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Highly Regio- and Stereoselective Hydrostannylation of Alkynols with A New Lewis Acidic Hydrostannane

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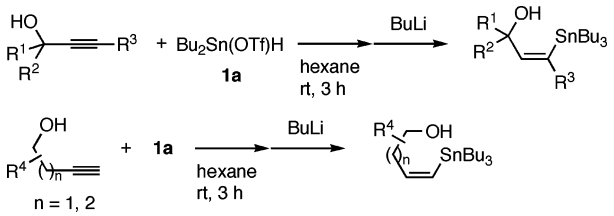
ABSTRACT



$Bu_2Sn(OTf)H$ (1a), easily prepared from Bu_2SnH_2 and TfOH, was found to be very valuable for highly regio- and stereoselective hydrostannylation of various propargyl alcohols leading to (*Z*)-γ-stannylated allyl alcohols. The stannylation with 1a is applicable to the synthesis of hydroxy-substituted (*Z*)-vinylstannanes from terminal alkynes bearing a hydroxy group at the homoallylic or bishomoallylic position. The coordination of the hydroxy group to the Lewis acidic tin center plays an important role for the observed regio- and stereochemistry.

Vinylstannanes are important reagents working as vinyl anion equivalents for stereo-controlled alkene synthesis.[1] Among various synthetic routes to vinylstannanes, hydrostannylation of alkynes with hydrostannanes is a most straightforward and convenient route. Much attention has been paid to the development of regio- and stereoselective hydrostannylation based on the elaboration of the promoter.[2−5] Radical-initiated reactions are valuable for the synthesis of functionalized vinylstannanes; however, the stereoselectivity is generally low.[2] We have recently described that the Et_3B-initiated hydrostannylation of γ-unsubstituted propargyl alcohols with Bu_2SnClH (**1b**) shows high levels of regio- and stereocontrol at low temperatures.[6,7] Unfortunately, this method is ineffective in selective hydrostannylation of other alkynols. We herein report that $Bu_2Sn(OTf)H$ (dibutyl(trifluoromethanesulfoxy)stannane, **1a**), a more Lewis acidic hydrostannane, realizes highly regio- and stereoselective hydrostannylation of various alkynols at room temperature.

Hydrostannane **1a** can easily be prepared by the dehydrogenative reaction of Bu_2SnH_2 with 1 equiv of TfOH without solvent at 0 °C.[8] The hydrostannane thus obtained

(1) (a) Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, 2004. (b) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(2) (a) Leusink, A. J.; Budding, H. A. *J. Organomet. Chem.* **1968**, *11*, 533−539. (b) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547−2549. (c) Mitchell, T. N.; Amamria, A. *J. Organomet. Chem.* **1983**, *252*, 47−56. (d) Nakamura, E.; Imanishi, Y.; Machii, D. *J. Org. Chem.* **1994**, *59*, 8178−8186.

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(5) Shibata, I.; Suwa, T.; Ryu, K.; Baba, A. *J. Am. Chem. Soc.* **2001**, *123*, 4101−4102.

(6) Miura, K.; Wang, D.; Matsumoto, Y.; Fujisawa, N.; Hosomi, A. *J. Org. Chem.* **2003**, *68*, 8730−8732.

(7) Quite recently, Mitchell et al. have reported similar results. Thiele, C. M.; Mitchell, T. N. *Eur. J. Org. Chem.* **2004**, 337−353.

(8) For the preparation of Bu_3SnOTf from Bu_3SnH, see: Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1984**, *25*, 2419−2422.

