Intramolecular Hydroamination/Cyclization of Aminoallenes Catalyzed by Organolanthanide Complexes. Scope and Mechanistic Aspects

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Organolanthanide complexes of the general type $Cp'_2LnCH(TMS)_2$ ($Cp' = \eta^5$-Me_5C_5; Ln = La, Sm, Y, Lu; TMS = $SiMe_3$) serve as effective precatalysts for the rapid, regioselective, and highly diastereoselective intramolecular hydroamination/cyclization (IHC) of aminoallenes having the general formula $RCH{=}C{=}CH(CH_2)_nCHR'NH_2$ to yield the corresponding heterocycles $RCH{=}CHCHNHCH(R')(CH_2)_{n-1}CH_2$ (R = CH_3, n-C_3H_7, n-C_5H_{11}; R′ = H, CH_3, n-C_4H_9, $CH_2{=}CHCH_2CH_2$; n = 2, 3). The mono- and disubstituted pyrrolidines and piperidines produced bear an α-alkenyl functionality available for further synthetic manipulation. Kinetic and mechanistic data parallel organolanthanide-mediated intramolecular aminoalkene and aminoalkyne hydroamination/cyclization, implying turnover-limiting allene insertion into the Ln−N bond followed by rapid protonolysis of the resulting Ln−C bond. The reaction rate is zero-order in [aminoallene] and first-order in [catalyst] over 3 or more half-lives. Hydroamination/cyclization of monosubstituted aminoallenes (R = H; R′ = H, CH_3; n = 1, 2) is less regioselective, with tetrahydropyridines being the predominant products.

Introduction

In the past decade, the use of f-element complexes as catalysts or reagents to effect synthetically useful organic transformations has become a ubiquitous, important interdisciplinary research activity bridging traditional organometallic and synthetic organic chemistry.[1] Catalytic C−N bond-forming processes are of fundamental importance in organic chemistry, and in particular catalytic N−H bond additions to unsaturated carbon−carbon multiple linkages remain both challenging and highly desirable reactions.[2] Until recently, efforts to catalytically effect such transformations in an efficient and general sense were only modestly successful. Two conventional approaches that have been employed involve either amine or unsaturated C−C bond activation.[2a] The amine activation approach utilizes alkali and alkaline-earth metals to generate highly nucleophilic species, which then undergo addition to the unsaturated functionality.[3] This approach affords modest yields and generally exhibits poor selectivity. On the other hand, late transition metals (e.g., Pd^{2+}) activate the unsaturated moiety via complexation, rendering it more susceptible to attack by amine nucleophiles.[4] Such transition-metal-mediated systems generally exhibit short catalyst lifetimes and low turnover frequencies.[5,6]

Organolanthanide complexes[7] exhibit unique reactivity characteristics for unsaturated organic substrate activation and heteroatom transformations vis-à-vis their typical middle- and late-transition-metal counterparts. This is a result of the high electrophilicity of f-element centers, relatively large ionic radii, nondissociable anionic ancillary ligation, absence of conventional oxidative-addition/reductive-elimination mecha-

(1) (a) Molander, G. A. *Chemtracts: Org. Chem.* **1998**, *11*, 237−263. (b) Taube, R. In *Applied Homogeneous Catalysis with Organometallic Complexes*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, Germany, 1996; Vol 2, pp 507−521. (c) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: San Diego, CA, 1994. (d) Molander, G. A. *Chem. Rev.* **1992**, *29*, 9−68.

(2) For leading reviews on catalytic amine additions to alkenes and alkynes, see: (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675−703 and references therein. (b) Roundhill, D. M. *Catal. Today* **1997**, *37*, 155−165. (c) Hegedus, L. S. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1113−1126. (d) Gasc, M. B.; Lattes, A.; Perie, J. J. *Tetrahedron* **1983**, *39*, 703−731.

(3) For hydroamination of alkenes mediated by alkali metals, see: (a) Pez, G. P.; Galle, J. E. *Pure Appl. Chem.* **1985**, *57*, 1917−1926. (b) Narita, T.; Yamaguchi, T.; Tsuruta, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3825−3828. (c) Narita, T.; Imai, N.; Tsuruta, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1242−1246. (d) Howk, B. W.; Little, E. L.; Scott, S. L.; Whitman, G. M. *J. Am. Chem. Soc.* **1954**, *76*, 1899−1902.

(4) Eisenstein, O.; Hoffmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4308−4320.

(5) For hydroamination of alkenes and alkynes mediated by late transition metals, see: (a) Larock, R. C.; Hightower, T. R.; Hasvold, L. A.; Peterson, K. P. *J. Org. Chem.* **1996**, *61*, 3584−3585. (b) Seligson, A. L.; Trogler, W. C. *Organometallics* **1993**, *12*, 744−751. (c) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738−6744. (d) Tamaru, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z.-I. *J. Am. Chem. Soc.* **1988**, *110*, 3994−4002. (e) Hegedus, L. S.; McKearin, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444−2451.

(6) For hydroaminations mediated by early transition metals, see: (a) McGrane, P. L.; Livinghouse, T. *J. Am. Chem. Soc.* **1993**, *115*, 11485−11489. (b) Baranger, A. M.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1993**, *115*, 2753−2763. (c) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *Organometallics* **1993**, *12*, 3705−3723. (d) McGrane, P. L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992**, *114*, 5459−5460.

(7) For leading general organolanthanide reviews, see: (a) Anwander, R.; Herrmann, W. A. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1996; Vol. 179, pp 1−32. (b) Edelmann, F. T. In *Topics in Current Chemistry*; Springer-Verlag: Berlin, 1996; Vol. 179, pp 247−276. (c) Deacon, G. B.; Shen, Q. *J. Organomet. Chem.* **1996**, *506*, 1−17. (d) Edelmann, F. T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2466−2488. (e) Schumann, H.; Meese-Marktscheffel, J. A.; Esser, L. *Chem. Rev.* **1995**, *95*, 865−986. (f) Schaverien, C. J. *Adv. Organomet. Chem.* **1994**, *36*, 283−362.

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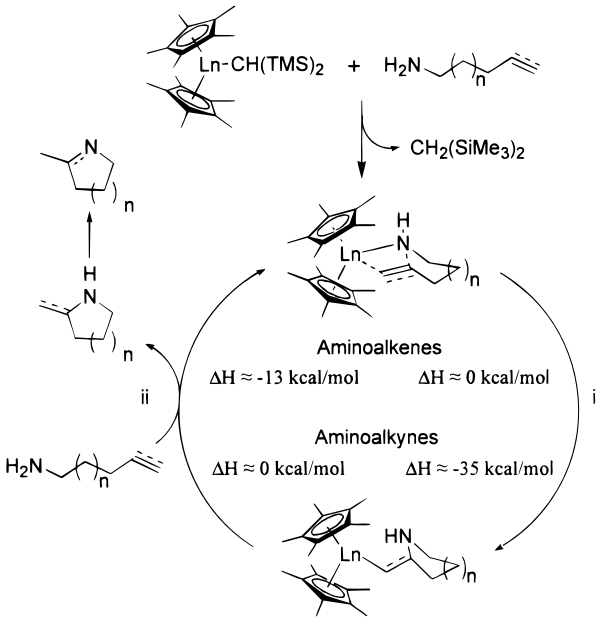
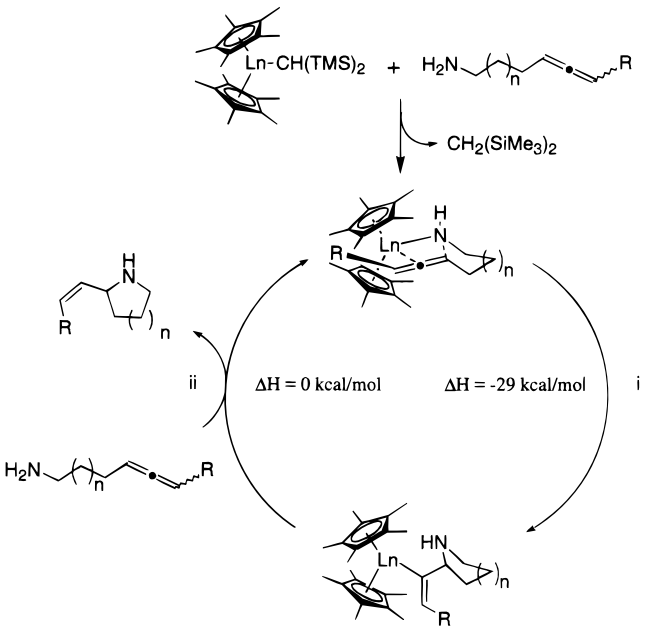
Scheme 1. Simplified Catalytic Cycle for the Organolanthanide-Mediated Intramolecular Hydroamination/Cyclization of Aminoalkenes and Aminoalkynes



Scheme 2. Proposed Catalytic Cycle for the Intramolecular Hydroamination/Cyclization of Aminoallenes



nistic pathways, and high kinetic lability. The facile catalytic, regioselective hydroamination/cyclization of aminoalkenes[8] and aminoalkynes[9] demonstrates that insertion of unsaturated C−C bonds into Ln−N bonds in lanthanocene environments can be coupled to rapid Ln−C protonolysis to effect efficient catalytic construction of numerous azacyclic classes (Scheme 1). However, cyclization of 1,2-disubstituted aminoalkenes for constructing azacycles bearing key substituents present in naturally occurring compounds has proven elusive.[10] To extend the scope of organolanthanide-mediated hydroamination methodology to applications in alkaloid synthesis, we envisioned highly reactive, sterically less encumbered aminoallenes[11] as attractive substrates for producing heterocycles bearing unsaturated α-substituents. Unlike alkenes and alkynes, the hydroamination of allenes has received limited attention. Thus, palladium(II), platinum(II), mercury(II), and silver(I) salts stoichiometrically mediate N−H addition to allenes, yielding allylic amines or enamines,[12] while silver-[13] and palladium-catalyzed[14] hydroaminations of nonactivated allenes have been reported only recently.[15] These latter conversions require long reaction times, high temperatures, and aromatic allenes or protected amines for best yields.[16]

Thermodynamic considerations[17,18] regarding unexplored allene−organolanthanide amide[19] reactivity (Scheme 2) predict that C═C insertion (step i) is ∼29 kcal/mol more exothermic than for alkenes and ∼6 kcal/mol less exothermic than for alkynes, whereas the subsequent protonolysis (step ii) is approximately thermoneutral.[20] That this transformation is indeed viable was reported earlier in a communication on the first catalytic intramolecular hydroamination/cyclization (IHC)

(8) (a) Molander, G. A.; Dowdy, E. D. *J. Org. Chem.* **1998**, 63, 8983−8988. (b) Roesky, P. W.; Stern, C. L.; Marks, T. J. *Organometallics* **1997**, *16*, 4705−4711. (c) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10241−10254. (d) Gagné, M. R.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1992**, *114*, 275−294. (e) Gagné, M. R.; Brard, L.; Conticello, V. P.; Giardello, M. A.; Stern, C. L.; Marks, T. J. *Organometallics* **1992**, *11*, 2003−2005.

(9) (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*, 9295−9306. (c) Li, Y.; Marks, T. J. *Organometallics* **1996**, *15*, 3770−3772. (d) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 707−708. (e) Li, Y.; Fu, P.-F.; Marks, T. J. *Organometallics* **1994**, *13*, 439−440.

(10) (a) Arredondo, V. M.; McDonald, F. E.; Marks, T. J., unpublished results. The turnover-limiting step in the catalytic cycle involves olefin insertion/cyclization, which is apparently impeded in sterically more demanding disubstituted aminoalkenes. However, 2,2-dimethyl-4-hexen-1-ylamine has been recently cyclized with a new class of organolanthanide precatalysts. (b) Tian, S.; Arredondo, V. M.; Marks, T. J. *Organometallics*, in press.

