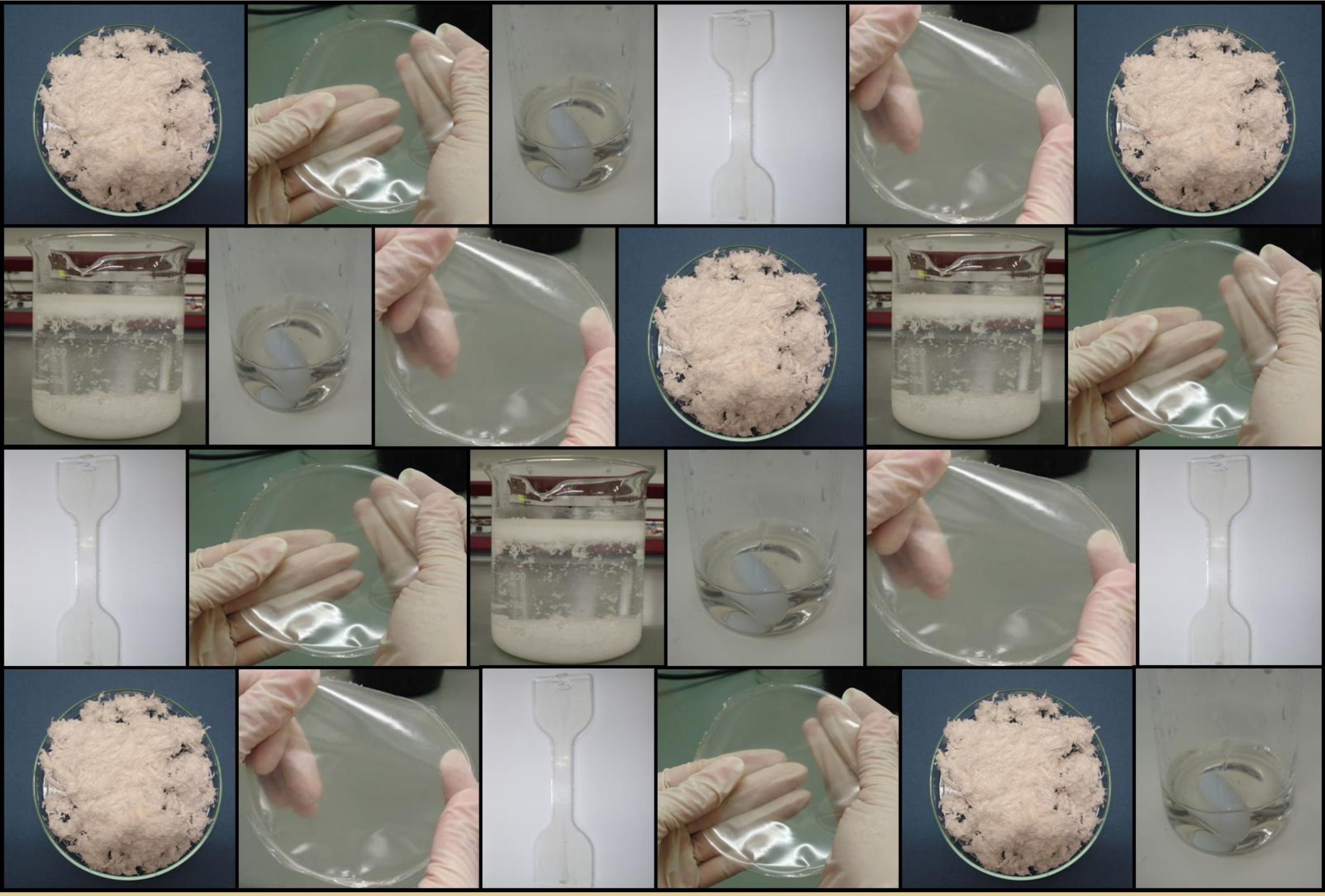

Dina Augusta Simões Marques

Studies on high molecular weight poly(lactic acid) synthesis

Doctoral Thesis

Coimbra
2012

Universidade de Coimbra

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This thesis submitted to the FACULTY OF SCIENCE AND TCHNOLOGY of the UNIVERSITY OF COIMBRA in partial fulfilment of the requirements for the degree of DOCTOR OF PHYLOSOPHY in CHEMICAL ENGINEERING, area of CHEMICAL PROCESSES

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Doctoral Thesis

Supervisors

Professor Doctor Maria Helena Mendes Gil
Professor Doctor Cristina Maria dos Santos Gaudêncio Baptista

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“Recomeça... se puderes, sem angústia e sem pressa e os passos que deres, nesse caminho duro do futuro, dá-os em liberdade, enquanto não alcances não descanses, de nenhum fruto queiras só metade.”

Miguel Torga

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ABSTRACT

The development of sustainable materials, as alternative to petrochemical origin ones, has registered an increasing effort in recent years. One of the most promising substitutes is the poly(lactic acid) (PLA), a synthetic biodegradable polymer obtained from a 100% renewable raw material, the lactic acid. The properties of PLA allow a wide range of applications, from biomedical and pharmaceutical to the conventional large scale polymer uses. Owing to a growing commercial interest it has been an intense research topic over the last few decades. Although it is already manufactured at a large scale, the need for a more cost-effective process remains.

Attempting to contribute to PLA competitiveness, this thesis is mainly devoted to studying conventional step-growth polymerization strategies as alternative approaches to synthesize PLA with a wide rage of molecular weights and different polymer structures. The main focus was achieving high molecular weight PLA, around 100 000 g.mol^{-1}, suitable for large scale applications, but the scope of the thesis was not limited to a particular end use.

PLA synthesis by step-growth polymerization is a reversible reaction requiring continuous by-product withdrawal. Unfortunately, an increase in polymer molecular weight is inevitably associated to an increase in viscosity which jeopardizes by-product removal. To improve by-product elimination, polymerization was carried out under vacuum, stirring, at high temperature and continuous nitrogen flow. The reaction conditions were optimized to reach the target molecular weight. Reaction time and yield, and the final polymer properties, including optical purity, were assessed.

Solution polymerization was the first strategy adopted to perform lactic acid polycondensation. Using organic solvents to reduce the viscosity of the reacting medium and enable continuous water removal, PLA with molecular weight up to 80 000 g.mol^{-1} was obtained in xylene. Although the molecular weight was high, a low yield, a high reaction time and using xylene as solvent that endangers process sustainability, supported the search for an alternative approach.

The use of lactic acid esters as monomers for the PLA synthesis by melt polytransesterification was reported. A catalyst screening step was undertaken and the differences in the chemical structures of the lactate esters tested led to different byproducts, greatly influencing reaction rate and final molecular weight. Ethyl L-lactate was found

particularly suitable for polytransesterification and, among the catalysts tested, the binary catalytic system $Sb_2O/Zn(O_2CCH_3)_2.2H_2O$ was the most effective.

A study on lactic acid polycondensation under melt conditions was performed to assess the direct synthesis of PLA from the monomer, and a new catalyst screening stage was required. Conversely to previous reports on direct lactic acid polyesterification, tin metal was found an efficient catalyst both in terms of molecular weight and yield. Moreover, this catalyst can be completely removed from the polymer matrix, a major asset for some applications, and therefore a great advantage over common tin salts.

Although interesting results were obtained both in bulk polyesterification and polytransesterification, relatively low molecular weights were reached. To overcome this, structure modifications were introduced into the PLA backbone. Two approaches were tested: introducing a branching co-monomer during lactic acid melt polycondensation obtaining star-shaped PLA and chain linking of the lactic acid melt polycondensation prepolymer. The final molecular weight and molecular architecture can be readily adjusted by the choice and the amount of the co-monomer. Chain lengths higher than 100 000 $g.mol^{-1}$, with relatively high optical purity and yields were successful produced. A clear evidence of the successful molecular weight increase was the dramatic raise in torque recorded in the later stage of melt polycondensation experiments. The mechanical performance (tensile strength higher than 40 MPa, elongation at break lower than 6 % and elastic modulus around 1100 MPa) are in the range of those reported for the unmodified polylactide, therefore fulfilling basic requirements for general applications. Thermal characterization results were strongly dependent on polymer composition and architecture. The influence of different central cores, as well as of the linking moieties, was assessed by DSC and TGA. According to WAXS results, no influence on crystalline structure was detected.

Side reactions were also registered in this process. These were: depolymerization into lactide reducing yield and the attainable molecular weight, racemization leading to the random introduction of D-lactyl units in the polymer chain and thermo-oxidation resulting in a yellow coloration. Crystallization was highly dependent on the racemization extent. An important feature of thermoplastic materials is its visual appearance. The yellow coloration of PLA films was evaluated by the standard L* a* b* colour system and compared to a commercial polylactide confirming important yellowing. To some extent colour formation may be avoided by using highly pure nitrogen and thermo stabilizers or, alternatively, colour correction may be applied.

Bioadhesives, from lactic acid condensation products, were also synthesized and assessed. Linear and star-shaped lactic acid oligomers were functionalized with carbon double bonds and further photocrosslinked into a well defined and self-supporting film after few minutes of UV exposure. According to the *in vitro* cell culture, linear lactic acid oligomers modified with methacrylic anhydride showed a moderate swelling ratio and enhanced cells proliferation and therefore may be envisaged as a new and promising material for tissue engineering.

RESUMO

O desenvolvimento de novos materiais, que constituam uma alternativa sustentável aos actuais materiais de origem petroquímica, tem registado um esforço muito significativo. O poli(ácido láctico), PLA, é um polímero sintético, biodegradável, obtido a partir de matéria prima 100 % renovável, o ácido láctico, e considerado um dos materiais mais promissores. As suas propriedades possibilitam um vasto leque de aplicações: biomédicas, farmacêuticas, ou mesmo convencionais. Devido ao crescente interesse comercial, o PLA tem sido alvo de inúmeros estudos científicos e, embora já seja produzido à escala industrial, o desenvolvimento de um processo alternativo mais eficiente permanece um desafio.

Com o intuito de contribuir para uma maior competitividade do PLA, esta tese discute a síntese de PLA por polimerização de reacção gradual, uma via alternativa ao actual processo de síntese por abertura de anel. O objectivo principal centra-se na obtenção de PLA de elevado peso molecular, cerca de 100 000 g.mol^{-1}, adequado para aplicações em larga escala. No entanto, o âmbito da tese não se encontra limitado a uma utilização em particular.

A produção de PLA por polimerização de reacção gradual é uma reacção reversível, requerendo a eliminação contínua do subproduto da reacção. Um peso molecular elevado está inevitavelmente associado a um aumento da viscosidade do meio, dificultando a remoção do subproduto. As condições de polimerização, realizada sob vácuo, a temperatura elevada, com agitação e fluxo contínuo de azoto, foram optimizadas de acordo com o peso molecular pretendido e as propriedades finais do polímero.

A policondensação do ácido láctico em solução foi a primeira via estudada. A utilização de solventes orgânicos permitiu reduzir a viscosidade do meio reaccional facilitando a remoção da água e o PLA obtido, usando xileno como solvente, atingiu um peso molecular de 80 000 g.mol^{-1}. Embora o peso molecular fosse elevado, o rendimento foi reduzido e o tempo de reacção longo. De salientar ainda que o recurso a solventes orgânicos põe em causa a sustentabilidade do processo, o que levou à procura de estratégias alternativas.

Na literatura não há informação sobre a utilização de ésteres derivados do ácido láctico na síntese de PLA por politransesterificação na massa, e este foi o segundo desafio deste trabalho. As estruturas químicas dos vários ésteres testados, bem como o catalisador adicionado, influenciaram significativamente a velocidade de polimerização e o peso molecular do produto final. O lactato de etilo conduziu aos melhores resultados obtidos nos

ensaios de politransesterificação e o sistema catalítico Sb2O/$Zn(O_2CCH_3)_2.2H_2O$ foi o mais eficiente.

A dificuldade em obter um polímero de elevado peso molecular levou ao estudo da síntese de PLA por policondensação directa do ácido láctico na massa, o que envolveu uma nova etapa de selecção de catalisador. Contrariamente aos estudos publicados, concluiu-se que o estanho metálico é um catalisador eficiente, tanto em termos de peso molecular como de rendimento. Uma vantagem adicional consiste no facto de este catalisador poder ser completamente removido da matriz polimérica, constituindo uma boa alternativa aos sais de estanho vulgarmente utilizados.

Os resultados obtidos por poliesterificação e por politransesterificação na massa foram interessantes, mas o desafio permanecia. O aumento do peso molecular passou pela introdução de alterações na estrutura do polímero. Foram estudadas duas abordagens diferentes: o uso de co-monómeros com vários grupos funcionais para promover a síntese de PLA com estrutura ramificada em estrela, e o uso de co-monómeros que conduzem à extensão de cadeia a partir de pré-polímeros de ácido láctico. Uma selecção cuidada do co-monómero e da quantidade a introduzir permite controlar o peso molecular e a estrutura da molécula final de PLA. Pesos moleculares superiores a 100 000 $g.mol^{-1}$, pureza óptica e rendimentos elevados foram assim atingidos. Os resultados da avaliação mecânica (resistência à tracção superior a 40 MPa, alongamento na ruptura inferior a 6 % e módulo de elasticidade de cerca de 1100 MPa) são semelhantes às propriedades do polilactídeo sem modificação. O comportamento térmico, avaliado por DSC e TGA, é fortemente dependente da composição e da estrutura do polímero final. De acordo com os resultados WAXS, não foi observada qualquer influência na estrutura cristalina.

Reacções secundárias estiveram presentes nos estudos de polimerização. As mais relevantes foram: despolimerização que origina lactídeo, reduzindo o rendimento da reacção e o peso molecular, racemização que leva à inversão da conformação e reacções de oxidação térmica, que resultam no amarelecimento do material. Verificou-se que a cristalização do polímero depende fortemente da extensão da racemização. A importância da cor nos materiais termoplásticos levou à sua avaliação pelo sistema L * a * b * e comparação com um PLA comercial, confirmando a ocorrência de amarelecimento. Confirmou-se que a formação de cor pode ser evitada usando estabilizantes térmicos ou azoto ultra puro durante a polimerização, na literatura a aplicação de correcção da cor é apresentada como uma alternativa.

Em paralelo aos estudos de polimerização avançou-se também no desenvolvimento de bioadesivos de base ácido láctico. Oligómeros lineares e com estrutura em estrela foram funcionalizados com ligações duplas e subsequentemente fotoreticulados, obtendo-se filmes bem definidos após poucos minutos de exposição a raios UV. De acordo com os resultados de cultura celular *in vitro*, o bioadesivo resultante de oligómeros lineares modificados com anidrido metacrílico mostrou uma capacidade de absorção de água moderada e uma boa proliferação celular, podendo ser encarado como um material novo e promissor para a utilização em engenharia de tecidos.

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Symbols	**Definition**
ATR-FTIR	Attenuated Total Reflectance - Fourier Transform Infrared Spectroscopy
b.p.	Boiling Point
DMTA	Dynamical Mechanical Thermal Analysis
E’	Storage Modulus
E’’	Loss Modulus
Σ	Stress
E	Strain
E	Modulus of Elasticity or Young’s Modulus
L* a* b*	Commission Internationale de l´Eclairage
ΔE*	Colour Difference
XYZ	Tristimulus values
YI	Yellowness index
DSC	Differential Scanning Calorimetry
Tg	Glass Transition Temperature
Tc	Crystallization Temperature
Tm	Melting Temperature
ΔHm	Melting Enthalpy
Xc	Percentage of Crystallinity
FDA	Food and Drug Administration of USA
GRAS	Generally Recognized as Safe
HPLC	High Performance Liquid Chromatography
^{1}H NMR	Proton Nuclear Magnetic Spectroscopy

MALDI-TOF	Matrix-Assisted Laser Desorption/Ionization – Time of Flight
SEC	Size Exclusion Chromatography
GPC	Gel Permeation Chromatography
PID	Polydispersity
Mn	Number-Average Molecular Weight
Mw	Weight-Average Molecular Weight
BD	1,4-Butanediol
mPET	Pentaerythritol
diPET	Dipentaerythritol
triPET	Tripentaerythritol
ECO	Castor Oil Glycidyl Ether
BADGE	Bisphenol A Diglycidyl Ether
PMDA	Pyromellitic Dianhydride
EDTA	Ethylenediamine Tetraacetic Acid
TEA	Triethanolamine
TAEA	Tris(2-aminoethyl) Amine
HDI	1,6-Hexamethylene Diisocyanate
TDI	Toluene 2,4-Diisocyanate
MAA	Methacrylic Anhydride
IEMA	2-Isocyanatoethyl Methacrylate
PE	Polyethylene
PVC	Poly(vinyl chloride)
PP	Polypropylene
PGA	Poly(glycolic acid)
PHAs	Polyhydroxyalkanoates
PCL	Polycaprolactone
PVA	poly(vinyl alcohol)
PBSs	poly(butylene succinate)s
PBS	Phosphate Buffer Solution
LDPE	Low-density polyethylene
PBAT	poly(butylene adipate-co-terephthalate)
PHB	poly(3-hydroxybutyrate)
PHB-PHV	Poly-(3-hydroxy-butyrate-valerate)

PTFE	Polytetrafluoroethylene
PEA	Poly(ester amide)
PEG	Poly(ethylene glycol)
PET	Poly(ethylene terephthalate)
PTT	Poly(trimethylene terephthalate)
PLA	Poly(lactic acid)
PLLA or L-PLA	Poly(L-lactic acid)
PDLA or D-PLA	Poly(D-lactic acid)
PDLLA	Poly(DL-lactic acid)
ppm	Parts Per Million
PS	Polystyrene
PLC	Programmable Logic Controller
ROP	Ring Opening Polymerization
TGA	Thermogravimetric Analysis
Td	Degradation Temperature
DBSA	4-Dodecylbenzenesulfonic Acid
THF	Tetrahydrofuran
TNBT	Titanium(IV) Butoxide
TMS	Tetramethylsilane
p-TSA	p-Toluenesulfonic Acid
PPh_3	Triphenylphosphine
MTS	3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium
OP	Optical Purity
SEM	Scanning Electron Microscopy
SSP	Solid State Polymerization
UV/vis	Ultraviolet-Visible Spectroscopy
WAXD	Wide-angle X-ray Diffraction
ASTM	American Society for Testing and Materials
EN	European Standard
ISO	International Organization for Standardization
LCA	Life-Cycle Assessment

I. SCOPE AND STRUCTURE OF THE THESIS

The increasing demand for biodegradable and biobased alternatives to the current petrol based materials triggered an increased interest in aliphatic polyesters. Among them poly(lactic acid), PLA, is a quite attractive polymer finding applications in the biomedical and pharmaceutical industry but also on large scale uses. Therefore, PLA has become a promising substitute for conventional polymers in some important markets such as food packaging, beverage bottles and disposable textiles, and a growing market is forecasted. Moreover, this biodegradable polymer can be easily processed by conventional techniques used for thermoplastics like injection moulding, thermoforming and extrusion.

The current process for PLA production is based on the synthesis and purification of an intermediate compound, the lactide, involving important costs that prevent its wider use. The literature often refers that the synthesis of high molecular weight PLA by direct lactic acid polycondensation would decrease production costs significantly. This reduction would be due to enabling avoiding the synthesis and purification of intermediate compounds but, on the other hand, process conditions would have to overcome a compromising reaction equilibrium. Until now polycondensation PLA has a low molecular weight and, consequently, poor mechanical properties for widespread applications.

The need for a more cost-effective approach to synthesize lactic acid based polymers is at the origin of this research project. This thesis is mainly concerned with the synthesis of high molecular weight poly(lactic acid), above 100 000 g.mol^{-1}, by conventional step-growth polymerization. Taking advantage of the background knowledge of polycondensation processes, different approaches were tested in order to set the reaction parameters. Step-growth polymerization is currently used in industrial production processes of several polycondensation polymers, but its potential for PLA based polymers production has not been thoroughly explored. Although reaching the target molecular weight may be difficult, this alternative route for poly(lactic acid) synthesis allows modifying the structure and properties, while reducing process complexity. Achieving this goal may lead to an increase in PLA competitiveness when comparing to petrol based polymers and to the current polylactide.

The thesis is organized in seven main chapters. A brief introduction, followed by information on the bioplastics market and its applications, advantages and disadvantages, with a special focus on PLA market is described in chapter 1. The relevance of lactic acid monomer to PLA synthesis and the current production process are discussed. A brief account on PLA properties and a review on different approaches to achieve properties modification are also introduced. An account on the most common methods used for PLA characterization, the experimental set-ups developed to perform the polymerization reactions and the experimental procedures adopted are described in chapter 2. The remaining chapters have several sections including introduction, discussion and conclusion.

Solution polycondensation of the lactic acid in the presence of organic solvents was studied in chapter 3, different lactic acid esters were assessed as monomers for the PLA production by melt polytransesterification in chapter 4 and the direct lactic acid melt polycondensation was investigated in chapter 5. In these chapters, the results obtained were discussed regarding the influence of the experimental parameters (catalyst, reaction time, reaction temperature and pressure) on the final polymer properties, mainly on molecular weight, optical purity and polymer colour. In chapter 3, the lactic acid polycondensation mechanism was also discussed. The influence of the reaction conditions on polymer optical purity and consequently on thermal behaviour was detailed in chapter 4. A careful discussion of the main reactions involved in the PLA synthesis by polycondensation is presented in chapter 5.

In chapter 6, two easily implementable strategies to attain high molecular weight PLA under melt conditions were investigated. The materials synthesized were evaluated from the perspective of large scale application by assessing preliminary hydrolytic degradation and carrying out thermal characterization. The mechanical performance of the selected samples was evaluated by tensile testing and DMTA experiments.

Since the step-growth polymerization experiments required considerably long reaction time, bioadhesives were developed in parallel, as a potential application for the lactic acid polycondensation products. Cytotoxicity was evaluated by *in vitro* cell culture with human fibroblasts. Given the specificity of this research work, the experimental section is included in chapter 7, alongside the discussion of the results obtained.

Finally, a brief account of other research works employing products obtained during the course of this project is reported in chapter 8 and in chapter 9 the overall conclusions are drawn along with some recommendations for further research lines.

1. INTRODUCTION

1.1. Bioplastics

Bioplastics are a large family of materials which, in contrast with conventional plastics, are biodegradable, biobased, or both. Biobased means that an important fraction of carbon in the polymer chain comes from renewable resources, whereas biodegradable means that at the end of product life it can be degraded by biological action [1, 2]. Bioplastics have already been introduced in the consumer market as short life products such as biodegradable mulch films, catering products, paper coating, packaging and waste bags, and also as biomaterials in the biomedical field [1-5]. More recently, durable applications in the consumer electronics, building and automotive industry are under development.

Bioplastics are usually classified according to their chemical composition or synthesis method [6]. However in the present work, they are classified in three different groups according to their biodegradability and biobased content, as shown in Figure 1.1. Comparable to the conventional plastics, properties can vary considerably from material to material.

Wholly or partly biobased no-biodegradable plastics consists on conventional polymers which monomers were obtained from biobased resources, usually from bioethanol modification. An example is the dehydration of bioethanol which leads to ethylene, an important chemical intermediate in the polyethylene (bio-PE) or poly(vinyl chloride) (bio-PVC) synthesis [1, 7]. Bio-PE and partially biobased poly(ethylene terephthalate) (bio-PET) are already being produced, polypropylene (bio-PP) from Braskem and bio-PVC from Solvay are under development. As expected, they have the same properties as their petrol based counterpart and are mainly intended to be used in the consumer electronics segment, textile and automotive industry [1, 7]. Although nearly all plastics are currently made from petrochemicals, this group of bioplastics is growing fast due to the development of new routes to obtain conventional monomers from biobased resources.

Biobased and biodegradable plastics largely used for packaging products include cellulose-based materials (regenerated-cellulose or cellulose-acetate), polyesters such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA) and polyhydroxyalkanoates (PHAs), modified starch and their blends. Similar to the former group, this group of bioplastics is increasing fast due to the development of a multitude of biobased monomers such as succinic acid, butane diol, propane diol or fatty acid derivatives [1, 7, 8].

Biodegradable plastics based on fossil resources are a comparatively small group, most important examples are: polycaprolactone (PCL), poly(vinyl alcohol) (PVA) and poly(butylene succinate)s (PBSs)[1, 7, 8].

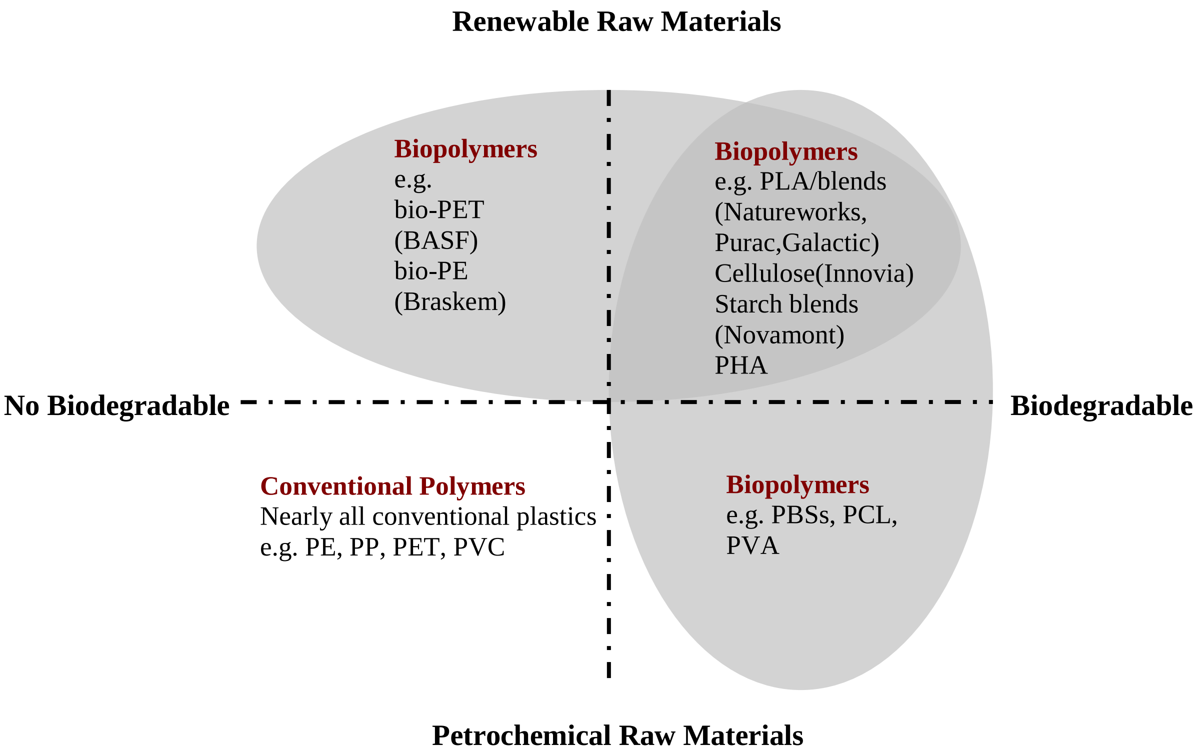

Figure 1.1: Different kinds of bioplastics according to their biodegradability and biobased content, and their producers [1, 7].

The renewable resources may come from agriculture, forestry or byproducts of the food industry. Proteins, starch and cellulose based products, as examples, can be used directly to make bioplastics or also used as raw materials for biological processes leading to polymers such as PHAs, or chemical precursors for further polymerization, such as lactic acid, succinic acid, etc. This is just an overview of the most relevant biopolymers used as bioplastics, detailed description of different biopolymers may be found in numerous review papers and textbooks [4-11]. In spite of the impressive number of biobased building blocks already available from biobased feedstock, the single most important group, which are aromatic based compounds, are not yet available on market [7]. Bioplastics only have advantages over polyolefins if they exhibit similar mechanical performance. Table 1.1 enables comparing properties of currently available bioplastics with some polyolefins [6].

Table1.1: Comparison of bioplastics and polyolefins properties [6].

Polymer	Tg (ºC)	Tm (ºC)	Tensile Strength (MPa)	Tensile Modulus (MPa)	Elongation at break (%)
LDPE	-100	98 – 115	8 - 20	300 - 500	100 - 1000
PS	70 - 115	100	34 - 50	2300 - 3300	1.2 - 2.5
PET	73 - 80	245 – 265	48 - 72	2800 - 4100	30 - 300
PCL	-60	59 – 64	4 - 28	390 - 470	700 - 1000
PVA	58 - 85	180 – 230	28 - 48	380 - 530	-
PBAT	-30	110 – 115	34 - 40	-	500 - 800
Starch	-	110 – 115	35 - 80	600 - 850	580 - 820
Cellulose acet.	-	115	10	460	13 - 15
PLA	40 - 70	130 – 180	48 - 53	3500	30 - 240
PHB	0	140 – 180	25 - 40	3500	5 - 8
PHA	-30 - 10	70 – 170	18 - 24	700 - 1800	3 - 25
PHB-PHV	0 - 30	100 – 190	25 - 30	600 - 1000	7 - 15
PGA	35 - 40	225 – 230	890	7000 - 8400	30
PEA	-20	125 - 190	25	180 - 220	400

1.1.1. Advantages/Disadvantages and Certification of Bioplastics

Following the recent efforts to move from a petrol to a biobased economy, bioplastics are the plastic industry response to the increasing political and social awareness to address the global environment issues and the depletion of the most easily accessible fossil reserves. They are predicted to have a major importance in the development of a future sustainable society offering equivalent functions as current petrol-based materials while reducing environmental impact [1, 9-14]. There are comprehensive advantages of using bioplastics over conventional ones. To quote some of them:

- Use of renewable resources.
- Less dependency on limited and increasingly expensive fossil resources.
- The potential for reducing greenhouse gas emissions.
- The potential for sustainable industrial production.
- Biodegradability and composting options offered by a number of bioplastics.
- Support rural development and innovation.
- An opportunity to differentiate from competition.
- High consumer acceptance

In spite of the motivations for supporting the use of bioplastics, they are also subject to some criticism, mainly, related to the feedstock supply. The majority of the available bioplastics production is based on rich carbohydrate food crops such as grains or beet/cane sugar, the same raw materials used for biofuels, consequently both are blamed to put pressure on food products. Nevertheless, the demand of raw materials for polymer' synthesis will always be very limited comparing to food requirements of an increasing population [7, 10, 15]. The few studies available addressing the impact of bioplastics on agriculture suggest that the potential production of sugar and ethanol from lignocellulosic biomass and food crops waste can be regarded as a possible approach to reduce conflict [2, 16]. Bad agricultural practices and deforestation of protected habitats must also be avoided. Implementing certification schemes may be a feasible solution in order to ensure sustainable biomass feedstock [1, 7].

Besides the current waste disposal alternatives available for conventional plastics, mainly incineration and recycling, biodegradability offers a new attractive recovery option for short life products such as food packaging, catering products or beverage bottles. These products are, by far, the larger market segment in the plastics industry and the major contributor to municipal solid waste. Legislation prevents the use of recycled polymers in direct food contact, and plastics with high technical specifications cannot be made from recyclates [17]. Therefore, biodegradability should be considered as a complement to the other disposal options.

It is important to define the biodegradability concept since it is highly dependent on the polymer chemical structure and biodegradation conditions. Biodegradable plastics can be subjected to industrial composting under oxygen rich conditions, high humidity, controlled temperature 50-70 ºC and a number of microorganisms such as bacteria, fungi, and algae, resulting in harmless products, e.g. water, carbon dioxide and compost [1, 17]. Nevertheless, it is important to emphasize that biodegradable polymers degradation in natural environments may take considerably longer, up to two years, being not a solution for inappropriate waste disposal [9]. The technical specifications for the compostability of bioplastics are available in two harmonised European standards, EN 13423 for packaging and EN 14995 for plastics, or ASTM 6400 and ISO 17088 [1, 17]. Certified compostable products according to these European standards may be treated in the existing composting facilities and advertised with a reliable compostability label, shown in Figure 1.2, being implemented across the entire EU. At the present time, there are no international standards for home compostability, just for industrial one. The European Standardization Committee is now working on developing a standard for determining the biobased content in bioplastics in order to allow consumer easily distinguishing biodegradable and/or biobased from conventional materials and therefore make more informed decisions [1].

Figure 1.2: Compostability logo for products certified according to EN 13432 or 14955 [1].

1.1.2. Bioplastics Market

Nowadays, plastics are key materials, and approximately 250 million tonnes are produced annually, but only a small fraction, less than 1 %, is from renewable resources. According to a recent study at the University of Utrecht the production of bioplastics is estimated to increase from around 700 thousand tonnes in 2010 to 1,7 million tonnes in 2015 [7]. At this early stage, a continuing and steady growth is expected mainly supported by recent governments' policies for promoting the transition from fossil-based to biobased economy such as: US "National Bioeconomy Blueprint" and European competitiveness strategy "Europe 2020". The later has as main targets a 20 % reduction in greenhouse gas emissions compared to 1990, a 20 % increase in energy efficiency and increasing to 20 % the share of renewables in final energy consumption. Bioplastics are regarded as important contributors to reaching the strategy targets [1, 7]. An in depth study [7] of current bioplastics' market, of the companies actively involved, of the emerging trends and projections under several scenarios in the time horizon of 2020 may be found in the PRO-BIP 2009 report of Utrecht University, with a special focus on the European market.

The first successful products in the bioplastics market were PLA compostable packaging, PHA, cellulose or starch-based materials and more recently durable biobased packaging and plastic components from bio-PE and bio-PET. Since 2009 some major brands such as Coca-cola, Volvic, Danone, Puma, Samsung and Toyota [1, 7], among others, have already introduced bioplastics packaging on their products which is an important step toward increasing consumer reconnaissance and acceptance. The biopolymers that contribute most to the current market and its market share (2010) are in Figure 1.3. One can notice that poly(lactic acid) (PLA) is one of the more significant bioplastics, being considered as a promising substitutes to some petrochemical origin materials due to its outstanding features of biodegradability, renewability and mechanical properties [1, 2, 18] similar to those of commodity plastics such as polyethylene (PE), polystyrene (PS) and PET.

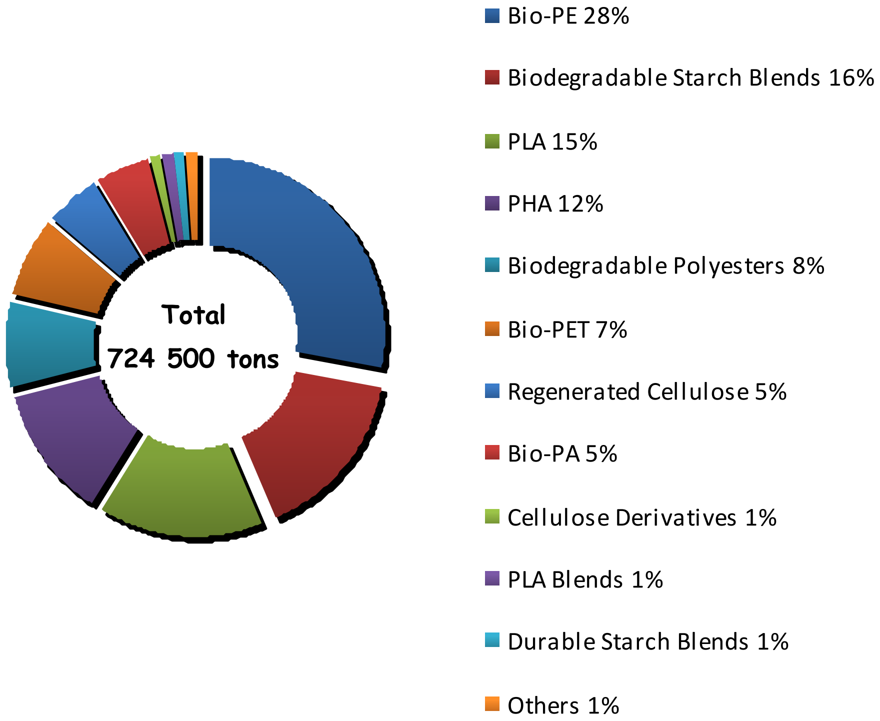

Figure 1.3: Bioplastics production in 2010 [1, 7].

1.2. Poly(Lactic Acid)

1.2.1. Poly(Lactic Acid) Market and Applications

Poly(lactic acid) or polylactide is a synthetic biodegradable polyester obtained from a 100 % renewable raw material, the lactic acid. It has huge potential to be used as bioplastic in large scale applications: in agriculture as mulch films, fertilizer and pesticides delivery devices; no woven fibres and disposable garments in the textile industry, such as wipes, nappies and in medical care [19]; in packaging for food and other items; in paper coating and composites [20]. There are already a number of PLA products in the market, mostly in the compostable packaging sector and disposable tableware [21] which represents 70 % of the current PLA market [20]. Additionally to its properties, this biodegradable polymer can be easily processed by conventional processing techniques used for thermoplastics like injection moulding, blow moulding extrusion, thermoforming, foaming extrusion or melt spinning [7, 16, 20]. Lim *et al*. [22] reported an excellent review of the processing technologies based on PLA properties. Current research studies are focused on broadening PLA range of applications to more durable applications such as building insulation, consumer electronics and automotive industry; increase its heat resistance to be used as woven fibre or to hold hot liquids; and improving its gas barrier properties.

Besides commodity applications, PLA was originally introduced in the biomedical market in the 70s as resorbable sutures under the brand name of Vicryl. Due to its biodegradability and biocompatibility features, it is approved by the US Food and Drug Administration (FDA) and currently used in a number of biomedical applications such as temporary scaffolds, sutures, systems for implant's fixation, stents, scaffolds, dialysis devices or drug delivering systems [23-26]. PLA has also been tested as the hydrophobic block of amphiphilic copolymers to form surfactants, and as vesicle membrane of drug carriers and in the growing niche of tissue engineering [4]. This polymer offers the possibility to set the appropriate mechanical strength and degradation rate by tailoring the molecular weight. For example, in an application where high degradation rate is required but mechanical strength is not important, a low molecular weight PLA is employed. Therefore, it is a polymer with a wide range of application from large scale to the biomedical industry and a huge potential market is predicted. Supporting this forecast is the number of scientific papers, patents and textbooks related to the synthesis, processing, properties' modification and applications published over the past two decades and the recent second edition of a conference devoted exclusively to this polymer, the 2nd PLA World Congress, May 2012 in Munich. Even though PLA price has been declining as production increases [18, 21, 22] it remains more expensive than many petroleum based plastics preventing its further usage as plastic commodity.

1.2.2. Lactic Acid, the Raw Material

PLA is a sustainable alternative to petrochemical-based materials, it fits very well within the biorefinary concept, since the lactic acid building block is obtained from the fermentation of carbohydrate rich products such as corn starch, maize, potato, sugar cane/beet or wheat. Although there is some controversy over this issue, it is stated in the literature [14, 27] that PLA requires 20-50% less fossil fuel resources than comparable petroleum-based plastics, according to environmental life-cycle assessment (LCA).

Lactic acid or 2-hydroxypropanoic acid is an alpha hydroxy acid bearing a hydroxyl and a carboxyl group linked to a chiral carbon, therefore existing under two optical isomers or stereoisomers: L-(+)-lactic acid and D-(-)-lactic acid (for simplicity, they will be referred as L-lactic acid and D-lactic acid from now on). The conformational differences between D- and L-lactic acid result in different physical properties such as solubility. The physical and chemical properties of different lactic acid stereoisomers, as well as a detailed review on lactic acid production, separation, purification and final applications can be found elsewhere [13, 18, 28, 29]. L-Lactic acid plays an important role in a number of biochemical processes and the human body produces it during normal metabolism and exercise. In the industry, L-lactic acid is predominantly produced by lactic acid bacteria, mainly Lactobacillus. Chemical synthesis, by hydrolysis of lactonitrile, is also feasible but it is not possible to control the stereoisomer composition, obtaining a racemic mixture of both L- and D- lactic acid isomers. The fermentation process is highly selective in producing pure L- or D- lactic acid by correct selection of the micro-organism(s) and much more environmentally friendly since it uses renewable resources in an aqueous solution. L-lactic acid is the only stereoisomer produced and metabolized by human beings. The D-lactic acid production has little commercial interest [23, 28, 29]. Nowadays, the main companies involved in the lactic acid production are Purac and Galactic.

Lactic acid is a chemical commodity with applications beyond PLA production, in 2006 the global production reached 275 thousand tonnes. It is largely employed in pharmaceutical industry [26] to produce water soluble lactates from insoluble active ingredients and in cosmetics and as acidity control agent. It is present in milk based products and as it is a GRAS chemical (Generally Recognized as Safe) it is used in food manufacturing and processing as food additive (E270), as flavour, as antibacterial agent and mainly as an acidity buffering agent. In the chemical industry [28], lactic acid is a raw material for the production of lactic acid esters, propylene glycol, 2,3-pentadione, propionic acid, acrylic acid, acetaldehyde and dilactides [26, 28].

Pure lactic acid, a white crystal, is difficult to obtain because during thermal dehydration lactic acid undergoes a condensation reaction. Therefore, it is typically supplied in 80 - 90 % aqueous solution at equilibrium with lactide and small oligomers [30]. As disclosed in patent EP 0 849 252 B1, lactic acid commercial solutions show a slightly yellow colour as a result of fermentation process impurities, which lead to coloration at high temperatures. These impurities from the bacterial fermentation process such as alcohols, acids, traces of nutrients, sugars and heavy metals also interfere with the course of polymerization. Therefore it is difficult to consistently prepare PLA with the same quality [31]. Low levels of sugars and nutrients are essential to avoid discoloration at high temperature, therefore the purification stage is of great relevance [29, 32]. Moreover, lactic acid solution and its vapours are quite corrosive requiring careful selection of the equipment materials to ensure low maintenance requirements [32].

Some reports state that lactic acid production represents around 40 to 50 % of the current PLA production cost [7], therefore it is important to reduce production costs in order to increase competitiveness.

1.2.3. Brief History of Poly(Lactic Acid) Production

PLA has been studied over the decades from different points of view. The first attempt to synthesise PLA was carried out by Carothers at DuPont in 1932 by direct lactic acid polycondensation but only low molecular weight PLA and cyclic side products were obtained, unsuitable for any application [20, 32]. The synthesis of PLA by direct lactic acid polycondensation relies on an esterification reaction between a carboxyl and a secondary hydroxyl group releasing a water molecule. As this is an equilibrium reaction, difficulties in removing trace amounts of water in the later stages of polymerization limit reaction extent and the ultimate molecular weight achievable by direct polycondensation. Low molecular weight polymers in the range of 10 000 to 20 000 $g.mol^{-1}$ are usually obtained. It is widely known [24] that tensile strength and PLA modulus increase by a factor of two when average molecular weight increases from 50 000 to 100 000 $g.mol^{-1}$ and remain relatively constant above this value. Efforts at that time were focused on an alternative approach for reaching higher molecular weights and in 1954 DuPont patented a process to synthesise high molecular weight PLA by ring opening polymerization (ROP) of the cyclic lactic acid product, the lactide [33-35].

