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Gel Permeation Chromatography as a Combinatorial Screening Method: Identification of Highly Active Heteroligated Phenoxyimine Polymerization Catalysts

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Combinatorial and high-throughput screening techniques were originally developed by the pharmaceutical industry to rapidly identify biologically active compounds, but they have become increasingly common in other areas of research.[1] In homogeneous catalysis, automated parallel devices are now used to screen potential catalysts and to optimize reaction conditions.[2] As more reactions are run simultaneously, the need for faster screening methods will increase. Although new techniques have been developed for the rapid screening of small-molecule catalysts, efforts to screen polymerization catalysts have focused on improving existing technologies, particularly gel permeation chromatography (GPC).[3]

Analyzing pooled catalyst (or substrate) mixtures increases efficiency, but screening methods must be carefully chosen to process the additional data accurately. Screening polymer mixtures formed by different species is difficult, and few pooled combinatorial experiments have been reported.[4] Mass spectrometry has been used to study a mixture of polymers formed by known catalysts and could potentially identify new compounds.[4e,f] We have used a pooled synthetic approach to identify a bis(phenoxyimine) titanium catalyst for the syndiospecific polymerization of propylene; the product mixture was analyzed by separating insoluble syndiotactic polypropylene (PP) from soluble atactic polymer.[4c] In this communication, we use GPC of polymer mixtures to identify a class of highly active heteroligated phenoxyimine (PHI) catalysts.

Since the initial discovery of PHI-based catalysts,[5a] research has focused on improving performance and understanding catalyst behavior.[5] Relevant to the work presented herein is the effect of electron-withdrawing groups: fluorine substitution at the ortho positions of the ligand *N*-aryl ring results in living behavior, while substitution at the meta or para positions increases catalyst activity.[6] Table 1 lists propylene polymerization data for a series of homoligated PHI catalysts. In the absence of any reports describing heteroligated PHI catalysts ($\mathbf{L^mL^n}TiCl_2$), we predicted the polymerization behavior of such complexes to fall between the known behavior of homoligated complexes $\mathbf{L^m}_2TiCl_2$ and $\mathbf{L^n}_2TiCl_2$. With this in mind, a heteroligated complex was synthesized using pentafluoro ligand $\mathbf{L^9}$ and 3,5-difluoro ligand $\mathbf{L^4}$ (Scheme 1).[7] Upon activation with methylaluminoxane (MAO), $\mathbf{L^4L^9}TiCl_2$ produced PP with the expected polydispersity ($M_w/M_n = 1.32$, between 1.06 and 1.75), but the catalyst was much more active (TOF = 1340 h^{-1}) and formed PP with much higher molecular weight (M_n = 117 700) than either $\mathbf{L^4}_2TiCl_2$ or $\mathbf{L^9}_2TiCl_2$. To ensure that ligands were not being exchanged under the polymerization conditions, equimolar amounts of $\mathbf{L^4}_2TiCl_2$ and $\mathbf{L^9}_2TiCl_2$ were mixed together, activated, and reacted with propylene. As expected, the catalyst mixture was much less active (TOF = 280 h^{-1}) than the heteroligated catalyst, and the GPC trace was bimodal.

To determine if the increase in activity and M_n observed for $\mathbf{L^4L^9}TiCl_2$ was characteristic of all heteroligated PHI complexes, we chose to investigate 10 ligands ($\mathbf{L^1}-\mathbf{L^{10}}$) that form highly syndiotactic ([r^4] > 0.75) polypropylene. To analyze the 45 possible heteroligated catalysts, pooled libraries were used. Combining five ligands per library results in five (known) homoligated compounds and 10 (unknown) heteroligated compounds. GPC analysis of the polymer mixtures formed by these libraries should be a viable screening technique for the identification of highly active catalysts with limited chain transfer, as they will form polymer with higher molecular weights. A test library was generated using equimolar amounts of ligands $\mathbf{L^4}$ and $\mathbf{L^9}$; ^{1}H NMR analysis indicated that complexes $\mathbf{L^4L^9}TiCl_2$, $\mathbf{L^4}_2TiCl_2$, and $\mathbf{L^9}_2TiCl_2$ were cleanly synthesized. A GPC of the polymer formed by the catalyst mixture contained three peaks, with the signal for the polymer from the heteroligated complex significantly more intense than those for the homoligated complexes (see Supporting Information).

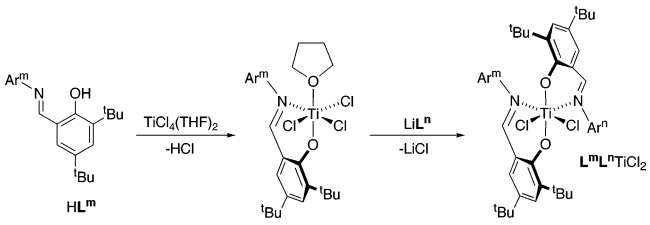
Encouraged by this result, we synthesized more diverse catalyst libraries. "Nonliving" ligands $\mathbf{L^1}-\mathbf{L^5}$ were combined into library **A**; "living" ligands $\mathbf{L^6}-\mathbf{L^{10}}$ were used to make library **B**. Libraries **C** ($\mathbf{L^2}$, $\mathbf{L^3}$, $\mathbf{L^5}$, $\mathbf{L^8}$, and $\mathbf{L^{10}}$) and **D** ($\mathbf{L^1}$, $\mathbf{L^4}$, $\mathbf{L^6}$, $\mathbf{L^7}$, and $\mathbf{L^9}$) contained both "living" and "nonliving" ligands. These catalyst mixtures were activated with MAO in the presence of propylene; the GPC traces of the resulting PP are shown in Figure 1. Libraries **A** and **B** generate polymers with relatively low molecular weights, while libraries **C** and **D** both form polymers with relatively high molecular weights (over 100 000 Da).[8] Libraries **A** and **B** contain all possible

Table 1. Propylene Polymerization with $\mathbf{L^n}_2TiCl_2$/MAO Catalysts[a]

L^n	*N*-aryl group	yield (g)	TOF[b]	M_n[c] (Da)	M_w/M_n[c]
$\mathbf{L^1}$	Ph	0.16	42	2 310	1.41
$\mathbf{L^2}$	4-F−Ph	0.52	138	5 830	1.66
$\mathbf{L^3}$	4-CF_3−Ph	0.59	157	5 720	1.70
$\mathbf{L^4}$	3,5-F_2−Ph	1.56	404	4 290	1.75
$\mathbf{L^5}$	3,4,5-F_3−Ph	1.95	516	2 780	1.83
$\mathbf{L^6}$	2,6-F_2−Ph	0.05[d]	7	1 020	1.05
$\mathbf{L^7}$	2,4,6-F_3−Ph	0.07	18	1 330	1.05
$\mathbf{L^8}$	2,3,5,6-F_4−Ph	0.55	143	15 560	1.07
$\mathbf{L^9}$	2,3,4,5,6-F_5−Ph	0.81	221	28 870	1.06
$\mathbf{L^{10}}$	2,3,5,6-F_4−4-CF_3−Ph	1.18	316	48 100	1.13

[a] General conditions: 0.03 mmol catalyst in toluene (5 mL) added to a propylene-saturated (30 psi) PMAO-IP solution (100 mL of toluene; [Al]/[Ti] = 150) at 0 °C for 3.0 h. [b] Turnover frequency: mol propylene/(mol Ti·h). [c] Determined by GPC in 1,2,4-trichlorobenzene at 140 °C vs polyethylene standards. [d] Reaction time = 6.0 h.

Scheme 1. Synthesis of Heteroligated PHI Complexes



10.1021/ja047236d CCC: $27.50

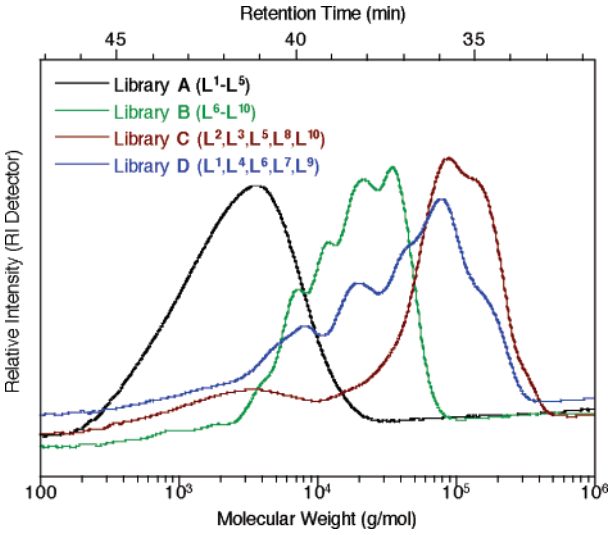


Figure 1. GPC traces of polypropylene formed by libraries **A**−**D**.

