ORGANIC
LETTERS

2003
Vol. 5, No. 19
3479−3481

Titanocene-Catalyzed Regioselective *syn*-Hydrosilation of Alkynes

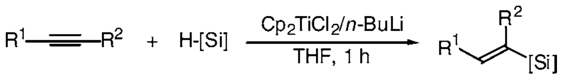
Tamotsu Takahashi,* Fengyu Bao, Guohua Gao, and Masamichi Ogasawara

*Catalysis Research Center and Graduate School of Pharmaceutical Sciences,
Hokkaido University, and CREST, Science and Technology Corporation (JST),
Kita-ku, Sapporo 060-0811, Japan*

tamotsu@cat.hokudai.ac.jp

Received July 11, 2003

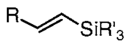
ABSTRACT



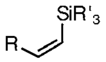
The titanium catalyst, which was generated in situ from titanocene dichloride and 2 equiv of butyllithium, was found to catalyze hydrosilation of a variety of alkynes with excellent regio- and *syn*-selectivity.

Alkenylsilanes have been used as important building blocks in organic synthesis. In addition to classical organic transformation of alkenylsilanes,[1] novel applications of these compounds to transition metal catalyzed reactions have been developed recently[2,3] that have enhanced synthetic usefulness of alkenylsilanes.

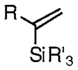
However, the utility of alkenylsilanes has been somewhat reduced by a lack of regio- and stereoselective synthetic methods of these compounds. Among the synthetic methods of alkenylsilanes, hydrosilation of alkynes is one of the most straightforward methods and the most attractive one from an atom-economical point of view.[4] Late transition metal catalysts of Pt, Pd, Rh, etc. have been frequently used for hydrosilation of alkynes; however, the late-transition metal catalyzed reactions have encountered difficulty in controlling stereochemistry of alkenylsilane products.[4] For instance, hydrosilation of terminal alkyne RC≡CH often afforded a mixture of three isomers **I**−**III** and complete control of stereochemistry in the hydrosilation of alkynes remains to be resolved.



I



II



III

In this paper, we wish to report highly regioselective *syn*-hydrosilation of alkynes catalyzed by titanocene species. Although titanocene derivatives have been utilized for hydrosilation of olefins,[5] ketones,[6] imines,[7] and pyridines,[8] to the best of our knowledge, this is the first example of the alkyne hydrosilation catalyzed by a group 4 metal catalyst except Lewis acid-catalyzed *trans*-hydrosilation of alkynes using MCl_4 (M = Ti, Zr, and Hf).[9] This paper also represents a rare example of hydrosilation of alkynes using early transition metal catalysts.[10]

---

(1) (a) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, 1981; p 44. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer: Berlin, 1983; p 79. (c) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic: London, 1988; p 7.

(2) For application of alkenylsilanes to palladium-catalyzed cross-coupling reactions, see: (a) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845. (b) Hiyama, T. Organosilicon Compounds in Cross-Coupling Reactions. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P., Eds.; Wiley-VCH: Weinheim, 1998.

(3) For application of alkenylsilanes to rhodium-catalyzed nucleophilic addition reactions, see: (a) Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 295. (b) Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 298. (c) Oi, S.; Honma, Y.; Inoue, Y. *Org. Lett.* **2002**, *4*, 667. (d) Oi, S.; Taira, A.; Honma, Y.; Inoue, Y. *Org. Lett.* **2003**, *5*, 97.

(4) (a) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley: Chichester, 1989; p 1479. (b) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, p 763. (c) Marciniec, B. *Comprehensive Handbook on Hydrosilylation*; Pergamon Press: Oxford, 1992; p 130.

(5) (a) Harrod, J. F.; Yun, S. S. *Organometallics* **1987**, *6*, 1381. (b) Kesti, M. R.; Abdulrahman, M.; Waymouth, R. M. *J. Organomet. Chem.* **1991**, *417*, C12. (c) Corey, J. Y.; Zhu, X.-H. *Organometallics* **1992**, *11*, 672. (d) Kesti, M. R.; Waymouth, R. M. *Organometallics* **1992**, *11*, 1095.

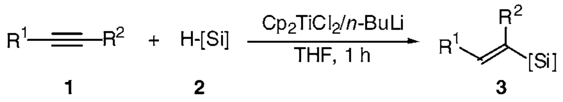
(6) Halterman, R. L.; Ramsey, T. M.; Chen, Z. *J. Org. Chem.* **1994**, *59*, 2642.