This process begins by synthesising low molecular weight lactic acid oligomers, about 2 000 $g.mol^{-1}$, by self-condensation. The prepolymer is synthesised under vacuum (70-250 mbar) at temperature up to 190 ºC [29] in a reaction that lasts about 6 hours. In the following step the lactic acid oligomers are catalytically depolymerised at 213 ºC and 4 mbar, for 1 hour to produce a cyclic dimmer, the lactide, by an internal transesterification reaction called “back-biting” as disclosed in USP 5,142,023 [36]. Around 70 % of conversion was reported [18, 29]. PLA is than produced from the lactate by ring-opening polymerization (ROP) usually with tin octoate as catalyst, at high temperature, 190-210 ºC, and vacuum for 2 to 5 hours to reach 95 % lactide conversion. In the last stage of the process additives are added to the polymer in an extruder to produce the required polymer grade and cut into pellets. Finally, the PLA pellets are dried under vacuum to remove the remaining monomer and traces of water, increasing polymer melt stability and preventing fouling in processing equipment [13, 37]. This ROP mechanism does not produce water, therefore, a wide range of molecular weights is attainable. A description of PLA synthesis by ROP process, as well as the process mathematical model which uses the commercial simulation software Polymer Plus from Aspen Technology's was published by Seavey and Liu in 2008 [37].

L-Lactic acid is the isomer predominantly used for lactide production (3,6-dimethyl-1,4-dioxane-2,5-dione). However, during the cyclization reaction, reversal of chiral center occurs at some extent, resulting in a mixture of different lactide isomers: L-lactide, D-lactide and *meso*-Lactate (DL-lactide). Similar to the lactic acid, lactide enantiomers also display different properties [29]. As it will be explained later, enantiomeric composition (ratio and distribution in the polymer backbone) greatly affects the final polymer properties. Therefore, an additional step for lactide purification and isomers' separation is required. In the original DuPont patent [29] the lactides separation was achieved by repeated recrystallization, at least three times. However, such recrystallization steps had relatively poor yields. Due to the high complexity and cost, this process was never implemented at an industrial scale. Later, in 1987, owning to the increasing environmental concerns, Cargill, the company which provided sugar feedstock, and Dow, a major player in the polymer market, joined efforts to study the PLA synthesis for bioplastic commodity. Ten years later, they announced a joint venture, NatureWorks LLC, entirely dedicated to the production of PLA and in 2001 the first large industrial plant in the USA started operating, with a global production capacity of 140 000 PLA tonnes per year. NatureWorks LLC is nowadays owned by Cargill. The continuous PLA production process developed by Gruber and colleagues at Cargill Dow relies on lactide purification by vacuum distillation taking advantage of the physical properties difference between lactide enantiomers and was described in several patents, USP 5,142,023, 5,247,059, 5,258,488 or 5,357,035, to quote some of them [35, 38-40]. The crude lactide obtained in the oligomers depolymerization is distilled in a first column to remove the lactic acid, oligomers and water, and then, the *meso*-lactide is removed in a second column [29, 38-40]. According to PRO-BIP-2009 report, the production and purification of lactide represents 30 % of the total PLA production costs, lactic acid monomer corresponds to about 40-50 % and the remaining includes the polymerization costs [7].

Figure 1.4 shows a simplified representation of the two possible mechanisms to synthesise PLA, directly from monomer by step-growth polymerization or by ring opening polymerization of an intermediate compound, the lactide [41].

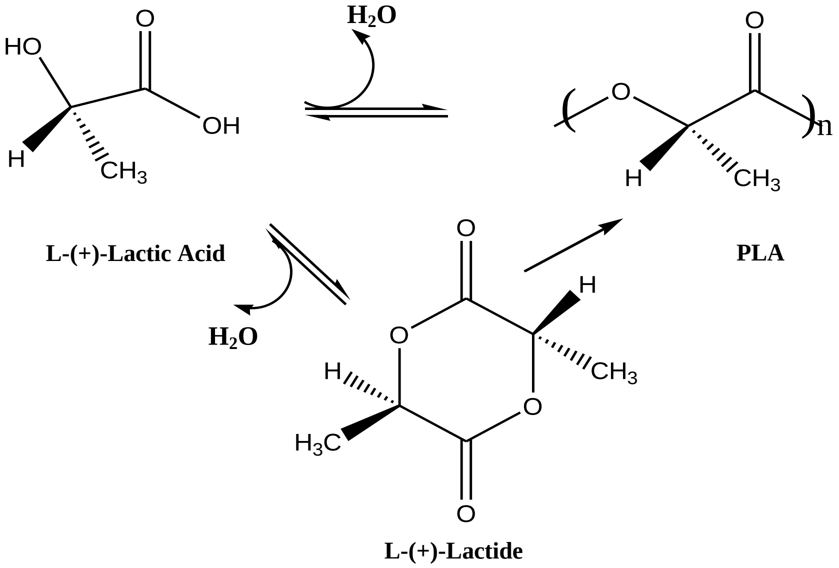

Figure 1.4: Simplified mechanism of lactic acid step-growth and lactide ring opening polymerization [13, 32, 41].

In some literature, PLA obtained by ROP is called of polylactide whereas PLA synthesised by polycondensation is referred as poly(lactic acid) [24], however they refer to the same material as they bear the same repeating unit.

1.2.4. Poly(Lactic Acid) Production

NatureWorks LLC is nowadays the world’s leading manufacturer of the bioplastic PLA under the brandname Ingeo™ for use as thermoplastic and in fibers production. Nature Works LLC has an integrated process from monomer production by corn starch fermentation to the final lactide polymerization. The demand for corn is 2.5 kg to produce 1 kg of PLA. A brief description of the NatureWorks LLC polymerization process was already given in the previous section and it is schematically illustrated in Figure 1.5. The different grades of PLA supplied by NatureWorks LLC make this bioplastic material suitable for a wide range of applications such as clothing, house ware, personal care products, food packaging, appliances, automotive, electronics, and durable goods [36, 38-40]. A second plant is to be built in Thailand [1].

As referred before, the PLA properties are highly related to the molecular weight and to the stereochemical composition. L-PLA has a very regular structure consequently develops a very high crystallinity degree being a material with high melting point whereas the presence of some D-lactic acid units into the polymer chain introduces irregularities in the crystalline structure, decreasing the melting temperature and the crystallinity degree. A racemic mixture, equimolar amounts of D- and L- enantiomers, is an amorphous polymer, therefore the polymer chirality allows a certain adjustment of the crystallitity, the mechanical performance and degradation rate thereof. Moreover, the amorphous polymer is soluble in most common organic solvents such as: ketones, tetrahydrofuran, benzene, acetonitrile, dioxane and chlorinated solvents, whereas a highly crystalline PLA material is only soluble either in chlorinated solvents or benzene [29]. Auras *et al.* [29] point out that one of the great advantages of ROP process is the ability of controling stereochemical composition by controlled polymerization of L-, D- or *meso*-lactide making use of a stereoselective catalyst to form pure L- or D-PLA, random or block stereocopolymers.

ROP can be performed via three different catalytic mechanisms: anionic, cationic and coordination-insertion. The anionic and cationic polymerizations are usually carried out in highly pure solvents. Although poorly understood, the melt coordination-insertion mechanism is the most widely studied in the literature and the one implemented in the large scale-process. Many types of metal catalysts containing free *p* or *d* orbitals may be used for ROP. Stannous octoate, often referred as tin(II) 2-ethylhexanoate, is the preferred catalyst since it allows achieving high molecular weight with reduced racemization and shows high solubility in the molten state and high stability at high temperatures [23, 25, 41, 42]. Tin based catalysts are approved by FDA for packaging and biomedical applications [29, 33] but some toxicity issues have been reported. In a 2007 review paper, Gupta and Kumar [25] reported an extensive compilation of more than 100 catalysts that had been studied for the lactide ROP and this remains an area of intense research.

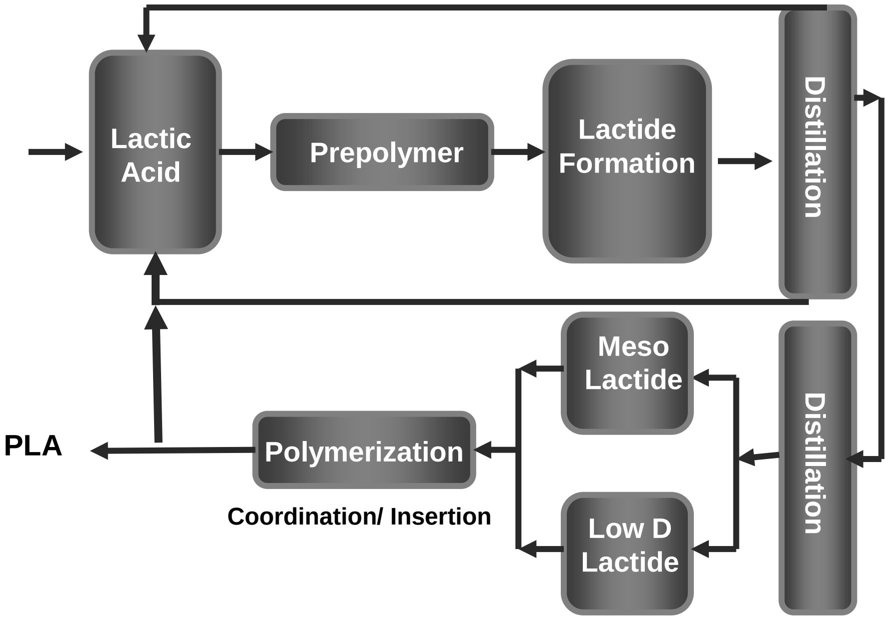

Figure 1.5: Simplified process for PLA synthesis by ROP [13, 33, 35-40].

PLA produced by ROP is a linear polymer with poor elasticity due to the low degree of molecular chain entanglement [35]. The strategy implemented by NatureWorks to increase de level of entanglement is to introduce long chain branching in a post polymerization step using epoxidized natural oils or epoxy acrylate copolymers. In some applications, modification involves the use of cross-linking agents such as peroxides [35]. Other additives to tailor PLA properties and to improve its melt stability, avoiding yellowing during processing, may include catalyst deactivators, inorganic fillers, mold release agents, plasticizers, thermal stabilizers, flame retardants, antioxidants, water scavengers and colorants. The use of antioxidants and water scavangers is widely referred in several patents and includes alkyl and aryl phosphites, phosphonites, hindered phenolic compounds, aromatic amines, thioethers, quinones and carbodiimides as disclosed in patents [40] and [43-48]. Thus, NatureWorks LLC commercializes several PLA grades which differ in stereochemical composition, molecular weight and other products they label as “additive packages”, also called masterbatch in some literature. Each grade is optimized for a processing technique and end-use application [13]. For example, 2000D PLA is designed as an extrusion grade typically for extruded sheet, or 7001D is designed as an injection stretching blow molding grade for bottles. More information about the PLA grades commercialized by NatureWorks may be found on the company web site or in the Utrecht University study [7, 49].

A number of small scale production facilities for medical applications are currently on the market such as Boeringer Ingelheim, Polysciences Inc., Hycail, B. V. and Purac, but information on production capacity is difficult to gather [24]. The most important in the medical applications field is Purac Biomaterials that has been producing PLA under the brand name of PURASORV^R for applications as diverse as resorbable surgical sutures, orthopedic implant devices, cosmetic surgery products and drug-delivery systems [18, 50].

Given the expected market growth, other companies have announced PLA production plans. In 2007 Galactic and Total Petrochemicals have announced a joint venture called Futerro and a PLA pilot plant in Belgium planning to produce 1,500 tonnes/year. Synbra started producing a PLA biofoam (EPLA) in 2010 [7, 51].

The PLA market growth is hindered by the lack of freely available production technology. To overcome this drawback the Uhde Inventa-Fischer, a leading company in polyamides and PET polymerization technologies, is the first engineering company developing an integrated process for both lactic acid and PLA, called PLAneo®. This process is being tested in a pilot plant with a capacity of 500 tons/year since 2010 [7, 52, 53].

Every process mentioned before is based on lactide melt ROP mechanism. New approaches to synthesize PLA have been recently reported but no industrial processes have been developed so far. The new paths include enzymatic approaches using bio-engineered Escherichia Coli [54], microwave assisted polymerization [55] and supercritical fluids [56].

1.2.5. Poly(Lactic Acid) Properties and Modifications

One of the distinctive features of PLA is the biodegradability. However PLA shows a different biodegradation mechanism comparing to other biodegradable polymers on the market which typically degrade in one single step involving bacterial attack. As micro-organisms are not able to digest high molecular weight PLA molecules they are not involved until the polymer molecular weight reaches around 20 000 g.mol^{-1}. Therefore, the PLA biodegradation process comprises two distinct steps. The first one consists in a hydrolytic degradation mechanism where the cleavage of the ester linkages entails a successive reduction in molecular weight. Then, micro-organisms present in the soil are able to digest lactic acid oligomers, producing carbon dioxide, water and compost. The PLA hydrolysis is greatly accelerated in composting conditions, while at low temperatures and/or low moisture contents PLA shows good stability over a long period of time [6].

PLA is a semi-crystalline, stiff and brittle material, with low ability to plastic deformation [57]. Common thermal and mechanical properties of PLA are listed in Table 1.1, enabling comparing with other polymers. Several approaches have been developed to tune the mechanical properties of PLA from a brittle thermoplastic to a rubber-like polymer. Those include well established plasticization in the traditional polymer industry using non-volatile and preferably biodegradable and renewable based compounds such as glucose monoesters, glycerol, citrate esters and oligomeric lactic acid. Co-polymerization employing a wide range of co-monomers, in particular caprolactone, and blending with flexible polymers have also been studied to reduce glass transition temperature and attenuate the brittle behaviour of PLA [29, 31, 58, 59]. Blends of PLA and starch have been extensively studied by several researchers [23, 29] not because of its outstanding properties but due to starch relative low cost. It has been reported that the addition of diisocyanates as compatibilizers improves the interfacial interaction between PLA and granular starch and consequently the mechanical performance, the Young's Modulus was reported to increase from 1.41 to 1.94 GPa [25, 29, 60]. Other PLA blends studied include blends with chitosan, poly(ethylene glycol) (PEG), poly(caprolactone) (PCL) and polyhydroyalkanoates with or without compatibilization [21, 24, 28, 41, 61, 62].

Mixing natural fibres with PLA is pointed out as a promising way for increasing mechanical properties, durability and heat resistance while reducing costs without compromising biodegradability. Strengthened PLA mechanical properties are usually achieved by reinforcing the polymer with natural fibres such as flax, hemp or kenaf by compatibilization with, usually, peroxides or diisocyanates. According to Shen *et al.* [7] and Sodergard and Stolt [24] these materials are seen as very promising structural composites for the automotive industry and building insulation.

Comparing with standard packaging materials like PET and PS, PLA shows superior flavour barrier but a higher UV transmission rate. Therefore, the application of transparent PLA films to pack daily products may require additives to block UV light transmission and thus, prevent sensitive food from damaging. PLA has excellent organoleptic characteristics, but one of its main drawbacks for use as an alternative packaging material is its poor gas barrier properties. This polymer shows a particularly high permeability to CO_2 comparing with PET, which maybe interesting for packing some fresh products, but limits PLA use in the important market of carbonated beverages [3, 11, 63, 64]. In addition, to overcome the inherent brittleness of PLA, the approaches described before can further lower the gas barrier properties of PLA. To improve the gas barrier properties of PLA, the addition of nanocomposites such as layered silicates, carbon nanotubes, nanofibers and nanowhiskers has been tested entailing, or not, surface modification [21, 29, 41]. For example, when blending kaolinite with the PLA a good interaction is observed, and an improvement in oxygen barrier properties by about 50 % is observed. Mechanical properties of PLA can also be significantly improved with nanocomposites. It has been demonstrated that various montmorillonite clays, blended with PLA at about 5 weight percentage, can increase PLA’s tensile modulus and elongation at break by 36 % and 48 %, respectively [28, 29, 65]. PLA is a slow crystallizing material, similar to PET, and blending with nanocomposites can improve this characteristic as they act as nucleating agents, increasing the nucleation density and decreasing the crystallization half-time [23, 66]. Therefore nanocomposites are regarded as a cost effective solution to overcome the slow crystallization rate of PLA. The latest advances in PLA nanocomposites, morphologies, mechanical properties, dynamic mechanical behaviour, rheological properties and evaluation of polymer-nanoparticles interactions, are thoroughly described in journals [21, 22, 23, 57] and in textbooks found elsewhere [6, 28, 29]. When properties such as high mechanical strength, high heat resistance, stiffness and high chemical resistance are required reducing crystallization half-time is the common approach pointed out in the literature.

An interesting phenomena in 50:50 wt % blends of poly(L-lactic acid) and poly(D-lactic acid) is the formation of a stereocomplex. The stereocomplex formation during co-crystalization of pure L-PLA blended with pure D-PLA was first reported by Ikeda *et al.* [67] and has a melting point 50 ºC higher than that of the pure enantiomeric polymers along with higher tensile properties and better resistance to hydrolysis. Therefore in the last decade the blend of the two enantiomers have been investigated [24, 41, 68, 69] as promising materials for heat stable and engineering plastics.

As referred before, to increase the PLA functionality and to prevent discoloration during melt processing the traditional polymer additives such as plasticizers, antioxidants and pigments have been employed [44-47]. However, to comply with the certification systems under development, bioplastics processing technologies require the use of preferably biobased and biodegradable additives. Moreover, for packaging only substances allowed to contact food can be considered. Some of these additives are not yet available, whereas some have already been developed for PLA processing, mainly by DuPont, Sukano, Clariant and Rohm&haas [7, 29, 57, 70, 71].

All the features mentioned above, the molecular weight, the polymer sterochemistry along with processing conditions and a judicious modification selection, allow PLA materials of a wide range of mechanical properties increasing the variety of potential applications and rendering PLA such an interesting material.

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2. MATERIALS AND METHODS

2.1. Introduction

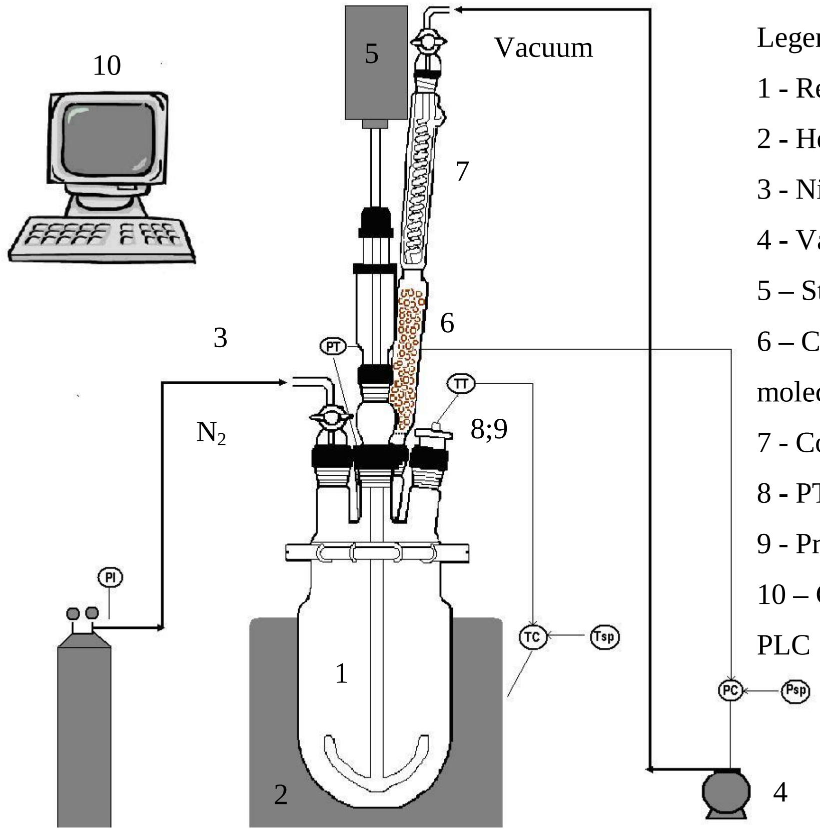
A detailed description of each experimental apparatus developed in this project to perform solution and melt polymerizations, as well the experimental procedures and the characterization techniques used to assess the influence of experimental conditions on final polymer properties are reported in the following subsections. Given the specificity of the chapter 7 content, the experimental procedures to synthesise lactic acid based adhesives and specific characterization techniques for this application will be described in chapter 7, not here.

2.2. General Set-up Description

Much effort and time of this project were put on the development and further adjustments of the experimental set-up. The main objective was to use a flexible and expandable plant, easy to scale-up, as it was intended to foresee and to assess difficulties that may arise when the synthesis routes tested are carried out at a larger scale.

The operating conditions required by the different polymerization approaches to synthesize PLA can be considered as severe: temperature up to 200ºC, pressure down to below 10 mbar, inert atmosphere, high stirrer rate, increasing viscosity of the reacting mixture and long reaction time. A set-up with these requisites was not found and had to be built. It is worth mentioning this was a time consuming task since several changes were introduced until reaching the final configuration of the experimental set-up and this was further updated whenever required by the polymerization technique in assessment.

Two different experimental set-ups have been assembled: one, to perform polycondensation in solution, and the other one to carry out the polycondensation and the polytransesterification reactions in molten state. The changes introduced in the second set-up were mainly due to the increase in viscosity. Each plant is schematically represented in Figures 2.1 and 2.2, respectively. A description of the equipment used in each plant developed and the reasons supporting the design adopted, as well as those responsible for the changes introduced, will be explained alongside the procedures.



Legend:

1 - Reactor 2000 mL

2 - Heating mantle

3 - Nitrogen inlet

4 - Vacuum pump

5 – Stirrer motor

6 – Column with molecular sieves

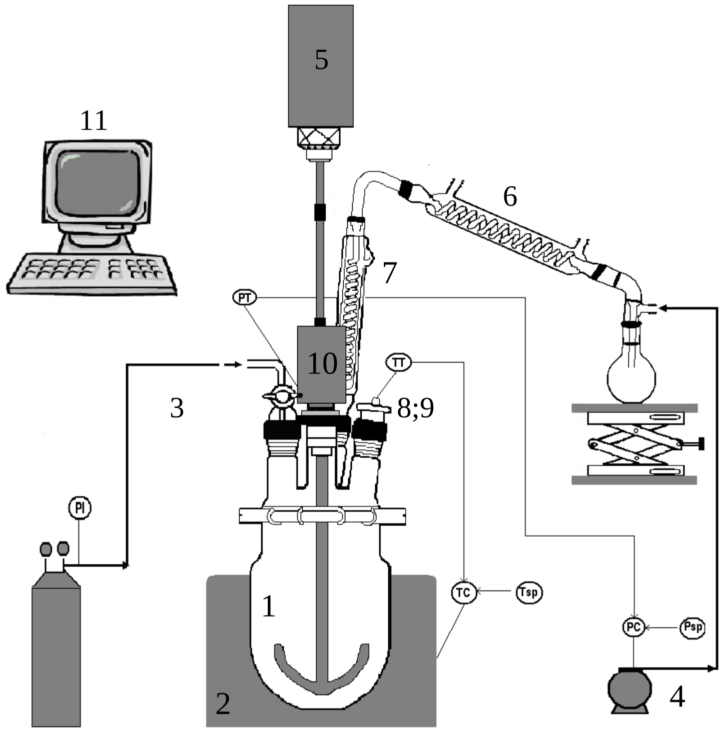
7 - Condenser

8 - PT100

9 - Pressure probe

10 – Computer & PLC

Figure 2.1: Schematic representation of the experimental plant used in the solution experiments.



Legend:

1 – Reactor 500 mL

2 - Heating mantle

3 - Nitrogen inlet

4 - Vacuum pump

5 – Stirrer motor

6 - Condenser

7 - Condenser

8 - PT100

9 - Pressure probe

10 - MRK 1/90 Magnetic coupling

11 – Computer & PLC

Figure 2.2: Schematic representation of the experimental set-up used in the melt experiments.

The batch reactors (number 1 in Figures 2.1 and 2.2) are equipped with a stirrer driven by an electric motor, a temperature sensor and a pressure probe. An inert atmosphere is achieved by a continuous flow rate of nitrogen bobbling into the reaction mixture, and a connection to a vacuum pump enables working at low pressure. An electrical mantle (number 2 in Figures 2.1 and 2.2) ensures the heating of the reactor and reaction mixture.

The reactor consists of a cylindrical ground bottom borosilicate glass vessel of 2000, 1000 or 500 mL, 10 cm in diameter and a separate five-necked glass cover both purchased from Afora S.A, Barcelona. These two parts are assembled through a metal clamp and a silicone O-ring. It is important to refer to the silicon O-ring since it is essential in order to reach high vacuum for long periods of time, at high temperature, while avoiding air leaks. The stirrer is inserted in the central neck of the cover and the side necks are used to place the pressure sensor, the PT100, the nitrogen feeding and connection to vacuum pump, as illustrated in Figures 2.1 and 2.2.

Regarding the mechanism of polycondensation reactions, temperature and pressure profiles are both fundamental. In the course of the experiments temperature profiles were set ranging from steady to increasing temperatures, whereas pressure started at atmospheric pressure that was later gradually reduced until reaching the set point. In order to achieve control of the temperature profiles in the reactor, a dedicated programmable logic controller (PLC) was employed. Both temperature and pressure measured inside reactor were recorded.

The heating system consists of an external electric heating mantle, model O from Glas-Col, connected to the PLC, and a PT100 temperature sensor, from Tecnisis, immersed in the reacting mixture and also connected to the PLC. Glass fiber was used as insulation material on the top of the reactor glass cover, minimizing heat loss.

The vacuum system comprises a vacuum controller CVC 3000, a solenoid valve VV-B 6C and a rotary vacuum pump model RZ6, all from Vaccubrand. Depending on the experimental procedure requirements one or more devices, Figure 2.1 and Figure 2.2 respectively, are inserted in series in the reactor top covers’ neck dedicated to the vacuum line. More detail will be given in the following experimental procedures sections of this chapter. In order to avoid oil contamination of the reacting mixture, two cold traps were placed between the reactor and the vacuum pump, not shown in Figures 2.1 and 2.2.

The stirring system is very important in order to ensure proper mixing and rapid water vapour diffusion throughout the reacting mixture. This is particularly relevant for the increasingly viscous mixture obtained in the melt experiments under high vacuum, and it was the most difficult system to set the final configuration. Polymerization in solution studies were carried out with a stirrer motor and a metallic anchor stirrer fitted to the reactor cover neck by means of a standard vacuum glass adaptor to avoid air leaks, as illustrated in Figure 2.1. When the experimental work evolved from solution polycondensation to the melt experiments this configuration became totally unsuitable, for two different reasons. Firstly, the glass material of the adaptor was not able to cope with the vibration as a result of the increasing polymer melt viscosity while ensuring tightness to avoid air leaking and eventually break in pieces. Secondly, some of the catalysts added to the process were found to interact with the metallic stirrer resulting in a heavily coloured polymer. To overcome these problems the metallic stirrer was replaced by a Teflon anchor stirrer (7 cm in diameter), specially designed for this project. The glass adaptor was replaced by a magnetic coupling MRK1/90 from Buddeberg and a double cardan was placed in the stirrer shaft, Figure 2.2. These changes allowed a much smoother operation, achieving higher stirring rates and lower pressures comparing with the solution experiments. During the melt experiments the stirrer motor was also replaced by a new one, model R100C from CAT, with torque display besides the information on stirring rate.

Oxygen has an influence in the progress of most polymerizations, in the case of polycondensation reactions at high temperatures oxidative degradation is a serious issue even at low oxygen concentrations. Unfortunately, the set-up designed is not entirely air tight. Figure 2.3 shows the pressure profile recorded inside the empty 500 mL reactor after the vacuum pump was turned off. As can be seen, the pressure inside reactor increases gradually over time approaching the atmospheric pressure. To ensure that polymerization reactions were performed under inert atmosphere, nitrogen sweep was used throughout the course of the reactions. To assess the influence of nitrogen composition in the final polymer properties, two nitrogen grades were tested: a standard grade and a higher purity one.

Conceptually, bulk polymerization reactions are relatively simple to perform. In practice, the viscosity increase introduces additional technical requirements as described above, even at the scale used in this work. These requirements are mainly set by the need to ensure very low pressure inside the reactor, which can only be achieved with an airtight system. This tightness is also relevant to prevent oxidation side reactions. Pressure and tightness requirements limited one of the initial objectives of this project which was sampling at selected time intervals enabling studying reaction rates. Unfortunately, under such temperature and pressure conditions, a reliable sampling system was not available and could not be designed.

The bulk experiments were carried out in a smaller capacity reactor, 500 mL vessel, owning to the need to facilitate water vapour diffusion from the melt during experiments. Diffusion rate increases with interfacial area and, according to the dimensions of the three cylindrical vessels available, the interfacial area/volume ratio was higher in the 500 mL reactor. Although the original plan was to carry out the experiments at a pilot scale, at this stage this was not feasible without putting at risk the performance reached in the process.

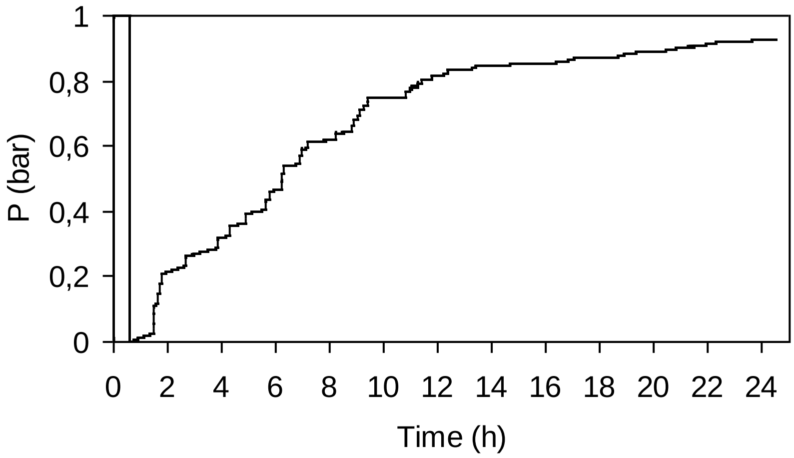


Figure 2.3: Pressure profile inside the 500 mL vessel confirming air leaks.

In this work, melt and bulk polymerizations are interchangeable terms since both mean a reaction carried out in the absence of solvents while the reacting mixture is in molten state. The results obtained during the experimental programme will be presented and discussed in the following Chapters. The chemicals used are presented in Section 2.3, a description of the experimental procedure followed in each polymerization route is given in the following Section 2.4 and the characterization techniques are presented in Section 2.5 of this Chapter.

2.3. Materials

All materials used in the experiments carried out in this work were purchased from Panreac, Sigma-Aldrich or Acros and used without further purification. The chemical structures as well as the main properties (molecular weight, boiling temperature, melting temperature and density) provided by the suppliers are listed in the *Appendix A*.

Monomer - Commercial lactic acid was the main monomer used in this project and budget limitations were decisive for purchasing an aqueous solution of L(+)-lactic acid (80 %). This monomer was purchased from Sigma-Aldrich and it is 99 % chemically pure [3]. Lactic acid obtained by fermentation is reported to be 99.8 % enantiomer pure and having traces of the following chemical compounds in its composition: alcohol < 250 ppm, sugar < 100 ppm, COOH < 250 ppm, chloride (Cl^-) < 50 mg/kg, sulphate (SO_4^{2-}) < 100 mg/kg, Ca < 100 mg/kg and Fe < 10 mg/kg [1-3]

In Chapter 4 PLA synthesis by polytransesterification L-lactic acid esters is assessed and four esters, all purchased from Sigma-Aldrich, were tested: ethyl L-lactate (98 %), methyl L-lactate (97 %), *iso*propyl L-lactate (97 %) and butyl L-lactate (97 %).

<u>*Co-monomers*</u> - 1,4-butanediol (BD) (99 %), pentaerythritol (mPET) (99 %), dipentaerythritol (diPET) (90 %), tripentaerythritol (triPET) (90 %), Castor oil glycidyl ether (ECO), bisphenol A diglycidyl ether (BADGE) (95 %), pyromellitic dianhydride (PMDA) (97 %), ethylenediamine tetraacetic acid (EDTA) (98.5 %), triethanolamine (TEA) (99 %), tris(2-aminoethyl) amine (TAEA) (96 %), 1,6-hexamethylene diisocyanate (HDI) (99 %) and toluene 2,4-diisocyanate (TDI) (98 %).

<u>*Solvents*</u> - Solution polycondensation, described in Chapter 3, was the first route tested in this work to obtain PLA. The two solvents used in the experiments were: anisole (96 %) and *m*-xylene (96 %).

Chloroform was used for dissolving the polymer remaining on vessel walls facilitating cleaning of the reactor. The polymer thus dissolved was purified by precipitation in ethanol for further characterization. Chloroform HPLC grade was used as eluent in the size exclusion chromatography analysis.

<u>*Catalysts*</u> - The performance of a large number of catalysts was tested in this work including: tin (II) chloride dihydrate ($SnCl_2.2H_2O$) (98 %), tin (II) octoate [Sn(II)Oct] (98 %), tin (II) oxide [Sn(II)O] (99,9 %), tin (IV) oxide [Sn(IV)O] (99.9 %), dibutyltin dilaurate (DBTL) (95 %), tin powder < 150 µm (Sn) (99.5 %), titanium (IV) butoxide (TNBT) (98 %), titanium(IV) oxide (TiO_2) (99.7 %), 4-dodecylbenzenesulfonic acid (DBSA) (90 %), antimony (III) oxide (Sb_2O_3) (99 %), zinc acetate dihydrate [Zn(acet)] (98 %), manganese(II) acetate tetrahydrate [Mn(acet)] (99 %), zinc (II) oxide [Zn(II)O] (99 %), cobalt acetate tetrahydrate [Co(acet)] (98 %) sulphuric acid (H_3SO_4) (95 - 98 %) and phosphoric acid (H_3PO_4) 85 wt % in water (99 %). *p*-Toluenesulphonic acid monohydrate (*p*-TSA) (98 %) and triphenylphosphine (PPh_3) (99 %) were assessed as co-catalyst in bulk polycondensation experiments described in Chapter 5.

Drying agent - Molecular sieves, 3 Å beads, 8-12 mesh, adsorption capacity of 21 % was used in solution experiments to reduce moisture content.

Inert gas - The inert gas used throughout the experimental work was nitrogen from Praxair. Two different purity grades were tested: standard nitrogen 99.99 % pure having $H_2O \leq 10$ ppmv and $O_2 \leq 10$ ppmv in its composition, and ultra pure nitrogen 9.999 % having $H_2O \leq 3$ ppmv, $O_2 \leq 2$ ppmv and $C_nH_m \leq 1$ ppmv. The information here reported was kindly supplied by Praxair.

2.4. Experimental Procedures

2.4.1. Polycondensation of Lactic Acid in Solution

The polymerization of lactic acid in solution was carried out using two high boiling point (b.p.) organic solvents: anisole (b.p. 154 ºC) or *m*-xylene (b.p. 139 ºC), which boiling points were used as reaction temperatures. The initial concentration of the monomer aqueous solution in the mixture with the solvent was 20 % (v/v). The reaction was performed in a 2 L borosilicate glass reactor. The first reaction step was the distillation of the aqueous solution of monomer which took *ca*. 8 hours using a Dean-Stark trap to collect the condensed water. Then, the catalyst was introduced (0.1 % mol) and the Dean-Stark trap was replaced by a tube packed with molecular sieves as drying agent as shown in Figure 2.1 (6). The polymerization was performed for several hours (up to 70 h) at the boiling point of the solvent under inert atmosphere (N_2). Some of the experiments were performed at reduced pressure (0.1 bar), by decreasing the pressure gradually, till reaching the set-point. The final polymer was recovered as a white powder from solvent precipitation when cooled in an ice bath. Further purification was performed by dissolution in chloroform and precipitation in 4-fold ethanol. After drying, the samples were stored in a dessicator for further characterization. The results obtained with this approach are presented and discussed in Chapter 3. Polymer yields of around 30 % were obtained.

2.4.2. Bulk Polytransesterification of L-Lactic Acid Esters

The polytransesterification experiments were carried out in the set-up described previously using the 500 mL borosilicate glass vessel equipped with a magnetic coupling

MRK1/90 and connected to the vacuum system through a cold trap as shown in Figure 2.2. Two reflux condensers, connected as shown in Figure 2.2 (6 and 7), were placed to remove the alcohol by-product and recycling the monomer removed during polymerization. The initial amount of L-lactic acid ester (200 mL) and catalyst or catalytic system were introduced in the reaction vessel and allowed to react overnight at atmospheric pressure, under inert atmosphere and at a stirring rate of 100 rpm. The heating up process, carried out under control using the PLC; took approximately 4 hours until reaching the temperature set-point, 170 ºC. Then, stirring rate was increased to 400 rpm, the temperature set point was increased to 180 ºC and a time span of one hour was allowed before starting gradual pressure reduction from atmospheric to around 10 mbar (set-point) carried out for 4 hours. Finally, after reaching the pressure set-point, the reaction proceeded under these conditions, T = 180 ºC and P = 10 mbar, for another 3 hours. Temperature and pressure were continuously recorded during the experiments.

The final polymer, in the form of a brown or light brown viscous melt, was allowed to cool to room temperature and recovered as powder after dissolution in chloroform and precipitation in 4-fold ethanol. After drying, the samples were stored in a dessicator for further characterization. The results obtained with this approach are presented and discussed in Chapter 4.

2.4.3. Bulk Polycondensation of Lactic Acid

The melt polycondensation experiments were carried out in the 500 mL glass vessel equipped with pressure and temperature control loops, using a mechanical stirrer with a magnetic coupling MRK1/90 and connected to the vacuum system through a cold trap as shown in Figure 2.2. Two reflux condensers, connected as shown in Figure 2.2 (6 and 7), were placed to remove the water by-product and recycling the monomer during polymerization in order not to jeopardize yield. The initial volume of L-lactic acid aqueous solution (200 mL) was introduced in the reaction vessel and allowed to react overnight under inert atmosphere, at atmospheric pressure and the stirring speed was set at 600 rpm. The temperature set-point was 170 ºC. On average, 79 g of water and 3 g of monomer were collected after the overnight distillation. Then, 0.4 wt % of catalyst was added to the reacting mixture (weight of catalyst/initial weight of monomer), the temperature set-point was increased to 180 ºC or 190 ºC and the experiment proceeded allowing reacting mixture temperature rise for one hour, before starting the gradual pressure reduction from atmospheric to 10 mbar for 7 h. Finally, after reaching the pressure set-point, the reaction system was kept under these conditions for, usually, 4 hours.

A dramatic increase in viscosity was registered during lactic acid bulk polycondensation experiments and, in spite of the efforts to improve the set-up to eliminate air leaks, this was not always achieved. The time elapsed in these experiments largely exceeded what had been scheduled as many experiments were not successful.

At the end of the polymerization, close to 130 g of melt polymer in the form of a brown or light brown viscous melt were poured onto a plate and allowed to cool. Few grams of polymer were purified by dissolution in chloroform and precipitation in 4-fold ethanol. After drying, the samples were stored in a dessicator for further characterization. On average 7 % of polymer samples is lost as low molecular weight oligomers. The results obtained with this approach are presented and discussed in Chapters 5 and 6.

2.5. Characterization Techniques

Assessment of the different alternative routes tested to produce poly(lactic acid) must be supported, not only on process design and its operating parameters, including global process time, but also on the properties of the final product. Many characterization techniques can be used for polymeric materials, some of them of a wide application scope that goes far beyond polymers. The different techniques used in this work enable characterizing the polymers obtained and evaluating its properties and usefulness. The information collected allows foreseeing some potential uses for these materials in different fields. A thorough product characterization would require more information, particularly relevant is the polymer melt rheology behaviour, unfortunately it was not feasible in the time frame of this study. The characterization methods employed throughout this project are described below.

2.5.1. Size Exclusion Chromatography (SEC)

Polymer properties are closely related to its molar mass distribution. Size exclusion chromatography, SEC, also known as gel permeation chromatography, GPC, is a very powerful method of polymer fractionation, thus it has become a standard method for determination of molecular weight distributions and relative molar masses [4].

The average molecular weight (*Mw*), the number molecular weight (*Mn*) and the polydispersity index (*PD*), (*PD*=M*w*/M*n*), were determined by size exclusion chromatography (SEC), calibrated with narrow-dispersity polystyrene (PS) standards (790, 4 000, 10 050, 19 880, 30 300, 66 350, 96 000 and 200 000 g.mol^{-1}). The column set consists of a Polymer Laboratory 5µm safe guard column (50x7.5mm) followed by one PLgel 5µm MIXED-D column (300x7.5mm). The WellChrom Maxi-Star K-1000 HPLC pump from Knauer was set with a flow rate of 0.6 mL.min^{-1} and the eluent was HPLC grade chloroform. Since only a column was used to perform the sample fractionation the flow rate was set at 0.6 mL.min^{-1} to increase the samples retention time, instead of the 1 mL.min^{-1} standard rate. The measurements were carried out at 25 ºC with a polymer sample concentration of ~ 2 mg.mL^{-1}, after purification by precipitation in ethanol. Before the injection (>50 µL), the samples were filtered through a PTFE membrane with a 0.45 µm pore. After column exclusion, the samples were analysed in an evaporative light scattering detector PL-EMD 960 working at 40 ºC. Data processing was carried out with GPC Clarity software from DataApex.

Briefly, this chromatographic technique is based on size-exclusion phenomena and enables the separation and assessment of polydisperse samples. Polymers are separated by their hydrodynamic volume. A highly dilute polymer solution passed through a column packed with a porous solid phase (polystyrene crosslinked with divinylbenzene). Small molecules are easily retained in these pores rather than larger ones, consequently, larger molecules are eluted first [4-6]. The technique requires a calibration with a series of polymers of known molecular weight, therefore it gives relative values and not absolute ones. Since the technique relies on the hydrodynamic volume of the polymer in solution, irrespective of its structure, size or composition the solvent is of major importance. Chloroform was chosen to perform the experiments since it is a very good PLA solvent at room temperature and shows a low boiling point. Figure 2.4 shows a typical calibration curve, conventional calibration, obtained in the SEC analysis, it is important to referrer that when new samples were assessed a new calibration curve was required.

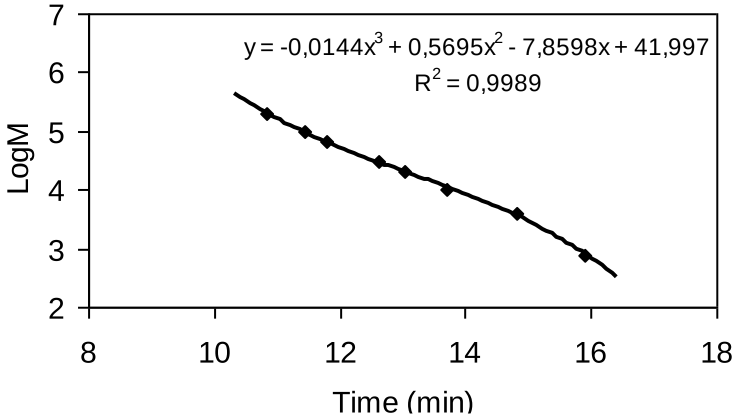


Figure 2.4: Typical conventional calibration curve obtained from PS standards.

