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Alkylidenesilacyclopropanes Derived from Allenes: Applications to the Selective Synthesis of Triols and Homoallylic Alcohols

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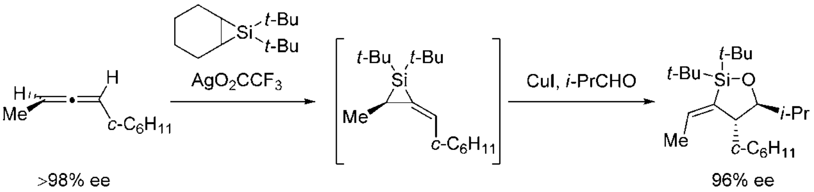
ABSTRACT



Several alkylidenesilacyclopropanes were prepared by silver-mediated silylene transfer to allenes. Oxasilacyclopentanes derived from allenes were prepared with high regio- and diastereoselectivity by a two-step, one-flask silacyclopropanation/carbonyl insertion reaction. Triols and homoallylic alcohols were formed diastereoselectively by functionalizing the oxasilacyclopentanes. An optically active allene (>98% ee) was utilized to synthesize an enantiopure homoallylic alcohol in 96% ee.

Allenes are unique scaffolds for organic synthesis because they have axial chirality that can be transferred to the products of subsequent reactions. Hydroamination,[1] three-component coupling,[2] Pauson–Khand-type cycloaddition,[3] and tandem coupling/cyclization[4] have all been applied to chiral allenes to give enantiopure products. The addition reactions of carbenes[5] and nitrenes[6] with allenes have also been employed in stereoselective synthesis. Silylene transfer to allenes would combine the chirality inherent to the allene with the high reactivity of the strained-ring silane[7] to allow the formation of enantiomerically pure products with new carbon–carbon bonds. Photochemical silacyclopropanation of allenes has been reported,[8] but the alkylidenesilacyclopropane products were formed with low regio- and diastereoselectivities.

In this paper, we demonstrate that metal-catalyzed silylene transfer[9] to allenes forms alkylidenesilacyclopropanes with high regio- and diastereoselectivity. These highly reactive intermediates undergo insertions of carbonyl compounds to yield synthetically useful oxasilacyclopentane products[8,10] (Scheme 1). After manipulation of the exocyclic alkene or the C–Si bond,

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[1] Nishina, N.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 3314–3317.

[2] (a) Ng, S.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2005**, *127*, 7320–7321. (b) Ng, S.-S.; Jamison, T. F. *Tetrahedron* **2005**, *61*, 11405–11417.

[3] Brummond, K. M.; Kerekes, A. D.; Wan, H. *J. Org. Chem.* **2002**, *67*, 5156–5163.

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[8] (a) Ando, W.; Saso, H. *Tetrahedron Lett.* **1986**, *27*, 5625–5628. (b) Saso, H.; Ando, W.; Ueno, K. *Tetrahedron* **1989**, *45*, 1929–1940.

[9] (a) Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 10659–10663. (b) Ćiraković, J.; Driver, T. G.; Woerpel, K. A. *J. Org. Chem.* **2004**, *69*, 4007–4012. (c) Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522–9523.

[10] (a) Marshall, J. A.; Ellis, K. C. *Org. Lett.* **2003**, *5*, 1729–1732. (b) O'Neil, G. W.; Phillips, A. J. *J. Am. Chem. Soc.* **2006**, *128*, 5340–5341. (c) Someya, H.; Kondoh, A.; Sato, A.; Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Synlett* **2006**, 3061–3064. (d) Robertson, J.; Middleton, D. S.; O'Connor, G.; Sardharwala, T. *Tetrahedron Lett.* **1998**, *39*, 669–672. (e) Robertson, J.; O'Connor, G.; Sardharwala, T.; Middleton, D. S. *Tetrahedron* **2000**, *56*, 8309–8320. (f) Leighton, J. L.; Chapman, E. *J. Am. Chem. Soc.* **1997**, *119*, 12416–12417. (g) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1992**, *57*, 1643–1645.

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Scheme 1. Formation of Oxasilacyclopentanes from Allenes

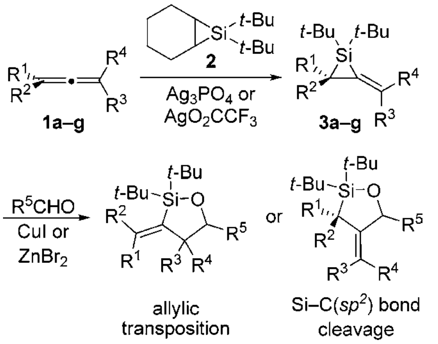
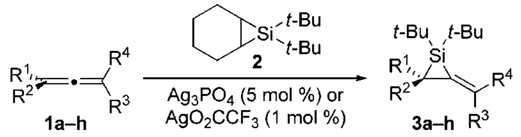
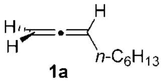
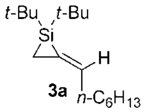
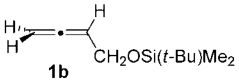
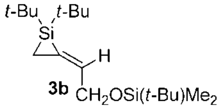
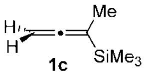
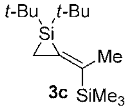
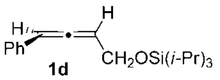
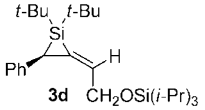
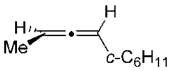
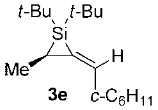
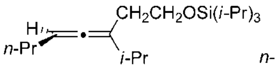
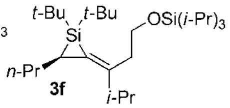
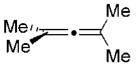
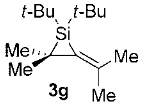
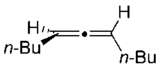
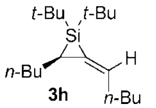


