Ring-opening polymerization of non-ionic eutectic mixtures for the synthesis of macroporous polyesters by emulsion templating
Castillo Santillan, Martin

DOI:
10.33612/diss.865369463

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2024

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Chapter 1

Facile and green alternative route to obtain polylactides and polylactones by the ROP of eutectic mixtures composed of lactide/lactones

This section provides the state-of-the-art for understanding the experimental work done in this thesis. The chapter started with an introduction to polymers and a variety of their applications, including their production around the world, as well as the environmental and health issues that are driving the present situation. Subsequently, the introduction of polylactides and polylactones, which are biodegradable polyesters, are described. The current production of polylactides and polylactones in industry, e.g., by bulk and by ring-opening polymerization (ROP), is also described. This process excludes the use of solvents, albeit it depends on the use of metal catalysts. In this chapter, an understanding of eutectic blends, and previous research on polyester production and applications of DESm are summarized. Finally, the challenges of synthesizing these polyesters using DESm are discussed.
1.1 Polymers and plastics sustainability

Polymers are macromolecules formed by the union of many smaller molecules called monomers. The reaction by which polymers are obtained is called polymerization. A single polymer can be composed of hundreds or thousands of monomers. Polymers are generally used as plastics, rubber, fibers, coatings, adhesives, foams, and films and have been widely used in all aspects of our society. Today, polymers have been designed with high quality and versatility, which has given us comfort and well-being. In addition, due to the ease of production and the enabled properties, such as durability, strength, and light weight, they have been applied in areas that have been limiting for other materials.

The words plastics and polymers are often used interchangeably. The word ‘Plastics’ comes from Latin or Greek words suggesting ‘able to be molded’. In practice, the word ‘plastics’ tends to be used only in the plural by people in the industry to avoid confusion with the adjective ‘plastic’ used to describe permanent changes of shape or ‘plastic deformation’ that can occur in any material. Additionally, ‘plastics’ commonly refer to commercial materials containing not only polymer macromolecules but also additives such as colorants, stabilizers, flow modifiers and other chemicals needed to produce stable commercial materials.

In parallel with petrochemical industry growth and progress in technological development, the demand for polymers is enormous, reaching 368 million metric tons in 2019, and is expected to grow to a total of 1.1 billion metric tons by 2050. In 2017 it was reported that there are 60,000 different plastic formulations and that just six polymer groups account for 90% of total plastic production: polypropylene (PP), high-density and low-density polyethylene (PE), polyethylene terephthalate (PET), polyvinyl chloride (PVC), polystyrene (PS), and polyurethanes (PU). The majority of these plastics are obtained from petroleum-based resources and are also single-use, i.e., once they have fulfilled their purpose, they are disposed of, and this represents losses of 95% of the materials, which are valued at between 80,000 and 120,000 million dollars annually. The increasing consumption of crude oil has an impact on its market price, which is also another issue that has generated considerable concern.
Fossil resources will be rapidly depleted within several hundred years; in parallel to their use as energy, their consumption in the polymer industry poses serious environmental concerns. Moreover, environmental concerns in polymer production are increasing, e.g., the use of toxic chemicals, such as metal catalysts and additives. Organic solvents are also typically used as auxiliaries in polymer production; they account for an estimated 80% of the total chemicals used in polymer synthesis, the vast majority of which are volatile and toxic.

The durability characteristics are intrinsic properties of polymers; most of them have a long period of degradation or decomposition. In 2003, plastics represented a large part of domestic and industrial waste (10-30%). Numerous forms of plastic waste have been found in the ecosystem, including their microscale fragments (microplastics). In addition to environmental pollution, microplastic waste is also known to have a negative impact on human health. The handling of plastic waste disposal has not been properly managed for many decades, and there are no appropriate end-of-life strategies for plastics. In a substantial majority of countries, the prevalent method of plastic disposal involves depositing plastic waste in landfills, leading to significant adverse environmental impact, and oftentimes, their capacity is insufficient to handle the increasing waste; and their capacity is insufficient. As a result, plastic waste is found in freshwater reservoirs, representing 57% of the total debris. Global plastic production exhibits a recycling rate of only 9%, while approximately 12% of the produced plastic undergoes incineration. Adverse health and environmental effects caused by the current production model of commercial polymers have triggered the demand for more environmentally friendly alternatives and formulations. Therefore, in recent decades, many efforts and studies have been performed on biodegradable, biobased polymers and greener polymer production.

1.2 Biodegradable polymers

Biobased polymers are those obtained from renewable resources or biomass. It is worth noting that not all plastics obtained from natural resources are biodegradable. Plastics themselves can be split into two categories: petroleum-derived and biobased plastics. However, a limited number of them are biodegradable. (See Figure 1).
Bioplastics, as defined by the official European Bioplastics industry association, encompass plastics that are either biobased, biodegradable, or both. Biobased plastics are derived from renewable biomass sources, while biodegradable plastics have the ability to break down through microbial action under specific conditions. Categorizing bioplastics based on their biobased or biodegradable properties is crucial for understanding their characteristics and environmental impact.\(^6\)

Bioplastics are a promising alternative to petroleum-derived plastics, possessing comparable properties that have the potential to reduce environmental impact by diverting challenging-to-degrade single-use plastic waste. However, the biodegradability of bioplastics, while beneficial for addressing plastic pollution, introduces complexities. Variability in biodegradation efficiency and uniformity across diverse environments may lead to incomplete degradation and the release of harmful byproducts. Therefore, maximizing the environmental benefits of biodegradable bioplastics requires meticulous consideration of their inherent characteristics and appropriate disposal strategies. Currently, bioplastics only account for 1% of the 370 million tons of total plastics generated.\(^21\) By 2025, however, annual growth rates of bioplastics are expected to be approximately 30%.\(^8,17\)

