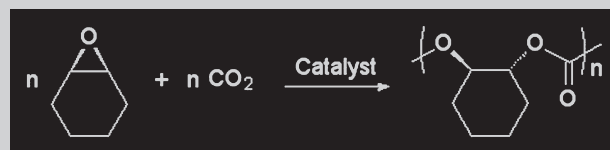


Summary: Copolymerization of CO₂ and oxiranes using high-pressure autoclaves typically allows one experiment per reactor per day. As a high-throughput approach for this chemistry would be extremely valuable, a parallel setup has been validated for the copolymerization of CO₂ and cyclohexene oxide (CHO) with two β -diiminato zinc complexes. Molecular weights, polydispersities and activities were found to be comparable with literature values.



Polycarbonate from cyclohexene oxide (CHO) and CO₂.

High-Throughput Automated Parallel Evaluation of Zinc-Based Catalysts for the Copolymerization of CHO and CO₂ to Polycarbonates

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Introduction

Although the physical properties of *aliphatic* polycarbonates do not yet approach the good impact strength, heat resistance and transparency of commercially available poly-(bisphenol-A carbonate),^[1] they are accessible by a very attractive route, a metal-catalyzed copolymerization of CO₂ and an oxirane.^[2] This process is much more environmentally friendly than the two routes currently used for the commercial production of *aromatic* polycarbonates.^[1] Carbon dioxide (Scheme 1) is a readily available, cheap, nonflammable, nontoxic and renewable monomer.^[3] The chain-growth mechanism of this process allows a much higher control of the molecular weight and unlike step-growth processes conversions do not have to approach 100% in order to obtain high-molecular-weight products. Since the discovery by Inoue et al.,^[4] extensive effort has been put into the development of more active catalysts that allow a better control over the polymerization process.^[5] Good examples are the zinc phenoxide complexes developed by Darensbourg et al.^[6] and the aluminum and chromium porphyrine complexes developed by the group of Inoue and Mang and co-workers, respectively.^[7] A system of specific interest was developed by the group of Coates and consists of β -diiminato zinc complexes.^[8] These species show high activity and selectivity

in CHO–CO₂ copolymerizations. More importantly, relatively low pressures (5–10 bar) are required as compared with the 80–120 bar needed for most other systems.^[5]

In this communication we like to demonstrate that a high-throughput approach towards further development and fine tuning of these copolymerizations is feasible with the current state of the art equipment available on the market, allowing a significant efficiency increase.

Experimental Part

Materials

Cyclohexene oxide (Aldrich) was dried over CaH₂, distilled and stored under argon on molsieves (4 Å) prior to use. Carbon dioxide (> 99.9993% pure) was purchased from HoekLoos. Toluene was dried over an alumina column and stored on molsieves. The β -diiminato (BDI) zinc catalysts [HC(C(CH₃)-N-2,6-R-C₆H₃)₂][Zn–N(SiMe₃)₂] (R = Et (1), *i*Pr (2)) were synthesized according to literature procedures.^[9]

Instruments

¹H NMR spectra were recorded on a Varian Gemini 2000 (300 MHz) and a Varian Mercury Vx (400 MHz) spectrometer. Size Exclusion Chromatography (SEC) spectra were recorded



Scheme 1. Polycarbonate from cyclohexene oxide (CHO) and CO_2 .

on Waters GPC equipped with a Waters model 510 pump and a model 410 differential refractometer (40°C). THF was used as the eluent at a flow rate of $1.0\text{ mL}\cdot\text{min}^{-1}$. A set of two linear columns (Mixed C. Polymer Laboratories, 30 cm , 40°C) was used. Molecular weights were calculated relative to polystyrene. Data acquisition and processing were performed using Waters Millennium32 software. The reactions were carried out in a custom made catalyst screening platform at Avantium Technologies. The system, which was specifically designed to avoid mass-transfer limitation issues, consists of modular blocks of twelve individual reactors (Figure 1) that after addition of the required components are sealed inside the glovebox. The sealed blocks are transferred from the glovebox to the reaction station (Figure 1), which consists of 2 beds, with 96 individually magnetically stirred positions. Each of the 2 beds can be operated at a different reaction temperature. Reaction time can be varied per block of 12 reactors by the modular feed-gas setup or by inserting/removing blocks at a desired time.

