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Synthesis and Structural Characterization of Group 4 Metal Alkoxide Complexes of *N*,*N*,*N*′,*N*′-Tetrakis(2-hydroxyethyl)ethylenediamine and Their Use As Initiators in the Ring-Opening Polymerization (ROP) of *rac*-Lactide under Industrially Relevant Conditions

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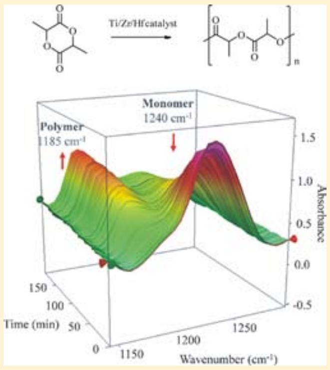
Supporting Information

ABSTRACT: A series of *N*,*N*,*N*′,*N*′-tetrakis(2-hydroxyethyl)ethylenediamine (TOEEDH$_4$) ligand precursors and their group 4 metal complexes have been prepared. The complexes have been characterized by single-crystal X-ray diffraction and ^{1}H NMR spectroscopy, highlighting the ability to systematically vary the number of TOEED ligands within the system. Initial catalytic data for the solvent-free, ring-opening polymerization of *rac*-lactide (*rac*-LA), a promising degradable polymer produced from renewable resources, is reported. At 135 °C, it has been demonstrated that the activity of the complexes is enhanced by increasing the number of labile isopropoxide groups. When the temperature was further increased to 165 °C, all complexes demonstrated a far higher activity irrespective of the identity of the metal or number of labile initiator groups. Polymerization kinetics were monitored in real time using FT-IR spectroscopy with a diamond composite insertion probe and Ti$_4$(TOEED)(O^{i}Pr)$_{12}$ was demonstrated to convert over 95% of the *rac*-LA within 160 min.



INTRODUCTION

Polylactide (PLA) is a degradable and biocompatible aliphatic polyester that is produced from the ring-opening polymerization (ROP) of lactide, the cyclic dimer of lactic acid, that can be derived from renewable resources such as corn starch. Lactide is currently produced on a kiloton industrial scale,[1] and as such, PLA is becoming a promising alternative to petrochemical-based polymers.[2−4] Various metals have been utilized in the ROP of cyclic esters including examples from groups 1 (Li, Na, K), 2 (Ca, Mg), 3 (Sc, Y), 4 (Ti, Zr, Hf), 12 (Zn), 13 (Al, In), and rare-earth metals (Y, Sm, Nd, Lu, Yb).[5−7] Group 4 metal initiators are recognized to give high activity and selectivity due to their strong Lewis acidic nature.[8−16] While there are numerous examples of using group 4 metal alkoxide initiators in solution, there are relatively few examples of these initiators under more industrially relevant, high-temperature, and solvent-free conditions.[17−20] Kricheldorf et al. first reported active group 4 metal alkoxides for the ROP of various cyclic esters.[12,21,22] Later, Kol and co-workers reported that titanium and zirconium centers complexed to bulky chelating tetradentate di- and trianionic ligands were highly active in the production of PLA from L-lactide.[11,22] In our work, zirconium and hafnium amine trisphenolate and bisphenolate complexes were shown to give a desirable combination of high activity (95% conversion in 30 min) with high stereoselectivity ($P_r > 0.90$) in the ROP of *rac*-LA under solvent-free conditions at 130 °C.[10,23]

Industrially, different PLA grades can be produced, dependent on the molecular weight chosen and the feed ratio of L- and D-lactide. Copolymers are typically random, as nonstereoselective catalysts such as tin(II) 2-eythylhexanoate (Sn(Oct)$_2$) are employed. To control the molecular weight of the resulting PLA, a co-initiator alcohol is used at typical loadings of 0.5 mol % to 3.0 × 10^{-3} mol %. In the bulk production of PLA, melt-crystallized lactide can carry trace levels of water and lactic acid that would deactivate most initiators at this loading. Therefore, robust alternatives that can be used with unsublimed lactide, while maintaining high activity under melt conditions, are being increasingly sought.

N,*N*,*N*′,*N*′-tetrakis(2-hydroxyethyl)ethylenediamine (TOEEDH$_4$), is an inexpensive, benign, and commercially available ligand. Group 4 metal complexes of this ligand in a 1:1 metal:ligand stoichiometry were shown by Tulloch and co-workers to be highly active initiators that displayed a high degree of air and water stability in polyurethane applications.[26] Other group 4 complexes derived from amino alcohols, such as

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triethanolamine, have also shown high activity in the ROP of L-lactide.[24−30]

Over the course of this work, a range of group 4 complexes of the TOEEDH$_4$ ligand were synthesized and structurally characterized. The aim of this approach was to increase the activity of the ROP of lactide by increasing the amount of labile isopropoxide groups within the structure, while retaining the stability necessary in the industrial conditions of PLA production.

■ EXPERIMENTAL SECTION

General Procedures. For the preparation and characterization of metal complexes, all reactions and manipulations were performed under an inert atmosphere of argon using standard Schlenk or glovebox techniques. All solvents were dried using a solvent purification system. The ligand, *N*,*N*,*N*′,*N*′-tetrakis(2-hydroxyethyl)-ethylenediamine (TOEEDH$_4$) (technical grade Sigma-Aldrich), was dried under vacuum, dissolved in dry THF to afford a 1 M solution, and stored under an inert atmosphere. $\mathrm{Ti(O^iPr)_4}$ (97%, Aldrich) was purified by vacuum distillation prior to use, $\mathrm{Zr(O^iPr)_4{}^iPrOH}$ (99.9%, Aldrich) and $\mathrm{Hf(O^iPr)_4{}^iPrOH}$ (99%, Aldrich) were used without further purification. L-lactide (Puralact L Polymer grade, 99+ %, Purac) and D-lactide (Puralact D Polymer grade, 99+ %, Purac) were recrystallized from toluene and sublimed twice before use. *Rac*-lactide was obtained by dissolving equal amounts of L- and D-lactide, recrystallized from toluene. Yields were obtained from recrystallized products.

