UNIVERSITAT ROVIRA I VIRGILI

FUNCTIONAL COPOLYESTERS FROM CASTOR AND SUNFLOWER OILS, POLY(L-LACTIDE) AND POLY(E-CAPROLACTONE) USING THIOL-CLICK CHEMISTRY

Zeynep Beyazkılıc

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Zeynep Beyazkılıc

Functional Copolyesters from Castor and Sunflower Oils, Poly(L-lactide) and Poly(ε-caprolactone) using Thiol-Click Chemistry

PhD thesis

Supervised by Prof. Marina Galià i Clua and Prof. Virginia Cádiz Deleito

Department of Analytical Chemistry and Organic Chemistry

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We STATE that the present study, entitled “Functional copolyesters from castor and sunflower oils, poly(L-lactide) and poly(ε-caprolactone) using thiol-click chemistry” presented by Zeynep Beyazkılıc for the award of the degree of Doctor, has been carried out under our supervision at the Department of Analytical Chemistry and Organic Chemistry of this University.

Tarragona, 6 February, 2015

Prof. Marina Galià i Clua   Prof. Virginia Cádiz Deleito

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To my family...

"Nunca consideres el estudio como una obligación sino como una oportunidad para penetrar en el bello y maravilloso mundo del saber"
Albert Einstein

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Chapter 1

Aim and Outline

Polymers are the most widely used materials due to their extraordinarily versatile and diversified structural and multifunctional characteristics. Modern life without polymers would not be possible because they assure the high quality of life with the development of novel tecnologies.

A significant increase of interest in biobased polymers has been observed in the last years due to at least two important reasons. The first one is related to the availability of raw materials for the synthesis of polymers. Currently, the majority of polymers is produced from crude oil with the problems associated with the high prices and rapid fluctuations. The second reason of interest is related to waste management. Expected solution to this problem cannot rely on only one approach but rather on combination of a variety of them. Taking advantage of chemistry, the efficient transformation of renewable resources avoiding the use of fossil reserves that contributes negatively to the planet's energy problem is an useful approach. Moreover, the obtention of degradable polymers is also pursued, decreasing the negative environmental impact of huge amounts of plastic waste generation.

Biobased polymers are now readily entering the green economy with a global production in 2011 of around 1.1 million tons. Further development of biobased polymers is expected with an estimated production in 2016 of around 5.8 million tons. By selecting appropriate biomass feedstock and appropriate transformation proccesses, a wide range of molecules are accessible and these bioplatform molecules are a new challenge for chemistry. Then, the question is if we can built on these molecules as we have done over the last 70 years with the well stablished petroplatform molecules. A substantial grow in research activity on the conversion of these platforms molecules to valuable and competitive products is needed.

The synthesis of polyesters and copolyesters made from monomers obtained by chemical modification of naturally-ocurring compounds such as vegetable oils may lead to renewable polyesters with improved properties regarding to those displayed by the traditional ones.

Poly(lactic acid) or poly(lactide) (PLA) and poly(ε-caprolactone) (PCL) are two of the leading and most mature biobased plastics among other aliphatic polyesters. However, the versatility and succesful use as commodity plastics are limited as is their exploitation in biomedical, electronic and optical sectors. The absence of reactive functionalities on the polymer backbone greatly limits their use. Thus, the introduction of functional groups can modulate their physical, chemical and biological properties.

The aim of this Thesis is to prepare renewable polyesters from vegetable oils and to develop environmentally friendly monomer and polymer synthesis strategies to keep moving toward more sustainable polymer chemistry. To achieve this goal the experimental work was focused on exploiting the reactivity of 10-undecenoic acid, a castor oil derivative, and oleic acid, a sunflower oil derivative, to synthesize monomers by using different methodologies. The specific objectives are:

- To prepare sulfur-containing castor and sunflower oil monomers using thiol-ene, thiol-yne and thiol-Michael click chemistries.
- To develop new functionalized thermoplastic polyesters by chemical or enzymatic polymerizations.
- To develop random and block copolyesters from L-Lactide (LA), ε-caprolactone (CL) and castor and sunflower oils derivatives.
- To carry out the post-polymerization modification of the linear polymers by oxidation, thiol-ene and ketoxime click chemistries.

The work presented in this Thesis consists of seven chapters including aim and outline, experimental part and conclusions.

The second chapter of this Thesis reviews both the state-of-the-art in biobased polyesters from fatty acid and the use of click chemistry on polymers from plant oils.

The third chapter describes the synthesis of a sulfur-containing hydroxyacid from castor oil and its homopolymerization. The block copolymerization with LA and the oxidation of thioether moiety is developed to investigate the properties of these triblock copolymers and their potential as PLA analogues.

Next chapter focuses on the synthesis of a vinylsulfide-containing hydroxyacid from castor oil and its homopolymerization. The random and block copolymerization with CL are studied. The thiol-ene post-modification has been demonstrated and applied to the surface modification and crosslinking.

The fifth chapter shows the synthesis of a thioetherketone-containing hydroxyester from sunflower oil and its homopoymerization. The copolymerization of this hydroxyester with the vinylsulfide-containing hydroxyacid allow the double main chain functionalization and the postmodification of polymer chain by thiol-ene and oxime click chemistries.

Chapter 2

General Introduction

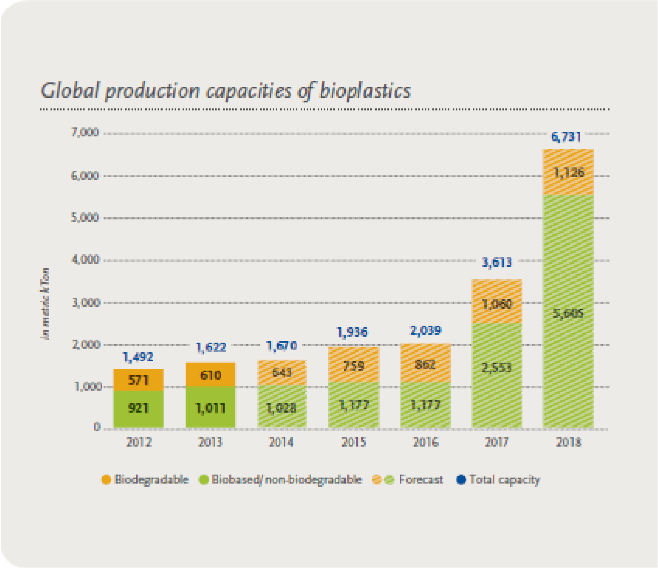
2.1. BIO-BASED POLYMERS

Due to the exceptional physical properties, low cost and easy processing, plastics become the most widely used materials which are also placed routinely in our daily life such as bags, containers and packages of food, drink bottles, clothes, objects and packaging of electronic devices, furniture, part of buildings and pieces of automobiles, etc. The worldwide annual production of plastics requiring multiple amounts of petroleum presumably exceed 300 millon tons in the time period of 2010 to 2015.[1] However, these amazing numbers in plastic production cause to release hundreds of millions of tons of CO_2 and along with other types of emissions resulting healt risks for humankind. One of the another considerable drawback is that giant amount of waste generation. According to the US Environmental Protection Agency reports, 32 millions tons of plastic waste are generated in United States in 2011, that represent 12.7% of the total municipal waste.[2] Moreover, traditional petrochemical based plastics and their wastes are not sustainable, persevere for hundreds or even thousands years after being thrown away. Therefore, they convert into toxic microfragments that could readily pass to surrounding ecosystems[3] and constitute a huge harm for terrestrial and see animals, in addition to birds that tend to eat plastic residues.[4]

These environment concerns that are related to continous consuming of non-renewable resources, greenhouse gas emissions and waste disposal together with dramatic fluctuations in the price of oil, have urgently led to develop new polymeric materials from biomass and renewable resources to avoid problems caused by the petrochemical plastics.[5] In recent decades, the utilization of renewable resources has an increasing interest as potential fossil substitutes in the field of industrial and academic researches. For example, poly(lactic acid) (PLA) is one of the most versatile and used sustainable polymer obtained from corn via fermentation process. PLA cost was around 15-20 times more than poly(ethylene terephthalate) (PET) in 1990s. Today, the surcharge of PLA towards PET is only 15-25%, an amount small enough to allow its development into several packaging markets such as drink cups which are especially used at the fast food restaurants.[6] In consequence, scientific efforts necessarily direct toward the design and production of innovative environmentally degradable green plastics to replace the conventional petroleum-based are requiered in order to decrease and prevent negative contributions of nonrenewable resources to our planet.

Although this renewed interest in polymers from renewable resources has gained wings recently, the idea is not new. Indeed, the first appearance of bio-based polymers is related to the birth of the macromolecular science and technology in the 19th century with the synthesis of some very well known materials such as celluloid,[7] vulcanized natural rubber[8], or linoleum.[9] On the other hand, the relative importance of macromolecular materials obtained from renewable resources fall into a gradual decline by the petrochemical revolution of the last century. Although polymeric materials based on fossil resource such as most important ones; polyethylene (PE), polypropylene (PP), poly(vinyl chloride) (PVC), PET and polystyrene (PS) inevitably surround our everyday life, the idea to find environmentally friendly alternative plastics based on renewable resources gain attention once again in the beginning of the 21st century. Polysaccharides (cellulose and starch), vegetable oils, proteins and wood are the most widely used renewable raw materials.[10]

Although the recent development of renewable polymers has shown great progress, the small share (<5%) of renewable polymers in the commercial market is largely due to their high cost and inferior performance compared with synthetic polymers produced from petroleum chemicals. Growing demand for more sustainable solutions is reflected in growing production capacities of bioplastics: in 2013 production capacities amounted to 1.6 million tonnes. Market data of European Bioplastics forecasts production capacities will multiply by 2018 to approximately 6.7 million tonnes (Figure 1).[11]

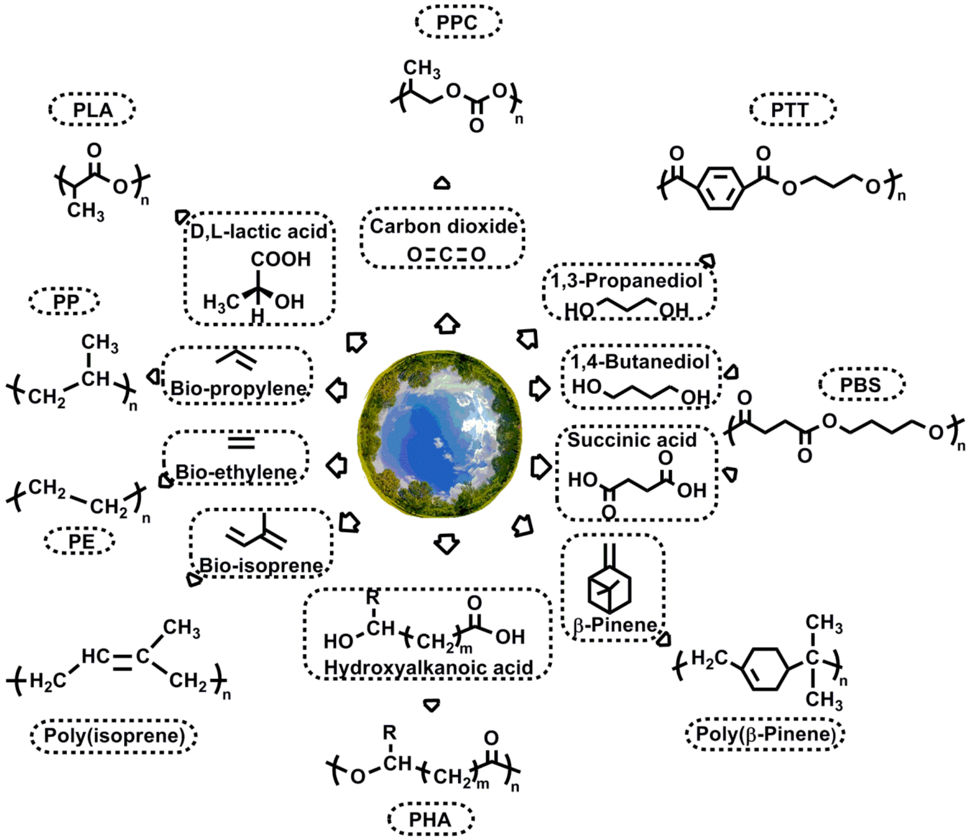


Source: European Bioplastics, Institute for Bioplastics and Biocomposites, nova-Institute (2014)
More information: www.bio-based.eu/markets and www.downloads.ifbb-hannover.de

Figure 1. Global production capacities of bioplastics

Generally, monomers derived from biological sources are classfied into four major categories which based on hydrogen, carbon and oxygen composition, according to their natural molecular biomass origins: (1) oxygen-rich monomers including carboxylic acids (lactic acid, succinic acid (SA), itaconic acid (IA), adipic acid (AA) and levulinic acid), polyols, dianhydroalditols and furans; (2) hydrocarbon-rich monomers including vegetable oils, fatty acids, terpenes, terpenoids and resin acids; (3) hydrocarbon monomers including bioolefins (bioethylene, biopropylene and bioisoprene) and (4) non-hydrocarbon monomers including carbon dioxide.[12]

These raw materials convert into a wide range various monomers that can produce many kind of biopolymers such as polyhydroxyalkanoates (PHA), PLA, poly(butylene succinate) (PBS), PE, poly(trimethylene terephthalate) (PTT), PP, PET and poly(propylene carbonate) (PPC)[13] (Scheme 1).



Scheme 1. Biobased monomers and their polymers

Most renewable carboxylic acids are obtained by fermentation of carbohydrates. In this class, glucose is one of the most common renewable material, produced from starch, cellulose, sucrose and lactose by enzymatic hydrolysis or from woody biomass by chemical transformation. Lactic acid is the simplest hydroxyl acid with an asymmetric carbon atom with D and L optically active configurations. It can be produced via either chemical synthesis or microbial fermentation. However, the chemical processes produce a racemic 50:50 mixture of D-lactic acid and L-lactic acid. Fermentation of carbohydrates such as glucose, maltose, sucrose, lactose, etc can produce very pure D-lactic acid, L-lactic acid or a mixture of them depending on the type of bacteria used.[14] Global producers of lactic acid include Purac, Galactic, NatureWorks and ADM. The current production of lactic acid is around 300-400 kton/year. SA is mainly obtained by microbial fermentation due to significant advantages from an environmental standpoint, as it uses CO_2 to convert the substrates into the product.[15] Feed stocks including corn starch, corn steep liquor, whey, cane molasses, glycerol, lignocelluloses, cereals and wood hydrolysates could be used for microbial fermentation by the activity of specific bacterias. SA could be also served as precursor to transform into γ-butyrolactone, 1,4-butanediol, tetrahydrofuran, and AA that can be used for the preparation of various polymers. Currently, SA are commercially produced by several important companies e.g. BASF and Purac joint, Bioamber, Reverdia, Myriant. The annual production is approximately 50 kton and also it is expected that this value reaches to 270 kton per year in the future years.[16] IA is another member of carboxylic acid renewable monomer family that can be obtained from carbohydrates by fermentation. Due to the similarity of the structure, IA may become suitable candidate to replace petrochemical-based acrylic or methacrylic acid.

1,3-propanediol (PDO) and 1,4-butanediol (BDO) are common examples of carbohydrate-based aliphatic diols. PDO can be prepared by chemical or biological processes from renewable resources.[17,18] Today, bio-based PDO which was developed and commercialized by the joint venture DuPont Tate & Lyle LLC. is produced by aerobic fermentation of glucose from corn starch, with an annual capacity of 45000 tons. BDO was developed by San Diego based Genomatica Inc. in a sucrose-based process by using an engineered microorganism. This process has considerable benefits in comparison to current petrochemical processes such as much less energy and releasing of less carbon dioxide.[19] Hydrogenation of SA to BDO can be carried out over mono- and bimetallic catalysts in an alternative production way.[20]

Terpenes, terpenoids and resin acids are one class of hydrocarbon-rich natural molecular biomass that have been used as precursors or derivatized into monomers for the production of some polymers. Many plants and trees serve to produce this kind of molecular biomass. [21]

Hydrocarbon biomass monomers are olefins such as bioethylene, biopropylene and bioisoprene that have also interest to develop their production from renewable resources.[22] Ethylene is one of the most important petrochemical precursor to produce many notable polymers on daily life such as high density polyethylene (HDPE) and low density polyethylene (LDPE), PVC, PET, etc. Although almost whole ethylene production is based on petroleum feedstock, much attention has been focused on renewable resources to produce ethylene precursors. Ethylene could be alternatively produced from bioethanol that is being produced from starch, sugar cane and lignocellulosic feedstocks via fermentation. Propylene is another petroleum based precursor that has many proposed routes from renewable feedstocks such as bioethanol and biobutanol. Isoprene is one the most important intermediate in the synthesis of renewable rubber. Therefore, using a biomass route such as microbial fermentation can be a promising development for the industrial field, especially automobile industry.

An abundant non-hydrocarbon nonflammable gas, CO_2 is also a specific class of renewable biomass feedstock. Due to its non-toxicity and low cost, CO_2 is an attractive resource in many applications, especially for the synthesis of polymers such as polycarbonates.[23]

All these current and certainly future efforts and developments based on renewable resources have an important role for a sustainable ecosystem by minimizing the obligation of fossil fuel, decreasing carbon emission and providing more environmentally friendly materials for our future.

2.1.1. Vegetable Oils as Renewable Monomers

Vegetable or plant oils are historically and currently one the most important renewable platform of the chemical industry due to their many promising advantages such as biodegradability, ready availability, low toxicity and relatively low price compared to petroleum-based chemicals. The utilization of vegetable oils as a feedstocks date back to old times for coating applications and soap manufacture and increased by time for wider and more developed uses including plasticizers, alkyd resins, inks and agrochemicals, etc. In recent years, there has been an increasing demand to produce biobased functional polymers and polymeric materials from oil-based feedstocks.[24] Figure 2 explains the life cycle of polymers based on plant oils and the importance of sustainability.

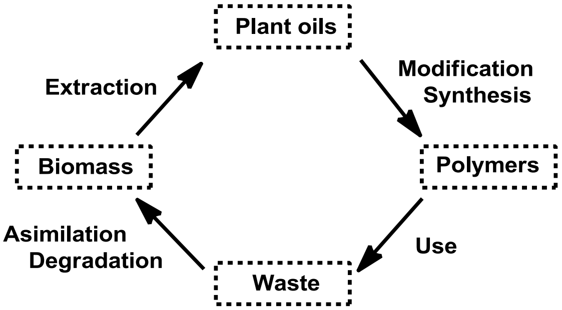
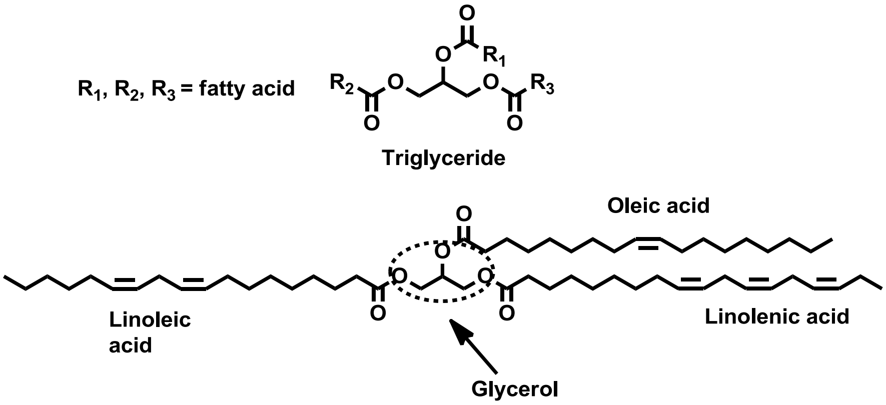


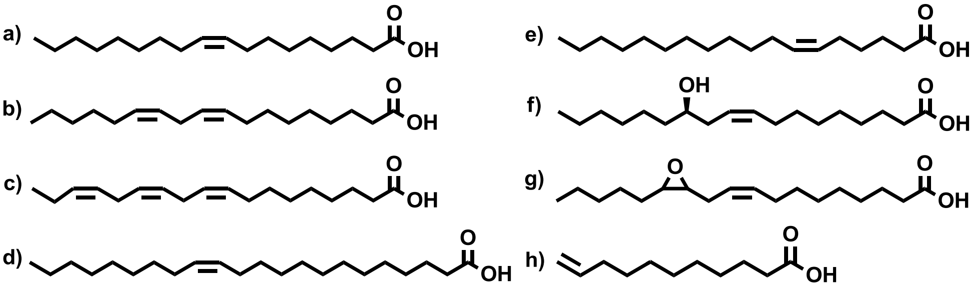
Figure 2. Life cycle of polymers based on plant oils

Vegetable oils are obtained by extraction from different species including palm trees, soybeans, rapeseeds, cotton, sunflower, palm kernel, olives and coconuts. The annual global production of the major vegetable oils amounted 90.5 million tons (Mt) in 2000/2001 and increased to 170 million tons (Mt) in 2013/2014 with an increase of 95%. About 20% is devoted to industrial applications primarily as sources of energy, compared with around 75% and 5% for the utilizations of food and feed. [25]

The main components of plant oils are triglycerides which are obtained from the esterification of one gylcerol molecule with three fatty acid molecules, as shown in scheme 2. Triglycerides are liquid at ordinary temperature and insoluble in water. Fatty acids account for 95% of the total weight of triglycerides and their content is characteristic for each plant oil. The chemical structures of the most common fatty acids in polymer chemistry and fatty acid composition of common plant oils are summarized in scheme 3 and table 1, respectively.



Scheme 2. Representative structure of triglycerides



Scheme 3. Fatty acids commonly used in polymer chemistry: (a) oleic acid, (b) linoleic acid, (c) linolenic acid, (d) erucic acid, (e) petroselinic acid, (f) ricinoleic acid, (g) vernolic acid, (h) 10-undecenoic acid

Table 1. Fatty acid composition of common plant oils

C:DB Plant Oils	16:0	16:1	18:0	18:1	18:1[a] OH	18:2	18:3	20:0	20:1	22:1
Canola	4.1	0.3	1.8	60.9	0.0	21.0	8.8	0.7	1.0	0.0
Corn	10.9	0.2	2.0	25.4	0.0	59.6	1.2	0.4	0.0	0.0
Linseed	5.5	0.0	3.5	19.1	0.0	15.3	56.6	0.0	0.0	0.0
Olive	13.7	1.2	2.5	71.1	0.0	10.0	0.6	0.9	0.0	0.0
Palm	44.4	0.2	4.1	39.3	0.0	10.0	0.4	0.3	0.0	0.0
Soybean	11.0	0.1	4.0	23.4	0.0	53.4	7.8	0.3	0.0	0.0
Sunflower	6.1	0.0	3.9	42.6	0.0	46.4	1.0	0.0	0.0	0.0
Sunflower high oleic	6.4	0.1	3.1	82.6	0.0	2.3	3.7	0.2	0.4	0.0
Sunflower high eruric	3.0	0.0	1.0	16.0	0.0	14.0	10.0	0.0	6.0	50.0
Castor	0.5-1	0.0	0.5-1	2-6	85-95	1-5	0.5-1	0.0	0.0	0.0

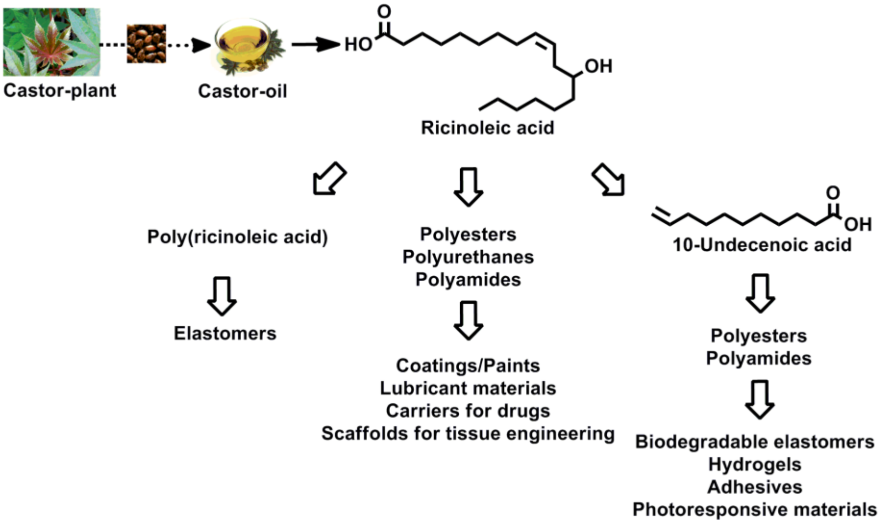
C: DB C number of carbon atoms, DB number of C=C, [a] contains a hydroxyl group

Most common oils are composed of fatty acids which have a chain lengths varying from 12 to 22 carbon atoms and with zero to three double bonds per chain. Fatty acids are defined with their number of carbon atoms in the chain and their number of unsaturation (Table 1). For example, oleic acid has 18 carbon atoms and one unsaturation therefore it is classified as 18:1 fatty acid derivative. Additionaly, some oils have fatty acid derivatives with different moieties namely hydroxyl or epoxy groups at various positions throughout the carbon chains.

The fatty acid composition of triglyceride diversifies depending on the crop, the plant, the season and the growing conditions. One of the most important feature affecting the physical and chemical properties of fatty acid and oils is the unsaturation degree as well as the carbon chain length of fatty acid. Iodine value is used to measure this average degree of unsaturation. For 100 g of sample, the amount of iodine that reacts with double bonds gives information of the degree of unsaturation. Plant oils are classified into three categories based on the iodine values: ‘drying oils’ have iodine value higher than 130, ‘semi-drying oils’ have iodine value between 90 and 130 and ‘non-drying oils’ have iodine value below 90.

The fatty acids structures thanks to their functionalities can be expanded into varios sophisticated starting materials such as α,ω-dicarboxylic acids, α,ω-dialcohols or α,ω-hydroxyacids by chemical modifications. Soybean, corn, tung, linseed and castor oils are the most used renewable resources used as precursors for the synthesis of vegetable oil-based monomers and polymers.[5b]

Castor oil contains 85-95 wt% of triglycerides of ricinoleic acid, which is the most used renewable monomer to produce various bio-based polymeric materials because of its hydroxyl and carboxyl groups and also its unsaturation in the C9 position makes it capable for the further modifications. The pyrolysis of ricinoleic acid under vacuum conditions yielded a fatty acid with a terminal double bond, 10-undecenoic acid that can be used in a wide range of applications (Scheme 4).[26,27]



Scheme 4. Biomass source of ricinoleic acid and some potential applications in the polymeric field

Most of the scientific literature avaible today has been centered on modifying vegetable oils to prepare well-defined linear structures, 3D networks and also matrices for biocomposites and hybrid materials. Figure 3 summarizes suitable approaches to obtain thermoplastic and thermosetting materials from triglycerides and triglyceride-derived building blocks.

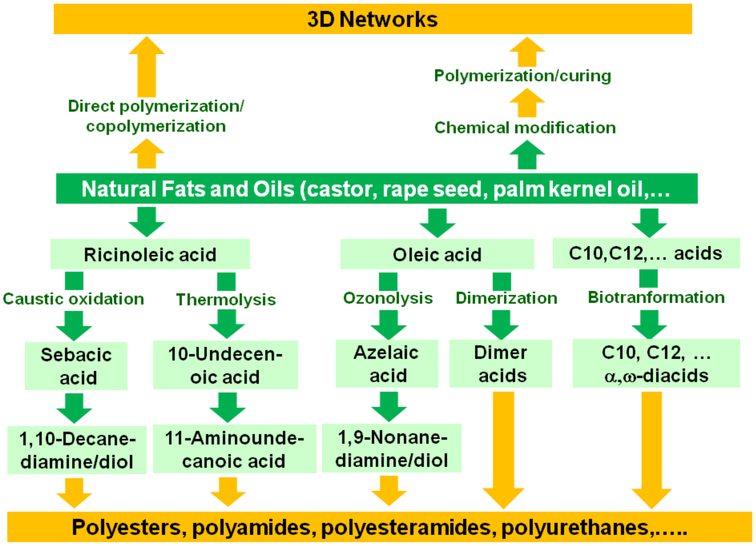


Figure 3. Main approaches to obtain thermoplastic and thermosetting materials from triglycerides and triglyceride-derived building blocks

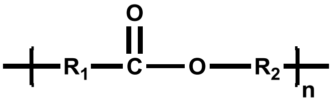
During the last decade, a great number of vegetable oil-based polymeric materials have been prepared.[28] Free radical[29], cationic[30], olefin metathesis such as ADMET[31], ROMP[32] and condensation polymerizations[24a,33] are important methods to generate and develop bio-based polymers as well.

These materials are used in a great number of applications not only restricted to material area (paints, coatings and adhesives) but also to biomedical field.[34] Particular attention is paid to investigating their suitability as future biomaterials due to properties like biocompatibility, shape memory effect and biodegradability.[35]

2.2. POLYESTERS

2.2.1. Historical Review

Polyesters are polymers in which the main chain is composed of aliphatic or aromatic moieties linked together by ester groups (Scheme 5). The polyester family is extremely large and depending on the nature of R_1 and R_2 exhibits an enormous variety of structures, properties and applications.



$$\left[R_1-\overset{O}{\overset{\|}{C}}-O-R_2 \right]_n$$

Scheme 5. General formula of polyesters

It has been known since the early 19th century that heating carboxylic polyacids with glycerol resulted in resinous compounds. In 1910-1920s, under the leadership of General Electric Company, extensive studies on the chemistry of phthalic anhydride-glycerol reaction were carried out and the technology of alkyd resins was developed. These type of resins are still widely used for the production of coatings, varnishes and paints.

In the 1930s the modern period of polyesters commenced by experimental studies of Carothers on reactions between aliphatic dibasic acids and diols.[36] These studies established the relationships between degree of polymerization, conversion, functionality and gel point, so that the base requirements on the relationships of step-growth polymerization were created. However, these polyesters had low melting point and were sensitive to hydrolysis and therefore they could not compete with aliphatic polyamides or nylons also discovered by Carothers in 1930 at the Dupont Company.

To increase the polyester melting points and to approach the thermomechanical properties obtained from nylons it was necessary to stiffen the polyester chain by using rigid aromatic monomers instead of flexible aliphatic. In the early 1940s at the laboratories of the Calico Printers Association in the United Kingdom, Whinfield carried out the reaction between terephthalic acid and aliphatic diols that yielded high melting point fiber-forming polyesters.[37] After World War II, the patent rights on these aliphatic-aromatic polyesters were shared between I.C.I. and DuPont, and several members of this family became, and are still today, major commercial polymers. PET is now one of the most produced polymers primarily for textile and packaging applications. Poly(butylene terephthalate) (PBT) finds uses as solid-state molding resin. PTT, though described in the Winfield's original patent, is a new comer in the commercial polyester family and has found its first application in the textile industry.

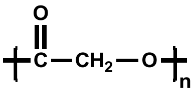
By the end of the 1930s, a new type of thermosetting resin was discovered when Carothers and Flory were studying aliphatic polyesters. Unsaturated polyesters were synthesized by reacting mixtures of saturated and unsaturated diacids or anhydrides with aliphatic diols.[38] Dissolving these linear aliphatic polyesters in an unsaturated monomer, such as styrene that could undergo free-radical copolymerization with the unsaturations in polyester chains led to the thermosetting resins. After radical polymerization in the presence of heat or catalysts, the liquid resin is converted into a rigid, insoluble and infusible crosslinked polymer. Unsaturated polyester resins found their first applications in combination with glass fibers for protective radar domes during World War II, but this technology was widely commercially available only in the mid of 1950s. Currently, they are one of the most important matrix resins for glass fiber reinforced composite materials.

Although aliphatic polyesters were the first step growth polymers fully characterized, they did not find commercial applications until late 1950s and the 1960s. The first commercial application of aliphatic polyesters appeared by the development of polyurethane foams and elastomers. In the 1970s there was a period of the intensive studies of block copolymers. At that time, block copolymers based on different polyesters were described in the literature, but the polyesterether block copolymers were the only successful commercial ones, marketed by DuPont under the tradename Hytrel, exhibiting the characteristics of thermoplastic elastomers.[39] During this period and with the arrival of 1980s, much attention was focused on high perfomance wholly aromatic polyesters. The commercial introduction of the first one, amorphous poly(bisphenol-A-isophthalate-terephthalate) (Union Carbide's Ardel) took place in the mid 1970s.[40] Despite their high cost, liquid crystalline thermotropic polyesters, such as poly(6-hydroxy-2-naphthoic acid-co-4-hydroxybenzoic acid) (Ticona's Vectra)[41] were described at the end of 1970s, found and still have a number of applications in high technology markets.

In 1990s, environmental concerns began to be gaining ground. The versatility of the ester linkage, able to undergo hydrolysis, alcoholysis and acidolysis in some conditions, makes polyesters the polymers of choice to fulfill the increasing demand for reciclable and/or biodegradable polymers. This resulted in a renewed interest in aliphatic polyesters such as PLA, poly(glycolic acid) (PGA), PCL or copolyesters containing aliphatic moieties.[42] PET production is also strongly driven by the demand of reciclable polymers.

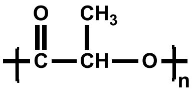
Depending on their structure, properties and synthetic methods, degradable polyesters can be divided into four groups: poly(α-esters), poly(β-esters), poly(lactones) and polyesters of aliphatic diols and diacids.[43]

Poly(α-esters)



$$\left[\overset{O}{\overset{\|}{C}} - CH_2 - O \right]_n$$

Poly(glycolic acid) (PGA)

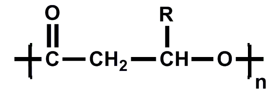


$$\left[\overset{O}{\overset{\|}{C}} - \overset{CH_3}{\overset{|}{CH}} - O \right]_n$$

Poly(lactic acid) (PLA)

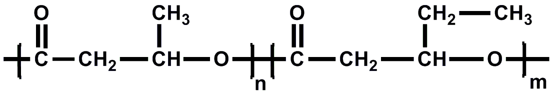
Poly(α-esters) are semicrystalline thermoplastic polymers with high melting points. PGA is the simplest aliphatic linear poly(α-ester) and its melting point is in the range of 220–225 °C which is the highest melting temperature in the aliphatic polyesters family. Pure enantiometric L-lactic acid and L-lactid (LA) produce isotactic poly(L-lactic acid), which is semicrystalline and melts around 170-190 °C. D-Lactic acid exists in some bacterial systems and leads to isotactic poly(D-lactic acid), a polymer with similar properties as isotactic poly(L-lactic acid). Sindiotactic poly(D,L-lactic acid) has been obtained by the estereoselective polymerization of D,L-lactide. Atactic poly(D,L-lactic acid) is obtained from the polycondensation of racemic lactic acid and also from sindiotactic poly(D,L-lactic acid) by the redistribution of stereosequences due to ester interchange in the melt. Consequently, the properties of PLA are strongly affected by the optical purity of starting monomers, by polymerization and processing conditions and by its thermal history. A wide range properties can also be achieved by copolymerization with glycolide or ε-CL. These general properties compare well with those of commodity thermoplastics such as PE, PS or PVC.[44]

Poly(β-esters)



$\left[\overset{O}{\overset{\|}{C}}-CH_2-\overset{R}{\overset{|}{CH}}-O \right]_n$

Poly(3-hydroxy alkanoic acid) (P3HA)

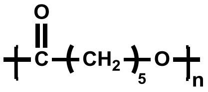


$\left[\overset{O}{\overset{\|}{C}}-CH_2-\overset{CH_3}{\overset{|}{CH}}-O \right]_n \left[\overset{O}{\overset{\|}{C}}-CH_2-\overset{CH_2-CH_3}{\overset{|}{CH}}-O \right]_m$

Poly(3-hydroxybutanoic-co-3-hydroxyvaleric acid) (PHBV)

Poly(3-hydroxy alkanoic acid)s (P3HAs), also known as poly(3-hydroxyalkanoates), are aliphatic polyesters naturally produced by bacteria as energy storage material.[45] Various P3HA homopolymers and copolymers such as, poly(3-hydroxybutanoic acid) (PHB) and poly(3-hydroxybutanoic-co-3-hydroxyvaleric acid) (PHBV), Monsanto's Biopol polyesters, can be obtained by fermentation of glucose or of various feedstock materials. The high cost of the fermentation process made the bacterial production uneconomical compared to other biodegradable plastics and the current trend is directed toward biosynthesis by genetically modified plants. Isotactic, sindiotactic and atactic P3HAs have been reported depending on the microbial or chemical synthesis. Moreover, the properties depend on their composition: PHB is highly crystalline, brittle polymer with melting temperature of 177 °C whereas PHBV copolymers exhibit lower melting temperature around 135-150 °C and display higher impact resistance and flexibility.[46]

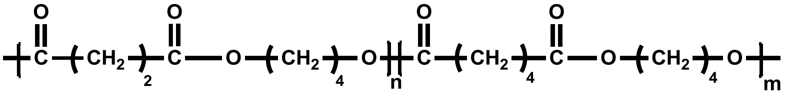
Poly(Lactones)



Poly(caprolactone) (PCL)

PCL, the most characteristic member of poly(lactones), is obtained by the ring opening polymerization of CL. It is a semicrystaline, tough and flexible plastic with a melting temperature of 60 °C and Tg below room temperature (-60 °C) that presents mechanical properties resembling those of the LDPE.

