J|A|C|S COMMUNICATIONS

Published on Web 08/15/2006

Stereoselective Synthesis of Vinylsilanes by a Gold(I)-Catalyzed Acetylenic Sila-Cope Rearrangement

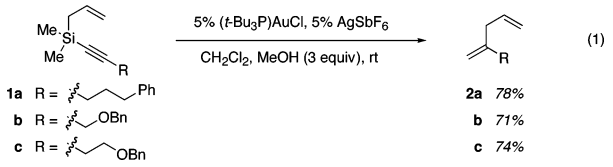
Yoshikazu Horino, Michael R. Luzung, and F. Dean Toste*

Department of Chemistry, University of California, Berkeley, California 94720

Received May 25, 2006; E-mail: fdtoste@uclink.berkeley.edu

Recent advances have dramatically increased the utility of organosilanes and silanolates as reagents for metal-catalyzed cross-coupling reactions.[1] The application of these reactions to stereoselective olefin synthesis is contingent on efficient and selective methods for the construction of vinylsilanes. Metal-mediated stereoselective addition to alkynes is commonly employed for this purpose.[2] For example, *trans*-allylsilylation[3] of alkynes and *cis*-allylmetalation of silylacetylenes[4] allow for the stereoselective construction of 1,4-dienylsilanes in which the allyl group is *trans* to silicon. On the other hand, application of allylmetalation reactions to the stereoselective synthesis of olefins substituted with the allyl group *cis* to silicon is rare.[5] The gold(I)-catalyzed rearrangement of propargyl vinyl ethers, which is hypothesized to proceed through a cyclization-induced rearrangement, was recently reported.[6] We envisioned that gold(I)-induced 6-*endo*-dig cyclization of acetylenic allylsilanes[7] would initiate a related rearrangement and provide a method for the stereoselective synthesis of *cis*-1,4-dienylsilanes.[8]

To this end, treatment of dimethylsilane **1a** with catalytic amounts of cationic tri-*tert*-butylphosphinegold(I), in the presence of 3 equiv of methanol, furnished 1,4-diene **2a** in 78% yield after 1 h at room temperature (eq 1).[9] While this reaction provided a general route to 2,2-disubstituted-1,4-dienes, it failed to afford the desired vinylsilane. We surmised that **2** was being formed through the desired rearrangement followed by rapid protodesilation of the resulting vinylsilane.

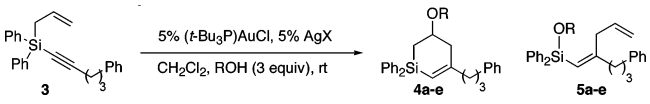


(1)

In accord with this hypothesis, gold(I)-catalyzed rearrangement of more robust diphenylsilane **3** furnished a mixture of silacycle **4a** and vinylsilane **5a** which slowly converted into 1,4-diene **2a** (Table 1, entries 1−3).[10] Changing the silver additive from $AgSbF_6$ to $AgBF_4$ resulted in improved selectivity for the formation of silacycle **4a** without deterioration of reaction efficiency (entry 4). While changing the sterics of the alcohol did not divert the reaction pathway from silacycle formation (entries 5−7), the use of phenol as a nucleophile completely reversed the selectivity in favor of vinylsilane **5e** (entry 8).

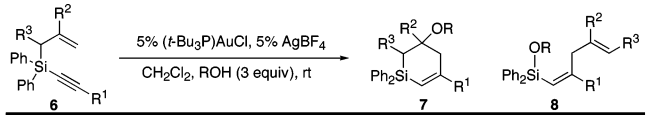
With these conditions in hand, the substrate scope of the gold(I)-catalyzed rearrangements was probed (Table 2). We were pleased to find that substitution at the acetylenic position (R^1) of allylsilane **6** was well tolerated and that the selectivity for cyclic and acyclic products is generally retained. For example, the gold(I)-catalyzed reaction of propargyl alcohol **6f** produced silacycle **7k** in 76% yield in the presence of 3 equiv of methanol (entry 11). When the nucleophile was changed to phenol, the reaction course was completely diverted to generate vinylsilane **8l** in 68% yield (entry 12). Notably, rearrangement of 1,5-enyne **6g** resulted in exclusive

