Hydrostannylation

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Studies on the Mechanism of $B(C_6F_5)_3$-Catalyzed Hydrostannylation of Propargylic Alcohol Derivatives**

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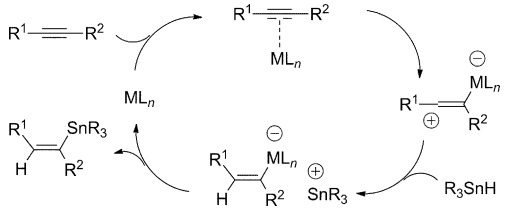
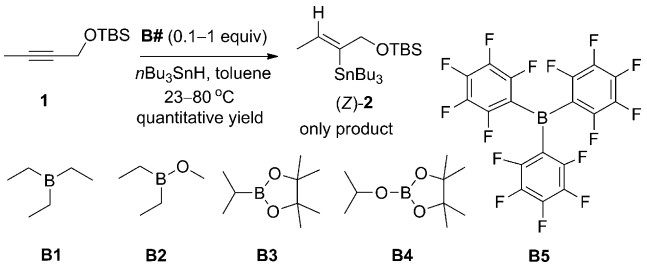
The ability to prepare vinyl organometallic compounds with high stereo- and regioselectivity is important in synthetic chemistry.[1,2] Vinylstannanes can be prepared from propargylic alcohol derivatives by using radical protocols (for example, nBu$_3$SnH/AIBN)[3] and palladium-catalyzed hydrostannylation (nBu$_3$SnH/Pd^0).[4] Unfortunately, the ability to prepare vinylstannanes with high regio- and stereochemical fidelity across a wide variety of substrates has remained elusive.[5] This problem is exacerbated for substrates containing coordinating functionality and those with steric constraints. The use of Lewis-acid promoters for the hydrostannylation[6] and hydrosilylation[7] of simple alkynes can give more reliable stereocontrol. Lewis acids such as $AlCl_3$, $EtAlCl_2$, Et_2AlCl, and $HfCl_4$ have been explored as catalysts in these hydrometalation reactions (see Scheme 1 for mechanism).[8]



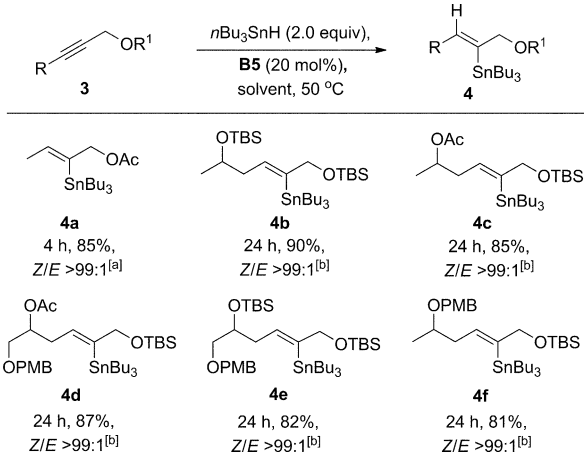
Scheme 1. Putative mechanism for the Lewis acid promoted hydrostannylation of alkynes.[6,7]

$B(C_6F_5)_3$ (**B5**) is an interesting catalyst for a variety of hydrometalation reactions[9] and Yamamoto and co-workers have illustrated the use of **B5** in the hydrostannylation of terminal alkynes and symmetrical internal alkynes.[9b] In pursuit of a synthetic route toward prunioside A, we needed a selective hydrostannylation of a complex internal alkyne and wondered whether **B5** could be used for this purpose. Ultimately, and described herein, we discovered that this catalyst operates under a mechanism that is unique among those of other catalysts that have been used for this transformation.

During the initial screening of boron-based Lewis acids for the hydrostannylation of alkyne **1**, we found that different alkyl- and alkoxyboranes (**B1**–**B4**), together with **B5** are effective catalysts (Scheme 2). When we examined the generality of this process (Scheme 3), differences emerged in the reactivity between **B5** and other catalysts. In one difference, **B1**–**B4** all require molecular oxygen for reactivity, whereas **B5** does not. The hydrostannylation of unhindered alkyne **1** proceeded well when **1** was treated with **B5** in toluene. However, whereas the use of **B2** led to successful hydrostannylation of hindered alkyne **3b** in toluene, the use of **B5** for this transformation led to no reaction. Finally, when THF was used in place of toluene, **B5** became an effective catalyst for the hydrostannylation of **3b** (Scheme 4).[10] This result suggests that the mechanism of **B5**-catalyzed hydrostannyla-



Scheme 2. Boron-based hydrostannylation catalysts.



