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# Selective Synthesis of Functionalized, Tertiary Silanes by Diastereoselective Rearrangement–Addition

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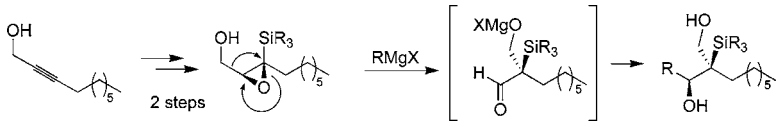
## ABSTRACT




**Treatment of hydroxy-substituted silyl epoxides with Grignard reagents induces a 1,2-carbon shift to reveal α-silyl aldehydes, which are trapped by highly diastereoselective addition reactions of the Grignard reagent. The starting epoxides are readily accessible from propargylic alcohols by regio- and diastereoselective hydrosilylation and epoxidation reactions. In addition to providing functionalized tertiary silane products, the method is shown to offer a tertiary olefin synthesis through chemo- and diastereoselective Peterson elimination of the product tertiary silane diols.**

Organosilicon compounds play an increasing role in organic synthesis, wherein the silyl group serves as a sterically demanding directing group,[1,2] as a placeholder for oxygenation though Tamao−Fleming oxidation,[3] as an organometallic species for transition-metal-catalyzed reaction,[4] or as a temporary, "traceless" tether for intramolecular reactions.[5] Additionally, allylic silanes are mild, stable nucleophiles.[2] However, in many respects, methodology for the incorporation of silicon into complex targets lags behind the utility of such products. Most traditionally, reactive organometallic species are trapped with silyl chlorides. However, this approach negates the benefits of functional-group tolerance available to organosilicon-based routes. In addition, the generation of reactive organometallics, such as Grignard reagents, may be impossible in a congested, densely functionalized target. Other important routes, such as hydrosilylation, can be robust methods for primary alkyl[6] and vinylsilanes.[6,7] However, they are not generally compatible with the synthesis of highly congested silanes.

We have examined the hydrosilylation of alkynes catalyzed by the ruthenium complex $[Cp^*Ru(MeCN)_3]PF_6$. Reactions catalyzed by this complex afford clean trans addition of a silane molecule to internal alkynes. A productive use of this method has been the hydrosilylation of propargylic alcohols, where (*Z*)-*β*-silyl allylic alcohols are formed selectively.[8] The placement of the silyl group offers the opportunity for diastereoselective epoxidation of the vinylsilane,[9] which can be further elaborated through silane oxidation (Scheme 1).

We are interested in investigating other methods for the elaboration of the silyl epoxide scaffold. Since allylic

(1) Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, 1981.

(2) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063−2192.

(3) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599−7662.

(4) (a) Oi, S.; Honma, Y.; Inoue, Y. *Org. Lett.* **2002**, *4*, 667−669. (b) Oi, S.; Taira, A.; Honma, Y.; Inoue, Y. *Org. Lett.* **2003**, *5*, 97−99. (c) Hiyama, T. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P., Eds.; Wiley-VCH: Weinheim, Germany, 1998. (d) Denmark, S. E.; Ober, M. H. *Aldrichimica Acta* **2003**, *36*, 75−85. (e) Denmark, S. E.; Sweis, R. F. *Acc. Chem. Res.* **2002**, *35*, 835−846.

(5) (a) Ishikawa, T.; Kudo, T.; Shigemori, K.; Saito, S. *J. Am. Chem. Soc.* **2000**, *122*, 7633−7637. (b) Stork, G.; Chan, T. Y.; Breault, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7578−7579. (c) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375−1408.

(6) Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 8, pp 763−792.

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(8) (a) Trost, B. M.; Ball, Z. T.; Laemmerhold, K. M. *J. Am. Chem. Soc.* **2005**, *127*, 10028−10038. (b) Trost, B. M.; Ball, Z. T.; Jöge, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 3415−3418.

