Inorganic Chemistry

Communication

Novel Chlorotitanium Complexes Containing Chiral Tridentate Schiff Base Ligands for Ring-Opening Polymerization of Lactide

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The selective synthesis of tri- and dichlorotitanium species containing chiral tridentate Schiff base ligands, derived from (1*R*,2*S*)-(−)-1-aminoindanol, was achieved by changing the solvent. Single-crystal X-ray analyses reveal that chlorotitanium complexes are monomeric and octahedral with the meridional occupation of the Schiff base. Although the chlorotitanium complexes lack typical initiating groups such as alkoxides or amides, they are effective catalysts for the controlled ring-opening polymerization of L-lactide (L-LA) as shown by the linearity of the molecular weight vs [L-LA]/[Ti] ratio plot as well as very narrow polydispersity index values.

Polylactide (PLA) is a biodegradable and renewable polymeric material for the use as controlled drug-release devices, absorbable sutures, medical implants for orthopedic use, disposable degradable plastic articles, and scaffolds for tissue engineering.[1] A large variety of new catalytic systems based on tin, aluminum, zinc, magnesium, iron, lanthanide, and lithium organometallic complexes containing initiating groups such as amides, carboxylates, and alkoxides have been reported as effective catalysts for the ring-opening polymerization (ROP) of lactide (LA).[2] In the case of group 4 metals, titanium and zirconium alkoxides are catalytically active for the ROP of LA;[3,4] however, the chlorotitanium system, in which chloride can play the role of an initiating group, remains undeveloped in this field. A dinuclear chlorotitanium complex containing a 2,2′-tellurobis(4-methyl-6-*tert*-butylphenoxo) ligand is the sole example of a controlled ROP catalyst of LA.[5]

In recent years, the research focus on PLA has been directed toward the introduction of stereoregularity such as heterotacticity and stereoblock to develop a new polymer system. Among various metal complexes that are known to produce stereoregular PLA,[6] chiral aluminum catalysts in particular draw attention since they can transform *meso*- and *rac*-LA into heterotactic and isotactic stereoblock PLA, respectively,[2d] revealing that the catalyst's chirality might be an important stereocontrol factor of the polymerization.

In order to develop a chiral chlorotitanium ROP catalyst of LA, chiral Schiff bases **L^H** and **L^Bu**, derived from (1*R*,2*S*)-(−)-1-aminoindanol, were taken as logical chelating ligands

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Figure 1. X-ray structure of **1**. Selected bond lengths (Å) and angles (deg): Ti—O1 1.807(2), Ti—O2 1.877(2), Ti—O3 2.101(2), Ti—N 2.178-(3), Ti—Cl2 2.3071(11), Ti—Cl1 2.3081(11), O2—Ti—O1 157.38(10), O1—Ti—O3 86.84(9), O2—Ti—N 76.45(9), O1—Ti—N 81.19(10), O2—Ti—Cl2 99.46(8), O1—Ti—Cl2 102.71(8), O3—Ti—Cl2 87.65(7), N—Ti—Cl2 175.12-(8), O2—Ti—Cl1 93.39(8), O1—Ti—Cl1 89.55(8), N—Ti—Cl1 88.94(7), Cl2—Ti—Cl1 93.99(4), C9—O2—Ti1 128.5(2), C1—O1—Ti1 128.5(2), C11—N1—Ti1 112.52(18), C6—N1—Ti1 127.0(2).

Scheme 1. Synthetic Routes to Complexes **1**−**3**
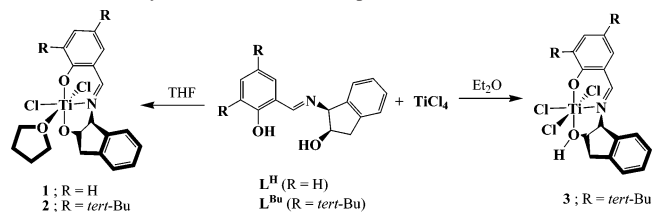
because they are easily synthesizable from cheap starting materials and are likely to form coordinatively saturated but sterically less congested titanium complexes. In this Communication, we report the synthesis and characterization of novel monomeric heteroleptic chlorotitanium complexes **1**−**3** containing chiral tridentate Schiff base ligands and their ROP behavior of L-LA.

