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Redox Control of Group 4 Metal Ring-Opening Polymerization Activity toward L-Lactide and ε-Caprolactone

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Supporting Information

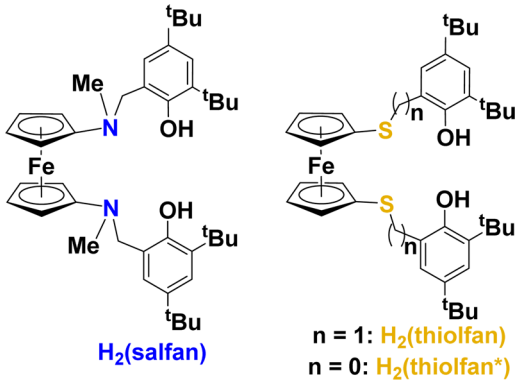
ABSTRACT: The activity of several group 4 metal alkoxide complexes supported by ferrocene-based ligands was controlled using redox reagents during the ring-opening polymerization of L-lactide and ε-caprolactone. Switching in situ between the oxidized and reduced forms of a metal complex resulted in a change in the corresponding rate of polymerization. Opposite behavior was observed for each monomer used. One-pot copolymerization of the two monomers to give block copolymers was also achieved.

Temporally switchable polymerization processes have received increased attention because they hold the promise of mimicking the selectivity exhibited by natural systems.[1,2] Allosteric,[3] chemical,[4] electrochemical,[5] photochemical,[6] and mechanochemical[7] control have been employed to turn on/off various polymerizations.[1] In the realm of chemical control, processes involving metal complexes containing redox-switchable groups are especially interesting because these groups provide a way to alter selectivity without the need for further, extensive synthetic steps to achieve ligand modification.[8] The first example using a metallocene redox switch in order to influence catalytic selectivity was reported by Wrighton's group in 1995.[9] In that seminal work, the authors showed that a rhodium complex containing cobaltocene (reduced form) is a better catalyst for the hydrogenation of olefins than the complex incorporating cobaltocenium (oxidized form). The reverse trend was observed for the hydrosilylation of acetone. Since then, several groups have reported switchable catalysts using redox-active substituents.[3,4,10−18] However, Wrighton's report is still the only example in which both the oxidized and reduced forms of a catalyst show activity and selectivity toward different substrates. Herein, we report a class of group 4 metal alkoxide complexes supported by ferrocene-based ligands that show switchable selectivity toward L-lactide and ε-caprolactone in the oxidized and reduced forms for the corresponding ring-opening polymerization processes. One-pot copolymerization of the two monomers to give block copolymers is also discussed.

In the area of switchable polymerization reactions,[19−22] Long et al. reported first that the rate of ring-opening polymerization of *rac*-lactide could be altered by changing the redox state of a ferrocenyl unit in a titanium salen bis(isopropoxide) catalyst.[4] We recently reported a similar behavior using a yttrium alkoxide.[18] In both cases, a decrease in reactivity toward lactide was observed after the oxidation of the ferrocene group. However, a change from yttrium to indium brought to light the opposite behavior: while the yttrium complex loses its activity toward trimethylene carbonate upon oxidation, the corresponding indium complex showed increased activity toward the same substrate.[18] A cerium(III)/(IV) redox switch presented analogous behavior to the yttrium system and allowed us to study it using DFT calculations.[17] On the basis of those results, we interpret the difference between the two oxidation states to be the result of large changes in the binding profile to the two oxidation states; i.e., for early transition metals, cationic complexes make stronger bonds with the polar substrates of interest than the corresponding neutral complexes. Guided by these results, we decided to turn to group 4 metal complexes in order to test whether a better balance between the oxidized and reduced complexes exists, such that the cationic/oxidized states would still show activity toward polar substrates.

