

การสังเคราะห์พอลิแล็กติกแอซิดที่มีประจุบวก

นายปิยะชัย ขอมอินทร์

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต

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ปีการศึกษา 2554

ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

บทคัดย่อและแฟ้มข้อมูลฉบับเต็มของวิทยานิพนธ์ตั้งแต่ปีการศึกษา 2554 ที่ให้บริการในคลังปัญญาจุฬาฯ (CUIR)

เป็นแฟ้มข้อมูลของนิสิตเจ้าของวิทยานิพนธ์ที่ส่งผ่านทางบัณฑิตวิทยาลัย

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SYNTHESIS OF POSITIVELY-CHARGED POLY(LACTIC ACID)

Mr. Piyachai Khomein

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Chemistry

Department of Chemistry

Faculty of Science

Chulalongkorn University

Academic Year 2011

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Thesis Title SYNTHESIS OF POSITIVELY-CHARGED
POLY(LACTIC ACID)
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ปิยะชัย ขอมอินทร์ : การสังเคราะห์พอลิแล็กติกแอซิดที่มีประจุบวก. (SYNTHESIS OF POSITIVELY-CHARGED POLY(LACTIC ACID)) อ. ที่ปรึกษาวิทยานิพนธ์หลัก : ผศ.ดร.วราวุฒิ ตั้งพสุธาตล, 44 หน้า.

ในงานวิจัยนี้ได้สังเคราะห์พอลิแล็กติกแอซิดที่มีประจุบวกเพื่อเพิ่มสมบัติความชอบน้ำให้กับพอลิเมอร์ชนิดนี้ สำหรับการสังเคราะห์จะเป็นการทำปฏิกิริยาโดยตรงระหว่างพอลิแล็กติกแอซิด (มวลโมเลกุล 3,500 ดาลตัน) กับไกลซิديلไตรเมทิลแอมโมเนียมคลอไรด์ (GTMAC) โดยสามารถสังเคราะห์พอลิแล็กติกแอซิดที่มีประจุบวกที่มีร้อยละการแทนที่ของ GTMAC ที่ละลายสายโซ่เท่ากับ 76% สำหรับการหาละการแทนที่ของ GTMAC ที่ละลายสายโซ่นั้นหาจากผลของการวิเคราะห์ด้วยเทคนิคโปรตอน-เอ็นเอ็มอาร์ สเปกโทรสโกปี นอกจากนี้ผลการสังเคราะห์พบว่าการแทนที่ของ GTMAC เกิดขึ้นส่วนใหญ่ที่ปลายสายโซ่ฝั่งหมู่คาร์บอกซิล (-COOH) และในงานวิจัยนี้ได้หาสมบัติความชอบน้ำของพอลิแล็กติกแอซิดที่มีประจุบวกโดยใช้เครื่องวัดมุมสัมผัสของหยดน้ำกับพื้นผิวของแผ่นฟิล์มพอลิเมอร์ โดยผลที่ได้พบว่าค่ามุมสัมผัสของฟิล์มพอลิแล็กติกแอซิดที่มีประจุบวก (47°) มีค่าน้อยกว่าค่ามุมสัมผัสของฟิล์มพอลิแล็กติกแอซิด (56°) สำหรับการวิเคราะห์สมบัติทางความร้อนด้วยเทคนิคดีฟเฟอเรนเชียลสแกนนิ่งแคลอริมิทรีและเทอร์มอลกราวิเมตริกอะนาไลซิส พบว่าสมบัติดังกล่าวของพอลิแล็กติกแอซิดที่มีประจุบวกไม่มีการเปลี่ยนแปลงอย่างมีนัยสำคัญเมื่อเทียบกับพอลิแล็กติกแอซิดทั้งนี้เป็นผลมาจากการปรับเปลี่ยนหมู่ฟังก์ชันของพอลิแล็กติกแอซิดที่บริเวณปลายสายโซ่นั้น

ภาควิชา.....เคมี.....ลายมือชื่อ.....
 สาขาวิชา.....เคมี.....ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....
 ปีการศึกษา.....2554.....

5372287323: MAJOR Chemistry

KEYWORDS: Poly(lactic acid) / Glycidyl trimethyl ammonium chloride /
Hydrophilicity

PIYACHAI KHOMEIN: SYNTHESIS OF POSITIVELY-CHARGED
POLY(LACTIC ACID). ADVISOR: ASST. PROF. VARAWUT
TANGPASUTHADOL, Ph.D. 44 pp.

In order to increase the hydrophilicity of biodegradable poly(L-lactic acid) (PLLA), PLLA with a terminal positively-charged ammonium ion (p-PLLA) was synthesized. PLLA with \bar{M}_n of 3,500 Da was reacted with glycidyl trimethyl ammonium chloride (GTMAC) to obtain up to 76% of substitution on the PLLA chain end. It was also confirmed that the attachment occurred mostly on the carboxyl chain end side. The degree of substitution was determined by $^1\text{H-NMR}$ spectroscopy. Hydrophilic property of the polymer was analyzed by measuring air-water contact angle of the modified PLLA films and it was found that the contact angles of p-PLLA (45°) was lower than that of the neat PLLA (57°). No significant change in the thermal properties when PLLA was transformed to p-PLLA as analyzed by DSC and TGA since PLLA was modified only at chain end position.

Department : Chemistry..... Student's Signature

Field of Study : Chemistry..... Advisor's Signature

Academic Year : 2011.....

ACKNOWLEDGEMENTS

I would like to express gratitude to my thesis advisor, Assistant Professor Varawut Tangpasuthadol for invaluable suggestion, guidance, encouragement and kindness throughout the course of this work. In addition, sincere appreciation is also extended to Assistant Professor Warinthorn Chavasiri, Associate Professor Voravee P. Hoven and Assistant Professor Chidchanok Meechaisue for acting as the chairman and examiners of my thesis committee, and for their valuable constructive comments and suggestions.

I would like to thank the Center for Petroleum, Petrochemicals and Advanced Materials, Chulalongkorn University and Development and Promotion of Science and Technology talent project (DPST) for financial support. Furthermore, I also thank Miss Hussaya Maneesuwan, a student of Petroleum and Petrochemical College, for her kindness of analyzing thermal properties of the products and I thank all members of Organic Synthesis Research Unit (OSRU), and all my friends, for their friendliness, helpful discussions, cheerful attitude and encouragements during my thesis work. Finally, I also wish to especially thank my family members for their love, kindness and support throughout my entire study.

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LIST OF ABBREVIATIONS

ROP	: Ring-opening polymerization
LA	: L-lactic acid, L-lactide
PLLA	: Poly(L-lactic acid), poly(L-lactide)
p-PLLA	: Positively-charged poly(L-lactic acid)
p-LA	: Positively-charged L-lactic acid
CDCl ₃	: Deuterated chloroform
DMSO-d ₆	: Deuterated dimethyl sulphoxide
TNBT	: Titanium(IV) n-butoxide
NMR	: Nuclear magnetic resonance spectroscopy
GPC	: Gel permeation chromatography
\overline{M}_n	: Number-average molecular weight
\overline{M}_w	: Weight-average molecular weight
PDI	: Polydispersity index
DSC	: Differential scanning calorimetry
TGA	: Thermal gravimetric analysis
T _g	: Glass transition temperature
T _c	: Crystallization temperature
T _m	: Melting temperature

CHAPTER I

INTRODUCTION

1.1 Statement of Problem

Poly(lactic acid) (PLA) can be produced from renewable resource such as corn, potato and cassava. It is a biodegradable polymer possessing biocompatibility and physical properties similar to the polymer obtaining from petroleum product. Nowadays, PLA is used in many applications such as materials for medical devices, textile and packaging. Hence, there are many interests in modification of the polymer property in order to meet the demand of applications.

PLA is water insoluble and considered to be rather hydrophobic. This limits its use in some applications, for example, as carriers for high polarity drugs. Furthermore, it is known that the product after degradation of PLA is acid, and was proved to cause inflammation to tissue when it was implanted in human body. Since the main route of degradation in PLA is hydrolysis, PLA with lower hydrophobicity would increase the degradation rate and therefore shorten the residence time of the device at the implanted site. For those reasons, increasing the hydrophilicity of PLA have been reported in recent years by blending poly(lactic acid) with hydrophilic polymers, copolymerizing PLA with hydrophilic monomers, or adding hydrophilic functional group such as carboxyl (-COOH) and amino (-NH₂) groups to PLA.

In this research PLA with increasing hydrophilicity was synthesized by reacting with glycidyl trimethyl ammonium chloride (GTMAC) which is a compound possessing epoxide ring and a positive charge on the quaternary ammonium group in its structure. It is expected that PLA will open the epoxide ring of GTMAC by using its hydroxyl group at the polymer chain end position giving a positively-charged polymer with more hydrophilicity and faster degradation.

1.2 Objectives

To synthesize poly(lactic acid) with positively-charged chain end to enhance the hydrophilicity of the polymer.

1.3 Scope of Investigation

1. Synthesis of positively-charged poly(lactic acid) by two methods
 - 1.1. PLA was direct reacted with GTMAC.
 - 1.2. Positively-charged lactic acid was first synthesized and then, polymerized with lactic acid.
2. Characterization of positively-charged PLA by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, gel permeation chromatography, contact angle goniometer and differential scanning calorimeter (DSC).

CHAPTER II

THEORY AND LITERATURE REVIEW

2.1 Lactic acid

Lactic acid is bi-functional monomer carrying a hydroxyl and a carboxyl groups and it is a monomer to produce PLA. Lactic acid can be produced by bacterial fermentation [1] of carbohydrates such as corn, potato and cassava which are renewable resource. Due to a chiral carbon in its structure, there are two active optically configurations of lactic acid. L-(+)-lactic acid or (S)-lactic acid is natural and the most common form of the acid [2, 3] but D-(-)-lactic acid or (R)-lactic acid can be produced by microorganisms or racemization reaction.

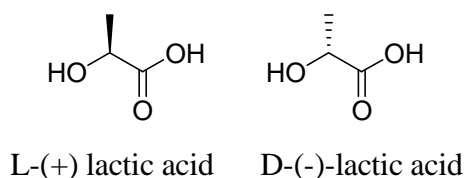


Figure 2.1 Two configurations of lactic acid: D-(-) and L-(+)-isomers

2.2 Poly(lactic acid)

Poly(lactic acid) (PLA) is an aliphatic polyester and considered to be a biodegradable polymer. Degradation of PLA occurs by hydrolysis, which is accelerated by enzyme or catalyst. The rate of the reaction depends on size and shape of the polymer and temperature of the reaction. Although PLA can be degraded if there is water present but under typical used conditions, it is very stable and will retain its physical properties for years. PLA is also a low releasing greenhouse gas polymer because the CO₂ generated during production and biodegradation of PLA is reduced by using CO₂ from the atmosphere during the growth of plant. Figure 2.2 is a life cycle of PLA in the environment.

