Department of Organic and Macromolecular Chemistry

Polymer Chemistry Research Group

Multifunctional polymer materials
based on sustainable thiolactone building blocks

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Chapter 1. Introduction and objectives

1.1 Introduction

Multifunctional polymers containing multiple chemical functional groups enable the development of complex materials with a combination of properties, such as toughness and surface activity. The overall performance of advanced materials relies on the combination of robust mechanical properties tailored for application requirements, as well as, additional chemical functionalities that enhance performance. For example, advanced polymer coatings incorporate specific functional components for targeted performance, such as antifouling or antibacterial properties, which will be described in Chapter 3. Multifunctional polymers find applications in composite materials,[1,2] packaging,[3] sensors,[4,5] tissue engineering,[6] and drug delivery[7,8]. Therefore, chemical techniques for incorporating multiple functional groups into polymers in simple and upscalable ways are necessary.

In addition, different strategies can be used to tailor the performance of functional groups on a macromolecular level, such as biomimetics, which harnesses design principles from nature. Biomolecules have inspired the design of multifunctional materials, due to their high specificity, hierarchical structure, and responsiveness to the environment. For example, the functionality of adhesive proteins in mussels has been replicated in coatings,[9] resulting in improved adhesion to a variety of substrates.[10] Notably, the interplay between the catechol hydrogen bonding functionalities, which are analogous to mussel proteins, as well as the polymer cross-link density affected the resulting mechanical and adhesive performance of the polymer networks.[10] Multifunctional polymers containing 3,4-dihydroxyphenyl-*L*-alanine (DOPA) with adhesion-promoting catechol functionalities were used in the "grafting to" approach for surface modification.[11] In addition, ionic functional groups were incorporated into the films in order to prevent protein fouling on the surface. Thereby, two biomimetic components were combined for both adhesion and antifouling performance.

The design of bio-inspired materials encompasses complex structure-property relationships, including specific functional groups, polymer structure, and the resulting intermolecular and

intramolecular interactions. Large-scale commercial production of bio-inspired materials remains a challenge due to the cost of building blocks and the complexity of preparation. The ability to introduce different functional groups in a simple and economic way is essential for enabling the future development of advanced materials with added value.

1.2 Objectives

The aim of this work was to develop multifunctional polymers and coatings using the thiolactone chemistry platform. Thiolactone chemistry imparts three key advantages for the preparation of functionalized polymers:

(1) bio-based thiolactone building blocks,
(2) versatility of functional groups,
(3) efficient thiol-ene polymerization.

The thiolactone building block is a cyclic thioester derived from renewable amino acids, which can be further derivatized and functionalized via nucleophilic ring-opening. The protected thiol contained in the thiolactone moiety can be released by ring-opening and employed in thiol-ene polymerization. The aim of this work is to use several thiolactone derivatives and functional groups to prepare thiol-ene polymers with different properties.

This work is part of the project "Sustainable multifunctional coating resins for scavenging applications" (SUSCOAT). The SUSCOAT project is a Marie-Curie European Industrial Doctorate program funded under the European 7th Framework scheme with the objective to develop sustainable polyurethane-based coating resins for the application of scavenging harmful chemical emissions, such as formaldehyde. In the first stage of the project, the preparation of UV-cured coatings using thiolactone chemistry was optimized in order to obtain high conversion of reactive groups and produce homogeneous polymer films. Subsequently, the properties of the polymer coatings with different functional groups were evaluated, including hardness, impact resistance, adhesion, solvent resistance, optical transparency and haze. The next objective was to

utilize functionalized polymer coatings for scavenging formaldehyde emissions originating from formaldehyde-containing adhesives which are commonly used in pressed wood products.

The thiolactone chemistry platform has been selected for the preparation of multifunctional polymer materials since it enables simple incorporation of functional groups into polymers in combination with photoinitiated thiol-ene polymerization. Polymers with different backbones, side chains and cross-links have been prepared in a straightforward manner from thiolactone derivatives and their properties were systematically evaluated.

Thiolactone chemistry was used to prepare bioinspired materials that mimic proteins by incorporating different polymer side chains that interact with molecules in their environment, such as formaldehyde or participate in intramolecular interactions that result in responsiveness to different stimuli. In Chapter 4, polymers with amino-side-chains were prepared for scavenging of formaldehyde, which is analogous to formaldehyde tissue fixation. Furthermore, amino acid side-chains in proteins participate in intermolecular interactions that affect the multiple levels of protein structure and function. In an analogous manner, polymers with different side-chains resulting in strong intermolecular interactions were prepared using thiolactone chemistry. Namely, polyampholytes with different types of complementary ionic functional groups were incorporated into polymers using thiolactone chemistry, in order to investigate their intermolecular interactions and properties. Finally, the latent thiol functionality derived from thiolactone building blocks was investigated for inhibiting radical species, which could be used for applications in polymer stabilizers and additives. The investigation of the thiol-containing radical inhibitors was inspired by glutathione, which is a powerful antioxidant in cells. Overall, this work demonstrates progressive development of functional polymer materials with advanced properties, while maintaining a simple and sustainable methodology enabled by the thiolactone chemistry.

1.3 Outline

Chapter 2 of this work provides an overview of functionalized polymers prepared using thiolactone chemistry, including functionalized polyamides, hydrogels for CO_2 sensing,

glycopolymer-containing nanoparticles, temperature responsive stationary phases for chromatography, and redox responsive polythiol layers. Chapter 3 is a second theoretical section providing an overview of polymer coatings prepared by thiol-ene chemistry, including their properties and applications. Recent advancements in the UV-cured and bio-based thiol-ene coatings are discussed with respect to their preparation, properties, and advantages compared to other coating resins.

Chapter 4 describes the conversion of thiolactone derivatives into UV-cured polymer networks, followed by a systematic screening of their coating properties. Different thiolactone monomers and amine-containing cross-linkers were used for a comparative evaluation of the polymer coating properties.

Chapter 5 focuses on the development of polymer coatings with amine functional groups that can trap formaldehyde and thereby prevent harmful airborne emissions. Different amine compounds have been incorporated into UV-cured polymer coatings and their efficiency of trapping formaldehyde was evaluated.

Chapter 6 covers the synthesis of multifunctional ionic polymers developed using thiolactone chemistry and their structure-property relationships, such as the isoelectric point and thermoresponsiveness.

Chapter 7 investigates the potential of the thiolactone building block to be used as bio-based antioxidant with tunable properties. Thiol functional groups from the thiolactone moiety were incorporated into a commercial styrene/maleic anhydride copolymer, which could be used to scavenge radicals.

Chapter 8 summarizes the objectives and results of this work, while raising new questions and opportunities for further research involving thiolactone chemistry in dynamic polymer materials.

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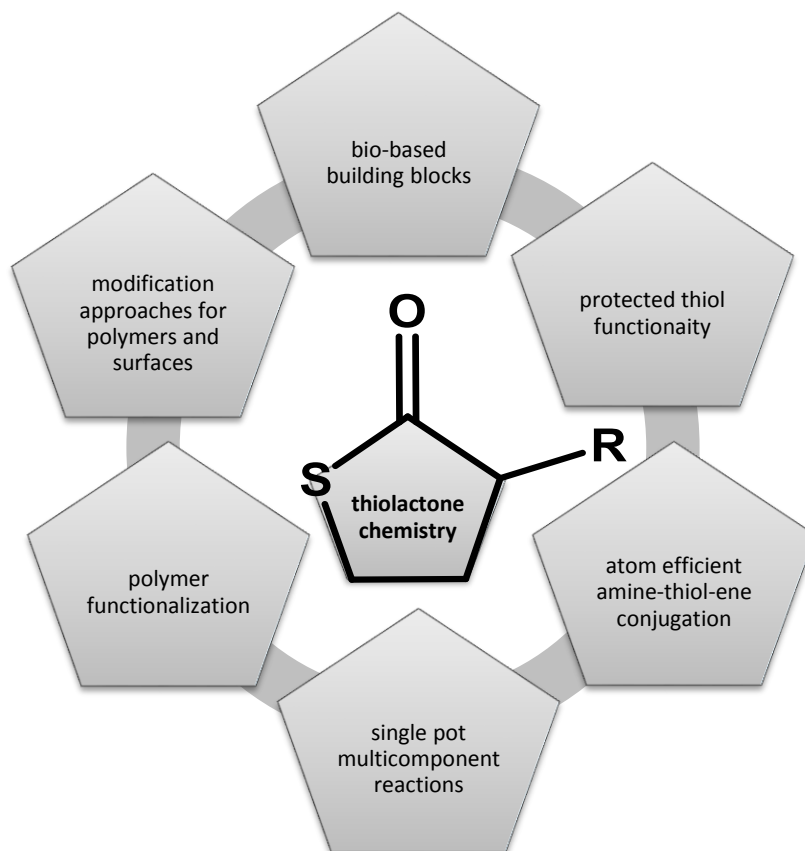
Abstract

Thiolactones are cyclic thioesters that can be obtained from amino acids, such as homocysteine. Various functionalized monomers have been prepared via the modification of the thiolactone side group with different reactive groups, such as acid chlorides, carboxylic acids, glycidyl ethers and anhydrides. Thiolactone-containing monomers with a double bond can be polymerized via radical or Michael-addition thiol-ene polymerization. In addition, thiolactones undergo ring-opening by nucleophilic addition with primary amines, which can be used to introduce different functionalities into polymers. The amine-thiol-ene reaction sequence can be conducted under mild conditions in a single pot. The thiolactone chemistry approach has been used for the preparation of various multifunctional polymers, including fluorescent poly(amide-imide)s, hydrogels for chemical sensing, thermoresponsive functionalized silica, and redox-responsive polythiol layers. Thiolactone chemistry is a powerful synthetic tool that contributes to sustainability via the integration of bio-based and functional building blocks in a simple and efficient manner.

Chapter 2. Thiolactone chemistry overview

2.1 Thiolactone chemistry in polymer science

In recent years, thiolactone chemistry has emerged as an effective method for one-pot multi-step synthesis of multifunctional polymers.[1] In previous research, thiolactone chemistry has been demonstrated as an effective strategy for the preparation of isocyanate-free polyurethanes,[2] diversely substituted polyamides,[3] hyperbranched polymers,[4] functionalized cyclic polymers,[5] poly(thioetherurethane)s[6] and crosslinked chitosan polymers.[7]

A recent review of thiolactone chemistry covers the synthetic aspects, as well as, a variety of polymer modification routes.[1] The main aspects of thiolactone chemistry are briefly covered here, followed by an overview of multifunctional polymers prepared via thiolactone chemistry, which is also the main focus of this PhD research.

Thiolactones are cyclic thioesters and homocysteine-γ-thiolactone (HTla) is a 5-membered thiolactone ring, which can be derived from homocysteine[8] and methionine[9] amino acids by acid-catalyzed intramolecular condensation. Hence, HTla is a bio-based building block that can be further derivatized into a variety of monomers via the conjugation reaction of the HTla amino group with acid halides,[10] carboxylic acids,[11] and anhydrides [12] (Scheme 2.1).

The synthesis and upscaling of the thiolactone-based monomers has been covered in previous work,[13] which provided the starting materials for further development of thiolactone-based coatings in this work. A variety of AB' monomers containing both a thiolactone and a double bond moiety have been prepared from the commercially available D,L-homocysteine thiolactone hydrochloride on multi-gram scale (Scheme 2.1).[13] The addition reaction between the amine side group of the D,L-homocysteine thiolactone hydrochloride and a variety of nucleophiles has been used to vary the side chain length and functionality of the thiolactone-based monomers. For example, 10-undecenoylthiolactonamide (Undec-TL) has been prepared from D,L-homocysteine thiolactone hydrochloride and 10-undecenoic acid, which is derived from castor oil (Scheme 2.1, A).[3] Undec-TL enhances the bio-based content of polymer materials and the aliphatic side-chain imparts hydrophobicity.
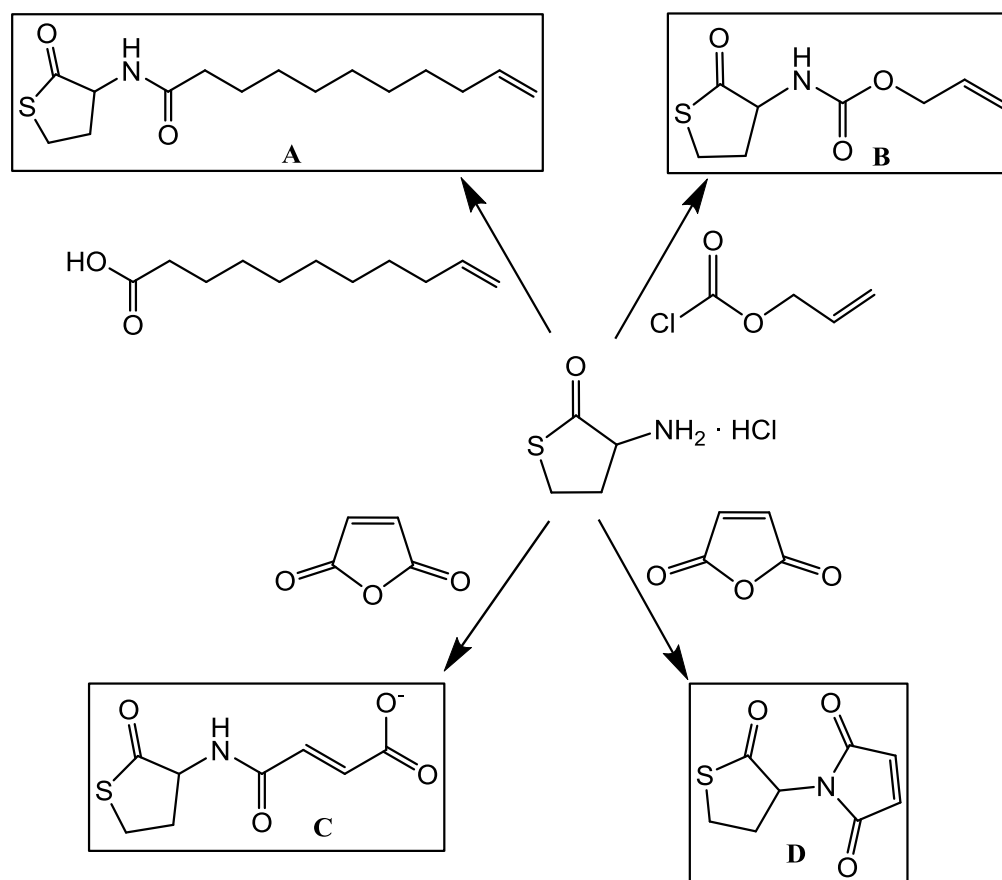
Scheme 2.1. Examples of monomers prepared from D,L-homocysteine thiolactone hydrochloride and 10-undecenoic acid (A), allyl chloroformate (B) , maleic anhydride (C, D).[13]

Alternatively, allyl chloroformate has been used to generate a thiolactone-containing monomer with a urethane moiety, which enabled the preparation of isocyanate-free polyurethanes with added functionalities (Scheme 2.1, B).[2] On the other hand, a hydrophilic ionic monomer has been prepared from *D,L*-homocysteine thiolactone hydrochloride and maleic anhydride, which introduces a carboxylic acid group to the monomer (Scheme 2.1, C).[14] The resulting *N*-maleamic acid homocysteine thiolactone monomer (MA-Tl) will be used to prepare pH-responsive ionic polymers with different functional groups. In addition, the same two precursors, namely, *D,L*-homocysteine thiolactone hydrochloride and maleic anhydride, have been used to synthesize a bicyclic thiolactone-maleimide monomer at higher temperatures (Scheme 2.1, D).[15] The thiolactone-maleimide monomer was polymerized using controlled and free radical polymerization methods, followed by polymer post-modification via the ring-opening of the

thiolactone moiety.[15] In conclusion, different side-chains can be incorporated into a thiolactone-containing monomer, resulting in a wide range of properties and applications.

2.2 Amine-thiol-ene conjugation

AB' thiolactone monomers have been used to prepare a variety of linear and cross-linked functionalized polymers following the general amine-thiol-ene reaction sequence (Scheme 2.2).
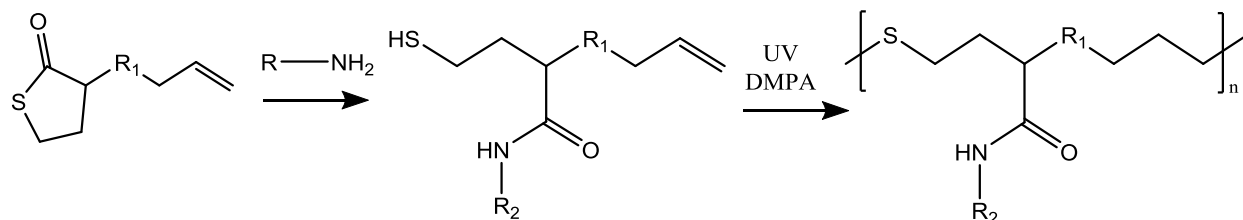
Scheme 2.2. Preparation of polymers from a thiolactone-containing monomer by aminolysis and ring-opening of the thiolactone moiety, followed by thiol-ene reaction.

In the first step, the ring-opening of the thiolactone moiety occurs by the nucleophilic addition with a primary amine, which releases the thiol functionality. Based on the kinetic studies and ab initio calculated rate coefficients of the aminolysis of *N*-acetyl-DL-homocysteine thiolactone with n-butylamine, the rate determining step is the formation of the neutral tetrahedral intermediate, which is stabilized mainly by the amine at low conversions and by the thiol at high conversions.[16] The liberated thiol group can react with a double bond by thiol-ene addition via the radical step-growth addition polymerization.[17] Further details and the optimization of the amine-thiol-ene conjugation for the preparation of UV-cured coatings are covered in Chapter 4. The advantage of using the radical thiol-ene addition polymerization is the spatial and temporal control, which can be achieved by UV or thermal initiation of the polymerization. For example, micropatterned polymer films were produced on thiolated surfaces via the photopolymerization of multifunctional thiol and ene precursors through a photomask.[18]

The orthogonality of the amine-thiol-ene conjugation depends on the mechanism of the thiol-ene addition, the reactivity of the reaction components, and the reaction conditions. The orthogonality of the amine-thiol-ene conjugation via the radical thiol-ene coupling mechanism is limited to functional groups that are stable in the presence of radical species. The drawbacks

associated with the amine-thiol-ene conjugation involving radical photopolymerization include side reactions of photoinitiators with certain amines, eg. 2,2-dimethoxy-2-phenylacetophenone (DMPA) and benzylamine.[17] In addition, some functional groups introduced in the first aminolysis step may be unstable in the presence of radicals, eg. furan, double and triple bonds.

Alternatively, if the double bond is more reactive (eg. acrylate, maleimide, imidazole, vinyl sulfone), the thiol-ene addition proceeds by the Michael addition mechanism, which can be catalyzed by a base.[2] Nucleophilic amine-thiol-ene conjugation is not entirely orthogonal and requires chemoselective discrimination between the amine and the thiol nucleophiles. The choice of the ene and the reaction conditions need to be optimized, such that the aminolysis of the thiolactone is followed by thiol-Michael addition, without the aza-Michael addition of the amine to a double bond. Espeel *et al.* have developed an optimized methodology for the one-pot nucleophilic amine-thiol-ene conjugation using model studies and online infrared spectroscopy.[2] This methodology enabled the preparation of functionalized polymers from AB'-type monomers, consisting of an acrylate and a thiolactone moiety in combination with several amine functional groups, such as double bond, triple bond, furfuryl, tertiary amine and morpholine. The orthogonality of the thiolactone aminolysis reaction was also confirmed by the fact that under the same reaction conditions, i.e. 50 equivalents of the nucleophile and neutral pH, water, alcohols, thiols and anilines did not react with the thiolactone ring. Disulfide formation can also occur concurrently with the amine-thiol-ene conjugation and it is more prominent at higher amine concentration and longer reaction times. The thiol-disulfide conversion is reversible and different reducing agents can be used to cleave disulfide bonds.[1]

In comparison with other conjugation approaches, such as the copper(I)-catalyzed cycloaddition of azides and alkynes, the orthogonality of amine-thiol-ene conjugation is more limited in terms of the reactivity of the ene components and the reaction conditions. However, amine-thiol-ene conjugation is a highly versatile technique that enables double polymer post-modification and double cross-linking with a wide variety of functional groups.

The versatility of the thiolactone chemistry was further expanded by combining Michael and radical thiol-ene addition to generate sequence-ordered polymers from thiolactone derivatives.[19] The ring-opening of thiolactones generated thiols in situ, followed by Michael addition with the

electron-deficient double bonds of allyl methacrylate (Figure 2.1). Subsequently, UV irradiation was used to trigger the radical thiol-ene reaction between thiols and the electron-rich allyl groups. This approach for the preparation of sequence-ordered polymers is notable for its simple one-pot process, enabled by the chemoselectivity of the three-component reaction system.
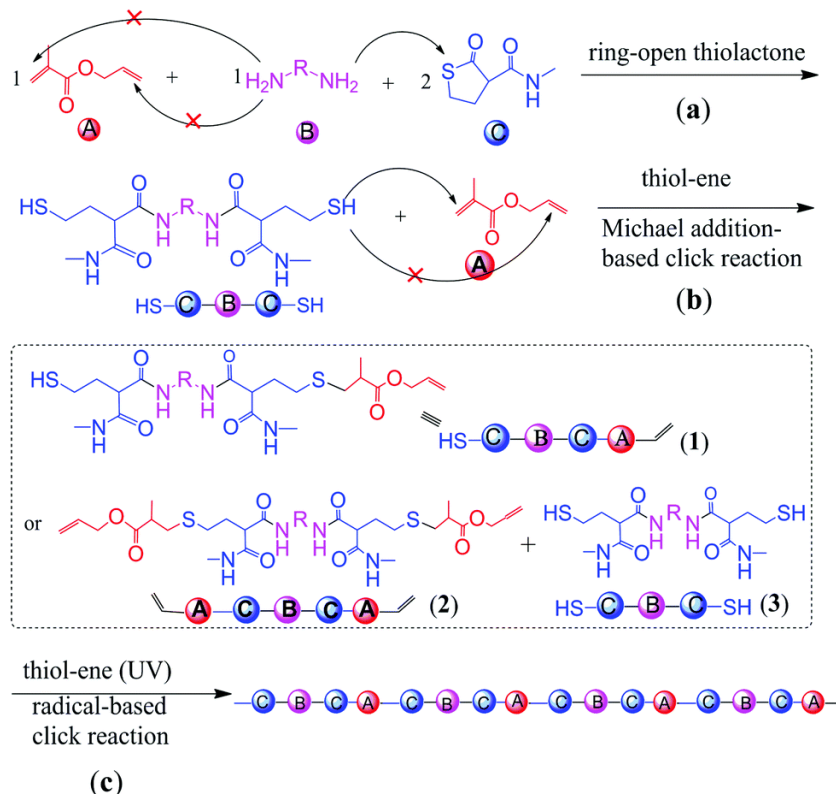
Figure 2.1 Preparation of sequence-ordered polymers via the multicomponent polymerization of bis(methacrylate)s, diamines and thiolactones, (a) ring-opening of thiolactones (b) Michael thiol-ene addition (c) free radical thiol-ene reaction.[19]

Mommer et al. developed another strategy for the preparation of thiolactone-based polymers starting from AB-type epoxy thiolactone monomers.[6] Aminolysis of the thiolactone moiety generated thiols in situ, which participated in the thiol–epoxy polymerization. Thereby, poly(thioether urethane)s with added side chains were prepared in a single pot (Figure 2.2).
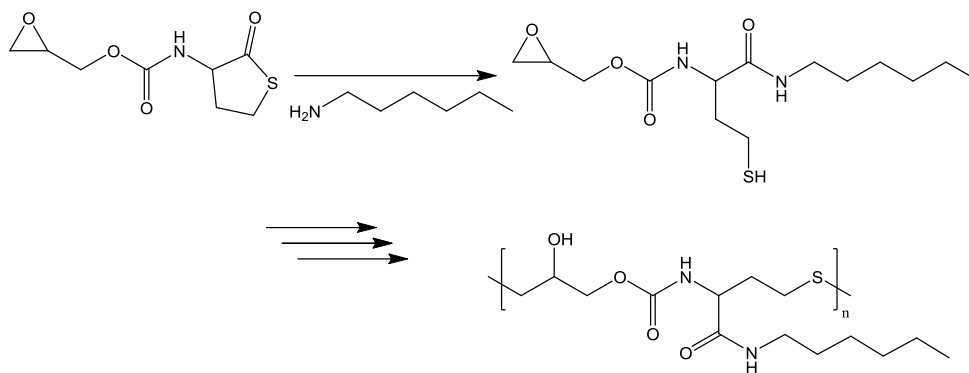
*Figure 2.2 Two-step cascade reaction of **1** generating poly(thioether urethane)s via an epoxy thiol intermediate.[6]*

Thiolactone chemistry is undoubtedly a versatile and powerful platform for the preparation of functionalized polymers. Many more opportunities exist in the application of thiolactone chemistry for the development of functionalized polymer materials with tailored properties, which will be described throughout this work.

2.3 Contribution of thiolactone chemistry towards sustainability

The contribution of thiolactone chemistry towards the sustainable development of polymers is several-fold, since sustainability encompasses multiple factors, such as renewable feedstocks and energy efficiency.[20] Thiolactone chemistry enables the incorporation of bio-based building blocks into polymers using mild reaction conditions and energy efficient processes, such as UV-initiated thiol-ene photopolymerisation. Thereby the combination of renewable feedstocks and energy-efficient processes can be used to achieve a high extent of sustainability in both polymer synthesis and processing.

First, the homocysteine thiolactone building block can be derived from renewable resources, namely, amino acids in proteins.[8] Secondly, the amine group of the homocysteine thiolactone can be derivatized with other bio-based molecules, such as the fatty acids from plant oils.[3] Additional bio-based functionalities can be integrated via the ring opening of the thiolactone by primary amines, such as those present in a variety of amino acids.[21] Moreover, the aminolysis of

thiolactone-containing precursors is an atom-efficient process, which occurs readily at room temperature and without catalysts.[2]

Furthermore, the versatility of the thiolactone building block has been used to incorporate desired functionalities into polymers, while avoiding the direct use of harmful components. For example, isocyanate-free polyurethanes have been prepared from a urethane-containing thiolactone monomer using thiol-ene photopolymerization.[17] Thus, thiolactone chemistry is suitable for industrial polymers, such as polyurethanes where greater sustainability has been a growing trend.[22]

Finally, the thiolactone moiety can be used as an in-situ source of a thiol functionality for thiol-ene polymerization. The UV-triggered thiol-ene radical polymerization is an energy-efficient process for the preparation of polymer materials with minimum consumption of organic solvents.[23] In addition, the synthesis of various thiolactone monomers from homocysteine thiolactone and acid derivatives with high yields can also be accomplished in benign solvents, such as water/ethyl acetate mixture.[13] Recyclability and biodegradability of polymers is also an important aspect of sustainability in terms of the material lifecycle and waste management. The versatility of the thiolactone chemistry could also be used to incorporate ester or disulfide linkages that could be broken down chemically or by microogranisms. Investigation of the decomposition and reprocessing of thiolactone-based polymers can be an important topic for future research due to the growing concern over plastic waste.

Therefore, thiolactone building blocks are excellent candidates for sustainable polymer materials with added value. Consequently, thiolactone derivatives have been used to prepare functionalized polymers with different properties and applications, as described in the next chapters.

2.4 Thiolactone chemistry for functionalized polymers and materials

Multifunctional polymers are an active area of research since functionalized polymers can be used to develop complex materials with added value in a variety of applications. Polymers with complementary chemical functionalities have enabled the production of "smart" or advanced materials, such as stimuli-responsive, shape-memory, and self-healing materials. Effective

strategies for the production of multifunctional materials include the incorporation of different moieties, establishing functions on different length scales, and forming multi-component systems, in which each component plays a role.[24]

In the field of multifunctional polymers, thiolactone chemistry plays an important role since it enables simple and efficient introduction of multiple functionalities into a variety of polymer structures. The next section provides an overview of functionalized polymers that have been prepared using thiolactone chemistry.

2.4.1 Functionalized polyamides prepared by thiolactone chemistry

The versatility of the amine-thiol-ene conjugation has been used to introduce a wide variety of functional groups prior and post polymerization.[1] For example, Goethals and coworkers prepared diversely substituted polyamides from a renewable 10-undecenoylthiolactonamide monomer and amine compounds with different chain lengths.[3] Polymers with longer side chains exhibited a lower E-modulus and a higher elongation at break. Oxidation of the thioether groups in the polymer backbone to sulfones led to more brittle materials with a higher E-modulus and lower elongation at break. Thereby, the mechanical properties of the polymers were varied both by the functional groups incorporated during polymer synthesis and polymer post-modification.

Another recent example of thiolactone chemistry for the preparation of functionalized polymers is the synthesis of fluorescent aliphatic poly(amide-imide).[12] The thiolactone chemistry approach was used to improve polymer solubility and tolerance to functional groups during the synthesis.[12] Thiolactone-maleimide monomer was prepared by the azide alkyne cycloaddition, followed by polycondensation with various diamines via a combination of aminolysis of thiolactones and amine-maleimide Michael addition (Figure 2.3). Thereby, poly(amide-imide) with 2-aminosuccinimide fluorophores were generated and the released thiols were combined with PEG via thiol-methacrylate Michael addition to improve polymer solubility.

A   Synthesis of thiolactone-maleimide monomer

B   Synthesis of fluorescent aliphatic poly(amide-imide)
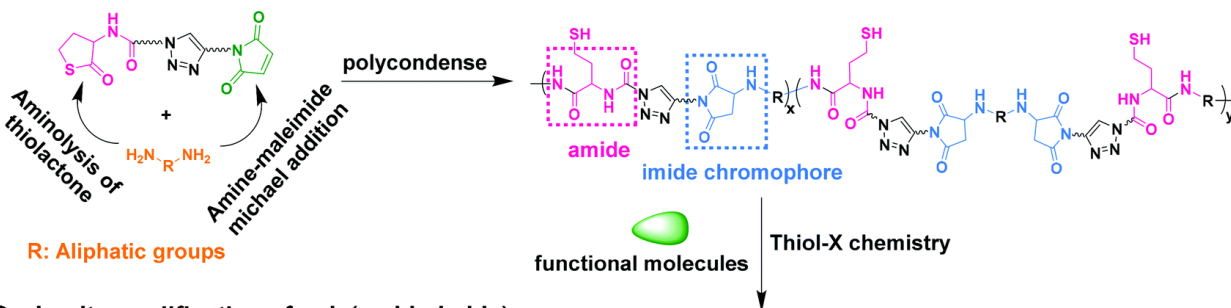
C   In-situ modification of poly(amide-imide)
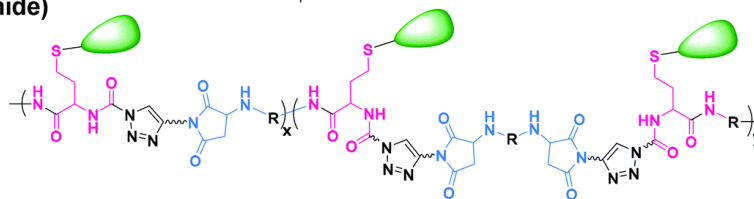
Figure 2.3 Synthesis of the thiolactone-maleimide monomer (A) and fluorescent aliphatic poly(amide-imide) (B), followed by polymer modification through thiol-ene addition (C).[12]

2.4.2 Functionalized hydrogels and particles prepared by thiolactone chemistry

Polymer hydrogels and particles are an important class of materials with a wide range of physical and chemical properties that make them suitable for many biomedical and environmental applications. Multifunctional hydrogels for sensing applications have been developed using the thiolactone functionalized poly(*N*-isopropylacryl amide) (p(NIPAAm-*co*-TlaAm)). For example, hydrogels for CO_2 sensing were prepared using (p(NIPAAm-*co*-TlaAm)).[25] The incorporation of basic moieties into the gels, such as imidazole and a morpholine by the aminolysis of thiolactone was employed to make them responsive to CO_2. The gels exhibited a significant increase in swelling in water in the presence of CO_2, which decreased the pH and caused the protonation of the polymer.

The modification of (p(NIPAAm-co-TlaAm)) via thiolactone chemistry was also implemented in other polymeric materials, such as glycopolymer-containing nanoparticles. [26] The thiolactone moiety in (p(NIPAAm-co-TlaAm) was reacted with different amines and the released thiol was

coupled with 2-bromoethyl-2′,3′,4′,6′-tetra-O-acetyl-α-*D*-mannopyranoside. The resulting amphiphilic graft copolymers self-assembled into micelles or larger vesicles, depending on the choice of amine functionality. The amine side-chain length determined the particle size, morphology, dispersity and bioactivity. Amines with shorter chain lengths led to the formation of micelles with a lower size distribution and greater bioactivity towards lectins.

Recently, Mommer *et al.* reported another example of functionalized nanoparticles prepared using thiolactone chemistry. [21] Polyelectrolytes were synthesized in one-pot from a bicyclic monomer with an epoxide and a thiolactone ring in combination with different amino acids.[21] Amino acids were introduced by the aminolysis of the thiolactone moiety, which released a thiol that subsequently reacted with the epoxide ring (Figure 2.4).
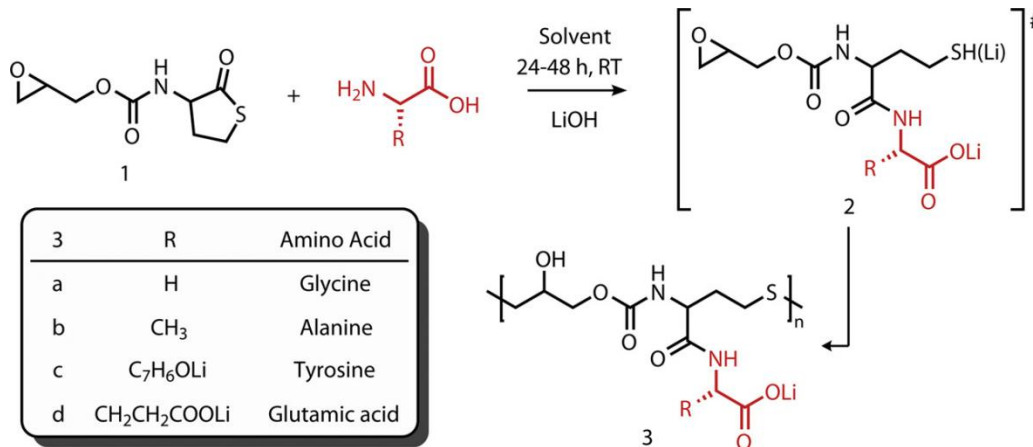
*Figure 2.4. Synthesis of poly(thioether urethane)s using epoxy thiolactone **1** and various amino acids.[21]*

Anionic and cationic polyelectrolyte precursors were obtained using glycine and lysine methyl ester, respectively. Polyelectrolyte complexes were formed by combining the two polyelectrolyte solutions. Thereby, complex macromolecular architectures were obtained using simple amine-thiol-ene conjugation with bio-based components.

Another application of functionalized poly(*N*-isopropylacryl amide), p(NIPAAm) was the preparation of temperature responsive stationary phases for aqueous liquid chromatography.[27] Thiolactone-containing p(NIPAAm) was grafted to aminopropylsilica by the aminolysis of the thiolactone moiety. High polymer coupling yields were achieved by thiolactone ring opening

with the primary amines in aminopropylsilica, which was facilitated by the relatively low polymer molecular weights. Thermal responsiveness of the resulting liquid chromatography columns was confirmed by the low and high retention of peptides at temperatures below and above the lower critical solution teperature (LCST) of p(NIPAAm), respectively. This work demonstrated that thiolactone chemistry is also an effective strategy for the surface modification of inorganic particles, which opens many opportunities for future research.

2.4.3 Functionalized polythiol layers prepared by thiolactone chemistry

In addition to hydrogels and particles, thiolactone chemistry can be used to prepare functionalized surfaces. For example, redox-responsive polythiol layers on gold substrates were prepared from water-soluble thiolactone-containing copolymers synthesized by RAFT copolymerization of thiolactone acrylamide and *N,N*-dimethylacrylamide.[28] The thiolactone functionality was used as a stable precursor for thiol groups, which can otherwise be unstable due to oxidation under ambient conditions. A thiolated dye was used as a model drug to demonstrate the dynamic release/regrafting to the polythiol layers under redox stimulation.
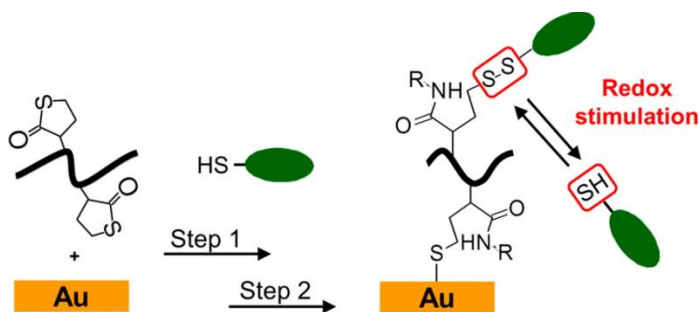
Figure 2.5 Redox-responsive polythiol layers on gold substrates prepared using thiolactone-containing polymers.

2.5 Conclusion

Thus, thiolactone chemistry has been demonstrated as an effective strategy for introducing different functional groups into polymers and materials. Amine-thiol-ene coupling has been conducted in one pot and under mild conditions using a wide range of substrates and functional

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groups. Notably, the length of the polymer side-chain introduced by the aminolysis of the thiolactone moiety has a significant impact on polymer properties, including E-modulus and lower elongation at break, as well as self-assembly behavior. In addition to D,L-homocysteine thiolactone hydrochloride being a renewable resource, other renewable building blocks have been incorporated into thiolactone-based polymers, such as 10-undecenoic acid derived from castor oil and amino acids. Evidently, thiolactone chemistry is a powerful synthetic tool for functionalized polymer materials with a wide range of properties and applications. The advantages of thiolactone chemistry can also be combined with those of thiol-ene chemistry, which is particularly attractive for the preparation of polymer coatings, which is described in the next chapter.

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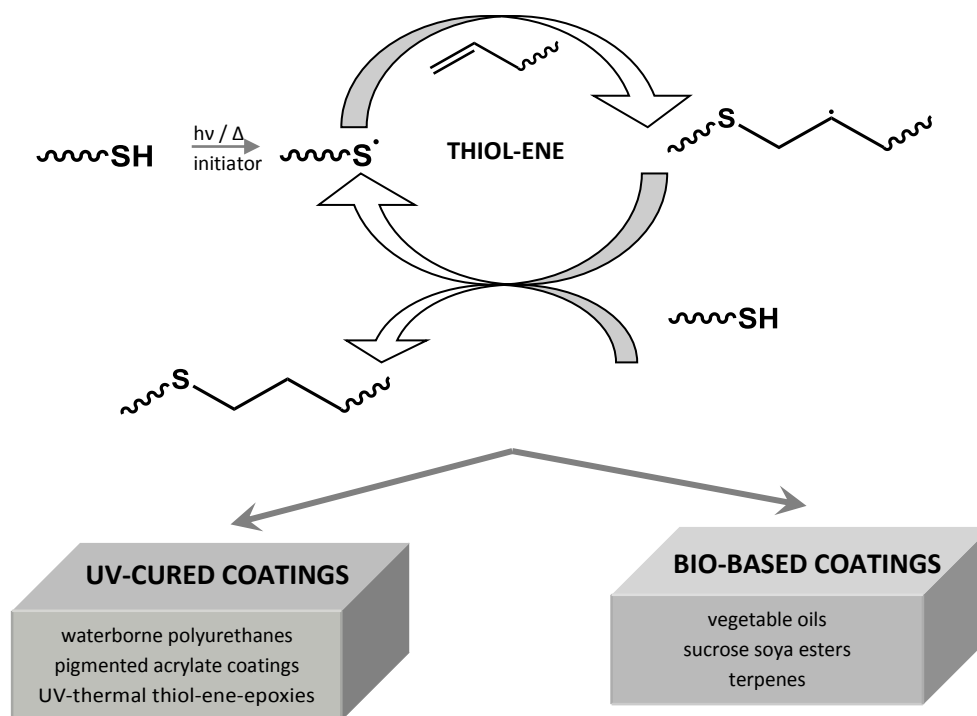
Abstract

Future advancement of coatings relies on new synthetic building blocks and methods that enable added functionality, while minimizing the environmental impact and cost. This overview highlights thiol-ene chemistry for coatings applications. Thiol-ene coupling has the advantages of rapid and uniform cross-linking, delayed gelation, reduced shrinkage, and insensitivity to oxygen. Thiol-ene chemistry has led to significant advances in UV-cured coatings, including pigmented acrylate coatings and waterborne polyurethane dispersions. Bio-based coatings were developed via thiol-ene coupling of unsaturated moieties in vegetable oils with multifunctional thiols, resulting in tunable properties. The homogeneous thiol-ene network formation has been employed in hybrid coatings yielding synergistic effects of the inorganic components within the thiol-ene matrix. Thus, thiol-ene chemistry is a powerful tool for the sustainable development of functional coatings with a variety of building blocks.

Chapter 3. Thiol-ene chemistry for polymer coatings

3.1 Introduction

Polymer coatings can be designed with a versatility of structures and functionalities, which lead to a broad range of properties and applications. While the primary function of most coatings is to protect the substrate, many specific coating functionalities have been developed, such as antifouling,[1,2] antimicrobial,[3,4] self-cleaning,[5,6] anti-reflective,[7,8] self-healing,[9-11] flame retardant[12,13] etc. Future advancement of coatings relies on new synthetic building blocks and methods that can enable added coating functionality, while minimizing cost and the environmental impact. This overview highlights thiol-ene chemistry for the preparation of polymer coatings, which has been an actively growing research field (Figure 3.1).
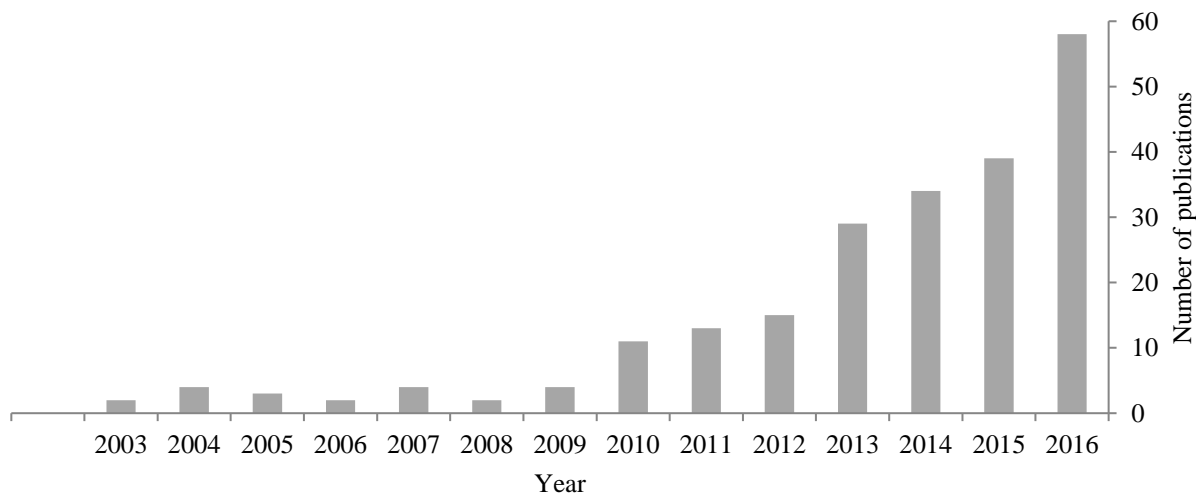
Figure 3.1: Publications on topic "Thiol-ene coatings". Source: Web of Science, 17/04/2017.

Thiol-ene chemistry has been used extensively for polymer synthesis and functionalization, which has been reviewed previously.[14-19] In this theoretical chapter, the focus is on the application of thiol-ene chemistry in coatings with different functionalities and applications, which is the starting point of this PhD research. The progress in UV-cured bio-based, and hybrid coatings is covered and the advantages of thiol-ene chemistry are highlighted.

3.2 Thiol-ene polymerization

Cross-linked polymer systems obtained by thiol-ene chemistry combine the advantages of the formation of uniform polymer networks, rapid cross-linking, delayed gelation, reduced shrinkage and insensitivity to oxygen, in comparison to network formation using acrylates.[14] The thiol–ene radical reaction can be triggered by a thermal or photochemical radical initiator which can abstract a hydrogen from the thiol, generating a thiyl radical.[20] The thiyl radical propagates by addition across the ene group. Subsequently, a chain-transfer between the carbon-centered radical and a thiol regenerates the thiyl radical that undergoes further reaction (Figure 3.2).[15] The molecular weight build-up occurs slowly during thiol-ene step-growth addition due to the chain transfer after each addition step.

Thiol-ene step-growth polymerization is characterized by delayed gelation compared to acrylates, since thiol-ene networks are typically formed from low-molecular multifunctional thiol and ene components, which maintain relatively low viscosity until high conversions are reached.[14]
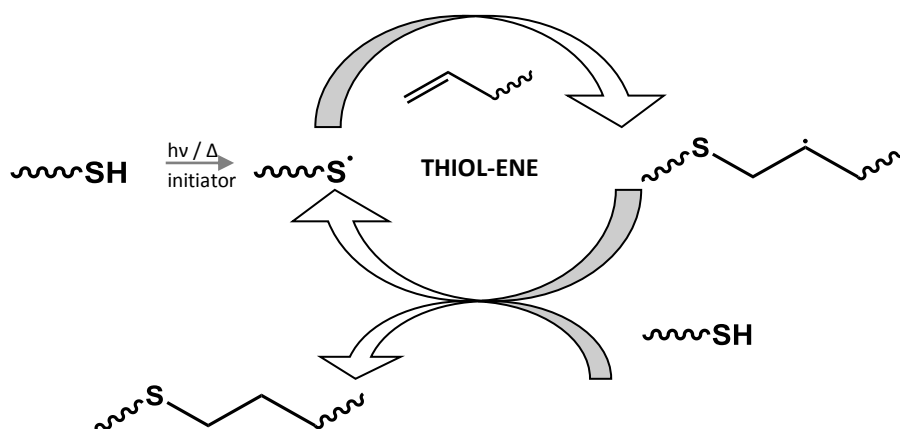
Figure 3.2: Radical thiol-ene reaction mechanism.

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Thiol-ene networks gel at much higher conversions than multifunctional acrylate networks, in which gels form at very low conversions. The gel point of thiol–ene crosslinked network formation at which diffusion rates are significantly reduced is determined by

$$\alpha = [1/r \, (f_{thiol} - 1)(f_{ene} - 1)]^{1/2}$$

where r is the thiol-ene molar ratio based on functional groups, f_{thiol} is the thiol functionality, and f_{ene} is the ene functionality. [14] Thereby, the gel point can be controlled by the choice of the thiol and ene.

Thiol-ene systems also exhibit uniform cross-link density, low polymerization stress and shrinkage. The low molecular weight of thiol and ene components, low formulation viscosity, and low polymerization stress contribute to improved adhesion of thiol-ene networks, which has been used for optical adhesive applications.[14]

Thiol-ene polymers typically have good thermal and oxidative stability, which can be attributed to the stabilizing effect of the thioether group that has antioxidant effects.[14] Thermogravimetric analysis of thiol-ene polymers indicated that the onset of thermal decomposition was above 250°C upon scanning at 10 °C/min without any weight loss after 40 minutes in air at 200 °C.[14]

3.3 Technical considerations of thiol-ene polymerization for applications

The main technical constraints of thiol-ene chemistry include the strong odor of thiols, limited shelf-life, and low polymer glass transition temperature (T_g) values and the corresponding mechanical properties, such as hardness. The shelf-life of unstabilized thiol-ene formulations can range from several hours to over a month, which is determined by the reactivity of the thiol and ene components, the presence of impurities and the storage conditions.[14] The possible reasons for limited stability of thiol-ene formulations include: (1) base-catalyzed thiol-ene additions, (2) decomposition of peroxide impurities that initiate a thermal free-radical reaction, (3) hydroperoxide impurities form thiyl radicals that initiate polymerization, (4) spontaneous initiation of polymerization via the formation of radicals through a ground-state charge-transfer complex between the thiol and ene components.[14]

Different approaches have been developed to overcome these drawbacks, which can be tailored for the desired coating formulation and application requirements. The strategies to minimize the thiol odor include selecting thiol compounds with reduced odor, or using high molecular weight thiol compounds with lower volatility.[21] The shelf life of thiol-ene formulations has been improved by adding stabilizers, such as radical scavengers.[22] Formulations with secondary thiols were found to exhibit improved storage stability and relatively low odor, with no change to the physical, mechanical and optical properties of the polymers.[23] A comparison between formulations with primary and secondary thiols with different ene components revealed that secondary thiol–ene formulations did not gel after 20 days of storage at room temperature, while primary thiol–ene formulations gelled after 12 hours to 15 days, depending on the ene component. [23]

An alternative strategy to overcome the disadvantages of free thiols in thiol-ene polymer preparation is to use protected thiol groups, such as the cyclic thiolactone.[24] As described in Chapter 2, DL-homocysteine thiolactone hydrochloride is a heterocyclic thioester with a protected thiol, which has improved storage stability and no offensive odor. The protected thiol can be released without any leaving groups by nucleophilic attack of a primary amine.

Thiol-ene polymers typically exhibit a relatively low T_g, below room temperature due to the flexible thioether linkages.[14] The T_g and the associated mechanical properties of polythioethers can be improved by including monomers with higher functionality, rigid structures,[25] hyperbranched[26,27] monomers or dendrimers.[28] Combinations of thiol-ene with epoxy[29] or polyurethane chemistries have also resulted in improved material properties.[30,31] For example, thiol-ene networks prepared with trimethylolpropane-tris(3-mercaptopropionate) and trimethylolpropanetriallyl ether exhibited a T_g = -5 °C, while analogous thiol-ene/epoxy networks exhibited a T_g = 25 °C, based on DMTA analysis.[29] In addition, dual cure systems with fast and slow reaction steps enable additional spatial-temporal control of the polymerization, which has been used in off-stoichiometry thiol-ene-epoxy thermosets.[32,33]

3.4 UV-cured thiol-ene coatings

3.4.1 Formulation of UV-cured thiol-ene coatings

UV-cured coatings have gained increased interest due to their low energy consumption, high curing speed, and low emissions of volatile organic compounds.[34,35] In the field of UV-curing technology, thiol-ene chemistry offers important advantages for both coating resin formulation and application. Thiols react with a variety of unsaturated compounds, such as the cyclic triallyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (TTT) and the linear tri(ethylene glycol) divinyl ether (TEGDVE), which results in polymer networks with a range of rigidity and physical and mechanical properties (Scheme 3.1).[23]

TEGDVE

HD-SH

TTT

CHDM-SH

HBPA-SH
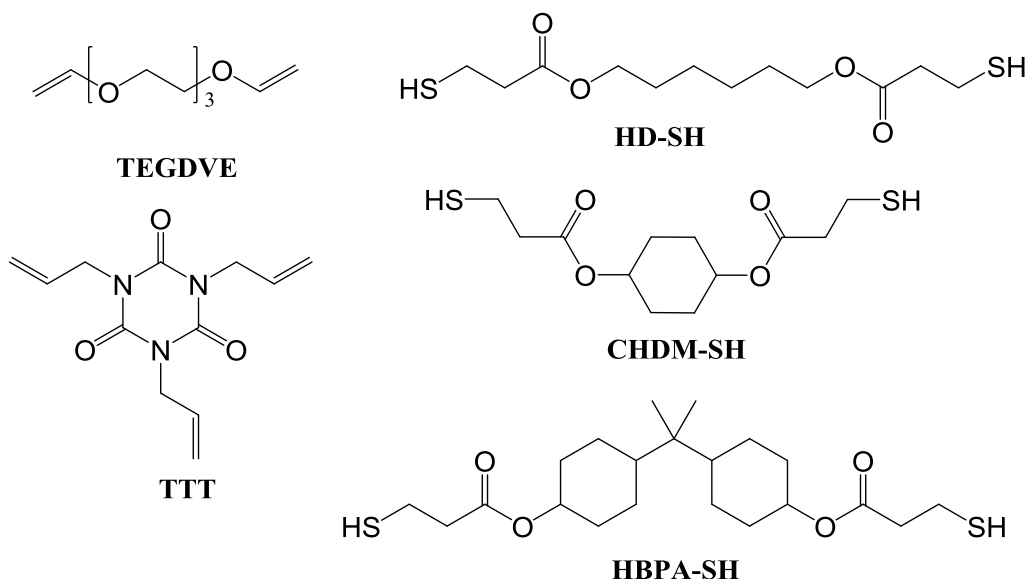
*Scheme 3.1 Examples of thiol and ene components used for the preparation of thiol-ene polymer coatings, tri(ethylene glycol) divinyl ether (**TEGDVE**), triallyl-1,3,5-triazine-2,4,6-trione (**TTT**), 1,6-hexane bis(3-mercaptopropionate) (**HD-SH**), trans-1,4-cyclohexanedimethyl bis(3-mercaptopropionate), 4,4'-isopropylidenedicyclohexane bis(3-mercaptopropionate) (**HBPA-SH**).*

The cyclic triallylic TTT compound contributes to higher T_g of thiol-ene polymer networks, while the polyether groups in the divinylic TEGDVE contribute to a reduced T_g, as well as a lower storage modulus and pendulum hardness.[23] Thereby, the properties of the thiol-ene

networks can be controlled by the thiol and ene functionality and the rigidity of the chemical structures.

Ternary experimental design has been employed for the investigation of the effect of three different thiol structures on the properties of thiol-ene photopolymerized coatings prepared with TTT.[36] Coatings prepared with the linear 1,6-hexane bis(3-mercaptopropionate) (HD-SH) resulted in high cross-link density of polymerized films, but poor thermomechanical and coating properties, which could be attributed to the flexibility of the linear alkyl thiol. The coatings with double-cycloaliphatic 4,4'-isopropylidenedicyclohexane bis(3-mercaptopropionate) (HBPA-SH) exhibited lower crosslink density and relative conversion due to the rigid and sterically hindered structure. However, the presence of HBPA-SH contributed to a higher tensile strength, tensile modulus, T_g, and pencil hardness. The combination of HBPA-SH and single-cycloaliphatic trans-1,4-cyclohexanedimethyl bis(3-mercaptopropionate) (CHDM-SH) resulted in a synergistic enhancement of the elongation-to-break and pull-off adhesion. Optimum coating properties were achieved using a mixture of thiols, including HBPA-SH for rigidity and toughness, as well as CHDM-SH, for a higher cross-link density.

Thiol-ene polymerization is not inhibited by oxygen, since a peroxyl radical can abstract a hydrogen from a thiol group, which forms a thiyl radical and thereby re-initiates polymerization (Scheme 3.2).[37]
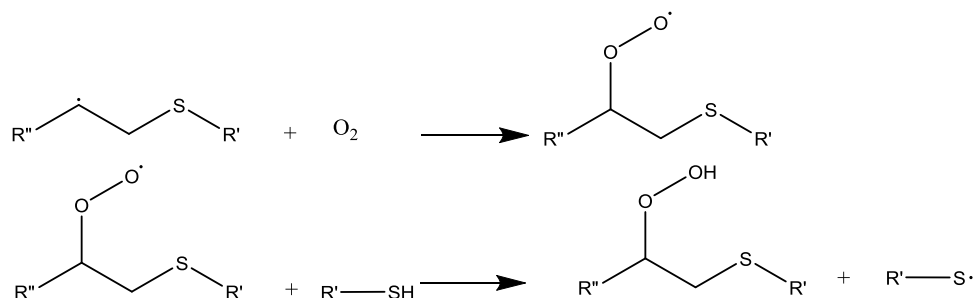
Scheme 3.2. Formation of a peroxyl radical during radical photopolymerization in the presence of oxygen and abstraction of hydrogen from a thiol by a peroxyl radical resulting in a thiyl radical, which can continue polymerizing.[27]

Thiols with higher functionality cause a more rapid increase in viscosity, which helps to reduce the diffusion of oxygen through the polymer film.[38] The UV-curing of pigmented formulations in

air was significantly improved by the addition of multifunctional thiols.[39] Addition of trimethylolpropane tris-(3-mercaptopropionate) to tripropylene glycol diacrylate with calcium lithol rubine pigment increased the photopolymerization rate in air due to the chain transfer from the peroxyl radicals to the thiols. Thiols were more effective in reducing oxygen inhibition compared to typical additives, such as *N*-methyldiethanolamine.

3.4.2 UV-cured waterborne polyurethane thiol-ene coatings

UV-cured waterborne polyurethane (PU) coating formulations are attractive due to their fast processing and sustainability associated with low emissions of volatile organic compounds (VOC's).[40-44] Multifunctional thiol- and ene-terminated PU aqueous dispersions have been developed for UV-curable coatings.[31,45] A PU prepolymer containing carboxylic acid groups was chain terminated with thiol and ene end-groups[31] (Figure 3.3). UV-cured coatings were prepared by neutralizing the PU prepolymers and dispersing them in water, followed by addition of a photoinitiator, application on a substrate and UV-curing. As the ratio of thiol/ene groups approached 1/1, the crosslink density increased, corresponding with an increase in T_g and the storage modulus above T_g, with maximum values of T_g =103°C and E'=25 MPa. The mixtures of thiol- and ene terminated PU aqueous dispersions exhibited high photopolymerization reactivity even after one month of storage, although stability was poor in acetone and in the presence of a photoinitiator. Multifunctional thiol-ene systems can have poor shelf-life under certain conditions, especially in the presence of oxygen and/or light. Therefore, the reactivity of the functional groups as well as the storage conditions have to be taken into account depending on the application requirements.
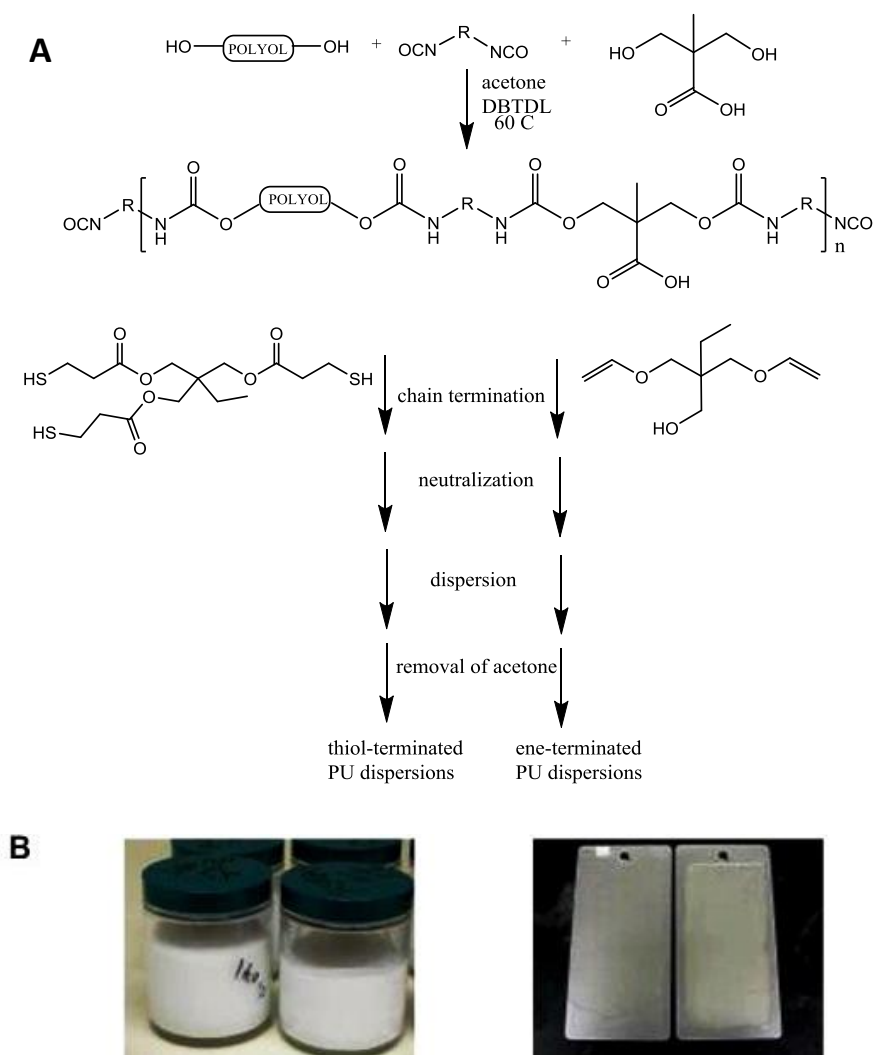
*Figure 3.3: Synthesis of multifunctional thiol- and ene-terminated polyurethanes (PU)s (**A**), PU dispersions and UV-cured waterborne coatings (**B**). [31]*

3.4.3 Dual-cured UV-thermal thiol-ene systems

Dual-cured polymer systems combine UV curable and thermally curable functional groups in order to achieve high cross-link densities throughout large three-dimensional objects[46] and minimize material defects.[47] Dual-cured UV-thermal systems have been developed by the photopolymerization of a thiol-ene system followed by thermally activated ring opening polymerization of epoxy monomers catalyzed by tertiary amines[27] or alkylsulfonium salts.[29] The presence of the epoxy monomer did not affect the conversion of thiol and ene reactive groups,

while 10-15% of epoxy groups have reacted by addition with thiols, which generated sulfides. Thiols are known to have an inhibiting effect on cationic ring-opening polymerization of epoxies.[48] However, when the sulfides react with the oxonium-terminated growing polyether chains, the resulting trialkyl sulfonium salts can act as thermal initiators for the cationic polymerization of epoxies. The typical thiol-ene polymers have flexible thioether linkages, which result in poor mechanical properties, especially surface hardness. The hybrid thiol-ene/epoxy systems with bisphenol A exhibited a higher T_g and storage modulus and improved thermal stability.

Besides, thiol-ene chemistry was also used to synthesize hyperbranched polymeric photoinitiators end-capped with benzophenone (BP) and tertiary amines.[49] Based on the differentiated scanning calorimetry (DSC) investigation, the photopolymerization rate of 1,6-hexanediol diacrylate initiated with 5 wt% of the hyperbranched polymeric photoinitiator containing BP was twice greater than that with BP itself. The hyperbranched polymeric photoinitiators exhibited good miscibility with acrylate resins and generated coatings with high cross-linking density.

3.4.4 Functionalized UV-cured thiol-ene coatings

Thiol-ene chemistry has been used to prepare functional UV-cured coatings, since the high efficiency of the thiol-ene reaction enables a high degree of incorporation of functional monomers and the step-growth polymerization enables the formation of homogeneous polymer networks with controlled structures. For instance, flame retardant coatings with allyl diphenyl phosphine oxide (ADPPO) were prepared using thiol-ene photopolymerization in order to improve the polymerization reactivity of the allyl moiety.[50] Previous attempts to incorporate ADPPO into epoxy acrylate coatings were problematic due to the intramolecular dimerization of ADPPO. However, the propagation rate of thiol-ene polymerization is higher than for acrylate polymerization, which resulted in the efficient incorporation of ADPPO and high gel content of the generated coatings. Coatings with greater amounts of ADPPO exhibited improved thermal stability and flame retardancy.

Furthermore, the thiol-ene reaction has been gaining increased interest for the preparation of antifouling UV-cured coatings due to its high efficiency and the ability to develop complex surface morphologies.[51-53] Controlled polymer structure is especially important for investigating structure-property relationships, while the traditional method of using acrylated PEG to make antifouling coatings generated poorly controlled and inhomogeneous hydrogel structures.

Lundberg *et al.* screened different thiol-ene coatings for antifouling performance depending on the thiol-cross-linker, molecular weight of PEG, and the vinylic end-group.[53] The thiol-allyl based systems exhibited higher selectivity in the thiol-ene coupling, compared to methacrylate systems, which involved some homopolymerization. Antifouling assays demonstrated that longer PEG chains improved the antifouling properties of the thiol-ene coatings.

Other types of UV-cured coatings with additional functionalities, such as antimicrobial[55,56] have been prepared using thiol-ene chemistry due to its high efficiency and simplicity. For applications dealing with medical and food industries, it is necessary to incorporate functional components without any potential for leaching in addition to avoiding the use of harmful additives or solvents.

3.5 Overview of building blocks for bio-based coatings

Bio-based coatings comprise an active area of research due to the limited availability of petroleum resources and growing concerns over sustainability. The main renewable building blocks used in coatings are described below, followed by the specific examples of thiol-ene bio-based coatings. There are many sources of renewable feedstock that can be generally classified as plant-based or animal-based. Plant-based feedstock commonly used in coatings can be further sub-divided into lipids, polysaccharides, terpenes and lignins (Figure 3.4).

In the lipid category, a wide variety of vegetable oil components have been used to prepare coatings, such as castor oil,[57-60] cotton seed oil,[61] linseed oil,[62-64] and soybean oil.[65-70] The fatty acids in vegetable oils are valuable building blocks for polymer coatings, since they contain carbon double bonds and carboxylic acid groups that can be incorporated into a variety of polymeric systems, such as alkyds, polyurethanes, epoxies, polyesteramides, and polyetheramides.[71]
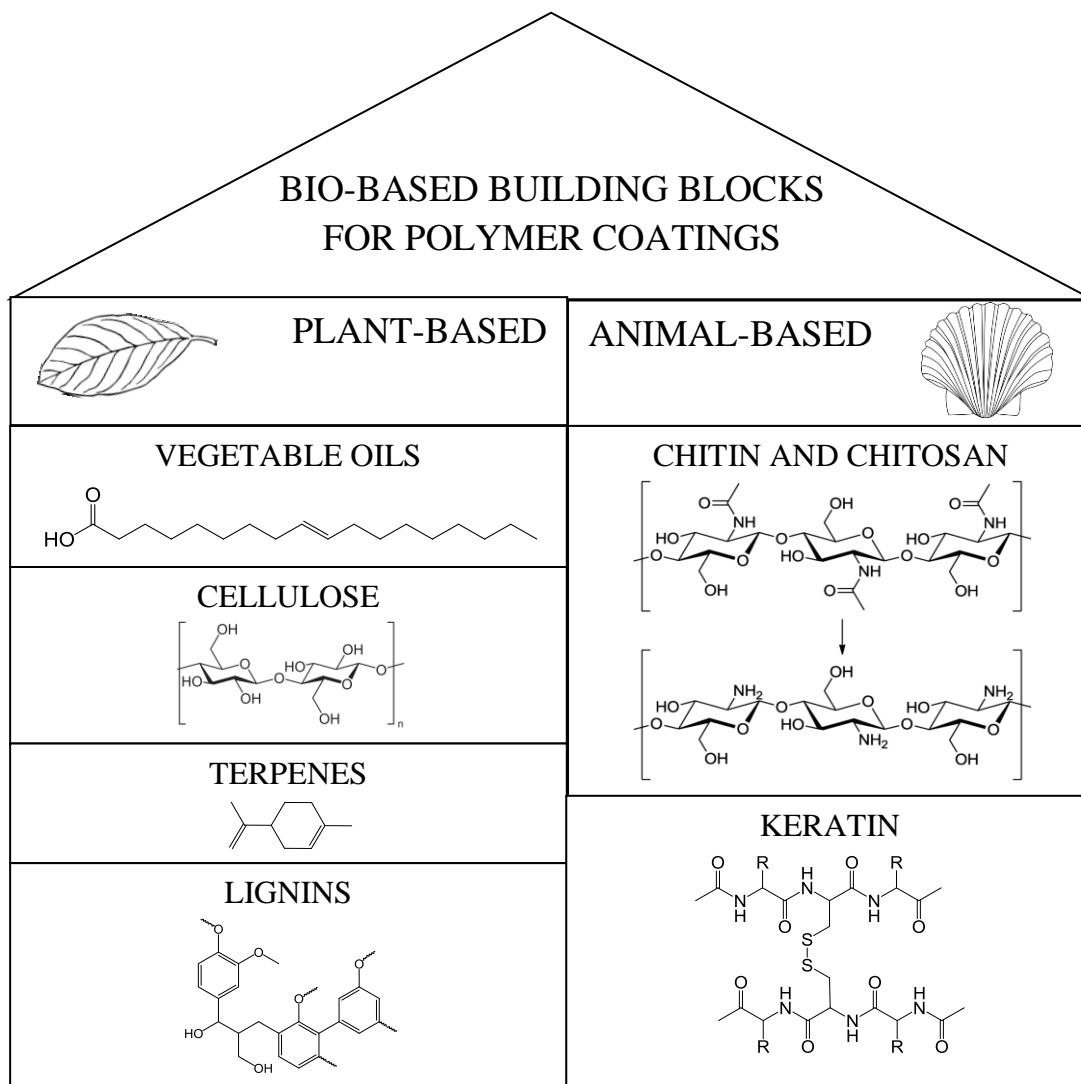
Figure 3.4. Examples of bio-based building blocks used for the formulation of polymer coatings.

The challenges with the incorporation of fatty acids into polymeric systems include the availability and purity of starting materials, the necessity for chemical modification, and the attainment of required coating properties. For example, waterborne UV-curable dispersion coatings were prepared from acrylated epoxidized soybean oil and a cross-linking agent synthesized by polycondensation of itaconic acid, glycerol and 1,4-butanediol. The resulting UV-

cured coatings exhibited improved hardness, flexibility, adhesion and solvent resistance compared to coatings without additional cross-linking agents.[65]

Many other plant-based renewable precursors for polymers are available, such as polysaccharides, which include cellulose, starch and products from the fermentation of carbohydrates, such as itaconic acid. Coatings containing cellulose[72] and starch[73-76] have gained increasing interest for packaging and food-contact material applications due to the growing emphasis on the environmental impact and recyclability of packaging. For instance, Dai and coworkers have developed a range of waterborne UV-cured polyester coatings by polycondensation of bio-based itaconic acid with different alcohols.[77-79] The resulting coatings exhibited high hardness, good water resistance and solvent resistance.

Terpenes and terpenoids are components of plant essential oils that contain one or more carbon-carbon double bonds and a wide variety of structures.[80] Terpenes have been used for the preparation of a variety of polymer coatings, including acrylates,[81] polyurethanes[82] and polyurethane/epoxies containing terpene-based polyols.[83] Thiol-ene chemistry has been widely used to transform the double bonds of terpenes into the desired functional groups for subsequent polymerization.[84]

Another widely occurring plant-based resource is lignin, which is a fiber with high molecular weight. Lignin can be broken down into a variety of functional aromatic compounds, such as p-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol.[85] Lignin derivatives provide added value in coatings due to their antibacterial properties. For example, Dai and coworkers prepared anti-bacterial cross-linked films containing eugenol allyl ether, which can be derived from lignin.[86]

In addition to plant-based raw materials, animal based feedstock has been used for the preparation of coatings. Chitosan and chitin are widely occurring amino-functionalized polysaccharides which form the shells of crustaceans.[87] Chitosan has been incorporated into coatings due to its antimicrobial[87,88] and corrosion inhibiting properties.[89-91] Chitosan imparts corrosion protection of metal substrates due to its good film-forming ability, excellent adhesion to metallic surfaces, and reversibility of ionization of the amine groups.[89]

In summary, a wide variety of bio-based building blocks have been used for the development of polymer coatings with different properties. Many challenges preclude large-scale industrial adoption of bio-based coatings due to the limited and unstable supply of natural resources, as well as their cost compared to petroleum feedstock. In addition, chemical transformation of bio-based resources into polymeric building blocks is not trivial and intensive research continues in this field.

In this context, thiol-ene chemistry has emerged as a simple and robust technique for chemical modification and polymerisation of natural starting materials. In particular, the carbon double bonds present in fatty acids of plant oils and terpenes are highly amenable to thiol-ene addition reactions, which have been used to prepare coatings with a wide range of properties.

3.5.1 Thiol-ene coatings prepared from vegetable oils

Thiol-ene polymerization is an effective approach for the incorporation of bio-based feedstock, such as unsaturated fatty acids derived from vegetable oil.[92] In the presence of a radical initiator the double bonds of unsaturated fatty acids are reactive towards thiols, which can be selected from a variety of multifunctional thiolated compounds, such as glyceryl dimercaptoacetate and pentaerythritol tetrakis(3-mercaptopropionate).[92]

Castor oil and its derivatives have been incorporated into a variety of polymer materials, since they contain double bonds amenable to thiol-ene reactions, as well as hydroxyl groups, which can be used to generate polyurethanes.[93] Allyl, acrylate, and vinyl ether derivatives of castor oil were prepared and combined with multifunctional thiols to produce thiol-ene UV-cured coatings.[94] The vinyl ether/thiol formulations resulted in the most homogeneous cross-linked polymer networks associated with nearly complete free radical step-growth thiol-ene polymerization, as evidenced by the narrow dynamic mechanical thermal (DMTA) analysis curves. On the other hand, allyl ether/thiol and acrylate/thiol formulations resulted in heterogeneous polymer networks, caused by a mixture of thiol-ene step-growth polymerization and homopolymerization of acrylates or allyl ethers. Auto-oxidation of the residual double bonds of the fatty acids upon aging resulted in increasing cross-link density of the polymer networks and associated improvement in solvent resistance, hardness, and chemical resistance.

The combination of fast UV-curing and slower auto-oxidation of the thiol-ene polymers containing fatty acids can generate coatings with a variety of properties. Photoinitiator-free UV-cured one-component bio-based coatings were prepared from a self-initiating oligomer synthesized by the esterification of castor oil with 3-mercaptopropionic acid.[59] The thiolated oligomer rapidly initiated photopolymerization under UV irradiation following the mechanism of step-growth addition and vinyl free radical polymerization.

A notable example of coatings with a high renewable carbon content are the waterborne polyurethanes prepared from a castor oil-derived undecylenic acid by Fu *et al*. (Figure 3.) [95]
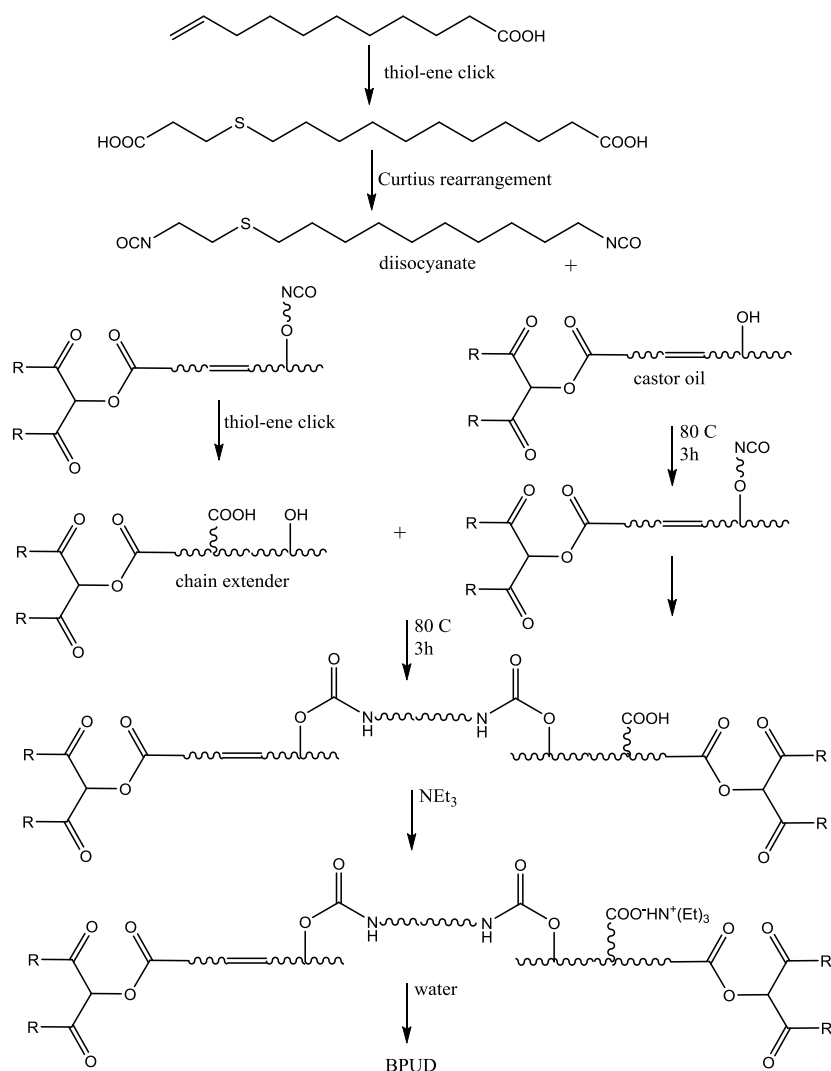
Figure 3.5: Preparation of bio-based waterborne polyurethane dispersion (BPUD) from undecylenic acid and castor oil.[95]

The undecylenic acid was transformed into a diisocyanate by thiol-ene coupling (TEC) with 3-mercaptopropionic acid and subsequent Curtius rearrangement.[95] This diisocyanate was combined with castor oil and a chain extender derived from thiol-ene reaction of castor oil and 3-mercaptopropionic acid to produce a bio-based waterborne polyurethane dispersion (BPUD). Thereby, BPUD with high renewable carbon content of 87 % was obtained. High renewable carbon content in coatings was also achieved using thiol-ene cross-linking of linseed oil triglycerides without photoinitator or solvent, resulting in final linseed oil content of 80 wt%.[63]

In addition to castor oil, epoxidized soybean oil has also been used extensively as a renewable feedstock for UV-cured thiol-ene coatings. For example, epoxidized soybean oil (SBO) was modified with multifunctional thiols or hydroxyl functionalized allyl compounds by Lewis acid-catalyzed ring opening (Figure 3.6).[67]
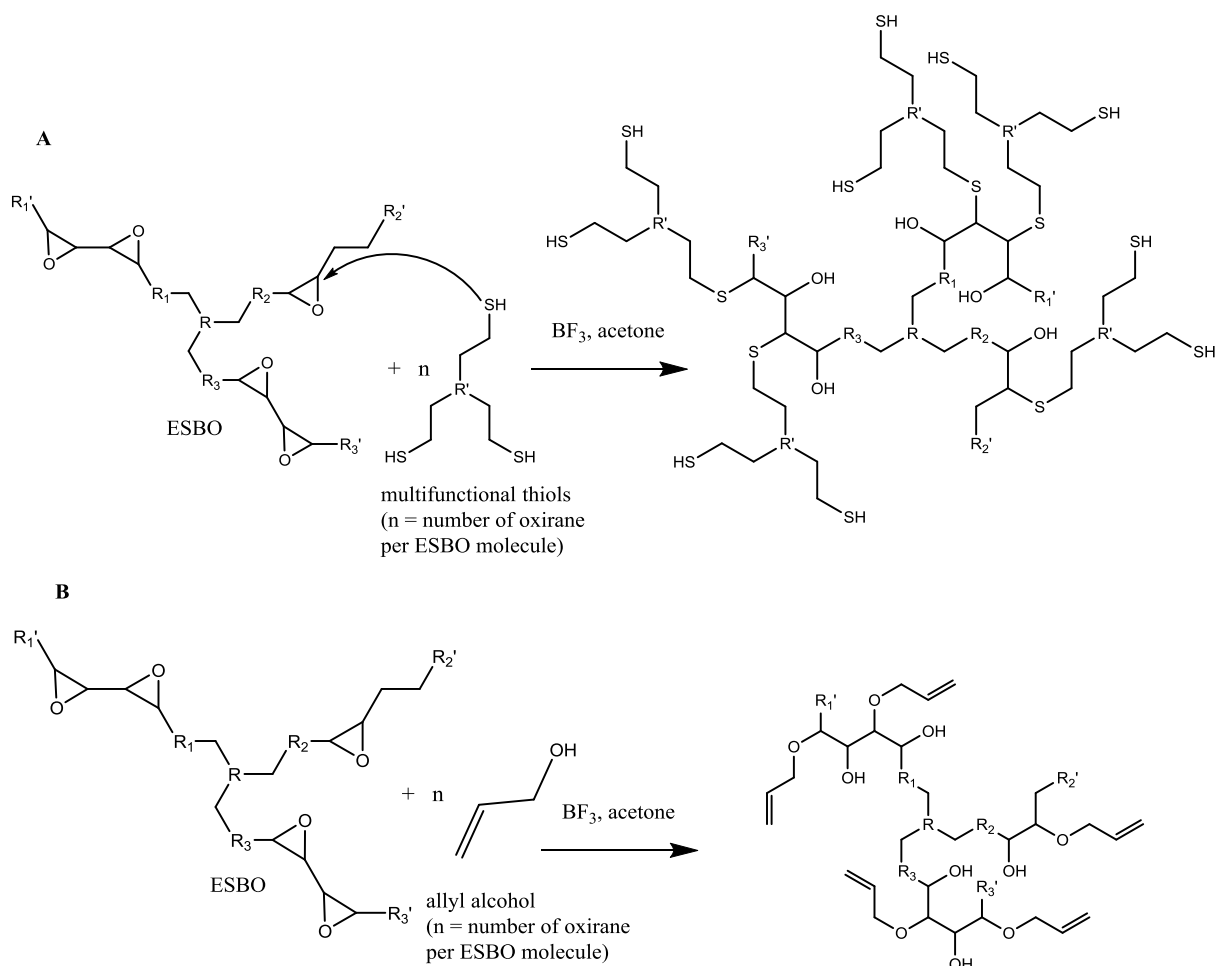
Figure 3.6: Modification of epoxidized soybean oil (ESBO) via epoxy ring opening by (a) multifunctional thiols and (b) hydroxyl functional enes.[67]

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Formulations with soy-based thiols and enes with higher functionality formed tack-free films. However, the glass transition temperatures were below 10°C, which was attributed to the flexible SBO structure and the flexible thioether bonds formed upon UV-curing. Improved coating properties were achieved by the addition of petroleum-based enes and thiols and hyperbranched acrylates (HBA). The HBA-toughened coatings exhibited higher cross-link densitiy, T_g, tensile modulus, and thermal stability.

In addition to the UV-initiated thiol-ene polymerization, thermally-initiated thiol-ene reactions have been used to prepare coatings with a bio-based sucrose soya ester (SSE). Webster and coworkers produced thiourethane thermoset coatings via the thermal thiol-ene coupling of SSE with multifunctional thiols, followed by a reaction with polyisocyanate trimer resins.[96] The thermal thiol-ene reaction resulted in the complete consumption of the double bonds in SSE, while the formed high-molecular-weight oligomers maintained low viscosity afforded by the branched structures. The thiourethane coatings exhibited good adhesion to aluminum substrates and high gloss. The flexible fatty acid chains contributed to low modulus, tensile strength, and chemical resistance. Substitution of the hexamethylene-diisocyanate (HDI) with a more rigid isophorone diisocyanate (IPDI) resulted in coatings with a higher T_g, hardness and impact resistance.

3.5.2 Thiol-ene coatings containing keratin as a reinforcing agent

Bio-based building blocks with thiol functional groups have also been utilized for coating preparation. For example, keratin is a widely occurring natural polymer, found in hair and nails. It contains a high content of sulfur within the cysteine and methionine amino acids.[97] Keratin has a three-dimensional fibrous structure that imparts high durability, chemical resistance, and stability.[97]

Keratin was employed as a natural reinforcing agent for photocured thiol-ene coatings, resulting in improvement of thermal stability, cross-linking density, T_g values and mechanical properties.[98] Addition of keratin up to a content of 15 w/w% did not change the thiol-ene UV-curing process significantly, as evidenced by nearly complete conversion of the double bonds and thiols, as well as a high gel content (>91%). The reinforcement effect of keratin was manifested in an increase in the polymer cross-link density and the storage modulus (E') in the rubbery region, as

determined by DMTA. Keratin is likely to be covalently linked to the thiol-ene polymer matrix via the thiol-containing cysteine residues, resulting in a mechanically robust three-dimensional network.

3.5.3 Thiol-ene coatings containing terpenes

Thiol–ene addition has been used for the modification of the bio-based terpenes in order to introduce alcohol and ester functional groups for the preparation of polyesters,[99] or amine groups for the synthesis of polyamides and polyurethanes.[100] In addition, the carbon-carbon double bonds in terpenes have been exploited for thiol-ene polymerization.

For example, a widely occurring bio-based monoterpene *D*-limonene (Figure 3.7, **1**) was used to prepare thermoset coatings by the free-radical thiol–ene polymerization.[101] The cycloaliphatic structure of limonene contributes to a higher glass-transition temperature and stiffness of the thiol–ene networks. *D*-Limonene contains two distinct double bonds, such that the thiol–ene reaction at the exo-olefinic bond is about 6.5 times faster than at the endocyclic double bond. The thiol-ene coupling at the isobutylene functionality could be promoted by increasing the ratio of monoterpene to thiol. The different ene reactivity was employed in the synthesis of multifunctional limonene-terminated precursors using polyfunctional mercaptan ester propionates (Figure 3., **4, 5**).

Subsequently, the limonene-terminated precursors with residual double bonds were used as alkene macromonomers in combination with multifunctional thiols to prepare thermoset coatings. The alicyclic ring of limonene enhanced the rigidity and T_g of the thiol-ene networks compared to allyl ether based thiol–ene systems.
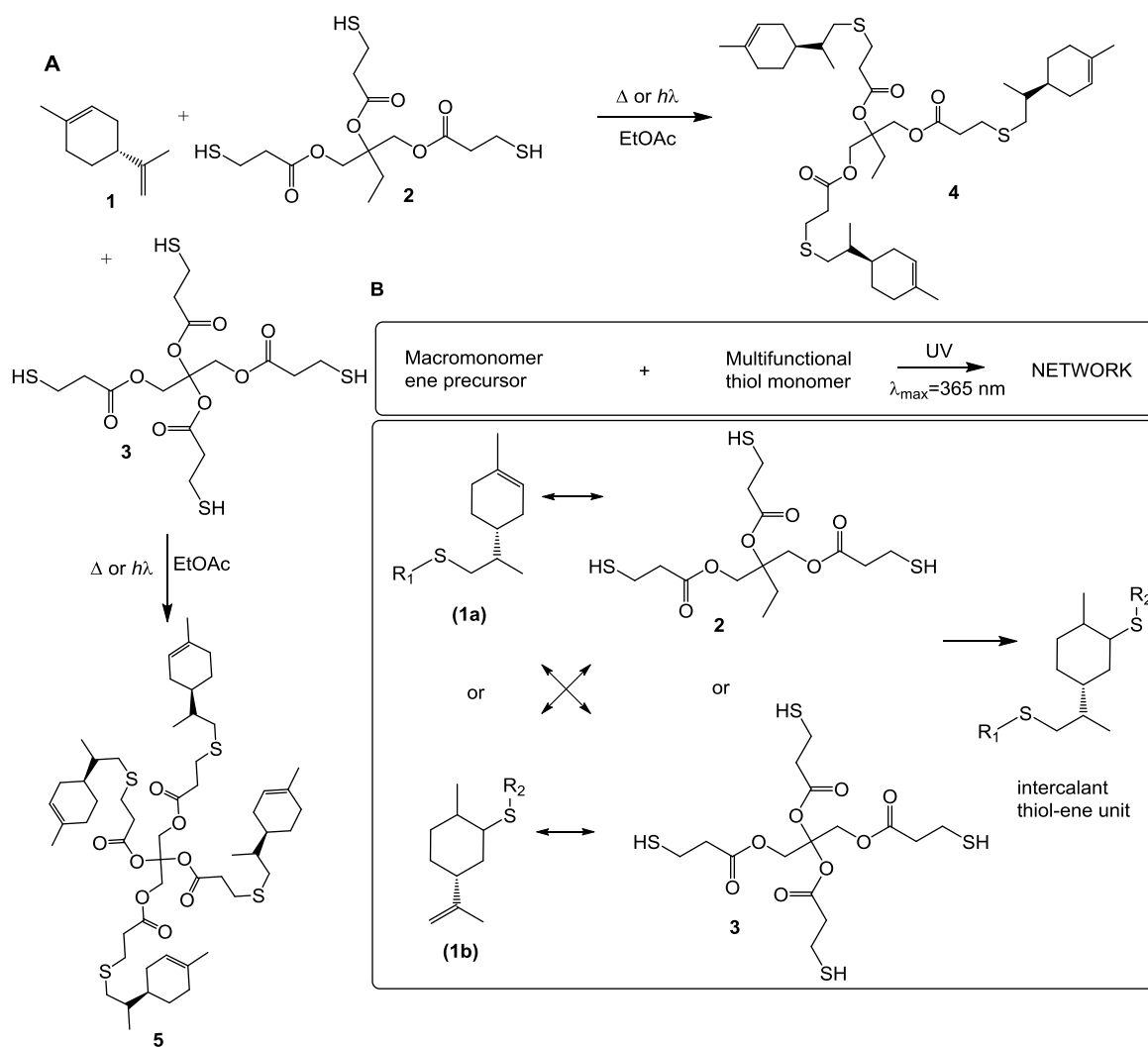
*Figure 3.7: Synthesis of limonene-terminated precursors **4** and **5** induced either in a thermal or photochemical way (a) and network formation based on equimolar amounts of multifunctional groups (b). [101]*

Thiol-ene chemistry has also been used for the post-modification of bio-based poly(limonene carbonate)s in order to introduce different quantities of hydroxyl groups with varying molecular weights for subsequent curing with polyisocyanates.[102] The quantity of hydroxyl groups could be used to tune the cross-link densities and thermal properties of the resulting thermosets, which also manifested good acetone resistance and high hardness. Multifunctional thiol-ene coatings containing a combination of the two bio-based terpenes, linalool and eugenol were demonstrated to have both antibacterial and antioxidant properties derived from the terpenes.[103] Thiol-ene

photopolymerization enabled fast curing at room temperature without inhibiting the activity of the terpenes.

3.5.4 Hybrid bio-based thiol-ene coatings

A variety of hybrid thiol-ene coatings have been formulated using both bio-based and synthetic components in order to achieve the desired coating properties. For example, hybrid coatings containing both bio-based castor oil and siloxanes were prepared by thiol-ene chemistry.[104] Castor oil was modified with 3-mercaptopropyl trimethoxysilane via thiol-ene reaction, which was a more efficient one-step process compared to previous strategies.[104] The hydroxyl groups in the silanized castor oil were subsequently reacted with isophorone-diisocyanate followed by hydrolysis and self-condensation of methoxysilane groups, resulting in polyurethane/siloxane coatings. The introduction of inorganic components into the polymer network with castor oil increased the cross-link density, gel content, T_g, hardness, thermal stability and water resistance of the coatings. The improved properties of the polyurethane/siloxane hybrid coatings were attributed to the covalent bonds between the organic and inorganic constituents and the homogeneous distribution of the silica throughout the polymer matrix.

3.6 Conclusion

Thiol-ene polymerization is a versatile methodology for the development of coatings with the advantages of the formation of uniform polymer networks, delayed gelation, reduced shrinkage stress, and insensitivity to oxygen. The radical step-growth addition of thiol and ene components has been used to generate polymer coatings with a range of properties, depending on the functionality and rigidity of the building blocks. Different functionalized and hybrid coatings have been developed using thiol-ene coupling due to its high efficiency and mild conditions that are suitable for a wide range of coating ingredients and substrates. Thiol-ene chemistry is also amenable to a wide variety of bio-based building blocks, including fatty acids, terpenes, and lignin derivatives. Overall,

thiol-ene polymerization is both an effective and sustainable technique that is a powerful enabler for the advancement of coatings technology.

3.7 References

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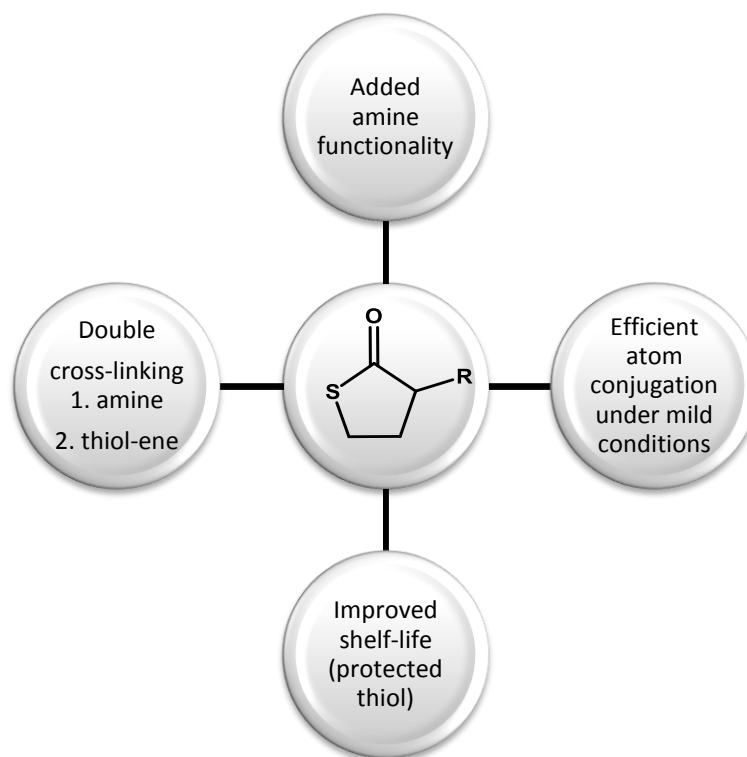
Abstract

A set of multifunctional UV-cured thiol-ene polymer resins were systematically prepared from thiolactone containing monomers and different amine compounds. Aminolysis of the thiolactone moiety enabled the introduction of different side chains and cross-linkers into the polymers. The glass transition temperature of the polymers varied between 22 and 90°C, depending on the type and molar ratio of amine-containing compounds relative to the monomer. Thiolactone-derived polymer films exhibited high transparency of 90%, pencil hardness in the range of 3B-HB, high impact resistance (>2 kg·m), and good adhesion to steel in dry conditions.

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Chapter 4. UV-cured multifunctional coating resins prepared from renewable thiolactone derivatives

4.1 Introduction

Cross-linked polymer systems obtained by thiol-ene chemistry combine the advantages of the formation of uniform polymer networks, rapid cross-linking, delayed gelation, reduced shrinkage and insensitivity to oxygen, in comparison to network formation by means of acrylates.[1] As highlighted in the previous chapter, thiol-ene chemistry has been used to prepare UV-curable polyurethane coatings,[2] antifouling hydrogel coatings,[3] pigmented coatings,[4] hybrid organic/inorganic nanostructured coatings,[5] flame retardant photocured coatings,[6] and functionalized trialkoxysilane coatings.[7] Moreover, thiol-ene polymerization is an effective approach for the incorporation of bio-based feedstock, such as vegetable oil.[8-10] In the presence of radical initiator the double bonds of unsaturated fatty acids are reactive towards thiols, which can be selected from a variety of multifunctional thiolated compounds, such as glyceryl dimercaptoacetate and pentaerythritol tetrakis(3-mercaptopropionate).[8]

However, applications of thiol-ene polymers in the coatings industry have been hindered by the strong odor and the limited shelf life of the free thiols. [11, 12] A strategy to overcome the disadvantages of free thiols in thiol-ene polymer preparation is to use thiolactone chemistry.[13] DL-homocysteine thiolactone hydrochloride is a heterocyclic thioester with a protected thiol, which has improved storage stability and no offensive odor. The protected thiol can be released by nucleophilic attack of a primary amine for subsequent reaction with an alkene. Both aminolysis and thiol-ene reactions proceed efficiently at room temperature and in the presence of oxygen.

In addition to the enhanced storage stability and reduced odor of thiolactone building blocks, thiolactone chemistry opens sustainable routes for the preparation of polymers with different backbones. For example, polyamides have been prepared from homocysteine DL-homocysteine thiolactone hydrochloride and renewable 10-undecenoic acid, which is derived from castor oil.[14]

45

Isocyanate-free polyurethanes have been synthesized via a scalable and high-yielding method from DL-homocysteine thiolactone hydrochloride and allyl chloroformate.[13]

Moreover, isocyanate-free formulations allow for the introduction of different functional groups in an orthogonal reaction sequence via amine-thiol-ene conjugation. Otherwise, isocyanates could react with amines/alcohols/thiols, which would make it difficult to prepare polymers with controlled functionality and structure. Isocyanate-free polyurethanes are especially important for coating applications, where emissions of volatile organic compounds pose a significant concern. The preparation of thiolactone-based polyurethanes does not require handling of isocyanates, which is advantageous from health and safety perspective. In addition, the shelf-life of coating formulations is not limited by the stability of isocyanates.

Renewable building blocks can be incorporated into polymer backbones via the synthesis of thiolactone-based monomers, as well as via subsequent aminolysis reaction with the thiolactone ring. Thiolactone chemistry opens opportunities to incorporate bio-based compounds, such as tyramine and dopamine. Sparks *et al.* observed that addition of dopamine to polymer coatings increases the glass transition temperature and improves adhesion to glass, aluminum, steel, and marble.[15]

Therefore, introduction of different functionalities into polymer coatings is essential for future development of biobased materials and advanced coatings with tailored properties. Furthermore, efficient, upscalable, and environmentally benign processes for the preparation of coating resins are important for addressing the multiple requirements of the coating industry.

Thiolactone chemistry has been demonstrated as an effective strategy for the preparation of isocyanate-free polyurethanes,[16] diversely substituted polyamides,[14] hyperbranched polymers,[17] functionalized cyclic polymers,[18] glycopolymer nanoparticles,[19] cross-linked chitosan polymers,[20] and formaldehyde scavenging coatings, which are discussed in Chapter 5.[21] Although functionalized polymers and coatings have been previously prepared using thiolactone chemistry, a systematic investigation of the effect of different functionalities on the coating properties is necessary, especially for coating applications that typically involve multiple performance requirements. In addition, the use of multifunctional amine compounds for amine-thiol-ene conjugation results in cross-linked polymers with new properties, which have not been

investigated yet. The functionality of building blocks as well as the molar ratios of the reactive groups in thiol-ene formulations affect the cross-link density and material properties.[11]

The initial hypothesis of this work is that the functionality of amine compounds and their molar ratios relative to the thiolactone monomers will also affect polymer structure and properties. The ability to vary polymer cross-link density as well as introduce different functional groups is particularly useful for the development of multifunctional coatings, where good mechanical and barrier properties are necessary in combination with specific surface and molecular characteristics tailored to the application.

In this work, cross-linked polymer networks are prepared using thiolactone chemistry and their coating properties are investigated (Figure 4.1). A systematic screening of different bio-based thiolactone building blocks with a variety of amine compounds has been conducted. The coating performance of the resulting polymer films was evaluated according to the standard test methods from the American Society for Testing and Materials (ASTM).

The general approach for the development of thiolactone-based coatings is illustrated in Figure 4.1, while the details are discussed further in this chapter. First, different thiolactone derivatives were combined with amine-containing compounds to obtain pre-polymers with thiol and ene functional groups for subsequent UV-initiated thiol-ene polymerization. In order to obtain homogeneous polymer films, an appropriate solvent mixture was selected based on the solubility parameters, solvent evaporation rates, and surface tension. The thiol-ene photopolymerization conditions were optimized in order to obtain high conversion of thiol and ene functional groups in the polymer. Finally, the coating properties of the polymer films with different functional groups were evaluated in order to determine the basic characteristics of thiolactone-based polymer resins.
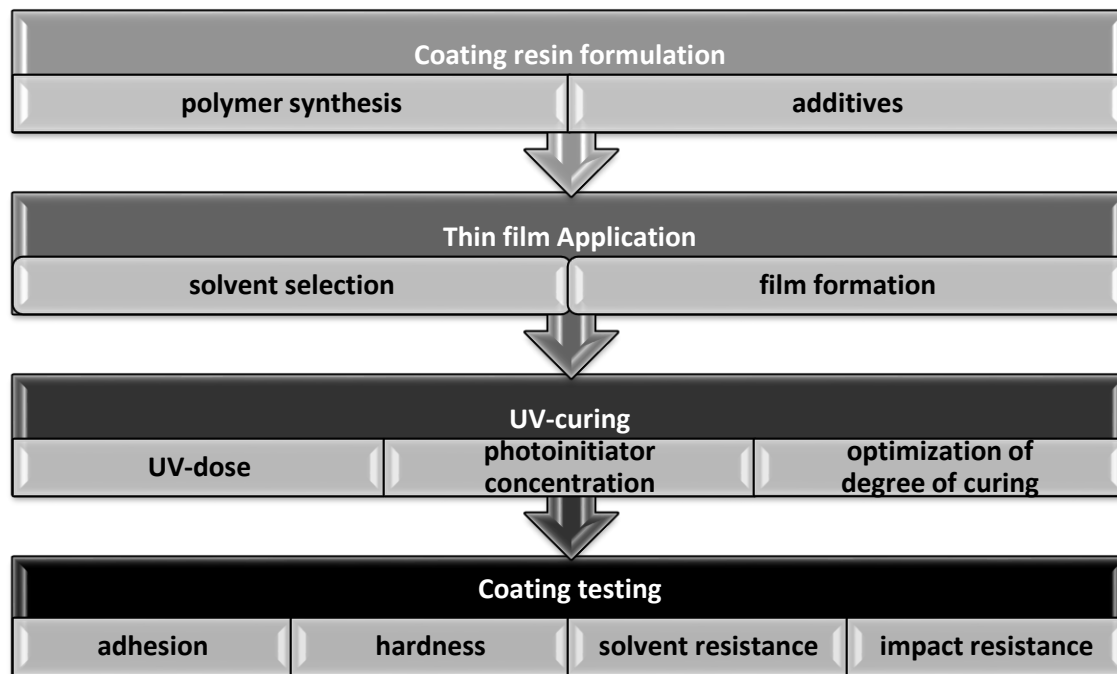
Figure 4.1. Schematic representation of the work process of preparing new coating resins.

4.2 Preparation of polymer films using thiolactone chemistry

First, two AB' monomers with both a double bond (A) and a thiolactone (B') unit were prepared (Scheme 4.1) based on the methodology developed in previous work.[11,12] Briefly, *N*-(allyloxy)carbonylhomocysteine thiolactone, referred to as Alloc-TL, was synthesized from *DL*-homocysteine thiolactone and allyl chloroformate, as previously reported.[11] Alloc-TL enables the preparation of isocyanate-free polyurethanes with additional functional groups that can be introduced via the ring opening of thiolactone moiety by amine-containing compounds. On the other hand, 10-undecenoylthiolactonamide (Undec-TL), was synthesized from *DL*-homocysteine thiolactone and 10-undecenoic acid, as previously described in Chapter 3.[12]

The coating properties are expected to vary with the choice of monomer, as well as, with the choice of the amine compound. The Alloc-TL monomer with a urethane moiety is expected produce polymers with higher rigidity due to hydrogen bonding between the urethane groups. On

the other hand, the Undec-TL monomer is expected to produce more flexible and less polar polymers ascribed to the presence of the long aliphatic chain.
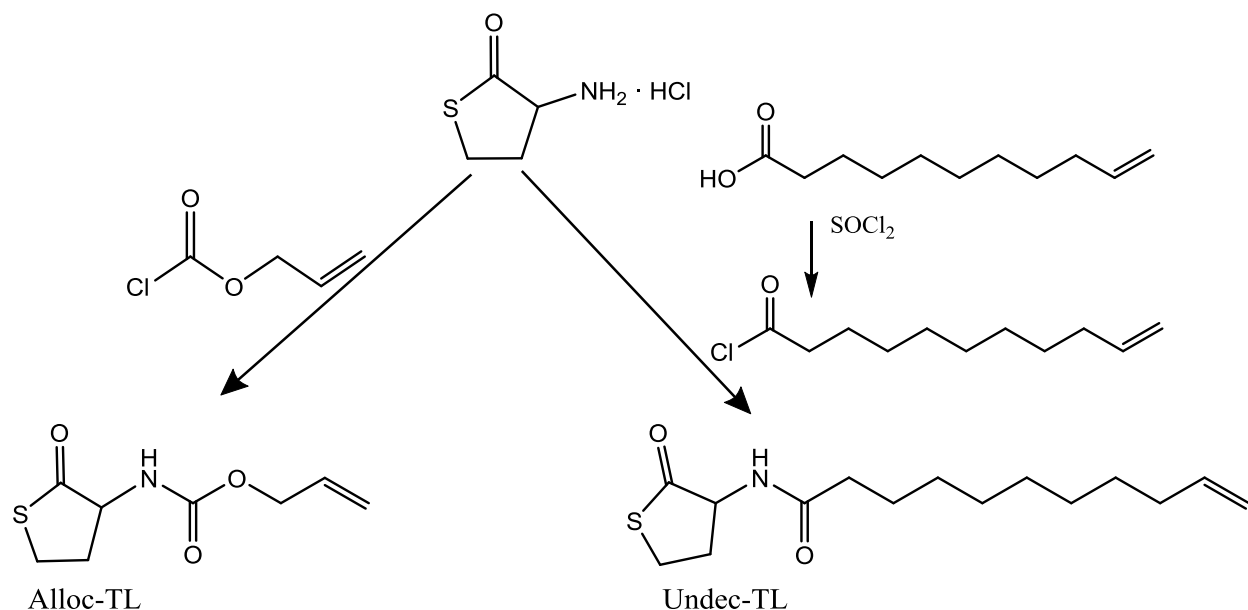
Scheme 4.1. Synthesis of N-(allyloxy)carbonyl homocysteine thiolactone (Alloc-TL) monomer from DL-homocysteine thiolactone hydrochloride and allyl chloroformate (left) and synthesis of 10-undecenoylthiolactonamide (Undec-TL) monomer from DL-homocysteine thiolactone hydrochloride and 10-undecenoic acid (right).

After the synthesis of the two thiolactone-containing monomers, multifunctional polymer coatings were prepared via a two-step amine-thiol-ene conjugation. In the first step, an amine compound was added to a thiolactone-containing monomer in solution, resulting in thiolactone ring-opening and amide formation, which simultaneously released a free thiol group (Scheme 4.2). The resulting formulation was applied on substrates and the solvent was evaporated. The second reaction step was initiated by UVA irradiation in the presence of a radical photoinitiator, which triggered the reaction between free thiol groups and the double bonds in the monomer, resulting in step-growth polymerization.
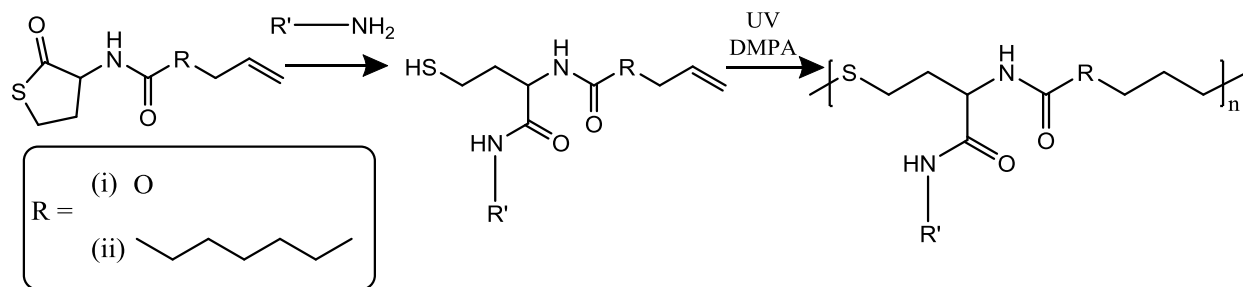
Scheme 4.2. Preparation of polymers from a thiolactone-containing monomer by aminolysis and ring-opening of the thiolactone moiety, followed by thiol-ene reaction in the presence of DMPA photoinitiator and UV irradiation.

The preparation of homogeneous thin films without any visible defects required systematic optimization of the solvent mixture used for film application. Indeed, solvents play several key roles in solvent-borne coatings by affecting the viscosity of the formulation, the rate of drying, and film leveling. As a result, both the coating-substrate and the coating-air interface can be affected by the choice of solvent. Inappropriate choice of solvent can lead to poor wetting of the formulation on the substrate and film defects, such as pinholes, bubbles or craters.

Film defects were observed for thiolactone-based coatings applied with only ethyl acetate solvent. Originally, ethyl acetate was chosen as a solvent for thiolactone-based formulations since it is a good solvent for the Alloc-TL monomer, does not react with formulation components and has low toxicity. However, polymer films prepared using ethyl acetate exhibited pinholes throughout the film, which was attributed to the high relative evaporation rate of ethyl acetate (Table 4.1). Subsequently the solubility parameters were determined for the coating components and common solvents in order to select appropriate solvents for the different formulations in this study. High solubility of coating components in a solvent is necessary to minimize the use of solvents in formulations, since solvents need to be evaporated from the substrates and cannot be reused or disposed of as chemical waste. Solvents with similar solubility parameters as the coating components can be used to prepare coating formulations with high solid contents (>30%w/w). Hansen solubility parameters for the coating components were calculated according to the Van Krevelen group contribution method based on solubility parameters of chemical groups (Figure 4.2).[23] The hydrogen bonding parameter and polar parameter for different amine compounds and thiolactone-containing monomers are plotted for relative comparison (Figure 4.8). The choice of amine-containing compounds covers a broad range of hydrogen bonding

parameters (7.2-13.9 $J^{1/2}/cm^{3/2}$) and polar parameters (2.9-7.2 $J^{1/2}/cm^{3/2}$), which is useful for controlling the intermolecular interactions between polymer functional groups and the associated coating properties. For example, a high extent of hydrogen bonding is expected to produce more rigid polymers with a higher glass transition temperature, while an abundance of polar functional groups is expected to increase the surface energy and hydrophilicity of the coatings. The choice of the thiolactone-containing monomer also influences the polymer intermolecular interactions, since Undec-TL monomer exhibits lower polar and hydrogen bonding parameters than Alloc-TL.
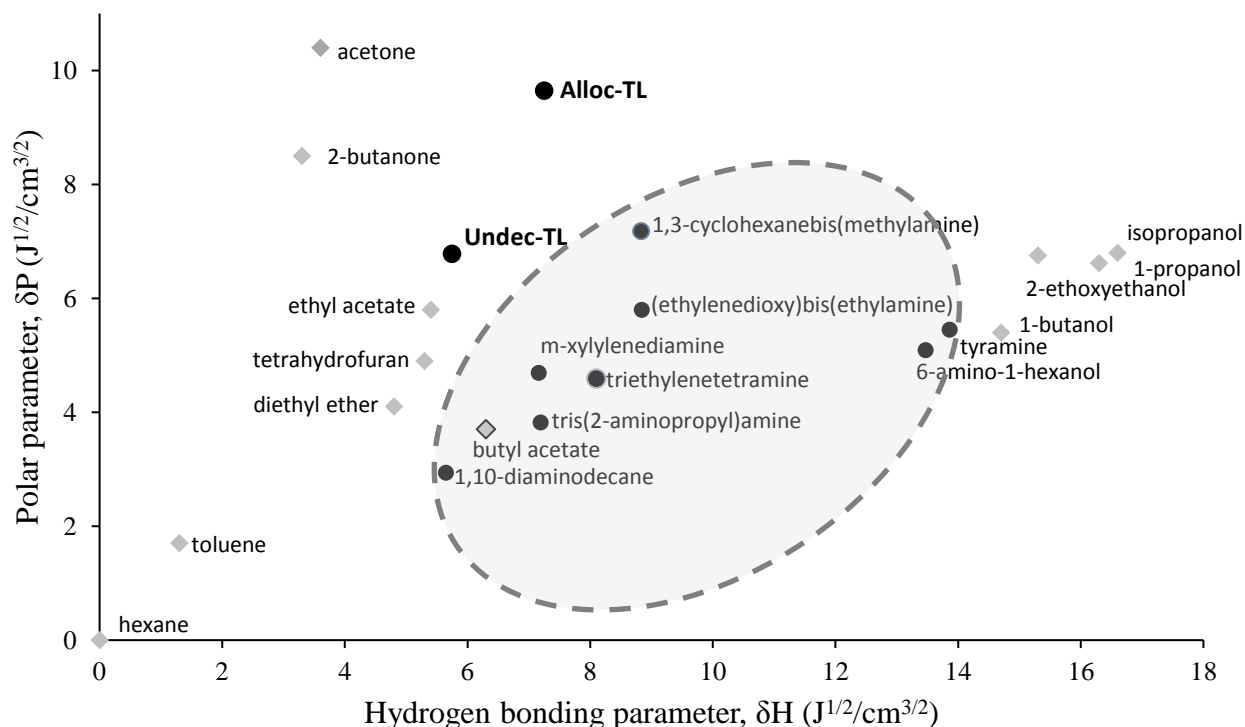
Figure 4.2. Hansen solubility parameters associated with hydrogen bonding and polar intermolecular interactions calculated for coating components by the Van Krevelen group contribution method. The range of solubility parameters covered by the different amine components is indicated by a dashed line.

Another solvent with a lower relative evaporation rate was used, namely 1-propanol. The resulting films exhibited significantly fewer pinholes, but there were still some pinholes throughout the film. Subsequently, different solvent mixtures were tested in order to generate homogeneous films without visible defects. However, trial and error testing of different organic solvents is very laborious and inefficient. Therefore, the key solvent properties were compiled from literature for different solvents (Table 4.1) and their effect on the quality of the resulting

polymer films were assessed. The main solvent properties that were found to affect film quality were the evaporation rate and surface tension.

Table 4.1. Properties of solvents obtained from literature and used for coating optimization.[22]

Solvent	Hansen solubility parameters $(J/cm^3)^{1/2}$			Relative evaporation rate (butyl acetate = 1 at 25°C)	Viscosity (mPa·s) (20°C)	Surface tension (dyne/cm) (25°C)
	dd (dispersion)	dp (dipolar)	dh (hydrogen bonding)			
Ethyl acetate	7.4	2.6	4.5	4.0	0.4	23.9
Butyl acetate	7.7	1.8	3.1	1.0	0.7	24.8
Acetone	7.6	5.1	3.4	6.1	0.31	22.9
1-Propanol	7.8	3.3	8.5	1.3	2.3	23.5
Isopropanol	7.7	3.0	8.8	2.9	2.4	21.0
1-Butanol	7.8	2.8	7.7	0.4	2.9	24.2
Tert-butanol	-	-	-	1.1	3.3 (30°C)	20.7

Table 4.2. Calculated average evaporation rate and surface tension for optimum solvent combination for thiolactone-based films containing Alloc-TL and different amine compounds: 2,2'-(ethylenedioxy)bis(ethylamine), tris(3-aminopropyl)amine, triethylenetetramine.

Solvent	Relative evaporation rate (butyl acetate = 1 at 25°C)	Surface tension (dyne/cm)	% solvent in mixture	Relative evaporation rate (butyl acetate = 1 at 25°C)	Surface tension (dyne/cm) (25°C)
1-Propanol	1.3	23.8	40	0.5	9.5
Isopropanol	2.9	21.4	30	0.9	6.4
Tert-Butanol	1.0	20.7	30	0.3	6.2
			target	1.7	22.1

The optimum solvent mixture for most of the coating formulations was 1-propanol/isopropanol/tert-butanol (40/30/30) (Table 4.2). The properties of this solvent mixture

were calculated based on the literature data values for pure solvents (Table 4.1) and the proportion of each solvent, yielding the approximate target evaporation rate, E.R.=1.7 (relative to butyl acetate E.R.=1.0) and surface tension 22.1 dyne/cm.
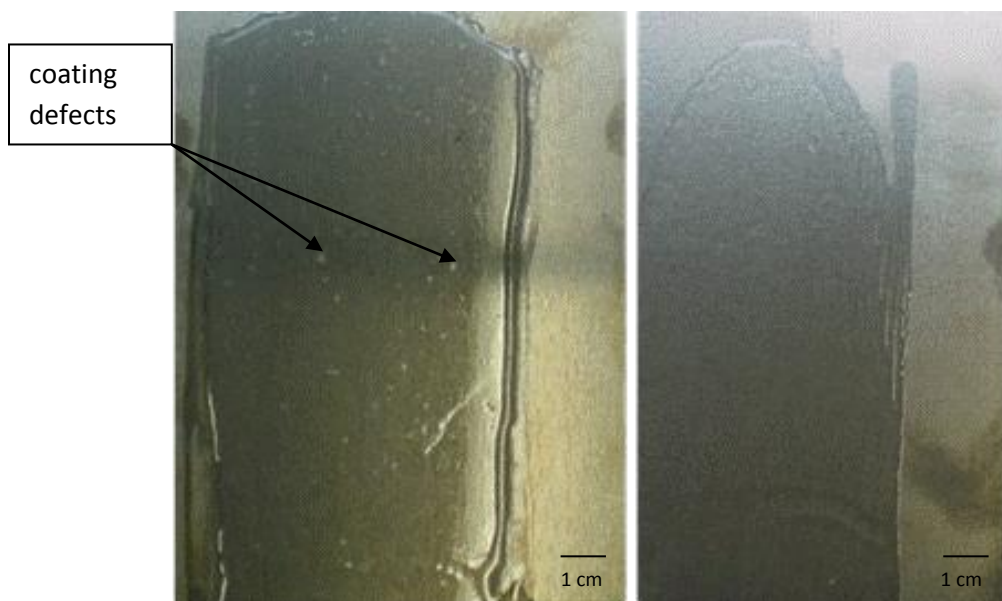
Figure 4.3. Thiolactone-based films prepared from Alloc-TL and triethylenetetramine applied on stainless steel panels with different solvent mixtures: 1-propanol (left), 1-propanol/isopropanol/tert-butanol (40/30/30) (right).
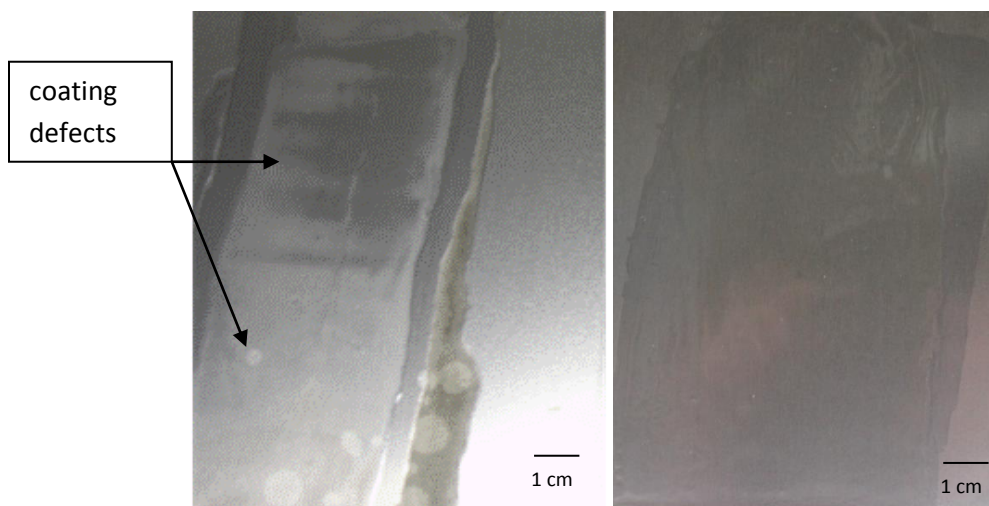

Figure 4.4. Coatings prepared using Alloc-TL:1,10-diaminodecane (1.5:1) with different solvent mixtures: 1-propanol/isopropanol/tert-butanol (40/30/30) (left), 60 w/w% acetone/butyl acetate (20/80) (right).

Tert-butanol was a key component in the solvent mixture because it reduced the overall surface tension of the formulation and enabled good wetting of the substrate. Otherwise, the presence of a high quantity of amine groups in the formulation inhibited good wetting of the substrate. The optimum solvent mixture also resulted in a slow evaporation rate compared to ethyl acetate. The slow evaporation rate contributed to better film formation and lack of observable surface defects (Figure 4.3).

However, not all formulations could be prepared using this mixture, as observed by the hazy and uneven film containing Alloc-TL and 1,10-diaminodecane (Figure 4.4, left). Therefore, an alternative solvent mixture was used, namely acetone/butyl acetate (20/80) (Figure 4.4, right). Butyl acetate has a low evaporation rate desirable for film formation, however it was too apolar to dissolve the coating components so that acetone, a more polar solvent was required. In addition, acetone has a lower surface tension than butyl acetate and thereby it reduces the overall surface tension of the solvent mixture. The calculated surface tension of the acetone/butyl acetate (20/80) solvent mixture is 24.4 dynes/cm and the calculated evaporation rate is 2.0, relative to the evaporation rate of pure butyl acetate at 25 °C. This solvent mixture is more suitable for coating formulations with less polar functional groups, such as 1,10-diaminodecane because butyl acetate has a lower polarity. The higher surface tension of the solvent mixture with butyl acetate is less problematic for formulations with lower polarity, since they also have a lower surface tension than highly polar components.

The acetone/butyl acetate solvent mixture does not contain any hydroxyl groups, which could be advantageous for certain coating formulations where a side-reaction with hydroxyls is possible. In addition, hydrogen bonding interactions between polymer and solvent can result in a significant amount of residual solvent left in the film. Thus, compared to the original ethyl acetate solvent, both the evaporation rate and surface tension of the coating formulation had to be reduced in order to obtain homogeneous films as illustrated by the differences in the solvent evaporation rate and surface tension in Figure 4.5.
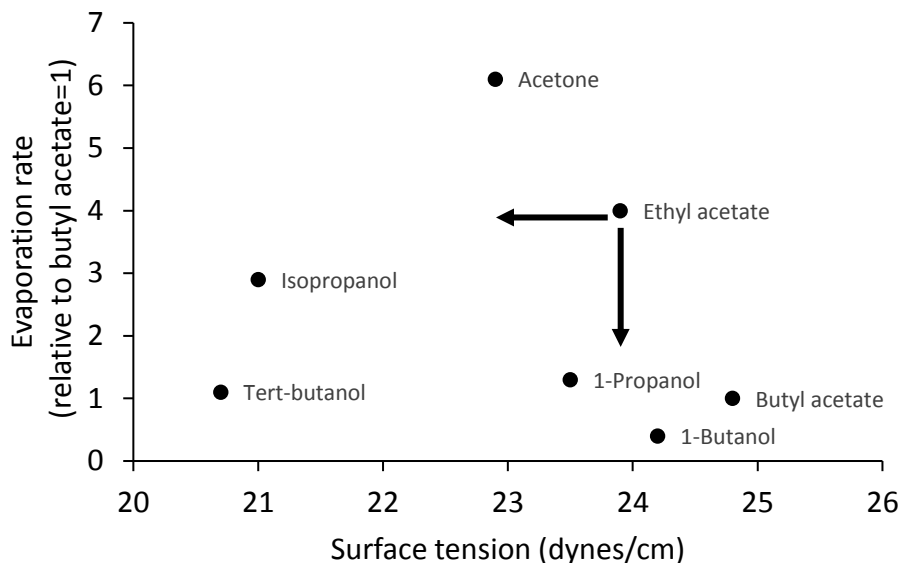
Figure 4.5. Evaporation rate and surface tension of different solvents in comparison with ethyl acetate.

Systematic investigation of the relevant solvent properties enabled more efficient optimization of the coating quality, even in the face of the challenge of a broad selection of different amine compounds used in the formulations.

Following the application of coating formulations with appropriate solvents and drying, the next stage involved the optimization of the conditions for UV-curing by varying the UV dose and content of photoinitiator. The objective of UV-curing was to obtain homogeneous conversion of functional groups throughout the thickness of the film (Table 4.3).

The conversion of carbon-carbon double bonds in the polymer was calculated based on the infrared absorption band at 1004-983 cm^{-1}. Another absorption band at 1776-1610 cm^{-1} was used as a reference because it corresponded to the carbonyl absorption, which was unaffected by the UV-curing (Table 4.3). The conversion of double bonds was determined on both the top and the bottom of each coating in order to confirm whether the curing of the film was homogeneous throughout the coating thickness. Polymer films with an average thickness of 30 µM were used for the optimization of UV-curing and a small section of the film was detached from the steel substrate in order to collect FTIR spectra from the top and the bottom of each film. The polymer

T_g was also determined in order to verify whether the highest photopolymerization conversion corresponded with the highest T_g.

Table 4.3. Optimization of UV-curing of polymer films prepared from Alloc-TL: 2,2'-(ethylenedioxy)bis(ethylamine) (1.5:1) with different quantities of DMPA photoinitiator and UV doses. FTIR absorption bands used to calculate conversion of double bonds on the top and bottom of each film are denoted A1, A2. SD – Standard deviation.

DMPA (w/w%)	UV Dose (mJ/cm^2)	A1=1776-1610 cm^{-1} (reference)	A2=1004-983 cm^{-1} (C=C)	A2/A1	C=C Conversion top of film	C=C Conversion bottom of film	C=C Conversion Average	C=C Conversion difference top vs. bottom of film	Tg (°C)
0.1	0.2	110	0.37	0.003	86	79	83	7	40
0.1	0.6	110	0.19	0.002	93	95	94	2	46
0.1	1.2	110	0.12	0.001	95	97	96	2	50
0.5	0.2	112	0.65	0.006	76	77	77	1	36
0.5	0.6	110	0.24	0.002	91	96	94	5	47
0.5	1.2	112	0.19	0.002	93	98	96	5	52
1	0.2	110	0.30	0.003	89	90	90	1	50
1	0.6	110	0.28	0.003	89	97	93	8	57
1	1.2	110	0.17	0.002	93	99	96	7	59
3	0.2	111	0.41	0.004	84	85	85	1	43
3	0.6	110	0.12	0.001	95	99	97	5	53
3	1.2	112	0.20	0.002	92	99	96	8	58
					SD=2	SD=1	SD=2	SD=2	SD=5

In general, higher DMPA concentration and higher UV doses are expected to yield higher conversions of carbon-carbon double bonds via thiol-ene photopolymerization. However, the results in Table 4.3 indicate that the difference between the degree of curing between the top and the bottom of the film becomes greater when higher DMPA concentrations or higher UV doses are employed. Differences in the degree of curing throughout the polymer film could be detrimental to the coating properties. For example, the penetration of UV irradiation may be inhibited in thicker films, which may result in higher degree of curing on the film surface, but lower degree of curing near the substrate, which would result in inferior coating properties, such as adhesion.

Figure 4.6 illustrates the dependence of the % conversion during photopolymerization of coating formulations with varying contents of photoinitiator, DMPA and varying UV doses. The results of the UV-curing optimization revealed that a high UV-dose (>0.6 J/cm^2) is necessary to obtain a high conversion ($>90\%$) of double bonds in the polymer film (Figure 4.6, left). On the other hand, the plot of the variation between the degree of conversion on the top and the bottom of the film revealed that low DMPA concentration (<0.5 w/w%) is necessary to minimize the difference between conversion on the top and bottom of film in order to achieve both high and uniform degree of curing (Figure 4.6, right).
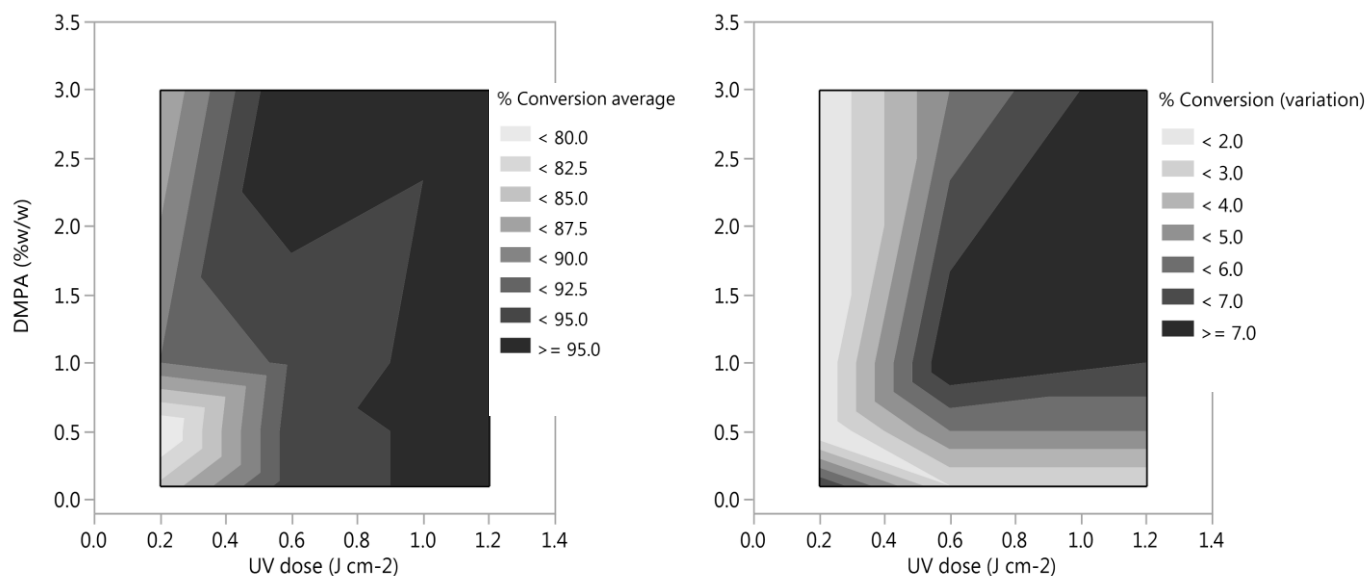
Figure 4.6. Plot of % conversion of double bonds as a function of DMPA photoinitiator quantity and UV dose used for the curing of thiolactone-based coatings (left); plot of the absolute difference in the conversion of double bonds on the top and the bottom of the coating (right).

In the initial stages of the investigation, it was unexpected that the conversion of double bonds on the top of the film was lower than on the bottom since UV irradiation is most intense at the top of the film. Several possible explanations were proposed for the difference in conversion between the top and bottom of the film: (1) radical recombination at high photoinitiator concentration and high UV intensity, (2) evaporation of coating components, such as photoinitiator or solvent from the top of the film, (3) oxygen inhibition, (4) heating of metal substrate increases the temperature of the film at the bottom enabling greater diffusion and faster

reaction rate. Experimental results support explanation (1), since the difference between the curing level at the top and bottom of the film decreases with decreasing photoinitiator concentration under high UV-doses (1.2 mJ/cm^2). A high photoinitiator concentration results in a high radical concentration, which increases the probability of radical recombination. On the other hand, at low UV-doses (0.2 mJ/cm^2) only 1% difference in conversion between the top and the bottom of the film is observed, which indicates that lower radical initiator concentrations also reduce the propensity for radical recombination, as expected. However, low UV-doses were ineffective in achieving a high degree of UV-curing, even at higher concentration of the photoinitiator, for example, 85%+/-1% average conversion of double bonds using 3 w/w% DMPA and 0.2 mJ/cm^2.

The observed FTIR peak wavenumbers and spectral assignments for thiolactone-based monomers and formulations are summarized in Table 4.4.

Table 4.4. FTIR spectral assignment of characteristic absorbance peaks of Alloc-TL and Undec-TL monomers and formulations.

Sample composition	Functional group	Wavenumber (cm^{-1})
Alloc-TL monomer	thioester C=O	1687
	urethane C=O	1705
	urethane C-N	1527
	CH=CH$_2$	995
Alloc-TL:tris(3-aminopropyl)amine (3:1) formulation	amide C=O,C-N	1647, 1525
	SH	2554
	C=C-H	995
	C=C-H	930
Undec-TL monomer	thioester C=O	1690
	amide C=O,C-N	1644, 1533
	CH=CH$_2$	995
Undec-TL:tris(3-aminopropyl)amine (3:1) formulation	SH	2554
	amide C=O,C-N	1630, 1537
	CH=CH$_2$	995
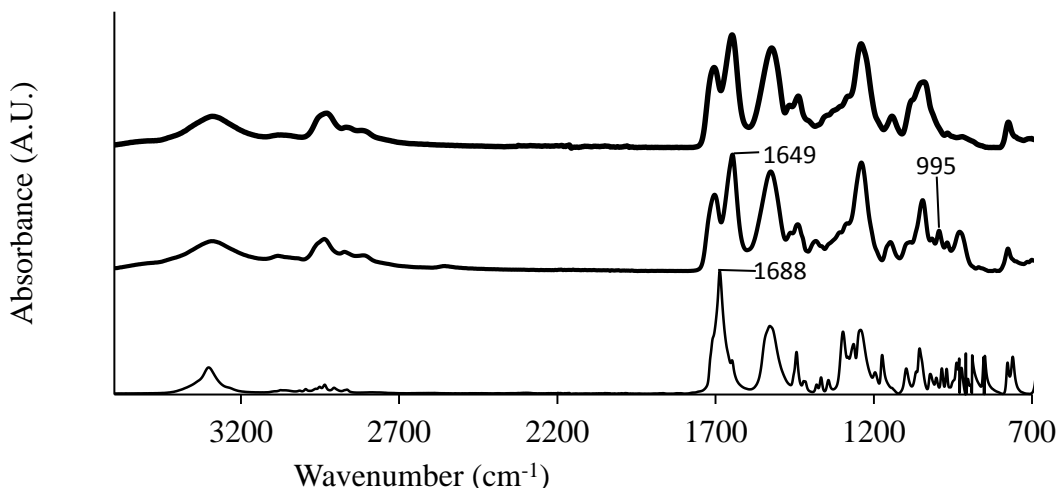
Figure 4.7. FTIR spectra of Alloc-TL monomer (bottom), formulation of Alloc-TL:tris(3-aminopropyl)amine (3:1) (middle), and the resulting UV-cured polymer (top).
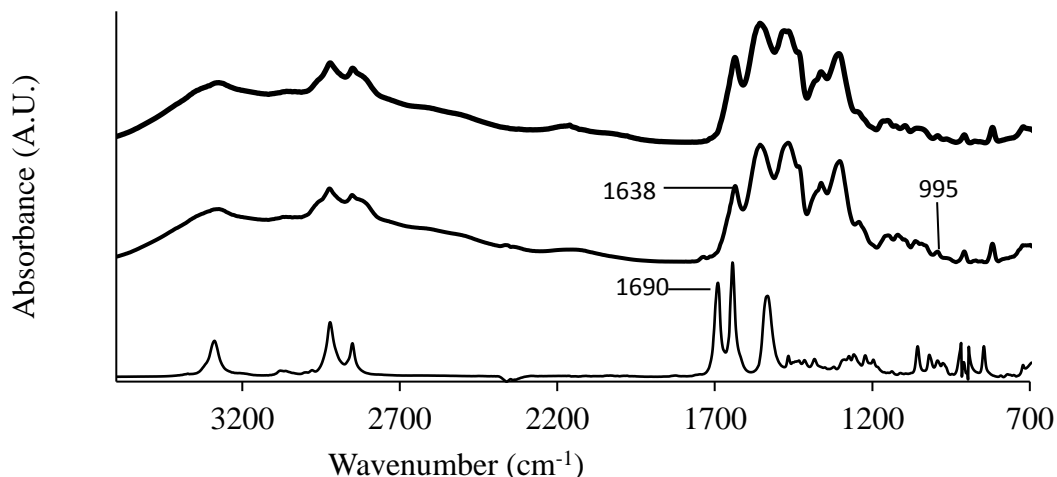
Figure 4.8. FTIR spectra of Undec-TL monomer (bottom), formulation of Undec-TL:tris(3-aminopropyl)amine (3:1) (middle), and the resulting UV-cured polymer (top).

The thioester group of the thiolactone has a characteristic carbonyl stretch vibration with a maximum at 1687-1690 cm^{-1} (Figure 4.7 and 4.8). After the addition of an amine compound to a thiolactone monomer, the thioester carbonyl vibration is replaced with a new carbonyl vibration with a maximum at 1638-1649 cm^{-1}, which corresponds to the amide functionality.

The ring opening of the thiolactone releases a free thiol group, which has an absorbance peak at 2554 cm^{-1}. The double carbon-carbon bond of the thiolactone-containing monomers exhibits an

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absorbance peak at 995 cm^{-1} associated with the C=C bending vibration, which decreases in intensity after UV-initiated polymerization (Figure 4.7).
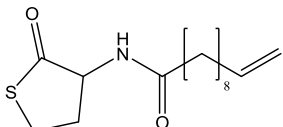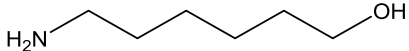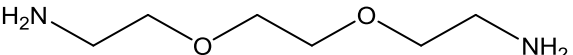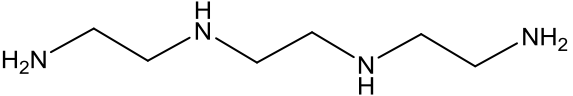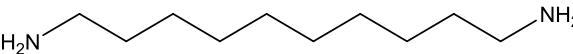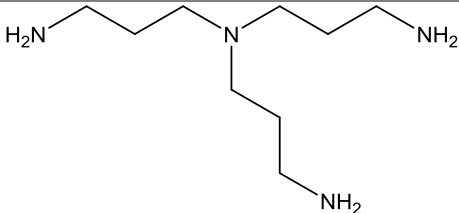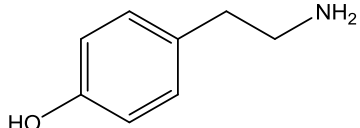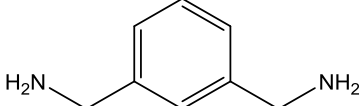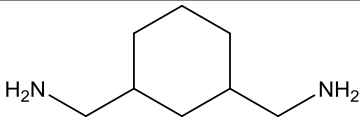
The change in the peak area at 995 cm^{-1} was used to calculate the percentage conversion of double bonds after UV-curing (Table 4.4). The standard deviation for the percentage conversion values calculated from FTIR spectra was 4%.

4.3 Coating formulation

Different primary amine compounds were combined with thiolactone-containing monomers in order to investigate the effect of amine structure and the monomer:amine molar ratio on the coating properties (Table 4.5). Compounds with two and three amine groups were used for cross-linking of the thiolactone-based polymers, which occurs at the monomer:amine molar ratio above 1. The rate of reaction for the aminolysis of thiolactone was lower with amine compounds containing aromatic functional groups, such as m-xylylenediamine and tyramine, which could be ascribed to the electron-withdrawing and steric hindrance effects. Therefore, 4-dimethylaminopyridine catalyst was added to facilitate the ring-opening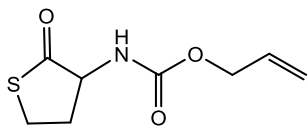 reaction of the thiolactone with aromatic amines, as previously reported.[11] The aminolysis of the Undec-TL monomer in the presence of the 4-dimethylaminopyridine catalyst was conducted in tetrahydrofuran solvent in order to avoid any side-reactions, such as the alcoholysis of the thiolactone in 1-propanol. Following the aminolysis reaction, 1-propanol solvent was added prior to coating application in order to obtain homogeneous polymer films.

For all of the formulations in Table 4.5, the degree of conversion of the thiolactone moiety via aminolysis was on average 96 ± 3% and the degree of conversion of the carbon-carbon double bonds after thiol-ene polymerization was 90 ± 3%. (Table 4.5). The efficiency of the overall amine-thiol-ene conjugation was similar for the different amine structures with the Alloc-TL and Undec-TL. Subsequently, differences in the polymer coating properties can be attributed to the composition of the formulation, rather than differences in the conversion of the reactive groups.

*Table 4.5. Clear coats prepared from Alloc-TL or Undec-TL monomer with different molar ratios of monomer: amine using primary amine compounds: 6-amino-1-hexanol (**1**), 2,2'-(ethylenedioxy)bis(ethylamine) (**2**), triethylenetetramine (**3**), 1,10-diaminodecane (**4**), tris(3-aminopropyl)amine (**5**), tyramine (**6**), m-xylylenediamine (**7**), 1,3-cyclohexanebis(methylamine) (**8**). Conversion of reactive functional groups is indicated in brackets (% conversion of thiolactone after aminolysis, % conversion of double bonds after polymerization).*

#		Alloc-TL	Undec-TL
1	6-amino-1-hexanol	1:1 (99%, 98%)	
2	2,2'-(ethylenedioxy)bis(ethylamine)	1:1 (89%, 86%) 1.5:1 (94%, 93%) 2:1 (89%, 88%)	
3	triethylenetetramine	1:1 (99%, 86%) 1.5:1 (93%, 92%) 2:1 (93%, 93%)	
4	1,10-diaminodecane	1:1 (96%, 84%) 1.5:1 (95%, 91%) 2:1 (99%, 91%)	
5	tris(3-aminopropyl)amine	1:1 (99%, 87%) 2:1 (96%, 86%) 3:1 (90%, 93%)	1:1 (99%, 90%) 2:1 (99%, 87%) 3:1 (99%, 86%)
6	tyramine		1:1 (99%, 90%)
7	m-xylylenediamine		2:1 (98%, 88%)
8	1,3-cyclohexanebis(methylamine)		2:1 (99%, 92%)

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4.4 Coating properties

The coating properties of thiolactone-based films were evaluated to determine the base properties of the polymer and the effect of the different amine functional groups and cross-linkers. Two main descriptor types were used to distinguish between the different polymer compositions. Constitutional descriptors include the amine functional groups in the polymers and their associated polar and hydrogen bonding solubility parameters. Topological descriptors relate to the connectivity of atoms in the polymers, in this case, the molecular weight between cross-links.

The glass transition temperature (T_g) of polymers prepared from Alloc-TL monomer and different amine compounds was determined by DSC (Figure 4.8). The effect of the different amine compounds and the monomer:amine molar ratio on the T_g of the resulting polymer films was assessed for the polymers containing the same Alloc-TL monomer. The comparison of the T_g values for the formulations with different amine compounds was conducted in order to elucidate whether multifunctional amines contributed to a higher polymer cross-link density and thereby a higher T_g. The polymer coatings exhibited a broad range of T_g of 21 °C to 90 °C, which could be controlled by the choice of amine compound and the molar ratio of the thiolactone-containing monomer and amine (Figure 4.8).

The normalized average molecular weight between cross-links (M_c) in each polymer was calculated from the stoichiometry of the formulations. Uncross-linked polymers prepared with monomer:amine molar ratio of 1:1 have a higher M_c (0.82-1.02), while cross-linked polymers prepared with monomer:amine molar ratio above 1 have a lower M_c (0.47-0.75). Amine compounds with higher functionality and lower molecular weight contributed to lower molecular weight between cross-links in a fully cross-linked polymer, which resulted in higher T_g. The monomer:amine ratio and the associated molecular weight between cross-links played the most prominent role in determining the T_g of the polymer films.
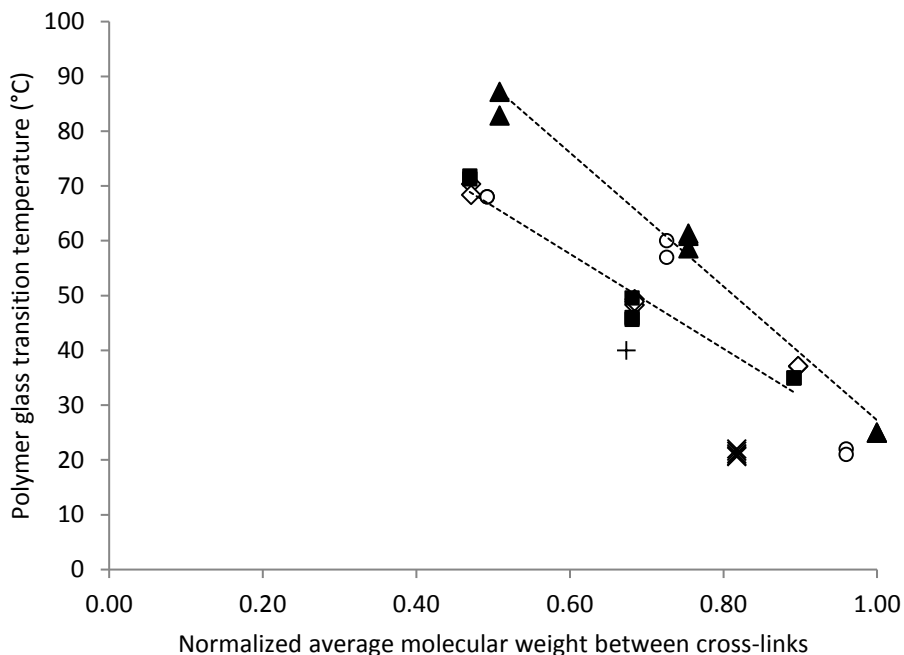
Figure 4.8. Glass transition temperature of polymer films prepared with Alloc-TL monomer and different amine compounds: ◊ (ethylenedioxy)bis(ethylamine), ■ triethylenetetramine, ▲ tris(3-aminopropyl)amine, x 6-amino-1-hexanol, + ethanolamine,o 1,10-diaminodecane.

The amine structure can also contribute to differences in the polymer T_g, as exhibited by the formulation #13 prepared with Undec-TL and m-xylylenediamine with T_g=69°C versus formulation #14 prepared with Undec-TL and 1,3-cyclohexanebis(methylamine), T_g=90°C. Both formulations #13 and #14 were prepared with monomer:amine ratio of 2 and exhibited final double bond conversion of 88% and 92%, respectively (Table 4.7). The increase in the T_g of 21°C observed for the polymer with 1,3-cyclohexanebis(methylamine) could be attributed to the three-dimensional conformation of the cyclohexane ring and the mixture of cis and trans isomers, which contribute to restricted mobility of the polymer segments.

Additional effects of the amine functional groups on the polymer T_g were observed for the uncross-linked polymers. For example, polymers prepared with 1,10-diaminodecane exhibited T_g=21.5°, while polymers prepared with 2,2'-(ethylenedioxy)bis(ethylamine) exhibited T_g=37° (Table 4.8). Greater polar and hydrogen bonding interaction parameters of 2,2'-(ethylenedioxy) bis(ethylamine) compared to 1,10-diaminodecane (Figure 4.2) was predicted from Hansen solubility parameters. Hydrogen bonding contributes to stronger intermolecular interactions of

the polymers prepared with 2,2'-(ethylenedioxy)bis(ethylamine), which is also reflected in a higher T_g. Typical thiol-ene polymers have flexible thioether linkages and relatively low T_g values, which limits their applications in coatings where high hardness is necessary. Therefore, the incorporation of amine cross-linkers via amine-thiol-ene conjugation can be used to increase the T_g and improve the mechanical properties of the thiol-ene polymers.

Thermogravimetric analysis (TGA) of the polymer films prepared in bulk from Alloc-TL and 2,2′-(ethylenedioxy)bis(ethylamine) exhibited 5% mass loss at 275 ±8 °C and the temperature for the maximum rate of mass loss was 380°C (Table 4.6). The same polymer formulations prepared using 1-propanol/isopropanol/tert-butanol (40/30/30) solvent mixture exhibited 5% mass loss at 244 ±34 °C and the temperature for the maximum rate of mass loss was 376° ±1 °C. The lower temperature at 5% mass loss for the polymer films prepared with solvent indicates that residual solvent is likely to be present in the film. Subsequently, all films were dried under vacuum in order to avoid the effect of the residual solvent in the film.

Table 4.6. TGA analysis of polymer films prepared by thiolactone chemistry, temperature at 5% mass loss ($T_{5\%}$), temperature at maximum rate of mass loss (T_{max}). PA/IPA/TBA refers to 1-propanol/isopropanol/tert-butanol (40/30/30) solvent mixture.

#	Sample composition (molar ratio of monomer:amine)	Solvent	$T_{5\%}$ (°C)	T_{max} (°C)
1	Alloc-TL: 2,2′-(ethylenedioxy)bis(ethylamine) (1.5:1)	bulk	271	380
2	Alloc-TL: 2,2′-(ethylenedioxy)bis(ethylamine) (1.5:1)	bulk	284	380
3	Alloc-TL: 2,2′-(ethylenedioxy)bis(ethylamine) (1.5:1)	bulk	269	380
4	Alloc-TL: 2,2′-(ethylenedioxy)bis(ethylamine) (1.5:1)	PA/IPA/TBA	208	375
5	Alloc-TL: 2,2′-ethylenedioxy)bis(ethylamine) (1.5:1)	PA/IPA/TBA	275	376
6	Alloc-TL: 2,2′-ethylenedioxy)bis(ethylamine) (1.5:1)	PA/IPA/TBA	249	377

The properties of the polymer films prepared from thiolactone-containing monomers have been tested per standard ASTM methods for coatings. The testing methodology is described in the materials and methods section of this chapter, which is based on the testing protocols for coatings published by ASTM. The main test results are summarized in Table 4.7 and the full dataset is in Table 4.8 and 4.9. The molar ratio of monomer to amine was varied in the coating

formulations to obtain polymer films with different molecular weight between cross-links and to investigate the resulting coating properties, which will be discussed in the following sections.

Table 4.7. Summary of test results obtained for UV-cured clear coats prepared from thiolactone-containing monomers and different amines with varying molar ratios of monomer to amine.

#	MONOMER	AMINE	MOLAR RATIO	Tg (°C)	IMPACT RESISTANCE (kg·m)	PENCIL HARDNESS	MEK RUBS	ADHESION DRY	ADHESION WET	TRANSPARENCY (%)	HAZE (%) D65/10
1	Alloc-TL	6-amino-1-hexanol	1.0	21	1.2	3B	>200	4	0	90	0.7
2	Alloc-TL	2,2′-(ethylenedioxy)bis(ethylamine)	1.0	37	>2	3B	>200	4	0	90	0.7
3	Alloc-TL	2,2′-(ethylenedioxy)bis(ethylamine)	2.0	72	>2	B	>200	4	0	91	0.6
4	Alloc-TL	1,10-diaminodecane	1.0	22	1	2B	>200	0	0	91	0.7
5	Alloc-TL	1,10-diaminodecane	2.0	68	>2	HB	>200	4	0	90	1.0
6	Alloc-TL	tris(3-aminopropyl)amine	1.0	39	>2	3B	>200	4	0	90	2.5
7	Alloc-TL	tris(3-aminopropyl)amine	2.0	61	>2	B	>200	4	0	91	0.2
8	Alloc-TL	tris(3-aminopropyl)amine	3.0	87	>2	HB	>200	4	0	90	0.6
9	Undec-TL	tris(3-aminopropyl)amine	1.0	36	>2	3B	30	4	0	90	3.1
10	Undec-TL	tris(3-aminopropyl)amine	2.0	68	>2	B	>200	4	0	91	0.3
11	Undec-TL	tris(3-aminopropyl)amine	3.0	76	>2	HB	>200	4	0	91	0.3
12	Undec-TL	tyramine	1.0	42	>2	2B	30	4	4	89	0.9
13	Undec-TL	m-xylylenediamine	2.0	69	>2	HB	>200	4	0	90	1.7
14	Undec-TL	1,3-cyclohexane bis(methylamine)	2.0	90	>2	HB	>200	4	0	90	1.7

Table 4.8. Test results obtained for UV-cured clear coats prepared from Alloc-TL monomer and different amine compounds with different molar ratios of monomer to amine.

#	AMINE	MONOMER: AMINE MOLAR RATIO	THICKNESS top (µM)	THICKNESS middle (µM)	THICKNESS bottom (µM)	% CONVERSION	Tg (°C)	ADHESION DRY	ADHESION WET	MEK RUBS	IMPACT RESISTANCE (kg·m)	PENCIL HARDNESS	TRANSPARENCY (%)	HAZE (%) D65/10
82-1	2.2′-(ethylenedioxy)bis(ethylamine)	1.0	8	8	9	83	37	3	0	>200	>2	3B	91	1.6
82-2	2.2′-(ethylenedioxy)bis(ethylamine)	1.0	84	82	69	89	37	4	0	>200	>2	3B	90	0.7
82-3	2.2′-(ethylenedioxy)bis(ethylamine)	1.5	35	41	42	93	61	4	0	>200	>2	3B	90	0.8
82-4	2.2′-(ethylenedioxy)bis(ethylamine)	1.5	24	30	34	95	62	4	0	>200	>2	3B	90	2.5
80-4.5	2.2′-(ethylenedioxy)bis(ethylamine)	1.5	25	28	28	92	60	4	0	>200	>2	3B	90	1.8
82-6	2.2′-(ethylenedioxy)bis(ethylamine)	2.0	10	9	10	90	70	4	0	>200	>2	B	91	0.3
82-7	2.2′-(ethylenedioxy)bis(ethylamine)	2.0	41	46	40	86	72	4	0	>200	>2	B	91	0.6
83-1	triethylenetetramine	1.0	15	12	8	85	31	4	0	>200	>2	2B	90	0.4
83-2	triethylenetetramine	1.0	43	47	43	86	35	4	0	>200	>2	2B	90	0.4
83-3	triethylenetetramine	1.5	30	38	39	92	46	4	0	>200	>2	B	91	0.2
83-4	triethylenetetramine	1.5	33	31	30	92	46	4	0	>200	>2	B	91	0.2
83-5	triethylenetetramine	1.5	20	19	17	91	50	4	0	>200	>2	B	91	0.2
83-6	triethylenetetramine	2.0	12	7	9	94	71	3	0	>200	>2	HB	91	0.2
83-7	triethylenetetramine	2.0	55	52	50	93	72	4	0	>200	>2	HB	91	0.2
85-1	6-amino-1-hexanol	1.0	n.d.	n.d.	n.d.	97	21	4	0	>200	1.2	3B	90	0.7
85-2	6-amino-1-hexanol	1.0	40	58	57	99	21	4	0	>200	1.2	3B	n.d.	n.d.
85-3	6-amino-1-hexanol	1.0	27	30	31	99	21	4	0	>200	1.2	3B	n.d.	n.d.
85-4	6-amino-1-hexanol	1.0	26	26	32	98	22	4	0	>200	1.2	3B	n.d.	n.d.
85-5	6-amino-1-hexanol	1.0	n.d.	n.d.	n.d.	97	22	4	0	>200	1.2	3B	n.d.	n.d.
86-1	tris(3-aminopropyl)amine	1.0	n.d.	n.d.	n.d.	n.d.	31	4	0	>200	>2	3B	90	2.5
86-2	tris(3-aminopropyl)amine	1.0	n.d.	n.d.	n.d.	n.d.	39	4	0	>200	>2	3B	n.d.	n.d.
86-3	tris(3-aminopropyl)amine	2.0	43	40	40	82	61	4	0	>200	>2	B	91	0.2
86-4	tris(3-aminopropyl)amine	2.0	48	50	53	87	61	4	0	>200	>2	B	91	0.3
86-5	tris(3-aminopropyl)amine	2.0	55	48	52	89	59	4	0	>200	>2	B	91	0.4
86-6	tris(3-aminopropyl)amine	3.0	8	9	10	90	87	4	0	>200	>2	HB	90	0.6
86-7	tris(3-aminopropyl)amine	3.0	58	67	62	97	83	4	0	>200	>2	HB	90	0.4
99-H	1.10-diaminodecane	1.0	10	12	12	84	22	0	0	>200	1	2B	91	0.7
99-K	1.10-diaminodecane	1.0	n.d.	n.d.	n.d.	n.d.	21	0	0	>200	1	2B	91	1.8
99-I	1.10-diaminodecane	1.5	9	10	9	91	60	0	0	>200	>2	B	n.d.	n.d.
99-L	1.10-diaminodecane	1.5	n.d.	n.d.	n.d.	n.d.	57	0	0	>200	>2	B	90	1.2
99-C	1.10-diaminodecane	2.0	15	12	13	91	68	4	0	>200	>2	HB	n.d.	n.d.
99-M	1.10-diaminodecane	2.0	n.d.	n.d.	n.d.	n.d.	68	4	0	>200	>2	HB	90	1.0

Table 4.9. Test results obtained for UV-cured clear coats prepared from Undec-TL monomer and different amine compounds with different molar ratios of monomer to amine.

#	AMINE	MONOMER: AMINE MOLAR RATIO	THICKNESS top (µM)	THICKNESS middle (µM)	THICKNESS bottom (µM)	% CONVERSION	Tg (°C)	ADHESION DRY	ADHESION WET	MEK RUBS	IMPACT RESISTANCE (kg·m)	PENCIL HARDNESS	TRANSPARENCY (%)	HAZE (%) D65/10
866B	tris(3-aminopropyl)amine	1.0	14	12	13	90	36	4	0	30	>2	3B	90	3.1
866C	tris(3-aminopropyl)amine	2.0	10	8	8	87	68	4	0	>200	>2	B	91	0.3
866D	tris(3-aminopropyl)amine	3.0	11	11	12	86	76	4	0	>200	>2	HB	91	0.3
869B	tyramine	1.0	10	9	8	90	42	4	4	30	>2	2B	89	0.9
869A	tyramine	1.0	n.d.	n.d.	n.d.	n.d.	n.d.	4	4	30	>2	2B	89	2.8
867B	m-xylylenediamine	2.0	9	8	7	88	69	4	0	>200	>2	HB	90	1.7
867A	m-xylylenediamine	2.0	n.d.	n.d.	n.d.	n.d.	n.d.	4	0	>200	>2	HB	90	1.2
868B	1,3-cyclohexanebis(methylamine)	2.0	9	9	7	92	88	4	0	>200	>2	HB	n.d.	n.d.
868A	1,3-cyclohexanebis(methylamine)	2.0	n.d.	n.d.	n.d.	n.d.	90	4	0	>200	>2	HB	n.d.	n.d.

The full dataset obtained during the evaluation of the thiolactone-based coatings in Table 4.8 and 4.9 includes replicates of coating samples. Some results were not determined (n.d.) due to the lack samples to conduct all of the testing with replicates. The coating thickness was determined using a magnetic gauge and three replicate measurements at three different positions on the coated steel panel, namely top, middle, and bottom in order to confirm homogeneous application of the film throughout the panel. The coating thickness was not found to affect the results, which provides an indication that the coating properties were homogeneous throughout the thickness of the film, which is in part due to the UV-curing optimization that was conducted. Based on the replicate coating samples, the coating preparation and UV-curing exhibited a high degree of reproducibility and robustness, as indicated by standard deviation of 1-4% in the degree of conversion after UV-curing.

4.4.1 Impact resistance

The clear coats prepared from thiolactone-containing monomers and different amines were tested for impact resistance by intrusion of a metal weight, according to ASTM D2794 under ambient conditions. The clear coats exhibited high impact resistance of 2 kg·m (19.6 J) for the majority of

the formulations. Only formulations #1 and 4 (Table 4.7) consisting of uncross-linked polymer films with monomer:amine molar ratio of 1:1 with long side chains had reduced impact resistance, which is attributable to the interference of the side chains in polymer chain packing and film formation. The introduction of different amine functional groups and the variation in polymer cross-linking did not affect the impact resistance of polymers with similarly high degree of conversion. In particular, the impact resistance of clear coats prepared from formulations #5 to 14 (Table 4.7) remained high, irrespective of the polymer T_g, which was in the range of 36-90 °C and exceeded the temperature during testing, 23 °C.

For amorphous polymers, the impact strength increases significantly as the temperature increases close to the T_g or higher due to the enhanced molecular mobility that can relieve stress and dissipate energy.[24] Impact resistance of the polymer coatings in this study was tested at room temperature (23°C), which is most of the time significantly below the T_g of most of the polymer coatings, which exhibited T_g in the range of 21-90°C. Therefore, the impact resistance of the clear coats prepared via thiolactone chemistry does not arise simply due to the polymer chain mobility in the rubbery state or the transition between glassy and rubbery state under mechanical impact. Rather, the clear coats exhibit high impact resistance that is characteristic of thiol-ene polymers ascribed to the flexibility of the thioether linkages and the homogeneity of the polymer networks that are formed by step-growth polymerization.[1] The advantage of the thiolactone chemistry approach for the preparation of clear coats is the possibility to tailor the properties of coatings via the choice of amine compounds without detrimental effects on the mechanical properties, such as impact resistance.

4.4.2 Hardness

The pencil hardness of the thiolactone-based coatings was in the range 2B-HB, based on the ASTM D3363 pencil hardness scale with a soft to hard range 6B-5B-4B-3B-2B-B-HB-F-H-2H-3H-4H-5H-6H. The lowest hardness was observed for coatings with monomer:amine ratio of 1:1 and different amine compounds, formulations #1, 2, 6 and 9 (Table 4.6). Greater hardness was observed for coatings prepared with higher monomer:amine ratios, formulations #5, 8, 11, 13 and 14 (Table 4.7). Higher monomer:amine ratios result in a greater degree of cross-linking and also a higher glass transition temperature, which translates into improved hardness. Therefore,

the monomer:amine ratio and the degree of polymer cross-linking has a significant influence over the hardness of the coatings.

4.4.3 Solvent resistance

The solvent resistance of coatings was evaluated with methyl ethyl ketone (MEK) double rubs, according to ASTM D5402 method. Thiolactone-based polymer films were resistant to 200 methyl ethyl ketone double rubs, without any noticeable change in transparency or thickness, with the exception of films prepared from formulations #9, 12 (Table 4.7). Further solvent resistance testing with greater than 200 MEK double rubs was not conducted, therefore, solvent resistance is reported as >200 MEK double rubs. The films prepared from the Undec-TL monomer without cross-linking by amines have greater chain mobility, which is reflected in the lower solvent resistance. In particular, Undec-TL monomer has a long aliphatic chain that imparts greater polymer chain mobility and flexibility, which is characteristic of materials prepared from fatty acids.

The advantage of thiolactone chemistry is that additional polymer cross-linking can be easily achieved with the multifunctional amine compounds, thereby imparting improved properties to the coatings. For example, coatings prepared from formulation #11 contain the same constituents as formulation #9 (Table 4.7), but a higher monomer:amine ratio leads to a greater chemical resistance, in addition to the higher T_g and higher pencil hardness.

4.4.4 Optical transparency and haze

Besides high impact and solvent resistance, the polymer films prepared from thiolactone-containing monomers and different amine compounds exhibited high optical transparency and low haze. The optical properties were measured under ambient conditions (25°C, 40% relative humidity) and standard D65 illumination, which replicates the average daylight in Europe defined by the International Commission on Illumination. Optical transparency is the percentage of incident light that is transmitted by the film. The haze measurement is a calculated value from the ratio of diffuse transmission and total transmission and provides an indication of the degree of cloudiness in a film. In general, 0% haze corresponds to complete transparency, up to 30% is

translucent, and more than 30% haze is considered opaque.[25] For comparison, US Patent 8357322 assigned to Mitsubishi Gas Chemical Company colorless and transparent polyimide films with a thickness of 200 μm, a total light transmittance of 89.8% and a haze of 0.74%.[26] Therefore, the polymer films in this study with an average optical transparency of 90% and haze in the range of 0.2-2.5% have suitable transparency and haze characteristics for optical applications.

High optical transparency is typical for thiol-ene polymers,[1] which is beneficial for optical applications. Thiolactone chemistry allows to introduce additional functional groups and cross-linkers into the thiol-ene polymers, while maintaining high transparency and low haze of the resulting polymer films.

4.4.5 Adhesion

The adhesion of thiolactone-based clear coats to stainless steel panels was evaluated according to the cross-hatch tape adhesion method on a scale of 0B (poor adhesion) to 5B (complete adhesion). Most polymer films exhibited good adhesion to steel under ambient conditions with only slight detachment of polymer from the areas of the cross-hatch marks, which was rated 4B. After the polymer samples were immersed in water for 2 hours at 60°C, the adhesion to steel was poor, rated 0B. Poor adhesion of thiolactone-based polymer films to steel in the presence of water is due to the presence of many polar functional groups in these polymers, as described by the Hansen solubility parameters (Figure 4.2). The presence of amide or urethane groups in the polymer backbone as well as amide side-chains contribute to high polarity and hydrophilicity of the coatings, which results in a high affinity for water in comparison with the substrate. Therefore, in the presence of water, these polymer films become easily detached from the steel substrate. In addition, the substrate preparation procedure has an effect on adhesion in terms of the surface roughness and the presence of contaminants. However, further investigation of the substrate preparation was not conducted in this study.

However, polymers prepared with tyramine exhibited good adhesion of 4B under both dry and wet conditions. The hydroxyl groups of tyramine are expected to improve polymer adhesion to

metals, similarly to the well-known effect of dopamine, as described in Chapter 1. Therefore, specific functional groups can be incorporated into thiolactone-based polymers in order to obtain the targeted coating performance.

Due to the significant influence of water on the adhesion of polymers to steel, the water uptake of the polymer coatings with different compositions was determined gravimetrically (Table 4.10). Multiple factors influence the water uptake of polymer coatings, including the hydrophilicity of the coating components and the degree of cross-linking. Coatings prepared using the less polar Undec-TL monomer exhibited water uptake of 6-16% (Table 4.10, #1- #3). Coatings prepared with the more polar Alloc-TL polymer exhibited water uptake of 14-69% (Table 4.10, #4 - #8). In addition, coatings with a higher monomer:amine ratio and a higher degree of cross-linking exhibited a lower water uptake (Table 4.10, #6). More cross-linked polymer networks generally have a lower degree of swelling in a solvent, which is also reflected in the water uptake values of polymer films with different monomer:amine ratios. The choice of amine compound and the presence of free amine groups in the coating also have an influence on the water uptake. Formulations prepared with amine compounds having additional secondary and tertiary amine groups and free primary amine groups have a higher water uptake (Table 4.10, #5 and #7).

Table 4.10 Water uptake of polymers prepared from Undec-TL or Alloc-TL monomer and different amine compounds.

#	MONOMER	AMINE	MONOMER: AMINE MOLAR RATIO	% WATER UPTAKE
1	Undec-TL	1,3-cyclohexane bis(methylamine)	2:1	6 ± 2
2	Undec-TL	m-xylylenediamine	2:1	11 ± 3
3	Undec-TL	tyramine	1:1	16 ± 2
4	Alloc-TL	1,3-cyclohexane bis(methylamine)	2:1	44 ± 9
5	Alloc-TL	tris(3-aminopropyl) amine	1:1	54 ± 11
6	Alloc-TL	tris(3-aminopropyl) amine	2:1	18 ± 4
7	Alloc-TL	triethylenetetramine	1:1	69 ± 11
8	Alloc-TL	2,2′-(ethylenedioxy)bis(ethylamine)	2:1	31 ± 7

The representative set of properties of thiolactone-based films are summarized in Table 4.11. Thiolactone-based polymer films are distinguished by their high transparency and low haze and

excellent impact resistance. These properties are also characteristic of thiol-ene polymer networks, since the thiol-ene step growth addition polymerization process produces homogeneous polymer structures with flexible thioether linkages.

Table 4.11. Overview of the properties of thiolactone-based coatings.

Polymer property	Testing methodology	Test results
thermal properties of polymers		
Glass transition temperature	Differential Scanning Calorimetry	-10 – 80 °C
Temperature at 5% mass loss	Thermogravimetric Analysis	249-284 °C
Temperature at maximum rate of mass loss		375-380 °C
optical properties of polymer films		
Transparency	UV-VIS Spectrophotometer	90 %
Haze		0,2 - 3 %
coating properties		
Adhesion to stainless steel (dry)	ASTM D3359 Tape test	4
Adhesion to stainless steel (wet)		0
Impact resistance	ASTM D2794 Impact resistance	> 2 kg·m
Methyl ethyl ketone (MEK) double rubs	ASTM D5402 Solvent Resistance	>200
Pencil hardness	ASTM D3363 Film hardness by pencil test	2B-H

The added value of the thiolactone building block is the enhanced storage stability of the protected thiol and the additional functionality that can be incorporated by aminolysis of the thiolactone ring. Furthermore, higher polymer cross-link densities can be easily achieved with multifunctional amine compounds via amine-thiol-ene conjugation, which enhances the T_g values of the resulting thiol-ene coatings and expands their potential applications. For example, thiol-ene polymers are particularly attractive for optical coating applications due to their high transparency, high refractive index, and homogeneous polymer networks. However, the flexible thioether polymer backbone contributes to low T_g values and low hardness, which results in poor

scratch-resistance of the coatings. The polymer coatings prepared using thiolactone chemistry also have the advantages of high optical transparency and low haze, while reaching T_g values above 80 °C.

4.5 Conclusion

The screening of the properties of new thiolactone-based coatings has established a foundation for the future development of multifunctional bio-based coatings via thiolactone chemistry. The high conversion of functional groups after a two-step amine-thiol-ene conjugation has been achieved, which is important for the development of tailored multifunctional coatings.

Coatings were evaluated according to standard ASTM tests for adhesion, impact resistance, hardness, and solvent resistance. Thiolactone-based films exhibited good adhesion to stainless steel under ambient conditions, but poor adhesion after immersion in water, with the exception of tyramine-containing films. Coatings with monomer:amine ratios of 2 or 3 exhibited higher T_g and also greater pencil hardness. Thiolactone-based coatings exhibited a high impact resistance of 2 kg·m, which is characteristic of thiol-ene polymers prepared by radical step-growth mechanism. Thiolactone-based films maintained high transparency of 90% and low haze (<5%) in the presence of different amine-containing functional groups.

Therefore, thiolactone-based polymers are promising for a variety of coating applications, enabled by the versatility of polymer backbone structures, side group functionalities, and cross-link densities. The high transparency and low haze of the thiolactone-based films could be further exploited for optical coatings, with additional functionality, such as anti-bacterial.

4.6 Materials and methods

4.6.1 Materials

Allyl chloroformate (97%), butyl acetate (≥99.5%), 4-(dimethylamino)pyridine (≥99%), DL-homocysteine thiolactone hydrochloride (≥99.0%), 1,3-cyclohexanebis(methylamine), mixture of isomers (99%), dichloromethane (99.8%), 2,2-dimethoxy-2-phenyl acetophenone (DMPA) (99%), 1,3-cyclohexanebis(methylamine), mixture of isomers (99%), 2,2′-(ethylenedioxy)bis(ethylamine) (98%), m-xylylenediamine (99%), tetrahydrofuran (≥99.0%),

triethylenetetramine (≥97.0% (T)), 1-propanol (≥99.5%), thionyl chloride (99.7%), triethylamine (99%), tyramine (99%), and 10-undecenoic acid (98%) were purchased from Sigma-Aldrich and were used as received, 6-amino-1-hexanol (>97.0%), tris(3-aminopropyl)amine (>95.0%) were purchased from TCI Chemicals and were used as received.

4.6.2 Methods

FTIR spectra (ATR mode) were recorded on a Perkin-Elmer Spectrum1000 FTIR infrared spectrometer by obtaining 16 scans for each sample.

Thermal properties of the UV-cured films were tested with TA Instruments 2920 Modulated DSC V2.6A under nitrogen gas flow of 19 mL/min. Measurements were performed in a temperature range of −20 to 150 °C with a heating and cooling rate of 10 °C/min. Glass transition temperatures were determined from the midpoint of the step change in the second measurement cycle. Thermogravimetric analyses were performed on a Mettler-Toledo TGA/SDTA851e instrument under nitrogen atmosphere at a heating rate of 10 °C/min from 25 to 600 °C. The thermograms were analyzed using the STARe software from Mettler-Toledo.

The thickness of polymer films on steel panels was determined using Erichsen Coating Thickness Gauge LAYERCHECK 750 USB-FN.

Polymer films were tested at room temperature and 40% R.H. according to the following standard ASTM methods. Coating hardness was tested according to the ASTM D 3363 − 00 Standard Test Method for Film Hardness by Pencil Test, employing the Elcometer 3086 Motorised Pencil Hardness Tester and graphite with hardness in the range 6B-5B-4B-3B-2B-B-HB-F-H-2H-3H-4H-5H-6H (Figure 4.10).

Figure 4.10 Elcometer 3086 Motorised Pencil Hardness Tester.

ASTM D2794 Standard Test Method for Resistance of Organic Coatings to the Effects of Rapid Deformation was conducted using Erichsen impact tester Model 304-ASTM via intrusion of a metal weight from a defined height on top of a coated steel panel (Figure 4.11).

Figure 4.11 Erichsen impact tester Model 304-ASTM.

Coating adhesion to steel under ambient conditions and after immersion in water was tested according to ASTM D 3359 Standard Test Methods for Measuring Adhesion by Tape Test, in reference to the hardness scale 0B (poor adhesion) to 5B (complete adhesion).

ASTM D5402 Standard Practice for Assessing the Solvent Resistance of Organic Coatings Using Solvent Rubs was carried out using methyl ethyl ketone (MEK) solvent and cotton swabs. Transparency and Haze (D65/10) of polymer films on microscope glass slides were measured by UltraScan VIS Hunterlab.

The water uptake of polymer films was determined gravimetrically using Mettler Toledo XS205 Dual range balance. Polymer films were suspended in deionized water for 24 hours.

% water uptake = (mass of wet sample − mass of dry sample)/ mass of dry sample

4.6.3 Synthesis of (N-allyloxy) carbonyl thiolactone (Alloc-TL)

Alloc-TL was synthesized following the procedure described by Espeel *et al.*[13] Briefly, DL-Homocysteine thiolactone hydrochloride (28 g, 0.1823 mol) was slowly added to a solution of NaHCO$_3$ (76.44 g, 0.91 mol) in H$_2$O/1,4-dioxane (1/1, 400 mL) and this mixture was stirred for 30 minutes at 0°C. Allyl chloroformate (38.76 mL, 0.3644 mol) was added dropwise and the reaction mixture was stirred overnight at ambient temperature. The reaction mixture was diluted with brine (800 mL) and extracted with ethyl acetate (4 x 800 mL). The organic phase was dried over MgSO$_4$. The drying agent was filtered and the solvent was evaporated under reduced pressure. The product was crystallized at 5°C during several days. ^{1}H-NMR (300 MHz, CDCl$_3$, ppm) 2.83 (m, 1H), 2.01 (m, 1H), 4.32 (m, 1H), 3.28 (m, 2H), 5.30 (m, 1H), 4.57 (dt, 17.2, 5.6, 1.4 Hz, 2H),5.25 (ddd, 10.4, 2.6, 1.3 Hz, 1H), 5.29 (ddd, 17.2, 3.0, 1.5 Hz, 1H), δ 5.90 (ddt, 17.2, 10.4, 4.7 Hz, 1H).

4.6.4 Synthesis of 10-undecenoylthiolactonamide (Undec-TL)

Undec-TL was synthesized following the procedure described by Goethals *et al.*[14] Briefly, 10-Undecenoylthiolactonamide was synthesized as previously described. Briefly, 10-undecenoic acid (292 mmol, 53.81 g) was dissolved in thionyl chloride (2.21 mol, 160 mL) and stirred under reflux for 90 min, after which thionyl chloride was evaporated. DL-Homocysteine thiolactone hydrochloride, (265 mmol, 40.71 g), was dissolved in dry dichloromethane (300 mL) and cooled to 0 °C, after which 10-undecenoyl chloride (292 mmol, 59.19 g), was added dropwise to the solution. Triethylamine (184.73 mL) was slowly added to the reaction mixture, and the mixture was allowed to reach room temperature under stirring for 24 h. The solution was washed with a saturated NaHCO$_3$ solution (500 mL), 1 M HCl solution (500 mL), and brine (500 mL), after which the organic layer was dried with anhydrous magnesium sulfate. The drying agent was filtered off and the resulting solution was evaporated under reduced pressure. ^{1}H NMR (300 MHz, CDCl$_3$, ppm): δ 1.31 (s, 10H,), δ 1.65 (m, 2H), δ 1.91 (m, 1H), δ 2.05 (m, 2H,), δ 2.25 (t,

2H), δ 2.99 (m, 1H), δ 3.34 (m, 2H), δ 4.52 (m, 1H), δ 4.97 (m, 2H), δ 5.82 (m, 1H), δ 5.90 (s, 1H).

4.6.5 Preparation of formulations with Alloc-TL and 6-amino-1-hexanol

A solution of *N*-(allyloxy)carbonylhomocysteine thiolactone (402 mg, 2 mmol) in butyl acetate (2 mL) and acetone (0.2 mL) was combined with 6-amino-1-hexanol (234 mg, 2 mmol). The reaction mixture was stirred for 4 hours at room temperature. DMPA (25 mg, 0.1 mmol) was added. All other formulations with the Alloc-TL monomer and different amine compounds were prepared using the same procedure.

4.6.6 Preparation of formulations with Undec-TL and tyramine

A solution of 10-undecenoylthiolactonamide (568 mg, 2 mmol) in tetrahydrofuran (3 mL) was combined with 4-(dimethylamino)pyridine (24 mg, 0,2 mmol) and tyramine (274 mg, 2 mmol). The reaction mixture was stirred for 4 hours at room temperature. DMPA (25 mg, 0.1 mmol) and 1-propanol (1 mL) was added. All other formulations with the Undec-TL monomer and different amine compounds were prepared using the same procedure.

4.6.7 Coating application and UV-curing

Prior to film application the glass and steel substrates were rinsed with isopropanol and acetone and dried in a fume hood. The coating formulations were applied on microscope glass slides with Erichsen Model 358 150 μM spiral applicator and on stainless steel Q-panels with Erichsen Quadruple Film Applicator Model 360 200 μm (Figure 4.12, right). Films with higher thickness were prepared by applying additional layers with the 150 μM spiral applicator. The polymer films were dried for 1 hour in a fume hood.


Figure 4.12 Erichsen spiral film applicators model 358 (left) and quadruple film applicators model 360 (right).

The films were irradiated with Xenon UVA lamp Model RC-847 Configuration 1-C3-H50 with irradiation dose of 2 J/cm^2 delivered in a pulsed mode with 34μsec pulses and 50% ON/OFF cycle. Polymer films with Undec-TL and 1,3-cyclohexanebis(methylamine) or m-xylylenediamine were prepared in a similar manner.

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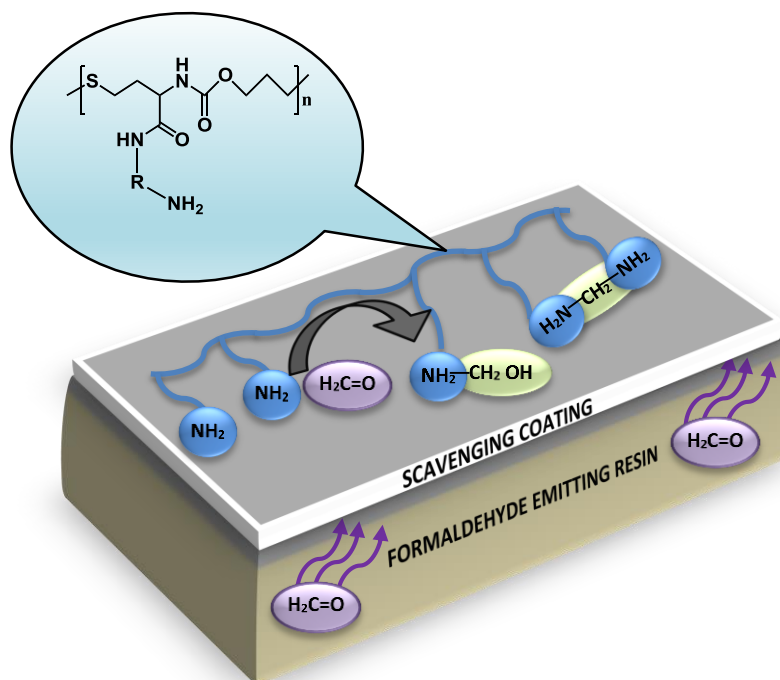
Abstract

A novel, straightforward chemical platform to prepare polymers with covalently bound amine functional groups has been developed for applications as coatings that scavenge formaldehyde emissions. For the polymer preparation, an amine-thiol-ene conjugation process was used to combine *N*-(allyloxy)carbonyl homocysteine thiolactone monomer with different amines, which simultaneously released a thiol group for subsequent thiol-ene radical polymerization. Results of the European standard formaldehyde release test by the flask method indicated that the obtained polymers with higher amine loadings resulted in a greater reduction in formaldehyde concentration. Urea-formaldehyde adhesive was overcoated with scavenging polymers, which resulted in a significant reduction in formaldehyde emissions.

Chapter 5. Thiolactone-based polymers for formaldehyde scavenging coatings

5.1 Introduction and aims

Smart coatings comprise a broad range of advanced coatings with multifunctional properties, such as self-healing, self-cleaning, superhydrophobic, stimuli-responsive, and antifouling.[1] Traditional protective coatings form a passive barrier that shields the substrate from environmental damage. In contrast, smart coatings typically contain active components in the polymer resin or additives that impart additional properties to coatings. The active components in coatings enable them to interact with environmental stimuli, such as pH, UV light, temperature, mechanical impact, or oxygen.[2] For example, smart barrier coatings in food packaging contain oxygen scavengers that actively trap oxygen, which prevents food spoilage and extends shelf-life.[3] Scavenging coatings are valuable in many applications for the reduction of undesired chemical species, such as volatile compounds,[4] radicals,[5] corrosive agents,[6] and moisture.[7] For the development of advanced coatings, techniques for introducing different scavenging functionalities into polymers are necessary.

Formaldehyde is an indoor air pollutant that can cause respiratory irritation and cancer after long-term exposure.[8] The International Agency for Research on Cancer (IARC) classified formaldehyde as carcinogenic to humans,[9] which led to stricter regulations on the emissions of this compound. The recommended limit for formaldehyde in residential indoor air was established at 0.1 mg/m^3 or about 0.08 ppm by the World Health Organization (WHO).[10] Many countries, such as Japan and the United Kingdom, have also adopted the 0.1 mg/m^3 limit.[8] Mass production of urea formaldehyde adhesives for medium density fiberboard, particleboard, and plywood resulted in a need for formaldehyde abatement.

Research efforts have been directed towards reduction of formaldehyde by reformulation of resins and incorporation of formaldehyde scavengers. In this respect, different additives have been investigated for formaldehyde scavenging, including chemical agents (eg. sodium metabisulfite, ammonium bisulfite)[11] and natural components (eg. wheat flour, tannin, rice husk and charcoal).[12] Compounds with amine groups can be effective in scavenging formaldehyde, since amines undergo an addition reaction with formaldehyde forming methylol groups, which

can react further to form methylene bridges.[13] At room temperature and under alkaline conditions, addition of formaldehyde to a primary amine produces the corresponding methylol derivative (Figure 5.1). The methylolamines can be condensed with a second molecule of amine to yield bis-(alkylamino)-methanes.
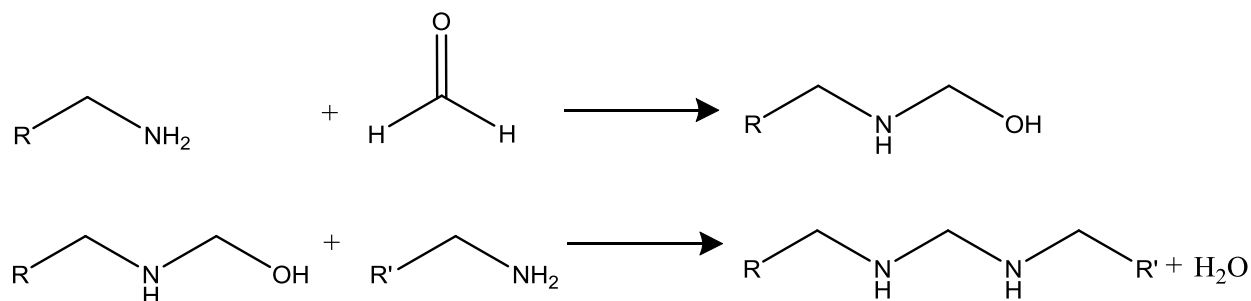

Scheme 5.1. Reaction of an aliphatic primary amine with formaldehyde, followed by condensation.

The effectiveness of amines in formaldehyde scavenging depends on several parameters (*vide infra*), including the amount of amine groups in the matrix, the structure of the amine compound, and the morphology of the matrix. Boran *et al.* determined that the emission of formaldehyde from medium density fiberboard panels, fabricated with urea formaldehyde resins, decreased with the addition of urea, propylamine, methylamine, ethylamine, or cyclopentylamine solution to the resin.[14] Addition of amine compounds led to an increase in water absorption and thickness swelling values of fiberboard. Medium density fiberboard panels with added amines exhibited higher internal bond strength, modulus of rupture, and modulus of elasticity. Therefore, scavenging additives can have an impact on the properties of the resin, which may be undesirable for certain applications. Nomura *et al.* impregnated polymeric amines, such as branched poly(ethyleneimine), linear poly(ethyleneimine), poly(allylamine) into mesoporous silica for the adsorption of airborne formaldehyde.[15] The formaldehyde adsorption capacity increased in proportion to the amount of amines, with maximum capacity corresponding to almost filled pores with slight residual porosity.

In contrast to the previous strategies of addition of formaldehyde scavengers to materials, this research aimed to use thiolactone chemistry for the covalent linkage of scavenging functional groups to a polymer backbone and the resulting polymer thin film. In particular, multifunctional

primary amine compounds can be readily incorporated into polymers via the aminolysis of the thiolactone moiety. The excess of primary amine groups in the polymer can be subsequently used for formaldehyde scavenging. Incorporation of scavenging functionalities by covalent linking to the polymer backbone is expected to reduce undesired migration and loss of scavengers over long time periods. This strategy could be effective for formaldehyde abatement in a wide range of products and applications without the need to reformulate existing resins.

An AB' monomer containing a double bond and a thiolactone unit has been synthesized by the addition of allyl chloroformate to DL-homocysteine thiolactone hydrochloride to form *N*-(allyloxy)carbonyl homocysteine thiolactone (Alloc-TL) (Scheme 5.2).
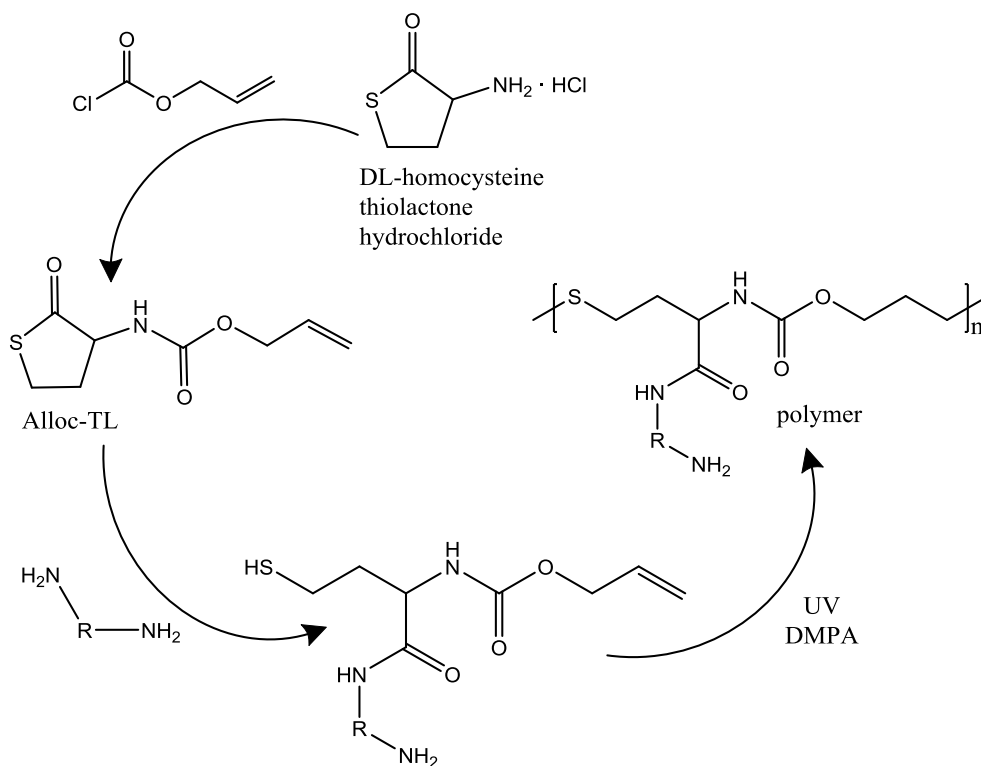
Scheme 5.2. Reaction of DL-homocysteine thiolactone hydrochloride and allyl chloroformate to form N-(allyloxy)carbonyl homocysteine thiolactone (Alloc-TL) monomer, followed by aminolysis and thiol-ene reaction in the presence of DMPA photoinitiator and UV light.

Polymers with different functional groups have been prepared from the Alloc-TL monomer, following the earlier described amine-thiol-ene conjugation.[16] Addition of primary amine

compounds to Alloc-TL results in thiolactone ring opening, which releases free thiol groups that can subsequently react via radical thiol-ene addition with double bonds (Scheme 5.2).

The aim of this research was the application of thiolactone chemistry to the preparation of UV-cured clear coats for scavenging formaldehyde. Formaldehyde emissions in the presence of polymer films with different types and loadings of amine compounds were evaluated according to the European standard formaldehyde release test by the flask method (Scheme 5.3).[17] The amine-functionalized polymers were characterized by High Resolution Magic Angle Spinning Nuclear Magnetic Resonance (HR-MAS NMR) spectroscopy, (Figure 5.5) and DSC (Figure 5.6) in order to elucidate any changes in polymer structure after exposure to formaldehyde.

5.2 Application of thiolactone chemistry for formaldehyde scavenging

The formaldehyde scavenging coatings were prepared using amine-thiol-ene conjugation, as described in Chapter 4. Briefly, Alloc-TL monomer reacted with a primary amine in solution, resulting in the release of the thiol functionality. The resulting solution was applied on substrates and the solvent was evaporated at ambient conditions. Next, polymer thin films were prepared by radical thiol-ene step growth addition that was triggered by UV irradiation in the presence of DMPA radical photoinitiator.

Four readily available diamines and triamines with primary amine groups, known to react with thiolactone groups, were chosen with the aim to obtain free amine groups that are available for scavenging formaldehyde (Figure 5.1). More specifically, aliphatic amine compounds with different chain length, composition, and branching were selected in order to investigate whether the structure of the amine compounds has an influence on the efficiency of formaldehyde scavenging.
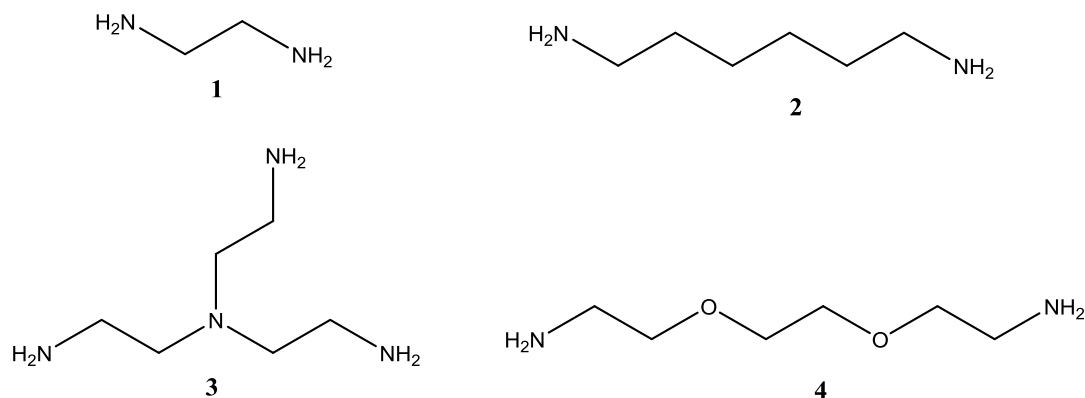
*Figure 5.1. Primary amine compounds used to prepare polymer coatings for formaldehyde scavenging: 1,2-diaminoethane (**1**), 1,6-diaminohexane (**2**), tris(2-aminoethyl)amine (**3**), 2,2'-(ethylenedioxy)bis(ethylamine) (**4**).*

FTIR spectroscopy was used to confirm the formation of an amide adduct from Alloc-TL and an amine. The infrared spectrum of the Alloc-TL contains a carbonyl absorbance peak at 1685 cm^{-1} that corresponds to the thioester group (Figure 5.2).
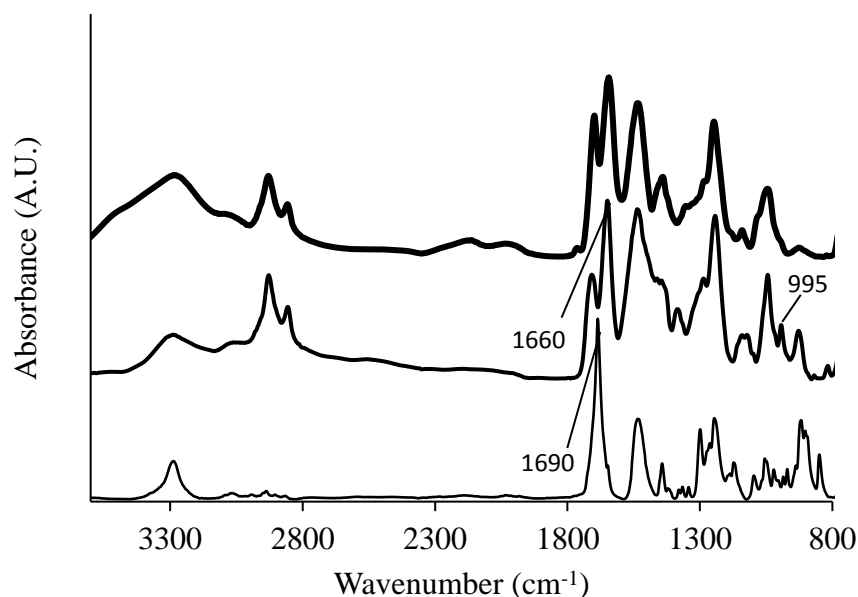

Figure 5.2. FTIR spectra of Alloc-TL monomer (bottom), formulation of Alloc-TL and 1,6-diaminohexane (middle), and the resulting UV-cured polymer (top).

Following the addition of an amine to Alloc-TL, a new carbonyl peak is observed at 1660 cm^{-1}, which corresponds to the amide product. An overlapping carbonyl peak at 1700 cm^{-1} is associated with the urethane functional group of Alloc-TL. The thiol-ene addition reaction results in the disappearance of the absorption at 995 cm^{-1}, which corresponds with the alkene C=C–H bending vibration. The overall conversion has been calculated from the integration of the alkene absorption peak before and after UV irradiation (Table 5.1).

5.3 Evaluation of formaldehyde scavenging

Systematic testing of polymers with different amine loadings was conducted in order to determine if they are effective in scavenging formaldehyde (Table 5.1).

Table 5.1. Formulations prepared from Alloc-TL and different amine compounds.

| #	Formulation	Molar ratio of components	NH$_2$ loading in polymer (mmol g^{-1})	% Conversion (C=C-H)
1	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 1.00 : 0	0.0	92
2	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 0.85 : 0.15	0.5	89
3	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 0.67 : 0.33	1.1	81
4	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 0.50 : 0.50	1.6	88
5	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 0.33 : 0.67	2.1	81
6	Alloc-TL: 1-aminohexane : 1,6-diaminohexane	1.00 : 0 : 1.00	3.2	89
7	Alloc-TL: 1,2-diaminoethane	1:1	3.8	81
8	Alloc-TL: 2,2′-(ethylenedioxy) bis(ethylamine)	1:1	2.9	97
9	Alloc-TL: tris(2-aminoethyl) amine	1:1	5.8	88
10	Alloc-TL: tris(2-aminoethyl) amine	2:1	3.6	88

The amine loading in dry polymers was calculated based on the stoichiometric molar ratio of the Alloc-TL monomer and amine compounds used to prepare the coatings. A series of UV-cured

polymer films with progressively increasing molar loadings of residual amine groups were prepared by varying the ratio of monofunctional 1-aminohexane and difunctional 1,6-diaminohexane (formulations #1-6). Formulation #1 contained only 1-aminohexane that reacted completely with Alloc-TL and resulted in the absence of residual amine groups. This formulation was used as a reference sample, which is not expected to scavenge formaldehyde. On the other hand, formulations prepared with the difunctional 1,6-diaminohexane contain residual amine groups, as indicated by the molar amine loading in Table 5.1. In most formulations, linear polymers are formed with pendant primary amine groups, while in formulation #10 cross-linked polymers are formed, since the trifunctional amine reacts with 2 equivalents of the Alloc-TL monomer.

The average mass of the polymer samples that were tested for formaldehyde scavenging was 55 +/- 3 mg. The total quantity of amine groups per sample ranged between 0.0275 mmol (0.5 mmol g^{-1}) and 0.319 mmol (5.8 mmol g^{-1}). The initial concentration of formaldehyde in solution that was added to each test flask was 0.2 ppm, which corresponded to the total amount of formaldehyde of 40 nmol per flask. The concentration of amine groups in the polymer was varied in different samples, while the initial formaldehyde concentration in a test flask was kept constant.

The total amount of amine groups in each sample was in a large excess compared to formaldehyde. An excess of scavenging groups is necessary to trap trace quantities of volatile compounds in a relatively short time. A long scavenging reaction time would limit the potential application of this methodology. Since the total amount of amine groups in the tested samples was in a large excess compared to the total amount of formaldehyde in the test flask, small variations in the mass of the polymers are not going to affect the total amount of formaldehyde scavenged.

Formaldehyde scavenging was investigated according to the EN 717-3 European standard flask method for the determination of formaldehyde release.[17] Polymer films with amine functional groups were suspended at the top of the flask containing 0.2 ppm formaldehyde solution in water at 40°C and samples of this solution were withdrawn over time (Scheme 5.3A).
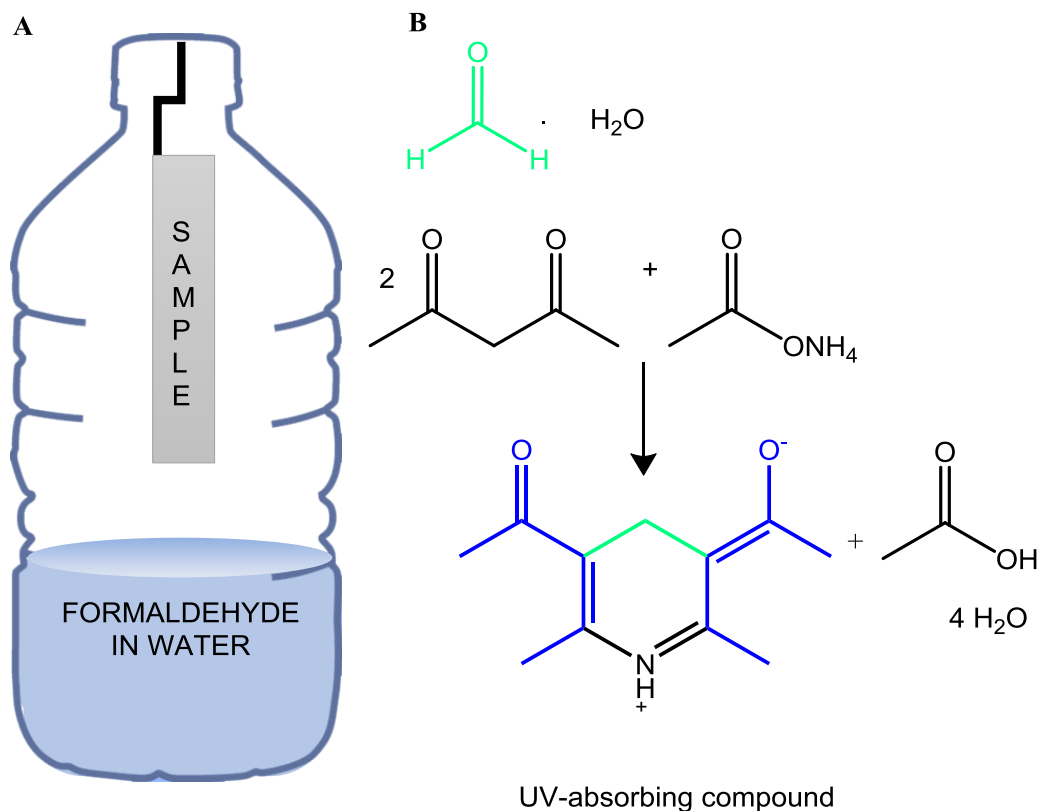
*Scheme 5.3. Schematic representation of the formaldehyde test in a flask (**A**); reaction scheme of formaldehyde with acetyl acetone and ammonium acetate (**B**) .* [17]

The samples with formaldehyde solution were combined with ammonium acetate and acetyl acetone, resulting in the formation of a UV-absorbing compound (Scheme 5.3B), which was analyzed by UV/Vis spectrophotometry. The concentration of formaldehyde in the samples was determined from a calibration curve prepared in the same way as the samples using a standard solution of formaldehyde. All samples were analysed in triplicate.

Figure 5.3 illustrates the change in the concentration of formaldehyde over time in the presence of polymer films containing different molar loadings of primary amine groups. Reduction of formaldehyde concentration was observed in the presence of the polymers with residual amine groups, as opposed to the reference sample. The concentration of formaldehyde was reduced to a greater extent in the presence of polymer samples with higher loadings of primary amines. For example, the polymers with a lower amine loading of 0.5 mmol g^{-1} resulted in a reduction of formaldehyde concentration from 0.2 ppm to 0.08 ppm, which corresponds to 60% reduction. Polymers with a higher amine loading of 3.2 mmol g^{-1} reduced the formaldehyde concentration

down to 0.006 ppm, which corresponds to 97% reduction. The standard error was 1-8% for measurements conducted with 3 replicates, n=3. Therefore, polymers with higher amine loading resulted in a greater reduction in formaldehyde concentration.
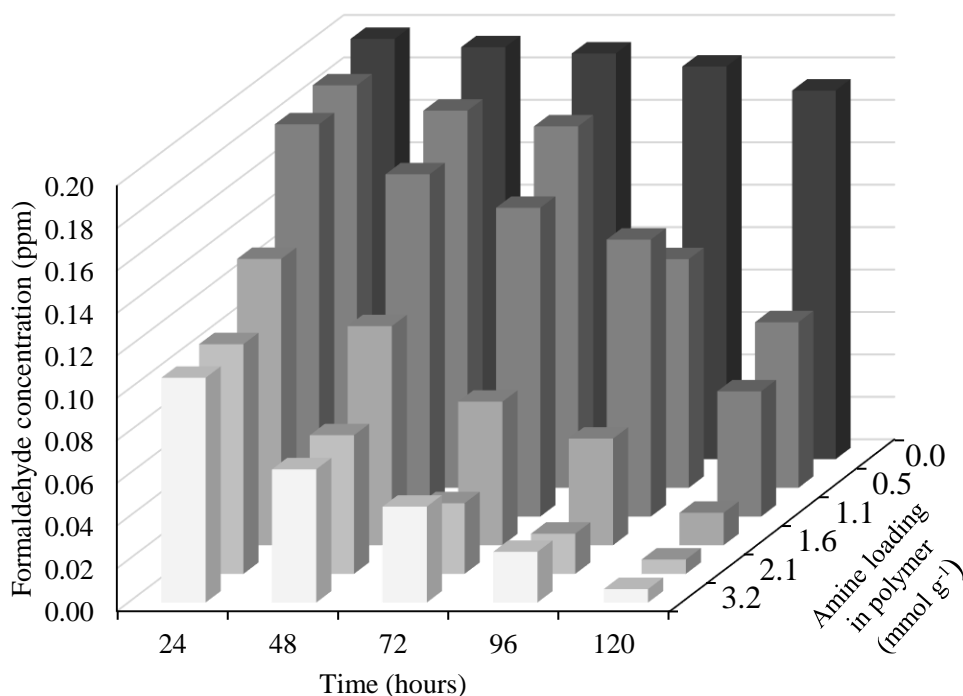

Figure 5.3. Formaldehyde concentration over time in the presence of 55 mg of polymer films with different molar quantities of primary amine groups prepared from Alloc-TL, 1-aminohexane and 1,6-diaminohexane in different molar ratios. Standard error is 1-8%.

The dependence of the formaldehyde concentration on the time of exposure and the amine loading of the polymer films has been modeled by linear regression using JMP 12 software, yielding the prediction expression: Formaldehyde concentration (ppm) = 0.247 − 0.050*(Amine loading in polymer, mmol g^{-1}) − 0.000934*(Time, hours), (Figure 5.4 A). The dependence of the formaldehyde on the amine loading in polymer is statistically significant, based on the p-value<0.0001 at 95% confidence interval. The leverage plots of the amine loading and exposure time show the impact of adding each of these parameters individually to the model, when the other parameters are already integrated into the model (Figure 5.4 B, C). The confidence curves for the line of fit are represented by dashed red lines, while the horizontal dashed blue lines

represent the mean value. The fact that the confidence curves for the line of fit cross the mean horizontal line indicates that both the amine loading and the exposure time have a significant effect on the formaldehyde concentration.
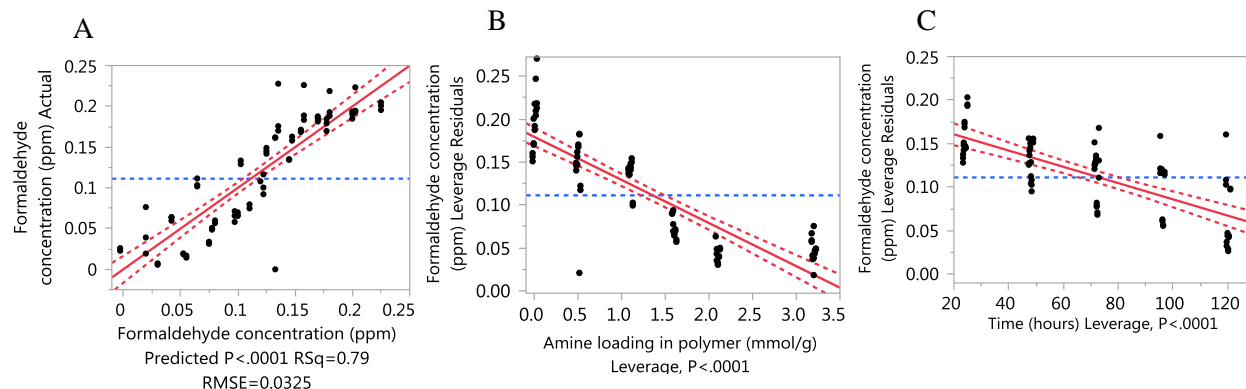

Figure 5.4 Plot of actual and predicted formaldehyde concentration using linear regression (A), partial-regression residual leverage plot of amine loading in polymer (B) and exposure time (C).

Various amine compounds were incorporated into polymers and their effect on formaldehyde concentration in a flask was investigated. Figure 5.4 illustrates the increase in the quantity of scavenged formaldehyde for a specific polymer film over time from a solution with 1.2 μg of formaldehyde. We observed a difference in the amount of formaldehyde scavenged by polymer films with different amines in the time period of 24 to 72 hours. The difference in scavenging was reduced over a longer time period, which suggests that at first, the orientation of the different amine molecules on the surface of the polymer film affected interactions with gaseous formaldehyde.

After 120 hours, the total amount of formaldehyde scavenged was the highest for amine compounds with linear aliphatic chains, compared to branched amine compounds. For example, formulations # 9 and 10 prepared with the branched tris(2-aminoethyl)amine at amine loading of 5.8 and 3.6 mmol g^{-1} resulted in a similar percentage of formaldehyde scavenged after 120 hours (respectively 90 % and 91 %), (Table 5.1).

Formulation #10 had a higher ratio of monomer to amine than formulation #9, resulting in greater cross-link density and lower amine loading. The results of formaldehyde scavenging indicated that branched amines with different loadings and cross-link densities are overall less

effective than linear amines. Formulations # 6 and 7 with linear aliphatic chain amines, 1,6-diaminohexane and 1,2-diaminoethane resulted in a higher percentage of formaldehyde scavenged after 120 hours (respectively 99 % and 97 %).
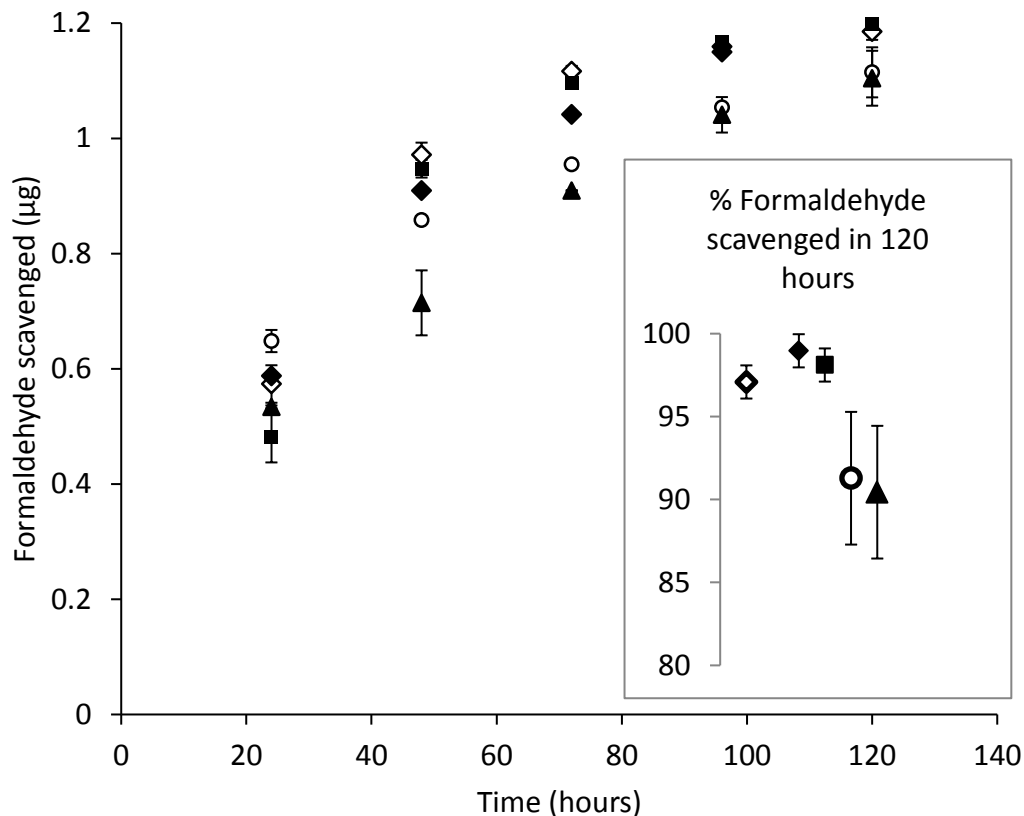

Figure 5.4. Formaldehyde scavenged by 55 mg of polymer films: ◊ Alloc-TL:1,2-diaminoethane (1:1), ■ Alloc-TL:2,2'-(ethylenedioxy)bis(ethylamine) (1:1), ○ Alloc-TL:tris(2-aminoethyl)amine (1:1), ▲ Alloc-TL:tris(2-aminoethyl)amine (2:1), ♦ Alloc-TL:1,6-diaminohexane (1:1). Standard error is 1-4%.

The difference between the formaldehyde scavenged by polymers with 1,6-diaminohexane and tris(2-aminoethyl)amine was 0.10 µg, while the standard error corresponded to 0.01 µg. Therefore, the difference in the amount of formaldehyde scavenged is related to the effect of polymers, rather than to differences in sample preparation or testing.

The reactivity of all the primary amine compounds used in this study with formaldehyde is expected to be similar. The difference in formaldehyde scavenging could be attributed to several secondary factors, such as the conformational constraints of the amine groups in the polymer and diffusion of formaldehyde through the polymer matrix.

5.4 Characterization of formaldehyde-scavenging polymers

The chemical change in the polymer structure after exposure to formaldehyde was elucidated by HR-MAS NMR spectroscopy. The HR-MAS technique provides enhanced resolution and sensitivity by adding a magnetic field gradient along the magic angle and by averaging the differences in magnetic susceptibility and residual dipolar coupling.[18] Thus, HR-MAS enables the analysis of cross-linked polymers swollen in deuterated solvents. This technique has been used for the analysis of polymer resins and gels and has become more popular for characterization of complex tissues in the biomedical field. [18]

HR-MAS NMR proved to be a valuable technique for characterizing the changes in the functional groups of the formaldehyde scavenging polymers. The HR-MAS NMR spectrum of the polymer prepared from Alloc-TL and 1,2-diaminoethane exhibited new peaks at 4.71 ppm and 4.82 ppm after exposure to formaldehyde (Figure 5.5). The new peaks were expected from the methylene and methylol protons that are incorporated into the polymer after reaction of amine groups in the polymer with formaldehyde.
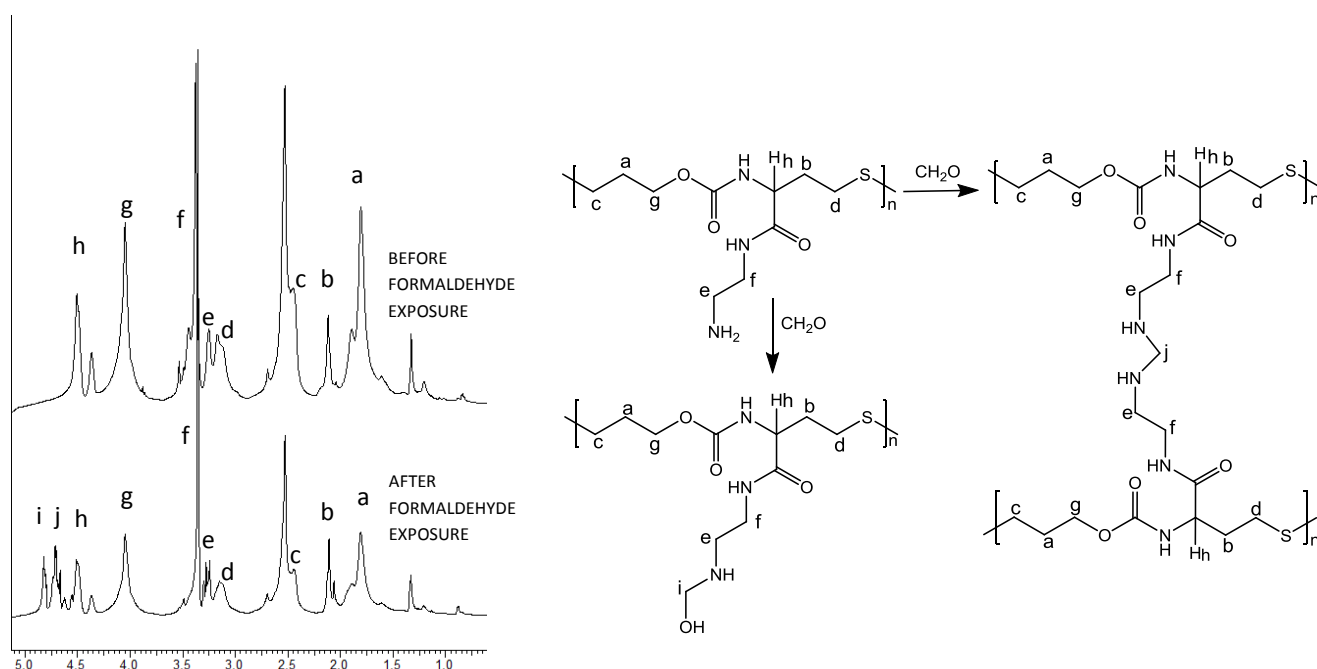
Figure 5.5. HR-MAS NMR spectra of polymer based on allyl thiolactone monomer and 1,2-diaminoethane in d6-DMSO (δ=2.5 ppm) before and after exposure to formaldehyde (left), chemical structures associated with the observed NMR spectra (right).

Similar results were obtained by Slonim *et al.* during an investigation of the structure of urea-formaldehyde resins by NMR, which revealed peaks at 4.39 ppm and 4.60 ppm corresponding to methylene diurea and methylol urea. [19] The difference in the chemical shift of the methylol and methylene peaks in the formaldehyde scavenging polymers compared to the urea-formaldehyde resins could be attributed to the influence of the urea functionality as opposed to aliphatic amines and the effect of solvent interactions, such as hydrogen bonding in the case of deuterated water.

The effect of formaldehyde exposure on the thermal properties of the polymer films was investigated by DSC. Figure 5.6 shows the T_g before and after exposure to formaldehyde while the difference in T_g is indicated on the scatter plot.
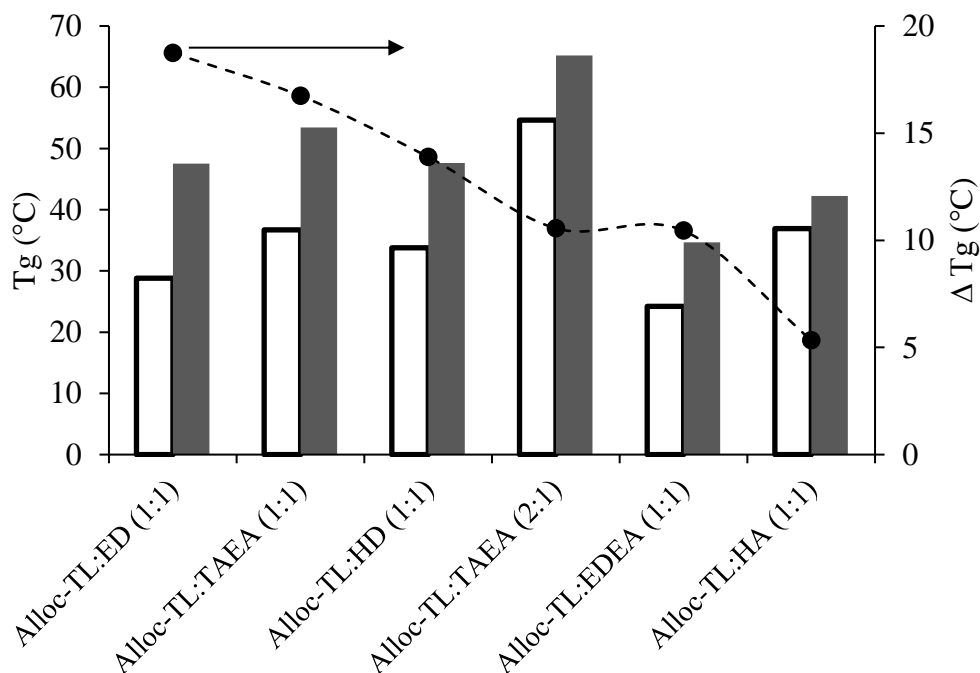
Figure 5.6. Glass transition temperature (T_g) of polymers before and after exposure to formaldehyde, represented by white and gray bars, respectively. Scatter plot represents the difference between the initial T_g and the final T_g after formaldehyde exposure. Polymers were prepared from Alloc-TL and different amines: 1,2-diaminoethane (ED), tris(2-aminoethyl)amine (TAEA), 1,6-diaminohexane (HD), 2,2'-(ethyenedioxy)bis(ethylamine) (EDEA) and 1-aminohexane (HA). Molar ratios of Alloc-TL and amines are indicated in brackets.

The T_g increased significantly by 10 to 19 °C after exposure to formaldehyde. The greatest increase in the T_g after formaldehyde exposure was observed for formulation #7 with 1,2-diaminoethane, which is a low-molecular weight aliphatic amine and was one of the most effective scavengers according to the formaldehyde testing (Figure 5.4). On the one hand, the formation of methylol groups upon addition of formaldehyde to amines can contribute to hydrogen bonding, resulting in a higher T_g of the polymer. On the other hand, methylene bridges formed by reaction of formaldehyde with several amine groups (Figure 5.5B) can increase the cross-link density and thus the T_g value. The formaldehyde emissions test was conducted at 40°C, which is close to the T_g value of the polymers assessed in this study. Greater mobility of the polymer segments close to their T_g could further enhance formaldehyde scavenging at 40°C. Therefore, the results of this test are useful as a proof of concept of the scavenging activity of the amine-containing coatings and for the relative comparison of the different coating formulations. Formaldehyde scavenging is expected to have slower kinetics at lower temperature, which could be the subject of future investigations.

The feasibility of using formaldehyde scavenging polymers as top coats was investigated using a urea-formaldehyde adhesive. The adhesive was applied and dried, followed by the application of the scavenging polymers. The results of the formaldehyde release test by the flask method indicated that formaldehyde emissions were significantly reduced by the scavenging polymers in comparison to the urea-formaldehyde adhesive as reference material (Figure 5.7). The reduction in formaldehyde emissions is due to a combination of the barrier effect of the polymer, as well as the scavenging groups. The polymers composed of Alloc-TL and 1-aminohexane, without any residual amines for scavenging, was expected to only have a passive barrier effect in preventing formaldehyde emission. A reduction was indeed observed for this polymer but to a much lower degree compared to the active scavenging polymers.

After incubation of the overcoated adhesive samples for 1 week at 40°C, the lowest concentration of emitted formaldehyde was 0.007 ppm in the presence of the polymer with 1,6-diaminohexane, while the highest formaldehyde concentration was 0.3 ppm in the presence of the polymer with tris(2-aminoethyl)amine. The limit of detection for formaldehyde was 0.002 ppm, based on 20 blank samples. These results are in agreement with the findings from the free

standing polymer films with amine scavengers, which confirmed that linear aliphatic chain amines are more effective in scavenging formaldehyde than branched amines.
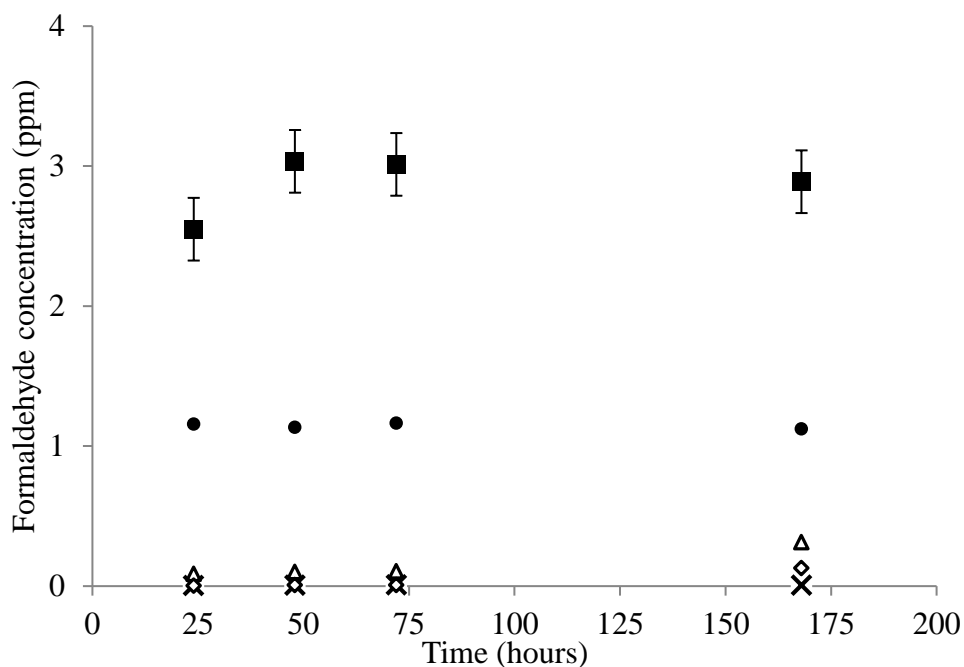

Figure 5.7. Formaldehyde emissions from urea- formaldehyde adhesive overcoated by polymers: × Alloc-TL:1,6-diaminohexane (1:1), Δ Alloc-TL:tris(2-aminoethyl)amine (1:1), ◊ Alloc-TL:tris(2-aminoethyl)amine (2:1), ● Alloc-TL:1-aminohexane (1:1), ■ urea-formaldehyde adhesive.

5.5 Conclusion

This work focused on the proof of concept that polymer films with amine side groups can react with formaldehyde and thereby reduce formaldehyde emissions. Multifunctional amine compounds were introduced into thiol-ene polymers via the Alloc-TL monomer, following a two-step amine-thiol-ene conjugation. Different ratios of monomer and amines resulted in branched or cross-linked polymers. Pendant amines in the polymer films reacted with formaldehyde, resulting in reduction of formaldehyde concentration in testing flasks. Reduction in formaldehyde emissions from coated urea-formaldehyde adhesive was demonstrated using the standard formaldehyde release test by the flask method. The versatility of the thiolactone chemistry enables efficient screening of functional groups in polymers for different applications

of interest. In addition, thiolactone-based polymers have favourable properties for top-coat applications due to their homogeneous cross-link density and a high degree of UV-cure. Therefore, functionalised thiolactone-based coatings are promising candidates for added-value coating applications.

5.6 Materials and methods

5.6.1 Materials

Allyl chloroformate (Sigma-Aldrich, 97%), DL-homocysteine thiolactone hydrochloride (Sigma-Aldrich, ≥99.0%), 2,2-dimethoxy-2-phenyl acetophenone (Sigma-Aldrich, 99%), 1-aminohexane (Sigma-Aldrich, 99%), tris(2-aminoethyl)amine (Sigma-Aldrich, 96%), 1,6-hexanediamine (Acros, 99.5+%), 2,2′-(ethylenedioxy)bis(ethylamine) (Sigma-Aldrich, 98%), 1,2-diaminoethane (Sigma-Aldrich, ≥ 99.5%), 1-propanol (Sigma-Aldrich, ACS reagent, ≥ 99.5%), formaldehyde in water, (Sigma-Aldrich, PE1380 Proficiency Testing Material) were used as received.

5.6.2 Methods

FTIR spectra in ATR mode were recorded on a Perkin-Elmer Spectrum1000 FTIR infrared spectrometer.

Thermal properties of the UV-cured polymer thin films were tested with TA Instruments 2920 Modulated DSC V2.6A under nitrogen gas flow of 19 mL/min. Measurements were performed in a temperature range of −20 to 150 °C with a rate of 10 °C/min over 2 cycles. Glass transition temperatures were determined from the midpoint of the step change in the second measurement cycle.

High Resolution Magic Angle Spinning Nuclear Magnetic Resonance (HR-MAS NMR) spectroscopy was performed on a Bruker Avance II 700 spectrometer (700 MHz). Samples were prepared by placing dry polymer into a 4 mm rotor and adding 30 µL of solvent (d6-DMSO) to

allow the material to swell. ^{1}H NMR spectra were recorded using a HR-MAS probe at spinning rate of 6 kHz and collecting 32 scans.

Formaldehyde testing was conducted according to the standard procedure for the determination of formaldehyde by the flask method.[17] UV-Vis spectra were obtained with AnalytikJena SPECORD 205 UV/Vis Spectrophotometer. A formaldehyde calibration curve was obtained using a standard solution of formaldehyde in water. Limit of detection of formaldehyde was determined from 20 blank samples and calculated by summation of the average value of the blank samples and the standard deviation multiplied by 3. All samples were tested in triplicate.

5.6. 3 Preparation of polymer films prepared from Alloc-TL and 1-aminohexane

A solution of *N*-(allyloxy)carbonyl homocysteine thiolactone (402 mg, 2 mmol) in 1-propanol (2 mL) was combined with 1-aminohexane (202 mg, 2 mmol). The reaction mixture was stirred for 4 hours at room temperature. DMPA (18 mg, 0.1 mmol) was added to the solution. The resulting formulation was dispensed by micropipette on microscope glass slides and spread with a 200 μm slot die, followed by drying for 1 hour. The thin film was irradiated with a 250 W mercury lamp (Hönle UVAHAND 250) at 1.4 J/cm^2. Two samples were prepared for each formulation. Each sample was weighed on a microbalance. Average sample mass was 55 +/- 3 mg. Average dry film thickness was 25 μm. Polymer thin films with other amine compounds were prepared in a similar manner.

5.7 References

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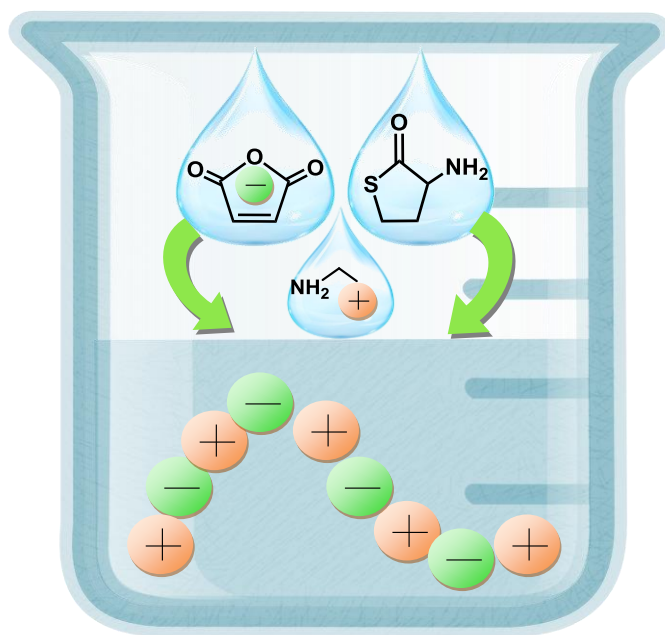
Abstract

Polyampholytes with precisely alternating cationic and anionic functional groups were prepared using sustainable thiolactone building blocks in a simple one-pot procedure at room temperature and in water. Ring-opening of *N*-maleamic acid-functionalized homocysteine thiolactone monomer enabled the introduction of different functional groups into the polymer chain, which contributed to both ionic and hydrogen bonding interactions. The resulting polyampholytes exhibited various isoelectric points, while maintaining high solubility in water under different pH and ionic strengths, which expands their potential for applications. The alternating polyampholytes exhibited upper critical solution temperature (UCST) thermoresponsive behavior in water/ethanol (30/70 %vol) solutions, which varied depending on the content of ionic and hydroxyl functional groups.

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Chapter 6. Precisely alternating functionalized polyampholytes prepared in a single pot from sustainable thiolactone building blocks

6.1 Introduction and aims

Polyampholytes are polymers containing functional groups that can exhibit both a positive or a negative charge, as opposed to polyelectrolytes, which are polymers with a single type of charged group (Figure 6.1). Inter- and intramolecular ionic interactions between the charged groups of polyampholytes can be used to control polymer structure and properties. Polyampholytes can exist in linear, coiled, helical or globular conformations, depending on the polymer composition and environment.[1]
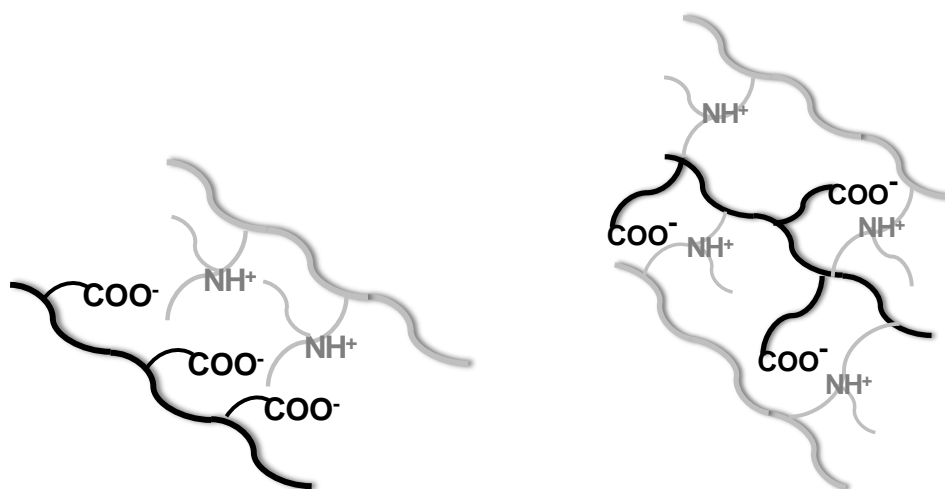
Figure 6.1. Representation of anionic or cationic polyelectrolytes (left) and polyampholytes (right).

The dynamic nature of the ionic groups in polyampholytes imparts stimuli-responsive properties, including pH,[2] ionic strength,[3] and temperature.[4] For example, thermoresponsive polymers exhibit a lower and/or upper critical solution temperature (LCST or UCST) in solution due to the phase separation at high and/or low temperatures, respectively. UCST polymers that become soluble upon heating are particularly attractive for biomedical applications, such as drug release and bioseparation,[5] although many applications include multiple requirements, such as a well-defined UCST transition at a certain temperature that occurs in water and is unaffected by pH or ionic strength.[6] Polyampholytes with different ionic functionalities display different

intramolecular interactions and solubility, which can be used to impart thermoresponsive behaviour. For example, Zhang *et al.* synthesized polyampholytes that exhibited UCST thermoresponsive behavior in alcohol-water mixtures, which was employed in temperature induced self-assembly into defined nanoparticles.[4]

Polyampholytes could also be employed as structural biomaterials, since they can be used to form tough and self-healing hydrogels.[7] Consequently, polyampholytes are valuable for many applications, including protein purification,[8] dry-strength additives for paper,[9] anti-fouling agents,[10] ice crystal inhibitors,[11,12] and drug delivery systems. [13,14]

The typical approach for the preparation of polyampholytes is radical copolymerization of different unsaturated monomers, which carry a positive or a negative charge.[15] The net charge of the polyampholyte is thus a result of the molar ratio of the cationic and anionic monomers, as well as their relative reactivity. The difference in the reactivity of monomers contributes to compositional drift and limits the control over the charge distribution throughout the polymer chain. In addition, the reactivity of ionic monomers can be significantly influenced by the pH, as in the case of methacrylic acid.[16] Nisato *et al.* noted that equimolar mixtures of two monomers tend to form polymers with an excess of positive charges at the beginning of the synthesis and an excess of negative charges at the end, which results in phase separation under certain ionic strengths.[17]

Control over the polyampholyte composition has been improved by regimenting comonomer feed throughout the polymerization or adjusting the pH of the reaction mixture.[18] However, these methods have to be adapted to each monomer composition, which poses a limitation to the development of different polyampholytes on a large scale. Moreover, the synthesis of polyampholytes often involves protecting groups,[19,20] which necessitates additional synthetic steps that reduces the overall atom-efficiency. For example, Kaur *et al.* employed solketal methacrylate and tert-butyl methacrylate and performed two deprotection steps after RAFT polymerization to obtain quaternary ammonium ions and methacrylic acid units in the polymer.[21]

The objective of this work is to develop a synthetic method for the preparation of alternating polyampholytes without any compositional drift. We employed thiolactone chemistry to prepare alternating polyampholytes with various functional groups in a simple and sustainable manner.

The amine-thiol-ene conjugation approach for the synthesis of polyampholytes contributes several advantages. First, thiol-ene polymerization can be carried out in water at room temperature and in the presence of oxygen. In contrast to radical polymerization of unsaturated monomers, there is no need for radical initiators or radical inhibitors for the polyampholyte precursors used in this study.

Secondly, the distribution of the net charge along polymers can be controlled starting from the thiolactone-derived monomer and can be further varied by introducing multifunctional amine compounds. The distribution of the net charge along the polymer backbone has a significant effect on the properties.[22] For example, Stubbs *et al.* quantitatively determined that regioregular alternating polyampholytes exhibit a greater ice recrystallization activity in comparison with random polyampholytes.[12] Furthermore, additional hydrophobic functionalities in polyampholyte side-chains could be used to further enhance ice crystal inhibition, which underscores the added value of multifunctional polymer materials.

Thirdly, the solubility of polyampholytes can be improved with additional polar or non-polar functional groups that can be introduced via the aminolysis of thiolactone. Indeed, broad regions of insolubility of polyampholytes near the isoelectric point often limit their characterization and applications.[18] Therefore, thiolactone chemistry contributes an important advancement in the field of polyampholytes and expands the range of functional and structural variations.

## 6.2 Incorporation of ionic groups into polymers via thiolactone chemistry

Thiolactone chemistry is an atom-efficient way to introduce functional groups into polymers, without the need for additional protecting groups, as described in Chapter 2. Four different strategies were considered for the introduction of ionic functional groups into polymers using thiolactone chemistry. The initial focus was to introduce an anionic carboxylic acid group, since there are already many options of cationic tertiary amine compounds that can be easily introduced via the aminolysis of the thiolactone moiety.
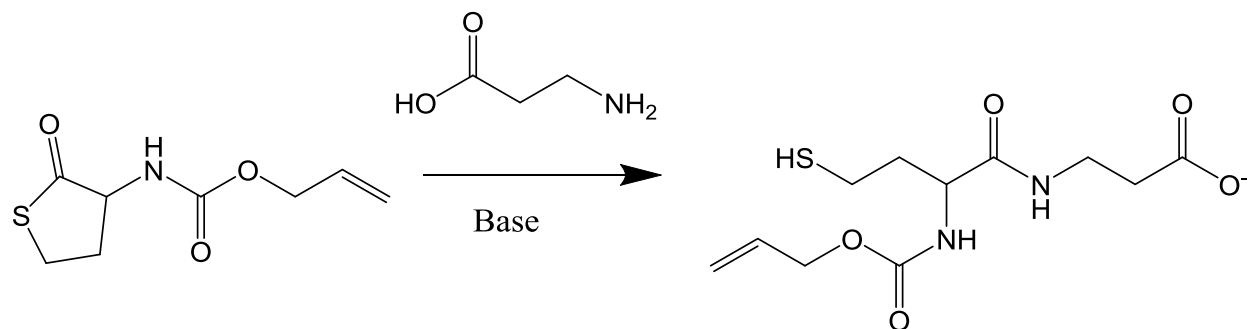
Scheme 6.1. Reaction of (N-allyloxy) carbonyl thiolactone (Alloc-TL) and β-alanine in the presence of different bases, KOH, pyridine, phosphate buffer pH=10.

In this context, the traditional strategy of introducing functional groups via the aminolysis of thiolactone was attempted using β-alanine, which contains both an amine and a carboxylic acid group (Scheme 6.1). The aminolysis of the thiolactone moiety with β-alanine was conducted in the presence of different bases, namely, KOH, phosphate buffer with pH=10, and pyridine in order to deprotonate the carboxylic acid group and facilitate the nucleophilic ring-opening. However, the presence of the carboxylic acid group hindered the amine reaction with the thiolactone moiety, resulting in low conversions of the thiolactone moiety. Different acid-base pairs of β-alanine were generated, such that the amine group did not react with the thiolactone.

The second strategy for introducing a carboxylic acid group using thiolactone chemistry was to react the thiolactone moiety with a diamine, such that the remaining amine groups could be subsequently reacted with maleic anhydride (Scheme 6.2). The ring-opening of maleic anhydride by an amine generates the desired carboxylic acid group. Finally, it was expected that another functional group could be introduced by thiol-ene addition with the double bond of the maleic anhydride.
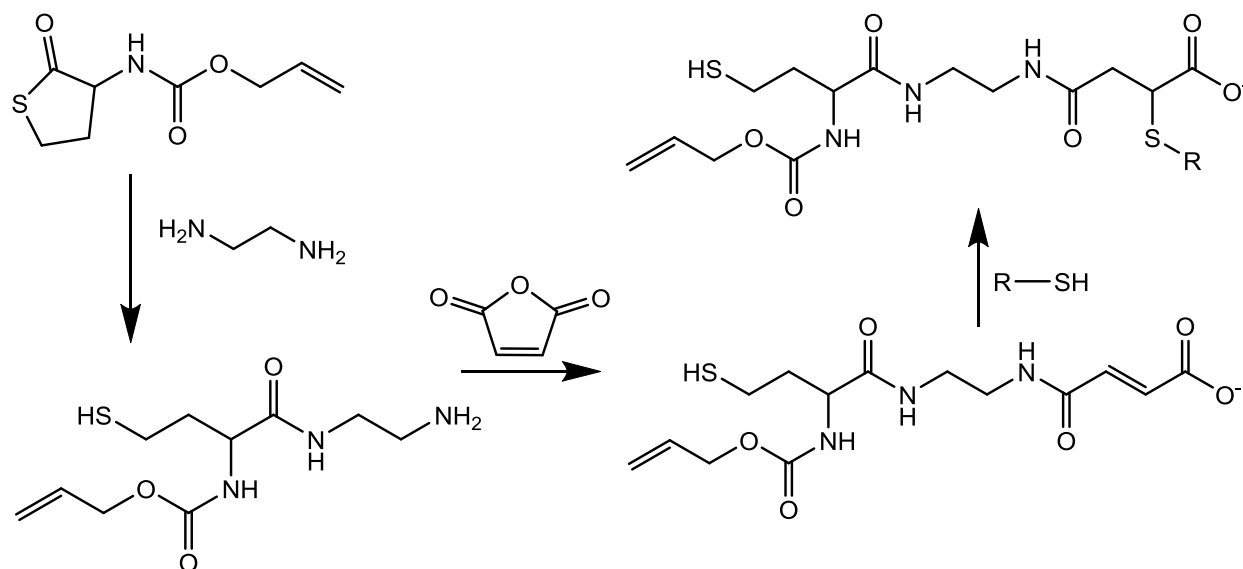
Scheme 6.2. General scheme of the reaction of Alloc-TL with 1,2-diaminoethane, followed by reaction with maleic anhydride and a thiol compound.

Although the final product could be obtained, the lack of control over the reaction of the diamine resulted in several side-products, such as the diamine combined with two equivalents of the thiolactone. It was not possible to control the reaction of the diamine with the thiolactone and maleic anhydride by adjusting the stoichiometry alone. Alternatively, a reaction of maleic anhydride with a diamine was attempted first, followed by a reaction of residual amine groups with the Alloc-TL. However, the same issue of side-products with the diamine was encountered and this approach was not pursued further, since the objective was to synthesize polyampholytes with controlled structures.

Therefore, a third strategy of introducing a carboxylic acid group into thiol-ene polymers was proposed, which involved simple hydrolysis of the thiolactone moiety under basic conditions (Scheme 6.3). Although this strategy is the simplest one and resulted in 100% ring-opening of the thiolactone, the disulfide dimer species formed concurrently under the basic conditions.
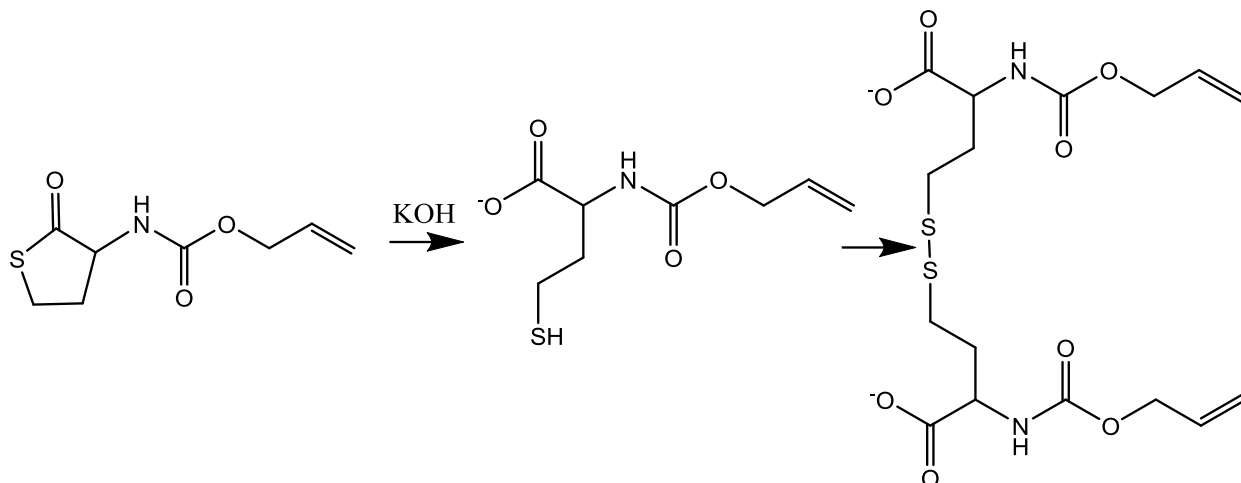
Scheme 6.3. General scheme for the ring-opening of Alloc-TL under basic conditions.

Thus, the final fourth strategy was successfully adopted, since it included the greatest control over the functionality of the polymer, which was achieved using an AB' thiolactone monomer with maleamic acid side chain. *N*-maleamic acid homocysteine thiolactone monomer **(MA-Tl)** has been synthesized in high yield (>70%) by a one-step addition reaction between D,L-homocysteine thiolactone hydrochloride and maleic anhydride (Scheme 6.4 (i)) with further details described in the Materials and methods section.

Preparation of the polyampholytes via amine-thiol-ene conjugation, starting with a thiolactone-containing monomer, involves two steps that occur sequentially in water in one pot and at room temperature (Scheme 6.4 (ii) and (iii)). First, the thiolactone ring is opened by aminolysis, which can be done with a variety of primary amine compounds. Second, the released thiol reacts with the double bond in the *N*-substituted homocysteine thiolactone by nucleophilic Michael addition, which results in step-growth addition polymerization. Activated electron-deficient double bonds, such as maleimides and maleates are known to readily react with thiols, especially under basic catalysis.[23,24]
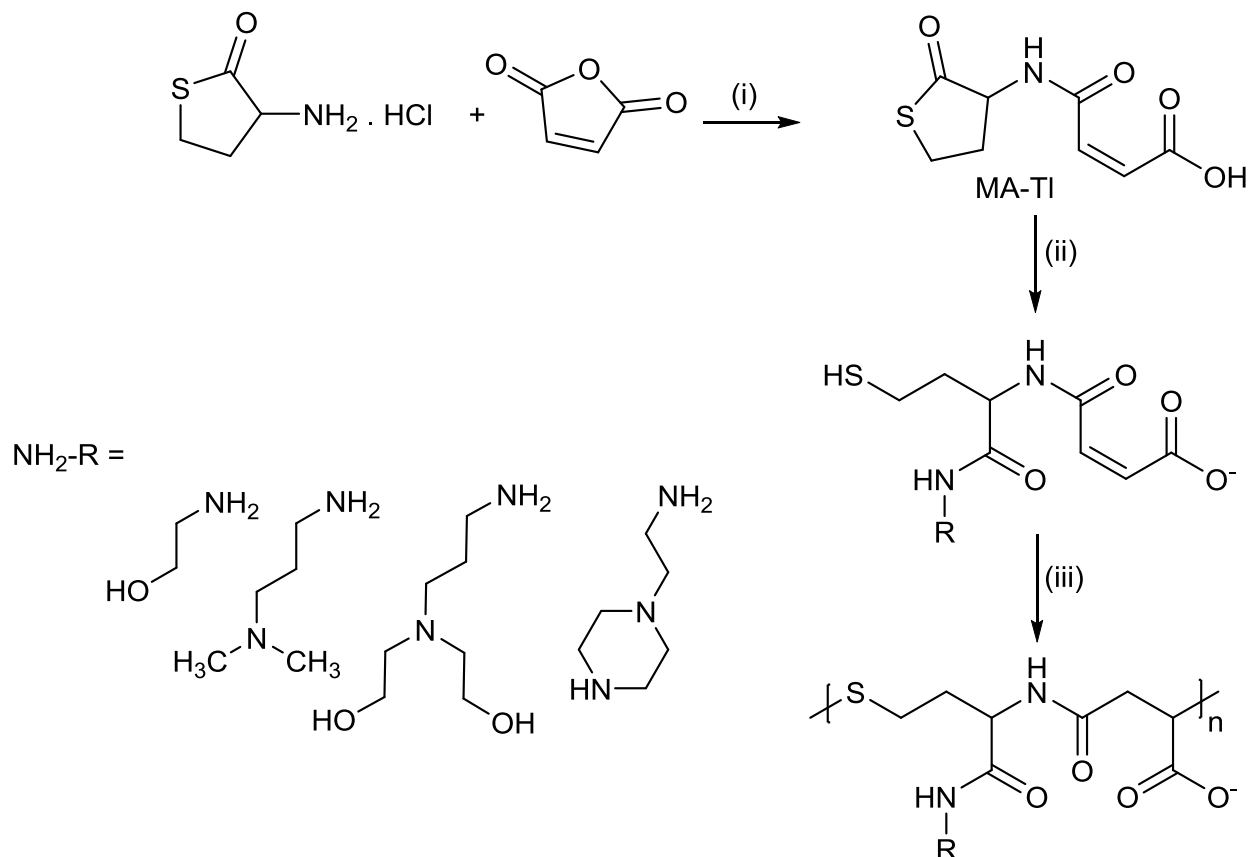
Scheme 6.4. Strategy used for the synthesis of polyampholytes: (i) synthesis of N-maleamic acid-functionalized homocysteine thiolactone monomer using maleic anhydride in water at room temperature; and one-pot formation of polyampholytes via (ii) thiolactone ring-opening with different R functionalized amines (i.e.: ethanolamine, 3-(dimethylamino)-1-propylamine, 1-(2-aminoethyl) piperazine, N-(3-aminopropyl)diethanolamine) in water at room temperature and subsequent (iii) step-growth thiol-ene polymerization in the same pot.

The functional groups and resulting net charge of the polymer is controlled via the choice of amine compound, as well as the ratio of the monomer to amine. For example, addition of ethanolamine to **MA-Tl** forms a polymer that can carry a negative charge, which is generated by the carboxylic acid groups at high pH. Alternatively, addition of 3-(dimethylamino)-1-propylamine creates positively charged groups due to the presence of the tertiary amine, which becomes protonated at low pH. The net charge of the resulting polymer can be controlled by adjusting the pH of the solution, which also affects polymer conformation.

6.3 Characterization of polyampholytes prepared by thiolactone chemistry

The presence of cationic and anionic groups in the polyampholyte structure determines in which range of pH the polyampholyte will be soluble. Various ionic polymers were prepared using **MA-Tl** and different amine compounds (Table 6.1). The amine-thiol-ene reaction sequence was investigated by NMR spectroscopy (Figure 6.2). The aminolysis of the thiolactone moiety was confirmed by the formation of a new proton signal at 1.98-2.11 ppm, which corresponds to the β proton of the ring-opened thiolactone.

Table 6.1. Polymers prepared by amine-thiol-ene conjugation with different functional groups.

Code	Amine	M_n^a(Da)	$Đ^a$	M_n^b(Da)	pI^c	T_{CP}^d
PA1	ethanolamine	3 750	2.0	12 450	-	9
PA2	3-(dimethylamino)-1-propylamine	2 350	2.8	10 200	7.1	23
PA3	1-(2-aminoethyl) piperazine	2 050	3.3	9 300	8.1	32
PA4	*N*-(3-aminopropyl) diethanolamine	1 250	1.8	4 050	7.9	5

[a] *Determined by aqueous SEC using dextran standards.*
[b] *Calculated from end-group (double bond) protons in ^1H NMR spectra in D_2O.*
[c] *Isoelectric points (pI) determined by potentiometric titration using HCl and NaOH.*
[d] *Cloud point temperature observed at 50% transmittance of 20mg/mL polymer solutions in water/ethanol (30/70 %vol) at pH=7.*

The consumption of the carbon-carbon double bonds during polymerization was confirmed by the disappearance of the proton peaks at 5.8-6.4 ppm (Figure 6.3). Both the aminolysis and the thiol-ene reactions were monitored online by ^1H NMR. Both reactions reached 96% conversion after 3 hours at room temperature (Figure 6.4). Finally, the polymers were purified by precipitation from the aqueous solution using acetone.

The ring opening of the thiolactone moiety was also confirmed by FTIR spectroscopy, which indicated a disappearance of the absorbance peak at 1696 cm^{-1}, associated with the thioester carbonyl of the thiolactone and the formation of a new peak at 1644 cm^{-1}, associated with the amide carbonyl of the aminolysis product (Figure 6.2).
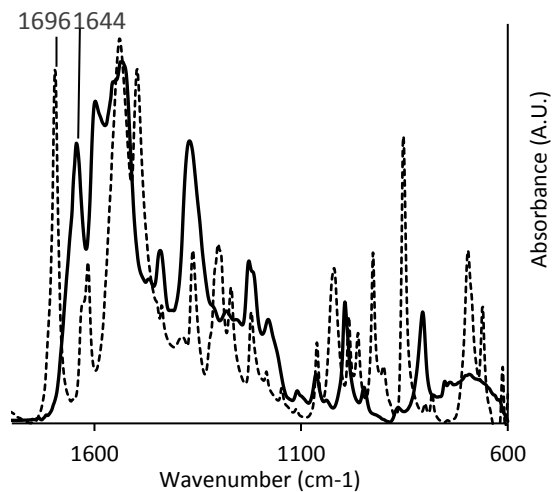
Figure 6.2. FTIR spectra of N-maleamic acid homocysteine thiolactone monomer (dashed line) and polymer prepared from N-maleamic acid homocysteine thiolactone and 3-(dimethylamino)-1-propylamine (solid line).
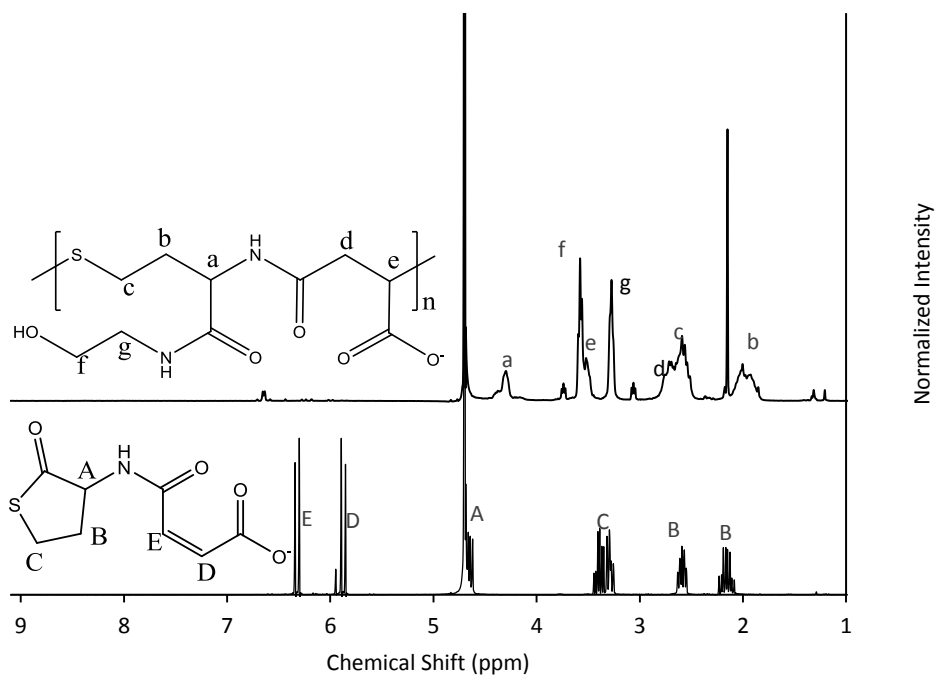

Figure 6.3. ^{1}H NMR spectra of ML-Tl (bottom) and PA1 polymer prepared from MA-Tl and ethanolamine (top) in D_2O.
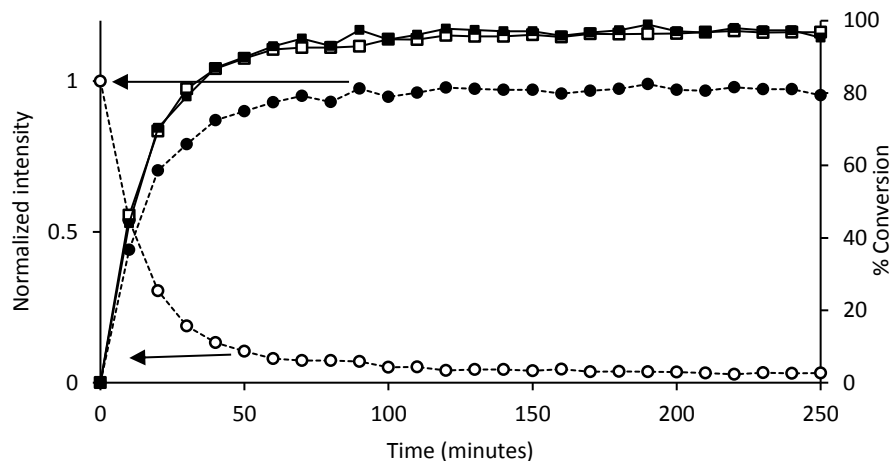
Figure 6.4. Kinetics of the amine-thiol-ene reaction monitored for PA1, --●—relative peak intensity of the thiolactone ring proton (1.98-2.11ppm), --o-- relative peak intensity of the double bond protons (5.8-6.4ppm), −□− % conversion of the thiolactone-ring opening by aminolysis, −■− % conversion of the thiol-ene reaction.

Polymer molecular weights were determined by SEC and carbon-carbon double bond end-group analysis by ^{1}H NMR (Table 6.1). The molecular weights of polyampholytes in Table 6.1 are experimentally estimated values with accuracy limited by the measurement techniques and conditions, such as the intermolecular and intramolecular interactions of the ionic side-chains of the polyampholytes in different solvents. As expected, the values for M_n and M_w obtained by SEC were lower than those determined from the ^{1}H NMR calculations, since polyampholyte chains are tightly coiled in solutions at pH values that are close to their isoelectric points, which coincides with the neutral pH used for the analysis. The polyampholytes exhibited dispersities in the range of 1.8-3.3, which are similar to the dispersities of other polymers prepared via amine-thiol-ene conjugation and step-growth addition polymerization.[25] Polyampholytes prepared via controlled radical polymerization techniques typically manifest lower dispersities. For example, reversible addition-fragmentation chain transfer (RAFT) copolymerization of cationic and anionic monomers produced polyampholytes with dispersities in the range of 1.24-1.34.[4] However, preliminary kinetic studies of the reactivity of the different monomers and subsequent adjustment of their feed ratio was necessary to obtain charge neutral polyampholytes.

6.4 Properties of polyampholytes prepared by thiolactone chemistry

6.4.1 Isoelectric points

The isoelectric points (pI) of the polyampholytes (Table 6.1) were determined by potentiometric titration (Figure 6.5-6.8). The potentiometric analysis showed that the isoelectric points of the polyampholytes varied between 6.9 and 8.1, depending on the choice of the functional group.

Moreover, all the polyampholytes tested remained fully dissolved in the range of pH=2-12. The high solubility of alternating polyampholytes over a broad pH range is characteristic of the interactions between the adjacent ionic groups, which inhibits complete charge compensation within the polyampholyte that is typically associated with insolubility. The higher solubility of polyampholytes with alternating versus random structure has been predicted theoretically by Wittmer et al.[22] The alternating arrangement of cationic and anionic groups results in shorter range intermolecular Coulomb interactions due to the influence of adjacent oppositely charged groups. Shorter range interactions of alternating polyampholytes inhibit aggregation and formation of polymer globules.[26]
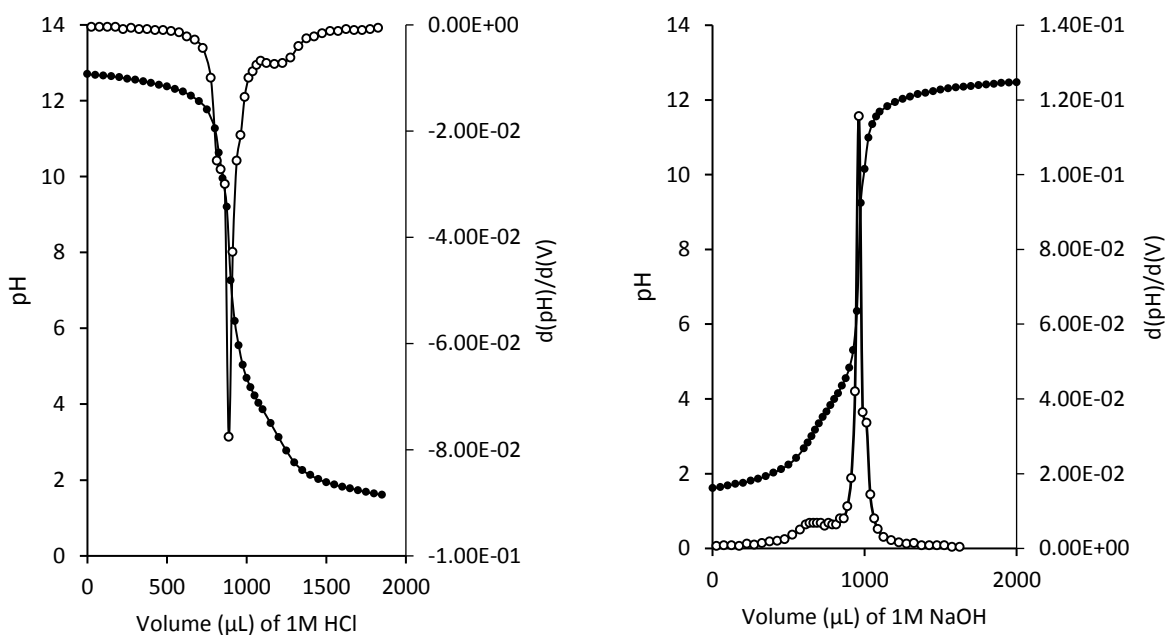
Figure 6.5. Potentiometric titration curves and first differentials of PA1 polyampholyte, prepared from N-maleamic acid homocysteine thiolactone and ethanolamine.
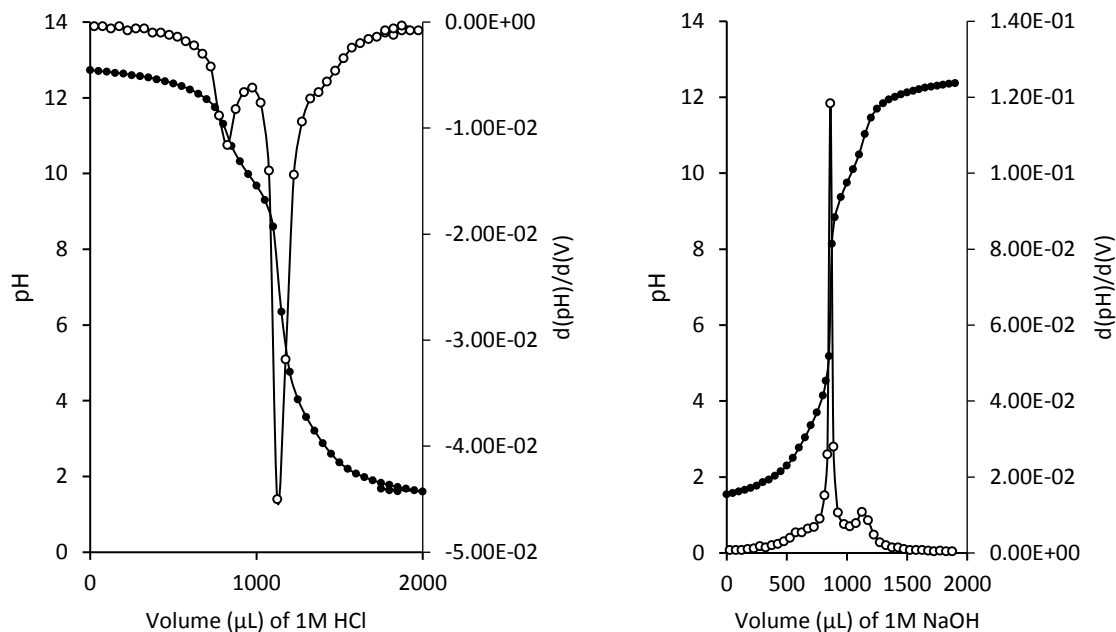
Figure 6.6. Potentiometric titration curves and first differentials of PA2 polyampholyte, prepared from N-maleamic acid homocysteine thiolactone and 3-(dimethylamino)-1-propylamine.
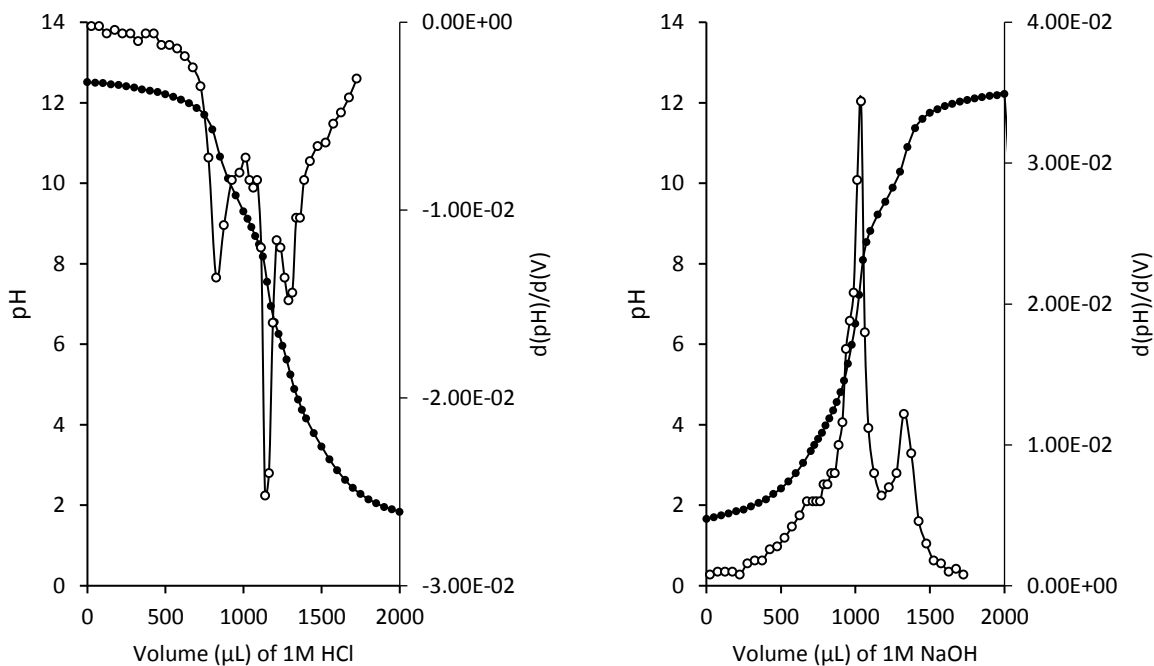

Figure 6.7. Potentiometric titration curves and first differentials of PA3 polyampholyte, prepared from N-maleamic acid homocysteine thiolactone and 1-(2-aminoethyl) piperazine.
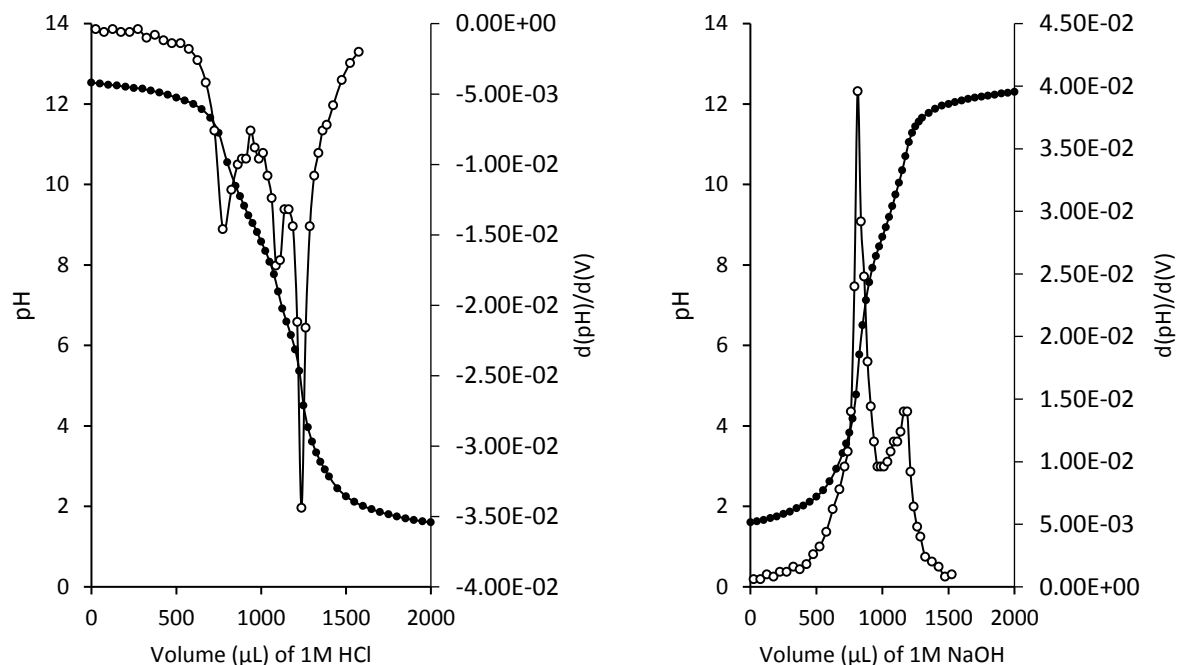
Figure 6.8. Potentiometric titration curves and first differentials of PA4 polyampholyte, prepared from N-maleamic acid homocysteine thiolactone and N-(3-aminopropyl) diethanolamine.

6.4.2 Turbidity

The high solubility of the alternating polyampholytes prepared from thiolactone derivatives was also reflected in the turbidity of polyampholytes in aqueous solutions at pH~7 with different salt concentrations (Figure 6.9). All the polyampholyte solutions tested remained transparent at [NaCl]=0-1 M and temperatures between 25 and 80°C (Figure 6.9). The concentration of polyampholytes in solution was 10 mg/mL, which is 100 times higher than in a previous study of polyampholyte turbidity (0.1 mg/mL), which demonstrated significant turbidity and polymer precipitation under different conditions of pH and ionic strength.[2]
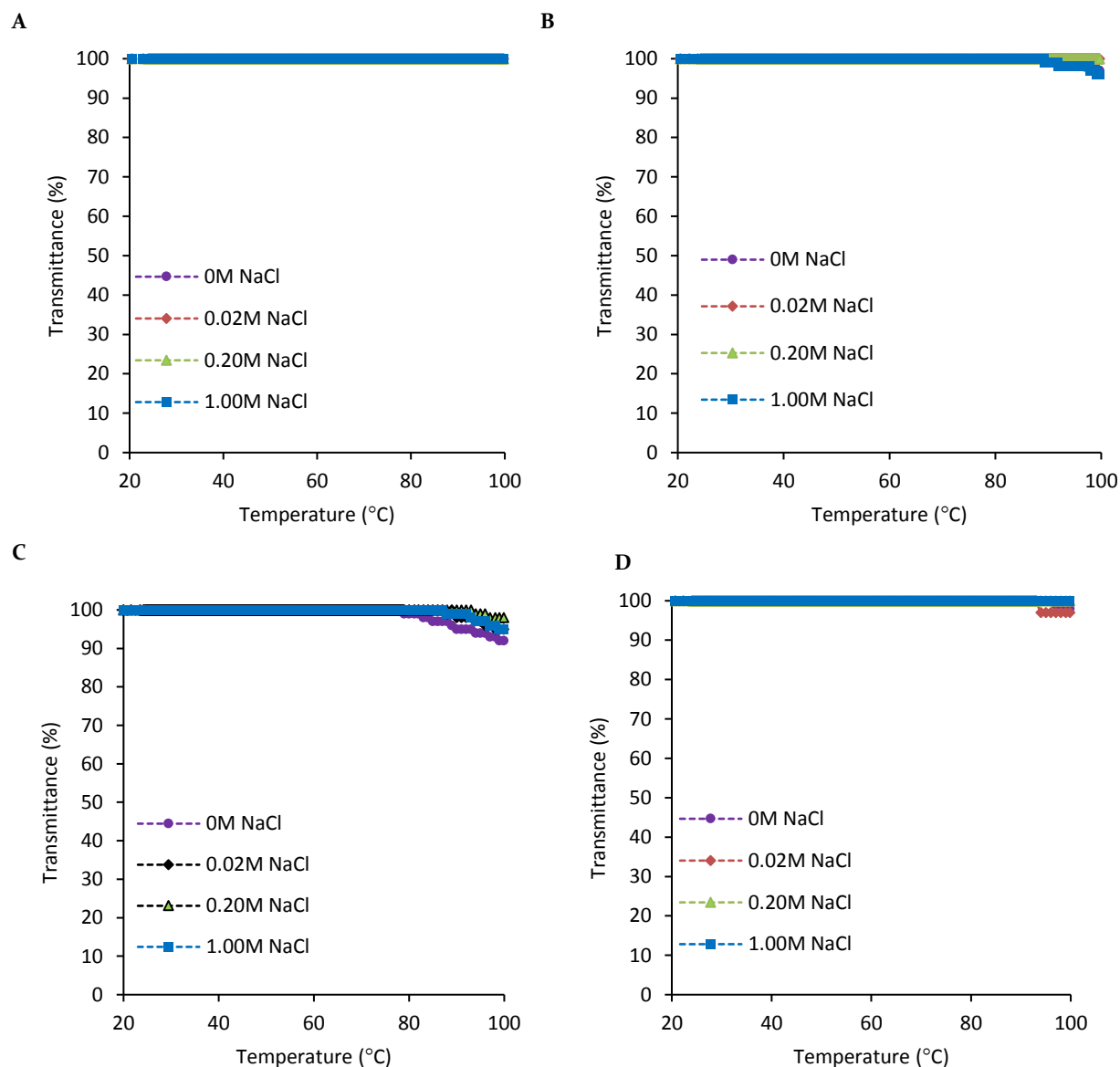
*Figure 6.9. Transmittance of aqueous solutions composed of N-maleamic acid homocysteine thiolactone and different amines: ethanolamine, PA1 (**A**), 3-(dimethylamino)-1-propylamine, PA2 (**B**), 1-(2-aminoethyl) piperazine, PA3 (**C**), N-(3-aminopropyl)diethanolamine, PA4, (**D**).*

The polyampholyte solution with PA2 exhibited a decrease in transmittance above 80°C, which was more pronounced without any added NaCl. The suppression of turbidity by NaCl is in accordance with the anti-polyelectrolyte effect, which is characteristic of polyampholytes. The anti-polyelectrolyte effect is exhibited by the polymer chain expansion at their isoelectric point due to the screening of intermolecular charge interactions.[1]

6.4.3 Thermoresponsive behaviour and UCST

The thermoresponsiveness of UCST polymers typically arises from the strong supramolecular interactions between the polymer functional groups. These interactions are sensitive to the nature of the solvent, presence of salts, the molecular weight and concentration of the polymer.[3] Since polyampholytes intrinsically have strong intermolecular interactions, they are suitable candidates for UCST thermoresponsive behaviour. The alternating polyampholytes synthesized using thiolactone chemistry were highly soluble in water in a wide range of pH values, as discussed previously. Therefore, a less polar solvent mixture was selected to study the thermoresponsive behaviour, namely water/ethanol mixture, which was also employed for the study of UCST behaviour of polyampholytes by Zhang *et al.*[4]

The polyampholytes with different functional groups introduced by thiolactone aminolysis exhibit UCST thermoresponsive behavior in water/ethanol (30/70 %vol) solutions (Figure 6.10). Intermolecular interactions of polyampholytes in a globule conformation render them insoluble, but upon heating, the intermolecular interactions are disrupted and polyampholytes adopt a coil conformation, which has higher solubility.
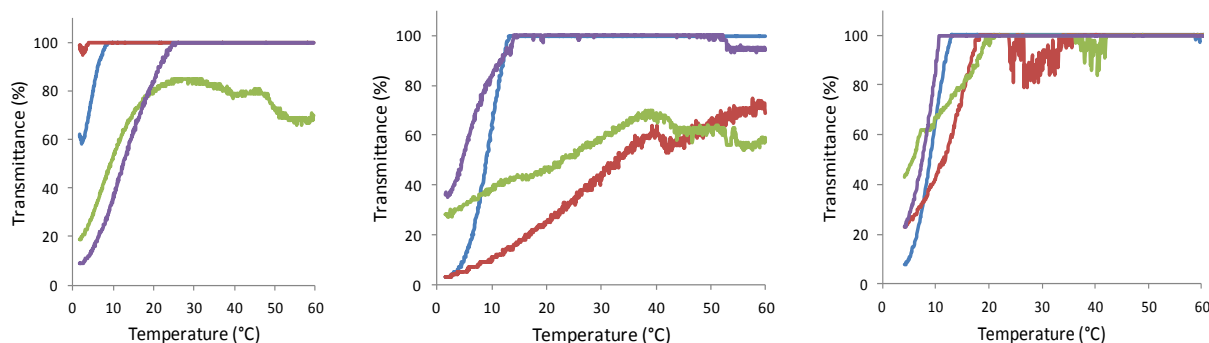

Figure 6.10. Transmittance of polyampholytes PA1 (blue), PA2 (red), PA3 (green), PA4 (purple) in water/ethanol 30/70 at pH=6 (left), pH=7 (center), pH=8 (right).

The cloud point temperatures (T_{CP}) at 50% transmittance of the polyampholytes were in the range of 5-32 °C (Table 6.1). PA1 and PA4 contained hydroxyl functionalities and the resulting

hydrogen bonding interactions were less strong than ionic interactions. Therefore, the cloud points for PA1 and PA4 were significantly lower compared to the polyampholytes PA2 and PA3, with a high content of ionic groups, which render stronger intermolecular interactions than hydrogen bonding.

At neutral pH, the polyampholytes PA2 and PA3 are close to their pI, which is associated with tightly coiled or globular polymer chain conformations and poor solubility. Consequently, PA2 and PA3 exhibit broad transitions in transmittance at pH=7 and limited solubility even at elevated temperatures, as expected for polyampholytes close to their pI. On the other hand, PA2 and PA3 exhibit sharper transitions at pH8 and higher solubility at elevated temperatures (> 30 C).

In contrast, PA4 contains multiple hydroxyl functionalities and consequently exhibits sharper transitions and higher solubility at all the pH values investigated. Therefore, the presence of hydroxyl groups has a significant effect on the thermoresponsive behaviour of polyampholytes and can be used in combination with the strong ionic interactions in order to tune the resulting properties.
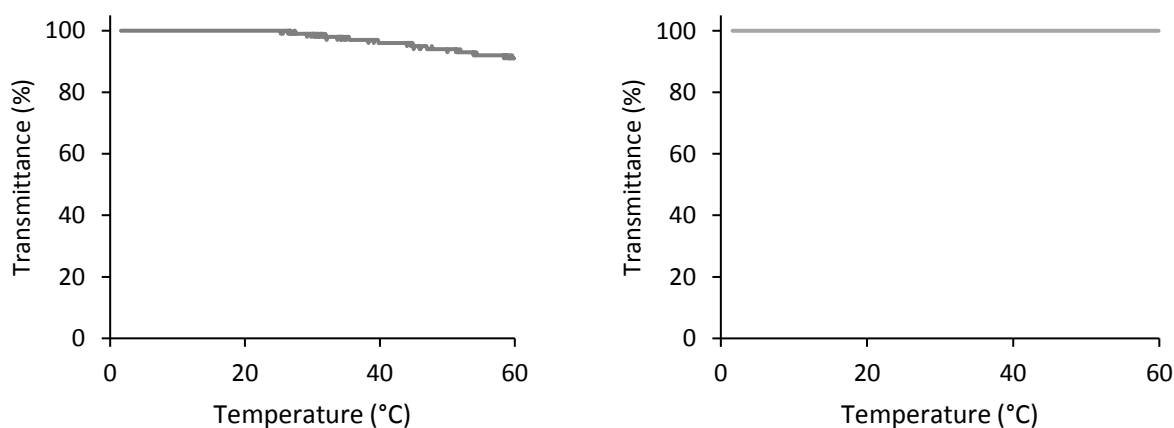

Figure 6.11. Transmittance of polyampholytes PA1 (blue) and PA2 (red) in water at pH=7.

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The turbidity of polyampholyte solutions at different temperatures was also measured in water at pH=7, which is more amenable to physiological conditions and potential biomedical research. However, the polyampholytes did not exhibit UCST behaviour in water, which is exemplified by the turbidity measurements of PA1 and PA2 polyampholytes (Figure 6.11) Similar results were obtained for all of the polyampholytes in this study, which is in accordance with the previous results that alternating polyampholytes have a high solubility in water (Figure 6.9).

 In the future, the thiolactone chemistry approach could be used to prepare polyampholytes with different side chains in order to tailor the T_{CP} and the sharpness of the UCST transition. Different structure-property relationships could be investigated, such as the effect of the pKa and polarity of the side chain, as well as the relative amount and distribution of the ionic groups.

6.5 Conclusion

Thiolactone chemistry has opened up a new route for the preparation of a variety of polyampholytes in a simple and sustainable way. The control over the alternating structure of polyampholytes has been efficiently achieved using amine-thiol-ene conjugation in one pot and at room temperature, in addition to incorporating different functional groups. The high solubility of polyampholytes over a wide temperature and concentration range is a unique characteristic of the alternating structure, which is advantageous for utilization of polyampholytes under a broad variety of conditions.

These alternating polyampholytes exhibit UCST thermoresponsive behavior, which further expands their interest for future research in the fields ionic polymers, gels, and stimuli-responsive polymer materials. In addition, the side-chains of the alternating polyampholytes could be further functionalized and their properties tailored towards applications, such as ice crystal inhibition.[11] Most importantly, the improvements in sustainability of the polyampholyte preparation via thiolactone chemistry is an important development for promoting the growth of polyampholyte applications.

6.6 Materials and methods

6.6.1Materials

1-(2-aminoethyl)piperazine (99%), bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride (≥95.0%), citraconic anhydride (98%), 3-(dimethylamino)-1-propylamine (99%), DL-homocysteine thiolactone hydrochloride (≥99.0%), (2-dodecen-1-yl)succinic anhydride (95%), ethanolamine (≥99.0%), itaconic anhydride (95%), maleic anhydride (99%), *N*-(3-aminopropyl)diethanolamine, sodium bicarbonate (≥99.7%), tryptamine (98%), β-Alanine (99%) were purchased from Sigma-Aldrich and were used as received. *N*-(3-aminopropyl)diethanolamine (>90.0%) was obtained from Tokyo Chemical Industry (TCI) and used as received.

6.6.2 Synthesis of N-maleamic acid homocysteine thiolactone monomer

DL-Homocysteine thiolactone hydrochloride (23 g, 0.15 mol, 1.0 equiv.) was dissolved in 50 mL water and 50 mL ethyl acetate in a round-bottom flask. The mixture was cooled to 0 °C and sodium bicarbonate 33.6 g (0.4 mol, 2.6equiv.) was added. Maleic anhydride 19.7 g (0.2 mol, 1.3 equiv.) as concentrated solution in acetone was added dropwise under vigorous stirring. The reaction mixture was stirred for 3 hours while warming up to room temperature. The reaction mixture was acidified with 6 M hydrochloric acid (pH < 4) and stirred for additional 30 minutes. The product precipitated upon acidification and was filtered off. The white, crystalline powder was rinsed with 20 ml water and dried under reduced pressure. The final product yield was 70 %. $C_8H_9NO_4S$ (215.02523 g/mol) HR-MS: $(M+H)^+$ (theoretical): 215.22636. $(M+H)^+$ (experimental): 215.02531. ^{1}H NMR (300 MHz, d6-DMSO, ppm) δ 8.98 (d, 8.1, 1H), 6.30 (m, 2H), 4.70 (m, 1H), 3.42 (m, 1H), 3.33 (m, 2H), 2.11 (m, 1H); ^{13}C NMR (125 MHz, d6-DMSO, ppm) δ 205.4 (C), 166.8 (C), 165.6 (C), 132.5 (CH), 130.5 (CH),58.8 (CH),30.6 (CH_2), 27.5 (CH_2).

6.6.3 General procedure for polyampholyte preparation

N-maleamic acid homocysteine thiolactone (4 mol, 860 mg) was dispersed in 6 mL water, resulting in a white solution. The solution was placed on ice for 10 minutes. $NaHCO_3$ (6 mmol, 504 mg) was combined with 10 mL water and added dropwise to the monomer solution and stirred until it became clear. Ethanolamine was added (6.4 mmol, 384 µL). The solution was stirred overnight at room temperature. The resulting polymer was precipitated with acetone and the supernatant was decanted. The polymer was a white powder and was dried under vacuum.

^{1}H NMR (300 MHz, D_2O, ppm) δ 4.30 (m, 1H), 3.57 (dd, 6.0, 2H), 3.51 (m, 1H), 3.27 (dd, 6.0, 2H), 2.71 (m, 2H), 2.58 (m, 2H), 1.96 (m, 2H) ; ^{13}C NMR (125 MHz, D_2O, ppm) δ 178.51 (C), 173.70 (C), 173.41(C), 60.10 (CH2), 53.20 (CH), 41.60 (CH2), 41.47 (CH2), 38.62 (CH), 30.79 (CH2), 27.19 (CH2).

6.6.4 Characterization

FTIR spectra were recorded in ATR mode on a Perkin-Elmer Spectrum1000 FTIR infrared spectrometer by obtaining 16 scans for each sample.

Nuclear magnetic resonance spectra were recorded on a Bruker AVANCE 300 MHz and 500 MHz spectrometer at room temperature using D_2O or d6-DMSO as solvent.

Potentiometric titrations were conducted on a Mettler Toledo S20 pH meter. Sample containing 100 mg dry polymer is dispersed in 10 mL of 0.1 M NaOH and equilibrated by stirring for 2 hours. Samples were titrated with 1 M HCl in 50µL aliquots until pH~2 and then back-titrated with 1 M NaOH in 50µL aliquots until pH~12.

Turbidity measurements were performed on Technobis Crystal16 multiple-reactor system with temperature controlled 16-sample holder for standard HPLC glass vials (1.5 mL volume). Sample solutions of 10 mg/mL polymer in deionized water adjusted with HCl or NaOH to a specific pH were heated and cooled at a rate of 1°C/min while continuously stirring at 700 RPM. Transmittance at 600 nm was measured. The cloud points were determined from the temperature

associated with 50% transmittance of 20 mg/mL polymer solutions in water/ethanol (30/70 %vol) at neutral pH.

Size exclusion chromatography (SEC) was conducted in phosphate buffer pH=7 using Waters instrument with 410 detector and two SB-806M HQ columns and dextran standards.

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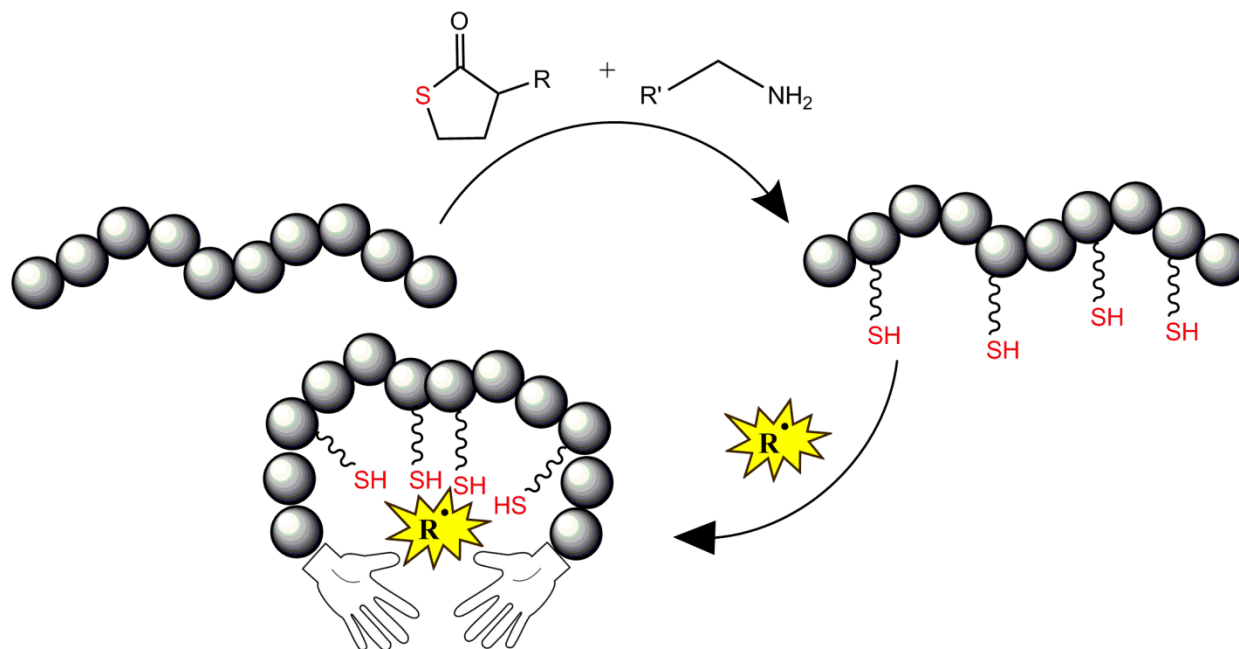
Abstract

Thiol-containing radical inhibitors were prepared from thiolactone-derivatives. Different primary amine compounds were used to open the thiolactone ring by aminolysis, thereby releasing a free thiol group. The antioxidant efficiency of the thiolactone-based derivatives was evaluated employing the 2,2-diphenyl-1-picrylhydrazyl (DPPH•) assay. The greatest antioxidant efficiency was obtained for the trifunctional thiol compound prepared using tris(2-aminoethyl)amine and 3 molar equivalents of *DL-N*-acetyl homocysteine thiolactone.

Next, thiolactone chemistry was used to functionalize maleic anhydride copolymers with thiols in order to generate macromolecular radical inhibitors. The functionalized polymers also exhibited radical inhibition capacity, which could be useful for potential applications in polymer master-batch stability additives. The thiolactone chemistry approach is a powerful technique for introducing thiol groups into a variety of molecular and polymer systems, which has expanded the versatility of radical inhibitors.

Chapter 7. Bio-inspired polymer-bound radical inhibitors prepared by thiolactone chemistry

## 7.1 Introduction and theoretical background

Natural antioxidants, such as glutathione,[1] are essential components in cells and provide protection from radical damage. In addition, there is a variety of synthetic antioxidants, such as butylated hydroxytoluene (BHT), which is widely added to many products to avoid degradation and spoilage.[2] Extensive comparative evaluations of different antioxidants have been carried out in terms of their antioxidant capacity, stoichiometry, and kinetics [3-5].

Many characteristics, such as antioxidant reactivity, stability, solubility and toxicity are important considerations for applications of antioxidants as additives in food, cosmetics, or materials. For example, hydrophilic antioxidants, such as Vitamin C have different solubility parameters than hydrophobic antioxidants, such as Vitamin E, which would be pertinent considerations for product development. Since different applications require specialized antioxidants, there is a need for development of tailored antioxidant compounds to meet specific requirements.

Thiol-containing compounds are known to inhibit radicals, such as the naturally occurring glutathione and cysteine.[1] Indeed, thiols can quench radical species, such as superoxide radicals, $O_2^-\bullet$ and $HO_2\bullet$, by forming a more stable R-S$\bullet$ species that subsequently forms a disulfide dimer (Scheme 7.1).[6]

The reactivity of thiol compounds can vary significantly depending on the substituent effects, including steric, pH, charge, and hydrogen bonding influences [5]. Therefore, understanding thiol reactions with radicals is both a challenge and an opportunity to develop different types of radical inhibitors and antioxidants. Herein, the distinction in terminology is made regarding radical inhibitors that quench radical species, versus antioxidants, which is a broad term used for substances that prevent oxidation reactions. Therefore, previous research on antioxidants and antioxidant analytical methods are applied in this work, but the focus is on studying radical

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inhibition by thiols using the stable radical 2,2-diphenyl-1-picrylhydrazyl (DPPH•), which has been used extensively in analytical chemistry[12] and will be described in detail later in this chapter.
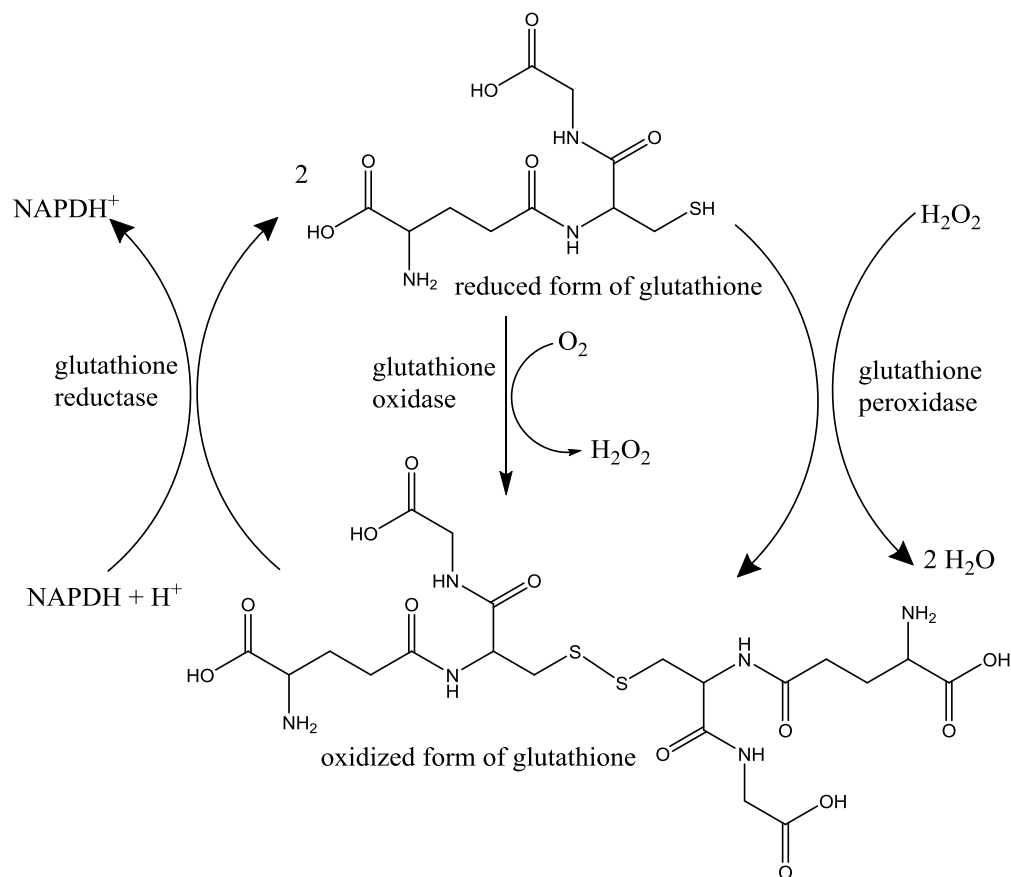
Scheme 7.1. Quenching of a radical species by glutathione (reduced form) and subsequent formation of the disulfide species of glutathione (oxidized form).[7]

Chemical modification of common antioxidant moieties, such as catechol or thiol is an alternative approach for enhancing the various properties of antioxidants in an efficient manner. For example, a series of prenylated phenol derivatives has been synthesized for radical scavenging applications, since the natural terpenyl phenols can only be isolated in very low yields.[8]

Another challenge in the effectiveness and sustainability of existing antioxidants is the migration of antioxidants and their degradation by-products into goods, especially food. Undesired chemical migration results in the loss of radical inhibition and poses health concerns. To address

the issue of antioxidant migration, antioxidants have been covalently bound to polymers, while maintaining their activity.[9-10] For example, 3,5-di-t-butyl-4-hydroxy-benzoyl chloride was reacted with hydroxyl groups of the hydroxyethyl methacrylate and butyl methacrylate copolymer for lubricant applications.[9] Polymer-bound p-phenylenediamine antioxidant showed improved aging resistance and reduced volatility, which is promising for stabilization of rubber products [10]. Chemical modification of antioxidants is typically necessary for subsequent reaction with polymer functional groups. Achieving a high efficiency of polymer modification with antioxidants, while maintaining antioxidant activity is challenging, especially on a large scale.

7.2 Research objectives

The objective of this work is to employ thiolactone chemistry to develop multifunctional thiolated radical inhibitors that can be covalently bound to polymers. The radical inhibition of thiolactone-based species is unknown to date, including the effect of different functional groups. Since thiols have different pKa's, which can be influenced by substituents, the radical inhibition process can also be significantly influenced. Therefore, several natural and commercially available thiol compounds will be compared in terms of their reactivity towards the DPPH• radical.

Inspired by the glutathione antioxidant in cells, which scavenges radicals via the thiol group, we will use biobased, commercially available D,L-homocysteine thiolactone hydrochloride as the starting material for radical inhibitors. Simple and upscalable synthetic routes based on amine-thiol-ene conjugation[11] will be utilized to incorporate different functional groups and thereby impart different properties to the radical inhibitors. The chemical structure and functionality of these radical inhibitors can be varied to achieve different radical inhibition capacity, kinetics, and molecular properties (solubility, melting point, etc.).

The antioxidant activity of the thiolactone derivatives will be evaluated by the DPPH• assay. [12] The objective is to systematically compare the antioxidant activity of the different thiolactone derivatives and the effect of different functional groups.

Thiolactone-based radical inhibitors were covalently bound to maleic anhydride copolymers and their antioxidant activity was evaluated. High loadings of covalently bound radical inhibitors in

polymers were achieved with multifunctional thiolactone chemistry, which could be used as master batch additives to polymer blends. Instead of chemically modifying existing antioxidants, the thiolactone moiety has been used as a bio-based source of the thiol radical inhibitor functionality that can be combined with a variety of other functional and polymeric matrices.

7.3 DPPH free radical assay

The DPPH free radical assay was used to evaluate radical inhibition, since it has a long history of use for both natural and synthetic antioxidants.[10] The DPPH• assay is conducted by combining a DPPH• solution with an antioxidant solution at different concentrations and measuring the absorbance of the DPPH• radical over time (Figure 7.1).
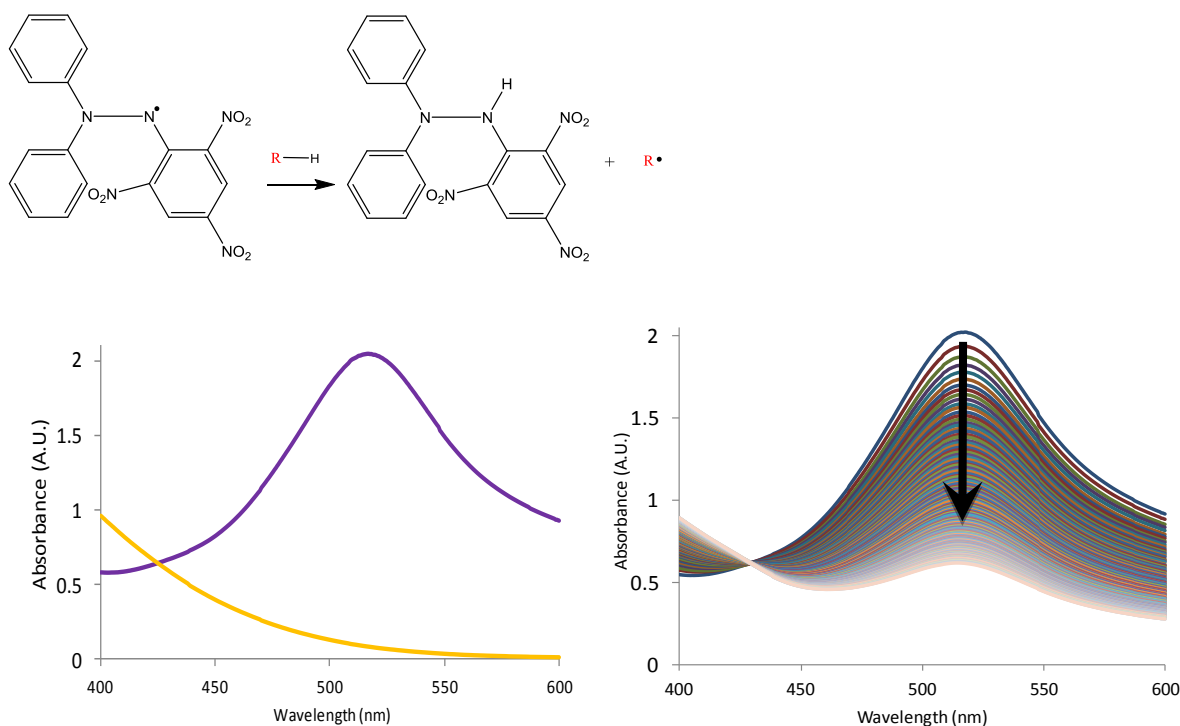
Figure 7.1. UV-Vis absorbance of the DPPH• (purple) and the reduced DPPH species (yellow) (left)[11]. Monitoring of the absorbance of DPPH• over time in 60 second intervals in the presence of glutathione, (right).

The maximum absorbance of DPPH• species occurs at 515 nm and once the radical is consumed, a reduction in this absorbance is observed. However, the reduced DPPH species has a non-zero absorption at 515 nm, which is observed by the isosbestic point at approximately 435 nm. Therefore, the DPPH• test was conducted at different antioxidant concentrations until a steady state was reached.

The results of the radical inhibition efficiency are typically described by the EC_{50} index, which is the concentration of antioxidant required to reduce 50% of DPPH•. The associated time at the steady state is referred to as TEC_{50}, which reflects the rate of reaction with the free radical. Since both the concentration of antioxidant species required, as well as the speed of radical inhibition are important parameters, a combined measure of antioxidant efficiency (AE) is used, $AE=1/(EC_{50} \times TEC_{50})$.[12]

7.4 Comparison of existing thiol radical inhibitors

The objective of comparing different existing thiol compounds for radical inhibition activity was to evaluate the effect of different substituents on the reactivity of thiols towards the DPPH• radicals. Glutathione is a powerful natural antioxidant, however, it has a complex structure that cannot be easily obtained using synthetic means at a low cost. Therefore, simpler thiol-containing structures were designed using *DL-N*-acetyl homocysteine thiolactone and different amine compounds.

Octanethiol was used as a model compound without any electron-withdrawing or electron-donating substituents. The reaction of octanethiol with DPPH• radical is relatively slow, since it requires 28 minutes to reduce the concentration of DPPH• in half (from 150µM to 75 µM) under equimolar conditions of DPPH• and the antioxidant (Figure 7.2). On the other hand, thioglycolic acid and cysteine exhibit a fast reaction rate with the DPPH• radical, resulting in the complete reduction of DPPH• in less than 8 minutes.
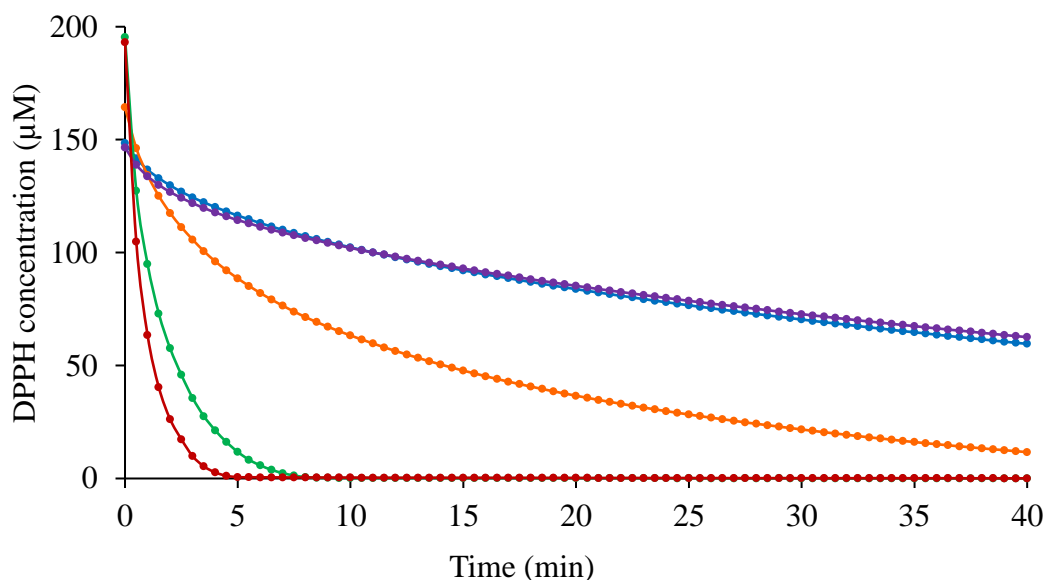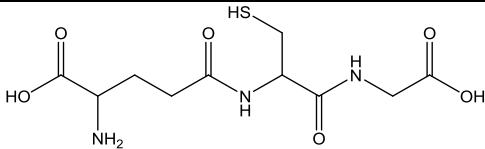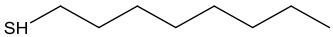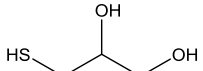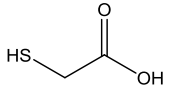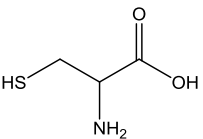
Figure 7.2. DPPH• concentration over time, in the presence of different thiol-containing compounds: glutathione (blue), 1-octanethiol (purple), thioglycerol (orange), thioglycolic acid (green), cysteine (red).

Table 7.1 provides a summary of the AE values of the common naturally occurring and synthetic thiol compounds (Table7.1). The molecular weights are provided for comparison, since for additive applications, smaller molecular weight with the comparable antioxidant efficiency would be preferable. All of the molecules in Table 7.1 contain a single thiol group, however, they display significantly different AE values. Although the thiol group is responsible for quenching radical species, as illustrated in Scheme 7.1, the substituent groups also play a role.

The reactivity and pKa values of thiols are known to be affected by the substituent effects, such as electron withdrawing or electron donating groups. [14] For example, Singh and Whitesides reported differences in the rate of thiol-disulfide interchange as a result of steric, acidic, charge, and hydrogen bonding substituent effects.[15] In this context, the reactivity of substituted thiol molecules with radical species also varies.

For example, among the molecules investigated, thioglycolic acid exhibited the highest AE, (8.77 μM^{-1} min^{-1}), while 1-octanethiol exhibited the lowest AE, (0.15 μM^{-1} min^{-1}). The carboxylic acid group is present in both thioglycolic acid and cysteine and it affects the dissociation constant (pKa) of the thiol functionality. The pKa determines the proportion of the thiol (SH) moiety to the thiolate anion (S⁻), which is more reactive. The cysteine thiol has pKa= 8.2, while glutathione thiol has pKa=9.2.[13] In a neutral solution, the species with a lower thiol pKa will have a greater proportion of the thiolate anion present compared to a species with a higher thiol pKa.[15] When substituted thiols preferentially exist in the thiolate form, they tend to react more readily with a radical.

Table 7.1. Natural and commercial thiol compounds and their antioxidant activity, concentration of antioxidant required to reach half of DPPH• concentration (EC₅₀), time required to reach EC₅₀ at steady state (TEC₅₀), antioxidant efficiency AE.

Chemical name	Structure	Molar mass (g/mol)	EC_{50} (µM)	TEC_{50} (min)	AE (10^{-3}) (μM^{-1} min^{-1})
glutathione		307	220	29	0.16
1-octanethiol		146	609	11	0.15
thioglycerol		108	158	12	0.55
thioglycolic acid		92	57	2	8.77
cysteine		121	98	10	1.02

7.5 Comparison of radical inhibitors prepared by thiolactone chemistry

Radical inhibitors were prepared from *DL-N*-acetylhomocysteine thiolactone (ACTLa) and different primary amine compounds in order to investigate if there is any effect of the functionality of the amine on the radical inhibiting activity of the thiols (Figure 7.3).
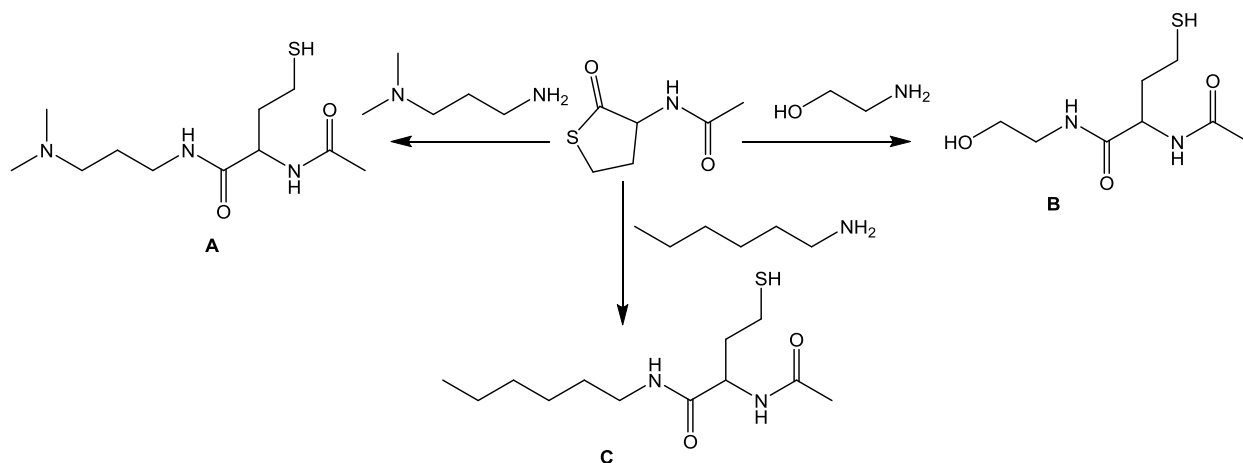

Figure 7.3. Thiol-containing compounds prepared from ACTla and different amine compounds: hexylamine (left), ethanolamine (center), 3-(dimethylamino)-1-propylamine (right).

The preparation of thiol-containing radical inhibitors from ACTla involves addition of a primary amine compound, which undergoes nucleophilic addition with the thiolactone moiety thereby releasing a free thiol group. The formation of the amide addition products was confirmed by ^{1}H NMR (Figure 7.4-7.6) and ESI LC-MS (Figure 7.7-7.9). The main products obtained were the expected amides with a free thiol group, however a small amount of the disulfide dimer was also detected by LC-MS as exemplified by peaks with m/z values double of the product (Figure 7.7-7.9). The product of the aminolysis of ACTla with a primary amine was observed to have three types of impurities: unreacted ACTla, unreacted amine, and the disulfide dimer of the addition product of ACTla and amine. These impurities do not contain free thiols or additional functional groups that could interfere with the DPPH• assay. The precursors used in this study, including ACTla and different amines, were tested using DPPH• assay and they did not reduce DPPH• concentration, meaning that these precursors did not have antioxidant effects. Further optimization of the synthesis could include varying the ratios of amine and thiolactone, using disulfide cleaving agents, adjusting pH, and conducting the reaction under anaerobic conditions

(not done because of time constraints). The focus of this work is to conduct a proof of concept that thiolactone-based compounds can be used as radical inhibitors and absolute purity of these compounds is not necessary to detect radical inhibiting activity.
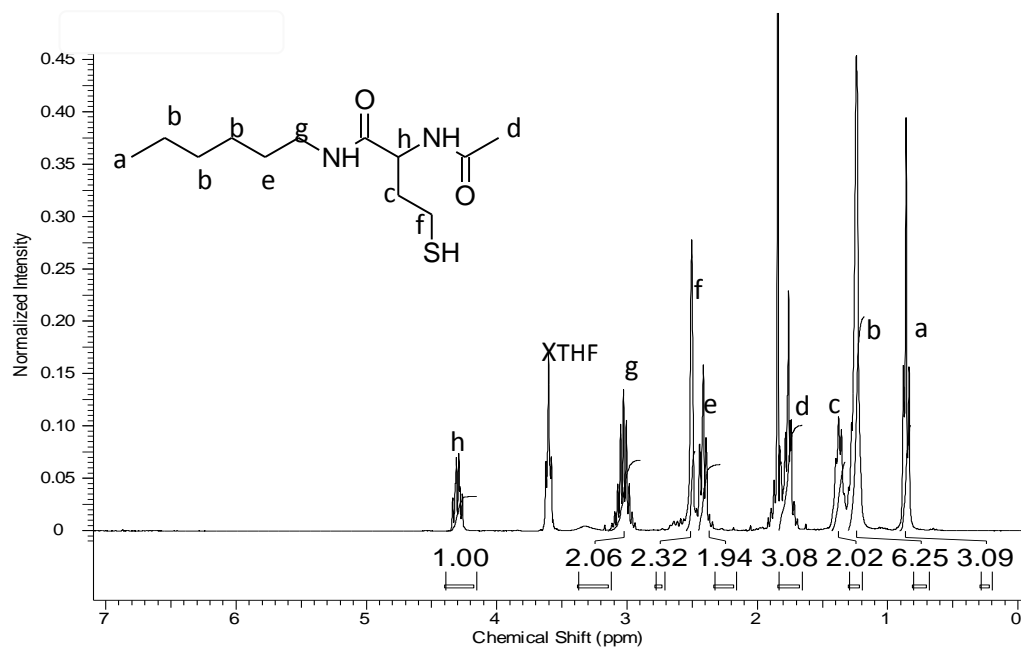

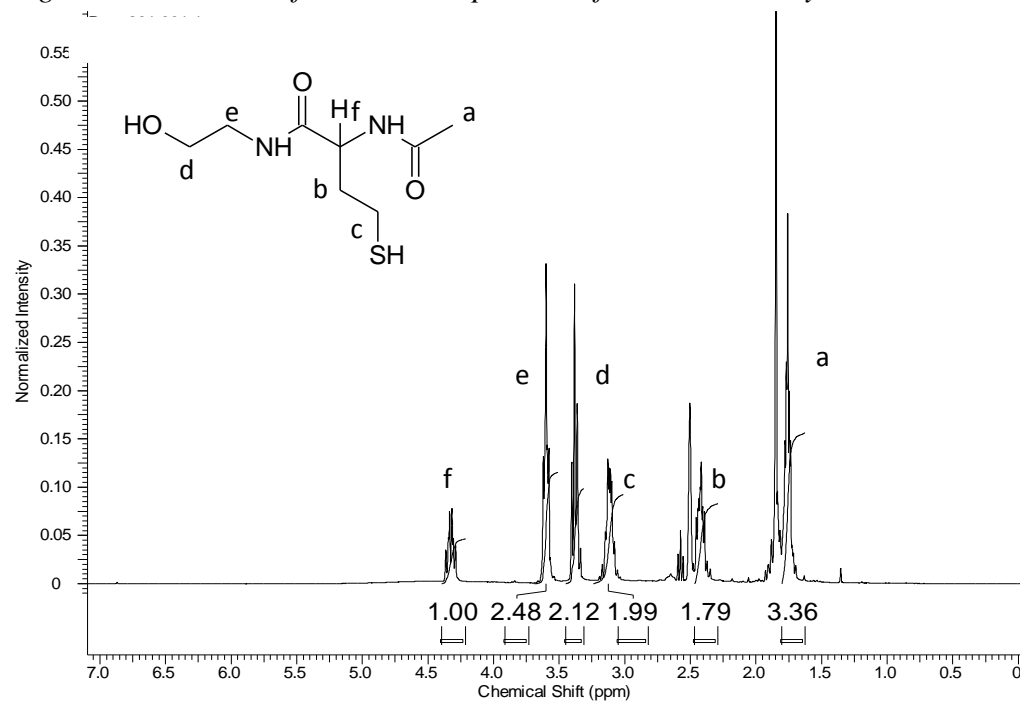*Figure 7.4. ${}^1H$ NMR of the addition product of ACTla and hexylamine in d6-DMSO.*

Figure 7.5. ${}^1H$ NMR of the addition product of ACTla and ethanolamine in d6-DMSO.
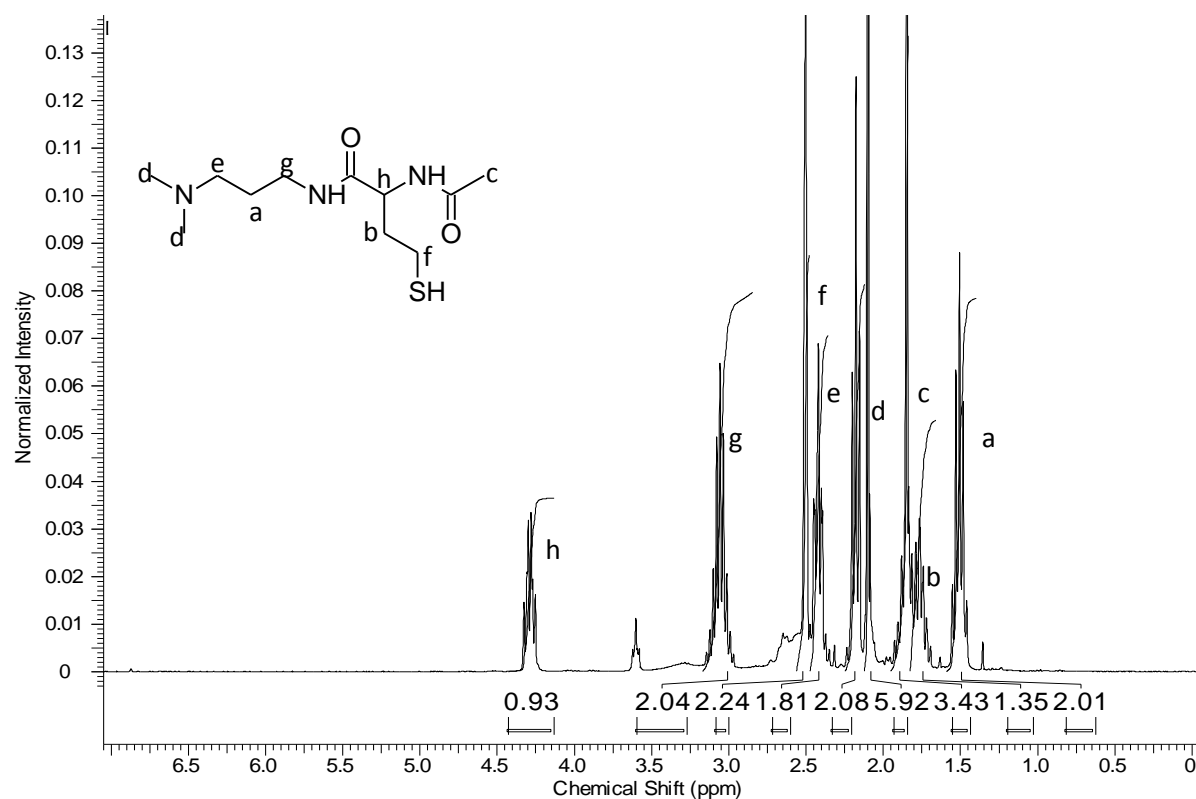
Figure 7.6. ^{1}H NMR of the addition product of ACTla and 3-(dimethylamino)-1-propylamine in d6-DMSO.

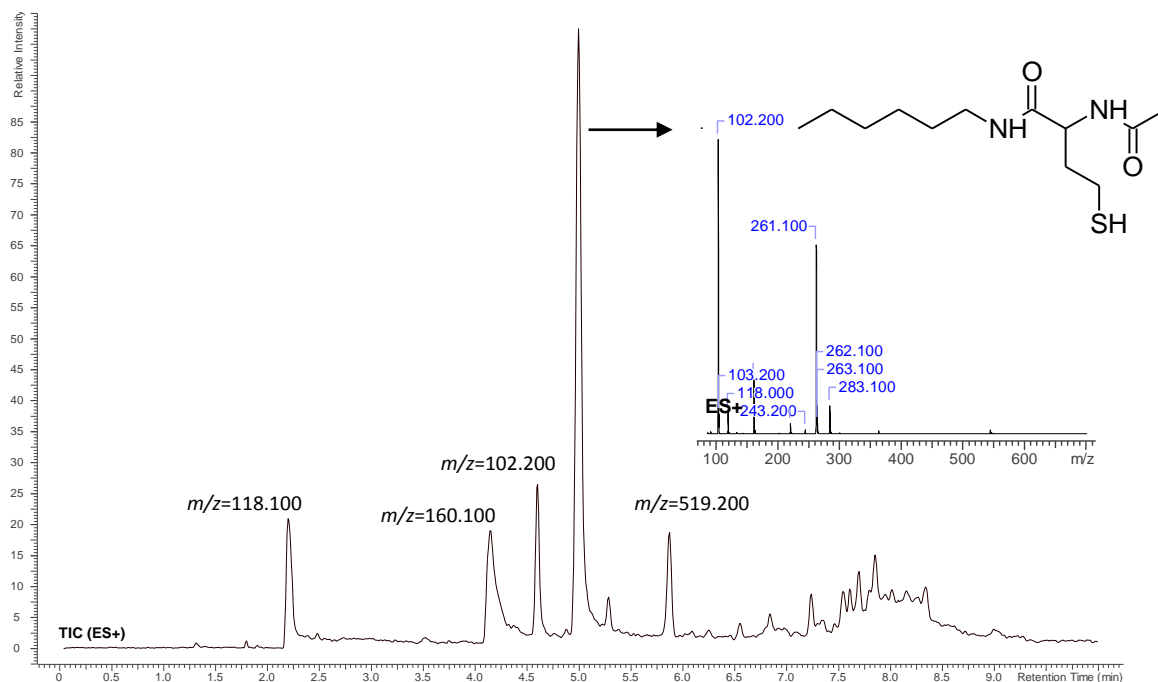*Figure 7.7. ESI LC-MS of the addition product of ACTla and hexylamine (m/z=261.100), hexylhydroxylamine (m/z=118.100), ACTla (m/z=160.100), hexylamine (m/z=102.200), dimer of the product of ACTla and hexylamine (m/z=519.200).*
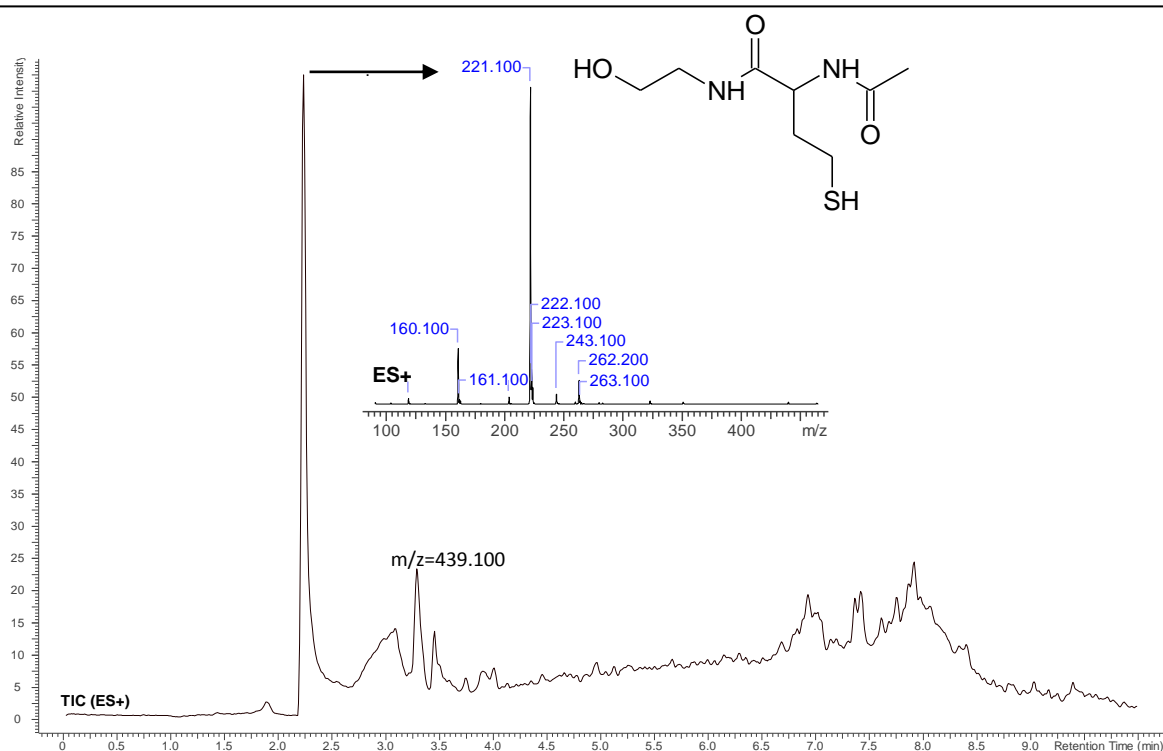
Figure 7.8. ESI LC-MS of the nucleophilic addition product of ACTla and ethanolamine (m/z=221.100) and the disulfide dime of the product (m/z=439.100).
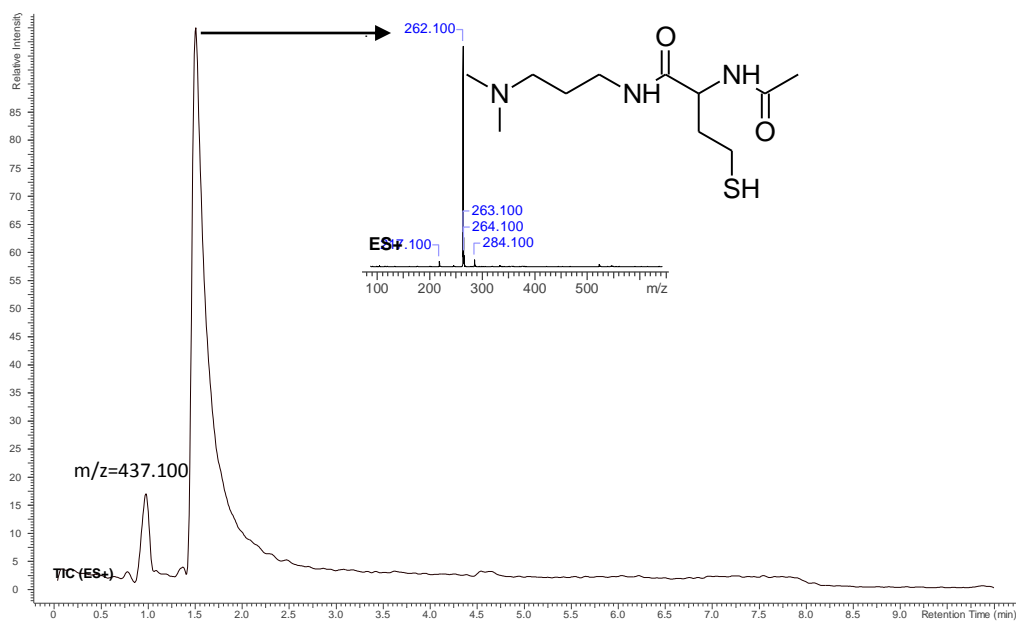

Figure 7.9. ESI LC-MS of the nucleophilic addition product of ACTla and 3-(dimethylamino)-1-propylamine (m/z=261.384).

The conversion of the thiolactone thioester into an amide by aminolysis with different amine compounds was also confirmed by FTIR spectroscopy (Figure 7.10). The absorption band at 1688 cm^{-1} corresponds to the thioester carbonyl of the thiolactone moiety. After the addition of an amine compound, the thioester band was replaced by the amide carbonyl absorbance at 1650 cm^{-1} due to the ring-opening of the thiolactone by an amine and the formation of an amide adduct.
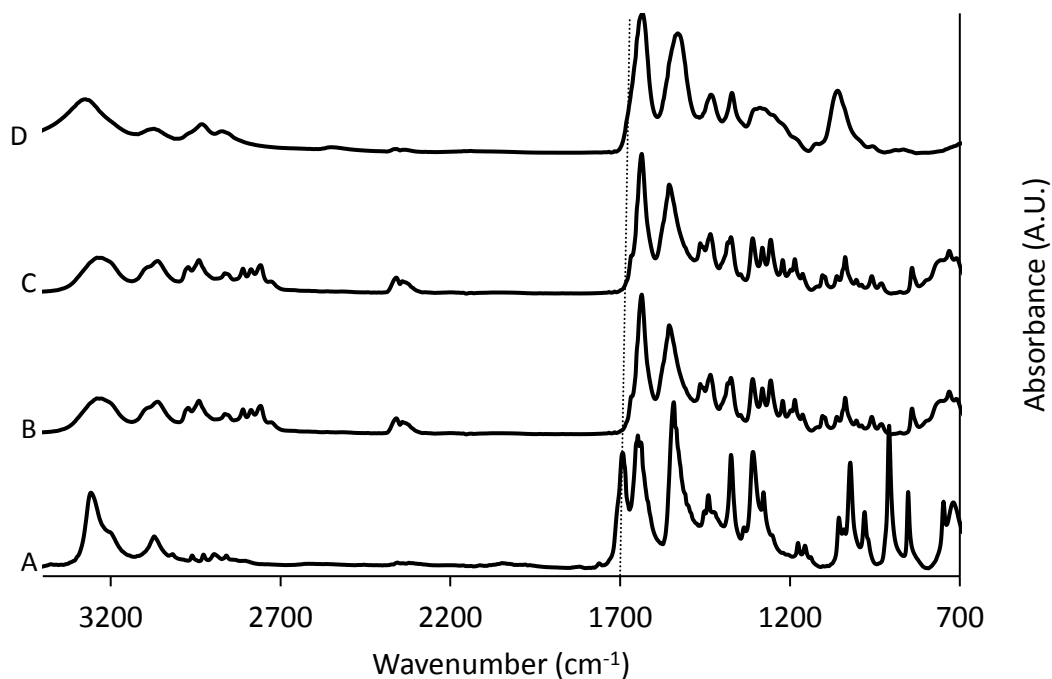

Figure 7.10. FTIR spectra of ACTla (A) and the aminolysis product of ACTla with hexylamine (B), 3-(dimethylamino)-1-propylamine (C), ethanolamine (D). The dotted line illustrates the 1688 cm^{-1} absorption band, which corresponds to the thioester carbonyl of the thiolactone moiety.

The efficiency of radical inhibition of the thiolactone-based compounds was investigated by the standard DPPH• assay, which was used to generate EC$_{50}$ (µM), TEC$_{50}$ (min.), and the overall antioxidant efficiency, AE (µM^{-1} min^{-1}). The EC$_{50}$ was calculated from the slope and intercept of the plot of the radical inhibitor concentration versus the % of the DPPH• remaining at the steady state during the reaction of the radical inhibitor with the DPPH• (Figure 7.11). The TEC$_{50}$ was calculated from the slope and intercept of the plot of the radical inhibitor concentration versus

the time taken to reach steady state during the reaction of the radical inhibitor with the DPPH•
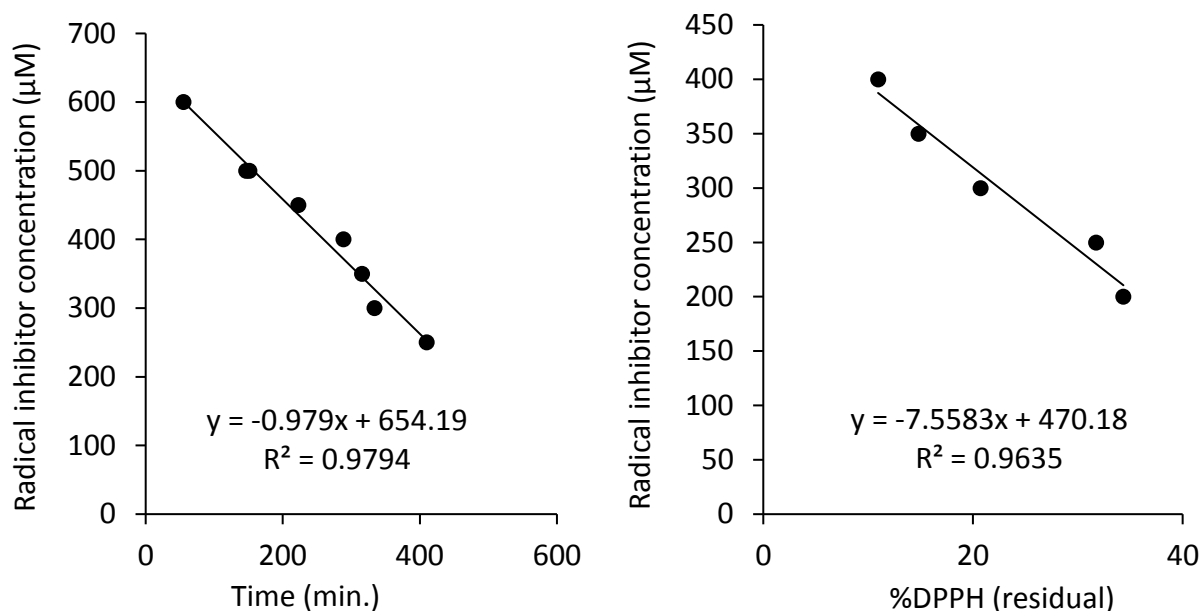(Figure 7.11).

*Figure 7.11. Representative plots and trend lines used to determine EC_{50} (μM), TEC_{50} (min.),
and the overall antioxidant efficiency, AE (μM^{-1} min^{-1}) for the radical inhibitor prepared from
ACTla and hexylamine.*

Both plots have negative slopes since the concentration of radical inhibitor is inversely
proportional to the time at steady state and DPPH• concentration at steady state, meaning that a
higher radical inhibitor concentration will require less time to lower DPPH• concentration and
will yield a lower final DPPH• concentration. Therefore, multiple concentrations of a radical
inhibitor need to be tested in order to obtain EC_{50}, TEC_{50} and the antioxidant efficiency.

The effectiveness of radical inhibitors depends on their kinetics of reactions with free radicals,
which is reflected by TEC_{50} as well as the stoichiometry of the reaction, which is reflected by the
EC_{50} (μM). Antioxidants with lower EC_{50} and TEC_{50} are more effective, since they inhibit
radicals on a shorter time scale and at lower concentrations. Therefore, the overall antioxidant
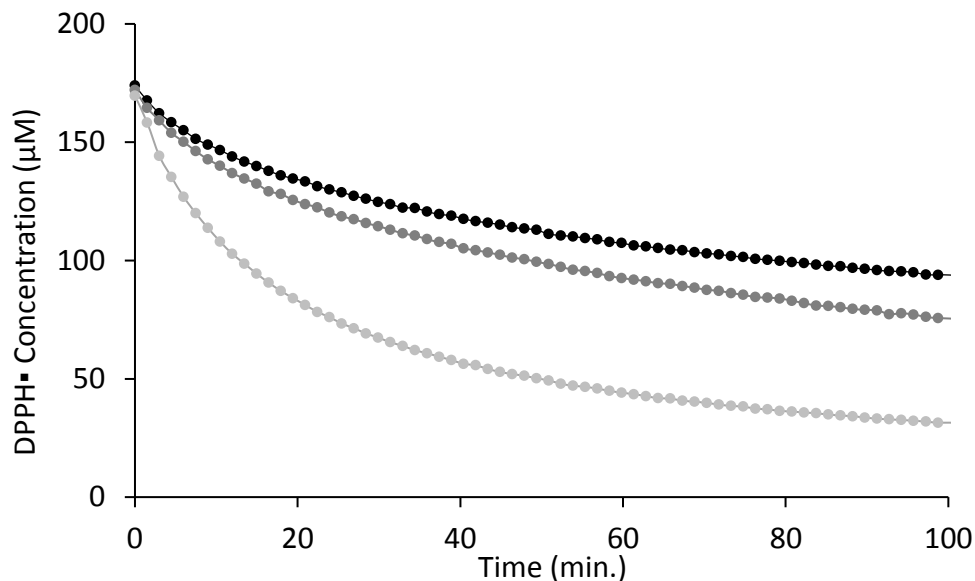efficiency is calculated to reflect both EC_{50} and TEC_{50}.

Figure 12. DPPH• concentration over time, in the presence of equimolar amounts of different thiol-containing compounds prepared from ACTla and different amine compounds: hexylamine (black); ethanolamine (grey); 3-(dimethylamino)-1-propylamine) (light grey).

The radical inhibitors prepared from ACTla and different amine functional groups exhibited slightly different inhibition capacities and kinetics. The highest antioxidant efficiency was observed for the radical inhibitor containing the 3-(dimethylamino)-1-propylamine) functional group, which can induce an electron withdrawing effect, thereby altering the pKa and reactivity of the thiol group (Table 7.2).

Table 7.2. Radical inhibitors prepared from different amine compounds and ACTla.

Component #1	Component #2	Molar ratio (#1:#2)	Molar mass (g/mol)	EC_{50} (μM)	TEC_{50} (min)	AE (10^{-3}) (μM^{-1} min^{-1})
ACTla	hexylamine	1:1	261	114	11	0.80
ACTla	ethanolamine	1:1	219	109	11	0.85
ACTla	3-(dimethylamino)-1-propylamine	1:1	261	117	10	0.89

In addition, thiolactone chemistry was used to prepare di, tri-functional thiols using di, tri-functional amine compounds (Figure 7.13), which are commercially available in order to compare with the monofunctional thiol compounds prepared previously (Figure 7.3). The structures of the radical inhibitors with several thiol groups were confirmed by ^{1}H NMR (Figure 7.14 and 7.15).
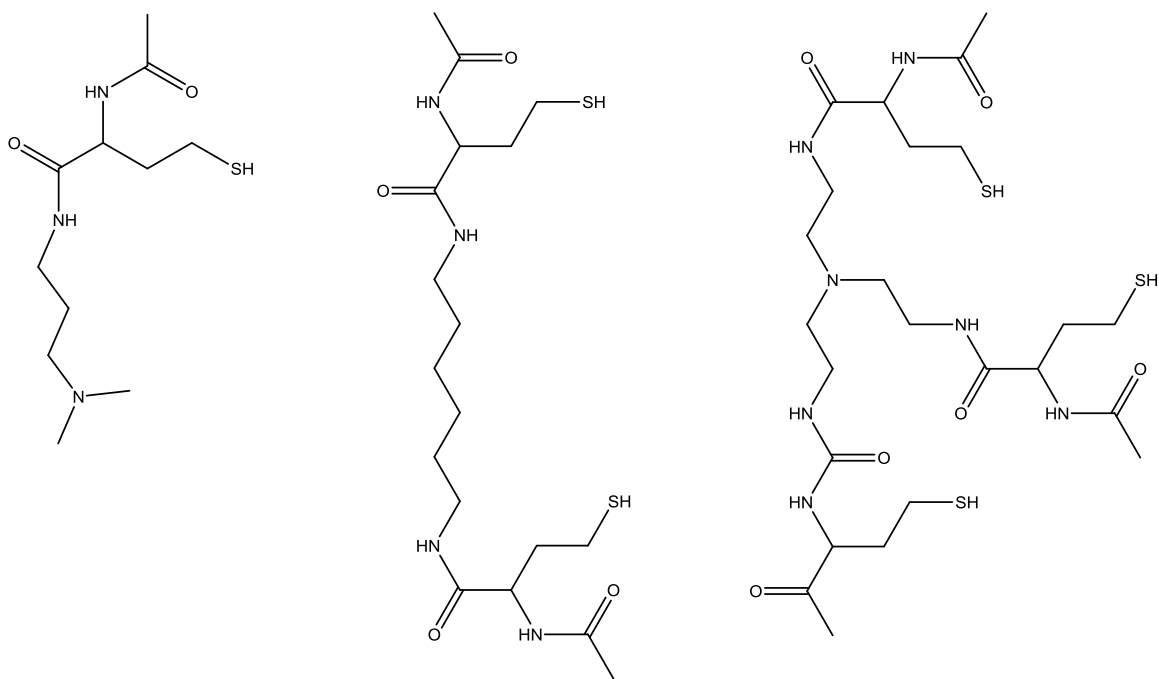

Figure 7.13. Thiol-containing compounds prepared from ACTla and different amines: 3-(dimethylamino)-1-propylamine (left), hexamethylenediamine (center), tris(2-aminoethyl)amine (right).

The presence of several thiol groups in a radical inhibitor is expected to increase the antioxidant efficiency. However, additional intramolecular effects of polythiols are possible, such as intramolecIlar disulfide bond formation. Therefore, molecules with two or three thiol groups will not necessarily have antioxidant efficiencies two or three times greater than monofunctional thiols. The following investigation is aimed at evaluating the antioxidant efficiency of molecules with multiple thiol groups.
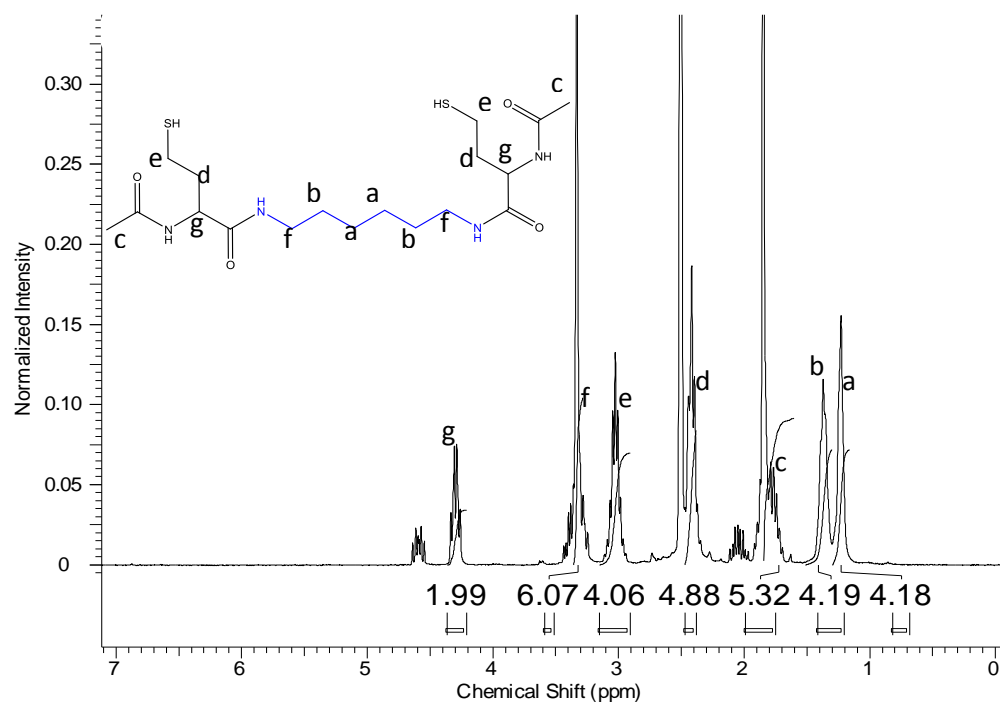
Figure 7.14. ^{1}H NMR of the addition product of ACTla and hexamethylenediamine in 2:1 molar ratio in d6-DMSO.
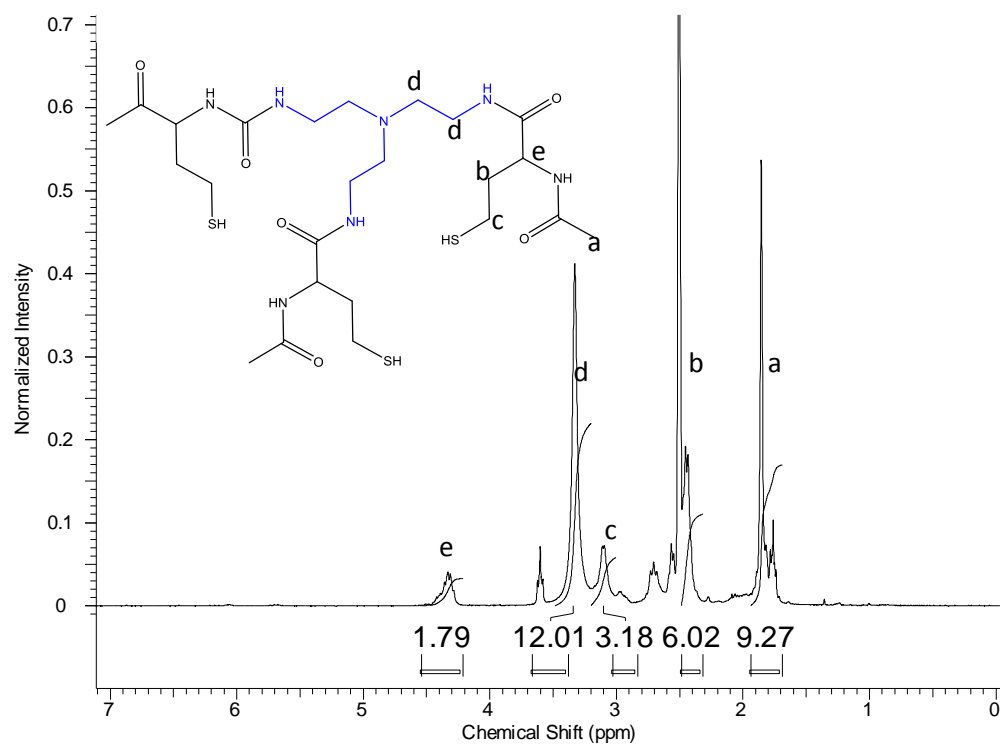

Figure 7.15. ^{1}H NMR of the addition product of ACTla and tris(2-aminoethyl)amine in 3:1 molar ratio in d6-DMSO.
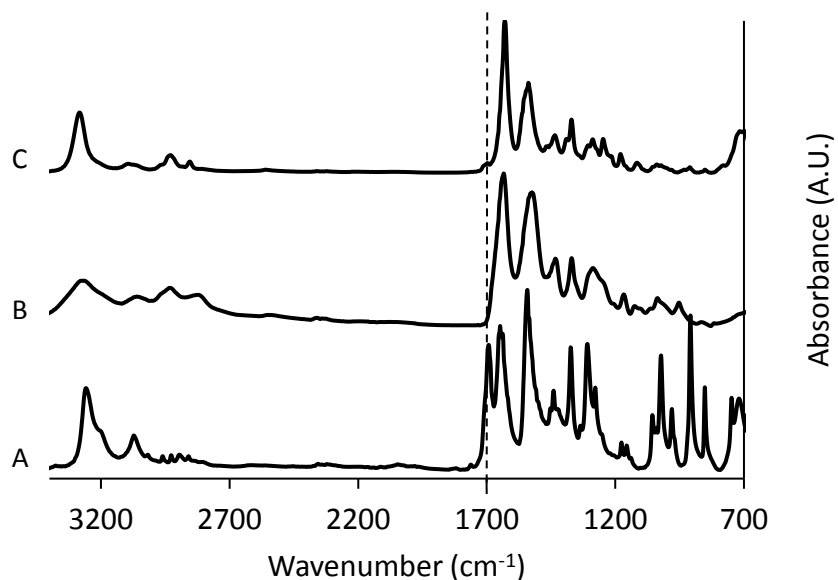
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Figure 7.16. FTIR spectra of DL-N-acetylhomocysteine thiolactone (ACTla) (A) and the aminolysis product of ACTla with hexamethylenediamine, (B); ACTla with tris(2-aminoethyl)amine, (C). The dotted line illustrates the 1688 cm^{-1} absorption band, which corresponds to the thioester carbonyl of the thiolactone moiety.

Thiolactone-based radical inhibitors with a greater thiol functionality exhibited a higher antioxidant efficiency, as expected (Table 7.3). The EC_{50} is lower for the radical inhibitors with greater thiol functionality, since the effective concentration of thiol groups in solution is higher than for monofunctional thiol compounds. However, the TEC_{50} is similar for all the thiolactone-based radical inhibitors, since the pKa and the thiol group reactivity is similar for the compounds derived from the same thiolactone building block. The similar reactivity of the radical inhibitors with multiple thiol groups is also illustrated by the similarity in the DPPH• reduction curves in Figure 7.17.
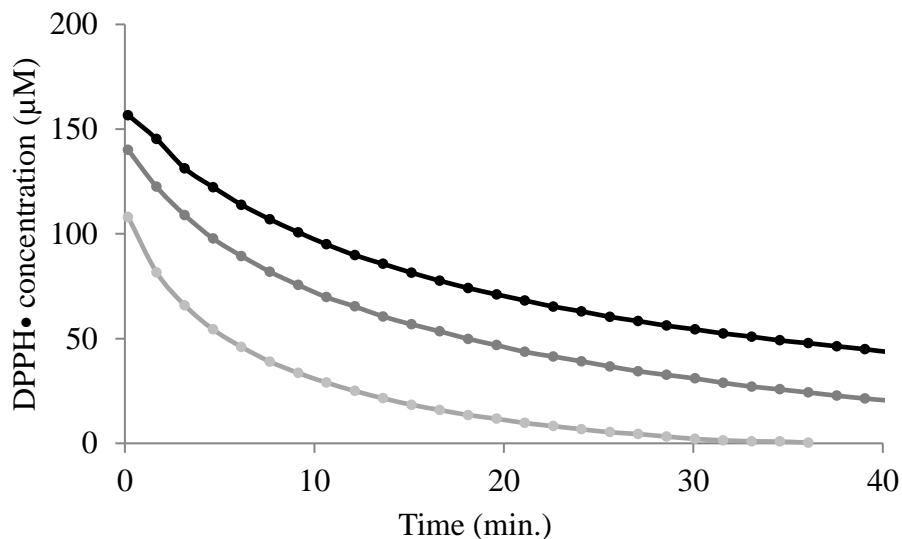
Figure 7.17. DPPH• concentration over time, in the presence of different thiol-containing compounds prepared from DL-N-acetylhomocysteine thiolactone (ACTla) and different amine compounds: ACTla with 3-(dimethylamino)-1-propylamine, (black); ACTla with 2,2'-(ethylenedioxy)bis(ethylamine), (grey); ACTla with tris(2-aminoethyl)amine, (light grey).

Table 7.3. Radical inhibitors prepared by nucleophilic addition of different amine compounds with ACTla. Molar ratios of components #1:#2 were varied to maintain ratio of thiolactone group to primary amine of 1.

Component #1	Component #2	Molar ratio (#1:#2)	Molar mass (g/mol)	EC_{50} (μM)	TEC_{50} (min)	AE (10^{-3}) (μM^{-1} min^{-1})
ACTla	3-(dimethylamino)-1-propylamine	1:1	261	127	12	0.63
ACTla	hexamethylenediamine	2:1	434	78	10	1.28
ACTla	tris(2-aminoethyl) amine	3:1	624	49	9	2.27
Glutathione	-	-	307	220	29	0.16
Cysteine	-	-	121	98	10	1.02

The antioxidant efficiency of the thiolactone-based radical inhibitors was compared to natural antioxidants, particularly cysteine, which was found to exhibit the greatest antioxidant efficiency among the natural antioxidants (Table 7.3). The monofunctional radical inhibitor prepared using 3-(dimethylamino)-1-propylamine exhibits lower overall antioxidant efficiency than cysteine, while the radical inhibitors with greater thiol functionality exhibited higher antioxidant efficiency than cysteine. These results demonstrate that thiolactone chemistry can be used to design radical inhibitors with tailored properties that can match or even exceed the antioxidant efficiency of existing thiol antioxidants.

7.6 Polymer modification by thiolactone chemistry

Commercially available copolymers of maleic anhydride were modified using thiolactone chemistry in order to introduce thiol functionalities on a polymer backbone for radical scavenging and test the antioxidant efficiency. For this proof of concept, two available maleic anhydride copolymers were used: (1) poly(styrene-co-maleic anhydride), cumene terminated with average M_n ~1,600 g/mol and ~1.3:1 mole ratio of styrene:maleic anhydride (2) poly(isobutylene-alt-maleic anhydride) with average M_w ~6,000 g/mol. These polymers were selected for the comparison of antioxidant efficiency on a macromolecular level, where steric hindrance and polymer chain configuration could contribute to secondary effects.

The ring-opening of maleic anhydride functional groups in maleic anhydride copolymers by primary amines has been reported previously for the preparation of amphiphilic graft copolymers based on poly(styrene-co-maleic anhydride)[16] and brush-like amphoteric poly[isobutylene-*alt*-(maleic acid)-*graft*-oligoethyleneamine)].[17]

A similar strategy was employed for the modification of maleic anhydride copolymers by amine-containing compounds with the additional thiol functionality derived from the thiolactone. First, ACTla was reacted with a difunctional amine, 2,2′-(ethylenedioxy)bis(ethylamine) or 4,7,10-trioxa-1,13-tridecanediamine at 1.2 molar equivalents (Figure 7.19).

The residual amine functional groups were subsequently reacted with the maleic anhydride functionalities in poly(isobutylene-alt-maleic anhydride) or poly(styrene-co-maleic anhydride) by nucleophilic ring opening. Thereby, the molecular weight of the diamine compound used for the polymer modification could be used to vary the length of the thiol-containing side-chain of the polymer.
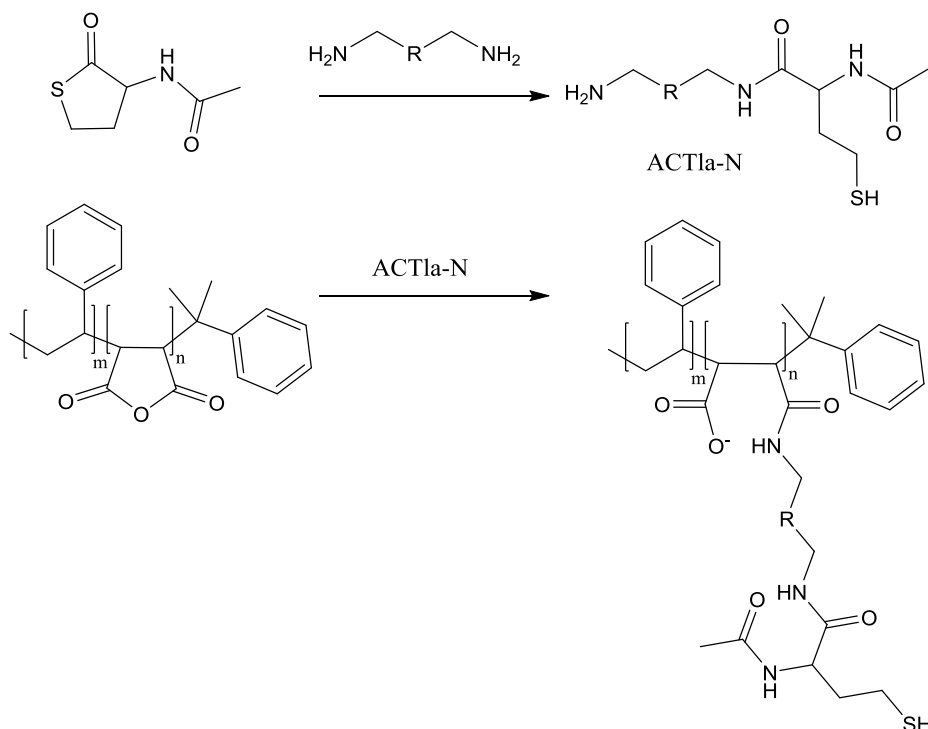
Figure 7.19. Aminolysis of DL-N-acetylhomocysteine thiolactone with a diamine (top), followed by reaction of excess amine groups with the anhydride functionality in a maleic anhydride copolymer, poly(styrene-co-maleic anhydride) (bottom).

Two diamines were used in this study in order to evaluate whether the side-chain length affects the antioxidant efficiency of the modified polymer. In addition, each maleic anhydride copolymer was modified with progressively increasing proportions of thiols in order to determine if there is an optimum degree of polymer modification for the antioxidant efficiency.

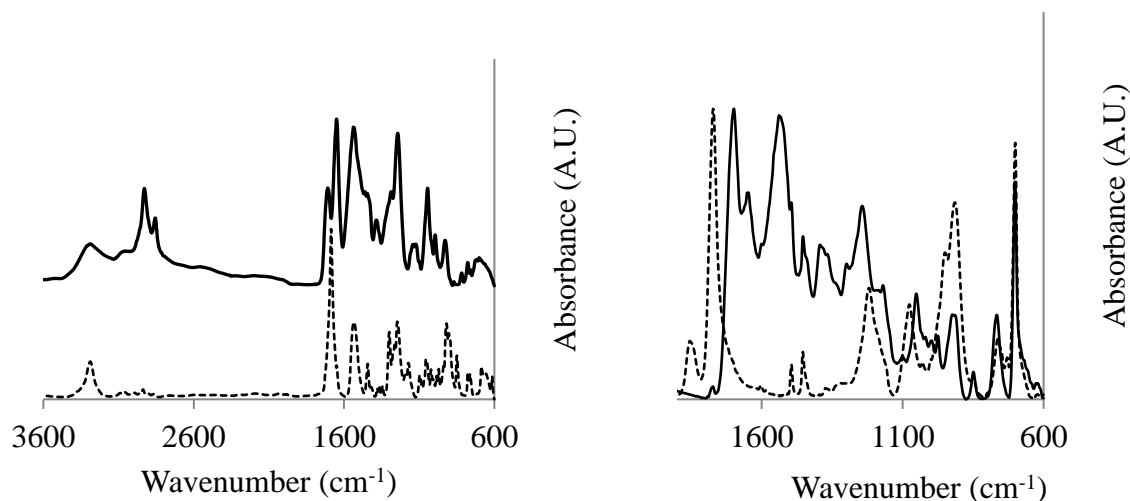*Figure 7.20. FTIR spectra of DL-N-acetylhomocysteine thiolactone (ACTla) (left, bottom dashed line) and the aminolysis product of ACTla (left, top solid line); poly(styrene-co-maleic anhydride) (right, bottom dashed line) and poly(styrene-co-maleic anhydride) after ring-opening (right, top solid line).*

The aminolysis of the thiolactone moiety by an amine was confirmed by FTIR and ^{1}H NMR. The thioester carbonyl absorbance at 1688 cm^{-1} of the thiolactone moiety was replaced by the amide carbonyl absorbance at 1650 cm^{-1} after the ring-opening of the thiolactone by an amine and the formation of an amide adduct (Figure 7.20, left). Similarly, the maleic anhydride functionality in poly(styrene-co-maleic anhydride) exhibits an absorbance at 1776 cm^{-1}, which is replaced by an amide carbonyl absorbance at 1698 cm^{-1} after ring-opening of the maleic anhydride by an amine (Figure 7.20, right).

The FTIR spectra of the maleic anhydride copolymers before and after modification by the ring-opening of the anhydride group clearly demonstrate the progressive decrease in the anhydride carbonyl absorbance at 1794 cm^{-1} and the formation of the new amide carbonyl absorbance at 1716 cm^{-1}, which exhibits a greater intensity for higher percentages of modification (Figure 7.21 and 7.22).

Figure 7.21. FTIR spectra of poly(isobutylene-alt-maleic anhydride) before and after modification with the addition product of ACTla and 2,2'-(ethylenedioxy)bis(ethylamine) in different amounts (A); poly(isobutylene-alt-maleic anhydride) before and after modification with the addition product of ACTla and 4,7,10-trioxa-1,13-tridecanediamine in different amounts (B).

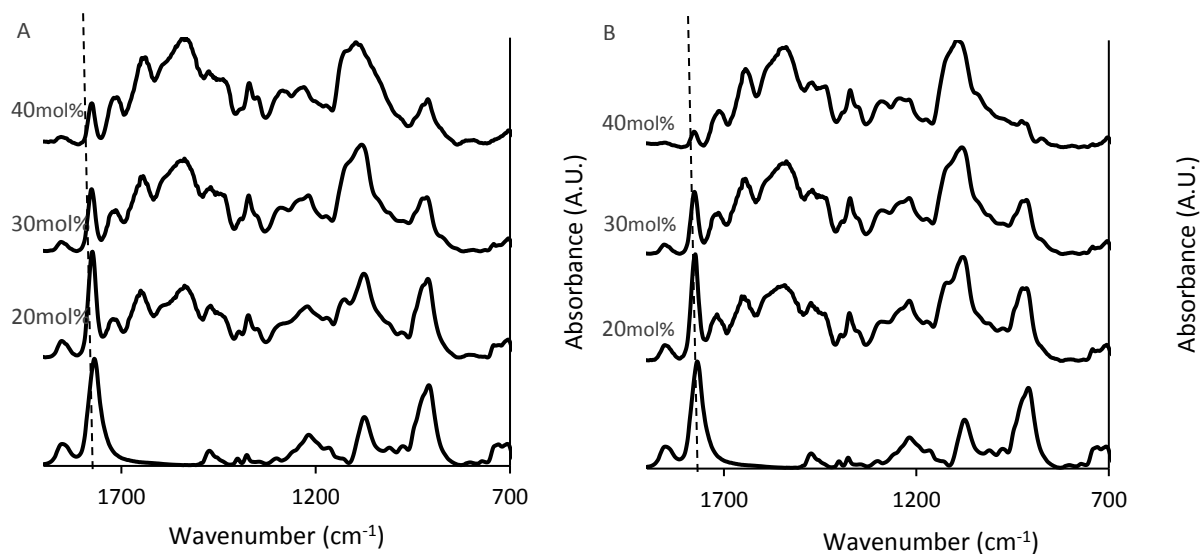*Figure 7.22. FTIR spectra of poly(styrene-co-maleic anhydride) before and after modification with the addition product of ACTla and 2,2'-(ethylenedioxy)bis(ethylamine) in different amounts (A); poly(isobutylene-alt-maleic anhydride) before and after modification with the addition product of ACTla and 4,7,10-trioxa-1,13-tridecanediamine in different amounts (B).*

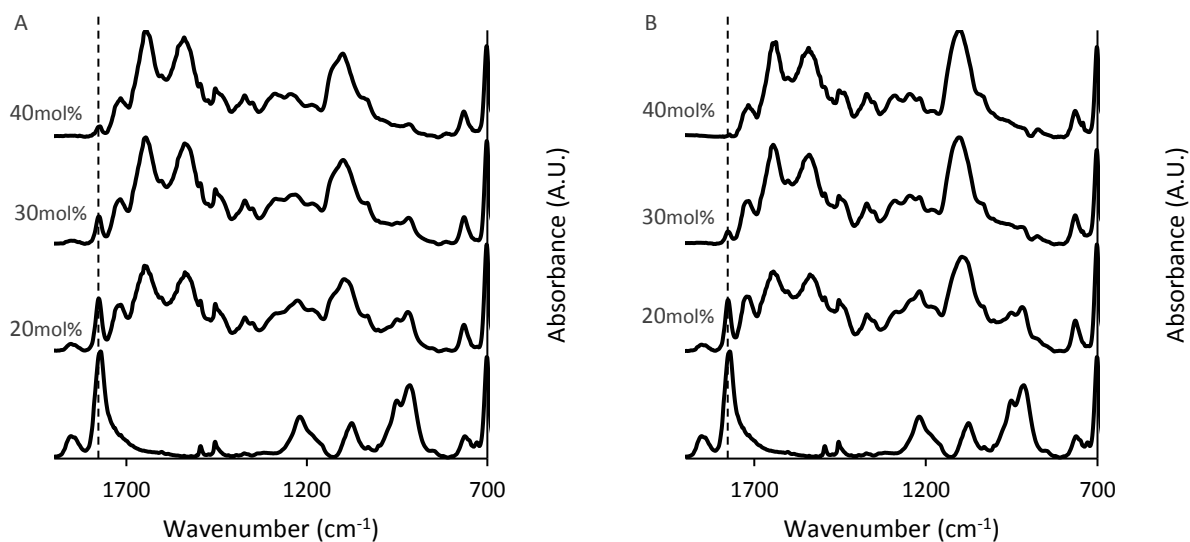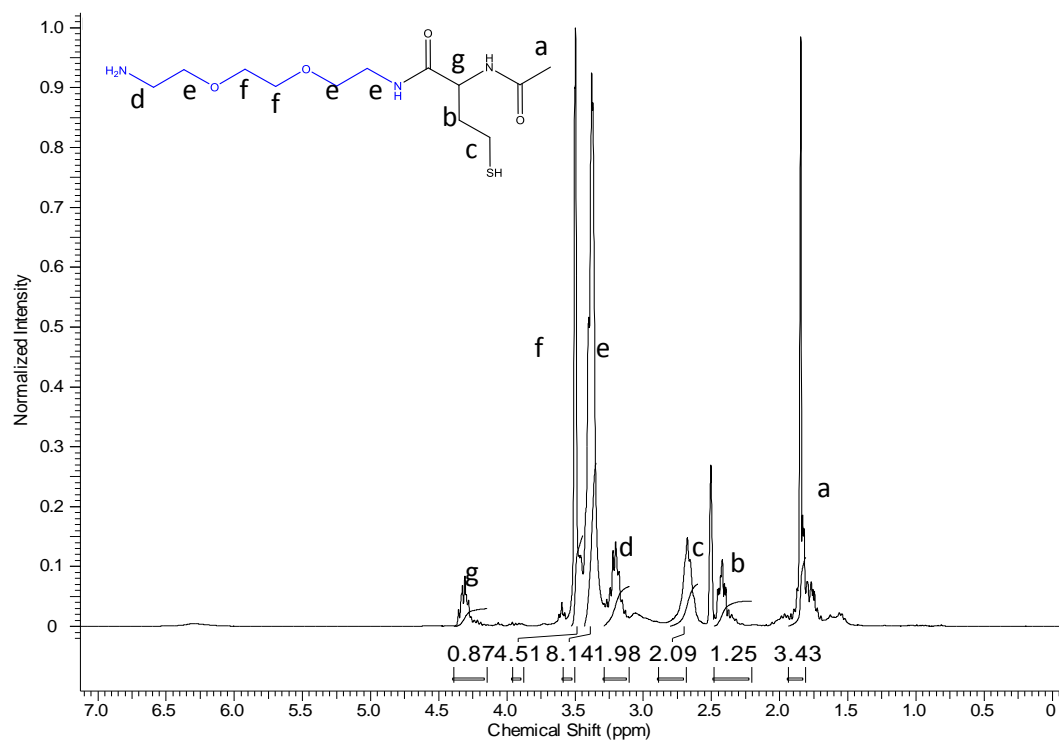*Figure 7.23. ¹H NMR of the nucleophilic addition product of ACTla and 2,2'-(ethylenedioxy)bis(ethylamine) (ACTla-EDEA) in d6-DMSO.*
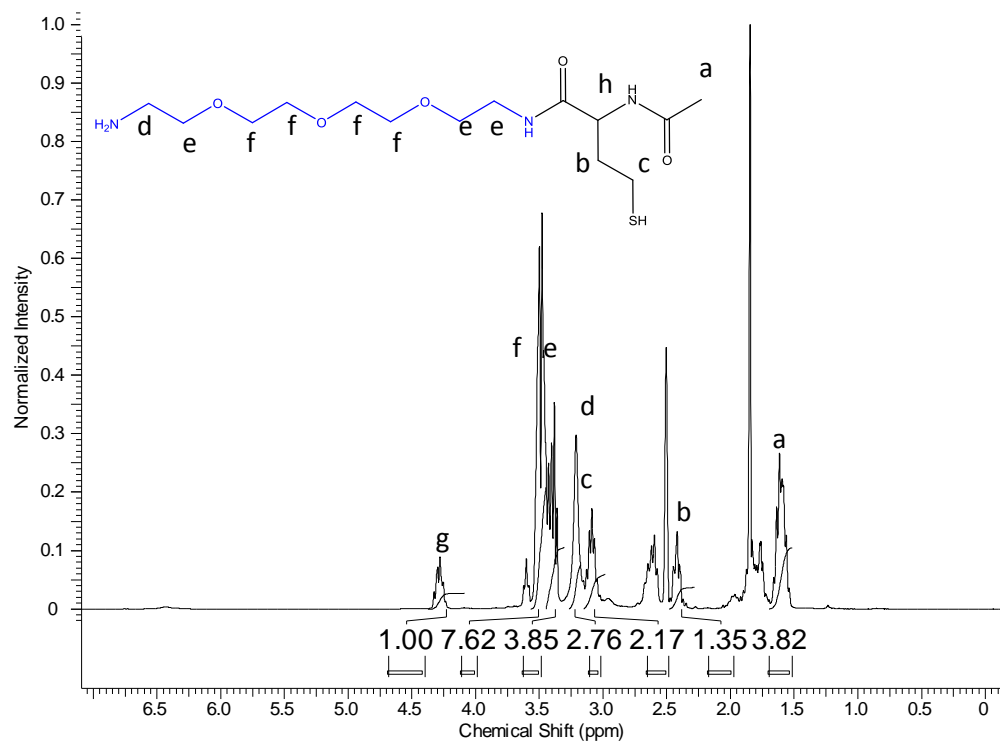
Figure 7.24. ¹H NMR of the nucleophilic addition product of ACTla and 4,7,10-trioxa-1,13-tridecanediamine (ACTla-TOTA) in d6-DMSO.

^{1}H NMR spectra confirmed the formation of ACTla adducts with 2,2′-(ethylenedioxy) bis(ethylamine) (Figure 7.23) and 4,7,10-trioxa-1,13-tridecanediamine (Figure 7.24). The ^{1}H NMR spectra of the modified maleic anhydride copolymers clearly demonstrate the presence of a new signal at 4.3 ppm, which is associated with the single proton on the β carbon of the homocysteine moiety (Figure 7.25 and 7.26).
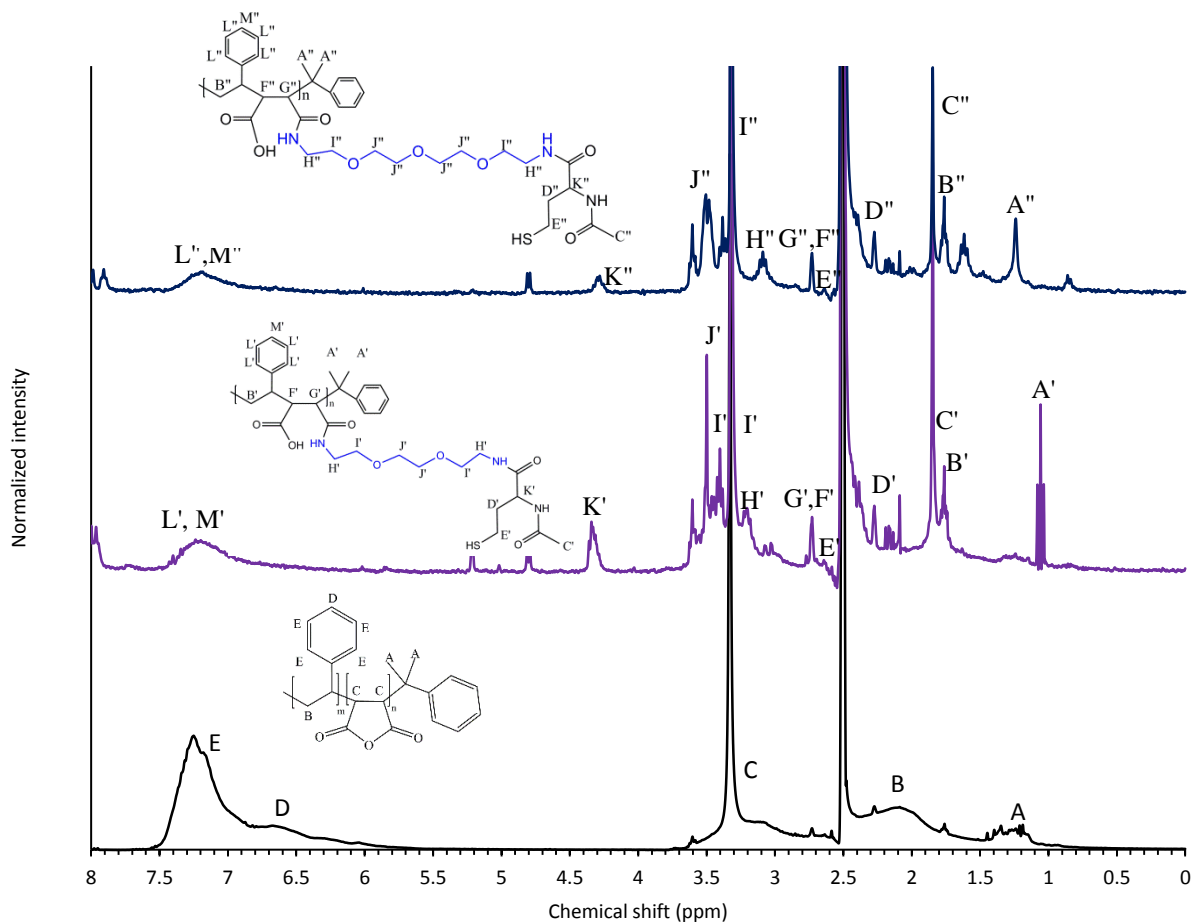
Figure 7.25. ^{1}H NMR of poly(styrene-co-maleic anhydride) (bottom) and modified poly(styrene-co-maleic anhydride) (middle, top) in d6-DMSO.

Both diamines used for the polymer modification, namely, 2,2′-(ethylenedioxy)bis(ethylamine) and 4,7,10-trioxa-1,13-tridecanediamine, contain polar and flexible ether groups. These polymer side chains are expected to contribute to a higher solubility and mobility, which should enhance the activity of the pendant thiol groups in quenching radical species.
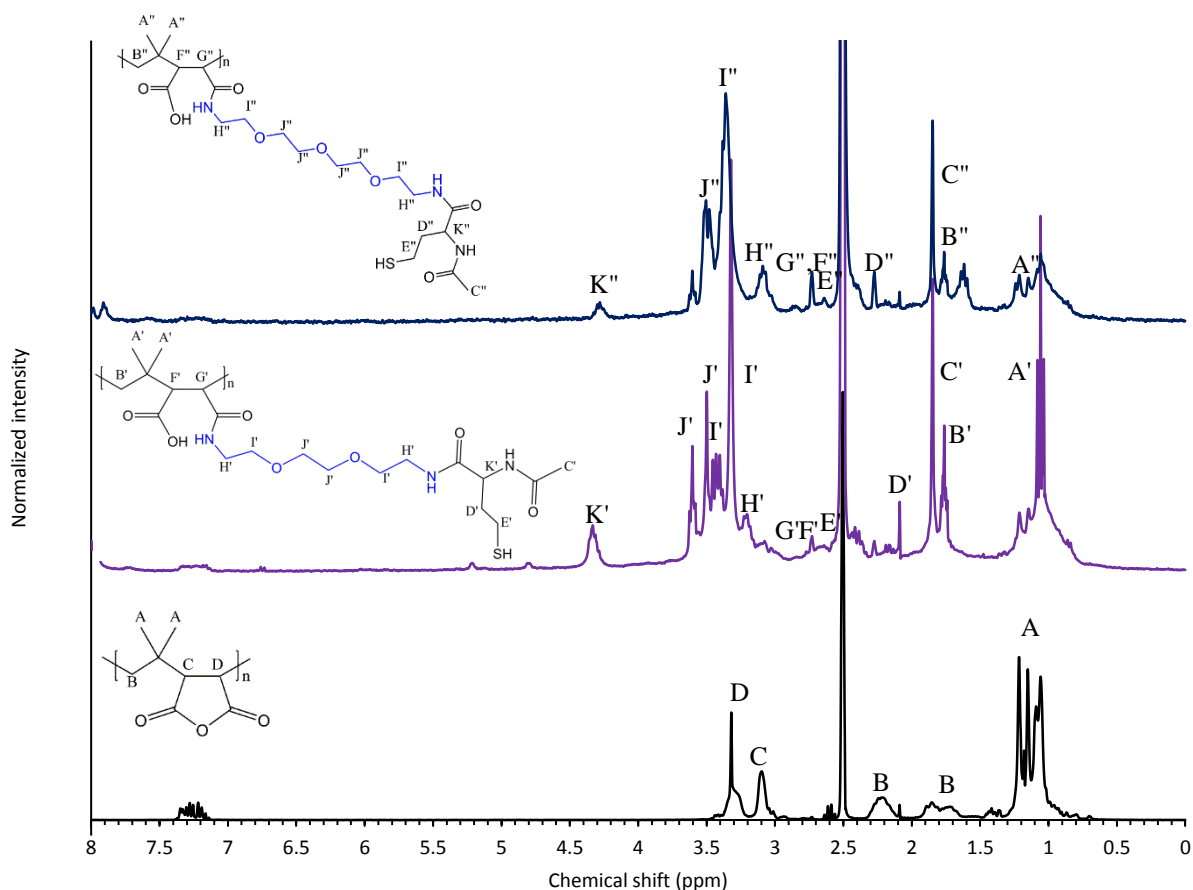
Figure 7.26. ^1H *NMR of poly(isobutylene-alt-maleic anhydride) (bottom) and modified poly(isobutylene-alt-maleic anhydride) in d6-DMSO.*

A control experiment was also conducted in order to determine if the free thiol groups could also open the anhydride ring via nucleophilic addition. Thus, poly(styrene-*co*-maleic anhydride) was combined with ethanethiol in excess in tetrahydrofuran and was stirred for 12 hours. There was no significant change observed in the ^1H NMR and FTIR spectra of poly(styrene-*co*-maleic anhydride) (Figure 7.27, left). In particular, the FTIR spectra were used to confirm that the carbonyl absorbance at 1772 cm^{-1} corresponding to the anhydride moiety in the polymer remained unchanged (Figure 7.27, right). Therefore, free thiols are not expected to interfere with the modification procedure of the anhydride copolymers and any remaining anhydride groups in the polymer should stay unaffected by the presence of free thiols.
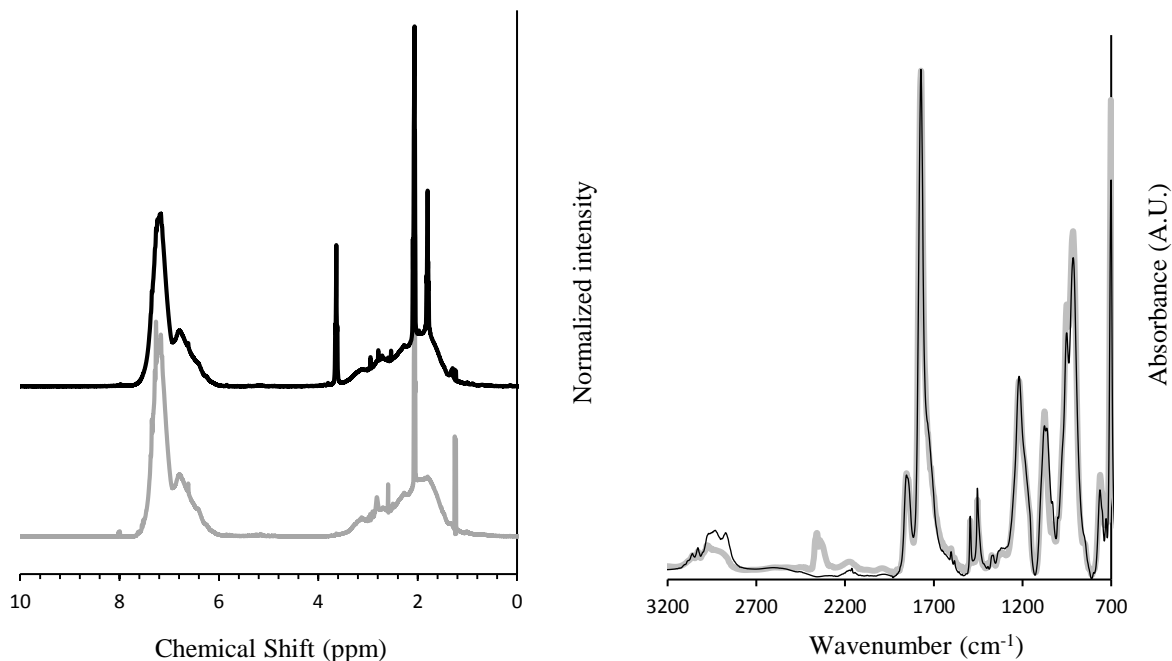
Figure 7.27. ^{1}H NMR of poly(styrene-co-maleic anhydride) (grey) and poly(styrene-co-maleic anhydride) after treatment with ethanethiol (black) in d6-DMSO. FTIR spectra of poly(styrene-co-maleic anhydride) (grey) and poly(styrene-co-maleic anhydride) after treatment with ethanethiol (black).

7.7 Evaluation of radical inhibition by polymers modified via thiolactone chemistry

The DPPH• free radical assay was performed with the modified poly(isobutylene-alt-maleic anhydride) and poly(styrene-*co*-maleic anhydride) using THF to dissolve the polymers. All of the modified polymers exhibited radical inhibition activity, which was evidenced by a significant decrease in the concentration of DPPH• (Figure 7.28 and 7.29). Polymers modified with ACTla and 4,7,10-trioxa-1,13-tridecanediamine were more effective in radical inhibition, which is likely due to the longer 4,7,10-trioxa-1,13-tridecanediamine side chain that imparts greater flexibility and less steric hindrance for the thiol group attached to the polymer.
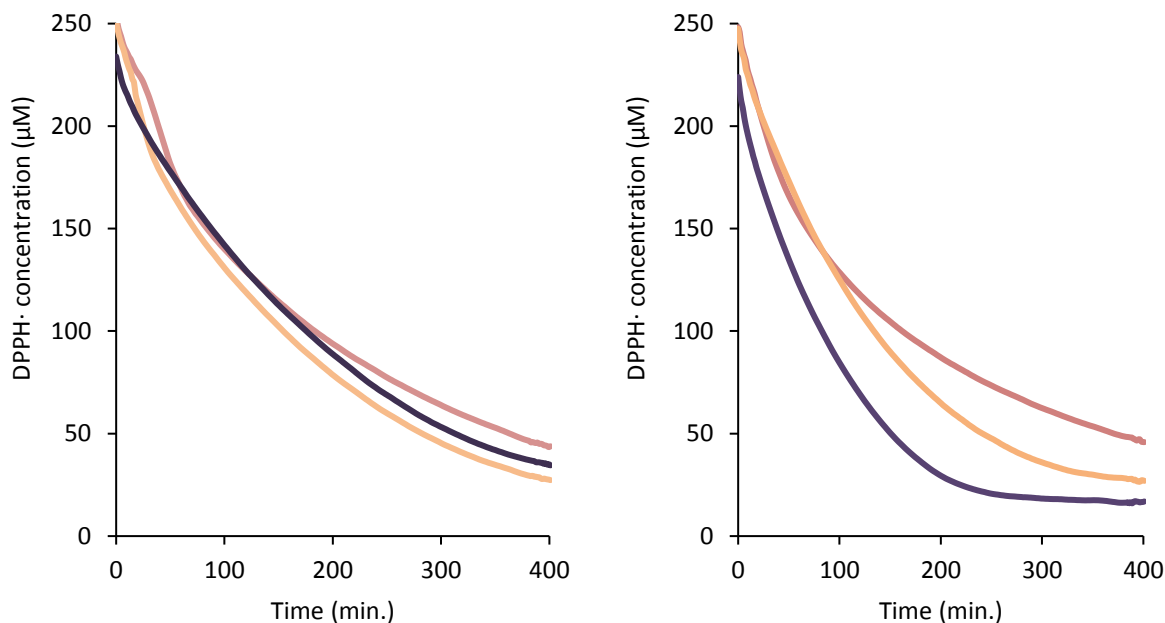
Figure 7.28. Decrease of DPPH• concentration in the presence of 1 mg/mL of poly(styrene-co-maleic anhydride) modified with 20 mol% (red), 30 mol% (orange), 40 mol% (purple) of ACTla and 2,2'-(ethylenedioxy)bis(ethylamine) (left) and 20 mol% (red), 30 mol% (orange), 40 mol% (purple) of ACTla and 4,7,10-trioxa-1,13-tridecanediamine (right).

Figure 7.29. Decrease of DPPH• concentration in the presence of 1 mg/mL of poly(isobutylene-alt-maleic anhydride) modified with 20 mol% (red), 30 mol% (orange), 40 mol% (purple) of ACTla and 2,2'-(ethylenedioxy)bis(ethylamine) (left) and 20 mol% (red), 30 mol% (orange), 40 mol% (purple) of ACTla and 4,7,10-trioxa-1,13-tridecanediamine (right).
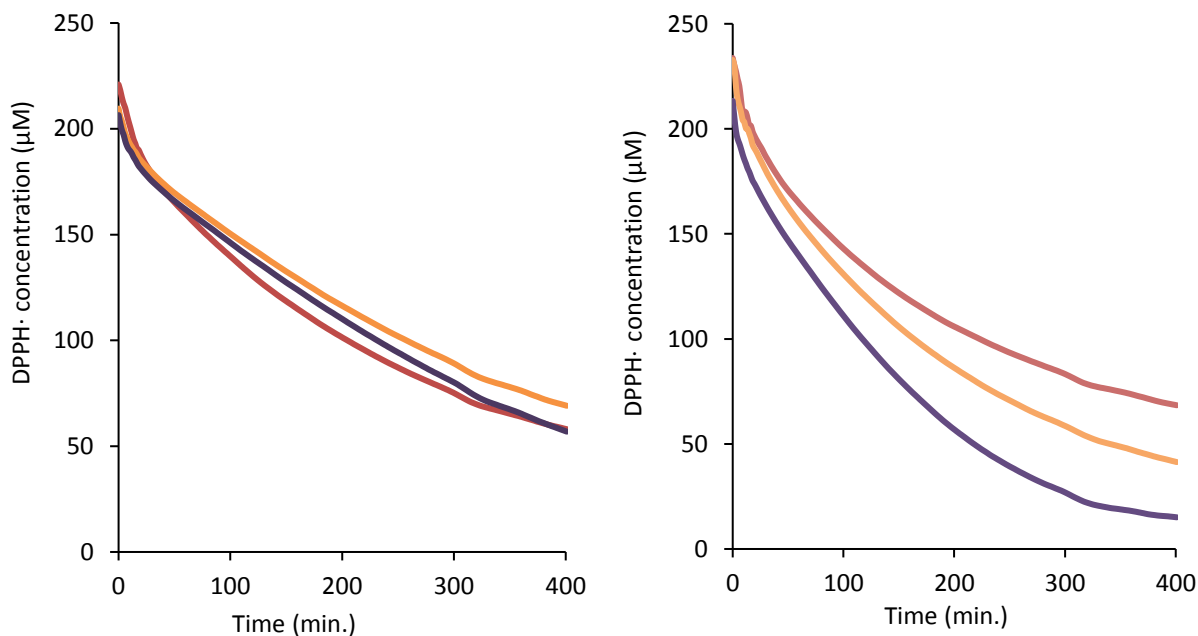
The main difference between the molecular radical inhibitors (Figure 7.13) and the polymeric radical inhibitors is the slower kinetics of the reaction with DPPH•. For example, the TEC_{50} of molecular radical inhibitors is in the range of 9-12 min (Table 7.3), while the TEC_{50} of polymeric radical inhibitors is in the range of 100-200 min (Figure 7.28 and 7.29). The slower kinetics of reaction of pendant thiol groups on a polymer level is expected due to the steric hindrance and polymer conformation that renders the thiol groups less accessible.

The polymers modified with ACTla and 4,7,10-trioxa-1,13-tridecanediamine exhibited strong radical inhibition capacity, as exhibited by nearly complete consumption of DPPH• species, as shown in Figure 7.28 and 7.29 (right). Therefore, thiolactone chemistry can be used to modify the side chain lengths of the maleic anhydride copolymers, which can render different properties. The proof of concept that maleic anhydride copolymers with thiol groups introduced via thiolactone chemistry have radical inhibition activity has been accomplished. Further investigation of the stability of these copolymers over time and at different temperatures would be useful for future applications.

7.8 Conclusion

Bioinspired thiolactone-based radical inhibitors were shown to be effective in reducing the concentration of the DPPH• based on the standard free radical assay. Thiolactone-based radical inhibitors with higher molar thiol contents exhibited greater antioxidant efficiency, since more thiol groups were available to react with DPPH•. Maleic anhydride copolymers were modified with thiol functional groups using thiolactone chemistry and their radical inhibition activity was confirmed. The polymers modified with ACTla and 4,7,10-trioxa-1,13-tridecanediamine exhibited a higher radical inhibition capacity compared to polymers modified with ACTla and 2,2′-(ethylenedioxy)bis(ethylamine). The longer 4,7,10-trioxa-1,13-tridecanediamine side chain is expected to improve the accessibility of the thiol groups attached to the polymer backbone. Overall, polymer-bound radical inhibitors reacted slower with DPPH• than the radical inhibitors with low molecular weights, which is expected from the steric constraint effects.

Thiolactone-based radical scavengers are promising candidates for tailored bio-based antioxidants with reduced migration and customized properties for different applications, such as coatings and food packaging. Further research is necessary to gain a greater understanding of the effect of different substituents on the thiol antioxidant efficiency in addition to stability testing under different temperatures and over longer time periods.

7.9 Materials and methods

7.9.1 Materials

1,1-Diphenyl-2-picrylhydrazine (DPPH•) 97% (Sigma-Aldrich), 1,4-dithiothreitol ≥97% (Ellman′s reagent) (Sigma-Aldrich), L-glutathione reduced ≥98.0% (Sigma-Aldrich), 1-thioglycerol ≥99.0% (GC) (Sigma-Aldrich), thioglycolic acid ≥98% (Sigma-Aldrich), 1-octanethiol ≥98.5% (Sigma-Aldrich), L-cysteine 97% (Sigma-Aldrich), *DL-N*-acetylhomocysteine thiolactone (3-acetamidotetrahydro-2-thiophenone), (ACTla) >98.0%(GC)(N) (TCI Europe N.V.), 3-(dimethylamino)-1-propylamine 99% (Sigma-Aldrich), tris(2-aminoethyl)amine 96% (Sigma-Aldrich) were used as received and were stored at 4°C.

For polymer modification, 2,2′-(ethylenedioxy)bis(ethylamine) 98% (Sigma-Aldrich), 4,7,10-trioxa-1,13-tridecanediamine 97% (Sigma-Aldrich), poly(styrene-co-maleic anhydride), cumene terminated average Mn ~1,600 by GPC (Sigma-Aldrich), poly(isobutylene-alt-maleic anhydride) average Mw ~6,000 (Sigma-Aldrich) were used as received and were stored at 4°C.

7.9.2 Preparation of antioxidants from DL-N-acetylhomocysteine thiolactone and different amine compounds

DL-N-acetylhomocysteine thiolactone, (2 mmol, 318 mg) was dissolved in 2 mL tetrahydrofuran. 3-(dimethylamino)-1-propylamine, (2.2 mmol, 225 mg, 277 µL) was added using a micropipette under vigorous stirring. The resulting solution was stirred for 3 hours at room temperature. The solution was then diluted with methanol to 100 mL (concentration of 0.2 M) for UV-Vis testing

with DPPH•. Solutions of antioxidants with other amine compounds were prepared in a similar manner, while adjusting the stoichiometry between the thiolactone and the amine groups.

7.9.3 Preparation of polymer-bound antioxidants using DL-N-acetylhomocysteine thiolactone and different amine compounds

An antioxidant solution was prepared by dissolving *DL-N*-acetylhomocysteine thiolactone, (4 mmol, 636 mg) in 3 mL tetrahydrofuran and adding 2,2′-(ethylenedioxy)bis(ethylamine), (4.8 mmol, 652 mg) in 3 mL tetrahydrofuran. The resulting solution was stirred for 3 hours at room temperature. The same procedure was repeated using 4,7,10-trioxa-1,13-tridecanediamine, (4.8 mmol, 968 mg) instead of the 2,2′-(ethylenedioxy)bis(ethylamine).

The antioxidant solution was diluted into 20 mL to obtain concentration of 0.2 M. Poly(styrene-co-maleic anhydride), (200 mg) was dissolved in 4 mL tetrahydrofuran in 3 different flasks and then 2 mL (0.4 mmol), 3 mL (0.6 mmol), and 4 mL (0.8 mmol) of the antioxidant solution (0.2 M) was added to each flask. The same procedure was repeated using poly(isobutylene-alt-maleic anhydride). The solutions with polymer and antioxidant were stirred for 15 hours at room temperature. Then 1,4-dithiothreitol was added to each sample, in equimolar amount to the antioxidant quantity. The resulting solutions were stirred for 4 hours at room temperature. The solutions were precipitated with diethyl ether, filtered, and dried under vacuum.

7.9.4 DPPH• free radical assay

DPPH• assay was conducted using the reagent concentrations in Table 7.4. DPPH• stock solution (400µM) was prepared using 0.04 mol, 15.78 mg DPPH• in 100 mL methanol or tetrahydrofuran. The solution was prepared daily and stored in the dark at 4°C. Antioxidant stock solution (2000 µM) in methanol was prepared. Samples of different antioxidant concentrations were prepared and combined with 1.5 mL DPPH• stock solution to a total volume of 3 mL for UV-Vis measurements.

UV-Vis measurements were conducted using Analytikjena SPECORD200 in an automatic cycle mode with 1 min frequency and absorption measurement at 515 nm.

Table 7.4. Reagents and concentrations used for DPPH• assay with [DPPH•] = 200 μM by UV-Vis spectroscopy.

	Methanol (mL)	**DPPH• (400μM) volume (mL)**	**Antioxidant (2000μM) volume (mL)**	**[Antioxidant] (μM)**
TEST100	1.35	1.5	0.15	100
TEST200	1.20	1.5	0.30	200
TEST300	1.05	1.5	0.45	300
TEST400	0.90	1.5	0.60	400
TEST500	0.75	1.5	0.75	500
TEST600	0.60	1.5	0.90	600
TEST700	0.45	1.5	1.05	700

FTIR spectra in ATR mode were recorded on a Perkin-Elmer Spectrum1000 FTIR infrared spectrometer by obtaining 16 scans for each sample.

Nuclear magnetic resonance spectra were recorded on a Bruker AVANCE 300 MHz spectrometer at room temperature using deuterium oxide or d6-DMSO as solvent.

7.10 References

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Chapter 8. Conclusions and outlook

8.1 Summary of objectives

The main objective of this work was to use thiolactone chemistry as a platform for the development of multifunctional polymer materials, including UV-cured coatings, formaldehyde scavenging coatings, radical inhibiting polymers and polyampholytes. The aim was to investigate how different functionalities in polymer backbones, side chains, and cross-links affect the resulting polymer properties.

Thiolactone chemistry has emerged as a powerful tool for polymer functionalization and modification via amine-thiol-ene conjugation. The thiolactone moiety itself is a bio-based source of thiols, which can participate in nucleophilic, radical, and redox reactions. Therefore, the combination of thiolactone and thiol-ene chemistries provides the means for the sustainable development of bio-inspired multifunctional materials, which was the focus of this work.

This PhD research encompasses some of the research questions and opportunities pertaining to the incorporation of thiolactone building blocks into materials with added value. The final aim was to elucidate new research directions and applications of thiolactone chemistry on both molecular and macromolecular level.

8.2 General conclusions

The final result of the research described herein is not only to answer a specific scientific question, but to also find new questions for future research. The original research objective was to develop multifunctional polymer materials using thiolactone chemistry. