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Formation of Poly(lactide) with Controlled Molecular Weight. Polymerization of Lactide by Aluminum Porphyrin

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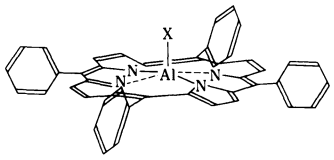
Poly(lactide) with narrow molecular weight distribution was obtained by the ring-opening polymerization of D-lactide with (5,10,15,20-tetraphenylporphinato)aluminum alkoxide as initiator. The polymerization was demonstrated to proceed via the ring--opening of lactide at the acyl-oxygen bond to give (porphinato)-aluminum alkoxide as the growing species.

Poly(lactide) (1) has attracted particular attention as non-toxic, biodegradable devices for controlled drug release and surgical sutures.[1] Thus, the control of molecular weight and its distribution is very important from practical as well as fundamental point of view.[2] Poly(lactide) can be synthesized by the ring-opening polymerization of lactide (2, 3,6-dimethyl-1,4-dioxacyclohexane-2,5--dione),[3] but no successful example of the formation of polymer with a desired molecular weight and the narrow distribution has been reported to date, except for the block copolymer of ε-caprolactone and D,L-lactide synthesized by $[(n\text{-}C_4H_9)_2AlO]_2Zn$ as initiator.[4]

In this paper is reported a novel example of the formation of poly(lactide) with narrow molecular weight distribution by the ring-opening polymerization of D-lactide (2, 3(R), 6(R)-) by using aluminum porphyrin (3) as initiator.[5]

For example, into a 20 cm^3 polymerization tube purged with dry nitrogen were added the CH_2Cl_2 solutions, respectively, of D-lactide (14 mmol, 5.7 cm^3) and a (tetraphenylporphinato)aluminum alkoxide (TPP)Al$\text{-}(\text{-}OCH(CH_3)CH_2\text{-})_n$Cl (n=20) ((TPP)AlPPO, 3a) (0.14 mmol, 2.8 cm^3), which was prepared by the polymerization of 1,2-epoxypropane (PO) by (TPP)AlCl (3b) with the ratio $[PO]_o/[(TPP)AlCl]_o$ of 20.[6,7] Then, the tube was placed in a liquid nitrogen bath, sealed off under vacuum, and allowed to stand at 100 °C with stirring magnetically. After a definite time, the tube was opened, and the volatile fractions were removed from the reaction mixture under reduced pressure at room temperature. For the determination of the conversion of lactide, and the molecular weight and its distribution of the polymer, a portion of the non-volatile fractions were dissolved in tetrahydrofuran, and subjected to gel permeation chromatography after filtering off the insoluble residue of aluminum porphyrin.



(TPP)AlX (3)

a : X=$\text{-}(\text{-}OCH(CH_3)CH_2\text{-})_n$Cl
b : X=Cl
c : X=OCH_3
d : X=C_2H_5

Under the conditions examined, the polymerization proceeded to give poly(lactide) in 30% conversion in 3 h, 65% in 24 h, and 94% in 96 h, respectively. The lower the temperature, the slower the polymerization. The polymerization attempted at room temperature led to no substantial formation of polymer even in a prolonged reaction.

Of particular interest to note is the narrow molecular weight distribution of the polymer, as demonstrated by a very sharp chromatogram shown in Fig. 1, for the reaction mixture at 94% conversion, where the ratio of the weight-average and number-average molecular weights ($\bar{M}w/\bar{M}n$) was estimated to be 1.12 with the number-average molecular weight ($\bar{M}n$) of 16400 (polystyrene as standard). The average molecular weight of polymer was observed to increase linearly with conversion, while keeping the ratio $\bar{M}w/\bar{M}n$ close to unity (Fig. 2). In such a case, the yield of polymer divided by $\bar{M}n$ should correspond to the number of the molecules of polymer (N_p). By taking advantage of this, the number of the poly(lactide) molecules with respect to that of aluminum porphyrin (N_p/N_{Al}) was calculated to be almost constant near 1.0 throughout the polymerization (Fig. 3), indicating that one molecule of initiator generates one polymer chain in the polymerization of lactide by (TPP)AlPPO (3a). Accordingly, the molecular weight of poly(lactide) can be controlled by the initial molar ratio of monomer to initiator and conversion; for another example, the polymerization starting from the ratio $[\text{D-lactide}]_o/[(\text{TPP})\text{AlPPO}]_o$ of 300 under the same conditions gave the polymer with the number-average molecular weight ($\bar{M}n$) of 24300 ($\bar{M}w/\bar{M}n$= 1.13) at 70% conversion.

Similarly, (TPP)$AlOCH_3$ (3c), prepared from (TPP)AlEt (3d) and CH_3OH,[6,8] gave rise to the polymerization of lactide under similar conditions to give the polymer with narrow molecular weight distribution. On the other hand, (TPP)AlCl[7] did not bring about the polymerization of lactide.