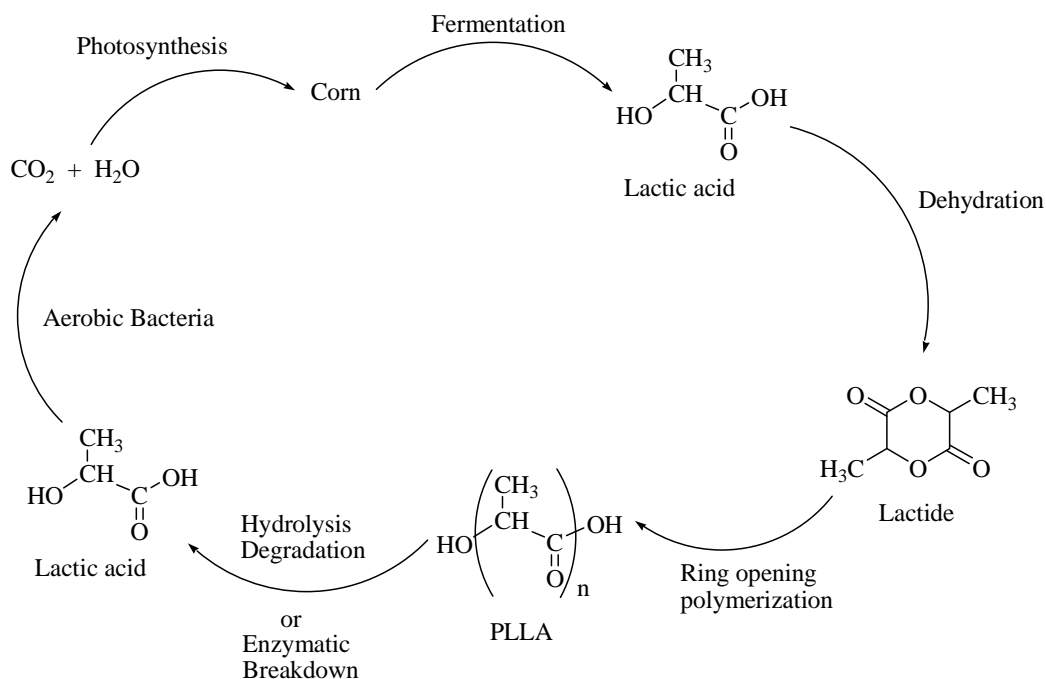


Figure 2.2 The cycle of PLA in the environment

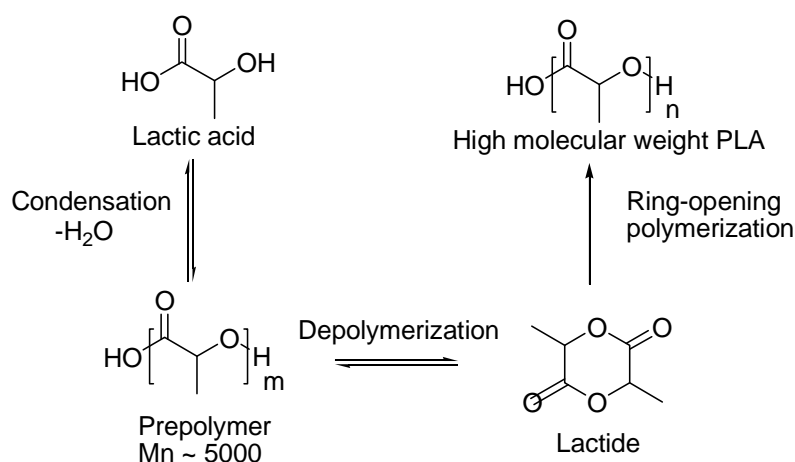
PLA is a rigid thermoplastic polymer which can be semi-crystalline or amorphous depending on the amount of L-lactic acid and D-lactic acid repeating units on the polymer backbone. PLA may be the polymer with broadest range of applications because the physical properties of PLA is similar to polyethylene (PE), poly(ethylene terephthalate) (PET) and polypropylene (PP) [4] and it possesses biocompatibility, therefore PLA can be used for either in industry packaging field or material medical devices [2, 4].

The thermal properties of the PLA depend on molecular weight of PLA and the amount of L-lactic acid and D-lactic acid repeating units on the polymer backbone. Glass transition temperature (T_g) and melting temperature (T_m) of PLA with various ratio of L-lactic acid and D-lactic acid repeating units are shown in the Table 2.1 [5].

Table 2.1 Glass transition temperature and melting temperature of selected PLA copolymer

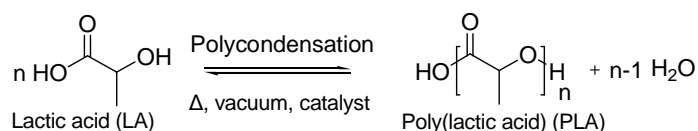
Copolymer ratio	Glass transition temperature (T_g) ($^{\circ}\text{C}$)	Melting temperature (T_m) ($^{\circ}\text{C}$)
100/0 (L/D,L)-PLA	63	178
95/5 (L/D,L)-PLA	59	164
90/10 (L/D,L)-PLA	56	150
85/15 (L/D,L)-PLA	56	140
80/20 (L/D,L)-PLA	56	125

PLA can be synthesized by two methods which are ring-opening polymerization (ROP) from lactide and direct condensation polymerization. For the ring-opening polymerization (Scheme 2.1), the starting material is lactide which is a cyclic di-ester of lactic acid produced by decomposing of low molecular weight of PLA using heat and catalyst [6, 7]. The advantages of the ROP are yielding high percent conversion and molecular weight with range of 20,000-600,000 Da depending on the type of catalysts. However, the cost to produce lactide is high due to complicated purification process of the lactide. The reaction mechanism can be either cationic [8], anionic [9], or coordination-insertion mechanisms [10].



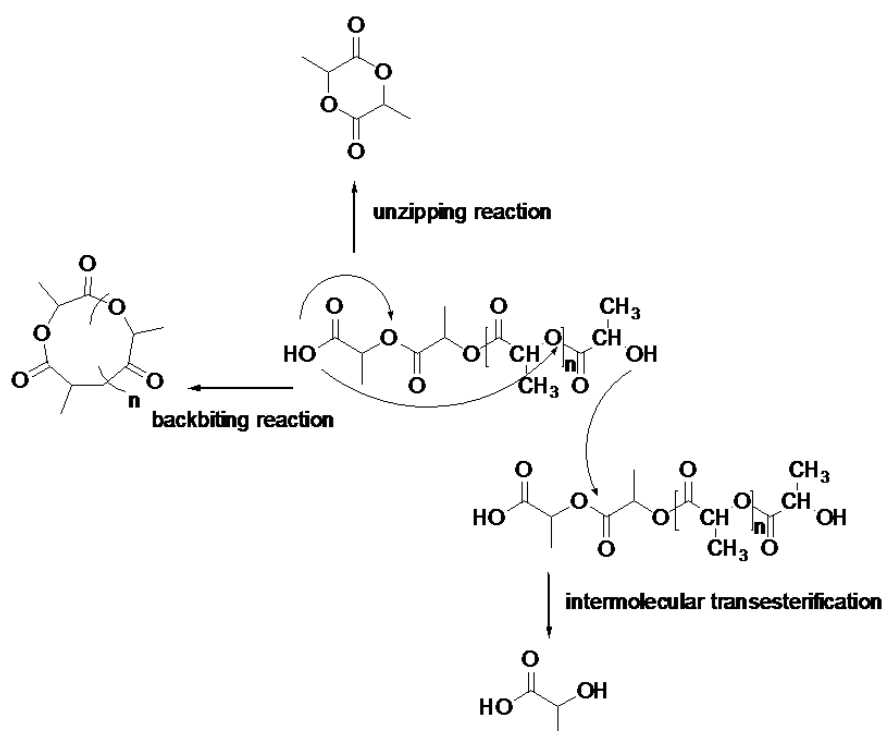
Scheme 2.1 Synthesis of PLA via ring-opening polymerization

Another method, direct condensation polymerization from lactic acid, is cheaper than the previous method. The molecular weight of synthesized PLA by this method, however, is generally low with range of 10,000-130,000 Da. because the direct condensation route is an equilibrium reaction and it is difficult to remove trace amounts of water in the late stages of polymerization because of the viscosity of the reaction. For the synthesis, lactic acid is used as a starting material and the reaction needs heat and vacuum condition in order to remove water out of the reaction to shift the equilibrium move to the product side as shown in scheme 2.2. A number of catalysts were suggested in literatures. PLA with molecular weight as high as 130,000 Da was synthesized by direct condensation polymerization at 180°C using titanium(IV) n-butoxide [TNBT] as the catalyst [11]. Another study reported that tin(II) oxide (SnO) was the most effective with regard to molecular weight but the percent yield was below 40% when performed at 180°C for 20 h [12]. Binary catalysts system was also studied. When *p*-toluenesulfonic acid was used as co-catalyst with SnCl₂, the molecular weight of the received PLA was 100,000 Da after 15h of reaction time. Solid state polymerization of PLA was reported to obtain PLA with molecular weight up to 320,000 [13].



Scheme 2.2 Synthesis of PLA via direct condensation polymerization

During the synthesis of PLA, thermal degradation can occur. Almost all active chain end groups, residuals catalyst and monomers can enhance the thermal degradation of PLA. It has been reported that the thermal degradation of PLA consists of random main-chain scission and unzipping depolymerization reactions. The random scission reaction involves hydrolysis, oxidative degradation, and inter- and intra-molecular transesterification (Scheme 2.3). Therefore, there are many studies trying to reduce the thermal degradation of PLA. In 2001 [14], the effect of chain end structure was studied. The -NH₂ and -Cl terminated PLA were synthesized. The modified chain end PLA were more resistant to thermal degradation than unmodified PLA.



Scheme 2.3 Thermal degradation reactions of PLLA at high temperature

PLA, however, is water insoluble and considered to be rather hydrophobic which limits its use in some applications. Therefore, there are studies trying to increase the hydrophilicity of PLA. In 2006 [15], multiple block copolymer of PLA, polyethylene glycol (PEG) and pyromellitic dianhydride was synthesized (Figure 2.3). The polymer contains PEG, hydrophilic polymer, and carboxyl group of pyromellitic dianhydride which could increase the hydrophilicity of the polymer. It was found the degradation time of the block copolymer was shorter than that of neat PLA.

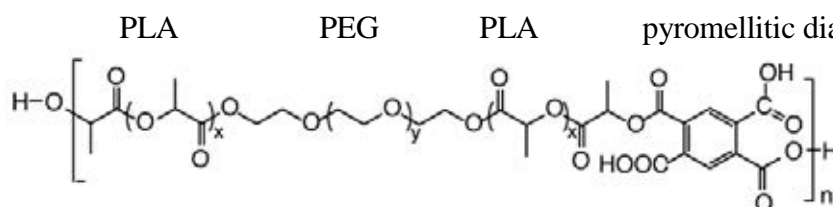


Figure 2.3 Multiblock copolymers of lactic acid and ethylene glycol containing periodic side-chain carboxyl groups

Gene therapy has been extensively studied due to its curing potential for many diseases. There are two systems to carry DNA to disease site, viral vectors and non-

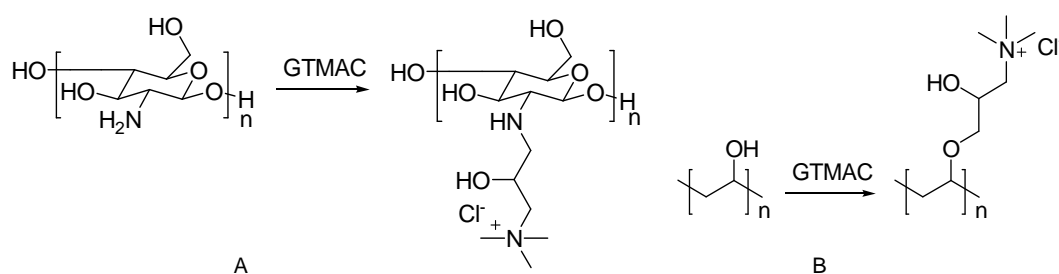
viral vectors. Although gene delivery by viral vector system is more effective but non-viral vector system is preferred due to lack of immunogenicity, more safety, and large scale production [16]. The material to use as a carrier in non-viral system should have a good biocompatibility so PLA has been used in many studies. Since DNA is a negatively-charged compound so several authors have been reported the using of cationic PLA microsphere as gene carrier which can form complex with DNA. In 2007 [17], cationic polyethylene glycolylated PLA (MePEG-PLA) nanoparticles can be prepared with high percent DNA loading (85%) and it exhibits low cytotoxicity to normal human liver cells. The positive part came from chitosan (CS) and MePEG-PLA/CS nanoparticles were prepared by diafiltration method.

For those reasons, this research aimed to synthesize positively-charged PLLA with positive charge permanently attached to the chain end position of PLLA. Glycidyl trimethyl ammonium chloride (GTMAC) was used to react with PLLA via epoxide ring-opening reaction. It is expected that the present of positive charge on the polymer helped increase the hydrophilicity of PLLA.

