Organolanthanide-Catalyzed Intra- and Intermolecular Tandem C−N and C−C Bond-Forming Processes of Aminodialkenes, Aminodialkynes, Aminoalkeneynes, and Aminoalkynes. New Regiospecific Approaches to Pyrrolizidine, Indolizidine, Pyrrole, and Pyrazine Skeletons

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Abstract: This contribution describes catalytic tandem C−N and C−C bond-forming reactions involving the intramolecular hydroamination/bicyclization and intermolecular hydroamination/cyclization of olefins and alkynes using the organolanthanide complexes $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ ($Cp' = \eta^5$-Me_5C_5; $Cp'' = \eta^5$-Me_4C_5; Ln = lanthanide) as precatalysts. In the case of the intramolecular processes, substrates of the structures $RC{\equiv}C(CH_2)_aNH(CH_2)_bC{\equiv}CR$, $RC{\equiv}C(CH_2)_cNH(CH_2)_dCH{=}CH_2$, and $H_2C{=}CH{-}(CH_2)_e$-$NH(CH_2)_fCH{=}CH_2$ are regiospecifically bicyclized to the corresponding pyrrolizidine and indolizidine skeletons, with turnover frequencies ranging from 2 to 777 h^{-1} at 21 °C and isolated product yields ranging from 85 to 93%. In the case of $e = 3$ and $f = 1$ mediated by Cp'_2Sm-, the kinetic rate law is zero-order in substrate concentration and first-order in lanthanide concentration. In the case of R = Ph, $c = 3$, and $d = 1$, the Cp'_2Ln-catalyzed turnover frequencies fall precipitously with decreasing Ln^{+3} ionic radius. In the intermolecular processes, substrates of the type $HC{\equiv}CCH_2NHR$ undergo regiospecific coupling and cyclization to the corresponding pyrroles $MeCC(H){=}C(\overline{CH_2}NHR)N(R)CH$ with high turnover frequencies where R and N_t (h^{-1}) are the following: $CH_2{=}CHCH_2$, 236 (60 °C); $CH_3CH_2CH_2$, 208 (60 °C); $CH_2{=}CHCH_2CH_2CH_2$, 58 (60 °C). In addition, hydroamination/cyclization processes after intermolecular insertion can be effected when R = $CH_2{=}CHCH_2$, to afford a 2,7-dimethyldipyrrolo[1,2-*a*:1′,2′-*d*]pyrazine derivative via two successive intramolecular olefin insertion processes. The mechanism for such tandem C−N and C−C bond formations is postulated to involve turnover-limiting intra- or intermolecular alkene/alkyne insertion into the Ln−N functionality, followed by rapid intramolecular insertion of a pendant C=C/C≡C-containing functionality into the resulting Ln−C bond (prior to protonolysis). Such a scenario is consistent with well-documented, stepwise transformations in organo-f-element-catalyzed insertions of unsaturated carbon−carbon multiple bonds into metal−amide and metal−alkyl functionalities.

Introduction

Carbon−nitrogen and carbon−carbon bond-forming reactions are important fundamental transformations in synthetic chemistry. Such reactions are in general most useful and efficient when performed catalytically, rather than stoichiometrically.[1,2] Catalytic carbon−carbon bond-forming transformations mediated by early and late transition metal catalysts have been studied extensively.[1,3,4] The addition of N−H bonds to unsaturated carbon−carbon functionalities (hydroamination) can likewise be catalyzed by a variety of metal complexes.[1,2,5−7] The

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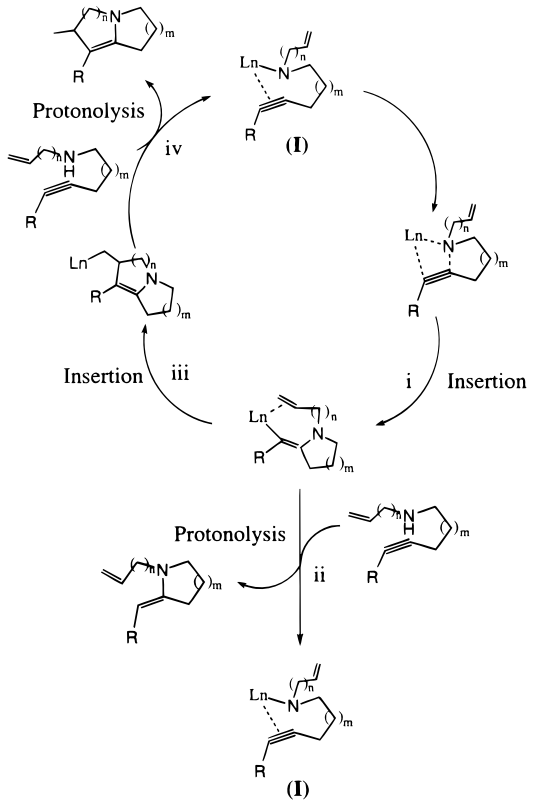
feasibility of such transformations therefore raises the interesting question of whether individual C−N and C−C bond-forming steps can be coupled in sequence to assemble more elaborate polycyclic, heteroatom-containing skeletons (e.g., pyrrole, pyrrolizidine, indolizidine, pyrazine, and other alkaloid frameworks)[8−10] using a single metal center in a single catalytic cycle. In this regard, lanthanide metal centers[11] exhibit a number of distinctive as well as potentially informative and useful characteristics for the activation not only of unsaturated carbon−carbon multiple bonds but of amine groups as well. The unique characteristics of lanthanide ions include high electrophilicity, very large ionic radii (resulting in high coordination numbers and coordinative unsaturation), relatively constrained/immobile yet tunable ancillary ligation, and facile bond activation via concerted four-centered σ bond metathesis processes rather than by conventional two-electron oxidative addition/reductive elimination sequences.

Scheme 1. Possible Scenarios for Organolanthanide-Catalyzed Aminoalkenyne Hydroamination/Cyclization



The facility of organolanthanide-catalyzed hydroamination/cyclization via olefin or alkyne insertion into the Ln−N bonds followed by rapid protonolysis (e.g., eqs 1 and 2; Cp′ = η^5-Me_5C_5; Ln = lanthanide) has been recently documented and mechanistically characterized (e.g., Scheme 1, steps i and ii).[6,7] It would therefore be of interest to determine if an alternative process (Scheme 1, step iii) to protonolysis (Scheme 1, step ii) could be coupled with metal−alkyl/alkenyl bond formation (Scheme 1, step i) to effect additional bond-forming processes (Scheme 1, steps i + iii).

Organolanthanide complexes of the type Cp'_2LnR (R = H, $CH(SiMe_3)_2$) are highly efficient catalysts for olefin insertion processes, exhibiting, for example, turnover frequencies in excess of 1500 s^{-1} at 25 °C and 1 atm of pressure for ethylene polymerization.[3j,12] Similar rapid processes involving intramolecular olefin insertions into Ln−C bonds might conceivably

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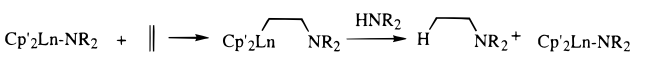
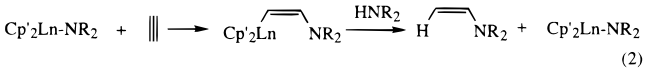
be competitive with Ln−C protonolysis in Scheme 1 (step ii). To test this hypothesis, a variety of bisunsaturated secondary amines were synthesized and investigated in catalytic reactions designed to facilitate tandem and sequential C−N and C−C bond-forming transformations.[3a]

Although the direct intermolecular addition of amines to olefins or alkynes is a priori an attractive transformation in organic synthesis, such simple hydroamination processes have not generally proven to be efficient and frequently lack generality as well as regioselectivity.[2,5e] The catalysts for these simple additions include alkali metals,[2,13] solid acids,[14] and late transition metals[15] which activate either the amine or carbon−carbon multiple bond functionality. However, efficient homogeneous processes are rare.[5d,6a,15,16] Of the effective intermolecular hydroamination processes, organolanthanide-mediated transformations offer some promise with significant turnover frequencies compared to most transition metal-catalyzed processes (eqs 1 and 2). Despite this, there remain problems



(1)



(2)

associated with limited reaction rates since a large excess of more nucleophilic amine substrates inhibits olefin or alkyne interactions with the strongly Lewis acidic metal centers, thereby retarding carbon−carbon multiple-bond insertions. An attractive alternative approach would be to employ olefin and alkyne substrates also containing a pendant Lewis basic group, such as an amine moiety, to temporarily anchor the substrate at the metal center. This would be expected to facilitate activation of the unsaturated carbon−carbon multiple bond by proximity within the lanthanide coordinative sphere. There is substantial precedent for $L_2LnNRR'(HNRR')$ adducts in organolanthanide chemistry (L = cyclopentadienyl-type ligand).[6b,c] Furthermore, if this approach were coupled with a subsequent rapid insertive C−C bond-forming process, the resulting two reactions (intermolecular C−N bond and intramolecular C−C bond formation) would afford pyrrole-type heterocycles in the same catalytic reaction and provide a new type of tandem inter- + intramolecular coupling reaction.

In this contribution, we present the first investigation of tandem C−N and C−C bond-forming processes catalyzed by organolanthanides.[3a] A full discussion of efficient, regiospecific intramolecular hydroamination/bicyclization and intermolecular hydroamination/cyclization within organolanthanide coordination spheres, including an investigation of reaction scope and metal ion size effects as well as kinetics and mechanism, is presented.

Experimental Section

Materials and Methods. All manipulations of air-sensitive materials were carried out with rigorous exclusion of oxygen and moisture using methodologies described previously.[6,7] Argon (Matheson, prepurified) was purified by passage through a MnO oxygen-removal column[17] and a Davison 4 A molecular sieve column. Before use, all solvents were distilled under dry nitrogen over appropriate drying agents (sodium benzophenone ketyl, metal hydrides, or 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 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, when appropriate, were distilled prior to use. For intramolecular hydroamination/bicyclization reactions, the substrates *N*-allyl-4-pentyn-1-amine[7b] (**5**), *N*-allyl-5-(trimethylsilyl)-4-pentyn-1-amine[7b] (**7**), *N*-4-penten-5′-(trimethylsilyl)-4′-pentyn-1-amine[7b] (**9**), *N*-4-pentyn-4′-penten-1-amine[7b] (**11**), and *N*-allyl-4-penten-1-amine[18] (**15**) were synthesized according to literature procedures. The new compounds *N*-allyl-5-phenyl-4-pentyn-1-amine (**1**), *N*-allyl-4-hexyn-1-amine (**3**), *N*-2-butyn-4′-hexyn-1-amine (**13**), *N*-allyl-5-hexen-1-amine (**17**), *N*-2-butyn-4′-penten-1-amine (**19**), *N*-3-(trimethylsilyl)-2-propyn-4′-penten-1-amine (**21**), and *N*-4-(trimethylsilyl)-3-butyn-4′-penten-1-amine (**23**) were synthesized via modifications of literature methods as described below. Substrates **1**, **3**, **7**, **9**, **13**, **15**, **17**, **19**, **21,** and **23** were dried by stirring over CaH_2, and substrates **5** and **11** were dried by stirring over BaO. All were then additionally dried by repeated vacuum transfer onto and from, freshly activated Davison 4 A molecular sieves, were degassed by freeze−pump−thaw cycles, and were finally stored in vacuum-tight containers. For intermolecular hydroamination/cyclization reactions, *N*-allyl-*N*-propargylamine (**25**), *N*-*n*-propyl-*N*-propargylamine (**27**), and *N*-4-pentenyl-*N*-propargylamine (**29**) were synthesized via modifications of literature methods as described below and were dried in a manner analogous to **5** and **11** above. The organolanthanide precatalysts $Cp'_2LnCH(SiMe_3)_2$ (Ln = La, Nd, Sm, Lu; Cp′ = η^5-Me_5C_5)[12a] and $Me_2SiCp''_2LnCH(SiMe_3)_2$ (Cp″ = η^5-Me_4C_5)[12b] were prepared by published procedures.

Physical and Analytical Measurements. NMR spectra were recorded on either a Varian VXRS 300 (FT, 300 MHz (^{1}H), 75 MHz (^{13}C)) or UNITYplus 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 detection 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 an MCT detector. Melting and boiling points are uncorrected.

Synthesis of *N*-Allyl-5-phenyl-4-pentyn-1-amine (1). A solution of 50.0 g (0.477 mol) of phenylacetylene in 200 mL of THF was treated with 0.477 mol of *n*-BuLi at 0 °C over a period of 2 h, warmed to room temperature, and stirred for 2 h. After the resulting solution was cooled to −78 °C, 110.0 g (0.534 mol) of $BrCH_2CH_2CH_2Br$ was rapidly

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syringed into the stirring solution and the mixture was stirred for 2 h at −78 °C, warmed to room temperature for 2 h, and then refluxed overnight. Next, 150 mL of water was poured into the cooled mixture, the organic phase was separated off, and the aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic phase and diethyl ether extracts were dried over $MgSO_4$ and filtered, and the solvents were removed by rotary evaporation. Distillation (111−114 °C/0.17 Torr) of the residue gave 41.7 g (39% yield) of $PhC{\equiv}CCH_2CH_2CH_2Br$. A solution of 19.0 g (0.085 mol) of 1-bromo-5-phenyl-4-pentyne and 34.0 g (0.590 mol) of allylamine in a sealed 150-mL storage tube was heated at 60 °C for 4 days. The reaction mixture was then poured into 250 mL of water, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phase and ether solution were dried over $MgSO_4$ and filtered, and the ether and excess allylamine were removed by rotary evaporation. Distillation (127−129 °C/0.15 Torr) gave **1** as a colorless oil (14.0 g, 83% yield).

^{1}H NMR (300 MHz, C_6D_6): δ 7.45 (m, 2H, Ph), 6.94 (m, 3H, Ph), 5.79 (m, 1H, CH═), 5.11−4.93 (m, 2H, CH_2═), 2.98 (d, J = 6.0 Hz, 2H, NCH_2−CH═), 2.47 (t, J = 6.8 Hz, 2H, CH_2N), 2.29 (t, J = 7.1 Hz, 2H, ≡C−CH_2), 1.52 (m, 2H, CH_2), 0.49 (br, 1H, NH). ^{13}C (75 MHz, C_6D_6): δ 137.6, 131.5, 128.1, 127.3, 124.4, 114.6, 90.2, 81.1, 52.2, 48.0, 29.2, 17.1. MS (relative abundance): M^+ (45), $M^+ - 1$ (86), $M^+ + 1$ (7), 184.1 (62), 172.1 (57), 156.0 (22), 141.0 (34), 128.0 (37), 115.0 (54), 91.0 (14), 82.0 (13), 70.0 (100), 56.0 (11), 41.0 (68). HRMS: Calcd for $C_{14}H_{17}N$: 199.1361. Found: 199.1351.