(11) (a) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; Wiley-Interscience: New York, 1984; Chapter 3, pp 59−85. (b) Brady, W. T.; Blake, P. In *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed.; Wiley-Interscience: New York, 1980; Vol. 1, Chapters 8, 9.

(12) (a) Arseniyadis, S.; Gore, J. *Tetrahedron Lett.* **1983**, *24*, 3997−4000. (b) De Renzi, A.; Ganis, P.; Panunzi, A.; Vitagliano, A.; Valle, G. *J. Am. Chem. Soc.* **1980**, *102*, 1722−1723.

(13) (a) Lathbury, D.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1986**, 114−115. (b) Arseniyadis, S.; Sartoretti, J. *Tetrahedron Lett.* **1985**, *26*, 729−732.

(14) (a) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421−5424. (b) Al-Masum, M.; Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1997**, *38*, 6071−6074. (c) Besson, L.; Gore, J.; Cazes, B. *Tetrahedron Lett.* **1995**, *36*, 3857−3860.

(15) For nonselective intermolecular hydroamination of allenes to afford allylamines, see: Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689−1708 and references therein.

(16) Catalyst lifetimes and turnover frequencies are generally modest.

(17) 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. *J. Am. Chem. Soc.* **1983**, *105*, 6824−6832.

(18) 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, A.22. (d) Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502−518.

(19) Allenylic complexes of rare-earth metals reamain unknown. For a recent review of metal allenyl complexes, see: Doherty, S.; Corrigan, J. F.; Carty, A. J.; Sappa, E. *Adv. Organomet. Chem.* **1995**, *37*, 39−130.

of aminoallenes mediated by organolanthanides.[21] In this contribution, we present a full account of the reaction scope, substrate selectivity, stereochemistry, lanthanide ion size effects, and kinetic/mechanistic aspects of this catalytic process.

Experimental Section

Materials and Methods. All manipulations of air-sensitive materials were carried out with rigorous exclusion of oxygen and moisture in flame-dried Schlenk-type glassware on a dual-manifold Schlenk line 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[22] and a Davison 4A molecular sieve column. All solvents were distilled before use under dry nitrogen from appropriate drying agents (sodium benzophenone ketyl, metal hydrides, Na/K alloy). Chloroform-*d* and THF-d_8 were purchased from Cambridge Isotope Laboratories. Benzene-d_6 and toluene-d_8 (Cambridge Laboratories; all 99+ atom % D) used for NMR reactions and kinetic measurements were stored 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 dried over CaH_2 overnight, dried twice over freshly activated Davison 4A molecular sieves, and then degassed by freeze−pump−thaw methods (except **11** and **12**). They were then stored in vacuumtight storage flasks. The organolanthanide precatalysts $Cp'_2LnCH(TMS)_2$ (Ln = Sm, La, Lu, Y; Cp′ = η^5-Me_5C_5),[23] $Cp'_2Sm(THF)_2$,[24] and $Me_2SiCp''_2$-$NdCH(TMS)_2$[25] were prepared by published procedures.

Physical and Analytical Measurements. NMR spectra were recorded on either a Varian Gemini VXR 300 (FT; 300 MHz, ^{1}H; 75 MHz, ^{13}C) or a Unity-400 (FT; 400 MHz, ^{1}H; 100 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. GC-MS analyses were performed using a HP6890 instrument with an HP-5MS (5% phenylmethylsiloxane, 30 m × 250 μm × 0.25 μm) capillary column and FID detector. The conditions were as follows: detector, 150 °C; injector, 250 °C; initial oven temperature, 55 °C for 3 min; 5 °C min^{-1} to 72 °C, hold for 0.1 min; 3 °C min^{-1} to 87 °C, hold for 0.1 min; 40 °C min^{-1} to 270 °C. HRMS studies were conducted on a VG 70-250 SE instrument with 70 eV electron impact ionization. IR spectra were recorded using a BioRad FT S60 FTIR instrument. Boiling points are uncorrected.

Synthesis of 4,5-Hexadien-1-ylamine (1). To a stirred solution of 1-chloro-4,5-hexadiene[26] (15.7 g, 135 mmol) and DMF (250 mL) was added potassium phthalimide (27.5 g, 148 mmol), and the resulting white suspension was heated at 107−110 °C for 20 h. After this suspension was cooled to room temperature, chloroform (100 mL) was added, and the mixture was poured into water (200 mL). The aqueous phase was separated and extracted with chloroform (3 × 25 mL). The combined chloroform extracts were washed with a 0.2 N NaOH solution and then with water. After the extracts were dried over Na_2SO_4 and filtered, the solvent was evaporated, yielding a thick oil, which upon trituration with ether furnished *N*-(4,5-hexadienyl)phthalimide as a white crystalline solid (17.5 g, 57% yield). A mixture of *N*-(4,5-hexadienyl)phthalimide (17.5 g, 77.0 mmol), MeOH (70 mL), and an 85% aqueous solution of hydrazine (77.0 mmol) was heated at reflux for 1 h. To the resulting yellow-green solution were added water (14 mL) and concentrated HCl (21 mL). The reaction mixture was then heated for an additional 3 min. After this mixture was cooled to room temperature, the creamy white precipitate was filtered and washed with cold water. The filtrate was next treated with a 1 N NaOH solution until strongly alkaline and was then extracted with ether (4 × 50 mL). The organic phase was dried over Na_2SO_4 and filtered and the solvent removed in vacuo to yield a yellow liquid. Purification of the product by reduced-pressure distillation afforded 2.3 g (30%) of **1** as a colorless liquid (bp 87−89 °C/56 mmHg). IR (KBr, thin film): ν_{max} 3355, 2923, 2852, 1955, 1584, 1438, 1311, 844 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.07 (1H, m, =CH), 4.63 (2H, m, $=CH_2$), 2.69 (2H, t, J = 6.9 Hz, CH_2NH_2), 2.06−1.96 (2H, m, $=CHCH_2$), 1.53 (2H, quintet, J = 7.2 Hz, $CH_2CH_2CH_2$), 1.08 (2H, s, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.4, 89.5, 74.9, 41.5, 32.9, 25.5. HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_6H_{11}N$, 96.0813; found, 96.0805.

Synthesis of 5,6-Heptadien-2-ylamine (2). 5,6-Heptadien-2-one[27] (4.50 g, 41.0 mmol) was suspended in water (18 mL) containing $H_2NOH{\cdot}HCl$ (2.83 g; 41.0 mmol). To this mixture was added solid Na_2CO_3 (2.16 g; 21.0 mmol), and to the resulting mixture was added EtOH (5 mL). The reaction mixture was stirred at room temperature for 4 days. The resulting solution was then diluted with ether and the organic layer separated. The aqueous layer was extracted with ether (4 × 25 mL), and the combined ethereal extracts were dried over Na_2SO_4. Filtration and removal of the solvent in vacuo yielded 5.01 g (98%) of the oxime as a mixture of isomers (2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 and 8.01 (1H, br s, =NOH), 5.10 (1H, m, =CH), 4.67 (2H, m, $=CH_2$), 2.48 and 2.27 (2H, t, $CH_2C{=}N$), 2.2−2.15 (2H, m, $=CHCH_2$), 1.87 (3H, s, $CH_3C{=}N$). The crude oxime (5.01 g, 40.0 mmol) in dry ether (50 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (2.28 g, 60 mmol) in ether at a rate sufficient to maintain a gentle reflux. Upon complete addition of the oxime, the reaction mixture was refluxed for an additional 2 h. The reaction mixture was then cooled to room temperature and quenched by the sequential addition of water (2.5 mL), a 15% NaOH solution (2.5 mL), and water (7.5 mL). The white precipitate which formed was filtered off and washed with ether. The filtrate was dried over Na_2SO_4, filtered, and the solvent evaporated. The residue was vacuum-distilled, affording **2** as a colorless liquid (bp 55 °C/7 mmHg), 1.94 g (67% yield). IR (KBr, thin film): ν_{max} 3356, 3276, 2958, 2918, 2851, 1955, 1586, 1441, 1372, 845 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.07 (1H, m, =CH), 4.63 (2H, m, $=CH_2$), 2.90 (1H, sextet, J = 6.3 Hz, CH_3CHNH_2), 2.05−1.97 (2H, m, $=CHCH_2$), 1.21 (2H, br s, NH_2), 1.03 (3H, d, J = 6.3, CH_3CHNH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.4, 89.7, 74.9, 46.3, 39.2, 25.1, 23.9. HRMS (*m*/*z*): $[M - H]^+$ calcd for $C_7H_{13}N$, 110.0970; found, 110.0962.

Synthesis of 5,6-Heptadien-1-ylamine (3). With stirring, Ph_3P (29.3 g, 112 mmol) was added in one portion to a 0 °C ether solution (120 mL) of 5,6-heptadienyl azide (15.3 g), prepared in a manner similar to **7c**, but from 5,6-heptadien-

(20) (a) ΔH for NH_3 addition to allene (to yield $CH_2{=}CHCH_2NH_2$) is estimated to be −24 kcal/mol. (b) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data for Organic Compounds*, 2nd ed.; Chapman and Hall: London, 1986.

(21) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871−4872.

(22) (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.

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

(24) Evans, W. J.; Grate, J. W.; Chei, H. W.; Bloom, I.; Hunter, W. E.; Atwood, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 941−946.

(25) Jeske, G.; Schock, L. E.; Mauermann, H.; Swepston, P. N.; Schumann, H.; Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 8103−8110.

(26) Arseniyadis, S.; Gore, J.; Roumestant, M. L. *Tetrahedron* **1979**, *35*, 353−363.

(27) Walkup, R. D.; Mosher, M. D. *Tetrahedron* **1993**, *49*, 9285−9299.

1-ol[28] (vide infra). After 1 h, the reaction mixture was then warmed to room temperature and stirred for an additional 1 h. Water (12 mL) was added to the reaction mixture, and stirring was continued for 1 day. The reaction mixture was then partitioned between ether and, sequentially, water and brine. The combined organic layers were dried over Na_2SO_4, filtered, concentrated to 70 mL, and cooled to 0 °C. Solid Ph_3PO was filtered off, and the ether solution was again concentrated. The crude product was distilled under reduced pressure (bp 103−105 °C/11 mmHg), to afford the title compound as a colorless liquid (6.2 g, 46% yield). IR (KBr, thin film): ν_{max} 3386, 3296, 2933, 2857, 1955, 1632, 1597, 1440, 1072, 843 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.03 (1H, m, =CH), 4.62 (2H, m, $=CH_2$), 2.42 (2H, t, J = 6.6 Hz, CH_2NH_2), 1.89−1.85 (2H, m, $=CHCH_2$), 1.31−1.18 (4H, m, CH_2CH_2), 0.53 (2H, br s, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.4, 89.8, 74.7, 42.1, 33.3, 28.0, 26.3. HRMS (*m*/*z*): $[M - H]^+$ calcd for $C_7H_{13}N$, 110.0970; found, 110.0978. Anal. Calcd for $C_7H_{13}N$: C, 75.62; H, 11.78; N, 12.60. Found: C, 75.17; H, 11.93; N, 12.62.

