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Intramolecular Hydroamination of Aminoalkenes by Calcium and Magnesium Complexes: A Synthetic and Mechanistic Study

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Abstract: The β-diketiminate-stabilized calcium amide complex [{ArNC(Me)CHC(Me)NAr}Ca{N(SiMe$_3$)$_2$}-(THF)] (Ar = 2,6-diisopropylphenyl) and magnesium methyl complex [{ArNC(Me)CHC(Me)NAr}Mg(Me)(THF)] are reported as efficient precatalysts for hydroamination/cyclization of aminoalkenes. The reactions proceeded under mild conditions, allowing the synthesis of five-, six-, and seven-membered heterocyclic compounds. Qualitative assessment of these reactions revealed that the ease of catalytic turnover increases (i) for smaller ring sizes (5 > 6 > 7), (ii) substrates that benefit from favorable Thorpe−Ingold effects, and (iii) substrates that do not possess additional substitution on the alkene entity. Prochiral substrates may undergo diastereoselective hydroamination/cyclization depending upon the position of the existing stereocenter. Furthermore, a number of minor byproducts of these reactions, arising from competitive alkene isomerization reactions, were identified. A series of stoichiometric reactions between the precatalysts and primary amines provided an important model for catalyst initiation and suggested that these reactions are facile at room temperature, with the reaction of the calcium precatalyst with benzylamine proceeding with $\Delta G°$(298 K) = −2.7 kcal mol^{-1}. Both external amine/amide exchange and coordinated amine/amide exchange were observed in model complexes, and the data suggest that these processes occur via low-activation-energy pathways. As a result of the formation of potentially reactive byproducts such as hexamethyldisilazane, calcium-catalyst initiation is reversible, whereas for the magnesium precatalyst, this process is nonreversible. Further stoichiometric reactions of the two precatalysts with 1-amino-2,2-diphenyl-4-pentene demonstrated that the alkene insertion step proceeds via a highly reactive transient alkylmetal intermediate that readily reacts with N−H σ bonds under catalytically relevant conditions. The results of deuterium-labeling studies are consistent with the formation of a single transient alkyl complex for both the magnesium and calcium precatalysts. Kinetic analysis of the nonreversible magnesium system revealed that the reaction rate depends directly upon catalyst concentration and inversely upon substrate concentration, suggesting that substrate-inhibited alkene insertion is rate-determining.

Introduction

Although the past two decades have overseen some dramatic advances in our appreciation of heavier alkaline-earth (Ca, Sr, and Ba) complex structures and coordination behavior,[1] a well-defined or applied reaction chemistry of these elements is now only beginning to emerge. This is in stark contrast to the widespread use of magnesium-based compounds (Grignard reagents, Hauser bases), which have been employed as *stoichiometric* reagents in organic synthesis since the beginning of the 20th century.[2]

The exclusively divalent compounds of the alkaline earths are redox-inactive[3] and unambiguously d^0 complexes, so the bonding is dictated only by ionic and nondirectional interactions between the metal and the auxiliary ligands. In this respect, parallels between the chemistry of the heavier alkaline-earth metals and that of the trivalent lanthanides have often been drawn. This latter series of elements has a well-defined and versatile reaction chemistry, and the pioneering research of Marks and subsequent researchers has demonstrated that trivalent organolanthanide compounds of the form L$_2$LnX, where L is a monoanionic (typically cyclopentadienyl) spectator ligand and X is a monoanionic σ-bonded (e.g., hydrido, alkyl, amido, phosphido) substituent, are applicable to a wide range of *catalytic* transformations.[4−6] This catalytic behavior is effectively founded upon two fundamental types of reactivity: (*i*) σ-bond metathesis and (*ii*) insertion of unsaturated carbon−carbon or carbon−heteroatom bonds into Ln−X σ bonds (Figure 1).

Incorporation of these two reaction steps into catalytic cycles has enabled the development of a vast number of lanthanide-mediated synthetic reactions, including *intra-* and *intermolecular* heterofunctionalization of carbon−carbon bonds,[4] polymerization of low-molecular-weight alkenes,[5,6] and C−H activation

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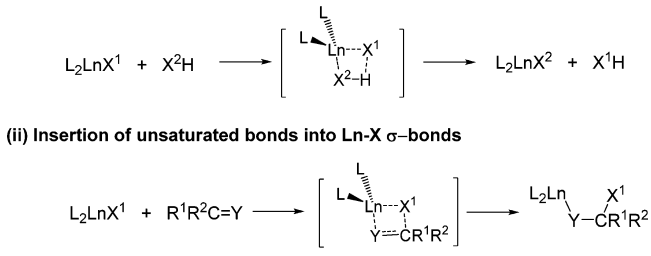

Figure 1. Fundamental reactions of trivalent lanthanide organometallics.

within even nonreactive hydrocarbons such as methane.[6a] Research in our laboratories and elsewhere has set out to investigate the potential for related reaction chemistries within the heavier alkaline-earth series. Although the intrinsic basicity of derivatives of these elements signifies that tolerance toward more delicate functional groups will be an issue for longer-term applicability,[7] these studies have sought to establish whether *well-defined* group-2 complexes may be employed as catalytic reagents using similar σ-bond metathesis and insertion reaction chemistries and to understand the potential relationship between any reactivity and the nature (radius, ionic character) of the metal dication involved.

In this regard, it is noteworthy that several precedents exist in stoichiometric heavier group-2 chemistry that are consistent with the fundamental reaction types observed for trivalent organolanthanide complexes. Westerhausen, for example, has observed the insertion of both 1,4-diphenylbutadiyne and benzonitrile into the metal−phosphorus bond of a series of homoleptic heavier alkaline-earth phosphides, $[M\{P(SiMe_3)_2\}_2(THF)_4]$ (M = Ca, Sr, Ba).[8] In a related study, it has been demonstrated that the analogous amide complexes $[M\{N(SiMe_3)_2\}_2(THF)_2]$ also undergo insertion reactions with benzonitrile.[9] Although in all cases the initial reaction products underwent decomposition with silyl-group migration, the isolated products can be rationalized in terms of the insertion step. This work parallels early studies by Gilman and Coles, which showed that ill-defined heavier alkaline-earth complexes containing metal−carbon σ bonds react with unsaturated substrates such as CO_2, benzonitrile, and 1,1-diphenylethene.[10,11] Mingos has demonstrated the insertion of carbonyl sulfide, carbon disulfide, and sulfur dioxide into group-2 metal−alkoxide bonds.[12] Perhaps more importantly, the work of Harder has shown that the highly reactive heavier group-2 benzyl complexes $[Ba\{C(Ph)_2(CH_2CH_2Ph)\}_2(THF)_2]$ and $[M(DMAT)_2(THF)_2]$ (M = Ca, Sr; DMAT = 2-dimethylamino-α-trimethylsilylbenzyl) are suitable initiators for the polymerization of styrene via reactions that occur through multiple insertions of the alkene into the metal−carbon σ bond of an intermediate organometallic species.[13] Harder has also reported that ligand control may be exerted to an extent in this reaction, and heteroleptic complexes of the form [LMX(THF)], where X is DMAT and L is a bulky silyl-substituted fluorenyl ligand, have been shown to initiate styrene polymerization with a degree of control over polymer tacticity.[13j]

In addition to these observations, σ-bond metathesis (or protonolysis) has frequently been employed in stoichiometric heavier group-2 chemistry to synthesize new organometallic species. Examples include the reaction of the heavier group-2 metal amides $[M\{N(SiMe_3)_2\}_2(THF)_n]$ (M = Ca, Sr, Ba; n = 0, 2) with alcohols, thiols, selenols and tellurols, pyrroles and pyrazoles, terminal alkynes, cyclopentadiene and derivatives, phosphines, or arsines to yield the corresponding metal alkox-

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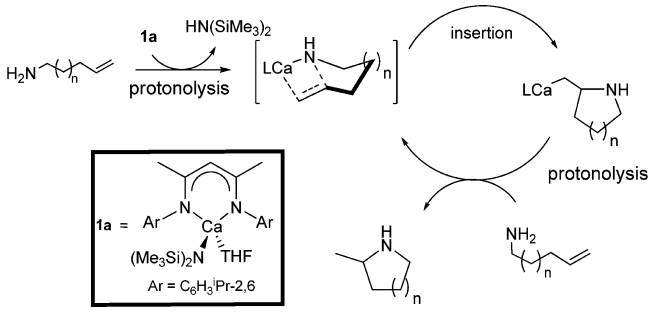

Figure 2. Generalized postulated catalytic cycle for calcium-mediated intramolecular hydroamination.

ide,[14] thiolate,[15] selenolate and tellurate,[16] pyrrolide and pyrazolide,[17] acetylide,[18] cyclopentadienide,[19] phosphide,[20] or arsenide[21] MX_2 species along with the reaction byproduct $HN(SiMe_3)_2$. The former homoleptic organometallic species commonly demonstrate low solubility in hydrocarbon solvents and are often isolated upon addition of a charge-neutral chelating ligand.

On the basis of these precedents, we previously reported in preliminary form that the β-diketiminate-stabilized calcium amide **1a** (Figure 2), a compound originally reported by Chisholm and co-workers as a catalyst for the polymerization of *rac*-lactide,[22] is a highly effective catalyst for the intramolecular hydroamination of aminoalkenes and aminoalkynes.[23] The reaction was postulated to occur by the generalized catalytic cycle outlined in Figure 2, which was assumed, by direct analogy to the experimentally validated cycle in lanthanide-mediated hydroamination reactions, to proceed via both σ-bond metathesis (protonolysis) and intramolecular C=C insertion for catalyst activation, thereby continuing the catalytic turnover.

