Addition of Metalloid Hydrides to Alkynes: Hydrometallation with Boron, Silicon, and Tin

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Abstract: This review covers the synthesis of isolabile vinylmetalloids through hydroboration, hydrosilylation, and hydrostannation, with special focus on recent developments, metal-catalyzed reactions, and synthetically useful methods.

Key words: hydroboration, hydrostannation, hydrosilylation, alkyne, organometallic reagent

1 Introduction

The selective synthesis of vinylmetal species plays a key role in organic synthesis due to the importance of vinylmetal intermediates in a wide range of applications. Hydrometallation is possibly the most straightforward, atom economical route to a wide range of vinylmetal intermediates. The demands placed by the need to access vinylmetals of many differing substitution patterns, stereochemistries, and functional groups requires a diverse, complementary set of methodologies.

Among vinylmetals, boron, silicon, and tin play a unique role primarily due to their significant stability and functional group tolerance. These vinylmetals function in oxidation and reduction (protodemetallation) reactions, as traditional nucleophiles, and as stereocontrol elements. Their broad application in palladium-catalyzed cross-coupling reactions ensures their status as important intermediates in synthesis. The metalloids boron, silicon, and tin allow for the mild coupling with diverse electrophiles in the presence of sensitive functionality of all kinds.

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This review covers hydrometallation reactions of the metalloids boron,[1–3] silicon,[4,5] and tin.[6] Our focus is equally the mechanistic understanding of these reactions and the synthetic utility of hydrometallation with these metals. At least some aspect of hydrometallation has been previously reviewed for all three metalloids.[1,2,4,6] However, hydrometallation by these metalloid hydrides is an active field, and important new synthetic and mechanistic developments have occurred in recent years that necessitate a new presentation. Furthermore, we feel that this presentation is particularly instructive. Mechanistically, the metalloid hydrides share much in common, and unique mechanistic proposals for reactions of one metalloid can impact our understanding of other processes. Additionally, synthetic chemists often require stable vinylmetalloid species and must make informed decisions about the relative merits of strategies built around different metals. We hope that this text simplifies the process of choosing vinylmetalloid species for use in synthetic applications of all types.

The review is organized by metalloid, first discussing mechanistic aspects of each in turn. Next, we cover hydrometallation of terminal alkynes, followed by reactions with internal alkynes. Since addition of a hydrometallation reagent to the same face of a triple bond (cis addition process) often results in the formation of the *E*-olefin product (trans olefin), to minimize confusion throughout this review we will use *E*/*Z* nomenclature to describe product stereochemistry and reserve the terms cis and trans to describe the orientation of the hydrogen and metalloid groups in the addition process.

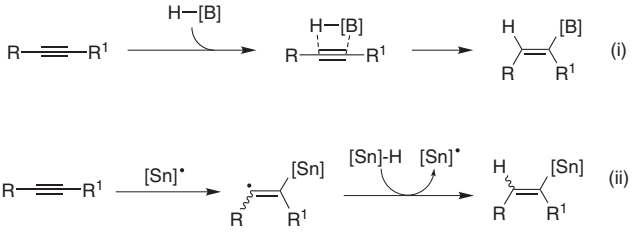
The formation of vinylmetals from alkynes is possible by other means, such as the synthetically important and useful silylcupration[7] and stannylcupration[8,9] of alkynes followed by cuprate protonation to afford vinylsilanes and vinylstannanes, respectively. These reactions provide products that can be complementary in nature to direct hydrometallation. Terminal vinylboranes are also accessible through the mechanistically related and synthetically similar dehydrogenative borylation of olefins.[10]

Heteroatom-substituted alkynes (i.e. alkoxy alkynes, thio alkynes) have also been used in hydrometallation reactions.[2,6] However, the factors important to these polarized triple bonds are significantly different from those of carbon-substituted cases, and the products are chemically quite different from simple vinylmetal species. These compounds are generally outside the scope of this review. Nonetheless, silyl and halide alkyne substituents are im-

portant and readily removable directing groups in hydrometallation reactions and are included where they have been shown to afford unique product selectivities.

2 Mechanistic Aspects of Hydrometallation

Hydrometallation occurs through a number of reaction types. Highly reactive hydrometallation reagents will react directly with alkynes through a four-centered transition state (shown for hydroboration in Scheme 1, i). Regiochemistry is determined in most cases by steric factors, though significant electronic factors exist as well. Uncatalyzed reactions are exclusively cis addition processes, though isomerization of the product is possible. Hydrozirconation[11] and hydroalumination[12] are synthetically useful reactions which react largely by this mechanism, resulting in an initial cis addition. In the case of aluminum, the initial olefin configuration may isomerize under the reaction conditions, resulting in clean trans addition products for substrates such as propargylic alcohols. Hydroboration, however, is the most important example of direct alkyne hydrometallation and is a mainstay in organic synthesis.[1,3] Hydrometallation can also proceed under radical conditions (shown for hydrostannation in Scheme 1, ii). In this case, initial regiochemistry is determined by the stability of the intermediate vinyl radical, and stereochemistry by the final hydrogen-atom abstraction step. In general, the products observed in radical hydrostannation often reflect thermodynamic rather than kinetic selectivities due to reversibility and product isomerization through addition–elimination reactions.



Scheme 1 Alkyne hydrometallation without metal catalysts.

Catalysis of the hydrometallation reaction by metal catalysts allows reaction with metalloid hydrides that do not typically react with alkynes, such as silanes. It also offers

Biographical Sketches

Born in Philadelphia, PA, in 1941 where, in 1959, he began his university training at the University of Pennsylvania (BA degree, 1962), **Barry Trost** obtained his Ph.D. degree in Chemistry just three years later at the Massachusetts Institute of Technology (1965). He directly moved to the University of Wisconsin, where he was promoted to Professor of Chemistry in 1969 and subsequently became the Vilas Research Professor of Chemistry in 1982. He joined the faculty at Stanford University as Professor of Chemistry in 1987 and became Tamaki Professor of Humanities and Sciences in 1990. In recognition of his many contributions, Professor Trost has received numerous awards, a few of which are the ACS Award in Pure Chemistry (1977), the ACS Award for Creative Work in Synthetic Organic Chemistry (1981), the Guenther Award in the Chemistry of Essential Oils and Related Products (1990), the Dr. Paul Janssen Prize (1990), the ACS Roger Adams Award (1995), the Presidential Green Chemistry Challenge Award (1998), the Herbert C. Brown Award for Creative Research in Synthetic Methods (1999), the Yamada Prize (2001), the ACS Nobel Laureate Signature Award for Graduate Education in Chemistry (2002), and the Arthur C. Cope Award (2004). Professor Trost's research interests include the invention and development of new synthetic reactions largely based upon catalysis using transition-metal complexes and their use to define strategies that result in the total synthesis of complex molecules largely of biological importance.

Zachary T. Ball was born in Columbus, Ohio in 1976. He obtained his bachelor's degree in 1999 from Harvard University under the guidance of Professor Gregory L. Verdine. Moving west to Stanford University, he began graduate study with Professor Barry M. Trost and received his Ph.D. in 2004. His graduate work focused on the selective hydrosilylation of alkynes and the application of vinylsilanes in synthesis. He is currently a postdoctoral fellow at the Miller Institute for Basic Research in Science, Univ. of California, Berkeley, studying with Professor Jean M. J. Fréchet.

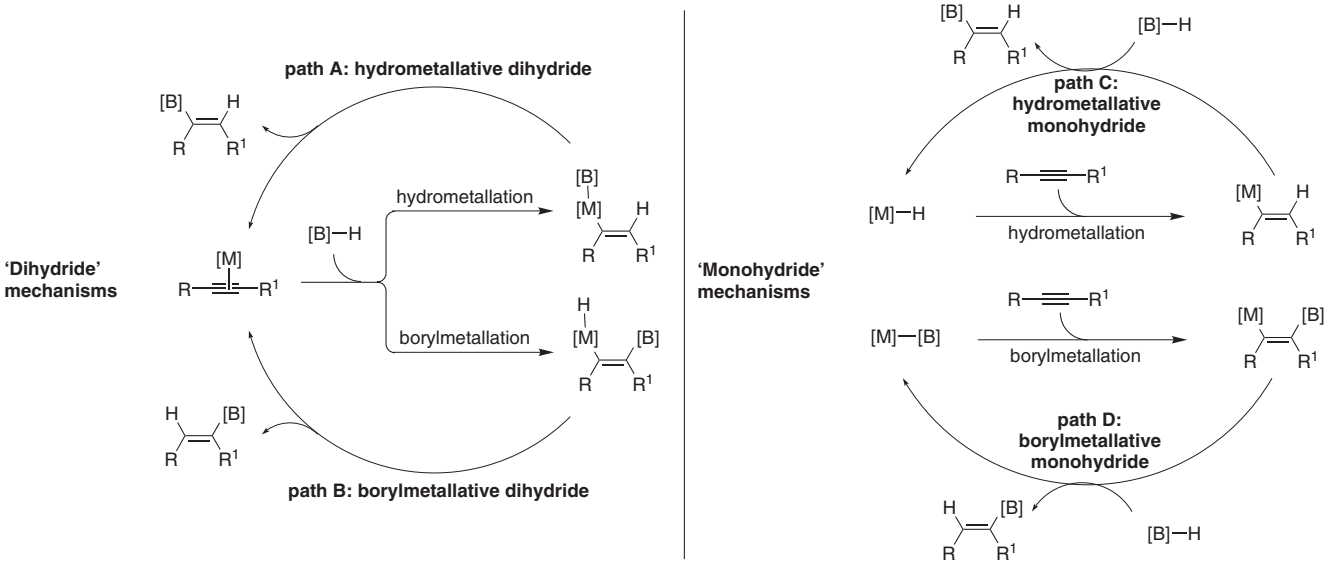
the possibility of achieving unique regio- and stereoselectivities and functional group tolerance for species such as catecholborane that react with alkynes in the absence of catalyst only slowly and at elevated temperatures, thus allowing the catalytic reaction to proceed under conditions where the background uncatalyzed process does not compete. Catalyzed hydrometallation occurs by an ever increasing array of mechanisms, though the majority of transition metal catalysts operate on some variation of the four pathways shown in Scheme 2 (depicted for catalyzed hydroboration). Divisions are based on the timing of the bond-forming step; initial bond formation occurs either for the H–C bond (hydrometallative, paths A, C) or for the B–C bond (borylmetallative, paths B, D). Further division is possible based on catalyst structure. By analogy to homogeneous hydrogenation, a 'dihydride' mechanism adds to an alkyne a hydride and a metalloid from the same metalloid hydride molecule (paths A, B), while a 'monohydride' mechanism adds a hydrogen and a metalloid from different metalloid hydride molecules (paths C, D). In many cases, all four mechanisms could in principle produce the same products, and uncertainty about the nature of the active catalyst can make the distinction between a monohydride-type and a dihydride-type catalyst difficult. This uncertainty makes identification of the factors controlling product outcome difficult.

This is not an exhaustive set of catalyzed hydrometallative classes. There are probably innumerable different mechanisms of hydrometallation if one considers all the details, and in several important examples significant differences almost assuredly exist. In the following sections, we hope to present the important mechanisms by which catalyzed and uncatalyzed hydrometallations are believed to proceed for individual metalloids, as well as to highlight mechanistic proposals for reactions generating unique product selectivities. As with much literature of transition-metal catalysis, most of the proposed hydrometallation mechanisms are largely conjecture; we focus here also on systems for which solid evidence of one kind or another exists. All generalizations into broad mechanistic classes must be approached with care, and certainly the reader should be aware that our understanding of catalyzed hydrometallation is far from complete.

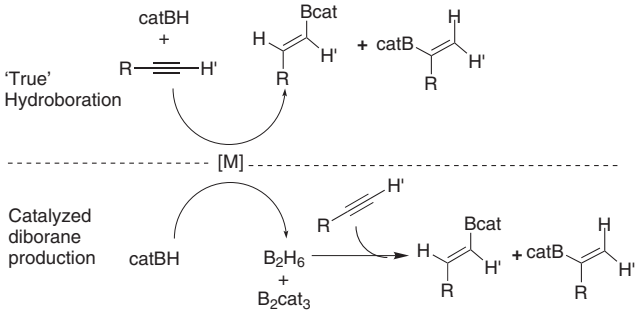
2.1 Hydroboration

Unlike hydrosilylation and hydrostannation, the addition of a boron-hydride to a triple bond proceeds readily without catalysis, providing the cis addition product. The mechanism is well-understood to proceed through the uncomplexed borane, though solvent and ligand effects do exist.[1,3,13] Metal-catalyzed processes have been studied to complement the standard hydroboration reaction. Late transition metals, notably rhodium, are among the most studied. Although a mechanism of oxidative addition followed by hydrometallation or borylmetallation is generally assumed, little convincing data exists. Studies are often complicated by the observation of several products. In many cases, rhodium-catalyzed hyroborations suffer from competitive diborane (B_2H_6) production (see section 3.1).[14] In this case, diborane becomes an extremely competitive uncatalyzed hyroborating reagent, and the metal catalyst is not explicitly involved in the hydroboration event. The two possibilities are shown in Scheme 3 for hydroboration with catecholborane (catBH).

Hartwig has recently demonstrated that titanium(II) complexes can function as true hydroboration catalysts without competing diborane production. Owing to the electronics of group IV d^0 complexes, the mechanism likely involves σ-bond metathesis between the borane and a titanium–alkyne complex (see Scheme 4). NMR and kinetic studies indicate a stepwise ligand exchange, losing both CO ligands to arrive at an alkyne–borane–titanium complex with partial boron–carbon bond character, de-

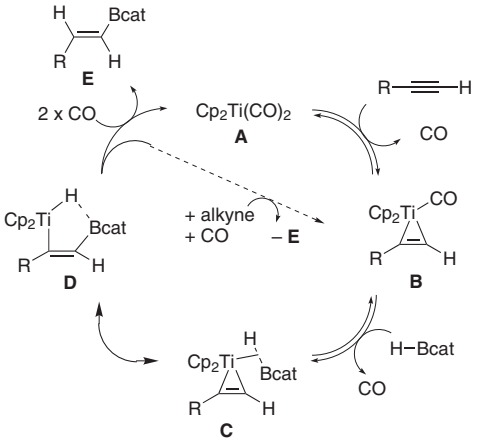


Scheme 2 Catalyzed hydrometallation pathways.



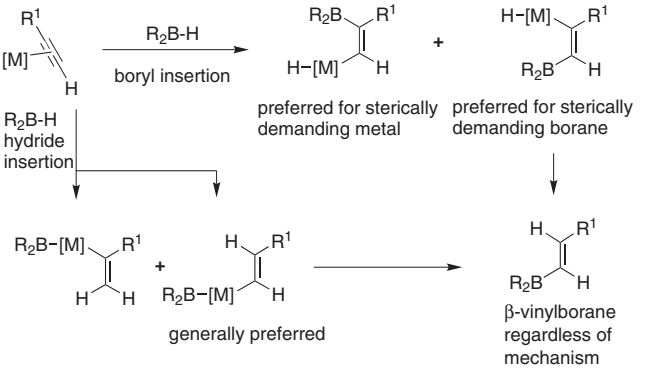
Scheme 3 Metal-catalyzed hydroboration.

scribed with the resonance structures **C** and **D**. Reductive elimination to produce the product vinylboronate **E** and ligand association resumes the catalytic cycle.[15,16]



Scheme 4 Well-defined titanium catalysis.

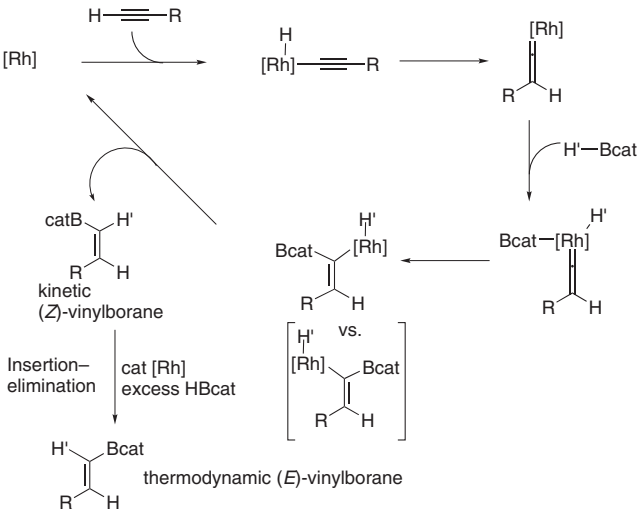
This is an example of a borylmetallation mechanism (i.e. proceeding through a β-borylvinyl titanium hydride, or more generally, a β-metalloidvinyl hydridometal). The mechanistic proposal is a good demonstration that borylmetallative and hydrometallative mechanisms are often indistinguishable by observation of product selectivities (see Scheme 5). Here, boryltitanation to produce [**C** ↔ **D**] occurs with titanium proximal to the bulky R group, with the borane acting as the sterically more demanding group proximal to the hydrogen atom. However, a hydrotitanation mechanism, as generally envisioned, would likely produce the same regiopreference, as titanium would be apt to occupy the opposite, less sterically demanding site leading to a β-vinyl boryltitanium species. This discussion implies an oxidative addition intermediate of the borane to the metal, or a σ-bond metathesis from a bound borane molecule as in Scheme 4, where the hydrogen and boron atoms transferred to the alkyne come from the same borane molecule – a 'dihydride' pathway by analogy to hydrogenation literature. However, the point is equally valid for 'monohydride' mechanisms in which the hydrogen and metalloid atoms come from separate metalloid hydride molecules (e.g. Scheme 9, vide infra).



Scheme 5 Confluence of mechanistic pathways.

Whether the initial insertion is a σ-bond metathesis or a discrete oxidative addition, hydrometallation reactions generally proceed by alkyne insertion mechanisms. However, Miyaura has recently discovered an alternative mechanistic pathway that also provides a solution to the problem of (*Z*)-vinylborane synthesis – the product of trans hydroboration (Scheme 6). In this reaction with rhodium(I) or iridium(I), deuterium labeling studies implicate a vinylidene rhodium intermediate.[17]

In addition to offering a new pathway for transition-metal catalyzed hydrometallation, the reaction illustrates another important consideration common to catalyzed hydrometallation in general: the observed ratio is not necessarily the kinetic one. In this case, when catecholborane is not the limiting reagent, a rhodium-catalyzed addition-elimination process equilibrates the mixture to the thermodynamic (*E*)-vinylborane. Only when alkyne is present in excess are trans addition selective processes possible.

