Lanthanocene Catalysts in Selective Organic Synthesis

Gary A. Molander* and Jan Antoinette C. Romero

Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, 231 South 34th Street, Philadelphia, Pennsylvania 19104-6323

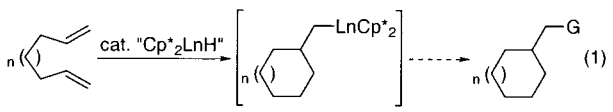
Received October 22, 2001

Contents

I. Introduction

Synthetic organic chemists have scoured the depths and breadth of the periodic table in search of novel, unique, and efficient methods to assemble small molecules. Metal-catalyzed reactions have risen to the forefront among bond-forming processes because they permit unprecedented molecular construction to be carried out with exquisite selectivity and efficiency.

Catalyzed carbon−carbon or carbon−heteroatom bond formation by direct insertion of alkenes or alkynes into metal−carbon or metal−heteroatom bonds represents one such useful process that has been developed extensively. Perhaps the most important example of this in the industrial realm is the polymerization of α-olefins. Group 3 organometallics and organolanthanides in particular are among the most active known catalysts for the Ziegler−Natta-type polymerization processes.[1] However, despite the spectacular ability of these complexes to generate new carbon−carbon bonds in polymerization reactions, only recently have efforts been made in applying these catalytic systems to small molecule synthesis through cyclization reactions of dienes, enynes, and related substrates (eq 1).



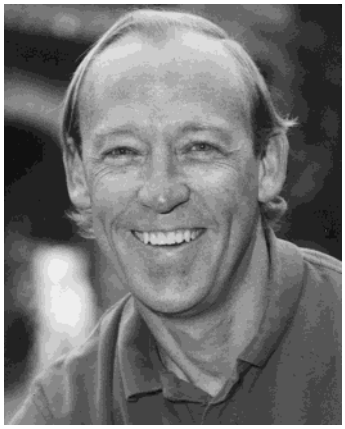
The reactivity of ethylene and propylene very rarely parallels that of highly functionalized organic molecules, and many limitations arise concerning the suitability of the aforementioned catalysts within this context. For example, only recently have available catalysts been able to polymerize anything but monosubstituted alkenes. Even allylic substitution on such alkenes has presented difficulties for the sterically sensitive organometallic complexes.[2] To be broadly applicable, catalysts had to be developed that would allow insertion of more highly substituted alkenes. Functional group compatibility was also of concern. Most polar functional groups (even ethers) were reported to either react with the organometallics[3] or irreversibly bind so as to inhibit catalysis.[4] To be regarded as part of a practical synthetic strategy, it was imperative that catalysts be developed that could tolerate a wide range of common organic functionality. Many of the lanthanocene complexes are generally air sensitive and benefit from glovebox or Schlenk-line techniques for their handling. The synthesis of reasonably air-stable complexes would facilitate the introduction of these catalysts to a broader range of applications. Finally, several issues of selectivity had to be addressed. First, chemoselectivity in the insertion of a single alkene or alkyne in a polyunsaturated system was required. A high degree of regioselectivity in this insertion was also essential. Diastereoselectivity in reactions of chiral substrates and prochiral unsaturated systems necessitated examination. Finally, chiral, nonracemic complexes would have to be developed in order to meet the challenges of modern enantioselective synthetic organic chemistry.

This contribution is intended to be a comprehensive review of the application of group 3 metal and lanthanide metallocenes to selective organic synthesis, covering published examples through September 2001. Emphasis has been placed upon the application of these catalytic species to novel methods for the selective synthesis of small organic molecules via alkene and alkyne insertion reactions.

II. General Features of the Catalytic Systems and the Olefin Insertion Reaction

The group 3 and lanthanide metallocenes possess a number of distinctive characteristics. The d^0 electron configuration of the metals combined with structural variations upon the ligands have been exploited to achieve a variety of transformations. Characteristic σ-bond metathesis/insertion reactions,

10.1021/cr010291+ CCC: $39.75
Published on Web 04/25/2002

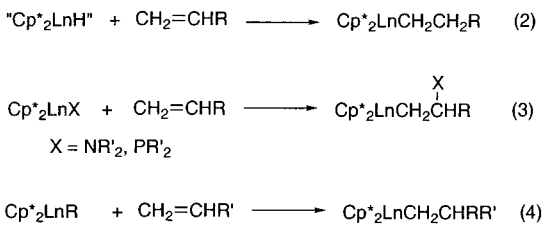


Professor Gary A. Molander was born in Cedar Rapids, IA. He received his B.S. degree at Iowa State University in 1975 working with Professor Richard C. Larock. He entered the graduate chemistry program at Purdue University in 1975, obtaining his Ph.D. degree in 1979 under the direction of Professor Herbert C. Brown. He joined Professor Barry Trost's group at the University of Wisconsin—Madison as a National Institutes of Health postdoctoral fellow in 1980, and in 1981 he accepted an appointment at the Unversity of Colorado, Boulder, as Assistant Professor of Chemistry. He was promoted to Associate Professor in 1988 and Professor of Chemistry in 1990. In 1999 he joined the faculty at the University of Pennsylvania. Professor Molander's research interests focus on the development of new synthetic methods for organic synthesis and natural product synthesis. A major focus of his research has been the application of organolanthanide reagents and catalysts to selective organic synthesis. More than 130 research paperes have emanated from his research program. He has received several honors for his work, including an Alfred P. Sloan Foundation Fellowship, the American Cyanamid Academic Award in 1989, and the Arthur C. Cope Scholar Award from the American Chemical Society in 1998. He has been a Visiting Professor at the Université de Paris-Sud, Orsay, France (1989, 1997); Philipps Universität, Marburg, Germany (1989); École Supérieure de Physique et de Chimie Industrielles de Paris (1993); Universidade Federal da Paraíbe, Brazil (1998); Universidade Federal da Pernambuco, Brazil (1998); Universidad Nacional del Litoral, Santa Fe, Argentina, (1998); Institute of Organometallic Chemistry, Russian Academy of Sciences, Nizhny Novgorod, Russia (1998); Institut de Recherche en Chimie Organique Fine, Rouen, France (1999), and Universidade Federal de Santa Maria, Brazil (2001). He has served on the American Chemical Society Division of Organic Chemistry Executive Committee. In 2001 he was the Executive Director for the 37th National Organic Symposium and currently serves on the Editorial Advisory Board of *Organometallics*.

Jan Romero was born in Los Angeles and raised in Orange County, CA. She received her B.S. degree from the University of California—Irvine in 1999, where she had the privilege of working for Professor Keith A. Woerpel. She was the recipient of a Presidential Undergraduate Fellowship and an Outstanding Undergraduate Researcher Award from UCI for work on nucleophilic substitution reactions of six-membered ring oxocarbenium ions. She is currently pursuing her Ph.D. degree at the University of Pennsylvania under the advisement of Professor Gary A. Molander. Her research focuses on the applications of organolanthanide and group 3 metallocenes to the functionalization of unsaturated molecules.

relatively constrained ligation, and highly electrophilic metal centers contribute to the unique reactivity of these complexes.

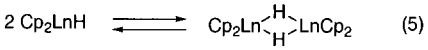
The key step in all of the catalytic processes to be discussed is olefin insertion into a metal−hydrogen (eq 2), metal−heteroatom (eq 3), or metal−carbon bond (eq 4). The hydrometalation and carbometalation processes also constitute the foundation for the polymerization of alkenes. Olefin insertions generally occur with the same regioselectivity as hydroboration reactions,[5] with the bulky, electrophilic metal and associated ligands residing at the less substituted of the two-carbon reactive unit.



In most instances these insertion reactions are extremely exothermic and effectively irreversible under reasonable reaction conditions.[6] Even *tert*-butyl-substituted organolanthanides (prepared by other methods) exhibit significant kinetic stability.[7]

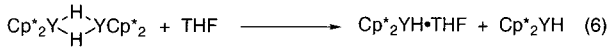
The rates of olefin insertion processes are greatly dominated by ligand substitution. Much of this can be attributed to the effects of coordinative unsaturation at the metal center. High reactivity is associated with accessibility to the metal center and terminal (nonbridging) ligands.[8] The requirement for free coordination sites dictates that noncoordinating solvents be utilized for the catalytic reactions. Thus, because of their high affinity for oxygen, common ether solvents lead to low catalytic turnover rates[6] and can even deactivate catalysts via ether cleavage reactions.[3,9] Consequently, hydrocarbon solvents are used exclusively in the catalytic reactions.

It would seem logical to utilize the least encumbered ligands about the metal to achieve maximum reactivity with highly substituted alkenes. However, providing a more open metal center also renders the organometallic hydride susceptible to a deactivating ligand redistribution[10] or to dimerization, forming hydride-bridged dimers (eq 5).[6]



These dimers are less reactive[11] or unreactive in catalytic reactions of interest, and thus, some substitution on the cyclopentadienyl ligands is necessary to prevent dimer formation through steric hindrance to association. Pentamethylcyclopentadienyl (Cp*) ligands are useful in this regard and lead to catalytic systems that are highly reactive and yet exquisitely selective in the insertion of monosubstituted alkenes. One such precatalyst system is the yttrium complex, $Cp^*_2YMe\cdot THF$. Although normally Lewis bases depress catalytic activity because they compete for empty coordination sites on the catalyst, in this

precatalyst the single THF of solvation appears to catalyze the hydrometalation process[12] in the same manner that Lewis bases catalyze the hydroboration of olefins with 9-BBN.[13] Thus, the THF provides a source of monomeric metal hydride that is more reactive in hydrometalation reactions (eq 6).



Comparison of reactions utilizing $Cp^*_2YCH(TMS)_2$, a complex lacking a molecule of solvation, and Cp^*_2-YMe·THF reaffirms the notion that THF association provides increased reactivity with monosubstituted alkenes. Addition of one molar equivalent of THF per equivalent of $Cp^*_2YCH(TMS)_2$ restores catalytic activity to the level of the methyl complex.[14] Apparently this THF also depresses the rate of σ-bond metathesis (vide infra) relative to olefin insertion,[6] with important ramifications for cyclization/termination processes to be discussed later. Curiously, this THF effect appears unique to the Cp^*_2YR system.

Unfortunately, the cyclopentadienyl ligand greatly hinders the metal center, thus inhibiting reactions with 1,1-disubstituted alkenes and more highly hindered olefins. Four general catalyst manipulations have been utilized to overcome this difficulty. The first is the incorporation of lanthanide metals with larger ionic radii. Because of the lanthanide contraction,[15] early lanthanides have a larger ionic radius than the late lanthanides. Placement of one of the larger metal ions into the ligand system has the effect of opening it up, allowing access to the metal by more hindered alkenes. This strategy has its limits, and to create even more accessible metal centers, the ligand system itself must be changed.

Incorporation of a single bulky substituent onto the cyclopentadienyl units has been utilized to open the reactive metal center. Substituents such as *tert*-butyl groups and trimethylsilyl groups appear to prevent extensive hydride dimer formation but at the same time leave the metal center relatively open for interaction with olefins. An example of such a precatalyst is displayed in Figure 1. Although the methyl precatalyst is a dimer, the active hydride catalyst is most likely a monomer and capable of rapid olefin insertion of most 1,1-disubstituted alkenes. Another interesting feature of the catalyst is its unusual stability. Members of this class of precatalysts have been weighed in the air and utilized in hydrosilylation reactions[16] performed with normal procedures for the benchtop handling of air-sensitive materials.[5,17]

The third strategy that has been utilized to provide more open access to the metal is to utilize "hinged"

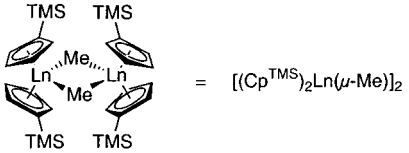


Figure 1. Lanthanocene complexes containing substituted cyclopentadienyl ligands.

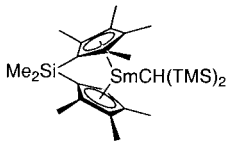


Figure 2. Samarium complex containing "hinged" cyclopentadienyl ligands.

or ansa-bridged cyclopentadienyl ligands. A one-atom bridge between two cyclopentadienyl units serves to increase the angle between them and again provides more facile approach of substrate to the metal. Figure 2 depicts one such precatalyst.[18]

The most recent addition to the stable of sterically open systems is the "constrained geometry" catalysts (Figure 3).[19] These have not been studied extensively but show promise in preliminary hydroamination studies (vide infra).

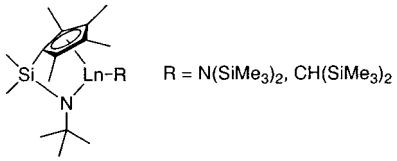


Figure 3. "Constrained geometry" catalysts.

With a wide range of metals and ligands available,[20] organolanthanide and group 3 organometallic catalysts are readily "tuned" to provide the desired reactivity and selectivity patterns in reactions of interest.

III. Catalyzed Hydrogenation Reactions

Organolanthanides and group 3 organometallics are extraordinarily reactive hydrogenation catalysts,[21] and catalysts possessing several different metal/ligand arrays have been utilized in the hydrogenation of simple alkenes.[22] Some of these catalysts are relatively challenging to prepare and handle. This, combined with their lack of tolerance to reactive functional groups, makes them less attractive than many transition-metal-based catalysts in standard hydrogenation reactions. It is instructive, however, to examine the catalytic cycle of hydrogenation reactions because it serves as a useful model for the other catalytic reactions to be discussed subsequently. Additionally, illuminating information concerning selectivity has been derived from studies of the hydrogenation reaction.

Transition-metal-based hydrogenation reactions most often operate on a catalytic cycle that involves oxidative addition, olefin insertion, and reductive elimination. In contrast, the mechanistic basis for organolanthanide hydrogenation involves olefin insertion and σ-bond metathesis (Figure 4).

The catalytic process is initiated by a σ-bond metathesis to generate the active metal hydride. Conversion of an organometallic precatalyst into the catalytic hydride species occurs through a four-centered exchange of ligands (eq 7).[23] Olefin insertion into the metal−hydrogen bond is the product-determining step of the process and is generally irreversible under optimal conditions for hydrogenation.[6] A σ-bond metathesis reaction constitutes the

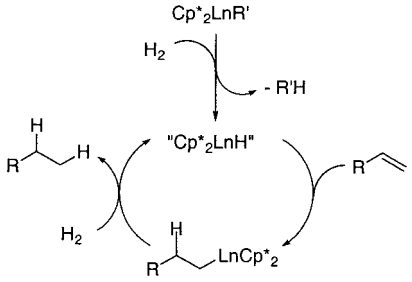
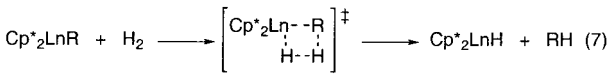
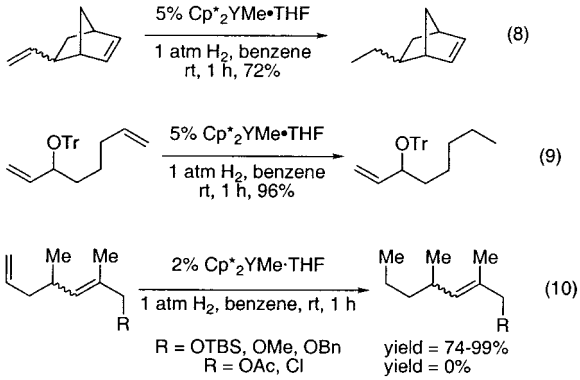


Figure 4. Mechanism of organolanthanide-catalyzed hydrogenation of olefins.

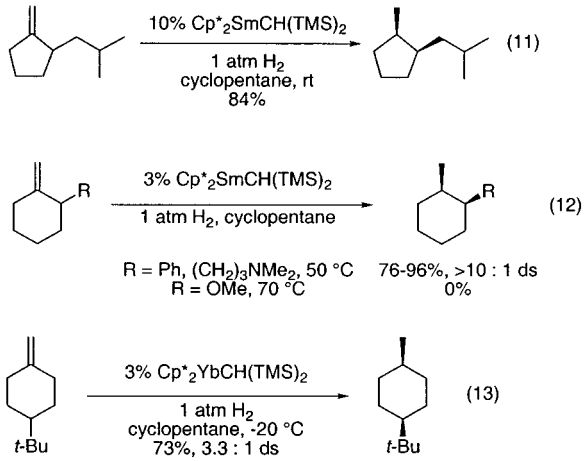
final step of the process, wherein the organometallic reacts with hydrogen to release the hydrocarbon and regenerate the active catalyst.



