

CHAIN LINKED LACTIC ACID POLYMERS: POLYMERIZATION AND BIODEGRADATION STUDIES

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ABSTRACT

The two-step polymerization method, including polycondensation and chain linking reactions, was conducted to obtain high-molecular-weight lactic acid polymers. The biodegradability of these polymers was subsequently investigated. Three polymerization routes were studied. Hydroxyl-terminated prepolymers were linked with diisocyanates, 1,6-hexamethylene diisocyanate (HMDI) or 1,4-butane diisocyanate (BDI), to produce poly(ester-urethanes) (PEU). Carboxyl-terminated prepolymers were linked with 2,2'-bis(2-oxazoline) (BOX) to produce poly(ester-amides) (PEA). In addition, lactic acid oligomers having both carboxyl and hydroxyl end-groups were linked, with sequential or simultaneous addition of HMDI and BOX, to produce both urethane and oxamide bonds in the lactic acid polymer (PEUA).

The structures of novel chain linked lactic acid polymers were identified and the polymerization behavior of carboxyl- and hydroxyl-reactive chain extenders with prepolymers was carefully evaluated with the use of SEC, NMR, and FTIR. BOX was found to be simultaneously an effective chain coupling agent and acid value reducer for lactic acid based prepolymer, whilst also increasing the thermal stability of PLA polymers. Side-reactions were detected, which can be utilized to obtain branches and crosslinks to PEU and PEUA during chain linking polymerizations. Amide groups, formed in the reaction between HMDI and the COOH group, played an important role in the branching and crosslinking, rather than the oxamide or urethane groups. Also, the mode of addition of chain extenders had a considerable effect on the branching.

The biodegradability of lactic acid polymers prepared by chain linking was demonstrated using hydrolysis and a controlled compost test. The quality of the compost after biodegradation was evaluated with biotests. All the polymers biodegraded to over 90% of the positive control in six months, which is the limit set by the CEN standard. Toxicity was detected with the Flash test and plant growth tests in PEU samples, where chain linking of lactic acid oligomers had been carried out with 1,6-hexamethylene diisocyanate. All other polymers showed no toxicological effect. The results clearly showed that 1,6-hexamethylene diisocyanate should not be used as a building block in biodegradable polymers on account of the environmental risk.

PREFACE

This work was carried out between 1996 and 2002 in the Laboratory of Polymer Technology at Helsinki University of Technology. The research was part of the National Technology Agency (TEKES) "Biodegradable Polymers Technology Programme 1992-1996" and targeted research projects thereafter. The financial support from TEKES is gratefully acknowledged.

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Jukka Tuominen

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LIST OF PUBLICATIONS

This thesis is based on the following six publications (Appendices I-VI), which are, throughout the summary, referred to by their Roman numerals.

- I Hiltunen, K., Tuominen, J., and Seppälä, J. V., Hydrolysis of lactic acid based poly(ester-urethane)s, *Polymer International* **47** (1998) 186-192.
- II Tuominen, J. and Seppälä, J. V., Synthesis and characterization of lactic acid based poly(ester-amide), *Macromolecules* **33** (2000) 3530-3535.
- III Helminen, A., Kylmä, J., Tuominen, J., and Seppälä, J.V., Effect of structure modification on rheological properties of biodegradable poly(ester-urethane), *Polymer Engineering and Science* **40** (2000) 1655-1662.
- IV Kylmä, J., Tuominen, J., Helminen, A., and Seppälä, J., Chain extending of lactic acid oligomers. Effect of 2,2'-bis(2-oxazoline) on 1,6-hexamethylene diisocyanate linking reaction, *Polymer* **42** (2001) 3333-3343.
- V Tuominen, J., Kylmä, J., and Seppälä, J., Chain extending of lactic acid oligomers. 2. Increase of molecular weight with 1,6-hexamethylene diisocyanate and 2,2'-bis(2-oxazoline), *Polymer* **43** (2002) 3-10.
- VI Tuominen, J., Kylmä, J., Kapanen, A., Venelampi, O., Itävaara, M., and Seppälä, J., Biodegradation of lactic acid based polymers under controlled composting conditions and evaluation of the ecotoxicological impact, *Biomacromolecules* **3** (2002) 445-455.

The author's contribution in the appended publications

Publication I: Jukka Tuominen and Kari Hiltunen are jointly responsible for research plan, experimental work, interpretation of the results, and the preparation of the manuscript.

Publication II: Jukka Tuominen is responsible for research plan, experimental work, interpretation of the results, and the preparation of the manuscript.

Publication III: Jukka Tuominen has participated in the preparation of the research plan, interpretation of the results, and the preparation of the manuscript. The experimental work was carried out by Antti Helminen.

Publication IV: Jukka Tuominen and Janne Kylmä are jointly responsible for research plan, experimental work, interpretation of the results, and the preparation of the manuscript. Rheological measurements and interpretation of these results were carried out by Antti Helminen.

Publication V: Jukka Tuominen and Janne Kylmä are jointly responsible for research plan, experimental work, interpretation of the results, and the preparation of the manuscript.

Publication VI: Jukka Tuominen, Janne Kylmä and Anu Kapanen are jointly responsible for research plan, experimental work, interpretation of the results, and the preparation of the manuscript. Compost and plant growth tests were carried out by Anu Kapanen and Olli Venelampi.

NOMENCLATURE

BD	1,4-butanediol
BDI	1,4-butane diisocyanate
BOX	2,2'-bis(2-oxazoline)
DMTA	dynamic mechanical thermal analysis
DSC	differential scanning calorimetry
E0%	lactic acid oligomer, 0 mol% BD or SA
E1%, E2%, E4%	lactic acid oligomer, 1, 2, 4 mol% BD
ESA2%	lactic acid oligomer, 2 mol% SA
FTIR	fourier transform infrared spectroscopy
HMDA	1,6-hexamethylenediamine
HMDI	1,6-hexamethylene diisocyanate
HPLC	high-performance liquid chromatography
DLA	DL-lactic acid
LA	lactic acid
LLA	L-lactic acid
NMR	nuclear magnetic resonance spectroscopy
NOE	nuclear overhauser effect
OX	oxazoline group
PC	positive control
PEA	poly(ester-amide)
PEU	poly(ester-urethane)
PEU4%B	1,4-butane diisocyanate based poly(ester-urethane)
PEU2%H	1,6-hexamethylene diisocyanate based poly(ester-urethane)
PEUA	lactic acid polymer having urethane and oxamide bonds in the main chain
PLA	poly(lactic acid)
PLLA	poly(L-lactide), poly(L-lactic acid)
RC	reference compost
SA	succinic anhydride
SEC	size exclusion chromatography

SYMBOLS

AV	acid value (mgKOH/g)
M_n	number average molecular weight (g/mol)
M_w	weight average molecular weight (g/mol)
MWD	molecular weight distribution
T_g	glass transition temperature (°C)
T_m	melting temperature (°C)

1 INTRODUCTION

1.1 Background

Biodegradable polymers are used and studied in an increasingly large number of mass produced applications such as packaging, paper coating, fibers, films, and other disposable articles, as well as in biomedical applications, such as resorbable surgical sutures, implants, and controlled drug-delivery devices.¹⁻⁹ These types of application sectors bring special requirements to the polymers and monomers which must be fulfilled before applications can be successfully launched on the market. These polymers need to be biodegradable and non-toxic or, in the biomedical applications, bioresorbable and biocompatible. On the other hand, polymers should have good chemical, mechanical, thermal and rheological properties. In addition, in the packaging sector, the raw materials should be annually renewable and the end products should be compostable to reduce the use of fossil resources. Furthermore, the raw materials and the end products should be low cost and the production processes on an industrial scale should be efficient, environmentally friendly and economically competitive.^{1,2,10-14}

However, only a few monomers and polymers can fulfill these demands. Among possible monomers, lactic acid (2-hydroxy propionic acid), which is a non-toxic, naturally occurring, and renewable raw material, fulfills most of these rigorous requirements.^{1-4,14} Lactic acid is the simplest hydroxy acid with an asymmetric carbon atom and it exists in two optically active configurations. The L-isomer is an intermediate of carbohydrate metabolism in humans and other mammals whereas both the D- and L-enantiomers are produced in bacterial systems. Pure L- and D-lactic acid can be obtained by fermentation or culture techniques, whereas synthetic lactic acid is a racemic mixture, referred to as DL-lactic acid. DL-lactic acid is optically inactive.¹⁵⁻¹⁹

Lactic acid based polyesters are well known and widely studied biodegradable polymers. Poly(lactic acid), a thermoplastic polyester, is suitable for packaging applications, since PLA's glass transition temperature (T_g about 60°C) is above the service temperature and therefore a good barrier material for solvents, flavors, and aromas, and a medium barrier for permanent gases.²⁰ Additional benefits for packaging applications are good heat sealability and processability with standard plastic equipment. Recent advances in the production process of poly(lactic acid), together with improvements in the material properties, have also opened up a promising market outlook in the sector of fibers and nonwovens, films, thermoformed and injection molded articles.²¹

The use of polymers in packaging, and the corresponding waste materials produced, results in considerable environmental impact. The removal of plastics from packaging is not a viable option. Mechanical recycling of polymers and energy recovery by incineration are primary strategies for reducing plastic waste. Despite the efforts to recycle used plastics, recycling is neither practical nor economical for certain applications, such as waste bags, agricultural mulch films, or food packaging. In this kind of application, the composting of items produced from biodegradable polymers has advantages compared to other types of municipal waste management. Another factor promoting the use of biodegradable polymers for packaging and other mass

volume applications is the criticism directed at industry for using non-renewable, oil-based chemicals for commodity polymers.^{2,22,23}

1.2 Polymerization methods for lactic acid

The existence of both a hydroxyl and a carboxyl group in lactic acid enables it to be converted directly into polyester via a polycondensation reaction. However, the conventional condensation polymerization of lactic acid does not increase the molecular weight sufficiently unless organic solvents are used for azeotropic distillation of condensation water and the polymerization time is very long. Conventional polycondensation of lactic acid yields a brittle glassy polymer, which is unusable for most applications.^{1,3,11,24-27}

The most common way to obtain high-molecular-weight poly(lactic acid) is through ring-opening polymerization of lactide.^{1,11,13,15,28-35} Carothers's³⁶ pioneering research suggested this two-step method that yields high-molecular-weight polymer. The intermediate lactide, a cyclic lactic acid dimer, is formed in the first step when the condensation product water is removed by evaporation during oligomerization. L-Lactic acid, D-lactic acid or mixtures thereof can be polymerized to corresponding low-molecular-weight poly(lactic acid) oligomer, which is in then catalytically depolymerized through an internal transesterification, i.e., by *back-biting* reaction to lactide. During depolymerization, three stereoisomers of lactide are possible: L-lactide, D-lactide, and *meso*-lactide. In the second step, purified L-lactide, D-lactide, DL-lactide (50:50 mixture of L and D isomers), or *meso*-lactide monomer is converted into the corresponding high-molecular-weight polyester by catalytic ring-opening polymerization. The ring-opening polymerization (ROP) has been performed as melt, bulk, solution or emulsion polymerization using a catalyst, which is always necessary to start the polymerization, and therefore usually referred to as initiator. Depending on the initiator/coinitiator system, the ring-opening polymerizations can be carried out via a coordination/insertion, anionic, cationic, zwitterionic, active hydrogen, or free-radical mechanism.

Due to the relatively complicated and expensive ring-opening polymerization of lactide, and the need for the modification of the polymer properties of poly(lactic acids) for many different type of applications, alternative polymerization routes for lactic acid are of considerable interest. An alternative way to achieve high-molecular-weight polyesters is to treat condensation polymers with chain extenders.^{37,38} Chain extenders are usually bifunctional low-molecular-weight compounds that will increase the molecular weight of polymers in a fast reaction. Feasible chain extending agents do not produce byproducts, which could cause contamination of the resulting polymer and would need to be removed.³⁹ The chain extending of polyesters can be conveniently and economically performed in an extruder if the reaction rate is high enough.^{40,41} Inata and Matsumura studied extensively carboxyl^{39,42,43} and hydroxyl-reactive⁴⁴⁻⁴⁶ addition-type chain extenders for polyesters. In the polyester chains, the hydroxyl end-group usually coexists with the carboxyl end-group. Carboxyl-reactive chain extender seems to be more advantageous, since the reduction of the acid value, resulting in improved thermal stability, is accompanied with the increase in molecular weight. However, hydroxyl end-groups are usually predominant over the carboxyl end-groups in the relatively low-molecular-weight polyesters prepared by the melt

polycondensation procedure. Thus, hydroxyl-reactive chain extenders can be more effective in increasing the molecular weight.⁴⁴ Suitable chain extenders for polyesters are bis(2-oxazolines), diisocyanates, bisepoxides, bis(ketene acetals), dianhydrides, bis[5(4H)-oxazolones], and bis(5,6-dihydro-4H-1,3-oxazines).^{37-51,56,57}

The two-step polymerization of lactic acid to high-molecular-weight thermoplastic poly(ester-urethanes) has been extensively studied at Helsinki University of Technology.⁵²⁻⁵⁷ Seppälä and coworkers introduced a poly(ester-urethane) process consisting of polycondensation of lactic acid to low-molecular-weight hydroxyl-terminated prepolymer⁵⁸, followed by chain linking with diisocyanate such as 1,6-hexamethylene diisocyanate⁵⁹ or isophorone diisocyanate^{60,61}. This feasible two-step process offers versatile possibilities for tailoring the structure and properties of lactic acid based polymers. Numerous monomers or comonomers can be introduced to both steps of the synthesis: other hydroxy acids than lactic acid can be used in the polycondensation step as well as different kinds of diols and diacids; and different type of chain extenders can be used in the chain extending step. Kylmä and Seppälä⁶² applied the two-step process by copolymerizing ϵ -caprolactone with lactic acid, which was followed by chain linking, thus introducing thermoplastic poly(ester-urethane) elastomer. The heat resistance of PEU has been improved by the copolymerization of lactic acid with DL-mandelic acid.⁶¹ The incorporation of various comonomers, which impede rotation of the molecule and stiffen the polymer chain, cause an increase in T_g .⁵⁷ Hiltunen and coworkers⁶³⁻⁶⁵ condensation polymerized different types of lactic acid prepolymers using various types of catalyst, diols, polymerization conditions and combinations of them. These types of structure modifications allow possibilities for the synthesis of materials for both high volume and biomedical applications.⁶⁶ In addition to the chemical modification of PEU, mechanical and thermal properties have been improved by physical modification. PEU composites have been prepared by the addition of fillers⁶⁷, rubber-toughening^{68,69} and combinations of both⁷⁰.