Synthesis of *N*-Allyl-4-hexyn-1-amine (3). A solution of 6.6 g (0.056 mol) of 1-chloro-4-hexyne and 50.0 g (0.86 mol) of allylamine was heated in a sealed tube at 60 °C for 1 week. After the solution was cooled to room temperature and poured into a separatory funnel containing 200 mL of diethyl ether and 30 mL of H_2O, the aqueous phase was separated and extracted with 3 × 100-mL portions 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 (108−110 °C) gave **3** as a colorless oil (6.0 g, 77% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.89 (m, 1H, CH═), 5.10 (m, 2H, CH_2═), 3.32 (d, J = 6.0 Hz, 2H, NCH_2CH═), 2.68 (t, J = 7.1 Hz, 2H, NCH_2), 2.16 (m, 2H, CH_2), 1.47 (br, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.8, 115.8, 78.6, 75.8, 52.3, 48.4, 29.1, 16.6, 3.45. MS (relative abundance): M^+ (25), $M^+ + 1$ (3), 122.1 (69), 110.1 (33), 94.1 (19), 79.1 (12), 70.1 (100), 53.1 (16), 41.1 (81). HRMS: Calcd for $C_9H_{14}N$ ($M^+ - H$): 136.1126. Found: 136.1122.

Preparation of *N*-2-Butynyl-4′-hexyn-1-amine (13). (a) 2-Butyn-1-amine. A suspension of 79.0 g (1.20 mol) of NaN_3 in 200 mL of DMF was treated dropwise at 25 °C for 30 min with 21.4 g (0.024 mol) of 2-butynyl 1-chloride, which was generated from 2-butynol (49.0 g, 0.699 mol), thionyl chloride (90.0 g, 0.756 mol), and 0.3 mL of pyridine in 250 mL of boiling anhydrous diethyl ether in the usual manner.[19] The mixture was stirred overnight, the precipitate removed by filtration, and the filtrate poured into a separatory funnel containing 800 mL of diethyl ether. The ether layer was washed with water (200 mL) and brine (100 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation to afford $CH_3C{\equiv}CCH_2N_3$, which was used immediately in the next step. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.88 (s, 2H, CH_2), 1.90 (s, 3H, CH_3). The $CH_3C{\equiv}CCH_2N_3$ in 150 mL of anhydrous diethyl ether was treated dropwise with LAH (0.177 mol, 4 equiv) in 50 mL of anhydrous diethyl ether at 0 °C for 30 min and then stirred for 30 min. The resulting mixture was quenched by careful addition of wet diethyl ether (ca. 200 mL) and a few drops of H_2O. After separation, the organic phase was washed with 200 mL of brine, dried over $MgSO_4$, filtered, concentrated with a rotary evaporator, and distilled at 110−112 °C to give 9.1 g (55% yield) of the title compound.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.35 (q, ^5J = 1.8 Hz, 2H, NCH_2), 1.78 (t, ^5J = 1.8 Hz, 3H, CH_3), 1.39 (br, 2H, NH_2).

(b) *N*-2-Butynyl-4′-hexyn-1-amine. To a solution of 12.0 g (0.068 mol) of crude 4-hexyn-1-yl methanesulfonate[19] and 200 mg of NaI in 40 mL of anhydrous DMSO was added 9.5 g (0.138 mol) of 2-butynyl-1-amine under Ar at room temperature. The reaction mixture was then heated in an oil bath at 55 °C for 5 h until the starting material was consumed (TLC monitoring) and then allowed to cool to 25 °C. The reaction mixture was poured into a separatory funnel containing 500 mL of aqueous NaOH solution (1%). The resulting solution was extracted with diethyl ether (3 × 200 mL). The combined ether extracts were washed with brine (50 mL), dried over $MgSO_4$, filtered, concentrated with a rotary evaporator, and purified by flash chromatography (hexane:diethyl ether = 1:1). After distillation (126−128 °C/19 Torr), 7.4 g (81% yield) of $CH_3C{\equiv}CCH_2CH_2CH_2NHCH_2C{\equiv}CCH_3$ was obtained as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 3.19 (m, 2H, $NCH_2C{\equiv}C$), 2.61 (t, J = 6.9 Hz, 2H, NCH_2), 2.11 (m, 2H, $CH_2C{\equiv}C$), 1.54−144 (m, 8H, CH_2, $2CH_3$), 0.53 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 79.3, 78.4, 78.2, 75.6, 47.9, 38.8, 29.7, 16.9, 3.4, 3.3. MS (relative abundance): M^+ (12), $M^+ - 1$ (35), $M^+ - 2$ (3), 134.1 (100), 120.1 (19), 106.1 (17), 94.1 (10), 82.1 (48), 68.1 (7), 53.1 (52), 42.0 (16). HRMS: Calcd for $C_{10}H_{14}N$ ($M^+ - H$): 148.1126. Found: 148.1110.

Synthesis of *N*-Allyl-4-penten-1-amine (15). A mixture of 25.0 g (0.168 mol) of 5-bromo-1-pentene and 38.0 g (0.64 mol) of allylamine in a sealed 150-mL storage tube was heated at 60 °C for 4 days. After the reaction mixture was poured into 250 mL of water, the organic layer was separated off and the aqueous phase washed with diethyl ether (3 × 50 mL). The combined organic phase and ether solution was dried over $MgSO_4$ and filtered, and the ether and excess allylamine were removed by rotary evaporation. Distillation (70−71 °C/25 Torr; lit.[18] bp 149−150 °C) of the residue gave 36.0 g (72% yield) of $CH_2{=}CHCH_2CH_2CH_2NHCH_2CH{=}CH_2$ as a colorless oil. The NMR data agree well with published data.[18]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.95 (m, 1H, NCH_2CH═), 5.85 (m, 1H, CH═), 5.14 (m, 2H, $NCH_2CH{=}CH_2$), 5.01 (m, 2H, CH_2═), 3.28 (d, J = 6.0 Hz, 2H, NCH_2CH═), 2.66 (t, J = 7.2 Hz, 2H, NCH_2), 2.13 (m, 2H, ═CH−CH_2), 1.63 (m, 2H, CH_2), 1.05 (br, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.0, 136.7, 115.2, 114.2, 52.1, 48.5, 31.2, 28.9. MS (relative abundance): $M^+ - 1$ (3), 110.1 (3), 97.1 (5), 84.1 (9), 82.1 (10), 70.1 (100), 65.1 (8), 42.0 (9). HRMS: Calcd for $C_8H_{14}N$ ($M^+ - H$): 124.1126. Found: 124.1117.

Synthesis of *N*-Allyl-5-hexen-1-amine (17). A procedure similar to that for **15** was used for *N*-allyl-5-hexenamine via reaction of 6-bromo-1-hexene (4.9 g, 0.030 mol) with allylamine (38.0 g, 0.570 mol). Distillation (119−121 °C/134 Torr) of the residue gave 3.0 g (72% yield) of $CH_2{=}CHCH_2CH_2CH_2CH_2NHCH_2CH{=}CH_2$ as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87 (m, 1H, NCH_2CH═), 5.77 (m, 1H, CH═), 5.11 (m, 2H, $NCH_2CH{=}CH_2$), 4.94 (m, 2H, CH_2═), 3.22 (d, J = 6.9 Hz, 2H, NCH_2CH═), 2.59 (t, J = 7.1 Hz, 2H, NCH_2), 2.04 (m, 2H, CH_2−CH═), 1.59 (br, 1H, NH), 1.49 (m, 2H, CH_2CH_2N), 1.39 (m, 2H, $CH_2CH_2CH_2N$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.7, 136.7, 115.9, 114.5, 52.4, 49.2, 33.6, 29.5, 26.6. MS (relative abundance): M^+ (7), $M^+ + 1$ (1), 110.1 (5), 96.1 (15), 84.1 (7), 70.0 (100), 56.0 (12), 41.0 (57). HRMS: Calcd for $C_9H_{16}N$ ($M^+ - H$): 138.1283. Found: 138.1285.

Preparation of *N*-2-Butynyl-4′-penten-1-amine (19). (a) 4-Penten-1-yl Methanesulfonate. A mixture of 9.9 g (0.12 mol) of 4-penten-1-ol and 26 mL of Et_3N in 300 mL of CH_2Cl_2 was cooled to ca. −5 °C, and 9.7 mL (0.13 mol) of methanesulfonyl chloride was slowly added over a period of 10 min. The solution was then stirred at ca. −5 °C for 40 min, and 40 mL of ice water was added to quench the reaction. The organic phase was separated and washed successively with 50 mL of 1 M HCl, 50 mL of saturated Na_2CO_3 solution, and 50 mL of brine and was then dried over $MgSO_4$. The solvent was removed from the filtrate by rotary evaporation to afford 18.5 g (98% yield) of $CH_2{=}CHCH_2CH_2CH_2OSO_2Me$ as a coloreless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.76 (m, 1H, CH═), 5.03 (m, 2H, CH_2═), 4.22 (t, J = 6.5 Hz, 2H, CH_2O), 2.99 (s, 3H, Me), 2.16 (m, 2H, CH_2CH═), 1.84 (m, 2H, CH_2).

(b) *N*-2-Butynyl-4′-penten-1-amine. Using a method similar to that for *N*-2-butynyl-4′-hexyn-1-amine (**9**), the title compound was prepared using 6.0 g (0.087 mol) of 2-butyn-1-amine and 7.0 g (0.043 mol) of 4-penten-1-yl methanesulfonate in 45 mL of anhydrous DMSO. By

(19) Arnold, H.; Overman, L. E.; Sharp, M. J.; Witschel, M. C. In *Organic Syntheses*; Meyers, A. I., Ed.; John Wiley & Sons Inc.: New York, 1992; Vol. *70*, pp 111−119.

following the procedure above, distillation (101−104 °C/25 Torr) gave **19** as a colorless oil (3.6 g, 62% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.80 (m, 1H, CH═), 4.97 (m, 2H, CH_2═), 3.35 (q, ^5J = 2.3 Hz, 2H, $NCH_2C{\equiv}C$), 2.66 (t, J = 7.2 Hz, 2H, CH_2N), 2.08 (m, 2H, CH_2C═), 1.80 (t, ^5J = 2.4 Hz, 3H, CH_3), 1.57 (m, 2H, CH_2), 1.02 (br, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 114.6, 78.7, 77.2, 48.3, 38.6, 31.5, 29.0, 3.5. MS (relative abundance): M^+ (4), $M^+ - 1$ (21), $M^+ - 2$ (2), $M^+ + 1$ (2), 122.1 (23), 108.0 (13), 94.0 (21), 82.0 (100), 70.0 (25), 53.0 (53), 42.0 (23). HRMS: Calcd for $C_9H_{14}N$ ($M^+ - H$): 136.1126. Found: 136.1122.

Preparation of *N*-3-(Trimethylsilyl)-2-propynyl-4′-penten-1-amine (21). A solution of 105.0 g (1.41 mol) of $HC{\equiv}CCH_2Cl$ in 300 mL of THF was treated with *n*-BuLi (1.41 mol) at −78 °C with stirring over a period of 2 h before 160.0 g (1.44 mol) of Me_3SiCl was injected into the reaction mixture. The solution was warmed to 25 °C, stirred for 2 h, and then heated at 60 °C for 1 h. The reaction mixture was cooled to 25 °C and poured into a separatory funnel containing 150 mL of H_2O. After separation, the aqueous phase was extracted with 3 × 150 mL of $CHCl_3$ and the combined extracts and organic phase were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Distillation (134−136 °C) afforded 128.5 g (62% yield) of $Me_3SiC{\equiv}CCH_2Cl$ as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.15 (s, 2H, CH_2), 0.19 (s, 9H, $SiMe_3$).

A stirring solution of 12.2 g (0.14 mol) of 4-penten-1-amine in 70 mL of anhydrous THF was treated dropwise by syringe with 5.0 g (0.034 mol) of $ClCH_2C{\equiv}CSiMe_3$ at 0 °C over a period of 20 min. The resulting mixture was stirred overnight at 25 °C before being poured into a separatory funnel containing 200 mL of H_2O. After separation, the aqueous phase was extracted with 3 × 150 mL of diethyl ether. The combined ethereal extracts and organic phase were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Distillation (128−130 °C/30 Torr) gave 2.5 g (38% yield) of the title compound as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.81 (m, 1H, CH═), 4.96 (m, 2H, CH_2═), 3.41 (s, 2H, $NCH_2C{\equiv}$), 2.66 (t, J = 7.4 Hz, 2H, CH_2N), 2.09 (m, 2H, CH_2C═), 1.57 (m, 2H, CH_2), 1.19 (br, 1H, NH), 0.14 (s, 9H, $SiMe_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.4, 114.7, 104.6, 87.7, 48.2, 39.2, 31.5, 29.0, 0.02. MS (relative abundance): M^+ (12), $M^+ - 1$ (12), $M^+ + 1$ (4), 180.1 (41), 166.1 (10), 152.1 (16), 140.1 (100), 122.1 (40), 11.0 (48), 97.0 (14), 83.0 (49), 73.0 (41), 63.0 (3), 41.0 (16). HRMS: Calcd for $C_{11}H_{21}NSi$: 195.1443. Found: 195.1434.

Preparation of *N*-4-(Trimethylsilyl)-3-butynyl-4′-penten-1-amine (23). A solution of 30.0 g (0.31 mol) of $Me_3SiC{\equiv}CH$ in 200 mL of THF was treated with *n*-BuLi (0.31 mol) at −78 °C with stirring over a period of 2 h before 44.6 g (0.310 mol) of $BrCH_2CH_2Cl$ was injected into the reaction mixture. The solution was warmed to 25 °C and stirred for 2 h, then heated at 60 °C for 2 h. The reaction mixture was next cooled to 25 °C and poured into a separatory funnel containing 200 mL of H_2O. After separation, the aqueous phase was extracted with 3 × 150 mL of $CHCl_3$ and the combined extracts and organic phase were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Distillation (145−148 °C) afforded 7.6 g (16% yield) of $Me_3SiC{\equiv}CCH_2CH_2Cl$ as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.47 (t, J = 7.4 Hz, 2H, CH_2Cl), 2.56 (t, J = 7.5 Hz, 2H, CH_2), 0.05 (s, 9H, $SiMe_3$).