Synthesis of 4,5-Heptadien-1-ylamine (7). 4,5-Heptadien-1-ol (7a). This compound was prepared from 4-pentyn-1-ol according to the literature procedure[29] in 43% overall yield. ^1H NMR (300 MHz, $CDCl_3$): δ 5.03 (2H, m, =CH), 3.60 (2H, t, J = 6.7, CH_2OH), 2.02 (2H, m, $=CHCH_2$), 1.70−1.58 (6H, m, $CH_3CH=$, CH_2, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.6, 89.6, 86.0, 62.3, 31.8, 25.0, 14.5. HRMS (*m*/*z*): $[M]^+$ calcd for $C_7H_{12}O$, 112.0888; found, 112.0884.

4,5-Heptadienyl-1-*p*-Toluenesulfonate (7b). Compound **7a** (6.44 g, 57.5 mmol) and TsCl (13.14 g, 68.9 mmol) were dissolved in ether (190 mL), and the mixture was cooled to between −5 and −10 °C. Freshly and finely powdered KOH (37.5 g) was added with efficient stirring. The addition was initially carried out in 5 g portions with intervals of 2 min. The evolution of heat was considerable, and efficient cooling was necessary to maintain the reaction temperature between −5 and 0 °C. After approximately half of the KOH had been added, the remainder was added over the next 5 min. The mixture was stirred for 1 h and then poured into ice water. After vigorous shaking, the layers were separated, and the aqueous layer was extracted with ether (2 × 50 mL). The organic layer and the two ethereal extracts were combined and dried over Na_2SO_4. After filtration, the solvent was removed in vacuo to yield tosylate **7b** as a yellow oil (14.58 g, 95% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.76 (2H, d, J = 7.9 Hz, Ph), 7.30 (2H, d, J = 8.0 Hz, Ph), 4.98 (2H, m, =CH), 4.03 (2H, t, J = 6.4 Hz, CH_2OSO_2Ar), 2.42 (3H, s, CH_3Ar), 1.97 (2H, m, $=CHCH_2$), 1.73 (2H, quintet, J = 7.1 Hz, CH_2), 1.57 (3H, dd, J = 6.9, 3.3 Hz, $CH_3CH=$).

4,5-Heptadienyl Azide (7c). NaN_3 (8.89 g, 136.8 mmol) was added in one portion to a stirred solution of **7b** (14.58 g, 54.7 mmol) in DMF (70 mL) at room temperature. After it was heated for 3 h at 50 °C, the reaction mixture was partitioned between ether and water. The aqueous layer was then back-extracted with ether (3 × 50 mL). The combined organic layers were washed (3×) with small portions of water, dried over Na_2SO_4, and then filtered. The filtrate was concentrated in vacuo to provide azide **7c** as a light yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 5.04 (2H, m, =CH), 3.29 (2H, t, J = 6.9 Hz, CH_2N_3), 2.04 (2H, m, $=CHCH_2$), 1.68 (2H, quintet, J = 7.0 Hz, CH_2), 1.63 (2H, dd, J = 6.8, 3.3 Hz, $CH_3CH=$).

4,5-Heptadien-1-ylamine (7). Compound **7c** dissolved in ether (50 mL) was added dropwise to a stirring suspension of $LiAlH_4$ (3.13 g, 82.5 mmol) in ether (170 mL) at a rate which maintained a gentle reflux. After addition was complete, reflux was continued for 2 h. The reaction mixture was then cooled to room temperature and quenched by the sequential addition of water (3 mL), a 15% solution of NaOH (3 mL), and water (10 mL). The white precipitate which formed was removed by filtration and washed with ether. The filtrate was then dried over Na_2SO_4, filtered, and the solvent evaporated. The product was purified by vacuum distillation (bp 85−87 °C/32 mmHg), yielding a colorless liquid (2.0 g, 31% overall yield from 4,5-heptadien-1-ol). IR (KBr, thin film): ν_{max} 3369, 3286, 2927, 2853, 1968, 1598, 1460, 1440, 1281, 1072, 872, 817 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.00 (2H, m, =CH), 2.69 (2H, t, J = 7.0 Hz, CH_2NH_2), 2.05−1.95 (2H, m, $=CHCH_2$), 1.60 (3H, dd, J = 5.1, 4.8 Hz, $CH_3CH=$), 1.51 (2H, quintet, J = 7.2 Hz, CH_2), 1.25 (2H, s, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 208.6, 89.7, 85.7, 41.5, 33.0, 26.0, 14.5. HRMS (*m*/*z*): $[M - H]^+$ calcd for $C_7H_{13}N$, 110.0970; found, 110.0964.

Synthesis of 5,6-Octadien-1-ylamine (8). Substrate **8** was obtained from 5,6-octadienyl azide[30] in the same way as described for **7** (vide supra) as a colorless liquid (4.8 g, 96% yield; bp 81−82 °C/5 mmHg). IR (KBr, thin film): ν_{max} 3369, 3294, 3182, 2933, 2858, 1966, 1600, 1467, 1438, 1069, 874 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.00 (2H, m, =CH), 2.66 (2H, t, J = 6.8 Hz, CH_2NH_2), 1.95 (2H, m, $=CHCH_2$), 1.61 (3H, t, J = 5.6, 5.6 Hz, $CH_3CH=$), 1.42 (4H, m, CH_2CH_2), 1.13 (2H, s, NH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.5, 89.9, 85.3, 41.9, 33.1, 28.5, 26.2, 14.4. HRMS (*m*/*z*): $[M]^+$ calcd for $C_8H_{15}N$, 125.120; found, 125.120.

Synthesis of 5,6-Decadien-2-ylamine (9). Crude allenic amine **9** was prepared from (*S*)-5,6-decadien-2-one[30] in the same way as described for **10** (vide infra). It was distilled under reduced pressure (bp 84−85 °C/0.1 mmHg) to afford a colorless liquid (2.6 g, 75%, yield). IR (KBr, thin film): ν_{max} 3347, 3287, 2957, 2928, 2871, 1961, 1576, 1459, 1376, 876 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.05 (2H, m, =CH), 2.90 (1H, sextet, J = 6.3 Hz, $CH_3CH(NH_2)$), 2.00−1.91 (4H, m, $=CHCH_2$), 1.40 (4H, m), 1.18 (2H, br s, NH_2), 1.04 (3H, d, J = 6.3 Hz, $CH_3CH(NH_2)$), 0.89 (3H, t, J = 7.3 Hz, $CH_3CH_2CH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.5, 90.7, 90.0, 46.0, 39.1, 30.7, 25.6, 23.6, 22.0, 13.3. HRMS (*m*/*z*): $[M - H^+]$ calcd for $C_{10}H_{19}N$, 152.14392; found, 152.14409.

Synthesis of 6,7-Nonadien-2-Amine (10). 6,7-Nonadien-2-one[30] (4.0 g, 28.9 mmol) was suspended in water (13 mL) containing $H_2NOH{\cdot}HCl$ (2.0 g; 28.9 mmol). To this mixture was added solid Na_2CO_3 (1.5 g; 14.5 mmol), and to the resulting mixture was added EtOH (5 mL). The reaction mixture was stirred at room temperature for 1.5 days. The resulting solution was then diluted with ether and the layers separated. The aqueous layer was extracted with ether (4 × 25 mL), and the combined ethereal extracts were dried over Na_2SO_4. Filtration and removal of the solvent in vacuo yielded the oxime as a mixture of isomers (2:1). ^1H NMR (300 MHz, $CDCl_3$): δ 8.19 and 8.01 (1H, br s, =NOH), 5.03 (1H, m, =CH), 2.39 and 2.20 (2H, t, J = 7.9 and 7.7 Hz, $CH_2C=NOH$), 1.98 (2H, m, $=CHCH_2$), 1.86 (3H, d, J = 2.4 Hz, $CH_3C(NOH)$), 1.62 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$): 204.7, 158.7, 158.4, 89.6, 89.5, 85.9, 85.8, 35.1, 28.7, 28.2, 28.1, 25.6, 24.8, 19.9, 14.5, 13.4. HRMS (*m*/*z*): $[M]^+$ calcd for $C_9H_{15}NO$, 153.1154; found, 153.1153. The crude oxime (5.01 g, 40 mmol) in dry ether (50 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (2.0 g, 53 mmol) in ether (100 mL) at a rate sufficient to maintain a gentle reflux. Upon addition, the reaction mixture was refluxed for an additional 4 h. The reaction mixture was next cooled to room temperature and quenched by sequential addition of water (2 mL), a 15% solution of NaOH (2 mL), and water (6 mL). The white precipitate which formed was filtered off and washed with ether. The filtrate was dried over Na_2SO_4, filtered, and the solvent evaporated, yielding a yellow liquid. Purification was carried out by redissolving the product in ether, acidifying with a 10% HCl solution, and separating the aqueous layer. The aqueous layer was made alkaline with

(28) Coates, R. M.; Senter, P. D.; Baker, W. R. *J. Org. Chem*. **1982**, *47*, 3597−3607.

(29) Bates, P. W.; Rama-Devi, T.; Ko, H.-H. *Tetrahedron* **1995**, *51*, 12939−12954.

(30) For detailed synthetic procedures and spectroscopic characterization data, see the Supporting Information.

NaOH and extracted with ether (3 × 70 mL). This process was repeated twice. The crude allenic amine **10** was then distilled under reduced pressure (bp 97−98 °C/14 mmHg) to afford a colorless liquid (3.5 g, 87% yield). IR (KBr, thin film): ν_{max} 3356, 3285, 2955, 2926, 2856, 1964, 1576, 1371, 1287, 872 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.01 (2H, m, =CH), 2.85 (1H, sextet, J = 6.2 Hz, CH_3CHNH_2), 1.96 (2H, m, =$CHCH_2$), 1.61 (3H, dd, J = 5.6, 4.5 Hz, CH_3CH=), 1.44−1.30 (4H, m), 1.28 (2H, br s, NH_2), 1.03 (3H, d, J = 6.3, $CH_3CH(NH_2)$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.6, 90.0, 85.5, 46.7, 39.5, 28.8, 25.9, 23.9, 14.5. HRMS (*m*/*z*): $[M]^+$ calcd for $C_9H_{17}N$, 139.1361; found, 139.1344.

(5*S*,8*S*)-5-Aminotrideca-8,9-diene (11). To a solution of (8*S*,5*R*)-trideca-8,9-dien-5-ol[31] (4.8 g, 24.3 mmol) in dry THF (300 mL) was added PPh_3 (12.8 g, 48.7 mmol), diethyl azodicarboxylate (DEAD; 8.5 g, 48.7 mmol), and diphenylphosphoryl azide (DPPA; 13. 4 g, 48.7 mmol). The reaction mixture was stirred for 30 min and then concentrated by rotary evaporation, filtered through a plug of Celite, and washed with 1/1 ether/pentane. The filtrate was concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (10% ether in pentane), yielding the azide as a light yellow oil (4.1 g, 75% yield). R_f = 0.88 (20% ether in pentane). IR (KBr, thin film): ν_{max} 2959, 2932, 2865, 2097, 1963, 1465, 1258 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.08 (2H, m, =CH), 3.30 (1H, quint, J = 6.6 Hz, $CH_2CH(N_3)CH_2$), 2.13−2.02 (2H, m, =$CHCH_2$), 1.99−1.91 (2H, m, =$CHCH_2$), 1.62−1.30 (10H, m, $5CH_2$), 0.93−0.87 (6H, m, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 204.1, 91.6, 89.7, 62.3, 34.1, 33.6, 31.0, 28.2, 25.3, 22.5, 22.4, 13.9, 13.6. A solution of this azide (4.1 g, 18.8 mmol) in dry ether (25 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (1.4 g, 36.5 mmol) in ether (50 mL) at a rate so as to maintain a gentle reflux. When addition was complete, reflux was continued for 24 h. The reaction mixture was then cooled to room temperature and quenched by the sequential addition of water (1.5 mL), a 15% solution of NaOH (1.5 mL), and water (4.5 mL). The white precipitate which formed was filtered off and washed with ether. The filtrate was dried over Na_2SO_4, filtered, the solvent was evaporated, and the crude product was purified by vacuum distillation (bp 135−136 °C/1 mmHg), yielding **11** as a colorless liquid (3.4 g, 92% yield). $[\alpha]^{23}_D$ = +26.6° (c = 2.0, $CHCl_3$). IR (KBr, thin film): ν_{max} 3373, 3303, 2958, 2929, 2859, 1962, 1465, 1378 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.05 (2H, m, =CH), 2.73 (1H, m, $CH_2CH(NH_2)CH_2$), 2.15−1.90 (4H, m, =$CHCH_2$), 1.58−1.25 (12H, m, $5CH_2$, NH_2), 0.92−0.87 (6H, m, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.8, 91.0, 90.4, 50.5, 37.7, 37.3, 31.0, 28.3, 25.6, 22.8, 22.3, 14.0, 13.6. HRMS (*m*/*z*): $[M]^+$ calcd for $C_{13}H_{25}N$, 195.19870; found, 196.19874. Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 79.73; H, 12.95; N, 7.13.

