J|A|C|S
COMMUNICATIONS

Regio- and Chemoselective Silylmetalation of Functionalized Terminal Alkenes

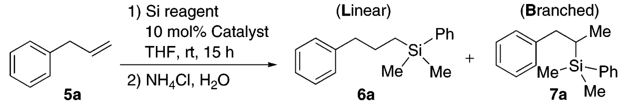
Shinji Nakamura*,† and Masanobu Uchiyama*,†,‡

Graduate School of Pharmaceutical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan, and Advanced Elements Chemistry Laboratory, Institute of Physical and Chemical Research, RIKEN, 2-1 Hirosawa, Wako-shi, Saitama 351-0198, Japan

Received September 23, 2006; E-mail: uchiyama@mol.f.u-tokyo.ac.jp

Organosilanes are versatile compounds in both synthetic and materials chemistry.[1] Though hydrosilylation of carbon−carbon multiple bonds such as alkynes, dienes, allenes, and alkenes is one of the most powerful methods for the preparation of organosilanes,[2] the nature of the group which can be introduced into these multiple bonds along with the silyl group is limited to a hydrogen atom. On the other hand, silylmetalation can simultaneously introduce both a silyl group and a metal that can be transformed into various functional groups, so it should be advantageous for synthesizing (multi)functionalized organosilanes. However, only limited success, such as bissilylation,[3] silylstannylation,[4] and silylboration[5] has been reported in silylmetalation to give alkylsilanes from alkenes. We present here a new and chemoselective silylmetalation of monosubstituted alkenes in the presence of a catalytic amount of copper salt.[6−8] We also show that the resultant alkylmetals can act as potent nucleophiles, making it possible to construct α-substituted alkylsilanes that could be converted smoothly into the corresponding alcohols.

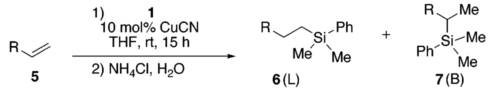
Table 1. Screening of Catalysts Using Allylbenzene (**5a**)[a]

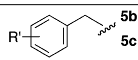


Entry	Catalyst	Si reagent	Yield (%)[b]	L/B	Entry	Catalyst	Si reagent	Yield (%)[b]	L/B
1	none	**1**	37	90/10	6	$Cu(OAc)_2$	**1**	80	76/24
2	CuI	**1**	73	89/11	7	$Cu(OTf)_2$	**1**	67	82/18
3	CuCN	$Me_2PhSiLi$	<24[c]	0/100	8	AgOTf	**1**	2	86/14
4	CuCN	**1**	82	83/17	9	none	**3**	<14[c]	0/100
5	$(CuOTf)_2$tol	**1**	86	82/18	10	none	**4**	32	81/19

[a] The silylation was carried out using Si reagent (1.1 equiv), allylbenzene (**5a**) (1.0 equiv) and catalyst (10 mol %) in THF at room temperature for 15 h. [b] Isolated yield. [c] Several minor products that were difficult to separate were observed but not identified.

Table 2. Silylation of Various Functionalized Terminal Alkenes[a]



Entry	R		Yield (%)	L/B	Entry	R		Yield (%)	L/B
1		**5b**: R' = 2-OMe	81	90/10	8	$^tBuS(CH_2)_3$	**5i**	76	79/21
2		**5c**: R' = 4-OMe	97	86/14	9	$PhCH_2NHC(O)(CH_2)_3$	**5j**	77	92/8
3		**5d**: R' = 3,4-OMe	88	84/16	10	$MeC(O)O(CH_2)_4$	**5k**	80	83/17
4	$Ph(CH_2)_2$	**5e**	85	81/19	11	$Me_2NC(O)O(CH_2)_3$	**5l**	90	82/18
5	$Cl(CH_2)_4$	**5f**	73	84/16	12	$EtOC(O)O(CH_2)_3$	**5m**	94	78/22
6	$TBSO(CH_2)_4$	**5g**	85	87/13	13	$NC(CH_2)_2$	**5n**	85	>99/1
7	$PhCH_2O(CH_2)_2$	**5h**	66	86/14	14	$Ph_2P(O)CH_2$	**5o**	79	>99/1

[a] The silylmetalation was carried out using **1** (1.1 equiv), substrate (1.0 equiv) and CuCN (10 mol %) in THF at room temperature for 15 h.

