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Recyclable Polymer-Supported Organolanthanide Hydroamination Catalysts. Immobilization and Activation via Dynamic Transamination

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A series of divinylbenzene cross-linked, amino-functionalized polystyrene resins such as aminomethylated polystyrenes of varying mesh size, piperazinomethyl polystyrene, 1,12-diaminododecanetrityl resin, 1,7-diaminoheptanetrityl resin, 1,2-diaminoethanetrityl resin, 1,4-bis-(aminomethyl)benzenetrityl resin, *N*-(2-aminoethyl)aminomethyl polystyrene, *cis*-1,2-diaminocyclohexanetrityl resin, and *trans*-1,2-diaminocyclohexanetrityl resin are used as supports for the intramolecular hydroamination/cyclization precatalysts $Cp'_2SmCH(SiMe_3)_2$, $Cp'_2LaCH(SiMe_3)_2$ ($Cp' = \eta^5\text{-}Me_5C_5$), and $CGCSmN(SiMe_3)_2$ ($CGC = Me_2Si[(\eta^5\text{-}Me_4C_5)(^tBuN)]$). It is shown that these catalyst precursors can be immobilized on the polymer supports via transaminative protonolysis to give the corresponding bound precatalysts, which, in the presence of aminoalkene substrates, are transaminatively released for efficient homogeneous intramolecular hydroamination/cyclization processes. Upon substrate consumption, the catalysts are readsorbed on the supports. In many cases, these catalysts exhibit activities comparable to the homogeneous precursors and are recoverable/recyclable with only minor to moderate loss of activity, depending on the particular resin amino substituents.

Introduction

Carbon−nitrogen bond-forming processes are of fundamental significance in synthetic chemistry, and olefin hydroamination by catalytic N−H bond addition to carbon−carbon unsaturation represents a challenging, highly desirable, and atom-economical transformation.[1,2] Traditionally, such reactions could be carried out only with alkali metals in liquid ammonia at high temperatures and pressures, affording modest yields and selectivities,[1b,d,3] or in transition metal-mediated systems with frequently limited catalyst lifetimes, modest turnover frequencies, and/or limited scope.[4,5] Recently, significant advances have been achieved using acidic additives and/or activated substrates, affording improved catalyst lifetimes and reaction rates.[4] In comparison to typical middle and late transition metal complexes, organolanthanides exhibit distinctively different reactivity character-

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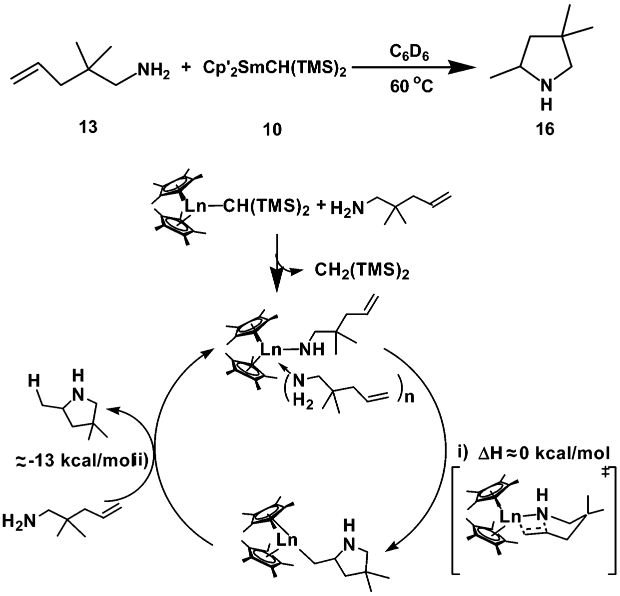
istics for unsaturated organic substrate activation and heteroatom transformations.[6] These reflect the great electrophilicity of f-element ions, polar metal−ligand bonding, large ionic radii, mechanistic pathways differing from conventional oxidative addition/reductive elimination sequences, nondissociable ancillary ligation, and high kinetic lability. Highly efficient homogeneous processes for the inter-[7] and intramolecular hydroamination/cyclization of C−C unsaturations such as aminoalkenes,[8,9] aminoalkynes,[10] aminoallenes,[11] and aminodienes[12] by organolanthanides[7−12] demonstrate efficient insertion of C−C unsaturation into Ln−N bonds coupled with rapid Ln−C protonolysis to effect a wide spectrum of regiospecific catalytic N−C bond-forming transformations (e.g., Scheme 1, Ln = lanthanide). Nevertheless, for practical laboratory-scale syntheses, the aforementioned organolanthanide precatalysts are difficult to recover from reaction mixtures. Since these catalysts can be expensive and laborious to synthesize,[7−12] devising flexible methods to recover and recycle them could potentially increase the utility and applicability of intramolecular hydroamination/cyclization. Although immobilizing transition metal catalysts on solid supports is well-developed,[13−18] as far as we are aware, this contribution represents the first immobilization of organo-

Scheme 1. Established Mechanism for Organolanthanide-Catalyzed Aminoalkene Hydroamination/Cyclization (Ln = lanthanide)



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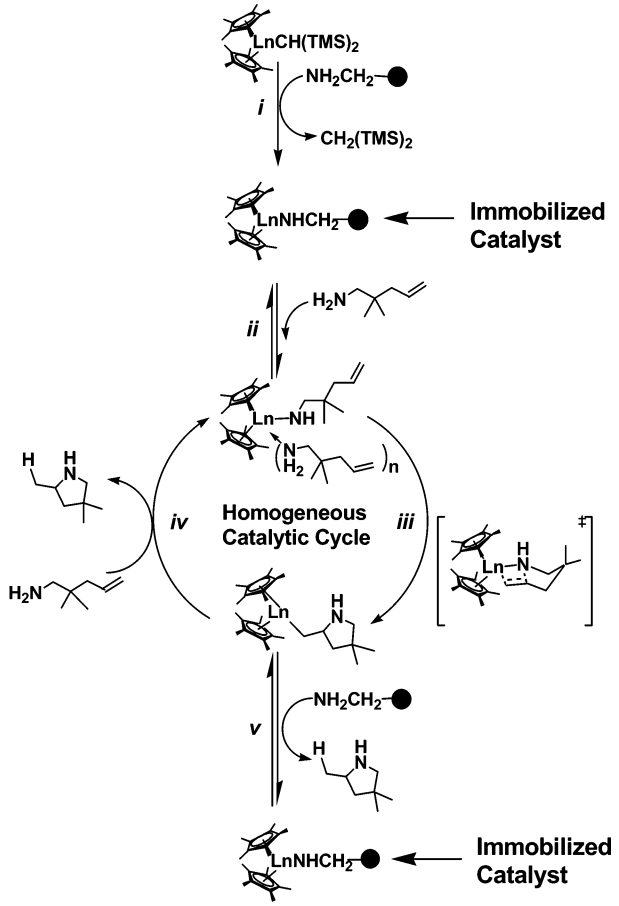
Scheme 2. Proposed Dynamic Transamination Mechanism for Intramolecular Hydroamination/Cyclization Mediated by Polymer-Bound Lanthanocenes



lanthanide catalysts on solid phases for hydroamination/cyclization. The approach we report is unconventional and capitalizes on the distinctive, frequently rapid interconvertability characteristics of Ln−C and Ln−N bonds.

