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Tandem intermolecular–intramolecular carbolithiation: application to the synthesis of silacyclopentanes

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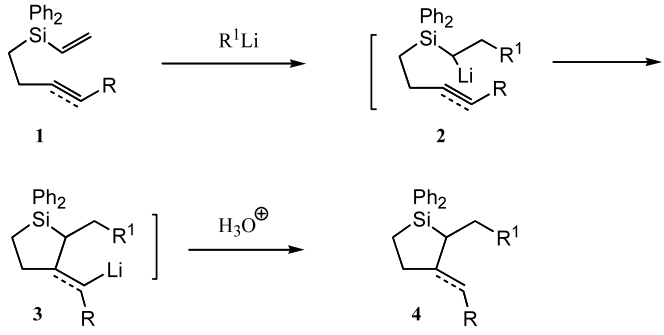
Abstract—Silacyclopentanes have been prepared from vinyl(homoallyl)silanes or vinyl(homopropargyl)silanes and organolithium reagents by a tandem intermolecular–intramolecular sequence involving a 5-*exo* cyclisation process. The unexpected stereochemical outcome of the sequence involving a 5-*exo*-*dig* cyclisation is rationalised.

Organosilicon compounds have received much interest in view of their versatility in organic transformations and their unique physical properties.[1] Silacyclic compounds, in which a silicon atom is embedded in a ring system, are useful synthetic building blocks as well as being interesting materials in their own right. Syntheses and reactions of five- and six-membered silicon–carbon heterocycles have been comprehensively reviewed.[2] We have recently studied organolithium addition reactions to styrenes and other activated alkenes including vinyl silanes.[3] As part of this programme we studied tandem processes such as the tandem intermolecular–intramolecular carbolithiation route to tetralins involving a 6-*exo*-cyclisation (Scheme 1).[3b]

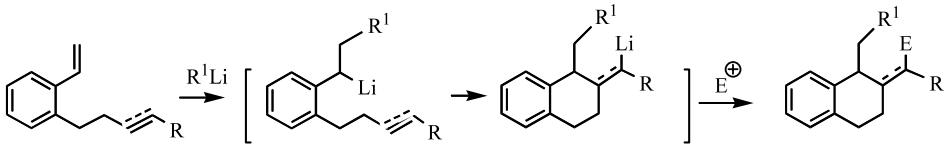
We now report that similar tandem intermolecular–intramolecular organolithium methodology can be utilised to convert vinyl silanes **1** into silacyclopentanes **4** as outlined in Scheme 2; in this sequence, the key intramolecular cyclisation (**2**→**3**) is of the well-precedented[3b,4] 5-*exo*-type.



Scheme 2.

Substrates **1a–d** (Scheme 3) were designed to facilitate the planned tandem intermolecular–intramolecular carbolithiation sequence in that:

(i) vinylsilanes are known to be good substrates for intermolecular organolithium addition[5] giving anionic adducts stabilised by an adjacent silicon group,[6]



Scheme 1.

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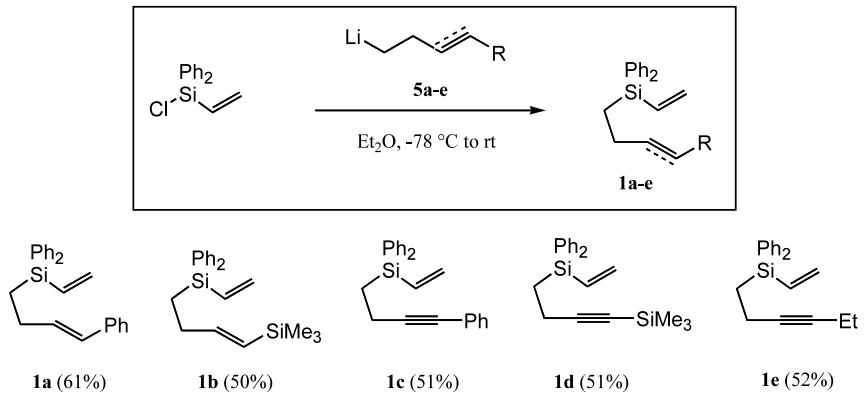


Scheme 3.