2.5.2 Nuclear Magnetic Resonance (NMR)

Nuclear magnetic resonance, NMR, is a unique technique for chemical identification, it was used here mainly to confirm the typical PLA structure, which means the sucess of the experimental procedure. The ^1H NMR spectra of PLA were recorded on a Varian 500-MHz spectrometer at 25 ºC using deuterated chloroform, $CDCl_3$, as solvent containing 1 % (v/v) of tetramethylsilane as internal standard for chemical shift reference. The sample amount in each NMR tube was keept near 15 mg.

The absorption peaks in the NMR spectrum correspond to nuclei in different chemical/electronic environments and each absorption area is proportional to the number of nuclei responsible for the absorption. Therefore, the area under the absorption band is related to the number of moles of that nuclei [4, 5]. Thus, a munber of information may be obtained, including molecular weight.

2.5.3. Ultraviolet/Visible Spectroscopy (UV/vis)

UV/vis is highly sensitive to detection of traces of chromophores. Therefore, it was chosen to give an insight into the thermo-oxidative degradation reactions of the final polymer samples. UV/vis spectra of polymer samples were obtained from chloroform solutions at room temperature in a Jasco V-550 UV/vis spectrophotometer. The study was performed in the wavelength range from 200 to 800 nm with a scanning speed of 200 $nm.min^{-1}$ and a bandwidth of 5 nm. Even though UV/vis spectroscopy is not very specific in the absorption band, it is highly sensitive and therefore much better than NMR or infrared spectroscopy [7, 8] to detect small amounts of chromophors.

2.5.4. End-group Titrations

The polyesterification kinetics is usually assessed by following the carboxyl end groups (*COOH)* disappearance by standard acid-base titration method. The polymer sample, 1 g, was dissolved in 20 mL of a mixture ethanol-chloroform (1/1 volume) and titrated with a solution of KOH in ethanol (0.05 $mol.L^{-1}$). This procedure was repeated 3 times. The concentration of free carboxyl groups in the sample, [*COOH*], is defined as the number of *COOH* moles per g of polyester [1, 9].

This procedure was applied to evaluate the progress of solution polycondensation ant it was found suitable for quantitative analysis of oligomers end groups, but rather erroneous and not quantitative for higher molecular weights. Most probably, aliphatic ester linkages undergo hydrolysis under the titration conditions. This drawback may explain why end groups quantification, and contrary to others commercial polyesters, is not a quality parameter shown in the commercial PLA datasheets. However, the identification and quantification of end groups is crucial when assessing reaction polycondensation kinetics and when any kind of modification or postpolymerization process is under consideration.

2.5.5. Specific Rotation Measurements

The stereoisomer composition of final polymers was obtained from specific rotation measurements. The specific rotation of PLA polymers, $[\alpha]_{\lambda}^{T}$, was measured in a AA-5 electrical polarimeter from Optical Activity Ltd at 25 ºC, wavelength of 589 nm and a concentration of 1 g.dL^{-1} in chloroform. The percentage of optical purity *(OP)* of the PLA polymers was calculated using the following relationship [10]:

$$OP(\%) = \frac{[\alpha]_{589}^{25}}{-156} \times 100 \tag{2.1}$$

Where -156 is the specific rotation of PLA with only L stereoisomer in its composition [10]. It is important to ensure a PLA sample free o lactic acid monomer as well as lactide by-product since the presence of these compounds will significantly affect the PLA specific rotation. Polarimetry was used to quantify the stereochemical defects, but it cannot distinguish its relative position in the PLA backbone. However, it is not relevant since lactic acid polycondensation results in an atactic structure, which means without specific order [11].

2.5.6. Gel Content Determination

The gel content of crosslinked samples were determined by extracting the soluble fraction of the material in refluxing chloroform for 4 hours. The amount of insoluble crosslinked fraction was determined gravimetrically after drying until a constant weight.

2.5.7. Differential Scanning Calorimetry Measurements (DSC)

Information on the thermal behaviour is relevant in order to evaluate the physical properties and processing conditions of semi-crystalline polymers. DSC is a common technique for measuring the temperature and enthalpy of phase transitions in materials.

Therefore, the polymer samples obtained in the frame of this work were subjected to DSC analysis. Glass transition temperature (*Tg*), crystallization temperature (*Tc*), melting temperature (*Tm*), and fusion enthalpy (*ΔHm*), were measured using a differential scanning calorimetry equipment, Q100 from TA Instruments, under nitrogen atmosphere, with a heating rate, typically, of 10 ºC.min^{-1}. The samples were accurately weighted and placed into aluminium pans (around 5 mg), sealed and analyzed in two heating scans in the 30-180 °C temperature range. The percentage of crystallinity (*Xc*) was calculated using the following relationship [10]:

$$Xc(\%) = \frac{\Delta Hm}{93} \times 100 \qquad (2.2)$$

Where 93 J.g^{-1} is the fusion enthalpy [10] of a PLA crystal of infinite size. Universal analysis 2000 software from TA Instruments was used for data processing.

The melting and crystallization temperatures were assigned as the maximum value of the respectively peaks and the glass transition temperature was taken as the midpoint of the glass transition. The melting temperature and the fusion enthalpy, used to calculate crystallinity degree, were obtained from the first heating scan, whereas the glass transition and crystallization temperature were obtained from second heating scan. The fusion enthalpy (*ΔHm*) is the area underneath the melting peak. Owing to the complex PLA crystallization process the second heating scan usually shows a double melting peak, therefore this is a common procedure when reporting DSC data from PLA samples [12-14]. Care must be taken when performing the analysis and never touch directly with hands in the pans, otherwise results may be altered.

2.5.8. Thermal Gravimetric Analysis (TGA)

The thermal degradation of PLA samples was performed in TGA equipment SDT Q600 from TA Instruments. The samples were heated from ambient temperature to 600°C at 10°C/min under nitrogen purge. Degradation temperatures (*Td*) at maximum decomposition rate taken from the differential weight loss curves were considered as the degradation temperatures. Universal analysis 2000 software from TA Instruments was used for data processing.

2.5.9. Dynamical Mechanical Thermal Analysis (DMTA)

Dynamical Mechanical Thermal Analysis (DMTA) is a convenient technique for investigating the viscoelastic properties of polymeric materials by applying a sinusoidal load to the specimen and measuring the resultant deformation as a function of frequency and temperature. In DTMA, the material is subjected to a forced mechanical vibration, E' characterizes the ability of the polymer to store energy (elastic component), whereas E'' reveals the ability of the material to dissipate energy (viscous component), allowing a clear evaluation of the material mechanical performance. The ratio of the two is the dissipation factor or tan δ which is an indicator of the relative importance of the two components [4, 5, 15].

Dynamical Mechanical Thermal measurements of thick specimens, ≈ 0.1 mm of thickness, were performed using a Triton Tritec 2000 in the tensile and multifrequency conditions using four frequencies (1Hz, 3 Hz, 5 Hz and 10 Hz), with a standard heating rate of 5 ºC.min^{-1}. The *Tg* was determined as the peak in tan δ (Tan δ =E''/E') at 1 Hz where E'' and E' are the loss and storage modulus, respectively. The specimens were cut from PLA films obtained from solvent casting.

2.5.10. Wide Angle X-ray Scattering (WAXS)

The morphology, arrangement of crystalline and amorphous phase, plays a great influence on semi-crystalline polymer properties. Using synchrotron as X-radiation source, X-ray diffraction patterns were recorded and used to investigate the influence of the chemical structure on cold crystallization (crystallization that occur in amorphous systems that are heated above the glass transition) consequently on crystal structure [16]. Wide angle X-ray diffraction analysis was performed on a x-ray diffractometer Bruker D8 Discover. The powder samples were scanned in the range of $2\theta = 10 - 30$ °. The analysis comprised two heating scans at 2ºC.min^{-1}.

2.5.11. Preparation of PLA Films by Solvent Casting

PLA solutions of the selected samples with a polymer concentration of 0.05 g.mL^{-1} were poured into a Petri dish and allowed chloroform evaporation, first at room temperature. The resulting film was then dried in an oven until constant weight. PLA films thus obtained, with a thickness of ≈ 0.1 mm, were used for the DMTA and CIELAB analysis. Only molecular weights around 80 000 g.mol^{-1} or higher were able to form a clear, transparent and self-supporting PLA film, otherwise it totally crystallizes. The visual appearance of the resulting films is exemplified in Figure 2.5.

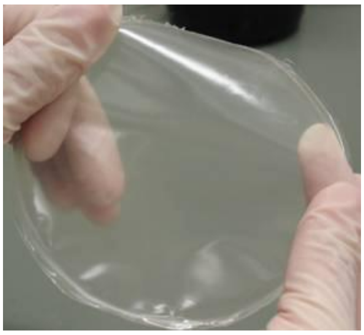


Figure 2.5: Visual appearance of a PLA film obtained by solvent casting.

2.5.12. Tensile Properties Analysis

Mechanical characterization is of major importance to assess the usefulness and the applicability as commercial material. Tensile analysis was performed by elongating a standard dog-bone shaped specimen and measuring the load carried by the specimen. The tensile properties of the selected PLA samples were determined using a Shimadzu tensile testing machine model Autograph AG-X 1KN at room temperature and a crosshead speed of 1 mm.min^{-1}. The dog-bone shaped specimens were prepared according to ISO 527-2 type 5A standard (20mm; 4mm; 2mm) in an injection moulding machine, Minijet II from Haake Thermo Scientific.

From the knowledge of the specimen dimensions, the load and elongation data, the stress-strain curve can be obtained. The stress (σ) was calculated by dividing the applied tensile force, *F*, by the area of the original cross sectional, A, as the follow:

$$\sigma = \frac{F}{A} \tag{2.3}$$

The strain (ε) was calculated by dividing the change in length, *ΔL*, by the original length or so-called gauge length (L_0= 20 mm) as the follow:

$$\varepsilon = \frac{\Delta L}{L_0} \times 100 \tag{2.4}$$

According to the Hooke's Law, modulus of elasticity or Young's modulus *(E)* is the ratio between stress and strain:

$$E = \frac{\sigma}{\varepsilon} \tag{2.5}$$

The E modulus presents the slope of the linear section of the stress-curves, the steeper the slope the stiffer the material. The maximum height of the stress-strain curve is called the tensile strength or yield point, which is a measure of the amount of the stress that a material can take before tearing. The point of rupture, or breaking strain, is the maximum extent of the stress-train curve [4]. Values of tensile strength and elongation at break were obtained based on the average tensile results of, usually, four tensile specimens.

2.5.13. Hydrolytic Degradation

The film specimens (2 mm of thickness) were placed in small bottles containing 10 ml a phosphate buffer solution (PBS) (pH 7.4) and subjected to hydrolytic degradation at room temperature, or 37 ºC for the bioadhesives materials, at a maximum of 12 weeks. Three samples were removed at predetermined times and the buffer solutions of the remaining samples were replaced. After, degradation the films were washed with fresh water and dried until constant weight. The degree of degradation was estimated from the weight loss, which was calculated using the following equation: $\textit{Weight loss}\ (\%) = \frac{(W_0 - W_t)}{W_0} \times 100$ (2.6)

where W_0 and W_t are the average weight of the three specimens before and after the hydrolytic degradation.

2.5.14. Optical Properties

One common system used to characterize colour in transparent plastic materials as described by the Commission Internationale de l´Eclairage is L* a* b* colour scale, Figure 2.6, also referred as the CIELAB system, which is used to determine and compare samples colour. The CIELAB method describes colour according to their position along three axes and can be visualized as a cylindrical coordinate system in which the axis of the cylinder is the brightness L*, ranging from 0 % (perfect black) to 100 % (white) and the radii are the chromatic variables a* and b*. Variable a* changes from green (negative) to red (positive) and variable b* changes from blue (negative) to yellow (positive). The L* value should be as high as possible and a* and b* as close to 0 as possible to provide a no colored material. From these variables an important parameter can be calculated, the colour difference between two points [17-20]: $\Delta E^* = \left[(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2\right]^{1/2}$ (2.7)

Another important parameter on the evaluation of transparent plastics is the Yellowness index obtained from the X, Y and Z tristimulus values of the CIE system, other colour scale, according to ASTM D 6290-98 [17]:

$$YI = \frac{100(1.2769X - 1.0592Z)}{Y} \tag{2.8}$$

PLA films obtained by solvent casting as explained above were analyzed in a spectrophotometer L&W Elrepho SE 070. The equipment was calibrated according to the working standards and references provided by the supplier. The values are reported in reference to the 2º standard observer, an illuminant C (light source) and are the average of 4 measurements.

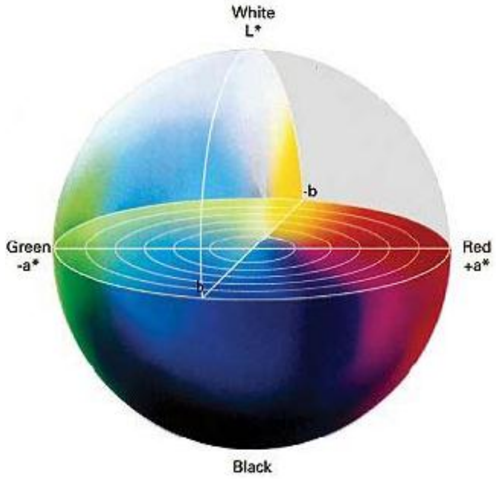


Figure 2.6: The representation of CIELAB System [20].

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3. SYNTHESIS OF POLY(LACTIC ACID) BY SOLUTION POLYCONDENSATION

D. A. S. Marques, S. Jarmelo, C. M. S. G. Baptista, M. Gil, Poly(lactic acid) Synthesis in Solution Polymerization, *Macromol Symp*, 296, 63-71, 2010.

D. A. S. Marques, S. Jarmelo, C. M. S. G. Baptista, M. H. Gil, Alternative Route to Poly(Lactic Acid) Synthesis**,** Proceedings of the 10th International Conference in Chemical Engineering-CHEMPOR2008, Braga, Portugal, 4-6 September, 2008.

This chapter is based on the above publications.

3.1. Introduction

Ring opening polymerization, ROP, is the current large scale process for Poly(lactic) acid, PLA, production. As explained in chapter 1, this process enables a precise control over polymer molecular weight but it is a quite complex process requiring the synthesis and purification of the intermediate lactide [1]. This contributes to the high price of PLA comparing to the petrol based thermoplastic competitors, restricting its further exploitation. The importance of developing more cost-effective PLA production technologies is therefore widely accepted in the literature. The direct step-growth polycondensation of lactic cid monomer is regarded [2] as the less expensive PLA production route. Its main advantage lies in eliminating the steps involving the production and purification of the intermediate lactide. Nevertheless, since the pioneer work of Carothers, only low molecular weight PLA was obtained by direct polycondensation, and therefore unsuitable for general purpose [2].

In 1994, a breakthrough in the PLA's state of the art was reported by Ajioka *et al*. [3]. They described the successful polycondensation of lactic acid in solution using a high boiling solvent to improve water removal. This polymerization route was carried out at the solvent boiling point, in the presence of a catalyst, and proved that it can be envisaged as an alternative route to ROP process. Water by-product was distilled from the reaction mixture together with the organic solvent while charging into the reaction mixture additional organic solvent with lower moisture content. The distilled solvent may pass through a drying agent bed, reducing moisture content to less than water solubility, and recicled to the reactor [3-5]. When the water content in the solvent was reduced to 50 ppm or less and the reaction proceeded for a long enough time, 30-40 h, molecular weights up to 1000 000 g.mol^{-1} were obtained directly from monomer. Nevertheless, other authors [6, 7] were not able to achieve the results reported by Ajioka *et al.* [3-5] and the information given by these authors on kinetics and process conditions was scarce.

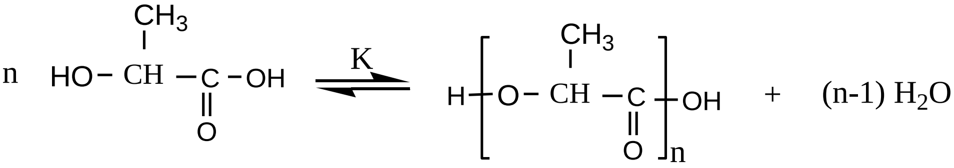
The lactic acid polycondensation, like any other esterification reaction, is a reversible process, where esterification and hydrolysis steps take place simultaneously, limiting reaction extent and the attainable molecular weight. Moreover, metal based catalysts, commonly employed in esterification reactions are reported to decompose or lose activity in the presence of protic substances such as water, acids or alcohols. New types of catalysts, such as tetrabutyl distannoxane, tetraphenyltin [8] and scandium trifluoromethanesulfonates [9], which are reported as water tolerant Lewis acids, have been exploited for lactic acid polycondensation in solution. These catalysts have bulky alkyl groups around the metal atoms and therefore exhibit a hydrophobic nature. Resistance to hydrolysis, usually, increases with increasing length of alkyl group. They have been tested for lactic acid solution polycondensation process, but the results obtained were not promising in terms of molecular weight and yield [8, 9]. Other catalytic systems have been reported for direct lactic acid solution polycondensation of which the most interesting is the system consisting of N,N'-dicyclohexylcarbodiimide/4-dimethylaminopyridine (DCC/DMAP) [10, 11]. This system enabled the synthesis of low molecular weight PLA at room temperature. The DMAP works as a catalyst and the DCC, in the presence of by-product water, precipitates as N-N'-dicyclohexyl-urea (DCU) being easily removed by filtration.

Aiming at developing an alternative route to ROP, the direct polycondensation of lactic acid in solution was studied during this project. This methodology employs a high boiling point solvent which helps removing the by-product, water. Attention was focused on the influence of the operating conditions (solvent, pressure, catalyst and drying agent) upon the final polymer's properties, such as molecular weight distribution (v*ide* chapter 2 section 2.5.1.) and optical purity (*vide* chapter 2 section 2.5.5.). The results reported in this chapter are based on publications at CHEMPOR2008 [12] and in the Macromolecular Symposia [13]. The experimental set-up and the experimental procedure followed in the solution polycondensation experiments were already described in chapter 2 (sections 2.2 and 2.4.1 respectively).

3.1.1. Step-Growth Polymerization of Lactic Acid

Lactic acid is an *alpha*-hydroxy acid, which comprises two functional groups that undergo a condensation reaction by releasing water as shown in the reaction scheme in Figure

3.1. This feature is particularly relevant, as it ensures stoichiometric concentration of both carboxyl, *–COOH*, and hydroxyl, *–OH*, end groups throughout the polymerization reaction avoiding undesired stoichiometric imbalance that may occur in same polycondensation systems [14, 15].



$$n\ HO-CH(CH_3)-C(=O)-OH \overset{K}{\rightleftharpoons} H-[O-CH(CH_3)-C(=O)]_n-OH + (n-1)\ H_2O$$

Figure 3.1: Dehydration reaction of lactic acid.

The polymer grows in a stepwise manner and, as the polymerization proceeds, the number of hydroxyl and the carboxyl end groups decreases. Kinetic studies usually assume that the reactivity of a functional group does not depend on molecule size. This assumption is referred in the literature [14, 15] as the concept of equal reactivity of functional groups, which was introduced originally by Flory [16] and proved to be valid when the functional groups are more than three atoms apart. When functional groups are separated by less than three atoms, as in the lactic acid monomer and dimmer molecules, their reactivity differs greatly. However, according to Roger and Long [14] the difference in reactivity diminishes rapidly with the increase in polymer length as the two functional groups become isolated from each other. It is a common mistake to consider that the lower diffusion rates of large molecules would lower the reactivity of its end groups. The reactivity of a functional group is dependent on the collision frequency of the end groups and not on the diffusion rate of the whole molecule. A terminal functional group attached to a growing polymer has a much bigger mobility than the polymer molecule as a whole, therefore the collision rate of such functional group with neighbouring groups remains roughly the same [14, 15].

Polyesterifications are slow reactions that are assumed to proceed through a substitution reaction at the carbonyl carbon with the formation of a tetrahedral intermediate, according to the $A_{AC}2$ addition-elimination mechanism in Ingold’s classification [14-15]. However, polyesterification mechanisms are not yet fully understood. Several factors affect the intermediate formation, an important one is the presence of bulky groups close to the reaction site which does not favour the formation of ester bond. This is particular relevant when studying lactic acid polycondensation due to the presence of the secondary hydroxyl group, explaining the lower polymerization rate comparing, for example, with the PET synthesis rate. In order to reach high molecular weight products an external catalyst is mandatory. Moreover, to continuously shift the reaction equilibrium towards polymer production, an efficient removal of water, the reaction by-product, must be accomplished. Once these experimental conditions are achieved, the polymerization can be considered irreversible [14, 15] leading to a rate of polymerization (r) that can be expressed as the rate of disappearance of carboxyl groups:

$$r = K[COOH]\,[OH]\,[cat] \tag{3.1}$$

Considering that the concentration of external catalyst, [cat], remains constant throughout the polymerization, $K' = K[cat]$ and as the concentration of the end groups is the same, [$COOH$]=[OH], the rate of polymerization can be written as:

$$r = K'[COOH]^2 \tag{3.2}$$

Integrating this equation gives information on the carboxyl groups concentration, $[COOH]$, during the batch polymerization:

$$\frac{1}{[COOH]} = K't + \frac{1}{[COOH]_0} \tag{3.3}$$

where $[COOH]_0$ represents the initial concentration of carboxyl groups. Considering that at time t, the extent of reaction, p, is $p = \frac{[COOH]_0 - [COOH]}{[COOH]_0}$, equation (3.3) becomes:

$$\frac{1}{1-p} = 1 + K'[COOH]_0 t \tag{3.4}$$

The concentration of carboxyl groups in the initial mixture and in the collected samples is usually measured by titration, allowing calculating the extent of reaction.

Another important relationship is the Carothers equation [15] calculated using the conversion of reactive end groups, not monomer conversion, which defines the theoretical degree of polymerization (DP):

$$DP = \frac{1}{(1-p)} \tag{3.5}$$

Step-growth polymerization of lactic acid has been studied, mainly as an intermediate step in the ROP process [17]. The understanding of its kinetics and reaction mechanism is crucial whatever the process under consideration, however very little has been written on this subject. Additional work must be carried out taking into account the side reactions that have been reported in polyesterification reactions such as transesterification, hydrolysis, degradation, cyclization [2, 13, 14], considering the stoichiometric imbalance in the presence of monomer impurities and water by-product diffusion constraints. The concept of equal reactivity of functional end groups at different chain lengths should also be assessed since some authors have shown evidences that this assumption is not always accurate, mainly, when the elimination of the side products of the reaction is hindered [18-20].

Until now, the major effort in the study of lactic acid polycondensation has been finding an efficient catalyst rather than studying the reaction mechanism. Actually, only one research group published a mathematical model for lactic acid polycondensation [21, 22] based on Flory's assumptions.

3.2. Results and Discussion

3.2.1. Polymerization Progress

The experiments in this project started with the thermal dehydration of the 80 % lactic acid solution. The chromatographs in Figure 3.2, were obtained by SEC (*vide* chapter 2 section 2.5.1), and enables to compare the broad molecular weight distribution of the mixture of lactic acid oligomers with different sizes, achieved by distillation of the monomer aqueous solution, to a narrower molecular weight distribution at lower retention time of the final polymer. Figure 3.3 shows the ^{1}H NMR spectrum of the PLA polymer (*vide* chapter 2 section 2.5.2). The bands of the $-CH_3$ and $-CH$ groups appear at 1.6 and 5.2 ppm, respectively, confirming the successful synthesis of PLA. The band at 7.3 ppm refers to the solvent used in the analysis, $CDCl_3$.

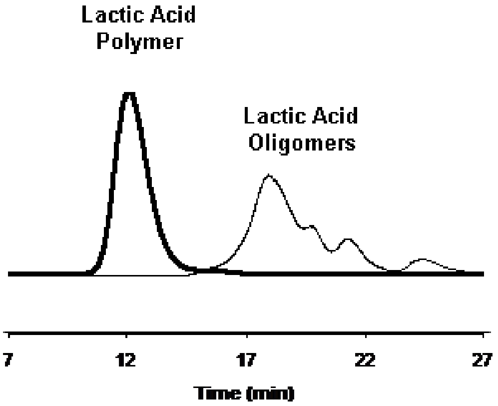


Figure 3.2: SEC curves of the mixture of oligomers and PLA.

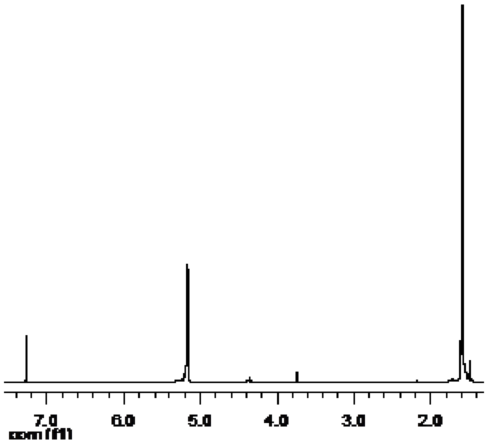


Figure 3.3: ^{1}H NMR spectrum of PLA.

Figure 3.4 presents the evolution of carboxyl end groups, (♦), and reaction extent, (▪). As expected for a step-growth polymerization, at the beginning of the reaction a steep decrease in carboxyl end groups concentration is registered, which corresponds to an increase in reaction extent. The initial lactic acid molecule contains a carboxyl and a hydroxyl group, which are responsible for the high polarity of the initial reaction mixture. Whilst the initial monomer is rapidly converted into a mixture of small oligomers with different chain lengths, the concentration of carboxylic groups decreases as well as the polarity of the reacting mixture [23]. This was reported by Moon *et al.* [23], who related polarity change to catalytic activity. Therefore, the initial thermal dehydration is self-catalyzed by the carboxyl group of the monomer and an external catalyst is added after oligomerization in order to further carry out the polymerization, avoiding a negative effect on catalyst activity.

Figure 3.5 shows the average molecular weight, (▲), obtained by SEC, and the polymerization degree, (♦), calculated with equation 3.5, during the course of experiment 6. These results point out a linear molecular weight increase along reaction time. On the other hand, the polymerization degree *(DP)* shows a steep increase later in the polymerization. This is consistent with the results presented in Figure 3.4, confirming that to reach high molecular weight PLA polymers, the conversion of carboxyl end groups must be very close to 100 %. Experimental results for esterification reactions presented in the literature show that the plot of $1/(1-p)$ *vs* reaction time is linear in the high conversion range [15] and Figure 3.5 confirms this pattern. The nonlinearity in the low conversion region is attributed by Flory [16] to the changes in reaction medium properties, mainly, the polarity decrease.

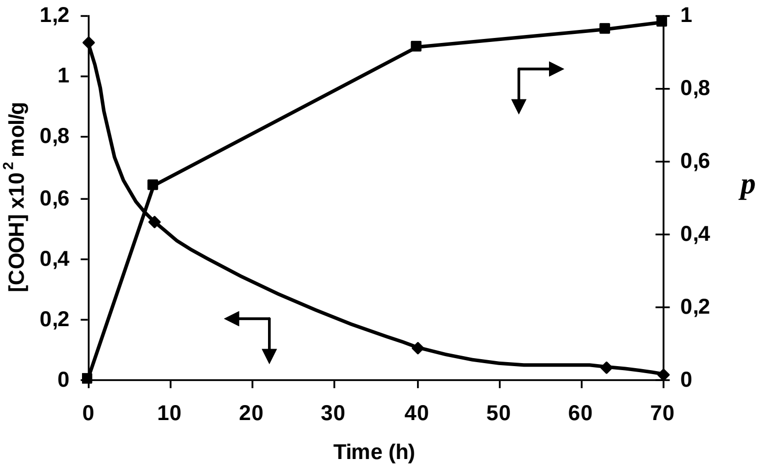


Figure 3.4: Evolution of carboxyl end groups concentration, [*COOH*], and reaction extent, *p*, during the experiment 6 in Table 3.1 (♦– represents the [*COOH*]; ▪ – represents the *p*).

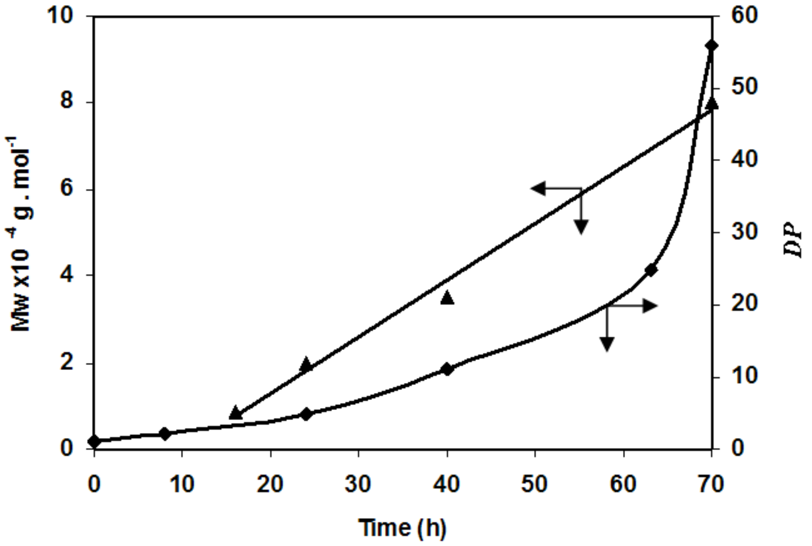


Figure 3.5: Average molecular weight, *Mw*, and degree of polymerization, *DP*, during reaction time for PLA6 in Table 3.1 (▲– represents the *Mw*; ♦– represents the *DP*).

3.2.2 Polymerization Conditions

Several experiments were carried out in order to set the experimental conditions to perform lactic acid polycondensation in solution. Table 3.1 summarizes the most relevant experiments and the experimental conditions used in each one: solvent, catalyst, pressure and reaction time. The average molecular weight (*Mw*), polydispersity index (*PD*) and optical purity (*OP*) is also shown. These polymer properties were measured using different characterization procedures described in chapter 2 section 2.5.

Table 3.1: Lactic acid solution polycondensation - experimental conditions and results.

Nº	**Solvent**	**Catalyst**	**Pressure (bar)**	**Time (h)**	***Mw*** **($g.mol^{-1}$)**	***PD***	***OP*** **(%)**
PLA1	*m*-Xylene	$SnCl_2.2H_2O$	1	30	3 200	1.5	83
PLA2	Anisole	$SnCl_2.2H_2O$	1	24	1 800	1.9	79
PLA3	*m*-Xylene	$SnCl_2.2H_2O$	1	24	7 900	1.3	83
PLA4	*m*-Xylene	$SnCl_2.2H_2O$	1	48	23 200	1.3	87
PLA5	*m*-Xylene	$SnCl_2.2H_2O$	0.3	40	45 400	-	54
PLA6	*m*-Xylene	$SnCl_2.2H_2O$	0.3	70	80 000	1.3	-
PLA7	*m*-Xylene	Sn(II)Oct	0.1	48	35 800	1.6	0
PLA8	*m*-Xylene	Ti(IV)But	0.1	40	40 800	3.2	-
PLA9	Anisole	$SnCl_2.2H_2O$	0.4	64	47 200	1.5	48
PLA10	*m*-Xylene	DBSA[a]	0.3	48	17 500	1.5	83

[a] 0.2 % v/v

The experimental programme used for the step-growth polymerization of lactic acid was intended to screen catalysts and solvents while studying the influence of process variables on the quality of the final polymer. It is well-known that PLA for commodity applications should exhibit high molecular weight and high stereoregularity, since these parameters have a strong influence on the mechanical properties and degradation rate of the polymer. Thus, the molecular weight and optical purity were chosen for evaluating the performance of the experiments.

Experiments 1 and 2 (PLA1 and PLA2, Table 3.1) were carried out at atmospheric pressure without removing the water during the polymerization. The results obtained by SEC technique show that the polymers synthesized under these experimental conditions have the lowest average molecular weight among the polymers analysed. To achieve high molecular weight polymers, it is essential to ensure an efficient water removal, as mentioned before. In order to increase the molecular weight, different strategies to control water content in the reacting mixture were tested in the subsequent experiments.

In the remaining set of experiments (3 to 10), after the initial distillation step, the Dean-Stark trap was replaced by a tube packed with molecular sieves, synthetic zeolites, which have the ability to adsorb small molecules such as water. This new set-up, illustrated in Figure 2.1 of previous chapter 2, allowed the evaporated solvent containing the by-product water to pass through the molecular sieves bed, the water was removed and the dry solvent was recycled into the reactor vessel. This approach allowed a considerable increase in the molecular weight (PLA3 and PLA4, Table 3.1), however, not enough for the intended target. In order to promote a more effective water removal, in the set of experiments 5 to 10, the pressure in the reaction vessel was gradually reduced through the course of the polymerization, leading to higher molecular weight polymers.

3.2.3 Catalyst Screening

As already mentioned, the esterification processes have a slow reaction rate and therefore an external catalyst is required. Proton acids, such as H_2SO_4 or H_3PO_3, are often used. However, metal ions, such as Lewis acids, can be more efficient than hydrogen ions in some esterification reactions [14]. According to the data shown in Table 3.1, the catalyst has a great influence on molecular weight and optical purity of the final product. Every polymer obtained (PLA1 to PLA10) has an optical purity lower than 100 %, suggesting the occurrence of some racemization reactions. At reduced pressure the optical purity of the polymers was drastically lower than that exhibited by the polymers synthesized at atmospheric pressure, experiments 1 to 4. Most probably, this result was due to a leak in the set-up, which may have allowed oxygen in, promoting the ester interchange reactions. These kind of reactions have also been reported for tin chloride ($SnCl_2.2H_2O$) used as catalyst in bulk/melt lactic acid polycondensation [23]. However, tin chloride was the most effective catalyst in these tests and allowed achieving the highest molecular weight, near 80 000 $g.mol^{-1}$ (PLA6, Table 3.1).

Sn(II)Oct, a Lewis acid catalyst, is ranked as an efficient catalyst for reaching high molecular weight PLA by ring opening polymerization [1]. However, Table 3.1 shows that for direct esterification of lactic acid tin chloride is more efficient. Sn(II)Oct was used in experiment 7. For this polymer an optical purity of 0 % was measured *i.e.*, the polymeric chain of PLA7 contains the same amount of L- and D- estereoisomers; therefore one can refer that Sn(II)Oct is a strong ester interchange catalyst promoting high levels of racemization. Titanium(IV) butoxide, (Ti(IV)but), is also a Lewis acid and proved to be an efficient polyesterification catalyst, although the final polymer exhibited a too broad molecular weight distribution.

Table 3.1 illustrates that reduced pressure improves the polymerization rate but this was not sufficient to enable achieving a high molecular weight PLA with 4-dodecylbenzenesulfonic acid, DBSA, a weak proton acid. Nevertheless, according to the data DBSA could be used to control the polymer stereoregularity. Dibutyltin dilaurate, DBTL, was also tested [24] but did not lead to encouraging results, data are not shown here.

As shown in Table 3.1 the course of the polymerization is also dependent on the solvent under consideration. The two solvents tested in this chapter were anisole in the experiment 9 (b.p. 154 ºC) and *m*-xylene on the remaining experiments (b.p. 139 ºC). Polar solvents are usually regarded as enhancing polymerazation rate due to specific interactions of the solvent with the functional groups. Surprisingly, the *m*-xylene seems to be a better solvent for PLA synthesis than anisole, producing less racemization reactions and, furthermore, it has a lower boiling point requiring a lower reaction temperature.

3.2.4 Chemistry of Lactic Acid Solution Polycondensation

The lactic acid polymerization by step-growth involves several reversible reactions and, the main one, is represented in Figures 3.1. The dehydration gives the major contribution to achieving a high molecular weight polymer and the equilibrium, in this reversible reaction, must privilege the direct reaction [24]. The key to obtaining a high molecular weight polymer is to promote efficient water removal, which in this work was accomplished by using drying agents and vacuum at the solvent boiling point. Depolymerization of growing PLA chains into lactide is the main degradation reaction. The organic solvent has an important role to control the extent of this reaction since it allows reintroducing the lactide into the reaction medium during the polymerization. Other cyclization reactions producing macrocyclic polymers have been identified in PLA synthesis [25]. Kricheldorf *et al* [26-30] have been studying several polycondensation reactions and concluded that high dilution conditions favour cyclization rather than linear macromolecules. According to this author, only a small weight fraction of cycles is present in bulk polycondensation, whereas the fraction of cycles increases rapidly upon dilution, since the probability of terminal end groups of the same molecule meeting and reacting increases. Moreover, after every end group has reacted, which means at 100 % of end groups conversion, all reaction products should be cycles, irrespectively of bulk or dilution conditions [26-30]. It has also been reported by other authors that commercial grades of polyesters have 0.25-2.0 % weight content of cyclic polymers [31]. Unfortunately, in this work it was not possible to assess the presence of these macrocycles. The macrocycles occurrence would help explaining the low yields obtained in the solution experiments, around 30 %. The optical purity results also show the occurrence of racemization reactions, which are attributed to transesterification [13, 24], this issue will better explained in the following chapters.

3.2.5. Additional Remarks

At the beginning of this project, it was aimed to study the kinetics of the polymerization process, but this proved to be very difficult due to the experimental conditions used. Online monomer and polymer concentration measurements are not achievable and sampling would have to be carried out during the reaction. The composition would be evaluated later by end groups titration. At this stage it is important to remind that experiments were carried out at a temperature in the 139-154ºC range and under vacuum. These operating conditions render sampling an arduous task, putting at risk the progress and success of the polymerization.

The accurate measurement of the concentration of the unreacted functional groups in the samples is mandatory for kinetic studies. This is usually accomplished by titration of unreacted carboxylic groups (*vide* chapter 2, section 2.5.4). Titration was found suitable for quantitative analysis of oligomers around 2 000 g.mol^{-1}, but rather erroneous and not quantitative for higher molecular weight molecules, as can be verified for the very low polymerization degrees of PLA6, Figure 3.5. This finding is probably due to the fact that aliphatic ester linkages undergo hydrolysis under titration conditions and titration is highly sensitive to the presence of reaction impurities. Alternatively to the carboxyl titration, hydroxyl groups may also be measured. This requires the previous acetylation of the *–OH* groups with phthalic or acetic anhydride in the presence of pyridine as catalyst, followed by back titration of excess *–COOH* groups [15]. This procedure is more complex and less accurate than carboxyl group determination, especially when secondary *–OH* groups are involved, therefore it was not considered in this project since the *–COOH* titration results were not encouraging for higher molecular weight samples.

Another technique for the determination of low chain length polymers end groups is RMN (*vide* chapter 2 section 2.5.2). According to some authors [32] RMN can be used for PLA with a polymerization degree lower than 18. This is the polymer size range that can already be assessed by the *–COOH* titration, and therefore also unsuitable for high molecular weight polymers.

Although difficult, the identification and quantification of the end groups is crucial when assessing reaction kinetics and also when any kind of modification or post-polymerization process is under consideration. Determination of water removal rate may also be applied for continuous follow up of esterification reactions, making use of reaction stoichiometry. This method is difficult to carry out because it requires continuous measurement of the water produced in the reaction and, in the experimental set-up used in this study water is adsorbed on the molecular sieves bed.

In spite of the challenges described in the previous paragraphs, samples were collected during experiment 6 and the information was shown and discussed above in section 3.2.1. Owing to the difficult to ensure that all the experiments were carried out under exactly the same conditions and the unavailability of accurate procedure for quantification of functional groups it was decided no longer to collect samples during the polymerization and no longer to perform kinetic studies. The performance of the process will be, mainly, assessed by measuring the molecular weight of the final polymer by SEC technique and by torque measurements.

3.3. Conclusion

Poly(lactic acid) was successfully synthesized by direct condensation of lactic acid in solution. The use of high boiling point solvents, of a drying agent and of reduced pressure, has been shown to be a good strategy to allow an efficient removal of the reaction by-product, water, and, consequently, obtaining high molecular weight polymers. This polymerization technique enabled producing high molecular weight PLA polymers directly from monomer, as an alternative to the three steps required by the ROP method.

The change of L- to D-lactyl units, supported by the optical purity results, confirmed to be a critical issue in PLA synthesis by polycondensation. Thus, its control is essential and can be attained by selecting a suitable catalyst. In order to avoid racemization reactions in lactic acid polymerization, protonic acids proved to be the best catalysts. More research work should be carried out to find the best catalyst that provides an enhanced molecular weight and lower racemization extent.

Solution processes involve the use of organic solvents rendering the processes environmentally unattractive. Moreover, the yields obtained were too low and the 70 hours reaction time required to achieve high molecular weight PLA can been considered as excessive from an industrial point of view, much higher than the one reported by Ajioka and co-workers [3-5], roughly 30-40 h. Nevertheless, the results reported here are consistent with results published by other authors [6-7], who were also not able to reproduce the Ajioka *et al.* [3-5] results. This may be due to difficulties in achieving an effective low moisture content in the solvent throughout the polymerization. These results did not encourage pursuing with experiments on solution polymerization. Aiming at reaching high molecular weight PLA, alternative routes were envisaged and studied in the following chapters.

3.4. References

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4. BULK POLYTRANSESTERIFICATION OF L-LACTIC ACID ESTERS

D. S. Marques, M. H. Gil, C. M. S. G. Baptista, Bulk Polytransesterification of L-Lactic Acid Esters: an Alternative Route to Synthesize Poly(Lactic Acid), *J Appl Polym Sci*, 2012, 125, S2, E283-E289.

D. S. Marques, M. H. Gil, C. M. S. G. Baptista, Synthesis of Poly(lactic acid) by Bulk Polytransesterification, Proceedings of CHISA 2010: 19th International Congress of Chemical and Process Engineering, Prague, Czech Republic, 28 August - 1 September 2010.

This chapter is based on the previous publications.

4.1. Introduction

Since the early studies carried out by Carothers, polyesters have become one of the most versatile classes of polymers [1, 2]. Among them, poly(ethylene terephthalate) (PET), is widely used to manufacture fibres and bottles. In the last decades, the need to develop sustainable alternatives to petrochemical origin materials associated with an increasing demand for biodegradability [3-6] has led to a remarkable interest in aliphatic polyesters such as poly(lactic acid) (PLA). Thus, the development and the improvement of synthesis processes involving environmentally friendly materials are extremely important in enabling its future implementation by the industry and therefore in expanding the use of these materials.

Since the results on lactic acid solution polycondensation, reported by Ajioka and coworkers in 1994 [7], a renewed interest in studying the synthesis of PLA by conventional step-growth polymerization methods has been registered. Step-growth polymerizations can be carried out either in solution or in the bulk, and for twenty years, poly(lactic acid) has been obtained by these two alternative processes by a large number of research groups [7-12]. However, the polytransesterification of lactic acid esters has not been reported.