Instead of covalently linking lanthanide ancillary ligands to polymer resins, which can be laborious and the results of which are likely to be highly catalyst/reaction specific, we investigated an alternative approach, dynamic transamination, in which the precatalyst is bound to the resin in a flexible, accessible way. The strategy is shown in Scheme 2. Here, Ln−N (immobilized catalyst molecules) are protonolytically released by the substrate, function as conventional homogeneous organolanthanide hydroamination catalysts, and are then readsorbed as substrate is converted to more sterically encumbered cyclization product. The attractions of this approach are as follows: (1) It has potential applicability to most organolanthanide catalysts (of which there are now a great many) without having to covalently attach an ancillary ligand to the support. (2) Diverse amine-functionalized polymer supports are commercially available. (3) The released catalysts offer all the benefits of the unencumbered, homogeneous catalysts in terms of reactivity and selectivity. Such characteristics are frequently compromised in immobilization.[19] (4) For some lanthanides (e.g., Sm), color changes in typical hydroamination reaction solutions should indicate when substrate has been consumed and the catalyst again immobilized. (5) This approach is more economical and environmentally benign than discarding catalysts after a single use. Nevertheless, this strategy has potential uncertainties: (1) The initial rate of catalyst release and the extent of release may strongly depend on unestablished aspects of equilibrium *ii*, Scheme 2. (2) Catalyst readsorption, hence recyclability, may strongly depend on unestablished aspects of equilibrium *v*, Scheme 2.

Here we report the first implementation of amino-functionalized polystyrene resins[17,20,21] as reversible binding supports for organolanthanide intramolecular hydroamination/cyclization (IHC) precatalysts. The supports are commercially available with the structures and specifications shown in Scheme 3. To explore the viability of the present approach and which types of supported catalysts afford the greatest activity and recyclability, a spectrum of amino-functionalized polystyrenes of varying structures and functionalities are surveyed, including resins having varied particle sizes (**1a** and **1b**), having only primary amine functionalities (**1**), without a primary amine (**2**), having both primary and secondary amines (**3**−**9**), having linkers of varying lengths between primary and secondary amines (**3**−**6**), having sterically hindered secondary amines (**3**−**6**, **8**, **9**), having unhindered secondary amines (**7**), and having primary and secondary amines in either *cis* (**8**) or *trans* relationships (**9**). It will be seen that a range of organolanthanides can be immobilized on these supports, affording bound precatalysts that can then be used for efficient IHC processes. In many cases, these catalysts exhibit activities comparable to those of the homogeneous precursors and are recoverable/recyclable with only modest loss of activity.

Experimental Section

Materials and Methods. All manipulations of air-sensitive materials were carried out with rigorous exclusion of O_2 and moisture using methodologies described previously.[7−12] Argon (Matheson, prepurified) was purified by passage through a MnO oxygen-removal column[22] and a Davison 4 Å molecular sieve column. Before use, all solvents were distilled under dry N_2 over appropriate drying agents (sodium benzophenone ketyl, metal

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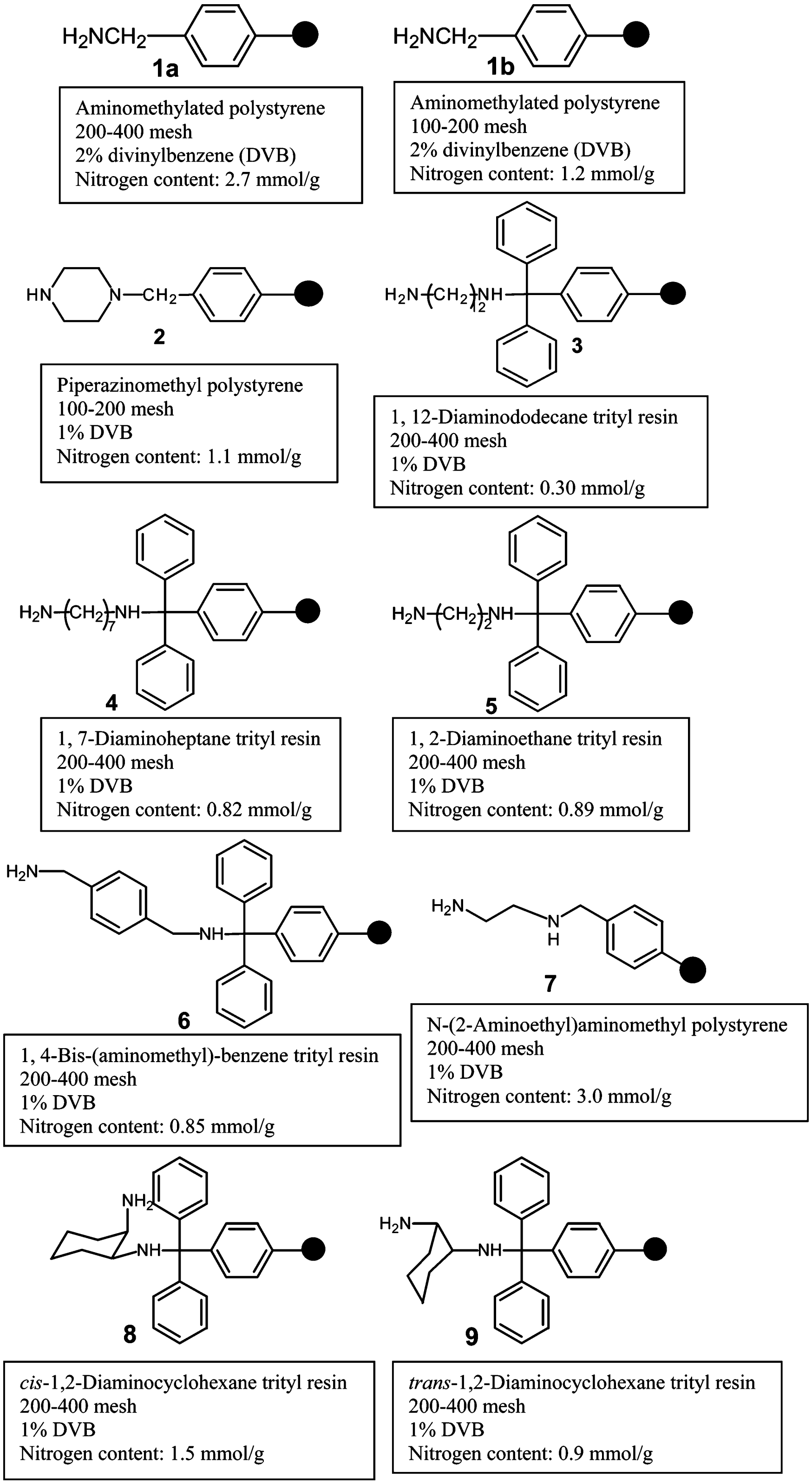
Scheme 3. Structures and Properties of Commercially Available Polymeric Supports 1−9 (● = cross-linked polystyrene bead)



1a

Aminomethylated polystyrene
200-400 mesh
2% divinylbenzene (DVB)
Nitrogen content: 2.7 mmol/g

1b

Aminomethylated polystyrene
100-200 mesh
2% divinylbenzene (DVB)
Nitrogen content: 1.2 mmol/g

2

Piperazinomethyl polystyrene
100-200 mesh
1% DVB
Nitrogen content: 1.1 mmol/g

3

1, 12-Diaminododecane trityl resin
200-400 mesh
1% DVB
Nitrogen content: 0.30 mmol/g

4

1, 7-Diaminoheptane trityl resin
200-400 mesh
1% DVB
Nitrogen content: 0.82 mmol/g

