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Titanium Alkoxides as Initiators for the Controlled Polymerization of Lactide

Youngjo Kim, G. K. Jnaneshwara, and John G. Verkade*

Department of Chemistry, Iowa State University, Ames, Iowa 50011

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Fourteen titanium alkoxides were synthesized for comparison of their catalytic properties in the bulk and solution polymerization of lactide (LA). In bulk polymerizations, they are effective catalysts in terms of polymer yield and molecular weight. Titanatranes gave polylactides with significantly increased molecular weight over more extended polymerization times, and those with five-membered rings afforded polymers in higher yields and with larger molecular weights than their six-membered ring counterparts. Steric hindrance of the rings was found to significantly affect polymer yields. Increased heterotactic-biased poly(*rac*-LA) was formed as the number of chlorine atoms increased in $TiCl_x(O\text{-}i\text{-}Pr)_{4-x}$. In solution polymerizations, titanium alkoxides catalyzed controlled polymerizations of LA, and end group analysis demonstrated that an alkoxide substituent on the titanium atom acted as the initiator. That polymerization is controlled under our conditions was shown by the linearity of molecular weight versus conversion. A tendency toward formation of heterotactic-biased poly(*rac*-LA) was observed in the solution polymerizations. The rate of ring-opening polymerization (ROP) and the molecular weight of the polymers are greatly influenced by the substituents on the catalyst, as well as by factors such as the polymerization temperature, polymerization time, and concentration of monomer and catalyst.

Introduction

Polylactide (PLA) polymers are biodegradable renewable materials, and they are proving to be valuable, for example, as packaging films, diapers, and a variety of medical implant devices including matrices for the slow release of pharmaceuticals.[1]

The ring-opening polymerization (ROP) of cyclic esters such as lactide (LA) and ϵ-caprolactone (CL) with metal complexes has been intensively studied over the past few decades.[2] Many types of metal alkoxides (e.g., of tin,[3] aluminum,[4] zinc,[5] magnesium,[5] iron,[6] lanthanide,[7] and lithium[8] organometallic complexes) have been found to be active LA polymerization catalysts, and many afford materials with controlled molecular weights and narrow molecular weight distributions. Despite the fact that some excellent initiators have been reported for the polymerization of LA, the search for new catalysts that generate well-defined polylactides remains of keen interest. The roles of the structure of metal alkoxide complexes in determining molecular weights and molecular weight distributions, as well as the polymerization pathway, are significant current research issues.

In view of the well-known significant number of similarities in the chemistries of tin and titanium, we were somewhat surprised to note that, until our entry into this area, no

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* To whom correspondence should be addressed. E-mail: jverkade@iastate.edu. Fax: 515-294-0105.

(1) (a) Chiellini, E.; Solaro, R. *Adv. Mater. (Weinheim, Ger.)* **1996**, *8*, 305−313. (b) Tullo, A. *Chem. Eng. News* **2000**, *78*, 13. (c) Bogaert, J. C.; Coszach, P. *Macromol. Symp.* **2000**, *153*, 287. (d) Vert, M. *Macromol. Symp.* **2000**, *153*, 333. (e) Drumright, R. W.; Gruber, P. R.; Henton, D. E. *Adv. Mater. (Weinheim, Ger.)* **2000**, *12*, 1841. (f) Dorgan, J. R.; Lehermeier, H. J.; Palade, L. I.; Cicero, J. *Macromol. Symp.* **2001**, *175*, 55.

(2) See: (a) Kuran, W. *Prog. Polym. Sci.* **1998**, *23*, 919. (b) O'Keefe, B. J.; Hillmyer, M. A.; Tolman, W. B. *J. Chem. Soc., Dalton Trans.* **2001**, 2215 and references therein.

(3) (a) Nijenhuis, A. J.; Grijpma, D. W.; Pennings, A. J. *Macromolecules* **1992**, *25*, 6419. (b) Kricheldorf, H. R.; Lee, S.-R.; Bush, S. *Macromolecules* **1996**, *29*, 1375. (c) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 3431. (d) Atthoff, B.; Trollsås, M.; Claesson, H.; Hedrick, J. L. *Macromol. Chem. Phys.* **1999**, *200*, 1333. (e) Duda, A.; Penczek, S.; Kowalsik, A.; Libiszowski, J. *Macromol. Symp.* **2000**, *153*, 41. (f) Kricheldorf, H. R. *Macromol. Symp.* **2000**, *153*, 55. (g) Kowalski, A.; Libiszowski, J.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 1964. (h) Stridsberg, K.; Ryner, M.; Albertsson, A. C. *Macromolecules* **2000**, *33*, 2862. (i) Dove, A. P.; Gibson, V. C.; Marshall, E. L.; White, A. J. P.; Williams, D. J. *Chem. Commun.* **2001**, 283. (j) Möller, M.; Nederberg, F.; Lim, L. S.; Kånge, R.; Hawker, C. J.; Hedrick, J. L.; Gu, Y.; Shah, R.; Abbott, N. L. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 3529. (k) Ryner, M.; Finne, A.; Albertsson, A. C.; Kricheldorf, H. R. *Macromolecules* **2001**, *34*, 7281. (l) Aubrecht, K. B.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules* **2002**, *35*, 644. (m) Finne, A.; Albertsson, A. C. *Biomacromolecules* **2002**, *3*, 684.

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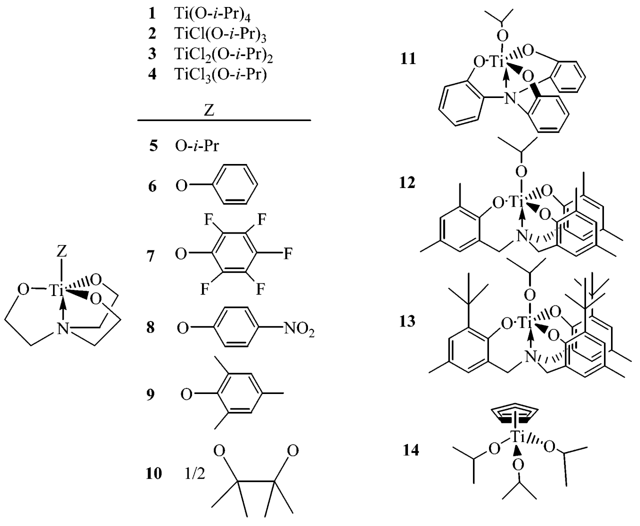
investigations of titanium alkoxides as potential catalysts in LA polymerization had been reported.[9] Interestingly, such compounds are well-known to homogeneously catalyze olefin polymerization,[10] and some Ti complexes have been found to polymerize CL.[11] Recently, we[9] reported that several titanium alkoxides showed reasonably good catalytic activity in the bulk homopolymerization of *l*-LA and *rac*-LA at 130 °C. Harada et al.[11d] also reported the living polymerization of LA by a Ti chloride complex, whose chloride apparently plays the same role as an alkoxide.

We thus believed it would be interesting to test titanium catalysts with well-defined ligand environments amenable to systematic variation, thus potentially facilitating more control of the molecular and physical properties of the PLA produced. Here, we describe discrete titanium alkoxide complexes for the study of the ROP of LA and CL under bulk and solution polymerization conditions. We also demonstrate that some of our titanium alkoxide catalysts allow well-controlled polymerizations of LA and CL, and that some of these catalysts give heterotactic-biased PLA derived from *rac*-LA.

The strategy we employed for choosing candidate titanium catalysts **1**−**14** is that, first of all, they should contain alkoxide groups, because such metal substituents have proven to be the initiation group of choice in the vast majority of previous studies. Second, the initiating alkoxide group should dissociate relatively easily from the titanium in the early stage of polymerization so that it can be utilized to initiate LA polymerization and provide a means of controlling the molecular weight by functioning as an end group. Alkoxy titanatranes seemed well-suited to these purposes because they possess a transannular Ti−N bond that could potentially labilize the *trans* axial OR group.



Results and Discussion

Syntheses. Except for minor modifications (see Experimental Section), compounds **2**−**4** were obtained by the reaction of **1** with the appropriate amount of $TiCl_4$ in pentane at room temperature.[12] Unlike slightly viscous **2**, compounds **3** and **4** precipitated as white solids within 20 min after combination of the reactants. To avoid generation of byproducts and mixtures of **2**−**4**, a solution of $TiCl_4$ in dry pentane was added dropwise to exactly the appropriate number of equivalents of **1** in pentane while stirring rapidly at room