We have already reported that the bulky zincate having one dimethylphenylsilyl (DMPS) group (DMPS)Zn^{t}Bu$(OR)_2$(MM′) (**1**) ($(OR)_2$ = 2,2′-biphenoxo, M = Li or MgCl, M′ = MgCl, abbreviated as SiBNOL-Zn-ate) can promote chemo- and regioselective silylzincation to terminal alkynes to give branched vinylsilanes.[9] However, simple applications of this protocol to terminal alkenes by using **1** proved unsuccessful because of low reactivity of the isolated C−C double bond (e.g., Table 1 entry 1). After extensive experimentation, we unexpectedly found that the combination of a catalytic amount of Cp_2TiCl_2 and the zincate having two DMPS groups $(DMPS)_2Zn(OR)_2(MM')$ (**2**) ($(OR)_2$ = 2,2′-biphenoxo, M = Li or MgCl, M′ = MgCl) promotes the silylmetalation of monosubstituted alkenes and the ready *β*-hydride elimination of the intermediary alkylmetals to give *γ*-substituted allylsilanes.[10] However, attempts at electrophilic trapping of the intermediary alkylmetals failed owing to the instability of the intermediate. Thus, we focused on screening of other catalysts for the addition of the zinc silyl complex to functionalized olefins, and we obtained some interesting results (Table 1): (1) Both Cu(I)/(II) salts catalyze the silylmetalation and the resultant zincate can be trapped by NH_4Cl (H^+). In contrast, Ag(I)OTf, containing a group 11 element like Cu, did not catalyze this transformation. On the basis of low cost, ready availability, and stability we chose CuCN as the best catalyst. (2) Reaction using an equimolar amount of cuprates such as $(DMPS)_2Cu(CN)Li_2$ (**3**) and (DMPS)Cu^{t}Bu(CN)-Li(MgCl) (**4**) in the absence of Zn(II) gave poor results. (3) The presence of Mg salts in the reaction mixture is essential for this silylmetalation. In the absence of Mg salts, the reactions became complicated and the yields became poor, though the regioselectivities were excellent. Addition of some Mg salts, such as $MgBr_2 \cdot OEt_2$, was also effective. It is noteworthy that though we routinely used 10 mol % of CuCN, as little as 0.66 mol % was sufficient. It is also important that unless otherwise noted, all reactions were conducted with only an equimolar amount of alkenes and zinc silyl complexes. Excess silyl reagents are required in most hydrosilylation and some silylmetalation reactions, and this often leads to synthetic problems.

Representative results of silylmetalation of various terminal alkenes by **1** are summarized in Table 2. Both allylbenzene derivatives and 4-phenyl-1-butene can be used in this reaction, and the yields and selectivities are comparable to those of **5a**. A substrate having a chloro group, which is a good leaving group, is also available. Furthermore, substrates that contain coordinative groups such as silyl and benzyl ether and thioether also cause no problems. A variety of electrophilic functional groups including amide, ester, carbamate, carbonate, nitrile, and phosphine oxide are also tolerated in the reaction.

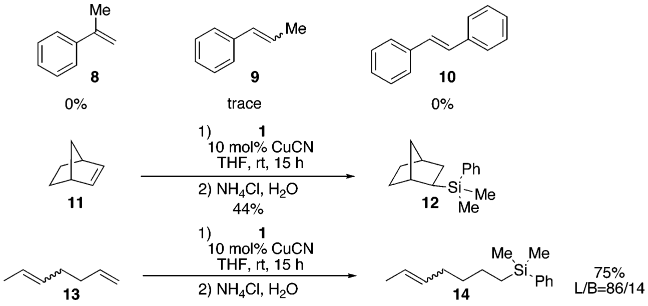
Two important conclusions regarding the regioselectivity of this silylmetalation can be drawn from these data. First, the silylation occurs regioselectively with monosubstituted alkenes at the terminal carbon atom. Second, coordinative functional groups have a little effect on the regioselectivity. Only when strongly coordinative

