Combinatorial Testing of Supported Catalysts for the Heterogeneous Polymerization of Olefins**

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Combinatorial chemistry, which has had a high impact on pharmaceutical and biotechnological research and development, has recently also been applied to catalysis research and is strongly connected with the development of high-throughput methods.[1] However, few efforts have been directed towards taking advantage of this approach in polymer science.[2] Herein we present a novel approach using tagged supports for the testing and direct comparison of silica-[3] or polymer-supported[4] heterogeneous catalysts for industrial olefin polymerizations.[5] In contrast to a process described in the literature[2c] which requires a chemical transformation, here direct detection of the different product beads obtained by different catalysts is available through fluorescence. This process accelerates the optimization and standardization of supported catalyst composition, polymerization conditions (e.g. temperature, pressure, and comonomer concentration), and product profiles because standard equipment can be applied.

This truly combinatorial approach starts with the tagging of different catalysts with fluorescent dyes, which exhibit different emission wavelengths. These labeled catalysts are then mixed and introduced into a single polymerization vessel. During the olefin polymerization each catalyst particle forms only one product granule through a particle growth process and can be considered as a microreactor.[6]

To assign the different components of the product mixture to the employed catalysts, the polymer products are exposed to UV light. Owing to the different emissions of the labels incorporated in the beads, the resulting products can be directly identified which permits manual separation and characterization. In this way the properties of each of the polymer products can be assigned to the characteristics of the employed catalyst. This protocol is illustrated in Figure 1.

For tagging the catalysts, we chose rylene dyes (see Figure 2) because of their chemical stability, their high tendency to physisorb on silica, and their high fluorescence quantum yields.[7] It had to be shown that these dyes do not influence the polymerization and are stable under different polymerization conditions (Table 1).

Catalyst **A**, consisting of metallocene **3** (dimethylsilylbis(2-methylbenzindenyl) zirconocene dichloride; Figure 2), silica-supported and activated with MAO (methylaluminoxane), was tagged with dye **2** (perylenemonoimide) and compared with the corresponding untagged catalyst at a range of pressures and temperatures (Table 1). In all cases similar

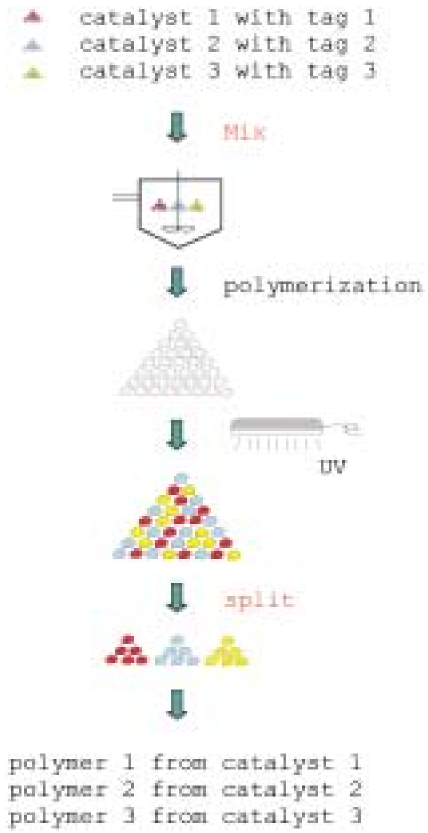

Figure 1. The combinatorial approach.

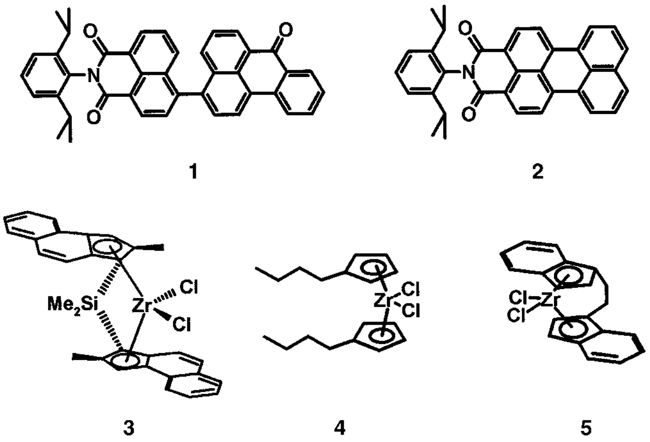

Figure 2. Dyes and catalysts.

Table 1. Comparison of the polymerization behavior of tagged and untagged catalyst **A**.[a]

Run	Dye	P [bar]	T [°C]	Productivity [g(PE) g(cat)$^{-1}$ h^{-1}]	M_n
1	–	40	70	1180	180000
2	**2**	40	70	1220	177000
3	–	40	50	320	188000
4	**2**	40	50	320	194000
5	–	40	30	60	277000
6	**2**	40	30	60	318000
7	–	20	70	200	78000
8	**2**	20	70	200	82000

[a] P: pressure, T: polymerization temperature, 5 mL triisobutylaluminum (TIBA).

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productivities from the corresponding experiments with and without dye were obtained and the polyethylene samples possessed the same molecular weight and polydispersity as well as the same particle morphology.

The preparation of the catalysts was performed by a facile impregnation method described in the Experimental Section (Figure 3).[8]

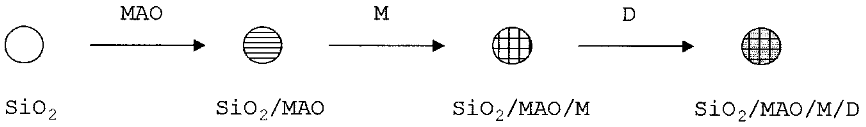

Figure 3. Preparation of labeled catalysts. M = metallocene, D = dye, MAO = methylaluminoxane.

To prove our concept of a combinatorial approach a set of two catalysts was used simultaneously. Catalyst **B** contained bis(*n*-butylcyclopentadienyl)zirconocene dichloride (**4**) with benzanthronylnaphthaleneimide **1** as a tag (Figure 2). Catalyst **C** consisted of ethylene–bis(indenyl)zirconocene dichloride (**5**) and perylenemonoimide **2** (Figure 2). Zirconocene **4** and ansa-zirconocene **5** were selected due to their similar activities. They gave product particles of nearly the same size and thus demonstrated the efficiency of our detection method. On the other hand, the two zirconocenes polymerize ethylene with different molecular weight and polydispersity.

By using catalysts **B** and **C** simultaneously, polyethylene products were obtained (see Experimental Section) as spherical granules within a range of 0.5 to 2 mm diameter. Upon exposure to UV light, particles prepared from the two different catalysts fluoresce with different colors. A fluorescence microscope image (Figure 4) clearly revealed two different kinds of particles: fluorescent and nonfluorescent ones. Owing to the different positions of the absorption maxima and the selection of suitable optical filters, each of the dyes could be excited separately: light with a wavelength of 436 nm only excited **2**, while dye **1** remained dark. The different fluorescence behavior of the dyes allowed an exact assignment of the particles resulting from catalysts **B** and **C**.

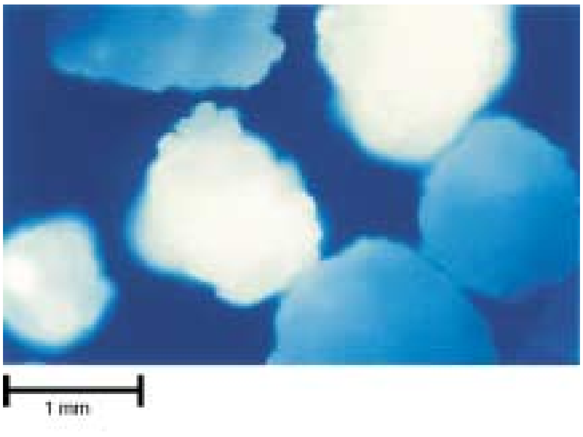

Figure 4. Fluorescence microscope image of the polymer products obtained from the labeled catalysts **B** and **C**.

For separation, the particles were exposed to UV light of 354 nm and 15 particles (ca. 15 mg) were collected. The amount of polymer collected was sufficient to allow a standard polymer characterization; thus we were able to determine copolymer composition (by NMR spectroscopy), melting temperatures (T_m) (by differential scanning calorimetry (DSC) measurements), molecular weights and distributions (by gel permeation chromatography (GPC)) and even crystallinity (by powder diffractometry).

The emission spectra as well as the fluorescence microscope images of the polyethylene samples showed that no migration of labels had occurred. Furthermore, the stability of the dyes under the aggressive reaction conditions with strong Lewis acids and alkylating reagents could be demonstrated.