5

1, 2-Diaminoethane trityl resin
200-400 mesh
1% DVB
Nitrogen content: 0.89 mmol/g

6

1, 4-Bis-(aminomethyl)-benzene trityl resin
200-400 mesh
1% DVB
Nitrogen content: 0.85 mmol/g

7

N-(2-Aminoethyl)aminomethyl polystyrene
200-400 mesh
1% DVB
Nitrogen content: 3.0 mmol/g

8

cis-1,2-Diaminocyclohexane trityl resin
200-400 mesh
1% DVB
Nitrogen content: 1.5 mmol/g

9

trans-1,2-Diaminocyclohexane trityl resin
200-400 mesh
1% DVB
Nitrogen content: 0.9 mmol/g

hydrides, or Na/K alloy, except for chlorinated solvents). Benzene-d_6 and toluene-d_6 (all 99+ atom % D), purchased from Cambridge Isotope Laboratories and used for NMR reactions and kinetic measurements, were stored in vacuo over Na/K alloy in resealable bulbs and vacuum-transferred immediately prior to use. All resins were purchased from Calbiochem-Novabiochem Co., washed with copious amounts of distilled benzene, and dried under high vacuum at 50 °C overnight. Other organic starting materials were purchased from Aldrich Chemical Co. and, when appropriate, were distilled prior to use. For intramolecular IHC reactions, the substrates 2,2-dimethyl-4-penten-1-amine (**13**), 2,2-dimethyl-5-hexen-1-amine

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(22) (a) He, M.-Y.; Xiong, G.; Toscano, P. J.; Burwell, R. L., Jr.: Marks, T. J. *J. Am. Chem. Soc.* **1985**, *107*, 641−652. (b) Moeseler, R.; Horvath, B.; Lindenau, D.; Horvath, E. G.; Krauss, H. L. Z. *Naturforsch.* **1976**, *31*, 892−893. (c) Mcllwrick, C. R.; Phillips, C. S. G. *J. Phys. E* **1973**, *6*, 1208−1210.

(**14**), and 4-penten-1-amine (**15**)[8] were synthesized according to literature procedures. Substrates **13**, **14**, and **15** were dried by stirring over CaH_2, then additionally dried by repeated vacuum transfer from freshly activated Davison 4 Å molecular sieves, degassed by freeze−pump−thaw cycles, and finally stored in vacuum-tight containers. Organolanthanide precatalysts $Cp'_2SmCH(SiMe_3)_2$ ($Cp' = \eta^5\text{-}Me_5C_5$) (**10**), $CGCSmN(SiMe_3)_2$ ($CGC = Me_2Si[(\eta^5\text{-}Me_4C_5)(^tBuN)]$) (**11**), and $Cp'_2LaCH(SiMe_3)_2$ (**12**)[8] were prepared by published procedures.

Physical and Analytical Measurements. NMR spectra were recorded on either Varian Gemini 300 (FT, 300 MHz, ^1H; 75 MHz, ^{13}C), Unity- or Mercury-400 (FT, 400 MHz, ^1H; 100 MHz, ^{13}C), Inova-400 (FT, 400 MHz, ^1H; 100 MHz, ^{13}C), or Inova-500 (FT, 500 MHz, ^1H; 125 MHz, ^{13}C) instruments. Chemical shifts (δ) for ^1H and ^{13}C are referenced to internal solvent resonances and reported relative to $SiMe_4$. NMR experiments on air-sensitive samples were conducted in Teflon valve-sealed tubes (J. Young). GC-MS analyses were performed using an HP6890 instrument equipped with an HP 5972 detector, an HP-5MS (5% phenyl methyl siloxane, 30 m × 250 μm × 0.25 μm) capillary column, and Chemstation software.

Representative NMR-Scale Preparation of Aminomethylated Polystyrene 1a Supported Catalyst Precursor 19a. In the glovebox, $Cp'_2SmCH(SiMe_3)_2$ (**10**, 2.9 mg, 5.0 μmol), aminomethylated polystyrene (**1a**, 3.7 mg, 10 μmol N content), and benzene-d_6 (0.5 mL) were loaded into an NMR tube equipped with a Teflon valve. The tube was then placed in a 60 °C oil bath, and the reaction was monitored over time by ^1H NMR until the two Cp'_2Sm peaks at ∼0.82 ppm were undetectable, indicating that the entire organosamarium complex had been immobilized. During this time period, the resin color turned gradually from yellow to red. All other supported precatalysts **19b** to **29** were prepared in a manner analogous to that for **19a**.

Representative NMR-Scale Intramolecular Hydroamination/Cyclization Catalyzed by Homogeneous Precatalyst $Cp'_2SmCH(SiMe_3)_2$ 10. In the glovebox, homogeneous precatalyst $Cp'_2SmCH(SiMe_3)_2$, **10** (2.9 mg, 5.0 μmol), and benzene-d_6 (0.5 mL) were loaded into an NMR tube equipped with a Teflon valve. Then on the vacuum line, a mixture of benzene-d_6 (0.10 mL) and 2,2-dimethyl-4-penten-1-amine, **13** (0.011 g, 100 μmol), was added via syringe under an argon flush while the tube was maintained at −78 °C to protect the precatalyst under the frozen benzene. The NMR tube was next evacuated and back-filled with argon three times at −78 °C and finally sealed. The ensuing catalytic reaction was monitored in situ by ^1H NMR. Upon completion of turnover, to separate the product and catalyst, the reaction solution was vacuum transferred to another NMR tube on the vacuum line. The product was identified by ^1H NMR. The intramolecular hydroamination/cyclization (IHC) of substrate **13** catalyzed by the other two homogeneous precatalysts **11** and **12** and the IHC of substrates **14** and **15** catalyzed by precatalyst **10** were conducted in the same manner.

Representative NMR-Scale Intramolecular Hydroamination/Cyclization Catalyzed by Polymer-Supported Catalyst Precursor 19a. On the vacuum line, to in situ generated, immobilized catalyst precursor **19a** prepared as described above (5.0 μmol in 0.5 mL of benzene-d_6) was added a mixture of benzene-d_6 (0.1 mL) and 2,2-dimethyl-4-penten-1-amine, **13** (0.011 g, 100 μmol), via syringe under an argon flush while the tube was maintained at −78 °C to protect the supported precatalyst under the frozen benzene. The NMR tube was next evacuated and back-filled with argon three times at −78 °C and finally sealed. The ensuing catalytic reaction was monitored by ^1H NMR. The IHC of substrate **13** by other precatalysts **19b** to **29** and the IHC of the other two substrates **14** and **15** by supported precatalyst **19a** were carried out in an identical way.

Representative NMR-Scale Recovery of Polymer-Supported Catalyst Precursor 19a. In the ^1H NMR, liberation of the samarocene catalyst from the resin and recapture of the catalyst by the resin was monitored by the appearance and disappearance of the Cp'_2Sm peak at δ ∼1.4 ppm. Thus, after completion of the catalytic reaction, the reaction solution was monitored by ^1H NMR until the Cp'_2Sm peak was undetectable, meaning that the maximum amount of catalyst had been recaptured by the resin. Then, in the glovebox, the product solution was withdrawn from the immobilized catalyst via syringe and the remaining solid rinsed with benzene-d_6 (0.3 mL × 10). The product was identified by ^1H NMR of the combined benzene-d_6 solutions. The recovered supported precatalyst **19a** was dried under vacuum at 50 °C overnight for reuse. The recovery of supported precatalysts **19b**−**29** was carried out analogously to that of **19a**.