Given the success of [OEEO]-type (E = N, O) bis(phenolato) ligands in group 4 metal catalysis,[23−25] we focused on the following three pro-ligands (Chart 1): H_2(salfan) (1,1′-di(2,4-di-*tert*-butyl-6-*N*-methylmethylenephenol)ferrocene), H_2(thiolfan) (1,1′-di(2,4-di-*tert*-butyl-6-thiomethylenephenol)-ferrocene), and H_2(thiolfan*) (1,1′-di(2,4-di-*tert*-butyl-6-thiophenol)ferrocene). Compounds (salfan)Zr(O^{t}Bu)$_2$ (**1**^{red}),

Chart 1. New Supporting Ferrocene-Based Pro-Ligands



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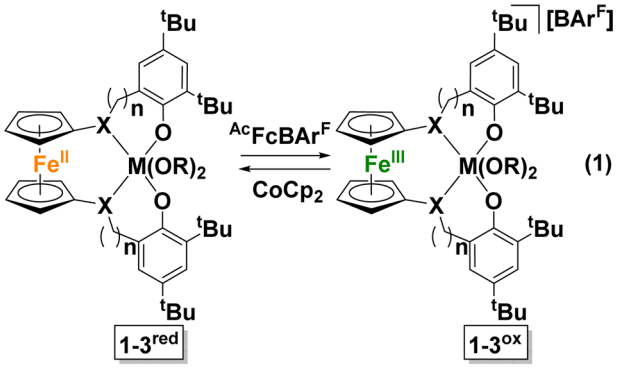
(thiolfan)Zr(O^tBu)$_2$ (2^{red}), and (thiolfan*)Ti(O^iPr)$_2$ (3^{red}) were synthesized from the reaction of Zr(O^tBu)$_4$ or Ti(O^iPr)$_4$ and each of the respective pro-ligands. All three metal complexes were characterized in the solid state by single-crystal X-ray diffraction (Figures S69–S72). The two alkoxide ligands coordinate cis to each other in all metal complexes; however, a difference between the two zirconium complexes is observed: both *t*-butoxide ligands are found trans to a sulfur donor in (thiolfan)Zr(O^tBu)$_2$, but, in (salfan)Zr(O^tBu)$_2$, one of them is trans to a nitrogen, while the other is found cis to both nitrogen donors. This relatively small difference in the zirconium coordination environments may cause some of the differences observed in their reactivity behavior (see below).

Electrochemical studies performed with (salfan)Zr(O^tBu)$_2$, (thiolfan)Zr(O^tBu)$_2$, and (thiolfan*)Ti(O^iPr)$_2$ ($E_{1/2}$ = −0.57, 0.07, and 0.02 V vs ferrocene, respectively) indicated that ferrocenium salts might oxidize the ferrocene backbone in these compounds. Indeed, the addition of 1 equiv of acetyl ferrocenium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate ($^{Ac}FcBAr^F$) in C_6D_6 resulted within minutes in dark-colored products, [(salfan)Zr(O^tBu)$_2$][BAr^F] (1^{ox}), [(thiolfan)Zr(O^tBu)$_2$][BAr^F] (2^{ox}), and [(thiolfan*)Ti(O^iPr)$_2$][BAr^F] (3^{ox}), respectively (eq 1). The ^{1}H NMR spectra of these



(1)

compounds indicated the formation of paramagnetic species, as expected. Each paramagnetic product could be reduced to the respective starting material, (salfan)Zr(O^tBu)$_2$, (thiolfan)Zr(O^tBu)$_2$, and (thiolfan*)Ti(O^iPr)$_2$, through the addition of 1 equiv of $CoCp_2$ (see the Supporting Information for details). Compound [(thiolfan)Zr(O^tBu)$_2$][BAr^F] was characterized by single-crystal X-ray diffraction (Figure S73).

Once the ferrocene and ferrocenium-based compounds were characterized, the polymerizations of L-lactide (LA) and ε-caprolactone (CL) were attempted (Table 1). At 100 °C in C_6D_6, (salfan)Zr(O^tBu)$_2$ polymerizes 100 equiv of L-lactide in 2 h with 90% conversion, while <5% conversion was observed in the presence of [(salfan)Zr(O^tBu)$_2$][BAr^F] under the same conditions. This difference in reactivity is maintained at various temperatures (80, 90, 100 °C, Table S1). A similar trend was observed for (thiolfan)Zr(O^tBu)$_2$, which achieves 93% conversion in 8 h, and (thiolfan*)Ti(O^iPr)$_2$, which leads to 82% conversion in 60 h, while <5% conversion was observed in the presence of [(thiolfan)Zr(O^tBu)$_2$][BAr^F] or [(thiolfan*)Ti(O^iPr)$_2$][BAr^F], respectively (Table 1).