1.3 Biodegradation

Biodegradable polymers in this connection are defined as those which are degraded in biological environments, where living cells or microorganisms are present, such as soils, composts, seas, rivers, lakes, bodies of human beings and animals through enzymatic or non-enzymatic hydrolysis.⁴ Biodegradation is a complex process including chemical and biological (i.e. enzymatic) reactions, which can occur simultaneously.⁷¹ In the mass volume applications, biodegradable polymers are designed to resist a number of environmental factors during use, but to be biodegradable under disposal conditions, for instance in the compost environment.⁷²

Polymer degradation occurs mainly through scission of the main chains or side chains of macromolecules. In nature, polymer degradation is induced by thermal activation, hydrolysis, biological activity (i.e. enzymes), oxidation, photolysis, or radiolysis. A variety of chemical, physical and biological processes and thus different degradation mechanisms can be involved with the degradation of a polymer. Combination of these mechanisms can also occur at some stage of the degradation. In addition to the environmental conditions such as pH, phase, temperature, exposure, mechanical stress, and biological activity, the process of polymer degradation is also

dependent upon the chemical and physical characteristics of the polymer. These include diffusivity, porosity, morphology, crosslinking, purity, chemical reactivity, mechanical strength, thermal tolerance, and resistance to electromagnetic radiation.^{2,4,71,73}

The hydrolysis of PLA polymers has been widely studied both *in vivo* and *in vitro*.⁷⁴⁻⁷⁹ The mechanism by which PLA polymers degrade depends on the biological environment to which they are exposed. In mammalian bodies, PLA is initially degraded by hydrolysis and the oligomers that form are metabolized or mineralized by cells and enzymes. Abiotic hydrolysis is known to participate at the initial stage of degradation before microbial biodegradation of PLA occurs in nature. However, the degradation rate has been shown to increase in the compost environment in the presence of an active microbial community compared to the abiotic hydrolysis.^{80,81} PLA polymers have suitable properties for many applications and composting of post consumer PLA items is a viable method for many PLA products.¹ The environmental degradation of PLA occurs by a two-step process. During the initial phases of degradation, the high molecular polyester chains hydrolyze to low-molecular-weight oligomers. This reaction can be accelerated by acids or bases and is affected by both temperature and moisture levels. At the level of about M_n 10 000 to 40 000 g/mol, microorganisms in the environment continue the degradation process by converting these low-molecular-weight components to carbon dioxide, water, and humus.^{1,3,10}

1.4 Scope of the study

This thesis discusses the work reported in the six appended publications (I-VI) and focuses on the synthesis of lactic acid based polymers via a chain linking reaction, their characterization, and on the biodegradation of these polymers. The aim of the thesis was to polymerize new types of biodegradable lactic acid based polymers.

Although biodegradable polyesters have found important uses in the high volume and biomedical applications, they often lack certain optimum properties and fail to meet all the requirements e.g. the mechanical, thermal, and processing properties, as well as the biodegradation behavior. Copolymerization with other monomers, crosslinking, and blending are proven tools for the modification of the polymer properties of polyesters.^{61,62,67-70,82-84} Likewise, the structure and the properties of polyesters can be tailored through the introduction of units other than ester groups on the polymer chain by chain linking of low-molecular-weight oligomers. Biodegradable poly(ester-urethanes) based on the two-step polymerization of lactic acid, which has been developed in our laboratory, have mainly been designed for high volume applications where the processability and cost of the material are of prime importance.^{52,53,56,57,85} Experiences with the polymerization method, and modification of properties and rates of biodegradation⁸⁶ of poly(ester-urethanes) indicated that the lactic acid based low-molecular-weight prepolymers could be used with other typical chain extenders such as bis(2-oxazolines) in the preparation of new biodegradable polymers.

The first part of the work focused on the two-step polymerization and characterization of lactic acid based polymers. The polymerization of poly(ester-urethane) (PEU) was studied in publications I and III by using different molecular weight prepolymers and by changing the

amount of diisocyanate linking agent (1,6-hexamethylene diisocyanate). To study the effect of different diisocyanates on the biodegradation and the ecotoxicity of the degradation products of PEU, 1,4-butane diisocyanate was introduced as a chain extender in publication VI. The chain extending method for producing lactic acid based poly(ester-amide) was introduced in the publication II, and the polymerization behavior of 2,2'-bis(2-oxazoline) with carboxyl-terminated prepolymer and the structure of PEA were characterized. In addition, the sequential and simultaneous addition of chain extenders in order to produce urethane and oxamide bonds on lactic acid polymers is discussed in publications IV and V. The use of two chain extenders provides more possibilities for modification of the polymer structures and thus the properties of lactic acid polymers.

Completely biodegradable polymers can be synthesized from petrochemical starting materials, renewable resources, or a combination of both. The origin of a material and its biodegradability are independent factors: biodegradability is only a function of the chemical structure and the degrading environment.⁸⁷ However, the materials used in the mass volume applications should be compostable after use, therefore it is important to clarify how these materials degrade during composting and their effect on the compost quality. The second part of the work, publications I and VI, concentrates on the hydrolytic degradation of lactic acid based PEU, biodegradation of the chain linked lactic acid based polymers under the controlled composting test and evaluation of the compost quality with biotests and high-performance liquid chromatography (HPLC).

2 POLYMERIZATION OF LACTIC ACID POLYMERS BY CHAIN EXTENDING

The two-step polymerization method, including polycondensation and polyaddition reactions, was conducted to obtain high-molecular-weight, chain linked lactic acid polymers.^{1-VI} Three types of polymerization routes were investigated for the preparation of polymers, as shown in Figure 1. Synthesis **route a**, polymerization of lactic acid based poly(ester-urethanes) (PEU), is discussed in publications I, III, and VI. Synthesis **route b**, polymerization of lactic acid based poly(ester-amides) (PEA), is discussed in publications II, and VI, and the sequential and simultaneous addition of chain extenders (**route c**) are discussed in publications IV and V.

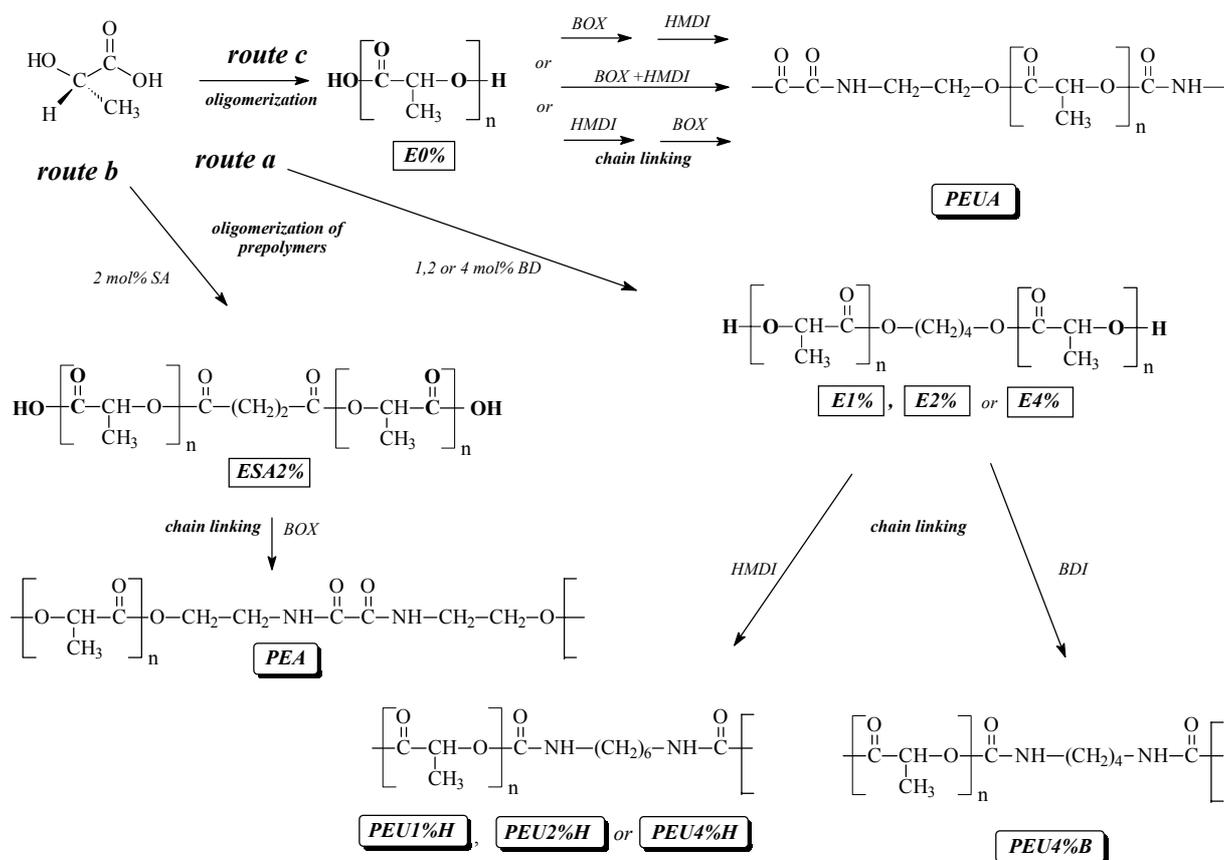


Figure 1. Studied synthesis routes for lactic acid based polymers.

In all these three routes, lactic acid was first condensation polymerized to low-molecular-weight oligomers, which were then chain extended with chain extender or extenders to high-molecular-weight polymer. Due to the selection of hydroxyl-reactive and carboxyl-reactive chain extenders, three types of telechelic prepolymers were synthesized for chain extending reactions. Hydroxyl-terminated prepolymers (E1\% , E2\% , or E4\%) were linked with diisocyanates, 1,6-hexamethylene diisocyanate (HMDI) or 1,4-butane diisocyanate (BDI), in order to produce poly(ester-urethanes) and carboxyl-terminated prepolymers (ESA2\%) were linked with 2,2'-bis(2-oxazoline) (BOX), which produced poly(ester-amides). In addition, lactic acid oligomers, having both carboxyl and hydroxyl end-groups (E0\%), were linked with sequential and simultaneous addition of HMDI and BOX in order to produce both urethane and oxamide bonds to lactic acid

polymer (PEUA). Due to the polymerization method used, and the type and size of the prepolymers, all synthesized PEUs, PEAs, and PEUAs consisted mainly of lactic acid units and only a small amount of chain extender units and butanediol or succinic acid units (if used).

2.1 Telechelic lactic acid prepolymers for chain extending polymerizations

The self-condensation of lactic acid, which is an equilibrium reaction between lactic acid, poly(lactic acid), water, and lactide¹⁶, yields a glassy low-molecular-weight polymer with an equimolar concentration of hydroxyl and carboxyl end-groups.^{IV,V} To avoid the different reaction rates of chain-linking, PLA oligomers can be modified to hydroxyl- or carboxyl-terminated. The use of a difunctional hydroxyl or carboxyl compound allows a change in the balance between the hydroxyl and acid groups towards favorable functional groups. The amount of difunctional compound added to the polycondensation of lactic acid defines the number of polymer chains, and thus the molecular weight of the prepolymer. It determines the amount of chain extender required, i.e., the amount of functional groups, which in turn influences the final properties of the polymer. These functional groups affect the mechanical and thermal properties of the chain linked polymer and especially its degradation behavior. In previous studies, Hiltunen *et al.*⁵⁸ used 1,4-butanediol (BD) or adipic acid in the condensation polymerization of lactic acid to obtain hydroxyl or carboxyl terminated prepolymers, which was also the method used in this study. 1-4 mol% of 1,4-butanediol was used in the preparation of prepolymers for the polymerization of poly(ester-urethanes)^{I,III,IV,VI} and 2 mol% of succinic anhydride (SA) was used in the preparation of prepolymers for the polymerization of poly(ester-amides)^{II,VI}. Despite the fact that there were differences with the batches used in the different publications, the molecular weights of the prepolymers were dependent on the amount of difunctional compound used (one BD or SA unit per polymer chain), as can be seen from the results shown in Table 1. The relatively narrow molecular weight distribution (MWD) is typical for the low-molecular-weight telechelic lactic acid polymers. The thermal properties of PLA oligomers depend on the molecular weight and stereostructure of the polymer chains, which are affected by the polymerization conditions and prepolymer composition.^{I-VI,58,63-65}

Table 1. Examples of the synthesized prepolymer compositions and their properties.

Prepolymer	Prepolymer composition in feed (mol%)				SEC			DSC		¹³ C NMR	AV
	LLA	DLLA	BD	SA	M _n g/mol	M _w g/mol	MWD	T _g	T _m	D-structures mol%	a)
								°C	°C		
E0% ^{IV}	100	-	-	-	8 800	19 600	2.2	47	-	21.9	11.3
E0% ^V	100	-	-	-	13 000	25 000	1.9	48	136	21.0	11.0
E1% ^I	99	-	1	-	15 300	22 200	1.5	46	-	25.9	n.m.
E1% ^{III}	99	-	1	-	5 300	11 700	2.2	36	-	n.m.	3.7
E2% ^{IV}	98	-	2	-	8 700	12 900	1.5	40	-	25.7	1.4
E2%DL50 ^I	49	49	2	-	5 300	9 500	1.8	33	-	64.1	n.m.
E2%DL100 ^I	-	98	2	-	5 300	10 000	1.9	31	-	76.4	n.m.
E4% ^I	96	-	4	-	3 400	4 900	1.4	27	-	26.9	n.m.
ESA2% ^{II}	98	-	-	2	6 200	10 000	1.6	49	-	16.0	30.5

a) mgKOH/g; n.m. not measured

Racemization is of particular importance for the properties of lactic acid polymers, regardless of the polymerization route. As noted by Kricheldorf and Serra⁸⁸, racemization is related to basicity, and monomer deprotonation is the likely mechanism. According to Witzke and Narayan⁸⁹, in ketone systems where the stereocenter is next to the carbonyl group, racemization occurs through formation of an intermediate enol form having an achiral planar configuration. The rate of racemization is equal to the rate of enolization, which is acid or base catalyzed. With lactic acid and poly(lactic acid), racemization was found to be first order with regard to acid end-group concentration, and thus higher molecular weight PLA has a lower racemization rate. Long reaction times and high temperatures considerably increase racemization. Usually, due to racemization during the condensation polymerization at 200°C with a strong ester interchange catalyst such as Sn(II) octoate, L-lactic acid prepolymers have not shown evidence of crystallinity in DSC measurements. The formation of D-structures (typically more than 20%) affects the stereoregularity of the chains and leads to an amorphous prepolymer. However, semi-crystalline low-molecular-weight prepolymer can be achieved by the use of suitable condensation conditions. Hiltunen and coworkers^{64,65,90} showed that the amount of D-lactic acid structures and thus the crystallinity of the L-lactic acid prepolymer can be affected by the choice of catalyst, diol, and polymerization temperature. In addition, Hiltunen *et al.*⁶³ and Fukuzaki *et al.*^{77,91} found that the direct polycondensation of lactic acid without a catalyst produced semi-crystalline oligomers at 180 and 200°C.

All prepolymers prepared and discussed in publications I-IV and VI were, as expected, totally amorphous due to the racemization during the condensation polymerization above 200°C with Sn(II) octoate catalyst. The only exception was the prepolymer used in publication V. The amount of racemization i.e. D-structures of this lactic acid oligomer (E0%^V), estimated by ¹³C NMR from the carbonyl region⁵⁸, was 21% and thus was in the normal range (Table 1). However, a clear melting endotherm was detected at 136°C, although the content of the crystalline phase was very low: ΔH was 1.5 J/g. By comparison, the melting enthalpy for 100% crystalline poly(L-lactide) is reported to be 93.6 J/g.^{92,93} The different capability of oligomers to crystallize is attributed to chain length. Without the use of a difunctional compound, the molecular weight of lactic acid oligomers is higher, reflecting the increased crystallisability of the PLA chain.

in mammalian cells^{97,98}. This would be especially beneficial, considering the biocompatibility of the prepared poly(ester-urethanes) for biomedical applications. For the synthesis of 1,4-butane diisocyanate based poly(ester-urethane) (PEU4%B), a hydroxyl-terminated prepolymer E4% was prepared using 4 mol% of 1,4-butanediol with lactic acid. The use of 4 mol% of 1,4-butanediol determined the molecular weight of prepolymer and thereby the amount of BDI units in the PEU4%B. Hydroxyl-terminated prepolymer was reacted with an equimolar amount of 1,4-butane diisocyanate relative to -OH groups. The reaction behavior of BDI was similar to HMDI (see paragraph 2.2.1).^{IV,VI,128,129} PEU4%B was a completely amorphous polymer, as was the prepolymer, having about the same T_g (45°C) as the corresponding HMDI based PEU.