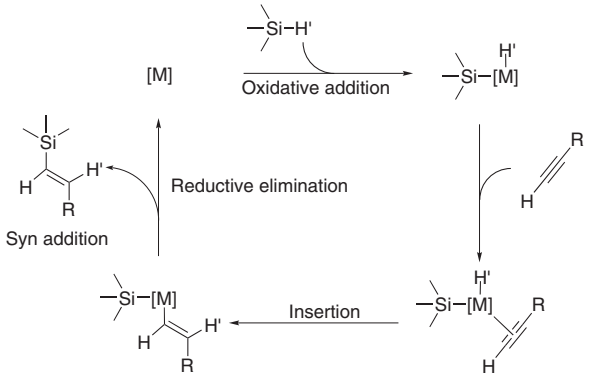


Scheme 6 Trans hydroboration with rhodium catalysts.

2.2 Hydrosilylation

Alkyne hydrosilylation was discovered as a radical-induced process, providing, for terminal alkynes, a trans addition to the thermodynamic product.[18] Additionally,

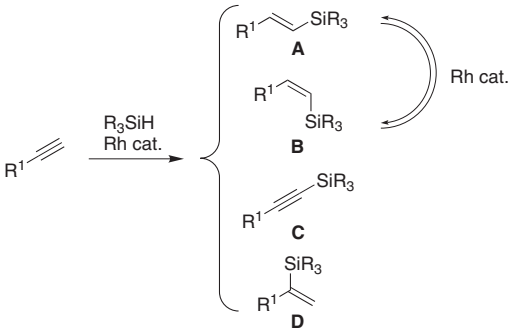
some work has focused on hydrosilylation with strong Lewis acid catalysts, which also give products of trans addition, presumably through an external attack mechanism.[19–21] However, the lion's share of work in the field involves transition-metal catalysis by one of the very many metals known to catalyze alkyne hydrosilylation. The Chalk–Harrod mechanism first proposed a pathway based on oxidative addition, migratory insertion, and reductive elimination (Scheme 7).[22] Though it arose from studies of cobalt-catalyzed olefin hydrosilylation, the Chalk–Harrod model was successfully applied to platinum-catalyzed hydrosilylation of alkenes and alkynes. This proposal correctly predicts terminal (β) silane products from placement of the bulky M-SiR^1_3 fragment distal to the alkyne substituent. The mechanism has received several refinements and challenges, largely to address the observation of unusual products from hydrosilylation reactions. These include (*Z*)-vinylsilanes from trans addition, the predominance of α-silyl products, and silylalkynes from dehydrogenative silylation.



Scheme 7 Chalk–Harrod hydrosilylation mechanism.

It quickly became clear that iridium and rhodium do not cleanly fit the Chalk–Harrod mechanism as does platinum. For electron-rich silanes and relatively unhindered terminal alkynes, the major product is the (*Z*)-vinylsilane (Scheme 8, **B**) from apparent unusual trans addition to the alkyne.[23] This observation was followed by important and confusing discoveries. First, rhodium, under appropriate conditions, will catalyze the isomerization of the (*Z*)-vinylsilane product **B** to the (*E*)-vinylsilane product **A**.[24] Second, rhodium can also catalyze the reverse, contrathermodynamic reaction of the (*E*)-vinylsilane **A** to the (*Z*)-vinylsilane **B**.[25]

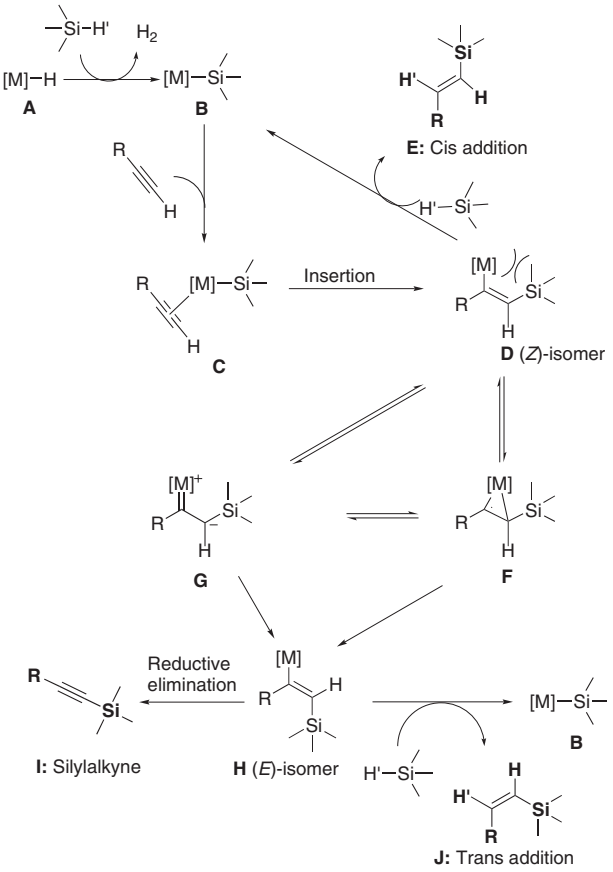
To account for the predominant appearance of trans addition products (**B**) with terminal alkynes, as well as smaller amounts of silylalkynes (**C**) from dehydrogenative silylation, Crabtree[26] (and similarly Ojima[27]) proposed a mechanism based on silylmetallation in the migratory insertion step and subsequent *E*/*Z* isomerization through either a metal carbene or metallocyclopropene intermediate. Noteworthy is the proposed 'monohydride'-type mechanism[26] (by analogy to homogeneous hydrogenation) that permits *E*/*Z* isomerization to out-compete reductive elimination, which must occur via intermolecular



Scheme 8 Rhodium-catalyzed processes of hydrosilylation.

reaction with a molecule of silane. Indeed, there is some evidence that a 'monohydride' mechanism may be active even in cases where it is not readily apparent from the precatalyst structure.[28] Focusing predominantly on the course of hydrosilylation reactions with a single metal, Crabtree (iridium) and Ojima (rhodium) sought answers to the longstanding questions, and significant overlap of the mechanism for the two metals is assumed.

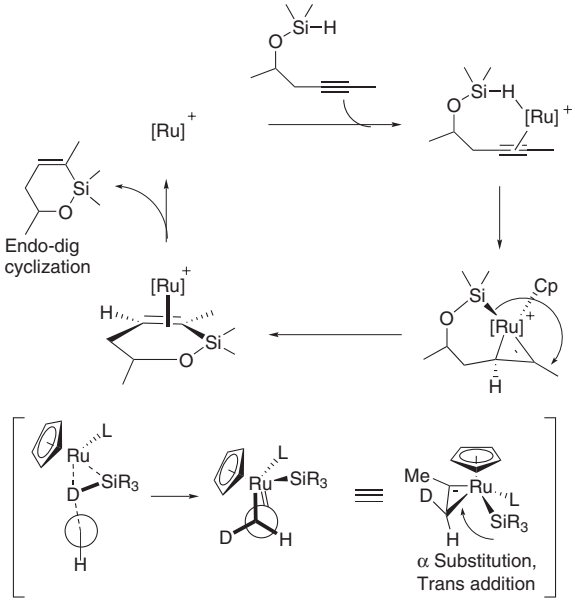
The mechanistic proposal fits well with the available data. Electron-rich silanes (e.g. Et_3SiH) provide good selectivity for the trans addition process to give (*Z*)-vinylsilane products, while electron-poor silanes [e.g. $(MeO)_3SiH$]



Scheme 9 Silylmetallation proposal for cis and trans addition processes.

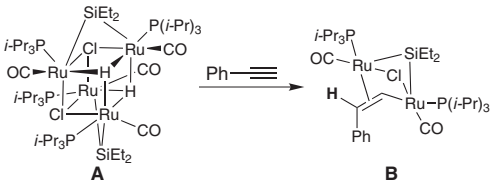
generally provide more (*E*)-vinylsilane product.[4,26,27] Electron-poor silanes are not as able to stabilize the positive charge at the β-position that is present in the isomerization intermediates **F** or **G** (Scheme 9), and so oxidative addition or transmetallation occurs prior to isomerization. It is argued that α-anion stabilization is not as dependent on the substituents at silicon.[27,29] The dehydrogenative product **I** is formed most readily for hindered terminal alkynes, where a large R group should favor strain release in a reductive elimination step.[26]

Recently, cationic ruthenium complexes of the type $[Cp^*Ru(MeCN)_3]PF_6$ have been shown to provide unique selectivities for inter- and intramolecular reactions that are difficult to reconcile with previously proposed mechanistic routes.[30–32] These observations led to a computational study and a new mechanistic proposal based on concerted oxidative addition and alkyne insertion to a stable ruthenacyclopropene intermediate (Scheme 10).[33] This proposal seems to best explain the unique selectivities. A similar mechanism in the context of C–H activation has recently been proposed from a computational study of a related ruthenium(II) catalyst.[34]



Scheme 10 Concerted oxidative addition–insertion.

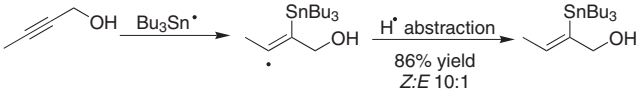
Recently, a proposal has been put forth that some ruthenium catalysts selective for the trans addition process may proceed through dinuclear ruthenium intermediates.[35] As shown in Scheme 11, reaction of tetraruthenium aggregate **A** with phenylacetylene results in the fully characterized bridging dinuclear alkenyl complex **B**. The authors propose that a direct trans delivery of hydride through a dinuclear intermediate may be active in the hydrosilylation catalyzed by **A**, though compound **B** itself is unreactive to Et_3SiH.



Scheme 11 Dinuclear ruthenium proposal.

2.3 Hydrostannation

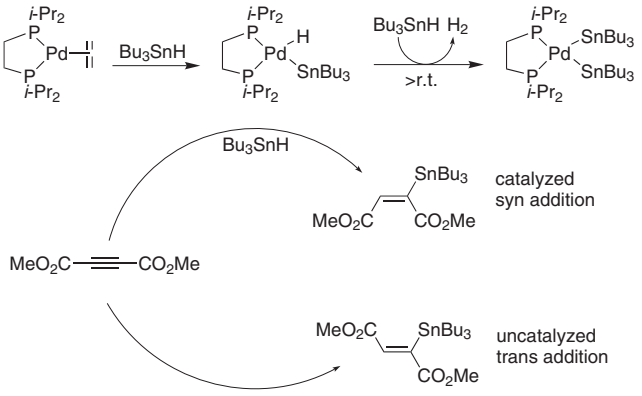
Radical hydrostannation of alkynes is believed to be a standard radical process, with a tin-centered radical reacting with the alkyne to produce the most stable vinyl radical intermediate (Scheme 12). In the example shown below, the propargylic alcohol induces complete regioselectivity for the distal radical, producing a (sometimes very selective) mixture of α-stannyl olefin stereoisomers.[36]



Scheme 12 Radical hydrostannation.

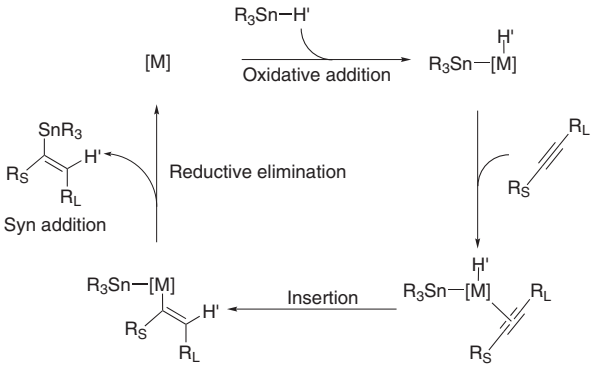
The metal-catalyzed hydrostannation is probably the least understood metalloid-hydride addition to alkynes. There is no kinetic or otherwise authoritative mechanistic study, and much assumed understanding is based on observed products in the hydrostannation of alkynes and related substrates, as well as by analogy to other reactions.[37] Recently, a palladium(II) oxidative addition product with stannanes was isolated by stabilizing the intermediate with bulky phosphine ligands (Scheme 13).[38] The intermediate will react with another stannane to produce dihydrogen and a distannylpalladium – illustrating a common side reaction in hydrostannation – and was shown to catalyze the hydrostannation of dimethyl acetylene dicarboxylate.

Much of the Chalk–Harrod hydrometallation proposal (vide supra) applies to hydrostannation as well, with sterically differentiated alkynes resulting in tin at the less sub-



Scheme 13 Isolable oxidation intermediate with palladium.

stituted terminus (Scheme 14). There is also the possibility of a stannylmetallation process, and little convincing evidence exists to distinguish between these pathways. We will address proposals that have been advanced to explain the results of individual studies as we come to them.



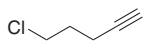
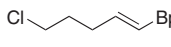
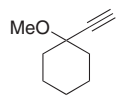
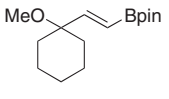
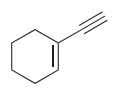
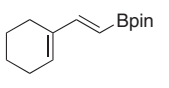
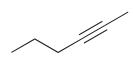
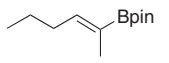
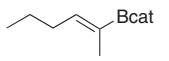
Scheme 14 Hydrostannation via hydrometallative mechanism.

3 Terminal Alkynes

3.1 Hydroboration of Terminal Alkynes

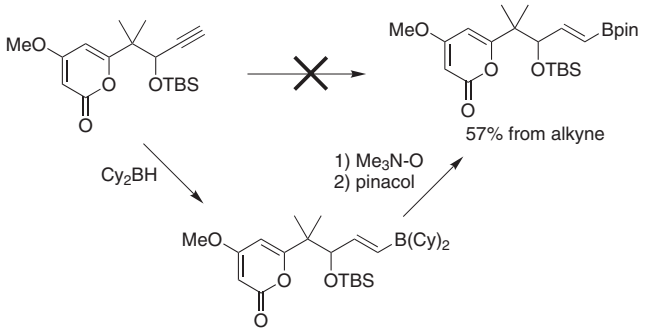
The cis hydroboration of terminal alkynes is generally a straightforward, well-understood reaction and typically requires no catalysis. The uncatalyzed process has been reviewed at length.[1] Unhindered boranes generally add to alkynes twice, producing diboryl alkanes. Hindered dialkylboranes, such as dicyclohexylborane, provide excellent regio- and chemoselectivity. For applications where boronic acids or boronate esters are required, the direct synthesis of these species is often desired. As such, catecholborane has been used, but suffers from low regioselectivity. Knochel disclosed that the more sterically discriminating pinacolborane (pinBH) overcomes this limitation, allowing facile synthesis of (*E*)-borate esters (Table 1).[39]

Table 1 Hydroboration of Alkynes with Pinacolborane

Entry	Alkyne	Major product	Yield (%)	Ratio[a]
1			85	99:1
2			85	100:1
3			83	99:1
4			75	93:7
5[b]				60:40

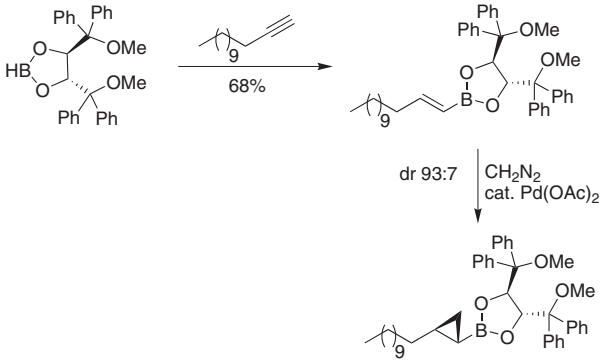
[a] Ratio of major product to all other isomers.
[b] For comparison, ratio for hydroboration with catacholborane.

It has been noted that the ease and success of uncatalyzed hydroboration requires that catalytic processes complement or improve on previous knowledge.[2] Catalytic processes that select for (*Z*)-vinylboranes and borates, or for 1,1-disubstituted species, are obvious goals. However, it is also worth noting that in model studies for a recent synthesis of deoxyfusapyrone, Organ was unable to effect the selective hydroboration of a relatively simple propargylic silyl ether with boronate reagents (Scheme 15).[40] Instead, the group resorted to an indirect synthesis using the highly selective dialkylborane hydroboration reagent dicyclohexylborane (Cy_2BH).



Scheme 15 Pinacol borane synthesis.

A recent development in the field of uncatalyzed terminal alkyne hydroboration is the design of chiral boronate esters, which can direct stereochemistry of subsequent transformations on the vinylboronate (Scheme 16).[41] The TADDOL-type auxiliary is stable to the high temperatures (90–120 °C) necessary for efficient hydroboration.[42] The product cyclopropylboronates are potentially useful in subsequent oxidative or cross-coupling reactions.



Scheme 16 Hydroboration with chiral dioxaborolanes.

Catalysis of alkyne hydroboration has been studied with both late and early transition metals. Rhodium catalysis garnered some of the earliest interest.[14,43,44] However, unlike rhodium-catalyzed alkene hydroboration,[2,45] which provided interesting and synthetically important alterations in regio-, diastereo-, and enantioselectivity, the catalyzed alkyne hydroboration was fraught with poor selectivity. Burgess[14] and Srebnik[43] performed early studies using Wilkinson's catalyst [$Rh(PPh_3)_3Cl$] and related

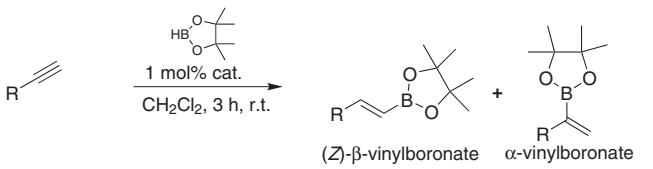
rhodium(I) species. The catalyzed reactions of pinacolborane and catecholborane proceed at room temperature, in contrast to the 80–120 °C regularly required for the uncatalyzed pathway, possibly permitting increased substrate scope and functional group tolerance. The plethora of products generated in Burgess's early experiments with phenylacetylene clearly demonstrated that multiple catalytic reactions are functioning (see Table 2).[14] While formation of the expected carbonyl compounds (**D** and **E**) is favored at short reaction times, other pathways occur on prolonged exposure. Hydrogenation (**B** and **C**) implies generation of rhodium hydrides, and double addition (**F**) indicates a slow, rhodium-catalyzed hydroboration of the vinylboronate products.

Burgess notes that NMR investigations of the intermediate boronates prior to oxidation sometimes reveals the presence of dialkylboranes from hydroboration with BH_3, presumably formed by rhodium-catalyzed decomposition of catBH.

Srebnik had significantly more success performing hydroborations with pinBH.[43] Hydroborations catalyzed by Wilkinson's catalyst with pinBH produce vinylboronates in very high yield (see Table 3, entries 1, 4, 7, 10). However, the regioselectivity remains poor, even for quite hindered substrates such as 3-methyl-1-butyne (entry 7). Only the very hindered *tert*-butylacetylene (entry 10) affords good selectivity for the (*E*)-β-vinylboronate. However, the exchange of one phosphine ligand for carbon monoxide alters the reactivity profile markedly. The resulting complex, $Rh(CO)(PPh_3)_2Cl$, provides essentially complete regioselectivity at ambient temperature. The same article reported that the nickel complex $CpNi(PPh_3)Cl$ offers similar high yields and complete selectivity for a range of substrates. Both catalysts selectively react at terminal alkynes in the presence of a trimethylsilyl alkyne (entries 13, 14).

