Metal-Catalyzed Hydrostannations

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Contents

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 these intermediates undergo.[1] As a consequence, there exists a variety of ways of forming a carbon−tin bond[2], the more widely used methods being: (a) the reaction of a tin−metal compound R_3SnM with an alkyl halide, (b) the reaction of an organometallic reagent, RM, with a tin halide, and (c) the overall addition of a 'tin hydride' to an alkyne, alkene, or allene.

Currently method c is the most frequently used strategy as the mild, neutral conditions allow for the formation of functionally rich vinyl and allyl organostannanes that are amenable to further manipulation. There are three general modes of addition of tin hydride that are used: (1) Hydrostannation under free-radical conditions; (2) Stannylmetalation−protonation of an alkene, allene, or alkyne; (3) Metal-catalyzed hydrostannation of an alkene, allene, or alkyne.

Neumann's book, published some 30 years ago, and the comprehensive book of Pereyre, Quintard, and Rahm highlight many of the subsequent transformations of organostannanes. Our focus will be on putting the hydrostannation reaction in context when selective methods for the preparation of organostannanes are desired.

1.1. Hydrostannation under Free-Radical Conditions

The hydrostannation of alkynes, alkenes, and allenes under free- radical conditions has been widely studied and gives, in general, a mixture of stereoisomers with the regiochemistry controlled by the relative stability of the two possible intermediate β-stannyl radicals (Scheme 1).[3] Since the benzylic radical is more stable, the β-product is favored.

Despite the high regioselectivity of radical hydrostannation, stereoselectivity is often a significant problem since the initially formed kinetic product is equilibrated by further addition−elimination processes under the reaction conditions. Good stereoselectivities may be obtained if this equilibration process leads to a thermodynamic product favored by other factors (often steric).[4] Recently, good cis selectivity has been reported by the use of sonochemical initiation of the radical cycle.[5]

Radical stannylation of unsaturated bonds is not applicable to all substrate types as discrimination between other sites of unsaturation (i.e., alkyne versus alkene) or reduction (alkyne versus halogen) in the molecule can lead to undesired side reactions.

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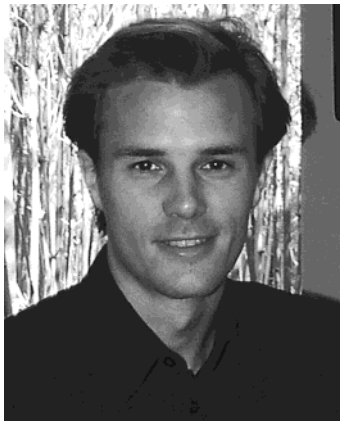
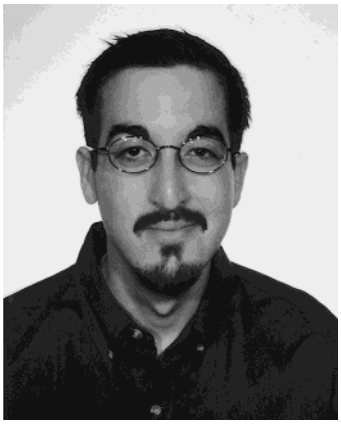
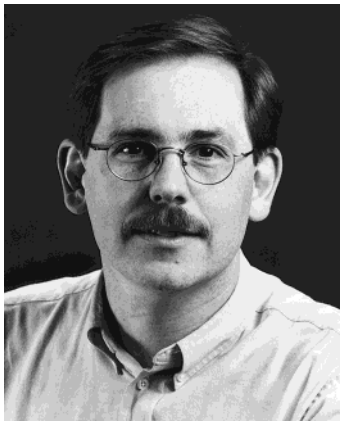


Nicholas Smith was born in Washington, D.C., in 1969. He received his B.Sc. degree at Southampton University, U.K., in 1992 and completed his doctoral degree with Professor Philip Kocienski at Southampton in 1996. Following postdoctoral work with Professor Mark Lautens at the University of Toronto, he joined the Medicinal Chemistry group at Tanabe Research Laboratories in San Diego. He is currently working at the Merck Research Laboratories in San Diego.

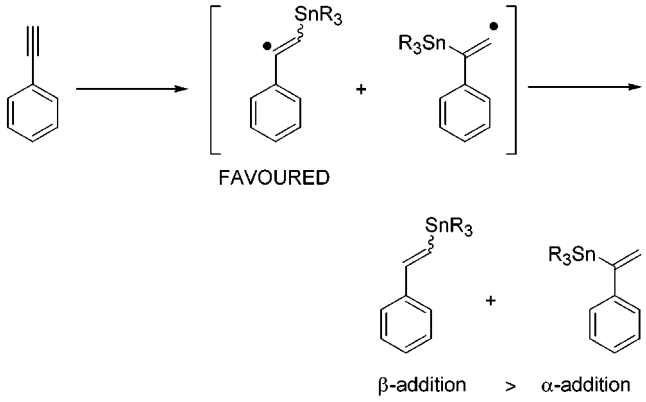


John Mancuso was born in Montreal, Canada, in 1975. He entered the Chemistry program at Concordia University, Montreal, and was a member of its Institute for Cooperative Education. He completed his final-year research project under the supervision of Dr. Y. S. Tsantrizos and obtained his B.Sc. degree in 1998. After brief internships at the Merck Frosst Centre for Therapeutic Research (Kirkland, Quebec) and at Merck Process Research (Rahway, NJ), he joined the group of Professor Mark Lautens at the University of Toronto. He is currently pursuing doctoral studies in the area of metal-catalyzed hydrostannations and Lewis-acid-mediated reactions of epoxides.

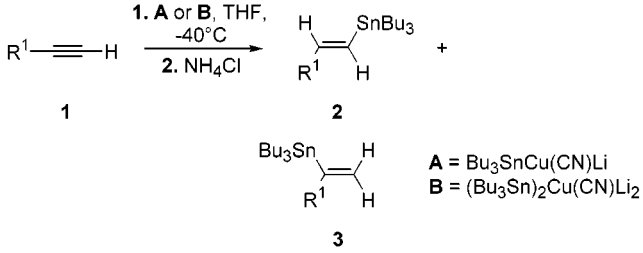


Mark Lautens was born in Hamilton, Ontario, Canada, in 1959. He received his B.Sc. degree at the University of Guelph in 1981 and his Ph.D. degree from the University of Wisconsin—Madison in 1985 with Barry Trost. He was an NSERC postdoctoral fellow with David A. Evans at Harvard University from 1985 to 1987 prior to taking a position a the University of Toronto, where he is now the AstraZeneca Professor of Organic Synthesis. His research interests include the development of new metal-catalyzed reactions, asymmetric catalysis, and natural product synthesis.

Scheme 1



Scheme 2



Enyne	R^1	Conditions	2:3	Yield(%)
1a	H_2C=C(Me)	**A**	19:81	56
1a	H_2C=C(Me)	**B**	3:97	95
1b	$HOCH_2CH$=CH	**A**	38:62	58
1b	$HOCH_2CH$=CH	**B**	18:82	91

1.2. Stannylmetalation–Protonation

Stannylmetalation of alkynes, alkenes, and allenes may be divided into two broad categories: stoichiometric stannylcupration and stannylmetalation in the presence of a transition-metal catalyst. For alkynes, both classes of stannylmetalations lead to cis addition of the bimetallic species unless equilibration occurs.[6] Stoichiometric stannylcuprations typically require an excess (2−4 equivalents) of reagent for the efficient consumption of starting material and the stereoselectivity of the addition depends not only on the substrate but also on the nature of the cuprate used (higher versus lower order, Scheme 2).[7]

Copper(I) sources are the most popular choice for catalysts in transition-metal-catalyzed stannylmetalations with the second metal often being Al, Zn, Mg, or B.[8] Palladium(II) catalysis has also been used widely in the stannylstannylation and silylstannylation of alkynes.[9]

As well as the structure of the substrate, the regiochemistry of transition-metal-catalyzed stannylmetalation depends on a number of factors including metal partner,[8b] catalyst,[8b,10] solvent,[11] and other additives.[12] Stannylmetalation reactions have been reviewed previously.[13]

This review will present the work to date that has been carried out on the last of these three techniques—

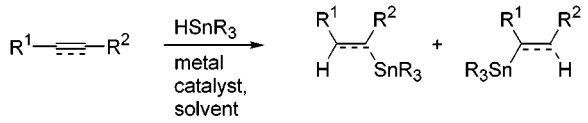
metal-catalyzed hydrostannation of alkynes, alkenes, and allenes.

1.3. Metal-Catalyzed Hydrostannation of Alkynes, Alkenes, and Allenes

1.3.1. General Reaction Conditions

A general equation for the hydrostannation of alkynes, alkenes, and allenes in the presence of a metal catalyst is shown in Scheme 3.

Scheme 3

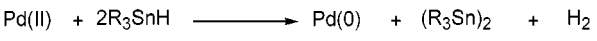


Metal-catalyzed hydrostannation usually occurs with cis stereoselectivity as a consequence of the reaction mechanism and, in many cases, good regioselectivity due to a combination of steric or electronic factors. Although a survey of the literature reveals that the nature of the substrate has the most profound effect on selectivity (vide supra), other variables will also influence the outcome of the reaction, and so they will be discussed briefly here.

1.3.2. Choice of Catalyst

As mentioned above, palladium is the most popular catalyst choice for the hydrostannation of alkynes, alkenes, and allenes with tetrakis(triphenylphosphine) palladium(0) ($Pd(PPh_3)_4$) and dichlorobis-(triphenylphosphine)palladium(II) ($PdCl_2(PPh_3)_2$) being most widely used. However, a number of other palladium sources have been successfully utilized including $Pd(OAc)_2/PPh_3$,[14] $Pd_2(dba)_3/PAr_3$,[15] $PdCl_2$(dppe),[16] and $Pd(OH)_2/C$.[17] It is believed that under the reaction conditions, palladium(II) complexes are reduced to catalytically active palladium(0) species (Scheme 4).

Scheme 4



Aside from palladium, a number of catalysts based on Mo[18] and Rh[19] have been described (often with divergent reactivities to those observed with Pd) in addition to a limited number of examples of Ni, Co, Pt, and Ru.[19,20] Good comparative studies of various catalyst sources have been published by Alami,[16] Guibé,[18a] and Kikukawa.[19]

1.3.3. Hydrostannation Reagent

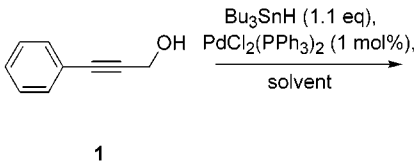
The most commonly used hydrostannation reagent is tri(*n*-butyl)tin hydride (noted Bu_3SnH) due to its price, ease of handling, and reactivity. Trimethyl- and triphenyltin hydride have also been used but the former is toxic and volatile[1] while the latter has adds to alkynes more slowly than Bu_3SnH.[21]

Recently, Maleczka elegantly demonstrated the in situ generation of Bu_3SnH from the reduction of Bu_3SnX with poly(methylhydrosiloxane) (PMHS) for a one-pot hydrostannation/Stille coupling sequence of terminal alkynes.[22] This discovery allows for the use of catalytic amounts of Bu_3SnX, which increase the importance of metal-catalyzed hydrostannation reactions.

1.3.4. Solvent

Metal-catalyzed hydrostannations of alkynes, alkenes, and allenes may be carried out in a wide variety solvents, but by far the most popular are THF, benzene, and toluene. No exhaustive studies on solvent effects have been carried out; however, in his study on the hydrostannation of aryl-substituted alkynes, Alami[16] noted a modest change in the regioselectivity on increasing solvent polarity (Scheme 5).

Scheme 5



Solvent	Conversion[a]	Regioselectivity[b] (2:3)
CH_2Cl_2	40	33:67
C_6H_5Me	100	45:55
C_6H_{12}	67	52:48
Et_2O	100	65:35
THF	100	80:20
TMU	61	77:23
AcOEt	100	67:33

[a] Conversion measured by ^{1}H-NMR analysis and is based on remaining alkyne. [b] Regioselectivity determined on the crude material by ^{1}H-NMR.

Similar observations have been reported by Greeves.[23]

1.3.5. Stoichiometry

Precise reaction stoichiometries vary widely; however, in general, 110−150 mol % of trialkyltin hydride is added dropwise to 0.5−10 mol % of catalyst and substrate at 0.1 M concentration in solvent at room temperature. An excess of tin hydride is required for two reasons: (i) the hydride is used to reduce a Pd(II) source to Pd(0) and (ii) trialkyltin hydride is destroyed by reductive coupling, generating hydrogen and the distannane. This undesired side reaction is minimized by maintaining a low concentration of tin hydride, which is more readily achieved by dropwise addition.

1.3.6. Purification

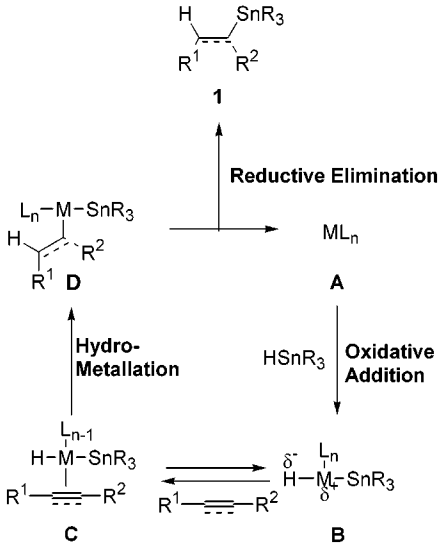
Purification of stannanes is usually achieved by silica-gel chromatography or distillation, the latter depending on the molecular weight of the compound. However, silica-gel-mediated protonolysis of alkenylstannanes resulting in destannylation is often a problem, giving low isolated yields. To this end, the

use of basic or neutral alumina can alleviate protodestannylation and for particularly sensitive compounds, performing the alumina chromatography at 0 °C using an ice-water-filled jacket column is optimal.[24] Triethylamine-treated silica gel can also be used to avoid destannylation.

1.3.7. Possible Reaction Mechanisms: Factors Affecting Stereo- and Regioselectivity

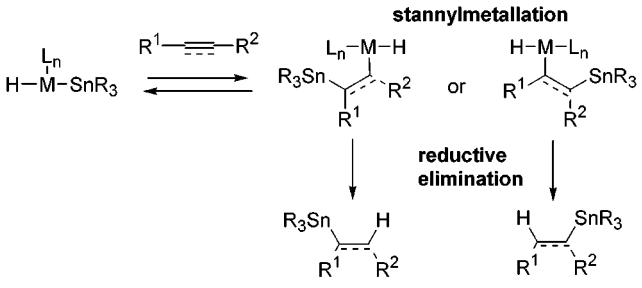
Through an understanding of the reaction mechanism for the metal-catalyzed hydrostannation of alkynes, alkenes, and allenes, we can attempt to rationalize the existing data and develop new reactions. Although the mechanistic details of the hydrostannation reactions are not fully understood, a general catalytic cycle based upon oxidative addition−hydrometalation−reductive elimination has been postulated by a number of authors and may be used to highlight the factors effecting selectivities (Scheme 6).[23,25,26]

Scheme 6



Although hydrometalation is shown as the initial reduction step, stannylmetalation−reductive elimination may also occur (Scheme 7).

