



Ni, Co, and Mo-catalyzed alkyne hydrostannations using $\text{Bu}_3\text{SnCl}/\text{PMHS}/\text{KF}/18\text{-crown-6}$ as an in situ Bu_3SnH source

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ABSTRACT

A number of terminal alkynes were subjected to nickel, cobalt, and molybdenum catalyzed hydrostannations in presence of tributyltin chloride, polymethylhydrosiloxane, potassium fluoride and 18-crown-6 as an in situ organotin hydride source to produce vinylstannanes.

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Vinylstannanes are useful and versatile building blocks for organic synthesis.¹ Among the many ways to generate these reactants,² transition-metal-catalyzed hydrostannations of alkynes³ (or alkenes⁴) with tributyltin hydride are widespread. Just as common though are the problems associated with the direct use of this reagent.⁵ For example, adventitious exposure to air can efficiently convert Bu_3SnH to $(\text{Bu}_3\text{Sn})_2\text{O}$, rendering the reagent useless. Similarly, in the presence of transition metals Bu_3SnH can immediately form $\text{Bu}_3\text{SnSnBu}_3$, often complicating the desired reaction and product purification.⁶ Similarly, overcoming any loss of Bu_3SnH to either the oxide or dimer often requires excess use of the relatively expensive and toxic Bu_3SnH .

To ameliorate the negatives associated with the direct use of Bu_3SnH , processes have been developed that use in situ generated organotin hydrides in hydrostannation reactions.⁷ Our own contributions to these efforts include the establishment of $\text{Bu}_3\text{SnCl}/\text{polymethylhydrosiloxane}$ (PMHS)/aqueous KF as an in situ source of Bu_3SnH for radical or palladium catalyzed alkyne hydrostannations.^{7a} This PMHS mediated hydrostannation protocol was integral to the invention of a one-pot hydrostannation/Stille coupling sequence that was catalytic in tin.⁸ In conjunction with efforts aimed at developing the next generation of Stille couplings that are catalytic in tin, we became interested in mixed catalyst systems where the hydrostannation and cross-coupling steps were catalyzed by different metals. With this goal in mind we set out to learn if other previously disclosed hydrostannation catalysts were compatible with our $\text{Bu}_3\text{SnCl}/\text{PMHS}/\text{KF}_{(\text{aq})}$ protocol and how

such conditions would impact the distal/proximal and *E/Z* ratios of the product vinyltins.

We began our study by employing $\text{NiCl}_2(\text{PPh}_3)_2$,⁹ $\text{CoCl}_2(\text{PPh}_3)_2$,⁹ and $\text{Mo}(\text{CO})_3(\text{NCT-Bu})_3$ (MoBI_3)¹⁰ under our $\text{Bu}_3\text{SnCl}/\text{PMHS}/\text{KF}_{(\text{aq})}$ conditions. With the Ni-catalyst, heating at 65 °C in THF for 1–2 days, afforded the expected vinylstannanes, but yields were very inconsistent and even in the best cases moderate. The Co- and Mo-catalysts behaved even worse in that no vinylstannanes were ever observed. We subsequently realized that water used to dissolve the KF was the offending element and that an anhydrous method would be required.

We had previously shown that the Bu_3SnF , PMHS, and catalytic quantities of tetrabutylammonium fluoride (TBAF) allowed for the in situ generation and reaction of Bu_3SnH under anhydrous conditions.^{7d} However, given the demands of our own Stille process and the relative availability and expense of triorganotin fluorides versus triorganotin chlorides,¹¹ our search for an anhydrous method was conducted with the criterion that Bu_3SnCl be employable.