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(4) (a) Dubois, P.; Jacobs, C.; Jerome, R.; Teyssie, P. *Macromolecules* **1991**, *24*, 2266. (b) Spassky, N.; Wisniewski, M.; Pluta, C.; Le Borgne, A. *Macromol. Chem. Phys*. **1996**, *197*, 2627. (c) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **1998**, *31*, 2114. (d) Emig, N.; Nguyen, H.; Krautscheid, H.; Réau, R.; Cazaux, J.-B.; Bertrand, G. *Organometallics* **1998**, *17*, 3599. (e) Cameron, P. A.; Jhurry, D.; Gibson, V. C.; White, A. J. P.; Williams, D. J.; Williams, S. *Macromol. Rapid Commun*. **1999**, *20*, 616. (f) Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc*. **1999**, *121*, 4072. (g) Eguiburu, J. L.; Fernandez-Berridi, M. J.; Cossío, F. P.; Román, J. S. *Macromolecules* **1999**, *32*, 8252. (h) Ko, B. T.; Lin, C. C. *Macromolecules* **1999**, *32*, 8296. (i) Bhaw-Luximon, A.; Jhurry, D.; Spassky, N. *Polym. Bull.* **2000**, *44*, 31. (j) Kitayama, T.; Yamaguchi, H.; Kanzawa, T.; Hirano, T. *Polym. Bull.* **2000**, *45*, 97. (k) Radano, C. P.; Baker, G. L.; Smith, M. R. *J. Am. Chem. Soc*. **2000**, *122*, 1552. (l) Ovitt, T. M.; Coates, G. W. *J. Polym. Sci., Part A: Polym. Chem*. **2000**, *38*, 4686. (m) Jhurry, D.; Bhaw-Luximon, A.; Spassky, N. *Macromol. Symp.* **2001**, *175*, 67. (n) Huang, C. H.; Wang, F. C.; Ko, B. T.; Yu, T. L.; Lin, C. C. *Macromolecules* **2001**, *34*, 356. (o) Chen, H. L.; Ko, B. T.; Huang, B. H.; Lin, C. C. *Organometallics* **2001**, *20*, 5076. (p) Liu, Y. C.; Ko, B. T.; Lin, C. C. *Macromolecules* **2001**, *34*, 6196. (q) Chisholm, M. H.; Navarro-Llobet, D.; Simonsick, W. J., Jr. *Macromolecules* **2001**, *34*, 8851. (r) Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1316. (s) Nomura, N.; Ishii, R.; Akakura, M.; Aoi, K. *J. Am. Chem. Soc.* **2002**, *124*, 5938.

(5) (a) Chisholm, M. H.; Eilerts, N. W. *Chem. Commun*. **1996**, 853. (b) Cheng, M.; Attygalle, A. B.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc*. **1999**, *121*, 11583. (c) Chisholm. M. H.; Eilerts, N. W.; Huffman, J. C.; Iyer, S. S.; Pacold, M.; Phomphrai, K. *J. Am. Chem. Soc*. **2000**, *122*, 11845. (d) Chisholm, M. H.; Huffman, J. C.; Phomphrai, K. *J. Chem. Soc., Dalton Trans*. **2001**, 222. (e) Chamberlain, B. M.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc*. **2001**, *123*, 3229. (f) Chisholm, M. H.; Gallucci, J. C.; Zhen, H. *Inorg. Chem.* **2001**, *40*, 5051. (g) Chisholm, M. H.; Navarro-Llobet, D.; Gallucci, J. *Inorg. Chem.* **2001**, *40*, 6506.

(6) (a) Stolt, M.; Sodergard, A. *Macromolecules* **1999**, *32*, 6412. (b) O'Keefe, B. J.; Monnier, S. M.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc*. **2001**, *123*, 339. (c) O'Keefe, B. J.; Breyfogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc*. **2002**, *124*, 4384.

(7) (a) Stevels, W. M.; Ankone, M. J. K.; Dijkstra, P. J.; Feijen, J. *Macromolecules* **1996**, *29*, 3332. (b) Stevels, W. M.; Ankone, M. J. K.; Dijkstra, P. J.; Feijen, J. *Macromolecules* **1996**, *29*, 6132. (c) Simic, V.; Spassky, N.; Hubert-Pfalzgraf, L. G. *Macromolecules* **1997**, *30*, 7338. (d) Chamberlain, B. M.; Sun, Y.; Hagadorn, J. R.; Hemmesch, E. W.; Young, V. G., Jr.; Pink, M.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules* **1999**, *32*, 2400. (e) Yuan, M.; Xiong, C.; Li, X.; Deng, X. *J. Appl. Polym. Sci.* **1999**, *73*, 2857. (f) Simic, V.; Pensec, S.; Spassky, N. *Macromol. Symp.* **2000**, *153*, 109. (g) Deng, X.; Yuan, M.; Li, X.; Xiong, C. *Eur. Polym. J.* **2000**, *36*, 1151. (h) Spassky, N.; Simic, V.; Montaudo, M. S.; Hubert-Pfalzgraf, L. G. *Macromol. Chem. Phys.* **2000**, *201*, 2432. (i) Chamberlain, B. M.; Jazdzewski, B. A.; Pink, M.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules* **2000**, *33*, 3970. (j) Aubrecht, K. B.; Chang, K.; Hillmyer, M. A.; Tolman, W. B. *J. Polym. Sci., Part A: Polym. Chem*. **2001**, *39*, 284. (k) Giesbrecht, G. R.; Whitener, G. D.; Arnold, J. *J. Chem. Soc., Dalton Trans*. **2001**, 923. (l) Save, M.; Schappacher, M.; Soum, A. *Macromol. Chem. Phys.* **2002**, *203*, 889.

(8) Ko, B.-T.; Lin, C.-C. *J. Am. Chem. Soc.* **2001**, *123*, 7973.

(9) (a) Kim, Y.; Verkade, J. G. *Organometallics* **2002**, *21*, 2395. (b) Kim, Y.; Kapoor, P. N.; Verkade, J. G. *Inorg. Chem.* **2002**, *41*, 4834. (c) Kim, Y.; Verkade, J. G. *Macromol. Rapid Commun*. **2002**, *23*, 917. (d) Kim, Y.; Verkade, J. G. In preparation.

(10) Gladysz, J. A., Ed. *Chem. Rev.* **2000**, *100*, 1167−1682.

(11) (a) Okuda, J.; Rushkin, I. L. *Macromolecules* **1993**, *26*, 5530. (b) Takeuchi, D.; Nakamura, T.; Aida, T. *Macromolecules* **2000**, *33*, 725. (c) Takeuchi, D.; Aida, T. *Macromolecules* **2000**, *33*, 4607. (d) Takashima, Y.; Nakayama, Y.; Watanabe, K.; Itono, T.; Ueyama, N.; Nakamura, A.; Yasuda, H.; Harada, A.; Okuda, J. *Macromolecules* **2002**, *35*, 7538.

(12) Kamigaito, M.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1995**, *28*, 5671.

temperature for 10 min. After washing thoroughly with cold pentane, these titanium compounds were used as catalysts for making PLA or as starting materials for other titanium alkoxides. Compounds **2**−**4** were soluble in toluene, dichloromethane, and ether. Displacement of the chloride from **2** with CpNa in toluene gave the desired product **14** as a reddish-yellow oil.

Our group[13] and Do's group[14] have synthesized several types of titanatranes by an amine or chloride displacement with an alkoxide or triethanolamine. Here, we synthesized the new titanatranes **6**−**9** in very good yield in a one-pot reaction containing Ti(O-*i*-Pr)$_4$, triethanolamine, and the appropriate phenol. These compounds were also synthesized by a two-step reaction in which **5** is made from Ti(O-*i*-Pr)$_4$ and triethanolamine, followed by reaction with the corresponding phenol. However, yields were lower than from a one-pot reaction (see Experimental Section). Although **6** and **9** showed good solubilities, **7** and **8** displayed limited solubility in a wide variety of solvents. Despite the limited solubility of **7** and **8**, we were able to isolate these compounds in analytically pure form. We previously showed that **10** could be synthesized in 70% overall yield by reacting 2 equiv of (diethylamino)titanatrane with 1 equiv of pinacol starting from tetrakis(diethylamino)titanium and triethanolamine.[13] However, in the present work, we found that the reaction between 2 equiv of **5** and 1 equiv of pinacol at room temperature generated **10** in an overall yield of 84% with a starting material (**5**) that is less expensive than tetrakis(diethylamino)titanium.

We first attempted to synthesize **11**, **12**, and **13** by transesterifying **1** with the tris(phenol)s tris(2-hydroxyphenyl)amine (2,2′,2″-nitrilotriphenol, THA),[15] tris(2-hydroxy-3,5-dimethylbenzyl)amine (THDA),[16] and tris(2-hydroxy-3-*tert*-butyl-5-methylbenzyl)amine (THBA),[16] respectively. However, **11**−**13** obtained in this manner were contaminated with *i*-PrOH despite extended drying under vacuum. For example, **11** consistently retained 0.5 equiv of *i*-PrOH after several recrystallizations from THF/toluene. In searching for a new synthetic route to **11**−**13**, **4** was chosen as the starting material. We had anticipated that the reaction of **4** with THDA in the presence of triethylamine under mild conditions could involve chloride displacement from the metal by THDA. This prediction was based on a somewhat lower Ti−Cl bond dissociation energy (430 kJ/mol for TiCl$_4$,[17]) compared with the analogous value for the Ti−O-*i*-Pr bond [444 kJ/mol for Ti(O-*i*-Pr)$_4$[17]]. However, the product obtained in the reaction of **4** with THDA was the corresponding chlorotitanatrane, which was also reported recently[18] to form in the reaction of CpTiCl$_3$ with THDA wherein the η^5-Cp ligand is displaced. Thus, as was reported earlier by others,[19] we synthesized **12** in high yield by reacting **14** with THDA, a reaction that also occurs by displacement of a η^5-Cp ligand (see Experimental Section). The C$_5$−Ti bond dissociation energy associated with the η^5-Cp−Ti moiety is 335 kJ/mol [an interpolated value between that of η^5-CpTiCl$_3$ and (η^5-Cp)$_2$TiCl$_2$[17]]. The leaving ability of these groups in their displacement by THDA decreases in the order Cp > O-*i*-Pr > Cl in which the last two members appear reversed considering only the bond dissociation energies involved. Because the difference between these latter two energies is only about 3%, greater relief of steric strain by departure of an O−*i*-Pr compared with that of a Cl substituent may dominate their leaving ability order. Compounds **11** and **13** were made starting from **1** (see Experimental Section). All the compounds evaluated as catalysts in the present work were prepurified by recrystallization or distillation.

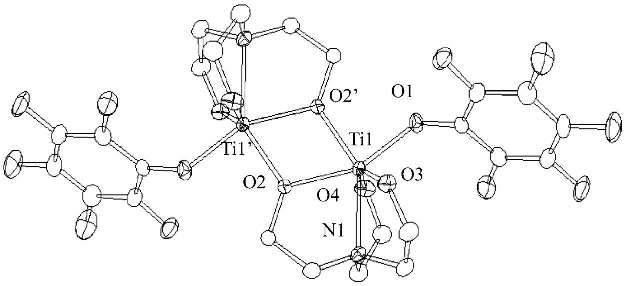

Figure 1. ORTEP drawing of **7** showing 50% probability thermal ellipsoids with H atoms and solvent omitted for clarity. Selected bond distances (Å): Ti1−O1 = 1.977(2), Ti1−O2 = 2.0588(19), Ti1−O3 = 1.8261(19), Ti1−O4 = 1.8320(19), Ti1−N1 = 2.284(2), Ti1−Ti1′ = 3.3107(11), Ti1−O2′ = 1.9881(18). Selected bond angles (deg): O1−Ti1−N1 = 128.95(8), O1−Ti1−O2 = 155.37(7), O1−Ti1−O3 = 90.46(9), O1−Ti1−O4 = 85.42(8), O2−Ti1−O3 = 100.87(9), O1−Ti1−O4 = 138.29(9).

Crystal and Molecular Structure of 7. The ORTEP depiction[20] of the structure is shown in Figure 1, and selected interatomic distances and angles are provided in the caption of Figure 1 and in Table 1. The X-ray analysis of **7** reveals that its molecular structure features an oxo bridge as is commonly observed for titanatranes in the solid state.[13,21] As the ORTEP drawing in Figure 1 illustrates, the geometry around each titanium in **7** can be viewed as a distorted octahedron. The four oxygen atoms of the ethylene arms form the equatorial plane, and the axial sites are occupied by a nitrogen atom of the tripodal ligand and an oxygen atom of the pentafluorophenoxy group.

Although the only difference between **5** and **7** is the Z substituent of the alkoxide, the coordination geometry of **7** differs substantially from the one in compound **5**[21] in that the axial Z substituent in **5** is *trans* to a nitrogen, whereas **7** is derived from **5** by a twist indicated by the curved arrows

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[13] (a) Menge, W. M. B. P.; Verkade, J. G. *Inorg. Chem.* **1991**, *30*, 4628. (b) Naiini, A. A.; Menge, W. M. B. P.; Verkade, J. G. *Inorg. Chem.* **1991**, *30*, 5009. (c) Naiini, A. A.; Ringrose, S. L.; Su, Y.; Jacobson, R. A.; Verkade, J. G. *Inorg. Chem.* **1993**, *32*, 1290.

[14] (a) Kim, Y.; Hong, E.; Lee, M. H.; Kim, J.; Han, Y.; Do, Y. *Organometallics* **1999**, *18*, 36. (b) Kim, Y.; Han, Y.; Hwang, J. W.; Kim, M. W.; Do, Y. *Organometallics* **2002**, *21*, 1127.

[15] Frye, C. L. Fr. Patent 1511256, 1968; *Chem. Abstr.* 70: 87303.

[16] (a) Chandrasekaran, A.; Day, R. O.; Holmes, R. R. *J. Am. Chem. Soc.* **2000**, *122*, 1066. (b) Timosheva, N. V.; Chandrasekaran, A.; Day, R. O.; Holmes, R. R. *Organometallics* **2000**, *19*, 5614. (c) Timosheva, N. V.; Chandrasekaran, A.; Day, R. O.; Holmes, R. R. *Organometallics* **2001**, *20*, 2331.

[17] Connor, J. A. *Top. Curr. Chem.* **1977**, *71*, 71.

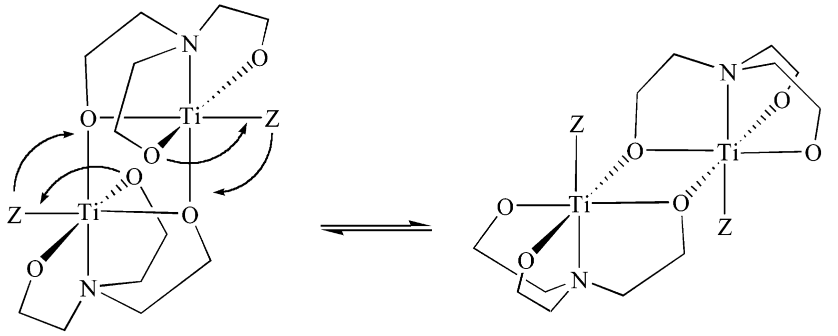
[18] Michalczyk, L.; de Gala S.; Bruno, J. W. *Organometallics* **2001**, *20*, 5547.

[19] Kol, M.; Shamis, M.; Goldberg, I.; Goldschmidt, Z.; Alfi, S.; Hayut-Salant, E. *Inorg. Chem. Commun.* **2001**, *4*, 177.

[20] Johnson, C. K. *ORTEP*; Report ORNL-5138; Oak Ridge National Laboratory, Oak Ridge, TN, 1976.

[21] Harlow, R. L. *Acta Crystallogr.* **1983**, *C39*, 1344.

Table 1. Comparison of Bond Angles (deg) and Bond Distances (Å) in Dimeric titanatranes



Z = O-*i*-Pr, **5**

Z = OC_6F_5, **7**
S-*i*-Pr, **15**
NMe_2, **16**

structural param	5	7	15	16
$O_{bridge}-Ti-Z$ (deg)	113.20(5)	155.37(7)	171.03(6)	179.46(6)
$N_{bridgehead}-Ti-O_{bridge}$ (deg)	75.23(4)	145.40(8)	148.44(9)	151.10(6)
$Ti-O_{bridge}-Ti'$ (deg)	109.66(5)	109.77(8)	107.40(9)	105.01(5)
Ti−Ti (Å)	3.356(1)	3.3107(11)	3.273(1)	3.2547(6)
$Ti-N_{bridgehead}$ (Å)	2.333(1)	2.284(2)	2.269(3)	2.270(2)
$Ti-O_{bridge}$ (Å)	2.053(1)	2.0235(19)	2.029(2)	2.050(1)
$Ti-O_{terminal}$ (Å)[a]	1.854(1)	1.8784(19)	1.875(1)	1.845(1)
ref	21	this work	13c	13b

[a] Average value.

in the transformation shown in Table 1. Previously, we suggested that a more electron-donating substituent Z such as S-*i*-Pr or NMe_2 in a titanatrane (**15** and **16**, respectively, in Table 1) would prefer to occupy a position *trans* to a bridging oxygen rather than to the more electron-donating tertiary bridgehead nitrogen atom.[13] However, no investigations of an oxo-bridged dimeric titanatrane bearing a strongly electron-withdrawing substituent Z have been reported. It appears that influences such as subtle steric and/or crystal packing effects may play a role in determining solid state conformations of these compounds.

Comparisons of pertinent bond angles and bond distances in the dimeric titanatranes **5**, **7**, **15**, and **16** are shown in Table 1. As the substituent Z changes from **5** to **7**, to **15**, and to **16**, a widening of the $O_{bridge}-Ti-Z$ bond angles [113.20(5)° in **5** to 179.46(6)° in **16**] occurs with concomitant opening of the $N_{bridgehead}-Ti-O_{bridge}$ bond angles [75.23(4)° in **1** to 151.10(6)° in **16**]. Even though **7** would be expected to have the shortest $Ti-N_{bridgehead}$ bond length and the longest Ti−Ti distance, the actual values curiously fall between these bond lengths for **5** and those for **15** or **16**. Like the situation for other oxo-bridged titanatrane dimers,[13,21] substantial Ti−Ti interaction was not indicated to be present in **7**. Also worthy of mention is that **7** has the shortest $Ti-O_{bridge}$ and the longest $Ti-O_{terminal}$ bond length of any oxygen-bridged dimeric titanatranes reported so far.[13,21] However, the average Ti−O bond distance for all the oxygens of **7** is similar to the average of this distance observed for other structurally characterized titanatranes.[13,14,21] The weaker interaction of $O_{terminal}$ with the titanium atom can be ascribed to repulsions from the combined effect of robust $Ti-O_{bridge}$ bonding and a strong transannular interaction from the bridgehead nitrogen. These observations suggest that the halves of **7** could be described as being bound together by predominantly alkoxy-type bridging bonds (similar to those in **15** and **16** in Table 1) while the analogous halves of **5** are bridged by predominantly donor−acceptor-like linkages.