Scheme 7



Oxidative addition of R_3SnH to the metal center (MLn) (**A** → **B**) occurs followed by coordination of the unsaturated bond leading to complex **C,** which may then undergo hydrometalation to give vinylmetal **D** followed by reductive elimination to furnish the organostannane.

This mechanism is in agreement with the following general observations from the literature. (i) Hydrostannation occurs with cis stereoselectivity furnishing the (*E*)-geometric isomer (in the case of alkynes). (ii) The relative steric bulk of R^1 and R^2 will effect the mode of addition (R_3Sn placed proximal to R^1 or R^2). Thus, a bulky R^1 substituent will orientate the substrate so that R^1 is distal to the bulky R_3Sn ligand on the metal, hence favoring complex **C** and so regioisomer **1**. (iii) In complex **B**, the electropositive metal center leads the H atom to show hydridic character. If there is also polarization of the π bond by R^1 and/or R^2, the regioselectivity of addition of R_3Sn-ML_n-H may be affected as well.[15] These steric and electronic effects will vary in their relative importance depending on the substrate and catalyst in use and together with secondary factors such as metal chelation by a suitably positioned heteroatom on R^1 or R^2,[21] which will control the regiochemistry of the hydrostannation.

1.4. Organization of Review

As mentioned previously, the literature indicates that the nature of the reacting center and neighboring functional groups of the substrate have the most profound effects on the selectivity of the hydrostannation reaction. For this reason, this review is arranged according to the reacting center (alkyne/alkene/allene) and then further subdivided according to nearby functional groups (ester, heteroatom, etc.).

Although palladium sources are most commonly used as catalysts, there are a number of studies where altering the 'traditional' catalyst source has resulted in effects on regio- and stereochemistries. These studies will be highlighted during the course of the discussion.

2. Hydrostannation of Alkynes

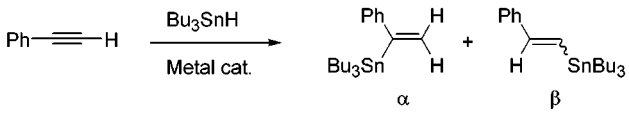
2.1. Hydrostannation of Aryl and Alkyl Alkynes

2.1.1. Hydrostannation of Aryl Alkynes

In 1987, Oshima and co-workers published one of the first reports exemplifying the hydrostannation of an alkyne.[27] Oshima found that in the presence of catalytic $Pd(PPh_3)_4$ and triphenyltin hydride, phenylacetylene was hydrostannated, leading predominantly to the formation of the β-substituted stannane. Kikukawa carried out a more detailed study in 1988, investigating the hydrostannation of phenylacetylene with tributyltin hydride using a variety of transition-metal catalysts (Table 1).[19]

Although Ni (entry 5), Pd (entry 6, 7),[28] Co (entry 9), and Mo (entry 11) catalysts were found to give poor regioselectivity (α/β = 1:1), Rh catalysts were found to give good α selectivity (entries 1−4)—in particular, Wilkinson's catalyst (entry 1) gave good yields and excellent selectivity for the α-isomer. Although $RuCl_2(PPh_3)_4$ (entry 10) gave good and complementary selectivity favoring the β regioisomer (compared to Rh), the stereoselectivity was poor (α/β = 1:1). Kikukawa also noted that the use of a cationic Rh complex (entry 4) significantly slowed the rate of the reaction compared to neutral complexes (entries

Table 1. Hydrostannation of Phenylacetylene Using Bu_3SnH and a Transition-Metal Catalyst



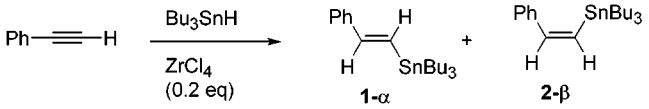
					Products (% ratio)[b]		
Entry	Catalyst	Temp (°C)	Time(h)	Yield (%)[a]	α	β(E/Z)	Reference
1	$RhCl(PPh_3)_3$	r.t.	0.5	86[e]	88	12(100/0)	19
2	$RhCl(CO)(PPh_3)_2$	0	0.5	99[e]	78	22(91/9)	19
3	$[RhCl(COD)]_2$	0	0.5	66[e]	81	19(32/68)	19
4	$[Rh(COD)(PPh_3)_2]^+PF_6^-$	0	2[c]	70[e]	80	20(55/45)	19
5	$NiCl_2(PPh_3)_2$	r.t.	0.2	80	45	55(91/9)	19
6	$PdCl_2(PPh_3)_2$	0	0.5	88[d]	43	51(100/0)	19
7	$Pd(PPh_3)_4$	r.t.	0.5	96	50	50(100/0)	28
8	$PtCl_2(PPh_3)_2$	r.t.	0.2	73	34	66(82/18)	19
9	$CoCl_2(PPh_3)_2$	0	4	40	43	57(84/16)	19
10	$RuCl_2(PPh_3)_4$	r.t.	68	78	11	89(47/53)	19
11	$Mo(\pi\text{-allyl})Br(CO)_2(CH_3CN)_2$	r.t.	---	56	47	53(100/0)	18a

[a]Isolated yields. [b]Determined by GC. [c]After 1 day 25% Bu_3SnH still remained. [d]Contaminated with Sn_2Bu_6 (6%). [e] the metal complex was mixed with the tin hydride prior to addition of the alkyne.

1−3). Miyake found rate effects when the ligand on Pd was changed; thus, the use of $Pd(PBu_3)_4$ required longer reaction times (2 h) than did $Pd(PPh_3)_4$ (entry 7, 30 min).[28]

Yamamoto has shown that excellent β-selectivity in the hydrostannation of phenylacetylene may be achieved through the use of Lewis-acid catalysis with $ZrCl_4$ (Scheme 8).[29] Contrary to the transition-metal

Scheme 8



Ratio (1−α : 2-β)	Yield (%)
5 : >95	73

catalysts presented in Table 1, the use of $ZrCl_4$ leads to *anti*-addition of the Bu_3SnH, furnishing the (*Z*)-isomer **2-**β. Although details of the mechanism are unknown, the authors postulate that $ZrCl_4$ may coordinate to the triple bond allowing hydride attack or that Bu_3SnH and $ZrCl_4$ may react to form an active hydrostannating species.[29b]

In 1990, Guibé published a wide-ranging study on the hydrostannation of variously substituted alkynes with Bu_3SnH using either Pd or Mo catalysis.[18a] Guibé found that poor regioselectivity was observed in the hydrostannation of phenylacetylene (i.e., entry 7, Table 1); however, 1-phenylprop-1-yne reacted with excellent α regioselectivity in the presence of Pd-$(PPh_3)_4$ (Scheme 2). A Mo-based catalyst, however, was found to be a poor catalyst for both substrates, giving negligible regioselectivity (Table 1, entry 11 and Scheme 9).

Scheme 9

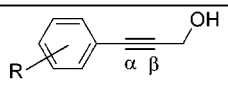
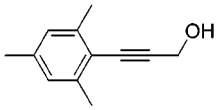
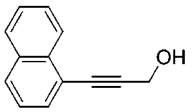
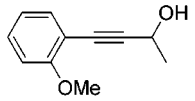
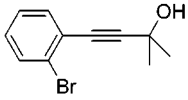
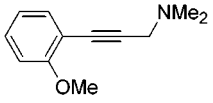
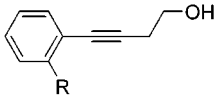
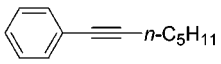
	α	β	yield (%)
$Pd(PPh_3)_4$	100	0	79
$Mo(\pi\text{-allyl})Br(CO)_2(CH_3CN)_2$	48	52	not isolated

Recently Alami published an extensive study on the $PdCl_2(PPh_3)_2$-catalyzed hydrostannation of aryl-substituted alkynes in which he noted that the regioselectivity was influenced by the nature and position of the ring substituent (Table 2).[16]

Alami found that an electron-withdrawing group in the *para*-position gave regiospecific formation of the α-isomer (entries 1, 2) but that this regioselectivity decreased upon substitution with an electron-donating group (entries 3, 4). However, upon switching the electron-donating group from the *para* to the *ortho* position, α-regioselectivity increased (entry 5). The authors postulate that such trends in regioselectivity are not only due to a coordination effect since this trend was followed for simple alkyl substituents as well (entries 6, 8). Furthermore, total α-regioselectivity was observed with a sterically congested *ortho*,*ortho*′-disubstituted aryl alkyne (entry 14) as well as for halogen substitution (entries 12, 13) and a range of propargylic substituents (entries 16−21). The precise contributions of steric, electronic, and coordinative factors controlling this regioselectivity have not been fully determined.

In summary, Rh-catalyzed hydrostannation of terminal aryl alkynes with Bu_3SnH occurs with *cis*-addition and with a preference for α-addition of the

Table 2. Palladium-Catalyzed Hydrostannation of Various Aryl-Substituted Alkynes

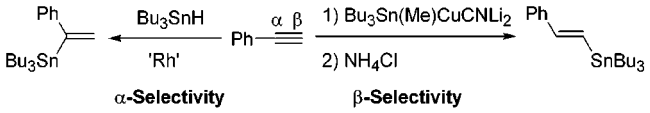
Entry	Aryl Alkyne		Isolated yield of (%) α-isomer	Isolated yield of (%) β-isomer
1		R = *p*-NO_2	68	---[a]
2		R = *p*-CHO	74	---[a]
3		R = *p*-OMe	65	20
4		R = *m*-OMe	67	17
5		R = *o*-OMe	87	6
6		R = *p*-Me	64	19
7		R = *m*-Me	59	11
8		R = *o*-Me	92	5
9		R = *o*-*i*-Pr	66	---[a]
10		R = *o*-CH_2OMe	51	---[a]
11		R = *o*-Cl	76	---[a]
12		R = *o*-Br	88	---[a]
13		R = *p*-Br	70	11
14			81	---[a]
15			80	---[b]
16			97	---[a]
17			96	---[a]
18			66	---[a]
19		R = Br	86	---[a]
20		R = H	87	---[a]
21			89	---[a]

[a] Not detected. [b] Less than 3% of another isomer detected whose structure could not be assigned.

tin moiety. Alami has shown that aryl-substituted internal alkynes undergo stereoselective α-addition with $PdCl_2(PPh_3)_2$. In a complementary fashion, the *β*-(*Z*)-product can be generated by Yamamoto's Lewis-acid-catalysis protocol,[29] while stannylcupration may be used to generate the *β*-(*E*)-product (Scheme 10).[8a,30]

Good *β*-regioselectivity is observed with radical hydrostannation; however, in the absence of steric factors, a mixture of stereoisomers is usually obtained.[31]

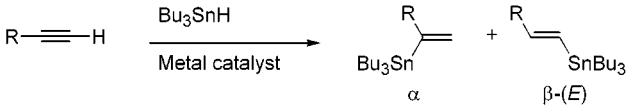
Scheme 10



2.1.2. Hydrostannation of Alkyl Alkynes

Both Oshima[32] and Guibé[18a] described the hydrostannation of alkyl-substituted alkynes in their early publications. Oshima found that hydrostanna-

Table 3. Hydrostannation of Alkyl Alkynes



Entry	R	Catalyst	α/β-(*E*)	Isolated yield
1	*n*-Hex	$PdCl_2(PPh_3)_2$	57/43	---[a]
2	*n*-Hex	$Mo(\pi\text{-allyl})Br(CO)_2(MeCN)_2$	50/50	---[a]
3	$CH(n\text{-}C_5H_{11})_2$	$PdCl_2(PPh_3)_2$	0/100	90
4	$CH(n\text{-}C_5H_{11})_2$	$Mo(\pi\text{-allyl})Br(CO)_2(MeCN)_2$	58/42	89

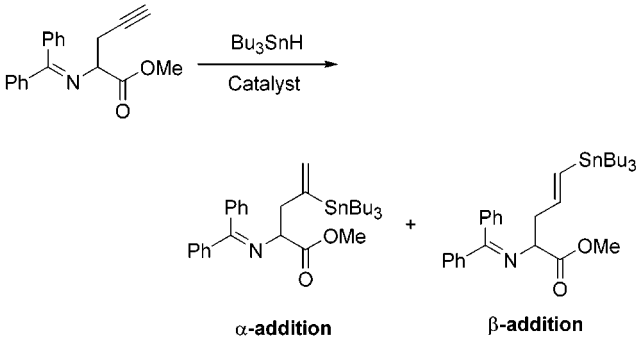
[a] Products not isolated.

tion of 1-dodecyne with Ph_3SnH and $Pd(PPh_3)_4$ led predominantly to the β-regioisomer (α/β = 11/89), whereas with Bu_3SnH and $PdCl_2(PPh_3)_2$, Guibé found negligible regioselectivity (Table 3, entry 1). However, upon increasing the steric bulk at the propargylic position, Guibé observed complete β-regioselectivity (entry 3).

These observations suggest the importance of steric factors in controlling the regioselectivity of addition in this substrate class. With the more reactive Mo catalyst, poor regioselectivity was observed with both substrates (entries 2,4).

Poor regioselectivity in the hydrostannation of an alkyl alkyne was reported in Crisp's recent publication on the hydrostannation of a propargylic glycine derivative (Scheme 11).[33] Despite surveying a wide

Scheme 11



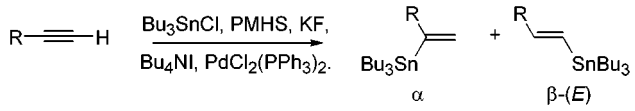
range of catalysts, Crisp was unable to achieve good yields of either regioisomer.

As part of an elegant study to develop a one-pot, hydrostannation/Stille coupling using substoichiometric quantities of Bu_3SnH generated in situ from poly(methylhydrosiloxane) and Bu_3SnCl, Maleczka investigated the hydrostannation of alkyl alkynes (Table 4).[22,34]

In agreement with the report by Guibé, Maleckza found that regioselectivity in the hydrostannation of alkyl alkynes with $PdCl_2(PPh_3)_2$ was poor (entries 1−3) in the absence of sterically bulky groups at the propargylic position (entries 4,5). As well as reducing toxicity concerns, the slow conversion of Bu_3SnCl to Bu_3SnH under the reaction conditions results in a low concentration of hydride, thus minimizing the formation of $(Bu_3Sn)_2$.