---

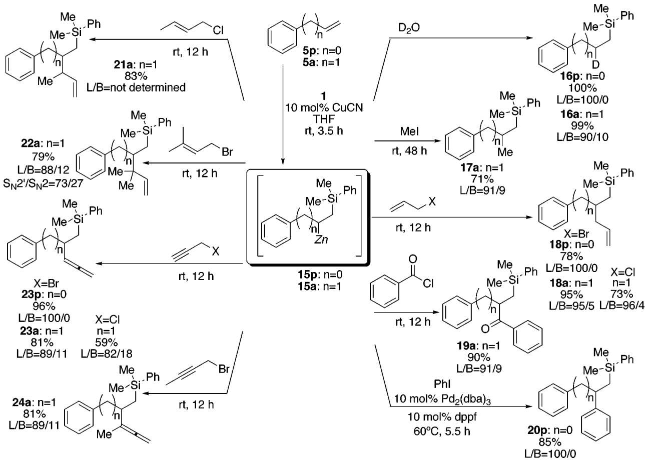
[†] The University of Tokyo.
[‡] RIKEN.

10.1021/ja066864n CCC: $37.00

Scheme 1. Reactivity and Selectivity of the Present Silylation



Scheme 2. Electrophilic Trapping of the Intermediary Species[a]



[a] The silylmetalation was carried out using **1** (1.1 equiv), substrate (**5a**, **5p**) (1.0 equiv), CuCN (10 mol %), and electrophiles (1.5 equiv).

groups such as cyano or phosphine oxide exist at a suitable position does the silylation occur practically regiospecifically at the terminal carbon atom.

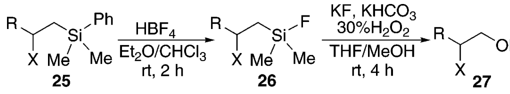
To investigate the scope of substitution patterns of this silylmetalation, the reactions with 1,1-/1,2-disubstituted alkenes were next examined (Scheme 1). The functional group specificity of this reaction is very high, and α-/β-methyl styrene (**8**, **9**) and *trans*-stilbene (**10**), which are among the most reactive disubstituted alkenes, did not react. However, it is noteworthy that norbornene (**11**), whose double bond is disubstituted, distorted, and hence reactive, was silylated in moderate yield. In the competitive reaction of terminal and internal alkenes in 1,5-heptadiene (**13**), silylmetalation at the terminal alkene proceeded with more than 99% selectivity.

We then demonstrated, as shown in Scheme 2, that the resultant alkylmetal intermediates can be utilized as a carbanion equivalent. Namely, the intermediates **15a** and **15p**, generated by the silylmetalation of **5a** and **5p**, respectively, were treated with D_2O, MeI, allyl halide, or benzoyl chloride to give the corresponding functionalized alkanes in satisfactory yields. The intermediate **15p** also undergoes Pd-catalyzed C−C bond-forming reactions in high yield and with high regioselectivity. We have also confirmed that the intermediates react with crotyl chloride, propargyl halide, or their derivatives in a high S_N2' manner.

Finally, the potential to generate α-substituted and functionalized alkylsilanes was examined (Table 3). The fact that alkylsilanes are alcohol equivalents is well-known[11] and we have verified that the resultant functionalized silanes could also be transformed into the desired multifunctionalized alcohols.

In conclusion, we have developed a new method for the chemoselective silylmetalation reaction of functionalized terminal alkenes, utilizing a catalyst system comprising catalytic Cu salt and a dianion-type Zn(II) ate complex (SiBNOL-Zn-ate). The method provides a simple and direct route for the regio-controlled synthesis of α-substituted alkylsilanes and alcohols from various terminal alkenes. Efforts to expand the scope of the reaction and to elucidate the reaction pathway with the help of theoretical and spectroscopic studies are in progress in our laboratory.

Table 3. Oxidation of the Resultant Functionalized Silylalkanes



Entry	R	X	Yield (%)	L/B
1	Ph	D	80	100/0
2	$PhCH_2$	D	74	88/12
3	$BnNHC(O)(CH_2)_3$	H	98	92/8
4	$Ph_2P(O)CH_2$	H	74	>99/1
5	$Me_2NC(O)O(CH_2)_3$	H	64	84/16

Acknowledgment. We thank the JSPS Research Fellowship for Young Scientists (to S.N.). We also thank Prof. T. Ohwada (The University of Tokyo) for his valuable comments.