In subsequent and related work, Harder has described the application of the heavier alkaline-earth complexes $[(DMAT)_2M(THF)_2]$ (M = Ca, Sr) to *intermolecular* hydrosilylation of styrenes and dienes with phenylsilane and phenyl(methyl)silane and the use of $[\{ArNC(Me)CHC(Me)NAr\}CaH(THF)]_2$ as a precatalyst for hydrogenation of activated alkenes and hydrosilylation of ketones.[24] While Roesky has reported aminotropinoate-supported calcium and strontium amides for intramolecular hydroamination catalysis,[25] further work in our laboratory has demonstrated both the application of **1a** to intermolecular hydrophosphination of alkenes, alkynes, and carbodiimides[26] and the use of the simple heavier group-2 amides $[M\{N(SiMe_3)_2\}_2(THF)_2]$ (M = Ca, Sr, Ba) as precatalysts for hydroamination of carbodiimides and isocyanates.[27]

In this submission, we provide a complete account of our experimental studies of the atom-efficient intramolecular hydroamination of aminoalkenes catalyzed by calcium and magnesium complexes. We also provide a mechanistic appraisal based upon stoichiometric reactivity and preliminary kinetic experiments.

Results and Discussion

Precatalyst Synthesis. An underlying challenge in the development of catalytic reagents based upon the heavier alkaline earths is the propensity of heteroleptic compounds of the form LMX to undergo Schlenk-like and/or irreversible solution redistribution reactions to the homoleptic compounds L_2M and MX_2. When X is sterically undemanding, the MX_2 species are often polymeric and/or have low solubility in noncoordinating solvents. Conversely, the "stabilizing" ligands L may encapsulate the alkaline-earth center to such an extent that the L_2M complexes are unreactive. In effect, solution redistribution may result in the formation of an ill-defined mixture from a potentially catalytically active species.

The β-diketiminate ligand series has a pedigree in the stabilization of low-coordinate and low-valent main-group

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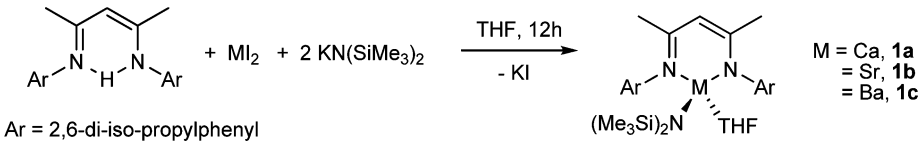
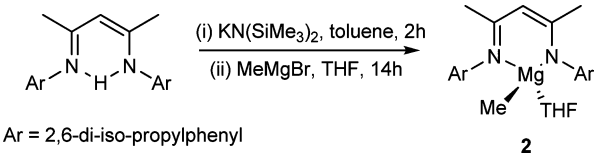
Scheme 1. Synthesis of β-Diketiminate-Stabilized Alkaline-Earth Amides **1a**−**c**



complexes, including a number of group-2 organometallics.[28,29] Following the conditions reported by Chisholm,[22] we reported previously that the reaction of the β-iminoenamine [ArNHC(Me)CHC(Me)NAr] (Ar = 2,6-diisopropylphenyl) with 2 equiv of potassium bis(trimethylsilyl)amide and 1 equiv of MI_2 in THF resulted in the formation of the series of heteroleptic complexes [{ArNC(Me)CHC(Me)NAr}M{N(SiMe$_3$)$_2$}(THF)] [M = Ca (**1a**), Sr (**1b**), Ba (**1c**)] (Scheme 1).[30] For the larger alkaline earths strontium and barium, formation of the desired heteroleptic products was accompanied by production of the known homoleptic compounds [{ArNC(Me)CHC(Me)NAr}$_2$M], which are subject to further dynamic equilibria. These initial observations suggested that the bulky β-diketiminate ligand [ArNC(Me)CHC(Me)NAr]$^-$ provided sufficient kinetic stabilization to heteroleptic calcium complexes but was of limited use for strontium and barium derivatives.

Scheme 2. Modified Synthesis of β-Diketiminate-Stabilized Magnesium Alkyl Complex **2**



These studies suggested that **1a** may be a useful compound with which to investigate hydroamination catalysis with heteroleptic calcium organometallics. Although the strontium and barium analogues of **1a** were deemed unsuitable for this purpose, for comparison we also synthesized the magnesium complex [{ArNC(Me)CHC(Me)NAr}Mg(Me)(THF)] (**2**) by modification of the literature procedure (Scheme 2).[28b] This compound proved to be stable under a number of reaction conditions and, although highly moisture-sensitive, provided no evidence of Schlenk-like redistribution in solution.

Intramolecular Hydroamination of Alkenes. Although it is thermodynamically feasible, the direct addition of amines across alkenes is kinetically unfavorable because of the high activation

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barrier to the reaction resulting from the repulsion of the lone pair of the nitrogen and the carbon−carbon π bond. The widespread search for homogeneous reagents capable of catalyzing this intramolecular process has given rise to a burgeoning and mechanistically diverse area of research[30] that has utilized alkali metal,[31c,32,33] Sc,[34,35] Ti and Zr,[36,37] Re,[38] Fe,[39] Ru,[40,41] Rh and Ir,[40,42] Pd,[40,43,44f] Pt,[44] Ag,[45] Au,[46] Zn,[47] Hg(II),[33b] and 4f-[48−58] and 5f-element[59] complexes. In addition, Brønstead acids have been reported to catalyze intramolecular hydroamination reactions.[36s,60]

Catalytic systems based upon trivalent organolanthanides of the form L_nLnX^1 devised and pioneered by Marks and co-workers,[48] are especially notable for being highly efficient in catalyzing the *intramolecular* hydroamination of aminoalkenes, aminoalkynes, aminoallenes, and aminodienes. The availability of a single common oxidation state (+3) precludes an oxidative addition/reductive elimination pathway as a viable mechanism for organolanthanide catalysts. Rather, the reactivity patterns are defined by alkene insertion into polar, largely ionic $Ln-X^2$ bonds and σ-bond metathesis, both of which may be modulated by judicious selection of the Ln^{3+} cationic radius and the supporting ligands. Both computational[58a] and experimental[48a,d] data are consistent with the *intramolecular* hydroamination of alkenes occurring via (*i*) σ-bond metathesis of the precatalyst $Cp^*_2LnX^1$ [$X^1 = H$, $CH(SiMe_3)_2$] with the aminoalkene to form a heteroleptic lanthanide amide intermediate, (*ii*) rate-limiting intramolecular insertion of the alkene into the Ln−N bond of the amide, and (*iii*) σ-bond metathesis of the resulting lanthanide alkyl species with a further equivalent of aminoalkene.[48d] While Marks has suggested that the observed rate law, $v \propto [\text{catalyst}]^1[\text{substrate}]^0$, and the moderate $\Delta H^{\ddagger}$ and large negative $\Delta S^{\ddagger}$ values of these reactions are consistent with a highly ordered polar transition state for carbon−nitrogen bond formation via a rate-determining insertion step, Hultzsch and co-workers have derived an alternative rate law and suggested that the reaction rate depends upon the substrate concentration at $t = 0$ because the substrate and product effectively inhibit the alkene insertion step to similar extents.[50e]

In subsequent studies, numerous 4f-element-based catalysts have been developed, and while initial studies centered upon the application of cyclopentadienyl and *ansa*-bridged cyclopentadienyl ligand sets, more recent investigations have included noncyclopentadienyl-based ligands with an emphasis on the design of nonracemic catalysts to effect stereocontrolled intramolecular hydroamination reactions.[49−57] Density functional theory computational studies of the intramolecular hydroamination of alkenes,[48a] dienes,[48b,e] allenes,[48c] and alkynes[48d] have been undertaken and recently reviewed.[48f]

Calcium compound **1a** and magnesium compound **2** were examined as catalysts for hydroamination of a variety of aminoalkenes. Reactions were conducted in NMR tubes using C_6D_6 as the solvent with tetrakis(trimethylsilyl)silane (TMSS) as an internal standard, and the yields were measured by integration of the ^{1}H NMR peaks. Subsequent repetition on a preparative scale allowed isolation of the heterocyclic products, which were purified by short-path (kügelrohr) distillation. The results of these experiments are provided in Table 1.

Reaction Scope. This group-2-catalyzed hydroamination/cyclization reaction allows access to derivatives of pyrrolidines, piperidines, and hexahydroazepines in near-quantitative yields under mild (25−80 °C) conditions using 2−20 mol % precatalyst. Structures of the reaction products were assigned using NMR spectroscopy by comparison to literature data where applicable and, in the case of Table 1, entries 16−18, using single-crystal X-ray diffraction of the hydrochloride salt of the isolated pyrrolidine (see the Supporting Information).

Examination of the data in Table 1 reveals that in all but one case (see below), the calcium precatalyst **1a** catalyzes the reaction with a shorter reaction time than the corresponding magnesium complex **2**. Although kinetically favorable (Thorpe−Ingold effect)[61] cyclizations could be achieved, more demanding substrates, such as those possessing substitution at the alkene terminus (either 1,1- or 1-substitution; Table 1, entries 12−15), were recovered unchanged. A limitation of the more active calcium system became apparent when reactions were conducted at higher temperatures and over extended times. In many of these cases, catalysis was accompanied by Schlenk-like, and effectively irreversible, redistribution of **1a** to the homoleptic calcium compound [{ArNC(Me)CHC(Me)NAr}$_2$Ca] (Ar = 2,6-diisopropylphenyl), as observed by ^{1}H NMR spectroscopy.[29a] In contrast, no such solution redistribution equilibria were apparent during catalysis with compound **2** containing the smaller Mg^{2+} cation.