Copolyesters from Diacids and Diols



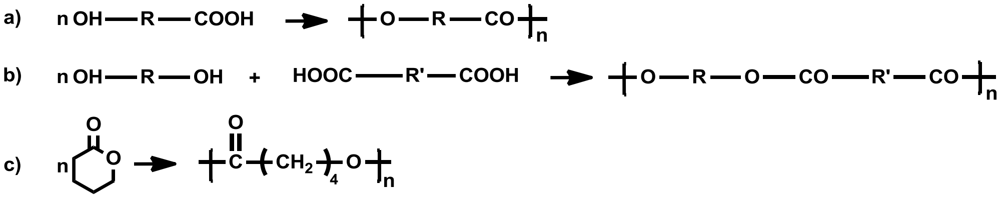
Poly(butylene succinate adipate) (PBSA)

Biodegradable aliphatic polyesters obtained from copolymerization reactions between diols and diacids have recently been commercially introduced. Bionolle (Showa Hypolymer) is a semicrystalline polyester obtained by the polycondensation reaction of BDO or 1,2-ethanediol with SA or mixture of SA and AA.[47] The properties and biodegradabilities of these copolyesters depend on the structure namely, the combination of diols and diacids used. Depending of composition the properties of Bionolle vary between those of LDPE and those of HDPE.

2.2.2. Synthetic methods

Polyesters are generally produced via several methods such as high-temperature bulk polyesterifications or enzyme-catalyzed polyesterifications. Solid state polymerization can be also used when low reaction temperatures are required which restrain side reactions and thermal degradation of the products. Moreover, polymerization can be carried out in solution but the use of environmentally unfriendly solvents make these polymerizations non suitable to be applied at industrial scale.

The synthesis of polyesters can be performed by polycondensation of hydroxyacids or diacids and diols or by ring opening polymerization of cyclic esters (Scheme 6).

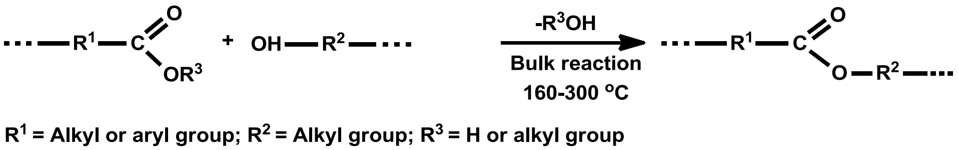


Scheme 6. Polyester synthesis: a) polycondensations of hydroxyacid b) polycondensation of diacid and diol c) ring-opening polymerization of lactones

2.2.2.1. High Temperature Bulk Polyesterifications

The synthesis of polyesters is carried out by a stoichiometric stepwise reaction between bifunctional reactants, which is accompanied by the formation of a low molecular weight condensation product in an equilibrium process. Since polyesterifications are step growth processes, the synthesis of high molecular weight polyesters requires maintaining proper end-group stoichiometry and the removal of the condensate to prevent depolymerization. Side reactions, which may cause imbalance of the reactive groups and limit the molecular weight, or may led to the formation of undesired changes in polymer structure, must also be carefully controlled.

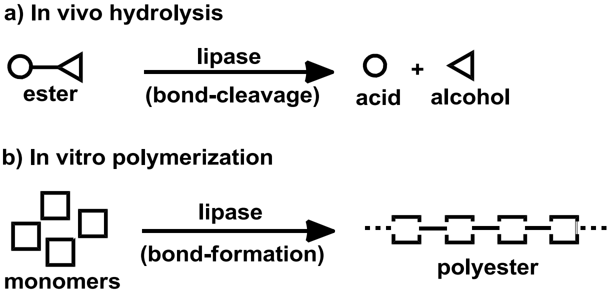
Direct esterification and transesterification polymerizations (Scheme 7) are rather slow at low temperature. These reactions must be carried out in the melt at high temperature with the presence of catalyst. Vacuum is generally applied during the last steps of the reaction to eliminate condensation by-products that form depending on the starting monomer (water or low molar mass alcohol), and to conduct the reaction toward the formation of high-molar-mass polyester. The presence of a catalyst is usually required for the preparation of high molecular weight polyesters. Metal salts and oxides, such as zinc acetate and diantimony trioxide, and organometallic compounds, mainly titanium and zirconium alkoxides are the preferred catalysts for bulk polyesterifications carried out in the 150-250 ºC temperature range.[48]



Scheme 7. Direct esterification and transesterification bulk polymerizations

2.2.2.2. Enzyme catalyzed Polyesterification

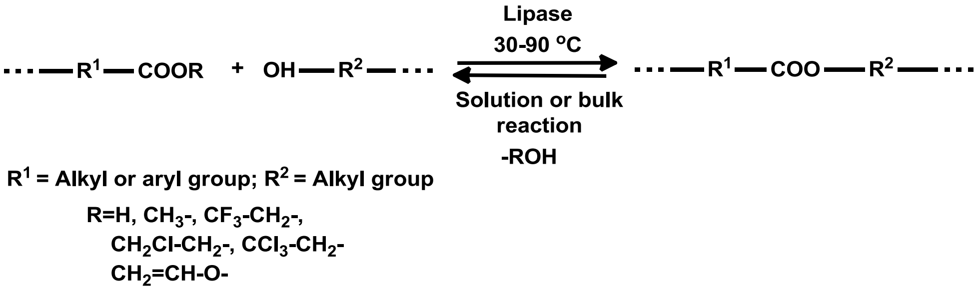
In vitro enzymatic polymerization, developed as an approach in the field of polymer synthesis, has received increasing interest during the last two decades due to some important benefits. Enzymes are biocatalysts that have high efficiency and specificity for a given chemical reaction. In the mid 1980s, in vitro synthesis of polyesters was first established by lipase catalyzed condensation reaction that yielded oligomers.[49] Lipases and esterases are hydrolylases that specifically catalyze in vivo hydrolysis of ester with bond cleavage. These type of enzymes, mainly lipases, were also found to catalyze a number of in vitro esterification and polyesterification reactions in organic medium (Scheme 8).[50]



Scheme 8. A model expression of lipase-catalyzed reactions: a) In vivo hydrolysis and b) In vitro polymerization of monomers to produce polyesters

Traditional chemical catalysts have some drawbacks including high reaction temperature (160-290 °C), toxicity and lack of selectivity, although they are widely used in the preparation of polyesters. However, in vitro enzyme catalyzed reactions occur under mild conditions such as temperatures below 100 °C, pressure and pH which enable notable energy efficiency. High substrate-, stereo-, regio- and chemoselectivities without any undesirable side reactions and the eco-friendly nature of these non-toxic substances make them appropriate candidates from the ‘green’ aspect. Enzyme catalyzed polyesterifications can proceed in solution or in bulk media by using free or immobilized enzymes. Solvent hydrophobicity plays an important role in enzymatic activity, particularly for lipases which normally act at oil-water interfaces in living cells.[51] The best reactivity is usually found for hydrophobic solvents such as hexane, toluene, diisopropylether or diphenlyether. Otherwise, hydrophilic polar solvents such as dimethylsulfoxide or methanol cause considerable modifications in enzyme conformation and for this reason decrease the catalytic activity of lipase.[52]

Many enzyme catalyzed polyesters have been prepared in organic medium by polyesterification of hydroxy acids,[53] hydroxy esters,[54] stoichiometric mixture of diols and diacids,[55] diols and diesters,[56] and diols and cyclic anhydrides.[57] Since lipases also catalyze the reverse reaction, both hydrolysis and alcoholysis of polyester, lipase-catalyzed polyesterification can be considered as equilibrium polycondensations (Scheme 9).



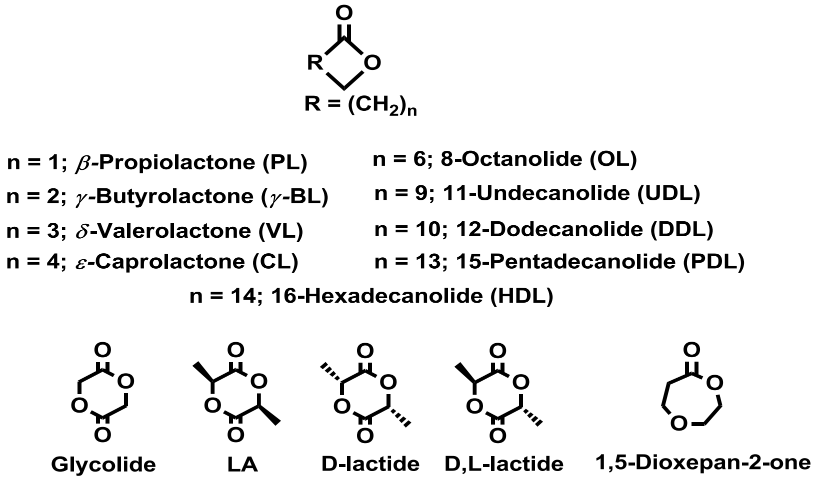
Scheme 9. Lipase catalyzed polyesterification

Various methods have been employed to remove the reaction by-product, water or alcohol, in order to displace the equilibrium toward the formation of polyester: addition of molecular sieves, Dean-Stark distillation of toluene-water azeotrope, or bubling inert gas in reaction medium. In the case of reactions carried out without solvent, vacuum can be applied to distill off the by-product.

Candida antarctica lipase B (CALB) has been widely used for the immobilized lipase-catalyzed polymerizations due to its high regio-, chemo- and enantio-selectivity and its high activity and thermal stability. This type of lipase CALB is available commercially as Novozyme 435 (N435) which consists of CALB physically adsorbed onto macroporous crosslinked beads of poly(methyl methacrylate) resin (PMMA, Lewatit VP OC 1600, Bayer).

2.2.2.3. Ring Opening Polymerization

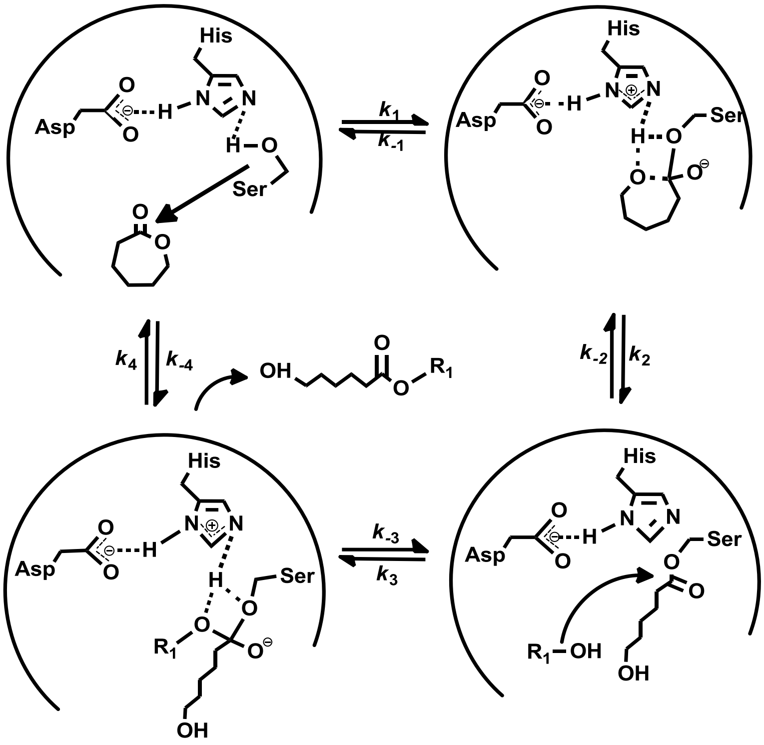
The ring opening polymerization (ROP) of cyclic esters is a very useful method to prepare degradable aliphatic polyesters. Small-sized rings such as glycolide, LA, γ-butyrolactone, δ-valerolactone and medium-sized ring such as CL, 1-5-dioxepan-2-one have been widely investigated for the studies of ROP during the past few years.[58] Scheme 10 shows some examples of lactones and lactides with different ring sizes.



Scheme 10. Lactones and lactides

Several efficient chemical catalysts have been proposed to convert the cyclic esters into well-defined and high molecular weight polyester derivatives, mainly salts or organocompounds of tin[59] , zinc[60] and aluminum.[61] In order to start the propagation of polymer chain, in some cases an initiator such as water, aliphatic alcohol or primary amine, is used.

In vitro enzyme-catalyzed ROP in a non-aqueous medium has been also extensively studied.[62] Scheme 11 shows the mechanism of enzyme-catalyzed ROP with the presence of CL as a substrate. The active site of a lipase comprises a catalytic triad consisting of serine, histidine and aspartate. The ester moiety of CL functions as the substrate and undergoes a nucleophilic attack from the primary alcohol group of serine of the enzime’s active site. Via the enzyme intermediate species, the original alkoxy group is released, forming the so-called enzyme-activated monomer (EAM) species. Subsequently, a nucleophile R_1OH can attack this EAM-species such that, via the new intermediate species, the final product is released, thereby regenerating the enzyme. In the propagation step, the EAM is attacked nucleophilically by the terminal hydroxy group of a propagating polymer to produce the polymer chain which is extended by one more monomer unit. Thus, the polymerization proceeds via an actived monomer mechanism, and the rate determining step of the overall polymerization is the formation of EAM.[63]



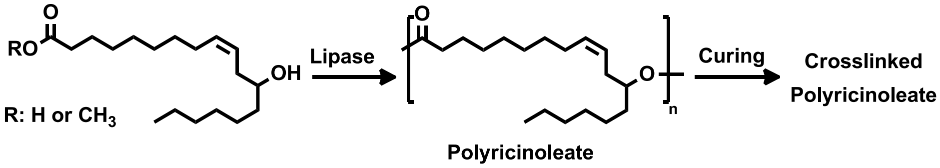
Scheme 11. Mechanism of enzyme-catalyzed ring opening polymerization of caprolactone

2.2.3. Polyesters from vegetable-oil derivatives

Aliphatic polyesters from renewable resources include together with the above mentioned PLA, PCL and PHAs, those obtained from vegetable oils, suberin, cutin, sugars and polycarboxylic acids and their corresponding derivatives. Other less common polyesters worth pointing out include the ones obtained from aminoacids which may serve as potential biocompatible materials for medical applications or terpenoids which display shape memory properties.[64]

Plant oils and more particularly fatty acids represent promising feedstock for aliphatic polyester formation as the substrate already provides aliphatic acidic or ester functions. Depending on the chemistry used, a huge range of different polyesters has been obtained. Some of recent developments are discussed in detail below.

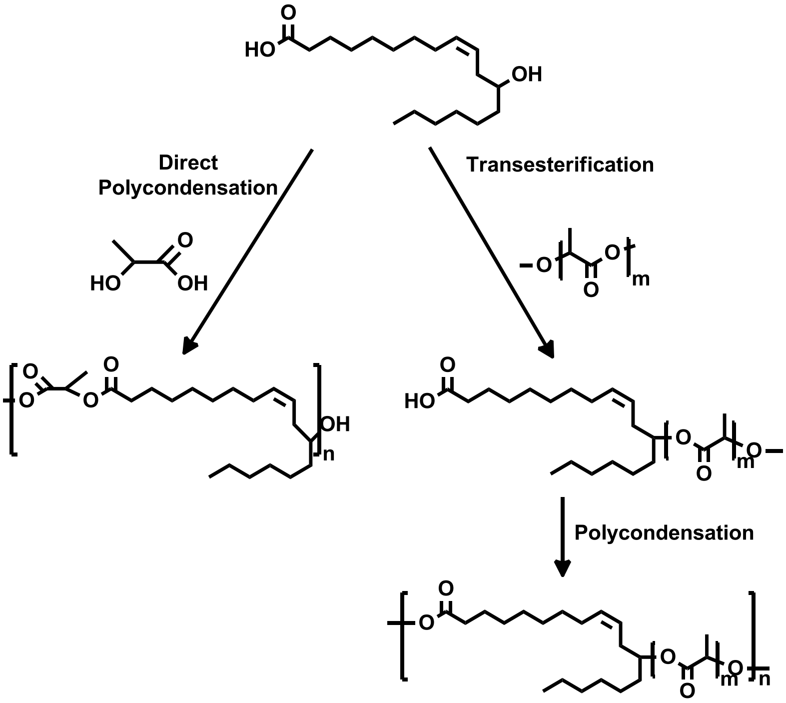
Castor oil is one the most interesting plant oil because it contains approximately 85-95% of ricinoleic acid (12-hydroxy-9-cis-octadecenoic acid), which can be readily used for the preparation of polyesters thanks to its hydroxyl functionalities.[65] Several remarkable examples of aliphatic polyesters based on the ricinoleic acid and its derivatives have been presented. In 1986, Matsumura synthesized polyricinoleate by enzymatic dehydration polycondensation of ricinoleic acid under mild reaction conditions, using lipases at 35 °C in a hydrocarbon solvent or benzene to obtain a polyester with molecular weight around 1000.[66] More recently, high molecular weight polyricinoleate was prepared by lipase catalyzed dehydration polycondensation of methyl ricinoleate (Scheme 12).[67] Methyl ricinoleic acid was polymerized at 80 °C for 7 days, with immobilized lipase PC (*Pseudomonas cepacia*). The obtained polyricinoleate with M_w of 100000 in a good yield, was further crosslinked to develop a new thermosetting elastomer.



Scheme 12. Lipase-catalyzed preparation and curing of polyricinoleate

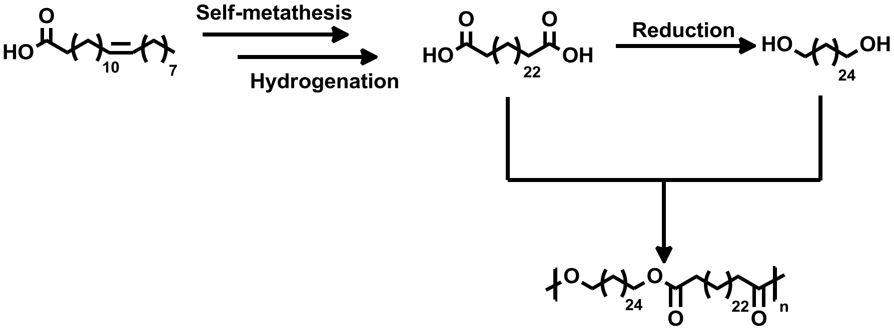
The results of this study showed the catalyst activity for ricinoleic acid polymerization although lipases are known to have low reactivity for the esterification of secondary hydroxyl groups.

In addition, castor oil has been used as a preferable resource to prepare hydroxyalkanoate based monomers that could be employed for the synthesis of versatile polyesters. Thus, Petrovic and co-workers[68] prepared high molecular weight linear polyesters from the methyl ester of 9-hydroxynonanoic acid that was obtained from ozonolysis of castor oil, followed by methanolysis of triglycerides. This polyester was synthesized in the presence of Ti(IV) isopropoxide by bulk transesterification. This bio-based polyester is an analogue of PCL but with a longer hydrocarbon chain between ester groups and has a high melting point (70 °C), glass transition temperature (-31 °C) and better thermal stability than PCL. Moreover, several investigations describe the copolyesters of ricinoleic acid with other monomers. In one example, Slivniak and Domb[69] carried out the copolyesterification with different ricinoleic acid:lactic acid ratios by direct polycondensation and by transesterification (Scheme 13). Copolymers obtained from direct polycondensation showed random character with molecular weights between 2000 and 8000 and were viscous liquids at room temperature when containing 20% ricinoleic acid. Semicrystalline multiblock copolymers were obtained from transesterification of high molecular weight PLA with ricinoleic and postpolyesterification, with molecular weight between 6000 and 14000. Because of the liquid form of these copolymers, they could be used in some applications including sealants and injectable drug carriers.



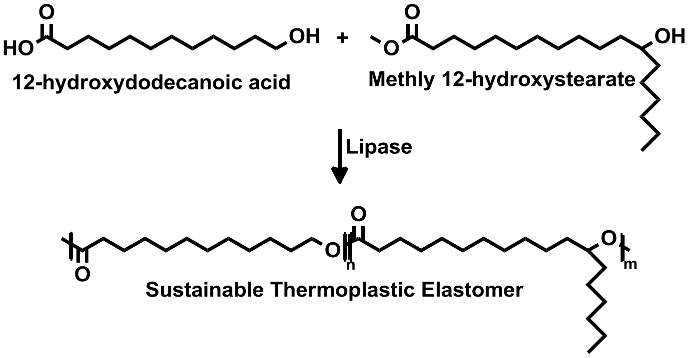
Scheme 13. Synthesis of poly(ricinoleic acid-co-lactic acid) by a) Random condensation of lactic acid and ricinoleic acid or b) Transesterification of PLA with ricinoleic acid and postpolyesterification

Other original contributions describe the preparation of long chain aliphatic polyesters from fatty acids with systems in which a fatty acid or ester is converted into a saturated α,ω-diacid or diester, which in turn is reduced to its diol counterpart in order to obtain the complementary monomer with which the corresponding polyester is synthesized by esterification or transesterification. Mecking et al. have extensively studied the preparation of linear saturated semicrystalline polyesters with long chain hydrocarbon segments, for example they synthesized aliphatic long chain C_{19}, C_{20}, C_{23} and C_{26} monomers generated from oleic acid, 10-undecenoic acid or erucic acid, by conversion into α,ω-diacids via carbonylation[70] and olefin metathesis[71] followed by reduction to α,ω-diols, which were then polymerized to yield saturated polyesters with high melting points. Vilela et al. prepared renewable long chain aliphatic polyesters from erucic acid using olefin self-metathesis for monomer synthesis (Scheme 14).[72] These above studies yielded aliphatic polyesters with chemical and physical properties which can mimic PE or other olefins.



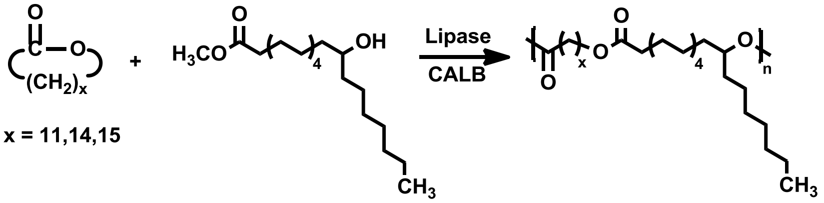
Scheme 14. Synthesis of aliphatic polyesters from erucic acid

Modification of the chemical structure of fatty acids was necessary as they usually present functionalization sites such as double bonds or hydroxyl functions in internal positions. However, this inherent internal position of the functionalization site can be great interest for the synthesis of soft materials. Indeed, after reaction of the internal function, an alkyl dangling chain remains in the structure of the fatty acid and serve as internal plastifizer. When copolymerized with linear monomers or crosslinked, thermoplastic or thermosetting elastomers are achivable. In this line, elastomers were prepared by polycondensation of 12-hydroxydodecanoic acid, which is obtained from vernolic acid, and methyl 12-hydroxystearate, hydrogenated methyl ricinoleate, using lipase Candida antarctica (IM-CA)[73] (Scheme 15). By varying of the two monomers a series of high molecular weight copolyesters were synthesized. In terms of physicochemical and mechanical properties, these biobased thermoplastic elastomers present close similarities to the well-known petroleum-based ethylene-octene and ethylene-hexene copolymers.



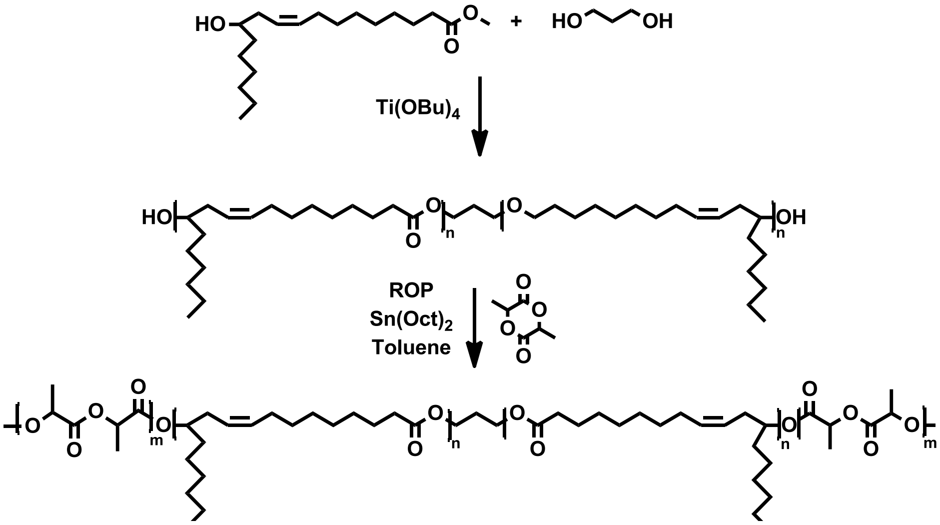
Scheme 15. Lipase catalayzed copolymerization of 12-hydroxydodecanoic acid and methyl 12-hydroxystearate

In 2011, a similar study by Matsumura[74] focused on the preparation of biodegradable and biobased thermoplastic elastomers from macrolides (dodecanolide, pentadecanolide and hexadecanolide) as a hard segment and methyl 12-hydroxystearate as a soft segment, by lipase catalyzed copolymerization (Scheme 16). Copolymers with a wide range of thermomechanical properties were obtained depending on the amount of hard or soft segments and improvement of the biodegradability is observed when the content of the soft segment content in the copolymer is increased.



Scheme 16. Enzymatic synthesis of thermoplastic elastomers

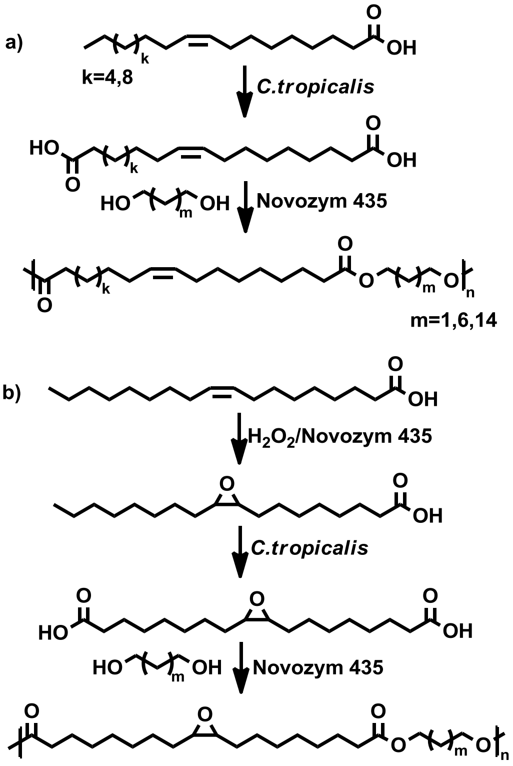
An other contribution is the synthesis and use of α,ω-hydroxy-terminated poly(ricinoleic acid) as a macroinitiator for the ring opening polymerization of LA.[75] In the first step, a hydroxy-telechelic prepolyester was prepared by self-condensation of methyl ricinoleate in the presence of a low amount of PDO and followed by ring opening polymerization of LA (Scheme 17). A series of triblock copolymers with a composition ranging from 35-83% of PLA was developed. The block structure provided good thermal properties and mechanical properties that range from thermoplastic to elastomeric, thus showing the high versatility of these copolymers.



Scheme 17. Two-step procedure to PLA-*b*-PRic-*b*-PLA triblock copolymers

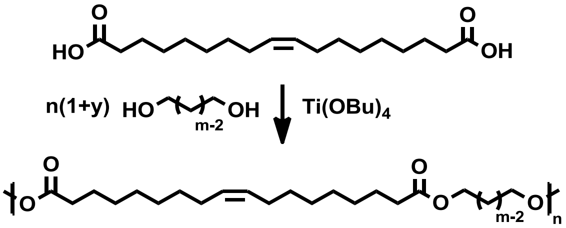
All these examples of aliphatic polyesters obtained from fatty acids are hydrophobic and free of functional groups for further modification. Reactions to induce branching, grafting or crosslinking as well as functionalization with macromolecules could be important pathways to improve thermomechanical, chemical and biological properties.[76]

An original contribution was reported by Gross and coworkers that explored also biobased functional polyesters from ω-carboxy fatty acids and diols by immobilized Candida antartica Lipase B (N435) catalyzed polycondensations (Scheme 18).[77] First, precursor biobased unsaturated and epoxy-bearing ω-carboxy fatty acid monomers, 1,18-cis-9-octadecenedioic, 1,22-cis-9-docosenedioic, and 1,18-cis- 9,10 epoxy-octadecanedioic acids were obtained from oleic, erucic and epoxy stearic acids by whole-cell biotransformations in the presence of Candida tropicalis ATCC20962. The polycondensation of these diacids with diols proceed in bulk and in diphenyl ether and linear unsaturated and epoxidized polyesters with molecular weight values ranging from 25000 and 57000 g/mol with low melting points (23-40 ^{o}C) were obtained. On the contrary, the analogous saturated polyesters from 1,18-octadecanedioic and 1,8-octanediol have a higher melting points (77-88 ^{o}C). As distinct from polyesters containing saturated diacids, the functionalizable sites of these unsaturated and epoxidized polyesters, can be modified, derivatized or crosslinked to be used as promising materials in many applications such as curable coatings or medical applications.



Scheme 18. Lipase-catalyzed polycondensation of a) unsaturated and b) epoxidized dicarboxylic acids with diols

Very recently, Roumanet et al. prepared novel aliphatic polyesters from an oleic acid based monomer.[78] 1,18-(Z)-octadec-9-enedioic acid, a derivative of high oleic sunflower oil, and aliphatic diols with different molecular weight including PDO or 1,12-dodecanediol, have been polymerized in bulk polycondensation with or without a metal catalyst (Scheme 19). Depending on the diol type, the polymer resulted to between viscous liquid and solid semi-crystalline at room temperature and gave molecular weights ranging around 7000 – 20000 g/mol. Subsequently, the double bonds of the polyester were epoxidized and the epoxy units were photochemically crosslinked. Moreover, the autors carried out the studies on the enzymatic degradation of these crosslinked polyesters that displayed no significant degradation over 8 weeks. This successful polyester synthesis can open new fields for the tailored-made new polymeric materials.

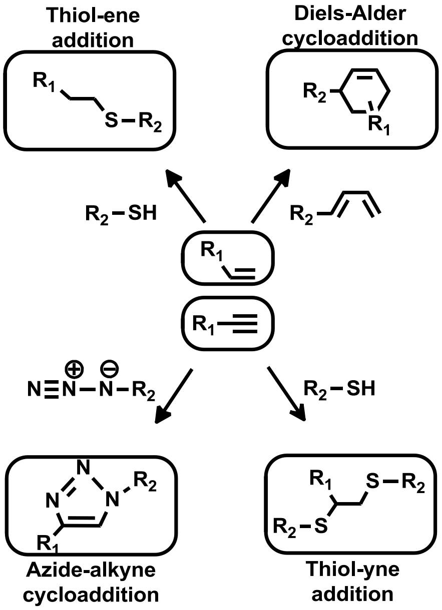


Scheme 19. Bulk polycondensation between 1,18-(Z)-octadec-9-enedioic acid and aliphatic diols

2.3. CLICK CHEMISTRY

Looking for a more environmentally friendly monomer and polymer synthesis the family of reactions collectively termed "click chemistry" helps to keep moving toward more sustainable polymer chemistry. Click chemistry reactions are often cited as a style of chemical synthesis that is consistent with the goals of green chemistry. This concept, introduced by Sharpless[79] encompasses a wide range of reactions and processes to generate organic substances and functional synthetic materials. Click reactions have many advantageous characteristics including extremely high yields, regiospecificity and stereospecificity, good tolerance to a variety of functional groups, applicability at ambient temperature and atmospheric conditions, facile experimental set-up and minimal synthetic work-up.

The copper catalyzed azide-alkyne 1,3-dipolar cycloaddition (CuAAC) is the most widely used click reaction and some extensive studies were published on the utilization of this chemistry.[80] However, the usage of copper catalyst is one of the main drawback of CuAAC click reactions. The potential toxicity of the metal catalyst is considered a major issue when the products are targetted to be used for biological applications, and thus, efforts moved to the development of metal-free variation of these reactions[81] but also other click reactions.[82] The click chemistry concept has been extended to many other highly efficient reactions such as thiol-ene[83], thiol-yne[84], Diels-Alder reactions[85] and Michael additions[86] (Scheme 20).



Scheme 20. Click chemistry reactions

Click chemistry reactions were rapidly integrated into the field of polymer chemistry. The distinctive features of these reactions, such as high efficiency, selectivity and easy purification, are of strong practical value in this discipline. The efficiency of chemical transformations is very important in the macromolecular framework. If the functionalization reaction is intended to take place at multiple sites within a single macromolecule or at the polymer end-groups, inefficiency leads to a final product in which reacted units are covalently linked to unreacted units. In these cases, no simple methods of separation lead to pure products, and the only manner to ensure purity is achieving quantitative transformations. Likewise, ortogonality is also of major concern if multiple transformations on a single polymer are desired, an ideal click functionalization procedure would allow simultaneous reactions to occur with no interferences.

As these characteristics are of special relevance in macromolecular synthesis, whereas in other fields probably not as much, the requirements of a reaction to achieve click status were adapted to this specific field.[87,88] According to the revisited concept, click reactions should use equimolar amounts of reagents to avoid complex purification techniques. For the same reason, reactions should reach very high conversions. Moreover, the reactions should proceed in a reasonable time scale and require no tedious fine-tuning of reaction conditions. This outlined requirements together with the unquestionable modularity, wide scope and chemoselectivity should be fulfilled. Satisfying or not this criteria would differentiate a click reaction from just an efficient or click-type reaction.

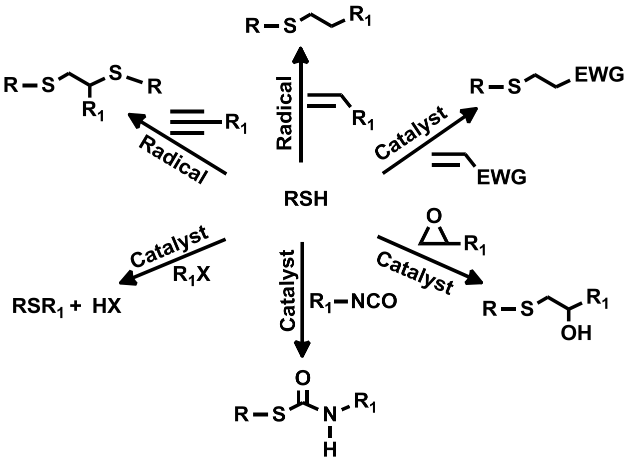
Click and click-type chemistries have been implemented in all levels of polymer science, having an important role in the functionalization of simple starting materials for monomer synthesis purposes, but also in the polymerization and even in the modification of polymers.

Some examples of the contribution of click chemistry reactions in the transformation into monomers and polymers are presented. The focus will be addressed to the obtention of polyesters

2.3.1. Thiol-Click Reactions

The thiol reactions have many attributes that incorporate the click concept, in part or in whole, and have been referred to in many circumstances as click reactions. In particular, the assignments of the thiol reactions as click reactions is done recognizing that one of the relative advantages of the thiol-click reactions, the great number of substrates that are able of reacting with the thiol due to its high reactivity, also represent one critical disadvantage in that their ortogonality is compromised. Thiols are prone to react either via radical or catalyzed processes under very mild conditions with a multitude of susbstrates. Controlling or in essence hiding the potential reactivity of thiols and inducing the selective reaction with a particular substrate is both the challenge and the oportunity for thiol-click chemistry. The reactivity of the thiols gives rise to a second relative advantage of the thiol-click reactions is that they proceed, under suitable conditions, more rapidly than many other click reactions, with reaction times to achieve high conversion frequently being less than 1-10 seconds. A distinguishing feature of these reactions is the ability to be triggered, either through photolatent base generators or through radical photoinitiating systems, by exposure to light. Finally, significant relative disadvantages of the thiol-click reactions relative to other reactions in the click family include the prevalent thiol odor, particularly for low molecular weight materials, as well as a lack of stability for many formulations.