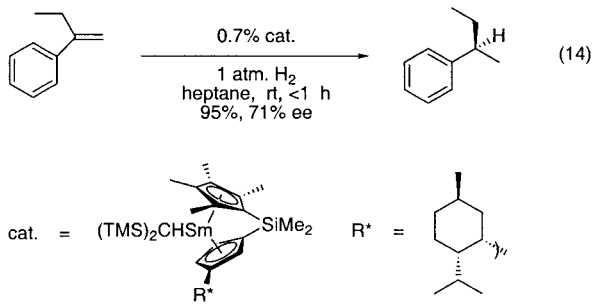
Extensive kinetic studies for organolanthanide-catalyzed hydrogenations have been performed.[21] Although there are some exceptions, for reactive olefins the rate of the reaction is proportional to the product of the catalyst concentration and hydrogen concentration, indicating a rapid olefin insertion and rate-limiting σ-bond metathesis. With the exception of cyclohexene, the relative rate constants for hydrogenation of monosubstituted alkenes and a variety of 1,2-disubstituted alkenes are remarkably similar. Nevertheless, synthetically useful selectivities can be achieved with a highly discriminating catalyst (eqs 8−10).[24] For most diene substrates wherein the two alkenes exhibit different reactivities, monitoring hydrogen uptake can be neglected. Even with a highly reactive, strained alkene such as is found in the bicyclo[2.2.1] system, the monosubstituted alkene is so much more reactive that a single equivalent of hydrogen is utilized even in the presence of a vast excess of hydrogen (eq 8). Perhaps even more impressive is the selectivity displayed in eq 9, wherein substitution at one allylic position of a diene system is sufficient to permit virtually complete selectivity. Most common alcohol protecting groups are tolerated (eq 10), but allylic acetate and allylic halide functionalities inhibit catalyst turnover.



More hindered, less reactive alkenes such as 1,1-disubstituted alkenes require a more open catalyst to achieve more efficient transformations.[25] For the hydrogenation reaction, the simple alternative of utilizing a samarium- or ytterbium-based catalyst permits these substrates to react effectively, often with high diastereoselectivities (eqs 11−13). A variety of alkyl and aryl substituents are tolerated, including a tertiary amine (eq 12). Allylic ether substitution, however, inhibits the reaction, even under more vigorous conditions. After initial insertion of the olefin, the Lewis acidic metal center forms a stable five-membered ring chelate with the oxygen, preventing further reaction. In general, the diastereoselectivity of the olefin insertion diminishes when the existing stereogenic center occupies a position that causes less interaction with the bulky organometallic reagent (eq 13). The stereochemistry of the products is that predicted by the approach of the bulky organometallic to the less hindered face of the exo-methylene unit.



Enantioselective catalytic hydrogenation and deuteration reactions have been reported and appear to offer synthetically useful results, although for a very limited set of alkenes.[6,26] Thus, deuteration of styrene and hydrogenation of substituted styrenes, molecules with essentially no functional group available to serve as a stereochemical control element, can be accomplished with modest to high asymmetric induction using a series of elegantly designed chiral, nonracemic catalysts (eq 14).



In contrast to the "1,2-addition" olefin insertions discussed previously, mechanistic and synthetic studies of the analogous hydrosilylation reaction of styrenes (vide infra)[6,26b] suggest that the catalytic hydrogenation cycle proceeds via another mechanism.[27] Thus, an irreversible, stereochemically determinant "2,1-insertion" probably initiates the reaction, with subsequent σ-bond metathesis completing

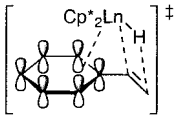


Figure 5. Transition structure for "aryl-directed" processes.

the process. Most remarkable is the fact that, if correct, this model demands that the olefin insertion takes place to orient the sterically encumbered metal center at a tertiary carbon center. This regioselectivity results from what is believed to be an "aryl-directed" phenomenon. Serving as a Lewis base, the aryl group interacts with the metal center of the catalyst in a Lewis acid/Lewis base manner. Least motion insertion of the alkene into the metal−hydrogen bond leads to a benzylic organometallic (Figure 5). Of further note is the lack of β-hydride elimination occurring from the resultant tertiary organometallic prior to σ-bond metathesis with hydrogen.

A "frontal trajectory" has been suggested to explain the sense of asymmetric induction in these reactions (Figure 6) and seems most valid based on steric effects. However, a "lateral trajectory" cannot be ruled out based upon the evidence available to date.[6,26b]

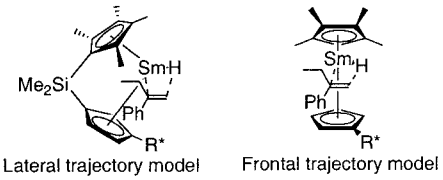
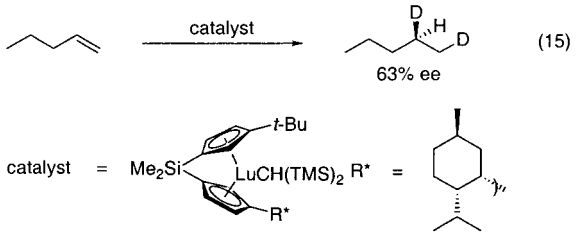


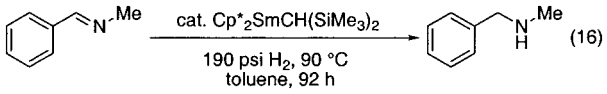
Figure 6. Models for asymmetric induction.

A second-generation catalyst was designed and utilized by the Marks group for the deuteration of 1-pentene.[28] This catalyst, based upon a slightly revised ligand platform, provided up to 63% ee of 1,2-dideuteriopentane, the highest reported at the time for this type of unfunctionalized alkene (eq 15).



Alkynes also undergo selective hydrogenation to generate *cis*-alkenes.[21,29] The process has not been developed, however, and at any rate it is unlikely to compete with more established methods.

The lanthanocene-catalyzed hydrogenation of imines has drawn little interest (eq 16).[30] Although it appears that organolanthanides may be competent catalysts for this process, the limited studies that have been carried out to date and the capricious nature of the reaction itself create some doubt as to the ultimate synthetic viability of this reaction.



IV. Catalyzed Hydrosilylation Reactions

Metal-catalyzed hydrosilylation reactions provide the most efficient and economical route to organosilanes.[31] Combined with a Tamao oxidation or related reactions, hydrosilylation methods permit access to the corresponding alcohols.[32] The overall process thus constitutes the synthetic equivalent of a catalytic hydroboration/oxidation sequence.[33] One advantage of the silylation/oxidation protocol is the stability of the intermediate silane, which allows the unmasking of the alcohol to be performed at a synthetically convenient time. Furthermore, the procedure avoids the use of the sometimes troublesome protection/deprotection sequence commonly used with the free hydroxyl. Despite the potential of hydrosilylation reactions in selective organic synthesis, relatively little effort has been made to develop procedures for the selective hydrosilylation of polyfunctional alkenes and alkynes, especially when compared to the analogous hydroboration reaction.

Organolanthanide and group 3 organometallic catalysts provide an alternative to the traditional platinum-based catalysts for the selective hydrosilylation of alkenes and alkynes. Mechanistically, the transformation is analogous to the catalytic hydrogenation reaction detailed previously.[11,21,27,34] When silane is utilized in place of hydrogen, the final σ-bond metathesis occurs to place the silane moiety on the alkyl unit and the organometallic hydride is again regenerated (Figure 7). In the overall process a rapid, exothermic, and essentially irreversible olefin insertion is followed by the slower, rate-determining σ-bond metathesis. Because the group 3 metallocenes and organolanthanides are highly effective catalysts for dehydrogenative polysilylation,[35] the desired process demands that olefin insertion and σ-bond metathesis occur much more rapidly than the generation of polysilanes.

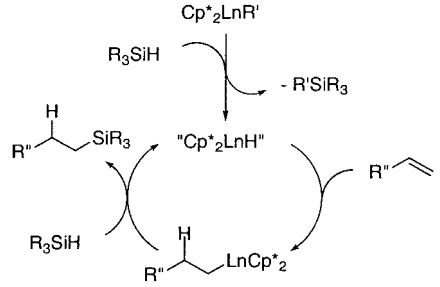
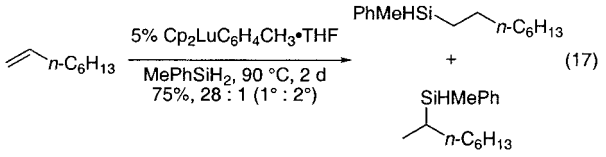


Figure 7. Catalytic cycle for organolanthanide-promoted hydrosilylation reactions.

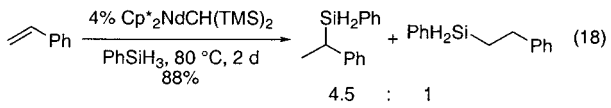
1. Silylation of Alkenes

The earliest reported examples of group 3 or organolanthanide-catalyzed hydrosilylation reactions emphasized reactions with simple alkenes (e.g., 1-octene, eq 17).[36] The lutetium- and neodymium-based catalysts utilized for these studies typically required prolonged reaction periods at high temperatures (80−90 °C) to react and provided modest to



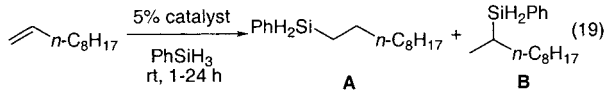
(17)

good yields of the desired terminal (linear) organosilanes. Styrene provided mixtures of linear and branched organosilanes (eq 18).



(18)

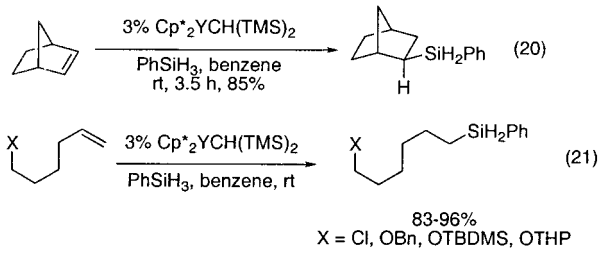
The regioselectivity of olefin insertion varies with the complex used in the reaction.[27,37] In the hydrosilylation of a monosubstituted olefin, the use of complexes with larger metals and more open ligands provides increased yields of the product derived from reversed ("2,1") insertion (eq 19). These results reveal that a variety of complexes give excellent selectivity for terminal insertion, but the conditions to elevate the amount of "2,1" insertion remain elusive.



(19)

catalyst	yield (% isolated)	A : B
$Cp^*_2LuMe•THF$	98	100 : 0
$Cp^*_2YbCH(TMS)_2$	91	100 : 0
$Cp^*_2YMe•THF$	84	100 : 0
$Cp^*_2SmCH(TMS)_2$	90	11 : 1
$Cp^*_2NdCH(TMS)_2$	85	3.2 : 1
$Cp^*_2LaCH(TMS)_2$	90	1.9 : 1
$Me_2SiCp"_2YCH(TMS)_2$	84	31 : 1
$Me_2SiCp"_2SmCH(TMS)_2$	98	1 : 2
$Me_2SiCp"_2NdCH(TMS)_2$	89	1 : 2

The development of organoyttrium catalysts provided a major breakthrough in terms of efficiency and selectivity in the synthesis of organosilanes.[38] Using these catalysts, reactions that once required harsh conditions were now realized within hours at room temperature, affording high yields of the desired organosilanes (eq 20). Furthermore, the mild reaction conditions allowed common organic functional groups (halides, ethers, and acetals) to be tolerated without disrupting catalytic activity (eq 21).

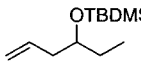
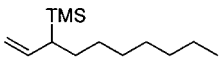
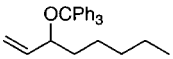


(20)

(21)

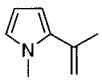
A relative rate study examining the organoyttrium-catalyzed hydrosilylation of various alkenes and alkynes was carried out.[39] This investigation, utilizing $Cp^*_2YMe•THF$ and $[Cp^{TMS}_2YMe]_2$ as catalysts, revealed important information concerning the reactivity of various alkenes and alkynes in these transformations. Somewhat surprisingly, conjugated aromatic alkenes were the most reactive among the alkenes examined (Table 1, entry 1). For example, *N*-methyl-2-vinylpyrrole reacted 7−10 times faster than the standard, 1-decene, in competitive reactions. Substitution at the allylic (entry 4) and even homoallylic positions (entry 3) noticeably slowed the hydrosilylation reaction relative to 1-decene. Allylic substituents that deactivated the alkene both sterically and electronically had the most dramatic effects on the rate of the hydrosilylation reaction of terminal, monosubstituted alkenes (entry 5).

Table 1. Relative Rates of Hydrosilylation of Terminal Alkenes

entry	substrate	$Cp^*_2YMe•THF$ (25 °C)	$[Cp^{TMS}_2YMe]_2$ (45 °C)
1		340	> 1000
2	1-decene	100	100
3		61	69
4		16	12
5		0.79	7.5

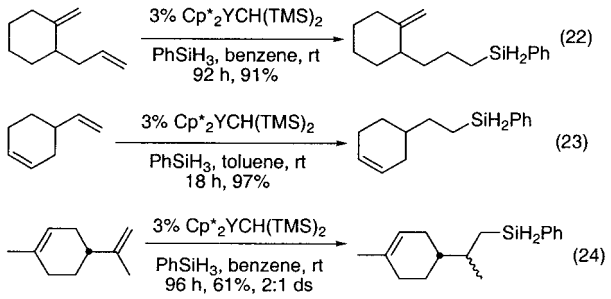
This same study revealed that internal alkynes could be hydrosilylated at rates that were as fast as, if not faster than, simple alkenes (Table 2). The comparison of relative rates uncovered in this study provided useful data for the strategic planning of sequenced reactions on polyunsaturated systems, as well as in the chemoselective monohydrosilylation of various dienes and enynes.

Table 2. Relative Rates of Hydrosilylation of Reactive Substrates

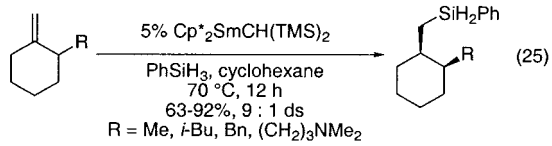
entry	substrate	$Cp^*_2YMe•THF$ (25 °C)	$[Cp^{TMS}_2YMe]_2$ (45 °C)
1	1-decene	100	100
2	2-decyne	670	140
3		--[a]	150

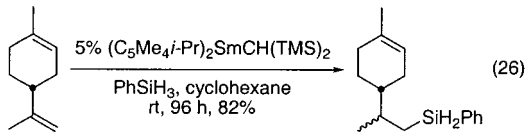
[a] Substrate is unreactive.

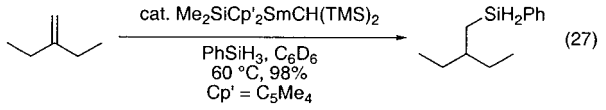
As an example, remarkable selectivity was demonstrated in the hydrosilylation of dienes with varying substitution patterns.[38] Virtually complete chemoselectivity was observed for the reaction of terminal olefins in the presence of disubstituted alkenes (eqs 22 and 23) and for the silylation of a 1,1-disubstituted olefin in preference to a trisubstituted double bond (eq 24).



The yttrium catalysts are less effective for more sterically hindered olefins, but the versatility afforded by being able to vary both the metal and the ligand system provides a means to adjust reactivity in a manner that allows hydrosilylation of more highly substituted alkenes. The simple modification of increasing the ionic radius of the metal permits the functionalization of 1,1-disubstituted alkenes (eq 25).[25] This effect dominates over slight ligand alterations, as a complex with more hindered ligands (C_5Me_4i-Pr) (eq 26) shows similar reactivity to the C_5Me_5-derived yttrium complex (eq 24).[40] A silicon-hinged catalyst further increases turnover frequency over nonbridged systems by a factor of 8 (eq 27).[27] Unfortunately, there is a tradeoff with the more open catalysts. Although increased activity with highly substituted alkenes is observed, monosubstituted alkenes react with poor regioselectivity.



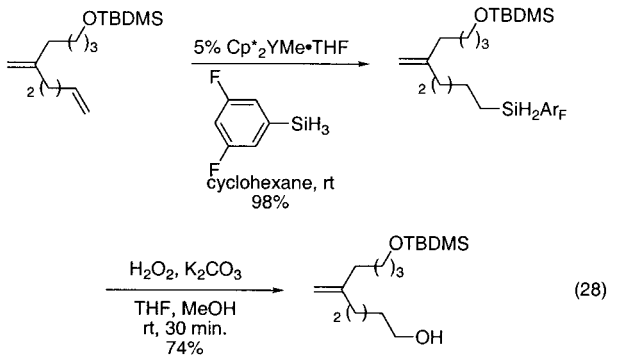




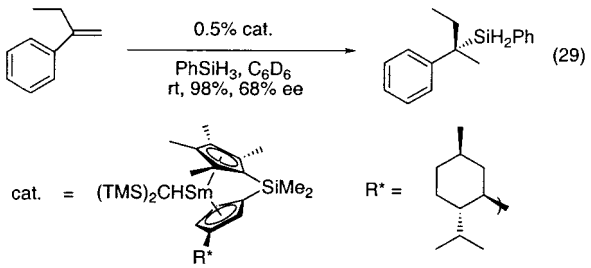
One of the principal values of the hydrosilylation reaction in organic synthesis is to providing a synthetic equivalent for alcohols. This transformation can be limited, however, by the reaction conditions used in the oxidation. Arylsilanes (as opposed to halo- or alkoxysilanes) must be used as the silylating agents in organolanthanide- and group 3 metal-catalyzed hydrosilylation protocols.[41] The use of arylsilanes in place of more readily oxidized alkoxysilanes requires the use of a protodesilylation protocol to remove the aryl moiety under strongly acidic conditions.[32] Basic oxidation protocols have also been developed for the cleavage of phenylsilanes, but they, like their acidic counterparts, require harsh conditions and long reaction times. Many functional groups are not compatible with these oxidation methods.[42] Mild protocols exist but are typically useful only when there is an allyl group or heteroatom bonded to the silicon atom.