To the best of our knowledge, there is no previous record on the use of lactic acid esters as monomers for the PLA synthesis by polytransesterification. On the other hand, the procedure for purification of lactic acid obtained by fermentation [13, 14] usually requires an esterification step with ethanol and a subsequent hydrolysis of the ester to revert it to lactic acid. In fact, the ethyl L-lactate is sold at a lower price than L-lactic acid. The use of these esters for PLA synthesis would enable simplifying the lactic acid purification process while avoiding the synthesis and purification of the lactide. Therefore, it would offer comprehensible advantages over ring opening polymerization process, ROP, and over lactic acid polycondensation. Moreover, the carboxylic end group protection in the polylactide has been reported as an additional factor towards thermal stability of the resulting polymer [15], increasing the degradation temperature by 10 ºC.

Preliminary experiments involving the polytransesterification of different L-lactic acid esters in molten state were successfully carried out, in the frame of this project. Figure 4.1 shows the simplified polytransesterification mechanism applicable to the different L-lactic acid esters tested in this experimental work. In a first stage the procedure was developed for ethyl L-lactate and later extended to other lactic acid lactates. The experimental set-up (*vide* Figure 2.2 and section 2.2) and the experimental procedure employed in the bulk polytransesterification experiments were already described in chapter 2, section 2.4.3. The polymerization main product was PLA with carboxylic end group protection and the by-product is an alcohol, whose chemical structure depends on the monomer used.

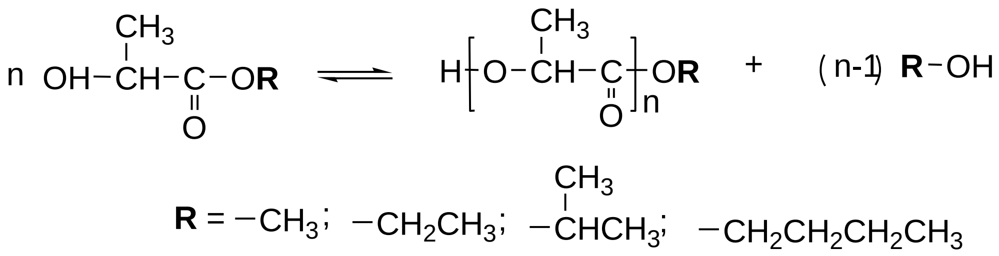

Figure 4.1: Polytransesterification mechanism for different L-lactic acid esters.

4.2. Results and Discussion

The experimental work reported here was mainly focused on assessing the experimental conditions required to synthesize PLA by bulk polytransesterification of different commercially available L-lactic acid esters in order to develop a reliable polytransesterification procedure for these monomers. The experimental procedure was followed as described in section 2.4.2, and different L-lactic acid esters were assessed. The experimental conditions: monomers, catalysts or catalytic systems and catalyst concentration; as well as the results achieved: molecular weight, thermal properties, optical purity and visual appearance are compiled in Table 4.1. The molecular weight information was assessed by SEC (*vide* section 2.5.1), the optical purity, *OP*, involved measuring the specific rotation (*vide* section 2.5.5) and the thermal properties were evaluated by DSC (*vide* section 2.5.7).

Table 4.1: Results obtained in different L-lactic acid esters bulk polytransesterification experiments using a two steps process (T_1=170ºC and P_1= 1 bar; T_2= 180ºC and 10 mbar< P_2 >1 bar).

PLA	**Lactate**	**Catalyst** ***(%w/w)***[a]	**Co-catalyst** ***(1% w/w)***	***Mw*** ***(g.mol^{-1})***	***PD***	***Tg*** ***(ºC)***	***Tm***[b] ***(ºC)***	***Xc*** ***(%)***	***OP*** ***(%)***	**Appearance**
PLA1	Ethyl	Sb_2O_3 (0.25)	-	12 700	1.7	53	154	43	86	White
PLA2	Ethyl	Sb_2O_3 (0.5)	-	15 300	1.3	50	152	37	85	pale yellow
PLA3	Ethyl	Sb_2O_3 (1)	-	14 300	1.4	50	152	37	85	pale yellow
PLA4	Ethyl	Sb_2O_3 (0.25)	Zn(acet)	22 300	1.4	54	155	47	85	White
PLA5	Ethyl	Sb_2O_3 (0.25)	Mn(acet)	11 300	1.5	48	147	34	82	White
PLA6	Ethyl	Sn(Oct) (0.25)	Zn(acet)	17 800	1.4	55	143	14	78	pale yellow
PLA7	Ethyl	$SnCl_2$ (0.25)	Zn(acet)	20 700	1.3	55	Nd	0	65	pale yellow
PLA8	Ethyl	TNBT (0.25)	Zn(acet)	5 000	1.4	47	145	41	88	White
PLA9	Ethyl	Sn (0.25)	Zn(acet)	6 500	1.8	49	144	48	83	White
PLA10	Methyl	Sb_2O_3 (0.25)	Zn(acet)	9 400	1.4	44	Nd	0	67	pale yellow
PLA11	*i*Propyl	Sb_2O_3 (0.25)	Zn(acet)	8 500	1.4	48	Nd	0	68	pale yellow
PLA12	Butyl	Sb_2O_3 (0.25)	Zn(acet)	17 200	1.6	52	144	41	87	White

[a] Weight ratio (catalyst/initial monomer)
[b] Taken from the first heating scan
[nd] Not detected

4.2.1 Bulk Polytransesterification of Ethyl L-lactate

The first stage of this work was carried out using ethyl L-lactate as monomer for the polytransesterification process (PLA1-PLA9). Preliminary experiments, not shown here, revealed that in the absence of a metal-based catalyst the entire volume of monomer was evaporated and withdrawn during the initial stage of the process and the polytransesterification reaction did not take place. This finding was contrary to previous lactic acid polycondensation results discussed in chapter 3 where it was reported that the lactic acid polymerizes in the absence of an external catalyst by self-catalysis of terminal carboxyl groups [12].

After this preliminary assessment, the experimental procedure was altered and carried out in two different steps. A first step in the presence of a metal-based catalyst, at temperature set-point of 170 ºC and atmospheric pressure under a gentle stream of nitrogen applied to remove the alcohol of the exchange reaction, allowing monomer transesterification and leading to viscous oligomers. The final step was carried out at 180 ºC and reduced pressure, in order to further shift the reaction equilibrium towards polymer production by means of a more efficient by-product withdrawal. During the polytransesterification process the partial condenser (*vide* Figure 2.2) has an important role to selectively distil off the by-product alcohol and reflux the monomer, avoiding its elimination and yield loss. At the end of the experiments, close to 100 g of polymer and 100 mL of distillate, alcohol and monomer, were collected.

The final product was a viscous melt with brown colour. After polymer precipitation the colour of the materials ranged from white to a pale yellow powder as can be seen in Figure 4.2, depending on experimental conditions. In trading, the polyesters colour is an important quality parameter and therefore it is used here for qualitative assessment. The typical molecular weight distributions of the oligomers and final polymer, obtained by SEC, are presented in Figure 4.3 confirming the expected increase in molecular weight in the second step of the polytransesterification.

Figure 4.2: Visual appearance of final polymers powder: white (a) and pale yellow (b).

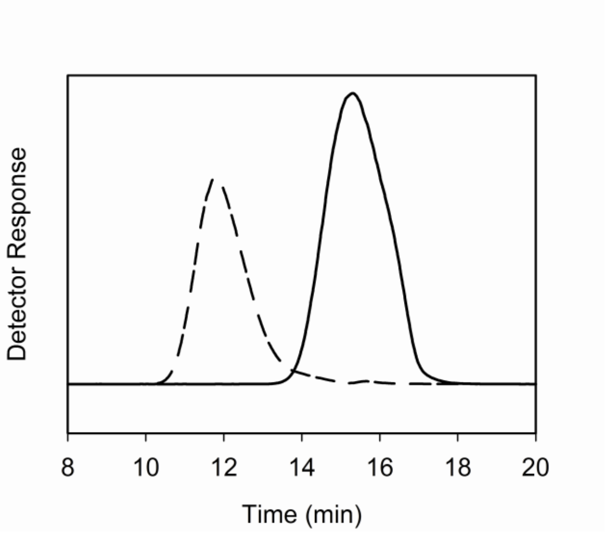

Figure 4.3: Typical molecular weight distribution obtained by SEC for polytransesterification products: oligomers after the first step (full line) and final polymer (hatched line).

4.2.2. Catalyst Screening

Polytransesterification, as explained above and confirmed in preliminary experiments, requires the addition of a metal-based catalyst. There is no information available in the literature regarding the synthesis of PLA by lactic acid esters polytransesterification. The information on the best catalysts to be screened was gathered from the PET polytransesterification process and from previous results on PLA synthesis by polycondensation [1-8, 16-18]. Table 4.1 summarizes the catalysts/catalytic systems studied and the results obtained (PLA1-PLA9) while studying the ethyl L-lactate polytransesterification. It is noticeable that the employed catalyst has a dramatic influence upon the properties of the final polymer, from molecular weight, to optical purity and even appearance.

The work began by studying antimony III oxide (Sb_2O_3) as catalyst and assessing the influence of catalyst concentration by introducing three different contents of Sb_2O_3.(PLA1-PLA3). Antimony III oxide is a Lewis acid widely used in the PET synthesis by dimethyl terephthalate polytransesterification with ethylene glycol [1, 2]. Slightly higher molecular weight was obtained when using a catalyst content of 0.5 and 1 % w/w (weight of catalyst/initial weight of monomer). However, appreciable colour change was registered in PLA2 and PLA3 suggesting that the occurrence of thermo-oxidative degradation reactions are promoted as catalyst content is increased. Based on these results and aiming at minimizing the resulting yellowing, 0.25 % w/w of Sb_2O_3 was selected as the optimal catalyst content for the following experiments, and the same initial catalyst content was used when testing the remaining catalysts (PLA6 – PLA9).

The next step consisted in testing two different metal acetates as co-catalysts of antimony III oxide, as suggested by PET related literature [2]. The addition of 1 % w/w of zinc acetate as a co-catalyst of Sb_2O_3 (PLA4) allowed a considerable increase in the molecular weight, from 12 700 to 22 300 g.mol^{-1}, the best result in Table 4.1 both in terms of molecular weight and polymer colour. Testing zinc acetate as sole catalyst, experiment not shown in Table 4.1, did not lead to a polymer. Although the catalytic mechanism has not been fully understood, the addition of zinc acetate as a co-catalyst of Sb_2O_3 showed a synergic effect. Manganese acetate was also assessed as a co-catalyst (PLA5) but the molecular weight was lower than the one obtained before when using only Sb_2O_3 (PLA1).

Several other compounds reported in the literature as efficient polyesterification or polytransesterification catalysts [1-8, 16-18] were then tested. Based on the better performance obtained in PLA4, these experiments implemented the use of the binary catalytic system approach (PLA6-PLA9) and, according to the results discussed above, zinc acetate was the selected co-catalyst. Among the catalytic systems screened for the polytransesterification of ethyl lactate, the Sb_2O_3/Zn acetate was confirmed as the most effective, enabling better polymer properties. The molecular weight of PLA7 was also greater than 20 000 g.mol^{-1}, ranking high the performance of $SnCl_2.2H_2O$ as a polytransesterification catalyst, but the yellowing of the final polymer and the low optical purity measured discourages its further utilization. $SnCl_2.2H_2O$ is also a strong Lewis acid and is largely used in bulk polycondensation of lactic acid [7]. Therefore the 68 % optical purity of PLA7, the lowest among the entire series of polymer samples, was an unexpected finding. The addition of titanium (IV) butoxide (TNBT) (PLA8) led to poor results in terms of molecular weight, but it was the most efficient catalytic system in terms of polymer stereoregularity control, exhibiting the highest optical purity degree, 88 %. The optical purity issue and its influence on polymer properties will be discussed in a further section of this work. The polydispersity index, *PD,* of all samples was below 2.

4.2.3. Influence of Different Monomers

Aiming at studying the influence of the alkyl substitute group of the L-lactate on the polytransesterification reaction, other L-lactic acid esters such as: methyl, *iso*propyl and butyl L-lactate were tested. The same experimental conditions (time, temperature and pressure) and the catalytic system selected from the ethyl L-lactate experiments (0.25 % w/w of Sb_2O_3 and 1 % w/w of Zn acetate) were implemented and the samples obtained are listed as PLA10, PLA11 and PLA12 (Table 4.1).

As it would be expected, the monomers specific structure, *i.e.* the length of the alkyl substitute group in the different L-lactic acid esters, has a great influence on the polymerization performance. Polytransesterification is a reversible reaction (Figure 4.1), reported in the literature [1] as an $A_{AC}2$ addition-elimination mechanism. This mechanism proceeds through a substitution reaction at the carboxyl carbon, with the formation of a tetrahedral intermediate, followed by the elimination of the leaving group, *i.e* the alkyl substitute group. According to Rogers and Long [1], nucleophilic attack on the carbonyl group by the alcohol is a key step in the substitution process, being strongly dependent on the nature of the leaving group. The steric effect of bulky groups close to the reaction site does not favour the ester formation, which might explain the poor result obtained while using *iso*propyl L-lactate (PLA11). However, the steric hindrance effects do not explain the poor results obtained when using methyl L-lactate (PLA10).

Among the L-lactic acid esters tested, methyl L-lactate has the lowest boiling point, 144ºC. Conversely to the other records, at the end of experiment 10, a larger volume of distillate, 140 mL, and a smaller weight of polymer, 50 g, were collected. The extent of methyl L-lactate vaporization, expressed in the distillate volume collected has certainly changed the monomer/catalyst ratio during the process having a negative effect on polymerization progress and explaining the poor properties of PLA10.

According to the experimental results in Table 4.1, ethyl L-lactate allowed achieving the best product and might be the best choice for PLA synthesis by polytransesterification. This finding is contrary to PET synthesis process, where dimethyl terephthalate is the monomer usually employed [2].

4.2.4. Thermal Characterization

Information on the thermal behaviour of materials is relevant in order to evaluate the physical properties of semi-crystalline polymers. Therefore, the polymer samples obtained in the frame of this work were subjected to DSC analysis (*vide* Section 2.5.7). The glass transition temperature (Tg), the melting point (Tm) and the crystallization degree (Xc), evaluated from fusion enthalpy of the first heating scan, are also summarized in Table 4.1. Figure 4.4 shows the DSC traces of the samples obtained in the second heating scan.

It is easily noticed in Figure 4.4 that the thermal properties of the samples are greatly different and the polymers range from semi-crystalline (PLA1-6, PLA8, PLA9 and PLA12) to amorphous behaviour (PLA7, PLA10 and PLA11). As expected, glass transition and melting temperature are highly dependent on molecular weight and the data registered in Table 4.1 are generally in agreement with this trend. As the molecular weight increases, the molecular mobility becomes restricted influencing its thermal behaviour. In Table 4.1 the glass transition temperature (Tg) ranges from 44 ºC to 55 ºC and the PLA's melting temperature (Tm) from 143 ºC to 155 ºC. Both temperature ranges are lower than those reported for commercial polylactides [3], but are in agreement with previous results for PLA in the same molecular weight range [7-9] produced by lactic acid polycondensation. Moreover, as shown in Figure 4.5, the experimental glass transition temperature, full symbols, is in good agreement with the theoretical values, empty symbols, calculated with Fox-Flory equation (Equation 4.1). Despite the clear trend (Figure 4.5) of increasing Tg with molecular weight, the experimental values are slightly scattered, which can be due to discrepancies in the optical purity degree. The introduction of D-lactyl unities into the polymer backbone alters the chain mobility and has a strong impact on thermal properties.

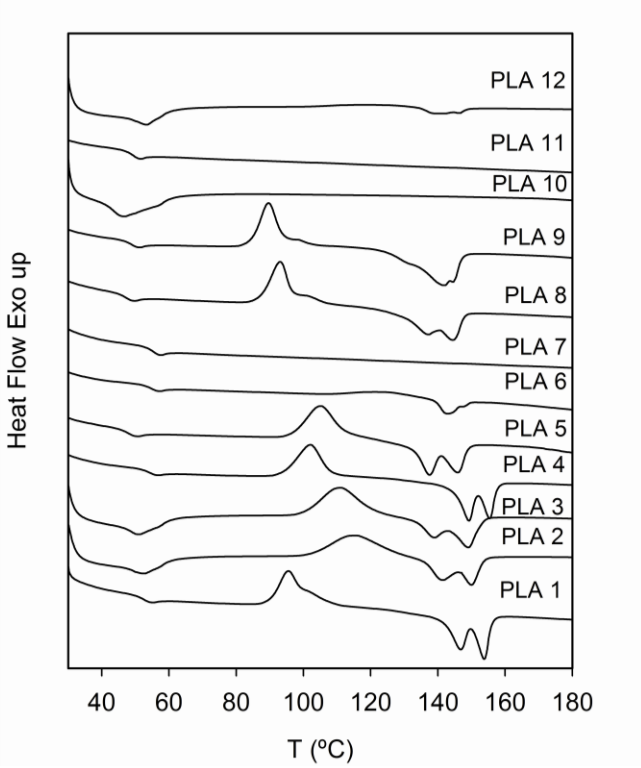

Figure 4.4: DSC traces from second heating scan of the PLA samples.

The glass transition temperature theoretical values were obtained with Fox-Flory equation [19]:

$$Tg(^{\circ}C) = Tg^{\infty} - \frac{K}{Mn} \tag{4.1}$$

where, according to Jamshidi *et al.* [19], the glass transition temperature of PLLA with a infinite molecular weight, Tg^{∞}, is 58 ºC, and K is $5.5\text{x}10^4$, a constant representing the influence of the excess free volume of the polymer end groups. It is worth mentioning that, according to experimental results, equation 4.1 fails in the low molecular weight region. This can be attributed to the influence of the carboxylic end group protection, which might have a stronger influence on the low molecular weight polymer chains. Additionally, the Fox-Flory parameters reported by Jamishidi *et al.* [19] were recorded for polylactides with free end groups and not protected ones, as those produced in this experimental work, which can further contribute to the differences between experimental and theoretical values registered in Figure 4.5.

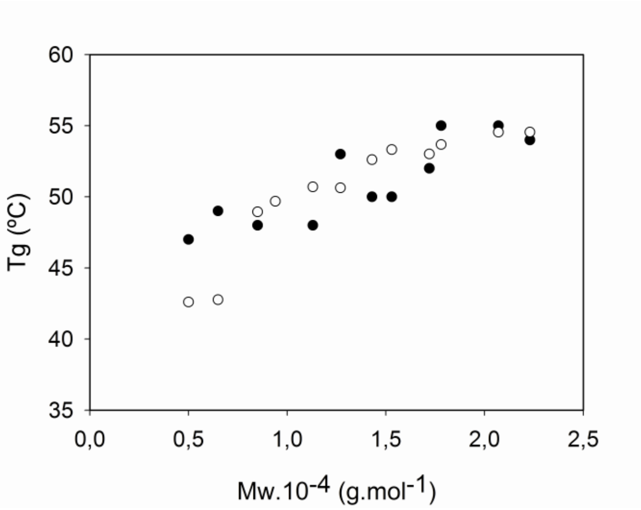

Figure 4.5: PLA sample's glass transition temperature *vs* molecular weight: (●) experimental obtained by DSC and (○) theoretical, obtained with Fox-Flory equation (eq. 4.1).

The Flory equation can also be used for predicting the melting point as function of the molecular weight and Jamshidi *et al.* [19] reported the Flory equation parameters for this purpose. This equation fits well for polymers with higher molecular weight but not in the low range [3, 19], therefore this comparation was not adressed here

Regarding the data in Table 4.1 it is important to refer that the crystallinity degree, *Xc*, (vide Section 2.5.7) showed to be highly dependent on the catalyst and monomer used during the polymerization and ranged from 0 to 48 %. The catalysts that allowed reaching the highest crystallinity degree were tin powder and Sb_2O_3, 48 % and 47 %, respectively. On the other hand, $SnCl_2.2H_2O$ led to the worst result, 0 %, as the DSC trace of PLA7 (Figure 4.4) does not exhibit the peak corresponding to the melting. Similar findings were reached with other polymer samples, specifically those synthesized from methyl and *iso*propyl L-lactate (PLA10 and PLA11) suggesting an amorphous structure in these polymers.

Several factors may affect the crystallization process of PLA such as: molecular weight, thermal history and L/D lactyl isomers ratio. The occurrence of two melting peaks in the second heating scan of PLA samples (Figure 4.4) is a consequence of its complex crystallization behaviour. According to Wang and Mano [20], several mechanisms have been proposed to explain the origin of this phenomenon, however this is still under discussion. Nevertheless, it is usually accepted that the presence of different crystalline structures and the simultaneity and competitiveness of the melting and recrystallization processes leads to this result.

4.2.5. Racemization

The yellowing of the final polymer suggests the occurrence of undesirable degradation reactions during the bulk polytransesterification, and this is further supported by the optical purity results (*OP*). The occurrence of racemization reactions, also identified in ROP and polycondensation mechanisms, are responsible for introducing some D-lactyl units in the polymer chain and, consequently, for affecting the polymer stereoregularity [21].

The PLA stereoregularity strongly influences its crystallinity and thermal behaviour, which can explain some disagreement between molecular weight and thermal characterization results discussed above. Aiming at clarifying this issue, the influence of optical purity on crystallization degree is addressed in Figure 4.6. It is clear that the crystallinity decreases sharply with the decrease in the optical purity and, for an optical purity, *OP,* lower than ~70 %, the polymers are amorphous. This finding is similar to the results reported earlier by Tsuji and Ikada [22]. This cumulative information cunfirmes that the D-lactyl units, introduced due to racemization reactions, hindered the crystallization process.

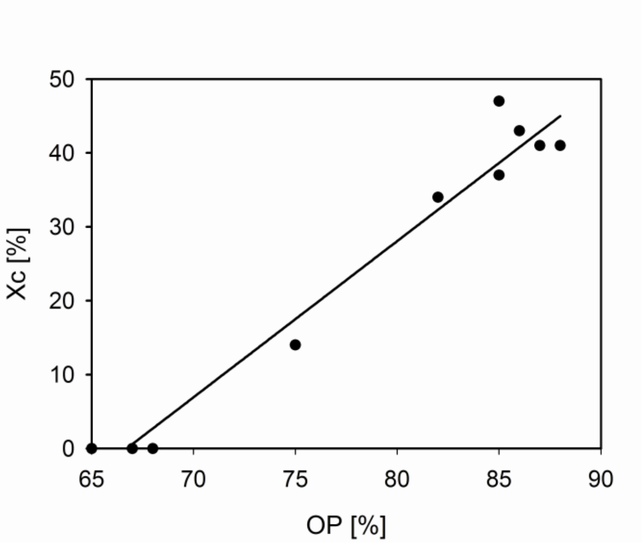

Figure 4.6: Crystallinity degree *vs* optical purity of the PLA samples.

4.2.6. NMR Spectroscopy

The typical chemical structure of PLA was confirmed in the ^{1}H NMR spectra (*vide* section 2.5.2) of the samples. Figure 4.7 shows the ^{1}H NMR spectrum corresponding to PLA4 (Mw=22 300 g.mol^{-1}), corroborating the successful polytransesterification of the ethyl L-lactate. The large quartet and doublet at 5.15 and 1.57 ppm are assigned to the methine, —C<u>H</u>(CH$_3$)—OCO—, and methyl, —CH(C<u>H</u>$_3$)—OCO—, protons in the main polymer chain. The weak quartet at 4.208 ppm in Figure 4.7 is assigned to the methine in the end chain units and the series of weak peaks downfield, 1.25 and 1.35 ppm, are assigned to the ethyl end groups. The corresponding PLA spectra of the samples obtained from the other L-lactates were entirely consistent with their expected structures.

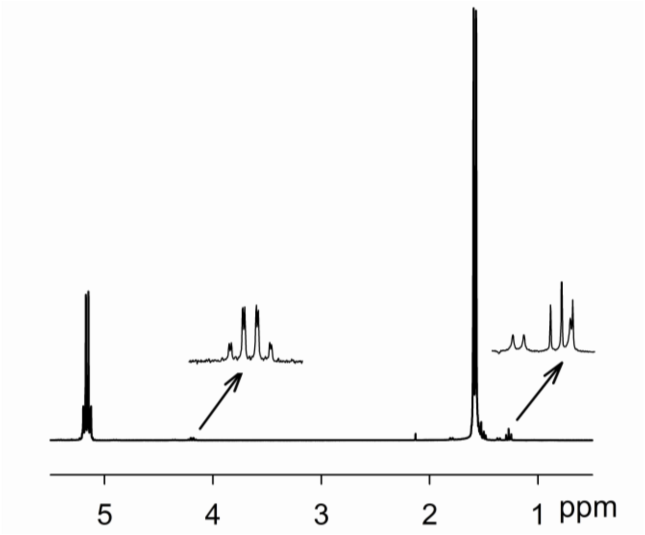

Figure 4.7: ^{1}H NMR spectrum of PLA4.

4.3. Conclusion

The polytransesterification process, originally developed for PETsynthesis, was applied to new monomers based on lactic acid esters and PLA was successfully produced using this mechanism. Several L-lactic acid esters were assessed and the results revealed that their structure influences the final molecular weight of the polymers which increased in the following order: *i*propyl < methyl < butyl < ethyl. The activity of the catalysts screened disclosed differences in the performance reached and pointed out to utilizing Sb_2O_3 for best results. These catalysts were part of a catalytic system, which consisted of a catalyst and a co-catalyst, zinc acetate. For this system TNBT led to the poorer results and improved performance followed the sequence: TNBT < Sn < Sn(Oct) < $SnCl_2$ < Sb_2O_3. The addition of $Zn(O_2CCH_3)_2.2H_2O$ to Sb_2O_3 showed a synergic effect, which enabled synthesizing the PLA sample with the highest molecular weight, 22 300 g.mol^{-1}. This binary catalytic system was also effective for suppressing racemization allowing a colourless polymer.

The thermal behaviour of the obtained materials is strongly dependent on final molecular weight and optical purity. Under certain experimental conditions the catalysts tested also promoted racemization reactions during polymerization, leading to a decrease in polymer crystallinity. The catalyst influence upon racemization extent was found to be ($SnCl_2$ > Sn(Oct) > Sn > Sb_2O_3 > TNBT). Specific rotation measurement confirmed to be a powerful technique to evaluate the racemization extent and the stereoisomer composition of the lactyl units in the polymer chain. Lactic acid polymers with an optical purity below 70 % showed an amorphous structure.

From the economic point of view, it is of best interest to develop an efficient, effective and less expensive route to produce poly(lactic acid). These results support that the polytransesterification can be envisaged as a promising alternative for PLA synthesis. However, the obtained molecular weights remain quite low for aliphatic polyesters, therefore further research work needs to be carried out to find the best reaction conditions enhancing the molecular weight and avoiding undesired side reactions.

4.4. References

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5. LACTIC ACID MELT POLYCONDENSATION

D. S. Marques, M. H. Gil, C. M. S. G. Baptista, Improving Lactic Acid Melt Polycondensation: the Role of Co-catalyst, *J Appl Polym Sci* (doi: 10.1002/app.38413).

D. A. S. Marques, C. M. S. G. Baptista, M. H. Gil, Process for Preparing High Molecular Weight Poly(Lactic Acid) by Melt Polycondensation, Provisional Patent Application nº 106360.

This chapter is based on the above publications.

5.1. Introduction

The commercial large scale process for producing high molecular weight PLA involves the ring opening polymerization (ROP) of an intermediate compound, the lactide, in the presence of stannous octoate catalyst [1-3]. This is an effective but quite complex process requiring highly energy consuming stages, increasing the production costs and the process environmental footprint, therefore, supporting the effort to develop an alternative approach.

The large-scale production of commercial polyesters such as poly(ethylene terephalate) (PET) and poly(trimethylene terephthalate) (PTT), [4,5] and the need to find a more cost effective process for PLA production has motivated several research groups [6-15] to study the synthesis of PLA by direct melt polycondensation of the monomer. However, the synthesis of high quality PLA under melt polycondensation conditions, which entangle temperature above melting point and long reaction times, remains a challenge. Under such operating conditions changes in the chemical structure of the growing polymer chain are introduced. The most jeopardizing ones are reduced optical purity and the yellowing phenomenon. The resulting reduction in optical purity has an adverse effect upon the thermal and mechanical properties of the polymer and discoloration becomes a critical issue when applications require optically clear materials. In some cases the degradation products may affect polymer organoleptic properties, being the acetaldehyde release during PET synthesis and processing a common example [4].

Moon *et al.* [7, 8] studied the direct lactic acid bulk polycondensation, but high molecular weight PLA could not be achieved due to inefficient water removal during the polymerization. Similar findings were recently published by Sedlarik *et al.* [11] where the highest molecular weight achieved by lactic acid bulk polycondensation was 17 200 g.mol^{-1}.

One of the most interesting studies on the direct melt polycondensation of lactic acid was carried out by Chen *et al.* [6] who were able to obtain high molecular weight PLA, 130 000 g.mol^{-1}, by increasing the reaction time up to 40 h. Nevertheless, a negative impact on polydispersity index and on the optical purity was reported, besides the yellowing phenomenon, observed during melt polymerizations, which was not discussed. Moreover, the reaction time required by their process is excessive from an industrial point of view. Interestingly, Harshe *et al.* were not successful to reproduce these results [16, 17].

Moon *et al.* [7, 8] was the first research group to discuss this process for PLA synthesis and to report that the addition of some compounds, such as proton acids, to a tin-based catalyst during polymerization could have a beneficial effect on the melt polymer stability [7, 8], as well as on the polymerization rate. Based on these results a sequential process of melt polycondensation followed by solid state polycondensation (SSP) was successfully developed [9, 10], clearly inspired in the PET process. The SSP process will be discussed in the following chapter 6.

In spite of all research work devoted to the development of an alternative to the ROP process, this goal remains a challenge. Having this aim in mind, this chapter details a study on the experimental conditions to perform lactic acid melt polycondensation and new interesting aspects are reported. Two co-catalysts were compared and both proved to be effective avoiding undesired yellowing. Specific rotation measurements (*vide* section 2.5.5) were used to evaluate the racemization extent in the polymer samples. UV/vis was employed to investigate the yellowing process and showed to be very sensitive to small changes in colour (*vide* section 2.5.3). The experimental set up and the experimental procedure were already described in chapter 2, section 2.2 and 2.4.3, respectively.

5.2. Results and Discussion

5.2.1. Lactic Acid Melt Polycondensation

Polycondensation is a stepwise reaction between lactic acid functional groups requiring the addition of an external catalyst to reach high molecular weight polymers, since the self-catalyzed reaction is too slow and side reaction may occur if the reaction mixture is kept at too high temperatures for a long reaction time. In the past two decades, a large number of studies on PLA synthesis by polycondensation have appeared in the literature [6-20] and some apparently contradictory results have been reported. An essential issue in understanding all information is that lactic acid polyesterification is equilibrium reversible reaction. In order to pull the reaction equilibrium towards polymer formation, the by-product water must be continuously withdrawn from the increasingly viscous reaction medium. This means that the kinetics of the reaction can not be understood without taking into account the method and efficiency of water vapour removal. Therefore, it depends on large extent on catalyst performance as well as on scale, geometry of the equipment in which polymerization is performed, and on the operating conditions controlling the water vapour diffusion throughout the increasingly viscous polymer bulk to the surface and its final withdrawal from the vapour phase [4, 21]. Factors such as: reactor design, stirring, temperature and pressure profiles assume special relevance in the final polymer molecular weight. These factors are difficult to reproduce at a different scale, consequently, making the product quality greatly sensitive to the scale of operation. Additionally, polarity changes in reaction medium have been reported as affecting catalytic activity [18] rendering results comparison rather difficult. Therefore, the experimental work began by assessing the most efficient catalyst/catalytic system to perform the lactic acid polycondensation under the same melt conditions.

The polycondensation reactions were carried out in bulk and the transfer of water from the increasingly viscous melt to the vapour phase was aggravated, comparing to the experiments described in Chapter 3. In the set-up available, an increase in interfacial area could only be achieved by using a smaller volume of reaction mixture. Therefore polymerization reactions were performed in a 500 mL bench-scale reactor, the same used in chapter 4, with pressure and temperature control loop and online record of process conditions, in order to obtain valuable information for possible process scale-up, and to achieve a strict control over reaction conditions.

After a literature survey on lactic acid melt polycondensation and some preliminary experiments, the experimental procedure was set with two sequential steps: an overnight monomer distillation at 170 ºC and atmospheric pressure followed by catalyst/catalytic system addition and final polycondensation at 180 or 190 ºC under vacuum. A detailed description of the experimental procedure is found in chapter 2, section 2.4.3. Typical temperature and pressure profiles employed throughout the experiments are illustrated in Figure 5.1.

During the experiments a dramatic increase in the reaction mixture viscosity was registered in the later stage of the polycondensation, as can be seen in Figure 5.1. Although it is common knowledge that the viscosity plays an important role in melt polycondensations, for the polymerization under study torque profiles have not been found in the open literature. A possible explanation may be related to the low reaction volumes typically employed while studying this reaction. At large scale polyesters production, the viscosity is often selected for inline monitoring by measuring torque. This is a very good method for melt viscosity estimation and correlates very well with average molecular weight.

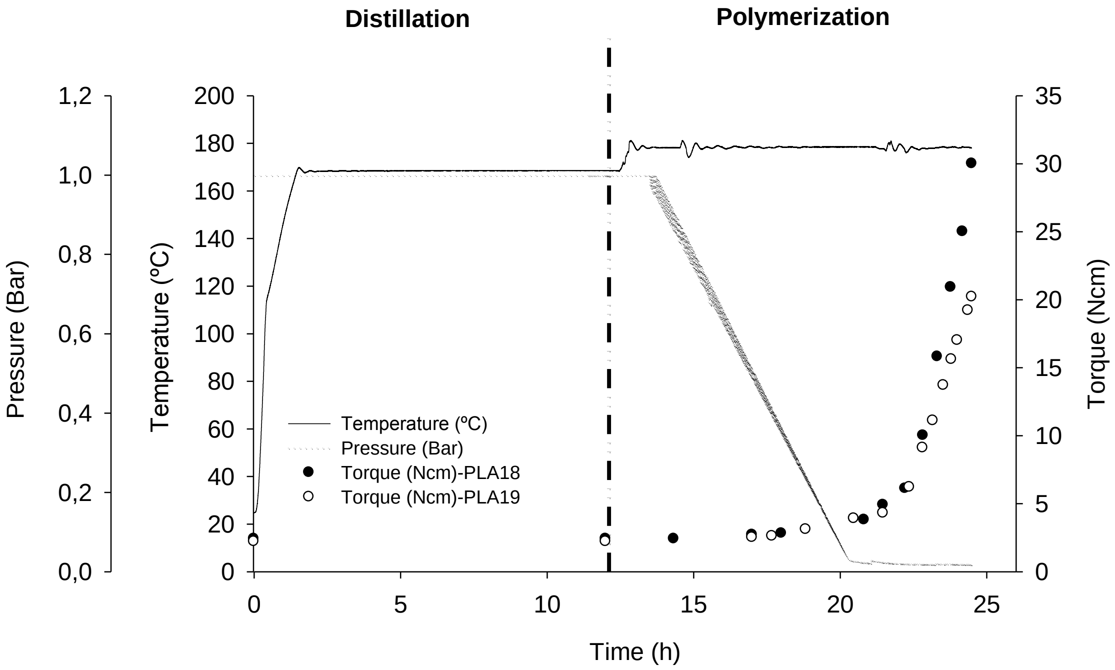

Figure 5.1: Typical temperature, pressure and torque profiles recorded during experiments 18 (full dots) and 19 (empty dots).

Even though no major viscosity change was recorded at the first stage during monomer distillation, other important changes occur during this period. The most important one is the pronounced volume reduction owing to the elimination of initial monomer free water and a high reduction in terminal end groups concentration by self-condensation. Based on the volume of water collected a volume reduction around 40 % was recorded. According to *COOH* end groups' titration (*vide* section 2.5.4), a polymerization degree *(DP)* about 16 was obtained. Figure 5.2 shows the typical molecular weight distributions obtained by SEC of distillation and polycondensation products for experiment 3. The curves show a typical broad distribution curve for the distillation product and a narrower distribution, at lower retention time, for the final polymer. Unfortunately, due to calibration limitations, it was not possible to assess the molecular weight of distillation oligomers by SEC technique. Therefore the result obtained by titration will be used.

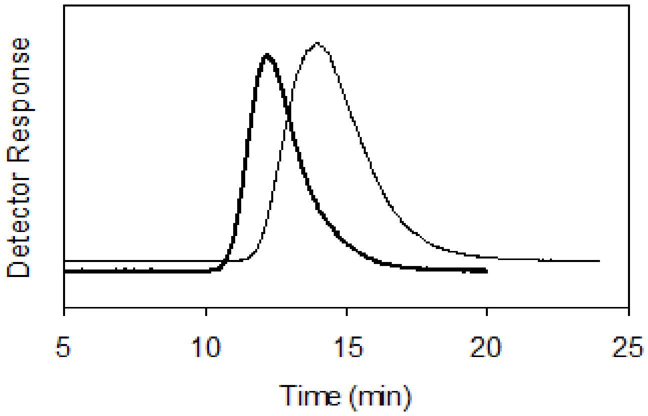

Figure 5.2: Typical molecular weight distribution of distillation and polycondensation products for PLA3.

It is important to emphasize that the distillation step was performed overnight for convenience, in order to add the catalyst and to follow the polycondensation during the day. A similar step is employed in the ROP process. Typically, vacuum pressure in the range 70-250 mbar and polymerization temperature at 190 ºC for around 6 h are used to synthesize a prepolymer with a polymerization degree around 29 [22]. Therefore, a substantial increase in polymerization degree, as well as an overall reaction time reduction can be obtained, if similar conditions are employed during monomer distillation. To ensure that water is efficiently removed during distillation a stream of nitrogen was flowing through the vessel, but, vacuum is essential to increase the polymerization degree and to reduce the distillation time.

As the viscosity increases with polycondensation progress, the level of vacuum is increased stepwise to around 10 mbar. While water removal is favoured, the operating conditions allow small molecules to be also removed from the reaction mixture, jeopardizing the polymer yield. A fractionating section (*vide* Figure 2.2), connected to a vacuum pump, is required at the top of the reactor throughout the process to selectively distil off the water and reflux these compounds. The water is then condensed and recovered in a cold trap. Therefore, the chemical reaction equilibrium is selectively shifted toward polymer formation. Recycle of these compounds is essential to ensure high molecular weight PLA and high yields. However, a small fraction crystallises as a thin film and remains trapped in the equipment walls. These compounds are, essentially, lactide, as confirmed by RMN analysis, Figure 5.3, and discussed below. The fractionating section is essential to suppress the lactide formation, otherwise considerable amounts of lactide, up to 30 g, would be removed from reaction medium.

The stirring, 600 rpm, is also used throughout the process to improve the water removal and the reaction extent. The combination of a rapid surface renewal obtained by stirring and bubbling of an inert gas stream into the reaction mixture enhances the mass transfer of the by-product water from the melt polymer to the vapour phase, which is then removed by vacuum. As polymerization proceeds and the melt viscosity increases, mass transfer becomes highly dependent on the surface renewal rate and surface area available. Therefore, polymerization reactors that offer high surface area are typically employed in the later stages of similar processes, namely, PET production process [4, 5]. The stirrer should be suitable for highly viscous materials therefore an anchor stirrer was employed.

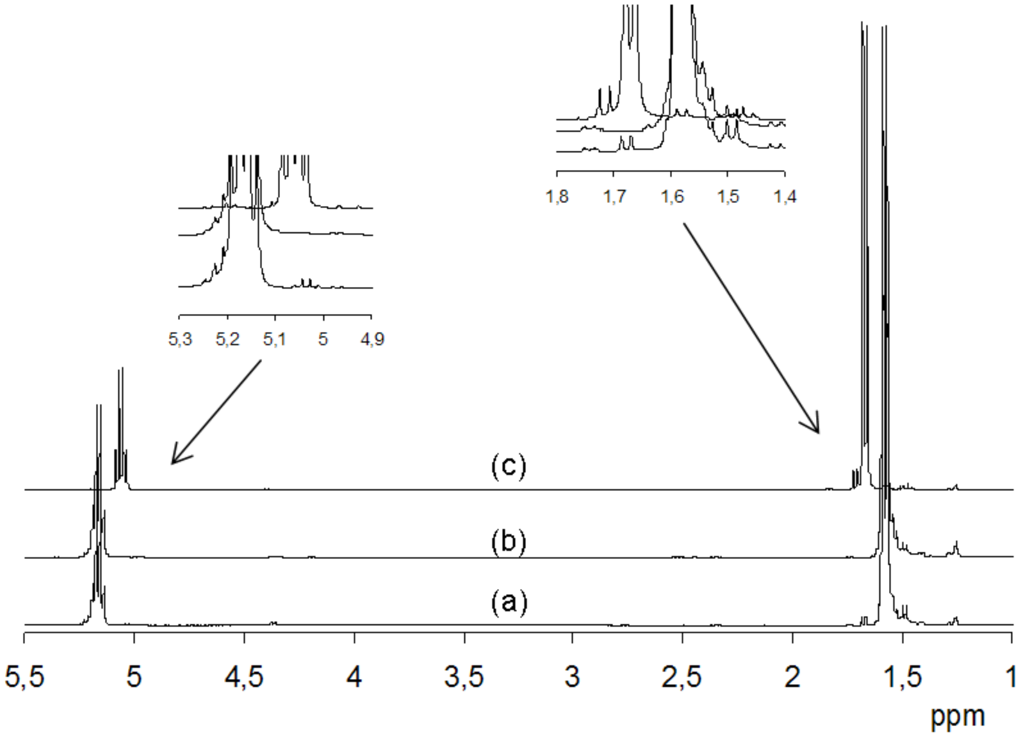

Figure 5.3: ^{1}H NMR spectra of a PLA sample as obtained at the end of polymerization (a), a PLA sample purified by precipitation (b) and lactide removed from equipment walls (c).

At the end of the polymerization either a brown or a light brown polymer was obtained. On average 6-7 % of final polymer samples were lost as low molecular weight oligomers during purification by precipitation. According to Inkinen *at al*. [23] lactic acid oligomers with molecular weight lower than 2 000 g.mol^{-1} are soluble in water and alcohols such as ethanol and methanol and, therefore, they are lost during the precipitation. The presence of these small oligomers will be a possible source of thermal instability during processing. In a large scale PLA production process, purification by precipitation is not feasible, therefore a final drying under vacuum would be required, similar to the PLA drying stage in the ROP process, to reduce lactide content [24], or in the PET process, to reduce acetaldehyde content [4].

Figure 5.3 shows the ^{1}H NMR spectra of a PLA sample as obtained at the end of polymerization without purification (a) and the PLA purified by precipitation (b). Spectrum (c) was collected from a white crystal sample removed from the reflux condenser walls. The polymer spectra show a typical methane quartet at 5,17 ppm and the methyl doublet at 1,59 ppm, while the crystal spectrum depicts a methane quartet at 5,05 ppm and the methyl doublet at 1,68 ppm. These chemical shifts are assigned to the lactide molecule and are in agreement with results reported by Sodergard *at al.* [25] and Braun *et al.* [26] while studying PLA composition obtained by ROP. The main difference registered between purified and no purified polymer in the ^{1}H NMR spectra was the disappearance of the small peaks assigned to the lactide molecule, as can be seen in the enlarged regions, showing that lactide formation is the main side reaction in melt lactic acid polycondensation, as it would be expected.