The nature of the thiol group and the corresponding thiyl and thiolate species provides for the highly efficient thiol-based reactions with a variety of very useful and readily available organic substrates. Specifically, electron rich enes (radical), alkynes (radical), electron poor enes (Michael addition), isocyanates (carbonyl addition), epoxies (S_N2 ring opening), and halogens (S_N2 nucleophilic substitution) all readily react with thiols, thus constituting a toolbox of efficient chemical reactions (Scheme 21).

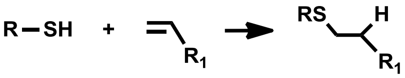


Scheme 21. Toolbox of thiol-click reactions

The two basic types of thiol-click chemistries, those proceeding by radical chain processes (thiol-ene and thiol-yne) and the one proceeding by nucleophilic reaction (thiol-Michael addition) will be discussed in the next section.

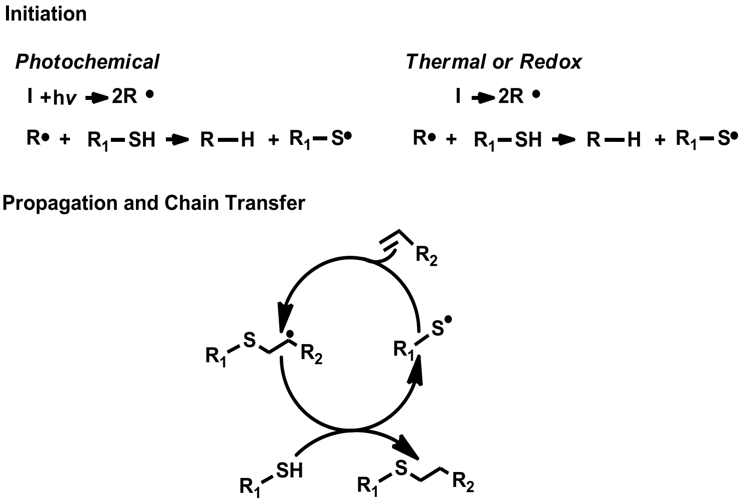
2.3.1.1. Thiol-Ene Radical Click Reactions

The earliest report on the addition of thiols to unsaturated compounds dates back to 1905 (Scheme 22).[89]



Scheme 22. Addition of thiols to double bonds

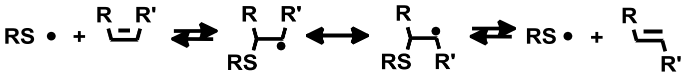
In the following decades the utilization of diolefins and dithiols to yield polymeric materials was described.[90] It was already known in the 1950s that thiols add to a double bond in the form of thiyl radicals and that the reaction involves radical chain propagation steps. Walling and Helmrich[91] reported the overall mechanism and the reversibility of some of the reactions. The mechanism comprises the “in situ” formation of thiyl radicals (both thermally or photochemically) which add to the double bond and yield a carbon radical which subsequently abstracts a hydrogen atom from another thiol compound resulting in the final addition product. A new thiyl radical is generated during the last step allowing the radical chain mechanism to propagate (Scheme 23). The rapid cis-trans isomerization during the addition of thiol to olefins make them conclude that the addition reaction is reversible.[92]



Scheme 23. The radical-mediated thiol-ene reaction mechanism

Any type of alkenes can be used in the coupling reaction with thiols. However, alkene compounds are not equally reactive, exhibiting different reactivities depending on their structures. Hoyle and coworkers[93] reported a general order of ene reactivity: Norbornene > Vinylether > Propenyl > Alkene ≈ Vinylester > N-vinylamide > Allylether ≈ Allyltriazine ≈ Allylisocyanurate > Acrylate > Unsaturated ester > N-substituted maleimide > Acrylonitrile ≈ Methacrylate > Styrene > Conjugated dienes. With the exception of norbornene, methacrylates, styrenes and conjugated dienes, the ene reactivity decreases, for the most part, with decreasing electron density of the C=C. Norbornene, methacrylates, styrenes and conjugated dienes are special cases. The rates of addition of thiols to norbornene are exceptionally rapid because a combination of the significant relief of ring strain and the subsequent rapid hydrogen-abstraction of a thiol hydrogen by the carbon centered radical. On the other hand, the rates of free radical addition of thiols to methacrylates, styrenes and conjugated dienes is low due to the high stability of the intermediate carbon-centered radicals yielding low hydrogen-abstraction rate constants in the propagation step.

According to this Hoyle's study on the reactivity of the ene depending on its substitution, terminal enes are higher reactive than internal enes. They carried out several model studies to demonstrate that 1-hexene is 8 times more reactive than trans-2-hexene and 18 times more reactive than trans-3-hexene. These results clearly revealed that steric effects are important factors in the reactivity of thiol-ene radical addition. However, these differences in reactivity are not due entirely to steric effects. As reported previously[94] thiyl radical addition to cis C=C bonds is reversible and is accompanied with an isomerization process, i.e. thiyl radicals can be employed as means of converting cis C=C bonds to trans C=C bonds with high efficiency (Scheme 24).



Scheme 24. Reversible addition of the thiyl radical to the disubstituted ene

In the following decades the addition of thiol compounds to unsaturations took its place among the most common organic reactions and a number of reviews were published, for example Griesbaum reviewed structure and reactivity relationship, reaction rate and reversibility.[95] Nuyken in 1990 reported the synthesis of telechelics from aromatic and/or aliphatic dithiols and diolefins via spontaneous addition under UV radiation.[96] In 1991, Klemm et al. reported the linear photopolymerization of the dithiols and diolefins to clarify the self-initiation mechanism and to find a potential inhibitor against the high reactivity of the homogenous thiol-ene mixtures.[97] Very recently, this mechanism of self initiated thiol-ene reaction was studied by Metzger.[98] The results clearly revealed the thermal generation of thiyl radicals and therefore the low self-life stability of alkene and thiol mixtures was explained.

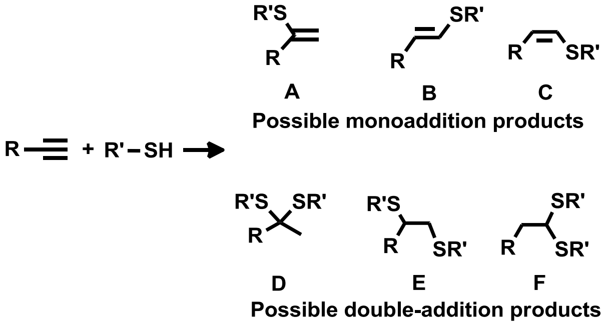
Apart from the discussion of the mechanism, the thiol-ene addition was already exploited for diverse functionalization protocols. For example in 1998 Boutevin et al.[99] employed this chemistry to introduce thiol functionality to phosphorus-compounds and to graft the phosphonated thiol to polybutadiene. Johansson et al.[100] studied the coupling reaction between mercapto acetate and propionate esters to methyl oleate and linoleate. Compared with linoleate, the isomerization ratio of oleate was higher, and this was attributed to a somewhat restricted rotation along the unreacted linoleate C=C bond.

Not only the structure of thiols and the unsaturated compounds, but also the reaction conditions play an important role in the overall success of the reaction. The first systematic study on the efficiency of the initiation reaction depending on the type of initiatior was reported by Yagci’s group in 2010. The thiol-ene reactions between a series of alkene with thiol-end functional polystyrene using both cleavage (Type I) and H-abstraction (Type II) type initiators and the classical thermal radical initiation were studied.[101] From the results, the authors conclude that the thiol-ene coupling reactions have the characteristics of a click reaction and the use of photochemical and thermal initiators Type I, such as (2,4,6-trimethlybenzoyl)diphenlyphosphine oxide or 2,2-dimethoxy-2-phenyl acetophenone (DMPA) leads to highest efficiencies.

2.3.1.2. Thiol-yne Radical Click Reactions

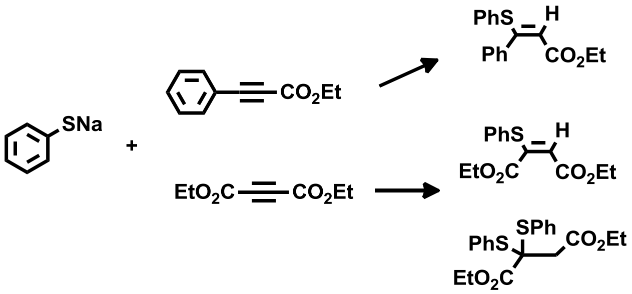
The thiol-yne reaction is regarded as a sister reaction of radical-mediated thiol-ene reaction and complementary reaction of Cu-mediated alkyne/azide cycloaddition reaction. The earliest reports on the hydrothiolation of a carbon-carbon triple bond have been known for the beginning of the twentieth century.[102] A distinguishing feature of thiol-yne reaction different from the Markovnikov and anti-Markovnikov addition of a thiol to a terminal alkene yielding two possible species, is that the addition of a thiol to terminal carbon-carbon triple bond yields six possible products. This means that carbon-carbon triple bond reacts with two equivalents of thiol resulting in a double addition product with 1,2-regioselectivity.

Scheme 25 presents six general possible modes of additions that are three possible monoaddition species **A-C** and the bis-addition products **D-F**. The monohydrothiolation of a thiol to terminal acetylenic bond can result in one Markovnikov product, **A** and two anti Markovnikov species, **B** and **C**, the cis and trans isomers of vinyl sulfide. For internal alkynes, **E** and **Z** stereoisomers are formed. There are three possible double-addition products by the addition of two equivalents of thiol; dithioacetal derivatives **D** and **F** or 1,2-addition product **E**.



Scheme 25. Possible addition products for the mono- and bis-hydrothiolation of terminal alkyne bond

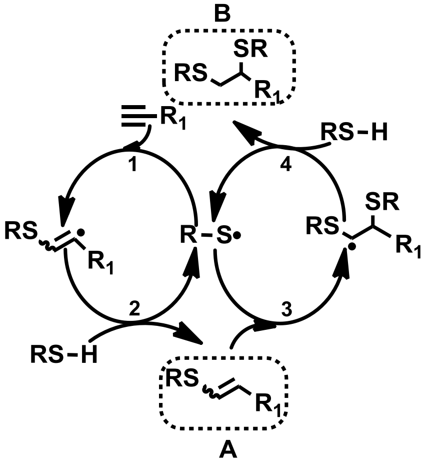
Rhuemann and coworkers[101a] discussed the reactions between sodium thiophenolate and two internal alkyne substrates, ethyl phenylpropiolate and ethyl acetylenedicarboxylate (Scheme 26). The formation of the monoaddition product at the more electrophilic C atom of ethyl phenylpropiolate occurs as expected in a Michael type conjugate addition reaction. In contrast, in the case of ethyl acetylenedicarboxylate, both mono- and bis-addition products were obtained. The double addition occured at the same carbon atom resulting in a dithioacetal derivative.



Scheme 26. Reaction of sodium thiophenolate with ethly phenylpropiolate or ethyl acetylenedicarboxylate

In 1949, Bader et al.[103] detailed the reaction between thiolacetic acid and several alkynes such as 1-hexyne, phenylacetylene, 1,7-octadiyne and methyl propargyl ether by using peroxides or UV irradiation. As an example, for 1-hexyne both the mono (1-substituted) and di-(1,2-substituted) addition products could be obtained with satisfactory yields. Additionally, the authors noted that the mono addition product could be readily converted into the 1,2-disubstituted species simply by heating in presence of additional thiolacetic acid.

The proposed mechanism of the double radical hydrothiolation to terminal alkyne bond is shown in scheme 27. Thiyl radical, R-S•, is generated thermally or photochemically, with the addition of photoinitiator or without photoinitiator. In step **1**, a thiyl radical undergoes to direct addition to yne bond to give a reactive intermediate vinylthioether radical. This intermediate radical realized a chain transfer reaction with additional thiol to give the vinylthioether intermediate, **A**. Then, highly reactive vinylthioether intermediate subsequently reacts with a second thiyl radical in step 3 as in a thiol-ene reaction, to yield an intermediate carbon-centered radical that undergoes a second chain transfer reaction resulting the 1,2-disubstituted dithioether product, **B** (Step 4).



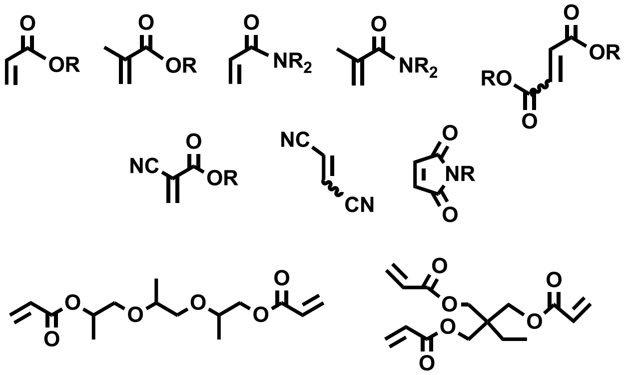
Scheme 27. The radical-mediated thiol-yne reaction mechanism

2.3.1.3. Thiol-Michael Addition Reactions

The Michael addition reaction is a versatile synthetic methodology for the efficient coupling reactions of electron poor olefins with a wide series of nucleophiles. The reaction, which is also commonly termed conjugate addition, has recently gained increased attention as a polymer synthesis strategy for tailored macromolecular architectures.[86] The Michael addition benefits from mild reaction conditions, high functional group tolerance, a large host of polymerizable monomers and functional precursors as well as high conversions and favourable reaction rates.

This reaction lends itself to both step growth and chain growth polymerization and has been employed in the synthesis of linear, graft, hyperbranched, dendritic and network polymers. Furthermore, post-polymerization modification and coupling of biological and synthetic polymers are often facilitated by the Michael reaction.[104] These features make the Michael addition reaction well-suited to numerous emerging technologies including biomedical applications.

A Michael addition requires the addition of a nucleophile, the ‘Michael donor’, to an activated electrophilic olefin, the ‘Michael acceptor’, leading to a ‘Michael adduct’. Although this reaction is generally considered the addition of enolate nucleophiles to activated olefins, a wide range of functional groups possess sufficient nucleophilicity to perform as Michael donors. Reactions involving non-enolate nucleophiles such as amines, thiols, and phosphines are typically referred to as Michael type additions or hetero-Michael additions. The Michael acceptor possesses an electron withdrawing and resonance stabilizing activating group, which stabilizes the anionic intermediate. Michael addition acceptors contain withdrawing activating groups that enable the Michael addition to olefins and alkynes. Acrylate esters, acrylonitrile, acrylamides, maleimides, alkyl methacrylates, cyanoacrylates and vinyl sulfones serve as Michael acceptors and are commercially available (Scheme 28). Less common, but equally important, vinyl ketones, nitro ethylenes, α,β-unsaturated aldehydes, vinyl phosphonates, vinyl pyridines, azocompounds and even β-keto acetylenes and acetylene esters also serve as Michael acceptors.[105] It is important to note that the product of the first Michael addition has a remaining active methylene hydrogen in many cases, which can undergo a second addition to another Michael acceptor.

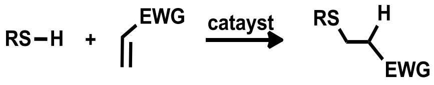


Scheme 28. Some Michael addition acceptors

The reactivity of the acceptor will decrease if the substituent of the α,β-unsaturated carbonyl compound is electron rich, such as in the case of alkyl, aryl or carboethoxy substituted olefins such as styrene derivatives or vinylethers. Sterics are also an important factor. The larger the groups substituted at the α and β positions, the slower the reaction rate and differences in reactivity between acceptors require differences in nucleophilicity of the Michael donors. For instance, alkyl methacrylates are relatively poor Michael acceptors and strong nucleophiles are necessary for successful

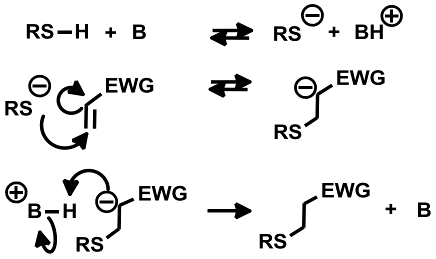
Michael additions. Better acceptors such as alkyl acrylates or acrylamide accept weaker amine and thiol nucleophiles.

Thiols are readily used as heteroatomic 'donors' in the Michael addition and this reaction has been known since the last peridos of 1940s.[106] Depending on the substrate, this reaction has been referred to as thia-Michael, thiol-Michael, thio-Michael, sulfa-Michael and more recently thiol-maleimide click and thiol-based click reaction.[107,108] In this thesis we simply refer to this click reaction as a thiol-Michael reaction, being the ene electron deficient, such as in acrylates, methacrylates, maleimides, α,β-unsaturated ketones, fumarates, acrylonitrile, cynamates and crotonates (Scheme 29). Traditionally, a wide variety of catalysts have been used to initiate the thiol-Michael addition including strong bases, metals, organometallics and Lewis acids.[86]



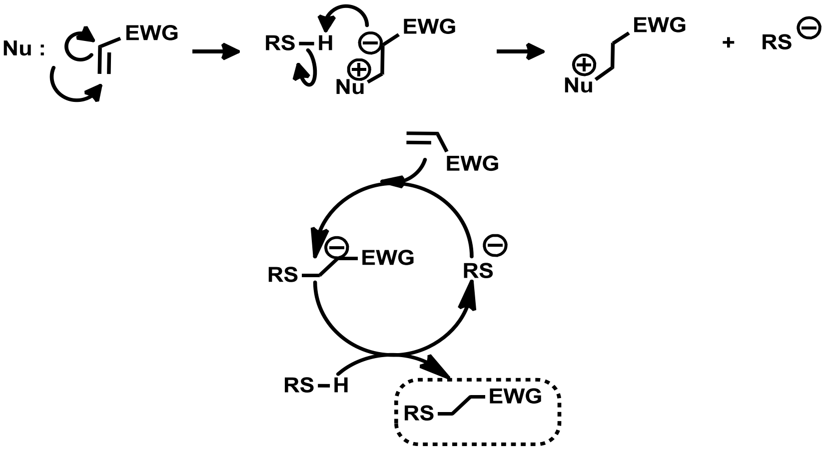
Scheme 29. Thiol-Michael addition a C=C bearing an electron-withdrawing group (EWG)

The proposed mechanism for base catalysed hydrothiolation of an activated C=C is shown in scheme 30. The base deprotonates the thiol to generate the thiolate anion RS^- and the corresponding conjugate acid BH^+. The powerful thiolate nucleophile attacks the electrophilic β-carbon of the activated C=C bond yielding an intermediate carbon-centered anion. This anion is a very strong base that abstracts a proton from the cation, the conjugated acid BH^+, resulting the thiol-Michael addition product by regeneration of the base catalyst.[109]



Scheme 30. Proposed base-catalyzed mechanism for the hydrothiolation of an activated C=C bond

While the traditional base-catalyzed thiol-Michael reaction is a highly versatile process, significant efforts are being expended on the development of novel catalytic systems that efficiently and cleanly effect such thiol-Michael additions. A strategy of using primary or secondary amines or even more powerful and efficient nucleophilic alkylphosphine catalysts for extremely efficient thiol-Michael addition has emerged during the last few years. A proposed mechanism for such a nucleophile mediated thiol-Michael addition reactions is given in scheme 31. The nucleophile (amine or phosphine) undergoes conjugate addition to the activated C=C bond generating the strong intermediate carbanion that deprotonates the thiol, generating a thiolate anion that then enters an anionic chain process in which the thiolate anion undergoes direct thiol-Michael addition, regenerating the strong carbanion that deprotonates more thiol with concomitant generation of the thiol-Michael product.



Scheme 31. Proposed mechanism for the nucleophile-mediated hydrothiolation of an activated C=C bond

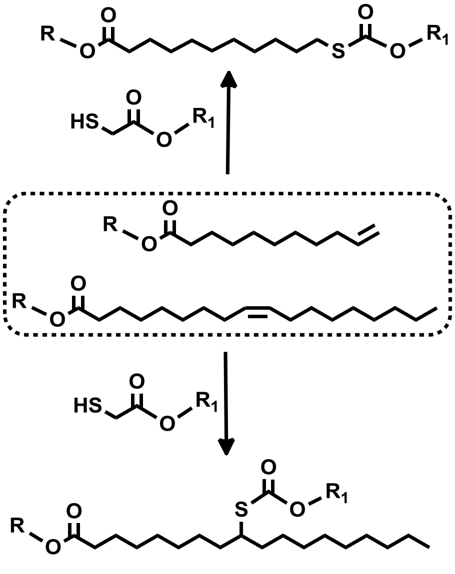
Thiol-Michael addition reactions can be also catalyzed by Lewis acids such as $Sc(OTf)_3$ chiral bipyridine complex used in assymetric Michael reactions.[110] Moreover, amphoteric vanadyl triflate catalyze Michael addition reactions with N-, P- and C- centered protic nucleophiles.[111]

Traditional base-catalyzed and nucleophile-mediated thiol-Michael addition reactions have the characteristic features of click reactions including rapid reaction rates, insensitivity of air and moisture, proceeding under bulk conditions, simple cleaning methods and quantitative yields.[112]

2.3.2. Applications of Thiol-Click Reactions to Plant Oils and Fatty Acid Derivatives for the synthesis of polyesters

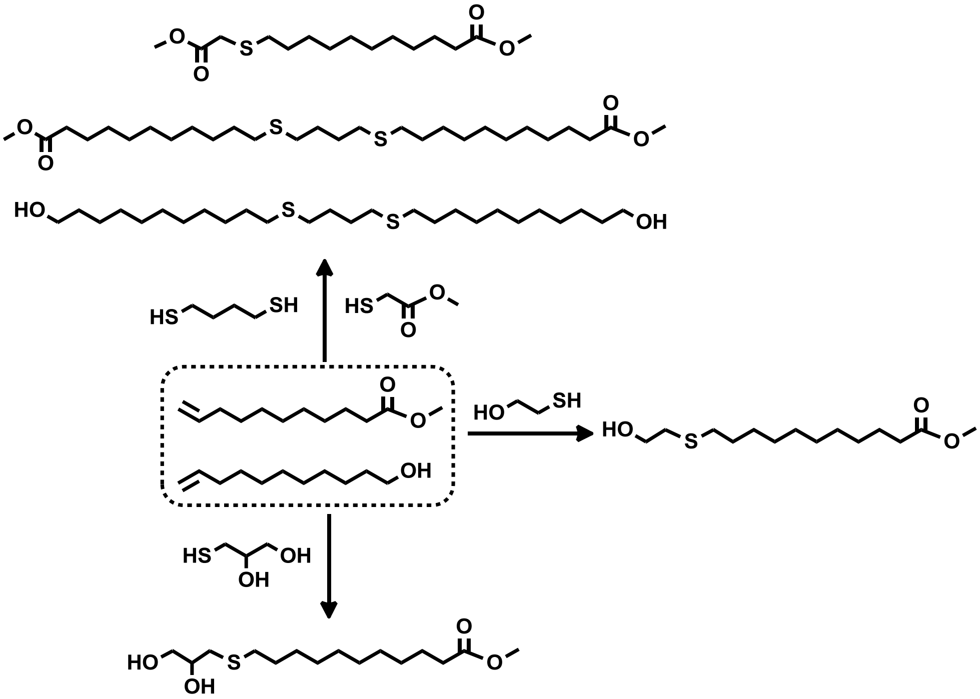
Although hydrothiolation reaction has been intermittently applied to fatty acids since more than 50 years ago, oleochemistry undoubtly has made the most of this reaction in the last years.[113] In particular, attention has been paid to the preparation of polycondensable monomers from isolated fatty acids for polyester synthesis. It is also worth noting at this point that hydrothiolation reaction has also been used as polymerization tool in the preparation of linear polymers from fatty acids, as well as a post-polymerization modification tool of well defined reactive fatty acid-based polymers. The thiol-ene click reaction is used to bring either an alcohol or a carboxylic function to a fatty acid backbone. All the attention has almost focused on monounsaturated fatty acids such as oleic and 10-undecenoic acids as well as their derivatives because their pòtential for the preparation of strictly bifunctional polymer precursors.

In 1957, Koenig and coworkers reported the first systematic studies on the modification of fatty acids and their esters including undecenoate and oleate with mercaptoacetate resulting various diester and/or diacid compounds (Scheme 32).[114]



Scheme 32. Modification of fatty acids with mercapto acetate

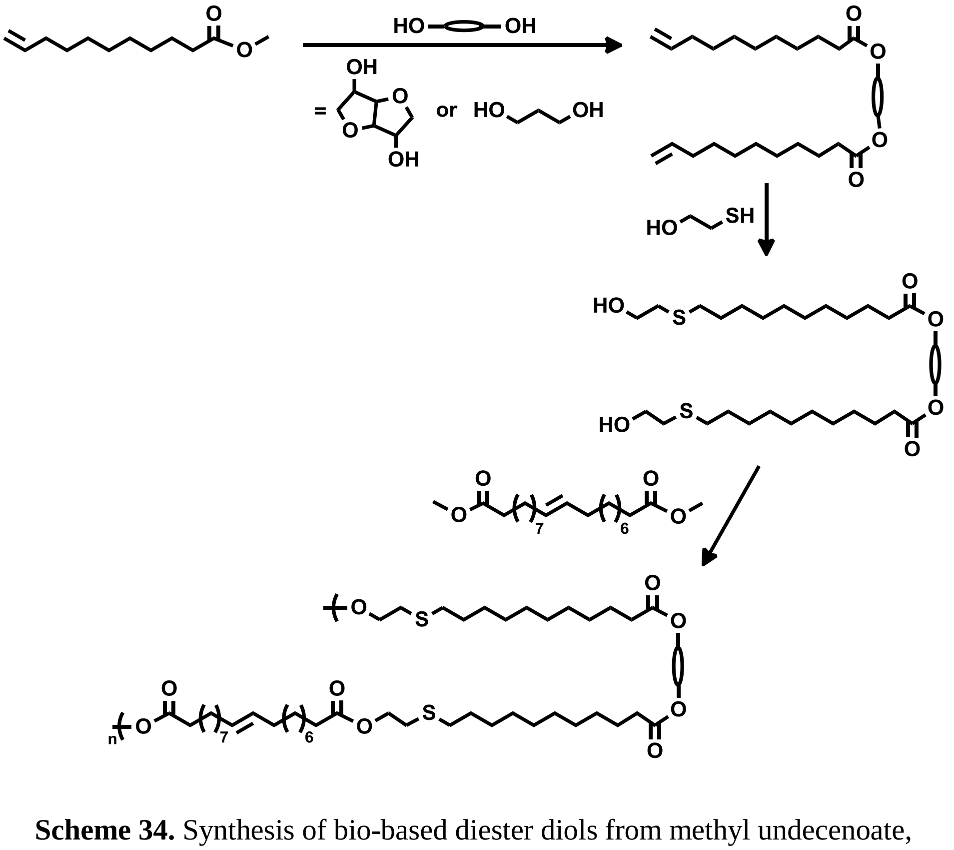
Recently, Meier and coworkers reported an efficient route to the development of a set of renewable monomers for polyester synthesis. These monomers were synthesized by thiol-ene reactions from castor oil derivatives such as methyl 10-undecenoate and 10-undecenol, and various thiols such as mercaptoethanol, butanedithiol, methylthioglycolate and thioglycerol (Scheme 33).[115] The hydrothiolation reactions were conducted at 1:1 ratio of reactive groups in solvent free conditions without adding any photochemical or thermal initator. The monomers were polymerized to linear and hyperbranched polyesters bearing thio-ether linkages by using 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) as a catalyst. The final polymers with molecular weights 4-10 kDa displayed melting points ranging between 50 °C and 71 °C and thermal stabilites up to 300 °C. A higher crystallization rate and melting point were observed for polyesters with longer chain lengths between ester linkages.



Scheme 33. Synthesis of new polycondensable monomers via thiol-ene coupling

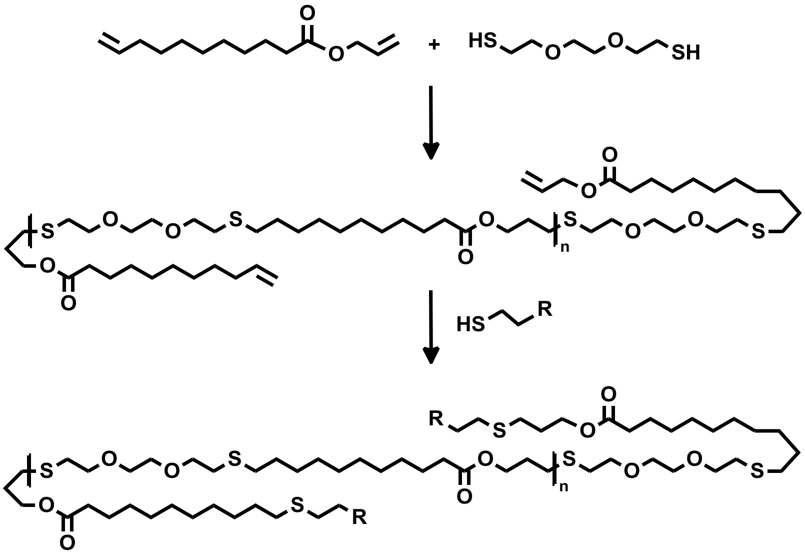
Li and coworkers also reported thioglycerol addition to methyl 10-undecenoate in a DMPA photoinitiated thiol-ene reaction. In this case higher yields and lower reaction times compared with the ones reported by Türünç and Meier are described. The obtained monomer was polymerized by self condensation under various reaction conditions to give hyperbranched polyesters with high molecular weights and unusual crystalline properties.[116]

Cramail also employed thiol-ene addition to introduce hydroxyl functionalities on unsaturated diester compounds obtained from methyl 10-undecenoate and 1,3-propanediol isosorbide.[117,118] The resulting diols were condensed with a methyl diester, obtained by self-metathesis of methyl 10-undecenoate, yielding various polyesters (Scheme 34). Regarding to thermal properties, the polyesters exhibited low melting temperatures, low glass transition temperatures from -31 °C to -24 °C and good thermal stability with no significant weight loss below 350 °C.



Scheme 34. Synthesis of bio-based diester diols from methyl undecenoate, propanediol and isosorbide as well as polyester synthesis

The outstanding efficiency and high reaction rate demonstrated by thiol-ene addition performed on terminal C=C bonds encouraged several researchers to investigate its performance as oligomerization/polymerization tool of 10-undecenoic acid-derived α,ω-dienes using bifunctional thiols. For example, our research group described the rapid synthesis of biobased oligomeric telechelics using two ‘‘one pot’’ thiol-ene click couplings.[119] In the first step, an excess of difunctional ene, allyl 10-undecenoate was photochemically reacted with a dithiol compound, 3,6-dioxa-1,8-octanedithiol, with DMPA as photoinitiator to give oligomers having allyl ester end groups. Subsequently, in order to obtain hydroxyl telechelics, the coupling with different thiols by photo-initiated thiol-ene reaction was carried out (Scheme 35).

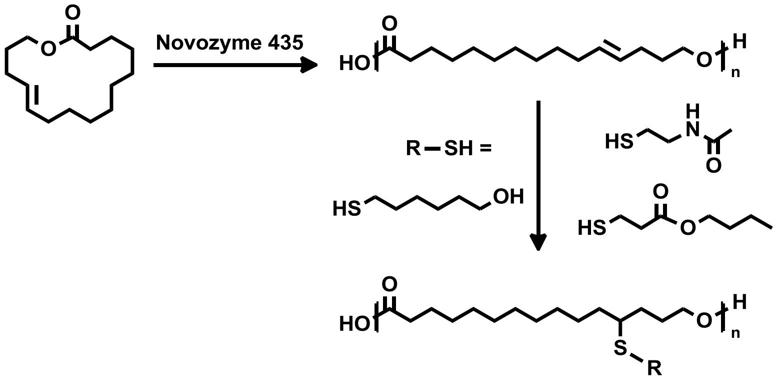


Scheme 35. Synthesis of telechelic polyester oligomers via sequential radical thiol-ene coupling

Meier and coworkers also reported the succesful preparation of medium molar mass polymers containing different functionalities in the main chain from dienes based on 10-undecenoic acid using a dithiol as coupling agent. For example, polyester from a bis-unsaturated diester, obtained by transesterification of methyl 10-undecenoate with biobased PDO, and bis (2-mercaptoethyl) ether was succesfully obtained by applying the AIBN thermally initiated version of thiol-ene addition.[120]

Beyond the synthesis and polymerization of fatty acid-based monomers, the thiol-ene addition has also been employed by several research groups as a facile and convenient tool for the post-polymerization modification at main chain, side chain and end groups of some plant oil derived polymers.

As an example, Heise and coworkers described the thiol-ene functionalization of a polyester from globalide, a unsaturated macrolactone synthesized from hydroxy fatty acid.[121] The double bond containing aliphatic polyester was modified on the main chain by three different thiols including butyl-3-mercaptopropionate, mercapto-1-hexanol and *N*-acetylcysteamine (Scheme 36). Thiol-ene modifications were performed with 6.6-11.0 equiv of thiol in the presence of AIBN as thermal initiator at 80 °C for 24 h. The degree of modification was higher than 95% for mercapto-1-hexanol and *N*-acetylcysteamine whereas lower efficiency (75%) was achieved on the addition of butyl ester.

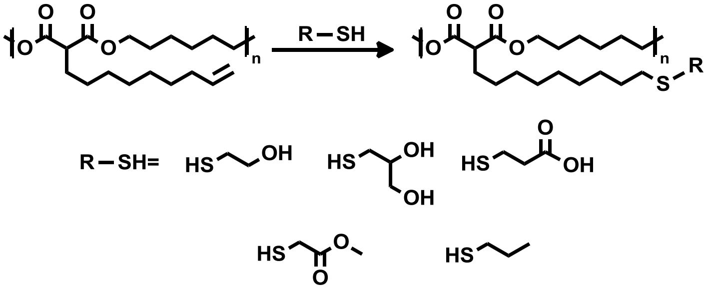


Scheme 36. Main chain modification of fatty acid derived aliphatic polyester from globalide

In a similar approach, the same group recently published a study on thiol-ene crosslinking of films of N-acetylcysteamine functionalized poly(globalide) and ethylene glycol bis(3-mercapto propionate) with various crosslinking ratios.[122] Subsequently, surface amine functionalization was achieved by thiol-ene grafting 2-(Boc-amino)ethanethiol onto the poly(globalide) surface.

Kolb and Meier investigated the modification of well-defined side-chain functional polymers prepared from 9-nonyl malonate and 1,6-hexanediol. High degrees of modification were reported when using several commercial available thiols bearing different functionalities such as hydroxyl, carboxylic acid and ester (Scheme 37).[123]

Side reactions such as radical-initiated ring closure of the side chain during the modification were not observed.



Scheme 37. Post-polymerization modification of the side chains of alkene-functionalized poly(malonate)s

Finally, the end groups functionalization of the above mentioned low-molecular-weight linear oligomers was also investigated (Scheme 35).[119] It was demonstrated that photo-initiated thiol-ene reaction at the chain ends of these oligomers with a slight excess of thiol allowed the preparation of perfect telechelics with hydroxyl, carboxyl or trimethoxysilyl groups in quantitative yields.

In a polymer chemistry context, the application of thiol-yne coupling to oleochemicals is limited to only two contributions focused to transform alkyne-derivatized fatty acids into (a) polyurethane building blocks and (b) functional comblike polymers. In both examples, the ability of acetylene groups to accept rapidly two thiols under radical conditions is exploited. In the search of biobased functional diols for polyurethane technology, our group[124] applied thiol-yne addition to 10-undecynoic and stearolic acid methyl esters. Unlike thiol-ene addition to fatty acids, thiol-yne addition to their alkyne derivatives allows double primary hydroxyl functionalization without compromising carboxylic acid group. Both synthesized diols, obtained in high yields as viscous oils, were combined with methylene diphenyl diisocyanate to yield thermoplastic polyurethanes containing pendant methyl ester groups. Alternatively, those products were also used to prepare two fatty acid-derived triols suitable for the preparation of polyurethane networks by subsequent reduction of the ester groups. Turunc and Meier[125] investigated the direct polymerization of monoalkynes via thiol-yne addition. First, optimal polymerization conditions were determined using 1-octyne and octanethiol, as model compounds, in the absence of initiator or using either thermally (AIBN) or photochemically (DMPA) radical initiation. Using an alkyne:thiol ratio of 1:2 UV initiated reaction gave the best results. Expanding on these initial findings, the authors examined the ability to prepare a range of functional polymers using the radical thiol-yne addition using dithiols. The polymerization of several functional monoalkynes such as 10-undecynoic acid and propargylic acid was investigated showing that highly functional comb-like linear polymers are accessible via this approach.

Finally, the ability of acetylene groups to accept only one thiol under radical conditions has been explored to obtain an unsaturated diol from 10-undecynol. A thiol-reactive linear polyurethane was synthesized by reaction with a commercial diisocyanate.[126]

As has been previously mentioned, the highly efficient thiol-Michael addition has been widely implemented in materials science.[108] However, it has not been applied to vegetable oil derivatives. Only one example describes the use of this reaction to synthesize an hydroxy acid from oleic acid and its polyesterification.[127]

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Chapter 3

Fully Biobased Triblock Copolyesters from L-lactide and Sulfur-Containing Castor Oil Derivatives

Introduction

As has been explained in the previous chapter, biodegradable and renewable derived polymers have attracted much attention due to the environmental concerns and sustainability issues associated with petroleum based polymers. One of such polymers is PLA, a biodegradable and bioabsorbable, renewable derived thermoplastic polyester extensively investigated over the last several decades.[1]

PLA development initiated with the lactide production formulas published by Bischoff and Walden in 1893. In 1932, Carothers and coworkers produced low molecular weight PLA. Dupont de Nemours and Ethicon, Inc. began marketing PLA in medical applications for sutures implants and drug delivery systems in 1954. Shimatzu Corporation and Canebo Johsen Ltd. Japan produced PLA fibers by melt spinning in the laboratoty in 1992 and started commercial production of PLA fibers under the trade name Lactron in 1994. Cargill Dow LLC, USA started commercial production of PLA from starch under the trade name NatureWorks at a capacity of 140.000 ton/year in 2002. In 2003, this company introduced PLA fiber in Ingeo™ spun from NatureWorks™.[2]

PLA offers many advantages. Apart from being derived from renewable resources (e.g. corn, wheat, rice) PLA is biodegradable, recyclable and compostable. Its production also consumes carbon dioxide. These sustainability and eco-friendly characteristics make PLA an attractive biopolymer. However, the most attractive aspect of PLA, specially with respect to biomedical applications, is its biocompatibility.[3,4] PLA does not produce toxic or carcinogenic effects in local tissues and hydrolyzes to its constituent α-hydroxy acid when implanted in living organisms, being incorporated into the tricarboxylic acid cycle and excreted. The food and drug administration (FDA) has also approved PLA for direct contacting with biological fluids. Other PLA advantage is its better thermal proccesibility compared to other biopolymers such as PHAs, poly(ethylene glycol) (PEG) and PCL. It can be processed by injection molding, film extrusion, blow molding, fiber spinning, and film forming. Finally, PLA requires 25-55% less energy to produce than petroleum based polymers and estimations show that this can be further reduced to less than 10% in the future.[5]

In spite of these advantages, PLA has drawbacks as well, which limit its use in certain applications. PLA is a very brittle material with less than 10% elongation at break. Although its tensile strength and elastic modulus are comparable to PET, the poor toughness limits its use in the applications that need plastic deformation at higher stress levels.

PLA degrades through hydrolysis of backbone ester groups and the degradation rate depends on crystallinity, molecular weight, molecular weight distribution, morphology, water diffusion rate into the polymer and the stereo isomeric content. The degradation rate is an important selection criterion for biomedical application since a slow degradation rate leads to a long in vivo life time, which could be up to years in same cases. The slow degradation rate is a serious problem with respect to disposal of consumer commodities as well. PLA is relatively hydrophobic with a static water contact angle of aproximately 80º. This results in low cell affinity, and can elicit an inflammatory response from the living host. Finally, PLA is chemically inert with no reactive side chain groups making its surface and bulk modifications a challenging task.

The succesful implementation of PLA in consumer and biomedical applications relies not only on mechanical properties being better than or comparable to conventional plastics but also an controlled surface properties. PLA has been bulk modified mainly to improve toughness and degradation rates. The surface modification of PLA has been attempted to control hydrophilicity, roughness and to introduce reactive groups.

The toughness improvement is a crucial necessity for many consumer applications and therefore many efforts have been made to improve PLA toughness including manipulation of crystallinity,[6] plasticization,[7,8] blending with other polymers[9-13] and incorporation into block copolymers.[14-18]

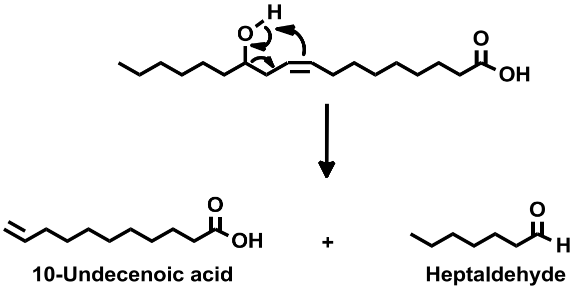
A recent trend for toughening PLA is to use degradable, renewable polymers including starch,[19] PBS,[20,21] PHAs,[22] polymerized soybean oil[23] and polyamide 11,[24] as a challenge to find a completely renewable and biodegradable toughening agent that enhances PLA properties. However, most tougheners derived from renewable resources are less effective than those derived from petroleum resources in improving the PLA toughness. Consequently, the obtention of block copolymers is a better approach to develop biocompatible, highly toughened PLA which retains both completely renewable origins and the ultimate degradability.[8]

Multiblock polymers attract interest because they are expected to have distinct microstructures, offering alluring opportunities to generate exquisitely tailored materials with unparalleled control over nanoscale-domain geometry, packing symmetry, and chemical composition, thus exhibiting different mechanical behaviour compared to conventional polymers with simple structures.[25] Moreover, advances in synthetic polymer chemistry methods allow access to numerous structures of multiblock copolymers and a considerable number of different strategies have been used. As concerns PLA-based block copolymers, one can distinguish between those synthesized by sequential ring opening polymerization (ROP) when comonomers are cyclic esters or carbonates, and block copolymers synthesized by distinct polymerization methods. In the latter case, most of the time, a macroinitiator is first synthesized by another polymerization method than ROP and then ROP of lactide is initiated by the reactive functions of the macroinitiator.

In this Chapter the synthesis and characterization of fully biobased triblock copolyesters from PLA and castor oil derivatives is described. The synthetic strategy selected was to design a dihydroxy telechelic polyester as a macroinitiator for ROP of L-lactide (LA). This approach consisted on the use of a sulfur-containing hydroxyacid derived from castor oil, which self-polycondensation initiated with low amounts of biobased BD, enables the obtention of a dihydroxy terminated prepolymer, which initiates the ROP of LA to reach the targeted triblock copolymer. The introduction of polar groups by oxidation of the main chain sulfide moiety to sulfone is expected to increase polarity and thus, changes in the thermal behaviour and crystallinity of the polymers are expected.

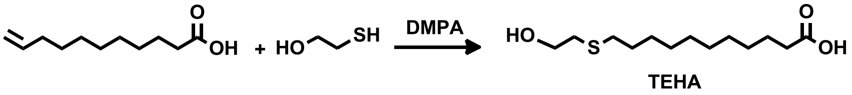
Monomer Synthesis

Castor oil is extracted from the seeds of the castor bean plant (*Ricinus communis*) which is a member of the large spurge family (Euphorblaceae), located in tropical Asia and Africa. Castor oil contains up to 90 % of ricinoleic acid, a mono-unsaturated 18-carbon fatty acid with a hydroxyl function at position 12, which tends to cleavage upon heating. Thus, 10-undecenoic acid can be obtained from the pyrolysis of castor oil at high temperature (>400 ºC) that cleaves the ricinoleate molecule yielding this compound and heptaldehyde. Several mechanisms, including a McLafferty-type rearrangement[26] (Scheme 1) and a free-radical mechanism[27] have been proposed for the transformation of ricinoleic acid into 10-undecenoic acid and heptaldehyde.



Scheme 1. McLafferty-type rearrangement of ricinoleic acid to 10-undecenoic acid and heptaldehyde

Thiol-ene coupling of mercaptoethanol and 10-undecenoic acid leads to an AB monomer containing both hydroxyl and carboxylic functionalities. Synthesis of this monomer was previously described by simply stirring mercaptoethanol and 10-undecenoic acid for 1.5 hours at 60 ºC. Moreover, reaction has also been described to take place when UV irradiated.[28] We carried out mercaptoethanol addition to obtain the thioether-containing ω-hydroxyacid (TEHA, Scheme 2) under irradiation at room temperature in presence of 2,2-dimethoxy-2-phenylacetophenone (DMPA) as photoinitiator. This monomer was obtained using equimolar amounts of mercaptoethanol, in short reaction times (10 min) with quantitative yield and characterization was carried out by spectroscopic techniques.



Scheme 2. Synthesis of thioether-containing ω-hydroxyacid (TEHA)

Polyester Synthesis

To explore the reactivity of the TEHA in the polyesterification reaction, tin (II) 2-ethyl-hexanoate (Sn(Oct)$_2$) and dibutyl tin oxide (DBTO) were tested under similar reaction conditions. Oligomerization of TEHA was performed in bulk under nitrogen atmosphere at 140 ºC for 1h and further dynamic vacuum. The reaction was conducted for 24 h and molecular weight values on non fractionated products were determined by SEC relative to PS standards. As can be seen in Figure 1, the highest Mn values were obtained for Sn(Oct)$_2$ while using DBTO resulted in lower Mn. Moreover, increasing catalyst percentage from 1 to 2 % mol decreases Mn.

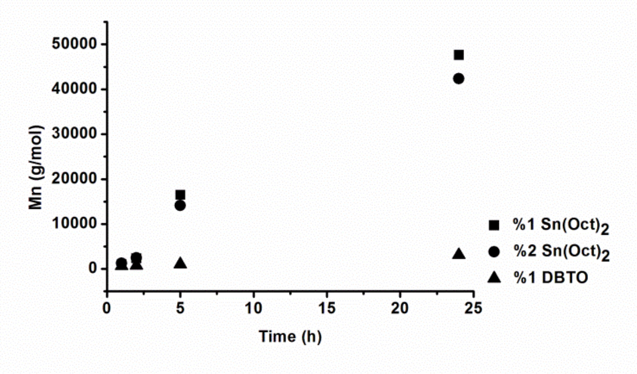
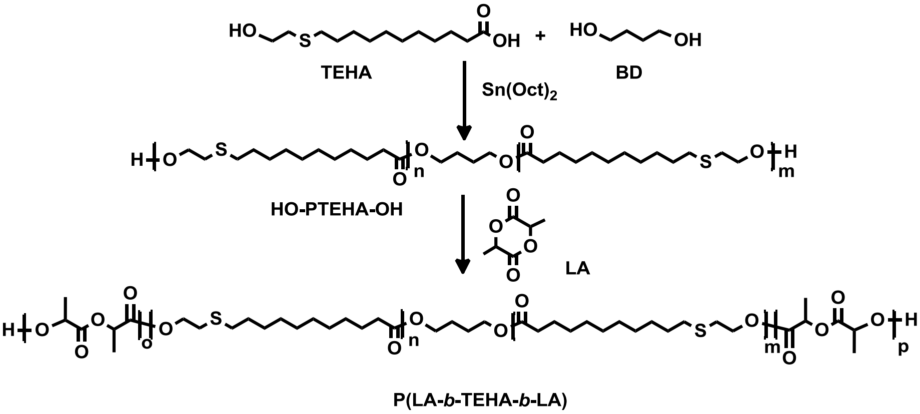


Figure 1. Mn versus time for TEHA self-condensations

Two dihydroxyl-terminated prepolymers were obtained by self-polycondensation of TEHA with two amounts of biobased 1,4-butanediol (BD) and 1% of Sn(Oct)$_2$ as catalyst, at 140 ºC (Table 1, Scheme 3). Reactions were carried out under the above described conditions for 6h.



Scheme 3. Two step procedure to P(LA-*b*-TEHA-*b*-LA) triblock copolymers: obtention of HO-PTEHA-OH and further ring opening of LA

^{1}H NMR spectroscopy allowed monitoring the polymer formation by the appearance of new signals in comparison to the starting TEHA (Figure 2). The characteristic peak of the proton linked to the carbon bearing the hydroxyl group in TEHA (Fig 2a, H_a) is shifted downfield as the conversion of TEHA increases, confirming the formation of ester functions. Also, the peak of the proton linked to the carbon bearing the carboxylic group in TEHA (Fig 2a, H_d) undergoes a slight shift upfield confirming the formation of ester. Furthermore, the appearance of a new signal H_x (Fig. 2b) at 4.09 ppm, characteristic of the oxymethylene protons linked to the carbon adjacent to the ester function in the BD unit, clearly confirms that the hydroxyl functions of BD efficiently reacted with the carboxylic acid moieties of TEHA. The ratio of BD to TEHA was determined from signals corresponding to oxymethylene units of BD at 4.1 ppm (H_x) and to one of the methylenes linked to sulfur at 2.73 ppm (H_b) from TEHA moiety, and the obtained values approaches well to theoretical values (Table 1). A high yield (93%) of dihydroxyl-terminated prepolymers was obtained allowing the use of these prepolymers for the ring opening of the LA.

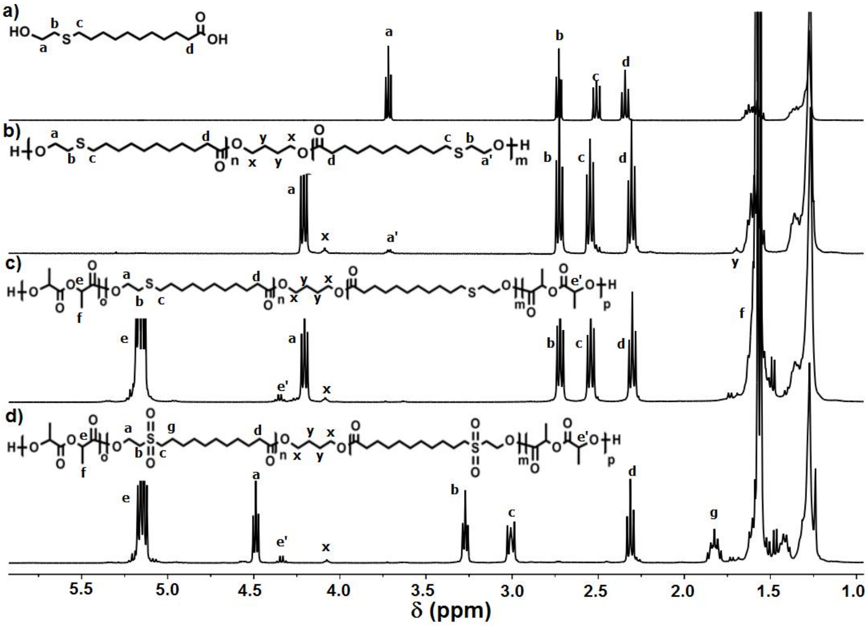


Figure 2. ^{1}H NMR spectra of a) monomer TEHA b) macroinitiator HO-PTEHA-OH1 c) triblock copolyester P(LA-*b*-TEHA1-*b*-LA)$_5$ d) polysulfone analogue PSO(LA-*b*-TEHA1-*b*-LA)$_5$

^{1}H NMR analysis, signals at 3.75 ppm corresponding to end-group ($H_{a'}$) and at 2.73 ppm corresponding to the repeating unit (H_b), was used to determine the molar mass of the HO-PTEHA-OH samples which was also characterized by SEC. As can be seen (Figure 1 and Table 1) when using BD as initiator (1:0.05 and 1:0.1 TEHA/BD molar ratio) lower Mn's than in absence of initiator were obtained. Moreover, as expected, higher Mn was obtained when using a 1:0.05 molar ratio. Significant differences were noticed between the absolute molecular weights calculated by ^{1}H NMR and the molecular weights evaluated by SEC using THF as solvent, giving an indication that the polystyrene standards calibration of our system over represents the molecular weight values.

Table 1. Molar composition and molecular weights of HO-PTEHA-OH prepolymers and P(LA-*b*-TEHA-*b*-LA)$_x$ copolyesters

	Composition TEHA/BD/LA					Molecular Weight (g mol^{-1})		
Polymer	**Molar ratio**	**Feed ratio^a**	**^{1}H NMR feed ratio**	**W (%)^b**	**W (%)^c**	**Mn NMR^d**	**Mn SEC^e**	**PDI**
HO-PTEHA-OH1	1:0.05:0	20	17.0	-	-	4679	15900	1.39
HO-PTEHA-OH2	1:0.1:0	10	9.5	-	-	2690	10400	1.43
P(LA-*b*-TEHA1-*b*-LA)$_2$	1:0.05:2	2	1.6	54	48	4176	15100	1.22
P(LA-*b*-TEHA1-*b*-LA)$_3$	1:0.05:3	3	2.6	63	60	5102	13200	1.23
P(LA-*b*-TEHA1-*b*-LA)$_5$	1:0.05:5	5	4.0	74	70	5583	16100	1.49
P(LA-*b*-TEHA1-*b*-LA)$_{10}$	1:0.05:10	10	8.4	85	83	9163	13200	1.58
P(LA-*b*-TEHA2-*b*-LA)$_2$	1:0.1:2	2	1.6	54	48	4119	14600	1.26
P(LA-*b*-TEHA2-*b*-LA)$_3$	1:0.1:3	3	2.2	63	57	3514	14500	1.26
P(LA-*b*-TEHA2-*b*-LA)$_5$	1:0.1:5	5	3.9	74	69	7898	13400	1.34
P(LA-*b*-TEHA2-*b*-LA)$_{10}$	1:0.1:10	10	8.5	85	83	11652	12800	1.62

^{a} TEHA/BD molar ratio for prepolymers and LA/TEHA molar ratio for block copolymers. ^{b} Theoretical weight percentage of PLA. ^{c} Weight percentage of PLA in block copolymers by ^{1}H NMR (from LA signal at 5.17 ppm and TEHA signal at 4.21 ppm). ^{d} Mn values were calculated from LA signal at 5.17 ppm and TEHA signal at 2.73 ppm related to the end group signal at 4.35 ppm. ^{e} THF as solvent.

These macroinitiators, α,ω-dihydroxy polyesters (HO-PTEHA-OH) were used for the ring opening of LA thus obtaining triblock copolymers (Scheme 3). Polymerizations were carried out in toluene due to the high viscosity of the hydroxyl-terminated prepolymer. Four copolymers from each initiator were prepared by changing the monomer to initiator molar feed as shown in Table 1. This enabled the preparation of block copolymers with various compositions ranging from 54 to 85% of PLA. Polymerizations were carried out using 1% of Sn(Oct)$_2$ at 140 ºC to avoid transesterification reaction for 4h. The ^{1}H NMR spectra (Figure 2c) shows the appearance of a quadruplet at 5.17 ppm (H$_e$) confirming the ring opening of LA. Moreover, the peak of the terminal unit of macroinitiator at 3.75 ppm (H$_{a'}$)

disappears according to initiation of LA polymerization. The composition of the copolymers was evaluated by ^{1}H NMR spectroscopy using signals corresponding to both repeating units, 5.17 ppm (H_e) and 4.21 ppm (H_a), and fits well to the theoretical values only for the lower feed ratios. This can be due to a lower number of growing chains when this ratio increases and to the viscosity increase with time that limits the accessibility of the monomer to the growing chain.

Molecular weights were evaluated from NMR analysis, using end group signal ($H_{e'}$) at 4.35 ppm and repeating LA unit signal at 5.17 ppm (H_e), and TEHA signal at 2.73 ppm (Table 1). Mn values increase as the percentage of PLA in the copolymer increases as can be expected from the higher reactivity of LA. Mn values obtained by SEC are significantly different from H^1 NMR according to the above mentioned behaviour.

Modification of Polyesters

It is known that thioethers can easily be oxidized to sulfones (via sulfoxides) by several oxidation reagents. Sulfones exhibit a high polarity and thus, changes in thermal behaviour and crystallinity of the related polymers are expected.[29] It was found that hydrogen peroxide is able to selectively oxidize the thioether to sulfoxide or to sulfone groups depending on the reaction temperature.[30] Thus, the sulfoxide intermediate oxidation product can be obtained when the reaction is carried out at room temperature while the sulfone derivative is obtained by heating at higher temperatures. Oxidation was carried out using H_2O_2 (50 vol %) in a thioether:H_2O_2 molar ratio 1:2, with $CHCl_3$ as solvent at 25 ºC. The reaction progress was followed by ^{1}H NMR spectroscopy. Signals at 2.72 ppm and 2.96 ppm attributable to α-protons of the sulfoxide moiety appear after 6 h of reaction. After 24h of reaction, when signals of the thioether can still be observed, signals at 3.02 ppm and 3.28 ppm attributable to the α-protons of sulfone moiety appears. Only after 48 h of reaction signals of thioether completely disappear, when a mixture of sulfoxide and sulfone is present, thus selective oxidation does not take place and long reaction time would be necessary to obtain fully conversion to sulfone. Oxidation with H_2O_2 at high temperature has been described to produce hydrolysis of ester groups that would lead to polymer degradation,[31] so alternative oxidants were considered. The oxidation process was finally performed in dichloromethane using m-chloroperbenzoic acid at room temperature.[32] Complete oxidation was achieved in 1 hour.

^{1}H NMR spectroscopy showed full conversion of the thioether functions by the appearance of unique signals for protons H_a, H_b and H_c (Figure 2d), at higher chemical shifts than for the parent polymer, indicating that only sulfone oxidation product is formed. It is known that sulfones give two characteristic bands in IR spectroscopy between 1160-1130 cm^{-1} and 1340-1300 cm^{-1}, whereas sulfoxides give only one band between 1060 and 1040 cm^{-1}. Figure 3 shows IR spectra of triblock copolymer parent P(LA-*b*-TEHA1-*b*-LA)$_3$ and its oxidized analogue. Several bands appear at the region between 1160-1130 cm^{-1} and 1060-1040 cm^{-1} for the non-oxidized polymer but a new band at 1300 cm^{-1} is only observed for the oxidized sample, thus indicating the formation of sulfone.

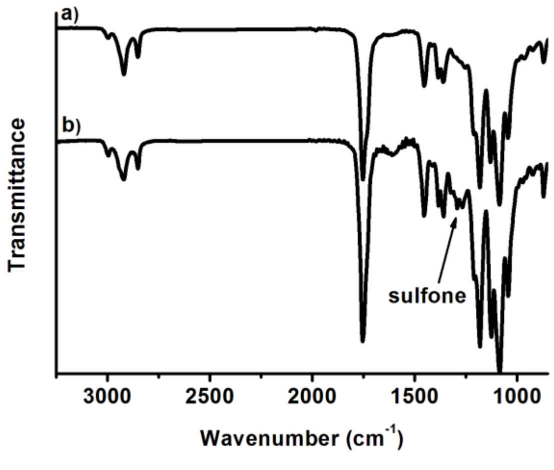


Figure 3. FT-IR spectra of a) triblock copolyester P(LA-*b*-TEHA1-*b*-LA)$_3$ and b) polysulfone analogue PSO(LA-*b*-TEHA1-*b*-LA)$_3$

Molecular weights of the polysulfones were obtained by ^{1}H NMR spectroscopy using signals of LA units (H_e) at 5.17 ppm and of oxidized TEHA units (SOTEHA) at 3.28 ppm (H_b) related to end group signal at 4.35 ppm ($H_{e'}$) (Table 2). Moreover, SEC analyses were carried out in DMF as polysulfones resulted insoluble in THF. As can be seen, no significant differences among Mn values previous and after oxidation were found, thus indicating that no degradation or crosslinking processes took place. It is noticeable the great difference among values obtained by the two techniques, even higher than when using THF as solvent in SEC. The composition of the polysulfones was calculated by ^{1}H NMR (from LA signal at 5.17 ppm and SOTEHA signal at 4.50 ppm) and approaches better to the theoretical values for the higher LA contents.

Table 2. Molecular weights of P(LA-*b*-TEHA1-*b*-LA)$_x$ copolyesters and corresponding polysulfones PSO(LA-*b*-TEHA1-*b*-LA)$_x$

Sample	**Copolyester**			**Polysulfone**				
	Mn NMR	**Mn SEC^a**	**PDI**	**Mn NMR**	**Mn SEC^a**	**PDI**	**W (%)^b**	**W (%)^c**
P(LA-*b*-TEHA1-*b*-LA)$_2$	4176	30265	1.06	5990	36467	1.17	51	44
P(LA-*b*-TEHA1-*b*-LA)$_3$	5102	36940	1.14	6100	37582	1.10	61	55
P(LA-*b*-TEHA1-*b*-LA)$_5$	5583	35592	1.06	6160	41281	1.11	72	68
P(LA-*b*-TEHA1-*b*-LA)$_{10}$	9163	37803	1.10	8980	39670	1.13	84	80

^{a} SEC values were obtained using DMF as solvent. ^{b} Theoretical weight percentage of PLA. ^{c} Weight percentage of PLA in polysulfones by ^{1}H NMR (from LA signal at 5.17 ppm and SOTEHA signal at 4.50 ppm).

Thermal properties

The thermal behaviour of triblock copolyesters under nitrogen atmosphere has been comparatively studied by thermal gravimetric analysis (TGA) and differential scanning calorimetry (DSC), taking as reference HO-PTEHA-OH and PLA homopolymers. The weight loss versus temperature plots registered for the two series of copolyesters and their corresponding derivative curves were very similar in both cases and P(LA-*b*-TEHA1-*b*-LA)$_x$ and P(LA-*b*-TEHA2-*b*-LA)$_x$ triblock copolyesters are shown in Figure 4 a-b) and c-d), respectively.

The temperatures at the decomposition onset and for maximum decomposition rate, together with the weight remaining after heating at 600 ºC are listed in Table 3**.**

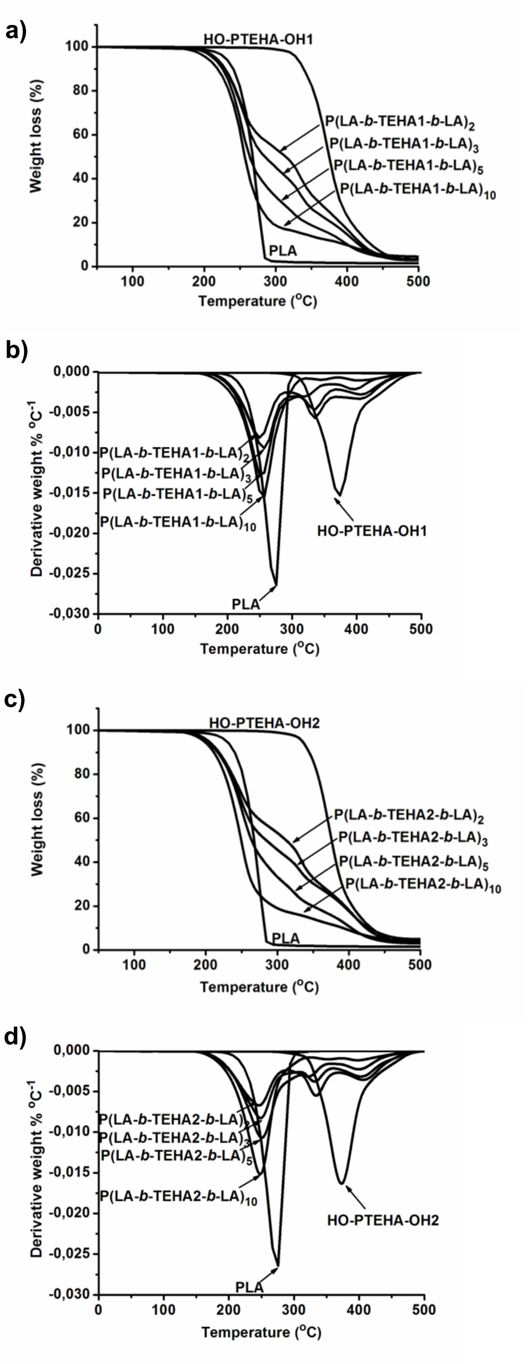


Figure 4. a) TGA weight loss curves and b) TGA derivative curves of HO-PTEHA-OH1, PLA and P(LA-*b*-TEHA1-*b*-LA)$_x$ triblock copolyesters, c) TGA weight loss curves and d) TGA derivative curves of HO-PTEHA-OH2, PLA and P(LA-*b*-TEHA2-*b*-LA)$_x$ triblock copolyesters

As can be seen, PLA and HO-PTEHA-OH1 have a unique degradation step with very different temperatures at the decomposition onset and for maximum rate, thus showing a noticeable higher stability for the dihydroxyl-terminated prepolymer. All the copolyesters started to decompose above 200 ºC with the maximum rate taking place in the proximities of 250 ºC to leave less than 5% of the initial mass after heating at 600 ºC. A common pattern of behaviour is followed by all them and slight differences associated to composition are noticeable.

As expected, all copolymers present a multi-step thermal decomposition. A first weight loss is observed at a temperature about 250 ºC which correspond to the degradation of PLA, followed by a two step thermal decomposition weight losses centered at 325-350 ºC and around 400 ºC, which seems to correspond to the decomposition of prepolymers HO-PTEHA-OH. The amount of the material degraded at these temperatures increases with the OH-PTEHA-OH content. This thermal decomposition pattern allows calculating the weight percentage of each block in the copolymer. As can be observed in Table 3, these weight percentages of PLA approach to the theoretical values (in brackets).

In spite of the higher initial degradation temperature of HO-PTEHA-OH, the effect of their incorporation into PLA is lowering the initial degradation temperature of copolymer and the higher the weight fraction of HO-PTEHA-OH in the copolymer, the higher the temperature corresponding to the 5% weight loss.

Table 3. Thermogravimetric properties of PLA, HO-PTEHA-OH and P(LA-*b*-TEHA-*b*-LA)$_x$ copolyesters.

Polymer	$T_{5\%}$ (ºC)[a]	Td (ºC)[b]	R (%)[c]	Wt PLA (%)[d]
PLA	230	272	1.5	-
HO-PTEHA-OH1	329	372	2.9	-
HO-PTEHA-OH2	335	373	2.8	-
P(LA-*b*-TEHA1-*b*-LA)$_2$	216	249-334-410	3.2	45 (54)
P(LA-*b*-TEHA1-*b*-LA)$_3$	215	255-334-411	2.7	55 (63)
P(LA-*b*-TEHA1-*b*-LA)$_5$	213	252-324-398	3.2	66 (74)
P(LA-*b*-TEHA1-*b*-LA)$_{10}$	204	254-345-413	4.3	83 (85)
P(LA-*b*-TEHA2-*b*-LA)$_2$	204	245-334-409	3.4	44 (54)
P(LA-*b*-TEHA2-*b*-LA)$_3$	202	248-332-406	4.7	53 (63)
P(LA-*b*-TEHA2-*b*-LA)$_5$	204	250-326-402	2.9	68 (74)
P(LA-*b*-TEHA2-*b*-LA)$_{10}$	198	248-352-397	4.0	83 (85)

[a] Temperature at which 5% weight loss was observed. [b] Temperature for maximum degradation rate. [c] Remaining weight at 600 ºC. [d] Weight percentage of PLA from TGA (Theoretical values in brackets).

The DSC heating scans recorded for copolyesters coming directly from synthesis showed two melting endotherms characteristic of melting of (HO-PTEHA-OH) and PLA and a small exotherm (Figure 5a). In the cooling scans, only the exotherm attributed to the prepolymer crystallization at temperatures around 40ºC can be seen (Figure 5b). A second heating run showed the two melting endotherms and a crystallization exotherm attributed to PLA crystallization by comparison to the second heating scan of PLA (Figure 5c).

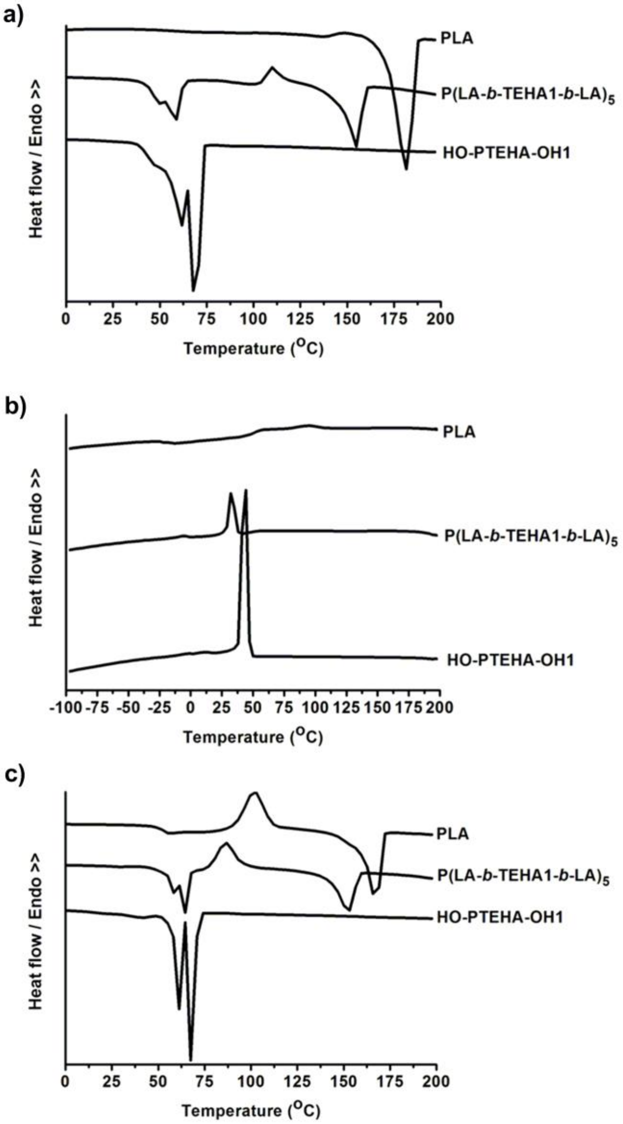


Figure 5. DSC plots of a) first heating b) cooling and c) second heating of PLA, HO-PTEHA-OH1 and P(LA-*b*-TEHA1-*b*-LA)$_5$ triblock copolyester

In block copolymers containing only crystallizable components, the competition between crystallization of the different crystalline blocks plays an important role and crystallization of one block may affect the crystallization and morphology of the other.[33,34] In our case, melting temperatures of the two blocks are far from each other and the crystallization behavior is very different. To study the effect of the lower melting temperature block on the crystallization of the PLA block, the polymers were subjected to annealing at 120 ºC, a temperature around 40 ºC below the melting temperature of PLA. All samples were heated from room temperature to 200 ºC, cooled from 200 ºC to 120 ºC and heated at this temperature for 2h, in order to produce maximum PLA block crystallinity, followed by cooling to -50 ºC. Melting points and enthalpies were then recorded while heating at 10 ºC/min from -50 ºC to 200 ºC. The obtained DSC heating scans are shown in Figure 6 and data are collected in Table 4. PLA showed a melting endotherm at 167 ºC which enthalpy increase from 53 J/g (second heating in figure 5c) to 69 J/g. Moreover, an increase of the melting enthalpy of HO-PTEHA-OH1 from 70 to 91 J/g is observed, indicating an increase of crystallinity in both cases.

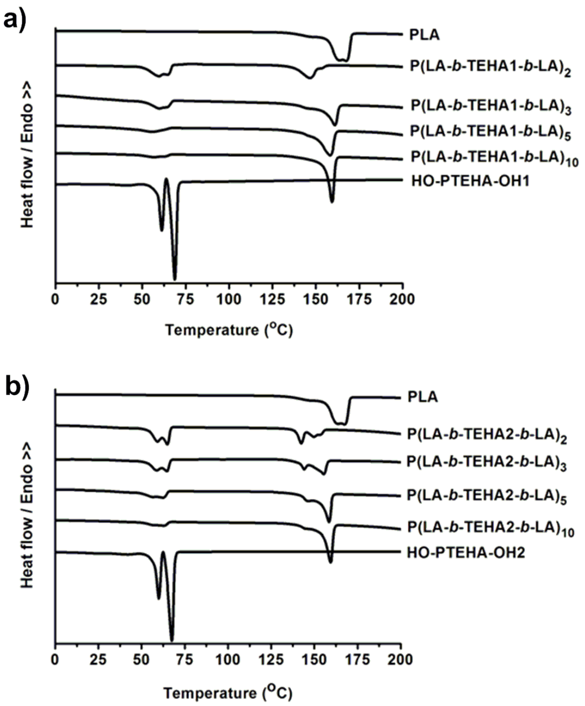


Figure 6. DSC plots after annealing a) PLA, HO-PTEHA-OH1 and P(LA-*b*-TEHA1-*b*-LA)$_x$ triblock copolyesters, b) PLA, HO-PTEHA-OH2 and P(LA-*b*-TEHA2-*b*-LA)$_x$ triblock copolyesters

For the block copolymers, while melting temperatures of the PTEHA block show slight variations, a decrease of the Tm related to the parent polymer is observed in all cases. Moreover, Tm of PLA block decreases as the weight percent of TEHA increases and copolyesters containing high weight percentages of PLA melt at temperatures close to the PLA homopolymer.