A mixture of 20.0 g (0.23 mol) of 4-penten-1-amine and 2.4 g (0.015 mol) of $Me_3SiC{\equiv}CCH_2CH_2Cl$ in a sealed storage tube was heated at 60 °C for 4 days before being poured into a separatory funnel containing 100 mL of H_2O. After separation, the aqueous phase was extracted with 3 × 50 mL of CH_2Cl_2. The combined extracts and organic phase were washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Distillation (138−140 °C/39 Torr) gave **23** as a colorless oil (1.1 g, 35% yield).

^{1}H NMR (300 MHz, C_6D_6): δ 5.69 (m, 1H, CH═), 4.95 (m, 2H, CH_2═), 2.53 (t, J = 6.8 Hz, 2H, $NCH_2CH_2C{\equiv}$), 2.32 (t, J = 7.1 Hz, 2H, CH_2N), 2.20 (t, J = 6.8 Hz, 2H, $CH_2C{\equiv}$), 1.94 (m, 2H, CH_2C═), 1.34 (m, 2H, CH_2), 0.63 (br, 1H, NH), 0.17 (s, 9H, $SiMe_3$). ^{13}C NMR (75 MHz, C_6D_6): δ 138.9, 114.6, 106.3, 85.6, 48.8, 48.6, 31.8, 29.7, 21.6, 0.29. MS (relative abundance): M^+ (2), 194.2 (3), 154.2 (7), 98.1 (100), 73.1 (19), 44.1 (39), 41.1 (15). HRMS: Calcd for $C_{12}H_{23}NSi$: 209.1600. Found: 209.1602.

Synthesis of *N*-Allylpropargylamine (25). A mixture of 7.0 g (0.092 mol) of propargyl chloride and 38.1 g (0.666 mol) of allylamine in a sealed 150-mL storage tube was heated at 60 °C for 2 days. The reaction mixture was then poured into a separatory funnel containing 100 mL of water and 200 mL of diethyl ether, the organic layer was separated off, and the aqueous phase was extracted with 3 × 150 mL of diethyl ether. The combined organic phase and ether solution was then dried over $MgSO_4$ and filtered, and the ether and excess allylamine were removed by rotary evaporation. Distillation (119−121 °C) of the residue gave 5.8 g (66% yield) of $CH_2{=}CHCH_2NHCH_2C{\equiv}CH$ as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 5.75−5.64 (m, 1H, C*H*═), 5.08−4.89 (m, 2H, CH_2═), 3.10 (d, ^4J = 2.4 Hz, 2H, $NCH_2C{\equiv}$), 3.07 (dt, ^4J = 1.5 Hz, 2H, CH_2N), 1.98 (t, ^4J = 2.3 Hz, 1H, HC≡), 0.82 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 136.9, 115.9, 82.7, 71.5, 50.9, 37.4. MS (relative abundance): M^+ (23), $M^+ + 1$ (3), $M^+ - 1$ (100), 80.0 (62), 68.0 (86), 56.1 (32), 52.0 (8), 39.0 (67). HRMS: Calcd for C_6H_8N ($M^+ - H$): 94.0657. Found: 94.0647.

Synthesis of *N*-*n*-Propylpropargylamine (27). A procedure similar to that for **1** above was used to synthesize *N*-*n*-propylpropargylamine by reaction of propargyl chloride (7.0 g, 0.092 mol) and *n*-propylamine (36.0 g, 0.608 mol). Distillation (110−112 °C) of the residue gave 5.0 g (56% yield) of $CH_3CH_2CH_2NHCH_2C{\equiv}CH$ as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 3.11 (d, ^4J = 2.7 Hz, 2H, $NCH_2C{\equiv}$), 2.40 (t, J = 7.1 Hz, 2H, CH_2N), 1.93 (t, ^4J = 2.4 Hz, 1H, HC≡), 1.26 (m, 2H, CH_2), 0.75 (t, J = 7.5 Hz, 3H, CH_3), 0.53 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 83.0, 71.1, 50.6, 38.3, 24.3, 11.9. MS (relative abundance): M^+ (12), $M^+ + 1$ (1), $M^+ - 1$ (2), 68.1 (100), 54.0 (7), 41.0 (29). HRMS: Calcd for $C_6H_{11}N$: 97.0891. Found: 97.0886.

Synthesis of *N*-Propargyl-4-penten-1-amine (29). A procedure similar to that for **1** above was used to synthesize *N*-propargyl-4-penten-1-amine from reaction of propargylamine (24.8 g, 0.449 mol) with 1-bromo-4-pentene (6.8 g, 0.0456 mol). Distillation (107−108 °C/55 Torr) of the residue gave 5.0 g (89% yield) of $CH_2{=}CHCH_2CH_2CH_2NHCH_2C{\equiv}CH$ as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 5.72 (m, 1H, CH═), 4.96 (m, 2H, CH_2═), 3.12 (d, ^4J = 2.5 Hz, 2H, $NCH_2C{\equiv}$), 2.46 (t, J = 7.0 Hz, 2H, CH_2N), 1.93 (m, 2H, CH_2C═), 1.90 (m, 1H, HC≡), 1.33 (m, 2H, CH_2), 0.48 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 138.8, 114.6, 82.9, 71.1, 48.1, 38.3, 31.7, 29.3. MS (relative abundance): M^+ (1), $M^+ + 1$ (1), $M^+ - 1$ (9), 108.1 (3), 94.0 (8), 80.0 (17), 68.0 (100), 54.0 (5), 41.0 (30). HRMS: Calcd for $C_8H_{12}N$ ($M^+ - H$): 122.0970. Found: 122.0989.

Typical NMR-Scale Catalytic Hydroamination/Bicyclization Reactions. In the glovebox, the $Cp'_2SmCH(SiMe_3)_2$ precatalyst (1.8 mg, 3.1 μmol) was loaded into an NMR tube equipped with a Teflon valve. On the vacuum line, the NMR tube was evacuated and back-filled with argon three times. Benzene (∼0.2 mL) was then vacuum transferred into the tube. Next a mixture (∼0.4 mL) of benzene-d_6 and *N*-allyl-5-phenyl-4-pentyn-1-amine (**1**, 12.0 mg, 61.0 μmol) was added via syringe under an argon flash while the tube which was maintained at −78 °C to protect the precatalyst under the frozen benzene. The NMR tube was next evacuated and back-filled with argon three times at −78 °C and finally sealed. The ensuing catalytic reaction was monitored by ^{1}H NMR. Upon completion, the reaction mixture was then chromatographed on a small alumina column (200 mg, neutral) using diethyl ether (7.0 mL) as eluant to remove the catalyst. The eluate was concentrated by rotary evaporation to yield 8.1 mg (68% yield) of **2** as a colorless oil. The products were identified by ^{1}H, ^{13}C, DEPT, and 2D NMR as well as by GC/MS, and HRMS.

Typical Preparative-Scale Catalytic Hydroamination/Bicyclization Reactions. In the glovebox, 49.0 mg (85 μmol) of $Cp'_2NdCH(SiMe_3)_2$ and 4.0 mL of C_6H_6 were loaded into a reaction vessel (30 mL) equipped with a magnetic stirbar. Next, 2.0 mL of a mixture of *N*-allyl-4-hexyn-1-amine (**3**, 0.116 g, 847 μmol, 10-fold molar excess) and benzene (∼1.9 mL) was added dropwise to the stirring precatalyst solution. The resulting reaction mixture was then allowed to stir for 1 h at room temperature before the second 2.0 mL of the amine substrate

mixture was added to the vessel. The procedure above was repeated until 0.58 g of *N*-allyl-4-hexyn-1-amine (4235 μmol, 50-fold molar excess) had been added to the vessel. The clear green solution was then stirred at 25 °C for 3 more days. The reaction mixture was next chromatographed on alumina (800 mg, neutral) using diethyl ether (30 mL) as the eluant to remove the catalyst. The eluate was concentrated by rotary evaporation to yield 0.51 g (88% yield) of 1-methyl-2-methylpyrrolizidine-8-ene (**4**) as a colorless oil. It was >95% pure by ^{1}H, ^{13}C NMR, and GC/MS.

Synthesis of 1-Phenyl-2-methylpyrrolizidin-8-ene (2). This compound was synthesized in both NMR and preparative-scale reactions. The typical preparative-scale reaction procedure described above was used with Cp′$_2$NdCH(SiMe$_3$)$_2$ (49.0 mg, 85 μmol) and **1** (0.575 g, 2890 μmol). Flash chromatography (diethyl ether) yielded **2** as a colorless oil (0.49 g, 85% yield).

^{1}H NMR (300 MHz, C_6D_6): δ 7.27−7.17 (m, 3H, Ph), 7.00−6.95 (m, 2H, Ph), 3.38 (m, 1H, CH), 2.84 (dd, ^3J = 8.7 Hz, ^2J = 2.4 Hz, 1H, NC*H*$_2$CH(ME)), 2.74 (dd, ^3J = 8.7 Hz, ^2J = 2.4 Hz, 1H, NC*H*$_2$-CHMe), 2.71 (m, 1H, NCH$_2$), 2.20 (m, 1H, CH$_2$C═), 2.08 (m, 1H, NCH$_2$), 2.05 (m, 1H, CH$_2$C═), 1.84 (m, 1H, NCH$_2$C*H*$_2$), 1.73 (m, 1H, NCH$_2$C*H*$_2$), 1.28 (d, J = 6.90 Hz, 3H, CH$_3$). ^{13}C NMR (75 MHz, C_6D_6): δ 153.5, 137.8, 129.1, 124.8, 123.5, 109.8, 60.0, 50.8, 43.3, 27.6, 25.1, 19.2. MS (relative abundance): M^+ (47), $M^+ - 1$ (9), $M^+ + 1$ (10), 184.1 (100), 156.1 (18), 128.1 (6), 115.0 (7). HRMS: Calcd for $C_{14}H_{17}N$: 199.1361. Found: 199.1373.

Synthesis of 1,2-Dimethylpyrrolizidin-8-ene (4). This pyrrolizidine derivative was prepared in both NMR and preparative-scale reactions. A procedure analogous to that for **2** above was used in the NMR-scale reaction using Cp′$_2$SmCH(SiMe$_3$)$_2$ (1.8 mg, 3.1 μmol) and *N*-allyl-4-hexyn-1-amine (**3**, 11.0 mg, 80.7 μmol). The reaction mixture was chromatographed on alumina (250 mg, neutral) using diethyl ether (5.0 mL) as eluant to remove the catalyst. The eluate was concentrated by rotary evaporation to yield 8.2 mg (75% yield) of **2** as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 3.15 (t, J = 8.0 Hz, 1H, N−C*H*$_2$−CH$_2$), 2.99 (m, 1H, C*H*−Me), 2.62 (m, 1H, N−C*H*$_2$), 2.33 (t, J = 8.4 Hz, 1H, N−C*H*$_2$−CH$_2$), 2.27 (m, 1H, N−C*H*$_2$), 1.99 (m, 2H, C*H*$_2$−C═), 1.84 (m, 2H, N−CH$_2$−C*H*$_2$), 1.62 (s, 3H, CH$_3$−C═), 1.07 (d, 3H, CH$_3$). ^{13}C NMR (77 MHz, C_6D_6): δ 150.2, 104.3, 61.9, 52.9, 46.7, 27.3, 21.1, 18.6, 11.3. MS (relative abundance): M^+ (36), $M^+ - 1$ (23), $M^+ + 1$ (4), 122.1 (100), 108.1 (7), 94.1 (16), 41.0 (7). HRMS: Calcd for $C_9H_{15}N$: 137.1204. Found: 137.1241.

Preparation of 1-Methyl-*Z*-2-ethylidenepyrrolizidin-8-ene (14) and 1-Methyl-2-ethyl-6,7-dihydro-5*H*-pyrrolizine (14a). A procedure analogous to that for **2** was used in the synthesis of bicyclic conjugated diene **14** with Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ (2.9 mg, 4.8 μmol) and *N*-2-butynyl-4′-hexyn-1-amine (**13**, 42.9 mg, 288.0 μmol). The yield (95%) was estimated by ^{1}H NMR and GC/MS after the product was isolated from the catalyst by vacuum transfer. The title compound was identified by NMR using^{1}H, ^{13}C, DEPT, 2D, and NOE difference techniques.

^{1}H NMR (300 MHz, C_6D_6): δ 4.80 (m, 1H, CH═), 3.60 (m, 2H, NCH$_2$C═), 2.47 (t, J = 6.6 Hz, 2H, NCH$_2$), 2.00 (t, J = 7.1 Hz, 2H, CH$_2$CN), 1.78 (m, 2H, CH$_2$), 1.61 (t, ^5J = 1.1 Hz, 3H, CH$_3$), 1.56 (td, ^5J = 2.1 Hz, 3H, CH$_3$). ^{13}C NMR (75 MHz, C_6D_6): δ 157.7, 150.1, 103.1, 100.9, 54.2, 50.1, 25.5, 21.3, 14.3, 9.1. MS (relative abundance): $M^+ + 1$ (7), M^+ (44), $M^+ - 1$ (18), 134.1 (100), 120.0 (8), 106.0 (8), 79.0 (7). HRMS: Calcd for $C_9H_{12}N$ ($M^+ - CH_3$): 134.0970. Found: 134.0945.

1-Methyl-(*Z*)-2-ethylidenepyrrolizidine-8-ene (**14**) was chromatographed on silica gel using diethyl ether as the eluent to yield the isomerization product **14a** in 95% yield.

^{1}H NMR (300 MHz, C_6D_6): δ 6.29 (s, 1H, CH), 3.27 (t, J = 6.9 Hz, 2H, NCH$_2$), 2.58 (q, J = 7.5 Hz, 2H, CH$_2$Me), 2.41 (t, J = 7.1 Hz, 2H, CH$_2$C═), 2.11 (s, 3H, CH$_3$), 1.80 (m, 2H, CH$_2$), 1.30 (t, J = 7.5 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (75 MHz, C_6D_6): δ 133.7, 129.5, 109.8, 107.1, 45.9, 27.6, 23.2, 19.9, 15.6, 10.0. MS (relative abundance): $M^+ + 1$ (7), M^+ (14), 134.1 (100), 120.1 (6), 106.1 (7), 91.1 (6), 84.1 (11), 77.0 (6), 43.0 (12). HRMS: Calcd for $C_{10}H_{15}N$: 149.1205. Found: 149.1210.

