SYNTHESIS OF VINYLSTANNANES WITH *IN SITU* GENERATED ORGANOTIN HYDRIDES

By

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ABSTRACT

SYNTHESIS OF VINYLSTANNANES WITH *IN SITU* GENERATED ORGANOTIN HYDRIDES
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Vinylstannanes are useful intermediates in organic chemistry as they undergo an important C-C bond forming reaction called the Stille coupling. Even though, these species can be accessed by a number of processes, transition-metal-catalyzed hydrostannations of alkynes with organotin hydrides are among the more synthetically attractive methods for their syntheses. Nonetheless, a number of issues, including storage, cost and toxicity associated with organotin hydrides besets the usefulness of hydrostannation protocols. Strategies have been developed to generate organotin hydrides *in situ* so as to carry out these transformations in more benign ways. Most of these strategies suffer from functional group compatibility issues or require excess tin. Here in, we describe protocols that could be efficiently carried out with *in situ* generated organotin hydrides under a number of transition-metal catalysts using less toxic organotin fluorides or less expensive organotin chlorides. We have also demonstrated a Lewis-acid mediated one-pot allylation-hydrostannation protocol to access structurally complex vinylstannane products that involves a recycling of the organotin species generated during the allylation step.

To my father Bivash Kumar Ghosh and my mother Archana Ghosh

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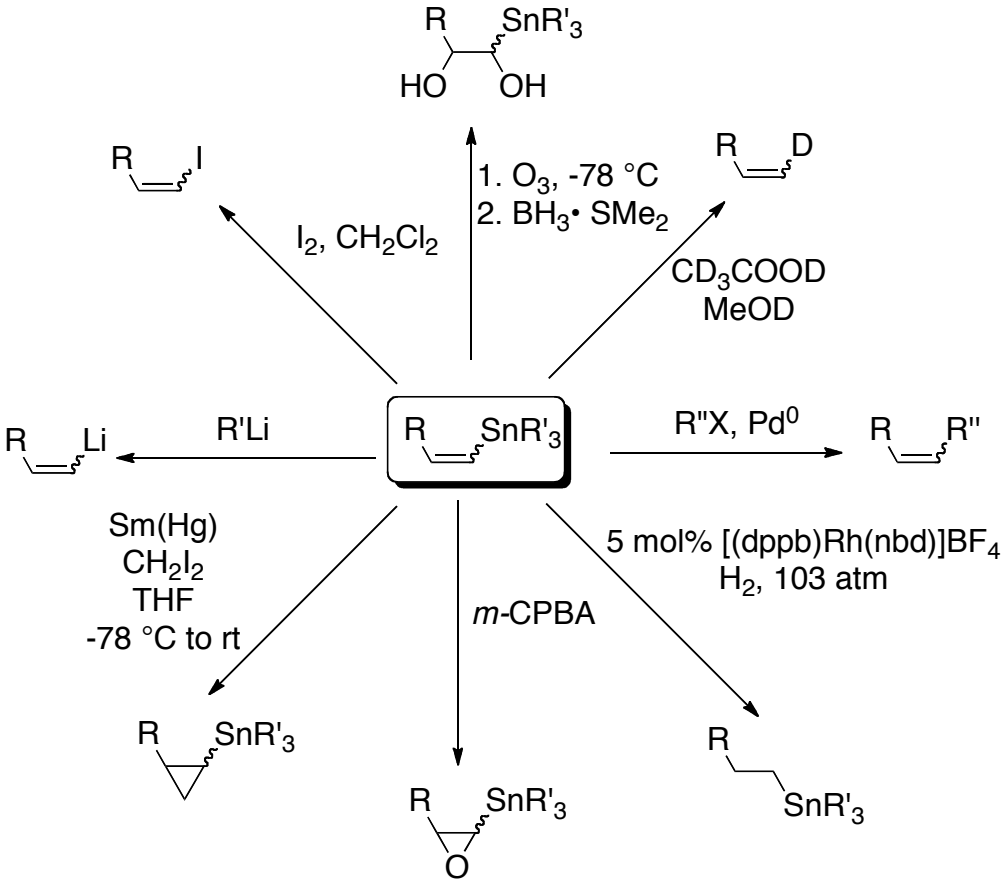
AIBN	2,2'-azobisisobutyronitrile
APCI	Atmospheric pressure chemical ionization
DMSO	Dimethyl sulfoxide
EI	Electron ionization
ESI	Electrospray ionization
h	hour
HMDS	Hexamethyldisiloxane
HRMS	High resolution mass spectrometry
NMR	Nuclear magnetic resonance spectroscopy
PMHS	Polymethylhydrosiloxane
Pt	Platinum
r.t.	Room temperature
TBAF	Tetrabutylammonium fluoride
TBAI	Tetrabutylammonium iodide
THF	Tetrahydrofuran
THP	Tetrahydropyranyl
TBS	*t*-butyldimethylsilyl
TLC	Thin layer chromatography
TMS	Trimethylsilyl
TMSA	Trimethylsilyl acetylene

Chapter 1. An introduction

Vinylstannanes constitute an important class of organic compounds. These species can undergo a variety of reactions, some that are specific to the double bond and others that are specific to the stannane.[1] Examples of such reactions are shown in Figure 1.

Figure 1. Reactions of vinylstannanes



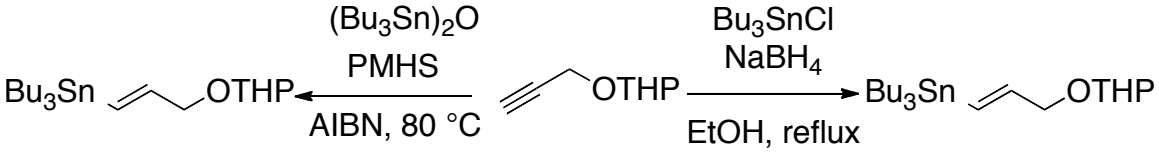
Among the most important type of reactions that this class of compounds undergoes are Stille couplings where these species form a C-C bond with organic electrophiles (R''X) when treated with a palladium (0) catalyst.[2] This reaction was pioneered by J. K. Stille in 1978. Over the last three decades, the Stille reaction has

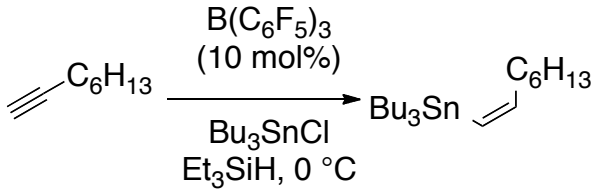
been the subject of further developments,[2c,d,e] mechanistic investigations[2f] and numerous applications in natural product syntheses.[2g]

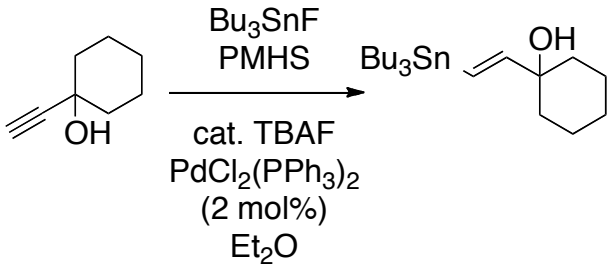
Vinylstannanes are important substrates for the Stille reactions. Due to their mild and neutral conditions, hydrostannation reactions of alkynes or allenes are among the most widely used methods for generating vinylstannanes. The reaction entails an overall addition of a tin hydride moiety across carbon-carbon multiple bonds. Organotin hydrides are the most commonly used reagents for such reactions. Nonetheless, there exist a number of problems in reactions that involve the use of organotin hydrides. First of all, commercial organotin hydrides are expensive (tributyltin hydride, $550.20/ 500g).[58] Organotins are also fairly prone to oxidation and hence, unstable. The toxic by-products can also create disposal issues. Similarly, tin by-products are often difficult to separate from non-polar organic products. While several methodologies involving use of catalytic amounts of tin and/or *in situ* generated tin hydrides have been developed for reductions and other related reactions,[3] only a handful of such methods have been developed for hydrostannation reactions. To the best of our knowledge, there are four hydrostannation protocols that use *in situ* generated organotin hydrides (Scheme 1). The first exploits the ability of polymethylhydrosiloxane (PMHS) to reduce bis(tributyltin) oxides.[4a] The second approach uses borohydrides to reduce tributyltin chloride.[4b] The third protocol utilizes Et_3SiH in conjunction with catalytic $B(C_6F_5)_3$ and generates the corresponding tin hydride by reducing tributyltin chloride.[4c] Our group documented the

fourth method, the basis of which lies in the ability of hypercoordinate polymethylhydrosiloxane to reduce less reactive organotin halides (organotin chlorides and their less toxic fluoride counter parts) to make corresponding tin hydrides *in situ*.[4d]

Scheme 1. *In situ* generated organotin hydrides in hydrostannations





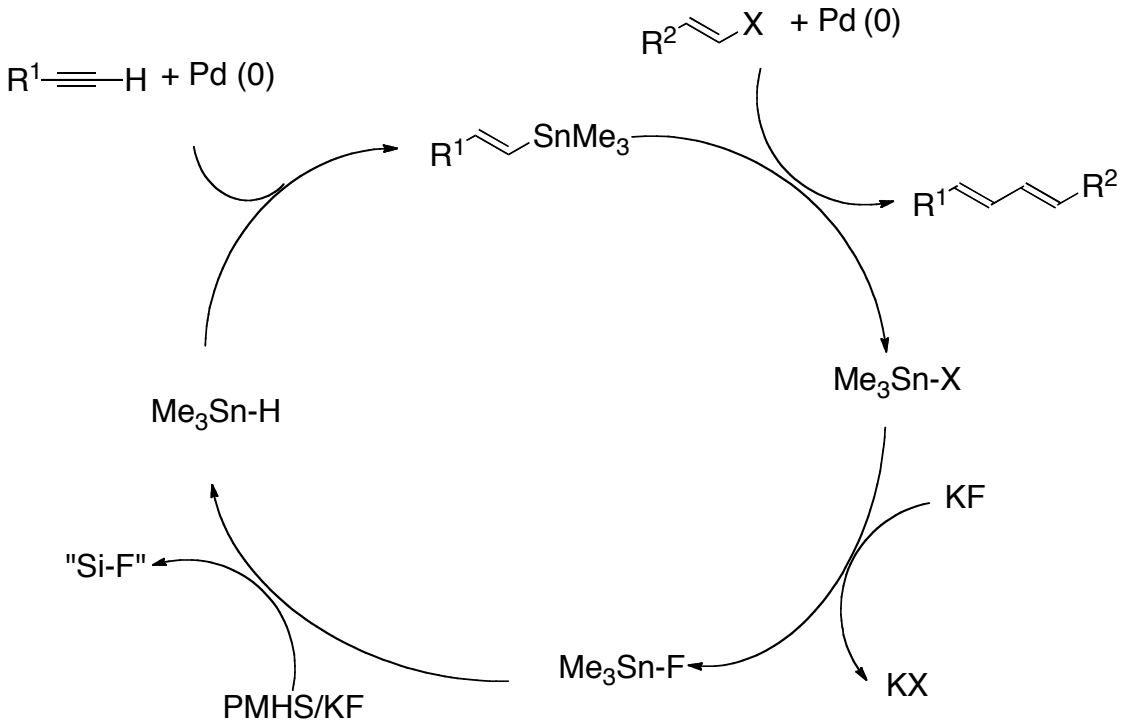


The first three protocols have their own disadvantages. Theoretically, one equivalent of organotin oxide should produce two equivalents of the corresponding tin hydride. However, in practice, only one equivalent of organotin hydride can be accessed from such reactions at room temperature. To generate the other equivalent of organotin hydride, distillation temperature is required. Moreover, many potentially useful organotin oxides (e.g. $(Me_3Sn)_2O$) are not commercially available. Hydrostannation methods involving $NaBH_4$ can have functional group (i.e. carbonyls, halogens etc.) compatibility issues. Similarly, processes involving $B(C_6F_5)_3$ might not be suitable for substrates

sensitive to Lewis acidic conditions (a substrate with Lewis basic functional groups). The hydrostannation protocol involving hypercoordinate PMHS is more general and can be applied to a wide array of alkynes in free radical and palladium-catalyzed hydrostannations producing vinylstannanes in good to excellent yields.

In 2001, our group showed that the PMHS mediated hydrostannation protocol can, also, be successfully extended to a one-pot hydrostannation/Stille coupling sequence catalytic in tin as illustrated in Scheme 2.[5] In described palladium mediated protocols, Bu_3SnH can reduce vinyl halides that are substrates for the subsequent Stille reaction. This unwanted process could be accelerated if the palladium catalyst has strong σ-donor ligands. Most palladium based hydrostannation catalysts have such ligands (e.g. $PdCl_2(PPh_3)_2$). Thus, if more than one Pd catalysts are used, proper tuning of the catalysts is essential.[6] An alternative to this could be a method that uses different non-palladium based catalysts for the hydrostannation and palladium catalyst for the Stille steps. However, in order to establish such an alternative protocol, development of non-palladium based hydrostannation processes is essential. In subsequent chapters, such non-palladium transition metal catalyzed hydrostannation protocols with *in situ* generated organotin hydrides will be presented.

Scheme 2. One-pot hydrostannation/Stille coupling sequence



The one-pot hydrostannation/Stille protcol recycles the tin waste of the Stille process back to organotin hydride, which, then, can undergo another cycle beginning with the alkyne hydrostannation. We wanted to extend this idea to other processes that use organotin compounds. We chose allylation chemistry for this purpose. Here in, we demonstrate a Lewis-acid mediated one-pot allylation-hydrostannation sequence that involves a tin recycling step. We, then, plan to develop a Lewis acid mediated hydrostannation protocol that uses these *in situ* generated organotin hydrides.

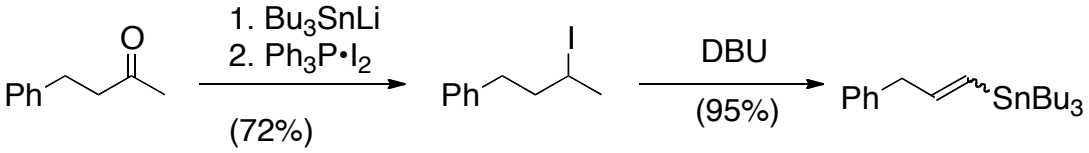
Chapter 2. Non-palladium transition-metal-catalyzed hydrostannation reactions with Bu_3SnF / PMHS/ catalytic TBAF as an *in situ* tin hydride source.

2.1 Introduction.

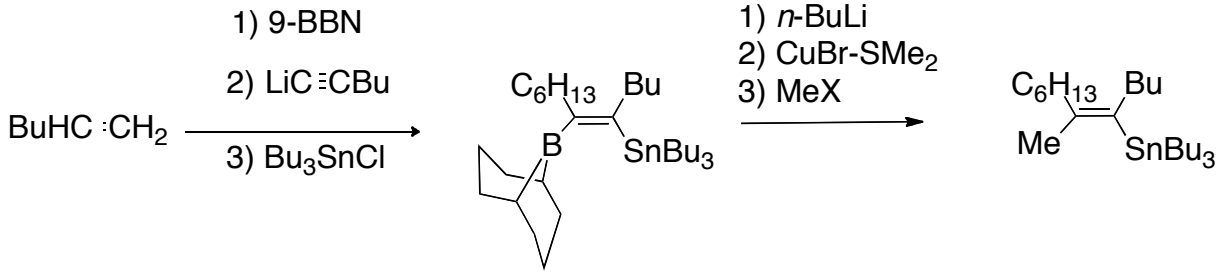
Organostannanes are of tremendous synthetic utility as building blocks in organic chemistry due to the large number of carbon-carbon bond forming reactions and other important structural transformations these molecules undergo.[1] Vinylstannanes represent one important class of organostannane compounds. Owing to their utility, a variety of ways of forming carbon-tin bonds in such species have been developed. The most widely used methods are: Elimination reactions,[7] Stille-type coupling reactions,[8] reactions of lithium trialkylalkynylborates with tin electrophiles,[9] reactions of organometallic compounds with tin halides,[1] nickel(0)-catalyzed carbostannylation reactions of alkynes,[10] reactions of distannanes with alkynes or allenes,[11] hydrogenation and hydrometalation reactions of alkynylstannanes,[12] and hydrostannylation reactions.[13] Some of these reactions are illustrated in Scheme 3.

Scheme 3. Synthesis of vinylstannanes using different methods

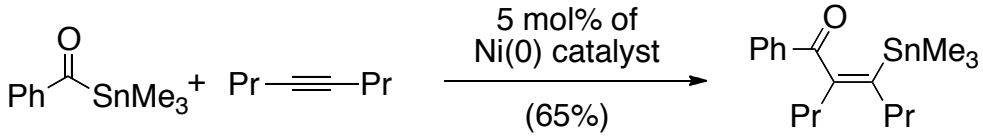
Elimination reactions[7]



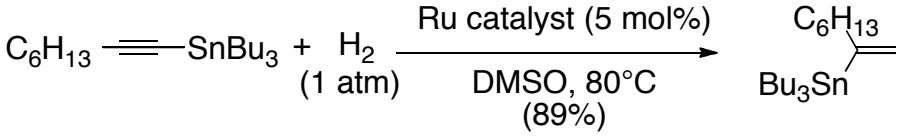
Reactions of lithium trialkynylborates with tin electrophiles[9]



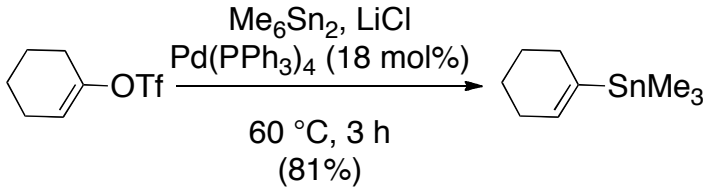
Nickel-catalyzed carbostannylation reactions[10]



Hydrogenation of alkynylstannanes[12]



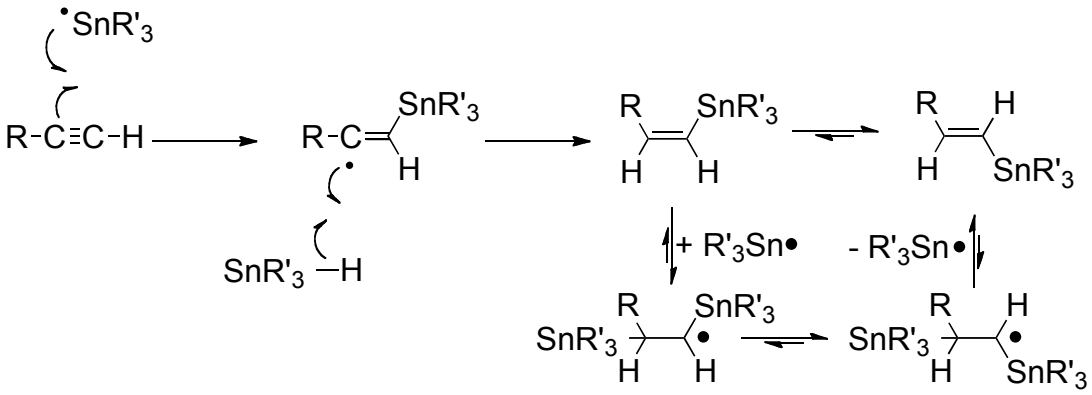
Stille-type coupling peocess[8]



The last and among the most frequently used strategies for the generation of vinylstannanes is hydrostannylation (a. k. a. hydrostannation) of an alkyne (or an allene), which is the overall addition of a tin hydride species to the organic moiety. The major advantage of this method is the mild and neutral conditions that allow for the formation of functionally rich vinyl organostannanes. There are three general modes of addition of a tin hydride species to C–C multiple bonds; hydrostannation under free-radical conditions, stannylmetalation-protonation of alkynes (or allenes), and, transition metal (or Lewis acid[48]) catalyzed hydrostannation reactions of alkynes (or allenes).

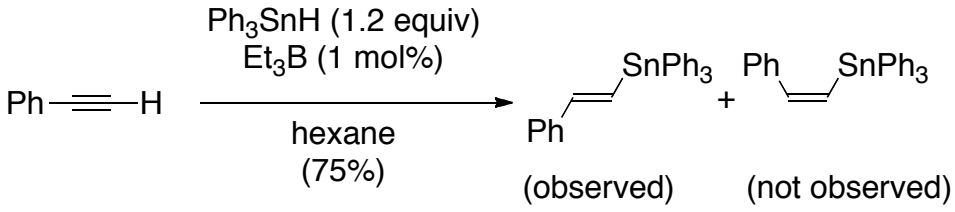
The hydrostannation of alkynes under free radical condition has been widely used.[14] With alkynes, the reaction follows a radical chain mechanism and is typically carried out at 60-80°C with a radical initiator like AIBN. The reaction can also be carried out at room temperature or below by initiation with UV light or sonication[14a] or with trialkylborane in the presence of a trace amounts of O_2.[14b] In these reactions, a (*Z*)-stannane is formed initially, because the tin hydride donates its hydrogen at the less hindered face of the vinyl radical.[1]

Figure 2. Mechanism of radical hydrostannation reactions



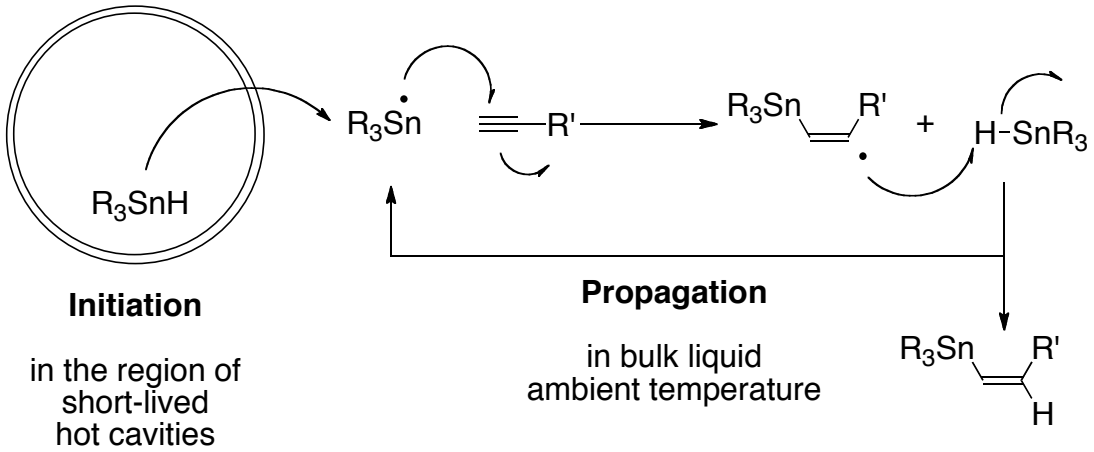
The initially formed kinetic (*Z*)-product is often equilibrated to the thermodynamic (*E*)-product by further reversible addition-elimination of a tin radical under the reaction conditions, particularly at elevated temperatures or prolonged reaction times (Figure 2). Good stereoselectivity may be obtained if this equilibrium leads to a thermodynamic product favored by other factors, especially, sterics. Good stereoselectivity has been reported by the use of catalytic amounts of Et_3B (1M in hexane, 0.1 mmol) to a solution of acetylenic compounds (1 mmol) and Ph_3SnH (1.2 mmol) in toluene producing vinyl stannanes with 8:2 to 7:3 E/Z ratios.[14b] Phenylacetylene and trimethylsilylacetylene provide *E*-isomers exclusively (Scheme 4). Bu_3SnH reactions with the same terminal alkynes need longer reaction times and yield corresponding vinylstannaes in lower yields. Non-terminal alkynes react much slower and produce *Z*-vinylstannanes as the major products.

Scheme 4. Et_3B induced radical addition of organotin hydrides to alkynes



On the other hand, sonochemical initiation of tin radical species and subsequent hydrostannation reactions can be smoothly initiated at temperatures under 0 °C (Figure 3).[14a] Reactions of excess terminal alkynes with triphenyltin hydride under argon atmosphere result in good to excellent yields of the vinylstannane products with excellent (*Z*) selectivity. Irradiation of homogeneous liquids with high-intensity ultrasound produces localized super-heated sonochemical cavities. These cavities can produce temperature as high as 2000 °K. It is hypothesized that an initiating tin radical is formed in these "hot cavities". The species, then, diffuses to the bulk medium after the adiabatic collapse of the cavity. The product forming propagation steps occur in the bulk medium.[14a]

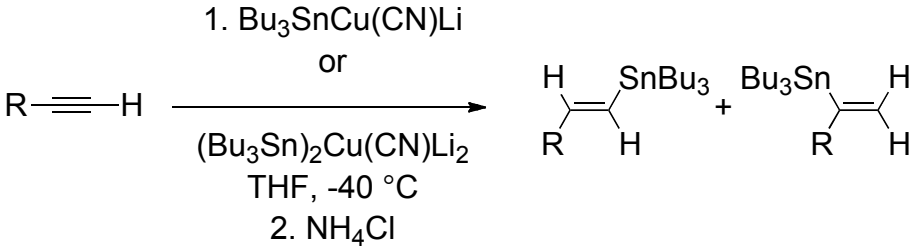
Figure 3. Sonochemical hydrostannation of terminal alkynes



Despite these positive outcomes, one area where the radical hydrostannation reactions really lack general applicability is in the discrimination of various sites of unsaturation (alkene vs. alkyne) or reductions (alkene vs. halogen reduction) that can lead to undesired side products.[13] Stannyl metalation and transition-metal catalyzed hydrostannation overcome these problems.

Stannylmetalation of alkynes may be divided into two broad categories: (1) Stoichiometric stannylcupration[15,16] (Scheme 5) and (2) stannylmetalation using transition metal catalysts.[17] Both lead to *syn* addition of the bi-metallic species. Stoichiometric stannylcupration can be performed with lower[15] or higher[16] order stannylcuprates. The stereochemistry of addition depends not only on the substrates but also on the nature of the cuprates.

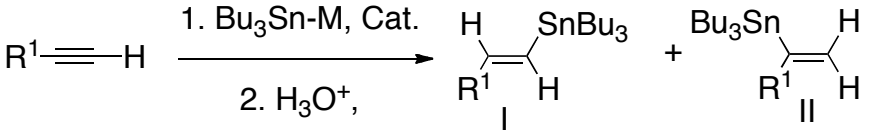
Scheme 5. Stoichiometric stannylcupration



Copper sources are the most popular choice for catalysts in transition metal-catalyzed stannylmetalation with the second metal often being Al, Zn, Mg or B. Pd(II) catalysts in the stannylation of alkynes have also been used. The regiochemistry of the transition metal-catalyzed stannylmetalation depends on a number of factors including the metal partner, catalyst, solvent and other additives. Several problems beset tin-

based bis-metallation reactions of alkynes. Reactions utilizing tin-based reagents where the metal is Al^{2+}, Mg^{2+}, Zn^{2+}, Mn^{3+} or Cu^{4+} often require a two or three fold excess of the reactant to achieve a high consumption of the alkyne. Following the stannylmetalation, most excess organotin reagent gets converted to hexaalkylditins, which often complicate product isolation. Addition of Sn-Cu reagents to alkynes requires consumption of one vinyl center by *in situ* protonolysis to overcome an unfavorable adduct-alkyne equilibrium. Regiospecificity is high for some stannylation reactions (Sn-Cu^{4+}, Sn-Zn^{2+}, Sn-Si) but low for others (Sn-Al^{2+}, Sn-Mg^{2+}) (Scheme 6).[17b]

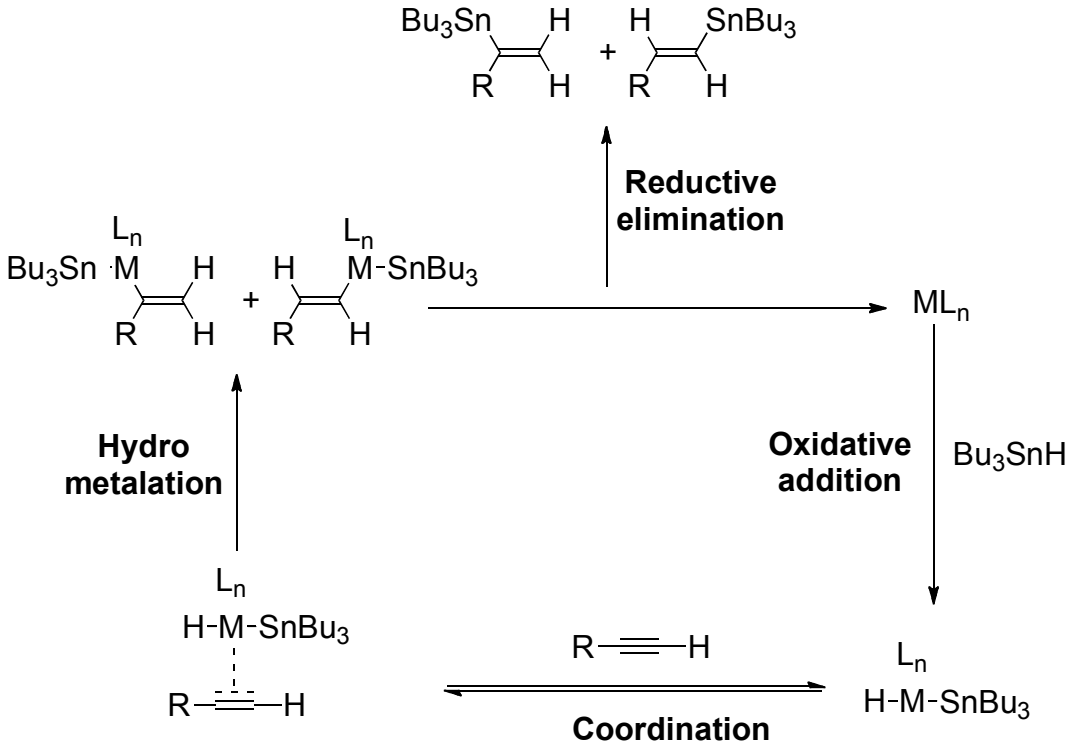
Scheme 6. Transition-metal catalyzed stannylmetalation of alkynes



Substrate	Reagent	Catalyst	Yield	Ratio	
				I	II
R = $PhCH_2OCH_2CH_2$	$(Bu_3Sn)_2CuCN$		78%	36	64
	$Bu_3SnMgMe$	CuCN	88%	100	0
	$Bu_3SnMgMe$	$CuBrSMe_2$	23%	34	66
	$Bu_3SnAlEt_2$	CuCN	86%	81	19
	$(Bu_3Sn)_2Zn$	CuCN	63%	26	74
	$(Bu_3Sn)_2Zn$	$Pd(PPh_3)_4$	81%	14	86

In 1987, Oshima and co-workers first reported a Pd-catalyzed hydrostannation protocol of alkynes.[33] Since then, transition-metal-catalyzed hydrostannation reactions have become among the most frequently used hydrostannation procedures. Hydrostannations under transition-metal catalysis occur via *syn* addition as a consequence of the reaction mechanism (Figure 4). In many cases, high regioselectivities are also observed based on a combination of both steric and electronic factors.[13]

Figure 4. Mechanism of transition-metal catalyzed hydrostannations



Mechanistically, organotin hydride oxidatively adds to the metal catalyst in the catalytic cycle followed by coordination to the triple bond of the alkyne, which may, then, undergo hydrometalation to give a vinyl metal followed by reductive elimination.[13,19] In

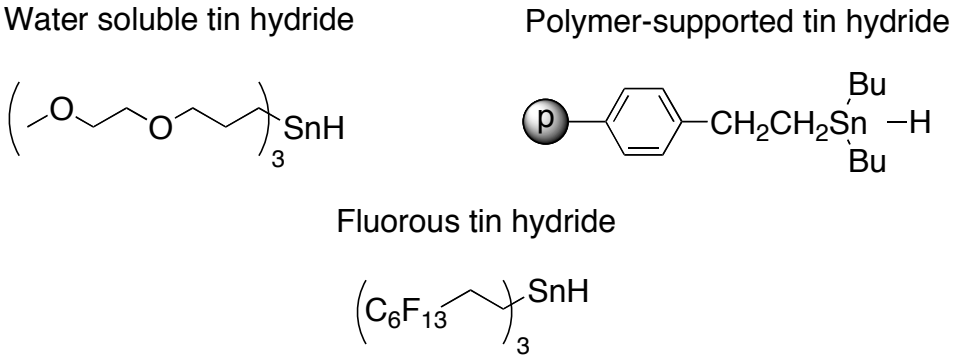
practice, the coordination of the alkyne to the metal could also take place prior to the oxidative addition. Although hydrometalation is shown as the initial reduction step in the cycle, stannylmetalation-reductive elimination may also occur. The process allows a *syn* addition of a tin hydride moiety to the alkyne resulting in the generation of proximal (a.k.a. internal) and distal (*E*) vinylstannanes.