The reasons behind the increased selectivity with $Rh(CO)(PPh_3)_2Cl$ are unclear; the less hindered CO ligand provides more selectivity in what is ostensibly a steric differentiation process. There is some evidence that rhodium hydroborations can proceed through insertion of a boron–rhodium bond[14] where limiting the steric bulk of rhodium would indeed favor the terminal β-vinylboronate

Table 3 Alkyne Hydroboration with Rhodium and Nickel Catalysts



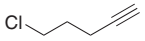
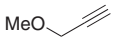
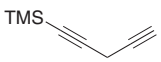
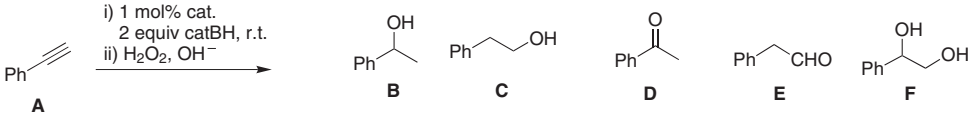
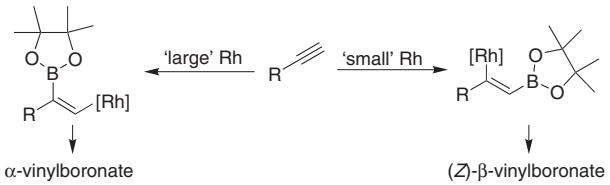
Entry	Alkyne	Catalyst	Yield (%)	Ratio β:α
1		$Rh(PPh_3)_3Cl$	99	40:60
2		$Rh(CO)(PPh_3)_2Cl$	99	99:1
3		$CpNiPPh_3Cl$	98	99:1
4		$Rh(PPh_3)_3Cl$	99	48:52
5		$Rh(CO)(PPh_3)_2Cl$	99	98:2
6		$CpNiPPh_3Cl$	99	98:2
7		$Rh(PPh_3)_3Cl$	99	79:21
8		$Rh(CO)(PPh_3)_2Cl$	99	99:1
9		$CpNiPPh_3Cl$	98	99:1
10		$Rh(PPh_3)_3Cl$	99	99:1
11		$Rh(CO)(PPh_3)_2Cl$	99	99:1
12		$CpNiPPh_3Cl$	99	99:1
13		$Rh(CO)(PPh_3)_2Cl$	99	99:1
14		$CpNiPPh_3Cl$	99	98:2

Table 2 Rhodium-Catalyzed Phenylacetylene Hydroboration



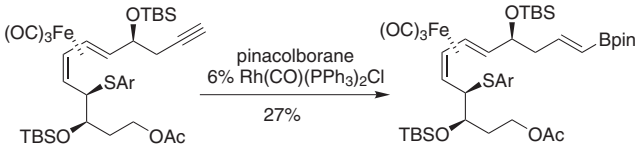
Entry	Catalyst	Time (h)	B	C	D	E	F
1	$Rh(PPh_3)_3Cl$	1	9	12	32	**47**	trace
2	$Rh(PPh_3)_3Cl+PPh_3$	1.5	2	3	35	**60**	trace
3	$Rh(PPh_3)_3Cl$	12	**20**	9	10	3	58
4	$Rh(PPh_3)_3Cl+PPh_3$	15	**29**	9	16	17	29
5	$[Rh(cod)Cl]_2+8\ PPh_3$	12	**54**	19	trace	trace	27

(Scheme 17). Conclusive evidence for insertion into a hydrogen–rhodium or boron–rhodium bond remains elusive.



Scheme 17 Borylmetallation.

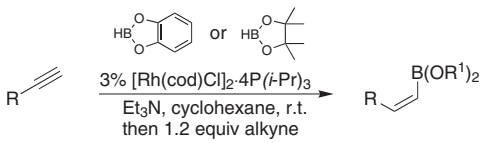
The catalyst $Rh(CO)(PPh_3)_2Cl$ has been used to obtain material for an approach to macrolactin A.[46] The rhodium-catalyzed process allowed hydroboration in the presence of an (*E*,*Z*)-dienyl–$Fe(CO)_3$ complex, though the isolated yield is quite low (Scheme 18).

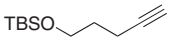
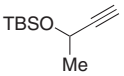


Scheme 18 An alkyne containing a dienyl–$Fe(CO)_3$ complex.

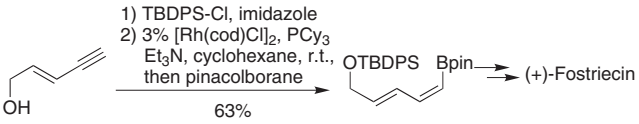
Miyaura recently published results from a study of hydroboration with rhodium and iridium catalysts.[17] Both $[Rh(cod)Cl]_2$ and $[Ir(cod)Cl]_2$ were found to provide extremely clean (*Z*)-vinylboranes. There is significant evidence that the reaction proceeds through a nonstandard vinylidene intermediate, providing further evidence for the value of vinylidene-type mechanisms to access new reactivity and selectivity for simple addition reactions to alkynes (see section 2.1).

Table 4 Trans Addition in Rhodium-Catalyzed Hydroboration



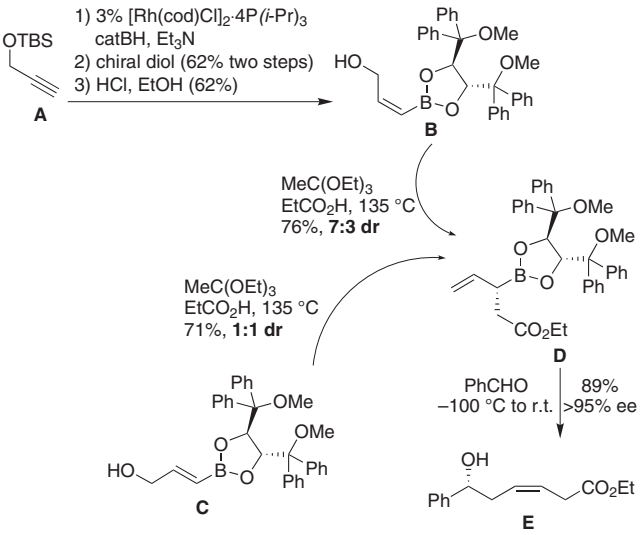
Entry	Alkyne	Borane	Yield (%)	Ratio *Z*:*E*
1		catBH	72	98:2
2		catBH	70	98:2
3		pinBH	59	90:10
4		pinBH	69	95:5
5		catBH	60	99:1

The initial report demonstrates that the trans hydroboration process is compatible with aryl as well as alkyl alkynes, silyl ethers, and substantial steric bulk (see Table 4). This very significant discovery has already made its mark on the synthesis of complex targets. Extension of the methodology to 1,3-enynes has led to its use in the course of a total synthesis of (+)-fostriecin (see Scheme 19).[47]



Scheme 19 Trans hydroboration en route to fostriecin.

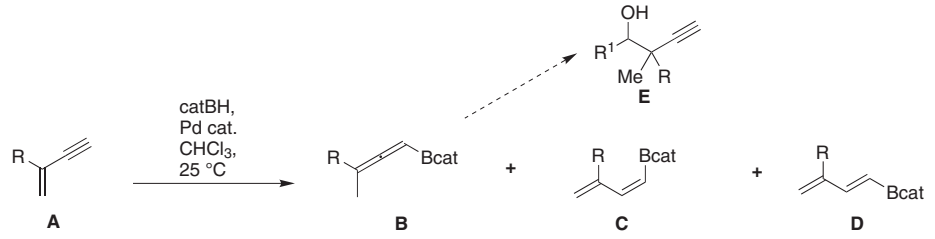
Rhodium-catalyzed trans hydroboration has also aided the synthesis of chiral allylboranes (Scheme 20).[48] The (*Z*)-vinylborane **B** allows modestly diastereoselective [3,3] sigmatropic rearrangement (dr 7:3) to afford readily separable allylborane **D** and its diastereomer. The allylborane undergoes clean addition to aldehydes, with absolute stereochemistry controlled by the C3 stereocenter (**E**).



Scheme 20 Chiral allylborane synthesis.

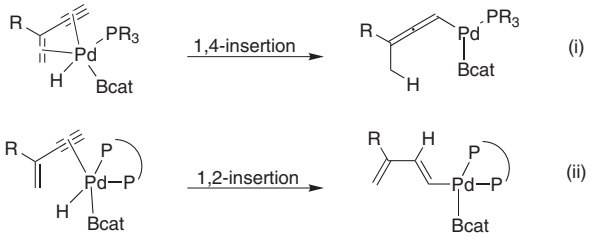
Another late transition metal providing unique reactivity in hydroboration catalysis is palladium. Palladium(0) catalysis of hydroboration with 1,3-enynes brings with it possibilities for 1,2- as well as 1,4-addition. Bidentate phosphine ligands provide selective formation of the alkyne 1,2-hydroboration product **D** (Table 5, entry 3), similar to that obtained with the uncatalyzed process (c.f. Table 1). The use of monodentate phosphines, however, gives selectively the allenylborane product **B**.[49] Allenylborane products are useful as carbonyl nucleophiles giving homopropargylic alcohols with quaternary stereocenters (**E**).

Table 5 Hydroboration of 1,3-Enynes with Palladium



Entry	R	Catalyst	Product ratio B	C	D	Yield (%)
1	Me	$Pd(PPh_3)_4$	60	34	6	75
2	Me	Pd(0) + $1.5PPh_3$	**84**	16	0	63
3	Me	Pd(0) + dppf	0	0	**100**	89
4	Me	Pd(0) + $2PPh_2(C_6F_5)$	**83**	17	0	73
5	*n*-C_5H_{11}	Pd(0) + $2PPh_2(C_6F_5)$	**88**	12	0	74
6	*t*-Bu	Pd(0) + $2PPh_2(C_6F_5)$	**83**	4	13	89

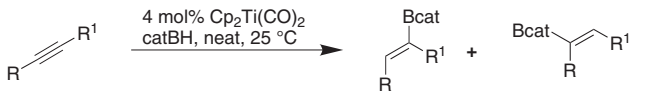
The authors explain the divergent reactivity by invoking a five-coordinate complex of palladium, with an η^4-enyne ligand necessary for 1,4-insertion (Scheme 21, i). By contrast, a palladium(II) species with a bidentate phosphine complex binds the enyne as an η^2-alkyne ligand as a result of the increased coordination number at palladium, resulting in 1,2-hydride insertion (Scheme 21, ii).

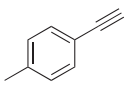
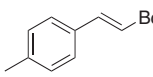
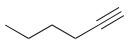
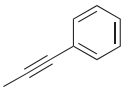
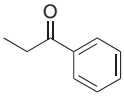


Scheme 21 Phosphine-based divergence in palladium-catalyzed hydroboration.

Early transition metals of the titanocene and zirconocene types have also been employed successfully for alkyne hydroboration. With titanium, various reports have demonstrated that the cheap, readily available early transition metals can act as hydroboration catalysts both for alkenes and alkynes, employing catecholborane or borohydride as borane sources.[44,50] However, a series of investigations has indicated that many of these, such as $Nb(mesityene)_2$, $TiCl_3$, and $Ti(O\textit{i}\text{-}Pr)_4$, primarily catalyze the decomposition of catechol, producing diborane and borate esters of the type $B(OR)_3$ (generally as $B_2(cat)_3$, see Scheme 3).[51] Diborane, then, is the actual hydroboration agent. This explains why such systems have generally provided selectivities very similar to borane itself.

Table 6 Titanium-Catalyzed Hydroboration

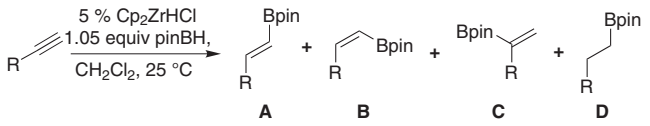


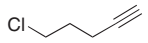
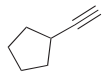
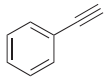
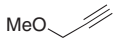
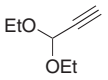
Entry	Alkyne	Major product	Yield[a]	Ratio[b]
1			96	100:0
2			96	100:0
3			89[c]	67:33

[a] Isolated total yield of both regioisomers.
[b] Ratio of regioisomers.
[c] Product mixture of regioisomers isolated after oxidation to ketone.

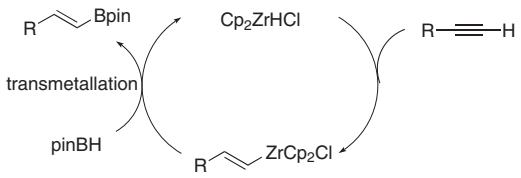
Careful design and experimentation have provided a titanocene catalytic system (Table 6) that appears to provide classic catalysis without borane production and subsequent uncatalyzed hydroboration. The system utilizing $Cp_2Ti(CO)_2$ provides improved selectivity over the already quite selective uncatalyzed process (cf. Table 1).[16] Roughly contemporaneous to this discovery, a similar zirconocene system was reported (Table 7). In this case, the more hindered pinacolborane was employed together with the Schwartz reagent (Cp_2ZrHCl).[52] As with $Cp_2Ti(CO)_2$, Cp_2ZrHCl provides very good stereoselectivity and reactivity at room temperature. The zirconium process tolerates substantial steric bulk (entry 3), and affords complete selectivity for terminal alkynes in the presence of a trimethylsilyl-capped alkyne (entry 5). The somewhat sensitive acetal functionality is tolerated as well (entry 7).

Table 7 Zirconium Catalysis of Hydroboration



Entry	Alkyne	Product ratio A	B	C	D	Yield (%)
1		97	2	0	1	94
2		97	1	0	2	94
3		100	0	0	0	95
4		97	1	1	1	75
5		96	3	1	0	82
6		95	3	3	0	87
7		82	11	7	0	82

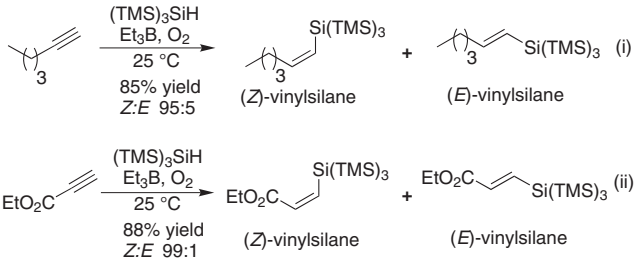
Perhaps surprisingly, the zirconocene and titanocene processes may have very different mechanisms. The titanocene process is postulated on the basis of kinetic and structural studies to proceed through a σ-bond metathesis pathway of alkyne insertion into a bound borane, producing a β-borylvinyl titanium hydride (see Section 2.1 and especially Scheme 4).[15] In contrast, hydroboration with the Schwartz reagent is proposed to proceed via alkyne hydrozirconation without involvement of the borane, followed by a precedented transmetallation with pinBH[53] to provide the product and regenerate Cp_2ZrHCl (see Scheme 22). The investigators note that regioselectivities are identical to those obtained when the zirconocene catalyst is allowed to react with an alkyne prior to addition of the catBH, and that no reaction between Cp_2ZrHCl and catBH occurs in the absence of alkyne. Presumably, this should imply that regioselectivity is independent of the borane employed, though this is not addressed.



Scheme 22 Proposed mechanism of zirconium catalysis.

3.2 Hydrosilylation of Terminal Alkynes

Although the most studied and utilized alkyne hydrosilylation processes are catalyzed by transition metals, other choices for reaction promoters exist. The reaction was discovered as a radical process more than 40 years ago.[18] More recently it was discovered that tris(trimethylsilyl)silane adds to alkynes cleanly under mild conditions. With activation by Et_3B/O_2, reaction temperatures as low as 0 °C are possible. Selectivity for the (*Z*)-β-vinylsilane from a trans addition process is often very good (>95:5), though erosion of selectivity occurs at higher reaction temperatures where isomerization to the thermodynamic product (*E*)-β-vinylsilane occurs (Scheme 23).[54]

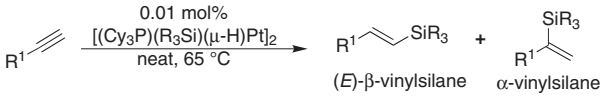


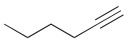
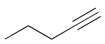
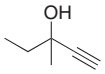
Scheme 23 Radical hydrosilylation with $(TMS)_3SiH$.

In contrast, strong Lewis acids have only been employed as hydrosilylation catalysts relatively recently.[19] Selectivities mirror those of the radical process above. Good yields and complete selectivity for the (*Z*)-β-vinylsilane are observed with 0.2 equiv $AlCl_3$ or $EtAlCl_2$ at 0 °C for several terminal alkynes. Although functional group compatibility is no doubt a concern with such aggressive reagents, the stability of a primary triisopropylsilyl ether and of a benzyl ether to the reaction conditions is demonstrated. The process has been used to bond alkyne molecules to a silane surface.[55]

Hydrosilylation of terminal alkynes with transition metal catalysts is a well-studied process. Speier's catalyst (H_2PtCl_6) has been used extensively for alkene hydrosilylation, and also functions in alkyne hydrosilylation. H_2PtCl_6 and platinum(0) catalysts have the advantages of excellent turnover numbers (often >10,000), clean cis hydrometallation leading only to (*E*)-vinylsilanes and the regioisomeric α-vinylsilane, and tolerance of a wide range of carbon and heteroatom substituents on the silane.[56] However, Speier's catalyst itself is quite nonselective in additions to typical alkynes (see Table 8, entry 1).[57] Platinum complexes with bulky trialkyl phosphines show improved steric discrimination. Complexes of the type $Pt(Cy_3P)(ethylene)_2$ or their silane adducts $[(Cy_3P)(R_3Si)(\mu\text{-}H)Pt]_2$ provide very useful regiochemical selectivity while retaining impressive catalyst loadings of about 0.01 mol% (Table 8, entries 2–8).[58] Also notably, phosphine complexes allow the use of phenyl-, alkoxy-, and chlorosilanes. However, for the important alkoxysilane substrates, there is a significant drop in regioselectivity (to 82:18, see entry 5), which is not explained solely on of the basis of electronegativity or lack of steric bulk, given the excellent selectivity with Cl_3SiH (96:4, entries 4, 6).