By modifying the electronic nature of the aryl group bonded to silicon, it was determined that the oxidative lability of the hydrosilylated product could be enhanced without the introduction of a heteroatom. Mechanistic work by Tamao demonstrated that the addition of electron-withdrawing groups to an aryl unit bonded to silicon increased its rate of cleavage under oxidizing conditions.[43] For example, the installation of fluorine atoms or trifluoromethyl groups on the aromatic ring of an arylsilane increased the reactivity of the organosilane products toward oxidizing agents.

This concept was incorporated into the lanthanocene-catalyzed hydrosilylation protocol.[44] In the process, an improved synthesis of arylsilanes was developed, and several of these fluorinated silanes proved to be competent in the catalyzed hydrosilylation reaction. Oxidation of the carbon−silicon bond could be effected under very mild conditions, providing access to the desired alcohols (eq 28).



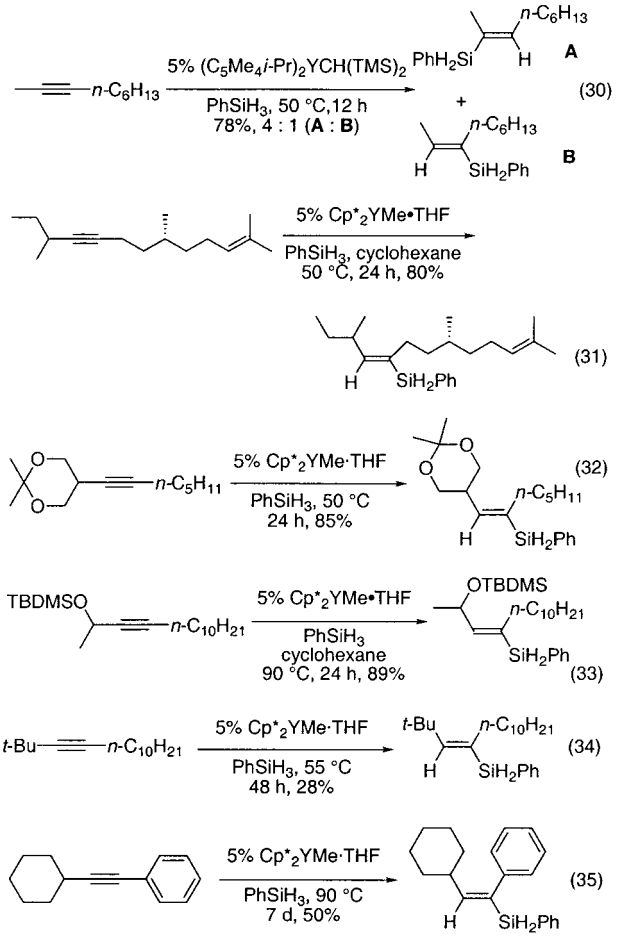
Styrene derivatives react with "2,1-"regioselectivity.[27] This reversal of selectivity varies considerably with the metal ionic radius and the ligand array present, with larger metals and bridged ligands giving higher ratios of the "2,1" product. As with the catalytic hydrogenation of styrene derivatives, the olefin insertion reaction defines the regiochemistry and stereochemistry of the final product. Thus, the olefin insertion is essentially irreversible under the reaction conditions and occurs with "aryl-directed" regioselectivity (see Figure 5). The σ-bond metathesis presumably occurs with retention of configuration, providing the observed products with remarkably high ee's considering the overall nature of the transformation (eq 29).



2. Silylation of Alkynes

Although terminal alkynes undergo metalation with organolanthanide hydrides and therefore cannot

be hydrometalated,[45] internal alkynes submit to effective hydrosilylation.[46] As expected from the mechanism, *cis*-addition of the organometallic hydride to the alkyne is observed (eq 30). Propargylic substitution is necessary to establish regioselectivity in unsymmetrical alkynes. A variety of branched substituents are suitable for use (eqs 31−35), expanding the structural possibilities of viable substrates. Placing a tertiary alkyl group on the alkyne (eq 34) slows the reaction, allowing the competitive dehydrogenative polymerization of silane to lower the yield of the desired product.



Equation 35 illustrates an interesting facet of this regioselectivity.[46] Although both substituents are branched, the phenyl group is effectively smaller than the cyclohexyl moiety, allowing good selectivity. The steric preference is likely buttressed by the electronic aryl-directing effects observed for styrene derivatives (see Figure 5).[27]

The critical and in fact rate-limiting step of alkyne hydrosilylation is the σ-bond metathesis.[46] Reactions must be heated overnight to achieve high yields of the desired alkenylsilanes. The hydrosilylation of alkynes is tolerant of a wide variety of functional groups (eq 36) including halides, amines, and several alcohol protecting groups.[46] A collection of substrates that were unreactive at temperatures up to 90 °C is pictured in Figure 8. The strongly Lewis acidic

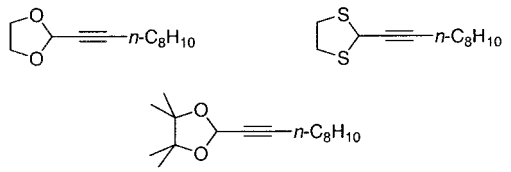
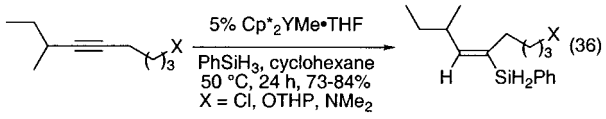
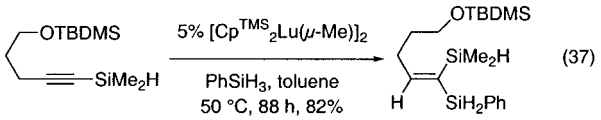


Figure 8. Substrates unreactive to organolanthanide catalysis.

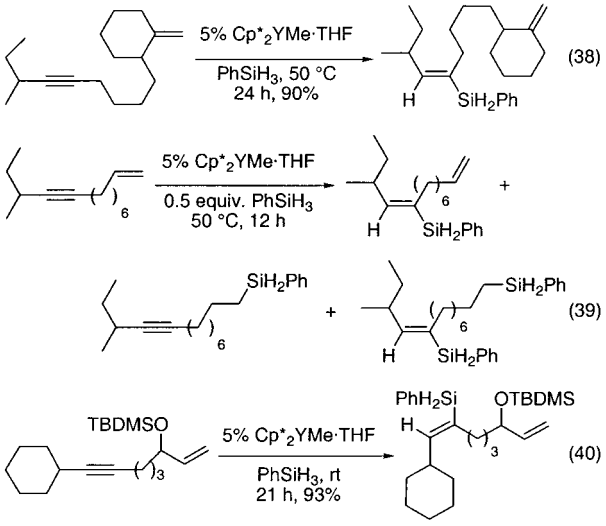
complexes probably cause catalyst-deactivating ionization of the propargylic acetals.



The organolanthanide-catalyzed hydrosilylation of alkynylsilanes provides 1,1-bis(silyl)alkenes as products of the reaction (eq 37).[47] The reactions are stereoselective for cis hydrosilylation and highly regioselective as well. From the nature of the products, one must conclude that the electronic directive effect of the silicon takes precedent over steric effects in the alkyne insertion event.



The lanthanocene catalysts have proven to be chemoselective for the insertion of alkynes over alkenes. Excellent discrimination is achieved in substrates containing an alkyne paired with a hindered olefin (eqs 31, 38).[46] When offered a monosubstituted olefin (eq 39), the catalyst is less selective, producing mixtures of alkyl- and alkenylsilanes. As previously noted for the hydrogenation of dienes, the allylic substitution of the alkene sterically shields the double bond and can electronically deactivate it as well (eq 40). This allows virtually complete selectivity for alkyne insertion.



V. Catalyzed Hydroboration Reactions

Hydroboration of olefins with catecholborane has been realized utilizing organolanthanide metal-

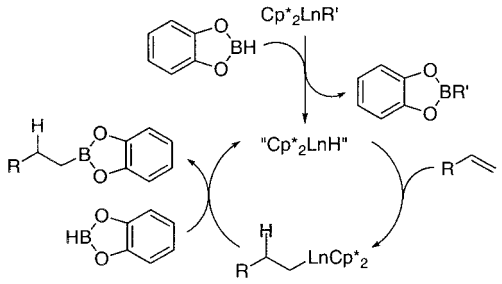
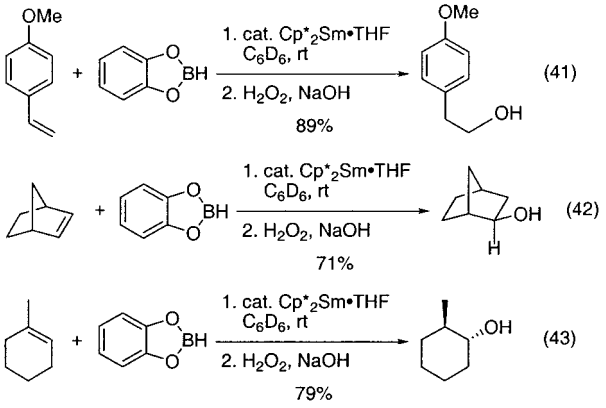


Figure 9. Mechanism of organolanthanide-catalyzed hydroboration of olefins.

locenes.[48] The mechanism is postulated to mimic that of hydrosilylation. The metal hydride is formed upon σ-bond metathesis with the boron−hydrogen bond. Olefin insertion into the metallocene hydride generates a metal−carbon bond. Subsequent σ-bond metathesis of the organometallic with catecholborane affords a boronate ester, thereby regenerating the catalyst (Figure 9).

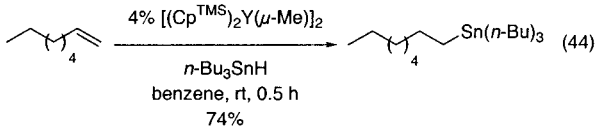
On the surface, the reaction appears to be completely general.[48a] Subjecting monosubstituted (eq 41), disubstituted (eq 42), and even trisubstituted alkenes (eq 43) to mild organolanthanide catalysis conditions all result in excellent yields of alcohols after oxidation of the reaction mixture. The regioselectivity and stereoselectivity of these reactions mimic that of the corresponding uncatalyzed hydroboration reactions.



A closer look at the reaction reveals many unanswered questions. Of the nearly 30 ostensibly related catalysts, few provide even modest catalytic activity in the hydroboration of the most reactive monosubstituted alkenes.[48b] A common observation under the reaction conditions is decomposition or disproportionation products of the boranes, in some cases generating BH_3. Second, organolanthanide-catalyzed hydrosilylations of styrenes afford the product resulting from "2,1-"hydrometalation of the alkene (eq 18). Although the same mechanism has been proposed for both the hydroboration and hydrosilylation reactions, the "1,2-"addition product prevails in the hydroboration reaction (eq 41).[48a] The latter is also the major product in the traditional hydroboration of styrene derivatives with BH_3. Finally, the fact that trisubstituted alkenes can be hydroborated under these conditions is extraordinary. These observations lead to some doubt as to the borane species involved in the product-determining hydroboration. Insertion and σ-bond metathesis reactions of this type in other systems have not been achieved. Although it is clear that some reactions (in particular those with monosubstituted alkenes) were carefully monitored for boronate ester formation as opposed to alkylborane formation,[48b] it appears possible that some of the observed results may be the result of hydroboration with BH_3 created by disproportionation with the Lewis acid catalysts.

VI. Catalyzed Hydrostannylation

Reports on catalytic hydrostannylation reactions are limited.[49] Despite the lack of experimental analysis, the mechanism of this process undoubtedly parallels that of the catalyzed hydrosilylation reaction discussed previously. In the only synthetic reaction reported along these lines, treatment of 1-octene with *n*-Bu_3SnH or Et_3SnH in the presence of the appropriate catalyst results in a high yield of the corresponding organostannane (eq 44). The crude reaction mixture was contaminated by distannanes. The increased acidity of stannanes relative to that of the analogous silanes leads to σ-bond metatheses in which metal−tin bonds are generated with release of H_2. A second σ-bond metathesis of this species with the tin hydride forms distannanes and regenerates the organometallic hydride. The olefin insertion process is claimed to be rate limiting in this reaction, although no kinetic details have been provided and it seems unlikely to be the case based upon detailed studies performed in analogous hydrogenation and hydrosilylation reactions. As expected for this very open class of catalysts, the organometallic hydride catalyst dimerizes slowly over time, losing catalytic activity.



VII. Catalyzed Hydroamination Reactions

Applications of organolanthanide-catalyzed processes extend beyond the ability to form carbon−carbon bonds. These organometallics are also known to generate new carbon−nitrogen bonds efficiently by insertion of alkenes and alkynes into the metal−nitrogen bond of organolanthanide amides.[26b,50] In addition to the metallocene versions of these catalysts, very effective nonmetallocene lanthanide and group 3 catalysts have been reported for alkene and alkyne hydroamination reactions.[51]

Of great synthetic utility is the employment of hydroaminations to the intramolecular cyclization of amino olefins. Intramolecular hydroamination reactions provide a powerful means to construct nitrogen heterocycles with high selectivity. The overall transformation follows a similar mechanism as the other catalytic processes (Figure 10). Conversion of a precatalyst to the resting state of the catalytic cycle occurs by a σ-bond metathesis. This protonolysis generates an organolanthanide amide, which under-

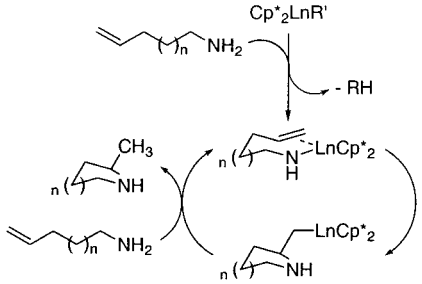


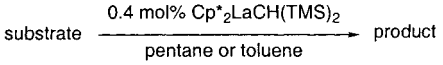
Figure 10. Mechanism of organolanthanide-catalyzed intramolecular hydroamination reactions.

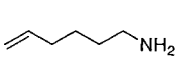
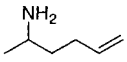
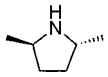
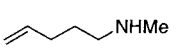
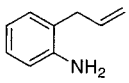
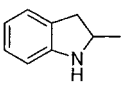
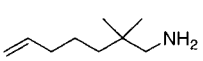
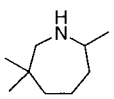
goes intramolecular olefin insertion in the rate-limiting step of the process. In the final step of the cycle, σ-bond metathesis with another molecule of amine regenerates the organolanthanide amide and releases the cyclic amine product.

Extensive studies have elucidated the mechanism of the hydroamination operation,[50c] but synthetic efforts have lagged behind. The majority of experiments have been performed in NMR tubes on a very small scale, and although isolated yields are reported to be high (>85%), larger scale reactions should be performed to substantiate the ultimate value of the method for organic synthesis. Nevertheless, transformations carried out to date are quite impressive and display highly promising generality. Five-, six-, and seven-membered rings have been created, and a variety of substitution patterns about the amine can be tolerated (Table 3).

Ligand systems other than the Cp* class have been explored in these reactions. Broene and co-workers exploited 1,2-bis(indenyl)ethane as a platform for the intramolecular hydroamination reaction.[52] Depending on the metal used for the metallocene, the *rac* or *meso* form of the catalysts can be formed preferentially. These complexes are more difficult to synthesize and, in particular, isolate than the Cp* systems.

Table 3. Organolanthanide-Catalyzed Intramolecular Hydroamination of Aminoalkenes

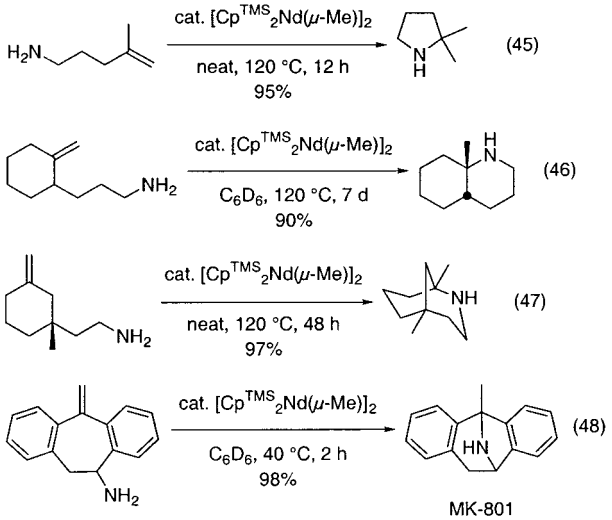


substrate	product
	
	
	
	
	

They offer no apparent advantages in the cyclization reactions themselves and thus are less desirable overall as hydroamination catalysts.