(5*S*)-5-Aminopentadeca-1,8,9-triene (12). From 942.4 mg of (5*R*)-pentadeca-1,8,9-triene-5-ol (**13**),[31] 538.7 mg of **12** was obtained after high-vacuum distillation using the same procedure as for **11**. $[\alpha]^{23}_D$ = −49.4° (c = 2.0, $CHCl_3$). IR (KBr, thin film): ν_{max} 3373, 3303, 2957, 2926, 2871, 2855, 1961, 1641, 1467, 1451, 1378, 910 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87−5.73 (1H, m, =CH alkene), 5.06 (2H, m, =CH allene), 4.99−4.91 (2H, m, $=CH_2$ alkene), 2.76 (1H, m, $CH_2CH(NH_2)CH_2$), 2.18−1.91 (6H, =$CHCH_2$), 1.58−1.44 (2H, m, CH_2), 1.41−1.21 (10H, m, $4CH_2$, NH_2), 0.86 (3H, t, J = 6.9 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.7, 138.7, 114.5, 91.4, 90.5, 50.1, 37.3, 37.1, 31.3, 30.5, 28.9 (2C), 25.6, 22.5, 14.1. HRMS (*m*/*z*): $[M + 1]^+$ calcd for $C_{15}H_{27}N$, 222.2222; found, 222.2226. Anal. Calcd for $C_{15}H_{27}N$: C, 81.38; H, 12.29; N, 6.33. Found: C, 80.5; H, 12.44; N, 6.05.

Typical NMR-Scale Catalytic Reactions. In the glovebox, the $Cp'_2LnCH(TMS)_2$ precatalyst (ca. 5 mg, 8 mmol) was weighed into an NMR tube equipped with a Teflon valve. On the high-vacuum line, the tube was evacuated, and C_6D_6 (700 μL) was vacuum-transferred into the tube, followed by 4,5-heptadien-1-ylamine (**7**). The tube was then sealed and the ensuing reaction monitored by ^{1}H NMR.

Preparative-Scale Catalytic Reactions. In the glovebox, $Cp'_2SmCH(TMS)_2$ (20 mg, 34 μmol) was loaded into a storage tube equipped with a magnetic stir bar and a J. Young Teflon valve. At −78 °C, benzene (or pentane; 2 mL) was vacuum-transferred onto the catalyst, and benzene (2 mL) containing **7** (500 mg, 4.5 mmol) was added by syringe. The clear yellow solution was stirred for 8 h at ambient temperature. The reaction mixture was next freeze−thaw-degassed, and the volatiles were vacuum-transferred into a separate flask. The solvent was removed on the rotary evaporator at 0 °C to give 465 mg (93% yield) of a slightly yellow liquid (>95% pure by GC-MS). Alternatively, for nonvolatile products, filtration of the reaction mixture through silica gel or aqueous/acidic workup effectively removes the catalyst and yields pure products.

2-Methyl-3,4,5,6-Tetrahydropyridine (4a).[32] This compound was prepared using both NMR- and preparative-scale reactions. Spectroscopic data agree with those in the literature.[32] IR (KBr, thin film): ν_{max} 2930, 2855, 1665, 1451, 1372, 1354, 1274, 1198, 996, 896 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.51 (2H, m, CH_2N=C), 2.10 (2H, tt, J = 6.6, 1.92 Hz, CH_2C=), 1.89 (3H, t, J = 1.68 Hz, CH_3C=), 1.68−1.62 (2H, m), 1.57−1.48 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.9, 49.1, 30.1, 27.4, 21.5, 19.5. GC-HRMS (*m*/*z*): $[M]^+$ calcd for $C_6H_{11}N$, 97.08915; found, 97.09015.

2,6-Dimethyl-3,4,5,6-Tetrahydropyridine (4b).[33] This compound was prepared using both NMR- and preparative-scale reactions. Spectroscopic data agree with those in the literature. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.28−3.42 (1H, m, CH_3CH), 1.99−2.08 (2H, m), 1.58−1.76 (4H, m), 1.90 (3H, d, J = 1.9 Hz), 1.22 (3H, d, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.3, 53.1, 29.9, 29.1, 27.4, 23.4, 18.7. GC−HRMS (*m*/*z*): $[M]^+$ calcd for $C_7H_{13}N$, 111.10480; found, 111.10488. MS *m*/*z* (relative intensity): $[M]^+$ (46), $[M - 1]^+$ (8), 96 (14), 83 (75), 70 (10), 68 (46), 55 (21), 42 (100), 39 (29).

2-Vinylpyrrolidine (5a). This compound was a minor component in the product mixture and was not isolated in pure form. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.83 (1H, ddd, J = 17.1, 10.2, 6.9 Hz, HC=CH_2), 5.12 (1H, td, J = 16.7, 1.4 Hz, HC=CH_2), 4.99 (1H, ddd, J = 10.2, 1.7, 1.0 Hz, HC=CH_2), 3.02 (1H, m, $CHHC$=CH_2), 2.96 (1H, m, CH_2N), 2.68 (1H, t, J = 7.4 Hz, CH_2N), 1.75 (1H, m), 1.4−1.6 (4H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.1, 113.9, 61.3, 46.3, 31.9, 25.1.

2-Methyl-5-Vinylpyrrolidine (5b). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81 (1H, ddd, J = 17.0, 10.2, 6.7 Hz, HC=CH_2), 5.08 (1H, td, J = 17.0, 2.0, 1.3 Hz, HC=CH_2), 4.96 (1H, ddd, J = 10.1, 2.0, 1.1 Hz, HC=CH_2), 4.10 (1H, quartet, J = 7.14 Hz), 3.71 (1H, m), 2.68 (2H, m), 1.48−1.62 (2H, m), 1.12 (3H, d, J = 6.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.7, 113.5, 60.4, 53.2, 34.1, 32.7, 22.1. GC-HRMS (*m*/*z*): $[M]^+$ calcd for $C_7H_{13}N$, 111.10480; found, 111.10479. MS (*m*/*z* (relative intensity)): $[M]^+$ (32), 96 (38), 83 (64), 68 (55), 56 (100), 49 (63), 41 (83), 39 (41), 32 (18).

6-Ethyl-2,3,4,5-Tetrahydropyridine (6).[32b] This compound was a pale yellow liquid obtained in 95% yield via reaction of $Cp'_2SmCH(TMS)_2$ (3 mol %) and **3** in benzene at 60 °C. Spectroscopic data agree with those in the literature.[32b] IR (KBr, thin film): ν_{max} 2926, 2855, 1666, 1444, 1359, 1277, 1139 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): δ 3.53 (2H, m,

(31) For detailed synthetic procedures and spectroscopic characterization data, see: Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J., *J. Am. Chem. Soc.*, in press.

(32) (a) Hua, D. H.; Miao, S. W.; Bharathi, S. N.; Katshira, T.; Bravo, A. A. *J. Org. Chem.* **1990**, *55*, 3682−3684. (b) Ansensio, G.; Gonzalez-Nunez, M. E.; Bernardini, C. B.; Mello, R.; Adam, W. *J. Am. Chem. Soc.* **1993**, *115*, 7250−7253. (c) Venanzi, M.; Pugin, B. *J. Am. Chem. Soc.* **1983**, *105*, 6877−6881.

(33) Vaultier, M.; Lambert, P. H.; Carrie, R. *Bull. Soc. Chim. Fr.* **1986**, 83−91.

CH_2N═C), 2.00 (2H, tq, J = 7.4, 1.7 Hz, CH_3CH_2C═N), 1.66 (2H, dt, J = 5.5, 1.8 Hz, $CH_3CH_2(CH_2)C$═NCH_2), 1.27 (4H, m, CH_2CH_2), 1.09 (3H, t, J = 7.4 Hz, CH_3CH_2C═N). ^{13}C NMR (75 MHz, C_6D_6): δ 169.0, 49.3, 33.7, 28.9, 22.4, 20.1, 10.5. HRMS (m/z): $[M - H]^+$ calcd for $C_8H_{15}N$, 110.0969; found, 110.0969.

2-[(*Z*)-Prop-1-enyl]pyrrolidine (13). This compound was obtained in 93% yield as a pale yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.45 (1H, ddd, J = 10.1, 6.6, 0.9 Hz, ═CH), 5.33 (1H, qdd, 10.7, 7.7, 1.7 Hz), 3.81 (1H, m), 3.04 (1H, ddd, J = 10.2, 7.5, 5.6 Hz), 2.83 (1H, dt, J = 6.1, 9.9 Hz, CH_2NH_2), 1.96−1.82 (1H, m), 1.80−1.69 (2H, m), 1.65 (3H, dd, J = 6.7, 1.6 Hz, CH_3CH═), 1.55 (1H, br s), 1.38−1.28 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.4, 125.0, 55.1, 46.5, 32.5, 25.5, 13.1. HRMS (m/z): $[M - H]^+$ calcd for $C_7H_{13}N$, 110.097; found, 110.097.

2-[(*E*)-Prop-1-enyl]pyrrolidine. ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.9, 125.2, 60.7, 46.3, 32.1, 25.2, 17.6. Both isomers exhibit indistinguishable mass spectra. MS (m/z (relative intensity)): M^+ (32), $[M - 1]^+$ (30), $[M + 1]^+$ (5), 96 (79), 83 (18), 68 (100), 41 (31), 36 (26).

2-[(*Z*)-Prop-1-enyl]piperidine (14). This compound was obtained as a pale yellow liquid in 95% yield. IR (KBr, thin film): ν_{max} 3289, 2931, 2853, 2818, 1661, 1441, 1374, 1205, 1051, 978, 759 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.51 (1H, qdd, J = 10.8, 8.2, 1.5 Hz ═CH), 5.38 (1H, dqd, J = 10.8, 6.6, 0.97 Hz, ═CH), 3.31 (1H, dd, J = 8.4, 2.7 Hz), 2.86 (1H, m), 2.47 (1H, m), 1.65 (1H, m), 1.53 (3H, dd, J = 6.7, 1.6 Hz), 1.42−1.37 (4H, m), 1.33−1.26 (1H, m), 0.98 (1H, br s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.1, 124.6, 53.9, 46.8, 32.4. 25.7, 24.6, 13.2. HRMS (m/z): $[M]^+$ calcd for $C_8H_{15}N$, 125.12045; found, 125.11841.

2-[(*E*)-Prop-1-enyl]piperidine. ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.9, 124.9, 59.0, 46.8, 32.8, 25.9, 24.6, 17.8. Both isomers exhibit indistinguisable mass spectra; MS (m/z (relative intensity)): $[M]^+$ (36), $[M - 1]^+$ (22), $[M + 1]^+$ (4), 110 (67), 97 (39), 96 (38), 82 (100), 68 (68), 55 (16), 41 (29).