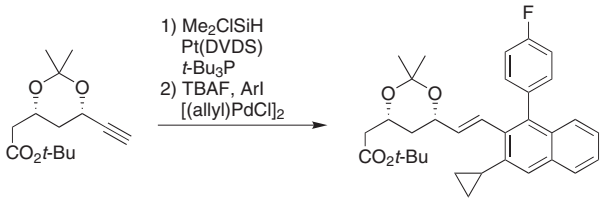
Table 8 Hydrosilylation with Platinum Phosphine Complexes



Entry	Alkyne	Silane	Yield (%)	Ratio[a] β:α
1[b]		Et_3SiH	78	42:58[b]
2		Et_3SiH	92	96:4
3		Cl_2MeSiH	86	95:5
4		Cl_3SiH	88	96:4
5		$(EtO)_3SiH$	83	82:18
6		Cl_3SiH	93	96:4
7		Et_3SiH	81	84:16
8		Et_3SiH	90	93:7

[a] In all cases, no (*Z*)-vinylsilane was produced.
[b] Reaction performed with Speier's catalyst, H_2PtCl_6.

Recently, the use of tri-*tert*-butylphosphine has produced still higher selectivities, allowing near total control in the synthesis of (*E*)-vinylsilanes including alkoxysilanes and disiloxanes.[59,60] In the context of a total synthesis of an HMG-CoA reductase inhibitor, hydrosilylation with a chlorosilane, followed by coupling with a 2,6-disubstituted aryl iodide, forged the key intermediate shown in Scheme 24.[59]



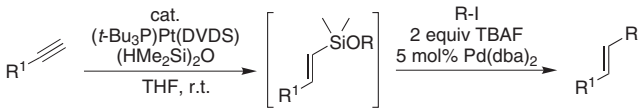
Scheme 24 Synthesis of HMG-CoA reductase inhibitor.

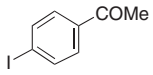
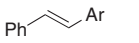
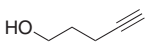
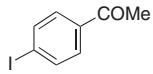
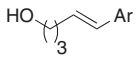
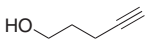
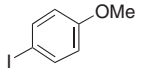
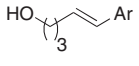
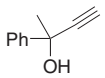
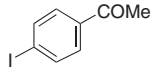
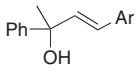
A separate, quite thorough study of terminal alkyne hydrosilylation with platinum arrived at a similar set of conditions.[60] This work utilized a one-pot hydrosilylation with the platinum(0) complex (t-Bu_3P)Pt(DVDS) (DVDS = 1,3-divinyl-1,1,3,3-tetramethyldisiloxane) and a palladium-catalyzed coupling reaction to demonstrate that the platinum catalyst is compatible with cross-coupling conditions, providing a convenient 'hydrocarbation' of terminal alkynes (Table 9).

The mechanistic and synthetic puzzle of alkyne hydrosilylation opened more fully with the discovery that rhodium will catalyze the trans hydrosilylation of terminal alkynes.[23] There is much work extant in this area, and good summaries of the various catalytic systems exist.[4] A trans addition process to give (*Z*)-β-silane products (**C**) is well-precedented with trialkylsilanes (Table 10), as well as with mixed Rh–Co complexes (entry 4).[23,27] However, the selectivity erodes significantly upon switching to Me_2PhSiH (entry 5), and due to the mechanistic requirements for equilibration of the β-silyl vinylrhodium intermediate (see section 2.2), electron poor silanes react exclusively to give (*E*)-β-silane products (**B**) (see entries 6, 7).

Efforts to tune the reactivity of rhodium catalysts by altering structure, solvent, and other factors have been pursued.[61,62] Although there is (justifiably) much attention given to catalysts that provide trans addition processes, it

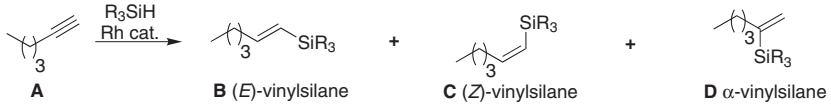
Table 9 One-Pot Hydrocarbation[a]



Entry	Alkyne	Iodide	Product [b]	Yield (%)
1[b]				89
2				82
3				89
4				72

[a] Reaction time for hydrosilylation: 30 min; for coupling: 10 min to 24 h.
[b] In all cases, <2% regioisomeric products detected.

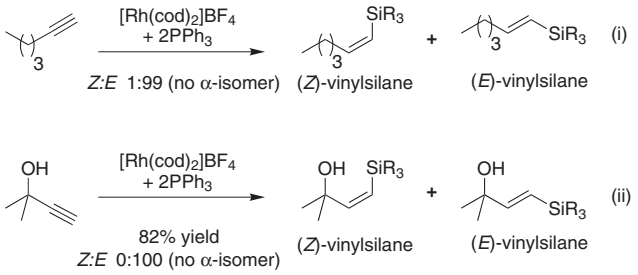
Table 10 Rhodium Catalysts for Selective Trans Addition Processes[a]



				Product ratio			
Entry	Silane	Temp (°C)	Catalyst	**B**	**C**	**D**	Yield (%)[b]
1	Et_3SiH	40	0.1% $Rh(PPh_3)_3Cl$	3	94	3	100
2	Et_3SiH	20	0.1% $Rh(PPh_3)_3Cl$	7	79	14	84
3	Et_3SiH	20	0.05% $Rh_4(CO)_{12}$	5	89	6	96
4	Et_3SiH	20	0.1% $Co_2Rh_2(CO)_{12}$	3	95	3	100
5	Me_2PhSiH	25	0.1% $Rh_4(CO)_{12}$	27	60	13	100
6	$(MeO)_3SiH$	0	0.1% $Rh_4(CO)_{12}$	95	0	5	98
7	$ClMe_2SiH$	0	0.1% $Rh_4(CO)_{12}$	74	0	26	85

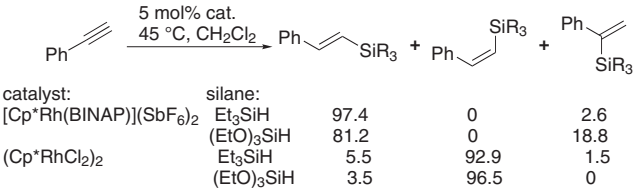
[a] Reactions generally 12–68 h.
[b] Yield determined by GC analysis.

is probably underappreciated that appropriate rhodium complexes, especially cationic phosphine complexes, can be very good and reliable catalysts for the formation of (*E*)-β-silane products from a cis addition process. The possibilities and range of substrate tolerance are demonstrated by the two examples in Scheme 25. A very bulky tertiary propargylic alcohol as well as a simple linear alkyne provide excellent access to the (*E*)-β-vinylsilane products.[61,63]



Scheme 25 Cis addition processes with rhodium.

However, the need for synthetically useful substituents on silicon limits the synthetic utility of most rhodium catalysts. The variable results with rhodium complexes was used to advantage by Faller, who showed that the complexes $[Cp^*Rh(BINAP)](SbF_6)_2$ and $[Cp^*RhCl_2]_2$ give opposite geometrical selectivities (Scheme 26), with the cationic system presumably following a Chalk–Harrod mechanism, while the neutral $(Cp^*RhCl_2)_2$ may be a precatalyst for a monohydride-type active catalyst such as $[Cp^*Rh(SiR_3)]^+$.[28] The significant success with $(EtO)_3SiH$

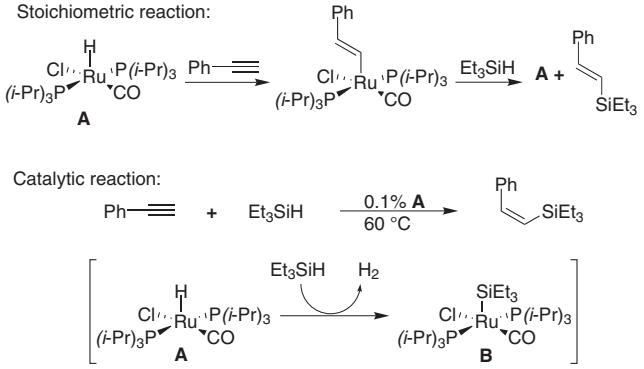


Scheme 26 Divergent selectivities with rhodium.

is noteworthy, and further analysis of substrate scope might lead to an extremely useful process.

The other well-characterized metal for trans addition processes to terminal alkynes, iridium, suffers from similar limitations.[64] While iridium provides good selectivity for (*Z*)-β-vinylsilanes (Table 11, **C**) with $MePh_2SiH$ (Table 11, entry 1), silanes with electron-withdrawing groups (entry 6) and bulky alkynes (entry 4) exhibit significant deterioration in selectivity.[26]

Ruthenium complexes do not have as extensive a history as alkyne hydrosilylation catalysts. Oro noted that a ruthenium(II) hydride (Scheme 27, **A**) will perform stepwise alkyne insertion, and that the resulting vinylruthenium will undergo transmetallation upon treatment with triethylsilane to regenerate the ruthenium(II) hydride and produce the (*E*)-β-vinylsilane in a stoichiometric reaction. However, when the same complex is used to catalyze the hydrosilylation reaction, in fact exclusive formation of the (*Z*)-β-vinylsilane is observed.[65] In the catalytic case, the active ruthenium species is likely not the hydride **A** but the Ru–Si species **B**. This leads to a monohydride silylmetallation mechanism (see Scheme 2). More recently,

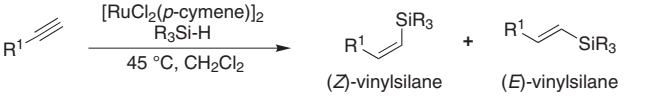


Scheme 27 Exclusive *trans* hydrosilylation.

small changes in catalyst structure have been shown to provide remarkable changes in stereoselectivity.[66]

Recently, the dissimilar complex $[RuCl_2(p\text{-cymene})]_2$ has also demonstrated excellent selectivity for the (*Z*)-vinylsilane products for a variety of substrates (see Table 12). Whether or not this complex also acts as a monohydride-type hydrosilylation catalyst – as do the majority of well-understood trans addition systems – is an open question. The selectivities for (*Z*)-β-vinylsilane products are some of the best yet reported, especially for α-branched substrates (entry 6). From a synthetic point of view, the catalyst is exciting, but at present is limited to trialkyl and triphenyl silanes, presenting problems for some applications.

Table 12 Ruthenium-Catalyzed Trans Hydrosilylation

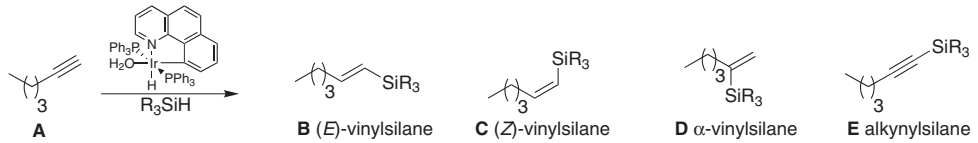


Entry	Alkyne	Silane	Yield (%)	Ratio[a] *Z*/*E*
1	Ph—	Et_3SiH	81	96:4
2		Ph_3SiH	94	96:4
3		Et_3SiH	88	96:4
4		Ph_3SiH	98	98:2
5	Cl	Ph_3SiH	87	96:4
6	OBn	Ph_3SiH	89	96:4

[a] In all cases, <1% of the α-silane was observed.

Interestingly, the $[RuCl_2(p\text{-cymene})]_2$ catalyst used for selective synthesis of (*Z*)-vinylsilanes produces instead the α-vinylsilanes with appropriately positioned hydroxyl groups.[67] For the homopropargylic system shown (Scheme 28), the selectivity is 98:2. For propargylic or bishomopropargylic systems only small amounts (2–13%) of the α-product are formed. Mechanistically, this result would seem to imply an initial hydroruthenation directed by ruthenium–hydroxyl interactions. Only recently has a proposal for achieving selectivity for a trans addition process by a hydrometallation mechanism appeared[33]

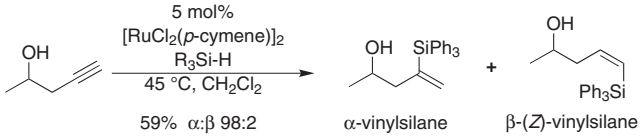
Table 11 Iridium Catalysis



				Product ratio			Yield (%)	
Entry	Silane	Temp	Alkyne[a]	**B**	**C**	**D**	**B** + **C** + **D**	**E**
1	$MePh_2SiH$	r.t.		2	97	1	87	2
2	$MePh_2SiH$	r.t.	Cy	4	74	22	81	6
3	$MePh_2SiH$	65 °C	Cy	45	44	11	75	13
4	$MePh_2SiH$	65 °C	*t*-Bu	58	29	15	28	32
5	Et_3SiH	r.t.	Ph	5.5	91	3.5	81	4
6	$(MeO)_3SiH$	r.t.	Ph	39	57	4	19	1

[a] Cy = cyclohexyl.

(Scheme 10), and the overall mechanism as well as the nature of the hydroxyl direction with $[RuCl_2(p\text{-cymene})]_2$ remain obscure.

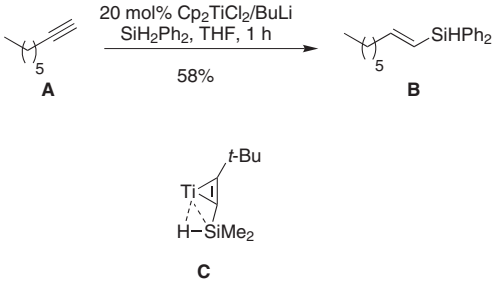


Scheme 28 Hydroxyl-directed terminal alkyne hydrosilylation.

While functional group direction is one strategy for the formation of α-vinylsilanes, cationic cyclopentadienylruthenium complexes have been shown to give selective α-vinylsilane formation without a directing group (Table 13).[31] The catalyst is compatible with alcohol, acid, protected amine, and internal alkyne functionality, and importantly succeeds with alkyl-, aryl-, halo-, and alkoxy-substituted silanes. Cyclopentadienylruthenium catalysts remain the only general method for accessing α-vinylmetal species by hydrometallation without the need for neighboring functional groups.[68]

Other metals have also been employed for alkyne hydrosilylation. A palladium-catalyzed reaction was recently reported to provide exclusive cis addition and good selectivity for the terminal silane, similar to platinum-based catalysts. The catalyst system, $Pd_2(dba)_3$ + 4 PCy_3, is unreactive to internal alkynes and succeeds with a range of aryl and alkyl terminal alkynes.[69]

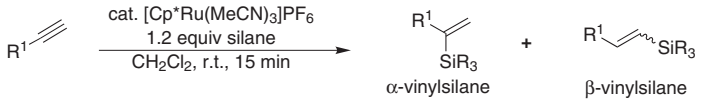
Early transition metal catalysts have been little used in alkyne hydrosilylation. Cp_2Ti (formed in situ) has been shown to catalyze the hydrosilylation of simple terminal and symmetrical internal alkynes in modest yield (see Scheme 29).[70] The authors postulate that the requirement for a silyl dihydride (or trihydride) may derive from a stabilizing agnostic interaction akin to that observed in a silyl alkyne complex **C**.[71a,b] Other explanations are possible, including titanium silylene intermediates.[71c]

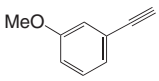
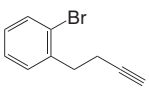
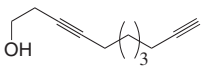
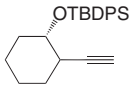
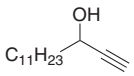
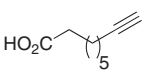


Scheme 29 Hydrosilylation catalyzed by titanocene.

The use of actinide catalysts of uranium and thorium has recently appeared. Complexes of the type $Cp^*_2UMe_2$ catalyze the hydrosilylation of terminal alkynes. The authors propose an unusual mechanism based on alkynyl actinide intermediates.[72a] A related mechanism has been invoked for thorium complexes, where increased activity is observed upon switching to a bridging *ansa*-$Me_2SiCp''_2$ ligand ($Cp'' = C_5Me_4$), which allows for a more open coordination site.[72b]

Table 13 Markovnikov Hydrosilylation of Terminal Alkynes

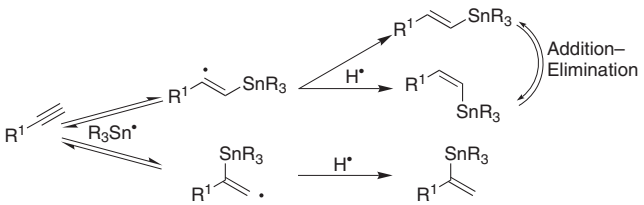


Entry	Alkyne	Silane	Cat (%)	Ratio α:β	Yield (%)
1		$(EtO)_2MeSiH$	1	9:1	86
2		$(EtO)_3SiH$	1	13:1	92
3		$(EtO)_3SiH$	1	9:1	71[a]
4		$(EtO)_3SiH$	5	20:1	87
5		$(EtO)_3SiH$	1	13:1	58
6[b]		Et_3SiH	1	20:1	89

[a] No reaction at the internal alkyne was observed with 1.05 equiv silane.
[b] $[CpRu(MeCN)_3]PF_6$ was used as catalyst.

3.3 Hydrostannation of Terminal Alkynes

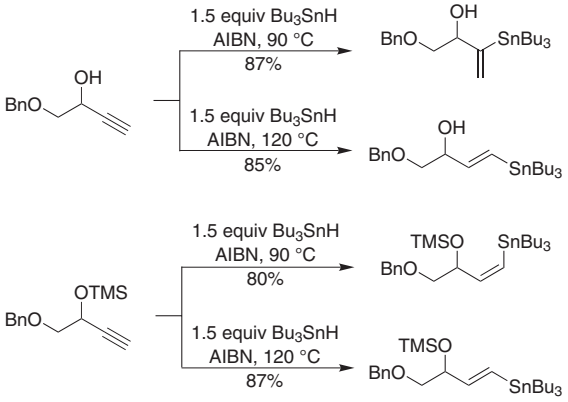
Hydrostannation of alkynes, like hydrosilylation, generally will not occur without catalysis except for reactions with highly activated electron-poor alkynes. Transition metal catalysts, therefore, play a significant role in the synthetic use of hydrostannation. The most important method for the addition of a H–Sn bond to an alkyne, however, has been the radical-induced process. Treatment of alkynes with a tin hydride and a radical initiator induces insertion of a tin-centered radical to create one of two regioisomeric vinylstannane radicals. Hydrogen atom abstraction then produces one of three isomeric vinylstannane products (see Scheme 30). In general, for terminal alkynes, the β-stannyl intermediate is favored due to the stability of the more substituted vinyl radical. Both kinetic and thermodynamic factors affect product distribution, as the two β-stannyl products may interconvert during the reaction by radical addition–elimination processes. This can be used to advantage in cases where one product olefin stereoisomer is strongly favored on thermodynamic grounds.[73]



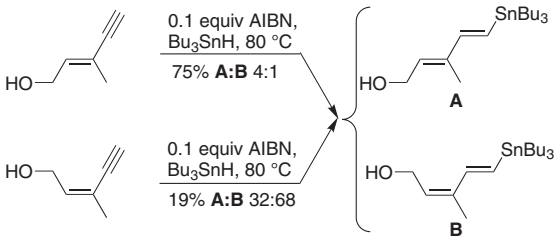
Scheme 30 Mechanism of radical alkyne hydrostannation.