Pd is the most popular catalyst choice for the hydrostannation of alkynes with $Pd(PPh_3)_4$ and $PdCl_2(PPh_3)_2$ being most widely used. However, other Pd sources have been successfully utilized including $Pd(OAc)_2/PPh_3$,[18] $Pd_2(dba)_3/PPh_3$,[20] $PdCl_2(dppe)$,[20] and, $Pd(OH)_2/C$.[21] Besides Pd, a number of catalysts based on Mo[22] and Rh[23] have been described. A limited number of examples of Ni, Co, Pt and Ru have also been documented.[23,24] In metal-catalyzed hydrostannation reactions, the most commonly used hydrostannation reagent is tributyltin hydride due to its facile reactions and commercial availability. Trimethyl and triphenyltin hydride have also been used, the former is toxic and volatile while reaction of the latter with alkyne is more sluggish than its tributyl counterpart.

Although metal-catalyzed hydrostannation is an attractive procedure in producing vinylstannanes, the use of organotin hydrides as the tin source can be problematic. Organotin hydrides are expensive, unstable and toxic. Moreover, separation of the tin by-products from non-polar organostannane products often poses a serious challenge for organic chemists. Water soluble[25] or polar[26] tin hydride can partly overcome the

problem as shown by several research groups. Organotin reagents based on cross-linked polystyrene of large pore size have also been developed.[27] This reagent is insoluble in common organic solvents and can be easily separated after its use simply by filtering and can be regenerated with *n*-octyl bromide and subsequent reduction. Use of fluorous tin reagents has also been exploited to overcome separation issues.[28] Nonetheless, none of these approaches has been widely embraced by others (Figure 5).

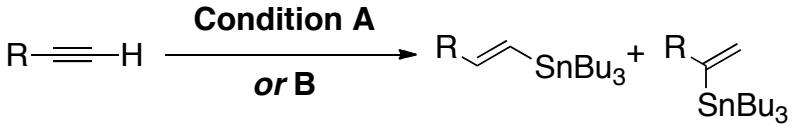
Figure 5. Organotin hydrides to solve separation and/or related issues



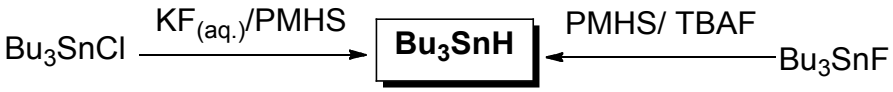
Another approach to resolve the problems related to cost, storage, toxicity and purification issues associated with organotin hydrides is *in situ* generation of the tin hydrides. As we have discussed in the previous chapter, there are only a few protocols available for hydrostannations using *in situ* generated organotin hydrides.[4] Fluoride catalyzed silane reductions of organotin halides are applicable to a wide array of alkynes and devoid of the issues associated with other protocols as described in Chapter 1. Fluoride-catalyzed silane reductions of organotin halides can be performed

in two different modes. One mode uses solid organotin fluoride polymers to generate corresponding organotin hydrides via silane reduction. The second protocol utilizes organotin chlorides for the same purpose. These protocols are illustrated in Scheme 7. Organotin chlorides are less expensive and commercially more accessible compared to their corresponding hydrides. On the other hand, organotin fluorides can be easily prepared from their chloride counterparts.[59] However, organotin fluorides are less toxic than the corresponding chlorides. Unlike their chloride counterparts, they are not readily absorbed through the skin and can be more easily filtered and disposed of. Given these advantages associated with organotin fluorides, a non-Pd transition-metal catalyzed version of the hydrostannation chemistry involving organotin fluorides was deemed worthwhile due to the reasons as discussed in Chapter 1.

Scheme 7. Fluoride-catalyzed silane reductions of organotin halides



Condition A	Condition B
Bu_3SnCl (1 mmol) PMHS (2 equiv) aq. KF (2 mmol) cat. Bu_4NF (1 mol%) $(Ph_3P)_2PdCl_2$ (1 mol%) Et_2O	Bu_3SnF (2.1 equiv) PMHS (2.1 equiv) cat. Bu_4NF (1 mol%) $(Ph_3P)_2PdCl_2$ (2 mol%) Et_2O

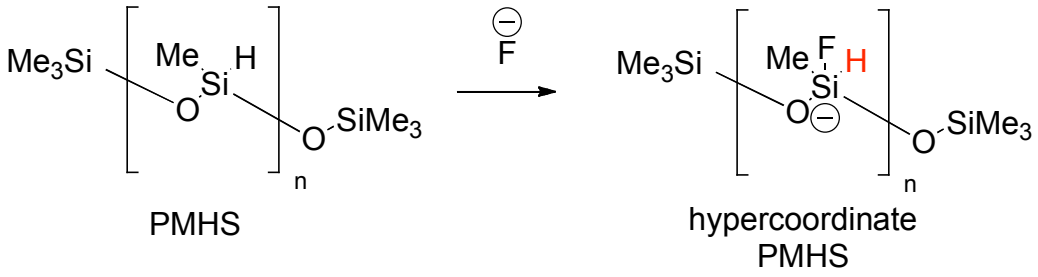


2.2 Initial Work

Kikukawa and co-workers have shown the applicability of various non-palladium catalysts in hydrostannation reactions of terminal alkynes.[23] However, further applications of these catalysts in hydrostannation reactions have not been well investigated. On the other hand, Kazmaier and co-workers demonstrated regioselective hydrostannation protocols using a molybdenum catalysts (a.k.a. $MoBI_3$). We wanted to explore the use of these catalysts in our protocols. However, the question of whether or not, the use of these transition metal catalysts would be compatible with our protocol involving *in situ* generation of tin hydride and subsequent hydrostannation was of general curiosity.

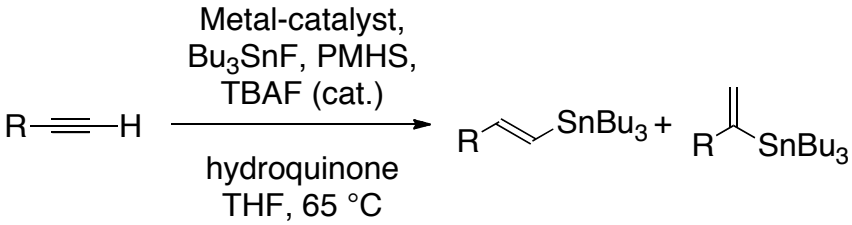
We hypothesized that the active species in the fluoride catalyzed PMHS reduction protocols is a hypercoordinate silane species, as neither R_3SnF nor R_3SnCl react with PMHS in absence of a fluoride source (Scheme 8).[30,31] However, we have not ruled out the involvement of "ate" species in this process.[32] For organotin chlorides, the reaction probably proceeds *via* the intermediacy of organotin fluorides which are reduced by hypercoordinate PMHS to organotin hydride (Scheme 7). Organotin hydrides thus generated then enter the catalytic cycle of Pd to generate desired vinylstannanes in our hydrostannation protocols.

Scheme 8. Formation of hypercoordinate PMHS



As palladium catalysts were applied successfully in our Bu_3SnF/PMHS protocols (Scheme 6, Conditions B), we were hopeful that other transition metals might also behave similarly. A general reaction scheme is given in Scheme 9.

Scheme 9. Bu_3SnF and PMHS mediated hydrostannation protocol



Tetrabutylammonium fluoride (TBAF) acts as an initial nucleophile source to PMHS. Use of hydroquinone in such reactions has been documented by Kazmaier. [22b,c,d] Hydroquinone functions as a radical inhibitor.

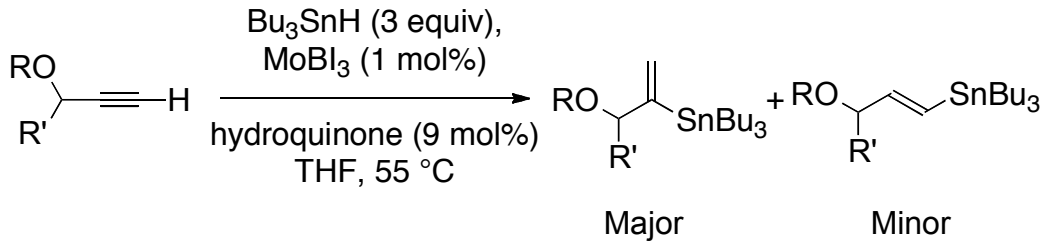
2.3 Results and Discussions

2.3.1. Molybdenum catalyzed hydrostannations

We began our study by looking at molybdenum-catalyzed hydrostannations. In 1990, Guibe found that $MoBr(allyl)(CO)_2(CH_3CN)_2$ was suitable for the hydrostannation of propargylic alcohol derivatives, but such reactions proceeded with poor regioselectivities.[22a] This problem was nicely addressed by Kazmaier and co-workers

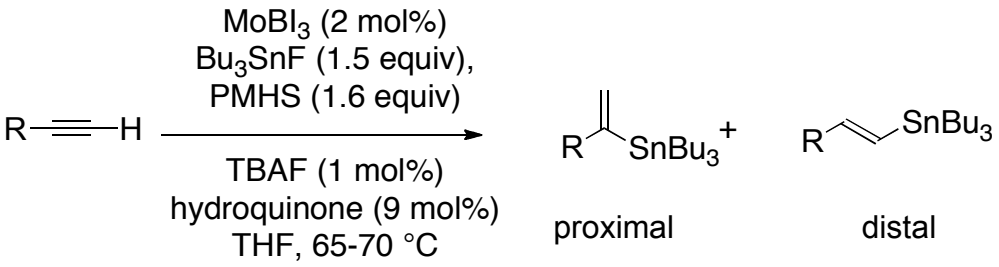
when they established that catalysis by $Mo(CO)_3(CN\textit{t}Bu)_3$ (a.k.a. $MoBI_3$) promoted the hydrostannations of variety of oxo-substituted alkynes with high selectivity for the proximal regioisomer (Scheme 10).[22 b,c,d]

Scheme 10. $MoBI_3$ as a hydrostannation catalyst



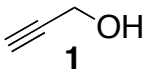
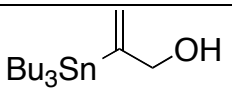
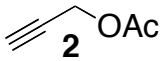
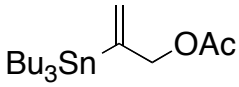
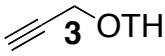
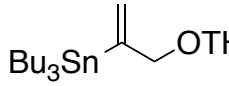
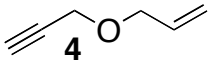
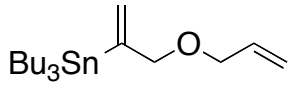
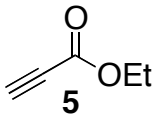
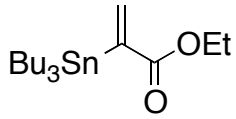
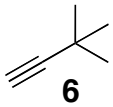
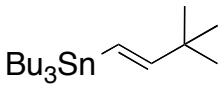
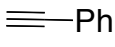
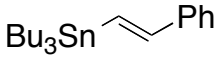
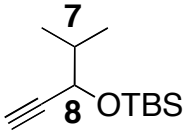
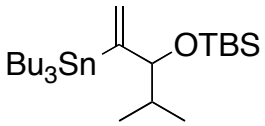
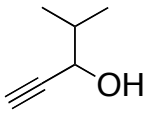
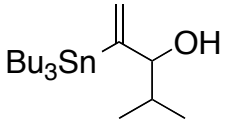
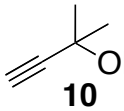
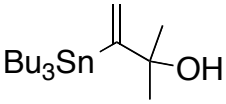
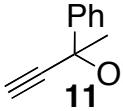
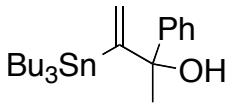
They also reported that fully active $MoBI_3$ could be recovered after column chromatography. We hoped that such robustness of the catalyst would bode well for a $MoBI_3$-catalyzed reaction with our *in situ* generated tin hydride protocols. However, it was clear that the hetero-atoms present in the substrates may likely play a directing role in these Mo-catalyzed reactions. As such we were both curious and apprehensive as to how our Bu_3SnF/PMHS conditions would fair in such hydrostannations. We were gratified to learn that our anhydrous Bu_3SnF/PMHS conditions gave positive results (Scheme 11). As shown in Table 1, a variety of alkynes were exposed to 1.5 equiv. Bu_3SnF, 1.6 equiv. PMHS, TBAF (1 mol%) and $MoBI_3$ (2 mol%) in THF.

Scheme 11. $MoBI_3$-catalyzed hydrostannations with *in situ* tin hydrides



Per Kazmaier's procedure, catalytic quantities of hydroquinone were added to suppress any free radical processes. After heating the resulting mixture at 65-70 °C, the corresponding vinylstannanes were obtained in 3 to 4 h. Consistent with the literature, derivatives of propargylic alcohol and propiolates predominantly gave the proximal vinyltins. Selectivity levels were generally comparable to those reported by Kazmaier for reactions with premade Bu_3SnH. In other ways, the hydrostannations with *in situ* generated Bu_3SnH actually held some advantages over standard protocols. For example, Bu_3SnF/PMHS reactions were typically complete in less time (3 vs 12 h) and could be run with half the amount of the catalyst used in the experiments reported by Kazmaier (1.5 equiv vs 3 equiv).[22b,c,d]

Table 1. $MoBI_3$-catalyzed hydrostannations of terminal alkynes

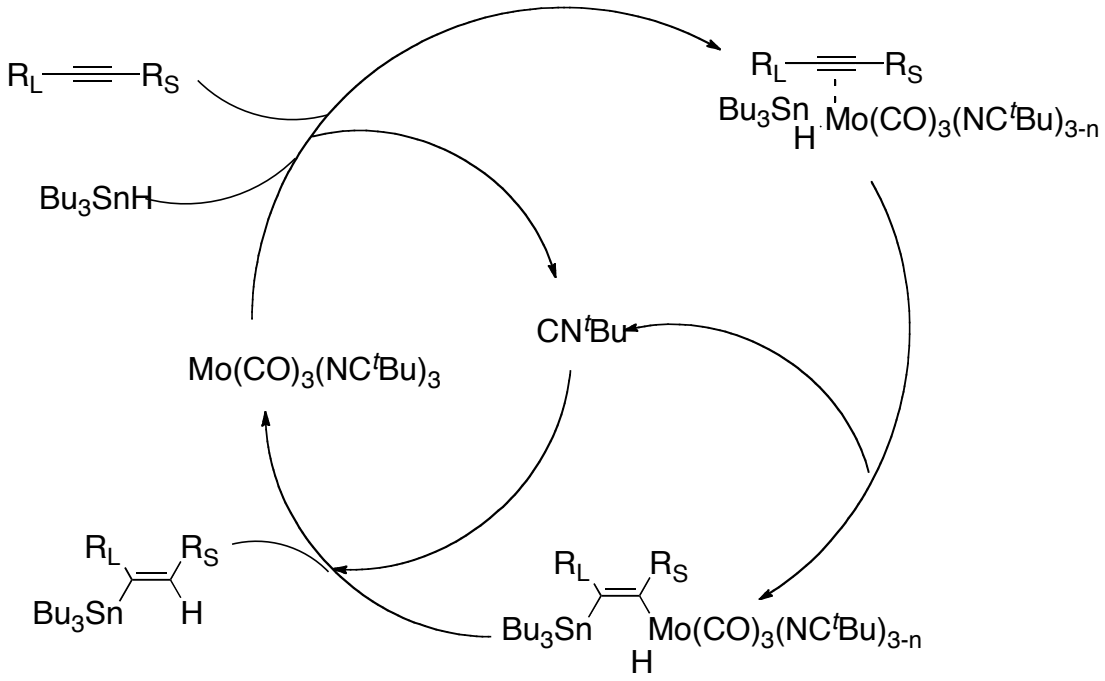
Entry	Alkyne	Major Product	Yields Bu_3SnH *(Conditions A)*	Yields Bu_3SnF/PMHS *(Conditions B)*
1	 **1**		94% Int/E (8.1:1)* **17a/17b**	90% Int/E (5:1)
2	 **2**		91% Int/E (24:1)* **18a/18b**	73% Int/E (99:1)
3	 **3**		91% Int/E (>19:1)* **19a/19b**	85% Int/E (19:1)
4	 **4**		43% Int/E (>19:1)* **20a/20b**	75% Int/E (19:1)
5	 **5**		98% Int/E (11.5:1)* **21a/21b**	92% Int/E (19:1)
6	 **6**		93% Int/E (1:2.1) **22a/22b**	57% Int/E (1:2.5)
7	 **7**		100% Int/E (1:99) **23a/23b**	88% Int/E/Z (1:1:1)
8	 **8**		57% Int/E (1.2:1) **24a/24b**	62% Int/E (3;1)
9	 **9**		86% Int/E (4:1) **25a/25b**	92% Int/E (2:1)
10	 **10**		81% Int/E (2.3:1) **26a/26b**	79% Int/E (6:1)
11	 **11**		99% Int/E (2.8:1) **27a/27b**	93% Int/E (3.7:1)

Conditions A: alkyne (1 mmoL), hydroquinone (9 mol%), catalyst (1 mol%), Bu_3SnH (3 mmoL), THF, 55-60 °C, 12 h ; Conditions B: alkyne (1 mmoL), Bu_3SnF (1.5 eq.), PMHS (1.6 eq.), hydroquinone (9mol%), $MoBI_3$ (2 mol%), THF, 65-70 °C, 3h ;* directly taken from Kazmaier's paper.

We also took the opportunity to answer some global questions surrounding substrate scope and $MoBI_3$ catalysis. To the best of our knowledge, $MoBI_3$-catalyzed hydrostannations of alkynes bearing non-heteroatom containing substituents at the propargylic positions had not been previously described by Kazmaier at the time of our study.

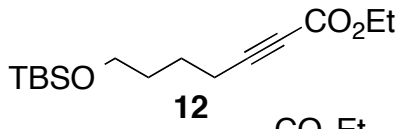
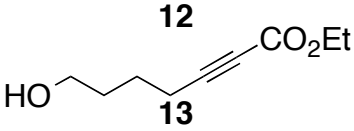
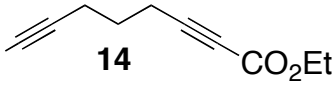
In discussing the reaction mechanism, Kazmaier suggested that insertion of alkyne into Mo-Sn bond is the product-determining step.[22c] The sterically demanding molybdenum fragment adds to the less hindered side of an alkyne (Figure 6). Any directing role of the heteroatoms was not discussed. When 3,3-dimethyl propyne and phenylacetylene (Table 1, entries 6 and 7) were subjected to the reaction conditions, the distal (*E*) vinylstannanes were the major products. We also examined propargylic alcohols that are sterically encumbered. In these cases, the proximal isomers were major, but with much lower levels of selectivity. These interesting results point toward the fact that sterics cannot be the only determining factor in product selectivity under $MoBI_3$ catalysis. Rather, it is a combination of both sterics and directing effects that decides the exact nature of product selectivity in this case.

Figure 6. Proposed mechanism of $MoBI_3$-catalyzed hydrostannations



The hydrostannation of alkynyl esters were also explored. In this case, stannylation occurred α to the ester preferentially. Our Bu_3SnF/PMHS method was comparable to that developed by Kazmaier in terms of both the isomeric ratio of stannane products and yields. It should also be noted that the isomeric ratio of stannanes thus produced is not affected by the presence of a hydroxyl group (Table 2 entry 2). The ratio also remains unchanged in the presence of a protecting group (Table 2 entry 1).

Table 2. $MoBI_3$-catalyzed hydrostannations of alkynyl esters

Entry	Alkyne	Yields	
		Bu_3SnH	Bu_3SnF/PMHS
1	 **12**	79% Int/E (3.7:1) **28a/28b**	88% Int/E (3.3:1)
2	 **13**	92% Int/E (3.8:1) **29a/29b**	81% Int/E (3.4:1)
3	 **14**	67% Int/E (2.8:1) **30a/30b**	88% Int/E (2.6:1)

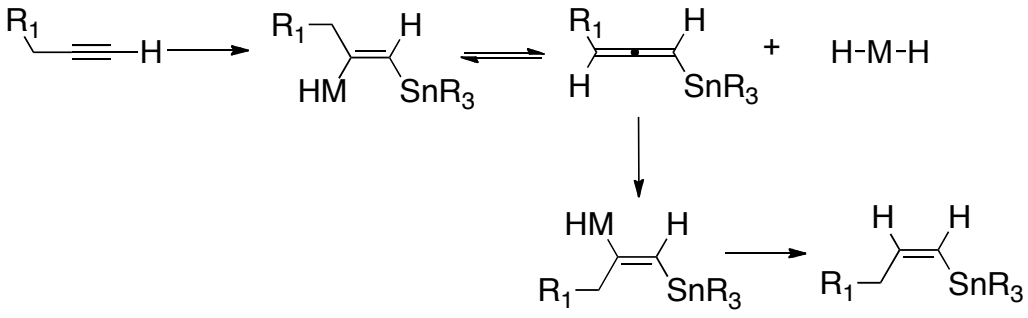
Bu_3SnH protocols: Alkyne (1 mmol), hydroquinone (9 mol%), $MoBI_3$ (2 mol%), Bu_3SnH (3 mmol), THF (1 mL), 55 °C. Bu_3SnF/PMHS protocols: Alkyne (1 mmol), hydroquinone (9 mol%), $MoBI_3$ (2 mol%), Bu_3SnF (1.5 mmol), PMHS (1.5 mmol), THF (1 mL), 55 °C. Yields refer to spectroscopically pure products.

2.3.2. Nickel catalyzed hydrostannations of alkynes

Driven, in part, by the ability of nickel to catalyze cross-couplings[2d], we next applied the conditions to hydrostannations catalyzed by $NiCl_2(PPh_3)_2$. With this catalyst, the Bu_3SnF/PMHS conditions again produced the corresponding vinylstannanes in good yields (Table 3). Use of this catalysts in hydrostannation reaction was previously documented by Kikukawa in 1988.[23] The selectivity for the propargylic derivative favored the internal isomer, as was the case under palladium catalysis. When the oxygen functionality at the propargylic position was removed, the selectivity switched to favor the *E*-isomer. In many cases, trace amounts of *Z*-isomers were also observed.

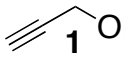
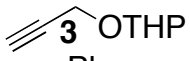
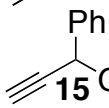
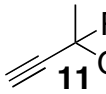
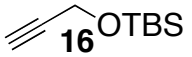
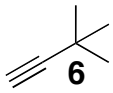
These by-products could be the result of adventitious radical reactions that were uninhibited by the hydroquinone. Alternatively, these *Z* products could be the result of β-hydride elimination followed by readdition-elimination of the catalytic species as previously proposed by Oshima and co-workers (Figure 7).[33]

Figure 7. Mechanism of formation of *Z*-isomer proposed by Oshima



According to this mechanism, alkynes having α-hydrogens can undergo a stannylmetalation followed by a reversible elimination of a metal(II) hydride. Its subsequent readdition can occur at the opposite end of the 1,2-diene. Finally, reductive elimination affords corresponding (*Z*)-stannanes. When 3,3-dimethyl propyne (**6**), which lacks α-hydrogens, was subjected to the nickel catalyzed reaction conditions, no detectable (*Z*)-stannane was observed in the NMR spectrum of the crude material. This result indicates that the processes suggested by Oshima and co-workers might be operative in our case.

Table 3. $NiCl_2(PPh_3)_2$-catalyzed hydrostannations

Entry	Alkyne	Yields	
		Bu_3SnH (*Conditions C*)	Bu_3SnF/PMHS (*Conditions D*)
1	 **1**	60% Int/E (4.1:1) **17a/17b**	70% Int/E (2.4:1)
2	 **3**	49% Int:E (7.1:1) **19a/19b**	61% Int/E (1.7:1)
3	 **15**	69% Int:E (1.3:1) **31a/31b**	87% Int/E (1.8:1)
4	 **11**	46% Int:E (1:3.4) **27a/27b**	66% Int/E (1:1.8)
5	 **16**	52% Int:E (4:1) **32a/32b**	52% Int/E (1.4:1)
6	 **6**	100% Int/E (1:4.3) **22a/22b**	83% Int/E (1:22)
7	 **7**	80% E/int/Z (10:9.1)* **23a/23b**	83% E/Int/Z(2.5:2.4:1)

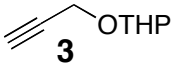
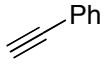
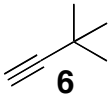
Conditions C: alkyne (1 eq.), Bu_3SnH (1.5 eq.), hydroquinone (9 mol%), catalyst (2 mol%), THF, 65 °C, 4h. Conditions D: alkyne (1 eq.), Bu_3SnF (1.5 eq.), PMHS (1.5 eq.), hydroquinone (9 mol%), Catalyst (2 mol%), THF, 65 °C, 4h. *Results taken from Kikukawa's paper.[23]

2.3.3. Cobalt catalyzed hydrostannations

Next we looked at the use of $CoCl_2(PPh_3)_2$ first put forth as a hydrostannation catalyst by Kikukawa.[23] Like molybdenum or nickel catalyst, this catalyst also gave fair to good results under our protocol with three functionally and sterically diverse alkynes.

Unfortunately, consistency was not the hallmark of these reactions. To date, the cause of such inconsistency is unclear. Somewhat usefully though, it is easy to identify when a reaction is not progressing properly as in those instances the reaction will fail to produce its typical blue color.

Table 4. $CoCl_2(PPh_3)_2$-catalyzed hydrostannations

Entry	Alkyne	Yields	
		Bu_3SnH (*Conditions E*)	Bu_3SnF/PMHS (*Conditions F*)
1	 **3**	84% Int/E (1.3:1) **19a/19b**	65% Int/E (1.5:1)
2	 **7**	40% Int/E/Z (4.8:5.3:1)* **23a/23b**	96% Int/E (1.5:1)**
3	 **6**	100% Int/E (1:5.3)** **22a/22b**	96% Int/E (1:9)

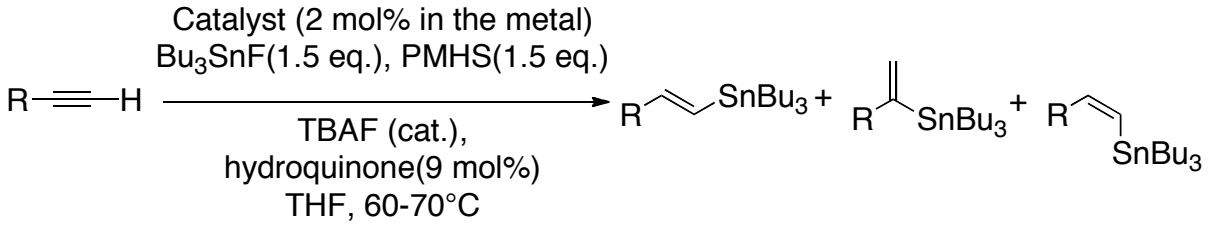
Conditions E: alkyne (1 eq.), Bu_3SnH (1.5 eq.), hydroquinone (9 mol%), catalyst (4 mol%), THF, 65 °C, 12h. Conditions F: alkyne (1 eq.), Bu_3SnF (1.5 eq.), PMHS (1.6 eq.), hydroquinone (9 mol%), Catalyst (4 mol%), THF, 65 °C, 1 d. *Results taken from Kikukawa's paper[23]. **Trace amount of (Z)-stannane was also observed.

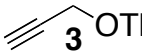
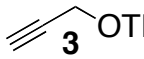
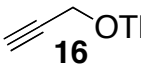
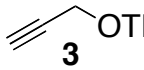
2.3. 4. Rhodium and Ruthenium catalyzed hydrostannations

Kikukawa and co-workers also found that Rh complexes, especially $[RhCl(COD)]_2$, catalyzed the hydrostannations of terminal acetylenes to give the proximal isomer regioselectively and in good yields.[23] Under our conditions, this catalyst

behaved poorly producing a trace amount of product with no detectable isomeric priority when the THP propargylic ether was used. Other Rh catalyst examined produced the *E*-isomers predominantly in modest to poor yields along with formation of trace amounts of *Z*-isomer for the alkynes tested. The use of $RuCl_2(PPh_3)_4$ was attempted, but little success and a complex mixture was obtained when THP propargylic alcohol was used as the substrate.

Table 5. Rhodium and Ruthenium-catalyzed hydrostannations



Entry	Alkyne	Catalyst	Yields	
			Bu_3SnH (Conditions G)	Bu_3SnF/PMHS (Conditions H)
1	 **3**	$[RhCl(COD)]_2$	59% Int/E (1.3:1) **19a/19b**	trace
2	 **3**	$RhCl(CO)(PPh_3)_2$	75% Int/E (1:1) **19a/19b**	17% Int/E (1:3.3)
3	 **16**	$RhCl(CO)(PPh_3)_2$	58% Int/E (1:1) **32a/32b**	55% Int/E (1:2.5)
4	 **3**	$RuCl_2(PPh_3)_4$	20% Int/E/Z (2.5:1.6:1) **19a/19b/19c**	Complex Mixture

Conditions G: alkyne (1 eq.), Bu_3SnH (1.5 eq.), hydroquinone (9 mol%), catalyst (2 mol% in metal), THF, 65 °C. Conditions H: alkyne (1 eq.), Bu_3SnF (1.5 eq.), PMHS (1.5 eq.), hydroquinone (9 mol%), Catalyst (2 mol% in metal), THF, 65 °C.