We tried to run heterogeneous reactions with KF being added as a solid, but not surprisingly such attempts failed to produce vinyltins. We quickly then moved to explore adding 18-crown-6 to the reactions, owing to this crown ether's ability to homogenize potassium salts and organic solvents.¹²

Starting with the marginally successful $\text{NiCl}_2(\text{PPh}_3)_2$ catalyzed⁹ reactions that we had run with aqueous KF, we ran reactions on alkynes with 1.5 equiv of Bu_3SnCl , 1.5 equiv of PMHS, 3 equiv of KF, and 3 equiv of 18-crown-6 (Table 1). Following our previous leads,^{7d} we also included 1 mol % TBAF as an additive. Likewise, we also added 9 mol % hydroquinone to inhibit unwanted free radical generation.¹⁰ Under these conditions the reactions

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Table 1
NiCl₂(PPh₃)₂ catalyzed hydrostannations

2 mol% NiCl₂(PPh₃)₂,
1.5 equiv Bu₃SnCl, 1.5 equiv PMHS,
3 equiv KF, 3 equiv 18-crown-6,
1 mol% TBAF, 9 mol% hydroquinone,
THF, 65 °C, 4–5 h *or*

2 mol% NiCl₂(PPh₃)₂,
1.5 equiv Bu₃SnH, THF,
9 mol% hydroquinone, 65 °C, 4–5 h

Entry	R	Products	Yield ^a (ratio of a/b) ^b	
			Bu ₃ SnCl/KF/PMHS	Bu ₃ SnH
1	CH ₂ OH (1)	9a/b	42% (1.5/1)	60% (4.1/1)
2	CH ₂ OTHP (2)	10a/10b	45% (1.7/1)	49% (7.1/1)
3	CH(OH)Ph (3)	11a/11b	42% (1.4/1)	69% (1.3/1)
4	C(OH)(CH ₃)Ph (4)	12a/12b	54% (1/1.7)	46% (1/3.4)
5	C(CH ₃) (5)	13a/13b	57% ^c (1/99)	100% ^d (1/4.3)
6	CH ₂ OTBS (6)	14a/14b	36% (1.4/1)	52% (4/1)

^a Yields refer to spectroscopically pure products unless otherwise noted.

^b Isomeric ratios were determined by ¹H NMR analysis of the crude reaction mixture. Entries 1–3 and 6 gave trace amounts of the Z-isomer (see Ref. 13 for a mechanistic explanation).

^c Reaction was run in Et₂O at room temperature for 12 h.

^d Yield determined by ¹H NMR using HDMS as an internal standard.

reproducibly gave moderate to good yields and required much less time (~4–5 h) to complete as compared to the aqueous KF protocols. On the other hand, while the regiochemical preferences were comparable to those observed in other reported protocols,^{3a,7d,9} regioselectivities and yields trended lower relative those observed for control reactions run using Bu₃SnH directly. Notably a TBS group survived this fluoride mediated protocol (Table 1, entry 6).

We next looked at CoCl₂(PPh₃)₂ catalyzed hydrostannations (Table 2). After some experimentation, it was found that these hydrostannations, which completely failed in the presence of water, could be achieved under the Bu₃SnCl/PMHS/KF/18-crown-6 conditions provided they were run at elevated temperatures. Specifically, reactions in toluene at 100–110 °C for 24 h afforded the vinylstannanes in fair to moderate yields. Regiochemical outcomes were similar to those observed during the Ni-catalyzed reactions. Entry 3 of Table 2 is of note because the TBS group survived in presence of the fluoride. That said, these Co-catalyzed reactions did exhibit some reliability problems. Successful

Table 2
CoCl₂(PPh₃)₂ catalyzed hydrostannations

2 mol% CoCl₂(PPh₃)₂,
1.5 equiv Bu₃SnCl, 1.6 equiv PMHS,
3 equiv KF, 3 equiv 18-crown-6,
1 mol% TBAF, 9 mol% hydroquinone,
toluene, 100–110 °C, 24 h, sealed tube

or 2 mol% CoCl₂(PPh₃)₂,
1.5 equiv Bu₃SnH, THF, 65 °C, 12 h
9 mol% hydroquinone, sealed tube

Entry	R	Products	Yield ^a (ratio of a/b) ^b	
			Bu ₃ SnCl/KF/PMHS	Bu ₃ SnH
1	CH ₂ CH ₂ CH ₂ OH (7)	15a/15b	45% (1.9/1)	–
2	CH ₂ OTHP (2)	10a/10b	51% (1.5/1)	65% (1.5/1)
3	C(CH ₃) ₃ (5)	13a/13b	39% ^c (1/99)	96% ^d (1/9)
4	CH ₂ OTBS (6)	14a/14b	31% (1.4/1)	–

^a Yields refer to spectroscopically pure products unless otherwise noted.

