Organolanthanide-Catalyzed Intramolecular Hydroamination/Cyclization of Aminoalkynes

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Abstract: This contribution reports the efficient and regiospecific $Cp'_2LnCH(SiMe_3)_2$ (Ln = La, Nd, Sm, Lu; Cp′ = η^5-Me_5C_5)- and $Me_2SiCp''_2LnCH(SiMe_3)_2$ (Ln = Nd, Sm; Cp″ = η^5-Me_4C_5)-catalyzed hydroamination/cyclization of aliphatic and aromatic aminoalkynes of the formula $RC{\equiv}C(CH_2)_nNH_2$ to yield the corresponding cyclic imines $RCH_2C{=}N(CH_2)_{n-1}CH_2$, where R, *n*, N_t h^{-1} (°C) = Ph, 3, 77 (21 °C); Ph, 3, 2830 (60 °C); Me, 3, 96 (21 °C); $CH_2{=}CMeCH_2$, 3, 20 (21 °C); H, 3, 580 (21 °C); Ph, 4, 4 (21 °C); Ph, 4, 328 (60 °C); Ph, 5, 0.11 (60 °C); and $SiMe_3$, 3, >7600 (21 °C), and of aliphatic secondary amino-alkynes of the formula $RC{\equiv}C(CH_2)_3NHR_1$ to generate the corresponding cyclic enamines $RCH{=}CNR_1(CH_2)_2CH_2$ where R, R_1, N_t h^{-1} (°C) = $SiMe_3$, $CH_2{=}CHCH_2$, 56 (21 °C); H, $CH_2{=}CHCH_2$, 27 (21 °C); $SiMe_3$, $CH_2{=}CH(CH_2)_3$, 129 (21 °C); and H, $CH_2{=}CH(CH_2)_3$, 47 (21 °C). Kinetic and mechanistic evidence is presented arguing that the turnover-limiting step is an intramolecular alkyne insertion into the Ln−N bond followed by rapid protonolysis of the resulting Ln−C bond. The use of larger metal ionic radius $Cp'_2LnCH(SiMe_3)_2$ and more open $Me_2SiCp''_2LnCH(SiMe_3)_2$ complexes as the precatalysts results in a *decrease* in the rate of hydroamination/cyclization, arguing that the steric demands in the −C≡C− insertive transition state are relaxed compared to those of the analogous aminoolefin hydroamination/cyclization.

Introduction

Carbon−nitrogen bond-forming processes are of fundamental importance in organic chemistry, and olefin or alkyne hydroamination by catalytic N−H bond addition to unsaturated carbon−carbon multiple bonds represents both a challenging and highly desirable transformation.[1,2] In many cases, such reactions only proceed with alkali metals in liquid ammonia at high temperatures and pressures, affording modest yields and selectivities,[1b,d,3] or in transition metal-mediated systems with generally short catalyst lifetimes, low turnover frequencies, and/or limited reaction scope (via metal activation of either the amine or the carbon−carbon multiple bond).[4,5] In comparison to typical middle and late transition metal complexes, organolanthanides exhibit distinctive reactivity characteristics for unsaturated organic substrate activation and heteroatom transformations.[6] These derive mainly from the high electrophilicity of f-element centers, mechanistic pathways different from conventional oxidative addition/reductive elimination sequences, relatively large ionic radii, nondissociable ancillary ligation, and high kinetic lability. The facile catalysis of aminoolefin hydroamination/cyclization by organolanthanides[7] demonstrates that the insertion of olefinic functionalities into Ln−N bonds in bis(cyclopentadienyl)lanthanide environments can be coupled

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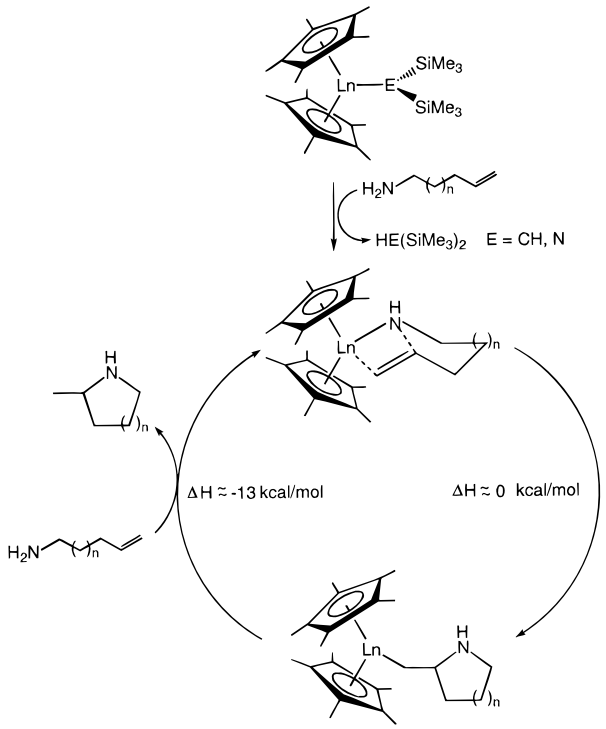
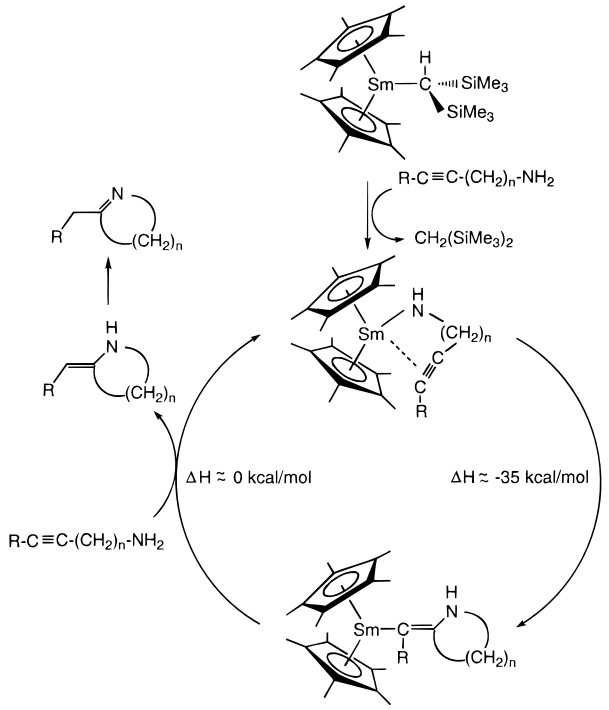
Scheme 1. Proposed Mechanism for Organolanthanide-Catalyzed Aminoolefin Hydroamination/Cyclization



with rapid Ln−C protonolysis to effect efficient and regiospecific catalytic N−C bond-forming processes (Scheme 1, Cp′ = η^5-Me_5C_5; Ln = lanthanide).

Literature precedent[8] for alkyne insertion into lanthanide metal−alkyl σ bonds and thermodynamic considerations[10−13] pose an interesting situation for aminoalkynes (Scheme 2). Alkyne insertion into Ln−N bonds (step 1) is estimated to be ∼35 kcal/mol more exothermic than for olefins,[10−13] while

Scheme 2. Simplified Catalytic Cycle for the Hydroamination/Cyclization of Aminoalkynes



amine protonolysis of the resulting Ln−C bond (step 2) is estimated to be ∼10−20 kcal/mol less exothermic (approximately thermoneutral). If the insertion of alkyne functionalities into Ln−N bonds were indeed efficient and analogous to those transformations established for aminoolefins,[7c−g,14] such aminoalkyne-based catalytic processes would offer a route to a diverse variety of heterocycles and natural product skeletons (e.g., indolizidines, quinolizidines) as well as a complement to recently reported organo group 4-centered stoichiometric[4a,d,e] and catalytic[4] alkyne hydroamination processes which proceed via an entirely different (noninsertive) mechanistic pathway.[4f]

In this contribution, we present a full discussion of our studies of efficient, regiospecific aminoalkyne hydroamination/cyclization processes within lanthanide coordination spheres, including studies of reaction scope, substrate substituent, metal, and ancillary ligand effects, as well as of kinetics and mechanism.[15]

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(9) An organoactinide-catalyzed intermolecular alkyne hydroamination process has recently been shown to occur via an actinide imido complex ($Cp'_2An{=}NR$): Haskel, A. H.; Straub, T.; Eisen, M. S., private communication.

(10) 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[13] 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[13] to be ∼14 kcal/mol more exothermic and ∼14 kcal/mol more exergonic than that to ethylene.

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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 (10^{-6} Torr) line, or in a nitrogen-filled Vacuum Atmospheres glovebox with a high-capacity recirculator (1−2 ppm of O_2). Argon (Matheson, prepurified) was purified by passage through a MnO oxygen-removal column[16] and a Davision 4A molecular sieve column. Before use, all solvents were distilled under dry nitrogen over appropriate drying agents (sodium benzophenone ketyl, metal hydrides of Na/K alloy except for chlorinated solvents). Deuterium oxide and chloroform-*d* were purchased from Cambridge Isotope Laboratories. Benzene-d_6 and toluene-d_8 (Cambridge Isotope Laboratories; all 99+ atom % D) used for NMR reactions and kinetic measurements were stored in vacuo over Na/K alloy in resealable bulbs and vacuum-transferred immediately prior to use. All organic starting materials were purchased from Aldrich Chemical Co., Farchan Laboratories Inc., or Lancaster Synthesis Inc. and, when appropriate, were distilled prior to use. The substrates 5-phenyl-4-pentyn-1-amine **(1)**,[4e] 4-hexyn-1-amine **(3)**,[17a] and 6-phenyl-5-hexyn-1-amine **(11)**[4e] were synthesized according to literature procedures. The substrates 4-octyn-7-methyl-7-en-1-amine **(5)**, 4-pentyn-1-amine **(7)**, 5-(trimethylsilyl)-4-pentyn-1-amine **(9)**, 7-phenyl-6-heptyn-1-amine **(13)**, *N*-allyl-5-(trimethylsilyl)-4-pentyn-1-amine **(15)**, *N*-allyl-4-pentyn-1-amine **(17)**, *N*-4-penten-5′-(trimethylsilyl)-4′-pentyn-1-amine **(19)**, and *N*-4-penten-4′-pentyn-1-amine **(21)** were synthesized via modifications of literature methods as described below. Substrates **1**, **3**, **5**, **9**, **11**, **13**, **15**, and **19** were dried by stirring over BaO, and substrates **7**, **17**, and **21** by stirring over CaH_2 overnight. Substrates were then repeatedly dried by vacuum transfer onto and from freshly activated Davison 4A molecular sieves and were degassed by freeze−pump−thaw methods. They were then stored in vacuum-tight storage flasks. The organolanthanide precatalysts $Cp'_2LnCH(SiMe_3)_2$ (Ln = La, Nd, Sm, Lu; $Cp' = \eta^5$-Me_5C_5)[14j] and $Me_2SiCp''_2LnCH(SiMe_3)_2$ (Ln = Nd, Sm; $Cp'' = \eta^5$-Me_4C_5)[18a] 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 XL-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). Analytical gas chromatography was performed on a Varian Model 3700 gas chromatograph with FID detectors and a Hewlett-Packard 3390A digital recorder/integrator using a 0.125 in. i.d. column with 3.8% (w/w) SE-30 liquid phase on Chromosorb W support. GC/MS studies were conducted on a VG 70-250 SE instrument with 70 eV electron impact ionization. IR spectra were recorded using a Nicolet 520 FT-IR spectrometer with MCT detector. Melting points and boiling points are uncorrected.

Synthesis of 5-Phenyl-4-pentyn-1-amine (1). (a) 5-Chloro-1-phenyl-1-pentyne (1a). A solution of 47.0 g (0.30 mol) of 3-bromo-1-chloropropane in 200 mL of THF was treated dropwise with 300 mL (0.30 mol) of lithium phenylacetylide while stirring at 0 °C for 2 h. The reaction mixture was then warmed to room temperature and refluxed for 3 h. The reaction solution was next poured into 120 mL of distilled H_2O, and the layers were separated. The aqueous phase was extracted with 3 × 25 mL of diethyl ether. The combined ether extracts and organic phase were washed with 100 mL of brine, dried over $MgSO_4$, and filtered, and the ether and THF removed from the filtrate by rotary evaporation. Distillation (96−100 °C (0.05 mmHg)) of the residue gave 47.0 g (88% yield) of colorless $ClCH_2CH_2CH_2C{\equiv}CPh$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (m, 2H, Ph), 7.32 (m, 3H, Ph), 3.74 (t, J = 6.38 Hz, 2H, CH_2Cl), 2.63 (t, J = 6.81 Hz, 2H, $CH_2C{\equiv}C$), 2.08 (m, 2H, CH_2).