2.4 Conclusions

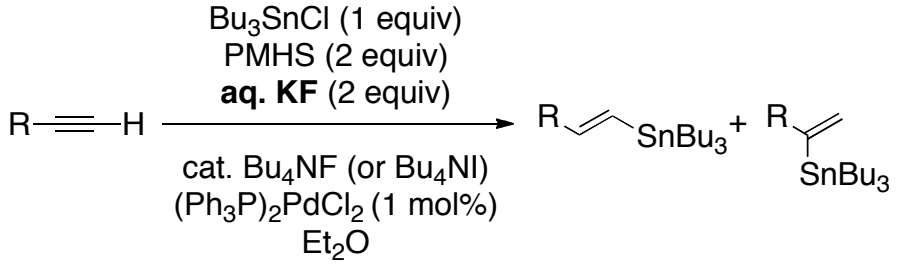
We have demonstrated that the use of Bu_3SnF/PMHS/TBAF (cat.) can serve as an effective *in situ* source of Bu_3SnH for non-Pd transition metal catalyzed hydrostannations of terminal alkynes. The use of $MoBI_3$ can be extremely useful for the formation of the proximal vinylstannanes. However, in the absence of an oxo-substitution at the propargylic positions of the alkynes, selectivity could favor the (*E*)-isomer. $NiCl_2(PPh_3)_2$ and $CoCl_2(PPh_3)_2$ were also used successfully in our protocols. While nickel-catalyzed reactions were fast and consistent, the yields were moderate in the case of a few alkynes (Table 2, entries 2, 4 and 5). Cobalt catalyzed reactions suffered from inconsistency. However, its typical blue color is useful in predicting whether the reaction is occurring successfully. Rh and Ru catalysts behaved poorly in our *in situ* protocols. Further optimizations might be necessary to use these Rh or Ru based catalysts successfully in our *in situ* processes.

Chapter 3. Non-palladium transition-metal-catalyzed hydrostannation reactions with Bu_3SnCl / PMHS/ KF / 18-crown-6 as an *in situ* tin hydride source.

3.1 Introduction.

In the last chapter we documented that Bu_3SnF/PMHS can act as an *in situ* tin hydride source for transition-metal catalyzed hydrostannation protocols. Unfortunately, besides tributyltin fluoride, most organotin fluorides are commercially unavailable. However, these organotin fluorides can be accessed from the corresponding organotin chlorides.[59] In 1999, our group demonstrsted that combination of R_3SnCl/PMHS/$KF_{(aq)}$ can substitute for R_3SnF/PMHS/TBAF reagent mix for the hydrostannations of terminal alkynes under palladium catalysis (Scheme 12).[4d] Thus, we wanted to explore other transition metal catalysts in our Bu_3SnCl/PMHS/$KF_{(aq)}$ mediated hydrostannation protocols. However, presence of water in these reactions raised concerns over how these transition metal catalysts would fair under such conditions. $NiCl_2(PPh_3)_2$, $CoCl_2(PPh_3)_2$ and $MoBI_3$ were chosen for initial screening.

Scheme 12. $Bu_3SnCl/PMHS/KF_{(aq)}$ as a hydride source in Pd catalyzed hydrostannations



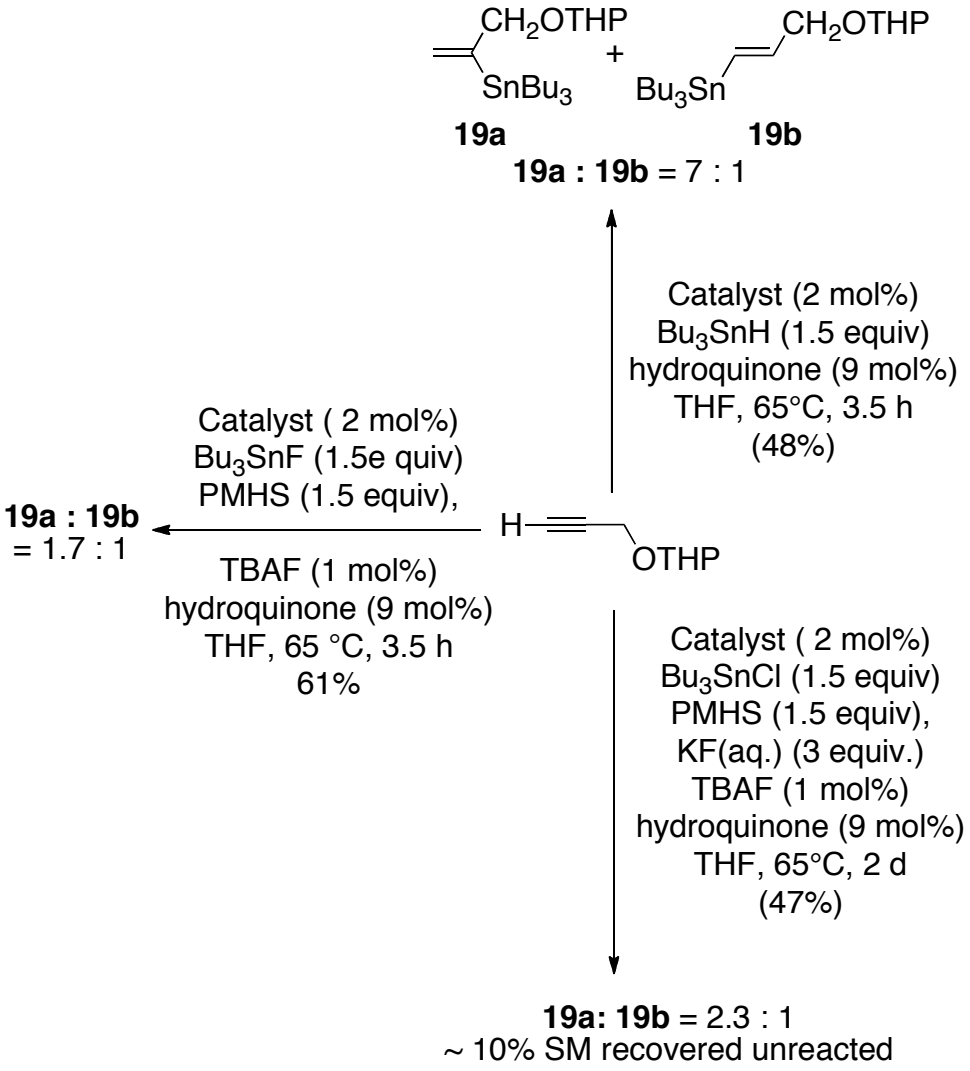
3.2 Intial study

We first looked at the use of the nickel(II) catalyst $NiCl_2(PPh_3)_2$. Previously, we showed that hydrostannations of terminal alkynes with the *in situ* generated tributyltin hydride from tributyltin fluoride could be performed with this catalyst with satisfactory outcome. When we tried to explore our $Bu_3SnCl/PMHS/KF_{(aq).}$ protocols with this catalyst, we were disappointed to observe that these aqueous conditions inhibited the reactions with this catalyst. Prolonged heating at 65°C in THF (in most cases 1 to 2 days) was required to get moderate yields of the product vinylstannanes, often, with irreproducible results.

When THP-protected propargyl alcohol (**3**) was subjected to nickel-catalyzed $Bu_3SnCl/PMHS/KF_{(aq.)}$ mediated hydrostannation protocols, vinylstannanes **19a** and **19b** were produced after 2 days and approximately 10% starting alkyne was found unreacted (Scheme 13). Propargyl alcohol (**1**) gave irreproducible yields (88% and 59% respectively) of products **17a** and **17b** after 1 day. Alkyne **15** also suffered similar

problems where the hydrostannated products **31a** and **31b** were formed with irreproducible yields in two different runs (43% and 13% respectively) after 1 day.

Scheme 13. Nickel-catalyzed hydrostannations of an alkyne



Cobalt ($CoCl_2(PPh_3)_2$) and molybdenum ($MoBI_3$) catalyst behaved even more poorly under our aqueous KF/PMHS protocols as the reactions shut down completely.

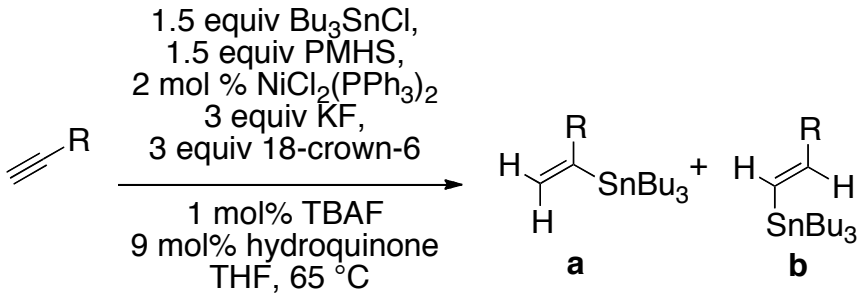
Realizing that water was likely the offending element in these systems, a non-aqueous system was sought. Two different approaches were taken: 1) Running the

reactions with dry KF and 2) designing systems that use homogenized KF. Our first approach was rendered ineffective as initial studies showed that dry KF alone in organic solvents was not effective in carrying out desired hydrostannations. We next investigated homogenization of KF in organic solvents. As 18-crown-6 is widely used to dissolve sodium or potassium salts in organic solvents, we wanted to explore the use of 18-crown-6 in our chemistry.[34] We were gratified to notice that in the presence of KF/18-crown-6, the nickel catalyst ($NiCl_2(PPh_3)_2$) produced the corresponding vinylstannanes in moderate to good yields comparable to our Bu_3SnF/PMHS protocol.

3.3 Nickel-catalyzed hydrostannylations

We first looked to see how the nickel catalyst responded to our Bu_3SnCl/KF/18-crown-6/PMHS protocol. Terminal alkynes were subjected to the reaction conditions. We were gratified to observe that use of 3 equivalents of KF/18-crown-6 mix facilitated the reaction producing vinylstannanes in moderate to good yields. The results were reproducible and required much less time (typically 3 to 5 h) to be completed (Scheme 14) when compared to our $Bu_3SnCl/KF_{(aq)}$/PMHS protocols under the same catalyst.

Scheme 14. Nickel-catalyzed hydrostannylation reactions with KF/18-crown-6



Entry	R	**a : b**	Yield
1	CH_2OH **(1)**	1.5 : 1 **17a/ 17b**	42%
2	CH_2OTHP **(3)**	1.7 : 1 **19a/ 19b**	45%
3	CH(OH)Ph **(15)**	1.4 : 1 **31a/ 31b**	42%
4	$C(OH)(CH_3)Ph$ **(11)**	1 : 1.7 **27a/27b**	54%
5[a]	$C(CH_3)_3$ **(6)**	1 : 99 **22a/22b**	57%
6	CH_2OTBS **(7)**	1.4 : 1 **32a/32b**	36%

[a] Reaction was run in ether at room temperature

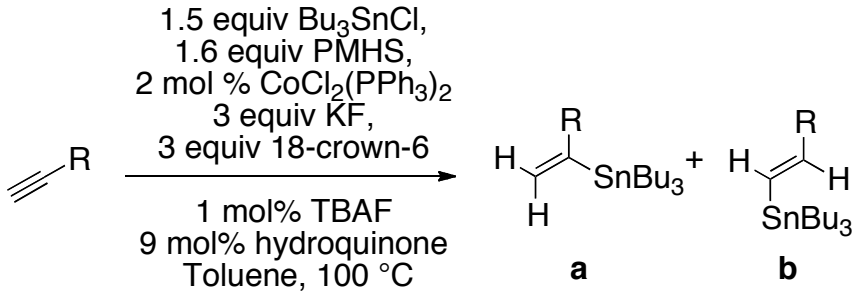
Alkynes with α–hydrogens resulted in the production of trace amounts of Z isomers, presumably, due to the Oshima mechanism previously presented.[33] Presence of a propargylic alcohol or its derivative favored the formation of the internal isomer except for entry 4. When the α-carbon was bulky, the selectivity switched to favor the *E*-isomer (Scheme 14, entry 4 and 5). Entry 4 was, presumably, a borderline case where bulky substituents at the α-carbon (methyl and phenyl) outweighed the directing effect of an alcohol functionality. We also found that a TBS group survives this fluoride mediated protocol (Scheme 14, entry 6).

3.4 Cobalt-catalyzed hydrostannylations

We next looked at cobalt-catalyzed hydrostannylations under $Bu_3SnCl/KF_{(aq)}$/PMHS conditions. $CoCl_2(PPh_3)_2$ was the catalyst of choice. Unlike the nickel catalyst, which exhibited slow rates and lack of reproducibility under our aqueous KF conditions, reactions with the cobalt catalyst completely shut down under $Bu_3SnCl/KF_{(aq)}$/PMHS conditions, presumably, due to the hygroscopic nature of the catalyst. Thus, our KF/18-crown-6 methodology was applied on this catalyst. After some optimizations, it was found that this catalyst works best in toluene at 100-110 °C. Reactions in toluene were still slow and needed prolonged reaction times. These reactions produced fair to moderate yields of the desired vinylstannanes. The reactions displayed a blue color when progressed as desired. When this characteristic blue color was absent, reactions failed to produce desired vinylstannaes. Similar to nickel, oxygen functionality in the alkyne favored proximal vinylstannanes over their distal (*E*)

counterparts (Scheme 15, entries 1,2 and 3). Absence of an oxygen functionality switched the selectivity in favor of the distal (*E*) isomer (Scheme 15, entry 4). Entry 3 is of special interest. Here a silicon group survived our reaction conditions.

Scheme 15. Cobalt-catalyzed hydrostannation reactions with KF/18-crown-6



Entry	R	**a:b**	Yield
1	$CH_2CH_2CH_2OH$ **(33)**	1.9 : 1 **34a/34b**	45%
2	CH_2OTHP **(3)**	1.5 : 1 **19a/19b**	51%
3	CH_2OTBS **(16)**	1.4 : 1 **27a/27b**	31%
4[a]	$C(CH_3)_3$ **(6)**	1 : 99 **22a/22b**	39%

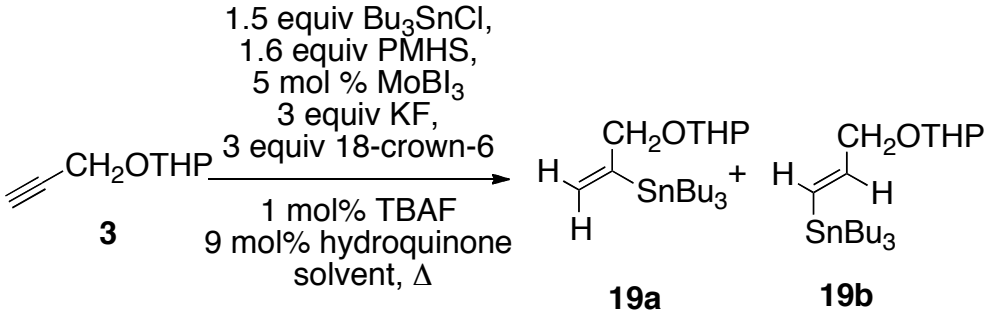
[a] Reaction was performed in THF in a sealed tube

3.5 Molybdenum-catalyzed hydrostannylations

Hydrostannylation reactions in presence of water failed completely under molybdenum ($MoBI_3$) catalyzed hydrostannylations. Gratifyingly, this catalyst behaved

well with our 18-crown-6 protocols. Reactions with THP-protected propargyl alcohol (**3**) were run in different solvents to optimize the reaction conditions.

Scheme 16. Optimizations of molybdenum-catalyzed hydrostannation reactions



19a **19b**

Entry	Solvent	temperature	rxn time	**19a : 19b**	Yield
1	THF	65 °C	18h	4 : 1	57%[a]
2	toluene	110 °C	1d	8.2 : 1	47%
3	benzene	80 °C	1d	4.2 : 1	80%

[a] based on starting material

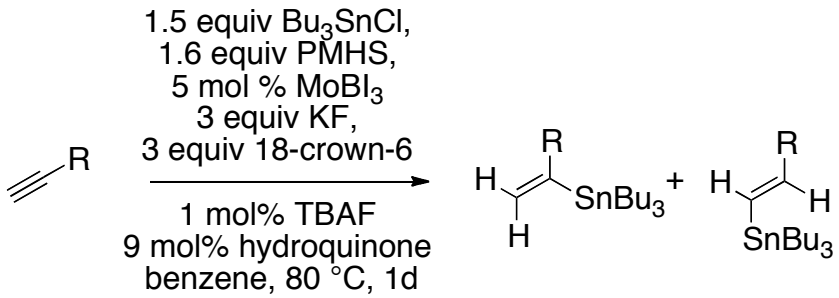
After 18 h, reaction of **3** in THF at 65 °C was quenched and subjected to column chromatography. The result of this was 13% unreacted alkyne along with 57% of the desired vinylstannanes in 4 : 1 proximal to distal (*E*) ratio. Reaction in toluene at 110 °C resulted in full conversion of the alkyne into products after a day. A higher selectivity was found for the proximal isomer in the products, but reaction yields were poor. Running the reaction in benzene 80 °C for a day met with erosion (~49%) of isomeric selectivity when compared to toluene reactions. No unreacted alkyne was found. The

yields of the product vinylstannes were found to be good (80%) and the reaction was reproducible.

Using benzene as the solvent for $MoBI_3$ catalyzed hydrostannation reactions, several alkynes were subjected to the reaction condition. Most alkynes behaved well giving good to excellent yields (Scheme 17). Oxygen functionality at the propargylic position, again, favored the proximal stannane product. Even when the oxo-group was further away from the alkyne functionality, the proximal isomer was favored over its *E* counterpart, albeit, to a smaller extent (Scheme 17, entry 3). Entry 6 was of special importance. Unlike Bu_3SnF/PMHS protocol, 3,3-methyl-1-butyne afforded proximal isomer as the major product. Control experiment showed that when hydrostannation reaction of the same alkyne was run in THF 65 °C under Bu_3SnCl/PMHS/18-crown-6 protocols, proximal to distal ratio changed to 1.3:1. Similarly, hydrostannation reaction of this alkyne in benzene at 80 °C under Bu_3SnF/PMHS protocol produced proximal and distal isomers in 1.2:1 ratio (as opposed to 2.5:1 when THF was used as solvent). This change in the isomeric ratio can be attributed partly to the solvent effect. Alami and co-workers showed that proximal to distal ratio in such reactions depends on the polarity of the solvent.[35] A more polar solvent (i.e. THF) favors the distal isomer and a non-polar solvent favors the proximal isomer. However, further studies are needed to have a thorough understanding of these observations.

The Bu_3SnCl/KF/18-crown-6/PMHS protocol required higher catalyst loadings (5 mol% vs 2 mol%) and longer time (1 d vs 3 h) compared to Bu_3SnF/PMHS protocols. Some erosion of proximal to distal selectivity was also observed compared to Bu_3SnF/PMHS protocol.

Scheme 17. $MoBI_3$-catalyzed hydrostannylation reactions with KF/18-crown-6



Entry	R	Internal : E	Yield
1	CH_2OH **(1)**	2 : 1 **17a/17b**	47%
2	CH_2OTHP **(3)**	4 : 1 **19a/19b**	82%
3	$C(CH_3)_2(OH)$ **(10)**	2.5 : 1 **26a/26b**	55%
4	$C(OH)(CH_3)Ph$ **(11)**	6 : 1 **27a/27b**	91%
5	$(CH_2)_3OH$ **(33)**	1.3 : 1 **34a/34b**	48%,
6	$C(CH_3)_3$ **(6)**	2.5: 1 **22a/22b**	63%

3.6. Rhodium and ruthenium-catalyzed hydrostannylations

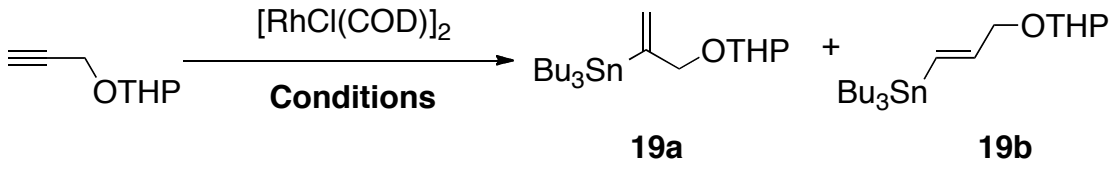
We next tried to explore the use of rhodium and ruthenium catalysts. $[RhCl(COD)]_2$, $RhCl(CO)(PPh_3)_2$, and $RuCl_2(PPh_3)_4$ were screened based on the high yields reported in hydrostannylation reactions with these catalysts by Kikukawa and co-workers.[23] First, we looked at $[RhCl(COD)]_2$. Application of our $Bu_3SnCl/KF_{(aq)}$/PMHS methodology in presence of this catalysts proved to be disappointing. We have seen in the last chapter that use of Bu_3SnF/PMHS afforded trace amounts of product when THP-protected propargylic alcohol (**3**) was subjected to the reaction conditions with $[RhCl(COD)]_2$. $Bu_3SnCl/KF_{(aq)}$/PMHS protocols resulted in a complex mixture when alkyne **3** was subjected to hydrostannation conditions under the same catalyst. Here, we took our opportunity to determine whether the presence of water and/or KF have any influence on the poor outcome of the reaction under this catalyst. Control experiments were run employing both *ex situ* tributyltin hydride and water and a combination of tin hydride, water and KF. We observed that the presence of H_2O or H_2O/KF reduced the yield significantly, and, to our surprise, the selectivity for the internal isomer increased markedly.

These results may be due to a change of the catalytic species in the presence of water, although, decompositions of (*E*)-isomer under the reaction conditions cannot be completely ruled out. A control experiment in the absence of the catalyst using our protocol revealed that the same sort of complex mixture formation could be accessed in the absence of the catalyst. When alkyne **3** was subjected to our

Bu_3SnCl/PMHS/KF/18-crown-6 protocols, similar complex mixture was formed. These results give us reasons to believe that the catalyst is probably decomposing in our PMHS mediated protocols.

Kikukawa recognized $[RhCl(COD)]_2$ catalyst to be highly proximal-vinylstannane selective. Initial control experiments using pre-made Bu_3SnH and THP-protected propargyl alcohol (**3**) produced similar yield as in Kikukawa's case. In contrast to Kikukawa's observation, we found the reaction afforded almost equal distribution of proximal and (*E*)-isomer with THP-protected propargyl alcohol (**3**). We rationalize this difference in product distribution as a result of solvent differences, as Kikukawa's reactions were performed in neat tin hydride in presence of the catalyst. We have previously mentioned that solvent could have pronounced influence on the outcome of such reactions.[35]

Scheme 18. $[RhCl(COD)]_2$-catalyzed hydrostannations



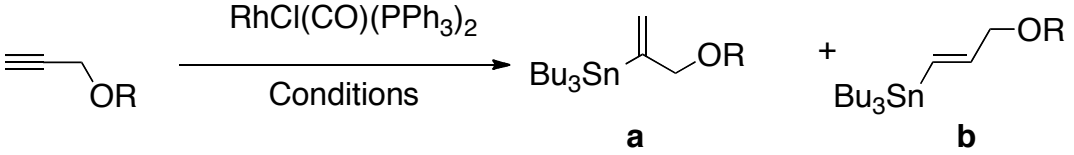
19a **19b**

Conditions	19a : 19b	Yield
Bu_3SnH[a]	1.3 : 1	59%
Bu_3SnH/H_2O[b]	5 : 1	32%
$Bu_3SnH/H_2O/KF$[c]	5.3 : 1	39%
$Bu_3SnF/PMHS$[d]	NA	trace
Bu_3SnCl/KF /PMHS[e]	NA	complex mixture

[a]Reaction conditions: alkyne (1.0 equiv.), catalyst (1 mol%), Bu_3SnH (1.5 equiv.), THF (7 mL), hydroquinone (9 mol%), 65 °C. [b]Reaction conditions: alkyne (1.0 equiv), catalyst (1 mol%), Bu_3SnH (1.5 equiv), H_2O (1 mL),THF (7 mL.), hydroquinone (9 mol%), 65 °C. . [c]Reaction conditions: alkyne (1.0 equiv), catalyst (1 mol%), Bu_3SnH (1.5 equiv), H_2O (1 mL), KF (3 equiv), THF (7 mL.), hydroquinone (9 mol%), 65 °C, [d]Reaction conditions: alkyne (1.0 equiv), catalyst (1 mol%), Bu_3SnF (1.5 equiv), PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C . [e]Reaction conditions: alkyne (1.0 equiv), catalyst (1 mol%), Bu_3SnCl (1.5 equiv), KF (3 equiv), 18-crown-6 (3 equiv) or H_2O (1 mL), PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C.

Use of $RhCl(CO)(PPh_3)_2$ proved to be modest to our $Bu_3SnCl/PMHS/KF_{(aq.)}$ protocol. Both THP and TBS-protected alcohol gave vinylstannanes in poor to moderate yields with $Bu_3SnCl/PMHS/KF_{(aq.)}$ (Scheme 19). The yields were comparable to the reactions where tributyltin hydride was directly added to the reaction of TBS-protected propargyl alcohol. Control experiments revealed that both H_2O or a combination of H_2O/KF do not affect the reaction with pre-made tin hydride (Scheme 19). The selectivity for the (*E*)-isomer was noticeable as oxygen functionality on the α-carbon normally favors the internal-isomer. At present the reason for this observation is not very clear to us. Unfortunately, this catalyst suffered from poor reactivity under $Bu_3SnCl/PMHS/KF$/18-crown-6 protocol. THP-protected propargyl alcohol (**3**) afforded a trace amount of product and unreacted starting alkyne was isolated.

Scheme 19. $RhCl(CO)(PPh_3)_2$-catalyzed hydrostannations

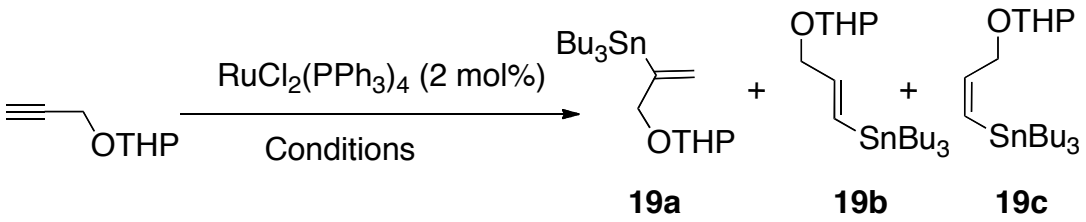


	Conditions					
R	Bu_3SnH[a]	Bu_3SnH /H_2O[b]	Bu_3SnH /H_2O/KF[c]	Bu_3SnF /PMHS[d]	Bu_3SnCl /$KF_{(aq.)}$ /PMHS[e]	Bu_3SnCl /KF/18-C-6 /PMHS[e]
THP	75% (a:b =1:1)	75% (a:b =1:1)	73% (a:b =1:1)	17% (a:b =1:3.3)	28% (a:b =1:1.8)	trace
TBS	58% (a:b =1:1)			55% (a:b =1:2.5)	50% (a:b =1:2.8)	

[a]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 equiv), THF (7 mL.), hydroquinone (9 mol%), 65 °C. [b]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 eq.), H_2O (1 mL),THF (7 mL.), hydroquinone (9 mol%), 65 °C. . [c]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 equiv), H_2O (1 mL), KF (3 equiv), THF (7 mL.), hydroquinone (9 mol%), 65 °C, [d]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnF (1.5 equiv), PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C . [e]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnCl (1.5 equiv), KF (3 equiv), H_2O (1 mL.) or 18-crown-6 (3 equiv) PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C.

$RuCl_2(PPh_3)_4$ catalyzed hydrostannations were attempted with little success. Both in presence of *ex situ* and *in situ* tributyltin hydride, the reaction afforded a mixture of (*E*), proximal and (*Z*)-isomer pointing to radical participations in the reaction in presence of the catalyst. H_2O or combination of H_2O/KF did not seem to have any major effects on the reaction where tributyltin hydride was added directly. Similarly, our KF/18-crown-6 protocols afforded a similar complex mixture when alkyne **3** was subjected to the reaction conditions under this catalyst.

Scheme 20. $RuCl_2(PPh_3)_4$-catalyzed hydrostannations



19a **19b** **19c**

Conditions	**19a : 19b : 19c**	**Yield**
Bu_3SnH[a]	3.8 : 3.8 : 1	29%
Bu_3SnH/H_2O[b]	3.3 : 2.9 : 1	21%
$Bu_3SnH/H_2O/KF$[c]	2.1 : 1.4 : 1	27%
Bu_3SnF/PMHS[d]	NA	complex mixture
Bu_3SnCl/KF /PMHS[e]	NA	complex mixture

[a]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 equiv), THF (7 mL.), hydroquinone (9 mol%), 65 °C. [b]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 eq.), H_2O (1 mL),THF (7 mL.), hydroquinone (9 mol%), 65 °C. . [c]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnH (1.5 equiv), H_2O (1 mL), KF (3 equiv), THF (7 mL.), hydroquinone (9 mol%), 65 °C, [d]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnF (1.5 equiv), PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C . [e]Reaction conditions: alkyne (1.0 equiv), catalyst (2 mol%), Bu_3SnCl (1.5 equiv), KF (3 equiv), H_2O (1 mL.) or 18-crown-6 (3 equiv) PMHS (1.5 equiv), TBAF (1 mol%), THF (7 mL.), hydroquinone (9 mol%), 65 °C.

3.7 Conclusions

We have demonstrated that Bu_3SnCl/PMHS/KF/18-crown-6 can serve as an *in situ* tin hydride source for hydrostannation reactions under several non-Pd transition metal catalysts. This non-aqueous protocol substituted for our $KF_{(aq)}$/ PMHS protocols for molybdenum, nickel and cobalt catalyzed reactions where $Bu_3SnCl/KF_{(aq)}$/PMHS conditions proved unsuccessful. However, these protocols suffered from longer reaction times, higher catalyst loadings and higher temperature compared to Bu_3SnF/PMHS protocols with the exception of the nickel catalyst. Yields of the product vinylstannanes were also lower under nickel, cobalt and molybdenum catalysts as compared to our Bu_3SnF/PMHS protocols. Molybdenum reactions showed erosion of isomeric selectivity of the proximal stannanes (58-79%). Rh and Ru catalyzed hydrostannations failed under these protocols. However, this method provides a means to perform desired hydrostannations under Bu_3SnCl/KF/PMHS protocols with nickel, cobalt and molybdenum catalysts where our aqueous KF method cannot be applied.

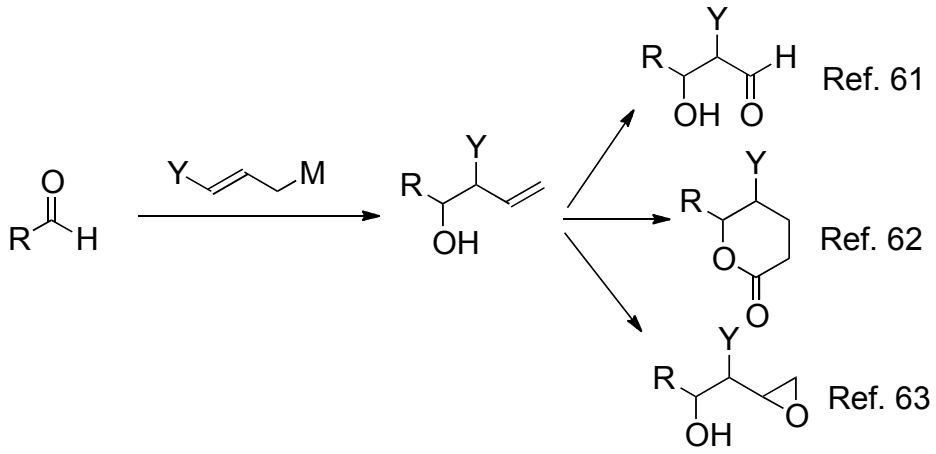
Chapter 4. Development of one-pot allylation hydrostannation sequence involving recycling of tin

4.1 Introduction.

In previous chapters, we documented non-Pd transitional metal catalyzed hydrostannation protocols in an attempt to examine the first step of our second-generation one-pot hydrostannation-Stille coupling process. We were driven, in part, from such one-pot processes where the tin by-products after the first step of the reactions were successfully recycled in the second step of the sequence. Next, we wanted to explore the concept of the tin recycling to other processes that also generate tin by-products. For this purpose, we chose allylation chemistry.