A second group of organometallics that does appear to offer advantages in terms of reactivity is the constrained geometry catalysts (see Figure 3).[53] These systems, although available only in modest yields from their dilithio precursors, afford up to 30-fold enhancement in turnover numbers per hour over the Cp* ligand arrays in the intramolecular hydroamination reaction while retaining regioselectivity in the insertion event.

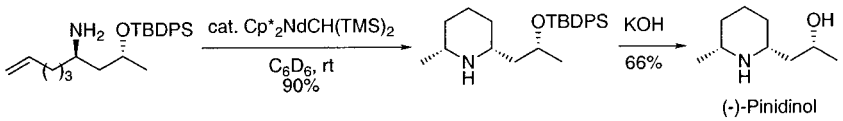
The $[Cp^{TMS}_2LnMe]_2$ catalyst provides yet another level of reactivity enhancement.[54] As it transpires, the intramolecular hydroamination reaction is sterically quite demanding. Although terminal, monosubstituted alkenes react with relative ease, even 1,1-disubstituted alkenes can create difficulties. Open access to the metal center afforded by the Cp^{TMS} ligands allowed a variety of cyclizations to be carried out for the first time. Varying substitution could be incorporated on the resultant heterocycles by utilizing the appropriate substrate. Monocyclic amines (eq 45), fused bicyclic systems (eq 46), and bridged heterobicycles (eq 47) created by hydroamination of 1,1-disubstituted alkenes could all be accessed for the first time utilizing this catalyst. The potent anticonvulsant and neuroprotective agent MK-801 was accessed using this strategy (eq 48).[55]



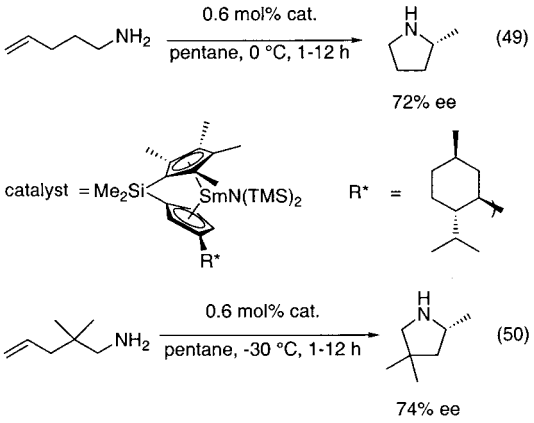
An investigation into the diastereoselectivity of the hydroamination reaction leading to piperidines was conducted, employing four different catalyst frameworks.[56] Among the systems examined, $Cp^*_2NdCH(TMS)_2$ provided the highest diastereoselectivity. Upon the basis of these results, a total synthesis of the alkaloid pinidinol was carried out (Scheme 1).

Enantioselective olefin hydroamination/cyclization employing C_1-symmetric organolanthanide complexes have been explored for a limited set of substrates.[26b] The source of asymmetric induction is the placement of a chiral auxiliary upon the ligand. The levels of enantiomeric excesses achieved are reasonably high for the synthesis of five-membered rings (eqs 49 and

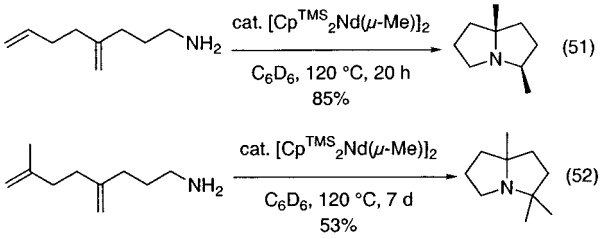
Scheme 1



50) but fall off rather dramatically (15% ee) in the related piperidine syntheses.



Double hydroamination reactions on dienyl primary amines have been carried out successfully.[54] Using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst, fused bicyclics were realized in good to excellent yields and high diastereoselectivities (eqs 51 and 52).

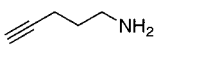
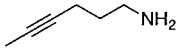
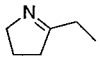
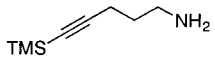
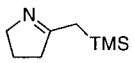
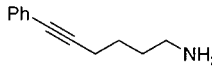
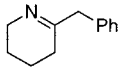
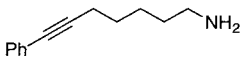
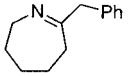
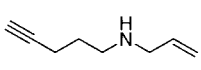
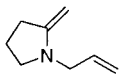
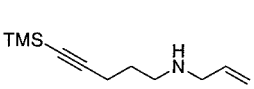
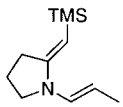


As with hydrogenation and hydrosilylation, alkynes also undergo smooth regiospecific intramolecular hydroamination (Table 4).[50h] Enamines generated in the cyclization tautomerize to the thermodynamically favored imines at room temperature.

Similar to the intramolecular cyclization onto alkenes, five-, six-, and seven-membered rings can be formed (entries 3−5). Interestingly, terminal alkynes readily undergo organolanthanide-catalyzed hydroamination (entries 1 and 6). Although the alkynyl proton is more acidic than the primary amine, metalation of the amine occurs preferentially, undoubtedly because of prior complexation to the metal center. Extension of this chemistry through an amination/cyclization process to achieve bicyclic products was not successful with certain substrates of this class (entries 6−7). After the alkyne initially inserts into the metal−nitrogen bond, subsequent insertion of the olefin can be arrested when the intermediate alkenyllanthanide is protonolyzed by another amine before cyclization onto the available alkene (entry 6). Additionally, if cyclization is slowed for steric reasons, isomerization of the remaining double bond can occur, making the cyclization effectively impossible (entry 7).

Table 4. Organolanthanide-Catalyzed Intramolecular Hydroamination of Aminoalkynes

substrate —(2 mol% $Cp^*_2SmCH(TMS)_2$, benzene, rt, 2 d)→ product

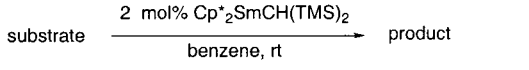
entry	substrate	product	% yield
1			47
2			59
3			92
4			95
5			92
6			52
7			91

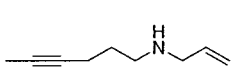
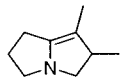
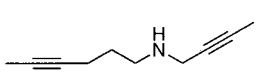
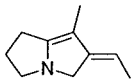
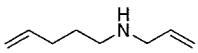
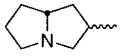
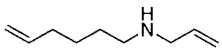
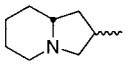
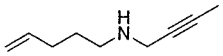
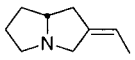
Sequential bicyclization of polyunsaturated molecules was achieved for select systems (Table 5).[50f] Enynes (entries 1 and 5), diynes (entry 2), and dienes (entries 3−4) are suitable substrates for the process. For example, the initial insertion into the metal−nitrogen bond can occur either at appropriately positioned alkynes (entries 1 and 2) or alkenes (entries 3−5). Similarly, the subsequent cyclization can be effected at alkenes (entries 1, 3, and 4) or alkynes (entries 2 and 5). The overall process offers a unique, efficient, and potentially valuable entry to pyrrolizidine and indolizidine skeleta. However, the results displayed in entries 6 and 7 in Table 4 also indicate that subtle steric and electronic effects can conspire to limit the scope of the process.[50h]

In addition to isolated alkenes and alkynes, allenes have proven to be excellent substrates for the intramolecular hydroamination process.[19c,57] Calculations indicate that insertion of allenes into the metal−nitrogen bond is about 29 kcal/mol more exothermic than that for alkenes but about 6 kcal/mol less exothermic than alkynes.

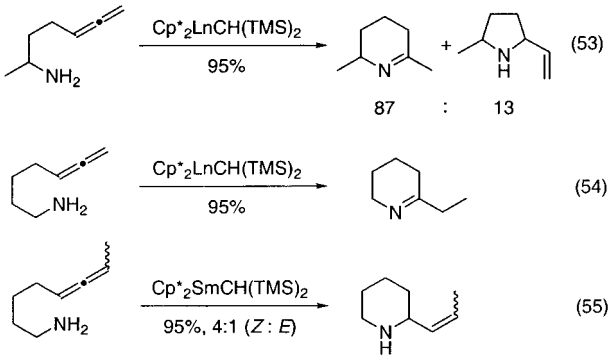
Regioselectivity issues arise for the cumulated alkenes.[57a,b] In a small sampling, monosubstituted allenes reacted predominantly at the terminal double bond in an exocyclic mode (eq 53). Homologation by one carbon affords exclusively the six-membered

Table 5. Organolanthanide-Catalyzed Intramolecular Hydroamination of Aminoenynes



entry	substrate	product	% yield
1			75
2			95
3			93
4			88
5			92

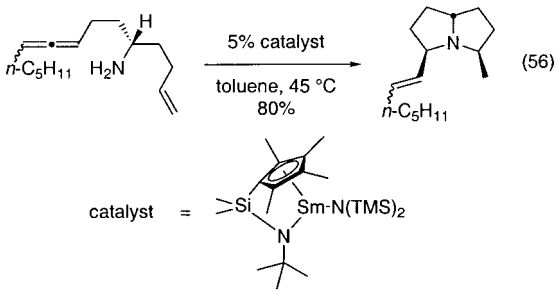
pyridine derivative (eq 54). 1,3-Disubstituted allenes react exclusively at the proximal double bond, providing mixtures of *Z:E* alkene products (eq 55). Changes in regioselectivity occur because the insertion event of the intramolecular hydroamination/cyclization reactions is highly sensitive to steric factors at the unsaturated moiety.



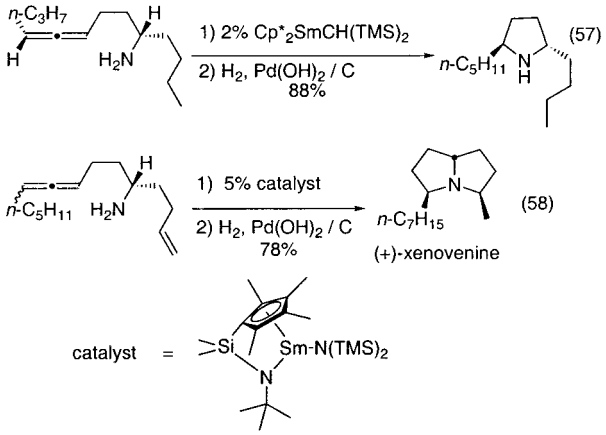
A variety of interesting and useful pyrrolidines and piperidines can be constructed using this method (Table 6).[57b] High diastereoselectivities at the ring stereocenters, affording *trans*-pyrrolidines (Figure 11) or *cis*-piperidines (Figure 12), were observed in all cases (Figure 11), but *Z:E* diastereoselectivity was highly variable.

The substrate depicted in entry 3 (Table 6) is interesting because, in principle, it is capable of undergoing a double hydroamination process. As indicated, under the conditions of the reaction with $Cp^*_2LaCH(TMS)_2$, high selectivity is achieved for reaction only at the allene. However, utilizing more reactive "constrained geometry" catalysts the double hydroamination occurs with facility, providing the nitrogen heterobicyclic system in excellent yield (eq 56).[53]

The lanthanocene-catalyzed hydroamination reaction of aminoallenes has been utilized as the key



cyclization step in the construction of the pyrrolidine alkaloid (+)-197B (eq 57) and the pyrrolizidine alkaloid (+)-xenovenine (eq 58).[57c]



Intermolecular versions of the catalyzed hydroamination reaction proceed at rates 1000 times slower than their intramolecular counterparts.[50g] To facilitate this process, a more open, more highly reactive catalyst has been utilized to effect the desired reaction. Even so, elevated reaction temperatures and extended reaction times are required to bring the transformations to completion (Table 7). High regioselectivities can be achieved in these reactions on unsymmetrical alkenes and alkynes (entries 1 and 3−5).

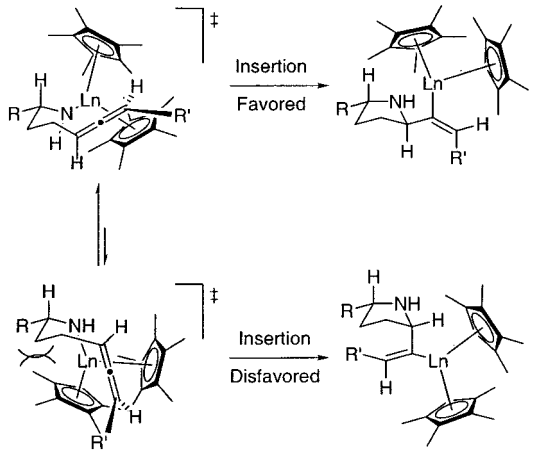
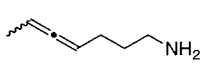
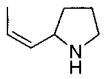
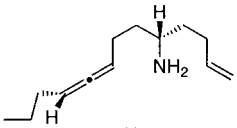
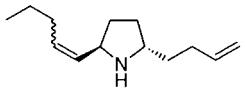
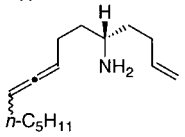
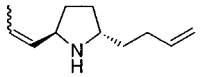
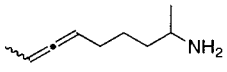
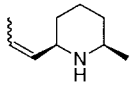


Figure 11. Transition structures explaining diastereoselectivity of intramolecular hydroamination/cyclization reactions of aminoallenes to afford *trans*-pyrrolidines.

As previously discussed, alkyne substrates undergo an initial insertion to provide an enamine, which subsequently isomerizes to the corresponding imine.

Table 6. Metallocene-Catalyzed Intramolecular Hydroamination of 1,3-Disubstituted Allenes

entry	substrate	catalyst	product	% yield	*Z*:*E*
1		$Cp^*_2YCH(TMS)_2$		93	6:1
2		$Cp^*_2SmCH(TMS)_2$		91	19:1
3		$Cp^*_2LaCH(TMS)_2$		85	2.6:1
4		$Cp^*_2LuCH(TMS)_2$		95	1:1

The observed product from the hydroamination reaction of 1-trimethylsilylpropyne is generated from a

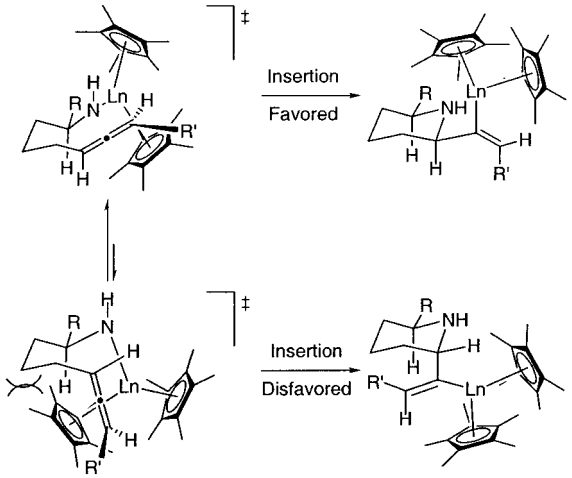


Figure 12. Transition structures explaining diastereoselectivity of intramolecular hydroamination/cyclization reactions of aminoallenes to afford *cis*-piperidines.

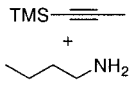
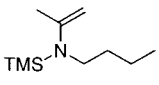
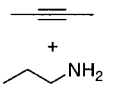
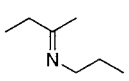
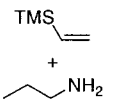
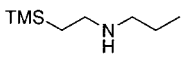
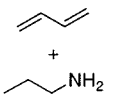
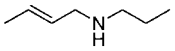
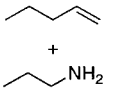
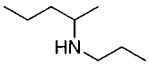
1,3-silatropic rearrangement of the imine (entry 1, Table 7, and Scheme 2). The regioselectivities observed in the silyl-substituted substrates in entries 1 and 3 reflect the tendency of silicon substituents to stabilize α-carbanionic and *β*-carbocationic character. Thus, the polarization of the metal−nitrogen bond is matched with the polarization of the alkene or alkyne in the four-centered insertion process. "2,1-"Insertion is also observed upon reaction with 1,3-butadiene, generating a stabilized allylmetallic species.[1,58] The resulting η^3-crotylmetallic intermediate is subsequently protonolyzed by another molecule of the amine, generating the observed product (entry 4, Table 7, and Scheme 3).