Figure 1. General classification of plastics (petroleum and biobased plastics).\(^20\) Polyethylene terephthalate (PET), polyethylene (PE), polypropylene (PP), polystyrene (PS), polycaprolactone (PCL), polybutylene succinate (PBS), polylactide (PLA).
Some bioplastics, as well biodegradable or compostable polymers, have the ability to degrade in CO₂, water, or biomass due to the action of microorganisms, whereas a specific amount of mass loss needs to be observed in a specific short-term and under specific conditions. Efforts have been made to enhance the production of biodegradable and compostable polymers in order to mitigate the environmental impact of plastic materials, and some of them are in growing demand as alternatives and have reached a stage of development where they offer nearly the same technical properties as plastics of fossil origin. However, despite its advantages, there are still some drawbacks associated with this material. One of the main concerns is its limited mechanical strength, which can make it less suitable for certain applications. Additionally, the use of non-degradable additives to enhance its properties is also a point of concern, as it can contribute to environmental issues.

Hence, the applications of biodegradable polymers still have limitations in being implemented for widespread use. In addition, biodegradable polymers have not yet been widely enhanced because of the lack of large-scale manufacturing and, in some cases, the high production cost compared to the production of fossil-based plastics. Moreover, technical limitations in their manufacturing often cause low production yields. Nevertheless, there are continuous efforts by academia and industry to overcome these shortcomings. Most biodegradable polymers comprise urethanes, orthoesters, carbonates, anhydrides, amides, and polyesters, as detailed below. The degradation mechanisms of polyesters, for example, are due to the susceptibility to hydrolyze the ester bond.

### 1.3 Polyesters

Polyesters are considered alternative to certain plastics since some of them are biodegradable or compostable. In addition, some polyesters are recyclable; thus, they offer a sustainability advantage in terms of low environmental impact after their disposal. The annual polyester production was estimated at 57.1 million tons in 2020 and is classified into two major groups according to their source of origin: natural and synthetic. Polyesters can also be classified as thermoplastics and thermosetting resins, and based on their monomer structure, polyesters can be classified as either aliphatic, aromatic, or semi-aromatic. The versatility of the properties presented in polyesters depends upon the type of monomers used in their synthesis.
Aliphatic polyesters have a linear chain structure and, for example, are mostly readily biodegradable and have poor mechanical properties. Furthermore, some aliphatic polyesters can be produced from biobased monomers, such as polylactic acid.\textsuperscript{32} In comparison to aliphatic polyesters, aromatic polyesters usually possess better mechanical and thermal properties. The incorporation of aromatic structures can improve mechanical properties but also impact their biodegradability.\textsuperscript{27} The general structure and example of polyesters are depicted in Figure 2. Some examples of polyesters are polyethylene terephthalate, polylactides, and polylactones, which account for 60\% of the overall plastic demand in Europe.\textsuperscript{27}

In general, there are two polymerization methods to synthesize them: polycondensation and ring-opening polymerization (ROP).\textsuperscript{33} Polycondensation is a common method used in industries; however, extreme conditions such as high temperatures above 150 °C, low pressures, long polymerization times, and metallic catalysts are often needed. Other drawbacks are the reaction's reversibility, which can reduce the yield, and the possibility of monomer evaporation.\textsuperscript{33} ROP is preferable due to the greater control obtained in the distribution and molecular weight of the product, fast polymerization time with fewer presence of byproducts. ROP synthesis is typically performed in several steps with metallic catalysts and generated cyclic oligomers as side reactions. Polylactides and polycaprolactone are polyesters that can be synthesized by ROP.\textsuperscript{34}

![Polyester structures](image)

Figure 2. (Left) General chemical structures of aliphatic and aromatic polyesters. (Right) Chemical structure of lactide isomers and lactones.
1.3.1 Polylactides

Polylactide is a biobased, biocompatible, and compostable plastic that has been widely studied. Polylactic acid (PLA) use in direct contact with food has been approved by the U.S. Food and Drug Administration (FDA). Their properties, such as innocuity and biocompatibility, enable it to be used in biomedical applications. PLA is the most extensively produced biopolymer and is mostly used for packaging, as well as other applications such as toys, automotive, construction, electronics, and agriculture. PLA’s properties can be similar to those of commercial petroleum-based polymers such as polyethylene terephthalate (PET) and polystyrene (PS). In addition to its versatile properties, PLA is widely used due to its lower price compared to other biodegradable polymers. However, despite their wide use in modern society, PLA still has some shortcomings to be used as materials, such as brittleness and fragility, and the price is high compared with traditional commodity plastics.

PLA holds a 13.9% share of the bioplastic market, which is projected to increase in production. In 2019, PLA production was reported at approximately 290,000 tons, while in 2024, it is expected to increase to 317,000 tons. PLA is produced from lactic acid, which is obtained through the fermentation of renewable feedstock such as rice, corn, and potato. PLA can be generally produced by two polymerization mechanisms: polycondensation and ring-opening polymerization (ROP). Although polycondensation is a simple and low-cost method, the yields and molecular weights are usually low and require extensive removal of water due to the occurrence of a reversible reaction. Conversely, the production of PLA by ROP has better processing control, and the molecular weights of the product obtained are higher in comparison to polycondensation, although it requires additional reaction steps, catalyst and higher temperatures. PLAs are typically produced from the ROP of lactide, of which there are three distinct optical isomers: L-, D- and meso-lactide (L-LA, D-LA and meso-LA, respectively) (See Figure 2). Hence, distinct homopolymer and copolymer structures of PLA can be obtained, such as poly(L-lactide) [PLLA], poly(D-lactide) [PDLA], or poly(L-co-D-lactide) [PLDLA]. The thermal, mechanical, processing and degradation properties of the resulting PLA also rely on the stereochemical sequence in their chains.
1.3.2 Polylactones

