A Fully Integrated High-Throughput Screening Methodology for the Discovery of New Polyolefin Catalysts: Discovery of a New Class of High Temperature Single-Site Group (IV) Copolymerization Catalysts

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Abstract: For the first time, new catalysts for olefin polymerization have been discovered through the application of fully integrated high-throughput primary and secondary screening techniques supported by rapid polymer characterization methods. Microscale 1-octene primary screening polymerization experiments combining arrays of ligands with reactive metal complexes $M(CH_2Ph)_4$ (M = Zr, Hf) and multiple activation conditions represent a new high-throughput technique for discovering novel group (IV) polymerization catalysts. The primary screening methods described here have been validated using a commercially relevant polyolefin catalyst, and implemented rapidly to discover the new amide-ether based hafnium catalyst $[\eta^2\text{-}$ $(N,O)-(2\text{-MeO}-C_6H_4)(2,4,6\text{-Me}_3C_6H_2)N]Hf(CH_2Ph)_3$ (**1**), which is capable of polymerizing 1-octene to high conversion. The molecular structure of **1** has been determined by X-ray diffraction. Larger scale secondary screening experiments performed on a focused 96-member amine-ether library demonstrated the versatile high temperature ethylene-1-octene copolymerization capabilities of this catalyst class, and led to significant performance improvements over the initial primary screening discovery. Conventional one gallon batch reactor copolymerizations performed using selected amide-ether hafnium compounds confirmed the performance features of this new catalyst class, serving to fully validate the experimental results from the high-throughput approaches described herein.

Introduction

Within the polyolefins industry, new single-site catalysts with improved performance features represent highly desirable research goals. Improvements in catalyst performance features such as temperature stability, productivity, comonomer incorporation capability, high molecular weight capability, comonomer sequence distribution control, and the ability to copolymerize new monomer combinations, are currently being sought through the design and modification of catalyst structures. Indeed, modifications of the ligand frameworks of single-site catalysts have led to impressive advances in catalyst technologies over the last twenty years. During this period, research has centered mostly on metallocene complexes comprising high-valent group (IV) metal centers supported by cyclopentadienyl-based ligands.[1] Structural modifications of the cyclopentadienyl ligand framework have led to substantial improvements in catalyst performance, and the emergence of commercial pro-

cesses employing metallocene complexes for the preparation of commodity polyolefins such as linear low-density polyethylene (LLDPE).[1-3] More recent developments include single-site catalyst classes based upon new noncyclopentadienyl ligands,[4] and mid-late transition metals.[5,6] Further discoveries of new classes of single-site catalysts will undoubtedly lead to improved and more versatile performance features, in addition to unique polymer product families with advanced properties.

An assessment of the development of polyolefin catalyst technologies over the last twenty years leads to the undeniable

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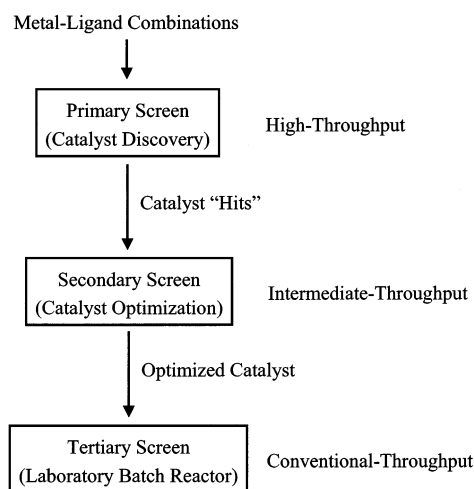
conclusion that a limited understanding of the complex relationships between catalyst structure and performance has impeded progress. For example, it is currently not possible to predict which new metal−ligand combinations will lead to active catalyst classes, and which metal−ligand combinations will have low or no activity. Furthermore, upon discovering a novel catalytically active metal−ligand combination, catalyst optimization is always desirable, and yet for any new catalyst class it is extremely difficult to predict the structural features necessary to impart the desired improvements in catalyst performance. Thus, research directed toward the discovery and optimization of new catalyst classes for commercial applications is an expensive, time-consuming "trial and error" process with an uncertain outcome. It is therefore not surprising that high-throughput synthesis and screening strategies are beginning to emerge within the field of polyolefin catalysis. In fact, such strategies are now being adopted for a broad range of catalytic transformations.[7−11] High-throughput approaches offer significant advantages over more conventional methods of catalyst

Scheme 1. High-Throughput Discovery Workflow

Metal-Ligand Combinations

↓

| Primary Screen (Catalyst Discovery) | High-Throughput

↓ Catalyst "Hits"

| Secondary Screen (Catalyst Optimization) | Intermediate-Throughput

↓ Optimized Catalyst

| Tertiary Screen (Laboratory Batch Reactor) | Conventional-Throughput

discovery. First, a high-throughput screen can (i) rapidly identify catalytically active systems, and importantly, identify and reject inactive systems, and (ii) allow a much broader range of catalysts candidates and conditions to be evaluated. As a consequence, time and resources may be directed toward maximizing the potential of the most promising catalyst candidates rather than optimizing catalyst structures around less important local "maxima" in catalyst performance. Additionally, the ability to generate sufficient quantities of meaningful catalyst performance data can provide the beneficiary with the opportunity to establish comprehensive and ultimately predictive structure−property relationships. Thus, to overcome the limitations of more conventional methods of polyolefin catalyst discovery, and to extend the capabilities of our own high-throughput program, we have designed and implemented a fully integrated, high-throughput discovery and optimization infrastructure targeted toward next-generation catalysts for olefin polymerization.

Our approach utilizes a microscale high-throughput primary screen in which arrays of new metal−ligand combinations are rapidly surveyed for catalytic activity. The purpose of our primary screen is to assess the potential of each metal−ligand combination as a polymerization catalyst for a specifically targeted application. Catalytically active metal−ligand combinations identified using this primary screening format are then subjected to a secondary screen in which the catalyst performance properties for the targeted application are assessed using larger scales and more commercially relevant conditions. Catalysts that meet predetermined performance criteria in these secondary screens are then subjected to rapid optimization through the structural elaboration of the newly discovered ligand class (Scheme 1). Secondary screens are typically intended to improve upon the catalyst performance, and importantly, to establish relationships between catalyst structure and catalyst performance. Rapid polymer characterization techniques have been developed to accommodate the synthetic throughput and the nature of the polymer products from our primary and secondary screens.

Herein, we report our first results in this area, including the design of a 1-octene primary screen, its validation through the use of a commercially relevant olefin polymerization catalyst, and the subsequent discovery of a new 1-octene polymerization catalyst using the primary screening methodology. Using our secondary screen, we then performed high-temperature ethylene-

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1-octene copolymerizations using a 96-member focus library comprising metal−ligand combinations structurally related to the primary screening discovery. The results illustrate that for this catalyst class, there is a strong dependence of copolymer yield, molecular weight and 1-octene content of the copolymer upon ligand structure. Additionally, many of the catalysts display substantial performance improvements relative to the performance of the initial primary screening discovery. Thus, our secondary screen has identified and developed a versatile new catalyst class capable of high-temperature ethylene-1-octene copolymerizations. Finally, conventional large scale batch reactor experiments performed on selected isolated catalysts confirm the performance features of this new class of catalyst, and further validate the high-throughput approaches adopted herein.

Results and Discussion

Strategy. High-throughput approaches to catalyst discovery typically require (i) an adaptation of catalyst synthesis and screening to smaller scales, which is necessary to accommodate arrays of reaction vessels,[12] (ii) large numbers of ligands that express suitably diverse electronic and steric properties, (iii) an efficient method of attaching the ligand to the metal to form the catalyst candidate, and (iv) a suitable rapid screening technique. Requirements (i), (ii), and (iii) will be addressed in the following sections. With regard to requirement (iv), the sample analysis times of traditional polymer characterization techniques such as GPC are too slow to accommodate arrays of polymer products produced in a high-throughput fashion. We have therefore utilized a Rapid◇GPC technique that can provide polymer concentration and molecular weight information at a rate of ninety seconds per sample. Additionally, for the products from our secondary screen, we used a Rapid◇FT-IR technique for the determination of weight % 1-octene incorporation within ethylene-1-octene copolymers. The details of these techniques have been reported elsewhere.[13]

Our previous work encompassing the requirements outlined in (i)−(iv) above utilized simple "mix and screen" methods for the discovery of late transition metal olefin polymerization catalysts.[9c−d] Because commercial single-site catalysts are based upon metallocene complexes comprising group (IV) metal centers, we wished to extend our high-throughput strategies to include new group (IV) metal−ligand combinations in our primary screen. There is also a growing recognition that nonmetallocene complexes hold great promise as olefin polymerization catalysts, and consequently we have turned our attention to high-throughput syntheses and screening of non-metallocene group (IV) complexes.

Design and Validation of the Primary Screen. The specific objective of this primary screen is to discover new catalysts with potential for the production of LLDPE.[14] Insertion barriers for α−olefins are higher than for ethylene, and catalysts capable of polymerizing α−olefins would be predicted to copolymerize ethylene with the α−olefin. We therefore rationalized that an assessment of activated metal−ligand complexes for their ability

to homopolymerize α−olefins would serve as a meaningful primary screen for new catalyst discovery.[15] Primary screening discoveries could then be screened for their ability to copolymerize ethylene with 1-octene under more controlled and commercially relevant conditions in our secondary screen (vide infra). We are aware that ethylene-1-octene copolymerization catalysts that are incapable of successive α−olefin insertions will not be detected using this primary screen. However, we adopted this approach in the belief that a rapid primary screen in which multiple arrays of metal−ligand combinations were assessed for their ability to polymerize 1-octene would provide sufficient numbers of new catalyst discoveries to offset such a limitation.