The crystallinity of the PLA block in the copolymers was calculated using the equation $Xc=(\Delta H_{m} / W\Delta H^{o}_{m}) \times 100$, where ΔH_{m} is the melting enthalpy of PLA given by DSC, ΔH^{o}_{m} the enthalpy of fusion of the completely crystalline state (93 J/g for PLA) and W the weight fraction obtained from ^{1}H NMR data. Considering the degree of crystallization, both series show a decrease of crystallinity with respect to the PLA homopolymer according to the influence of the molten PTEHA chains on the crystallization of the PLA. The crystallinity increases as the weight percentage of PLA increases.

Table 4. DSC properties of PLA, HO-PTEHA-OH and P(LA-*b*-TEHA-*b*-LA)$_x$ copolyesters

Polymer	**Tm_1 (ºC)**	**ΔHm_1 (J g^{-1})**	**Tm_2 (ºC)**	**ΔHm_2 (J g^{-1})**	**Xc^{a}**
PLA	-	-	167	69	74
HO-PTEHA-OH1	61, 68	91	-	-	-
HO-PTEHA-OH2	59, 67	84	-	-	-
P(LA-*b*-TEHA1-*b*-LA)$_2$	60	22	146	24	54
P(LA-*b*-TEHA1-*b*-LA)$_3$	60	13	161	33	59
P(LA-*b*-TEHA1-*b*-LA)$_5$	56	10	158	43	66
P(LA-*b*-TEHA1-*b*-LA)$_{10}$	57	5	160	48	62
P(LA-*b*-TEHA2-*b*-LA)$_2$	65	25	142	21	47
P(LA-*b*-TEHA2-*b*-LA)$_3$	64	25	155	27	51
P(LA-*b*-TEHA2-*b*-LA)$_5$	62	20	158	41	64
P(LA-*b*-TEHA2-*b*-LA)$_{10}$	63	7	159	45	58

[a] Degree of crystallinity

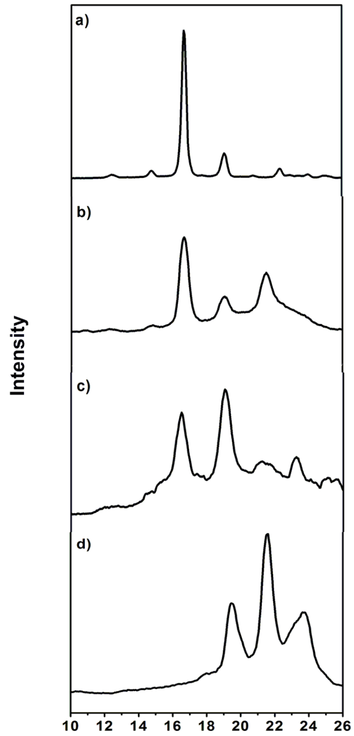


Figure 7. WAXD patterns of a) PLA b) P(LA-*b*-TEHA1-*b*-LA)$_2$
c) PSO(LA-*b*-TEHA1-*b*-LA)$_2$ d) HO-PTEHA1-OH

The crystallinity of both blocks was confirmed by wide angle X-ray experiments. Figure 7 compares WAXD intensity profile of copolyester with that of PLA and HO-TEHA-OH1 homopolymers recorded after annealing. PLA can crystallize in different forms depending on the processing conditions, being the most stable the α-form with a 10^3 helical chain conformation where two chains interact in a orthorhombic unit cell.[35] Typical reflections at (010), (110/200), (203) and (015) corresponding to this form are identified at 2θ = 14.7º, 16.7º, 19.1º and 22.3º. Moreover, reflections corresponding to PTEHA unit at 2θ = 19.5º, 21.5º and 23.7º can be seen. Both characteristic homopolymer reflections are visible in the block copolymer sample and the most significant trend is the increase of the amorphous halo which can be related to the crystallinity decrease.

The thermal behaviour of polysulfone derivatives under nitrogen atmosphere has been comparatively studied by thermal gravimetric analysis (TGA) and differential scanning calorimetry (DSC) taking as reference PLA, HO-PSOTEHA-OH1 and the parent triblock copolyesters. Thermogravimetric analysis show that the synthesized polysulfones are stable until at least a temperature of 235ºC, so the oxidation process increases the thermal stability of the block copolymers (Figure 8 and Table 5). While the polysulfones containing the lowest percentage of LA show the same pattern as copolyester precursors on the derivative curves, the copolymers containing higher LA percentages show only two degradation steps. The first degradation step, that can be attributed to PLA degradation, appears at higher temperatures than in the parent copolymers, according to the increased thermal stability and overlaps to the second degradation step for PSO(LA-*b*-TEHA1-*b*-LA)$_5$ and PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$. The weight percentages of each block calculated from these degradation patterns approach well the theoretical values only in the last two cases.

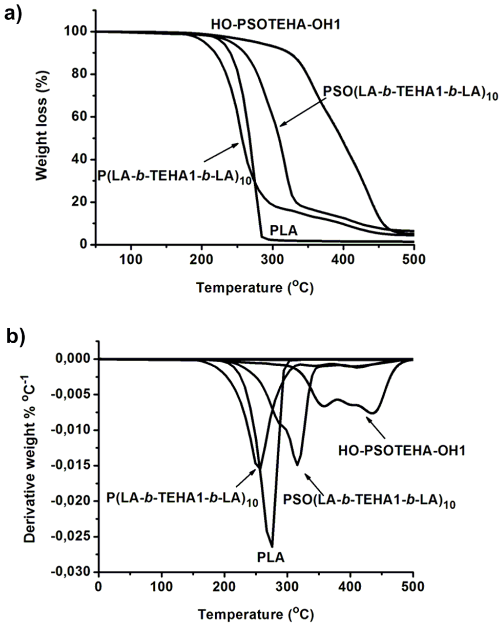


Figure 8. a) TGA weight loss curves and b) TGA derivative curves of PLA, P(LA-*b*-TEHA1-*b*-LA)$_{10}$, PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$, HO-PSOTEHA-OH1

Table 5. Thermogravimetric properties of PSO(LA-*b*-TEHA-*b*-LA)$_x$ polysulfone

Sample	$T_{5\%}$[a] (ºC)	Td[b] (ºC)	W[c] (%)	Wt PLA[d] (%)
HO-PSOTEHA-OH1	278	358-435	5.3	-
PSO(LA-*b*-TEHA1-*b*-LA)$_2$	235	273-316-423	6.1	38 (51)
PSO(LA-*b*-TEHA1-*b*-LA)$_3$	243	289-310-413	5.4	40 (61)
PSO(LA-*b*-TEHA1-*b*-LA)$_5$	255	292-413	5.4	72 (72)
PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$	241	316-412	6.2	84 (84)

[a] Temperature at which 5% weight loss was observed. [b] Temperature for maximum degradation rate.
[c] Remaining weight at 600 ºC. [d] Weight percentage of PLA (Theoretical values in brackets).

Oxidation of the thioether to sulfone resulted in a significant increase of the melting temperature of the PSOTEHA block of around 40ºC, but not significant differences with the PTEHA block melting enthalpies were found (Figure 9, Table 6). Regarding the PLA block, the melting temperatures do not differ significantly from the parent copolymers and lower crystallinities can be observed, showing the influence of the oxidized melting chains on the PLA crystallization. WAXD intensity profile of PSO(LA-*b*-TEHA1-*b*-LA)$_2$ (Fig. 7c) show a similar pattern to the parent copolyester with the above mentioned reflections but different relative intensities.

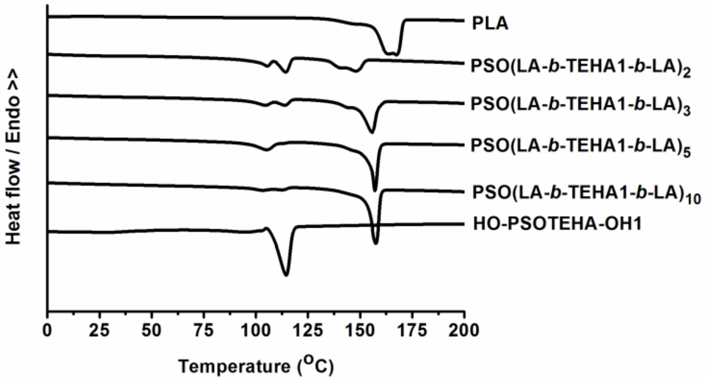


Figure 9. DSC plots of PLA, HO-PSOTEHA-OH1 and PSO(LA-*b*-TEHA1-*b*-LA)$_x$ polysulfones

Table 6. DSC properties of PSO(LA-*b*-TEHA-*b*-LA)$_x$ polysulfones

Sample	T_{m1} (ºC)	ΔH_{m1} (J g^{-1})	T_{m2} (ºC)	ΔH_{m2} (J g^{-1})	X_c[a]
HO-PSOTEHA-OH1	114	45	-	-	-
PSO(LA-*b*-TEHA1-*b*-LA)$_2$	114	16	148	18	44
PSO(LA-*b*-TEHA1-*b*-LA)$_3$	114	10	156	28	55
PSO(LA-*b*-TEHA1-*b*-LA)$_5$	105	10	157	32	51
PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$	103	4	158	44	59

[a] Degree of crystallinity

Water contact angle measurements were carried out on PLA and copolyesters P(LA-*b*-TEHA1-*b*-LA)$_3$ and P(LA-*b*-TEHA1-*b*-LA)$_{10}$ (Figure 10). The obtained contact angles were 83º, 91º and 91º respectively, showing the more hydrophobic character of the triblock copolyesters related to PLA. The contact angles of corresponding polysulfones PSO(LA-*b*-TEHA1-*b*-LA)$_3$ and PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$ were 78º and 80º confirming the more hydrophilic character of polysulfones related to the parent copolymers.

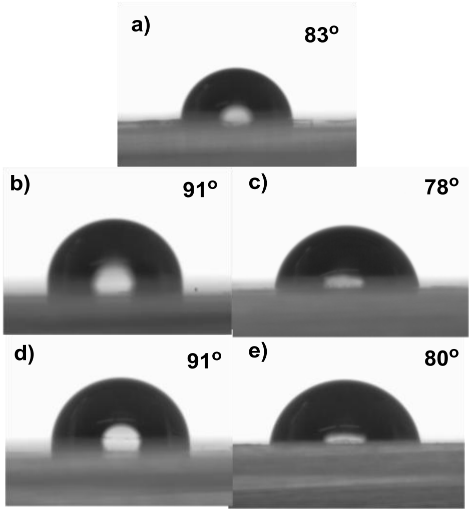


Figure 10. Contact angle images for a) PLA b) P(LA-*b*-TEHA1-*b*-LA)$_3$ c) P(LA-*b*-TEHA1-*b*-LA)$_{10}$ d) PSO(LA-*b*-TEHA1-*b*-LA)$_3$ e) PSO(LA-*b*-TEHA1-*b*-LA)$_{10}$

As a conclusion of this chapter, fully biobased ABA triblock copolyesters from PLA and castor oil derivatives have been synthesized. The synthetic strategy used a dihydroxy telechelic polyester, from a sulfur-containing hydroxyacid derivative of 10-undecenoic acid, which self-polycondensation with low amounts of biobased 1,4-butanediol, enables the obtention of a macroinitiator for the ROP of LA. Two series of triblock copolyesters with different LA/HO-PTEHA-OH ratio were prepared and characterized by ^{1}H NMR spectroscopy and Mn determined by NMR and SEC. DSC results of the triblock copolyesters showed a significant decrease on the melting temperature of PLA block related to percentage of PTEHA in the polymer chain. Both series of copolyesters showed a decrease of crystallinity with respect to the PLA homopolymer. The thermal stability of the copolymers was found to increase as TEHA units increased in the copolymer. Triblock copolyesters were modified to polysulfone analogues by the oxidation of thioether functionality. After oxidation a decrease of crystallinity was observed and thermal analysis demonstrated improved stability of these oxidized polymers compared to the copolyester parents. From water contact angle measurements a higher hydrophobic character of the triblock copolyester and a similar hydrophilicity of the polysulfone analogues related to PLA is observed.

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Chapter 4

Vinylsulfide-Containing Polyesters and Copolyesters from Fatty Acids

Introduction

Aliphatic polyesters are a class of interesting polymeric materials. In particular, biodegradable and biocompatible aliphatic polyesters are highly attractive and valuable biomaterials which can be used in a white range of applications.[1,2,3] While polymeric materials based on CL, LA and glycolide are currently used in numerous biomedical applications; such polyesters are limited in scope due to their hydrophobic and semicrystalline properties and the absence of functionality on the polymer backbone, which could otherwise be used for tailoring physical properties and introducing bioactive moieties.[4] Numerous examples of chain-end functionalized aliphatic polyesters have been reported, prepared most commonly by the use of functional nucleophiles to initiate ring-opening lactone polymerization.[5] However, pendent functionalization provides a unique opportunity to alter physical and chemical properties by distributing functionality along the polymer backbone.[6] Pendent functionalization of aliphatic polyesters can be achieved by polymerization of functionalized monomers, post-polymerization modification or a combination of the two approaches and numerous reports can be found describing the introduction of a broad palette of functionalities. Functional groups provide versatile routes to conjugate bioactive molecules and can further transform the polymers to branched and networks polymers.

Fatty acids have been proven as an ideal renewable starting material for the synthesis of aliphatic polyesters.[7-9] Fatty acid-based polycondensates may be provided with a great diversity of chemical structures and unusual properties; they typically display enhanced hydrophilicity, less toxicity, and higher susceptibility to biodegradation than petrochemical-based polycondensates, offering therefore a wide possibility of applications in food packaging and medical devices. The terminal functionalization of fatty acids or their derivatives can be carried out by enzymatic ω-oxidation, or alternatively ω-hydroxy fatty acids can be obtained by fermentation with modified yeast strains.[10,11] Chemical routes for the preparation of α,ω-dicarboxylic acid esters from unsaturated fatty acids by means of isomerising alkoxycarbonylation,[12] and of ω-hydroxyfatty acids by ozonolysis/hydrogenation[13] have also been described. Moreover, metathesis and thiol-ene reactions have been used to prepare linear and hyperbranched polyols and hydroxyesters for polyesters production.[14-18]

The derivatization reaction of fatty acids by thiol-yne coupling (TYC) is a convenient approach to prepare ω-hydroxy fatty acids. The ability of an acetylene group to accept one or two thiols rapidly, without any metallic catalyst, is used as a powerful tool for creating highly functional polymer structures.[19,20] The outcomes of the TYC reactions strongly depend on the experimental conditions (e.g., temperature, solvent and alkyne/thiol ratio) but these can be properly adjusted to achieve selective production of either mono- or bis-coupling products.[21] Thus, under suitable reaction conditions the vinyl sulphide intermediate fatty acid can be obtained. The self-polycondensation of these functional α,ω-hydroxyacids is a rapid strategy to efficiently synthesize functional polyesters by using chemical catalysts[22] or by means of enzymatic synthesis.[23-25]

Considered as environmentally friendly and valuable thermoplastics, PCLs have gained much interest since they can be functionalized and tailored for special applications in a straight forward manner.[5,26,27] Because its biodegradability and biocompatibility PCL is of great interest for tissue engineering and drug delivery applications. Specially PCL is an excellent material for tissue engineering since it is of nontoxic nature and revealed to be cyto-compatible with diverse body tissues. Moreover, PCL can be used as drug carrier enabling a homogeneous drug distribution and long-term drug release.

Industrially, the CL monomer is prepared by Bayer-Villiger oxidation of cyclohexanone using peracetic acid, whereas for lab scale synthesis preferentially *m*-chloroperbenzoic acid is used as oxidant. Organic peracides are usually non environmental benign and the reactions are preferably carried out in chlorinate solvents thus, green alternatives and environmentally benign oxidation procedures making use of, e.g. diverse metal or enzyme catalysts and hydrogen peroxide as clean oxidant or potassium peroxymonosulfate ($KHSO_5$) as green oxidant are of great interest for the synthesis of the CL monomers. Besides of development of greener and more efficient Bayer-Villiger oxidation procedures there is a great interest in CL monomers from renewable resources. The synthesis of CL was achieved by catalytic transformation of 5-hydroxymethylfurfural, which can be obtained from, e.g. fructose starch or cellulose.[28] Moreover, the synthesis of diverse CL monomers from carvone or menthol has also been described.[29,]

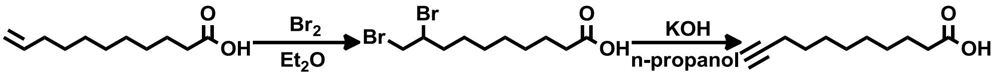
The use of these renewable monomers enables the synthesis of functional PCLs with different material properties. Generally, the attachment of functional groups along the aliphatic chains of PCL allows tailoring material properties and one common approach is to directly attach pendent functional groups to the lactone ring. However, usually multistep synthesis procedures and extensive purification steps are needed to obtain the desired pure monomers. Considering the importance of functionalized PCLs, a strategy that has even greater appeal because of the ability to precisely control properties involves the preparation of block copolymers. While there are examples of such polymers in the literature,[30,31] the goal of wholly renewable and degradable examples still represents a significant challenge. Furthermore, establishing foundational structure-property relationships in such materials is still needed.

In this work, we describe the synthesis of a vinyl sulphide-containing α,ω-hydroxy fatty acid (VSHA) from castor oil. Polymerization of VSHA has been studied using metal and enzymatic catalysts. The approach of copolymerizing lactones with functionalized comonomers has been established for the direct functionalization of polyester backbone.[32] So, we also investigated the copolymerization of VSHA with ε-CL and among the reported strategies, two were selected.[33,34] The first one used the direct copolymerization of hydroxyacid with lactone to obtain random copolyesters. Alternatively, the preparation of a dihydroxy telechelic polyester and its use as a macro-initiator for ring-opening polymerization of ε-CL enabled the preparation of triblock copolymers. Due to the particularly valuable application of click chemistry to aliphatic polyesters,[35,36] we finally investigate the thiol-ene click post-modification reaction showing that material performance can be enhanced by attaching the required moieties.

Monomer Synthesis

Synthesis of 10-undecynoic acid

Whilst alkenic fatty acids occur abundantly in nature, alkynic fatty acids are rare. However, alkynic fatty acid can be obtained by the dehydrogenation of alkenes through a sequence of bromation/dehydrobromation as an efficient methodology. 10-undecynoic acid was obtained in moderate yield from 10-undecenoic acid in these two stages (Scheme 1).[37]



Scheme 1. Synthesis of 10-undecynoic acid

Figure 1a shows the ^{1}H NMR spectrum of crude reaction after bromation of 10-undecenoic acid. The disappearance of C=C proton signals and the appearance of three characteristic signals at 3.60, 3.82 and 4.14 ppm, corresponding to the two diastereotopic protons of methylene 11 and 11’and methine proton 10, can be observed.

The dehydrobromation of 10,11-dibromoundecanoic acid using a strong base, such as potassium hydroxide, in n-propanol/water mixture as solvent, was carried out. The 10-undecynoic acid was obtained as white solid with in a 70% yield. The ^{1}H NMR spectrum (Figure 1b), confirms the presence of triple bond unit, HC≡C by the appearance of a triplet at 1.94 ppm.

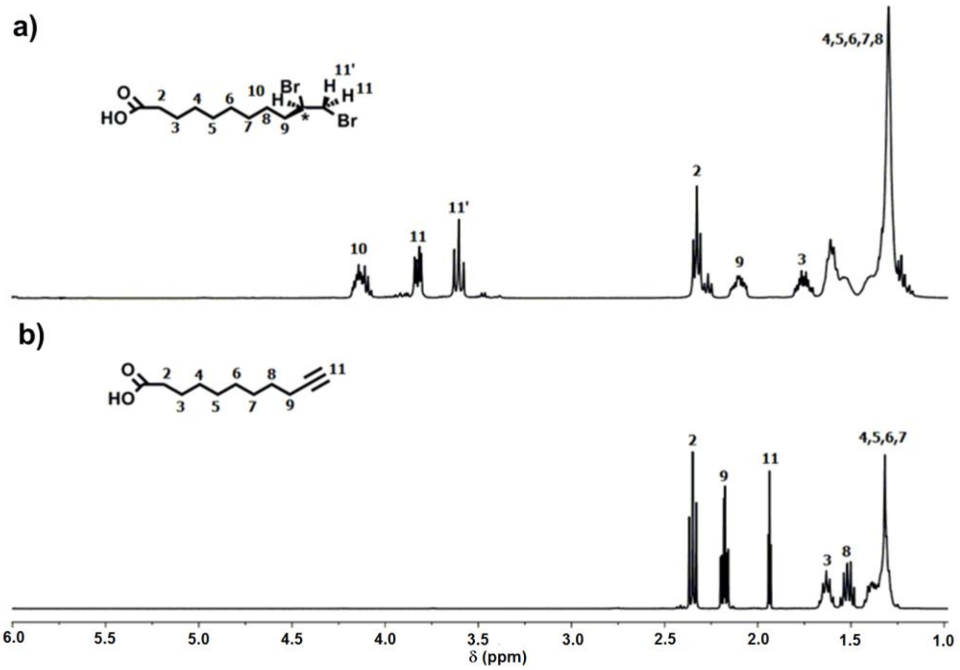
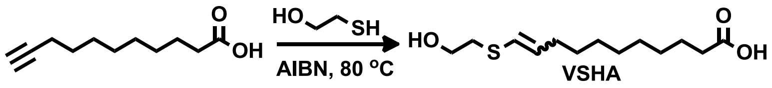


Figure 1. ^{1}H NMR spectrum of a) 10,11-dibromoundecanoic acid b) 10-undecynoic acid

Synthesis of vinyl sulphide containing hydroxyacid (VSHA)

The vinyl sulphide-containing hydroxyacid (VSHA, Scheme 2) was obtained from an alkyne-derivatized fatty compound 10-undecynoic acid, using hydrothiolation.



Scheme 2. Synthesis of vinyl sulfide-containing hydroxyacid (VSHA)

Coupling between alkyne derivative fatty acids and thiols under thermal and photo inititiated conditions were previously described. Meier et al.[38] reported the formation of equimolar amounts of mono-addition (E and Z vinyl sulfide isomers) and di-addition (disulfide) products when using equimolar amounts of alkyne and thiol under thermal initiated conditions (80º C).

We studied the coupling reaction between 2-mercaptoethanol and 10-undecynoic acid at 80º C in bulk or in toluene solution in presence of 10% mol AIBN as radical initiator, as summarized in Table 1.

Table 1. Thiol-yne couplings of 2-mercaptoethanol with 10-undecynoic acid

Run	Thiol/Alkyne Molar ratio	Time (min)	Concentration (M)	Mono Addition (%)	Di Addition (%)	Triple Bond (%)
1	1.05/1	20	-	48	46	6
2	1.05/1	60	-	41	53	4
3	1.05/1	15	5	45	42	13
4	1.05/1	20	5	57	34	9
5	1.05/1	30	5	50	40	10
6	1/1	20	5	62	27	10
7	1/1	20	1	70	15	15
8	1.05/1	20	1	77	20	3

The addition reaction was carried out in bulk using a slight excess of thiol for 20 min (Run 1). The ^{1}H NMR spectrum of crude reaction mixture (Figure 2) showed signals at 5.90-5.58 ppm (H_{c-d}) corresponding to the vinyl-thioether unit and at 2.84 ppm (H_b) corresponding to methylene protons linked to sulfur atom of mono addition product. Moreover, peaks of di-addition product between 2.84 and 2.71 ppm ($H_{b',d',c',i}$) were observed. Signals corresponding to unreacted alkyne and to disulfide at 1.94 ppm and 3.90 ppm could be detected in the spectrum. The vinyl sulfide was obtained as mixture of E and Z isomers in a 48% yield and the di-addition compound with 46% yield. Increasing reaction times increase the di-addition process (Run 2). Using toluene as solvent increases the monoaddition (Run 4 versus 1). Using equimolar amounts of thiol/alkyne seems to increase the monoaddition aduct for the highest concentration (Run 6 versus 4), however an increase is observed for the lowest concentration (Runs 7 and 8). Thus, the highest amount of vinyl sulfide was obtained using a slight excess of thiol (1.05:1 SH/C≡C) and 10% mol AIBN at 80º C and toluene as solvent.[39]

The monoaddition compound as a mixture of E and Z isomers could be isolated by column chromatography. Figure 3 shows the 2-D NMR gHSQC spectrum of the isolated mixture.

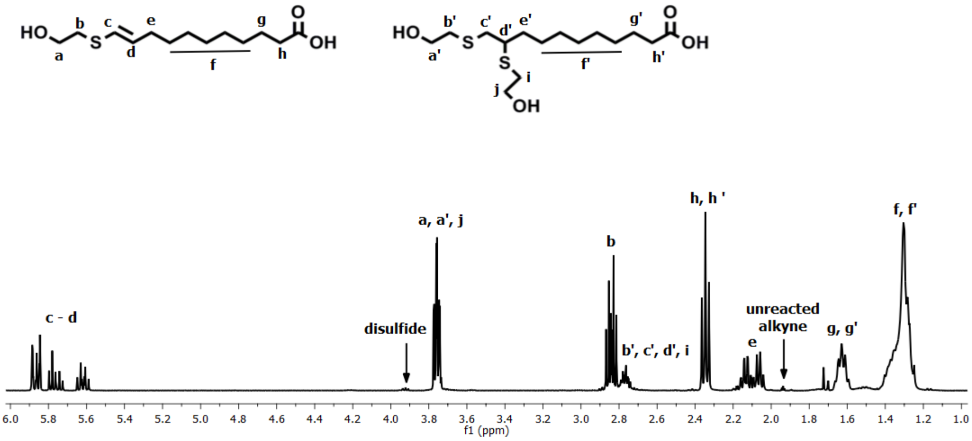


Figure 2. ^{1}H NMR spectrum of the crude reaction of thiol-yne coupling between 2-mercaptoethanol and 10-undecenoic acid

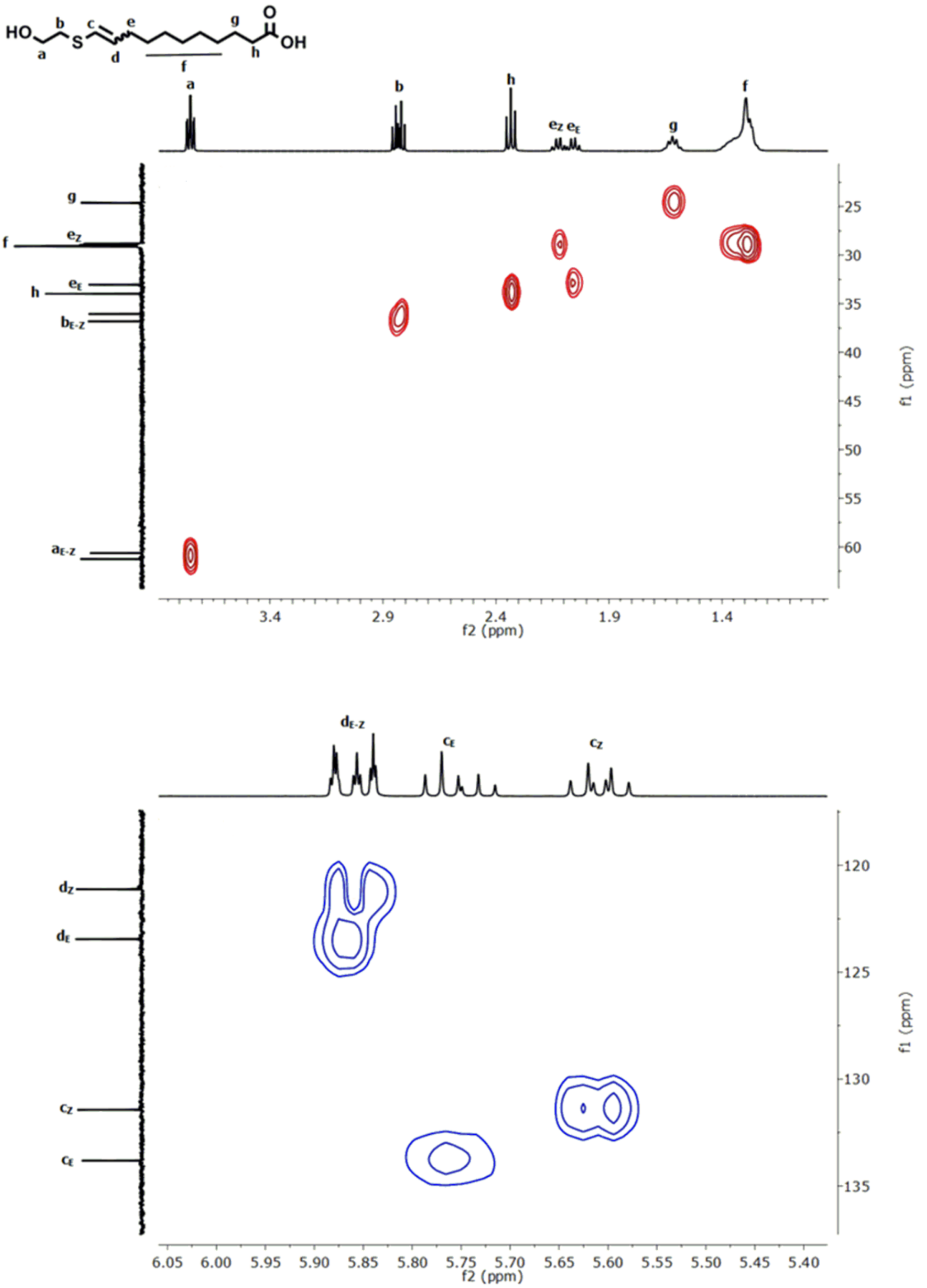


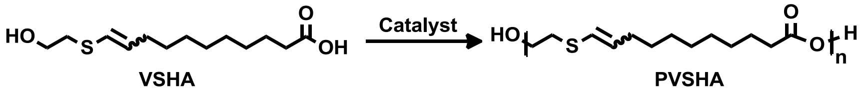
Figure 3. 2-D NMR gHSQC spectrum of isolated mixture of Z and E isomers of VSHA

The presence of the vinyl thioether moiety was confirmed by the presence of two sets of signals between 5.58-5.90 ppm corresponding to the *E* and *Z* C-C double bond protons in the ^{1}H NMR and the signals at 120-140 ppm in the ^{13}C NMR. The ratio E/Z was 1:1 calculated from vinyl proton signals in ^{1}H NMR spectrum. Signals a, b and e appear to split in ^{13}C NMR spectrum into two signals due to the presence of both isomers but only e_E and e_Z can be assigned from empirical calculations. The unequivocally ^{1}H NMR assignments could be carried out using 2-D NMR gHSQC experiments.

Polyester Synthesis

Condensation polyesterifications are conducted under organometallic catalysis, producing high molecular weight products with accelerated polymerization rates. Metal catalysts dominate the industrial condensation polymerization processes, but their negative environmental impact push replacing these original catalysts. Titanium alkoxides are emerging as important polyesterification catalysts due to their high activity, general view that they do not cause environmental problems and acceptable pricing for low cost industrial processes. Using these catalysts for polycondensation requires metals potentially problematic for certain product end uses and hard reaction conditions. These conditions can limit product molecular weight and reduce available building blocks as many can be unstable at such temperatures. In contrast, enzyme-catalyzed condensation polymerization offers a successful and energy-minimizing process of polymerization as an environmentally benign synthetic method. It is metal free and function at moderate temperatures, especially relevant for temperature-sensitive monomers, like those with functional groups as epoxy and vinyl moieties.[40,41] The feasibility of lipase-catalyzed polyesterification of hydroxy acids has been demonstrated, but slow reactions, including solvent and using excessive quantities of lipase are described.

Taking into account these considerations, both kinds of catalysis, chemical and enzymatic, were used to explore the reactivity of the vinylsufide-containing ω-hydroxyacid in the polyesterification reactions (Scheme 3).



Scheme 3. Enzymatic or chemical polymerization of VSHA

On the basis of literature revision, tin(II) 2-ethylhexanoate $Sn(Oct)_2$, dibutyl tin oxide (DBTO) and titanium(IV) butoxide $Ti(OBu)_4$ were tested under similar reactions conditions. In a first stage, oligomerization of VSHA was performed in bulk with 2% mol under nitrogen atmosphere at 120ºC for 1h and subsequently the pressure was reduced to <0.1 mmHg. The reaction was conducted for 48h and molecular weight values were determined on non- fractionated products by SEC relative to polystyrene standards. As can be seen in Figure 4, the highest Mw values were obtained for $Sn(Oct)_2$ while using $Ti(OBu)_4$ and DBTO resulted in lower molecular weights. Polydispersities around 2 were obtained in all cases.

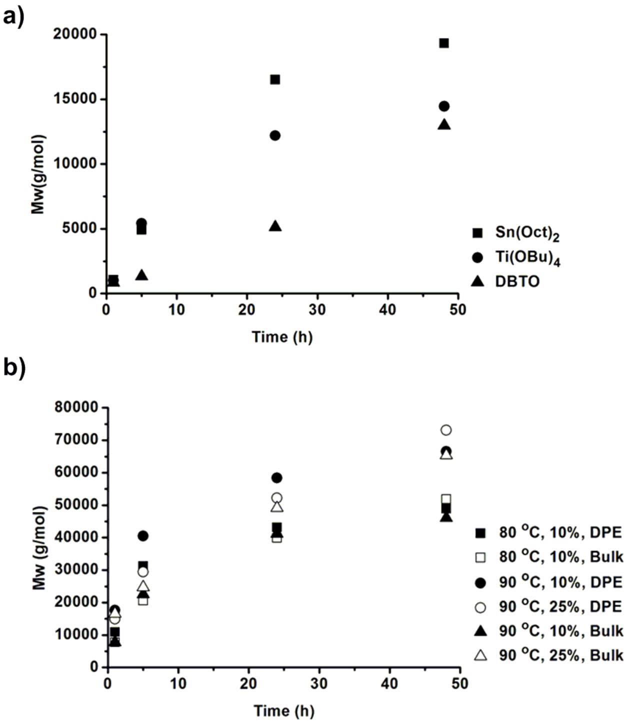


Figure 4. Mw versus time for a) chemical and b) enzymatic polymerization

The enzymatic synthesis of the polyvinylsulfide ester derived from VSHA was carried out under vacuum using Novozyme 435, *Candida Antarctica* Lipase B physiadsorbed to a macroporous acrylic resin and molecular weight values were obtained by SEC (Figure 5b). The SEC analysis for the control reaction in absence of Novozyme 435 verified that chain growth occurs due to enzyme catalysis. Concentrations of 10 and 25%wt relative to monomer were used and as expected the polymerizations with higher catalyst loading took place relatively faster and achieved higher molecular weights. Polymerizations were carried out in bulk or using diphenylether (DPE) as solvent, and higher molecular weights were obtained using a 50% w/v of solvent, according to a greater constrains on chain diffusion for bulk polymerizations and/or to an enhanced activity when the reaction is carried out in DPE.[42] To test the effect of temperature, polymerizations were carried out at 80 and 90ºC since higher temperatures are described to cause decreased monomer conversion presumably because of protein denaturation. Higher molecular weighs were obtained at 90ºC and significant differences can be found between both temperatures at longer reaction times. ^{1}H NMR spectroscopy allowed monitoring the polymer formation by the appearance of a new signal at 4.20 ppm corresponding to the methylene protons in α position to the ester in the repeating unit an the disappearance of the signal at 3.75 ppm corresponding to the methylene protons of the hydroxylic moiety respectively. ^{1}H NMR spectrum of PVSHA can be seen in Figure 5a.

Hydroxy acid chain length seems to have an important effect on the enzymatic polyesterification. It has been described that the lipases exhibits a preference for substrates with chain lengths similar to the fatty acids and the polymerizations of 16-, 12-, and 10-carbon chain length ω-hydroxyacids were described to give products with DP from 115 to 125 while the DP for polymerizations of the 6-carbon hydroxyacid was 80.[43] In our case, the polymerization of VSHA under similar reaction conditions gave products with a DP of 110. Our results seem to indicate that the presence of the vinylsufide moiety in the chain does not influence the enzyme activity, thus being the chain length the main factor that affects the polymerization.

The lower molecular weight obtained when using organometallic catalysts can be explained on the basis of a competitive binding by the catalyst not only at both intrachain ester units and chain-end groups, e.g. hydroxyl and carboxyl moieties, but also at the sulfur atoms. As the molecular weight increases, the terminal group concentration decreases and as a consequence, increased metal ion binding to intrachain oxygen and sulfur atoms occurs, leading to the deactivation of the catalysts and to chain scissions reactions. Moreover, enzyme-catalyzed step polymerizations lead to polydispersities below the ones obtained by traditional chemical catalysts, suggesting that chain growth for lipase-catalyzed condensations occurs with some selectivity and that transesterification occurs less frequently, thus giving products with relatively higher chain uniformity and lower polydispersity.