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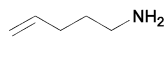
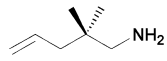
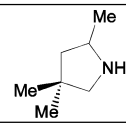
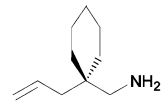
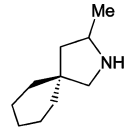
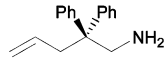
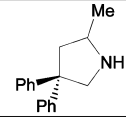
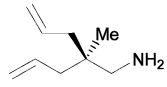
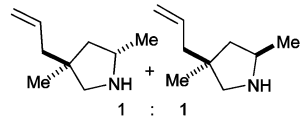
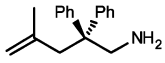
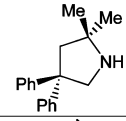
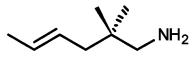
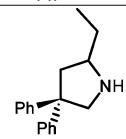
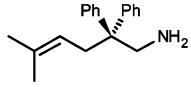
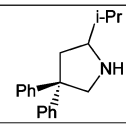
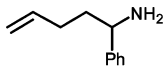
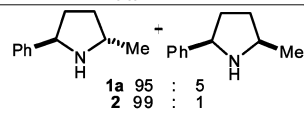
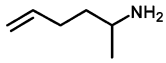
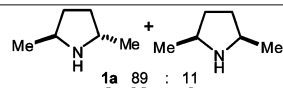
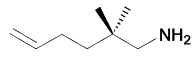
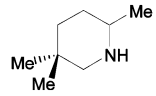
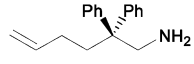
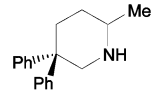
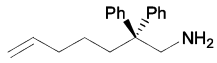
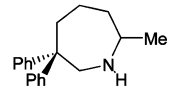
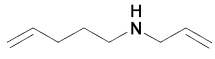
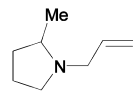
Table 1. Scope of Calcium- and Magnesium-Mediated Intramolecular Hydroamination Reactions

Entry	Substrate	Product	Catalyst (mol %)	Time / h	Temp / °C	NMR yield / %[a]
1			**1a** (10 mol %)	21	25	90
2			**1a** (2 mol %)	2	25	>95
3			**1a** (10 mol %)	0.25	25	>99
4			**1a** (5 mol%)	0.25	25	93
5			**1a** (2 mol %)	1	25	98
6			**2** (5 mol %)	2	25	96
7			**1a** (2 mol %)	0.25	25	99
8			**2** (2 mol%)	2	25	99
9		 1 : 1	**1a** (2 mol %)	1	25	>95
10			**1a** (5 mol %)	0.5	25	94
11			**2** (5 mol %)	0.5	25	86
12			**1a** (20 mol %)	24	80	0
13			**2** (20 mol %)	24	80	0
14			**1a** (20 mol %)	18	60	0
15			**2** (15 mol %)	18	60	0
16		 **1a** 95 : 5 **2** 99 : 1	**1a** (5 mol %)	5	25	87
17			**1a** (10 mol %)	2	25	91
18			**2** (10 mol %)	96	25	72
19		 **1a** 89 : 11 **2** 92 : 8	**1a** (20 mol %)	48	25	99
20			**2** (20 mol %)	48	25	81
21			**1a** (10 mol %)	72	60	85[b]
22			**1a** (20 mol %)	6	60	86[b]
23			**1a** (2 mol %)	24	25	69[b]
24			**1a** (10 mol %)	4	25	83[b]
25			**2** (10 mol %)	4	25	97
26			**1a** (20 mol %)	24	80	0
27			**2** (5 mol %)	5.5 d	80	88
28			**1a** (10 mol %)	48	25	60

[a] NMR yields were measured against TMSS as an internal standard; reactions were conducted in C_6D_6 or toluene-d_8. [b] Products were accompanied by alkene isomerization byproduct (see text for details).

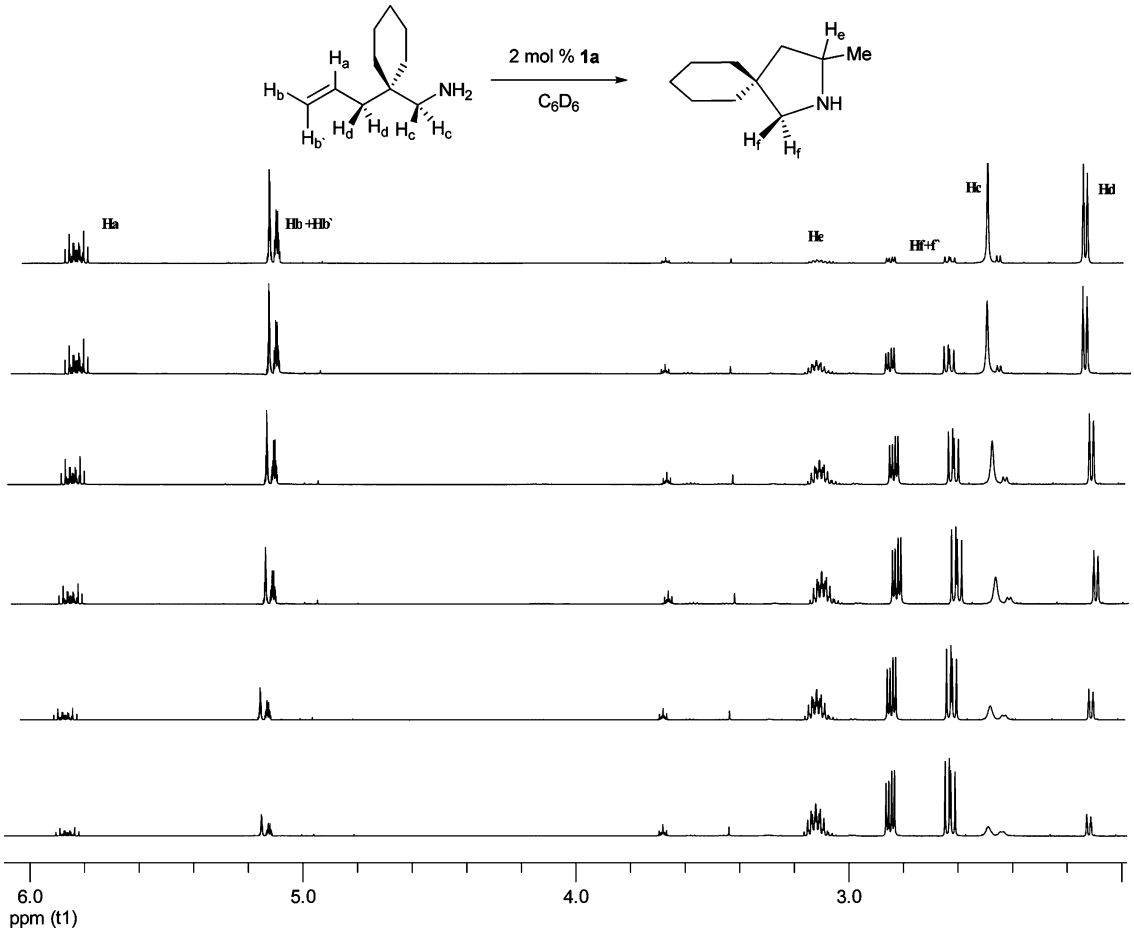


Figure 3. Stack plot of NMR spectra for the reaction of (1-allylcyclohexyl)methylamine with 2 mol % **1a** taken at 10 min intervals.

The empirical experimental observations listed in Table 1 are consistent with the calcium amide catalyst **1a** effecting the cyclization of aminoalkenes at a higher rate than the magnesium species **2**. In moving from Mg^{2+} to Ca^{2+}, there is an increase in the ionic radius of the dication [from 0.72 to 1.00 Å for Mg^{2+} and Ca^{2+} in six-coordinate complexes].[61] Although not isoleptic, both species would be expected to form similar group-2 primary amide intermediates following the initial protonolysis reaction with the aminoalkene substrate (see below). The trend within the lanthanide series is a marked increase in turnover frequency (TOF) with increasing coordinative unsaturation at the metal center.[48a,d] Hence, for a given ligand set, the activity decreases across the lanthanide series with increasing atomic number because of contracting Ln^{3+} radii. In order to further quantify this observation, the kinetics of the cyclizations of (1-allylcyclohexyl)methylamine in C_6D_6 mediated by **1a** and **2** were followed by ^1H NMR spectroscopy. The in situ NMR studies revealed clean conversions of the substrate to the spirocyclic hydroamination product (Figure 3), and the kinetic data were taken from the integration of the substrate and product peaks relative to the TMSS peak. The reactions were conducted with identical initial concentrations of 0.44 M in aminoalkene and ~0.01 M in catalyst (2−3 mol %) in the two experiments and monitored by consumption of the aminoalkene over 3 half-lives. TOFs were calculated using linear-fit data derived from the plot of log[aminoalkene] versus time (Figure 4). Although only a preliminary analysis, this kinetic data revealed a marked increase in TOF with increasing ionic radius of the metal: **1a** and **2** effected the cyclization of 1-aminomethyl-1-allylcyclohexane with TOFs of 54.5 and 17.0 h^{-1}, respectively. Indeed, attempts to monitor the cyclization reaction at higher concentrations of

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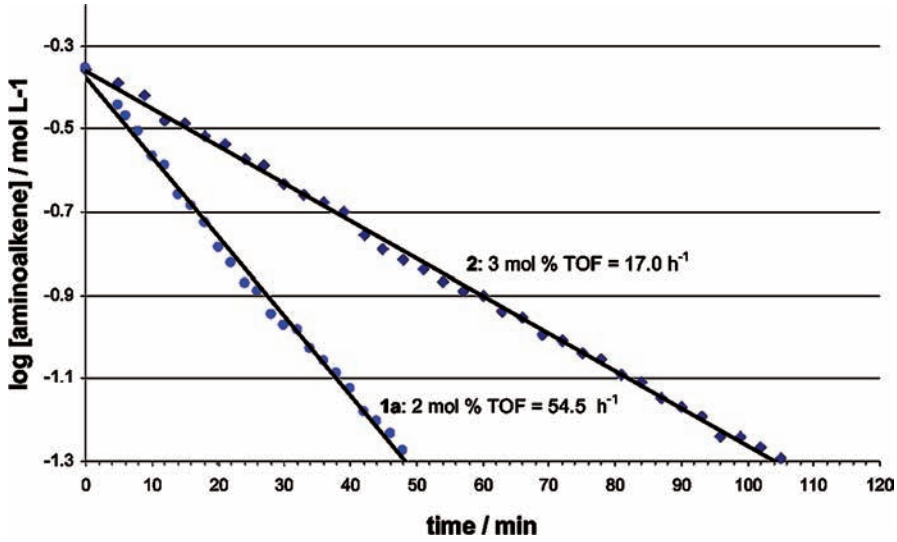

Figure 4. Plots of log[aminoalkene] vs time for the cyclization of (1-allylcyclohexyl)methylamine with **1a** (blue ●) and **2** (dark-blue ◆).

