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Directing Group-Controlled Hydrosilylation: Regioselective Functionalization of Alkyne

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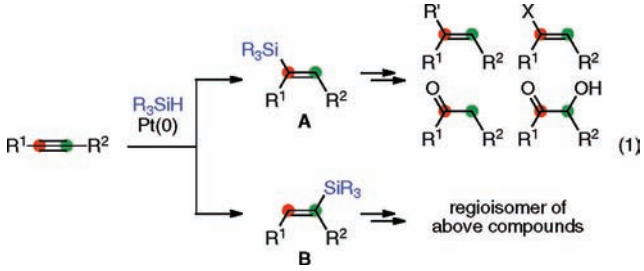
Supporting Information

ABSTRACT: Pt(0)-catalyzed hydrosilylation of unsymmetric alkynes proceeds in a highly regioselective manner with a dimethylvinylsilyl (DMVS) group as the directing group. This hydrosilylation affords a single regioisomer of silylalkenes from propargylic and homopropargylic alcohol derivatives. DMVS also has an accelerating effect that allows group-selective hydrosilylation of the DMVS-attached alkyne prior to that of other alkynes. Combined hydrosilylation and transformation reactions of the resulting silylalkenes afford various tri-substituted alkenes and multi-oxy-functionalized compounds with high regioselectivity from unsymmetric alkynes.

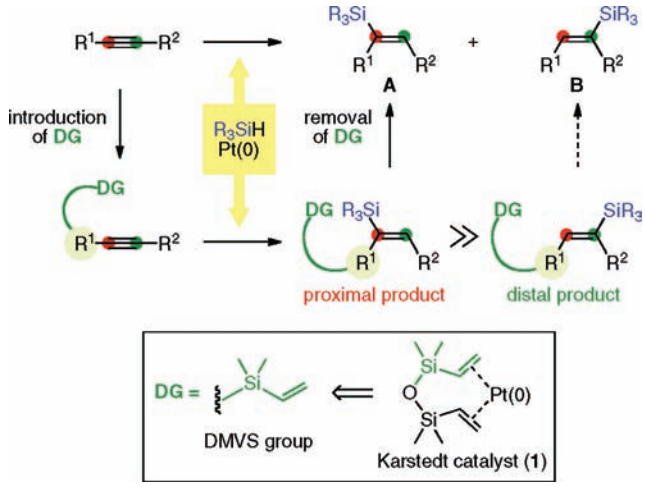
The importance of transformation reactions of alkynes in organic synthesis is undisputed, and various methods have been developed to introduce functional groups to sp carbons of alkynes.[1] Among them, Pt(0)-catalyzed hydrosilylation is a well-established reaction[2] that provides *E*-silylalkene, a versatile precursor for tri-substituted alkenes, ketones, acyloins, etc.[3−6] The difficulty of regiocontrol in the hydrosilylation, however, has prevented its application to an unsymmetric alkyne system



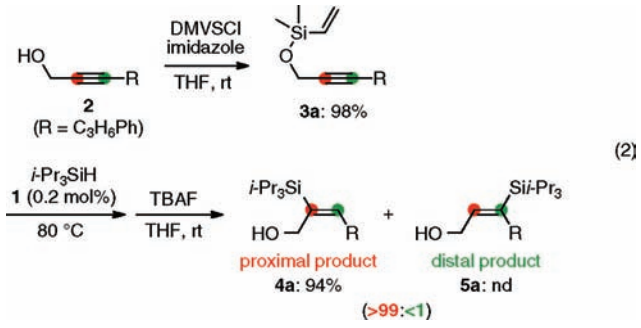
to obtain a mixture of regioisomers of **A** and **B**, as shown in eq 1.[7,8]

To address this problem, we planned to introduce a directing group (DG) into a substrate to control the regioselectivity of the hydrosilylation in an unsymmetric alkyne system (Scheme 1). In this approach, it is most important to select a DG that can coordinate with the Pt(0) catalyst to adequately restrict the reaction pathway. After several attempts, we found that a dimethylvinylsilyl (DMVS) group, a substructure of the Karstedt catalyst, [Pt(0)-1,1,3,3-tetramethyl-1,3-divinyldisiloxane] (**1**),[9] is an excellent DG for proximal-selective hydrosilylation of alkynes.[10−13] Herein, we provide the details of our novel approach to achieve regioselective hydrosilylation and the synthetic value of the resulting silylalkenes.