Compounds **1**−**3** were obtained by adding dropwise a solution of TiCl$_4$ to an equimolar solution of **L^H** or **L^{Bu}** in tetrahydrofuran (THF) or Et$_2$O at −78 °C, as outlined in Scheme 1. For a given ligand **L^{Bu}**, the nature of the product is dependent on the solvent: THF and Et$_2$O led to six-coordinated dichlorotitanium complex **2** and trichlorotitanium complex **3**, respectively. In the case of **L^H**, the use of THF produced dichlorotitanium complex **1**, while the Et$_2$O system resulted in the formation of an intractable insoluble solid.

The molecular structure of **1**, displayed in Figure 1, shows that a fully deprotonated **L^H** in the meridional position, two chlorides, and THF form a distorted octahedral coordination around the metal center.[7] Compound **2** is also considered to have a similar coordination geometry as judged by various spectroscopic data including ^{1}H and ^{13}C{^{1}H} NMR and mass spectra. The X-ray analysis reveals that **3** also adopts a distorted octahedral geometry consisting of mono-deprotonated **L^{Bu}** in the meridional position and three chlorides[8] (see Figure 2). Spectroscopic data of **3** are totally different from those of **2**. The ligand **L^{Bu}** has two deprotonating sites of

(7) Crystal data for **L^H**TiCl$_2$THF (**1**; C$_{20}$H$_{21}$NO$_3$Cl$_2$Ti): orthorhombic, space group $P2_12_12_1$, $a = 8.0799(17)$ Å, $b = 13.225(3)$ Å, $c = 19.270$-(4) Å, $\alpha = \beta = \gamma = 90.00°$, $V = 2059.1(7)$ Å^3, $Z = 4$, $F(000) = 912$, $D = 1.426$ g/m^3, R1 = 0.0457, wR2 = 0.1084 for 3591 reflections with $I_0 > 2\sigma(I_0)$.

(8) Crystal data for **L^{Bu}**TiCl$_3$ (**3**; C$_{24}$H$_{30}$NO$_2$Cl$_3$Ti·C$_4$H$_{10}$O): orthorhombic, space group $P2_12_12_1$, $a = 10.9666(6)$ Å, $b = 12.2922(7)$ Å, $c = 23.8353(13)$ Å, $\alpha = \beta = \gamma = 90.00°$, $V = 3213.1(3)$ Å^3, $Z = 4$, $F(000) = 1248$, $D = 1.226$ g/m^3, R1 = 0.0347, wR2 = 0.0607 for 4009 reflections with $I_0 > 2\sigma(I_0)$.
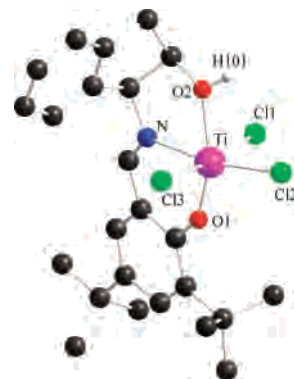
Figure 2. X-ray structure of **3**. Selected bond lengths (Å) and angles (deg): Ti—O1 1.7924(16), Ti—O2 2.0514(17), Ti—N 2.1570(19), Ti—Cl2 2.2782(8), Ti—Cl3 2.3028(8), Ti—Cl1 2.3475(9), O2—H101 0.808(24), O1—Ti—O2 157.81(8), O1—Ti—N 83.68(7), O2—Ti—N 74.29(8), O1—Ti—Cl2 106.34(5), O2—Ti—Cl2 95.38(6), N—Ti—Cl2 168.70(6), O1—Ti—Cl3 94.52-(6), O2—Ti—Cl3 88.52(5), Cl2—Ti—Cl3 93.43(3), O2—Ti—Cl1 84.92(5), N—Ti—Cl1 84.55(5), Cl3—Ti—Cl1 172.84(3).

