Catalytic Intramolecular Hydroamination of Hindered Alkenes Using Organolanthanide Complexes

Gary A. Molander* and Eric D. Dowdy

Department of Chemistry and Biochemistry, University of Colorado at Boulder, Boulder, Colorado 80309-0215

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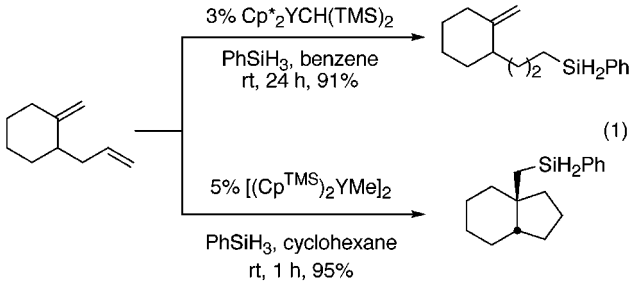
The intramolecular hydroamination of hindered alkenes has been developed as a versatile route to heterocyclic systems. The current process utilizes the unhindered catalyst system $[Cp^{TMS}_2LnMe]_2$ (Ln = Sm, Nd) to effect the cyclization of hindered amino olefins, providing products containing quaternary centers. The process tolerates a wide variety of substitution patterns, allowing the construction of monocyclic as well as fused and bridged bicyclic heterocycles. Two experimental procedures were employed in this study: one without solvent, minimizing waste streams, the other in deuterated solvents, allowing NMR monitoring of the reaction. The yield of each reaction was high, with NMR analysis of the reactions in progress showing clean conversion from starting material to a single product in most cases.

Introduction

Alkene hydroamination is a potentially powerful entry into a variety of heterocyclic systems.[1] Traditional methods to facilitate this transformation include aminomercuration/demercuration[2] and palladium-catalyzed addition of nitrogen nucleophiles to alkenes. Although many interesting structures have been formed via intramolecular reactions,[2a] the aminomercuration route suffers from the need to use stoichiometric quantities of mercury salts. The method is also complicated by the reversible nature of some reactions and nitrogen migration when exposed to the workup conditions,[3] leading to reduced yields and impure products. The palladium procedure is limited by the poisoning effect many amines have on the reactive center.[4] This makes many of the reactions possible only under stoichiometric conditions. A limited set of conjugated amines permits catalytic cyclization to proceed,[5] with obvious constraints on synthetic utility.

Organolanthanide complexes have been studied as catalysts for the selective hydrogenation,[6] hydrosilylation,[7] hydroamination,[8] and hydrostannylation[9] of alkenes and alkynes. The most powerful transformations performed take advantage of the ability of these complexes to insert multiple alkenes before the final functionalization step to give polycyclic products from acyclic substrates.[7a,b,d,f,h,j,k,l,8e] The flexibility of these catalysts is increased by their variability: substitution patterns on the ligands can be altered and the metal can be varied with a concomitant change in ionic radius to provide the desired steric environment necessary to facilitate a certain transformation selectively. Many ligands have been prepared bearing a wide variety of steric directors or coordinating groups,[10] some in asymmetric form.[5c,d,11] Coupled with the fact that these ligands complex with almost any of the lanthanide or group 3 metals, a wide array of catalyst variation is possible.[12] This approach



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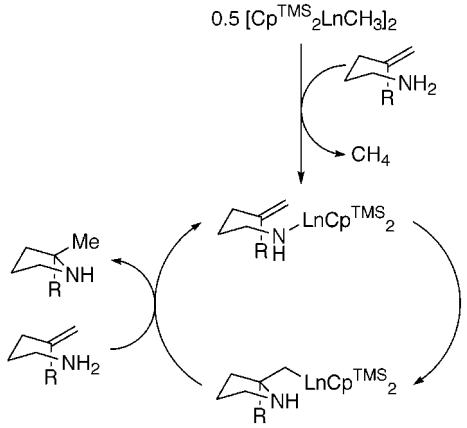
Scheme 1. Catalytic Cycle for Intramolecular Hydroamination