Polycaprolactone (PCL) is a hydrophobic and biodegradable polymer with adequate mechanical strength and flexibility for many applications related to the biomedical field. PCL can be obtained from the polymerization of ε-caprolactone (ε-CL), a cyclic monomer (See Figure 2). PCL is a biocompatible polymer, and it has been widely used for some medical applications, as certified by the (FDA) and marked by the European Community. The viscoelastic and mechanical properties of PCL make it a perfect candidate for use in packaging, coatings, adhesives, textiles, and other areas. PCL degradation occurs through to the ester bonds that can be cleaved by hydrolysis under physiological temperature. The biodegradable features of PCL have drawn attention, and over the last decades, their fields of application have diversified. For example, combining PCL with other biopolymers is a way to improve the properties and enhance the sustainability features, providing that the biocompatibility and biodegradability are maintained; PCL blendings with PLA, for example, improve their toughness. Copolymerization of ε-caprolactone (ε-CL) with different lactide isomers allows polymers with different crystallinities, mechanical properties, and degradability profiles to be obtained. PCL is typically synthesized via bulk ROP of ε-CL using ionic and metal catalysts, where the mechanism of ROP proceeds depending upon the initiator/catalyst employed. Secondary reactions usually occur during syntheses by ROP, such as transesterification, loss of reaction control, and polydispersity. Such reactions are avoided by using tin or aluminum metal-based catalysts, which are widely employed in the industry to produce PCL.

Other cyclic monomers, such as hexadecalactone, δ-valerolactone (see Figure 2), and ω-pentadecalactone, can be polymerized to obtain polylactones, which exhibit similar behavior and mechanical properties to low-density polyethylene glycol. Poly-(δ-valerolactone) [PVL], a member of the lactone family, is a biodegradable polymer that, similar to PCL, has also been used in biomedical applications. PVL possesses low mechanical strength, reduced gas permeability, solvent resistance, and degradation profile, which could be useful in other areas similar than PCL or in packaging applications. PVL is obtained from the lactone monomer with 5 methyl groups, namely, δ-valerolactone, via ROP.
1.4 Industrial production of PLLA, PCL, and PVL

1.4.1 Industrial production of PLLA

There are two mechanisms by which PLLA is produced in the industry: polycondensation and ROP. Although polycondensation appears to be the simplest, the throughput is relatively low, the mechanical properties are weak, and its application is limited. Another problem with polycondensation is the high cost of purification.\textsuperscript{28} ROP of lactide is the route preferred by the industry since it provides better control in the molecular weight dispersion of PLA and results in high molecular weights. ROP catalyzed by sulfonic acid compounds generally offers high reactivity and selectivity and low product racemization.\textsuperscript{51} ROP of lactide is also carried out using anionic and cationic catalysts, and the reaction is generally carried out under solution conditions. However, there are some drawbacks, such as the toxicity of the catalysts as well as the reaction sensitivity to the presence of impurities.\textsuperscript{51} Tin-based catalysts are the most common catalyst type used for ROP of lactide in the industry.\textsuperscript{38,52} This reaction typically yields a high molecular weight PLA with conversions of approximately 90% and low racemization. ROP of lactide can also be carried out at temperatures below 100 °C using tin octoate as an organocatalyst and tetrahydrofuran (THF) as the solvent.\textsuperscript{46} Tin octoate is approved for food and medical applications by the FDA; however, its presence in trace amounts could compromise the corresponding bio-related applications. Therefore, their complete removal is necessary, or at least the concentration in the final product should be less than 10 ppm. For this purpose, they are usually deactivated and extracted from molten polyesters by using aggressive chemicals such as phosphoric acid or acetic anhydride.\textsuperscript{28}

1.4.2 Industrial production of PCL and PVL

Similar to PLLA, lactones polymerization via ring-opening polymerization (ROP) are favored over polycondensation polymerization due to offer better control, which yields products with narrow polydispersity and high molecular weight. Typically, this can be achieved by tuning the molar ratio of the monomer and the initiator.\textsuperscript{33,53} The initiator and catalyst are the drivers that lead the mechanism of the reaction, either via coordination-insertion or complexation-monomer mechanisms.\textsuperscript{33,44}
In industry, polylactones are usually produced in a solvent-free process, with metal catalysts at temperatures between 120-200 °C. Tin derivatives and aluminum alkoxides are two of the most commonly used catalysts for this reaction. Tin-based catalysts are known to perform very well in controlling and obtaining high molecular weight polylactones.44

Twin-screw extruders have also been used in the industry to produce polylactones, and ROP can be performed through the appropriate selection of monomers and temperatures. The synthesis of polymers and their extrusion is carried out in a continuous process, which shortens costs and polymerization time and provides high conversions. Nevertheless, in some cases, high temperatures cause secondary reactions such as transesterifications. The most widely used metal catalysts are aluminum alkoxides and titanium alkoxides, which are capable of polymerizing ε-CL. However, tin octoate does not allow reaching a PCL with high molecular weight due to the longer polymerization time required in the extruder. Alternatively, polymerization of ε-CL has been carried out at lower temperatures using aluminum-based catalysts in tetrahydrofuran at 80 °C.