Preparation of $\mathbf{Zr_2(TOEED)_2}$, 1. $\mathrm{Zr(O^iPr)_4(HO^iPr)}$ (0.55 g, 2.32 mmol) in THF (5 mL) was added to 1 M solution of TOEEDH$_4$ in THF (2.32 mL, 2.32 mmol) with a syringe. The reaction was stirred overnight at 50 °C. The solvent was removed in vacuo, and the dry residue was recrystallized from THF. Isolated crystalline yield = 28%. El. Anal.: Calcd. for $\mathrm{C_{20}H_{40}N_4O_8Zr_2}$ C: 37.13%; H: 6.23%, N: 8.66%. Found C: 37.01%; H: 6.23%, N: 8.47%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.71−3.90 (16H, m, O−C*H*$_2$), 3.80−2.38 (24H, m, N−C*H*$_2$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 66.98 (O(CH$_2$)), 60.83 (N(CH$_2$)).

Preparation of $\mathbf{Hf_2(TOEED)_2}$, 2. $\mathrm{Hf(O^iPr)_4(HO^iPr)}$ (0.42 g, 1.01 mmol) in THF (10 mL) was added to 1 M solution of TOEEDH$_4$ in THF (1.0 mL, 1.0 mmol) dropwise with a syringe and stirred for 16 h. The solvent was removed in vacuo, and the dry residue was recrystallized from dichloromethane. Isolated crystalline yield: 14%. El. Anal.: Calcd. for $\mathrm{C_{20}H_{40}N_4O_8Hf_2}$ C: 29.24%; H: 4.91%, N: 6.82%. Found C: 29.13%; H: 5.00%, N: 6.72%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.75−4.01 (m, 16H, O−C*H*$_2$), 3.79−3.49 (m, 2H, N−C*H*$_2$), 3.49−3.18 (m, 8H, N−C*H*$_2$), 3.18−2.50 (m, 14H, N−C*H*$_2$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 66.53(O-(CH$_2$)), 60.87 (N(CH$_2$)).

Preparation of $\mathbf{Ti_4(TOEED)_3(O^iPr)_4}$, 3. $\mathrm{Ti(O^iPr)_4}$ (1.5 mL, 5.06 mmol) was added to 1 M solution of TOEEDH$_4$ in THF (3.81 mL, 3.81 mmol) dropwise with a syringe and stirred for 16 h at 50 °C. The solvent was removed in vacuo, and the dry residue was recrystallized from dichloromethane. Isolated crystalline yield = 24%. El. Anal.: Calcd. for $\mathrm{C_{42}H_{88}N_6O_{16}Ti_4}$ C: 44.85%; H: 7.89%, N: 7.47%. Found C: 44.68%; H: 7.81%, N: 7.39%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.92−4.74 (m, 4H, OC*H*), 4.73−4.18 (m, 20H, ROC*H*$_2$), 4.17−3.93 (m, 4H, ROC*H*$_2$), 3.69−3.53 (m, 4H, RNC*H*$_2$), 3.51−3.15 (m, 14H, RNC*H*$_2$), 3.14−3.00 (m, 4H, RNC*H*$_2$), 3.00−2.70 (m, 14H, RNC*H*$_2$), 1.31−1.15 (m, 24H, RC*H*$_3$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 74.16 (O(CH)), 71.39 (O(CH$_2$)), 69.44 (O(CH$_2$)), 69.09 (O(CH$_2$)), 64.78 (N(CH$_2$)), 61.61 (N(CH$_2$)), 61.04 (N(CH$_2$)), 60.98 (N(CH$_2$)), 60.52 (N(CH$_2$)), 60.06 (N(CH$_2$)), 26.64 (RCH$_3$), 25.43 (RCH$_3$).

Preparation of $\mathbf{Ti_4(TOEED)(O^iPr)_{12}}$, 4. $\mathrm{Ti(O^iPr)_4}$ (1.48 mL, 5.00 mmol) was added to 1 M solution of TOEEDH$_4$ in THF (1.25 mL, 1.25 mmol) dropwise with a syringe and stirred for 16 h at 50 °C. The solvent was removed in vacuo, and the dry residue was recrystallized from dichloromethane. Isolated crystalline yield =28%. El. Anal.: Calcd. for $\mathrm{C_{46}H_{104}N_2O_{16}Ti_4}$ C: 48.77%; H: 9.25%, N: 2.47%. Found C: 48.65%; H: 9.15%, N: 2.39%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.85 (sept, *J* = 6.0 Hz, 2H, O−C*H*), 4.79−4.53 (m, 4H, O−C*H*$_2$), 4.48 (sept, *J* = 6.0 Hz, 10H, O−C*H*), 4.42−3.96 (m, 4H, O−C*H*$_2$), 3.73−3.32 (m, 4H, N−C*H*$_2$), 3.32−3.03 (m, 4H, N−C*H*$_2$), 3.02−2.69 (m, 4H, N−C*H*$_2$), 1.23 (d, *J* = 6.0 Hz, 60H, RC*H*$_3$), 1.19 (d, *J* = 6.0 Hz, 12H, RC*H*$_3$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 72.04 (O(CH)), 68.50 (O(CH$_2$)), 64.06 (O(CH$_2$)), 61.28 (N(CH$_2$)), 55.46 (N(CH$_2$)), 50.96 (N(CH$_2$)), 26.52 (RCH$_3$), 25.32 (RCH$_3$).

Preparation of $\mathbf{Zr_3(TOEED)(O^iPr)_8}$, 5. $\mathrm{Zr(O^iPr)_4(HO^iPr)}$ (0.97 g, 2.50 mmol) in THF (10 mL) was added to 1 M solution of TOEEDH$_4$ in THF (0.83 mL, 0.834 mmol) dropwise with a syringe and stirred for 16 h at room temperature. The solvent was removed in vacuo, and the dry residue was recrystallized from toluene. Isolated crystalline yield = 34%. El. Anal.: Calcd. for $\mathrm{C_{34}H_{76}N_2O_{12}Zr_3}$ C: 41.72%; H: 7.82%, N: 2.86%. Found C: 42.27%; H: 7.86%, N: 2.74%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.67 (sept, *J* = 6.0 Hz, 2H, O−C*H*), 4.36−4.32 (m, 2H, O−C*H*$_2$), 4.32−4.24 (m, 6H, O−C*H*), 4.24−4.19 (m, 2H, O−C*H*$_2$), 4.18−4.11 (m, 2H, O−C*H*$_2$), 4.10−4.03 (m, 2H, O−C*H*$_2$), 3.68 (td, *J* = 6.0 Hz + 12.0 Hz, 2H, N−C*H*$_2$), 3.43−3.27 (m, 2H, N−C*H*$_2$), 3.26−3.13 (m, 2H, N−C*H*$_2$), 2.80−2.64 (m, 6H, N−C*H*$_2$), 1.28 (d, *J* = 6.0 Hz, 6H, RC*H*$_3$), 1.20 (d, *J* = 6.0 Hz, 6H, R−C*H*$_3$), 1.14 (d, *J* = 6.0 Hz, 36H, R−C*H*$_3$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 69.61 (O(CH)), 69.10 (O(CH)), 67.73 (O(CH$_2$)), 64.64 (N(CH$_2$)), 64.11 (O(CH$_2$)), 62.12 (N(CH$_2$)), 59.81 (N(CH$_2$)), 27.50 (RCH$_3$), 26.60 (RCH$_3$), 26.29 (RCH$_3$).