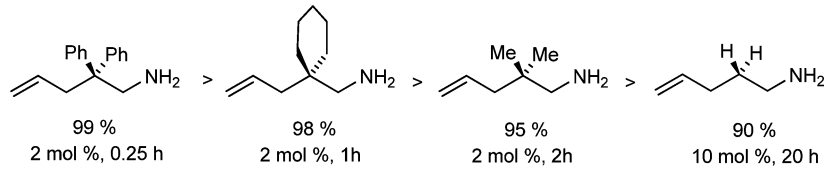

Figure 5. Thorpe−Ingold effect in intramolecular hydroamination catalyzed by **1a** at room temperature.

the calcium compound **1a** proved unsuccessful because of the high rate of the reaction.

The intramolecular hydroamination reaction was influenced greatly by the substitution pattern on the aminoalkene. Typically, geminally disubstituted alkenes gave the shortest reaction times and could be cyclized using just 2 mol % **1a** or 2−5 mol % **2**. These substrates benefited from a favorable kinetic effect due to the fact that the geminal groups decrease

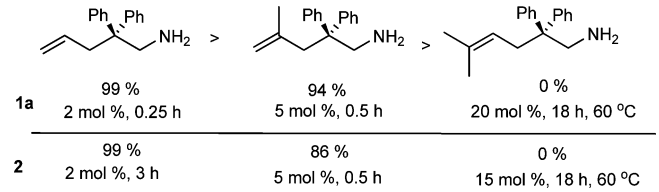

Figure 6. Effect of alkene substitution upon intramolecular hydroamination catalysis.

the conformational freedom of the aminoalkene, favoring reactive conformations. Although rigorous quantitative kinetic experiments were not performed, it can be seen from the data in Figure 5 that for a given catalyst, both the loading and reaction time decreased with increasing steric demand of the geminal substituents.

Substitution about the C═C bond lengthened the reaction time (Figure 6). Mono- and disubstitution at the terminal carbon caused the hydroamination reaction to shut down completely under the conditions utilized (Table 1, entries 12−15). It is likely that increasing the substitution on the alkene raises the energy of the transition state for M−C and C−N bond formation, not only because of steric factors but also the formation of energetically unfavorable transition-state structures with partial 2° and 3° group-2 alkyl character in the insertion step (see

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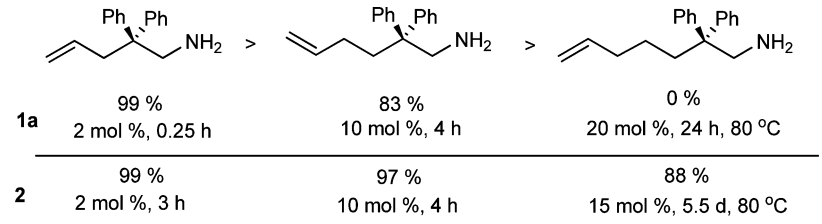

Figure 7. Effect of ring size on intramolecular hydroamination catalysis.

below). Similar observations have been made in organolanthanide chemistry, and a number of coordinatively unsaturated half-sandwich organolanthanide catalysts have been designed to effect the hydroamination/cyclization of highly substituted aminoalkenes.[48n,p,u]

Consistent with Baldwin's guidelines for ring formation, the ease of the catalytic reactions increases with decreasing ring size (5 > 6 > 7).[63] In all cases, more forcing reaction conditions (higher reaction temperatures, higher catalyst loadings) were required for the hydroamination/cyclization of aminoalkenes to produce piperidines and hexahydroazepines (Figure 7). The last case provided a notable exception to the trends in these catalytic reactions. While calcium amide **1a** proved ineffective in the intramolecular hydroamination of 1-amino-2,2-diphenyl-6-heptene, the magnesium catalyst **2** gave the corresponding seven-membered-ring product in 88% yield, albeit in an exceedingly slow reaction (5.5 days at 80 °C). While alternative scenarios may be envisaged, this observation is likely an effect of the relative stability of the two precatalysts **1a** and **2**, with the magnesium species being more robust at higher temperatures.

Cyclization of aminoalkenes possessing two prochiral centers potentially results in the formation of a mixture of diastereoisomeric products. Although substitution at the β position of the aminoalkene had little effect upon the diastereoselectivity of the reaction (entry 9 in Table 1 gave a 1:1 mixture of diastereoisomers), α-substituted aminoalkenes underwent diastereoselective intramolecular hydroamination cyclization reactions. Thus, the catalytic reactions of 1-amino-1-phenyl-4-pentene and 2-amino-5-hexene with **1a** or **2** yielded the corresponding *trans*-pyrrolidines with diastereoisomeric excesses of 90 or 98% (Table 1, entries 16−18) and 78 or 84% (Table 1, entries 19 and 20), respectively. The reaction of 1-amino-1-phenyl-4-pentene with the magnesium-based catalyst **2** was considerably slower, requiring 96 h to reach 72% conversion at room temperature. Under the same reaction conditions, calcium amide **1a** effected the cyclization of this substrate in under 2 h and in effectively quantitative yield, albeit with lower diastereoisomeric excess. The relative stereochemistry of the product was assigned by single-crystal X-ray diffraction of the hydrochloride salt isolated by treatment of the product with HCl in diethyl ether (see the Supporting Information). Similar trends in the intramolecular hydroamination of α-substituted aminoalkenes have been observed for the organolanthanide series, and the reaction of 2-amino-5-hexene with [{$(C_5Me_4)_2SiMe_2$}-La{$CH(SiMe_3)_2$}] has been reported to yield an 8:1 trans/cis mixture of heterocyclic products at 0 °C.[48d] The magnesium-centered catalyst also provided the greater degree of diastereodifferentiation in the cyclization of 2-amino-5-hexene, and it is notable that for a given ligand set, the diastereoselectivity of this reaction has also been shown to increase for the later, smaller lanthanides.[48n]

The stereochemistry of reaction is most readily explained by consideration of the energetically dissimilar transition states for carbon−nitrogen bond formation in the insertion step. Of the four seven-membered-ring transition states that can be envisaged for the carbon−nitrogen bond-forming step (Figure 8), the enantiomeric transition conformers **A** and **D** leading to the *cis*-pyrrolidine possess a potentially destabilizing 1,3-diaxial steric interaction. This latter conformation may raise the activation energy for carbon−nitrogen bond formation and hence favor the trans diastereoisomer via transition states **B** and **C**.[48d] The higher degree of diastereodifferentiation observed for the cyclization of 1-amino-1-phenyl-4-pentene for either **1a** or **2** may be related to the greater steric demands of the 1-phenyl substituent versus the 1-methyl one. In this regard, it appears that substitution at the β position does not result in differentiation of the transition states for carbon−nitrogen bond formation, as such unfavorable diaxial interactions are not present. The

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(59) (a) Stubbert, B. D.; Stern, C. L.; Marks, T. J. *Organometallics* **2003**, *22*, 4836. (b) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 4253. (c) Stubbert, B. D.; Marks, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 6149. (d) Andrea, T.; Eisen, M. S. *Chem. Soc. Rev.* **2008**, *37*, 550.
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(62) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751.
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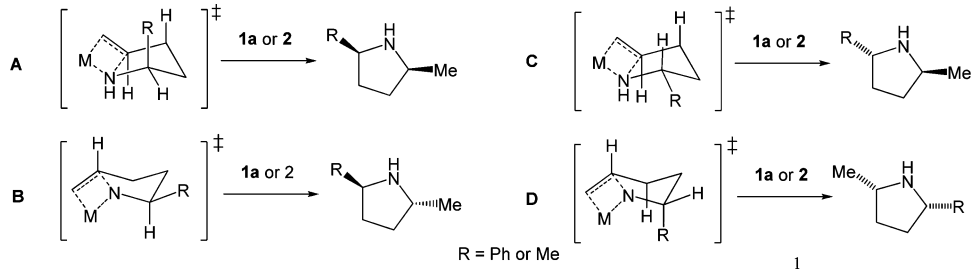
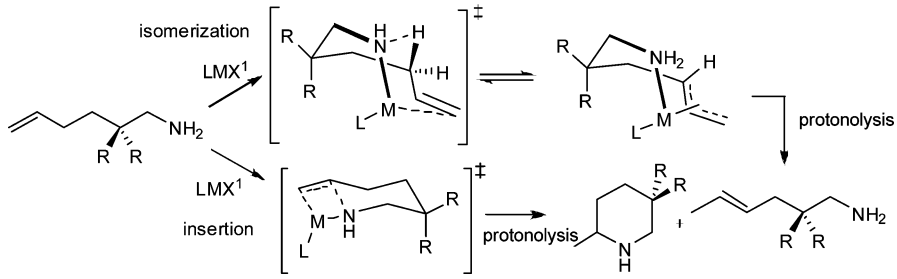


Figure 8. Four possible transition states **A**−**D** for the hydroamination/cyclization of 1-amino-1-phenyl-2-pentene and 2-amino-5-hexene.