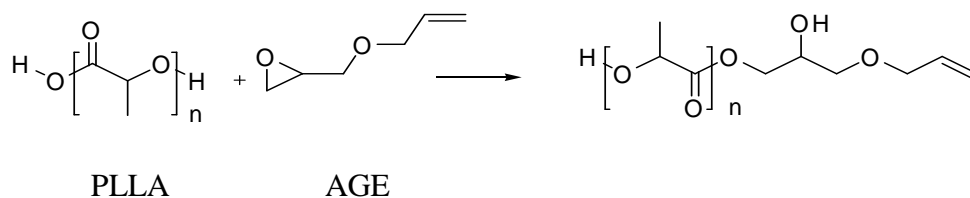
2.3 Glycidyl trimethyl ammonium chloride

GTMAC is a compound consisting of a quaternary ammonium group which presents a positive charge. The compound also contains an epoxide ring which easily reacts with nucleophile so this compound has been used in many works to synthesize positively-charged polymer (Scheme 2.4). In 2000 [18], positively-charged chitosan was synthesized by using GTMAC. The substitution percentage of GTMAC on the repeating unit of chitosan was up to 90%. In 2011 [19], positively-charged polyvinyl alcohol (PVA) was also synthesized by using GTMAC and the result showed that the positive charge density of derivative of PVA was about 1.3 meq/g which was higher than the result obtained from other reagents such as diallyldimethyl ammonium chloride (DADMAC) [20]. From the two studies, GTMAC is a very effective reagent to react with the hydroxyl group, which is also present on one end of PLLA chain. In fact PLLA possesses two reactive functional groups on its chain ends; one hydroxyl and one carboxyl groups. Therefore the probability for PLLA to react with GTMAC is less than chitosan and PVA. Reaction condition for the end-capping reaction must be optimized

by studying choice of solvent, temperature, and catalyst. In 2008 [21], there was a report preparing unsaturated PLLA by the reaction between PLLA and allyl glycidyl ether (AGE) to prepare biodegradable microgels. The reaction was performed at 80°C in solvent of DMSO and Zn powder as catalyst (Scheme 2.5). The $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra of the product confirmed that the unsaturated PLLA was successfully synthesized. The degree of AGE substitution on PLLA chain end was, however, not mentioned anywhere in the paper.



Scheme 2.4 Synthesis of A) positively-charged chitosan and B) positively-charged PVA

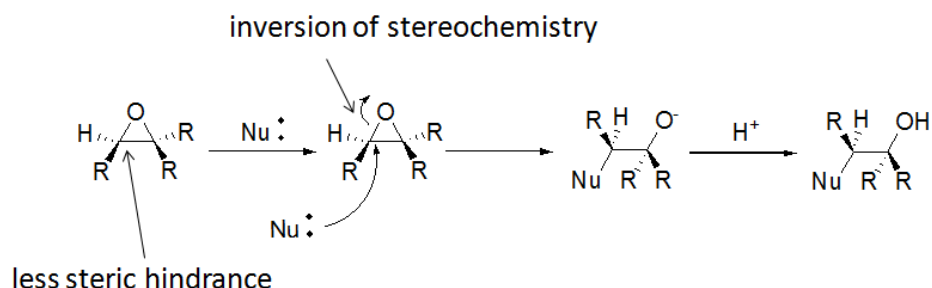


Scheme 2.5 Synthesis of PLLA carrying an unsaturated group the carboxyl chain end

2.4 Epoxide ring opening reaction

Epoxides are much reactive than simply ethers because of highly ring strain. The ring can be attacked by large range of nucleophiles causing the break of C-O bond resulting in the relieving of the ring strain. There are two types of mechanism of the reaction depending on the condition. If the reaction condition is basic or strong nucleophile is used in the reaction, $\text{S}_{\text{N}}2$ mechanism will occur. For asymmetric epoxide,

nucleophile will attack the least steric hindrance of epoxide ring and the inversion of stereochemistry will occur. The reaction mechanism is showed in Scheme 2.6.



Scheme 2.6 Epoxide ring opening reaction via S_N2 mechanism

For acidic condition reaction and poor nucleophile, S_N2 -like mechanism (loose S_N2 mechanism) will occur. For asymmetric epoxide, nucleophile will attack the most steric hindrance of epoxide ring and the inversion of stereochemistry will occur. The difference between S_N2 and S_N2 -like mechanisms is the position in which nucleophile attacks. Since the reaction is acidic, the epoxide ring will be protonated making the epoxide more electrophile and if the mechanism is considered as S_N1 mechanism, the C-O bond of the protonated epoxide will break generating carbocation. The more stable carbocation is favored then the nucleophile attacks the more substituted end of the epoxide. In reality it is usually that the epoxide C-O bond of the more substituted center is weaker resulting in carbocation character at that carbon atom (Figure 2.4) and the nucleophile will attacks there. The reaction mechanism is showed in Scheme 2.7.

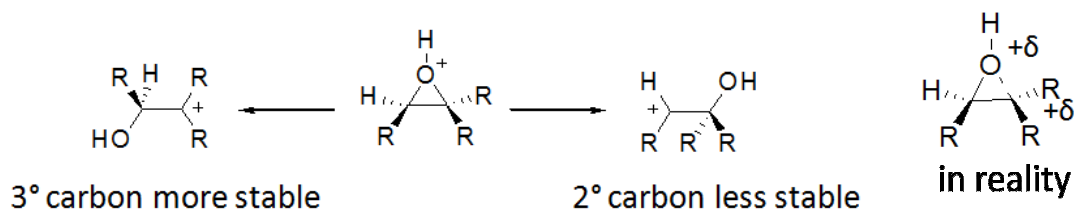
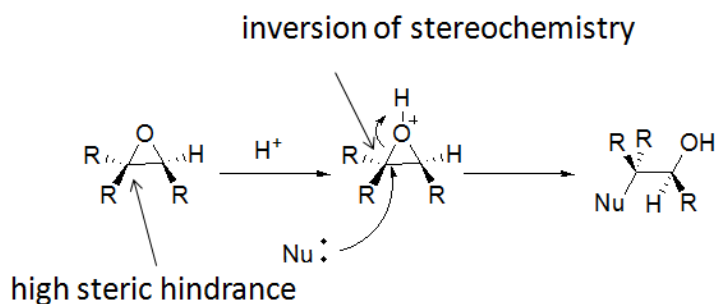


Figure 2.4 Description of S_N2 -like mechanism as S_N1 mechanism



Scheme 2.7 Epoxide ring opening reaction via S_N2 -like mechanism

In summary, this research intends to add positively-charged functional group to the chain end position of PLLA in order to increase the hydrophilicity. The advantage of end-capping modification is that the bulk properties of the polymer such as melting temperature and crystallinity remain but only the surface property change. In 2004 [22], the carboxyl group at the chain end position of PLLA was modified to dodecyl group which was a hydrophobic functional group, and 2-(2-(2-methoxyethoxy)ethoxy)ethyl (MEEE) group which was a hydrophilic functional group so as to study the change of wettability of PLLA derivatives. The results of air-water contact angle measurement showed that when dodecyl group was added to the PLLA chain end, the polymer surface has higher air-water contact angle ($93-112^\circ$) meaning that the polymer was more hydrophobic. When MEEE was added to the chain end, the polymer surface has lower air-water contact angle ($74-82^\circ$) meaning that the polymer was more hydrophilic compared with that of neat PLLA ($87-89^\circ$).

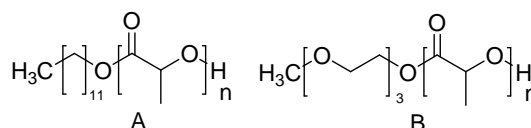


Figure 2.5 Structure of A) dodecyl group and B) 2-(2-(2-methoxyethoxy)ethoxy)ethyl (MEEE)

CHAPTER III

EXPERIMENTAL

3.1 Chemicals

L-lactic acid (88% by wt) was purchased from Carlo Erba Reagent (France). Titanium(IV) n-butoxide (TNBT, reagent grade 97%) and glycidyl trimethyl ammonium chloride (20-25% by wt of water) were purchased from Sigma-Aldrich (USA). Methanol, sodium chloride, chloroform-d and deuterium oxide were purchased from Merck (Germany). Chloroform, tetrahydrofuran (THF) (HPLC grade), and dimethyl formamide (DMF) were purchased from RCI Labscan Limited (Thailand).

3.2 Instruments

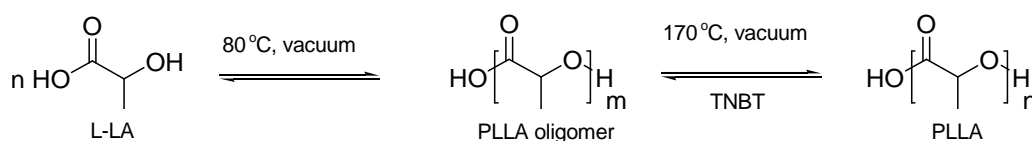
A Varian model Mercury-400 (USA) operating at 400 MHz and a Bruker Advance-III 300 operating at 300 MHz nuclear magnetic resonance spectrometers were used to characterize all products. Molecular weight of PLLA and positively-charged PLLA were analyzed by gel permeation chromatography (GPC) using Waters 600 controller chromatograph equipped with HR1 and HR4 columns (Waters, MW resolving range = 100-500,000) at 35 °C and a refractive index detector (Waters 2414). THF was used as an eluent with the flow rate of 1.0 mL/min. Sample injection volume was 50 µL. Five polystyrenes standards (996-188,000 Da) were used for calibration. The hydrophilicity of the polymer was analyzed by measuring contact angle between water and surface of the polymer film using Ramé-Hart Contact Angle Goniometer Model 100-00 equipped with Gilmont syringe and 24-gauge flat-tipped needle. All polymer films were prepared by melt-casting the polymer in an oven to obtain a film of about 0.5-0.9 mm thick. Filtrate after precipitation of the products was freeze-dried to collect the dissolving product (freeze dryer model Freezone 77520, Benchtop, Labconce). The thermal properties of the products were analyzed by differential scanning calorimetry

(DSC) technique using METTLER TOLEDO STARE SYSTEM, DSC 822e Module and thermal gravimetric analysis (TGA) using Perkin Elmer, Pyris Diamond TG/DTA.

3.3 Methods

3.3.1 Synthesis of PLLA

PLLA was synthesized following a modified method reported by Chen et al [11]. L-lactic acid was dehydrated under vacuum at 80 °C for 4 hours. Then, the reaction was placed in N₂ atmosphere and heated up to 170 °C. TNBT (0.1 mol% of monomer) was then added to the reaction. After stirring for 30 min, the pressure was reduced gradually to vacuum. The reaction was left with stirring in this step for 5 hours. The obtained product was purified by dissolved in chloroform and precipitated in methanol and washed with methanol 3 times. Then, the product was further dried under vacuum until dry giving white powder PLLA with 30-45 % yield.

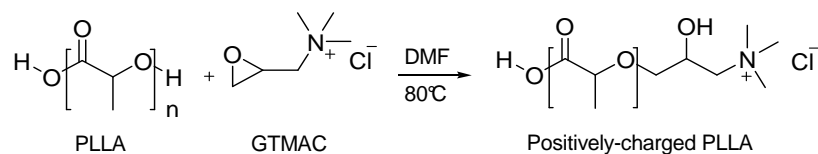


Scheme 3.1 Synthesis of poly(L-lactic acid) by direct condensation polymerization from L-lactic acid

3.3.2 Synthesis of positively-charged PLLA

- Method 1

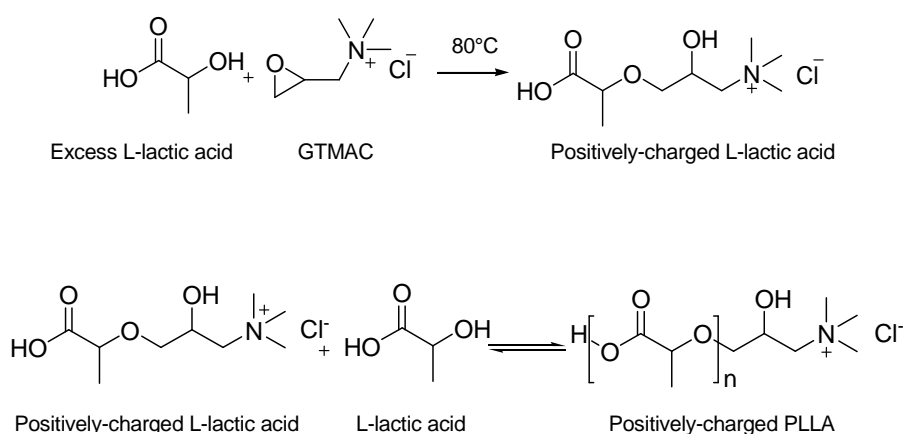
PLLA and GTMAC were dissolved in DMF. The solution was stirred for 1 day at 80 °C. After that, the solution was precipitated in 1M NaCl in deionized water and the precipitate was collected by centrifuge at 3,500 rpm. The precipitate was washed with deionized water 4 times and dried under vacuum for 1 day giving white solid with 40-47 % yield. The substitutions of GTMAC on PLLA-COOH chain end was more than 76%.