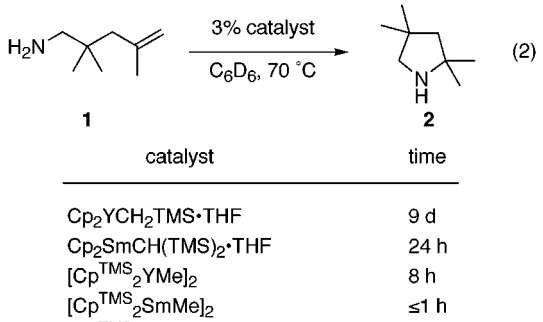
has led to the successful expansion of substrate compatibility in organolanthanide-catalyzed olefin hydrosilylation by the rational modulation of the ligand array (eq 1, Cp* = C_5Me_5).[7l]

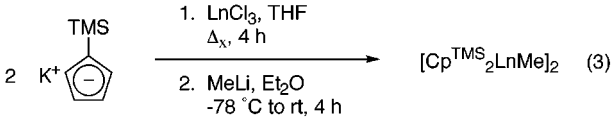
Organolanthanide-catalyzed hydroamination has been developed to overcome the difficulties inherent with other similar transformations while taking advantage of the variability of this catalytic platform.[8] This transformation is mechanistically distinct from the other hydroamination protocols (Scheme 1).[8a] The organometallic complex enters the catalytic cycle with metalation of the amine nitrogen. This is followed by an intramolecular olefin insertion to generate a hydrocarbyl intermediate that undergoes σ-bond metathesis with another primary amine to complete the cycle. Intra-[8a,b,d,e] and intermolecular[7c] reactions have been performed with relatively hindered catalyst systems. This protocol allows the assembly of a wide variety of heterocyclic and bicyclic products, the nature of which is only limited by the requirement that cyclization occur with internal alkynes or monosubstituted alkenes. The current research was undertaken to alleviate this requirement by appropriate modification of the catalyst.

Results and Discussion

An initial survey of catalysts was undertaken to discover the most efficient complexes to perform the intramolecular hydroamination of a hindered alkene. A test substrate, 1-amino-2,2,4-trimethylpent-4-ene (**1**), was exposed to a broad assortment of group 3 and lanthanide-based metallocene complexes. The complexes chosen possessed varying amounts of substitution on the cyclopentadienyl ligands and a range of metal ionic radii. The results (eq 2, Cp" = C_5Me_4) illustrate that reduced substitution about the ligand and a larger metal ionic radius contribute to accelerated reaction with hindered olefins. When also considering the ease of preparation (eq 3),[13] we decided to use $[Cp^{TMS}_2LnMe]_2$ (Ln = Sm, Nd) as catalysts for the remainder of the study.

The hydroamination reaction was performed by two procedures: the two components, substrate and catalyst,





dissolved in C_6D_6 in a sealed NMR tube with NMR monitoring or neat in a sealed tube with GC analysis of small aliquots. The former procedure was utilized with higher molecular weight amines that could be easily separated from the solvent during workup and purification. The latter procedure allowed the isolation of volatile products by vacuum transfer of the product away from the catalytic species. In general, the neat procedure required longer reaction periods than the same transformation in solution, probably because of the increased viscosity of the reaction medium. The continued catalytic activity of the complexes used under the rigorous thermal conditions and lengthy reaction times required for some reactions to reach completion is remarkable in light of their moderately low decomposition temperatures.[14]

Varied structural motifs (Table 1) were incorporated into the amino olefin substrates to examine the generality and scope of the reaction. Most of the substrates were prepared through Wittig olefination of a keto nitrile followed by LAH reduction of the pendant nitrile. Both steps were rapid and high yielding, making this an efficient entry to heterocycles. Pyrrolidines bearing quaternary centers α to the nitrogen could be prepared in good yield, regardless of the substitution along the rest of the chain (entries 1−4, 7, 8). Substitution along the linking chain accelerated the cyclization when comparing results from runs utilizing unsubstituted substrates under similar conditions (procedure B). Thus, the Thorpe−Ingold effect may be harnessed to facilitate a sluggish reaction.[15]

The hydroamination of an exocyclic alkene was also successful in constructing bicyclic amines from monocyclic precursors (entries 5, 6). In this manner, azabicyclo[4.3.0]nonane and azabicyclo[4.4.0]decane ring systems bearing methyl groups at one ring junction were prepared in good yields. The cyclization onto a hindered alkene leading to a six-membered ring is an expansion of carbometalation/cyclization chemistry wherein products from related dienes are exclusively acyclic in nature (eq

