ORGANIC LETTERS

2007
Vol. 9, No. 19
3773−3776

Metal-Catalyzed Silylene Transfer to Imines: Synthesis and Reactivity of Silaaziridines

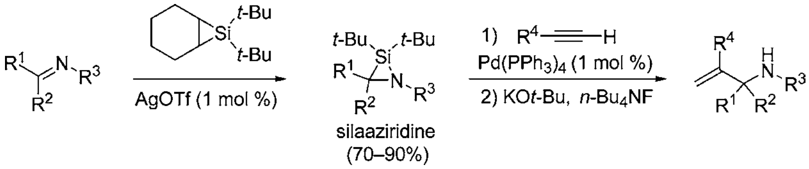
Zulimar Nevárez and K. A. Woerpel*

Department of Chemistry, University of California, Irvine,
Irvine, California 92697-2025

kwoerpel@uci.edu

Received June 18, 2007

ABSTRACT



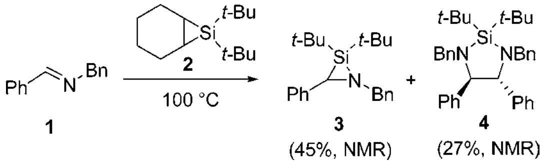
Metal-catalyzed silylene transfer to imines provides an efficient synthesis of silaaziridines. These strained cyclic silanes undergo selective bond-forming reactions, permitting the synthesis of nitrogen-containing compounds after protodesilylation of the resulting vinyl silane.

The chemistry of three-membered ring compounds composed of silicon, nitrogen, and carbon atoms remains unexplored because these compounds have proven to be challenging to synthesize. Brook prepared silaaziridines from isocyanides and photolytically generated silenes, but the generality of this method is limited.[1] Although silaaziridines have been proposed as reactive intermediates in thermal[2] and photochemical[3] silylene transfer reactions to imines, the strained-ring silanes were not isolated; instead, rearranged products were obtained. Because no general synthesis of silaaziridines has emerged, the reactivity of these intermediates has not been explored,[4−6] and no applications to organic synthesis have appeared.

In this paper, we demonstrate that silver-catalyzed silylene transfer to imines provides a general method for the synthesis of stable silaaziridines. These compounds engage in selective bond-forming reactions that can be applied to the synthesis of nitrogen-containing products.

An indication that stable silaaziridines could be prepared from imines emerged from our studies of thermal silylene transfer. Heating a mixture of imine **1** and silacyclopropane **2** provided silaaziridine **3** in 45% yield along wih 27% of a dimer byproduct[7] (Scheme 1). We surmised that the elevated temperatures required to transfer t-Bu$_2$Si caused the dimerization and that milder conditions would permit the isolation of silaaziridines without unwanted side products.

Scheme 1. Thermal Silylene Transfer to Imines



The mild silver-catalyzed silylene transfer reaction allowed for the clean conversion of a variety of imines to silaaziri-

---

(1) Brook, A. G.; Young, K. K.; Saxena, A. K.; Sawyer, J. F. *Organometallics* **1988**, *7*, 2245−2247.

(2) Belzner, J.; Ihmels, H.; Pauletto, L. *J. Org. Chem.* **1996**, *61*, 3315−3319.

(3) Weidenbruch, M.; Piel, H. *Organometallics* **1993**, *12*, 2881−2882.

(4) Brook, A. G.; Saxena, A. K.; Sawyer, J. F. *Organometallics* **1989**, *8*, 850−852.

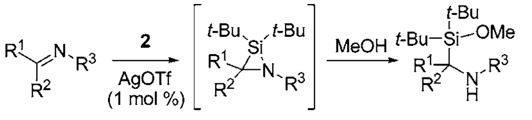
(5) Brook, A. G.; Azarian, D.; Baumegger, A.; Hu, S. S.; Lough, A. J. *Organometallics* **1993**, *12*, 529−534.

(6) Brook, A. G.; Habtemariam, A. *Can. J. Chem.* **2003**, *81*, 1164−1167.