NMR Spectra. The chemical shift of the *i*-Pr group in the ^1H NMR spectra of **1**−**4** moves downfield in the same order as expected on the basis of the electron-withdrawing effect of the chlorides. Titanatranes **5**−**10** can be divided into four categories on the basis of their ^1H and $^{13}C\{^1H\}$ NMR spectra. In the first category is **5**, whose solution ^1H and $^{13}C\{^1H\}$ NMR spectra are quite temperature-independent, displaying sharp resonances for two types of CH_2CH_2O protons. The spectra are consistent with monomeric behavior in solution, though it is a dimer in the solid state. Compounds **6**−**8** constitute a second category, for which the ^1H and $^{13}C\{^1H\}$ NMR spectra are broadened at room temperature, presumably owing to an exchange process that is relatively slow on the NMR time scale. Because dilution of solutions of these dimers does not affect the breadth of their ^1H NMR spectra, the exchange process can be envisioned as being dominated by an intramolecular “gearing” type of fluxionality around their Z−Ti−N axes rather than by dissociation into monomers.[13] This gearing motion requires the breakage of only one bridge bond at a time with the subsequent formation of a new one as opposite rotations about the Z−Ti−N axes occur. Thus, ^1H NMR spectroscopic data for **7** in $CDCl_3$ are consistent with retention of the dimeric unit in solution. Room temperature ^1H and $^{13}C\{^1H\}$ NMR spectra of **9** display sharp resonances which are consistent with the presence of two types of CH_2CH_2O groups in a 1:1 ratio. Because of the bulky nature of the apical substituent Z, this compound is monomeric in solution as well as in the solid state, thus representing a third category of titanatranes. Dimeric compound **10** is a member of a trivial fourth category for which the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra are sharp over a wide temperature range.

The structures of **11**−**13** can be described as a 3-bladed turbine of C_3 symmetry.[9a,18,19] Although the presence of a transannular bond in **11** has not been verified, it is likely to exist on the basis of its presence in a titanatrane[18] and in several silatranes[22] containing the THA ligand. The ^{1}H NMR spectra of **11**−**13** display well-defined resonances possessing expected integrations. Compounds **12** and **13** should have *pseudo*-C_3 symmetry on the NMR time scale, and therefore, the benzylic CH_2 protons should not be equivalent. Indeed, the proximity of these protons to the aromatic rings may be responsible for the ca. 1.1 ppm chemical shift difference displayed in the room temperature spectra. Upon heating, compounds **12** and **13** assume *pseudo*-C_{3v} symmetry on the NMR time scale, and all six CH_2 protons become equivalent. Similar observations for (2,6-di-*i*-PrC_6H_3O)-Ti(O-2,4-$Me_2C_6H_2CH_2)_3N$ (**17**) and *i*-PrOTi(O-2,4-*tert*-$Bu_2C_6H_2CH_2)_3N$ (**18**) were reported recently by us[9a] and by Kol et al.,[19] respectively.

Bulk Polymerization of LA. Bulk ROP of LA initiated by **1**−**14** was carried out at 130 °C with the [LA]/[Ti] ratio fixed at 300, and Table 2 shows that all of these compounds were effective catalysts. The end groups of PLA produced by **1**−**14** are the corresponding alkoxy ester units as indicated by ^{1}H NMR spectroscopy.[23] Because chloride ion is also known to function as an initiator in LA polymerization,[11d] $TiCl_4$ was also evaluated (Table 2, entry 43). Thus, initiation occurs through the insertion of the alkoxy group from the titanium catalyst into *l*-LA or *rac*-LA, consistent with a polymerization process that proceeds via a coordination−insertion mechanism. This was further supported by homonuclear decoupled ^{1}H NMR spectroscopy. Such spectra of PLA derived from *rac*-LA display the characteristic five methine resonances, whereas spectra of PLA derived from *l*-LA exhibit only one methine peak.[23] However, we believe at this stage that some transesterification occurred during polymerization, because the PDI values of the resulting polymers were somewhat higher than expected for a controlled polymerization.

Proceeding from **1** to **4**, catalytic activity and molecular weights generally increased, though the corresponding PDI values generally decreased in that order (Table 2, entries 1−8). We were unable to distinguish between the relative catalytic activities of **3** and **4** and also between those of **1** and **2** on the basis of yield at the end of 2 h. Therefore, the polymerizations were terminated at the end of 30 min when the trend in the yields for **1** to **4** was more apparent (Table 2, entries 9−12). With these catalysts, we also observed that the homonuclear decoupled ^{1}H NMR spectra of poly(*rac*-LA) derived from **3** and **4**, respectively, in Figure 2c and d are quite different from the spectra in Figure 2a and b which were derived from **1** and **2**, respectively. This result is consistent with that predicted from a Bernouillian analysis of totally random poly(*rac*-LA).[23] The methine region in the homonuclear decoupled ^{1}H NMR spectrum of poly(*rac*-LA) derived from **3** and **4** displays *rmr* and *mrm* tetrads which are much more intense than expected. These observations are consistent with a heterotactic-biased poly(*rac*-LA) because the *rmr* microstructure can only arise from two consecutive D−L or L−D interchanges. Each *rmr* tetrad is accompanied by two *mrm* tetrads in agreement with the NMR integration (Table 2, entries 6 and 8). The preference for heterotacticity in our poly(*rac*-LA) is not as strong as reported previously by Coates et al.[5b,e] and Kasperczyk et

Table 2. Bulk Polymerization of LA at 130 °C

entry	catalyst[a]	lactide type	time	yield (%)	M_w[b]	M_n[b]	PDI[b]
1	**1**	*l*-LA	2 hr	75	35 700	16 000	2.24
2		*rac*-LA	2 hr	71	41 100	19 600	2.10
3	**2**	*l*-LA	2 hr	79	40 700	27 600	1.47
4		*rac*-LA	2 hr	75	38 000	23 800	1.60
5	**3**	*l*-LA	2 hr	92	36 900	19 900	1.85
6		*rac*-LA	2 hr	90	34 900	28 400	1.23
7	**4**	*l*-LA	2 hr	94	79 500	60 900	1.31
8		*rac*-LA	2 hr	93	97 600	68 600	1.42
9	**1**	*l*-LA	30 min	20	*c*	*c*	*c*
10	**2**	*l*-LA	30 min	29	*c*	*c*	*c*
11	**3**	*l*-LA	30 min	37	*c*	*c*	*c*
12	**4**	*l*-LA	30 min	46	*c*	*c*	*c*
13	**5**	*l*-LA	2 h	69	135 400	80 000	1.69
14		*rac*-LA	2 h	66	132 600	78 200	1.70
15		*l*-LA	15 h	92	270 300	73 500	3.68
16		*rac*-LA	15 h	90	303 600	119 200	2.55
17	**6**	*l*-LA	4 h	71	73 500	39 500	1.86
18		*rac*-LA	4 h	75	38 900	21 800	1.78
19		*l*-LA	15 h	91	188 200	101 100	1.86
20		*rac*-LA	15 h	88	136 500	76 900	1.78
21	**7**	*l*-LA	4 h	92	91 100	63 200	1.44
22		*rac*-LA	4 h	88	61 000	39 500	1.56
23		*l*-LA	15 h	98	273 700	94 500	2.90
24		*rac*-LA	15 h	93	245 000	93 200	2.63
25	**8**	*l*-LA	4 h	89	112 700	66 500	1.69
26		*rac*-LA	4 h	84	44 000	25 500	1.72
27		*l*-LA	15 h	96	223 100	110 900	2.01
28		*rac*-LA	15 h	95	142 500	82 700	1.72
29	**9**	*l*-LA	4 h	84	65 800	43 900	1.50
30		*rac*-LA	4 h	82	30 900	19 600	1.57
31		*l*-LA	15 h	94	131 400	82 600	1.59
32		*rac*-LA	15 h	91	115 500	67 900	1.70
33	**10**	*l*-LA	15 h	95	98 200	46 700	2.10
34		*rac*-LA	15 h	91	72 800	34 700	2.10
35	**11**	*l*-LA	4 h	95	161 800	80 800	2.00
36		*rac*-LA	4 h	94	194 400	96 000	2.02
37	**12**	*l*-LA	4 h	55	76 100	52 000	1.46
38		*rac*-LA	4 h	53	51 400	38 000	1.35
39	**13**	*l*-LA	14 h	26	38 400	28 400	1.35
40		*rac*-LA	14 h	24	43 400	30 200	1.44
41	**14**	*l*-LA	2 h	97	38 300	29 200	1.31
42		*rac*-LA	2 h	94	31 200	20 000	1.56
43	$TiCl_4$	*l*-LA	2 h	0			

[a] Oil bath temperature: 130 (±3) °C, [LA]/[Ti] = 300, 2 g of LA. [b] The weight average molecular weights (M_w), the number average molecular weights (M_n), and the polydispersity indices (PDI = M_w/M_n) were determined by GPC. [c] Not determined.

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(22) (a) Frye, C. L.; Vincent, G. A.; Hauschildt, G. L. *J. Am. Chem. Soc.* **1966**, *88*, 2727. (b) Boer, F. P.; Turley, J. W.; Flynn, J. J. *J. Am. Chem. Soc.* **1968**, *90*, 5102. (c) Livant, P.; Northcott, J.; Webb, T. R. *J. Organomet. Chem.* **2001**, *620*, 133.

(23) (a) Thakur, K. A. M.; Kean, R. T.; Hall, E. S.; Kolstad, J. J.; Lindgren, T. A.; Doscotch, M. A.; Siepmann, J. I.; Munson, E. J. *Macromolecules* **1997**, *30*, 2422. (b) Thakur, K. A. M.; Kean, R. T.; Hall, E. S.; Doscotch, M. A.; Munson, E. J. *Anal. Chem.* **1997**, *69*, 4303. (c) Thakur, K. A. M.; Kean, R. T.; Hall, E. S.; Kolstad, J. J. Munson, E. J. *Macromolecules* **1998**, *31*, 1487. (d) Thakur, K. A. M.; Kean, R. T.; Zell, M. T.; Padden, B. E.; Munson, E. J. *Chem. Commun.* **1998**, 1913.

