DOI: 10.1021/ma101202g

Macromolecules
ARTICLE

Facile Synthesis of Hydroxyl-Ended, Highly Stereoregular, Star-Shaped Poly(lactide) from Immortal ROP of *rac*-Lactide and Kinetics Study

Wei Zhao,[†,‡] Dongmei Cui,*[,†] Xinli Liu,[†] and Xuesi Chen[†]

[†]*State Key Laboratory of Polymer Physics and Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China, and* [‡]*Graduate School of the Chinese Academy of Sciences, Beijing 100039, China*

Received May 30, 2010; Revised Manuscript Received July 16, 2010

ABSTRACT: Triethanolamine (TEA) reacted with 3 equiv of yttrium alkyl complex **1** bearing *O*,*N*,*N*,*O*-tetradentate Salan ligand to give a trinuclear yttrium alkoxide counterpart **2** via metathesis reaction. Complex **2** initiated the ring-opening polymerization of *rac*-lactide in a livingness mode under mild conditions. Remarkably, **2** was so tolerant of the protic TEA that under various TEA-to-yttrium molar ratios ranging from 1:3 up to 81:1, the polymerization performed smoothly, suggesting an immortal characteristic. The resultant polylactides had variable molecular weights (M_n = $1.36 \times 10^4$to 32.54×10^4) but narrow molecular weight distributions (PDI = 1.02−1.09), and, especially, pure heterotactic (P_r = 0.99), hydroxyl-functionalized and star-shaped architecture, which were fully characterized by NMR spectroscopy and MALDI−TOF mass spectrum analyses and confirmed further by calculating the contraction factor value g' (g' = 0.96) via Mark−Houwink equations. Detailed investigation of the "immortal" polymerization gave a unique kinetics law of $-d[LA]/dt = k_p[LA][TEA]^{-0.352}$.

Introduction

In recent years, biodegradable polymers as a promising alternative of synthetic petrochemical-based plastics have attracted a considerable attention.[1] Of the variety of biodegradable polymers known, polylactide (PLA) derived from lactic acid of nonpetroleum sources has become one of the most important candidates because of its favorable degradation rate and mechanical properties. In the meantime, owing to its good biocompatibility, PLA has been also widely applied in medicine and pharmaceutics, for instance, as the media for controlled release of drugs and for delivery of antibodies and genes and in tissue engineering as the scaffolds.[2] On the other hand, the properties of the linear PLA, such as the crystallinity, brittleness, degradation when processing at temperatures higher than its melting point, impermeability to many drugs with low molecular weights,[3a] and difficulty in filming, limit a broader spectrum of its possible applications. Therefore, aiming at modulating further the physical and chemical properties of linear PLA and thereby to extend its application field, researches have directed to copolymerize lactide with other monomers such as glycolide and lactones,[3b] or to modify the topologies via creating novel macromolecular architectures, which lead to formation of the linear/grafted block copolymers or star-shaped and dendritic polymers.[4−6] The star-shaped polymers known for their interesting morphologies and rheological properties and low melting viscosity as compared with their linear structural counterparts, have gathered an increasing attention.[7] To date, 3- to 10-armed polylactides have been synthesized mainly through the "core-first" method by using tin(II) octoate ($Sn(Oct)_2$) combined with polyols such as 1,1,1-tris(hydroxymethyl)propane,[8] pentaerythritol,[8−10] dipentaerythritol and its derivatives,[11] natural sugars[12] and polyglycerines, etc.[9] Recently a number of catalysts based on potassium,[13] lithium,[14] zinc,[15] magnesium,[14a,15i−15l,15n,16] iron,[17] and calcium[15c,d,18] or organic[19] and enzymatic[20] systems have been investigated. However, there are problems remained to be solved: (i) in the obtained PLA the amount of catalyst residue is still high, although the use of tin element has been approved by the U.S. FDA, concerns have been raised in the literature regarding the potential health issues associated with the toxicity of tin-based residues;[21] (ii) the nonuniform reactivity of the hydroxyl functions in the polyols with $Sn(Oct)_2$ and the presence of transesterification during the polymerization process make good control of the molecular weight of the side arms a challenging project; (iii) owing to lack of stereoselectivity for most of the above systems when *rac*-LA is employed, good control of stereotacticity of the side arms has not been achieved yet.

During our previous studies on the ring-opening polymerization (ROP) of LA,[22] we found that an achiral yttrium alkyl complex **1** was an excellent heteroselective initiator for the ROP of *rac*-LA (Chart 1).[22c] Herein we wish to report that by treatment of complex **1** with triethanolamine (TEA), a trinuclear yttrium alkoxide complex **2** was obtained *in situ* via metathesis reaction, which initiated living ROP of *rac*-LA. Moreover the polymerization can proceed in an "immortal" fashion that each Y−alkoxide species generated an up to 81 star-shaped PLA molecules with adjustable molecular weight and very narrow polydispersity as well as high heterotacticity. In addition the side-arms of PLA were automatically capped with hydroxyl functionality without any extra process. The hydroxyl-ends will facilitate the incorporation of bioactive substituents such as drugs or fluorescent tags to construct novel PLA-contained functionalized biopolymers.[23,24]

Results and Discussion

Synthesis of Trinuclear Initiator and Star-Shaped Heterotactic PLA. Heterospecific ROP of *rac*-LA can be achieved by using indium trichloride,[25] bis(phenolato)scandium,[26] and a range of germanium, zirconium, and hafnium complexes.[27]

*Corresponding author. Fax: +86-431-85262773. E-mail: dmcui@ciac.jl.cn.

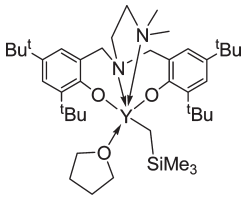
 Published on Web 07/28/2010

Recently, we reported that the ONNO-tetradentate Salan ligated yttrium alkyl complex **1** initiated efficiently the ROP of *rac*-LA to afford PLA with the highest heterotacticity (P_r = 0.99) under mild conditions. The distinguished specific selectivity was governed mainly by the "cage-like" geometry of the Salan ligand. The polymerization proceeded in a controllable manner but not livingness, which might be ascribed to the highly active Y−alkyl initiator.[22c] In this work, complex **1** was employed to react stoichiometrically with TEA (Y-to-OH = 1). The reaction was monitored by NMR technique in THF-d_8 solvent (Supporting Information, Figure S7), which showed that the Y−alkyl moiety in **1** was alkoxylated via metathesis reaction by releasing TMS (tetramethyl silane) to generate a trinuclear Y−alkoxide counterpart **2**, exclusively (Scheme 1). No ligand abstraction was observed. Complex **2** initiated efficiently the ROP of *rac*-LA to reach higher than 90% conversion within 1 h in THF at 10 °C (Table 1, entry 1). Moreover the trinuclear **2** remained the excellent selectivity of its mononuclear precursor **1** by giving pure heterotactic PLA (Supporting Information, Figure S1). This confirmed further that the protic TEA reacted with the yttrium−alkyl moiety selectively while the Salan ligand remained untouched and kept bonding to yttrium ion to govern the selectivity via its steric environment.