2.2.1 Reaction of diisocyanate with hydroxyl-terminated prepolymer

Chain extending reactions with diisocyanate take place by addition across the C=N double bond. With hydroxyl-terminated prepolymer, at an equimolar amount of diisocyanate relative to hydroxyl groups, the molecular weight increased rapidly within the first few minutes, as seen in Figure 3.^{IV} After obtaining the maximum, a decrease occurred due to lack of reactive groups and degradation of thermally unstable prepolymer chains, which is typical for lactic acid polymers^{99-103,II,III}. With an increase in the NCO/OH ratio, the molecular weight curves gradually became flatter. When the NCO/OH ratio was 1.2:1, the weight average molecular weight increased at the beginning of the reaction to a level 50% lower than with a ratio of unity. The excess of the chain extending agent in the reaction mixture caused a rapid decrease in the hydroxyl group concentration as the lactic acid oligomers became terminated with isocyanate groups. Further increase in the molecular weight is prevented by the lack of -OH groups. Isocyanate groups can further react with -OH or -COOH groups formed by thermal and hydrolytical degradation of the lactic acid chain, but the observed gradual increase in M_w during the reaction and faster increase at a certain point of the polymerization is caused by branching and crosslinking reactions. The excess of HMDI also retards these reactions, in such a way that the highest molecular weights were achieved at 80 and 100 min for OH/NCO ratios of 1:1.1 and 1:1.2, respectively. Concurrent with the fast increases in M_w , the number average molecular weight remains essentially unchanged for the whole period of time. This is observed as an instant broadening of the molecular weight distributions from 2 to 4.5, as seen in Figure 3 (dashed lines). Samples were soluble, however, and gel fractions were not observed. In contrast, with the OH/NCO ratio of 1:1, the MWD was consistently 2 during the polymerization.

The termination of the prepolymer was found to play an essential role in chain linking polymerization.^{III} It was found that when the acid value of hydroxyl-terminated prepolymer was higher (over 2), the maximum extent of the linking reaction was about ten prepolymer units. Also, the acid end-groups in the prepolymer impede the reaction, which was seen in the longer polymerization times and the increase in the amount of chain extender required. Several side reactions were present, which were capable of producing branches in the polymer, especially when the chain extender was used in excess. An increase in the amount of chain extender (1.05:1 to 1.35:1, NCO/OH) broadened the MWD of the polymer from 2.2 to 3.5.^{III}

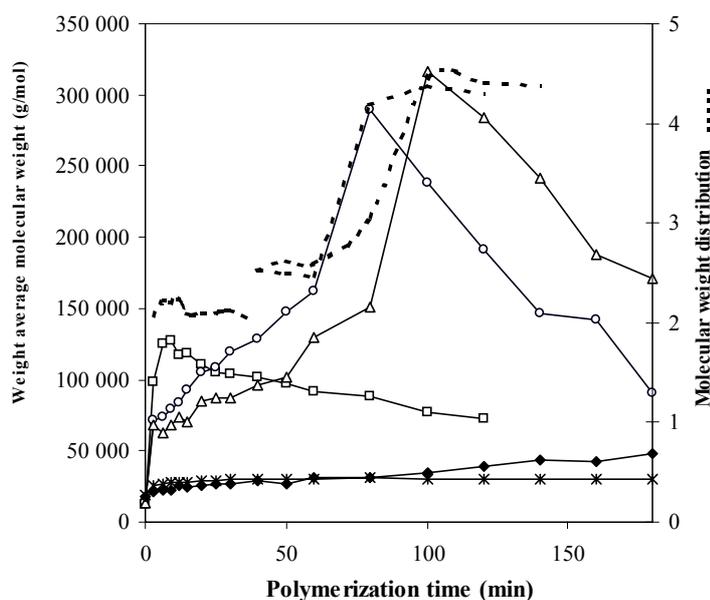


Figure 3. Development of the weight average molecular weight and molecular weight distribution (dashed line) for prepolymer E2% (open symbols) with OH/NCO ratios of 1:1 (\square), 1:1.1 (o), and 1:1.2 (Δ), and for prepolymer E0% (solid symbols) with OH/NCO ratios of 1:1.1 (\times) and 1:2 (\blacklozenge).^{IV}

2.2.2 Reaction of diisocyanate with unmodified lactic acid oligomer

The clear hindering effect of the high acid value of prepolymer E1% on the molecular weight of PEU and the reaction behavior, indicated a very different reactivity of hydroxyl end-groups compared to carboxyl end-groups with isocyanates, as demonstrated in publication III. To study the reaction between isocyanate and carboxyl group in the presence of hydroxyl groups, lactic acid prepolymer that was not modified with difunctional compound, i.e. lactic acid oligomer (E0%) having a hydroxyl group at one end of the polymer chain and a carboxyl group at the other, was allowed to react with HMDI. If the reactivity of -OH was much higher than the reactivity of -COOH, chain linking with equimolar amounts of -NCO and -OH groups would connect two chains together to form a longer acid-terminated chain. Thus, in the case of E0%, the molecular weight was doubled in the linking reaction (OH/NCO ratios of 1:1.1), as seen in Figure 3, and the AV stayed at a level of 11.^{IV} As noted earlier, isocyanates can also react with carboxyl end-groups, leading to amides, carboxylic anhydrides or ureas. The reactivity in the present system was tested by using an amount of isocyanate corresponding to both -OH and -COOH end-groups (OH/NCO ratios of 1:2). As seen in Figure 3, the molecular weight increased slowly (M_w from 13 000 to 48 000 g/mol) during the three hours reaction time and at the same time the acid value decreased from eleven to seven. Isocyanate groups thus reacted with carboxyl groups, but not fast enough to be utilized in the chain linking of lactic acid oligomers. It was also noted that the molecular weight distribution of prepolymer E0% narrowed immediately in the beginning of the reaction, as the smaller molecules reacted first.

Representative samples of this chain linking with HMDI at a OH/NCO ratio of 1:2 were analyzed by NMR spectroscopy (Figure 4a).^V In ¹H NMR, the formation of amide bonds can be seen as a broad peak at 6.21 ppm. The urethane bonds are partly overlapped by the solvent peak at 7.23 ppm and are not seen well, but the formation of the urethane peak in this region was confirmed with the use of deuterated acetone as solvent. The reactions of HMDI with both the hydroxyl and carboxylic acid end-groups of the prepolymer can be seen more clearly in the region 4.5-2.5 ppm. The formation of urethane bonds is seen at 3.12 ppm (Figure 4a). The partly overlapped peak observed as a shoulder at 3.31-3.16 ppm is due to the amide bond. The identification of this resonance was confirmed by reacting an acid-terminated prepolymer with HMDI (Figure 4b). In addition, some indication of side-reactions, such as the formation of allophanates and urea groups (Figure 2c and 2d), i.e., branching of the polymer, was observed as a broad shoulder on the NH peak at 6.50-6.26 ppm.

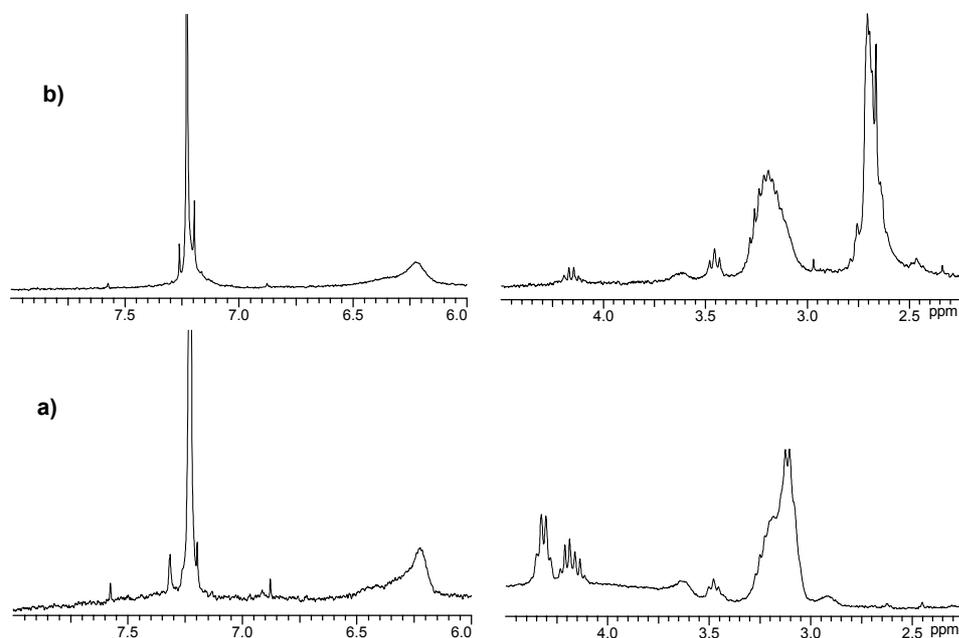


Figure 4. ¹H NMR spectra of (a) unmodified lactic acid prepolymer chain linked with HMDI and (b) acid-terminated prepolymer chain linked with HMDI.^V

In the ¹³C NMR spectra, the formed urethane and amide groups were detected at 155.5 and 156.3 ppm, respectively.^V The resonance at 169.4 ppm (partly overlapping), which is assigned to the carbonyl group of the carboxyl end-groups of the prepolymer, diminished substantially after just 6 min polymerization time. This indicated that the reaction between carboxyl groups and isocyanate groups was surprisingly fast. However, the FTIR and AV results indicated that a large number of carboxyl groups were left, even after 180 min reaction time. More interesting and unexpected was that the resonances assigned to the terminal lactic acid units (i.e., units bonded directly to hydroxyl end-groups with resonances at 175.1 and 66.7 ppm due to the carbonyl groups and methine carbons, respectively) did not disappear during the reaction with isocyanate. This showed clearly, in accordance with publication III, that the presence of carboxyl groups retarded the rate of reaction between isocyanate and hydroxyl groups. These results were also in agreement with the deceleration or inhibition of isocyanate-alcohol reactions due to -COOH

groups suggested by Draye and Tondeur¹⁰⁴ and favored the use of carboxyl-reactive coupling agent and acid value reducer such as BOX together with HMDI (Section 3.1.4).

The HMDI reactions were also studied with FTIR.^V In the 3600-3100 cm^{-1} range, the characteristic peaks of hydroxyl (3600-3440 cm^{-1}) and carboxylic acid (broad band between 3450 and 3150 cm^{-1}) end-groups of the oligomer E0% remained substantially unchanged. However, the appearance of the characteristic peak of NH groups (3405 cm^{-1}) indicated the formation of urethane and amide groups. Furthermore, the disappearance of the characteristic peaks of -NCO groups (2270 cm^{-1}) was evident. In the region between 1800 and 1400 cm^{-1} , the urethane bond formed by the reaction between -OH and -NCO groups was coincident with the carbonyl absorption of the LA oligomer, but an amide II band of the urethane bond also appeared at 1525 cm^{-1} (Figure 5(a), hydroxyl-terminated LA oligomer linked with HMDI). When the isocyanate group reacts with the carboxyl group, amide I absorption bands of the amide bond appear in the 1595-1700 cm^{-1} region. This was further demonstrated with a model reaction where acid-terminated oligomer was linked with diisocyanate (Figure 5(b), COOH/NCO 1:1). In the case of the amide II peak, a slight shift to higher wave number (1537 cm^{-1}) relative to urethane was observed. At the beginning of the reaction between lactic acid oligomer E0% and HMDI (after 6 min, Figure 5(c)), a clear shoulder indicative of these acid-HMDI reactions was formed beside the urethane amide II peak, but as the reaction time increased the shoulder diminished (Figure 5(d)). Correspondingly, the intensity of the amide I peak at 1640 cm^{-1} decreased. The FTIR results supported NMR data and the formation of urethane and amide bonds was assured.

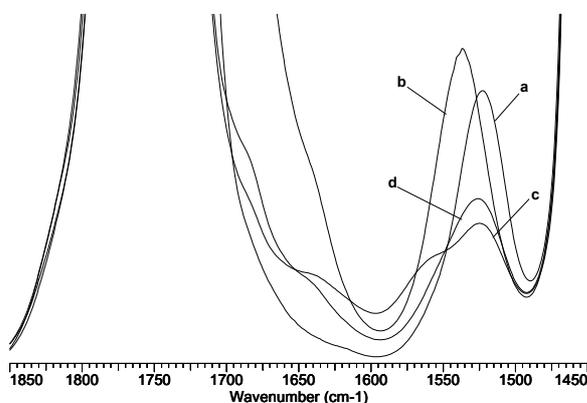


Figure 5. FTIR spectra of (a) hydroxyl-terminated LA oligomer linked with HMDI, (b) acid-terminated LA oligomer linked with HMDI, (c) E0% reacted with HMDI for 6 min and (d) E0% reacted with HMDI for 160 min.^V

2.3 Synthesis and characterization of poly(ester-amide)

The polymerization method for producing lactic acid based poly(ester-amide) was introduced in publication II. PEA was polymerized using a carboxyl-terminated prepolymer (ESA2%) and 2,2'-bis(2-oxazoline) as chain extender. The fact that 2-oxazolines are inert towards aliphatic alcohols enables the selective modification of the carboxyl end-group of the polyester.¹⁰⁵ As a matter of fact, polymerization of lactic acid in a two-step process including polycondensation and chain linking enables the introduction of new functionalities, and thus new properties to lactic

acid polymers.^{II,VI} 2-Oxazolines react with carboxylic acids through the ring opening between positions 1 and 5 of the oxazoline, producing compounds possessing both amide and ester bonds. The incorporation of unstable amide or oxamide linkages in the polyester chain by means of polymerization involving hydroxy acids is a promising approach to the synthesis of biodegradable poly(ester-amides).^{66,II,VI,106-108} Synthetic aliphatic polyamides are not usually biodegradable but may possess favorable crystallization properties, thermal stability, and high modulus and tensile strength. The combination of polyesters and polyamides could lead to materials that combine the favorable properties of both.¹⁰⁹⁻¹¹¹ Aliphatic poly(ester-amides) have been suggested as a family of biodegradable polymers endowed with good mechanical and thermal properties and processability.¹¹²⁻¹¹⁴

2.3.1 Effect of polymerization temperature and molar ratio of end-groups

The molecular weight of the poly(ester-amide) was strongly dependent on the polymerization temperature and the molar ratio of OX/COOH end-groups.^{II} High-molecular-weight polymer was produced only within a narrow range of these polymerization parameters. A polymerization temperature of 190°C did not favor high molecular weights at any molar ratio of end-groups (OX/COOH ratio from 1.0:1.0 to 1.3:1.0). Evidently, this temperature is too low for an efficient chain extending reaction. The highest molecular weights were obtained at 200°C with the molar ratio of end-groups 1.2:1.0 (OX/COOH). A polymerization temperature of 210°C was too high to produce a high-molecular-weight polymer; thermal degradation of the PEA was marked. The effects of polymerization temperature and molar ratio of the end-groups on the molecular weight of the poly(ester-amide) can be seen in Figure 6. Comparison of the molar ratios 1.1/1.0 and 1.2/1.0 at each polymerization temperature showed that in all cases the highest values were obtained in ten minutes. After that, the thermal degradation of the polymer was faster than the polymerization reaction and the molecular weight started to decrease. The same tendency was noticed at all polymerization temperatures and all molar ratios of end-groups, although the thermal degradation slowed down with decreasing temperature.

The polymerization behavior, and the requirement of an excess of 2,2'-bis(2-oxazoline) for producing high-molecular-weight PEA, can be explained in terms of the thermal instability of the lactic acid based prepolymer at the high temperatures required for effective chain extending. At the beginning of the chain extending reaction, 2,2'-bis(2-oxazoline) reacts quickly with prepolymer chains, forming high-molecular-weight PEA. Evidently, the chain extending reaction is faster than the blocking reaction, where one of the 2-oxazoline rings has reacted, and high-molecular-weight polymer is produced rapidly, even when the 2,2'-bis(2-oxazoline) is used in excess. At the same time, however, thermally unstable prepolymer chains start to degrade and the thermal degradation of the prepolymer chain in PEA generates new carboxyl and hydroxyl end-groups. The excess of oxazoline groups allows them to react readily with carboxyl groups but not with hydroxyl groups. The molecular weight of the poly(ester-amide) increases until all oxazoline groups have reacted or the hydroxyl end-group concentration becomes too high and degradation occurs faster than polymerization. The amount of oxazoline must be optimized, since with too

high an excess of oxazoline the blocking reaction becomes dominant and the molecular weight of PEA remains low.