(b) *N*-(5-Phenyl-4-pentynyl)phthalimide (1b). Compound **1a** and 54.0 g (0.29 mol) of potassium phthalimide were heated at 100 °C overnight in 350 mL of DMF. After cooling, the solution was poured into a mixture of $CHCl_3$ (500 mL) and H_2O (500 mL). The aqueous phase was separated and extracted with 3 × 40 mL of $CHCl_3$. The combined $CHCl_3$ solutions and the organic phase were washed with 300 mL of 0.2 N KOH (to remove unreacted phthalimide) and 300 mL of H_2O, respectively. After drying over $MgSO_4$ and filtration, the $CHCl_3$ and DMF were removed in vacuum, and the crystalline residue was triturated with 2 × 80 mL of diethyl ether. After collection by filtration, the solid residue was dried at reduced pressure to give 55.0 g (69% yield) of colorless crystalline $C_8H_4O_2N\ CH_2CH_2CH_2C{\equiv}CPh$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 2H, Ph), 7.69 (m, 2H, Ph), 7.32 (m, 2H, Ph), 7.25 (m, 3H, Ph), 3.90 (t, J = 7.00 Hz, 2H, CH_2N), 2.54 (t, J = 7.00 Hz, 2H, $CH_2C{\equiv}$), 2.06 (m, 2H, CH_2).

(c) 5-Phenyl-4-pentyn-1-amine (1). Compound **1b** and 20.0 g (0.40 mol) of hydrazine monohydrate in 450 mL of CH_3OH were refluxed for 1 h. The reaction mixture was then cooled to 0 °C and filtered. The colorless solids were washed with 3 × 10 mL of CH_3OH, and the organic phase was concentrated to an oily residue by rotary evaporation. Distillation (88−89 °C (0.05 mmHg)) afforded 7.0 g (22% yield) of $H_2NCH_2CH_2CH_2C{\equiv}CPh$ as a colorless oil. The NMR data agree with literature data:[4e] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 2H, Ph), 7.24 (m, 3H, Ph) 2.84 (t, J = 6.87 Hz, 2H, CH_2N), 2.45 (t, J = 6.89 Hz, 2H, $CH_2C{\equiv}C$), 1.71 (m, 2H, CH_2), 1.22 (br s, 2H, NH_2); ^{13}C NMR (75 MHz, ^{1}H-decoupled, $CDCl_3$) δ 131.5 (CH), 128.2 (CH), 127.6 (CH), 123.8 (C of Ph), 89.5 (C≡C) 80.9 (C≡C), 41.3 (CH_2N), 32.4 (CH_2), 16.8 (CH_2).

Synthesis of 4-Hexyn-1-amine (3). A solution of 75.0 g (0.73 mol) of 5-chloro-1-pentyne in 500 mL of THF at −78 °C was treated while stirring with *n*-BuLi (0.73 mol) for 1 h, and then CH_3I (0.73 mol) was added dropwise. The reaction mixture was then stirred while warming to room temperature. After 1 h reflux, the solution was poured into 250 mL of distilled H_2O, followed by separation. The aqueous phase was extracted twice with diethyl ether (2 × 100 mL). The combined organic phase and ether extracts were then washed with a saturated NaCl solution (100 mL), dried over $MgSO_4$, and filtered. Removal of the solvents from the filtrate by rotary evaporation gave 6-chloro-2-hexyne **(3a)**. The reaction of **3a** with sodium phthalimide (0.23 mol) in 300 mL of DMF at 60 °C overnight afforded *N*-4-hexynylphthalimide. This compound was used directly for the next step without further purification. *N*-4-Hexynylphthalamide and hydrazine monohydrate (0.18 mol) in 500 mL of EtOH were heated with stirring at 60 °C overnight. After the mixture was cooled to room temperature, followed by addition of 70 mL of concentrated HCl, the solution was heated at 60 °C for an additional 4 h. The mixture was then cooled and filtered, and the colorless precipitate washed with 2 × 100 mL of EtOH. Removal of solvent from the filtrate at reduced pressure gave a white precipitate. The white solid was then treated with a mixture of KOH (2 N, 150 mL) and diethyl ether (300 mL). After separation, the organic phase was extracted with 3 × 200 mL of diethyl ether. The ether phase was then washed with a saturated NaCl solution and dried over $MgSO_4$. After filtration and removal of solvent from the filtrate by rotary evaporation, distillation (68−69 °C (23 mmHg)) afforded 5.0 g (34% yield) of $H_2NCH_2CH_2CH_2C{\equiv}CCH_3$ **(3c)** as a colorless oil. The NMR spectra agree with published data:[17a] ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.80 (t, J = 6.87 Hz, 2H, CH_2N), 2.20 (m, 2H, $CH_2C{\equiv}C$), 1.78 (t, J = 2.51 Hz, 3H, CH_3), 1.63 (m, 2H, CH_2), 1.63 (br s, NH_2); ^{13}C NMR (75 MHz, ^{1}H-decoupled, $CDCl_3$) δ 78.5 (C≡CMe), 75.9 (≡CCH_3), 41.2 (CH_2N), 32.5 (CH_2CH_2N), 16.1 ($CH_2C{\equiv}C$), 4.13 (Me); ^{13}C NMR (100 MHz, ^{1}H-coupled, $CDCl_3$) δ 78.5 (s, C≡CMe), 75.9 (s, ≡CCH_3), 41.9 (t, J_{CH} = 135 Hz, CH_2N), 33.2 (t, J_{CH} = 128 Hz, CH_2CH_2N), 16.8 (t, J_{CH} = 131 Hz, $CH_2C{\equiv}C$),

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4.1 (q, J_{CH} = 132 Hz, CH_3); IR ($CHCl_3$) 2050, 1588 cm^{-1}; MS (rel abundance) M^+ (10), $M^+ - 1$ (55), 82.1 (100), 80.1 (43), 79.1 (30), 77.0 (17), 65.0 (100), 56.0 (15), 53.0 (25), 51.0 (14), 44.0 (11), 43.0 (34); high-resolution mass spectrum, calcd for $C_6H_{11}N$ (M^+) 97.0891, found 97.0895.

Compound **3** was dissolved in dry diethyl ether; hydrogen chloride gas was then bubbled into the solution to form a white precipitate. After filtration, the solid was washed with dry diethyl ether and recrystallized from a mixture of EtOH and ethyl acetate to give $HCl{\cdot}H_2NCH_2CH_2CH_2C{\equiv}CCH_3$: ^{1}H NMR (300 MHz, D_2O) δ 2.88 (t, J = 8.34 Hz, 2H, CH_2N), 2.06 (m, 2H, $CH_2C{\equiv}C$), 1.61 (m, 2H, CH_2), 1.54 (t, ^5J = 2.55 Hz, 3H, CH_3).

Synthesis of 4-Octyn-7-methyl-7-en-1-amine (5). A solution of 18.0 g (0.175 mol) of $ClCH_2CH_2CH_2C{\equiv}CH$ in 150 mL of pentane was treated with 0.175 mol of *n*-BuLi at 0 °C over a period of 1 h. The reaction mixture was stirred for 10 h at room temperature and then refluxed for an additional 2 h. Next, the reaction mixture was cooled to 0 °C, and 25.0 g (0.275 mol) of $ClCH_2C(Me){=}CH_2$ in 150 mL of THF was syringed into the solution over a period of 10 min. The mixture was then stirred at 0 °C for 10 h, warmed to room temperature, stirred for 2 h, and then refluxed for 8 h. The mixture was cooled to room temperature, and 300 mL of water was added to the solution. After separation of organic and aqueous phases, the aqueous phase was extracted with 3 × 100 mL of diethyl ether. The combined organic phase and ether extracts were washed with 150 mL of saturated NaCl solution and then dried over $MgSO_4$ overnight. Removal of the solvent by rotary evaporation followed by trap-to-trap distillation gave 11.2 g (41% yield) of colorless $CH_2{=}C(Me)$-$CH_2C{\equiv}CCH_2CH_2CH_2Cl$.

The reaction of 11.2 g (0.072 mol) of $CH_2{=}C(Me)CH_2C{\equiv}CCH_2$-$CH_2CH_2Cl$ with 20.0 g (0.11 mol) of sodium phthalimide in 300 mL of DMF at 60 °C overnight afforded *N*-4-octynyl-7-methyl-7-enephthalimide. This compound was used directly for the next step without further purification. *N*-4-Octynyl-7-methyl-7-enephthalimide and hydrazine monohydrate (0.202 mol) in 250 mL of EtOH were heated with stirring at 60 °C for 4 days. After the mixture was cooled to room temperature, the colorless precipitate was then filtered off. Removal of solvent from the filtrate by rotary evaporation gave a colorless crude product. Distillation (80−83 °C (8 mmHg)) of the residue afforded 2.43 g (total, 10% yield) of $H_2NCH_2CH_2CH_2C{\equiv}CCH_2C$-$(Me){=}CH_2$ as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.96 (s, 1H, CH═), 4.79 (s, 1H, CH═), 2.84 (s, 2H, ═$CCH_2C{\equiv}$), 2.78 (t, J = 6.74 Hz, 2H, NCH_2), 2.24 (m, 2H, $CH_2C{\equiv}$), 1.75 (s, 3H, Me), 1.62 (m, 2H, CH_2), 0.47 (br, 2H, NH_2); ^{13}C (75 MHz, $CDCl_3$) δ 141.2, 111.2, 81.9, 77.5, 41.2, 32.5, 27.5, 22.1, 16.2; MS (rel abundance) M^+ (85), $M^+ + 1$ (34), 122.1 (74), 120.1 (30), 109.1 (97), 105.1 (85), 91.1 (94), 82.0 (88), 77.0 (81), 65.0 (35), 51.0 (40), 41.0 (351), 39.0 (100); high-resolution mass spectrum, calcd for $C_9H_{15}N$ (M^+) 137.1204, found 137.1201.

Synthesis of 4-Pentyn-1-amine (7). A suspension of 49.0 g (0.487 mol) of 5-chloro-1-pentyne, 109.0 g (0.582 mol) of sodium phthalimide, and 300 mg of NaI in 300 mL of DMF was heated at 100 °C overnight to afford *N*-4-pentynylphthalimide. This compound was used directly for the next step without further purification. *N*-4-Pentynylphthalimide and hydrazine monohydrate (1.00 mol) in 800 mL of MeOH were heated with stirring at 60 °C overnight. After the mixture was cooled to room temperature, followed by addition of 70 mL of concentrated HCl, the solution was heated at 60 °C for an additional 4 h. The mixture was then cooled and filtered, and the white precipitate washed with 2 × 100 mL of EtOH. Removal of solvent from the combined filtrates at reduced pressure gave a white precipitate. The colorless solid was then treated with a mixture of KOH (2 N, 350 mL) and diethyl ether (300 mL). After separation, the organic phase was extracted with 3 × 200 mL of diethyl ether. The ether phase was then washed with brine (100 mL) and dried over Na_2SO_4. After filtration and removal of solvent from the filtrate by rotary evaporation, distillation (124−125 °C) afforded 12.5 g (32% yield) of $H_2NCH_2CH_2CH_2C{\equiv}CH$ as a colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 2.44 (t, J = 6.75 Hz, 2H, CH_2N), 1.98 (m, 2H, $CH_2C{\equiv}C$), 1.79 (m, 1H, HC≡), 1.31 (m, 2H, CH_2), 0.38 (br s, NH_2); ^{13}C NMR (75 MHz, C_6D_6) δ 84.3, 68.8, 41.1, 32.6, 15.9; MS (rel abundance) M^+ (92), $M^+ - 1$ (1), $M^+ + 1$ (32), 65.1 (16), 55.1 (52), 51.0 (22), 43.0 (100), 39.0 (52); high-resolution mass spectrum calcd for C_5H_8N ($M^+ - 1$) 82.0657, found 82.0628. Anal. Calcd for C_5H_9N: C, 72.24; H, 10.91; N, 16.84. Found: C, 72.16; H, 11.33; N, 16.88.