Remarkably, the Y−alkoxide species in **2** showed the living fashion that linear correlation between molecular weight of the obtained PLA and conversion was observed meanwhile the polydispersity indices maintained almost constant (PDI = 1.02−1.04) (Figure 1, I). The living mode could be confirmed further by adding a second portion of *rac*-LA to a 100% conversion *rac*-LA ROP system to reach a total 200% conversion and to give PLA with doubled molecular weight (Table 1, entry 5). These results were also in agreement with the previous reports that the Ln−O species induce more controllable polymerization than the corresponding Ln−C and Ln−N species (Ln: lanthanide element).[22,28,29] Noteworthy was that the molecular weights of the resultant PLAs were very close to the theoretic values, suggesting a 100% catalytic efficiency of the system.

The ^{1}H NMR and the ^{13}C NMR spectra of the obtained PLA showed clearly the resonances from three HOCH(CH_3)-CO end-groups and a triethanolamine-core for each macromolecule, as the integral ratio of H_a to H_e is 2:1 while the integral ratio of C_a to C_e is 1:1 (Figure 2 and Figure S2, Supporting Information). This result suggested that *rac*-LA monomers inserted into the three Y−alkoxy bonds in **2** and propagated into the three-armed architecture. The three-arm architecture of oligomeric PLA was confirmed further by MALDI−TOF mass spectrum analysis as shown in Figure 3. According to the m/z value, a formula of [H−(OCHMeCOOCHMeCO)$_n$−OCH$_2$CH$_2$]$_3$N·H$^+$ (n = 2 to 4) was established, which was in well agreement with a three-armed PLA oligomer having HOCHMeCO− and TEA end-groups (M_{MS} = 1371, PDI_{MS} = 1.02). No peaks arising from cyclic oligomers and oligomers with nonintegral LA repeat units were found

Chart 1. Salan-Ligated Yttrium Alkyl Complex 1



1

Scheme 1. Synthesis of Star-Shaped Polylactide from *rac*-Lactide Initiated by Complex 2

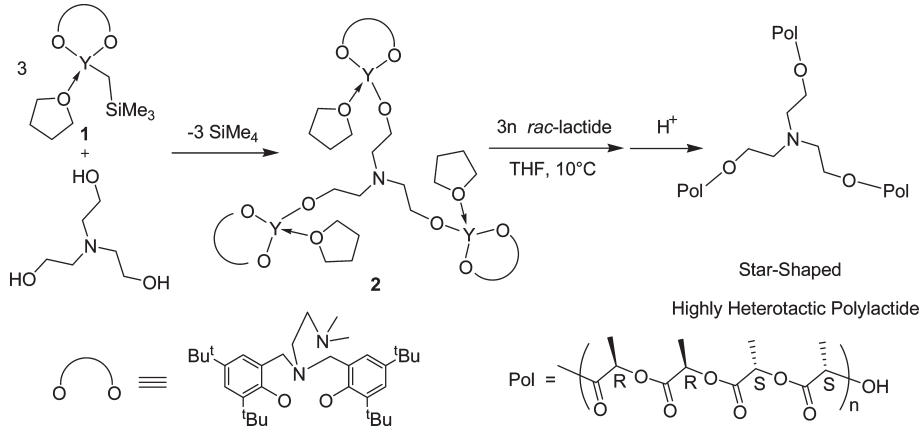


Table 1. ROP of *rac*-Lactide by Complex 1 in the Presence of Triethanolamine (TEA)

entry[a]	$[LA]_0/[Y]_0$	$[TEA]_0/[Y]_0$	time (min)	convn (%)[b]	$M_{n,calcd} \times 10^{-4}$ [c]	$M_{n,LS} \times 10^{-4}$ [d]	$M_{w,LS} \times 10^{-4}$ [d]	M_w/M_n [d]	P_r [e]
1	900	1/3	65	93	36.20	32.54	33.84	1.04	0.98
2	900	1	60	93	12.08	11.42	11.76	1.03	0.99
3	900	2	50	87	5.66	5.70	5.81	1.02	>0.99
4	300	2	1440	100	2.18	2.10	2.21	1.05	0.98
5	300 + 300	2	1440 + 1440	200	4.34	3.73	4.07	1.09	0.98
6	900	3	70	85	3.69	4.35	4.44	1.02	>0.99
7	900	9	60	68	1.00	1.36	1.40	1.03	0.97
8	900	9	570	100	1.46	1.81	1.86	1.03	0.97
9	2700	27	1440	100	1.46	1.52	1.56	1.03	0.98
10	8100	81	1440	100	1.46	1.42	1.55	1.09	0.98

[a] Polymerizations were performed in THF, 10 °C, $[LA]_0$ = 2.08 M. [b] Obtained from ^{1}H NMR analysis. [c] Calculated by $([LA]_0/[TEA]_0) \times 144.13 \times X$ (X = convn) + 149.19. [d] Determined by SEC-MALLS. Number-average molecular weight ($M_{n,LS}$), weight-average molecular weight ($M_{w,LS}$), and polydispersity index $(M_w/M_n)_{LS}$ were measured using the light scattering (LS) detector. [e] P_r is the probability of racemic linkages between monomer units determined from the methine region of the homonuclear decoupled ^{1}H NMR spectrum.

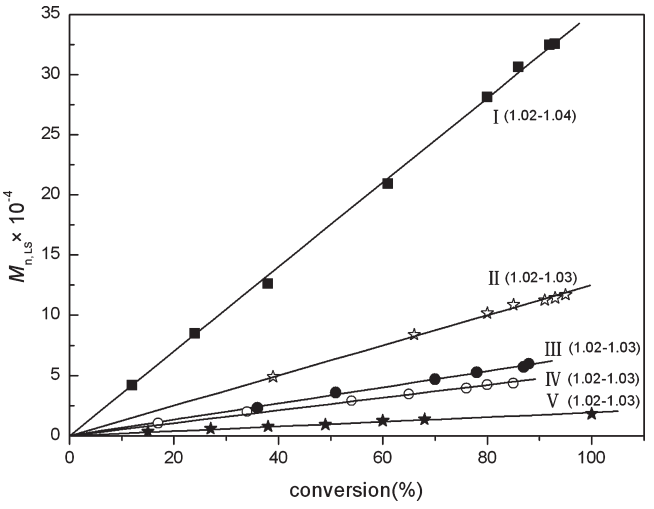


Figure 1. Plots of $M_{n,LS}$ vs conversion (PDI indicated in parentheses) for the ROP of *rac*-LA. Conditions: [TEA]-to-[Y] ratio = 1/3 (I), 1 (II), 2 (III), 3 (IV) and 9 (V); $[rac\text{-LA}]_0/[Y]_0 = 900$, $[rac\text{-LA}]_0 = 2.08$ M; THF, 10 °C.