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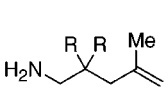
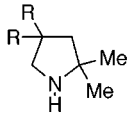
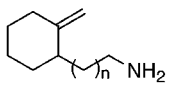
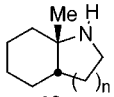
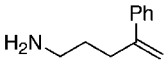
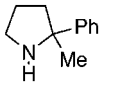
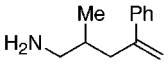
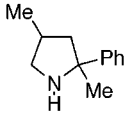
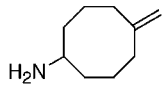
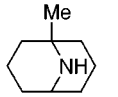
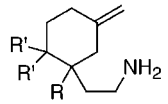
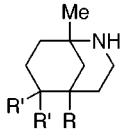
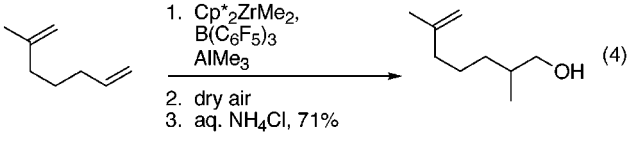
Table 1. Hydroamination of Hindered Alkenes Catalyzed by $[(Cp^{TMS})_2LnMe]_2$[a]

entry	substrate	product	procedure,[b] temp, time, isolated yield
			
1	**1** R = Me	**2**	A,[c] 70 °C, 2 h, 93% B, 70 °C, 1 h, 70%
2	**3** R = H	**4**	A, 120 °C, 12 h, 95%
3	**5** R = Ph	**6**	B,[c] rt, 1 h, 98%
4	**7** R = -$(CH_2)_5$-	**8**	B,[c] rt, 1 h, 92%
			
5	**9** n = 1	**10**	A, 140 °C, 14 d, 90% B, 120 °C, 2 d, 80%
6	**11** n = 2	**12**	B, 140 °C, 7d, 90%
7	 **13**	 **14**	B, 120 °C, 7 d, 90%
8	 **15**	 **16**	B,[c] 120 °C, 2 d, 100%
9	 **17**	 **18**	B, 120 °C, 5 min, 94%
			
10	**19** R = Me, R' = H	**20**	B, 120 °C, 48 h, 97%
11	**21** R = H, R' = Me	**22**	B, 120 °C, 3 d, 91%

[a] $[Cp^{TMS}_2NdMe]_2$ was used as the precatalyst unless otherwise noted. [b] Procedure A: The reaction was run neat in a sealed tube. Procedure B: The reaction was run in C_6D_6 in a sealed NMR tube. [c] $[Cp^{TMS}_2SmMe]_2$ was used as the precatalyst.

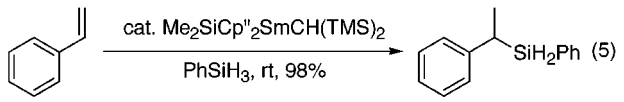
4).[16] Cyclization is the major reactive pathway available to the amino olefin, whereas in the zirconium-catalyzed carbometalation systems the intermediates can react with the trapping reagent before the entropically less favorable six-membered ring-forming event.



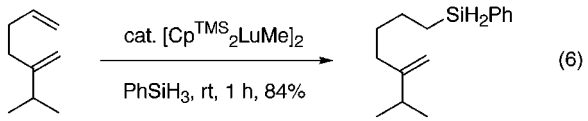
(4)

Another area in which the hydroamination chemistry excels beyond other lanthanide-catalyzed reactions is the toleration of branched substituents on the alkene. In the current study styrene derivatives (entries 7, 8) were found to cyclize with only moderate reduction of the reaction rate. In the olefin silylation reaction styrenes react with inverted regiochemistry (eq 5),[7a] and branching α to the hindered olefin precluded cyclization (eq 6).[7l]

Again, the difference in observed reactivity stems from the lack of competing side reactions in the hydroamination process. The incorporation of a single methyl group along the molecular backbone (entry 8) opened up the possibility for diastereomeric products. Unfortunately, no preference for the orientation of this substituent during cyclization was observed and a mixture of diastereomers was obtained.