For validation purposes, we chose to assess the feasibility of performing small-scale 1-octene polymerizations using the well-studied catalyst $[(\eta^5\text{-}C_5Me_4)SiMe_2(\eta^1\text{-}NBu^t)]TiMe_2$, a highly active olefin polymerization catalyst known to be effective for the commercial production of ethylene-1-octene copolymers.[3c−f] Additionally, we wished to determine relevant conditions under which to perform the primary screening experiments using new metal−ligand combinations. The validation experiment was performed using an [8 × 12] array of 1 mL glass vials fitted with miniature stir-bars. Polymerizations were conducted for 1 h in 220 μL total reaction volume containing 120 μL of 1-octene. Reagents were added as toluene solutions using a commercially available liquid handling robot driven by Symyx software packages.[16] Figure 1 illustrates the experiment design, which encompasses three catalyst concentrations, three activation methods (plus one control with no activator), and importantly, eight replicates for each polymerization condition. Figure 2 displays the resultant 1-octene conversion data and clearly demonstrates the excellent reproducibility for the eight replicates. Moreover, some of the known performance features of $[(\eta^5\text{-}C_5Me_4)SiMe_2(\eta^1\text{-}NBu^t)]TiMe_2$ were captured in these experiments (e.g., single-site behavior and dependence of M_w on 1-octene conversion). A detailed description of the experiment and the results can be found in the Supporting Information. Importantly, reliable data from this well-studied, highly active polymerization catalyst can be used as a figure of merit for new metal−ligand combinations studied using our primary screen. On the basis of these results, we conclude that meaningful polymerization experiments can be conducted at microliter scales.

Primary Screening Discovery Experiments: Ligand Selection. Our starting point for discovery screening was a small ligand array (arranged in a [8 × 3] format) containing an assortment of simple bidentate and tridentate ligands with

(12) Pooled approaches can also be used, see refs 7 and 9.

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(14) Linear low-density polyethylene is an ethylene-α−olefin copolymer in which the α−olefin, typically 1-hexene or 1-octene, is statistically distributed throughout the polymer chain. Commercial solution-phase polymerizations are conducted at temperatures in excess of 100 °C. New high-temperature catalysts that are capable of producing high molecular weight, high α−olefin content copolymers with high productivities are highly desirable, see: Klosin, J.; Kruper, W. J., Jr.; Nickias, P. N.; Roof, G. R.; De Waele, P.; Abboud, K. A. *Organometallics* **2001**, *20*, 2663−2665.

(15) Additionally, the use of a liquid α−olefin, such as 1-octene, in a primary screening format is convenient, since this allows liquid handling robots to deliver reagents and monomer rapidly to an array of reaction vessels. Furthermore, poly-1-octene is a soluble material that can be conveniently and rapidly manipulated using automated liquid handling equipment. See: Diamond, G. M.; Goh, C.; Leclerc, M. K.; Murphy, V.; Turner, H. W. WO Patent Application 01/98371 2001.

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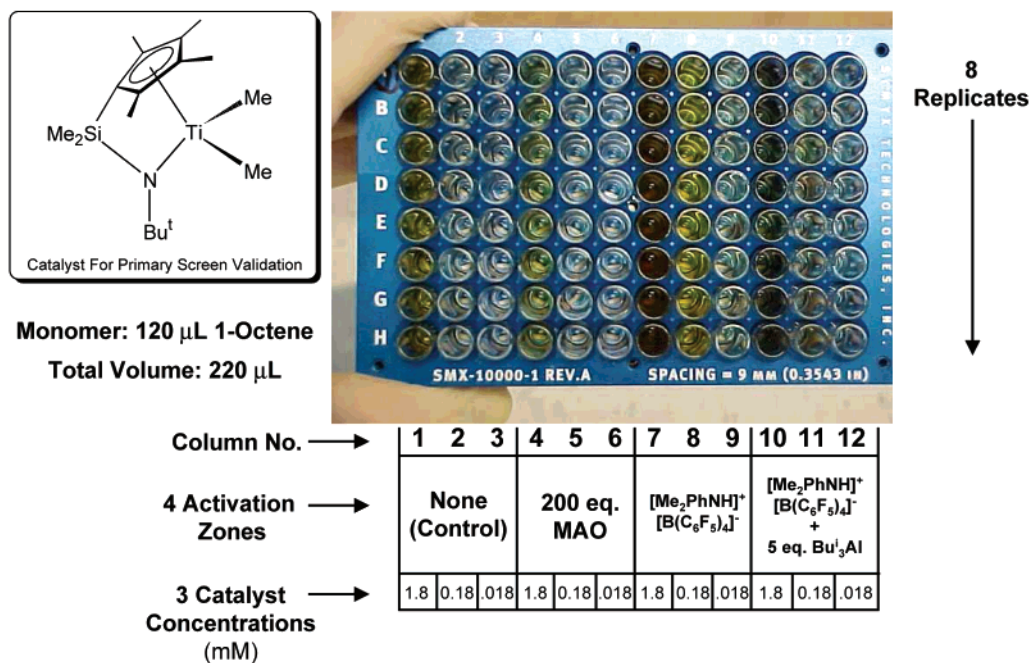
Figure 1. [8 × 12] Array design for the primary screening validation experiment.
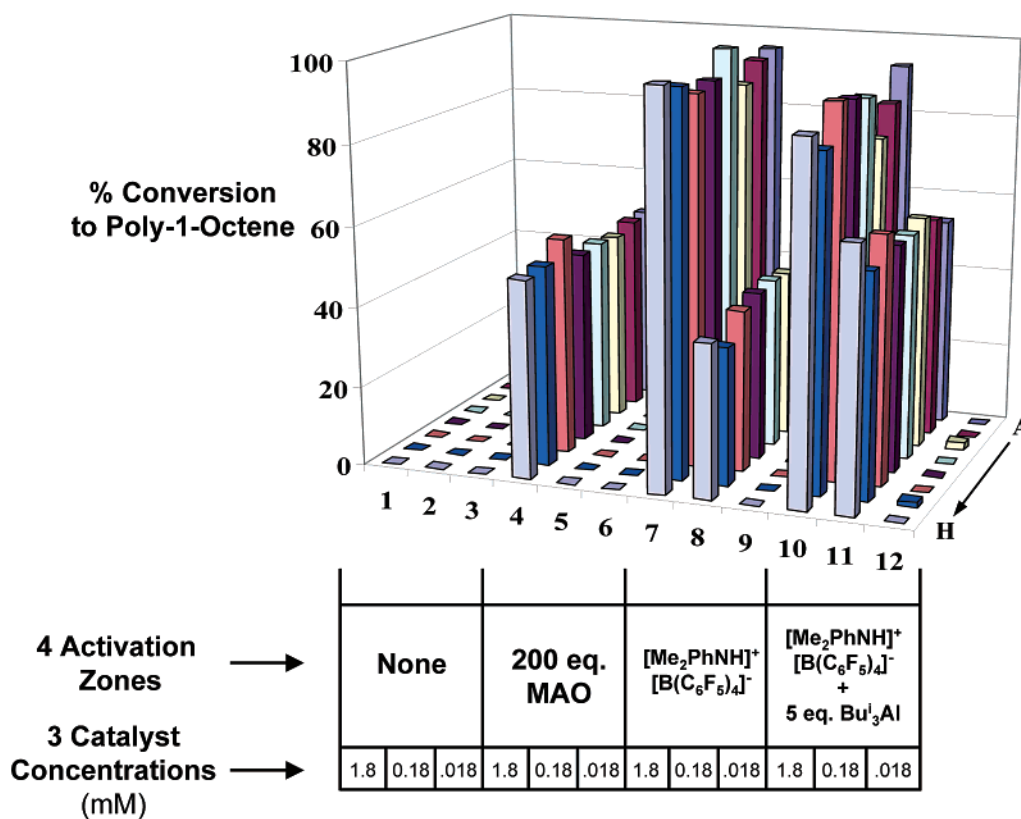

Figure 2. Conversion data from the primary screening validation experiment.

considerable diversity (Figure 3). Because this primary screening experiment was directed toward the discovery of new early metal catalysts, the ligands chosen mostly contain "hard" oxygen or nitrogen based donor atoms with one or two acidic protons. Oxygen donors include ethers, aliphatic and aromatic alcohols, whereas nitrogen donors include imines, aliphatic and aromatic amines and pyridines. Through these donor sets, ligands with considerable differences in steric demands, electronic properties and potential bite angles are represented. It is important to note

that the control cell [IIC], which contains no ligand, provides a valuable measure of the catalytic activity of the $M(CH_2Ph)_4-$ activator combinations alone, allowing us to determine the effect of the presence of each ligand upon the polymerization. Finally, we are aware that some of the ligands present in this initial array have been investigated previously as supporting ligands for new group (IV) polyolefin catalysts.[17]

Primary Screening Discovery Experiments: Metal−Ligand Complexation and Activation. As previously dis-

