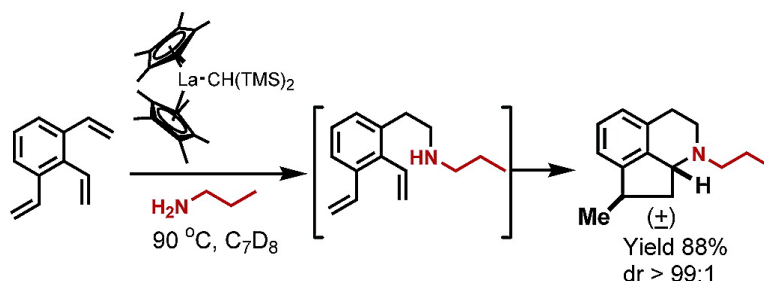Article

Organolathanide-Catalyzed Regioselective Intermolecular Hydroamination of Alkenes, Alkynes, Vinylarenes, Di- and Trivinylarenes, and Methylenecyclopropanes. Scope and Mechanistic Comparison to Intramolecular Cyclohydroaminations

Jae-Sang Ryu, George Yanwu Li, and Tobin J. Marks

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 35 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Organolathanide-Catalyzed Regioselective Intermolecular Hydroamination of Alkenes, Alkynes, Vinylarenes, Di- and Trivinylarenes, and Methylenecyclopropanes. Scope and Mechanistic Comparison to Intramolecular Cyclohydroaminations
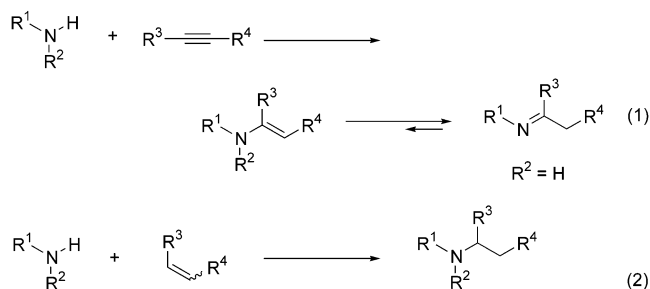
Jae-Sang Ryu, George Yanwu Li,[†] and Tobin J. Marks*

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60208-3113

Received April 30, 2003; E-mail: t-marks@northwestern.edu

Abstract: Organolanthanide complexes of the type $Cp'_2LnCH(SiMe_3)_2$ ($Cp' = \eta^5\text{-}Me_5C_5$; Ln = La, Nd, Sm, Lu) and $Me_2SiCp''_2LnCH(SiMe_3)_2$ ($Cp'' = \eta^5\text{-}Me_4C_5$; Ln = Nd, Sm, Lu) serve as efficient precatalysts for the regioselective intermolecular hydroamination of alkynes $R'C\equiv CMe$ ($R' = SiMe_3$, C_6H_5, Me), alkenes $RCH=CH_2$ ($R = SiMe_3$, $CH_3CH_2CH_2$), butadiene, vinylarenes $ArCH=CH_2$ (Ar = phenyl, 4-methylbenzene, naphthyl, 4-fluorobenzene, 4-(trifluoromethyl)benzene, 4-methoxybenzene, 4-(dimethylamino)benzene, 4-(methylthio)benzene), di- and trivinylarenes, and methylenecyclopropanes with primary amines $R''NH_2$ ($R'' = n$-propyl, n-butyl, isobutyl, phenyl, 4-methylphenyl, 4-(dimethylamino)phenyl) to yield the corresponding amines and imines. For $R = SiMe_3$, $R = CH_2=CH$ lanthanide-mediated intermolecular hydroamination regioselectively generates the anti-Markovnikov addition products ($Me_3SiCH_2CH_2NHR''$, (E)-$CH_3CH=CHCH_2$-NHR''). However, for $R = CH_3CH_2CH_2$, the Markovnikov addition product is observed ($CH_3CH_2CH_2$-$CHNHR''CH_3$). For internal alkynes, it appears that these regioselective transformations occur under significant stereoelectronic control, and for $R' = SiMe_3$, rearrangement of the product enamines occurs via tautomerization to imines, followed by a 1,3-trimethylsilyl group shift to stable N-SiMe$_3$-bonded $CH_2=CMeN$-$(SiMe_3)R''$ structures. For vinylarenes, intermolecular hydroamination with n-propylamine affords the anti-Markovnikov addition product β-phenylethylamine. In addition, hydroamination of divinylarenes provides a concise synthesis of tetrahydroisoquinoline structures via coupled *intermolecular* hydroamination/subsequent *intramolecular* cyclohydroamination sequences. Intermolecular hydroamination of methylenecyclopropane proceeds via highly regioselective exo-methylene C=C insertion into Ln−N bonds, followed by regioselective cyclopropane ring opening to afford the corresponding imine. For the $Me_2SiCp''_2Nd$-catalyzed reaction of $Me_3SiC\equiv CMe$ and $H_2NCH_2CH_2CH_2CH_3$, $\Delta H^\ddagger = 17.2$ (1.1) kcal mol^{-1} and $\Delta S^\ddagger = -25.9$ (9.7) eu, while the reaction kinetics are zero-order in [amine] and first-order in both [catalyst] and [alkyne]. For the same substrate pair, catalytic turnover frequencies under identical conditions decrease in the order $Me_2SiCp''_2$-$NdCH(SiMe_3)_2 > Me_2SiCp''_2SmCH(SiMe_3)_2 > Me_2SiCp''_2LuCH(SiMe_3)_2 > Cp'_2SmCH(SiMe_3)_2$, in accord with documented steric requirements for the insertion of olefinic functionalities into lanthanide−alkyl and −heteroatom σ-bonds. Kinetic and mechanistic evidence argues that the turnover-limiting step is intermolecular C=C/C≡C bond insertion into the Ln−N bond followed by rapid protonolysis of the resulting Ln−C bond.

Introduction

Carbon−heteroatom bond-forming reactions involving olefins and alkynes are important synthetic transformations in organic chemistry, and the direct addition of amines to such bonds is a conspicuously challenging and highly desirable process.[1] The simple catalytic addition of an N−H bond to C−C unsaturation, the hydroamination reaction, offers an efficient synthetic route to primary, secondary, and tertiary amines, imines, and enamines, by converting readily accessible alkenes and alkynes into desirable, more highly substituted nitrogen-containing products in a single step (e.g., eqs 1 and 2). The hydroamination of

$$R^1R^2N\text{-}H + R^3\text{—}\!\!\equiv\!\!\text{—}R^4 \longrightarrow \quad (1) \quad R^2 = H$$

$$R^1R^2N\text{-}H + \text{(alkene)} R^3R^4 \longrightarrow \quad (2)$$

alkynes[1a,b] (eq 1) affords relatively reactive enamines and imines, which can be used for further synthetic manipulations, while

† Current address: CombiPhos Catalysts, Inc., Princeton, NJ 08542-0220.

the hydroamination of alkenes directly provides a convenient access to stable saturated amines (eq 2). Although catalytic intermolecular homogeneous hydroamination of alkynes[1a,b] mediated by transition metals has progressed substantially in the last several years, the intermolecular hydroamination of alkenes[1] is generally recognized to be limited in scope due to a high activation barrier, which plausibly arises from electrostatic repulsion between the nitrogen lone pair electrons and the electron-rich π-bond of the olefin. Moreover, these *intermolecular* processes are generally much more difficult to achieve and far less developed than *intramolecular* processes, which are kinetically and thermodynamically favored.

Traditionally, intermolecular hydroamination has required the presence of alkali metals or metal hydrides at high temperatures and pressures.[2,3] More elegant processes have recently been developed using early- and late-transition-metal catalysts. In general, the advantage of late-transition-metal catalysts is their greater tolerance of polar functional groups. The first successful demonstration of this process was employed using Rh(III)[4] and Ir(III)[5] complexes. More recently, $Ru_3(CO)_{12}$[6,7] and $[Rh(cod)_2]$-BF_4[8] have been applied to the catalytic intermolecular hydroamination of aniline derivatives and terminal alkynes. In addition, Pd complexes in the presence of acid additives also mediate intermolecular alkyne hydroamination.[9] Note also that Pd-complex-catalyzed intermolecular hydroamination of vinylarenes[10] and dienes[11] has been reported.
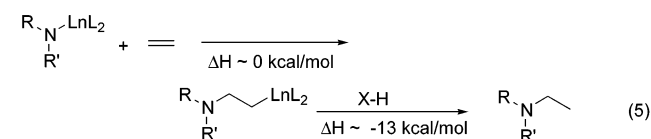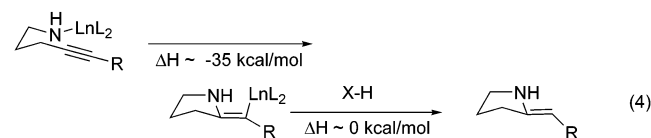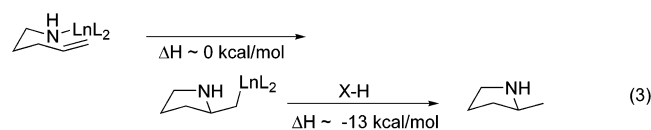
With regard to early transition metals,[1a] zirconocene-catalyzed intermolecular hydroamination of alkynes and allenes with aromatic amines has been extensively studied[12] as the first example of group IV metal mediated intermolecular hydroamination.[1a] Such transformations proceed via rather uncon-

ventional mechanisms involving metal imide (M=NR) complexes, and less sterically demanding amines cannot be used with alkynes or allenes, due to the formation of catalytically inactive dimers. Analogous actinide complexes also exhibit catalytic activity for terminal alkyne hydroamination in variable yields (7−80%) and presumably operate via a similar mechanism.[13] Recently, notable progress in Ti-catalyzed[14] intermolecular hydroamination of alkynes with primary aryl- and alkylamines has been achieved. Thus, $Ti(NMe_2)_4$,[15] $Ti(NMe_2)_2$-(dpma),[16] and Ti−guanidinate complexes[17] mediate hydroamination of alkynes with arylamines, while with aniline and sterically hindered amines react smoothly in the presence of Cp_2TiMe_2, but with lower reactivity for less sterically hindered *n*-alkylamines, due to unfavorable equilibria between Ti−imido monomers, dimers, and bis(amides).[18] Improved reactivity for less sterically hindered *n*-alkylamines with bulky $Cp^*_2TiMe_2$ has also been reported.[19] However, to date, no example of intermolecular alkene hydroamination has been reported for such catalysts. In the past decade, significant progress has been made with late- and early-transition-metal-mediated intermolecular hydroamination of alkynes, but the intermolecular hydroamination of alkenes and aliphatic amines still remains a challenge.[1b]

In regard to organolanthanides,[20] the remarkable kinetic facility with which early lanthanide−alkyl and −heteroatom bonds undergo *intramolecular* insertion of unactivated alkene,[21] alkyne,[22] allene,[23] and diene[24] functionalities (e.g., eqs 3 and

(1) For reviews of catalytic amine addition to C−C multiple bonds, see: (a) Bytschkov, I.; Doye, S. *Eur. J. Org. Chem.* **2003**, *6*, 935−946. (b) Pohlki, F.; Doye, S. *Chem. Soc. Rev.* **2003**, *32*, 104−114. (c) Nobis, M.; Driessen-Holscher, B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3983−3985. (d) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−703 and references therein. (e) Roundhill, D. M. *Catal. Today* **1997**, *37*, 155−165. (f) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113−1126. (g) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 768−770, and references therein. (h) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapters 7.4 and 17.1. (i) Bäckviall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335−342. (j) Trost, B. M.; Verhoeven, T. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, U.K., 1982; Vol. 8, pp 892−895 and references therein.
(2) For catalytic intermolecular hydroamination of olefins using alkali metals at high temperatures and pressures, see: (a) Pez, G. P.; Galle, J. E. *Pure Appl. Chem.* **1985**, *57*, 1917−1926. (b) Howk, B. W.; Little, E. L.; Scott, S. L.; Whitman, G. M. *J. Am. Chem. Soc.* **1954**, *76*, 1899−1902.
(3) (a) For recent examples of base-catalyzed hydroamination, see: Tzalis, D.; Koradin, C.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 6193−6195. (b) For a review on base-catalyzed hydroamination reactions, see: Seayad, J.; Tillack, A.; Hartung, C. G.; Beller, M. *Adv. Synth. Catal.* **2002**, *344*, 795−813.
(4) Coulson, D. R. *Tetrahedron Lett.* **1971**, 429−430.
(5) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738−6744.
(6) Uchimaru, Y. *Chem. Commun.* **1999**, 1133−1134.
(7) Tokunaga, M.; Eckert, M.; Wakatsuki, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3222−3225.
(8) (a) Hartung, C. G.; Tillack, A.; Trauthwein, H.; Beller, M. *J. Org. Chem.* **2001**, *66*, 6339−6343. An example of $[Rh(cod)_2]BF_4$-mediated intermolecular hydroamination of acrylonitrile and piperidine has been reported; see: (b) Kawatsura, M.; Hartwig, J. F. *Organometallics* **2001**, *20*, 1960−1964. (c) For $[Rh(cod)_2]BF_4$-mediated intermolecular hydroaminomethylation and oxidative amination, see: Beller, M.; Breindl, C.; Eichberger, M.; Hartung, C. G.; Seayad, J.; Thiel, O. R.; Tillack, A.; Trauthwein, H. *Synlett* **2002**, *10*, 1579−1594 and references therein.
(9) (a) Kadota, I.; Shibuya, A.; Lutete, L. M.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4570−4571. (b) Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12670−12671.
(10) Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 9546−9547.
(11) Löber, O.; Kawatsure, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366−4367.
(12) (a) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753−2763. (b) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *Organometallics* **1993**, *12*, 705−3723. (c) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708−1719. This article reviews a variety of conventional hydroamination processes for unsaturated carbon−carbon bonds. (d) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729−8730.
(13) Straub, T.; Haskel, A.; Neyroud, T. G.; Kapon, M.; Botoshansky, M.; Eisen, M. S. *Organometallics* **2001**, *20*, 5017−5035. (b) Haskel, A.; Straub, T.; Eisen, M. S. *Organometallics* **1996**, *15*, 3773−3775.
(14) For the early work on Ti-mediated intramolecular hydroamination of aminoalkynes, see: (a) McGrane, P. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489. (b) McGrane, P. L.; Livinghouse, T. *J. Org. Chem.* **1992**, *57*, 1323−1324.
(15) Shi, Y.; Ciszewski, J. T.; Odom, A. L. *Organometallics* **2001**, *20*, 3967−3969.
(16) (a) Cao, C.; Shi, Y.; Odom, A. L. *J. Am. Chem. Soc.* **2003**, *125*, 2880−2881. (b) Cao, C.; Ciszewski, J. T.; Odom, A. L. *Organometallics* **2001**, *20*, 5011−5013.
(17) Ong, T.-G.; Yap, G. P. A.; Richeson, D. S. *Organometallics* **2002**, *21*, 2839−2841.
(18) Haak, E.; Bytschkov, I.; Doye, S. *Angew. Chem., Int. Ed.* **1999**, *38*, 3389−3391.
(19) Heutling, A.; Doye, S. *J. Org. Chem.* **2002**, *67*, 1961−1964.
(20) For recent organolanthanide reviews, see: (a) Aspinall, H. C. *Chem. Rev.* **2002**, *102*, 1807−1850. (b) Edelmann, F. T.; Freckmann, D. M. M.; Schumann, H, *Chem. Rev.* **2002**, *102*, 1851−1896. (c) Arndt, S.; Okuda, J. *Chem. Rev.* **2002**, *102*, 1953−1976. (d) Molander, G. A.; Romero, A. C. *Chem. Rev.* **2002**, *102*, 2161−2186. (e) Shibasaki, M.; Yoshikawa, N. *Chem. Rev.* **2002**, *102*, 2187−2210. (f) Inanaga, J.; Furuno, H.; Hayano, T. *Chem. Rev.* **2002**, *102*, 2211−2226. (g) Molander, G. A. *Chemtracts: Org. Chem.* **1998**, *18*, 237−263. (h) Edelmann, F. T. *Top. Curr. Chem.* **1996**, *179*, 247−276. (i) Edelmann, F. T. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, U.K., 1995; Vol. 4, Chapter 2. (j) Schumann, H.; Meese-Marktscheffel, J. A.; Esser, L. *Chem. Rev.* **1995**, *95*, 865−986. (k) Schaverien, C. J. *Adv. Organomet. Chem.* **1994**, *36*, 283−362. (l) Evans, W. J. *Adv. Organomet. Chem.* **1985**, *24*, 131−177. (m) Marks, T. J.; Ernst, R. D. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, U.K., 1982; Chapter 21.
(21) (a) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10241−10254. (b) Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275−294. (c) Gagné, M. R.; Nolan, S. P.; Marks, T. J. *Organometallics* **1990**, *9*, 1716−1718. (d) Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 4108−4109. For cyclohydroamination of amine-tethered 1,2-disubstituted alkenes, see: (e) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *Org. Lett.* **2001**, *3*, 3091−3094. (f) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. *J. Org. Chem.*, in press.
(22) (a) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 9295−9306. (b) Li, Y.; Fu, P.-F.; Marks, T. J. *Organometallics* **1994**, *13*, 439−440.

4; $L_2 = (\eta^5\text{-Me}_5C_5)_2$, $Me_2Si(\eta^5\text{-Me}_4C_5)_2$; $X = NH, NR$; $Ln =$

$$\Delta H \sim 0 \text{ kcal/mol} \quad (3)$$
$$\Delta H \sim -13 \text{ kcal/mol}$$

$$\Delta H \sim -35 \text{ kcal/mol} \quad (4)$$
$$\Delta H \sim 0 \text{ kcal/mol}$$

$$\Delta H \sim 0 \text{ kcal/mol} \quad (5)$$
$$\Delta H \sim -13 \text{ kcal/mol}$$

lanthanide) raises the question of whether similar processes could be used to effect intermolecular alkyne and alkene hydroamination (e.g., eq 5). Indeed, limited examples of organolanthanide-catalyzed intermolecular hydroamination have been reported in a previous communication.[25]

Thermochemical data argue that the enthalpic constraints on the intermolecular insertion and protonolysis steps in eq 5 should be similar to those in the successful intramolecular processes (eqs 3 and 4, overall $\Delta H_{\text{calcd}} \approx -13$ and -35 kcal/mol, respectively).[26-29] However, it is likely that cyclohydroamination benefits from substantial intramolecular entropic advantages[30,31] over the corresponding intermolecular process (conceivably both thermodynamic and kinetic),[32,33] so that the feasibility, selectiv-

ity, and generality of organolanthanide-catalyzed intermolecular alkene and alkyne hydroamination are not fully known. To characterize the nature of organolanthanide-catalyzed intermolecular alkene and alkyne hydroamination, we have undertaken a detailed study of catalytic scope including aliphatic olefin, butadiene, styrenic olefin, and methylenecyclopropanes. In addition, we have investigated the regioselectivity, substrate substituent effects, catalytic ancillary ligand and metal ion size effects, kinetics, and mechanism, all of which are described herein.

Experimental Section

Materials and Methods. All manipulations of air-sensitive materials were carried out with rigorous exclusion of oxygen and moisture in flame- or oven-dried Schlenk-type glassware on a dual-manifold Schlenk line or interfaced to a high-vacuum line (10^{-6} Torr) or in a nitrogen-filled Vacuum Atmospheres glovebox with a high-capacity recirculator (<1 ppm of O_2). Argon (Matheson, prepurified) was purified by passage through a MnO oxygen-removal column[34] and a Davison 4Å molecular sieve column. All solvents were distilled before use under dry nitrogen over appropriate drying agents (sodium benzophenone ketyl, metal hydrides, Na/K alloy). Chloroform-*d* was purchased from Cambridge Isototope Laboratories. Benzene-d_6, toluene-d_8, *o*-xylene-d_{10}, and cyclohexane-d_{12} (Cambridge Laboratories; all 99+ atom % D) used for NMR-scale reactions and thermolysis experiments were stored in vacuo over Na/K alloy in resealable bulbs and were vacuum-transferred immediately prior to use. All organic starting materials were purchased from Aldrich Chemical Co., Farchan Laboratories Inc., or Lancaster Synthesis Inc., and were used without further purification unless otherwise stated. All substrates were vacuum-distilled over CaH_2, next dried twice over freshly activated Davison 4A molecular sieves, and then were degassed by freeze−pump−thaw methods. They were stored in vacuumtight storage flasks. Butadiene was purified by passing through a MnO oxygen-removal column and a Davison 4A molecular sieve column. The reagent 2-vinylnaphthalene was vacuum-sublimed before use. The organolanthanide precatalysts $Cp'_2LnCH(TMS)_2$ (Ln = Sm, La; $Cp' = \eta^5\text{-Me}_5C_5$)[35] and $Me_2SiCp''_2$-$LnCH(TMS)_2$ (Ln = Sm, La; $Cp'' = \eta^5\text{-Me}_4C_5$)[36] were prepared by published procedures. The reagents 4-(dimethylamino)styrene[37] [2039-80-7] and 4-(methylthio)styrene [18760-11-7] were synthesized from the corresponding benzaldehydes by Wittig reactions according to published procedures. The reagents 1,2-divinylbenzene [91-14-5], 2,3-divinylnaphthalene[38] [34299-60-0], 1,2,3-trivinylbenzene[39] [114310-41-7], and methylenecyclopropane[40] [6142-73-0] were synthesized according to published procedures. The reagent 2-phenylmethylenecyclopropane [29817-09-2] was purchased from Lancaster Synthesis Inc. and was vacuum-distilled from CaH_2.