As with the hydrostannation of phenylacetylene (section 2.1.1), Yamamoto demonstrated that excel-

Table 4. Hydrostannation of Alkyl Alkynes Using in Situ Generated Bu_3SnH



PMHS: poly(methylhydrosiloxane)

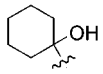
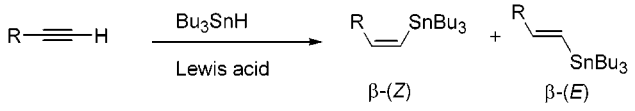
Entry	R	α:β	Yield (%)
1	$CH_2(CH_2)_3OH$	1 : 1.4	72
2	$CH_2(CH_2)_3OTBS$	1 : 1	51
3	$CH_2(CH_2)_2Cl$	1 : 1.4	84
4		1 : 17	62
5	*t*-Bu	1 : 99	59

Table 5. Lewis-Acid-Catalyzed Hydrostannation of Alkyl Alkynes



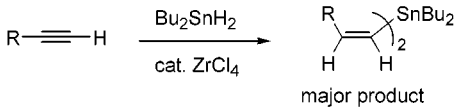
R	Lewis Acid (eq.)	(*Z*:*E*)[a]	Yield (%)[b]
$CH_3(CH_2)_5$	$ZrCl_4$ (1.1)	>95 : 5	30
$CH_3(CH_2)_5$	$ZrCl_4$ (0.2)	>95 : 5	76
$CH_3(CH_2)_5$	$ZrCl_4$ (0.2)	>95 : 5	86
$TBMDSO(CH_2)_3$	$ZrCl_4$ (0.2)	>95 : 5	87(48)
$CH_3(CH_2)_5$	$ZrCl_4$ (0.2)	>95 : 5	47(40)
$CH_3(CH_2)_4$	$ZrCl_4$ (1.0)	>95 : 5	56

[a] Stereoisomeric ratio determined by ^{1}H-NMR and came from isomer detection limits. [b] Yields determined by ^{1}H-NMR spectra using *p*-xylene as internal standard. Figures in parentheses indicate isolated yields. Protodestannylation occurred on silica gel column chromatography.

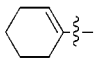
lent regio- and stereocontrol for the β-(*Z*)-isomer may be achieved via Lewis-acid-catalyzed hydrostannation of alkyl alkynes (Table 5).[29b]

Yamamoto's methodology was also shown to be useful in the construction of divinyl tin derivatives

Table 6. Hydrostannation of Alkyl Alkynes with Bu_2SnH_2



major product

R	Yield (%)[a]	product :other isomers
$CH_3(CH_2)_5$	85 (60)	>95:5
$PhCH_2$	78 (54)	>95:5
	76	>95:5

[a] Yields determined by ^{1}H-NMR spectra, isolated yields in parentheses.

by reaction with Bu_2SnH_2 (Table 6). Such compounds could be viewed as "atom-economical" building blocks in the Stille reaction, allowing transfer of both vinyl groups.

In summary, good β-(*E*)-regioselectivity in the hydrostannation of alkyl alkynes may be achieved with Pd(0) catalysis when controlled by bulky propargylic substituents. Alternatively the β-(*Z*)-product may be obtained via the use of catalytic $ZrCl_4$. To date, useful levels of α-regioselectivity have not been obtained for this substrate class.

2.2. Hydrostannation of Propargylic Alcohol Derivatives

2.2.1. Hydrostannation of Propargylic Alcohols and Ethers

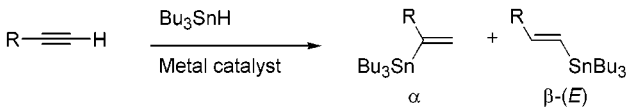
Miyake[28] and Guibé[18a] were among the first to publish studies that contained results on the hydrostannation of propargylic alcohols and ethers. They found that for ethers with no substitution at the propargylic position, slight α-regioselectivity was observed, probably due electronic and/or coordinative effects (Table 7, entries 1−4).

However, as with alkyl alkynes, steric effects upon substitution at the propargylic position changed the regioselectivity, leading to a preference for the β-addition product (entries 5−8). Interestingly, Guibé's Mo catalyst maintained modest α-selectivity with both these substrate types (entries 9−12).

As shown by selected examples from Maleczka's and Pancrazi's studies, virtually complete β-regioselectivity can be obtained by further increasing the steric bulk at the propargylic position (Table 7).[22,7c]

Recently an important advance was made with Kazmaier's development of $Mo(CO)_3(t\text{-BuNC})_3$ as a catalyst for the α-regioselective hydrostannation of propargylic alcohols and ethers.[18b] By replacing the CO ligands on $Mo(CO)_6$ with isoelectronic *tert*-butyl isocyanide ligands, Kazmaier was able to increase catalyst selectivity, turn over, and stability. Thus, as

Table 7. Hydrostannation of Propargylic Alcohols and Ethers



Entry	R	Catalyst	α:β	Yield (%)	Ref.
1	$HOCH_2$	$Pd(PPh_3)_4$	1.6 : 1	95	28
2	$BnOCH_2$	$Pd(PPh_3)_4$	1.9 : 1	95	28
3	$HOCH_2$	$PdCl_2(PPh_3)_2$	1.2 : 1	41	18a
4	$THPOCH_2$	$PdCl_2(PPh_3)_2$	2 : 1	68	18a
5	$CH_3(OH)CH$	$PdCl_2(PPh_3)_2$	1 : 4	---[a]	18a
6	$C_5H_{11}(OH)CH$	$PdCl_2(PPh_3)_2$	1 : 3	---[a]	18a
7	$C_5H_{11}(OTBS)CH$	$PdCl_2(PPh_3)_2$	1 : 2.6	94	18a
8	$Ph(OH)CH$	$PdCl_2(PPh_3)_2$	1 : 3.2	---[a]	18a
9	$HOCH_2$	Mo(π-allyl)$Br(CO)_2(MeCN)_2$	2 : 1	---[a]	18a
10	$THPOCH_2$	Mo(π-allyl)$Br(CO)_2(MeCN)_2$	1.8 : 1	---[a]	18a
11	$C_5H_{11}(OH)CH$	Mo(π-allyl)$Br(CO)_2(MeCN)_2$	1.3 : 1	67	18a
12	$C_5H_{11}(OTBS)CH$	Mo(π-allyl)$Br(CO)_2(MeCN)_2$	2.7 : 1	---[a]	18a

[a] Products not isolated.

Scheme 12

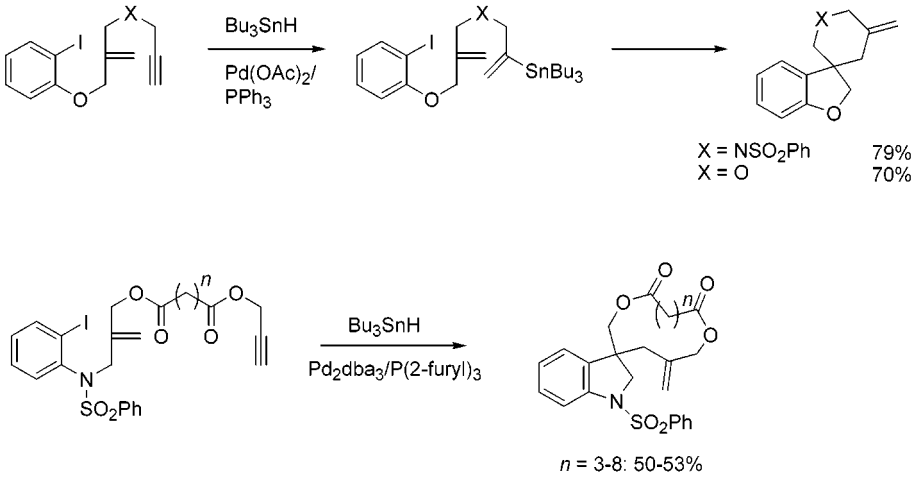
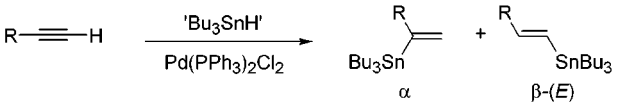
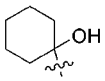
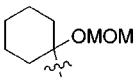
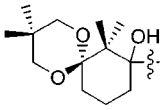


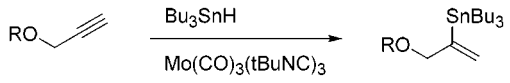
Table 8. Hydrostannation of Propargylic Derivatives

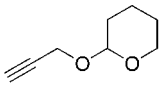
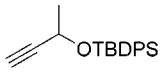
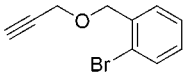
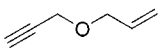


Entry	R	α:β	Yield (%)	Ref.
1	HO(Ph)(Me)C	1 : 12	86[a]	22
2	HO(*i*-Bu)(Me)C	1 : 24	66[a]	22
3		1 : 17	62[a]	22
4		0 : 1[b]	65	7c
5		0 : 1[b]	70	7c

[a] Bu_3SnH generated *in-situ* from Bu_3SnCl and poly(methylhydrosiloxane)
[b] Complete selectivity for the α isomer was reported

Table 9. Hydrostannation of Propargylic Derivatives Using $Mo(CO)_3(tBuNC)_3$



Substrate	Yield (%)	Selectivity (α:β)[a]
	81	91:9
	98	98:2
	88	90:10
	44	>95:<5
	38	>95:<5

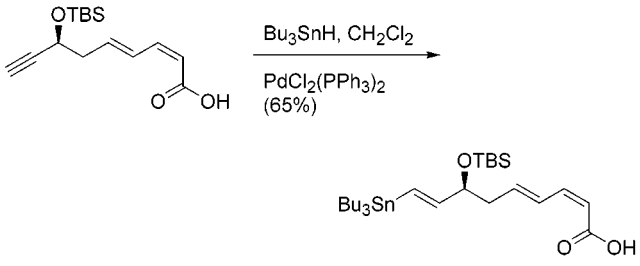
shown in Table 9, propargylic alcohols and ethers undergo highly regioselective α-hydrostannation regardless of their substitution patterns and with low catalyst loadings (0.1−1.0 mol %).

Applications of the hydrostannation of propargylic derivatives have been described in the literature and include Grigg's cascade hydrostannation/cyclization for the synthesis of spirocyclic heterocycles (Scheme 12).[14] In these studies Grigg reported regioselectivities for the hydrostannation step of $\alpha:\beta = 2-3:1$.

During a synthesis of the polyene antiviral macrolactin (A), Smith used a β-regioselective hydrostannation of a propargylic ether to generate the desired (*E*)-vinyl stannane (Scheme 13).[35] This example is notable because the (*E*,*Z*)-dienoic acid was stable and did not isomerize.

In summary, good levels of β-regioselectivity are observed in the Pd(0)-catalyzed hydrostannation of substituted propargylic ethers whereas good levels of α-regioselectivity on a range of substrates may be

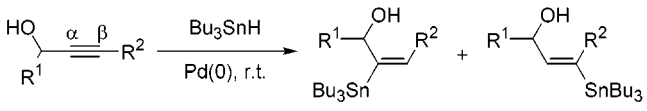
Scheme 13



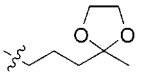
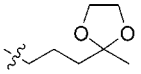
obtained via the use of Kazmaier's molybdenum catalyst.

As would be expected, radical stannylation leads to regioselective formation of the β-adduct but with poor stereoselectivity.[36] There are no universal rules for the regioselectivity of tin addition under stannylcupration conditions as selectivites vary with the substrate and cuprate used; however optimization on

Table 10. Hydrostannation of Disubstituted Propargylic Alcohols



α - addition β - addition

Entry	R^1	R^2	Yield % (α : β)[a]
1	Ph	*n*-Bu	21 : 67
2	2-Furyl	*n*-Bu	12 : 65
3	2-Furyl		8 : 64
4	*i*-Pr	*n*-Bu	0 : 86
5	*i*-Pr		0 : 80

[a] Isolated material

a case-by-case basis can afford good regioselectivites.[37,38,39]

2.2.2. Hydrostannation of Disubstituted Propargylic Alcohols

As with the hydrostannation of terminal propargyl alcohols and ethers, α/*β*-regioselectivity in the hydrostannation of disubstituted propargylic alcohols is influenced by the relative steric bulk of proximal substituents. Thus, in Greeves' 1994 study, moderate *β*-regioselectivity is observed in the $PdCl_2(PPh_3)_2$-catalyzed hydrostannation of phenyl- and furyl-substituted alkynes (entries 1−3, Table 10), but upon increasing steric bulk at the propargylic position (R^1), complete *β*-regioselectiviy was reported (entries 4,5).[23]

Further support for the controlling effects of the steric enviroment on the regioselectivity of addition may be obtained from a selection of individual examples in the literature. Thus, with steric bulk at the propargylic position, excellent *β*-selectivity was obtained by Oikawa in his synthesis of tautomycetin (compare entries 1 and 2, Table 11).[40]

Conversely, high α-regioselectivity may be achieved by increasing the steric bulk at the *β*-alkynyl carbon as shown in Semmelhack's studies toward the synthesis of tetronomycin (compare entries 3 and 4).[41]

Stannylcupration (under specific quenching conditions) of disubstituted propargylic alcohols can lead to excellent *β*-selectivity, as demonstrated in Pancrazi's comparative study (entry 1, Table 12).[7c] Radical hydrostannation shows complete selectivity for the α-regioisomer but with poor stereoselectivity (entry 2), while for this substrate, hydrostannation using $PdCl_2(PPh_3)_2$ shows moderate *syn*-α-regioselectivity (entry 3).

In summary, good α- or *β*-regioselectivity in the hydrostannation of disubsituted propargylic alcohols and ethers may be achieved when sufficient steric control is in effect.

2.3. Hydrostannation of Alkynyl Esters and Ketones

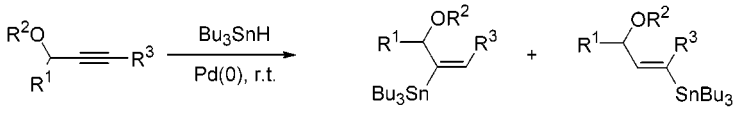
Studies by Guibé, Cochran, and Rossi on the Pd(0)-catalyzed hydrostannation of alkynyl esters have shown that in contrast to other substrate classes, good regioselectivity for the α-addition product is observed across a range of substrate substitution patterns, i.e., steric considerations play a lesser role (Table 13).[18a,21,42]

It has been proposed that the uniformly good α-regioselectivity observed is due to polarization of the acetylenic bond resulting in addition of hydride to the more electron-deficient *β*-carbon of the triple bond (placing the tin moiety α).[15]

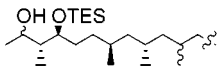
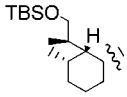
The Pd(0)-catalyzed hydrostannation of alkynyl ketones was also described by Guibé and Cochran as shown in Table 14.