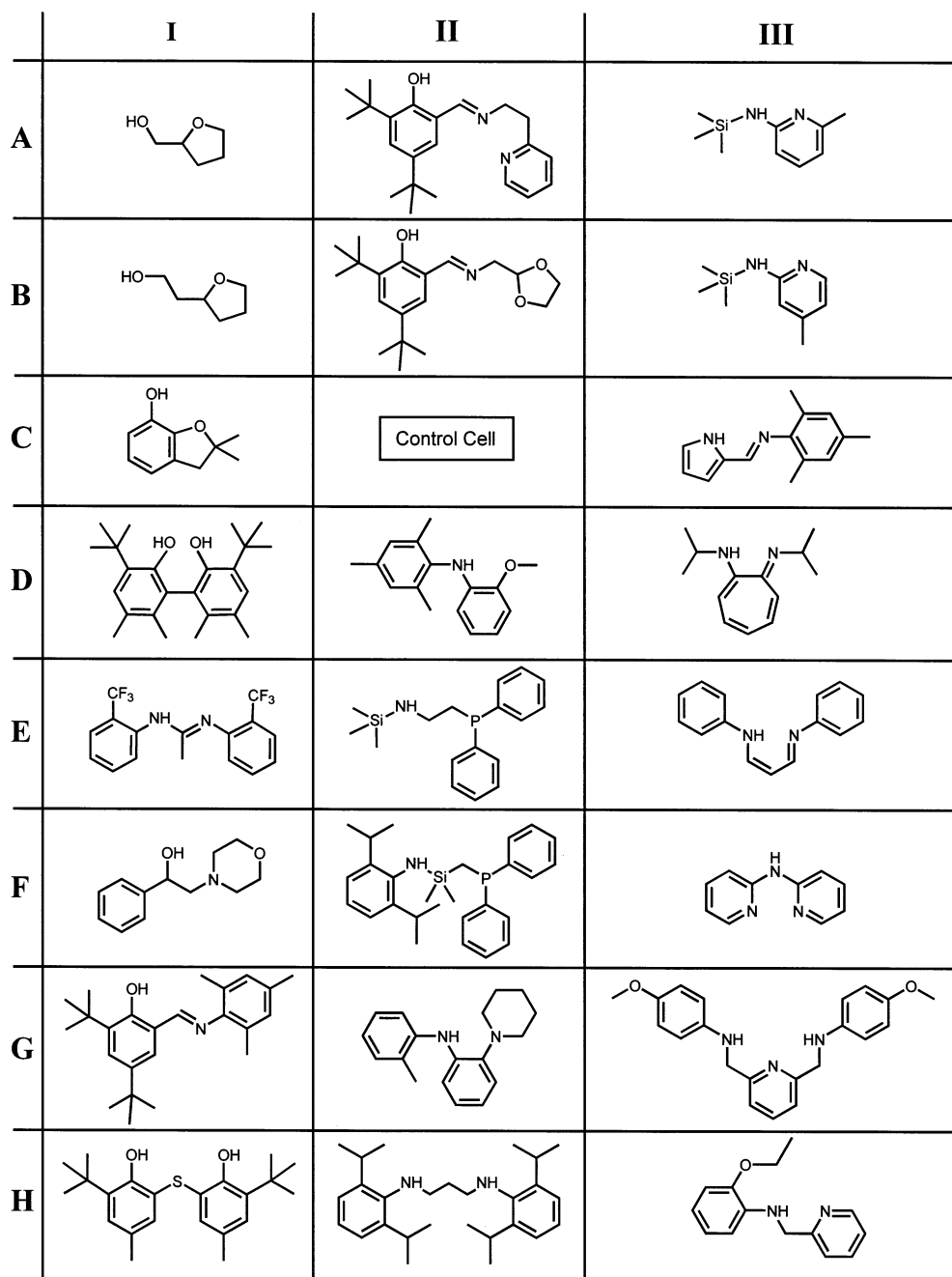|	**I**	**II**	**III**
A			
B			
C		Control Cell	
D			
E			
F			
G			
H			

Figure 3. [8 × 3] Discovery ligand array.

cussed, high-throughput approaches to catalyst discovery require an efficient method of attaching the ligand to the metal to form the catalyst candidate. Our strategy for metal−ligand complex-

(17) (a) Ligand [IH] see: van der Linden, A.; Schaverien, C. J.; Meijboom, N.; Ganter, C.; Orpen, A. G. *J. Am. Chem. Soc.* **1995**, *117*, 3008−3021; Katayama, H.; Nabika, M.; Imai, A.; Kawamura, N.; Hanaoka, H. Eur. Patent Appl. 0−761−694, 1996. (b) Ligand [IIH] see: Scollard, J. D.; McConville, D. H.; Vittal, J. J. *Organometallics* **1997**, *16*, 4415−4420; Shaffer, T. D.; Squire, K. R. WO Patent Application 98/37109, 1998; Imuta, J.; Saito, J.; Sugimura, K.; Fujita, T. WO Patent Application 98/34961, 1998. (c) Ligand [IIIA] and [IIIB], see: Fuhrmann, H.; Brenner, S.; Arndt, P.; Kempe, R. *Inorg. Chem.* **1996**, *35*, 6742−6745. For related ligands, see: Polamo, M.; Leskelä, M.; Hakala, K.; Löfgren, B. WO Patent Application 97/45434, 1997. (d) Ligand [IIIC] see: Nitabaru, M.; Yoshida, Y.; Mitani, M.; Terunori, F. Eur. Patent Appl. 1-008-595-A3, 2000. (e) Ligand [IIID] see: Takahashi, F.; Naito, Y. JP 11060624, 1999. (f) Ligand [IIIE], see: Theopold, K. H.; Kim, W.-K.; Power, J. M.; Mora, J. M.; Masino, A. P. WO Patent Application 01/12637, 2001. (g) For ligands related to [IG] see: Fujita, T.; Tohi, Y.; Mitani, M.; Matsui, S.; Saito, J.; Nitabaru, M.; Sugi, K.; Makio, H.; Tsutsui, T. Eur. Patent Appl. 0-874-005-A1 1998.

Scheme 2. Metal−Ligand Complexation Strategy Employed for the Discovery Screen
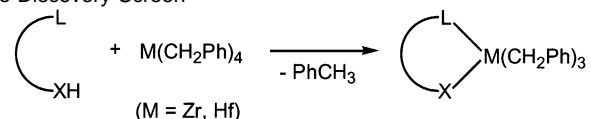
ation in our primary screen involves contacting a solution of one equivalent of each ligand with a solution of $M(CH_2Ph)_4$ (M = Zr, Hf) for sufficient time to afford the products of a toluene elimination reaction. Scheme 2 illustrates one such reaction between a bidentate ligand containing one acidic proton (the ligand is represented generically as L-XH in Scheme 2) and $M(CH_2Ph)_4$ (M = Zr, Hf). The targeted reaction products from this approach would contain the associated ligands and, importantly, metal−carbon bonds to support olefin insertion

events in the presence of a suitable activator. Additionally, because the removal of undesirable byproducts is not necessary using this approach, activators can be added directly to the reaction mixture in the presence of 1-octene to initiate the primary screen. To assess the feasibility of this approach, we conducted ^{1}H NMR experiments to investigate the reactivity of $M(CH_2Ph)_4$ (M = Zr, Hf) with representative ligands from the [8 × 3] ligand array. These studies revealed that reactions between the less sterically encumbered ligands, such as ligand [IIIC] (Figure 3), and $M(CH_2Ph)_4$ (M = Zr, Hf) proceeded rapidly through toluene elimination to generate metal–ligand complexes containing metal–carbon bonds.[18] Unfortunately, reactions between more sterically encumbered ligands (such as [IIH]) and $M(CH_2Ph)_4$ (M = Zr, Hf) were either very slow, or did not proceed at all. However, we recognized that additional opportunities for the ligand to react with the group (IV) metal center could arise through the use of carefully chosen activation conditions. For example, alkyl aluminum reagents (e.g., R_3Al), are known to undergo facile alkyl group exchange reactions with group (IV) metals, potentially generating a group (IV) metal alkyl or metal hydride bond that may react more readily with the acidic proton(s) on the ligand.[19] Additionally, the alkyl aluminum reagents may react directly with the acidic proton(s) on the ligands, producing an aluminum-ligand species which can subsequently react with $M(CH_2Ph)_4$ (M = Zr, Hf) to form the targeted group (IV) metal–ligand compound(s). Furthermore, the use of ionizing activators such as [Me$_2$PhNH]-[B(C$_6$F$_5$)$_4$] may generate an open coordination site available for coordination of the ligand. In our view, the use of carefully chosen activation conditions increases the likelihood of ligand association to the metal, and decreases the likelihood of missing a new catalyst.[20] Thus, in an attempt to overcome limitations in complexation, and to minimize the probability of missing a new catalyst, we chose to use *eight* different activation conditions for each ligand/$M(CH_2Ph)_4$ combination. Specifically, we chose to combine the ionizing activators [Me$_2$PhNH][B(C$_6$F$_5$)$_4$], [Ph$_3$C][B(C$_6$F$_5$)$_4$] and B(C$_6$F$_5$)$_3$, with two aluminum alkyl reagents, Et$_3$Al and Bu$^i_3$Al (Figure 4). In fact, the combination of [Me$_2$PhNH][B(C$_6$F$_5$)$_4$] with Bu$^i_3$Al was shown to be particularly effective for the activation of [(η^5-C$_5$Me$_4$)SiMe$_2$-(η^1-NBu^t)]TiMe$_2$ in our primary screening validation experiment. In summary, we adopted this approach believing that high-throughput screening of multiple arrays of metal–ligand combinations under multiple activation conditions would provide sufficient numbers of new catalyst discoveries to offset any limitations in the complexation chemistry.