Physical and Analytical Measurements. NMR spectra were recorded on a Varian Gemini (FT; 300 MHz, ^1H; 75 MHz, ^{13}C), Mercury-400 (FT; 400 MHz, ^1H; 100 MHz, ^{13}C), Unity-400 (FT; 400

(23) For cyclohydroamination of amino−allenes, see: (a) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *Organometallics* **1999**, *18*, 1949−1960. (b) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871−4872.

(24) For cyclohydroamination of amino−dienes, see: (a) Hong, S.; Marks, T. J. *J. Am. Chem. Soc.* **2002**, *124*, 7886−7887. (b) Hong, S.; Marks, T. J. *J. Am. Chem. Soc.*, in press.

(25) Li, Y.; Marks, T. J. *Organometallics* **1996**, *15*, 3770−3772.

(26) Requisite experimental thermochemical data are not available to compare the thermodynamics of amine addition to olefins with that to alkynes. However, ΔH for NH_3 addition to ethylene can be estimated from thermochemical data[28,29] to be -13 kcal/mol. Calculations at the AM-1 level place NH_3 addition to acetylene (to yield $CH_3CH=NH$) as 17 kcal/mol more exothermic than to ethylene. Furthermore, the addition of CH_4 to acetylene is estimated from thermochemical data[28,29] to be $\sim$14 kcal/mol more exothermic than that to ethylene.

(27) Metal−ligand bond enthalpies from: (a) Nolan, S. P.; Stern, D.; Hedden, D.; Marks, T. J. *ACS Symp. Ser.* **1990**, *No. 428*, 159−174. (b) Nolan, S. P.; Stern, D.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 7844−7853. (c) Schock, L. E.; Marks, T. J. *J. Am. Chem. Soc.* **1988**, *110*, 7701−7715. (d) Bruno, J. W.; Marks, T. J.; Morss, L. R. *J. Am. Chem. Soc.* **1983**, *105*, 6824−6832.

(28) Organic fragment bond enthalpies from: (a) Griller, D.; Kanabus-Kaminska, J. M.; Maccoll, A. *J. Mol. Struct.* **1988**, *163*, 125−131. (b) McMillan, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493−532 and references therein. (c) Benson, S. W. *Thermochemical Kinetics,* 2nd ed.; Wiley: New York, 1976; Appendix Tables A.10, A.11, and A.22. (d) Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502−518.

(29) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds,* 2nd ed.; Chapman and Hall: London, 1986; Appendix Tables 1 and 3.

(30) For a discussion of the thermodynamic and kinetic advantages of intramolecular reactions over intermolecular analogues, see: (a) Smith, G. M.; Carpenter, J. D.; Marks, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 6805−6807 and references therein. (b) Page, M. I. In *The Chemistry of Enzyme Action*; Page, M. I., Ed.; Elsevier: New York, 1984; pp 1−54. (c) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183−278. (d) Page, M. I.; Jencks, W. P. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1678−1683.

(31) March, J. *Advanced Organic Chemistry,* 4th ed.; Wiley: New York, 1992; pp 210−214.

(32) For discussions of entropy and enthalpy effects on ring-closing reactions, see: (a) Mandolini, L. *Bull. Soc. Chim. Fr.* **1988**, *2*, 173−176. (b) Detar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505−4512. (c) For a related discussion, see: Menger, F. M. *Acc. Chem. Res.* **1985**, *18*, 128−134.

(33) Steinborn, D.; Taube, R. *Z. Chem.* **1986**, *26*, 349. The $\Delta S°$ value for the intermolecular NH insertion of NH_3 into ethylene is $\sim$−30 cal/mol K. The negative reaction entropy of the hydroamination of course drives the equilibrium to the starting materials with increasing temperature.

(34) (a) He, M. Y.; Toscano, P. J.; Burwell, R. L.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 641−652. (b) McIlwrick, C. R.; Phillips, C. S. G. *J. Chem. Phys., E* **1973**, *6*, 1208−1210.

(35) Jeske, G.; Lauke, H.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8091−8103.

(36) (a) Jeske, G.; Schock, L. E.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8103−8110. (b) Stern, D.; Sabat, M.; Marks, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 9558−9575.

(37) Hollywood, F.; Suschitzky, H.; Hull, R. *Synthesis* **1982**, *8*, 662−665.

(38) Takeuchi, M.; Tuihiji, T.; Nishimura, J. *J. Org. Chem.* **1993**, *58*, 7388−7392.

(39) Nakamura, Y.; Hayashida, Y.; Wada, Y.; Nishimura, J. *Tetrahedron* **1997**, *53*, 4593−4600.

(40) (a) Liptay, W. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 177−188. (b) Salaun, J. R.; Champion, J.; Conia, J. M. *Org. Synth.* **1977**, *57*, 36−40.

MHz, ^{1}H; 100 MHz, ^{13}C), or Inova-500 (FT; 500 MHz, ^{1}H; 125 MHz, ^{13}C) instrument. Chemical shifts (δ) for ^{1}H and ^{13}C are referenced to internal solvent resonances and reported relative to SiMe$_4$. NMR experiments on air-sensitive samples were conducted in Teflon valve sealed tubes (J. Young). Elemental analyses were performed by Midwest Microlabs, Indianapolis, IN. GCMS analyses were performed using an HP6890 instrument with an HP-5MS (5% phenyl methyl siloxane, 30 m × 250 μm × 0.25 μm) capillary column and an FID detector. HPLC analyses were performed using a Waters Breeze system consisting of a Model 1525 binary pump, Model 77251 manual injector, and Model 2487 dual-λ UV/vis detector. HRMS studies were conducted on a VG 70-250 SE instrument with 70 eV electron impact ionization or chemical ionization using CH$_4$ as the reagent gas. IR spectra were recorded using a Biorad FT S60 FTIR instrument.

Typical NMR-Scale Catalytic Intermolecular Hydroamination Reactions for Alkynes, Aliphatic Olefins, and Butadiene. In a glovebox, the Me$_2$SiCp''$_2$NdCH(SiMe$_3$)$_2$ precatalyst (2.0−35.0 mg, 3.3−58.0 μmol), olefin or alkyne (0.575−2.85 mmol, ∼35- to 333-fold molar excess), and benzene (∼0.6 mL) were loaded into an NMR tube equipped with a Teflon valve. On the high-vacuum line, the NMR tube was evacuated and back-filled with argon three times. Then amine (∼1.0−1.57 mmol, ∼10- to 52-fold molar excess; absolute concentrations of amines were determined by internal FeCp$_2$ calibration) was vacuum-transferred in. The NMR tube was next back-filled with argon and finally sealed. The reaction mixture was heated to 60 °C and periodically monitored by ^{1}H NMR spectroscopy. The final products were identified by ^{1}H, ^{13}C, DEPT, and 2D NMR, GC/MS, and high-resolution mass spectrometry.

Typical Preparative-Scale Catalytic Intermolecular Hydroamination Reactions for Alkynes, Aliphatic Olefins, and Butadiene. Scale-up catalytic reactions were carried out using the following procedure. In the glovebox, 20.0 mg (33.2 μmol) of Me$_2$SiCp''$_2$Nd-CH(SiMe$_3$)$_2$, 1-(trimethylsilyl)propyne (295 mg, 2.63 mmol, 79-fold excess), and C$_6$H$_6$ (5.0 mL) were loaded into a storage tube (25.0 mL) equipped with a magnetic stir bar. Next, *n*-butylamine (183 mg, 2.5 mmol, 75-fold excess) was vacuum-transferred onto the precatalyst. The mixture was then freeze−pump−thaw degassed and warmed to room temperature. The resulting solution was stirred with heating to 60 °C for 3 days. Distillation of the C$_6$H$_6$ and excess 1-(trimethylsilyl)-propyne at atmospheric pressure followed by vacuum transfer afforded a mixture of *N*-(1-methyl-2-(trimethylsilyl)ethylidene)butylamine and *N*-(trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine. After the mixture was heated to 120 °C for 72 h, the *N*-(1-methyl-2-(trimethylsilyl)-ethylidene)butylamine underwent isomerization to *N*-(trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine. *N*-(Trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine (**2**; 0.29 g, 62% isolated yield) was obtained as a colorless oil. It was >95% pure by ^{1}H and ^{13}C NMR and GC/MS. See the section below for characterization data.

Synthesis of *N*-(Trimethylsilyl)-*N*-(1-methylethyl-1-enyl)propyl-amine (1) [180140-30-1]. The title amine derivative was synthesized catalytically using the procedure as described in typical NMR-scale reactions. Me$_2$SiCp''$_2$NdCH(SiMe$_3$)$_2$ precatalyst (2.0 mg, 3.3 μmol), 1-(trimethylsilyl)propyne (76 mg, 675 μmol, 205-fold molar excess), and *n*-propylamine (9.3 mg, 160 μmol, 48-fold molar excess) in 0.6 mL of C$_7$D$_8$ afforded (*E*)- and (*Z*)-*N*-(1-methyl-2-(trimethylsilyl)-ethylidene)propylamine (intermediate imine) as a colorless liquid in the NMR-scale reaction. The intermediate imine concentrations were determined by integration versus a ferrocene internal standard. ^{1}H NMR (300 MHz, C$_6$D$_6$) of the major isomer (70% yield by ^{1}H NMR): δ 3.05 (t, J = 6.7 Hz, 2H, CH$_2$N), 1.75 (s, 2H, CH$_2$Si), 1.67 (m, 2H, CH$_2$), 1.49 (s, 3H, =CMe), 0.95 (t, J = 7.4 Hz, 3H, CH$_3$), −0.07 (s, 9H, SiMe$_3$). ^{1}H NMR (300 MHz, C$_6$D$_6$) of the minor isomer (30% yield by ^{1}H NMR): δ 3.02 (t, J = 6.7 Hz, 2H, CH$_2$N), 1.84 (s, 2H, CH$_2$Si), 1.70−1.61 (m, 2H, CH$_2$), 1.66 (s, 3H, CH$_3$), 0.98 (t, J = 7.4 Hz, 3H, CH$_3$), −0.06 (s, 9H, SiMe$_3$). ^{13}C NMR (75 MHz, ^{1}H-coupled,

C$_6$D$_6$): 165.8, 164.9, 53.8, 53.4, 34.1, 34.1, 29.7, 25.1, 25.0, 19.3, 12.5, 12.4, −0.41, −0.92. ^{13}C NMR (75 MHz, ^{1}H-coupled, C$_6$D$_6$): δ 165.9 (s), 164.9 (s), 53.7 (t, J_{CH} = 129.0 Hz), 53.5 (t, J_{CH} = 129.7 Hz), 34.1 (t, J_{CH} = 119.1 Hz), 34.1 (t, J_{CH} = 119.1 Hz), 29.7 (q, J_{CH} = 125.0 Hz), 25.1 (t, J_{CH} = 116.6 Hz), 25.0 (t, J_{CH} = 128.9 Hz), 19.3 (q, J_{CH} = 125.2 Hz), 12.5 (q, J_{CH} = 124.0 Hz), 12.4 (q, J_{CH} = 122.0 Hz), −0.41 (q, J_{CH} = 118.7 Hz), −0.92 (q, J_{CH} = 118.7 Hz).

The mixture of imine isomers described above in 0.6 mL of C$_7$D$_8$ was heated in a sealed NMR tube for 8 h at 120 °C to afford *N*-(trimethylsilyl)-*N*-(1-methylethyl-1-enyl)propylamine (**1**), the rearrangement product, as a colorless liquid. The product was identified by ^{1}H, ^{13}C, and 2D NMR and GC/MS. The yield (>90%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. ^{1}H NMR (300 MHz, C$_7$D$_8$): δ 4.10 (d, J = 3.9 Hz, 2H, CH$_2$=), 2.90 (t, J = 7.5 Hz, 2H, CH$_2$N), 1.77 (s, 3H, =CCH$_3$), 1.41 (m, 2H, CH$_2$), 0.77 (t, J = 7.5 Hz, 3H, CH$_3$), 0.15 (s, 9H, Si-(CH$_3$)$_3$). ^{13}C NMR (75 MHz, C$_7$D$_8$): δ 148.5 (NC=), 93.2 (=CH$_2$), 48.4 (NCH$_2$), 23.5 (CH$_2$), 22.7 (=CCH$_3$), 11.6 (CH$_3$), 1.79 (SiMe$_3$). MS (relative abundance): M$^+$ (54), M$^+$ − 1 (3), M$^+$ + 1 (13), 156.1 (88), 142.1 (37), 128.1 (15), 114.1 (65), 98.1 (17), 73.1 (100), 59.0 (20), 45.0 (18). HRMS: calcd for C$_9$H$_{21}$NSi, 171.1443; found, 171.1431.

Synthesis of *N*-(Trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butyl-amine (2) [180140-31-2]. The title compound was synthesized in both NMR- and preparative-scale reactions. Following the procedure above, Me$_2$SiCp''$_2$NdCH(SiMe$_3$)$_2$ precatalyst (2.0 mg, 3.3 μmol), 1-(trimeth-ylsilyl)propyne (124 mg, 1.1 mmol, 333-fold molar excess), and *n*-butylamine (2.3 mg, 31 μmol, 9.3-fold molar excess) in 0.6 mL of C$_7$D$_8$ yielded the intermediate imine *N*-(1-methyl-2-(trimethylsilyl)-ethylidene)butylamine, as a colorless liquid in the NMR-scale reaction. ^{1}H NMR (300 MHz, C$_7$D$_8$): δ 3.10 (t, J = 6.6 Hz, 2H, CH$_2$N), 1.74 (s, 2H, CH$_2$Si), 1.61 (m, 2H, CH$_2$CH$_2$N), 1.51 (s, 3H, CH$_3$), 1.44 (m, 2H, CH$_2$CH$_2$CH$_2$N), 0.92 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (75 MHz, C$_7$D$_8$): δ 166, 51.3, 34.1, 33.9, 25.1, 21.1, 14.3, −0.99.

The imine compound above in 0.6 mL of C$_7$D$_8$ was heated in a sealed NMR tube for 8 h at 120 °C to afford *N*-(trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine (**2**). The yield (>90%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. The scale-up catalytic reaction was carried out using the following procedure. In the glovebox, 20.0 mg (33.2 μmol) of Me$_2$SiCp''$_2$NdCH-(SiMe$_3$)$_2$ was loaded into a storage tube (25 mL) equipped with a magnetic stir bar. Next, C$_6$H$_6$ (5.0 mL), 1-(trimethylsilyl)propyne (295.2 mg, 2.63 mmol), and *n*-butylamine (182.9 mg, 2.5 mmol) were successively vacuum-transferred onto the precatalyst. The mixture was then freeze−pump−thaw degassed and warmed to room temperature. The resulting solution was stirred with heating at 60 °C for 72 h. Distillation of C$_6$H$_6$ and excess 1-(trimethylsilyl)propyne at atmospheric pressure followed by vacuum transfer afforded a mixture of *N*-(1-methyl-2-(trimethylsilyl)ethylidene)butylamine and the title compound **2**. After the mixture was heated at 120 °C for 72 h, *N*-(1-methyl-2-(trimethylsilyl)ethylidene)butylamine underwent isomerization to *N*-(tri-methylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine (**2**). *N*-(Trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine (**2**; 0.29 g, 62% isolated yield) was obtained as a colorless oil. ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 4.18 (s, 2H, CH$_2$Si), 2.98 (t, 2H, J = 7.5 Hz, CH$_2$N), 1.81 (s, 3H, CH$_3$C=N), 1.45 (m, 2H, CH$_2$CH$_2$N), 1.20 (m, 2H, CH$_2$CH$_3$), 0.84 (t, J = 7.2 Hz, 3H, CH$_2$CH$_3$). 0.19 (s, 9H, Si(CH$_3$)$_3$). ^{13}C NMR (75 MHz, ^{1}H-decoupled, C$_6$D$_6$): δ 148.9, 92.9, 46.6, 32.8, 23.1, 20.9, 14.4, 2.1. ^{13}C NMR (75 MHz, ^{1}H-coupled, C$_6$D$_6$): δ 148.9 (s), 92.7 (t, J_{CH} = 157.0 Hz), 46.6 (t, J_{CH} = 132.5 Hz), 32.8 (t, J_{CH} = 123.5 Hz), 23.1 (q, J_{CH} = 120.0 Hz), 20.9 (t, J_{CH} = 121.5 Hz), 14.5 (q, J_{CH} = 123.5 Hz), 2.1 (q, J_{CH} = 106.6 Hz). MS (relative abundance): M$^+$ (11), M$^+$ − 1 (2), 170.2 (66), 156.3 (4), 142.1 (48), 128.1 (18), 114.1 (82), 100.1 (6), 73.0 (100), 59.1 (16), 45.0 (17). HRMS: calcd for C$_{10}$H$_{23}$NSi, 185.1600; found, 185.1602.

Synthesis of *N*-(Trimethylsilyl)-*N*-(1-methylethyl-1-enyl)isobutylamine (3) [180140-32-3]. A procedure analogous to that for *N*-(trimethylsilyl)-*N*-(1-methylethyl-1-enyl)butylamine (**2**) above was used in the synthesis of the title compound with Me$_2$SiCp″$_2$NdCH-(SiMe$_3$)$_2$ (2.0 mg, 3.3 μmol), 1-(trimethylsilyl)propyne (76 mg, 680 μmol, 205-fold molar excess), and isobutylamine (9.0 mg, 120 μmol, 37-fold excess) in 0.6 mL of C$_6$D$_6$. The yield (>90%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. The intermediate imine was characterized by ^{1}H NMR. ^{1}H NMR (300 MHz, C$_7$D$_8$): δ 2.88 (d, J = 6.0 Hz, 2H, CH$_2$N), 1.94 (m, 1H, CH), 1.74 (s, 2H, CH$_2$Si), 1.50 (s, 3H, =CCH$_3$), 0.99 (d, J = 6.7 Hz, 6H, 2CH$_3$), 0.04 (s, 9H, SiMe$_3$). ^{13}C NMR (75 MHz, ^{1}H-coupled, C$_7$D$_8$): δ 165.9 (s, C=N), 59.7 (t, J_{CH} = 128.7 Hz, CH$_2$N), 34.0 (t, J_{CH} = 119.1 Hz, CH$_2$Si), 30.5 (d, J_{CH} = 126.2 Hz, CH), 29.6 (q, J_{CH} = 125.0 Hz, CH$_3$), 21.1 (q, J_{CH} = 128.2 Hz, 2CH$_3$), −0.92 (q, J_{CH} = 117.5 Hz, SiMe$_3$).

The imine was heated at 120 °C for 8 h to afford the title compound as a colorless liquid. ^{1}H NMR (300 MHz, C$_7$D$_8$): δ 4.21 (d, J = 5.1 Hz, 2H, CH$_2$=), 2.72 (d, J = 7.2 Hz, 2H, CH$_2$N), 1.74 (s, 3H, =CCH$_3$), 1.51 (m, 1H, CH), 0.80 (d, J = 6.6 Hz, 6H, 2CH$_3$), 0.15 (s, 9H, SiMe$_3$). ^{13}C NMR (75 MHz, C$_7$D$_8$): δ 148.7, 96.7, 53.8, 28.3, 2.0, 20.6, 1.63. MS (relative abundance): M$^+$ (33), M$^+$ − 1 (2), M$^+$ + 1 (9), 170.1 (52), 142.1 (70), 128.1 (15), 114.0 (40), 98.1 (9), 73.0 (100), 57.1 (22), 41.0 (21). HRMS: calcd for C$_{10}$H$_{23}$NSi, 185.1600; found, 185.1581.

Synthesis of *N*-(1-Methyl-2-phenylethylidene)propylamine (4) [180140-33-4]. A procedure analogous to that for **1** above was used in the synthesis of the title imine with Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ (3.0 mg, 5.0 μmol), 1-phenylpropyne (78 mg, 675 μmol, 135-fold molar excess), and *n*-propylamine (15.5 mg, 260 μmol, 52-fold excess) in 0.6 mL of C$_6$D$_6$. The yield (>85%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. ^{1}H NMR (300 MHz, C$_7$D$_8$): δ 7.16−7.09 (m, 5H, Ph), 3.44 (s, 2H, CH$_2$Ph), 3.03 (t, J = 6.8 Hz, 2H, CH$_2$N), 1.70 (m, 2H, CH$_2$), 1.32 (s, 3H, =CCH$_3$) 0.95 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (75 MHz, C$_6$D$_6$): δ 166.6, 129.4, 128.7, 126.6, 123.4, 53.4, 49.8, 24.6, 16.1, 12.4. MS (relative abundance): M$^+$ (4), 146.2 (5), 115.2 (5), 105.2 (5), 91.1 (23), 84.2 (65), 65.1 (8), 42.1 (100). HRMS: calcd for C$_{12}$H$_{17}$N, 175.1361; found, 175.1359.