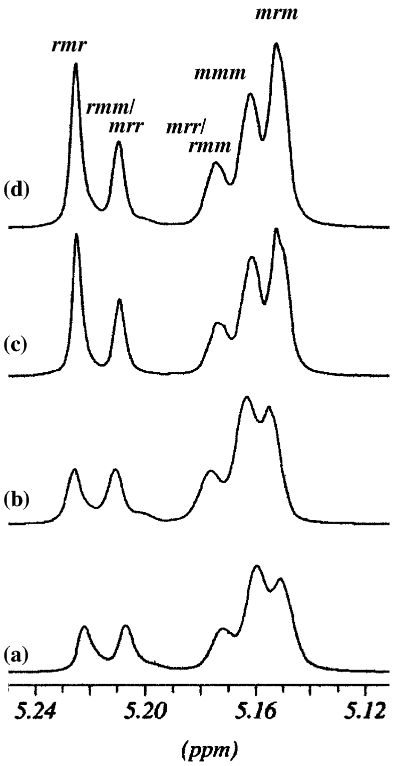

Figure 2. Methine region of homonuclear decoupled ^{1}H NMR spectra for poly(*rac*-LA) produced by (a) **1**, (b) **2**, (c) **3**, and (d) **4** under bulk polymerization conditions.

al.,[24] but our tacticity bias is similar to that reported by Gibson and co-workers.[3i] It is interesting that in proceeding from **1** to **4** (Table 2, entries 2, 4, 6, and 8), the intensity of heterotactic-biased poly(*rac*-LA) augments significantly for reasons that are not obvious, especially because the precise mechanism for preferred heterotacticity is currently unknown.

It is worth noting that titanatranes **5**−**9** provide PLA with significantly increased molecular weights which are associated with the polymerization time (Table 2, entries 13−32). The same result was also observed in the syndiospecific polymerization of styrene using Cp*Ti(OCH_2CH_2)$_3$N, in which there is also a transannular bond from the bridgehead nitrogen to the titanium.[14] The unexpectedly high molecular weights may be due to a faster rate of propagation than initiation. This notion was supported by the observation of bimodal GPC traces for some of the polymer samples. Thus, although such traces of the polymers prepared using **5**−**9** with [LA]/[Ti] = 300 were unimodal up to 80% conversion, they began to show bimodal peaks at conversions greater than 90%, which is consistent with the predictable effects of transesterification processes in lactone polymerization.[2] Thus, when transesterification effectively competes with ROP, the PDI values of the resultant polymers should rise with increasing conversion, and molecular weight distributions may be bimodal.[25] The same bimodal GPC patterns were observed in PLA prepared with **10** (which is a dialkoxide-bridged bis-titanatrane) and by **11** (Table 2, entry 33−36).

Compound **10** contains a pinacolate ligand, which could allow this catalyst to behave as a difunctional initiator in the polymerization of LA, thus leading to a significant increase in molecular weight than with other titanatranes. However, no significant increase of molecular weight was observed with the use of **10**. Moreover, elemental analysis revealed that there is less than 0.003% titanium in the polymer obtained with this catalyst, which is far less than the 0.049% expected had not the titanatrane structure at both ends of the anticipated polymer chain been solvolyzed by the excess MeOH used to isolate and purify the polymers.

In terms of yield and molecular weight, titanatrane **11** is the most effective PLA bulk polymerization catalyst among the 14 catalysts studied. According to an elemental analysis of the product polymer obtained with this five-membered ring catalyst, the residual titanium content is less than 0.001%. The question then arises as to whether *six*-membered ring titanatranes with fused *ortho*-phenyls in the bridges may be more active catalysts for making PLA than five-membered ring **11**, for example. Titanatranes such as **12** and **13** might be expected to exhibit weak/long bridgehead−bridgehead Ti−N interactions. Despite the absence of X-ray structural data for **12** and **13**, two similar compounds [(2,6-di-*i*-Pr−PhO)Ti(O-2,4-$Me_2C_6H_2CH_2$)$_3$N (**17**) and *i*-PrOTi(O-2,4-*tert*-$Bu_2C_6H_2CH_2$)$_3$N (**18**)] structured by us[9a] and by Kol et al.[19] revealed Ti−N distances of 2.306(2)[9a] and 2.334(5) Å,[19] respectively, which signify the presence of transannular bonds that fall at the long end of the range between 2.264(3) and 2.342(9) Å observed in other structurally characterized titanium trialkanolamine derivatives.[13,14] The data in entries 37−40 in Table 2 reveal that **12** and **13** are considerably poorer catalysts than **5** or **11**. We believe this is primarily due to the greater steric protection of the titanium in **12** or **13**, particularly in the region above the equatorial plane in these molecules, where the methyl or *tert*-butyl substituent on the six-membered rings can accentuate blockage of titanium ligation in the coordination−insertion step. In accord with this idea is the observation that less sterically hindered **12** shows higher activity and affords a greater polymer molecular weight than **13**. Although the PDI values associated with the PLA polymers produced by **12** and **13** were smaller than those for the products provided by **5** and **11**, the polymer molecular weights are also considerably lower for **12** and **13**.

In the presence of methylaluminoxane, CpTi(OR)$_3$ compounds are well-known to catalyze the syndiospecific polymerization of styrene.[26] Compound **14** also contains alkoxide groups that could function as initiators of LA polymerization, and entries 41 and 42 in Table 2 show that it too is a good catalyst, giving PLA in high yields and with moderate PDI and molecular weight values.

Solution Polymerization of LA and CL. Although **1**−**14** are catalysts for bulk polymerization of LA, the PDI values

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(24) (a) Kasperczyk, J. E. *Macromolecules* **1995**, *28*, 3937. (b) Bero, M.; Dobrzynski, P.; Kasperczyk, J. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 4038.

(25) Baran, J.; Duda, A.; Kowalski, A.; Szymanski, R.; Penczek, S. *Macromol. Rapid Commun.* **1997**, *18*, 325.

(26) Ishihara, N.; Seimiya, T.; Kuramoto, M.; Uoi, M. *Macromolecules* **1986**, *19*, 2464.

Table 3. Solution Polymerization of LA

entry	catalyst	monomer type	[M]/[Ti]	T^d (°C)	time	yield[e] (%)	M_w[g]	M_n[g]	PDI[g]
1	**1**	*l*-LA[a]	300	70	24 h	85	28 700	14 300	2.01
2		*rac*-LA[a]	300	70	24 h	70	16 900	9 200	1.83
3	**2**	*l*-LA[b]	200	70	4 h	15 (20)[f]	4600	4200	1.10
4		*l*-LA[b]	200	70	16 h	55 (58)[f]	13 600	12 800	1.06
5		*l*-LA[b]	200	70	20 h	65 (69)[f]	16 300	15 100	1.08
6		*l*-LA[b]	200	70	24 h	81 (85)[f]	20 200	18 400	1.10
7		*l*-LA[b]	300[h]	70	36 h[h]	78	30 700	27 300	1.12
8		ϵ-caprolactone[c]	125	70	24 h	52	12 000	10 600	1.13
9		ϵ-caprolactone[c]	175	70	24 h	77	16 700	15 800	1.06
10		*rac*-LA[b]	200	70	24 h	87	17 600	16 300	1.07
11	**3**	*l*-LA[a]	200	70	6 h	26	6200	5600	1.10
12		*rac*-LA[a]	200	70	6 h	28	5600	5200	1.08
13	**4**	*l*-LA[a]	300	130	24 h	53	61 500	51 100	1.20
14		*rac*-LA[a]	300	130	24 h	48	44 500	37 000	1.20
15	**5**	*l*-LA[b]	300	70	3 h	7 (8)[f]	3000	2800	1.09
16		*l*-LA[b]	300	70	10 h	21 (25)[f]	11 500	10 000	1.15
17		*l*-LA[b]	300	70	14 h	29 (31)[f]	13 500	12 500	1.08
18		*l*-LA[b]	300	70	17 h	28 (35)[f]	14 200	13 300	1.07
19		*l*-LA[b]	300	70	36 h	58 (70)[f]	28 900	28 000	1.03
20		*l*-LA[b]	300	130	24 h	81	34 300	25 400	1.35
21		*rac*-LA[b]	300	50	15 h	16	14 400	13 200	1.09
22		ϵ-caprolactone[b]	200	70	24 h	89	19 400	17 600	1.10
23	**6**	*l*-LA[b]	200	130	24 h	43	12 300	9400	1.31
24	**7**	*l*-LA[b]	300	130	24 h	58	25 800	18 600	1.39
25	**8**	*l*-LA[b]	400	130	24 h	51	43 200	35 200	1.23
26	**9**	*l*-LA[b]	200	130	24 h	17	13 600	10 500	1.29
27	**10**	*l*-LA[a]	300	130	24 h	26	25 800	17 400	1.49
28		*rac*-LA[a]	300	130	24 h	24	23 000	15 800	1.45
29	**11**	*l*-LA[a]	300	130	24 h	68	18 500	11 100	1.66
30		*rac*-LA[a]	300	130	24 h	64	17 500	13 100	1.34
31	**12**	*l*-LA[a]	300	130	24 h	0			
32	**13**	*l*-LA[a]	300	130	24 h	0			
33	**14**	*l*-LA[a]	300	130	12 h	63	8000	6700	1.20
34		*rac*-LA[a]	300	130	12 h	59	9000	8300	1.09

[a] Solvent: 40 mL of toluene, 2 g of LA. [b] Solvent: 30 mL of toluene, 2 g of LA. [c] Solvent: 30 mL of toluene, 2 g of ϵ-caprolactone. [d] Oil bath temperature: 130 (±3) °C. [e] Isolated yield. [f] Conversion determined via integration of the methine resonances of LA and PLA ($CDCl_3$). [g] See Table 1, footnote b. [h] Continuation of polymerization after equilibrium was established (see Results and Discussion section).