VIII. Catalyzed Hydrophosphinylation

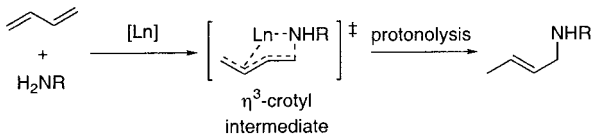
In analogy to the hydroamination reaction described above, unsaturated phosphines have also been utilized as substrates in lanthanocene-catalyzed cyclization processes (Table 8).[59] At present the synthetic value of this transformation is quite limited. Only a few substrates have been examined, and

Table 7. Organoneodymium-Catalyzed Intermolecular Hydroamination[a]

substrate —(1.3 mol% $Me_2SiCp'_2NdCH(TMS)_2$, benzene, 60 °C, 3 d)→ product

entry	substrates	product	% yield
1			62
2			91
3			93
4			90
5			90

Scheme 3



Scheme 2

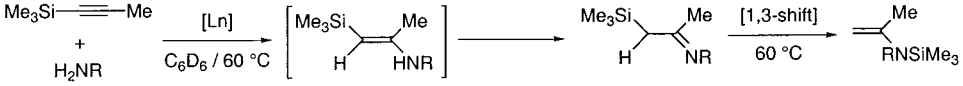
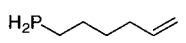
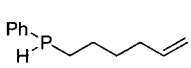
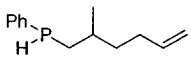
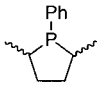
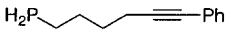
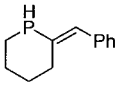
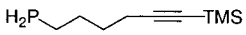
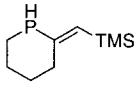


Table 8. Lanthanocene-Catalyzed Intramolecular Hydrophosphinylation

substrate	catalyst	product
	$Cp^*_2SmCH(TMS)_2$	
	$Cp^*_2LaCH(TMS)_2$	
	$Cp^*_2LaCH(TMS)_2$	
	$Cp^*_2LaCH(TMS)_2$	
	$Cp^*_2LaCH(TMS)_2$	

isolated yields for these reactions have not been reported. Shortcomings of the method encountered during experimental studies limit the scope of the reaction. For example, significant side reactions of the cyclization of phosphinoalkenes (entries 1−3) are noncatalyzed, light-induced cyclizations to afford undesired phosphorinanes. Furthermore, it is apparent that isolation of pure products is often difficult because some of the products themselves appear unstable. Nevertheless, the process is an important and unique one, worthy of further development.

IX. Catalyzed Cyclization/Functionalization Reactions

The inclination for organolanthanides and group 3 organometallics to undergo polymerizing olefin insertion reactions with α-olefins provides the possibility of cyclization of polyunsaturated systems. A reasonable catalytic cycle for such a transformation is depicted in Figure 13. There are several requirements for successful reduction of this process to reality. First, selective reaction at a single π-system

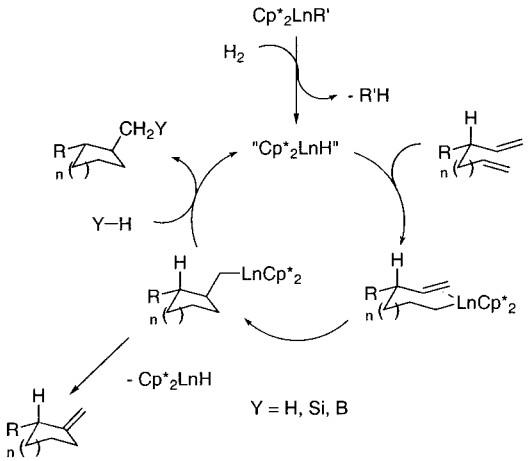
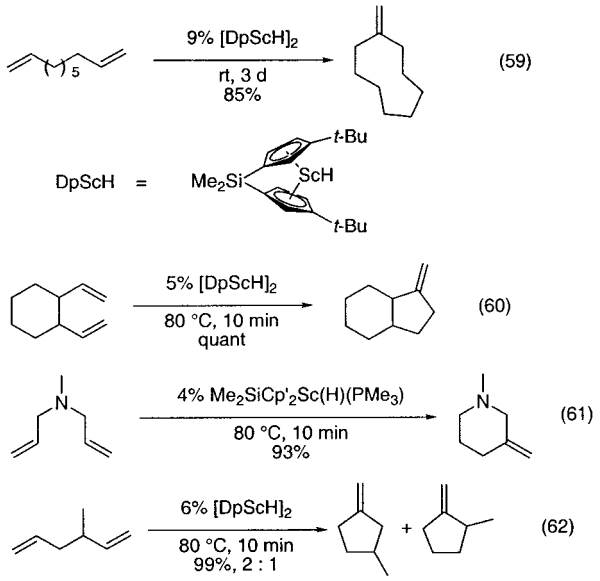


Figure 13. Mechanism of organolanthanide-catalyzed cyclization/functionalization reactions.

within an unsymmetrical diene is necessary to avoid mixtures of regioisomeric products. As noted previously, this prerequisite has been addressed with a number of catalysts (eq 9).[24] Second, transformations carried out with a functionalizing reagent (e.g., silane or borane) or under a hydrogen atmosphere require that the rate of cyclization must be faster than that of intermediate termination. That is, intramolecular olefin insertion must occur more rapidly than intermolecular σ-bond metathesis of the newly formed organometallic with the external agent. Furthermore, diastereoselectivity established in the process should be reliable and predictable based upon a simple chair transition structure for the cyclization. Intramolecular coordination of an alkene to an alkylyttrium metallocene has been documented,[60] and such an intermediate undoubtedly precedes cyclization, which provides a cyclized organometallic intermediate. Finally, in the absence of a functionalizing reagent, the catalytic cycle can be completed by β-hydride elimination to afford the exomethylene-substituted cycloalkane.

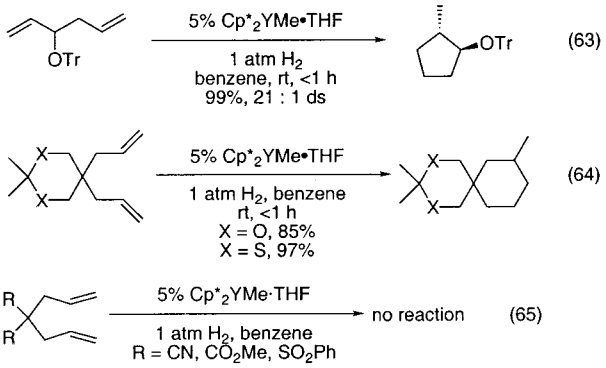
1. Termination by β-Hydride Elimination

Small- and medium-sized carbocycles and heterocycles have been synthesized utilizing organoscandium metallocenes (eqs 59−62).[4] These reactions were carried out in the absence of hydrogen or other "terminating agents". Consequently, the organometallic generated after initial olefin insertion was more persistent and is therefore provided the time to cyclize to ring sizes that are normally inaccessible. After cyclization upon the pendant olefin, β-hydride elimination furnishes the observed product and regenerates the metal hydride. Diastereoselectivity issues were not addressed in this study nor was the tolerance of the catalysts for a wide range of functional groups. From the reported studies, it is clear that discrimination of the catalysts for a monosubstituted alkene in the presence of an allylically substituted monosubstituted alkene is not high (eq 62).

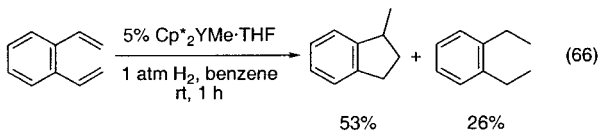


2. Termination by Hydrogenation

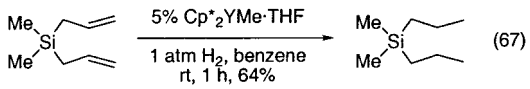
The cyclization of 1,5- and 1,6-dienes under reductive conditions was successfully realized utilizing organoyttrium catalysts.[6,61] Excellent selectivity was achieved in these reactions between two monosubstituted alkenes leading to a single regioisomeric product (eq 63), and the diastereoselectivity was consistent with the simple chair transition structure model (Figure 13). Incorporation of allylic substitution provided sufficient steric influence to force the yttrium hydride to selectively react at the more electron-rich, less encumbered olefin. If a heteroatom-directed reaction had occurred, predominance of a 1,3-disubstitution pattern would have been observed. Both acetals and thioacetals were tolerated (eq 64), whereas nitriles, esters, and sulfones precluded product formation (eq 65).



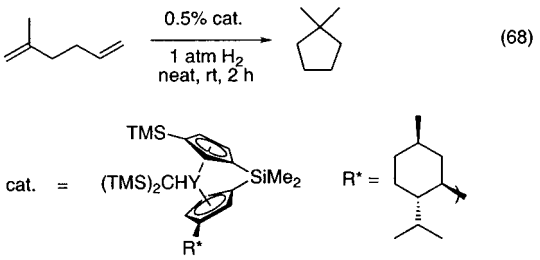
An attenuated yield of the cyclized product accompanied by reduced uncyclized material is obtained in the reaction of 1,2-divinylbenzene (eq 66).[61] This could be caused by the rigid aryl group skewing the geometry of the transition state, making cyclization more difficult. Additionally, it seems likely that a substantial amount of inverse ("2,1") addition occurs in the initial olefin insertion event. The failure of the secondary benzylic organometallic thus formed to cyclize would lead to formation of reduced uncyclized material.



Significant reduction is also observed in the attempted cyclization of diallyldimethylsilane (eq 67).[61] Presumably, the relatively long Si−C bond perturbs the cyclization transition state to prevent annulation.



More highly hindered (e.g., 1,1-disubstituted) alkenes are generally unreactive with the Cp^*_2YH catalysts. However, "tuning" the catalyst by providing a more accessible metal center permits rapid cyclization under extraordinarily mild conditions (eq 68).[6]



3. Termination by Silylation

Although the cyclization reactions described above represent a potentially powerful means for the construction of carbocycles, under reductive (hydrogenolysis) conditions the method utilizes a highly functionalized diene substrate and leaves an essentially unfunctionalized product in its wake. The utilization of silylation as a terminating event provides a convenient means to place functionality back into the molecule after the cyclization (Figure 14). The sequential process provides the selective assembly of both a carbon−carbon and a carbon−silicon bond in one step.

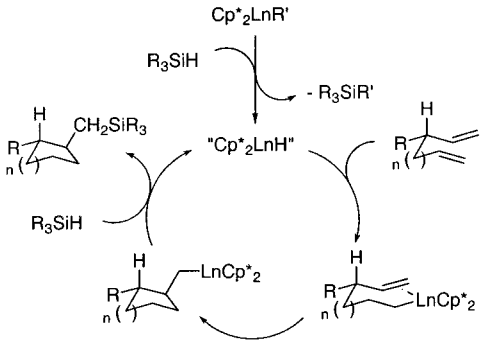
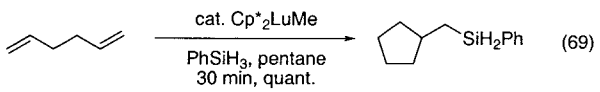


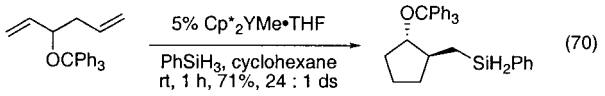
Figure 14. Mechanism of organolanthanide-catalyzed cyclization/silylation reactions.

Preliminary studies for the cyclization of 1,5-hexadiene and homologues centered on the utilization of organolutetiums (eq 69),[35a] organoneodymiums,[36c] and organosamariums.[27] These investigations of the cyclization/silylation process included only the simplest of substrates, leaving questions of regioselection, diastereoselection, and functional group toleration unanswered. A more thorough study of this chemistry that focused on the application to small molecule synthesis was performed utilizing organoyttrium complexes.[62] The organoyttrium-catalyzed process employed on monosubstituted dienes appears to be quite general for the synthesis of both five- and six-membered rings.



For the synthesis of five-membered rings, phenylsilane is a convenient "terminator". It provides high

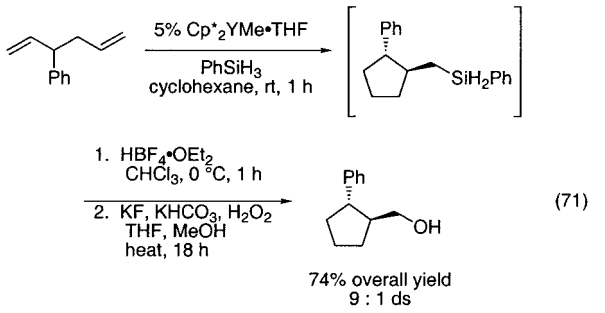
yields of cyclized/silylated products with no stereocenters introduced as a result of the incorporation of the silicon atom. High diastereoselectivities are achieved in many instances (eq 70).



(70)

An attractive feature of these organolanthanide-catalyzed reactions is the fact that they proceed with complete "atom economy",[63] i.e., all of the atoms from the substrates and reagents are incorporated into the desired product and there are no byproducts produced. Many of these reactions are so clean, in fact, that pouring the reaction mixture through a short bed of Florisil to remove the catalyst, followed by evaporation of the solvent and bulb-to-bulb distillation, leads to essentially quantitative yields of analytically pure product.

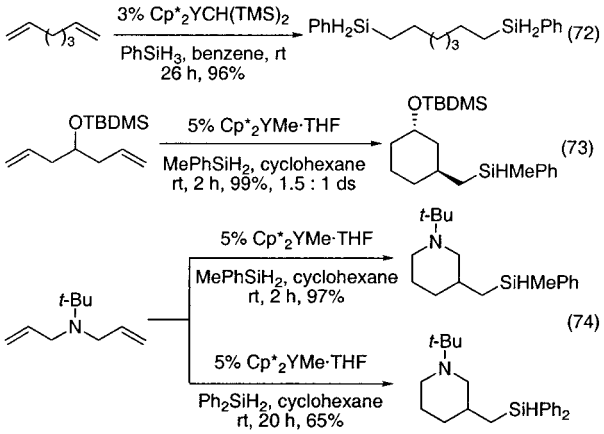
The synthetic equivalence of a silane to an alcohol can be easily demonstrated by subjecting the crude silane product to any of a variety of available oxidizing conditions (eq 71).[32,62] The resultant alcohol can be functionalized or elaborated further in the subsequent steps.



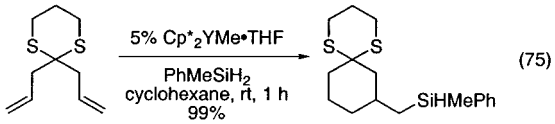
(71)

Cyclohexane formation is entropically less favorable than cyclopentane generation, and treatment of 1,6-dienes under the conditions listed in eq 70 leads to the production of uncyclized, disilylated products (eq 72)[38] or silicon-bridged dimers.[62] To promote cyclization, premature trapping of the organometallic must be slowed relative to the rate of intramolecular insertion of the olefin. Utilizing a more hindered silane, such as phenylmethylsilane, as the terminator delays σ-bond metathesis sufficiently to prevent dimerization (eq 73). Untimely conversion of the organometallic can also be retarded by the use of diphenylsilane (eq 74). The advantage in this case is that no new stereocenter at silicon is introduced into the product. Thus, not only can the metal and the ligand array be manipulated to bring about the desired result in the catalytic process, but the properties of the silane reagent itself can also be adjusted to meet the demands of the envisioned transformation.

The functional group compatibility of this process is similar to that described previously.[62] Protected alcohols (eq 73), tertiary amines (eq 74), and protected ketones (eq 75) are all inert to the reaction conditions.

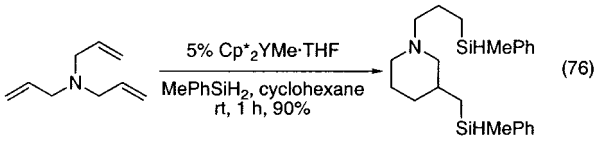


(72) (73) (74)



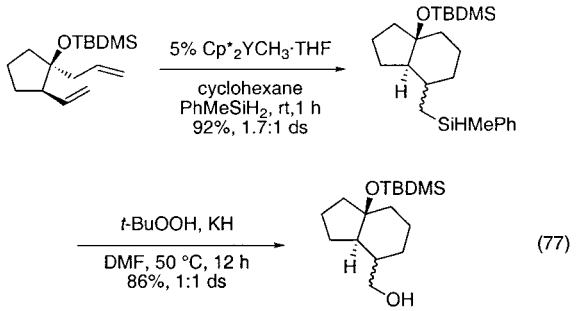
(75)

In the reaction of triallylamine (eq 76),[62] after the first ring-forming event the organometallic is trapped by σ-bond metathesis with the silane instead of undergoing an entropically unfavorable intramolecular olefin insertion to yield a bridged bicyclic structure. The remaining double bond then competes effectively for the catalyst, making the isolation of monocyclic silylated product bearing a free allyl group impossible.