Allylation reactions are the reactions of carbonyls (i.e. aldehydes) with allylic organometallic compounds. One type of allylic organometallic compounds used in such reactions is allyl (crotyl) stannane. Allylation reactions of allylstannanes and aldehydes can take place under thermal[68] or Lewis acidic[36,37,38] (or transition metal-catalyzed[41]) conditions. Allylation reactions have special synthetic importance as the products of the reaction (homoallylic alcohols) can be viewed as synthetic equivalent to aldol products. The product homoallylic alcohols can undergo several structural manipulations, e.g. their conversions to β-hydroxyaldehydes[61], δ-lactones[62] and epoxides[63] (Figure 8). They can also be successfully utilized in ring closing metathesis[64a] and cross-coupling reactions[64b]. Indeed, over the years, allylation of aldehydes has become one of the most powerful tools in organic synthesis.

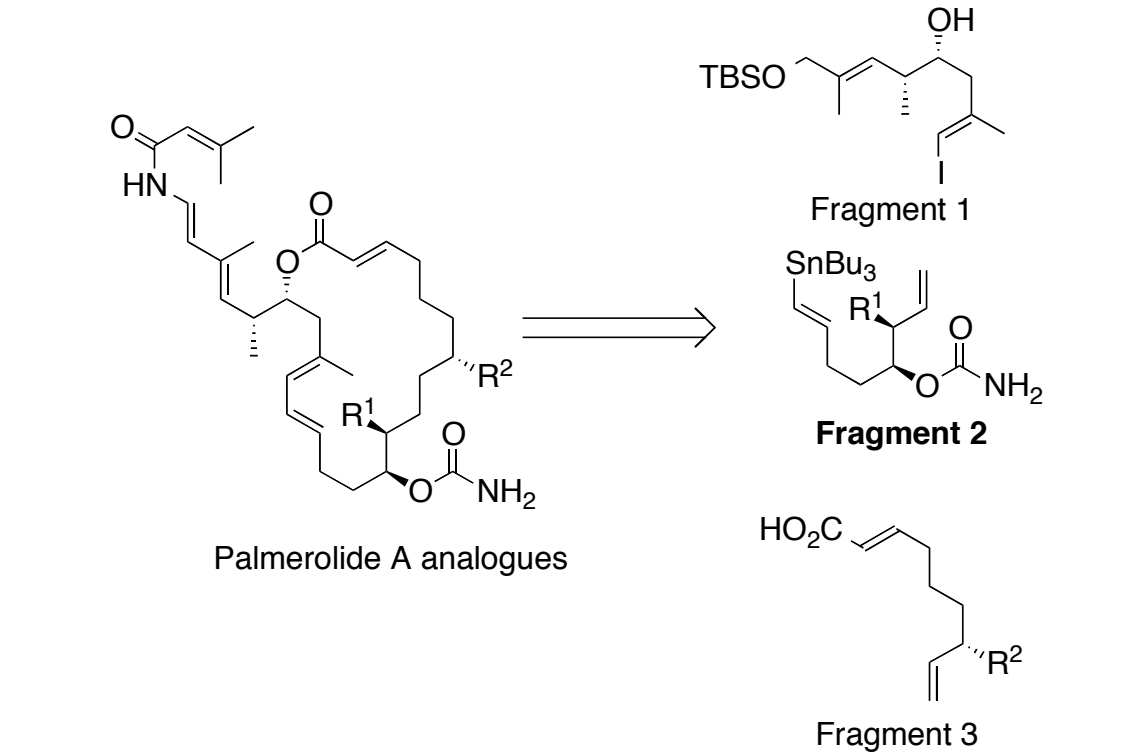
Figure 8. Synthetic utility of homoallylic alcohols

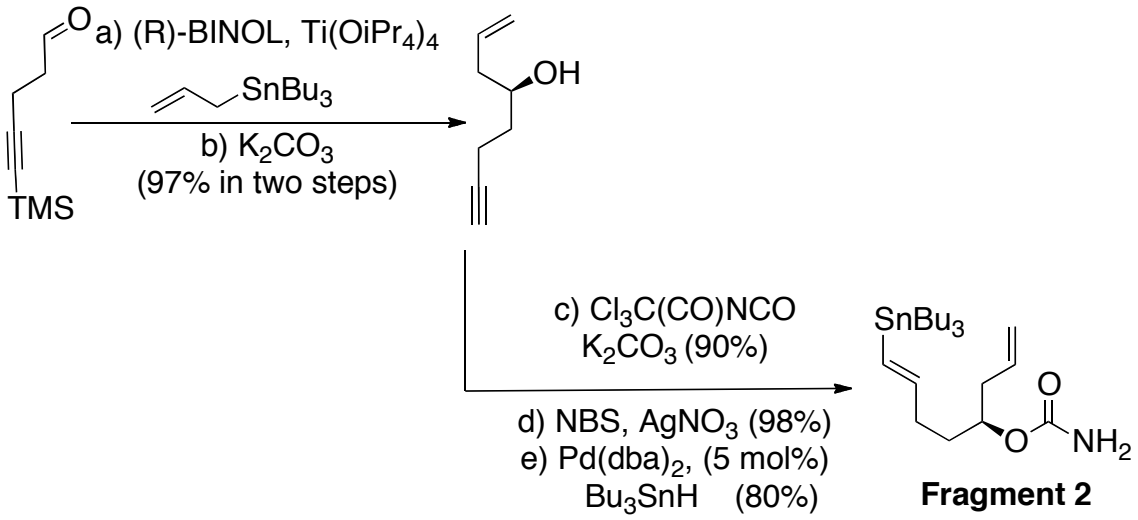


However, in developing protocols that use allylation chemistry to generate organotin products that can be successfully utilized in another reaction in the same pot, the nature of the tin-byproducts of the allylation step should be known. Moreover, choice of the second reaction partner in such combined processes also needs to be judicious.

A report by Chen and coworkers caught our attention.[67] In an attempt to synthesize palmerolide A (a natural product having selective cytotoxicity against melanoma cancer cells) analogues, this group utilized allylation and hydrostannation chemistry in a sequence.

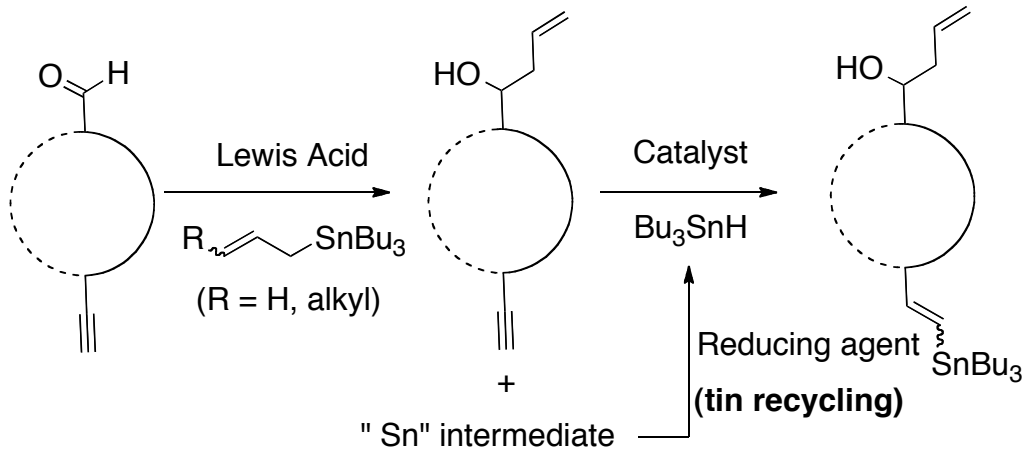
Scheme 21. Total synthesis of palmerolide A analogues





We realized, to access structurally complex molecules, combination of the allylstannane mediated allylation and hydrostannation reactions could be attractive. The advantage of the combined process would be usage of reduced amounts of the toxic tin reagents compared to if the allylation and the hydrostannation steps were performed separately. However, in order to couple an allylation and a hydrostannation in the same reaction pot, the allylation tin-intermediates must undergo facile conversion to organotin hydrides by known protocols. A general reaction protocol is illustrated in Scheme 22.

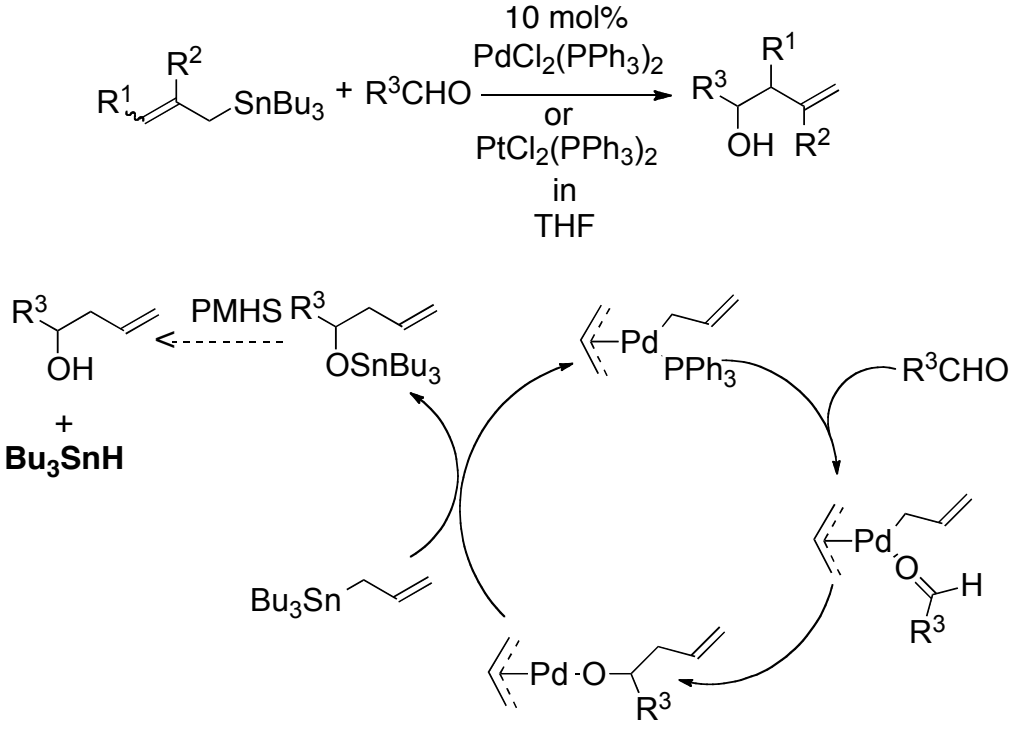
Scheme 22. General reaction of one-pot allylation-hydrostannation sequence



First, we looked at studies that give an idea about the nature of such tin intermediates. While the regiochemical[40] and stereochemical[36-39] aspects of such allylation reactions have been heavily studied over the last three decades, only a handful of these studies provide information about the tin intermediates in such reactions. Two examples caught our attention. The first one was Yamamoto's palladium (or platinum) catalyzed condensation of allylstannanes with aldehydes shown in Scheme 22.[41] In these reactions, allylstannanes were reacted with aldehydes in

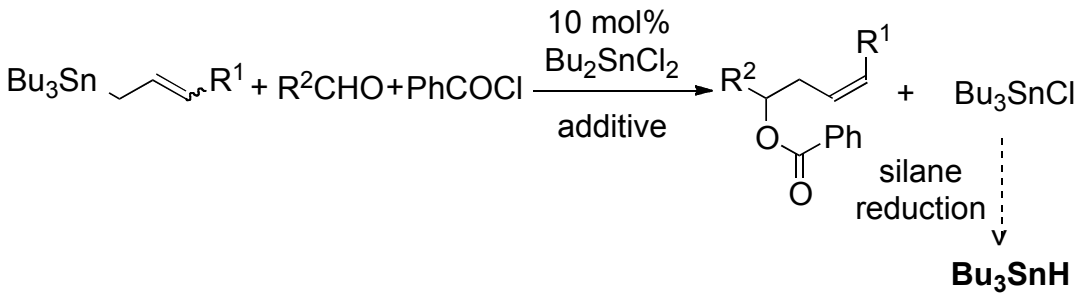
presence of Pd(II) or Pt (II) catalysts (10 mol%) either at ambient temperature or at reflux to produce the corresponding homoallylic alcohols in good yields. Such reactions, according to Yamamoto and coworkers, proceed via intermediacy of stannyl ethers as illustrated below (Scheme 23). We anticipated that with proper choice of a reducing agent (e.g. PMHS), this Sn-O bond would be cleaved and tributyltin hydride produced.[31,42]

Scheme 23. Palladium/ platinum-catalyzed allylation of aldehydes



The second example was allylation/ crotylation of aldehydes with catalytic amount of Bu_2SnCl_2 complex documented by Baba and co-workers.[43] Addition of coordinating reagents like tetrabutylammonium iodide (TBAI) and benzoyl chloride as a quencher were required to perform a successful allylation (Scheme 24).

Scheme 24. Bu_2SnCl_2 catalyzed allylation of aldehydes



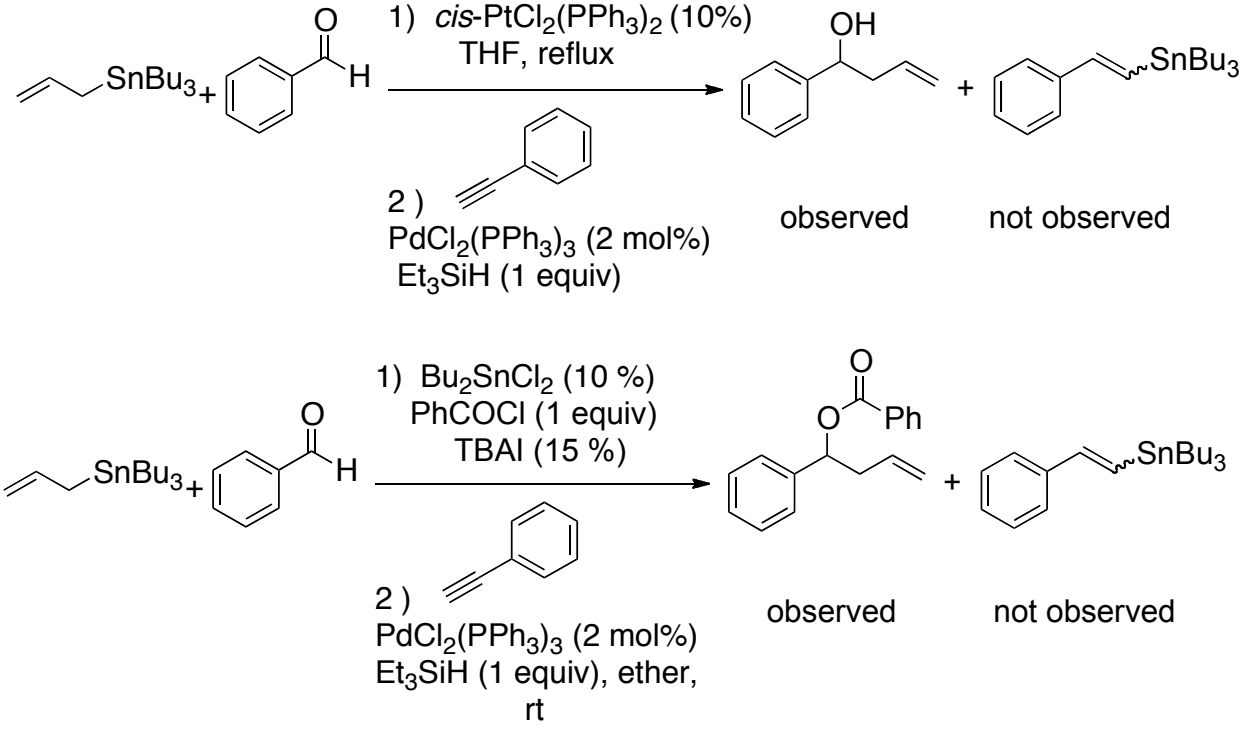
It is known that tributyltin chloride can, also, be effectively reduced by silanes to Bu_3SnH and hydrostannation reactions could be performed on alkynes and alkenes with this *in situ* generated tin hydride.[4c,4d] So, we wanted to explore these protocols in our one-pot allylation-hydrostannation sequence (Schemes 23 and 24).

4.2. Results and discussions

We were very disappointed to learn that neither of these methods was effective in our one-pot allylation hydrostannation protocols. When benzaldehyde was subjected to allylation reaction in presence of 10% *cis*-$PtCl_2(PPh_3)_2$ and allylstannane in THF at rt and the resulting allylation product mixture was reacted with 2 mol% $PdCl_2(PPh_3)_2$, PMHS, TBAF and phenyl acetylene, no vinylstannane was ever detected. The results did not change even when the mixture was refluxed and/or when Et_3SiH was used as a reducing agent instead of PMHS. On the other side, use of catalytic amount of Bu_2SnCl_2 in conjunction with stoichiometric PhCOCl was, again, successful in carrying out the desired allylation when bezaldehyde and allylstannane were subjected to the conditions, but treatment of the resulting mixture with 2 mol% $PdCl_2(PPh_3)_2$, Et_3SiH and

phenyl acetylene to perform a hydrostannation reaction was rendered ineffective (Scheme 25).

Scheme 25: Attempted one-pot allylation-hydrostannation with Yamamoto's and Baba's protocol



We, then, turned to a classic allylation reaction method mediated by BF_3•OEt_2.[44] Even though, little was known about the tin intermediates that form in these reactions, we wanted to explore the possibility of a reduction of these intermediates. It was observed that $PdCl_2(PPh_3)_2$ and $MoBI_3$ were unable to survive the BF_3•OEt_2 conditions. So, $B(C_6F_5)_3$ was chosen as a hydrostannation catalyst. To our gratification, with 10 mol% of $B(C_6F_5)_3$ and 1 equiv. Et_3SiH as the reductant, formation of 56% of homoallylic

alcohol (**54**) and 32% *z*-vinylstannane (**23c**) was observed in CH_2Cl_2 using hexamethyldisiloxane (HMDS) as an external standard (Scheme 26).

Scheme 26. BF_3•OEt_2 and $B(C_6F_5)_3$ mediated allylation-hydrostannation

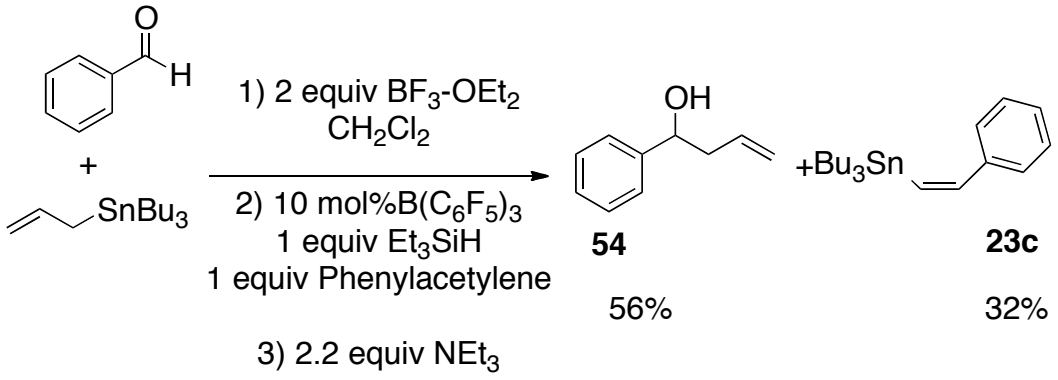


Table 6. Optimization of one-pot allylation-hydrostannation sequence[a]

Entry	BF_3•OEt_2 (equiv)	Solvent	Tem (° C)	$B(C_6F_5)_3$ (mol%)	Reductant (equiv)	Alcohol (%)	Stannane (%)
1	2	CH_2Cl_2	0	10	Et_3SiH (1)	56	32
2	2	CH_2Cl_2	0	20	Et_3SiH (1)	60	55
3	2	toluene	0	20	Et_3SiH (1)	72	65
4	2	toluene	0	100	Et_3SiH (1)	12	-

Table 6 (cont'd)

Entry	BF_3•OEt_2 (equiv)	Solvent	Tem (° C)	$B(C_6F_5)_3$ (mol%)	Reductant (equiv)	Alcohol (%)	Stannane (%)
5	2	toluene	0	20	Et_3SiH (1.5)	63	85
6	2	toluene	0	30	Et_3SiH (2)	62	35
7	2	toluene	0	0	Et_3SiH (1.5)	71	8
8	2	toluene	0	20	Et_3SiH (2)	46	76
9	2	toluene	0	20	PMHS (1) +TBAF (cat)	75	62
10	2	toluene	0	20	PMHS (2) +TBAF (cat)	71	86
11	2	toluene	0	20	PMHS (3) +TBAF (cat)	38	52
12	2	toluene	-35	20	PMHS (2) +TBAF (cat)	73	92

Table 6 (cont'd)

Entry	BF_3•OEt_2 (equiv)	Solvent	Tem (° C)	$B(C_6F_5)_3$ (mol%)	Reductant (equiv)	Alcohol (%)	Stannane (%)
13	1.05	toluene	-35	20	PMHS (2)	74	93
14	3	toluene	-35	20	PMHS (2)	61	99

[a] Yields are based on using HDMS as an external standard.

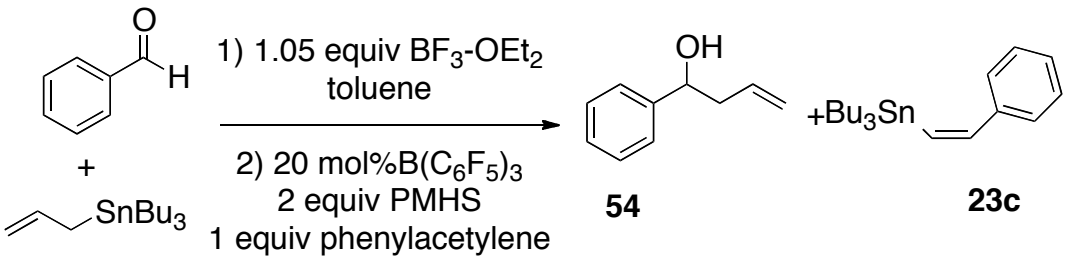
Table 6 describes the set of reactions performed in order to optimize our reaction conditions. Use of a higher amount of catalyst loading (20 mol%) increased yields of both the homoallylic alcohols and vinylstannanes. Toluene as a solvent was found superior to CH_2Cl_2. Stoichiometric loading of $B(C_6F_5)_3$ was detrimental to the formation of both the alcohols and vinylstannanes. A loading of 30 mol% catalyst also produced poor outcome. Higher amounts of Et_3SiH (1.5 equiv) produced a better yield of the stannanes, but the yield of the alcohols decreased. When 2.0 equiv of the same reductant was used, yield of both the stannanes and the alcohols decreased significantly. To our delight and in contrast to Yamamoto's observations,[4c] PMHS in conjunction with TBAF proved to be an excellent reducing agent. While developing a Lewis acid catalyzed hydrostannation protocol for C–C multiple bonds, Yamamoto and co-workers commented on the efficiency of PMHS as a reducing agent under Lewis acid-catalyzed hydrostannation conditions: "*In general, the preparation of commercially available tributyltin hydride is carried out by the reduction of tributyltin oxide and hydrosiloxane. Accordingly, we attempted to employ this method…..under the*

conditions of the Lewis acid catalyzed hydrostannation reaction. However, no hydrostannation product was detected…..It is probable that due to the strong affinity of the Lewis acid for the oxygen of the reactants (tributyltin oxide or hydrosiloxane) or of the byproduct, it is deactivated and thus not effective as a catalyst in the hydrostannation reaction".[4c]

The yields of the alcohols and the stannanes improved fairly when the reaction was carried out at – 35 °C. Reactions could also be run without TBAF. A little over 1 equiv of BF_3•OEt_2 and 2 equiv PMHS seemed to offer similar yields of the product homoallylic alcohols and vinylstannanes compared to when the reaction was run in presence of 2 equiv of both BF_3•OEt_2 and PMHS and catalytic load of TBAF.

Experiments were also undertaken to optimize the work-up conditions. It was observed that H_2O or sat. $NaHCO_3$ were detrimental to the stannane. Work-up with hexane reduced the yield of the vinylstannane to a significant extent. Lower amounts of NEt_3 (1.4 equiv) proved to provide the best results and thus, chosen as the optimized work-up condition. Table 7 summarizes the results of optimization of the work-up procedure for conditions depicted in Table 6 entry 13.

Table 7. Optimization of the work-up

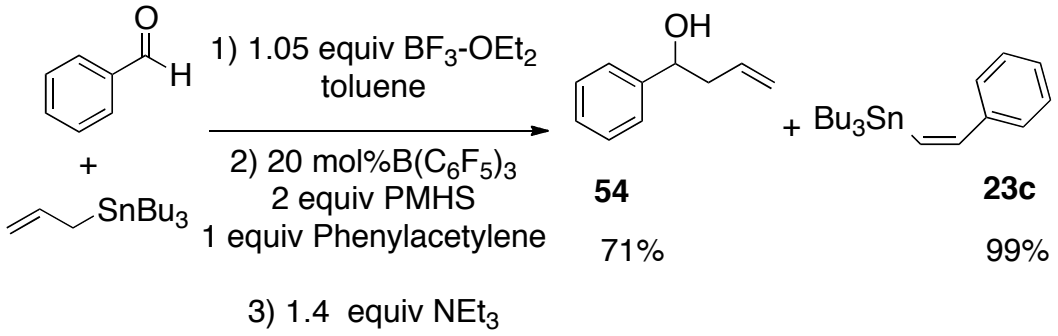


Entry	Work-up procedure[a]	Alcohol (%)	Stannane (%)
1	2.2 equiv NEt_3	74	93
2	H_2O	60	-
3	Sat. $NaHCO_3$	90	-
4	hexanes	80	24
5	1.4 equiv NEt_3	78	100

[a]These reagents were added after the completion of the reaction at step 3

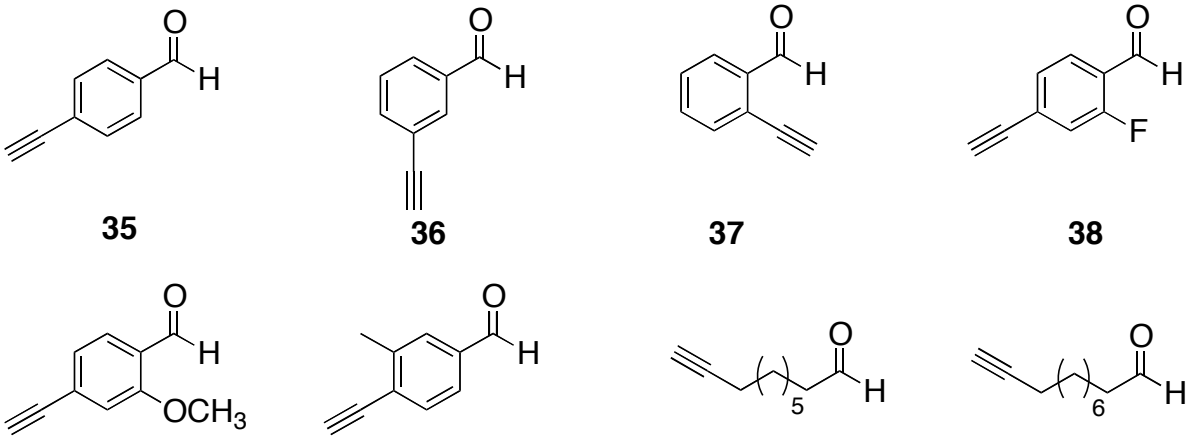
Selecting Table 7, entry 5 as the optimized conditions, the homoallylic alcohol (**54**) and vinylstannane (**23c**) were isolated in 71% and 99% yield respectively from the reaction of bezaldehyde, allylstannane and phenylacetylene. This is illustrated in Scheme 27.

Scheme 27. Isolation of the homoallylic alcohol and allylstannane



Having had success with our one-pot allylation-hydrostannation protocol with separate aldehyde and alkyne moieties, we decided to design and synthesize different alkynals to demonstrate the effectiveness of this protocol. The following alkynals were targeted (Figure 9).

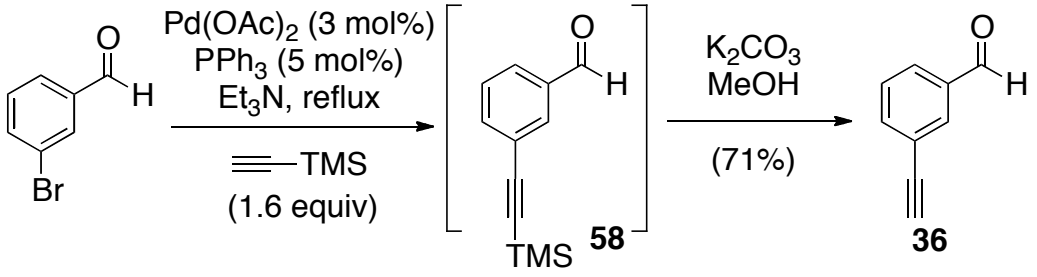
Figure 9. Prospective alkynals for one-pot allylation /hydrostannation



As most of these compounds were commercially inaccessible (aside from **35** and **37**), facile syntheses of these alkynals were necessary. It was envisioned that the aromatic alkynals could be synthesized from commercially available bromo/ iodo substituted aromatic aldehydes *via* Sonogashira coupling, whereas, the aliphatic

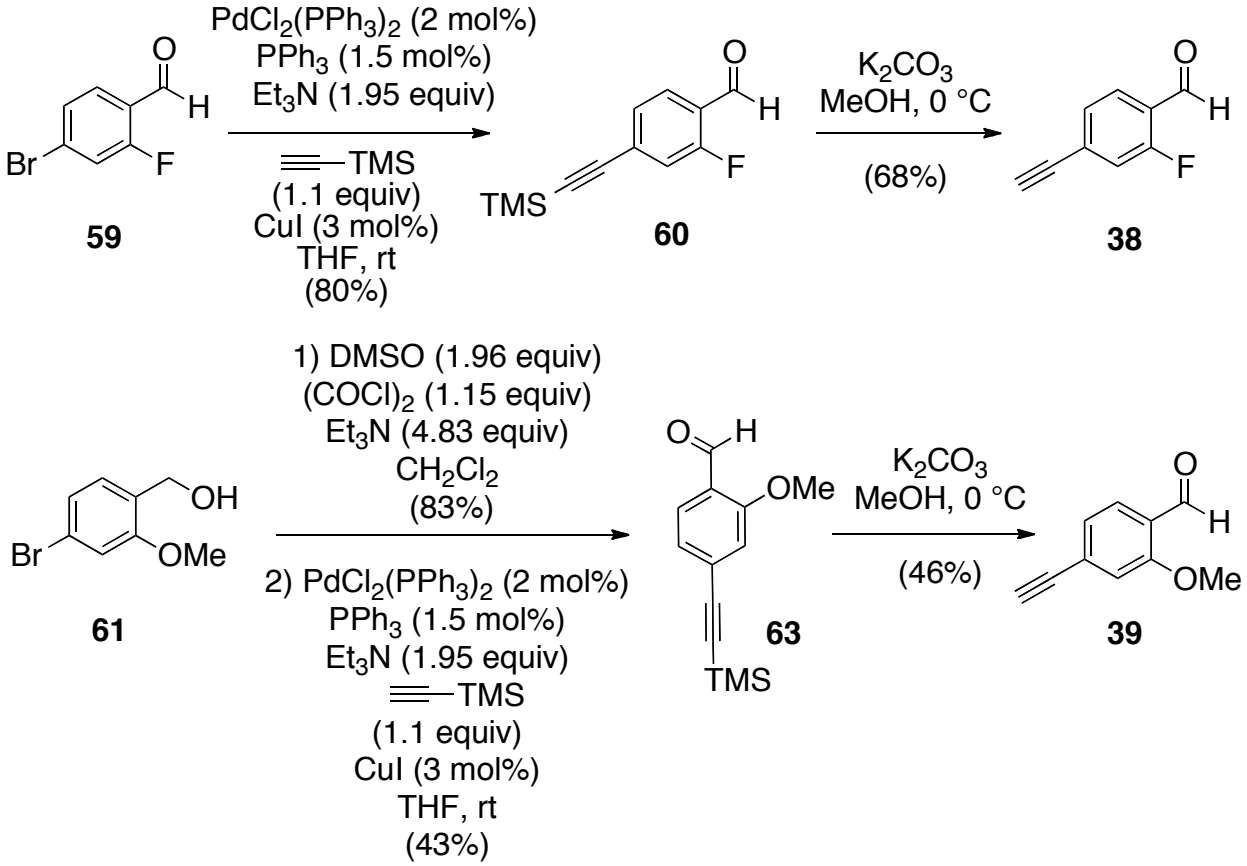
alkynals could be synthesized from commercially available alkynols *via* Swern oxidation. Scheme 28 illustrates the synthesis of **36**. The TMS-alkyne (**58**) was formed from the coupling of 3-bromobenzaldehyde and trimethylsilylacetylene using Heck's condition.[45] It was, then, subjected to K_2CO_3 catalyzed desilylation without purification to afford **36** in 71% yield.