Good regioselectivity for the α-addition of tin is again observed (entries 1−4), but the stereoselectvity is poor when Me_3SnH/D is used as the hydrostannation reagent. Significant quantities of the α-(*Z*)-isomer are obtained (i.e., overall anti hydrostannation, entries 1 and 3).[43] Protodestannylation during purification is also reported to be a problem with this

Table 11. Hydrostannation of Various Disubstituted Propargylic Alcohols and Ethers

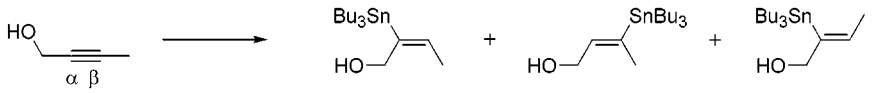


α - addition β - addition

Entry	R^1	R^2	R^3	Catalyst	α:β	Yield(%)	Ref.
1	*n*-Bu	H	*n*-Bu	$PdCl_2(PPh_3)_2$	1 : 2	65	18a
2		TBS	Et	$Pd(PPh_3)_4$	1 : 19	98	40
3	H	H	Me	$Pd(PPh_3)_4$	5 : 1	84	28
4	H	H		$PdCl_2(PPh_3)_2$	*a*	80	41

[a] High regioselectivity for the α-isomer was reported

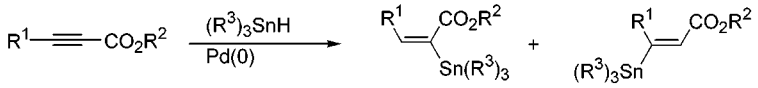
Table 12. Comparative Study of the Hydrostannation of But-2-yn-1-ol



syn-α *syn*-β *anti*-α

Entry	Conditions	Yield (%)	*syn*-α	*syn*-β	*anti*-α
1	2 eq. $Bu_3Sn(Bu)CuCNLi_2$, MeOH/THF, -10°C, 12 h	71	---	100	---
2	1.2 eq Bu_3SnH, AIBN, 80°C	64	30	---	70
3	1.2 eq Bu_3SnH, 2 mol% $PdCl_2(PPh_3)_2$	58	75	25	---

Table 13. Hydrostannation of Alkynyl Esters

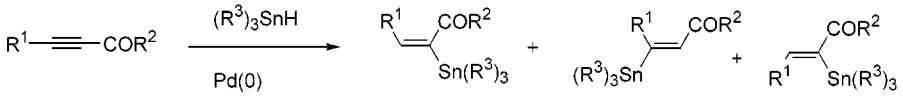


α β

Entry	R^1	R^2	R^3	Catalyst	α:β	Yield (%)[a]	Ref.
1	H	Me	Me	$Pd(PPh_3)_4$	100 : 0	71	21
2	H	Me	Ph	$Pd(PPh_3)_4$	100 : 0	42	21
3	H	Me	*n*-Bu	$PdCl_2(PPh_3)_2$	100 : 0	94	18a
4	*n*-Pent	Me	*n*-Bu	$Pd(PPh_3)_4$	92 : 8	85	42
5	$TBSOCH_2$	Et	*n*-Bu	$Pd(PPh_3)_4$	91 : 9	84	42
6	$C_2H_5CH(Me)$	Et	*n*-Bu	$Pd(PPh_3)_4$	98 : 2	93	42
7	Ph	Et	*n*-Bu	$Pd(PPh_3)_4$	90 : 10	71	42

[a] Isolated yield

Table 14. Hydrostannation of Alkynyl Ketones



α-(*E*) β-(*E*) α-(*Z*)

Entry	R^1	R^2	R^3	Catalyst	α(*E*) : β(*E*) : α(*Z*)	Yield (%)[a]	Ref.
1	H	Me	Me	$Pd(PPh_3)_4$	50 : 0 : 50[b]	51	21
2	H	Me	*n*-Bu	$PdCl_2(PPh_3)_2$	82 : 18 : 0	65	18a
3	Et	Me	Me	$Pd(PPh_3)_4$	0 : 0: 100	58	21
4	*n*-Hex	Me	*n*-Bu	$PdCl_2(PPh_3)_2$	100 : 0 : 0	---[c]	18a

[a] Isolated yield. [b] Use of Me_3SnD gives a mixture of α-(*E*):α-(*Z*) = 1:1. [c] Total protodestannylation by column chromatography

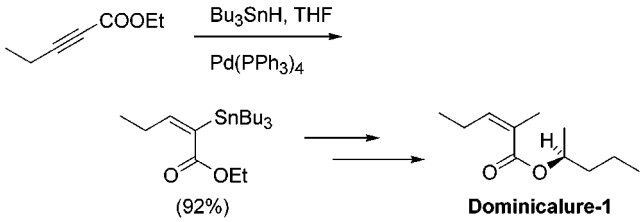
substrate class (entry 4) and has been investigated in detail.[21]

Kazmaier recently developed catalyst $Mo(CO)_3(t\text{-}BuNC)_3$ as a catalyst (previously discussed in section 2.2.1) which also demonstrated good yields and α-regioselectivity in the hydrostannation of alkynyl esters (Table 15).[18b]

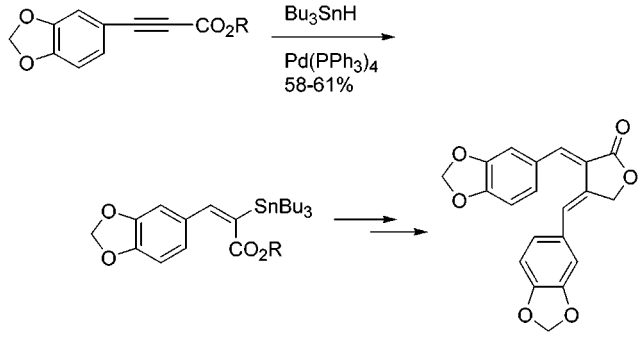
Of note is the compatibility of the Mo catalyst toward an allyl ester (which is incompatible with Pd(0) catalysis, entry 1) and toward an alkynoic acid (entry 5). Although good α-regioselectivity was also observed in the hydrostannation of an alkynyl ketone, protodestannylation of the product during purification was again reported (entry 6).

Applications of the hydrostannation of alkynyl esters in the literature include Rossi's synthesis of the aggregation pheromone dominicalure-1 (Scheme 14)[44] and Horikawa's synthesis of taiwanin A (Scheme 15):[45]

Scheme 14



Scheme 15



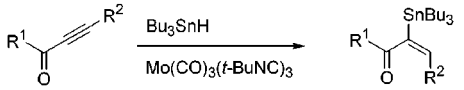
In summary, the Pd- and Mo-catalyzed hydrostannation of alkynyl esters and ketones proceeds with α-regioselective addition of tin, although protodestannylation of the product is a major problem with alkynyl ketones. In contrast, under stannylmetalation conditions, regio- and stereoselective hydrostannation of alkynyl acids and esters occurs leading predominantly to the *β*-(*E*)-adduct.[46,47] Once again, radical conditions tend to lead to a mixture of stereo- and/or regioisomers.[48]

2.4. Hydrostannation of Enynes

In a 1994 report on the preparation of dienyl stannane synthons, Trost performed one of the first studies on Pd-catalyzed hydrostannation of enyne−esters. High α-regio- and stereoselectivity was observed with a variety of substrates as shown in Table 16.[15]

The formation of the α-regioisomer was rationalized on the basis of polarization of the alkyne via

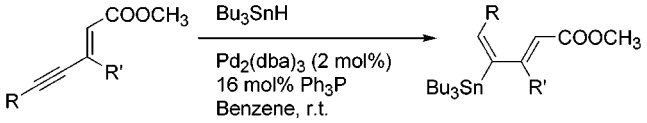
Table 15. Mo-Catalyzed Hydrostannation of Alkynyl Esters, Ketones and Acids

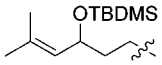


Entry	R^1	R^2	Yield (%)	Selectivity (α:β)[a]
1	$OCH_2CH=CH_2$	*n*-Pr	80	91 : 9
2	OEt	H	98	92 : 8[b]
3	OBn	*n*-Pr	68	90 : 10
4	OBn	$CH_2(CH_2)_3C=CH$	74	82 : 18
5	OH	*n*-Bu	88[c]	63 : 37
6	*i*-Pr	*n*-Pr	---	95 : 5[b]

[a] Ratio determined by ^{1}H-NMR. [b] Ratio determined by HPLC. [c] Isolated yield after esterification with CH_2N_2 and flash chromatography.

Table 16. Hydrostannation of Enyne−Esters



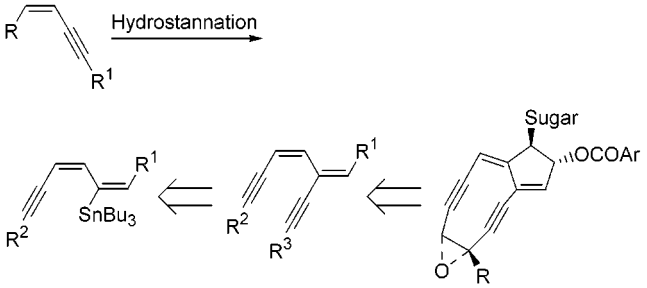
R	R'	Yield (%)[a]
$HOCH_2$	Me	85
$HOCH_2CH_3$	*n*-Pr	87
n-Pr	Me	85
	Me	80
$HOCH_2C{\equiv}C(CH_2)_3CH_2$	Me	46
$TBDMSOCH_2$	Me	81
$OHCCH_2CH_2CH_2$	Me	78

[a] Isolated yields.

conjugation to the ester moiety—in an analogous manner to that observed with alkynyl esters (Section 1.3)

In 1996, in methodology studies toward the synthesis of the powerful antitumor agent neocarzinostatin, Alami reported on the $PdCl_2(PPh_3)_2$-catalyzed hydrostannation of chloroenynes (Scheme 16).[49]

Scheme 16



Neocarzinostatin chromophore

Alami found that good α-regioselectivity was observed with both (*E*)- and (*Z*)-chloroenynes across a range of substrates including those containing potentially coordinating heteroatoms (Table 17).

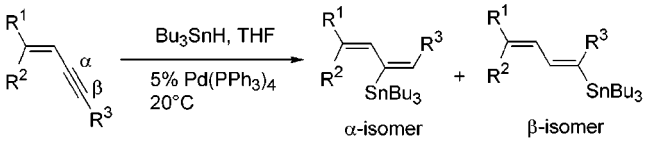
When the chlorine of the enyne was replaced with an alkyl group, good α-regioselectivity was again observed with (*Z*)-enynes (Table 18).

However (*E*)-enynes exhibited a reversal of regioselectivity with the *β*-regioisomer favored, although the level of selectivity was modest (Scheme 17).

In a more direct route to the dienyne unit of neocarzinostatin, Alami examined the hydrostannation of variously substituted enediynes.[50] He found that with symmetrically substituted (*Z*)-endiynes, excellent selectivity for the α-regioisomer was observed regardless of the nature of the R substituent (Table 19).

With unsymmetrical (*Z*)-enediynes bearing a trimethylsilyl group, excellent chemo- and regioselectivity was observed due to the deactivating effect of

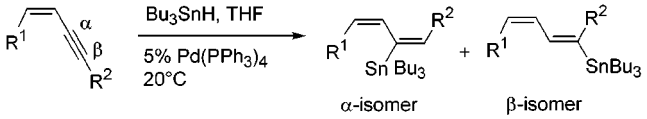
Table 17. Hydrostannation of (*E*)- and (*Z*)-Chloroalkynes



			Isolated yields	
R^1	R^2	R^3	α-isomer	β-isomer
Cl	H	CH_2OEt	62	15
Cl	H	$(CH_2)_2OH$	70	16
Cl	H	Ph	86[a]	14[a]
Cl	H	*n*-Pent	86	0
Cl	H	CH(OH)Me	74	0
Cl	H	CH_2NMe_2	89	0
H	Cl	$(CH_2)_2OH$	85	0
H	Cl	CH_2OH	92	2
H	Cl	CH_2OEt	68	0
H	Cl	CH_2NMe_2	85	0
H	Cl	Ph	93	0
H	Cl	*n*-Pent	91	0

[a] Not isolated - regioisomer ratio determined by ^{1}H-NMR.

Table 18. Hydrostannation of Alkyl-substituted Enynes



		Isolated yields	
R^1	R^2	α-isomer	β-isomer
n-C_4H_9	$(CH_2)_2OH$	55[a]	---[b]
n-C_4H_9	CH_2OH	83	8
n-C_4H_9	$CH(OH)C_5H_{11}$	92	---[b]
Ph	CH(OH)Me	84	---[b]

[a] 23% of starting material recovered at the end of the reaction. [b] Less than 2% of another isomer was obtained whose structure could not be assigned.

silicon on one of the alkynes (see also section 2.6.3), (Table 20).

However, although the analogous, unsymmetrical (*E*)-enediynes again exhibited total chemoselectivity, only moderate α-regioselectivity was observed (Table 21).

These results suggest that coordination of both alkynes to the palladium center may be an important controlling factor in the regioselectivity of addition—an effect that was invoked by Lautens in the hydrostannation—cyclization of 1,6-enynes (see section 2.4) and 1,6-diynes (see section 2.5).[17b,51]

Scheme 17

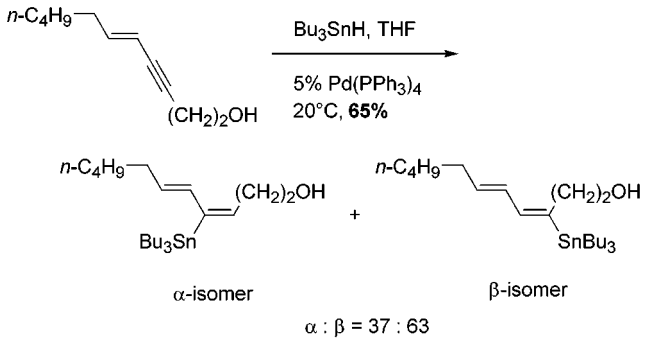
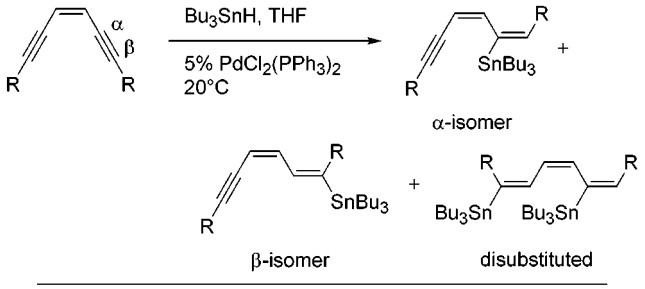


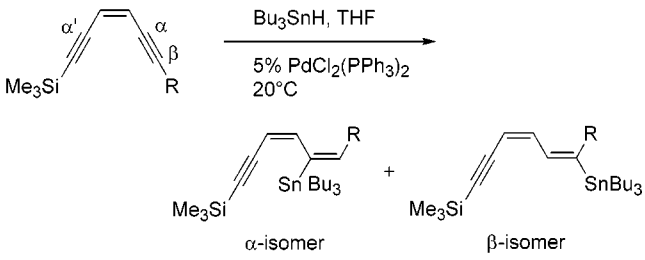
Table 19. Hydrostannation of Symmetrical (*Z*)-Enediynes



	Isolated yields		
R	α-isomer	β-isomer	disubstituted
$(CH_2)_2OH$	78	0	8
$CH(OH)C_5H_{11}$	50	0	---[a]
n-Pent	82	0	---[a]
Ph	77	0	---[a]

[a] Less than 2% of another isomer was obtained whose structure could not be assigned.