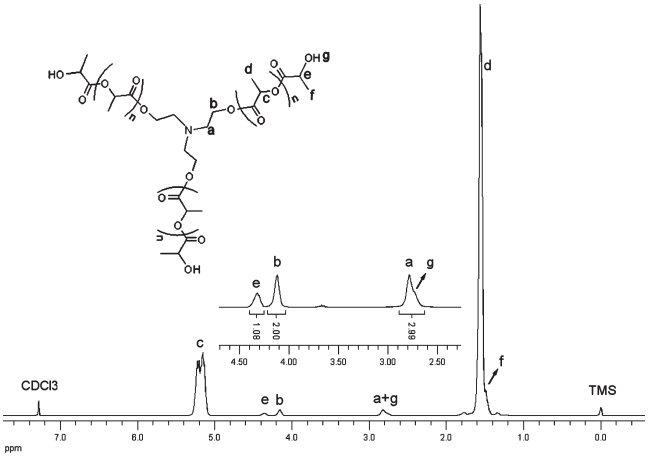


Figure 2. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) spectrum of trihydroxyl-functionalized highly heterotactic star-shaped polylactide. Conditions: $[LA]_0 = 2.08$M, $[LA]_0$:$[TEA]_0$:$[Y]_0 = 100$:1:3, THF, 100% conversion, $T_p = 10$ °C.

in the spectrum, indicating the absence of intramolecular and intermolecular transesterification. To prove the star-shaped microstructures of higher molecular weight PLAs obtained, the contraction factor (g') was determined (in this case the MALDI−TOF-MS method is not possible). g' was defined as the ratio of intrinsic viscosity of star-shaped polymer to that of linear polymer of equal molecular weight. For all star-shaped polymers with perfect three-armed architecture in their good solvents, g' value is about 0.95.[30] Therefore, intrinsic viscosity [η] of PLA samples in THF at 25 °C were measured by means of Ubbelohde viscometer, and their absolute molecular weights were characterized by SEC-MALLS. According to the experimental data, the Mark−Houwink equation was established as $[\eta]_{star} = 0.01180 M_{W,LS}^{0.743}$ (mL/g) for the narrow-distributed star-shaped PLA while $[\eta]_{linear} = 0.01234 M_{W,LS}^{0.744}$ (mL/g) for the narrow-distributed linear PLA (Supporting Information, Figure S3). Thus, the g' value was determined to be about 0.96, indicating the symmetric three-arm-star topology of the obtained PLA.

Immortal ROP of *rac*-LA. Addition of excess amount of TEA (based on Y) to complex **2** did not abstract the Salan ligand as usually happened to give homoleptic (usually uncontrollable) yttrium alkoxides, leading to termination of the active propagation species by releasing "dead" PLA. Strikingly, complex **2** was so tolerant of the protic TEA that the presence of increasing amount of TEA only led to regular decrease of molecular weight of the resultant PLA without any change of the molecular weight distribution (Figure 4). Under a broad range of TEA-to-Y molar ratios, the polymerizations could perform fluently all in livingness modes (Figure 1, II−V), to give PLAs with variable molecular weights ($M_n = 1.36 \times 10^4 - 32.54 \times 10^4$) and narrow molecular weight distributions (PDI = 1.02−1.09). The highest TEA-to-Y molar ratio was 81:1 (OH-to-Y molar ratio was 243), suggesting that each initiator molecule generated up to 81 three-armed PLA macromolecules. Therefore, a very high catalytic efficiency had been achieved successfully and the amount of catalyst residue was negligible (Table 1). These results demonstrated that the ROP of *rac*-LA with **2** was "immortal", suggesting there existed rapid and reversible exchange reaction among the active propagation species and the protic TEA and the resultant hydroxyl-ended PLA (Scheme 2). The star-shaped architecture and heteroregularity of the side arms had been sustained in the process (Figure 5). It should be noted that the immortal characteristic of this polymerization should be attributed to the concert effects of chain-transfer-agent TEA and the Y−alkoxide active species. The kinetics study of the polymerization confirmed further there was no aggregate active species.[31] Previously, we attempted repeatedly to treat complex **1** with one equiv of primary alcohol such as methanol, ethanol, and 2-propanol to synthesize its alkoxide analogues to isolate the corresponding alkoxide counterpart but failed, because **1** was so fragile to these protic alcohols to afford uncontrollable products that were definitely inert for the ROP of *rac*-LA.

Immortal polymerization presents advantages such as atom economy, molecular weight control, and polymer end-functionality, whereas to date only polymerizations of epoxides and β-lactone by using aluminum porphyrin systems,[32,33] ROP of ε-caprolactone by using biphenol supported aluminum alkoxides, and ROP of trimethylene carbonate by using [Zn(BDI){N(SiMe$_3$)$_2$}] (BDI = CH(CMeNC$_6$H$_3$-2,6-^{i}Pr$_2$)$_2$) have been reported to show immortal fashion,[34] and a limited number of immortal ROP of LA initiated by rare-earth metal amido and alkoxide complexes in combination with primary alcohols have been reported very recently.[35] However the synthesis of the star-shaped and specific regular side-armed PLA via immortal ROP, is, as far as we are aware, unprecedented. At the same time, the high ratio of monomer-to-catalyst (up to 8100) also provides a facile way to obtained "clean" PLA materials applied in some special fields.

