3-*H*), 2.14 (1H, m, 2-*H*), 1.98 (1H, d, *J* 14), 1.80–1.69 (3H, m), 1.62–1.59 (1H, d, *J* 14), 1.31–1.16 (4H, m), 1.10–1.01 (2H, m), 0.65 (3H, d, *J* 7, 2-CH_3); δ_C (126 MHz, $CDCl_3$) 144.7 (*ipso*-Ar-*C*), 137.3 (3-*C*H=), 128.1 (Ar-*C*), 127.1 (Ar-*C*), 126.8 (Ar-*C*), 117.5 (=*C*H_2), 89.5 (*C*-4), 76.0 (*C*-1), 61.6 (O*C*H_3), 51.0 (*C*-3), 41.0 (4-*C*H), 40.3 (*C*-2), 30.0 (*C*H_2), 29.6 (*C*H_2) 26.5 (*C*H_2), 26.3 (*C*H_2), 26.0 (*C*H_2), 17.7 (2-*C*H_3); *m/z* (ES$^+$) 325 (MNa^+), 627 ($2MNa^+$); HRMS (ES$^+$) Found MNa^+ 325.2137, $C_{20}H_{30}O_2$ requires M^+ 325.2138.

X-Ray crystallography

X-Ray diffraction experiment was carried out at $T = 120$ K on a Siemens 3-circle diffractometer with a SMART 1K CCD area detector, using graphite-monochromated Mo-K$_\alpha$ radiation ($\bar{\lambda} =$ 0.71073 Å) and a Cryostream (Oxford Cryosystems) open-flow N_2 cryostat. The structure was solved by direct methods using *SIR92* program,[34] and refined by full-matrix least squares (against F^2) using *CRYSTALS* software (version 12.80).[35] *Crystal data*: **45**, $C_{20}H_{30}O_2$, $M = 302.46$, monoclinic, space group $P2_1/c$ (No. 14), $a = 16.9623(4)$, $b = 9.9591(2)$, $c = 11.0721(3)$ Å, $\beta = 96.287(1)°$, $U = 1859.15(8)$ Å^3, $Z = 4$, $D_c = 1.081$ g cm^{-3}, $\mu = 0.07$ mm^{-1}, 23555 reflections with $2\theta \leq 61°$, semi-empirical absorption correction on Laue equivalents,[36] $R_{int} = 0.023$, $R(F) = 0.039$ on 2621 data with $I \geq 2\sigma(I)$, $wR(F^2) = 0.143$ on all 5273 unique data. CCDC reference number 298852. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b709318g

Acknowledgements

We thank the EPSRC (DTA studentships to JDS and NJH) and GlaxoSmithKline for financial support of this work (CASE award to NJH). The EPSRC Mass Spectrometry Service for accurate mass determinations. Dr A. M. Kenwright for assistance

with NMR experiments, Dr M. Jones for mass spectra and Dr A. S. Batsanov for help with the X-ray data.