Representative NMR-Scale Recycle of Polymer-Supported Catalyst Precursor 19a. In the glovebox, recovered supported precatalyst **19a** was mixed with benzene-d_6 (0.5 mL). Then on the vacuum line, a mixture of benzene-d_6 (0.1 mL) and 2,2-dimethyl-4-penten-1-amine, **13** (0.011 g, 100 μmol), was added via syringe under an argon flush while the tube was maintained at −78 °C to protect the supported precatalyst under the frozen benzene. The NMR tube was then evacuated and back-filled with argon three times at −78 °C and finally sealed. The ensuing catalytic reaction was monitored by ^1H NMR. The recycling of immobilized precatalysts **19b**−**29** was carried out in the same manner.

Mass Transfer Effect Study. To assess the possible importance of mass transfer effects, a sealed NMR tube was loaded with the supported precatalyst and substrate as described above, and the ensuing catalytic reaction was carried out with the NMR tube clamped in an electric drill so that the spinning axis was perpendicular to the long axis of the tube. At the same time, a duplicate NMR tube was loaded with the same supported precatalyst and substrate. The ensuing catalytic reaction was carried out under the same reaction conditions for both samples with the only difference being agitation of the NMR tube. The reactivity and recyclability of these two sets of reactions were compared to assess possible mass transfer effects.

Preparative-Scale Synthesis of Aminomethylated Polystyrene 1a Supported Catalyst Precursor 19a. In the glovebox, $Cp'_2SmCH(SiMe_3)_2$, **10** (0.087 g, 0.15 mmol), aminomethylated polystyrene **1a** (0.111 g, 0.30 mmol N content), and benzene (15 mL) were loaded into a 50 mL storage tube equipped with a J. Young valve and a magnetic stir bar. The tube was then sealed and removed from the glovebox. The reaction mixture was vigorously stirred under a 60 °C oil bath for 2.2 days until the color of the resin turned from yellow to red. Preparative-scale syntheses of supported precatalysts **22** and **25** were carried out in a manner analogous to that for **19a**.

Preparative-Scale Intramolecular Hydroamination/Cyclization Catalyzed by Polymer-Supported Catalyst Precursor 19a, Product Isolation, and Catalyst Recovery. In the glovebox, to the immobilized catalyst precursor **19a** prepared as described above (0.15 mmol in 15 mL of benzene) was added a mixture of benzene (3.0 mL) and 2,2-dimethyl-4-penten-1-amine, **13** (0.33 g, 3.00 mmol). The sealed reaction flask was then removed from the glovebox, and the resulting reaction mixture was vigorously stirred in a 60 °C oil bath for 2 h. The color of the solution turned first to red and then back to colorless. Next in the glovebox, the product solution was separated from the immobilized catalyst via filtration, and the collected solid was rinsed with benzene (3.0 mL × 5). After removing it from the glovebox, the combined benzene solution was cooled to 0 °C, diluted with Et_2O (8 mL), and treated with 2 N NaOH (6 mL). Then, benzyl chloroformate (Cbz-Cl) (0.84 mL, 6 mmol) was added dropwise, and the mixture was allowed to warm to room temperature and stirred vigorously for 1 h. Next, the aqueous layer was separated and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, filtered, and concentrated to afford the crude Cbz-protected amine as a pale yellow oil. The crude product was purified by flash column chromatography (silica gel, hexanes/Et_2O, 6:1) to afford 0.31 g (2.9 mmol, 96% yield) of **Cbz-16** as a colorless, clear oil, which was identified by ^1H NMR.[12b] The recovered supported precatalyst **19a** was dried under vacuum at 50 °C overnight for reuse. The preparative-scale recovery of precatalysts **22** and **25** and isolation and purification of the corresponding azacyclic product were analogous to that of **19a**.

Preparative-Scale Recycle of Polymer-Supported Catalyst Precursor 19a. In the glovebox, recovered supported precatalyst **19a** was mixed with a solution of 2,2-dimethyl-4-penten-1-amine, **13** (0.33 g, 3.0 mmol), in benzene (18 mL). The sealed reaction flask was then removed from the glovebox, and the reaction mixture was vigorously stirred in a 60 °C oil bath. The ensuing catalytic reaction, recovery of the catalyst, and isolation and purification of the azacyclic product were realized in the same manner as described above. The preparative-scale recycle of immobilized precatalysts **22** and **25** was carried out in the same way.

Kinetic Studies of Intramolecular Hydroamination/Cyclization. In a typical experiment, an NMR sample was prepared as described above (see NMR-scale homogeneous catalytic reactions), but maintained at −78 °C until kinetic measurements were begun. The sample tube was then inserted into the probe of the INOVA-500 spectrometer, which had been previously set to the appropriate temperature ($T \pm 0.2$ °C; checked with a methanol or ethylene glycol temperature standard). A single acquisition (nt = 1) with a 45° pulse was used during data acquisition to avoid saturation. The reaction kinetics were usually monitored from intensity changes in one of the olefinic resonances over three or more half-lives. The substrate concentration was measured from the olefinic peak area, standardized to the methyl peak area of the internal standard, (p-$CH_3C_6H_4)_4Si$. For the supported system, the catalyst concentration was measured from the Cp′ peak area and also standardized to the methyl peak area of the (p-$CH_3C_6H_4)_4Si$ internal standard. For the homogeneous system, the data collected up to 2 half-lives could be convincingly fit by least-squares to eq 1, where $[\text{substrate}]_o$ is the initial concentration of substrate. The turnover frequency (h^{-1}) was calculated from the least-squares-determined slope (m) according to eq 2, where $[\text{catalyst}]_o$ is the initial formal concentration of the precatalyst.

$$[\text{substrate}] = mt + [\text{substrate}]_o \qquad (1)$$

$$N_t\ (h^{-1}) = -(60\ \text{min}\ h^{-1}) \times m/[\text{catalyst}]_o \qquad (2)$$

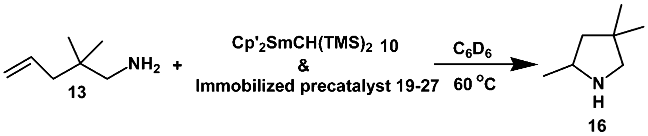
Results

Table 1. Time Required for Complete NMR-Scale Resin Reactions with Homogeneous Organosamarium Precatalyst 10[a]

entry	resin	time (days)	mol resin N/mol catalyst	yield (%)[b]
1	**1**	5.4	1.5	99
2	**1**	3.0	2.0	99
3	**1**	1.1	10.0	99
4	**2**	10.3	1.5	99
5	**2**	7.0	2.0	99
6	**3**	2.1	2.0	99
7	**4**	2.4	2.0	99
8	**5**	2.9	2.0	99
9	**6**	2.2	2.0	99
10	**7**	1.5	2.0	99
11	**8**	5.8	2.0	99
12	**9**	5.1	2.0	99

[a] All reactions performed in C_6D_6 at 60 °C. [b] NMR yield.