5.2.2. Catalyst Screening

The information on the best catalysts to be screened was gathered from the literature on polyesters synthesis such as PET and PLA [1, 2, 5-21]. The catalysts used in this study, as well as the results achieved, are compiled in Table 5.1 (PLA1-PLA15). The final product from each experiment was investigated by molecular weight distribution measurements (*vide* section 2.5.1), optical purity (*vide* section 2.5.5) and visual appearance, after polymer precipitation from chloroform solutions. According to the data presented in Table 5.1 catalysts have a dramatic influence on these properties. It is important to refer that the molecular weight information, as well as the optical purity results, were obtained from purified samples.

The experimental work began by testing $SnCl_2$ (PLA1), a strong Lewis acid largely used in direct lactic acid polycondensation in solution [18, 20] and in molten state [7-10], by using the frequently reported 0.4 wt % catalyst amount. As previously reported [8], it is a very effective catalyst promoting the synthesis of high molecular weight PLA, but ester interchange reactions are also favoured. TNBT is also a Lewis acid and proved to be an efficient polymerization catalyst [6]. However, the final polymer exhibits low optical purity showing that it is a strong ester interchange catalyst promoting high levels of racemization (PLA2).

Table 5.1: Lactic acid melt polycondensation results using different catalysts.

PLA	Catalyst (0.4 wt %)	*Mw* (g.mol^{-1})	*PD*	*OP* (%)	Yield (%)	Appearance
1	$SnCl_2$	32 500	2.7	77	93	Pale yellow
2	TNBT	27 000	2.5	76	94	Pale yellow
3	Sn	39 000	2.1	85	94	Pale yellow
4	Sn(Oct)	17 000	2.4	82	91	White
5	Sb_2O_3	24 000	2.8	77	85	Pale yellow
6	Zn(acet)	26 000	2.7	90	80	White
7	DBTL	18 000	2.3	89	91	White
8	Sn(II)O	18 000	2.3	88	88	Pale yellow
9	Zn(II)O	16 500	2.4	86	81	Pale yellow
10	Co(acet)	17 000	1.7	71	72	Pale pink
11	Sn(IV)O	13 300	2.2	72	90	Pale yellow
12	TiO_2	13 000	2.3	64	81	Pale yellow
13	DBSA	11 300	2.7	94	96	Pale yellow
14	H_3PO_4	10 000	2.7	82	96	White
15	H_3SO_4	26 000	2.7	-	-	Black

Tin powder was tested in experiment 3 and, surprisingly, it allowed the synthesis of the highest molecular weight PLA (39 000 g.mol^{-1}) with a relatively high optical purity (85 %). Tin powder has been successfully used in the lactic acid solution polycondensation [19] but with little success on melt polycondensation [14, 15]. As catalyst, tin powder requires an additional purification step to be removed from the final polymer bulk, which may explain the little interest comparing with other tin based compounds that are soluble in the polymer bulk. In applications in the commodity field the purification stage jeopardizes process cost balance. Nevertheless, for biomedical applications, where high purity PLA grades are required, purification may be a great advantage in order to avoid further cytotoxicity problems. Additionally, it has been reported [27] that the complete removal of residual catalysts enhances the polymer melt stability during subsequent melt processing stages. Therefore, purification requirements may not be always envisaged as a limitation to proceed with catalyst testing. In experiment 3, when tin metal was used, in the end, right after turning off the heating, the catalyst solidified in aggregates (Figure 5.4) which are easily removed from the reactor bottom allowing easily recovering the catalyst. This unexpected observation may be related to the catalyst melting point, within reaction temperature range. Tin metal has another great advantage as it is cheaper than its derivatives. An experiment was performed to assess the possibility of tin recovery and reuse but there was a significantly lost in catalytic activity after the first utilization.

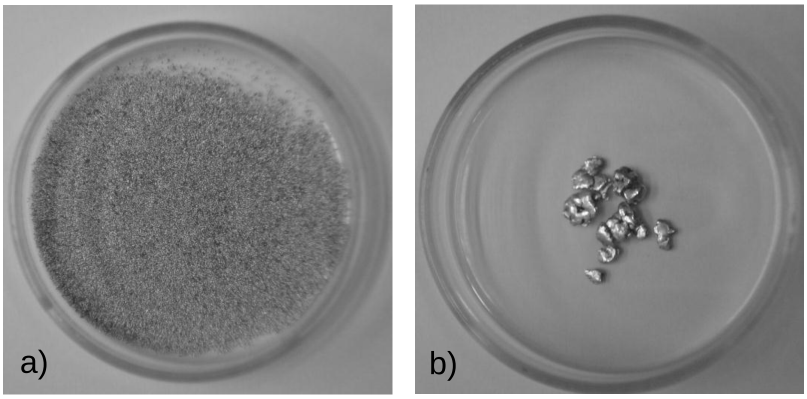

Figure 5.4: Visual appearance of tin metal catalyst before (a) and after polymerization (b).

Tin (II) octoate (Sn(II)Oct), a strong Lewis acid, is the catalyst usually employed in the ROP process [1, 20] and it was also reported by Hiltunen *et al.* [12] as an efficient lactic acid melt polycondensation catalyst. Nevertheless, under the conditions tested in this work, it did not lead to encouraging results (PLA4). Antimony oxide (Sb_2O_3) and zinc acetate [Zn(acet)], both widely used in the PET synthesis by both melt polytransesterification and polycondensation, [4, 5] were tested in experiment 5 and 6, respectively, showing low catalytic activity in lactic acid melt polycondensation. Other standard esterification catalysts such as DBTL, Sn(II)O, Zn(II)O and Co(acet) were also tested in experiments 7 to 10, respectively, leading to similar results, which are not very encouraging for PLA synthesis under melt polycondensation conditions. A few other compounds mentioned in the literature [5, 12] as efficient polycondensation catalysts such as tin (IV) oxide (PLA11), titanium (IV) oxide (PLA12), DBSA (PLA13) and phosphoric acid (PLA14) were also assessed, revealing a low catalytic activity towards lactic acid polycondensation. However, it is worth mentioning that DBSA allowed synthesizing the polymer (PLA 13) with higher optical purity (94 %) and may be preferred to control the polymer stereoregularity, when relevant. Sulphuric acid, tested in experiment 15, showed a high catalytic activity, but the resulting polymer was black in colour.

The results above, Table 5.1, clearly illustrate that different catalysts produce different polymers in terms of molecular weight and stereoregularity, which should be taken into account when planning further studies. Yield is another important criterion to assess a process, therefore included in Table 5.1. Considering that during polymerization each mole of monomer releases one mole of water, the yield was calculated using the following equation:

$$Yield\left(\%\right) = \frac{Weight \quad of \quad product}{Weight \quad of \quad monomer \times 0.8} \times 100 \qquad (1)$$

The yields in Table 5.1 are nearly all above 80%, quite high for melt polycondensation reactions [28], and slightly dependent on the catalyst.

The colour of the final materials ranged from white to slightly yellow powder, depending on the catalyst, suggesting the occurrence of thermo-oxidative degradation reactions, besides racemization. The polyester's colour is an important quality parameter and therefore it has been used for qualitative assessment while checking the catalyst performance. In the last column of Table 5.1 the appearance of the polymers is described. This issue will be explained in more detail, later. However, it can be pointed out that the results do not suggest a clear relationship between polymerization rate, optical purity and colour formation, not even whether they are competitive phenomena or not. Therefore these parameters will be independently analyzed in the following sections taking into account only the catalyst and the reaction conditions influence.

5.2.3. Co-Catalysts

In the catalyst screening stage tin chloride ($SnCl_2$) and tin powder (Sn) (experiments 1 and 3) were assessed as the most efficient catalysts and therefore selected for further experiments. Nevertheless, as referred before, these catalysts also favour side reactions leading to melt polymer yellowing and racemization. Aiming at overcoming this problem and following Moon *et al.* [7] and Degée *et al.* [29] works, in a second set of experiments two co-catalysts were tested (PLA16 to PLA19 in Table 5.2). These two co-catalysts, added to the catalyst in an equimolar ratio, were *p*-toluenesulphonic acid (*p*-TSA) [7], a protonic acid, and triphenylphosphine (PPh_3) [29] a Lewis base.

The results in Table 5.2 reveal major differences regarding the catalysts performance in the presence of these compounds. The addition of co-catalysts to neat tin powder (PLA16 and PLA17) does not significantly influence the polymerization degree, but the addition of PPh_3 (PLA17) allowed the synthesis of the higher (91 %) optical purity polymer. On the other hand, when added to $SnCl_2$ (PLA18 and PLA19) they speed up polymerization rate. Indeed, the molecular weight reached when using $SnCl_2$ combined with co-catalysts increased from

32 500 to 52 000 g.mol^{-1}, together with a narrower molecular weight distribution and a slightly higher optical purity, regardless the co-catalyst employed. Thus, in general, it can be stated that these co-catalysts enforce a better controlled polymerization leading to a higher optical purity polymer, while reducing yellowing. Moreover, when added to the $SnCl_{2,}$ polymerization rate is also enhanced. The role of these compounds while improving polymerization reactions is still under discussion.

Table 5.2: Lactic acid melt polycondensation results employing co-catalysts.

PLA	Catalyst (1 M %)	*Mw* (g.mol^{-1})	*PD*	*OP* (%)	Yield (%)	*Td* (ºC)	Appearance	Torque (Ncm)
16	Sn/*p*-TSA	37 000	3.2	86	81	271	White powder	5.4
17	Sn/PPh_3	35 000	3.3	91	83	339	White powder	3.3
18	$SnCl_2$/*p*-TSA	52 000	1.4	83	73	278	White powder	30
19	$SnCl_2$/PPh_3	52 000	1.3	81	77	302	White powder	20

According to the literature, metal-catalyzed polyesterifications proceed to the complexation of carbonyl group on the metal atom, which induces a positive charge on the carbonyl carbon atom and favours the nucleophilic attack of the hydroxyl groups [4]. As the polymerization proceeds, both terminal hydroxyl and carboxyl groups contents decrease, leaving the coordination sites of catalyst centre unfilled, which induces side reactions causing discoloration and racemization. It has been proposed that the co-catalysts added fill the open coordination sites of the catalyst and therefore prevent side reaction [7, 19, 20]. In the particular case of $SnCl_2$/*p*-TSA catalytic system [7] a mechanism has been put forward by Moon *et al*.

It is worth mentioning that racemization reactions occur whatever the catalytic system used and cannot be completely prevented, as the optical purity results in Table 5.1 and Table 5.2 show. The occurrence of racemization reactions, previously identified in ROP and melt/solution polycondensation mechanisms [12, 16, 20, 30, 31], are responsible for the random introduction of some D-lactyl units in the polymer chain and, consequently, for affecting the polymer stereoregularity. The origin of this kind of reactions will be discussed below.

In the polycondensation process, rheologic behaviour changes continuously. At large scale polyesters production, the viscosity is often selected for inline monitoring, by measuring torque in the stirring system. The addition of these co-catalysts also affects the polymer melt viscosity and therefore torque measurements were recorded during the experiments. Figure 5.1 shows the torque progress during the overall reaction, from monomer distillation to the final polymerization stage after catalytic system addition, for experiments 18 and 19. In these experiments $SnCl_2$ was employed as catalyst combined either with *p*-TSA, experiment 18 (full dots), or with PPh_3, experiment 19 (empty dots). The torque curves depict a slow increase in torque while molecular weight is low, less than ≈ 30 000 $g.mol^{-1}$, and an exponential increase as polymer chain grows further. The high viscosity of PLA in the later stages of the melt polycondensation process restricts water removal and therefore limits the final molecular weight achieved by this approach. Nevertheless, as it stands out in Figure 5.1, the use of PPh_3 allows a significant melt viscosity reduction close to the end of the process and may be regarded as an advantage to *p*-TSA.

5.2.4. Thermal Characterization

Information on the thermal behaviour of polymer samples obtained by DSC (*vide* section 2.5.7) analysis is summarized in Table 5.3. It is easily noticed that the thermal properties of the samples greatly differ from each other, ranging from semi-crystalline (PLA3-PLA8 and PLA10-PLA19) to amorphous behaviour (PLA1, PLA2 and PLA9). Glass transition and melting temperatures are regarded as highly dependent on molecular weight. However, according to the data recorded in Table 5.3 this trend is not clear. The glass transition temperature ranges from 36 ºC to 55 ºC, the crystallization temperature from 90 to 111 ºC and the melting temperature ranges from 131 ºC to 156 ºC. These temperatures are in good agreement with previous results for PLA with the same molecular weight range [11, 13], produced by lactic acid polycondensation.

Regarding the data presented in Table 5.3, the crystallinity degree shows, in general, a close correlation with the optical purity. For instance, the polymer with the highest crystallinity degree also presents the highest optical purity (PLA8). It is well known [12, 32] that PLA stereoregularity strongly influences its crystallinity and thermal behaviour, which can explain the disagreement between molecular weight and thermal characterization results discussed above, as already explained in chapert 4.

The stereochemical composition of the PLA polymer significantly affects the crystallization kinetics, spherulite size and ultimate extent of crystallinity. According to the theory of polymer chain folding, structural defects are rejected from crystalline domains, thus resulting in a reduction of the lamellar thickness and consequently in a reduction of melting enthalpy [33]. The racemization reactions that occur during the lactic acid polymerization result in a polymer with an atactic structure, *i.e.*, with a random distribution of the L- and D-lactyl units [31], which prevent the crystallization process.

Table 5.3: Thermal characterization of the polymer samples.

PLA	*Tg* (ºC)	*Tc* (ºC)	*Tm* (ºC)	*Xc* (%)
1	nd	nd	nd	nd
2	nd	nd	nd	nd
3	55	nd	156	36
4	48	108	142	36
5	nd	nd	138	35
6	54	110	152	46
7	nd	nd	141	29
8	53	103	153	49
9	nd	nd	nd	nd
10	52	nd	150	42
11	nd	nd	124	45
12	50	99	150	45
13	54	111	154	54
14	nd	78	144	36
15	-	-	-	-
16	nd	90	135	24
17	45	102	143	43
18	36	nd	134	41
19	41	nd	131	34

nd Not detected

Since the addition of co-catalysts was found to significantly prevent yellowing during melt polycondensation, TGA experiments of PLA 16 to PLA19 were performed in order to assess whether they also have an influence on PLA thermal stabilization. The degradation profiles obtained are shown in Figure 5.5 and the degradation temperatures at maximum decomposition rate, recorded from the differential weight loss curves (not shown), are presented in Table 5.2. The degradation patterns clearly point out that when PPh_3 is added as co-catalyst it also has the ability to work as an effective thermal stabilizer, irrespectively of the main catalyst under study, whereas no stabilizing effect were registered in the presence of *p*-TSA.

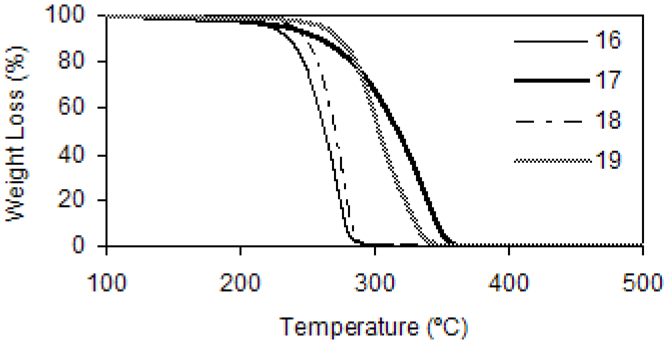

Figure 5.5: TGA thermograms of selected samples (PLA16, PLA17, PLA18 and PLA19).

5.2.5. Yellowing

The optical purity results in Table 5.1 and Table 5.2 and the slightly yellowish colouration of some polymer samples undoubtedly suggest the occurrence of undesirable degradation reactions during the melt lactic acid polycondensation. It is clear that the addition of the co-catalysts considered in this work hinders the colour formation and transesterification reactions to some extent (PLA16 to 19), as the samples are now white and the optical purity slightly increased.

Since the visual examination of the polymer samples after purification is rather subjective, UV/vis spectroscopy (*vide* chapter 2 section 2.5.3) was employed to enable identifying which catalyst has a stronger influence upon colour formation, as well as the role of co-catalysts, Figure 5.6. The literature confirms that UV/vis spectroscopy has been successfully applied to follow the effect of melt processing on the properties of PLA [34] and also the effect of ionizing radiation on thermoplastic polymers such as PET, LDPE and polyamides [35]. Surprisingly, so far it has not been used to assess lactic acid polymerization, although it is a unique technique allowing highly sensitive detection of traces of chromophores.

The ultraviolet-visible spectra of selected PLA samples dissolved in chloroform and measured in the wavelength region from 200 to 500 nm are presented in Figure 5.6. Above 500 nm no absorbance was recorded. All spectra show a maximum absorbance peak at 240 nm and, according to Garlotta, [1] this is attributed to the ester group present in the polymer main chain. After this maximum absorbance peak, with increasing wavelength, all spectra depict a continuous decrease in absorbance which, in some cases, extends to the visible region of the spectrum. UV/vis spectroscopy was previously used by Wang *et al.* [34] to study the effect of melt extrusion conditions on PLA thermal degradation in the range of 300 to 1000 nm, and a similar behaviour was registered. This absorption tail was ascribed to the creation of chromophores during melt processing, small amounts of conjugated double bonds with carbonyl groups, which are responsible for the perceived polymer colour [34-36], the origin of this reaction will be explained below. In the low wavelengths region, from 200 to 240 nm, small absorbance peaks are exhibited in each spectrum. These peaks are assigned to the hydroxyl and carboxyl end groups. However, owing to the high noise in this spectral region, the small peaks registered will not be considered here.

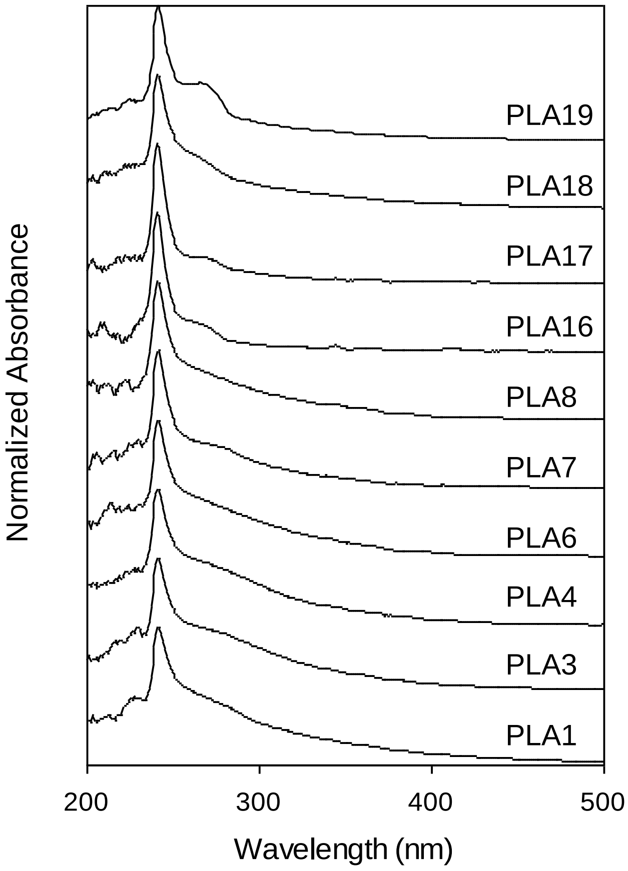

Figure 5.6: Ultraviolet-visible spectra of selected PLA samples.

To deepen the understanding of the influence of co-catalysts upon polymerization, Figure 5.7 shows the enlarged absorbance profiles of PLA1 and PLA3 synthesized with $SnCl_2$ and tin powder (see Table 5.1), and PLA16 to PLA19, obtained by adding co-catalysts (see Table 5.2).

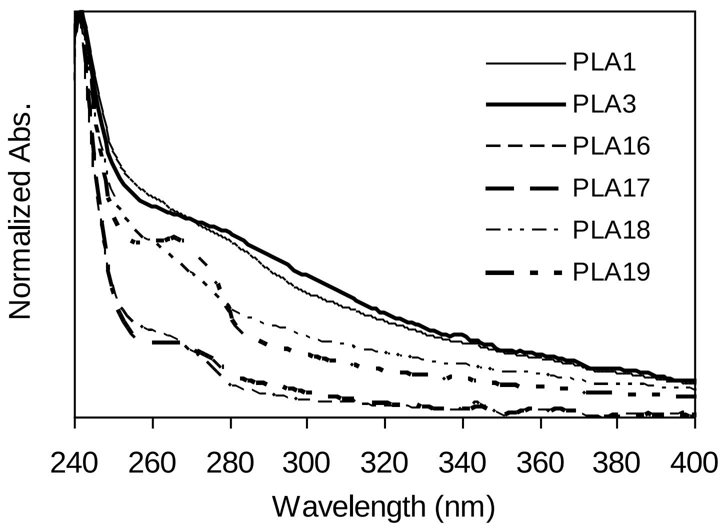

Figure 5.7: Ultraviolet-visible spectra of some PLA samples in the 240 to 400 nm wavelength region.

It is reported in the literature [21] that thermo-oxidative degradation is greatly accelerated in the presence of traces of oxygen and monomer impurities. Considering that besides the catalyst used, the reaction conditions were unaltered from batch to batch, the results in Figure 5.7 show that during melt polycondensation catalysts promote not only polymerization but, to a certain extent, degradation reactions as well. The striking information in Figure 5.7 is that undesirable reactions may be retarded in the presence of a suitable co-catalyst.

5.2.6. Effect of Oxygen

To evaluate the actual effect of oxygen on final polymer yellowing, nitrogen with low oxygen content ($O_2 \leq 2$ ppmv) was assessed as alternative to the standard nitrogen ($O_2 \leq 10$ ppmv). The ultraviolet-visible spectrum of a PLA sample obtained with tin powder as catalyst, another one synthesized with tin chloride, both at 190 ºC, and the comparison with a commercial polylactide (2002D) are presented in Figure 5.8. The curves exhibit an absorption shoulder much less intense than the previous ones shown on Figure 5.7 as a result of fading of the yellowing, and the absorption profile of the PLA sample obtained with tin powder is quite similar to the commercial polylactide. These results provide a clear insight into the negative effect of oxygen on polymer properties and point out that, to prevent yellowing, highly pure nitrogen is much more effective than co-catalysts, although the tin chloride still displays a clearly distinguishable absorption tail. Moreover, using ultra-pure nitrogen allowed increasing reaction temperature from 180 ºC to 190 ºC with lower yellowing, similar optical purity and improved average molecular weight *(Mw)*: 45 000 g.mol^{-1} and *PD*=1.9 for tin powder; 38 000 g.mol^{-1} and *PD*=2.9 for tin chloride, respectively, without extra reaction promoters. These results compare with the PLA1 and PLA3 information in Table 5.1 synthesized at 180 ºC.

Due to budget limitation only this preliminary assessment was carried out employing ultra-pure nitrogen. Further experiments were performed with standard nitrogen. However the results obtained were essential to set the following experimental parameters: tin metal as catalyst and 190 ºC as polymerization temperature.

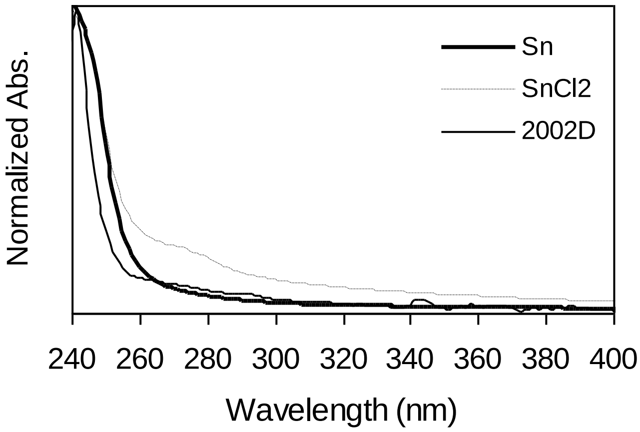

Figure 5.8: Ultraviolet-visible spectra of PLA samples obtained from ultra-pure nitrogen at 190 ºC and the comparison with a commercial polylactide, 2002D.

5.2.7. Chemistry of Lactic Acid Melt Polycondensation

High temperature, long reaction times in the presence of a metal catalyst, traces of oxygen and other monomer impurities, besides chain growth, also promote side reactions that may affect mechanical properties and cause processing problems [37]. However, few studies have been carried out to address the PLA degradation pathway at polymerization conditions. The main reactions involved in the melt lactic acid polycondensation, based on previously discussed results, are put forward in Figure 5.9. All reactions are catalyzed by the same compounds, therefore, a careful screening of PLA catalysts was performed in order to find the catalyst that reconciles high molecular weight and low side reactions.

Polycondensation or polyesterification, Figure 5.9 (a), is equilibrium reversible reaction between carboxyl and hydroxyl end groups and has the major contribution to achieve high molecular weight PLA polymers. Removal of released water is essential, otherwise chain scission through hydrolysis of the ester bonds occurs, leading to low molecular weight oligomers. It is well accepted in the literature [4, 38-39] that polycondensation mechanism proceeds through nucleophilic attack of hydroxyl oxygen of one end group on the carbonyl carbon at another end. Since the lactic acid bears a secondary hydroxyl group, melt polycondensation requires longer time than, for example, PET synthesis, which requires 5-10 h. The activation mechanism in the presence of an external catalyst it still under discussion, two main mechanisms have been proposed: alkaline compounds activate the attacking hydroxyl oxygen whereas acids, mostly used, activate the carbonyl carbon lowering the electron density on the carbonyl and facilitating nucleophilic attack by an activated hydroxyl. The polycondensation mechanism has been intensively studied in order to better understand the PET synthesis process [4, 38, 39]. To the best of our knowledge, only Moon *et al.* [7] have proposed a reaction mechanism of lactic acid melt polycondensation for the SnCl2/p-TSA catalytic system, as referred above.

Inter or intramolecular transesterification reactions, Figure 5.9 (b), are ester interchange reactions giving origin to a random redistribution of molecular weights. These reactions are usually reported as the origin of racemization and consequent introduction of D-lactyl units in the polymer chain. According to Hiltunen *et al.* [12], during the ester interchange reactions, there are two ways in which ester linkage can cleave: by acyl-oxygen cleavage, not involving the chiral carbon; or by alkyl-oxygen cleavage, in which the covalent bond between oxygen and the chiral carbon breaks and subsequently reforms [12]. This leads to a random inversion of the conformation (L- is converted into D-) and, consequently, to a decrease of PLA optical purity. Ester-semiacetal tautomerization mechanism has also been proposed as racemization mechanism on the PLA main chain [37, 40] but when temperature exceeds 200 ºC, which is not he case.

The ring-chain equilibrium, illustrated in reaction (c) Figure 5.9, is a particular intramolecular transesterification reaction that involves the depolymerization of PLA into lactide, when few water molecules are present. This is pointed out as the main PLA degradation reaction. Reintroducing the lactide by-product into the reaction medium is essential to control the extent of this reaction and, simultaneously, to promote the insertion of the cyclic oligomers into the linear polymer. The reaction pathway proposed involves the reaction of a hydroxyl end group in a "back-biting" ester interchange reaction to form lactide [7, 12, 18, 37, 41].

Yellowing was an unavoidable problem occurring at high temperature in melt polycondensation reactions. It has been widely reported in other polyesters synthesis and melt processing, including during PLA processing studies [34-36, 42-48]. However the discolouration problem is usually not reported during PLA melt synthesis. It is ascribed to the formation of small amounts of conjugated double bonds by thermal pyrolytic elimination. The pyrolytic elimination results in new species containing an acid end group and unsaturated carbon-carbon bonds [34, 36, 49, 50], as illustrated in reaction (d) Figure 5.9. According to PLA specific degradation studies, pyrolytic elimination is not the dominant degradation reaction even at high pyrolysis temperatures [50-52]. However, the presence of trace amounts of chromophores lead to a negative consumer perception. An effective strategy to delay thermal degradation and to mask the resulting yellowing during PET process was developed and may be adapted to a PLA melt polycondensation process. This strategy relies on the use of thermal stabilizers and radical scavengers during melt polycondensation and an appropriate combination of toners to adjust final colour properties [42, 54-57]. Some of these compounds have also been reported in the ROP patent literature [58, 59].

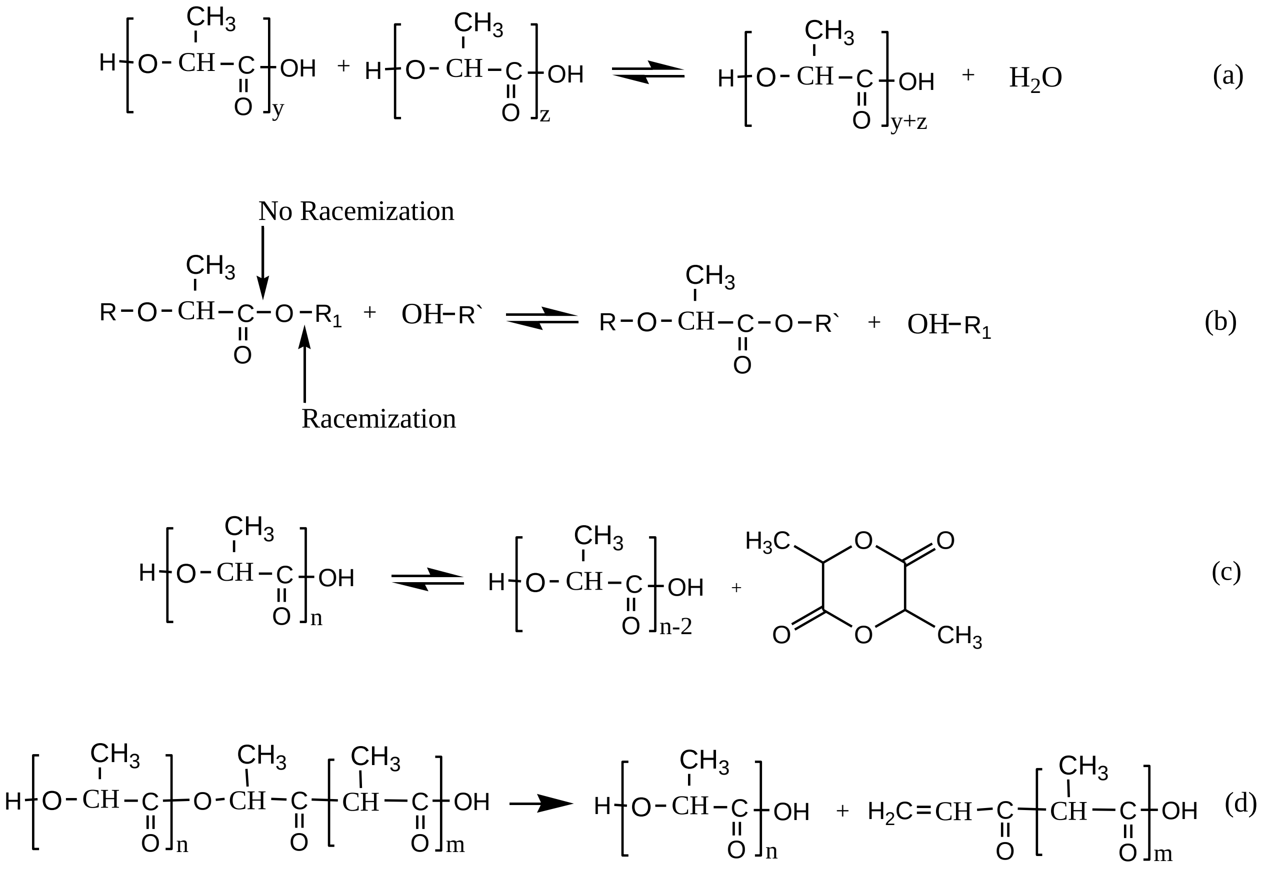

Figure 5.9: Main reactions involved in lactic acid melt polycondensation: (a) polycondensation; (b) transesterification equilibrium; (c) ring-chain equilibrium; (d) pyrolytic elimination.

PLA degradation reactions are reported to be greatly accelerated in the presence of oxygen [21, 53]. Therefore, the reaction should be careful conducted under inert atmosphere.

An approach to delay undesired thermal degradation is the additon of stabilizers. Phosphorous based coumpound (PPh3) was found a particular efficient stabilizer. Although not tested in this project, to mask yellowing during PLA processing a blue toner has been tested [46, 60]. Radical reactions and acetaldehyde formation have also been reported when subjecting PLA to severe degradation conditions [60-62]. To the best of our knowledge, acetaldehyde has not been found as a degradation product during PLA polymerization or processing.

Owing to the high mechanistic complexity of polycondensation reactions, and the number of functional groups involved, it is likely that other side reactions took place although the resulting products were not identified during the course of this project. However, based on experimental observations, the most significant are surely the ones illustrated in Figure 5.9.

5.3. Conclusion

Catalysts screening was the first stage in this work on PLA synthesis by lactic acid melt polycondensation. Tin powder and $SnCl_2$ were selected as the most efficient catalysts. Besides polymerization, these catalysts also promoted racemization and thermo-oxidation reactions which could be better controlled by using a suitable co-catalyst. The addition of PPh_3 or *p*-TSA has a tremendous effect on molecular weight, optical purity and colour and even on polymer melt viscosity, allowing the synthesis of PLA polymers with enhanced properties. Thus, the catalytic system selection for PLA production may be based on the target molecular weight, purity grade and accurate control over stereoregularity.

The development of colour during melt polymerization limits the polymerization time and therefore contributes to reducing the advantages of using this process for large scale PLA production. Minimization of degradation during melt polycondensation and improved role of commonly tin based catalysts will be a major asset, enabling developing a more cost effective process for commercial production of PLA. Further studies are crucial to obtain high molecular weight PLA by lactic acid melt polycondensation, up to 100 000 g.mol^{-1}, without compromising its quality.

5.4. References

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6. PROCEDURES TO INCREASE PLA MOLECULAR WEIGHT

D. A. S. Marques, C. M. S. G. Baptista, M. H. Gil, Process for Preparing High Molecular Weight Poly(lactic Acid) by Melt Polycondensation, Provisional Patent Application nº 106360.

This chapter is partly based on the above publication, some of the results have not been published elsewhere.

6.1. Introduction

In spite of all the efforts to synthesize high molecular weight PLA directly from the monomer by melt polycondensation, with good quality and in feasible reaction conditions, this goal remains a challenge. The polymers synthesized have low molecular weight for general melt processing technologies, usually lower than 50 000 g.mol^{-1}. On the other hand, these are suitable for some biomedical applications. Whenever a high molecular weight is required, an additional reaction step is essential for increasing it, until reaching around 100 000 g.mol^{-1} or higher. In the literature two post-polymerization strategies have been studied to deal with this problem: solid-state polymerization (SSP) [1-7] and chain extension [8-21]. Both have shown promising results leading to PLA polymers with mechanical properties similar to the polymer obtained by ROP but, to the best of our knowledge, none of them has been scaled-up and performed at industrial scale.

Moon and co-workers [22, 23] were one of the first research groups publishing results on lactic acid melt polycondensation. To increase molecular weight, conventional solid-state polymerization (SSP) was adapted for the PLA thermal specifications. Originally developed for polycondensation related processes, mainly PET and Nylons [24-27], SSP is a post-polymerization stage intended to further increase molecular weight of high viscosity polycondensation polymers. Briefly, the melt polycondensation resulting polymer is transformed into pellets or flakes and subsequently submitted to temperature above glass transition to promote crystallization. The temperature is further raised, although not reaching melting point, and the polymer is allowed to react. During the crystallization process segregation of reactive end groups and catalyst to the amorphous region occurs. A further polycondensation takes place in the amorphous region, promoted by the increased concentration of both reactive groups and catalyst. The polycondensation by-products are continuously removed from the reactor by a continuous flow of an inert gas or by operating the reactor under high vacuum [24-29].

The melt process followed by solid-state polymerization has already led to PLA with molecular weight up 500 000 g.mol^{-1} [1, 2, 4-7]. In this consecutive process PLA with 20 000 g.mol^{-1} was first obtained by melt polycondensation, afterwards crystallized at 105 ºC for 1-2 hours and finally heated till 140 to 150 ºC remaining at this temperature for another 10-30 hours and under high vacuum, since the reaction rate is faster than when using an inert gas stream to withdraw the by-products [1, 2, 4-7]. Although effective, this process takes a very long reaction time and a special dryer would be required to prevent pellets agglomeration. At industrial scale, a fluidized bed heat exchanger would be used, adding complexity and energy costs to the process. To overcome the SSP drawbacks Lurgi Zimmer [30] and Uhde Inventa-Fischer [31], two worldwide leading companies in supplying PET and copolymers related technologies, have recently developed equipments to handle highly viscous polyesters in order to avoid SSP stage. A considerable reduction in capital and production costs is claimed by these new processes [30, 31].

Given that PLA synthesis by solid-state polymerization has already received much attention by the research community [1, 2, 4-7] and that recent research and development trend in the polycondensation field appears to be avoiding the SSP stage [30, 31], this approach was not considered in this project for increasing PLA molecular weight. However, solid-state polymerization seems to be a very promising alternative to solution for obtaining PLA stereocomplexes (sc-PLA) to be used as high performance biobased polymers [32-39], but not to synthesize thermoplastic PLA.

Chain Extension

Another process that has been reported in the literature as a feasible production route for high molecular weight polymers is the so-called chain extension. This approach increases PLA chain length by coupling two or more low molecular weight prepolymers, around 15 000 g.mol^{-1}, previously modified with hydroxyl or carboxyl end groups [40-42], using bifunctional coupling agents. The prepolymers are usually obtained by lactic acid polycondensation at 200 ºC and for 24 hours [8-21]. Lab-scale chain extension of PLA by reactive blending has been reported [8-9] for a limited number of linking agents. Diisocyanates were often employed as coupling agents of hydroxyl terminated prepolymers forming a lactic acid based poly(ester-urethane), while bisoxazolines were used as coupling agents of carboxyl terminated prepolymers leading to a poly(ester-amide) [8-9]. Although the content of coupling agent required for effective chain linking is low, it offers the possibility of extending the PLA properties range by copolymerization [43] and chain linking selection. Besides thermoplastics, chain extenders containing crosslinkable moieties, usually carbon double bonds, have enabled stiff and elastic biodegradable cross-linked lactic acid based polymers [16, 44-47].

Chain extension has also been extensively reported in the literature as a very effective approach for increasing stability during ordinary melt processing. It is argued to increase final molecular weight while restoring polymer degraded chains [48-57]. Chain extenders may be any bifunctional or multifunctional compound, thermal stable and non-volatile, which can react within few minutes with polyesters end groups under melt conditions, without releasing undesired by-products. In addition to diisocyanates and bisoxazolines [8-9] also diepoxides [49-55] and dianhydrides [54-58] have been reported as particular suitable chain linking agents for PET and copolymers. In the few studies reporting chain linking agents for polylactides melt processing two types have been tested: epoxidized vegetable oils and epoxy acrylate copolymers were assessed as plasticizers and melt rheology modifiers [59-64], respectively, while diisocyanates have been mainly used as compatibilizers to improve the interfacial interaction through covalent bonding in blends [65, 66].

In practice, the use of these chain extenders offers the possibility to link two or more low molecular weight PLA chains in a linear, branched or crosslinked arrangement. Employing common compounding strategies such as reactive extrusion, a wide range of materials from biobased and biodegradable thermoplastics to networks may be obtained. Reactive extrusion is a particular extrusion process that involves the use of an extruder as a chemical reactor in which polymerization or other chemical modification is carried out *in situ*, while processing is in progress. Twin screw extruders are usually chosen for the reactive extrusion process [67-70] due to the excellent mixing properties and the ability to deal with high viscous materials. Reactive extrusion is used in the polymers industry including in the ring opening polymerisation of lactide to produce PLA [71-75]. Futerro [71], the first large scale European company in the PLA market, employs this process demonstrating the effectiveness of this approach at large scale.

Large melt phase polycondensation plants always include an extruder after the polymerization reactor(s) for melt mixing additives and produce pellets [24]. Therefore, this same extruder could be used for chain extension without increasing investment costs. Chain extension is studied in this chapter as a possible approach to increase PLA molecular weight.

It is important to highlight that chain extension was performed in the last stage of polycondensation reaction, in the same reactor and without additional catalyst. A schematic representation of the PLA chain extension with hexamethylene diisocyanate (HDI) is illustrated in Figure 6.1. The ultimate goal would be combining chain extension and reactive extrusion to increase PLA molecular weight in a short reaction time while transform the resulting material into pellets or into the final item. Unfortunately, performing these experiments in an extruder is beyond the scope of this project as this equipment was not available.

Branching

Branching was studied as another alternative route for increasing polymer molecular weight. Differently from chain extension, performed with low molecular weight prepolymers, the branching co-monomers were added to the monomer at the beginning of the polymerization to promote the synthesis of high molecular weight star-shaped PLA, as illustrated in figure 6.1.

As discussed in chapter 1, some grades of NatureWorks branching is introduced into the polylactide backbone to increase its flexibility and improve melt rheologic properties using reactive extrusion [62]. Owning to the chemistry of the catalytic co-ordination insertion mechanism, branching can not be introduced during main polymerization stage of the current industrial ROP process [63, 76-80].

It has been stated by different researchers that the co-ordination insertion mechanism in the ring opening process of cyclic esters is strongly influenced by the presence of impurities such as alcohol or carboxylic acid. Alcohol has been reported as jeopardizing the ring opening polymerization as it may interfere with initiator formation, or induce chain transfer and transesterification. On the other hand carboxylic acid promotes deactivation reactions and both impurities reduce the final PLA molecular weight attained by ROP [76-80]. As discussed in US patents nº 5,998,552 [76] and 7,566,753 B2 [63] the co-ordination insertion mechanism requires the presence of trace amounts of initiator to promote polymerization. However, the lactide obtained by distillation of oligomeric lactic acid depolymerization contains sufficient trace amounts of impurities with active hydroxyl groups, such as water and free lactic acid, to act as initiator. The addition of branching molecules containing free functional groups would compete with the lactide impurities, and therefore jeopardize the molecular weight of the final polymer and, consequently, its mechanical performance. A successful synthesis of branched PLA by ROP could only be achieved with extra pure lactide. To reach this purity grade the lactide would have to undergo recrystallization from dry toluene or diethyl ether, usually repeating the recrystallization three times, and this procedure is not feasible in a large scale process [62, 76]. Therefore a post-polymerization stage is required to successful accomplish polylactide structure modification.