Kinetics Study of *rac*-Lactide "Immortal" Polymerization with Complex 1/TEA. To establish the reaction orders in *rac*-LA and TEA for the ROP of *rac*-LA with yttrium complex **1** in THF at 10 °C, kinetics study was conducted by monitoring the conversion of *rac*-LA versus time with ^{1}H NMR spectrum. The kinetics equation could be written as $-d[LA]/dt = k_p[LA]^a[TEA]^b$ where k_p is the rate constant. Fixing the initial concentration $[TEA]_0$ at 0.77, 2.31, 4.62, 6.94, and 20.87 mM, respectively, the $\ln([LA]_0/[LA]_t)$ values were calculated according to the conversions observed, which were plotted versus polymerization time to give straight lines accordingly (Figure 6), indicating that polymerization proceeded in a first-order dependence on *rac*-LA concentration. Thus, the polymerization rate equation could be simplified as $-d[LA]/dt = k_{app}[LA]$ where $k_{app} = k_p[TEA]^b$. According to the slops of the straight lines, the k_{app} values were calculated to be 0.055, 0.046, 0.038, 0.027, and 0.018 min^{-1}, respectively. The order in TEA concentration b was determined as the slope of ln k_{app}

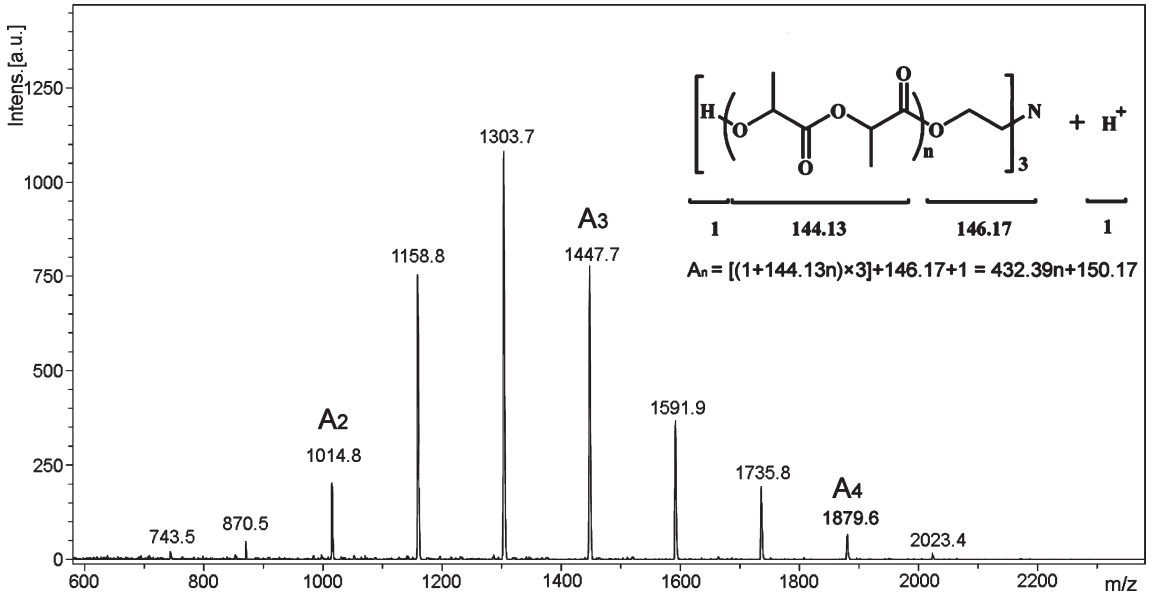


Figure 3. MALDI−TOF mass spectrum of the star-shaped polylactide obtained by complex **1**/TEA (doped with H^+). Conditions: $[LA]_0$ = 2.08 M, $[LA]_0$:$[TEA]_0$:$[Y]_0$ = 10:1:3, THF, 100% conversion, T_p = 10 °C.

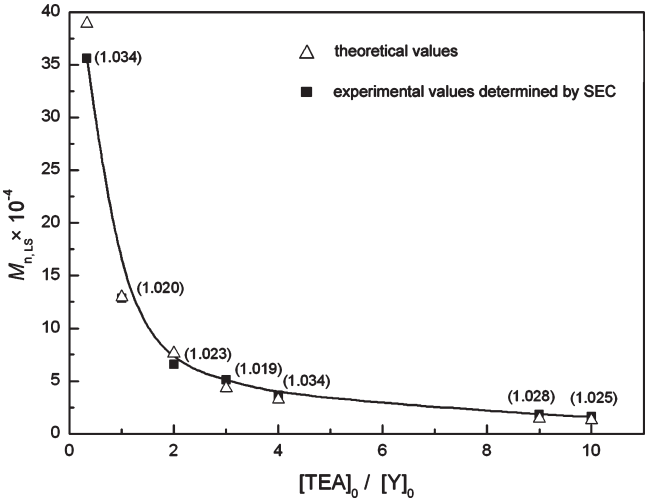


Figure 4. Dependence of the molar mass $M_{n,LS}$ (PDI indicated in parentheses) on $[TEA]_0/[Y]_0$ ratio. Conditions: $[LA]_0$-to-$[Y]_0$ ratio =900, $[LA]_0$ = 2.08M, solvent, THF, T_p = 10 °C.

vs $\ln[TEA]_0$ line being −0.352, while the rate constant k_p as intercept being 0.0049, respectively (Figure 7). The overall kinetic law was depicted as $-d[LA]/dt = k_p[LA][TEA]^{-0.352}$. Noteworthy was that the rate law was different from those reported previously for the other initiation systems,[15o,29] in which the minus exponent was observed. This is consistent with the immortal characteristic of the system, although the exchange among the active species, the transfer agent and the macromolecules was claimed to be rapid and reversible, the slowdown of the polymerization rate should be not avoided,[33] unless chain transfer agents could be added endlessly.

Conclusion

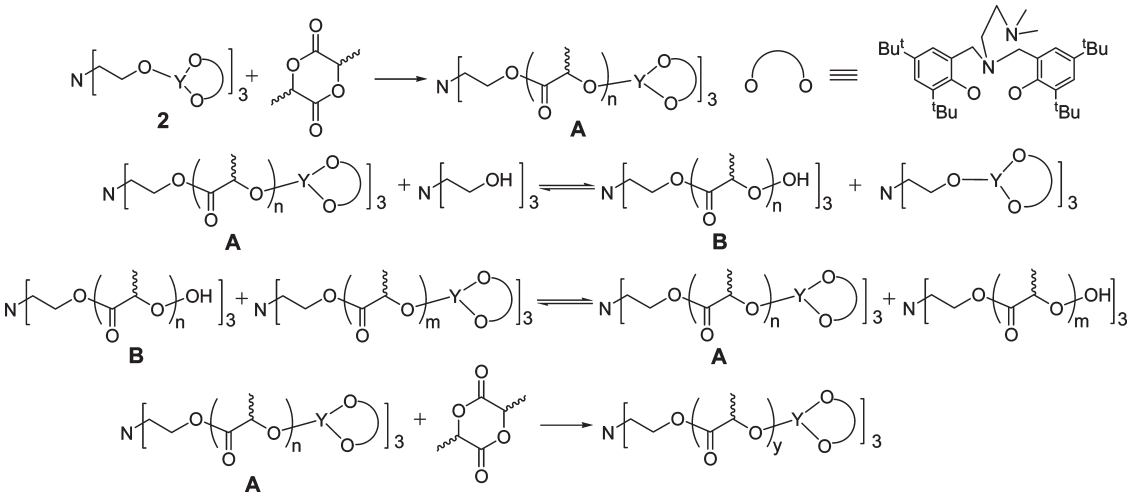
We have demonstrated that by properly choosing a specific selective coordination catalyst, the yttrium alkyl complex bearing the Salan ligand, and a polyol such as triethanolamine (TEA), a star-shaped catalyst-core was generated, which initiated efficiently the ROP of *rac*-LA to give the unprecedented PLA with highly heterotactic three side arms. This was contributed significantly to the clean metathesis reaction between the polyol agent and the yttrium−alkyl species, leaving the Salan ligand attaching to the metal center to govern the selectivity. In addition, the system showed a livingness mode and the remarkable immortal nature with each active species generating up to 81 macromolecules, to afford hydroxyl-functionalized, star-shaped polylactides with stereocontrolled side arms. We are sure that the "specific control catalyst core first" strategy conveyed an idea to synthesize homo- and copolymeric materials with totally new architectures.

