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Polymerization Catalysts

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Nonconventional Catalysts for Isotactic Propene Polymerization in Solution Developed by Using High-Throughput-Screening Technologies

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Industrial methods for the manufacture of commodity polyolefins are presently dominated by gas- and slurryphase processes in which the catalysts are formulated on solid supports.^[1] Homogeneous processes in solution offer greater operational flexibility and wider ranges of products, but for technical and economical reasons they operate most effectively at higher temperatures to prevent precipitation of the polymer, with low concentrations of monomer and short catalyst residence times.^[2] These restrictions impose a highly demanding set of requirements on the performance of the catalyst, in particular with respect to the thermal stability, the molecular weight capability, and the stereoselectivity (when needed). In the case of ethene polymerization, metallocene and hemi-metallocene catalysts matching the requirements were identified, and solution processes became commercial in the 1990s,^[3] yielding an impressive portfolio of high-value ethene/1-alkene copolymers, in particular, that were once thought to be beyond the capability of polyethylene process technology.^[4] For propene polymerization, on the other hand, the quest proved to be much more problematic. The performance of C_2 -symmetric ansa-zirconocenes, which represent the state-of-the-art homogeneous catalysts for isotactic polypropylene,^[5] rapidly deteriorates with increasing temper-

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Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author. ature and decreasing concentration of monomer.^[6] Herein, we report on the development, aided by high-throughput-screening (HTS) technologies, of a new family of homogeneous Hf catalysts with non-conventional structure, that are now used commercially for the unprecedented production of materials based on isotactic polypropylene in a high-temperature solution process.^[7,8]

The catalyst discovery workflow using the Symyx HTS infrastructure (introduced elsewhere^[9]) moves from a microscale high-throughput primary screen (250 µL working volume), in which large arrays of (new) metal-ligand combinations are rapidly surveyed for catalytic activity with 1-octene (a liquid monomer convenient for robotic handling^[10]), with automated procedures enabling several hundred experiments per day. Promisingly active metal-ligand combinations thus identified ("hits") are subjected to a secondary screen in which the catalyst performance properties for the targeted application are assessed using larger scales, with less experiments run under more commercially relevant conditions; typically, 48 experiments in parallel are carried out with real-time monitoring in individually controlled high-pressure reactors (Parallel Pressure Reactor Technology (PPR); 5-6 mL working volume). Catalysts that meet predetermined performance criteria ("leads") are then optimized through structural elaboration. Specially developed rapid polymer characterization techniques accommodate the synthetic throughput and assess the nature of the polymer products from primary and secondary screens.^[11]

In a previous project on ethene/1-octene copolymerization,^[9] a number of new non-metallocene^[12] catalysts with remarkable high-temperature stability and molecular weight capability were uncovered. Our attention, in particular, had been raised by the combinations of two closely related pyridyl-amine ligands with HfBn₄ (Bn = benzyl), because under primary screening conditions they yielded high-molecular-weight polyoctene with high l-octene conversions. Before evaluating these hits in a secondary screen with propene, a greater number of pyridyl-amine ligands with enhanced structural diversity were synthesized (Figure 1). In designing the expanded ligand array, three convenient positions for structural amplification were identified and are labeled as R¹, R^2 , and R^3 . The amine substituent R^1 was known to influence catalyst performance dramatically from prior reports of other amide-stabilized systems.^[12] Substituent R² was chosen to alter the steric and electronic properties of pyridine ligation, while R³ gave the opportunity to introduce a stereogenic center on the ligand, albeit at a position remote from the propene-binding site in the metal complex, and test whether it can influence the stereoselectivity of the catalyst. In total, 39 pyridyl-amine structures were prepared by using synthetic procedures adapted from known transformations.^[13] As can be seen from Figure 1, considerable steric and electronic diversity is represented in this ligand array.