On the other hand, the activity toward ε-caprolactone shows the opposite trend: at 25 °C in C_6D_6, (salfan)Zr(O^tBu)$_2$ converts <5% of 100 equiv in 24 h, while 98% conversion

Table 1. Reactivity of Oxidized and Reduced Complexes toward L-Lactide (LA) and ε-Caprolactone (CL)[a]

				M_n		
initiator	monomer	time (h)	conversion (%)	GPC	calcd	PDI
1^{red}	LA	2	90	7.31	6.77	1.16
1^{ox}	LA	2	<5			
2^{red}	LA	8	93	7.83	6.70	1.10
2^{ox}	LA	8	<5			
3^{red}	LA	60	82	4.49	5.90	1.14
3^{ox}	LA	36	<5			
1^{red}	CL	24	<5			
1^{ox}	CL	24	98	6.95	5.59	1.06
2^{red}	CL	1.5	57	3.87	3.25	1.10
2^{ox}	CL	1.5	92	8.26	5.24	1.14
3^{red}	CL	2	<5			
3^{ox}	CL	4	48	3.20	2.70	1.12

[a]Conditions: monomer (0.50 mmol), initiator (0.005 mmol), oxidant (0.005 mmol, 5.5 mg), d_6-benzene as solvent (0.5 mL), 1,3,5-trimethoxybenzene as an internal standard. All experiments were performed at 100 °C, except for those corresponding to entries 7 and 8, which were performed at 25 °C. M_n are reported in 10^3 g/mol; PDI = M_w/M_n; theoretical M_n values were calculated by assuming dual propagation chains. d*n*/d*c* values: PLA, 0.044 mL/g; PCL, 0.075 mL/g.

was observed in the presence of [(salfan)Zr(O^tBu)$_2$][BAr^F] under the same conditions (Table 1). As with L-lactide, this difference in reactivity is maintained at various temperatures with only a slight decrease in selectivity (80, 90, 100 °C, Table S2). Similarly, [(thiolfan)Zr(O^tBu)$_2$][BAr^F] or [(thiolfan*)Ti(O^iPr)$_2$][BAr^F] show higher activity toward ε-caprolactone than their reduced counterparts (Table 1).

Since (salfan)Zr(O^tBu)$_2$ showed better activity and selectivity toward the two substrates, we decided to focus our selectivity studies on this compound. Switching in situ between the oxidized and reduced forms of (salfan)Zr(O^tBu)$_2$ was examined in the presence of both monomers (Figure 1). After 54 min at 95 °C, the polymerization of L-lactide by (salfan)Zr(O^tBu)$_2$ reached 43% conversion. Upon oxidation with $^{Ac}FcBAr^F$, the polymerization halted. Once $CoCp_2$ was added to the reaction mixture, the polymerization resumed with the same rate as before the switch was performed (see the Supporting Information for details, Figure S56). In the case of ε-caprolactone (Figure S58), starting with [(salfan)Zr(O^tBu)$_2$][BAr^F], the polymerization reached 39% conversion after 38 min at 80 °C. Upon reduction with $CoCp_2$, the polymerization almost stopped; once $^{Ac}FcBAr^F$ was added to the reaction mixtures, the polymerization resumed with a rate similar to that before the switch was performed. In addition, in situ switching was performed three consecutive times; it was found that there was minimal change in the rate of the reaction before or after changing the iron oxidation states (see the Supporting Information for details, Figures S57 and S59).

The polymers obtained from the above reactions were characterized by gel permeation chromatography (GPC). The molecular weights are close in value to the corresponding theoretical molecular weights and the PDIs (PDI = M_w/M_n) are ca. 1.1–1.2; these data indicate a controlled polymerization process in all cases (Table 1). End-group analysis of lactide polymerization (Figure S44) indicates that this reaction proceeds through a coordination–insertion mechanism. Unfortunately, a similar study could not be performed for the