***trans*-2-Methyl-5-[(*Z*)-pent-1-enyl]pyrrolidine (15).** ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.43 (1H, td, J = 12.4, 6.2 Hz, ═CH), 5.30−5.35 (1H, m), 4.01 (1H, m), 3.29 (1H, m), 1.88−1.96 (4H, m), 1.20−1.47 (4H, m), 1.68 (1H, s), 1.09 (3H, d, J = 6.2 Hz, CH_3CH), 0.86 (3H, t, J = 7.4, CH_3CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.5, 129.8, 54.1, 53.1, 34.4, 34.2, 33.3, 22.9, 22.3, 13.7. GC-HRMS (m/z): $[M]^+$ calcd for $C_{10}H_{19}N$, 153.15175; found, 153.15275. Both isomers exhibit indistinguishable mass spectra. MS (m/z (relative intensity)): M^+ (28), 138 (32), 124 (44), 110 (61), 96 (56), 82 (100), 67 (27), 55 (17), 41 (44).

***trans*-2-Methyl-5-[(*E*)-pent-1-enyl]pyrrolidine.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.47 (1H, td, J = 15.2, 6.2 Hz, ═CH), 5.30−5.35 (1H, m), 3.63 (1H, m), 3.29 (1H, m), 1.97−2.05 (4H, m), 1.68 (1H, s), 1.20−1.47 (4H, m), 1.08 (3H, d, J = 6.3 Hz, CH_3CH), 0.84 (3H, t, J = 7.4, CH_3CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.9, 130.1, 59.8, 53.2, 34.3, 33.7, 29.4, 22.4, 22.2, 13.6. GC-HRMS (m/z): $[M]^+$ calcd for $C_{10}H_{19}N$, 153.15175; found, 153.15190.

Hydrogenation of 15 (Mixture of *Z*/*E* Stereoisomers). The product mixture from the reaction above (10 mg) was dissolved in dry CH_2Cl_2 (2 mL), and PtO_2 (5 mg) was added. Hydrogen was bubbled into the reaction vessel using a balloon and a syringe needle. The reaction mixture was vigorously stirred for 30 min. The catalyst was removed by filtration and the solvent by rotary evaporation, yielding 10 mg (99% yield) of *trans*-2-methyl-5-pentylpyrrolidine (**15a**)[34] as a pale yellow liquid. A single peak is observed by GC-MS analysis corresponding to the product, and the spectroscopic data are in agreement with the published data.[34] The relative stereochemistry was established by NOE difference techniques. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.74 (1H, m), 3.61 (1H, m), 2.15 (2H, d, m), 1.87−1.99 (1H, m), 1.53−1.72 (4H, m), 1.49 (3H, d, J = 6.6 Hz), 1.20−1.43 (6H, m), 0.83 (3H, t, J = 7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 59.2, 55.1, 32.7, 32.1, 31.3, 30.4, 26.3, 22.4, 18.0, 13.9. HRMS (m/z): calcd for $C_{10}H_{21}N$ ($[M - 1]^+$), 154.15958; found, 154.15756.

***cis*-2-Methyl-6-[(*Z*)-prop-1-enyl]piperidine (16).** ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.41−5.46 (1H, m, CH_3CH═), 5.34 (1H, ddq, J = 11.8, 7.0, 1.5 Hz, ═CH), 3.43 (1H, ddd, J = 10.8, 8.2, 2.8 Hz), 2.65(1H, m), 1.68−1.78 (1H, m), 1.62 (3H, d, J = 6.7 Hz, CH_3CH═), 1.46−1.58 (2H, m), 1.26−1.40 (1H, m), 1.21−1.15 (1H, m), 1.04 (3H, d, J = 6.15, CH_3CH), 0.96−1.02 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.1, 124.3, 54.1, 52.1, 33.6, 31.8, 24.5, 22.9, 13.2. GC-HRMS (m/z): calcd for $C_9H_{17}N$ ($[M]^+$), 139.13609; found, 139.13780. Both isomers exhibit indistinguishable mass spectra. MS (m/z (relative intensity)): $[M]^+$ (35), 124 (100), 111 (26), 96 (94), 82 (76), 68 (67), 55 (25), 41 (60).

***cis*-2-Methyl-6-[(*E*)-prop-1-enyl]piperidine.**[35] Spectroscopic data agree with those in the literature.[35] ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.54 (1H, dqd, J = 18.7, 6.0, 0.8 Hz, CH_3CH═), 5.41−5.46 (1H, m), 3.02 (1H, ddd, J = 10.8, 6.7, 2.9 Hz), 2.65 (1H, m), 1.68−1.78 (1H, m), 1.63 (3H, dd, J = 6.5, 0.9 Hz, CH_3CH═), 1.46−1.58 (2H, m), 1.26−1.40 (1H, m), 1.21−1.15 (1H, m), 1.04 (3H, d, J = 6.15, CH_3CH), 0.96−1.02 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.9, 124.8, 59.3, 52.1, 33.7, 32.1, 24.6, 22.9, 17.7. GC-HRMS (m/z): calcd for $C_9H_{17}N$ ($[M-H]^+$), 139.13609; found, 139.13737.

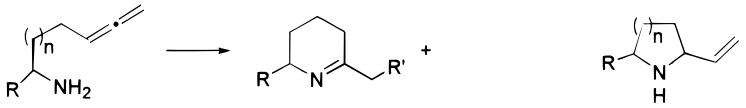
(2*S*,5*S*)-*trans*-2-Butyl-5-[(*Z*)-pent-1-enyl]pyrrolidine (17). In the glovebox, $Cp'_2SmCH(TMS)_2$ (15 mg, 25.8 μmol) was loaded into a storage tube equipped with a magnetic stirring bar and a J. Young Teflon valve. At −78 °C, pentane (1.5 mL) was vacuum-transferred onto the catalyst and **11** (264.5 mg, 1.35 mmol) was syringed in. The clear yellow solution was then stirred for 1 h at ambient temperature. The reaction mixture was next loaded onto a short column of silica gel and eluted with ether, yielding the title compound as a 95:5 mixture of *Z*/*E* isomers. ^{1}H NMR (300 MHz, $CDCl_3$; *Z* isomer): δ 5.36 (2H, m, ═CH), 4.01 (1H, m, ═CHC*H*NH), 3.18 (1H, m, CH_2CHNH), 2.52 (1H, br s, NH), 2.06−1.92 (4H, m, $2CH_2$), 1.48−1.23 (10H, m, $5CH_2$), 0.87 (6H, t, J = 7.2 Hz, $2CH_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.1, 130.5, 58.2 (2C), 36.5, 33.2, 32.5 (2C), 29.5, 22.9, 22.8, 14.1, 13.8. HRMS (m/z): $[M]^+$ calcd for $C_{13}H_{25}N$, 195.1987; found, 195.1983.

(2*S*,5*S*)-2-(3-Butenyl)-5-(hept-1-enyl)pyrrolidine (18). In the glovebox, $Cp'_2LaCH(TMS)_2$ (4.6 mg, 8.1 μmol) and C_6D_6 (~700 μL) were loaded into an NMR tube equipped with a Teflon valve. On the high-vacuum line, the tube was evacuated after freezing the precatalyst solution. Under a stream of Ar gas **12** (20 mg, 90.4 μmol) was then syringed in. The tube was sealed, and the frozen reaction mixture was warmed to room temperature. After the tube was shaken until a clear colorless solution was formed, the progress of the ensuing reaction was monitored by ^{1}H NMR spectroscopy. Upon reaction completion (<15 min), the reaction mixture was next loaded onto a short column of silica gel and eluted with ether, affording **18** (17 mg, 85%) as a ~2.5:1 mixture of *Z*/*E* isomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.87−5.73 (1H, m, ═CH), 5.54−5.32 (2H, m, ═CH), 5.02−4.89 (2H, m, $=CH_2$), 3.97 and 3.59 (1H, m, ═CHC*H*NH), 3.16 (1H, m, CH_2CHNH), 2.10−1.90 (m, 6H), 1.66 (1H, br s, NH) 1.52−1.21 (10H, m, $5CH_2$), 0.85 (3H, t, J = 6.8 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.7, 133.1, 130.7, 114.4, 59.9, 57.4, 36.5, 33.1, 32.3, 32.2, 31.6, 31.4, 29.0, 22.5, 14.1 and 138.7, 133.5, 130.4, 114.4, 57.5, 54.1, 36.3, 33.4, 32.5, 31.4, 30.3, 29.5, 27.4, 14.1. HRMS (m/z): $[M]^+$ calcd for $C_{15}H_{27}N$, 221.21436; found, 221.21376.

(34) Fugami, K.; Miura, K.; Morizawa, Y.; Oshima, K.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1989**, *45*, 3089−3098.

(35) (a) Todd, F. G.; Stermitz, F. R.; Blokhin, A. V. *Phytochemistry* **1995**, *46*, 401−406. (b) Schneider, M. J.; Montali, J. A.; Hazen, D.; Stanton, C. E. *J. Nat. Prod.* **1991**, *54*, 905−909. (c) Gessner, W.; Takahashi, K.; Brossi, A.; Kowalski, M.; Kaliner, M. A. *Helv. Chim. Acta* **1987**, *70*, 2003−2010. (d) Tawara, J. N.; Blokhin, A.; Foveraro, T. A.; Stermitz, F. R.; Hope, H. *J. Org. Chem.* **1975**, *40*, 2151−2153.

Table 1. Results for the Catalytic Intramolecular Hydroamination/Cyclization of Monosubstituted Aminoallenes[a]



aminoallene	combined yield (%)[b]	tetrahydropyridine	2-vinylpyrrolidine	**4**:**5**[c]
1 (R = H, *n* = 1)	91	**4a** (R = R′ = H)	**5a** (R = H, *n* = 1)	90:10
2 (R = CH_3, *n* = 1)	95	**4b** (R = CH_3, R′ = H)	**5b** (R = CH_3, *n* = 1)	87:13
3 (R = H, *n* = 2)	95	**6** (R = H, R′ = CH_3)		**6** only

[a] All reaction were carried out using Cp′. [b] Isolated yields. [c] Determined by ^{1}H NMR spectroscopy and GC-MS.

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 VXR-300 or Unity-400 spectrometer which had been previously set to the appropriate temperature ($T \pm 0.2$ °C; checked with a methanol or ethylene glycol temperature standard). Data were acquired using two scans per time interval with a long pulse delay (10 s) to avoid signal saturation. The kinetics were usually monitored from intensity changes in the substrate allenic resonances over 3 or more half-lives. The substrate concentration, *C*, was measured from the allenic peak area, A_s, standardized to the area A_I of the free $CH_2(TMS)_2$ formed as turnover commenced (Scheme 1). All data collected could be convincingly fit ($R = 0.986-0.998$) by least-squares to eq 1, where C_0 is the initial concentration of substrate ($C_0 = A_s(0)/A_I(0)$). The ratio of catalyst to substrate (*E*) was then accurately determined from the ratio of $A_s(0)$ and $A_I(0)$. The turnover frequency (h^{-1}) was calculated from the least-squares-determined *x* intercept ($t = -C_0/m$, min) according to eq 2.

$$C = mt + C_0 \quad (1)$$

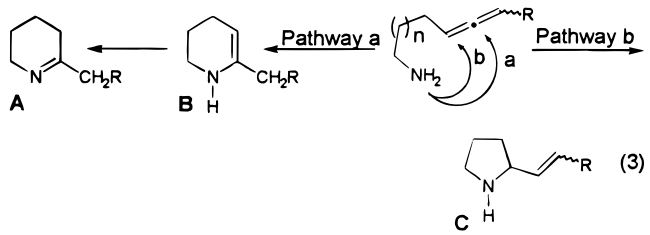
$$N_t\ (h^{-1}) = (60\ \text{min}\ h^{-1}/-t)E \quad (2)$$

Results

The goal of this study was to further explore the scope and selectivity of the organolanthanide-catalyzed intramolecular hydroamination/cyclization (IHC) reaction. We previously communicated[21] that aminoallenes are excellent substrates for constructing heterocyclic frameworks via IHC, overcoming some of the limitations previously identified in aminoalkene and aminoalkyne hydroamination/cyclization reactions.[8,9] This section begins by discussing alternative routes into the catalytic manifold of the present system, followed by examination of the reaction scope in terms of product ring size, as well as regio- and stereoselectivity. Variations in reaction turnover frequency as a function of metal ion size and ancillary ligation are then examined. Finally, the kinetics and the rate law for this reaction are discussed.