Synthesis of *N*-(2-Butylidene)propylamine (5) [3332-11-4]. A procedure analogous to that for **1** above was used in the synthesis of the title compound with Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ (3.0 mg, 5.0 μmol), 2-butyne (37 mg, 680 μmol, 135-fold molar excess), and *n*-propylamine (9.3 mg, 160 μmol, 32-fold molar excess) in 0.6 mL of C$_6$D$_6$. The yield (91%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 3.09 (t, J = 6.4 Hz, 2H, CH$_2$N), 2.09 (q, J = 7.4 Hz, 2H, MeCH$_2$C=N), 1.75 (m, 2H, CH$_2$), 1.36 (s, 3H, CH$_3$C=N), 1.09 (t, J = 7.4 Hz, 3H, CH$_3$CH$_2$C=), 1.00 (t, J = 7.4 Hz, 3H, CH$_3$). ^{13}C NMR (100 MHz, C$_6$D$_6$): δ 167.9, 53.2, 35.3, 24.7, 12.4, 10.7, 1.4. MS (relative abundance): M$^+$ (23), M$^+$ + 1 (2), M$^+$ − 1 (2), 98.1 (7), 84.1 (100), 56.1 (40), 42.1 (65). HRMS: calcd for C$_7$H$_{15}$N: 113.1204; found, 113.1186.

Synthesis of *N*-(2-(Trimethylsilyl)ethyl)-*N*-*n*-propyl-1-amine (6) [41269-62-9]. An NMR tube with a Teflon valve was charged with Me$_2$SiCp″$_2$SmCH(SiMe$_3$)$_2$ precatalyst (10.0 mg, 16.4 μmol) and a mixture of 1-(trimethylsilyl)ethylene (58 mg, 570 μmol, 35-fold molar excess) and *n*-propylamine (9.6 mg, 160 μmol, 10-fold molar excess) in 0.6 mL of C$_6$D$_6$. The reaction mixture was heated to 60 °C while being monitored by ^{1}H NMR spectroscopy. Only the title compound was detected in 93% yield. The yield was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 2.57 (m, 2H, CH$_2$N), 2.45 (m, 2H, CH$_2$N), 1.41 (m, 2H, CH$_2$CH$_3$), 0.89 (t, J = 7.4 Hz, 3H, CH$_3$), 0.68 (t, J = 8.0 Hz, 2H, CH$_2$SiMe$_3$), 0.31 (br s, 1H, NH), 0.03 (s, 9H, Si(CH$_3$)$_3$). ^{13}C NMR (75 MHz, C$_6$D$_6$): δ 52.1, 46.1, 23.8, 18.5, 12.2, 1.2. MS (relative abundance): M$^+$ (14), M$^+$ + 1 (3), M$^+$ − 1 (3), 145.1 (4), 130.1 (39),

116.1 (43), 102.1 (35), 84.1 (21), 73.0 (100), 59.0 (21), 45.0 (13). HRMS: calcd for C$_8$H$_{21}$NSi, 159.1443; found, 159.1432.

Synthesis of *N*-(*trans*-2-Butenyl)-*N*-*n*-propyl-1-amine (7) [180140-34-5]. In a glovebox, the Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ precatalyst (35.0 mg, 58.0 μmol) was weighed into an NMR tube having a Teflon valve. Next, 1.0 mL of C$_6$D$_6$, 1,3-butadiene (154 mg, 2.85 mmol, 49-fold molar excess), and *n*-propylamine (93 mg, 1.57 mmol, 27-fold molar excess) were vacuum-transferred into the tube on the high-vacuum line. Only the trans-1,4-addition product was detected in the ^{1}H NMR spectrum (90% yield) by comparison with an authentic sample prepared from the reaction of *n*-propylamine with *trans*-1-chloro-2-butene. ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 5.65−5.45 (m, 2H, 2CH=), 3.04 (d, J = 6.0 Hz, 2H, =CCH$_2$N), 2.40 (t, J = 7.5 Hz, 2H, CH$_2$N), 1.58 (d, J = 4.8 Hz, 3H, CH$_3$C=), 1.48 (m, 2H, CH$_2$), 0.88 (t, J = 7.8 Hz, 3H, CH$_3$), 0.57 (br s, 1H, NH). ^{13}C NMR (75 MHz, C$_6$D$_6$): δ 129.6, 126.7, 51.6, 51.2, 23.1, 17.5, 11.6. MS (relative abundance): M$^+$ (7), M$^+$ -1 (11), M$^+$ + 1 (7), 98.2 (13), 84.1 (100), 66.1 (23), 55.1 (100), 43.1 (19). HRMS: calcd for C$_7$H$_{15}$N, 113.1204; found, 113.1201.

Synthesis of *N*-*n*-Propyl-1-methyl-*n*-butyl-1-amine (8) [39190-86-8]. An NMR tube with a Teflon valve was charged with Me$_2$SiCp″$_2$-NdCH(SiMe$_3$)$_2$ precatalyst (3.0 mg, 5.0 μmol) and a mixture of 1-pentene (125 mg, 1780 μmol, 365-fold molar excess) and *n*-propylamine (1.5 mg, 25 μmol, 5-fold molar excess) in 0.6 mL of C$_6$D$_6$. The reaction mixture was heated to 60 °C while being monitored by ^{1}H NMR spectroscopy. Only the Markovnikov addition product was detected in the ^{1}H NMR spectrum by comparison with an authentic sample prepared from the reaction of *n*-propylamine with 2-bromopentane. The yield (90%) was determined by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products. ^{1}H NMR (300 MHz, C$_6$D$_6$): δ 2.54−2.36 (m, 3H), 1.42−1.33 (m, 2H), 1.31−1.17 (m, 4H), 0.95 (d, J = 6.3 Hz, 3H), 0.87 (t, J = 7.2 Hz, 6H), 0.61 (br s, 1H, NH). ^{13}C NMR (75 MHz, C$_6$D$_6$): δ 53.2, 49.5, 40.1, 24.2, 20.8, 19.5, 14.6, 12.1. MS (relative abundance): M$^+$ (3), M$^+$ − 1 (3), M$^+$ + 1 (1), 114.2 (15), 100.2 (12), 86.1 (100), 70.1 (5), 58.1 (8), 44.1 (36). HRMS: calcd for C$_8$H$_{19}$N, 129.1517; found, 129.1514.

Typical NMR-Scale Catalytic Intermolecular Hydroamination Reactions for Vinylarenes and Di- and Trivinylarenes. In a nitrogen-filled glovebox, the (η^5-Me$_5$C$_5$)$_2$LaCH(SiMe$_3$)$_2$ precatalyst (7.2 mg, 12.6 μmol) was weighed into an NMR tube equipped with a Teflon valve, and C$_7$D$_8$ (0.4 mL), *n*-propylamine (7.4 mg, 126 μmol), and vinylarene (1.26 mmol) were added in turn. The tube was then removed from the glovebox. The catalyst:amine:vinylarene ratio was confirmed as 1:10:100 by ^{1}H NMR, on the basis of the quantitatively generated internal CH$_2$(SiMe$_3$)$_2$ standard. The tube was then brought to the indicated reaction temperature (90 °C) and the ensuing catalytic reaction monitored by ^{1}H NMR. After the reaction was complete, Et$_2$O (1.0 mL) was added to the reaction mixture. The instantaneously precipitated polystyrene and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with Et$_2$O (1.0 mL). The solvent was carefully removed on the rotary evaporator, and then the residue was diluted with anhydrous Et$_2$O (1 mL). A 2.0 M solution of Et$_2$O·HCl (0.15 mL, 0.3 mmol) was next added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. The final product was purified by recrystallization from hot benzene−pentane.

Preparative-Scale Catalytic Intermolecular Hydroamination Reactions. Synthesis of *N*-Propylphenethylamine (9) [27906-91-8]. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), styrene (208 mg, 2.0 mmol), and C$_6$D$_6$ (1.0 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 40 h at 90 °C behind a blast shield. Et$_2$O (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polystyrene and catalyst were filtered off through a pad of Al$_2$O$_3$, which was then washed with Et$_2$O (2.0 mL). The solvent was removed in vacuo. Column chromatography on silica gel (meth-

ylene chloride−hexane−isopropylamine, 1:15:0.8) afforded pure amine **9** (146 mg; 90% yield) as a colorless liquid, $R_f = 0.43$. ^{1}H NMR (400 MHz, C_6D_6): δ 7.19−7.06 (m, 5H), 2.72 (t, $J = 6.4$ Hz, 2H), 2.65 (2H, $J = 6.4$ Hz, 2H), 240 (t, $J = 7.2$ Hz, 2H), 1.34 (sextet, $J = 7.2$ Hz, 2H), 0.83 (t, $J = 7.2$ Hz, 3H), 0.63 (br s, 1H). ^{13}C NMR (100 MHz, C_6D_6): δ 141.326, 129.444, 129.004, 126.631, 52.565, 52.209, 37.681, 24.290, 12.666. MS (relative abundance): M$^+$ + 1 (15), M$^+$ (100), 154.0 (20), 145.1 (4), 124.1 (5), 122.0 (5), 97.1 (5), 95.1 (7), 91.1 (15), 85.1 (32), 81.1 (35), 79.1 (37), 71.1 (56), 69.1 (72), 67.1 (50); HRMS: calcd for $C_{11}H_{18}N$, 164.1434; found, 164.1433.

Synthesis of Propyl(2-(*p*-tolyl)ethyl)amine (10) [181495-51-2] Hydrochloride. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-methylstyrene (236 mg, 2.0 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 68 h at 90 °C behind a blast shield. Et$_2$O (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polystyrene and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with Et$_2$O (2.0 mL). The solvent was carefully removed on the rotary evaporator, and then the residue was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure HCl salt of amine **10** as a white crystalline solid (198 mg; 93% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.72 (br s, 2H), 7.12−7.08 (m, 4H), 3.22 (m, 2H), 3.15 (m, 2H), 2.93 (m, 2H), 2.30 (s, 3H), 1.96 (m, 2H), 1.00 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 136.8, 133.6, 129.6, 128.7, 49.7, 49.4, 32.0, 21.2, 19.7, 11.5. MS (relative abundance): M$^+$ − Cl (2), 162.2 (10), 148.0 (6), 119.2 (19), 105.2 (11), 91.1 (10), 72.1 (100), 44.9 (12), 34.4 (26). HRMS: calcd for $C_{12}H_{19}N^+$, 177.15175; found, 177.15268. Anal. Calcd for $C_{12}H_{20}NCl$: C, 67.43; H, 9.43; N, 6.55. Found: C, 67.28; H, 9.36; N, 6.52.

Synthesis of (2-(Naphthalen-2-yl)ethyl)propylamine (11) [181495-57-8] Hydrochloride. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 2-vinylnaphthalene (308 mg, 2.0 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was next closed and the clear solution stirred for 72 h at 90 °C behind a blast shield. Et$_2$O (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polyvinylnaphthalene and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was then washed with Et$_2$O (2.0 mL). The solvent was carefully removed on the rotary evaporator, and then the residue was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure HCl salt of amine **11** as a white crystalline solid (229 mg; 92% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.87 (br s, 2H), 7.78−7.70 (m, 2H), 7.74 (d, $J = 8.5$ Hz, 1H), 7.68 (s, 1H), 7.44−7.42 (m, 2H), 7.35 (d, $J = 8.5$ Hz, 1H), 3.50 (t, $J = 8.0$ Hz, 2H), 3.29 (m, 2H), 2.99 (m, 2H), 2.01 (sextet, $J = 7.5$ Hz, 2H), 1.02 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 134.1, 133.6, 132.5, 128.8, 127.8, 127.7, 127.4, 126.9, 126.4, 126.0, 49.8, 49.2, 32.6, 19.8, 11.5. Anal. Calcd for $C_{15}H_{20}NCl$: C, 72.13; H, 8.07; N, 5.61. Found: C, 72.04; H, 8.12; N, 5.56.

Synthesis of 4-Fluoro-*N*-propylphenethylamine (12) Hydrochloride. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-fluorostyrene (244 mg, 2.0 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was next closed and the clear solution stirred for 6 days at 100 °C behind a blast shield. MeOH (2.0 mL) was then added to the reaction mixture. The instantaneously precipitated polystyrene and catalyst were filtered

off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was then removed in vacuo. Column chromatography on silica gel (methylene chloride−hexane−isopropylamine, 1:15:0.8) afforded the pure amine **12** (159 mg; 88% yield), $R_f = 0.41$. ^{1}H NMR (500 MHz, C_6D_6): δ 6.86−6.79 (m, 4H), 2.60 (t, $J = 7.0$ Hz, 2H), 2.50 (t, $J = 7.0$ Hz, 2H), 2.38 (t, $J = 7.0$ Hz, 2H), 1.34 (sextet, $J = 7.0$ Hz, 2H), 0.84 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 162.3 (d, $J_{CF} = 242$ Hz), 136.9, 130.8 (d, $J_{CF} = 7.75$ Hz), 115.6 (d, $J_{CF} = 20.9$ Hz), 52.3, 51.9, 36.5, 24.0, 19.3.

The amine **12** (159 mg, 0.88 mmol) was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure HCl salt of amine **12** as a white crystalline solid (174 mg; 91% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.19 (dd, $J_{HH} = 8.5$ Hz, $J_{HF} = 5.0$ Hz, 2H), 6.96 (dd, $J_{HH} = 8.5$ Hz, $J_{HF} = 8.5$ Hz, 2H), 3.26 (m, 2H), 3.14 (m, 2H), 2.93 (m, 2H), 1.94 (sextet, $J = 7.5$ Hz, 2H), 1.00 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 162.1 (d, $J_{CF} = 244$ Hz) 132.4 (d, $J_{CF} = 2.88$ Hz), 130.3 (d, $J_{CF} = 7.75$ Hz), 115.9 (d, $J_{CF} = 21.3$ Hz), 49.8, 49.3, 31.6, 19.3, 11.5. Anal. Calcd for $C_{11}H_{17}NClF$: C, 60.69; H, 7.87; N, 6.43. Found: C, 60.37; H, 7.79; N, 6.32.

Synthesis of *N*-Propyl-4-(trifluoromethyl)phenethylamine (13) Hydrochloride. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-(trifluoromethyl)styrene (344 mg, 2.0 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was next closed and the clear solution stirred for 34 h at 90 °C behind a blast shield. MeOH (2.0 mL) was then added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was then removed in vacuo. Column chromatography on silica gel (methylene chloride−hexane−isopropylamine, 1:15:0.8) afforded the pure amine **13** (192.0 mg; 83% yield): $R_f = 0.40$. Data for free amine **13** are as follows. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.55 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 2.91−2.85 (m, 4H), 2.60 (t, $J = 7.2$ Hz, 2H), 1.49 (sextet, $J = 7.2$ Hz, 2H), 0.90 (t, $J = 7.2$ Hz, 3H).

The amine **13** (192 mg, 0.83 mmol) was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure HCl salt of amine **13** as a white crystalline solid (187 mg; 84% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.86 (br s, 2H), 7.55 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 3.38 (m, 2H), 3.18 (m, 2H), 2.96 (m, 2H), 1.95 (sextet, $J = 7.5$ Hz, 2H), 1.02 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 140.7, 129.8 (q, $J_{CF} = 32.4$ Hz), 129.2, 126.0 (q, $J_{CF} = 3.9$ Hz), 125.2 (q, $J_{CF} = 270$ Hz), 49.8, 48.9, 32.2, 19.8, 11.5. Anal. Calcd for $C_{12}H_{17}NClF_3$: C, 53.84; H, 6.40; N, 5.23. Found: C, 53.98; H, 6.42; N, 5.21.

Synthesis of 4-Methoxy-*N*-propylphenethylamine (14) Hydrochloride [101566-01-2]. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-methoxystyrene (268 mg, 2.0 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 7 days at 90 °C behind a blast shield. Et$_2$O (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with Et$_2$O (2.0 mL). The solvent was carefully removed on the rotary evaporator, and then the residue was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure

HCl salt of amine **14** as a white crystalline solid (188 mg; 82% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.73 (br s, 2H) 7.15 (d, $J = 8.5$ Hz, 2H), 6.82 (d, $J = 8.5$ Hz, 2H), 3.77 (s, 3H), 3.23 (m, 2H), 3.16 (m, 2H), 2.93 (quintet, $J = 7.5$ Hz, 2H), 1.96 (sextet, $J = 7.5$ Hz, 2H), 1.01 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 158.8, 129.9, 128.7, 114.4, 55.4, 49.7, 49.5, 31.6, 19.7, 11.5. Anal. Calcd for C$_{12}$H$_{20}$-NOCl: C, 62.73; H, 8.77; N, 6.10. Found: C, 61.68; H, 8.80; N, 6.03.

Synthesis of 4-(Dimethylamino)-*N*-propylphenethylamine (15). In a glovebox, (η^5-Me$_5$C$_5$)LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-(dimethylamino)styrene (294 mg, 2.0 mmol), and C$_6$D$_6$ (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 10 days at 90 °C behind a blast shield. MeOH (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was then removed in vacuo. Column chromatography on silica gel (methylene chloride−hexane−isopropylamine, 1:15:0.8) afforded pure amine **15** (62.0 mg; 30% yield), $R_f = 0.48$. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.00 (d, $J = 8.5$ Hz, 2H), 6.80 (d, $J = 8.5$ Hz, 2H), 2.93 (s, 6H), 2.84 (t, $J = 7.5$ Hz, 2H), 2.73 (t, $J = 7.0$ Hz, 2H), 2.58 (t, $J = 7.0$ Hz, 2H), 1.49 (sextet, $J = 7.5$ Hz, 2H), 0.90 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 149.4, 129.5, 128.4, 113.2, 52.0, 51.7, 41.1, 35.5, 23.4, 12.0. Anal. Calcd for C$_{13}$H$_{22}$N$_2$: C, 75.68; H, 10.75; N, 13.58. Found: C, 75.64; H, 10.79; N, 12.29.

Synthesis of 4-(Methylthio)-*N*-propylphenethylamine (16) Hydrochloride. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 4-(methylthio)-styrene (300 mg, 2.0 mmol), and C$_6$D$_6$ (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 34 h at 90 °C behind a blast shield. MeOH (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was removed in vacuo. Column chromatography on silica gel (methylene chloride−hexane−isopropyl-amine, 1:15:0.8) afforded pure amine **16** (178 mg; 85% yield), $R_f = 0.40$. Data for the free amine are as follows. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.20 (d, $J = 8.8$ Hz, 2H), 7.13 (d, $J = 8.8$ Hz, 2H), 2.84 (t, $J = 6.8$ Hz, 2H), 2.76 (t, $J = 6.8$ Hz, 2H), 2.57 (t, $J = 7.2$ Hz, 2H), 2.46 (s, 3H), 1.48 (sextet, $J = 7.2$ Hz, 2H), 0.88 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 137.4, 129.4, 127.2, 126.7, 52.0, 51.4, 36.1, 23.4, 16.5, 12.0.

The amine **16** (178 mg, 0.85 mmol) was diluted with anhydrous Et$_2$O (2.0 mL). A 2.0 M ether solution of HCl (1.0 mL, 2.0 mmol) was added dropwise with stirring at 0 °C. After the mixture was stirred at 0 °C for 30 min, the solvent was removed in vacuo. Washing the resulting solid with Et$_2$O (2 × 2.0 mL) afforded the analytically pure HCl salt of amine **16** as a white crystalline solid (160 mg; 77% yield). ^{1}H NMR (500 MHz, CDCl$_3$): δ 9.77 (br s, 2H), 7.18 (AB doublet, $J = 8.0$ Hz, 2H), 7.15 (AB doublet, $J = 8.0$ Hz, 2H), 3.26 (m, 2H), 3.15 (m, 2H), 2.94 (t, $J = 7.0$ Hz, 2H), 2.46 (s, 3H), 1.96 (sextet, $J = 7.5$ Hz, 2H), 1.02 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 137.5, 133.4, 129.3, 127.2, 49.8, 49.3, 31.9, 19.8, 16.1, 11.5. Anal. Calcd for C$_{12}$H$_{20}$NClS: C, 58.63; H, 8.20; N, 5.70; S, 13.04. Found: C, 58.52; H, 8.10; N, 5.75; S, 13.02.

