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Silenes as novel synthetic reagents: synthesis of diols and lactones from simple alkyldienes

Malcolm B. Berry,[b] Russell J. Griffiths,[a] Mahesh J. Sanganee,[b] Patrick G. Steel[a,*] and Daniel K. Whelligan[a]

[a] *Department of Chemistry, University of Durham, Science Laboratories, South Road, Durham DH1 3LE, UK*
[b] *Synthetic Chemistry, GlaxoSmithKline, Gunnels Wood Road, Stevenage, Herts SG1 2NY, UK*

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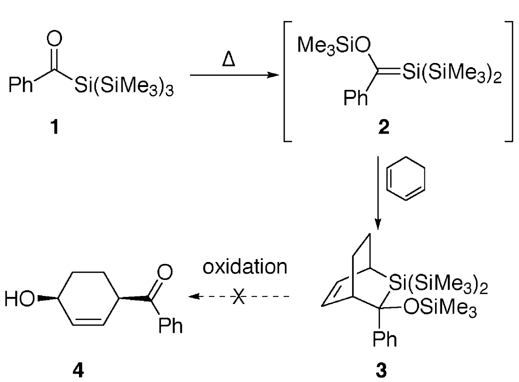
Abstract—Aryl substituted silenes can be generated by a modified Peterson olefination reaction and trapped in situ to afford silacycles with high diastereoselectivity. These silacycles can be elaborated by 'Fleming–Tamao' type oxidation to provide access to functionalized diols and lactones.

Since the first reported demonstration of their existence by Gusel'nikov and Flowers,[1] silenes, compounds containing a C=Si bond, have been the subject of a number of theoretical, structural and mechanistic studies.[2] This has led to their detection as highly reactive intermediates, an understanding of their basic reactivity and finally to the isolation and structural characterisation of 'stable' silenes.[3] However, relatively little effort has been expended in the application of these species in organic synthesis. In this communication we report our initial results describing how silenes can be exploited to provide a strategy for the elaboration of butadienes into polyols and lactones.

Our premise was that the generation of a silene, in the presence of a diene would afford the corresponding [4+2] silacycloadduct,[4] which on Fleming–Tamao oxidative extrusion of the silicon centre would provide access to a highly functionalised building block.[5] In earlier studies, we had been able to generate silacycles through the thermal rearrangement of acylpolysilanes and in situ trapping with a number of dienes (Scheme 1).[6] In all cases the [4+2] cycloadduct was formed selectively in high yields consistent with the known chemistry of reversed polarity silenes. However, the trisilane unit resisted all attempts to initiate the oxidation and we therefore considered alternative silene generation strategies and precursors.

Based on the seminal studies by Fleming, we recognised that the incorporation of an aryl silyl substituent would provide a trigger to facilitate the oxidation. Furthermore, in a number of cases, the diastereoselectivity of the thermal cycloaddition was only moderate and we speculated that this could be enhanced through the use of a low temperature modified Peterson olefination strategy to produce silenes.[7]

In earlier work on the sila-Peterson reaction, Oehme has demonstrated that a magnesium counter ion (silyl



Scheme 1.

Keywords: silene; Diels–Alder cycloaddition; silacycles; Fleming–Tamao oxidation; diols; lactones.

* Corresponding author. Fax: +44-191-384-4737; e-mail: p.g.steel@durham.ac.uk

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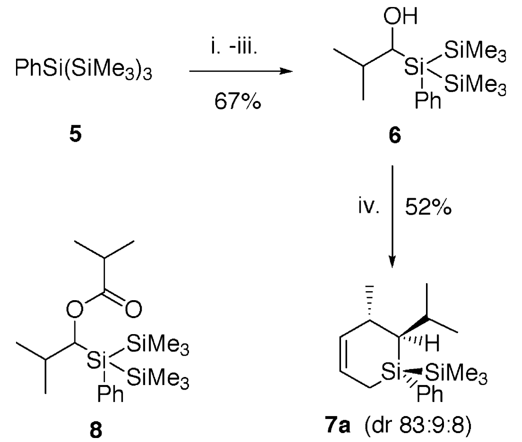
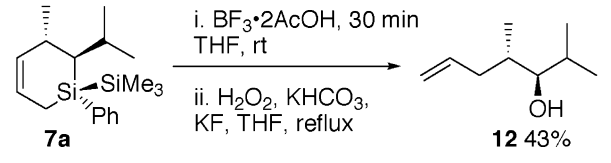