Using previously reported secondary screening protocols,^[9] the ligands were complexed in situ with suitable Hf precursors,^[14] namely HfBn₄ or, for the more sterically hindered ligands, Hf(NMe₂)₄ (see Supporting Information). The complexes were then tested in the polymerization of propene at 75 °C in toluene. As many as 34 combinations





Figure 1. The pyridyl amine ligands used in this study. Bn = benzyl; Anthr = anthracenyl; Nap = naphthyl.

turned out to be active. In the vast majority of cases, the produced polypropylenes came out of the reactor as clear solutions in toluene and were determined by rapid FTIR analysis^[9,11] to be stereoirregular (Figure 2). In two reactors, however, opaque suspensions were obtained, which is a clear indication of high-polymer crystallinity, and indeed rapid FTIR analysis indicated an isotactic polypropylene structure. This structure was confirmed by a subsequent NMR spectroscopic characterization of the isolated polymers (see below).

From the members of the library screened in the present study, the two ligands that led to this breakthrough have a very similar structure, with the same R^1 (2,6-*i*Pr₂C₆H₃) and R^3 (phenyl) groups, and with R^2 = phenyl in one case (ligand L1-

H₂) and $R^2 = 1$ -naphthyl in the other (ligand $L2-H_2$). Note that all other substitution patterns in this library, some of which are apparently similar to L1-H₂ and L2-H₂, resulted in poorly stereoselective or non-stereoselective catalysts. For example, replacing $R^1 = 2.6 - i Pr_2 C_6 H_3$ with another 2,6-substituted aryl, such as 2,4,6-Me₃-C₆H₂, resulted in a substantial loss of the stereocontrol. This observation demonstrates that the stereoselectivity is exquisitely sensitive to the nature of the substituents on the ligand, suggesting that the discovery would likely have taken significantly longer without the synthesis of a suitably diverse ligand array coupled with the use of HTS.

The ¹³C NMR spectrum of the polypropylene sample obtained using ligand **L2**-H₂ is shown in Figure 3. The isotacticity is strikingly high, and the occasional (0.9 mol%) $m_x rrm_y$ (m = meso and r = racemo) stereodefects are typical of stereocontrol exerted by an intrinsically chiral active species.^[15] Low amounts of

regiodefects (0.9 mol %) are also seen in the form of isolated head-to-head/tail-to-tail enchainments with an unprecedented stereostructure^[5,15] (see Figure 3), which can be attributed to the preference of the catalyst to insert the *same* propene enantioface irrespective of the regiochemistry. Results of ¹H and ¹³C NMR chain end group analysis on suitable polymer samples indicated that the favored propene insertion mode is 1,2 (primary).^[16]

More insight into the novel catalyst class was gained from an investigation of the metal-ligand complexation and alkylation chemistry. The reaction of $L1-H_2$ with $Hf(NMe_2)_4$ (Scheme 1, upper) proceeded smoothly with the elimination of two equivalents of dimethylamine, instead of one as



Figure 2. Results from rapid FTIR analysis of polymers obtained from the secondary screening protocol.

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Figure 3. ¹³C NMR spectrum (100 MHz, (CDCl₂)₂, 120°C; δ scale relative to tetramethylsilane at δ =0 ppm) of the polypropylene obtained with the in situ combination and activation of L2-H₂ with Hf(NMe₂)₄, with explicit attributions of peaks owing to regio- and stereodefects. The main peaks of the isotactic polypropylene (marked with \approx) are out of scale.