Table 1. Catalyst Optimization



entry	AgX	time	R	4	5	2a
1	$AgSbF_6$	20 min	Me (**a**)	52%	48%	trace
2		30 min		35%	45%	3%
3		2 h		0%	0%	78%
4	$AgBF_4$	50 min		78%	12%	
5		1 h	Bn (**b**)	91%	0%	
6		12 h	*i*-Pr (**c**)	84%	trace	
7		12 h	*t*-Bu (**d**)	44%	0%	
8		12 h	Ph (**e**)	trace	77%	

Table 2. Scope of Gold(I)-Catalyzed Sila-Cope Rearrangement[a]



entry	R^1	R^2	R^3	ROH	7[b]	8[b]
1	H	H	H (**6a**)	MeOH	78%(**7a**)	<5%(**8a**)
2				PhOH	0%(**7b**)	99%(**8b**)[c]
3	*n*-C_4H_9	H	H (**6b**)	MeOH	82%(**7c**)	16%(**8c**)
4				PhOH	0%(**7d**)	50%(**8d**)
5[f]	CH_2OBn	H	H (**6c**)	MeOH	74%(**7e**)	5%(**8e**)
6				PhOH	9%(**7f**)	72%(**8f**)
7[f]	$(CH_2)_2OBn$	H	H (**6d**)	MeOH	81%(**7g**)	12%(**8g**)
8				PhOH	0%(**7h**)	79%(**8h**)
9	*c*-C_6H_{11}	H	H (**6e**)	MeOH	82%(**7i**)	0%(**8i**)
10[f]				PhOH	0%(**7j**)	75%(**8j**)
11		H	H (**6f**)	MeOH	76%(**7k**)[d]	0%(**8k**)
12				PhOH	0%(**7l**)	68%(**8l**)
13		H	H (**6g**)	MeOH	68%(**7m**)[d]	0%(**8m**)
14[f]				PhOH	0%(**7n**)	69%(**8n**)
15	CO_2Me	Me	H (**6h**)	MeOH	75%(**7o**)	0%(**8o**)
16[f]				PhOH	0%(**7p**)	46%(**8p**)
17	Ph	Me	H (**6i**)	MeOH	33%(**7q**)	64%(**8q**)
18[f]				PhOH	0%(**7r**)	56%(**8r**)[c]
19		Me	H (**6j**)	MeOH	39%(**7s**)	27%(**8s**)
20				PhOH	0%(**7t**)	76%(**8t**)
21	$(CH_2)_3Ph$	H	Me (**6k**)	MeOH	0%(**7u**)	66%(**8u**)[e]

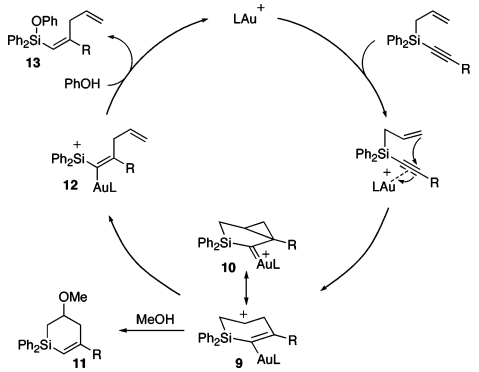
[a] Reaction conditions: 0.2 M **6** in CH_2Cl_2, rt. [b] Isolated yield after chromatography. [c] 7−8:1 mixture of olefin isomers. [d] 1:1 mixture of diastereomers. [e] 2:1 mixture of crotyl olefin isomers. [f] Run at 50 °C.

formation of desired adducts without significant competing enyne cycloisomerization (entries 13 and 14).[11,15c]

Substitution on the allyl moiety is also tolerated but has consequences on the product distribution. For example, C2-substituted allylsilane **6h** underwent the gold(I)-catalyzed cyclization onto an alkynoate to afford silacycle **7o** in 75% yield (entry 15) and vinylsilane **8p** in 46% yield (entry 16) in the presence of methanol and phenol, respectively. It is noteworthy that, in contrast to typical β-addition of nucleophiles to alkynoates,[8c] in this reaction, allylsilane regioselectively adds to the α-position. On the other hand, substituted allylsilanes **6i** and **6j** underwent addition of methanol to provide mixtures of cyclic and acyclic products (entries 17 and 19); however, the gold(I)-catalyzed reaction of phenol with **6i** and **6j** afforded vinylsilanes **8r**[12] and **8t**, respectively (entries 18 and 20). Furthermore, gold(I)-catalyzed rearrangement of an allylsilane (**6k**) that is substituted adjacent to the silicon produced vinylsilane