Scheme 2. *Reagents*: (i) KO^{t}Bu, THF; (ii) $MgBr_2$, Et_2O; (iii) ^{i}PrCHO, Et_2O, −78°C; (iv) ^{n}BuLi, 1,3-pentadiene, Et_2O, rt then LiBr −45 to −30°C, 16 h.

Grignard reagent) is required to avoid premature generation of the silene.[7] Consequently, adapting this precedent, treatment of phenyltris(trimethylsilyl)silane[8] **5** with KO^{t}Bu in THF at room temperature for 2 h[9] followed by transmetallation with $MgBr_2$ produced the required silyl Grignard reagent. This reagent was then directly combined with isobutyraldehyde to afford the desired silene precursor **6** as a stable colourless oil in 50–67% yield, Scheme 2, accompanied by varying amounts of the ester **8**, presumably derived via a Tishchenko type transformation.[10] Subsequently, treatment of a solution of alcohol **6** and 1,3-pentadiene in Et_2O with BuLi at room temperature, cooling to −45°C and addition of 10 mol% of LiBr followed by warming to −30°C and stirring at this temperature for 16 h afforded the desired silacyclohexene **7a** in 52% yield accompanied by small amounts of minor diastereoisomers (dr 83:9:8).[11,12] Trace amounts of products from alternative silene reaction pathways (ene, [2+2] and dimerisation) could be detected (GCMS) but were not isolated.

The high diastereoselectivity observed in silacycle formation suggested that both silene generation and subsequent Diels–Alder reaction are highly stereoselective. Given that we were unable to ascertain the stereochemistry of silacycle **7a** by simple 2D NMR experiments, we explored the oxidative extrusion of the silicon centre (Table 1). Following reduction of the alkene (H_2, Pd–C), treatment with BF_3·2AcOH complex to afford the corresponding fluorosilane (detectable by ^{19}F NMR but not isolated), silicon oxidation with H_2O_2, KF, $KHCO_3$ yielded the desired diol **9a** (85% over two steps). Further oxidation using TPAP, NMO produced the lactone **10a** as a 92:8 mixture of diastereoisomers. 2D NOESY experiments (Fig. 1) established the *anti* stereochemistry of the methyl and isopropyl groups. This was confirmed by independent synthesis of the alternative *cis* lactone diastereoisomer **11** following established literature precedents.[13]



Scheme 3.

The silene geometry was established through the reaction with 2,3-dimethylbutadiene. The [4+2] cycloadduct **7b** could be isolated as a single stereoisomer although in this case there was considerably greater competition from ene and [2+2] pathways (82:8:10 by GC). NOESY experiments (Fig. 1) clearly established a *trans* relationship between the Ph and ^{i}Pr groups for the major silene cycloadduct. In a similar fashion to that described above, this adduct could be converted to the corresponding lactone. However, with this more hindered alkene, reduction required the use of PtO_2 and resulted in a significant amount of *trans* addition of hydrogen, entry b Table 1.