For this feasibility study, one block of 12 reactors was used. Each stainless steel reactor was used with a Teflon insert which reduced the maximum working volume to about 5 mL . The 96-position bed was heated by both electrical heating and by a circulating oil thermostat. The lab-scale copolymerization was performed in a Hastelloy Premex reactor equipped with a bottom tap for sampling purposes.

High-Throughput Experiments

Prior to use, the reactor block was heated to 70°C for an hour and was left to cool under vacuum in the antechamber of the

glovebox for 10 min. After two more evacuation cycles the reactor block was transferred to the glovebox and all reactors were equipped with a Teflon insert. The inserts were filled with 3 mL of CHO and 1 mL of catalyst solution of the appropriate concentration in toluene. After filling, the reactor block was sealed and transferred outside the glovebox to the heating jack. Once the reactors were placed in the reaction bed, the gas-lines were purged with CO_2 and the reactors were pressurized to 10 bar and heated to 50°C , using a gas-on-demand (constant pressure) mode of operation. After 3 h the reactors were cooled and depressurized. A sample from each reactor was taken for $^1\text{H NMR}$ analysis (300 MHz , CDCl_3) to determine the conversion. Conversions were determined by integration of the methine peaks in the $^1\text{H NMR}$ spectrograms: $^1\text{H NMR}$ (300 MHz , CDCl_3): δ 4.65 (br, CH (PCHC), 2H), 3.11 (s, CH (CHO), 2H). The samples for SEC analyses were prepared as follows: About 0.5 mL of each of the reaction mixtures was added dropwise to a 10-fold excess of petroleum ether ($40\text{--}70$) upon which the poly(cyclohexene carbonate) (PCHC) precipitated. After separation, the polymer was redissolved in the GPC eluent THF.

Reference Polymerization in 380 mL Autoclave

(BDI-2)ZnAmide (190 mg ; $295\text{ }\mu\text{mol}$; $0.06\text{ mol-}\%$) was dissolved in a mixture of CHO (50 mL ; 495 mmol) and toluene (16.7 mL). After complete dissolution of the catalyst, the mixture was injected into an autoclave that was previously dried under vacuum at 100°C for eight hours. At regular intervals samples ($\pm 1\text{ mL}$) were collected by the bottom needle valve which was rinsed with THF after every sample to avoid cross-contamination. Isolation and characterization were performed as described above.

Results and Discussion

Known catalysts were used as the objective of this study was the validation of a research method. We selected the

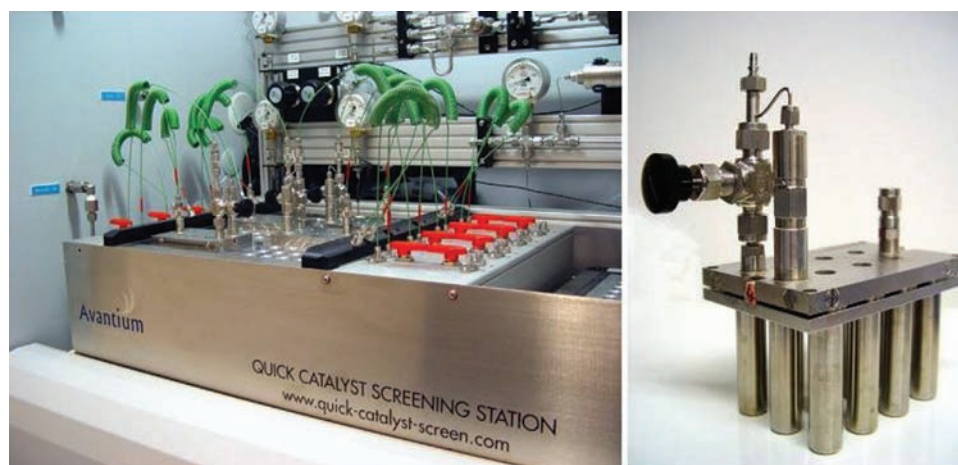
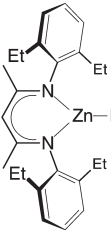
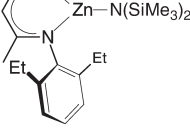
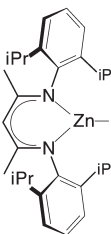
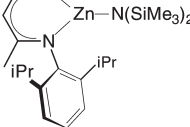


Figure 1. Reaction station with several blocks of 12 reactors connected to gas-inlet tubes (left) and block of 12 reactors which can be filled in the glovebox (right).