Scheme 1. Regioselective Hydrosilylation Using a Directing Group



We first performed the hydrosilylation of propargylic alcohol derivatives.[14] The requisite DMVS ether **3a** was prepared from alcohol **2** by reaction with commercially available DMVSCl in the presence of imidazole (eq 2). DMVS ether **3a** was isolated



in 98% yield as a sufficiently pure form after purification using Celite column chromatography,[15] even though we observed partial hydrolysis of DMVS ether after purification using silica gel column chromatography. Hydrosilylation of **3a** was performed with *i*-Pr_3SiH at 80 °C in the presence of **1** (0.2

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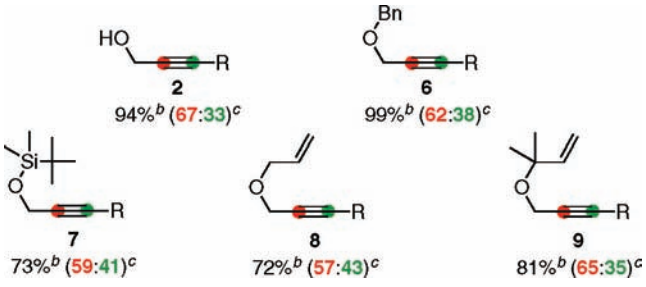
mol%) without solvent, followed by TBAF treatment to remove DMVS. As expected, the reaction provided the proximal-silylated product **4a** in excellent yield (94%) *with no trace of the distal product* **5a** (proximal:distal = >99:<1).[16−18]

Similar reactions using solvents at a concentration of 0.2 M, such as THF, hexane, toluene, dioxane, and 1,2-dichloroethane, also afforded **4a** exclusively in excellent yields (88−95%) without a significant decrease in the reaction rate.[19] Moreover, hydrosilylation of **3a** using Et_3SiH, $i\text{-}Pr_2ClSiH$, and $(EtO)_3SiH$ proceeded with excellent proximal selectivity (proximal:distal = >99:<1, 77−87% yields). This flexibility in choosing the hydrosilane is highly advantageous compared with the intramolecular variant.[7a−c]

In sharp contrast to the reaction of **3a**, hydrosilylation of the parent alcohol **2** and other ether derivatives **6**−**9** afforded *E*-silylalkenes as a mixture of regioisomers, proximal:distal = 57:43−67:33 (Scheme 2). These results clearly indicate that

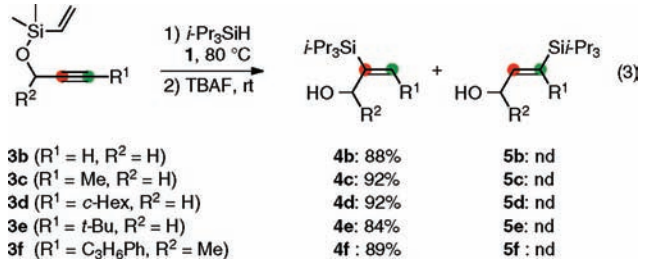
Scheme 2. Hydrosilylation of Propargylic Alcohol 2 and Its Derivatives 6−9 (R = C_3H_6Ph)[a]



[a]Reagents and conditions: $i\text{-}Pr_3SiH$ (1.0 equiv), **1** (0.2 mol%), 80 °C. [b]Combined yield of the proximal- and distal-silylated products. [c]Ratio of proximal- and distal-silylated products (proximal:distal).