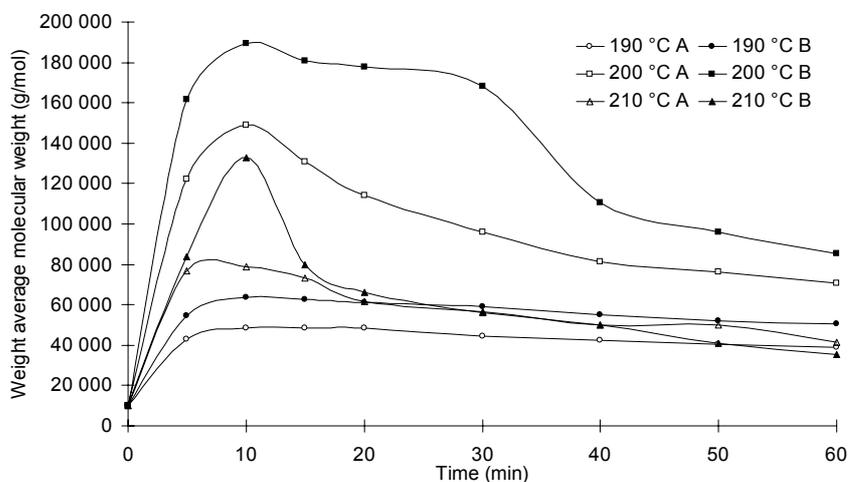


Figure 6. The development of weight average molecular weights in the chain extending reaction with 1.1/1.0 (A) and 1.2/1.0 (B) molar ratios of end-groups at temperatures of 190, 200, and 210°C.^{II}

2.3.2 Characterization of the formed structure

The structure of PEA was identified through comparison of the ^{13}C NMR spectra of L-lactic acid, L-lactide, succinic anhydride, 2,2'-bis(2-oxazoline), prepolymer ESA2%, and poly(ester-amide), and according to Douhi *et al.*¹¹⁵ and Hiltunen *et al.*⁵⁸ The results of the peak assignment are summarized in Table 2. According to ^{13}C NMR analysis of the poly(ester-amide), a chain extending reaction took place and the structure of the PEA was as shown in Figure 1 on page 14. ^{13}C NMR also showed that no significant side reactions occurred during the chain extending reaction.^{II} The carboxyl end-group peak (169.60 ppm) in the prepolymer spectrum disappeared in the chain extending reaction and two new peaks were formed, but all other polymer peaks in the carbonyl area remained the same. The new peaks were due to oxamide carbonyl (159.77 ppm) and to the end-group carboxyl of prepolymer (169.95 ppm), which had reacted with oxazoline group. The three peaks (155.70, 68.37, and 55.10 ppm), due to the 2,2'-bis(2-oxazoline) monomer, could not be seen in the poly(ester-amide) spectrum, which confirms that all of the BOX monomer reacted during the chain extending reaction. In the methine area of the poly(ester-amide) there was a new peak (63.56 ppm) due to the 2,2'-bis(2-oxazoline) unit (CH_2) in the polymer chain, and the CH peak (68.78 ppm) near the end-group carboxyl peak in the prepolymer spectrum had disappeared. The other CH_2 peak (38.51 ppm) due to the 2,2'-bis(2-oxazoline) unit in the polymer chain was in the methyl area. Carbons of the succinic acid unit were in the methyl (28.61 ppm) and carbonyl (170.21 ppm) areas. FTIR and titrimetric results were in accordance with ^{13}C NMR analysis.

Table 2. Identified groups and ^{13}C NMR spectral data (ppm) of prepolymer ESA2% and poly(ester-amide).^{II}

<i>Group</i>	<i>Lactic acid chain units in prepolymer</i>	<i>Lactic acid units near COOH end-groups</i>	<i>Succinic acid chain units</i>	<i>Lactic acid units near succinic acid units</i>	<i>Oxazoline chain units</i>	<i>Lactic acid units near oxazoline units</i>
$\underline{\text{C}}\text{H}_3$	16.63					
$\underline{\text{C}}\text{H}_2$			28.61			
$\underline{\text{C}}\text{H}$	69.01	68.78				
$\underline{\text{C}}\text{OO}$	169.64		170.21	169.77, 171.63		169.95
$\underline{\text{C}}\text{OOH}$	169.60					
$\text{CONH}\underline{\text{C}}\text{H}_2\text{CH}_2$					63.56	
$\text{CONHCH}_2\underline{\text{C}}\text{H}_2$					38.51	
$\underline{\text{C}}\text{ONH}$					159.77	

2.4 Sequential and simultaneous addition of chain extenders

Hydroxyl group containing compounds are the most important reactants for isocyanates. Isocyanates also react at different rates with other compounds having acidic protons as mentioned earlier. Among the property requirements for polyester prepolymers, acid value is of particular importance, since the residual acid content of the polyester negatively affects the catalysis of the urethane reaction and decreases the thermal stability of the poly(ester-urethane).^{III,V} Bifunctional carboxyl-reactive chain extenders, such as 2,2'-bis(2-oxazoline), have two advantages: the molecular weight is increased by coupling of two chains and the content of carboxyl end-groups decreases, resulting in improved thermal stability.^{42,115,116,II,IV,V} When these two types of chain extenders are used together, both types of end-groups of the lactic acid oligomers can be exploited for the production of high-molecular-weight poly(lactic acids). The utilization of two chain extenders provides a new way to influence the chain linking of lactic acid polymers: to produce both urethane and oxamide bonds to lactic acid polymer and the possibilities for variations in the polymer structures (e.g. branching), which also affect the properties of the final polymers. In addition, the introduction of sequential or simultaneous addition of 2,2-bis(2-oxazoline) and 1,6-hexamethylene diisocyanate during the final steps of melt polycondensation, allows the use of a lower polymerization temperature and shortens the polycondensation time, which prevents thermal degradation and lactide formation.^{IV,V}

2.4.1 Effect of BOX on the HMDI linking reaction

In the BOX-HMDI chain linking polymerizations^{IV}, the function of 2,2'-bis(2-oxazoline) was to lower the acid value and couple two oligomers to hydroxyl-terminated prepolymer (Figure 7), which was then further chain extended with diisocyanate. In general, reaction behavior between bis(2-oxazoline) and carboxyl terminal groups can be classified into three types: coupling, blocking, where only one of the two rings have reacted, and unreacted.⁴² Both blocking and coupling reactions certainly decrease the carboxyl content of the prepolymer, which is

advantageous for the HMDI linking reaction, but only coupling increases the molecular weight. The coupling and blocking efficiency of bis(2-oxazoline) depends on the structure of the compound and the electron-withdrawing property of the substituent at position 2 in the oxazoline ring. Previously, Inata *et al.*⁴³ have found that once one of the two rings of 2,2'-bis(2-oxazoline) is involved in the reaction, it increases the reactivity of the other ring and thus accelerates the coupling reaction. Moreover, in this system the high reactivity is partly due to the structure of the terminal carboxylic acid, which determines the acidity of the end-groups and thus affects the reactivity of carboxyl-terminated prepolymer with bis(2-oxazoline).

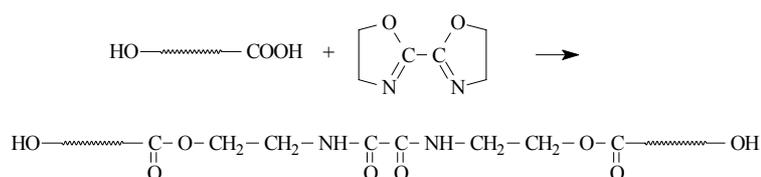


Figure 7. Reaction between BOX and carboxyl groups of lactic acid oligomer.

As seen in Figure 8, the increase in molecular weight is twofold when 2,2'-bis(2-oxazoline) connects two E0% oligomer chains together. Similarly, as in the HMDI coupling, once the BOX linking begins, the small molecules will disappear from the MWD curves. The acid value decreased from 11 to 3 mgKOH/g in 30 min reaction time, to the level of typical hydroxyl-terminated lactic acid prepolymer. Nevertheless, this acid value level is slightly higher than for the prepolymers generally used in urethane chemistry. In E2% prepolymer, where the initial acid value is already low, the addition of BOX did not seem to have an effect on either the acid value or the molecular weight.

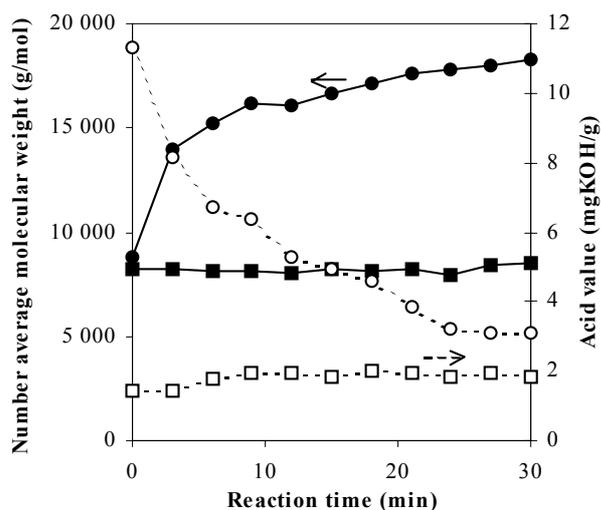


Figure 8. Effect of BOX in COOH/OX ratio 1:1.1 on molecular weight (—) and acid value (---) of E0% (○) and E2% (□) prepolymers.^{IV}

The effect of the amount of 2,2'-bis(2-oxazoline) on the acid value of prepolymer E0% is shown in Figure 9a. If totally hydroxyl-terminated prepolymer is to be obtained, an equimolar

amount of BOX to the carboxyl groups of the oligomer should be sufficient, since it is not reactive with hydroxyl groups¹⁰⁵. In 30 min reaction time, an equimolar amount of BOX decreased the acid value from 11 to 5 mgKOH/g, whereas without BOX the acid value of the prepolymer increased slightly due to the thermal degradation. When the amount of BOX was increased from 1:1 to 1:2 (COOH/OX), the acid value decreased faster, reaching a considerably lower level. Since the molecular weight increased in proportion to the BOX content (Figure 9b), obtaining prepolymer with doubled molecular weight at a large excess of 2,2'-bis(2-oxazoline), the greater effectiveness of BOX coupling than of blocking reaction was confirmed.

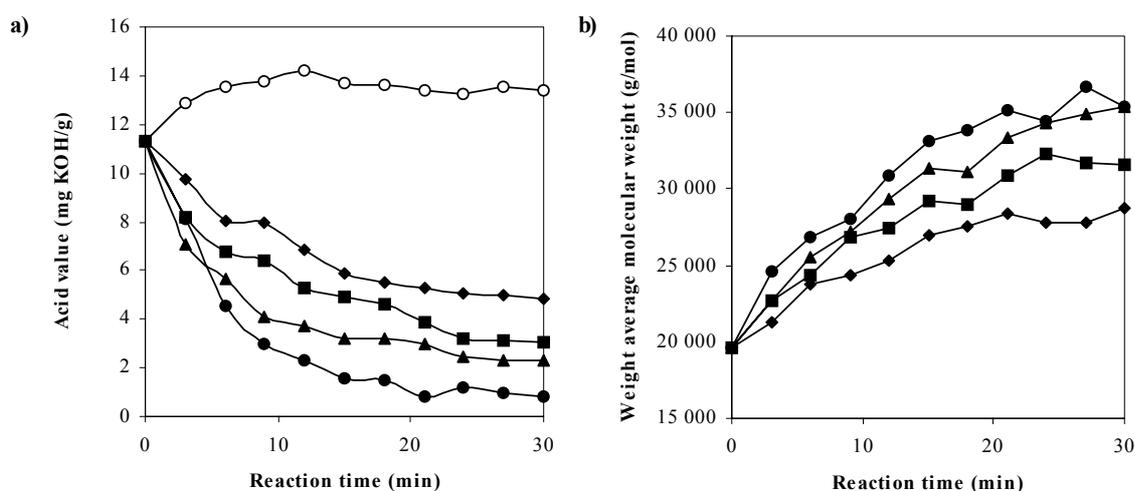


Figure 9. Effect of COOH/OX ratio on a) acid value and b) weight average molecular weight of prepolymer E0%: plain polymer without BOX (○), COOH/OX ratio of 1:1 (◆), 1:1.1 (■), 1:1.4 (▲), and 1:2 (●).^{IV}

The significance of the acid value for the chain linking polymerization behavior of HMDI is shown in Figure 10a, where BOX reacted with the oligomer E0% (COOH/OX ratio of 1:1.1) for a predetermined time (5, 10, and 25 min). The acid values achieved levels of 10, 7, and 5 mgKOH/g, respectively, and then the diisocyanate was added. If the reaction time of BOX was not long enough to reduce the amount of acid end-groups, the result of the HMDI linking was modest; the weight average molecular weight of PEUA was at a low level of 75 000 g/mol. When the acid values were lower before the diisocyanate linking reaction, the molecular weight of the polymer increased significantly, exceeding 170 000 - 190 000 g/mol, and the polymerization rate was much faster. The linking behavior of the two polymers with AV 5 and 7 mgKOH/g was basically the same, although the increase in the reaction rate at the beginning of the polymerization was more dramatic with lower acid values. Indeed, as noticed earlier, the acid content inhibited the reaction between hydroxyl and isocyanate groups. It is also worth noting that the acid values of 5 and 7 mgKOH/g were still fairly high, compared for example with the acid value of hydroxyl-terminated prepolymer E2% (AV 1.4 mgKOH/g).

The BOX ratio of 1:2 with 20 min reaction time before diisocyanate addition decreased the acid value from 11.3 mgKOH/g to as low as 1.5 mgKOH/g. The polyurethane reactions were then conducted at OH/NCO ratios of 1:1, 1:1.1, and 1:1.2, as plotted in Figure 10b. The low acid value had a marked effect on the polymerization rate. If the development of the molecular weight of polymer with OH/NCO ratio 1:1.1 (Figure 10b) is compared with the curves presented in Figure

10a, which are drawn for the same OH/NCO ratio and under the same polymerization conditions, it can be seen that M_w increased distinctly faster with the low acid value, achieving 120 000 g/mol within 15 min. Although there were differences in reaction behavior, the obtained molecular weights were roughly the same. The important observation was that the large excess of BOX prevents the drop in polymer molecular weight at longer reaction times, such as occurred without BOX and with BOX ratio 1:1.1 (Figures 3 and 10a). This is because the BOX or oxazoline end-groups would react with newly formed carboxyl groups, which are formed by thermal degradation of poly(lactic acid) chains, and thus improve the thermal stability of the polymer. It was interesting, however, that the molecular weights stayed at the highest level for as long as 40 min. This is very important from the practical point of view, regarding further processing, for example.