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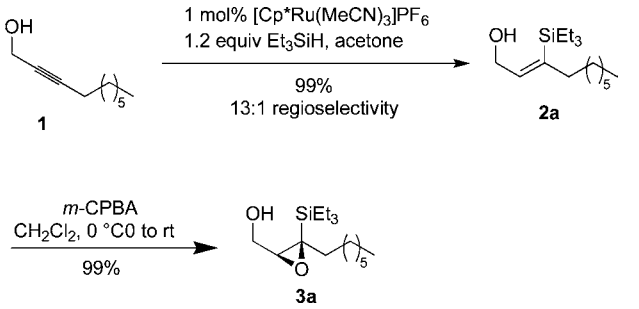
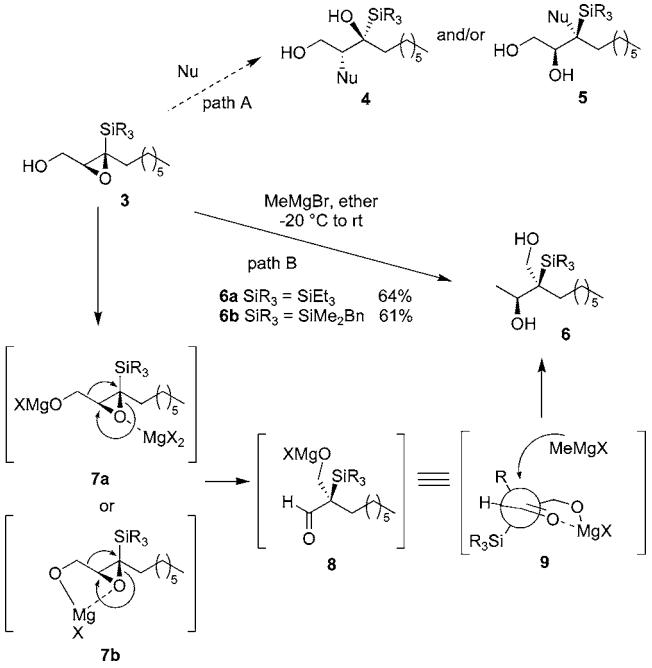
**Scheme 1.** Synthesis of Silyl Epoxides from Propargylic Alcohols




epoxides, in general, have a robust chemistry of selective ring-opening reactions,[10] we examined the possibility of selectively adding nucleophiles to silyl epoxide **3** to afford 1,2-diol **4** or 1,3-diol **5**.[11] Treatment of silyl epoxide **3** with methylmagnesium bromide and catalytic CuCN or CuI did indeed produce a diol product with incorporation of a methyl group (Scheme 2). However, instead of the expected

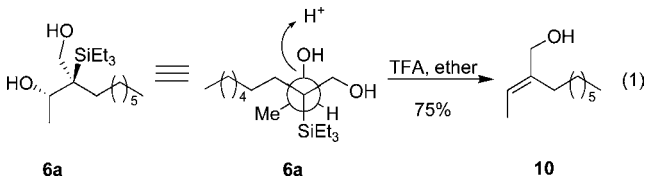
**Scheme 2.** Rearrangement−Addition of Silyl-Substituted Epoxy Alcohols with Grignard Reagents




products, we isolated the diol **6**, the product of a rearrangement process. Similar processes have been observed in all-carbon systems.[12] Presumably, the product is formed by means of an epoxide ring opening mediated by magnesium(II), wherein the 1,2-carbon shift is accelerated by the added electron density of the magnesium alkoxide. It is instructive to note that ring opening occurs at the carbon α to the silane, despite the conventional wisdom that silicon stabilizes positive charge at the $\beta$ position. Poor orbital overlap with incipient positive charge at the $\beta$ position—enforced by epoxide ring geometry—likely contributes to this result. We initially employed catalytic copper salts known to aid in epoxide ring opening, but they are not necessary for the rearrangement process and similar yields are obtained without copper salts.

Notably, the diol is formed as a single diastereomer—presumably the result of chelation-controlled addition, as shown (Scheme 2, **9**). The large size of the silyl group may play an important role in what is a surprising level of selectivity—complete diastereocontrol for a Grignard addition to an aldehyde at ambient temperature. The rearrangement also offers an in situ generation of a sensitive and synthetically challenging α-silyl aldehyde moiety.[13]

The relative stereochemistry of the product diols could be determined by acid-mediated Peterson elimination (eq 1).[14] The geometry of olefin **10**, determined by nOe studies, establishes the relative stereochemistry of the diol **6**. It is noteworthy that two $\beta$-hydroxy groups are present, which could potentially eliminate, yet under acidic conditions, only the secondary alcohol reacts, due to better carbocation stabilization in an E1 elimination mechanism.