^b Isomeric ratios were determined by ¹H NMR analysis of the crude reaction mixture.

^c Reaction was run in THF.

^d Yield determined by ¹H NMR using HDMS as an internal standard.

reactions displayed a blue color when progressing as desired. When this characteristic blue color was present, reaction yields were consistent from run to run. On occasions when the mixture did not go to blue, no reaction was always the result.

We also explored the hydrostannation of **2** in the presence of catalytic amounts of [RhCl(COD)]₂, RhCl(CO)(PPh₃)₂, or RuCl₂(PPh₃)₄.⁹ Unfortunately, all three of these catalysts proved incompatible with not only water, but with the Bu₃SnCl/PMHS/KF/18-crown-6 combination in general. Additional studies are aimed at identifying the exact offender as well as conditions that could be amenable to the use of these catalysts.

Perhaps our most interesting results came about during the application Bu₃SnCl/PMHS/KF/18-crown-6 conditions to Mo-catalyzed hydrostannations. Kazmaier has shown that Mo(CO)₃(NCt-Bu)₃ (aka MoBl₃) catalyzed hydrostannations typically favor formation of the proximal vinylstannanes.¹⁰ As illustrated in Scheme 1, this regiochemical preference has been explained by the addition of an intermediate Mo–Sn species across the triple bond whereby the sterically demanding molybdenum fragment ends up on the less hindered side of the alkyne (distal to R_L). This of course, places the triorganotin moiety on the more hindered side of the alkyne and forms the proximal stannane as the major isomer.^{10c} To the best of our knowledge though, all of the reported MoBl₃ hydrostannations were carried out on heteroatom substituted and/or highly polarized alkynes. As such, we used our own study herein to address the more global question of how alkynes that are incapable of heteroatom direction would perform under MoBl₃ catalysis.

To begin our examination, THP-protected propargyl alcohol (**2**) was subjected to Bu₃SnCl/PMHS/KF/18-crown-6 and 5 mol % MoBl₃ in different solvents and at different temperatures (Table 3). After 18 h, reaction of **2** in THF at 65 °C afforded a 4:1 ratio of the proximal to distal vinylstannanes (**10a** and **10b**) in 57% yield (based on 13% recovered **2**). Reaction in toluene at 110 °C resulted in disappearance of the alkyne after 24 h. However, the combined yields of **10a** and **10b** was lower (47%), although the ratio of **10a/10b** was higher (8:1). In contrast, running the reaction in benzene at 80 °C for 24 h gave the highest yield (66%) of the proximal isomer albeit with a return to the 4:1 ratio of **10a/10b** (82% combined yield).

Using the highest yielding solvent, benzene, several alkynes were subjected to MoBl₃ catalyzed hydrostannations. Most alkynes behaved well giving good to excellent yields of the vinylstannane products (Table 4). The ratio of proximal to distal isomer also

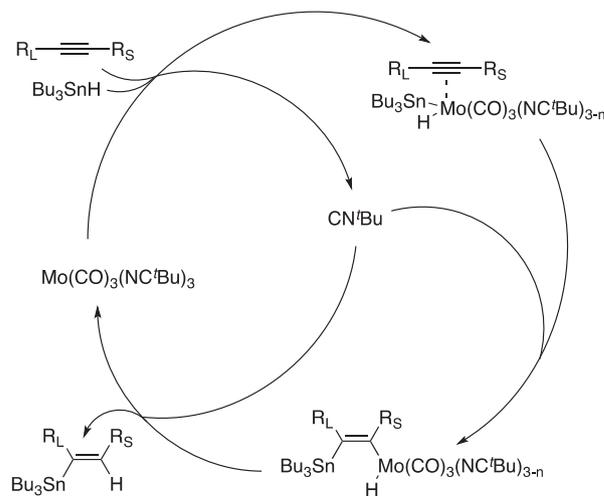
**Scheme 1.** Mechanism of MoBl₃-catalyzed hydrostannations proposed by Kazmaier and co-workers.¹⁰