Table 1. Summary of ROP of L-LA Using **1**−**3**[11]

entry[a]	catalyst	[L-LA]/[Ti]	yield (convn) (%)[b]	M_n[c]	M_w/M_n[c]
0	**L^H** or **L^{Bu}**	50	0		
1	**1**	200	56 (61)	8300	1.26
2	**2**	200	81 (85)	9300	1.26
3	**3**	50	75 (100)	2900	1.19
4	**3**	100	82 (100)	5600	1.27
5	**3**	150	85 (100)	7700	1.20
6	**3**	200	86 (100)	12400	1.25
7	**3**	250	81 (100)	13900	1.17
8[d]	**3'**	200	45 (50)	10100	1.28
9[d]	**3 + 3'**	100	80 (100)	10300	1.33

[a] Polymerization conditions: catalysts = 0.05 mmol, temp = 100 °C, time = 10 h, toluene = 1 mL. [b] Yield = obtained yield; conversion was calculated by integration of the ^{1}H NMR peak. [c] Determined by gel permeation chromatography relative to polystyrene standards. [d] Complex **3'** is a kind of enantiomeric analogue **3** containing an enantiomer of **L^{Bu}**.[14]

phenolic OH and indanolic OH, and it is reasonable to note that the more acidic phenolic OH is deprotonated in **3**, as judged by the spectroscopic data and the longer Ti—O2 in **3** (2.05 Å) than in **1** (1.88 Å). **1** and **3** constitute the first structurally characterized heteroleptic titanium complexes containing a chiral tridentate Schiff base.[9]

The possible removal of THF from **1** and **2** or HCl from **3** can make them attractive candidates for the ROP catalyst of LA even though they have no normal initiating groups such as amides, carboxylates, and alkoxides. Somewhat lower Ti—Cl bond dissociation energy ($\Delta H_f^{298} = 494$ kJ/mol)[10] compared with the analogous value for the Ti—O bond [$\Delta H_f^{298} = 662(16)$ kJ/mol][10] may support the foregoing speculation. Table 1 summarizes the results of the evaluation of **1**−**3** as a ROP catalyst of L-LA.

The activity of **1**−**3** is comparable to those of previously reported titanium alkoxide ROP catalysts,[3] and a reasonably low polydispersity index (PDI) for the molecular weight

(9) A structurally characterized homoleptic titanium system containing two chiral tridentate Schiff base ligands is known: Flores-Lopes, L. Z.; Parra-Hake, M.; Somanathan, R.; Walsh, P. J. *Organometallics* **2000**, *19*, 2153.

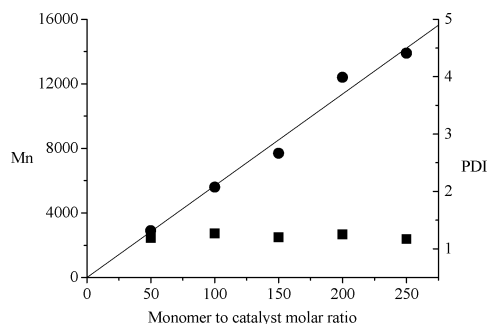(10) Speight, J. G. *Lange's Handbook of Chemistry*, 16th ed.; McGraw-Hill: Seoul, 2005; p 1.160.

Figure 3. Graph of the number-average molecular weight (●) and PDI (■) values in different monomer-to-catalyst molar ratios in ROP of complex **3**.

distribution implies that the polymerization is well-controlled. In general, an external source of alcohol such as benzyl alcohol is needed when the ROP catalysts do not contain alkoxide or amide groups.[1,2] However, the systems **1**−**3** are active for PLA even in the absence of an external source of alcohol. The end groups of PLA produced by **1**−**3** are neither **L^H** nor **L^{Bu}**, as checked by ^{1}H NMR spectroscopy.[2−5] In addition, the ligands **L^H** and **L^{Bu}** are inactive for ROP of L-LA (see Table 1, entry 0). Thus, the initiation may occur through the insertion of a chloride ion from the titanium catalysts into L-LA, being consistent with a polymerization process that proceeds via a coordination−insertion mechanism.[2] This was further supported by the observation of only one methine peak in the homonuclear-decoupled ^{1}H NMR spectra of PLA[2−5] and by the end-group analysis of short oligomers of L-LA with matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) spectrometry studies.[12]