Experimental Section

General Methods. All reactions were carried out under a dry and oxygen-free argon atmosphere by using Schlenk techniques or under a nitrogen atmosphere in an MBraun glovebox. Solvents were purified by an MBraun SPS system. Ligands H_2L were synthesized according to modified literature procedures.[36] The phenols and amines were purchased from Aldrich or Fluka. All liquids were dried over 4 Å molecular sieves for a week and distilled before use, and solid materials were used without purification. The synthesis of lanthanide tris(alkyl)s followed the established method with minor alteration.[37] D,L-Lactide (Aldrich) was recrystallized three times with dry ethyl acetate. Triethanolamine was dried over calcium hydride prior to distillation under vacuum.

Instruments and Measurements. Organometallic samples for NMR spectroscopic measurements were prepared in a glovebox by use of NMR tubes and then sealed by paraffin film. ^1H, ^{13}C NMR spectra were recorded on a Bruker AV300 (FT, 300 MHz for ^1H; 75 MHz for ^{13}C) spectrometer. Homonuclear decoupled ^1H NMR spectra were recorded on a Bruker AV400 spectrometer. Assignments were confirmed by $^1H-^1H$ (COSY), $^1H-^{13}C$ (HMQC), and ^{13}C NMR (DEPT) experiments when necessary. SEC−MALLS were carried out by combining a Waters 515 GPC instrument with a light scattering apparatus at 25 °C. The system included a Styragel HMW6E column, a 515 HPLC pump, an IR OPTILAB DSP detector, and a DAWN EOS multiangle laser-light scattering (MALLS) detector (Wyatt Technology). The eluent was DMF at a flow rate of 0.5 mL min^{-1}. Matrix-assisted laser desorption/ionization time-of-flight (MALDI−TOF) mass spectra were recorded using a Bruker Reflex III mass spectrometer (Bremen, Germany) equipped.

Scheme 2. "Living" and "Immortal" Polymerization of *rac*-Lactide Initiated by Complex 2/TEA



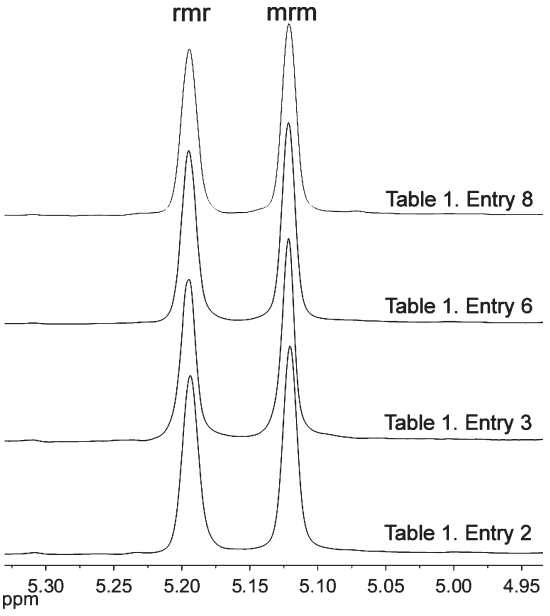


Figure 5. Representative homonuclear decoupled ^{1}H NMR spectra of the methine region of star-shaped PLAs (Table 1, entries 2, 3, 6, and 8) at 25 °C (400 MHz, $CDCl_3$).

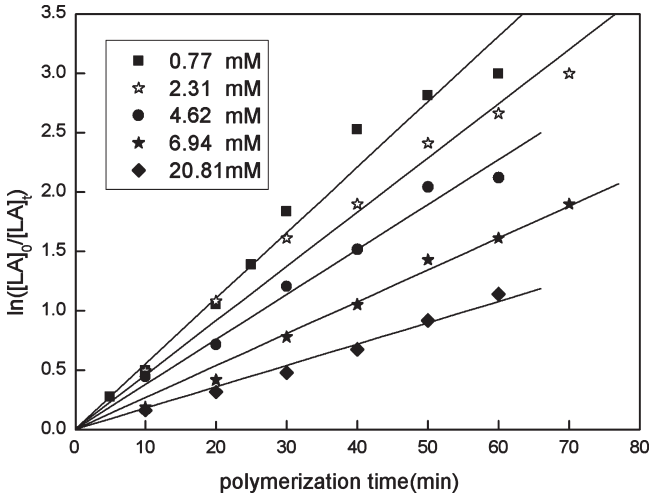


Figure 6. ln($[LA]_0/[LA]_t$) vs time for the ROP *rac*-LA initiated by **1**/TEA. Conditions: [TEA]-to-[Y] ratios, 0.33 ($[TEA]_0$ = 0.77 mM, ■), 1 ($[TEA]_0$ = 2.31 mM, ☆), 2 ($[TEA]_0$ = 4.62 mM, ●), 3 ($[TEA]_0$ = 6.94 mM, ★), 9 ($[TEA]_0$ = 20.81 mM, ♦); $[Y]_0$ = 2.31 mM; $[LA]_0$-to-$[Y]_0$ = 900; solvent, THF; T_p = 10 °C.

The ions were accelerated with pulsed ion extraction by a voltage of 19 kV and detected using a microchannel plate detector. Samples were dissolved in THF, 2,5-dihydroxybenzoic acid (DHBA) was used as the matrix material. Viscosity of the synthesized star-shaped as well as linear PLAs were measured at 25 °C with a 1836 Ubbelohde viscometer in THF solution. Under a series of PLA concentrations, special viscosities (η_{sp}) and relative viscosities (η_r) were measured and evaluated. Furthermore, intrinsic viscosities ([η]) were estimated via the extrapolation of the η_r vs polymer concentration plot for the synthesized polyesters.

Synthesis of Complex 2. To a THF (2.5 mL) solution of complex **1** (0.51 g, 0.66 mmol) was dropwise added $^1/_3$ equiv of TEA (0.033 g, 0.22 mmol, in 2.5 mL of THF) slowly. After being stirred at 10 °C for 10 min, Volatile materials were then removed *in vacuo*, giving complex **2** in quantitative yield (0.44 g). ^{1}H NMR (300 MHz, THF-d_8, 25 °C) δ 7.19 (d, ^4J (H, H) = 3.0 Hz, 6H, C_6H_2), 6.90 (d, ^4J (H, H) = 3.0 Hz, 6H, C_6H_2), 4.30 (brs, 6H, NCH_2CH_2O), 4.24−3.94 (m, 6H, $ArCH_2N$), 3.52 (brs, 6H, NCH_2CH_2O), 3.24−2.89 (m, 6H, $ArCH_2N$), 2.55 (brs, 6H, $N(CH_2)_2N$), 2.03 (s, 18H, $N(CH_3)_2$), 1.91 (brs, 6H, $N(CH_2)_2N$), 1.50 (s, 54H, $C(CH_3)_3$), 1.26 (s, 54H, $C(CH_3)_3$) ppm. ^{13}C NMR (100 MHz, THF-d_8, 25 °C): δ 163.0 (6C, *ipso*-2,4-tBu$_2$-C_6H_2), 136.0 (6C, *ipso*-2,4-tBu$_2$-C_6H_2), 135.8 (6C, *ipso*-2,4-tBu$_2$-C_6H_2), 126.3 (6C, 2,4-tBu$_2$-C_6H_2), 125.5(6C, 2,4-tBu$_2$-C_6H_2), 124.2 (6C, *ipso*-2,4-tBu$_2$-C_6H_2), 65.8 (6C, $ArCH_2N$), 63.1 (3C, NCH_2CH_2O), 59.8 (3C, $N(CH_2)_2N$), 49.9 (3C, $N(CH_2)_2N$), 47.8 (3C, NCH_2CH_2O), 46.5 (6C, $N(CH_3)_2$), 35.8 (6C, $C(CH_3)_3$), 34.4 (6C, $C(CH_3)_3$), 32.3 (18C, $C(CH_3)_3$), 30.6 (18C, $C(CH_3)_3$) ppm.

General Kinetics Procedure. A typical procedure for polymerization of *rac*-LA was performed in a 25 mL round flask under an N_2 atmosphere. To a vigorously stirred THF solution (3 mL) of complex **1** were added a THF solution (2 mL) of triethanolamine and then *rac*-LA. The polymerization took place immediately at 10 °C. After specified time intervals, an aliquot was withdrawn and quenched quickly with 1.0 mL of HCl/CH_3OH/$CHCl_3$ (0.1/10/60 v/v) solution, and then 1.0 mL of THF was added to obtain a clear solution. Several drops of the quenched solution was taken, removed volatiles and subjected to ^{1}H NMR spectrum analysis to determine the monomer conversion by integrating methine or methyl resonances of monomer vs polymer ($CDCl_3$). The residue solution was quenched by an excess amount of ethanol, filtered, washed with ethanol, and then dried

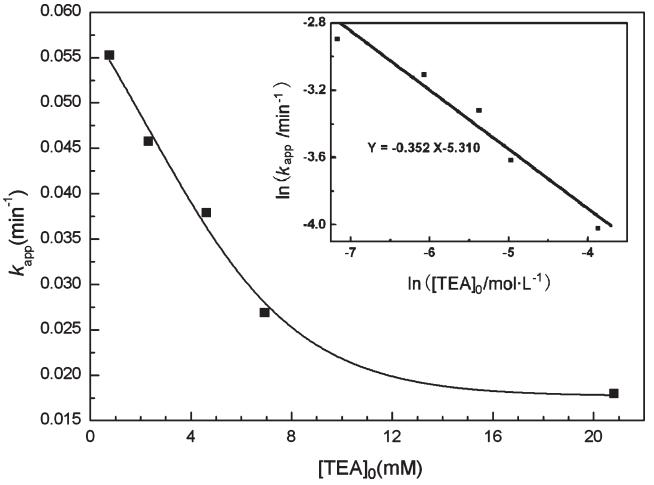


Figure 7. k_{app} vs $[TEA]_0$ for the ROP *rac*-LA initiated by **1**/TEA. (The inset is a linear plot of $\ln k_{app}$ vs $\ln[TEA]_0$.) Conditions: $[LA]_0 = 2.08$ M; solvent, THF; $T_p = 10$ °C.

at 40 °C for 24 h *in vacuo* to give the polymer product. The molecular weight and the molecular weight distribution of the resulting polymer were determined by SEC−MALLS. The tacticity of the PLA was calculated according to the methine region homonuclear decoupling ^{1}H NMR spectrum. Each sample quenched at specified time was used as one data point.

Acknowledgment. We thank The National Natural Science Foundation of China (Project No. 20904051) for financial support.