Catalyst Generation. Routes into the catalytic cycle (Scheme 2) have been developed from Cp'_2LnR (R = H, $CH(TMS)_2$, $N(TMS)_2$; Ln = La, Nd, Sm, Y, Lu) complexes. For these precatalysts, rapid and quantitative substrate N−H protonolysis of the Ln−H, Ln−C, or Ln−N σ bonds occurs, producing H_2, $CH_2(TMS)_2$, or $NH(TMS)_2$ respectively, together with the catalytically active organolanthanide amido species (presumably a $Cp'_2Ln(HNR)(H_2NR)_x$ amine−amido complex).[8c] The mechanism likely involves amine coordination followed by well-documented, rapid four-centered protonolysis,[8c,36] forming the active catalytic species (Schemes 1 and 2). Furthermore, readily prepared divalent $Cp'_2Sm(THF)_2$[24] also serves as a precatalyst for the IHC of aminoallenes. For example, anaerobic reaction of **7** with $Cp'_2Sm(THF)_2$ affords pyrrolidine **13** (Table 2). In situ ^{1}H NMR spectroscopy reveals the decrease of paramagnetic, broad divalent $Cp'_2Sm(base)_n$ resonances and the appearance and growth of new (also paramagnetic), sharper resonances corresponding to a trivalent organosamarium species. Changes in reaction mixture color (purple → orange-red) are also in agreement with previous assignments of a Sm(II) → Sm(III) oxidative-addition process.[37] The $Cp'_2Sm(THF)_2$ precatalyst has the advantage of being more convenient and economical to synthesize than the trivalent hydride, $CH(TMS)_2$, or $N(TMS)_2$ complexes.

Scope of Aminoallene Hydroamination/Cyclization. The catalytic IHC of aminoallenes can, in principle, generate two different regioisomeric products (**A, C**; eq 3). Both pathways are favorable according to the



(3)

Baldwin ring closure rules.[38] The anaerobic, anhydrous reaction of $Cp'_2LnCH(TMS)_2$ ($Cp' = \eta^5$-Me_5C_5; Ln = La, Sm, Y, Lu; TMS = Me_3Si) precatalysts with dry, degassed *monosubstituted* aminoallenes[39] **1** and **2** (20−100-fold stoichiometric excess) in hydrocarbon solvents affords mixtures of regioisomers **4** and **5**, regardless of precatalyst and/or reaction conditions. The homologous substrate **3** gives exclusively 2-ethyl-3,4,5,6-tetrahydropyridine (**6**) (Table 1). In marked contrast, the reaction of *1,3-disubstituted* aminoallenes proceeds exclusively through exocyclic pathway b (eq 3). For example, **7** affords 2-(prop-1-enyl)pyrrolidine (**13**), whereas **8** undergoes cyclization to yield 2-(prop-1-enyl)piperidine

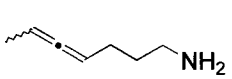
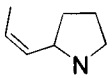
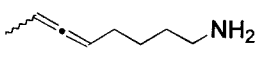
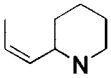
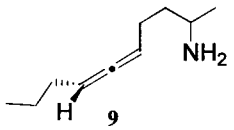
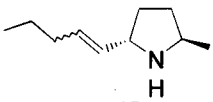
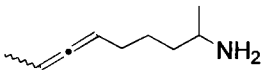
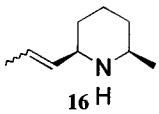
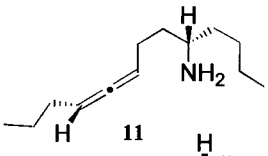
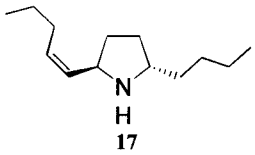
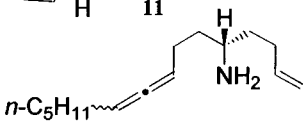
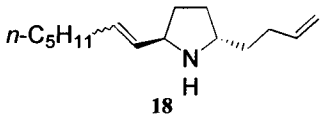
(36) (a) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74−84. (b) Thompson, M. E.; Baxter, S. M.; Bulls, A. R.; Burger, B. J.; Nolan, M. C.; Santarsiero, B. D.; Schaefer, W. P.; Bercaw, J. E. *J. Am. Chem. Soc.* **1987**, *109*, 203-219.

(37) Gagné, M. R.; Nolan, S P.; Marks, T. J. *Organometallics* **1990**, *9*, 1716−1718.

(38) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; pp 212−214.

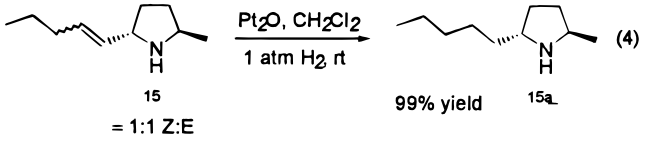
(39) In this paper we will also refer to them as *terminal* aminoallenes.

Table 2. Organolanthanide-Catalyzed Intramolecular Hydroamination/Cyclization of 1,3-Disubstituted Aminoallenes

Entry	Substrate	Product	Conversion (%)[c] (Yield) (%)[b]	Product Ratio (Z/E)[c]	N_t, h^{-1} (°C)
1	 **7**	 **13**	>95, (93)[b]	86:14[d] 88:12[f]	31.4 (23)[d]
2	 **8**	 **14**	>95, (95)[b]	80:20[f] 95:5[d]	0.15 (60)[e]
3	 **9**	 **15**	>95	67:33[e] 58:42[f] 55:45[g]	>630 (23)[e]
4	 **10**	 **16**	>95	55:45[f]	0.23 (23)[e]
5	 **11**	 **17**	>95, (91)[b]	95:5[e]	>1000 (23)[e]
6	 **12**	 **18**	>95, (85)[b]	72:28[g]	Not Determined

[a] All rates measured in benzene-d_6. [b] Isolated yields. [c] Determined by ^{1}H NMR spectroscopy and GC-MS. [d] $Cp'_2YCH(SiMe_3)_2$ as precatalyst. [e] $Cp'_2SmCH(SiMe_3)_2$ as precatalyst. [f] $Cp'_2LuCH(SiMe_3)_2$ as precatalyst. [g] $Cp'_2LaCH(SiMe_3)_2$ as precatalyst.

(**14**), in excellent combined yield and good *Z* selectivity (Table 2, entries 1 and 2). Thus, the present process is effective for the catalytic formation of five- and six-membered heterocycles. As observed for aminoalkene and aminoalkyne cyclizations, the ring-size dependence of cyclization rates (N_t) for aminoallenes is 5 > 6, consistent with classical, stereoelectronically controlled cyclizations.[40] Aminoallene **9** exclusively generates *trans*-2-methyl-5-(pent-1-enyl)pyrrolidine (**15**), as a mixture of *Z* and *E* stereoisomers in high combined yield (entry 3). Hydrogenation of **15** (PtO_2/1 atm of H_2) yields the fully saturated *trans*-2,5-disubstituted pyrrolidine **15a** as a single compound by GC-MS analysis (eq 4).



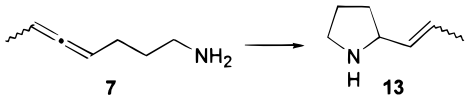
Spectroscopic characterization and NOE difference experiments on the fully saturated pyrrolidine **15a** establish the relative substituent stereochemistry. In contrast, cyclization of substrate **10** affords *cis*-2-methyl-6-(prop-1-enyl)piperidine (**16**), in excellent yield as a 1/1 Z/E stereoisomer mixture (entry 4).

In the course of our recent syntheses of naturally occurring alkaloids via organolanthanide-catalyzed IHC, enantiomerically enriched aminoallenes **11** and **12** (Table 2) were prepared. Substrate **11** undergoes rapid cyclization ($N_t \geq 1000$ h^{-1}, $Cp'_2SmCH(TMS)_2$) at room temperature to furnish **17** in excellent yield and *Z* selectivity (entry 5), and aminoallene−alkene substrate **12** readily reacts with $Cp'_2LnCH(TMS)_2$ (Ln = La, Sm, Y) and $Me_2SiCp''_2NdCH(TMS)_2$ to exclusively yield *trans*-2,5-disubstituted pyrrolidine **18** as a *Z*/*E* alkene stereoisomeric mixture (entry 6). The latter result shows that the Ln−N bond preferentially adds to the allene rather than to the alkene moiety when both functional groups are positioned at essentially equal distances from the amino group within the same molecule (three CH_2 units away). It is clear from this study that aminoallenes containing the amino group at a secondary carbon (entries 3 and 4) undergo cyclization far more rapidly with the same catalyst than those substrates bearing the amino group at a primary carbon (entries 3 vs 1 and 4 vs 2). With regard to turnover frequencies, the Cp'_2LnR-mediated hydroamination/cyclization of aminoallenes is significantly more rapid than for the corresponding aminoalkenes[8c] and slower (~5−20×) than for the corresponding aminoalkynes.[9b]

As in the case of the organolanthanide-catalyzed IHC of aminoalkenes and aminoalkynes, $4f^n$ ($n \neq 0$ or 14) precatalysts such as $Cp'_2SmCH(TMS)_2$ and $Me_2SiCp''_2NdCH(TMS)_2$ react with aminoallenes, giving rise to

(40) (a) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*, 2nd ed.; Plenum: New York, 1984; Part A, Chapter 3.9. (b) De Tar, D. F.; Luthra, N. P. *J. Am. Chem. Soc.* **1980**, *102*, 4505−4512. (c) Mandolini, L. *J. Am. Chem. Soc.* **1978**, *100*, 550−554.