(76)

In addition to accessing monocyclic rings, monosubstituted diene systems have been employed for the synthesis of fused ring systems (eq 77).[14,64] The simplest manner to accomplish this is to construct a second ring onto an existing structure. Production of fused ring skeleta is initiated at the alkene lacking allylic substitution. The formation of the six-membered ring necessitates the use of methylphenylsilane as the silylating reagent. Because the silane itself comprises a new stereocenter, it must be removed by oxidation to accurately assess the diastereoselectivity of cyclization. Fluxionality of the five-membered ring results in a mixture of diastereomers at the silylmethyl-substituted stereocenter.



(77)

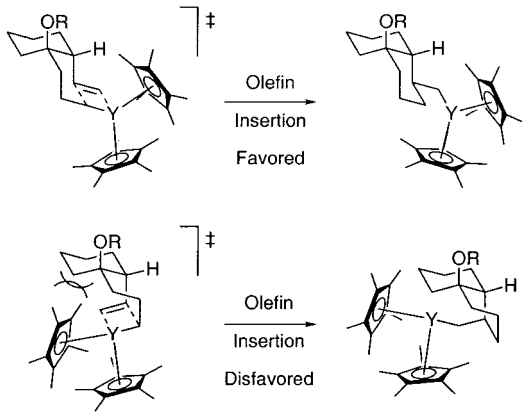
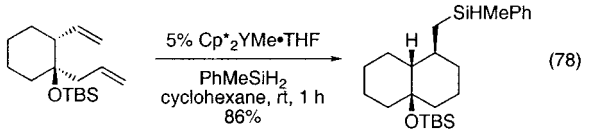


Figure 15. Transition structures demonstrating diastereoselectivity of polyene cyclizations producing *cis*-decalins.

On the basis of the mechanism, the stereochemistry at the ring juncture is passed undisturbed from the substrate. Thus, generation of substrates with a fixed relationship between the olefin-bearing centers grants access to either ring fusion (eq 78).[14,64] After oxidation of the silane product and deprotection to the corresponding diol, the stereochemistry of the single isomer was determined by single-crystal X-ray analysis. In this case, the high diastereoselectivity observed may be explained by the transition structures shown in Figure 15. The bulky organometallic is oriented away from the existing ring, leading to the observed *cis*-decalin product.



A *trans*-decalin system can be produced by using a substrate with the opposite diastereomeric relationship (eq 79 and Figure 16).[14,64] Of interest is the heightened stereoselectivity observed when the relatively rigid cyclohexane unit is substituted for the fluxional cyclopentane moiety (compare with eq 77). Constraining the transition state accentuates the steric interactions governing the stereochemical course of the reaction.

If the substituents are arranged to form a *trans*-decalin with complementary substitution, no cyclization occurs (eq 80).[14,64] The slow six-membered ring formation compounded by steric encumbrance at the alkene results in premature silylation. This allows

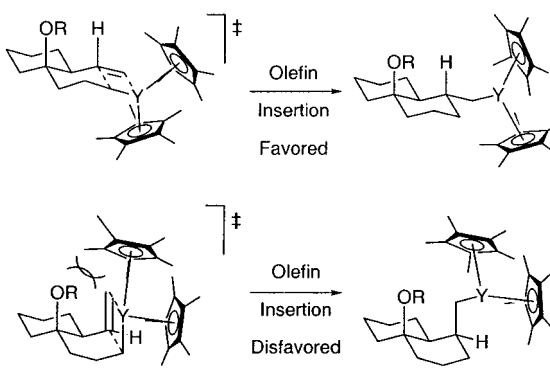
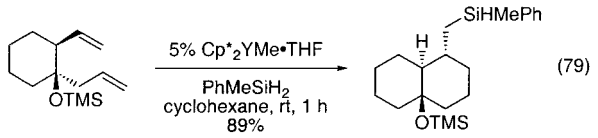
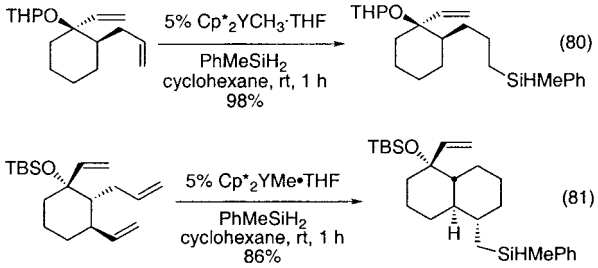


Figure 16. Transition structures demonstrating diastereoselectivity of polyene cyclizations producing *trans*-decalins.





impressive chemoselectivity in polyene substrates. When presented with a substrate possessing three monosubstituted olefins with varying steric environments, the catalyst can elect the least hindered alkene for initial insertion and will only cyclize onto the less hindered of the two remaining double bonds (eq 81). A mechanistic outline and depiction of the steric environments is provided in Figure 17.

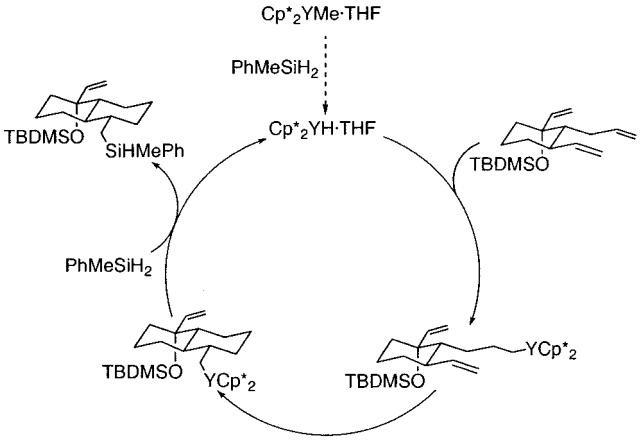
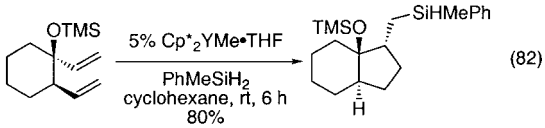


Figure 17. Transition structures demonstrating chemoselectivity of polyene cyclizations.

The failure to insert quaternary vinyl groups in a cyclization process is limited to 1,6-diene systems.[14,64] When a similar competition for selective insertion is attempted on a 1,5-diene, cyclization occurs because of the inherent entropic advantage of five-membered ring formation (eq 82). The close approach of the bulky organometallic to the axial alkoxy substituent in the chairlike transition structure (Figure 18b) causes the reaction to proceed through the less hindered boat conformation (Figure 18a).



In addition to their ability to assemble bicyclic structures on a monocyclic scaffold, the organoyttrium catalysts can also convert trienes to bicyclics

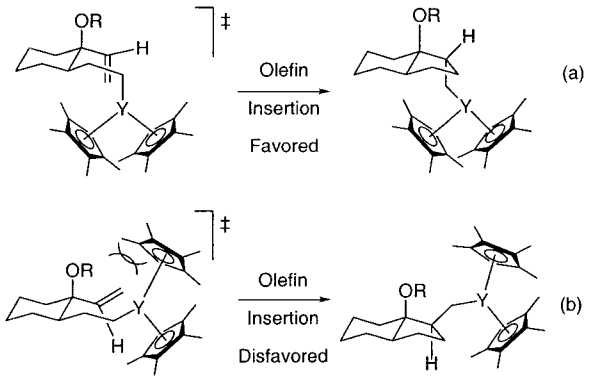
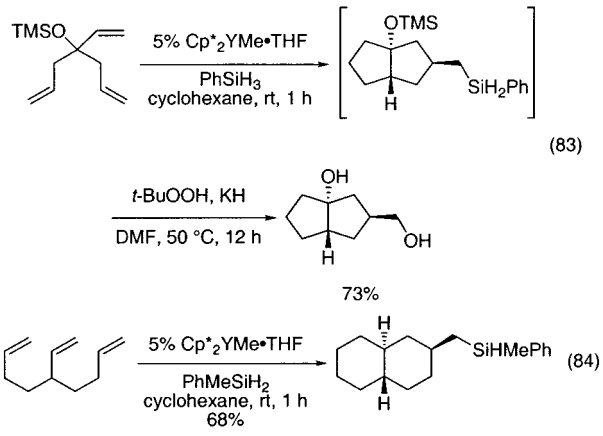


Figure 18. Transition structures explaining diastereoselectivity of polyene cyclizations producing *trans*-5,6 ring systems.

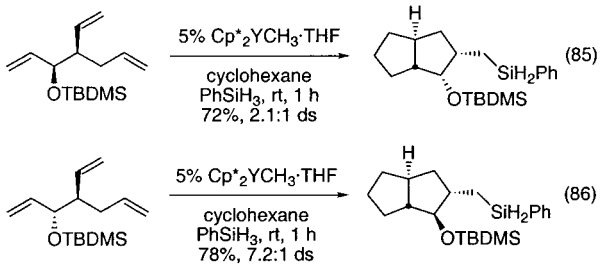
in a cascading process (eqs 83 and 84).[14,64] Both five- and six-membered rings can be constructed from the proper acyclic polyunsaturated systems. In these cases, the stereochemistry at the ring fusion is a result of the chairlike transition structures operative during the intramolecular olefin insertions (Schemes 4 and 5). There are two notable features of this reaction. First, after the initial olefin insertion, a 5-exo cyclization at the allylically substituted alkene is chosen over a 6-exo cyclization at an unhindered alkene. The second is the formation of the *trans*-bicyclo[3.3.0] ring system. Currently, the number of methods available to prepare this highly strained system is quite limited.[65] The formation of single product isomers attests to the high chemo- and stereoselectivity of each individual reaction step.

The chemoselectivity of these catalysts allows the discriminating construction of bicyclic systems bearing additional substitution (eqs 85 and 86).[14,64] Thus, the stereochemistry of the final product can be easily manipulated from simple acyclic precursors utilizing the cyclization/silylation protocol.

Despite their recognized Lewis acidity and their propensity to complex with heteroatoms (particularly in an intramolecular chelate),[4] the organoyttrium complexes can be utilized for the synthesis of nitrogen

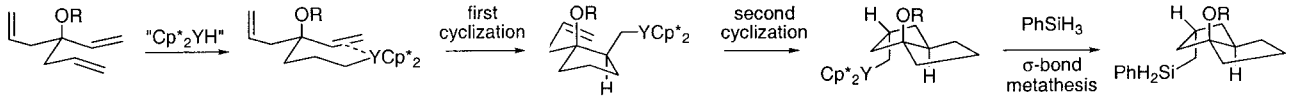


heterocycles. This strategy has been employed in a concise synthesis of (±)-epilupinine (Scheme 6).[66]

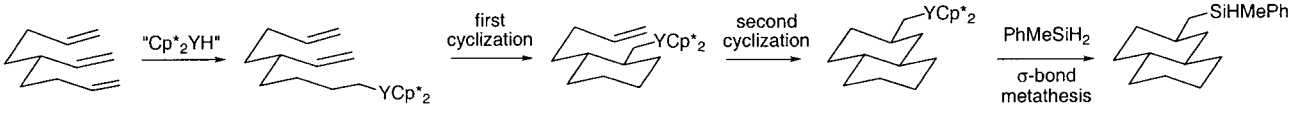


As mentioned previously, the utility of the relatively closed organoyttrium catalysts is limited to monosubstituted alkenes. To broaden the scope of the reaction, more open ligand arrays were developed to allow incorporation of 1,1-disubstituted alkenes. A first-generation catalyst was designed that exhibited moderate reactivity with these systems, albeit at somewhat elevated temperatures and protracted reaction times.[67] The ligand possessed a silicon hinge that served to open the clamshell comprised of the cyclopentadienyl rings. The rings themselves possessed a single trimethylsilyl group to prevent dimer formation upon generation of the metal hydride.

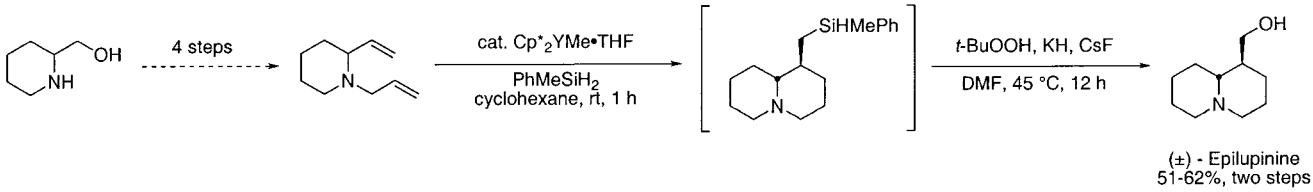
Scheme 4



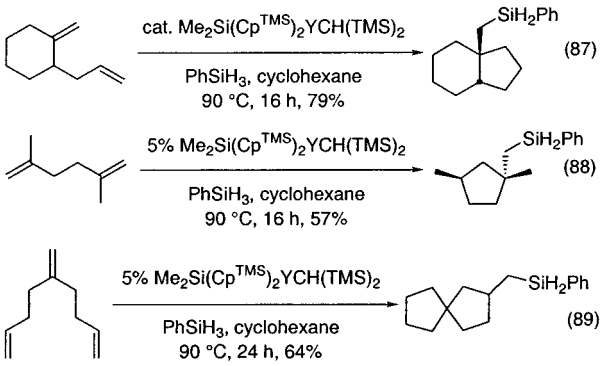
Scheme 5



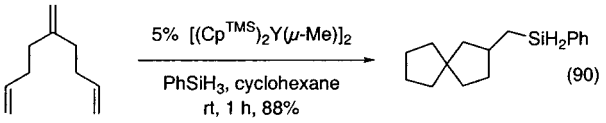
Scheme 6



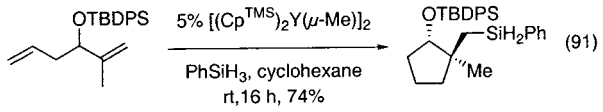
Cyclization/silylation reactions of various dienes demonstrated that monosubstituted alkenes reacted in preference to 1,1-disubstituted alkenes (eq 87). Remarkably, both alkenes can be disubstituted, generating a quaternary center with complete stereochemical control (eq 88). Trienes reacted in a sequential process, in one case leading to a spirocyclic system (eq 89). The first ring formation is selective for the construction of a five-membered ring, reacting with the 1,1-disubstituted olefin in preference to the terminal olefin. The intermediate monocyclic hydrocarbyl undergoes a second insertion reaction to afford the spirocycle in good yield.



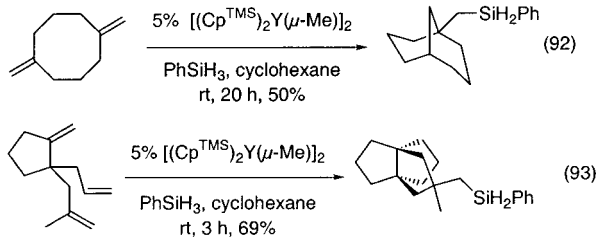
To improve upon the reactivity of the catalyst, a second-generation catalyst was tested in similar systems (eq 90).[67] The new ligand system lacked the



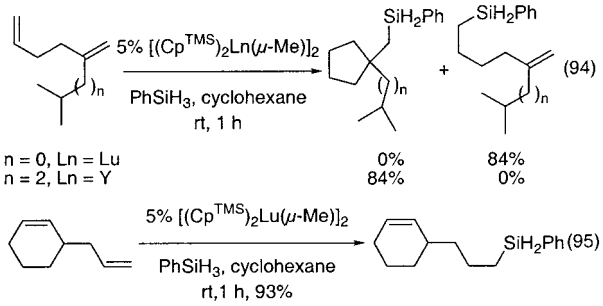
silicon hinge, and upon reactions with a number of dienes, the catalysts proved to be extraordinarily reactive. In comparison with previous investigations, the newly developed metallocenes were orders of magnitude more reactive than any other neutral catalyst to date (compare eqs 89 and 90). The enhanced performance of the catalysts allowed the reaction in eq 88 to be performed on a 20 mmol scale with a catalyst loading as little as 0.5 mol %. After essentially the same period of time as the small-scale reaction, the product was isolated in good yield (~80%). Despite the increased reactivity of the catalysts, they displayed unexpected stability to air, thereby enabling the handling of the catalysts on the benchtop using standard techniques for the handling of air-sensitive reagents.[5] Furthermore, the catalyst also endures the presence of the standard functional groups for this general class of catalysts (eq 91). One drawback with the catalyst is that it apparently becomes deactivated over time because of hydride dimer formation. Ideal reaction conditions for slow-reacting substrates thus involve addition of smaller portions of the catalyst at fixed intervals to maintain an active concentration of the catalyst.



The expanded capabilities of this catalyst allowed the construction of additional ring systems.[67] A transannular olefin insertion of hindered systems formed a bicyclo[3.3.1]nonane structure (eq 92). Multiple insertion steps can selectively transform a monocyclic substrate into a propellane derivative (eq 93). The catalytic cycle begins at the monosubstituted olefin, followed by the insertion of the remaining double bonds to form five-membered rings.



Although the catalyst supports transformations of 1,1-disubstituted alkenes, the metallocene is intolerant of branching on a hindered olefin (eq 94).[67] The addition of two methylene units between the alkene and the branch point is required to provide good yields of cyclized product. Another limitation is the inability of the complex to insert an endocyclic olefin (eq 95).