Synthesis of 5-(Trimethylsilyl)-4-pentyn-1-amine (9). (a) 5-Bromo-1-(trimethylsilyl)-1-pentyne (9a). A procedure similar to that for **1a** utilizing the lithium (trimethylsilyl)acetylide obtained from the reaction of *n*-butyllithium (0.25 mol) with (trimethylsilyl)acetylene (25.0 g, 0.25 mol) and 1,3-dibromopropane (50.0 g, 0.25 mol) instead of 3-bromo-1-chloropropane gave 36.0 g (65% yield) of $BrCH_2CH_2CH_2C{\equiv}CSiMe_3$. ^{1}H NMR (300 MHz, $CDCl_3$) data agree with literature data:[17c−e] δ 3.52 (t, J = 6.48 Hz, 2H, CH_2Br), 2.42 (t, J = 6.66 Hz, 2H, $CH_2C{\equiv}C$), 2.05 (m, 2H, CH_2), 0.16 (s, 9H, $SiMe_3$).

(b) *N*-[5-(Trimethylsilyl)-4-pentynyl]phthalimide (9b). The procedure was the same as for **1b** except that the solid product was recrystallized from 100 mL of distilled H_2O and washed with 2 × 20 mL of H_2O. The product, $C_8H_4O_2NCH_2CH_2CH_2C{\equiv}CSiMe_3$, was isolated in 53% yield (24.5 g), mp 77.5−78.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (m, 2H, Ph), 7.74 (m, 2H, Ph), 3.78 (t, J = 6.93 Hz, 2H, CH_2N), 2.32 (t, J = 7.14, 2H, $CH_2C{\equiv}C$), 1.94 (m, 2H, CH_2), 0.09 (s, 9H, $SiMe_3$).

(c) 5-(Trimethylsilyl)-4-pentyn-1-amine (9). A procedure similar to that for **1** was used except that the reaction mixture was refluxed for 24 h, yielding 5.1 g (38% yield) of **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.79 (t, J = 6.87 Hz, 2H, CH_2N), 2.28 (t, J = 7.00 Hz, 2H, $CH_2C{\equiv}C$), 1.85 (br s, NH_2) 1.64 (m, 2H, CH_2), 0.12 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, ^{1}H-decoupled, $CDCl_3$) δ 106.8 (C≡C), 84.97 (C≡C), 41.2 (CH_2N), 32.1 (CH_2, 17.4 (CH_2), 0.2 ($SiMe_3$); ^{13}C NMR (75 MHz, ^{1}H-coupled, $CDCl_3$) δ 106.5 (s, C≡C), 85.1 (s, C≡C), 41.0 (t, J_{CH} = 134 Hz, CH_2N), 31.7 (t, J_{CH} = 128 Hz, CH_2), 17.4 (t, J_{CH} = 131 Hz, CH_2), 0.2 (q, J_{CH} = 119 Hz, $SiMe_3$); IR ($CHCl_3$) 2171, 1589 cm^{-1}. MS (rel abundance) M^+ (7), $M^+ - 1$ (5), $M^+ + 1$ (2), 140.1 (30), 138.1 (37), 123.1 (38), 109.0 (20), 98.0 (13), 82.1 (100), 73.0 (73), 67.0 (10), 59.0 (20), 43.0 (49), 35.0 (9); high-resolution mass spectrum, calcd for C_8H_{17}-$NSi(M^+)$ 155.1130, found 155.1135.

Synthesis of 6-Phenyl-5-hexyn-1-amine (11). (a) 6-Chloro-1-phenyl-1-hexyne (11a). 11a was synthesized in a manner analogous to that for **1a** using 38.0 g (0.30 mol) of 1,4-dichlorobutane in place of 3-bromo-1-chloropropane. Distillation at 94−95 °C (0.2 mmHg) gave 19.5 g (34% yield) of $Cl(CH_2)_4C{\equiv}CPh$ as a colorless oil. The ^{1}H NMR (300 MHz, $CDCl_3$) spectra agree with the published data:[4a] δ 7.35 (m, 2H, Ph), 7.24 (m, 3H, Ph), 3.57 (t, J = 6.59 Hz, CH_2Cl), 2.43 (t, J = 6.86 Hz, 2H, $CH_2C{\equiv}$), 1.93 (m, 2H, CH_2CH_2Cl), 1.73 (m, 2H, CH_2).

(b) *N*-(6-Phenyl-5-hexynyl)phthalimide (11b). 11b was prepared in a fashion analogous to **1b** using **11a**. After washing with diethyl ether and drying in vacuum, 21.0 g (69% yield) of $C_8H_4O_2NCH_2CH_2$-$CH_2CH_2C{\equiv}CPh$ was obtained as a colorless solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (m, 2H, Ph), 7.71 (m, 2H, Ph), 7.39 (m, 2H, Ph), 7.27 (m, 3H, Ph), 3.76 (t, J = 7.00 Hz, CH_2N), 2.48 (t, J = 7.00 Hz, $CH_2C{\equiv}C$), 1.88 (m, 2H, CH_2CH_2N), 1.66 (m, 2H, CH_2).

(c) 6-Phenylhex-5-yn-1-amine (11). 11 was synthesized in a manner analogous to **1** using **11b** and $H_2NNH_2{\cdot}H_2O$. Distillation (88−89 °C (∼0.05 mmHg)) afforded 2.1 g (18% yield) of $H_2NCH_2CH_2$-$CH_2CH_2C{\equiv}CPh$ as a colorless oil. The NMR data agree with published data:[4e] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (m, 2H, Ph), 7.27 (m, 3H, Ph), 2.75 (t, J = 6.80 Hz, 2H, CH_2N), 2.44 (t, J = 6.56 Hz, 2H, $CH_2C{\equiv}C$), 1.64 (m, 4H, $2CH_2$), 1.23 (br, 2H, NH_2); ^{13}C NMR (75 MHz, ^{1}H-decoupled, $CDCl_3$) δ 131.5 (CH), 128.2 (CH), 127.5 (CH), 123.9 (C of Ph), 90.0 (C≡C), 80.8 (C≡C), 41.8 (CH_2N), 33.1 (CH_2), 26.1 (CH_2), 19.3 (CH_2).

Synthesis of 7-Phenylhept-6-yn-1-amine (13). (a) 7-Bromo-1-phenyl-1-heptyne (13a). A procedure similar to those described above was used to prepare **13a** using 84.0 g (0.36 mol) of 1,5-dibromopentane in place of 3-bromo-1-chloropropane. Distillation (164−167 °C (0.05 mmHg)) afforded 49.0 g (52% yield) of $Br(CH_2)_5C{\equiv}CPh$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (m, 2H, Ph), 7.24 (m, 3H, Ph), 3.41 (t, J = 7.00 Hz, 2H, CH_2Br), 2.40 (t, J = 6.20 Hz, 2H, $CH_2C{\equiv}C$), 1.89 (m, 2H, CH_2CH_2Br), 1.60 (m, 4H, $2CH_2$).

(b) *N*-(7-Phenyl-6-heptynyl)phthalimide (13b). 13b was synthesized in a manner analogous to that for **1b**. Recrystallization from diethyl ether gave 46.0 g (74% yield) of $C_8H_4O_2NCH_2CH_2CH_2CH_2$-$CH_2C{\equiv}CPh$ as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (m, 2H, Ph), 7.69 (m, 2H, Ph), 7.34 (m, 2H, Ph), 7.24 (m, 3H, Ph),

3.71 (t, J = 7.20 Hz, 2H, CH_2N), 2.41 (t, J = 6.81 Hz, $CH_2C{\equiv}C$), 1.71 (m, 2H, CH_2CH_2N), 1.65 (m, 2H, $CH_2CH_2C{\equiv}C$), 1.51 (m, 2H, CH_2).

(c) 7-Phenylhept-6-yn-1-amine (13). **13** was prepared by a method similar to that for **1** except that the reaction mixture was refluxed for 2 days. After distillation (169−170 °C (11 mmHg)), 7.7 g (28% yield) of $H_2N(CH_2)_5C{\equiv}CPh$ was obtained: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (m, 2H, Ph), 7.26 (m, 3H, Ph), 2.71 (t, J = 6.24 Hz, 2H, CH_2N), 2.41 (t, J = 6.98 Hz, 2H, $CH_2C{\equiv}C$), 1.84 (br s, 2H, NH_2), 1.62 (m, 2H, CH_2CH_2N), 1.49 (m, 4H, $2CH_2$); ^{13}C NMR (75 MHz, ^{1}H-decoupled, $CDCl_3$) δ 131.5 (CH), 128.1 (CH), 127.5 (CH), 123.8 (C of Ph), 90.1 (CC), 80.6 (CC), 42.0 (CH_2N), 33.1 (CH_2), 28.5 (CH_2), 26.1 (CH_2), 19.3 (CH_2); ^{13}C NMR (75 MHz, ^{1}H-coupled, $CDCl_3$) δ 130.8 (d, CH), 127.5 (d, CH), 126.9 (d, CH), 123.4 (s, C of Ph), 89.6 (s, C≡C), 80.1 (s, C≡C), 41.4 (t, J_{CH} = 132 Hz, CH_2N), 32.6 (t, J_{CH} = 125 Hz, CH_2), 27.9 (t, J_{CH} = 128 Hz, CH_2), 25.5 (t, J_{CH} = 126 Hz, CH_2), 18.7 (t, J_{CH} = 129 Hz, CH_2); IR ($CHCl_3$) 2233, 1599 cm^{-1}; MS (rel abundance) M^+ (98), $M^+ - 1$ (18), $M^+ + 1$ (32), 170.1 (27), 158.1 (52), 141.1 (43), 128.1 (62), 115.0 (85), 91.0 (31), 82.1 (36), 56.0 (100), 43.0 (19); high-resolution mass spectrum, calcd for $C_{13}H_{17}N(M^+)$ 187.1361, found 187.1359.

Compound **13** was dissolved in dry diethyl ether; then hydrogen chloride gas was bubbled into the solution to form a colorless precipitate. After filtration, the solid was washed with dry diethyl ether and recrystallized from an EtOH/ethyl acetate mixture to given $HCl{\cdot}H_2N(CH_2)_5C{\equiv}CPh{\cdot}2H_2O$: ^{1}H NMR (300 MHz, D_2O) δ 7.24 (m, 2H, Ph), 7.16 (m, 3H, Ph), 2.79 (t, J = 7.41 Hz, 2H, CH_2N), 2.24 (t, J = 6.83 Hz, 2H, $CH_2C{\equiv}C$), 1.40 (m, 6H, $3CH_2$). Anal. Calcd for $C_{13}H_{18}NCl{\cdot}2H_2O$: C, 60.10; H, 8.53; N, 5.39. Found: C, 59.80; H, 7.13; N, 5.41.

Synthesis of *N*-Allyl-5-(trimethylsilyl)-4-pentyn-1-amine (15). A solution of 40.0 g (0.39 mol) of $ClCH_2CH_2CH_2C{\equiv}CH$ in 200 mL of THF was treated with 0.39 mol of *n*-BuLi at −78 °C over a period of 30 min. The reaction mixture was stirred for 1.5 h at −78 °C, warmed to room temperature for 2 h, and then refluxed for 2h. Next, the reaction mixture was cooled to −78 °C, 42.5 g (0.39 mol) of $ClSiMe_3$ was syringed into the solution over a period of 10 min, and the mixture was stirred at −78 °C for an additional 2 h, warmed to room temperature, stirred for 2 h, and then refluxed for 2 h. The mixture was next cooled to room temperature, and 150 mL of water was added to the solution. After separation of the organic and aqueous phases, the aqueous phase was extracted with 100 mL of $CHCl_3$. The combined organic phase and $CHCl_3$ extract was washed with 150 mL of saturated NaCl and then dried over $MgSO_4$ overnight. Removal of the solvent by rotary evaporation followed by distillation gave 57.8 g (85% yield) of $Me_3SiC{\equiv}CCH_2CH_2CH_2Cl$: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (t, J = 6.45 Hz, 2H, $ClCH_2$), 2.39 (t, J = 6.75 Hz, 2H, $\equiv CCH_2$), 1.94 (m, 2H, CH_2), 0.13 (s, 9H, $SiMe_3$).