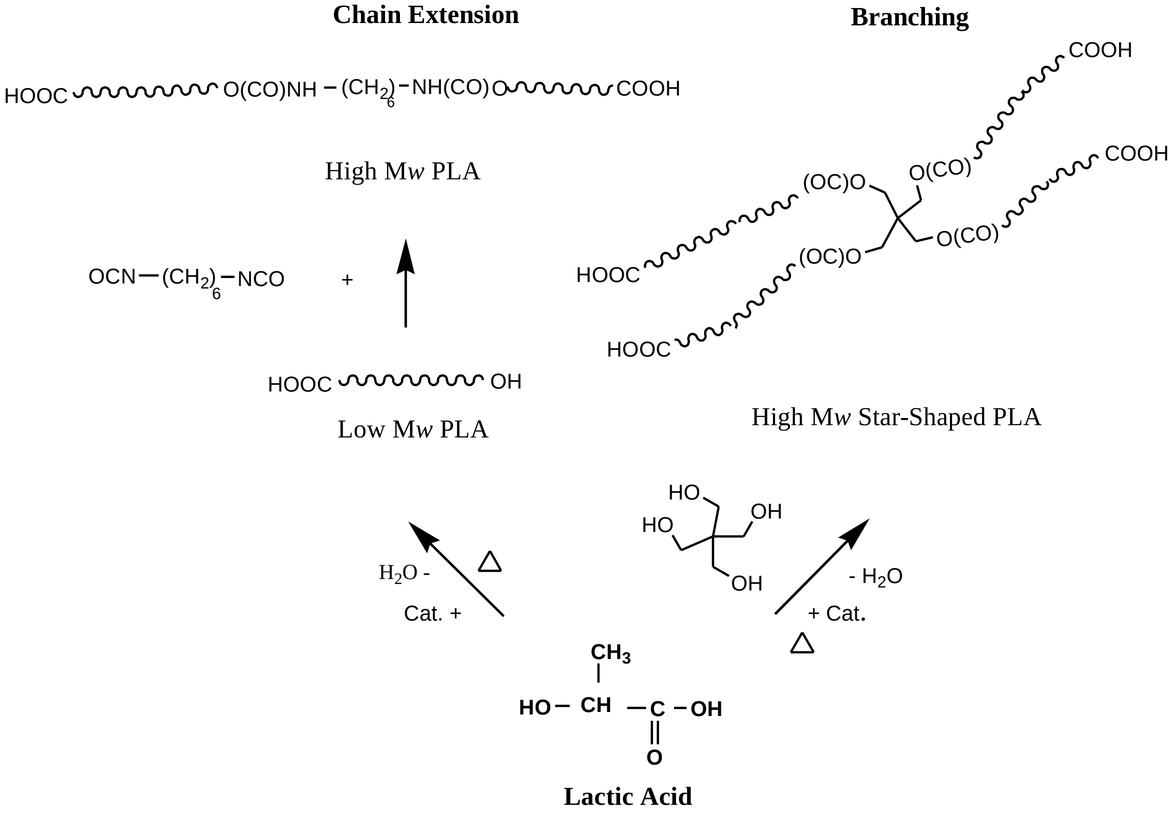

Figure 6.1: Schematic representation of the PLA chain extension with hexamethylene diisocyanate (HDI) (left) and branching with pentaerythritol (mPET) (right).

Although not feasible from an industrial point of view, the advantages of introducing long chain branching into PLA backbone have been reported in recent academic studies using multifunctional hydroxyl co-monomers as initiators of the lactide ROP [80-88], obtaining well defined star-shaped architectures. Interestingly, the resulting high molecular weight branched polymers show enhanced melt rheology properties without significantly altering polymer melt temperature and crystallinity degree. According to the literature [88-90], this is owed to the low amount of branching initiator required for effective structure modification

Biodegradable aliphatic polyesters of high molecular weight, suitable for conventional melt processing, have in common a narrow processability window. Bionolle™, known as pioneer in the green plastic materials field [91], is the tradename for a series of aliphatic polyesters such as poly(ethylene succinate), poly(butylene succinate) (PBSs) and poly(butylene adipate). They have been successfully synthesised since the 90s by melt polycondensation of aliphatic glycols with dicarboxylic acids. High molecular weight Bionolle™ polymer grades are reported to be obtained by chain extension using diisocyanates [92] and branching with compounds such as glycerol, pentaerythritol, citric acid or combining both [93]. The star-shaped Bionolle™ polymer is marketed as particularly suitable for blow molding articles, such as beverage bottles [93-96], showing that branching co-monomers also have potential for the preparation of very attractive materials.

Branching agents are multifunctional compounds enabling attaching several linear PLA chains in a star arrangement (Figure 6.1) with a higher molecular weight and, additionally, offering the possibility of internal plasticizing effect. Surprisingly, the use of branching agents during lactic acid melt polycondensation and its evaluation for large scale applications has not been reported yet. To the best of our knowledge the literature [89, 97-99] only refers to relatively low molecular weight star-shaped PLA, up to 30 000 $g.mol^{-1}$. These low molecular weight structures may be useful for some biomedical application to control PLA biodegradability and crystallinity by introducing hydrophilic or hydrophobic end groups [89, 99, 100], but are unsuitable for general purposes.

It is important to highlight that, in the frame of this project, only low branching degree star-shaped PLA polymers (low number of branches) were investigated. Therefore, their mechanical performance is expected to be similar to that of linear poly(lactic acid) with similar molecular weight. A large degree of branching in a polymer backbone (referred in the literature as hyperbranched and dendrimers) has a very pronounced effect on physical properties providing high solubility, low viscosity, low crystallinity and low mechanical performance [94]. Therefore, highly branched structures, even with high molecular weight, are not advantageous for the intended purpose.

To sum up to a very careful literature survey on polyesters synthesis related literature, two easily implementable strategies for obtaining high molecular weight poly(lactic acid) are assessed in this chapter. Branching, which consists in the addition of branching co-monomers during lactic acid melt polycondensation to promote star-shaped structures *(method I)* and chain extension, by adding highly reactive linking agents after the polycondensation step to promote chain extension *(method II).* A schematic illustration of the two approaches is presented in Figure 6.1. The materials obtained were investigated by different techniques and the most relevant results: molecular weight distribution, mechanical performance, thermal and optical properties are presented and discussed in the following sections.

Having in mind future applications, some concerns were taken into consideration when selecting potential co-monomers. All substances used throughout this project are common chemicals and easily available in the market. Moreover, the list of authorized monomers and other starting substances in the European Directive 2002/72/EC [101], relating to plastics intended to come into contact with foodstuffs, was verified. The chemical structure and properties of these compounds may be found in the *appendix A.*

The properties of the poly(lactic acid) polymers synthesized by different routes in the course of this project, including those obtained by lactic acid melt polycondensation (Chapter 5), confirm that the polymer molecular weight reached is too low to enable their use as thermoplastic materials. Using the set-up illustrated in Figure 2.2, the experimental polymerization procedure described in Chapter 2 and the operating conditions previously discussed, two strategies for polymer molecular weight increase will be assessed in this chapter: melt polycondensation in the presence of branching agents *(method I)* and chain extension of the polycondensation resulting prepolymer *(method II).*

6.2. Branching

6.2.1. Molecular Weight increasing

The set-up illustrated in Figure 2.2 and the experimental polymerization procedure described in section 2.4.3 from Chapter 2, were used in the experiments designed to assess melt polycondensation in the presence of branching agents *(method I).* The operating conditions were those discussed in Chapter 5 and the amount of co-monomers introduced at the beginning of the monomer distillation was calculated according to the target molecular weight, Mn_{th}, in table 6.1.

The first experimental evidence of chain growth was a remarkable increase in stirrer torque, registered when adding branching co-monomers during lactic acid melt polycondensation and illustrated in Figure 6.2. Since melt viscosity is directly related to molecular weight the pattern in Figure 6.2 suggests successful molecular weight increasing. In spite of some irregularities, the data in Table 6.1 show that a higher torque corresponds to a higher molecular weight as demonstrates PLA4_mPET sample.

Table 6.1: Results of lactic acid melt polycondensation experiments with branching agents, *method I*.

Nº	Branching Agent Molar Ratio (10^{-4})	Mn_{th} (g.mol^{-1})	Mw (g.mol^{-1})	*PD*	*OP* (%)	Torque (Ncm)	Yield (%)	*Tg* (ºC)	*Tc* (ºC)	*Tm* (ºC)	*Xc* (%)	*Td* (ºC)	Visual Appearance
PLA0	-	-	41 000	1.7	87	24	90	47	93	153	33	277	Pale yellow
PLA1_mPET	mPET – (9.6)	75 000	87 000	1.4	89	90	84	54	-	152	28	266	Pale yellow
PLA2_mPET	mPET – (7.2)	100 000	113 000	1.3	84	86	87	56	-	152	28	276	Pale yellow
PLA3_mPET	mPET – (5.8)	125 000	95 000	1.3	89	85	81	57	-	149	32	270	Pale yellow
PLA4_mPET[a]	mPET – (7.2)	100 000	180 000	4.0	77	130	84	59	-	125	15	275	Brown
PLA5_diPET	diPET – (14.4)	50 000	79 000	1.4	91	84	88	51	-	145	28	-	Pale yellow
PLA6_diPET	diPET – (9.6)	75 000	114 000	1.4	91	86	80	53	-	147	26	269	Pale yellow
PLA7_diPET	diPET – (7.2)	100 000	105 000	1.5	90	85	83	56	-	148	23	263	Pale yellow
PLA8_triPET	triPET – (9.6)	75 000	102 000	1.4	85	66	82	55	-	145	25	263	Pale yellow
PLA9_triPET	triPET – (7.2)	100 000	120 500	1.5	86	79	82	54	-	141	23	273	Pale yellow
PLA10_triPET	triPET – (5.8)	125 000	82 000	1.6	88	35	79	55	-	150	26	271	Pale yellow
PLA11_ECO	ECO – (9.6)	75 000	72 000	1.4	84	58	85	55	-	150	26	270	Pale yellow
PLA12_ECO	ECO – (7.2)	100 000	74 000	1.4	92	60	81	53	-	145	27	-	Pale yellow
PLA13_ECO	ECO – (5.8)	125 000	89 000	1.4	89	60	84	54	-	147	28	-	Pale yellow
PLA14_BADGE	BADGE – (9.6)	75 000	78 000	1.4	86	77	77	56	-	146	26	-	Pale yellow
PLA15_BADGE	BADGE – (7.2)	100 000	114 500	1.4	88	94	81	55	-	147	27	282	Pale yellow
PLA16_BADGE	BADGE – (5.8)	125 000	72 000	1.4	91	77	79	52	-	143	29	276	Pale yellow
PLA17_PMDA	PMDA – (9.6)	75 000	45 000	2.6	85	31	84	48	118	151	37	-	Pale yellow
PLA18_EDTA	EDTA – (9.6)	75 000	66 500	1.5	87	34	86	-	-	147	15	340	Brown
PLA19_TEA	TEA – (9.6)	75 000	58 500	1.6	89	70	80	58	-	146	23	255	Black
PLA20_ TAEA	TAEA – (9.6)	75 000	-	-	74	12	74	-	-	-	-	-	Black

[a] Total reaction time, 27h;

Star-shaped PLA with different central cores, different arm lengths and arm numbers were prepared. All these features may have a great impact on the properties of the final polymers, therefore a full characterization is of major importance. However, quantitative description of long branching polymers, as the ones obtained in this study, is a hard task particularly for molecular weights characterization [94, 102, 103]. Molecular weight information, in table 6.1 were obtained by SEC technique (section 2.5.1), using conventional calibration obtained from narrow linear polystyrene standards. A first conclusion from Table 6.1 is that some of the branching comonomers added to the lactic acid melt polycondensation allow synthesizing PLA polymers with molecular weight above 100 000 g.mol^{-1}.

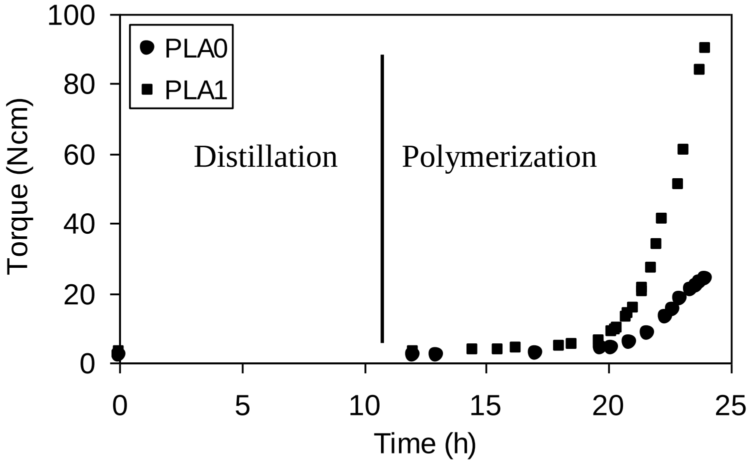

Figure 6.2: Torque profile of lactic acid melt polycondensation in the absence of branching agent (PLA0) and in the presence of pentaerythritol as branching agent (PLA1-mPET).

In size exclusion chromatography, SEC, the separation of macromolecules occurs according to the hydrodynamic volume rather than to molecular weight. In solution, branched polymers have a more compact structure and therefore a smaller hydrodynamic volume than the linear molecules with the same molecular weight. To better understand this concept one can think about a macromolecule with three branches. If the branch point is located close to one of the chain ends, the architecture and the hydrodynamic volume of the branched polymer does not differ much from the linear molecule. However, if the branch point is located at equal distance from all the three chain ends, the molecule assumes the shape of a well defined three arms star and its hydrodynamic volume is considerably smaller than the linear counterpart [102]. This effect is even more pronounced for star-shaped polymers with higher arm numbers. It is well known in the literature [84, 90, 104-108] that this hydrodynamic volume reduction will lead to an underestimated molecular weight. Consequently, experimental determination of molecular weight of branched polymers by SEC is not a reliable technique [94] and should be used just as an indication. Nevertheless, having this information in mind, size exclusion chromatography still provides very useful data to elucidate the branching effect based on molecular weight and its distribution. All branched polymers obtained in this study depicted a monomodal distribution with low apparent polydispersity showing a good polymerization control and that linear PLA formation, as side reaction, was not significant.

The accurate determination of molecular weight of branched polymers by SEC would require the use of several detectors (namely refractive index, viscosimeter and light scattering) simultaneously in order to determine the different parameters required for the calculation of the molecular weight directly from the detectors. In this work, due to low refractive index (dn/dc) of PLA [109] the light scattering detector could not be used. Branched samples were also analysed by MALDI-TOF technique, in an attempt to determine its absolute molecular weight, but only low molecular weight oligomers, 2 000 g.mol^{-1}, were detected. Therefore, further discussion will be based on SEC data.

The experimental work began by assessing pentaerythritol (mPET) and its derivatives, dipentaerythritol (diPET) and tripentaerythritol (triPET), as chain branching agents (PLA1_mPET to PLA10_triPET). These compounds were first selected as they bear 4, 6 and 8 primary hydroxyl groups, respectively. Each hydroxyl group has the ability to work as a branching point, therefore star-shaped PLAs with different arm numbers and arm lengths could be prepared. The reaction mechanism for synthesizing a star-shaped PLA by conventional polycondensation reaction relies on the difference in reactivities of the polyhydroxyl co-monomers and the lactic acid [97], which bears a secondary hydroxyl group. In the initial stage of the reaction it is expected that all primary hydroxyl groups in the co-monomer react by esterification with the lactic acid carboxyl group to form a small star-shaped structure, whose arms grow further by subsequent lactic acid esterification. The quite narrow apparent molecular weight distribution registered in PLA1_mPET to PLA10_triPET (Table 6.1) suggests a well defined star-shaped structure and a parallel and steady growth of the linear side arms.

To illustrate the corresponding branched structures, ^{1}H NMR spectra of selected samples were recorded. Spectra of 4-arms star-shaped PLA obtained with pentaerythritol (PLA2_mPET), 6-arms star-shaped PLA obtained with dipentaerythritol (PLA6-diPET) and 8-arms star-shaped PLA obtained with tripentaerythritol as branching agent (PLA9_triPET) are depicted in Figure 6.3.

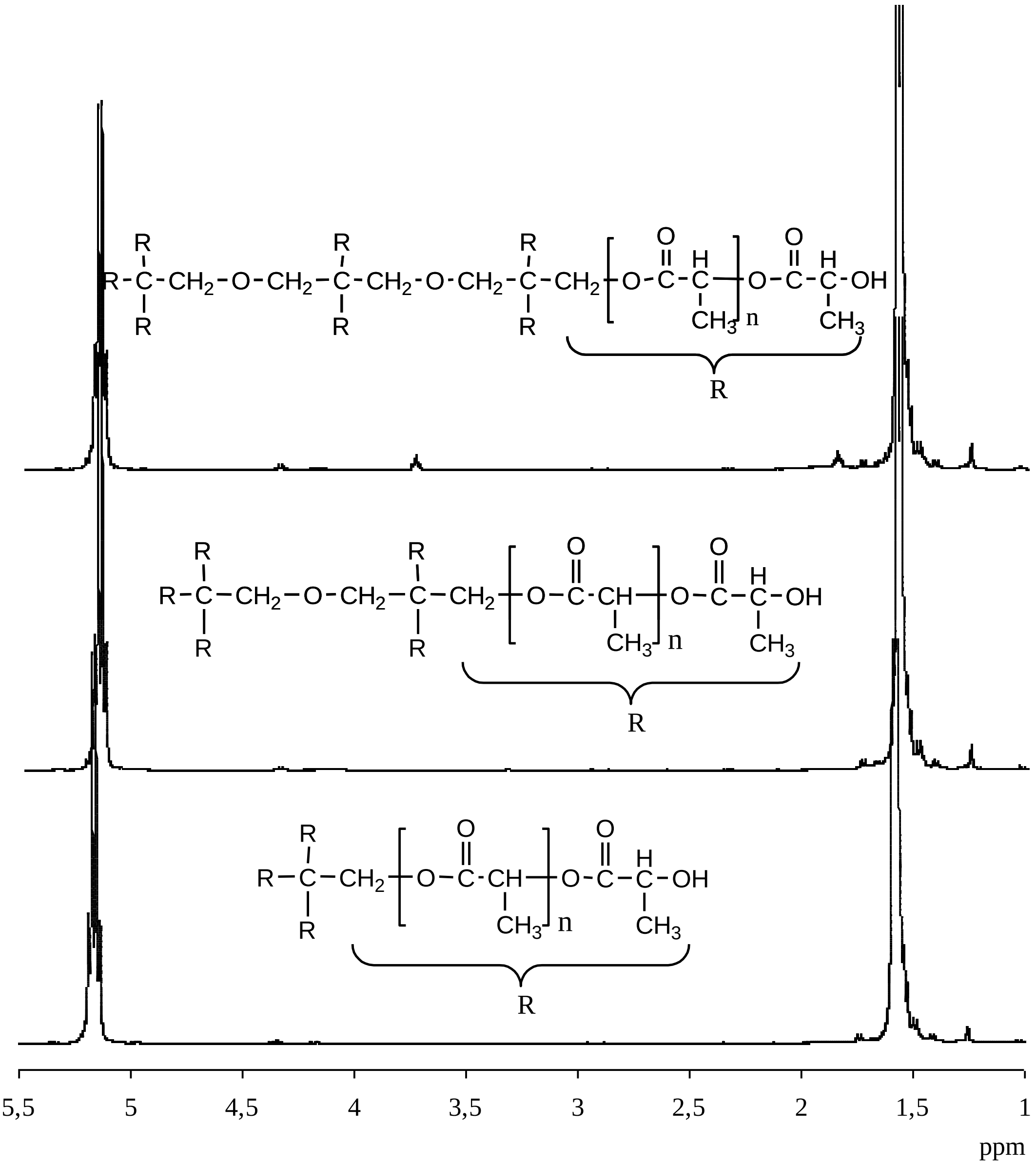

Figure 6.3: ^{1}H NMR spectrum of 4-arms star-shaped PLA obtained with pentaerythritol (PLA2_mPET), 6-arms star-shaped PLA obtained with dipentaerythritol (PLA6_diPET) and 8-arms star-shaped PLA obtained with tripentaerythritol (PLA9_triPET).

Owing to the low amount of branching agent required for effective structure modification, which is insufficient for detection, the ^{1}H NMR spectra of star-shaped PLA in Figure 6.3 do not differ much from the ^{1}H NMR spectra obtained for linear PLA molecules and discussed in chapter 3, Figure 3.3. Therefore it is not possible to use nuclear magnetic resonance spectroscopy for measuring the branching degree of such high molecular weight polymers, and this is in agreement with the finding of Korhonen *et al.* [88] when studying star-shaped polylactides. The most significant change in the spectra in Figure 6.3 is an additional peak at 3.75 ppm recorded in the 8-arms star-shaped PLA (PLA9_triPET). This new peak is assigned to the –C$\underline{H}_2$ protons in the tripentaerythritol central core, being another strong evidence of successful structure modification. Attempting to use NMR results to determine number molecular weight of star-shaped samples, the same limitations were found as the ones discussed in chapter 3. Taking the 4-arms star-shaped PLA2_mPET sample as example, the integration of the –C$\underline{H}$ peak in the polymer main chain and close to the terminal hydroxyl groups led to a number molecular weight of 38 000 g.mol^{-1}, considerably lower than the one expected according to reaction stoichiometry (theoretical) and to the value obtained by SEC and reported in the Table 6.1.

After the promising results achieved with pentaerythritol and its derivatives, other branching agents were tested. Particularly good results were obtained employing epoxidized castor oil (ECO) (PLA11_ECO to PLA13_ECO), a renewable monomer, and bisphenol A diglycidyl ether (BADGE) (PLA14_BADGE to PLA16_BADGE), both chemical compounds bearing epoxy groups that react preferably with lactic acid carboxyl groups. At the experimental conditions in this study, it might be expected that, in the presence of water, the oxirane ring structure opens and the two resulting hydroxyl groups would participate in a further step-growth polymerization. Therefore, ECO would originate a 6-arms star-shaped PLA, whereas BADGE would originate a 4-arms star-shaped PLA. However, due to steric effects resulting from the presence of secondary hydroxyl groups in the reaction system, star-shaped polymers with no uniform arm lengths may be expected.

The amount of multifunctional component restricts stoichiometrically the achievable polymerization degree. To assess the influence of the initial branching agent content on the final molecular weight, Figure 6.4 depicts the number molecular weights obtained by SEC $(Mn=Mw/PD)$ and the theoretical ones, Mn_{th}, for each of the co-monomers discussed above (mPET, diPET, triPET, ECO and BADGE). Three contents, based on different targeted molecular weights, were tested for each co-monomer. Although rather difficult to compare due to the reliability of SEC results, the results point out a clear influence of branching agent amount on final molecular weight. Higher molecular weights seem to be obtained when initial content is calculated based on a theoretical molecular weight of 100 000 g.mol^{-1}, except for diPET which seems to be 75 000 g.mol^{-1}. Regarding the epoxydized castor oil results, molecular weights are considerably lower and show a monotonous increasing trend, suggesting that a lower content should be tested to find the optimum amount.

Other kinds of multifunctional compounds with different functionalities: pyromellitic dianhydride (PMDA), ethylenediaminetetraacetic acid (EDTA), triethanolamine (TEA) and tris(2-aminoethyl)amine (TAEA); were also assessed as branching agents (PLA17_PMDA, PLA18_EDTA, PLA19_TEA, PLA20_TAEA), but the results were not promising both in terms of molecular weight and resulting polymer colour.

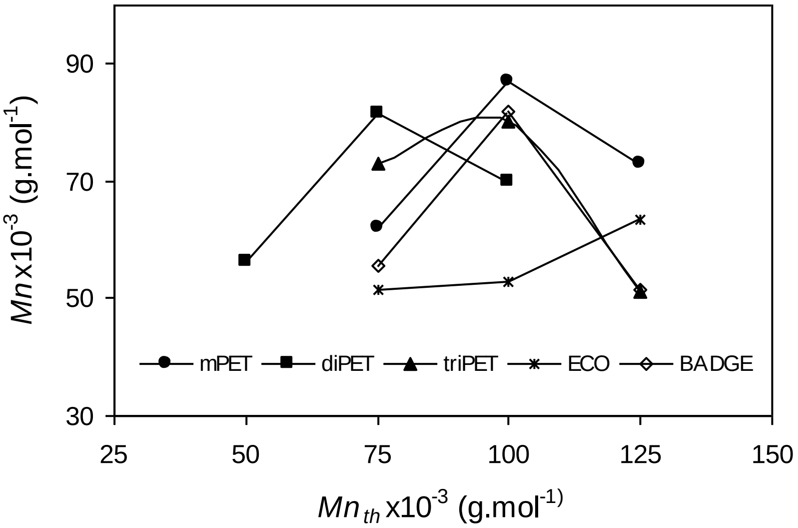

Figure 6.4: Molecular weight for star-shaped PLA obtained with different branching agents - experimental (SEC) *(Mn) versus* theoretical *(Mn_{th})*.

As previously discussed in Figure 6.2, the addition of branching agents usually results in a considerable increase in the torque comparing to when these are not used (PLA0). Figure 6.5 depicts the torque recorded throughout the melt polycondensation as a function of the molecular weight when using mPET as branching agent (PLA4_mPET). No significant changes on melt viscosity were recorded for molecular weights lower than ≈ 30 000 g.mol^{-1}. After that turning point, a fast and steady increase was registered. The apparent slope declining for the higher chain length is due to a broader molecular weight distribution (higher *Mw* and lower *Mn*). The experiment PLA4_mPET was carried out at the same conditions of PLA2_mPET but with a longer reaction time (3 hours more), inducing side reactions such as racemization, depolymerisation and discoloration of the final material. Thus, increasing reaction time may not be advantageous from the polymer quality point of view.

Torque data in Table 6.1 points out the influence of the number of arms and central cores on the star-shaped polymers melt viscosity. For example, the 8-arms PLA9_triPET has a lower torque than its 4-arms PLA2_mPET counterpart (79 and 86 Ncm, respectively) and PLA15_BADGE shows the highest value (94 Ncm) likely as a result of its stiffer central core.

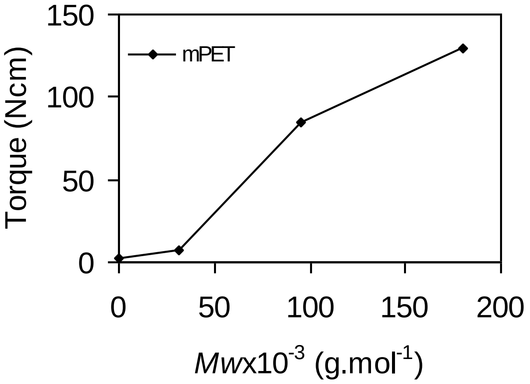

Figure 6.5: Torque and molecular weight relationship using mPET as branching agent.

6.2.2. Thermal Characterization

In addition to the molecular weight and optical purity also the number of arms, arm length and the nature of the central core, which PLA arms are attached, should have a great influence on thermal properties of star-shaped polymers. Therefore, DSC (*vide* chapter 2 section 2.5.7) and TGA measurements (*vide* chapter 2 section 2.5.8) were performed and the data collected (*Tg*, *Tc, Tm, Xc* and *Td*) are summarized in Table 6.1.

Concerning the glass transition temperature *(Tg)*, an expected increase was observed for the branched polymers, comparatively to the PLA0, owing to a significant molecular weight increase, but the influence of arm numbers is not clear (Table 6.1). The highest *Tg*, 59 ºC, was obtained for the PLA4_mPET sample which corresponds to the highest molecular weight. The influence of the number of arms upon melting temperature, *Tm*, is much more evident as all branched samples show a melting point lower than the linear PLA (PLA0), since the presence of branching increases chain mobility [110-112]. Considering samples of higher molecular weight PLA2_mPET (4-arms), PLA6_diPET (6-arms) and PLA9_triPET (8-arms) as examples, a gradual decrease is observed as the number of arms increases (152 ºC, 147 ºC and 141 ºC, respectively). This finding is in agreement with previous results for star-shaped PCL [110] and star-shaped polylactides [111, 112]. A decrease in crystallinity degree was also recorded for these samples (28 %, 26 % and 23 %, respectively). Star-shaped polymers with increasing number of arms and same molecular weight have shorter arms and increased number of free end groups, which may difficult chain folding and regular packing during crystallization process. On the other hand, star-shaped polymers with same molecular weight and fewer arms, each arm has a higher chain length. Therefore it is less sensitive to the nature of the central core enabling to form more perfect crystals [110].

Interestingly, at the DSC standard heating rate of 10 ºC/min, no crystallization peak was detected for every branched sample, corroborating the finding of crystallization delay relatively to the linear architecture. PLA17_PMDA sample was an exception, showing a cold crystallization temperature of 118 ºC, significantly higher than the linear PLA0, and the highest crystallinity degree, 37 %. This finding may be due to the ability of pyromellitic anhydride (PMDA) to act as nucleating agent.

It is expected that branching may change polymers thermal stability and therefore degradation profiles of selected samples are shown in Figure 6.6. Degradation temperatures, *Td*, at maximum decomposition rate were recorded from the differential weight loss curves (not shown) and are listed in Table 6.1. Figure 6.6 enables comparing polymer weight loss *versus* degradation temperature. All curves show a single degradation stage with roughly similar onset temperature, regardless of number of arms or central core nature, but different degradation rates. In spite of the higher molecular weights of PLA2_mPET, PLA6_diPET and PLA9_triPET samples, they show a faster degradation comparing to the linear PLA0 sample. The relatively poor thermal stability of branched polymers can be ascribed to the increased content of thermally unstable free end groups [88, 112]. Regarding the influence of number of arms on degradation rate, and similarly to the aforementioned when discussing glass transition temperature, no clear conclusions can withdrawn. This result is probably due to the limitations molecular weight assessment by SEC and optical purity dissimilarities.

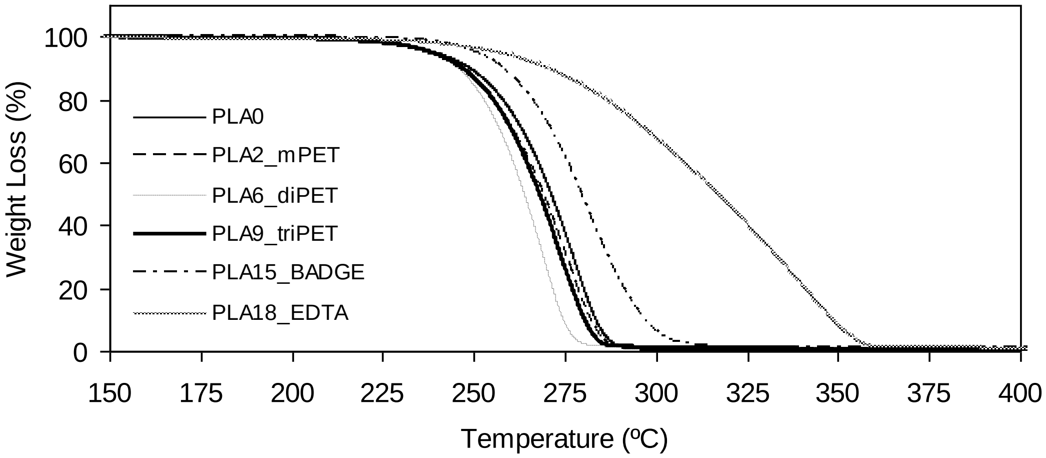

Figure 6.6: TGA thermograms of selected samples (PLA0, PLA2_mPET, PLA6_diPET, PLA9_triPET, PLA15_BADGE and PLA18_EDTA).

A very surprising result was obtained for PLA18_EDTA. This sample was synthesized using ethylenediaminetetraacetic acid (EDTA) as branching agent and the thermal degradation rate was dramatically slowed down, Figure 6.6. EDTA has been widely used in the pulp industry as chelating agent [113] to reduce metal ions concentration, such as Ca^{2+} and Fe^{3+}, also present in this polymerization system as monomer impurities. The EDTA ability to coordinate with metal compounds, reducing its activity, can explain the poor molecular weight result and the unexpected thermal stability enhancement. Being residual metals reported as one of the main causes affecting PLA thermal stability during ordinary melt processing [114], EDTA may be envisaged as an interesting masterbatch.

Although difficult to make direct comparisons with commercial polylactides, since thermal stability is strongly dependent on polymer structure, stereoregularity, amount of residual catalyst, presence of residual monomer among others, it is evident that the samples here assessed show a thermal stability lower than commercial polylactides. To enable comparison, a thermograph of a NatureWorks PLA (2002D) was recorded and *Td* was 358 ºC while the degradation onset was at around 300 ºC.

The analysis of the weight residues after TGA heating ramp experiments, until 600 ºC, revealed that the prepared samples had lower weight residues (≈ 0.7 %) comparing to 1.5 % of the commercial 2002D PLA also purified by precipitation. The only exception was PLA18_EDTA with 1.3 % weight residue. This result for the NatureWorks polymer is quite high having in mind that the ring opening polymerization process requires highly pure lactide. This finding may be partly explained by a lower catalyst content as a consequence of tin metal precipitation at the end of the polymerization experiments, as previously discussed in chapter 5.

6.2.3. Crystal Structure

Depending on preparation conditions three different crystalline forms have been identified for PLA (α, β and γ). The most common polymorph is by far the α form, which consists in two chains with left-handed 10_3 helical conformation packed into a pseudo-orthorhombic unit cell with dimensions of a = 10.7 Å, b = 6.45 Å and c = 27.8 Å [115-117]. Attempting to investigate branching effect on resulting PLA crystal structure, wide-angle X-ray scattering (WAXS) patterns of selected samples were recorded (*vide* chapter 2 section 2.5.10).

The WAXS profiles of the samples recorded at 100 ºC are shown in Figure 6.7. All samples, linear and branched ones, show two easily distinguishable peaks. The most intense one occurs at a Bragg angle around 16.7^o, which is attributed to the diffraction from (110) and/or (200) planes, and the second most intense peak around 19.1^o arising from (203) and/or (113) diffraction planes [89, 115-118]. In addition, two weaker reflections may be observed in some samples. These peaks are consistent with the α-crystals of PLA that have been fully described in the literature and show that branching may affect crystallization rate but not the resultant crystal structure [119]. Similar results were obtained for branched PCL [110] as well as for 4-arms star-shaped polylactides [89].

Wide-angle X-ray scattering can also be used to quantify the degree of crystallinity, however the temperature control in the DSC is much more accurate than the X-ray set-up and only well defined crystalline entities give detectable scattering peaks by WAXS. For that reason, this technique was used mainly to confirm crystalline structure formed during cold crystallization [119].

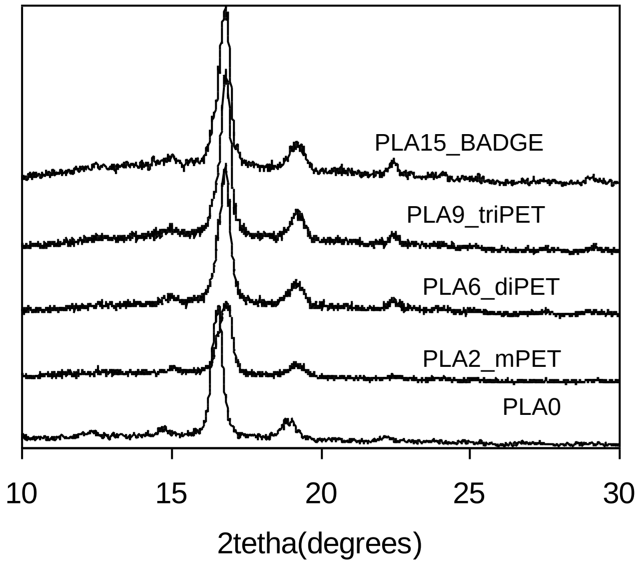

Figure 6.7: WAXD patterns of selected samples (PLA0, PLA2_mPET, PLA6_diPET, PLA9_triPET and PLA15_BADGE) recorded at 100 ºC during the second heating scan at 2ºC.min^{-1}.

6.3. Chain Extension

6.3.1. Molecular Weight Increasing

Slight modifications were introduced into the melt polycondensation procedure described in chapter 2, section 2.4.3 to perform the chain extension reactions, *method II.* The lactic acid prepolymer was first obtained by polycondensation under vacuum as previously described in chapter 5, the overnight distillation was followed by melt polycondensation at 190 ºC for 10 h. Then vacuum was turned off and the reactor was filled with nitrogen prior to a drop by drop addition of the chain extender into the reactor. Chain extension reaction was further carried out under melt conditions for two hours under nitrogen sweep and at atmospheric pressure. The most relevant linking agents tested, molar ratio, and the results obtained are summarized in Table 6.2.

The reaction progress was once more followed by measuring the torque since it is an indirect measurement of polymer molecular weight and may give a valuable insight into resulting polymer structure. Figure 6.8 shows the typical torque profile recorded during a chain extension experiment (PLA24_HDI) and it depicts a sharp increase after the linking agent addition, suggesting a fast molecular weight increase. High molecular weight, up to 140 000 g.mol^{-1}, were further confirmed by SEC measurements. However, broader molecular weight distributions were obtained in these chaining experiment samples, which may explain the low torque values comparing with the branching results, Figure 6.2, discussed above.

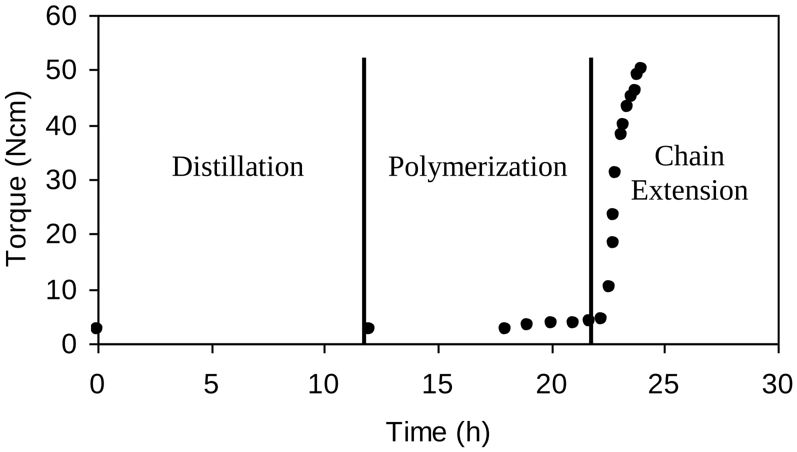

Figure 6.8: Typical torque profile recorded during chain extension reaction with 1,6-hexamethylene diisocyanate (PLA24_HDI).

The chain extension experiments started with the study of 1,6-hexamethylene diisocyanate (HDI) as linking agent of a low molecular weight PLA prepolymer obtaining a poly(ester-urethane) copolymer. However, the amount of chain extender is always considerably smaller than the lactic acid units and it is expected that polymer properties remain close to the PLA homopolymer ones. HDI was selected since it is widely used in polyurethanes synthesis and is relatively inexpensive comparing to other available isocyanates.

Table 6.2: Results of the lactic acid polycondensation experiments using chain extenders, *method II*.

Nº	**1,4-Butanediol Molar Ratio (10^{-3})**	**Chain Extender Molar Ratio (10^{-3})**	***Mw*** **($g.mol^{-1}$)**	***PD***	***OP*** **(%)**	**Torque (Ncm)**	**Yield (%)**	***Tg*** **(ºC)**	***Tc*** **(ºC)**	***Tm*** **(ºC)**	***Xc*** **(%)**	***Td*** **(ºc)**	**Visual Appearance**
PLA21_prep	None	None	32 000	1.7	89	7.7	88	49	98	150	37	272	Pale yellow
PLA22_HDI	None	HDI – (9)	41 000	1.9	85	24	89	48	-	146	28	-	Brown
PLA23_HDI	None	HDI – (18)	56 000	1.8	84	35	90	56	-	-	-	-	Pale yellow
PLA24_HDI	None	HDI – (24)	142 000	3.6	87	50	80	56	-	148	34	-	Pale yellow
PLA25_HDI	None	HDI – (30)	145 000	2.6	81	41	90	55	-	145	27	286	Pale yellow
PLA26_HDI	None	HDI – (35)	-	-	-	30	95	-	-	-	-	-	Pale yellow
PLA27_OH	2.8	None	33 000	1.4	90	7.7	84	46	97	151	36	292	Pale yellow
PLA28_HDI	2.8	HDI – (18)	84 000	1.8	87	43	86	57	-	144	34	-	Pale yellow
PLA29_HDI	2.8	HDI – (24)	89 000	2.0	84	47	91	-	-	-	-	-	Pale yellow
PLA30_HDI	2.8	HDI – (30)	108 000	2.4	85	46	92	54	-	142	32	287	Brown
PLA31_HDI	7	HDI – (18)	65 000	1.7	84	34	88	55	-	141	21	-	Pale yellow
PLA32_TDI	None	Toluene 2,4-Diisocyanate – (30)	56 000	2.8	82	23	92	63	-	143	23	283	Pale yellow
PLA33_ECO	None	Epoxydized Castor Oil – (9)	35 000	4.0	82	10	86	-	-	-	-	-	Pale yellow

HDI- Hexamethylene Diisocyanate

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The isocyanate group is reported to react predominantly with the hydroxyl groups of the lactic acid [8, 9, 120]. Thus, to assess the influence of terminal end groups on final molecular weight, two lactic acid based prepolymers were tested: a prepolymer as obtained by polycondensation, with an equimolar concentration of both carboxyl and hydroxyl end groups (PLA21_prep); and a hydroxyl terminated prepolymer (PLA27_OH). This last one was synthesized with 1,4-butanediol as co-monomer during the initial distillation step, as reported in the literature [8, 9, 18, 19, 45, 120], to avoid differences in end groups reactivity. The results in Table 6.2 clearly indicate that, under the experimental conditions set in this work, there is no advantage in hydroxyl end group modification. Surprisingly, enhanced molecular weights were obtained with unmodified prepolymers containing both hydroxyl and carboxyl end groups (PLA24_HDI to PLA25_HDI), comparing to the hydroxyl terminated ones (PLA29_HDI to PLA31_HDI). This result contrasts with those in the literature were PLA chain extension with diisocyanates is always preceded by the synthesis of telechelic hydroxyl prepolymers and the presence of carboxyl end groups is reported to hinder chain extension [8, 9, 18, 19, 45, 120].

The molecular weight of the prepolymer sets the distance between urethane linkages and the amount of chain extender defines de number of prepolymers linked to the final molecule, consequently both determine the final polymer length. Therefore the higher the prepolymer chain length (PLA28_HDI and PLA31_HDI) as well as the amount of diisocyanate, the higher the final molecular weight (PLA22_HDI to PLA25_HDI or PLA28_HDI to PLA30_HDI). For the higher diisocyanate molar ratio tested (PLA26_HDI) the final polymer showed some gel formation (around 5 wt % from chloroform extraction, *vide* chapter 2 section 2.5.6), indicative of crosslinking. For that reason, molecular weight determination was not carried out. Although interesting for some kind of applications, the study of crosslinked PLA was beyond the scope of this work.