1.5 Organocatalysts in polyester synthesis

Aluminum alkoxide or tin-based metal catalysts are typically used in ROP of polylactones and polylactides, these catalysts have excellent thermal stability and offer good control of the dispersion or molecular weight of the final products. Tin-based catalysts allow the reaction to proceed in a relatively short time with high yields. However, the use of these metal-based catalysts has raised some environmental and health concerns, and removal of the metal residues in the final products is challenging. Also, the complexity of removing the remaining catalyst increase the cost of processing. In addition, the use of metal catalysts can compromise the polymer’s applicability and create new environmental problems at the end of the polymer’s lifetime. The toxicity of metals or organometallic catalyst residues also remains a concern for a certain specialized polymeric products, for example, in medical or electrical applications.
Additionally, concerns have emerged in the polymer industry due to the forthcoming regulations that limit the use of tin-based catalysts. The restrictions to the use of metal catalysts have stimulated the exploration of other (nontoxic) alternative catalysts. Considerable research emphasis is being focused on the use of green catalysts, such as enzymes and organocatalysts. Enzymes and organocatalysts have been reported to catalyze ROP, providing metal-free routes for polyester synthesis. However, to date, enzyme catalysis still has some disadvantages, such as a slow polymerization rate, high cost, and less control of the final polymer properties. Organocatalysts, on the other hand, have become a powerful method for diverse polymerization routes due to their versatility and easy recovery.

Organocatalysts have several attractive properties, such as good control and high selectivity in polymerizations, accessibility, and compatibility with several functional groups and monomer structures. Organocatalysts are small organic molecules whose activity can be electrophilic or nucleophilic. Polymer syntheses using organocatalysts include those obtained via ROP, step-growth polymerization, and controlled radical polymerization. Henrick and Waymouth pioneered the organocatalyzed ROP of lactones using N-heterocyclic carbenes. In addition, acids have been studied as organocatalysts; for instance, trifluoromethanesulfonic acids proved highly effective in polymerizing lactides via ROP, which was faster and more controlled. Hoashi, Y. et al. reported a dual organocatalyst combination of amines with thiourea for obtaining polylactides. In general, the organocatalysts used in ROP are classified into two main groups: organic bases and organic acids. Phosphazenes, N-heterocyclic carbenes, pyridines, thioureas/amines, guanidines, and amidines are included in the organic bases category. For example, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) is an amidine organocatalyst that is able to catalyze L-lactide polymerization. Sulfonic acids, trifluoromethanesulfonic acid, benzoic acid, and phosphonic acid are examples of acid organocatalysts. Herein, methanesulfonic acid was reported to have excellent control in the ROP of ε-CL.
Despite the advantages that organocatalysts offer, their use in industry is still limited, this is because the typical industrial synthesis of polymers such as PET, polyamides, polyurethane, or polyurethanes is normally conducted in the temperature range of 100-300 °C. While most organocatalysts are quite volatile and subject to thermal decomposition.

Organocatalyst poor thermal stability leads to their degradation during bulk polymerization and remains as an attractive issue to be addressed for future research (see Figure 3). Recently, it was reported that acid and basic organocatalyst combinations retain their catalytic performance and are capable of enduring the high temperature of polymerization. Acids such as phosphonic and sulfonic acid, act as proton carriers for basic oxygen atoms while bases, such as pyridines and guanidine, play the role of a hydrogen bond acceptor. This dual catalyst system has been demonstrated to be stable at temperatures above 400 °C, due to the hydrogen-bond.

Examples of bifunctional organocatalyst systems include sparteine/thiourea, N,N(-dimethylamino)/pyridine, diphenyl phosphate/4-dimethylaminopyridine, imidazole/trifluoroacetic acid, 4-dimethylaminopyridine, and methanesulfonic acid, which have been reported as catalysts for the ROP of lactide. It is noteworthy that the latter allowed the polymerization of ε-CL with high control in the absence of side reactions. Similarly, the ROP of ε-CL was also reported by using a combination of sulfonic acids and their conjugated bases, urea, and thiourea, or guanidine-methanesulfonic acid. These dual acid-base system organocatalysts proved to be efficient systems with reasonable control and, in some cases, prevent side reactions. However, they still have some drawbacks for industrial applications, such as their commercial availability (e.g., alkyl urea) and high cost, which prevents their potential scale-up.
The efficiency and versatility of the organocatalysts, together with their facile elimination from the final products, aid in enhancing the green character of the synthesis of biodegradable and biocompatible polymers. To prevent organocatalysts thermal degradation during polymerization, it is recommended to develop a dual-system organocatalysts. Another alternative approach is using organocatalysts at low reaction temperatures and in the presence of organic solvents. For example, ROP of L-lactide (LLA) was catalyzed by triazabicyclodecene, or phosphazene-thiourea/urea at room temperature in CH₂Cl₂. However, the use of chlorinated organic solvents is known to causing an environmental problem. Thus, the development of new alternatives for producing polyesters via environmentally friendly routes remains a crucial challenge to be addressed. Therefore, the search for alternatives to volatile organic solvents, high temperatures, and the use of metal-base catalysts in the ROP to produce polyesters will be addressed in this work with the aid of deep eutectic system (DESs).

1.6 Family of green solvents as alternative for polymerizations

1.6.1 Deep eutectic solvent (DES)

Many of the most useful organic solvents in chemical laboratories and industries are volatile, flammable, toxic, and hazardous. They are associated with potentially serious health problems and concerns regarding the safety of handling them and the appropriate use of these chemicals. Volatile organic solvents are derived from petroleum feedstock and are widely used in chemical synthesis processes such as extraction, purification, and cleaning.
In addition, there is a potentially serious environmental impact on polymer production due to the organic solvents used in synthesis and processing, which are primarily responsible for the largest generation of waste in the polymer industry. Thus, there is an increased awareness from academia as well as industry to pursue new routes for more sustainable solvent alternatives, for example, water, glycerol, ionic liquids (ILs), low-transition temperature mixtures, CO₂ tunable solvents, bioderived lignin solvents from oil, and dihydrolevoglucosenone (Cyreneᵀᴹ). However, some of these alternatives have certain limitations in terms of solute dissolution or processes that require a vacuum and temperatures above 100 °C, toxicity in the long term, and price.