(5)

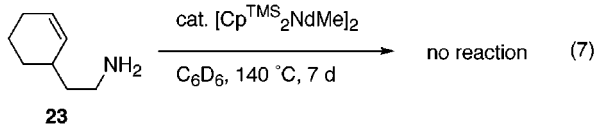


(6)

Bridged bicyclic amines can also be produced by the hydroamination of exocyclic alkenes. Entry 9 illustrates one scenario for this transformation—the transannular cyclization of a medium-membered ring. The rapidity of the reaction at elevated temperatures is interesting because the reaction proceeds sluggishly if at all at ambient temperature. This energy requirement is probably reflective of the need to invert the conformation of the eight-membered ring to bring the reactive partners in close proximity.[17]

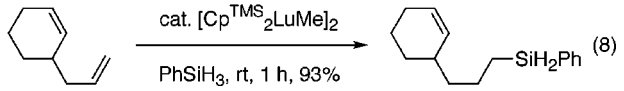
Another entry into bridged bicyclic amines providing complementary location of the nitrogen is the hydroamination of an exocyclic alkene by a chain pendant from the β carbon (entries 10 and 11). The cyclization is tolerant of changes in the substitution pattern at other ring locations, allowing the amine products to be limited only by the feasibility of substrate preparation.

In contrast to the remainder of these experimental results, endocyclic alkenes remain resistive to cyclization. Upon exposure of **23** to a variety of reaction conditions, no reaction was observed (eq 7). This echoes the results of the hydrosilylation study in which no cyclized products were obtained from similar substrates (eq 8).[7l]



(7)

23



(8)

The power of performing multiple bond insertions in a single step has previously been harnessed in the one-step construction of bicyclic amines (eq 9).[8e] Precisely balanced reactivity must be obtained for success in this type of reaction. The rate of the second double bond insertion must be far greater than the intermolecular trapping of the intermediate hydrocarbyl by metathesis with the substrate. A lack of selectivity would result in a mixture of products. A similar multiple bond insertion process was attempted in the hydroamination of a doubly unsaturated amine **24** (eq 10). After the insertion of the first double bond, the molecule has the choice of reaction with another free amine, generating an unsaturated

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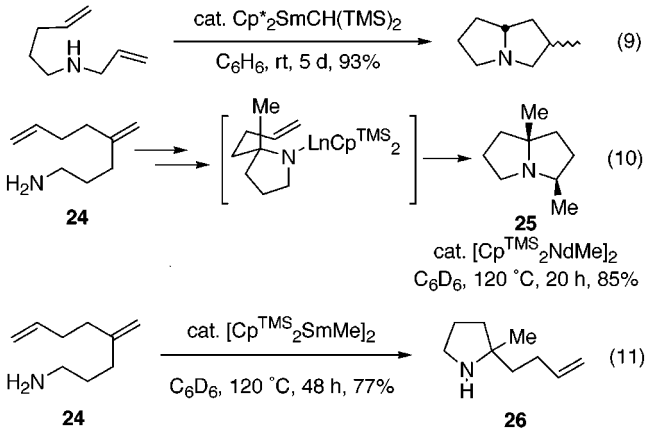
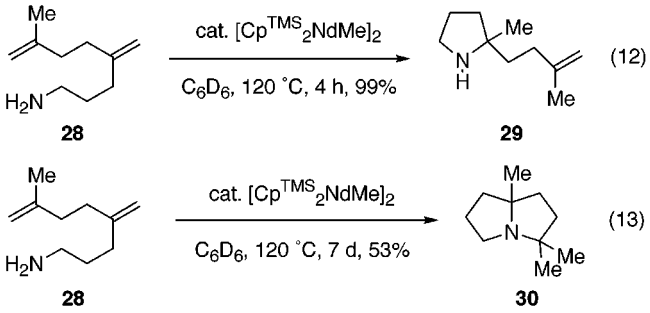
pyrrolidine, or insertion of the remaining double bond, leading to a bicyclic product. When **24** was exposed to the catalyst, the latter process dominated and the reaction proceeded through two discrete ring-forming steps to give **25** as the major product. The high diastereomeric selectivity of the second cyclization event may be explained by the chairlike transition structure of the intermediate organolanthanide (eq 10). The use of a slightly more hindered complex ([Cp^{TMS}_2SmMe]$_2$) coupled with careful monitoring of the reaction by NMR allowed the isolation of **26** contaminated by small amounts of **24** and bicyclic product **25** (eq 11). On extended reaction **26** is converted completely to bicyclic product **25** by the hydroamination of the remaining olefin with the secondary amine. The structure of **25** was determined unambiguously by conversion to its picrate (**27**) and X-ray diffraction analysis of the resulting crystalline product.



Analogous products were generated in the hydroamination of **28** where both alkenes are hindered and the intermediate is a secondary amine. The first step of the reaction proceeded cleanly to unsaturated pyrrolidine **29** (eq 12). Bicyclic amine **30** was produced after prolonged exposure to the catalyst (eq 13). Either product could be generated selectively with careful NMR monitoring because of the much slower progress of the second cyclization. The high catalyst loading and rigorous reaction conditions required for this conversion indicate that this represents the practical limit of steric encumbrance about the amine and olefin allowable by this class of catalysts.