Table 1. Polymerization results of high-throughput experiments.

| Reaction No. | Catalyst | Mol-% catalyst ^{a)} | Conversion ^{b)} | | TOF ^{c)} | | \bar{M}_w ($\times 10^3$ g/mol) ^{d)} | | \bar{M}_w/\bar{M}_n | |
|--------------|---|------------------------------|--------------------------|-------|-------------------|-------|--|-------|-----------------------|-------|
| | | | Exp 1 | Exp 2 | Exp 1 | Exp 2 | Exp 1 | Exp 2 | Exp 1 | Exp 2 |
| #1 |  | 0.03% | 3% | 0% | 32 | 0 | 2.6 | 0 | 1.1 | 0 |
| #2 |  | 0.06% | 20% | 21% | 105 | 111 | 19.4 | 20.6 | 1.1 | 1.1 |
| #3 | (BDI-1)ZnAmide | 0.09% | 11% | 25% | 38 | 88 | 9.3 | 23.8 | 1.2 | 1.2 |
| #4 |  | 0.03% | 4% | 5% | 41 | 51 | 3.4 | 3.5 | 1.2 | 1.1 |
| #5 |  | 0.06% | 23% | 25% | 122 | 131 | 25.1 | 30.0 | 1.1 | 1.2 |
| #6 | (BDI-2)ZnAmide | 0.09% | 30% | 27% | 105 | 93 | 31.5 | 28.1 | 1.2 | 1.2 |

^{a)} mol-% of catalyst with respect to the monomer.

^{b)} Determined by ^1H NMR spectroscopy.

^{c)} mol CHO \cdot mol \cdot catalyst $^{-1}$ \cdot hour $^{-1}$.

^{d)} Polystyrene equivalents.

β -diiminato zinc amide catalysts with ethyl- (BDI-1) and *iso*-propyl- (BDI-2) substituted aryl groups (see Table 1) for their proven high copolymerization activities.^[10] For the high-throughput experiments, twelve copolymerization reactions were performed simultaneously. The two zinc catalysts ((BDI-1)ZnAmide and (BDI-2)ZnAmide) were applied in three different concentrations (0.03%, 0.06% and 0.09% with respect to the amount of CHO used). To test the reproducibility of the setup, each combination was performed in

duplicate. Conversions were determined by integration of the polymeric versus the monomeric methine proton resonance in the ^1H NMR spectra. A summary of the results is presented in Table 1. Several interesting features can be derived from the results depicted in Table 1 and Figure 2. Let us first look at the reproducibility of the results. Except for experiment 2 of reaction #1 and experiment 1 of reaction #3, the conversions obtained are as expected and the duplicate runs are similar with a small deviation of approximately 3%.

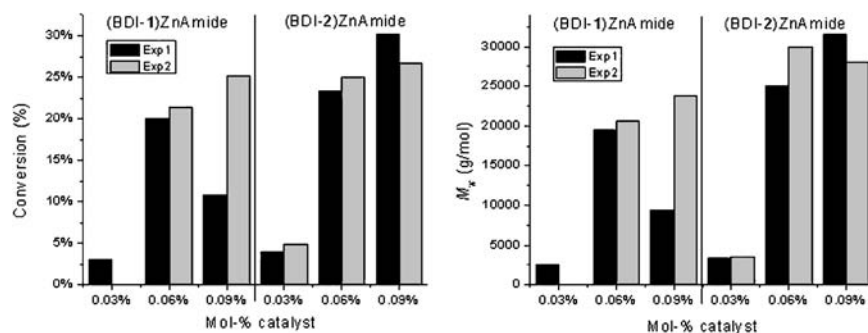


Figure 2. CHO conversions from ^1H NMR analyses and \bar{M}_w values from SEC analyses.