Scheme 3. Scope study of $B(C_6F_5)_3$-catalyzed regioselective tin-hydride addition to propargylic alcohol derivatives. Isomeric ratio was determined by ^{1}H NMR spectroscopy of the crude reaction mixture. Yield was determined after purification by silica-gel chromatography. [a] Reaction conditions: alkyne (0.5 M in toluene), **B5** (0.2 equiv), nBu$_3$SnH (2 equiv), 50 °C. [b] Reaction conditions: alkyne (0.5 M in THF), **B5** (0.2 equiv), nBu$_3$SnH (2 equiv), 50 °C.

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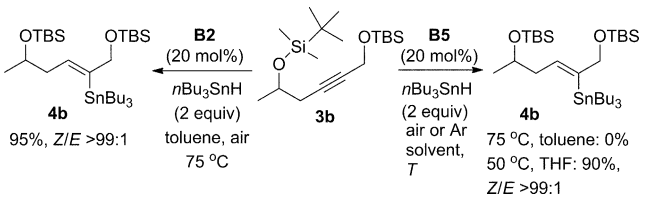
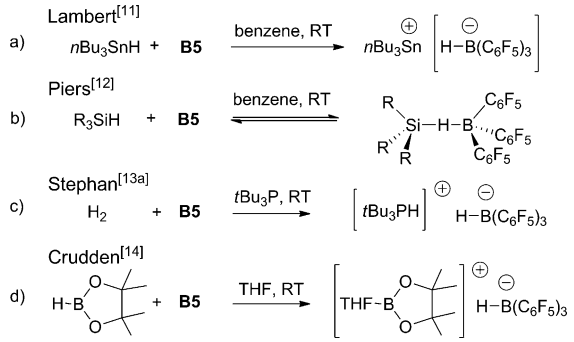


Scheme 4. **B5**-catalyzed hydrostannylation of hindered alkyne **3b**.

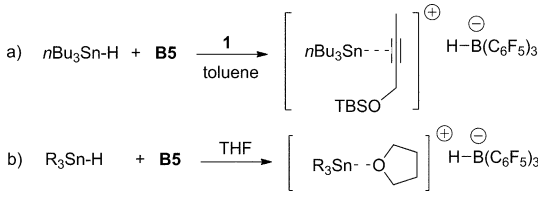
tion in toluene and in THF are different. Furthermore, although the hydrostannylation of hindered alkynes is only successful when conducted in THF, the hydrostannylation of unhindered alkynes does not have such a restriction.

Lambert and Kuhlmann first reported that the three-coordinate tributylstannyl cation could be generated by hydride abstraction from nBu$_3$SnH by **B5** in pure benzene (Scheme 5a).[11a] Piers and co-workers demonstrated that **B5** forms complexes with R$_3$SiH (Scheme 5b)[12a] whereas the



Scheme 5. Hydride abstraction by **B5** for tin hydrides, silanes, hydrogen, and borane.

research groups of both Stephan and Rieger have independently shown that **B5** is sufficiently Lewis acidic to abstract a hydride from hydrogen gas in the presence of Lewis bases (Scheme 5c).[13] Later, Crudden and Lata reported the formation of a THF-stabilized borenium ion (Scheme 5d) that was active in rhodium-catalyzed hydroboration.[14] The reaction of nBu$_3$SnH and **B5** would generate the nonstabilized tributylstannyl cation [nBu$_3$Sn]$^+$, which in the presence of an alkyne would become stabilized through interaction with the alkyne, thus initiating hydrostannylation (Scheme 6a). If the alkyne is sufficiently hindered (**3b**), stabilization of the stannyl cation would become impaired. In this case, the stannyl cation can either reversibly react with HB(C$_6$F$_5$)$_3^-$ to



Scheme 6. Hydride abstraction by **B5** in THF and toluene.

regenerate nBu$_3$SnH and **B5**, or degrade at the reaction temperature.[15] Conversely, a coordinating solvent such as THF would assist in stabilization of the stannyl cation and protect it from degradation at elevated temperatures (Scheme 6b).