Conclusions

The organolanthanide catalyzed hydroamination reaction has been successfully extended to more highly hindered substrate classes than previously explored. The flexibility of the method allows the rapid construction of many mono- and bicyclic heterocycles with varying substitution. The catalysts utilized are readily prepared by standard organometallic synthesis. The procedures developed in this study allow the easy monitoring of each reaction's progress as well as facile isolation of the products.

Experimental Section

2,2,4,4-Tetramethylpyrrolidine (2). Representative Procedure for Neat Hydroamination (Procedure A). In a nitrogen filled glovebox [Cp^{TMS}_2SmMe]$_2$ (0.038 g, 5.6 mol %) was weighed into a storage tube with a Teflon screw top valve. Next, 1-amino-2,2,4-trimethyl-4-pentene (0.196 g, 1.54 mmol) was added to form a light yellow solution, and the vessel was sealed and removed from the glovebox. The solution was then heated to 70 °C for 2 h. GC analysis of an aliquot confirmed that the reaction was complete. The product was then vacuum transferred away from the catalyst into another storage tube. The material obtained in this manner was analytically pure (0.182 g, 1.42 mmol, 93%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.66 (s, 2 H), 1.70 (br s, 1 H), 1.40 (s, 2 H), 1.14 (s, 6 H), 1.02 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 60.42, 59.93, 54.75, 41.19, 30.52, 28.82; IR (neat) 3276.1, 2954.8, 2866.2 cm^{-1}; HRMS calcd for $C_8H_{17}N^+$ 127.1361, found 127.1367; LRMS (EI+) *m*/*z* 127 (2), 112 (100), 71 (56).

2,2-Dimethylpyrrolidine (4). Prepared from **3** according to procedure A given above using [Cp^{TMS}_2NdMe]$_2$ as the precatalyst. Using 3.9% catalyst loading the reaction was complete after 12 h at 120 °C. Analogous workup and purification provided the title compound in 95% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94−2.92 (m, 2 H), 1.79−1.73 (m, 2 H), 1.49−1.46 (m, 2 H), 1.29 (br s, 1 H), 1.11 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 58.85, 46.00, 39.50, 28.76, 26.05; IR (neat) 3269.0, 2959.2, 2868.2 cm^{-1}; HRMS calcd for $C_6H_{13}N^+$ 99.1048, found 99.1055; LRMS (EI+) *m*/*z* 99 (4), 84 (100), 71 (27). Anal. Calcd for $C_6H_{13}N$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.56; H, 13.22; N, 13.92.

2,2-Dimethyl-4,4-diphenylpyrrolidine (6). Representative Procedure for NMR Scale Hydroamination (Procedure B). In a nitrogen filled glovebox [Cp^{TMS}_2SmMe]$_2$ (0.009 g, 4 mol %) was weighed into a vial and dissolved in 0.5 mL of C_6D_6. Next, 0.139 g (0.557 mmol) of **5** was added and the light yellow solution was transferred into an NMR tube equipped with a Teflon valved top using another 0.5 mL of C_6D_6 to rinse the vial. The mixture was then removed from the glovebox and the progress of the reaction was monitored by NMR. After 1 h the starting material was completely consumed. The solution was filtered through Florisil with Et_2O to remove the catalyst, and the filtrate was concentrated in vacuo. The residue was purified by Kugelrohr distillation to yield 0.137 g (0.545 mmol, 98%) of the title compound as a colorless oil: ot 112 °C/0.07 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.22 (m, 8 H), 7.14−7.10 (m, 2H), 3.61 (s, 2 H), 2.51 (s, 2 H), 1.67 (br s, 1 H), 1.12 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.60, 128.38, 126.95, 125.84, 59.25, 58.41, 57.26, 52.04, 30.75; IR (neat) 3200 (br), 3084.7, 3026.8, 2961.4 cm^{-1}; HRMS calcd for $C_{18}H_{21}N^+$ 251.1674, found 251.1662; LRMS (EI+) *m*/*z* 251 (5), 236 (10), 91 (6), 71 (100). Anal. Calcd for $C_{18}H_{21}N$: C, 86.01; H, 8.42; N, 5.57. Found: C, 86.22; H, 8.62; N, 5.53.

