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Ring-opening polymerization of ε-caprolactone and L-lactide using organic amino calcium catalyst

Longhai Piao, Mingxiao Deng, Xuesi Chen, Liansheng Jiang, Xiabin Jing*

State Key Laboratory of Polymer Physics and Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, 159 Renmin Street, Changchun 130022, People's Republic of China

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Abstract

Poly (ε-caprolactone) (PCL) and poly (L-lactide) (PLA) were prepared by ring-opening polymerization catalyzed by organic amino calcium catalysts (Ca/PO and Ca/EO) which were prepared by reacting calcium ammoniate $Ca(NH_3)_6$ with propylene oxide and ethylene oxide, respectively. The catalysts exhibited high activity and the ring-opening polymerization behaved a quasi-living characteristic. Based on the FT-IR spectra and the calcium contents of the catalysts, and based on the ^{1}H NMR end-group analysis of the low molecular weight PCL prepared using catalysts Ca/PO and Ca/EO, it was proposed that the catalysts have the structure of $NH_2-Ca-O-CH(CH_3)_2$ and $NH_2-Ca-O-CH_2CH_3$ for Ca/PO and Ca/EO, respectively. The ring-opening polymerization of CL and LA follows a coordination-insertion mechanism and the active site is the Ca–O bond.

Keywords: Calcium catalyst; Poly (ε-caprolactone); poly (L-lactide)

1. Introduction

Biodegradable aliphatic polyesters such as poly (ε-caprolactone) (PCL), poly (L-lactide) (PLA) and poly (glycolide) (PGA) and their copolymers have received much attention because of their potential applications in tissue engineering, bone fixation, and controlled drug delivery due to their bioresorbable and biocompatible properties [1–5].

Usually, these polymers can be synthesized by ring-opening polymerization of cyclic ester monomers. Many effective catalysts have been employed [6–8]. But, it is highly preferable to use nontoxic catalysts in the preparation of clinic materials, since to remove the catalyst residue from resulted polymers is very difficult. It was reported that the residues of stannous octoate catalyst might present some cytotoxicity [9]. Recently, catalysts based on Ca, Mg, Zn and Fe received great interest because these elements can participate in the human metabolism [10–17].

Calcium ammoniate catalyst appeared in early 1960s and was modified in 1980s, for the ring-opening polymerization of olefin oxides [18–20]. It was also effective in the polymerization of ε-caprolactone (CL) and L-lactide (LLA) as shown in our previous studies [17]. But, because it can not dissolve in any organic solvents and is very unstable and sensitive to moisture, its structure or its catalytic mechanism has not been clear yet.

In this paper we wish to report on the recent results of the polymerization of CL and LLA, using calcium ammoniate catalyst treated with ethylene oxide (EO) and propylene oxide (PO), respectively. And, the structure of the catalysts was studied with ^{1}H NMR, FT-IR and elemental analysis.

2. Experimental section

2.1. Materials

ε-Caprolactone (Aldrich) was dried over CaH_2 and distilled at reduced pressure before use. L-lactide (LLA, Purac) was recrystallized from ethyl acetate under argon atmosphere. Xylene and 1,4-dioxane were dried by refluxing over Na/Ka alloy. Ethyl acetate and propylene oxide were dried by refluxing over CaH_2. Ethylene oxide was dried using CaH_2. Metallic calcium was used without further treatment.

* Corresponding author. Tel.: +86-431-5262224; fax: +86-431-5685653.
E-mail address: xbjing@ns.ciac.jl.cn (X. Jing).

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2.2. Preparation of catalysts

Gaseous NH_3 was purified over two columns filled with sodium sulfate and sodium hydroxide, respectively, to remove water and aldehyde impurities in it, and was liquidized with dry ice. The liquidized NH_3 was introduced into a flask that contained metal Ca and magnetic stirrer. EO or PO was added dropwise using a syringe. The molar ratio of Ca/EO or Ca/PO was 1/1. Ten minutes later, the excess NH_3 was evaporated by raising the temperature from −40 to 100 °C. The obtained white solid was crashed into fine powders and added into desired solvent to prepare a suspension in a glove box filled with dried nitrogen.