Synthesis of 1-Methyl-*N*-propyl-1,2,3,4-tetrahydroisoquinoline (18). In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 1,2-divinylbenzene (260 mg, 2.0 mmol), and C$_6$D$_6$ (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 22 h at 90 °C behind a blast shield. MeOH (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was removed in vacuo. Column chromatography on

silica gel (EtOAc−hexane, 1:1) afforded pure amine **18** (155 mg; 82% yield), $R_f = 0.22$. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.14−7.09 (m, 4H), 3.90 (q, $J = 6.5$ Hz, 1H), 3.09 (m, 1H), 2.94 (m, 1H), 2.79 (m, 1H), 2.72 (dt, $J = 16$ Hz, $J = 4.0$ Hz, 1H), 2.56 (m, 2H), 1.62 (m, 2H), 1.36 (d, $J = 6.5$ Hz, 3H), 0.95 (t, $J = 8.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$): δ 140.5, 134.4, 129.0, 127.6, 125.9, 125.8, 56.6, 56.1, 44.1, 27.4, 21.0, 19.4, 12.2. Anal. Calcd for C$_{13}$H$_{19}$N: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.41; H, 10.16; N, 7.40.

Synthesis of 1-Methyl-2-propyl-1,2,3,4-tetrahydrobenzo[*g*]iso-quinoline (20). In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 2,3-divinylnaphthalene (360 mg, 2.0 mmol), and C$_6$D$_6$ (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 22 h at 90 °C behind a blast shield. MeOH (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was removed in vacuo. Column chromatography on silica gel (EtOAc−hexane, 1:1) afforded pure amine **20** (220 mg; 92% yield), $R_f = 0.32$. ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 7.66 (t, $J = 9.0$ Hz, 2H), 7.40 (s, 1H), 7.37 (s, 1H), 7.30−7.28 (m, 2H), 3.95 (q. $J = 6.5$ Hz, 1H), 3.00−2.89 (m, 2H), 2.72 (dt, $J = 17.0$ Hz, 5.0 Hz, 1H), 2.58 (dt, $J = 12.0$ Hz, 5.0 Hz, 1H), 2.50−2.41 (m, 2H), 1.52 (sextet, $J = 7.5$ Hz, 2H), 1.33 (d, $J = 6.5$ Hz, 3H), 0.94 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 140.4, 134.2, 133.1, 133.1, 128.1, 127.7, 127.5, 126.3, 125.8, 125.6, 57.8, 56.5, 45.0, 28.7, 21.8, 20.7, 12.5. HRMS (*m/z*): calcd for C$_{17}$H$_{21}$N (M$^+$), 239.1674; found, 239.1669. Anal. Calcd for C$_{17}$H$_{21}$N: C, 85.30; H, 8.84; N, 5.85. Found: C, 85.61; H, 8.96; N, 5.60.

Synthesis of (±)-(1*R*,2a*R*)-1-Methyl-3-propyl-1,2,2a,3,4,5-hexahy-dro-3-azaacenaphthylene (22). In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH-(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 1,2,3-trivinylbenzene (312.0 mg, 2.0 mmol), and C$_6$D$_6$ (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 24 h at 90 °C behind a blast shield. MeOH (2.0 mL) was next added to the reaction mixture. The instantaneously precipitated polymer and catalyst were filtered off through a pad of Al$_2$O$_3$, and the pad was washed with MeOH (2.0 mL). The solvent was removed in vacuo. Column chromatography on silica gel (EtOAc−hexane, 1:1) afforded pure amine **22** (189 mg; 88% yield), $R_f = 0.40$. ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 7.13 (dd, $J = 7.5$ Hz, $J = 7.0$ Hz, 1H, H$_7$), 6.94 (d, $J = 7.0$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 3.21 (dd, $J = 8.5$ Hz, $J = 6.0$ Hz, 1H), 3.01−2.95 (m, 2H), 2.84 (m, 1H) 2.61−2.53 (m, 2H), 2.26 (quintet, $J = 5.5$ Hz, 1H), 2.14 (td, $J = 12.5$ Hz, $J = 5.5$ Hz, 1H), 2.04 (m, 1H), 1.46 (m, 2H), 1.36 (dd, $J = 11.0$ Hz, $J = 10.5$ Hz, 1H), 1.12 (d, $J = 6.5$ Hz, 3H), 0.91 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 146.7, 143.4, 132.5, 127.9, 125.4, 120.5, 66.9, 57.9, 51.8, 45.1, 37.8, 28.7, 21.1, 18.9, 12.7. Anal. Calcd for C$_{15}$H$_{21}$N: C, 83.67; H, 9.83; N, 6.50. Found: C, 83.51; H, 9.77; N, 6.69.

All ^{1}H NMR resonances were assigned by COSY, and the relative stereochemistry of H(2a) and Me(1) was confirmed by a NOESY experiment. H(2a) shows an NOE correlation with H$_{eq}$(2), which is cis to H(2a) at δ 3.12 ppm. H$_{eq}$(2) at δ 2.26 ppm exhibited an NOE correlation with Me(1) at δ 1.12 ppm and was confirmed as cis to Me(1).
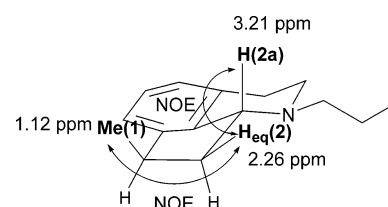
Synthesis of *N*-(1-Methylpropylidene)-1-propanamine (28a) [3332-11-4]. In a nitrogen-filled glovebox, the (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$

precatalyst (28.5 mg, 15.8 μmol) was weighed into an NMR tube equipped with a Teflon valve, and C_6D_6 (1.0 mL) was added. The tube was then removed from the glovebox. On the high-vacuum line, the NMR tube was evacuated and back-filled with argon three times. Then *n*-propylamine (59 mg, 1.0 mmol) and methylenecyclopropane (54 mg, 1.0 mmol) were vacuum-transferred in. The NMR tube was next back-filled with argon and finally sealed. The catalyst to substrate ratio was confirmed as 1:20.1 by ^{1}H NMR, on the basis of the quantitatively generated internal $CH_2(TMS)_2$ standard. The reaction mixture was heated to 60 °C and periodically monitored by H NMR spectroscopy. After 24 h, the reaction had proceeded to >95% conversion, as determined by ^{1}H NMR and GC-MS on the basis of the $CH_2(TMS)_2$ internal standard. ^{1}H NMR (500 MHz, C_6D_6): δ 3.08 (t, J = 7.5 Hz, 2H), 2.09 (q, J = 7.5 Hz, 2H), 1.71 (sextet, J = 7.5 Hz, 2H), 1.42 (s, 3H), 1.06 (t, J = 7.5 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 168.2, 53.6, 35.7, 25.1, 12.7, 17.1, 11.0.

Synthesis of *N*-Propyl-4-phenyl-2-butylamine (33a) [68164-01-2]. In a glovebox, (η^5-Me$_5$C$_5$)$_2$SmCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *n*-propylamine (59.1 mg, 1.0 mmol), 2-phenylmethylenecyclopropane (156 mg, 1.2 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 24 h at 60 °C. Et$_2$O (2 mL) was next added to the reaction mixture. The resulting precipitate was filtered off through a pad of Al$_2$O$_3$ and washed with Et$_2$O (2 mL). The solvent was removed carefully in vacuo to yield crude imine **29a** as a pale yellow liquid. ^{1}H NMR (500 MHz, C_6D_6): δ 7.17−7.11 (m, 5H), 3.09 (t, J = 7.0 Hz, 2H), 2.92 (t, J = 7.5 Hz, 2H), 2.37 (t, J = 7.5 Hz, 2H), 1.73 (sextet, J = 7.0 Hz, 2H), 1.42 (s, 3H), 0.99 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 166.8, 143.2, 129.2, 128.9, 126.3, 53.6, 44.3, 32.9, 25.1, 17.8, 12.8.

10% Pd/C (100 mg, 0.1 mmol) was added to the crude imine **29a** dissolved in anhydrous THF (2 mL), and the resulting suspension was stirred under 1 atm of H$_2$ at room temperature. After 2 days, the reaction mixture was filtered through a pad of Al$_2$O$_3$. The solvent was removed in vacuo. Column chromatography on silica gel (methylene chloride−hexane−isopropylamine, 1:15:0.8) afforded pure amine **33a** (168 mg; 88% yield), R_f = 0.41. ^{1}H NMR (500 MHz, C_6D_6): δ 7.23−7.10 (m, 5H), 2.63 (dt, J = 9.5 Hz, 7.5 Hz, 2H), 2.41 (m, 1H), 1.68 (m, 1H), 1.58 (m, 1H), 1.42 (sextet, J = 7.5 Hz, 2H), 0.99 (d, J = 6.0 Hz, 3H), 0.92 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 143.5, 129.1, 128.9, 126.3, 53.1, 49.7, 39.9, 33.0, 24.1, 21.1, 12.5. Anal. Calcd for $C_{13}H_{21}N$: C, 81.61; H, 11.06; N, 7.32. Found: C, 81.51; H, 11.21; N, 7.04.

Synthesis of *N*-Phenyl-4-phenyl-2-butylamine (34a) [72641-00-0]. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), aniline (91 μL, 1.0 mmol), 2-phenylmethylenecyclopropane (156 mg, 1.2 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 2 days at 60 °C. Et$_2$O (2.0 mL) was next added to the reaction mixture. The resulting precipitate was filtered off through a pad of Al$_2$O$_3$, and the pad was washed with Et$_2$O (2.0 mL). The solvent was removed carefully in vacuo to yield crude imine **30a** and **30b** as a pale yellow liquid. A 10% Pd/C mixture (100 mg, 0.1 mmol) was added to the crude imine **30a** and **30b** dissolved in anhydrous THF (2.0 mL), and the resulting suspension was stirred under 1.0 atm of H$_2$ at room temperature. After 2 days, the reaction mixture was filtered through a pad of Al$_2$O$_3$. The solvent was removed in vacuo. Column chromatography on silica gel (ethyl acetate−pentane, 1:22) afforded pure amine **34a** (155 mg; 69% yield), R_f = 0.43, and a diastereomeric mixture of *syn*-**34b** and *anti*-**34b** (27 mg, 12% yield), R_f = 0.46, as a colorless liquid.

Data for the major product **34a** [72641-00-0] are as follows. ^{1}H NMR (500 MHz, C_6D_6): δ 7.16−7.12 (m, 4H), 7.05 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 7.5 Hz, 2H), 6.72 (t, J = 7.5 Hz, 1H), 6.39 (d, J = 7.5 Hz, 2H), 3.20 (m, 1H), 2.88 (d, J = 7.0 Hz, 1H), 2.46 (t, J = 7.0 Hz, 2H), 1.50 (td, J = 12.5 Hz, J = 7.0 Hz, 1H), 1.43 (td, J = 12.5 Hz, J =

7.0 Hz, 1H), 0.86 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 147.4, 141.7, 129.0, 128.1, 128.0, 125.5, 116.7, 112.9, 47.1, 38.3, 32.1, 20.1. HRMS (*m/z*): calcd for $C_{16}H_{19}N$ (M)$^+$, 225.1512; found, 225.1509. LRMS (relative abundance): [M$^+$ + 1] (40), [M$^+$] (87), 210.1 (60), 132.1 (12), 121.1 (63), 120.1 (100), 93.1 (33), 91.1 (70), 77.0 (35), 65.0 (13).

Data for the minor products, a diastereomeric mixture of *syn*-**34b** [91859-40-4] and *anti*-**34b** [91859-39-1], are as follows. ^{1}H NMR (500 MHz, C_6D_6): δ 7.18−7.11 (m, 12H), 7.05 (d, J = 7.0 Hz, 2H), 6.99 (d, J = 7.0 Hz, 2H), 6.75−6.69 (m, 2H), 6.44 (t, J = 7.5 Hz, 2H), 3.41 (dq, J = 16.5 Hz, J = 6.5 Hz, 1H), 3.07 (d, J = 8.5 Hz, 1H), 2.96 (d, J = 9.5 Hz, 1H), 2.78 (m, 1H), 2.69 (m, 1H), 1.11 (d, J = 7.0 Hz, 3H), 1.05 (d, J = 7.0 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H), 0.72 (d, J = 6.5 Hz, 3H). ^{13}C NMR (500 MHz, C_6D_6): δ 148.5, 144.6, 144.1, 130.1, 129.9, 129.0, 128.9, 128.8, 127.0, 126.9, 117.8, 117.7, 117.5, 114.1, 114.0, 113.9, 53.7, 51.9, 44.6, 44.2, 18.7, 17.8, 17.7, 16.2.

Synthesis of *N*-(4-Methylphenyl)-4-phenyl-2-butylamine (35a) [289895-12-1]. In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *p*-toluidine (107 mg, 1.0 mmol), 2-phenylmethylenecyclopropane (156 mg, 1.2 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 2 days at 60 °C. The reaction mixture was next added to a suspension of ZnCl$_2$ (136 mg, 1 mmol) and NaBH$_3$CN (126 mg, 2 mmol) in THF (5 mL). The resulting white suspension was stirred at room temperature. After 20 h, the reaction mixture was filtered through a pad of Al$_2$O$_3$. The solvent was removed in vacuo. Column chromatography on silica gel (ethyl acetate−pentane, 1:22) afforded pure amine **35a** (201 mg; 84% yield), R_f = 0.46, and a diastereomeric mixture of *syn*-**35b** and *anti*-**35b** (20 mg, 8% yield), R_f = 0.49, as a colorless liquid.

Data for the major product **35a** [289895-12-1], are as follows. ^{1}H NMR (500 MHz, C_6D_6): δ 7.16−7.13 (m, 5H), 7.03 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H), 6.38 (d, J = 8.5 Hz, 2H), 3.23 (m, 1H), 2.61 (br s, 1H), 2.48 (t, J = 7.0 Hz, 2H), 2.18 (s, 3H), 1.53 (dt, J = 15 Hz, J = 7.0 Hz, 1H), 1.45 (dt, J = 15 Hz, J = 7.0 Hz, 1H), 0.88 (d, J = 6.0 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 144.2, 142.8, 130.5, 129.1, 129.0, 126.5, 126.4, 114.2, 48.4, 39.4, 33.1, 21.1, 20.9. Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 8.84; N, 5.85. Found: C, 85.42; H, 8.97; N, 5.84; HRMS (*m/z*): calcd for $C_{17}H_{21}N$ (M)$^+$, 239.1669; found, 239.1666. LRMS (relative abundance): [M$^+$ + 1] (25), [M$^+$] (100), 238.2 (5), 225.1 (5), 224.1 (30), 216.9 (3), 211.9 (3).

Data for the minor products, a diastereomeric mixture of *syn*-**35b** and *anti*-**35b**, are as follows. ^{1}H NMR (500 MHz, C_6D_6): δ 7.15−6.94 (m, 14H), 6.41 (d, J = 8.0 Hz, 4H), 3.50 (m, 1H), 3.44 (m, 1H), 3.00 (br s, 1H), 2.99 (br s, 1H), 2.82 (quintet, J = 7.0 Hz, 1H), 2.74 (quintet, J = 7.0 Hz, 1H), 2.20 (s, 3H), 2.17 (s, 3H), 1.14 (d, J = 7.0 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 0.85 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6): δ 146.2, 144.5, 144.0, 142.8, 130.6, 130.5, 129.0, 128.9, 128.8, 128.7, 127.0, 126.9, 126.5, 126.4, 114.4, 114.3, 54.2, 54.1, 44.5, 44.2, 21.2, 20.9, 18.7, 17.8, 17.7, 16.1.

Synthesis of *N*,*N*-Dimethyl-*N'*-(1-methyl-3-phenylpropyl)benzene-1,4-diamine (36a). In a glovebox, (η^5-Me$_5$C$_5$)$_2$LaCH(TMS)$_2$ precatalyst (28.5 mg, 50 μmol), *N*,*N*-dimethyl-*p*-phenylenediamine (107 mg, 1.0 mmol), 2-phenylmethylenecyclopropane (156 mg, 1.2 mmol), and C_6D_6 (1 mL) were loaded into a storage tube equipped with a magnetic stir bar and J. Young valve. The valve was then closed and the clear solution stirred for 2 days at 60 °C. The reaction mixture was next added to a suspension of ZnCl$_2$ (136 mg, 1 mmol) and NaBH$_3$CN (126 mg, 2 mmol) in THF (5 mL). The resulting white suspension was stirred at room temperature. After 22 h, the reaction mixture was filtered through a pad of Al$_2$O$_3$. The solvent was removed in vacuo. Column chromatography on silica gel (ethyl acetate−pentane, 1:2) afforded pure amine **36a** (150 mg; 56% yield) as a pale yellow liquid, R_f = 0.40. ^{1}H NMR (500 MHz, C_6D_6): δ 7.16−7.13 (m, 3H), 7.06 (d, J = 6.5 Hz, 2H), 6.71 (d, J = 8.5 Hz, 2H), 6.48 (d, J = 8.5 Hz, 2H), 3.24 (m, 1H), 2.58

(s, 6H), 2.55 (t, $J = 8.0$ Hz, 2H), 1.61 (m, 1H), 1.49 (m, 1H), 0.94 (d, $J = 6.0$ Hz, 3H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 144.8, 143.0, 140.9, 129.2, 129.0, 126.4, 116.6, 115.8, 49.3, 42.5, 39.6, 33.2, 21.5. Anal. Calcd for C$_{18}$H$_{24}$N$_2$: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.52; H, 9.03; N, 10.35. HRMS (*m/z*): calcd for C$_{18}$H$_{24}$N$_2$ (M$^+$), 268.1934; found, 268.1929. LRMS (relative abundance): [M$^+$ + 1] (22), [M$^+$] (100), 266.9 (22, 263.9 (11), 256.2 (7), 253.1 (12), 247.9 (6), 243.9 (9), 235.9 (18), 231.9 (6).

Kinetic Studies of Hydroamination/Cyclization. In a typical experiment, an NMR sample was prepared as described above (see Typical NMR Catalytic Reaction) but maintained at −78 °C until kinetic measurements were begun. The sample tube was then inserted into the probe of the Inova-500 or Unity-400 spectrometer, which had been previously set to the appropriate temperature (T ±0.2 °C; checked with a methanol or ethylene glycol temperature standard). Data were acquired using four scans per time interval with a long pulse delay (8 s) to avoid signal saturation. The reaction kinetics were usually monitored from the intensity changes in the substrate resonances and in the product resonances over 3 or more half-lives on the basis of amine consumption. The substrate concentration, C, was measured from the area, A_s, standardized to the area A_1 of the free CH$_2$(SiMe$_3$)$_2$ formed as turnover commences. The CH$_2$(SiMe$_3$)$_2$ is present as a result of quantitative protonolytic ligand cleavage during catalyst generation. All data collected could be convincingly fit by least squares to eq 6,

$$C = mt + C_0 \tag{6}$$

$$N_t\,(\mathrm{h}^{-1}) = -(60\ \mathrm{min\ h}^{-1})m \tag{7}$$

where C_0 is the initial concentration of substrate ($C_0 = A_{s,0}/A_{1,0}$). The catalyst to substrate ratio was then accurately determined from the ratio of $A_{s,0}$ and $A_{1,0}$ or from the area of the product to A_1. Accurate calibration of catalyst and substrate concentrations was achieved with an internal FeCp$_2$ standard. The turnover frequency (h^{-1}) was calculated from the least-squares-determined slope (m) according to eq 7.

Results and Discussion

The principal goal of this study was the development of catalytic intermolecular hydroamination methods which could be generally applied to broad substrate classes: specifically, closely related objectives involved defining the scope, regioselectivity, effects of varying lanthanide ionic radius and ancillary ligation, kinetics, and mechanism of organolanthanide-mediated intermolecular hydroamination of aliphatic olefins, alkynes, vinylarenes, divinylarenes, and methylenecyclopropanes. To compare and contrast with the intramolecular cyclohydroamination of aminoalkenes[21] and aminoalkynes,[22] as well as bicyclizations involving both C≡C and C=C functionalities,[41] the present work focused on varying C−C unsaturation while holding the amine and catalyst constant. The scope, regioselectivity, and kinetic and mechanistic aspects of *intermolecular* hydroamination of alkynes and vinylbenzenes are discussed first, followed by *intermolecular* hydroamination coupled to subsequent cyclohydroamination of di- and trivinylbenzenes, and finally, the hydroamination of methylenecyclopropanes.