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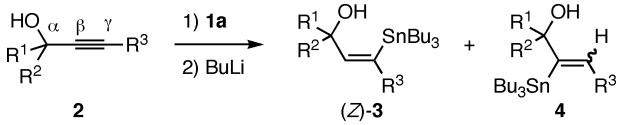
was used without purification. Propargyl alcohol **2a** reacted spontaneously with **1a** at room temperature. Treatment of the resulting mixture with BuLi gave (*Z*)-vinylstannane **3a** in a high isolated yield (entry 1 in Table 1). The regio- and

Table 1. Hydrostannylation of Propargyl Alcohols **2** with **1a**[a]



2 (*Z*)-**3** **4**

	propargyl alcohol					
entry	R^1	R^2	R^3		yield (%)[b]	(*Z*)-**3**:**4**
1	*n*-C_8H_{17}	H	H	(**2a**)	89	>99:1[c]
2[d]	*n*-C_8H_{17}	H	H	(**2a**)	83	93:7
3	*c*-C_6H_{11}	H	H	(**2b**)	93	>99:1[c]
4[e]	H	H	H	(**2c**)	85	>99:1
5	Me	Me	H	(**2d**)	90	96:4
6	H	H	Me	(**2e**)	88 (50)[f]	71:26 (>99:1)[f]
7[d]	H	H	Me	(**2e**)	77	7:93 [g]
8	H	H	*n*-$C_{10}H_{21}$	(**2f**)	91 (77)[f]	91:9 (>99:1)[f]
9	H	H	$SiMe_3$	(**2g**)	64 (85)[h]	>98:2 (>99:1)[h]
10	Me	H	*n*-C_6H_{13}	(**2h**)	72 (89)[h]	97:3 (97:3)[h]

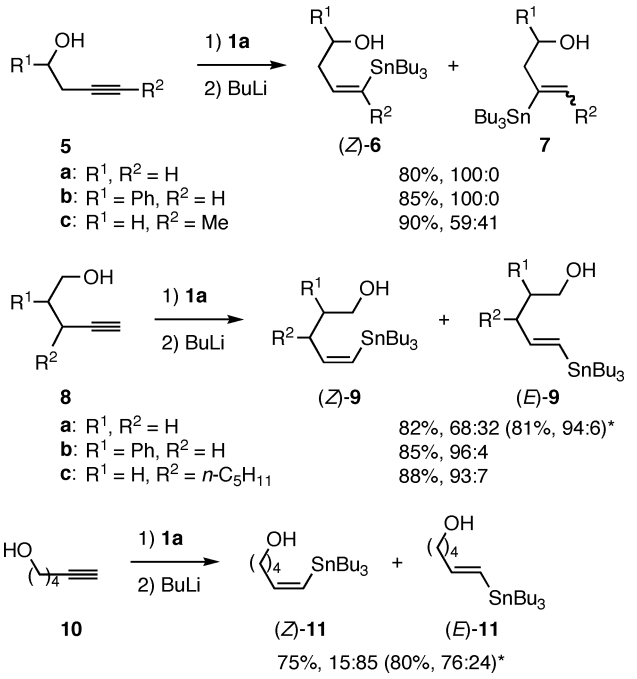
[a] Unless otherwise noted, the initial step was carried out with **2** (1.00 mmol) and **1a** (1.10 mmol) in hexane (2 mL) at room temperature for 3 h. The resultant mixture was diluted with Et_2O (2 mL) and treated with BuLi (1.6 M in hexane, 2.2−2.5 mmol) at 0 °C for 20 min. [b] Isolated yield of a mixture of (*Z*)-**3** and **4**. [c] A trace amount of (*E*)-**3** (<1%) was formed. [d] **1b** was used instead of **1a**. [e] BuMgBr (in Et_2O) was used instead of BuLi. [f] After the reaction of **2** with **1a**, the reaction mixture was concentrated under reduced pressure and heated at 80 °C for 3 h. The resultant mixture was diluted with Et_2O and treated with BuLi. The results are shown in parentheses. [g] (*Z*)-**3e**:(*Z*)-**4e**:(*E*)-**4e** = 7:64:29. [h] Et_3B (0.10 mmol) and dry air were used as initiator. The results are shown in parentheses. (*Z*)-**3h** could be isolated in 86% yield.

stereoisomers, **4a** and (*E*)-**3a**, were hardly formed. Since the hydrostannylation of **2a** was effectively inhibited by adding 5 mol % of galvinoxyl, a radical scavenger, it would involve a radical chain mechanism. Hydrostannane **1b** is known to have a similar reactivity causing spontaneous, homolytic hydrostannylation.[9] The use of **1b** instead of **1a** resulted in lower regioselectivity under the same conditions (entry 2).[10] The present method using **1a** is valuable also for highly selective, efficient hydrostannylation of other γ-unsubstituted propargyl alcohols **2b**−**d** (entries 3−5).

It has been reported that the radical-initiated reaction of γ-substituted propargyl alcohols (e.g., **2e**) with Bu_3SnH (**1c**) yields (*Z*)-β-stannylated products (e.g., (*Z*)-**4e**) exclusively.[11] In contrast, **1a** added spontaneously to **2e** to form (*Z*)-γ-stannylated product **3e** as the major product (entry 6). Although the regiochemistry was not well controlled, the γ-stannylation showed complete *Z*-selectivity. Under the same conditions, the stannylation with **1b** took place mainly at the β-position as the stannylation with **1c** does, but with low *Z*-stereoselectivity (entry 7). Internal alkyne **2f** was stannylated with better γ-regioselectivity than **2e** (entry 8). In the reactions of **2e,f** with **1a**, heating the reaction mixture before butylation led to exclusive formation of (*Z*)-**3e,f**, although the total yields of stannylated products decreased. The seeming improvement in regioselectivity is probably due to thermal decomposition of the precursors leading to **4e,f** by deoxystannylation.[11b] Actually, the formation of 1,2-tridecadiene was observed in the reaction of **2f** by the improved method. Propargyl alcohols **2g,h** underwent highly regio- and stereoselective hydrostannylation to give (*Z*)-**3g,h** in moderate yields (entries 9 and 10). The use of Et_3B as initiator effected higher yields of (*Z*)-**3g,h**.[2b]

We next examined the hydrostannylation of other alkynols with **1a** (Scheme 1). Terminal alkynes **5a,b**, bearing a hydroxy group at the homopropargylic position, were stannylated with complete regio- and stereoselectivity.[12] The reaction of internal alkyne **5c** formed both regioisomers with low regioselectivity, although the stannylation at the sp-carbon more remote from the hydroxy group gave only the *Z*-isomer of **6c**. Similar to the case of **5a,b**, the stannylation of terminal alkynes **8b,c** proceeded with high *Z*-selectivity.

Scheme 1. Hydrostannylation of Alkynols **5**, **8**, and **10** with **1a**[a]



[a] A small excess of an alkynol was used (alkynol:**1a** = 1.1:1) in the reactions marked with an asterisk (*).

(9) (a) Neumann, W. P.; Pedain, J. *Tetrahedron Lett.* **1964**, 2461−2465. (b) Davies, A. G.; Kinart, W. J.; Osei-Kissi, D. K. *J. Organomet. Chem.* **1994**, *474*, C11−C13. (c) Mitchell, T. N.; Moschref, S.-N. *Chem. Commun.* **1998**, 1201−1202.

(10) The hydrostannylattion of **2a** with Bu_3SnH was much slower even in the presence of Et_3B (rt, 6 h, 49% conversion with 10 mol % Et_3B) and showed low *Z*-selectivity ((*Z*)-**3a**:(*E*)-**3a**:**4a** = 66:26:8).

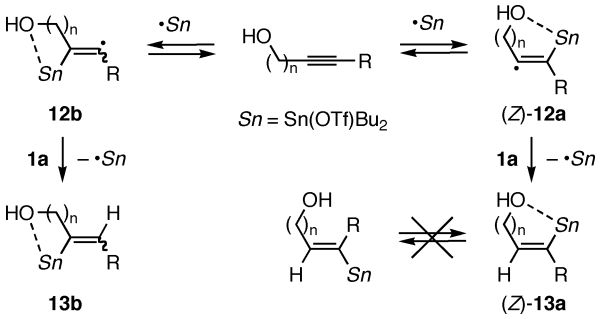
(11) (a) Ensley, H. E.; Buescher, R. R.; Lee, K. *J. Org. Chem.* **1982**, *47*, 404−408. (b) Konoike, T.; Araki, Y. *Tetrahedron Lett.* **1992**, *33*, 5093−5096.