When (TPP)AlPPO carrying a long polyether chain ($\bar{M}n$, PPO=4900, $\bar{M}w/\bar{M}n$=1.07, based on standard poly(oxyethylene)) was used as initiator for the polymerization of lactide ($[\text{D-lactide}]_o/[(\text{TPP})\text{AlPPO}]_o$=100, in CH_2Cl_2 at 100 °C), the GPC chromatogram of the reaction mixture at 100% conversion showed no peak corresponding to the starting polyether, while a new unimodal

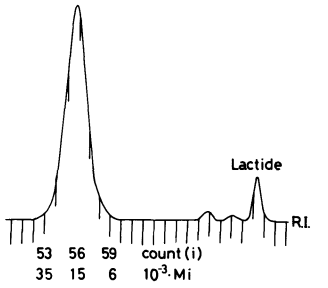


Fig. 1. Polymerization of D-lactide initiated with (TPP)AlPPO (3a, n=20), CH_2Cl_2 at 100°C. $[\text{D-lactide}]_o/[(\text{TPP})\text{AlPPO}]_o$=100, $[(\text{TPP})\text{AlPPO}]_o$=16.5 mmol·dm^{-3} GPC profile at 94% conv. (96 h). $\bar{M}n$=16400, $\bar{M}w/\bar{M}n$= 1.12

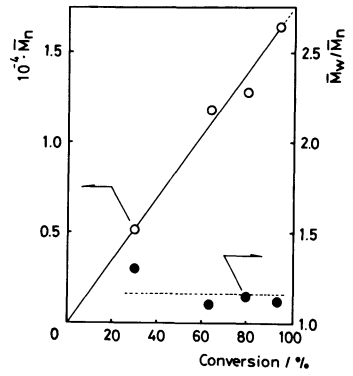


Fig. 2. Polymerization of D-lactide initiated with (TPP)AlPPO (3a, n=20). Reaction conditions : see Figure 1. Relationship between $\bar{M}n$(o) ($\bar{M}w/\bar{M}n$(●)) and conversion.

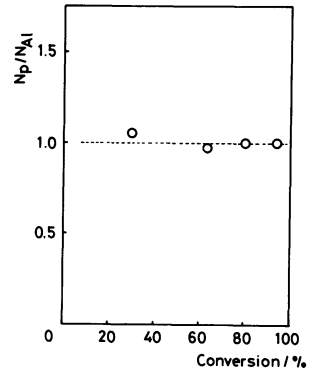


Fig. 3. Polymerization of D-lactide initiated with (TPP)AlPPO (3a, n=20). Reaction conditions : see Figure 1. Relationship between N_p/N_{Al} (number of polymer molecules/number of aluminum atoms) and conversion.

peak was observed at the higher molecular weight region ($\bar{M}n$=10300, $\bar{M}w/\bar{M}n$=1.24), indicating the formation of a block copolymer consisting of the starting polyether (PPO) and poly(lactide). Thus, the polymer of lactide initiated with (porphinato)aluminum alkoxide carries the alkoxyl group at the terminal.

In order to elucidate the structure of the growing species, the ^{1}H NMR analysis was made on the mixture of (TPP)AlOCH$_3$ (3c) and five molar equivalents of D-lactide in CDCl$_3$. The reaction at room temperature for 1 h gave the ^{1}H NMR spectrum shown in Fig. 4, where the signal P$_1$ (δ 9.1) is due to the pyrrole-β protons of the porphyrin ring, the signals P$_2$ (δ 8.2) and P$_3$ (δ 7.8) the o- and m-/p- protons of its phenyl substituents, respectively, and the signals A (δ 1.65) and B (δ 4.95) the methyl and methine protons of D-lactide, respectively. At the upfield region, a complete disappearence of the signal c at δ -1.3 due to the CH$_3$O-Al group of (TPP)AlOCH$_3$ was noted, while two doublet signals a (δ -1.56) and a' (δ 0.97), two quartet signals b (δ -1.95) and b' (δ 3.95), and one singlet signal c' (δ 3.29) were newly observed. When this spectrum is compared with that of (TPP)Al-OCH(CH$_3$)CO$_2$CH$_3$ (δ -1.57 (CH$_3$), δ -1.91 (CH), and δ 2.59 (OCH$_3$)), prepared by the exchange reaction between (TPP)AlOCH$_3$ and methyl lactate,[9,10] a set of the signals a and b can be assigned to the (Al)-OCH(CH$_3$)CO- group directly linked to the aluminum porphyrin, while another set a' and b' the penultimate -OCH(CH$_3$)CO- group shielded more weakly by the porphyrin. The signal c', which is observed to shift downfield by 0.7 ppm from the CH$_3$O- group of (TPP)AlOCH(CH$_3$)CO$_2$CH$_3$, is assignable to the methoxyl group attached to the carbonyl of the penultimate -OCH(CH$_3$)CO- group. Under the conditions examined, no signal was observed at δ 5.20 (CH) characteristic of poly(lactide). The relative intensities of the signals were in conformity with the assigned structure. Thus, the insertion of one molecule of lactide into the Al-OCH$_3$ bond of (TPP)AlOCH$_3$ takes place via the ring cleavage at the acyl-oxygen bond, to give the corresponding (porphinato)aluminum alkoxide (4$_1$)

