

Stereocontrolled Polymerization of Racemic Lactide with Chiral Initiator: Combining Stereoelection and Chiral Ligand-Exchange Mechanism

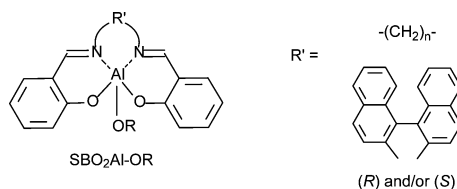
Katarzyna Majerska and Andrzej Duda*

Department of Polymer Chemistry, Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Sienkiewicza 112, PL-90-363 Lodz, Poland

Received October 6, 2003; E-mail: anduda@bilbo.cbmm.lodz.pl

Polymerization of lactides (LA) and other cyclic aliphatic esters provides an excellent model system for fundamental studies of thermodynamics, kinetics, and mechanism of the ring-opening polymerization (ROP) of heterocyclic monomers. The best control of LA polymerization, with regard to molar masses and end-group structures in the resultant poly(lactide) (PLA), has been achieved with multivalent metal (e.g., Ca, Zn, Sn(II), Al, La, Y, Sn(IV), Ti) alkoxides as initiators and catalysts.¹ A concept of a "single-site" initiator/catalyst in LA polymerization has thoroughly been explored^{2–7} to avoid the mechanistic complexity resulting from the aggregation equilibria, in which "multiple-site" alkoxides are usually engaged.

Stereochemical microstructure of PLA macromolecules formed in the ROP of LA, can be controlled by the monomer composition in the feed (proportion of (R,R)-, (S,S)-, and (R,S)-LA diastereoisomers) and/or by the stereochemical preference of the initiating/catalytic system. The idea of a single-site, enantioselective (or enantioelective) catalyst for polymerization of racemic lactide (rac-LA) has been realized by Spassky, who applied aluminum alkoxides of general structure SBO_2Al-OR , bearing Schiff's base ligands.³



The method originally developed by Spassky was then followed by methods by Baker,⁴ Coates,^{2,5} Feijen,⁶ and Nomura.⁷ It has been revealed that polymerization of rac-LA mediated with either achiral ($R' = -(CH_2)_m-$) or chiral racemic (R' : (R,S)-(1,1'-binaphthyl-2,2')-diyl) catalyst SBO_2Al-OR led to the multiblock stereocopolymers $[(S)\text{-PLA-}b\text{-}(R)\text{-PLA}]_p$ (Scheme 1), due to a chain-end control or an enantiomorphic site control of the monomer addition, respectively.

$[(S)\text{-PLA-}b\text{-}(R)\text{-PLA}]_p$ copolymers are able to form a stereocomplex due to van der Waals interactions between homochiral PLA sequences of opposite configuration, and therefore, they show enhanced thermal stability compared to the homochiral PLAs.⁸ The highest melting temperatures (T_m) of a stereocomplex obtained by the stereoselective polymerization of rac-PLA were equal to 191–192 °C.^{3–7}

The present communication aims at reporting a new approach to the chiral Schiff's base/aluminum alkoxide/rac-LA system, based on a consecutive addition of homochiral (S)- and (R)-Schiff's bases to the $Al(O^iPr)_3$ /rac-LA polymerization mixture, employing a chiral ligand-exchange mechanism.

Two-step polymerization of rac-LA was initiated by 2,2'-[1,1'-binaphthyl-2,2'-diylbis(nitrylomethylidene)]diphenol ($SB(OH)_2$)/

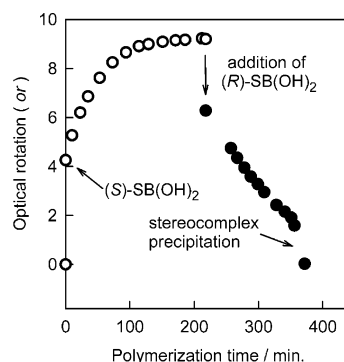
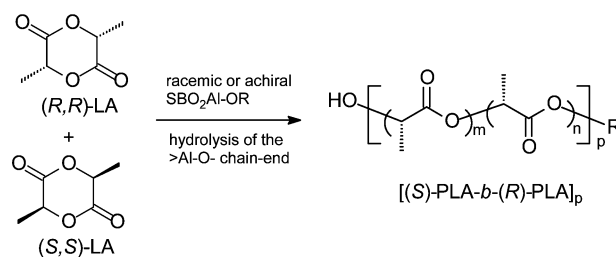