Table 2. NMR-Scale Intramolecular Hydroamination/Cyclization of 2,2-Dimethyl-4-penten-1-amine, 13,[a] **by Homogeneous Precatalyst 10 and Corresponding Supported Precatalysts 19−27**[b]

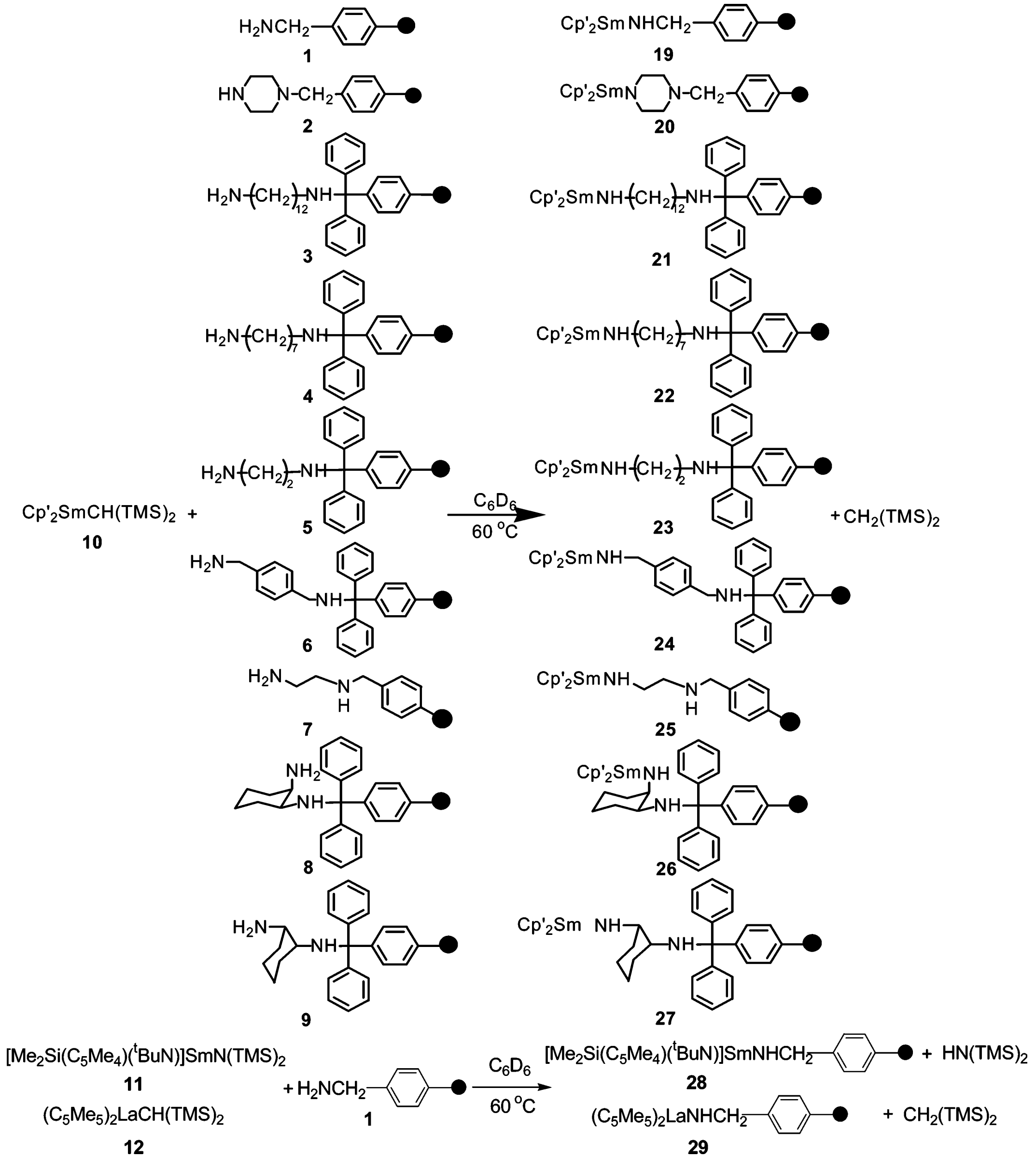


entry	catalyst precursor	mol resin N/ mol catalyst	cycle	time (h)[c]
1	**10**		1	0.6
2	**19a**	1.5	1	0.8
3	**19a**	1.5	2	1.6
4	**19a**	1.5	3	2.9
5	**19a**	2.0	1	1.1
6	**19a**	2.0	2	2.6
7	**19a**	2.0	3	4.2
8	**19a**	10.0	1	39.0
9	**19a**	10.0	2	59.0
10	**19b**	2.0	1	1.5
11	**19b**	2.0	2	2.9
12	**19b**	2.0	3	4.6
13	**20**	1.5	1	4.1
14	**20**	1.5	2	6.7
15	**20**	1.5	3	10.1
16	**20**	2.0	1	8.0
17	**20**	2.0	2	11.1
18	**20**	2.0	3	15.0
19	**21**	2.0	1	0.9
20	**21**	2.0	2	1.6
21	**21**	2.0	3	2.5
22	**22**	2.0	1	0.9
23	**22**	2.0	2	1.7
24	**22**	2.0	3	2.8
25	**23**	2.0	1	1.2
26	**23**	2.0	2	1.9
27	**23**	2.0	3	3.2
28	**24**	2.0	1	1.0
29	**24**	2.0	2	1.8
30	**24**	2.0	3	2.9
31	**25**	2.0	1	7.4
32	**25**	2.0	2	8.9
33	**25**	2.0	3	10.1
34	**26**	2.0	1	4.7
35	**26**	2.0	2	7.3
36	**26**	2.0	3	10.9
37	**27**	2.0	1	4.1
38	**27**	2.0	2	6.9
39	**27**	2.0	3	9.9

[a] All reactions performed in C_6D_6 at 60 °C. [b] Substrate:catalyst = 20:1. [c] Time required for 90% catalytic reaction completion as assayed by in situ NMR.

Synthesis of the Polymer-Supported Catalyst Precursors. In NMR-scale reactions, the amino-functionalized polymer support was impregnated with organosamarium complexes **10** and **11** and organolanthanum complex **12** by simply mixing a C_6D_6 solution of the precatalysts with a suspension of the dried, degassed polymer beads and heating the mixture to 60 °C. The course of the immobilization and catalytic reactions can be monitored in situ by ^1H NMR spectroscopy. Sufficient time was allowed to ensure that >99% of the precatalyst was immobilized on the resin (the immobilized catalyst is essentially NMR-silent). Taking $Cp'_2SmCH(SiMe_3)_2$ (**10**, Cp′ = η^5-Me_5C_5) as an example, immobilization of **10** on the cross-linked resins is indicated by disappearance of the two Cp'_2Sm signals at $\delta \sim 0.82$ ppm and the appearance of $CH_2(SiMe_3)_2$ signals at $\delta \sim 0.10$ and ~ 0.38 ppm. In preparative practice, the color change of the resin from yellow to red can also be conveniently used to monitor the course of the reaction. Under these conditions, the protonolytic transaminative binding of complexes **10**, **11**, and **12** to the resins gives rise to polymer-bound precatalysts **19**−**29** (Scheme 4). The time required for the reaction to be >99% complete varies for the various resins, presumably reflecting an interplay of steric and Brønsted acidity characteristics (Table 1). The rate of resin **7** reaction with samarium complex **10** is

Scheme 4. Synthesis of Polymer-Supported Catalyst Precursors

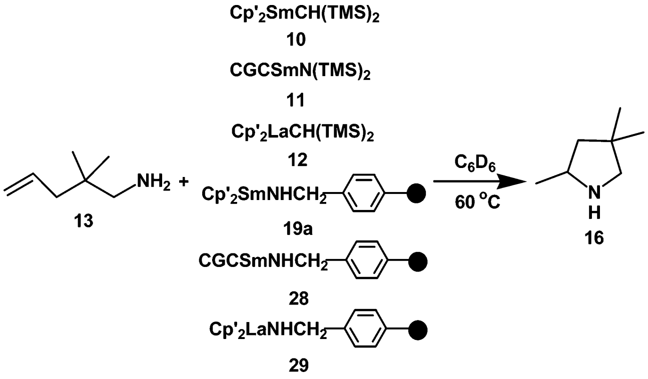


the greatest of the resins surveyed, while the corresponding reaction rate with resin **2** is the least under identical reaction conditions (Table 1, entries 5 and 10). For the same resin, the greater the NH:precatalyst ratio, the greater the reaction rate (Table 1, entries 1−3).