Preparation of $\mathbf{Hf_3(TOEED)(O^iPr)_8}$, 6. $\mathrm{Hf(O^iPr)_4(HO^iPr)}$ (0.42 g, 1.01 mmol) in THF (10 mL) was added to 1 M solution of TOEEDH$_4$ in THF (0.33 mL, 0.33 mmol) dropwise with a syringe and stirred for 16 h at room temperature. The solvent was removed in vacuo, and the dry residue was recrystallized from dichloromethane. Isolated crystalline yield = 14%. El. Anal.: Calcd. for $\mathrm{C_{34}H_{76}N_2O_{12}Hf_3}$ C: 32.92%; H: 6.18%, N: 2.26%. Found C: 32.78%; H: 6.06%, N: 2.33%. ^{1}H NMR (300.22 MHz, CDCl$_3$, 298 K): δ 4.79 (sept, *J* = 6.0 Hz, 2H, O−C*H*), 4.50−4.41 (m, 2H, O−C*H*$_2$), 4.41−4.28 (m, 6H, O−C*H*), 4.28−4.19 (m, 2H, O−C*H*$_2$), 4.19−4.08 (m, 2H, O−C*H*$_2$), 4.08−3.94 (m, 2H, O−C*H*$_2$), 3.67 (td, *J* = 6.0 Hz + 12.0 Hz, 2H, N−C*H*$_2$), 3.38−3.29 (m, 2H, N−C*H*$_2$), 3.29−3.16 (m, 2H, N−C*H*$_2$), 2.89−2.83 (m, 2H, N−C*H*$_2$), 2.77−2.65 (m, 4H, N−C*H*$_2$), 1.28 (d, *J* = 6.0 Hz, 6H, R−C*H*$_3$), 1.20 (d, *J* = 6.0 Hz, 6H, R−C*H*$_3$), 1.18−1.09 (m, 36H, R-C*H*$_3$). ^{13}C{^{1}H} NMR (300.22 MHz, CDCl$_3$, 298 K): δ 68.52 (O(CH)), 66.90 (O(CH$_2$)), 64.76 (N(CH$_2$)), 63.59 (O(CH$_2$)), 62.36 (N(CH$_2$)), 60.03 (N(CH$_2$)), 26.58 (RCH$_3$), 26.12 (RCH$_3$), 25.48 (RCH$_3$).

General X-ray Crystal Structure Information. Single crystal X-ray diffraction data were obtained for compounds **3**, **4**, and **6**. Suitable single crystals were selected using the oil drop technique, in perfluoropolyether oil and mounted at 150(2) K. Intensity data were collected on an Nonius Kappa CCD single crystal diffractometer using graphite monochromated Mo−Kα radiation (λ = 0.71073 Å). Data were processed using the Nonius Software.[31] A symmetry-related (multiscan) absorption correction was applied. Crystal parameters and details on data collection, solution, and refinement for the complexes are provided in Table S1 of the Supporting Information (SI).

The structures were solved by direct methods using the program SIR97[32] followed by full-matrix least-squares refinement on F^2 using SHELXL-97 implemented in the WINGX-1.80 suite of programs throughout.[33] Hydrogen atoms were placed in calculated positions and isotropically refined using a riding model.

Additional programs used for analyzing data and graphically manipulating them included the following: SHELXle,[34] PLATON,[35,36] and ORTEP 3 for Windows.[37]

Polymerization of *rac*-Lactide. The group 4 initiators were used in the polymerization of sublimed *rac*-LA (2 g) at 135 and 165 °C under solvent-free conditions. A monomer to initiator ratio of 300:1 was employed and benzyl alcohol (1 equiv.) was added as a co-initiator with the initiators Zr$_2$(TOEED)$_2$, **1**, and Hf$_2$(TOEED)$_2$, **2**. For initiators with isopropoxide groups no co-initiator was added. Initially, polymerizations were screened using Schlenk techniques, before the most promising initiators were examined on larger scales and the conversion monitored by FT-IR. Conversions were determined by ^1H NMR spectroscopy with aliquots taken from the reaction mixture every hour for 4 h and at 24 h. Samples were also analyzed by homonuclear decoupled NMR spectroscopy for tacticity and GPC (calibrated with polystyrene standards, in THF, 35 °C, 1.0 mL/min) for molecular weights. For IR measurements a Bruker Matrix-MF FT-IR spectrometer equipped with a diamond ATR probe (IN350 T) suitable for Mid-IR in situ reaction monitoring was used. Reactions were performed under inert conditions in a specifically designed jacketed vessel fitted with a mechanical stirrer and connected to a Huber PETITE FLEUR-NR circulation thermostat (Figure 1).

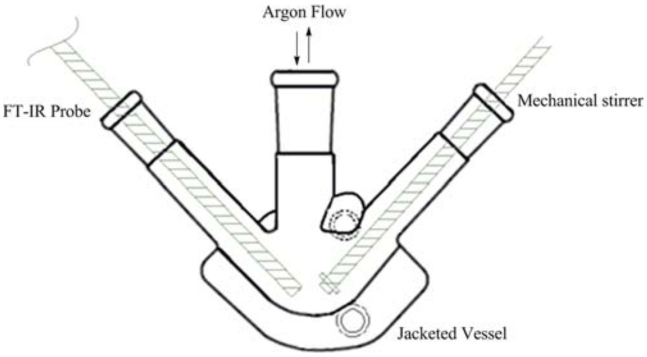


Figure 1. Schematic drawing of FT-IR reaction vessel.