In this context, systems known as "deep eutectic solvents" (DESs), more generally deep eutectic systems, have emerged as a new family of green solvents as potential alternatives for replacing traditional organic solvents in biotechnology, chemical, and materials sciences. DES are promising candidates for the substitution of the approximately 600 existing volatile organic compounds (VOCs). A DES is defined as a mixture of different compounds with no reaction between them, which results in a decrease in the freezing point of the final system in comparison with the melting points of the pure compounds. Usually, the compounds are in the solid state, but this is not necessary; the final system is in the liquid phase under operating temperatures. DESs were first reported by Abbott et al., who first coined the term to refer to binary mixtures of crystalline urea \((T_m \approx 133 \, ^\circ C\), acting as hydrogen bond donor (HBD)), and choline chloride salt \((T_m \approx 302 \, ^\circ C\), acting as a hydrogen acceptor, (HBA)), at a 2:1 molar ratio composition, which possessed a freezing point of 12 °C. As mentioned before, the resulting DES mixture has a lower melting point in comparison with the melting point of the constituents. The decrease in the melting point is due to the self-associative intermolecular interactions between the components, likely driven by the entropy, van der Waals interactions, hydrogen bonding, and ionic bonding interactions. DES are typically clear viscous liquids with varying colors from white to amber to cloudy, they are usually in the liquid phase at room temperature, and their melting point is generally below 100 °C. Properties such as low to negligible vapor pressure, good chemical and thermal stability, and ionic conductivity (when composed of salts) are characteristics of DESs.
Contrary to ionic liquids (ILs), DESs are relatively cheaper and therefore more viable for application on a larger production scale. Another advantage of DESs over ILs is that they tend to be easier to prepare, i.e., the most common method is by simple stirring and heating. The preparation of DES is dependent on several factors, including the equipment's limitations and the water content. Alternative methods of DES synthesis include grinding and mixing until a clear liquid is obtained, evaporation and freeze-drying of solutions with DES counterparts. The starting materials for DESs are typically inexpensive and ubiquitous, but more sophisticated HBDs and HBAs are growing for new applications. Furthermore, their synthesis is sustainable, and nearly 100% atom economy can be achieved in most cases. Purity of DES often only depends on the purity of the starting components, i.e., generally, there are no byproducts. DES can be recycled, from which the respective solvent components can be recovered. They can be considered nontoxic since many of their constituent precursors are nontoxic, although recent concerns have arisen about toxic effects due to acidification and eutrophication of wastewater. To date, the choline/urea combination is the most studied DES. Choline chloride (ChCl) is a component of vitamin B and is currently produced on a scale of megatons per year as a livestock feed supplement, while urea is commonly used in fertilizers. Even though the constituent components are considered safe, DES cytotoxicity still needs to be further evaluated. Since the initial reports on the principle behind eutectic mixture formation, the research area has broadened, now involving a wide range of novel components. The large diversity of the constituents to produce DES systems is estimated in the range from $10^6$ to $10^8$ possible binary combinations. Currently, DES systems exhibit an unusually large solvation capacity, and because of their tunable composition, they may include either ionic or nonionic compounds.

In general, depending on their compositions, DES can be classified as types I, II, III and IV. Types I and II combine relevant Lewis acids, such as quaternary ammonium base, phosphonium, or sulfonium salts, with their counterparts Lewis bases, such as a metal chloride and a hydrated metal chloride, respectively. Whereas type III encompasses the most extensively studied DESs, they consist of a quaternary ammonium salt and its counterpart, a hydrogen bond donor (HBD), such as alcohols, amines, amides, and carboxylic acids.
Type IV DES comprises a hydrate metal chloride and HBD.^{100} Recently, a new class named type V was reported and consists of nonionic components. Hydrogen bonds are particularly predominant in all types of DESs (See Figure 4).^{101} The composition of DESs has expanded to include mixtures such as natural deep eutectic solvents (NADES),^{102,103} whose components include derivatives of renewable and/or biological raw materials, low-transition-temperature mixtures (LTTM),^{89} or even aqueous dilutions of DES.^{84}

![Figure 4. Classification of Deep Eutectic Solvents](image)

DES are typically chemically and thermally stable, however some undesirable reactions during their preparation were reported in literatures, like thermal degradation,^{104} or certain reactivity between their constituents such as the formation of ester groups when the DES are mixtures of carboxylic acids and bases or alcohols.^{105} Furthermore, DES typically possesses a very high viscosity compared to traditional solvents, up to 100 times higher.^{106} This may be considered a significant drawback in regard to handling or dissolution, but pose interesting properties for gels and other topics.^{106}

High viscosity results in reduced mobility of molecules and thus hinders the dissolution of compounds, but water addition has solved these problems while also enhancing the ionic conductivity. DESs are in general hydrophilic, therefore the presence of water may be helpful or hampering the applications where viscosity or conductivity is important.^{107}
DES has been applied in various fields, with much ongoing investigation in areas such as nanoparticle synthesis,\textsuperscript{106} metallurgy and electrodeposition,\textsuperscript{107} gas separation and capture,\textsuperscript{108} metallic carbon dioxide fixation,\textsuperscript{109} energy systems, and battery technologies,\textsuperscript{110} biocatalysts and organic chemistry,\textsuperscript{109} biomass processing,\textsuperscript{111} genomics,\textsuperscript{112} and production of polymers which is the focus of the next section.