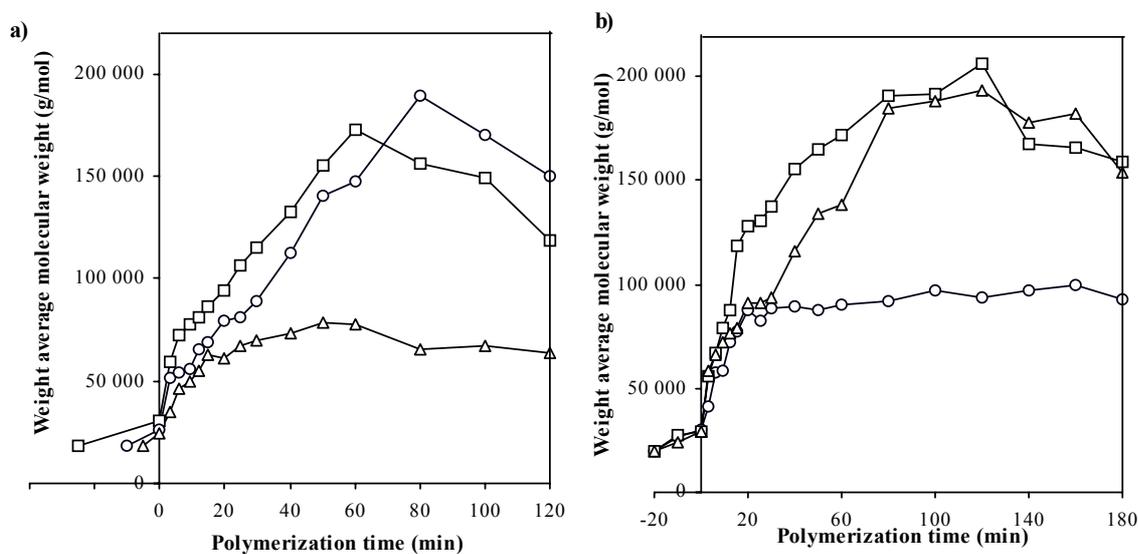


Figure 10. a) Molecular weight development of E0% prepolymer with different acid values (COOH/OX 1:1.1) before chain linking with HMDI (OH/NCO 1:1.1); acid value 10 (Δ), 7 (○), and 5 (◻). b) Molecular weight development versus polymerization time for prepolymer E0% chain linked with BOX (ratio 1:2) and with different amounts of HMDI: OH/NCO ratios of 1:1 (○), 1:1.1 (◻), and 1:1.2 (Δ).^{IV}

The development of the molecular weight was also dependent on the amount of HMDI, and was similar to that for E2% (Figure 3). Since the M_w of prepolymer E0% after BOX linking was three-times that of prepolymer E2%, it was unexpected that the molecular weight obtained was at a somewhat lower level than for E2% in analogous HMDI linking. Similarly, however, a slight excess of diisocyanate (ratio 1:1.2) retarded the development of the molecular weight before M_w reached the high level of 200 000 g/mol. The most striking difference was that the rapid leap in weight average molecular weight and broadening of the molecular weight distribution, which we saw earlier in Figure 3, was absent in these BOX-HMDI chain linking polymerizations.

In hydroxyl-terminated prepolymer E2%, the acid groups were almost totally absent, but because of equilibrium in the polycondensation reaction there are always some residual carboxyl groups. The results, obtained with E2% using a COOH/OX ratio of 1:2 with different ratios of HMDI, were in line with data set out in Figure 3. Indeed, the effect of excess hexamethylene diisocyanate that was noted earlier for E2% can also be seen in Figure 11. In addition, as discussed above, the excess of BOX impeded the drop in molecular weight and the thermal

degradation effect was less pronounced. In this BOX-HMDI combination, the clearest difference associated with BOX was seen for OH/NCO ratio 1:1.2. The 2,2'-bis(2-oxazoline) reacted with the remaining carboxyl groups in the prepolymer and with the carboxyl groups formed by thermal degradation, which meant that there were slightly more isocyanate groups than in the basic HMDI chain extending polymerization. This additional diisocyanate led to branching and crosslinking reactions, which were observed as insoluble fractions in the SEC eluent (Figure 11). The gel fraction measurements, however, demonstrate that the gel content of samples (OH/NCO ratio of 1:1.2) was less than 1%; i.e., polymers were clearly thermoplastic.

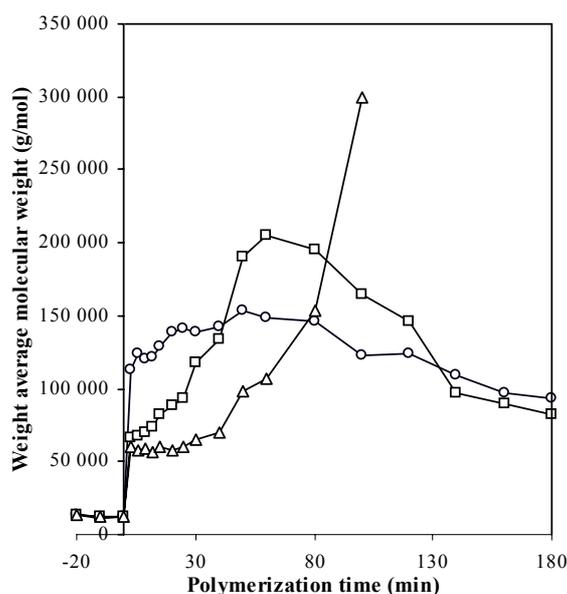


Figure 11. Development of the weight average molecular weight of E2%, which is first linked with BOX (COOH/OX ratio 1:2) and then with HMDI, with OH/NCO ratios of 1:1 (o), 1:1.1 (□), and 1:1.2 (Δ).^{IV}

Characterization of BOX-HMDI chain coupling reactions

An inspection of chain coupling reactions was carried out with FTIR in the spectral regions of 3600 - 3150 and 1850 - 1420 cm^{-1} . BOX reacted with carboxyl groups (broad band between 3400 - 3150 cm^{-1}) of the prepolymer forming oxamide groups shown as a NH peak at 3380 cm^{-1} and amide I and amide II bands at 1685 and 1510 cm^{-1} , respectively. When a large excess of BOX was used in the chain extending reaction, the unreacted 2-oxazoline groups were detected as an absorption band at 1645 cm^{-1} . It is worth noting that the OH peak at 3510 cm^{-1} remained unchanged after BOX treatment, showing that the OX and OH groups did not react with each other. When reaction between prepolymer and 1,6-hexamethylene diisocyanate took place, the hydroxyl peak diminished to a small peak. Meanwhile, an absorption peak for urethane NH formed at 3410 and 1525 cm^{-1} . In addition to these peaks, during the reaction the stretching band of diisocyanate at 2270 cm^{-1} decreased, and in all polymerizations it disappeared upon completion of the reactions.

The coupling reaction between BOX and oligomer E0% was also characterized with ^1H NMR spectroscopy in the spectral region of 5.0 - 3.3 ppm. The two methylenes of reacted oxazoline moieties gave resonances at 4.20 and 3.55 ppm (Figure 12a). Figure 12b shows the spectrum of BOX reacted with E0% at 150°C for 3 min with the molar ratio of COOH/OX 1:2. Besides the reacted oxazoline, the methylenes of unreacted 2,2'-bis(2-oxazoline) can be seen in the triplets at 4.43 and 4.05 ppm and the methylenes of the terminal 2-oxazoline group, whose one ring had reacted with the carboxyl group, at 3.75 and 3.46 ppm.

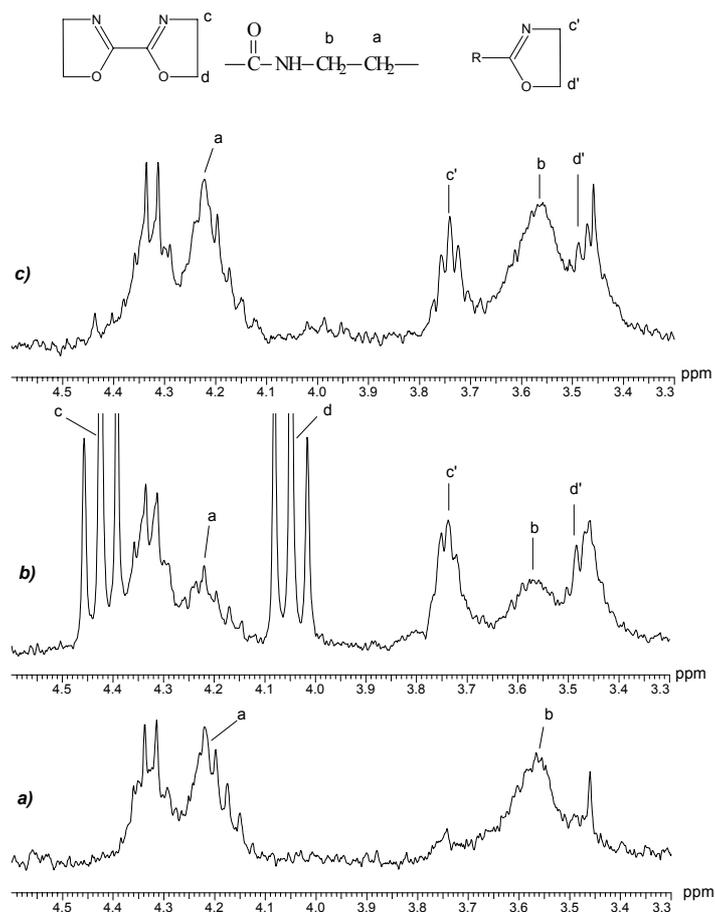


Figure 12. ^1H NMR spectra of E0% coupled with BOX: a) COOH/OX 1:1, b) COOH/OX 1:2 after 3 min reaction time, and c) COOH/OX 1:2 after 15 min reaction time.^{IV}

The reaction of 2-oxazoline and the carboxylic acid end-group is fast, since in the samples taken past 3 minutes reaction time, the triplets of the methylene groups in the monomeric oxazoline ring had disappeared almost completely. In this situation, where the amount of BOX was twofold to carboxyl groups, it could be estimated from integrals that about 60% of BOX monomers had linked two oligomers, i.e. both of the two rings of 2,2'-bis(2-oxazoline) had reacted (Figure 12c). The result suggested that a slight excess of BOX should be used. It was assumed that a small amount of BOX was lost by volatilization from the reaction system and, besides that, some of the monomers were consumed with carboxylic acid groups formed in the thermal decomposition of oligomer. From the rest of the additional BOX, only one ring has reacted. Because these reactions did not prevent the increase of the molecular weight of prepolymer as

seen in Figure 9a, it is improbable that a blocking reaction with the COOH group dominates. The only possible side reaction was the reaction between oxamide and oxazoline groups.^{49,117} Because of the low concentration of the formed bond, this could not be verified by NMR measurements. The essential OH-groups were shown to be unreacted (the peak at 4.32 ppm).

In these BOX-HMDI chain linking reactions, when BOX was allowed to react before HMDI addition, both chain extending reactions took place, as was evident from the FTIR and ¹H NMR spectra mentioned above. In addition, in the case where BOX was used in excess (COOH/OX 1:2), the assigned signals at 3.75 and 3.46 ppm for unreacted terminal 2-oxazoline ring disappeared in the course of the reaction when the highest molecular weight had been reached. It was deduced from the measurements that the 2-oxazoline group did not react with an isocyanate group.

2.4.2 Effect of HMDI on the BOX linking reaction

The effects of 1,6-hexamethylene diisocyanate on the 2,2'-bis(2-oxazoline) linking reaction were studied by adding the chain extenders sequentially and in different amounts.^V The M_w of the prepolymer E0% increased only slightly, from 25 000 to 30 000 g/mol during the first 10 min, when HMDI was in the reaction system (Figure 13), and only the isocyanate reactions described earlier took place. At time point 0 min, BOX was added and M_w started to increase very rapidly. The reaction behavior with the two amounts of BOX (COOH/OX 1:1.1 and 1:2) was clearly different. The M_w increased more rapidly with the larger amount, and similarly AV decreased with BOX1:2 from 8.6 to 0.6 during 20 min reaction time. With the smaller amount of BOX, AV decreased to 3.6 during the same time. Thus, the use of BOX decreased the AV, which also accelerated the reaction between HMDI and -OH and allowed the formation of high-molecular-weight polymer within a short reaction time. The molecular weights obtained were similarly on two different levels, although with the lower ratio of BOX they were also far above the threshold for realizing good mechanical properties in PLA derivatives. It should be noted that some formation of gel occurred during these chain-linking reactions, and thus the molecular weights above the dashed line (Figures 13 and 17) are the M_w values of the soluble fraction. However, the M_w values were proportional to the torque values measured during the chain extending polymerizations. The molecular weights started to decrease after obtaining the maximum values due to lack of reactive groups and degradation of thermally unstable lactic acid prepolymer chains.

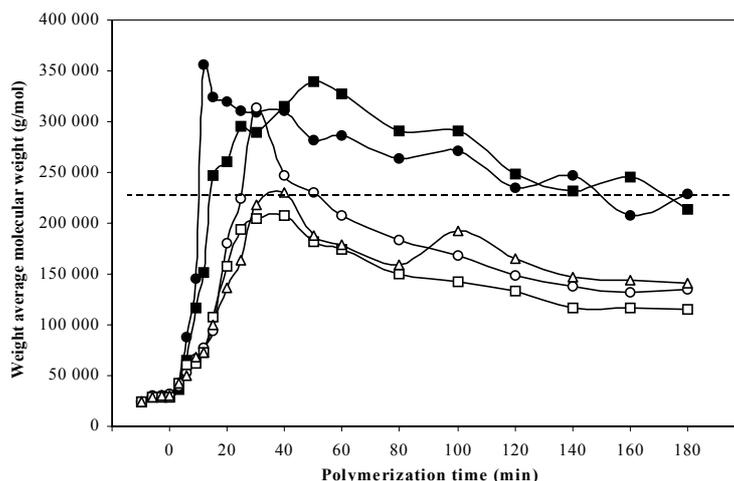


Figure 13. Development of weight average molecular weight for sequential addition of HMDI with OH/NCO ratios of 1:1(o), 1:1.1(\square) and 1:1.2 (Δ), and BOX with COOH/OX ratios of 1:1.1 (open symbols) and 1:2 (solid symbols).^V

The maximum values for gel contents were observed at the highest torque values, i.e., at the highest molecular weights shown in Figure 13. These gel contents were 21 and 41 wt.% for HMDI1:1.0/BOX1:2 and HMDI1:1.1/BOX1:2, respectively. With the lower amount of BOX (COOH/OX 1:1.1), some network formation was observed (13 wt.% gel content) only with the highest amount of HMDI. In the sequential linking, which was performed in the opposite order (BOX-HMDI), no sign of gel formation was observed, even when BOX was used in high excess. In the chain-linking polymerizations of lactic acid based poly(ester-urethanes), gradual branching and network formation have always been observed when the amount of diisocyanate was increased over the unity ratio of NCO/OH.^{59,62,68} Again, in these present polymerizations, gel content was increased when the amount of HMDI was increased, but evidently the mode of addition and the amount of BOX also had a considerable effect on the branching. Other reactions that may lead to branched and crosslinked structures, besides the HMDI reactions presented in Figure 2 c and d, are reactions between BOX and urethane NH or oxamide NH (Figure 14 a and b). In addition, HMDI can react with oxamide NH (Figure 14 c).

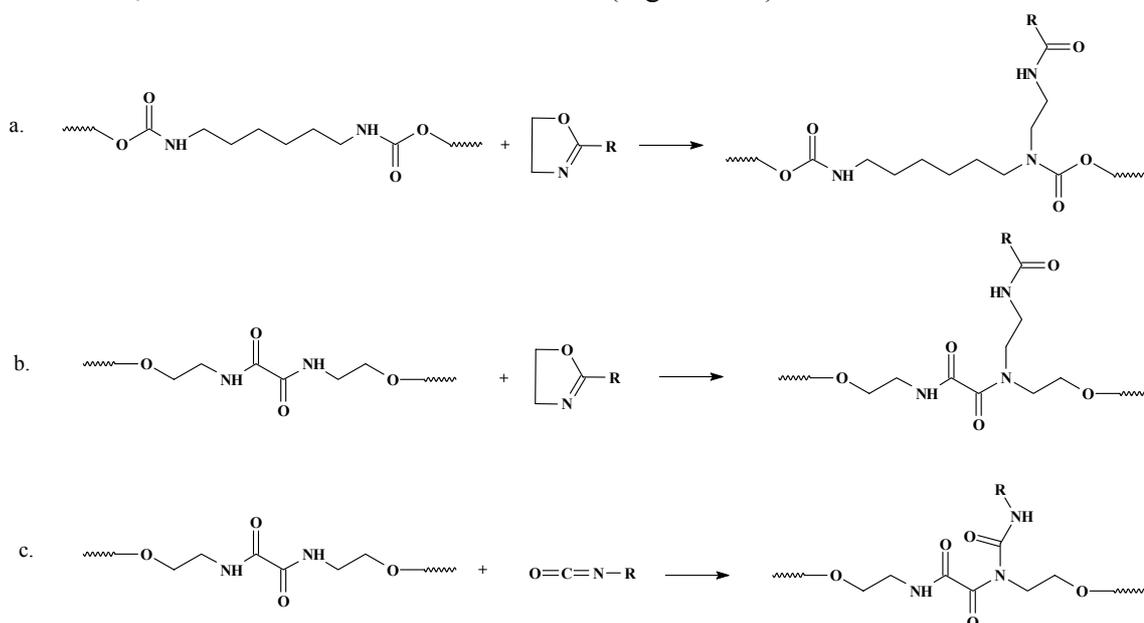


Figure 14. Branching and crosslinking reactions in PEUA polymers.