Scheme 3. Reaction Products from the Hydroamination/Cyclization of 1-Amino-5-hexenes with **1a**



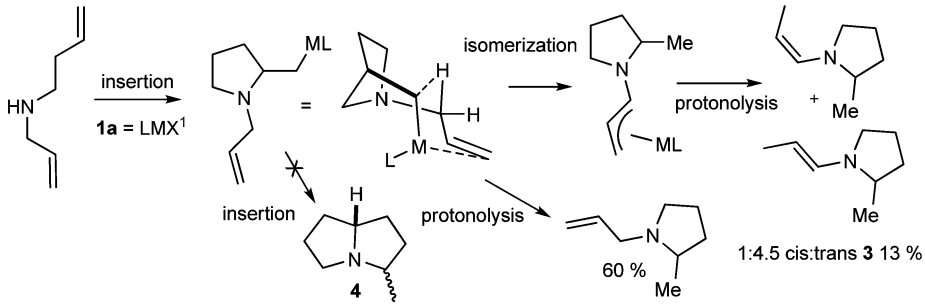
improved diastereoselectivity in the case of the magnesium catalyst can be similarly attributed to the shorter M−N and M−C bond lengths in magnesium-containing complexes than in calcium-containing ones, tightening the transition state of the insertion reaction in the former and therefore increasing any effects exerted by nonbonding interactions.

These data suggest that the scope of group-2-mediated intramolecular hydroamination catalysis is dictated by stereoelectronic effects. While the nature of the metal dication and auxiliary coordination at the metal is undoubtedly important, the facility of substrate cyclization appears to depend upon the ease with which a reactive conformation can be obtained as the alkene approaches the metal center. In the case of the cyclizations of 1-amino-2,2-dimethyl-5-hexene and 1-amino-2,2-diphenyl-5-hexene catalyzed by 10 mol % **1** in C_6D_6 at room temperature, in addition to the expected intramolecular hydroamination products (Table 1, entries 17 and 20), the corresponding alkene isomerization byproducts *trans*-1-amino-2,2-dimethyl-4-hexene (14% yield) and *trans*-1-amino-2,2-diphenyl-4-hexene (12% yield) were identified by ^{1}H NMR spectroscopy (Scheme 3). Monitoring of the reaction of 1-amino-2,2-diphenyl-5-hexene with **1a** by ^{1}H NMR spectroscopy revealed that the isomerization occurred in tandem with the hydroamination, suggesting that both products are derived from the aminoalkene rather than further reaction of the hydroamination products (see Figure S5 in the Supporting Information). Although unprecedented in organolanthanide(III) chemistry and not reported by Roesky and co-workers during the application of aminotropinoate calcium and strontium complexes to hydroamination catalysis, alkene isomerization products have been observed during Na/K alloy- and *n*-BuLi-catalyzed intramolecular hydroaminations of 1-amino-4-pentenes.[32] For the reactions presented herein, the byproduct may be rationalized in terms of stereoelectonic effects: following precatalyst initiation to form a β-diketiminate calcium amide intermediate (see below), these reactions may proceed via either (*i*) an eight-membered-ring transition state yielding the hydroamination cyclization product via insertion of the alkene into the metal−nitrogen bond or (*ii*) a boatlike six-membered-ring transition state leading to a group-2 allyl species via intramolecular proton transfer (Scheme 3). Subsequent σ-bond metathesis (protonolysis) of this latter species with a further equivalent of amine may regenerate the starting materials or yield the alkene isomerization product.

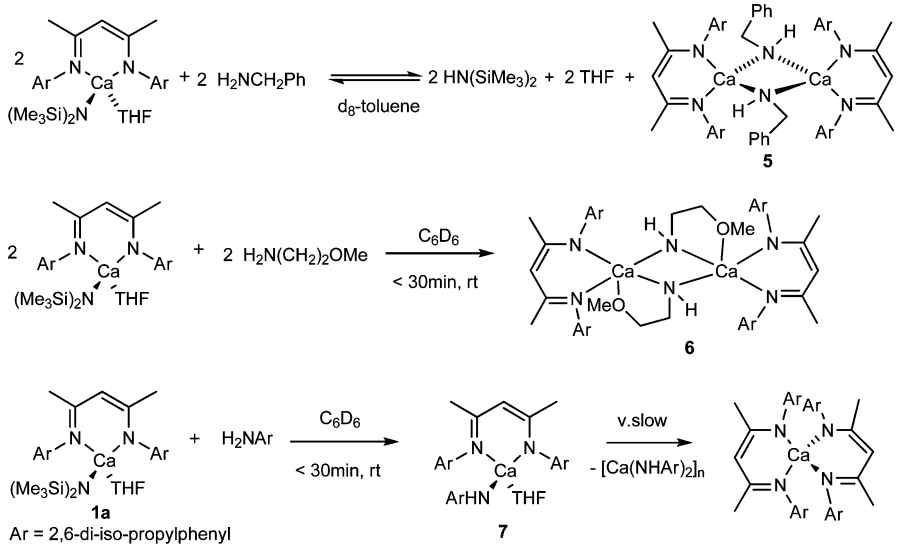
It is noteworthy that under these catalytic conditions, the isomerization products do not undergo subsequent catalyzed intramolecular hydroamination. Furthermore, no such byproducts were observed when catalytic reactions were conducted with the magnesium complex **2**. The isomerization products were observed as single geometric isomers that were assigned as trans on the basis of $^3J_{1H-1H}$ values, with 1-amino-2,2-diphenyl-2-hexene and 1-amino-2,2-dimethyl-2-hexene both possessing 13.5 Hz coupling constants for the proton resonances of the 1,2-disubstituted alkene. This stereochemistry was unambiguously defined by an independent synthesis of 1-amino-2,2-diphenyl-2-hexene and may be rationalized in terms of either a reversible reaction (forming the most thermodynamically stable alkene) or protonolysis of the pro-trans intermediate allyl complex represented in Scheme 3.

Alkene isomerization byproducts were also observed during the cyclization of *N*-allyl-1-amino-4-pentene catalyzed by 10 mol % **1a** in C_6D_6. In this instance, both *cis*- and *trans*-**3** were apparent on the basis of ^{1}H NMR spectroscopy (13% yield, 1:4.5 cis/trans), as characterized by a series of high-field enamide resonances [*trans*-**3**, 4.22 (dq, 1H, J = 6.4, 12.4 Hz); *cis*-**3**, 4.42 (dq, 1H, J = 7.0, 8.9 Hz). NMR monitoring of the reaction revealed that the concentration of these species began to increase only at longer reaction times. As with the byproducts observed from the hydroamination of 1-amino-5-hexenes, isomerization may occur via an intramolecular proton transfer, albeit in this case from the transient metal alkyl intermediate, followed by protonolysis with a further equivalent of aminoalkene (Scheme 4). In this regard, it is possible that as the substrate is depleted, the rate of isomerization increases relative to the rate of σ-bond metathesis of the intermediate alkyl complex with a further equivalent of aminoalkene. Thus, isomerization products are only observed at higher substrate conversion, and their formation is likely to be highly dependent upon the initial substrate and catalyst concentrations. Marks and co-workers have reported that *N*-allyl-1-amino-4-pentene undergoes an organolanthani-

Scheme 4. Reaction Products from the Hydroamination/Cyclization of *N*-Allyl-1-amino-4-pentene with **1a**



Scheme 5. Reaction of **1a** with Primary Amines

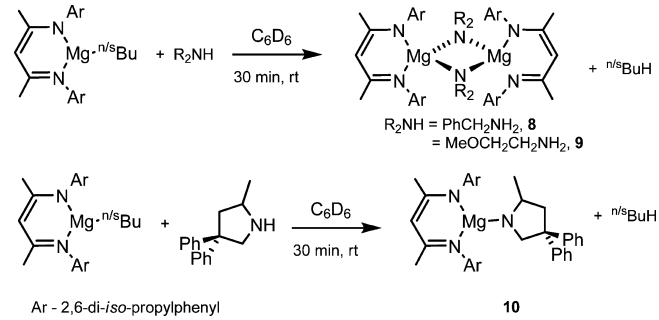


de(III)-mediated tandem hydroamination/cyclization reaction to form the bicyclic product **4**.[48g] The catalytic reaction of *N*-allyl-1-amino-4-pentene with **1a** has not been studied at higher temperatures or low substrate concentrations, and it remains possible that the bicyclic product **4** may be formed under different reaction conditions.

The σ-Bond Metathesis (Protonolysis) Step. By analogy to the mechanism for organolanthanides, the first step of the proposed mechanism of the alkaline-earth-mediated intramolecular hydroamination involves the reaction of the precatalyst, **1a** or **2**, with the aminoalkene to form a group-2 primary amide species (Figure 2). Our understanding of the catalytic hydroamination reaction was enhanced through further consideration of our previously reported studies of the stoichiometric reaction of **1a** with a range of primary amines and anilines.[30,64]

We reported previously that the reaction of **1a** with benzylamine is reversible and forms a quantifiable dynamic equilibrium, as depicted in Scheme 5. Through pulsed-gradient spin-echo (PGSE) NMR experiments, it was shown that the isolated reaction product **5** [i.e., in the absence of $HN(SiMe_3)_2$], which was characterized by X-ray crystallography, retains a dimeric constitution in solution. A van't Hoff analysis of the equilibrium mixture was conducted, and the concentrations of **1a**, **5**, and

Scheme 6. Reactions of **2** with Primary and Secondary Amines

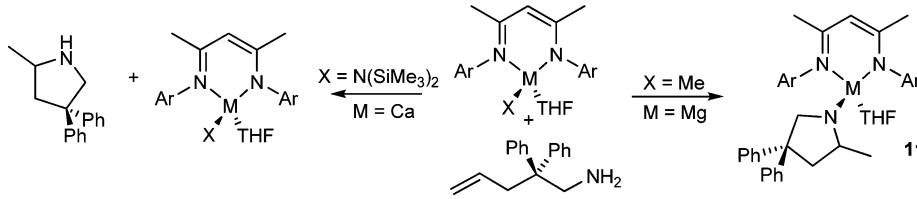


benzylamine were measured by ^{1}H NMR using TMSS as an internal standard, allowing $\Delta H°$ and $\Delta S°$ for the forward process depicted in Scheme 5 to be calculated as -12.2 kcal mol^{-1} and -32 cal K^{-1} mol^{-1}, respectively, thereby leading to the derivation of $\Delta G°$(298 K) as -2.7 kcal mol^{-1}.[64b]

A further reaction of **1a** with the potentially bidentate species 2-methoxyethylamine resulted in quantitative formation of the corresponding calcium primary amide **6** (Scheme 5),[64a] demonstrating that under certain conditions the position of the amine/amide equilibrium may be perturbed significantly to one side. Again through detailed studies of its solution dynamics and X-ray crystallography, we showed that compound **6** maintains its dimeric constitution in solution and in the solid state. In C_6D_6 solution, **6** was characterized by a distinctive resonance for the calcium amide proton, which occurred as a heavily shielded triplet at -1.63 ppm and in the current context provided a useful model for the initial primary amide σ-bond metathesis product

(64) (a) Avent, A. G.; Crimmin, M. R.; Hill, M. S.; Hitchcock, P. B. *Dalton Trans.* **2004**, 3166. (b) Barrett, A. G. M.; Crimmin, M. R.; Hill, M. S.; Kociok-Köhn, G.; Lachs, J. R.; Procopiou, P. A. *Dalton Trans.* **2008**, 1292. (c) Barrett, A. G. M.; Casely, I. J.; Crimmin, M. R.; Hill, M. S.; Lachs, J. R.; Mahon, M. F.; Procopiou, P. A. *Inorg. Chem.* **2009**, *48*, 4445.