Scheme 28. Synthesis of 3-ethynylbenzaldehyde (**36**)



Synthesis of **38**, **39** and **40** proved to be challenging. Aside from a few isolated examples, there are not many systematic appoaches toward synthesis of aromatic alkynals in the literature.[46] Attempted synthesis of the above compounds using Heck's conditions and then, subjecting the crude product to K_2CO_3 catalyzed desilylation proved ineffective. A competing polymerization reaction was observed in most cases. So we turned to classic Sonogashira conditions.[47] It was also learned that the desilylation reactions are most effective on these subtrates at low concentrations and low temperature. Scheme 29 demonstrates the syntheses of **38** and **39** using Sonogashira conditions.

Scheme 29. Syntheses of **38** and **39**

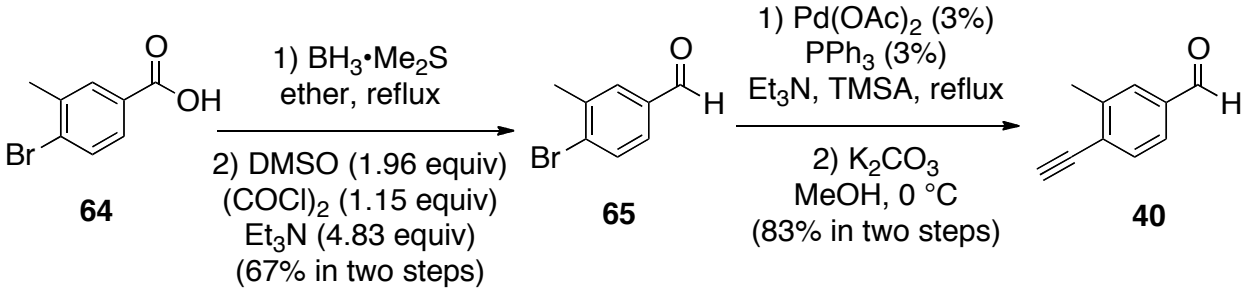


With 3% CuI, the desired Sonogashira coupling was accomplished at room temperature in both cases. Using Sonogashira conditions, 4-bromo-2-fluorobenzaldehyde afforded the coupled product in 80% yield. Finally, desilylation reaction with catalytic K_2CO_3 afforded **38** in 68% yield. Likewise, commercially available, 4-bromo-2-methoxyphenylbenzylalcohol was subjected to Swern oxidation to produce 4-bromo-2-methoxybenzaldehyde (**62**), Sonogashira coupling followed by desilylation reaction on **62** afforded **39** in 46% yield.

Synthesis of**40** began with available 4-bromo-3-methylbenzoicacid that was first converted to 4-bromo-3-methylbenzylalcohol by treatment with $BH_3 \cdot Me_2S$ and,

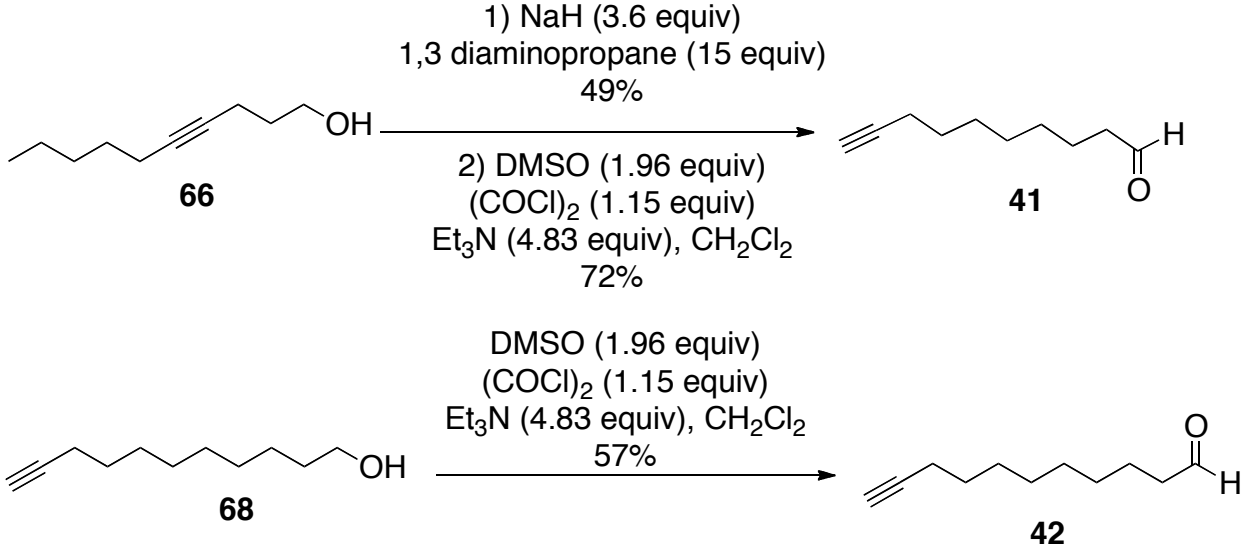
then, subjected to Swern oxidation. The resulting 4-bromo-3-methylbenzaldehyde did not respond to our standard Sonogashira protocol as described in Scheme 29. Turning to Heck conditions provided positive results. Finally the Sonogashira coupled product was subjected to desilylation to afford a partially separable mixture of desired 4-ethynyl-3-methylbenzaldehyde and a hitherto unknown aldehyde in 7:1 ratio (Scheme 30).

Scheme 30. Synthesis of 4-ethynyl-3-methylbenzaldehyde (**40**)



The acyclic alkynals were prepared from commercially available alkynols *via* Swern oxidation (or isomerization followed by Swern oxidation). Scheme 31 illustrates syntheses of **41** and **42**.

Scheme 31. Syntheses of **41** and **42**



Commercially available alkynals **35** and **37** and synthesized alkynals **36**, **38**, **39**, **40**, **41** and **42** were then subjected to our optimized one-pot allylation hydrostannation protocol. Most alkynals responded favorably, producing “allylation-hydrostannation” products in the same reaction pot in moderate yields. Figure 10 and Table 8 summarizes the results of our one-pot allylation hydrostannation protocol.

Figure 10. One-pot allylation-hydrostannation protocols

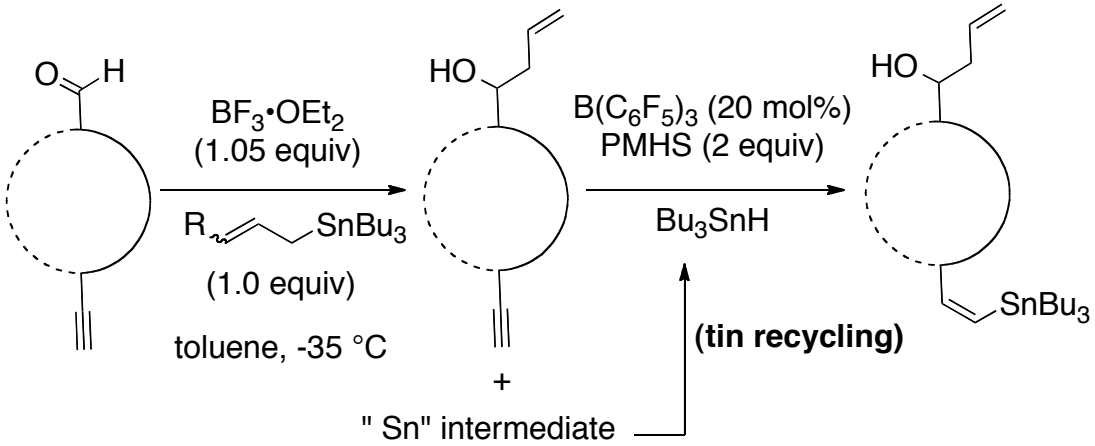
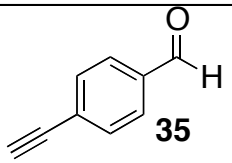
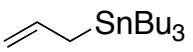
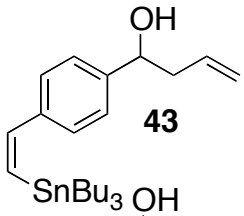
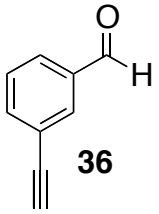
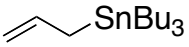
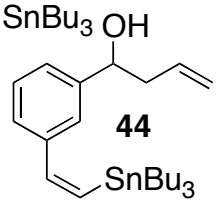
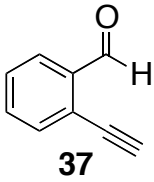
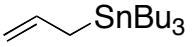
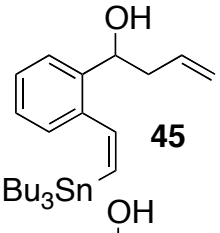
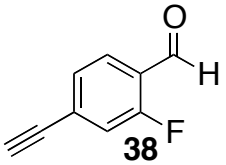
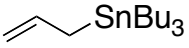
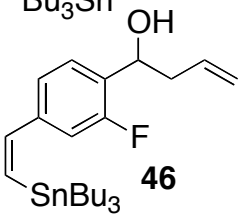
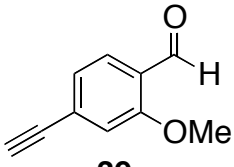
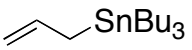
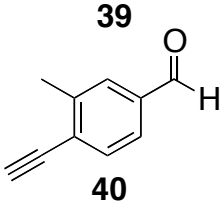
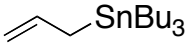
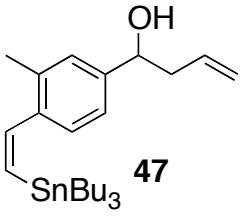
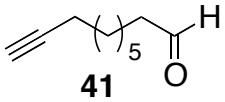
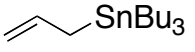
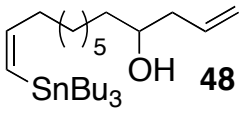
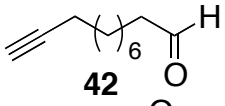
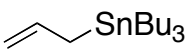
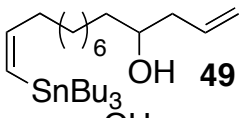
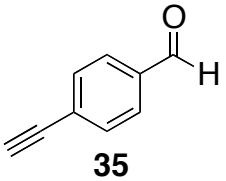
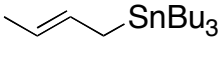
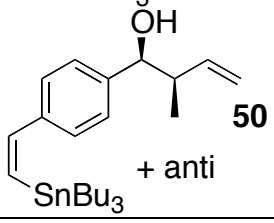


Table 8. Results of one-pot allylation-hydrostannation protocols

Entry	Alkynal	Stannylating agent	Product	Yield
1	 **35**		 **43**	51%
2	 **36**		 **44**	48%
3	 **37**		 **45**	57%
4	 **38**		 **46**	50%
5	 **39**		—	— [a]
6	 **40**		 **47**	trace
7	 **41**		 **48**	41%
8	 **42**		 **49**	43%
9	 **35**		 **50** + anti	38%[b]

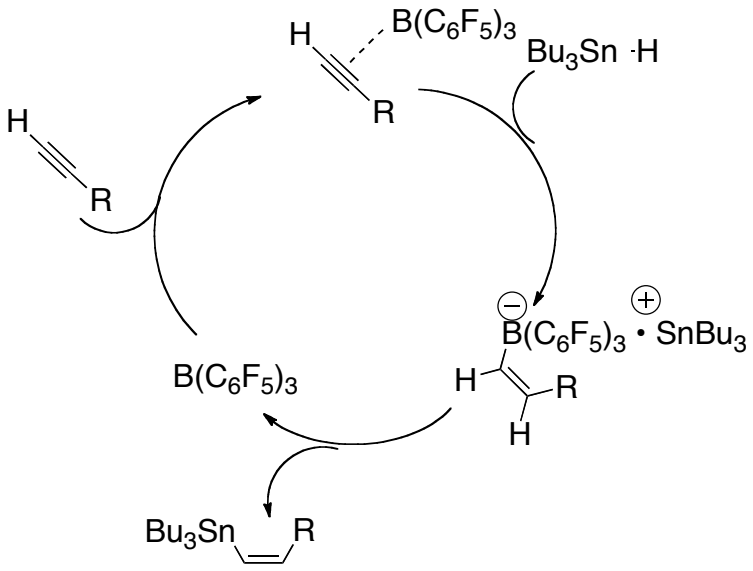
[a]No vinylstannane was observed. [b]based on the mass of the degraded material

Even though the first step of the reaction (allylation) was fast for all substrates examined (15 to 60 minutes, with the exception of the crotylation (Table 8, entry 9), both sterics and electronics governed the fate of the hydrostannation step. While the hydrostannation reaction of allylated 4-ethynylbenzaldehyde (**35**) was the fastest (1h), the same reaction became increasingly slower when the ethynyl group was moved closer to the aldehyde moiety (14 h for 3-ethynylbenzaldehyde (**36**) and 1d for 2-ehtnylbenzaldehyde (**37**)). An electron withdrawing group (Table 8, entry 4) was tolerated in the reaction, but, again, slower reactions compared to allylated 4-ethynylbenzaldehyde (entry 1) were observed. Entries 5 and 6 are interesting. These substrates underwent the first step of the reaction (as shown by TLC) failed to undergo successful hydrostannations. When $B(C_6F_5)_3$ was added to the allylation mixture of **39** under nitrogen, the color of the mixture turned deep orange and bubbling was observed after addition of PMHS. A hydrostannated product was never isolated. ^{1}HNMR of the crude matter indicated disappearance of all vinyl peaks after one hour of the reaction. Similarly, **40** (7:1 mixture with another unknown aldehyde) produced only trace amount (~7%) of the hydrostannated product **47**. While the reasons for some of these observations are not entirely clear, we believe that an electron donating group, possibly, inhibits the hydrostannation step. For the aliphatic alkynals **41** and **42** (entries 7 and 8), the second step of the reaction was the slowest and yields were lower compared to most of their aromatic counterparts. Finally, crotylation reaction of 4-ethynylbenzaldehyde (**35**) with (*E*)-crotylstannane proved to be slower than its allylation counterpart (1.5 h vs. 15 minutes). The reaction yielded partially separable syn and anti

products, but most of the products degraded on silicagel. Switching to neutral alumina column chromatography also proved ineffective as a similar degradation was observed. Timed TLC spotting revealed, the compound degrades even on a TLC plate.

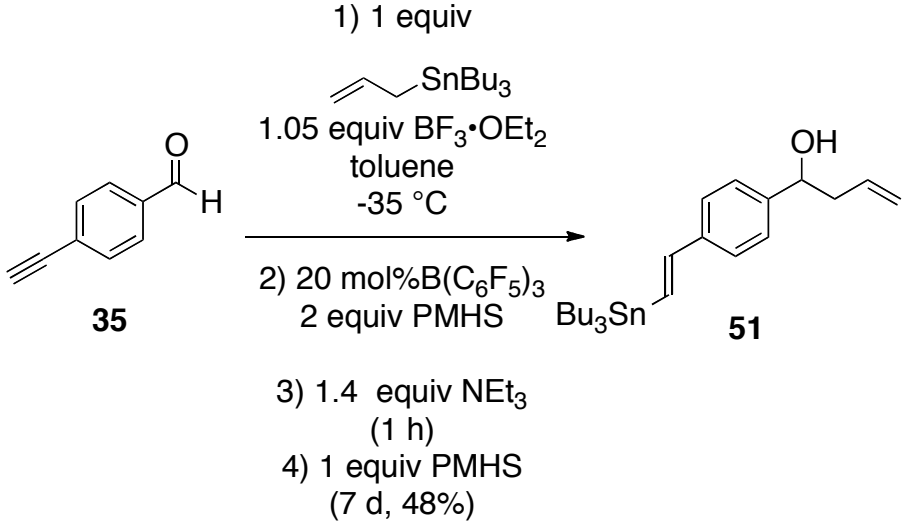
Stereochemistry of the vinylstannanes, thus generated is of special interest. In all cases, (*Z*)-vinylstannanes were observed as exclusive or predominantly major products, possibly, due to the Lewis acid catalyzed protocol.[48] A plausible mechanism for the Lewis acid catalyzed hydrostannation is shown in Figure 10. The coordination of the acetylenic bond of the alkyne to the Lewis acid ($B(C_6F_5)_3$) would produce the π-complex. A hydride from Bu_3SnH (*in situ* generated) would attack an electron deficient carbon from the side opposite to Lewis acid to produce an “ate” complex. The “ate” complex then undergoes a trans-metalation from boron to tin with retention of geometry to produce the (*Z*)-stannanes and Lewis acid.

Figure 11. Lewis acid-catalyzed hydrostannation mechanism for alkynes



An interesting phenomenon was observed when the crude of the one-pot reaction of **35**, (Table 8, entry 1) was treated with one additional equivalent of PMHS after Et_3N work-up. Over a duration of 4 d, the (*Z*)-vinylstannane was isomerized to its (*E*)-counterpart. Finally, after 7 days, the (*E*)-product was isolated in 48% yield (Scheme 31).

Scheme 32. Isomerization of **43** with 1 additional equiv of PMHS

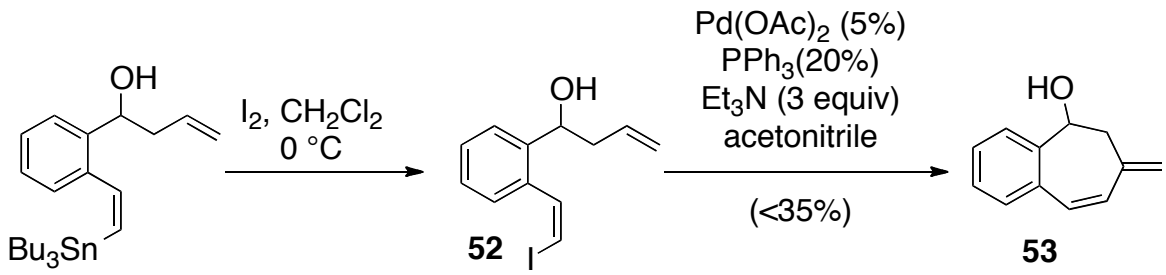


Such *Z* to *E* conversions became significantly reduced after 4 days (*Z*/*E* = 1.2:1) when a radical scavenger (hydroquinone) was added to the reaction crude. Moreover, similar *Z* to *E* equilibration was observed when the reaction crude was flushed with air and refrigerated. Both of these facts point toward radical participation in the process of equilibration. Silane mediated radical reactions are known in the literature.[49] The separated (*E*)-vinylstannane, however, does not equilibrate to its (*Z*)-counterpart when subjected to the same reaction conditions.

On the other hand, 2 and 3-ethynylbenzaldehyde do not respond to the excess PMHS protocol in a similar manner, as (*E*)-stannanes were never observed for this species over a duration of 4-days. At this point, the reasons for these observations are unclear.

Finally, we took our opportunity to show a synthetic application of our one-pot allylation-hydrostannation protocol. When **45** was treated with I_2 and the corresponding vinyliodide was subjected to Pd-catalyzed Heck reaction, smooth intramolecular Heck cyclization afforded **53** in two steps (Scheme 33). Even though, the product **53** had impurities, its partial characterization was possible. However, yield (<35%) of the product is not satisfactory and should be subjected to further optimizations.

Scheme 33. Synthetic application of one-pot allylation-hydrostannation protocol



4.3. Conclusions

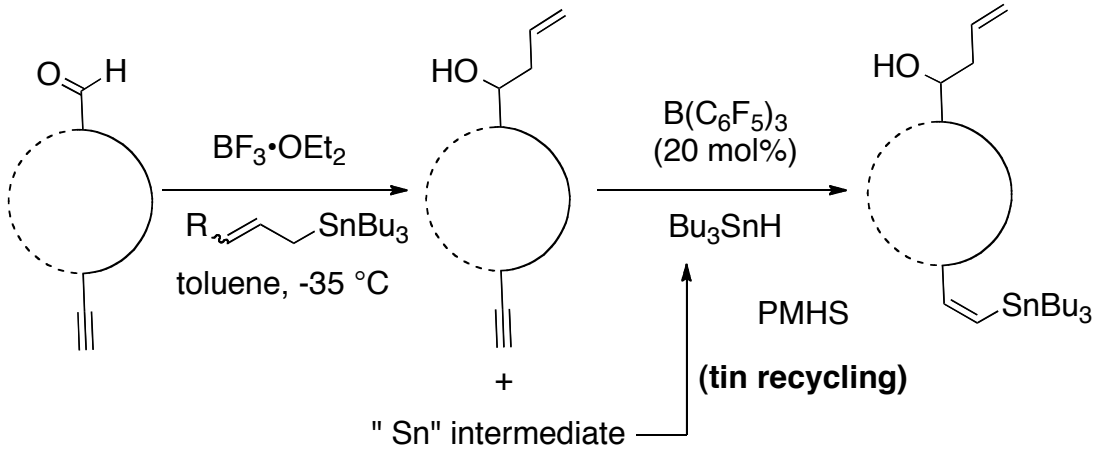
We have demonstrated a novel one-pot allylation-hydrostannation sequence that involves the in situ recycling of the tin species. This reaction can be performed on a number of alkynals with satisfactory outcome. Electron withdrawing groups are tolerated in the reaction. However, this reaction is inhibited by the presence of electron donating groups (e.g. OMe, Me) and cyanide. Reactions of the aromatic alkynals are more efficient (faster reactions with higher yields) than their aliphatic counterparts. The overall yields of the two-step process define an area of future improvement. Moreover, functional group susceptibility also constitutes another domain where this protocol needs to show its efficiency.

Chapter 5. Mechanistic investigation of Lewis acid catalyzed one-pot allylation-hydrostannation sequence

5.1 Introduction

Previously, we demonstrated that an allylation-hydrostannation sequence can be efficiently carried out on a variety of alkynals in one pot by using BF_3•OEt_2 as an allylation promoter and a reagent mix of catalytic $B(C_6F_5)_3$ and stoichiometric PMHS as a promoter of hydride formation/hydrostannation (Scheme 34). To answer the question whether these reactions proceed *via* an intermediacy of a "Sn-O" species or a "Sn-F" species, we decided to investigate the this reaction in more depth.

Scheme 34. One-pot allylation-hydrostannation protocol

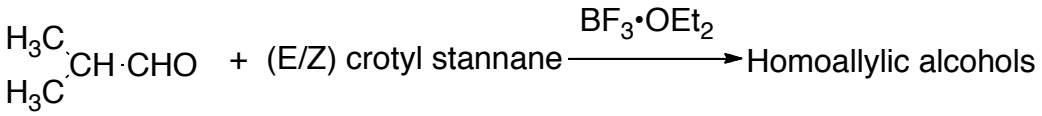


Our hypothesis was that a hydride was being produced *in situ* in the media from the "Sn intermediates" produced from the first step of the one-pot protocol. It was deemed worthwhile to explain the nature of these "Sn intermediates".

Metathesis reactions between allyltriorganostannanes and Lewis acids prior to allylation are documented in the literature,[50] but such reactions between stannanes and

BF_3•OEt_2 have not been conclusively proven. Tagliavini and co-workers showed that when (*E/Z*) crotylstannanes were added to a solution of aldehyde and BF_3-OEt_2 at –78 °C, erythro and threo homoallylic alcohols were formed along with their *E* and *Z* counterparts.[50a] The last two products, as they suggested, might come from intermediates formed from the initial organotin substrates and the added Lewis acid. The proportions of these isomeric products changed when aldehyde was added to the solution of organostannanes premixed with BF_3•OEt_2. They argued that this different proportion of the products originated from reaction of aldehyde with a mixture of new allylmetal substrates (generated from the organotin and the Lewis acid) the composition of which is different from the reaction species generated when the inverse addition was used. On the other hand, when chlorodiorganostannane was added to a mixture of premixed aldehyde and Lewis acid, no formation of *E* and *Z* homoallylic alcohol was observed indicating inactivity of the Lewis acid toward the organostannane substrate in this case (Scheme 35).

Scheme 35. An observation by Tagliavini and co-workers



Entry	Crotylstannane	E/Z ratio	% yield	product composition			
				erythro	threo	Z	E
1.	$Bu_3SnH_2CHC\ CHCH_3$	70/ 30	88	55	9	36	–
2.	$Bu_3SnH_2CHC\ CHCH_3$	52/ 48	89	54	11	5	30
3.	$Bu_2ClSnH_2CHC\ CHCH_3$	46/ 54	75	33	66	–	–

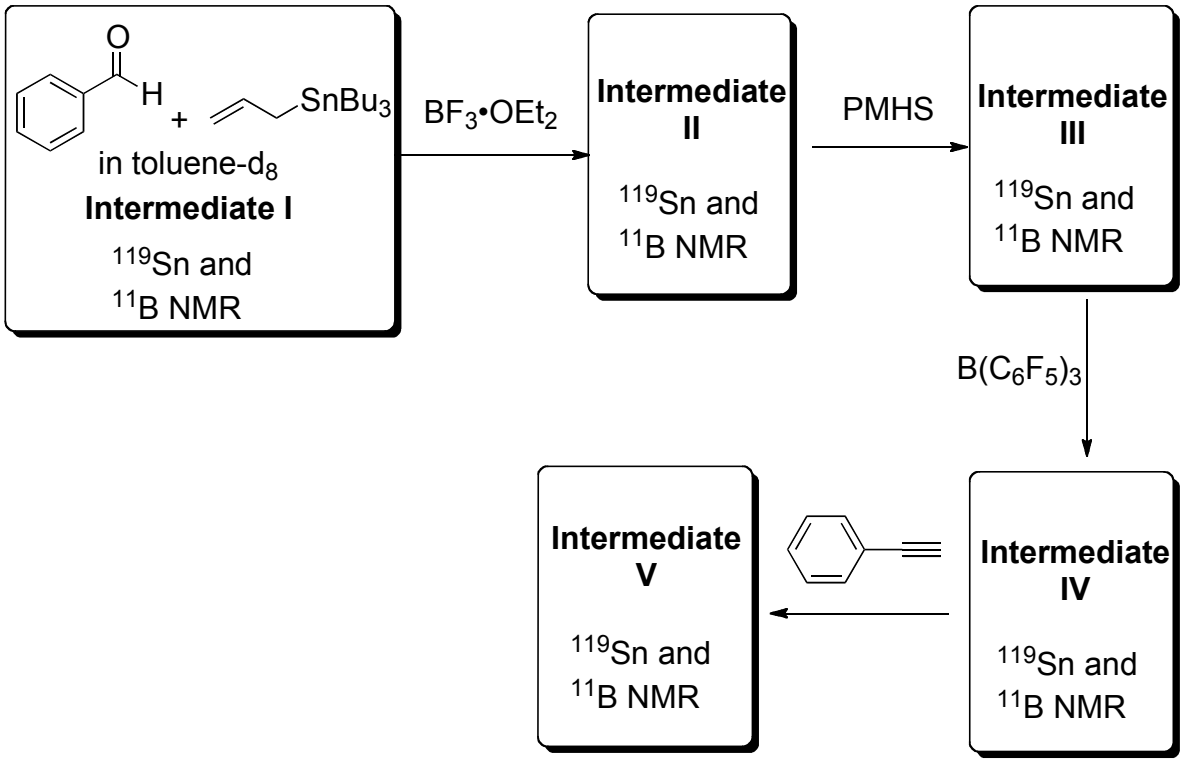
Denmark and co-workers also observed an interaction of trimethylallylstannane and BF_3•OEt_2.[51] In a ^{13}C NMR study, they observed a rapid 1,3-shift of Me_3Sn groups of the stannane. They suggested that such 1,3 shifts labilize the allyl groups for bimolecular exchange to another tin center by a process involving BF_3•OEt_2. However, formation of a Bu_3SnF•BF_3 complex was refuted based on absence of the corresponding peaks. They also observed that the allylation product was formed as diastereomeric boron ethers and Me_3Sn ethers were never detected in their study. The absence of extensive metathesis between allylstannanes and BF_3•OEt_2 and the absence stannylethers in the product made us wonder how PMHS in conjunction with $B(C_6F_5)_3$ could carry out the conversion of the tin intermediates formed during the allylation step that presumably were required for the hydrostannation step. We decided

to monitor the reaction by ^{119}Sn and ^{11}B NMR to unravel the mystery behind the chemistry.

5.2 Results and discussions

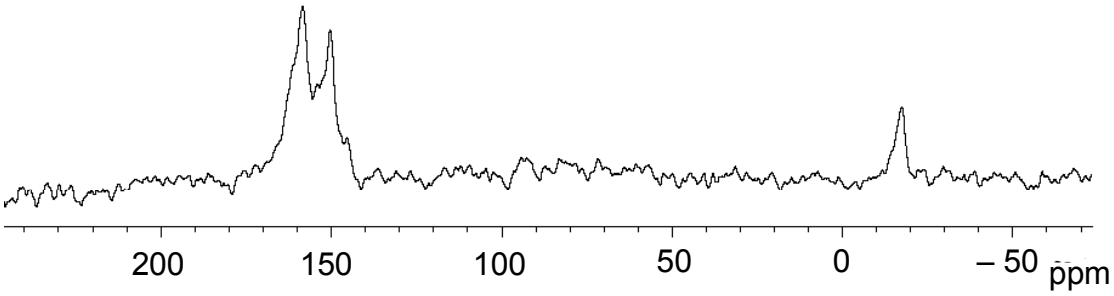
We first looked at the reaction between benzaldehyde and allyltributylstannane in presence of $BF_3 \cdot OEt_2$ by ^{119}Sn NMR. Benzaldehyde (0.04 mL, 0.375 mmol), and allyltributylstannane (0.12 mL, 0.375 mmol) were dissolved in toluene-d8 in an NMR tube under nitrogen and vortexed. ^{119}Sn NMR was observed after each addition of $BF_3 \cdot OEt_2$ (0.05 mL, 0.393 mmol), PMHS (0.05 mL) and $B(C_6F_5)_3$ (0.0384 mg, 20%). Finally, phenylacetylene was added (0.04 mL, 0.375 mmol) and ^{119}Sn NMR was taken. These steps were repeated when ^{11}B NMR spectra were obtained. Scheme 36 shows the stage of the process at which ^{119}Sn and ^{11}B spectra were obtained.