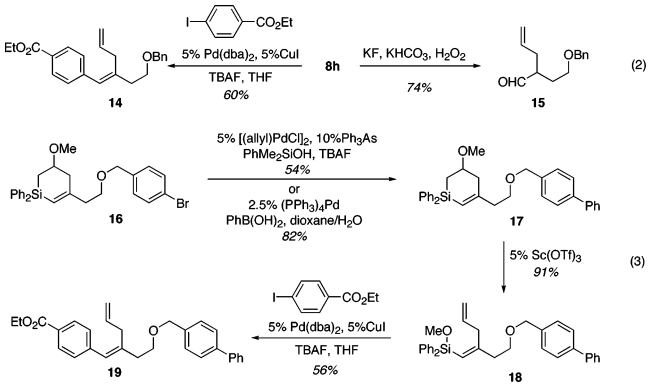
10.1021/ja0636800 CCC: $33.50

Scheme 1. Proposed Mechanism of Au(I)-Catalyzed Rearrangement



product **8u** even when methanol was employed as a nucleophile (entry 21).

A proposed mechanism involving S_E2' addition of the allylsilane onto a gold(I)-complexed alkyne to generate a gold-stabilized cation is outlined in Scheme 1.[13] While β-silyl fragmentation is generally faster than trapping of the cation,[14] stabilization of **9** by back-bonding from gold(I) (i.e., resonance structure **10**)[15] allows for methanol addition to afford cyclic silane **11**. On the other hand, when the relative rate of nucleophilic trapping is decreased, selective trapping occurs at silyl cation **12** to afford vinylsilane **13**. Presumably, this is the case when the less nucleophilic phenol is used and when addition to the cation is sterically encumbered (Table 2, entries 17 and 19). Furthermore, an increase in the relative rate of β-silyl fragmentation as a result of the steric clash of the methyl group and the silicon substituents accounts for the observation that α-substituted allylsilane **6k** affords only vinylsilane **8u** (Table 2, entry 21).



The products of the gold(I)-catalyzed acetylenic sila-Cope rearrangement serve as useful reagents in a number of transformations. For example, palladium-catalyzed cross-coupling[1] of vinylsilane **8h** with ethyl 4-iodobenzoate produced trisubstituted olefin **14** in 60% yield (eq 2). Moreover, α-allylated aldehyde **15** was prepared through a Tamao oxidation[16] of **8h**. Additionally, the silacycles can be viewed as latent vinylsilanes that can be revealed on treatment with a mild Lewis acid. This allowed for chemoselective cross-coupling reactions of arylbromide **16** to be performed, while the vinyl silane remained protected as the silacycle (eq 3). Reaction of **17** with 5 mol % of $Sc(OTf)_3$ generated vinylsilane **18**, which was subjected to a second cross-coupling reaction to afford trisubstituted olefin **19**.

In conclusion, a cationic gold(I) complex has been developed as a catalyst for the first transition-metal-catalyzed acetylenic sila-Cope rearrangement.[17] The reaction allows for the stereoselective synthesis of vinylsilanes substituted with a wide range of functional groups. Furthermore, depending on the choice of nucleophile, either cyclic or acyclic vinylsilanes were produced. Both of these reagents can be employed for stereoselective synthesis of trisubstituted[18] olefins through transition-metal-catalyzed cross-coupling reactions.

Acknowledgment. We gratefully acknowledge the University of California, Berkeley, NIHGMS (R01 GM073932-01), Merck Research Laboratories, Bristol-Myers Squibb, Amgen Inc., DuPont, GlaxoSmith-Kline, Eli Lilly & Co., Pfizer, AstraZeneca, Abbott, and Roche for financial support. Y.H. thanks JSPS for a postdoctoral fellowship.

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

References

(1) (a) Denmark, S. D.; Baird, J. D. *Chem.—Eur. J.* **2006** *12*, 4954. (b) Denmark, S. E.; Sweis, F. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; De Meijere, A., Diderich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Chapter 4. (c) Hiyama, T.; Shirakawa, E. *Top. Curr. Chem.* **2002**, *219*, 61.