The typical preparative-scale reaction procedure described above was used in a reaction with Cp′$_2$NdCH(SiMe$_3$)$_2$ (49.0 mg, 85 μmol) and **13** (0.280 g, 1879 μmol). The reaction mixture was chromatographed on alumina (700 mg, neutral) using diethyl ether (20 mL) as the eluant to remove the catalyst. The eluate was concentrated by rotary evaporation to yield 0.26 g (92% yield) of **14** as a colorless oil.

Synthesis of *cis*- and *trans*-2-Methylpyrrolizidine (16a,b). These pyrrolizidine derivatives[18,20b,d] were synthesized in both NMR- and preparative-scale reactions. The Cp′$_2$SmCH(SiMe$_3$)$_2$ precatalyst (5.7 mg, 9.8 μmol) in benzene-d_6 (~0.4 mL) and *N*-allyl-4-pentenamine (58.8 mg, 470.0 μmol, 47-fold molar excess) were used for the NMR-scale reaction. The products were identified by ^{1}H and ^{13}C NMR and by GC/MS. The NMR data agree well with the literature data.[18,20c]

^{13}C NMR of *cis*-2-methylpyrrolizidine (**16a**) (75 MHz, ^{1}H-decoupled, C_6D_6): δ 64.6, 63.4, 56.7, 41.4, 34.0, 33.5, 27.3, 18.6. ^{13}C NMR of *trans*-2-methylpyrrolizidine (**16b**) (75 MHz, ^{1}H-decoupled, C_6D_6): δ 65.8, 64.5, 55.9, 42.9, 37.6, 32.9, 27.0, 18.0. The isomers exhibit indistinguishable mass spectra. MS (relative abundance): M^+ (55), $M^+ - 1$ (43), $M^+ + 1$ (6), 110.0 (23), 97.0 (59), 83.0 (100), 68.0 (9), 55.0 (70), 41.0 (24) for *trans*-2-methylpyrrolizidine (ca. 55% yield by ^{1}H NMR and GC). HRMS: Calcd for $C_8H_{15}N$: 125.1204. Found 125.1201. MS (relative abundance): M^+ (45), $M^+ - 1$ (30), $M^+ + 1$ (64), 110.0 (19), 97.0 (59), 83.0 (100), 68.0 (9), 55.0 (81), 41.0 (31) for *cis*-2-methylpyrrolizidine (ca. 45% yield by ^{1}H NMR and GC). HRMS: Calcd for $C_8H_{15}N$: 125.1204. Found: 125.1201.

The reaction was scaled up using the following procedure. In the glovebox, 14.5 mg (25.0 μmol) of Cp′$_2$SmCH(SiMe$_3$)$_2$ was loaded into a reaction vessel (25 mL) equipped with a stirbar. Next, 2 mL of C_6H_6 was vacuum-transferred onto the precatalyst, followed by syringing 2.0 mL of a mixture of *N*-allyl-4-pentenamine (**15**, 0.21 g, 1680 μmol, 67-fold molar excess) 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 5 days. Filtration followed by vacuum transfer afforded a mixture of C_6H_6, *cis*-2-methylpyrrolizidine, and *trans*-2-methylpyrrolizidine. After the benzene was removed by distillation at atmospheric pressure, 194 mg (93% yield) of **16a**,**b** (cis: trans ratio = 45:55 by comparison with lit.[18,20c] NMR data) was obtained as a colorless oil. It was >95% pure by ^{1}H NMR and GC/MS.

Synthesis of *cis*- and *trans*-2-Methylindolizidine (18a,b). A procedure similar to that used for **2** above in the NMR-scale reaction was used for *cis*-2-methylindolizidine (**18a**) and *trans*-2-methylindolizidine (**18b**). The Cp′$_2$SmCH(SiMe$_3$)$_2$ precatalyst (3.0 mg, 5.2 μmol) in benzene-d_6 (~0.4 mL) and *N*-allyl-5-hexenamine (**17**, 8.8 mg, 64.0 μmol) were used. The reaction mixture was chromatographed on alumina (50 mg, neutral) using diethyl ether (7.0 mL) as eluant. The eluate was concentrated by rotary evaporation to yield 7.0 mg (88% yield) of **18** as a colorless oil.

^{13}C NMR of the major isomer **18a** (85% yield by ^{1}H NMR and GC/MS; 75 MHz, C_6D_6): δ 63.9, 63.5, 53.3, 40.1, 31.6, 29.5, 26.1, 25.2, 20.8. The stereochemistry of *trans*-2-methylindolizidine was assigned by comparison with literature chemical shift values.[20a] ^{13}C NMR of the minor isomer **18b** (15% yield by ^{1}H NMR and GC/MS; 75 MHz, C_6D_6): δ 65.4, 62.5, 53.3, 41.1, 31.8, 29.5, 26.1, 25.1, 23.2. The isomers exhibit indistinguishable mass spectra. MS (relative abundance) of the major isomer: $M^+ - 1$ (100), M^+ (47), $M^+ + 1$ (4), 124.4 (16), 110.3 (34), 97.3 (78), 83.2 (16), 69.2 (24), 55.2 (16), 41.1 (25). High-resolution mass spectrum: Calcd for $C_9H_{16}N$ ($M^+ - H$): 138.1283. Found: 138.1278. MS (relative abundance) of the minor isomer: $M^+ - 1$ (100), M^+ (43), 124.4 (15), 110.3 (32), 97.3 (74), 83.2 (14), 69.2 (20), 55.2 (16), 41.1 (23). HRMS: Calcd for $C_9H_{16}N$ ($M^+ - H$): 138.1283. Found: 138.1278.

Synthesis of 2-Ethylidenepyrrolizidine (20). A 5-mm NMR tube with a Teflon valve was charged with 2.8 mg (4.6 μmol) of Me$_2$SiCp″$_2$-NdCH(SiMe$_3$)$_2$ and *N*-2-butynyl-4′-penten-1-amine (**19**, 18.9 mg, 138.0

(20) (a) Stereochemistry assigned from NMR comparisons to similar compounds: Heidt, P. C.; Bergmeier, S. C.; Pearson, W. H. *Tetrahedron Lett.* **1990**, 5441−5444. (b) Newcomb, M.; Deeb, T, M. *J. Am. Chem. Soc.* **1987**, *109*, 3163−3165. (c) Skvortsov, I. M.; Antipova, I. V. *J. Org. Chem. USSR* **1979**, *15*, 777−783. (d) Surzur, J.-M.; Stella, L. *Tetrahedron Lett.* **1974**, 2191−2194.

μmol) in 0.6 mL of C_6D_6 as described above, and the mixture was maintained at 25 °C. The progress of the reaction was monitored by ^{1}H NMR. The products were vacuum transferred via a short Y-type connecting tube to give a mixture of **20**, $CH_2(SiMe_3)_2$, and C_6D_6. The title compound was identified by NMR spectroscopy including ^{1}H, ^{13}C, DEPT, 2D, and NOE difference spectroscopy. The yield of **20** (92%) was estimated by ^{1}H NMR and GC/MS**.**

^{1}H NMR (300 MHz, C_6D_6): δ 5.23 (m, 1H, CH═), 3.67 (d, J = 15.0 Hz, 1H), 3.38 (m, 1H), 3.05 (d, J = 14.7 Hz, 1H), 2.97 (m, 1H), 2.45 (m, 2H), 1.90 (m, 1H), 1.61 (m, 4H), 1.45 (d, J = 6.9 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, C_6D_6): δ 142.4, 114.7, 64.6, 55.7, 54.8, 38.7, 31.2, 25.7, 14.7. MS (relative abundance): $M^+ - 1$ (69), M^+ (100), $M^+ + 1$ (11), 122.1 (73), 109.1 (35), 94.1 (25), 83.1 (22), 67.1 (39), 55.1 (31), 49.0 (20), 41.0 (46), 36.0 (20). HRMS: Calcd for $C_9H_{15}N$: 137.1204. Found: 137.1203.

Synthesis of 2-((Trimethylsilyl)methylidene)pyrrolizidine (22). A 5-mm NMR tube with a Teflon valve was charged with 3.3 mg (5.5 μmol) of $Me_2SiCp''_2NdCH(SiMe_3)_2$ and *N*-3-(trimethylsilyl)-2-propyn-4′-penten-1-amine (**21**, 19.3 mg, 99.0 μmol) in 0.6 mL of C_6D_6 as described above, and the reaction mixture was allowed to stand at 25 °C. The progress of the reaction was monitored by ^{1}H NMR. The title compound was identified by NMR spectroscopic analysis including ^{1}H, ^{13}C, DEPT, 2D, and NOE difference spectroscopy. The yield of **22** (80%) was estimated by ^{1}H NMR and GC/MS after the product was isolated by vacuum transfer of the volatiles.

^{1}H NMR (300 MHz, C_6D_6): δ 5.48 (m, 1H, CH═), 3.77 (d, J = 15.0 Hz, 1H), 3.40 (m, 1H), 3.19 (d, J = 15.0 Hz, 1H), 2.97 (m, 1H), 2.47 (m, 2H), 2.14 (m, 1H), 1.63 (m, 4H), 0.46 (s, 9H, $SiMe_3$). ^{13}C NMR (100 MHz, C_6D_6): δ 147.1, 119.2, 63.9, 58.6, 54.7, 42.7, 31.4, 25.7, −0.20. MS (relative abundance): $M^+ - 1$ (22), M^+ (20), $M^+ + 1$ (4), 180.1 (19), 166.0 (14), 152.1 (11), 122.1 (100), 111.0 (7), 94.1 (11), 83.0 (23), 73.0 (66), 59.0 (14), 45.0 (8). HRMS: Calcd for $C_{11}H_{21}NSi$: 195.1443. Found: 195.1436.

Synthesis of 2-Methyl-1-(4-(trimethylsilyl)-3-butynyl)pyrrolidine (24). This cyclized pyrrolidine derivative was prepared using 3.3 mg (5.5 μmol) of $Me_2SiCp''_2NdCH(SiMe_3)_2$ and *N*-4-(trimethylsilyl)-3-butynyl-4′-penten-1-amine (**23**, 18.4 mg, 88.0 μmol) in 0.6 mL of C_6D_6 as described above. The yield (>90%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer of the volatiles.

^{1}H NMR (400 MHz, C_6D_6): δ 2.94 (m, 2H), 2.38 (t, J = 7.5 Hz, 2H), 2.26 (m, 1H), 2.09 (m, 1H), 1.86 (m, 1H), 1.59 (m, 2H), 1.36 (m, 1H), 1.21 (m, 1H), 0.94 (d, J = 6.0 Hz, 3H, Me), 0.22 (s, 9H, $SiMe_3$). ^{13}C NMR (100 MHz, C_6D_6): δ 106.4, 84.7, 59.1, 53.4, 52.7, 32.8, 21.8, 20.3, 19.0, 0.08. MS (relative abundance): M^+ (1), $M^+ -$ Me (11), 98.0 (100), 69.0 (12), 41.0 (9). HRMS: Calcd for $C_{11}H_{20}NSi$ ($M^+ -$ Me): 194.1365. Found: 194.1374.

Synthesis of 4-Methyl-2-((2-allylamino)methyl)-1-allylpyrrole (26). A 5-mm NMR tube with a Teflon valve was charged with 3.0 mg (5.2 μmol) of $Cp'_2SmCH(SiMe_3)_2$ and *N*-allylpropargylamine (**25**, 35.4 mg, 372.2 μmol) in 0.6 mL of C_6D_6 as described above, and the mixture was heated at 60 °C. The progress of the reaction was monitored by ^{1}H NMR. The title compound was identified by GC/MS and NMR including ^{1}H, ^{13}C, DEPT, 2D, and NOE difference spectroscopy. The yield of **26** (92%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products.

^{1}H NMR (300 MHz, C_6D_6): δ 6.29 (s, 1H, CH═), 6.01 (s, 1H, CH═), 5.85−5.66 (m, 2H, 2CH═), 5.12−4.78 (m, 4H, $2CH_2$═), 4.26 (m, 2H, N−CH_2−CH═), 3.49 (d, J = 6.3 Hz, 2H, C−CH_2−NH), 3.03 (m, 2H, NH−CH_2−CH═), 2.21 (s, 3H, CH_3), 0.68 (br. 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 136.1, 130.7, 128.5, 119.6, 117.2, 115.3, 115.2, 110.3, 51.8, 48.9, 45.4, 12.3. MS (relative abundance): M^+ (33), $M^+ + 1$ (5), $M^+ - 1$ (17), 148.1 (10), 134.1 (100), 120.1 (19), 107.1 (18), 94.1 (18), 80.0 (6), 68.1 (12), 41.0 (30). HRMS: Calcd for $C_{12}H_{18}N_2$: 190.1470. Found: 190.1458.

Synthesis of 4-Methyl-2-((3-propylamino)methyl)-1-propylpyrrole (28). A 5-mm NMR tube with a Teflon valve was charged with 3.0 mg (5.2 μmol) of $Cp'_2SmCH(SiMe_3)_2$ and *N*-*n*-propylpropargylamine (**3**, 64.9 mg, 669.1 μmol) in 0.6 mL of C_6D_6 as described above, and the mixture was heated at 60 °C. The progress of the reaction was monitored by ^{1}H NMR. The yield of **28** (95%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer of the volatiles.

^{1}H NMR (300 MHz, C_6D_6): δ 6.29 (s, 1H, CH═), 6.02 (s, 1H, CH═), 3.63 (t, J = 7.2 Hz, 2H, CH_2N), 3.54 (d, J = 5.7 Hz, 2H, C−CH_2−NH), 2.39 (m, 2H, $CH_3CH_2CH_2$NH), 2.24 (s, 3H, CH_3), 1.54 (m, 2H, CH_2CH_2N), 1.30 (m, 2H, CH_2CH_2NH), 0.80 (t, J = 7.1 Hz, C$H_3CH_2CH_2$NH), 0.72 (t, J = 7.5 Hz, C$H_3CH_2CH_2$N), 0.50 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 129.3, 119.1, 116.9, 109.7, 51.5, 48.0, 46.4, 25.1, 23.5, 12.4, 11.9, 11.4. MS (relative abundance): M^+ (27), $M^+ + 1$ (5), $M^+ - 1$ (13), 136.1 (100), 120.1 (11), 108.1 (6), 94.1 (28), 41.0 (7). HRMS: Calcd for $C_{12}H_{22}N_2$: 194.1783. Found: 194.1779.