Table 3
Optimization of MoBI₃-catalyzed hydrostannations

Entry	Solvent	Temperature (°C)	Time (h)	Yield ^a (ratio of 10a/10b) ^b
1	THF	65	18	57% ^c (4/1)
2	Toluene	110	24	47% (8.2/1)
3	Benzene	80	24	82% (4/1)

^a Yield refer to spectroscopically pure products unless otherwise noted.^b Isomeric ratios were determined by ¹H NMR analysis of the crude reaction mixture.^c Based on 13% recovered.

increased when the alkyne had a more bulky substituent (entry 1 vs 2 and 3 vs 4), as should be expected from Kazmaier's model.

Comparing entries 3 and 6 of Table 4 is also interesting. Under our Bu₃SnCl/KF/18-crown-6/PMHS conditions the proximal to distal ratios of the products are the same for both substrates, suggesting that heteroatom direction is not a regiochemical driver. Yet, the hydrostannation of 3,3-dimethyl-1-butyne under Kazmaier's conditions (Bu₃SnH)¹⁰ (Table 4, entry 6) afforded a 2:1 mixture favoring the distal isomer. Furthermore, hydrostannation of **5** in THF at 65 °C under Bu₃SnCl/PMHS/KF/18-crown-6 protocols, saw the proximal to distal ratio change to 1.3:1. Similarly, MoBI₃ catalyzed hydrostannation of this alkyne in benzene at 80 °C under Bu₃SnF/PMHS/TBAF(cat.) protocol produced proximal and distal isomers in 1:1.2 ratio and 1:2.5 when THF was used as solvent for this same protocol.¹⁴ Thus the regiochemical course of these MoBI₃ catalyzed reactions, and in turn the general reliability of the proposed mnemonic, is dependent on reaction conditions. Here the mnemonic held best when reactions were run in benzene and Bu₃SnCl/KF/18-crown-6/PMHS was used to generate Bu₃SnH in situ. Changing the solvent to THF lowered the regioselectivity.¹⁵ When Bu₃SnH is used directly proximal selectivity may benefit from (if not requiring) a nearby heteroatom.

Table 4
MoBI₃-catalyzed hydrostannations

Entry	R	Products	Yield ^a (ratio of a/b) ^b	
			Bu ₃ SnCl/KF/PMHS	Bu ₃ SnH
1	CH ₂ OH (1)	9a/9b	47% (2/1)	94% (8.1/1) ^c
2	CH ₂ OTHP (2)	10a/10b	82% (4/1)	98% (>19/1) ^c
3	C(CH ₃) ₂ OH (8)	16a/16b	55% (2.5/1)	81% (2.3/1)
4	C(OH)(CH ₃)Ph (4)	12a/12b	91% (6/1)	99% (2.8/1)
5	CH ₂ CH ₂ CH ₂ OH (7)	15a/15b	48% (1.3/1)	—
6	C(CH ₃) ₃ (5)	14a/14b	63% ^d (2.5/1)	93% ^d (1/2.1)

^a Yields refer to spectroscopically pure products unless otherwise noted.^b Isomeric ratios were determined by ¹H NMR analysis of the crude reaction mixture.^c Data from Ref. ¹⁰.^d Yield determined by ¹H NMR using HDMS as an internal standard.

Conclusions

We have demonstrated that Bu₃SnCl/PMHS/KF can serve as an in situ tin hydride source for hydrostannation reactions under several nonPd transition metal catalysts. Key to the success of these moisture sensitive reactions is the use of 18-crown-6 and dry (rather than aqueous) KF. Our results show for the first time that MoBI₃ catalyzed hydrostannations of nonheteroatom containing alkynes can afford proximal vinyltins as the major product, although further studies are clearly required to have a thorough understanding of the mechanistic origins of the observed regiochemical outcomes.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.08.005.

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