FT-IR Spectroscopy. The jacketed vessel was placed under a positive pressure of argon and heated to the reaction temperature of 165 °C. The lactide was added (35 g) and allowed to melt with stirring from the overhead mechanical stirrer. A background spectra was recorded at this point before the probe was placed in the reaction solution. The initiator was dissolved in a minimal amount of toluene and transferred using a cannula into the reaction under argon. Spectra were collected over a set period of time, and the decrease in the C−O−C lactide peak was calibrated against ^1H NMR spectrum measurements, the time-resolved spectra were then used to accurately assess the kinetics.[38−41]

RESULTS AND DISCUSSION

Synthesis and Characterization of Ti, Zr and Hf Complexes. The ligand, TOEEDH$_4$, was reacted with Ti(O^{i}Pr)$_4$, Zr(O^{i}Pr)$_4$(HO^{i}Pr) and Hf(O^{i}Pr)$_4$(HO^{i}Pr) in varying stoichiometries yielding a range of well-defined complexes with degrees of ligand substitution (Scheme 1). All complexes were characterized by ^1H, ^{13}C NMR spectroscopy, and elemental analysis. Single crystal X-ray structures were obtained for Ti$_4$(TOEED)$_3$(O^{i}Pr)$_4$, **3**, Ti$_4$(TOEED)(O^{i}Pr)$_{12}$, **4**, and Hf$_3$(TOEED)(O^{i}Pr)$_{12}$, **6**. Initially, a 1:1 stoichiometric reaction of Ti(O^{i}Pr)$_4$ and TOEEDH$_4$ was examined. However, instead of forming Ti$_2$(TOEED)$_2$, as reported by Tulloch and co-workers,[26] the NMR spectrum was consistent with a 3:4 TOEED:O^{i}Pr ratio, and the reaction was repeated under the correct stoichiometry to yield Ti$_4$(TOEED)$_3$(O^{i}Pr)$_4$, **3**. In the solid state, Ti$_4$(TOEED)$_3$(O^{i}Pr)$_4$, **3**, was shown to consist of four metal centers bound to three TOEED ligands, two in a 6-coordinate environment bridged by one ligand and two terminal metal centers in a 7-coordinate environment (Figure 2).

Ti(2) exhibits a distorted octahedral geometry (Table S1 of the SI) and two mutually cis isopropoxide ligands. The ligand geometry around Ti(1) favors mutually cis N atoms.

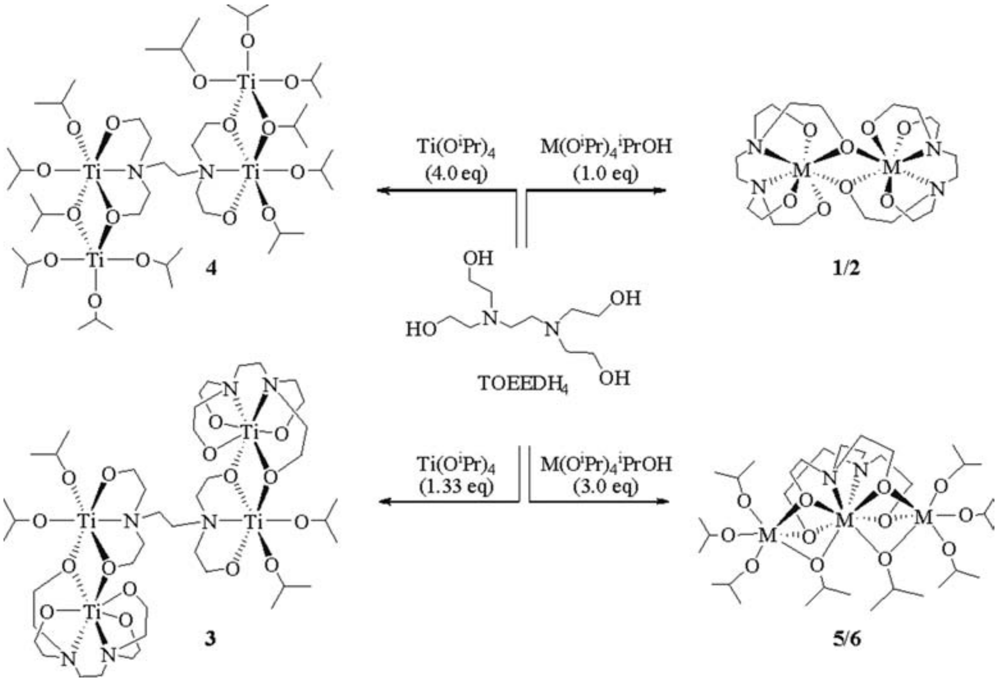
The similar reaction procedure with Ti(O^{i}Pr)$_4$ and TOEEDH$_4$ in 4:1 stoichiometry yielded Ti$_4$(TOEED)(O^{i}Pr)$_{12}$, **4**. The presence of twelve isopropoxide groups per TOEED ligand in the NMR spectrum is consistent with the solid-state structure in which all four metal centers are bound to one bridging ligand, two in a 6-coordinate environment and two terminal metal centers in a 5-coordinate environment (Figure 3). This structure is closely related to that of **3** with the

Table 1. Crystallographic Data

compound reference	(3)	(4)	(6)
chemical formula	$C_{44}H_{92}Cl_4N_6O_{16}Ti_4$	$C_{46}H_{104}N_2O_{16}Ti_4$	$C_{34}H_{76}Hf_3N_2O_{12}$
formula mass	1294.64	1132.91	1240.44
crystal system	triclinic	triclinic	monoclinic
space group	$P\bar{1}$	$P\bar{1}$	$C2/c$
a (Å)	8.84810(10)	9.7827(3)	23.6691(6)
b (Å)	9.8772(2)	10.9231(3)	10.3738(2)
c (Å)	17.3948(3)	15.2538(5)	19.0472(5)
α (deg)	83.6010(10)	87.910(2)	90.00
β (deg)	78.3720(10)	75.866(2)	97.2430(10)
γ (deg)	80.9510(10)	79.555(2)	90.00
unit cell volume (Å^3)	1465.47(4)	1554.39(8)	4639.50(19)
temperature (K)	150(2)	150(2)	200(2)
no. of formula units per unit cell, Z	1	1	4
absorption coefficient, μ/mm^{-1}	0.775	0.553	6.748
no. of reflections measured	28775	20206	34294
no. of independent reflections	6714	6993	5326
R_{int}	0.0624	0.0564	0.1251
final R_1 values $(I > 2\sigma(I))^a$	0.0409	0.0446	0.0413
final $wR(F^2)$ values $(I > 2\sigma(I))^b$	0.0879	0.1044	0.1026
final R_1 values (all data)	0.0531	0.0656	0.0539
final $wR(F^2)$ values (all data)	0.0926	0.1161	0.1099
goodness of fit on F^{2c}	1.103	1.045	1.034

$^aR_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. $^bwR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]\}^{1/2}$. $^c\mathrm{GOF} = S = \{\Sigma[w(F_o^2 - F_c^2)^2]] / (n - p)\}^{1/2}$.

