Hosomi–Sakurai reactions of silacyclic allyl silanes†

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Substituted silacyclohexenes, generated through silene–diene [4 + 2] cycloaddition reactions, undergo Lewis acid promoted Sakurai type reactions with acetals to afford, following oxidation of the resultant fluorosilane, 1,4-diols with four contiguous chiral centres.

Allyl silanes are widely used in organic chemistry and have been shown to undergo a plethora of reactions at both the silicon and olefinic moieties.[1] In particular, the Hosomi–Sakurai reaction, which involves the Lewis acid promoted addition of allyl silanes to acetals and related electrophiles, has found considerable use in synthesis.[2] The reaction is generally considered to proceed *via* 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 stabilisation is believed to arise from orbital overlap between the empty P_π orbital on the carbocation and the co-planar C–Si σ-bond, structure **1**, Fig. 1.[3] Whilst such an alignment is trivial in acyclic systems this is not the case for cyclic substrates. Reflecting this difficulty, with the exception of the unique bridgehead allyl silane **2**, recently described by Shea *et al.*, in which the silicon atom is held at an angle of 78° to the C=C plane,[4] there have been no reports describing the use of silacyclic allyl silanes in the Hosomi–Sakurai reaction or related transformations.

As a component of a project exploring the application of silenes, compounds containing a C=Si bond, as novel synthetic reagents, we have previously described efficient synthetic routes for the preparation of substituted silacyclohexenes. These have proved to be versatile intermediates for the generation of diols and lactones.[5] As a continuation of this theme, we were interested in using these cyclic allyl silanes in the Hosomi–Sakurai reaction. Whilst protiodesilylation reactions of various related silacyclic substrates have been described, there are no examples of analogous reactions involving carbon based electrophiles.[6] In this communication we demonstrate that silacyclic allyl silanes are capable of participating in the Hosomi–Sakurai reaction with both aryl and alkyl acetals to provide substituted 1,4-diols with moderate levels of stereoselectivity.

The silacyclohexenes **5** used in this study were prepared through the reaction of 1,3-pentadiene with silenes, generated *in situ* by a modified sila-Peterson reaction. In each case the cycloaddition proceeds with high chemo- and regioselectivity to afford an inseparable mixture of diastereoisomeric products. The major diastereoisomer **5** obtained, Scheme 1, 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.

With the silacyclic allyl silanes in hand we then commenced an exploration of the Sakurai reaction, Scheme 2. Initial attempts to generate the oxonium ion from an acetal prior to addition of the cycloadducts were unsuccessful leading to an intractable mixture of products. However, addition of BF₃·OEt₂ to a precooled (0 °C) mixture of the silacyclohexene **5a** and benzaldehyde dimethyl acetal in DCM afforded, after aqueous workup and purification by flash column chromatography, the anticipated silyl fluoride **7a** in 60% yield, as a 2 : 1 mixture of stereoisomers as ascertained by ¹⁹F NMR spectroscopy [$\delta_F = -184.72$ (d, $J = 15.8$ Hz); $\delta_F = -185.57$ (d, $J = 17.8$ Hz)]. 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 H₂O₂ in the presence of KHCO₃ to yield the monoprotected 1,4-diol in 80% yield. Importantly, this compound was also produced as a 2 : 1 mixture of diastereoisomers. At this stage a single crystal X-ray study, Fig. 2, confirmed the stereochemistry of the major isomer as the *syn*, *anti*, *anti* isomer **8a**.‡ Given that the Tamao oxidation is known to proceed with retention of configuration at carbon,[7] this suggested that the silyl fluoride was formed as a single
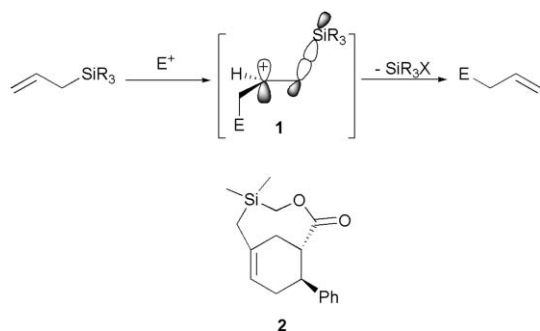