A single report has appeared outlining efforts to develop an enantioselective version of the diene cyclization/silylation reaction.[68] A C_2-symmetrical yttrocene catalyst (Figure 19) was tested on several representative substrates (Table 9). Yields in the desired transformations were excellent; however, the observed enantioselectivities were disappointing. This frontier awaits further evaluation, design, and testing.

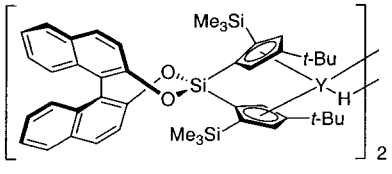


Figure 19. Bercaw's [(*R*,*S*)-BnBpY-H]$_2$ catalyst.

Table 9. Asymmetric Cyclization-Silylation of α,ω-Dienes with Bercaw's [(*R*,*S*)-BnBpY−H]$_2$ Catalyst

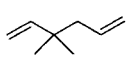
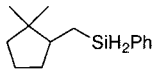
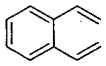
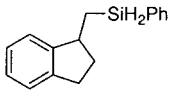
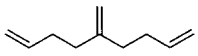
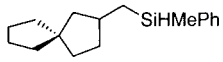
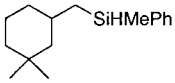
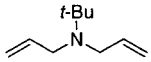
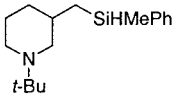
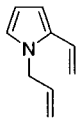
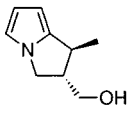
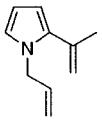
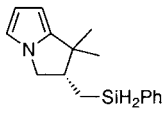
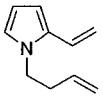
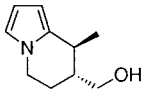
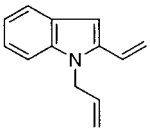
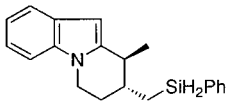
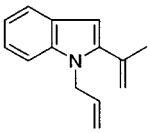
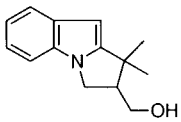
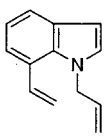
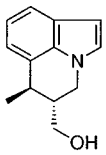
substrate	silane	product	% yield	% ee
	$PhSiH_3$		95	50
	$PhSiH_3$		84	10
	$PhMeSiH_2$		72	23
	$PhMeSiH_2$		80	14
	$PhMeSiH_2$		74	< 5

Table 10. [Cp$^{TMS}_2$Y(μ-Me)]$_2$-Catalyzed Cyclization/Silylation Reactions of Heteroaromatic Dienes[a]

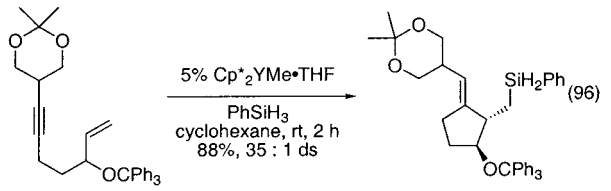
entry	substrate	product	% isolated yield (ds)
1			90 (98:2)
2			94
3			60 (98:2)
4			85 (98:2)
5			68
6			58 (9:1)

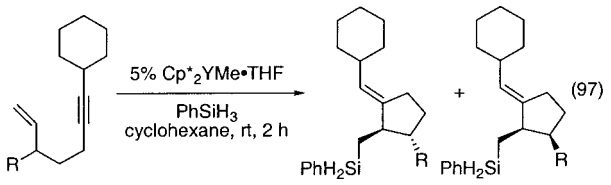
[a] Some phenylsilanes were converted directly to the corresponding alcohols by known methods.

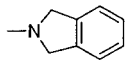
The "aryl-directed" regioselectivity observed for styrene in many of the processes described previously (see, for example, Figure 5) has been effectively applied to pyrrole and indole derivatives in cyclization/silylation sequences (Table 10).[69] The chemoselectivity observed in some of these reactions (entries 2 and 5) is remarkable given the results of competitive rate studies, which indicated that isolated monosubstituted alkenes and disubstituted alkenes conjugated with the pyrrole ring reacted at similar rates (see Table 2). Further, the observation that the tertiary organometallics generated in the initial olefin insertion cyclize so efficiently is also surprising given the dominant role that steric effects play in the reactivity of the catalysts toward alkenes. The overall transformation provides a useful synthetic method to access functionalized five- and six-membered nitrogen aromatic heterocycles.

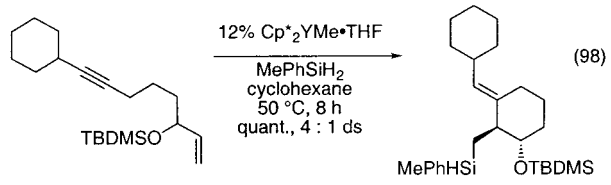
Elaboration of the cyclization/silylation sequential reaction from polyolefins to enynes has been tremendously successful.[70] Organoyttrium metallocenes have proven to be chemoselective, undergoing preferential reaction at the electron-rich alkyne. Propargyl branching is required to direct the regiochemistry of the initial insertion. The alkenylyttrium formed in the initial insertion event is converted smoothly via the cyclization/silylation process to afford the desired products. Compatibility with a variety of functional groups at key positions in these substrates was demonstrated in the process (eqs 96 and 97). The diastereoselection varies reliably with the size of the substituent, as would be expected from the chairlike transition structure for insertion. Six-membered rings can also be generated in high yields and with modest diastereoselection when phenylmethylsilane is employed (eq 98). In this case, varying the silylating reagent allows for complete cyclization of the substrate (compare with eq 40).

The cyclization protocol can be carried a step further by judiciously placing another olefin in the substrate.[71] In the process, a fused ring system is generated with the selective formation of two carbon−carbon bonds and one carbon−silicon bond. The incorporation of an additional allylic group results in low yields of bicyclic products (eq 99). The reduced yield is certainly because of the poor chemoselectivity between the alkyne and the allylic olefin in the initial

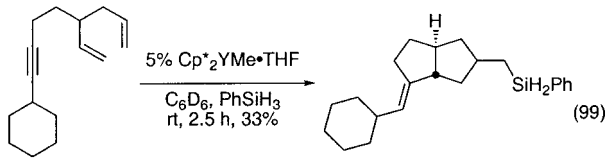




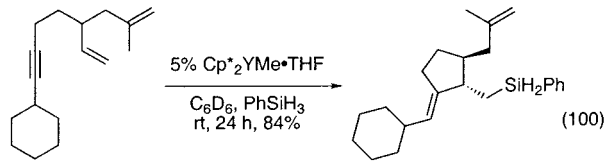
R	% yield	ds
OTBDMS	93	6.5 : 1
OTIPS	93	12 : 1
OTr	84	24 : 1
Et	88	>50 : 1
CH_2OMe (100 °C)	80	20 : 1
$CH_2OTBDMS$	76	>50 : 1
	91	40 : 1



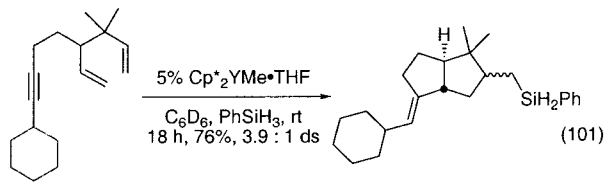
insertion event. Steric distinction between the unsaturated systems is necessary to provide for a successful reaction. Alkyl substitution on the allyl



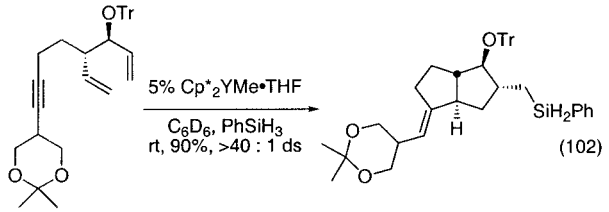
group provides complete selectivity for initial alkyne insertion, but the hindered olefin prevents bicyclic product formation (eq 100). Geminal dimethyl sub-

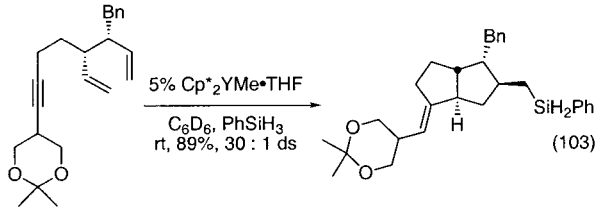


stitution at the allylic position, however, provides selectivity in the initial insertion without stopping the second intramolecular insertion from taking place (eq 101). This dienyne cyclization allows another entry into the strained *trans*-bicyclo[3.3.0]octane system and incorporates an additional handle for further functionalization.

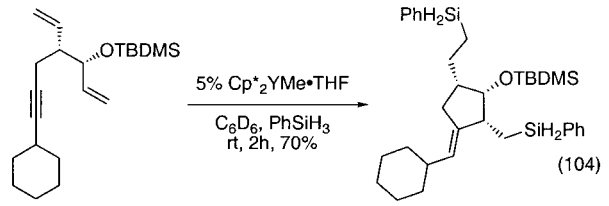


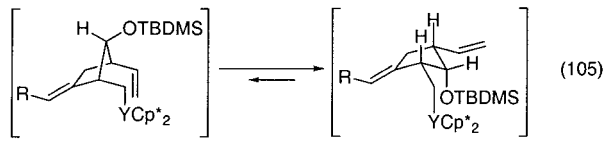
A single substituent allylic to the monosubstituted olefin is sterically large enough to make the initial insertion selective (eqs 102 and 103).[46] Either substrate diastereomer can be prepared, leading to different steric interactions in the transition states (Figures 20 and 21) and different product stereochemistry patterns.





Shortening the alkyl chain by one carbon provides a substrate that is capable of bicyclo[2.2.1]heptane generation (eq 104).[46] After the initial alkyne insertion, the catalyst must choose between cyclobutane and cyclopentane formation. The five-membered ring is formed because of the lower strain involved, but the remaining olefin is not inserted because the lowest energy conformation of the organometallic intermediate places the olefin out of reach of the carbon−metal bond (eq 105).





In addition to carbocycles, nitrogen heterocycles can be synthesized using the enyne cyclization/silylation protocol.[72] In the preparation of five-membered rings, Cp^*_2LuMe•THF was determined to provide maximum yields (Table 11). Utilizing a lanthanide with a small ionic radius impedes intramolecular coordination of the metal center with the nitrogen atom in the alkyne-inserted intermediate. Monocyclic (entry 4), bicyclic (entries 1 and 2), and tricyclic cores (entry 3) can all be accessed utilizing this strategy.

For six-membered ring formation, chelation of the nitrogen through a five-membered ring is not as significant and the Cp^*_2YMe•THF precatalyst provided good to excellent yields of the desired products (Table 12). The development of these reactions pro-

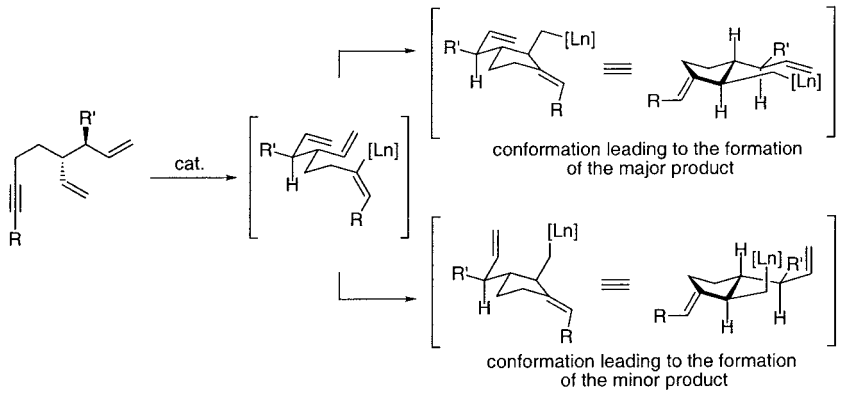


Figure 20. Transition structures in the formation of bicyclic products from *anti*-dienynes.

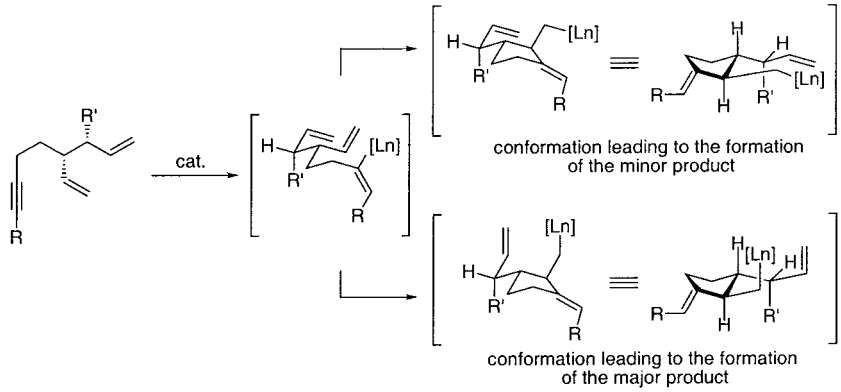
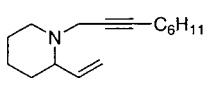
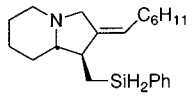
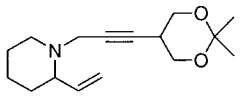
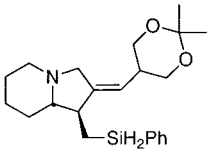
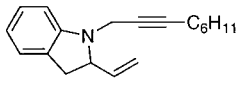
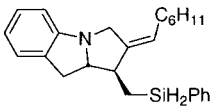
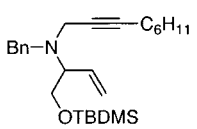
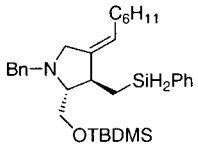


Figure 21. Transition structures in the formation of bicyclic products from *syn*-dienynes.

Table 11. Cyclization/Silylation of Enynes with Cp*$_2$LuMe·THF To Afford Five-Membered Nitrogen Heterocycles

entry	substrate	product	% isolated yield
1			92
2			78
3			43
4			90

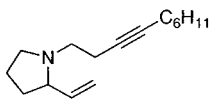
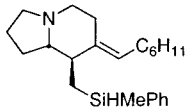
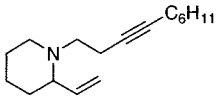
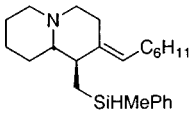
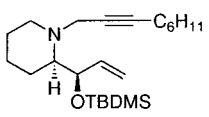
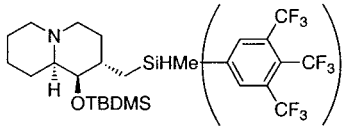
vided further evidence that "tuning" of the catalysts can be easily carried out to achieve optimum conversions in transformations of interest.

4. Termination by Boration

The synthetic utility of the lanthanocene-catalyzed cyclization/silylation reactions described above are somewhat restrictive because synthetically useful conversions of the resulting organosilicon compounds are limited. To address this issue, a study was undertaken to examine the possibility of a cyclization/boration process (Figure 22). In the event that such a transformation could be accomplished, numerous functional groups could be incorporated into the eventual product of these reactions via well-known organoboron chemistry.