Scope and Regiochemistry of Intermolecular Hydroamination of Alkynes, Alkenes, and Dienes. The complexes Cp′$_2$-SmCH(SiMe$_3$)$_2$ and Me$_2$SiCp″$_2$LnCH(SiMe$_3$)$_2$ (Ln = Nd, Sm, Lu) effectively and regioselectively catalyze the intermolecular hydroamination of a variety of alkenes and alkynes to yield the corresponding amines and enamines, the latter of which undergo

Scheme 1. Proposed Catalytic Cycle for Organolanthanide-Catalyzed Intermolecular Alkyne Hydroamination
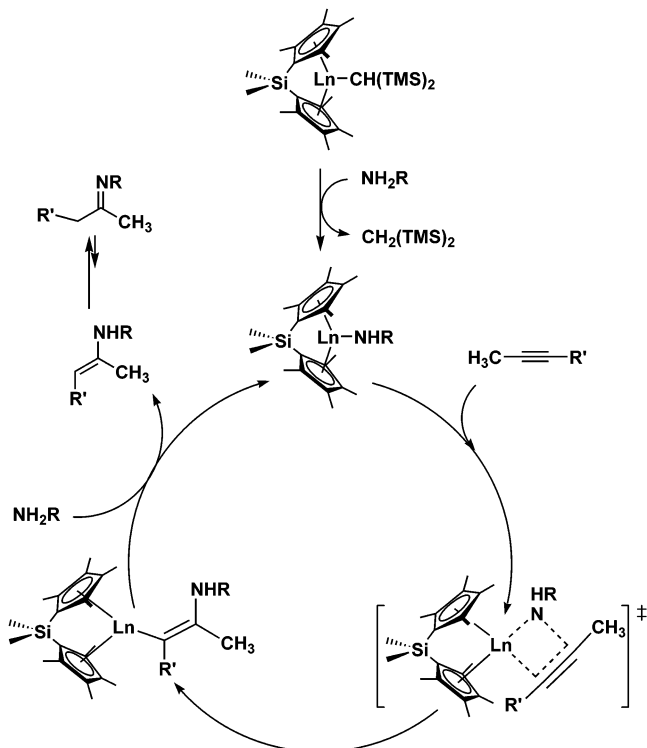
thermal tautomerization to the more stable imines,[42] as shown in Scheme 1. The intermolecular hydroamination reactions in general proceed under an inert atmosphere at 60 °C under conditions of excess alkene or alkyne (typically 50−250 [alkene/alkyne]:[catalyst]; 10−50 [amine]:[catalyst] to minimize amine inhibition)[21a,b] to >95% amine consumption. These catalytic processes are conveniently monitored by the disappearance of the amine NCH$_2$ signal (δ ~2.6−2.2 ppm) and/or by appearance of the imine =NCH$_2$ signal (δ ~3.1−2.8 ppm) using ^{1}H NMR spectroscopy. For paramagnetic Ln = Nd, Sm, broadened ^{1}H NMR amine substrate and product resonances are observed during catalytic turnover at room temperature and at 60 °C. This behavior is analogous to the known coordination to/amine exchange with paramagnetic LnNHR(NH$_2$R)$_x$ amine−amido complexes (vide infra).[21b] The known hydroamination products were identified by comparison with literature data and/or data of authentic samples. New compounds were characterized by ^{1}H/^{13}C and 2D NMR as well as by high-resolution mass spectrometry. General product isolation procedures involve high-vacuum transfer of the products, excess olefins or alkynes, and other volatiles, followed by distillative removal of unreacted olefins or alkynes, solvent, and CH$_2$(SiMe$_3$)$_2$. A preparative-scale reaction was carried out in a storage tube with the product being isolated in 62% yield. All the products in NMR or preparative-scale reactions were >95% pure by ^{1}H NMR and GC-MS.

Intermolecular hydroamination results are summarized in Table 1. It can be seen that the present organolanthanide-centered process catalyzes a variety of alkene, alkyne, and diene hydroaminations. Aliphatic (entries 1−3 and 5) and aromatic

(41) (a) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 1757−1771. (b) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 707−708.
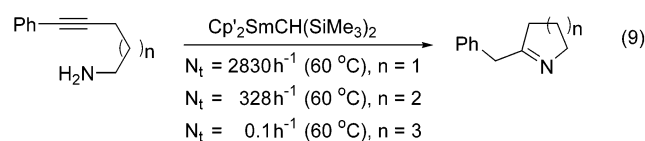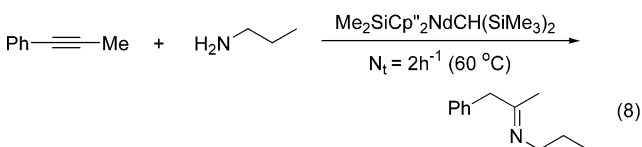
(42) Shainyan, B. A.; Mirskova, A. N. *Russ. Chem. Rev. (Engl. Transl.)* **1979**, *48*, 107−117 and references therein.

Table 1. Intermolecular Hydroamination[a] Results for Alkynes, Alkenes, and Butadiene

Entry	Alkyne/Olefin	Amine	Product	N_t, h^{-1} (°C)	Yield (%)
1.	H_3C≡TMS	H_2N∼	**1**	14 (60)	90[b]
2.	H_3C≡TMS	H_2N∼	**2**	13 (60)	62[c]
3.	H_3C≡TMS	H_2N∼	**3**	10 (60)	90[b]
4.	H_3C≡Ph	H_2N∼	**4**	2 (60)	85[b]
5.	H_3C≡CH_3	H_2N∼	**5**	1 (60)	91[b]
6.	TMS∼	H_2N∼	**6**	2 (60)	93[b]
7.	∼∼	H_2N∼	**7**	0.3 (21)	90[b]
8.	∼∼	H_2N∼	**8**	0.4 (60)	90[b]

[a] $Me_2SiCp''_2NdCH(SiMe_3)_2$ as precatalyst. [b] NMR-scale reactions and yield determined by ${}^1H$ NMR and GC/MS after vacuum transfer of volatile products. [c] Preparative-scale reactions and isolated yield.
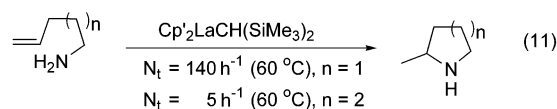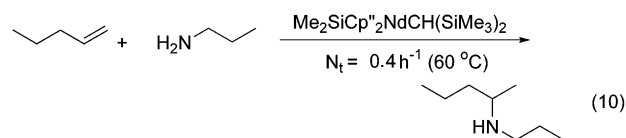
(entry 4) alkynes, aliphatic (entries 7 and 8) and trimethylsilyl-substituted (entry 6) olefins, and a diene (entry 7) all undergo intermolecular hydroamination to afford the corresponding amines or enamines. Several features of the present intermolecular catalytic transformation are especially noteworthy and provide informative, useful quantitative parallels and contrasts to the corresponding organolanthanide-catalyzed intramolecular cyclohydroamination processes.[21–24,41] The present process is applicable not only to polarized olefins (entries 6 and 7) and alkynes (entries 1–4) but also to nonpolarized olefins (entry 8) and alkynes (entry 5) as well. In comparison to the corresponding organolanthanide-catalyzed intramolecular hydroamination, these intermolecular transformations are slower for both alkyne and alkene substrates. For example, comparison of the Me_2-$SiCp''_2Nd$-catalyzed conversion of 1-phenylpropyne + *n*-propylamine to *N*-(1-methyl-2-phenylethylidene)propylamine (entry 4, eq 8) to the Cp'_2Sm-catalyzed conversion of 5-phenyl-

$$Ph\text{—}≡\text{—}Me + H_2N\diagdown \xrightarrow[N_t = 2h^{-1} (60 °C)]{Me_2SiCp''_2NdCH(SiMe_3)_2} \quad (8)$$

$$Ph\diagdown\diagup{=N}\diagdown$$

$$Ph\text{—}≡\diagdown_{H_2N} \xrightarrow[\substack{N_t = 2830h^{-1} (60 °C),\ n = 1 \\ N_t = 328h^{-1} (60 °C),\ n = 2 \\ N_t = 0.1h^{-1} (60 °C),\ n = 3}]{Cp'_2SmCH(SiMe_3)_2} \quad (9)$$

4-pentyn-1-amine to 2-benzyl-1-pyrroline (eq 9, *n* = 1) under comparable catalytic conditions (catalyst and substrate concentrations, solvent, temperature) reveals a decrease in N_t of $\sim$1400× ($N_t = 2$ h^{-1} versus 2830 h^{-1}, respectively). Since it will be seen that the ring-bridged Nd catalyst is significantly more active than the Cp'_2Sm– catalyst (vide infra), the actual
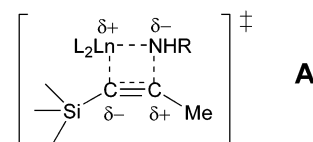
disparity in rates between inter- and intramolecular processes is likely greater for the same catalyst. A similar trend is also observed in the conversion of 2-butyne/*n*-propylamine to *N*-(2-butylidene)propylamine (entry 5, $N_t = 1$, using $Me_2SiCp''_2Nd$– catalyst at 60 °C) vs that of 4-hexyn-1-amine to 2-ethyl-1-pyrroline ($N_t = 96$, using Cp'_2Sm– catalyst at 21 °C).

In the case of unactivated aliphatic olefin hydroamination, modest N_t values are observed for the intermolecular conversion of 1-pentene + *n*-propylamine to *N*-propyl-1-methylbutylamine (entry 8, eq 10) vs conversion of 4-penten-1-amine to 2-meth-

$$\diagdown\diagdown\diagup + H_2N\diagdown \xrightarrow[N_t = 0.4\,h^{-1} (60 °C)]{Me_2SiCp''_2NdCH(SiMe_3)_2} \quad (10)$$

$$\diagdown\diagup\diagdown_{HN\diagdown}$$

$$\diagup{=}(\ )_n \xrightarrow[\substack{N_t = 140\,h^{-1} (60 °C),\ n = 1 \\ N_t = 5\,h^{-1} (60 °C),\ n = 2}]{Cp'_2LaCH(SiMe_3)_2} \quad (\ )_n \text{ pyrrolidine (N–H)} \quad (11)$$

ylpyrrolidine (eq 11, *n* = 1). It can be seen that under comparable catalytic conditions, the intramolecular process can be up to $\sim$350× more rapid ($N_t = 0.4$ h^{-1} versus 140 h^{-1}, respectively).

The above comparisons likely reflect the kinetic advantages[30,31] of intramolecular over intermolecular processes in both olefinic and acetylenic hydroamination. However, these advantages diminish with increasing ring size, due apparently to the greater steric impediments to the C≡C/C=C insertion and the increasing loss of entropy in attaining the transition state[30] for the greater numbers of chain conformations. The intermolecular alkyne processes are $\sim$3–7× more rapid than the corresponding alkene transformations under identical reaction conditions (Table 1), in congruence with analogous intramolecular alkyne and alkene comparisons.[21,22] The greater alkyne insertion rates can be associated with the sterically more accessible, cylindrical C≡C π system, more nucleophilic sp-hybridized carbon atoms,[43] greater C≡C π-donating capacity, greater thermodynamic driving force, and greater stabilization of the insertive transition state. The largest intermolecular (and intramolecular) alkyne hydroamination rates are observed for silyl-substituted alkynes (entries 1–3), and the reason likely reflects the known stabilizing tendency by silicon substituents of α-carbanionic and β-carbocationic centers[44] in what is a reasonable portrayal of the insertive transition state (**A**). The proposed transition state **A** is

$$\left[\begin{array}{c} \overset{\delta+}{L_2Ln}\text{- - -}\overset{\delta-}{NHR} \\ | \quad\quad | \\ \overset{}{Si}\text{—}\underset{\delta-}{C}{≡}\underset{\delta+}{C}\text{—Me} \end{array} \right]^{‡} \quad \textbf{A}$$

also in accord with the observed regiochemistry, delivering the lanthanide ion to the α-carbanionic position.

(43) For a comparison of nucleophilic additions of alkenes and alkynes, see for example: Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987; Chapter 7, and references therein.

(44) (a) Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappaport, Z., Eds.; Wiley: Chichester, U.K., 1989; Chapter 14. (b) Fleming, I. In *Comprehensive Organic Chemistry*; Jones, N. D., Ed.; Pergamon Press: Oxford, U.K., 1979; Chapter 13.

The hydroamination results for trimethylsilyl- or phenyl-substituted internal alkynes are examples of regioselective insertion processes (entries 1−4). For example, for the trimethylsilyl-substituted α-alkynes, *N*-alkyl-1-methyl-2-(trimethylsilyl)ethylimines are formed exclusively, as judged by in situ NMR studies. These imines undergo subsequent, known 1,3-sigmatropic silyl rearrangement[45] under the catalytic reaction conditions (rapidly brought to completion at higher temperatures) to yield the more stable enamine-like structures (enties 1−3, eq 12). In the case of silyl-substituted α-olefins, only the

$$R = \textit{n}\text{-propyl, } \textit{n}\text{-butyl, } \textit{i}\text{-butyl} \qquad (12)$$
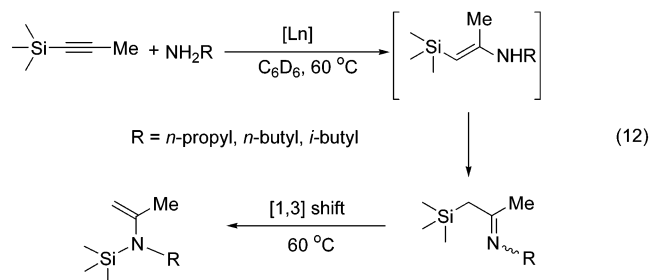
anti-Markovnikov addition product is observed (entry 6; N delivered to the terminal carbon position).

The present hydroamination process for α-functionalized olefins and alkynes likely involves significant stereoelectronic control via metal-induced positive polarization of the evolving carbon skeleton, which ultimately leads to olefin or alkyne insertion products. The marked regioselectivity of the organolanthanide-mediated α-functionalized olefin and alkyne hydroamination demonstrates that important factors other than simple sterics are operative, as previously observed in organolanthanide-mediated styrenic olefin and arylalkyne hydrosilylation.[46] These kinetic and directing effects argue for SiMe₃ activating effects known in organosilicon chemistry,[44] i.e., a β-Si−C bond interaction with the metal to stabilize the electrophilic lanthanide center (e.g., **B**),[20k] as suggested by ab initio calculations,[47] as well as interaction of the electrophilic lanthanide center with adjacent arene π systems (e.g., **C**).[48,49]
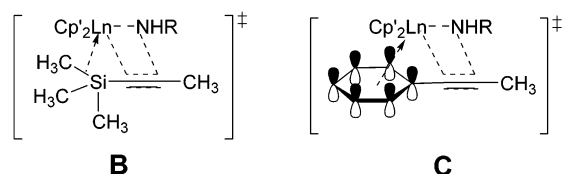

The insertion of a conjugated diene into the Ln−N bond is also noteworthy. The results of the 1,3-butadiene hydroamination illustrate that 1,4-addition is favored over 1,2-insertion (entry 7) and suggest a possible pathway involving an η³-crotyl

(45) For examples of 1,3-silyl rearrangement from C to N, see: (a) Hitchcock, P. B.; Lappert, M. F.; Liu, D.-S. *J. Chem. Soc., Chem. Commun.* **1994**, 1699−1700. (b) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 204−205. (c) Bassindale, A. R.; Brook, A. G. *Can. J. Chem.* **1974**, *52*, 3474−3483. (d) Belavin, I. Yu.; Fedoseeva, N. A.; Baukov, Yu. I.; Lutsenko, I. F. *J. Gen. Chem. USSR (Engl. Transl.)* **1973**, *43*, 443.
(46) (a) Molander, G. A.; Romero, J. A. C.; Corrette, C. P. *J. Organomet. Chem.* **2002**, *647*, 225−235. (b) Fu, P.-F.; Brard, L.; Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1995**, *117*, 7157−7168.
(47) Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 108−112.
(48) For η^n-benzylic structures, see: (a) Evans, W. J.; Ulibarri, T. A.; Ziller, J. W. *J. Am. Chem. Soc.* **1990**, *112*, 219−223. (b) Mintz, E. A.; Moloy, K. G.; Marks, T. J.; Day, V. W. *J. Am. Chem. Soc.* **1982**, *104*, 4692−4695.
(49) For arene−lanthanide complexes, see: Bochkarev, M. N. *Chem. Rev.* **2002**, *102*, 2089−2117.

Table 2. Amine Substituent Group Effects on Turnover Frequencies for Intermolecular Hydroamination[a]

| R	N_t, h[−1 b]
CH₃CH₂CH₂	14
CH₃CH₂CH₂CH₂	13
(CH₃)₂CHCH₂	10

[a] Using Me₂SiCp″₂NdCH(SiMe₃)₂ as precatalyst. Starting amine, alkyne, and catalyst concentrations are identical in each experiment. [b] Turnover frequencies measured in C₇D₈. The temperature was 60 °C in all cases.

complex (**D**). There is considerable precedent for such η³-allylic insertion products in organo-f-element chemistry (e.g., eq 13).[50,51]

$$(13)$$
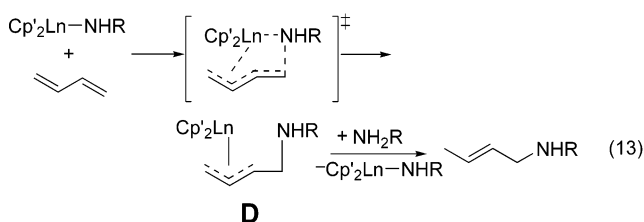
In the case of *terminal alkynes*, a previously characterized[52] alkyne oligomerization process is considerably more rapid than hydroamination and dominates the catalytic chemistry under the conditions[53] of Table 1.

With regard to amine substrate effects, the hydroamination process slightly favors less sterically encumbered amines, with N_t falling in the order *n*-propyl > *n*-butyl > isobutyl (Table 2) for identical catalyst, alkyne, and reaction conditions. This likely reflects steric demands during the alkyne insertion processes (Scheme 1). With regard to catalyst effects, the reaction rate for the present intermolecular process can be modulated considerably by varying the lanthanide size and ancillary ligation, as shown in Table 3. For example, under identical amine, alkyne, and catalyst concentrations as well as reaction temperature, increasing the Ln³⁺ ionic radius[54] and opening the

(50) For related Cp′₂Ln(η³-allyl)complexes, for examples, also see: (a) *Topics in Organometallic Chemistry*; Kobayashi, S., Ed.; Springer: Berlin, Germany, 1999; Vol. 2. (b) Edelmann, F. T. *Top. Curr. Chem.* **1996**, *179*, 247−276. (c) Evans, W. J.; Gonzales, S. L.; Ziller, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 2600−2608. (d) Evans, W. J.; Keyer, R. A.; Rabe, G. W.; Drummond, D. K.; Ziller, J. W. *Organometallics* **1993**, *12*, 4664−4667. (e) Scholz, A.; Smola, A.; Scholz, J.; Loebel, J.; Schimann, H.; Thiele, K. H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 435−436. (f) Nolan, S. P.; Stern, D.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 7844−7853.
(51) (a) For diene insertion into Sc−H bonds, see: (a) Bunel, E.; Burger, B. J.; Bercaw, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 978−976. (b) For diene insertion into Ln−C bonds, see ref 35.
(52) (a) Heeres, H. J.; Nijhoff, J.; Teuben, J. H. *Organometallics* **1993**, *12*, 2609−2617. (b) Evans, W. J.; Keyer, R. A.; Ziller, J. W. *Organometallics* **1993**, *12*, 2618−2633. (c) Heeres, H. J.; Teuben, J. H. *Organometallics* **1991**, *10*, 1980−1986 and references therein. (d) Heeres, H. J.; Meetsma, A.; Teuben, J. H. *Organometallics* **1990**, *9*, 1508−1510. (e) Heeres, H. J.; Meetsma, A.; Teuben, J. H.; Rogers, R. D. *Organometallics* **1989**, *8*, 2637−2646. (f) Den Haan, K. H.; Wielstra, Y.; Teuben, J. H. *Organometallics* **1987**, *6*, 2053−2060.
(53) For terminal alkynes HC≡CR (R = *n*-butyl, Ph, SiMe₃), the typical catalytic reaction was carried out by the following procedure. Under an Ar atmosphere, a mixture of Me₂SiCp″₂NdCH(SiMe₃)₂ (3.0 mg, 5.0 μmol), 1-hexyne (75.2 Mg, 915.0 μmol), and *n*-propylamine (3.1 mg, 52.4 μmol) in 0.60 mL of C₆D₆ was heated at 60 °C while being monitored by ¹H NMR. The ¹H/¹³C NMR and GC/MS results indicate 2-butyl-1-octen-3-yne as the major product (96%) along with other unidentified minor products. The yield was estimated by ¹H NMR and GC/MS after vacuum transfer of the volatile products. The product NMR spectroscopic data agree well with the literature data: Straub, T.; Haskel, A.; Eisen, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 6364−6365.
(54) Shannon, R. D. *Acta Crystallogr.* **1976**, *32*, 751−760.