The isocyanate group is highly reactive and it is well known from the literature that, besides hydroxyl groups, it also reacts with other functional groups containing active hydrogen, such as acids, water impurities or even with themselves in a self-addition reaction undergoing dimerization, trimerization and carbodiimidization [17, 45, 120, 121]. In particular, under the temperature and catalytic conditions in this polycondensation system, isocyanate chemistry may lead to a number of reactions. The reaction of isocyanate with prepolymer hydroxyl group leads to the formation of well known urethane linkage (Figure 6.9 a), whereas the reaction with carboxyl end group leads to the formation of an amide bond (figure 6.9 b). As chain linking reaction proceed the prepolymer free end group content decreases and becomes scarce. The urethane and amide groups can further react with free isocyanate, leading to the formation of allophonate (Figure 6.9 c) and urea linkages (Figure 6.9 d), which may result in branching and crosslinking of the final polymer [17, 45, 120], as observed for PLA26_HDI sample. The urea linkage can even react further with free isocyanate giving biuret bonds. The most likely reactions are illustrated in Figure 6.9. Once again, it must be noticed that uncertainties in SEC measurements can arise if branching occurs, however SEC results will always provide clear evidence of chain length increasing.

Torque, as a measure of melt viscosity, can give an insight into the polymer structure. For example, PLA25_HDI shows a lower torque than PLA24_HDI in spite of its slightly higher chain length, which may be related to some branching. Branching enhances the flow properties and therefore may be beneficial for polymer processing.

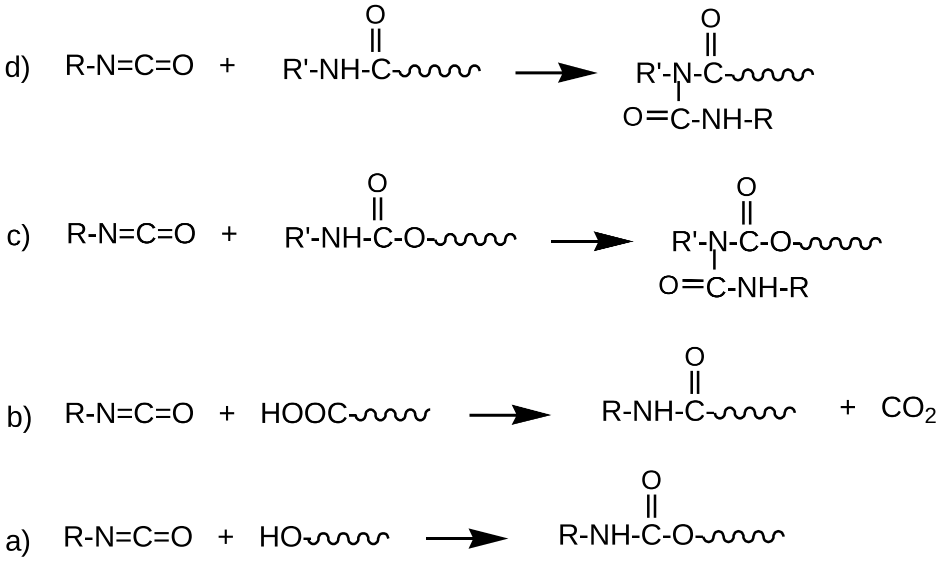

Figure 6.9: Simplified illustration of isocyanate reactions with a) hydroxyl group, b) carboxylic group, c) urethane and d) amide [18, 45, 120, 121].

The ^{1}H NMR spectrum of a selected sample obtained with HDI as linking agent (PLA24_HDI) can be seen in Figure 6.10. A new broad peak at 3.15 ppm, assigned to the –C$\underline{H}_2$ group in HDI units close to the urethane bond, can be clearly distinguished providing evidence of successful chain extension reaction. A magnification of the spectrum shows a shoulder of a partly overlapped peak that may be assigned to the amide bond, supporting the hypothesis of reaction between isocyanate and carboxyl end group [120]. The urethane peak itself is not observed since it is probably overlapped with the solvent, C<u>H</u>Cl$_3$, peak at 7.21 ppm [20, 120]. Although not shown, the urethane bonds were easily identified by ATR-FTIR.

Besides HDI other chemicals were assessed as potential chain linking agents, including an aromatic diisocyanate. Toluene 2,4-diisocyanate (TDI) was tested in the experiment referred as PLA32_TDI, but the resulting molecular weight was significantly lower comparing to HDI (PLA25_HDI and PLA30_HDI). This finding indicates that the chemical structure of the diisocyanate plays an important role on its reactivity. Conversely to the aliphatic HDI, TDI has an asymmetric structure therefore its isocyanate groups show different reactivities.

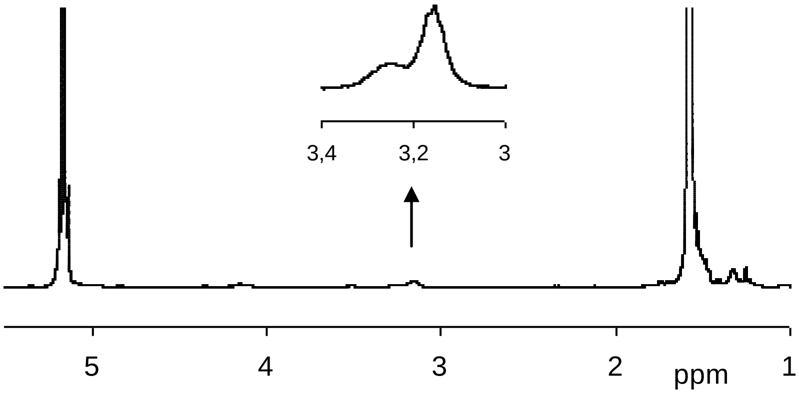

Figure 6.10: ^{1}H NMR spectrum of PLA24_HDI sample, linked with 1,6-hexamethylene diisocyanate.

In some applications care must be taken when choosing chain extender agents. Aromatic compounds are more likely to degrade into toxic products, whereas HDI is commonly used in the synthesis of biodegradable polyurethanes and they are generally regarded as biocompatible [122].

As aforementioned, in the PET process branching and length increasing is performed simultaneously employing compounds containing epoxy groups [49-55] rather than diisocyanates. The epoxy group is reported to react with both carboxyl, predominantly, and hydroxyl end groups [51, 55]. Attempting to study the effectiveness of this kind of functional groups on lactic acid prepolymer chain extension, biobased and biodegradable epoxydized castor oil was tested (PLA33_ECO), but the molecular weight achieved was rather disappointing (35 000 g.mol^{-1}). A reasonable explanation for the lack of reactivity is the low reaction temperature in this study (190 ºC) comparing to the temperature, 280 ºC, in PET modification process.

6.3.2. Thermal Characterization

Chain extension reaction introduces new segments, new linkages and possibly some branching into the PLA molecular structure and it certainly affects thermal transitions compiled in Table 6.2. The glass transition temperature, *Tg*, of chain-extended polymers is higher than that of the starting prepolymers (PLA21_prep and PLA27_OH) owing to the reduced mobility of the longer chains. However, the melting temperature, *Tm*, and crystallinity degree, *Xc*, show a decreasing trend, since these new segments hinder crystallization to some extent. Interestingly, PLA32_TDI obtained with a rather stiff diisocyanate shows a considerably higher *Tg*, in spite of its relatively low molecular weight.

Degradation temperatures at maximum decomposition rate (*Td*), taken from the differential weight loss curves, show an opposite trend according to the starting prepolymer. When PLA21_prep, without end group modification, is employed *Td* increases, PLA25_HDI and PLA32_TDI, owing to the raise in molecular weight. However, when hydroxyl terminated prepolymer is used (PLA27_OH), *Td* decreases (PLA30_HDI) with chain extension. The surprisingly high *Td* of the hydroxyl terminated PLA27_OH prepolymer may be attributed to the lack of thermally unstable carboxyl end groups. The *Td* decrease over the two hours chain extension reaction may be a strong evidence of new carboxyl groups appearance due to the occurrence of degradation reactions. This is further corroborated by the lower *OP* of the chain-extended polymer, relatively to the starting prepolymers.

As discussed in the previous section, the results in Table 6.2 point out that, for an effective linking reaction, a prior functionalization with hydroxyl groups is not necessary. An additional difference between HDI chain-extended PLA samples obtained in this project and the ones reported in the literature lies in the semi-crystalline nature. Chain-extended PLA was previously described as an amorphous material due to the high level of racemization [13, 120] originated from inappropriate experimental procedure, rather than the disrupting effect of the linking segments into the polymer backbone. Moreover, yellowing degree of resulting polymers was never discussed or even referred. These features are of major importance since it is well known that amorphous PLA has inferior mechanical properties as compared with semi-crystalline one [116] and polymers with an yellow appearance cannot be used as prime material. Therefore, the conditions of the prepolymer synthesis play a critical role in attaining good polymer quality.

To assess the influence of linking reactions on resultant crystal structure, WAXS profiles were recorded. The information gathered confirms the results for the branched PLA samples discussed in section 6.2.3, and therefore it is not included here.

6.4. Mechanical Performance Assessment

Tensile testing (*vide* chapter 2, section 2.5.12.) and dynamic mechanical analysis (DMTA) (*vide* chapter 2, section 2.5.9.) of selected samples were carried out in order to determine the influence of molecular weight increasing strategy, *method I* and *method II*, on general mechanical performance, as well as the usefulness of the resulting polymers as commodity materials. Figure 6.11 depicts the stress *versus* strain curves for PLA samples obtained by two molecular weight increasing methods described above.

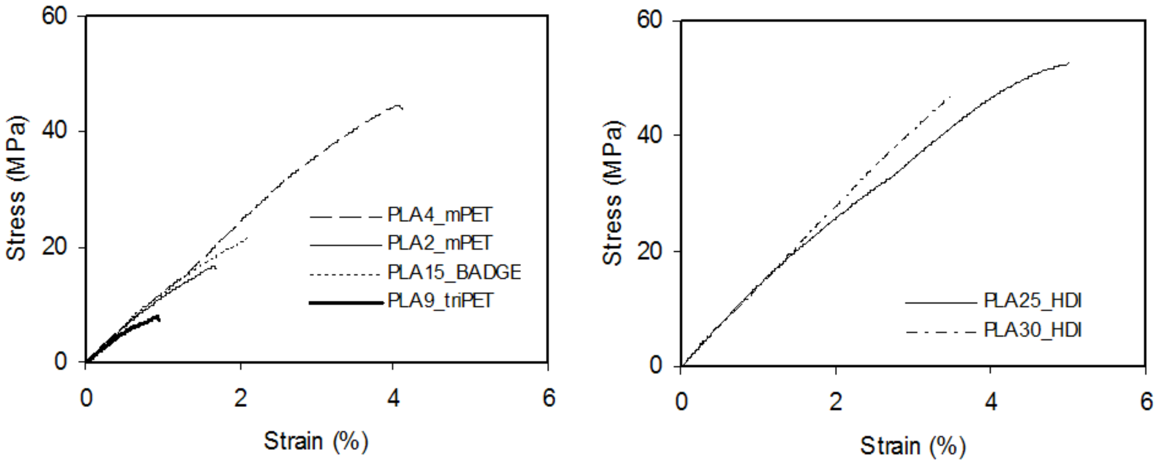

Figure 6.11: Poly(lactic acid) samples stress *vs* strain curves: *method I* - using branching comonomers (a - left) and *method II* - using chain linking agents (b - right).

An overall analysis of stress-strain curves in Figure 6.11 concludes that these are steep, almost linear, and flatten, only slightly, near to the breaking point, without exhibiting yielding point and subsequent plastic deformation. Samples with higher molecular weight (PLA4_mPET and PLA25_HDI), irrespectively of the length increasing approach, deform only to a very small extent (less than 6 %) at relatively high loads (higher than 40 MPa) with roughly the same elastic modulus (around 1100 MPa), showing a rather hard and brittle nature. In spite of the introduction of branching or small amounts of urethanes linkages into the PLA backbone, these samples behave like rigid and brittle materials, comparable to the reported values for unplasticized and unoriented polylactides (tensile strength 47-53 MPa, elongation at break 3-8 % and elastic modulus 1500-2170 MPa) [59, 61, 123-130] or chain linked PLA (tensile strength 57 MPa, elongation at break 5.8 % and elastic modulus 1750 MPa) [8, 120].

Figure 6.11-a clearly depicts the marked effect of molecular weight on PLA mechanical performance, but also of the molecular structure, since the 8-arm star shaped PLA9_triPET broke at a much lower tension than the 4-arm star shaped PLA2_mPET (7 and 16 MPa, respectively). Moreover, the 4-arm star shaped PLA15_BADGE has a tension at break of 21 MPa, as a consequence of its stiffer central core. However, this remains substantially lower than the tension at break recorded for the linear PLA30_HDI (47 MPa), in the same molecular weight range.

From the mechanical performance point of view, the results suggest that, to achieve similar mechanical performance to the linear polymer with a given molecular weight, the branched PLA polymer must have an higher molecular weight and, moreover, no plasticizing effect was perceived. Therefore, to increase ductility, plasticizers additives should be tested.

Figures 6.12 represents the dynamic mechanical traces (storage modulus (*E'*) and loss tangent (tan δ)) against temperature for representative poly(lactic acid) samples synthesized according to *method I* (PLA4_mPET, solid lines) and *method II* (PLA25_HDI, hatched lines). The thermomechanical behaviour was evaluated in multifrequency mode to allow an easy identification of polymer α relaxation or glass transition. The thick specimens were cut from PLA films obtained by solvent casting (*vide* chapter 2, section 2.5.11), the lower molecular weight PLA films were fragile and underwent fracture during measurement. Therefore, no reliable viscoelastic results could be obtained through the whole range of temperature. This explains why the samples in Figure 6.12 have the highest molecular weights.

The DMTA patterns in Figure 6.12 are characterized by a steep drop in storage modulus E', associated with an intense relaxation peak in tan δ. This relaxation phenomenon corresponds to the glass-to-rubber state transition, at temperature higher than the glass transition resulted in a rapid loss of the film strength. No other relaxation phenomenon is noticed below α relaxation which may explain the brittleness of glassy PLA. Moreover, the pattern observed for these samples corresponds to the one previously reported for PLA polymers [64, 131-132].

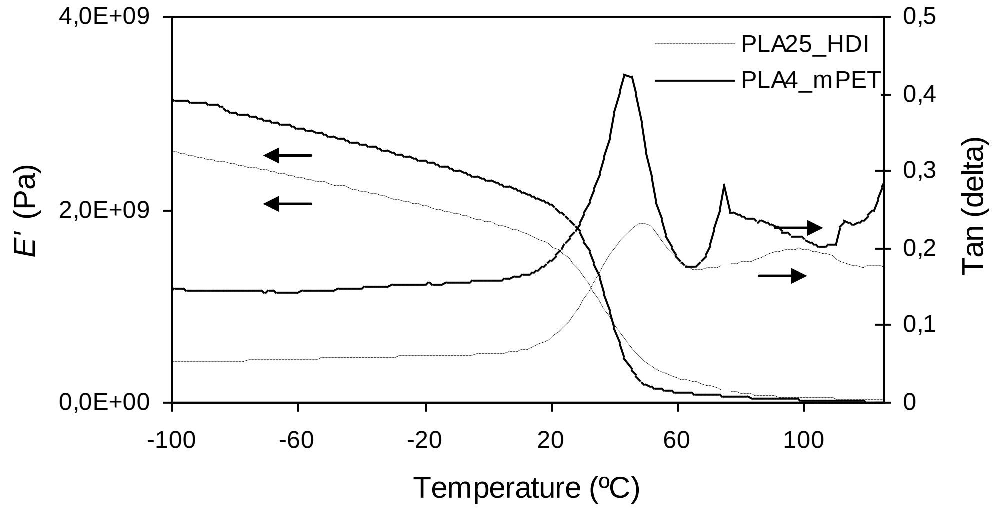

Figure 6.12: Dynamic mechanical traces of PLA4_mPET and PLA25_HDI (1 Hz).

The tan δ peaks of the two samples under consideration in Figure 6.12 show a different shape. PLA25_HDI exhibits a broader peak, whereas PLA4_mPET displays a sharper and more intense peak, showing that a large fraction of the sample was frozen in a glassy amorphous state. This can be explained by the degree of crystallinity. Amorphous polymers are reported to have a very sharp and intense peak because there is no restriction on chain motion, whereas larger crystallinity inhibits chain mobility and reduces the number of polymer chains participating in the glass transition, resulting in the reduction of sharpness and height of the tan δ peak [64, 133-135].

6.5. Preliminary Hydrolytic Degradation

Being poly(lactic acid) an aliphatic polyester, it is susceptible to undergo hydrolysis. Regarding the intended large scale applications as for example in food or beverage packaging, long-term hydrolytic stability is of major importance and was assessed in this study. Hydrolytic behaviour of PLA specimens with 2 mm thickness was studied *in vitro* by immersion in phosphate buffered solution (PBS) (*vide* section 2.5.13), kept at room temperature for predetermined periods of time, at a maximum of three months. The weight loss recorded (%) for representative polymer samples (PLA2_mPET, PLA4_mPET, PLA_triPET and PLA25_HDI) during different degradation periods is plotted in Figure 6.13.

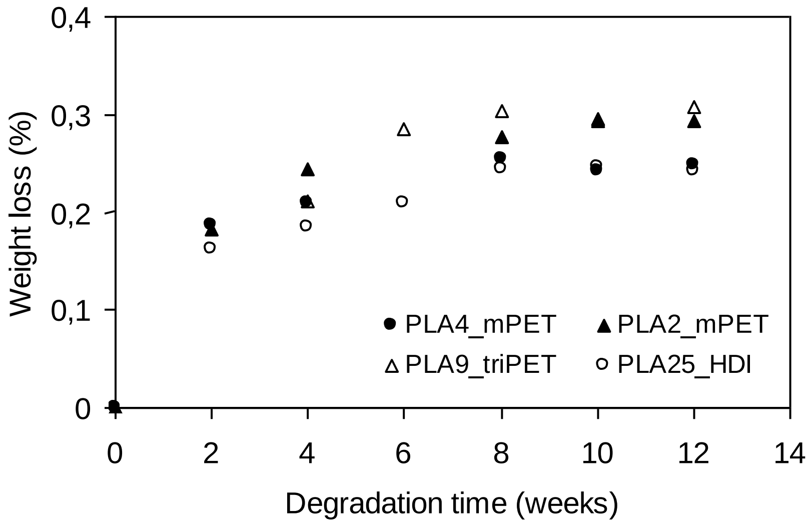

Figure 6.13: Poly(lactic acid) samples weight loss against hydrolysis time in phosphate buffered solutions.

The data presented in Figure 6.13 point out that weight loss was not significant in the time span of the study. After a small weight loss in the early stages further weight loss was not recorded. The diffusion of low molecular weight compounds trapped in the polymer matrix might explain the weight loss, rather than chain scission products. Moreover, PLA films fully preserved its integrity throughout the experiments. The only perceptible change was a decline of transparency due to the development of crystallinity. It is generally recognized that molecular weight and crystallinity degree are crucial factors determining the hydrolytic degradation of biodegradable polyesters, particularly in the initial induction period [136-137]. Indeed, for 60 weeks, no significant weight loss was reported for very high molecular weight amorphous PLA films (*Mw* = 1.1x10^{6} g.mol^{-1}, *Mw/Mn* = 2.0, thickness = 50 μm) [137], whereas at 31 weeks a 4.0 % weight loss was observed for lower molecular weight sample (*Mw* = 1.3x10^{5} g.mol^{-1}, *Mw/Mn* = 1.8, thickness = 2 mm) [138]. Malin *et al.* [139] reported about 10 % weight loss in PLA films after 10 weeks of hydrolytic degradation (*Mw* = 1.15x10^{5} g.mol^{-1}, *Mw/Mn* = 2.3, thickness = 4 mm). Although preliminary, the results clearly suggest that PLA polymers synthesized in this project are able to preserve its long term stability in moisture environments. In order to confirm these results, and to assess the effect of molecular structure on degradation profile, degradation experiments should be carried out at different temperatures (preferable at room temperature, 37 ºC and 60 ºC) and extended to up to two years, till fragmentation. The degraded samples should be fully characterized by gravimetric measurements, SEC, DSC and tensile testing. Hydrolytic profiles of high molecular weight star-shaped PLA were not found in the literature.

The weight loss is an indication of the content of water soluble products (lactic acid, lactide and small oligomers) released from polymer films into the surrounding medium. Lactic Acid is a safe food substance naturally present or added to food, mainly as a flavouring agent and for pH control. In accordance with FDA guidelines, Conn and coworkers [140] performed a polylactide safety assessment where PLA was “Generally Recognized as safe” (GRAS). Although, in this project, the nature of the migrant substances was not identified it seems reasonable to consider that they do not represent a significant risk, since migrating species are expected to ultimately convert into lactic acid, also classified as GRAS.

6.6. Optical Properties of PLA Films

The yellow colour that usually arises in melt phase polycondensations may create a negative consumer perception, particularly in the packaging field. In the industry this problem is overcome by mixing approved food contact blue and/or pink coloured toners [141]. Therefore, measuring standard colour parameters is of major importance in order to formulate suitable correcting toners to produce the desired colour specification. Although hardly reported in academic studies, colour characterization and correction is common practice in polyesters patent literature [141-146]. The colour of PLA cast films and of the commercial polylactide 2002D, were measured using the widespread L* a* b* tristimulus colour system (*vide* chapter 2 section 2.5.14) and the results are compiled in Table 6.3, as well as the colour shift (ΔE*) using the commercial polylactide as reference and the yellowness index (YI).

The results in table 6.3 point out clear differences relatively to the commercial PLA and, between batches, contradictory results were obtained. L* values of almost all samples are higher than that of polylactide 2002D indicating a higher brightness, which is in contrast with visual observations. This may be explained by occurrence of crystallization during the storage period, prior to colour measurements. Chain extended polymers show higher YI values than branched ones, which is attributed to the experimental procedure. During chain linking addition to the reaction vessel, some atmospheric oxygen may have leaked leading to thermal-oxidation and racemisation reactions. This is also corroborated by overall lower optical purities reported in Table 6.2, comparatively to those in Table 6.1. PLA4_mPET sample exhibited the higher YI, which is in agreement with the highest value of b* observed and with the lowest value of L*, as a result of the longer reaction time and consequent thermo-oxidation reactions.

Table 6.3: Optical properties of selected poly(lactic acid) samples and a commercial polylactide, 2002D.

Nº	L*	a*	b*	ΔE*	YI
2002D	73.4	-0.83	0.28	0.00	0.00
PLA2_mPET	74.9	-1.01	0.73	1.34	0.77
PLA4_mPET	71.7	-1.00	2.72	3.16	5.63
PLA6_diPET	74.3	-1.08	0.78	1.09	0.84
PLA9_triPET	74.7	-1.05	0.77	0.79	0.82
PLA24_HDI	74.9	-1.37	1.68	1.88	2.73
PLA25_HDI	79.2	-1.33	1.93	5.74	3.23
PLA30_HDI	74.3	-1.55	2.26	2.17	3.84

The discrepancies between colour shift (ΔE*) and yellowness (YI) are ascribed to the influence of crystallization. Yellowness index in Figure 6.14 is less prone to the crystallization influence since it is a specific parameter for assessing yellowing in plastic films. These experiments were performed mainly to assess the samples yellowness that was hardly or not visually perceptible.

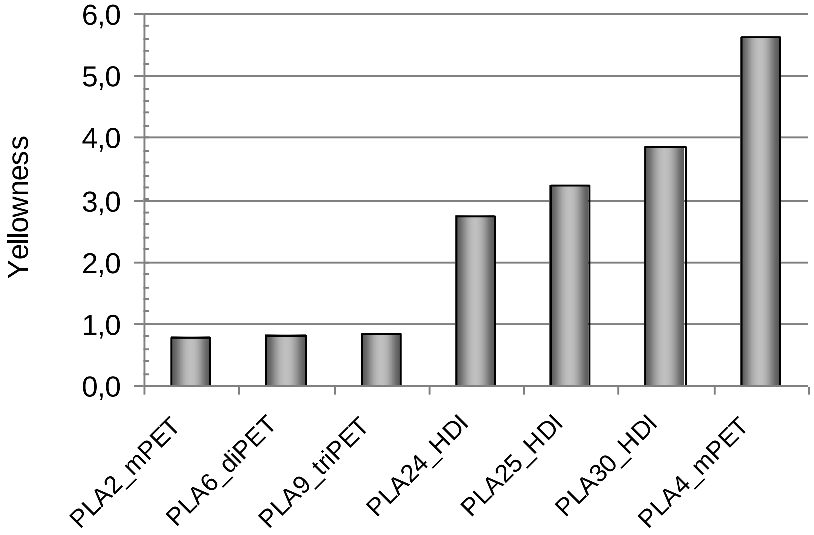

Figure 6.14: Yellowness index of several PLA cast films.

The yellowness index differences recorded shown in the Figure 6.14 are attributed to the yellowish colour and are a strong evidence that PLA obtained by melt polycondensation may require colour compensation. The lack of studies addressing PLA colour compensation renders difficult to draw conclusions from results in Table 6.3. Nevertheless, for PET it was reported that difference in b* values lower than 10 can be compensated [141].

6.7. Conclusion

The best polymerization system and experimental conditions resulting from the melt polycondensation studies were used for assessing two different molecular weight increasing strategies. Branching agents allowed obtaining a star-shaped PLA and chain linking agents linked PLA prepolymers in a predominantly linear arrangement. Poly(lactic acid) polymers with more than 100 000 g.mol^{-1} molecular weight, relatively high optical purity, narrow molecular weight distributions, and quantitative gravimetrical yields were successfully produced

High molecular weight star-shaped PLA was produced using branching co-monomers as central cores. The selection of branching agent proved to control the number of arms and their length and, consequently, the thermal properties and thermal stability of final star-shaped polymers. Compounds containing hydroxyl groups were found particularly good branching agents for lactic acid melt polycondensation. The molecular shape and terminal end groups of the resulting branched polymers were determined by the structure of the comonomer and the chemistry involved.

Modified PLA containing urethane linkages was synthesized by chain extension of a lactic acid prepolymer (≈ 30 000 g.mol^{-1}) previously obtained by melt polycondensation using high reactive linking agents able to react with both hydroxyl and carboxyl PLA end groups. The appropriated amount of chain extender and reaction time allowed obtaining thermoplastic PLA with remarkably high molecular weight or even crosslinked materials. Among the chain extenders studied, aliphatic 1,6-hexamethylene diisocyanate was found to be the most effective. Chain extension of lactic acid prepolymers had been reported, however the conditions affecting polymer properties were not thoroughly investigated. Conversely to the results in the literature, better results were achieved with unmodified chain end prepolymers and semi-crystalline PLA with high degree of crystallinity (≈ 30 %) was produced.

The mechanical performance of the high molecular weight polymers obtained is comparable to that reported for polylactide, irrespectively of polymer structure. Moreover, its hydrolytic stability over a relatively large period of time is another evidence that materials fulfil requirements for large scale applications.

Based on the aforementioned findings, the addition of small amounts of co-monomers proved to be a good way to attain high molecular weight poly(lactic acid) by conventional step-growth polymerization. The Thermal and mechanical properties similar those of the PLA homopolymer were attained, while the synthesis and purification of intermediate products was avoided, achieving the main goal of this research project.

As a final remark it is important to recall that poly(lactic acid) properties should be evaluated according to the intended uses. Among the co-monomers tested, the Commision Directive 2002/72/EC [101] prohibits BADGE in materials intended to come into contact with foodstuffs. Amine, isocyanate and epoxy containing substances have restrictions in the permitted residual quantity in the final material.

6.8. Bibliography

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7. PHOTOCROSSLINKABLE BIOADHESIVES BASED ON LACTIC ACID

7.1. Introduction

Throughout this work, lactic acid based bioadhesives were developed in an attempt to find other potential uses for the lactic acid condensation products, beyond large scale applications, and taking advantage of our research group expertise in the tissue engineering field [1, 2].

The use of bioadhesives for human tissue regeneration as an alternative to suturing has recently increased. Among the advantages, bioadhesives allow a fast and less invasive application and can also be designed for localized drug release, increasing the healing process efficiency. Antibiotic and anti-inflammatory drugs can be incorporated in the adhesive formulation. A suitable bioadhesive must have adequate viscosity prior to application, adhere to the tissue easily, cure rapidly, provide strong closure throughout the healing process and degrade into non-toxic products when no longer necessary [1-4]. Currently approved surgical glues, which are based on fibrin and cyanoacrylates, have been associated with some safety issues. Fibrin presents risk of blood transmitted diseases and cyanoacrylates are reported to degrade into formaldehyde [1-4]. Thus, efforts to develop non-toxic, biodegradable, biocompatible and commercially viable bioadhesives remain relevant.

Several studies [1-5] have already been conducted by other authors trying to develop a bioadhesive that fulfils the previously described requirements. Polymeric materials with photocrosslinkable groups have shown good adhesion results and fast-curing rate at physiological temperature which make them promising materials to be explored in surgical applications. Aliphatic polyesters and its copolymers have arose much interest, mainly because ester bonds are susceptible to hydrolytic and enzymatic degradation under physiological conditions and the resulting products are naturally occurring metabolites. Ferreira e*t al.* 2008 [1] reported the successful modification of commercial polycaprolactone diol with 2-isocyanatoethyl methacrylate followed by photocrosslinking via UV irradiation using a biocompatible photoinitiating agent, Irgacure 2959®. In that work [1], biocompatibility characterization gave promising results. Another biodegradable polyester, approved by FDA and largely used in the medical industry is PLA. It has been largely used in biodegradable sutures, scaffolds, clamps and controlled release devices [3]. However, its use as a bioadhesive has not been thoroughly studied.

Commercial PLA has high molecular weight, high glass transition temperature and low solubility in non-toxic solvents, which prevents its straight use as a tissue adhesive, requiring structure modification or copolymerization to adjust these properties. In 2002 Helminen *et al.* [5] reported the synthesis of star lactide based prepolymers by ring opening polymerization (ROP) in the presence of pentaerythritol as initiator, followed by modification with methacrylic anhydride and further thermal crosslinking at 90 ºC. Nevertheless, the resulting material showed a relatively high glass transition temperature, unsuitable for bioadhesive applications [5]. More recently, Karikari *et al.* 2005 [6] reported the synthesis of a 4-arms star-shaped polylactide end functionalized either with methacrylic anhydride or with 2-isocyanatoethyl methacrylate, and cured by photopolymerization with 2,2-dimethyl-2-phenylacetophenone as the radical photoinitiator. Since the prepolymers' molecular weight were higher than 2 000 g.mol^{-1}, the procedure resulted in a glassy solid at room temperature, and chloroform was used as solvent. As it is well known, chloroform is a very toxic solvent, and therefore a unsuitable formulation. According to the ICH guidelines (The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use) the maximum chloroform content in biomedical materials is set at 60 ppm [7]. Although its synthesis was intended for bioadhesives application, no biocompatibility assessment was reported, the authors [6] focused only on chemical, thermal and mechanical characterization. Ho *et al.* 2006 [8] studied the synthesis of poly(lactide-propylene glycol) dimethacrylate adhesives but, again, biocompatibility was not investigated.

Moreover, ring opening polymerization of lactide, as well as other lactones, requires a tin based catalyst which has been reported as a source of toxicity in brain and nervous tissues and to cause DNA damage [8]. The limit for the residual amount of tin in commercially used medical polymers was set at 20 ppm by the FDA. Common purification techniques by solvent precipitation are not effective to remove tin catalysts since they remain partially coordinated to the polymer end functionalities [9-11]. To overcome this limitation, great attention has been paid to the development of non-toxic initiator and catalyst systems for replacing tin based compounds in lactide ring opening polymerization, ROP. Catalysts based on Fe, Mg, Na, K, and Ca have been presented as suitable alternatives, since they play a role in human metabolism, but the molecular weight achieved remain too low comparing with tin compounds [3, 9, 10, 12, 13].

Based on previous reports [1-6], a new strategy was developed for obtaining lactic acid based adhesives following a three reaction steps approach. Telechelic lactic acid prepolymers with low molecular weight and different architectures, linear and star-shaped, were synthesized by self-condensation, subsequently modified with double bonds and further crosslinked. The resulting films were characterized in order to assess its potential for bioadhesive applications. The low molecular weight oligomers are expected to allow its application as a viscous liquid but also to increase the double bonds density, therefore requiring short curing time [8].

Among the crosslinking methods, photopolymerization has many advantages for biomedical applications, in particular with the development of biocompatible photoinitiators. Photopolymerization allows fast curing rates *in situ* under mild temperature conditions [14]. Therefore it was the technique chosen to successfully accomplish final adhesives, which means with a rapid liquid to solid transition.

7.2. Synthesis of Lactic Acid Based Adhesives

7.2.1. Materials

All materials were purchased from Acros or Sigma-Aldrich and were used without further purification: aqueous solution of L(+)-lactic acid (80 %), 1,4-butanediol (BD) (99 %), pentaerythritol (mPET) (99 %), methacrylic anhydride (MAA) (94 %), 2-isocyanatoethyl methacrylate (IEMA) (98 %), diethyl ether (99 %). Irgacure 2959 (97 - 99 %) was an exception as it was supplied by Ciba, now part of BASF.

7.2.2. Synthesis of Telechelic Prepolymers

Two telechelic prepolymers with OH end groups were synthesized: a linear one and a star-shaped one. Lactic acid solution (100 mL) and co-monomers (1,4-butanediol or pentaerythritol) were introduced into a neck round-bottom glass flask, equipped with a magnetic stirrer and a glass condenser, and were allowed to react at 150 ºC under nitrogen sweep. When the whole water had been removed (around 9h of reaction) the process was stopped and the products were stored for further functionalization. The amount of co-monomers introduced was calculated according to the reaction stoichiometry and the target molecular weights presented in Table 7.1. From now on in this chapter, the linear prepolymer obtained is referred as PLA and the star-shaped prepolymer as StarPLA.

7.2.3. Prepolymers Functionalization

PLA and StarPLA prepolymers were modified with two different compounds containing carbon double bonds: methacrylic anhydride (MAA) and 2-isocyanatoethyl methacrylate (IEMA), involving different experimental procedures as described below.

7.2.3.1. Modification with Methacrylic Anhydride

Methacrylic anhydride was added either to the linear or to the star-shaped prepolymer in the reaction flasks and the reaction allowed to proceed at 130ºC, under stirring and nitrogen stream, overnight. The molar ratio used was 1 mole of MAA per 2 moles of OH end groups, considering that the methacrylic acid resultant from the anhydride reaction also undergoes esterification reaction with the free OH end groups. The functionalized prepolymers thus obtained are further referred as PLA-MAA0 and StarPLA-MAA0, respectively.

7.2.3.2. Modification with 2-Isocyanatoethyl Methacrylate

The amount of 2-isocyanatoethyl methacrylate added to each of the prepolymers was set to fulfil an equimolar ratio to the OH prepolymer end groups. Besides these chemicals, 20 mL of diethyl ether were added to the reaction flasks and the reactions were allowed to proceed at 60ºC, under reflux, stirring and nitrogen atmosphere for 24 h. The functionalized prepolymers synthesized according to this procedure are further referred as PLA-IEMA0 and StarPLA-IEMA0, respectively.

7.2.4. Synthesis of Crosslinked Networks by UV Irradiation

The photoinitiator, in a percentage of 6 % of the double bonds moles, was previously dissolved in 20 mL of diethyl ether, and than added to each of the modified prepolymers at 60 ºC and the mixture was stirred under reflux until obtaining an homogeneous solution. The solutions were poured onto Petri dishes and then irradiated for different periods of time (2 minutes for linear prepolymers and 3 minutes for star-shaped prepolymers) obtaining four well-defined and uniform films. Finally, the films were dried in an oven at 40 ºC to remove the diethyl ether and characterized. The UV lamp used was a Multiband UV UVGL-48 model from Mineral Light.

7.2.5. Characterization

Some characterization techniques further discussed in this chapter, such as DMTA and hydrolytic degradation in phosphate buffered solution, PBS, were previously described in Chapter 2 sections 2.5.9 and 2.5.13, respectively.

7.2.5.1. Attenuated Total Reflectance - Fourier Transform Infrared Spectroscopy (ATR-FTIR)

ATR-FTIR was used for identification of reactions products. The spectra were recorded by a Jasco FT/IR-4200 Spectrometer equipped with a Golden Gate Single Reflection Diamond ATR, at. an average of 128 scans at a resolution of 4 cm^{-1}.

7.2.5.2. Swelling

Dried samples of each crosslinked films were weighted (*Wd*) and placed in a container with a saturated solution of pentahydrate copper sulphate at room temperature [1]. Specimens of each sample were removed and weighted at predetermined times (*Ws*) until maximum weight was achieved. Experiments were carried out in triplicate. The swelling ratio was evaluated using the following equation:

$$\text{Swelling ratio (\%)} = \frac{(Ws - Wd)}{Wd} \times 100 \tag{7.1}$$

7.2.5.3. Cytotoxicity

Cytotoxicity was evaluated by *in vitro* cell culture with human fibroblasts in direct contact with the films. The films' surfaces were first washed by immersion in a culture medium and then placed in tissue culture polystyrene plates. Cells suspended in culture medium were seeded on films surfaces at a density of $3x10^4$ per sample and incubated for 24 h, 48 h and 72 h. Cell viability was assessed by the MTS assay. After adding the MTS solution into each plate the absorbance was measured at 492 nm. Each of the results shown in Figure 7.6 is the mean of three experiments.

7.2.5.4. Scanning Electron Microscopy (SEM)

In order to visualize the surface and cross section morphology of the films, SEM was performed. Samples were placed over a carbon ribbon in an appropriated support and then covered with a gold thin layer. When necessary, films were cooled in liquid nitrogen and then easily fractured. The analyses were carried out in a Scanning Microscope JSM-5310 from Joel.

7.3. Results and Discussion

7.3.1. Bioadhesives Synthesis

The experimental procedure described in the sections above enabled obtaining four different bioadhesive films. Making use of different co-monomers, lactic acid was submitted to thermal dehydration and, afterwards, two distinct functionalization agents (MAA and IEMA) led to different modified prepolymers. These first steps were performed without adding external catalysts and the modified prepolymers showed a viscous oil appearance, with potential for *in situ* injection administration. The content of photoinitiator agent to be added, 6% of the double bonds introduced, was set after preliminary assessment to limit curing time to few minutes.

Irgacure 2959 was found to be rather insoluble in the viscous prepolymers requiring a prior solubilisation in diethyl ether before addition to the prepolymers flask. These four different functionalized prepolymers: PLA-MAA-0, PLA-IEMA-0 StarPLA-MAA-0 and StarPLA-IEMA-0, resulted in four films after UV radiation exposure: two films obtained from linear prepolymers: PLA-MAA and PLA-IEMA and another two from star-shaped precursors: StarPLA-MAA and StarPLA-IEMA.

A schematic representation of the star-shaped prepolymers synthesis, functionalization and curing reactions is shown in Figure 7.1. The reactions involved in the linear and star-shaped prepolymers synthesis are the same. Therefore, the schematic representation for the linear prepolymers is shown in *appendix B.*

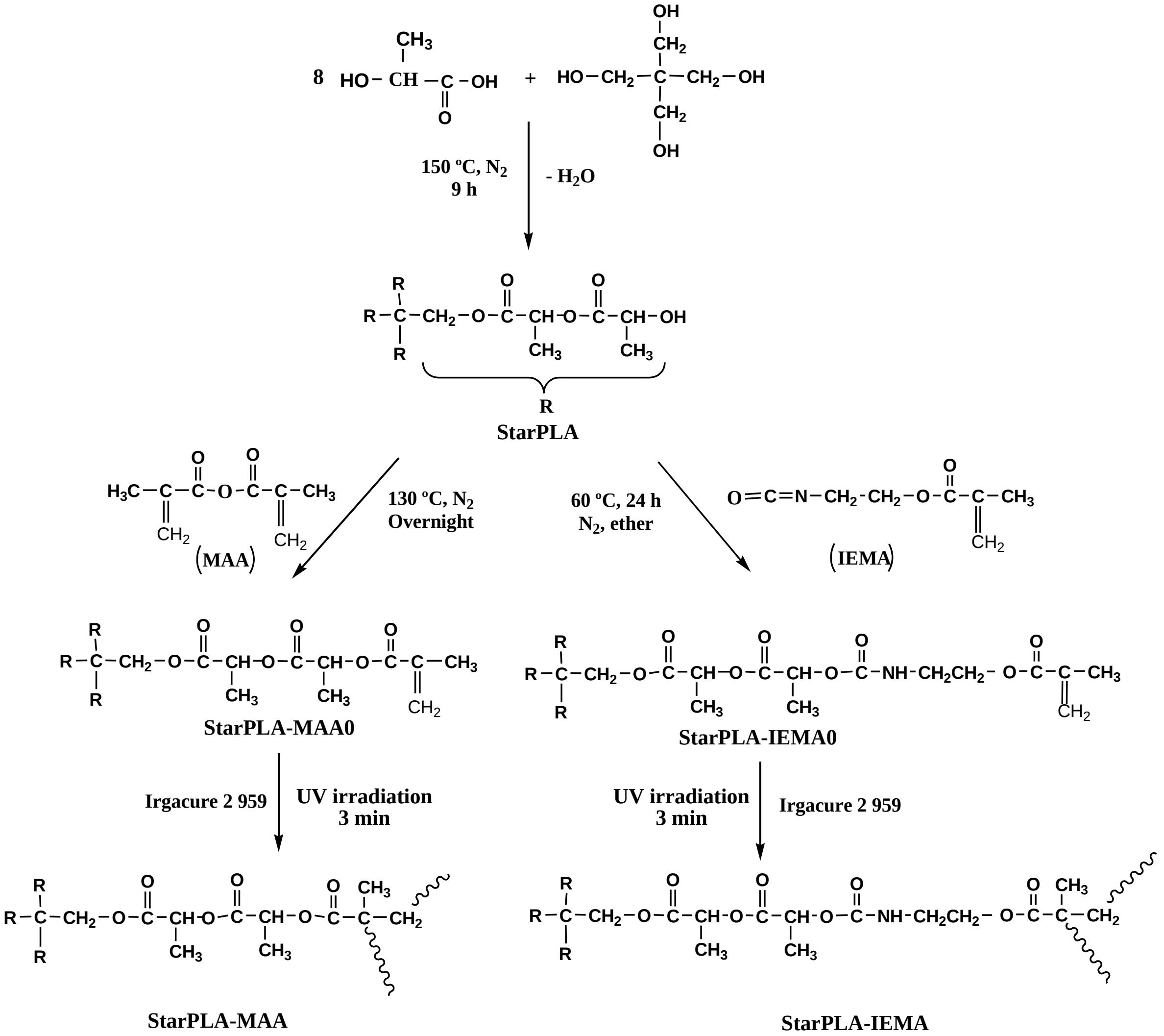

Figure 7.1: Schematic representation of the star-shaped prepolymers synthesis, functionalization and crosslinking reactions.

The information related to the target molecular weight for each prepolymer, the curing time elapsed till obtaining a self-supporting film, the glass transition temperature and water sorption ability of the four films are compiled in Table 7.1.

