Published in final edited form as:

Org Lett. 2009 May 21; 11(10): 2173–2175. doi:10.1021/ol900456v.

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

Kay M. Buchner, Timothy B. Clark, Janice M. N. Loy, Thong X. Nguyen, and K. A. Woerpel
Department of Chemistry, University of California, Irvine, California 92697-2025, kwoerpel@uci.edu

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/cyclization⁴ have all been applied to chiral allenes to give enantiopure products. The addition reactions of carbenes⁵ and nitrenes⁶ 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 silane⁷ 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 transfer⁹ 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, 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 transfer⁹ (Table 1). The reaction is general for a wide variety of substitution patterns, including for a tetrasubstituted allene (entry 7). Silylene transfer is highly 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

Correspondence to: K. A. Woerpel.

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>.

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 oxasilacyclopentanes⁸ 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 °C 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 spiro-epoxide **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 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 synthesized 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

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by the National Institute of General Medical Sciences of the National Institutes of Health (GM-54909). K.M.B. thanks the Department of Education (GAANN) for a predoctoral fellowship. K.A.W. thanks Amgen and Lilly for awards to support research. We thank Dr. P. Dennison (UCI) for assistance with NMR spectroscopy, Dr. J. W. Ziller and M. K. Takase (UCI) for X-ray crystallography, and Dr. J. Greaves and S. Sorooshian (UCI) for mass spectrometry.

References

1. Nishina N, Yamamoto Y. *Angew Chem Int Ed* 2006;45:3314–3317.
2. (a) Ng SS, Jamison TF. *J Am Chem Soc* 2005;127:7320–7321. [PubMed: 15898774] (b) Ng SS, Jamison TF. *Tetrahedron* 2005;61:11405–11417.
3. Brummond KM, Kerekes AD, Wan H. *J Org Chem* 2002;67:5156–5163. [PubMed: 12126400]
4. Ma S, Yu F, Gao W. *J Org Chem* 2003;68:5943–5949. [PubMed: 12868930]
5. Brandi A, Goti A. *Chem Rev* 1998;98:589–635. [PubMed: 11848910]
6. Shipman M. *Synlett* 2006:3205–3217.
7. Seyferth D. *J Organomet Chem* 1975;100:237–256.
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 TG, Woerpel KA. *J Am Chem Soc* 2003;125:10659–10663. [PubMed: 12940750] (b) Ćiraković J, Driver TG, Woerpel KA. *J Org Chem* 2004;69:4007–4012. [PubMed: 15176824] (c) Clark TB, Woerpel KA. *J Am Chem Soc* 2004;126:9522–9523. [PubMed: 15291539]
10. (a) Marshall JA, Ellis KC. *Org Lett* 2003;5:1729–1732. [PubMed: 12735763] (b) O'Neil GW, Phillips AJ. *J Am Chem Soc* 2006;128:5340–5341. [PubMed: 16620095] (c) Someya H, Kondoh A, Sato A, Ohmiya H, Yorimitsu H, Oshima K. *Synlett* 2006:3061–3064. (d) Robertson J, Middleton DS, O'Connor G, Sardharwala T. *Tetrahedron Lett* 1998;39:669–672. (e) Robertson J, O'Connor G, Sardharwala T, Middleton DS. *Tetrahedron* 2000;56:8309–8320. (f) Leighton JL, Chapman E. *J Am Chem Soc* 1997;119:12416–12417. (g) Hale MR, Hoveyda AH. *J Org Chem* 1992;57:1643–1645.
11. Clark TB, Woerpel KA. *Org Lett* 2006;8:4109–4112. [PubMed: 16928086]
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.
15. Myers AG, 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 JJ, Sliwinski M, Harrington LE, Pandey S. *Eur J Org Chem* 2007:5669–5673. (b) Evans DA, Tedrow JS, Shaw JT, Downey CW. *J Am Chem Soc* 2002;124:392–393. [PubMed: 11792206] (c) Abiko A. *Acc Chem Res* 2004;37:387–395. [PubMed: 15196048]

Scheme 1.
Formation of Oxasilacyclopentanes from Allenes

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

Scheme 3.

Scheme 4.

Table 1

Silacyclopropanation of Allenes

entry	allene
-------	--------	--

1

2

entry

allene

3

entry

allene

4

entry

allene

entry

allene

6

entry

allene

7

8

^a All regio- and diastereoselectivities were $\geq 93:7$ 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 ^1H NMR spectroscopic analysis of the product relative to an internal standard (PhSiMe_3).

^c Details regarding isolated yields are provided as Supporting Information.

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	<i>n</i> -Pr	60 °C	4b	15 h	82
4	<i>n</i> -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

^aTime needed for the reaction to proceed to 100% conversion.

^bAs determined by ¹H NMR spectroscopic analysis of the product relative to an internal standard (PhSiMe₃).