8-Aza-9,9-dimethylspiro[5.4]decane (8). Prepared from **7** according to procedure B given above using [Cp^{TMS}_2SmMe]$_2$ as the precatalyst. Using 3.8% catalyst loading the reaction was complete after 1 h at room temperature. Analogous workup and purification provided the title compound in 92% yield: ot 90 °C/10 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.73 (s, 2 H), 1.60 (br s, 1 H), 1.43−1.26 (m, 12 H), 1.14 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 59.25, 45.39, 38.17, 30.26, 26.05, 23.84; IR (neat) 3275.7, 2955.2, 2923.8, 2855.6 cm^{-1}; HRMS calcd for $C_{11}H_{21}N^+$ 167.1674, found 167.1676; LRMS (EI+) *m*/*z* 167 (1), 152 (100), 71 (50).

(±)-(1*R,6*R**)-9-Aza-1-methylbicyclo[4.3.0]nonane (10).** Prepared from **9** according to procedure A given above using [Cp^{TMS}_2NdMe]$_2$ as the precatalyst. Using 4.8% catalyst loading the reaction was complete after 14 days at 120 °C. Analogous

workup and purification provided the title compound in 90% yield: ot 80 °C/40 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.04−2.90 (m, 2 H), 1.91−1.80 (m, 1 H), 1.71−1.27 (m, 11 H), 1.08 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 59.51, 44.38, 42.79, 33.84, 30.10, 26.79, 26.35, 22.90, 22.08; IR (neat) 3275.0, 2924.8 cm^{-1}; HRMS calcd for $C_9H_{17}N^+$ 139.1361, found 139.1361; LRMS (EI+) *m*/*z* 139 (17), 124 (50), 96 (100).

(±)-(1*R,6*R**)-2-Aza-1-methylbicyclo[4.4.0]decane (12).**[18] Prepared from **11** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 4.9% catalyst loading the reaction was complete after 7 days at 120 °C. Analogous workup and purification provided the title compound in 90% yield: ot 95 °C/30 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$, spectra taken at 60 °C) δ 2.85−2.81 (m, 2 H), 1.83−1.75 (m, 1 H), 1.65−1.25 (m, 11 H), 1.13 (s, 3 H), 1.15−1.04 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.46, 41.34, 40.56, 35.42, 28.36, 27.50, 26.29, 24.92, 23.27, 22.90; IR (neat) 3277.7, 2926.6, 2860.9 cm^{-1}; HRMS calcd for $C_{10}H_{19}N^+$ 153.1517, found 153.1512; LRMS (EI+) *m*/*z* 153 (14), 138 (53), 110 (100).

2-Methyl-2-phenylpyrrolidine (14). Prepared from **13** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 4.5% catalyst loading the reaction was complete after 7 days at 120 °C. Analogous workup and purification provided the title compound in 90% yield: ot 100 °C/10 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.44 (m, 2 H), 7.38−7.27 (m, 2 H), 7.21−7.15 (m, 1 H), 3.15−3.06 (m, 1 H), 3.01−2.93 (m, 1 H), 2.11−2.02 (m, 1 H), 1.93−1.82 (m, 2 H), 1.79−1.62 (m, 2 H), 1.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.18, 128.10, 126.01, 125.43, 65.12, 45.83, 40.10, 30.30, 25.50; IR (neat) 3300 (br), 3021.2, 2961.0, 2870.0 cm^{-1}; HRMS calcd for $C_{11}H_{15}N^+$ 161.1204, found 161.1217; LRMS (EI+) *m*/*z* 161 (2), 146 (100), 132 (28).