(ii) the presence of terminal phenyl or trimethylsilyl substitutents on the pendant alkene/alkyne unit should facilitate anionic cyclisation because of their known anion stabilising ability.[3e]

The starting vinyl silanes **1a–e** were successfully prepared in moderate yields by the addition of commercially available chloro(diphenyl)vinylsilane to a freshly prepared solution of homoallyl- or homopropargyllithium reagents **5a–e** in diethyl ether at −78°C and slowly warming the reaction mixture to room temperature (rt) as shown in Scheme 3.[7] The organolithium reagents **5** were prepared from the corresponding organo-iodides by lithium–halogen exchange at −78°C using the Negishi/Bailey method.[8]

The reactions of the above vinylsilanes **1a–d** with organolithium reagents were explored at different temperatures. Although reactions at temperatures lower than 0°C were very sluggish, the desired tandem reactions went smoothly (20–60 min) in diethyl ether at room temperature giving the desired silacyclopentanes **4** in good to excellent yields (62–81%) as shown in Table 1.[7,9]

It is noteworthy that the intermolecular organolithium addition step is regioselective for the vinylsilane group: addition of butyllithium to the remote disubstituted alkene or alkyne group was not observed in any of the examples.

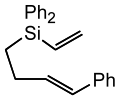
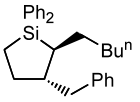
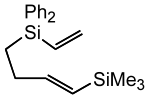
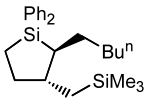
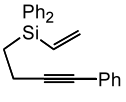
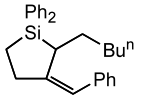
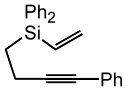
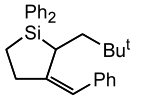
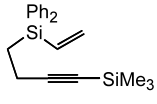
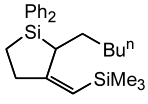
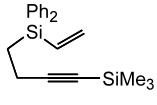
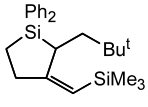
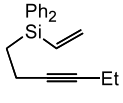
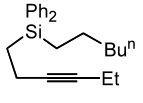
For reactions of the homoallyl vinylsilanes **1a**,**b**, silacyclopentanes **4a**,**b** were obtained in good yield with both phenyl and trimethylsilyl substituted starting materials (entries i and ii). In each case, as expected, the *trans*-isomeric products predominated based on NOE experiments.

Reactions of the activated homopropargyl vinylsilanes **1c**,**d** were equally effective, giving the expected products **4c**,**d** (entries iii–vi) with both *n*-butyllithium and *t*-butyllithium. Interestingly, COSY and NOE studies indicated that these products derived from 5-*exo*-*dig* cyclisation were formed predominantly as the *Z*-isomers (entries iii–vi). Given the fast isomerisation of phenyl- and trimethylsilyl-stabilised vinyl anions[10] we speculate that the ether-coordinated lithium atom may have a greater steric demand than the trimethylsilyl or phenyl groups. The variation of *Z*:*E* ratio over **4c**, **4c**^{t}, **4d** and **4d**^{t} certainly gives credence to this proposal as going from the relatively sterically undemanding *n*-butyl/phenyl combination of substituents through *t*-butyl/phenyl and *n*-butyl/trimethylsilyl to the challenging *t*-butyl/trimethylsilyl arrangement, the *Z*:*E* ratios increase from 3:1 to 10:1 to 19:1 to 24:1. This process is illustrated in Scheme 4. Possibly due to the steric hindrance between the *t*-butyl and trimethylsilyl groups, the exocyclic vinyl compound **4d**^{t} slowly isomerised to the more stable silacyclopentene **6** on standing at room temperature for 24 h (Scheme 4).

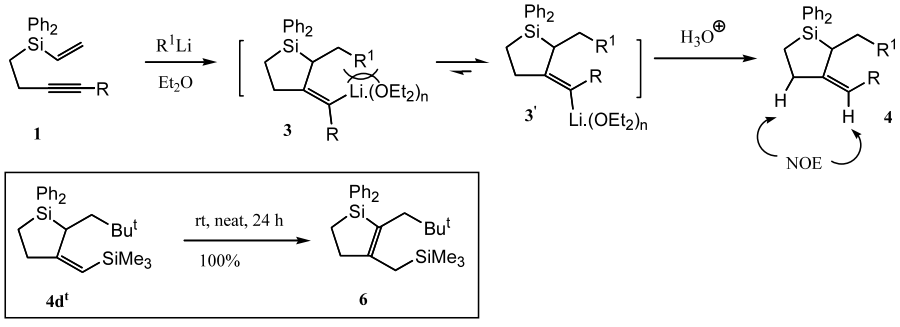
Finally, we established the importance of having an activated receptor group containing an anion-stabilising substituent (Table, entry vii). When the ethyl substituted alkyne **1e** was treated with *n*-butyllithium in diethyl ether, no cyclisation to give a silacyclopentane was observed and the major isolated product was the simple *n*-butyllithium adduct **7**.