Intramolecular Hydroamination/Cyclization (IHC) Activity of Polymer-Supported Catalyst Precursors. NMR-scale in situ generated polymer-supported catalyst precursors **19**−**29** were used in IHC reactions with representative amino-olefin substrate **13**. The course of the reaction was monitored in situ by ^{1}H NMR. The rate of the catalytic reaction is represented by the time required for a measured amount of substrate to be converted. In terms of NMR spectroscopy, this can be quantified by the progressive disappearance of the $CH_2=$ signals at $\delta \sim 5.0$ ppm. In this contribution, to compare the rate of IHC reactions catalyzed by the various immobilized catalysts, the time required for 90% substrate conversion, calculated by integration of the $CH_2=$ spectral signals, is reported. Furthermore, as discussed above, color changes during the reaction course can be used to roughly gauge reaction completion for some lanthanides. Taking immobilized organosamarium catalysts as an example, the reaction solution turns from colorless to bright red after substrate introduction, reflecting liberation of the red organosamarium complex from the resin. The reaction solution reverts to a colorless/near-colorless appearance after substrate conversion is complete and the free samarium in the solution is recaptured by the resin. It is found that all of the immobilized catalyst precursors efficiently mediate IHC of substrate **13** and can be recovered and recycled at least twice (readsorption is not 100% efficient, as described below).

Results are summarized in Table 2 and compared with those for homogeneous analogue **10**. Comparing polymer-supported catalyst precursors **19**−**27** at the same resin:lanthanide complex ratio, precatalyst **21** and **22** IHC activities are greatest, while **20** is the lowest among all the precursors for all three cycles (Table 2, entries 19−24, 16−18). The greatest activities observed for **21** and **22** are comparable to that of their homogeneous analogue **10** (Table 2, entry 1), while the most efficient recyclability observed by far is from polymer-supported catalyst precursor **25** (Table 2, entries 31−33). Recyclability here describes how efficiently the immobilized catalyst can be recycled after recovery. If, for the second IHC cycle, the rate of the supported catalyst is indistinguishable from that of the first cycle, recyclability is denoted 100%. If the supported

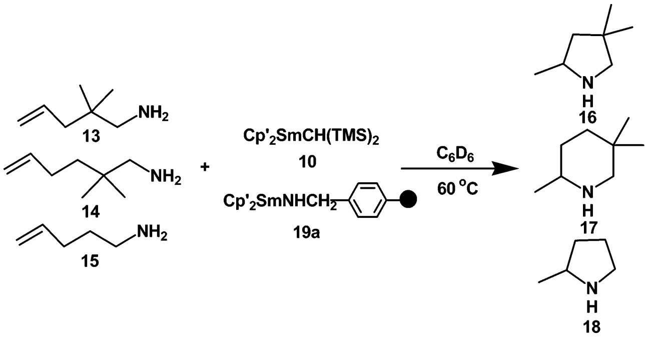
Table 3. NMR-Scale Intramolecular Hydroamination/Cyclization of 2,2-Dimethyl-4-penten-1-amine, 13,[a] by Homogeneous Precatalysts 10, 11, and 12 and Their Corresponding Supported Precatalysts 19a, 28, and 29[b]



substrate	catalyst precursor	cycle	time (h)[c]	mol resin N/ mol catalyst
13	**10**	1	0.60	
13	**19a**	1	1.10	2.0
13	**19a**	2	2.60	2.0
13	**19a**	3	4.20	2.0
13	**11**	1	0.12	
13	**28**	1	0.37	2.0
13	**28**	2	0.61	2.0
13	**28**	3	1.08	2.0
13	**12**	1	0.25	
13	**29**	1	0.56	2.0
13	**29**	2	0.99	2.0
13	**29**	3	1.80	2.0

[a] IHC reactions catalyzed by precursors **10** and **19a** performed in C_6D_6 at 60 °C; IHC reactions catalyzed by precursors **11**, **12**, **28**, and **29** performed in C_6D_6 at 23 °C. [b] Substrate:catalyst = 20:1. [c] Time required for 90% catalytic reaction completion as assayed by in situ NMR.

Table 4. NMR-Scale Intramolecular Hydroamination/Cyclization of 2,2-Dimethyl-4-penten-1-amine, 13, 2,2-Dimethyl-5-hexen-1-amine, 14, and 4-Penten-1-amine, 15,[a] Catalyzed by Homogeneous Precatalyst 10 and Supported Analogue 19a[b]



substrate	catalyst precursor	cycle	time (h)[c]	mol resin N/ mol catalyst
13	**10**	1	0.6	
13	**19a**	1	1.1	2.0
13	**19a**	2	2.6	2.0
13	**19a**	3	4.2	2.0
14	**10**	1	4.3	
14	**19a**	1	5.6	2.0
14	**19a**	2	7.0	2.0
14	**19a**	3	8.7	2.0
15	**10**	1	2.2	
15	**19a**	1	3.5	2.0
15	**19a**	2	4.7	2.0
15	**19a**	3	5.8	2.0

[a] Catalytic reactions for substrates **13** and **15** performed in C_6D_6 at 60 °C; catalytic reaction for substrate **14** performed in C_6D_6 at 23 °C. [b] Substrate:catalyst = 20:1. [c] Time required for 90% catalytic reaction completion as assayed by in situ NMR.

catalyst exhibits negligible activity after recovery, recyclability is denoted zero. For all immobilized catalysts synthesized here, none exhibit 100% recyclability, while even the poorest recyclability observed is far greater than zero. For the same immobilized precatalyst, the higher the resin:lanthanide ratio, the lower the activity observed (Table 2, entries 2, 5, 8), while a higher ratio also correlates with greater recyclability (Table 2, entries 5, 6, 8, 9). The smaller the resin particle size employed, the greater the observed catalytic activity (Table 2, entries 5−7, 10−12). Also, smaller steric hindrances provided by the resin environment correlate with greater catalytic activity (Table 2, entries 34−39). All of the present homogeneous precatalysts can be recovered and recycled; however activity is reduced to varying degrees for successive catalytic cycles, depending on the quantity of catalyst retained (Table 2, entries 2−4). As mentioned above, the polymeric resins are applicable to a variety of organolanthanides. Table 3 compares IHC results for polymer-based catalyst precursors **19a**, **28**, and **29** vs their homogeneous parents **10**, **11**, and **12** with aminoalkene **13** as the substrate. This demonstrates that a variety of organolanthanides can be immobilized by the polystyrene resins and give acceptable to good IHC reactivity and recyclability. There is no evidence that, in the absence of oxygen and moisture, nonleaching chemical reasons prohibit indefinite recycling, as is the case for the homogeneous analogues.[6a,8c]