Table 3. Metal Ion Size Effects on Turnover Frequencies for the Hydroamination/Cyclization of 7



7 13

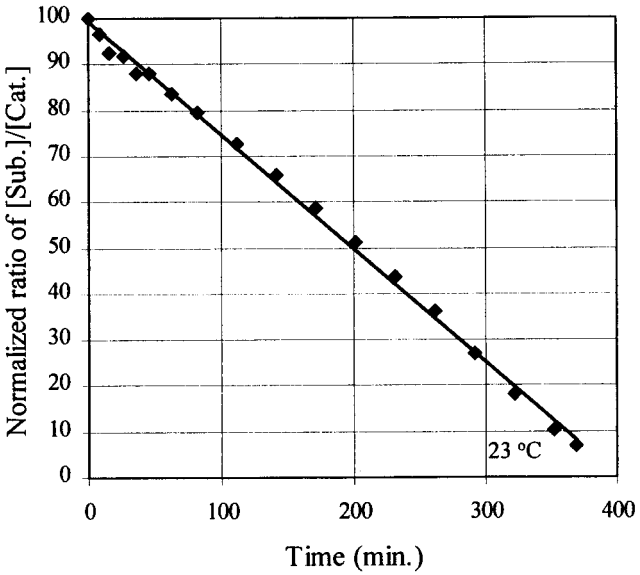
catalyst	ionic radius,[a] Å	N_t,[b] h^{-1} (23 °C)
Cp'_2La-	1.106	4
Cp'_2Sm-	1.079	13
Cp'_2Y-	1.019	31
Cp'_2Lu-	0.977	7

[a] Eight-coordinate ionic radii from ref 41. [b] All rates measured in benzene-d_6.

distinctive color changes associated with catalytic initiation and termination. Thus, the original green and orange solutions (C_6D_6 or C_7D_8) of the paramagnetic Nd^{3+} ($4f^3$) and Sm^{3+} ($4f^5$) alkyl precatalysts, respectively, immediately turn to the characteristic blue and yellow colors, respectively, of the corresponding amine−amide complexes upon substrate addition.[8c] The resulting reaction solutions revert to the original colors upon aminoallene substrate consumption. Product isolation generally involves vacuum transfer of volatiles from the catalyst, acidic−aqueous workup followed by ether extraction, or flash chromatography through a short column of silica gel. In general, the products are isolated in high yield and are >95% pure by GC-MS. Reactions are conveniently monitored by ^{1}H NMR spectroscopy, and the proton spectra of completed experiments only show resonances attributable to cyclized product. All reactions proceed well in pentane, toluene, benzene, and other hydrocarbon solvents.

Metal and Ancillary Ligation Effects on the Catalytic Process. It was previously reported that both increasing the Ln^{3+} ionic radius[41] and opening the metal coordination sphere by connecting the ancillary ligands ($Cp'_2Ln \rightarrow Me_2SiCp''_2Ln$) increase the turnover frequencies (N_t) for the IHC of aminoalkenes.[8c] Interestingly, the opposite effect is observed for the IHC of aminoalkynes; i.e., turnover frequencies decrease upon making identical changes in Ln^{3+} ionic radius or ancillary ligation.[9b] In contrast to the above trends, the present kinetic results for the Cp'_2Ln-catalyzed transformation **7** → **13** exhibit *maximum* N_t values at Y^{3+} (1.019 Å), on proceeding from the largest eight-coordinate lanthanide ionic radius, La^{3+} (1.160 Å), to the smallest, Lu^{3+} (0.977 Å) (see Table 3). In addition, replacement of Cp'_2Y with the more open Me_2SiCp''-(^{t}BuN)Y precatalyst[10b] depresses N_t from 31.4 to <0.1 h^{-1} for the transformation **7** → **13**. Thus, it appears that the reactivity of 1,3-disubstituted aminoallene substrates falls between those of the aminoalkene and aminoalkyne counterparts, presumably reflecting an interplay of substrate−ancillary ligand and substrate−substrate steric repulsions as well as reactant-like versus product-like characters of the cyclization transition state.[8c,9b]

Kinetic Studies of Aminoallene Hydroamination/Cyclization. The kinetic data obtained in this study were acquired using the diamagnetic precatalyst $Cp'_2LuCH(TMS)_2$, which allows convenient ^{1}H NMR monitoring of reactions. Thus, the IHC reaction of a 40−70-fold molar excess of 4,5-heptadien-1-ylamine (**7**) was monitored at constant catalyst concentration until complete substrate consumption. The decrease of the allene proton resonances (δ ~5.0 ppm) was normalized to the proton resonances of the stoichiometrically generated $CH_2(TMS)_2$ reaction byproduct (δ ~0.2 ppm). Figure 1A presents kinetic data for this reaction (typical of many runs), which shows the reaction rate to be zero-order in substrate concentration over at least 3 half-lives and over at least a 100-fold range, in analogy to the IHC of aminoalkenes and aminoalkynes.[8c,9b] This result argues that the turnover-limiting step involves intramolecular allene insertion into the Ln−N bond (Scheme 2, step i), followed by rapid protonolysis of the resulting C−N bond (step ii). A plot of reaction rate vs precatalyst concentration (Figure 1B) indicates the reaction to be first-order in [Ln] when the initial



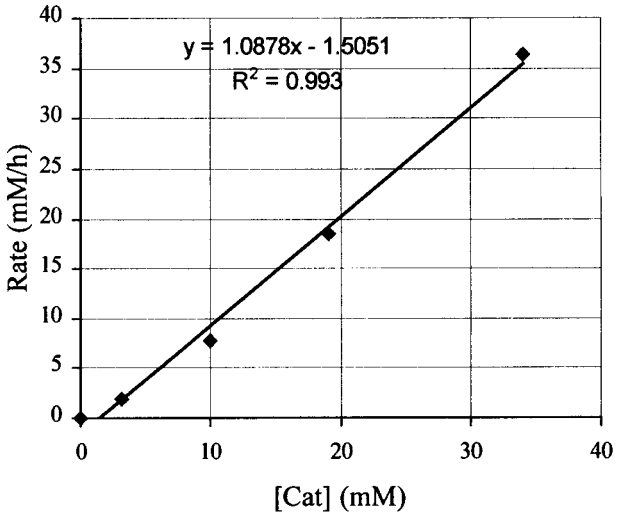


Figure 1. (A, top) Normalized ratio of substrate to lanthanide concentration as a function of time for the IHC of 4,5-heptadien-1-ylamine (**7**) using the precatalyst $Cp'_2LuCH(TMS)_2$ in benzene-d_6 at 23 °C. (B, bottom) Determination of reaction order in lanthanide concentration for the IHC of 6,7-nonadien-2-ylamine (**10**) mediated by $Cp'_2YCH(TMS)_2$ in benzene-d_6 at 25 °C. The lines represent the least-squares fits to the data points.

(41) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751−760.

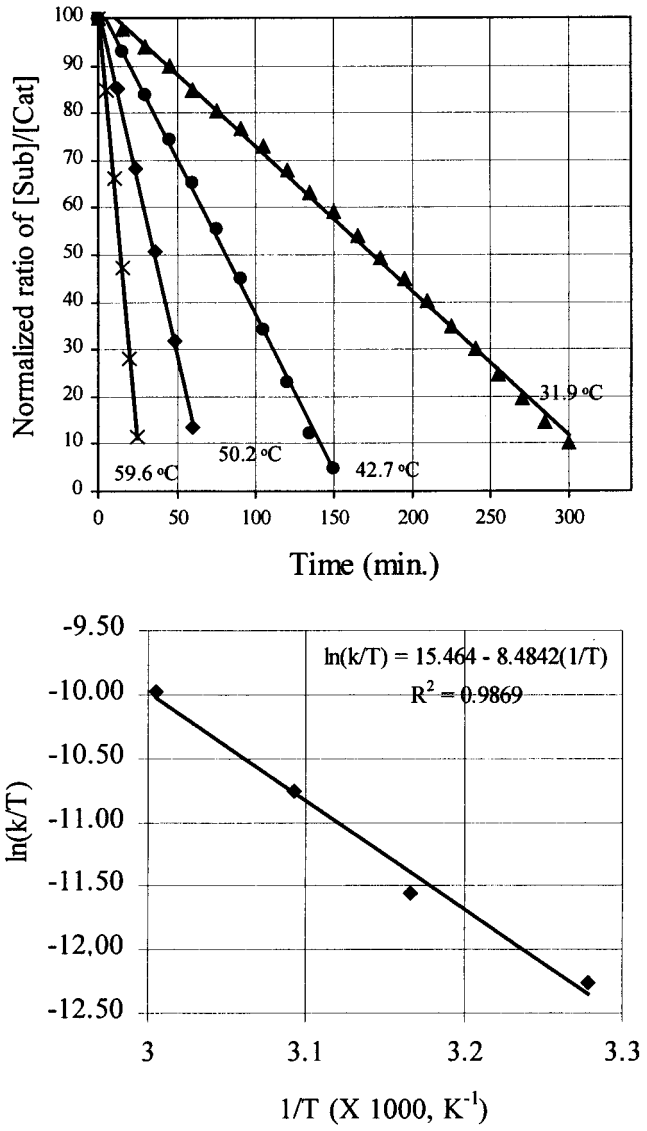


Figure 2. (A, top) Normalized ratio of substrate to lanthanide concentration as a function of time and temperature for the hydroamination/cyclization of 4,5-heptadien-1-ylamine (**7**) using the precatalyst $Cp'_2LuCH(TMS)_2$ in toluene-d_8. (B, bottom) Eyring plot for the hydroamination/cyclization of 4,5-heptadien-1-ylamine (**7**) using the precatalyst $Cp'_2LuCH(TMS)_2$ in toluene-d_8. The lines are least-squares fits to the data points.

substrate concentration is held constant and the precatalyst concentration is varied over a 10-fold range. Therefore, the empirical rate law can be expressed as in eq 5 and is identical with that for organolanthanide-catalyzed aminoalkene[8c] and aminoalkyne[9b] IHC.

$$v = k[\text{substrate}]^0[\text{Ln}]^1 \qquad (5)$$

Kinetic studies of the **7** → **13** transformation catalyzed by $Cp'_2LuCH(TMS)_2$ reveal the reaction rate to be independent of substrate concentration (zero-order) over a 30 °C temperature range (30−60 °C; Figure 2A). The activation parameters derived from standard Eyring and Arrhenius kinetic analyses (Figure 2B) are $\Delta H^{\neq}$ = 16.9(1.3) kcal/mol, $\Delta S^{\neq}$ = −16.48(4.3) eu, and $E_a^{\neq}$ = 17.6(1.4) kcal/mol.

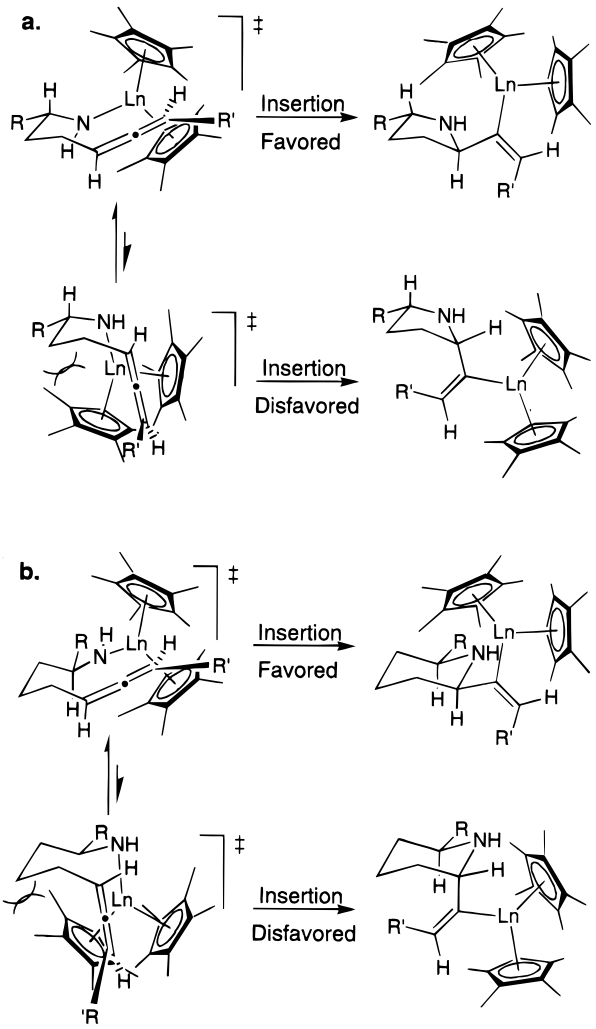
Discussion

The results presented in Tables 1 and 2 illustrate that $Cp'_2LnCH(TMS)_2$ complexes are effective precatalysts for the efficient catalytic formation of five- and six-membered heterocycles derived from both terminal and internal aminoallene substrates. Noteworthy is the facile, regioselective, and diastereoselective IHC of internal aminoallenes to yield pyrrolidines and piperidines bearing unsaturated α-substituents. Furthermore, the more conveniently synthesized $Cp'_2Sm(THF)_2$ complex also serves as an efficient precatalyst for this transformation. The present work therefore represents an important step forward in making the organolanthanide-catalyzed hydroamination/cyclization reaction a general method for the catalytic synthesis of nitrogen-containing heterocyles. It extends the scope of known hydroamination/cyclization processes, namely the IHC of aminoalkenes and aminoalkynes, and opens a window for applications to alkaloid synthesis, the details of which are presented elsewhere.[31] In the following paragraphs, we discuss the factors influencing the course and rate of this hydroamination/cyclization reaction.