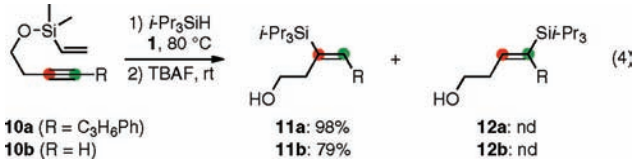
DMVS is highly capable of controlling the regioselectivity of Pt(0)-catalyzed hydrosilylation in an unsymmetric alkyne system.

Hydrosilylation of other DMVS ethers **3b**−**f**, which were prepared from propargyl alcohol (R^1 = H, R^2 = H), 2-butyn-1-ol (R^1 = Me, R^2 = H), 3-cyclohexyl-2-propyn-1-ol (R^1 = *c*-Hex, R^2 = H), 4,4-dimethyl-2-pentyn-1-ol (R^1 = *t*-Bu, R^2 = H), and a secondary propargylic alcohol (R^1 = C_3H_6Ph, R^2 = Me), respectively, also afforded proximal-silylated allylic alcohols **4b**−**f** *as the sole product* in excellent yield (84−92%), irrespective of steric hindrance at the proximal and distal positions of the alkyne carbons (eq 3). Therefore, the present

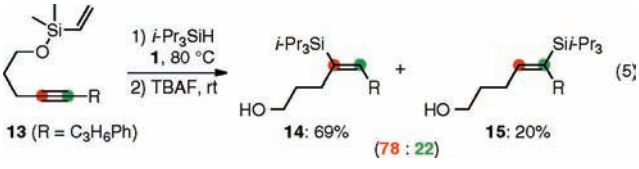


method complements the previously developed methods with regard to regioselectivity, particularly in a terminal alkyne system.

The developed DMVS method is also efficient in the homopropargylic system. Hydrosilylation of DMVS ethers **10a,b** afforded exclusively proximal products **11a,b** in 98% and 79% yield, respectively (eq 4).

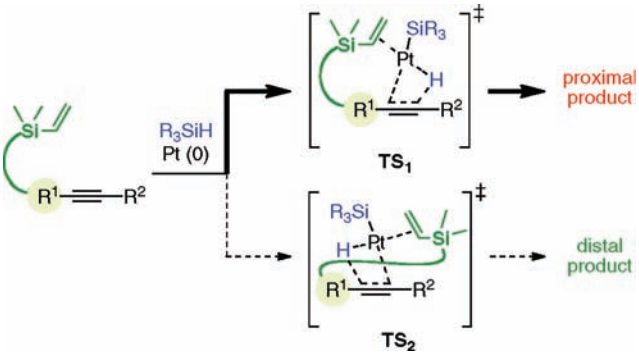


Even when DMVS was placed three carbons away from the alkyne, hydrosilylation of the bis-homopropargylic alcohol derivative **13** proceeded in a proximal-selective manner, albeit with moderate selectivity (proximal:distal = 78:22) (eq 5).



To clarify the origin of the observed high regioselectivity of hydrosilylation, we formed hypotheses regarding the reaction pathway and transition-state models. It is well accepted that the regioselectivity of hydrosilylation with a Pt(0) catalyst is determined at the hydroplatination step.[20,21] Therefore, the regioselectivity of the present hydrosilylation might also occur at the hydroplatination step, in which a Pt center properly coordinates with a vinyl moiety of DMVS. Based on these hypotheses, transition-state models $\mathbf{TS_1}$ and $\mathbf{TS_2}$ are probable, providing the proximal product and distal products, respectively (Scheme 3). Comparison of both models indicated that $\mathbf{TS_2}$ is

Scheme 3. Proposed Reaction Mechanism for Hydrosilylation of DMVS Ethers



disfavored by the highly strained ring structure; hence, hydrosilylation would proceed via the less strained $\mathbf{TS_1}$ to afford the proximal-silylated product.