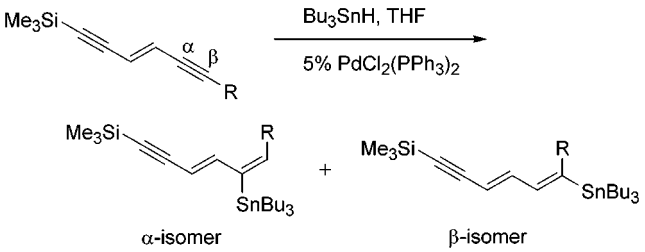
Table 20. Hydrostannation of Unsymmetrical (*E*)-Enediynes



	Isolated yields	
R	α-isomer	β-isomer
$(CH_2)_2OH$	96	0
CH_2OH	90	0
CH_2NMe_2	96	0
Ph	79	0
n-Pent	92	0

In 1997, Pancrazi reported on the hydrostannation of eneynols under $PdCl_2(PPh_3)_2$ catalysis, stannylcupration, and radical conditions. His study illustrated the importance of proximate heteroatom effects as

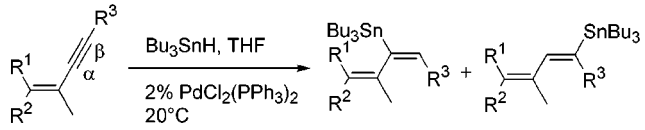
Table 21. Hydrostannation of Unsymmetrical (*E*)-Enediynes



	Isolated yields	
R	α-isomer	β-isomer
$(CH_2)_2OH$	61	34
n-Pent	59	23
$CH(OH)C_5H_{11}$	58	11
CH_2NMe_2	82	5

well as steric effects in controlling regioselectivitity of addition for this class of substrates (Table 22).[7c]

Table 22. Hydrostannation of Terminal and Alkyl-Substituted Enynes

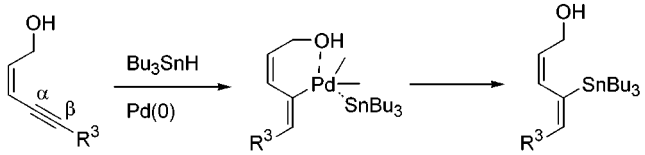


Entry	R^1	R^2	R^3	Yield (%)	α : β
1	H	CH_2OH	CH_3	92	100 : 0
2	CH_2OH	H	CH_3	62	100 : 0
3	H	CH_2OH	H	>99	---[a]
4	CH_2OH	H	H	54	88 : 12

[a] β-isomer and reduced diene isolated in 60:40 ratio.

Thus, the authors suggest that with disubstituted alkynes (R^3 = Me, entries 1, 2), exclusive formation of the α-addition product occurs due to the steric requirements of the R^3 and Bu_3Sn groups. Conversely, with no R^3 substituent and hence no steric restriction, a reversal in stereochemistry occurs furnishing the *β*-regioisomer as the major product (entry 3). However, predominant α-regioselectivity was again obtained with an unsubstituted but (*Z*)-eneynol (entry 4) wherein the heteroatom is proposed to be able to coordinate to the Pd center of the intermediate and hence control the regiochemistry of addition (Scheme 18).

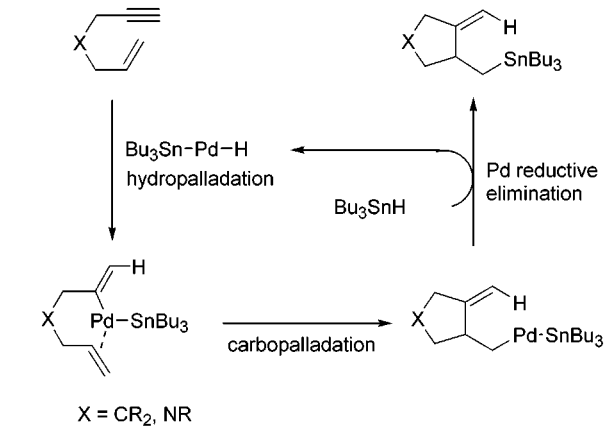
Scheme 18



Recently, Lautens and Mancuso showed that 1,6-enynes can undergo a hydrostannylative cyclization to generate methylenecyclopentanes bearing a [tri(*n*-butyl)stannyl]methyl moiety. The presence of a nitrogen at the propargylic position leads to the formation of pyrrolidines.[51]

The reaction is believed to proceed by the sequence shown in Scheme 19. Thus, chelation of the enyne to

Scheme 19

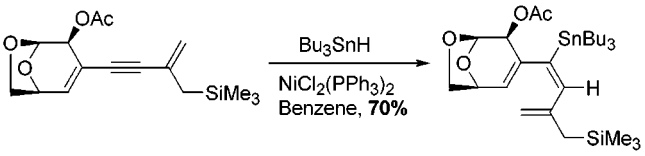


the palladium center and subsequent hydropalladation of the triple bond occurs to give an intermediate vinylpalladium(II) complex. Cyclization via carbopalladation of the double bond then occurs followed by reductive elimination to give the observed product. Reaction with tributyltin deuteride gives >90% deuterium incorporation into the (*E*)-vinyl proton.

In this study, phosphine-free sources of palladium [$Pd(OAc)_2$, $PdCl_2$, $Pd_2(dba)_3$] were found to generate higher yields of products compared to phosphine-containing palladium catalysts, a phenomenon also seen in the hydrostannylative−cyclization of 1,6-diynes (see section 2.5).

Examples of the use of the hydrostannation of enynes include Isobe's regio- and stereoselective nickel-catalyzed hydrostannation of a sterically congested dienyne in his study on the synthesis of (−)-tetrodotoxin (Scheme 20).[20]

Scheme 20

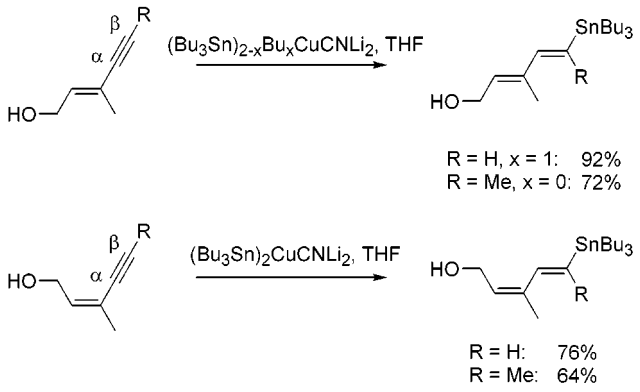


In summary, the Pd-catalyzed hydrostannation of substituted enynes generally leads to the α-addition product, although both Alami's and Pancrazi's studies illustrated that substrate chelation effects may alter the regioselectivity of addition.

In contrast, Pancrazi's comparative study illustrates that complementary *β*-regioselectivity may be obtained for a range of eneynols using stannylcupration conditions (Scheme 21).[7c]

Pancrazi also demonstrated that although hydrostannation of enynols under free-radical conditions leads to good *β*-regioselectivity, poor stereoselectivity was observed.

Scheme 21



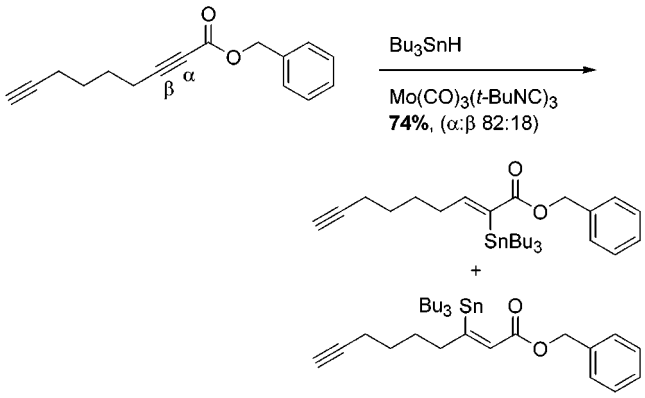
2.5. Hydrostannation of Diynes

Guibé examined the hydrostannation of conjugated diynes with catalytic $PdCl_2(PPh_3)_2$ in his extensive 1990 study.[18a] Although only three examples of this substrate class were described, some basic information on steric and electronic effects was apparent (Table 24).

Thus, an alkyl-substituted symmetrical diyne (entry 1) underwent α-regioselective hydrostannation at one of the alkynes to furnish the corresponding stannylenyne in 78% yield. Even on addition of further equivalents of hydride, no further hydrostannation of the remaining alkyne was observed—presumably due to steric constraints. With unsymmetrical terminal (entry 2) and silyl (entry 3) diynes, chemo- and regioselective hydrostannation was observed, again furnishing the α-addition product. As with Alami's hydrostannation of silyl−enediynes (section 2.4), Guibé suggested that the silicon substituent leads to deactivation of the proximal alkyne while polarizing the distal alkyne leading to both chemo- and regioselectivity.

Chemoselectivity may also be achieved by activating one diyne over another (as opposed to deactivating one) as demonstrated recently by Kazmaier et al.[18b] In a single example using $Mo(CO)_3(t\text{-BuNC})_3$, chemoselectivity was achieved in the hydrostannation of a diynoic ester (Scheme 22). As would be expected with an alkynyl ester (section 2.3), the regioselectivity was moderately high, favoring the α-addition product.

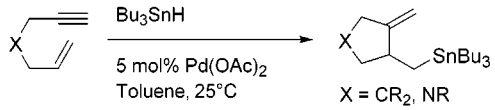
Scheme 22



As discussed in section 2.4, the hydrostannation of enediynes suggested that the presence of a second alkyne group, oriented properly, can exert a directing effect on the hydrostannation selectivity.[50] Further evidence for this directing effect was demonstrated by Lautens et al. in their application of the divergent reactivity of $Pd(OH)_2/C$ (when compared to palladium catalysts containing phosphine ligands) to the hydrostannation of 1,6-diynes.[17b] They found that upon treatment of a variety of terminal 1,6-diynes with Bu_3SnH in the presence of $Pd(OH)_2/C$, a hydrostannation/cyclization sequence occurred generating synthetically useful 1,2-bis(methylene)cyclopentanes containing a tributylstannyl moiety (Table 25).

A variety of heteroatoms were tolerated in the propargylic position including N, O, and S. In addition, a survey of catalysts demonstrated that phosphine-free systems including $Pd(OH)_2/C$, Pd/C, $Pd(OAc)_2$, and $Pd_2(dba)_3$ all gave excellent conversion to the cyclized product whereas $Pd_2(dba)_3$ in the presence of 1 or 2 equiv of PPh_3 led to a complex mixture consisting of nonregioselective hydrostannation of one or both of the alkynes. These observations were rationalized when considering the proposed mechanism in (Scheme 23).

Table 23. Hydrostannylative Cyclization of 1,6-Enynes



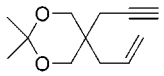
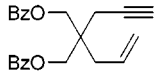
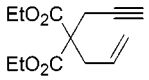
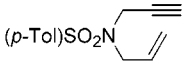
Substrate	Isolated Yield (%)
	61
	50
	67
	41

Table 24. Hydrostannation of Diynes

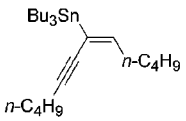
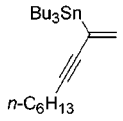
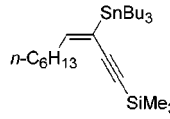
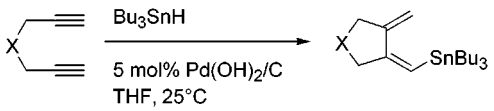
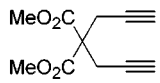
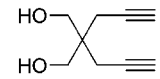
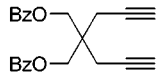
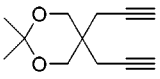
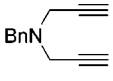
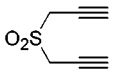
Entry	Substrate	Product	Isolated Yield (%)
1	$n\text{-}C_4H_9C{\equiv}C\text{-}C{\equiv}C\text{-}n\text{-}C_4H_9$		78
2	$n\text{-}C_6H_{13}C{\equiv}C\text{-}C{\equiv}C\text{-}H$		54
3	$n\text{-}C_6H_{13}C{\equiv}C\text{-}C{\equiv}C\text{-}SiMe_3$		86

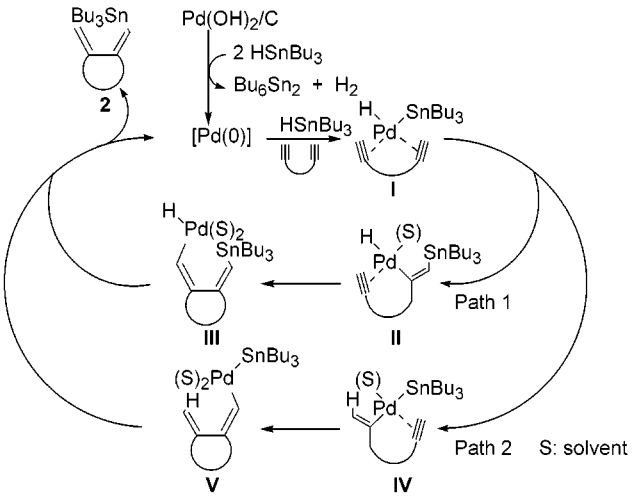
Table 25. Hydrostannylative-Cyclization of 1,6-Diynes



Substrate	Isolated Yield (%)
	95
	61
	60
	70
	85
	68
	58[a]
	77

[a] 9% mono-hydrostannated acyclic product also isolated.

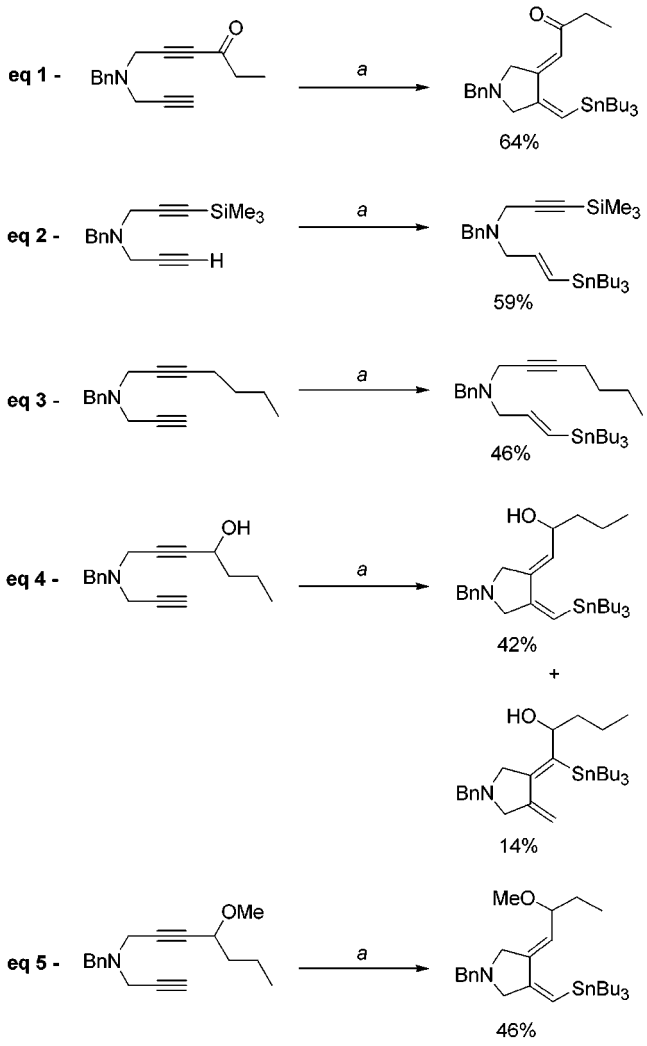
Scheme 23



Thus, in the absence of strongly coordinating phosphine ligands, a chelate **I** may form between the diyne and the Pd center. Upon stannylpalladation of one alkyne, coordination to the second alkyne is maintained (**II**), which upon carbopalladation (**III**) and reductive elimination furnishes the observed dienyl stannane **2**—effectively one alkyne is directing the hydrostannation of the second alkyne. Alternatively, a hydropalladation (**I** to **IV**), carbopalladation (**IV** to **V**), reductive elimination sequence (path 2) may occur.