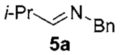
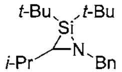
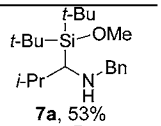
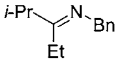
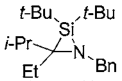
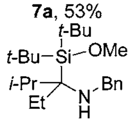
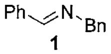
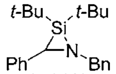
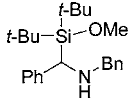
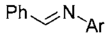
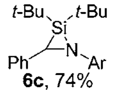
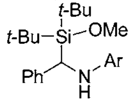
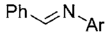
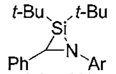
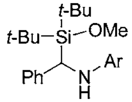
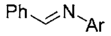
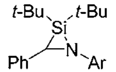
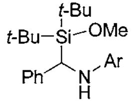
(7) Bodnar, P. M.; Palmer, W. S.; Ridgway, B. H.; Shaw, J. T.; Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 4737−4745.

10.1021/ol701424a CCC: $37.00

Table 1. Silver-Catalyzed Silylene Transfer Followed by Methanolysis



1, 5a–e 3, 6a–e 7a–f

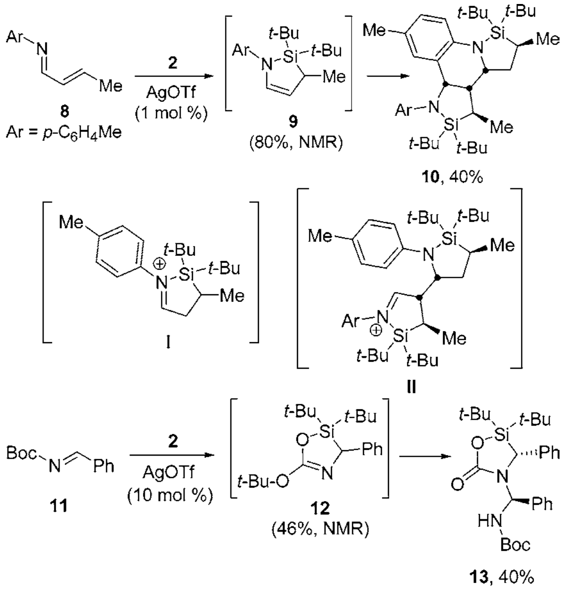
entry	imine	silaaziridine[a]	methanolysis[b]
1[c]	 **5a**	 **6a**, 88% (84%)	 **7a**, 53%
2	 **5b**	 **6b**, 74%	 **7b**, 55%
3[c]	 **1**	 **3**, 90% (80%)	 **7c**, 62%
4[c]	 **5c** Ar = *p*-MeC$_6$H$_4$	 **6c**, 74% (73%)	 **7d**, 40%
5[d]	 **5d** Ar = *p*-MeOC$_6$H$_4$	 **6d**, 76%	 **7e**, 46%
6	 **5e** Ar = *p*-CF$_3$C$_6$H$_4$	 **6e**, 70%	 **7f**, 42%

[a] As determined by ^{1}H NMR spectroscopic analysis of the product relative to an internal standard (PhSiMe$_3$). [b] Isolated yields after purification by flash chromatography. Some decomposition was observed during purification. [c] Silaaziridines were isolated by bulb-to-bulb distillation in the corresponding yields in parentheses. [d] 13:1 mixture of isomers with **7e** as the major isomer. The minor isomer is the result of cleavage of the Si−C bond; characterization data are provided as Supporting Information.

dines (Table 1).[8] Imines with aromatic and benzyl substituents on the nitrogen atom underwent silylene transfer to provide silaaziridines in good yields. Silylene transfer occurred to alkyl imines (entries 1 and 2) and even to a sterically hindered ketimine **5b** (entry 2). The reactivity of the trisubstituted C−N double bond contrasts with the observations that trisubstituted alkenes are unreactive to the silylene transfer conditions.[9] Despite the sensitivity of these compounds to air and water, silaaziridines **6a**, **3**, and **6c** could be isolated in good yields (entries 1, 3, and 4). In general, however, silaaziridines were characterized as their methanolysis products.