Figure 1. Plot of optical rotation versus time for two-step polymerization of rac-LA initiated with $Al(O^iPr)_3$ trimer (A_3)/(S)- $SB(OH)_2$ mixture and mediated with (R)- $SB(OH)_2$ added consecutively (THF, 80 °C, $3[A_3]_0 = [(S)\text{-}SB(OH)_2]_0 = [(R)\text{-}SB(OH)_2]_0 = 0.023$ M, $[rac\text{-}LA]_0 = 1.54$ M).

Scheme 1



aluminum isopropoxide trimer (A_3)⁹ mixture in which the actual initiator (SBO_2Al-O^iPr) was formed in situ. First, (S)- $SB(OH)_2/A_3$ mixture was reacted for 24 h in THF as solvent at 80 °C, and then rac-LA was introduced. Progress of the polymerization was followed using polarimetry (Figure 1) and size exclusion chromatography (SEC) (Table 1, entries 1 and 4).

Optical rotation (*or*) readings increased with polymerization time and eventually leveled off. SEC measurement revealed approximately 50 mol % consumption of LA (α). In the second step, an equimolar quantity of (R)- $SB(OH)_2$, with regard to (S)- $SB(OH)_2$, was introduced (Table 1, entries 2 and 5). Further polymerization was accompanied by a gradual decrease of *or*, and finally ($\alpha > 90$ mol %) the polymerization product precipitated out.

M_n values of PLAs obtained in the first and second polymerization steps were controlled by the concentration ratios of the reacted LA and O^iPr groups in the feed (Table 1, entries 1, 2, 4, and 5).

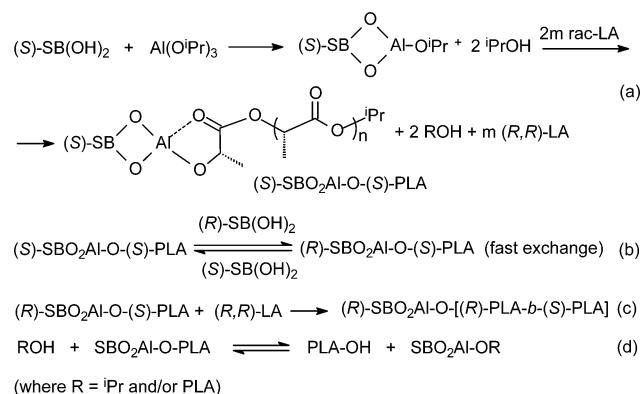
Low polydispersity indexes ($PDI = M_w/M_n$) (1.08–1.12) suggested the living polymerization mechanism, accompanied by a dynamic chain transfer to (macro)alcohol.

Moreover, the ²⁷Al NMR spectrum of the living polymerization mixture revealed the presence of one absorption band at $\delta \approx 67$ ppm,¹⁰ characteristic of the tetracoordinate $SBO_2Al-O-PLA$ active

Table 1. Polymerization of rac-LA Using SB(OH)₂/Al(OⁱPr)₃ Mixture^a

entry	[rac-LA] ₀ M	[Al] ₀ M × 10 ²	[(S)-SBH ₂] ₀ M × 10 ²	[(R)-SBH ₂] ₀ M × 10 ²	time (min)	α ^b mol %	M _n × 10 ⁻³ (calcd) ^c	M _n × 10 ⁻³ (SEC) ^d	PDI (SEC) ^e	T _m ^f (°C)	ΔH _{fus} ^g kJ/mol
1	1.54	2.30	2.30	0	220	53	1.8 ₀	1.8 ₀	1.1 ₂	130.8	56.5
2	1.54	2.30	2.30	2.30	400	93	3.1 ₀	3.4 ₈	1.1 ₂	189.7	70.7
3	1.54	2.30	2.30	0	16000	96	3.1 ₄	3.1 ₁	1.6 ₄	129.0	14.3
4	2.0	0.55	1.10	0	750	47	8.2 ₇	8.5 ₀	1.0 ₈	158.1	50.4
5	2.0	0.55	1.10	1.10	1500	~90 ^h	15.7 ₈	12.3 ₀ ^h	1.1 ₁	210.0	70.9

^a See ref 10 for polymerization conditions. ^b The conversion of rac-LA to PLA measured by SEC. ^c $M_n(\text{calcd}) = 144.13\alpha[\text{rac-LA}]_0/3[\text{Al}]_0 + 60.10$. ^d The average molar mass measured by SEC (PLA standards, CH₂Cl₂). ^e Polydispersity index (M_w/M_n). ^f PLA melting temperature measured by DSC. ^g Enthalpy of PLA melting measured by DSC. ^h PLA partially insoluble in CH₂Cl₂.

Scheme 2

species, with an additional coordination of the Al atom by the acyl oxygen from the first repeating unit (Scheme 2).^{1c,d,9a,b}

T_m 's of the isolated poly(rac-LA) were well above those expected for the homochiral PLA and reached 210 °C for the molar masses high enough ($M_n \approx 10^4$, Table 1, entry 5). The pertinent enthalpies of melting (ΔH_{fus} , entries 2 and 5) indicated a degree of crystallinity of ~70%. Thus, the experimental evidence reported above pointed out the appearance of a stereocomplex composed of the block stereocopolymer (S)-PLA-*b*-(R)-PLA, formed according to the polymerization mechanism shown in Scheme 2.

The independent kinetic measurements, carried out for the (S)-SB(OH)₂/A₃/(S,S)-LA and (S)-SB(OH)₂/A₃/(R,R)-LA systems, exhibited a 28:1 preference for the polymerization of (S,S)-LA over (R,R)-LA.¹⁰ Thus, for the final poly(rac-LA), the gradient poly-[(S)-LA-*grad*-(R)-LA], rather than the pure block copolymer structure, should have been expected. Indeed, decoupled ¹H NMR spectra showed a presence apart from the strong signal of the isotactic *mmm* tetrad and also peaks of lower intensity,¹⁰ which could be ascribed to the *mmr*, *rmm*, and *rmr* tetrads, according to the reported stereochemical microstructure to chemical shift assignments.^{4–6}

Attempts to synthesize poly[(S)-LA-*grad*-(R)-LA] from rac-LA, resulting in the stereocomplex formation with (S)-SB(OH)₂ only and without introducing the (R)-ligand in the second step, failed. PDI, DSC data (Table 1, entry 3), and ¹H NMR spectra¹⁰ revealed an important role of transesterification during the very slow polymerization of (R,R)-LA on the (S)-SBO₂Al-O-... active centers.

In conclusion, we reported new opportunities provided by the SB(OH)₂/Al(OⁱPr)₃/rac-LA polymerization system employing a combination of stereoelection with (S) and (R) ligand exchange at Al-alkoxide active centers. Two-step polymerization of rac-LA was initiated by (S)-SBO₂Al-OⁱPr and mediated in the second step by (R)-SB(OH)₂, adding to the reacting mixture. The stereoelectivity

was close to that determined for the process with an additional synthetic step of isolation and purification of the SBO₂-Al-OⁱPr alkoxide. The resultant poly(rac-LA) had a gradient stereocopolymer structure and exhibited enhanced thermal stability due to a stereocomplex formation ($T_m = 210$ °C). This is the highest melting temperature reported until now for PLA prepared directly from rac-LA.

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Supporting Information Available: Experimental procedures, discussion of the polymerization mechanism, figures of 75 MHz ²⁷Al and decoupled 500 MHz ¹H NMR spectra, DSC traces of PLA stereocopolymers, and kinetic data (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (10) See the Supporting Information.

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