A mixture of 10.0 g (0.057 mol) of 1-chloro-5-(trimethylsilyl)-4-pentyne and 35.0 g (0.60 mol) of allylamine in 0.3 g of NaI was sealed in a storage tube and heated at 60 °C for 7 days. After the reaction solution had cooled to room temperature, it was poured into a separatory funnel containing 100 mL of H_2O. The aqueous phase was then separated and extracted with 3 × 50 mL of diethyl ether. The combined extracts and the organic phase were washed with 70 mL of brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Distillation (143−145 °C (55 mmHg)) gave 6.1 g (55% yield) of $Me_3SiC{\equiv}CCH_2CH_2CH_2NHCH_2CH{=}CH_2$ as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93−5.83 (m, 1H, CH═), 5.19−5.04 (m, 2H, CH_2), 3.23 (d, J = 5.7 Hz, 2H, $NCH_2CH{=}$), 2.69 (t, J = 7.05 Hz, 2H, NCH_2), 2.27 (t, J = 7.05 Hz, 2H, CCH_2), 1.67 (m, 2H, CH_2), 1.33 (br, 1H, NH), 0.11 (s, 9H, $SiMe_3$); ^{13}C (75 MHz, $CDCl_3$) δ 136.8, 115.8, 106.8, 84.9, 52.3, 48.2, 28.6, 17.8, 0.1; MS (rel abundance) M^+ (5), $M^+ - 1$ (4), $M^+ + 1$ (1), 180.1 (38), 168.1 (7), 152.1 (9), 122.1 (95), 109.1 (7), 96.1 (6), 82.1 (14), 70.1 (100), 59.0 (14), 41.0 (38); high-resolution mass spectrum, calcd for $C_{11}H_{21}NSi$ (M^+) 195.1443, found 195.1439.

Synthesis of *N*-Allyl-4-pentyn-1-amine (17). A mixture of 8.0 g (0.046 mol) of 1-chloro-5-(trimethylsilyl)-4-pentyne, 43.0 g (0.75 mol) of allylamine, and 0.3 g of NaI was sealed in a storage tube and heated at 60 °C for 4 days. After the reaction solution cooled to room temperature, it was poured into a separatory funnel containing 200 mL of NaOH (10% solution). The aqueous phase was then separated and extracted with 3 × 100 mL of diethyl ether. The combined ethereal extracts and the organic phase were washed with 70 mL of brine, dried over $MgSO_4$, and concentrated by rotary evaporation. Distillation (99−101 °C (34 mmHg)) gave 4.9 g (55% yield) of $HC{\equiv}CCH_2CH_2CH_2NHCH_2CH{=}CH_2$ as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (m, 1H, CH═), 5.13 (m, 2H, $CH_2{=}$), 3.23 (d, J = 4.50 Hz, 2H, $NCH_2CH{=}$), 2.70 (t, J = 7.05 Hz, 2H, NCH_2), 2.25 (m, 2H, $CH_2C{=}$), 1.93 (t, J = 2.70 Hz, 1H, HC≡), 1.70 (m, 2H, CH_2), 1.57 (br, 1H, NH); ^{13}C (75 MHz, $CDCl_3$) δ 136.7, 116.0, 84.0, 68.6, 52.3, 48.1, 28.6, 16.3; MS (rel abundance) M^+ (16), $M^+ - 1$ (43), $M^+ - 2$ (10), 108.1 (11), 96.1 (25), 80.1 (13), 70.1 (100), 65.1 (6), 54.1 (13), 41.1 (94); high-resolution mass spectrum, calcd for $C_8H_{12}N$ ($M^+ - 1$) 122.0970, found 122.0970.

Preparation of *N*-4-Pentenyl-5′-(trimethylsilyl)-4′-pentyn-1-amine (19). The title compound was synthesized in a manner analogous to that for *N*-allyl-5-(trimethylsilyl)-4-pentyn-1-amine **(15)** using 4.0 g (0.023 mol) of 1-chloro-5-(trimethylsilyl)-4-pentyne and 17.7 g (0.208 mol) of 4-penten-1-amine to afford 3.1 g (61% yield) of $Me_3SiC{\equiv}CCH_2CH_2CH_2NHCH_2CH_2CH_2CH{=}CH_2$ (bp 70−73 °C (0.10 mmHg)) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (m, 1H, CH═), 4.95 (m, 2H, $CH_2{=}$), 2.68 (t, J = 7.05 Hz, 2H, NCH_2), 2.59 (t, J = 7.35 Hz, 2H, NCH_2), 2.26 (t, J = 7.05 Hz, 2H, $\equiv C{-}CH_2$), 2.06 (m, 2H, $CH_2CH{=}$), 1.67 (m, 2H, CH_2CH_2N), 1.58 (m, 2H, $NCH_2CH_2CH_2CH{=}$), 1.20 (br, 1H, NH), 0.11 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 114.6, 106.9, 84.8, 49.3, 48.8, 31.5, 29.3, 28.7, 17.8, 0.10; MS (rel abundance) $M^+ - 1$ (1), 208.1 (8), 194.0 (1), 180.0 (2), 168.0 (27), 155.0 (18), 140.0 (19), 123.0 (5), 98.0 (35), 73.0 (100), 59.0 (15), 44.0 (43); high-resolution mass spectrum, calcd for $C_{13}H_{24}NSi$ ($M^+ - 1$) 222.1678, found 222.1683.

Preparation of *N*-4-Pentenyl-4′-pentyn-1-amine (21). The title compound was synthesized in a manner analogous to that for *N*-allyl-4-pentyn-1-amine **(17)** using 0.86 g (4.9 mmol) of 1-chloro-5-(trimethylsilyl)-4-pentyne and 3.8 g (44.6 mmol) of 4-penten-1-amine to afford 0.40 g (54% yield) of $HC{\equiv}CCH_2CH_2CH_2NHCH_2CH_2CH_2CH{=}CH_2$ (bp 132−133 °C (31 mmHg)) as a colorless oil: ^{1}H NMR (300 MHz, C_6D_6) δ 5.75 (m, 1H, CH═), 4.99 (m, 2H, $CH_2{=}$), 2.43 (t, J = 6.75 Hz, 2H, NCH_2), 2.34 (t, J = 7.05 Hz, 2H, NCH_2), 2.07 (td, ^3J = 7.20 Hz, ^4J = 2.70 Hz, 2H, $CH_2C{\equiv}$), 1.98 (m, 2H, CH_2), 1.77 (t, ^4J = 2.70 Hz, 1H, HC≡), 1.46 (m, 2H), 1.37 (m, 2H), 0.46 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 114.6, 84.4, 68.8, 49.4, 46.7, 31.8, 29.8, 29.3, 16.4; MS (rel abundance) M^+ (12), $M^+ - 1$ (5), $M^+ + 1$ (2), 136.2 (7), 123.2 (19), 108.2 (10), 96.1 (100), 83.1 (9), 69.1 (19), 55.1 (100, 41.1 (15); high-resolution mass spectrum, calcd for $C_{10}H_{17}N$ (M^+) 151.1361, found 151.1356.

Typical NMR-Scale Catalytic Hydroamination/Cyclization Reactions. In the glovebox, the $Cp'_2SmCH(SiMe_3)_2$ precatalyst (6.0 mg, 10.5 μmol) was loaded into an NMR tube equipped with a Teflon valve. On the high-vacuum line, the NMR tube was evacuated and refilled with argon three times. Benzene (0.2 mL) was next vacuum-transferred into the tube, and then a mixture (0.5 mL) of benzene-d_6 and 5-phenylpent-4-yn-1-amine (**1**, 2.60 mmol, 248-fold molar excess) was transferred in via syringe under an argon flush while the tube was cooled to −78 °C to seal the precatalyst under the frozen benzene. The NMR tube was then evacuated and refilled with argon three times at −78 °C and finally sealed. The ensuing reaction was monitored by ^{1}H NMR. The product was identified by ^{1}H and ^{13}C NMR, GC/MS, and high-resolution mass spectrometry.

Typical Preparative-Scale Catalytic Hydroamination/Cyclization Reactions. Scale-up catalytic reactions were carried out using the following procedure. In the glovebox, 20.0 mg (34.5 μmol) of $Cp'_2SmCH(SiMe_3)_2$ was loaded into a reaction vessel (25 mL) equipped with a magnetic stir bar. Next, 2.0 mL of C_6H_6 was vacuum-transferred onto the precatalyst, followed by syringing 2.0 mL of a mixture of 5-(trimethylsilyl)-4-pentyn-1-amine (**9**, 0.250 g, 1.62 mmol) and benzene (1.5 mL) onto the frozen benzene and precatalyst mixture. The mixture was then freeze−pump−thaw degassed and warmed to room temperature. The clear yellow solution was stirred under argon for 2 days. Anaerobic filtration of the solution followed by vacuum transfer afforded a mixture of C_6H_6 and 5-[(trimethylsilyl)methyl]-3,4-dihydro-2*H*-pyrrole **(10)**. After the benzene was distilled off at atmospheric pressure, 0.23 g (92% yield) of **10** was obtained as a colorless oil. It was >95% pure by ^{1}H NMR and GC/MS.

2-Benzyl-1-pyrroline (2). This pyrrole derivative was synthesized catalytically using the procedure described under typical NMR-scale reactions. The NMR data agree with the literature data.[4e,19d] The yield (>95%) was estimated by the ^{1}H NMR spectrum and GC/MS: ^{1}H NMR (300 MHz, C_6D_6): δ 7.16−7.03 (m, 5H, Ph), 3.75 (t, J = 7.20 Hz, 2H, CH_2N), 3.55 (s, 2H, CH_2Ph), 2.02 (t, J = 8.13 Hz, 2H, CH_2C=N), 1.42 (m, 2H, CH_2); ^{13}C NMR (75 MHz, ^{1}H-decoupled, C_6D_6) δ 174.9 (C=N), 137.9 (C of Ph), 129.3 (CH), 128.8 (CH), 126.6 (CH), 61.4 (CH_2N), 40.8 (CH_2), 36.4 (CH_2), 22.9 (CH_2); ^{13}C NMR (75 MHz, ^{1}H-coupled, C_6D_6) δ 175.0 (s, C=N), 138.0 (s, C of Ph) 129.4 (d, CH), 128.8 (d, CH), 126.7 (d, CH), 61.5 (t, J_{CH} = 138 Hz, CH_2N), 40.9 (t, J_{CH} = 127 Hz, CH_2), 36.4 (t, J_{CH} = 129 Hz, CH_2), 23.0 (t, J_{CH} = 130 Hz, CH_2); MS (rel abundance) M^+ (100), $M^+ - 1$ (76), $M^+ + 1$ (33), 144.1 (4), 130.1 (13), 117.1 (19), 91.1 (71), 84.1 (51), 68.0 (15), 54.0 (10), 42.0 (11), 41.0 (13), 39.0 (13); high-resolution mass spectrum, calcd for $C_{11}H_{13}N$ 159.1048, found 159.1042.

2-Ethyl-1-pyrroline (4). The reaction of $Cp'_2SmCH(SiMe_3)_2$ (8.7 mg, 15.0 μmol) with **3** (1.36 mmol) in benzene-d_6, as described under typical NMR-scale reactions, afforded cyclized pyrrole derivative **4**. The yield (>95%) was estimated by the ^{1}H NMR spectrum and GC/MS. The NMR data agree with the published spectra:[19a,c,e,f] ^{1}H NMR (300 MHz, C_6D_6) δ 3.73 (m, 2H, CH_2N), 2.09 (q, J = 7.56 Hz, 2H, CH_2CH_3), 1.99 (t, J = 8.16 Hz, 2H, CH_2C=N), 1.47 (m, 2H, CH_2), 1.09 (t, J = 7.41 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, ^{1}H-decoupled, C_6D_6) δ 176.89 (C=N), 61.3 (CH_2N), 37.0 (CH_2C=N), 27.0 (CH_2-CH_2N), 22.9 (CH_2CH_3), 10.9 (CH_3); ^{13}C NMR (75 MHz, ^{1}H-coupled, C_6D_6) δ 176.9 (s, C=N), 61.3 (t, J_{CH} = 137.58 Hz, CH_2N), 37.0 (t, J_{CH} = 128 Hz, CH_2C=N), 27.0 (t, J_C = 122 Hz, CH_2CH_2N), 22.9 (t, J_{CH} = 130 Hz, CH_2CH_3), 10.8 (q, J_{CH} = 126 Hz, CH_3); MS (rel abundance): M^+ (58), $M^+ - 1$ (43), $M^+ + 1$ (6) 69.1 (100), 56.1 (37), 54.0 (28); high-resolution mass spectrum, calcd for $C_6H_{11}N$ 97.0891, found 97.0912.