Characterization of HMDI-BOX chain coupling reactions

Although the reaction rate of urethane formation was relatively slow before BOX addition, due to the poor reactivity between the -NCO and -OH groups in the presence of -COOH, the urethane bond was seen at 155.5 ppm in the carbon spectrum and at 3.12 ppm in the proton spectrum (Figure 15a and 15b). The amide peak due to the reaction between the -NCO and -COOH groups was not observed in either the ^{13}C NMR or the ^1H NMR spectra (156.3 ppm and 6.21 ppm, respectively) confirming the lower reactivity of -NCO with -COOH than with -OH. Immediately after the addition of BOX, the formation of an oxamide group due to the reaction between BOX and -COOH groups was seen at 159.6 ppm (^{13}C NMR) and 7.69 ppm (^1H NMR), (Figure 15c and 15d). Some indications of side-reactions were evident as peaks in the NH-region between 155 and 160 ppm in ^{13}C NMR and broadening of the NH peak in the ^1H NMR spectra was observed when the amount of BOX was high. The peaks were due to branching and crosslinking reactions, which were also confirmed by gel content measurements. The amount of branching increased when the amounts of BOX and HMDI were increased.

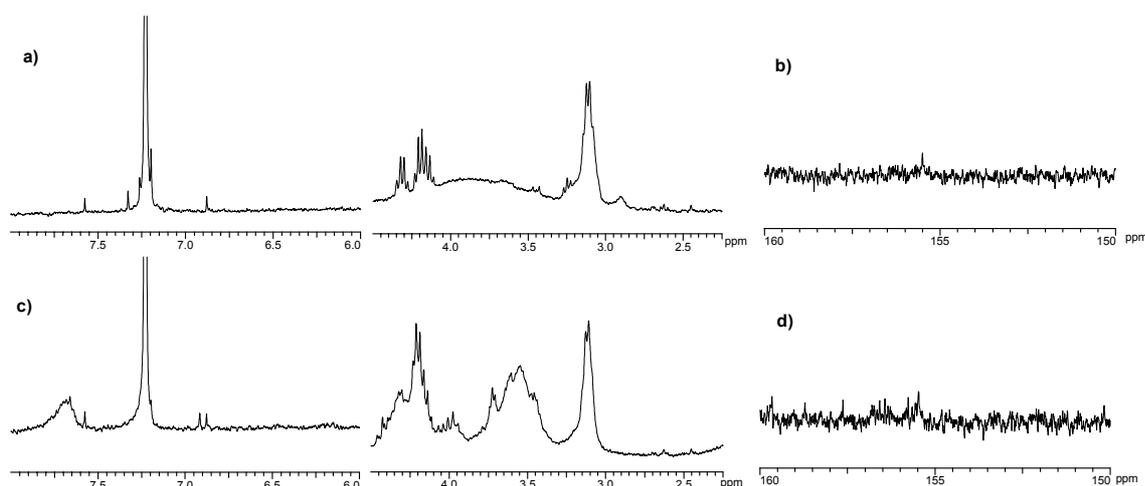


Figure 15. NMR spectra of HMDI-BOX sequential addition polymerizations. (a) ^1H NMR and (b) ^{13}C NMR spectra of E0% chain extended with HMDI in OH/NCO ratio of 1:1.1 at time point 0 min, and (c) ^1H NMR and (d) ^{13}C NMR spectra 12 min after BOX addition at COOH/OX ratio of 1:2.^V

Figure 16 shows the FTIR spectra recording the progress of the sequential linking reaction with HMDI1:1.1 and BOX1:2 during the first 30 min. At time point 0 min, when HMDI has reacted for 10 min with both -OH and -COOH groups, the amide II peak of urethane at 1520 cm^{-1} and the broad absorption bands caused by COOH-HMDI reactions at $1590\text{--}1550\text{ cm}^{-1}$ and $1650\text{--}1595\text{ cm}^{-1}$ can be observed. Immediately after the addition of BOX (3 min), the top of the peak at 1520 cm^{-1} shifted to 1512 cm^{-1} , which was earlier assigned as amide II peak formed by the reaction between BOX and -COOH groups. However, this absorption had a very broad shoulder, which also includes all the other amide II peaks due to the side reactions. The amide I peak of the oxamide group at 1684 cm^{-1} was similarly observed immediately after BOX addition, and this gradually increased in intensity with the reaction time. The peak at 1645 cm^{-1} , which appeared

after 6 min and likewise increased in intensity with reaction time, is associated with the C=O peak of a tertiary amine. This again revealed the formation of branched and crosslinked structures.

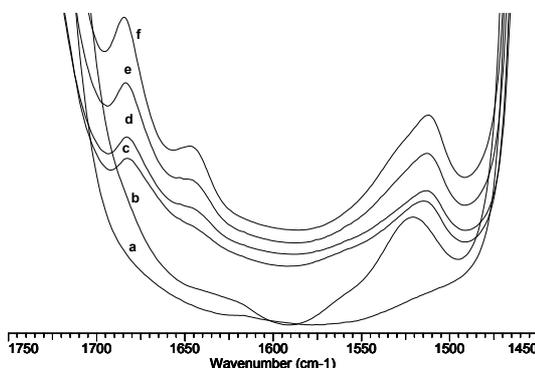


Figure 16. FTIR spectra of (a) prepolymer E0%, E0% chain linked with sequential addition of HMDI (OH/NCO 1:1.1) and BOX (COOH/OX 1:2) after (b) 0 min, (c) 3 min, (d) 6 min, (e) 9 min, and (f) 30 min polymerization time.^v

2.4.3 Effect of simultaneous addition of HMDI and BOX on the linking reaction

In the case of simultaneous addition of chain extenders, i.e. HMDI and BOX fed to the reactor at the same time, immediately after the prepolymer had melted, many competing reactions occurred concurrently in the reaction system.^v As can be seen in Figure 17, the M_w of the polymer increased rapidly after addition of chain extenders, especially with the higher amount of BOX (COOH/OX ratio of 1:2). The molecular weights achieved with the COOH/OX ratio of 1:1.1 and 1:2 were again on two different levels. When the results of the chain linking polymerizations of the same prepolymer E0% with simultaneous addition of HMDI and BOX (Figure 17) and HMDI-BOX sequential addition (Figure 13) are compared, it can be seen that the molecular weights increase somewhat more slowly in the simultaneous addition. Even with the prepolymer E0% from a different batch^{IV}, a slightly faster increment in the molecular weights was also seen at the beginning of BOX-HMDI sequential addition polymerizations (Figure 10b) compared with simultaneous addition. In the simultaneous addition, corresponding acid values at time point 20 min were 1.9 mgKOH/g for BOX1:2 and 4.1 mgKOH/g for BOX1:1.1. The molecular weights obtained for BOX 1:2 were roughly the same as in the HMDI-BOX sequential addition polymerizations, but with BOX 1:1.1 the levels reached were not so high. The maximum values for gel content were in simultaneous additions with BOX1:2, 23% for HMDI1:1.0 and 27% for HMDI1:1.1, so that there was no significant difference between the two. With BOX1:1.1, in contrast, no gel formation was observed. The effect of the amount of HMDI on the formation of gel was not as obvious as in the case of the HMDI-BOX sequential addition of chain extenders, where the amount of gel increased with the amount of HMDI. The decrease in molecular weight due to the thermal degradation after the maximum was observed, similar to the case with HMDI-BOX sequential addition.

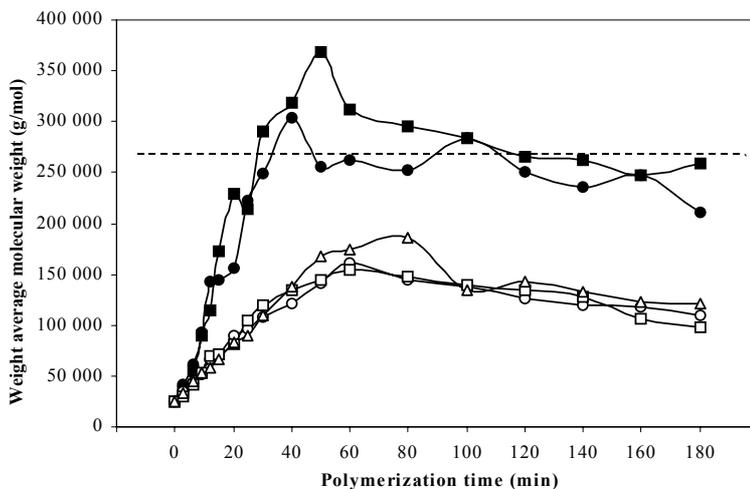


Figure 17. Development of M_w for lactic acid prepolymer chain extended with simultaneous addition of HMDI and BOX: COOH/OX ratios of 1:1.1 (open symbols) and 1:2 (solid symbols) and OH/NCO ratios of 1:1(o), 1:1.1(\square), and 1:1.2 (Δ).^V

Characterization of simultaneous HMDI and BOX chain coupling reactions

FTIR signals were in accordance with the above results and with the expected structures. Amide I (at 1684 cm^{-1}) and amide II (at 1512 cm^{-1}) peaks due to the oxamide group were of the same shape as peaks in the HMDI-BOX sequential addition and were seen immediately after the addition of the chain extenders. The tertiary amine peak at 1645 cm^{-1} , indicating branched or crosslinked structures was also detected, after just 6 min, although the shape of the peak was flatter than in the HMDI-BOX sequential addition. The weak absorption bands at $1590\text{--}1550\text{ cm}^{-1}$ and $1650\text{--}1595\text{ cm}^{-1}$, due to the COOH-HMDI reactions, were only seen with the COOH/OX ratio of 1:1.1 (after 3 min), as in the sequential addition, and not with the COOH/OX ratio of 1:2, i.e., when there was a large excess of BOX that could react with the -COOH groups. ^{13}C NMR and ^1H NMR studies supported the FTIR results indicating the formation of branched structures, but a smaller amount than in the HMDI-BOX sequential addition.

In the case of the HMDI-BOX sequential addition of chain extenders, HMDI accomplished a wide variation in structures, increasing the possibilities for side-reactions. The probability for the formation of crosslinked structures increased when HMDI was added first, and the gel formation was fast after BOX addition. In the case of simultaneous addition and BOX-HMDI sequential addition, by contrast, the fast reactions of BOX favor chain extending reactions over the branching reactions. It was confirmed, therefore, that the branching and crosslinking were highly dependent not only on the amount of chain extenders but on the order of addition.

It can be concluded that BOX reacts with -COOH groups more selectively than HMDI reacts with -OH groups. Both chain extending reactions are accompanied by side-reactions, but the chain extending efficiency of BOX outweighed the other reactions. BOX reacted very rapidly with the carboxylic acid end-groups, which otherwise retarded the reaction between HMDI and

hydroxyl groups. In addition, the blocking reaction of HMDI seemed to be more probable than the chain coupling reaction, especially when HMDI was used in excess. This partly explains, together with the differences in the prepolymers, the lower molecular weights in the BOX-HMDI sequential additions. Moreover, these COOH-BOX reactions reduced the probability of the reaction between HMDI and carboxylic acid end-groups. Thus, fewer amide groups, able to participate in further branching reactions, are formed in the simultaneous and BOX-HMDI sequential addition of chain extenders than in the HMDI-BOX sequential addition. In the HMDI-BOX sequential addition, HMDI had more time to react with -COOH groups, and through reactions with amide and urethane formed branches before BOX addition. The formation of amide bonds seemed to play an important role in the formation of branches and crosslinks. The BOX addition before HMDI supported this, since when BOX was allowed to react with all carboxylic acid end-groups before the HMDI addition, crosslinking or gelation did not occur, even with a large excess of BOX. Thus, it seems probable that the formed amide groups rather than the oxamide or urethane groups reacted further, forming branches.

2.5 Properties of the chain linked lactic acid based polymers

The physical properties of the chain linked lactic acid polymers are determined by the chemical nature of the repeating ester chain, the chain extender and BD or SA units to lesser extent, the molecular weights and molecular weight distributions, the stereochemistry, and the molecular architecture e.g., linear, branched, or crosslinked structure. Basically, the properties of the chain linked lactic acid based polymers were typical for lactic acid polymers: high strength and high modulus polymer with T_g around 50°C. All synthesized PEUs, PEAs, and PEUAs, excluding PEUA in publication V, were completely amorphous, as were the prepolymers.^{I-IV,VI} The PEUAs, which were made of slightly crystalline prepolymer E0%^V, showed a melting endotherm in the range 134-138°C. However, the highest melting endotherm was as low as 3.2 J/g. The glass transition temperatures of PEU, PEA, PEUA were dependent on the molecular weight, amount of D-structures, linearity, and amount of crosslinking. Crosslinking and branching increased the T_g of the polymer by introducing restrictions in chain mobility. Also, stiff BOX units stiffened the polymer chains, which was seen in slightly higher tensile modulus and strength, and lower strain. The properties of PEUs, PEAs, PEUAs, and a reference polymer PLLA are collected in Tables 3, 4, and 5.

The advantage with the use of a chain extender or two chain extenders, in order to produce urethane, oxamide or both bonds to lactic acid polymers or to other biodegradable polyesters, can be seen in the special characteristics compared to pure homopolymers. The benefit of these structure units in lactic acid polymers can be seen as new properties in the different applications. The hydrolysis and biodegradation rate were especially accelerated.^{I,VI} This can be utilized in waste management, as well as in biomedical applications such as controlled drug release device materials with new degradation or release profiles¹⁰⁶⁻¹⁰⁸ and fracture fixation materials having high strength combined with amorphous nature and fast degradation^{114,128,129}. In addition, chain linking provides a new way to influence the molecular architecture of polymer structures (e.g., branching and crosslinking) and molecular weight distribution, which also affect the rheological

properties and processability of polymers in the different processing equipment and can be utilized e.g. in film extrusion coating of paper and fiber spinning applications.

Table 3. Mechanical properties of PEU, PEA, and PEUA.

<i>Polymer</i>	<i>COOH/ OX ratio</i>	<i>OH/ NCO ratio</i>	<i>M_n g/mol</i>	<i>M_w g/mol</i>	<i>MWD</i>	<i>Tensile modulus MPa</i>	<i>Tensile strength MPa</i>	<i>Strain at break %</i>
PEU2% ^{H^{IV}}	-	1:1.1	63 000	188 000	3.0	1 640±30	55±4	11±2
PEUA ^{IV}	1:2	1:1.1	53 000	162 000	3.0	1 750±20	57±3	6±3
PEA ^{II}	1:1.2	-	74 000	390 000	5.3	1 720±30	67±4	9±3
PLLA ^a	-	-	n.m.	n.m.	n.m.	1 630±60	62±2	7±1

a) reference, n.m. not measured

3 BIODEGRADATION OF LACTIC ACID BASED POLYMERS

Hydrolysis studies and the controlled compost test were used for the evaluation of the biodegradation of the synthesized chain linked lactic acid based polymers.^{1,VI} In compost environment, biodegradation is a complex process, including both chemical (hydrolysis) and biological processes, which can occur simultaneously. Biodegradation of polymers in the compost should lead to harmless, natural decomposition products such as water, carbon dioxide, and biomass.^{71,VI,118,119} The ecotoxicity of the compost after the composting test was assessed with the test scheme including the Flash test and plant growth experiments. The release of possible toxic components from these lactic acid polymers during the biodegradation was analyzed by high-performance liquid chromatography (HPLC).