For each sample the shape of the GPC curves showed a monomodal distribution. Catalyst **B** produced polyethylene with a molecular weight M_n of 207000 Da and a molecular weight distribution D of 2.24; polyethylene from catalyst **C** exhibited almost half the molecular weight M_n of 124000 Da and a broad polydispersity D of 3.47. These results agreed exactly with GPC data obtained from single runs with each catalyst. Additionally, the shape of the GPC curves as well as the values indicated that no exchange of catalyst between the particles took place.

To prove that there is no exchange either of catalyst or of the dyes on the product beads, two different catalysts were used known for having strongly different behavior in the copolymerization of ethylene/hexene. By means of DSC measurements the melting temperatures were used as a probe to determine the amount of incorporated hexene. A migration of the metallocenes should easily be detectable by any deviation from the expected melting temperatures.

Catalyst **D** contained **4** and **2** as a tag. Catalyst **E** consisted of metallocene **3** and was labeled with **1**. Each catalyst system was run separately with and without dye, and then as a mixture. Table 2 indicates that the dye had no influence on T_m, and that the M_n values (GPC measurements) were essentially unaffected. This clearly demonstrates that the copolymerization behavior was independent of the dye. More importantly, however, the polymers obtained in the isolated mixture of different tagged product beads have the same properties as in the single experiment.

Table 2. Copolymerization of ethylene/hexene (40 bar, 70 °C, 5 mL TIBA).

	Dye	Zirconocene	T_m	M_n
D	–	**4**	129.3	113000
	1	**4**	129.9	107000
E	–	**3**	119.5	227000
	2	**3**	119.0	234000
mixture of **D** + **E**				
particles of **D**	**1**	**4**	129.3	117000
particles of **E**	**2**	**3**	120.3	221000

The concept described herein can be implemented in present polymerization and analytical facilities. The sets of two catalysts can be easily enlarged because a great variety of rylene dyes covering the whole visible spectra is available.[9] Our rapid testing and comparison of supported metallocene catalysts under identical experimental conditions is suitable for other heterogeneous polymerization processes. In order to create larger libraries of heterogeneous catalysts, on-line methods for the detection and characterization of the particles will have to be developed and applied.

Experimental Section

Procedure for supporting and labeling zirconocenes: All experiments were performed under argon by using standard Schlenk techniques. Catalyst **B**: SiO_2/MAO (2.50 g, 25 % MAO on silica, TA 02794/HL, Witco GmbH, Bergkamen, Germany) was suspended in toluene (100 mL) followed by addition of **4** (7 mg) in toluene (50 mL) at room temperature and stirred for 2 h. Subsequently, a solution of dye **1** (60 mg) in toluene (50 mL) was added dropwise and the mixture was stirred for 1 h. The almost colorless solution was removed by filtration and the resulting silica/MAO/zirconocene/dye catalyst system was washed twice with toluene and dried in vacuum. Catalysts **C**–**E** were prepared in a similar way.

Polymerization: General procedure: Two catalysts were mixed and used simultaneously in a single vessel for the polymerization of ethylene. Isobutane (400 mL) and triisobutylaluminum (TIBA)(5 mL; 10 % in n-hexane) were introduced into a Büchi stainless steel reactor (1 L) equipped with a magnetic stirrer and saturated with ethylene (standard conditions: 40 bar, 70 °C). The mixture of catalysts was introduced into the reactor using a pressure gate. After 90 min the polymerization was stopped by releasing the pressure.[10]

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[10] All polymerization experiments presented herein were repeated at least two times to prove the reproducibility.

An Allosteric Ribozyme Regulated by Doxycyline**

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Specific ligand-binding nucleic acid molecules (aptamers) can be isolated by searching the "shape-space" of vast combinatorial nucleic acid libraries for functional sequences in vitro.[1–3] Selection strategies for the isolation of aptamers usually involve incubation of a complex library of nucleic acids with the immobilized target molecule or the immobilization of a preformed target/nucleic acid complex.

A considerable number of RNA aptamers that bind a variety of targets with high affinity and specificity have been isolated and extensively characterized. Detailed structural investigations of many aptamer/ligand complexes have established that complex formation in most cases is accompanied by extensive conformational changes only in the presence of the cognate ligand by adaptive binding events.[4–11] This property of small-molecule-binding aptamers allowed the rational design of artificial allosteric ribozymes inhibited or activated by a ligand that is bound to an aptamer which has been positioned in immediate proximity to a ribozyme sequence.[12–15]

We have applied a novel in vitro selection strategy based on allosteric inhibition of a hammerhead ribozyme fused to a

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