Reaction with a variety of substituted diynes illustrates the profound effects that steric, electronic, and chelating factors exert on the reaction. As shown in Scheme 24,[52] an electronically activated alkynone

Scheme 24



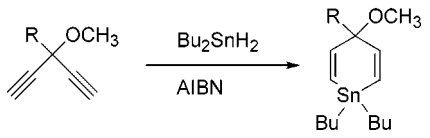
a: Bu_3SnH, $Pd(OH)_2/C$ (5 mol%), THF.

undergoes stannylative—cyclization efficiently (eq 1) whereas the analogous trimethylsilyl derivative containing an electronically and sterically deactivated alkyne does not (eq 2). Chelation as well as electronic factors may also be in effect as an *n*-butyl-substituted diyne undergoes simple hydrostannation as the major reaction pathway (eq 3) whereas the presence of a propargylic alcohol or ether once again furnishes the hydrostannation/cyclization product (eqs 4, 5).

In a related hydrostannation—cyclization reaction of 1,2-diynes under radical conditions, the use of dibutyltin hydride led to the formation of a stannacyclohexadiene (Scheme 25).[53]

In summary, good levels of chemoselectivity in the hydrostannation of diynes may be obtained via

Scheme 25



R = Ph, 68%, *c*-C_6H_{11}, 58%, *t*-Bu, 61%

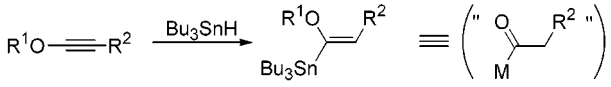
electronic and/or steric discrimination. Regioselectivities are also good, generally forming the α-addition product. Diyne chelation effects may be exploited via the use of phosphine-free palladium catalysts to perform a hydrostannation−cyclization reaction.

2.6. Hydrostannation of α-Heteroalkynes

2.6.1. Hydrostannation of α-Alkoxy Alkynes

α-Regioselective hydrostannation of alkoxyacetylenes **1** is of interest as it offers access to acylanion equivalent **3** (Scheme 26).

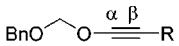
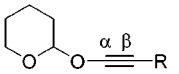
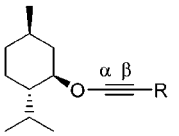
Scheme 26



1 **2** **3**

Although Guibé reported a single example of a hydrostannation of ethoxyacetylene in 1990 (α/β = 1/1, no yield given),[18a] Kocienski's comprehensive 1993 study demonstrated the scope of the reaction for this substrate class. Kocienski found that the regioselectivity of the $Pd(PPh_3)_4$-catalyzed hydrostannation of alkoxyalkynes was controlled predominantly by the steric bulk of the R^1 and R^2 substituents (Scheme 26) on the acetylene (Table 26).[54]

Table 26. Hydrostannation of α-Alkoxy Alkynes

Substrate	Entry	R	Yield (%)[a]	α : β[b]
	1	*n*-Bu	46	1.8 : 1
	2	*s*-Bu	57	5.1 : 1
	3	*t*-Bu	71	100 : 1
	4	*n*-Bu[c]	74	1.5 : 1
	5	*n*-Bu	28	1.2 : 1
	6	*s*-Bu	46	3.9 : 1
	7	*t*-Bu	51	13.8 : 1
	8	*n*-Bu[c]	81	1.1 : 1
	9	Me	23	1 : 3
	10	Me[c]	89	1 : 3

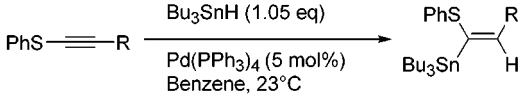
[a] Isolated by chromatography on basic alumina. β-isomer destroyed under these conditions. [b] Determined by ^{1}H-NMR after 30 min. [c] Me_3SnH used instead of Bu_3SnH.

Thus, when R had relatively low steric bulk (entries 1, 5), the bias in favor of the α-regioisomer was minimal. However, as the steric demand of R increased, so did the α-regioselectivity (entries 1−3, 5−7). Similarly, on increasing the steric demand of the alkoxy substituent, a reversal to β-regioselectivity was observed (entries 9, 10). Although Kocienski found that the resulting vinylstannanes were susceptible to protodestannylation during chromatographic purification, the greater lability of the β-regioisomer serendipitously allowed easy isolation of the desired α-regioisomer. Interestingly, the use of Me_3SnH led to derivatives that showed more resistance to protodestannylation furnishing higher yields of stannylated material (entries 4, 8, 10) as well as allowing isolation of the β-regioisomer.

2.6.2. Hydrostannation of α-Phenylthio, Phenylseleno Alkynes

In 1991, Magriotis reported that the hydrostannation of phenylthioalkynes with catalytic $Pd(PPh_3)_4$ was highly regio- and stereoselective, furnishing the α-regioisomer for a range of substrates (Table 27).[55]

Table 27. Hydrostannation of α-Phenylthio Alkynes



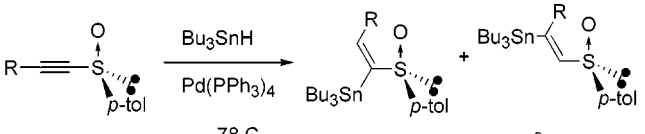
Entry	R	Yield (%)[a]
1	H	87
2	Me	79[b]
3	Ph	75[b]
4	CH_2OH	84
5	CH_2OTBS	90
6	$CH(OH)CH_2OTBS$	80
7	$C(O)CH_2OTBS$	88
8	$SiMe_3$	85

[a]Isolated yield. [b]Regioselectivity α/β=19/1

Thus, irrespective of steric (entries 1, 2, 3, 6), electronic (entries 3, 7, 8), or chelation (entries 2, 4, 6) considerations, sulfur-induced polarization of the alkyne led to the α-regioisomer. Later in 1992, Kocienski illustrated the use of α-phenylthiovinyl stannanes as potential a^1d^1 (acceptor/donator) synthons in Pd(0)-catalyzed couplings of the corresponding alkenylzincs.[56]

Similar levels of α-regioselectivity were observed by Paley in his low-temperature hydrostannation of chiral alkynyl sulfoxides (Scheme 27).[57]

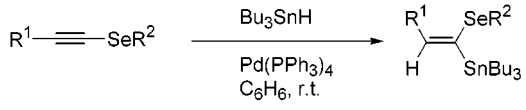
Scheme 27



R = Bu, 86%, (α:β 40:1)
R = $(CH_2)_4OPMB$, 83%, α-only

In 1997, Ma demonstrated that α-selenoalkynes also undergo α-regioselective hydrostannation with $Pd(PPh_3)_4$, again presumably due to polarization of the alkyne by selenium (Table 28).[58]

Table 28. Hydrostannation of α-Alkynyl Selenides

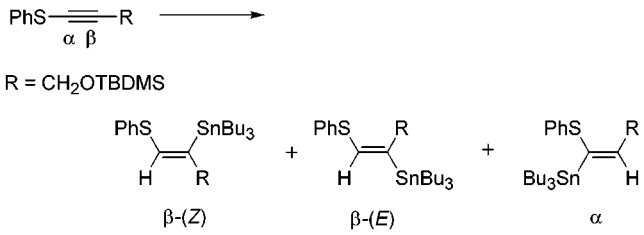


R^1	R^2	Yield (%)[a]
CH_3OCH_2	Me	76[b]
CH_3OCH_2	Ph	73[c]
Ph	Ph	68
Ph	Et	65
Ph	Me	70

[a] Isolated yield. [b] Proton NMR ratio α:β 98:2. [c] Proton NMR ratio α:β 95:5.

In comparison to Pd(0)-catalyzed hydrostannation of thioalkynes, Magriotis showed that although radical stannylation gave formation of the *β*-regioisomer, the stereoselectivity was poor (Table 29).[55,59] Stannylcupration was found to give moderate yields of the α-regioisomer but with some loss of stereoselectivity.

Table 29. Formation of α-Thioalkenyl Stannanes via Various Hydrostannation Methods



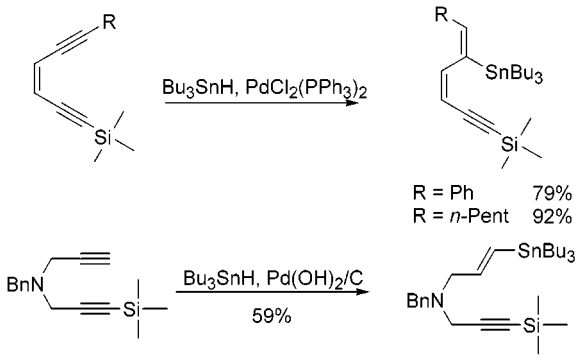
Conditions	Yield (%)[a]	β-(*Z*)	β-(*E*)	α
1.05 eq. Bu_3SnH, 5 mol% $Pd(PPh_3)_4$, 23°C	90	---	---	>99[b]
1.3 eq. Bu_3SnH, AIBN, 95°C	---[c]	17	83	---
2 eq. $Bu_3Sn(Bu)CuCNLi_2$, THF, -50°C	65	---[d]	---[d]	---[d]

[a] Isolated yields. [b] *Cis*-addition product only. Trace amount of β-isomers detected by GC and NMR. [c] Not reported. [d] α-addition major product with 10:1 E:Z ratio. *Cis*-alkene also isolated in 15% yield.

2.6.3. Hydrostannation of α-Trimethylsilyl Alkynes

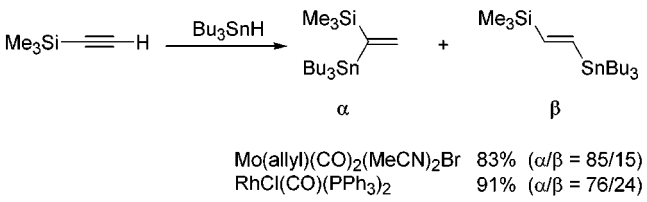
In 1987, Oshima reported a $Pd(PPh_3)_4$-catalyzed, *β*-regiospecific hydrostannation of trimethylsilylacetylene with Ph_3SnH.[27] However, subsequent groups have reported a deactivating effect of silicon with α-substituted alkynes.[18a] This deactivating effect was clearly illustrated by chemoselective hydrostannation of unsymmetrical diynes in both Alami's and Lautens' studies (Scheme 28).[50,17b] However, α-regioselective

Scheme 28



hydrostannation of silylalkynes may be achieved via the use of Mo[18a] or Rh[19] catalysis (Scheme 29).

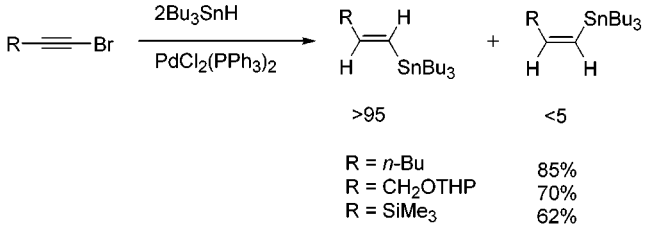
Scheme 29



2.6.4. Hydrostannation of α-Haloalkynes

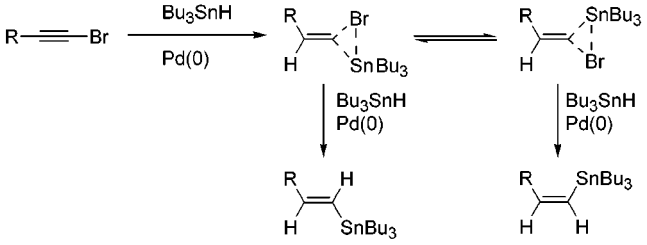
Of synthetic value for the regio- and stereocontrolled synthesis of disubstituted (*E*)-vinyl stannanes, Guibé found that the hydrostannation of 1-bromoalk-1-yne with 2 equiv of tributyltin hydride led to selective formation of the corresponding (*E*)-1-(tributylstannyl)alkenes with only trace amounts of the (*Z*)-isomer (Scheme 30).[18a]

Scheme 30



Guibé proposed that the first equivalent of hydride adds to the acetylene to regioselectively form an alkylidene carbenoid intermediate, which undergoes palladium-catalyzed C−Br cleavage by a second mole of hydride (Scheme 31). The formation of small

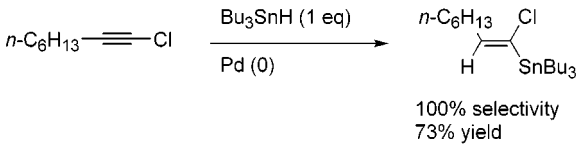
Scheme 31



quantities of the (*Z*)-isomer is believed to be due to the configurational lability of the carbenoid intermediate.

Support for this proposed mechanism came from the isolation of 1-chloro-1-(tributylstannyl)- oct-1-ene from the α-regioselective hydrostannation of 1-chloro-oct-1-yne (Scheme 32). In this case, no reduction of

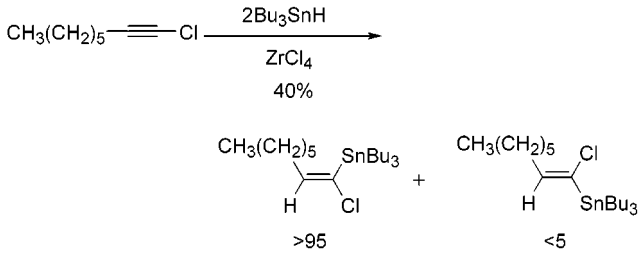
Scheme 32



the vinyl chloride was observed upon the addition of further equivalents of hydride.

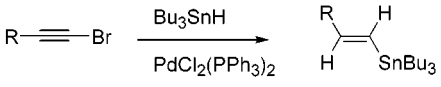
Synthesis of the corresponding (*Z*)-vinyl stannane may be achieved using Yamamoto's $ZrCl_4/Bu_3SnH$ system as shown in Scheme 33.[29]

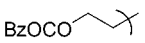
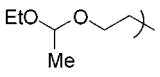
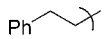
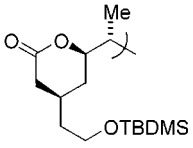
Scheme 33



Pattenden further extended the scope of Guibé's observations by illustrating that a variety of substrates underwent the hydrostannation−reduction sequence giving good yields and selectivities for the desired (*E*)-isomer (Table 30).[60]

Table 30. Hydrostannation of α-Bromoalkynes



R	Yield (%)[a]
	78
	80
	74
	82
	70

[a] *E*:*Z* > 95:5 in all cases

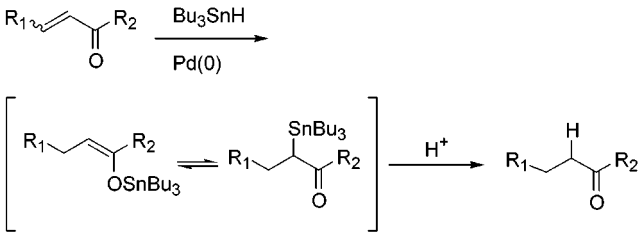
In summary, the polarization of the alkyne bond by an α-thio, seleno, or halo substituent leads to good α-regioselectivity during the hydrostannation. In the case of α-bromo alkynes, in-situ reduction allows access to (*E*)-vinyl stannanes providing a convenient alternative to the radical addition of $Bu_3Sn^•$ to a terminal alkyne.