This methodology can be extended to other alkyl substituted butadienes (Table 1), to provide a novel route to substituted lactones. High diastereoselectivity in the silene cycloaddition was observed in all cases although, not surprisingly, isoprene and 3-methyl-1,3-pentadiene demonstrated lower regioselectivity (entries **c** and **d**). As with cycloadduct **7b**, reduction of silacycles containing olefinic methyl substituents required more forcing conditions and was accompanied by significant scrambling of stereochemistry at these positions. A further limitation of the strategy with these more hindered silacycles is that the Fleming–Tamao oxidation is somewhat less efficient and we are currently exploring alternative procedures to enhance this process. Attempts to extend this result to more hin-

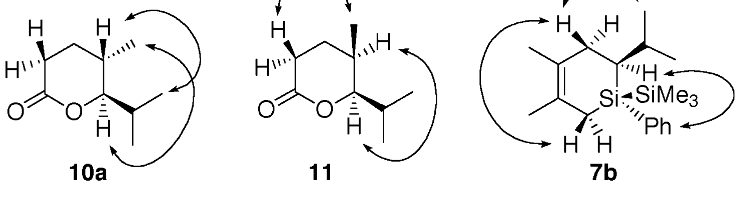
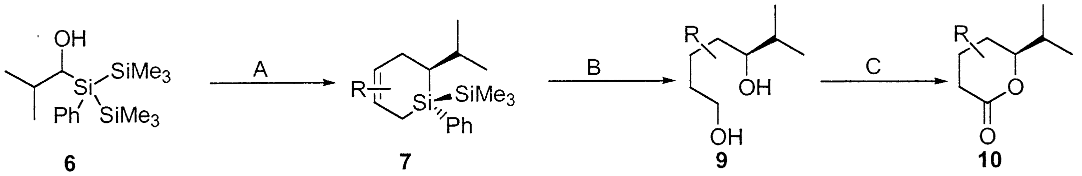


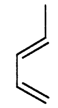
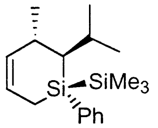
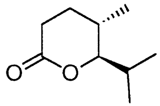
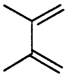
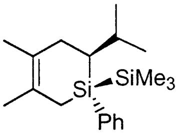
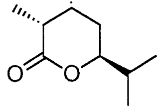
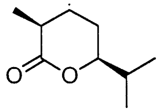
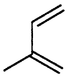
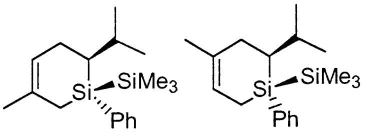
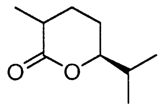
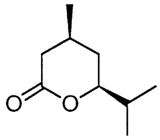
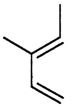
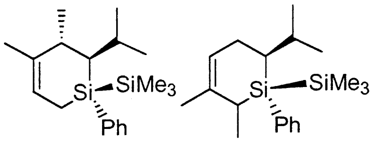
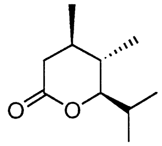
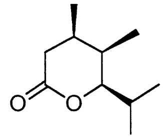
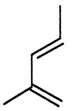
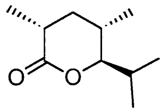
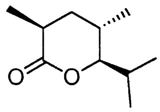
Figure 1. Selected NOESY responses.

Table 1.



6 **7** **9** **10**

Reagents: A. diene, ^{n}BuLi, Et_2O, rt, 3 h then LiBr, Et_2O, -20°C,16 h; B. i. H_2Cat[b]; ii. $BF_3{\bullet}2AcOH$, $CHCl_3$, reflux, 18 h iii. H_2O_2, $KHCO_3$, KF, THF/MeOH, reflux; C. TPAP, NMO, DCM

	Dienes	[4+2] Silacycloadducts[a]	Reduction[b]	Oxidation	Lactones[a]	
a		 50% (83 : 9 :8)	74%[bi]	85%	 76% (92 : 8)	
b		 48%	64%[bii]	63%[c]	 39%	 24%
c		 31% (79 : 21)	58%[bii]	19%[c]	 35% (66 : 44)	 12%
d		 38% (86 : 9) : (4 : 1)	35%[biii]	18%[c]	 13%	 60% (87 : 10 : 3)
e		 44% (80 : 14 : 4 : 2)	74%[bii]	20%[c]	 45%	 26% (79 : 11 : 8 : 2)

a. ratio of isomers in parenthesis;
b. i. Pd-C, toluene, ii. PtO_2, EtOAc, iii. $Ir(cod)(pyr)(PCy_3)PF_6$, DCM;
c. The redox sequence produced isomeric mixtures of diols. Quoted yield refers to combined overall yield of purified diol mixtures.