(1.31−3.68) of the polymers obtained are higher than the ideal value of 1.00 for a completely controlled polymerization. Therefore, we investigated the possibility that better polymerization control might be achieved under solution conditions. In Table 3 are shown the results of our experiments carried out in toluene solution with different [LA]/[Ti] ratios, with various polymerization times, and at temperatures higher than 50 °C (owing to a lack of sufficient solubility of the monomer and polymers at lower temperatures[27]). The yields and molecular weights of the polymers obtained using **1**−**14** in toluene were inferior compared with those synthesized in the bulk polymerization experiments. The PDI values of the polymers obtained using catalysts other than **1** and **10**−**13** in Table 3 are quite small, indicating a substantial degree of molecular weight control. Even though the polymerizations were carried out in toluene, **1** gave rise to PLA with a high PDI value, which may be associated with the dissociation of more than one O-*i*-Pr group from **1**, thus generating more than one initiating site (Table 3, entries 1−2). On the other hand, **2** and **3**, which contain more than one chlorine atom, generated PLA with very narrow PDI values (entries 3−12, Table 3). This suggests that the presence of chlorine atoms in chlorotitanium alkoxides may permit only one O-*i*-Pr group to dissociate. In keeping with this suggestion, the methine region in the homonuclear decoupled ^{1}H NMR spectrum of poly(*rac*-LA) derived from **4** displayed *rmr* and *mrm* tetrads that were much more intense than expected [as was also observed under bulk polymerization conditions for this catalyst (Figure 3d)].[23] In progressing from **1** to **4** (Table 3, entries 2, 10, 12, and 14), the intensity in the ^{1}H NMR spectra of heterotactic-biased poly(*rac*-LA) increased, although to a lesser degree than in such spectra of the bulk polymerization product (Figure 3).

For a further investigation of the degree of control in these polymerizations, we selected catalysts **2** and **5**. The PDI values of PLA obtained with **2** ranged from 1.06 to 1.12. These values vary linearly with M_n and with conversion as shown in Figure 4 (Table 3, entries 3−6), implying a very substantially controlled polymerization process. The controlled nature of these polymerizations was further confirmed by a polymerization resumption experiment that resulted in further ROP of LA. In this experiment (Table 3, entry 7), an additional 100 equiv of LA monomer was added to the reaction medium corresponding to that of entry 6 in Table 3. The GPC traces in Figure 5 show that the molecular weight increased for the final polymer (peak e, M_n = 27 300, PDI = 1.12) relative to the initial product (peak d, M_n = 18 400, PDI = 1.10).

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(27) Although these compounds did catalyze the polymerization of LA at room temperature in toluene and also in THF, yields, molecular weights, and PDI values were not sufficiently reproducible.

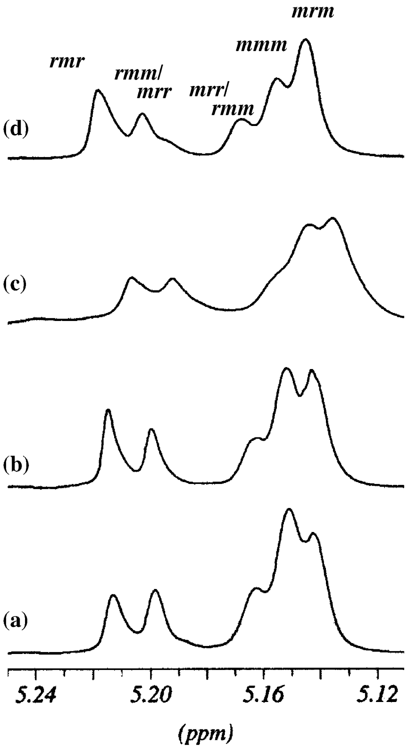

Figure 3. Methine region of the homonuclear decoupled ^{1}H NMR spectra for poly(*rac*-LA) produced by (a) **1**, (b) **2**, (c) **3**, and (d) **4** under solution polymerization conditions.

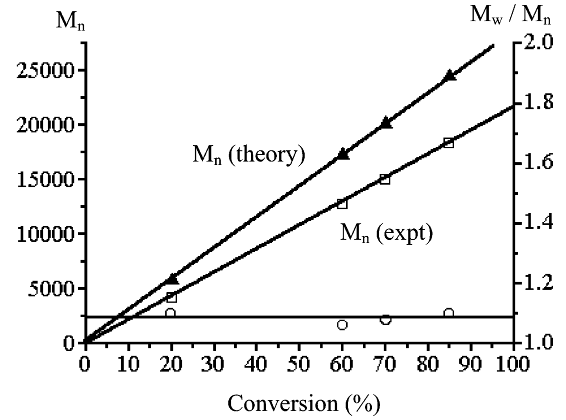

Figure 4. Plot of M_n and PDI values (employing polystyrene standards) for PLA as a function of conversion at 70 °C in toluene with [LA]/[Ti] = 200 using **2** as the catalyst. M_n (theory) was calculated from the formula (M_w of LA) × ([LA]/[Ti]) × (conversion).

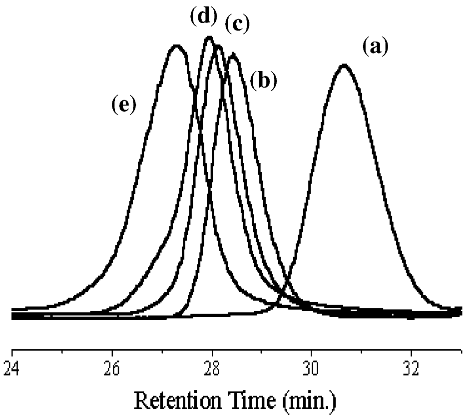

Figure 5. GPC traces of isolated PLA produced with **2** ([LA]/[Ti] = 200) at (a) 4 h, (b) 16 h, (c) 20 h, (d) 24 h, and (e) 36 h. The corresponding PDI values are 1.10, 1.06, 1.08, 1.10, and 1.12, respectively.

In an effort to better understand the initiating process, ^{1}H NMR studies on PCL [poly(ϵ-caprolactone)] formation initiated by **2** were carried out as shown in Figure 6. The ^{1}H NMR spectrum of PCL indicates that initiation occurs through the insertion of an O-*i*-Pr group from compound **2** to CL, giving a titanium alkoxide intermediate that further reacts with excess CL (ϵ-caprolactone) giving PCL (Table 3, entries 8 and 9). This result is in agreement with our expectation that the polymer chain should terminate with one *i*-Pr ester and one hydroxy end group, the latter arising from methanolysis of the metal alkoxide terminus present during polymerization.

This experiment was also carried out for PLA obtained with catalyst **2** with the analogous result, suggesting that back-biting reactions do not occur to any appreciable extent under our conditions. This conclusion was further verified by the following observations. First, the homonuclear decoupled ^{1}H NMR spectrum reveals only one resonance and five resonances in the methine region for poly(*l*-LA) and poly(*rac*-LA), respectively.[23] Thus, if back-biting reactions had occurred, side peaks would have been observed. Second, if intermolecular cyclization reactions had taken place during polymerization, the PDI values of the resulting PLA would have been substantially higher than the nearly ideal values we observed. Interestingly, epimerization of the chiral centers in poly(*l*-LA) apparently does not occur to a detectable extent according to the homonuclear decoupled ^{1}H NMR spectra for the methine region.

In the case of **5**, PLA polymers with narrow PDI values were obtained from reactions conducted with a fixed [LA]/[Ti] ratio of 300 at 70 °C. The linear relationship between Mn and the conversion shown in Figure 7 (Table 3, entries 15−19) implies that polymerization was substantially controlled. To aid in understanding the initiating process in PCL formation initiated by **5**, ^{1}H NMR studies were carried out (Table 3, entry 22). These spectra indicate that initiation occurs through the insertion of an O-*i*-Pr group from **5** into the CL molecule, giving a titanium alkoxide intermediate. This observation accords with our expectation that the polymer chain should possess an *i*-Pr ester and a hydroxy end group.