Synthesis of 4-Methyl-2-((5-pentenylamino)methyl)-1-(4-pentenyl)pyrrole (30). A 5-mm NMR tube with a Teflon valve was charged with 2.0 mg (3.5 μmol) of $Cp'_2SmCH(SiMe_3)_2$ and *N*-propargyl-4-penten-1-amine (**5**, 3.48 mg, 28.3 μmol) in 0.6 mL of C_6D_6 as described above, and the reaction mixture was heated at 60 °C. The progress of the reaction was monitored by ^{1}H NMR. The yield of **30** (95%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer of the volatile products.

^{1}H NMR (300 MHz, C_6D_6): δ 6.29 (s, 1H, CH═), 6.01 (s, 1H, CH═), 5.68 (m, 2H, 2CH═), 4.97 (m, 4H, $2CH_2$═), 3.67 (t, J = 7.2 Hz, 2H, CH_2N), 3.51 (d, J = 6.3 Hz, 2H, C−CH_2−NH), 2.42 (m, 2H, CH_2NH), 2.23 (s, 3H, CH_3), 1.93 (m, 2H, CH_2), 1.86 (m, 2H, CH_2), 1.61 (m, 2H, CH_2), 1.37 (m, 2H, CH_2), 0.92 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 138.8, 138.0, 130.8, 119.0, 117.0, 114.9, 114.5, 109.8, 48.9, 46.3, 45.7, 31.8, 31.0, 30.9, 29.6, 12.3. MS (relative abundance): M^+ (3), $M^+ - 1$ (10), 206.8 (6), 161.9 (100), 133.9 (16), 108.0 (29), 94.0 (16), 41.0 (8). HRMS: Calcd for $C_{16}H_{26}N_2$: 246.2096. Found: 246.2103.

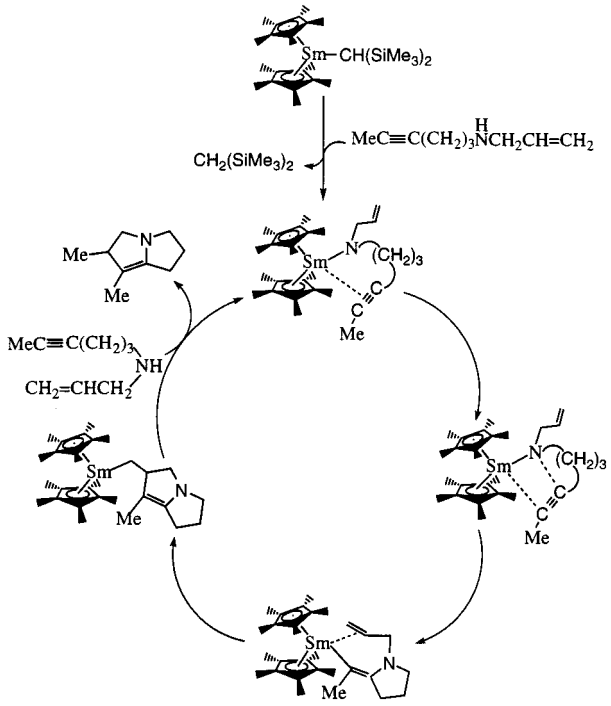
Synthesis of *cis*-1*H*,2*H*,3*H*,5*H*,10*H*-2,7-Dimethyldipyrrolo[1,2-*a*:1′,2′-*d*]pyrazine (31). A 5-mm NMR tube with a Teflon valve was charged with 3.0 mg (5.2 μmol) of $Cp'_2SmCH(SiMe_3)_2$ and *N*-allylpropargylamine (**1**, 3.4 mg, 36 μmol) in 0.6 mL of C_6D_6 as described above, and the mixture was heated at 60 °C. The progress of the catalytic reaction was monitored by ^{1}H NMR. The title compound was identified by GC/MS and NMR spectroscopic analysis including ^{1}H, ^{13}C, DEPT, 2D, and NOE difference spectroscopy. The reaction mixture was chromatographed on alumina (50 mg, neutral) using diethyl ether (5.0 mL) as the eluant to remove the catalyst. The eluate was concentrated by rotary evaporation to yield 3.2 mg (93% yield) of the title compound as a colorless oil.

^{1}H NMR (300 MHz, C_6D_6): δ 6.20 (s, 1H, CH═), 5.88 (s, 1H, CH═), 4.00 (d, J = 13.2 Hz, 1H), 3.43 (d, J = 3.9 Hz, 1H), 3.39 (d, J = 3.9 Hz, 1H), 3.30 (t, J = 10.7 Hz, 1H), 3.14 (d, J = 13.2 Hz, 1H), 3.06 (d, J = 8.0 Hz, 1H), 2.26 (s, 3H, CH_3), 2.19−2.13 (m, 2H), 1.56 (t, J = 8.9 Hz, 1H), 1.09 (m, 1H), 0.79 (d, J = 6.9 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, C_6D_6): δ 129.3, 118.0, 116.6, 104.6, 63.2, 60.3, 51.0, 50.5, 36.7, 30.8, 20.1, 12.5. MS (relative abundance): M^+ (64), $M^+ + 1$ (10), $M^+ - 1$ (69), 175.1 (6), 133.1 (9), 107.1 (100), 94.1 (7), 79.0 (6), 41.0 (7). HRMS: Calcd for $C_{12}H_{18}N_2$: 190.1470. Found: 190.1450.

Synthesis of *N*-Allyl((1′-octen-3′-yn-2′-yl)methyl)methanamine (32). A 5-mm NMR tube with a Teflon valve was charged with 3.0 mg (5.2 μmol) of $Cp'_2SmCH(SiMe_3)_2$, *N*-allylpropargylamine (**1**, 5.4 mg, 56.9 μmol), and 1-hexyne (4.25 mg, 52.0 μmol) in 0.6 mL of C_6D_6 as described above, and the mixture was heated at 60 °C. The progress of the reaction was monitored by ^{1}H NMR. The title compound was identified by GC/MS and NMR spectroscopic studies including ^{1}H, ^{13}C, DEPT, and NOE difference spectroscopy. The yield of **32** (39%) was estimated by ^{1}H NMR and GC/MS after vacuum transfer of the volatiles. This reaction also generates **31** (22%) and 2-butyl-1-octen-3-yne[4a] (39%).

^{1}H NMR (300 MHz, C_6D_6): δ 5.89−5.79 (m, 1H, C*H*═CH_2), 5.47 (d, J = 1.8 Hz, 1H, CH_2═), 5.29 (d, J = 1.8 Hz, 1H, CH_2═), 5.18−4.97 (m, 2H, CH_2═), 3.25 (s, 2H, C−CH_2−NH), 3.09 (d, J = 6.0 Hz, 2H, HN−CH_2−CH═), 2.11 (t, J = 6.9 Hz, 2H, CH_2−C), 1.29 (m, 4H, $2CH_2$), 0.76 (t, J = 7.2 Hz, 3H, CH_3), 0.45 (br, 1H, NH). ^{13}C NMR (75 MHz, C_6D_6): δ 137.3, 131.7, 119.3, 115.0, 91.1, 81.7, 54.1, 51.0, 30.8, 21.9, 18.9, 13.4. MS (relative abundance): M^+ (5), $M^+ +$

Scheme 2. Proposed Pathway for Organolanthanide-Catalyzed Sequential C−N and C−C Bond Formation



1 (1), $M^+ - 1$ (3), 150.2 (3), 134.1 (20), 120.1 (33), 70.1 (100), 41.1 (34). HRMS: Calcd for $C_{12}H_{19}N$: 177.1517. Found: 177.1521.

Kinetic Study of Hydroamination/Bicyclization. In a typical experiment, an NMR sample was prepared as described in the typical NMR-scale catalytic reaction section but the tube was maintained at −78 °C until kinetic measurements were initiated. Before the measurements, the spectrometer probe was equilibrated at the appropriate temperature ($T \pm 0.2$ °C, checked with a methanol or ethylene glycol temperature standard). The NMR tube was then quickly warmed with shaking for ∼8 s and inserted into the probe. Data were acquired using 4−8 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 concentration (C) was measured from the area (A_S) of integrals of the ^{1}H-normalized CH_2═ signal, standardized to the area (A_I) of free $CH_2(SiMe_3)_2$, which is quantitatively generated by reaction of the precatalysts with the substrate (Scheme 2). All data could be convincingly fit ($R > 0.98$) by least-squares to eq 3, where C_O ($C_O = A_{SO}/A_{I0}$) is the initial concentration of substrate (relative to precatalyst) and C (A_S/A_I) is the substrate concentration at time, t. The ratio of catalyst to substrate was

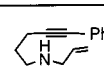
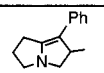
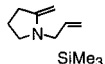
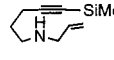
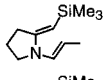
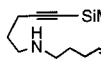
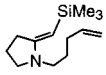
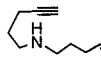
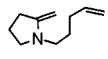
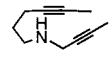
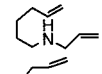
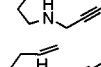
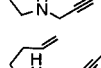
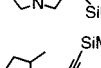
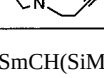
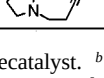
$$mt = (C_O - C) \tag{3}$$

accurately measured from the ratio of A_{SO} and A_{I0} or from the area of product and A_I. The absolute concentrations of catalyst and substrate were determined with an internal $FeCp_2$ standard. 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 0.13−0.60 M, and typical catalyst concentrations in the range 3.0−17 mM.

Results

The principal goal of this study was to exploit the possibility of coupling sequences of organolanthanide-mediated element−element bonding-forming reactions into catalytic cycles for construction of polycyclic heteroatom-containing frameworks (e.g., pyrrolizidines, indolizidines, pyrroles, pyrazines, and other frameworks).[8−10] A closely related objective involved examination of the scope, stereoselectivity, lanthanide ion sensitivity, ancillary ligand sensitivity, kinetics, and mechanism of these organolanthanide-catalyzed tandem C−N, C−C bond-forming transformations. The *intramolecular* hydroamination/bicyclizations of aminodialkynes, aminodialkenes, and aminoalkenynes are discussed first, followed by the *intermolecular* hydroamination/cyclizations of aminoalkynes. This study capitalized upon our previous success in organolanthanide-catalyzed carbon−heteroatom bond formation[6,7] and upon well-characterized organolanthanide-catalyzed carbon−carbon bond formation processes.[3,4]

Table 1. Intramolecular Hydroamination/Bicyclization Results

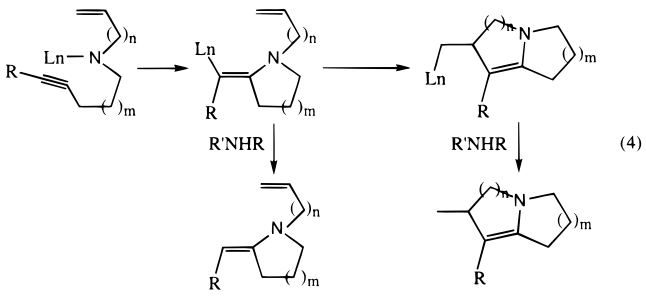
Entry	Substrate		Product		N_t, h^{-1}(^{0}C)	Yield (%)
1.		**1**		**2**	17(21)[a] 12(21)[b]	68[d] 85[e]
2.		**3**		**4**	777(21)[a] 124(21)[b]	75[d] 88[e]
3.		**5**[f]		**6**	27 (21)[a]	85[c] 52[e]
4.		**7**[f]		**8**	2.6(60)[a] 1.7(60)[b]	91[c]
5.		**9**[f]		**10**	129(21)[a]	90[c]
6.		**11**[f]		**12**	47(21)[a]	85[c]
7.		**13**		**14**	74(21)[a] 132(21)[b]	95[c] 92[e]
8.		**15**		**16**	55(21)[a] 1(60)[b]	93[e]
9.		**17**		**18**	5(21)[a]	88[d]
10.		**19**		**20**	2(21)[a] 14(60)[a] 10(21)[b]	92[c]
11.		**21**		**22**	16(21)[b]	80[c]
12.		**23**		**24**	16(60)[b]	90[c]

[a] $Cp'_2SmCH(SiMe_3)_2$ as precatalyst. [b] $Me_2SiCp''_2NdCH(SiMe_3)_2$ as precatalyst. [c] NMR-scale reaction with the yield determined by ^{1}H NMR and GC/MS after vacuum transfer of volatile products. [d] NMR-scale reaction and isolated yield. [e] Preparative-scale reaction and isolated yield. [f] Data from ref 7a.

Scope of Organolanthanide-Catalyzed Intramolecular Bicyclization. The organolanthanides $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ are precatalysts for intramolecular hydroamination/bicyclization of aliphatic and aromatic aminodialkynes, aminodialkenes, and aminoalkenynes to yield the corresponding monocyclic and/or bicyclic organonitrogen compounds as shown in Table 1, where N_t is the catalytic turnover frequency at the temperature indicated. The catalytic bicyclization reactions in general proceed to completion at room temperature under inert atmosphere and are conveniently monitored by ^{1}H NMR spectroscopy. As in the case of organolanthanide-catalyzed hydroamination/cyclization of aminoolefins[6b,c] and aminoalkynes,[7a] the reaction of $Cp'_2NdCH(SiMe_3)_2$, $Cp'_2SmCH(SiMe_3)_2$, and $Me_2SiCp''_2SmCH(SiMe_3)_2$ with the present substrates results in distinct color changes concurrent with catalytic initiation and termination. The original green and orange solutions of the neodymium and samarium alkyl precatalysts, respectively, in C_6D_6 or C_7D_8 instantaneously turn to the characteristic blue and yellow colors of the

corresponding amine−amido complexes[6b,c] with initiation of catalytic turnover. Upon consumption of the amine substrates, the resulting reaction solutions return to the original colors. The pyrrolidine, pyrrolizidine, and indolizidine products were characterized by NMR spectroscopy (^{1}H, ^{13}C, and 2D), GC/MS, and high-resolution mass spectroscopy or by comparison with literature ^{1}H/^{13}C NMR spectral data and data for authentic samples. Isolation procedures for products involved chromatography, or high vacuum transfer of the products and other volatiles followed by removal of solvent and $CH_2(SiMe_3)_2$. Preparative-scale reactions were carried out in sealed tubes, affording isolated products in 52−93% yields as shown in Table 1. All products in NMR or preparative-scale reactions were separated from the catalysts and were >95% pure by ^{1}H NMR and GC/MS.