An important substrate class that has been shown to offer good selectivities is propargylic alcohols.[74] Terminal alkyne propargylic alcohols direct radical cyclization to provide the α-stannyl isomer (see Scheme 31).[74a] It was demonstrated, however, that more extensive heating produces instead the (*E*)-β-vinylstannane.[74c] Furthermore, protection of the alcohol as its TMS derivative leads to the formation of the normal kinetic product, the (*Z*)-β-vinylstannane, and that increased temperatures in this case also produce the (*E*)-β-vinylstannane.[74] Unfortunately, rigorous identification of product selectivity is not given. The hydrostannation of propargylic alcohols has until recently been the only general hydrometallative synthesis of such α-vinylmetal species (see Table 13).

Systems with extended conjugation are typically good substrates. Enynes and enynols exhibit good (*E*)-β-vinylstannane selectivity (Scheme 32).[9] In general, radical hydrostannation suffers from poor selectivities, with outcomes in more complicated systems difficult to predict. Furthermore, the high temperatures necessary for reactivity (generally 80–120 °C) often cause problems with complicated substrates. 9-BBN has been introduced as an alternative radical activator active at low temperatures to circumvent these problems.[75]



Scheme 31 Altering selectivities for propargylic alcohols and ethers.



Scheme 32 Radical addition to enynes.

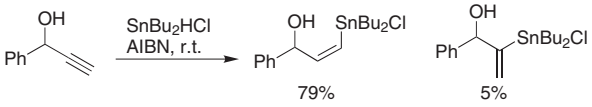
Sonochemical activation by ultrasound irradiation has been employed to initiate hydrostannation of terminal alkynes. A limited study (Table 14) found that irradiation in air effected hydrostannation, without the need for traditional activators such as AIBN, at low temperatures (reaction at –55 °C, entry 2). Selectivity for the kinetic (*Z*)-vinylstannane is obtained for 1-hexyne and phenylacetylene (entries 1–4).[76] Although the underlying basis for the observed reactivity is not yet known, the process may be a mild alternative to the high temperatures typically required for radical hydrostannation.

Table 14 Sonochemical Initiation of Radical Hydrostannation

Entry	Alkyne	Solvent	Temp (°C)	Ratio *Z*:*E*	Yield (%)[a]
1	Ph	toluene	6	73:23	83
2	Ph	THF	–55	87:13	61
3	*n*-Bu	none	7	92:8	95
4	*n*-Bu	THF	7	93:7	72
5	TMS	toluene	–8	8:92	78

[a] Total yield of both isomers.

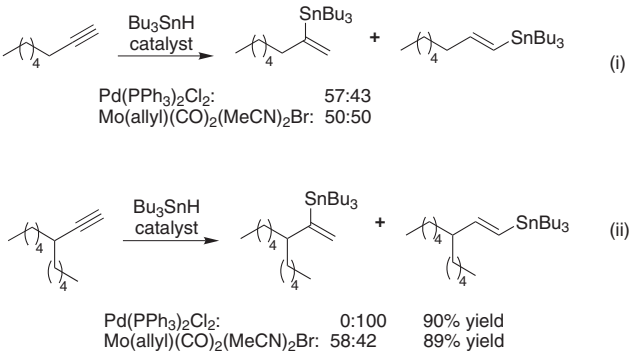
Dialkyltin hydride halides (e.g. Bu_2SnHCl) have recently been introduced as a more Lewis acidic hydrostannation reagent, and a large study indicates good selectivity for the (*Z*)-β-vinylstannane with a variety of propargylic alcohols (Scheme 33), though other directing groups meet with less success.[75b] The authors attribute the selectivity to coordination effects with the more Lewis-acidic tin.



Scheme 33 Use of dialkyltin hydride halides.

Metal-catalyzed hydrostannation of alkynes is a field of continuing development. A significant amount of initial work focused on phenylacetylene and its derivatives, where a host of metal complexes have been investigated (see Table 15).[6,77–80] While several rhodium complexes (entries 1–3) provide useful levels of α-stannane selectivity, perhaps the most surprising message of these results is the difficulty in obtaining selective formation of either of the synthetically important β-stannane stereoisomers with transition metal catalysts. Only ruthenium results in good regioselectivity, but provides the β-stannane product as a nearly 1:1 mixture of isomers (entry 9). Palladium catalysis, on the other hand, offers the advantage of displaying complete selectivity for the (*E*)-β-vinylstannane stereoisomer **B** without contamination from the *Z*-olefin isomer (entries 5, 6). This apparent stereospecificity has made palladium the most studied catalyst in a wide variety of substrate types. The Lewis-acidic $ZrCl_4$ (entry 11) does provide clean trans addition to give only the (*Z*)-β-stannane product in reasonable yield, a result which has been shown to be general for alkyl alkynes and terminal enynes as well.[79]

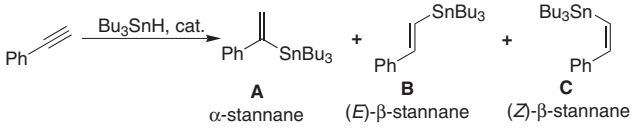
Simple alkyl alkynes are even more troublesome. Although an early report indicates some reason for optimism,[81] palladium or molybdenum catalyses provide almost no selectivity with 1-octyne (Scheme 34, i).[82] However, palladium is capable of delivering a single product isomer for terminal alkynes with significantly bulky substituents (Scheme 34, ii).



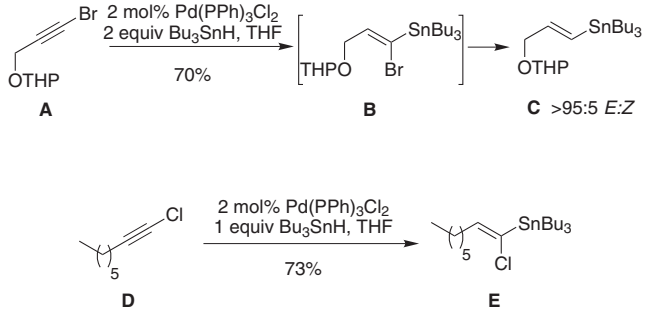
Scheme 34 Hydrostannation of alkyl alkynes.

The problems with simple terminal alkyne hydrostannation are illustrated by an attempt to perform selective hydrostannation of a propargyl glycine derivative. It was hoped that coordination to either of two heteroatom groups might allow selectivity, but an extensive screen

Table 15 Metal-Catalyzed Hydrostannation of Phenylacetylene



Entry	Catalyst	Temp (°C)	Product ratio A	B	C	Yield (%)
1	$Rh(PPh_3)_3Cl$	r.t.	88	12	0	86
2	$Rh(CO)(PPh_3)_2Cl$	0	78	20	2	99
3	$[Rh(cod)Cl]_2$	0	81	13	6	66
4	$Ni(PPh_3)_2Cl_2$	r.t.	45	50	5	80
5	$Pd(PPh_3)_2Cl_2$	0	46	54	0	82
6	$Pd(PPh_3)_4$	r.t.	50	50	0	96
7	$Pt(PPh_3)_2Cl_2$	r.t.	34	52	14	73
8	$Co(PPh_3)_2Cl_2$	0	43	48	9	40
9	$Ru(PPh_3)_4Cl_2$	r.t.	11	42	47	78
10	$Mo(allyl)(CO)_2(MeCN)_2Br$	r.t.	47	53	0	56
11	$ZrCl_4$	0	0	0	100	73



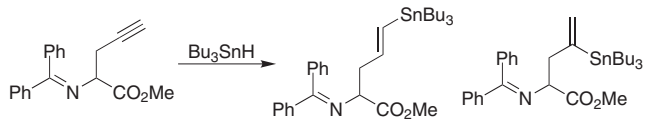
Scheme 35 Haloalkynes as directing groups for hydrostannation.

was unable to determine an appropriate catalyst.[83] Several attempts are shown in Table 16.

A solution, albeit an indirect one, to the problem of poor regiocontrol with unbranched linear alkynes is the use of haloalkynes (Scheme 35).[82] For bromoalkynes (**A**), excess Bu_3SnH and a palladium catalyst result in the formation of the (*E*)-α-stannane **C** with >20:1 regio- and stereocontrol. The reaction likely proceeds through a bromo-vinylstannane from normal hydrosilylation, followed by debromination through a palladium-catalyzed pathway or possibly an α-elimination to an alkylidene carbene. In the case of chloroalkynes, the 1-chloro-1-stannyl olefin (Scheme 35, **E**) was stable enough to allow its isolation as a single isomer.

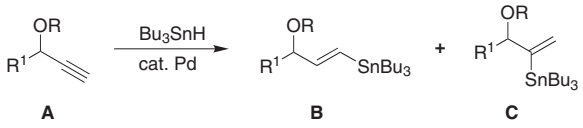
As a general rule, selective hydrostannations of terminal alkyl alkynes have thus far been demonstrated only for (*E*)-β-stannane products of alkynes substituted with sterically bulky groups using palladium catalysis. Propargylic alcohols are a substrate class that has been particularly well-exploited (see Table 17). Although primary propargyl alcohols give poor selectivity for the α-vinylstannane with palladium catalysts (entries 1–3),[78,82] secondary alcohols begin to show some selectivity for the β-vinylstannane (entries 4, 5).[82] Tertiary propargylic alcohols provide very good selectivity.[9,84]

Table 16 Hydrostannation of a Phenylglycine Derivative

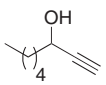
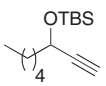
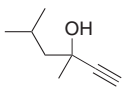
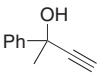
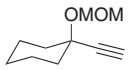
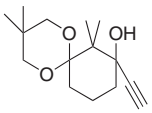


Entry	Catalyst	Product yield (%) β-Stannane	α-Stannane	Reduction (terminal olefin)
1	$Pd(PPh_3)_4$	43	46	0
2	$Pd(PPh_3)_2Cl_2$	35	50	0
3	$Pd(MeCN)_2Cl_2$	21	16	21
4	$Rh(PPh_3)_3Cl$	13	8	10
5	$Pt(PPh_3)_2Cl_2$	8	31	4

Table 17 Hydrostannation of Propargylic Alcohols Catalyzed by Palladium

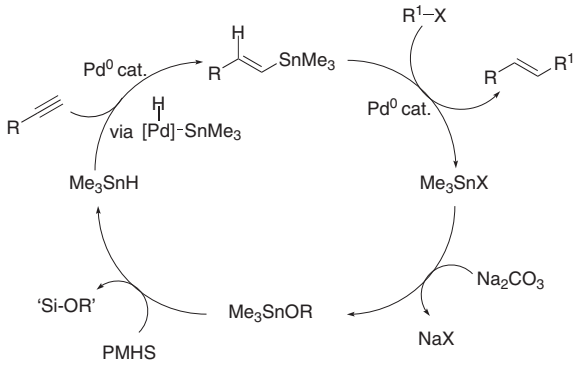


A B C

Entry	Alkyne	Catalyst	Yield (%)	Ratio **B**:**C**	Ref.
1		$Pd(PPh_3)_4$	95	1:1.6	78
2		$Pd(PPh_3)_4$	95	1:1.9	78
3		$Pd(PPh_3)_2Cl_2$	68	1:2	82
4		$Pd(PPh_3)_2Cl_2$	–[a]	3:1	82
5		$Pd(PPh_3)_2Cl_2$	94	2.6:1	82
6		$Pd(PPh_3)_2Cl_2$	66[b]	24:1	84
7		$Pd(PPh_3)_2Cl_2$	86[b]	12:1	84
8		$Pd(PPh_3)_2Cl_2$	65	1:0	9
9		$Pd(PPh_3)_2Cl_2$	70	1:0	9

[a] Yield not reported.
[b] Reactions performed with in situ generation of Bu_3SnH from Bu_3SnCl and poly(methylhydrosiloxane). See Table 18.

These selectivities form the basis for the design of a new reaction catalytic in tin. There are obvious benefits to vinyltin species: they are highly reactive, relatively stable, and very well-studied. However, the significant cost and especially the toxicity of organostannanes raises concerns about their use in research settings and is a huge problem in large-scale industrial applications. In addressing this concern, one of the most exciting recent discoveries is the development of a one-pot hydrostannation–cross coupling, catalytic in tin, and employing polymethylhydrosiloxane (PMHS) as the terminal reductant.[85]

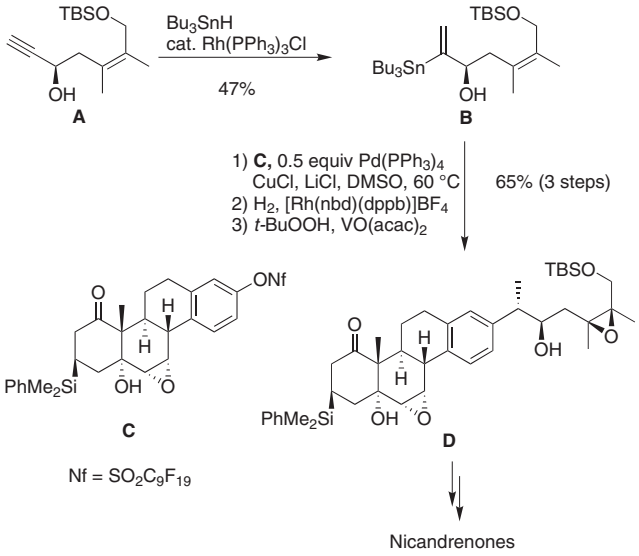


Scheme 36 Proposed mechanism of Stille reaction catalytic in tin.

The reaction uses the known ability of PMHS to reduce organotin oxides to the corresponding hydrides[86] (the authors propose that a tin carbonate is the oxidizing agent in their system) to regenerate tin hydrides from the Sn-X species formed from Stille coupling (see Scheme 36). Since both the hydrostannation and the coupling reaction are palladium-catalyzed processes, a single metal can be active in both cycles; the authors, however, found that the addition of two different palladium sources together with an electron poor phosphine provided the most satisfying results (see Table 18). Starting from hindered alkynes bearing α-heteroatoms, very good yields of the *E*-olefin cross coupling products can be obtained. The use of less sterically demanding and more reactive trimethylstannanes is essential to ensure that coupling occurs faster than decomposition pathways.

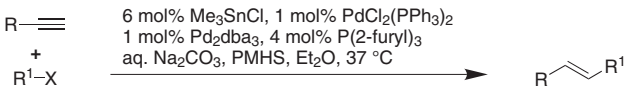
For the purposes of this review, another noteworthy aspect of the work is that its most significant drawback appears to be the lack of general, selective hydrostannation catalysts. This requires the use of tertiary propargylic amines and alcohols to selectively obtain vinylstannanes. If this issue could be remedied, the catalytic tin Stille reaction might be a more widely useful process. Recently, the use of hydrostannation in tandem processes has been expanded to include a rhodium-catalyzed process of tandem hydrosilylation–conjugate addition of alkynes.[87]

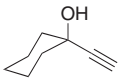
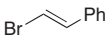
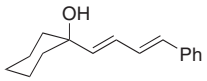
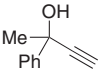
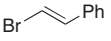
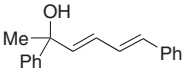
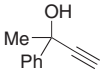
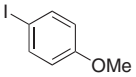
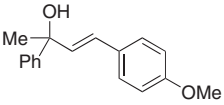
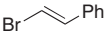
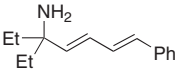
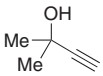
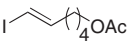
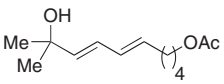
A rhodium-catalyzed hydrostannation of terminal propargylic alcohols has been used in a synthesis of the nicandrenones.[88] A modest-yielding process accesses the vinylstannane **B** (Scheme 37) necessary for a challenging key coupling reaction with the complex perfluorononylsulfonate **C**, a coupling which required substantial study and optimization.[89]



Scheme 37 Synthesis of nicandrenones.

Table 18 Hydrostannation–Stille Coupling Catalytic in Tin



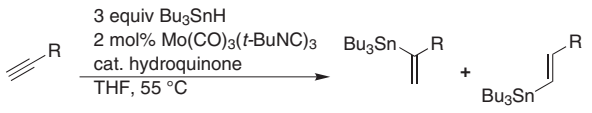
Entry	Alkyne	R^1-X	Product	Yield (%)
1				90
2				85
3				80
4				86
5				80[a]

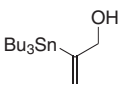
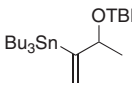
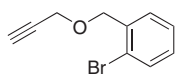
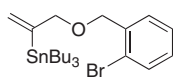
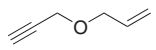
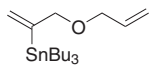
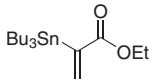
[a] Both the starting vinyl iodide and the product were 4:1 mixtures of *E/Z* isomers.

The limited scope of alkynes that render selective palladium-catalyzed hydrostannations spurs chemists to find more selective catalysts. Molybdenum has emerged as one possible solution. From some early results,[82] screening several molybdenum(0) complexes yielded the stable isocyanide complex $Mo(CO)_3(t\text{-BuNC})_3$.[80,90] The complex was designed with the notion that the more labile (relative to CO) isocyanide ligands would create a more active catalyst, while at the same time being more likely than the volatile CO ligands to remain available to stabilize coordinatively unsaturated centers, thus extending catalyst lifetime. The results are shown in Table 19. Useful regioselectivities are observed for a large range of alkynes with propargylic oxygenation, including internal alkynes (see section 4.3, Table 32, vide infra). This interesting work leaves open several questions. The authors argue for steric differentiation in determining regioselectivity, yet no substrates without propargylic oxygenation are reported. Coordination to a propargylic oxygen could also help account for the selectivities, but in that case the high selectivity observed in entry 2 with a TBDPS ether, normally considered a poor coordinating group, seems an anomaly. An oxidative addition followed by stannylmetallation is favored by the authors, though more work is probably merited to fully reconcile a mechanistic hypothesis with these results. The simple molybdenum catalyst does, however, appear to be a useful advance in the selective synthesis of α-vinylstannanes.

As a class, α,β-alkynyl esters and ketones exhibit good selectivity for the (*E*)-α-vinylstannane (Table 19, entry 5), and several applications have been demonstrated. Terminal alkynes and internal alkynes are both possible and successful substrates, but as most examples and applications deal with internal alkynes, the topic will be addressed in section 4.3.

Table 19 Molybdenum-Catalyzed Hydrostannation



Entry	Alkyne	Major product	Yield (%)[a]	Ratio α:β
1			94	89:11
2			88	90:10
3			44	>95:5
4			43	>95:5
5			98	92:8

[a] Isolated total yield of both regioisomers.