Table 3. Metal and Ancillary Ligand Effects on Turnover Frequencies for Intermolecular Hydroamination[a]

H$_3$C≡≡—SiMe$_3$ + H$_2$N⁓⁓ → Me$_3$Si⁓ (=N—⁓⁓)

catalyst	N_t, h^{-1} [b]
Cp′$_2$Sm—	0.01
Me$_2$SiCp″$_2$Lu—	0.1
Me$_2$SiCp″$_2$Sm—	4
Me$_2$SiCp″$_2$Nd—	14

[a] Starting amine, alkyne, and catalyst concentrations are identical in each experiment. [b] Turnover frequencies measured in C$_7$D$_8$. The temperature is 60 °C in all cases.
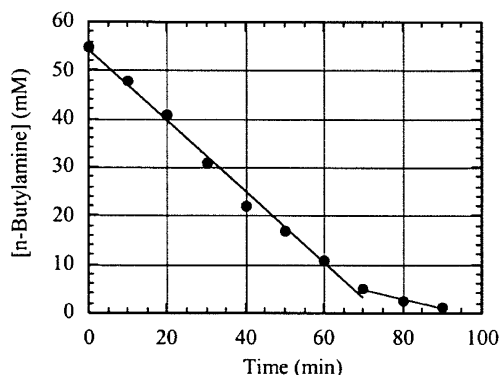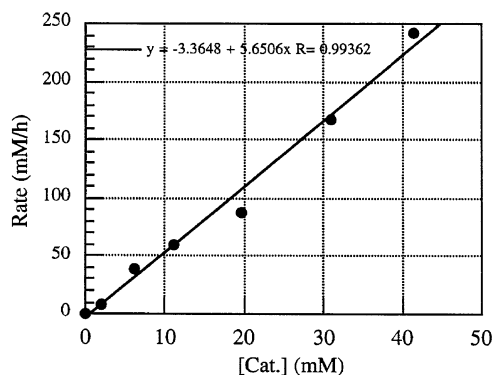

Figure 1. Plot of amine concentration vs time for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. The line represents the least-squares fit to the data points.

Figure 2. Plot of observed reaction rate vs alkyne concentration for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$-CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. The line represents the least-squares fit to the data points.

Figure 3. Plot of observed reaction rate vs catalyst concentration for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$-CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. The line represents the least-squares fit to the data points.

metal coordination sphere by connecting the ancillary π-ligands (Cp′$_2$Ln → Me$_2$SiCp″$_2$Ln) enhances the turnover frequency (N_t) for the hydroamination of 1-(trimethylsilyl)propyne with *n*-propylamine from 0.01 h^{-1} using Cp′$_2$Sm as a catalyst to 0.1, 4, and 14 h^{-1} using Me$_2$SiCp″$_2$Lu—, Me$_2$SiCp″$_2$Sm—, and Me$_2$-SiCp″$_2$Nd—, respectively, as the catalyst. Such tendency for larger metal ions and more open coordination spheres to accelerate carbon—carbon multiple bond insertion into Ln—N bonds is in accord with observations made in organolanthanide-mediated intramolecular amino—olefin hydroamination[21] and amino—alkyne—alkene bicyclization.[41] It likely reflects the steric demands accompanying unsaturated carbon—carbon bond insertion at the lanthanide center.

Kinetics and Mechanism of Intermolecular Hydroamination. Quantitative kinetic studies of the Me$_2$SiCp″$_2$Nd-catalyzed hydroamination of 1-(trimethylsilyl)propyne with *n*-butylamine at 60 °C were carried out by in situ ^{1}H NMR. Initially, the catalyst concentration was held constant, the alkyne to amine molar ratio was held at greater than 12:1 (the excess alkyne concentration not only maintains approximately zero-order conditions but also minimizes amine inhibition), the amine to catalyst ratio was held at 15—20:1, and amine was monitored until >90% consumption. The disappearance of ^{1}H resonances of the NCH$_2$ (δ ∼2.3 ppm) in the amine and appearance of =NCH$_2$ (δ ∼3.3 ppm) in the imine product were normalized to an internal CH$_2$(SiMe)$_3$ standard. The kinetic data shown in Figure 1 reveal a linear dependence of amine concentration on reaction time over a ∼15-fold concentration range, which agrees with an essentially zero-order dependence of the catalytic rate on amine concentration. Kinetic plots for the catalytic reaction rate as a function of alkyne concentration (varied over a 3-fold concentration range; [alkyne]:[amine] > 12:1, [amine]:[catalyst]
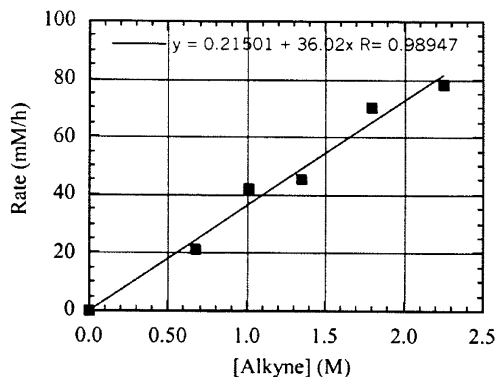
> 10:1, Figure 2) and the concentration of catalyst precursor varied over a 17-fold concentration range (Figure 3) indicate that the reaction rate is first-order in alkyne and catalyst. Taken together, the empirical rate law is given in eq 14, which stands

$$v = k[\text{amine}]^0[\text{alkyne}]^1[\text{Sm}]^1 \qquad (14)$$

in stark contrast to the zero-order amine substrate kinetics observed for both organolanthanide-catalyzed amino—olefin[21] and amino—alkyne intramolecular cyclohydroamination.[22] In both these cases, turnover-limiting alkyne and alkene insertion is inferred from these results and other evidence (vide infra). The present results suggest a similar turnover-limiting step involving intermolecular unsaturated carbon—carbon bond insertion into the Ln—N bond. For the intermolecular process, the rate of hydroamination decreases as the conversion progresses beyond ∼90%, which is consistent with some competitive catalyst inhibition by enamine or imine product coordination (vide infra).[12c,21b]

Variable-temperature studies of the intermolecular hydroamination of 1-(trimethylsilyl)propyne and *n*-propylamine mediated by Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ were performed by ^{1}H NMR, as discussed in the kinetic study above. Results are summarized in Figure 4. Standard Eyring (Figure 5) and Arrhenius analyses (Figure 6) derived from the kinetic data afford the following

(55) (a) Benson, S. W. *ThermochemicalKinetics*, 2nd ed.; Wiley: New York, 1986; pp 8—10. (b) Robinson, P. J. *J. Chem. Educ.* **1978**, *55*, 509—510.
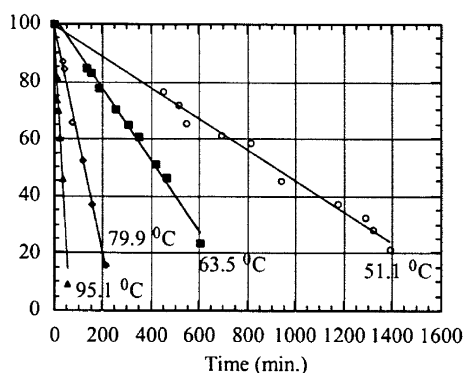
Figure 4. Normalized ratio of amine to lanthanide concentration as a function of time and temperature for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. Starting amine, alkyne, and catalyst concentrations are held constant. The line represents the least-squares fit to the data points.
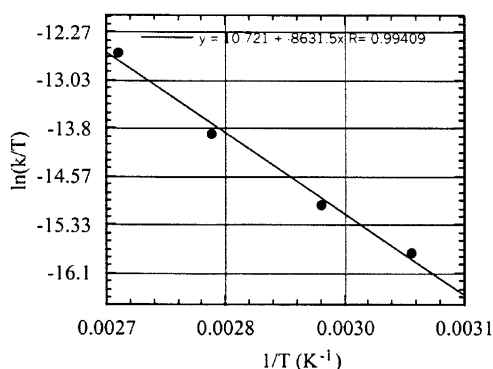
Figure 5. Eyring plot for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. The line represents the least-squares fit to the data points.
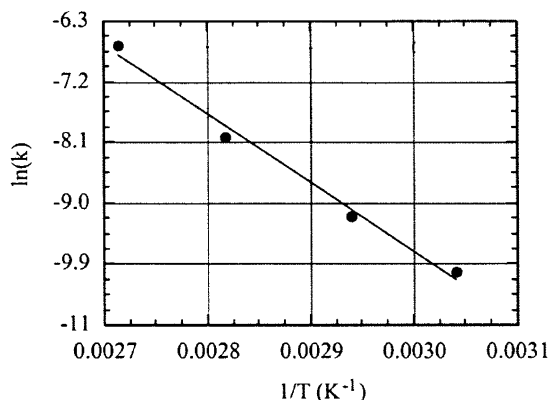
Figure 6. Arrhenius plot for the intermolecular hydroamination of MeC≡CSiMe$_3$ with NH$_2$CH$_2$CH$_2$CH$_2$CH$_3$ using Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ as the precatalyst in toluene-d_8. The line represents the least-squares fit to the data points.

activation parameters: $\Delta H^\ddagger = 17.2(1.1)$ kcal/mol, $\Delta S^\ddagger = -25.9(9.7)$ eu, and $E_a = 17.8(1.8)$ kcal/mol,[55] Similar analyses for intramolecular amino−olefin cyclohydroamination (Table 4, entry 4) yield $\Delta H^\ddagger = 12.7(1.4)$ kcal/mol, $\Delta S^\ddagger = -27.0(4.6)$ eu, and $E_a = 13.4(1.5)$ kcal/mol,[21b] while for 4-pentyn-1-amine cyclohydroamination (Table 4, entry 5) $\Delta H^\ddagger = 10.7(1.8)$ kcal/mol, $\Delta S^\ddagger = -27.4(11.9)$ eu, and $E_a = 11.3(2.0)$ kcal/mol[22a] and for 2,2-dimethyl-hept-4-enylamine (Table 4, entry 2) $\Delta H^\ddagger = 17.7(2.1)$ kcal/mol, $\Delta S^\ddagger = -24.7(5)$ eu, and $E_a =$

Table 4. Activation Parameter Comparison for Intermolecular Hydroamination and Intramolecular Hydroamination/Cyclization Reactions
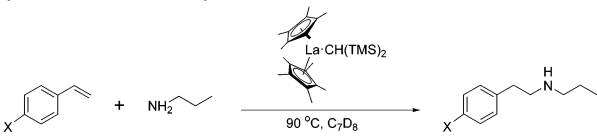

Entry	Substrate	Product	$\Delta H^\ddagger$ Kcal/mol	$\Delta S^\ddagger$ eu	E_a Kcal/mol
1.[a]			17.2 (1.1)	-25.9 (9)	17.8 (1.8)
2.[b]			17.7 (2.1)	-24.7 (5)	18.5 (2.0)
3.[c]			16.9 (1.3)	-16.5 (4)	17.6 (1.4)
4.[d]			12.7 (1.4)	-27.0 (5)	13.4 (1.5)
5.[e]			10.7 (8)	-27.4 (6)	11.3 (2.0)

[a] Determined using Me$_2$SiCp″$_2$NdCH(TMS)$_2$ in toluene-d_8. [b] Determined using Me$_2$SiCp″$_2$SmCH(TMS)$_2$ in *o*-xylene-d_{10}.[21f] [c] Determined using Cp′$_2$LaCH(TMS)$_2$ in toluene-d_8.[23a] [d] Determined using Cp′$_2$LaCH(TMS)$_2$ in toluene-d_8.[21b] [e] Determined using Cp′$_2$SmCH(TMS)$_2$ in toluene-d_8.[22a]

18.5 (2.0) kcal/mol.[21f] In these cases, the *intramolecular* processes proceed with substantially lower activation enthalpies and activation energies than the *intermolecular* process, except in the case of intramolecular internal amino−olefin processes suffering significant electrostatic and steric impediments;[21f] however, the large, negative $\Delta S^\ddagger$ values are interestingly comparable in both cases of *intramolecular* and *intermolecular* processes. This argues that the *intramolecular* processes do not benefit from major activation entropic advantages and that the transition states are all highly organized/constrained.

Further mechanistic evidence for steric constraints in the transition state for intermolecular hydroamination derives from metal/ancillary ligand effects on the rate of the Me$_3$SiC≡CMe + *n*-propylamine reaction (Table 3). A pattern of decreasing N_t with a more constricting metal coordination sphere is seen here with N_t(60 °C) = 14 h^{-1}(Me$_2$SiCp″$_2$Nd−) > 4 h^{-1} (Me$_2$SiCp″$_2$Sm−) > ≤0.1 h^{-1} (Me$_2$SiCp″$_2$Lu−) > ≤0.01 h^{-1} (Cp′$_2$Sm) and is observed for numerous other organolanthanide-catalyzed processes where olefin insertion is the turnover-limiting step.[21b,e,f,41] Interestingly, the only significant exception to this pattern is in the intramolecular amino−alkyne cyclohydroamination. Additional support for steric impediments in the present intermolecular process is found in RNH$_2$ substituent effects, where N_t declines in the order *n*-Pr > *n*-Bu > *i*-Bu in the reaction with Me$_3$SiC≡CMe (Table 2).

With regard to the proposed mechanism of the present organolanthanide-mediated intermolecular hydroamination (Scheme 1), the first step appears to be analogous to that proposed for intramolecular hydroamination.[21−24] The protonolytic reaction of organolanthanide Cp′$_2$LnCH(SiMe$_3$)$_2$ and Me$_2$SiCp″$_2$LnCH(SiMe$_3$)$_2$ complexes with amines generates the catalytically active species. The products are likely amine−amido adducts, which would be expected to undergo rapid bound amine−amido exchange as well as rapid bound-free amine exchanges, as found in intramolecular amino−olefin[21] and amino−alkyne[22] cyclohydroaminations. The second step in this catalytic process most likely involves turnover-limiting intermolecular alkyne or alkene insertion into the resulting Ln−N bonds via well-documented insertive transition states[21b] as

Table 5. Organolanthanide-Catalyzed Intermolecular Hydroamination of Vinylarenes[a]

Entry	Olefin	Product	N_t (h^{-1})[a]	Conversion[a] (Isoation Yield %)[b]
1.	(styrene)	**9**	2.0 (90 °C)	93 (90)
2.	(4-methylstyrene, H$_3$C)	**10**	1.5 (90 °C)	> 95 (93)[c]
3.	(2-vinylnaphthalene)	**11**	1.6 (90 °C)	> 95 (92)[c]
4.	(4-fluorostyrene, F)	**12**	0.94 (120 °C)	94 (88)
5.	(4-CF$_3$-styrene, F$_3$C)	**13**	3.4 (90 °C)	93 (83)[d]
6.	(4-methoxystyrene, MeO)	**14**	0.2 (90 °C)	89 (82)[c]
7.	(4-Me$_2$N-styrene, Me$_2$N)	**15**	0.05 (90 °C)	55 (30)
8.	(4-MeS-styrene, MeS)	**16**	3.6 (90 °C)	89 (85)
9.	(4-vinylpyridine, N)	—		No reaction

[a] Turnover frequencies (N_t) measured in C$_7$D$_8$. NMR reaction conditions: [cat]:[amine]:[vinylarene] = 1:10:100 employed for pseudo-zero-order kinetic plot; [cat] = 0.03 mM. [b] Isolated yield in preparative-scale reaction: the reactions were conducted in C$_6$D$_6$. Preparative reaction conditions: [cat]: [amine]:[vinylarene] = 1:20:40 employed; [cat] = 0.05 mM. [c] Isolated yield of the corresponding HCl salt in preparative-scale reaction. [d] [anti-Markovnikov]:[Markovnikov] = 96:4 regiochemistry was observed.

discussed above, to yield metal−alkyl or metal−alkenyl complexes which then undergo rapid intra- or intermolecular protonolysis with amine moieties, generating the corresponding amine or enamine products and regenerating the catalysts as depicted in Scheme 1.

Intermolecular Hydroamination of Vinylarenes. Organolanthanide-catalyzed intermolecular hydroamination of most vinylarenes proceeds under an inert atmosphere at 90 °C. All of the NMR-scale reactions were carried out under identical reaction conditions in order to compare the relative reactivities. In addition, an [olefin]:[amine]:[catalyst] ratio of 100:10:1 was employed to minimize amine inhibition and to shorten reaction times. Turnover frequencies were determined over 3 half-lives in toluene-d_8 at 90 °C from the slope of the kinetic plots of [substrate]/[catalyst] vs time. All reactions in Table 5 exhibit pseudo-zero-order kinetic behavior in the presence of excess vinylarene. The relative reactivities of vinylarenes can be compared by N_t. Preparative-scale reactions were carried out in sealed tubes at 90 °C, employing a 40:20:1 ratio of [olefin]: [amine]:[catalyst]. Less than 5 mol % of precatalyst and a slight excess (1.2−1.5 equiv) of olefin suffice for practical reaction rates.[56] The final phenethylamine products were worked up by filtration through a short plug of Al$_2$O$_3$ and treated with anhydrous HCl·Et$_2$O. The resulting amine−HCl salts were

purified by recrystallization. Alternatively, the free amine products can be isolated from the reaction mixture by column chromatography.

The scope of organolanthanide-mediated intermolecular hydroamination of vinylarenes is summarized in Table 5. Cp′$_2$-LaCH(SiMe$_3$)$_2$ catalyzes the hydroamination of a variety of vinylarenes, and this process is compatible with polar functional groups such as −F (entry 4), −CF$_3$ (entry 5), −OMe (entry 6), −NMe$_2$ (entry 7), and −SMe (entry 8). However, when a strongly coordinating substrate, 4-vinylpyridine, is added to a catalyst solution (entry 9), instant precipitation[57] is observed. With regard to substituent effects, in general electron-donating substituents decrease turnover frequencies (entry 1 vs entries 2, 4, 6, and 7). Weakly electron-donating methyl substitution and π-donating fluorine substitution exhibit slightly decreased N_t's compared to styrene, whereas the strongly electron-donating methoxy and dimethylamino substituents exhibit significantly decreased N_t's. In contrast, electron-withdrawing trifluoromethyl substitution exhibits a significantly enhanced N_t (entry 2 vs 5). Most likely, N−H bond insertion across electron-rich styrenic olefin is hampered by electrostatic repulsion between the nitrogen lone pair electrons and the π electrons of the styrenic olefin. Therefore, decreased styrenic olefin electron density lowers the barrier to insertion into Ln−N. The present organolanthanide-catalyzed intermolecular process is broad in scope, from electron-deficient styrenes to electron-rich styrenes, compared to the Pd-catalyzed hydroamination of vinylarene, in which the scope encompasses only electron-deficient and electron-neutral styrenes.[10]

Organolanthanide-mediated intermolecular vinylarene hydroamination proceeds in good isolated yields and excellent regioselectivities to afford anti-Markovnikov products. ^{1}H NMR spectra of completed in situ monitored experiments exhibit only resonances attributable to the addition product and excess olefin, with no detectable traces of regioisomers except (∼4%) in the case of (trifluoromethyl)styrene (Table 5, entry 5). As noted before, these regiochemical preferences are reasonably attributed to aryl-directing interactions[46,49] of the weakly coordinating arene π system and the electrophilic lanthanide center (Scheme 2, **T1**). Weakly Lewis basic arene π electrons stabilize the electron-deficient Lewis acidic lanthanide center and deliver lanthanide to the benzylic position. There is substantial precedent for η^n-benzylic structures in organo-f-element chemistry[46] and for the 2,1-addition of organolanthanide center to styrenic olefins.[46,58] Such processes are favored by sterically open metal coordination spheres,[46b] and lanthanide ion delivery is biased to the benzylic position by stereoelectronic factors other than simple sterics. With regard to substitution effects on regioselectivity, the intermolecular hydroamination of electron-deficient vinylarenes (Table 5, entry 5) proceeds,

(56) Due to the polymerization properties of styrene derivatives, a small excess of styrene derivatives was employed. In situ NMR monitoring confirmed the complete consumption of *n*-propylamine in the reaction with 1.2−1.5 equiv of styrenes.

(57) For known lanthanide−pyridine complexes, see: (a) Berg, D. J.; Boncella, J. M.; Andersen, R. A. *Organometallics* **2002**, 21, 4622−4631. (b) Schultz, M.; Boncella, J. M.; Berg, D. J.; Tilley, T. D.; Andersen, R. A. *Organometallics* **2002**, *21*, 460−472. (c) Clark, D. L.; Gordon, J. C.; Scott, B. L.; Watkin, J. G. *Polyhedron* **1999**, *18*, 1389−1396. (d) Den Haan, K. H.; Teuben, J. H. *J. Organomet. Chem*. **1987**, *322*, 321−329. (e) 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*, 203−219.

(58) Molander, G. A.; Schmitt, M. H. *J. Org. Chem.* **2000**, *65*, 3767−3770.