Scheme 36. ^{119}Sn NMR study of one-pot allylation-hydrostannation protocol



In the absence of BF_3•OEt_2, the reaction mixture of the aldehyde and stannane only showed the characteristic peak for allyltributylstannane (δ ~18 ppm) by ^{119}Sn NMR. When BF_3•OEt_2 was added, a doublet at δ 154 ppm slowly grew as the peak corresponding to allyltributylstannane decayed (Figure 12). The coupling constant (*J*) of this doublet was found to be in the range of 1650 Hz. Such a large coupling constant is consistent with many Sn–F species.[52] However, both peaks appeared to be very broad, implying possible involvements of the corresponding species in the intermediate(s).

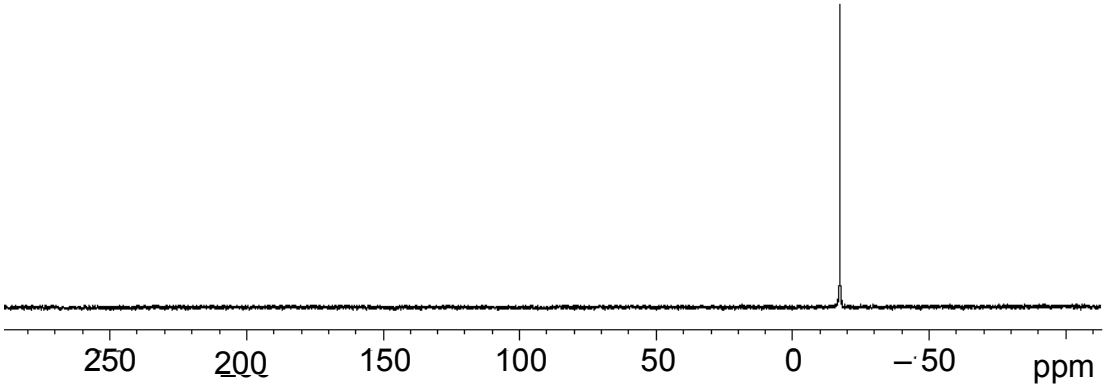
Figure 12. ^{119}Sn NMR spectrum of Intermediate II



A ^{11}B NMR study of the same mixture (Intermediate II) showed two major peaks at δ 0.152 and –1.136 ppm respectively. The first peak grew over time indicating gradual formation of the boron ether where as the other sharp peak (BF_3•OEt_2) decayed over the course of the reaction .

At this point, we were curious whether the tin species was being produced as a direct result of metathesis between allylstannane and the Lewis acid. So, BF_3•OEt_2 and allyltributylstannane was premixed and vortexed in an NMR tube. The ^{119}Sn NMR of the solution thus produced showed only one peak characteristic to the allylstannane, thereby, reiterating the absence of metathesis between these two species (Figure 13).

Figure 13. ^{119}Sn NMR spectrum of premixed allylstannane and BF_3• OEt_2



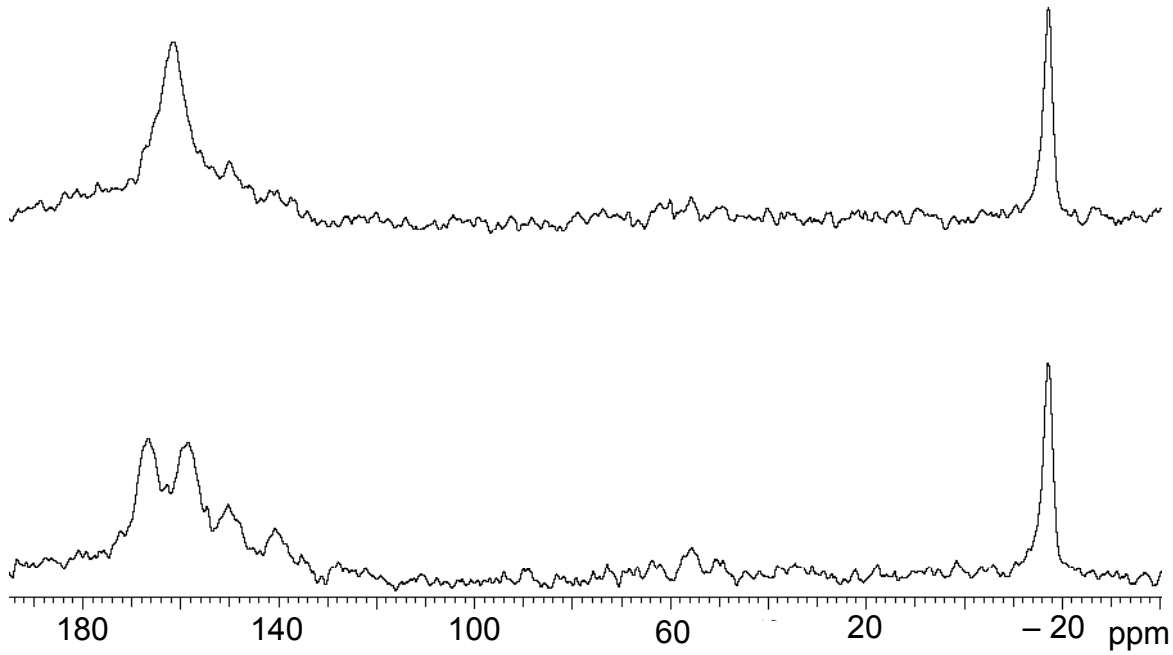
However, when benzaldehyde was added to this solution, the tin doublet reappeared. This indicates that the aldehyde is involved in the transformation of the allylstannane to the new species, presumably, because of the coordination of the aldehyde with boron that leads to the allylation reaction.

We further speculated that if the "Sn species" formed during the course of the reaction that is responsible for the formation of the organotin hydride is an oxygen bound tin species, PMHS should be able to cleave its Sn-O bond without any assistance from $B(C_6F_5)_3$.[31] ^{119}Sn chemical shifts for oxygen bound tins are normally observed in the range of 70-150 ppm (our tin doublet appears at ~154 ppm).[1]

In fact, $(Bu_3Sn)_2O$ reacts with PMHS at –35 °C forming tributyltin hydride, albeit, at a much slower rate compared to that observed at room temperature. The rate at which $(Bu_3Sn)_2O$ forms tributyltin hydride at –35 °C increased a great deal when $B(C_6F_5)_3$ was added. On the other hand, when PMHS was added to a mixture of benzaldehyde, allylstannane and BF_3•OEt_2 (Intermediate III) after the tin doublet

appeared by NMR, no change in the shape of the peak was observed, even after an hour. Nevertheless, the chemical shift of the doublet moved ~ 12 ppm downfield. At this point, it is not clear whether it is a due to formation of a different species or change of dielectric constant of the media upon addition of PMHS. Here, we took advantage of the opportunity to obtain a fluorine-decoupled ^{119}Sn NMR spectrum of the mixture. A clean transformation of the doublet to a singlet peak was observed upon decoupling (Figure 14).

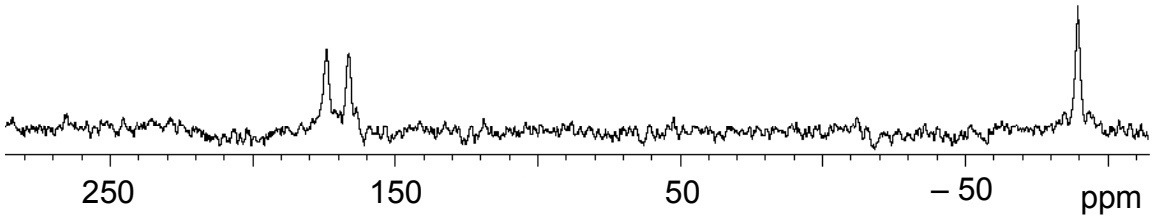
Figure 14. Fluorine-decoupled spectrum of Intermediate III



This result conclusively proves that a "Sn-F" species is being produced in the reaction. This species is not tributyltin fluoride which typically appears as a triplet at ~ δ -10 ppm in hexane solution with a coupling constant (*J*) of ~1350 Hz.[53]

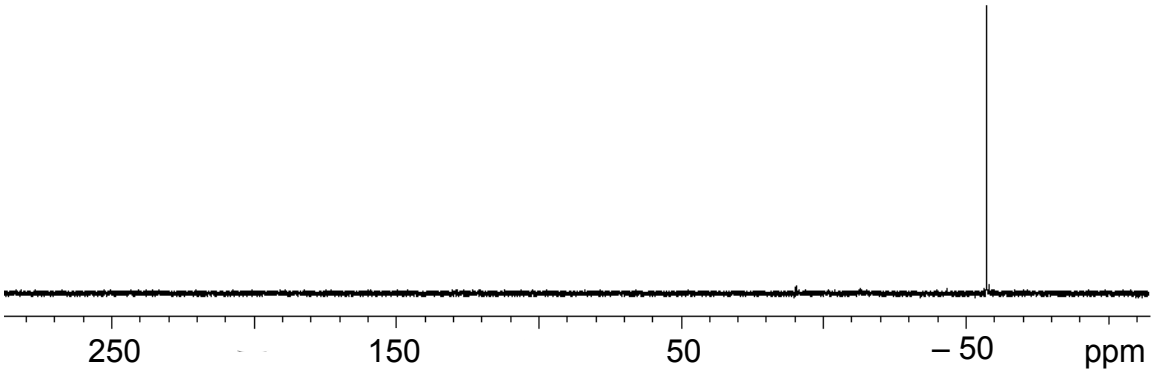
When $B(C_6F_5)_3$ was added to the mixture containing PMHS (Intermediate IV), a clear, but not unexpected, change was observed as a new peak started appearing at ~ δ -90 ppm (Figure 15). This is a characteristic peak for tributyltin hydride. This transformation, however, is very slow. Chandrasekar showed that $B(C_6F_5)_3$ can function as a PMHS activator.[54] So, it is not unrealistic to believe that $B(C_6F_5)_3$ activates PMHS to reduce the "Sn-F" species formed during the course of the reaction to tributyltin hydride.

Figure 15. ^{119}Sn NMR spectrum of the mixture after addition of PMHS and $B(C_6F_5)_3$



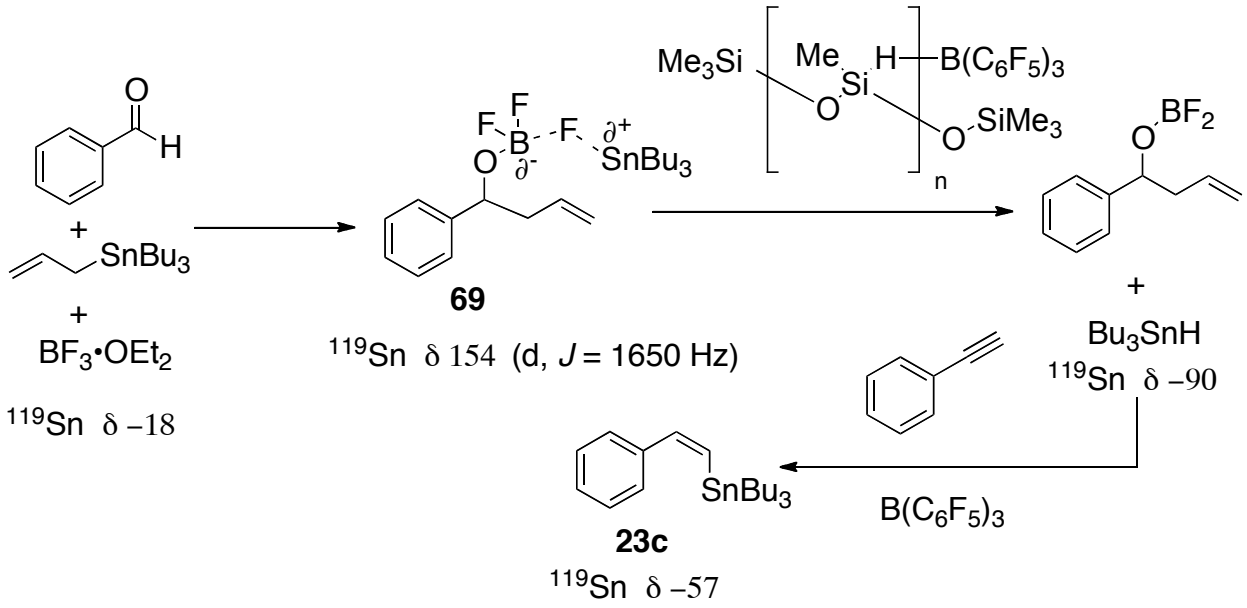
Finally, when phenyl acetylene was added to this solution (Intermediate V), the tributyltin hydride and tin doublet disappeared and corresponding peak of the vinylstannane species appeared almost instantaneously at δ – 57 ppm (Figure 16).

Figure 16. ^{119}Sn NMR spectra of Intermediate V



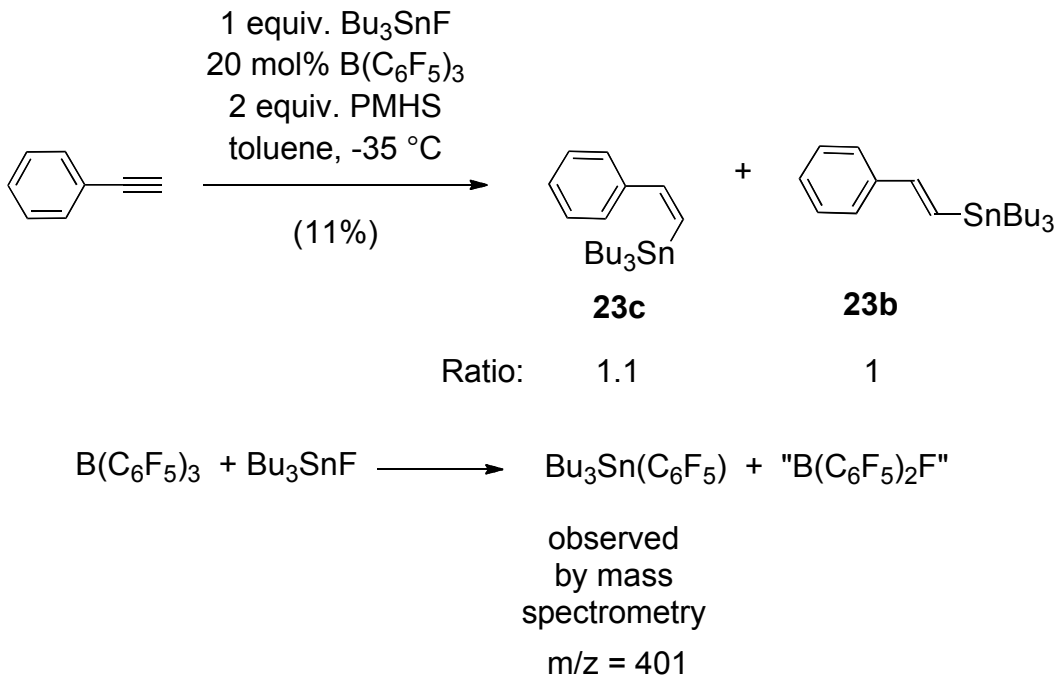
After studying the kinetics of the reaction, we propose the following course for the reaction. Aldehyde reacts with allylstannane in presence of BF_3•OEt_2 to form a boron-ether and the "Sn-F" intermediate. This "Sn-F" intermediate might be associated with the boron ether through Sn–F–B linkage (Scheme 37, **69**). Compounds with such linkages are known in the literature.[55] The downfield ^{119}Sn chemical shift (~154 ppm) of this intermediate is consistent with the positive (or partially positive) nature of the tin moiety.[55,69] PMHS, activated by $B(C_6F_5)_3$ reduces this "Sn-F" intermediate into tributyltin hydride, which, then, enters the Lewis acid catalytic cycle to produce the corresponding vinylstannanes as described earlier.

Scheme 37. Mechanistic rationale of one-pot allylation-hydrostannations



The proposal described in Scheme 37 is also based on additional experimentations. To eliminate the possibility of Bu_3SnF involvement, reactions were performed with premade tributyltin fluoride for 1h (exact same time length as our typical hydrostannation step for phenyl acetylene in our optimized allylation-hydrostannation protocol). The result of this reaction (Scheme 38) produced an enigma where (*Z*) and (*E*) vinylstannanes were produced in almost equal amounts with a combined 11% yield. From experiments done in our group, it was known that Bu_3SnF undergoes unusual boron to tin ligand exchange reaction as observed by mass spectrometry (Scheme 38). So, this erosion of yield is not unexpected. Non-selective product formation and the low yield obtained in the reaction in conjunction with the chemical shift of the species formed all indicate that it is unlikely for Bu_3SnF to be the species being reduced to Bu_3SnH in our allylation-hydrostannation reaction.

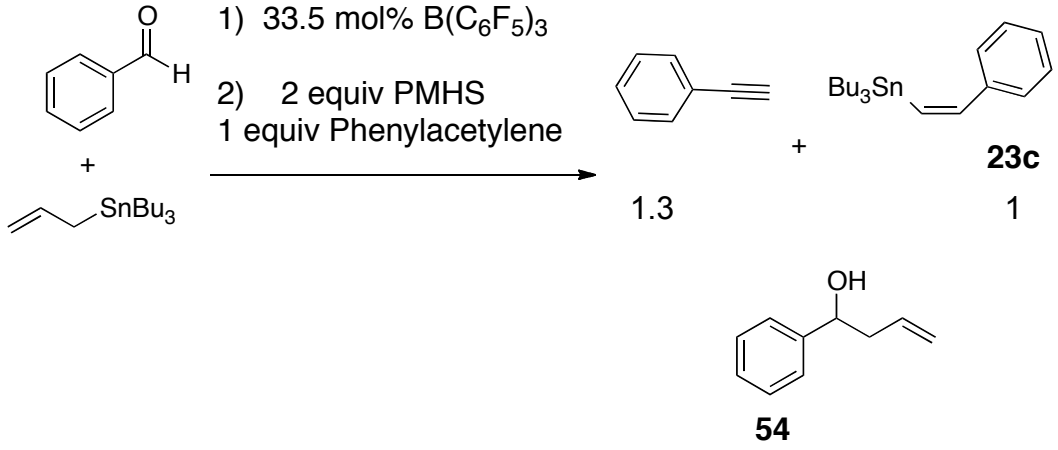
Scheme 38. Hydrostannation of phenylacetylene with Bu_3SnF



Finally, it was essential to show whether the one-pot allylation-hydrostannation reaction could proceed without BF_3•OEt_2. In fact, fluorine of the "Sn-F" species produced during the first step of our reaction must have been coming from BF_3•OEt_2. In that sense, BF_3•OEt_2 has an indirect but indispensable role in the second step of the reaction, a.k.a. hydrostannation. $B(C_6F_5)_3$ is known to be used as an allylation reagent.[55] Indeed, when benzaldehyde and allyltributylstannane were subjected to $B(C_6F_5)_3$ mediated allylation followed by addition of phenylacetylene and PMHS in an NMR tube, the corresponding *Z*-vinylstannane peak was observed in ^1H NMR. However, the rate of hydrostannation was slow. Even after 4 h, the phenyl acetylene to

vinylstannane ratio was found to be 1.3 to 1 (Scheme 39). For the BF_3•OEt_2 mediated reactions, the conversion of phenylacetylene to vinylstannane took place almost instantaneously, reiterating the indirect but important role of BF_3•OEt_2 in the one-pot protocol.

Scheme 39. Allylation/hydrostannation sequence with $B(C_6F_5)_3$



Piers and co-workers have extensively studied the allylation of orthoanisaldehyde in presence of allylstannane and $B(C_6F_5)_3$.[55a] Formation of stannyl ether after the allylation reaction was suggested in these cases. So, it is not unreasonable to believe that a similar stannyl ether (which was never seen in our one-pot reactions) is being produced when the reaction proceeds without BF_3•OEt_2. That, then, gets cleaved by PMHS to produce tributyltin hydride at a slower rate at – 35 °C, as we have previously observed in case of $(Bu_3Sn)_2O$. Tributyltin hydride is, then, entering the catalytic cycle of $B(C_6F_5)_3$ to carry out hydrostannation of the alkyne.

5.3 Conclusions

We have demonstrated that our one-pot allylation/hydrostannation protocols can be applied to a number of alkynals. These processes proceed via a “Sn-F” intermediate produced in the allylation step of one-pot allylation-hydrostannation protocols. Activated PMHS, then, reduces this species to Bu_3SnH. Thus, organotin intermediates formed in the allylation step, gets recycled to the Lewis acid catalyzed hydrostannation step, the second step of the sequence. No metathesis is observed between allylstannane and Lewis acid species, reiterating the observations made by Denmark and co-workers. However, to the best of our knowledge, our observations provide the first spectroscopic evidence of formation of a fluorine bound tin species in $BF_3{\bullet}OEt_2$ mediated allylation reactions of aldehydes.

Chapter 6. Experimental Details

Materials and Methods: Reactions were carried out in oven or flame-dried glassware under nitrogen in round bottom flasks or in sealed tubes unless otherwise noted. All commercial reagents were used without purification. All solvents were reagent grade. Diethyl ether and THF were freshly distilled from sodium/benzophenone under nitrogen. Benzene, toluene and triethylamine were freshly distilled from calcium hydride under nitrogen. Except as otherwise indicated, all reactions were magnetically stirred and monitored by thin-layer chromatography with 0.25-mm pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 Å (230-400 mesh ASTM). Yields refer to chromatographically and spectroscopically pure compounds unless otherwise mentioned. In a few cases where the vinylstannanes were impossible to separate from the tin dimmer impurity, external-standard yields were reported. Melting points were determined on a Thomas-Hoover Apparatus, uncorrected. ^{1}H NMR spectra were recorded at 300 or 500 MHz Spectrometer. ^{13}C NMR spectra were recorded at 75 or 125 MHz. Chemical shifts are reported relative to the residue peaks of solvent $CDCl_3$ (δ = 7.24 for ^{1}H and δ = 77 for ^{13}C). IR spectra were obtained at Michigan State University and Grand Valley State University. High-resolution mass spectra (HRMS) data were obtained at Michigan State University Mass Spectrometry Service center.

Representative procedure for molybdenum ($MoBI_3$)-catalyzed hydrostannations using Bu_3SnF/PMHS protocol (Table 1, Conditions B): To the sealed tube were

added THF (7 mL), alkyne (1 mmol), Bu_3SnF (464 mg, 1.5 mmol), hydroquinone (10 mg, 0.09 mmol), PMHS (0.10 mL, 1.6 mmol), $MoBI_3$ (8.6 mg, 0.02 mmol) and TBAF (2 drops of a 1M solution in THF). The mixture was then heated in an oil bath at 65°C. Once complete (~3h), the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^1H NMR spectrum of the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (buffered with 1% Et_3N). Compound **17**, **18**, **19**, **20**, **21**, **24**, **25, 28, 29 and 30** were prepared previously in the group using the same protocol. Alkyne **1**, **3**, **6**, **7**, **9**, **10** and **11** were bought from Aldrich. Alkyne **2**, **4**, **5** and **8** was also prepared previously in the lab from commercially available alkynes.

General Procedure for Molybdenum-Catalyzed Hydrostannations with Bu_3SnH (Table 1, Conditions A): To the sealed tube were added THF (2 mL) and alkyne (1 mmol) and stirred for a 5 mins. $MoBI_3$ (4.3 mg, 0.01 mmol) and hydroquinone (10 mg, 0.09 mmol) were added and stirred followed by the addition of Bu_3SnH (0.8 mL, 3 mmol). The mixture was then heated in an oil bath at 55°C until complete by TLC analysis. Once complete (~12h), the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^1H NMR spectrum of

the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (buffered with1% Et_3N).

Preparation of 22a and 22b (Table 1, entry 6)

Applying Conditions B on alkyne **6** (82 mg, 1 mmol) afforded **22a** and **22b** (1:2.5) after 3 h as oils. Using Hemethyldisiloxane (HMDS) as an external standard, the yield was calculated to be 54%.

Applying Conditions A on alkyne **6** (82 mg, 1 mmol) afforded after 12 h a mixture of **22a** and **22b** (1:2.1) as oils. Using Hemethyldisiloxane (HMDS) as an external standard the yield was calculated to be 93%. Spectroscopic data were consistent with the literature and that reported earlier.[56,65]

Preparation of 23a and 23b (Table 1, entry 7)

Applying the conditions B on alkyne **7** (102 mg, 1 mmol) afforded after 3 h a mixture of 23a and 23b and 23c (1:1:1) as a clear oil. Using Hemethyldisiloxane (HMDS) as an external standard, the yield was calculated to be 88%.

Applying Conditions B on alkyne **7** (102 mg, 1 mmol) afforded after 12 h a mixture of **23a** and **23b** (1:20) as a clear oil. Using Tetrahydrofuran (THF) as an external standard

the yield was calculated to be quantitative. Spctroscopic data were consistent with the literature. [57,66]

Preparation of 24a and 24b (Table 1, entry 8)

Applying Conditions A on alkyne **8** (212 mg, 1 mmol) afforded after 12 h a mixture of **24a** and **24b** (1.2:1) as clear oil. After column chromatography [silica; hexanes, 1% TEA] a separable mixture of **24a** and **24b** was obtained as clear oils (287 mg, 57%).

Data for **24a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (d, *J* = 8.9, 6 H), 0.81-0.93 (m, 30 H), 1.22-1.37 (m, 6 H), 1.39-1.55 (m, 7 H), 3.73 (t, *J* = 5.7 Hz, 1 H), 5.17 (m, 1 H), 5.70 (m, 1 H) ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.7, -3.8, 10.3, 13.7, 18.3, 19.8, 26.1, 27.5, 29.1, 33.9, 85.8, 124.8, 158.4.

Data for **24b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (d, *J* = 8.9, 6 H), 0.81-0.89 (m, 30 H), 1.22-1.34 (m, 6 H), 1.43-1.53 (m, 6 H), 1.57-1.67 (m, 1 H), 3.72 (t, *J* = 5.7 Hz), 5.77-6.08 (m, 2 H), ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.8, -4.2, 9.5, 13.7, 18.0, 18.5, 25.9, 27.3, 29.2, 34.4, 81.9, 127.7, 150.5. Spectroscopic data was consistent with that reported earlier.[56]

Preparation of 25a and 25b (Table 1, entry 9)

Applying Conditions A on alkyne **9** (98 mg, 1 mmol) afforded after 12 h a mixture of **25a** and **25b** (4:1) as clear oil. After column chromatography [silica; 95:5 hexanes/EtOAc, 1% TEA] a separable mixture of **25a** and **25b** was obtained as clear oils (322 mg, 86%).

Data for **25a**: ^{1}HNMR (300 MHz, $CDCl_3$) δ 0.82-0.94 (m, 21 H), 1.24-1.36 (m, 6 H), 1.40-1.64 (m, 7 H), 3.71-3.91 (m, 1 H), 5.13-5.35 (m, 1 H), 5.52-5.98 (m, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 13.7, 17.5,19.8, 27.4, 29.1, 33.2, 85.0, 124.8, 158.4.

Data for **26b**: ^{1}HNMR (300 MHz, $CDCl_3$) δ 0.76-0.98 (m, 21 H), 1.23-1.35 (m, 6 H), 1.41-1.57 (m, 6 H), 1.67-1.80, (m, 1 H), 3.79-3.94 (m, 1 H), 5.76-6.27 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.5, 13.7, 17.5, 18.2, 27.2, 29.1, 33.5, 80.5, 128.8, 149.4. Spectroscopic data were consistent with that reported earlier.[56]

Preparation of 26a and 26b (Table 1, entry 10)

Applying conditions B on alkyne **10** (84 mg, 1 mmol) afforded after 3 h a mixture of **26a** and **26b** (6:1) and column chromatography [silica; 95:5 hexanes/EtOAc, 1% TEA] produced a separable mixture of **26a** and **26b** as clear oils (296 mg, 79%).

Applying conditions A on alkyne **10** (84 mg, 1 mmol) afforded after 12 h a mixture of **26a** and **26b** (2.3:1) and column chromatography [silica; 95:5 hexanes/EtOAc, 1% TEA] produced a separable mixture of **26a** and **26b** (2.3:1) as clear oils (304 mg, 81%).

Data for **26a:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85-0.92 (m, 15 H), 1.24-1.34 (m, 12 H), 1.42-1.53 (m, 6 H), 5.12 (d, *J* = 1.5 Hz, 1 H), 5.7 (d, *J* = 1.37 Hz, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.7, 13.7, 27.4, 29.1, 30.6, 75.7, 120.6, 165.0.

Data for **26b** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84-0.90 (m, 15 H), 1.22-1.34 (m, 12 H), 1.42-1.52 (m, 6 H), 6.08 (d, *J* = 1.47 Hz, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.4, 13.7, 27.2, 29.0, 29.4, 72.4, 122.4, 155.6. Spectroscopic data was consistent with the literature.[22a]

Preparation of 27a and 27b (Table 1, entry 11) Applying Conditions B on **11** (146 mg, 1 mmol) afforded after 3 h and column chromatography [silica; 95:5 hexanes/EtOAc, 1% TEA] a separable mixture of **27a** and **27b** (3.7:1) as clear oils (407 mg, 93%).

Applying the Conditions A on **11** (146 mg, 1 mmol) afforded after 3 h and column chromatography [silica; 95:5 hexanes/EtOAc, 1% TEA] a separable mixture of **27a** and **27b** (2.8:1) as clear oils (432mg, 99%).

Data for **27a:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.62-0.87 (m, 15 H), 1.17-1.43 (m, 12 H), 1.65 (s, 3 H), 1.84, (s, 1 H), 5.29 (d, *J* = 1.5 Hz, 1 H), 5.77 (d, *J* = 1.5 Hz, 1 H), 7.17-7.23 (m, 1 H), 7.26-7.32 (m, 2 H), 7.38-7.42 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.5, 13.7, 27.4, 29.0, 30.0, 79.1, 122.6, 125.5, 126.7, 128.0, 147.1, 163.4.

Data for **27b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82-0.91 (m, 15 H), 1.22-1.34 (m, 6 H), 1.43-1.53 (m, 6 H), 1.62 (s, 3 H), 1.91 (s, 1 H), 6.25 (d, *J* = 6.8 Hz, 2H), 7.20-7.25 (m, 1 H), 7.29-7.35 (m, 2 H), 7.35-7.47 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.5, 13.7, 27.2, 29.1, 29.4, 76.1, 124.5, 125.3, 126.8, 128.1, 146.8, 153.8. Spectroscopic data was consistent with that reported earlier.[56]

General Procedure for Nickel-Catalyzed Hydrostannations (Table 3, Conditions D): To a sealed tube were added THF(7 mL), alkyne (1 mmol), Bu_3SnF (464 mg, 1.5 mmol), hydroquinone (10 mg, 0.09 mmol), PMHS (0.09 mL, 1.5 mmol), $NiCl_2(PPh_3)_3$ (13.2 mg, 0.02 mmol) and TBAF (2 drops of a 1M solution in THF). The mixture was then heated in an oil bath at 65°C until complete by TLC analysis. Once complete (~ 4h), the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^{1}H NMR spectrum of the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (buffered with 1% Et_3N).