(7) (a) Verdaguer, X.; Lange, U. E. W.; Reding, M. T.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 6784. (b) Tillack, A.; Lefeber, C.; Peulecke, N.; Thomas, D.; Rosenthal, U. *Tetrahedron Lett.* **1997**, *38*, 1533.

(8) Hao, L.; Harrod, J. F.; Lebuis, A.-M.; Mu, Y.; Shu, R.; Samuel, E. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 3126.

10.1021/ol035277t CCC: $25.00

Scheme 1



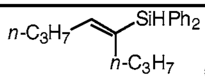
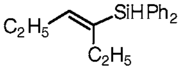
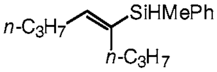
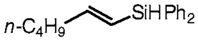
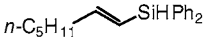
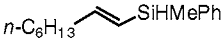
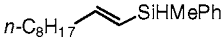
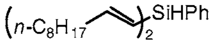
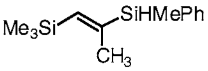
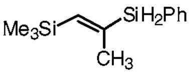
1a: $R^1 = R^2 = n\text{-}C_3H_7$
1b: $R^1 = R^2 = Et$
1c: $R^1 = n\text{-}C_4H_9$, $R^2 = H$
1d: $R^1 = n\text{-}C_5H_{11}$, $R^2 = H$
1e: $R^1 = n\text{-}C_6H_{13}$, $R^2 = H$
1f: $R^1 = n\text{-}C_8H_{17}$, $R^2 = H$
1g: $R^1 = SiMe_3$, $R^2 = Me$

2a: [Si] = $SiHPh_2$
2b: [Si] = SiHMePh
2c: [Si] = SiH_2Ph

It was found that hydrosilation of alkynes was efficiently catalyzed by a titanium species, which was generated in situ from titanocene dichloride and 2 equiv of butyllithium (Scheme 1). Generally, reactions proceeded smoothly at room temperature. A representative procedure for the Ti-catalyzed hydrosilation of alkyne is as follows. To a solution of Cp_2TiCl_2 (50.0 mg, 0.200 mmol) in THF (5 mL) was added *n*-BuLi hexane solution (1.60 mol/L, 0.25 mL, 0.40 mmol) at −78 °C. After the solution was stirred for 1 h at this temperature, 4-octyne (**1a**; 110 mg, 1.00 mmol) and diphenylsilane (**2a**; 203 mg, 1.10 mmol) were added subsequently by means of syringe. The reaction mixture was warmed to room temperature and stirred for 1 h. After aqueous workup, GC analysis of the reaction mixture showed formation of 4-(diphenylsilyl)-4-hexene **3a** in 87% yield (Table 1, entry 1).

The geometry of **3a** was determined to be (*E*) by comparison of the ^1H and ^{13}C NMR spectra with those reported previously.[11] No formation of the corresponding (*Z*)-isomer was detected by NMR and GC analysis. The (*E*)-geometry in **3a** indicates that the reaction proceeded through a *syn*-addition of the hydrosilane to the carbon−carbon triple bond in **1a**. Analogous highly selective *syn*-addition was also observed for the reaction of **1b** and **2a** (entry 2). With hydrosilane **2b**, the reaction proceeded as well giving an (*E*)-product **3c** exclusively (entry 3).

Table 1. Titanium-Catalyzed Hydrosilation of Alkynes[a]

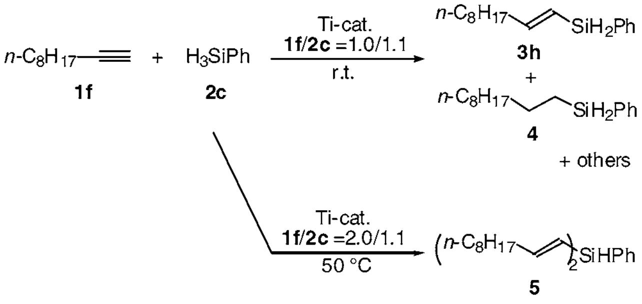
entry	alkyne	hydrosilane	alkenylsilane	yield (%)[b]
1	**1a**	**2a**	 **(3a)**	87 (70)
2	**1b**	**2a**	 **(3b)**	96 (67)
3	**1a**	**2b**	 **(3c)**	97 (66)
4	**1c**	**2a**	 **(3d)**	78 (59)
5	**1d**	**2a**	 **(3e)**	72 (58)
6	**1e**	**2b**	 **(3f)**	82 (63)
7	**1f**	**2b**	 **(3g)**	92 (67)
8[c]	**1f**	**2c**	 **(5)**	52 (31)
9	**1g**	**2b**	 **(3i)**	82 (54)
10	**1g**	**2c**	 **(3j)**	68 (44)