Scheme 7. Stoichiometric Reaction of **1a** and **2** with 1-Amino-2,2-diphenyl-4-pentene



from the reaction of **1a** with primary aminoalkenes (see below). A similar stoichiometric reaction of **1a** with 2,6-diisopropylaniline cleanly gave the corresponding calcium primary anilide [{ArNC(Me)CHC(Me)NAr}Ca(NHAr){THF}] (**7** in Scheme 5).[30] This latter compound illustrated the potential for solution redistribution observed in catalytic hydroamination reactions conducted with **1a** and proved to be unstable toward a (nonreversible) equilibration in solution to give [{ArNC(Me)-CHC(Me)NAr}$_2$Ca] (~30% conversion after 20 days at room temperature) and the precipatation of an insoluble material assumed to be polymeric/oligomeric calcium anilide or imide species. In related studies, Harder and co-workers demonstrated that **1a** reacts with ammonia to form the corresponding metal amide/amine complex [{ArNC(Me)CHC(Me)NAr}Ca(NH$_2$)-(NH$_3$)$_2$]$_2$, which exhibits facile intramolecular interconversion of the amine and amide ligand sets as evidenced by ^{1}H NMR spectroscopy.[29f]

Similarly, an easily prepared analogue of **2**, [{ArNC(Me)-CHC(Me)NAr}MgBu$^{n/s}$], reacts with 2-methoxyethylamine and benzylamine at room temperature to yield the corresponding magnesium amide complexes (**8** and **9** in Scheme 6). In this instance, although monitoring of the reactions by ^{1}H NMR spectroscopy revealed complete conversion to the products by the first point of analysis (20 min) at room temperature, these σ-bond metathesis reactions were found to be nonreversible, proceeding with liberation of alkane byproducts, which played no further part in the reactivity. A further reaction of [{ArNC(Me)CHC(Me)NAr}MgBu$^{n/s}$] with the isolated hydroamination product 2-methyl-4,4-diphenylpyrrolidine provided the model complex **10**, which in turn was used in the investigation of the insertion step (see below). These studies suggest that while **8** and **9** are dimeric in solution and the solid state, complex **10** retains a monomeric constitution at room temperature in hydrocarbon solutions.[64c]

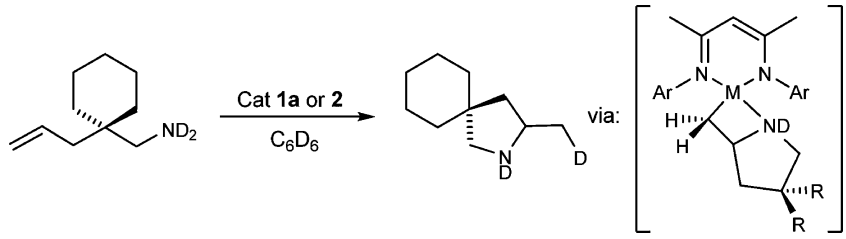
This series of experiments demonstrated several important features of the group-2-mediated hydroamination catalysis: (*i*) σ-Bond metathesis reactions of amines with **1a** or **2** are facile, with the reaction of **1a** with benzylamine occurring with negative Gibbs' free energy of $\Delta G^\circ = -2.7$ kcal mol^{-1} at room temperature. (*ii*) This reaction may be reversible, and the potential exists to form equilibrium mixtures of the form LMX^1 + HX^2 $\rightleftarrows$ LMX^2 + HX^1 when the species HX^1 has a pK_a value similar to that of HX^2. (*iii*) Compound **5** was shown to undergo fast external amine/amide exchange in the presence of an excess of benzylamine. (*iv*) Intramolecular site exchange between amine and amide ligands was observed by Harder and co-workers in [{ArNC(Me)CHC(Me)NAr}Ca(NH$_2$)(NH$_3$)$_2$]$_2$ (Ar = 2,6-diisopropylphenyl), and NMR studies yielded an activation Gibbs free energy of $\Delta G^\ddagger = 11.3 \pm 0.1$ kcal mol^{-1},[29f] which compares favorably to the value of 12.0 ± 0.1 kcal mol^{-1} reported by Marks and co-workers for [(Cp*)La(NHMe)-(NH$_2$Me)].[48d] (*v*) For reactions with simple unbranched primary amines, dimeric products are observed in solution and the solid state for both magnesium and calcium analogues. (*vi*) At elevated temperatures and/or over long reaction times, the heteroleptic calcium primary amide compounds show a propensity to undergo deleterious Schlenk-like equilibria. No such equilibria are observed for magnesium complexes.

When this study began, previous examples of heavier alkaline-earth primary amides reported in the literature remained confined to polymeric species that are soluble only in liquid ammonia.[65] Although several reports have since documented the synthesis and characterization of heavier group-2 primary amide complexes,[66] the examples discussed herein are well-defined hydrocarbon-soluble compounds that provide useful models for the intermediacy of heteroleptic calcium amide species in the intramolecular hydroamination of aminoalkenes with **1a**.

The Insertion Step. Because of the instability of the proposed group-2 alkyl intermediate under catalytic reaction conditions, specifically in the presence of N−H bonds, the nature of the insertion step is more challenging to investigate through stoichiometric reaction studies. Nevertheless, a series of reactions of the catalysts **1a** and **2** with 1-amino-2,2-diphenyl-4-pentene and (1-allylcyclohexyl)methylamine-d_2 were conducted. The stoichiometric reaction of **1a** with 1-amino-2,2-diphenyl-4-pentene in C_6D_6 yielded a mixture apparently containing the catalyst starting material and 2-methyl-4,4-diphenylpyrrolidine, which arose from the intramolecular hydroamination reaction, as monitored by ^{1}H NMR (Scheme 7). This experimental observation can be explained by considering that the reversible σ-bond metathesis step occurs with the liberation of HN(SiMe$_3$)$_2$. Following the cyclization, the alkylmetal intermediate may react with HN(SiMe$_3$)$_2$ to reform the catalyst **1a** and liberate the hydroamination/cyclization product.

In order to isolate the metal-bound insertion product, the initial σ-bond metathesis step must be nonreversible. Such conditions are met with the heteroleptic magnesium alkyl complex **2**. The methane byproduct from the initiation step is a volatile gas that is insufficiently acidic to undergo proton transfer under these reaction conditions and, once produced, plays no further part in the reaction. A stoichiometric reaction between **2** and 1-amino-2,2-diphenyl-4-pentene in C_6D_6, therefore, gave the corresponding cyclic magnesium amide **11** in near-quantitative yield (Scheme 7). Complex **11** was characterized by ^{1}H and ^{13}C NMR, including COSY, NOESY, and PGSE NMR experiments. The PGSE experiments confirmed that **11** is a single compound in solution, not a mixture of pyrrolidine and catalyst, and gave a single value for the diffusion coefficient in C_6D_6. Importantly, the multinuclear NMR data are consistent with those acquired for not only the recently reported solvent-free complex formed upon reaction of [{ArNC(Me)CHC(Me)NAr}Mg($^{n/s}$Bu)] with 2-methyl-4,4-diphenylpyrrolidine in C_6D_6 solution[64c] but also the isoelectronic cationic scandium complex [{ArNC(Me)CHC(Me)-NAr}Sc{N(CH(Me)CH$_2$CPh$_2$CH$_2$)}]$^+$[MeB(C$_6$F$_5$)$_3$]$^-$ reported by Piers, Schafer, and co-workers in the context of intramolecular hydroamination catalysis.[34] The connectivity of the amide moiety was confirmed by the COSY experiments. The ^{1}H resonances of the magnesium-bound heterocycle were shifted

Scheme 8. Catalytic Reaction of **1a** or **2** with (1-Allylcyclohexylmethyl)amine-d_2



noticeably upfield from those in the free pyrrolidine, with those adjacent to the amide nitrogen exhibiting the strongest effect.