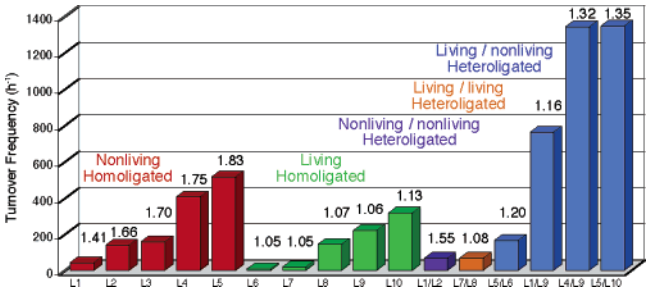


Figure 2. Polymerization activity and M_w/M_n data for homo- and heteroligated PHI catalysts.

heteroligated catalysts with either two "nonliving" or two "living" ligands, and thus it appears that a combination of one "living" and one "nonliving" ligand is required for a heteroligated catalyst to form polymer with unusually high molecular weight.

The high molecular weight polypropylene in libraries **C** and **D** could be formed by highly active catalysts (with much faster propagation rates) or by living catalysts (with much slower termination rates). To verify that only "living"/"nonliving" ligand combinations result in highly active catalysts, several individual heteroligated complexes were synthesized and reacted with propylene (Figure 2). Catalyst $\mathbf{L^7L^8}TiCl_2$, with two "living" ligands, generates polymer with narrow polydispersity and has an activity less than $\mathbf{L^8}_2TiCl_2$ but greater than $\mathbf{L^7}_2TiCl_2$. Catalyst $\mathbf{L^1L^2}TiCl_2$, with two "nonliving" ligands, has a similar activity but forms polymer with a broader molecular weight distribution. Catalyst $\mathbf{L^5L^6}TiCl_2$ has one "living" and one "nonliving" ligand and is less active than $\mathbf{L^5}_2TiCl_2$ (possibly due to the extremely deactivating nature of ligand $\mathbf{L^6}$), but $\mathbf{L^5L^{10}}TiCl_2$ and $\mathbf{L^1L^9}TiCl_2$ are both much more active than the corresponding homoligated catalysts.

In summary, GPC analysis of polymers formed by a set of pooled catalyst libraries has been used to identify a class of syndiospecific heteroligated PHI catalysts that are unusually active for propylene polymerization. A combinatorial approach was used to drastically reduce the number of reactions needed to identify these compounds. GPC can be an effective tool for identifying high molecular weight polymer formed by either fast catalysts or catalysts with limited chain transfer, although there is a limit to the number of catalysts that can be analyzed per GPC run. At this point, it is not clear why the combination of a "living" ligand (with an *ortho*-fluorinated *N*-aryl group) with a "nonliving" ligand (without *ortho*-fluorination) is needed for high activity. Ligand differences may result in faster rates for both catalyst racemization[5f,g] and monomer insertion. We are now investigating the mechanistic questions these findings raise and plan to develop heteroligated catalysts incorporating a wider range of PHI ligands.

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Supporting Information Available: Experimental procedures, polymerization, and GPC data (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Früchtel, J. S.; Jung, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 17−42. (b) Balkenhohl, F.; von dem Bussche-Hünnefeld, C.; Lansky, A.; Zechel, C. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2288−2337. (c) Jandeleit, B.; Schaefer, D. J.; Powers, T. S.; Turner, H. W.; Weinberg, W. H. *Angew. Chem., Int. Ed.* **1999**, *38*, 2494−2532.