To examine these hypotheses, nBu$_3$SnH and **B5** were mixed in C$_6$D$_6$/THF (1:1) at room temperature and monitored by ^{11}B NMR spectroscopy (Figure 1a and b). The rapid formation of HB(C$_6$F$_5$)$_3^-$ was confirmed by the quantitative shift of the boron resonance from 2.68 to −24.99 ppm, a shift that also occurred with Ph$_3$SnH (Figure 1c). These values are

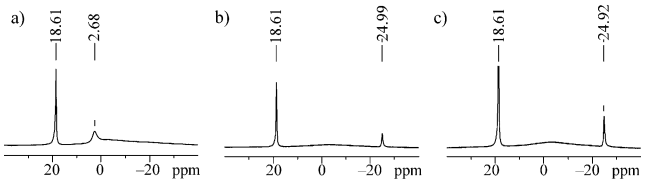


Figure 1. ^{11}B NMR spectra: a) **B5** in 1:1 C$_6$D$_6$/THF; spectrum shows the resonance of the B(C$_6$F$_5$)$_3$·THF adduct at 2.68 ppm. b) **B5** (1 equiv) and nBu$_3$SnH (5 equiv) in 1:1 C$_6$D$_6$/THF; spectrum shows the formation of HB(C$_6$F$_5$)$_3^-$, the resonance of which appears at −24.99 ppm. c) **B5** (1 equiv) and Ph$_3$SnH (5 equiv) in 1:1 C$_6$D$_6$/THF; spectrum shows the formation of HB(C$_6$F$_5$)$_3^-$, the resonance of which appears at −24.92 ppm. B(OEt)$_3$ was used as the internal reference in a sealed capillary (18.61 ppm).

in strong agreement with those of HB(C$_6$F$_5$)$_3^-$ that is formed by the reaction of R$_2$BH and **B5** in the presence of Lewis bases, as reported by Lata and Crudden,[14] and Welch and Stephan[13a]. We also used ^{119}Sn NMR spectroscopy to confirm the formation of the [nBu$_3$Sn·THF]$^+$ complex. The peaks at −76.79 and +141.99 ppm correspond to nBu$_3$SnH and [nBu$_3$Sn·THF]$^+$, respectively (Figure 2a and b).[16] A downfield shift was observed for the nonsolvated tributylstannyl cation [nBu$_3$Sn]$^+$ at +360 ppm.[11a] When the [nBu$_3$Sn]$^+$ HB(C$_6$F$_5$)$_3^-$ adduct was heated in benzene above 30 °C, and monitored by ^{119}Sn NMR spectroscopy, only degradation of the stannyl cation was observed. In contrast, the solvated [nBu$_3$Sn·THF]$^+$HB(C$_6$F$_5$)$_3^-$ adduct remained stable up to 70 °C, above which degradation eventually began to occur.

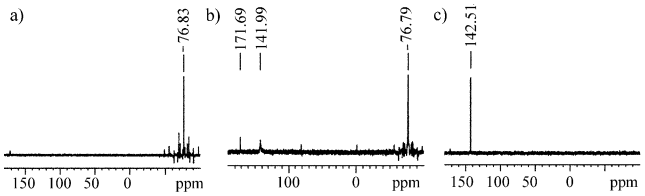
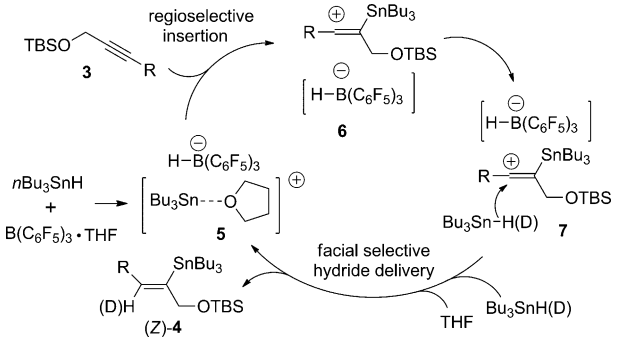