The typical preparative-scale reaction procedure described above was used in a scale-up reaction with $Cp'_2SmCH(SiMe_3)_2$ (20.0 mg, 34.5 μmol) and **3** (0.47 g, 4.85 mmol) except that the reaction mixture was stirred for 4 days. Isolated yield: 59%.

2-(3-Methyl-3-butenyl)-1-pyrroline (6). The reaction of $Cp'_2SmCH(SiMe_3)_2$ (10.0 mg, 17.2 μmol) with **5** (23.6 mg, 172.0 μmol) in benzene-d_6 as described under typical NMR-scale reactions afforded cyclized pyrrole derivative **6**. The yield (>95%) was estimated by the ^{1}H NMR spectrum and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 4.77 (s, 2H), 3.76 (t, J = 7.20 Hz, 2H), 2.33 (s, 4H), 1.98 (t, J = 8.33 Hz, 2H), 1.63 (s, 3H), 1.46 (m, 2H); ^{13}C NMR (75 MHz, ^{1}H-decoupled, C_6D_6) δ 175.7, 145.5, 110.3, 61.3, 37.2, 34.6, 32.1, 22.9, 22.6; MS (rel abundance) M^+ (25), $M^+ - 1$ (22), $M^+ + 1$ (4), 122.2 (60), 108.2 (49), 84.2 (69), 53.1 (27), 41.2 (100); high-resolution mass spectrum, calcd for $C_9H_{15}N$ 137.1204, found 137.1228.

2-Methyl-1-pyrroline (8). A procedure analgous to that for **2** was used in an NMR-scale reaction for the synthesis of title pyrrole derivative using $Cp'_2SmCH(SiMe_3)_2$ (3.2 mg, 5.5 μmol) and **7** (500.3 μmol). The yield (>90%) was estimated by the ^{1}H NMR spectrum and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 3.71 (m, 2H, CH_2C=), 1.94 (t, J = 8.10 Hz, 2H, CH_2N), 1.77 (s, 3H, CH_3), 1.45 (m, 2H, CH_2); ^{13}C NMR (75 MHz, C_6D_6) δ 174.4, 61.5, 38.5, 23.2, 19.4; MS (rel abundance) M^+ (69), $M^+ - 1$ (12), $M^+ + 1$ (8), 69.1 (16), 55.1 (100), 42.0 (61); high-resolution mass spectrum, calcd for C_5H_9N 83.0735, found 83.0749.

2-[(Trimethylsilyl)methyl]-1-pyrroline (10). The cyclized pyrrole derivative was synthesized in both NMR- and preparative-scale reactions. A procedure analogous to that for **2** was used in the NMR-scale reaction using $Cp'_2SmCH(SiMe_3)_2$ (4.0 mg, 6.9 μmol) and **9** (164.0 mg, 1059.0 μmol). The yield (>95%) was estimated from the ^{1}H NMR spectrum and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 3.77 (t, J = 7.95 Hz, 2H, CH_2N), 2.07 (t, J = 8.11 Hz, 2H, CH_2C÷bN), 1.78 (s, 2H, CH_2SiMe_3), 1.51 (m, 2H, CH_2), 0.04 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, ^{1}H-decoupled, C_6D_6) δ 174.26 (C=N), 61.43 (CH_2N), 39.86 (CH_2C=N), 24.68 (CH_2C=N), 23.48 (CH_2), 1.06 ($SiMe_3$); ^{13}C NMR (75 MHz, ^{1}H-coupled, C_6D_6) δ 174.1 (s, C=N), 61.3 (t, J_{CH} = 138 Hz, CH_2N), 39.8 (t, J_{CH} = 128 Hz, CH_2C=N), 24.6 (t, J_{CH} = 120 Hz, CH_2SiMe_3), 23.5 (t, J_{CH} = 130 Hz, CH_2), 1.1 (q, J_{CH} = 118 Hz, $SiMe_3$); MS (rel abundance) M^+ (43), $M^+ - 1$ (28), $M^+ + 1$ (10), 140.1 (56), 127.1 (8), 114.1 (11), 102.1 (10), 84.1 (100), 73.0 (73), 59.0 (27), 42.0 (17); high-resolution mass spectrum, calcd for $C_8H_{17}NSi$ 155.1130, found 155.1124.

2-Benzyl-3,4,5,6-tetrahydropyridine (12). The procedure described above was employed except that $Cp'_2SmCH(SiMe_3)_2$ (15.0 mg, 26.0 μmol) and **9** (564.0 μmol) were used to prepare this cyclized compound. The NMR data agree with the published data.[4e,17a,19d] The yield (>95%) was estimated by ^{1}H NMR and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 7.17−6.99 (m, 5H, Ph), 3.52 (m, 2H, CH_2N), 3.37 (s, 2H, CH_2Ph), 1.63 (m, 2H, CH_2C=N), 1.13 (m, 4H, $2CH_2$).

2-Benzyl-3,4,5,6-tetrahydro-2*H*-azepin (14). This cyclized seven-membered ring azepin derivative was prepared as described for **2** above except that $Cp'_2SmCH(SiMe_3)_2$ (5.6 mg, 9.7 μmol) and **13** (2.76 mmol) were used. The NMR results agree with literature data.[19b,d] The yield (>92%) was estimated by ^{1}H NMR and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 7.28−7.05 (m, 5H, Ph), 3.59 (t, J = 4.50 Hz, 2H, CH_2N), 3.52 (s, 2H, CH_2Ph), 1.99 (t, J = 4.50 Hz, CH_2C=N), 1.39 (m, 4H, $2CH_2$), 0.98 (dd, 2H, CH_2); ^{13}C NMR (75 MHz, ^{1}H-decoupled, C_6D_6) δ 175.2 (C=N) 137.0 (C of Ph), 129.7 (CH), 128.7 (CH), 126.7 (CH), 52.3 (CH_2N), 49.9 (CH_2), 32.5 (CH_2), 31.8 (CH_2), 26.9 (CH_2), 24.1 (CH_2); MS (rel abundance) M^+ (100), $M^+ - 1$ (82), $M^+ + 1$ (12), 172.1 (4), 158.1 (27), 144.1 (19), 130.0 (44), 115.0 (14), 110.1 (13), 84.0 (9); high-resolution mass spectrum, calcd for $C_{13}H_{17}N$ 187.1361, found 187.1346.

Synthesis of 2-[(Trimethylsilyl)methylidene]-1-allylpyrrolidine (16) and 2-[(Trimethylsilyl)methyliden]-1-(1-propenyl)pyrrolidine (16a). Cyclized pyrrolidine derivative **16** were prepared as described for **2** but using $Cp'_2LuCH(SiMe_3)_2$ (3.1 mg, 5.0 μmol) and **15** (52.2 mg, 267.9 μmol). The yield (>90%) was estimated by ^{1}H NMR and GC/MS: ^{1}H NMR (400 MHz, C_6D_6) δ 5.64 (m, 1H, CH=), 4.97 (m, 2H, CH_2=), 3.75 (s, 1H, CH), 3.46 (d, J = 5.64 Hz, 2H, NCH_2C=), 2.79 (t, J = 6.68 Hz, 2H, CH_2N), 2.37 (t, J = 7.67 Hz, 2H, CH_2CN), 1.40 (m, 2H, CH_2), 0.30 (s, 9H, $SiMe_3$); ^{13}C NMR (100 MHz, ^{1}H-decoupled, C_6D_6) δ 158.6, 133.8, 116.0, 76.5, 51.0, 48.9, 32.1, 21.7, 1.4; MS (rel abundance) M^+ (26), $M^+ - 1$ (9), $M^+ + 1$ (5), 180.2 (38), 152.1 (8), 136.1 (8), 122.1 (100), 108.1 (14), 84.1 (19), 73.1 (52), 59.1 (15), 41.1 (14); high-resolution mass spectrum, calcd for $C_{11}H_{21}NSi$ 195.1442, found 195.1441.

Cyclized derivative **16a** was synthesized in a procedure analogous to that for **2** in the NMR-scale reaction except using 3.0 mg (4.9 μmol) of $Cp'_2SmCH(SiMe_3)_2$ and *N*-allyl-5-(trimethylsilyl)-4-pentyn-1-amine (**15**, 17.9 mg, 92.0 μmol). The NMR and GC/MS results indicate that **16a** is the major product (91%) and that two other isomers (8%) are present, which have identical molecular masses. The yield (91%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer or volatile products: ^{1}H NMR (300 MHz, C_6D_6) δ 6.70 (d, J = 13.7 Hz, 1H, NCH=), 4.49 (m, 1H, =CHMe), 4.19 (s, 1H, =CH($SiMe_3$)), 2.91 (t, J = 6.8 Hz, 2H, NCH_2), 2.29 (t, J = 7.7 Hz, 2H, CH_2C=), 1.68 (d, J = 6.6 Hz, 3H, CH_3), 1.32 (m, 2H, CH_2), 0.26 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz), C_6D_6) δ 154.6, 128.1, 100.0, 80.3, 48.3, 31.9, 21.2, 15.7, 1.1; ^{13}C NMR (75 MHz, ^{1}H-coupled, C_6D_6) δ 154.9 (s), 128.6 (d, J_{CH} = 157.0 Hz), 100.4 (d, J_{CH} = 157.7 Hz), 80.5 (d, J_{CH} = 132.7 Hz), 48.6 (t, J_{CH} = 137.3 Hz), 32.3 (t, J_{CH} = 130.3 Hz), 21.5 (t, J_{CH} = 131.9 Hz), 16.1 (q, J_{CH} = 119.4 Hz), 1.5 (q, J_{CH} = 117.5 Hz); MS (rel abundance): $M^+ - 1$ (10), M^+ (73), $M^+ + 1$ (14, 180.2 (92), 166.2 (9), 150.1 (9), 140.2 (42), 122.2 (100), 106.1 (12), 97.1 (7), 83.1 (5), 73.1 (65), 59.1 (26), 41.0 (11); high-resolution mass spectrum, calcd for $C_{11}H_{21}NSi$ 195.1443, found 195.1427.

Synthesis of 2-Methylene-1-allylpyrrolidine (18). Cyclized pyrrolidine derivative **18** was prepared as described for **2** above using $Cp'_2SmCH(SiMe_3)_2$ (3.0 mg, 5.2 μmol) and **17** (32.6 mg, 169.3 μmol). The yield (>85%) was estimated by the ^{1}H NMR and GC/MS: ^{1}H NMR (300 MHz, C_6D_6) δ 5.72 (m, 1H, CH=), 5.02 (m, 2H, CH_2=), 3.77 (d, J = 20.7 Hz, 2H, CH_2=CN), 3.46 (d, J = 5.70 Hz, 2H, NCH_2CH=), 2.82 (t, J = 6.60 Hz, 2H, CH_2N), 2.36 (m, 2H, CH_2CN), 1.44 (m, 2H,

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CH_2); ^{13}C NMR (75 MHz, ^1H-decoupled, C_6D_6) δ 152.6, 134.0, 116.0, 71.6, 51.7, 49.8, 32.0, 22.0; ^{13}C NMR (75 MHz, ^1H-coupled, C_6D_6) δ 152.6 (s), 134.0 (d, J_{CH} = 150.8 Hz), 116.0 (t, J_{CH} = 149.5 Hz), 71.6 (t, J_{CH} = 156.3 Hz), 51.7 (t, J_{CH} = 134.2 Hz), 49.8 (t, J_{CH} = 128.2 Hz), 32.0 (t, J_{CH} = 132.7 Hz), 22.0 (t, J_{CH} = 134.2 Hz); MS (rel abundance) M^+ (77), $M^+ - 1$ (100), $M^+ + 1$ (8), 108.1 (25), 96.1 (25), 80.1 (21), 67.1 (19), 54.1 (31), 41.1 (51); high-resolution mass spectrum, calcd for $C_8H_{12}N(M^+ - H)$ 122.0970, found 122.0963.