Scheme 1. Synthesis of Group 4 TOEED Complexes (M = Zr or Hf, Structures 1/2 or 5/6, Respectively)



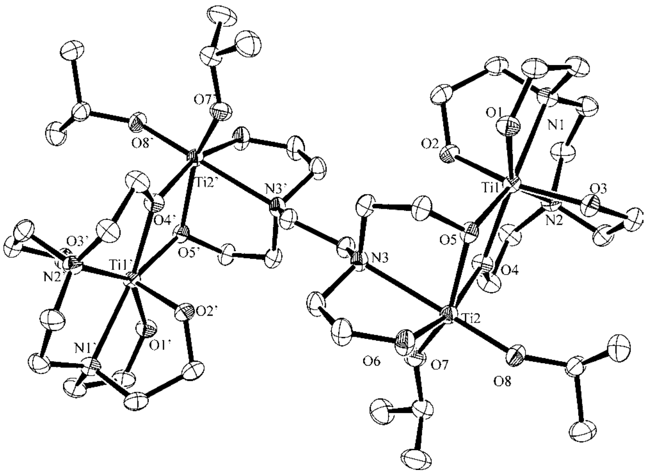


Figure 2. X-ray molecular structure of **3** ($Ti_4(TOEED)_3(O^iPr)_4$) (Thermal ellipsoids are drawn at 50% probability level. H atoms were omitted for clarity.).

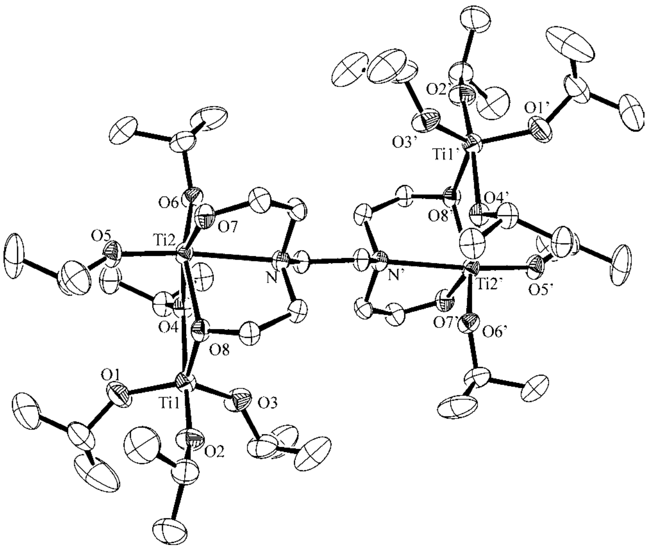


Figure 3. X-ray molecular structure of **4** ($Ti_4(TOEED)(O^iPr)_{12}$) (Thermal ellipsoids are drawn at 50% probability level. H atoms were omitted for clarity.).

terminal TOEED ligand bound to Ti(1) being replaced by four O^iPr groups.

For the reaction of $Zr(O^iPr)_4(HO^iPr)$ and $TOEEDH_4$ a 1:1 stoichiometric ratio was used in a modified synthesis as reported by Tulloch et al.[26] $Zr_2(TOEED)_2$, **1**, was isolated as a crystalline solid and analyzed by ^1H and ^{13}C NMR spectroscopy. The NMR spectrum was consistent with the replacement of all isopropoxide groups with the chelating TOEED ligand. While the solid-state structure was found to be highly disordered, it is clear that two metal centers, both in a 7-coordinate geometry, are bound to two ligands. $TOEEDH_4$ acts as a hexadentate chelate to the metal centers and the ligand geometry around zirconium metal centers favors mutually cis N atoms (Figures S2, S3, and S4 of the SI).

Reacting a 2:1 stoichiometry of $Zr(O^iPr)_4(HO^iPr)$ and $TOEEDH_4$ afforded $Zr_3(TOEED)(O^iPr)_8$, **5**, as the major product. The reaction was repeated under the correct stoichiometry of 3:1. Due to weak diffraction, the resulting structure was of poor quality, although the molecular structure is clearly elucidated (see Figures S14, S15, and S16 of the SI). The NMR spectrum of **5** was consistent with the presence of eight isopropoxide groups per TOEED ligand, which is comparable to **6**. In the solid state, the adduct consists of three metal centers bound to one ligand. Two zirconium centers, Zr(1) and Zr(3), lie in a 6-coordinate environment and one central metal center, Zr(2), lies in an 8-coordinate environment (Figure S14 of the SI).

$Hf_2(TOEED)_2$, **2**, was synthesized by reacting $Hf(O^iPr)_4(HO^iPr)$ and $TOEEDH_4$ with a 1:1 stoichiometric ratio.[26] The adduct was isolated and analyzed by NMR spectroscopy (Figure S5, S6, and S7 of the SI). The NMR spectra are consistent with the replacement of all isopropoxide groups with the ligand TOEED and the structure is analogous to zirconium complex, **1**.

Reaction of $Hf(O^iPr)_4(HO^iPr)$ with $TOEEDH_4$ under similar conditions in a 3:1 stoichiometry yielded $Hf_3(TOEED)(O^iPr)_8$, **6**, (Figure 4) which is isostructural with its zirconium congener **5**.