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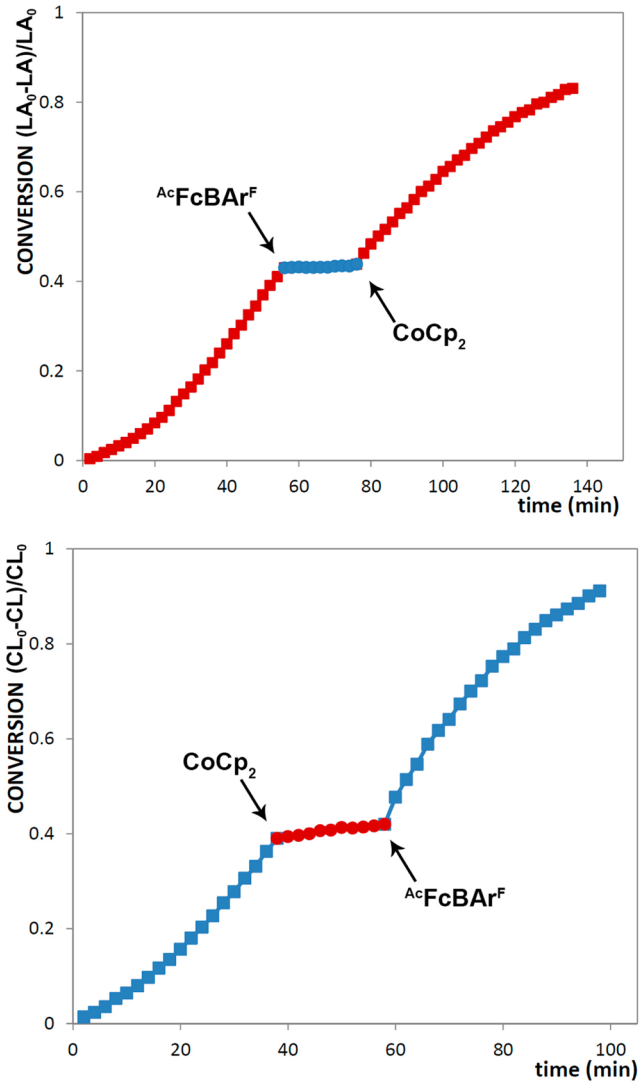


Figure 1. Plot of conversion vs time for the polymerization of L-lactide (50 equiv, 0.5 M) starting with (salfan)Zr(O^tBu)$_2$ (top) and ε-caprolactone (100 equiv, 1.0 M) starting with [(salfan)Zr(O^tBu)$_2$][BAr^F] (bottom) in C_6D_6 using in situ oxidation and reduction with $^{Ac}FcBAr^F$ and $CoCp_2$, respectively.

polymerization of ε-caprolactone because of overlap between the *tert*-butyl peaks and the alkyl peaks of polycaprolactone. GPC analysis of the polymers produced from L-lactide or ε-caprolactone by switching in situ between (salfan)Zr(O^tBu)$_2$ and [(salfan)Zr(O^tBu)$_2$][BAr^F] shows that the polymerization is also controlled when using redox agents, with PDIs in the 1.08−1.20 range (Tables 2 and S3).

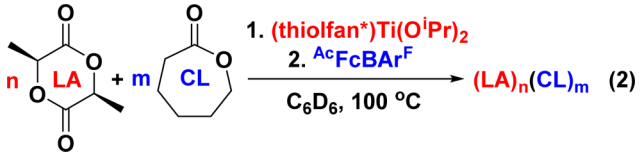
As a proof of concept, one-pot copolymerization of L-lactide and ε-caprolactone by in situ switching the redox states of the initiator was attempted. Although L-lactide was polymerized by the reduced form of (salfan)Zr(O^tBu)$_2$, polymerization of ε-caprolactone did not occur upon addition of the oxidant. We attribute this lack of reactivity to a strong coordination of L-lactide to the oxidized zirconium complex (see below). We reasoned that the titanium complex might alleviate this problem since its complexes are less electrophilic than the corresponding zirconium counterparts.

Gratifyingly, the one-pot copolymerization of L-lactide and ε-caprolactone catalyzed by (thiolfan*)Ti(O^iPr)$_2$ was successful (eq 2): L-lactide was first polymerized with 58% conversion at

Table 2. In Situ Switching during the Polymerization of L-Lactide (1.0 M in Benzene) with (salfan)Zr(O^tBu)$_2$[a]

complex	time (min)	conversion (%)	M_n	PDI
(salfan)Zr(O^tBu)$_2$	40	57	4.68	1.08
add $^{Ac}FcBAr^F$	20	56	4.24	1.09
add $CoCp_2$	40	92	7.68	1.15

[a]Conditions: monomer (0.50 mmol), initiator (0.005 mmol), oxidant (0.005 mmol, 5.5 mg), 100 °C, d_6-benzene as solvent (0.5 mL), 1,3,5-trimethoxybenzene as an internal standard. Experiments were performed individually. M_n are reported in 10^3 g/mol; PDI = M_w/M_n. d*n*/d*c* values: PLA, 0.044 mL/g; PCL, 0.075 mL/g.