At the higher polymerization temperature of 130 °C and at the higher [LA]/[Ti] ratio of 300, the PDI value for PLA using initiator **5** increases (M_n = 25 400, PDI = 1.35, Table 3, entry 20), but a significant increase in polymer yield did not occur. This tendency toward increased PDI values at this temperature was also observed for titanatranes **6**−**11** (Table 3, entry 23−30) along with dramatically decreased polymer yields. At the higher polymerization temperatures, titanatranes increasingly initiate transesterification reactions, which could account for the augmented PDI values. Interestingly, **12** and **13** did not show any catalytic activities for the solution polymerization of LA though they showed moderate catalytic activity in bulk polymerizations. In addition, **14** gave

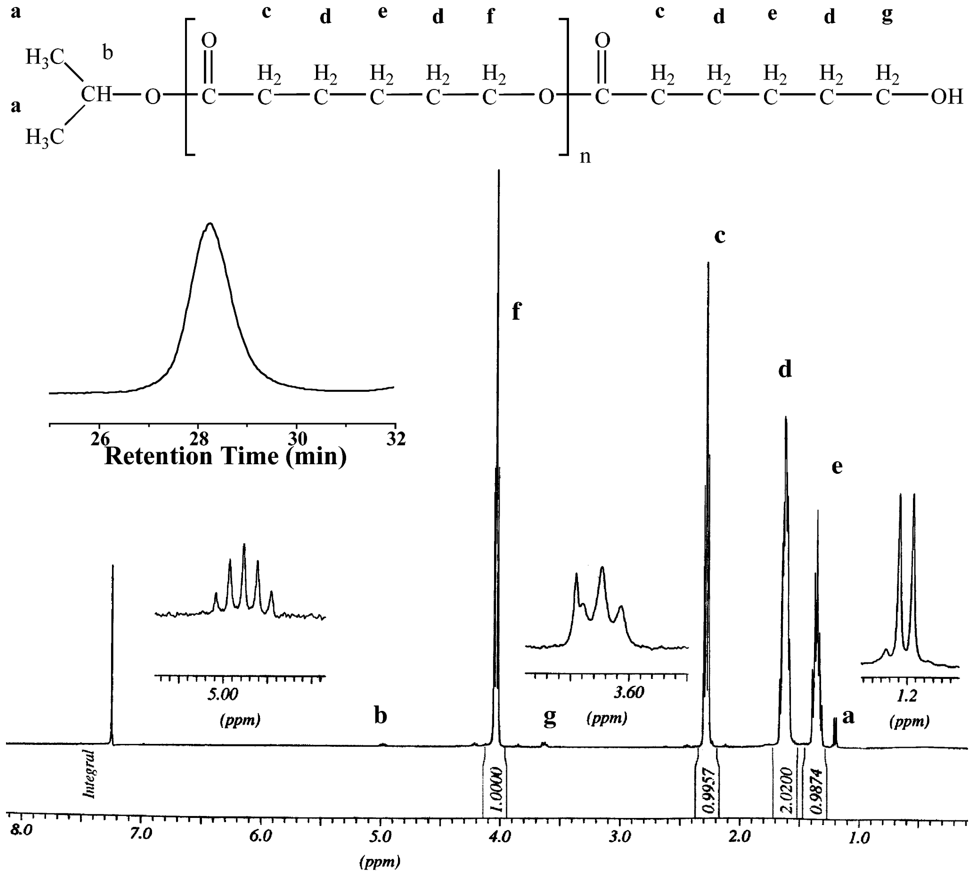

Figure 6. ^{1}H NMR spectrum of PCL synthesized in toluene at 70 °C along with a typical GPC trace (PDI = 1.06).

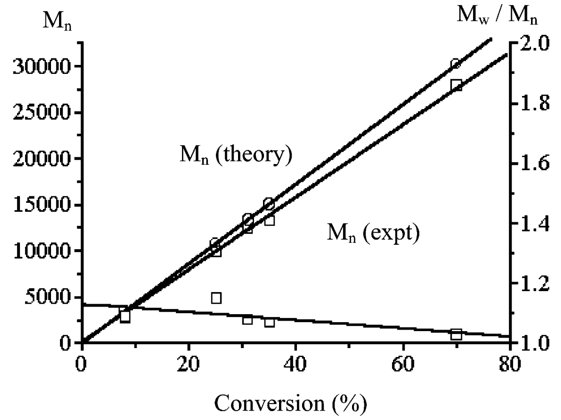

Figure 7. Plot of M_n and PDI values (employing polystyrene standards) for PLA as a function of conversion at 70 °C in toluene with [LA]/[Ti] = 300 using **5** as the catalyst. M_n (theory) was calculated from the formula of (M_w of LA) × ([LA]/[Ti]) × (conversion).

PLA of very low molecular weight when compared with other titanium compounds, although the PDI values are quite narrow.

Summary and Conclusions

We have synthesized a series of titanium alkoxides from readily available starting materials by simple procedures in high yields. These compounds showed remarkably high catalytic activity in bulk and solution polymerizations of LA, revealing interesting correlations of catalyst structure with polymer activity. The catalysts can be roughly divided into two categories: simple tetracoordinate titanium complexes (**1**−**4** and **14**) and pentacoordinate complexes (**5**−**13**) derived from tetradentate trisalkoxy- or trisaryloxyamine podands. Additionally, pentacoordinate **5**−**13** break down into a set of three five-membered ring titanatranes (**5**−**11**) and three six-membered ring analogues (**12** and **13**). Although the different ring sizes result in only minor structural changes in these compounds, they give rise to a major effect on their polymerization activity and the characteristics of the resulting polymers, with five-membered ring systems affording polymers in higher yields and with larger molecular weights than their six-membered ring counterparts.

Increased heterotactic-biased poly(*rac*-LA) was formed as the number of chlorine atoms increased in $\mathrm{TiCl}_x(\mathrm{O}\text{-}i\text{-}\mathrm{Pr})_{4-x}$. In solution polymerizations, titanium alkoxides catalyzed controlled polymerizations of LA, and end group analysis demonstrated that an alkoxide group acted as the initiator. That polymerization is controlled under our conditions was shown by the linearity of molecular weight versus the conversion of LA into PLA.

Experimental Section

General Considerations. All reactions were carried out under an argon atmosphere using standard Schlenk and glovebox techniques.[28] All chemicals were purchased from Aldrich and were used as supplied unless otherwise indicated. Pentane, dichloromethane,

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(28) Shriver, D. F. *The Manipulation of Air-Sensitive Compounds*; McGraw-Hill: New York, 1969.

THF, and toluene (Fischer HPLC grade) were dried and purified under a nitrogen atmosphere in a Grubbs-type nonhazardous two-column solvent purification system[29] (Innovative Technologies) and were stored over activated 3 Å molecular sieves. All deuterium solvents were dried over activated molecular sieves (3 Å) and were used after vacuum transfer to a Schlenk tube equipped with a J. Young valve. CL was distilled under reduced pressure (90 °C/7 micron Hg pressure) from calcium hydride and stored in vacuo over 4 Å molecular sieves. *l*-LA and *rac*-LA were purified twice by sublimation at 70 °C under 7 μm Hg pressure before use.

Measurements. ^{1}H, ^{13}C{^{1}H}, and ^{19}F NMR spectra were recorded at ambient temperature on a Varian VXR-300 or VXR-400 NMR spectrometer using standard parameters. The chemical shifts are referenced to the peaks of residual $CDCl_3$ (δ 7.24, ^{1}H NMR; δ 77.0, ^{13}C{^{1}H} NMR) and acetone-d_6 (δ 2.05, ^{1}H NMR). Elemental analyses were performed by Desert Analytics Laboratory. Molecular weights of polymers were determined by gel permeation chromatography (GPC), and the measurements were carried out at room temperature with THF as the eluent (1 mL/min) using a Waters 510 pump, a Waters 717 Plus Autosampler, four Polymer Laboratories PLgel columns (100, 500, 10^4, 10^5 Å) in series, and a Wyatt Optilab DSP interferometric refractometer as a detector. The columns were calibrated with polystyrene standards.

Syntheses. Compounds **2**−**4**,[12] **5**,[13,21] **10**,[13c] **11**,[15] **12**,[19] THBA,[16] and **14**[30] were synthesized using literature procedures except that these procedures were modified for the synthesis of **2**−**4**, **10**, and **11**. In the case of **2**−**4**, pentane and a shortened reaction time (1 h) were used. Compound **10** was obtained by a reaction between **5** and pinacol at room temperature instead of the reaction between $Et_2NTi(OCH_2CH_2)_3N$ with pinacol. Compound **11** was synthesized by mixing Ti(O-*i*-Pr)$_4$ and THA in dichloromethane instead of THF. Compounds **7**−**9** were made by procedures analogous to both of those given for **6**.

Synthesis of 6. Method 1: In a 250 mL Schlenk flask containing a stirring bar, phenol (0.471 g, 5.00 mmol), triethanolamine (0.746 g, 5.00 mmol), and **1** (1.42 g, 5.00 mmol) were charged in the order given. Then, 50 mL of THF was added, and the reaction mixture was refluxed overnight. After cooling to room temperature, volatiles were evaporated under vacuum, leaving an orange-yellow solid to which was added 15 mL of toluene. The orange solution was filtered, and the desired product **6** was isolated as orange-yellow crystals after the solution remained at −15 °C in a refrigerator for several days (1.21 g, 84%). ^{1}H NMR ($CDCl_3$, 400.147 MHz): δ 7.13 (t, J = 7.4 Hz, 2H, aryl-H), 7.01 (s, 1H, aryl-H), 6.76 (t, J = 6.6 Hz, 2H, aryl-H), 4.60 (br s, 6H, CH_2O), 3.27 (br s, 6H, NCH_2). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.626 MHz): δ 165.0, 128.7, 119.5, 119.0, 129.4 (aryl), 72.43 (CH$_2$O), 61.10 (NCH$_2$). Anal. Calcd for $C_{12}H_{17}NO_4Ti$: C, 50.20; H, 5.97; N, 4.88. Found: C, 49.15; H, 6.14; N, 5.13. Method 2: To a solution of triethanolamine (0.746 g, 5.00 mmol) in 10 mL of THF was added dropwise at room temperature a solution of **1** (1.42 g, 5.00 mmol) in 10 mL of THF. After stirring overnight at room temperature, all volatiles were evaporated under vacuum, leaving a yellow solid **5** (1.19 g, 94%). To a THF solution of **5** (1.00 g, 3.95 mmol) in 10 mL of THF was added dropwise at room temperature a solution of phenol (0.371 g, 3.95 mmol) in 10 mL of THF. The reaction mixture was refluxed overnight, and then, the volatiles were evaporated under vacuum, leaving an orange-yellow solid, to which was added 15 mL of toluene. The orange solution was filtered, and the desired product **6** was isolated as orange-yellow crystals after the solution remained at −15 °C in a refrigerator for several days. Yield = 62% (0.62 g).