2.3. Polymerization

All polymerizations were carried out in an argon-filled glass reactor which had been flame-dried. ε-Caprolactone, xylene, and catalyst suspension in xylene were introduced into the reactor with dried syringes in that order. The volume ratio of CL to xylene was 2/5, and the reaction temperature was 70 °C. In the case of PLA, the weight ratio of LLA to 1,4-dioxane was 1/2, and the reaction temperature was 80 °C. The polymerization was conducted for predetermined time. The reaction product was dissolved in $CHCl_3$, precipitated into alcohol, filtrated, washed several times with alcohol, and finally dried in vacuum at room temperature for 24 h.

2.4. Measurements

NMR spectra were recorded with a Unity-400 NMR spectrometer at room temperature, with $CDCl_3$ as solvent and TMS as internal reference. The GPC measurement was conducted at 25 °C with a Waters 410 GPC instrument equipped with a Waters Styragel HT6E column and a differential refractometer detector. THF was used as eluent at a flow rate of 1.0 ml/min, and the molecular weights were calibrated with polystyrene standards. FT-IR spectra were recorded on a Bio-Rad Win-IR instrument.

To determine calcium content in the catalyst, known-amount of the catalyst was dissolved in nitric acid and a PEAA800 atomic absorption spectrophotometer was employed to carry out the analysis.

The intrinsic viscosity $[\eta]$ of PCL was measured in benzene at 30 °C using an Ubbelohde viscometer. For PLA, the measurement was carried out at 25 °C using $CHCl_3$ as solvent. The viscosity–average molecular weight (Mv) of PCL and PLA were calculated according to the following equations [21,22]:

$$\text{PCL}: [\eta] = 9.94 \times 10^{-5} \text{Mv}^{0.82}$$

$$\text{PCL}: [\eta] = 5.54 \times 10^{-4} \text{Mv}^{0.73}$$

3. Results and discussion

The polymerizations of ε-caprolactone (Figs. 1 and 2) and L-lactide (Figs. 3–5) were conducted using calcium ammoniate catalysts treated with PO (abbreviated as Ca/PO) and EO (abbreviated as Ca/EO), respectively. The reaction system was in suspension state in the very early stage of polymerization, since the catalysts had low solubility in xylene or 1,4-dioxane. The mixture became homogenous and viscous about 15 min after the beginning of polymerization, indicating that the catalyst species became a part of the growing polymer chain and got dissolved into the system.

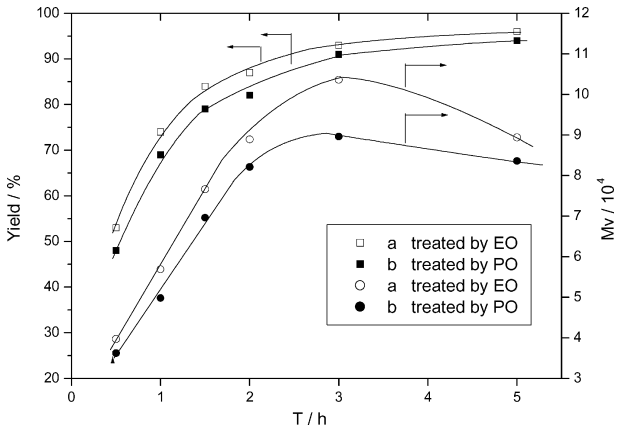


Fig. 1. Yield and Mv of PCL vs. polymerization time. Catalyst: Ca/EO (a) and Ca/PO (b). Other polymerization conditions: $M/I = 650$, 70 °C.

The variations of yield and Mv of PCL versus reaction time were shown in Fig. 1, with the weight ratio of monomer to catalyst, M/I, of 650 and at 70 °C. The polymerization of CL was very fast for both catalysts. The yield of more than 90% was achieved within 3 h. In the early stage of the polymerization, Mv increased linearly with the reaction time, indicating that the polymerization has certain living characteristics. After reaching the highest value (at about 2.5–3 h), Mv decreased with time, implying the occurrence of intermolecular or intramolecular transesterification.