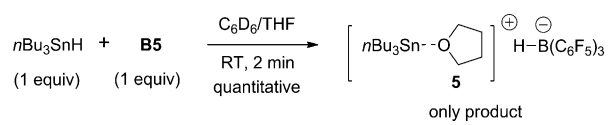
Figure 2. ^{119}Sn NMR spectra: a) nBu$_3$SnH in 1:1 C$_6$D$_6$/THF; spectrum shows a Sn resonance at −76.83 ppm. b) **B5** (1 equiv) and nBu$_3$SnH (5 equiv) in 1:1 C$_6$D$_6$/THF; spectrum shows the formation of [nBu$_3$Sn·THF]$^+$, the resonance of which appears at 141.99 ppm. c) **B5** (1 equiv) and nBu$_3$SnH (1 equiv) in 1:1 C$_6$D$_6$/THF; spectrum shows quantitative formation of [nBu$_3$Sn·THF]$^+$, the resonance of which appears at 142.51 ppm (see Scheme 8 for exact reaction). Me$_3$SnCl was used as the internal reference in sealed capillary (171.69 ppm) for all spectra.

These studies reveal that hydride transfer from the tin reagent to **B5** is rapid and irreversible in the presence of THF, a process that is aided by the formation of the stabilized ion pair.[11] For comparison, we carried out ^{11}B NMR studies on the bulky, but less Lewis acidic three-coordinate boron compound **B4**. Mixing **B4** (1 equivalent) and nBu$_3$SnH (5 equivalents) in C_6D_6/THF (1:1) at room temperature did not lead to hydride abstraction by **B4** (see the Supporting Information). Consistent with this lack of reactivity, the ^{119}Sn NMR spectra of these mixtures showed no evidence of a coordinate Sn–O bond. Because both **B4** and **B5** mediate hydrostannylation, these results strongly suggest that they do so by a different mechanism. Based on the above spectroscopic studies, we propose that the first step in the **B5**-catalyzed hydrostannylation of alkynes in THF is hydride transfer from the stannane to **B5**, thus generating a reactive ion pair (**5**, Scheme 7). The triple bond of alkyne **3** then nucleophilically attacks **5** to give vinyl cation **6**. We attribute the absolute regioselectivity of this insertion to the β-oxygen effect whereby the presence of the oxygen atom inhibits the development of cationic character two positions away.[18] Hydride delivery should occur opposite the bulky tributylstannyl moiety in **6**, thus leading to vinylstannane (*Z*)-**4** via **7** and regenerating the catalyst.

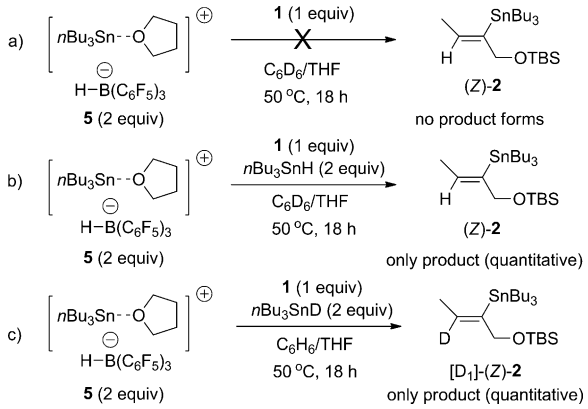


Scheme 7. Plausible catalytic cycle for **B5**-catalyzed hydrostannylation of hindered alkynes in polar solvents, for example, THF.

We then focused on the manner in which hydride is delivered to the alkyne. At first glance, it would seem reasonable to assume that the borohydride ($HB(C_6F_5)_3^-$) is the hydride donor. However, it has been proposed that nBu$_3$SnH is a suitable hydride donor for the Lewis acid catalyzed hydrostannylation.[6,17] When nBu$_3$SnH and **B5** (1:1) were dissolved in a mixture of benzene/THF (1:1), complex **5** formed rapidly, quantitatively, and irreversibly as indicated by ^{119}Sn NMR spectroscopy (Scheme 8) and Figure 2c). The peak at m/z 363.1710 in the mass spectrum of complex **5** confirmed it as the four-coordinate tributylstannyl cation [nBu$_3$Sn·THF]$^+$. Interestingly, when **1** was reacted with freshly prepared **5** (2 equivalents), no hydrostannylation product was obtained (Scheme 9a). When two additional equivalents of nBu$_3$SnH were added to preformed **5**, and then **1** was added, hydrostannylation product (*Z*)-**2** was formed quantitatively (Scheme 9b). To confirm that $HB(C_6F_5)_3^-$ is just a spectator counterion, we performed another experiment in which following the formation of **5**, nBu$_3$SnD and **1** was added. This time only the deuterated product [D$_1$]-(*Z*)-**2** was obtained (Scheme 9c), thus confirming that the stannane is the sole hydride donor (Scheme 7).