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

References

(1) For recent reviews: (a) Nicole, L.; Boissier, C.; Grosso, D.; Quach. A.; Sanchez. C. *J. Mater. Chem.* **2005**, *15*, 2598. (b) Hosomi, A.; Miura, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 835.

(2) For reviews: (a) Barnea, E.; Eisen, M. S. *Chem. Rev.* **2006**, *250*, 855. (b) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, *6*, 853. (c) Brunner, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 2749. (d) Ojima, I.; Li, Z.; Zhu, J. *Chem. Org. Silicon Compd.* **1998**, *2*, 1687.

(3) For alkenes. (a) Beletskaya, I.; Moberg, C. *Chem. Rev.* **2006**, *106*, 2320. (b) Suginome, M.; Iwanami, T.; Ohnori, Y.; Yamamoto, A.; Ito, Y. *Chem.—Eur. J.* **2005**, *11*, 2954. (c) Pohlmann, T.; de Meijere, A. *Org. Lett.* **2000**, *2*, 3877. (d) Delpech, F.; Mansas, J.; Leuser, H.; Sabo-Etienne, S.; Chaudret, B. *Organometallics* **2000**, *19*, 5750. (e) Hayashi, T.; Kobayashi, T.; Kawamoto, A. M.; Yamashita, H.; Tanaka, M. *Organometallics* **1990**, *9*, 280.

(4) For alkenes. (a) Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2002**, *124*, 1566. (b) Watanabe, H.; Saito, M.; Sutou, N.; Obora, Y.; Tsuji, Y.; Asayama, M.; Kawamura, T. *Organometallics* **1993**, *12*, 4697. See also ref 3a.

(5) For alkenes. (a) Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *680*, 43. (b) Suginome, M.; Nakamura, H.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2516. See also ref 3a.

(6) For recent examples on silylcupration: (a) Barbero, A.; Blanco, Y.; Pulido, F. *J. Org. Chem.* **2005**, *70*, 6876. (b) Barbero. A.; Pulido F. *Acc. Chem. Res.* **2004**, *37*, 817 and references therein. See also: (c) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

(7) For recent examples on copper-catalyzed silylzincation: (a) Auer, G.; Oestreich, M. *Chem. Commun.* **2006**, 311. (b) Wakamatsu, K.; Nonaka, T.; Okuda, Y.; Tückmantel, W.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1986**, *42*, 4427. (d) Okuda, Y.; Wakamatsu, K.; Tückmantel, W.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 4629.

(8) Though silylcupration and silylzincation of reactive substrates including terminal alkynes, allenes, and 1,3-dienes have been thoroughly investigated and are well known for their versatility in the preparation of multisubstituted vinylsilanes and allylsilanes, reactions of alkenes, which are considered as unreactive substrates, remain unexplored. Very limited but pioneering work on silylcupration of styrene, a reactive alkene, has been reported by Bäckvall et al. Liepins, V.; Bäckvall, J.-E. *Chem. Commun.* **2001**, *3*, 265. Copper-catalyzed silylzincation of styrene has also been reported by Oestreich et al. See ref 7*a*.

(9) Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2004**, *126*, 11146.

(10) (a) Nakamura, S.; Uchiyama, M.; Ohwada, T. *J. Am. Chem. Soc.* **2005**, *127*, 13116. See also: (b) Uchiyama, M.; Furuyama, T.; Kobayashi, M.; Matsumoto, Y.; Tanaka, K. *J. Am. Chem. Soc.* **2006**, *128*, 8404. (c) Kobayashi, M.; Matsumoto, Y.; Uchiyama, M.; Ohwada, T. *Macromolecules* **2004**, *37*, 4339. (d) Uchiyama, M.; Nakamura, S.; Ohwada, T.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 10897.

(11) (a) Fleming, I.; Henning, R.; Parker, D. C.; Plaut, H. E.; Sanderson, E. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317. (b) Tamao, K.; Ishida, N.; Ito, Y.; Kumada, M. *Org. Synth.* **1993**, *8*, 315; **1990**, *69*, 96 and references therein.

JA066864N