Scheme 3.2 Synthesis of positively-charged PLLA from PLLA and GTMAC

- Method 2

First, positively-charged L-lactic acid was prepared. L-lactic acid was dehydrated under vacuum at 80 °C for 4 hours. Then, the reaction was placed in N₂ atmosphere and added GTMAC (1/70 times the mole of LA). The reaction was stirred for 2 hours. Next, the reaction was heated to 170 °C. TNBT (0.1 mol% of L-lactic acid) was then added to the reaction. After stirring for 30 min, the pressure was reduced gradually to vacuum. In this step the remaining of L-lactic acid will polymerize with positively-charged L-lactic acid to produce positively-charged PLLA. The reaction was left with stirring for 5 hours. The obtained product was purified by dissolved in DMF and precipitated in 1M NaCl in DI water and washed with DI water for 3 times. Then, the product was dried under vacuum for 1 day giving waxy-light brown product with 20-35 % yield.



Scheme 3.3 Synthesis of positively-charged PLLA from lactic acid and positively-charged lactic acid

3.3.3 Characterization of the products by $^1\text{H-NMR}$ spectrum

There are three solvents using to dissolve the products. D_2O was used to dissolve L-lactic acid and GTMAC. CDCl_3 and DMSO-d_6 were used to dissolve PLLA and positively-charged PLLA. Varian model Mercury-400 nuclear magnetic resonance spectrometer was used to provide all 1D $^1\text{H-NMR}$ spectra and a Bruker Advance-III 300 was used to provide all 2D $^1\text{H-NMR}$ spectra.

3.3.4 Molecular weight determination

A polymer product (6 mg) was dissolved in 1 ml THF (HPLC grade). Then the solution was filtered through a nylon filter with pore size of 0.45 μm . After that 50 μl of the solution was injected into the GPC. Molecular weight of products was defined by using standard calibration curve of five standard polystyrenes with molecular weight range of 996-188,000 Da.

3.3.5 Air-water contact angle measurement

Samples were tested for their hydrophobic/hydrophilic property in the form of flat films. Positively-charged PLLA from 1st method was melt-cast into films at heating the polymer on metal sheet in an oven (150 $^\circ\text{C}$). Using Ramé-Hart Contact Angle Gonio-meter, each data point reported was averaged from 4 measurements, each from a different spots on two films.

Air-water contact angle can be defined the hydrophobicity and hydrophilicity on polymer surface [23]. If the angle is almost 0° , the polymer surface is completely wetting and the result refer that the polymer surface is super hydrophilic. If the angle is in range between 0° to 90° , the polymer surface is good wetting and the result refer that the polymer is hydrophilic. If the angle is in range between 90° to 150° , the polymer surface is poor wetting and the result refer that the polymer is hydrophobic. If the angle is more than 150° , the polymer surface is non-wetting and the result refer that the polymer is super hydrophobic.

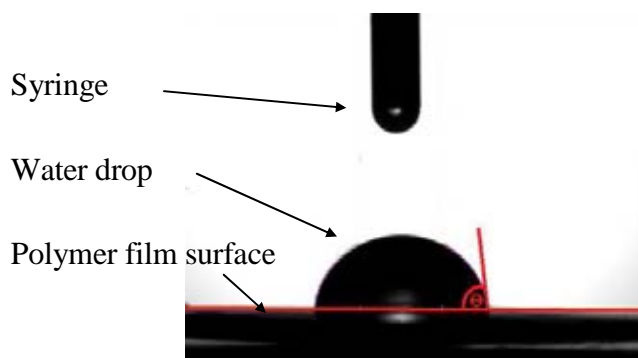


Figure 3.1 An air contact angle image from the goniometer

3.3.6 Thermal properties measurement

The measurements of thermal properties were performed using differential scanning calorimeter (DSC 822e) and thermo gravimetric analyzer. For DSC measurements, the sample was subjected to two consecutive heating scans to ensure an identical thermal history for the sample. All scans were measured under nitrogen atmosphere. In the first scan, 10 mg of the sample was heated from 30 to 150°C at 20°C/min and the temperature was hold at 150°C for 5 min. Then, the sample was cooled down to -20°C at 30°C/min. The second scan was performed immediately at rate of 10°C/min from -20-150°C. Glass transition temperature (T_g), crystallization temperature (T_c), and melting temperature (T_m) of the sample were determined in the second scan. For TG measurements, 10 mg of the sample was heated from room temperature to 800°C at rate of 10°C/min under nitrogen atmosphere.

CHAPTER IV

RESULTS AND DISCUSSION

4.1 Synthesis of PLLA

In the present work, PLLA was synthesized by direct condensation polymerization following the method reported in 2006 [11] with a slight modification in the 1st dehydration step in which it was performed at 80°C and under vacuum. This was done to increase the amount of water being removed from the starting material which was 88% by weight of lactic acid in aqueous solution. After the dehydration step, TNBT catalyst was added to the reaction with an increase of reaction temperature and the pressure was gradually reduced to vacuum. The effect of reaction temperature in the range of 170-190°C on the polymerization was studied and the results are shown in Table 4.1. Percent yield of the products was calculated by using Eq. 1.

$$\begin{aligned} \% \text{ yield} &= \frac{\text{mole of lactide unit in PLLA}}{\text{mole of L-lactic acid}} && \text{(Eq.1)} \\ &= \frac{\text{amount of PLLA (g)} \div \text{molecular weight of lactide unit}}{\text{amount of L-lactic acid solution (g)} \times \frac{88}{100} \div \text{molecular weight of L-lactic acid}} \end{aligned}$$

Table 4.1 The effect of reaction temperature on the polymerization of L-lactic acid in the presence of TNBT catalyst

Entry	Reaction temperature (°C)	Amount of lactic acid solution (g)	\bar{M}_n (Da) ¹	\bar{M}_w (Da) ¹	PDI ²	Yield (%)
1	170	10	9,200	12,900	1.39	47
2	180	10	10,100	15,300	1.50	33
3	190	10	13,800	21,400	1.54	30
4	170	20	3,500	4,600	1.31	33
5	180	5	12,200	15,800	1.30	27

¹determined by GPC

²polydispersity index

From Table 4.1, the PLLA yield increased when the reaction temperature increased. This finding was similar to the result reported earlier by Achmad, et al. [24]. Moreover the study also reported that thermal degradation of the PLLA occurred at the temperature higher than 200 °C without the catalyst. Since the thermal degradation reactions such as hydrolysis reaction and transesterification reaction produced lactide and lactic acid, they were vaporized and freed from the reaction at high temperature and low pressure, causing the reduction of the PLLA yield. In addition, the synthesis of PLLA in this work used the catalyst which can accelerate those thermal degradation reactions so the thermal degradation might occur at temperature lower than 200°C. In order to increase the PLLA yield, the condition to synthesize PLLA oligomer was employed in the method of synthesis of PLLA reported by Wang, et al.[25]. Since L-lactic acid was lost easily when the temperature reached 180°C under vacuum because the boiling point of lactic acid was lower than 140°C (1.8 kPa). Therefore after removing free water, the reaction was set at 140°C for 5 h to convert L-lactic acid to PLLA oligomer. Then a catalyst was added to the reaction, temperature was heated to 180°C and pressure was reduced to vacuum to synthesize PLLA. The percent yield of PLLA received by this method was 76%.

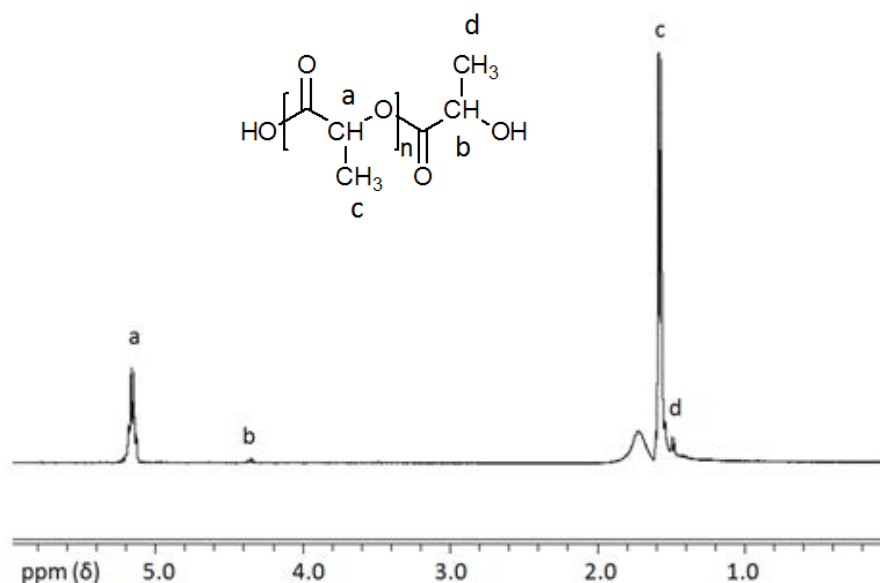


Figure 4.1 ¹H-NMR spectrum of PLLA in CDCl₃

$^1\text{H-NMR}$ spectrum of PLLA in CDCl_3 is shown in Figure 4.1. The proton signals at 5.16 and 1.56 ppm were assigned to methine (a) and methyl (c) protons of PLLA repeat unit, respectively. The signals of methine (b) and methyl (d) protons of hydroxyl-side chain end unit were found at 4.36 and 1.48 ppm, respectively.

4.2 Synthesis of positively-charged PLLA

The preparation of positively-charged PLLA (p-PLLA) was based on the ring-opening reaction of the epoxide in GTMAC by the hydroxyl-chain end or carboxyl-chain end of PLLA. To follow the extent of reaction, the relative amount of reacted GTMAC was monitored by NMR analysis. The 1D and 2D $^1\text{H-NMR}$ spectra of GTMAC are shown in Figure 4.2. The proton signals in the epoxide ring of GTMAC are located at 2.65 and 2.92 ppm for the two protons in methylene group (d) and at 3.49 ppm for the methine proton (c). In 2D $^1\text{H-NMR}$ spectrum, the three signals correlate with each other and the proton signal at 3.49 also correlates with the signals at 3.07 and 3.85 ppm so the two proton signals were assigned to methylene proton (b). After the reaction with the epoxide ring opened, the peaks of epoxide ring should be shifted to lower field (higher chemical shift numbers). Three methyl groups (a) adjacent to the quaternary ammonium atom in GTMAC were assigned to the proton signal at 3.16 ppm.