Synthesis of 2-[(Trimethylsilylmethylidene]-1-(4-pentenyl)pyrrolidine (20). The reaction of $Cp'_2SmCH(SiMe_3)_2$ (3.0 mg, 5.1 μmol) with *N*-4-pentenyl-5′-(trimethylsilyl)-4′-pentyn-1-amine (**19**, 81.2 mg, 364.0 μmol) in benzene-d_6 was carried out as described for **2** and afforded the cyclized pyrrolidine derivative **20** (90% yield): ^1H NMR (300 MHz, C_6D_6) δ 5.64 (m, 1H, CH═CH_2), 4.91 (m, 2H, CH_2═), 3.70 (s, 1H, ═CH($SiMe_3$), 2.86 (t, J = 7.35 Hz, 2H, $NCH_2CH_2CH_2$-CH═CH_2), 2.74 (t, J = 6.75 Hz, 2H, NCH_2), 2.36 (t, J = 7.65 Hz, CH_2C═), 1.81 (m, 2H, CH_2CH═), 1.43 (m, 2H, $NCH_2CH_2CH_2$C═), 1.37 (m, 2H, CH_2), 0.28 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, C_6D_6) δ 159.0, 138.4, 114.9, 75.6, 51.4, 45.7, 32.3, 31.7, 26.1, 21.8, 1.5; MS (rel abundance) $M^+ - 1$ (18), M^+ (16), $M^+ + 1$ (5), 208.2 (19), 182.2 (10), 168.2 (40), 155.2 (24), 140.1 (29), 123.1 (18), 110.1 (14), 98.1 (46), 73.1 (100), 59.1 (14), 44.1 (30); high-resolution mass spectrum, calcd for $C_{12}H_{22}NSi$ (M^+ − Me) 208.1522, found 208.1495.

Synthesis of 2-Methylene-1-(4-pentenyl)pyrrolidine (22). This cyclized pyrrolidine derivative was prepared as described for **2**, but using $Cp'_2SmCH(SiMe_3)_2$ (1.0 mg, 1.7 μmol) and **21** (8.0 mg, 53.1 μmol): ^1H NMR (400 MHz, C_6D_6) δ 5.74 (m, 1H, CH═), 4.98 (m, 2H, CH_2═), 3.76 (d, J = 25.5 Hz, 2H, CH_2═CN), 2.88 (d, J = 7.20 Hz, 2H), 2.79 (t, J = 6.00 Hz, 2H), 2.38 (m, 2H), 1.90 (m, 2H), 1.59−1.42 (m, 4H); ^{13}C NMR (100 MHz, ^1H-decoupled, C_6D_6) δ 152.9, 138.5, 114.8, 70.7, 51.9, 46.5, 32.2, 31.7, 26.1, 22.1; ^{13}C NMR (100 MHz, ^1H-decoupled, C_6D_6) δ 152.9 (s), 138.5 (d, J_{CH} = 146.4 Hz), 114.9 (t, J_{CH} = 154.4 Hz), 70.7 (t, J_{CH} = 156.3 Hz), 51.9 (t, J_{CH} = 138.4 Hz), 46.5 (t, J_{CH} = 130.5 Hz), 32.3 (t, J_{CH} = 131.2 Hz), 31.7 (t, J_{CH} = 122.9 Hz), 26.1 (t, J_{CH} = 127.8 Hz), 22.1 (t, J_{CH} = 129.4 Hz); MS (rel abundance) M^+ (13), $M^+ - 1$ (4), $M^+ + 1$ (2), 136.2 (6), 123.2 (23), 108.2 (9), 96.1 (100), 82.1 (8), 69.1 (21), 55.1 (18), 41.1 (29); high-resolution mass spectrum, calcd for $C_{10}H_{17}N$ 151.1361, found 151.1352. The yield (>85%) was estimated by the ^1H NMR spectrum and GC/MS.

Kinetic Studies of Hydroamination/Cyclization. In a typical experiment, an NMR sample was prepared as described under typical NMR-scale catalytic reactions but the NMR tube was maintained at −78 °C until kinetic measurements were initiated. Before the measurements, the NMR probe was equilibrated to the appropriate temperature ($T \pm 0.2$ °C; checked with a methanol or ethylene glycol temperature standard), and the NMR sample was quickly warmed with shaking for ~8 s and inserted into the probe. Data were acquired using four or eight scans per time interval with a long pulse delay to avoid saturation of the signal. The kinetics were usually monitored by the intensity changes in the substrate resonances over three or more half-lives. The substrate concentrations (C) were measured from the area (A_s) of the ^1H-normalized NCH_2 signals, standardized to the area (A_l) of free CH_2-($SiMe_3$)$_2$ in the solution, which is quantitatively generated by reaction of the precatalysts with amines (Schemes 1 and 2). All the data collected could be convincingly fit over approximately three half-lives (R > 0.98) by least squares to eq 1, where C_0 ($C_0 = A_{s0}/A_{l0}$) is the

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

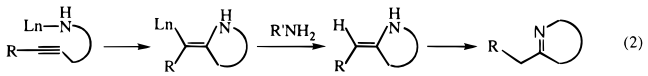
initial concentration of substrate (relative to precatalyst) and C (A_s/A_l) is the substrate concentration at time, t.

The ratio of the catalyst to substrate was accurately measured from the ratio of A_{s0} and A_{l0}, or from the area of product and A_l. The exact concentrations of catalysts and substrates were determined by internal $FeCp_2$ calibration. The turnover frequency (N_t, h^{-1}) was calculated from the least-squares determined slope *(m)* of the resulting plot. Typical initial substrate concentrations were in the range 0.1−4.6 M, and typical catalyst concentrations were in the range 1.5−35 mM.

Results

The goal of this investigation was to examine the scope, stereoselectivity, lanthanide ion sensitivity, ancillary ligand sensitivity, kinetics, and mechanism of the organolanthanide-catalyzed intramolecular hydroamination/cyclization of aminoalkynes. This study represents an extension of, and comparison to, our previous investigation of the catalytic hydroamination/cyclization of unprotected aminoolefins.[7c−g] In the ensuing discussion, we focus on reaction scope, alkyne substituent effects on the reaction, metal ion size and ancillary ligand effects on the reaction, and kinetics and the rate law.

Reaction and Scope of Hydroamination/Cyclization. The organolanthanides $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ efficiently and regiospecifically catalyze the intramolecular hydroamination/cyclization of a variety of aliphatic and aromatic aminoalkynes to yield the corresponding heterocycles (Table 1). The reactions are conveniently monitored by ^1H NMR spectroscopy. The initial reaction of $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ complexes with aminoalkynes quantitatively generates lanthanide amides (presumably amine−amide complexes of the type $Cp'_2LnNHR(H_2NR)_x$/$Me_2SiCp''_2$-$LnNHR(H_2NR)_x$)[7c,d] and $CH_2(SiMe_3)_2$ (within seconds as monitored by ^1H NMR; Scheme 2). The mechanism of this process likely involves a four-centered protonolytic transition state.[20] Hydroamination/cyclization of primary aminoalkynes yields enamines, which subsequently and expectedly undergo tautomerization to the more stable imines[21] at room temperature (eq 2). The intermediate enamines are in some cases observable



by ^1H NMR spectroscopy during the course of the reactions. Not surprisingly, the cyclization of secondary amines results only in enamines.

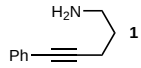
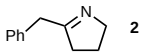
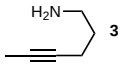
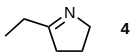
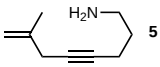
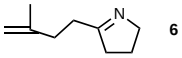
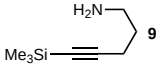
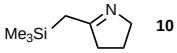
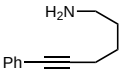
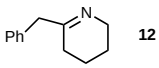
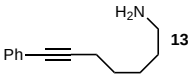
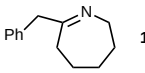
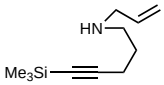
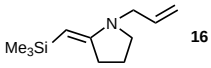
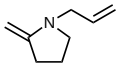
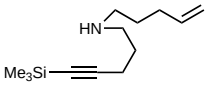
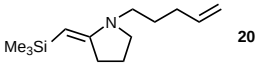
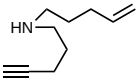
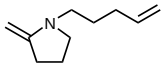
As in the case of organolanthanide-catalyzed hydroamination/cyclization of aminoolefins,[7c−g] the reaction of $Cp'_2NdCH(SiMe_3)_2$, $Cp'_2SmCH(SiMe_3)_2$, and $Me_2SiCp''_2SmCH(SiMe_3)_2$ with aminoalkynes effects distinctive color changes associated with catalytic initiation and termination. Thus, the original green and orange solutions of the Nd and Sm hydrocarbyl precatalysts, respectively, in C_6D_6 or C_7D_8 instantaneously turn to the characteristic blue and yellow colors of the corresponding amine−amide complexes[7c,d] in conjunction with the initiation of catalytic turnover. Upon consumption of the aminoalkynes, the resulting reaction solutions revert to the original colors. In the presence of the paramagnetic Nd^{3+} (4 f^3) and Sm^{3+} (4 f^5) catalysts, only paramagnetically broadened amine product and substrate ^1H NMR resonances are detected during catalytic turnover at room temperature. This behavior is analogous to that observed during aminoolefin hydroamination/cyclization and can be associated with rapid intramolecular exchange of bound amine and amide groups as well as intermolecular exchange of bound and free amine (substrate and product) groups involving complexes of the type $Cp'_2LnNHR(NH_2R)_x$.[7c,d]

The present tetrahydropyrrole, pyrroline, and pyrrolidine products were characterized by ^1H and ^{13}C NMR spectroscopy, GC/MS, and high-resolution mass spectroscopy and/or by comparison with literature ^1H/^{13}C NMR spectral data and data for independently synthesized product samples (see Experimental Section for details). The ^1H NMR spectra show that the aminoalkyne substrates are quantitatively and regiospecifically

(20) (a) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74−84. (b) Thompson, M. E.; Baxer, 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. (c) Doherty, N. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 2670−2682.

(21) Shainyan, B. A.; Mirskova, A. N. *Russ. Chem. Rev.* **1979**, *48*, 107−117, and references therein.

Table 1. Intramolecular Hydroamination/Cyclization Results

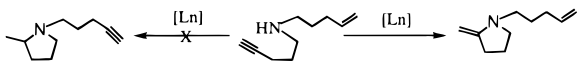
entry	substrate	product	N_t, h^{-1} (°C)	yield (%)
1	 **1**	 **2**	77 (21)[a] 2830 (60)[a] 2 (21)[b]	95[d]
2	 **3**	 **4**	96 (21)[a] 28 (21)[b]	95[d] 59[e]
3	 **5**	 **6**	20 (21)[a]	95[d]
4	 **7**	 **8**	580 (21)[a]	90[d] 47[e]
5	 **9**	 **10**	>7600 (21)[a,d]	95[d] 92[e]
6	 **11**	 **12**	4 (21)[a] 328 (60)[a]	95[d]
7	 **13**	 **14**	0.11 (60)[a] 0.03 (60)[b]	92[d]
8	 **15**	 **16**	56 (21)[c]	90[d]
9	 **17**	 **18**	27 (21)[a]	85[d] 52[e]
10	 **19**	 **20**	129 (21)[a]	90[d]
11	 **21**	 **22**	47 (21)[a]	85[d]

[a] $Cp'_2SmCH(SiMe_3)_2$ as precatalyst. [b] $Me_2SiCp''_2SmCH(SiMe_3)_2$ as precatalyst. [c] $Cp'_2LuCH(SiMe_3)_2$ as precatalyst; see text. [d] NMR scale reaction and the yield determined by ^1H NMR spectroscopy and GC/MS. [e] Preparative-scale reaction and isolated yield.

converted to the cyclized compounds shown in Table 1 with negligible traces of starting materials or other byproducts. General product isolation procedures involve high-vacuum transfer of the products and other volatiles, followed by removal of solvents and $CH_2(SiMe_3)_2$. Preparative-scale reactions were carried out in the storage tubes with products isolated in 59−92% yields (Table 1). All the products in NMR or preparative-scale reactions were >95% pure by GC/MS.

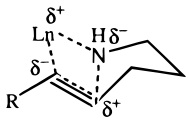
Table 1 presents the results of the organolanthanide-catalyzed aminoalkyne cyclizations. The present process is capable of regiospecifically forming five-, six-, and seven-membered heterocycles from substrates having several classes of substituents on the acetylenic moiety. The transformations **15** → **16**, **17** → **18**, **19** → **20**, and **21** → **22** indicate that the hydroamination/cyclization is not limited to primary amines and that secondary amines also undergo rapid cyclization. The present process is effective in the cyclization of both internal alkynes (entries 1−3, 5−8, and 10) and terminal alkynes (entries 4, 9, and 11). The catalytic process is also applicable to alkynes substituted with a number of functional groups, such as alkyl **(3)**, allyl **(5)**, phenyl **(1, 11, 13)**, H **(7, 17, 21)**, and trimethylsilyl **(9, 15, 19)**. This catalytic process exhibits similar efficiencies for *N*-allyl- **(15, 17)** and *N*-alkenyl- **(19, 21)** substituted secondary amines in the synthesis of 2-methylidenepyrrolidine derivatives (entries 8−11).