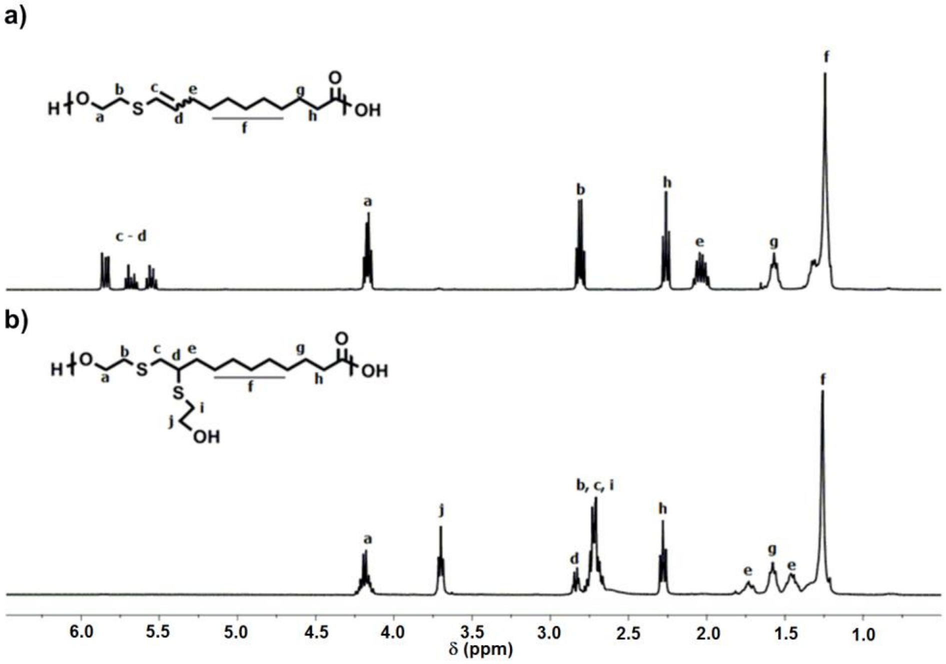
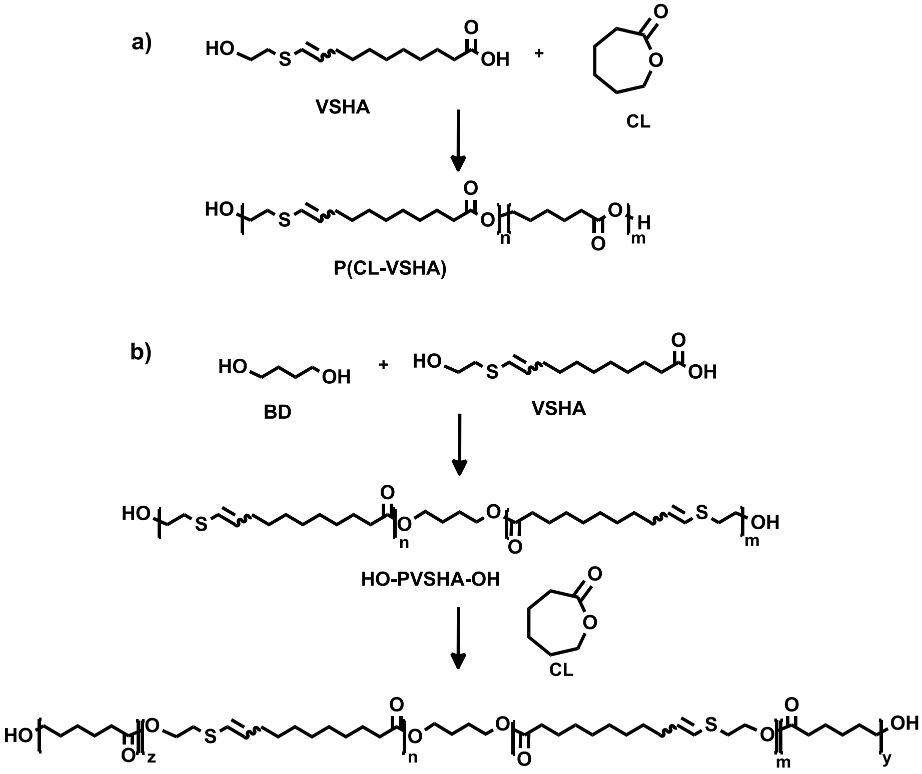


Figure 5. ^{1}H NMR spectra of a) PVSHA and b) modified PVSHA with 2-mercaptoethanol

Copolyester Synthesis

In view of the results obtained for the homopolymerization of VSHA, copolymerization with ε-CL was carried out using Novozyme 435 due to its better performance as a catalyst and to the absence of potential contaminating catalyst or co-reagents for potential biological applications (Scheme 4a).



Scheme 4. Synthesis of a) random P(CL-VSHA) and b) triblock copolymers P(CL-*b*-VSHA-*b*-CL)

Polymerizations were carried out using 10% of enzyme to avoid higher catalyst loadings and at 80 ºC to ensure that partial distillation of monomers or initiator does not take place. DPE in a 50%w/v as solvent was used in all cases. Polymerization of CL was also carried out and a molecular weight higher that the one for VSHA was obtained. Varying monomer ratios were used to prepare P(CL_x-$VSHA_y$).Because of the unknown reactivity ratio of the monomers, all polymerizations were carried out over at least 24h to ensure incorporation of both monomers. Chemical constitution and composition of the resulting copolyesters were ascertained by ^{1}H NMR. Monomer composition of the copolymers was determined by ^{1}H NMR spectroscopy from the ratio of peak intensity of oxymethylene protons of CL and VSHA units at 4,06 and 4,20 ppm respectively (Figure 6a). As can be seen in Table 2, it was found nearly equal to the initial monomer feed ratio. Molecular weights as determined by SEC, increased with the CL/VSHA ratio according to the higher reactivity of CL.

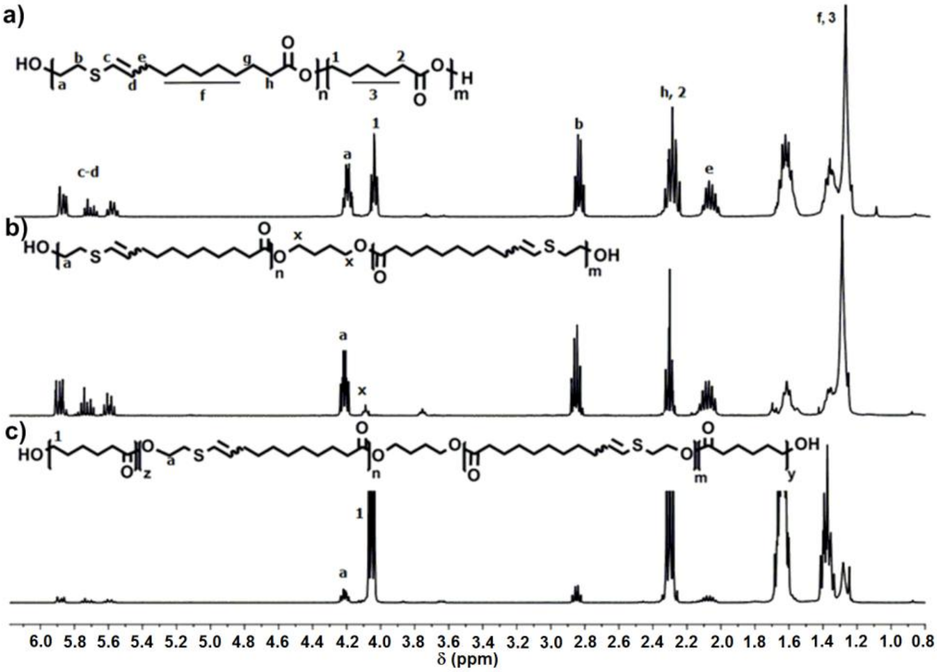


Figure 6. ^{1}H NMR spectra of a) random copolymer P(CL$_{50}$-VSHA$_{50}$) b) dihydroxyl terminated prepolymer HO-PVSHA-OH c) triblock copolymer P(CL-*b*-VSHA-*b*-CL)$_{10}$

Table 2. Molar composition and molecular weights of P(CL$_x$-VSHA$_y$) copolyesters

	Molar Composition[a] CL/VSHA		**Molecular Weight[b] (g mol^{-1})**		
Polymer	**Feed ratio**	**^{1}H NMR ratio**	**Mn**	**Mw**	**PDI**
PCL	-	-	65500	87800	1.3
P(CL$_{80}$-VSHA$_{20}$)	4.0	4.1	30800	46500	1.5
P(CL$_{60}$-VSHA$_{40}$)	1.5	1.6	20700	31300	1.5
P(CL$_{50}$-VSHA$_{50}$)	1.0	1.1	15000	23600	1.6

[a] Molar compostion determined by ^{1}H NMR. [b] Number and weight-average molecular weights measured by SEC.

The polyesters microstructure could be determined by ^{13}C NMR. As it is depicted in Figure 7, the spectra show signals corresponding to the carbon adjacent to the oxygen of the ester function sensitive to sequence distributions al the level of dyads. These signals appear to split with enough resolution into four peaks between 64 and 62 ppm due to the different environments occurring along the polyester chain. The assignment of the peaks was possible by comparison to the ^{13}C NMR spectra of the homopolymers.

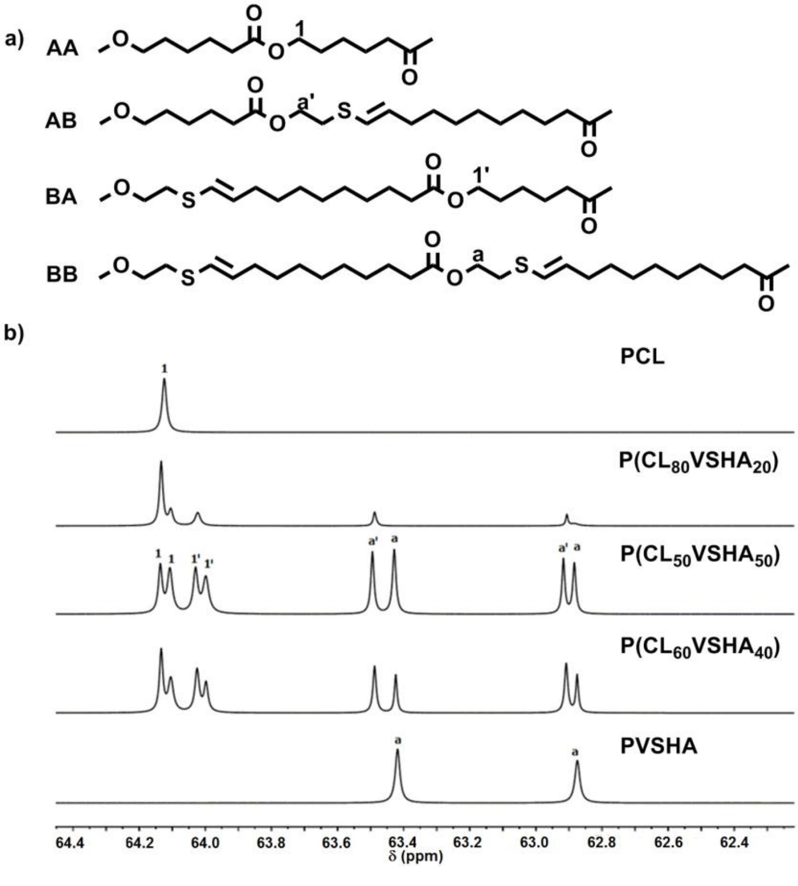


Figure 7. a) The four possible dyads present in P(CL$_x$VSHA$_y$) copolyesters; b) ^{13}C NMR spectra of the indicated polyesters with assignments of the peaks to different carbons. A: CL; B: VSHA

The number-average sequence lengths n_A and n_B can be calculated as follows:

$n_A = 1/ P_{AB}$

$n_B = 1/ P_{BA}$

were P_{AB} and P_{BA} are the probability of finding unit B next to unit A and the probability of finding unit A next to unit B, respectively. P_{AB} and P_{BA} can be calculated by integrating peak areas of the ^{13}C NMR spectrum

$P_{AB} = I_{AB} / (I_{AA} + I_{AB})$
$P_{BA} = I_{BA} / (I_{BA} + I_{BB})$

where I_{AA}, I_{AB}, I_{BA} and I_{BB} are the peak areas for AA, AB, BA and BB sequences, respectively. The degree of randomness R is defined as:

$R = P_{AB} + P_{BA}$

The value of R is 1 for random copolymers, <1 for blocky structures and 0 for block copolymers.

Results from these calculations are summarized in Table 3 and the degree of randomness is between 1.0 and 1.1, close to the expected value for fully random copolyesters. This suggests that despite of the potentially different reactivity ratios of the monomers, the copolymers are randomly distributed because of the rapid transesterification by Novozyme 435.

Table 3. Microstructure analysis of P(CL_x-$VSHA_y$) copolyesters

	Microstructure[a]					
	Dyads (mol %)			**Number Average Sequence Lengths**		**Randomness**
Polymer	**AA**	**AB/BA**	**BB**	**n_A**	**n_B**	**R**
P(CL_{80}-$VSHA_{20}$)	66.8	32.5	0.7	5.1	1.0	1.1
P(CL_{60}-$VSHA_{40}$)	32,4	51.3	16.3	2.2	1.6	1.0
P(CL_{50}-$VSHA_{50}$)	26,0	49,0	25,0	2.1	2.0	1.0

[a] Microstructures were determined statistically by calculation on the basis of the ^{13}C NMR analysis. A: CL; B: VSHA.

After obtaining random P(CL_x-$VSHA_y$) copolymers, triblock copolymers were obtained in two steps (Scheme 4b). A dihydroxyl-terminated VSHA diol (HO-PVSHA-OH) was used to initiate the polymerization of CL and four copolymers P(CL-*b*-VSHA-*b*-CL)$_x$ were synthesized by changing the monomer to initiator molar feed as shown in Table 4. The macroinitiator was prepared by self-polycondensation of VSHA with a low amount of 1,4-butanediol (BD) using the previously described reaction conditions for 16h and its formation was verified by ^{1}H NMR. The total disappearance of the methylene unit adjacent to the carboxylic acid proves that all these groups have reacted with hydroxyl groups of VSHA and BD (Figure 6b). Moreover, the disappearance of signal at 3.6 ppm attributed to the hydroxyl moieties in the BD unit and the appearance of a signal at 4.1 ppm characteristic of the oxymethylene protons confirm that BD efficiently reacted. The ratio of BD to VSHA was determined from signals corresponding to oxymethylene units of BD at 4.09 ppm and to the methylene adjacent to the vinylsulfide moiety of VSHA at 2.10 ppm and the obtained value of 8.8 approaches well to the feed ratio. Moreover, ^{1}H NMR end group analysis was used to determine the molar mass of the macroinitiator by integrating signals at 3.75 and 2.10 ppm. The degree of polymerization and molecular weight (DP = 9.6, Mn = 2323 g mol^{-1}) gave a lower value than the obtained by SEC, given an indication that the polystyrene standards calibration of our system over represents the molecular weight values.

Table 4. Molar compositon and molecular weights of P(CL-*b*-VSHA-*b* -CL) triblock copolyesters

	Molar Composition CL / HO-VSHA-OH		**Molecular Weight[b] (g mol^{-1})**		
Polymer	**Feed ratio**	**^{1}H NMR ratio**	**Mn**	**Mw**	**PDI**
HO-PVSHA-OH	10[a]	8.8	8600	11800	1.4
P(CL-*b*-VSHA-*b*-CL)$_5$	5	4.9	13000	17700	1.4
P(CL-*b*-VSHA-*b*-CL)$_{10}$	10	8.9	27000	45100	1.7
P(CL-*b*-VSHA-*b*-CL)$_{20}$	20	8.7	35100	49600	1.4
P(CL-*b*-VSHA-*b*-CL)$_{30}$	30	19.6	35000	53400	1.5

[a] VSHA/BD ratio for the prepolymer. [b] number and weight-average molecular weights measured by GPC.

HO-VSHA-OH was then used as macroinitiator for the ring opening of CL. The polymerization was carried out for 24h and monomer conversion was complete as determined by ^{1}H NMR spectroscopy for copolymers with monomer to initiator ratios of 5 and 10 (Figure 6c). The conversion decreased with increasing monomer to initiator ratio of 20 and 30, and signals of CL monomer can be seen in the spectrum. This can be due to a lower number of growing chains when this ratio increases and to the viscosity increase with time what limits the accessibility of the monomer to the growing chain. In this way, monomer to initiator ratio as determined by ^{1}H NMR spectroscopy fits well to the theoretical values only in the first two cases.

Thermal properties

The thermal behaviour of copolyesters has been comparatively studied by DSC and TGA; the thermal parameters resulting from these analyses are given in Table 5, where the corresponding data for the parent homopolyesters, PVSHA and PCL, are also included for comparison. DSC measurements showed a melting endotherm in the first heating and a crystallization peak in the subsequent cooling. The second heating DSC traces of the two series of copolyesters are comparatively depicted in Figure 8. As expected the effect of the copolymer composition is a decrease of the melting temperature with an increase of the VSHA molar fraction. Indeed, copolymers containing high percentages of CL melt at a temperature close to the melting point of PCL (57 ºC). When incorporating 50% mol of VSHA into the copolymer, Tm drops to 8 ºC, even lower than the melting point of PVSHA (18 ºC). It can also be noticed that melting enthalpy values slightly decrease with the presence of high amounts of PVSHA. It is interesting to note that this behaviour seems to be independent of the random or block nature of the copolymers and DSC traces for copolymers P(CL_{80} -$VSHA_{20}$) and P(CL-*b*-VSHA-*b*-CL)$_5$ are very similar. By DSC measurements glass transition could be observed in all cases below -40º C.

Data of thermal stability of copolyesters are collected in Table 4. In all cases, decomposition process happens in a single stage with a maximum rate at a range between 400 to 410 ºC. Copolyesters start to lose weight above 325 ºC. The most significant effect in the 5% weight loss temperature ($T_{5\%}$) is a decrease when VSHA is incorporated.

Table 5. Thermal properties of polyesters

Polymer	Tm (ºC)	ΔH (J/g)	T5% (ºC)	Tmax
PVSHA	18	37	337	354-451
PCL	57	67	378	410
P(CL_{80}-$VSHA_{20}$)	34	43	341	402
P(CL_{60}-$VSHA_{40}$)	9	38	-	-
P(CL_{50}-$VSHA_{50}$)	8	31	-	-
P(CL-*b*-VSHA-*b*-CL)$_5$	36	55	337	403
P(CL-*b*-VSHA-*b*-CL)$_{10}$	48	62	354	401
P(CL-*b*-VSHA-*b*-CL)$_{20}$	51	65	370	410
P(CL-*b*-VSHA-*b*-CL)$_{30}$	54	66	374	410

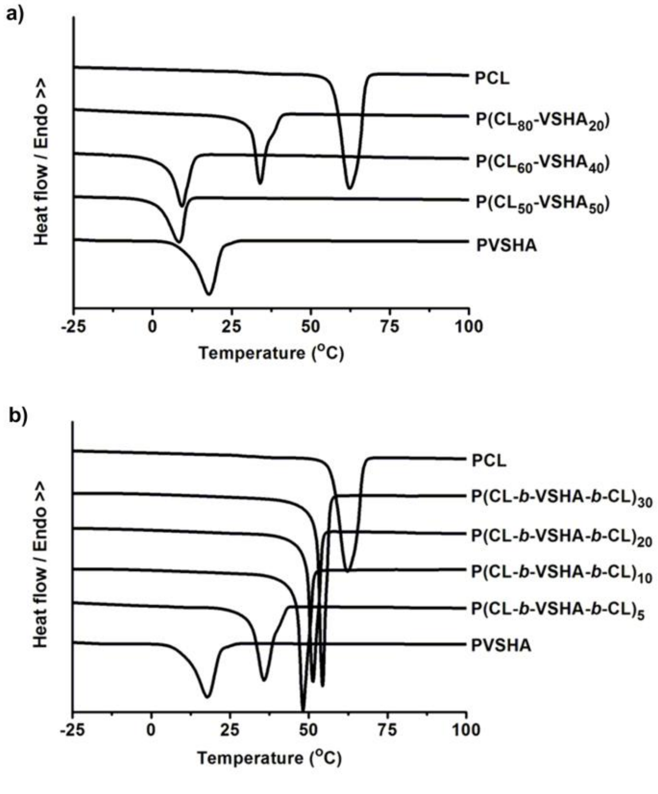


Figure 8. DSC plots of a) random copolymers and b) triblock copolymers

Modification of polyesters

The key feature of the polymers and copolymers is the incorporation of a vinyl sulfide functional group into the repeating unit of the polyester. The addition reaction between this unsaturated group and a thiol is a powerful conjugation strategy that allows for a variety of ligands to be covalently immobilized. The reaction is chemoselective, rapid and mild resulting in hydrolytically stable non-degraded materials. To demonstrate this strategy, commercially available 2-mercaptoethanol was chosen as a model compound.

The reaction was first carried out using PVSHA under stoichiometric conditions but a molar ratio 1:1.3 (vinyl sulfide/thiol) was needed to ensure complete conversion in 15 min. The reaction was carried out at room temperature, under UV irradiation (λ=365 nm) using 1% of DMPA as photoinitiator in THF solution. The course of the reaction was followed by ^{1}H NMR analysis (Figure 5b) by the disappearance of signals at 5.90-5.58 ppm of double bond C=C, and the appearance of new signals at 3.71 and 2.87 ppm corresponding to the C$\underline{H_2}$OH of ME moiety and the CH-S of the main chain. New peaks appeared, at 1.75 and 1.40 ppm that are assigned to the two diastereotopic protons of methylene in α-position to the carbon attached to the sulfur atom, instead of the peak at 2.10 ppm corresponding to methylene protons linked to double bond. Moreover, GPC analysis of PVSHA and modified PVSHA gave similar molecular weights values and a slight increase in polymer polydispersity (Mn=17764, PDI=2.15 and Mn=18661, PDI=2.60, respectively), as can be seen in Figure 9. Thus, no significant degradation of the polyester backbone seems to take place.

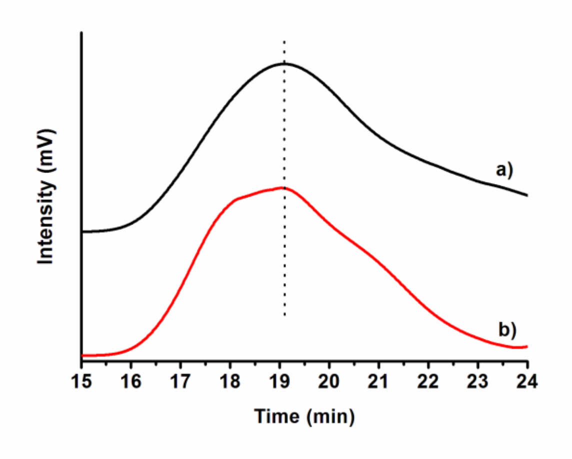


Figure 9. GPC traces of a) PVSHA b) modified PVSHA with 2-mercaptoethanol

A similar strategy can be applied to obtain crosslinked materials by using dithiols. Thus, PVSHA and 1,4-butanedithiol (BDT) were reacted at room temperature, under UV irradiation (λ=365 nm) using 1% of DMPA as photoinitiator in equimolar amounts of vinyl sulfide and thiol. By IR spectroscopy could be observed the disappearance of the signal at 1520 cm^{-1} corresponding to the vibration of double bond C=C after 1h (Figure 10). Insoluble fraction after extraction with chloroform was 90%, proving the efficiency of the reaction in the crosslinking process. DSC analysis of the obtained crosslinked polymer shows an increase of T_g value and the disappearance of melting endotherm of PVSHA (Figure 11).

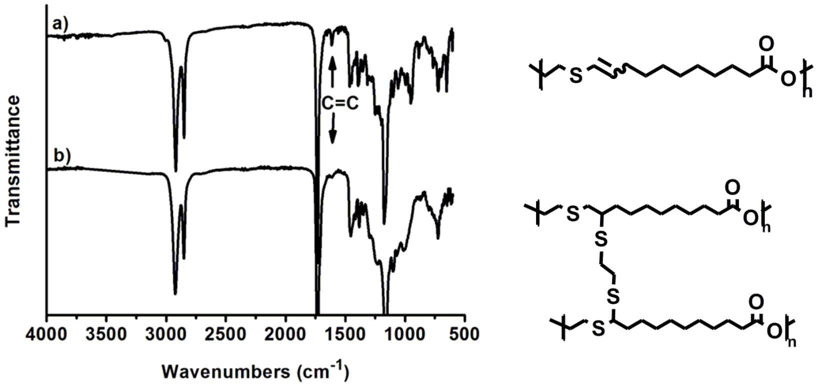


Figure 10. IR spectrum of a) PVSHA and b) PVSHA crosslinked with BDT

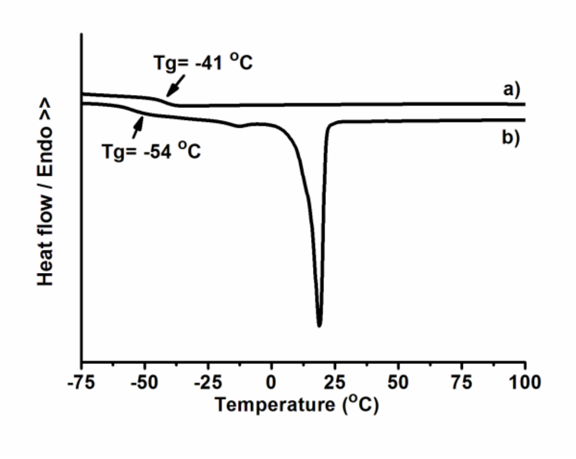


Figure 11. DSC plots of a) PVSHA crosslinked with BDT and b) PVSHA

The surface modification of copolyesters was also investigated. Films from triblock copolyesters were prepared by solution casting and 7-mercapto-4-methylcoumarin (Cm-SH) was used as a probe.[39] Figure 12 shows the fluorescence emission spectrum of P(CL-*b*-VSHA-*b*-CL)$_{30}$ film at different reaction times. As the reaction proceeds, an emission band appears at 425 nm and its intensity increased, with sufficient sensitivity to monitor the thiol-ene addition of Cm-SH to vinyl sulfide groups present on copolymer surface.

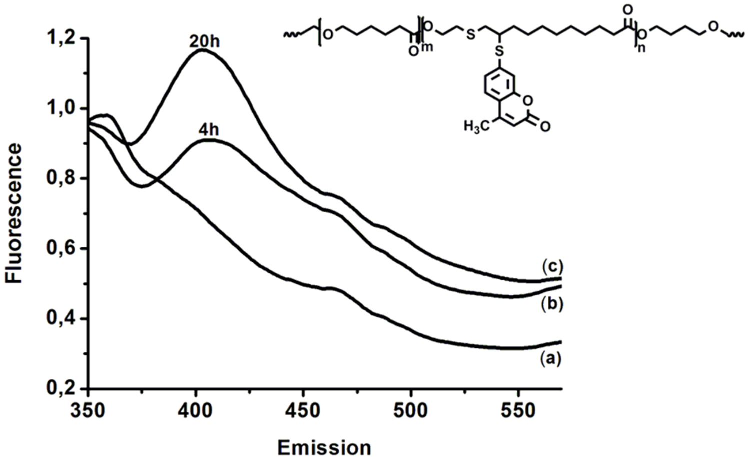


Figure 12. Fluorescence spectra of P(CL-*b*-VSHA-*b*-CL)$_{30}$ and Cm-SH reaction a) initial film b) at 4h c) at 20h

As a conclusion of this chapter, the preparation of a vinyl sulfide-containing hydroxy acid (VSHA) from undecylenic fatty acid via thiol-yne monoaddition has been carried out. The compound has been obtained with moderate yield as a mixture of E/Z isomers. Metal- and enzymatic- catalyzed polycondensation of VSHA was investigated to obtain functional polyesters. Higher molecular weights were obtained when using enzymatic polymerization and the best results were obtained using 25% of Novozyme-435, in DPE solution at 90ºC. Random copolymers were prepared by direct enzymatic copolymerization of VSHA and CL. Triblock CL-VSHA-CL copolymers were obtained by VSHA self-condensation with BD as initiator, and using this macroinitiator for ring-opening polymerization of CL. The copolymers displayed semicrystalline behaviour with melting temperatures from 8 to 57 ºC, and a good thermal stability with no significant weight loss below 300ºC. Thiol-ene chemistry type crosslinking and surface functionalization have been employed to open new application fields. Evidence of the successful reactions was obtained by NMR, IR and fluorescence spectroscopies.

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Chapter 5

Post-Polymerization Modification of Functional Polyesters from Castor and Sunflower Oils

Introduction

As mentioned in the previous chapters, aliphatic polyesters continue to receive significant attention in the design and construction of synthetic materials for use in biomedical applications due to their biocompatibility and biodegradability.[1] However, their versatility and successful use as commodity plastics is limited as it is their exploitation in biomedical, electronic and optical sectors. The absence of reactive functionalities on the polymer backbone greatly limits their use in a series of demanding applications where the precise control and placement of functionality is critical. The introduction of functional groups on the backbone can modulate the physical, chemical and biological properties of polyesters. However, the synthesis of functional aliphatic polyesters remains a challenge in polymer science.[2]

A traditional approach for generating new biomaterials has been to design one polymer for one particular application. In order to streamline the discovery process, a more efficient strategy would be to design new and versatile materials capable of successful performance in multiple diverse applications. With this approach, materials can be versatile in terms of mechanical characteristics and chemical functionality. Mechanical versatility implies that a single technique can achieve a spectrum of strength-related properties. Chemical versatility can be defined as the ability to introduce a wide range of functional moieties into the polymer at various time points in the synthesis, during the prepolymer stage or as a crosslinked film. A material that possess both mechanical and chemical versatility could potentially allow for the modulation of both sets of properties independently.

Strategies have emerged that employ a variety of routes and chemistries for the functionalization of synthetic polyesters via copolymerization with specialty monomers, post-polymerization modification or a combination of these two strategies.[3] These approaches include the polymerization of monomers with moieties that are inert towards the polymerization conditions, but which can be quantitatively converted into a broad range of functional groups. In this way, a simple polyester platform with a versatile chemistry for coupling of numerous pendant units could allow for the construction of multifunctional materials.

Ideally, the modification reactions must be highly efficient and occur without the use of harsh reactions conditions and reagents. Thus, click reactions are particularly well suited for modification of polymer chains. To avoid polymerization methods that often require toxic chemical catalysts, enzyme-catalyzed polymerization provides a strategy for producing useful polymeric materials with many advantages including mild reaction conditions, high tolerance of functional groups, high catalyst activity and the use of nontoxic biocatalysts.[4]

To create multifunctional copolymers having a high degree of versatility in the structure and composition, a few criteria must be met regarding the types of chemistries and reaction conditions employed. The reaction environment should be sufficiently mild to avoid premature degradation of the polymer while allowing for the incorporation of numerous polymer and small molecules ligands onto the polymer backbone. The choice of highly efficient chemistry would improve the consumption of the polymer reagents and, as it is often difficult to remove free polymer remaining in the desired material, would produce a more pure product. Additionally, when working with a hydrolytically degradable polymer system the ability to incorporate different units in a single step to afford a multifunctional copolymer is beneficial, as it minimizes the premature degradation of the polyester backbone that may result from sequential functionalization reactions.

The work of this chapter is focused in extending the use of sunflower and castor oils in the synthesis of functionalized polyesters by design of specialty monomers. Click reactions are particularly well suited for modification of polymer chains. We applied thiol-ene and oxime chemistries to the modification of vinyl sulfide- and ketone-containing polyesters. The oxime ligation is particularly attractive but has received much less attention than other click type reaction such as thiol-ene, most probably due to the difficulties associated with the synthesis, manipulation and storage of modified molecules containing amino-oxy moieties. Oxime bond formation is faster at mild acidic pH and above millimolar range concentration. When neutral pH and sub-millimolar concentrations are necessary, nucleophiles can be used to catalyze the reaction. Indeed, oxime exchange is sluggish, especially at neutral pH, and required catalysis, such as heat, acids and nucleophiles. Thus, oximes are ideally suited for preparing bioconjugates that are stable at physiological pH, as complete or partial hydrolysis requires strong acid conditions. Oxime ligation has emerged as powerful tool for the engineering of various types of bioconjugates that have already been successfully used as artificial vectors for drug delivery, imaging proves, synthetic vaccines and functional arrays.[5]

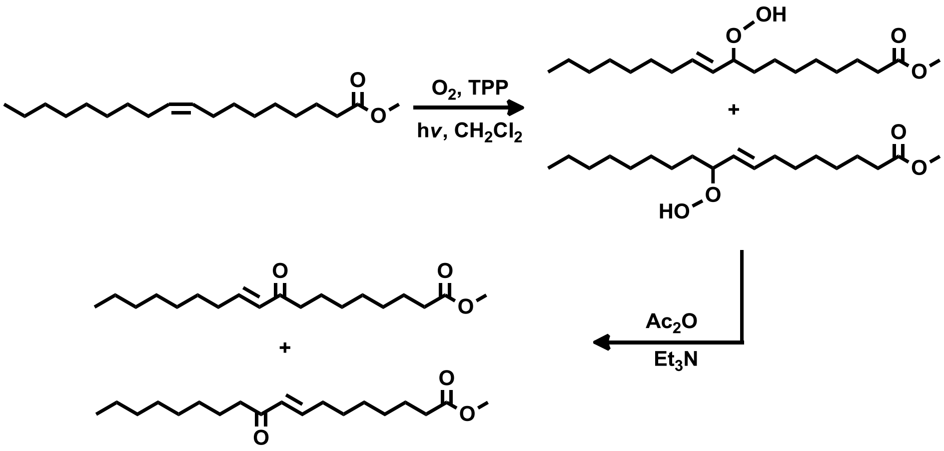
The investigations using these two reactions, thiol-ene and oxime, for the derivatization of polyesters are addressed to demonstrate how sequential postpolymerization reactions can be utilized for multiple functionalization and also highlight complications with a multiple stage process versus the advantages of a single step strategies.

Below we describe the enzymatic synthesis of copolyesters from vinyl sulfide-containing hydroxyacid (VSHA) and ketone-containing hydroxyester, obtained by thiol-Michael addition to the α-β-unsaturated ketone derived from methyl oleate. We applied the chemo selective thiol-ene and oxime reactions to these copolyesters with two “clickable” moieties in a sequential process or in a one-pot single step functionalization.

Monomer Synthesis

Synthesis of enone derivative of methyl oleate

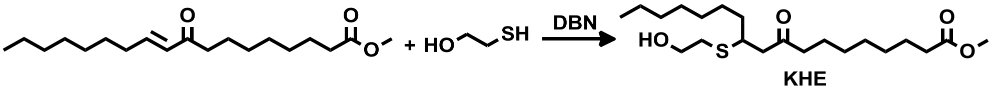
The synthesis of the enone containing-fatty acid was carried out by an environmentally friendly chemical procedure from the methyl oleate derived from high oleic sunflower oil. We used the singlet oxygen “ene” reaction which is one of the most investigated processes in organic chemistry to functionalize the allylic C-H bonds of unsaturated compounds. This reaction was discovered in 1948 by Schenck,[6] who demonstrated that allylic hydroperoxides are handily prepared by reaction of alkenes with photochemically generated singlet oxygen. The mechanism of this reaction has been widely studied and it is actually well established.[7] For synthetic applications, the unsaturated substrate can be photoxygenated “in situ” with singlet oxygen generated by means of a high pressure sodium-vapor lamp and *meso*-tetraphenylporphiryn (TPP) as sensitizer in an oxygen saturated medium, to give a mixture of isomeric allylic hydroperoxides (Scheme 1). This reaction has been used to oxidize the allylic position of fatty acids and their derivatives[8,9] such methyl oleate. The mild conditions utilized and the use of oxygen, as the only reagent, makes this process particularly favorable from both an economical and ecological viewpoint. One of the most interesting reactions of the allylic hydroperoxides is its conversion into a regioisomeric mixture of enones using acetic anhydride and pyridine or tertiary amines. We have applied this reaction to obtain an α,β-unsaturated ketone-containing fatty acid derivative.[10]



Scheme 1. Enone-containing fatty acid derivative

Synthesis of ketone-containing hydroxyester (KHE)

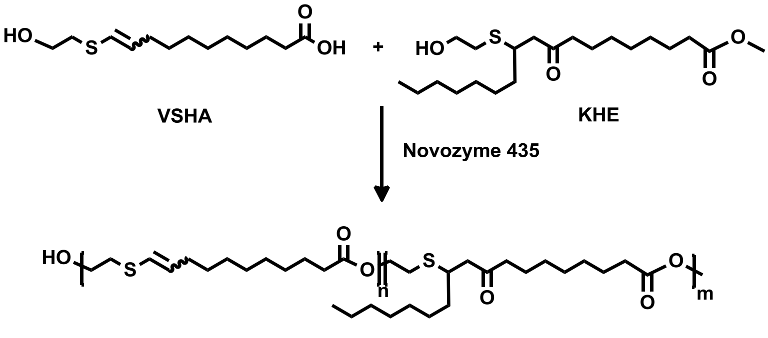
Thiol-Michael addition is an efficient route that can be used for the synthesis of novel monomers from renewable resources due to the ability of adding a broad range of functionalities to the double bond of α,β-unsaturated carbonyl compounds. Thus, the ketone-containing hydroxyester (KHE) was synthesized from the enone derivative of methyl oleate via thiol-Michael addition.[11] 2-Mercaptoethanol was chosen to obtain the hydroxyester by bringing primary hydroxyl functionalities to enone-containing fatty ester. Thiol-Michael addition was carried out under acid and basic/nucleophilic conditions. The use of vanadyl triflate ($VO(OTf)_2$) to catalyze Michael reactions with N-, P-, C- and S- centered protic nucleophiles has been described.[12] Conjugate addition of 2-mercaptoethanol to α,β-unsaturated carbonyl compounds was examined in the presence of 5 mol % of $VO(OTf)_2$. This reaction proceeded chemoselectively due to the amphoteric character of $VO(OTf)_2$ by which the more acidic thiol end gets activated more efficiently that the corresponding alcohol end. The addition was carried out at room temperature using an excess of 1.2 mol of thiol and the complete conversion was reached in 1h in a 98% yield. The thiol-Michael addition has been also examined in the presence of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) due to its both basic and nucleophilic character.[13] The reaction was carried out with 0.1% of DBN and an equimolar ratio of reactants at room temperature and the total consumption of enone took place in 1h (Scheme 2).



Scheme 2. Thiol-Michael addition to enone-containing fatty acid

Copolyester Synthesis

Our goal was to design a versatile copolyester platform capable of bearing multiple functional ligands by means of a post-polymerization modification strategy. Two comonomers were choosen (Scheme 3): VSHA was selected because it contains a vinyl sulfide moiety capable to accept a thiol rapidly, without any metal catalyst allowing for a variety of ligands to be covalently inmobilized.[14] KHE was chosen as a monomer due to the presence of a ketone, which has the ability to react chemoselectively with oxyamine-, hydrazine-, and hydrazide-terminated ligands. This reaction is mild and it can proceed rapidly at physiological conditions and without need of any co-reagents or catalyst.[5]



Scheme 3. Copolymerization of VSHA and KHE

The synthesis was designed in view of biological applications and therefore, copolymers were generated without any potential contaminating catalyst or co-reagents. Novozyme-435, *Candida antarctica* lipase B physi-adsorbed to a macroporous acrylic resin, was successfully used in the synthesis of poly vinylsulfide ester derived from VSHA[15] and poly ketoester from KHE.[11] In this way, homopolymerization of both monomers with 10% of catalyst at 90 ºC and using DPE as solvent led to polymers of 70000 and 40000 g/mol^{-1} respectively, after 48 h (Figure 1a).

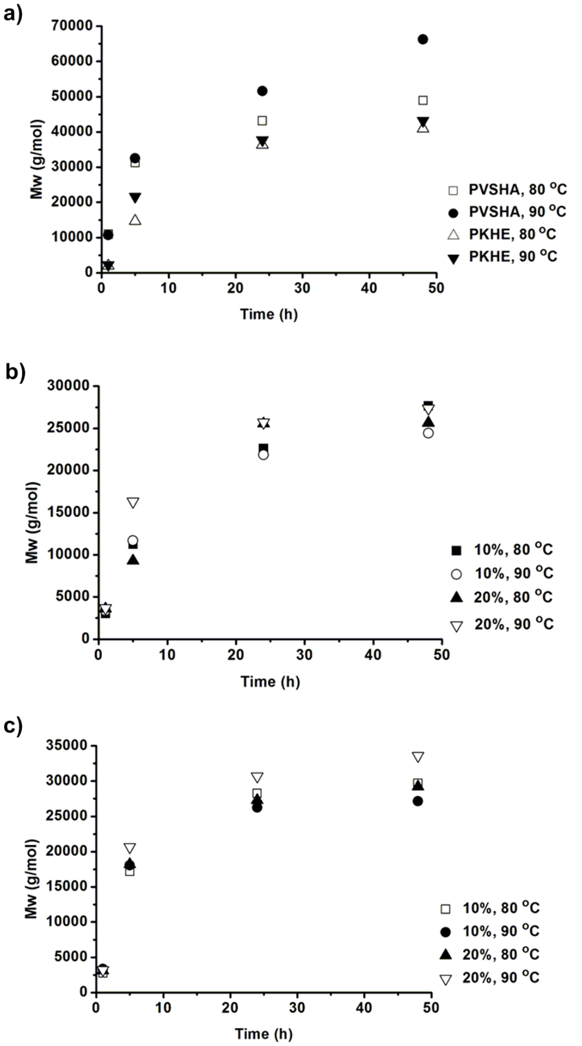


Figure 1. M_w versus time for a) homopolymers of VSHA and KHE in DPE b) copolyesters (VSHA:KHE, 1:1) in bulk c) copolyesters (VSHA:KHE, 1:1) in DPE

In view of these results, copolymers using 1:1 molar ratio of comonomers and 10% of catalyst were obtained by heating in bulk at 80 and 90 º C. Similar molecular weights around 25000 g mol^{-1} and polydispersities of 1.6-1.8 were obtained after 48 h of reaction as can be seen in Figure 1b. No significant differences were observed by increasing catalyst loading to 20% at both temperatures (Figure 1b). Polymerizations were also carried out in the same conditions but using 50% w/v of DPE as solvent. Higher molecular weights were obtained by solution polymerization, according to greater constraints on chain diffusion for bulk polymerizations and/or to an enhanced activity when the reaction is carried out in DPE.[16] Using the two monomers, copolymers of different composition were also obtained. Molar ratios of VSHA:KHE of 1:4 and 4:1 were considered and to obtain high molecular weights and low polydispersity indices, temperature of 90 ºC, 20% of Novozyme-435 and 50% w/v of DPE were used. In this way, higher molecular weights were obtained in both cases (Table 1).

Table 1. Molar composition and molecular weights of P(VSHA$_x$KHE$_y$) copolyesters

	Molar Composition VSHA / KHE		**Molecular Weight (g/mol)**		
Polymer	**Feed ratio**	**^{1}H NMR^a ratio**	**Mn NMR^b**	**Mn SEC^c**	**PDI**
P(VSHA$_{80}$KHE$_{20}$)	4.00	3.88	32460	63810	1.9
P(VSHA$_{50}$KHE$_{50}$)	1.00	0.98	15530	27140	1.7
P(VSHA$_{20}$ KHE$_{80}$)	0.25	0.32	24810	41000	1.6

[a] Molar composition determined from ^{1} H NMR by using using VSHA signal at 2.10 ppm and KHE signal at 0.87 ppm. [b] Mn values were calculated by using VSHA signal at 2.10 ppm and KHE signal at 0.87 ppm and end group signal at 3.73 ppm (C$\underline{H}_2$-OH). [c] THF as solvent.

The chemical structure of the copolyester was determined by ^{1}H NMR (Figure 2a). A new signal at 4.22-4.14 ppm corresponding to the ester repeating units appears. The presence of the vinyl thioether moiety was confirmed by the appearance of two sets of signals between 5.55 and 5.90 ppm corresponding to the E and Z C-C double bond protons. Moreover, the signal corresponding to methylene protons vicinal to double bonds appear at 2.10 ppm. The presence of KHE moiety was confirmed by signals at 3.14 ppm corresponding to the methine linked to sulfur, signals at 2.64

and 2.40 ppm corresponding to methylene in α-positions to the ketone and signal at 0.87 ppm due to side chain methyl group.

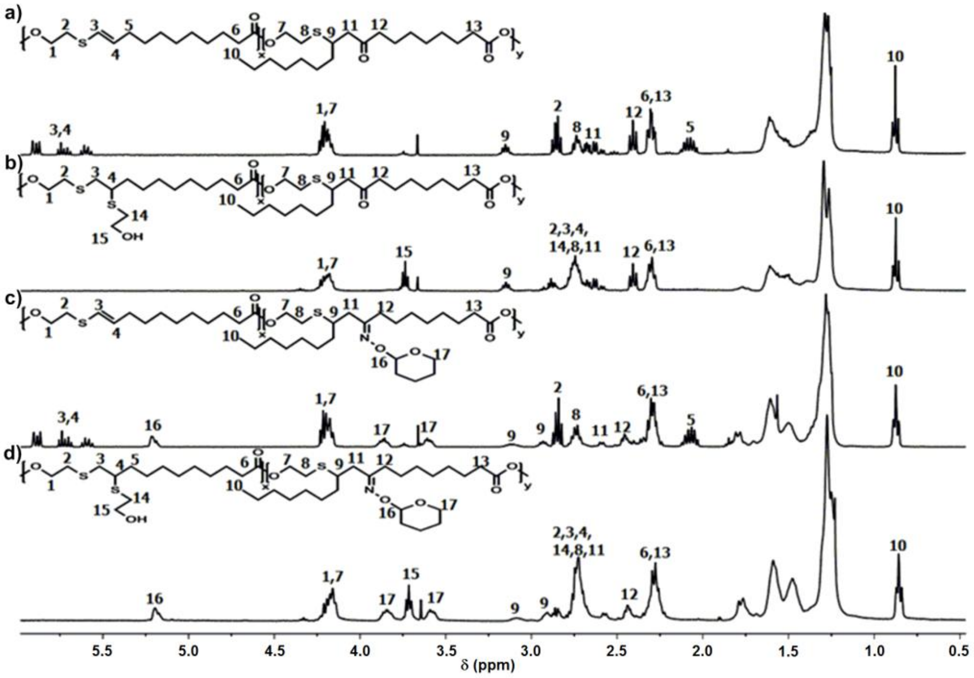


Figure 2. ^{1}H NMR spectra of a) P(VSHA$_{50}$KHE$_{50}$) copolymer
b) P(MVSHA$_{50}$KHE$_{50}$) c) P(VSHA$_{50}$MKHE$_{50}$) d) P(MVSHA$_{50}$MKHE$_{50}$)

By integrating VSHA signal at 2.10 ppm and KHE signal at 0.87 ppm, copolyester composition was calculated and resulted very close to monomer feed (Table 1). Moreover, molecular weight was obtained from VSHA signal at 2.10 ppm and KHE signal at 0.87 ppm and end group signal at 3.73 ppm (C$\underline{H}_2$-OH). Significant differences were noticed between the absolute molecular weights calculated by ^{1}H NMR and the molecular weights evaluated by SEC using THF as solvent, giving an indication that the polystyrene standards calibration of our system over represents the molecular weight values.

To obtain more detailed information about the structure of the copolyesters ^{13}C NMR spectra were obtained. The signals attributable to the ester repeating unit appear at 173.7 ppm (C=O) and at 63.7 and 63.0 ppm (CH$_2$-OCO). Moreover, signals of VSHA unit at 133.2, 131.2, 123.9 and 121.5 ppm (C=C, E and Z isomers) and those of the KHE at 209.1 ppm (CO) can be seen.

The sensitivity of the ^{13}C NMR to small differences in the chemical environment enables us to determine the different dyads (AA, AB, BA and BB) structures (Figure 3). The determination is possible assuming that the methylene carbons adjacent to the oxygen of the ester function have chemical shifts identical to those to the corresponding homopolyesters as found for other copolymers.[17] These signals appear to split with enough resolution into several peaks between 64.0 and 63.0 ppm due to the different environments occurring along the polyester chain.

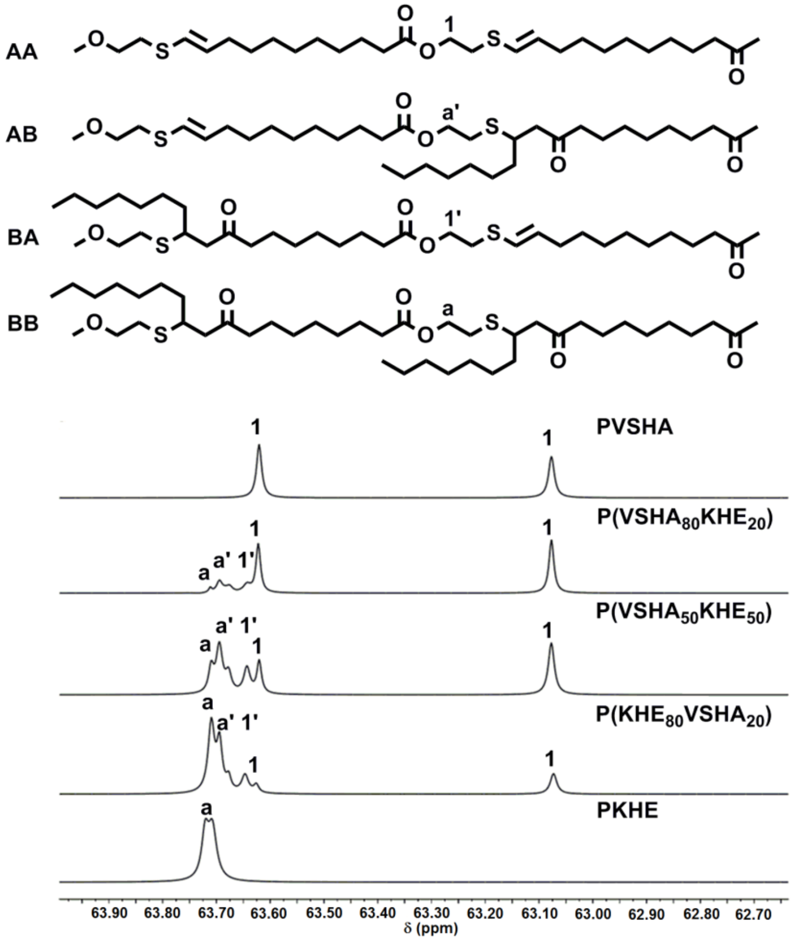


Figure 3. The four possible dyads present in P(VSHA$_x$-KHE$_y$) copolyesters and ^{13}C NMR spectra of the indicated copolyesters with assignments of the peaks to different carbons

The number average sequence lengths n_A and n_B can be calculated as follows:

$$n_A = 1/ P_{AB}$$

$$n_B = 1/ P_{BA}$$

were P_{AB} and P_{BA} are the probability of finding unit B next to unit A and the probability of finding unit A next to unit B respectively. P_{AB} and P_{BA} can be calculated by integrating peak areas of the ^{13}C NMR spectrum

$$P_{AB}= I_{AB} / (I_{AA} + I_{AB})$$

$$P_{BA} = I_{BA} / (I_{BA} + I_{BB})$$

were I_{AA}, I_{AB}, I_{BA} and I_{BB} are the peak areas for AA, AB, BA and BB sequences respectively. The degree of randomness R is defined as:

$$R = P_{AB} + P_{BA}$$

For fully random copolymers, R is equal to 1, whereas it is >1 for alternating and close to 0 for block copolymers.

As seen from Table 2 all copolymers present almost ideal random microstructure with R independent of the copolymer composition. This suggests that even if there exist differences in reactivity ratios of the monomers, the copolymers are randomly distributed because of the rapid transesterification by Novozyme-435.

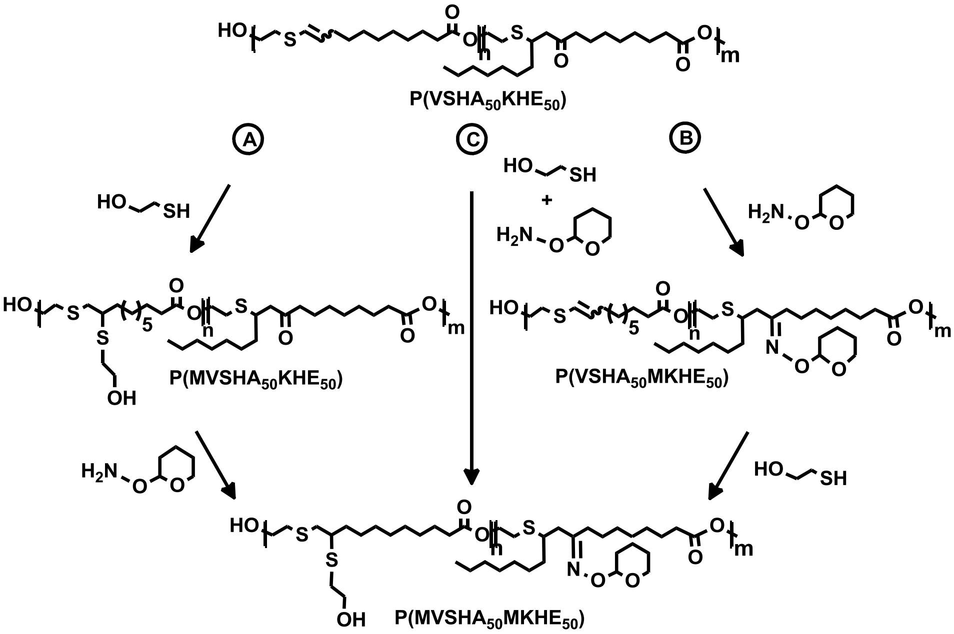
Table 2. Microstructure analysis of P(VSHA$_x$-KHE$_y$) copolyesters

	Microstructure[a]					
	Dyads (mol %)			**Number Average Sequence Lengths**		**Randomness**
Polymer	**AA**	**AB/BA**	**BB**	**n_A**	**n_B**	**R**
P(VSHA$_{80}$ -KHE$_{20}$)	74	25	1	6.7	1.0	1.05
P(VSHA$_{50}$ –KHE$_{50}$)	39	49	12	2.6	1.5	1.05
P(VSHA$_{20}$ –KHE$_{80}$)	15	54	31	1.5	2.2	1.10

[a] Microstructures were determined statistically by calculation on the basis of the ^{13}C NMR analysis A: VSHA; B: KHE.

Copolyester Modification

We attempted sequential and single steps reactions for modification of vinylsulfide-ketone-containing copolyesters (Scheme 4). We have examined if sequential post-polymerization reactions are complicated by the presence of both moieties and if the analogous one-pot single step reaction yields isolated polymers with agreement between stoichiometries of the reactants and the functionalized polymers.



Scheme 4. Sequential and one-pot modifications of P(VSHA$_{50}$-KHE$_{50}$)

Sequential post-polymerization modification was first conducted with 2-mercaptoethanol using a molar ratio 1:1.3 (vinylsulfide/thiol), under UV irradiation (λ = 365 nm) with 1% of DMPA as photoinitiator in THF solution to lead to P(MVSHA-KHE) (Scheme 4, route A). The course of the reaction after 30 min was followed by ^{1}H NMR analysis (Figure 2b) by the disappearance of signals between 5.90 and 5.55 ppm (H_3,H_4) corresponding to the double bond in the polymer precursor and the appearance of a new signal at 3.75 ppm corresponding to CH_2OH (H_{15}) of 2-mercaptoethanol moiety linked to main chain. Moreover, the peak at 2.10 ppm corresponding to methylene protons linked to double bonds of the precursor dissapears. By ^{13}C NMR, the disappearance of C=C signals between 133.2 and 121.5 ppm and the appearance of the new methine signal at 46.2 ppm and the new methylene signals at 38.6 ppm (CH_2-S) and 61.4 ppm (CH_2-OH) are observed.

After thiol-ene addition, molecular weight from ^{1}H NMR analysis could not be determined because of the new signals from mercaptoethanol moiety overlap to the end group signals. By SEC analysis the modified polymer had lower polystyrene equivalent molecular weight with an increase in polydispersity (Table 3). Thiol-ene modification of main chain[18] or side chain[19] has been reported that occurs without side reaction as degradation or polymer coupling. By thiol-ene grafting a branched polymer is produced, which makes complex the comparison of SEC results with the linear precursor and accurate molecular weight assignments upon thiol-ene grafting are difficult.

Oximes could be easily generated by the coupling reaction between ketones and oxyamines. Initially, to demonstrate this conjugation strategy, we studied several model oxime modifications using ketone moiety of polyhydroxyester (PKHE) and *O*-(tetra-hydro-2H-pyran-2yl) hydroxylamine, chosen as model ligand. Therefore, the reaction was first carried out with 50% excess of oxyamine relative to ketone moiety at room temperature. After 8 h, the reaction achieved complete conversion and the ^{1}H NMR spectrum of a polymer, that was fully converted to its ketoxime analogue, showed new characteristic resonances at 5.20 ppm, 3.85 ppm and 3.60 ppm corresponding to the tetrahydropyranyl moiety (Figure 4). Additionaly, new proton resonance was detected at 2.91 ppm correlated with a decrease in the intensity of methine signal at 3.14 ppm (H_3). The further spectroscopic analysis, 2-D NMR gHSQC confirmed that the peak at 2.91 ppm corresponds to a methine. These two methine signals can be attributed to the two isomeric configuration of the oximes. Moreover, ^{13}C NMR spectrum confirmed the formation of the oxime by the appearance of signals attributable to the oxime bond at 160.6 ppm and the oxyamine moiety at 100.6 ppm and 62.8 ppm together with the disappearance of ketone carbonyl signal at 209.1 ppm. No degradation of the polyester backbone was observed by GPC.

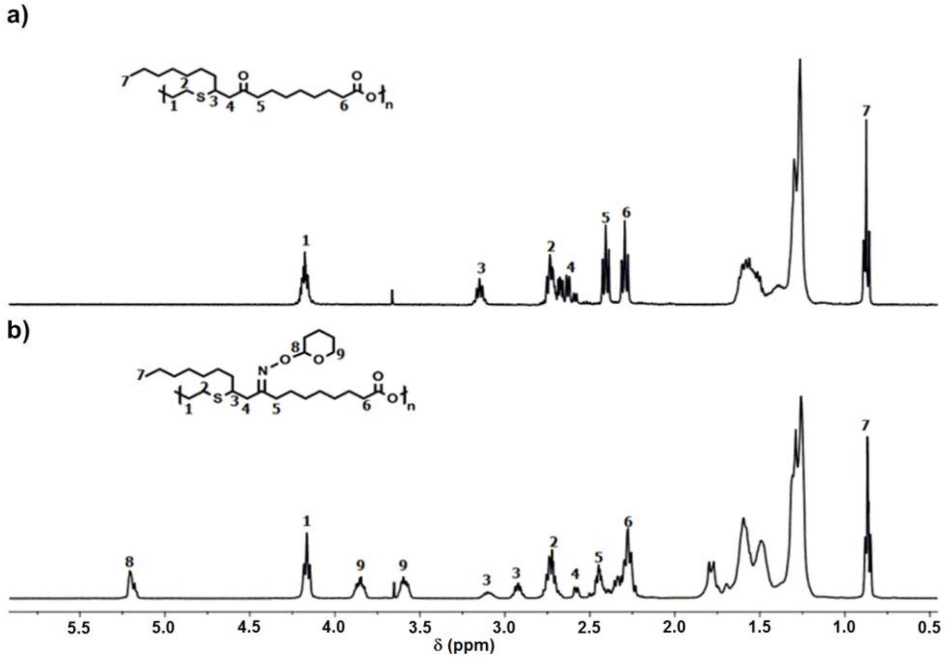


Figure 4. ^{1}H NMR spectra of a) PKHE homopolymer b) PKHE modified with *O*-(tetra-hydro-2H-pyran-2 yl)hydroxylamine

The modification of ketone moiety of copolyester P(VSHA$_{50}$KHE$_{50}$) was performed with *O*-(tetra-hydro-2H-pyran-2yl) hydroxylamine at room temperature using a 50% excess of oxyamine relative to ketone content, to give P(VSHA$_{50}$MKHE$_{50}$) (Scheme 4, route B). After 8 h complete conversion of ketone to oxime is observed. Figure 2c shows the ^{1}H NMR spectrum of the copolymer with the new proton resonances at 5.20 ppm (H$_{16}$), 3.85 ppm and 3.60 ppm (H$_{17}$) attributed to the tetrahydropyranyl moiety. The methine proton linked to sulfur atom (H$_9$) was also detected with resonances appearing at 3.10 ppm and 2.91 ppm. Moreover, ^{13}C NMR spectrum shows signals attributable to the oxyamine moiety at 100.6 and 62.8 ppm together with the disappearance of ketone carbonyl signal at 209.1 ppm and the appearance of the new signal at 160.6 ppm of the oxime bond.

Next, the modification of ketone moiety of P(MVSHA$_{50}$-KHE$_{50}$) (Scheme 4, route C) with *O*-(tetra-hydro-2H-pyran-2yl) hydroxylamine was performed using the above mentioned conditions. After 8 h complete conversion of ketone to oxime is observed obtaining P(MVSHA$_{50}$-MKHE$_{50}$). Figure 2d shows the ^{1}H NMR spectrum of the copolymer with the new proton resonances at 5.20 ppm (H_{16}), 3.85 ppm and 3.60 ppm (H_{17}) attributed to the tetrahydropyranyl moiety. The methine proton linked to sulfur atom (H_9) was also detected with resonances appearing at 3.10 ppm and 2.91 ppm, confirmed by spectroscopic analysis, 2-D NMR gHSQC (Figure 5).

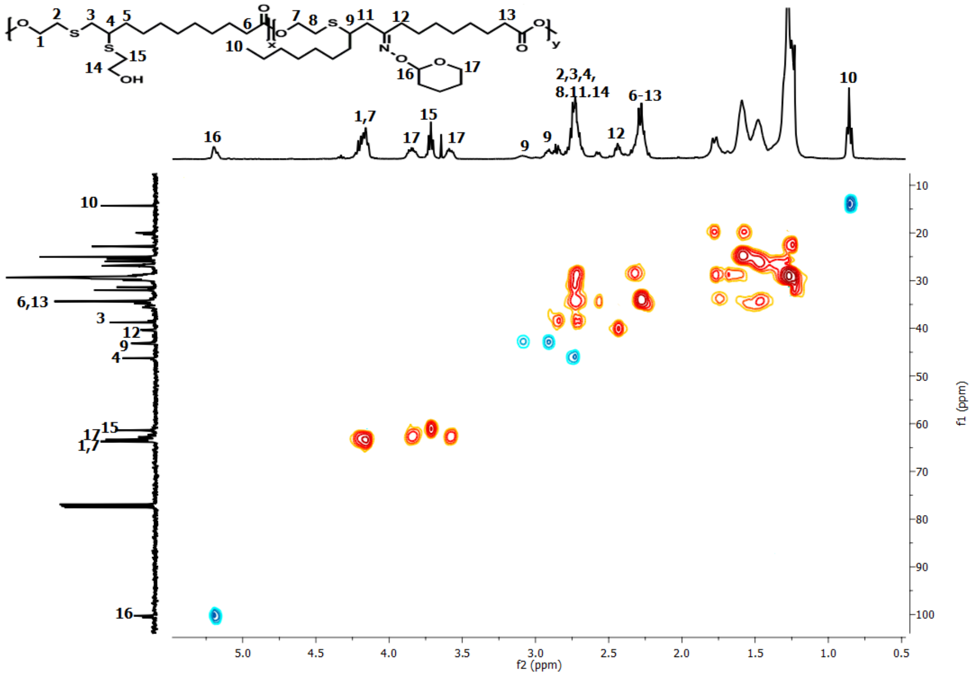


Figure 5. 2-D NMR gHSQC spectrum of P(MVSHA$_{50}$MKHE$_{50}$)

Likewise, the modification of P(VSHA$_{50}$-MKHE$_{50}$) with 2-mercaptoethanol (Scheme 4, route B) was carried out leading to P(MVSHA$_{50}$-MKHE$_{50}$). Similar results as sequential modification route A, were obtained.

To explore the utility of acid-catalyzed oxime formation, the reaction was also carried out by using p-toluenesulfonic acid. In this case, and using 1:1 molar ratio ketone/oxyamine, complete reaction took place in 5 h. and without significant variations on molecular weights after this second modification were observed by SEC (Table 3). Thus, although the copolymer was produced through an acidic reaction, no significant degradation of the polyester backbone was observed.

Table 3. Molecular weights of copolyesters

Polymer	Mn[a]	Mw	PDI
P(VSHA$_{50}$KHE$_{50}$)	15532	27142	1.74
P(MVSHA$_{50}$KHE$_{50}$)	9022	20330	2.25
P(MVSHA$_{50}$MKHE$_{50}$)[b]	9037	19791	2.19
	(9219)[d]	(20032)	(2.17)
P(VSHA$_{50}$MKHE$_{50}$)	15754	26226	1.66
P(MVSHA$_{50}$MKHE$_{50}$)[b]	8170	12725	1.55
P(MVSHA$_{50}$MKHE$_{50}$)[c]	4153	6873	1.65

[a] SEC values were obtained using THF as solvent. [b] Copolyester obtained by sequential modification.[c] Copolyester obtained by one pot modification.
[d] In brackets values when acid catalyst was used.

Sequential reactions were performed in the opposite order of addition to generate first the ketoxime and followed by the thioether formation. Using the acid catalyzed reaction and the same reaction conditions in both steps as above described, similar results were obtained.

Additionally, we explored the one pot functionalization to achieve the single-step preparation of the bifunctionalized copolyester. Reaction was carried out by adding 2-mercaptoethanol and *O*-(tetra-hydro-2H-pyran-2yl) hydroxylamine and UV irradiating for 30 min. After 8 h of reaction, lower modification degrees than those obtained by sequential addition were obtained (92% for thioether and 67% for ketoxime formations). Lower molecular weights than those obtained by sequential modificacion were also observed (Table 3).

Thermal properties

The thermal behavior of copolyesters has been comparatively studied by DSC and TGA taking as reference their parent homopolyesters from VSHA and KHE (Table

4). Data for the parent homopolymers are also included for comparison. PVSHA showed a melting endotherm centered at 19 ºC with a melting enthalphy of 38 J/g according to its crystalline nature, while PKHE showed the glass transition at -60 ºC according to its amorphous character. Thermal stability of PVSHA is significantly higher than the one of PKHE. Although a common pattern of degradation is followed by all of the unmodified copolymers, initial degradation temperatures show the influence of the composition, and the higher the amount of VSHA, the higher the thermal stability. However, the modified copolyester, show a noticeable decrease on thermal stability and the appearance of a new degradation step. A decrease on the thermal stability of the oxime modified copolymer was previously described.[11]

Table 4. DSC and TGA properties of the copolymers

Polymer	Tg(ºC)	Tm (ºC)	$T_{5\%}$ (ºC)	Tmax	R (%)[a]
PVSHA	-54	19 (38J/g)	337	354-451	2.5
PKHE	-60	-	256	349-447	0.5
P(VSHA$_{80}$-KHE$_{20}$)	-57	-7 (12J/g)	315	349-448	0.4
P(VSHA$_{50}$-KHE$_{50}$)	-57	-	296	347-449	0.7
P(VSHA$_{20}$-KHE$_{80}$)	-61	-	282	343-447	0.3
P(MVHA$_{50}$MKHE$_{50}$)	-46	-	226	268-338-448	2.5

[a] Remaining weight at 800 ºC

As conclusion, copolymers carrying both vinyl sulfide and ketone functional groups have been obtained by enzymatic polymerization. Sequential and single step one pot post-polymerization modifications of both functional groups have been carried out. Sequential modification yields materials with good agreement between the reaction stoichiometry and the observed incorporation of thiol and oxyamine, and the order of addition seems not to be a significant parameter. One pot functionalization strategy allows for the single step modification but not quantitative either thiol-ene or oxime reaction were achieved. In spite of the differences in molecular weights obtained by SEC, no significant degradation seems to take place as observed by NMR spectroscopy since no unexpected signals can be observed.

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Chapter 6

Experimental Part

6.1. MATERIALS

The following chemicals were obtained from the sources indicated and used as received: 10-undecenoic acid (Fluka), methyl oleate (96%, Alfa Aesar), L-lactide (LA) (98% Aldrich), ε-caprolactone (CL) (97%, Aldrich), 2-mercaptoethanol (99%, Aldrich), 1,4-butanedithiol (97%, Aldrich), 7-mercapto-4-methylcoumarin (Cm-SH) (97%, Aldrich), *O*-(tetrahydro-2*H*-pyran-2-yl)hydroxylamine (96%, Aldrich), 1,4-butanediol (BDO) (99%, Aldrich), 3-chloroperbenzoic acid (mCPBA) (≤77%, Aldrich), hydrogen peroxide (H_2O_2) (50% Aldrich), bromine (99%, Aldrich), potassium hydroxide (90%, Scharlau), hydrochloric acid solution HCl (35%, Scharlau), acetic anhydride (Pure, Sharlau), 4-(dimethylamino)pyridine (DMAP) (≥99%, Aldrich), meso-tetraphenylporphyrin (TPP) (Aldrich), 2,2-dimethoxy-2-phenylacetophenone (DMPA) (99%, Aldrich), 2,2′-azobis(2-methylpropionitrile) (AIBN) (99%, Aldrich), Novozyme-435 (lipase acrylic resin from candida antarctica), tin(II) 2-ethylhexanoate ($Sn(Oct)_2$) (95%, Aldrich), dibutyl tin oxide (DBTO) (98%, Aldrich), titanium(IV) butoxide ($Ti(OBu)_4$) (97%, Aldrich), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) (98%, Aldrich). Solvents were purified by standart procedures.

6.2. INSTRUMENTATION

Nuclear Magnetic Resonance (NMR) analysis

NMR spectra were recorded on Agilent VNMRS400 spectrometer. The samples were dissolved in deuterated chloroform, and ^{1}H and ^{13}C NMR spectra were recorded at room temperature with tetramethylsilane (TMS) as an internal standard. About 10 and 50 mg of sample dissolved in 1 mL solvent were used for ^{1}H and ^{13}C NMR, respectively. Sixty-four scans were acquired for ^{1}H and 1000-10000 for ^{13}C NMR with 32K and 64K data points as well as relaxation delays of 1 and 2 s, respectively. 2D ^{1}H-^{1}H homonuclear (gCOSY) and ^{13}C-^{1}H gradient heteronuclear Single Quantum Coherence (gHSQC) spectra were recorded as a means of obtaining the hh and hx correlation respectively.

Fourier Transform Infrared Spectroscopy (FT-IR)

The IR analyses were performed on a FTIR- 680PLUS spectrophotometer with a resolution of 4 cm^{-1} in the transmittance mode.

Liquid Chromatography-Mass Spectrometry (ESI MS)

The chromatographic system was an Agilent 1200 liquid chromatograph coupled to 6210 Time of Flight (TOF) mass spectrometer from Agilent Technologies (Waldbronn, Germany) with an ESI interface, using a Zorbax Eclipse XDB C18 column (4.6 mm × 150mm × 5 µm) provided by Agilent Technologies.

Size exclusion chromatography (SEC)

Polymer molecular weight analysis was perfomed on two different systems. The THF-SEC was carried out with an Agilent 1200 series system equipped with an Agilent 1100 series refractive-index detector. The analysis was perfomed on the three following column system: 3 µm PLgel MIXED-E, 5 µm PLgel MIXED-D, 20 µm PLgel MIXED-A at a nominal flow rate of 1.0 ml/min and a sample concentration of 0.1% w/w in THF as solvent. The DMF-SEC was carried out with an Agilent 1260 infinity system equipped with an Shimadzu RID-6A refractive index detector. The analysis was performed on the three following column system: 3 µm PLgel MIXED-E, 5 µm PLgel MIXED-C, 5 µm PLgel MIXED-D running in dimethylformamide containing 0.025 M lithium bromide at a flow rate of 1ml/min. Both instruments were calibrated with linear monodisperse polystyrene standards from Polymer Laboratories with molecular wieghts ranging from 500 to 400,000 Da.

Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) measurements were carried out with a Mettler DSC822e thermal analyzer with N2 as the purge gas. Samples, 6-12 mg, were used for DSC analysis. Non-isothermal crystallization behaviors were evaluated by cooling the samples from the melt. The samples were heated from -80 to 200 °C with a heating rate of 20 °C /min, cooled down to -80 °C with a cooling rate of -20 °C /min, and then heated again to 200 °C at the same heating rate. Measurement of Tm values were obtained from the second heating curves. Isothermal crystallization investigation was performed by cooling (10°C/min) of the samples from the melt to a fixed temperature (120 °C) and by keeping the samples at this temperature for 2h.

Thermogravimetric analysis (TGA)

Thermal stability studies were carried out with a Mettler TGA/SDTA851e/LF/1100 with N_2 as the purge gas at a scanning rate of 10 °C/min.

Fluorescence Spectroscopy

The spectrofluorimetric data were adquired on an Aminco-Bowman series 2 Luminescence spectrometer (SLM Amino, Rochester, NY, USA) equipped with a 150W continuous xenom lamp and a PMT detector.