The molecular weights nicely follow the same trend as the conversions. For example, the somewhat higher conversion in experiment 1 of reaction #2 and #6 or experiment 2 of reaction #5 is reflected in a slightly higher molecular weight. Reaction #1 and #3 clearly show different results for the duplicate experiments. The conversion of experiment 1 of reaction #3 is only half of what was expected, while no conversion at all was observed for experiment 2 of reaction #1. These observations are most likely due to the poisonous effect of water^[9] present in small but different amounts in the reactors of the specific experiments, which most probably is the result of improper manual filling of the reactor block. With automated filling and sampling such errors can be avoided in the future.

Another interesting feature is the observed conversion and molecular weights of the polymers obtained at different catalyst concentrations. For a living catalyst system (meaning a system with no chain termination or transfer) like $[\text{HC}(\text{C}(\text{CH}_3)\text{N}-2,6\text{-R}-\text{C}_6\text{H}_3)_2\text{Zn}-\text{N}(\text{SiMe}_3)_2]$ ($\text{R} = \text{Et}$ (**1**), $i\text{Pr}$ (**2**)), one would expect a linear increase in conversion with increasing catalyst concentration at low conversions, while the molecular weight of the polymer remains the same. At higher conversions, a decrease in molecular weight is expected with increasing catalyst concentration since the same amount of monomer is consumed by more chains. As can be seen from Table 1 the CHO conversion strongly increases when going from a catalyst concentration of 0.03 mol-% to 0.06 mol-% but hardly increased when the catalyst concentration is increased further to 0.09 mol-%. Theoretically one would expect an increase of the conversion of 1.5 times going from a catalyst concentration of 0.06% to 0.09% and halving of the conversion when going from a catalyst concentration of 0.06% to 0.03%. The lower observed conversion for the system with a catalyst concentration of 0.03% can readily be explained by the presence of traces of water. For these low catalyst concentrations (30 ppm), which are at the lower limit of what is possible in the current setup, traces of water effectively “kill” the catalyst soon after the start of the polymerization. Since the molecular weights that were obtained are also very low (Figure 2) it seems unlikely that only a part of the catalyst is rendered inactive by the water. Hence, initiation of the catalyst is fast compared with the poisoning by water. The possibility of water acting as a chain transfer agent (as Colomb et al. observed for the ring opening polymerization of trimethylene carbonate with alcohols) is unlikely since the Zn–OH species formed will dimerize very easily forming and inactive species.^[11] This is further supported by the low polydispersities (< 1.2) found here and the living nature of the catalyst as suggested by Coates and co-workers.^[9]

Both the conversion and the molecular weights for the systems with a catalyst concentration of 0.09 mol-% (reactions #3 and #6) are only slightly higher than those observed for the systems with a catalyst concentration of

0.06 mol-% (reactions #2 and #5). For these polymerizations, the viscosity rapidly increases with conversion, which has a pronounced retarding effect on the polymerization rate. However, it is not likely that mass transport limitations at higher conversion cause the relative low conversion and molecular weight for the 0.09% system, since the effect is similarly strong for catalyst systems **1** and **2**. Since catalyst **1** results in both a lower conversion and a lower molecular weight, the reaction mixtures for catalyst system **1** are significantly less viscous than for catalyst system **2**. Therefore one would expect a larger difference in conversion and molecular weight for reaction #2 and #3, compared with reaction #5 and #6, which is not observed.

A possible explanation for the unexpected low conversion and molecular weight for reactions #4 and #6 might be the presence of a monomer–dimer equilibrium of the catalyst although this effect is not fully understood yet. Based on the observation that catalyst system **2** gave a bimodal distribution of the molecular weight, Rieger et al.^[12] reported that the active catalyst exists both in monomeric and dimeric form in solution. These bimodal distributions (small shoulder at higher molecular weights) have also been observed in our experiments. Rieger and co-workers found that the concentration of the dimeric species decreased with increasing temperature, leading to a relative decrease of the high-molecular-weight polymer fraction. Thermodynamically, the concentration of dimeric zinc complex should also increase with increasing initial catalyst concentration. Further study will be undertaken to fully understand the consequences of this observed equilibrium on the catalyst performance.

