Remarkable Stereocontrol in the Polymerization of Racemic Lactide Using Aluminum Initiators Supported by Tetradentate Aminophenoxide Ligands

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There is currently much interest in the development of new catalyst systems for the production of polylactide (PLA), a relatively new commodity polymeric material derived from biorenewable feedstocks such as corn starch.[1] The mechanical properties of PLA are intimately linked to its microstructure, and hence, the stereoregular polymerization of lactide has become a key focus of attention. Some of the most significant advances in stereocontrolled polymerization have been seen using aluminum alkoxides stabilized by salen-type ligands (Scheme 1). For example, **I** was found to polymerize *rac*-LA with a pronounced isotactic bias,[2] while enantiopure (−)-**II** afforded a tapered block copolymer p(D-LA)−p(L-LA).[3] The enantiomorphic site selectivity of (−)-**II** has more recently been exploited to prepare highly syndiotactic PLA from *meso*-LA.[4] The racemic form of this initiator, (±)-**II**, converts *rac*-LA into an isotactic stereoblock material which exhibits a higher softening temperature than p(L-LA);[5] each enantiomer of **II** preferentially consumes either D-LA or L-LA, with low levels of stereochemical imperfections arising from the exchange of propagating chains between Al centers of opposing chirality.[5b,c] Isotactic PLA stereocopolymers have also been prepared in the melt phase using **III**,[6] and highly isotactic PLA has been produced from *rac*-LA using a mixture of *achiral* **IV** and benzyl alcohol (Scheme 1).[7]

Here, we report a new family of aluminum catalysts stabilized by tetradentate phenoxyamine (salan-type[8]) ligands which shows an hitherto unprecedented degree of stereocontrol in the polymerization of racemic lactide. Such ligands have previously been attached to zirconium and exploited by Kol and co-workers to catalyze the living polymerization of 1-hexene.[9] In general, they can be accessed by a modified Mannich condensation reaction.[10] However, this route is not applicable to the unsubstituted phenoxy derivatives which we have therefore synthesized via the stepwise condensation of an *N,N*-disubstituted ethylenediamine with the appropriate salicylaldehyde, followed by reduction.[11]
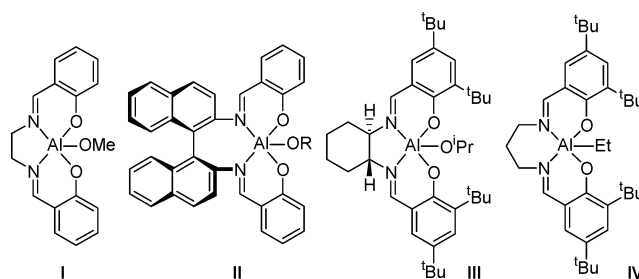
The aminophenols reacted smoothly with Me₃Al to afford the desired methyl complexes, **1**−**8** (Scheme 2). Unlike the highly conjugated salen ligands, which typically form colored metal complexes, the N-alkylated bis(aminophenoxide) complexes are white solids, an important factor for the commercial production of polymers since costly decolorization (catalyst removal) steps may be avoided.

Crystals of **2** were grown from toluene and a single-crystal X-ray analysis revealed a distorted trigonal bipyramidal coordination geometry at the aluminum center (Figure 1). C, N(8) and O(18) form the equatorial plane from which the metal atom deviates by ca. 0.20 Å in the direction of the axial atom O(1); a weakly associated fifth donor atom [Al−N(11), 2.4532(19) Å] occupies the other axial site. With the exception of this long axial contact, the coordination distances are unexceptional, the axial Al−O(1) bond length [1.7930(16) Å] being, as expected, noticeably longer than its equatorial counterpart [Al−O(18), 1.7570(15) Å].
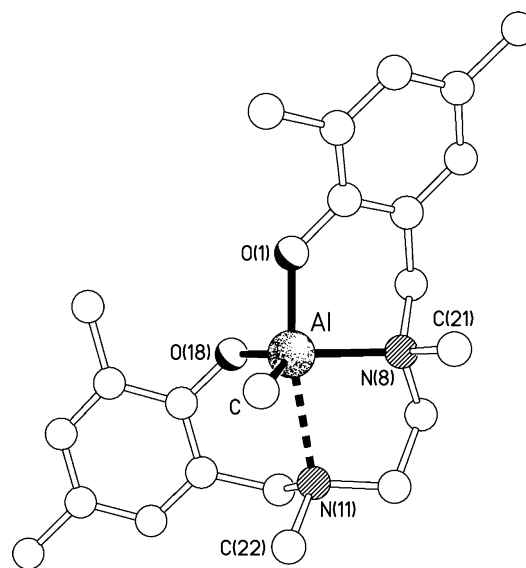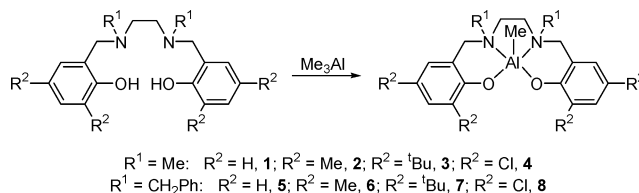

Figure 1. Molecular structure of **2**. Selected bond lengths (Å) and angles (deg): Al−C 1.955(3), Al−O(1) 1.7930(16), Al−N(8) 2.0550(18), Al−N(11) 2.4532(19), Al−O(18) 1.7570(15), C−Al−N(8) 119.93(12), C−Al−O(18) 122.84(12), N(8)−Al−O(18) 113.86(8), O(1)−Al−C 100.23(10), O(1)−Al−N(8) 90.95(7), O(1)−Al−O(18) 96.69(8), O(1)−Al−N(11) 167.97(7).