X-Ray diffraction

XRD measurements were made using a Siemens D5000 diffractometer (Bragg-Brentano parafocusing geometry and vertical Ө-Ө goniometer) fitted with a curved graphite diffracted-beam monochromator, incident- and diffractedbeam Soller slits, a 0.06° receiving slit, and a scintillation counter as a detector. The angular 2Ө diffraction range was between 1° and 40°. Samples were dusted onto a low background Si(510) sample holder. The data were collected with an angular step of 0.05° at 3 s per step. Cu KR radiation was obtained from a copper X-ray tube operated at 40 kV and 30 mA.

Contact angle

The contact angle of deionized water against polymer surfaces was measured by the water drop method (3mL) at 25 °C, using Kruss contact angle instrument (Hamburg, Germany) equipped with a motorized pipet (Matrix Technology, Nashua, NH.

6.3. SYNTHETIC METHODS OF MONOMERS AND POLYMERS

6.3.1. MONOMER SYNTHESIS

Synthesis of thioether-containing ω-hydroxyacid TEHA

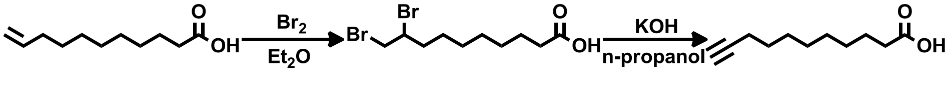
An equimolar mixture of 10-undecenoic acid (1.0 g, 5.43 mmol) and 2-mercaptoethanol (0.4 g, 5.43 mmol) was irradiated in dichloromethane solution at λ=365 nm in the presence of DMPA (2% mol relative to C=C) as photoinitiator. After 10 min, the reaction mixture solidified and the completion of the reaction was confirmed by the completely disappearance of C=C double bonds from ^{1}H NMR. The crude product was crystallized from hexane to obtain the pure product as a white powder (yield % 98, mp: 54 ^{o}C, LC-(ESI) MS: m/z calcd: 262.16 ; found: 262.16).

^{1}H NMR ($CDCl_3$, δ, ppm): 3.72 (t, 2H), 2.72 (t, 2H), 2.50 (t, 2H), 2.34 (t, 2H), 1.69-1.27 (m, 16H)

^{13}C NMR ($CDCl_3$, δ, ppm): 179.7 (s), 60.3 (t), 35.4 (t), 34.1 (t), 31.8 (t), 29.9-24.8 (t)

Synthesis of vinylsulfide-containing hydroxyacid VSHA

a) Synthesis of 10-Undecynoic Acid



In a 1000 ml two-necked round bottom flask provided with a Teflon-coated magnetic bar and a pressure equalized dropping funnel, 10-undecenoic acid (46.0 g, 0.25 mol) dissolved in diethyl ether (500 mL) was added with stirring at 0°C within 75 min bromine (48 g, 300 mmol). The mixture was allowed to warm up gradually to the temparature of laboratory and after stirring overnight, the solvent and the excess of bromine were remowed at reduced pressure. To a 2L round-bottomed flask the brown liquid dibromo acid was transferred, n-propanol (800 mL) and 85% aqueous potassium hydroxide (1.8 mol, 120 g in 140 ml agua) were added and the mixture was refluxed for 20 h. Then water (1500 mL) was added and the cold solution was neutralized with 2 N (≈ 800 ml) hydrochloric acid solution. After several extractions with diethyl ether the combined organic phases dried with anhydrous magnesium sulfate and the solvent evaporated under reduced pressure. The residue was distilled under reduced pressure (0.5 mmHg) and the fraction at 120-130 °C was collected. The product solidifies on cooling and was recrystallized from hexane to obtain a white solid (yield 70%, mp 41-42 °C).

^{1}H NMR ($CDCl_3$, δ, ppm): 11.10 (s, 1H), 2.35 (t, 2H), 2.18 (dt, 2H), 1.94 (t, 1H), 1.67-1.29 (m, 12H)

^{13}C NMR ($CDCl_3$, δ, ppm): 180.6 (s), 84.9 (s), 68.3 (d), 34.3 (t), 28.5-24.8 (t), 18.5 (t)

b) Thiol-yne addition to 10-Undecynoic acid

A mixture of 10-undecynoic acid (1.00 g, 5.50 mmol) and 2-mercaptoethanol (0.45 g, 5.77 mmol) was heated in toluene solution at 80°C in presence of AIBN (10 % mol init./mol C≡C). The product was purified by column chromatography using 1:1 hexane-ethyl acetate as eluent to afford a mixture of E and Z vinyl sulfides as a white solid (yield 77%, mp: 35-36ºC, E/Z ratio 1:1 from ^{1}H NMR, LC-(ESI) MS m/z calculated: 260,39; found : 260,14).

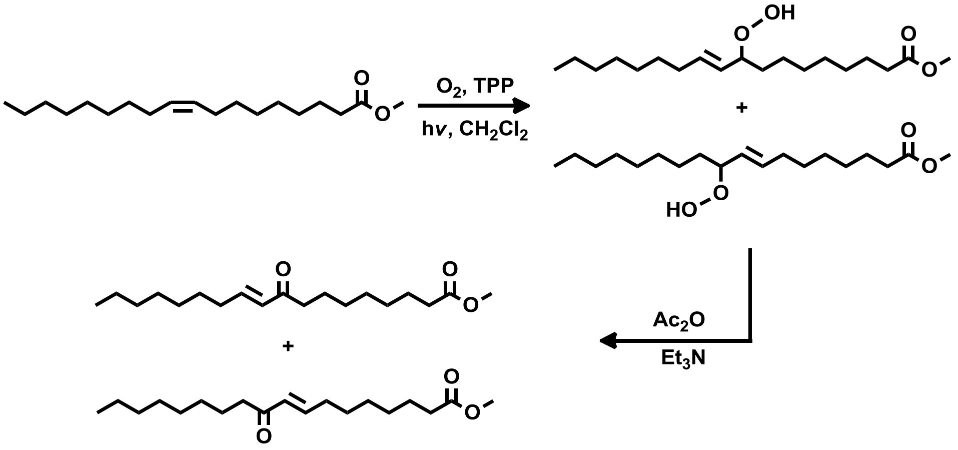
^{1}H NMR ($CDCl_3$, δ, ppm): 5.90-5.84 (2 dt , 1H), 5.79-5.58 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz, Jcis= 8,8 Hz, Jvec=8 Hz, 3.75 (dt, 2H), 2.84 (dt, 2H), 2.34 (t, 2H), 2.16-2.03 (dq, 2H), 1.66 (m, 2H), 1.42-1.25 (m, 10H)

^{13}C NMR ($CDCl_3$, δ, ppm): 179.9 (s), 133.9 (d), 131.6 (d), 123.7 (d), 121.3 (d), 61.4 (t), 60.8 (t), 36.9 (t), 36.2 (t), 34.2 (t), 33.2 (t), 29.4-24.8 (t)

Synthesis of ketone containing hydroxyester KHE

a) Synthesis of enone derivative of methyl oleate

Enone derivative of methyl oleate has been obtained as a mixture of methyl-9-oxo-10-octadecenoate and methyl-10-oxo-8-octadecenoate following a reported procedure.

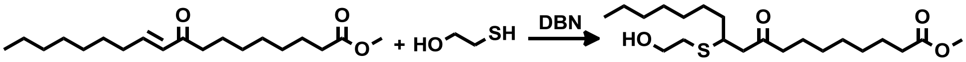


The reactor was charged with a solution of methyl oleate (20.0 g, 67.5 mmol), acetic anhydride (6.68 mL, 70.8 mmol), pyridine (2.73 mL, 33.8 mmol), TPP (50.2 mg), and DMAP (0.167 g, 1.37 mmol) in methylene chloride (325 mL). After 2 h of irradiation, TLC (3:1 pentane/ether) indicated no remaining starting material and an intense UV active spot for the enone. The mixture was diluted with ether (1 L) and washed successively with 100-mL portions of water, saturated $NaHCO_3$, 1 N HCl, saturated $CuSO_4$ water, and saturated NaC1. After drying ($MgS0_4$) and concentration, the dark residue was bulb-to-bulb distilled (165 °C at 0.04 mm) to afford a 1:l mixture of methyl 9-oxo-10-octadecenoate and methyl 10-oxo-8-octadecenoate as a light yellow liquid (yield 97%).

^{1}H NMR ($CDCl_3$, δ, ppm): 6.84-6.75 (m, H), 6.07 (dt, H), 3.65 (s, 3H), 2.50 (t, 2H), 2.29 (dt, 2H), 2.20 (m, 2H), 1.63-1.25 (m, 20 H), 0.86 (t, 3H)

^{13}C NMR ($CDCl_3$, δ, ppm): 200.5 (s), 173.9 (s), 147.1 (d), 130.3 (d), 51.30 (q), 40.0 (t), 33.9 (t), 32.3-22.5 (t), 14.0 (q)

b) Thiol-Michael addition to enone derivative of methyl oleate



A equimolecular mixture of enone derivative (1.0 g, 3.22 mmol) and 2-mercaptoethanol (0.3 g, 3.22 mmol) was stirred at room temperature in the presence of DBN (0.1 % mol) to one hour. The crude product was washed with distilled water, dried over anhydrous magnesium sulfate, and filtered (yield 97%).

^{1}H NMR ($CDCl_3$, δ ppm): 3.75 (m, 2H), 3.65 (s, 3H), 3.15 (m, 1H), 2.72 (m, 2H), 2.64 (m, 2H), 2.40 (t, 2H), 2.29 (t, 2H), 1.62-1.26 (m 20H), 0.86 (t, 3H)

^{13}C NMR ($CDCl_3$, δ ppm): 209.8 (s), 174.4 (s), 61.5 (t), 51.6 (q), 48.7 (t), 43.9 (t), 43.8 (t) , 40.3 (t), 36.1 (d), 34.7 (t), 34.2 (t), 32.0 (t), 31.9 (t), 29.5-22.8 (t), 14.2 (q)

6.3.2. MACROINITIATORS AND POLYMERS SYNTHESIS

Synthesis of PTEHA: General procedure for polyesterification of hydroxyacid TEHA

Tin(II) 2-ethylhexanoate $Sn(Oct)_2$ (1% or 2% mol), or dibutyl tin oxide (DBTO) (1% mol) were added to VSHA (0.20 g, 0.76 mmol). The reaction was carried out in bulk at 140ºC under nitrogen atmosphere for 1h and subsequently the pressure was reduced. The polymer was recovered by precipitating a concentrated dichloromethane solution into cold methanol, filtered and dried under reduced pressure (yield 96%).

^1H NMR ($CDCl_3$, δ, ppm): 4.21 (t, 2H), 3.72 (m, 2H) 2.73 (t, 2H), 2.54 (t, 2H), 2.30 (t, 2H), 1.63-1.25 (m, 16H)

^{13}C NMR ($CDCl_3$, δ, ppm): 173.8 (s), 63.5 (t), 34.4 (t), 32.6 (t), 30.7 (t), 29.9-29.0 (t), 25.1 (t)

Synthesis of dihydroxyl-terminated prepolymers OH-PTEHA-OH

Hydroxyacid TEHA (2g, 7.63 mmol) and BDO (0.034g, 0.38 mmol in 1:0.05 molar ratio or 0.068g, 0.76 mmol in 1:0.1 molar ratio) were stirred at 140 ^oC under a argon atmosphere. The polymerization was carried out with tin(II) 2-ethylhexanoate $Sn(Oct)_2$ (1% mol). After the completion of 1 hour argon flow, dynamic vacuum was applied during the 6 hours. The resulted polyester was obtained as a white solid and was dissolved in dichloromethane, precipitated into methanol, filtered and dried under reduced pressure (yield % 93).

^1H NMR ($CDCl_3$, δ, ppm): 4.21 (t, 2H), 4.09 (t, 2H), 3.75 t, 2H, terminal unit), 2.73 (t, 2H), 2.54 (t, 2H), 2.30 (t, 2H), 1.70 (t, 2H), 1.63-1.25 (m, 16H)

^{13}C NMR ($CDCl_3$, δ, ppm): 173.8 (s), 63.5 (t), 34.4 (t), 32.6 (t), 30.7 (t), 29.9-29.0 (t), 25.1 (t)

Synthesis of triblock copolyesters P(LA-*b*-TEHA-*b*-LA)

The triblock copolymers were prepared by ring-opening polymerizaton of LA using dihydroxy terminated prepolymer as a macro-initiator. The desired amounts of dihyroxy-terminated prepolymer and LA were refluxed in dry toluene (0.1 g/ml) at 140 ^{o}C under argon atmosphere for 4 hours with addition of tin(II)2-ethylhexanoate (1% relative to LA). After completion of the reaction, toluene was removed under reduced pressure, the copolymer was dissolved in dichloromethane followed by precipitation into methanol and dried under reduced pressure (yield %84-88).

^{1}H NMR ($CDCl_3$, δ, ppm): 5.17 (q, H), 4.35 (q, H, terminal unit), 4.21 (t, 2H), 4.09 (t, 2H), 2.73 (t, 2H), 2.55 (t, 2H), 2.31 (t, 2H), 1.70 (t, 2H), 1.58 (d, 3H), 1.50-1.25 (m, 16H)

^{13}C ($CDCl_3$, δ, ppm): 173.6 (s), 169.8 (s), 69.2 (d), 63.5 (t), 34.4 (t), 32.6 (t), 30.7 (t), 29.9-29.0 (t), 25.1 (t), 16.8 (q)

Synthesis of PVSHA: General procedure for polyesterification of hydroxyacid VSHA

Tin(II) 2-ethylhexanoate $Sn(Oct)_2$, dibutyl tin oxide (DBTO) or titanium(IV) butoxide $Ti(OBu)_4$ (2% mol) were added to VSHA (0.20 g, 0.77 mmol). The reaction was carried out in bulk at 120ºC under nitrogen atmosphere for 1h and subsequently the pressure was reduced. Enzymatic polymerizations were carried out using Novozyme-435 dried in a vacuum desiccator (10 or 25 % w/w relative to total weight of monomer). VSHA (0.20 g, 0.77 mmol) was dissolved in diphenylether (DPE) (2:1 w/v monomer /DPE) and the catalyst was added. Reactions were carried out at 80º or 90ºC and vacuum was applied to remove water. Both polymerizations were terminated by adding excess of chloroform, stirring and removing the enzyme by filtration for enzymatic process and precipitating in cold methanol (yield 95%).

^{1}H NMR ($CDCl_3$, δ, ppm): 5.91-5.84 (2 dt, 1H), 5.79-5.58 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz; Jcis= 8,8, Hz, Jvec=8 Hz, 4,20 (dt, 2H), 2.84 (dt, 2H), 2.30 (t, 2H), 2.10 (m, 2H), 1.61 (m, 2H), 1.38-1.25 (m, 10H)

^{13}C NMR (CDCl$_3$, δ, ppm): 173.8 (s), 133.2 (d), 131.2 (d), 124.0 (d), 121.5 (d), 63.6 (t), 63.1 (t), 34.4 (t), 33.3 (t), 32.2 (t), 31.5 (t), 29.4-29.0 (t), 25.1 (t)

Synthesis of polycaprolactone PCL

Enzymatic polymerization of ε-caprolactone was carried out using Novozyme-435 (10 % w/w relative to total weight of monomer) in diphenylether (DPE) (2:1 w/v monomer /DPE) at 80 ºC. The polymerization was terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 98%).

^{1}H NMR (CDCl$_3$, δ, ppm): 4.06 (t, 2H), 2.30 (t, 2H), 1.69-1.34 (m, 3H)

^{13}C NMR (CDCl$_3$, δ, ppm): 173.7 (s), 64.3 (t), 34.3 (t), 28.5-24.7 (t)

Synthesis of random copolymers P(CL-VSHA)

The desired amounts of CL and VSHA (in molar ratio CL/VSHA 4:1, 3:2 and 1:1) were dissolved in DPE (2:1, monomer /DPE), w/v) and Novozyme-435 (10% w/w relative to weight of monomers) was added. The reactions were carried out under vacuum at 80ºC for 24h. The polymerization was terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 91-94%).

^{1}H NMR (CDCl$_3$, δ, ppm): 5.90-5.84 (2 dt , 1H), 5.76-5.57 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz; Jcis= 8,8, Hz, Jvec=8 Hz, 4,22 (m, 2H), 4.06 (dt, 2H), 2.84 (q, 2H), 2.30 (m, 4H), 2.10 (m, 2H), 1.70-1.25 (m, 18 H)

^{13}C NMR (CDCl$_3$, δ, ppm): 174.1 (s), 173.7 (s), 133.2 (d), 131.2 (d), 124.0 (d), 121.5 (d), 121.4 (d), 64.3 (t), 64.2 (t), 63.7 (t), 63.6 (t), 63.1 (t), 63.0 (t), 34.5 (t), 34.3 (t), 34.2 (t), 33.3 (t), 32.2 (t), 31.5 (t), 29.9-29.0 (t), 28.5 (t), 25.7-24.7 (t)

Synthesis of dihydroxyl terminated prepolymer OH-PVSHA-OH

VSHA (1 g, 3.8 mmol) and BDO (0.034 g, 0.38 mmol) were dissolved in DPE (2:1, monomer /DPE), w/v). Novozyme-435 (10% w/w relative to weight of monomer) was added and the misture was heated at 80ºC for 16h under vacuum. The polymerization was terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 90%).

^{1}H NMR ($CDCl_3$, δ, ppm): 5.90-5.84 (2 dt , 1H), 5.76-5.57 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz; Jcis= 8,8, Hz, Jvec=8 Hz, 4,22 (dt, 2H), 4.09 (t, 2H), 3.75 (t, 2H, terminal unit), 2.85 (dt, 2H), 2.31 (t, 2H), 2.13-2.04 (m, 2H), 1.70 (t, 2H), 1.63-1.25 (m, 12H)

^{13}C NMR ($CDCl_3$, δ, ppm): 173.8 (s), 133.2 (d), 131.2 (d), 124.0 (d), 121.5 (d), 63.6 (t), 63.1 (t), 34.4 (t), 33.3 (t), 32.2 (t), 31.5 (t), 29.4-29.0 (t), 25.1 (t)

Synthesis of triblock copolymers P(CL-*b*-VSHA-*b*-CL)

The desired amounts of dihydroxyl terminated prepolymer OH-PVSHA-OH and CL (ratio monomer/initiator 5, 10, 20 and 30) were dissolved in DPE (2:1, monomer /DPE), w/v) and Novozyme-435 (10% w/w relative to weight of monomer) was added. The reaction was carried out at 80ºC for 24h. The polymerization was terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 82-85%)

^{1}H NMR ($CDCl_3$, δ, ppm): 5.90-5.87 (2 dt , 1H), 5.76-5.57 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz; Jcis= 8,8, Hz, Jvec=8 Hz, 4,22 (dt, 2H), 4.06 (t, 2H), 2.85 (dt, 2H), 2.31 (t, 4H), 2.10 (m, 2H), 1.70-1.24 (m, 20H)

^{13}C NMR ($CDCl_3$, δ, ppm): 173.8 (s), 173.5 (s), 133.11 (s), 131.07 (d), 123.7 (d), 121.2 (d), 64.12 (t), 64.01 (t), 63.4 (t), 62.9 (t), 34.3 (t), 34.0 (t), 33.9 (t), 33.1 (t), 32.0 (t), 31.3 (t), 29.6-28.3 (t), 25.5-24.4 (t)

Synthesis of PKHE: General procedure for polyesterification of hydroxyester KHE

Enzymatic polymerizations were carried out using Novozyme-435 dried in a vacuum desiccator (10 % w/w relative to total weight of monomer). KHE (0.20 g, 0.51 mmol) was dissolved in diphenylether (DPE) (2:1 w/v monomer /DPE) and the catalyst was added. Reactions were carried out at 80º or 90ºC and vacuum was applied to remove water. The polymerization was terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 90%).

^{1}H NMR ($CDCl_3$, δ, ppm): 4.18 (m, 2H), 3.75 (t, 2H, terminal unit), 3.64 (s, 3H, terminal unit), 3.14 (m, 1H), 2.72 (m, 2H), 2.64 (m, 2H), 2.40 (t, 2H), 2.28 (t, 2H), 1.60-1.26 (m, 20H), 0.87 (t, 3H)

^{13}C NMR ($CDCl_3$, δ, ppm): 209.1 (s), 173.7 (s), 63.7 (t), 49.0 (t), 43.8 (t), 41.2 (d), 35.7 (t), 34.3 (t), 34.2 (t), 32.0 (t), 29.8-22.8 (t), 14.2 (q)

Synthesis of random copolymers P(VSHA-KHE)

Enzymatic copolymerizations were carried out using Novozyme-435 dried in a vacuum desiccator (10 or 20 % w/w relative to total weight of monomer). Different molar ratios of hydroxyacid (VSHA) and hydroxyester (KHE) were copolymerized with in diphenylether (DPE) (2:1 w/v monomer /DPE) or in bulk by the corresponding amount of enzyme catalyst. Reactions were carried out at 80º or 90ºC and vacuum was applied to remove the esterifications products water and methanol. The polymerizations were terminated by adding excess of chloroform, stirring and removing the enzyme by filtration and precipitating in cold methanol (yield 88-91 %).

^{1}H NMR ($CDCl_3$, δ, ppm): 5.90-5.85 (2 dt , 1 H), 5.74-5.55 (2 dt, 1H) Jtrans=14,8 Hz, Jvec=8 Hz; Jcis= 8,8, Hz, Jvec=8 Hz, 4.22-4.14 (m, 4 H), 3.64 (s, 3H), 3.14 (m, 1H), 2.80 (dt, 2 H), 2.72 (m, 2H), 2.64 (m, 2H), 2.40 (t, 2H), 2.29 (dt, 4H), 2.10 (m, 2 H), 1.61-1.25 (m, 34H), 0.87 (t, 3H)

^{13}C NMR ($CDCl_3$, δ, ppm): 209.1 (s), 173.7 (s), 133.2 (d) , 131.0 (d), 123.9 (d), 121.5 (d), 63.7 (t), 63.0 (t), 49.0 (t), 43.8 (t), 41.2 (d), 35.7 (t), 34.3 (t), 34.2 (t), 33.3 (t), 32.0 (t), 31.9 (t), 31.4 (t), 29.8-22.8 (t), 14.2 (q)

6.3.3. MODIFICATION OF POLYESTERS

Synthesis of PSO(LA-b-TEHA-b-LA): Oxidation of thioether-containing triblock copolyesters to polysulfone

a) Thioether-containing triblock copolyesters (0.3 g, 1,14 mmol) were dissolved in dicloromethane, 3-chloroperbenzoic acid (mCPBA) (0.5 g, 2.28 mmol) was added and the mixture was stirred at room temperature. After 1 hour of reaction, the formed polymer was washed with 5% $Na_2S_2O_3$ and 5% $NaHCO_3$ prior to drying under reduced pressure (yield 86%).

^{1}H NMR ($CDCl_3$, δ, ppm): 5.17 (q, H), 4.50 (t, 2H), 4.35 (q, H, terminal unit), 4.09 (t, 2H), 3.28 (t, 2H), 3.02 (t, 2H), 2.31 (t, 2H), 1.84 (m, 2H), 1.70-1.25 (m, 16 H)

^{13}C ($CDCl_3$, δ, ppm): 173.1 (s), 169.8 (s), 69.2 (d), 57.7 (t), 54.4 (t), 51.8 (t), 34.3 (t), 29.9-22.0 (t), 16.8 (q)

b) Thioether-containing triblock copolyester (0.2 g, 0.82 mmol) were dissolved in chloroform and subsequently 50% hydrogen peroxide solution (0.09 ml) was added to the reaction flask. The mixture was stirred at room temperature. After 48 hour of reaction, the formed polymer was washed with 5% $NaHCO_3$ and water prior to drying under reduced pressure (yield 80%).

Functionalization of vinylsulfide-containing polyester PVSHA

A solution of 0.1 g (0.41 mmol) of the polymer in THF was mixed with the corresponding amount of 2-mercaptoethanol (1:1.3 mol C=C/mol SH) and DMPA (1% mol init./mol C=C) as a radical photoinitiator. The reaction was carried out at room temperature, without deoxygenation, by irradiation with two 9 W UV-lamps (λ=365 nm). The completion of the reaction was confirmed after 30 min by ^{1}H NMR. The crude product was washed with distilled water to eliminate the excess of mercaptoethanol and dried over anhydrous magnesium sulfate, and filtered (yield 75%).

^{1}H NMR ($CDCl_3$, δ, ppm): 4.21 (m, 2H), 3.71 (t, 2H), 2.89-2.69 (m, 7H), 2.31 (t, 2H), 1.76-1.24 (m, 14H)

^{13}C NMR ($CDCl_3$, δ, ppm): 174.0 (s), 63.3 (t), 61.4 (t), 46.2 (d), 38.7 (t), 34.4 (t), 31.4 (t), 29.5-25.0 (t)

Crosslinking of vinylsulfide-containing polyester PVSHA

To a solution of 0.2 g of polyester and 0.04 g of 1,4-butanedithiol (1:0.5 mol C=C/mol SH) in chloroform, 1% of photoinitiator DMPA/mol C=C was added. The mixture was placed on a petri dish and was irradiated at λ=365 nm for 1h. The disappearance of C=C was followed by IR spectroscopy. The final product was extracted with chloroform and fractions soluble and insoluble appear in 10/90 ratio.

Surface modification of copolyester P(CL-*b*-VSHA-*b*-CL)$_{30}$

A film from triblock copolyester was prepared by solution casting from chloroform and dried under atmospheric pressure at room temperature for 24 h and under vacuum for 1 day until constant weight. Copolyester sample (0.7 x 0.7 x 0.02 cm^3) reacted with Cm-SH (molar ratio C=C/ Cm-SH 1/2). The corresponding amount of Cm-SH and the radical initiator in a proportion 10% mol init./mol C=C were dissolved in the minimum amount of DMSO. Copolyester was immersed into the solution and the reaction was carried out at room temperature without deoxygenation by irradiation with two 9 W UV-lamps (λ = 365 nm). The thiol-ene addition was followed by fluorescence at different times. The emission spectra of the copolymer films were measured at excitation wavelengths of 358 nm. The resulting films were extensively washed with DMSO at different times, to remove the residual unreacted Cm-SH on the surface.

Functionalization of ketone containing hydroxyester KHE

A solution of 0.1 g of the polymer in THF was mixed with corresponding amount of *O*-(tetra-hydro-2H-pyran-2 yl)hydroxylamine to obtain an oxyamine/ketone mole ratio 1:1 with p-TsOH or 1:1.5 for 8h. The reaction mixture was stirred at room temperature and samples were taken to monitor the reaction progress. The final product was dissolved in chloroform and precipitated in cold methanol.

^{1}H NMR ($CDCl_3$, δ, ppm): 5.20 (m, 1H), 4.18 (m, 2H), 3.85 (m, 1H), 3.65 (s, 3H, terminal unit), 3.60 (m, 1H), 3.10 (m, 1H), 2.91 (m, 1H), 2.72 (m, 2H), 2.64 (m, 2H), 2.44 (t, 2H), 2.28 (t, 2H), 1.74-1.26 (m, 26H), 0.87 (t, 3H)

^{13}C NMR ($CDCl_3$, δ, ppm): 173.7 (s), 160.6 (s), 100.6 (d), 63.7 (t), 62.8 (t), 43.1 (d), 40.5 (t), 35.5 (t), 34.8 (t), 34.2 (t), 32.0 (t), 29.9-22.8 (t), 14.3 (q)

Sequential and one-pot functionalization of P($VSHA_{50}KHE_{50}$)

Route A: Random copolyester P($VSHA_{50}KHE_{50}$), (0.200 g, 0.330 mmol) was mixed with 2-mercapthoethanol (0.064 g, 0.826 mmol) in THF and DMPA (1 % mol) as a radical photoinitiator was added. The reaction was carried out at room temperature,without deoxygenation by irradiation with two 9 W UV-lamps (λ=365 nm). The completion of the reaction was confirmed after 30 min by ^{1}H NMR. The copolyester P($MVSHA_{50}KHE_{50}$) (0.033 g, 0.28 mmol) was then mixed with *O*-(tetra-hydro-2H-pyran-2 yl)hydroxylamine (0.017g , 0.148 mmol) in THF and two drops of a 0.02 M p-TsOH was added. The reaction was proceed at RT for 5h. The final copolyester P($MVSHA_{50}MKHE_{50}$) was washed with water to remove all unreacted products and dried under vacuum.

Route B: Sequential modification was carried out in the opposite order of route A to generate first the ketoxime containing P($VSHA_{50}MKHE_{50}$) and followed by the thioether formation P($MVSHA_{50}MKHE_{50}$).

Route C: The single step preparation was carried out by adding 2-mercapthoethanol and *O*-(tetra-hydro-2H-pyran-2-yl)hydroxylamine into copolyester P($VSHA_{50}KHE_{50}$) dissolved in THF with UV irradiation for 30 min and stirring at RT for 7h.

a) Thiol-ene functionalization P(MVSHA$_{50}$KHE$_{50}$)

^{1}H NMR (CDCl$_3$, δ, ppm): 4.22-4.15 (m, 4H), 3.75 (t, 2H), 3.65 (s, 3H), 3.14 (m, 1H), 2.88-2.58 (m, 11H), 2.40 (t, 2H), 2.29 (dt, 4H), 1.77-1.25 (m, 36 H), 0.87 (t, 3H)

^{13}C NMR (CDCl$_3$, δ, ppm): 209.2 (s), 173.7 (s), 63.7 (t), 63.2 (t), 61.4 (t), 49.0 (t), 46.2 (d), 43.9 (t), 41.2 (d), 38.6 (t), 35.6 (t), 34.4 (t), 34.3 (t), 31.9 (t), 31.4 (t), 29.8-22.8 (t), 14.3 (q)

b) Oxime functionalization P(MVSHA$_{50}$MKHE$_{50}$)

^{1}H NMR (CDCl$_3$, δ, ppm): 5.20 (m, 1H), 4.22-4.15 (m, 4H), 3.85 (m, 1H), 3.75 (t, 2H), 3.65 (s, 3H), 3.60 (m, 1H), 3.10 (m, 1H), 2.92-2.58 (m, 11H), 2.43-2.28 (m, 6H), 1.79-1.23 (m, 42H), 0.87 (t, 3H)

^{13}C NMR (CDCl$_3$, δ, ppm): 173.7 (s), 160.6 (s), 100.6 (d), 63.7 (t), 63.2 (t), 62.8 (t), 61.4 (t), 46.2 (d), 43.2 (d), 40.5 (t), 38.7 (t) , 35.7 (t), 34.8 (t), 34.3 (t), 34.2 (t), 32.0 (t), 31.4 (t), 30.0-22.8 (t), 14.3 (q)

Chapter 7

Conclusions

It has been demonstrated in this Thesis that fatty acids from castor and sunflower oils are a good option for the preparation of biobased polyesters with improved properties. Likewise the use of click chemistry (thiol-ene, thiol-yne and thiol-Michael) has been a succesful tool to obtain a set of functionalized copolyesters with a wide range of compositions and displaying diverse behavior are now accessible.

The conclusions of these research are summarized as follows:

- The thiol-ene addition to 10-undecenoic acid under photoinitiated catalyst yields quantitative conversion, in short reaction times, using equimolar ratio of reagents.
- The thiol-yne mono-addition to 10-undecynoic acid using thermal initiators yields a mixture of E and Z vinylsulfide isomers in good yield in short reaction times and using slight excess of thiol.
- The thiol-Michael addition to the enone derivative of methyl oleate using a basic/nucleophilic catalyst yields quantitative conversion under stoichiometric conditions in short reaction times.
- The hydroxyacids (TEHA, VSHA) and the hydroxyester (KHE) can be chemically and enzymatically homopolymerized to medium molecular weight polyesters.
- The poly(vinylsulfide ester) can be quantitatively functionalized with thiol compounds in short reaction times.
- The poly(keto ester) can be quantitatively functionalized with an oxyamine compound using a large excess of oxyamine and long reaction times.

- Random copolymers can be obtained by copolymerization of the vinylsulfide-containing hydroxyacid (VSHA) from castor oil and ε-caprolactone (CL).

- Block copolymers can be obtained by ring opening of L-lactide (LA) or ε-caprolactone (CL) by using dihydroxy telechelic polyesters from castor oil as macroinitiators.

- Random copolymers from the vinylsulfide-containing hydroxyacid (VSHA) and ketone-containing hydroxyester (KHE), can be obtained.

- Both sequential and one pot thiol-ene and oxime modifications of the double functionalized copolyesters can be carried out being more effective the first strategy.

- PLA copolyesters and polysulfone analogues, showed a decrease of crystallinity and an increase of thermal stability with respect to the PLA homopolymer.

Appendix A: List of abbreviations

AA	Adipic acid
ADMET	Acyclic diene metathesis polymerization
AIBN	2,2′-azobis(2-methylpropionitrile)
BDT	1,4-butanedithiol
BDO	1,4-Butanediol
CALB	Candida antarctica lipase B
CL	ε –caprolactone
CuAAC	Copper-catalyzed azide-alkyne cycloaddition
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBTO	Dibutyl tin oxide
DMF	N,N' -dimethylformamide
DMSO	Dimethyl sulfoxide
DMPA	2,2-dimethoxy-2-phenylacetophenone
DPE	Diphenyl ether
DSC	Differential scanning calorimetry
EAM	Enzyme-activated monomer
EWG	Electron-withdrawing group
FTIR	Fourier transform infrared spectroscopy
IA	Itaconic acid
KHE	Ketone containing hydroxyester
LA	L-Lactide
M_n	Number average molecular weight
M_w	Weight average molecular weight

N435	Novozyme 435
PBS	Poly(butylene succinate)
PBT	Poly(butylene terephthalate)
PCL	Poly(ε-caprolactone)
PDI	Polydispersity index (Mw/Mn)
PDO	1,3-Propanediol
PE	Polyethylene
PET	Poly(ethylene terephthalate)
PGA	Poly(glycolic acid)
PHA	Polyhydroxyalkanoate
P3HA	Poly(3-hydroxy alkanoic acid)
PHB	Poly(3-hydroxybutanoic acid)
PHBV	Poly(3-hydroxybutanoic-co-3-hydroxyvaleric acid)
PLA	Polylactide or Poly(lactic acid)
PP	Polypropylene
PPC	Poly(propylene carbonate)
PS	Polystyrene
PVC	Poly(vinyl chloride)
PTT	Poly(trimethylene terephthalate)
ROMP	Ring-opening metathesis polymerization
SA	Succinic acid
SEC	Size exclusion chromatography
TBD	1,5,7-triazabicyclo[4.4.0]dec-5-ene
TEHA	Thioether-containing ω-hydroxyacid
Tg	Glass-transition temperature

THF	Tetrahydrofuran
TGA	Thermogravimetric analysis
Tm	Melting temperature
Tmax	Temperature of maximum weight loss
TMS	Tetramethylsilane
TYC	Thiol-yne coupling
UV	Ultraviolet
VSHA	Vinyl sulphide-containing hydroxyacid
WAXD	Wide-angle X-ray diffraction

Appendix B: List of Publications

Title: Vinylsulfide-containing polyesters and copolyesters from fatty acids: Thiol-yne monomer synthesis and thiol-ene functionalization

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Ref.: Macromolecular Chemistry and Physics, Vol. 215, Issue 22, pp. 2248-2259, 2014.

Title: Fully biobased triblock copolyesters from L-lactide and sulfur-containing castor oil derivatives: preparation, oxidation and characterization

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Ref.: Polymer, submitted

Title: Post-polymerization modification of functional polyesters from vegetable oils

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Ref.: to be submitted

Appendix C: Meeting Contributions

Authors: Z. Beyazkilic, R. J. González-Paz, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Poster Presentation: Thiol-yne coupling to undecylenic acid derivatives. Synthesis of polyurethanes.

European Polymer XII GEP 2011 Congress, Proceedings of The European Polymer Congress 2011, June 2011, Granada, Spain.

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Poster Presentation: Fatty acid-based functional polyesters. Synthesis and modification.

XIII Meeting of the Group of Polymers (GEP) of the Spanish Royal Chemistry and Royal Physics Societies, September 2014, Girona, Spain.

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Poster Presentation: Fully biobased polylactide triblock copolyesters based on a castor oil derivative.

Frontiers in Polymer Science, May 2015, Riva del Garda, Italy.

Authors: Z. Beyazkilic, G. Lligadas, J. C. Ronda, M. Galià, V. Cádiz.

Poster Presentation: Post-polymerization modification of functional polyesters from castor and sunflower oils: Sequential and single step functionaization using thiols and alcoxyamines.

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