(12) In general, homolytic hydrostannylation of terminal alkynes proceeds with high regioselectivity. See ref 2. As an exception, the reaction of γ-unsubstituted propargyl alcohols shows slightly lower regioselectivity.

Interestingly, the selectivity with **8a** was rather low under the standard conditions; however, a small excess of **8a** over **1a** achieved high *Z*-selectivity.[13] Furthermore, 5-hexyn-1-ol (**10**) was used as a substrate. As shown in the reaction of **8a**, the molar ratio of **10** to **1a** strongly affected the stereoselectivity: a small excess of **1a** led to *E*-selectivity, whereas *Z*-selectivity was observed with a small excess of **10**.

The stereochemistry of homolytic hydrostannylation of alkynes is determined by H-abstraction of β-stannylated vinyl radical intermediates and the subsequent stannyl radical-induced isomerization of the vinylstannanes formed.[6] The high *Z*-selectivity with **1a** can be rationalized by conformational fixation of the intermediate **12a** to the *Z*-form and suppression of the isomerization of the product (*Z*)-**13a**, both of which are directed by a strong interaction between Sn and O atoms (Scheme 2).[14,15] The origin of the high

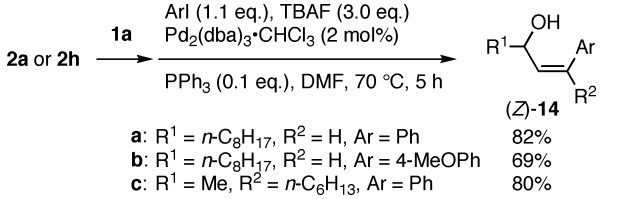
Scheme 2. Origin of Regio- and Stereocontrol



γ-selectivity with **2** would be that the reversible addition of •Sn(OTf)Bu_2 forms the radical intermediate with a five-membered chelate ring, (*Z*)-**12a** (n = 1), in preference to that with a four-membered chelate ring, **12b** (n = 1), by thermodynamic control.

Vinylstannanes prepared by the present method can be directly used for the Pd-catalyzed cross-coupling reaction with aryl halides (Scheme 3).[16] The hydrostannylation of **2**

Scheme 3. Pd-Catalyzed Cross-Coupling of Vinylstannanes



with **1a** followed by treatment with TBAF, iodoarenes, and catalytic amounts of $Pd_2(dba)_3$ and PPh_3 (one-pot procedure) gave allyl alcohols (*Z*)-**14** (*Z*:*E* = >99:1) in good yields.

In conclusion, we have developed a novel hydrostannylating agent with a strong Lewis acidity, which is very valuable for highly selective synthesis of functionalized vinylstannanes from various alkynols. It is noteworthy that the use of **1a** enables γ-selective stannylation of γ-substituted propargyl alcohols in sharp contrast to β-selective stannylation with **1b** and **1c**. The present study has demonstrated that the high Lewis acidity of **1a** is quite effective in both regio- and stereocontrol of homolytic hydrostannylation of alkynols.

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Supporting Information Available: Experimental details, characterization data (^{1}H NMR, ^{13}C NMR, IR, elemental analysis), and discussions on the Lewis acidity of **1a** and the reaction mechanism. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) Under the standard conditions, the excess **1a** may interfere with the O−Sn coordination in (*Z*)-**12a** or (*Z*)-**13a** when the chelate ring is not tight.

(14) The NMR analysis of the (trifluoromethanesulfoxy)vinylstannane prepared from **1a** and **2a** revealed the presence of a highly coordinated tin center. See Supporting Information.

(15) The reaction mechanism possibly involves pre-coordination of **1a** with a substrate and intramolecular radical addition leading to **12**. See Supporting Information for further discussion on the reaction mechanism.

(16) For the cross-coupling reaction using organohalostannanes, see: Fugami, K.; Ohnuma, S.; Kameyama, M.; Saotome, T.; Kosugi, M. *Synlett* **1999**, 63−64 and references therein.