(2)

100 °C for 36 h by the reduced form of the initiator, while almost no conversion was observed for ε-caprolactone at this stage. After addition of the oxidant at room temperature, ε-caprolactone was then polymerized with 18% conversion at 100 °C for another 2 h, while almost no conversion was observed for L-lactide during this step (Figure S48). The resulting block copolymer was isolated and characterized by ^1H NMR spectroscopy and GPC that indicate that the copolymer is best described as poly[block(LA-minor-CL)-block(CL-minor-LA)]; i.e., some incorporation of the monomer that is not predominantly converted was still observed. The protons corresponding to the juncture of the two blocks could be identified by ^1H NMR spectroscopy (Figure S53), while the polymer chain extension was clearly demonstrated by comparing its GPC trace with that of the polymer obtained with the same initiator before the oxidation event (Figure 2). At

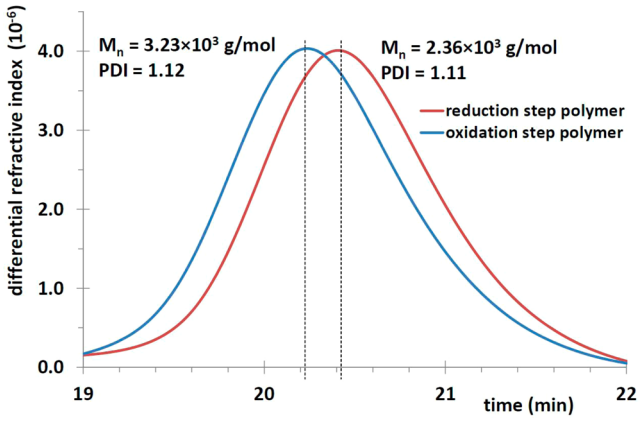


Figure 2. GPC traces of the LA-CL copolymer produced by redox switching copolymerization (blue) and the polymer produced before switching (red) using (thiolfan*)Ti(O^iPr)$_2$.

the same time, the PDIs of both polymers are narrow (1.11 for the homopolymer and 1.12 for the copolymer), indicating that the copolymerization process is well controlled. Attempts to increase the amount of ε-caprolactone by increasing the reaction time led to a decrease in selectivity and higher incorporation of L-lactide (Table S4).

We propose that the lack of copolymerization activity observed with the oxidized zirconium complexes stems from

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the higher Lewis acidity of zirconium compared to that of titanium that increases the bond strengths of all intermediates for the cationic compound.[17] As mentioned earlier, a softer Lewis acid is likely to balance this effect.[18] In addition, the reaction of a cationic yttrium complex (obtained from the oxidation of a ferrocene-based ligand) and 1 equiv of L-lactide showed that the product did not react with another 1 equiv of L-lactide,[18] presumably because L-lactide could not open the five-membered ring formed after the ring opening of the first molecule (compound B in Scheme S1; see also Figures S45−47 for further studies).

In conclusion, we described the first example of substrate selectivity by using redox control of a zirconium precatalyst in the ring opening polymerization of L-lactide and ε-caprolactone. The reduced forms, compounds (salfan)Zr(O^tBu)$_2$, (thiolfan)Zr(O^tBu)$_2$, and (thiolfan*)Ti(O^iPr)$_2$, showed higher activity toward lactide, while the oxidized counterparts, [(salfan)Zr(O^tBu)$_2$][BAr^F], [(thiolfan)Zr(O^tBu)$_2$][BAr^F], and [(thiolfan*)Ti(O^iPr)$_2$][BAr^F], showed higher activity toward caprolactone. The precatalysts based on salfan had higher activity and selectivity toward both substrates and were studied for in situ redox switching experiments, which could be repeated three times. Individual experiments and GPC data indicate controlled polymerization processes. In addition, the one-pot copolymerization of the two monomers to give a block copolymer was also achieved by using the titanium analogue. Further copolymerization studies and mechanistic investigations are currently ongoing.

■ ASSOCIATED CONTENT

Supporting Information

Synthetic details, NMR spectra, and data from kinetics, electrochemistry, and crystallographic studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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