Because of the uncertainties alluded to previously concerning catalyzed versus noncatalyzed processes

Table 12. Cyclization/Silylation of Enynes with Cp*$_2$YMe·THF To Afford Six-Membered Nitrogen Heterocycles

entry	substrate	product	% isolated yield
1			100
2			94
3			61

in lanthanocene-induced hydroborations (see section V), a survey of various hydroborating agents was conducted to determine if a suitable reagent could

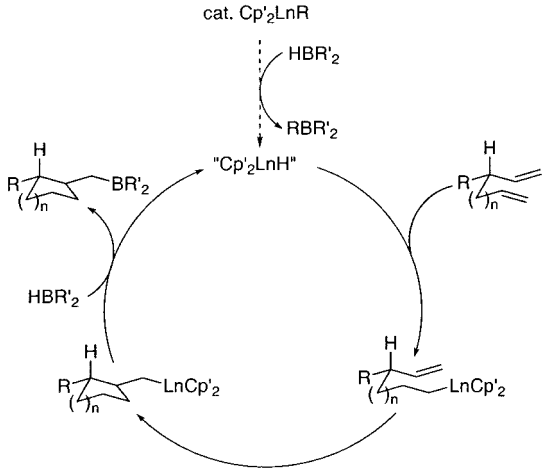
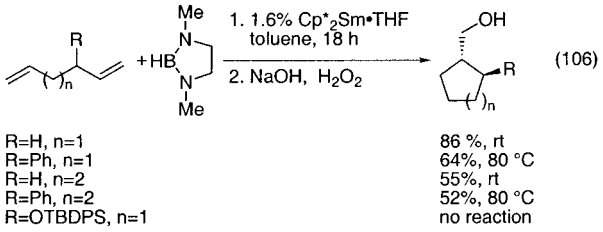
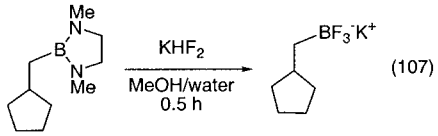


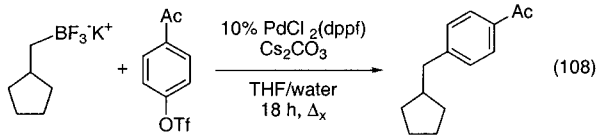
Figure 22. Mechanism of organolanthanide-catalyzed cyclization/boration reactions.

be developed for this process. Indeed, the reagent claimed to provide good yields of hydroboration product in previous studies completely failed in these reactions.[48] Fortunately, *N*,*N*-dimethyl-1,3-diazaboracyclopentane proved to be an adequate reagent for the desired transformation, providing reasonable yields of the cyclized products (eq 106).[73]



As shown, the resulting organoboron compounds could be readily oxidized under standard conditions to the corresponding alcohols. Alternatively, conversion to the alkyltrifluoroborates could be effected (eq 107). The latter serve as effective substrates in palladium-catalyzed Suzuki-type coupling reactions (eq 108).[74]





X. Conclusions

The lanthanide and group 3 metallocenes display bounteous chemistry that can be exploited for the selective synthesis of small molecules. At least one class of catalysts exhibits reasonable stability in the air. Consequently, they are readily accessible to practicing synthetic organic chemists. Catalysts have been developed that permit reactions of monosubstituted and 1,1-disubstituted alkenes as well as internal alkynes. Various substitution patterns on the substrate can be accommodated by exploiting different combinations of ligand and metal. Practical solutions for the inability of more highly substituted alkenes to insert have yet to be reduced to practice. Terminal alkynes are rapidly metalated by these catalysts and are unlikely to be adaptable to many of the processes outlined in this contribution. The catalysts tolerate a variety of functional groups (halides, acetals, thioacetals, ethers, and amines), and thus, highly functionalized substrates of interest in complex molecule synthesis should be amenable to utilization in selected processes. A high degree of chemoselectivity can be achieved in polyunsaturated systems, and regiochemistry in the olefin insertion reactions can also be directed. Both of these conspire to provide an effective means to control the direction of cyclization in unsymmetrical systems. Excellent diastereoselectivity can often be achieved, taking advantage of both the inherent selectivity of the catalysts themselves as well as the highly ordered transition structures involved in the intramolecular

processes they promote. Finally, elegant asymmetric catalysts have been synthesized and utilized in selective reactions. Further developments in this arena are certain to produce a class of catalysts that provide rapid and efficient entry to a wide range of complex structures in enantiopure form.

XI. Acknowledgments

Our work in this area was supported by a research grant from the National Institutes of Health (GM48580). The authors thank a very talented group of co-workers whose names appear in the references below for their dedicated effort to this chemistry.

XII. References

(1) Jeske, G.; Lauke, H.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8091.
(2) (a) Borricello, A.; Busico, V.; Sudemijer, O. *Macromol. Rapid Commun.* **1996**, *17*, 589. (b) Sinclair, K. B.; Wilson, R. B. *Chem. Ind.* **1994**, 857.
(3) (a) Watson, P. L. *Chem. Commun.* **1983**, 276. (b) Evans, W. J.; Chamberlain, L. R.; Ulibarri, T. A.; Ziller, J. W. *J. Am. Chem. Soc.* **1988**, *110*, 6423.
(4) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74.
(5) Brown, H. C. *Organic Syntheses via Boranes*: Wiley: New York, 1975.
(6) Haar, C. M.; Stern, C. L.; Marks, T. J. *Organometallics* **1996**, *15*, 1765.
(7) (a) Schumann, H.; Genthe, W.; Bruncks, N. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 119. (b) Evans, W. J.; Wayda, A. L.; Hunter, W. E.; Atwood, J. L. *Chem. Commun.* **1981**, 292.
(8) Evans, W. J. *Polyhedron* **1987**, *6*, 803.
(9) Deelman, B.-J.; Booij, M.; Meetsma, A.; Teuben, J. H.; Kooijman, H.; Spek, A. L. *Organometallics* **1995**, *14*, 2306.
(10) Stern, D.; Sabat, M.; Marks, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 9558.
(11) Voskoboynikov, A. Z.; Shestakova, A. K.; Beletskaya, I. P. *Organometallics* **2001**, *20*, 2794.
(12) den Haan, K. H.; Wielstra, Y.; Teuben, J. H. *Organometallics* **1987**, *6*, 2053.
(13) Wang, K. K.; Brown, H. C. *J. Am. Chem. Soc.* **1982**, *104*, 7148.
(14) Nichols, P. J. Ph.D. Thesis, University of Colorado at Boulder, 1997.
(15) Abram, U.; DellAmico, D. B.; Calderazzo, F.; Porta, C. D.; Englert, U.; Marchetti, F.; Merigo, A. *Chem. Commun.* **1999**, 2053.
(16) Schumann, H.; Keitsch, M. R.; Demtschuk, J.; Molander, G. A. *J. Organomet. Chem.* **1999**, *582*, 70.
(17) Shriver, D. F.; Drezdzon, M. A. *The Manipulation of Air-Sensitive Compounds*, 2nd ed; Wiley-Interscience: New York, 1986.
(18) Jeske, G.; Schock, L. E.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8103.
(19) Mu, Y.; Piers, W. E.; MacDonald, M.-A. Zaworotko, M. J. *Can. J. Chem.* **1995**, *73*, 2233−2238. (b) Tian, S.; Arrendondo, V. M.; Stern, C. L.; Marks, T. J. *Organometallics* **1999**, *18*, 2568−2570. (c) Hultzsch, K. C.; Voth, P.; Beckerle, K.; Spaniol, T. P.; Okuda, J. *Organometallics* **2000**, *19*, 228−243. (d) Arndt, S.; Voth, P.; Spaniol, T. P.; Okuda, J. *Organometallics* **2000**, *19*, 4690−4700.
(20) (a) Marks, T. J.; Ernst, R. D. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 3. (b) Evans, W. J. In *The Chemistry of the Metal−Carbon Bond*; Hartley, F. R., Patai, S., Eds.; John Wiley & Sons: Chichester, 1982. (c) Schumann, H.; Genthe, W. In *Handbook on the Chemistry and Physics of Rare Earths*; Gschneidner, K. A., Jr., Eyring, L., Eds.; Elsevier: Amsterdam, 1984. (d) Schumann, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 474. (e) Evans, W. J. *Adv. Organomet. Chem.* **1985**, *24*, 131. (f) Schumann, H.; Meese-Marktscheffel, J. A.; Esser, L. *Chem. Rev.* **1995**, *95*, 865. (g) Schaverien, C. J. *Adv. Organomet. Chem.* **1994**, *36*, 283.
(21) Jeske, G.; Lauke, H.; Mauermann, H.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8111.
(22) Ye, C.; Qian, C.; Yang, X. *J. Organomet. Chem.* **1991**, *407*, 329.
(23) (a) Zinnen, H. A.; Pluth, J. J.; Evans, W. J. *Chem. Commun.* **1980**, 810. (b) Brothers, P. J. *Prog. Inorg. Chem.* **1981**, *28*, 1. (c) Evans, W. J.; Meadows, J. H.; Wayda, A. L.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1982**, *104*, 2008. (d) Schumann, H.; Genthe, W. *J. Organomet. Chem.* **1981**, *213*, C7. (e) Marks, T. J. *Inorg. Chim. Acta* **1987**, *140*, 1. (f) Thompson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schaefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203.
(24) Molander, G. A.; Hoberg, J. O. *J. Org. Chem.* **1992**, *57*, 3266.
(25) Molander, G. A.; Winterfeld, J. *J. Organomet. Chem.* **1996**, *524*, 275.
(26) (a) Conticello, V. P.; Brard, L.; Giardello, M. A.; Tsuji, Y.; Sabat, M.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 2761. (b) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10241.
(27) Fu, P.-F.; Brard, L.; Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 7157.
(28) Roesky, P. W.; Denninger, U.; Stern, C. L.; Marks, T. J. *Organometallics* **1997**, *16*, 4486.
(29) Evans, W. J.; Bloom, I.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 6507.
(30) (a) Radu, N. S.; Buchwald, S. L.; Scott, B.; Burns, C. J. *Organometallics* **1996**, *15*, 3913. (b) Obora, Y.; Ohta, T.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1997**, *119*, 3745.
(31) (a) Speier, J. L. *Adv. Organomet. Chem.* **1979**, *17*, 407. (b) Ojima, I. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley & Sons Ltd.: London, 1989. (c) Yamamoto, K.; Takemae, M. *Synlett* **1990**, 259. (d) Takahashi, T.; Hasegawa, M.; Suzuki, N.; Saburi, M.; Rousset, C. J.; Fanwick, P. E.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 8564. (e) Boudjouk, P.; Han, B.-H.; Jacobsen, J. R.; Hauck, B. J. *Chem. Commun.* **1991**, 1424. (f) Kesti, M. R.; Abdulrahman, M.; Waymouth, R. M. *J. Organomet. Chem.* **1991**, *417*, C12. (g) Kesti, M. R.; Waymouth, R. M. *Organometallics* **1992**, *11*, 1095.
(32) (a) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1649. (b) Bergens, S. H.; Nogeda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2121. (c) Taber, D. F.; Yet, L.; Bhamidipati, R. S. *Tetrahedron Lett.* **1995**, *36*, 351. (d) Fleming, I.; Hennings, R.; Plaut, H. *Chem. Commun.* **1984**, 29. (e) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229. (f) Fleming, I.; Winter, S. B. D. *Tetrahedron Lett.* **1993**, *34*, 7287. (g) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044. (h) Taber, D. F.; Yet, L.; Bhamidipati, R. S. *Tetrahedron Lett.* **1993**, *34*, 7287.
(33) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179.
(34) Voskoboynikov, A. Z.; Parshina, I. N.; Shestakova, A. K.; Butin, K. P.; Beletskaya, I. P.; Kuz′mina, L. G.; Howard, J. A. K. *Organometallics* **1997**, *16*, 4041.
(35) (a) Watson, P. L.; Tebbe, F. N. U. S. Patent 4,965,386; *Chem. Abstr.* **1991**, *114*, 123331p. (b) Forsyth, C. M.; Nolan, S. P.; Marks, T. J. *Organometallics* **1991**, *10*, 1450. (c) Radu, N. S.; Tilley, T. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 8293. (d) Radu, N. S.; Tilley, T. D. *J. Am. Chem. Soc.* **1995**, *117*, 5863.
(36) (a) Beletskaya, I. P.; Voskoboinikov, A. Z.; Parshina, I. N.; Magomedov, G. K.-I. *Izv. Akad. Nauk SSR, Ser. Khim.* **1990**, 693. (b) Sakakura, T.; Lautenschlager, H.-J.; Tanaka, M. *Chem. Commun.* **1991**, 40. (c) Onozawa, S.; Sakakura, T.; Tanaka, M. *Tetrahedron Lett.* **1994**, *35*, 8177.
(37) Molander, G. A.; Dowdy, E. D.; Noll, B. C. *Organometallics* **1996**, *17*, 3754.
(38) Molander, G. A.; Julius, M. *J. Org. Chem.* **1992**, *57*, 6347.
(39) Molander, G. A.; Knight, E. E. *J. Org. Chem.* **1998**, *63*, 7009.
(40) Schumann, H.; Keitsch, M. R.; Winterfeld, J.; Muhle, S.; Molander, G. A. *J. Organomet. Chem.* **1998**, *559*, 181.
(41) *Comprehensive Handbook on Hydrosilylation*; Marciniec, B., Ed.; Pergamon: Oxford, U.K., 1992.
(42) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599 and references therein.
(43) Tamao, K.; Hayashi, T.; Ito, Y. In *Frontiers of Organosilicon Chemistry*; Bassindale, A. R., Gaspar, P. P., Eds.; Royal Society of Chemistry: Cambridge, U.K., 1991; pp 197−207.
(44) Molander, G. A.; Corrette, C. P. *Organometallics* **1998**, *17*, 5504.
(45) (a) Heeres, H. J.; Heeres, A.; Teuben, J. H. *Organometallics* **1990**, *9*, 1508. (b) Heeres, H. J.; Teuben, J. H. *Organometallics* **1991**, *10*, 1980.
(46) Molander, G. A.; Retsch, W. H. *Organometallics* **1995**, *14*, 4570.
(47) Molander, G. A.; Romero, J. A. C.; Corrette, C. P. *J. Organomet. Chem.*, in press.
(48) (a) Harrison, K. N.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 9220. (b) Bijpost, E. A.; Duchateau, R.; Teuben, J. H. *J. Mol. Catal.* **1995**, *95*, 121.
(49) Voskoboynikov, A. Z.; Beletskaya, I. P. *New J. Chem.* **1995**, *19*, 723.
(50) (a) Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 4108. (b) Gagné, M. R.; Nolan, S. P.; Marks, T. J. *Organometallics* **1990**, *9*, 1716. (c) Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275. (d) Gagné, M. R.; Brard, L.; Conticello, V. P.; Giardello, M. A.; Stern, C. L.; Marks, T. J. *Organometallics* **1992**, *11*, 2003. (e) Li, Y.; Fu, P.-F.; Marks, T. J. *Organometallics* **1994**, *13*, 439. (f) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 707. (g) Li, Y.; Marks, T. J. *Organometallics* **1996**, *15*, 3770. (h) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 9295.

(51) (a) Bürgstein, M. R.; Berberich, H.; Roesky, P. W. *Organometallics* **1998**, *17*, 1452. (b) Kim, Y. K.; Livinghouse, T.; Bercaw, J. E. *Tetrahedron Lett.* **2001**, *42*, 2933.
(52) Gilbert, A. T.; Davis, B. L.; Emge, T. J.; Broene, R. D. *Organometallics* **1999**, *18*, 2125.
(53) Tian, S.; Arredondo, V. M.; Stern, C. L.; Marks, T. J. *Organometallics* **1999**, *18*, 2568.
(54) Molander, G. A.; Dowdy, E. D. *J. Org. Chem.* **1998**, *63*, 8983.
(55) Molander, G. A.; Dowdy, E. D. *J. Org. Chem.* **1999**, *64*, 6515.
(56) Molander, G. A.; Dowdy, E. D.; Pack, S. K. *J. Org. Chem.* **2001**, *66*, 4344.
(57) (a) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871. (b) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *Organometallics* **1999**, *18*, 1949. (c) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633.
(58) Bunel, E.; Burger, B. J.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 976.
(59) Douglass, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 1824.
(60) (a) Casey, C. P.; Hallenbeck, S. L.; Wright, J. M.; Landis, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 9680. (b) Casey, C. P.; Klein, J. F.; Fagan, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 4320.
(61) Molander, G. A.; Hoberg, J. O. *J. Am. Chem. Soc.* **1992**, *114*, 3123.
(62) Molander, G. A.; Nichols, P. J. *J. Am. Chem. Soc.* **1995**, *117*, 4415.
(63) (a) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259. (b) Trost, B. M. *Science* **1991**, *254*, 1471.
(64) Molander, G. A.; Nichols, P. J.; Noll, B. C. *J. Org. Chem.* **1998**, *63*, 2292.
(65) (a) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K. V. *J. Am. Chem. Soc.* **1992**, *114*, 8053. (b) Cooke, M. P.; Gopal, D. *Tetrahedron Lett.* **1994**, *35*, 2837. (c) Davis, J. M.; Whitby, R. J.; Jaxa-Camiec, A. *Tetrahedron Lett.* **1992**, *33*, 5655. (d) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* **1998**, *30*, 5105. (e) Doi, T.; Yanagisawa, A.; Takahashi, T.; Yamamoto, K. *Synlett* **1996**, 145. (f) Piers, E.; Kaller, A. M. *Tetrahedron Lett.* **1996**, *37*, 5857.
(66) Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040.
(67) Molander, G. A.; Dowdy, E. D.; Schumann, H. *J. Org. Chem.* **1998**, *63*, 3386.
(68) Murci, A. R.; Bercaw, J. E. *Tetrahedron Lett.* **2000**, *41*, 7609.
(69) Molander, G. A.; Schmitt, M. H. *J. Org. Chem.* **2000**, *65*, 3767.
(70) Molander, G. A.; Retsch, W. H. *J. Am. Chem. Soc.* **1997**, *119*, 8817.
(71) Molander, G. A.; Retsch, W. H. *J. Org. Chem.* **1998**, *63*, 5507.
(72) Molander, G. A.; Corrette, C. P. *J. Org. Chem.* **1999**, *64*, 9697.
(73) Molander, G. A.; Pfeiffer, D. *Org. Lett.* **2001**, *3*, 361.
(74) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.

CR010291+