The regioselectivity of hydrostannation of alkoxyalkynes was found to be predominantly controlled by steric considerations; however, the vinyl stannane products were susceptible to proto-destannylation during purification. A silicon substituent was found to deactivate alkynes toward Pd(0) catalysis, although hydrostannation could be effected with Mo or Rh catalysis.

3. Hydrostannation of Alkenes

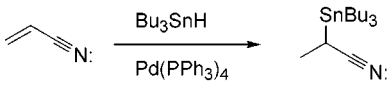
Although the hydrostannation of alkynes has been widely studied, there has been relatively little research on the hydrostannation of alkenes. The first examples were reported in 1982 by Keinan and Gleize[61] and Guibé and Four[62] in studies on the palladium-catalyzed conjugate reduction of α,*β*-unsaturated carbonyl compounds with Bu_3SnH. Keinan proposed that palladium-catalyzed hydrostannation occurs to give an enol stannane intermediate, which decomposes in the presence of a proton donor (i.e., during workup) to give the reduced carbonyl compounds (Scheme 34).[61]

Scheme 34



As proof of this mechanism, Guibé treated the crude conjugate reduction material of cyclohexenone with allyl bromide and obtained the mono-*C*-allylated product. In addition, isolation of α-tributyltin proprionitrile was possible upon treatment of acrylonitrile with Bu_3SnH in the presence of a Pd catalyst (Scheme 35).[62]

Scheme 35



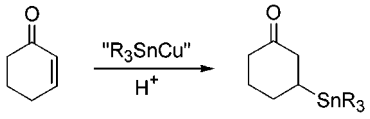
α-Enones that bear two or more substituents on the alkene are not reduced in acceptable yields. The use of anhydrous $ZnCl_2$ as a co-activating agent overcame this limitation and broadened the scope of the reaction, allowing reduction of carvone and other substituted species.

In contrast to palladium-catalyzed alkene hydrostannation, radical conditions are known to favor isomeric *β*-trialkylstannyl derivatives. Stannylcupration of α,*β*-unsaturated ketones is a good method for the regioselective *β*-addition of the tin moiety with to this substrate class (Scheme 36[63]).[37]

Stereoselective addition occurs if one face of the alkene is blocked by a nearby substituent.[64,65]

Radical stannylation of the activated alkene of alkynyl esters also leads to regioselective *β*-addition

Scheme 36



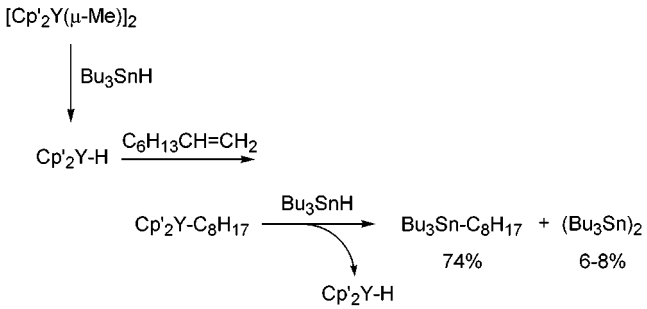
of the tin moiety with stereoselectivity again controlled by steric factors.[5a,66]

In a later study, Miyake reported on the hydrostannation of dienes using $Pd(PPh_3)_4$ as a way of generating synthetically useful allyl stannanes.[67]

With the exception of 1,3-pentadiene, the conjugate–addition was stereo-and regioselective. The stereoselectivity is believed to be due to a s-*cis*-coordination of the diene to the Pd(0) center. In addition, steric factors were found to be important since hindered dienes such as 2,3-dimethyl-1,3-butadiene and 1,3-cyclooctadiene could not be hydrostannated under these conditions. Miyake and Yamamura investigated further the mechanism using tri(*n*-butyl)tin deuteride and found that the intermediate π-allyl palladium complex plays an important role in determining the regioselectivity of the reaction.[68]

In 1995, Voskoboynikov and Beletskaya reported the use of a yttrium hydrocarbyl ($[Cp_2Y(\mu\text{-Me})]_2$) to hydrostannate 1-octene and obtained the linear isomer in 74% yield.[69] The reaction was found to proceed at room temperature using approximately 4 mol % of the hydrocarbyl. The mechanism was believed to involve conversion of the hydrocarbyl to the hydride in situ, followed by hydroyttration of the double bond and then transmetalation to the organostannane (Scheme 37).

Scheme 37



As part of continuing work on the utility of oxabicyclic compounds in the generation of highly functionalized and synthetically useful cycloalkenols, Lautens and Klute reported the palladium-catalyzed hydrostannation of oxa- and azabicyclo[3.2.1]alkenes (Scheme 38).[70]

Scheme 38

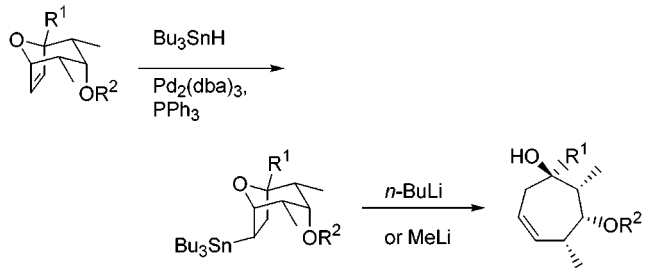
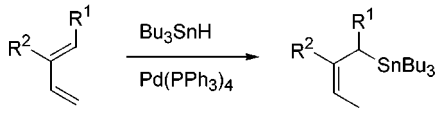


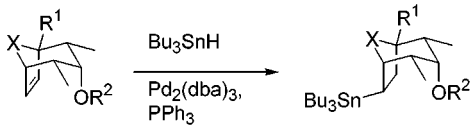
Table 31. Hydrostannation of 1,3-Dienes



R^1	R^2	Yield (%)[a]	*E*	*Z*
H	H	91	0	100
H	Me	61	0	100
Me	H	45	36	64
H	OAc	72	100	0

[a] Isolated by column chromatography. Yields are based on conversion of Bu_3SnH

Table 32. Hydrostannation of Oxa- and Azabicycles



X	R^1	R^2	Yield (%)[a]
O	Me	H	80
O	Me	TBS	97
O	Me	Me	88
O	CH_2OH	Me	62
O	CH_2OTBS	Me	98
O	CONHBn	H	61
NBn	H	H	77

[a] Isolated yields - in all cases selectivity was greater or equal to 97:3 by ^{1}H-NMR

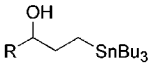
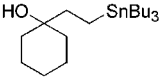
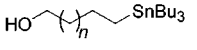
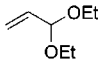
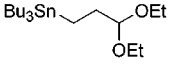
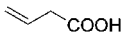
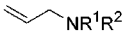
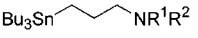
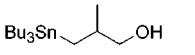
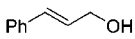
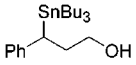
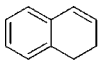
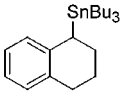
As can be seen from the results in Table 32, a wide variety of strained alkenes undergo stereo- and regioselective hydrostannation furnishing tetraalkylstannanes with the tin moiety placed on the least sterically hindered carbon in an *exo* fashion.

The mechanism is proposed to involve a hydropalladation of the alkene moiety followed by reductive elimination of the palladium to generate the tetraalkylstannane. Upon treatment with MeLi or *n*-BuLi, either the pentavalent stannate or the transmetalated lithioalkane is formed, which undergoes elimination, generating the desired cycloalkenols

Early examples of homogeneous palladium-catalyzed hydrostannations were carried out on *activated* alkenes. The use of catalytic systems to hydrostannate unactivated alkenes had not been reported due to the ease of decomposition of tin hydride and the inefficiency of the reaction with an alkene. In 1996, Lautens, Kumanovic, and Meyer showed that a catalyst based on $Pd(OH)_2/C$ efficiently hydrostannated unactivated alkenes.[17a]

As illustrated in Table 33, a wide variety of alkene systems, including those containing secondary and tertiary alcohols, may be regioselectively hydrostannated using $Pd(OH)_2/C$ furnishing the corresponding tetraalkylstannanes in good to excellent yields. Ter-

Table 33. Hydrostannation of Various Alkenes with $Pd(OH)_2/C$

Entry	Alkene	Product	Yield (%)[a]
1			R = Ph, 96 R = 2-furyl, 92
2			94
3			n = 1, 91 n = 8, 80
4			85
5			78
6			R^1 = H, R^2 = CO_2tBu, 89 R^1 = H, R^2 = Bn, 81 R^1 = R^2 = Bn, 80 R^1 = H, R^2 = COPh, 88
7			90
8			X = CN, 84 X = *N*-pthaloyl, 60
9			94
10			90

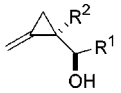
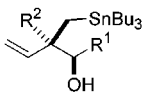
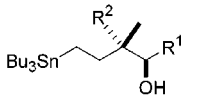
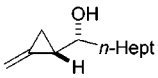
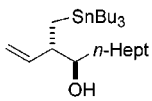
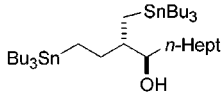
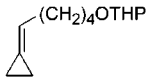
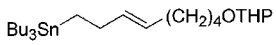
[a] Isolated yields - conditions: 1.5 equivalents Bu_3SnH, 10 mol% $Pd(OH)_2/C$, THF r.t., 1h.

minal alkenes (entries 1−8) are regioselectively hydrostannated with the tin moiety placed at the terminus regardless of the steric environment or proximity of heteroatoms. Styrene derivatives (entries 9 and 10) are also regioselectively hydrostannated with the tin moiety placed in the benzylic position. For acrylonitrile (entry 8), it was previously shown that under homogeneous catalysis conditions, the α-addition product was obtained (Scheme 35), thus suggesting that catalysis by $Pd(OH)_2/C$ follows a similar polar pathway to $Pd(PPh_3)_4$.

The divergent reactivity of $Pd(OH)_2/C$ compared to $Pd(PPh_3)_4$ was further illustrated in 1996 when Lautens, Lorenz, and Meyer reported on their investigations on the ring-opening−hydrostannation of methylenecyclopropanes (Table 34).[26]

Thus, it was found that upon treatment of a methylenecyclopropane with 1.5 equiv of Bu_3SnH in the presence of $Pd(PPh_3)_4$, a hydrostannation−ring-opening sequence occurred furnishing homoallylstannanes **1** in good yields. However, the same reaction carried out in the presence of $Pd(OH)_2/C$ led to a mixture of the homoallylstannane **1** and the diorganostannane **2** as a result of a double hydrostannation. This phenomenon was found only to occur under "heterogeneous" conditions. Exclusive formation of the diorganostannane could be achieved by increasing

Table 34. Hydrostannation of Methylenecyclopropanes Using $Pd(PPh_3)_4$ and $Pd(OH)_2/C$

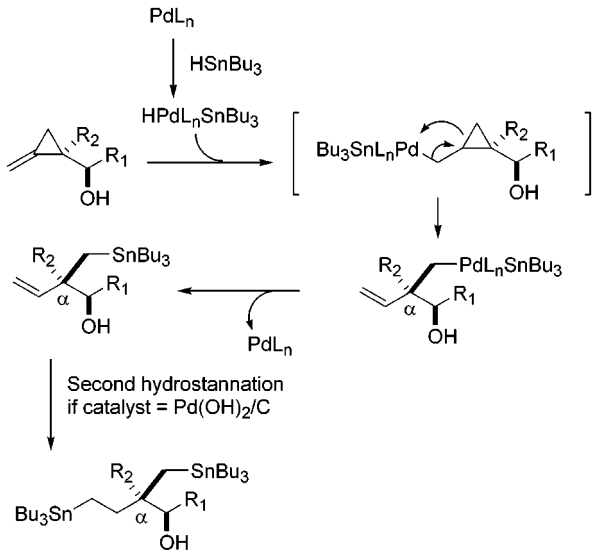
Substrate		Product[a]	
		$Pd(PPh_3)_4$[b]	$Pd(OH)_2/C$[b]
			
R^1	R^2	Yield (%)	Yield (%)
Ph	H	68, **1a**	64, **2a**
c-Hex	H	65, **1b**	62, **2b**
n-Hept	H	67, **1c**	59, **2c**
c-Hex	Me	90, **1d**	85, **2d**
c-Hex	OMe	not isolated	61, **2e**
			
		58, **1f**	60, **2f**
			
		87	76

[a] Bu_3SnH (1.5 eq. or 3 eq.) was added over 1 or 1.5 h to 0.1M solution of the substrate in THF containing $Pd(PPh_3)_4$ (3 to 5 mol%) or $Pd(OH)_2/C$ (3 to 5 mol%). [b] Isolated yields of analytical pure products.

the amount of tin hydride to 3 equiv. As seen with unactivated alkenes, the hydrostannation is regioselective, placing the tin moiety at the terminus. For methylenecyclopropanes bearing substituents on the double bond, the (*E*)-homoallylstannane **3** was isolated regardless of the catalytic system.

The mechanism is believed to proceed as depicted in Scheme 39. Oxidative addition of palladium into

Scheme 39



the tin−hydrogen bond of tributyltin hydride generates a stannylpalladium hydride species which hy-

dropalladates the methylenecyclopropane, forming a (cyclopropylmethyl)palladostannane. This species undergoes a highly regioselective ring-opening reaction to generate a primary homoallylpalladostannane. Reductive elimination of the palladium occurs to generate the homoallyl stannane. No loss of stereochemical information at the α stereocenter is observed, suggesting that the homoallylpalladium species does not *β*-eliminate to generate the diene and then re-add palladium hydride.

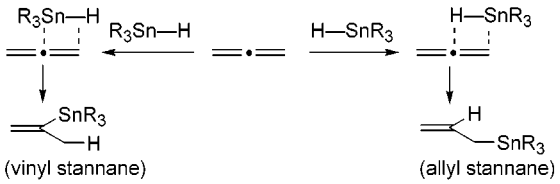
The reaction stops at this stage when a homogeneous catalyst such as $Pd(PPh_3)_4$ is used, and excess hydride disproportionates to Bu_6Sn_2 and H_2. In the presence of a heterogeneous catalyst, such as $Pd(OH)_2/C$, further hydrostannation of the vinyl moiety can occur to give the distannane. In general, the metal-catalyzed hydrostannation of a terminal alkene leads to introduction of the tin to the terminal position. The internal position is favored when the alkene is adjacent to a heteroatom or a strongly electron-withdrawing group (e.g., nitrile, ester).[62]

Although heterogeneous catalysis using $Pd(OH)_2/C$ is ideal for the hydrostannation of activated and inactivated alkenes, it is not amenable to effecting asymmetric induction. This factor becomes especially important in the cases where branched products predominate. The development of an enantioselective hydrostannation has not yet been achieved but remains a subject of interest.