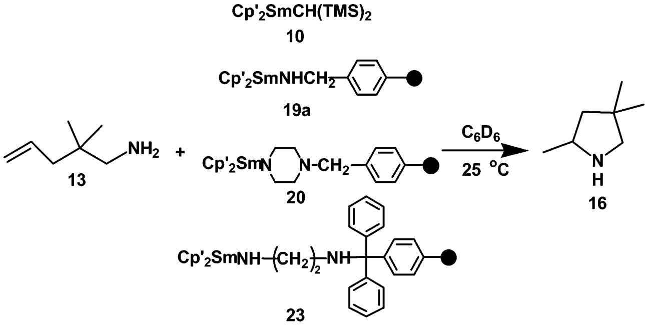
Reaction Scope. The aforementioned polymer-based precatalyst **19a** can also be applied to the hydroamination of other aminoalkene substrates. Table 4 summarizes the IHC activities of 2,2-dimethyl-4-penten-1-amine (**13**), 2,2-dimethyl-5-hexen-1-amine (**14**), and 4-penten-1-amine (**15**) in hydroamination/cyclizations mediated by homogeneous precatalyst **10** and supported catalyst precursor **19a**. It shows that the supported precatalyst can be used to cyclize both five-membered and six-membered substrates with or without a *gem*-dimethyl functional group to give piperidine and pyrrolidine products in acceptable to good reactivity and recyclability.

Mass Transfer Effects. To determine the magnitude of mass transfer effects on activity, NMR-scale intramolecular hydroamination/cyclization of amino-olefin substrate **13** by supported precatalysts **19a**, **23**, and **25** was carried out with/without agitation. The results are summarized in Table 5, showing that reactions that are continuously agitated have rates and recyclabilities similar to those that are not agitated. This demonstrates that mass transfer effects do not play an important role in IHC processes mediated by these polymer-supported precatalysts.

Kinetic Studies. A comparative kinetic study of IHC catalyzed by supported precatalyst **19a** and homogeneous precatalyst **10** was undertaken by in situ ^{1}H NMR spectroscopy. The transformation of a ∼20-fold molar excess of 2,2-dimethyl-4-penten-1-amine (**13**) catalyzed by supported precatalyst **19a** and its homogeneous parent **10** was monitored to greater than 90% substrate consumption. For the heterogeneous system, the appearance of the homogeneous paramagnetic Cp'_2Sm resonance (δ ∼1.4 ppm) in the ^{1}H NMR spectrum was also normalized to a tetrakis(4-tolyl)silane internal standard. The spectral signal at δ ∼1.4 ppm is the only peak that can be related to the catalyst, and bound catalyst is not observed in the NMR, reflecting the relatively large rotational correlation times of species bound to the highly cross-linked resins.[15,17] Kinetic plots are shown in Figures 1 and 2.

In contrast to the homogeneous analogue, kinetic plots of the heterogeneous system (Figures 1, 2) reveal a slight s-like dependence of substrate concentration on reaction time over a

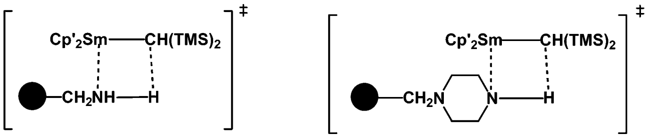
Table 5. NMR-Scale Intramolecular Hydroamination/Cyclization of 2,2-Dimethyl-4-penten-1-amine, 13,[a] Catalyzed by Homogeneous Precatalyst 10 and Supported Precatalysts 19a, 23, and 25[b] with/without Agitation



substrate	catalyst precursor	cycle	time (h)[c]	mol resin N/ mol catalyst
13	**10**	1	4.8	
13[d]	**19a**	1	6.7	2.0
13	**19a**	2	8.3	2.0
13	**19a**	3	10.9	2.0
13[e]	**19a**	1	6.5	2.0
13	**19a**	2	8.2	2.0
13	**19a**	3	10.9	2.0
13[d]	**20**	1	22.1	2.0
13	**20**	2	25.9	2.0
13	**20**	3	30.2	2.0
13[e]	**20**	1	21.8	2.0
13	**20**	2	26.1	2.0
13	**20**	3	30.0	2.0
13[d]	**23**	1	7.5	2.0
13	**23**	2	10.4	2.0
13	**23**	3	13.1	2.0
13[e]	**23**	1	7.2	2.0
13	**23**	2	10.4	2.0
13	**23**	3	13.0	2.0

[a] All reactions were performed in C_6D_6 at 25 °C. [b] Substrate:catalyst = 20:1. [c] Time required for 90% catalytic reaction completion as assayed by in situ NMR. [d] Three cycles of IHC were carried out without agitation. [e] Three cycles of IHC were carried out with continuous agitation.

Scheme 5. Possible Transition States for the Formation of Polymer-Supported Precatalysts 19 and 20

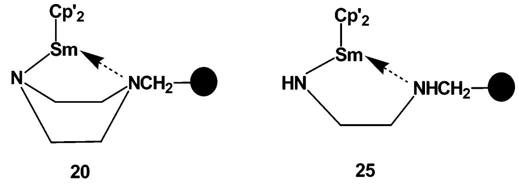


~10-fold substrate concentration range, suggesting that the catalytic rate increases gradually, reaches a maximum, and then decreases gradually rather than strictly adhering to zero-order dependence. Also note the trend of the catalyst concentration released from the polymer to the solution with reaction time. The catalyst concentration rises gradually until it reaches a maximum and then declines slowly, approximately paralleling substrate consumption.

Discussion

Mechanism. The proposed pathway for IHC conversion of substrate **13** catalyzed by supported catalyst precursor **19a** is depicted in Scheme 2. In this mechanism, the catalyst is first transaminatively released from the polymer matrix into the solution and mediates the IHC reaction as in the conventional homogeneous catalytic scenario.[8] Upon substrate consumption, the catalytically active Cp'_2Ln species are ultimately transaminatively recaptured by the resin amino groups, which are available in stoichiometric excess. This proposed "boomerang" mechanism is strongly supported by the kinetic results in Figure 1, which reveal that as substrate is consumed, the quantity of catalyst recaptured by the resin increases substantially. Binding of Cp'_2Sm- by the resin will be favored as the accessible/unhindered substrate $-NH_2$ groups are depleted.

Scheme 6. Possible Structures of Polymer-Supported Precatalysts 20 and 25



Rate of Resin Reaction with Homogeneous Precatalyst 10. Table 1 shows that the rate of resin **7** reaction with precatalyst **10** is the greatest, while that of resin **2** is the lowest among the resins investigated. This can tentatively be explained by the fact that resin **7** contains both primary and secondary amino sites and is the least sterically hindered compared to the secondary amines of the other resins. In contrast, resin **2** has only a secondary amine, lower Brønsted acidity, and greater steric encumbrance, all of which should render $Sm-CH(TMS)_2$ protonolysis more sluggish compared to that of a primary amine (Scheme 5).