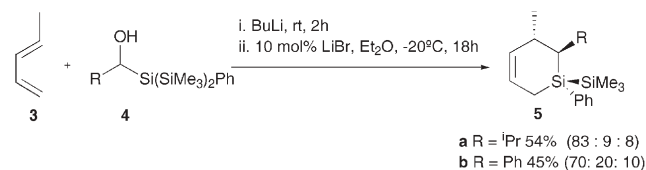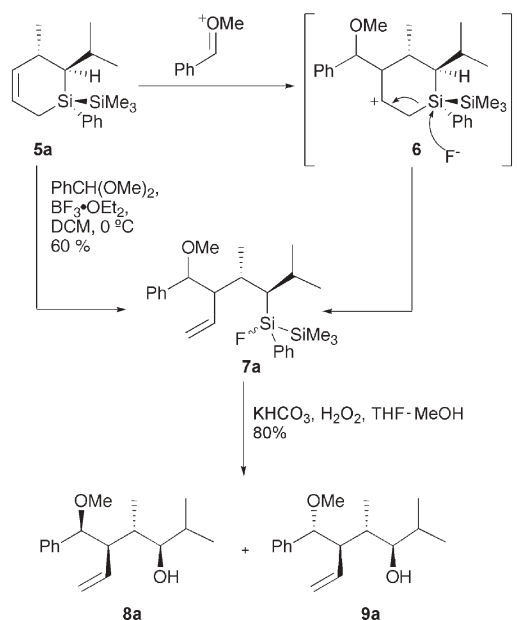**Fig. 1** β Si stabilisation in the reaction of allyl silanes.

Department of Chemistry, University of Durham, Science Laboratories, South Road, Durham, UK DH1 3LE. E-mail: p.g.steel@durham.ac.uk; Fax: +44 (0)191 384 4737; Tel: +44 (0)191 334 2131

i. BuLi, rt, 2h
ii. 10 mol% LiBr, Et₂O, -20°C, 18h

a R = ᵢPr 54% (83 : 9 : 8)
b R = Ph 45% (70 : 20 : 10)

Scheme 1

Scheme 2

Scheme 3

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). Such an approach to the silacycle can be rationalised on the basis of simple stereoelectronic arguments. Co-planarity of the C–Si and alkene π-orbital requires a pseudo boat structure. Whilst this is possible for the major silacycle isomer the alternative diastereoisomer is prevented from adopting such a conformation by eclipsing interactions between the Si–Ph and C-2 substituent.§ Selectivity in the major isomer is then a matter of approach from the least hindered face of the conformation which avoids prow interactions between the C-3 methyl group and a C-6 hydrogen, Scheme 4.

Whilst the silyl fluorides proved to be stable species, amenable to chromatography, it is possible to combine the two stages. After complete consumption of the silacyclohexene, the crude reaction mixture is directly subjected to the oxidation process to afford the same product mixture in comparable yields. Using this "single operation" process a range of acetals have been explored, Table 1. Whilst both aromatic and alkyl acetals react, somewhat lower yields are observed with alkyl acetals. Whilst both electron withdrawing and electron donating aryl substituents are tolerated,
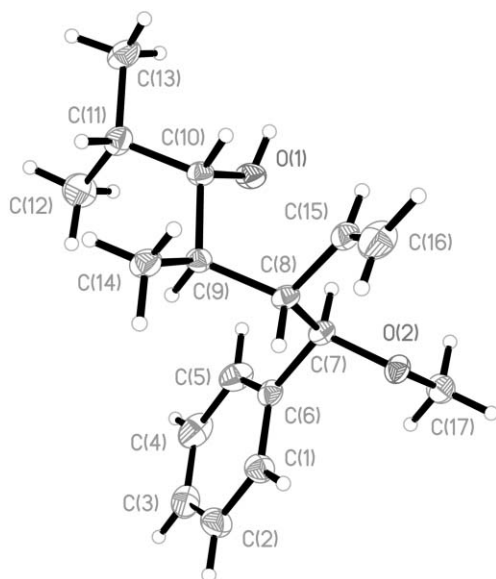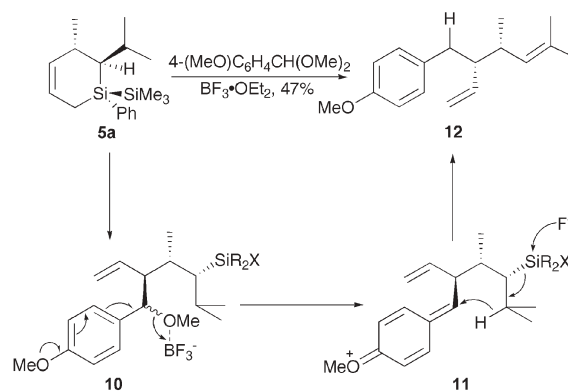

Fig. 2 ORTEP structure of **8a** (ellipsoids at 50% probability level). The co-crystalline phenol has been omitted for clarity.