4 Internal Alkynes

In contrast to terminal alkynes, where reactivity, chemoselectivity, regioselectivity, stereochemistry, and mechanism are often well-investigated, internal alkynes have received far less attention. Given the challenges of trisubstituted olefin synthesis in general, this lack of attention is probably to the detriment of the synthetic community. The issues of stereochemistry and even reactivity are rather poorly documented, despite significant recent work in these areas. There are probably four approaches to achieving regioselectivity with internal alkynes: (1) straight steric differentiation of the two alkyne substituents; (2) interaction (coordination) with neighboring heteroatom functional groups; (3) electronic differentiation of, for example, aromatic alkynes or α,β-alkynyl esters where the triple bond is significantly polarized; and (4) intramolecular delivery of tethered metal hydrides. Substrates and approaches may, of course, overlap one or more of these methods; in some cases, such as for secondary propargylic alcohols, it is difficult to say with certainty which of steric effects, coordination, or electronic effects is the most important factor.

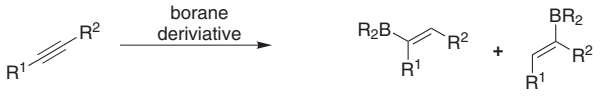
The mechanistic discussion in section 2 was presented almost entirely for terminal alkynes because the vast majority of the literature focuses on these substrates. However, most broad mechanistic classes should apply to internal alkynes as well, with the exception of a few mechanisms likely inoperable for internal alkynes such as those involving vinylidene intermediates (see Scheme 6).

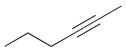
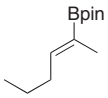
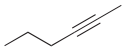
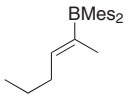
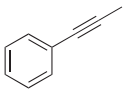
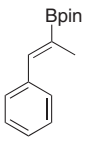
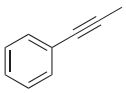
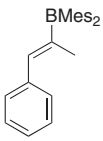
4.1 Hydroboration of Internal Alkynes

The uncatalyzed hydroboration process typically offers excellent yield with internal alkynes. Hindered dialkyl boranes (e.g. dimesitylborane[91]) as well as the boronate ester pinacolborane[39] (pinBH) provide excellent regioselectivity, based on steric discrimination, for the less hindered vinylborane product (Table 20).

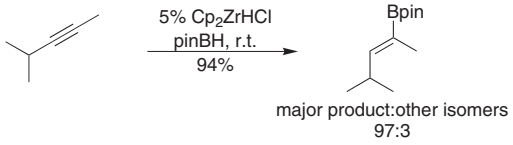
Catalyzed reactions that provide complementary regioselectivity, employ substrate coordination for regiocontrol, or provide access to the trans addition product for hydroboration of internal alkynes have not yet been reported. It has been shown, for instance, that zirconium catalysis provides good selectivity for hydroboration of 4-methyl-2-pentyne (Scheme 38).[52] This selectivity could certainly be achieved by the conventional, uncatalyzed process, though it does proceed at lower temperature, perhaps allowing enhanced chemoselectivity in some applications. The mechanism of this process is assumed to be analogous to that for the reactions of terminal alkynes (see Scheme 22).

Table 20 Uncatalyzed Hydroboration of Internal Alkynes



Entry	Alkyne	Borane[a]	Major product	Yield (%)	Ratio
1		pinBH		75	93:7
2		Mes_2BH		95	9:1
3		pinBH		69	85:15
4		Mes_2BH		94	98:2

[a] pinBH = pinacolborane, Mes_2BH = dimesitylborane.



Scheme 38 Zirconium-catalyzed hydroboration of an internal alkyne.

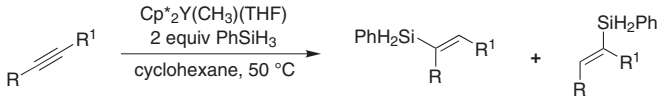
4.2 Hydrosilylation of Internal Alkynes

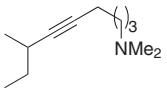
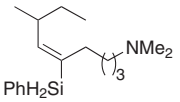
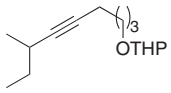
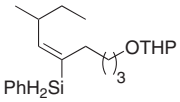
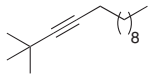
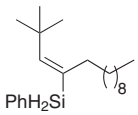
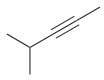
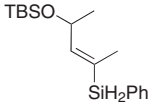
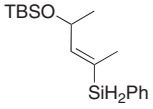
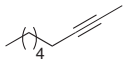
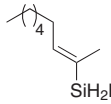
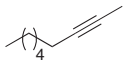
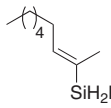
Probably the only very successful, broad method of steric differentiation of internal alkynes employs an yttrium catalyst.[92] As shown in Table 21, exceptional regioselectivity is observed for alkynes bearing an α-branch point on one side (entries 1,2). Even the discrimination of methyl for straight-chain alkyl is possible, providing a 7.2:1 mixture of regioisomers when the more discriminating catalyst $Cp^*_2Y[CH(TMS)_2]$ is used (entry 7). A secondary propargylic silyl ether (entry 4) provides complete selectivity for the β-silyl product, though similar selectivity with a primary propargylic silyl ether (entry 5) indicates that factors others than sterics – such as electronics or catalyst coordination – must also be involved. Noteworthy is the tolerance of the reaction for an unprotected tertiary amine (entry 1) and an acid-sensitive tetrahydropyranyl ether (entry 2). The catalyst system does have limitations, however. Severely hindered substrates (entry 3) suffer from poor turnover, as do even modestly electron-poor alkynes (entry 5). Perhaps the most important limitation is that of the silane. Only $PhSiH_3$ was employed in the study, limiting the adaptability and utility of the system for some applications. However, the phenylsilane dihydride products of the yttrium process are stable to chromatography and hydridosilanes have been employed in a host of subsequent transformations.[93,94]

One of the few other studies of internal alkynes involves the ruthenium catalyst $[Cp^*Ru(MeCN)_3]PF_6$. This complex provides exclusively trans addition to give (*Z*)-vinylsilane products (Table 22). Although trans addition processes to terminal alkynes are well-known, such catalysts generally provide cis addition processes for internal alkynes,[95] and Table 22 illustrates the first reported transition-metal catalyst affording a clean trans addition process with internal alkynes in intermolecular reactions. For unconjugated alkynes, some selectivity can be obtained (entries 1–4). Substrates with nearby olefins (entry 1) or alcohols (entry 3) may indicate the presence of directing effects. In general, however, the selectivity is modest and predictive ability is low. A substrate class with clean, predictable selectivity are α,β-alkynyl esters and ketones. Here, strong preference for the (*Z*)-β-silyl ester or ketone is observed, especially for silanes without an alkoxy substituent (entries 5–8).[31,96]

Propargylic alcohols are a substrate class that has also shown regioselectivity with the $[Cp^*Ru(MeCN)_3]PF_6$ catalyst (Table 23). The complex provides exclusive trans addition for all alkynes, and in this context provides the distal, (*Z*)-β-vinylsilane product.[96] The use of alkoxysilanes provides products that cyclize under the reaction conditions to give the cyclic siloxane. The poor stability of these species makes them difficult to isolate in good yield for sterically unhindered substrates (entry 1). Trialkylsilanes generally provide better regioselectivity, and

Table 21 A Sterically Discriminating Yttrium Catalyst



Entry	Alkyne	Major product	Yield (%)	Ratio[a]
1			73	100:0
2			84	100:0
3			28	100:0
4[b]			82[b]	100:0
5[b]			23[b]	100:0
6			81	4.1:1
7[c]			n.d.	7.2:1

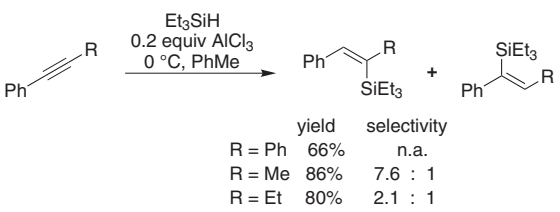
[a] Regioselectivity of (*E*)-vinylsilane isomers. No (*Z*) isomers were observed.
[b] Reaction temperature was 90 °C.
[c] Catalyst used was $Cp^*_2Y[CH(TMS)_2]$.

the use of benzyldimethylsilanes (BDMS) provides more robust vinylsilane products useful in subsequent oxidative[96] and cross-coupling[97] pathways. Regioselectivities vary somewhat (5:1 to 20:1) but are typically synthetically useful. An enyne (entry 7) provides very good regioselectivity and a vinylmetal product with stereochemistry complementary to that obtained for similar substrates in palladium-catalyzed hydrostannation (see Scheme 46).

Quite recently, ruthenium carbene complexes, more typically known as olefin metathesis catalysts, have been shown to act as alkyne hydrosilylation catalysts.[98] Trans addition is the major pathway with trialkylsilanes, even in a single example with an internal alkyne.[98a] This result represents one of the very few examples of the trans hydrosilylation of an internal alkyne.

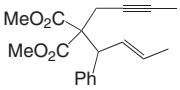
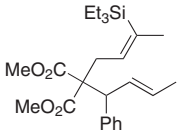
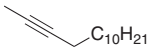
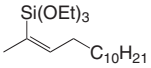
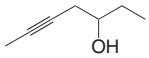
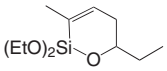
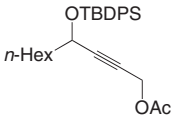
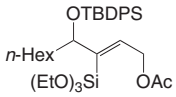
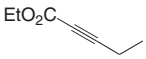
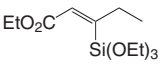
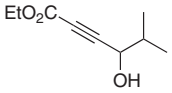
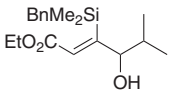
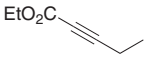
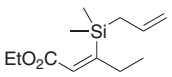
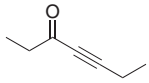
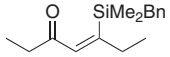
Strong Lewis acid catalysts have also been demonstrated to catalyze the addition of silanes to internal and terminal alkynes. Exclusive formation of the (*Z*)-vinylsilane from a trans addition process is reported. Yields are generally reasonable, though only two examples of unsymmetrical substrates are reported (Scheme 39).[19,21]

An important means of obtaining regioselectivity for intramolecular alkynes is tethering a silane to the alkyne, thereby creating an intramolecular hydrosilylation that is often very regio- and stereoselective. Pioneering studies



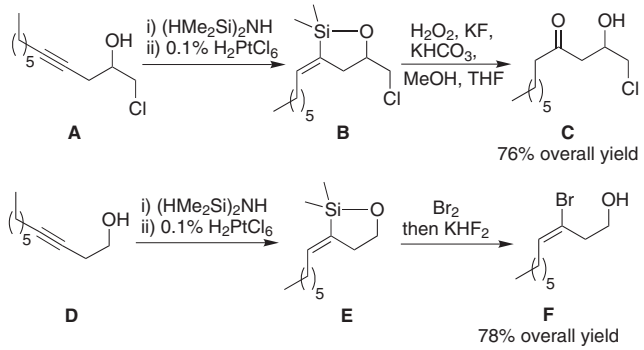
Scheme 39 Lewis acid hydrosilylation catalysis.

Table 22 Trans Hydrosilylation of Internal Alkynes[a]

Entry	Alkyne	Major product	Ratio[b]	Total yield (%)
1[d]			>20:1	70[c]
2			2.4:1	100
3			5:1	71[c]
4[d]			6:1	92
5			5:1	99
6			8:1	83
7			>20:1	85[c]
8			>20:1	94[c]

[a] Reactions performed in CH_2Cl_2 with 1 mol% $[Cp^*Ru(MeCN)_3]PF_6$ unless otherwise indicated.
[b] Ratio of two regioisomeric (*Z*)-vinylsilanes. No evidence of *cis* addition process was observed.
[c] Yield is given for pure major product.
[d] 5% catalyst loading.

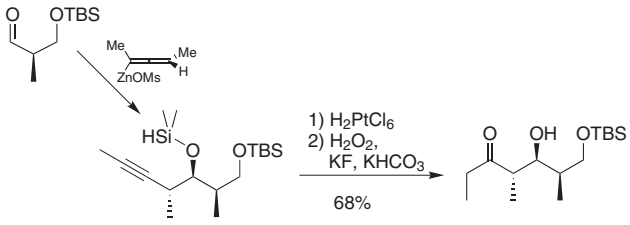
established that platinum catalysis (H_2PtCl_6) allows clean 5-exo-dig cyclization of silylated homopropargylic alcohols (Scheme 40).[99a] The resulting cyclic vinylsiloxanes were elaborated through bromination and oxidation[93] reactions. Alcohol silylation in intramolecular hydrosilylation reactions is typically performed through mild heating (40–80 °C) of the substrate alcohol in neat 1,1,3,3-tetramethyldisilazane (TMDS).[99]



Scheme 40 Intramolecular platinum hydrosilylation.

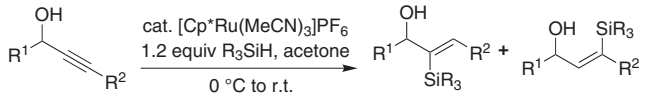
More recent applications of the intramolecular hydrosilylation of homopropargylic alcohols with platinum catalysis have expanded the utility of this reaction. Marshall has linked stereoselective aldehyde propargylation with hydrosilylation–oxidation sequences, providing access to stereodefined, highly substituted polyketide fragments (Scheme 41).[99b] Importantly, the strained 5-membered siloxacycle intermediate permits oxidation in the presence of primary TBS ethers, which is not generally true of Tamao–Fleming oxidations.[93]

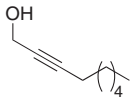
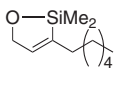
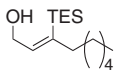
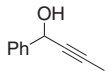
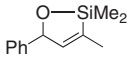
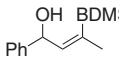
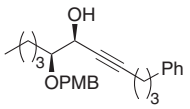
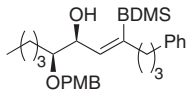
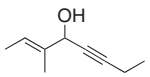
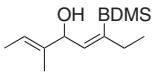
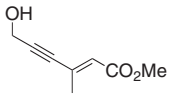
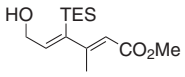
Denmark pursued intramolecular alkyne hydrosilylation in the context of generating stereodefined vinylsilanes for



Scheme 41 Hydrosilylation-based polyketide synthesis.

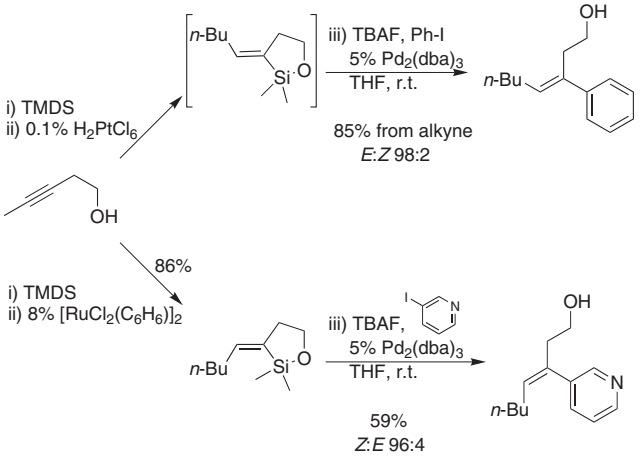
Table 23 Hydrosilylation of Propargylic Alcohols



Entry	Alkyne	Major product	Yield (%), ratio[b]
1[c]			30 N.D.
2			99 13:1
3			73[c] 5:1
4			91[c] 14:1
5			78[c] (91) N.D.
6			58 5:1
7			63[c] (84) >20:1

[a] Reactions performed in CH_2Cl_2 with 1–5 mol% $[Cp^*Ru(MeCN)_3]PF_6$.
[b] Ratio of two regioisomeric (*Z*)-vinylsilanes. No evidence of cis addition process is observed. Numbers in parenthesis refer to yield based on unreacted starting material. N.D. = not determined.
[c] Isolated yield of pure major isomer.

cross-coupling chemistry (Scheme 42). Cyclic siloxanes from platinum-catalyzed hydrosilylation were used in a coupling reaction, affording good yields with a variety of aryl iodides.[100] The three steps are mutually compatible and can be carried out as a one-pot 'hydro-arylation' of propargylic alcohols. The isomeric trans exo-dig addition was also achieved. Despite the fact that many catalysts for terminal alkyne hydrosilylation react poorly with internal alkynes, the group found that areneruthenium(II) chloride complexes – which provide complete selectivity for trans addition in terminal alkynes[67] (see Table 12) – facilitate a trans addition for intramolecular hydrosilylation with silylated homopropargylic alcohols as well.[101]

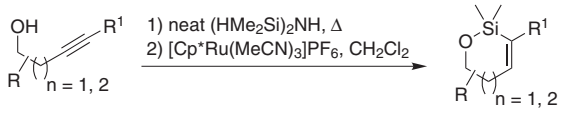


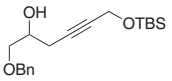
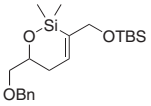
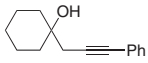
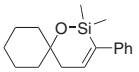
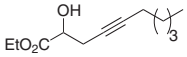
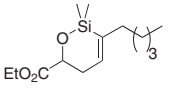
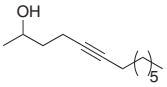
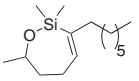
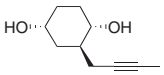
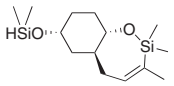
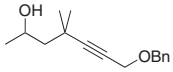
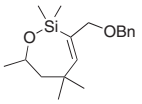
Scheme 42 Cross-coupling of cyclic siloxanes.

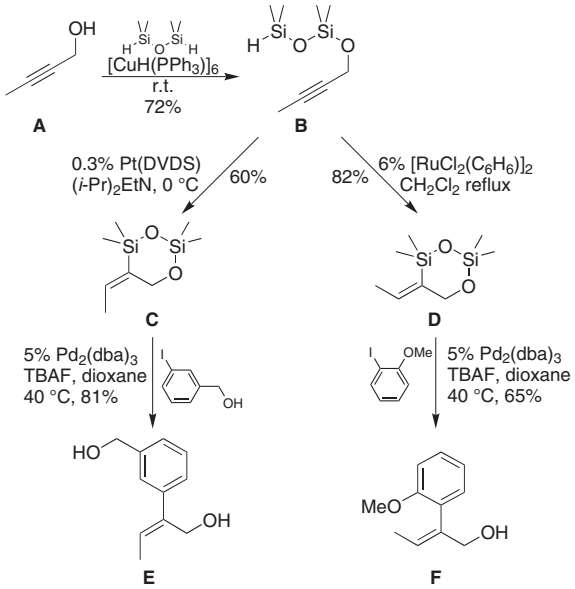
The final cyclization manifold has recently been realized with a different ruthenium catalyst. The cationic $[Cp^*Ru(MeCN)_3]PF_6$ induces exclusive endo-dig cyclization (Table 24) of both homopropargylic (entries 1–3) and bishomopropargylic (entries 4–6) alcohols.[30] The clean reaction to form a 7-membered ring is noteworthy for several reasons: intramolecular exo-dig cyclization with bishomopropargylic alcohols is not well-established, the platinum-catalyzed case has been reported to be problematic,[98] and the selectivity for 7-membered ring formation over the exo-dig cyclization to form a 6-membered ring is likely not thermodynamic. The endo-dig cyclization manifold was thus significant evidence that a re-examination of alkyne hydrosilylation mechanisms is necessary (see section 2.2).