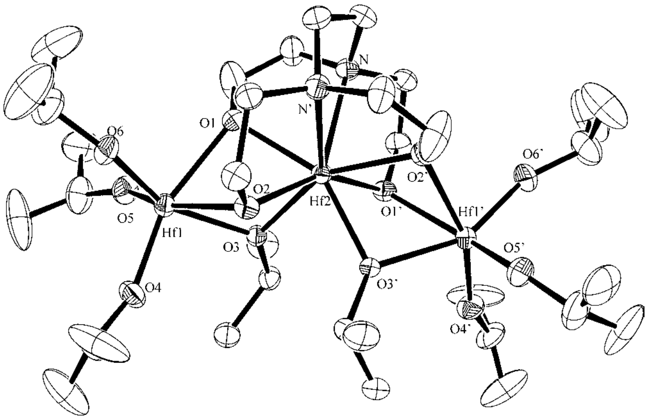
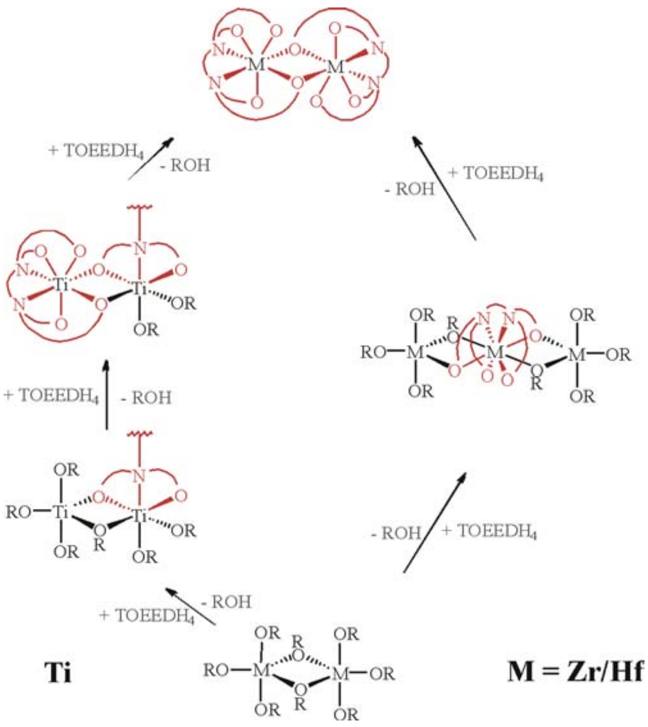


Figure 4. X-ray crystal structure of **6** ($Hf_3(TOEED)(O^iPr)_8$) (Thermal ellipsoids are drawn at 50% probability level. H atoms were omitted for clarity.).

A number of general observations can be made regarding the structural data described above. As the stoichiometry of the TOEED ligand to metal is increased, the coordination number of the group 4 species increases (Scheme 2). $M_2(TOEED)_2$ is the common structure for Ti, Zr, and Hf complexes. $Ti_4(TOEED)(O^iPr)_{12}$, **4**, and $Ti_4(TOEED)_3(O^iPr)_4$, **3**, can be thought of as successive intermediates between the starting material $Ti(O^iPr)_4$ and the coordinatively saturated $Ti_2(TOEED)_2$. $Zr_3(TOEED)(O^iPr)_8$, **5**, can be considered an intermediate originating from $Zr(O^iPr)_4.HO^iPr$. As the ligand is introduced and coordinates to the metal center, isopropoxide groups are lost and the coordination number of the metal center increases giving, **5**. Further addition of ligand leads to the loss of remaining isopropoxide groups affording $Zr_2(TOEED)_2$, **1**. The same is true for analogous complexes $Hf_3(TOEED)(O^iPr)_8$, **6** which is an isolated intermediate between $Hf(O^iPr)_4{\cdot}HO^iPr$ and $Hf_2(TOEED)_2$, **2**.

Scheme 2. Schematic Diagram Summarizing Complexes Synthesized Illustrating Ligand to Dimer Stoichiometry (R = ^iPr)



ROP of *rac*-Lactide. An initial screening of complexes **1**−**6** as initiators in the ROP of sublimed *rac*-LA was completed under solvent-free conditions at 135 °C with a 300:1 monomer to initiator ratio (Figure 5).

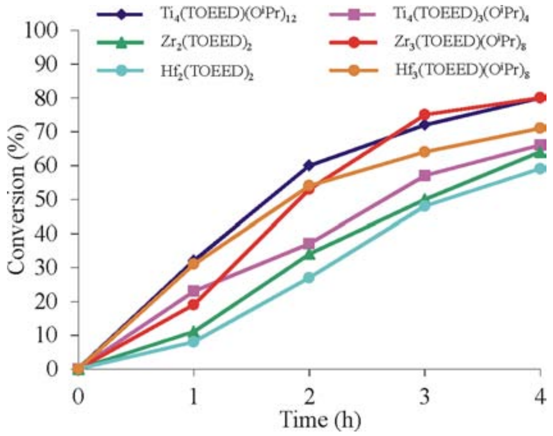


Figure 5. Reaction rate of lactide to PLA in solvent-free polymerizations of sublimed *rac*-LA at 135 °C, 300:1 monomer to initiator ratio.

The initiators $Zr_3(TOEED)(O^iPr)_8$, **5**, and $Ti_4(TOEED)(O^iPr)_{12}$, **4**, showed moderate activity at 135 °C with over 80% conversion of the monomer in 4 h. $Zr_2(TOEED)_2$, **1**, and $Hf_2(TOEED)_2$, **2**, were the least active initiators. Both species are more stable than the equivalent complexes with labile isopropoxide groups, making the metal center far less accessible to the approaching lactide monomer. This is demonstrated by the large increase in activity observed when using initiators $Zr_3(TOEED)(O^iPr)_8$, **5**, and $Hf_3(TOEED)(O^iPr)_8$, **6**. A similar step change in activity was observed for the two titanium species, **3** and **4**, for which a large increase in activity was observed as the number of labile groups was increased 3-fold. Under these conditions, the identity of the metal was found to be of less importance than the number of isopropoxide groups on the metal complex (Figure 5). The total number of isopropoxide groups in the initiator complex does however influence the kinetics at 135 °C. This implies that the resulting polymers could be initiated from different sites of the complex, including the TOEED ligand, and accordingly, long-chain branched or even star-shaped PLA could be the result. All polymerizations were quenched with methanol after 24 h, and the resulting solid was extracted into dichloromethane. The solvents were removed in vacuo, and the resulting polymer was washed with methanol to remove any unreacted monomer. The final conversions were calculated using ^1H NMR spectroscopy ($CDCl_3$), and the weight average molecular weight (M_w), number average molecular number (M_n), and polydispersity

Table 2. Solvent-Free Polymerizations of *rac*-LA at 135 °C

initiator	T (°C)	time (h)	conversion (%)	M_n (kg·mol^{-1})	M_w (kg·mol^{-1})	PDI	P_r
$Ti_4(TOEED)(O^iPr)_{12}$ **4**	135	24	92	7.2	10.8	1.49	0.52
$Ti_4(TOEED)_3(O^iPr)_4$ **3**	135	24	90	7.0	10.0	1.43	0.52
$Zr_2(TOEED)_2$[a] **1**	135	24	78	2.6	3.9	1.53	0.52
$Zr_3(TOEED)(O^iPr)_8$ **5**	135	24	93	4.2	5.9	1.41	0.55
$Hf_2(TOEED)_2$[a] **2**	135	24	64	2.1	3.3	1.62	0.56
$Hf_3(TOEED)(O^iPr)_8$ **6**	135	24	81	12.2	16.4	1.34	0.51

[a] Addition of benzyl alcohol (1 equiv.) as co-initiator.

index (PDI) were determined by GPC. P_r (the probability of heterotactic linkages) was determined by analysis of the methine region of the homonuclear decoupled ^1H NMR spectrum, the equations used to calculate P_r and P_m are used from Coates et al.[42]

All polymerizations gave atactic PLA with P_r ranging from 0.52 to 0.56. The initiators showed reasonable activity at 135 °C with $Zr_3(TOEED)(O^iPr)_8$, **5**, and $Ti_4(TOEED)(O^iPr)_{12}$, **4**, converting over 90% of the monomer in 24 h (Table 2). All initiators gave lower molecular weight polymers than expected, as theoretically calculated M_w of 43.0 kg·mol^{-1} is expected. This may be part due to the high abundance of initiator groups within the complexes. All of the initiators investigated facilitated controlled polymerization reactions with PDIs of between 1.34 and 1.62. In order to determine the effect of a co-initiator on M_w control, $Hf_2(TOEED)_2$, **2**, with various quantities of benzyl alcohol was applied to the polymerization of lactide. Good control over the M_w was observed (Table S22 of the SI). MALDI-ToF analyses of polymers produced using $Zr_3(TOEED)(O^iPr)_8$, **5**, $Ti_4(TOEED)(O^iPr)_{12}$, **4**, and $Ti_4(TOEED)_3(O^iPr)_4$, **3**, initiators all showed the expected series due to PLA capped with an isopropoxide end group. However, in all cases, this was a minor series which was accompanied by an unidentified major series, suggesting a ligand fragmentation polymerization pathway. There is also evidence of transesterification based on an observed repeat unit of 72.1 Da in both major and minor series (Figure S23 of the SI).

Complexes **1**−**6** were then examined for their activity in the ROP of sublimed *rac*-LA at an elevated temperature of 165 °C (Figure 6).

With the increase in temperature to 165 °C, all of the complexes were markedly more active than at the lower temperature, demonstrating the potential applicability of this particular ligand motif to industrial applications. All of the complexes tested converted over 90% of the monomer within four hours, irrespective of the identity of the metal or number of labile initiator groups. This observation suggests that the complexes may be degrading under the harsher conditions into species of similar activity, regardless of the original motif. This is supported by an induction period observed through in situ FT-IR monitoring of reactions.

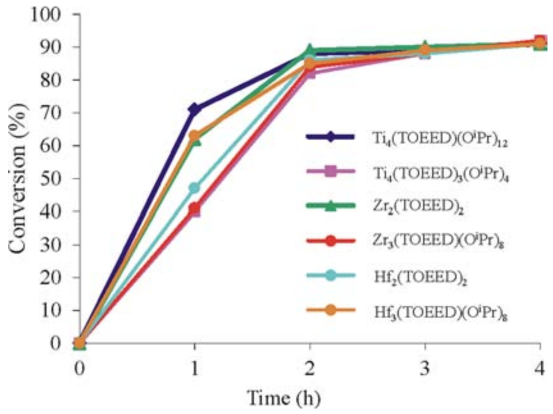


Figure 6. Conversion of lactide to PLA in the solvent-free polymerizations of sublimed *rac*-LA at 165 °C, 300:1 monomer to initiator ratio.

All polymerizations at 165 °C gave atactic PLA except for $Zr_3(TOEED)(O^iPr)_8$, **5**, which showed a slight heterotactic bias (P_r = 0.59) (Table 3). Some of the M_w values were found to be lower than values at 135 °C, presumably due to increased levels of transesterification at higher temperatures. This is also consistent with an increase in the PDIs of the polymers at the higher temperature. The measured molecular weights were still markedly lower than theoretically calculated M_w of 43.0 kg·mol^{-1} assuming that one initiator complex initiates one polymer chain. This again reflects the possibility of the production of branched polymers (Table S24 of the SI).

Solvent-Free Polymerizations under Industrially Relevant Conditions. As all of the initiators screened demonstrated a similar activity at higher temperature, $Ti_4(TOEED)(O^iPr)_{12}$, **4**, was selected for further investigation, to give a better understanding of the activity in the ROP of lactide and determine viability as a replacement for $Sn(Oct)_2$. To assess the applicability of the Ti species under industrially relevant conditions, nonsublimed *rac*-LA was polymerized at 165 °C with a far lower 5000:1 initiator loading (Table 4). The polymerization kinetics were assessed using in situ FT-IR with a jacketed vessel and a mechanical stirrer under a positive argon flow. The peak at 1240 cm^{-1}, corresponding to the C−O−C stretch, was used to assess the depletion of the monomer, while the peak at 1185 cm^{-1} (which corresponds to the C−O−C asymmetric vibrations in the polymer chain) was used to assess the growing concentration of PLA. The peaks can be integrated to determine the relative monomer and polymer concentration respectively (Figure 7).[38]

The initiator was dissolved in a minimal amount of dry toluene, and transferred into the reaction vessel under argon. The reaction mixture was stirred with a mechanical stirrer and after 5 min the initiator dissolved and the reaction proceeded, converting 99% of the monomer to PLA over three hours.

The polymerization of recrystallized (but nonsublimed) *rac*-LA with $Ti_4(TOEED)(O^iPr)_{12}$, **4**, reached near completion within 3 h, whereas $Sn(Oct)_2$ reached near completion within an hour (Figure 8a). A semilogarithmic plot of the results gave an apparent rate constant (k_{app}) of 0.0204 mol l^{-1} min^{-1} for $Ti_4(TOEED)(O^iPr)_{12}$ and a k_{app} of 0.0385 mol l^{-1} min^{-1} for $Sn(Oct)_2$ (Figure 8b).

The polymerization of recrystallized *rac*-LA using the initiator $Ti_4(TOEED)(O^iPr)_{12}$, **4**, produced a relatively low

Table 3. Solvent-Free Polymerizations of Lactide at 165 °C

initiator	T (°C)	time (h)	conversion (%)	M_n (kg·mol^{-1})	M_w (kg·mol^{-1})	PDI	P_r
$Ti_4(TOEED)(O^iPr)_{12}$ **4**	165	24	92	4.8	8.2	1.79	0.49
$Ti_4(TOEED)_3(O^iPr)_4$ **3**	165	24	96	6.0	9.6	1.60	0.55
$Zr_2(TOEED)_2$^{a} **1**	165	24	97	5.4	8.9	1.65	0.54
$Zr_3(TOEED)(O^iPr)_8$ **5**	165	24	96	5.9	8.8	1.49	0.59
$Hf_2(TOEED)_2$^{a} **2**	165	24	94	2.1	4.4	2.07	0.49
$Hf_3(TOEED)(O^iPr)_8$ **6**	165	24	97	17.5	24.8	1.42	0.49

[a] Addition of benzyl alcohol (1 equiv.) as co-initiator.