Primary Screening Discovery Experiments: 1-Octene Primary Screening Results. Based upon results from the primary screening validation experiments described above, the $M(CH_2Ph)_4$/ligand concentration was set at 1.6 mM, and polymerizations were conducted for 1 h in 250 μL total reaction volume containing 120 μL 1-octene. As described previously, reagents were added as toluene solutions using a liquid handling robot. Figure 4 illustrates the experiment design in which the
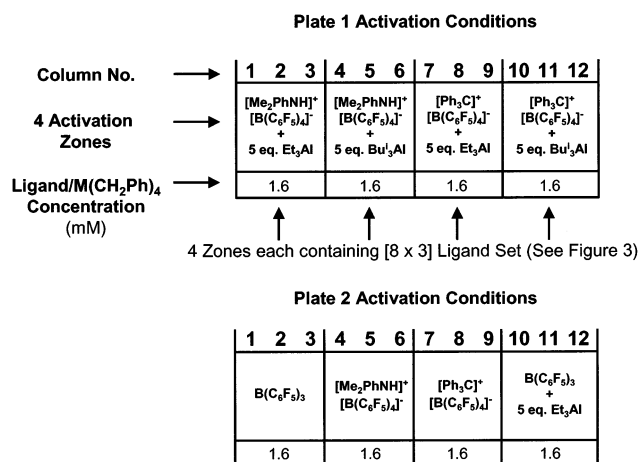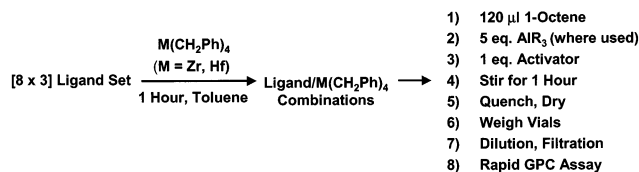
(18) The products are dependent upon the ligand. For example, with [IIIC] the reaction proceeds cleanly to one product of the type [ligand]Hf(CH$_2$Ph)$_3$; with [IIIA], product mixtures containing species of the types [ligand]M-(CH$_2$Ph)$_3$ and [ligand]$_2$M(CH$_2$Ph)$_2$, (along with unreacted $M(CH_2Ph)_4$) were observed. The notation [ligand] used here refers to the deprotonated ligand.
(19) Siedle, A. R.; Newmark, R. A.; Schroepfer, J. N.; Lyon, P. A. *Organometallics* **1991**, *10*, 0, 400−404.
(20) We have seen evidence that activation conditions can assist the reaction between bulky ligands and $M(CH_2Ph)_4$ (M = Zr, Hf).

Plate 1 Activation Conditions

Column No. ⟶	1 2 3	4 5 6	7 8 9	10 11 12
4 Activation Zones ⟶	[Me$_2$PhNH]$^+$ [B(C$_6$F$_5$)$_4$]$^-$ + 5 eq. Et$_3$Al	[Me$_2$PhNH]$^+$ [B(C$_6$F$_5$)$_4$]$^-$ + 5 eq. Bu$^i_3$Al	[Ph$_3$C]$^+$ [B(C$_6$F$_5$)$_4$]$^-$ + 5 eq. Et$_3$Al	[Ph$_3$C]$^+$ [B(C$_6$F$_5$)$_4$]$^-$ + 5 eq. Bu$^i_3$Al
Ligand/M(CH$_2$Ph)$_4$ Concentration (mM) ⟶	1.6	1.6	1.6	1.6

4 Zones each containing [8 x 3] Ligand Set (See Figure 3)

Plate 2 Activation Conditions

1 2 3	4 5 6	7 8 9	10 11 12
B(C$_6$F$_5$)$_3$	[Me$_2$PhNH]$^+$ [B(C$_6$F$_5$)$_4$]$^-$	[Ph$_3$C]$^+$ [B(C$_6$F$_5$)$_4$]$^-$	B(C$_6$F$_5$)$_3$ + 5 eq. Et$_3$Al
1.6	1.6	1.6	1.6

Figure 4. Activation conditions and plate designs for the primary screening discovery experiment.

Scheme 3. Sequence of Reagent Additions and Polymer Work-Up Protocol for the Primary Screening Discovery Experiment

$$[8 \times 3] \text{ Ligand Set} \xrightarrow[\text{1 Hour, Toluene}]{\substack{M(CH_2Ph)_4 \\ (M = Zr, Hf)}} \text{Ligand/M(CH}_2\text{Ph)}_4 \text{ Combinations} \longrightarrow$$

1) 120 μl 1-Octene
2) 5 eq. AlR$_3$ (where used)
3) 1 eq. Activator
4) Stir for 1 Hour
5) Quench, Dry
6) Weigh Vials
7) Dilution, Filtration
8) Rapid GPC Assay

[8 × 3] ligand array was repeated in four zones conveniently allowing four different activation methods to be employed per plate (1 plate = 1 [8 × 12] array). To accommodate eight activation conditions, two plates were used for each of the metal compounds Zr(CH$_2$Ph)$_4$ and Hf(CH$_2$Ph)$_4$, totaling four plates comprising 384 polymerization experiments. Scheme 3 displays the sequence of reagent additions to initiate the screen. It is noteworthy that using the high-throughput methodologies described herein, these 384 polymerization experiments were completed in just a few hours.[21] The results indicate that of the eight activation conditions chosen, the four conditions employed in plate 1 proved to be the most productive for both Zr(CH$_2$Ph)$_4$ and Hf(CH$_2$Ph)$_4$. Figures 5 and 6 illustrate the resultant 1-octene conversion data for Zr(CH$_2$Ph)$_4$ and Hf(CH$_2$Ph)$_4$ respectively, for the plate 1 activation conditions. It is important to note that the control cells containing $M(CH_2Ph)_4$ (M = Zr, Hf) in the absence of ligands, yield poly-1-octene with very low 1-octene conversions for all eight activation conditions (≤1−8%, for plate positions 2C, 5C, 8C, and 11C in Figures 5 and 6). Figure 5 indicates that for Zr(CH$_2$Ph)$_4$ in combination with this ligand set, 1-octene conversions range from < 1% to 60% using the conditions described, with five ligand/Zr(CH$_2$Ph)$_4$ combinations yielding poly-1-octene with conversions > 10%. Figure 6 indicates that for Hf(CH$_2$Ph)$_4$ in combination with this ligand set, 1-octene conversions range from < 1% to 100% using the conditions described, with five ligand/Hf(CH$_2$Ph)$_4$ combinations yielding poly-1-octene with conversions > 10%. Interestingly, the same five ligand structures form productive combinations with both Zr(CH$_2$Ph)$_4$ and Hf(CH$_2$Ph)$_4$ (Ligands [IC], [IE], [IID], [IIIA], and [IIIC] from Figure 3). Strikingly, using eight activations conditions, 1-octene conversions can vary dramatically for a given metal–ligand combination. For example, 1-octene conversions for the combination

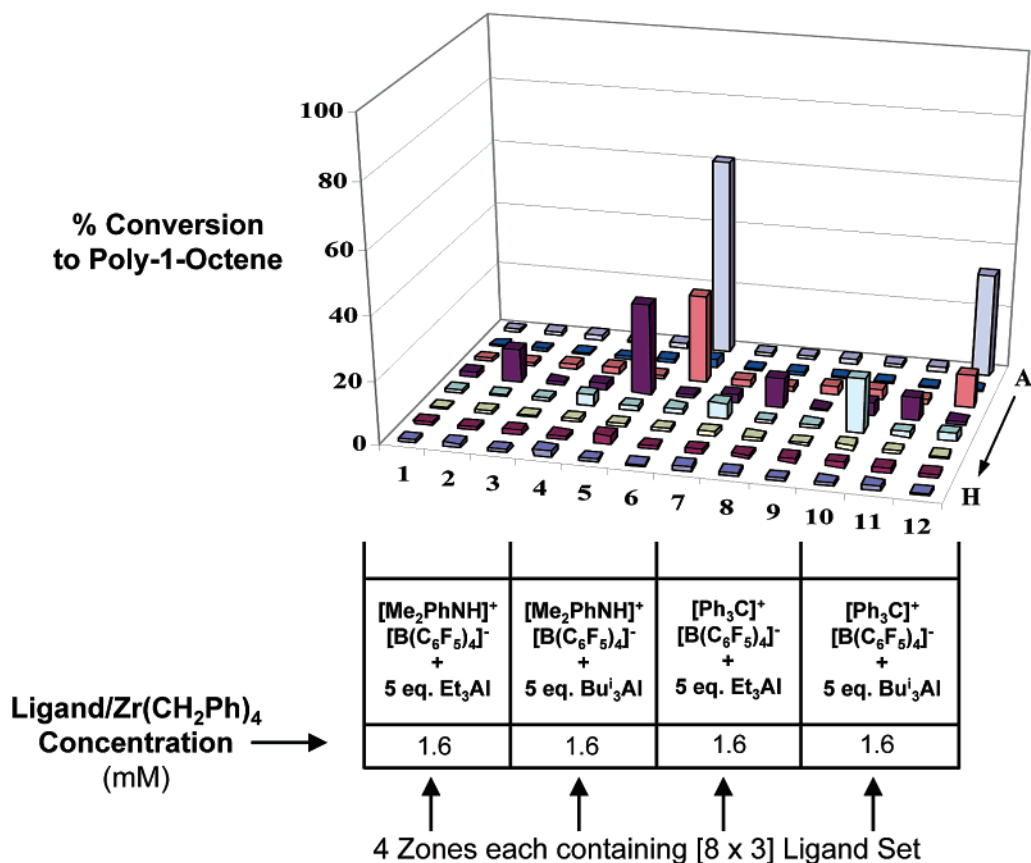(21) Polymer yields were determined using an automated weighing assay.