expected, and the concomitant formation of the pyridylamide complex $[{\eta^3-(N,N,C)-L1}]$ Hf $(NMe_2)_2$]. ¹H NMR and single-crystal X-ray diffraction data are consistent with the phenyl group at R^2 being the source of the proton necessary for the elimination of the second equivalent of dimethylamine, in addition to that coming from the amine functionality. The structure obtained from single-crystal X-ray studies (see Figure 4A and Supporting Information), in particular, reveals the presence of a Hf–C(aryl) σ bond formed by *ortho*metalation of the phenyl group^[17] and, consequently, tridentate ligation of L1. The complex reveals C_1 symmetry, with a highly distorted trigonal-bipyramidal coordination of the Hf center and the two NMe₂ groups that occupy equatorial diastereotopic sites. Alkylation with 10 equivalents of AlMe₃^[18] gave the dimethyl derivative [{ η^3 -(N,N,C)-L1]HfMe₂] (1-Me₂), with the protons of the two diastereotopic methyl groups on Hf resonating at $\delta = 0.91$ and 0.61 ppm in the ¹H NMR spectrum.



Figure 4. Single-crystal X-ray diffraction structures of A) [$\{\eta^3$ -(N,N,C)-L1}Hf(NMe_2)_2] and B) [$\{\eta^2$ -(N,N)-L2-H}Hf(NMe_2)_3].

Less exotically, the reaction of L2-H₂ with Hf(NMe₂)₄ (Scheme 1, lower) proceeded with the elimination of one equivalent of dimethylamine to give the complex [{ η^2 -(N,N)-L2-H}Hf(NMe₂)₃]. In this case, the pyridyl-amide ligand is bidentate, as shown in the single-crystal structure (see Figure 4B and Supporting Information). However, during the subsequent alkylation step with 10 equivalents of AlMe₃, the evolution of methane was observed, along with the



Scheme 1. Reactions of L1-H₂ (upper) and L2-H₂ (lower) with $Hf(NMe_2)_4$ and concomitant formation of the corresponding pyridyl-amide complexes.

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formation of three equivalents of Al₂Me₅(NMe₂). This observation points to the formation of an *ortho*-metalated dimethyl complex [{ η^{3} -(N,N,C)-L2}HfMe₂] (2-Me₂), strictly similar to the corresponding species with ligand L1. Consistently, the ¹H NMR spectrum displayed two inequivalent resonances of methyl protons on Hf at $\delta = 0.93$ and 0.65 ppm.

It is plausible to identify $1-Me_2$ and $2-Me_2$ as catalyst precursors, from which cationic active species would be formed by methide abstraction, similar to what is known for metallocenes.^[19] Indeed, when $2-Me_2$ was screened in the PPR by activation with $[Me_2PhNH][B(C_6F_5)_4]$ in combination with an alkylaluminum reagent (see Supporting Information for details), propene polymerization led to a highly isotactic polymer, which was identical to that produced starting from an in situ combination of ligand $L2-H_2$ with $Hf(NMe_2)_4$ (when screened under identical conditions). That such cations should be highly isotactic-selective in the polymerization of propene up to very high temperatures, however, is not at all obieous.

The effect of temperature on the stereoselectivity of the catalyst derived from 2-Me₂ by activation with $[(C_6H_5)_3C]$ $[B(C_6F_5)_4]$ in toluene is shown in Figure 5, in which $\ln[\sigma/$



Figure 5. Plot of $\ln[\sigma/(1-\sigma)]$ versus 1/RT for propene polymerization with 2-Me₂/[(C₆H₅)₃C][B(C₆F₅)₄] in toluene (see text for details).

 $(1-\sigma)$] is plotted versus 1/RT; σ and $1-\sigma$ are the stochastic probabilities of propene insertion in the predominant 1,2 regiochemistry with the two (re or si) enantiofaces. The limiting cases of $\sigma = 1$ or $\sigma = 0$ correspond to complete enantioselectivity, while $\sigma = 0.5$ corresponds to a complete lack of enantioselectivity. For a single-center isotactic-selective catalytic species with two homotopic active sites (i.e., with local C_2 symmetry), the function is usually a straight line, whose derivative is the difference in activation energy (ΔE^{\dagger}) between the two competing diastereomeric propene insertion paths (unless additional routes for the generation of stereodefects, such as growing chain epimerization,^[6] are viable), that intercepts at the origin ($\Delta S^{\dagger} \approx 0$). The case of interest here is in principle more complicated, because the two active sites of the C_1 -symmetric catalytic species are diastereotopic. However, the experimental data points are well interpolated by a straight line through the origin, as if the two active sites were equivalent or, more likely, as if propene insertion occurred predominantly at one of the two, with a robust enantioselectivity ($\Delta E^{\pm} = 3.4 \text{ kcal mol}^{-1}$). Notably, at each given temperature the stereoselectivity turned out to be independent of the concentration of propene (in the explored 0.5–5 M range), which is not always the case for a C_1 -symmetric catalyst.^[5,15]