[a] The reaction was carried out with **1** (1.0 mmol) and **2** (1.1 mmol) in THF at room temperature in the presence of titanocene catalyst (20 mol % to **1**) generated in situ from Cp_2TiCl_2 and *n*-BuLi (2 equiv to Cp_2TiCl_2) unless otherwise noted. [b] GC yields. Isolated yields are given in parentheses. [c] At 50 °C with **2c** (0.55 mmol).

The titanium-catalyzed hydrosilation could be applied to terminal alkyne substrates. A reaction of 1-hexyne (**1c**) and **2a** in the presence of 20 mol % of the titanocene catalyst afforded an alkenylsilane **3d** in 78% yield (entry 4). The ^1H and ^{13}C NMR analysis of the product revealed that **3d** consisted of a single isomer. A mode of the addition reaction was found to be 2-hydro-1-silation, and the large coupling constant between the two olefinic hydrogens in **3d** ($^3J_{HH}$ = 18.3 Hz) indicates the product being an (*E*)-isomer. The titanocene-catalyzed hydrosilation is highly stereoselective in the reactions of other terminal alkynes **1d**−**f** as well (entries 5−7). All the products were 1-silylalkenes of (*E*)-isomers exclusively, and no other regio- or geometrical isomers were detected.

When a reaction was carried out using sterically compact phenylsilane **2c** at room temperature, a product was obtained as a complex mixture, which contained a single-hydrosilation product **3h** (15% GC yield), a hydrogenated product **4** (18% GC yield), and other uncharacterized products (Scheme 2). However, a double-hydrosilation product **5** was prepared in

Scheme 2



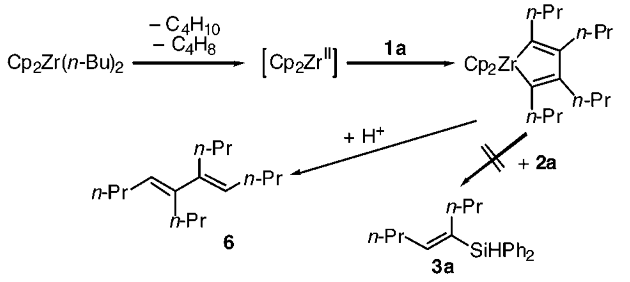
---

[9] (a) Asao, N.; Sudo, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 7654. (b) Sudo, T.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2494. (c) Sudo, T.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **2000**, *65*, 8919.

[10] (a) Molander, G. A.; Retsch, W. H. *Organometallics* **1995**, *14*, 4570. (b) Schumann, H.; Keitsch, M. R.; Winterfeld, J.; Muhle, S.; Molander, G. A. *J. Organomet. Chem.* **1998**, *559*, 181. (c) Dash, A. K.; Wang, J. Q.; Eisen, M. S. *Organometallics* **1999**, *18*, 4724. (d) Dash, A. K.; Wang, J. X.; Berthet, J. C.; Ephritikhine, M.; Eisen, M. S. *J. Organomet. Chem.* **2000**, *604*, 83. (e) Dash, A. K.; Gourevich, I.; Wang, J. Q.; Wang, J.; Kapon, M.; Eisen, M. S. *Organometallics* **2001**, *20*, 5084.

[11] (a) Tillack, A.; Pulst, S.; Baumann, W.; Baudisch, H.; Kortus, K.; Rosenthal, U. *J. Organomet. Chem.* **1997**, *532*, 117. (b) Lee, S. J.; Park, M. K.; Han, B. H. *Silicon Chem.* **2002**, *1*, 41.