2,4-Dimethyl-2-phenylpyrrolidine (16). Prepared according to procedure B given above using $[Cp^{TMS}_2SmMe]_2$ as the precatalyst. Using 5.3% catalyst loading the reaction was complete after 2 days at 120 °C. Analogous workup and purification provided the title compound in 100% yield as a 1:1 mixture of diastereomers: ot 125 °C/10 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.44 (m, 2 H), 7.32−7.27 (m, 2 H), 7.20−7.15 (m, 1 H), 3.29−3.23 (m, 0.5 H), 3.12 (dd, J = 10.5, 8.0 Hz, 0.5 H), 2.67−2.61 (m, 0.5 H), 2.52 (dd, J = 11.0, 8.0 Hz, 0.5 H), 2.40−2.33 (m, 1 H), 2.22 (dd, J = 12.2, 7.6 Hz, 0.5 H), 2.11−2.04 (m, 0.5 H), 1.74 (br s, 1 H), 1.62 (dd, J = 12.2, 9.0 Hz, 0.5 H), 1.46 (s, 1.5 H), 1.46−1.40 (m, 0.5 H), 1.40 (s, 1.5 H), 1.02 (d, J = 6.6 Hz, 1.5 H), 0.98−0.96 (m, 1.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.59 (149.41), 128.12 (128.02), 125.93 (125.87), 125.36 (125.25), 65.49 (65.44), 54.45 (53.86), 49.65 (49.07), 34.64 (34.13), 31.43 (31.39), 19.35 (18.94); IR (neat) 3320 (br), 3057.6, 3027.5, 2955.3, 2925.2, 1599.9 cm^{-1}; HRMS calcd for $C_{12}H_{17}N^+$ 175.1361, found 175.1364; LRMS (EI+) *m*/*z* 176 (6), 175 (4), 161 (52), 160 (100), 132 (75). Anal. Calcd for $C_{12}H_{17}N$: C, 82.23. H, 9.78. N, 7.99. Found: C, 81.95; H, 10.02; N, 7.77.

9-Aza-1-methylbicyclo[3.3.1]nonane (18). Prepared from **17** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 10.5% catalyst loading the reaction was complete after 5 min at 120 °C. Analogous workup and purification provided the title compound in 94% yield: ot 80 °C/21 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.18−3.16 (m, 1 H), 2.08−1.98 (m, 2 H), 1.76−1.53 (m, 9 H), 1.43−1.36 (m, 2 H), 0.95 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 48.08, 47.45, 37.59, 33.67, 30.32, 21.27; IR (neat) 3254.1, 2986.0, 2951.9, 2919.1, 2839.8 cm^{-1}; HRMS calcd for $C_9H_{17}N^+$ 139.1361, found 139.1346; LRMS (EI+) *m*/*z* 139 (30), 124 (8), 110 (76), 97 (100).

2-Aza-1,5-dimethylbicyclo[3.3.1]nonane (20). Prepared from **19** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 8% catalyst loading the reaction was complete after 48 h at 120 °C. Analogous workup and purification provided the title compound in 97% yield: ot 100 °C/20 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.41 (td, J = 13.0, 5.2 Hz, 1 H), 2.86−2.82 (m, 1 H), 2.09−1.98 (m, 1 H), 1.67−1.63 (m, 1 H), 1.60−1.53 (m, 2 H), 1.47−1.43 (m, 1 H), 1.40−1.29 (m, 2 H), 1.26−1.19 (m, 2 H), 1.13 (dt, J = 12.3, 2.5 Hz, 1 H), 0.99 (s, 3 H), 0.85 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 49.43, 48.99, 42.81, 38.27, 37.99, 37.44, 33.03, 32.61, 30.31, 22.74; IR (neat) 3275.2, 2947.7, 1455.6 cm^{-1}; HRMS calcd for $C_{10}H_{19}N^+$ 153.1517, found 153.1510; LRMS (EI+) *m*/*z* 153 (8), 138 (13), 110 (38), 30 (100).

2-Aza-1,6,6-trimethylbicyclo[3.3.1]nonane (22). Prepared from **21** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 14% catalyst loading the reaction was complete after 3 days at 120 °C. Analogous workup and purification provided the title compound in 91% yield: ot 95 °C/10 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.35 (td, J = 13.1, 4.7 Hz, 1 H), 2.82−2.78 (m, 1 H), 1.92−1.77 (m, 3 H), 1.65−1.50 (m, 4 H), 1.32−1.27 (m, 2 H), 1.13 (br s, 1 H), 0.98 (s, 3 H), 0.953 (s, 3 H), 0.950 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 47.82, 41.91, 38.90, 38.50, 36.88, 36.26, 32.58, 32.54, 29.74, 28.84, 28.01; IR (neat) 3274.3, 2947.3, 2867.4, 1452.0 cm^{-1}; HRMS calcd for $C_{11}H_{21}N^+$ 167.1674, found 167.1673; LRMS (EI+) *m*/*z* 167 (5), 152 (2), 96 (100).