A full quantum mechanics study (see Supporting Information) was undertaken on the two diastereoisomers [2'-iBu]⁺ and [2''-iBu]⁺ of a putative active cation [{ η^3 -(N,N,C)-L2}Hf(iBu)]⁺, with the ligand in R configuration and an isobutyl residue simulating the growing polypropylene chain (Figure 6). In both cases, propene insertion into the Hf–iBu



Figure 6. Transition states for 1,2-propene insertion at the two diastereomers of an $[{\eta}^{3}-(N,N,C)-L2]$ Hf(*i*Bu)]⁺ model cation, as obtained from quantum mechanics calculations (see text for details). Propene dark green, *i*Bu light green, N blue, C(L2) orange, H white, Hf orange sphere. A) *re* enantioface (favored) and B) *si* enantioface of $[2''-iBu]^{+}$. C) *si* enantioface (favored) and D) *re* enantioface of $[2''-iBu]^{+}$.

bond was found to proceed according to a standard Cosseetype chain-migratory path,^[5,15] and with predominant 1,2 regiochemistry $(G_{2,1}^{\#}-G_{1,2}^{\#}>2 \text{ kcal mol}^{-1})$ in agreement with experiment. According to the calculations, for $[\mathbf{2}'-i\mathbf{Bu}]^+$ at the transition states the metal is in a distorted trigonalbipyramidal coordination (Figure 6A,B) and insertion with the *re* enantioface is strongly favored $(G_{si}^{\#}-G_{re}^{\#}=4.5 \text{ kcal} \text{ mol}^{-1})$. The lowest-energy paths for insertion at $[\mathbf{2}''-i\mathbf{Bu}]^+$, on the other hand, involve square-pyramidal transition states

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(Figure 4C,D), and it is the *si* enantioface that is slightly preferred ($G_{si}^{\#}-G_{re}^{\#}=-0.8 \text{ kcal mol}^{-1}$). In both cases, the flow of chiral information from the active species to the incoming monomer is mediated by the growing polymer chain, as is common in Ziegler–Natta catalysis.^[5,15] In brief, the steric hindrance of the ancillary ligand framework reduces the conformational freedom of the chain, which is constrained in a chiral orientation, with the first C–C bond pointing towards the more open of the two accessible quadrants. In turn, 1,2 propene insertion is favored with the enantioface that directs the methyl substituent *anti* to the first C–C bond.

In view of the above, the observed stereoselectivity (Figure 5) can be explained assuming that the monomer inserts in preference at $[2'-P]^+$ (P = polymeryl in the place of iBu). The few stereodefects in the polymer can be traced to faults of enantioselection at the same diastereomer and/or to occasional insertions at $[2''-P]^+$. This interpretation is consistent with all presently available experimental data, including results of solution-state NMR studies on [2-Me][MeB- $(C_6F_5)_3$ ion couples showing a single diastereoisomer with the methyl group on Hf at the same site of the *i*Bu group in [2' $iBu]^{+,[20]}$ and of chiral 1-alkene oligomerization with enantiopure [(R)-2]-Me₂-based catalysts confirming the preferential uptake of propene with the *re* enantioface,^[16] as will be reported in due course. The fact that the stereoselectivity is independent of the concentration of propene suggests that the rate of chain/anion relocation^[19,21,22] is fast relative to that of monomer insertion (Curtin-Hammett regime^[22]).