### 1.7 Polymerization in DES

DESs can be used in polymer synthesis and may replace conventional organic solvents as well as enables reaction conditions that may not be possible in organic solvents e.g., reaction with vacuum and temperatures above 100 °C, electrochemical deposition, catalysis, or dissolution of resilient biomass.\textsuperscript{113} The first polymerization using a eutectic mixture was reported in 1985, where the electrochemical synthesis of polyanilines was obtained by oxidation of aniline in a eutectic mixture with NH\textsubscript{4}F in different acid or salt solutions.\textsuperscript{114} DES applications go beyond being mere alternative solvent substitutes for reactions. Where typically DES acts as an inert solvent, not participating in polymerization. For instance, in addition to the reaction medium, DESs can enhance the solvation of monomers and initiators, providing an optimized medium and chemical environment for the reactions to proceed.\textsuperscript{115} Most DES systems are polar, but hydrophobic DESs have the capability to solubilize aliphatic, aromatic, and nonpolar monomers, e.g., methacrylate and styrene. Polymerization by free radical polymerization of such monomers is beneficial when polymerization is performed in hydrophobic DESs, in which additional co-solvents are required in polar DESs.\textsuperscript{83,84}

Other benefits of using DES are the improvement of reaction kinetics to obtain polymeric materials with better thermal and/or mechanical properties.\textsuperscript{83} In this regard, Fazende et al. reported that the polymerization rate of methacrylic and methyl methacrylic acid improved five-fold in eutectic mixtures that contained choline chloride when diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide was used as a photoinitiator. They demonstrated that the viscosity and polarity of the mixture were responsible for these results.\textsuperscript{83} It is noteworthy that the role of DES in this polymer synthesis is, besides the reaction medium, the precursors or monomers that form the final polymer products.
1.8 Polymers obtained from Deep Eutectic Solvent monomers.

Whenever single or various components comprising a DES system are capable of being polymerized, they are referred to as "polymerizable eutectics mixtures" or "deep eutectic solvent monomers" (DESm). Given suitable conditions, including the appropriate triggering of the initiator of the polymerization, the monomer that forms DESs then polymerizes, creating a unique situation in which the monomer has the dual role of being part of the medium and a reagent at the same time. 

Hence, DESs can perform different functions, including solvents, monomers, and templating agents. Cooper et al. reported that if one of the constituents of DESs undergoes a chemical transformation, its counterpart can play the role of a final directing agent of the final material’s structure. A similar scenario occurs in the polymerization of a DESm: the monomer that is part of the DES then polymerizes, whereas its counterpart remains embedded in the resulting output product. Notably, the inert counterpart determines the overall spatial composition of the finished product, such as porosity. Important aspects that are relevant to polymerizable eutectic mixtures and the final spatial composition are the relation between the reaction rate, the separation rate of the DES system components, and its overall viscosity evolution during the reaction.

DES monomers are particularly attractive as sustainable systems because some of their components, which are solid in their original form, are liquid when forming the eutectic mixture, therefore enabling reactions under mild and solvent-free conditions. Another advantage of eutectic polymerizable mixtures is that the often its gives high yields or atomic economy of ca. 100%, allowing synthesis to be performed at conditions that are impossible in traditional solvents. They also allow for an enhanced rate of polymerization, and provides better control in the reactions. DESm polymerizations have been reported through several mechanisms of polymerization, such as free radicals, polycondensation, and ring opening, including another methods such as, atom transfer radicals polymerization, and electrochemical.
1.8.1 Free-radical polymerization of eutectic mixtures monomers

The polymerization of vinyl acrylate monomers forming DESm systems has been studied mainly by the free-radical polymerization (FRP) mechanism. For example, Mota-Morales et al.\textsuperscript{120} reported the polymerization of DESm comprising acrylic or methacrylic acid with choline chloride. The polymerization was carried out in a column in the presence of benzoyl peroxide as an initiator and ethylene glycol dimethacrylate as a crosslinker. Due to their hydrogen-bonding nature, acrylic monomers play the role of HBD in DES. The high viscosity of DESm stabilizes the polymerization reaction, while ChCl catalyzes the polymerization.\textsuperscript{120}

Polymerization of other acrylates, such as acrylamide and N-isopropylacrylamide, which were part of DESm, was also performed by the FRP mechanism.\textsuperscript{121} Sánchez-Leija et al. synthesized a polymer-lidocaine complex that was produced from a DESm composed of lidocaine hydrochloride (as ammonium salt) and acrylic acid. The synthesis of polyacrylic acid was carried out by the FRP mechanism, allowing the final polymer to be applied as a drug delivery system.\textsuperscript{122} Bednarz et al. reported the copolymerization of a DESm from itaconic acid, ChCl and bisacrylamide.\textsuperscript{123} A macroporous polymer composite (carbon nanomaterials or nitrogen-carbon nanotubes, with conversions of approximately 76%) was successfully obtained from FRP of DESm composed of acrylic acid/ChCl.\textsuperscript{124,125}

Free-radical enzymatic polymerizations of acrylamide in the ChCl DES system have also been reported. The reaction was conducted at 50 °C using horseradish peroxidase (HRP) enzyme, hydrogen peroxide, and 2,4-pentanedione.\textsuperscript{126} Furthermore, the FRP mechanism of DESm, which includes photoinitiators, has been extensively studied in recent years. Fazende et al.,\textsuperscript{127} reported the polymerization of DESm composed of acrylic acid, methacrylic acid and ChCl, and the photoinitiator used was diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide. It was observed that the rate of polymerization of acrylates was enhanced by the polarity of its counterpart ChCl in DES and the viscosity of the mixture.\textsuperscript{127} Similarly, Mecerreyes et al.,\textsuperscript{119} reported the photopolymerization of DESs consisting of 2-cholinium bromide methacrylate and citric acid or amidoxime. The reaction was carried out at room temperature with UV light using 2-hydroxy-2-methylpropiophenone as an initiator, and resulted in poly(ionic) liquids that were applied for CO\(_2\) capture.\textsuperscript{119}
In addition, Li Ren'ai et al.,\textsuperscript{128} also photopolymerized acrylic acid/ChCl DES using 2-hydroxy-4-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959\textsuperscript{®}) as a photoinitiator and ethylene glycol diacrylate as a crosslinker. The final product obtained from the polymerization of DESm, poly(DES), was used as inks and deposited on paper via screen-printing into various forms and shapes, enabling the fabrication of origami paper circuits.\textsuperscript{128} Similar works were reported by the same groups and applied as conductive paper and strain sensors.\textsuperscript{129}