Table 1. Silacyclopropanation of Allenes



entry	allene	product[a]	yield[b] (%)
1	 **1a**	 **3a**	77[c]
2	 **1b**	 **3b**	77
3	 **1c**	 **3c**	85[c]
4	 **1d**	 **3d**	84
5	 **1e**	 **3e**	70[c]
6	 **1f**	 **3f**	81
7	 **1g**	 **3g**	91[c]
8	 **1h**	 **3h**	90[c]

[a] All regio- and diastereoselectivities were ≥93:7 except for **3b** (83:17 dr), **3d** (79:21 regioisomers) and **3f** (78:22 dr). Details are provided as Supporting Information. [b] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard (PhSiMe$_3$). [c] Details regarding isolated yields are provided as Supporting Information.

oxygenated compounds such as triols and homoallylic alcohols can be formed.[9c,11] When enantiomerically enriched allenes were employed, enantioenriched products were formed.

Several alkylidenesilacyclopropanes were prepared with high regio- and diastereoselectivity using silver-catalyzed silylene transfer[9] (Table 1). The reaction is general for a wide variety of substitution patterns, including for a tetrasubstituted allene (entry 7). Silylene transfer is regioselective for substrates that have a steric difference between the substituents on the 1- and 3-positions of the allene (entries 1−6). For 1,3-disubstituted allene **1e**, the silacyclopropane was initially formed as a 70:30 mixture of regioisomers, but the more sterically hindered isomer decomposed,[12] and silacyclopropane **3e** remained in 70% yield (entry 5). Diastereoselectivity for these reactions, like regioselectivity, was high when the two groups on the newly formed exocyclic alkene were significantly different in size. A decrease in diastereoselectivity was observed for trisubstituted allene **1f**, which provided a 3:1 mixture of alkene isomers, favoring **3f** (entry 6).

Alkylidenesilacyclopropanes participate in insertion reactions with carbonyl compounds to yield oxasilacyclopentanes[8] with high regio- and diastereoselectivity. Silacyclopropane **3h** underwent allylic transposition with benzaldehyde and butyraldehyde to provide oxasilacyclopentanes **4a** and **4b**, respectively (Table 2, entries 1−4). Cleavage of the Si−C(sp^2) bond occurred when silacyclopropane **3h** was treated with ethyl formate, resulting in oxasilacyclopentane **5** (entries 5 and 6). Although these insertion reactions can be performed without catalyst (22 to 100 °C), the use of a copper salt reduced both the temperature and reaction time.[12,13]

Reaction conditions were developed for a two-step, one-flask silacyclopropanation/carbonyl insertion method to avoid handling sensitive alkylidenesilacyclopropanes. Oxasilacyclopentane products like **6**, **7**, and **8** were synthesized (Scheme 2) with silver salts catalyzing silylene transfer and copper and zinc salts promoting insertion of carbonyl compounds.

The double bond of the oxasilacyclopentane can be elaborated to provide highly functionalized products. Oxasilacyclopentane **6** underwent epoxidation to form spiroepoxide **9** in 72% yield and 98:2 diastereoselectivity. Under protodesilylation conditions, the epoxide was converted into triol **10** as a single isomer in 84% yield (Scheme 3).[14] The triol is presumed to form by removal of the di-*tert*-butylsilyl moiety under the protodesilylation conditions with concomitant opening of the epoxide by adventitious water.

To determine the stereochemical course of the carbonyl insertion with allylic transposition, silylene transfer to an enantiopure allene was performed (Scheme 4). Allene (+)-**1d** was prepared from an enantiopure (>98% ee) alcohol

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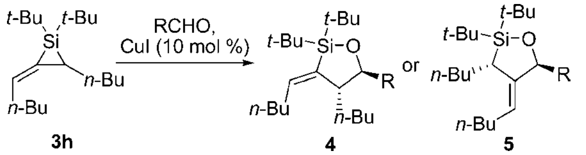
[11] Clark, T. B.; Woerpel, K. A. *Org. Lett.* **2006**, *8*, 4109–4112.

[12] More information is provided as Supporting Information.

[13] It is not clear how copper salts catalyze carbonyl insertion. The mechanism of this reaction is currently being investigated.

[14] The relative stereochemistry of **10** was determined by X-ray crystallography.

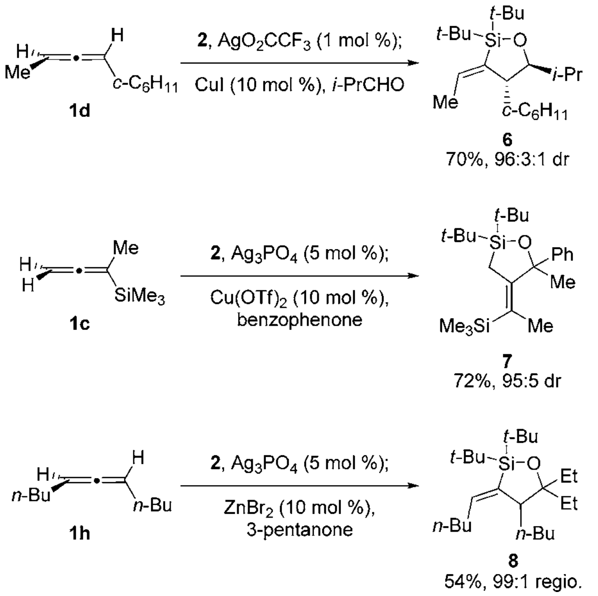
Table 2. Thermal vs. Cu-Catalyzed Carbonyl Insertion Reactions



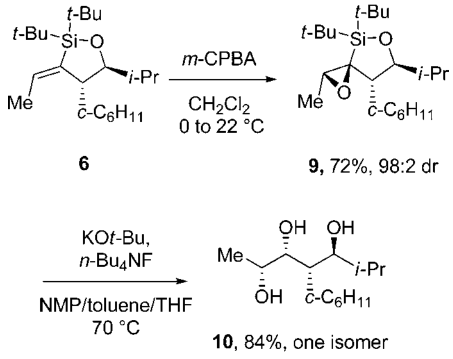
entry	R	conditions	product	time[a]	yield[b] (%)
1	Ph	22 °C	**4a**	1.5 h	82
2	Ph	CuI, 22 °C	**4a**	30 min	90
3	*n*-Pr	60 °C	**4b**	15 h	82
4	*n*-Pr	CuI, 22 °C	**4b**	30 min	89
5	EtO	100 °C	**5**	7 d	82
6	EtO	CuI, 60 °C	**5**	21 h	90

[a] Time needed for the reaction to proceed to 100% conversion. [b] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard (PhSiMe$_3$).

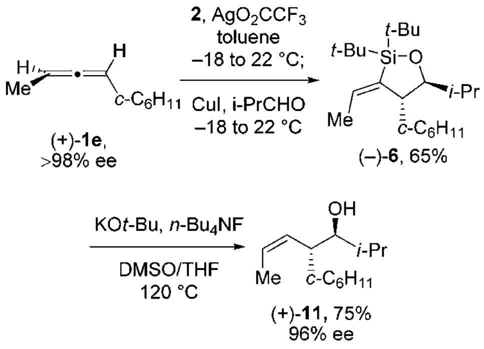
Scheme 2. Two-Step, One-Flask Silacyclopropanation/Carbonyl Insertion Reactions



Scheme 3. Functionalization to Form a 1,2,4-Triol



Scheme 4. Formation of an Enantiopure Homoallylic Alcohol



following a known procedure,[2a,15] then subjected to the two-step, one-flask silacyclopropanation/carbonyl insertion reaction to provide oxasilacyclopentane (*R*,*S*)-(−)-**6** in 65% yield. Oxasilacyclopentane (−)-**6** underwent protodesilylation to afford alcohol (*R*,*S*)-(+)-**11** in 75% yield and 96% ee.[16] These results indicate that upon allylic transposition, the new carbon−carbon bond formation occurs on the face opposite to the substituent of the three-membered ring.

In conclusion, alkylidenesilacyclopropanes were synthesized from allenes with high regio- and diastereoselectivity. Oxasilacyclopentanes derived from allenes were prepared in a two-step, one-flask reaction with high regio- and diastereoselectivity. The oxasilacyclopentanes were functionalized to form triols and homoallylic alcohols diastereoselectively. An enantiopure homoallylic alcohol was synthesized from optically active starting material, which demonstrated the synthetic utility of this method. This process could be used to make a variety of highly branched homoallylic alcohols that cannot easily be made using existing methods.[17]

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

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(15) Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492–4493.

(16) Absolute stereochemistry was determined by X-ray crystallographic analysis of a chiral carbamate derivative. Details are provided as Supporting Information.

(17) (a) McNulty, J.; Nair, J. J.; Sliwinski, M.; Harrington, L. E.; Pandey, S. *Eur. J. Org. Chem.* **2007**, 5669–5673. (b) Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2002**, *124*, 392–393. (c) Abiko, A. *Acc. Chem. Res.* **2004**, *37*, 387–395.