The present catalytic process, as illustrated in eq 4, for the transformations of unsaturated secondary amines, may in principle generate bicyclic or undesired monocyclic heterocycles (due to premature Ln−C protonolysis). However, the results of the cyclizations summarized in Table 1 demonstrate that C−N/C−C fusions can be regiospecifically coupled in sequence to exclusively assemble bicyclic rather than monocyclic products



(4)

3. R = H, n = 1, m = 1
4. R = $SiMe_3$, n = 1, m = 1
5. R = $SiMe_3$, n = 3, m = 1
6. R = H, n = 3, m = 1

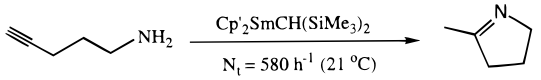
1. R = Ph, n = 1, m = 1
2. R = Me, n = 1, m = 1

when catalysts with less coordinative unsaturation at the metal center (e.g., $Cp'_2LnCH(SiMe_3)_2$-type complexes) are used at room temperature (Table 1, entries 1, 2, 7, 8, 9, 10, and 11). However, small amounts (3−15%) of monocyclic byproducts are observed when more "open" $Me_2SiCp''_2LnCH(SiMe_3)_2$ precatalysts and/or high substrate concentrations are employed and at slightly elevated temperatures (e.g., 60 °C). In lieu of this observation, optimization of the catalytic reaction conditions was carried out using the **3** → **4** transformation. It is found that using less "open" organolanthanide catalysts, relatively low operating substrate:catalyst molar ratios (substrate:catalyst = 12−60), and carrying out the reactions at room temperature ensures regiospecific pendant olefin insertion to close the second ring in the catalytic cycle (e.g., entry 2, in Table 1; Scheme 2). Similar effects are found in the insertion of the terminal olefin into the α-phenylvinyl−lanthanide bond in the bicyclization of *N*-allyl-5-phenyl-4-pentyn-1-amine (entry 1).

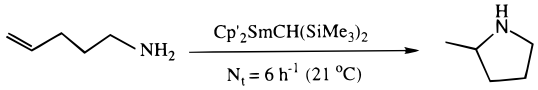
It can be seen that the present process, using the aforementioned optimized conditions, effects efficient coupling of alkyne/alkene (entries 1 and 2), alkene/alkene (entries 8 and 9), alkene/alkyne (entries 10 and 11), and alkyne/alkyne (entry 7) moieties in catalytic cycles, by the insertion of carbon−carbon multiple bonds into the Ln−N and Ln−C bonds, in sequence. This catalytic reaction is capable of forming five−five and six−five polycyclic skeletons (entries 1, 2, and 7−11). The results indicate that both internal alkynes (entries 1, 2, and 7) and terminal alkenes (entries 8−11) undergo addition to Ln−N bonds, followed by insertion of a second olefin (entries 1, 2, 8, and 9) or alkyne (entries 7, 10, and 11) into the resulting Ln−C bonds to yield bicyclized pyrrolizidine (entries 1, 2, 7, 8, 10, and 11) and indolizidine (entry 9) skeletons. Entries 7, 10, and 11 illustrate that internal alkynes are effective insertive groups yielding exo-alkene functionalized pyrrolizidines. Entry 7 indicates rapid sequential alkyne/alkyne insertive bicyclization to introduce two regions of heterocyclic unsaturation. Entries 8 and 9 illustrate alkene/alkene bicyclization to produce known saturated pyrrolizidine **16**[18,20b−d] and indolizidine **18** (cis:trans ratios = 45:55 and 85:15,[20a] respectively).

Attempts to couple terminal alkyne/alkene insertions in substrates **5** and **11** (entries 3 and 6) to form bicyclized compounds were unsuccessful, and monocyclized pyrrolidines, the products of competing, premature protonolysis (eq 4), are obtained instead. It is likely that closure to form a seven-membered ring is kinetically disfavored in **11**, judging from prior aminoalkene results. Entries 4 and 5 also reveal that a second (olefinic) insertion into an α-(trimethylsilyl)vinyl−lanthanide bond is also impeded; instead a slow, precedented catalytic[3k] double-bond migration occurs in the case of entry 4. Entry 12 illustrates that the second ring-closing reaction fails for alkyne insertion into an Ln−C bond to form a six-membered ring, and a monocyclic structure is instead preferentially generated.

In regard to reaction rate, the present disubstituted amine bicyclizations are comparable in turnover frequency to the corresponding cyclizations of primary aminoalkenes and aminoalkynes for the same catalysts, temperatures, and reaction conditions.[6,7] For example, entry 2 illustrates that *N*-allyl-4-hexyn-1-amine is bicyclized regiospecifically to the corresponding pyrrolizidine derivative with N_t as high as 777 h^{-1} at room temperature. In comparison, the turnover frequencies for the cyclization of 4-pentyn-1-amine and 4-penten-1-amine to the corresponding heterocycles are 580 h^{-1} and 6 h^{-1}, respectively (eqs 5 and 6).[6b,c,7a] It can be seen in Table 1 that substrates lacking alkynyl functionalities undergo bicyclization with more modest N_t values (entries 8 and 9). In addition, in two directly



(5)

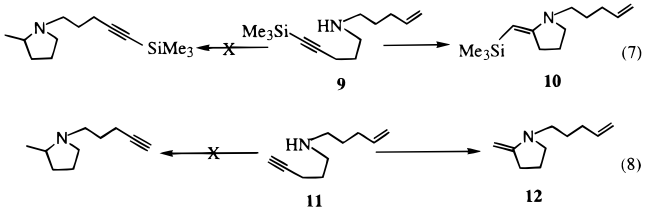


(6)

competitive intramolecular cyclizations, a distinct preference for alkyne insertion over alkene insertion is observed (**9** → **10**, **11** → **12**; eqs 7 and 8). This is in accord with earlier regiospecificity observations on organolanthanide-mediated olefin and alkyne hydroamination/cyclization and is not surprising in view of the known activating effects of $SiMe_3$ substitution,[21] the greater exothermicity of additions to alkynes versus those to alkenes,[22−24] and the enhanced nucleophilic reactivity of alkynes over alkenes.[25]

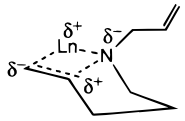
Substrate Substituent, Lanthanide, and Ancillary Ligand Effects on the Bicyclization Process. Kinetic and mechanistic studies of the Cp'_2Ln-catalyzed hydroamination/bicyclization reactions to be discussed below argue that the turnover-limiting

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



step is the intramolecular insertion of an unsaturated carbon−carbon bond into the Ln−N bond, followed by a more rapid second ring closure and/or protonolysis of the intermediate Ln−C bond (Scheme 2, eq 4). In analogy to earlier observations on the hydroamination/cyclization of aminoolefins and aminoalkynes mediated by organolanthanides,[6,7] the transition states involved in the first ring-closing step for multifunctional substrates should be both electronically and sterically sensitive to the environment of the four-membered insertive transition state configuration.[26] Entries 1, 2, and 7 of Table 1 indicate that the first ring-closing process involving C≡C addition to the Ln−N bond is considerably more rapid than that for alkenes (entries 8−11). These results are consistent with previous observations on organolanthanide-catalyzed cyclization of aminoalkenes and aminoalkynes.[6,7] For diolefinic amines, that bicyclization of *N*-allyl-4-penten-1-amine (entry 8) is more rapid under the same conditions than that of *N*-allyl-5-hexen-1-amine (entry 9) is consistent with initial insertion via a preferred quasi-seven-membered transition state in the former (e.g., **A**). Similar ring size-reaction rate relationships prevail in organolanthanide-mediated aminoolefin cyclizations.[6c]

A



In regard to substrate substituents, Table 1 reveals that the rate of bicyclization is decreased by sterically encumbered substituents for the same alkyne/alkene (entries 1 and 2) and alkene/alkyne (entries 8 and 10) frameworks. It can also be seen that the course of bicyclization depends on the pattern of amine substitution. Attempts to effect six- or seven-membered ring closure with initial cyclization via insertion of pendant γ or δ unsaturation were unsuccessful (entries 5, 6, and 12), mirroring trends noted previously for monofunctional substrates.[6,7]

In regard to metal ion size effects, interestingly, and in marked contrast to the analogous hydroamination/cyclization of aminoalkynes,[7] the present results illustrate an *acceleration* rather than a deceleration in rate when lanthanides with larger ionic radii[27] are used as the catalysts. Thus, the turnover frequency for conversion of *N*-allyl-5-phenyl-4-pentyn-1-amine to 1-phenyl-2-methylpyrrolizidin-8-ene (**1** → **2**) under identical reaction conditions increases dramatically from the smallest Lu^{3+} (0.977 Å), to intermediate Sm^{3+} (1.079 Å), to Nd^{3+} (1.109 Å), and to the largest La^{3+} (1.160 Å) (Figure 1; Table 2). Similar trends have been observed in a variety of Ln-catalyzed processes where the turnover-limiting step is olefin insertion.[3c,d,6b,c] In the case of organolanthanide-catalyzed aminoolefin hydroamination/cyclization, opening the metal coordination sphere by connecting ancillary Cp ligands (Cp'_2Ln → $Me_2SiCp''_2Ln$ or Me_2SiCp''-(R*Cp)Ln)[6b,12b] results in higher turnover frequencies, presumably reflecting steric demands in turnover-limiting olefin insertion step (e.g., **A**). However, in the present bicyclizations, a decrease in N_t for aminodiolefin substrates is observed for $Me_2SiCp''_2NdCH(SiMe_3)$ as the precatalyst (entry 8). A similar

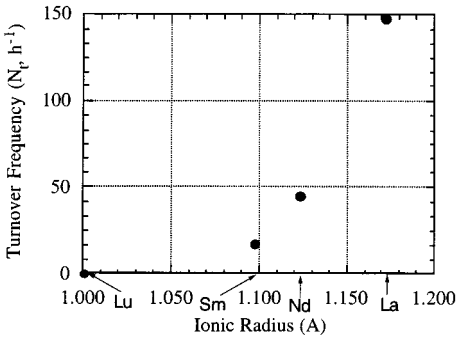
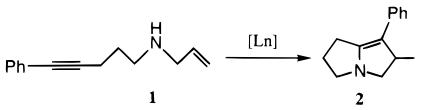


Figure 1. Plot of turnover frequency (N_t) as a function of eight-coordinate Ln^{3+} ionic radius for the intramolecular hydroamination/bicyclization of $PhC{\equiv}CCH_2CH_2CH_2NHCH_2CH{=}CH_2$ (**1** → **2**) in benzene-d_6 using $Cp'_2LnCH(SiMe_3)_2$ complexes as the precatalysts.

Table 2. Lanthanide Ion Size Effects on the Turnover Frequency for Hydroamination/Bicyclization



catalyst	ionic radius (Å)[a]	N_t, h^{-1}(°C)
Cp'_2La-	1.172	148 (21)
Cp'_2Nd-	1.123	45 (21)
Cp'_2Sm-	1.098	17(21)
Cp'_2Lu-	1.001	0.21(60)

[a] Eight-coordinate ionic radii from ref 27.

(22) Requisite experimental thermochemical data are not available to compare the thermodynamics of amine addition to olefins versus that to alkynes. However, ΔH for NH_3 addition to ethylene can be estimated from thermochemical data[23,24] 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[23,24] to be ∼14 kcal/mol more exothermic and ∼14 kcal/mol more exergonic than that to ethylene.

(23) Metal−ligand bond enthalpies from: (a) Nolan, S. P.; Stern, D.; Hedden, D.; Marks, T. J. *ACS Symp. Ser.* **1990**, *428*, 159−174. (b) Nolan, S. P.; Stern, D.; Marks, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 7844−7853. (c) Schock, L. E.; Marks, T. J. *J. Am. Chem. Soc.* **1988**, *110*, 7701−7715. (d) Bruno, J. W.; Marks, T. J.; Morss, L. R. *J. Am. Chem. Soc.* **1983**, *105*, 6824−6832. (e) Reference 6d.

(24) Organic fragment bond ethalpies 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.; John Wiley and Sons: New York, 1976; Appendix Tables A.10, A.11, A.22. (d) Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502−518. (e) Pedley, J. B.; Naylor, R. D.; Kirby, S. P. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall: London, 1986; Appendix Tables 1 and 3.

(25) For a comparison of nucleophilic addition chemistry involving 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.

(26) (a) Eshuis, J. J. W.; Tan, Y. Y.; Meetsma, A.; Teuben, J. H.; Renkema, J.; Evens, G. G. *Organometallics* **1992**, *11*, 362−369. (b) Piers, W. E.; Shapiro, P. J.; Bunel, E. E.; Bercaw, J. E. *Synlett* **1990**, 74−84. (c) Burger, B. J.; Thompson, M. E.; Cotter, W. D.; Bercaw, J. E. *J. Am. Chem. Soc.* **1990**, *112*, 1566−1577. (d) 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. (e) Doherty, N. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1985**, *107*, 2670−2682.

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

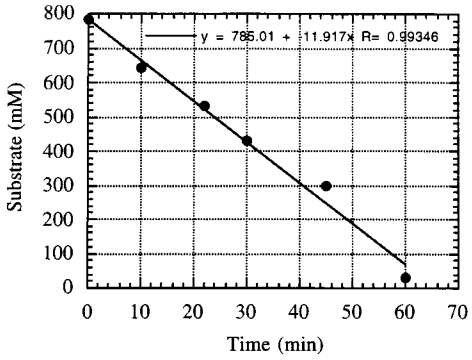


Figure 2. Plot of $CH_2{=}CHCH_2CH_2CH_2NHCH_2CH{=}CH_2$ concentration as a function of time at constant catalyst concentration for the hydroamination/ bicyclization of $CH_2{=}CHCH_2CH_2CH_2NHCH_2CH{=}CH_2$ (**15** → **16**) using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst in benzene-d_6. The line represents least-squares fit to the data points.

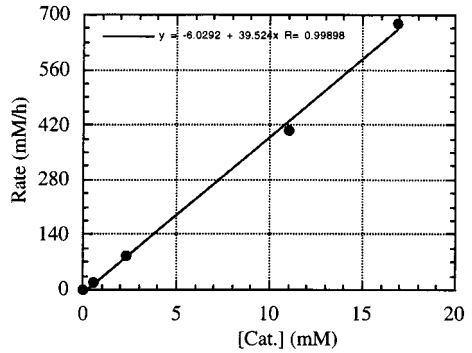
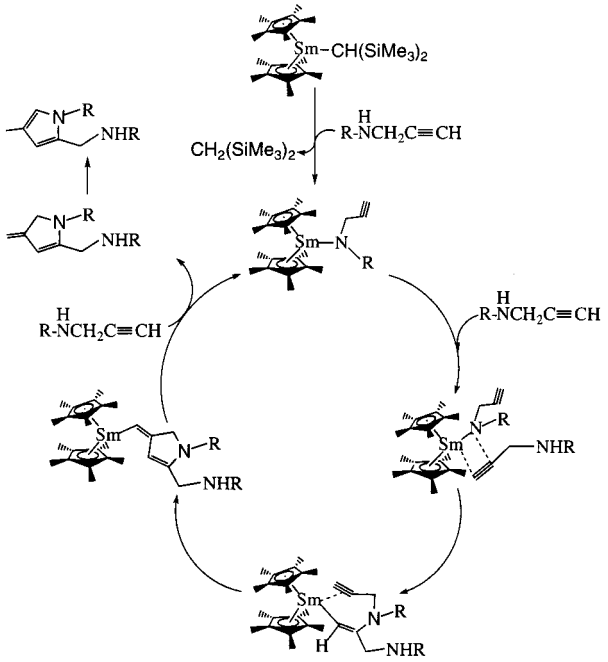


Figure 3. Plot of reaction rate vs catalyst concentration for the intramolecular hydroamination/bicyclization of $CH_2{=}CHCH_2CH_2CH_2NHCH_2CH{=}CH_2$ (**15** → **16**) using $Cp'_2SmCH(SiMe_3)_2$ as the precatalyst in benzene-d_6. The line represents a least-squares fit to the data points.

relationship between N_t and ancillary ligation-based Ln^{3+} unsaturation is observed in bicyclization of internal alkynes and terminal olefins (entries 1 and 2). However, as in the case of aminoolefin cyclization,[6b,c] increasing N_t values with more open coordination spheres are observed in bicyclization of apparently more sterically demanding internal alkyne/alkyne and terminal olefin/internal alkyne substrates (entries 7 and 10).

Kinetic Studies of Bicyclization. The kinetics of the aminodiolefin bicyclization **15** → **16** were investigated by in situ ^{1}H NMR. With constant catalyst concentration, the conversion of a 40−50-fold molar excess of *N*-allyl-4-penten-1-amine mediated by $Cp'_2SmCH(SiMe_3)_2$ was monitored over >3 half-lives. The disappearance of the allyl olefinic ^{1}H resonances ($CH_2{=}$, δ ∼5.2 ppm) was normalized to $CH_2(SiMe_3)_2$ as an internal standard. The kinetic data (Figure 2) reveal a linear dependence of aminodialkene concentration on reaction time over a ∼10-fold concentration range, which indicates an essentially zero-order dependence of the catalytic rate on substrate concentration, in analogy to organolanthanide-catalyzed aminoolefin[6b,c] and aminoalkyne cyclization.[7] This argues for a similar turnover-limiting step involving intramolecular unsaturated carbon−carbon bond insertion into the Ln−N bond. When the initial substrate concentration is held constant and the catalyst precursor concentration is varied over a 10-fold range (Figure 3), a plot of reaction rate vs precatalyst concentration indicates the reaction to be the first-order in catalyst. The empirical rate law is thus given by eq 9, and is identical to that for organo-f-element catalyzed aminoolefin[6b,c] and aminoalkyne cyclization.[7a,b] The derived rate

Scheme 3. Proposed Pathway for Organolanthanide-Catalyzed Intermolecular Hydroamination/Cyclization

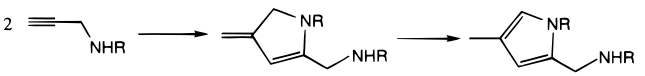


constant (k) for the **15** → **16** conversion at 21 °C is 0.011(2) s^{-1}.

$$v = k[\text{substrate}]^0[\text{Sm}]^1 \qquad (9)$$

In the presence of the Nd^{3+} ($4f^3$) and Sm^{3+} ($4f^5$) catalysts, both paramagnetically broadened ^{1}H NMR substrate and product resonances are observed during turnover. This behavior is analogous to that of aminoolefin and aminoalkyne cyclizations where amine−amido $Cp'_2LnNHR(NH_2R)_x$ complexes undergo bound amine−amide and bound-free amine (substrate and product) exchange, which is fast on the NMR time scale at 25 °C.[6b,c]

Organolanthanide-Catalyzed Intermolecular Hydroamination/Cyclization. Coupled intermolecular hydroamination and intramolecular cyclizations, mediated by organolanthanides, are also efficiently incorporated into catalytic cycles. The efficiency of such processes was first investigated with substituted secondary propargylamines (eq 10). In a typical intermolecular hydroamination/cyclization procedure (see the Experimental Section for details), a 70:1 molar ratio of substrate:catalyst was

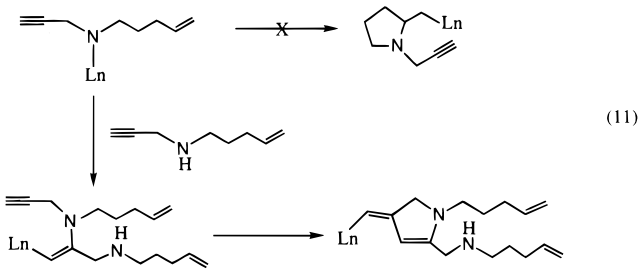


(10)

employed in C_6D_6 solution with $Cp'_2SmCH(SiMe_3)_2$ and the process monitored by ^{1}H NMR. Intermolecular amination of a secondary amine having a pendant terminal alkyne generates a metal−alkenyl species as a presumed intermediate, which then undergoes intramolecular insertion of the pendant terminal alkyne moiety to yield an exomethylene dihydropyrrole derivative (Scheme 3). This product subsequently undergoes isomerization to the more stable aromatic pyrrole skeleton.[9,10,28] In ^{1}H NMR monitoring of the reaction, exomethylene resonances

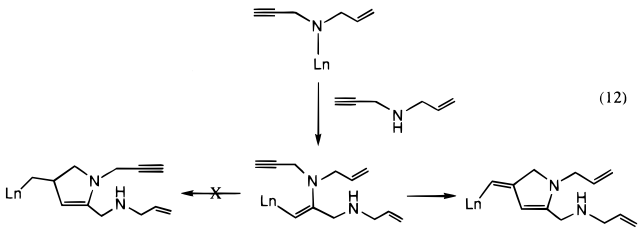
at δ 6.0−5.2 initially grow in and then gradually disappear during the catalytic turnover, while aromatic pyrrole-type signals at δ 6.3−5.8 evolve as the final product. This conversion is clean and quantitative under catalytic conditions. GC/MS and NMR of the final reaction mixtures indicate the presence of only cyclized pyrrole derivative, C_6D_6, and the expected quantity of $CH_2(SiMe_3)_2$. The products were characterized by GC/MS, HRMS and ^{1}H, ^{13}C, DEPT, 2D, and NOE difference NMR spectroscopy.

Although more sterically encumbered secondary amines generally exhibit lower turnover frequencies than primary amines in catalytic aminoolefin and aminoalkyne hydroamination/cyclization,[6c,7b] it can be seen in Table 3 that the secondary propargylamines exhibit substantial cyclization rates compared to analogous intramolecular hydroamination/cyclizations[6c] and intermolecular primary amine hydroaminations.[6a] For example, the turnover frequency for intermolecular conversion of *N*-allylpropargylamine (**25**) to *N*-allyl-2-(1′-allyl-3′-methylpyrrolyl)methylamine (**26**) can be as high as 236 h^{-1} at 60 °C using Cp′$_2$Sm− as the catalyst (entry 1, in Table 3). More interestingly, and in marked contrast to the aforementioned intramolecular secondary amine hydroamination/bicyclizations (entries 8−12, in Table 1), *N*-propargyl-4-penten-1-amine (**29** in Table 3) preferentially undergoes *intermolecular* hydroamination/cyclization rather than intramolecular hydroamination/bicyclization or hydroamination/cyclization (**29** → **30**, in Table 3, eq 11), arguing for a more rapid intermolecular insertion of the terminal alkyne moiety into the Ln−N bond than intramolecular olefin insertion (intramolecular C≡C insertion would yield a highly strained three-membered ring).



(11)

The regiospecific, tandem C−N and C−C coupling of *N*-allylpropargylamine (**25** → **26** in Table 3) is unprecedented, and the proposed reaction sequence is shown in eq 12. The Ln−C bond initially generated via intermolecular insertion of the C≡C bond into the Ln−N functionality preferentially

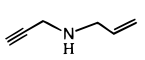
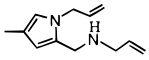
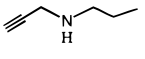
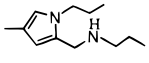
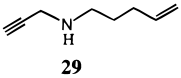
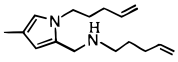
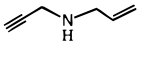
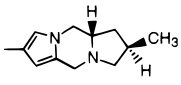
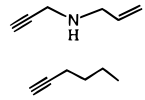
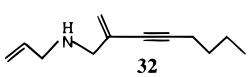


(12)

undergoes regiospecific terminal alkyne insertion rather than alkene insertion to form a five-membered pyrrole structure. The greater insertive reactivity of Ln−N groups with respect to alkynes than to alkenes was noted above in intramolecular hydroamination/ bicyclizations (**9** → **10**, **11** → **12** in Table 1).

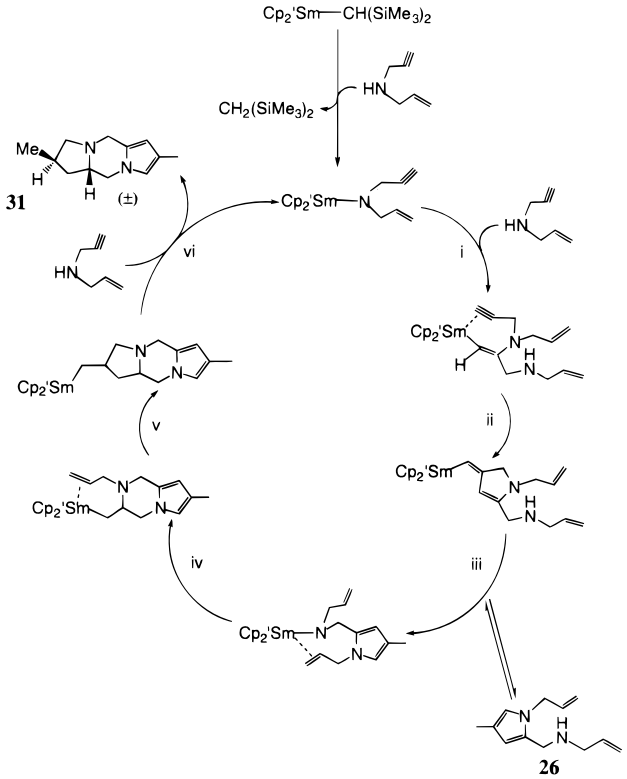
(28) For a discussion of such thermal [1, *j*] sigmatropic rearrangements, see: (a) March, J. *Advanced Organic Chemistry*, 4th ed.; J. Wiley & Sons: New York, 1992; pp 1121−1125 and references therein. (b) Boger, D. L.; Ishizak, T.; Kitos, P. A.; Suntornwak, O. *J. Org. Chem.* **1990**, *55*, 5823−5832.

Table 3. Intermolecular Hydroamination/Cyclization Results

Entry	Substrate	Product	N_t, h^{-1}(°C)	Yield(%)
1.	 **25**	 **26**	236 (60)[a]	92[c]
2.	 **27**	 **28**	208 (60)[a]	95[c]
3.	 **29**	 **30**	58 (60)[a] 15 (60)[b]	95[c]
4.	 **25**	 (±) **31**	1 (60)[a]	93[d]
5.		 **32**	10 (60)[a]	39[c,e]

[a] Cp′$_2$SmCH(SiMe$_3$)$_2$ precatalyst in C_6D_6. [b] Me$_2$SiCp″$_2$NdCH(SiMe$_3$)$_2$ precatalyst in C_6D_6. [c] Yield determined by ^{1}H NMR and GC/MS after vacuum transfer of volatile products. [d] Isolated yield. [e] See text.

Scheme 4. Proposed Pathway for Organolanthanide-Catalyzed Inter- and Intramolecular Hydroamination/ Tricyclization



Additionally, *N*-allyl-2-(1′-allyl-3′-methylpyrrolyl)methylamine (**26**), produced by organolanthanide-mediated intermolecular hydroamination followed by intramolecular cyclization (Scheme 4, steps i and ii), undergoes subsequent activation on longer reaction times (Scheme 4, step iii), intramolecular hydroamination/bicyclization (Scheme 4, step iv), tricyclization (Scheme 4, step v), and finally protonolysis (Scheme 4, step vi) to generate a tricyclic polyheterocycle (**31**). Furthermore, tricyclization beginning with *N*-allylpropargylamine (**25**, Table

3) or **26** (Table 3) is regiospecific, yielding exclusively a structure assigned to the trans isomer by 2D and NOE difference NMR spectroscopy. Attempts to intermolecularly couple a simple terminal alkyne such as 1-hexyne with substituted propargylamines followed by hydroamination/cyclization were unsuccessful, yielding only acyclic coupling products (**32**) and homodimers (entry 5, Table 3).

Discussion

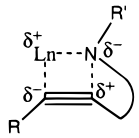
The present study reveals efficient, sequential coupling of organolanthanide-mediated carbon−nitrogen and carbon−carbon bond formation/cyclization processes to constitute catalytic cycles, and considerably extends the scope of known organolanthanide-mediated olefin and alkyne hydroamination/cyclization, as well as diolefin, dialkyne, and enyne cyclization processes. In the ensuing discussion, we focus on factors affecting the course and rates of both inter- and intramolecular catalytic variants of these reactions, and interpret them in terms of likely mechanistic patterns.