1.8.2 Polycondensation of eutectic mixtures monomers

In addition to other polymerization techniques, polycondensation reactions are also utilized as polymerization methods for deep eutectic mixture monomers. For example, Serrano et al. reported the synthesis of an elastomer polyester obtained from 1,8-octanediol/lidocaine DES and citric acid via polycondensation at 90 °C. Lidocaine degradation occurs at approximately 100°C, and it was prevented by the use of DES, allowing polycondensation at temperatures below 100°C.\textsuperscript{130} An example of this is the production of a similar DESm using a combination of 1,8-octanediol and other salts such as tetraethylammonium bromide, hexadecyltrimethylammonium bromide, or methyl triphenylphosphonium bromide. The resulting elastomers possess antibacterial properties due to the presence of nonpolymerizable ammonium or phosphonium salts in the DESm.\textsuperscript{131} Moreover, polycondensation of DESm composed of ammonium salts mixed with citric acid, terephthalic acid, or amidoxide has been reported without the need for a catalyst.\textsuperscript{119} Del Monte et al. developed carbon monoliths with mesoporosity, narrow pore size distribution, and large surface area through the polycondensation of DESm composed of resorcinol/ChCl or ChCl/urea DES with formaldehyde, followed by carbonization.\textsuperscript{124} The same DES system was further explored by adding polymerizable ternary eutectic mixtures, i.e., resorcinol/3-hydroxypyridine/ChCl,\textsuperscript{132,133} 3-hydroxypyridine/tetraethylammonium bromide,\textsuperscript{134} and 4-hexylresorcinol/tetraethylammonium bromide.\textsuperscript{135} The advantages of the synthesis of such materials were high yields, low cost, and exclusion of additives. The carbon surface was functionalized with nitrogen to enhance the adsorption of carbon dioxide,\textsuperscript{134,136} or included iron acetate,\textsuperscript{134} to provide electrical conductivity. Finally, a phosphorus-doped carbon composite was obtained from polycondensation of triethyl phosphate/p-toluene sulfonic acid/furfural alcohol DES and carbon nanotubes.\textsuperscript{137}
1.8.3 Ring--opening polymerization (ROP) of eutectic mixtures monomers

More recently, DES monomers composed of lactides, carbonates, and lactones were studied as alternatives to traditional ROP in bulk or solution. Under suitable conditions, it is possible to polymerize these DESm to produce polyesters under mild temperature conditions and through a simple and overall sustainable route, i.e., it allows them to be produced in a solvent-free method.

Coulembier et al.\textsuperscript{138} carried out a pioneering study in which they prepared a nonionic DESm consisting of an equimolar combination of L-lactide (LLA) and trimethylene carbonate (TMC). They performed ring-opening polymerization (ROP) in this nonionic DES at 23 °C using 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) as the organocatalyst and benzyl alcohol as the initiator. LLA was able to polymerize first due to its liquid phase at room temperature, and the selectivity of DBU, allowing mild temperature conditions and the absence of organic solvents. Subsequent polymerization of TMC onto the blend led to a final poly(LLA-g-TMC) copolymer with a gradient composition.\textsuperscript{138} Similarly, Pérez-García et al. produced a eutectic mixture composed of L-lactide (LLA) and ε-caprolactone (CL) in a molar ratio of 3:7, respectively. The melting point of the mixture was -19 °C, which is below the melting point of the constituents. Taking advantage of the liquid nature of LLA, polymerization was possible under mild temperature conditions (37°C) through sequential ROP, resulting in a blend of poly(L-lactide) and polycaprolactone homopolymers with high crystallinity.\textsuperscript{139}

1.9 Polymers from the eutectic mixture and their applications

Utilizing DES monomers presents an attractive approach to replace volatile organic solvents, achieve high yields, or enhance the rate of polymerization when synthesizing various polymers. As previously discussed, polymers can be produced by different mechanisms from DESm with several advantages over conventional systems. Furthermore, the benefits of implementing DES monomers are not restricted to polymer synthesis applications; they can also be employed to create diverse materials, including supramolecular hydrogels, porous monoliths, and molecular imprinted polymers.
Bernardz et al. reported the production of a poly(itaconic acid-co-N,N'-methylenebisacrylamide (BIS) hydrogel obtained from DESm consisting of itaconic acid and ChCl. Wu et al. produced a deep eutectic supramolecular polymer gel from cyclodextrin/natural acids DES. Li et al. mixed glycerol with urea to prepare acrylamide polymers for molecular printing. Ndizeye et al., used non-ionic DESs as a porogen in the synthesis of porous polymer monoliths.

Porous polymers have garnered significant interest due to their potential applications in fields like biomedicine, separation processes, and energy storage. The morphology, size, and connectivity of the pores in these polymers are directly linked to their intended use. To achieve these properties, various pore-generation methodologies have been developed, including macromolecular design, self-assembly, phase separation, solid-liquid melt, sol-gel, and foam formation.