Scheme 1

Scheme 2

R^1 = Me: R^2 = H, **1**; R^2 = Me, **2**; R^2 = ᵗBu, **3**; R^2 = Cl, **4**
R^1 = CH₂Ph: R^2 = H, **5**; R^2 = Me, **6**; R^2 = ᵗBu, **7**; R^2 = Cl, **8**

Alkoxide initiators for lactide polymerization were generated by in situ alcoholysis of **1**−**8** using PhCH₂OH. Polymerizations were carried out at 70 °C in toluene; the results are collected in Table 1. All of the initiator systems exhibit molecular weights in close agreement with calculated values [M_n(calcd) PLA₁₀₀ = 14 400] and

Table 1. Polymerization Data for Complexes **1**–**8**[a]

	time (hr)	conv[b] (%)	M_n[c]	M_w/M_n[c]	k_{app} (10^{-6} s^{-1})	P_r/P_m[d]
1	23	97	18 920	1.04	182	0.32:0.68
2	24	87	12 725	1.09	25.4	0.80:0.20
3[e]	1464	66	4730	1.08	0.28	0.42:0.58
4	24	94	12 500	1.11	38.2	0.88:0.12
5	21	98	21 180	1.08	79.8	0.21:0.79
6	24	75	13 350	1.06	12.4	0.83:0.17
7	120	77	11 290	1.05	3.4	0.61:0.39
8	21	94	17 770	1.06	37.8	0.96:0.04

[a] [LA]/[Al] = 100, toluene, 70 °C. [b] Monomer conversion determined by ^{1}H NMR spectroscopy. [c] Determined by GPC. [d] P_r and P_m are the probability of hetero- and iso-tactic enchainment determined by ^{1}H NMR spectroscopy.[13a] [e] [LA]/[Al] = 50.
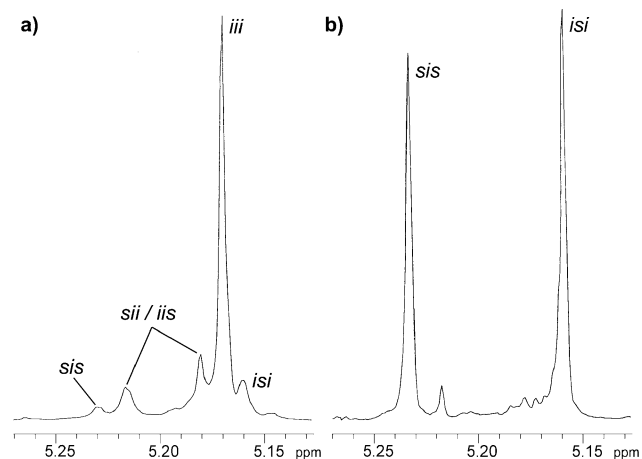
Figure 2. Homonuclear decoupled ^{1}H NMR spectra (methine region) of PLA generated from (a) **5**/PhCH$_2$OH and (b) **8**/PhCH$_2$OH (CDCl$_3$, 298 K, 500 MHz).

narrow molecular weight distributions, characteristic of well-controlled living propagation. The high level of control afforded by these initiators is further exemplified by linear correlations between M_n and conversion for all eight complexes (see Supporting Information).

Kinetic analyses showed that, as the size of the phenoxide alkyl substituent increases (from H to Me to ^{t}Bu), the rate of polymerization decreases. Further, the 3,5-dichlorophenoxides, **4** and **8**, are appreciably more active than their dimethyl analogues, most likely a consequence of the greater electrophilicity of the aluminum centers in **4** and **8**.

Table 1 also reveals the remarkable range of microstructures accessible using these initiators. Where the phenoxide groups are unsubstituted (**1** and **5**), high levels of isoselectivity are observed (as high as 79% in the case of **5**; see Figure 2a). However, when the phenoxide units contain substituents in the 3 and 5 positions, the tacticity is changed dramatically to a strong heterotactic bias. In the case of **8**, 96% heterotactic PLA is obtained (Figure 2b).[12,13] This is lowered to 83% for the sterically comparable 3,5-dimethyl derivative, **6**, implying that the chloro substituents exert an influence beyond a straightforward steric effect.

It can also be seen that the tacticity is significantly influenced by the substituents (R^1) attached to the amino nitrogen donors. For example, the benzylamine derivatives **6** and **8** afford higher heterotacticities than their methylamine analogues **2** and **4**, while

the unsubstituted phenoxide derivative **5** affords a higher isotactic content than **1**. Examination of the X-ray structure of the precatalyst **1** (Figure 1) reveals a possible explanation: the N(8)–C(21) bond of the equatorial amine donor, and especially the N–Me [N(1)–C(22)] bond of the axial amine unit, eclipses the Al–C bond, showing that the alkylamino backbone substituents can closely approach the site of polymer chain growth and thereby influence monomer selectivity.

In conclusion, we have found quite remarkable stereocontrol in the polymerization of *rac*-lactide by aluminum initiators supported by tetradentate aminophenoxide ligands. The polymerizations are well-controlled and living, affording PLA materials that range from highly isotactic to highly heterotactic, depending upon the ligand substitution pattern. To our knowledge, this is the first time aluminum-based systems have been found to give heterotactic PLA and the first time a dramatic switch in tacticity has been observed for a lactide polymerization system upon small changes to the remote ligand substituents. Work is continuing in our laboratories to understand the origin of stereocontrol in this new family of lactide polymerization initiators.

Supporting Information Available: Full experimental details for the synthesis of complexes **1**–**8**, including crystallographic data for **2** and polymerization data (M_n vs conversion plots, homonuclear decoupled NMR spectra for P_r/P_m determination, and kinetic data) (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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JA038757O