Silylene transfer to conjugated imines did not provide three-membered ring products, but instead afforded five-membered ring adducts. Treatment of α,*β*-unsaturated imine **8** to the silylene transfer conditions resulted in the formation of enamine **9** in 80% yield by ^{1}H NMR spectroscopy (Scheme 2).[10] Attempted isolation of the enamine **9**, however, resulted in dimerization to yield compound **10** as a single diastereomer. The relative stereochemistry of **10** was determined by X-ray crystallography.[11] This transformation likely occurred through nucleophilic addition of the enamine **9** to its conjugate acid **I** to form iminium ion **II**, which underwent electrophilic aromatic substitution.

Scheme 2. Silylene Transfer to Conjugated Imines



Silylene transfer to *N*-acylimines also led to five-membered ring products. Treatment of carbamate-protected imine **11** under silver-catalyzed conditions provided oxazoline **12** in 46% yield.[12] The low yield of this reaction may be the result of binding of the product to the catalyst, which would inhibit turnover.[13] Concentration of **12** resulted in reaction with remaining imine **11** to yield **13** as a single diastereomer. The relative stereochemistry was determined by X-ray crystallography.[11]

A mechanism for silylene transfer to imines can be proposed to account for both three- and five-membered ring products (Scheme 3). Addition of the nucleophilic heteroatom to the electrophilic silylene[13] or silylenoid would generate ylides **III** or **IV**. Intermediate **III** can undergo a 4*π*-electrocyclic reaction to form silaaziridine products **3** and

---

(8) Other silver catalysts such as AgOCOCF$_3$, AgBF$_4$, and AgOTf gave products in comparable yields. Copper catalysts at higher temperatures also provided products, although in low yields.

(9) For examples of metal-catalyzed silylene transfer to mono- and disubstituted alkenes, see: Ćiraković, J.; Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc*. **2002**, *124*, 9370−9371.

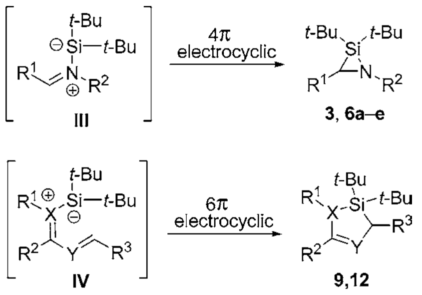
(10) Formal [4+1] products have been observed for other silylene transfer reactions to unsaturated imines and dienes: (a) Bobbitt, K. L.; Gaspar, P. P. *J. Organomet. Chem*. **1995**, *499*, 17−26. (b) Vinylsilacyclopropanes, however, have been prepared: Zhang, S.; Conlin, R. T. *J. Am. Chem. Soc*. **1991**, *113*, 4272−4278.

(11) The details are provided as Supporting Information.

(12) The analogous reaction was observed for α,*β*-unsaturated esters and ketones: Calad, S. A.; Woerpel, K. A. *J. Am. Chem. Soc*. **2005**, *127*, 2046−2047 and references therein.

(13) Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc*. **2004**, *126*, 9993−10002.

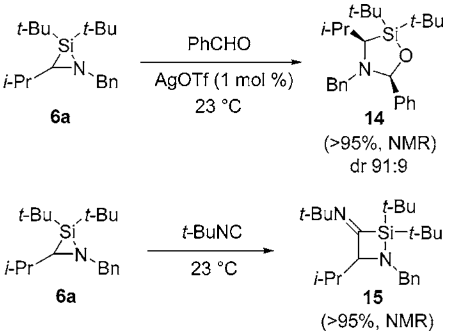
Scheme 3. Proposed Mechanism for Silylene Transfer to Imines



6a−**e**. In the case of conjugated imines, the resulting intermediate **IV** could undergo a 6*π*-electrocyclic reaction to provide five-membered ring products **9** and **12**.[12]

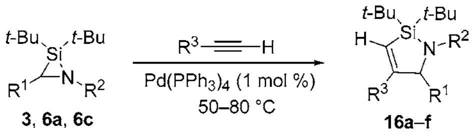
Because little was known about the reactivity of silaaziridines,[4−6] we examined their reactions with various electrophiles. Reaction of silaaziridine **6a** with benzaldehyde resulted in insertion into the Si−N bond to provide *N*,*O*-acetal **14** (Scheme 4).[14,15] The *cis*-stereochemistry of **14** was determined by NOE experiments. Insertion with the opposite selectivity occurred with isocyanides. When silaaziridine **6a** was treated with *tert*-butyl isocyanide, insertion occurred solely through the Si−C bond to give imine **15** in quantitative yield.[16] The chemoselectivity for these insertion reactions is consistent with Pearson's hard-soft acid-base theory.[17] Hard electrophiles such as PhCHO and MeOH reacted at the more ionic Si−N bond, whereas the softer isocyanide electrophile inserted at the more covalent Si−C bond.