A good linear relationship between Mv and M/I was found when M/I was lower than 700 (Fig. 2). This linear

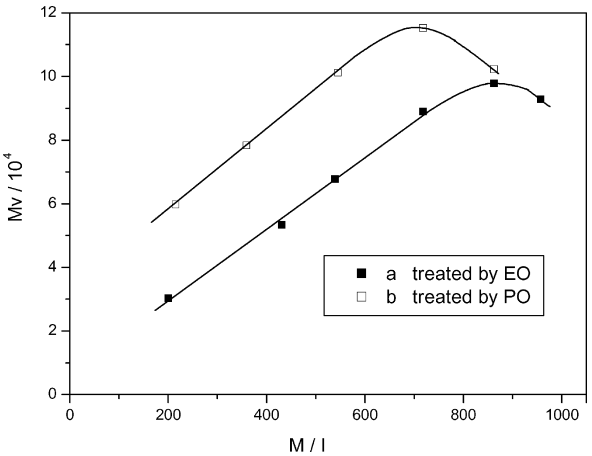


Fig. 2. Relationship between the Mv and M/I ratio. Catalyst: Ca/EO(a) and Ca/PO(b). Other polymerization conditions: 70 °C, 24 h.

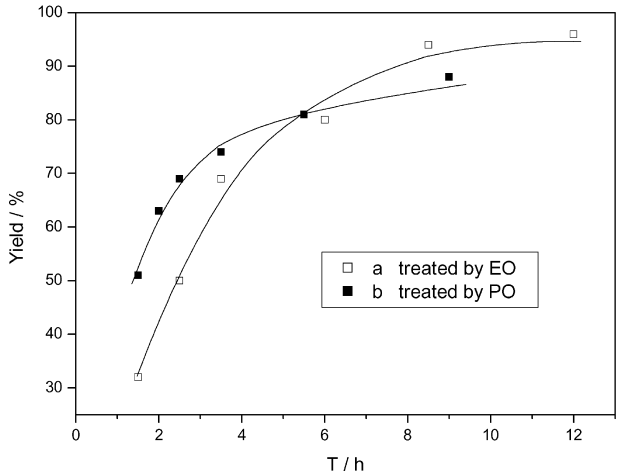


Fig. 3. Yield of PLA vs. polymerization time. Catalyst: Ca/EO (a) and Ca/PO (b). Other polymerization conditions: $M/I = 650$, 80 °C.

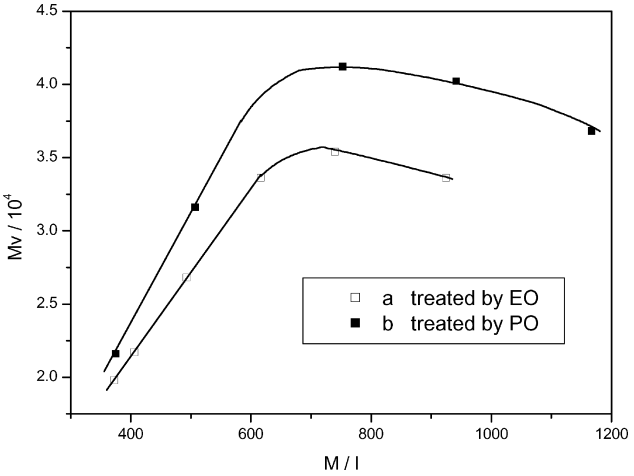


Fig. 5. Relationship between the Mv and M/I ratio. Catalyst: Ca/EO (a) and Ca/PO (b). Other polymerization conditions: 80 °C, 24 h.

relationship provided another support for the quasi-living polymerization, and could be used to control the molecular weight of PCL. The Mv of PCL using Ca/EO was higher than that using Ca/PO, probably due to the difference in availability of the both catalysts in the reaction system. In fact, the solubility of Ca/EO in xylene was slightly worse than Ca/PO. Owing to the limited availability of Ca/EO, the real M/I for Ca/EO was higher than that for Ca/PO and led to higher Mv of PCL. In Fig. 2, the data curves intersect with the y-axis at Mv > 0, probably because only the precipitated polymer with high enough molecular weight was collected for the Mv measurement.