It must be added, though, that experimental and quantum mechanics results indicate that monomer insertion into the *ortho*-metallacycle is also viable, leading to an in situ ligand modification.^[16] The relevance of this issue for catalysis is currently under investigation.

The performance of the new catalysts in toluene at 90 °C and a partial pressure of propene of 6.9 bar (100 psi) is compared in Table 1 with the state-of-the-art C_2 -symmetric metallocene, *rac*-[Me₂Si(2-Me-4-phenyl-1-indenyl)₂Zr(η^4 -1,4-(phenyl)₂-1,3-butadiene)].^[23] Strikingly, under the conditions explored, the unoptimized pyridyl-amide catalysts displayed productivities up to 20% of that of the highly optimized metallocene. The complex [{ η^2 -(N,N)-L2-H}Hf(NMe₂)₃], moreover, afforded a polypropylene with nearly the same melting temperature (141 vs 142 °C). The metallocene-made polymer, however, revealed an average molecular weight of $M_w \approx 95$ kDa. If it is considered that M_w of typical commercial

Table 1: Typical results of propene polymerization at 90°C with the new catalysts as well as with metallocene *rac*-[Me₂Si(2-Me-4-phenyl-1-indenyl)₂Zr(η^4 -1,4-(phenyl)₂-1,3-butadiene)], for comparison.

Precatalyst	Productivity ^[a]	M _w [kDa]	$M_{\rm w}/M_{\rm n}$	<i>Τ</i> _m [°C] ^[b]
[{η ³ -(N,N,C)- L1 }Hf(NMe ₂) ₂]	1.9	300	2.1	127
$[{\eta^2-(N,N)-L2-H}Hf(NMe_2)_3]$	0.3	710	3.2	141
Zr metallocene	9.2	95	2.0	142

Conditions: toluene (4.4 mL), propene (6.9 bar), $Al(iBu)_2H$ (10– 30 equiv), $[Me_2PhNH][B(C_6F_5)_4]$ (1.1 equiv). See Supporting Information for details. [a] Units: kilograms of polymer per mmol metal per minute. [b] Maximum of the differential scanning calorimetry melting endotherm on the second heating scan (heating rate: 10°Cmin⁻¹). products is in the range of 300–400 kDa, and that an industrial solution process would operate well above 90 °C at which temperature a further drop of M_w is expected, it is clearly confirmed that the molecular weight capability of this high-performance metallocene is not adequate to the application of interest. The polypropylenes produced with $[{\eta^3-(N,N,C)-L1}Hf(NMe_2)_2]$ and $[{\eta^2-(N,N)-L2-H}Hf(NMe_2)_3]$, on the other hand, revealed much higher values of M_w with narrow polydispersities; the molecular weight capability of $[{\eta^2-(N,N)-L2-H}Hf(NMe_2)_3]$, in particular, with molecular weights of polypropylene above 700 kDa, is truly extraordinary at these polymerization conditions, opening exciting perspectives for a new industrial process.

In fact the readily synthesized pyridyl-amine ligand system facilitated rapid optimization of the catalyst. By further examining the substituent effects at R¹,R²,R³ through a positional scanning approach^[24] coupled with iterative rounds of secondary screening, we could achieve significant improvements in the catalyst performance. In particular, new catalysts with bulky R³ substituents such as ortho-tolyl, 2biphenyl, and 2-cyclohexylphenyl were identified, which displayed higher productivity and molecular weight capability. At process temperatures above 100°C, these catalysts yield isotactic polypropylenes with $T_{\rm m} \approx 150 \,^{\circ}{\rm C}$ and $M_{\rm w}$ values that are compatible with commercial application. As a result, an industrial high-temperature solution process for the production of new isotactic polypropylene based materials has been introduced in less than four years from the launch of the catalyst discovery program.^[7]

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