IHC Reactivity and Recyclability Trends for the Polymer-Supported Precatalysts. 1. Effect of *trans* and *cis* Resin Cyclohexyl Conformation on IHC Activity. Table 2 shows that polymer-supported precatalyst **27**, which has a *trans*-cyclohexyl conformation, exhibits greater catalytic activity than its *cis* counterpart **26**. This presumably reflects the fact that the catalytically-active lanthanide center must be first accessed by the substrate to be released to the solution. Organolanthanide bonding to a primary amine should be less sterically hindered for the *trans*-cyclohexyl conformation than for the *cis*. Furthermore, steric hindrance also explains why precursors **19**, **21**, **22**, **23**, and **24** exhibit superior activity to **26** and **27**. The chairlike six-membered ring in **26** and **27** should render the polymer-bound Sm far less accessible to substrate and therefore more difficultly released.

2. Effect of Sm−Polystyrene Phenyl Ring Distance on IHC Activity. Table 2 shows that immobilized catalyst precursors **21** and **22** have the greatest hydroamination/cyclization activity. This again can be explained by the relative accessibility of the substrate to the bound Ln center, a prerequisite for release from the resin. The greater the Ln−phenyl ring distance, the less hindered the metal ion and the more accessible it should be to substrate, hence the greater the effective IHC rate. When the distance is sufficiently great, resin reactivity differences become negligible, as in **21** and **22**.

3. Polymer Denticity Effects on Catalytic Activity and Recyclability. Table 2 shows that polymer-supported precatalysts **20** and **25** exhibit the lowest IHC activity. This likely reflects chelation effects (Scheme 6), with Ln coordination by the two nitrogen ligands favoring resin binding. Interestingly, this minimized Ln dissociation (Scheme 2 equilibria *ii* and *v* lie far to the resin-bound side) likely reduces catalyst leaching, explaining why immobilized precatalysts **20** and **25** also exhibit the greatest recyclability. For other polymer-based precusors **21**, **22**, **23**, **24**, **26**, and **27**, chelation effects are probably minor due to the steric hindrance between the secondary amine and proximate phenyl groups as well as the sizable distance between primary and secondary amine sites.

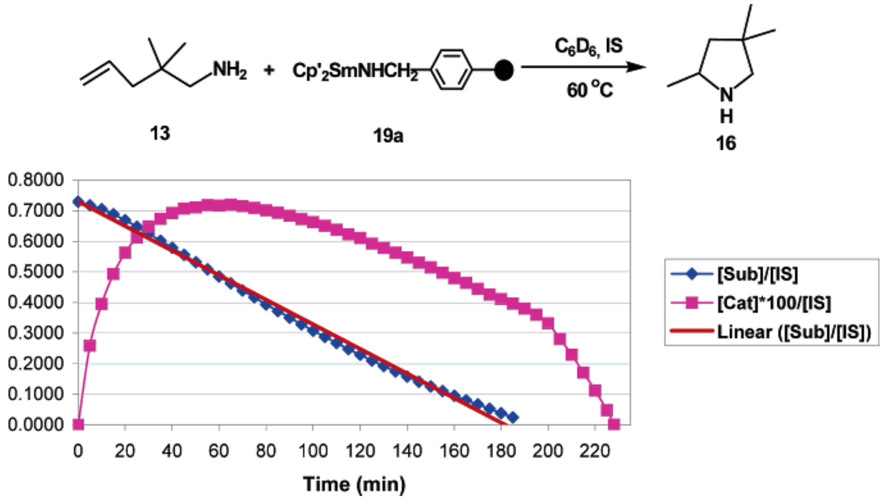


Figure 1. Plot of the 2,2-dimethyl-4-penten-1-amine (**13**):tetrakis(4-tolyl)silane (internal standard) ratio as a function of time, and plot of the homogeneous $(C_5Me_5)_2Sm-$:tetrakis(4-methylphenyl)silane (internal standard) ratio as a function of time for the IHC reaction of 2,2-dimethyl-4-penten-1-amine (**13**) as mediated by supported precatalyst **19a** in benzene-d_6 at 60 °C.

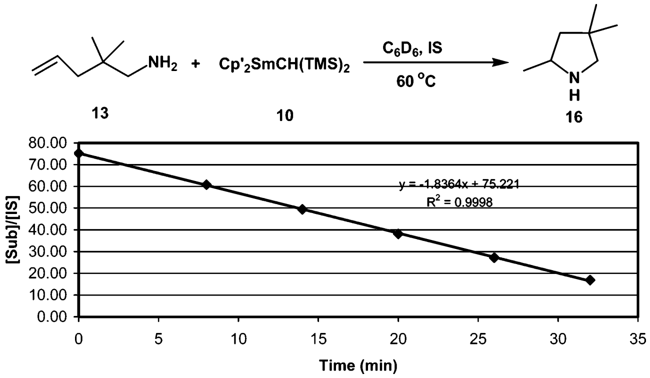


Figure 2. Plot of the 2,2-dimethyl-4-penten-1-amine (**13**):tetrakis-(4-methylphenyl)silane (internal standard) ratio as a function of time for the IHC reaction of 2,2-dimethyl-4-penten-1-amine (**13**) as mediated by homogeneous precatalyst **10** in benzene-d_6 at 60 °C.

Effect of Resin N:Complex Ratio on Activity and Recyclability. Table 2 shows that the greater the resin N:Ln ratio, the lower the IHC activity but the greater the recyclability. Scheme 2 shows that there exists competition between substrate and resin for the catalytically-active organolanthanide species. As substrate is depleted, competition between the resin and the azacyclic IHC product for the organolanthanide may become important. Thus, leaching of the polymer-bound catalyst by the azacyclic product may influence recyclability to some degree. However, the data in Table 2 show that the greater the stoichiometric excess of resin, the weaker the competition of substrate and product for the resin, hence the lower the catalytic activity but the greater the recyclability.

Preparative-Scale Catalytic Reactions. As described in the Experimental Section, preparative-scale catalytic reactions are readily carried out with the present supported catalysts. For colored Ln ions, the reaction course is conveniently monitored by the color change of the reaction solution. After completion of the reaction, the azacyclic product can be isolated with good purity, and the immobilized precatalysts can be recovered and practically recycled for at least two times.

Conclusions

A wide spectrum of homogeneous organolanthanide catalysts is presently available, and this contribution focuses on general ways to immobilize them as well as on the activity and recyclability of the immobilized catalysts. Instead of covalently binding ancillary ligands to polymeric resins, the approach here is to bind the homogeneous precatalyst in a flexible and simple way. Nine commercially available polymer-based resins were examined. For the first time, homogeneous lanthanocene and CGC Sm and La precatalysts have been grafted to the above resins to give supported precatalyst systems for catalytic intramolecular aminoalkene hydroamination/cyclization (IHC). Some of the polymer-supported precatalysts display activities comparable to that of their homogeneous counterparts. All of the immobilized precatalysts can be recovered and recycled at least two times, and some demonstrate very effective recyclability. The effect of particle size, structure of the various resins, and the ratio of resin to homogeneous precatalyst on IHC activity and recyclability has been defined. Kinetic studies of the heterogeneous system suggest a "boomerang" mechanism for IHC reactions catalyzed by the immobilized precatalyst. The reaction scope includes both five- and six-membered heterocycles with or without *gem*-dimethyl groups. On the basis of the reactivity and recyclability of the corresponding polymer-supported precatalysts, resins **1**, **5**, and **6** are recommended for general preparative use. With this contribution, the scope and limitations of immobilized organolanthanide precatalysts for IHC reactions are now better defined, and studies aimed toward the synthesis of more active and more recyclable supported catalysts are underway.

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