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Formation and Utility of Oxasilacyclopentenes Derived from Functionalized Alkynes

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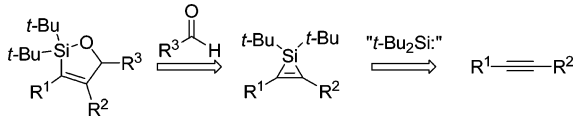
Reductive coupling reactions of alkynes with ketones and aldehydes represent powerful methods for the synthesis of functionalized allylic alcohols from simple starting materials.[1−7] While these reactions are typically accomplished using transition metal promoters, we envisioned that the use of silicon in the coupling of carbonyls to alkynes would provide intermediate oxasilacyclopentenes which could then be unmasked to form allylic alcohols. Silacyclopropenes, prepared from alkynes,[8] undergo insertion reactions with carbonyl compounds to form oxasilacyclopentenes,[9] which would serve as masked allylic alcohol derivatives (Scheme 1). This process would form cyclic vinylsilanes that are available for further functionalization, including oxidation of the carbon−silicon bond,[10] expanding the transformation scope beyond the preparation of allylic alcohols. In this Communication, we describe a mild method for the synthesis of silacyclopropenes from functionalized alkynes and demonstrate that these reactive compounds can be converted, without isolation, to oxasilacyclopentenes with high regioselectivity. Further transformations of these products occur diastereoselectively, leading to the assembly of a number of architecturally diverse products.

Scheme 1. Formation of Oxasilacyclopentenes from Alkynes

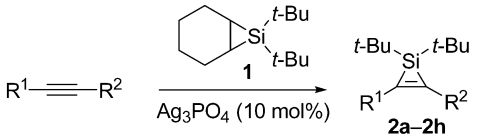


We initially developed the metal-catalyzed silacyclopropenation of a range of functionalized alkynes.[8,11] Utilizing Ag_3PO_4 as catalyst,[12] high yields of disubstituted silacyclopropenes were achieved with internal alkynes (Table 1, entries 1, 2, 6). Terminal alkynes, which are normally difficult substrates for silylene transfer,[13,14] also provided high yields of the desired silacyclopropenes (entries 3−5, 7−8). Propargyl ethers and amines also participate in this reaction (entries 5−8). In addition, selective silacyclopropenation to an alkyne in the presence of an olefin was achieved (entry 8).[15]

Because silacyclopropenes are highly reactive and difficult to isolate,[9] an in situ procedure for the functionalization of these intermediates was developed. The use of $CuBr_2$ as the insertion catalyst proved to be optimal. Reactions of saturated and unsaturated aldehydes and ketones provided high yields and regioselectivities (eq 2, Table 2).[16] In all cases, copper-catalyzed ring expansion resulted from insertion into the more substituted C−Si bond of the silacyclopropene. Selectivity likely arises from disfavored interactions between the silacyclopropene substituent and the *t*-Bu groups upon insertion into the less substituted C−Si bond.[17]

The scope of the one-flask formation of oxasilacyclopentenes from internal and terminal alkynes was explored with acetophenone and butyraldehyde (eq 3, Table 3). While CuI provided increased yields for terminal alkynes (entries 1 and 2), $Cu(OTf)_2$ proved to be the best catalyst for formation of insertion products derived from internal alkynes (Table 3, entries 3−5). Alkynes containing additional functionality, such as a propargylamine (Table 3, entry 2), were tolerated under the optimized conditions.

Table 1. Silacyclopropenation of Alkynes (Eq 1)

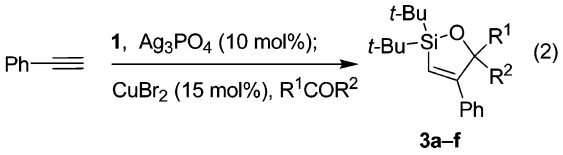


(1)

Entry	Alkyne	Yield[a] (%)
1	Ph—≡—Me	91 (**2a**)
2	Et—≡—Et	84 (**2b**)
3	Ph—≡	95 (**2c**)
4	*n*-Bu—≡	92 (**2d**)
5[b]	Me, Bn–N, ≡	97 (**2e**)
6	TIPSO, ≡, Me	94 (**2f**)
7[b]	MeO, ≡	79 (**2g**)
8	TIPSO, ≡	81 (**2h**)

[a] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard ($PhSiMe_3$). [b] The reaction mixture was heated in a sealed NMR tube at 80 °C (**2e**) or 50 °C (**2g**).

Table 2. One-Flask Silacyclopropenation/Carbonyl Insertions of Phenylacetylene (Eq 2)



(2)

Entry	Carbonyl	Yield[a] (%)	Regioselectivity[b]
1	Ph, H, O	79 (**3a**)	≥99:1
2	*n*-Pr, H, O	79 (**3b**)	99:1
3	Et, Et, O	85 (**3c**)	≥99:1
4	Ph, Me, O	83 (**3d**)	≥97:3[c]
5	Ph—≡—C(=O)Me	80 (**3e**)	≥99:1
6	EtO, H, O	68 (**3f**)	≥99:1

[a] Isolated yield from phenylacetylene after purification by flash chromatography. [b] As determined by GCMS analysis of the unpurified product mixture. [c] As determined by ^{1}H NMR spectroscopic analysis of the unpurified product mixture.

Transformations involving the vinylsilane functionality of the oxasilacyclopentene were explored, displaying the synthetic versatility of these intermediates. Simple removal of the *t*-Bu_2Si moiety by protodesilylation of oxasilacyclopentene **6a** afforded highly substituted allylic alcohol **8** (eq 4). This regioisomer is typically-

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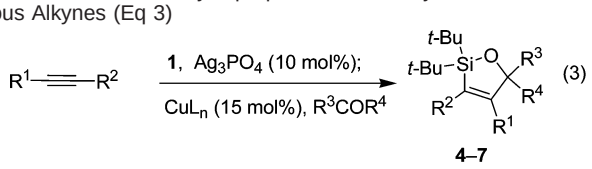
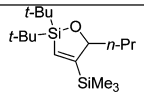
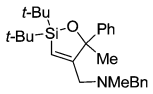
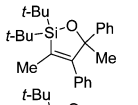
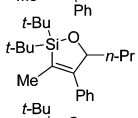
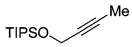
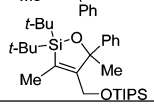
Table 3. One-Flask Silacyclopropenation/Carbonyl Insertions of Various Alkynes (Eq 3)



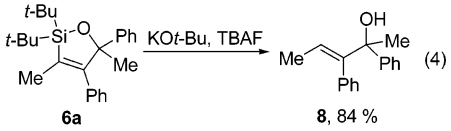
(3)

4–7

Entry	Alkyne	CuL_n	Product[a]	Yield[b](%)
1	Me_3Si—≡	CuI		78 (**4**)
2[c]		CuI		72 (**5**)
3	Ph—≡—Me	$Cu(OTf)_2$		94 (**6a**)
4	Ph—≡—Me	$Cu(OTf)_2$		54 (**6b**)
5		$Cu(OTf)_2$		90 (**7**)

[a] Insertions provided ≥95:5 regioselectivity, except **5** (90:10), as determined by GC analysis of the unpurified product mixture. [b] Isolated yield from alkyne after purification by flash chromatography.

challenging to obtain using other methods.[18]

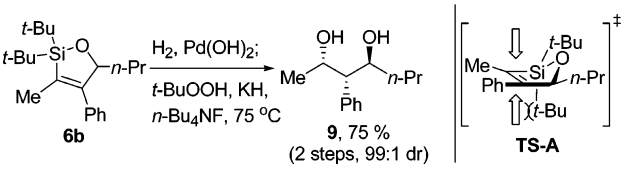


(4)

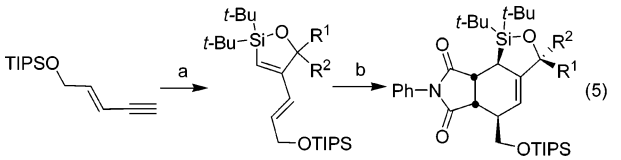
6a **8**, 84 %

The alkene moiety of the oxasilacyclopentene was also reactive. Hydrogenation of the oxasilacyclopentene, followed by oxidation[10] of the resulting oxasilacyclopentane, provided 1,3-diol **9** diastereoselectively. The observed diastereomer may have resulted from addition of hydrogen to the face opposite the pseudoaxial *t*-Bu group (**TS-A**, Scheme 2).[19,20]

Scheme 2



Upon establishing the reactivity of simple oxasilacyclopentenes, we utilized the olefin to increase the molecular complexity through a cycloaddition reaction. Oxasilacyclopentenes **11** and **12** were constructed using typical conditions (vide supra) utilizing enyne **10** (eq 5). Heating diene **11** with *N*-phenylmaleimide provided the Diels−Alder adduct **13** as a 99:1 mixture of diastereomers favoring the exo adduct (vide infra). Although the exo-selective Diels−Alder was not expected to give high facial selectivity with a chiral oxasilacyclopentene such as **12**, 4:1 diastereoselectivity was achieved upon thermal cycloaddition with *N*-phenylmaleimide.[21] The formation of adduct **14** represents a cyclohexene core with five stereogenic centers. We propose that the endo transition state in these reactions was disfavored due to steric interactions between the dienophile and the *t*-Bu groups on silicon.



(5)

10 **11** (R^1 = R^2 = Et) **13** (R^1 = R^2 = Et)
12 (R^1 = Ph, R^2 = Me) **14** (R^1 = Ph, R^2 = Me)

a) i. 10 mol% Ag_3PO_4, **1**; ii. **11**: CuI, Et_2CO, 54% from **10**, 98:2 regiosel.; **12**: CuI, PhCOMe, 58% from **10**, 89:11 regiosel.; b) *N*-phenylmaleimide, 130 °C, 6-9 d, **13**: 76%, 99:1 dr, **14**: 69%, 4:1 dr

In conclusion, alkynes can be transformed into synthetically valuable masked allylic alcohols through the in situ functionalization of silacyclopropenes. The potential synthetic utility of the intermediate oxasilacyclopentenes was demonstrated through the Diels−Alder reactions to provide highly substituted carbocycles **13** and **14**.

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Supporting Information Available: Experimental procedures; spectroscopic, analytical, and X-ray data for the products (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) Details are provided as Supporting Information.

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