dered dienes (e.g. cyclohexadiene) have not been successful with silene dimerisation becoming competitive with the desired [4+2] cycloaddition.

In conclusion, silenes can be employed as novel reagents for alkene functionalisation providing stereoselective access to diols and lactones. Further extensions of these studies to explore variables in both silene and silenophile and alternative functionalisation strategies are in progress and will be reported in due course. For example, in a preliminary experiment (Scheme 3) simple omission of the reduction step exploits the latent allylsilane nature of the silacycle and, following oxidation, produces the bis homoallylic alcohol **12**.

Acknowledgements

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10. All new compounds had satisfactory spectroscopic and analytical data.
11. The presence of LiBr was found to be essential to promote efficient generation of the silene. A number of other lithium salts were explored but none was found to be as effective.
12. Typical experimental procedure for silene generation and trapping: **1-phenyl-1-trimethylsilyl-2-(prop-2′-yl)-3-methylsilacyclohex-4-ene (7a)** *n*-butyllithium (1.6 M solution in ether, 0.58 ml, 0.92 mmol) was added to a stirred solution of silyl alcohol **6** (0.29 g, 0.88 mmol) and *trans*-1,3-pentadiene (0.53 ml, 5.28 mmol) in dry ether (10 ml) at rt. The mixture was stirred for 3 h after which time TLC showed complete consumption of starting material. The solution was cooled to −45°C and an anhydrous suspension of LiBr in ether (0.31 M, 0.14 ml, 0.044 mmol) was added. The mixture was warmed to −30°C and stirred for 20 h. Saturated ammonium chloride solution (10 ml) was added and the mixture allowed to reach rt. The aqueous layer was separated and extracted with diethyl ether (3×10 ml). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and dried in vacuo. Flash column chromatography (pet. ether) gave the title compound **7a** as a colourless oil (0.133 g, 52%) along with small amounts of diastereoisomers in an 83:9:8 ratio (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}; 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, 5-H), 5.54 (1H, ddt, *J* 10.5, 4.4, 1.8, 4-H), 2.36 (1H, m, 3-H), 2.10 (1 H, septet d, *J* 6.8, 3.3, C**H**(CH_3)$_2$), 1.68 (1H, ddt, *J* 17.2, 5.2, 1.8, 6-**H**H), 1.47 (1H, ddt, *J* 17.2, 5.2, 1.8, 6-H**H**), 1.20 (1H, dd, *J* 6.5, 3.3, 2-H), 1.03 (3H, d, *J* 6.8, CH(C**H**$_3$)$_2$), 0.93 (3H, d, *J* 7.2, 7-H), 0.88 (3H, d, *J* 6.8, CH(C**H**$_3$)$_2$), 0.14 (9H, s, Si(C**H**$_3$)$_3$); δ_C (126 MHz; $CDCl_3$) 139.36 (*ipso*-Ar-C), 137.41 (4-C), 134.48 (Ar-C), 128.19 (Ar-C), 127.66 (Ar-C), 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(**C**H$_3$)$_3$); *m*/*z* (EI) 302 (M$^+$, 7%), 259 (M$^+$–^{i}Pr, 4%), 229 (M$^+$–SiMe$_3$, 56%), 218 (27%), 203 (47%), 185 (11%), 173 (29%), 161 (100%), 145 (31%), 135 (82%), 121 (69%); HRMS (EI) Found: 302.1889; $C_{18}H_{30}Si_2^+$ requires *M*, 302.1886.
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