Scheme 2. Proposed Catalytic Cycle for Organolanthanide-Catalyzed Intermolecular Vinylarene Hydroamination
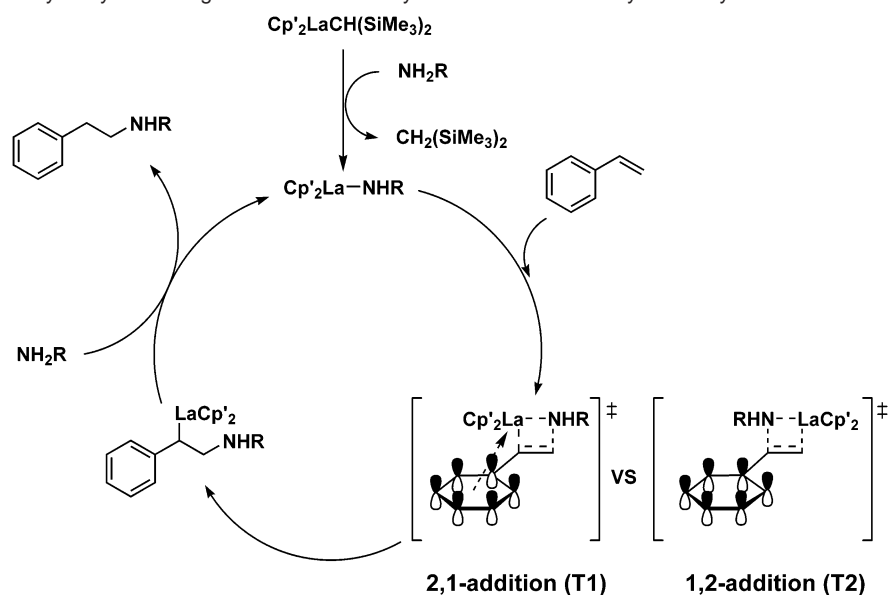
as noted above, in slightly decreased regioselectivity (96:4 anti-Markovnikov product:Markovnikov product), while electron-rich and electron-neutral vinylarenes provide exclusively aniti-Markovnikov products. Most likely, the highly electron-withdrawing −CF$_3$ functionality decreases the electron density in the arene π system, resulting in lessened arene coordinative tendencies.

Intermolecular Hydroamination/Cyclization of Divinyl/Trivinylarenes. In comparison with intramolecular hydroamination, one of the advantages of intermolecular hydroamination is the facile and concise synthesis of amine-containing, synthetically useful structures from commercially available substrates or from readily synthesized substrates. This advantage is illustrated by the synthesis of tetrahydroisoquinolines (THIQs) by intermolecular hydroamination coupled with subsequent cyclization.

Tetrahydroisoquinolines (THIQs) are of great interest, due to their interesting biological and pharmaceutical properties. For instance, 1-MeTHIQ,[59] an endogenous Parkinsonism-preventing
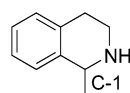
1-Methyltetrahydroisoquinoline (1-MeTHIQ)

substance,[60] is involved in the treatment of nerve diseases, and some THIQ family natural products include potent cytotoxic agents that display a range of antitumor and antimicrobial activities.[61] The substantial literature on this class of heterocycles reflects their importance. Notable synthetic methods include the Pictet−Spengler cyclization,[62] the reduction of 3,4-dihydroisoquinolines,[63] the Pomeranz−Fristch reaction,[64] α-alky-

lation of chiral formamidines,[65] organolithium additions to imines followed by condensation,[66] and metal-catalyzed cyclization reactions.[67] These synthetic methods permit the synthesis of 1-substituted THIQ in two steps: cyclization and creation of the stereocenter. However, only the Pictet−Spengler approach creates the stereogenic carbon at C-1 concurrent with ring closure. In contrast to these results, organolanthanide-catalyzed intermolecular hydroamination + subsequent cyclization of divinylbenzene affords the THIQ structure in a single step, while creating a stereogenic center at the C-1 position. The success of the present process is based on the excellent regioselectivity of the intermolecular vinylarene hydroamination described above. Regioselective Ln−N bond insertion into the styrenic C=C functionality through aryl-directed 2,1-addition provides the anti-Markovnikov product in excellent yield, and this process is efficiently coupled with intramolecular cyclohydroamination of the phenylethylamine intermediate (eq 15).

(15)
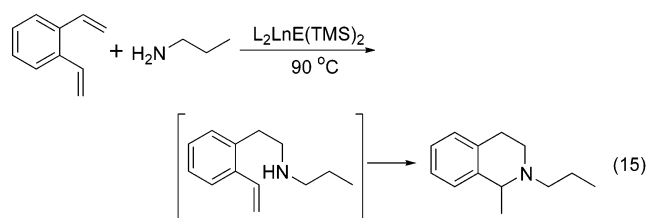
The polyvinylarene intermolecular hydroamination plus subsequent cyclization results are summarized in Table 6. In

(59) For a review on asymmetric synthesis of 1-substituted tetrahydroisoquinolines, see: Rozwadowska, M. D. *Heterocycles* **1994**, *39*, 903−931 and references therein.
(60) (a) Abe, K.; Taguchi, K.; Wasai, T.; Ren, J.; Utsunomiya, I.; Shinohara, T.; Miyatake, T.; Sano, T. *Brain Res. Bull.* **2001**, *56*, 55−60. (b) Parrado, J.; Absi, E.; Ayala, A.; Castano, A.; Cano, J.; Machado, A. *J. Neurochem.* **2000**, *75*, 65−71.
(61) Scott, J. D.; Williams, R. M. *Chem. Rev.* **2002**, *102*, 1669−1730.
(62) Whaley, W. M.; Govindachari, T. R. *Organic Reactions*; Wiley: New York, 1951; Vol. 6, p 151.
(63) (a) Davis, F. A.; Mohanty, P. K.; Burns, D. M.; Andemichael, Y. W. *Org. Lett.* **2000**, *2*, 3901−3903. (b) Comins, D. L.; Badawi, M. M. *Heterocycles* **1991**, *32*, 1869−1873. (c) Polniaszek, R. P.; Dillard, L. W. *Tetrahedron Lett.* **1990**, *31*, 797−800. (d) Polniaszek, R. P.; Kaufman, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 4859−4863.
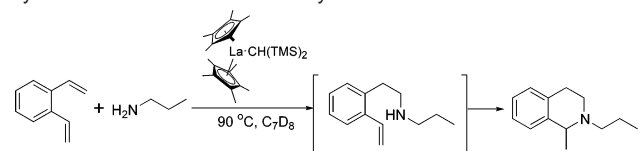(64) (a) Schlosser, M.; Simig, G.; Geneste, H. *Tetrahedron* **1998**, *54*, 9023−9032. (b) Kaufman, T. S. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2497−2505.
(65) (a) Meyers, A. I.; Dickman, D. A. *J. Am. Chem. Soc.* **1987**, *109*, 1263−1265. (b) Meyers, A. I.; Warmus, J. S.; Gonzalez, M. A.; Guiles, J.; Akahane, A. *Tetrahedron Lett.* **1991**, *32*, 5509−5512. (c) Meyers, A. I. *Tetrahedron* **1992**, *48*, 2589−2612.
(66) Wunsch, B.; Nerdinger, S. *Eur. J. Org. Chem.* **1998**, 711−718.
(67) (a) Richter-Addo, G. B.; Knight, D. A.; Dewey, M. A.; Arif, A. M.; Gladysz, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 11863−11873. (b) Wirth, T.; Fragale, G. *Synthesis* **1998**, 162−166.
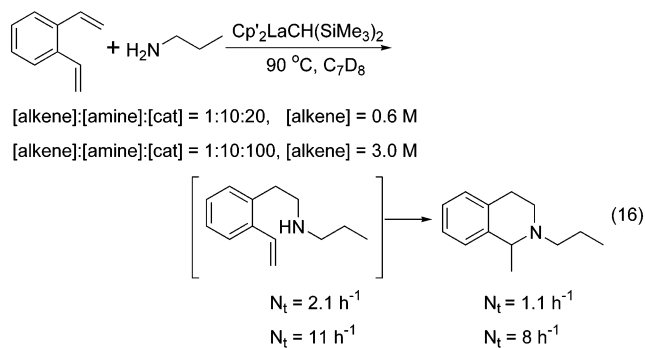
Table 6. Organolanthanide-Catalyzed Intermolecular Hydroamination of Di- and Trivinylarenes

Entry	Olefin	Intermediate	$N_t{}^a$	Product	$N_t{}^a$	Yield (%)[b]
1.		**17**	11	**18**	8.0	82
2.		**19**	9.6	**20**	6.0	92
3.		**21**	6.0	**22 (±)**	22.2	88

[a] Turnover frequencies (N_t) measured in C_7D_8. NMR reaction conditions: [cat]:[amine]:[vinylarene] = 1:10:100 employed for pseudo-zero-order kinetic plot; [cat] = 0.03 mM. [b] Isolated yield of free amine in preparative-scale reaction. Preparative reaction conditions: [cat]:[amine]:[vinylarene] = 1:20:40 employed; [cat] = 0.05 mM.

comparison to the corresponding organolanthanide-catalyzed intermolecular hydroamination of vinylarenes, notably enhanced N_t's in intermolecular hydroamination of divinylarenes are observed under identical reaction conditions. For example, comparison of the Cp′₂La-catalyzed intermolecular hydroamination of *n*-propylamine and styrene (Table 5, entry 1) to the Cp′₂La-catalyzed intermolecular hydroamination of *n*-propylamine and divinylbenzene (Table 6, entry 1) under comparable catalytic conditions reveals a substantial increase in N_t ($N_t = 2$ h⁻¹ versus 11 h⁻¹). Presumably, additional electron-withdrawing alkene substitution at the ortho position decreases the electron density at the other olefin and reduces the electrostatic repulsion between the Ln−N and C=C functionalities. The rate enhancement for vinylnaphthalene (Table 5, entry 3) versus divinyl-naphthalene (Table 6, entry 2) is consistent with this trend. This effect is particularly significant in the intramolecular cyclization of the intermediate 2-ethenylphenethylamines: $N_t = 8.0$ h⁻¹ for **17** (Table 6, entry 1) versus $N_t = 22.2$ h⁻¹ for **21** (Table 6, entry 3).

As shown above, the intermolecular hydroamination of alkynes follows the empirical rate law $v = k[\text{amine}]^0[\text{alkyne}]^1$-[catalyst]¹, while intramolecular cyclohydroamination of aminoalkenes follows the empirical rate law $v = k[\text{aminoalkene}]^0$-[catalyst]¹. Therefore, in principle, the rate of intermolecular hydroamination should vary with divinylarene concentration, while the subsequent cyclization should be independent of divinylarene concentration and intermediate phenethylamine concentration. However, when lower divinylbenzene concentrations (∼0.6 M vs 3.0 M) are employed with the identical initial amine and catalyst concentrations ([DVB]:[PA]:[catalyst] = 20:10:1), the turnover frequencies of both the first addition and the cyclization decrease from 11 to 2.1 h⁻¹ and from 8.0 to 1.1 h⁻¹, respectively (eq 16). Presumably, in the case where

[alkene]:[amine]:[cat] = 1:10:20, [alkene] = 0.6 M
[alkene]:[amine]:[cat] = 1:10:100, [alkene] = 3.0 M

$$N_t = 2.1 \text{ h}^{-1} \qquad N_t = 1.1 \text{ h}^{-1}$$
$$N_t = 11 \text{ h}^{-1} \qquad N_t = 8 \text{ h}^{-1}$$

the intermolecular hydroamination is relatively slow, a significant portion of the catalyst may be tied up in the first intermolecular catalytic cycle and therefore delay initiation of the second intramolecular catalytic cycle (vide infra).

The intermolecular hydroamination followed by subsequent bicyclization of trivinylbenzene (Table 6, entry 3) is especially noteworthy. Intermolecular hydroamination proceeds chemoselectively, only at the *β-o*lefin moiety rather than at the sterically hindered α olefin (eq 17). La−NHR bond addition to an α-*o*lefin
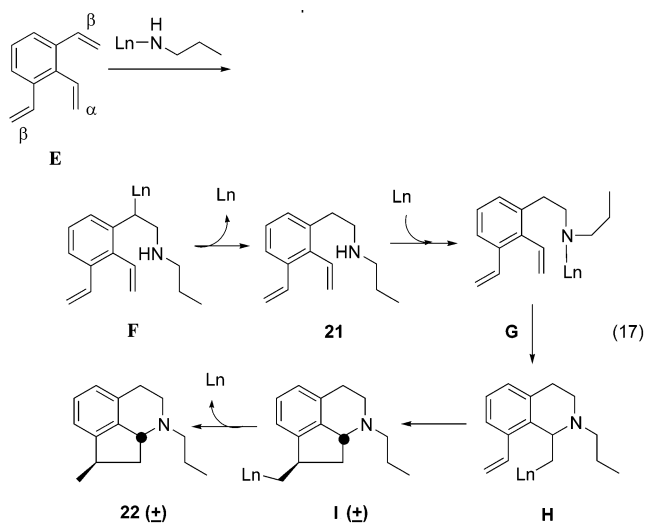
having two ortho substituents is efficiently blocked. After the rapid protonolysis of the Ln−C bond by *n*-propylamine, only the single intermediate **21** is observed by ¹H NMR. The ensuing intramolecular cyclization of **21** likely affords Ln−C species **H** by analogy to the transformation of divinylbenzene **17** → **18**. The intramolecular cyclization is observed by ¹H NMR after >70% consumption of the *n*-propylamine (vide infra). Therefore, the Ln−C bond protonolysis of **H** by *n*-propylamine is efficiently prevented, due to the low *n*-propylamine concentration. In addition, the Ln−C bond protonolysis of **H** by the sterically hindered secondary amine intermediate **21** is moderately slow[68] compared to the sequential second cyclization, which affords the hexahydrocyclopent[*ij*]isoquinoline species **22**. In contrast to the previously reported[41] bicyclization of aminodiene **J** (eq 18), which provided a cis/trans product mixture, the present intermolecular hydroamination/bicyclization of trivinylbenzene proceeds with excellent diastereoselectivity.

(68) (a) In general, Ln−C protonolysis for Cp′₂La−CH(SiMe₃)₂ by diethylamine requires ∼2 h at 60 °C. (b) For the organolanthanide-catalyzed tandem bicyclizations of secondary amino dienes, amino diynes, and amino enynes, see ref 41.

Scheme 3. Proposed Stereochemical Pathways for Organolanthanide-Catalyzed Intramolecular Hydroamination/Ensuing Cyclization of Trivinylbenzene and *n*-Propylamine To Afford *trans*-(±)-1-Methyl-3-propyl-1,2,2a,3,4,5-hexahydro-3-azaacenaphthylene (22)


1, 2a-Trans

1, 2a-Cis

(18)

15 : 85
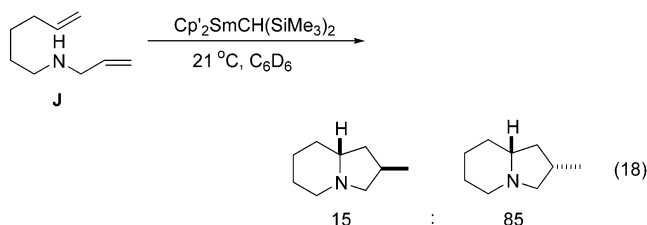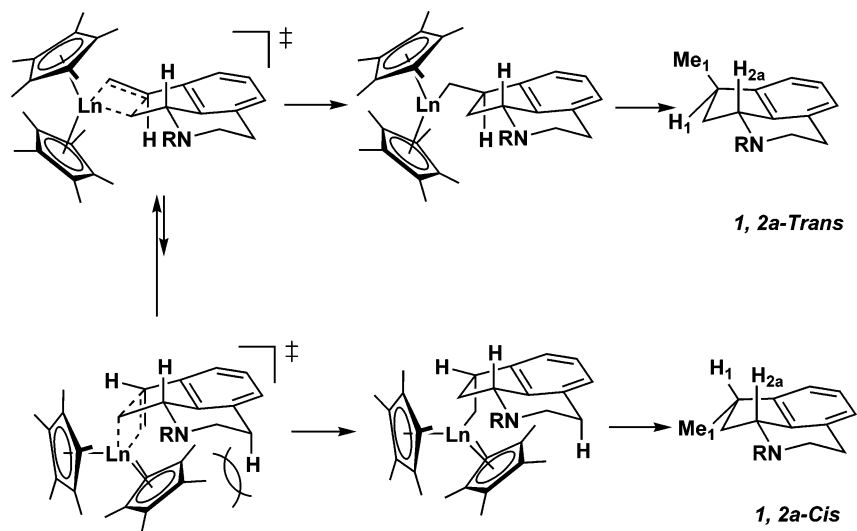
^{1}H NMR spectra and GC/MS spectra of completed in situ monitored experiments shows only resonances attributable to the trans isomer. The stereochemical and conformational assignments of **22** were supported by rigorous one- and two-dimensional NMR experiments (see the Experimental Section). The diastereoselectivity can be understood by an analogy to the cyclohydroamination of α-substituted amino−olefins,[21] α-substituted amino−allenes,[23] and α-substituted amino−diene[24] (Scheme 3).

An attempt was also made to effect the catalytic intermolecular hydroamination of divinylveratrole **K** to the corresponding tetrahydroisoquinoline (eq 19). However, it was not

(19)

L

68% conversion in ^{1}H NMR
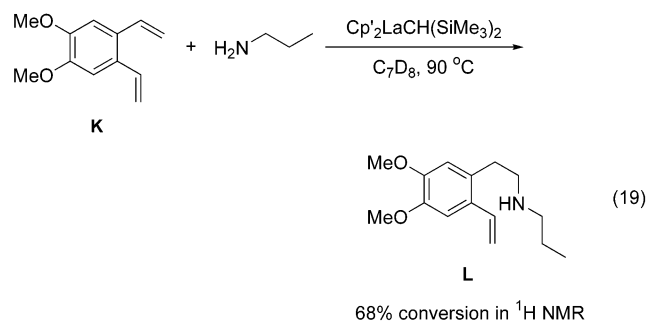
successful, due to the high competing polymerization reactivity of **K**. The substrate was rapidly polymerized under typical catalytic reaction conditions, and ∼68% conversion to intermediate phenethylamine **L**, which could not be isolated from polymeric byproducts, was observed during in situ ^{1}H NMR experiments.

Quantitative kinetic studies of the Cp′$_2$La-catalyzed reaction of divinylarenes with *n*-propylamine at 90 °C were carried out
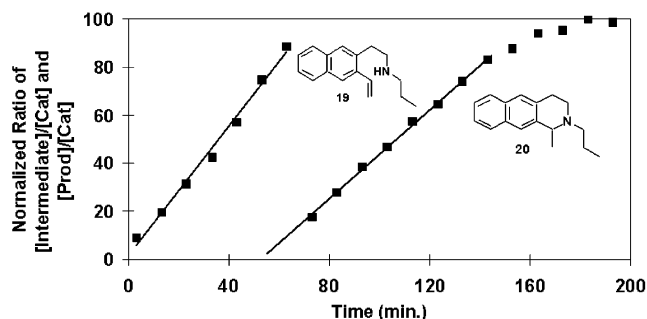
Figure 7. Normalized ratios of intermediate to lanthanide and of product to lanthanide concentration as a function of time and temperature for the intermolecular hydroamination plus ensuing cyclohydroamination of 2,3-divinylnaphthalene and *n*-propylamine using Cp′$_2$LaCH(SiMe$_3$)$_2$. The lines represent least-squares fits to the data points for the second half-life of the reaction. After 70% conversion, the intermediate **19** resonance overlapped with the product **20** resonance.

by ^{1}H NMR spectroscopy. The divinylarene:amine:catalyst molar ratio was held at 100:10:1. The decrease of the NCH$_2$ (δ ∼2.5 ppm) resonance in the *n*-propylamine, the increase of the MeCH$_2$CH$_2$NH (δ ∼1.4 ppm) resonance in the intermediate phenethylamine, and the H resonance at the C1 position (∼δ 3.8 ppm) in the THIQ product were monitored over time and normalized versus the CH$_2$(SiMe$_3$)$_2$ internal standard (δ ∼0.05 ppm). The kinetic plot of Figure 7 reveals approximately zero-order behavior in the intermolecular hydroamination step in the presence of excess divinylarene. Intermediate **19** is generated with consumption of propylamine, and the cyclized product **20** begins to appear after ∼70% consumption of *n*-propylamine and ∼70% generation of intermediate **19**. The ensuing intramolecular cyclization of the intermediate occurs, before the intermolecular hydroamination of propylamine and divinylbenzene is complete, after approximately 2 half-lives. Scheme 4 illustrates the proposed mechanistc pathway based on the kinetic studies. Rapid protonolysis of the Cp′$_2$La−CH(SiMe$_3$)$_2$ bond by *n*-propylamine produces CH$_2$(SiMe$_3$)$_2$ and generates the lanthanide−amido complex **23**. Subsequent olefin insertion via a four-centered transition state (**T3**) affords the lanthanide−alkyl species **24**. This intermediate is quickly protonolyzed by *n*-propylamine and

Scheme 4. Proposed Catalytic Cycle for Organolanthanide-Catalyzed Intermolecular Hydroamination plus Subsequent Cyclohydroamination of Divinylarenes
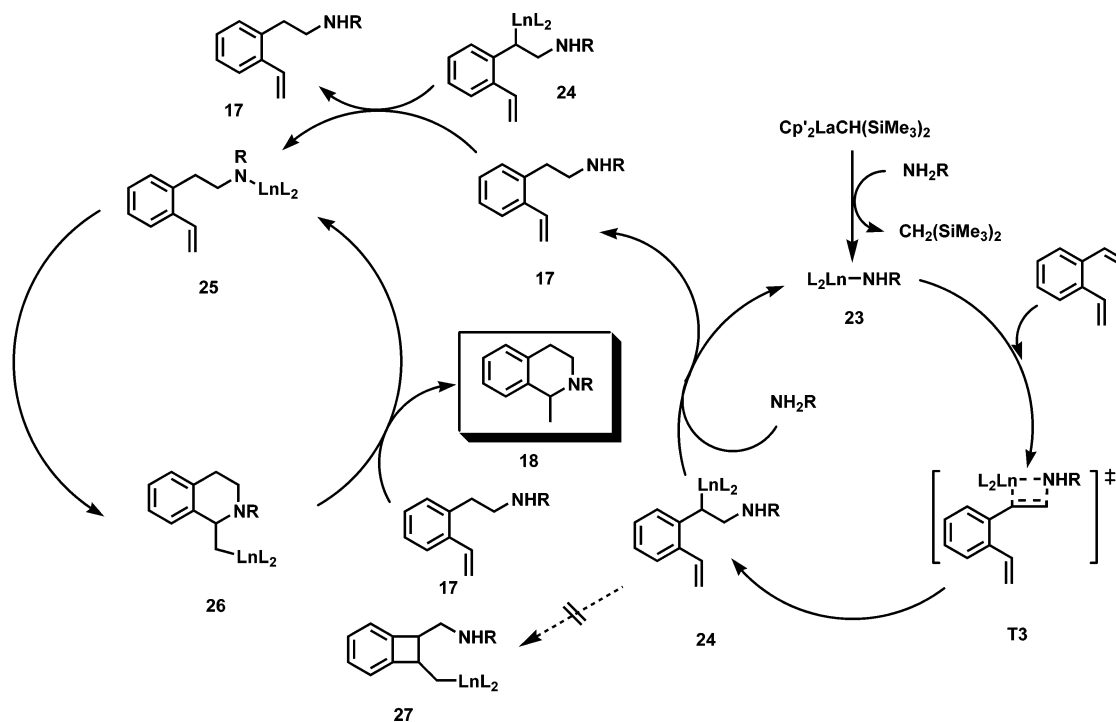
regenerates the lanthanide−amido complex **23**. The direct addition of Ln−C to the styrenic olefin of **24** without protonolysis does not occur, presumably due to unfavorable strain energies associated with formation of a four-membered ring. As the concentration of the phenethylamine intermediate **17** bearing a styrenic olefin functionality increases, protonolysis by intermediate **17** competes with the protonolysis by *n*-propylamine. Thus, the increased concentration of the intermediate **17** favors the formation of the lanthanide−amido complex **25**, and the second catalytic cycle begins to turnover before complete consumption of *n*-propylamine. Styrenic olefin insertion via a four-centered transition state into the Ln−N bond of **25** affords the corresponding lanthanide−alkyl complex **26**. Subsequent protonolysis by *n*-propylamine and/or intermediate **17** releases the final THIQ product **18**.