Regioselectivity and Diastereoselectivity in Aminoallene IHC. A priori, two regioisomeric cyclic products are possible in the IHC of aminoallenes (eq 3). For the terminal aminoallene substrate **1** (entry 1, Table 1), these regioisomeric products are 5-exo (2-vinylpyrrolidine) and 6-endo (2-methyltetrahydropyridine). The formation of both isomers is favorable according to the Baldwin ring closure rules, and such product structures have been reported in Pd- and Pt-mediated hydroamination/cyclization processes.[42] In the present study, terminal aminoallene substrates **1** and **2** undergo hydroamination/cyclization to yield mixtures of regioisomers **4** and **5** with nitrogen addition occurring predominantly via endocyclic pathway a (eq 3) (entries 1 and 2, Table 1), whereas substrate **3** gives exclusively 2-ethyl-3,4,5,6-tetrahydropyridine (**6**) (entry 3, Table 1). Our previous work on the IHC of aminoalkenes[8] and aminoalkynes[9] showed the reaction to be highly regioselective, and mechanistic studies revealed the turnover-limiting insertion of the unsaturated moieties to be highly sensitive to steric factors. This led us to the hypothesis that more encumbered internal aminoallene substrates might undergo exo-regioselective cyclization, and indeed, the reaction of 1,3-disubstituted aminoallenes proceeds exclusively via exocyclic pathway b (eq 3), as is evident in Table 2. This transformation is also highly diastereoselective. Cyclization of **9**, **11**, and **12** furnishes only *trans*-2,5-disubstituted pyrrolidines **15**, **17**, and **18**, respectively (entries 3, 5, and 6; Table 2). On the other hand, aminoallene substrate **10** affords only *cis*-2-methyl-6-(prop-1-enyl)pieperidine (**16**). These results can be understood on the basis of steric/conformational effects in proposed transition-state structures for allene insertion (Scheme 3). Nonbonding interactions arising from congestion in the metal coordination sphere (alkyl substituents, binding of additional substrate

(42) Pd- and Pt-catalyzed aminoalkene cyclizations give mixtures of endo and exo heterocycles: (a) Reference 5e. (b) Pugin, B.; Venanzi, L. M. *J. Organomet. Chem.* **1981**, *214*, 125−133. For Pd-catalyzed endo and exo cyclization of aminoalkynes, see: Fukuda, Y.; Matsubara, S.; Utimoto, K. *J. Org. Chem.* **1991**, *56*, 5812−5816.

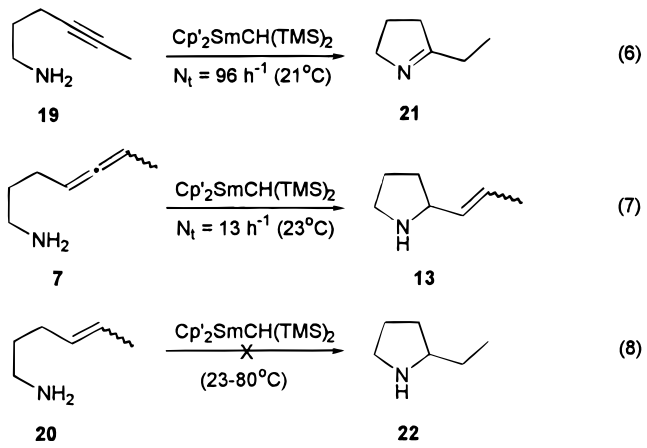
Scheme 3. Stereochemical Pathways for Organolanthanide-Catalyzed Intramolecular Hydroamination/Cyclization of Aminoallenes To Afford (a) *trans*-Pyrrolidines and (b) *cis*-Piperidines



molecules)[8c] determine the stereochemical outcome. The depicted stereochemical pathways account well for the observed diastereoselectivity.

Kinetics and Mechanism of Aminoallene IHC. All in situ NMR-scale reactions of $Cp'_2LnCH(TMS)_2$ with aminoallene substrates instantaneously generate $CH_2(TMS)_2$ by protonolysis of the Ln−C bond, and the concentration of this byproduct remains constant throughout the course of the catalytic reaction (internal standard). Variation of the Ln^{3+} ionic radius significantly affects the reaction rate for transformation **7** → **13** (Table 3). This reaction rate dependence on metal ion size has been previously observed in other organolanthanide-mediated hydroamination processes.[8,9] For example, turnover frequencies for the IHC of aminoalkene $H_2C{=}CHCH_2C(CH_3)_2CH_2NH_2$ are metal ion size dependent with $N_t = 95\ s^{-1}$ (25 °C) for $Ln^{3+} = La^{3+}$ and $N_t < 1\ s^{-1}$ (80 °C) for $Ln^{3+} = Lu^{3+}$.[8c] The catalytic activities for the IHC of aminoalkyne $HC{\equiv}CCH_2CH_2CH_2NH_2$ also depend on the metal ion size with $N_t = 135\ s^{-1}$ (21 °C) for $Ln^{3+} = La^{3+}$ and $N_t = 711\ s^{-1}$ (21 °C) for $Ln^{3+} = Lu^{3+}$, following the general order $Lu^{3+} > Sm^{3+} > Nd^{3+} > La^{3+}$ (opposite to the IHC of aminoalkenes).[9a] The aforementioned transformations cycle through turnover-limiting alkene and alkyne insertion steps, respectively. In contrast, the reaction rates for **7** → **13** exhibit a maximum N_t value at Y^{3+} (1.019 Å), on proceeding from the largest eight-coordinate Ln^{3+} ionic radius, La^{3+} (1.160 Å), to the smallest, Lu^{3+} (0.977 Å), at constant catalyst concentration and 23 °C.

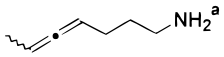
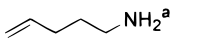
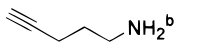
Aminoallene hydroamination/cyclization reactions are significantly more rapid than those of the corresponding aminoalkenes but are slower than those of the corresponding aminoalkynes. For example, comparison of cyclization rates for 4,5-heptadien-l-ylamine (**7**) versus 4-hexen-l-ylamine (**20**) and 4-hexyn-l-ylamine (**19**),[9b,10a] under identical reaction conditions, reveals that aminoallenes exhibit reactivity intermediate between that of the aminoalkene and aminoalkyne counterparts (eqs 6−8). The distinctive insertive reactivity of C=C and



C=C=C multiple bonds is obvious from the IHC of substrate **12** to yield only **18** (entry 6, Table 2). This intramolecular insertive competition between the allene and alkene tethers clearly indicates that the allene moiety is substantially more reactive than the alkene counterpart. It is possible to explain this outcome on the basis of a sterically more accessible C=C=C π-system and a greater enthalpic driving force. Skeletal alkyl substitutions also dramatically affect reaction rates. Thus, the cyclization rates for **9** → **15** and **11** → **17** are respectively at least 20 and 30 times more rapid than for **7** → **13**, while methyl substitution of **8** increases the cyclization rate for **10** → **16**.

The kinetic results for the transformation **7** → **13** catalyzed by $Cp'_2LuCH(TMS)_2$ indicate zero-order dependence in substrate concentration inagreement with previous findings on aminoalkene and aminoalkyne IHC.[8,9] The proposed turnover-limiting insertion transition state exhibits activation parameters that are typical of organized, polar transition states of d^0- and f^n-centered transformations. The activation parameters for the reaction of **7** → **13** can be compared to the values obtained from the IHC of aminoalkenes and aminoalkynes (Table 4). The aminoallene hydroamination/cyclization displays a substantially higher enthalpic barrier, suggesting a concerted transition state with modest bond formation. However, the smaller magnitude of $\Delta S^{\neq}$ (less negative) suggests that the transition state is perhaps somewhat less highly organized than for aminoalkenes and aminoslkynes.[43] Kinetic and mechanistic studies of aminoalkene and aminoalkyne

Table 4. Activation Parameter Comparison for the Intramolecular Hydroamination/Cyclization Reaction

Substrate	$\Delta H^{\ddagger}$, Kcal/mol	$\Delta S^{\ddagger}$, eu
	16.9 (1.3)	-16.5 (4)
	12.7 (1.4)	-27.0 (5)
	10.7 (8)	-27.4 (6)

[a] Determined using $Cp'_2LaCH(TMS)_2$ in toluene-d_8. [b] Determined using $Cp'_2SmCH(TMS)_2$ in toluene-d_8.

IHC strongly argue that alkene and alkyne insertion into the Ln−N bond is the turnover-limiting step in the catalytic cycle, followed by rapid Ln−C bond protonolysis which releases the azacycle and regenerates the catalytically-active amide species. The present results obtained from the kinetic studies and from factors affecting cyclization rates (metal ion size, ring size, and substrate architecture) basically support an analogous mechanistic scenario. Thus, the precatalyst $Cp'_2LnCH(TMS)_2$ immediately undergoes reaction with aminoallene substrates in hydrocarbon solvents to quantitatively form $CH_2(TMS)_2$ and the putative amine−amido species $Cp'_2LnNH(CH_2)_nC{=}C{=}CHR[H_2N(CH_2)_nC{=}C{=}CHR]_x$ (R = alkyl). NMR spectroscopy reveals that this species undergoes rapid bound amine−amide exchange and/or bound-free amine substrate exchange.[8c] Therefore, a simplified reasonable nechanistic picture for the present catalytic system is put forward in Scheme 2.

Conclusions

The results presented in this account demonstrate that the insertion of allenes into Ln−N bonds in bis(cyclopentadienyl)lanthanide environments can be coupled with rapid Ln−C protonolysis to effect catalytic C−N bond formation. Lanthanocenes are therefore versatile precatalysts for the efficient, regioselective, and diastereoselective construction of pyrrolidines and piperidines bearing unsaturated α-substituents. The turnover frequencies for this catalytic process are highly dependent on the size of the metal ion, temperature, and substrate architecture. A mechanism very similar to the IHC of aminoalkenes and aminoalkynes is operative in the present catalytic system.

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Supporting Information Available: Text giving detailed synthetic procedures and analytical data for some intermediate compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OM981037J

(43) (a) Similar $\Delta S^{\neq}$ values (−10 to −24 eu) are observed for Cp'_2ThR_2-centered cyclometalation reactions which are believed to proceed via analogous four-center cyclic transition states. (b) Smith, G. M.; Carpenter, J. D.; Marks, T. J. *J. Am. Chem. Soc.* **1986**, *108*, 6805−6807. (c) Bruno, J. W.; Smith, G. M.; Marks, T. J.; Fair, C. K.; Schultz, A. J.; Williams, J. M. *J. Am. Chem. Soc.* **1986**, *108*, 40−56.