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# *Communications*

## Novel Intramolecular Ene Reactions of Allenylsilanes

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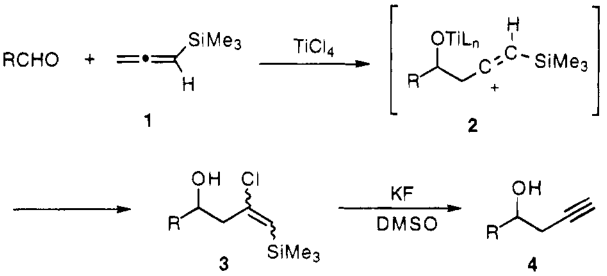
In a series of elegant papers which appeared in the 1980's, Danheiser and co-workers described a number of reactions of allenylsilanes with a variety of carbon electrophiles.[1] For example, it was found that an allenylsilane such as **1** reacts with an aldehyde in the presence of a Lewis acid to afford a (chlorovinyl)silane **3**, presumably via a $\beta$-silyl-stabilized cation **2** (Scheme 1). Compound **3** can then be converted to a homopropargyl alcohol **4** with fluoride ion. In the course of a total synthesis of the marine alkaloid papuamine,[2] we attempted to effect an intramolecular version of this Danheiser reaction using an imine as the electrophile,[1c] but instead discovered a new type of pericyclic imino ene reaction involving the allenylsilane. We have subsequently found that allenylsilanes are in fact prone to a wide range of facile intramolecular ene processes and in this paper describe some of the preliminary results of this study.

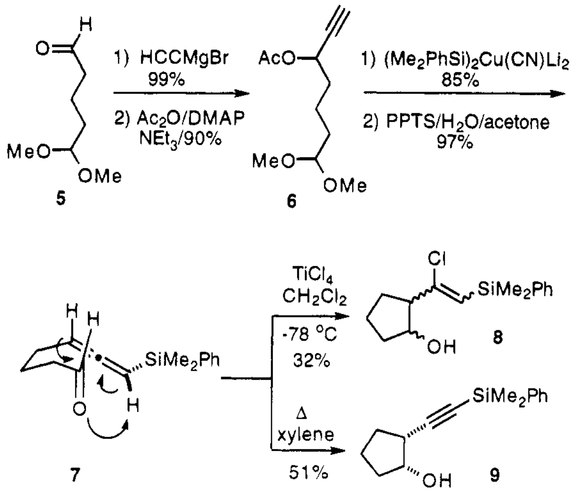
A simple model substrate was first prepared as outlined in Scheme 2. Known aldehyde **5**[3] was converted to propargyl acetate **6** and then transformed to the allenylsilane via the methodology of Fleming,[4] affording aldehyde **7** upon acetal cleavage. When subjected to conditions of Danheiser,[1b] allenylsilane aldehyde **7** cyclized to a complex mixture of stereoisomeric (chlorovinyl)silanes **8** in poor yield. However, we were pleased to find that upon refluxing in xylene for 16 h, compound **7** cyclized stereoselectively to *cis*-hydroxy silylacetylene **9** in moderate yield.[5] We believe this latter transformation occurs via a concerted pericyclic carbonyl ene reaction through the conformation shown in structure **7**.[6,7]

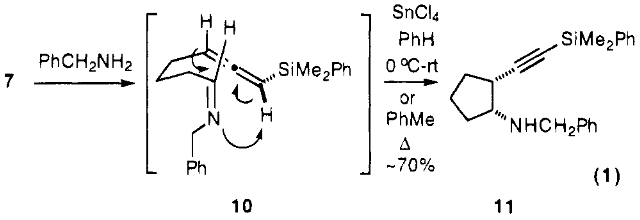
This system also was found to readily undergo a pericyclic imino ene reaction.[8] *N*-Benzylimine **10**, which was prepared from aldehyde **7** (eq 1), was observed to cyclize stereoselectively to *cis*-amino silylacetylene **11** either thermally or at low temperature in the presence of stannic chloride in good yields.[5] Once again, this process is believed to occur via an ene cyclization through conformation **10**.

**Scheme 1**



**Scheme 2**





(1)

The methodology has also been successfully applied to synthesis of six-membered rings. Thus, thermolysis of allenylsilane aldehyde **12** afforded *cis*-hydroxy acetylene **14** after silyl group cleavage (Scheme 3).[9] Imine **13**, derived from aldehyde **12**, when treated with stannic chloride produced a $\beta$-amino ketone, characterized as its *cis*-*N*-acetyl derivative **15**. It appears that in this case the silylacetylene initially produced in the ene cyclization is prone to hydrolysis upon workup.[10] However, if imine **13** is simply heated in mesitylene (162 °C) for 16 h, followed by desilylation, *cis*-amino acetylene **16** is formed which is more stable to hydrolysis.

In order to probe the role of the silyl group in this ene chemistry, substrates **17a** and **17b** were prepared (Scheme 4). In both cases, the derived imines **18**, when treated

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[1] See, for example: (a) Danheiser, R. L.; Carini, D. J. *J. Org. Chem.* **1980**, *45*, 3925. (b) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870. (c) Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1985**, *107*, 7233. (d) Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407. (e) Becker, D. A.; Danheiser, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 389.

[2] Borzilleri, R. M.; Weinreb, S. M.; Parvez, M. *J. Am. Chem. Soc.* **1994**, *116*, 9789.

[3] Claus, R. E.; Schreiber, S. L. *Org. Synth.* **1985**, *64*, 150.

[4] Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, *264*, 99.

[5] Stereochemistry was proven by appropriate $^1$H NMR NOE experiments.

[6] For reviews of the ene reaction, see: (a) Snider, B. B. Ene Reactions with Alkenes as Enophiles. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 5, p 1. (b) Mikami, K; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. (c) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876.

[7] For a review of the carbonyl ene reaction, see: Snider, B. B. The Prins and Carbonyl Ene Reactions. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 527.

[8] For a review of the imino ene reaction, see: Borzilleri, R. M.; Weinreb, S. M. *Synthesis* **1995**, 347. For an example of an intermolecular imino ene reaction involving an allene, see: Baumann, H.; Duthaler, R. O. *Helv. Chim. Acta* **1988**, *71*, 1025.

[9] All attempts at cyclizing a similar homologated substrate to produce the seven-membered ring analog failed.

[10] It is also conceivable that the ketone is formed via a cyclization involving a vinyl cation.[1] However, one would not expect such a high selectivity for the *cis* isomer in this case. We have, in general, found that the (cyclohexylamino)silyl alkynes are rather unstable relative to the cyclopentyl systems and thus were desilylated immediately. For example, chromatography of the silylacetylene from thermolysis of **13** gave the methyl ketone.

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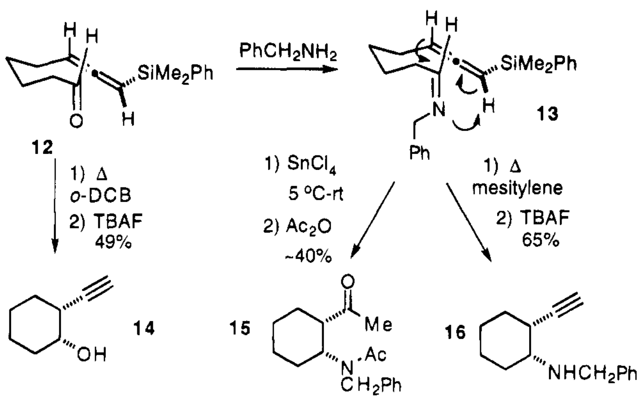
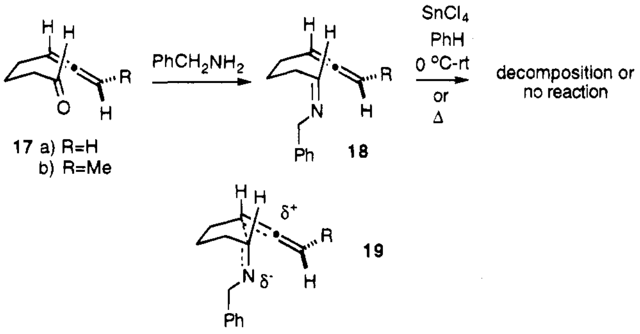
**Scheme 3**

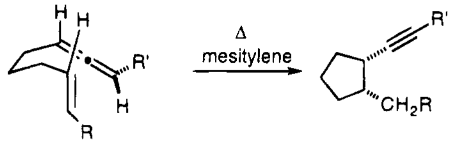


**Scheme 4**



with Lewis acids or heated, failed to give any observable ene cyclization products. A reasonable explanation for this lack of reactivity is that the ene transition state has dipolar character (*cf.* **19**) and the silyl group is necessary for stabilization of the partial positive charge at the central carbon of the allene.[11]

The silyl group has also been found to facilitate intramolecular "all-carbon" ene reactions. It has been previously reported[12] that allene olefin **20a**, upon heating at 400 °C, produces a complex mixture of ene product **21a** along with two [2 + 2]-cycloadducts (eq 2). However,



(2)

20 a) R, R'=H
b) R=H, R'=Me$_2$PhSi
c) R=CO$_2$Me, R'=Me$_2$PhSi

21 a) R, R'=H
b) R=H, R'=Me$_2$PhSi (62%)
c) R=CO$_2$Me, R'=Me$_2$PhSi (70%)

silyl allene **20b** cyclizes stereoselectively to *cis*-silyl acetylene **21b** upon refluxing in mesitylene.[5] Similarly, α,β-unsaturated ester allenylsilane **20c** undergoes ene cyclization to *cis*-disubstituted cyclopentane **21c** in good yield.

We are continuing to explore the scope and applications of these facile intramolecular allenyl silane ene reactions.[13]

**Acknowledgment.** We are grateful to the National Institutes of Health (CA-34304) for support of this research.

**Supporting Information Available:** Synthetic procedures for substrate **7** and cyclizations of **7**, **10**, **12**, **13**, **20b**, and **20c** (10 pages).

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[11] Allene aldehyde **17a** is known to react with Me$_2$AlCl to give 2-(chloromethyl)-2-cyclohexenol via addition of the carbonyl group to the central carbon of the allene. See: Snider, B. B. In *Selectivities in Lewis Acid Promoted Reactions;* Schinzer, D., Ed.; Kluwer: Dordrecht, 1989; Chapter 8. See also: Bertrand, M.; Roumestant, M. L.; Sylvestre-Panthet, P. *Tetrahedron Lett.* **1981**, *22*, 3589 and references cited therein.

[12] Huntsman, W. D.; Li, Y.; Giannamore, V. P. *Isr. J. Chem.* **1985**, *26*, 88. See also: Meyer, C.; Marek, I.; Courtemanche, G.: Normant, J. F. *J. Org. Chem.* **1995**, *60*, 863.

[13] Interestingly, thermolysis of allenyl stannane imine **i** afforded *trans*-amino acetylene **ii** in low yield. This product may derive from a stepwise ionic cyclization mode (*cf.* Scheme 1).