Figure 5. Poly-1-octene conversion data for $Zr(CH_2Ph)_4$ with discovery ligand set.

of $Zr(CH_2Ph)_4$ and ligand [IIIA] varied from 1 to 60%! Thus, the right choice of activation condition can be essential for detecting new catalytically active metal−ligand combinations, and since this is not possible to predict, the use of multiple activation conditions is warranted.

Overall, from the 384 primary screening experiments described here, 10 ligand/$M(CH_2Ph)_4$ combinations (M = Zr, Hf) were identified as 1-octene polymerization catalysts when combined with appropriate activation conditions.[22,23] Thus, using our high-throughput strategies, these 10 metal−ligand combinations would be selected for secondary screening. Of the ligands that have been reported as supporting ligands for group (IV) polyolefin catalysts in the literature, [IIIA] and [IIIC] were identified as poly-1-octene catalysts when combined with both $Zr(CH_2Ph)_4$ and $Hf(CH_2Ph)_4$ under the conditions of our primary screen.[24] The most exciting observation is that from these small-scale primary screening experiments, many catalytically active metal−ligand combinations were identified, thereby demonstrating the power of this high-throughput approach.

(22) The catalytically active metal−ligand combinations produced poly-1-octenes with a wide range of molecular weights. Data for all 384 experiments can be found in the Supporting Information.
(23) A repeat experiment in which the ligand-to-metal ratio was adjusted to 2:1 significantly altered the 1-octene conversions. However, no new catalytically active metal−ligand combinations were identified.
(24) With respect to zirconium and hafnium complexes of the other ligands listed in ref 17, α−olefin polymerization activity has only been reported for the combination of ligand [IIH] with zirconium. The [IIH]/zirconium combination, when activated with $[Ph_3C][B(C_6F_5)_4]$, has been reported as a low activity α−olefin oligomerization catalyst.[17b] In our primary screen, the combination of [IIH]/$Zr(CH_2Ph)_4$/$Ph_3C][B(C_6F_5)_4]$/5 Bu^i_3Al produced small quantities of a material that was not detected by our Rapid◊GPC technique. The Rapid◊GPC protocol chosen has a low molecular weight detection limit of around 1000.

Scheme 4. Reaction Scheme for the Preparation of 1
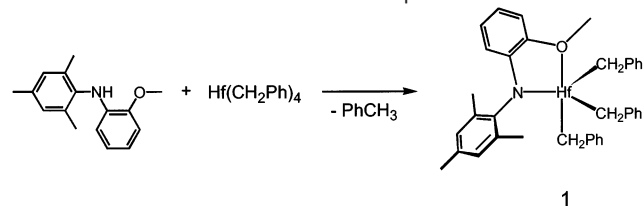
Of particular interest to us was the combination of $Hf(CH_2Ph)_4$ with ligand [IID] (plate positions 2D, 5D, 8D, and 11D in Figure 6). When activated with $[Me_2PhNH][B(C_6F_5)_4]$ and 5 eq. Et_3Al, this ligand/$Hf(CH_2Ph)_4$ combination generates a catalyst capable of polymerizing 1-octene with 100% conversion under the conditions of our primary screen. We felt that this observation warranted an investigation into the reaction between $Hf(CH_2Ph)_4$ and ligand [IID]. The reaction between $Hf(CH_2Ph)_4$ and [IID] leads quantitatively, and rapidly via toluene elimination, to the formation of the new amide-ether hafnium tribenzyl complex $[\eta^2\text{-}(N,O)\text{−}(2\text{-MeO−}C_6H_4)(2,4,6\text{-Me}_3C_6H_2)N]\text{-}Hf(CH_2Ph)_3$ (**1**) (Scheme 4). The molecular structure of **1** has been determined by X-ray diffraction (Figure 7) and indicates a distorted trigonal bipyramid structure with η^1-benzyl groups. Selected bond lengths and angles for **1** are presented in Table 1, crystal, intensity collection and refinement data for **1** are presented in the Supporting Information.

Interestingly, there is no evidence for the formation of the 2:1 complex upon addition of excess [IID] to **1**. The results from the NMR and X-ray studies are consistent with the notion that compound **1** was formed in our primary screening experiment, and under suitable activation conditions is capable of
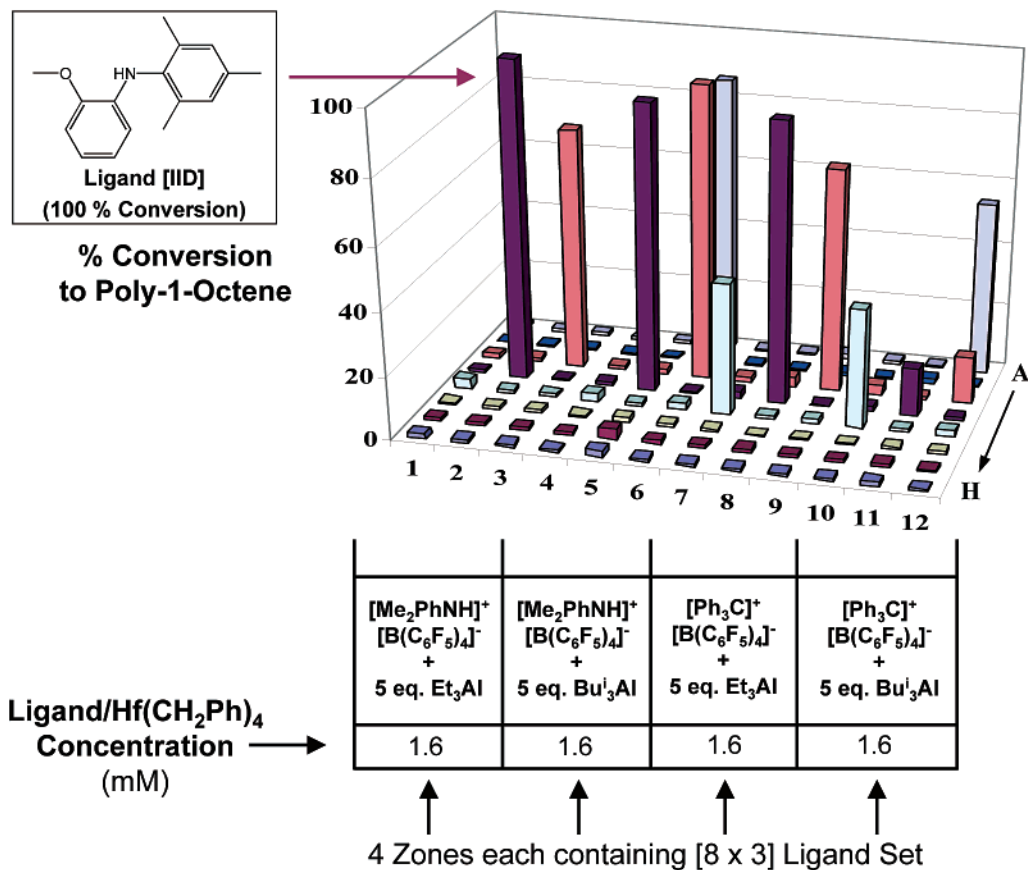
Figure 6. Poly-1-octene conversion data for Hf(CH2Ph)4 with discovery ligand set.
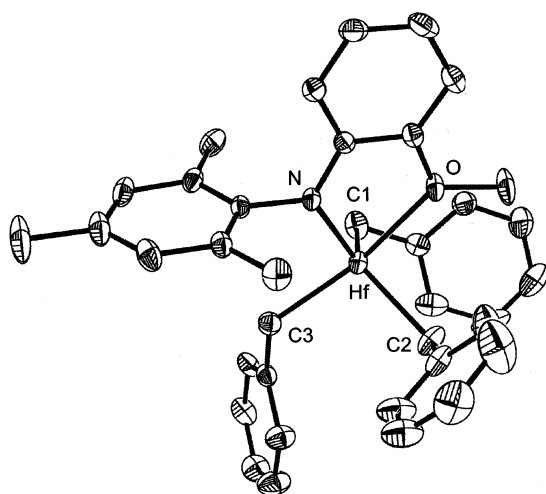

Figure 7. Molecular structure of **1**.

Table 1. Selected Bond Lengths (Å) and Angles (deg) for **1**[a]

Hf−N	2.094 (3)	Hf−O	2.311 (2)	Hf(1)−C(1)	2.226 (4)
Hf−C(2)	2.254 (4)	Hf−C(3)	2.236 (3)		

N−Hf−C(1)	114.0 (1)	N−Hf−C(2)	122.8 (1)
N−Hf−C(3)	91.0 (1)	O−Hf−C(1)	92.9 (1)
O−Hf−C(2)	86.5 (1)	O−Hf−C(3)	160.8 (1)
C(1)−Hf−C(2)	119.0 (2)	C(1)−Hf−C(3)	100.3 (2)
C(2)−Hf−C(3)	98.9 (2)	O−Hf−N	70.8 (1)

[a] average of two crystallographically independent molecules.

polymerizing 1-octene to high conversions. In the following sections, we describe preliminary secondary screening results for this novel ligand/Hf(CH2Ph)4 [IID] combination, along with new ligand/Hf(CH2Ph)4 combinations through the preparation of a 96-member focus library of structurally related ligands.