Intermolecular Hydroamination of Methylenecyclopropanes. Although methylenecyclopropanes (MCPs)[69] are highly strained, they are remarkably stable and readily accessible molecules that have served as versatile building blocks in organic synthesis.[70] The release of strain energy associated with the cleavage of a cyclopropane ring results in driving force in numerous organic transformations. Especially, increasing attention has been paid to the transition-metal-catalyzed reactions of MCPs,[71] which have been employed for construction of a number of complex organic molecules.[70] Organolanthanide-mediated MCP transformations[72] represent one notable class of reactions. We show here that MCPs also can serve as starting

materials in organolanthanide-mediated intermolecular hydroamination processes.

The organolanthanide complexes Cp′$_2$LnCH(SiMe$_3$)$_2$ (Ln = La, Sm) mediate the intermolecular hydroamination of MCP to the corresponding enamine, which undergoes subsequent tautomerization to the more stable imine[42] (eq 20). Subsequent

(20)
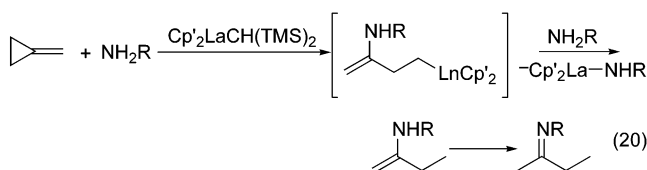
hydrogenation of the initially formed imine with 10 mol % Pd/C or NaBH$_3$CN−ZnCl$_2$[73,74] affords the corresponding amines. The intermolecular hydroamination results for symmetrical MCPs (entry 1) and unsymmetrical MCPs (entries 2−5) are shown in Table 7. This intermolecular process is not restricted to aliphatic amines (Table 7, entries 1 and 2) and is also applicable to aromatic amines (Table 7, entries 3−5). In the case of intermolecular MCP hydroamination with aromatic amines, slightly decreased N_t values are observed with respect to those of aliphatic amines ($N_t = 0.8$ h^{-1} for entry 2 vs $N_t = 0.25$ h^{-1} for entry 3). Most likely, this reflects the decreased nucleophilicity of the aromatic amines. Likewise, electron-rich aromatic amines (entries 4 and 5) exhibit slightly enhanced N_t values compared to electron−neutral aromatic amines (entry 3). The greater amine addition rate can be associated with the increased nucleophilicity of amine. Selectivity is discussed below.

(69) For the synthesis of MCPs see: Brandi, A.; Goti, A. *Chem. Rev.* **1998**, *98*, 589−635.

(70) Reviews: (a) Ohta, T.; Takaya, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, U.K., 1991; Vol. 5, p 1185. (b) Binger, P.; Buch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77−151. (c) Dzhemilev, U. M.; Khusnutdinov, R. I.; Tolstikov, G. A. *J. Organomet. Chem.* **1991**, *409*, 15−65.

(71) Review: (a) Nakamura, I.; Yamamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111−129. (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92.

(72) (a) Jia, L.; Yang, X.; Seyam, A. M.; Albert, I. D. L.; Fu, P.-F.; Yang, S.; Marks. T. J. *J. Am. Chem. Soc.* **1996**, *118*, 7900−7913. (b) Yang, X.; Seyam, A. M.; Fu, P.; Marks, T. J. *Macromolecules* **1994**, *27*, 4625−4626. (c) Jensen, T. R.; Marks, T. J. *Macromolecules* **2003**, *36*, 1775−1778.

(73) Bytschkov, I.; Doye, S. *Eur. J. Org. Chem.* **2001**, 4411−4418.

(74) Kim, S.; Oh, C. H.; Ko, J. S.; Ahn, K. H.; Kim, Y. J. *J. Org. Chem.* **1985**, *50*, 1927−1932.

Table 7. Organolanthanide-Catalyzed Intermolecular Hydroamination of Methylenecyclopropanes[a]

Entry	MCP	Amine	Products	N_t, h^{-1} (°C)[a]	Conversion[b] (Yield %)
1.			**28a**	1.2 (60)[e] 0.80 (60)[f]	> 95 > 95
2.			**29a**	0.8 (60)[e] 0.22 (60)[f]	> 95 > 95 (88)[c]
3.			**30a** **30b**	0.25 (60)[e]	> 95 (81)[c]
4.			**31a** **31b**	0.38 (60)[e]	> 95 (92)[d]
5.			**32a** **32b**	0.40 (60)[e]	94 (56)[d]

[a] Reaction conditions: 5 mol % [Cp′$_2$LnCH(SiMe$_3$)$_2$]; 1.2 equiv of MCP; turnover frequencies (N_t) measured in C$_6$D$_6$. [b] Determined by ^{1}H NMR spectroscopy and GC-MS. [c] Isolated yield of the corresponding free amines in preparative-scale reaction after H$_2$ Pd/C reduction. [d] Isolated yield of the corresponding free amines in preparative-scale reaction after the reduction using ZnCl$_2$ and NaBH$_3$CN. [e] Cp′$_2$LaCH(SiMe$_3$)$_2$ as precatalyst. [f] Cp′$_2$SmCH(SiMe$_3$)$_2$ as precatalyst.

With regard to regioselectivity and mechanistic pathways, the MCP olefin insertion into the Ln−N bond can in principle afford two different regioisomers as a result of either 1,2-addition or 2,1-addition (Scheme 5). Following 1,2-addition of the Ln−N functionality to the MCP exo methylene (Scheme 5, **T4**), ensuing β-alkyl eliminative cyclopropane ring opening of the Ln−alkyl cyclopropane species **33** affords the Ln−alkyl enamine species **34**. Rapid protonolysis of **34** by the amine substrate gives the enamine intermediate **35**, which is tautomerized to the more stable corresponding imine product. On the other hand, 2,1-addition of the Ln−N bond (Scheme 5, **T5**) would provide the Ln−alkyl species **37**. Subsequent β-alkyl shift-based ring opening and followed by protonolysis of the Ln−C bond should afford the allylamine product **39**. Organolanthanide centers sensitive to steric factors should prefer 1,2-addition (Scheme 5, **T4**) over 2,1-addition (Scheme 5, **T5**). Moreover, the C2−C3 bond of 1,2-addition product **33** can be syn oriented with respect to the Ln−C bond, while the C3−C4 bond of 2,1-insertion product **37** is perpendicular to the Ln−C bond. Thus, the β-alkyl shift of 2,1-addition product **37** is conformationally

33 (1,2-addition)   **37** (2,1-addition)

disfavored. Importantly, the proposed transition state **T4** in Scheme 5 is in accord with the observed regiochemical outcome in Table 7, entry 1. ^{1}H NMR spectra of completed, in situ monitored experiments reveal only resonances attributable to the 1,2-addition product with no trace of the 2,1-addition product, allylamine.

It is well-known that β-alkyl elimination processes represent a major chain termination pathway in lanthanide and cationic zirconocenium-catalyzed α-olefin polymerization processes.[75] In addition, this unique reactivity has been additionally har-

(75) (a) Yang, X.; Stern, C.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10015−10031. (b) Resconi, L.; Piemontesi, F.; Francisco, G.; Abis, L.; Fiorani, T. *J. Am. Chem. Soc.* **1992**, *114*, 1025−1032. (c) Eshuis, J. W.; Tan, Y. Y.; Teuben, J. H. *J. Mol. Catal.* **1990**, *62*, 277−287. (d) Evans, W. J. *Adv. Organomet. Chem.* **1985**, *24*, 131−177. (e) Watson, P. L.; Parshall, G. W. *Acc. Chem. Res.* **1985**, *18*, 51−55.

Scheme 5. Proposed Catalytic Cycle for Organolanthanide-Catalyzed Intermolecular Methylenecyclopropane Hydroamination
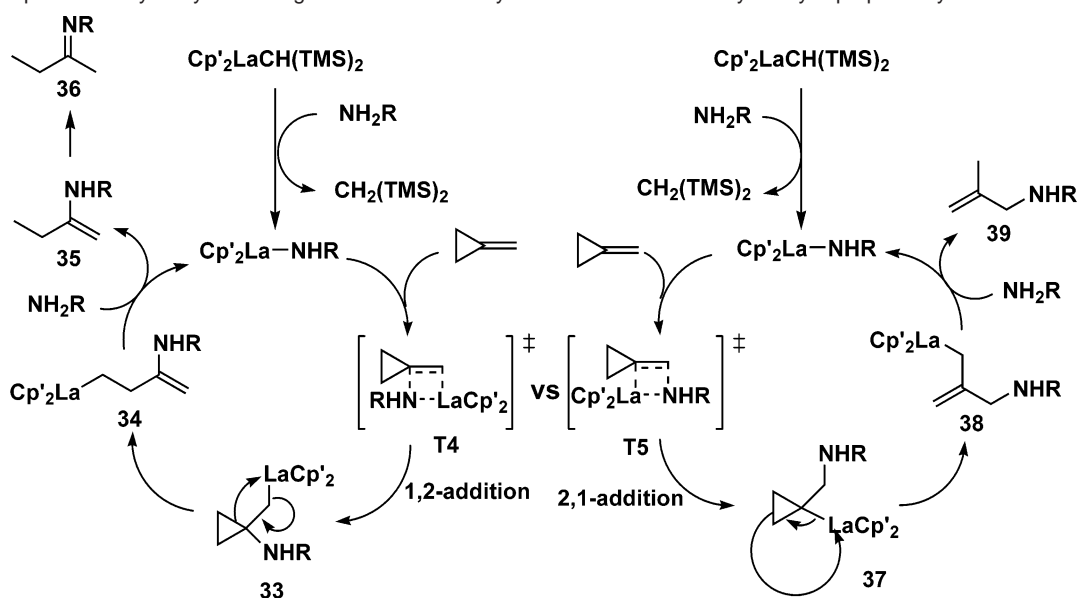
Scheme 6. Proposed Catalytic Pathways for Organolanthanide-Catalyzed Intermolecular Hydroamination of 2-Phenylmethylenecyclopropane
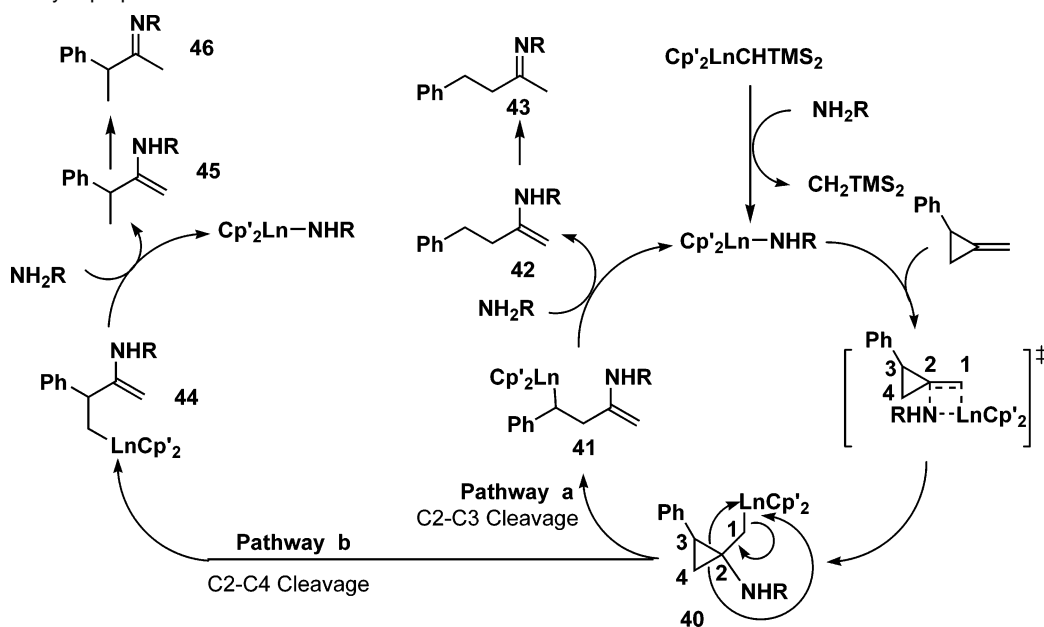
nessed as a ring-opening step in chain propagation and has provided functionalized polyolefins with backbone exo-methylene groups.[76] The organolanthanide and zirconocenium-mediated alkyl shift-based ring-opening mechanisms for methylenecycloalkanes have been well-established by ^{13}C labeling copolymerization experiments of methylenecyclobutane (MCB) and ethylene (eqs 21 and 22),[72a] in which the C2−C3/C2−C5 bond is exclusively cleaved (eq 21) rather than the C3−C4/C4−C5 bond (eq 22).

With regard to hydroamination, an additional intriguing question arises concerning regioselective ring opening of unsymmetrical phenylmethylenecyclopropane (PhMCP). In principle, two different β-alkyl shift pathways are possible in the intermolecular hydroamination of PhMCP (Scheme 6). C2−

$$(21)$$

$$(22)$$
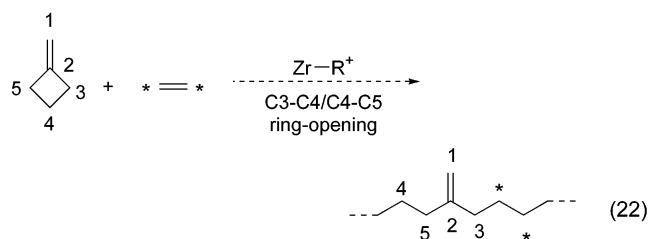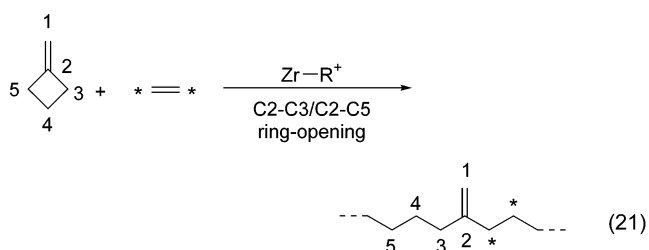
(76) (a) Yang, X.; Jia, L.; Marks, T. J. *J. Am. Chem. Soc.* **1993**, *115*, 3392−3393. (b) Jia, L.; Yang, X.; Yang, S.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 1547−1548.

Table 8. Ring-Opening Selectivity in the Intermolecular Hydroamination of 2-Phenylmethylenecyclopropane


| Entry	Amine	Precatalyst	Products	Selectivity[a] (Linear/Branch) (%)
1.	H_2N ⌒⌒	Cp'$_2$LaCH(SiMe$_3$)$_2$	**33a**	> 99%
2.	H_2N ⌒⌒	Cp'$_2$SmCH(SiMe$_3$)$_2$	**33a**	> 99%
3.	H_2N—Ph	Cp'$_2$LaCH(SiMe$_3$)$_2$	**34a** **34b**	88%
4.	H_2N—C$_6$H$_4$—Me	Cp'$_2$LaCH(SiMe$_3$)$_2$	**35a** **35b**	89%
5.	H_2N—C$_6$H$_4$—NMe$_2$	Cp'$_2$LaCH(SiMe$_3$)$_2$	**36a** **36b**	95%

[a] Determined by GC-MS and ^{1}H NMR spectroscopy.

C3 bond cleavage would proceed via pathway a. The Ln–alkyl species **41** generated affords a linear imine product after protonolysis and ensuing tautomerization. On the other hand, C2–C4 bond cleavage would provide the homobenzylic lanthanide species **44** via pathway b, which would convert rapidly to branched imine product **46** after protonolysis and tautomerization. Table 8 summarizes the regioselectivites observed in PhMCP ring opening. In all cases, linear products are observed as the major product. These results can be understood on the basis of the same arguments advanced in connection with aryl directing effects in the regioselectivity of intermolecular vinylarene hydroamination.[46,49] Presumably, the lanthanide alkyl species **40** generated from 1,2-insertion is stabilized by weak
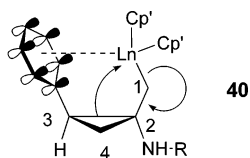
coordination to adjacent arene π-electrons. The arene–lanthanide interaction would then favor a syn orientation of Ln–C and C2–C3 bonds, which would lead to preferential C2–C3 cleavage. Interestingly, in the case of *n*-propylamine hydroamination (Table 8, entries 1 and 2), excellent regioselectivities

are observed with both Cp′$_2$La– and Cp′$_2$Sm– catalysts, while aromatic amines exhibit somewhat decreased selectivities compared to aliphatic amines (entries 3–5). Possibly, the availability of additional arene π-electron density from aromatic amine reagents disfavors the preferred conformation (eq 23).

(23)
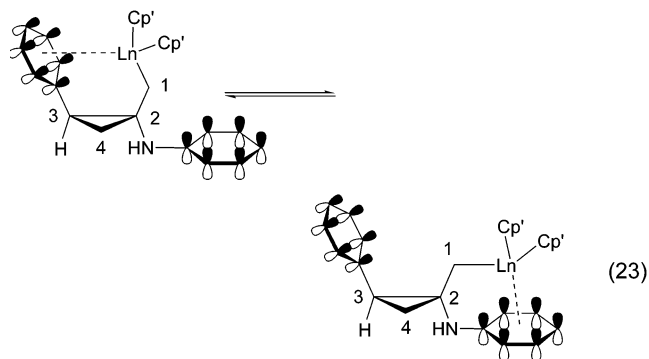
Conclusions

Intermolecular organolanthanide-mediated hydroamination processes exhibit a broad reaction scope in substrate type, including alkynes, alkenes, styrenes, butadiene, and methylenecyclopropanes. Complexes such as Me$_2$SiCp″$_2$NdCH-

(SiMe$_3$)$_2$ efficiently and regioselectively catalyze the intermolecular hydroamination of a variety of polarized and nonpolarized alkenes and alkynes to provide the corresponding amines and imines with relatively high turnover frequencies. Mechanistic data implicate turnover-limiting insertion of C−C unsaturation into Ln−N bonds (involving a highly organized transition state) with subsequent, rapid Ln−C protonolysis. In addition, the reaction proceeds with electron-deficient styrenes in good regioselectivity and yield as well as with electron-rich styrenes. Remarkably, these processes exhibit stereoelectronically controlled α-substituted effects on regioselectivity. Such transformations, based on excellent regioselectivities, can be readily integrated into intramolecular processes following intermolecular hydroamination to afford highly substituted N-containing complex molecules such as tetrahydroisoquinolines in a single catalytic cycle. Significantly, preferential intermolecular insertion over intramolecular insertion and sequential tandem bicyclization can provide an efficient route to polycyclic alkaloid skeletons.

JA035867M