References

1 M. A. Brook, *Silicon in Organic, Organometallic and Polymer Chemistry*, Wiley, Chichester, 2000.
2 G. Rabbe and J. Michl, in *The Silicon-Carbon Multiple Bond*, ed. Z. Rappoport and S. Patai, J. Wiley, Chichester, 1989.
3 T. Muller, W. Ziche and N. Auner, in *Silicon Carbon and Silicon-Nitrogen Multiply Bonded Compounds*, ed. Z. Rappoport and Y. Apeloig, J. Wiley, Chichester, 1998.
4 A. G. Brook, F. Abdesaken, B. Gutekunst, G. Gutekunst and R. K. Kallury, *J. Chem. Soc., Chem. Commun.*, 1981, 191.
5 Y. Apeloig, M. Bendikov, M. Yuzefovich, M. Nakash, D. Bravo-Zhivotovskii, D. Blaserand and R. Boese, *J. Am. Chem. Soc.*, 1996, **118**, 12228.
6 N. Wiberg, G. Wagner, G. Reber, J. Riede and G. Muller, *Organometallics*, 1987, **6**, 35.
7 N. Wiberg and G. Wagner, *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 1005.
8 N. Wiberg and G. Wagner, *Chem. Ber.*, 1986, **119**, 1467.
9 K. Schmohl, H. Reinke and H. Oehme, *Eur. J. Inorg. Chem.*, 2001, 481.
10 K. Sakamoto, J. Ogasawara, Y. Kon, T. Sunagawa, C. Kabuto and M. Kira, *Angew. Chem., Int. Ed.*, 2002, **41**, 1402.
11 T. Guliashvili, I. El-Sayed, A. Fischer and H. Ottosson, *Angew. Chem., Int. Ed.*, 2003, **42**, 1640.
12 H. Ottosson and P. G. Steel, *Chem.–Eur. J.*, 2006, **12**, 1576.
13 M. B. Berry, R. J. Griffiths, M. J. Sanganee, P. G. Steel and D. K. Whelligan, *Org. Biomol. Chem.*, 2004, **2**, 2381.
14 M. J. Sanganee, P. G. Steel and D. K. Whelligan, *Org. Biomol. Chem.*, 2004, **2**, 2393.
15 M. B. Berry, R. J. Griffiths, M. J. Sanganee, P. G. Steel and D. K. Whelligan, *Tetrahedron Lett.*, 2003, **44**, 9135.
16 A. S. Batsanov, I. M. Clarkson, J. A. K. Howard and P. G. Steel, *Tetrahedron Lett.*, 1996, **37**, 2491.
17 J. D. Sellars and P. G. Steel, *Org. Biomol. Chem.*, 2006, **4**, 3223.
18 L. Chabaud, P. James and Y. Landais, *Eur. J. Org. Chem.*, 2004, 3173.
19 A. Hosomi and K. Miura, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 835.
20 A. Hosomi, M. Endo and H. Sakurai, *Chem. Lett.*, 1976, 941.
21 A. Hosomi and H. Sakurai, *Tetrahedron Lett.*, 1976, 1295.
22 N. Auner and H. U. Steinberger, *Z. Naturforsch., B: Chem. Sci.*, 1994, **49**, 1743.
23 P. R. Jones and M. E. Lee, *J. Am. Chem. Soc.*, 1983, **105**, 6725.
24 M. E. Lee, J. H. Kim and C. H. Kim, *Bull. Korean Chem. Soc.*, 1994, **15**, 729.
25 G. Manuel, A. Faucher and P. Mazerolles, *J. Organomet. Chem.*, 1984, **264**, 127.
26 R. Lauchli, J. M. Whitney, L. Zhu and K. J. Shea, *Org. Lett.*, 2005, **7**, 3913.
27 J. D. Sellars, P. G. Steel and M. J. Turner, *Chem. Commun.*, 2006, 2385.
28 I. Fleming, *Chemtracts, Org. Chem.*, 1996, **9**, 1; K. Tamao, *Adv. Silicon Chem.*, 1996, **3**, 1; G. R. Jones and Y. Landais, *Tetrahedron*, 1996, **52**, 7599.
29 R. S. Ward, *Phytochem. Rev.*, 2004, **2**, 391.
30 R. S. Ward, *Synthesis*, 1992, 719.
31 R. S. Ward, *Tetrahedron*, 1990, **46**, 5029.
32 A. Pelter, R. S. Ward, M. C. Pritchard and I. T. Kay, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1603.
33 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978, **43**, 2923.
34 A. Altomare, G. Cascarano, G. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori and M. Camalli, *J. Appl. Crystallogr.*, 2003, **27**, 435.
35 P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout and D. J. Watkin, *J. Appl. Crystallogr.*, 2003, **36**, 1487.
36 G. M. Sheldrick, *SADABS, version 2.10*, Bruker AXS, Madison, Wisconsin, USA, 2003.

This journal is © The Royal Society of Chemistry 2007