Intramolecular Hydroamination/Bicyclization. Kinetics and Mechanism. The results in Table 1 illustrate that both $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ complexes are competent precatalysts for the hydroamination/bicyclization of aminodialkenes, aminodialkynes, and aminoalkenynes. In all in situ NMR-scale reactions, instantaneous formation of $CH_2(SiMe_3)_2$ from protonolytic reaction of the precatalysts with the amine substrates is observed, and the concentration remains constant throughout the course of the catalytic reaction. It can be seen in Table 2 that variation of Ln^{3+} ionic radius significantly affects the reaction rate of the **1** → **2** transformation. When catalyst and substrate concentration are held constant at room temperature, the **1** → **2** turnover frequencies increase with increasing eight-coordinate Ln^{3+} ionic radius[26] (Figure 3). However, as mentioned in the Results Section, high amine concentrations and the more "open" $Me_2SiCp''_2LnCH(SiMe_3)_2$ precatalyst, along with high reaction temperatures can result in monocyclic byproducts (3−15%), presumably via competing intermolecular protonolysis of Ln−C intermediates (Scheme 1, step ii). The more "open" catalysts and high amine concentrations likely enhance amine coordination at the lanthanide center, thus facilitating Ln−C protonolysis.

In regard to substrates, the present intramolecular catalytic coupling process is capable of regiospecifically assembling aminodialkenes, aminodialkynes, and aminoalkenynes in a single catalytic cycle to generate pyrrolizidine and indolizidine skeletons.[8,10] Note in Table 1 that alkyne, alkene (entries 1 and 2); alkyne, alkyne (entry 7); alkene, alkene (entries 8 and 9); and alkene, alkyne (entry 11) substrates all undergo organolanthanide-mediated sequential bicyclization as exemplified by Scheme 2. However, only regiospecific five-membered cyclization is observed in significant yields for the second ring-closing reaction. The diminished activity for six- and seven-membered second ring bicyclitive closure likely reflects a sterically controlled process[5a,29−32] in competion with Ln−C protonolysis (Scheme 1, steps ii and iii) which leads to monocyclic products. For example, *N*-allyl-4-pentyn-1-amine (**5**) could potentially form a pyrrolizidine skeleton; however, the second ring-closing reaction is unrealized, presumably due to intervention of rapid Ln−C protonolysis of the intermediate by a free or bound substrate containing an acidic N−H and/or ≡C−H moiety (Scheme 1, step ii). Although *N*-allyl-5-(trimethylsilyl)-4-pentyn-1-amine (**7**) also contains the elements of a pyrrolizidine skeleton, a combination of what are apparently electronic[33] and steric impediments prohibits the second (olefinic) insertion into the α-(silylvinyl)lanthanide linkage in the Ln−C bonded intermediate (Scheme 1, step iii). In the case of second rings greater than five-membered (Table 1, entries 5, 6, and 12), apparently the greater steric encumbrance and greater entropic loss[32] in the formation of cyclization transition states renders the second ring closure uncompetitive with rapid Ln−C bond protonolysis.

With regard to reaction rate, the present bicyclizations are kinetically comparable to the corresponding aminoalkene[6b,c] and aminoalkyne[7a,b] monocyclizations for the same catalysts, temperatures, and reaction conditions. Furthermore, insertion in the first ring-closing reaction largely appears to govern the overall bicyclization rate, and bicyclizations involving alkyne insertions in the initial ring formation are more rapid than the corresponding alkene transformations. As noted above, an appealing explanation for such insertion sequences and rate effects invokes a sterically more approachable, electron-rich, and cylindrical C≡C π system, a stereoelectronically influenced four-center transition state (**B**; electron-withdrawing groups in the terminal alkyne moieties (R) stabilize; electron-donating groups in the terminal position destabilize), more nucleophilic alkynyl sp hybridized carbon atoms,[25] as well as a more exothermic and exergonic alkyne insertion process.[22−24]

B



In regard to reaction mechanism, the ^1H NMR monitoring results indicate that intermolecular substrate protonolysis of the catalyst hydrocarbyl precursors, similar to the case of organolanthanide-catalyzed aminoalkene[6b,c] and aminoalkyne cyclization,[7a,b] rapidly forms $CH_2(SiMe_3)_2$ and a catalytically active $LnNRR'(NHRR')_x$ species. As evidenced by the ^1H NMR of the paramagnetic catalysts, this complex undergoes rapid exchange of bound amine-amide ligands and/or of bound and free amines[6b,c] (eq 13). Next, as examplified by in Scheme 2, the insertion of an unsaturated carbon−carbon moiety into the Ln−N amido bond yields a five-membered ring. This insertion is expected to be more rapid and exothermic than the formation of a strained three-membered ring.

$$Cp'_2LnNRR'(HNRR')_x \rightleftharpoons Cp'_2LnNRR'(HNRR')_{x-1} + HNRR' \quad (13)$$

The process of olefin insertion into the Ln−C bond generated in the initial ring-forming amination/cyclization undoubtedly occurs via a concerted four-center transition state. Such processes generally have very low activation barriers, as

(29) For reviews of the cyclization of acyclic molecules, see; (a) Nakagaki, R.; Sakuragi, H.; Mutai, K. *J. Phys. Org. Chem.* **1989**, *2*, 187−204. (b) Mandolini, L. *Adv. Phys. Org. Chem.* **1986**, *22*, 1−111.

(30) For a review of the cyclization and conformation of hydrocarbon chains, see: Winnik, M. A. *Chem. Rev.* **1981**, *81*, 491−524.

(31) For a review of steric and electronic effects in heterocyclic ring closures, see: Valters, R. *Russ. Chem. Rev.* **1982**, *51*, 788−801.

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

(33) For discussions of unusual aspects of d^0 metal-α-silylvinyl electronic structure and bonding, see: (a) Horton, A. D.; Orpen, A. G. *Organometallics* **1991**, *10*, 3910−3918. (b) Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 108−112. (c) Eisch, J. J.; Piotrowski, A. M.; Brownstein, S. K.; Gabe, E. J.; Lee, F. L. *J. Am. Chem. Soc.* **1985**, *107*, 7219−7220.

suggested by theoretical calculations,[34] and numerous examples of such insertions,[3] including spectroscopic[3c] and X-ray crystal structure[35] studies designed to model such insertions. The results of the present bicyclizations are consistent with Scheme 1, involving a rapid second C═C/C≡C insertion (Scheme 1, step iii) into the resulting Ln−C bond formed via previous carbon−carbon multiple bond insertion into the Ln−N bond (Scheme 1, step i).

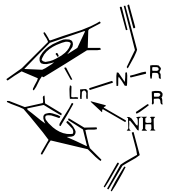
The kinetic results for the Cp'_2Sm-catalyzed **15** → **16** transformation indicate zero-order behavior in [substrate] and first-order behavior in [Sm] (eq 9) in analogy to organo-f-element-mediated intramolecular aminoolefin,[6b,c] and aminoalkyne[7a,b] hydroamination/cyclization. This implies a similar intramolecular insertive process during the first ring-closing reaction (carbon−carbon multiple bond insertion into the Ln−N bond) arguably as the turnover-limiting step. Further support for such a turnover-limiting insertion scenario is found in the pronounced correlation of **1** → **2** turnover frequencies (at constant $[Cp'_2Ln]$, [substrate], and temperature) with decreasing eight-coordinate Ln^{3+} ionic radius[26] [Ln (ionic radius, Å), N_t]: La (1.16), 148; Nd (1.11), 45; Sm (1.08), 17; Lu (0.977), <0.2 h^{-1}) (Figures 2 and 3). This tendency of large Ln^{3+} ions to accelerate unsaturated carbon−carbon bond insertion is consistent with the known patterns in organolanthanide-mediated olefin hydrogenation,[3j,6b,12b,c,36] polymerization,[12a,c,36f] hydrophosphination,[6d] hydrosilylation,[3d,e] and hydroamination.[6] Further evidence for this turnover-limiting insertion process derives from bicyclization turnover frequencies. For example, in the case of *N*-allyl-4-hexyn-1-amine (**3**) vs *N*-allyl-4-penten-1-amine (**15**) (Table 1), which have sterically similar structures, the former alkyne insertion into the Ln−N bond exhibits a far greater N_t (777 h^{-1}) than the latter alkene insertion (N_t = 55 h^{-1}).

Organolanthanide-Catalyzed Intermolecular Sequential C−N and C−C Bond Formation. The organolanthanides $Cp'_2LnCH(SiMe_3)_2$ and $Me_2SiCp''_2LnCH(SiMe_3)_2$ also serve as effective catalyst precursors for rapid, coupled intermolecular C−N + intramolecular C−C bond formation sequences to yield pyrrole derivatives in a single catalytic cycle. The principal reaction mechanism for the present intermolecular hydroamination/cyclization likely appears to be the pathway previously proposed for both intermolecular hydroamination[6a] and intramolecular hydroamination/bicyclization.[3a] This would involve rapid protonolysis of the precatalysts by the amine substrates to form $LnNRR'(NHRR')_x$ complexes. These subsequently undergo (presumably) turnover-limiting intermolecular alkyne insertion into the Ln-N bonds (a similar turnover-limiting insertion was identified in related intermolecular hydroamination[6a]) followed by a second rapid intramolecular alkyne insertion into the resulting Ln−C bond (Scheme 3; the same type of insertion was observed in intramolecular cyclizations[3a,4b−g]). Subsequent rapid intra- or intermolecular protonolysis of the Ln−C bonds generates exo-methylene heterocycles which undergo precedented thermal isomerization to conjugated pyrrole derivatives.[7,8] Such catalytic cycles proceed via rather different mechanisms than other lanthanide- and actinide-mediated terminal alkyne dimerizations or oligomerizations.[4] In those processes, the plausible pathway involves protonolysis of the metal−alkyl precursor with simple terminal alkynes to yield $[Ln-C{\equiv}CR]_n$ species which then undergo subsequent alkyne insertion into the Ln−C≡CRbond affording Ln−alkenyl complexes. These species then undergo protonolysis by an incoming alkyne, yielding an acetylene dimer and regenerating the Ln−alkynyl complex.

In the present catalytic processes, the substrate contains a Lewis basic/acidic amine group,[37] arguing that rapid protonolysis by N−H functionalities limits the lifetimes/effective concentrations of any $Ln-C{\equiv}CCH_2NHR$ species, as shown in Scheme 3. Intra- or intermolecular protonolysis of $Ln-N(R)CH_2C{\equiv}CH$ complexes by a ≡CH moiety to yield a $Ln-C{\equiv}CCH_2NHR$ complex is estimated from thermochemical data[22−24] to be exothermic by ∼7 kcal/mol, however this pathway is apparently not competitive with the far more exothermic insertion of alkyne into the Ln−N bond ($\Delta H \approx -35$ kcal/mol). It is therefore not surprising that significant quantities of alkyne dimers or trimers formed via alkyne insertion into metal−carbon bonds[4] are not observed.

The substantial turnover frequencies in the present dimerization process are especially noteworthy compared to more conventional organolanthanide-catalyzed intermolecular hydroamination processes (amine + olefin; amine + alkyne).[6a] For example, the secondary amines in the present process are rather sterically encumbered for efficient intermolecular insertion of carbon−carbon multiple bonds into the Ln−N functionalities. However, it is likely that amine substrates bearing pendant alkyne functionalities are involved in strong acid−base, catalyst−substrate preorganization, which would facilitate subsequent insertion of the proximate alkyne moiety into the Ln−N bond (e.g., **D**, Scheme 3). Similar $LnNHR(NH_2R)_x$ amine−amido adducts[38] are detected in chiral organolanthanide systems[6b] via ^1H NMR, and in achiral catalyst systems by both ^1H NMR and

D



X-ray crystal structure studies.[6c] In the present intermolecular hydroamination/cyclization process, the formation of amine−

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amido adducts is expected to readily place the attached alkyne moieties in favorable geometries within the lanthanide coordination spheres for facile alkyne insertion into the Ln−N bonds. It is therefore not surprising that such intermolecular insertion processes can compete favorably with intramolecular insertion (eq 11). That products resulting from simple alkyne insertion into an Ln−N bond are not detected in the organolanthanide-mediated intermolecular reaction of *N*-allylpropargylamine with excess 1-hexyne (Table 3, entry 5) also supports the proposed catalyst−substrate preinteraction.

The observation that Ln−C bonds generated by intermolecular amination undergo cyclization with the pendent alkyne moieties rather than intra- or intermolecular amine protonolysis is in accord with the aforementioned rapid carbon−carbon bond formation processes as demonstrated in the intramolecular bicyclization. Furthermore, this insertion is favored for alkynes over alkenes (eq 12), and is analogous to the aforementioned intra- and intermolecular additions of Ln−N moieties to carbon−carbon multiple bonds, reflecting the aforementioned preferential alkyne nucleophilic addition.[22,24,25] That the only observed products are those expected on the basis of sequential C−N, C−C coupling, strongly supports such a cyclization mechanistic scenario. However, note that this intermolecular hydroamination/cyclization can be followed by subsequent sequential intramolecular hydroamination/cyclization to generate a tricyclic heterocycle via the aforementioned bicyclization process (Scheme 4). Also noteworthy here is the stereochemical course of the tricyclization process. Only the *trans*-isomer is observed in the sequential intermolecular C−N, intramolecular C−C, C−N, and C−C bond formation process. This result argues for substantial steric control as well as intramolecular amine coordination to the lanthanide center during the intramolecular amination/bicyclization (Scheme 4, step iv) and tricyclization (Scheme 4, step v) leading to the unique fused pyrrole-pyrazine-pyrrole skeleton.[9,10f−i]

The present intermolecular C−N + intramolecular C−C bond fusion processes represent a direct and efficient method for catalytically generating unusual amino-pyrrole derivatives from simple substituted propargylamines. The apparently straightforward reaction mechanism, extendible reaction scope, substrate versatility, as well as the regiospecific and stereospecific product formation represents a potentially useful approach to important heterocycle skeletons such as pyrrole and pyrazine derivatives.

Conclusions

Organolanthanide centers can mediate unusual tandem sequences of insertive C−N and C−C bond-forming processes in intramolecular as well as intermolecular hydroamination/cyclization, and such transformations can be readily integrated into novel and regioselective catalytic cycles with high turnover frequencies. Of note is the attraction of assembling pyrrolizidine, indolizidine, and pyrrole−pyrazine−pyrrole skeletons having varying degrees of unsaturation and substitutable groups, hence points for subsequent functionalization, in a single catalytic cycle. Significantly, the catalyst−substrate interaction via adduct formation can be applied to intermolecular catalytic reactions, resulting in preferential intermolecular insertion over intramolecular insertion. Followed by intramolecular cyclization, this provides an efficient route to pyrrole and pyrazine derivatives. Additional applications are currently under investigation.

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