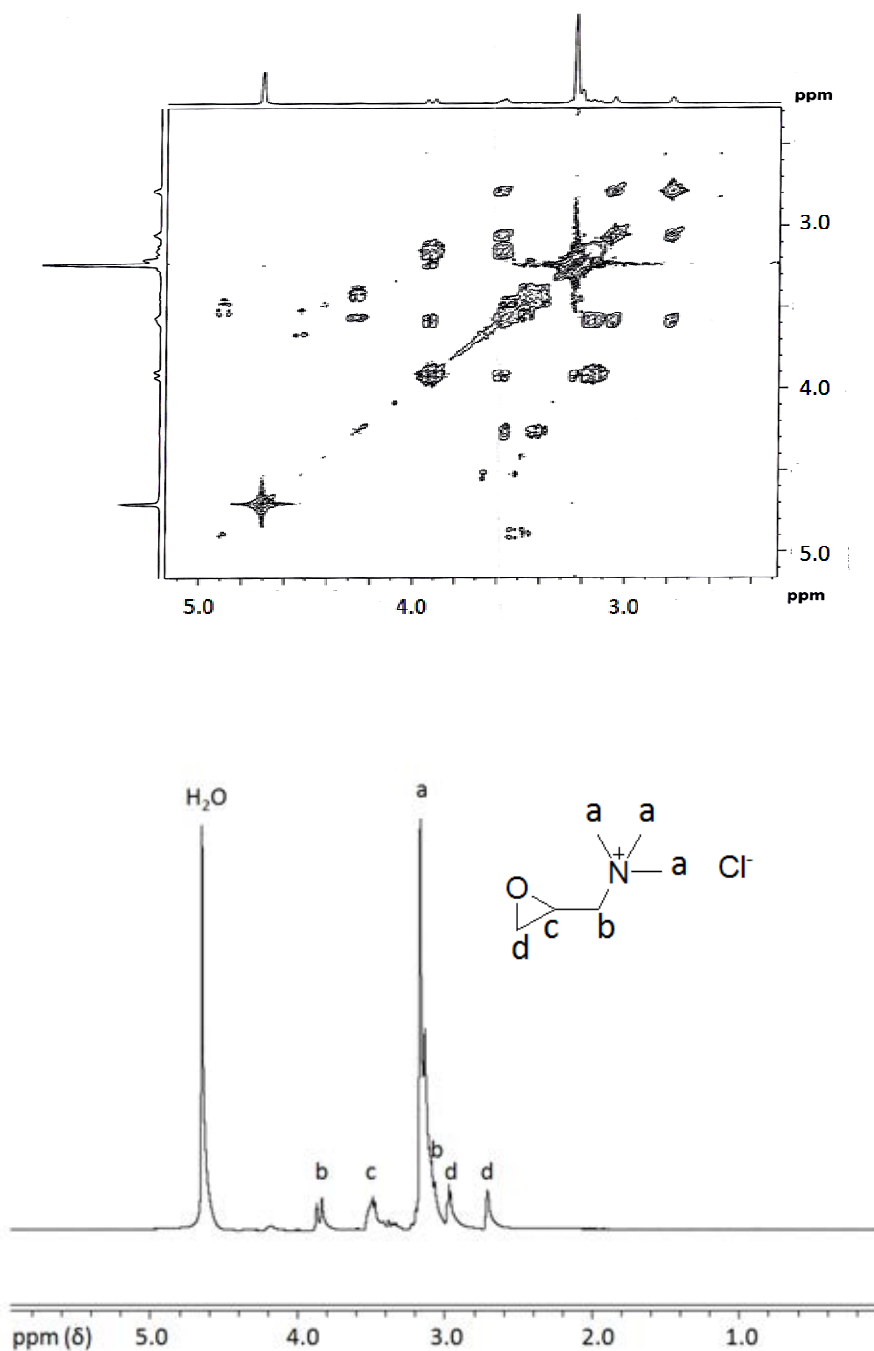


Figure 4.2 A) COSY-NMR spectrum of GTMAC in D₂O and B) ¹H-NMR spectrum of GTMAC in D₂O

Considering the structure of PLLA, there are two active functional groups on each chain; hydroxyl and carboxyl, one on each chain end. Both can in fact react with the epoxide ring of GTMAC. In 2010 [25], multifunctional group PLLA was

synthesized by reacting with an epoxy compound. The structure of the product was proposed that PLLA connected with the epoxy compound via carboxyl chain end unit, proven by $^1\text{H-NMR}$ spectrometry. In this work, however, confirmation on which chain ends, the hydroxyl or carboxyl group or both, reacted with GTMAC was somewhat inconclusive because only the hydroxyl terminal lactide unit was present in the spectrum when CDCl_3 was the solvent (Figure 4.1). In other words, the lactide end unit at the carboxyl side was not resolved in the chloroform-d solvent. Therefore DMSO-d₆ was tried as the solvent used for $^1\text{H-NMR}$ analysis of p-PLLA since it was reported that both hydroxyl and carboxyl terminal lactide units was resolved clearly in this solvent [26]. Additional signals were observed in Figure 4.3 as follows. The proton signal at 5.09 ppm was assigned to methine proton (f) of penultimate lactide unit, next to the hydroxyl terminal lactide unit. Importantly, the proton signals of hydroxyl and carboxyl terminal lactide unit were clearly seen. The methyl and methine proton signals of the lactide unit at hydroxyl chain end appear at 1.26 (a) and 4.19 (d) ppm while those at the carboxyl end appear at 1.39 (b) and 4.97 (e) ppm, respectively.

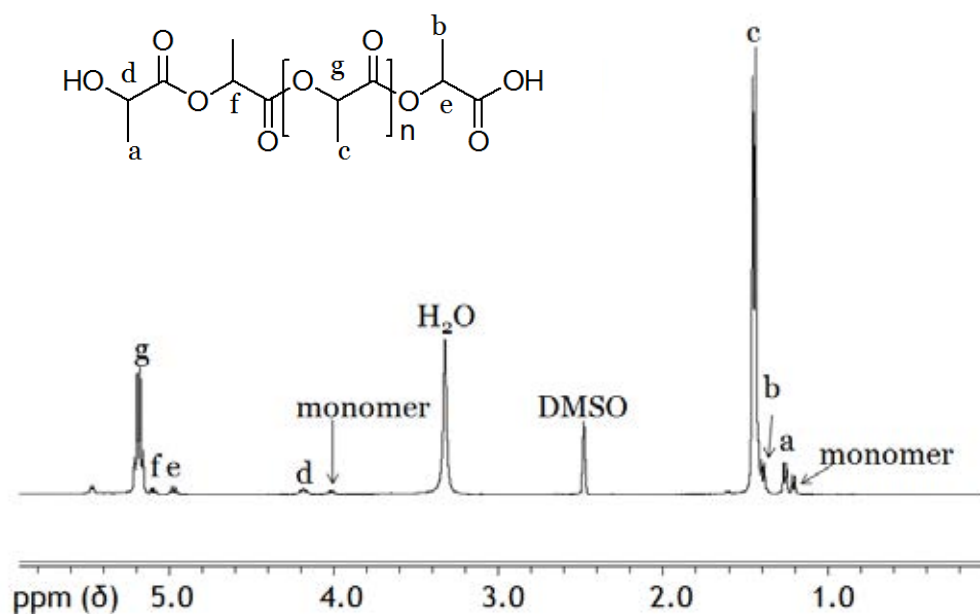


Figure 4.3 $^1\text{H-NMR}$ spectrum of PLLA in DMSO-d₆

4.2.1 Synthesis method 1

In this method, PLLA with \bar{M}_n of 3,500 Da was reacted with GTMAC directly to synthesize p-PLLA. After purification, the p-PLLA products were characterized by $^1\text{H-NMR}$ in CDCl_3 and the spectrum is shown in Figure 4.4. The proton signals of the GTMAC epoxide ring (2.65 and 2.92 ppm) were disappeared and a new set of signals apart from those of PLLA were found at 3.31, 3.60, 3.78, 4.21 and 4.60 ppm. The high intensity signals from lactide repeat unit were clearly seen at 1.58 ppm for the methyl (b) and 5.16 ppm for the methine (f) protons. Nevertheless the proton signals at 1.47 and 4.35 ppm assigned to the methyl (a) and methine (d) group of the free hydroxyl terminal lactide unit remained. This suggested that a portion of PLLA chains did not react with the GTMAC. In addition, the signal at 4.98 ppm was believed to belong to the methine proton (j) of the chain end lactide unit connecting to GTMAC, which was confirmed by 2D-NMR (COSY, Figure 4.4). A complete assignment list of NMR signals is shown in Table 4.2.

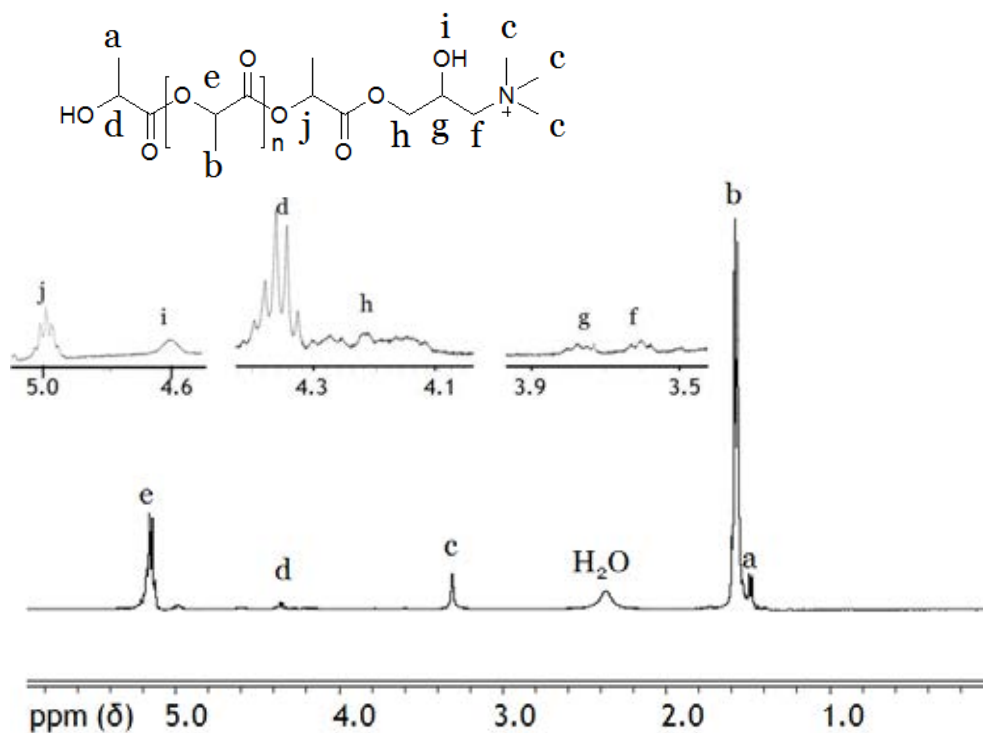


Figure 4.4 $^1\text{H-NMR}$ spectrum of p-PLLA in CDCl_3

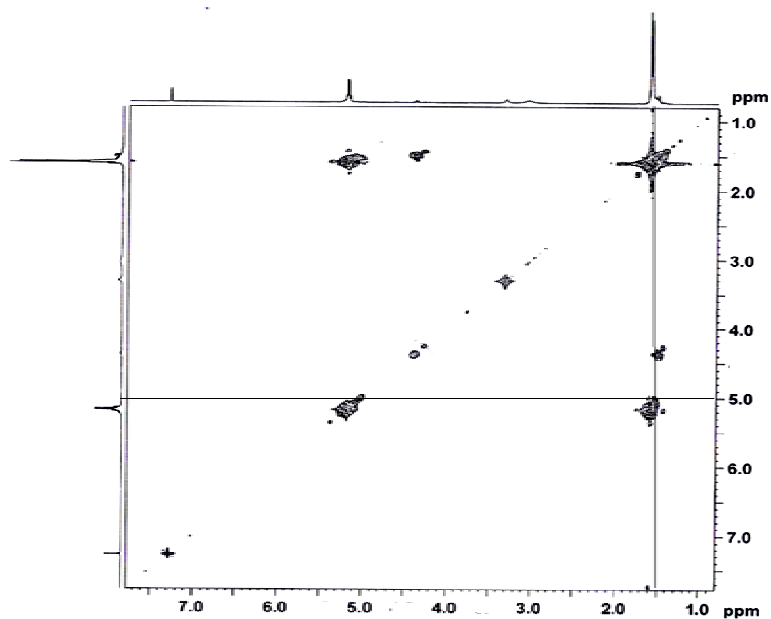
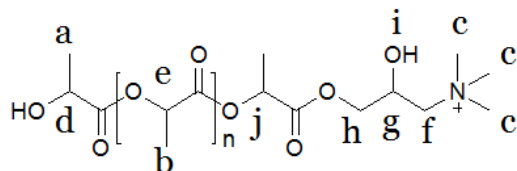


Figure 4.5 COSY-NMR spectrum of p-PLLA in CDCl_3

Table 4.2 Complete assignment of ^1H -NMR chemical shifts (δ , in ppm) of p-PLLA (CDCl_3)



Unit	Chemical shifts	Unit	Chemical shifts
a	1.47	f	3.60
b	1.58	g	3.78
c	3.31	h	4.21
d	4.35	i	4.60
e	5.16	j	4.98

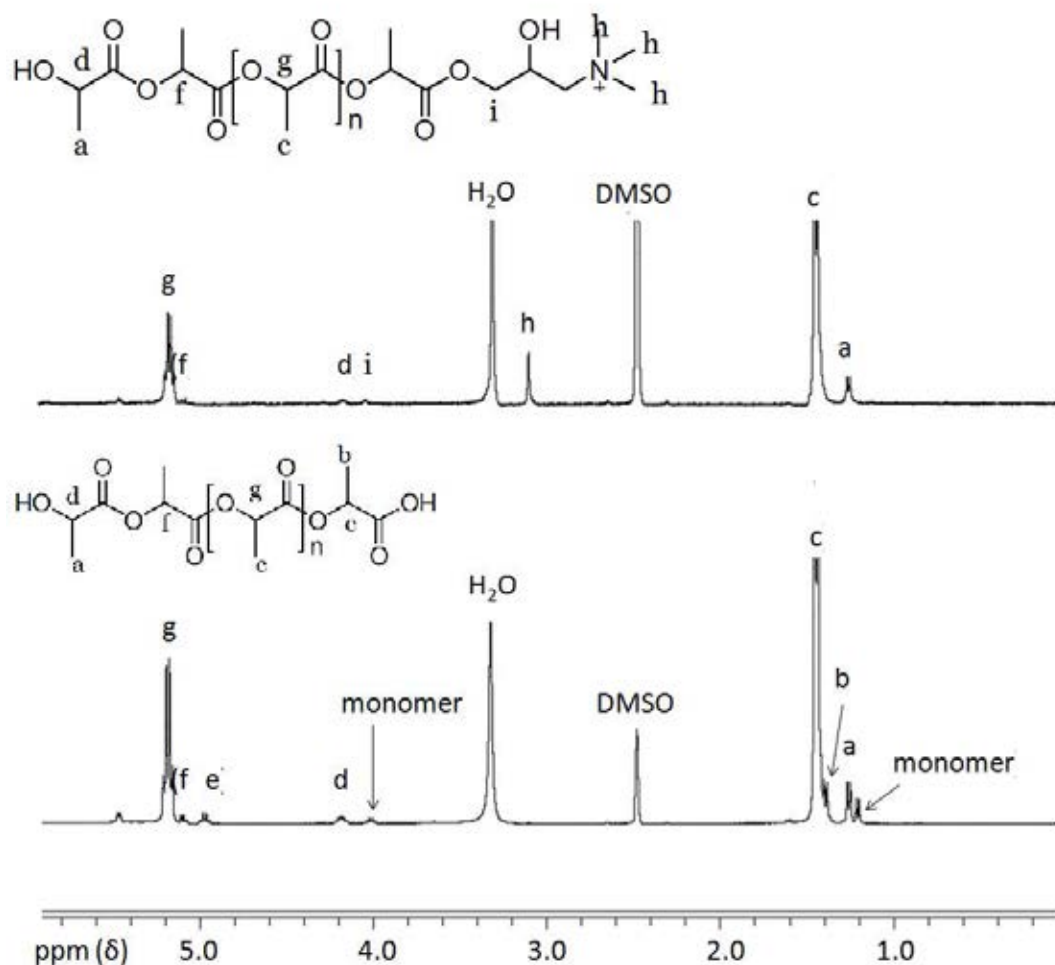


Figure 4.6 ¹H-NMR spectra of PLLA (bottom) and p-PLLA (top) in DMSO-d₆

In Figure 4.6 the spectrum of p-PLLA in DMSO-d₆ is also presented for comparison with the starting PLLA. The signal of methyl protons adjacent to quaternary ammonium atom was again found at 3.10 ppm confirming the presence of positive charge on the polymer. Interestingly, the proton signals of ‘carboxyl’ terminal lactide unit (1.39 and 4.97 ppm) were disappeared. Moreover, the ratio between the peak area of methine proton (d) of ‘hydroxyl’ chain end and the methine proton (5.09 ppm, (f)) of penultimate lactide unit was 0.89, lower than a theoretical value of 1, indicating that GTMAC was rarely attached to PLLA on the hydroxyl chain end side. The attachment of GTMAC on the –OH chain end of PLLA occurred about 11% of the total polymer. This result came as a surprise since it was initially believed that the nucleophilicity of hydroxyl group was higher than that of the carboxyl. Nevertheless the

degree of GTMAC substitution on PLLA chain end was calculated based on their relative ratio of the three methyl groups on the attached GTMAC ($\delta = 3.31$ ppm) and the methine group of lactide repeat unit of PLLA ($\delta = 5.16$ ppm). The calculation formula exhibits in Eq.2.

$$\% \text{Substitution} = \int \frac{H \text{ of } -N^+(CH_3)_3/9}{H \text{ of } -CH \text{ of PLLA}/n} \times 100 \quad (\text{Eq.2})$$

$$n = \text{Repeat units of PLLA} = \frac{\text{Molecular weight of PLLA}}{72}$$

Table 4.3 shows the synthesis results after the mole ratios of PLLA:GTMAC were varied in order to determine the optimum amount of GTMAC in the reaction to achieve the highest substitution at the polymer chain end. From Table 4.3, increasing the equivalent of GTMAC from 1 to 4 folds resulted in an increase of the substitution percentage from about 2 to 77, but when increasing the GTMAC amount beyond 4 equivalents, no clear impact on the reaction was obtained. It was, however, found that the conversion and \overline{M}_n of the product unexpectedly decreased. A possible explanation was that during the purification step some portions of low molecular weight p-PLLA were lost. Water was the solvent of choice to purify the intended product p-PLLA because it was able to dissolve GTMAC that was excessively added in the reaction. The presence of the ammonium group in the low molecular weight PLLA could result in an increase of solubility in water. Concerns about product degradation during the water washing step was also investigated. The purification step usually lasted about 20 min at room temperature. A trial study was set up by monitoring the molecular weight change of p-PLLA that was immersed in water at room temperature for up to 60 min. Analysis result by GPC is presented as the chromatograms shown in Figure 4.7. The molecular weight change was observed when the product was in contact with water for longer than 20 min. It was thus concluded that during the 20 min washing step, the obtained p-PLLA was not hydrolyzed.

Table 4.3 The effect of mole ratio of PLLA:GTMAC on the synthesis of p-PLLA by fixing the reaction temperature at 80°C

PLLA: GTMAC	\overline{M}_n of starting PLLA (PDI)	%Conversion	%Substitution	\overline{M}_n of p-PLLA (PDI)	%Weight change
1:1	3,503(1.31)	87.5	2.17	2,785(1.36)	20.5
1:2	9,285(1.39)	75.4	15.9	7,706(1.39)	17.0
1:4	3,503(1.31)	46.6	76.5	2,029(1.33)	42.1
1:8	3,503(1.31)	45.0	54.8	1,505(1.32)	57.0
1:13	9,285(1.39)	47.8	75.5	4,309(1.38)	53.6
1:15	2,978(1.17)	Very low	56.1	1,117(1.24)	62.5

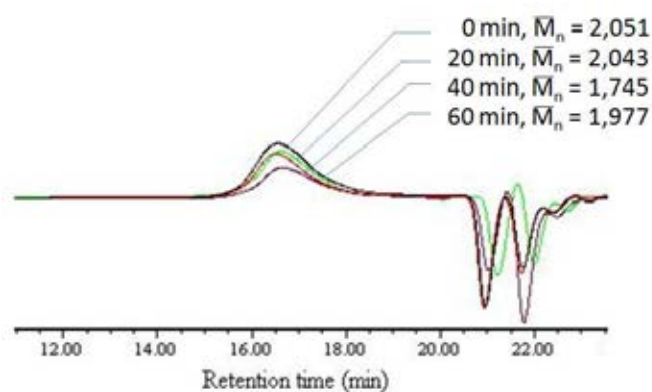


Figure 4.7 GPC chromatograms of p-PLLA after immersed in water for 20, 40, and 60 min

A similar drop of conversion was also obtained from the study in which reaction temperature was optimized (Table 4.4). The substitution of ammonium group at the polymer chain end increased with the reaction temperature, but less yield and molecular weight were obtained. It was possible that the increase of temperature led to faster rate of epoxide ring-opening of GTMAC by the hydroxyl end of PLLA as well as the degradation rate of the ester bonds in p-PLLA.

Table 4.4 The effect of reaction temperature on the synthesis of p-PLLA by fixing the mole ratio of PLLA:GTMAC at 1:4

Temp	\overline{M}_n of starting PLLA (PDI)	%Conversion	%Substitution	\overline{M}_n of p-PLLA (PDI)	%Weight change
30°C	2,978(1.17)	90.5	9.97	3,047(1.17)	-2.3
50°C	2,978(1.17)	85.6	11.6	2,945(1.17)	1.1
60°C	3,503(1.31)	85.0	59.3	3,135(1.35)	10.5
80°C	3,503(1.31)	46.6	76.5	2,029(1.33)	57.0

To confirm the assumption that low molecular weight p-PLLA can dissolve in 1M NaCl, the filtrate after purification was freeze dried under vacuum to collect the all dissolved chemicals in the filtrate. After freeze dry step, white solid was obtained and then the solid was stirred in THF to extract the low molecular weight p-PLLA. After THF removal, light yellow film was found coating on the container. The received products were analyzed by GPC and $^1\text{H-NMR}$ spectrometry. The results are shown in Table 4.5 and Figure 4.8. The results show that there was some low molecular weight of the product dissolved in water and the pattern of $^1\text{H-NMR}$ spectrum in Figure 4.8 also confirmed that the products in filtrate consisted of p-PLLA because the pattern was similar to the pattern of $^1\text{H-NMR}$ spectrum of the product p-PLLA (Figure 4.4).

Table 4.5 Analyzed results of products in filtrate

Temp	PLLA:GTMAC	%Conversion	%Filtrate	\overline{M}_n ^a (PDI)
80°C	1:4	59	15	1,145(1.27), 270 ^b
80°C	1:0	76	9	N/A

^a \overline{M}_n of product in filtrate. ^b out of calibration curve range.

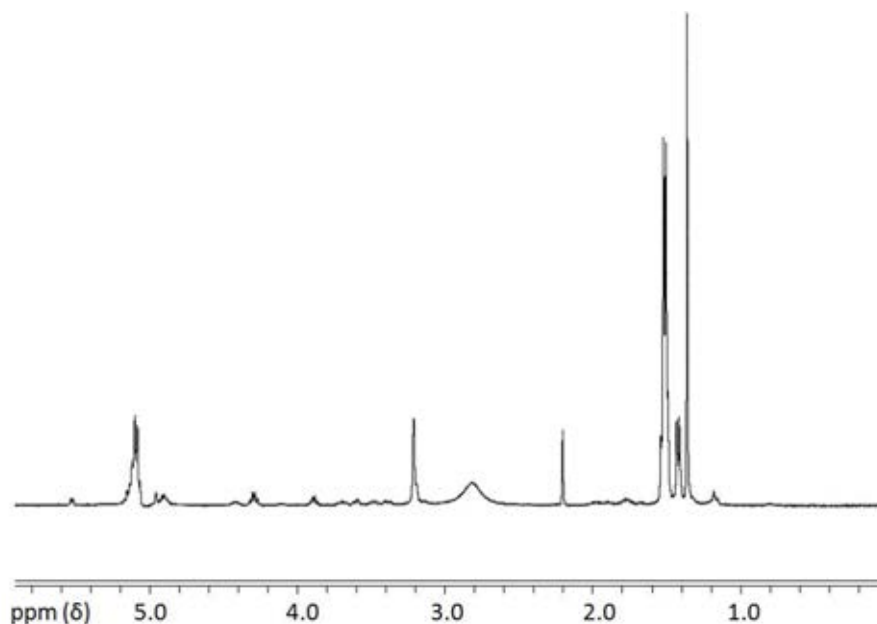


Figure 4.8 ^1H -NMR spectrum of products in filtrate in CDCl_3

Since it was found that the degradation of PLLA causing the reduction of molecular weight which most likely occurred during the synthesis step. The cause of the result might be water containing in GTMAC (20-25% by wt, as received from Sigma-Aldrich). Hence, GTMAC was dehydrated under vacuum condition at 50°C for 4 h. The dehydration of GTMAC was performed at low temperature to avoid thermal degradation. After 4 h, the received GTMAC was white paste. Then, it was used to synthesize p-PLLA at 80°C with PLLA:GTMAC equaled 1:4 by mole for 24 h and the results are shown in the Table 4.6. The reduction of the molecular weight of p-PLLA still occurred but with less extent than the synthesis using GTMAC without dehydration. The degree of substitution using the dehydrated GTMAC slightly increased (15%). The increase of GTMAC attached to the PLLA chain end could be due to the fact that the dehydrated reagent contained less water which was somewhat reactive towards the epoxide of GTMAC.

Table 4.6 Synthesis results of p-PLLA at 80°C with PLLA:GTMAC = 1:4 by mole using dehydrated GTMAC

p-PLLA	\overline{M}_n of starting PLLA (PDI)	%Conversion	%Substitution	\overline{M}_n of p-PLLA (PDI)	%Weight change
1	2,978(1.17)	50.2	86.1	2,069(1.24)	30.5
2	3,503(1.31)	48.0	90.0	2,838(1.24)	19.0
3*	3,503(1.31)	46.6	76.5	2,029(1.33)	42.1

*Using as-received GTMAC (containing 20-25% wt H₂O)

The degradation rates of PLLA and p-PLLA were studied by dissolving the polymer in 5% by volume of water in DMF. The solution was kept stirring at 80°C for 24 h. After that, the polymer was precipitated out of the solution by pouring in 1M NaCl solution. The precipitate was washed with water 3 times. The changes of molecular weight are showed in the Table 4.7. The decrease of molecular weight of p-PLLA (53%) was greater than the change of PLLA (34%). It can be concluded that the presence of positive charge on to PLLA chain end can increase the degradation rate of the polymer.

Table 4.7 Molecular weight changes of PLLA and p-PLLA after dissolved in 5% water in DMF at 80°C for 24 h

Sample	\overline{M}_n before incubation (PDI)	\overline{M}_n after incubation (PDI)	%Weight change
PLLA	3,503 (1.31)	2,322 (1.38)	33.7
p-PLLA (%DS = 90)	2,838 (1.24)	1,343 (1.47)	52.7

The two catalysts, TNBT and 98% sulphuric acid (H₂SO₄), were used in the synthesis of p-PLLA in order to improve reaction efficiency because both catalysts can activate epoxide ring. Since the titanium metal in TNBT and the proton from sulphuric

acid can coordinate to the lone pair electrons of oxygen atom in epoxide, facilitating the ring opening reaction by a nucleophile, in this case which is the hydroxyl chain end of PLLA. For TNBT, 1 mole of the catalyst was added directly to the reaction at 80°C with PLLA:GTMAC was equaled to 1:4 and the reaction was stirring for 24 h. However, it was found that TNBT was immiscible with the reaction mixture in which DMF was used as a solvent. After adding the catalyst, the reaction color was changed from colorless to opaque white. For H₂SO₄, 1 mole of the catalyst was added directly to the same reaction condition of the synthesis using TNBT. The results of the synthesis of the both methods showed that the degrees of substitution of received p-PLLA were 39% for TNBT and 23% for H₂SO₄, lower than the product received by the synthesis without catalyst (76%). This result might be due to over activating by the catalyst at the epoxide ring of GTMAC. So water containing in the reaction was also able to attack the epoxide ring, lowering the desired reaction with p-PLLA. However, the reduction of molecular weight of the product from the synthesis using H₂SO₄ was similar to the product with high degree of substitution when no catalyst was used. Sulfuric acid could accelerate the hydrolysis reaction of the polymer since this catalyst was miscible with the reaction mixture.

In summary, there are two problems for the synthesis of p-PLLA in this method. The first is the degradation of the product during the reaction. The cause of this problem is water containing in the reaction. To solve the problem the reagents using in the reaction must be dehydrated and completely dry especially GTMAC. However, GTMAC can be degraded by heat so to avoid this problem freeze drying technique may be useful to dehydrate GTMAC. The second problem is the dissolving of product in 1M NaCl causing the reduction of product yield. To solve this problem, the solvent in purification step should be studied. The use of mixing solvent may be useful to solve this problem.

4.2.2 Synthesis method 2

The 2nd method to prepare p-PLLA was carried out by first synthesizing positively-charged L-lactic acid (p-LA), which was subsequently used in the polymerization reaction with L-lactic acid. The p-LA was first synthesized by the

reaction between dehydrated L-lactic acid and GTMAC. The $^1\text{H-NMR}$ spectrum of p-LA is shown in Figure 4.10. The proton signals of lactic acid were clearly seen at 1.15 and 4.07 ppm which were the signals of methyl (d) and methine (e) protons. The evidence to confirm the epoxide ring-opening was the disappearing of the proton signals of the GTMAC epoxide ring at 2.65 and 2.92 ppm. Since the lactic acid solution consists of lactic acid monomer and a few dimers and oligomers as seen in $^1\text{H-NMR}$ spectrum of as-received L-lactic acid in Figure 4.9. After the reaction with GTMAC, it was found that the signals of carboxyl terminal lactide unit (c and g) of dimer and oligomer was disappeared as well. The result suggested that lactic acid connected to GTMAC by its carboxyl group, as was also found from the product obtained by the 1st synthesis method. The signals at 4.09 could be assigned to methine or/and methylene protons of GTMAC connecting to carboxyl end group of PLLA since the carboxyl group can react to both methine and methylene of epoxide ring. However, splitting pattern of this peak is quartet so the signal should be assigned to methine proton. The peak area of signal at 4.09 was calculated to be 10% of all products containing of ammonium atom by compared to the peak area of signal at 3.01 ppm, which are the signal of methyl protons next to ammonium atom. Therefore, there was only 10% of p-LA connecting to GTMAC by carboxyl group. The 90% left might be p-LA connecting to GTMAC by hydroxyl group and some by-products since there was water containing in GTMAC.

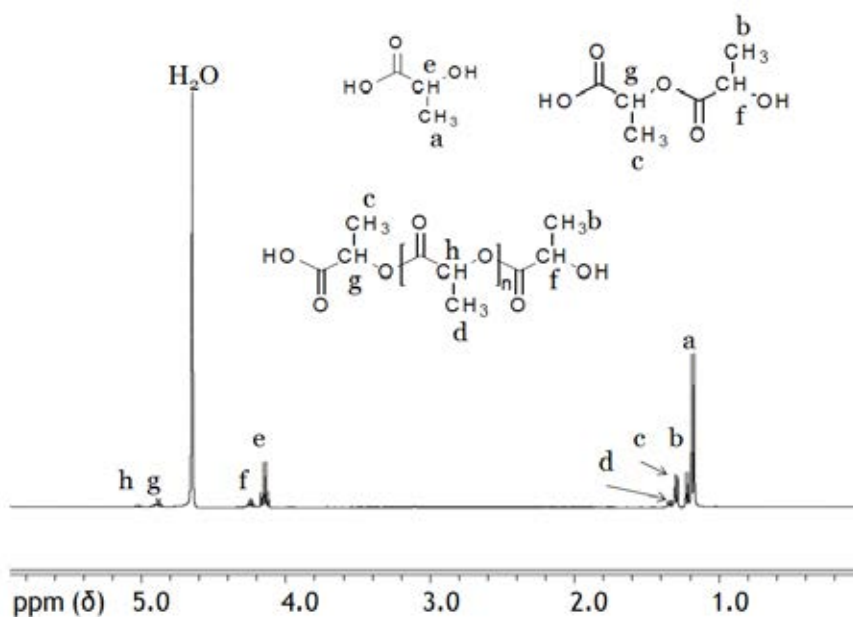


Figure 4.9 $^1\text{H-NMR}$ spectrum of L-lactic acid in D_2O

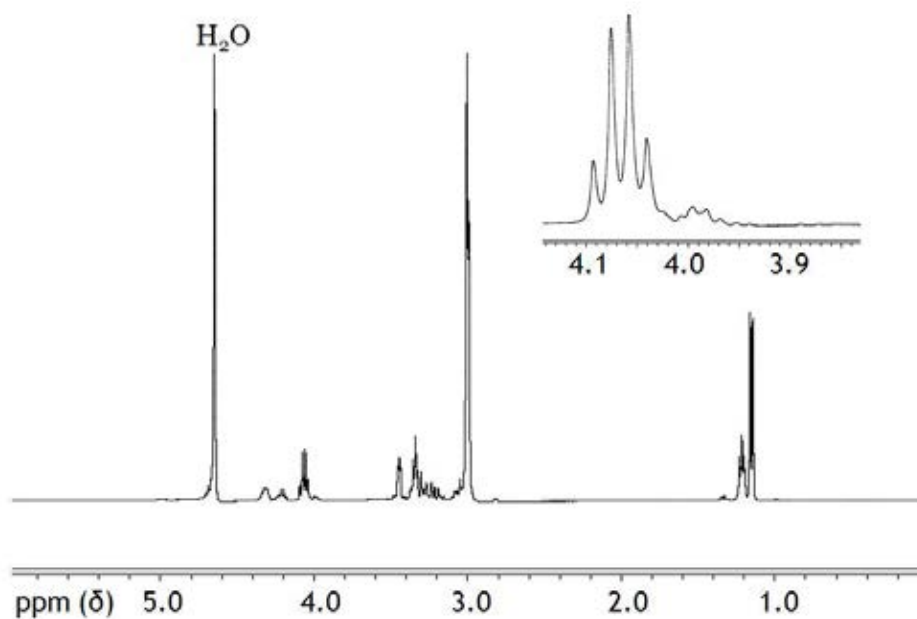


Figure 4.10 $^1\text{H-NMR}$ spectrum of p-LA in D_2O

p-LA was then polymerized with lactic acid to yield p-PLLA. The relative amount of p-LA to L-lactic acid was 1:70. The received product was rather viscous with yellow in color. $^1\text{H-NMR}$ spectrum was different from p-PLLA received from the 1st synthesis method in which GTMAC reacted with the chain end of PLLA

(Figure 4.11). The reason of these observations could be the decomposition of GTMAC at high temperature (170 °C) which was required in the polymerization of L-lactic acid. In fact it was found that the color of GTMAC changed from colorless to brown starting at 150 °C. The $^1\text{H-NMR}$ spectrum, however, exhibits the proton signal of methyl group adjacent to quaternary ammonium atom of GTMAC (3.75 ppm,(a)), which was used to calculate the substitution degree of GTMAC on PLLA. The substitution ranged from only 15-30%. Moreover, the highest molecular weight of the product obtained by the 2nd method was 7,053 Da which was lower than the neat PLLA synthesized using the same reaction condition but without adding p-LA (9,285 Da). This may be caused by the reduction of polymerization rate of L-lactic acid with added p-LA. Since, p-LA has only one site to polymerize with L-lactic acid, the rate of reaction may be less than the polymerization from only L-lactic acid. It was therefore concluded that the 2nd synthesis method was inferior to the 1st one.

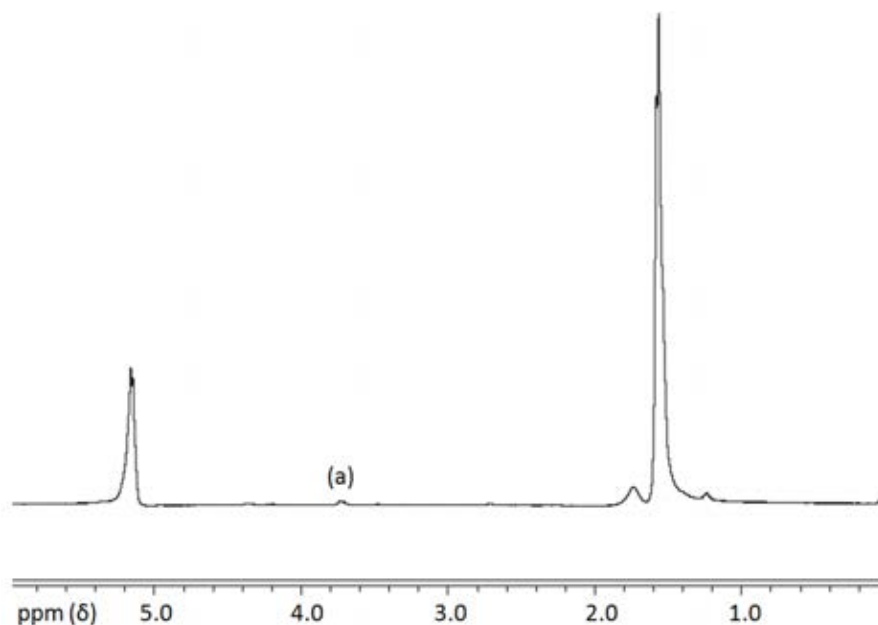


Figure 4.11 $^1\text{H-NMR}$ spectrum of p-PLLA in CDCl_3

4.3 Hydrophilicity determination

The degree of hydrophilicity of the obtained p-PLLA was determined by measuring air-water contact angle of the polymer film surface. From Table 4.8, the

PLLA with \overline{M}_n of 2,978 Da showed contact angle value of $57\pm 2^\circ$. For p-PLLA with different degrees of substitution, the contact angle value remained unchanged when the DS was as high as 24% but decreased to 51, 45, and 47 degrees when the substitution was increased to 59, 77, and 90%, respectively. The attachment of ammonium group on the PLLA chain end enhanced the hydrophilicity of the film surface. At low substitution (11-24%), the charge density might be too low to cause any change of surface hydrophilicity.

Table 4.8 Air-water contact angle measurement of the PLLA films with different degrees of GTMAC substitution on the polymer chain end

Sample (\overline{M}_n)	Degree of substitution	Contact angle
PLLA(2,978)	-	$57\pm 2^\circ$
p-PLLA(2,945)	11.6	$55\pm 2^\circ$
p-PLLA(2,079)	23.7	$56\pm 1^\circ$
p-PLLA(3,135)	59.3	$51\pm 1^\circ$
p-PLLA(2,029)	76.5	$45\pm 4^\circ$
p-PLLA(2,838)	90.0	$47\pm 1^\circ$

4.4 Thermal properties

DSC thermogram of PLLA ($\overline{M}_n = 3,503$ Da, Figure 4.12 A) shows T_g and T_c at 37.86 and 92.94 °C, respectively while the thermogram of p-PLLA ($\overline{M}_n = 2,838$ Da, %substitution = 90.0, Figure 4.12 B) shows T_g , and T_c , at 34.46 and 103.23 °C, respectively. However, above 100 °C in both thermograms show two endothermic peaks expecting to be the melting point (T_m) of the polymers. The T_m of PLLA are at 115.3 and 126.8 °C and T_m of p-PLLA are at 115.3 and 127.0 °C.

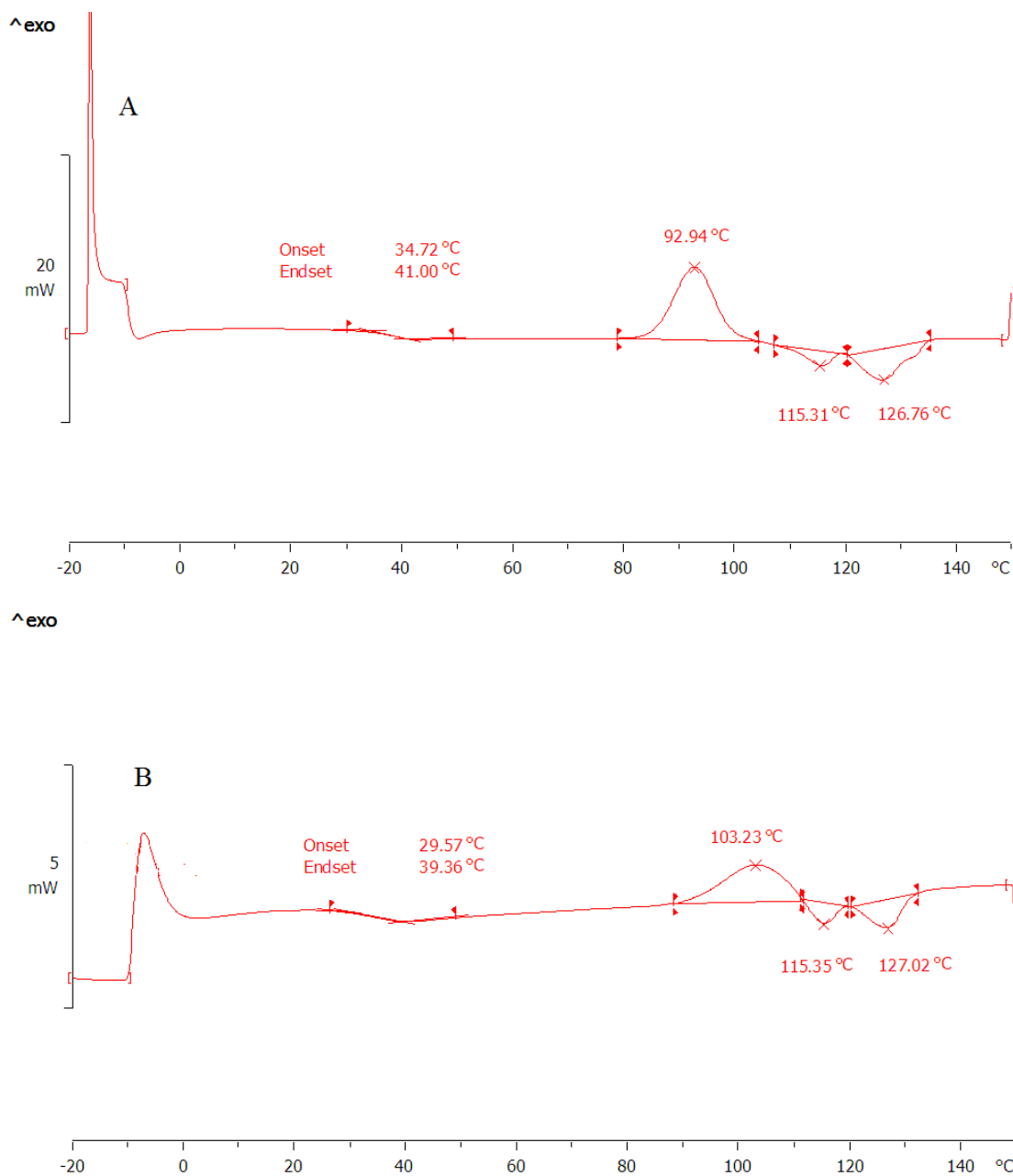


Figure 4.12 DSC thermograms of A) PLLA and B) p-PLLA

TGA thermograms of both PLLA and p-PLLA are shown in Figure 4.13. It was found that on-set decomposition temperatures (T_d) of PLLA and p-PLLA were 253.4 and 250.5°C, respectively. The results from both DSC and TGA indicated that adding of positive charge on PLLA chain end had no effect on the thermal properties of PLLA.

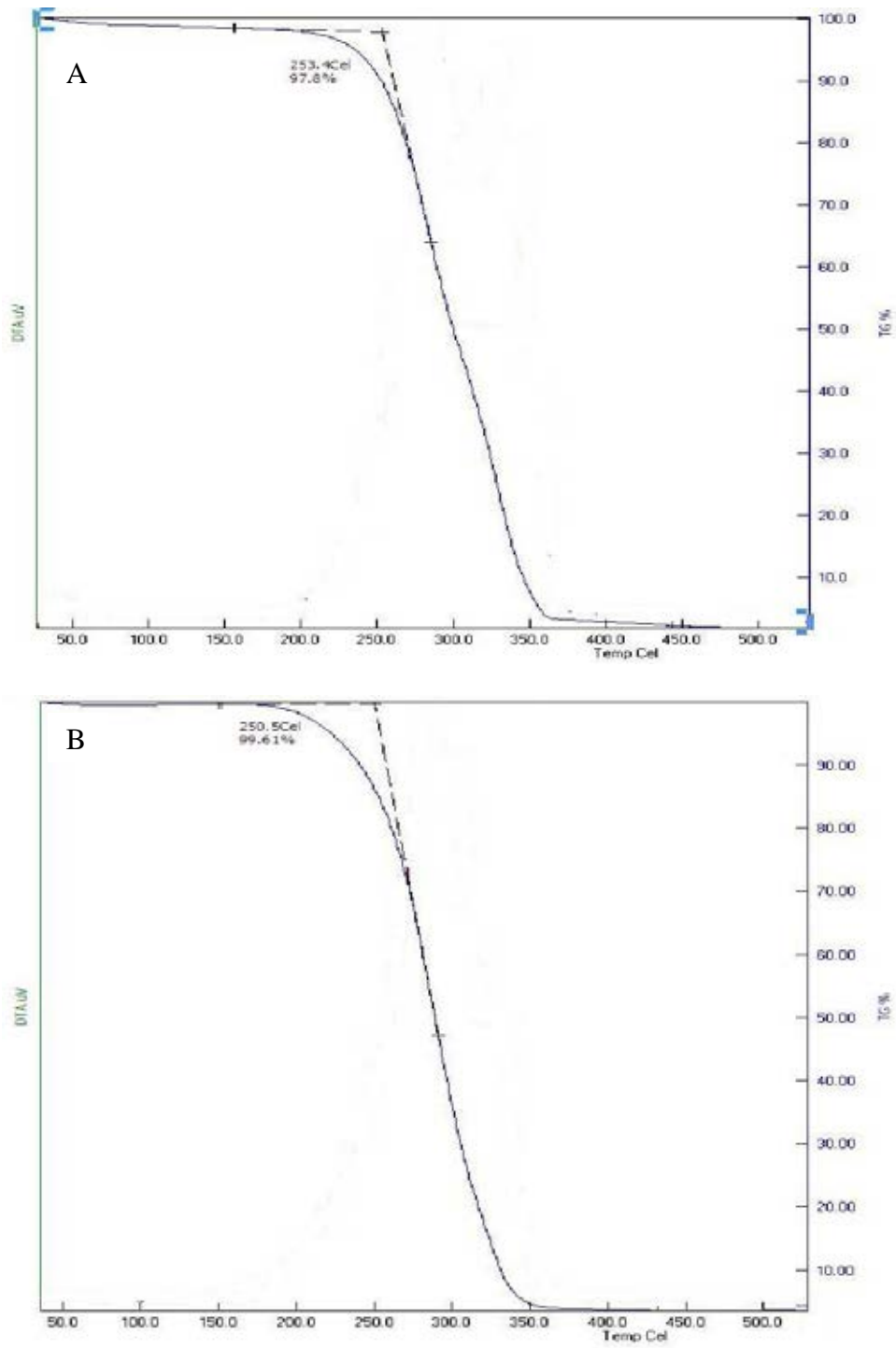


Figure 4.13 TGA thermograms of A) PLLA and B) p-PLLA

CHAPTER V

CONCLUSION

5.1 Conclusions

Poly(lactic acid) having a positively-charged quaternary ammonium group on the chain end was synthesized by reaction between PLLA and GTMAC via epoxide ring-opening reaction. There were two methods to synthesize the p-PLLA. The 1st method was performed by reacting between PLLA and GTMAC directly. The 2nd method was conducted by synthesizing p-LA first and then polymerizing with LA. The product from the 2nd method was inferior to that from the 1st method because its color, appearance, and characteristic of the product which could be contaminated by the decomposed products from GTMAC at high temperature. The ¹H-NMR spectrum confirmed that the carboxyl chain end of PLLA was the main end group to react with the epoxide group of GTMAC to obtain polyester with terminal positively-charged ammonium group. The hydrophilic property of the polymer surface was analyzed by means of air-water contact angle measurement of the melt-cast films. The positive charge on PLLA chain end was able to reduce the hydrophobicity of the polymer film surface. No significant change in the thermal properties when PLLA was transformed to p-PLLA as analyzed by DSC and TGA. However, the molecular weight of the product was quite low so the polymer could be applied to be used as an additive to blend with high molecular weight PLLA to increase the hydrophilicity of the polymer or used as drug carrier to deliver negatively-charged compounds such as DNA.

5.2 Future Direction

Two problems arise in the synthesis step of positively-charged PLLA. The 1st one was the hydrolytic degradation of the polymer product. The cause of the problem may be water containing in the starting material. Hence, the technique to dehydrate the reagents should be further explored. Freeze dry technique may be useful to dehydrate

the reagents. Another problem was the dissolving of the low molecular weight product in 1M NaCl during the purification step. An alternate solvent should be studied to solve the problem.

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APPENDIX



Certificate of Participation

This is to certify that

Piyachai Khomein
Chulalongkorn University

has participated as an

Oral Presenter

in the 6th Pure and Applied Chemistry International Conference (PACCON 2012)
at The Empress Convention Center, Chiang Mai, Thailand
11 - 13 January 2012

Kate Grudpan

Professor Dr. Kate Grudpan

Chairman
Academic Committee

Jintana Siripitayananon

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Presentation in Conference:

January 11-13, 2012 Oral presentation with proceeding in The 6th Pure and Applied Chemistry International Conference 2012 (PACCON 2012), The Empress Convension Center, Chiang mai, Thailand.