General Procedure for Nickel-Catalyzed Hydrostannations with Bu_3SnH (Table 3, Conditions C): To the flask were added THF (7 mL), alkyne (1 mmol), Bu_3SnF (464 mg, 1.5 equiv), hydroquinone (10 mg, 0.09 mmol), PMHS (0.10 mL, 1.6 mmol), $NiCl_2(PPh_3)_2$ (13.2 mg, 0.02 mmol) and TBAF (2 drops of a 1M solution in THF). The mixture was then heated in an oil bath at 60°C until complete by TLC analysis. Once complete (~ 4h), the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^1H NMR spectrum of the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (buffered with 1% Et_3N).

Preparation of 17a and 17b (Table 3, entry 1)

Under Conditions D described above, propargyl alcohol (**1**) produced **17**a and **17b** (2.4:1) 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **17a** and **17b** as clear oils (243 mg, 70%).

Under Conditions C described above, propargyl alcohol (**1**) produced **17a** and **17b** (4.1:1) 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **17a** and **17b** as clear oils (208 mg, 60%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 19a and 19b (Table 3, entry 2)

Under Condition D described above, THP-protected propargyl alcohol (**3**) produced **19a** and **19b** (1.7:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (263 mg, 61%).

Under Conditions C described above, alkyne **3** produced **19a** and **19b** (7.1:1) 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (211 mg, 49%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 31a and 31b (Table 3, entry 3)

Under Conditions D described above, alkyne **15** produced **31a** and **31b** (1.8:1) in 5 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **31a** and **31b** as clear oils (368 mg, 87%).

Under Conditions C described above, alkyne **15** produced **31a** and **31b** (1.3:1) in 5 h. The reaction was cooled to room temperature and subjected to column chromatography

[silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **31a** and **31b** as clear oils (292 mg, 69%).

Data for **31a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.70-0.86 (m, 15H), 1.16-1.40 (m, 12H), 1.94 (bs, 1H), 5.30-5.33 (m, 2H), 5.90 (m, 1 H), 7.23-7.32 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.9, 13.6, 27.3, 28.9, 80.5, 124.3, 126.5, 127.4, 128.3, 143.0, 158.1.

Data for **31b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83-0.91 (m, 15H), 1.24-1.34 (m, 6H), 1.42-1.53 (m, 6H), 1.99 (bs, 1H), 5.16 (d, *J* = 4.6 Hz, 1H), 6.11-6.33 (m, 2H), 7.24-7.37 (m, 5H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 9.5, 13.7, 27.2, 29.1, 77.6, 126.4, 127.5, 128.5, 128.6, 143.0, 149.5. Spectroscopic data was consistent with the literature.[57]

Preparation of 27a and 27b (Table 3, entry 4)

Under Conditions D described above, alkyne **11** (146 mg, 1 mmol) produced **27a** and **27b** (1:1.8) in 5 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 95:2 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **27a** and **27b** as clear oils (288 mg, 66%).

Under Conditions C as described above, alkyne **11** (146 mg, 1 mmol) produced **27a** and **27b** (1:3.4) in 5 h. The reaction was cooled to room temperature and subjected to

column chromatography [silica gel; 95/2 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **27a** and **27b** as clear oils (201 mg, 46%). For spectroscopic data, see page 92.

Preparation of 32a and 32b (Table 3, entry 5)

Under Conditions D as described above, alkyne **16** produced **32a** and **32b** (1.4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a separable mixture of the isomers **32a** and **32b** and trace amount of *Z*-stannane as clear oils (240 mg, 52%).

Under Conditions C as described above, alkyne **16** produced **32a** and **32b** (4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a separable mixture of the isomers 32a and 32b and trace amount of *Z*-stannane as clear oils (240 mg, 52%). Spectroscopic data was consistent with the literature.[57]

Preparation of 22a and 22b (Table 3, entry 6)

Under Conditions D as described above, alkyne **6** produced **22a** and **22b** (1:22) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford isomer **22b** (**22a** was never recovered) as a clear oil (310 mg, 83%).

Under the reaction condition described above, alkyne **6** produced **22a** and **22b** (1:4.3) in 4 h. Using Hemethyldisiloxane (HMDS) as an external standard, the yield was calculated to be quantitative.

Data for **22b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82-0.92 (m, 15 H), 0.98 (s, 9 H), 1.23-1.35 (m, 6 H), 1.43-1.56 (m, 6 H), 5.59-6.19 (dd, *J* = 19.6, 40.6 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.4, 13.7, 27.2, 29.1, 29.2, 35.9, 119.7, 160.0. Spectroscopic data was consistent with that reported earlier.[56,65]

Preparation of 23a, 23b and 23c (Table 3, entry 7)

Under Conditions D as described above, alkyne **7** produced **23a** and **23b** (2.5:2.4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **23a**, **23b** and **23c** as a yellow oil (326 mg, 83%).[57.66]

General Procedure for cobalt-catalyzed Hydrostannations (Table 4, Conditions F):

To a sealed tube were added THF(7 mL), alkyne (1 mmol), Bu_3SnF (464 mg, 1.5 mmol), hydroquinone (10 mg, 0.09 mmol), PMHS (0.10 mL, 1.6 mmol), $CoCl_2(PPh_3)_3$ (27 mg, 0.04 mmol) and TBAF (2 drops of a 1M solution in THF). The mixture was then

heated in an oil bath at 65°C for 1 d. Then the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^{1}H NMR spectrum of the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (1% Et_3N).

General procedure for cobalt-Catalyzed Hydrostannations with Bu_3SnH (Table 4, Conditions E): In a sealed tube, the alkyne (1 mmoL) was dissolved in 7 mL of THF. To this were added hydroquinone (10 mg, 9 mol%), catalyst (27 mg, 2 mol%) and tributyltin hydride (0.4 mL, 1.5 mmoL). The mixture was heated to 65°C for 12 h. After the reaction, the mixture was concentrated and isomeric ratio was calculated from the crude. Finally, the products were then purified by flash silica gel chromatography (1% Et_3N).

Preparation of 19a and 19b (Table 4, entry 1)

Under Condition F described above, THP-protected propargyl alcohol (**3**) produced **19a** and **19b** (1.5:1). The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils. The yield was calculated as an average of three runs (281 mg, 65%).

Under Conditions E, as described above, alkyne 3 produced **19a** and **19b** (1.3:1) 12 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (361 mg, 84%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 23a and 23b (Table 4, entry 2)

Under Conditions F as described above, phenylacetylene (**6**) produced **23a** and **23b** (1.5:1). The yield was calculated by using HMDS as external standards (96%).[57]

Preparation of 22a and 22b (Table 4, entry 3)

Under Conditions F as described above, alkyne 6 produced **22a** and **22b** (1:9) in 1 d. The reaction was cooled to room temperature and the yield was calculated using both HMDS as external standard (96%).

Under the Conditions E as described above, alkyne 6 produced **22a** and **22b** (1:5.3) in 12 h. The reaction was cooled to room temperature. The yield was calculated using HMDS as external standard (100%).[56,65]

General Procedure for rhodium/ruthenium-catalyzed Hydrostannations (Table 5, Conditions H): To a sealed tube were added THF(7 mL), alkyne (1 mmol), Bu_3SnF

(464 mg, 1.5 mmol), hydroquinone (10 mg, 0.09 mmol), PMHS (0.10 mL, 1.6 mmol), catalyst (2 mol% in metal) and TBAF (2 drops of a 1M solution in THF). The mixture was then heated in an oil bath at 65°C for 1 d. Then the reaction mixture was concentrated, the crude was passed through a short plug of silica gel to remove the catalyst, ^{1}H NMR spectrum of the concentrated crude material was taken to determine the isomeric ratio. The products were then purified by flash silica gel chromatography (1% Et_3N).

General procedure for rhodium/ruthenium-catalyzed Hydrostannations with Bu_3SnH (Table 5, Conditions G): In a sealed tube, the alkyne (1 mmoL) was dissolved in 7 mL of THF. To this were added hydroquinone (10 mg, 9 mol%), catalyst (2 mol% in metal) and tributyltin hydride (0.4 mL, 1.5 mmoL). The mixture was heated to 65 °C until complete. After the reaction, the mixture was concentrated and isomeric ratio was calculated from the crude. Finally, the products were then purified by flash silica gel chromatography (1% Et_3N).

Preparation of 19a and 19b with $[RhCl(COD)]_2$ as catalyst (Table 5, entry 1)

Under Condition H described above, THP-protected propargyl alcohol (**3**) with [RhCl(COD)], (5 mg, 1mol%), failed to produce **19a** and **19b** even after 2.5 d. The reaction was cooled to room temperature and subjected to column chromatography

[silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford trace amount of **19a** and **19b** as clear oils (<5%).

Under Conditions G, as described above, alkyne **3** produced **19a** and **19b** (1.2:1) 1 d. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (255 mg, 59%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 19a and 19b with $RhCl(CO)(PPh_3)_2$ as catalyst (Table 5, entry 2)

Under Condition H described above, THP-protected propargyl alcohol (3) with $RhCl(CO)(PPh_3)_2$, (14 mg, 2 mol%) afforded **19a** and **19b** (1:3.3) after 8 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford mixture of **19a** and **19b** as clear oils (73 mg, 17%).

Under Conditions G, as described above, alkyne 3 produced **19a** and **19b** (1:1) 12 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (324 mg, 75%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 32a and 32b with $RhCl(CO)(PPh_3)_2$ as catalyst (Table 5, entry 3)

Under Condition H described above, TBS-protected propargyl alcohol (**16**) with $RhCl(CO)(PPh_3)_2$, (14 mg, 2 mol%) afforded **32a** and **32b** (1:2.5) after 8 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford partially separable mixture of **32a** and **32b** as clear oils (254 mg, 55%).

Under Conditions G, as described above, alkyne **16** produced **32**a and **32**b (1:1) 12 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a partially separable mixture of the isomers **32a** and **32b** as clear oils (267 mg, 58%). Spectroscopic data were consistent with the literature.[57]

Preparation of 19a and 19b with $RuCl_2(PPh_3)_4$ as catalyst (Table 5, entry 4)

Under Condition H described above, THP-protected propargyl alcohol (**3**) with $RuCl_2(PPh_3)_4$ (20 mg, 2 mol%), failed to produce **19a** and **19b** and a complex mixture resulted after 8 h.

Under Conditions G, as described above, alkyne **3** produced **19a** and **19b** and the **19c** (2.5:1.6:1) after 18h. The reaction was cooled to room temperature and subjected to

column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** and **19c** as clear oils (86 mg, 20%). Spectroscopic data were consistent with the literature.[22c]

Preparation of TBS-protected propargyl alcohol (16): TBSCl (3.81g, 25.3 mmol) was added to a solution of propargyl alcohol (1.29 g, 23 mmol), imidazole (1.88 g, 27.6 mmol) and DMAP (0.28 g, 2.3 mmol) in CH_2Cl_2 (125 mL) at 0 °C and stirred overnight at 0 °C. The reaction was then poured into a saturated solution of NH_4Cl and layers were separated. The organic phase was washed with saturated NH_4Cl (3x50 mL) and dried with $MgSO_4$. Column chromatography [silica gel; hexane] afforded desired alkyne (2.3g, 59%). Spectroscopic data was consistent with the literature.[70]

Representative procedure for $NiCl_2(PPh_3)_2$ catalyzed hydrostannations using Bu_3SnCl/ $KF_{(aq)}$/ PMHS protocol (Scheme 13): Preparation of **19a** and **19b** is representative. Alkyne **3** (14 mg, 1 mmol), KF (174 mg, 3 equiv), H_2O (1 mL), Bu_3SnCl (0.41 mL, 1.5 equiv), catalyst (13 mg, 2 mol%), PMHS (0.09 mL, 1.5 equiv), TBAF (2 drops, 1 mol%) and hydroquinone (10 mg, 9 mol%) in 7 mL THF were heated to reflux in a round bottom flask for 48 h. The reaction was quenched with 2 mL 0.5 M NaOH solution. The aqueous layer was extracted with CH_2Cl_2 (3x5 mL), dried with $MgSO_4$ and

concentrated. The crude was subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a column chromatographically inseparable mixture of the isomers **19a** and **19b** as clear oils (203 mg, 47%) and starting alkyne 3 (~14 mg, 10%).

Representative procedure for $NiCl_2(PPh_3)_2$ catalyzed hydrostannations using Bu_3SnCl/ KF / 18-crown-6/ PMHS protocol (Scheme 14): Alkyne (1 mmol) was dissolved in THF (7 mL) in a sealed tube under nitrogen atmosphere. Hydroquinone (10 mg, 9 mol%), KF (174 mg, 3 equiv) and 18-crown-6 (793 mg, 3 equiv) were added to the solution followed by sequential addition of catalyst (13 mg, 2 mol%), Bu_3SnCl (0.41 mL, 1.5 equiv), PMHS (0.09 mL, 1.5 equiv) and TBAF (2 drops, 1 mol%). The stirred reaction mixture was heated in an oil bath. Once complete, the reaction mixture was concentrated, eluted through a 1" plug of silica gel with 300 mL of hexane : EtOAc mixture (9:1) and concentrated. Crude NMR was taken to determine the isomeric ratio. Finally, the mixture was purified by column chromatography. Isomeric ratio and chromatographic yields are calculated as averages of two runs, unless otherwise mentioned.

Preparation of 17a and 17b (Scheme 14, entry 1)

Under the reaction condition described above, propargyl alcohol (**1**) produced **17a** and **17b** (1.5:1) 4 h. The reaction was cooled to room temperature and subjected to column

chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **17a** and **17b** as clear oils (147 mg, 42%). Spectroscopic data were consistent with the literature.[22a,c]

Preparation of 19a and 19b (Scheme 14, entry 2)

Under the reaction conditions described above, THP-protected propargyl alcohol (**3**) produced **19a** and **19b** (2.4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford an inseparable mixture of the isomers **19a** and **19b** as clear oils (194 mg, 45%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 31a and 31b (Scheme 14, entry 3)

Under the reaction condition described above, alkyne **15** produced **31a** and **31b** (2.4:1) in 5 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford an inseparable mixture of the isomers **31a** and **31b** as clear oils (179 mg, 42%). For spectroscopic data, see page 95.

Preparation of 27a and 27b (Scheme 14, entry 4)

Under the reaction condition described above, alkyne **11** (146 mg, 1 mmol) produced **27a** and **27b** (1:1.7) in 5 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **27a** and **27b** as clear oils (236 mg, 54%). For spectroscopic data, see page 92.

Preparation of 22a and 22b (Scheme 14, entry 5)

Alkyne 6 produced **22a** and **22b** (1.99) in 12 h in ether at ambient temperature when subjected to otherwise unchanged reaction conditions as above. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford an isomer 22b as clear oil (213 mg, 57%). For spectroscopic data, see page 97.

Preparation of 32a and 32b (Scheme 14, entry 6)

Under the reaction condition described above, alkyne **16** produced **32a** and **32b** (1.4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a separable mixture of the isomers **32a** and **32b** as clear oils (166 mg, 36%). Spectroscopic data were consistent with the literature.[57]

Representative procedure for $CoCl_2(PPh_3)_2$ catalyzed hydrostannations using Bu_3SnCl/ KF / 18-crown-6/ PMHS protocol (Scheme 15): Alkyne (1 mmol) was dissolved in Toluene (10 mL) in a sealed tube under nitrogen atmosphere. Hydroquinone (10 mg, 9 mol%), KF (174 mg, 3 equiv) and 18-crown-6 (793 mg, 3 equiv) were added to the solution followed by sequential addition of catalyst (13 mg, 2 mol%), Bu_3SnCl (0.41 mL, 1.5 equiv), PMHS (0.10 mL, 1.6 equiv) and TBAF (2 drops, 1 mol%). The stirred reaction mixture was heated in an oil bath for 1 d. Then, the reaction mixture was concentrated, eluted through a 1" plug of silica gel with 300 mL of hexane: EtOAc mixture (9:1) and rotavapped. Crude NMR was taken to determine the isomeric ratio. Finally, the mixture was purified by column chromatography. Isomeric ratio and chromatographic yields are calculated as averages of two runs, unless otherwise mentioned.

Preparation of 34a and 34b (Scheme 15, entry 1)

Under the reaction condition described above, alkyne **33** produced **34a** and **34b** (1.9:1). The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a partially separable mixture of the isomers **34a** and **34b** as clear oils (168 mg, 45%).

Data for **34a:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81-0.95 (m, 15 H), 1.26-1.33 (m, 6 H), 1.45-1.52(m, 6 H), 1.61-1.67 (m, 2 H), 2.30 (t, *J* = 7.6 Hz, 2 H), 3.61-3.64 (m, 2 H), 5.12 (m, 1 H), 5.69 (m, 1 H. ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.6, 13.7, 27.4, 29.1, 32.4, 37.4, 62.6, 125.2, 154.9.

Data for 34b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.83-0.90 (m, 15 H), 1.26-1.32 (m, 6 H), 1.43-1.50 (m, 6 H), 1.64-1.69 (m, 2 H), 2.18-2.22 (m, 2 H), 3.64 (t. *J* = 6.5 Hz, 2 H), 5.85-6.00 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.4, 13.7, 27.2, 29.0, 31.8, 34.1, 62.6, 128.2, 148.6. Spectroscopic data was consistent with the literature.[57]

Preparation of 19a and 19b (Scheme 15, entry 2)

Under the reaction conditions described above, THP-protected propargyl alcohol (**3**) produced **19a** and **19b** (2.4:1) in 4 h. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford an inseparable mixture of the isomers **19a** and **19b** as clear oils. The yield was calculated as an average of three runs (220 mg, 51%). Spectroscopic data were consistent with the literature.[22c]

Preparation of 32a and 32b (Scheme 15, entry 3)

Under the reaction condition described above, alkyne **16** produced **32a** and **32b** (1.4:1). The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford a partially separable mixture of the isomers **32a** and **32b** as clear oils (143 mg, 31%). Spectroscopic data were consistent with the literature.[57]

Preparation of 22a and 22b (Scheme 15, entry 4)

Alkyne **6** produced **22a** and **22b** (1.99) in 12 h in THF at ambient temperature when subjected to otherwise unchanged reaction conditions as above. The reaction was cooled to room temperature and subjected to column chromatography [silica gel; hexane, 1% TEA] to afford an isomer **22b** as clear oil (146 mg, 39%). For spectroscopic data, see page 97.

Representative procedure for $MoBI_3$ catalyzed hydrostannations using Bu_3SnCl/ KF / 18-crown-6/ PMHS protocol (Scheme 17): Alkyne (1 mmol) was dissolved in benzene (7.5 mL) in a sealed tube under nitrogen atmosphere. Hydroquinone (10 mg, 9 mol%), KF (174 mg, 3 mmol) and 18-crown-6 (793 mg, 3 mmol) were added to the solution followed by sequential addition of catalyst (21.5 mg, 5 mol%), Bu_3SnCl (0.41 mL, 1.5 mmol), PMHS (0.1 mL, 1.6 mmol) and TBAF (2 drops, 1 mol%). The stirred

reaction mixture was heated in an oil bath for 1 day. Once complete, the reaction mixture was concentrated, eluted through a 1" plug of silica gel with 300 mL of hexane: EtOAc mixture (9:1) and concentrated. Crude NMR was taken to determine the isomeric ratio. Finally, the mixture was purified by column chromatography. Isomeric ratio and chromatographic yields are calculated as averages of two runs, unless otherwise mentioned.

Preparation of 17a and 17b (Scheme 17, entry 1)

Under the reaction condition described above, propargyl alcohol (**1**) produced **17a** and **17b** (2:1). The crude was subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **17a** and **17b** as clear oils (162 mg, 42%).[22a,c]

Preparation of 17a and 17b (Scheme 17, entry 2)

Under the reaction condition described above, THP-protected propargyl alcohol (**3**) produced **19a** and **19b** (4:1). The crude was subjected to column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford a mixture of the isomers **19a** and **19b** as clear oils (354 mg, 82%).[22c]

Preparation of 26a and 26b (Scheme 17, entry 3)

Under the reaction condition described above, 2-methyl-3-propyn-2-ol (**10**) produced **26a** and **26b** (2.5:1). The crude was subjected to column chromatography [silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **26a** and **26b** as clear oils (206 mg, 55%). For spectroscopic data, see page 91.

Preparation of 27a and 27b (Scheme 17, entry 4)

Under the reaction condition described above, 2-phenyl-3-propyn-2-ol (**11**) produced **27a** and **27b** (6:1). The crude was subjected to column chromatography [silica gel; 95/5 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **27a** and **27b** as clear oils (397 mg, 91%). For spectroscopic data, see page 92.

Preparation of 34a and 34b (Scheme 17, entry 5)

Under the reaction condition described above, 4-pentyn-1-ol (**33**) produced **34a** and **34b** (1.3:1). The crude was subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford a separable mixture of the isomers **34a** and **34b** as clear oils (180 mg, 48%). For spectroscopic data, see page 108.

Preparation of 22a and 22b (Scheme 17, entry 6)

Under the reaction condition described above, 3,3-dimethyl-1-butyne (**6**) produced **22a** and **22b** (2.5:1). The yield was calculated by using hexamethyldisiloxane as an external standard (63%).

Procedure for $[RhCl(COD)]_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride (Scheme 18): See page100.

Procedure for $[RhCl(COD)]_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride and H_2O (Scheme 18): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmoL) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (5 mg, 1 mol%, 2 mol% in Rh) and stirred for 5 minutes. Tributyltin hydride (0.4 mL, 1.5 mmoL) and water were sequencially added to it. The mixture was heated at 65 °C for 1 d. The mixture was concentrated and isomeric ratio of **19a** and **19b** was detected (5:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (138 mg, 32%).

Procedure for $[RhCl(COD)]_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride KF and H_2O (Scheme 18): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), and catalyst (5 mg, 1 mol%, 2 mol% in Rh) and stirred for 5 minutes.

Tributyltin hydride (0.4 mL, 1.5 mmol), KF (174 mg, 3 mmol) and water were sequencially added to it. The mixture was heated at 65 °C for 1 d. The mixture was concentrated and isomeric ratio of **19a** and **19b** was detected (5.3:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (168 mg, 39%).

Procedure for $[RhCl(COD)]_2$ catalyzed hydrostannation of alkyne 3 with Bu_3SnF/ PMHS/ protocol (Scheme 18): See page 100.

Procedure for $[RhCl(COD)]_2$ catalyzed hydrostannation of alkyne 3 with Bu_3SnCl/ KF/ PMHS/ TBAF protocol (Scheme 18): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (5 mg, 1 mol%, 2 mol% in Rh). KF (174 mg, 3 mmol), water (1 mL) (or 18-crown-6 (793 mg, 3 mmol), Tributyltin chloride (0.41 mL, 1.5 mmol) and PMHS (0.09 mL, 1.5 mmol) were sequencially added to it. The mixture was heated at 65 °C for 1 d. The mixture was concentrated. Crude NMR revealed a complex mixture.

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride (Scheme 19): See page 101.

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride and H_2O (Scheme 19): In sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmoL) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (14 mg, 2 mol%) and stirred for 5 minutes. Tributyltin hydride (0.4 mL, 1.5 mmoL) and water were sequencially added to it. The mixture was heated at 65 °C for 12 h. The mixture was concentrated and isomeric ratio of **19a** and **19b** was detected (1:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (324 mg, 75%).

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride KF and H_2O (Scheme 19): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), and catalyst (14 mg, 2 mol%) and stirred for 5 minutes. Tributyltin hydride (0.4 mL, 1.5 mmol), KF (174 mg, 3 mmol) and water were sequencially added to it. The mixture was heated at 65 °C for 12 h. The mixture was concentrated and isomeric ratio of **19a** and **19b** was detected (1:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (315 mg, 73%).

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with Bu_3SnF/ PMHS/ protocol: See page 101.

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with Bu_3SnCl/ KF_{aq}/ PMHS/ TBAF protocol (Scheme 19): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (14 mg, 2 mol%). KF (174 mg, 3 mmol), water (1 mL), Tributyltin chloride (0.41 mL, 1.5 mmol) and PMHS (0.09 mL, 1.5 mmol)were sequencially added to it . The mixture was heated at 65 °C for 8 h. The mixture was concentrated and isomeric ratio of **19a** and **19b** was detected (1:1.8). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (121 mg, 28%).

Procedure for $RhCl(CO)(PPh_3)_2$ catalyzed hydrostannation of alkyne 3 with Bu_3SnCl/ KF / 18-crown-6/ PMHS/ TBAF protocol (Scheme 19): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (14 mg, 2 mol%). KF (174 mg, 3 mmol), 18-crown-6 (793 mg, 3 mmol), Tributyltin chloride (0.41 mL, 1.5 mmol) and PMHS (0.09 mL, 1.5 mmol) were sequencially added to it . The mixture was heated at 65 °C for 8 h. The mixture was concentrated. Trace amounts of stannane product

was detected. Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford starting alkyne (**3**) (406 mg, 29%).

Procedure for $RuCl_2(PPh_3)_4$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride (Scheme 20): See page 102.

Procedure for $RuCl_2(PPh_3)_4$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride and H_2O (Scheme 20): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmoL) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (20 mg, 2 mol%) and stirred for 5 minutes. Tributyltin hydride (0.4 mL, 1.5 mmoL) and water were sequencially added to it. The mixture was heated to 65 °C for 12 h. The mixture was concentrated and isomeric ratio of **19a**, **19b** and **19c** was detected (3.3:2.9:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a**, **19b** and **19c** as a mixture (91 mg, 21%).

Procedure for $RuCl_2(PPh_3)_4$ catalyzed hydrostannation of alkyne 3 with tributyltin hydride KF and H_2O (Scheme 20): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), and catalyst (14 mg, 2 mol%) and stirred for 5 minutes. Tributyltin hydride (0.4 mL, 1.5 mmol), KF (174 mg, 3 mmol) and water were sequencially added to it. The mixture was refluxed for 12 h. The mixture was concentrated and isomeric ratio

of **19a** and **19b** was detected (1:1). Finally, the crude was purified by column chromatography [silica gel; 98/2 hexane/EtOAc, 1% TEA] to afford **19a** and **19b** as a mixture (315 mg, 73%).

Procedure for $RuCl_2(PPh_3)_4$ catalyzed hydrostannation of alkyne 3 with Bu_3SnF/ PMHS/ protocol (Scheme 20): See page 102.

Procedure for $RuCl_2(PPh_3)_4$ catalyzed hydrostannation of alkyne 3 with Bu_3SnCl/ KF / PMHS/ TBAF protocol (Scheme 20): In a sealed tube, THP-protected propargyl alcohol (140 mg, 1 mmol) (**3**) was dissolved in 7 mL of THF. To this was added hydroquinone (10 mg, 9 mol%), catalyst (14 mg, 2 mol%). KF (174 mg, 3 mmol), water (1 mL) (or 18-crown-6 (793 mg, 3 mmol)), Tributyltin chloride (0.41 mL, 1.5 mmol) and PMHS (0.09 mL, 1.5 mmol)were sequencially added to it . The mixture was heated to 65 °C for 12 h. The mixture was concentrated. A complex mixture resulted.

Represeantative procedure for optimization of one-pot allylation-hydrostannation (Table 6): A 5 mL round bottom flask was charged with benzaldehyde (1 mmol), allyltributylstannane (1 mmol) and dissolved in toluene (2 mL). Temperature was maintained as required. $BF_3 \cdot OEt_2$ was added slowly and the reaction was allowed to go until complete. The round bottom flask was, then, taken inside glove bag where $B(C_6F_5)_3$ was weighed and added. Reducing agent was added followed by alkyne and

the reaction was allowed to go until complete (~ 1 h) and then, quenched. Crude NMR was taken with HMDS as internal standard.

Preparation of 54 and 23c by one-pot allylation-hydrostannation (Scheme 27)

A 5 mL round bottom flask was charged with benzaldehyde (212 mg, 2 mmol), allyltributylstannane (0.62 mL, 2 mmol) in toluene (4 mL) and cooled to –35 °C. BF_3•OEt_2 was added slowly and the reaction was allowed to go until complete (~15 minutes). $B(C_6F_5)_3$ (205 mg, 20%) was weighed and added under nitrogen. PMHS (0.24 mL, 2 equiv) was added to it followed by phenylacetylene (0.22 mL, 2 mmol) and and the reaction was allowed to go for 1 h. NEt_3 (0.36 mL) was added. The crude was subjected to column chromatography [silica gel; 90/10 hexane/EtOAc, 1% TEA] to afford **54** (209 mg, 71%), and **23c** (781 mg, 99%).

Data for **54:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.49-2.56 (m, 3 H), 4.72-4.76 (m, 1 H), 5.14-5.19 (m, 2 H), 5.79-5.87 (m, 1 H), 7.28-7.33 (m, 1 H), 7.38 (d, J = 4.2, 4 H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 43.7, 73.2, 118.1, 125.8, 127.4, 128.3, 134.5, 143.9.

Data for **23c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.77-0.99 (m, 15 H), 1.23-1.30 (m, 6 H), 1.38-1.48 (m, 6 H), 6.23 (d, J =13.7 Hz, 1 H), 7.10-7.54 (m, 5 H), 7.64 (d, J = 14.0 Hz, 1

H) ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.8, 13.6, 27.2, 29.0, 127.1, 127.2, 128.1, 132.8, 141.5, 147.4.[66]

Preparation of 36 (Scheme 28)

A turbid solution of 3-bromobenzaldehyde, (1.17 mL, 10 mmol) ethynyltrimethylsilane (2.26 mL, 16 mmol), $Pd(OAc)_2$ (270 mg, 4 mol%) and triphenylphosphine (52 mg, 2 mol%) in anhydrous NEt_3 (8.7 mL) was rapidly heated to gentle reflux under N_2. After 4 h the mixture was cooled and the filtered. The filtrate was concentrated, mixed with $NaHCO_3$, extracted with CH_2Cl_2 (3 x10 mL). The organic fractions were combined, dried over $MgSO_4$ and concentrated to yield an oil (**58**).

This oil was treated with anhydrous K_2CO_3 (121 mg) in MeOH (23 mL) under N_2 at rt for 3 h. The solvent was evaporated. The residue was mixed with 10 mL aq. $NaHCO_3$ and extracted with CH_2Cl_2 (3x10 mL). The combined organic fractions were dried over $MgSO_4$ and concentrated to yield a yellow mass. This mass was subjected to sublimation at 50 °C at 4 torr for overnight. White crystalline solid of **36** resulted (923 mg, 71%).

Data for **36**: ^1H NMR (300 MHz, $CDCl_3$) δ 3.14 (s, 1 H), 7.47 (t, J = 7.7, 1 H), 7.67-7.70 (m, 1 H), 7.82-7.84 (m, 1 H), 7.95 (s, 1 H), 9.96 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ

78.8, 82.1, 123.3, 129.1, 129.4, 133.4, 136.4, 137.6, 191.3. Spectroscopic data was consistent with the literature.[46]

Preparation of 60 and 38 (Scheme 29)

Under nitrogen atmosphere, 4-bromo-2-fluoro-benzaldehyde (1.42 g, 7 mmol), $PdCl_2(PPh_3)_2$ (98 mg, 2 mol%), PPh_3 (28 mg, 1.5 mol%), were dissolved in anhydrous THF (22 mL), followed by addition of NEt_3 (1.89 mL, 13.65 mmol) and ethynyltrimethylsilane (1.09 mL, 7.7 mmol). After stirring for 20 minutes, CuI (40 mg, 3 mol%) was added. The reaction mixture was stirred overnight at rt. The solvent was removed. The resulting brown residue was, then, dissolved in pentane and passed through celite using pentane as eluent. Yellow solution, thus obtained was concentrated. The resulting solid was subjected to sublimation at 52-54 °C at 5 torr to produce a white crystalline solid of **60** (1.234 g, 80%).

Data for **60**: mp 63-65 °C. IR (neat): 1693 cm-^{1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.24 (s, 9 H), 7.21-7.24 (m, 1 H), 7.31 (d, *J* = 8.1 Hz, 1 H), 7.78 (t, *J* = 7.7 Hz, 1 H), 10.30 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -0.4, 100.5, 102.5 (d, *J* = 3.6 Hz), 119.6, (d, *J* = 22.2 Hz) 123.7 (d, *J* = 8.4 Hz), 128.2 (d, *J* = 3.4), 128.4 , 131.3 (d, *J* = 10.6), 164.1 (d, *J* = 259.6), 186.5 (d, *J* = 7.0). HRMS (ESI) m/z calcd for $C_{14}H_{16}NOFNaSi$ $[M+CH_3CN+Na]^+$, 284.0883, found: 284.0887.

60 (0.88 g, 4 mmol) was treated with anhydrous K_2CO_3 (54 mg) in MeOH (11 mL) at 0 °C. After 1 h, the mixture was treated with 10 mL of sat. $NaHCO_3$ and extracted with CH_2Cl_2 (3x10 mL), dried with $MgSO_4$ and concentrated. The resulting solid was subjected to sublimation at 58-60 °C at 3 torr for 2h to obtain a yellowish white crystal of **38** (402 mg, 68%).

Data for **38**: mp 95-97 °C. IR (neat): 1684 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 3.32 (s, 1 H), 7.24 (dd, *J* = 10.7, 1.4 Hz, 1 H) 7.32 (d, J = 7.9 Hz, 1 H), 10.29 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.5 (d, *J* = 3.3 Hz), 82.2, 119.9, (d, *J* = 22.9 Hz) 124.1 (d, *J* = 8.5 Hz), 128.2 (d, *J* = 3.4), 128.4 (d, *J* = 3.7 Hz), 128.6 (d, J = 3.1 Hz), 130.1 (d, *J* = 10.9), 164.0 (d, *J* = 259.1), 186.2 (d, *J* = 6.3). HRMS (ESI) m/z calcd for C_9H_5OFNa $[M+Na]^+$, 171.0222, found: 171.0229.

Preparation of 62, 63 and 39 (Scheme 29)

A solution of anhydrous DMSO (1.08 mL, 13.82 mmol) in anhydrous CH_2Cl_2 (46 mL) was added to a solution of oxalyl chloride (0.71 mL, 8.12 mmol) anhydrous CH_2Cl_2 (28 mL) at – 78 °C over 20 minutes. The mixture was stirred for 30 minutes. A solution of alcohol **61** (1.53 g, 7.04 mmol) in anhydrous CH_2Cl_2 (9 mL) was added over it for 10

minutes. This solution was stirred for 1 h. Et_3N (4.7 mL, 34 mmol) was added and stirred for 1 h. The reaction mixture was allowed to warm to 0 °C. After addition of water, two layers were separated. The aqueous layer acidified with 1% HCl (saturated with NaCl) and then back extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were washed with 1% HCl (saturated with NaCl, 3x50 mL), sat $NaHCO_3$ (3x50 mL) and brine (3x50 mL). This was dried with $MgSO_4$ and concentrated. Resulting white crystalline solid **62** was subjected to the next step without purification.

Data for **62**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3 H), 7.13-7.18 (m, 2 H), 7.66 (d, *J* = 8.1 Hz, 1 H), 10.37 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.0, 115.3, 123.7, 124.2, 129.7, 130.5, 161.9, 188.7.

Under nitrogen atmosphere, 4-bromo-2-methoxy-benzaldehyde (**62**, 0.645 g, 3 mmol) , $PdCl_2(PPh_3)_2$ (42 mg, 2 mol%), PPh_3 (12 mg, 1.5 mol%), were dissolved in anhydrous THF (9.6 mL), followed by addition of NEt_3 (0.81 mL, 5.85 mmol) and ethynyltrimethylsilane (0.51 mL, 3.6 mmol). After stirring for 20 minutes, CuI (17 mg, 3 mol%) was added. The reaction mixture was stirred overnight at rt. The solvent was removed. The resulting brown residue was, then, dissolved in pentane and passed through celite using pentane as eluent. Yellow solution, thus obtained was

concentrated. The resulting solid was recrystallized from hexane to provide orange crystals of **63** (300 mg, 43%).

Data for **63**: mp 58-60 °C. IR (neat): 1672 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.23 (s, 9 H), 3.91 (s, 3 H), 7.03-7.11 (m, 2 H), 7.74 (d, *J* = 7.6 Hz, 1 H), 10.40 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ -0.2, 55.8, 98.6, 104.0, 124.4, 124.6, 128.4, 130.5, 161.3, 189.1. HRMS (ESI) m/z calcd for $C_{13}H_{17}O_2FSi$ $[M+H]^+$, 233.0998, found: 233.1001.

63 (232 mg, 1 mmol) was treated with anhydrous K_2CO_3 (14 mg) in MeOH (3 mL) at 0 °C. After 45 minutes, the mixture was treated with 5 mL of sat. $NaHCO_3$ and extracted with CH_2Cl_2 (3x5 mL), dried with $MgSO_4$ and concentrated. The resulting solid was subjected to sublimation at 57 °C at 4 torr for overnight to obtain a white crystal of **39** (73 mg, 46%).

Data for **39**: mp 84-85 °C. IR (neat): 1672 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.25 (s, 1 H), 3.91 (s, 3 H), 7.07 (s, 1 H) 7.12 (d, *J* = 8.1 Hz, 1 H), 7.76 (d, *J* = 7.8 Hz, 1 H) 10.41 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.8, 80.6, 80.8, 115.1, 115.3, 124.4, 124.6, 128.4, 128.5, 189.0. HRMS (ESI) m/z calcd for $C_{10}H_9O_2$ $[M+H]^+$, 161.0603, found: 161.0610.

Synthesis of 65 and 40 (Scheme 30):

In a three-necked round bottom flask equipped with a condenser was dissolved **64** (2.22 g, 10 mmol) in Et_2O (28 mL), This solution was cooled to 0 °C and BH_3•Me_2S complex (10M, 1.12 mL) was added dropwise to it. The milky white acid turned yellowish and the solution looked thicker. The mixture was then refluxed overnight. The solution turned milky white and lucid. This was poured into 50 mL MeOH and stirred for 2 h. MeOH was evaporated and the alcohol, thus produced, was subjected to the next step without purification.

A solution of anhydrous DMSO (1.08 mL, 13.82 mmol) in anhydrous CH_2Cl_2 (46 mL) was added to a solution of oxalyl chloride (0.71 mL, 8.12 mmol) anhydrous CH_2Cl_2 (28 mL) at – 78 °C over 20 minutes. The mixture was stirred for 30 minutes. A solution of the crude alcohol (1.42 g) in anhydrous CH_2Cl_2 (9 mL) was added over it for 10 minutes. This solution was stirred for 1 h. Et_3N (4.7 mL, 34 mmol) was added and stirred for 1 h. The reaction mixture was allowed to warm to 0 °C. After addition of water, two layers were separated. The aqueous layer acidified with 1% HCl (saturated with NaCl) and then back extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were washed with 1% HCl (saturated with NaCl, 3x50 mL), sat $NaHCO_3$ (3x50 mL) and brine (3x50 mL). This was dried with $MgSO_4$ and concentrated. Resulting oil

was subjected to column chromatography [silica gel; 90:10 hexane/EtOAc] to afford **65** (0.942 g, 67%).

Data for **65**: IR (neat): 1704 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 3 H), 7.59-7.76 (m, 3 H), 9.98 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 128.2, 131.4, 132.2, 133.2, 135.4, 139.1, 191.3 HRMS (ESI) m/z calcd for C_8H_6OBr $[M+H]^+$, 196.9602, found: 196.9606.

A solution of **65** (0.215 g, 1.08 mmol), PPh_3 (8.5 mg, 3 mol%), $Pd(OAc)_2$ (22 mg, 3 mol%), and ethynyltrimethylsilane (0.23 mL, 1.62 mmol) in Et_3N (2.2 mL) was heated to refulx for overnight. It was, then concentrated, dissolved in pentane and passed through a celite plug. After concentrating the resulting brownish solution (121 mg) in MeOH (1 mL) was, then, slowly added to a solution of anhydrous K_2CO_3 (7.6 mg) in MeOH (0.5 mL) at 0 °C. The reaction was run for 1 h when TLC showed the completion of the reaction, the mixture was treated with 5 mL sat. $NaHCO_3$ and extracted with CH_2Cl_2 (3x5 mL), dried with $MgSO_4$ and concentrated. Finally, column chromatography [silica gel; 97:3 hexane/EtOAc] to afford partially separable yellow solid **40** (0.0807 g, ~83%) from the impurity. Note: This aldehyde was contaminated with a small amount of another unknown aldehyde.

Data for **40**: m.p. 49-51 °C IR (neat): 1692 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56 (s, 3 H), 3.53 (s, 1 H), 7.62-7.76 (m, 3 H), 10.02 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.5,

81.6, 84.7, 126.8, 128.2, 130.3, 133.1, 135.9, 141.7, 191.7. HRMS (ESI) m/z calcd for $C_{10}H_6O$ $[M]^+$, 144.0575, found: 144.0574.

Preparation of 67 and 41 (Scheme 31)

To a solution of sodium hydride (2 g, 60% in oil) at an ice bath was added 1,3-diaminopropane (17.5 mL). The suspension was heated gradually to 80 °C over a period of 2 h with stirring. At this point the color of the solution turned dark brown. This was cooled to –10 °C and 3-decyne-1-ol (**66**, 12.16 g, 14 mmol) was added to it over a period of 5 minutes. The mixture was heated gradually to 100 °C over 40 minutes and stirred for 80 minutes at 100 °C. The mixture was cooled in an ice bath and extracted with hexanes. The organic layer was washed with water, sat $NaHCO_3$, and brine successively and dried over $MgSO_4$. Column chromatography [silica gel; 7:3 hexane/EtOAc] , then, afforded **67** as an oil (1.06 g, 49%).

Data for **67**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.14-1.34 (m, 9 H), 1.43-1.50 (m, 4 H) 1.88 (s, 1 H), 2.11-2.13 (m, 2 H), 3.53-3.58 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.3, 25.6, 28.3, 28.6, 29.0, 29.1, 32.6, 62.8, 68.0, 84.6. Spectroscopic data was consistent with the literature.[71]

A solution of anhydrous DMSO (0.98 mL, 11.76 mmol) in anhydrous CH_2Cl_2 (39 mL) was added to a solution of oxalyl chloride (0.61 mL, 6.9 mmol) anhydrous CH_2Cl_2 (23 mL) at – 78 °C over 20 minutes. The mixture was stirred for 30 minutes. A solution of alcohol **67** (0.925 g, 6 mmol) in anhydrous CH_2Cl_2 (8 mL) was added over it for 10 minutes. This solution was stirred for 1 h. Et_3N (4.0 mL, 29 mmol) was added and stirred for 1 h. The reaction mixture was allowed to warm to 0 °C. After addition of water, two layers were separated. The aqueous layer acidified with 1% HCl (saturated with NaCl) and then back extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were washed with 1% HCl (saturated with NaCl, 3x50 mL), sat $NaHCO_3$ (3x50 mL) and brine (3x50 mL). This was dried with $MgSO_4$ and concentrated. Resulting oil was purified by column chromatography [silica gel; 4:1 hexane/EtOAc] , then, afforded **67** as an oil (0.656 g, 72%).

Data for **67**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19-1.41 (m, 6 H), 1.43-1.50(m, 2 H), 1.52-1.64 (m, 2 H), 1.89 (t, J = 2.6 Hz, 1 H), 2.14 (dt, J = 6.9, 2.6 Hz, 2 H), 2.38 (dt, J = 7.3, 1.9 Hz, 2 H), 9.72 (t, J = 1.8, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 21.9, 28.2, 28.4, 28.7, 28.9, 43.7, 68.1, 84.4, 202.6. Spectroscopic data was consistent with the literature.[71]

Preparation of 42 (Scheme 31)

A solution of anhydrous DMSO (1.08 mL, 13.82 mmol) in anhydrous CH_2Cl_2 (46 mL) was added to a solution of oxalyl chloride (0.71 mL, 8.12 mmol) anhydrous CH_2Cl_2 (28 mL) at – 78 °C over 20 minutes. The mixture was stirred for 30 minutes. A solution of alcohol **68** (1.185 g, 7.04 mmol) in anhydrous CH_2Cl_2 (9 mL) was added over it for 10 minutes. This solution was stirred for 1 h. Et_3N (4.7 mL, 34 mmol) was added and stirred for 1 h. The reaction mixture was allowed to warm to 0 °C. After addition of water, two layers were separated. The aqueous layer acidified with 1% HCl (saturated with NaCl) and then back extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were washed with 1% HCl (saturated with NaCl, 3x50 mL), sat $NaHCO_3$ (3x50 mL) and brine (3x50 mL). This was dried with $MgSO_4$ and concentrated. Resulting oil was subjected column chromatography [silica gel; 95:5 hexane/EtOAc] to afford **42** as an oil (0.6718, 57%). Spectroscopic data was consistent with the literature.[71]

General procedure of one-pot allylation hydrostannations on alkynals (Table 8): Alkynal was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (1 equiv) was added followed by $BF_3 \cdot OEt_2$ (1.05 equiv) The reaction was monitored until complete (typically 15 minutes to 90 minutes). At this point,

$B(C_6F_5)_3$ (20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (2 equiv) was added and the reaction was run until complete. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200-300 mL) The solution was concentrated and subjected to column chromatography, if vinylstannane was present.

Note: Geometries of stannane **45** and **48** were confirmed by NOE studies. Geometries of the other stannanes were determined by analogy.

Synthesis of 43 (Table 8, entry 1):

Alkynal **35** (130 mg, 1 mmol) was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.31 mL, 1 mmol) was added followed by $BF_3{\bullet}OEt_2$ (0.14 mL, 1.05 equiv) The reaction was monitored until complete (15 minutes). At this point, $B(C_6F_5)_3$ (103 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.12 mL, 2 equiv) was added and the reaction was run for 1 h. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column

chromatography [silica gel; 80:20 hexane/EtOAc, 1% Et_3N] to afford **43** (236 mg, 51%) as a clear oil.

Data for **43**: IR (neat): 3386 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.76-0.98 (m, 15 H), 1.25-1.34 (m, 6 H), 1.41-1.54 (m, 6 H), 2.12 (s, 1 H), 2.50-2.60 (m, 2 H), 4.76-4.81 (m, 1 H), 5.16-5.24 (m, 2 H), 5.76-5.90 (m, 1 H), 6.2 (d, J = 13.7, 1 H), 7.28-7.36 (m, 4 H), 7.6 (d, J = 13.7, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.8, 13.6, 27.2, 29.0, 43.8, 73.1, 118.4, 125.6, 127.1, 132.8, 134.3, 141.0, 142.9, 146.9. HRMS (EI) m/z calcd for $C_{20}H_{31}O^{116}Sn$ $[M\text{-}Bu]^+$, 403.1392, found: 403.1406.

Synthesis of 44 (Table 8, entry 2)

Alkynal **36** (65 mg, 0.5 mmol) was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.16 mL, 0.5 mmol) was added followed by $BF_3 \cdot OEt_2$ (0.07 mL, 1.05 equiv) The reaction was monitored until complete (20 minutes). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 14 h. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc

solution (200 mL) The solution was concentrated and subjected to column chromatography [silica gel; 80:20 hexane/EtOAc, 1% Et_3N] to afford **44** (111 mg, 48%) as a clear oil.

Data for **44**: IR (neat): 3408 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.76-0.89 (m, 15 H), 1.19-1.26 (m, 6 H), 1.34-1.45 (m, 6 H), 1.97 (s, 1 H), 2.45-2.55 (m, 2 H), 4.71-4.73 (m, 1 H), 5.13-5.17 (m, 2 H), 5.76-5.84 (m, 1 H), 6.2 (d, *J* = 13.9, 1 H), 7.15-7.30 (m, 4 H), 7.6 (d, *J* = 13.8, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.8, 13.6, 27.2, 29.0, 43.9, 73.3, 118.5, 124.5, 124.7, 126.4, 128.3, 132.9, 134.4, 141.6, 143.8, 147.2. HRMS (EI) m/z calcd for $C_{20}H_{29}Sn$ $[M\text{-}Bu\text{-}H_2O]^+$, 385.1287, found: 385.1305.

Synthesis of 45 (Table 8, entry 3)

Alkynal **37** (65 mg, 1 mmol) was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.16 mL, 1 mmol) was added followed by $BF_3{\bullet}OEt_2$ (0.07 mL, 1.05 equiv) The reaction was monitored until complete (20 minutes). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 1 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column

chromatography [silica gel; 80:20 hexane/EtOAc, 1% Et_3N] to afford **45** (132 mg, 57%) as a clear oil.

Data for **45**: IR (neat): 3403 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.74 (t, *J* = 8.1 Hz, 6 H), 0.88 (t, *J* = 7.2 Hz, 9 H), 1.20-1.35 (m, 6 H), 1.37-1.48 (m, 6 H), 2.03 (bs, 1 H), 2.36-2.47 (m, 1 H), 2.52-2.61 (m, 1 H), 5.01 (m, 1 H), 5.17-5.25 (m, 2 H), 5.82-5.96 (m, 1 H), 6.34 (d, *J* = 13.7, 1 H), 7.17-7.38 (m, 3 H), 7.52-7.55 (m, 1 H), 7.80 (d, *J* = 13.4, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.6, 13.6, 27.2, 29.0, 42.5, 69.7, 118.3, 124.8, 127.2, 127.8, 127.8, 134.7, 135.2, 139.5, 141.4, 145.6. LRMS (APCI) m/z 447.2 $[M\text{-}OH]^+$.

Synthesis of 46 (Table 8, entry 4)

Alkynal **38** (74 mg, 0.05 mmol) was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.16 mL, 1 mmol) was added followed by $BF_3{\bullet}OEt_2$ (0.07 mL, 1.05 equiv) The reaction was monitored until complete (~30 minutes). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 3 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column

chromatography [silica gel; 4:1 hexane/EtOAc, 1% Et_3N] to afford **46** (121 mg, 50%) as a clear oil.

Data for **46**: IR (neat): 3378 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.76-0.90 (m, 15 H), 1.19-1.27 (m, 6 H), 1.35-1.45 (m, 6 H), 2.04 (bs, 1 H), 2.44-2.50 (m, 1 H), 2.54-2.59 (m, 1 H), 5.03-5.05 (m, 1 H), 5.12-5.17 (m, 2 H), 5.75-5.84 (m, 1 H), 6.23 (d, *J* = 13.7, 1 H), 6.90-6.93 (m, 1 H), 7.03-7.05 (m, 1 H), 7.39 (t, *J* = 7.9 Hz, 1 H), 7.52 (d, *J* = 13.9 Hz, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.8, 13.6, 27.2, 29.0, 42.6, 67.3 (d, *J* = 1.9 Hz), 113.7 (d, *J* = 22.4 Hz), 118.7, 123.0 (d, *J* = 3.0 Hz), 127.0 (d, *J* = 5.0 Hz), 129.6 (d, *J* = 13.6 Hz), 134.0, 134.6, 142.7, (d, *J* = 7.0 Hz) . 145.8 (d, *J* = 2.0 Hz), 159.5 (d, *J* = 245.3 Hz). HRMS (EI) m/z calcd for $C_{20}H_{30}OFSn$ $[M\text{-}Bu]^+$, 421.1298, found: 421.1317.

Attempted one-pot allylation/hydrostannation with 39 (Table 8, entry 5)

Alkynal **39** (40 mg, 0.25 mmol) was dissolved in toluene in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.08 mL, 0.25 mmol) was added followed by $BF_3 \cdot OEt_2$ (0.04 mL, 1.05 equiv) The reaction was monitored until complete (15 minutes). At this point, $B(C_6F_5)_3$ (26 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. The solution turned red. PMHS (0.03 mL, 2 equiv) was added, bubbling was observed and the reaction was run for 1 h. At this

point, TLC revealed multiple spots. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated. NMR of the crude material indicated disappearance of all vinyl peaks.

Synthesis of 47 (Table 8, entry 6)

Alkynal **40** (7:1 mixture with another unknown aldehyde, ~0.4 mmol) was dissolved in toluene (0.8 mL) in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.14 mL, 0.45 mmol) was added followed by BF_3•OEt_2 (0.07 mL, 1.05 equiv) The reaction was monitored until complete (20 minutes). At this point, $B(C_6F_5)_3$ (40 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.05 mL, 2 equiv) was added and the reaction was run for 2 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column chromatography [silica gel; 9:1 hexane/EtOAc, 1% Et_3N] to afford **47** (13 mg, 7%) as a clear oil.

Data for **47**: IR (neat): 3349 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.68 (t, *J* = 8.1 Hz, 6 H), 0.81 (t, *J* = 7.3 Hz, 9 H), 1.13-1.25 (m, 6 H), 1.29-1.39 (m, 6 H), 1.93 (d, *J* = 3.2 Hz, 1 H), 2.26 (s, 3 H), 2.46-2.51 (m, 2 H), 4.66-4.72 (m, 1 H), 5.10-5.18 (m, 2 H), 5.71-5.85 (m, 1 H), 6.21 (d, *J* = 13.7, 1 H), 7.11 (s, 3 H), 7.61 (d, *J* = 13.5, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.7, 13.7, 19.7, 27.2, 29.0, 43.8, 73.2, 118.3, 123.1, 126.9, 127.3, 133.3, 134.5, 136.0, 140.8, 143.1, 146.6. HRMS failed for this compound.

Synthesis of 48 (Table 8, entry 7)

Alkynal **41** (76 mg, 0.5 mmol) was dissolved in toluene (1 mL) in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.16 mL, 0.5 mmol) was added followed by $BF_3{\bullet}OEt_2$ (0.07 mL, 1.05 equiv) The reaction was monitored until complete (1 h). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 3 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column chromatography [silica gel; 9:1 hexane/EtOAc, 1% Et_3N] to afford 43 (99 mg, 41%) as a clear oil.

Data for **48**: IR (neat): 3349 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) 0.81-0.94 (m, 15 H), 1.25-1.36 (m, 15 H), 1.41-1.55 (m, 10 H), 1.96-2.02 (m, 2 H), 2.09-2.15 (m, 1 H), 2.25-2.31 (m, 1 H), 3.59-3.65 (m, 1 H), 5.09-5.14 (m, 2 H), 5.66-5.85 (m, 2 H), 6.33-6.64 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.2, 13.7, 25.7, 27.3, 29.2, 29.4, 29.6, 29.6, 29.9, 36.8, 37.1, 41.9, 70.7, 118.0, 127.7, 134.9, 149.2. HRMS (EI) m/z calcd for $C_{21}H_{41}O^{116}Sn$ $[M-Bu]^+$, 425.2175, found: 425.2168.

Synthesis of 49 (Table 8, entry 8)

Alkynal **42** (166 mg, 1 mmol) was dissolved in toluene (2 mL) in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.31 mL, 1 mmol) was added followed by $BF_3 \cdot OEt_2$ (0.14 mL, 1.05 equiv) The reaction was monitored until complete (1 h). At this point, $B(C_6F_5)_3$ (103 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.12 mL, 2 equiv) was added and the reaction was run for 3 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL) The solution was concentrated and subjected to column chromatography [silica gel; 9:1 hexane/EtOAc, 1% Et_3N] to afford **49** (217 mg, 43%) as a clear oil.

Data for **48**: IR (neat): 3355 cm^{-1}. . ^{1}H NMR (500 MHz, $CDCl_3$) 0.80-0.94 (m, 15 H), 1.23-1.36 (m, 17 H), 1.39-1.50 (m, 9 H), 1.54-1.58 (m, 1 H), 1.97-2.02 (m, 2 H), 2.08-2.14 (m, 1 H), 2.25-2.30 (m, 1 H), 3.59-3.64 (m, 1 H), 5.09-5.13 (m, 2 H), 5.66-5.90 (m, 2 H), 6.31-6.62 (m, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 10.2, 13.7, 25.6, 27.3, 29.2, 29.4, 29.4, 29.6, 29.6, 29.9, 36.8, 37.1, 41.9, 70.7, 118.0, 127.6, 134.9, 149.3. HRMS (EI) m/z calcd for $C_{22}H_{43}O^{116}Sn$ $[M\text{-}Bu]^+$, 439.2331, found: 439.2340.

Synthesis of 50 and attempted separation (Table 8, entry 9)

(*E*)-crotylstannane was prepared following Brückner's protocol.[60] Alkynal **35** (65 mg, 0.5 mmol) was dissolved in toluene (1 mL) in a round-bottom flask and the mixture was cooled to –35 °C. Crotylstannane (207 mg, 0.6 mmol) was added followed by $BF_3{\bullet}OEt_2$ (0.07 mL, 1.05 equiv) The reaction was monitored until complete (90 minutes). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 2 d. NEt_3 was added to quench the reaction. The crude was passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL). The solution was concentrated. NMR of the crude material showed desired stannane. However, isomeric ratio was difficult to calculate. The reaction crude was subjected to column chromatography [silica gel; 9:1 hexane/EtOAc, 1% Et_3N]. However, the isolated

product seemed to have additional peaks in the ^{1}HNMR (between 3-4 ppm). Reaction was repeated and column chromatography was performed with neutral alumina (3% deactivated). The similar peaks were observed after chromatography. The reported yield was based on 0.917 g of recovered material (38% for the desired stannane)

Synthesis of 51 (Scheme 32)

Alkynal **35** (65 mg, 0.5 mmol) was dissolved in toluene (1 mL) in a round-bottom flask and the mixture was cooled to –35 °C. Allylstannane (0.16 mL, 1 mmol) was added followed by BF_3•OEt_2 (0.07 mL, 1.05 equiv) The reaction was monitored until complete (15 minutes). At this point, $B(C_6F_5)_3$ (53 mg, 20 mol%) was added to the solution under N_2 (glove bag) and it was cooled to –35 °C. PMHS (0.06 mL, 2 equiv) was added and the reaction was run for 1 h. NEt_3 was added to quench the reaction. At this point, another equiv of PMHS (0.03 mL, 1 equiv) was added to the crude and it was refrigerated for 7 d. The solution was then passed through a short silica plug (1") buffered with 1% NEt_3 with 4:1 hexane/EtOAc solution (200 mL), concentrated and subjected to column chromatography [silica gel; 80:20 hexane/EtOAc, 1% Et_3N] to afford 43 (111 mg, 48%) as a clear oil.

Data for **51**: IR (neat): 3353 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.6 Hz, 9 H), 0.95 (t, *J* = 8.0 Hz, 6 H), 1.28-1.36 (m, 6 H), 1.46-1.59 (m, 6 H), 1.98 (b, 1 H), 2.44-2.54 (m, 2 H), 4.70-4.73 (m, 1 H), 5.11-5.16 (m, 2 H), 5.74-5.83 (m, 1 H), 6.84 (s, 2 H), 7.3 (dd, J = 34.9, 8.3 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.6, 13.7, 27.3, 29.1, 43.8, 73.1, 118.4, 126.0, 126.0, 129.7, 134.4, 138.2, 143.1, 145.6. HRMS (EI) m/z calcd for $C_{20}H_{31}O^{116}Sn$ $[M\text{-}Bu]^+$, 403.1392, found: 403.1403.

Synthesis of 53 (Scheme 33)

To a stirred solution of stannane (62 mg, 0.133 mmol)in CH_2Cl_2 (2.3 mL) cooled to 0 °C was added a solution of iodine in CH_2Cl_2 (0.7 mL) until the purple iodine persisted for a few minutes. At this point, the solvent was removed and purification of the vinyliodide was attempted using column chromatography [silica gel; 80:20 hexane/EtOAc, 1% Et_3N]. However, the vinyliodide had impurities. So, it was subjected to the next Heck-coupling step.

Crude vinyliodide, triethylamine (0.05 mL, 3 equiv), palladium acetate (4.5 mg, 5 mol%) and triphenylphosphine (7 mg, 20%) was stirred in acetonitrile (1.2 mL) in a sealed tube under nitrogen at 80 °C for 12 h. At this point, black Pd-mirror deposited on the walls of the tube which indicated the end of the reaction. The reaction mixture was diluted with brine and extracted with ether. The ether layers were combined, dried with $MgSO_4$ and

concentrated. Finally, the crude was subjected to column chromatography [silica gel; CH_2Cl_2] to afford **53** (~8 mg, <35%) This product had certain impurities between (1-2 ppm). However, structure of this compound has been confirmed from, IR, ^{1}HNMR, ^{13}CNMR, HRMS and HMQC studies.

Data for **53**: IR (neat): 3380 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) 1.98 (bm, 1 H), 2.76-2.82 (m, 1 H), 2.92-3.00 (m, 1 H), 4.88 (m, 1 H), 5.12 (m, 1 H), 5.23-5.24 (m, 1 H), 6.35 (s, 2 H), 7.18-7.38 (m, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ. 41.9, 72.0, 121.1, 127.5, 127.8, 127.9, 129.2, 131.9, 132.3, 133.9, 142.2, 142.5. HRMS (ESI) m/z calcd for $C_{12}H_{13}O$ $[M+H]^+$, 173.0966, found: 173.0960.

^{119}Sn NMR and ^{11}B NMR study of one-pot allylation/hydrostannation protocol (Scheme 36): Benzaldehyde (0.04 mL, 0.375 mmol), and allyltributylstannane (0.12 mL, 0.375 mmol) were dissolved in toluene-d8 in an NMR tube under nitrogen and vortexed. ^{119}Sn NMR was observed. BF_3•OEt_2 (0.05 mL, 0.393 mmol) was added to the tube and ^{119}Sn NMR was observed again. PMHS (0.05 mL) was added followed by addition of $B(C_6F_5)_3$ (0.0384 mg, 20%). After each addition, ^{119}Sn NMR was observed. Finally, phenyl acetylene was added (0.04 mL, 0.375 mmol) and ^{119}Sn NMR was taken.

These steps were repeated for taking ^{11}B NMR.

Hydrostannation of phenylacetylene with Bu_3SnF and catalytic $B(C_6F_5)_3$ (Scheme 38)

$B(C_6F_5)_3$ (102 mg, 20 mol%) was weighed in a glove bag under nitrogen and dissolved in toluene (2 mL). Phenylacetelene (106 mg, 1 mmol) was added to it. This solution was stirred for 5 minutes. Bu_3SnF (309 mg, 1 equiv) was weighed and added to the above solution under nitrogen followed by the addition of PMHS (0.12 mL, 2 equiv). The reaction was stirred for 1 h. The solution was then passes through a silica plug as usual using hexanes (200 mL) as eluent. This solution was concentrated to afford **23b** and **23c** (1.1:1). Finally, column chromatography [silica gel; hexane, 1% Et_3N] afforded a mixture of **23c** and **23b** as a yellow oil (42 mg, 11%). Spectroscopic data was consistent with the literature.[57,66]

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