Recently, emulsion templates have become a popular choice for developing porous materials, and they can be further extended to fabricate interconnected macroporous polymeric monoliths by utilizing a high internal phase emulsion (HIPE) as a template, where a DES monomer comprises the continuous phase. HIPE is a packed emulsion that has a higher internal phase of 74% v/v and is stabilized by surfactants. The closed-pack emulsion droplets provide the template where the subsequent polymerization of the continuous phase followed by the elimination of the internal phase gives rise to a macroporous polymer with interconnected pores. Pérez García et al. exploited the liquid nature of the mixture of L-lactide and ε-caprolactone monomers at room temperature, which otherwise are separately solid and liquid, respectively. To prepare the HIPE, the eutectic mixture of L-lactide and ε-caprolactone, liquid at RT, was mixed with nonpolar solvents and stabilized with nonionic surfactants. Polymerization of the DESm in the continuous phase was performed at 37 °C, and the resulting polyHIPE (pHIPE) was reported to possess pores with a diameter close to 20 μm. pHIPES has found numerous applications in biomedical applications, separations, or catalyst supports.
The polymerization of DESm and eutectic systems has flourished over the last decade with exciting results that have translated into new materials and applications. Nevertheless, in the case of other methods of polymerization, apart from free radicals, the literature is scarce, with only a handful of works published concerning polycondensation and ROP, for instance. Hence, this work aims to fill the gap in understanding and exploring the ROP of eutectic mixtures composed of lactones for the synthesis of biodegradable polyesters through a sustainable approach. The synthesis of porous polyesters with properties that can be tailored to adjust their biodegradability is one of the expected results. Such materials will add to the existing toolbox for applications in areas such as biomedicine and separation processes.

1.10 Scope and Outline of the Thesis
Chapter 2 provides a fundamental study on the Ring Opening Polymerization (ROP) of deep eutectic solvent monomers (DESm) composed of L-lactide and ε-caprolactone, leading to the synthesis of polymer blends and a block copolymer. The Chapter discusses the influence of various parameters in producing polyesters with tunable number average-molecular weight (in the range of 2000 to 6900 g/mol⁻¹), crystallinity (from 37% to 70 %), and polymer architectures with controlled degradation profiles. The outcome strongly depends on the selection of organocatalysts, including 1,5-Diazabicyclo (4.3.0) non-5-ene (DBN), a new catalyst for the ROP of L-lactide/ε-caprolactone DESm. The use of this organocatalyst not only allows an increase in the polymerization temperature (up. to 92 °C) but also facilitates the formation of a block copolymer P(LLA-b-CL) for the first time using this methodology. Additionally, the Chapter discusses the influence of the stereoisomer D-lactide in the DESm and water content (ca. 0.2 wt.%) during the ROP process.

Chapter 3 introduces new DESm capable of undergoing ROP to produce biodegradable polyesters by mixing various lactones with L-lactide. These lactones encompass a range of molecular weights and structures, including δ-valerolactone and δ-decalactone. The Chapter provides fundamental insights into ROP kinetics and explores the impact of different organocatalysts, benzyl alcohol initiator concentration, and reaction temperatures (37 and 60°C).
These factors significantly influence the achieved number average molecular weight (in the range of 2400 to 8700 g/mol\(^{-1}\)), crystallinity, and polymer architectures of the resulting polyesters, including blends and block copolymers.

Chapter 4 investigates the incorporation of multifunctional macroinitiators in the ROP of a DESm composed of L-lactide and ε-caprolactone to enhance the properties of the resulting polyesters. These macroinitiators include poly(caprolactone triol (PCL segments of 900 g/mol\(^{-1}\)) and polyethylene glycol (6000 g/mol\(^{-1}\)), both OH-terminated. The thorough understanding of the ROP kinetics of the DESm, considering factors such as hydrophobicity and molecular weight of the final bulk polyesters (from Mn 2400 to 9500 g/mol\(^{-1}\)), serves as the basis for the synthetic conditions applicable to the design and synthesis of high internal phase emulsions (HIPEs).

These HIPEs consist of highly viscous emulsions of tetradecane-in-DESm, which are stabilized by Pluronic F-127 surfactant, and acts as a template for the ROP of the continuous (external) phase. The macroinitiators enable precise control over the hydrophilic characteristics of the polyesters, whether in bulk or polyHIPEs, providing control over the degradability, average-molecular weight, and polymer architectures of the resulting polymers. Notably, the macroporous polyHIPEs (with pores in the range of 33 to 42 μm) exhibit excellent crude oil sorption capabilities, with a competitive sorption capacity of 2 grams of oil per gram of sorbent.

These chapters provide a comprehensive exploration of a solventless ROP process at low temperatures (e.g., 37°C), using organocatalysts to synthesize biodegradable polyesters with tailored properties. The research contributes to the development of alternative protocols in polymer synthesis and offers valuable insights for sustainable development. The solvent-free ROP of lactide and lactones in the form of DESm, conducted under mild temperature conditions without metal catalysts and volatile organic solvents, demonstrates a versatile process for polyester synthesis with rapid degradability and controllable properties. The use of mild temperatures and organocatalysts in preparing polyesters with programmable degradation profiles represents important environmentally friendly features for the development of new materials.
These findings are expected to have significant implications for biomaterials science and polymer chemistry, enabling the exploration of sustainable materials engineering or degradable biomaterials. Such materials, with controllable degradation profiles, hold potential applications in separation processes, cell culture scaffolds, and drug delivery. Overall, this research lays the foundation for an alternative, greener methodology for polyester production, opening new avenues for sustainable materials development in the field of biomaterials and beyond.

1.11 References


Facile and green alternative route to obtain polylactides and polylactones


Facile and green alternative route to obtain polylactides and polylactones | 49