Further investigation into the degree of control in the polymerization was carried out with the catalyst **3**. As the monomer-to-catalyst molar ratio [L-LA]/[Ti] increases from 50 to 250, the relative number-average molecular weight M_n increases linearly while the PDI values of PLA remain unchanged within the range of 1.19−1.27 under the conditions of the same conversion (100%), implying the presence of a substantially controlled polymerization process (Figure 3 and Table 1, entries 3−7). Thus, the catalytic systems **1**−**3** constitute the first examples of monomeric chlorotitanium complexes having high reactivity in controlled ROP of LA initiated by chloride.

The observed relative M_n values of PLA listed in Table 1 are almost half of the expected M_n values. For example, for

entry 6 the relative and expected M_n values are 12 400 and 28 800, respectively. MALDI-TOF spectra[12] of the separately prepared short oligomers of L-LA show sets of peaks that are equally spaced by the half mass unit of L-LA, implying the involvement of transesterification in the propagation process.[2g] Although transesterification, in particular intramolecular transesterification, is known to contribute to the decrease of the observed M_n values,[2b] the foregoing significant decrease is hardly rationalized by the transesterification term. Thus, it can be suggested that the catalysts **1**−**3** act as dual-site catalysts[13] and two polymer chains are growing at the same metal center with a high frequency of intramolecular transesterification. The meridional occupancy of **L^H** or **L^{Bu}** at the titanium centers may provide a sterically suitable spatial environment for the growth of two polymer chains initiated by chlorides.

The polymerization of L-LA has been further tested with **3′**, a kind of enantiomeric analogue **3** containing an enantiomer of **L^{Bu}**,[14] to confirm whether the catalytic systems show selectivity with respect to the chirality of the monomer or not. The system **3′** shows a lower activity than **3** (see Table 1, entry 8). Such a difference in activity might lead to control of the stereocenter in the ROP of *rac*-LA. Thus, the preparation of stereoblock-type PLA was tried by taking *rac*-LA and a *rac* catalyst (**3** + **3′**) as the monomer and catalyst, respectively, affording PLA that is dominantly atactic but with an increased isotactic portion of 45% (see Table 1, entry 9). Therefore, the current catalytic systems may have monomer selectivity to a certain extent but not large enough to give stereochemically controlled PLA.

In conclusion, new di- and trichlorotitanium catalyst systems were easily prepared, and their catalytic behavior in ROP of L-LA was investigated. Although **1**−**3** are lacking normal initiating groups such as alkoxides or amides, they showed high activities in the controlled polymerization of L-LA.

Supporting Information Available: Syntheses and characterization for **1**−**3**, X-ray data for compounds **1** and **3**, and MALDI-TOF spectra of oligomers of L-LA. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Polymerization of LA was carried out by charging a stirring bar and LA to a 20 mL round-bottomed flask in the glovebox, and then the flask was immersed in an oil bath of 100 °C. Polymerization began with the addition of a 1 mL stock toluene solution of the titanium compound. After 10 h, the polymerization was terminated by the addition of 5 mL of MeOH. After a small amount of the reaction mixture was taken as a sample for conversion measurement by ^{1}H NMR study, the reaction mixture was washed with excess methanol several times. The precipitated polymer was collected by filtration, washed with methanol (40 mL, washing five times), and dried in a vacuum oven at 40 °C for 12 h.

(12) See entry 6 of the Supporting Information.

(13) Systems with dual catalytic sites are known: (a) Takeuchi, D.; Nakamura, T.; Aida, T. *Macromolecules* **2000**, *33*, 725. (b) Perez, Y.; Hierro, I. d.; Sierra, I.; Gomez-sal, P.; Fajardo, M.; Otero, A. *J. Organomet. Chem.* **2006**, *691*, 3053.

(14) An enantiomer of **L^{Bu}** was prepared by Schiff base condensation of (1*S*,2*R*)-(+)-1-aminoindanol and 3,5-di-*tert*-butylsalicylaldehyde in ethanol. See the Supporting Information.