To probe this potential mechanism further, we performed a DFT computational study of the reaction of **3c** with Me_3SiH as a model (Scheme 4).[22] Initially, a $\mathbf{TS_1}$-type transition state, $\mathbf{TS_a}$, was computed, and then an intrinsic reaction coordination calculation of $\mathbf{TS_a}$ was performed to analyze the reaction pathway.[23] The results revealed that the starting intermediate $\mathbf{IM_a}$ overcame the energy barrier of $\mathbf{TS_a}$ (+10.7 kcal/mol) while maintaining the chelation structure. $\mathbf{TS_a}$ converted to the proximal-hydroplatination product $\mathbf{IM_b}$ with a decrease in energy of 6.6 kcal/mol from $\mathbf{IM_a}$. The calculated results supported the observed proximal selectivity of the hydrosilylation.

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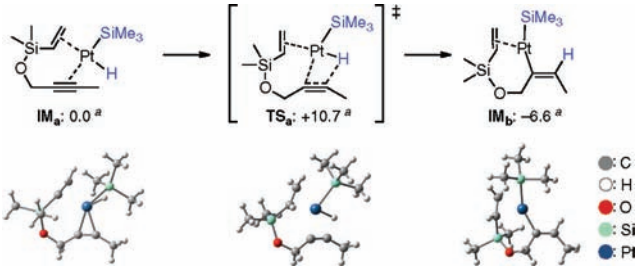
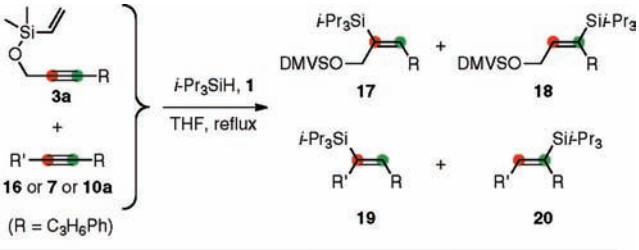
Scheme 4. Reaction Pathway Analysis of Hydrosilylation in the DMVS Ether System Using DFT Calculation



[a]Relative zero-point energies (ΔE_0) based on $\mathbf{IM}_a$ in kcal/mol.

The DMVS acts not only as the DG but also as the accelerating group for the hydrosilylation. For example, hydrosilylation of a 1:1:1 mixture of DMVS ether **3a**, alkyne **16** (R′ = C_3H_6Ph), and *i*-Pr_3SiH afforded products from **3a** and **16** in 93% and 2% yield, respectively, indicating that hydrosilylation of **3a** proceeds 46.5 times faster than that of **16** (Table 1, entry 1).[24] Furthermore, DMVS ether **3a** reacts

Table 1. Competitive Experiments on Hydrosilylation between 3a and Other Alkynes



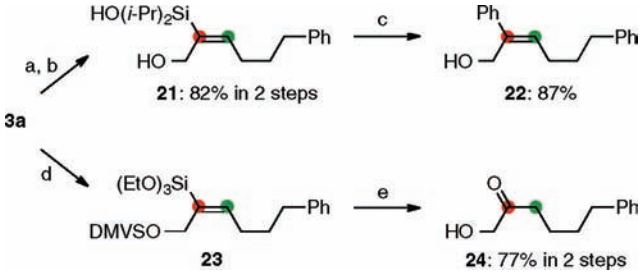
entry	substrates	products (%) 17 + 18 (proximal:distal)	19 + 20	recovered substrates (%)	ratio (17+18)/(19+20)
1	**3a** + **16** (R′ = C_3H_6Ph)	93[a] (99:1)[a]	2[a]	**3a**: 7[a] **16**: 90[a]	46.5
2	**3a** + **7** (R′ = CH_2OTBS)	87[a] (>99:<1)[a]	11[a] (64:36)[a]	**3a**: 6[a] **7**: 89[a]	7.9
3	**3a** + **10a** (R′ = C_2H_4ODMVS)	84[b] (>99:<1)[c]	16[b] (>99:<1)[c]	**3a**: 13[b] **10a**: 84[b]	5.3

[a]Determined by GLC analysis. [b]Isolated yields of the corresponding alcohols after TBAF treatment of the hydrosilylation products. [c]Determined by ^1H NMR analysis.