Scheme 4. Chemoselective Ring Expansion Reactions



Silaaziridines undergo regioselective palladium-catalyzed alkyne insertion reactions to provide synthetically valuable products in high yields. Treatment of selected silaaziridines with terminal alkynes in the presence of $Pd(PPh_3)_4$ resulted in the formation of azasilacyclopentenes **16** (Table 2).[18] These compounds are masked 1,3-amino alcohols,[19] and embedded in their structure is an allylic amine.[20]

Table 2. Palladium-Catalyzed Alkyne Insertions

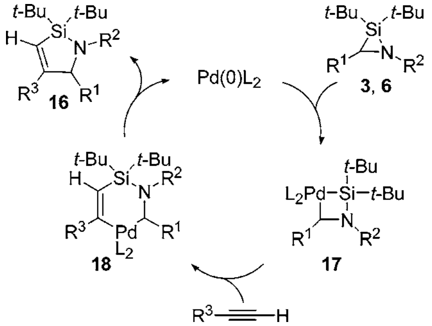


entry	R^1	R^2	R^3	product[a,b]
1	*i*-Pr	Bn	Ph	**16a**, 90%
2	*i*-Pr	Bn	CH_2SiMe_3	**16a**, 85%
3	*i*-Pr	Bn	CH_2OP[c]	**16c**, 94%
4	*i*-Pr	Bn	CH_2NMe_2	**16d**, 87%
5	Ph	Bn	Ph	**16e**, 95%
6	Ph	Ar[d]	Ph	**16f**, 98%

[a] Clean products were obtained after acetonitrile/hexane extractions. [b] Purification by flash chromatography resulted in hydrolysis of the Si−N bond. [c] P = $SiMe_2$*t*-Bu. [d] Ar = *p*-MeC_6H_4.

A catalytic cycle that illustrates the palladium-catalyzed C−C bond formation process between a silaaziridine and an alkyne is shown in Scheme 5.[21] Oxidative addition of the weaker Si−C bond[22] of the silaaziridine would provide azapalladasilacyclobutane **17**. Migratory insertion of the alkyne into the Si−Pd bond[22] would lead to azapalladasilacyclohexene **18**. The observed regioselectivity could result from minimizations of steric interactions between the alkyne substituent and the *t*-butyl groups on the silicon. Reductive elimination from **18** would provide azasilacyclopentene **16** and regenerate the catalyst.[23]

Scheme 5. Catalytic Cycle for Alkyne Insertion of Silaaziridines



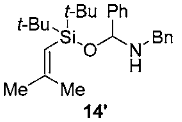
The proposed palladium-catalyzed alkyne insertion mechanism is supported by data from a control experiment. When silaaziridine **6a** was treated with a catalytic amount of

---

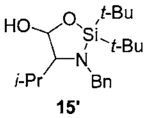
(14) Product **14** was also obtained in the absence of a silver catalyst, although the reaction was slower and low-yielding.

(15) Upon purification of **14** by flash chromatography, a significant amount of *N*,*O*-acetal hydrolysis and elimination to form **14′** were observed. Vinyl silane **14′** was isolated in 13% yield.

(16) Purification of **15** by flash chromatography gave a mixture of hydrolyzed products. Compound **15′** was isolated in 55% yield.



14'

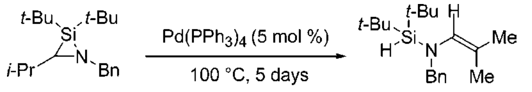


15'

(17) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* **1967**, *89*, 1827−1836.