LLA was successfully polymerized with Ca/EO and Ca/PO. As shown in Figs. 3–5, similar relationships of yield–Mv–time and of Mv–M/I were observed. Compared to CL, the polymerization of LLA was slower: over 10 h was needed to achieve a conversion of 90%. Ca/PO exhibited higher activity than Ca/EO. This was evidenced by the higher yield (Fig. 3, in the first 4 h) and Mv (Fig. 4) at a given time, and the higher Mv (Fig. 5) at a given M/I for the Ca/PO catalyzed system than for the Ca/EO catalyzed system. Because the polymerization was carried out in 1,4-dioxane and the both catalysts showed similar solubility in it, heterogeneity was not the predominant factor as in the case of PCL. The Mv of PLLA was mainly determined by the molar ratio of monomer to catalyst. Taking the molecular weights of the both catalysts (see below) into consideration and converting the weight ratio in Figs. 3–5 into molar ratio, the above differences could be reasonably explained.

Calcium catalysts have been studied for many years, but their structure was not clear yet, because of their poor solubility in organic solvents and instability under ambient condition. Therefore, efforts were made to get more information on their composition and structure, and to deduce their active center and polymerization mechanism.

The FT-IR spectra of the Ca/PO and Ca/EO are shown in Figs. 6 and 7, respectively. In both spectra the bands at 3400–3200 cm^{-1} and the characteristic peak at 1590 cm^{-1} can be assigned to NH_2 group. Therefore, it is concluded that the Ca/PO and Ca/EO catalysts both contain NH_2

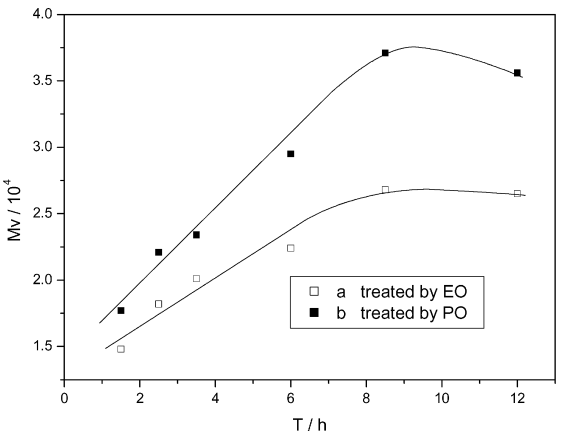


Fig. 4. Molecular weight of PLA vs. polymerization time. Catalyst: Ca/EO (a) and Ca/PO (b). Other polymerization conditions: $M/I = 650$, 80 °C.

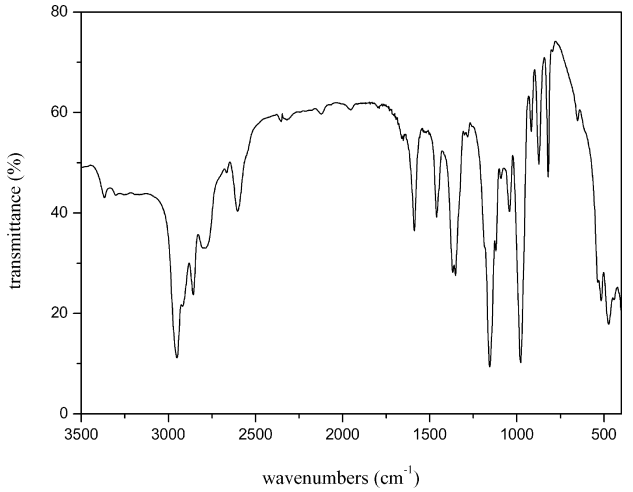


Fig. 6. FT-IR spectrum of the Ca/PO catalyst.

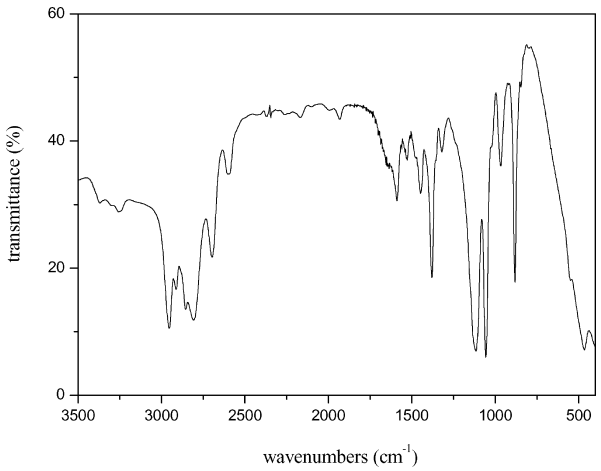


Fig. 7. FT-IR spectrum of the Ca/EO catalyst.

groups. Usually amine salts exhibit characteristic absorption peaks in the range of 2800–2500 cm^{-1}. The peaks at 2790, 2600 cm^{-1} in Fig. 6 and peaks at 2700, 2600 cm^{-1} in Fig. 7 might provide evidence for the presence of amine group in the catalysts. On the other hand, when metal calcium was reacted with isopropanol to form its isopropanoxide, similar weak peaks in this region were observed. Thus they might be assigned to the overtone of the propoxy or ethoxy groups and serve as the evidence for these groups.

In Fig. 6, the peaks at 2950, 2860 cm^{-1} are due to the asymmetric and symmetric C–H stretching vibrations of CH_3 group. The doublet bands at 1353 and 1368 cm^{-1} as well as the peak at 1460 cm^{-1} are characteristic of the CH_3 in an isopropyl group. The strong band at 1156 cm^{-1} is related to the C–O stretching. So, it is concluded that the Ca/PO catalyst has a structure of $NH_2–Ca–O–CH(CH_3)_2$.

The similar spectral analysis is applied to Fig. 7. That is, bands over 2950–2850 cm^{-1} and over 1448–1382 cm^{-1} are due to $–CH_2CH_3$; peak at 1117 cm^{-1} is due to O–C stretching. So, similar to the case of Ca/PO, the Ca/EO catalyst has a structure of $NH_2–Ca–O–CH_2CH_3$.

To examine this conclusion, determination of Ca content in the catalysts was conducted by using atomic absorption spectrophotometer. The determined values, 34.3 and 39.6% for Ca/PO and Ca/EO, respectively, were close to the theoretical data, 34.8 and 37.3%, calculated for the formula $NH_2–Ca–O–CH(CH_3)_2$ and $NH_2–Ca–O–CH_2CH_3$, respectively.

Therefore, although we failed to obtain reliable and reproducible elemental analysis data because of the instability of the catalysts under ambient conditions, it is concluded that the catalysts have a structure of $NH_2–Ca–O–R$ and their preparation can be described in Scheme 1. First, metal calcium is reacted with liquid ammonia to form a blue calcium ammoniate solution [23], and then it is reacted with olefin oxide to form a white catalyst.

The end group analysis can provide powerful evidence for catalyst structure and polymerization mechanism. In order to analyze the end groups of the polymer obtained, low molecular weight PCL was prepared with $M/I = 10$ and at room temperature. The solution ^1H NMR in $CDCl_3$ of such PCL prepared with Ca/PO is shown in Fig. 8. The strong peaks at 4.1, 2.3, 1.6, 1.4 ppm all are assigned to the methylene protons (a, e, b + d, c) of the PCL repeat unit. The doublet peak at 1.23 ppm (g) and the multiplet peak at 5.00 ppm (f) are attributed to isopropoxy end-group. The triplet peak at 3.65 ppm (h) is assigned to the methylene proton adjacent to the hydroxy end-group. The integral area ratio of peaks f, h and g is close to 1:2:6 within the NMR experimental errors.

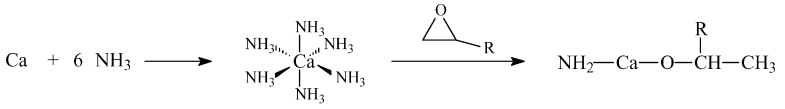
The ^1H NMR spectrum of low molecular weight PCL using Ca/EO is shown in Fig. 9. Similar to Fig. 8, the peaks of a, b, c, d and e are assigned to the PCL repeat unit and peak h to the methylene proton linked with hydroxy end-group. The triplet peak at 1.26 ppm (g) and the peak at 4.13 ppm (f) which is partly overlapped with peak a are attributed to the ethyl ester end-group.

From the above analysis, it is reasonably concluded that the polymers obtained by Ca/PO and Ca/EO contain two end-groups. One is hydroxyl group and the other is isopropoxy or ethoxy group. Obviously, the former is derived from the polymerization active center, and the latter is transferred from the catalyst used.

There are not any peaks assignable to the amine group in the ^1H NMR spectra of the both polymers obtained, indicating that the bond $Ca–NH_2$ is not active in the polymerization.

Therefore, it is deduced that the active species of polymerization is Ca–OR, where $R = CH(CH_3)_2$ in the case of Ca/PO and $R = CH_2CH_3$ in the case of Ca/EO. And the ring-opening polymerization of CL and LA follows a 'coordination–insertion' mechanism as other metal alkoxides do [14], as shown in Scheme 2.

First, the carbonyl of cyclic monomer is coordinated with the Ca atom in the catalyst and thus the ester bond gets weakened, and finally cleaved and inserted in between the calcium and oxygen atoms, forming a new active center. The monomer is continuously inserted into the active center, and the chain is growing. Hydrolysis of the active calcium alkoxide bond leads to the formation of a hydroxyl end-



R=CH_3 for Ca/PO and H for Ca/EO

Scheme 1. Preparation and structure of the Ca/PO and Ca/EO catalysts.

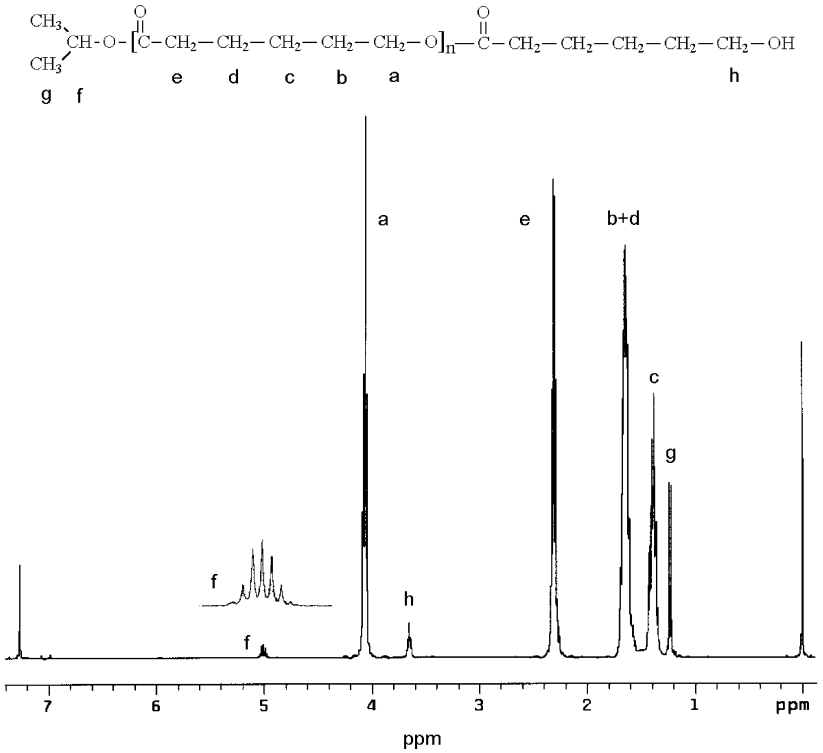


Fig. 8. The ^{1}H NMR spectrum of low molecular weight PCL using Ca/PO catalyst.

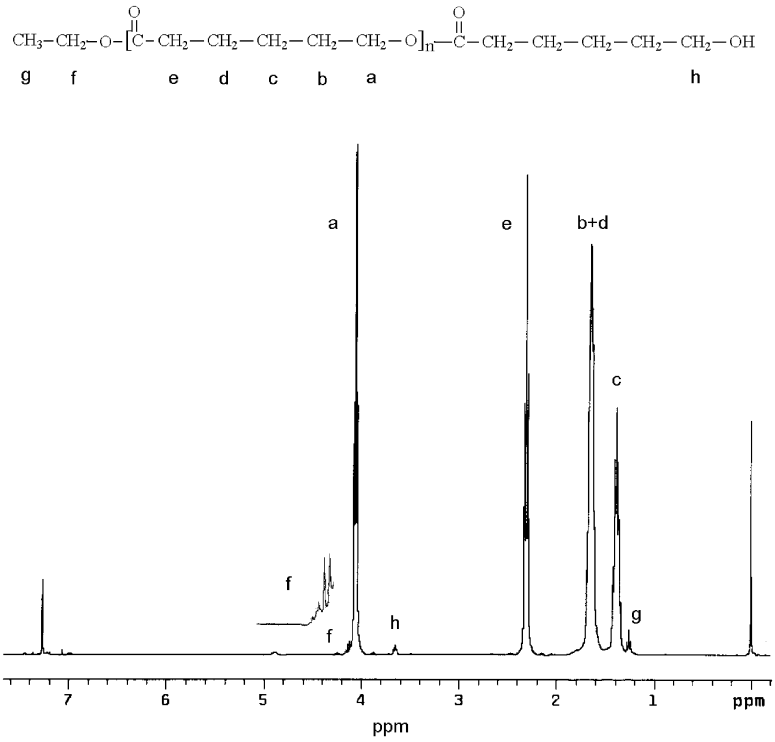
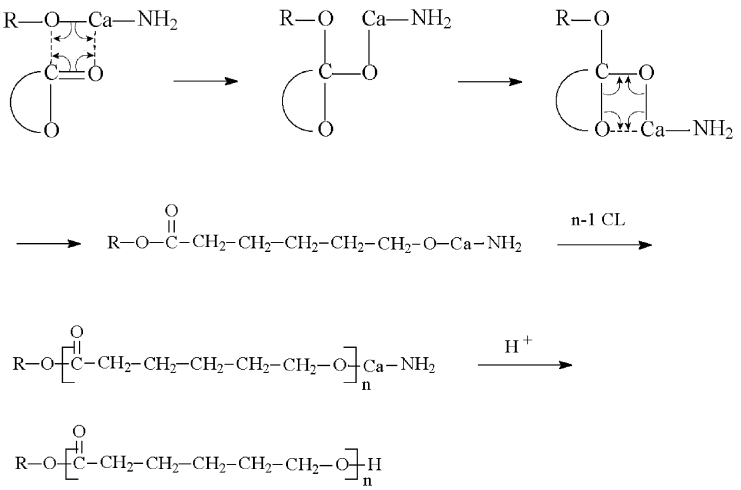


Fig. 9. The ^{1}H NMR spectrum of low molecular weight PCL using Ca/EO catalyst.



Scheme 2. Possible ring-opening polymerization mechanism of ε-caprolactone catalyzed by Ca/PO or Ca/EO.

group. The other chain end is capped with an ester, carrying the alkyl group R from the catalyst.

4. Conclusion

Poly (ε-caprolactone) and poly (L-lactide) were prepared by ring-opening polymerization catalyzed by organic amino calcium catalysts Ca/PO and Ca/EO which were prepared by reacting calcium ammoniate $Ca(NH_3)_6$ with propylene oxide and ethylene oxide, respectively. The catalysts exhibited high activity and the ring-opening polymerization behaved a quasi-living characteristic. Based on the FT-IR spectra and the calcium contents of the catalysts, and based on the ^{1}H NMR end-group analysis of the low molecular weight PCL prepared using catalysts Ca/PO and Ca/EO, it could be concluded that the catalysts have the structure of $NH_2-Ca-O-CH(CH_3)_2$ and $NH_2-Ca-O-CH_2CH_3$ for Ca/PO and Ca/EO, respectively. The ring-opening polymerization of CL and LA follows a coordination-insertion mechanism and the active site (insertion position) is the Ca–O bond, not the Ca–NH_2 bond.

Acknowledgements

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