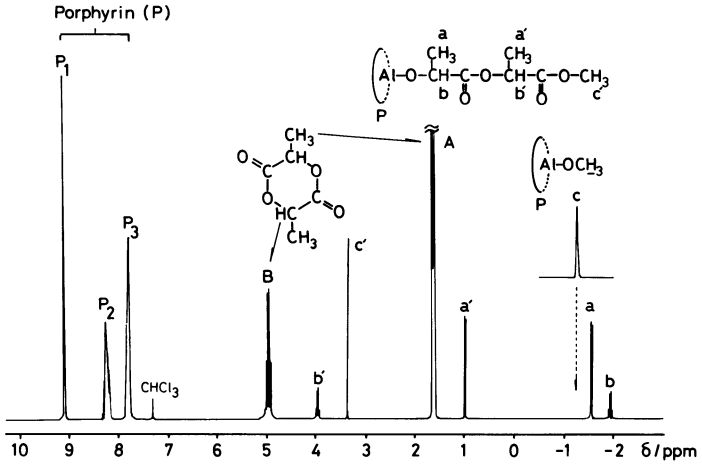
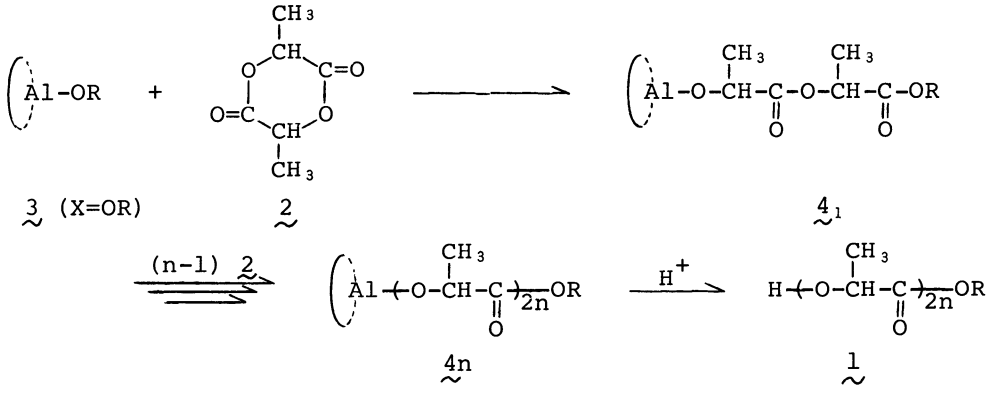


Fig. 4. ^{1}H NMR spectrum in CDCl$_3$ of the reaction mixture between D-lactide and (TPP)AlOCH$_3$ (3c) at room temperature in 1 h. [D-lactide]$_o$/[(TPP)AlOCH$_3$]$_o$=5/1.



quantilatively at room temperature. Upon heating this reaction mixture at 100 °C, the signals due to poly(lactide) appeared and increased in intensity with time at the expense of lactide monomer. At the same time, a decrease in intensity was observed for the signal c', while a new singlet at δ 3.68 appeared and increased.[9] Similarly, a new doublet signal at δ 1.02 assigned to (TPP)Al-OCH(CH_3)CO--OCH($\underline{CH}_3$)CO-OCH(CH_3)CO- appeared and increased in intensity with decreasing the intensity of the signal due to (TPP)Al-OCH(CH_3)CO-OCH($\underline{CH}_3$)CO-OCH_3 (a', δ 0.97). These facts indicate the successive insertions (polymerization) of lactide into the Al-O bond of $\underset{\sim}{4}_1$ to give $\underset{\sim}{4}n$. The alkyl-oxygen cleavage of lactide ring was also excluded by the infrared spectrum of the reaction mixture between (TPP)AlOCH_3 and D-lactide (1/0.5) in $CHCl_3$, where the carbonyl absorption characteristic of (porphinato)aluminum carboxylate[11] was not observed.

Thus, aluminum porphyrin is an excellent initiator for the "living" polymerization of lactide to give the polymer with controlled molecular weight, and has the potential utility for the molecular elaboration of biodegradable materials based on poly(lactide).

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