In regard to turnover frequency, the present cyclizations are ∼10−100× more rapid than the corresponding aminoolefin transformations for the same catalyst, temperature, and reaction conditions.[7d] Indeed, N_t for process **9** → **10** considerably exceeds the rate that can be accurately measured at room temperature. Furthermore, in direct competition studies it can be seen that the Ln−N bond preferentially adds to the 4-alkyne functionality rather than to the 4-alkene in the hydroamination/cyclization of **21** → **22** (eq 3).



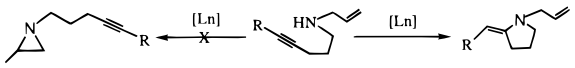
(3)

As in the case of aminoolefin cyclization, the present ring-size dependence of cyclization rates is 5 > 6 ≫ 7, consistent with classical, stereoelectronically controlled cyclization processes.[7d,22] A preference for a quasi-seven-membered transition state (e.g., **A**) is in accord with the aforementioned ring-size effects and earlier stereochemical observations on organolanthanide-catalyzed intramolecular aminoolefin hydroamination/cyclization.[7c,d] In regard to the possible formation of three-



A

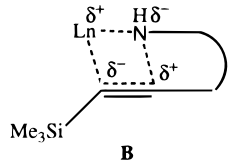
membered rings, the preferences for five-membered-ring formation observed in transformations of **15** → **16** and **17** → **18** (e.g., eq 4) are presumably due, among other factors, to unfavorable strain



(4)

energies in the product three-membered rings.

Substituent Effects on the Catalytic Process. The kinetic and mechanistic studies of the Cp'_2Ln-catalyzed hydroamination/cyclization process to be discussed below argue that the turnover-limiting step is intramolecular alkyne insertion into the Ln−N bond followed by rapid protonolysis of the resulting Ln−C bond (Schemes 1 and 2). The transition states involved in this process should therefore be electronically and sterically sensitive to the environment of the insertive transition state (e.g., **A**). In an effort to investigate such effects, a study of the turnover frequency as a function of alkyne substituent groups was undertaken. Table 2 shows that, for similar primary aminoalkynes, N_t is rather sensitive to the identity of the R group on the alkyne moiety. Thus, when R = $SiMe_3$, a very large N_t value is observed **(9 → 10)**, despite the considerable steric encumbrance of this group. This substituent kinetic effect is in accord with proposed transition state electronic demands **(B)**



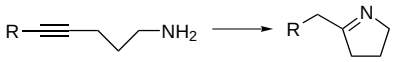
B

since silyl functionalities are known to stabilize α-carbanions and β-carbocations.[23,24]

In the case of R = H, the appreciable N_t may reflect minimal steric impediment of alkyne insertion into the Ln−N bond **(7 → 8)**. Comparing these kinetic results to those for **1** → **2**, **3** → **4**, and **5** → **6** suggests that steric effects may be somewhat more important than electronic ones since for N_t(R), H > Me ≥ Ph > 2-propenyl. For more encumbered secondary amines, the silyl accelerating effect is not as dramatic (compare entries 8 vs 9 and 10 vs 11). The kinetic results in Tables 1 and 2 therefore likely reflect subtle combinations of R- and N-centered electronic and steric effects.

Metal and Ancillary Ligation Effects on the Catalytic Process. In the case of organolanthanide-catalyzed hydroamination/cyclization of aminoolefins,[7c,d] both increasing the Ln^{3+} ionic radius[25] and opening the metal coordination sphere by connecting the ancillary ligands (Cp'_2Ln → $Me_2SiCp''_2Ln$ or $Me_2SiCp''(R*Cp)Ln$)[18a,7c] *increase* turnover frequencies, presumably reflecting significant steric demands in the insertive transition state.[7c,d,14j,18a] Interestingly, and in marked contrast to the olefin cyclization,[7c,d] for constant substrate and reaction conditions, the present kinetic results for the Cp'_2Ln-catalyzed transformation **7** → **8** (Table 3) evidence *increasing* N_t values on proceeding from the largest eight-coordinate ionic radius lanthanide ion, La (1.160 Å), to intermediate Nd (1.109 Å), Sm (1.079 Å), to smallest, Lu (0.977 Å). Furthermore, replacement of Cp'_2Nd with the more open $Me_2SiCp''_2Nd$ catalyst also effects a *decrease* in N_t from 207 to 78 h^{-1} for the transformation **7** → **8**. The same ancillary ligand reactivity effects are also observed in the five- and seven-membered-ring closures of phenyl-substituted aminoalkynes (Table 1, entries 1 and 7). Thus, the organolanthanide-catalyzed cyclization of aminoalkynes experiences a deceleration rather than an acceleration or identity in rate when larger ionic radius Ln^{3+} catalysts or more open $Me_2SiCp''_2Ln$ coordination spheres are employed.

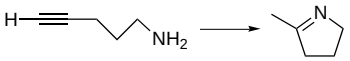
Table 2. Substituent Group Effects on the Turnover Frequencies for Primary Aminoalkyne Hydroamination/Cyclization[a]



R	N_t, h^{-1} [b] (at 21 °C)
CH_2═$CMeCH_2$	20
Ph	77
CH_3	96
H	580
Me_3Si	7600

[a] Using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst. [b] Turnover frequencies measured in C_6D_6.

Table 3. Metal Size and Ancillary Ligation Effects on the Turnover Frequencies for Primary Aminoalkyne Hydroamination/Cyclization



catalyst	ionic radius[a] (Å)	N_t, h^{-1} (at 21 °C)
$Me_2SiCp''_2Nd$−	1.109	78
Cp'_2La−	1.160	135
Cp'_2Nd−	1.109	207
Cp'_2Sm−	1.079	580
Cp'_2Lu−	0.977	711

[a] Eight-coordinate ionic radii from ref 25.

Kinetic Studies of Aminoalkyne Hydroamination/Cyclization. A kinetic study of the **3** → **4** transformation was undertaken by *in situ* ^1H NMR spectroscopy. The reaction of a 40−50-fold molar excess of 5-methyl-4-pentyn-1-amine with $Cp'_2SmCH(SiMe_3)_2$ was monitored with constant catalyst concentration until complete substrate consumption. The disappearance of CH_2N (δ ∼2.8 ppm) ^1H resonances was normalized to the $CH_2(SiMe_3)_2$ signal as an internal standard. The turnover frequency of cyclization was calculated from the slope of the kinetic plots of substrate to catalyst ratio vs time. The kinetic plots as shown in Figure 1 reveal a linear dependence of aminoalkyne substrate concentration on reaction time over a ∼10-fold substrate concentration range, which indicates an essentially zero-order dependence of the catalytic rate on substrate concentration under these conditions, in analogy to organolanthanide-catalyzed aminoolefin cyclization.[7c,d] This

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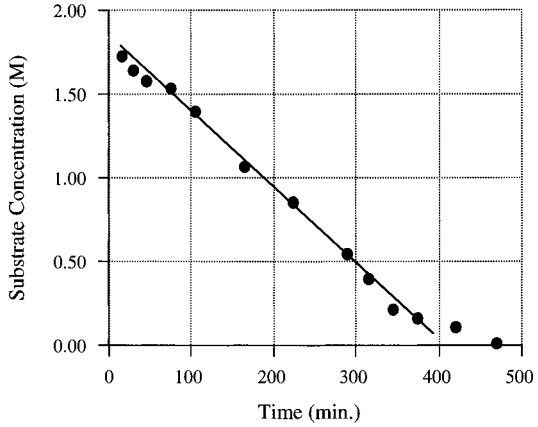


Figure 1. Plot of $H_2NCH_2CH_2CH_2C{\equiv}CMe$ concentration as a function of time for the hydroamination/cyclization of $H_2NCH_2CH_2CH_2C{\equiv}CMe$ **(3 → 4)** using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst in benzene-d_6 at 21 °C. The deviation from linearity at high conversions likely reflects product inhibition (see text).

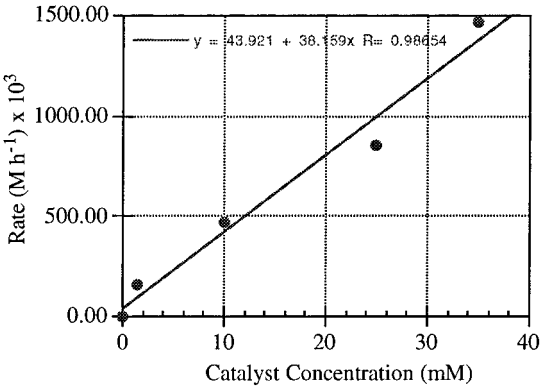


Figure 2. Determination of reaction order in lanthanide concentration for the hydroamination/cyclization of $H_2NCH_2CH_2CH_2C{\equiv}CMe$ **(3 → 4)** mediated by $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst in benzene-d_6 at 21 °C.

result is consistent with a similar turnover-limiting step involving intramolecular C≡C insertion into the Ln−N bond followed by rapid protonolysis of the resulting Ln−C bond. Considering the rapidity of Ln−C protonolysis by amines in these systems, it seems unreasonable that intramolecular (or intermolecular) proton transfer could be turnover-limiting under most catalytic conditions. It is also observed (Figure 1) that the rate of aminoalkyne cyclization begins to decrease (depart from zero-order behavior) as the catalytic reaction progresses to ≥90% completion, which is consistent with previously analyzed examples in aminoolefin hydroamination of competitive inhibition of substrate coordination/cyclization by the product heterocycle as high product concentrations are attained.[7c,d]

When the initial concentration of the aminoalkyne is held constant and the concentration of catalyst precursor is varied over a 50-fold concentration range (Figure 2), a plot of reaction rate vs precatalyst concentration indicates the reaction to be the first-order in catalyst. Taken together, the empirical rate law for the organolanthanide-catalyzed hydroamination/cyclization **3 → 4** is given by eq 5, which is identical to the aminoolefin cyclization rate law.[7c,d]

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

The derived rate constant for the **3 → 4** conversion at 21 °C is $k = 0.011(2)\ s^{-1}$. The terminal aminoalkyne cyclization **7 → 8** catalyzed by Cp'_2Sm exhibits a similar kinetic independence of amine concentration over a 0−35 °C temperature range

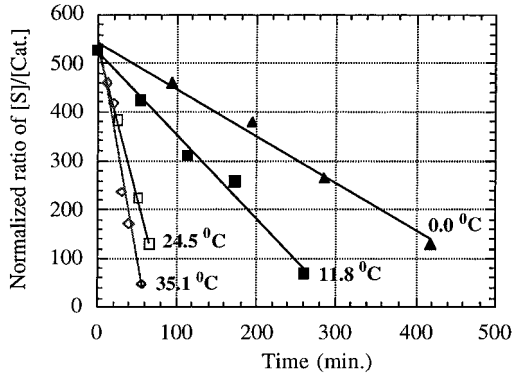


Figure 3. Normalized ratio of aminoalkyne to lanthanide concentration as a function of time and temperature for the intramolecular hydroamination/cyclization of $H_2NCH_2CH_2CH_2C{\equiv}CH$ **(7 → 8)** using the precatalyst $Cp'_2SmCH(SiMe_3)_2$ in toluene-d_8. Starting amine and catalyst concentrations are identical in each experiment. The lines are least-squares fits to the data points.

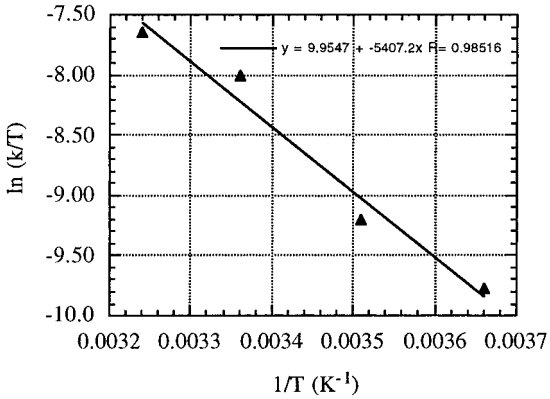
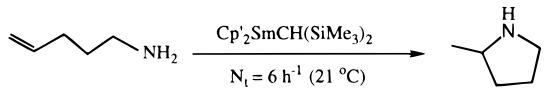


Figure 4. Eyring plot for the intramolecular hydroamination/cyclization of $H_2NCH_2CH_2CH_2C{\equiv}CH$ **(7 → 8)** using the precatalyst $Cp'_2SmCH(SiMe_3)_2$ in toluene-d_8. The line represents the least-squares fit to the data points.