Supporting Information Available: Text discusing the typical polymerization of *rac*-lactide and the kinetics of polymerization and figures showing ^{1}H NMR (300 MHz, THF-d_8, 25 °C) spectrum, ^{13}C NMR (100 MHz, THF-d_8, 25 °C) spectrum, and ^{1}H−^{1}H (COSY) spectrum of complex **2**, ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) spectrum of trihydroxyl-functionalized highly heterotactic star-shaped polylactide, homonuclear decoupled ^{1}H NMR spectra of the methine region of star-shaped PLA, and Mark−Houwink plots of linear and star-shaped polylactide. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) Drumright, R. E.; Gruber, P. R.; Henton, D. E. *Adv. Mater.* **2000**, *12*, 1841–1846. (b) Mecking, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1078–1085.
(2) (a) Finne, A.; Albertsson, A. C. *Biomacromolecules* **2003**, *3*, 684–690. (b) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 689–695. (c) Kikkawa, Y.; Abe, H.; Iwata, T.; Inoue, Y.; Doi, Y. *Biomacromolecules* **2002**, *3*, 350–356.
(3) (a) Schindler, A.; Jeffcoat, R.; Kimmel, G. L.; Pitt, C. G.; Wall, M. E.; Zweidinger, R. In *Contemporary Topics in Polymer Science*; Pearce, E. M., Schaefgen, J. R., Eds.; Plenum: New York, 1977; Vol. *2*, p 251.(b) Chen, W.; Yang, H.; Wang, R.; Cheng, R.; Meng, F.; Wei, W.; Zhong., Z. *Macromolecules* **2010**, *43*, 201–207.
(4) Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev.* **2004**, *104*, 6147–6176.
(5) Baker, G. L.; Vogel, E. B.; Smith, M. R. *Polym. Rev.* **2008**, *48*, 64–84.
(6) Albertsson, A. C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, 1466–1486.
(7) Lang, M.; Wong, R.; Chu, C. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 1127–1141.
(8) Kricheldorf, H. R.; Ahrensdorf, K.; Rost, S. *Macromol. Chem. Phys.* **2004**, *205*, 1602–1610.
(9) Korhonen, H.; Helminen, A.; Seppälä, J. V. *Polymer* **2001**, *42*, 7541–7549.
(10) Kim, S. H.; Han, Y. K.; Kim, Y. H.; Hong, S. I. *Makromol. Chem.* **1992**, *193*, 1623–1631.
(11) Biela, T.; Duda, A.; Pasch, H.; Rode, K. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 6116–6133.
(12) Hao, Q.; Li, F.; Li, Q.; Li, Y.; Jia, L.; Yang, J.; Fang, Q.; Cao, A. *Biomacromolecules* **2005**, *6*, 2236–2247.
(13) (a) Lemmouchi, Y.; Perry, M. C.; Amass, A. J.; Chakraborty, K.; Schacht, E. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 5348–5362. (b) Lemmouchi, Y.; Perry, M. C.; Amass, A. J.; Chakraborty, K.; Schacht, E. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 3966–3974. (c) Lemmouchi, Y.; Perry, M. C.; Amass, A. J.; Chakraborty, K.; Schué, F. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 2235–2245.
(14) (a) Dobrzynski, P.; Kasperczyk, J.; Jelonek, K.; Ryba, M.; Walski, M.; Bero, M. *J. Biomed. Mater. Res., Part A* **2006**, *79*, 865–873. (b) Hsueh, M. L.; Huang, B.; Wu, J.; Lin, C. *Macromolecules* **2005**, *38*, 9482–9487. (c) Ko, B.; Lin, C. *J. Am. Chem. Soc.* **2001**, *123*, 7973–7977.
(15) (a) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *Polym. Int.* **1998**, *46*, 177–182. (b) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *Biomaterials* **2002**, *23*, 993–1002. (c) Rashkov, I.; Manolova, N.; Li, S. M.; Espartero, J. L.; Vert, M. *Macromolecules* **1996**, *29*, 50–56. (d) Li, S. M.; Rashkov, I.; Espartero, J. L.; Manolova, N.; Vert, M. *Macromolecules* **1996**, *29*, 57–62. (e) Hiemstra, C.; Zhong, Z.; Li, L.; Dijkstra, P. J.; Feijen, J. *Biomacromolecules* **2006**, *7*, 2790–2795. (f) Kricheldorf, H. R.; Kreiser-Saunders, I.; Damrau, D. O. *Macromol. Symp.* **2000**, *159*, 247–257. (g) Williams, C. K.; Breyfogle, L. E.; Choi, S. K.; Nam, W.; Young, V. G., Jr.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.* **2003**, *125*, 11350–11359. (h) Huang, M. H.; Coudane, J.; Li, S.; Vert, M. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, *43*, 4196–4205. (i) Breyfogle, L. E.; Williams, C. K.; Young, V. G., Jr.; Hillmyer, M. A.; Tolman, W. B. *J. Chem. Soc., Dalton Trans.* **2006**, 928–936. (j) Chisholm, M. H.; Eilerts, N. W.; Huffman, J. C.; Iyer, S. S.; Pacold, M.; Phomphrai, K. *J. Am. Chem. Soc.* **2000**, *122*, 11845–11854. (k) Chisholm, M. H.; Gallucci, J.; Phomphrai, K. *Inorg. Chem.* **2002**, *41*, 2785–2794. (l) Chisholm, M. H.; Huffman, J. C.; Phomphrai, K. *J. Chem. Soc., Dalton Trans.* **2001**, 222–224. (m) Huang, B.; Lin, C.; Hsueh, M. L.; Athar, T.; Lin, C. *Polymer* **2006**, *47*, 6622–6629. (n) Wu, J.; Huang, B.; Hsueh, M. L.; Lai, S.; Lin, C. *Polymer* **2005**, *46*, 9784–9792. (o) Chen, H.; Huang, B.; Lin, C. *Macromolecules* **2005**, *38*, 5400–5405. (p) Chisholm, M. H.; Gallucci, J. C.; Zhen, H.; Huffman, J. C. *Inorg. Chem.* **2001**, *40*, 5051–5054. (q) Chisholm, M. H.; Lin, C.; Gallucci, J. C.; Ko, B.-T. *J. Chem. Soc., Dalton Trans.* **2003**, 406–412. (r) Cheng, M.; Attygalle, A. B.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 11583–11584. (s) Hung, W.; Huang, Y.; Lin, C. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 6466–6476.
(16) (a) Kricheldorf, H. R.; Damrau, D. O. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1998**, *35*, 1875–1887. (b) Wei, Z.; Liu, L.; Yu, F.; Wang, P.; Qu, C.; Qi, M. *Polym. Bull.* **2008**, *61*, 407–413. (c) Yu, T.; Wu, C.; Chen, C.; Huang, B.; Wu, J.; Lin, C. *Polymer* **2005**, *46*, 5909–5917. (d) Shueh, M.; Wang, Y.; Huang, B.; Kuo, C.; Lin, C. *Macromolecules* **2004**, *37*, 5155–5162.
(17) (a) Wang, X.; Liao, K.; Quan, D.; Wu, Q. *Macromolecules* **2005**, *38*, 4611–4617. (b) Gibson, V. C.; Marshall, E. L.; Navarro-Llobet, D.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Dalton Trans.* **2002**, 4321–4322. (c) O'Keefe, B. J.; Monnier, S. M.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.* **2001**, *123*, 339–340. (d) O'Keefe, B. J.; Breyfogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc.* **2002**, *124*, 4384–4393. (e) Stolt, M.; Sodergard, A. *Macromolecules* **1999**, *32*, 6412–6417.
(18) (a) Zhong, Z.; Schneiderbauer, S.; Dijkstra, P. J.; Westerhausen, M.; Feijen, J. *Polym. Bull.* **2003**, *51*, 175–182. (b) Zhong, Z.; Schneiderbauer, S.; Dijkstra, P. J.; Westerhausen, M.; Feijen, J. *J. Polym. Environ.* **2001**, *9*, 31–38. (c) Zhong, Z.; Dijkstra, P. J.; Birg, C.; Westerhausen, M.; Feijen, J. *Macromolecules* **2001**, *34*, 3863–3868. (d) Piao, L.; Sun, J.; Zhong, Z.; Liang, Q.; Chen, X.; Kim, J. H.; Jing, X. *J. Appl. Polym. Sci.* **2006**, *102*, 2654–2660. (e) Piao, L.; Deng, M.; Chen, X.; Jiang, L.; Jing, X. *Polymer* **2003**, *44*, 2331–2336. (f) Darensbourg, D. J.; Choi, W.; Karroonnirun, O.; Bhuvanesh, N. *Macromolecules* **2008**, *41*, 3493–3502. (g) Chen, H.; Tang, H.; Lin, C. *Polymer* **2007**, *48*, 2257–2262. (h) Chisholm, M. H.; Gallucci, J.; Phomphrai, K. *J. Chem. Soc., Chem. Commun.* **2003**, 48–49. (i) Chisholm, M. H.; Gallucci, J. C.; Phomphrai, K. *Inorg. Chem.* **2004**, *43*, 6717–6725.
(19) (a) Wang, C.; Li, H.; Zhao, X. *Biomaterials* **2004**, *25*, 5797–5801. (b) Coulembier, O.; Lohmeijer, B. G. G.; Dove, A. P.; Pratt, R. C.; Mespouille, L.; Culkin, D. A.; Benight, S. J.; Dubois, P.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 5617–5628. (c) Myers, M.; Connor, E. F.; Glauser, T.; Möck, A.; Nyce, G.; Hedrick, J. L. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 844–851. (d) Nederberg, F.; Lohmeijer, B. G. G.; Leibfarth, F.; Pratt, R. C.; Choi,