Secondary Screening: The Parallel Polymerization Reactor. The next step in our high-throughput discovery research is an assessment of primary screening catalyst discoveries using larger scales under more controlled and more commercially relevant copolymerization conditions. As previously discussed, the rationale for our primary screen is that catalysts capable of polymerizing α−olefins would be predicted to copolymerize ethylene with the α−olefin to produce a LLDPE copolymer. However, because commercial solution processes for the production of LLDPE operate at temperatures in excess of 100 °C, high-temperature stability is an additional requirement for new catalysts. Therefore, in our secondary screen we chose to perform ethylene-1-octene copolymerization experiments at 130 °C. To meet the throughput required to perform secondary screening on primary screening discoveries within our program, we have designed and built our own 48-cell parallel polymerization reactor. Although this parallel reactor has been described elsewhere, the important features of this instrument are worth mentioning.[13b,25] The instrument consists of 48 individually controlled 15 mL high-pressure batch reactors with magnetically coupled mechanical overhead stirring. Each reactor cell possesses its own pressure and temperature control, and gaseous monomer feed line. Reagent stations with liquid dispensing robots are situated alongside the reactors, and are used to mix reagents where necessary, and add reagents to each cell of the reactor. Because reagents can be added to the reactor cells at

(25) Turner, H. W.; Dales, G. C.; Van Erden, L.; van Beek, J. A. M. U.S. Patent 6,306,658, 2000.
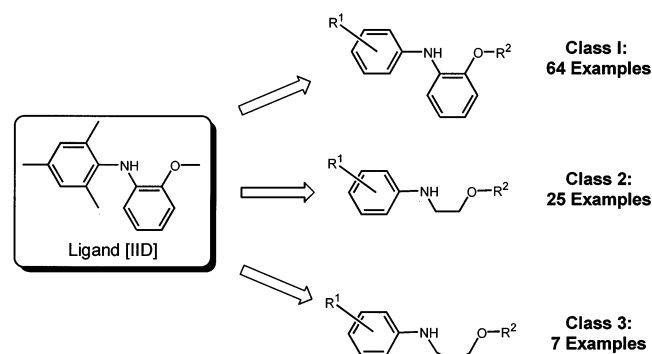
Figure 8. 96-Member focus library containing 3 classes of amine-ether ligands.

Scheme 5. Reaction Scheme for the Preparation of the Amine-Ether Focus Library

high pressures and high temperatures, metal−ligand combinations can be prepared, activated and quickly injected into each cell at the equilibrated temperature and pressure of the copolymerization. Moreover, upon catalyst injection, real-time temperature, pressure and ethylene uptake measurements can be made on each of the 48 cells simultaneously. Thus, 48 individual polymerization events can be monitored in real-time under conditions that provide meaningful information about the performance capabilities of each catalyst at high temperatures. Typically, 100−200 mg of copolymer product is targeted from our secondary screening studies. Such a quantity allows a comprehensive analysis of the polymer properties, but will not foul the reactor or prevent the diffusion of the monomer to the catalyst sites during the polymerization experiment.

Secondary Screening: Focus Library Preparation. The objective of our secondary screen is the optimization of catalyst performance, and the development of relationships between catalyst structure and catalyst performance. Preliminary reactor experiments performed at 130 °C revealed that **1** is capable of producing high molecular weight ethylene-1-octene copolymers with high levels of 1-octene incorporation.[26] To determine the structural features necessary to further improve the performance of **1**, we prepared a focused 96-member amine-ether ligand library containing significant structural variations on ligand [IID]. As depicted in Figure 8, three structurally similar classes of ligands were synthesized for this library, all of which were based upon amine-ether binding groups, but contain three different linkers situated between the amine and ether moieties, namely 1,2-phenyl (both with and without additional substituents on the linker; Class I), 1,2-ethyl (Class II), and 1,3-propyl linkers (Class III). Within each of the three structural classes, additional steric and electronic diversity is expressed by substituents on the amine and ether moieties, denoted generically as R^1 and R^2 respectively in Figure 8. Because the principal focus of this library was the structural elaboration of the ligand framework discovered in the primary screening experiment, ligand Class I is represented by 64 of the 96 ligands. Additionally, to examine the influence of the linker group situated between the amine and ether moieties, we prepared a total of 32 examples from ligand Classes II and III. All ligand structures were prepared using a previously developed aryl-amination procedure (Scheme 5).[27] For a list of the 96 structures prepared, see the Supporting Information.
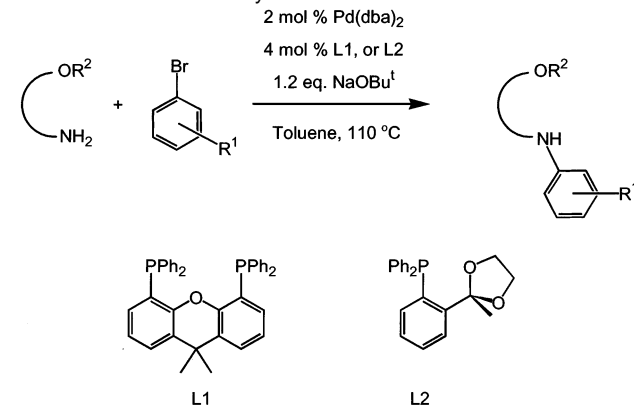
Secondary Screening: High-Temperature Ethylene-1-Octene Copolymerizations. Catalysts were prepared in situ by mixing solutions of the ligands (1 eq.) with $Hf(CH_2Ph)_4$, in a manner similar to that used in the primary screen. A high-temperature reactor study comparing the performances of **1** and the in situ prepared combination of $Hf(CH_2Ph)_4$ and ligand [IID] (Figure 3) revealed little difference in the yield of polymer obtained or the nature of the polymer produced.[28] Only one activation condition was chosen for this catalyst optimization experiment, the combination of $[Me_2PhNH][B(C_6F_5)_4]$ with Bu^i_3-Al, which was selected from a combination of primary screening data and preliminary high-temperature secondary screening runs with compound **1**.[29] Thus, 96 high-temperature ethylene-1-octene copolymerization experiments were performed in toluene solutions (6.1 mL total reaction volume containing 0.25 mL 1-octene, and Bu^i_3Al as an impurity scavenger). Upon addition of toluene, 1-octene and Bu^i_3Al to the reactor cells, the stirring rate was set to 600 rpm, the reactor temperature was set to 130 °C, and the pressure was set to 100 psi with ethylene. Using the reagent station situated alongside the reactor cells, solutions of the ligands were treated with solutions of $Hf(CH_2Ph)_4$, and allowed to mix for 1 h at room temperature, whereupon the resultant mixtures were treated with Bu^i_3Al. At this point, solutions of $[Me_2PhNH][B(C_6F_5)_4]$ were injected into each reactor cell, followed immediately by an aliquot[30] from each solution containing the ligand/$Hf(CH_2Ph)_4$ combinations to initiate the copolymerizations. The copolymerizations were then allowed to continue for 30 min, whereupon the reactors were vented and cooled. The polymer products were isolated, weighed, and characterized using our Rapid◇FT-IR and Rapid◇GPC techniques. Figure 9 displays the results from this experiment, plotted as polymer yield against molecular weight for each ligand/$Hf(CH_2Ph)_4$ combination. Selected ligand structures are also displayed in Figure 9.

Several important conclusions can be drawn from this experiment: (i) many of these catalysts are clearly capable of

(26) An earlier version of our parallel polymerization reactor was used for these experiments.

(27) See the Supporting Information, and: (a) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805−818. (b) Hartwig, J. F. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2046−2067.

(28) It should be noted that for bulkier ligands, particularly those containing phenyl ether moieties, we typically observe identical products, but lower polymer yields using the in situ preparation method. Thus, catalyst performance is convoled with complexation efficiency, and this limitation needs to be considered when analyzing the results of this study.

(29) It should be noted that this activation condition is unlikely to be optimal for every ligand/$Hf(CH_2Ph)_4$ combination.