While homopropargylic and bishomopropargylic silyl ethers can provide clean intramolecular reactivity, propargylic ethers have been unsuccessful in intramolecular hydrosilylation due to the strain of small-ring intermediates.[102] A successful approach to this problem using a disiloxane tether has recently appeared (Scheme 41). Tackling rather formidable technical obstacles, an O–Si–O–Si–H linkage was shown to allow exo-dig cyclization to the six-membered ring product, despite that fact that such cyclizations are known to be difficult in the analogous case of bishomopropargylic silyl ethers. The approach relies on a copper-catalyzed dehydrogenative silylation to produce the requisite, rather sensitive, tetramethyldisiloxane **B** (Scheme 43).[103] This substrate then participates in both a cis addition process with a platinum catalyst and a trans addition process catalyzed by $[RuCl_2(C_6H_6)]_2$ to afford vinylsilanes **C** and **D**, respectively. The approach showcases the result in the synthesis of the trisubstituted olefins **E** and **F** through palladium coupling reactions to access either olefin stereoisomer through choice of hydrosilylation catalyst.[104]

Table 24 Endo-Dig Hydrosilylation



Entry	Alkyne	Ru cat.	Product	Yield (%)[a]
1		1%		86
2[b]		5%		95
3		3%		77
4		1%		97
5		3%		85
6[c]		10%		92



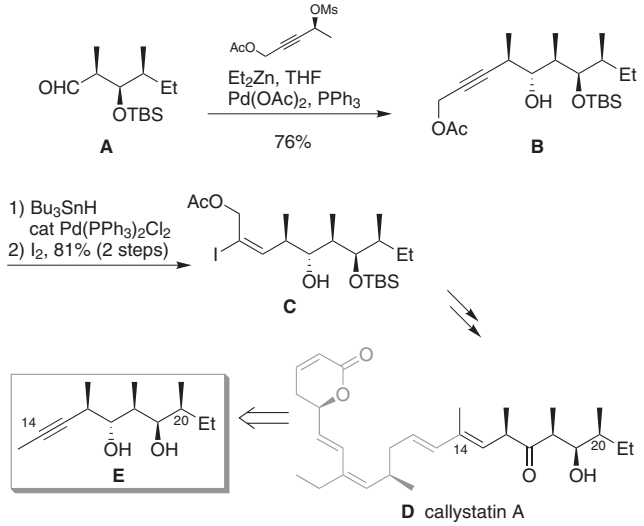
Scheme 43 Disiloxane tethers with a propargylic alcohol.

4.3 Hydrostannation of Internal Alkynes

Dialkyl alkynes have generally provided inconsistent and nonselective results in hydrostannation. There are some early results suggesting that neighboring hydroxyl groups might have a directing effect,[9,105] and Marshall pursued this in the context of a callystatin A synthetic project (Scheme 44).[106a] The approach required a trisubstituted vinylmetal species of the C14 to C20 fragment. All attempts to access such a species by hydrometallation of internal alkynes such as **E** – including hydrostannation, which provided very poor yield – failed. Propargylic oxygenation, later reductively deoxygenated, allowed the approach to succeed through vinyliodide **C**. Hydrostannation of the alkyne piece (**B**) provided the desired vinylstannane in good yield and complete regioselectivity.

In the course of this work, the group published a study of similar substrates (Table 25).[106b] In general, a propargylic primary alcohol appears to improve reactivity (the parent methyl alkyne **E** in Scheme 44 reacted slowly and gave poor yields) and to provide very moderate directing abilities for the proximal stannane product (**A** in Table 25). Together with a synergistic effect of steric bulk at the other alkyne substituent, excellent selectivities are obtained for several substrates. In general, acetoxy and hydroxyl subtrates behave similarly (c.f. entries 3,6), but some unexpected results are hard to explain; the TBS ether substrates (entries 5,7) are very selective with a free hydroxyl (>20:1), but results in only 3:1 selectivity with a propargylic acetoxy group.

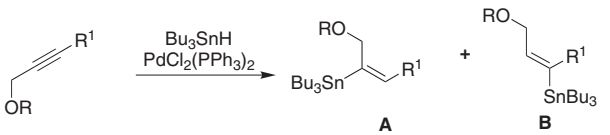
Recently, it was reported that performing palladium-catalyzed hydrostannations in hydrocarbon solvent greatly aided reaction efficacy (Scheme 45).[107] Tetrahydrofuran, as well as several other polar solvents resulted in a poor reaction. The use of the bulky tricyclohexylphosphine was

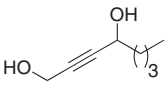
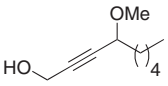
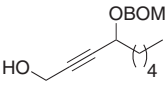
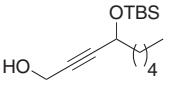
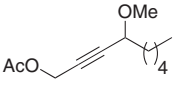
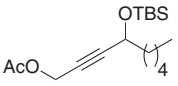
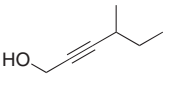


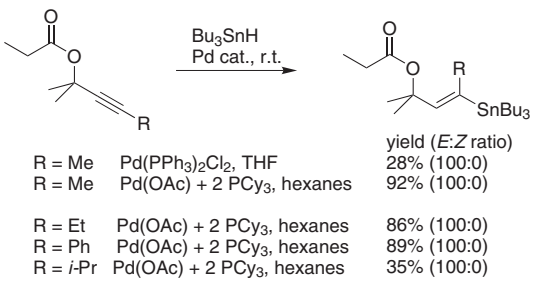
Scheme 44 Synthesis of callystatin A.

also found to be optimal, allowing hydrostannation to proceed for more substituted substrates. The generality of this ligand and solvent study to hydrostannation is an open question.

Table 25 Primary Propargylic Alcohol Hydrostannation



Entry	Alkyne	Total yield (%)	Ratio (**A**:**B**)
1		73	7:1
2		71	2.9:1
3		66	6.3:1
4		70	>20:1
5		69	>20:1
6		73	6.3:1
7		73	3:1
8		75	>20:1

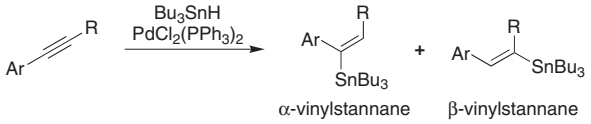


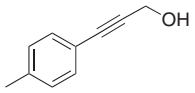
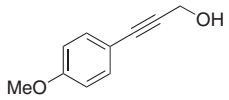
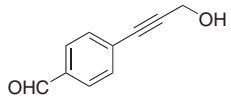
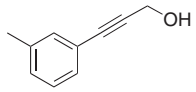
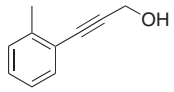
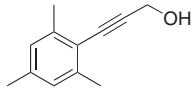
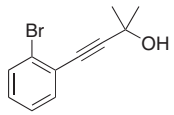
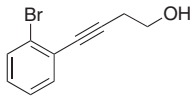
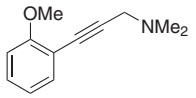
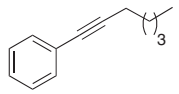
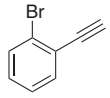
Scheme 45 Hydrocarbon solvents for hydrostannation.

While aromatic groups provide poor to modest selectivity in the hydrostannation of terminal alkynes (see Table 15), aromatic groups are moderate to excellent directing groups for palladium-catalyzed hydrostannation of internal alkynes.[108,109] Possibly for electronic reasons, the α-vinylstannane is favored in all cases (Table 26). Initial substituent studies determined that electron-poor aromatics provided very good selectivity (entry 3), while neutral or donating groups had only very modest α-stannane selectivity. Very intriguing results appear with a study of substitution pattern. While meta (entry 4) and para groups have only a minor effect on regioselectivity, ortho groups of all kinds result in extremely high selectivity for the same (*E*)-α-styrenylstannane product (entries 5–9). The reaction tolerates propargylic amines and alcohols – problematic groups for many transition-metal catalyzed reactions – but does not require the presence of propargylic heteroatoms for reactivity or selectivity (entries 8 and 10).

The ortho-substituent regiocontrol concept has been extended to include diaryl and heteroaryl-aryl alkynes, where the presence of an ortho substituent on one side of the alkyne dictates the sense of regioselectivity.[109] Electron-withdrawing groups could be used to bring about the same effect (Table 27, entries 1–3), but selectivity eroded for modest electron-withdrawing groups such as the ester of entry 3. All ortho-substituted diaryl alkynes provided good selectivity for a single regio- and stereoisomer, regardless of electronics, and heteroaryl substituents are tolerated as well (entry 6). The origin of this unique ortho-effect is not immediately clear. It does not appear to be a coordination effect (alkyl groups induce high selectivity, i.e. Table 27, entry 9), nor solely a steric effect (highly hindered alkyl groups do not affect the regioselectivity, i.e. Table 26, entry 7). The authors postulate that ortho-substituent-induced electronic perturbations of the alkyne may be the source of the observed selectivity. They cite ^{13}C NMR data showing a 2–5 ppm downfield shift in the C_β of the alkyne for ortho-substituted substrates compared to the corresponding para-substituted species.[109] However, the modest directing effects of para substituents with rather strong electron-donating and -withdrawing abilities would argue strongly against a solely electronic basis for selectivity. Another possible explanation is the extent to which aryl-olefin conjugation is maintained in the transition state, with ortho substituents generating significant strain for conjugated conformations. Again, the lack of

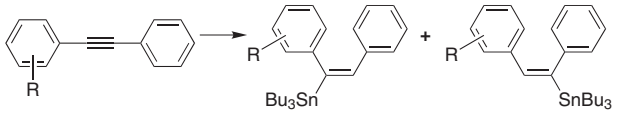
Table 26 Hydrostannation of Internal Aryl-Alkyl Alkynes

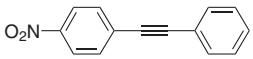
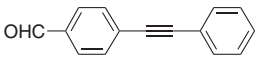
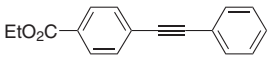
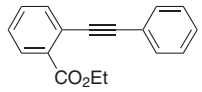
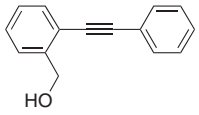
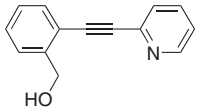
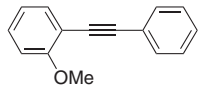
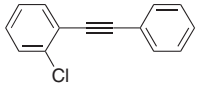
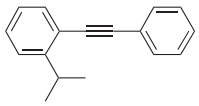
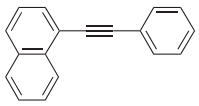


Entry	Alkyne	α-Product[a]	β-Product[a]
1		64	19
2		65	20
3		74	0
4		59	11
5		92	5
6		81	0
7		96	0
8		86	0
9		66	0
10		89	0
11		93	0

[a] Isolated yield of pure regioisomers. In all cases no (*Z*)-vinylstannanes from trans addition are observed.

Table 27 Hydrostannation of Diaryl Alkynes with Palladium



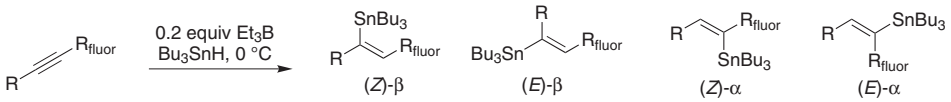
Entry	Alkyne	Total yield (%)[a]	Ratio α:β
1		75	100:0
2		98	85:15
3		81	75:25
4		81	100:0
5		95	100:0
6		81	100:0
7		94	90:10
8		85	100:0
9		76	100:0
10		67	100:0

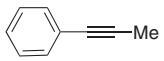
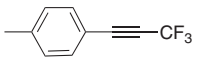
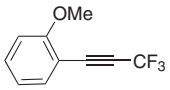
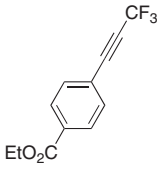
[a] Isolated yield. All reactions performed at r.t. in THF with 1 mol% $Pd(PPh_2)_2Cl_2$ for 15 min.

mechanistic data hinders efforts to explain the observed selectivity; at the crudest level, it is not clear if C–H bond formation occurs before or after C–Sn bond formation. The regiocontrolled vinylstanne products have been used in subsequent cross-coupling chemistry as a selective access to diaryl- and triaryl-substituted olefins.[110]

A study of trifluoromethyl derivatives of aryl alkynes revealed a unique regiopreference. The parent 1-phenyl-1-propyne under Et_3B-mediated conditions has been shown to provide selectively the β-vinylstannane with poor *E*/*Z* selectivity (Table 28, entry 1).[111] Although the reaction could be catalyzed by transition metals, the best results were obtained under radical conditions.[112] Good isomeric selectivity for the trans addition process with aryl-trifluoromethyl alkynes affords the product with regioselectivity opposite to that seen in simple aryl-alkyl alkynes (product (*Z*)-α, entries 2, 3; cf. Table 26). Unfortunately, an alkyl derivative (entry 5) displayed significantly diminished yield and isomeric purity. The electron-poor arene substrate (entry 4) suffers from an erosion in regioselectivity and provides only (*E*)-vinylstannane products.

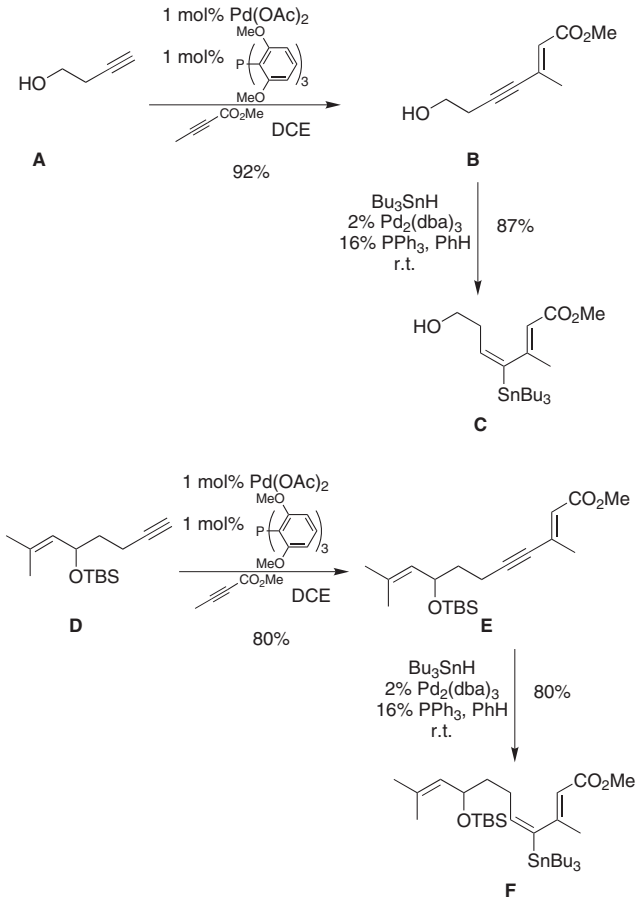
Table 28 Hydrostannation of Fluorous Alkynes



		Product ratio				
Entry	Alkyne	(*Z*)-β	(*E*)-β	(*Z*)-α	(*E*)-α	Yield
1		75	25	0	0	74
2		0	0	98	2	91
3		0	0	100	0	89
4		0	35	0	65	78
5	*n*-$C_{10}H_{21}$—≡—CF_3	0	0	62	38	32

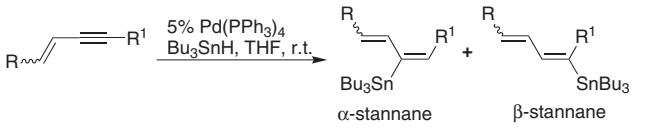
Other conjugated internal alkynes have also been shown to function well in regioselective hydrostannations. An initial study of enynes focused on electron-poor enynoate systems, which are readily accessible through palladium-catalyzed alkyne addition,[113] as shown in Scheme 46. Completely regiocontrolled hydrostannation produced the γ-stannyl unsaturated ester (**C**, **F**).[114] The sense of addition is the same as that observed for α,β-alkynyl esters (vide infra), and is complementary to that observed in a hydrosilylation reaction (Table 23).

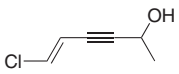
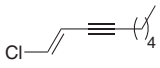
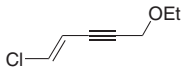
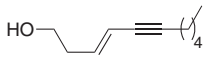
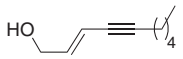
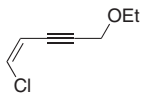
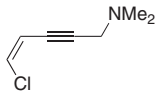
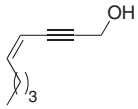
Since that time, groups have expanded the use of conjugated olefins to direct regioselectivity in alkyne hydrostannation. In an initial study of chloroenynes as building blocks for the synthesis of endiyne natural products such as neocarzinostatin, the *cis*-chloro compounds exhibited uniformly high α-stannane selectivity and produced only the *E*-olefin isomer products (Table 29, entries 6, 7). The corresponding *trans*-chloroenynes (entries 1–3) exhibited markedly lower selectivity in some cases (entry 3), despite excellent selectivity for other cases. Expanding the scope of investigation to alkyl substituents, the same trend emerged, with *cis*-olefins (entry 8) providing complete selectivity and *trans*-enynes (entries 4, 5) producing mixtures of products.[115]



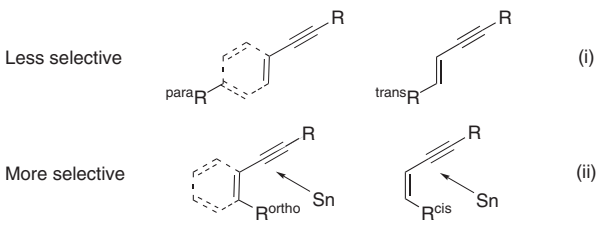
Scheme 46 Dienylstannane synthesis by palladium catalysis.

Table 29 *Cis*- and *Trans*-Enynes



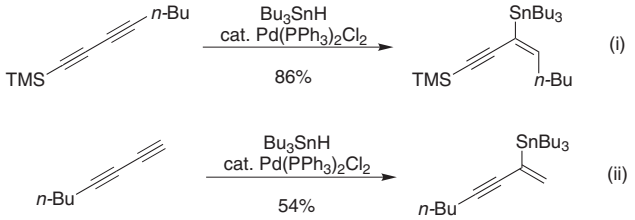
Entry	Alkyne	Yield α-stannane (%)	Yield β-stannane (%)
1		74	0
2		86	0
3		62	15
4		41	24
5		17	34
6		68	0
7		85	0
8		83	8

There appear to be significant effects from proximal substrate heteroatoms clouding the data from this study. However, the general trend mirrors that for aryl alkynes (Table 26 and Table 27), and the structural similarity of the more and less selective isomers (Scheme 47) indicates that similar factors may be at work. As discussed previously (see section 2.3), if the generally accepted mechanism of insertion of the alkyne into a Pd–H bond is operative, then the effect is not simply one of sterics, as an ortho/cis substituent should favor more β-stannane, the opposite of what is observed. It may be that stannylpalladation best explains these results.



Scheme 47 Isomer effects on hydrostannation.

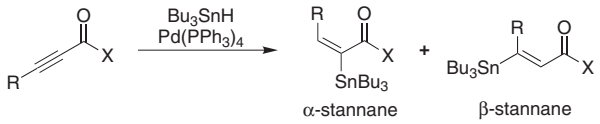
A few examples of diyne hydrostannation have been published, with encouraging results in line with the enyne preference for α-stannylated products (Scheme 48). A TMS group serves to block stannylation in a chemoselective reaction of internal alkynes, while the terminal alkyne reacts preferentially in a monosubstituted diyne system.[82]

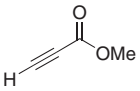
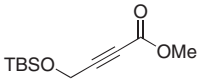
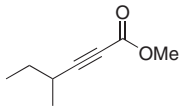


Scheme 48 Diyne substrates for hydrostannation.

Alkynyl esters are a generally reliable substrate class with palladium catalysis, providing the (*E*)-α-stannyl enoate in useful selectivity and yield.[82,116,117] A few representative examples are shown in Table 30.

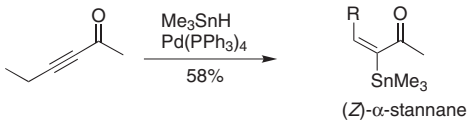
Table 30 Hydrostannation of Electron-Poor Alkynes



Entry	Alkyne	Yield (%)[a]	Ratio α:β
1		94[b]	100:0
2		84	91:9
3		93	98:2

[a] Isolated total yield of both regioisomers.
[b] Catalyst used is $Pd(PPh_3)_2Cl_2$.

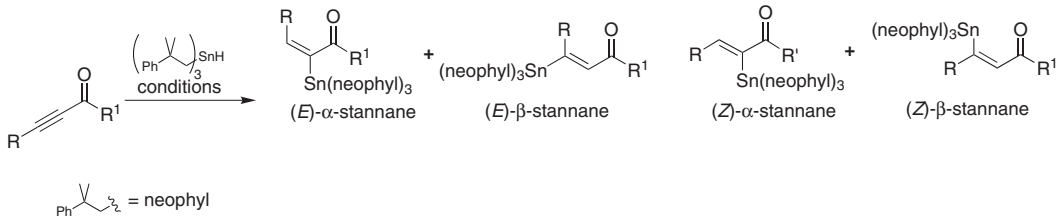
Ketones have significantly more difficulty in selective hydrostannation; protodestannylated products and olefin isomers can prevent clean conversion to the desired product. The nature of the groups on tin also have an effect on the products observed. For example, the use of trimethyltin hydride with catalytic $Pd(PPh_3)_4$ provided a modest yield of isomerically pure (*Z*)-α-stannane (Scheme 49).[116]

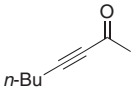
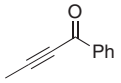
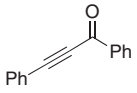
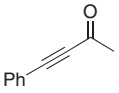
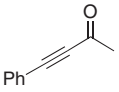
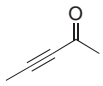


Scheme 49 Ketone hydrostannation with palladium.

The problem has been addressed in a recent paper demonstrating that the more hindered trineophyltin hydride circumvents many of the protodestannylation and isomerization problems that plague reactions with tributyl and trimethyl analogues.[118,119] While terminal alkynones

Table 31 Trineophyltin in Catalytic Hydrostannation

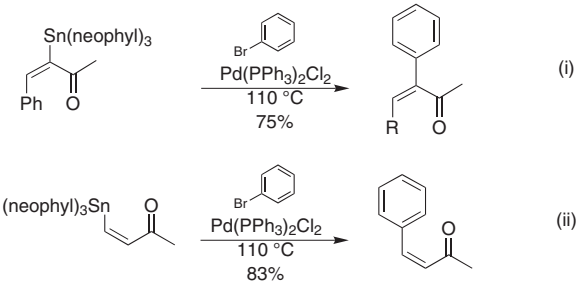


Entry	Alkyne	Conditions	Yield (%)	Product ratio (*E*:*Z*) α-Stannane	Product ratio (*E*:*Z*) β-Stannane
1		Pd^0 [a]	94	58 (n.a.)	42 (52:48)
2		Pd^0 [a]	90	100 (100:0)	0
3		Pd^0 [a]	80	100 (100:0)	0
4		Pd^0 [a]	88	93 (100:0)	7 (100:0)
5		Pd^0 [a]	92	38 (100:0)	62 (100:0)
6		Et_3B [b]	79	0	100 (0:100)
7		AIBN [c]	88	94 (100:0)	6 (0:100)
8		AIBN [c]	60	72 (57:43)	28 (0:100)

[a] 2 mol% $Pd(PPh_3)_2Cl_2$ in THF, 25 °C.
[b] 0.1 equiv Et_3B, 25 °C.
[c] 0.01 mol% AIBN, 80–90 °C.

give rather unselective reactions (Table 31, entry 1), several substrates with alkyl substituents show very good selectivity and reactivity with a palladium catalyst. The products are reported to be stable to workups and chromatography. Alkynes with aryl substituents show decreased selectivity, though to an extent that seems variable and difficult to predict (entries 4, 5). The authors also demonstrate that trineophyltin hydride reacts selectively with terminal- and aryl- substituted alkynes under radical conditions (entries 6–8), providing complementary conditions for substrates that do not proceed well under palladium catalysis. Alkyl-substituted alkynes do not react in a highly selective manner under radical conditions (entry 8).

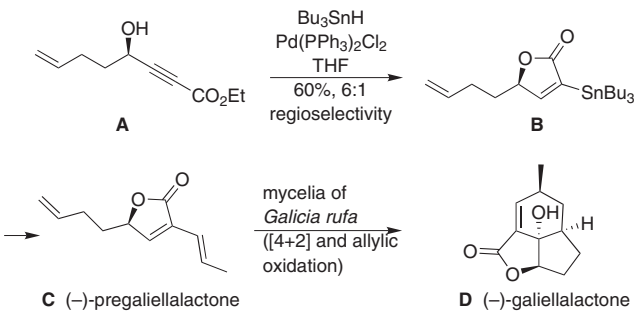
The vinyl trineophyltin products are iodinated upon treatment with I_2, and, perhaps surprisingly, are competent species for Stille cross-coupling reactions with bromobenzene (Scheme 50). The additional steric demand of the neophyl group does not prevent transmetallation to palladium, as might be feared, and the stereochemical integrity of the vinyltin species is maintained.[119]



Scheme 50 Coupling trineophyltin derivatives.

Molybdenum-catalyzed hydrostannation also functions well for electron-deficient internal alkynes (see also section 3.3, Table 19).[80,90] Mirroring trends seen with palladium – though a free alkynyl acid demonstrates poor selectivity – alkynyl esters and an alkynyl ketone offer significant selectivity and useful yields (Table 32). Chemoselectivity for electron-poor alkynes in the presence of other alkynes and allyl esters is also achieved (entry 4). One alkynyl ketone results in a product of poor stability toward protodestannylation. This product is isolated in 40% yield after iodination (entry 5).

The selective α-stannation of alkynyl esters has recently been used in a facile route to (–)-galiellalactone. Alcohol **A** (Scheme 51), obtained from asymmetric ketone reduction, was treated with Bu_3SnH and a palladium(0) catalyst, resulting in the cyclized product **B**, which could be readily transformed into (–)-pregaliellalactone (**C**). The simple route allowed study of the biosynthetic [4+2] and allylic oxidation steps.[120]

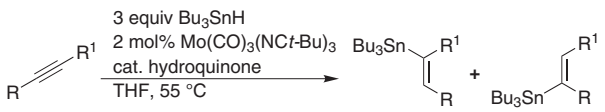


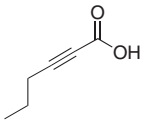
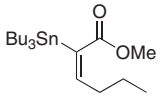
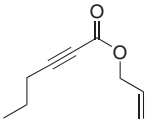
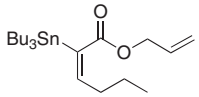
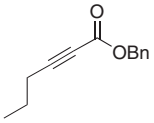
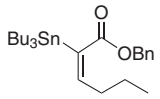
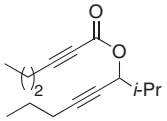
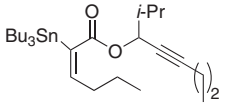
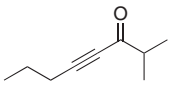
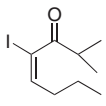
Scheme 51 (–)-Pregaliellalactone synthesis.

Similarly, an alkynyl amide is also a useful substrate (Scheme 52). Hydrostannation of alkyne **A** allows creation of vinylstannane **B** in good yield. This fragment was then employed in a double Stille coupling with diiodide **C**, allowing for a late-stage double asymmetric intramolecular Heck reaction in the synthesis of (–)-quadrigemine C and psycholeine.[121]

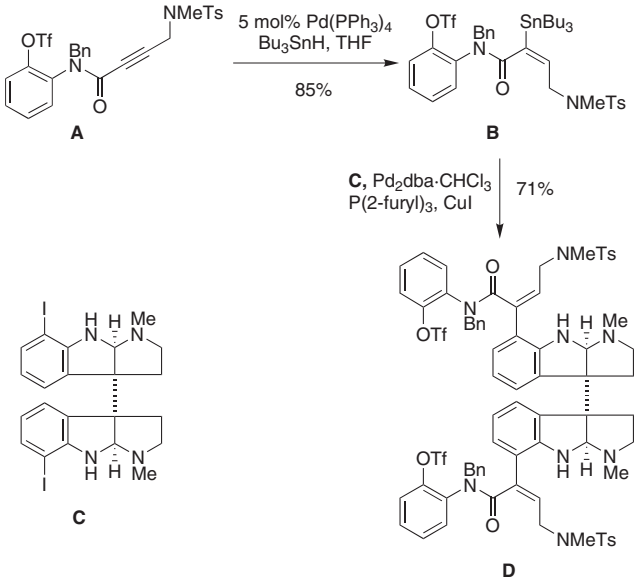
Palladium catalysis of hydrostannation permitted the late-stage introduction of a dienyl nitrile (Scheme 53, **C**) during a synthesis of borrelidin.[122] The approach required selective hydrostannation of the advanced intermediate enyne **A**. A model study (Scheme 54) indicated that the propargylic enyne alcohols and ethers did not provide the desired selectivity, instead providing mostly β-stannyl alcohol derivatives. The use of the more electron-withdrawing acetoxy group negated this preference, permitting

Table 32 Molybdenum Catalysis of Internal Alkyne Hydrostannation



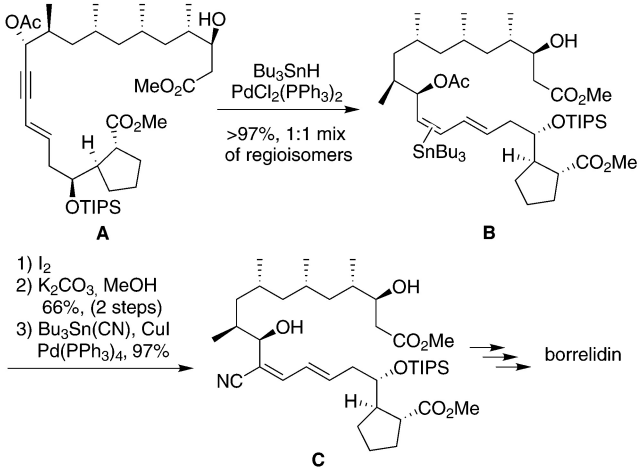
Entry	Alkyne	Major product	yield (%)[a]	Ratio α:β
1			88[b]	63:37
2			80	91:9
3			68	90:10
4			87	85:15
5			40[c]	92:8

[a] Isolated total yield of both regioisomers.
[b] Isolated yield after esterification with CH_2N_2.
[c] Isolated yield after iodination with I_2. Product vinylstannane is unstable to protodestannylation during workup.

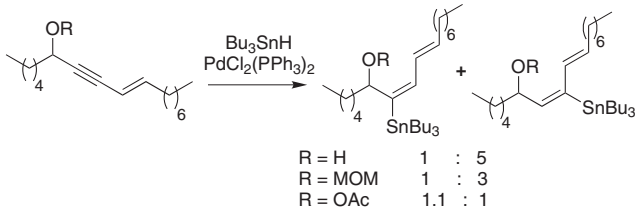


Scheme 52 Synthesis of (–)-quadrigemine C and psycholeine.

access to a roughly equal mixture of the two isomers, which in turn allowed completion of the synthesis. Although the work highlights limitations in extant hydrostannation methodology, no trans addition or 1,4-addition isomers were detected in the nearly quantitative manipulation of a rather complex substrate.



Scheme 53 Synthesis of borrelidin.



Scheme 54 Model study of internal alkyne hydrostannation.

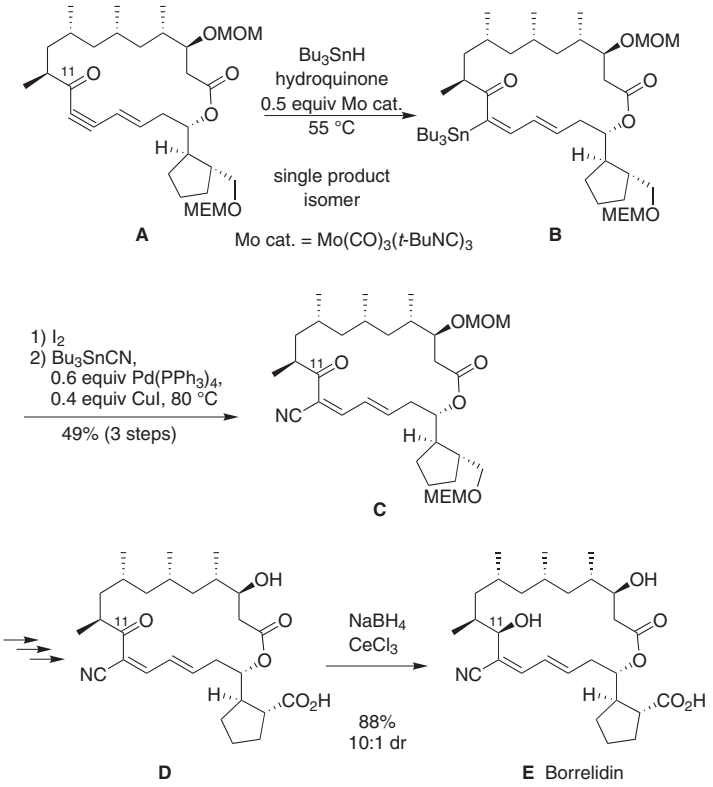
The problems associated with non-selective palladium-catalyzed hydrostannation have recently been remedied through the use of molybdenum catalysis (Scheme 55). By altering the oxidation state at C11, Theadorakis was able to take advantage of the excellent selectivity of molybdenum(0) catalysts as previously described. Working on the fully constructed macrocycle, hydrostannation with the complex $Mo(CO)_3(t\text{-BuNC})_3$ provided a single isomeric vinylstannane (Scheme 55, **B**).[123] In a manner similar to the previous effort, iodination and cyanation then installed the necessary nitrile functionality. Importantly, the requisite $C11_\beta$ stereochemistry was readily introduced with 10:1 stereoselectivity in the last step of the synthesis (**D** → **E**). The authors note that palladium catalysis was completely nonselective in the alkyne hydrostannation reaction. Protodestannation of the α-stannyl enone does not seem to be a problem in this case, though it was troublesome in a much simpler substrate (see Table 32). The newly developed routes to α-stannyl enones afforded by molybdenum catalysis may bring about a better understanding of the stability and synthetic utility of these species.

5 Conclusion

Organometallic reagents continue to play a major role in the elaboration of olefins in organic synthesis. Most commonly, vinylmetalloid species are made from the corresponding halide for use in subsequent cross-coupling reactions. A main goal of hydrosilylation methods is to supplant often circuitous vinylhalide routes with efficient reactions that provide more atom-economical access to similar organometallics. Reliable access to either geometrical isomer for a given target would be a major expansion of the method.

The goal of creating methods to synthesize any given geometrical isomer by hydrometallation is not necessarily unachieveable. Recent reports employ hydrometallation for the synthesis of vinylmetal isomers that, based on previous methods, were impossible to imagine; among these, clean trans addition processes and a small number of selective reactions with internal alkynes. There appear to be new mechanisms operating in several recent reports as well. For example, rhodium vinylidene intermediates in hydroboration reactions and concerted oxidative addition–alkyne insertion to a metallacyclopropene intermediate in ruthenium-catalyzed hydrosilylation reactions are fundamentally new reaction manifolds proposed to explain unique selectivities obtained in recently disclosed reactions. Strategic use of the mechanistic diversity of hydrometallation reactions may be a key to discovering solutions to selectivities that remain elusive.

It is apparent from even a cursory read that there remain large gaps in the ability of synthetic chemists to employ hydrometallation for the synthesis of vinylmetalloid structures. Solutions to the problem of terminal alkyne hydrostannation are not entirely satisfactory. As a whole,



Scheme 55 Molybedenum catalysis to afford a more selective hydrometallation.

though, the hydrometallation of internal alkynes is the less studied field and presents many unsolved problems. In particular, the catalyzed hydroboration of internal alkynes is an area without current solutions. With hydrosilylation – the oldest and most widely studied field presented here – the substituents on silicon are often crucial to the subsequent utility of the vinylsilane products, so the search for methods that tolerate a variety of carbon- and heteroatom-substituted silanes is important in order to provide interesting selectivities in important synthetic reactions.

Mechanistic studies continually shine new light on the basis of hydrometallation reactivity and selectivity. However, current thinking is based as much on speculation as it is on solid data. More than likely, continued, detailed exploration of the mechanistic underpinnings of hydrometallation reactions will lead to new understanding and better reactions. For hydrostannation mechanisms in particular, very little is known; this lack of knowledge hampers the understanding of reported reactivity and the expansion of current methods to new settings.

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