Scheme 3

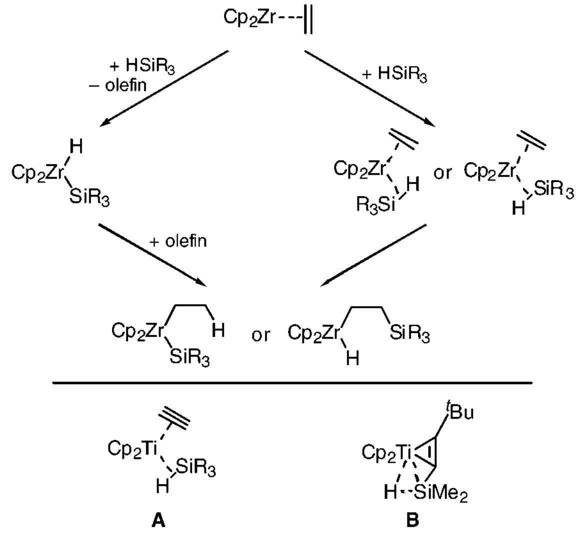


moderate yield (52%) at higher temperature (50 °C) with a molar ratio of **1f**/**2c** = 2.0/1.1 (Table 1, entry 8). Each step of the hydrosilation reactions giving **5** also took place in a stereoselective manner, and thus **5** was obtained as a single isomer. Analogous double-hydrosilation was not observed with the disubstituted dihydrosilanes **2a** or **2b**, and no triple-hydrosilation was detected with **2c**.

The highly regio- and *syn*-selective hydrosilation could be realized for a certain unsymmetrically substituted internal alkyne. The titanocene-catalyzed reaction of 1-(trimethylsilyl)propyne (**1g**) with **2b** gave an 1,2-disilyl olefin **3i** of (*E*)-geometry in 82% yield as a sole hydrosilation product (Table 1, entry 9). With this internal alkyne **1g**, the monophenyltrihydrosilane **2c** reacted cleanly to give a single-hydrosilation product **3j** in 68% yield (entry 10).

The present catalytic hydrosilation of alkynes is characteristic to titanocene species among group 4 metals. Zirconocene and hafnocene species do not catalyze the reactions under the analogous conditions, although zirconium and hafnium complexes have been known to catalyze hydrosilation of olefins.[5b−d,12] A transient divalent zirconocene Cp$_2$Zr^{II}, which is generated in situ by thermal decomposition of Cp$_2$Zr(n-Bu)$_2$,[13] reacts with 2 equiv of alkynes to form a stable zirconacyclopentadiene species.[13,14] The zirconacyclopentadiene is inert to hydrosilanes, and thus a catalytic cycle of alkyne hydrosilation is not operative with the zirconocene species. Indeed, aqueous workup of a reaction mixture of Cp$_2$Zr(n-Bu)$_2$, **1a**, and **2a** afforded a substituted butadiene derivative **6** with unreacted **2a**, but no **3a** was detected (Scheme 3).

Scheme 4



Two possible paths have been suggested for the zirconocene-catalyzed olefin hydrosilation (Scheme 4, top).[15] One is oxidative addition of an H−Si bond to a divalent Zr center, and the other is via a zirconium−olefin−silane complex Cp$_2$Zr(η^2-olefin)(η^2-H-SiR$_3$). It is reasonable to assume that the present titanocene-catalyzed hydrosilation of alkynes also proceeds through a reaction mechanism similar to either of the two. Recently, Rosenthal and coworkers reported a *trans*-η^2-alkyne complex of titanocene (**B**) in which strong (η^2-Si-H)−Ti agostic interaction was evident.[16] Although we have no evidence supporting either of the two (or other) possible reaction paths, Rosenthal's complex could be regarded as a stabilized intermediate of the latter reaction path (**A**).

In summary, we have developed a novel catalytic hydrosilation reaction of alkynes using the titanocene derivative as a catalyst. The reaction proceeded with excellent regioselectivity, and *syn*-addition products were obtained exclusively for a variety of substrates.

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

OL035277T

---

[12] Takahashi, T.; Hasegawa, M.; Suzuki, N.; Saburi, M.; Rousset, C. J.; Fanwick, P. E.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 8564.

[13] Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829.

[14] (a) Takahashi, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* **1987**, 623. (b) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788. (c) Negishi, E.; Holms, S. J.; Tour, J.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336. (d) Van Wagenen, B. C.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 3495.

[15] Ura, Y.; Hara, R.; Takahashi, T. *Chem. Lett.* **1998**, 233.

[16] (a) Ohff, A.; Kosse, P.; Baumann, W.; Tillack, A.; Kempe, R.; Görls, H.; Burlakov, V. V.; Rosenthal, U. *J. Am. Chem. Soc.* **1995**, *117*, 10399. (b) Peulecke, N.; Ohff, A.; Kosse, P.; Tillack, A.; Spannenberg, A.; Kempe, R.; Baumann, W.; Burlakov, V. V.; Rosenthal, U. *Chem. Eur. J.* **1998**, *4*, 1982. (c) Fan, M.-F.; Lin, Z. *Organometallics* **1997**, *16*, 494.