To assess the scalability of the results, viscosity behavior and catalyst stability at longer reaction time and high conversion, reaction #5 was repeated on a larger scale (50 mL CHO, 0.06 mol-% Zn, 16.7 mL toluene) in an autoclave. During this lab-scale reaction, samples were taken at regular intervals to follow the conversion and molecular weight development in time (Figure 3).

For the CHO–CO₂ copolymerization the viscosity is known to rapidly increase with increasing conversion. Consequently, conversions higher than 40% are difficult to achieve as a result of severe mass transport limitation. Figure 3 clearly shows a decreasing activity at longer reaction times as a result of diffusion limitation, which also influences the expected linear correlation of \bar{M}_n versus time for a living system. However, the plot of \bar{M}_n versus the conversion (Figure 3) shows a straight line and confirms the living nature of the catalyst and indicates that the catalyst is active for prolonged reaction time.

The catalyst activities for the high-throughput experiments are in the same order as reported in literature (a TOF of 219 was reported by Coates et al. against the 126 (± 5) found here).^[9] The slightly lower values can be explained by the fact that in this study a more diluted system was used in combination with a somewhat longer

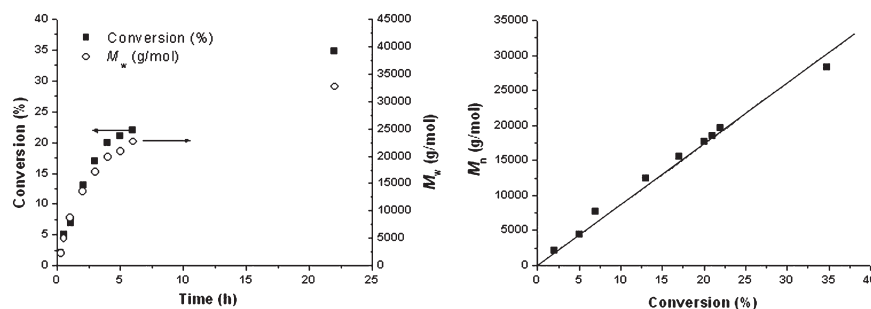


Figure 3. Conversion and molecular weight development over time and \bar{M}_n plotted against conversion.

reaction time (3 against 2 hours).^[13] The activity and molecular weight for the lab-scale reaction are lower than those found in the high-throughput experiment (a TOF of 92 was found after a reaction time of 3 hours against the 132 found in reaction #5 experiment 2), probably caused by a more pronounced mass transfer limitation in the larger scale equipment.

Currently, we are expanding the high-throughput approach to evaluate different catalysts for the copolymerization of a large variety of oxiranes with carbon dioxide at higher pressures and temperature.

Conclusion

In this communication we reported the successful application of a high-throughput approach for the copolymerization of carbon dioxide and cyclohexene oxide with two β -diiminato zinc complexes. It was shown that the polymerizations were controlled and reproducible although not every reaction was successful. Catalyst activities suggest that there can be up to 9 micromol of water present in the reactors. Most likely a mistake in the addition or traces of moisture deactivates the very small catalyst amounts involved. Until the reason for this failure is known duplicate experiments are obligatory.

A scaled-up experiment to conventional lab-scale, which was sampled and analyzed over time, showed a living system, although with somewhat lower activity than in the high-throughput experiment. We assume this to be caused by more severe mass-transfer limitation in the larger scale equipment.

With automated catalyst addition, the reactor system described will be used to further investigate catalyst systems for the copolymerization of CHO and CO₂.

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- [13] TOFs reported here are based on a longer reaction time than TOFs reported by Coates. Since the viscosity rapidly increases with increasing conversion, the TOF will drop with time and therefore the average TOF will consequently be lower.