4. Hydrostannation of Allenes

Vinylstannanes and allylstannanes have a variety of uses in organic synthesis, and routes to access these compounds are an area of continuing interest. The two modes by which hydrostannation of an allene can occur would provide a novel route to either or both of these moieties. Addition of tin to the central sp-hybridized carbon leads to the formation of a vinyl stannane, while addition to the terminal sp^2-hybridized carbon gives an allyl stannane (Scheme 40).

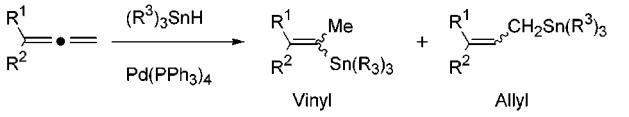
Scheme 40

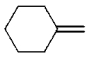


Oshima was the first to report on the hydrostannation of allenes using $Pd(PPh_3)_4$ as catalyst in 1988. He obtained selective formation of allyl stannanes but the range of substrates examined was limited.[71] The mechanism proposed involved the stannylpalladation of the allene, with the palladium binding to the central carbon and the tin moiety to the terminal carbon. Subsequent studies by Mitchell explored the effect substitutents and heteroatoms had on the regio- and stereochemistry (Table 35).[72]

For example, Mitchell observed regioselective addition of the tin moiety to the terminal carbon of the allene resulting in the formation of the corresponding allyl stannane in preference to the vinyl stannane (regioselectivity typically >7:1) in analogy with Oshima. However, the stereoselectivity was poor with the *E*/*Z* ratio of the allyl stannane varying considerably with substrate.

Table 35. Hydrostannation of Allenes Using $Pd(PPh_3)_4$

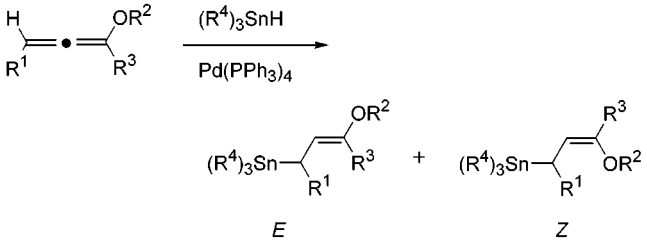


			Yield[a]		
R^1	R^2	R^3	Vinyl (*E*:*Z*)	Allyl (*E*:*Z*)	Reference
H	H	Ph	---	40%[b]	71
n-Bu	H	Me	10%, (2 : 1)	71%, (1 : 1.6)	72
Ph	H	Me	2%, (*E*) only	67%, (6.4 : 1)	72
c-Hex	H	Me	5%, 1 : 1	57%, (1 : 2.3)	72
MeO	H	Me	9%, (*E*) only	68%, (1 : 6.4)	72
		Me	---	76%	72

[a] Yields and ratios determined by GLC and ^{119}Sn-NMR. [b] Yield based on amount of Ph_3SnH used and product isolated by preparative TLC on silica gel.

Goré also reported the $Pd(PPh_3)_4$-catalyzed hydrostannation of alkoxyallenes leading to the regiospecific formation of alkoxyallyl stannanes (Table 36)—potentially versatile acyl anion equivalents.[73]

Table 36. Hydrostannation of Alkoxy Allenes

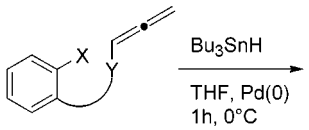


R^1	R^2	R^3	R^4	Yield (*E*:*Z*)[a]
H	Me	H	*n*-Bu	72%, (25 : 75)
H	Me	H	Ph	72%, (9 : 91)
H	*t*-BuMe$_2$Si	H	*n*-Bu	70%, (23 : 87)
H	Me	*n*-Bu	*n*-Bu	45%, (55 : 45)[b]
H	Me	SMe	*n*-Bu	52%, (53 : 47)[b]
H	Me	SiMe$_3$	*n*-Bu	82%, (0 : 100)
n-Bu	Et	H	*n*-Bu	41%, (45 : 55)
H	Me	H	*n*-Bu	52%, (8 : 92)[c]

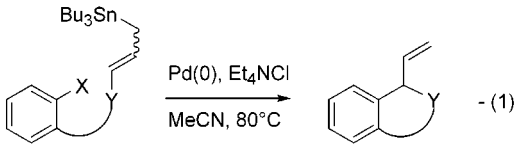
[a] Isolated yield after column chromatography. [b] Geometry of the double bond of each isomer was not determined. [c] $Mo(CO)_6$ was used as catalyst.

The tin moeity was again found to favor addition to the terminal carbon to produce allyl stannanes but with poor diastereoselectivity. However, with sterically bulky substituents (e.g., TBDMS) proximal to the oxygen, good selectivity for the (*Z*)-isomer was obtained.

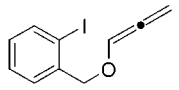
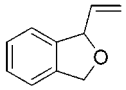
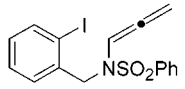
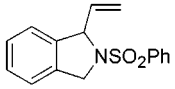
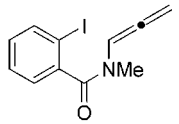
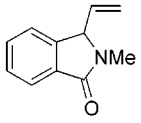
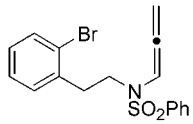
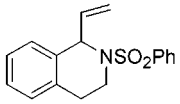
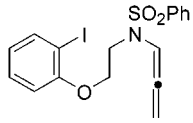
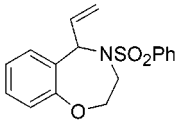
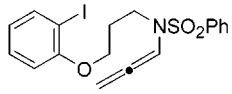
Table 37. Tandem Allene Hydrostannation/ Palladium-Catalyzed Cyclization



X = I, Br
Y = O, NSO_2Ph



- (1)

Entry	Substrate	Time	Product	Yield(%)[a]
1		1		85[b]
2		1		66
3		1		72
4		4		52
5		3[c]		50
6		4-8	—	—

[a]Isolated yields. [b]Yield of crude material. Product decomposes on silica. [c]Concentration was ca. 0.05M maintaining the concentration of $Et_4NCl.H_2O$ at 0.15M

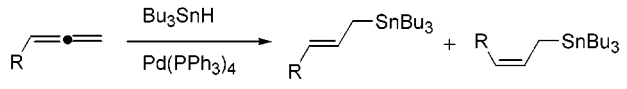
Despite its lower reactivity, $Mo(CO)_6$ is effective as a catalyst and gave good regio- and stereoselectivity, favoring the (*Z*)-isomer.

An example of the application of the hydrostannation of alkoxy allenes to the synthesis of spirocyclic rings was reported by Grigg in 1997 in which a "one-pot" hydrostannation−cyclization sequence was reported (Table 37).[74]

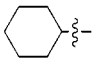
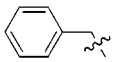
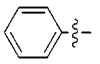
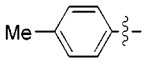
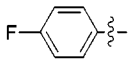
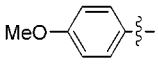
As with Goré's study, Grigg reported regiospecific formation of an allylstannane intermediate, but contrary to Goré's observed (*Z*)-alkene stereoselectivity with alkoxyallenes, Grigg reported (*E*)-alkene stereoselectivity of the intermediate allyl stannane when aza allenes (entries 2−5) were used.

Grigg's one-pot methodology successfully gave good yields of five−seven-membered heterocycles (entries 1−5); however, attempted cyclization to form an eight-membered ring was unsuccessful (entry 6).

Table 38. Hydrostannation of Alkyl and Aryl Allenes



E *Z*

R	Yield (%)[a]	(*E*:*Z*)[b]
C_8H_{17}	78[c]	33 : 67
	52[c]	18 : 82
	66[c]	38 : 62
	60	>95 : 5
	62	>95 : 5
	77	>95 : 5
	75	>95 : 5
MeO	69[d]	19 : 81
TIPSO	73[d]	29 : 71

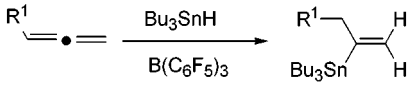
[a] Isolated yield. [b] Determined by 270MHz proton NMR, ratios were not dependent on reaction temperatures. [c] Isolated as mixtures of *E*- and *Z*-isomers. [d] Readily separated by silica gel chromatography.

In 1997, Yamamoto described the hydrostannation of aryl- and alkyl-substituted allenes in the presence of a Lewis acid $[B(C_6F_5)_3]$ or transition-metal $[Pd(PPh_3)_4]$ catalyst.[25]

As shown in Table 38, alkyl allenes undergo regioselective hydrostannation to generate the corresponding allyl stannane as a mixture of stereoisomers. However, Yamamoto demonstrated that variously substituted aryl allenes give very high stereoselectivities producing the (*E*)-isomer in excellent yields. The reaction was concluded to be under kinetic control as the isomeric ratios did not vary with temperature.

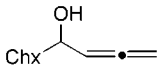
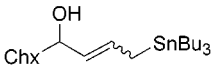
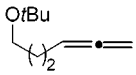
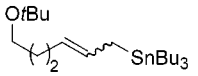
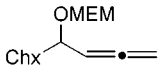
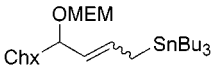
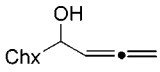
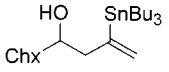
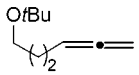
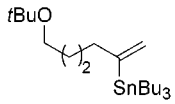
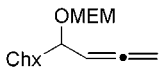
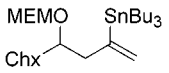
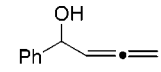
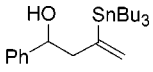
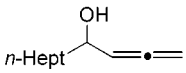
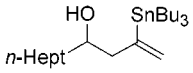
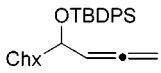
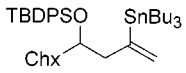
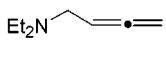
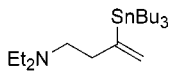
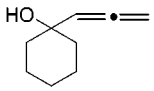
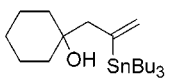
In a complementary fashion, Yamamoto found that the use of $B(C_6F_5)_3$ gave internal addition of the tin moiety producing vinyl stannanes (Scheme 41).

Scheme 41



In 1997, Lautens, Ostrovsky, and Tao showed the importance of the catalyst in influencing the reaction pathway. For example, the use of $Pd(OH)_2/C$ as a catalyst for the regioselective generation of vinyl stannanes from alkyl-substituted allenes was achieved (Table 39).[75] In a comparative study using $Pd(PPh_3)_4$

Table 39. Hydrostannation of Various Allenes with $Pd(PPh_3)_4$ and $Pd(OH)_2/C$

Entry	Substrate	Catalyst	Product	Yield (E:Z)[a]
1		$Pd(PPh_3)_4$		55%, 1 : 1
2		$Pd(PPh_3)_4$		67%, 1 : 1
3		$Pd(PPh_3)_4$		56%, 1 : 1
4		$Pd(OH)_2/C$		57%
5		$Pd(OH)_2/C$		67%
6		$Pd(OH)_2/C$		57%
7		$Pd(OH)_2/C$		58%
8		$Pd(OH)_2/C$		57%
9		$Pd(OH)_2/C$		55%
10		$Pd(OH)_2/C$		41%
11		$Pd(OH)_2/C$		42%

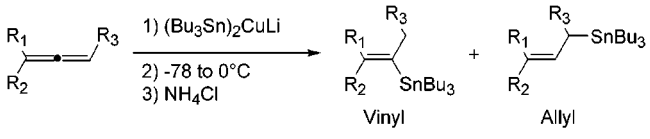
[a]Isolated yields. Starting materials treated with 1.5 equivalents Bu_3SnH and 5mol% Pd catalyst.

and $Pd(OH)_2/C$, Lautens showed the complementary reactivity between the two palladium sources. $Pd(PPh_3)_4$ gave, as previously reported, the allyl stannane as a mixture of geometric isomers and $Pd(OH)_2/C$ gave only the vinyl stannane. In comparison to Mitchell's study using $Pd(PPh_3)_4$ and Me_3SnH, the formation of small amounts of vinyl stannanes was not observed. Hydrostannation of the allenols was found to proceed regardless of the steric bulk of the protecting group (i.e., TBDPS) or the presence of chelating groups (i.e., MEM). The nature of the R group on the alkyl chain did not have any significant effect. An allenylamine also underwent hydrostannation.

As can be seen from Table 39, good conversion to the vinyl stannane is observed for a range of substrates including aryl and alkyl allenols (entries 4,7,8), protected allenols (entries 5,6,9), and allenylamines (entry 10).

In comparison to metal-catalyzed hydrostannations, Barbero demonstrated that good regioselectivities may be obtained in the stannylcupration of alkyl allenes leading to the allyl stannane.[7] Aryl allenes predominantly led to the vinyl stannane via internal addition (Scheme 42).

Scheme 42



$R_1 = R_2 = Me, R_3 = H$		99%
$R_1 = Ph, R_2 = R_3 = H$	91%	
$R_1 = Me, R_2 = H, R_3 = Ph$	89%	

While good selectivities are observed with palladium-catalyzed hydrostannation and stannyl-

cupration, radical stannylation of allenes often leads to a multitude of products.[72]

The use of $Pd(OH)_2/C$ is ideal for the selective generation of a (*E*)-vinyl stannane from an allene. Although the use of $Pd(PPh_3)_4$ is optimal for generation of allyl stannanes, stereoselectivity remains an issue and only aryl allenes show high selectivity for the (*E*)-isomer. This remains an area for further development.

5. Conclusions

Transition-metal-catalyzed hydrostannation of alkynes continues to be a widely used method of accessing vinyl stannanes—useful intermediates in a variety of synthetic manipulations. The reaction occurs via stereospecific syn addition of tin hydride with the regiochemistry, in general, controlled by substrate steric considerations. Notable exceptions to this general steric control are the α-regioselectivities obtained with substituted phenylacetylenes, alkynyl esters, enynes, and phenylthioalkynes. In addition, recently developed catalyst systems such as $Mo(CO)_3(t\text{-BuNC})_3$ have demonstrated good levels of α-regioselectivity across a range of substrate classes.

Although less widely utilized, hydrostannation of allenes allows access to both allyl- and vinylstannanes by the use of 'traditional' homogeneous or Pearlman catalysts, respectively. Further, the recent application of Pearlman's catalyst has allowed for the first time the hydrostannation of unactivated alkenes.

In comparison to metal-catalyzed hydrosilation, hydroboration, and hydroalumination, hydrostannation is clearly a much less investigated reaction. The synthetic utility of vinyl and allyl stannanes suggest further studies are warranted and will yield additional surprises and opportunities for synthetic chemists.

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