(30) The aliquot contained 1 μmol of the ligand/$Hf(CH_2Ph)_4$ mixture. Final reactor concentrations: ligand/$Hf(CH_2Ph)_4$ mixture: 0.16 mM.; [PhMe₂-NH][B(C₆F₅)₄]: 0.16 mM.; Bu^i_3Al: 1.97 mM.
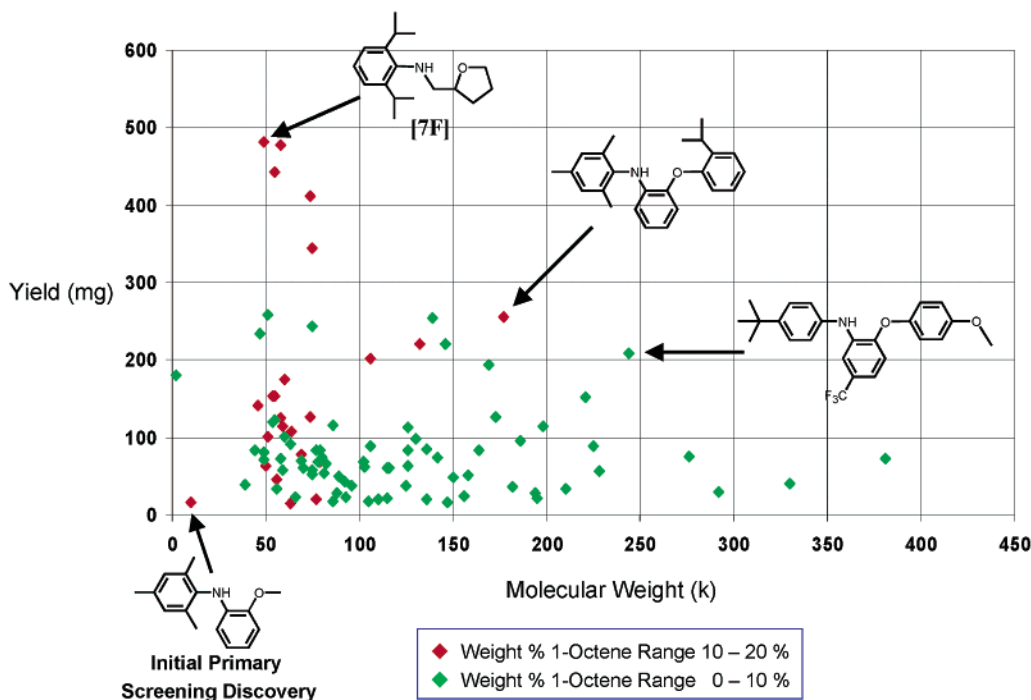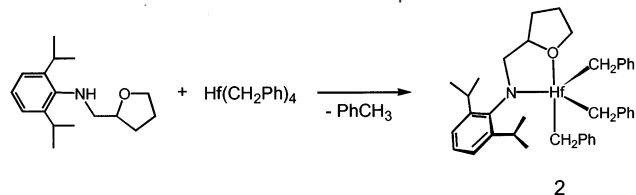
Figure 9. Results from the 96 Ligand/Hf(CH$_2$C$_6$H$_5$)$_4$ ethylene-1-octene copolymerizations performed at 130 °C.

ethylene-1-octene copolymerizations at 130 °C which, we believe, represents a significant technological advance for nonmetallocene olefin polymerization catalysts; (ii) the data displayed in Figure 9 illustrates that for this class of catalyst there is a strong dependence of polymer yield, molecular weight and 1-octene incorporation on the ligand structure, with many of the catalysts demonstrating significant performance improvements over the initial primary screening discovery. For instance, M_w varied between 2k and 381k, 1-octene incorporation values varied between 0 and 20 wt. %, and yields varied between 15 and 482 mg; and (iii) many of the product polymers possess low polydispersities, demonstrating that under these conditions, single-site catalysts are being generated.[31] Thus, the results suggest that we have discovered a new and versatile class of high temperature, single-site LLDPE catalyst that can provide access to many different types of polymer products through structural changes to a very simple ligand framework.[32]

It is also important to discuss the limitations of screening this many catalysts under a single set of experimental conditions (refer to Figure 9). Using the conditions employed in this experiment, we are aware that the highest activity catalysts perform at an activity level that exceeds the ethylene diffusion limitations of the reactor.[33] Under these conditions, the results for these catalysts, including polymer yields and polymer properties will *not* represent the capabilities of the catalysts. To properly assess the performances of the higher activity catalysts would require a reduction in the catalyst concentrations. Additionally, for the lowest activity catalysts, the yields are too low to fully assess the polymer properties, and catalyst

(31) Of the 24 copolymers containing > 10 wt % 1-octene, 20 had polydispersities below 3.5, see the Supporting Information.
(32) Goh, C.; Diamond, G. M.; Murphy, V.; Leclerc, M. K.; Hall, K.; Lapointe, A. M.; Boussie, T. R.; Lund, C.; Uno, T. WO Patent Application 01/74910, 2001.
(33) At a stirring rate of 600 rpm. The real-time ethylene uptake monitoring capabilities of these reactors enable us to readily identify catalysts that are running under ethylene diffusion limitations.

Scheme 6. Reaction Scheme for the Preparation of 2

performance properties, and thus, a proper assessment of the performances of the lower activity catalysts would therefore require an increase in catalyst concentrations. The conditions employed for these preliminary experiments necessarily represent a compromise, and clearly, the results should be considered with this in mind.[34] Additionally, we are aware that the results from this experiment are convolved with the complexation efficiency of the ligands with Hf(CH$_2$Ph)$_4$.[28] In view of these limitations, further experiments employing isolated complexes are therefore necessary to establish quantitative structure−property relationships.

Scaled-Up Batch Reactor Copolymerizations. To rigorously test the quality of the results from our parallel polymerization reactor, we prepared two amide-ether hafnium tribenzyl complexes for larger scale batch reactor experiments. For this comparison, **1** was chosen for along with a second catalyst, the combination of Hf(CH$_2$Ph)$_4$ and ligand [7F], identified from the secondary screening experiments as possessing superior performance features in comparison to **1** (Figure 9). The reaction between Hf(CH$_2$Ph)$_4$ and ligand [7F] proceeds rapidly and quantitatively, via toluene elimination, to the formation of the new amide-ether hafnium tribenzyl complex **2** (Scheme 6).[35]

Batch reactor evaluations of compounds **1** and **2** were performed in a 1 gallon autoclave under commercially relevant

(34) Under identical conditions, the results from this secondary screening experiment are reproducible.
(35) The analogous zirconium compound has been reported, see: Murray, R. E. U.S. Patent 6,103,657, 2000.

Table 2. One Gallon Batch Reactor Copolymerization Data

complex[a]	CGC	1	2
activity[b]	52.30	7.56	13.76
M_w	59 500	97 000	181 000
M_w/M_n	2.0	3.0	2.8
polymer density (g/mL)	0.912	0.910	0.917

[a] Conditions: 1440 g Isopar E; 126 g 1-Octene, 130 °C, 450 psi Ethylene, 10 mmol H_2. [b] grams of polymer/μmol metal.

high-temperature solution polymerization conditions. The runs were performed at 130 °C and 450 psig of ethylene pressure, using an isoparaffinic solvent, 1-octene as comonomer, and hydrogen for molecular weight control. A comparative run was performed using the titanium based catalyst [(η^5-C$_5$Me$_4$)SiMe$_2$-(η^1-NBu^t)]Ti(η^4-C$_5$H$_8$) (CGC), which has proven performance as a commercially viable catalyst in the Dow solution polyethylene process.

Key results from these runs are summarized in Table 2. It is clear from these results that the new hafnium complexes **1** and **2** perform at a level comparable to a commercially relevant catalyst system, particularly in the areas of polymer molecular weight and comonomer incorporation (reflected by the polymer density), where the new complexes equal or exceed the performance of the CGC complex. Polymerization activity is somewhat lower than the CGC complex, although still reasonable considering the early stage of development of these catalyst systems. It is particularly significant that the molecular weight and activity trends from the commercial screening results for **1** and **2** mirror the results from the high-throughput screens. The correspondence between the large-scale catalyst performance and the secondary screening results clearly serves to validate the new high-throughput screening methodologies for the discovery and optimization of polyolefin catalysts.

Conclusions

For the first time, new polyolefin catalysts have been discovered and developed through the application of a fully integrated high-throughput primary and secondary screening approach supported by rapid polymer characterization techniques. Using this approach, 384 microscale primary screening polymerization experiments were performed in just a few hours and resulted in the identification of 10 interesting 1-octene polymerization catalysts. Larger scale secondary screening experiments performed on a focused 96-member library led to the development of a new and versatile high temperature LLDPE catalyst class based upon a nonmetallocene ligand. Moreover, we have subsequently used our high-throughput infrastructure to screen many thousands of catalyst candidates for a variety of targeted applications. Numerous catalyst discoveries have emerged that were entirely unpredictable, and that most likely would not have been discovered through more conventional methods of catalyst research. The results described herein illustrate the power of well-designed high-throughput experiments, and highlight the tremendous advantages of the high-throughput approach over more conventional methods of catalyst discovery. Polyolefin catalysts can now be discovered and optimized at unprecedented rates.

Experimental Section

General. All reactions were performed under a purified argon or nitrogen atmosphere in a glovebox. All solvents used were dried, deoxygenated and purified according to known techniques. All glassware

was oven-dried. Polymerizations were carried out in a parallel pressure reactor, which is fully described in ref 25. High-temperature Size Exclusion Chromatography was performed using an automated Rapid◇GPC system as described, for example in ref 13, and U.S. Patents 6,294,388; 6,260,407; 6,296,771; and 6,265,226. All of the molecular weight data were measured relative to linear polystyrene standards. Rapid◇FT-IR was performed on a Bruker Equinox 55 + IR Scope II in reflection mode to determine weight % (wt %) of 1-octene incorporated in the copolymer. Samples were prepared in a thin film format by evaporative deposition techniques. Wt.% 1-octene was obtained from ratio of peak heights at 1378 and 4335 cm^{-1}. This method was calibrated using a set of ethylene-1-octene copolymers with a range of known wt. % 1-octene content.[13] NMR spectra were recorded using a Bruker ADVANCE DPX 300 MHz spectrometer. GC–MS analyses were recorded using a Hewlett-Packard 6898 gas chromatograph coupled to a Hewlett-Packard 5973 Mass Selective Detector. For detailed descriptions of (i) the primary screening validation and discovery experiments, and (ii) the secondary screening high-temperature ethylene-1-octene copolymerizations, see the Supporting Information.