$Pd(PPh_3)_4$, in the absence of alkyne, a slow rearrangement was observed to form silane **19** (Scheme 6). Compound **19** was characterized by ^{1}H NMR and IR spectroscopy.[24] The rearranged product **19** likely results from β-hydride elimination of intermediate **17** followed by reductive elimination.[21a,25]

Scheme 6. Palladium-Catalyzed Rearrangement



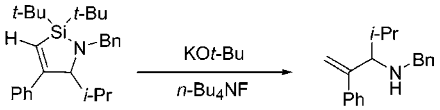
6a

19

34%, NMR

Synthetic manipulations of the vinylsilane functionality of azasilacyclopentene products **16** demonstrated the synthetic value of these intermediates. To release the allylic amines embedded in structure **16a**, the t-Bu_2Si moiety was removed by protodesilylation (Scheme 7).

Scheme 7. Synthesis of Allylic Amines



16a

20

In conclusion, silver-catalyzed silylene transfer is a general method for the synthesis of silaaziridines. These strained compounds undergo selective insertion reactions to afford ring-expanded products. The azasilacyclopentenes obtained from palladium-catalyzed alkyne insertion can be converted into allylic amines by protodesilylation of the vinyl silane moiety.

Acknowledgment. This research was supported by the National Institute of General Medical Sciences of the National Institutes of Health (GM-54909). Z.N. thanks the National Institutes of Health for a predoctoral fellowship. K.A.W. thanks Amgen and Lilly for awards to support research. We thank Dr. Phil Dennison (UCI) for assistance with NMR spectroscopy, Dr. Joseph W. Ziller (UCI) for X-ray crystallography, and Dr. John Greaves (UCI) for mass spectrometry.

Supporting Information Available: Complete experimental procedures and product characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

OL701424A

---

(18) For other transition-metal-mediated alkyne insertion reactions of strained intermediates, see: (a) Barluenga, J.; Rodríguez, F.; Álvarez-Rodrigo, L.; Zapico, J. M.; Fañanás, F. J. *Chem. Eur. J.* **2004**, *10*, 109−116. (b) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486−4494. (c) Grossman, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 2321−2322. (d) Gao, Y.; Yoshida, Y.; Sato, F. *Synlett* **1997**, 1353−1354. (e) Ohkubo, M.; Hayashi, D.; Oikawa, D.; Fukuhara, K.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **2006**, *47*, 6209−6212. (f) Seyferth, D.; Shannon, M. L.; Vick, S. C.; Lim, T. F. O. *Organometallics* **1985**, *4*, 57−62. (g) Ohshita, J.; Ishikawa, M. *J. Organomet. Chem*. **1991**, *407*, 157−165. (h) Saso, H.; Ando, W.; Ueno, K. *Tetrahedron* **1989**, *45*, 1929−1940. (i) Saso, H.; Ando, W. *Chem. Lett.* **1988**, 1567−1570.

(19) (a) Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 11276−11282. (b) Ohno, H.; Hamaguchi, H.; Tanaka, T. *Org. Lett.* **2000**, *2*, 2161−2163. (c) O'Brien, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 326−329.

(20) (a) Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689−1708. (b) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed*. **2003**, *42*, 1364−1367. (c) Miller, K. M.; Molinaro, C.; Jamison, T. F. *Tetrahedron: Asymmetry* **2003**, *14*, 3619−3625.

(21) (a) Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 1097−1099. (b) Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 4824−4827.

(22) (a) Walsh, R. In *The Chemistry of Organic Silicon Compounds*, *Part 1*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989; pp 371−391. (b) Armitage, D. A. In *The Chemistry of the Silicon-Heteroatom Bond*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1991; pp 245−439.

(23) For other metal-catalyzed reductive coupling strategies of imines and alkynes, see: (a) Black, D. A.; Arndtsen, B. A. *Org. Lett.* **2006**, *8*, 1991−1993. (b) Black, D. A.; Arndtsen, B. A. *Org. Lett*. **2004**, *6*, 1107−1110. (c) See ref. 20c.

(24) The proton chemical shift (δ 4.13 ppm) and IR band (ν = 2137 cm^{-1}) for the Si−H are similar to other aminosilanes: Gu, T.-Y. Y.; Weber, W. P. *J. Organomet. Chem.* **1980**, *184*, 7−11.

(25) A 1,3-dipolar cycloaddition between dipole **III** (Scheme 3) and an alkyne would also account for the formation of compounds **16a**−**f**. We have not, however, observed the cycloaddition under thermal conditions (120 °C).