This experiment suggests that the alkyl intermediate is not long-lived in the catalytic cycle and readily forms the more stable alkaline-earth amide by either an *intra-* or *intermolecular* σ-bond metathesis (or protonolysis) reaction. In order to infer the formation of the alkyl complex, deuterium-labeling experiments were conducted. Thus, catalytic reactions of (1-allylcyclohexyl)methylamine-d_2 (>95% deuteration) with **1a** and **2** in C_6D_6 solutions not only provided evidence for the formation of the alkyl intermediate but also demonstrated that no further proton migration steps or ligand activation reactions occurred under the catalytic conditions. In both cases, exclusive deuteration of the exocyclic methyl group, characterized by a 1:1:1 triplet resonance at 21.3 ppm in the ^{13}C NMR spectrum ($^1J_{^{13}C-D}$ = 19.3 Hz), was observed, consistent with deuteronolysis of an intermediate group-2 alkyl complex (Scheme 8). Reactions conducted at high catalyst loadings (25 mol %) also revealed that no deuteration of the β-diketiminate ligand occurred during catalytic turnover, consistent with the latter species acting solely as a spectator during hydroamination catalysis.[67]

Kinetic Studies. Once it had been established that intramolecular hydroamination reactions catalyzed by the magnesium alkyl complex **2** proceed via fast, nonreversible catalyst initiation, further kinetic studies were undertaken to determine the effect of the catalyst and substrate concentrations upon the reaction rate. Reactions of (1-allylcyclohexyl)methylamine with **2** with either variable catalyst concentration at constant substrate concentration or variable substrate concentration at constant catalyst concentration were monitored by ^1H NMR spectroscopy. NMR-scale reaction mixtures were prepared in C_6D_6 solution in a glovebox, instantly frozen to 193 K, and then thawed and transferred directly to the NMR spectrometer. The results of these experiments are presented in Figures 9 and 10.

The reaction rate increased linearly with increasing catalyst concentration, indicating that the reaction is first-order in **2** (Figure 9). The data acquired at 283 K provided a good fit over the 10−50 mM catalyst concentration range relevant to the experiments presented in Table 1. While similar first-order data were observed at 298 K, at higher temperatures (313 and 328 K) the reactions became too rapid to monitor effectively over the same concentration range using ^1H NMR spectroscopy. This difficulty prevented further data analysis and left the authors reluctant to quantify these data.

In line with the findings of Hultzsch and co-workers,[50e] the reaction of (1-allylcyclohexyl)methylamine catalyzed by **2** at constant catalyst concentration at 298 K in C_6D_6 showed a dependence upon the initial substrate concentration, with the reaction rate increasing with decreasing initial concentration of the substrate (Figure 10). This behavior is not consistent with a rate-determining σ-bond metathesis reaction step but rather indicates substrate/product inhibition of catalysis of the rate-determining alkene insertion step. Thus, it may be considered that alkene coordination (and polarization) is required to effect the insertion, and this requires a vacant "coordination site" at the metal.

With the use of steady-state theory and neglecting the effect of THF, the rate law presented in Figure 11 can be derived. In this simplified model, the reaction rate is dictated by catalytic turnover governed by a rate-determining intramolecular insertion reaction of intermediate **B**. The substrate and product both effectively inhibit catalytic turnover by formation of **A** and **A′**, and on the basis of the acquired linear plots of log[aminoalkene] versus time (Figures 9 and 10), the effect of the product can be assumed to be approximately equal to the effect of the substrate. Thus, it may be concluded that the rate of the reaction should increase with increasing initial catalyst concentration and increasing amine dissociation rate constant k_d and decrease with increasing initial substrate concentration and increasing amine association rate constant k_a.

Although Marks also proposed a similar model as a candidate to explain the reactivity, it was argued that the observed kinetic isotope effects, k_{H2}/k_{D2} [2.7(4) for 1-amino-4-pentene at 60 °C; 5.2(8) for 1-amino-1-methyl-4-pentene at 25 °C; 4.1(8) for 1-amino-2,2-dimethyl-4-pentene at 25 °C], militate against rate-determining alkene insertion occurring from a coordinatively unsaturated lanthanide amide species.[48d] For group-2 catalysis occurring with nonreversible catalyst initation, the studies detailed herein provide a weight of evidence for rate-determining alkene insertion with similar rates of reaction inhibition by substrate and product. It may be envisioned that catalytic turnover is occurring from a coordinatively unsaturated compound, i.e., through dissociation from $[L_nM(NHR)S_n]$ to form $[L_nM(NHR)S_{n-1}]$ (S = Lewis base).

Proposed Mechanism. On the basis of these data, it is now possible to present a clearer picture of hydroamination catalysis mediated by group-2 diketiminate complexes. It is proposed that the two catalyst systems described herein give rise to two independent catalytic cycles occurring with (a) nonreversible and (b) reversible catalyst initiation for **2** and **1a**, respectively (Figures 12 and 13).

For nonreversible initiation, the kinetic analysis suggests rate-limiting alkene insertion, and while the complexity of the system proceeding with reversible catalyst initiation precluded such studies for that case, similar rate-determining insertion is expected by analogy. Further anecdotal evidence for this model is provided by the observed Thorpe−Ingold effect on cyclization, the fact that the ease of cyclization followed Baldwin's guidelines (5 > 6 > 7), and the dramatic effect of alkene substitution upon the reaction, all of which are more easily explained by rate-determining alkene insertion than rate-limiting protonolysis. Rate-limiting protonolysis also seems unlikely in light of the fast and potentially reversible σ-bond metathesis reactions of group-2 alkyls and amides with amines documented herein.

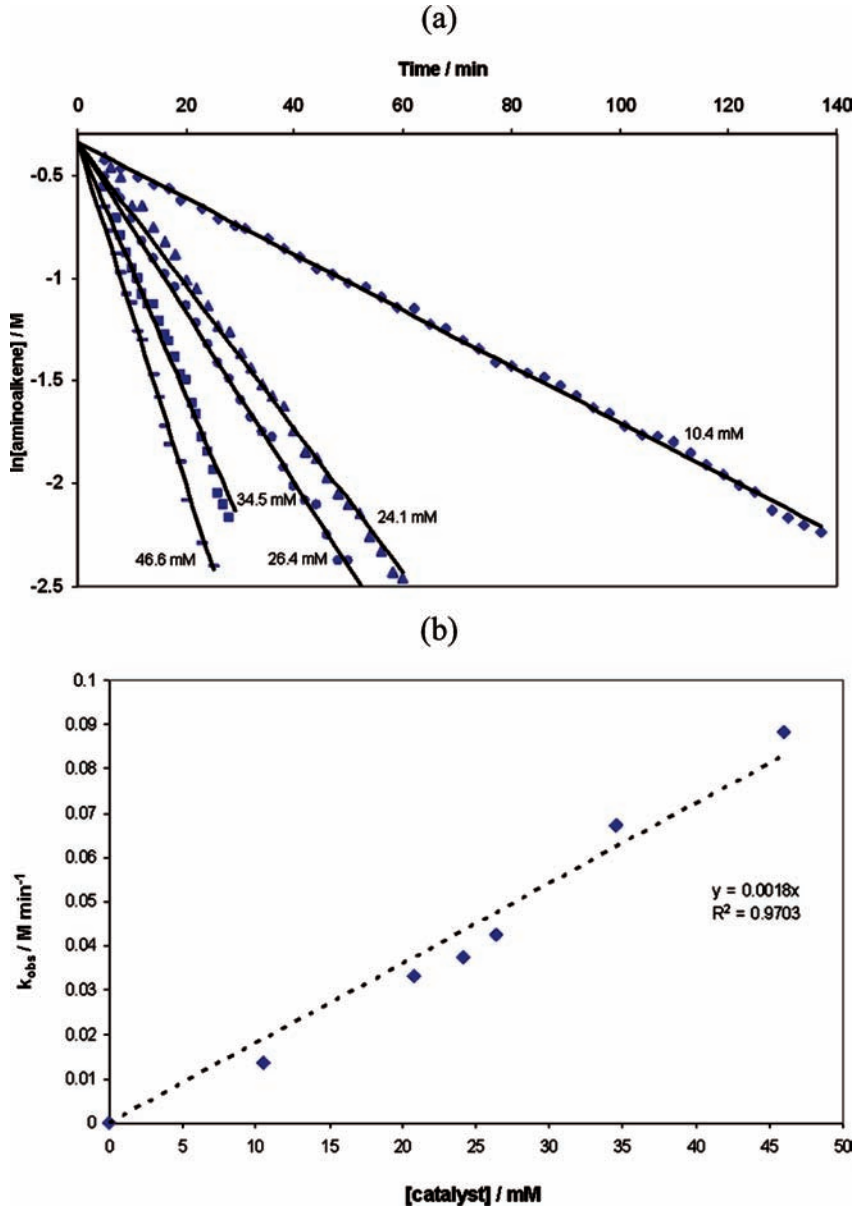


Figure 9. Plots of (a) log[aminoalkene] vs time for a series of different concentrations of **2** and (b) k_{obs} vs [**2**]. Data were collected with [aminoalkene]$_0$ = 0.6 M at 283 K in C_6D_6.

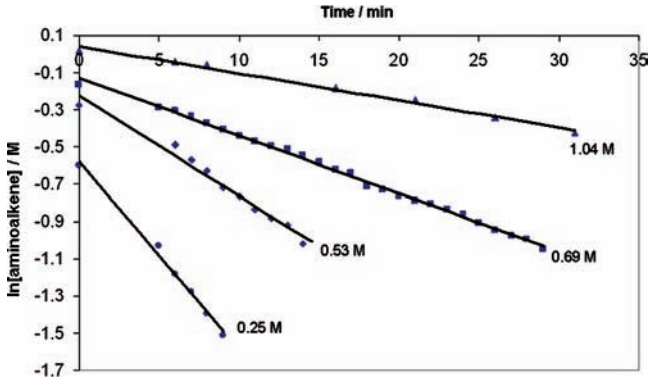


Figure 10. Inhibition kinetics: Plot of log[aminoalkene] vs time for different substrate concentrations at a constant [**2**] of 25 mM at 298 K.