J.; Dove, A. P.; Waymouth, R. M.; Hedrick, J. L. *Biomacromolecules* **2007**, *8*, 153–160. (e) Lohmeijer, B. G. G.; Pratt, R. C.; Leibfarth, F.; Logan, J. W.; Long, D. A.; Dove, A. P.; Nederberg, F.; Choi, J.; Wade, C.; Waymouth, R. M.; Hedrick, J. L. *Macromolecules* **2006**, *39*, 8574–8583. (f) Zhang, L.; Nederberg, F.; Pratt, R. C.; Waymouth, R. M.; Hedrick, J. L.; Wade, C. G. *Macromolecules* **2007**, *40*, 4154–4158. (g) Tang, H.; Chen, H.; Huang, J.; Lin, C. *Macromolecules* **2007**, *40*, 8855–8860.

(20) (a) Sinnwell, S.; Ritter, H. *J. Macromol. Sci., Part A: Pure Appl. Chem*. **2007**, *44*, 1155–1160. (b) Numata, K.; Srivastava, R. K.; Finne-Wistrand, A.; Albertsson, A. C.; Doi, Y.; Abe, H. *Biomacromolecules* **2007**, *8*, 3115–3125. (c) Namekawa, S.; Uyama, H.; Kobayashi, S.; Kricheldorf, H. R. *Macromol. Chem. Phys*. **2000**, *201*, 261–264.

(21) (a) Appel, K. E. *Drug Metab. Rev*. **2004**, *36*, 763–786. (b) Nakanishi, T. *J. Health Sci*. **2007**, *53*, 1–9.

(22) (a) Shang, X.; Liu, X.; Cui, D. *J. Polym. Sci., Part A: Polym. Chem*. **2007**, *45*, 5662–5672. (b) Miao, W.; Li, S.; Cui, D.; Huang, B. *J. Organomet. Chem*. **2007**, *692*, 3823–3834. (c) Liu, X.; Shang, X.; Tang, T.; Hu, N.; Pei, F.; Cui, D.; Chen, X.; Jing, X. *Organometallics* **2007**, *26*, 2747–2757.

(23) Wang, S.; Cui, W.; Bei, J. *Anal. Bioanal. Chem*. **2005**, *381*, 547–556.

(24) (a) Noga, D. E.; Petrie, T. A.; Kumar, A.; Weck, M.; García, A. J.; Collard, D. M. *Biomacromolecules* **2008**, *9*, 2056–2062. (b) Williams, C. K. *Chem. Soc. Rev*. **2007**, *36*, 1573–1580.

(25) Pietrangelo, A.; Hillmyer, M. A.; Tolman, W. B. *Chem. Commun*. **2009**, 2736–2737.

(26) (a) Ma, H.; Spaniol, T. P.; Okuda, J. *Inorg. Chem*. **2008**, *47*, 3328–3339. (b) Ma, H.; Spaniol, T. P.; Okuda, J. *Angew. Chem., Int. Ed*. **2006**, *45*, 7818–7821.

(27) (a) Chmura, A. J.; Davidson, M. G.; Frankis, C. J.; Jones, M. D.; Lunn, M. D. *Chem. Commun*. **2008**, 1293–1295. (b) Chmura, A. J.; Chuck, C. J.; Davidson, M. G.; Jones, M. D.; Lunn, M. D.; Bull, S. D.; Mahon, M. F. *Angew. Chem., Int. Ed*. **2007**, *46*, 2280–2283.

(28) Amgoune, A.; Thomas, C. M.; Roisnel, T.; Carpentier, J. F. *Chem.−Eur. J*. **2006**, *12*, 169–179.

(29) Ma, H.; Okuda, J. *Macromolecules* **2005**, *38*, 2665–2673.

(30) Zimm, B. M.; Kilb, R. W. *J. Polym. Sci*. **1959**, *37*, 19–42.

(31) See details in Supporting Information. The integral order (= 1) in precatalyst concentration observed in detail kinetics study suggested that the species were unimeric and nonaggregate. The polymer chains propagated on one type of active center according to the literature: (a) Aubrecht, K. B.; Hillmyer, M. A.; Tolman, W. B. *Macromolecules* **2002**, *35*, 644–650. (b) O'Keefe, B. J.; Breyfogle, L. E.; Hillmyer, M. A.; Tolman, W. B. *J. Am. Chem. Soc*. **2002**, *124*, 4384–4393.

(32) Aida, T.; Maekawa, Y.; Asano, S.; Inoue, S. *Macromolecules* **1988**, *21*, 1195–1202.

(33) Inoue, S. *J. Polym. Sci., Part A: Polym. Chem*. **2000**, *38*, 2861–2871.

(34) (a) Helou, M.; Miserque, O.; Brusson, J. M.; Carpentier, J. F.; Guillaume, S. M. *Chem.−Eur. J*. **2008**, *14*, 8772–8775. (b) Wu, J.; Yu, T.; Chen, C.; Lin, C. *Coord. Chem. Rev*. **2006**, *250*, 602–626.

(35) (a) Amgoune, A.; Thomas, C. M.; Carpentier, J. F. *Macromol. Rapid Commun*. **2007**, *28*, 693–697. (b) Ajellal, N.; Lyubov, D. M.; Sinenkov, M. A.; Fukin, G. K.; Cherkasov, A. V.; Thomas, C. M.; Carpentier, J. F.; Trifonov, A. A. *Chem.−Eur. J*. **2008**, *14*, 5440–5448.

(36) Tshuva, E. Y.; Goldberg, I.; Goldschmidt, Z.; Kol, M. *Organometallics* **2001**, *20*, 3017–3028.

(37) Lappert, M.; Pearce, R. *Chem. Commun*. **1973**, 126–127.