Preparation of 96-Member Amine-Ether Ligand Library. Reactions were performed on a 1 mmol scale in 20 mL glass vials. In a typical procedure, Pd(dba)$_2$, NaOBu^t, and L1 or L2 (Scheme 5) were first combined in the glass vial under an atmosphere of argon. A degassed toluene solution (ca. 5 mL) containing the amine and the aryl bromide were then added to the reaction mixture by syringe transfer. The mixture was then heated to 100 °C overnight. The crude reaction product was then filtered, concentrated and purified using column chromatography (silica gel; 5% ethyl acetate in hexane). L1 was initially used for the preparation of this library, but was found to be less effective for aryl bromides with bulky substituents at the 2 and 6 positions. For these transformations L2 was used with an extended reaction time of 48 h.[36] The aryl bromides employed for this library are commercially available. The anilines were either obtained commercially or prepared using simple procedures. All ligands were assayed for purity using GCMS, and ^{1}H and ^{13}C NMR were recorded for representative members of the 96 ligands (see Supporting Information).

Preparation of [η^2-(N,O)−(2-MeO−C$_6$H$_4$)(2,4,6-Me$_3$C$_6$H$_2$)N]Hf-(CH$_2$Ph)$_3$ (1). A solution of (2-MeO−C$_6$H$_4$)(2,4,6-Me$_3$C$_6$H$_2$)NH (0.076 g, 0.31 mmol) in 5 mL toluene was added to a solution of Hf(CH$_2$Ph)$_4$ (0.18 g, 0.33 mmol) in 5 mL toluene. After stirring the resultant mixture for 12 h the toluene was removed under a stream of argon and the product was then dried in vacuo. The product was then washed with cold hexane and isolated as a pale yellow solid. (0.15 g, 70%). Crystals for an X-ray structure determination were grown from a hexane/diethyl ether solution at −35 °C. ^{1}H NMR data (C$_6$D$_6$): δ 7.10, t, 6.82, t, 6.75 d [15H, Hf(CH$_2$*Ph*)$_3$], 6.9, [2H, s, [η^2-(N,O)−(2-MeO−C$_6$H$_4$)(2,4,6-Me$_3$C$_6$*H*$_2$)N]Hf(CH$_2$Ph)$_3$], 6.75, t 6.50, t, 6.35, d 6.14, d [4H, [η^2-(N,O)−(2-MeO−C$_6$*H*$_4$)(2,4,6-Me$_3$C$_6$H$_2$)N]Hf(CH$_2$Ph)$_3$], 2.98 [3H, s, [η^2-(N,O)−(2-*Me*O−C$_6$H$_4$)(2,4,6-Me$_3$C$_6$H$_2$)N]Hf(CH$_2$Ph)$_3$], 2.18 [9H, s, [η^2-(N,O)−(2-MeO−C$_6$H$_4$)(2,4,6-*Me*$_3$C$_6$H$_2$)N]Hf(CH$_2$Ph)$_3$], 2.00 [6H, s, Hf(C*H*$_2$Ph)$_3$]; ^{13}C{^{1}H} (C$_6$D$_6$): δ 148.7, 144.6, 143.1, 141.1, 135.9, 135.6, 130.4, 128.9, 124.6, 122.7, 117.2, 112.9, 109.3 [η^2-(N,O)−(2-MeO−C$_6$H$_4$)(2,4,6-Me$_3$*C*$_6$H$_2$)N]Hf(CH$_2$*Ph*)$_3$], 87.1 [Hf(*C*H$_2$Ph)$_3$], 58.6 [η^2-(N,O)−(2-*Me*O−C$_6$H$_4$)(2,4,6-Me$_3$C$_6$H$_2$)N]Hf(CH$_2$Ph)$_3$] 21.0, 18.3 [η^2-(N,O)−(2-MeO−C$_6$H$_4$)(2,4,6-*Me*$_3$C$_6$H$_2$)N]Hf(CH$_2$Ph)$_3$].

Preparation of [η^2-(N,O)−(C$_4$H$_7$O-2-CH$_2$)(2,6-Pr^i$_2$−C$_6$H$_3$)N]Hf-(CH$_2$Ph)$_3$ (2). A solution of (C$_4$H$_7$O-2-CH$_2$)(2,6-Pr^i$_2$−C$_6$H$_3$)NH (0.084 g, 0.32 mmol) in 5 mL toluene was added to a solution of Hf(CH$_2$Ph)$_4$ (0.20 g, 0.37 mmol) in 5 mL toluene. After stirring the resultant mixture

(36) (a) Bei, X.; Crevier, T.; Guram, A. S.; Jandeleit, B.; Powers, T. S.; Turner, H. W.; Uno, T.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40 (20)*, 3855–3858. (b) Bei, X.; Guram, A. S.; Turner, H. W.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40 (7)*, 1237–1240. (c) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Petersen, J. L. *J. Org. Chem.* **1999**, *64*, 6797–6803. (d) Bei, X.; Uno, T.; Norris, J.; Turner, H. W.; Weinberg, W. H.; Guram, A. S. *Organometallics* **1999**, *18*, 1840–1853.

for 12 h, the toluene was removed under a stream of argon and dried in vacuo. The product was then washed with cold hexane and isolated as a white solid. 0.16 g (70%). ^{1}H NMR data (C_6D_6): δ 7.22−7.15 [3H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 7.15 t, 6.88 t, 6.81 d [15H, Hf(CH_2Ph)$_3$], 4.11 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$-CH}$_2$−C_6H_3)N], 3.99 [1H, sept, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 3.56 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 3.35 [1H, sept, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 3.24 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 2.93 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 2.78 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 2.08 [6H, m, Hf(CH_2Ph)$_3$], 1.37 [3H, d, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 1.29 [3H, d, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 1.22 [3H, d, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 1.20 [3H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$-CH}$_2$−C_6H_3)N], 1.20−1.02 [3H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 0.82 [1H, m, (C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N]; ^{13}C{^{1}H} (C_6D_6): δ 149.6, 145.8 (br), 145.4, 144.9, 128.8, 127.3, 126.0, 124.6, 124.4, 122.0 [(C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N]Hf-(CH_2Ph)$_3$, 86.5 [(C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 83.0 [br, Hf(CH_2Ph)$_3$,], 72.0 [(C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 63.9 [(C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N], 28.5, 28.4, 27.8, 27.1, 26.8, 26.2, 24.22, 24.17 [(C_4H_7O−2-CH_2)(2,6-{(CH_3)$_2$CH}$_2$−C_6H_3)N].

X-ray Structure Determination for Compound 1. X-ray diffraction data were collected on a Bruker P4 diffractometer equipped with a SMART CCD detector. The structure was solved using direct methods and standard difference map techniques, and were refined by full-matrix least-squares procedures on $F2$ with SHELXTL (Version 5.03).[37] Hydrogen atoms on carbon were included in calculated positions.

One Gallon Batch Reactor Copolymerization Procedure. Polymerization experiments were performed using a 1 gallon stirred Autoclave Engineers reactor. The reactor was charged with 1440 g of Isopar E (mixture of isoparaffins, available from ExxonMobil Chemical), 126 g of 1-octene, and 10 mmol of hydrogen, then heated to 130 °C and saturated with ethylene to 450 psig. Solutions of compounds **1** and **2**

(0.005 M in toluene) were prepared in the drybox, and the catalyst was activated using a soluble anilinium borate activator, [($C_{18}H_{37}$)$_2$-PhNH][B(C_6F_5)$_4$] (1.2 equivs). An alumoxane (MMAO Type 3A from Akzo Nobel Polymer Chemicals) was used as an impurity scavenger (5 eq). In the comparative run, the titanium complex [(η^5-C_5Me_4)SiMe$_2$-(η^1-NBu^t)]Ti(η^4-C_5H_8) was activated using B(C_6F_5)$_3$ (3 eq) and MMAO-3A (10 eq). The mixture of the metal complex, borane or borate, and alumoxane was injected to the reactor over several minutes using a flow of high pressure solvent, and the polymerization was allowed to proceed for 10 min, with ethylene provided on demand to maintain the pressure at 450 psig. The amount of ethylene consumed during the reaction was monitored using a mass flow meter. The polymer solution was dumped from the reactor into a nitrogen-purged glass kettle containing 10−20 mL of 2-propanol. An aliquot of an additive solution (prepared by dissolving 6.66 g of Irgaphos 168 and 3.33 g of Irganox 1010 in 500 mL of toluene) was added to this kettle and the solution stirred thoroughly. The polymer solution was dumped into a tray, air-dried overnight, and then thoroughly dried in a vacuum oven for 2 d. The weights of the polymers were recorded and the efficiency calculated as grams of polymer per micromole of transition metal.

Supporting Information Available: Tables of crystal structure data for compound **1**. Experimental designs and results from the primary screening validation and discovery experiments. Experimental designs and results from the secondary screening ethylene-1-octene copolymerization experiments. GCMS data for the 96-member amine-ether ligand library, and ^{1}H and ^{13}C NMR data for representative examples. This material is available free of charge via the Internet at http://pubs.acs.org.

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