In summary, we have shown that organolithium addition to vinylsilanes can be coupled with a subsequent intramolecular 5-*exo*-cyclisation to generate silacyclopentanes in good yields. In the case of the 5-*exo*-*dig* cyclisation of homopropargyl silanes, the products were obtained mainly as the *Z*-isomers which are difficult to obtain by other procedures. The methodology is versatile in that by varying the structure of the organolithium reagents, the vinylsilanes and the quenching electrophiles, a wide range of substituted silacyclopentanes should be available.

Table 1. Tandem intermolecular–intramolecular carbolithiation of **1a**–**e**[a]

i	 **1a**	*n*-BuLi	 **4a** (*trans:cis* = 2:1)	70%
ii	 **1b**	*n*-BuLi	 **4b** (*trans:cis* = 3:1)	71%
iii	 **1c**	*n*-BuLi	 **4c** (*Z:E* = 3:1)	67%
iv	 **1c**	*t*-BuLi	 **4c**^{t} (*Z:E* = 10:1)	62%
v	 **1d**	*n*-BuLi	 **4d** (*Z:E* = 19:1)	81%
vi	 **1d**	*t*-BuLi	 **4d**^{t} (*Z:E* = 24:1)	78%
vii	 **1e**	*n*-BuLi	 **7**	50%

[a] *n*-Butyllithium or *t*-butyllithium was added to a solution of vinylsilane **1** in diethyl ether at rt and the reaction monitored by TLC. When the reaction was complete, water was added followed by normal workup and purification.[9]



Scheme 4.

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7. All novel compounds were fully characterised (including by high field ^{1}H and ^{13}C NMR spectroscopy and high-resolution mass spectrometry).
8. (a) Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404–5406; (b) Negishi, E.-i.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5406–5409.
9. *General procedure for the synthesis of silacyclopentanes* **4**: *n*-Butyllithium (0.14 mL, 1.6 M solution in hexanes, 0.225 mmol) was added to a solution of vinylsilane **1** (0.15 mmol) in dry diethyl ether (8 mL) at rt over 5 min. The reaction mixture was stirred for 20 min and then quenched with water (5 mL). The organic layer was washed with water (8 mL) and dried over sodium sulphate. After removal of solvent in vacuo the residue was purified by column chromatography on silica gel (petroleum ether–dichloromethane, 20:1). Data for **4d**: obtained as a colourless oil (Z:E = 19:1 by NMR spectroscopy), 81%, R_f 0.40 (petroleum ether–CH_2Cl_2, 10:1), IR (neat): 3068, 2953, 1606, 1598, 1428, 1247, 1112, 837, 699 cm^{-1}; δ_H (300 MHz, $CDCl_3$) Z-isomer: 0.08 (9H, s, Me_3Si), 0.74 (3H, t, J = 6.5 Hz, CH_3), 0.85–1.54 (10H, m, 4×CH_2 and CH_2Si), 2.27 (1H, t, J = 6.5 Hz, CH), 2.44–2.57 (1H, m, CH_aH_bC=CH), 2.70–2.85 (1H, m, CH_aH_bC=CH), 5.31 (1H, s, =CHSi), 7.31–7.44 (6H, m, Ph), 7.54–7.61 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) Z-isomer: 0.5, 9.5, 13.9, 22.3, 29.2, 31.9, 32.0, 33.4, 37.1, 121.9, 127.7, 127.8, 129.3, 129.5, 134.2, 134.9, 135.5, 136.3, 165.8; MS (EI): 392 (M^+, 22%), 377 (7), 318 (8), 242 (65), 185 (65), 73 (100); HRMS (EI): 392.2354. Calcd for $C_{25}H_{36}Si_2$, 392.2356 (0.4 ppm error).
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