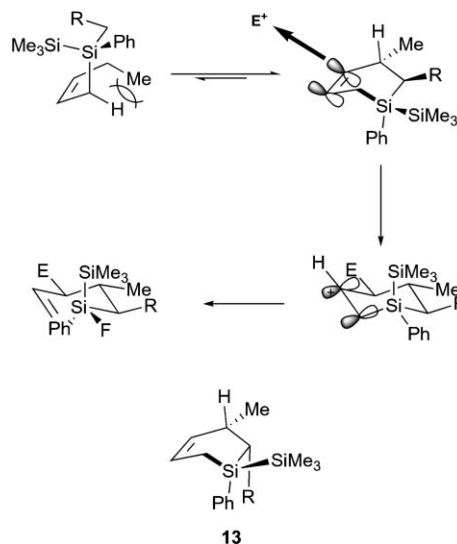Si stereoisomer and the mixture of isomers reflects the relative configurations at C-1 and C-2.

A second experiment using 4-methoxybenzaldehyde dimethyl acetal was then undertaken. However, in this case, the addition of BF₃·OEt₂ to the mixture of silacyclohexene and acetal led directly to the formation of the non-conjugated diene **12** in 47% yield. We account for this product, Scheme 3, through a sequence of steps involving initial addition of the oxonium ion to the silacycle followed by generation of a vinylogous oxacarbenium ion (*para*-quinone methide) **11**. Intramolecular hydride transfer affords a silicon stabilised carbocation which undergoes rapid desilylation to generate the second alkene. Importantly, in this case, the product was formed as a single diastereoisomer suggesting that the initial
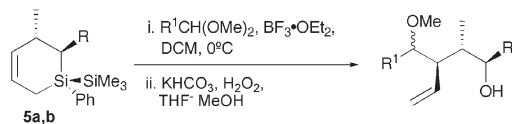

Scheme 4

Table 1 Hosomi–Sakurai reaction of silacycles **5a** and **5b** with acetals

Entry	R	R^1	Yield[a] (%)	dr
1	^iPr	C_6H_5	50	2 : 1
2	^iPr	4-MeOC_6H_4	47	**12**
3	^iPr	$4\text{-CF}_3C_6H_4$	23	2 : 1 : 1
4	^iPr	4-BrC_6H_4	23	2 : 1
5	^iPr	CH_3	21	2 : 1
6	Ph	C_6H_5	55	2 : 1
7	Ph	$4\text{-CF}_3C_6H_4$	50	4 : 1.5 : 1
8	Ph	4-BrC_6H_4	46	3 : 1
9	Ph	CH_3	32	2 : 1
10	Ph	$c\text{-}C_6H_{11}$	36	1 : 2[b]
11	Ph	C_6H_{13}	22	1 : 1

[a] Yield over two steps. [b] Major isomer confirmed by X-ray diffraction.

the latter can lead to further reaction under the Lewis acidic conditions through activation of the initially formed benzylic ether, entry 2 (Scheme 3). Attempts to minimise this second pathway through the use of sub-stoichiometric amounts of $BF_3 \cdot OEt_2$ resulted in lower yields and recovered starting silacyclohexene.

In conclusion silene–diene cycloadducts represent convenient sources of silacyclic allyl silanes which can undergo Hosomi–Sakurai type addition to acetals. This represents the first examples of C–C bond formation of such cyclic allyl silanes. Work is currently in progress to further optimise the selectivity and fully delineate the scope of this transformation.

Notes and references

‡ The X-ray crystallography revealed that **8a** crystallised as a 1 : 1 H-bonded complex with phenol: $C_{23}H_{32}O_3$, $M = 356.49$, triclinic, space group $P\bar{1}$, $a = 8.2609(3)$ Å, $\alpha = 79.854(2)°$, $b = 10.8798(4)$ Å, $\beta = 79.837(2)°$, $c = 11.7925(5)$ Å, $\gamma = 89.219(2)°$, $V = 1026.76(7)$ Å^3, $Z = 2$, absorption coefficient $= 0.074$ mm^{-1}, reflections collected $= 7400$, independent reflections $= 4610$ [R(int) $= 0.0271$], final R indices [$I > 2 \sigma(I)$] $R1 = 0.0511$, $wR2 = 0.1088$, R indices (all data) $R1 = 0.0849$, $wR2 = 0.1226$. CCDC 298851. For crystallographic data in CIF or other electronic format see 10.1039/b602642g

§ Trace amounts of the less reactive minor silacycle diastereoisomers can be recovered from the reaction mixture. Details will be given in a full account.

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