(2) (a) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, *6*, 853. (b) Marek, I.; Chinkov, N.; Banon-Tenne, D. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; De Meijere, A., Diderich, F., Eds.; Wiley- VCH: Weinheim, Germany, 2004; Chapter 4. (c) Normant, J. F.; Alexakis, A. *Synthesis* **1981**, 902.

(3) For Lewis acid-mediated *trans*-allylsilylation, see: (a) Yeon, S. H.; Han, J. S.; Hong, E.; Do, Y.; Jung, I. N. *J. Organomet. Chem.* **1995**, *499*, 159. (b) Asao, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4874. (c) Yoshikawa, E.; Gevorgyan, V.; Asao, N.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6781. For a review, see: (d) Asao, N.; Yamamoto, Y. *Bull. Chem. Soc. Jpn* **2000**, *3*, 1071.

(4) (a) Yamguchi, M.; Sotokawa, T.; Hirama, M. *Chem. Commun.* **1997**, 743. (b) Klaps, E.; Schmid, W. *J. Org. Chem.* **1999**, *64*, 7537. Allylmetalation of silylacetylenes is often not stereoselective: (c) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2318. (d) Molander, G. A. *J. Org. Chem.* **1983**, *48*, 5409.

(5) For selected examples of metal-catalyzed *cis*-allylmetalation, see: (a) Okada, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1996**, *118*, 6076. (b) Shirakawa, E.; Yamasaki, K.; Yoshia, H.; Hiyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 10221. (c) Nishikawa, T.; Yorimitsu, H.; Oshima, K. *Synlett* **2004**, 1573. For a review, see: (d) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(6) (a) Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978. (b) Suhre, M. H.; Reif, M.; Kirsch, S. F. *Org. Lett.* **2005**, *7*, 3925. (c) Binder, J. T.; Kirsch, S. F. *Org. Lett.* **2006**, *8*, 2151. (d) Sherry, B. D.; Maus, L.; Lafortezza, B. N.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 8132. For a review of cyclization-induced rearrangements, see: (e) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579.

(7) For a recent report of Au(III)-catalyzed reactions of allylsilanes, see: Georgy, M.; Boucard, V.; Campagne, J.-M. *J. Am. Chem. Soc.* **2005**, *127*, 14180.

(8) (a) Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 1221. (b) Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem.* **2002**, *67*, 5197. For an *endo*-selective intramolecular *trans*-addition of allylsilanes to alkynes, see: (c) Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem.* Soc. **1998**, *120*, 5339.

(9) Under identical conditions, $(Ph_3P)AuCl$ required 10 h to afford 72% yield of **2a**. On the other hand, no reaction was observed on treatment of **1** with $AgSbF_6$, 10% $AgSbF_6$/4% PPh_3, $PtCl_2$, or $(PhCN)_2PdCl_2$.

(10) Reaction of **3** with $(Ph_3P)AuCl/AgBF_4$ gave **4a** and **5a** in 15 and 7% yield, respectively. No reaction was observed on treatment of **3** with $AgSbF_6$, $AgBF_4$, $PtCl_2$, $(PhCN)_2PdCl_2$, $(PhCN)_2PdCl_2/AgBF_4$, or CuOTf.

(11) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2005**, *45*, 200.

(12) The allyl analogue of **6i** (R^1 = Ph; R^2, R^3 = H) did not undergo the gold(I)-catalyzed reaction with methanol and gave a complex mixture with phenol at 50 °C.

(13) Deuterium labeling is consistent with protonation of a vinylgold intermediate (see Supporting Information).

(14) (a) Hollis, T. K.; Bosnich, B. *J. Am. Chem. Soc.* **1995**, *117*, 4570. (b) Kim, K.-C.; Reed, C. A.; Elliot, D. W.; Mueller, L. J.; Than, T.; Lin, L.; Lambert, J. B. *Science* **2002**, *297*, 825. (c) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857 and references therein.

(15) (a) Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402. (b) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654. (c) Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858. (d) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11807. (e) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178. (f) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260. (g) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

(16) (a) Tamao, K.; Kumada, H. *Tetrahedron Lett.* **1984**, *25*, 321. (b) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599.

(17) Slutsky, J.; Kwart, H. *J. Org. Chem.* **1973**, *38*, 3658.

(18) Reiser, O. *Angew. Chem., Int. Ed.* **2006**, *45*, 2838.

JA0636800