Table 4. Solvent-Free Polymerization Using $Sn(Oct)_2$ and $Ti_4(TOEED)(O^iPr)_{12}$

initiator	T (°C)	time (min)	conversion (%)	M_n (kg·mol^{-1})	M_w (kg·mol^{-1})	PDI
$Sn(Oct)_2$	165	80	99	94.3	114.1	1.21
$Ti_4(TOEED)(O^iPr)_{12}$ **4**	165	180	99	8.2	10.8	1.32

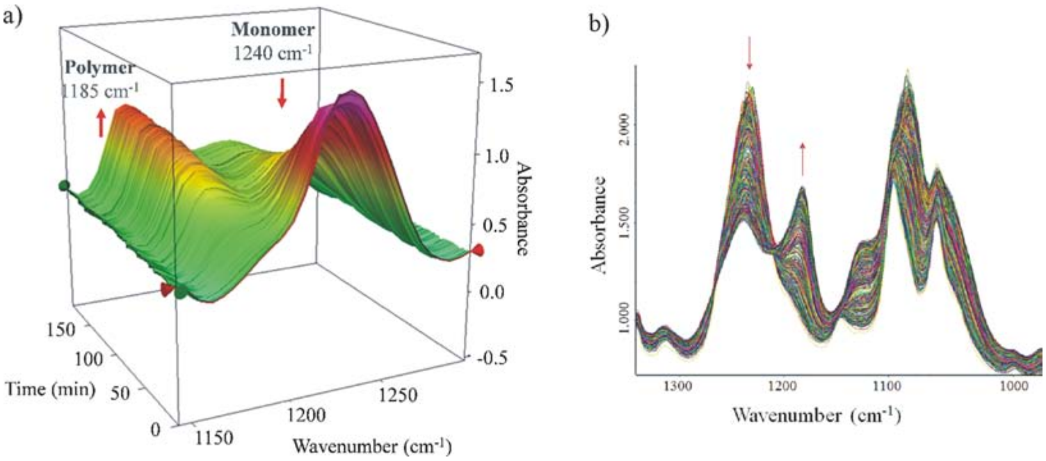


Figure 7. (a) 3D time-resolved FT-IR spectra, (b) 2D time-resolved FT-IR spectra of the polymerization of *rac*-LA with $Ti_4(TOEED)(O^iPr)_{12}$, **4**.

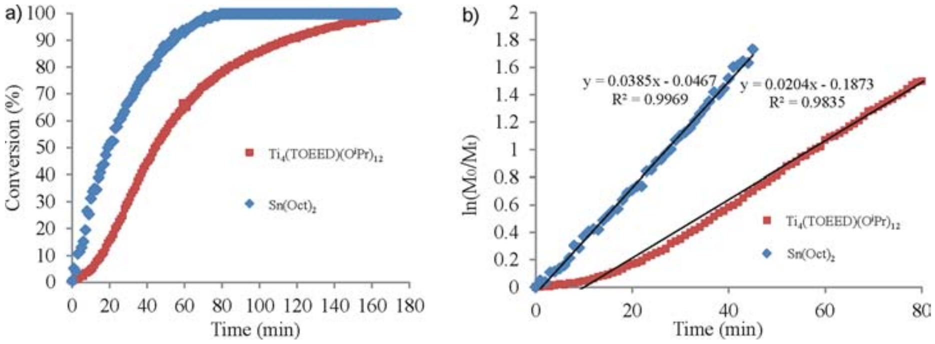


Figure 8. (a) Solvent-free polymerization rate of unsublimed *rac*-LA at 165 °C, 5000:1 with $Sn(Oct)_2$ (blue) and $Ti_4(TOEED)(O^iPr)_{12}$ **4** (red). (b) Semi -log plot of ln[M_0/M_t] against time for ROP using $Sn(Oct)_2$ (blue) and $Ti_4(TOEED)(O^iPr)_{12}$ **4** (red).

molecular weight polymer for the amount of initiator and the PDI was reduced significantly using a lower initiator loading. For comparison, the widely available metal alkoxides titanium isopropoxide ($Ti(O^iPr)_4$) and zirconium isopropoxide ($Zr(O^iPr)_4(HO^iPr)$ were also tested. At high catalyst loading (300:1), $Ti_4(TOEED)(O^iPr)_{12}$, **4**, was comparable to $Ti(O^iPr)_4$ (92% conversion in 4 h); however, $Zr(O^iPr)_4(HO^iPr)$ was much less active (12% conversion in 4 h) (Figure S25 of the SI). Under more industrially relevant conditions using unsublimed *rac*-LA and a lower catalyst loading (5000:1), $Ti(O^iPr)_4$ exhibited much lower activity than $Ti_4(TOEED)(O^iPr)_{12}$, **4** (55% and 90% conversion in 2 h, respectively) (Figure S26 of the SI).

■ CONCLUSIONS

Several new group 4 complexes have been prepared and characterized by NMR spectroscopy and single crystal X-ray diffraction. The activity of these complexes was assessed for the ROP of sublimed *rac*-LA under solvent-free conditions at 135 °C. The activity of the complexes was found to increase with an increase in the number of labile isopropoxide groups. Under these conditions, the identity of the metal was found to be of less importance than the number of labile initiator groups present, with similar Zr, Hf, and Ti complexes giving similar conversions. On increasing the temperature to 165 °C, all of the complexes demonstrated a higher activity irrespective of the identity of the metal or number of labile initiator groups. The most active titanium species was further examined under conditions more closely replicating industrial polymerizations: at 165 °C with a low initiator loading (5000:1) and using unsublimed lactide. Under these conditions, and in contrast to commercially available group 4 metal alkoxides ($Ti(O^iPr)_4$ and $Zr(O^iPr)_4(HO^iPr)$), $Ti_4(TOEED)(O^iPr)_{12}$, **4**, was found to be highly active, facilitating a >99% polymerization of the monomer to PLA within 3 h thus highlighting the potential of group 4 complexes as initiators for the commercial production of PLA.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Crystallographic data, NMR spectra, MALDI-ToF, and polymerization data. 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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