Compound 7. Characterization data for **7** include the following: colorless crystals; yield, 90% (method 1), 66% (method 2). ^{1}H NMR ($CDCl_3$, 400.147 MHz): δ 4.72 (br s, 6H, CH_2O), 3.44 (br s, 6H, NCH_2). ^{19}F NMR ($CDCl_3$, 376.479 MHz): δ −9.74 (s, 2F), −14.05 (s, 2F), −20.43 (s, 2F). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.626 MHz): δ 74.37 (CH$_2$O), 62.01 (CH$_2$N). Aromatic carbons could not be observed because of the low solubility of **7** in $CDCl_3$. Anal. Calcd for $C_{12}H_{12}F_5NO_4Ti$: C, 38.22; H, 3.21; N, 3.75. Found: C, 38.35; H, 3.08; N, 3.75.

Compound 8. Characterization data for **8** include the following: yellow powder; yield, 88% (method 1), 61% (method 2). ^{1}H NMR (acetone-d_6, 400.147 MHz): δ 8.13 (d, J = 11 Hz, 2H, aryl-H), 7.01 (d, J = 12 Hz, 2H, aryl-H), 4.62 (br s, 6H, CH_2O), 3.49 (br s, 6H, NCH_2). Anal. Calcd for $C_{12}H_{16}N_2O_6Ti$: C, 43.39; H, 4.86; N, 8.43. Found: C, 43.40; H, 5.22; N, 8.30.

Compound 9. Characterization data for **9** include the following: yellow crystals; yield, 81% (method 1), 56% (method 2). ^{1}H NMR ($CDCl_3$, 400.147 MHz): δ 6.70 (s, 2H, aryl-H), 4.51 (t, J = 5.6 Hz, 6H, CH_2O), 3.25 (t, J = 5.6 Hz, 6H, NCH_2), 2.31 (s, 6H, aryl-Me), 2.17 (s, 3H, aryl-Me). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.626 MHz): δ 160.3, 128.9, 128.0, 127.0 (aryl), 71.20 (CH$_2$O), 57.00 (CH$_2$N), 20.65, 17.02 (aryl-Me). Anal. Calcd for $C_{15}H_{23}NO_4Ti$: C, 54.72; H, 7.04; N, 4.36. Found: C, 54.49; H, 7.67; N, 4.36.

Synthesis of $N[CH_2(Bu^tMeC_6H_2)O]_3TiO^iPr$ (13). A solution of **1** (5 mmol, 1.42 g) in dichloromethane (30 mL) was added to a solution of THBA (5 mmol, 2.73 g) in dichloromethane (40 mL) with stirring at room temperature over a period of 10 min, and then, the solution was stirred for an additional 14 h. The solvent was removed from this solution in vacuo, and the residue was recrystallized from dichloromethane/hexane (1:2, 30 mL). The yellowish crystalline product **13** was washed with cold pentane and dried (yield, 2.76 g, 85.2% before recrystallization; yield, 2.12 g, 65.4% after recrystallization). Mp 366−368 °C. ^{1}H NMR (299.94 MHz, $CDCl_3$, ppm): δ 6.95 (d, J = 1.7 Hz, 1H, aryl), 6.74 (d, J = 1.5 Hz, 1H, aryl), 5.20 (m, 1H, OCHMe$_2$), 3.93 (d, J = 13 Hz, 3H, NCH_2), 2.82 (d, J = 13 Hz, 3H, NCH_2), 2.24 (s, 9H, aryl-Me), 1.49 (d, J = 6.1 Hz, 6H, OCHMe_2), 1.42 (s, 27H, *tert*-butyl). ^{13}C{^{1}H} NMR (75.43 MHz, $CDCl_3$, ppm): δ 160.5, 135.7, 128.8, 127.9, 126.6, 124.8 (aryl), 79.53 (CHMe$_2$), 58.40 (NCH$_2$), 34.72 (CHMe_2), 29.50, 20.95 (aryl-Me). Anal. Calcd for $C_{39}H_{55}NO_4Ti$: C, 72.09; H, 8.53; N, 2.16. Found: C, 71.96; H, 8.66; N, 2.37.

X-ray Crystallography for 7. Crystallographic measurements for **7** were performed at 173 K using a Bruker CCD-1000 diffractometer with Mo Kα (λ = 0.71073 Å) radiation and a detector-to-crystal distance of 5.03 cm. Specimens of suitable quality and size (0.2 × 0.08 × 0.05 mm^3) were selected and mounted onto glass fibers with silicon grease. The initial cell constants were obtained from three series of ω scans at different starting angles. Each series consisted of 30 frames collected at intervals of 0.3° in a 10° range about ω with an exposure time of 50 s per frame. All the intensity data were corrected for Lorentz and polarization effects. The structures were solved by the direct method and were refined by a full-matrix anisotropic approximation. All hydrogen atoms were placed at idealized positions in the structure factor calculation and were allowed to ride on the neighboring atoms with relative isotropic displacement coefficients. Final least-squares refinement of 208 parameters against 2752 independent reflections converged to R (based on F^2 for $I > 2.0\ \sigma$) and R_w (based on F^2 for $I > 2.0\sigma$) values of 0.0408 and 0.0986, respectively. Further details are listed in Table 4.

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(29) Pangborn A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

(30) Kucht, A.; Kucht, H.; Barry, S.; Chien, J. C. W.; Rausch, M. D. *Organometallics* **1993**, *12*, 3075.

Table 4. Crystallographic Data for Compound **7**

empirical formula	$C_{24}H_{24}F_{10}N_2O_8Ti_2$
fw	377.13
temp (K)	173(2)
cryst syst	triclinic
space group	$P\bar{1}$
a (Å)	7.0985(15)
b (Å)	7.2229(15)
c (Å)	13.930(3)
α (deg)	103.976(4)
β (deg)	93.096(4)
γ (deg)	101.600(4)
V (Å^3)	675.0(2)
Z	1
D_{calcd} (Mg/m^3)	1.856
abs coeff (mm^{-1})	0.715
F(000)	380
θ range (deg)	2.97−28.25°
reflections collected	3461
independent reflections	2752
no. of parameters refined	208
GOF	0.975
final R indices[a] [$I > 2\sigma(I)$]	R1 = 0.0408, wR2 = 0.0986
R indices (all data)	R1 = 0.0550, wR2 = 0.1040
largest diff. peak and hole (e Å^{-3})	0.425 and −0.409

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$ and $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.

Polymerization Procedure. LA bulk polymerizations were carried out by charging a stirring bar, 2.00 g of LA, and then the appropriate amount of catalyst precursor to a 10 mL Schlenk flask. The flask was then immersed in an oil bath at 130 °C, and after the appropriate time, the reaction was terminated by the addition of 5 mL of methanol. The precipitated polymers were dissolved in a minimum amount of methylene chloride, and then, excess methanol was added. The resulting reprecipitated polymers were collected, washed with 3 × 50 mL of methanol, and dried in vacuo at 50 °C for 12 h.

Solution polymerizations of LA were carried out by charging a stirring bar and LA to a 50 mL Schlenk flask in the glovebox, and then, the appropriate amount of toluene was added to the flask at the desired polymerization temperature. Polymerization began with the addition of a stock toluene solution of the titanium compound. After the appropriate time, the reaction was terminated by the addition of 5 mL of methanol. The precipitated polymers were dissolved in a minimum amount of methylene chloride, and then, excess methanol was added. The reprecipitated polymers were collected, washed with 3 × 50 mL of methanol, and dried in vacuo at 50 °C for 12 h. ^{1}H and ^{13}C{^{1}H} NMR spectra of PLA samples were recorded in $CDCl_3$.

A polymerization resumption experiment was carried out after the desired polymerization time had been reached. The toluene reaction mixture was transferred via cannula to a 50 mL Schlenk flask containing a stirring bar, and then, another portion of LA that had been heated to the desired polymerization temperature was added. The remaining workup steps were the same as those described earlier in this section. ^{1}H and ^{13}C{^{1}H} NMR spectra of PLA samples were recorded in $CDCl_3$.

Acknowledgment. This work was generously supported by the National Science Foundation through a grant. We thank Dr. Arkady Ellern for carrying out the X-ray structure determination of **7** and Mr. Erik C. Hagberg in Prof. Valerie Sheares-Ashby's group in this department for obtaining the GPC data.

Supporting Information Available: GPC traces, homonuclear decoupling ^{1}H NMR spectra of the methine region for PLA, and tables of crystal data, atomic coordinates, thermal parameters, bond distances, bond angles and ORTEP diagrams for compound **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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