(±)-(2*R,5*R**)-2,5-Dimethyl-1-azabicyclo[3.3.0]octane (25).** Prepared from **24** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 5.5% catalyst loading the reaction was complete after 20 h at 120 °C. Analogous workup and purification provided the title compound in 85% yield. The material obtained was determined to be a 30:1 mixture of two stereoisomers. The structure of the major stereoisomer was determined by the conversion of the amine to picrate **27** by treatment with picric acid. The yellow solid obtained was recrystallized from $CHCl_3$/hexanes for X-ray analysis: ot 50 °C/30 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94−2.86 (m, 1 H), 2.62−2.56 (m, 2 H), 1.84−1.68 (m, 4 H), 1.63−1.44 (m, 4 H), 1.13 (s, 3 H), 1.11 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 70.52, 63.35, 53.35, 40.10, 39.18, 34.28, 30.47, 25.65, 21.78; IR (neat) 2955.6, 2863.2, 2800.1, 1452.9 cm^{-1}; HRMS calcd for $C_9H_{17}N^+$ 139.1361, found 139.1333; LRMS (EI+) *m*/*z* 139 (9), 124 (100), 111 (12), 96 (19).

2-(3-Butenyl)-2-methylpyrrolidine (26). Prepared from **24** according to procedure B given above using $[Cp^{TMS}_2SmMe]_2$ as the precatalyst. Using 6.3% catalyst loading the reaction was complete after 48 h at 120 °C. Analogous workup and purification provided the title compound in 77% yield. The material obtained was contaminated by 6% **24** and 1% **25** as determined by GC: ot 60−70 °C/35 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89−5.76 (m, 1 H), 5.04−4.89 (m, 2 H), 3.00−2.86 (m, 2 H), 2.14−2.01 (m, 2 H), 1.81−1.68 (m, 2 H), 1.58−1.43 (m, 4 H), 1.29 (br s, 1 H), 1.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.28, 114.01, 61.37, 45.45, 41.30, 38.11, 29.60, 26.22, 25.84; IR (neat) 3286.1, 3076.3, 2957.6, 1640.2 cm^{-1}; HRMS calcd for $C_9H_{17}N^+$ 139.1361, found 139.1348; LRMS (EI+) *m*/*z* 139 (4), 124 (19), 84 (100).

2-Methyl-2-(3-methyl-3-butenyl)pyrrolidine (29). Prepared from **28** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 5.7% catalyst loading the reaction was complete after 4 h at 120 °C. Analogous workup and purification provided the title compound in 99% yield: ot 90 °C/25 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.67−4.66 (m, 2H), 2.98−2.88 (m, 2H), 2.14−1.96 (m, 2 H), 1.84−1.72 (m, 2 H), 1.71 (s, 3 H), 1.59−1.45 (m, 4 H), 1.40 (br s, 1 H), 1.08 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.45, 109.26, 61.41, 45.91, 40.14, 38.02, 33.36, 26.13, 25.82, 22.72; IR (neat) 3285.0, 3072.4, 2958.2, 1648.0 cm^{-1}; HRMS calcd for $C_{10}H_{19}N^+$ 153.1517, found 153.1517; LRMS (EI+) *m*/*z* 153 (1), 138 (14), 84 (100).

1-Aza-2,2,5-trimethylbicyclo[3.3.0]octane (30). Prepared from **28** according to procedure B given above using $[Cp^{TMS}_2NdMe]_2$ as the precatalyst. Using 41% catalyst loading the reaction was complete after 7 days at 120 °C. Analogous workup and purification provided the title compound in 53% yield. GC analysis of the material isolated revealed the isolated material to be 85% the major component, 5% **28**, and 10% a mixture of unidentified isomers: ot 95 °C/35 mmHg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.83−2.79 (m, 1 H), 2.75−2.70 (m, 1 H), 1.79−1.62 (m, 7 H), 1.48−1.42 (m, 1 H), 1.19 (s, 3 H), 1.10 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

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70.40, 61.57, 48.85, 41.08, 38.91, 38.55, 31.75, 30.53, 26.94, 24.18; IR (neat) 2955.7, 2864.5, 1455.4 cm^{-1}; HRMS calcd for $C_{10}H_{19}N^+$ 153.1517, found 153.1525; LRMS (EI+) *m*/*z* 153 (9), 138 (100), 121 (10).

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Supporting Information Available: Experimental details and characterization for substrates **1**, **3**, **5**, **7**, **9**, **11**, **13**, **15**, **17**, **19**, **21**, **23**, **24**, and **28** and their precursors, NMR spectra for compounds without reported elemental analyses, and details of the X-ray stucture determination of **27** (130 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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