We have explored the generality of this process. The methodology readily tolerates the use of the benzyldimethylsilyl (BDMS) group, which allows mild activation for subsequent chemistry.[8] As shown in eqs 2−6, aryl (eq 2) and alkenyl (eq 3) Grignard reagents react efficiently. An alkynylmagnesium reagent (eq 5) provides the same products of rearrangement, affording diol **13a**. In this case, however, the product diol was rather unstable, and we also isolated a small quantity of the eliminated compound, **13b**. The chemoselectivity in this base-promoted *cis*−*syn* elimination to form **13b** may be derived from a preference for a transition state with silyl coordination to the more sterically accessible and more electron-rich primary alkoxide. On the other hand,

(10) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437−475.

(11) Other reactions of epoxysilanes: (a) Hudrlik, P. F.; Hudrlik, A. M.; Rona, R. J.; Misra, R. N.; Withers, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1993−1996. (b) Hudrlik, P. F.; Hudrlik, A. M.; Misra, R. N.; Peterson, D.; Withers, G. P.; Kulkarni, A. K. *J. Org. Chem.* **1980**, *45*, 4444−4448. (c) Hudrlik, P. F.; Hudrlik, A. M. *Advances in Silicon Chemistry*; JAI Press: Greenwich, CT, 1993; Vol. 2, pp 1−89. (d) Hudrlik, P. F.; Ma, D.; Bhamidipati, R. S.; Hudrlik, A. M. *J. Org. Chem.* **1996**, *61*, 8655−8658.

(12) (a) Jung, M. E.; Damico, D. C. *J. Am. Chem. Soc.* **1995**, *117*, 7379−7388. (b) Jung, M. E.; Anderson, K. L. *Tetrahedron Lett.* **1997**, *38*, 2605−2608. (c) Maruoka, K.; Ooi, T.; Nagahara, S.; Yamamoto, H. *Tetrahedron* **1991**, *47*, 6983−6998. (d) Matsubara, S.; Yamamoto, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2002**, *41*, 2837−2840.

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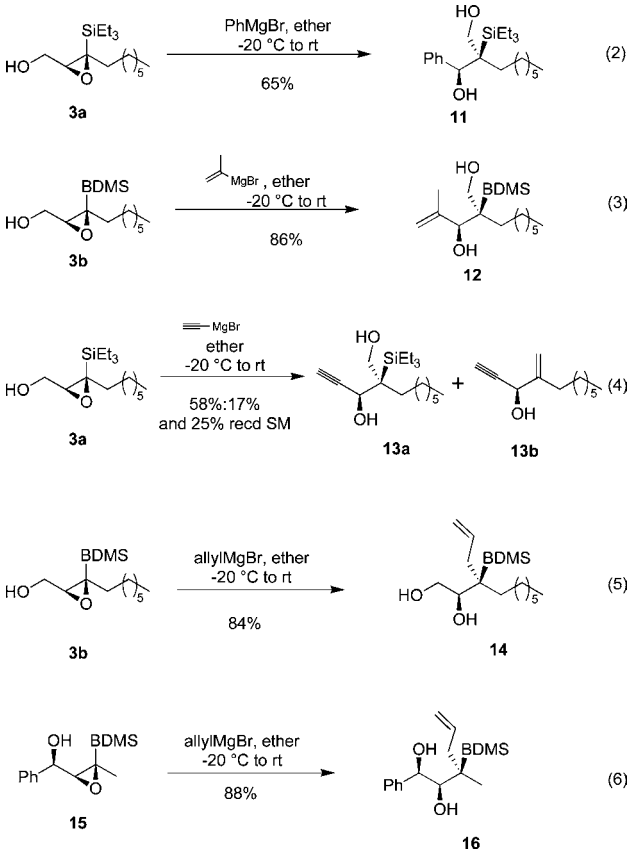
(14) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin 1983; Chapter 6, pp 58−78.

the use of allylmagnesium bromide alters the reactivity, and the direct addition products **14** (eq 5) and **16** (eq 6) could be isolated in good yield.




The method described here provides an efficient access to highly functionalized, sterically congested tertiary silanes. Such structures are difficult to access with current methodology and should facilitate the generation of molecular complexity with organosilicon methods. We are unaware of any extant method to prepare tertiary α-silyl aldehydes, which are produced in situ in this work. The highly diastereoselective addition of a Grignard reagent to an intermediate aldehyde at room temperature is a noteworthy feature of the process and demonstrates results from the additive effects of several unique features of the molecular intermediates. The simplicity of the conditions indicates that other nucleophiles might also be employed to trap the rearrangement products, providing a more general route to tertiary silanes. Selective elimination of the silane product also allows the stereoselectivity of the addition to be employed for stereoselective trisubstituted olefin synthesis.

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

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