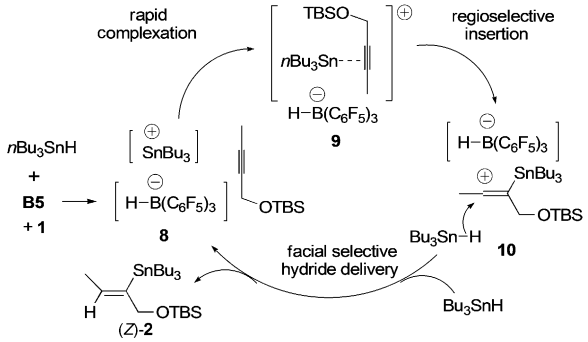


Scheme 8. Formation of **B5** hydride/THF·stannyl cation complex.



Scheme 9. Reaction of **B5** hydride/THF·stannyl cation complex with **1**.

What remained in this study was to account for the ability of **B5** to catalyze hydrostannylation of unhindered alkynes in toluene (Scheme 10). We propose that the catalytic cycle begins in a way that is similar to the catalytic cycle that operates in THF, that is, hydride abstraction. In the case of unhindered alkynes, fast complexation of **1** with the stannyl cation to form complex **9** is essential for catalysis. Complex **9** is then reduced by the stannane via complex **10**.



Scheme 10. Plausible catalytic cycle for **B5**-catalyzed hydrostannylation of unhindered alkynes in toluene.

In conclusion, we have carried out the first regio- and stereoselective hydrostannylation of internal propargylic alcohol derivatives by using $B(C_6F_5)_3$ as a catalyst under very mild reaction conditions.[19] ^{11}B- and ^{119}Sn NMR spectroscopy has been used to identify the reactive intermediates that are formed in the catalytic cycle. This analysis uncovered

that hydride transfer from the stannane to **B5** to generate $[n\mathrm{Bu_3Sn}]^+\mathrm{HB}(\mathrm{C_6F_5})_3^-$ (**8**) is rapid and irreversible. In THF, the stannyl cation is stabilized by the solvent through the formation of a strong chelate (**5**), an interaction that increases stannyl-cation lifetime, especially above room temperature. In the absence of a coordinating solvent, the alkyne itself forms an ion pair with the stannyl cation. Consequently, whereas unhindered alkynes hydrostannylate readily with **B5**, hindered alkynes, which cannot form intimate complexes with $[n\mathrm{Bu_3Sn}]^+\mathrm{HB}(\mathrm{C_6F_5})_3^-$ (**8**) as it is forming, do not undergo hydrostannylation. The lack of solvent dependence on the stereochemical outcome of these reactions (exclusive *Z*-product formation) suggests that both the tributylstannyl-cation insertion and hydride delivery could occur in a more synchronized manner and not as discrete steps as shown above. Finally, deuterium-labeling experiments have identified the stannane as the hydride source for the reduction of complexes **7** and **10**, and not $\mathrm{HB}(\mathrm{C_6F_5})_3$ as would have been expected.

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[19] Hydrostannylation proceeds equally well in the absence of propargylic alcohol functionality (see the Supporting Information, p S12).

Communications

Hydrostannylation

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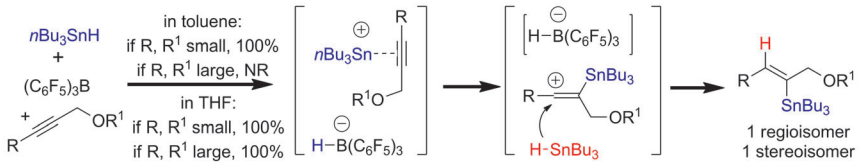

Sleight of hydride: $B(C_6F_5)_3$ catalyzes the hydrostannylation of propargylic alcohols in a regio- and stereoselective manner (see scheme). This Lewis acid first abstracts a hydride from the stannane, thus forming a borohydride/stannyl cation pair, the stability of which depends on solvent and ligands. Deuterium-labeling experiments showed that the source that delivers a hydride to the alkenyl cation is not the borohydride but rather a second molecule of stannane.