3.1 Hydrolytic degradation of poly(ester-urethane)

The hydrolysis behavior of amorphous lactic acid based poly(ester-urethanes) (Table 4) was studied in a buffer solution of pH 7.0 at 37 and 55°C.¹ The effect of temperature on the hydrolysis rate was clearly shown. At 55°C, the decrease in molecular weight and the weight loss were remarkably fast, as shown in Figure 18a. At 37°C, the molecular weight decreased slower than at 55°C and the weight loss occurred later (Figure 18b). The decrease in molecular weight and weight loss were also dependent on the amount of different stereostructures and the length of the ester chain: an increasing amount of D-structures and shortening of the ester chain increased the degradation rate. Both of these lowered T_g of the PEU, which in turn increased the water absorption.

Hetero-chain polymers, particularly those containing oxygen and/or nitrogen atoms in the main chain, are generally susceptible to hydrolysis. For hydrolysis to occur, the polymer must contain hydrolytically unstable bonds such as ester, amide, or urethane, and show some degree of hydrophilicity, as is the case with PEUs and PEAs. In addition, the hydrolysis rate of the polymer is affected by the polymer properties such as molecular weight, glass transition temperature, and crystallinity and also hydrolysis conditions such as pH, temperature, and the presence of enzymes and microorganisms.^{71,120-125,I,VI} The degradation rate and behavior of lactic acid polymers have also been shown to be dependent on the purity of the polymer. Purification of lactic acid polymers removes monomers, oligomers, lactide, catalyst residuals and other impurities, which all promote hydrolysis, and thus reduce water absorption and the degradation process.^{126,127} Unpurified lactic acid based poly(ester-urethanes)¹, absorb much more water and degrade much faster than solvent precipitation purified PEUs^{128,129}.

Table 4. Properties of poly(ester-urethanes) used in the hydrolysis study. (Data from publication I)

<i>Polymer</i>	<i>Prepolymer</i>	<i>D-structures</i> ^a <i>mol%</i>	<i>M_n</i> ^b <i>g/mol</i>	<i>M_w</i> ^b <i>g/mol</i>	<i>MWD</i> ^b	<i>T_g</i> ^c <i>°C</i>
PEU1%H	E1%	25.9	79 700	127 600	1.6	50
PEU2%H	E2%	27.2	68 800	110 200	1.6	47
PEU2%HDL100	E2%DL100	76.4	62 800	103 700	1.7	41
PEU2%HDL50	E2%DL50	64.1	66 200	106 900	1.6	43
PEU4%H	E4%	26.9	46 700	71 500	1.5	44

a) NMR b) SEC c) DSC

Hydrolytic degradation of poly(DL- and L-lactic acids) proceeds by random hydrolytic chain scission of the ester linkages, eventually producing the monomeric lactic acid.¹³⁰ This is the probable hydrolysis mechanism for lactic acid based PEUs^{1,86} and also for lactic acid based PEAs^{106,114,VI}. The molecular weight of the bulk degradable polymers, such as PLA and poly(ϵ -caprolactone) or their copolymers, has to be reduced substantially during the hydrolysis to permit mass loss through solubilization.¹³¹ Mass loss usually begins when molecular weight has decreased to 15 000 g/mol or less.¹³² As can be seen in Figure 18, the weight loss of PEUs began when the M_w was under 20 000 g/mol (or M_n was about 10 000 g/mol), which is in accordance with the known results for PLA polymers. Also, the MWD behaved as expected for lactic acid polymers: MWD started to broaden when the mass loss began.¹³³ At the end of the test period, MWD narrowed again.

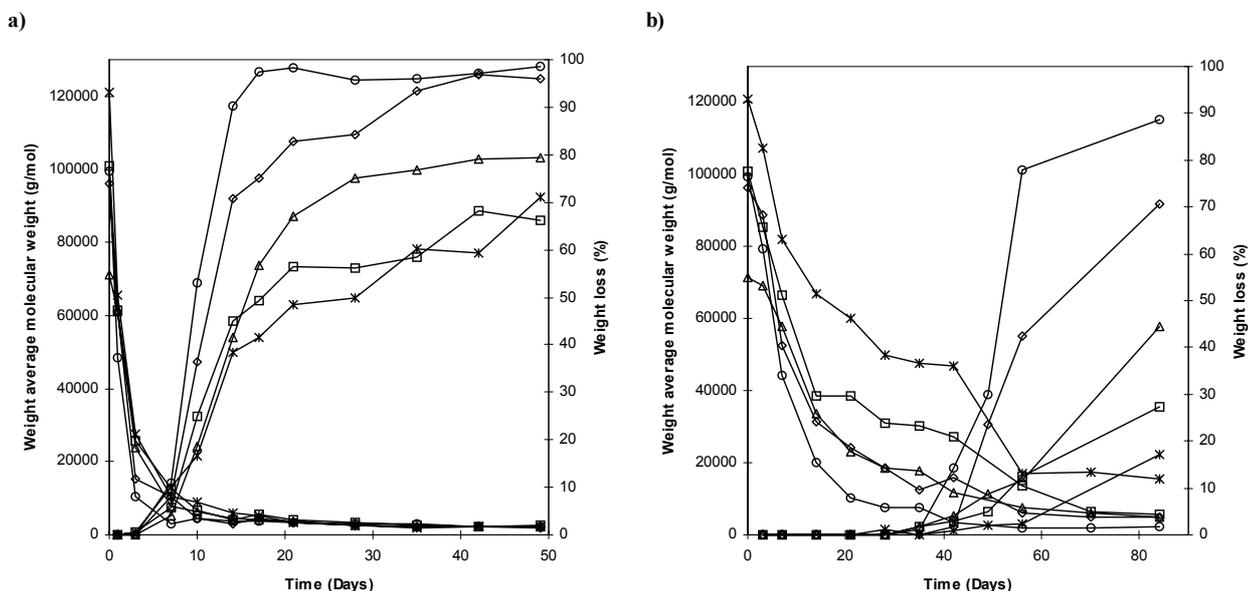


Figure 18. The decrease in weight average molecular weight and the weight loss of PEU1%H (x), PEU2%H (□), PEU2%HDL100 (o), PEU2%HDL50 (◇), PEU4%H (Δ) during hydrolysis at a) hydrolysis temperature of 55°C and b) hydrolysis temperature of 37°C. (Data from publication I)

As discussed earlier, hydrolytic degradation of lactic acid polymers is believed to occur before mineralization occurs in the compost environment.^{80,81,I,VI} Thus, the hydrolysis results at 55°C showed that these types of lactic acid polymers could be composted with other biodegradable material and all of the polymer will degrade during the normal composting cycle.^I The molecular weight of all PEUs had already collapsed after three days hydrolysis. This was remarkably fast, even when considering that the hydrolysis temperature was above T_g .

3.2 Biodegradation in the compost environment

The biodegradation of different lactic acid based polymers was studied under controlled composting conditions (CEN prEN 14046) and the quality of the compost was evaluated (publication VI). The ecotoxicological impact of compost samples, i.e., the ecotoxicity of polymers and their degradation products, was evaluated by biotests, i.e., by the Flash test, and by plant growth tests with cress, radish, and barley. The Flash test is based on kinetic measurement of the bioluminescence of *Vibrio fischeri*, a heterotrophic bacterium capable of light production as a part of its metabolism.

Table 5 summarizes the compositions and the properties of poly(lactic acids), poly(ester-urethanes), and poly(ester-amide) used in the study. All synthesized polyester prepolymers and chain linked PEUs and PEAs were amorphous. Differences in the structural units of these polymers caused variation in the glass transition temperature (Table 5). PLLA was used as a reference polymer.

Table 5. Characteristics of the lactic acid polymers used in biodegradation tests.^{VI}

Polymer	Prepolymer composition (in feed, mol%)			Chain extending reaction		Carbon content	SEC		DSC		
	LA	BD	SA	extender	wt. %	Carlo-Erba wt. %	M_w g/mol	MWD	T_g °C	T_m °C	% ^{a)}
E1%	99	1	-	-	-	50.2	14 000	1.8	45	-	-
E4%	96	4	-	-	-	50.3	5 500	1.5	25	-	-
PEU1%H	99	1	-	HMDI	2.0	50.0	97 000	3.2	48	-	-
PEU4%H	96	4	-	HMDI	8.3	51.1	71 000	1.7	44	-	-
PEU4%B	96	4	-	BDI	7.2	50.8	180 000	3.0	45	-	-
PEA	98	-	2	BOX	3.7	50.7	200 000	3.0	52	-	-
PLLA ^b	-	-	-	-	-	50.2	305 000	1.7	61	176	50

a) crystallinity; 93.6 J/g was used as the melting enthalpy for 100% crystalline poly(L-lactide)^{92,93} b) reference

3.2.1 The effect of polymer structure on biodegradation

All the studied polymers biodegraded to 90% of the positive control (PC), i.e., produced 90% of the theoretical CO₂ during six months, and thereby met the requirements set in the CEN standard for biodegradability of packaging materials. The biodegradation results are shown in Figure 19.

The biodegradation percentage of the prepolymer E4% was 85% ($\pm 3\%$) during 112 days, which was equivalent to 90% biodegradation relative to the biodegradation of the positive control. As expected, the biodegradation of the prepolymer began with a shorter lag-period than that of the actual polymer samples. The biodegradation percentages of the tested polymers were 87% ($\pm 4\%$) for PEU1%H, 95% ($\pm 6\%$) for PEU4%H, and 100% ($\pm 9\%$) for PEA in 112 days; and 91% ($\pm 0.2\%$) for PEU4%B in 70 days.

The difference between the degradation of PEU1%H and PEU4%H with different length poly(lactic acid) chain and different amounts of 1,6-hexamethylene diisocyanate was about 8%. The biodegradation of PEU4%H was slightly faster throughout the whole composting experiment. This is in agreement with a previous biodegradability study, which was carried out using the headspace test⁸⁶. To determine the effect of different chain extender on degradation, PEU prepared with 1,4-butane diisocyanate was also tested. Even though the biodegradation of PEU4%H and PEU4%B was tested in separate composting experiments, it can be concluded that PEU4%B biodegraded faster than PEU4%H. The lag-time was slightly longer, but after that the degradation rate was faster. This faster biodegradation was attributed to the activating effect of a degradation product of BDI, since the chain linking agent was the only chemical difference between these polymers. In poly(ester-amide), the chain extender was replaced with 2,2'-bis(2-oxazoline), and so oxamide groups were introduced to the polymer structure. Moreover, 1,4-butanediol was substituted with succinic acid in the prepolymer chain. Indeed, it was found that the degradation behavior of PEA was similar to that of PEU1%H and PEU4%H. PEA began to biodegrade after a longer lag-period than that of PEUs, but it reached an even higher level of biodegradation. The extensive biodegradation (100%) of PEA was explained by an error in the measurement arising during the long test period, i.e. diminishing CO₂ levels, or the sample might have activated the degradation of the compost matrix itself, a phenomenon known as the priming effect¹³⁴.

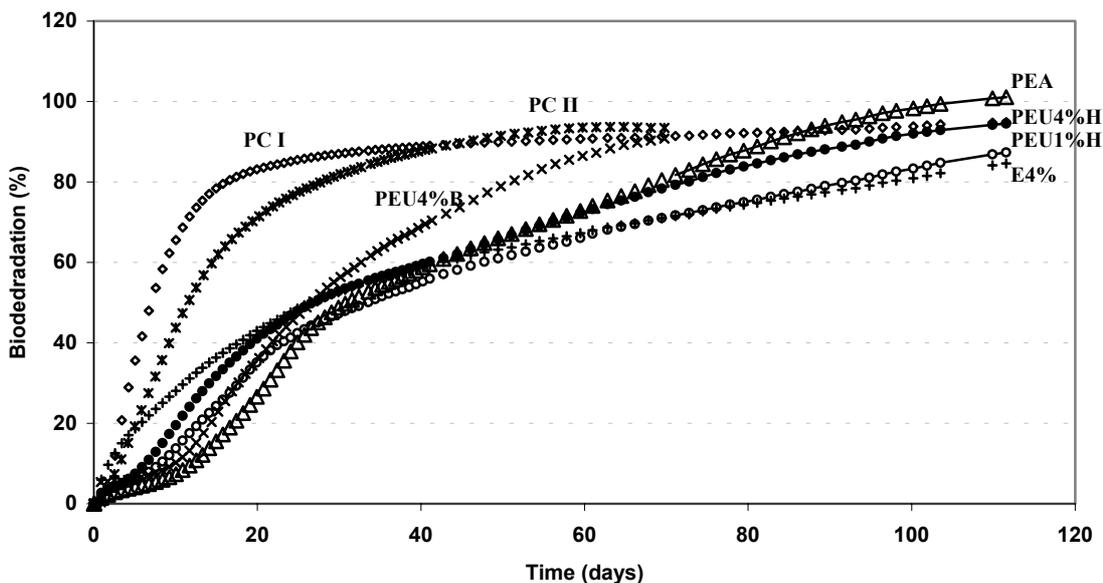


Figure 19. Biodegradation in the controlled composting test: E4% (+), PEU1%H (o), PEU4%H (●), PEU4%B (x), PEA (Δ), PC I (\diamond) and PC II (*).^{VI}

3.2.2 The effect of polymer structure on ecotoxicological impact

Evaluation of toxicity of compost samples by the Flash test

The Flash test, based on the kinetic measurement of bioluminescence of *Vibrio fischeri*, was applied to evaluate the formation of potentially toxic metabolites in the compost matrix during the biodegradation.^{VI} The Flash test measurements were carried out for compost samples after 10, 20, 33, and 45 days of composting and at the end of the composting test, as shown in Figure 20.

Two of the composted polymers, PEU1%H and PEU4%H, produced a toxic response in the test. Toxicity, reported as inhibition in the light production of *V. fischeri*, was highest (73%) with PEU4%H after 33 days of composting. At that point, over 50% of the polymer had already been mineralized to CO₂. The toxic effect was not pronounced, though evident, at the beginning of the composting experiment. As the biodegradation proceeded, more degradation products were released into the compost matrix, raising the acute toxicity level. However, at no point did the toxicity slow the biodegradation rate. The toxicity dropped to 30% inhibition after 112 days when the biodegradation was 95%. Polymer PEU1%H produced a toxic response between 20 and 45 days of composting (biodegradation at 35 to 60%), when the inhibition decreased from 37% to 17%. No toxicity was observed in samples originating from PEU1%H at the end of the composting experiment. The amount of light generated was increased in all the other compost samples, and those samples were declared to be non-toxic to *V. fischeri*.

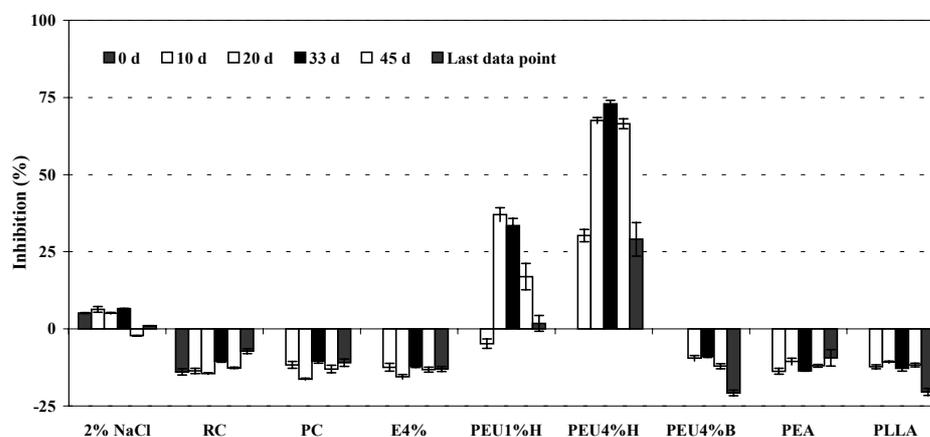


Figure 20. Inhibition in light production of *V. fischeri* in the Flash test: 2% NaCl=test control, RC=reference compost, PC=positive control. Last data point for RC, PC, E4%, PEU1%H, PEU4%H, PEA was 112 days, for PEU4%B 70 days, and for PLLA 202 days.^{VI}

Toxicity evaluation by plant growth test

The growth of cress, radish, and barley were examined to assess the effect of biodegradation intermediates on the quality of the compost product. After a 2-week growth period, plants were harvested; germination and visual growth were observed and gravimetric measurements were

made. The compost samples after the controlled composting test did not have an adverse effect on seedling emergence in any of the tested plant species. However, the compost sample containing PEU4%H caused 33, 24, and 12% inhibition in the plant growth with cress, radish, and barley, respectively. Cress was the most sensitive and barley the most resistant of the three plant species. PEU1%H showed only a minor negative effect on cress growth. With all the other polymers – E4%, PEU4%B, PEA and PLLA – plant growth was excellent.

PEU4%H and PEU1%H had a severe effect on plant metabolism, resulting in chlorosis and damage to the shoot tips. As seen in Figure 21a, 21b, and 22a for PEU4%H, the shoot tips of barley were curled and the edges of the leaves of cress and radish were damaged. The effect of PEU4%H was greater than the similar effect of PEU1%H, which contained fewer 1,6-hexamethylene diisocyanate units. PEU4%B, a similar polymer to PEU4%H but with a different diisocyanate (1,4-butane diisocyanate) used as chain extender, did not cause any visible damage or have a growth inhibiting effect on the plants (Figure 22b). Likewise, PEA and the control samples of E4% and PLLA did not cause any visible changes. Therefore, these polymers can be considered as ecotoxicologically safe.

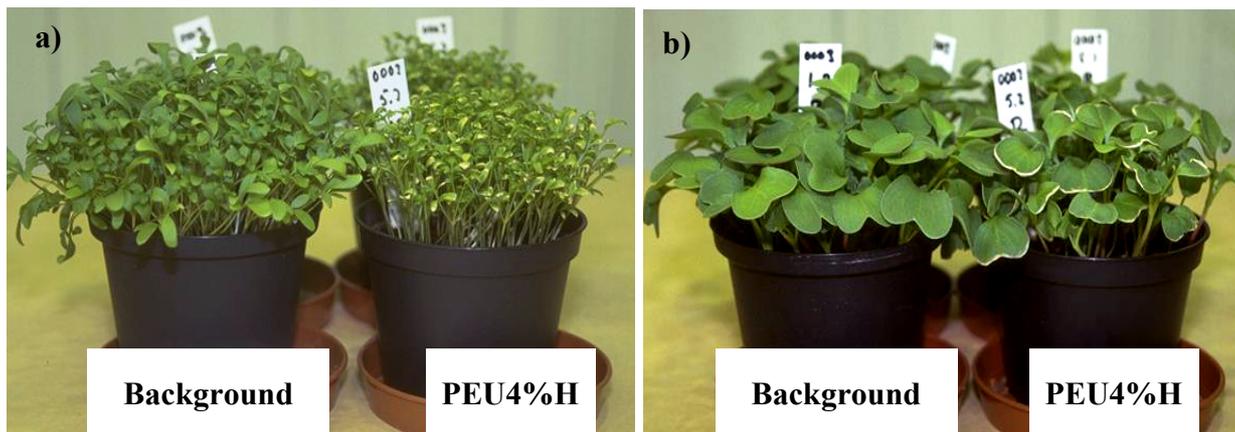


Figure 21. Growth of a) cress, and b) radish in PEU4%H/compost medium, and in background compost medium.^{VI}

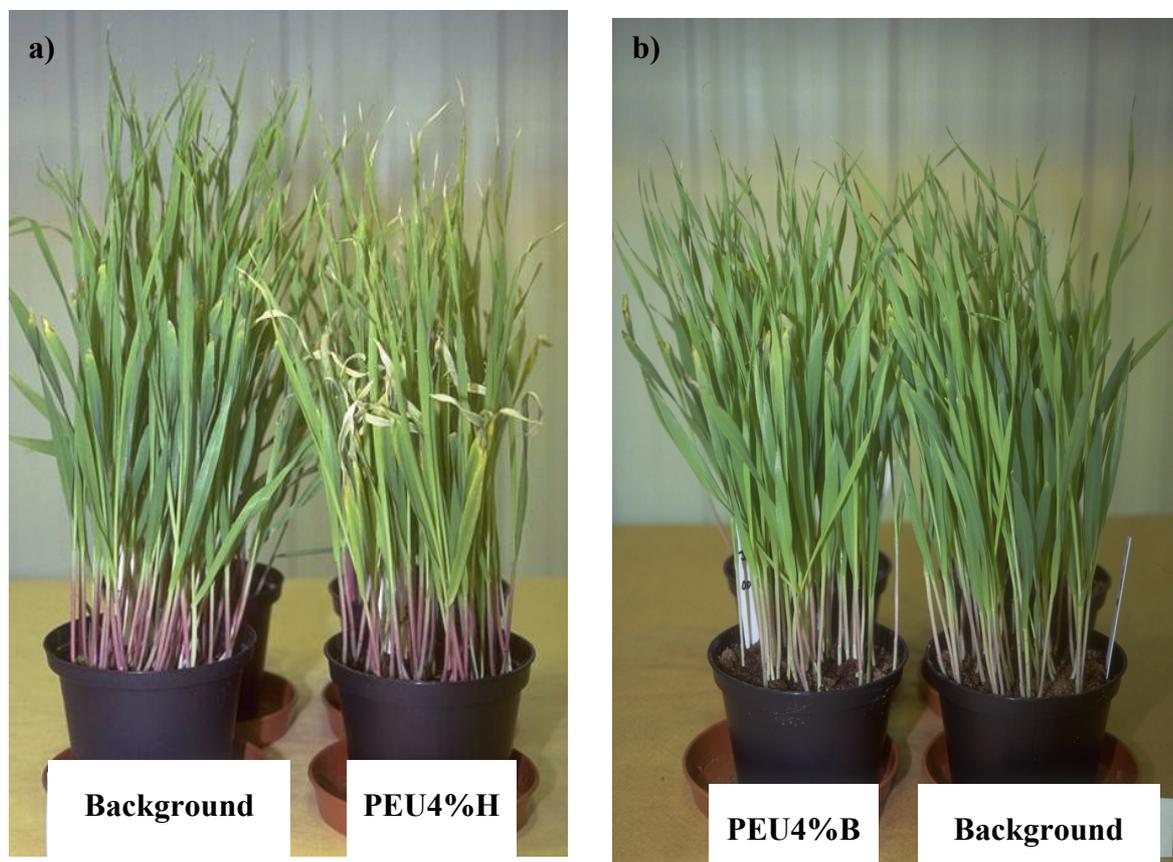


Figure 22. Growth of barley a) in PEU4%H/compost medium, b) in PEU4%B/compost medium, and in background compost medium.^{VI}

3.2.3 Investigation of the ecotoxic substance

As demonstrated both in the Flash test and the plant growth experiments, a clear toxic effect was observed with poly(ester-urethane) samples where chain linking was carried out with HMDI. Since the other tested polymers did not show any ecotoxicological effect, not even PEU4%B where the chain linking was carried out with BDI, the toxicity was evidently due to the breakdown product of HMDI units. The different HMDI concentrations in the PEU1%H and PEU4%H polymer samples caused significant difference in the detection of toxicity, although both samples showed an inhibitory effect. Initially, PEU4%H contained approximately 8 wt.% and PEU1%H 2 wt.% of HMDI. In the Flash test, the inhibition in light production due to PEU4%H was twofold or more, relative to PEU1%H. Also, in plant growth experiments, the toxicity effect was more distinct with the higher concentration of HMDI.

Although HMDI was evidently indirectly responsible for the toxicity, the form in which the toxicity was expressed was not self-evident. It is generally accepted that, in the degradation of polyurethanes, diisocyanate units hydrolyze to the corresponding amines. In particular, the

aromatic amines, which are considered toxic, have been the subject of intensive discussion, since they are formed in the degradation of aromatic diisocyanates (e.g. diphenylmethane diisocyanate).¹³⁵⁻¹³⁷ On the other hand, polyester-based polyurethanes contain many ester bonds that are vulnerable to hydrolysis. Thus, microbial degradation of ester-based polyurethanes is thought to be mainly a consequence of the hydrolysis of ester bonds, at least at the beginning of degradation in the compost environment.¹³⁸ The formation of small molecules in the hydrolysis allows microbiological degradation to begin. The degradation of the diurethane molecules has been found to be highly ineffective relative to the degradation of the poly(ϵ -caprolactone) chain, and thus it has been thought that complete degradation of the polyester would yield undegradable diurethane residue.¹³⁹ However, in this study, the toxicity in the Flash test was already evident in the 10-day sample of PEU4%H (in the 20-day sample for PEU1%H). At that point, only about 20% of the polymer had been mineralized to CO₂. Thus, it is likely that urethane bonds in fact tend to degrade (or hydrolyze) at a surprisingly early stage.

It was established that the toxic compound cannot be the supposed hydrolysis product of the HMDI unit, 1,6-hexamethylenediamine (HMDA), since the concentration at which HMDA showed toxicity in the Flash test was at least 15-times (EC20_{30s}) the highest possible amount in the compost. The toxicity results for the pure chemicals show the threshold values for each compound in the Flash or standardized luminescent bacteria test, i.e., the possible toxicity levels in compost that can be detected with these biotests. This approach does not, however, take into account the combined effects of substances in the compost sample. EC values of all tested chemicals except HMDI were so high that such concentrations could not reasonably be expected to appear after the composting process. The highest possible amount of HMDA that could originate in the hydrolysis of PEU is 2.14 g/kg of compost, calculated from the amount of HMDI in the feed, which is still far below the toxicity level measured in the Flash or the standardized luminescent bacteria test.

Owing to the highly complex organic composition of the compost medium, the extraction and analytical detection of residuals or toxic intermediates at low concentration tended to be more complicated than in a synthetic aqueous environment^{140,141}. Despite this, HMDA was identified in the compost from the controlled compost test by HPLC. The chromatograms showed that only traces of HMDA were left in the compost after the controlled compost test with PEU4%H. Similarly, only traces were seen in the control samples where a known amount of HMDA was allowed to be in contact with native compost slurry. HPLC, like the Flash test above, confirmed that urethane bonds degraded first to HMDA, which then, chemically or biochemically, further converted to a more toxic compound with a concentration that decreased during composting. HPLC analysis, together with the biotests, showed that the toxic compound in the compost was not HMDA, but the toxicity was due to the derivatives or degradation products of HMDA.

The concentrations of polymers and of the degradation products formed during our composting study were much higher than could be expected in a real composting process. The amount of polymer in the biodegradation experiment was about 16% of the dry weight of the compost, whereas the amount of biodegradable polymers in future biowaste is assumed to be a maximum 1 wt.%¹⁴¹. Thus, where toxicity was not detected, the polymer can be considered safe, without negative effects on the compost quality.

4 CONCLUSIONS

Major findings in this work concerning chain linking polymerization, characterization, and the biodegradation of lactic acid based polymers are summarized in the following:

- New lactic acid polymers were synthesized with the use of highly effective hydroxyl- and carboxyl-reactive chain extenders.
 - Poly(ester-amides) provided an alternative to existing biodegradable polymers. Incorporation of a small amount of hydrolytically unstable oxamide linkages to the degradable ester chain changed the degradation behavior and the properties of the polymer.^{II,VI}
 - 2,2'-Bis(2-oxazoline) was an effective chain coupling agent to obtain high molecular weights with a fast reaction rate.^{II,IV,V}
 - With the use of 1,4-butanediisocyanate as a chain extender, the ecotoxicity problem of 1,6-hexamethylene diisocyanate based PEU was solved without altering the other properties.^{VI}
 - PEUA polymers exhibited a combination of the properties of PEU and PEA, thus widening the application field of chain linked lactic acid polymers.^{IV,V}
 - The structures of synthesized polymers were identified and the polymerization behavior of chain extenders with oligomers was evaluated with the use of SEC, NMR and FTIR.^{I-VI}
 - Variations in the polymer structure (e.g., branching) and molecular weight distribution can be achieved, which affect the processability of the polymer and can be utilized e.g. in film extrusion coating of paper and fiber spinning applications.^{II-V}

- The use of 2,2'-bis(2-oxazoline) increased the thermal stability of PLA polymers.^{II,IV,V}
 - BOX can be used to increase the thermal stability of biodegradable polyesters, which is very important from the processing point of view.

- Sequential and simultaneous addition of two chain extenders was a valuable chain extending method.
 - Because BOX effectively decreased the acid value, it enabled a reduction in the polycondensation time of lactic acid polymers and a lowering of the reaction temperature, preventing the thermal degradation and lactide formation.^{IV,V}
 - With this method, oxamide and urethane groups can be introduced into lactic acid polymers and the properties of the polymers are modified.^{IV,V}
 - The mode of addition of chain extenders had a considerable effect on the branching.^{IV,V}
 - Side-reactions for producing branching and crosslinking were detected: amide groups, formed in the reaction between HMDI and the COOH group, rather than

the oxamide or urethane groups, reacted further and played an important role in the formation of branches and crosslinks.^{II,IV,V}

- All the studied chain linked lactic acid polymers biodegraded, i.e. produced 90% of the theoretical CO₂ during the six months set in the CEN standard for biodegradability of packaging materials.^{VI}
 - Lactic acid polymers prepared by the chain extending method were hydrolytically degradable.^I
 - 1,4-Butane diisocyanate and 2,2'-bis(2-oxazoline) based lactic acid polymers were completely biodegradable and showed no ecotoxicological effect.^{VI}
 - 1,6-Hexamethylene diisocyanate based PEUs were biodegradable. However, they showed ecotoxicological effects with the Flash test and plant growth experiment.^{VI}
- 1,6-Hexamethylene diisocyanate should not be used as a structural unit in biodegradable polymers on account of the environmental risk.^{VI}
 - With the applied test scheme, Flash test and plant growth experiment, it was possible to detect the release of toxic components from polymers during biodegradation.^{VI}
 - Urethane bonds, i.e. HMDI units, degraded first to HMDA, which then chemically or biochemically converted to a toxic compound, which caused the detected toxic effect.^{VI}

The benefit of the chain extending polymerization, and the introduction of new functional groups and thus new properties to lactic acid polymers or to other polyesters, can especially be seen in the field of applications. Poly(ester-amide) has been shown, in addition to being compostable and thus suitable for high volume applications, to be a potential polymer for medical applications. The benefit of the PEA structure has been shown in the controlled release of active agents¹⁰⁶ and self-reinforcing¹¹⁴ studies. The use of BOX and the chain extending polymerization have also been utilized in the polymerization of ϵ -caprolactone based poly(ester-amides), which have been shown to be suitable for the preparation of microparticles for controlled delivery of drugs.¹⁰⁷ In addition, the degradation and drug release were enhanced with the aid of these new bonds when compared with poly(ϵ -caprolactone).¹⁰⁸ 1,4-Butane diisocyanate based poly(ester-urethanes) have been studied *in vitro* as a composite material with bioceramic fillers. The PEU composites were biocompatible and were considered suitable for application as fracture fixation materials.^{128,129} The additional benefit of the chain extending polymerization is that the polymerization can be conveniently and economically carried out using the extruder as a polymerization reactor.⁸⁵ Finally, when the applications of the polymers involve commercial products, in contact with the biological environment, polymer properties and toxicological aspects should be taken into account and properly tested at each stage of the life cycle of the product.

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