For reversible catalyst initiation (Figure 13), the stoichiometric studies suggest that the catalyst resting state is characterized by an equilibrium mixture partitioned between **1a** and monomeric and/or dimeric calcium amide species (exemplified by the model complexes **5**−**7**). Indeed, for many reactions, primary amide complexes were observed, as evidenced by the presence of a highly shielded NH resonance occurring at high field in the ^{1}H NMR spectra (−0.5 to −1.7 ppm). Specifically, in the attempted intramolecular hydroamination of 1-amino-2,2-diphenyl-6-heptene with **1a**, for which no conversion to the reaction product was recorded, high catalyst loadings led to the observation of a broad resonance at −1.72 ppm, which compares well to the value of −1.63 ppm reported for **6**. For nonreversible catalyst initiation (Figure 12), the catalyst resting state may lie with either monomeric or dimeric primary amide complexes. Despite the formation of dimeric complexes as catalyst resting states, on the basis of the coordination chemistry of **10** along with

(65) (a) Juza, R. *Angew. Chem.* **1964**, *76*, 290. (b) Juza, R.; Schumacher, H. *Z. Anorg. Allg. Chem.* **1963**, *324*, 278. (c) Kaupp, M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1992**, *114*, 491.

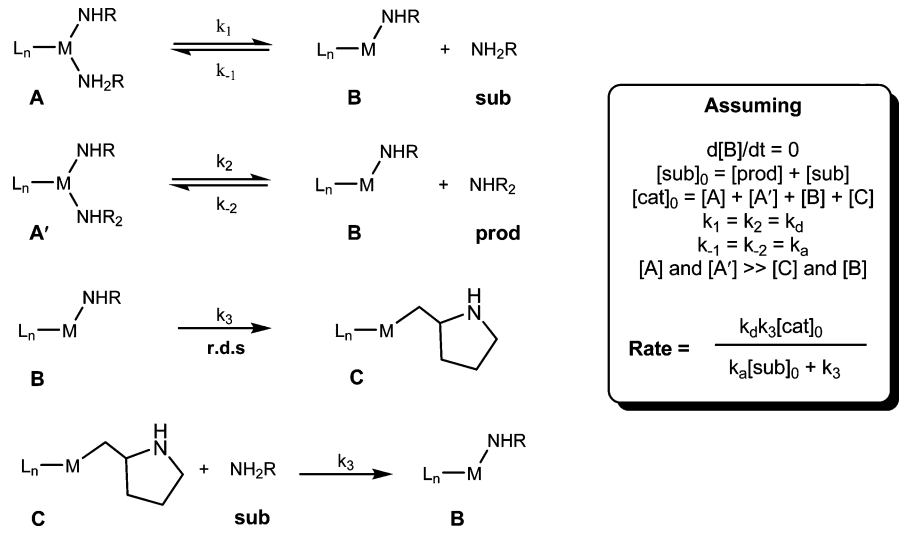


Figure 11. Proposed model for hydroamination catalysis mediated by **2**.

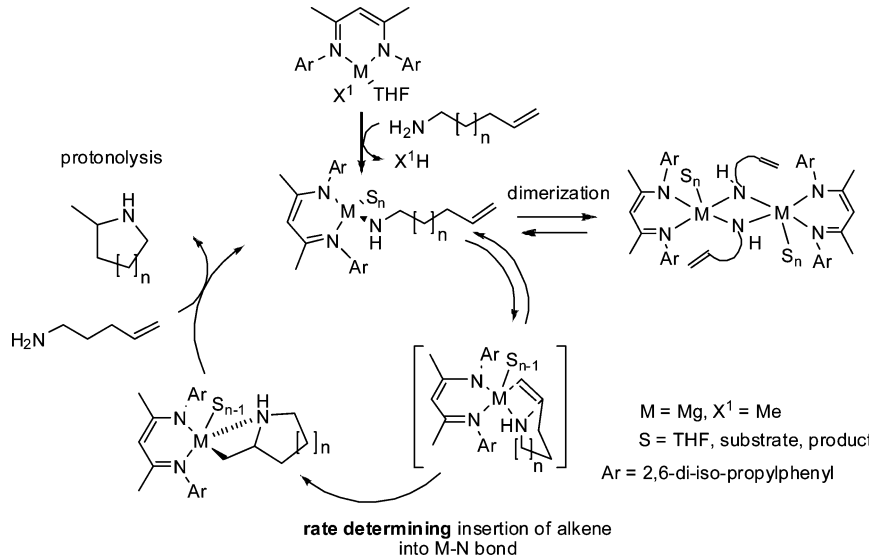


Figure 12. Proposed mechanism of group-2-mediated intramolecular hydroamination catalysis for nonreversible catalyst initiation.

the first-order behavior with respect to catalyst, we propose that catalytic turnover occurs from discrete monomeric species and that the formation of dimeric group-2 amide complexes is simply a nonreactive pathway in the catalytic cycle.

Hence, it becomes apparent that there are several mechanisms for inhibiting catalytic turnover, involving either formation of organometallic intermediates that are no longer able to re-enter the catalytic cycle or inhibition of the rate-limiting step. Important reactions include (*i*) dimerization of intermediate metal amide species, (*ii*) deleterious Schlenk-like equilibria that form homoleptic species of the form L_2M and $M(X^1)_2$, and (*iii*) coordinative saturation of intermediate species by auxiliary Lewis bases such as THF, substrate, or product.

Summary and Conclusions

The β-diketiminate-stabilized calcium amide **1a** and its magnesium analogue **2** are reported to be efficient precatalysts for hydroamination/cyclization of aminoalkenes. The reactions proceed under mild conditions, allowing the synthesis of five-, six-, and seven-membered heterocyclic products. Qualitative assessment of these reactions has revealed that the ease of catalytic turnover increases (*i*) for smaller ring sizes (5 > 6 > 7), (*ii*) substrates that benefit from favorable Thorpe−Ingold effects, and (*iii*) substrates that do not possess additional substitution on the alkene component. Extension of this chemistry to the known strontium and barium analogues **1b** and **1c** was not undertaken because of the propensity of these species to undergo deleterious Schlenk-like solution equilibria to form ill-defined mixtures under catalytically relevant conditions. In this regard, it is apparent that the kinetic stabilization provided

(66) (a) Gärtner, M.; Görls, H.; Westerhausen, M. *Inorg. Chem.* **2007**, *46*, 7678. (b) Gärtner, M.; Görls, H.; Westerhausen, M. *Dalton Trans.* **2008**, 1574.

(67) It has previously been reported that the exocyclic methyl groups of the β-diketiminate ligand may undergo C−H activation in the presence of a calcium−benzyl σ bond. See: Harder, S. *Angew. Chem., Int. Ed* **2003**, *42*, 3430.

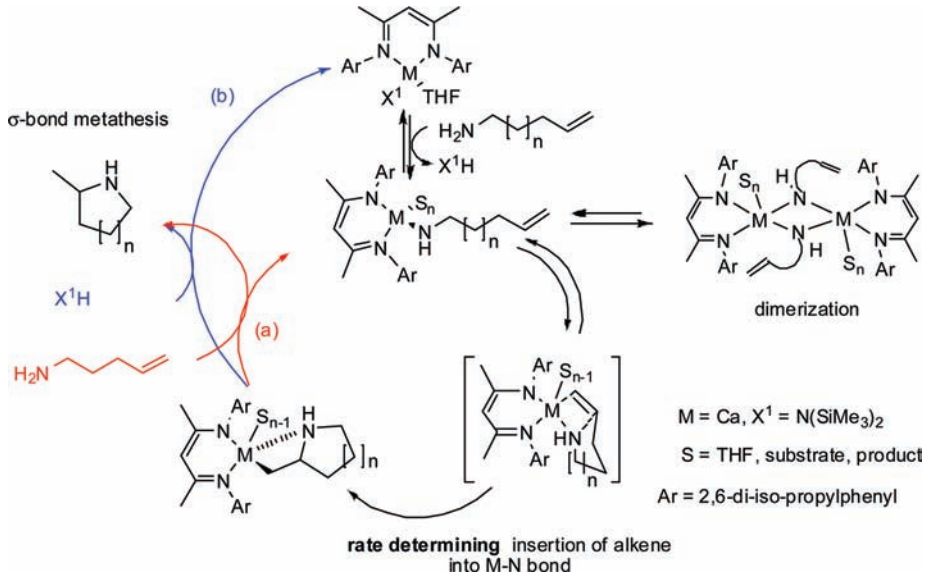


Figure 13. Proposed mechanism of group-2-mediated intramolecular hydroamination catalysis for reversible catalyst initiation.

by the diketiminate ligand to the calcium and magnesium species is of vital importance.

In organolanthanide(III)-mediated hydroamination catalysis, the effect of ionic radius on reaction kinetics is well-documented. For a given substrate, intramolecular hydroamination with a given precatalyst proceeds at lower rates with decreasing size of the metal ionic radius as a result of the greater degree of coordinative saturation at the electrophilic metal center, which increases the energy of the transition state for the rate-determining insertion step. As such, the choice of metal, with consideration of the lanthanide contraction, may be used as means of tuning the reactivity/selectivity of the catalyst. In contrast to the relatively small change in ionic radius of M^{3+} in crossing the period from lanthanum to lutetium (19.9%),[62] there is a drastically large change in the M^{2+} ionic radius (87.5%) in descending group-2 from magnesium to barium.[62] The effect of metal radius upon reaction rate in the group-2 system is evidently more complex. Although the results presented herein suggest that the calcium complex **1a** is superior to the magnesium analogue **2** as a catalyst, further studies in our group and that of Roesky have demonstrated that this trend does not extend neatly to strontium.[23,25] It is clear that large variations in the size and resultant charge density of M^{2+}, as well as Schlenk-like redistribution and/or aggregation of complexes of the heavier alkaline earths of the form LMX (M = Mg, Ca, Sr, Ba) in solution, have dramatic effects on reactivity. In contrast to the situation for the trivalent organolanthanides, the reaction rates and selectivity cannot be considered simply in terms of increasing ionic radius that decreases the coordinative saturation at the metal center. We are continuing to study the reaction chemistry of organometallic compounds of the heavier alkaline earths and will report our findings in subsequent publications.

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Supporting Information Available: Full experimental details and details of the X-ray analysis of the (±)-*trans*-1-phenyl-4-methylpyrrolidine·HCl cyclization product (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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