(2) (a) Dahmen, S.; Bräse, S. *Synthesis* **2001**, *10*, 1431−1449. (b) Shimizu, K. D.; Snapper, M. L.; Hoveyda, A. H. *Chem.−Eur. J.* **1998**, *4*, 1885−1889. (c) Gruter, G. M.; Graham, A.; McKay, B.; Gilardoni, F. *Macromol. Rapid Commun.* **2003**, *24*, 73−80. (d) Boussie, T. R.; Diamond, G. M.; Goh, C.; Hall, K. A.; LaPointe, A. M.; Leclerc, M.; Lund, C.; Murphy, V.; Shoemaker, J. A. W.; Tracht, U.; Turner, H.; Zhang, J.; Uno, T.; Rosen, R. K.; Stevens, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 4306−4317. (e) Jones, D. J.; Gibson, V. C.; Green, S. M.; Maddox, P. J. *Chem. Commun.* **2002**, 1038−1039. (f) Adams, N.; Arts, H. J.; Bolton, P. D.; Cowell, D.; Dubberley, S. R.; Friederichs, N.; Grant, C. M.; Kranenburg, M.; Sealey, A. J.; Wang, B.; Wilson, P. J.; Cowley, A. R.; Mountford, P.; Schröder, M. *Chem. Commun.* **2004**, 434−435.

(3) Meier, M. A. R.; Hoogenboom, R.; Schubert, U. S. *Macromol. Rapid Commun.* **2004**, *25*, 21−33.

(4) (a) Boussie, T. R.; Coutard, C.; Turner, H.; Murphy, V.; Powers, T. S. *Angew. Chem., Int. Ed.* **1998**, *37*, 3272−3275. (b) Boussie, T. R.; Murphy, V.; Hall, K. A.; Coutard, C.; Dales, C.; Petro, M.; Carlson, E.; Turner, H. W.; Powers, T. S. *Tetrahedron* **1999**, *55*, 11699−11710. (c) Tian, J.; Coates, G. W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3626−3629. (d) Stork, M.; Herrmann, A.; Nemnich, T.; Klapper, M.; Müllen, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 4367−4369. (e) Hinderling, C.; Chen, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 2253−2256. (f) Chen, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 2832−2847.

(5) (a) Matsui, S.; Tohi, Y.; Mitani, M.; Saito, J.; Makio, H.; Tanaka, H.; Nitabaru, M.; Nakano, T.; Fujita, T. *Chem. Lett.* **1999**, 1065−1066. (b) Makio, H.; Kashiwa, N.; Fujita, T. *Adv. Synth. Catal.* **2002**, *344*, 477−493. (c) Mitani, M.; Furuyama, R.; Mohri, J.; Saito, J.; Ishii, S.; Terao, H.; Nakano, T.; Tanaka, H.; Fujita, T. *J. Am. Chem. Soc.* **2003**, *125*, 4293−4305. (d) Tian, J.; Hustad, P. D.; Coates, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 5134−5135. (e) Hustad, P. D.; Tian, J.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 3614−3621. (f) Talarico, G.; Busico, V.; Cavallo, L. *J. Am. Chem. Soc.* **2003**, *125*, 7172−7173. (g) Milano, G.; Cavallo, L.; Guerra, G. *J. Am. Chem. Soc.* **2002**, *124*, 13368−13369. (h) Lamberti, M.; Pappalardo, D.; Zambelli, A.; Pellechia, C. *Macromolecules* **2002**, *35*, 658−663. (i) Gagieva, S. C.; Sukhova, T. A.; Savinov, D. V.; Optov, V. A.; Bravaya, N. M.; Belokon, Y. N.; Bulychev, B. M. *Russ. Chem. Bull., Int. Ed.* **2003**, *52*, 1693−1697.

(6) (a) Mitani, M.; Mohri, J.; Yoshida, Y.; Saito, J.; Ishii, S.; Tsuru, K.; Matsui, S.; Furuyama, R.; Nakano, T.; Tanaka, H.; Kojoh, S.; Matsugi, T.; Kashiwa, N.; Fujita, T. *J. Am. Chem. Soc.* **2002**, *124*, 3327−3336. (b) Mason, A. F.; Tian, J.; Hustad, P. D.; Lobkovsky, E. B.; Coates, G. W. *Isr. J. Chem.* **2002**, *42*, 301−306.

(7) (a) Pennington, D. A.; Hughes, D. L.; Bochmann, M.; Lancaster, S. J. *J. Chem. Soc., Dalton Trans.* **2003**, 3480−3482. (b) Owiny, D.; Parkin, S.; Ladipo, F. T. *J. Organomet. Chem.* **2003**, *678*, 134−141.

(8) A library containing all 10 ligands was also made, but did not provide any additional information; the GPC was similar in appearance to library **C**.

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