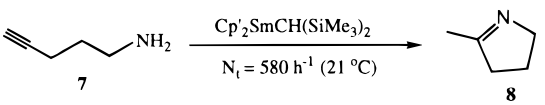
(Figure 3). The derived $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values from an Eyring analysis (Figure 4) are 10.7(8) kcal mol^{-1}, and −27.4(6) eu, respectively.

Discussion

Catalytic Reaction Scope and Mechanism. The present catalytic results for aminoalkyne hydroamination/cyclization demonstrate that a substantial range of substrates can be cyclized to the corresponding heterocycles, including not only primary and secondary amines but also internal and terminal alkynes. Five-, six-, and seven-membered heterocycles with several classes of substituents α to the acetylenic moiety can be regiospecifically synthesized by the present catalytic process. With regard to rate, the present process exhibits significant rate enhancements over aminoolefin cyclization.[7c,d] For example, comparison of 4-pentyn-1-amine cyclization to that of 4-penten-1-amine under identical reaction conditions using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst reveals that N_t increases ∼100× (N_t = 6 h^{-1} vs 580 h^{-1}, respectively; eqs 6 and 7). The activation

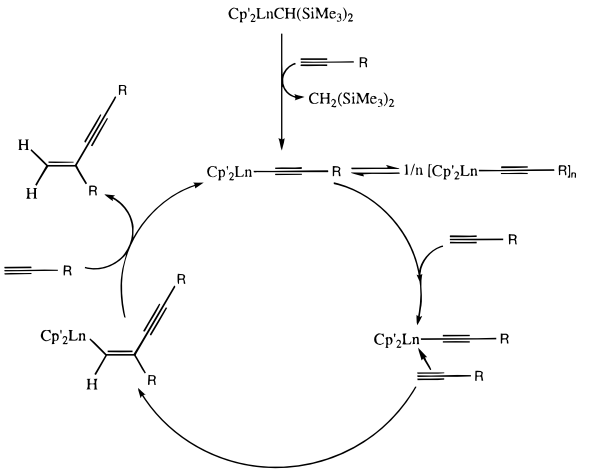


(6)



7 8 (7)

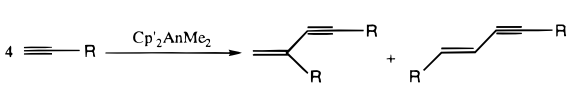
Scheme 3. A Plausible Pathway for the Organolanthanide-Catalyzed Coupling Reactions of Terminal Alkynes



energetics for the **7** → **8** conversion of $\Delta H^{\ddagger} = 10.7(8)$ kcal/mol and $\Delta S^{\ddagger} = -27.4(6)$ eu can be compared to $\Delta H^{\ddagger} = 12.7(1.4)$ kcal/mol and $\Delta S^{\ddagger} = -27.0(4.6)$ eu for the aminoolefin process in eq 6.[7d] While the aminoalkyne hydroamination/cyclization has a substantially lower activation enthalpic barrier, it appears from $\Delta S^{\ddagger}$ that eqs 6 and 7 proceed with similar overall degrees of entropic reorganization on approaching the transition state.

The present kinetic results doubtless reflect the differing insertive reactivities of the C═C and C≡C multiple bonds. This hypothesis is further supported by the results in the previous section showing that the competitive transformation **21** → **22** favors aminoalkyne rather than aminoolefin ring closure (eq 3). An appealing explanation for the preferential insertion into Ln−N bonds of alkyne over olefinic functionalities involves the sterically more accessible, cylindrical C≡C π system, the more nucleophilic sp-hybridized carbon atoms,[26] the greater C≡C π-donating capacity, the greater thermodynamic driving force,[10] and possibly the greater electronic stabilization of the four-center transition state **(B)**.

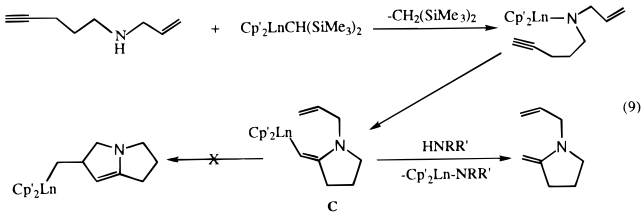
With regard to substrates, the present process is able to effect hydroamination/cyclization of both internal and terminal alkyne functionalities. An interesting contrast is presented by other organo-f-element-catalyzed alkyne reactions. Thus, Teuben and co-workers have reported $Cp'_2LnCH(SiMe_3)_2$-catalyzed terminal alkyne dimerization and/or oligomerization processes which doubtless proceed via initial protonolysis to yield Ln−C≡CR species which then undergo subsequent C≡C insertion to generate metal−alkenyl complexes. Further alkyne insertion competes with intermolecular RC≡CH protonolysis to yield alkene−alkyne dimers or trimers (Scheme 3).[8b−g] In addition, Eisen and co-workers recently reported analogous terminal alkyne dimerization and oligomerization processes mediated by organoactinides (eq 8; An = Th, U).[8a]



(8)

The present results, and those on intermolecular alkene and alkyne hydroamination to be discussed elsewhere,[7b,15b] argue that rapid N−H protonolysis of incipient metal−carbon bonds limits the lifetimes/effective concentrations of the metal−alkynyl and −alkenyl species shown in Scheme 3, and significant quantities of alkyne coupling products are therefore not observed.[27] However, in cases where alkyne or olefin functionalities are "tethered" to the reaction center, as in recently described bicyclizations involving difunctional amines,[7a] incipient metal−carbon bonds can be insertively intercepted.

In contrast to our recently reported aminoalkene−eyne bicyclizations mediated by organolanthanides,[7a] attempts to effect bicyclization of terminal alkene−enes **15** and **17** to the corresponding pyrrolizidine derivatives (e.g., eq 9), were



(9)

unsuccessful (entries 8 and 9). This is presumably due to the unfavorable strain in the bicyclic cyclopentene which would form and competing protonolysis of the metal−alkenyl intermediate **(C)** by substrates containing active hydrogen in NH and/or ≡CH moieties. In the case of $Cp'_2SmCH(TMS)_2$ as the precatalyst for **15** → **16**, isomerization of the allylic double bond is also detected[7a] (see Experimental Section for details). Isomerization is not observed with smaller $Cp'_2LuCH(TMS)_2$ as the precatalyst.

The previous mechanistic studies of organolanthanide-catalyzed aminoolefin hydroamination/cyclization argued that olefin insertion into the Ln−N bond is the turnover-limiting step and that this is followed by rapid intra- and intermolecular Ln−C protonolysis, affording the product heterocycle and regenerating the metal−amide catalyst.[7c,d] In the present aminoalkyne hydroamination/cyclization processes, the catalytic results derived from the kinetic data, as well as substrate substituent, metal ion size, and ancillary ligand effects on the turnover frequency, argue for a basically similar mechanistic picture. The catalyst precursors $Cp'_2LnCH(SiMe_3)_2$ react rapidly with aminoalkynes in benzene-d_6 or toluene-d_8 to form $CH_2(SiMe_3)_2$ (used as an internal NMR standard) and the putative, catalytically active $Cp'_2LnNR(CH_2)_nC{\equiv}CR'[HNR(CH_2)_nC{\equiv}CR']_x$ species (R = H, alkyl; R′ = H, phenyl, alkyl, trimethylsilyl). This species undergoes bound amine−amide exchange and/or bound-free amine substrate or product exchange, which is rapid on the NMR time scale during catalytic turnover at room temperature and above. Analogous species were identified in variable-temperature NMR studies of aminoolefin hydroamination/cyclization,[7c] and one was characterized crystallographically.[7d] A reasonable, minimal scenario for the present catalytic mechanism is depicted in Scheme 2. Turnover-limiting insertion of alkyne into the Ln−N bond would be followed by rapid intramolecular or intermolecular protonolysis of the resulting Ln−C bond, which would afford tautomerizable (eq 2) enamines and regenerate $Cp'_2Ln\text{-}NR(CH_2)_nC{\equiv}CR'$ species.

Substituent, Metal, and Ancillary Ligation Effects on the Catalytic Process. As discussed above, the turnover frequencies for the organolanthanide-catalyzed cyclization of variously substituted aminoalkynes exhibit marked substituent effects under constant catalyst and reaction conditions. For 4-pentynyl substrates, N_t decreases in the order $SiMe_3 > H > CH_3 \geq Ph > CH_2{=}CMeCH_2$. For the sterically bulky, but transition state-

(26) For a comparison of nucleophilic additions to 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.

(27) For a terminal acetylene, the reaction with a Cp'_2LnNHR complex to yield a $Cp'_2LnC{\equiv}CR$ complex and H_2NR is estimated from thermochemical data[11−13] to be slightly exothermic by ~7 kcal/mol. Apparently this pathway is not competitive with the far more exothermic insertion of the acetylene into the Ln−N bond.

stabilizing $SiMe_3$ group, the turnover frequency is $\gtrsim$7600 h^{-1} at room temperature using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst (Table 1, entry 5), while N_t decreases to 580 h^{-1} for less sterically encumbered and less electronically distinctive 4-pentyn-1-amine. A similar but less dramatic decline in rate is observed in the cyclization of secondary amines, where the turnover frequency decreases from 56 to 27 h^{-1} (Table 1, entries 8 and 9) and from 129 to 47 h^{-1} (Table 1, entries 10 and 11) upon changing the substituent from $SiMe_3$ to H. For sterically and electronically less distinctive substituents such as Ph and alkyl (CH_3, $CH_2{=}CMeCH_2$), steric impediments appear to have an important effect on the cyclization rates, suggesting a combination of intrasubstrate-based steric encumbrance to cyclization within the metal coordination sphere, electronic stabilization of the transition state, and differing steric interactions between substituted alkynyl groups and the metal ancillary ligands.

In the case of aminoolefin cyclization, the reaction rates increase with increasing Ln ionic radius and more "open" lanthanide coordination spheres.[7c,d] An analogous enhancement with large metal ions and more open coordination spheres has also been observed for organo-f-element-mediated olefin hydrosilylation,[14c,d] hydrophosphination,[7e] olefin hydrogenation,[7c,14g−j,18b,28] and olefin polymerization,[19a,d,28c] arguing for a sterically demanding transition state in turnover-limiting olefin insertion into Ln−X bonds (X = H, P, C). Interestingly, and in marked contrast to these olfein insertion reactions, the present process involving alkyne insertion reactions clearly reveals a modest *deceleration* rather than an *acceleration* in rates when the larger lanthanide ions and more open $Me_2SiCp''_2Ln-$ coordinate spheres are used as the catalysts (Tables 1 and 3). It would appear that the steric demands in lanthanide-mediated alkyne insertions are considerably relaxed. The results likely reflect a combination of smaller substrate C≡C steric bulk, differences in number and/or orientation of substrate coordination,[7d] and, in a Hammond-type picture,[29] a more reactant-like, sterically distinct transition state for such an exothermic insertion process.

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Conclusions

The evidence presented here shows that organolanthanide centers are competent for the efficient, regioselective insertion of alkynes into metal−amide bonds and that such processes can be incorporated into efficient catalytic cycles for the hydroamination/cyclization of a variety of aminoalkynes. The present process provides an efficient method for the catalytic synthesis of pyrrole, pyridine, and azepin derivatives. The catalytic reaction scope includes primary amines, secondary amines, terminal alkynes, and internal alkynes. The turnover frequencies for this organolanthanide-catalyzed aminoalkyne cyclization are found to be highly dependent on substrate substituents, on the size of the lanthanide ion, and on the catalyst ancillary ligation. Compared to the corresponding aminoolefin cyclizations, a similar mechanism and rate law appear operative. Nevertheless, substantially different metal, ancillary ligation, and substrate substituent effects are observed in the present catalytic cyclizations.

Acknowledgment. We thank NSF for generous support of this research under Grant CHE9104112. We thank Dr. I. D. L. Albert for the AM-1 calculations.

JA9612413

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