~8 and 5 times faster than TBS ether **7** (R′ = CH_2OTBS) and the DMVS ether of homopropargylic alcohol **10a** (R′ = C_2H_4ODMVS), respectively (Table 1, entries 2 and 3).[25] The significant acceleration effect of DMVS on the propargylic alcohol **3a** is most likely due to preferential chelation with the Pt center, as proposed in Scheme 4.

The reported hydrosilylation offers an efficient approach to the synthesis of highly functionalized alkenes and ketones with regioselective introduction of functional groups to the unsymmetric alkynes. For examples, **3a** can be converted to tri-substituted *Z*-alkene **22** without the formation of any other isomers via hydrosilylation with *i*-Pr_2SiClH, followed by hydrolysis of the chlorosilane moiety to silanol **21** (82% yield in two steps) and the Hiyama coupling reaction with iodobenzene (87% yield) (Scheme 5).[26] On the other hand, hydrosilylation with $(EtO)_3SiH$ followed by oxidation using

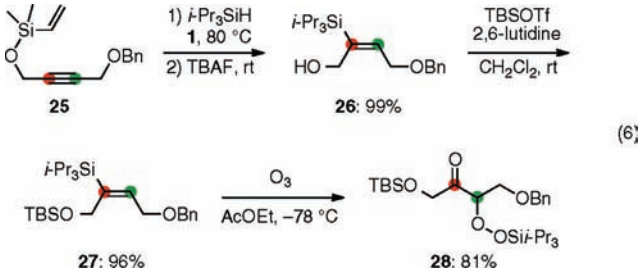
Scheme 5. Transformation of 3a Using Hydrosilylation[a]



[a]Reagents and conditions: (a) *i*-Pr_2ClSiH (1.0 equiv), **1** (0.2 mol%), 80 °C; (b) K_2CO_3, H_2O, THF, rt; (c) PhI (1.0 equiv), TBAF, $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol%), THF, rt; (d) $(EtO)_3SiH$ (1.0 equiv), **1** (0.2 mol%), 80 °C; (e) H_2O_2, $NaHCO_3$, THF−MeOH, 50 °C.

Tamao's condition converted **3a** to the acyloin product **24** (77% yield in two steps) exclusively.[27]

Furthermore, the current hydrosilylation combined with our previously reported addition-type ozone oxidation produces poly-oxy-functionalized compounds regioselectively.[5] For example, DMVS ether **25**, easily available from 2-butyne-1,4-diol, was converted to silylalkene **26** by hydrosilylation with *i*-Pr_3SiH (eq 6, 99% yield, proximal:distal = >99:<1). After TBS



etherification, ozone oxidation of the thus-obtained silylalkene **27** in AcOEt at −78 °C afforded the α-silylperoxy ketone **28** with different oxy-functional groups on all four carbons in 81% yield.[28,29]

In summary, we described a highly regioselective Pt(0)-catalyzed hydrosilylation of unsymmetric alkynes using DMVS as a directing group. The novel sequential conversion of alkynes via hydrosilylation and transformations of the resulting *E*-silylalkene moiety is an efficient approach to the synthesis of versatile multi-substituted alkenes and oxy-functionalized compounds. Further studies toward expanding the present directing group method for other reactions and their applications are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Recently, we developed an addition-type ozone oxidation for silylalkenes that affords α-silylperoxy carbonyl compounds in excellent yield. The ozone oxidation products can be converted to poly-oxy-functionalized compounds such as acyloin derivatives: (a) Murakami, M.; Sakita, K.; Igawa, K.; Tomooka, K. *Org. Lett.* **2006**, *8*, 4023. (b) Igawa, K.; Sakita, K.; Murakami, M.; Tomooka, K. *Synthesis* **2008**, 1641. (c) Igawa, K.; Kawasaki, Y.; Tomooka, K. *Chem. Lett.* **2011**, *40*, 233.

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(10) We describe as "proximal" the product of silylation at the carbon closer to the DG and as "distal" the opposite one.

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(12) Brookhart et al. reported Co-catalyzed intramolecular hydrogen transfer from an amine moiety to a DMVS group and proposed that DMVS acts as a DG: Bolig, A. D.; Brookhart, M. *J. Am. Chem. Soc.* **2007**, *129*, 14544.

(13) Jamison et al. reported alkene-directed coupling reactions of enyne and aldehyde using Ni catalyst: (a) Miller, K. M.; Luanphaisarnnont, T.; Molinaro, C.; Jamison, T. F. *J. Am. Chem. Soc.* **2004**, *126*, 4130. (b) Moslin, R. M.; Jamison, T. F. *Org. Lett.* **2006**, *8*, 455. (c) Moslin, R. M.; Miller, K. M.; Jamison, T. F. *Tetrahedron* **2006**, *62*, 7598.

(14) It is recognized that regiocontrol of hydrosilylation of propargylic alcohol derivatives is difficult, even with an intramolecular variant system. Pt-catalyzed intramolecular hydrosilylation of hydrosilyl ethers derived from propargylic alcohols does not afford the corresponding four-membered cyclic silylalkenes owing to its strained structure. To solve this problem, Denmark et al. developed disiloxane-tethered intramolecular hydrosilylation of propargylic alcohol derivatives.[7c]

(15) Removal of concomitantly produced imidazole hydrochloride salt by Celite column chromatography is important to achieve the high regioselectivity of the hydrosilylation of DMVS ethers.

(16) The DMVS group of **3a** was intact after hydrosilylation. In fact, ^{1}H NMR analysis of the crude products of hydrosilylation confirmed that there was no trace of products missing the vinyl moiety on DMVS.

(17) We also observed partial hydrolysis of DMVS of the hydrosilylation products during purification using silica gel chromatography. To avoid confusion, purifications were performed after removal of DMVS.

(18) Authentic samples of distal products from DMVS ethers were prepared independently; e.g., **5a** was isolated from the isomer mixture obtained by hydrosilylation of alcohol **2**. See SI for details.

(19) The presented reactions were completed in 1.0−1.5 h at 66−80 °C.

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(21) Tsipis and Kefalidis reported a pioneering theoretical study on alkyne hydrosilylation using a Pt(0) catalyst, where acetylene and phosphane were used as substrate and ligand, respectively: Tsipis, C. A.; Kefalidis, C. E. *Organometallics* **2006**, *25*, 1696.

(22) All calculations were performed at the B3LYP/cep-121G level of theory using the Gaussian 09 program; see SI for details.

(23) We estimated the initial structure for the calculation of $\mathbf{TS}_a$ from the transition structure of hydrosilylation of acetylene reported by Tsipis and Kefalidis.[21]

(24) Chemical yields of hydrosilylation products in the competitive experiments of **3a** with **7** and **16** were determined by GLC analysis using biphenyl as an internal standard. Retention times of all products in GLC analysis were independently confirmed using separately prepared authentic samples. See SI for details.

(25) These results clearly indicate that hydrosilylation of TBS ether **7** is faster than that of alkyne **16**. Regarding the substituent effect of the oxy-functional group at the propargylic position, Tsipis reported that hydrosilylation of propargylic alcohols is faster than that of non-substituted alkynes: Tsipis, C. A. *J. Organomet. Chem.* **1980**, *188*, 53.

(26) Pioneering work on the coupling reaction of silyl alkene: (a) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918. (b) Denmark, S. E.; Wehrli, D. *Org. Lett.* **2000**, *2*, 565.

(27) Tamao, K.; Maeda, K. *Tetrahedron Lett.* **1986**, *27*, 65.

(28) We observed slight decomposition of **28** during purification using silica gel chromatography. Therefore, the chemical yield of **28** was determined by ^{1}H NMR analysis of the crude product with 1,3,5-trimethoxybenzene as an internal standard. See SI for details.

(29) The silylperoxide moiety of **28** can be transformed into silyl ether, alcohol, ketone, and so on.[5]