ATR-FTIR spectroscopy was used to monitor prepolymer synthesis, functionalization and crosslinking reactions. The FTIR spectra in Figure 7.2 show the successful functionalization of the star-shaped prepolymers with MAA and IEMA and its subsequent photocrosslinking. The spectra obtained from linear prepolymers modification are quite similar to those in Figure 7.2, allowing the same conclusions, therefore not shown.

Table 7.1: Characterization of: prepolymers, functionalized prepolymers and photocrosslinked products.

Product	*Mn* target (g.mol^{-1})	Tg_{DMTA} (ºC)	Curing Time (min)	Swelling (%)
PLA	500	-	-	-
PLA-MAA0	654	-	-	-
PLA-IEMA0	810	-	-	-
PLA-MAA	-	1	2	10
PLA-IEMA	-	21	2	4
StarPLA	760	-	-	-
StarPLA-MAA0	1 068	-	-	-
StarPLA-IEMA0	1 380	-	-	-
StarPLA-MAA	-	15	3	29
StarPLA-IEMA	-	11	3	6

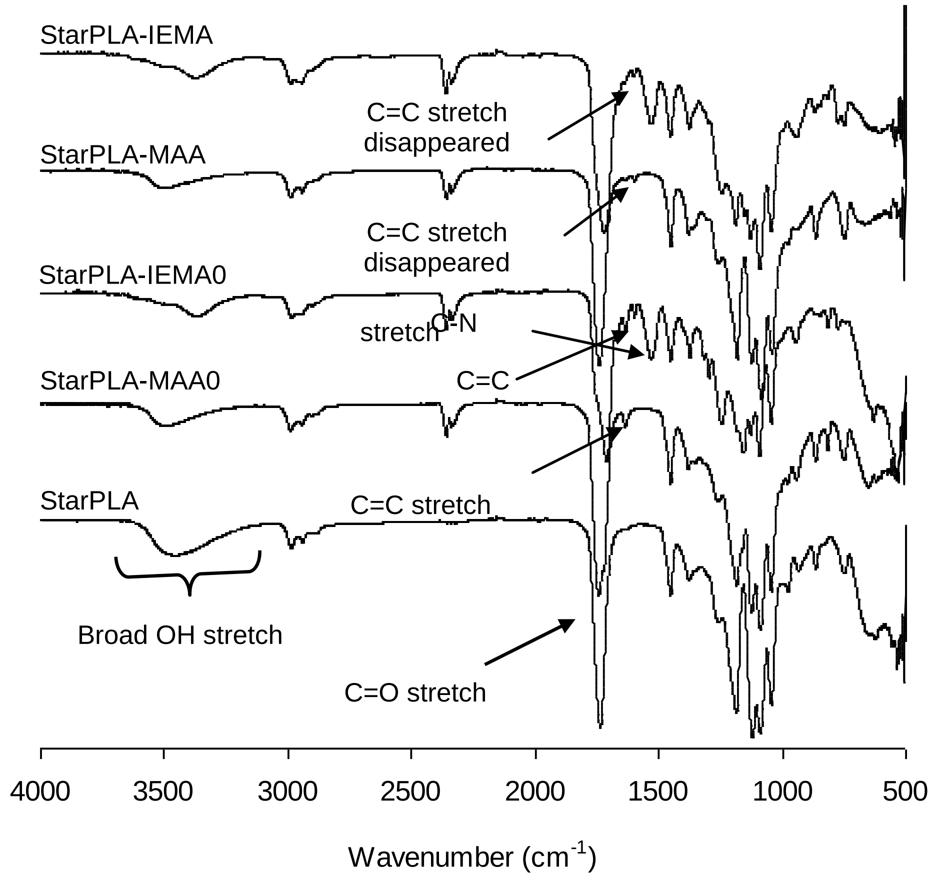

Figure 7.2: ATR-FTIR spectra of the star-shaped PLA prepolymers and their, functionalized and photocrosslinked products.

Carbon double bounds were introduced into the lactic acid prepolymers by reaction of its hydroxyl end groups with MAA and IEMA. The presence of carbon double bonds after functionalization was confirmed by a new band at 1636 cm^{-1} and by the decreasing intensity of the hydroxyl stretching peak at 3460 cm^{-1}. When IEMA was used as functionalizing agent the formation of urethane bonds was identified by the detection of one peak at 3390 cm^{-1} assigned to the NH stretch and another one at 1540 cm^{-1}, which corresponds to the urethane carboxyl absorbance. Peaks matching the free isocyanate groups or the anhydride bonds were not detected in the functionalized prepolymers. After UV irradiation the ATR-FTIR spectra of the bioadhesives show the disappearance of the double stretching peak as a consequence of photocrosslinking.

In this work curing time is the time needed to obtain a well defined and uniform membrane and corresponds to the disappearance of the peak assigned to the double bond in the ATR-FTIR. The linear lactic acid prepolymers required a shorter curing time for effective cosslinking (2 minutes) than that registered for the star-shaped prepolymers (3 minutes).

It is important to underline that in resorbable systems for biological applications a complete conversion of the free isocyanates and double bounds must be accomplished to ensure that potentially reactive and toxic compounds are not released upon degradation.

7.3.2. Thermal Properties

DMTA technique (*vide* section 2.5.9) was selected for identifying the materials glass transition temperature (*Tg*) since it has a higher sensibility to the α-relaxation (glass to rubber transition) than the widespread DSC [6]. The measurements were carried out in the Single Cantilever Bending mode and in multifrequency to allow a ready identification of α-transition. The DMTA traces obtained at 1 Hz are shown in Figure 7.3 and the glass transition temperatures taken from the Tan δ peak at 1 Hz are recorded in Table 7.1. All crosslinked products depict a *Tg* lower than physiological temperature, in the range of 1 to 21 ºC, fulfilling the requirements for the intended purpose. It is worth mentioning that star-shaped prepolymer films exhibit similar glass transition temperatures. Whereas *Tg* obtained from linear prepolymers are very dissimilar, showing a higher influence of the functionalizing co-monomer.

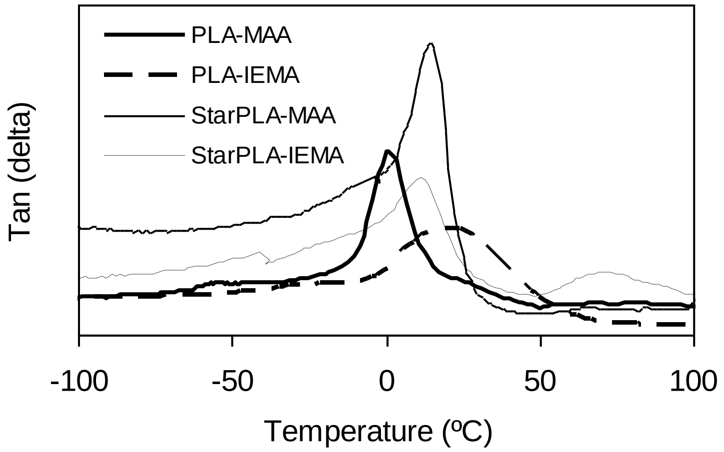

Figure 7.3: Photocrosslinked products Tan δ traces at 1 Hz registered by DMTA.

7.3.4. Swelling Ratio and Hydrolytic Degradation

The results obtained for the hydrolytic degradation of the films, in PBS solutions at 37 ºC, are illustrated in Figure 7.4, clearly showing that crosslinked films preserve its hydrolytic instability, which is fundamental for short-term applications such as bioadhesives. Every sample underwent a substantial weight loss in the first days followed by a slower process in the remaining experiment time. Some of the initial weight loss may be attributed to the release of low molecular weight compounds such as monomer or photoinitiator molecules trapped in the polymer network. Weight loss proved to be strongly dependent on prepolymers structure and on functionalization co-monomers. Films obtained from MAA prepolymers exhibited a faster hydrolytic degradation than the ones obtained from IEMA prepolymers. Comparing films synthesized from different prepolymers architecture, it seems that linear prepolymers impart lower hydrolytic stability than branched ones, which may be related to a lower crosslinking density.

The hydrolytic degradation of PLA in aqueous solution is reported to proceed through random scission of the ester bond [15, 16], being strongly influenced by the swelling behaviour of the polymer matrix. Therefore, hydrolytic degradation should be closely related to the swelling ability reported in Table 7.1. Similar to the hydrolytic degradation results, films previously functionalized with MAA depicted a much higher water absorption capacity than the ones functionalized with IEMA. Films obtained from branched prepolymers also showed higher swelling ratio, for instance the highest swelling ratio, 29 %, in Table 7.1 correspond to the StarPLA-MAA. Since the polymer swelling is followed by volume increasing, damage of the surrounding tissues may be observed when placed *in vivo* [1].

Therefore, such a high swelling ratio and consequent volume increasing may put at risk its use as bioadhesive.

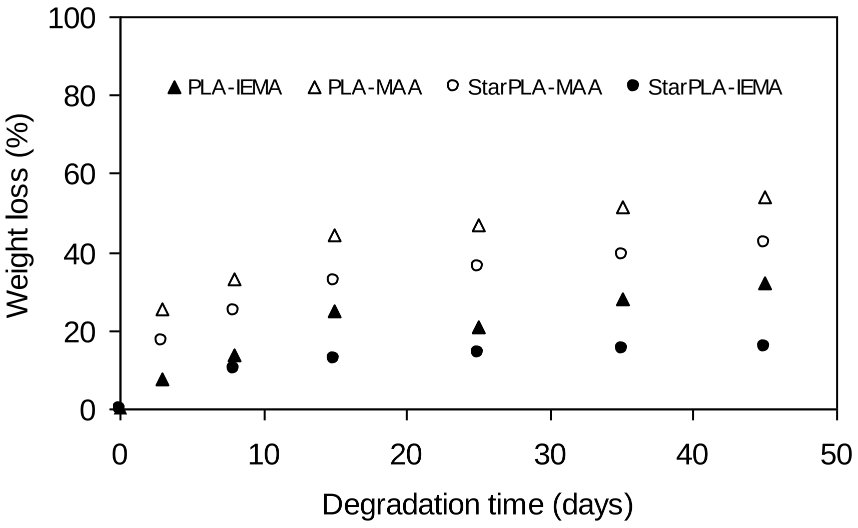

Figure 7.4: Bioadhesives weight loss against hydrolysis time, in PBS solutions at 37 ºC.

The results obtained highlight that the incorporation of urethane linkages in the prepolymers terminals hinders water absorption and hydrolysis. This finding may be related to a higher hydrophobicity or to the occurrence of some urethane hydrogen bond interactions [6].

7.3.5. Scanning Electron Microscopy (SEM)

The SEM technique was chosen to provide an insight into the morphology of the films obtained. As visible in Figure 7.5 (a) and (c), films obtained from branched prepolymers show a very compact structure and no significant differences were noticed regardless the functionalizing co-monomers used for crosslinking. Similar observations were registered for the films obtained from linear prepolymers.

The samples undergoing *in vitro* hydrolytic degradation were also characterized by SEM after 45 days in PBS solutions. Figure 7.5 (b) and (d) show that no differences were perceptible in the inner cross sections after degradation. Since considerable weight losses were recorded after 45 days degradation, particularly for the StarPLA-MAA sample, one can assume that, under these conditions, the dominant hydrolytic degradation mechanism was surface erosion. This finding is further confirmed by observing what seems to be the degraded surface of the StarPLA-MAA sample, Figure 7.5 (b). Similar degradation behaviour was previously reported for crosslinked poly(ester anhydrides) based on poly(ε-caprolactone) oligomers [17].

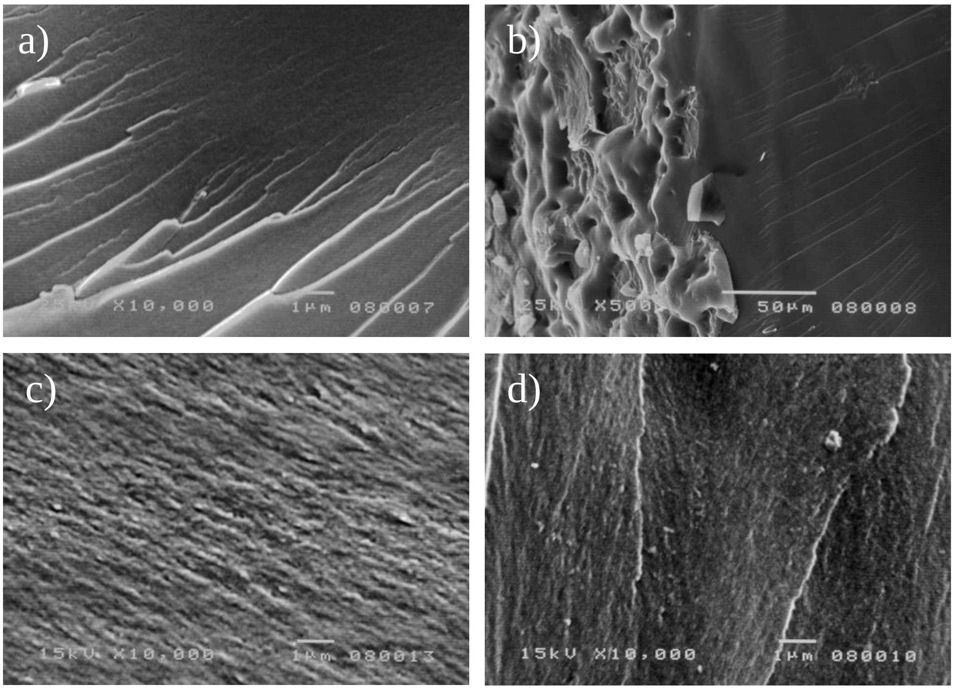

Figure 7.5: SEM images obtained for the cross section of the films: a) StarPLA-MAA as synthesized; b) StarPLA-MAA after 45 days of hydrolytic degradation; c) StarPLA-IEMA as synthesized and d) StarPLA-IEMA after 45 days of hydrolytic degradation.

7.3.6. Cytotoxicity

The preparation of cell compatible materials is extremely important in view of its application in tissue regeneration. Therefore, biocompatibility of the films was assessed by their cytotoxic potential. Cytotoxicity of the potential tissue adhesives was evaluated by cells adhesion, proliferation and viability in direct contact with films surface. Fibroblasts were chosen for these experiments since they are involved in the healing process. Figure 7.6 displays the cellular activity measured by the MTS assay after 24, 48 and 72 hours incubating in contact with the material.

MTS assay is a colorimetric test to measure cellular metabolic activity, therefore indicating cellular proliferation. Living cells can metabolize MTS producing formazan, a purple dye, which leads to a coloured solution. The absorbance of this coloured solution is measured in a spectrophotometer, at the wavelength of 490-500 nm [18]. In other words, higher values of absorbance reflect higher cell viability and proliferation.

Comparing the samples results to the negative control they show an overall good biocompatibility *in vitro* with no significant cytotoxic effect. However, there are visible differences mainly regarding the functionalizing co-monomer. Generally, films obtained from prepolymers functionalized with MAA display better biocompatibility than those synthesized with IEMA, since the last ones showed cytotoxic effect at 72 h incubating. PLA-MAA film, obtained from linear prepolymer functionalized with MAA, showed enhanced proliferation results throughout the incubation periods. Cells adhered and proliferated on the PLA-MAA film surface during 24 and 48 h of incubation. After that period, a decrease in the cellular viability was registered at 72 h however, remaining, higher than the negative control. This decrease may be ascribed to the accumulation of acidic degradation products since PLA-MAA film was the one with the fastest hydrolytic degradation, as shown in Figure 7.4.

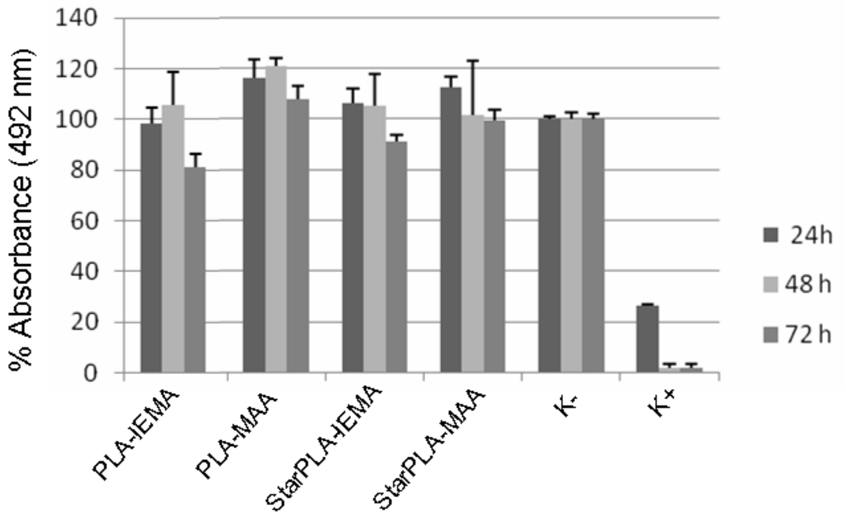

Figure 7.6: Cellular activities measured by the MTS assay after 24, 48 and 72 hours in contact with the materials: K^-, negative control, K^+, positive control.

Among the biomaterial properties, hydrophilicity/hydrophobicity balance is a key aspect controlling interactions with cells. It has been reported that cells adhere, spread and grow easier on surfaces with moderate hydrophilicity rather than on those highly hydrophilic or hydrophobic, regardless of the cell type tested [19], which is the case for PLA-MAA sample according to its 10 % swelling ratio. Consistently, PLA-IEMA film showed the lowest swelling ratio, only 4 %, and also the worst of all cellular activities.

7.4. Conclusion

A new strategy to synthesize potential bioadhesives based on lactic acid was developed. Lactic acid oligomers were obtained by direct esterification, then carbon double bonds were introduced into the OH terminal groups, and finally curing was achieved by photopolymerization in the presence of a biocompatible photoinitiator. The influence of precursor molecular architecture, linear and star-shaped, and end group functionalization, MAA or IEMA, was investigated.

The curing time required to obtaining well defined films and the resulting glass transition temperatures were considered acceptable for the intended application and all the films preserved its hydrolytic instability. However, significant differences were registered in the swelling ratio, hydrolytic degradation and even in its cytotoxicity.

Films obtained from prepolymers functionalized with MAA showed higher swelling ratio, faster degradation and also enhanced biocompatibility in the presence of human fibroblasts than IEMA functionalized bioadhesives. In particular, the film resulting from the linear PLA-MAA prepolymer showed moderated swelling ratio and enhanced cells proliferation during the test period and may be envisaged as a promising new material for further studies in tissue engineering.

7.5. Bibliography

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8. RELATED WORKS

Some products obtained in the course of this project were supplied to other research projects that were being carried out simultaneously at CIEPQPF. A brief description of three very different projects is here presented.

L-Lactic acid oligomers with increasing size obtained at different stages of L-lactic acid thermal dehydration were studied by Doctor Susana Jarmelo to determine the conformation preferentially adopted by PLLA homopolymer chains. A thorough investigation based on three different contributions: density functional theory (DFT) for energetic calculations, and NMR and vibrational spectroscopies of these small L-lactic acid oligomers was carried out. The study confirmed that, making use of computational chemistry, complex systems, such as polymers, can be explained using quite small models. In this particular case, data from a small molecule such as the L-lactic acid pentamer was enough to simulate the structural and spectroscopic properties of PLLA homopolymer [1].

It is worth mentioning that providing the lactic acid based materials, after a discussion about the intended application, was the main contribution to the following research studies.

Branched PLA terminated with carboxyl end groups were blended with commercial polycaprolactone (PCL) to develop a nanomembrane by electrospinning. Enzymes are to be immobilized in this membrane and the whole system used in biotechnological processes. This approach to increase PCL membrane functionalization was more efficient than conventional surface modification with plasma or UV radiation followed by further copolymerization with acrylic monomers containing free functional groups. The resulting membrane showed good mechanical resistance, higher hydrophilicity and better enzyme carrier function [2].

A relatively low molecular weight PLA, around 30 000 $g.mol^{-1}$, was tested by Florbela Rouxinol to develop new drug delivery systems for the treatment of ophthalmologic diseases. Two active substances, vancomycin, an antibiotic, and Avastin®, an antibody, were encapsulated in PLA nanoparticles reaching encapsulation efficiency above 95 %. Controlled release studies and cellular viability assays were performed *in vitro*. Vancomycin loaded nanoparticles showed a very interesting delivery rate, within 15 days [3].

The research works briefly described above, underline a broad diversity of uses for the materials synthesized under the scope of this project.

References:

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9. EPILOGUE

9.1. Concluding Remarks

An intensive study on poly(lactic acid), PLA, synthesis by conventional step-growth polymerization approaches was carried out in the frame of this work. This included: lactic acid solution polycondensation, lactic acid esters melt polytransesterification and lactic acid melt polycondensation. The polymer samples were characterized in order to identify the best polymerization conditions for PLA production.

Although encouraging, the results of melt polytransesterification of lactic acid esters did not enable reaching very high molecular weight polymers. Moreover, racemization reactions influenced polymer crystallinity and other properties. Nevertheless the relevance of the catalytic system upon polytransesterification was confirmed and $Sb_2O_3/Zn(O_2CCH_3)_2.2H_2O$ was found the most efficient one.

Among the three routes tested for PLA production, direct lactic acid melt polycondensation was selected for further studies since it allowed a much faster and greener process than solution polycondensation. In addition, free functional end groups in the monomer and in the final polymer allow different strategies for accomplishing effective molecular weight increase. The failure to attain a high molecular weight polymer by melt phase step-growth polymerization of the monomer is attributed to the competitive depolymerization reactions favoured by high temperature and long reaction time and to limitations on by-product elimination due to increasing melt viscosity. Initial monomer distillation followed by melt polycondensation for 12 h, at 190 ºC, under vacuum enabled minimizing undesirable side reactions, improve by-product removal and increase reaction yield.

High molecular weight PLA, above 100 000 $g.mol^{-1}$, with different structures, was successfully synthesized by lactic acid melt polycondensation using different co-monomers. High molecular weight star-shaped PLA was obtained by performing melt polycondensation in the presence of branching co-monomers. Predominantly linear PLA was synthesized by chain extension of PLA prepolymers, using highly reactive chain linking co-monomers. The influence of the molecular weight increasing approach upon the final polymer properties was investigated. Besides evaluating the molecular weight distribution, performing thermal characterization and measuring optical rotation, the general-purpose suitability of the polymers was further assessed by mechanical characterization, L* a* b* colour system evaluation and preliminary log-term hydrolytic degradation studies, affording promising results.

Chain extension and branching are common practice in industrial scale melt polycondensation processes, such as in PET and in PBSs production, forecasting they may be feasible and economic routes for the synthesis of lactic acid based polymers for commercial use. The yellowing of the final polymer, frequent in melt phase processes, when critical may also be minimized using highly pure nitrogen or an effective thermal stabilizer, such as triphenylphosphine. Alternatively or additionally, colour correction using a suitable pigment formulation may also be employed.

The main achievements and conclusions of this research study are as follows:

1. High molecular weight star-shaped PLA, up to 8 arms, was successfully synthesized using branching co-monomers during melt polycondensation. Depending on the starting co-monomer functionalities, star-shaped PLA with free carboxyl or hydroxyl end groups was obtained. Multifunctional co-monomers containing hydroxyl groups such as pentaerythritol, dipentaerythritol and tripentaerythritol were found particular effective for the synthesis of star-shaped PLA with controlled molecular weight and controlled number of arms.

2. Chain extension of hydroxyl and carboxyl terminated PLA prepolymers were achieved by means of highly reactive chain extenders. Starting with a 32 000 g.mol^{-1} prepolymer, a 4.5 fold molecular weight enhancement was achieved with 1,6-hexamehylene diisocyanate as chain linking co-monomer. The coupling efficiency was limited by crosslinking reactions when higher chain extender contents were assessed. Although chain extension of PLA had been reported previously, the strategy developed here led to semi-crystalline polymers, avoiding prepolymer end group modification, since isocyanates are effective hydroxyl and carboxyl chain extenders.

3. Lactic acid melt polycondensation is a simple and versatile polymerization mechanism, which enables the production of PLA based polymers with controlled molecular weight and different molecular architectures, ranging from linear and branched thermoplastics to networks. The structure, the molecular weight and

therefore the properties of the synthesized polymers can be readily varied by changing the types and ratio of co-monomers.

9.2. Further Research Topics

Following the promising results obtained in this project a number of possible research lines may be recommended as future challenges. These include:

- Developing mathematical models describing the lactic acid melt polycondensation kinetics, including the side reactions.
- Studying the process scale-up using a melt polycondensation reactor followed by a melt extruder.
- Developing new materials such as composites, foams or lactic acid based copolymers for a number of different applications, using renewable co-monomers.
- Deepen polymer characterization by evaluating additional mechanical properties, barrier properties and crystallization kinetics.
- Finishing the hydrolytic degradation assessment by complementing with molecular weight measurements and DSC analysis. Study PLA degradation by compostability including evaluating the toxic potential of the end products.

Besides the list presented above, that could be easily extended, the processability and yellowing of the materials obtained should be thoroughly assessed to complement the study and assess the materials usefulness for large scale applications.

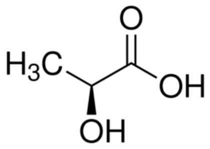
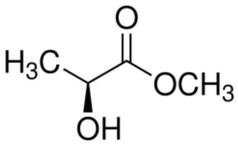
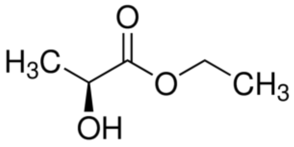
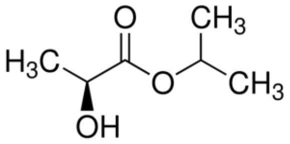
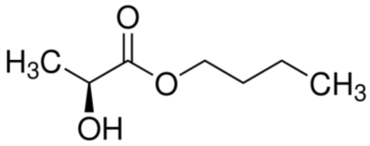
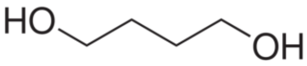
For better understanding the influence of reaction conditions (time, pressure, temperature, catalyst, nitrogen and/or thermal stabilizer) on the yellowing phenomenon, and to what extent yellowing could be limited, further experiments would have to be carried out. A critical combination of operating conditions could be based on design of experiments techniques.

Colour correction studies would allow determining the suitable L* a* b* limits at the end of melt polycondensation, to avoid colour compensation or, alternatively, the values permitting colour correction.

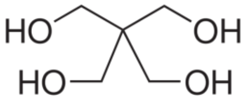
Melt rheology is also relevant to assess the material processability and the influence of branching and chain extension of the polymer backbone. It is important to keep in mind that, during processing, hydrolysis of the polymer and further thermo-oxidation reactions are expected, therefore melt stabilization may be required.

APPENDIX A

Table I: Properties and chemical structures of monomers and comonomers.

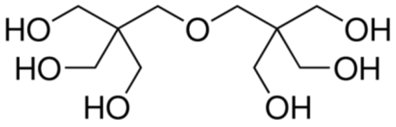
Properties	Chemical Structure
(S)-2-Hydroxypropionic acid or L-(+)-Lactic acid Molecular Weight: 90.08 g.mol-1 Boiling point: 122° C at 12 mmHg Melting point: 53° C Density (80% solution): 1.209 g.mL-1	
Methyl L-lactate Molecular Weight: 104.10 g.mol-1 Boiling point: 144 - 145 ºC Melting point: - Density: 1.092 g.mL-1	
Ethyl L-lactate Molecular Weight: 118.13 g.mol-1 Boiling point: 151 - 155 ºC Melting point: -26 ºC Density: 1.03 g.mL-1	
isoPropyl L-lactate Molecular Weight: 132.16 g.mol-1 Boiling point: 166 - 168 ºC Melting point: - Density: 0.988 g.mL-1	
Butyl L-lactate Molecular Weight: 146.18 g.mol-1 Boiling point: 183 - 190 ºC Melting point: - Density: 0.981 g.mL-1	
1,4-Butanediol Molecular Weight: 90.12 g.mol-1 Boiling point: 230 ºC Melting point: 16 ºC Density: 1.0171 g.mL-1	

Pentaerythritol



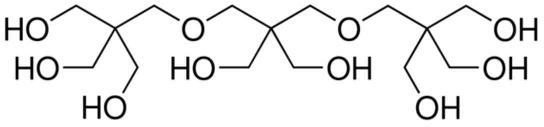
Molecular Weight: 136.15 g.mol-1
Boiling point: 276 °C at 30 mmHg
Melting point: 253 - 258 °C

Dipentaerythritol



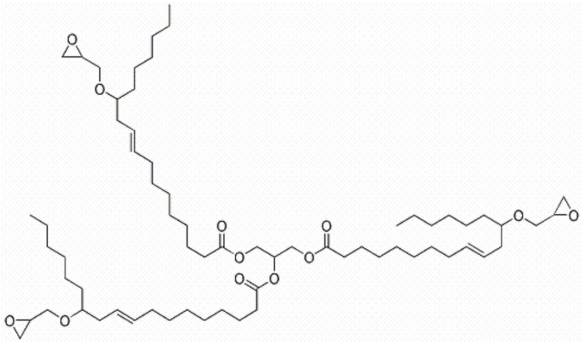
Molecular Weight: 254.28 g.mol-1
Boiling point: -
Melting point: 215 - 218 °C

Tripentaerythritol



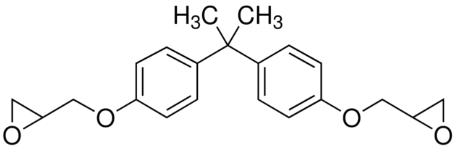
Molecular Weight: 372.41 g.mol-1
Boiling point: -
Melting point: 225 °C

Castor oil glycidyl ether



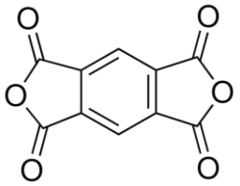
Molecular Weight: 1101.62 g.mol-1
Boiling point: -
Melting point: -
Density: 1.02 g.mL-1

Bisphenol A diglycidyl ether



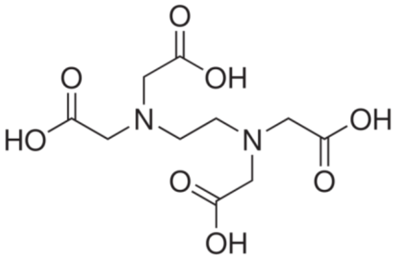
Molecular Weight: 340.41 g.mol-1
Boiling point: -
Melting point: 40 - 44 ºC

Pyromellitic dianhydride



Molecular Weight: 218.12 g.mol-1
Boiling point: 397 - 400 °C
Melting point: 283-286 °C

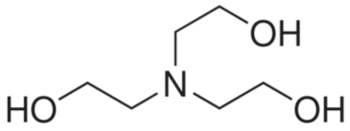
Ethylenediaminetetraacetic acid



Molecular Weight: 292.24 g.mol-1
Boiling point:-
Melting point: 250 °C

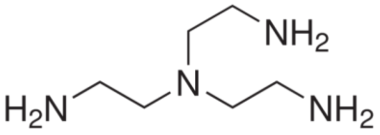
Triethanolamine

Molecular Weight: 149.19 g.mol-1
Boiling point: 335 ºC
Melting point: 22 ºC
Density: 1.124 g.mL-1



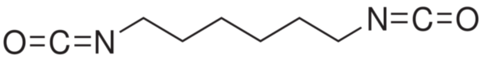
Tris(2-aminoethyl)amine

Molecular Weight: 146.23 g.mol-1
Boiling point: 114 °C at 15 mmHg
Melting point: - 16 ºC
Density: 0.976 g.mL-1



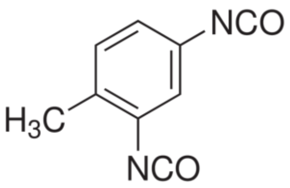
Hexamethylene diisocyanate

Molecular Weight: 168.19 g.mol-1
Boiling point: 255 ºC
Melting point:-
Density: 1.047 g.mL-1



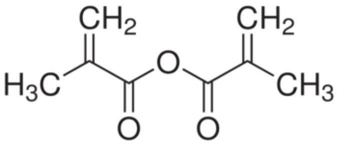
Toluene 2,4-diisocyanate

Molecular Weight: 174.16 g.mol-1
Boiling point: 251 ºC
Melting point: 19.5 - 21.5 °C
Density: 1.21 g.mL-1



Methacrylic anhydride

Molecular Weight: 154.16 g.mol-1
Boiling point: 87 °C at 13 mmHg
Melting point:-
Density: 1.035 g.mL-1



2-isocyanatoethyl methacrylate

Molecular Weight: 155.15 g.mol-1
Boiling point: 211 ºC
Melting point: - 45 ºC
Density: 1.098 g.mL-1

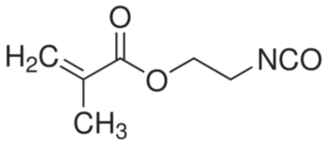
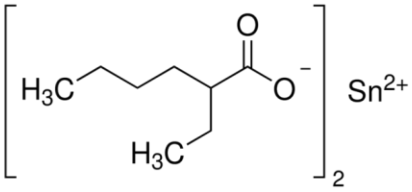
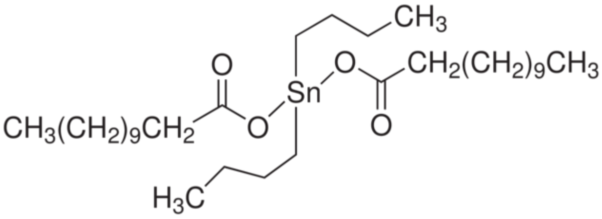
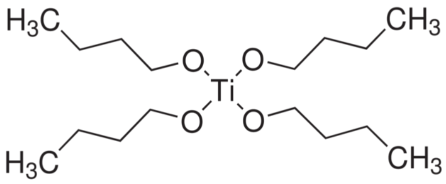


Table II: Properties and chemical structures of catalysts and phoinitiator.

Properties	**Chemical Structure**
M Tin (II) chloride dehydrate Molecular Weight: 225.65 g.mol-1 Boiling point: 652 °C Melting point: 37 - 38 °C	$SnCl_2 \bullet 2H_2O$
Tin(II) 2-ethylhexanoate or tin (II) octoate Molecular Weight: 405.12 g.mol-1 Boiling point: - Melting point: - Density: 1.251 g.mL-1	
Tin (II) oxide Molecular Weight: 134.71 g.mol-1 Boiling point: - Melting point: -	SnO
Tin (IV) oxide Molecular Weight: 140.71 g.mol-1 Boiling point: - Melting point: -	SnO
Dibutyltin dilaurate Molecular Weight: 631.56 g.mol-1 Boiling point: - Melting point: - Density: 1.0661 g.mL-1	
Tin Molecular Weight: 118.71 g.mol-1 Boiling point: - Melting point: 177.3 - 231.9 °C	Sn
Antimony (III) oxide Molecular Weight: 291.52 g.mol-1 Boiling point: 1550 ºC Melting point: 655 ºC	Sb_2O_3

Titanium (IV) butoxide

Molecular Weight: 340.32 g.mol-1
Boiling point: -
Melting point: -



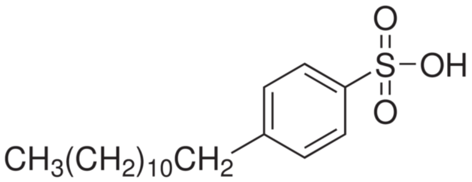
Titanium (IV) butoxide

Molecular Weight: 79.87 g.mol-1
Boiling point: -
Melting point: -

TiO_2

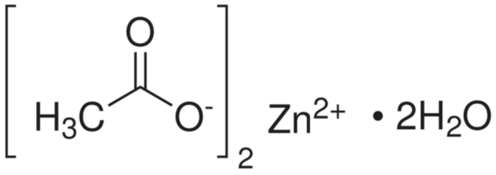
4-Dodecylbenzenesulfonic acid

Molecular Weight: 326.49 g.mol-1
Boiling point: -
Melting point: -
Density: 1.06 g.mL-1



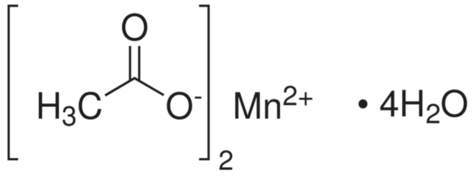
Zinc acetate dehydrate

Molecular Weight: 219.51 g.mol-1
Boiling point: -
Melting point: -



Manganese(II) acetate tetrahydrate

Molecular Weight: 245.09 g.mol-1
Boiling point: -
Melting point: -



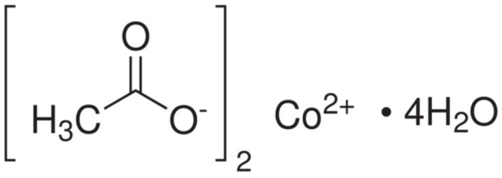
Zinc oxide

Molecular Weight: 81.39 g.mol-1
Boiling point: -
Melting point: -

ZnO

Cobalt acetate tetrahydrate

Molecular Weight: 249.08 g.mol-1
Boiling point: -
Melting point: -



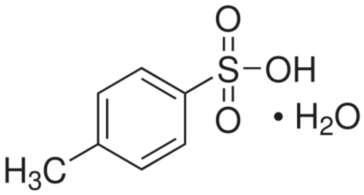
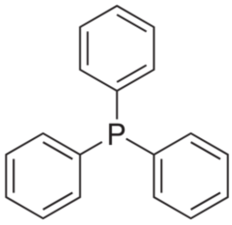
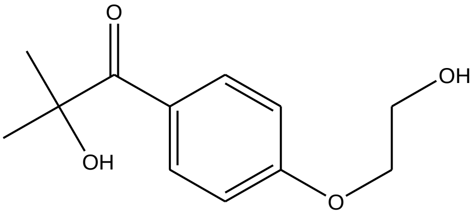
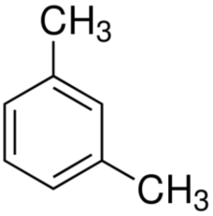
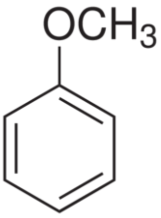
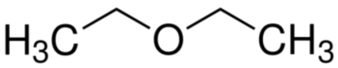
p-Toluenesulphonic acid monohydrate Molecular Weight: 190.92 g.mol-1 Boiling point: - Melting point: -	
Triphenylphosphine Molecular Weight: 262.29 g.mol-1 Boiling point: 377 °C Melting point: 79-81 °C	
4-(2-hydroxyethoxy)phenyl-(2-hydroxy-2-propyl)ketone or Irgacure 2959 Molecular Weight: 224.3 g.mol-1 Boiling point: - Melting point: 86.5 - 89.5°C	

Table III: Properties and chemical structures of the solvents.

Properties	**Chemical Structure**
m-Xylene Molecular Weight: 106.17 g.mol-1 Boiling point: 138 - 139 °C Melting point: -	
Anisole Molecular Weight: 108.14 g.mol-1 Boiling point: 154 °C Melting point: -	
Chloroform Molecular Weight: 119.38 g.mol-1 Boiling point: 61 °C Melting point: -	$CHCl_3$
Diethyl ether Molecular Weight: 74.12 g.mol-1 Boiling point: 35 °C Melting point: -	

APPENDIX B

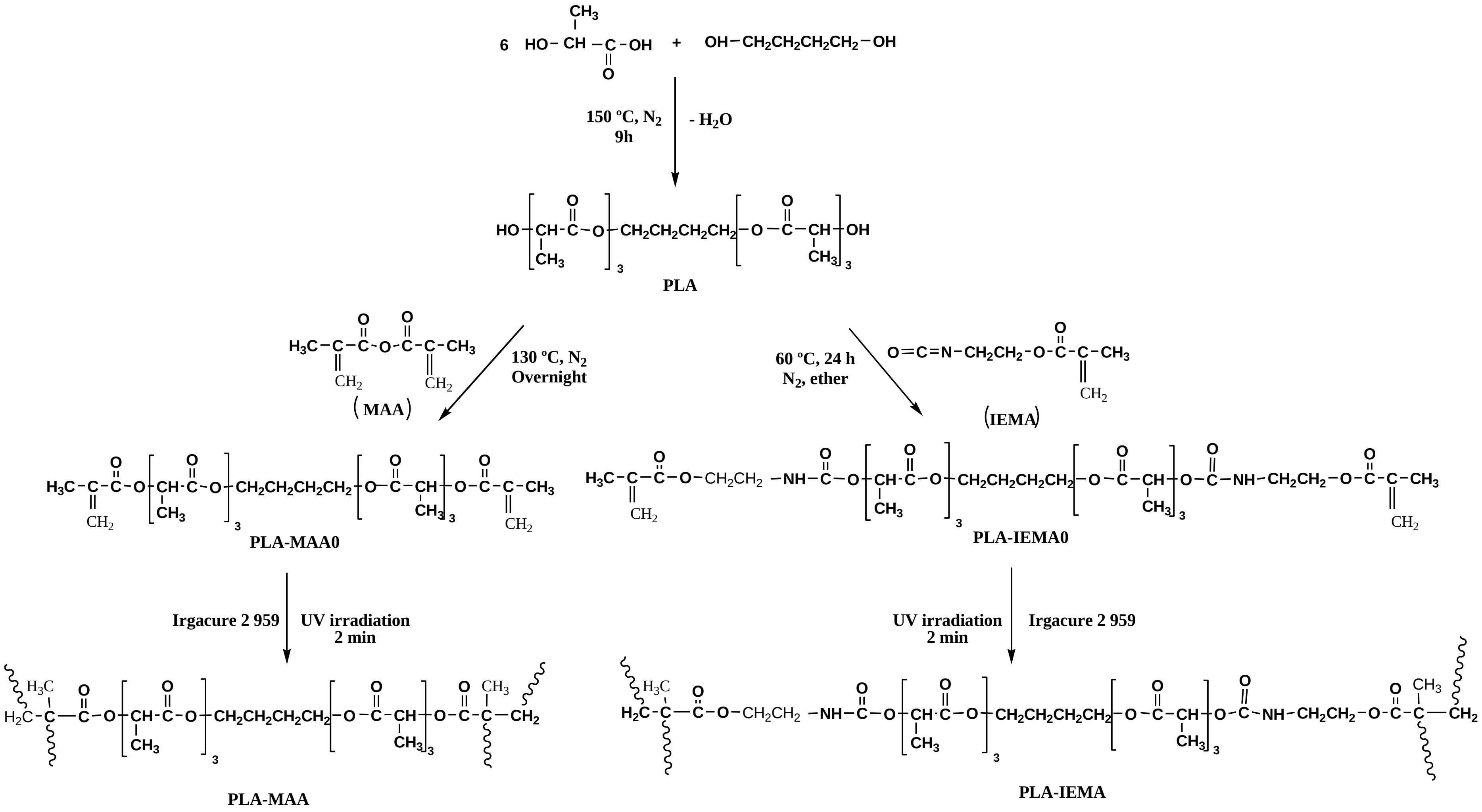


Figure I: Schematic representation of the linear prepolymers synthesis, functionalization and crosslinking reactions.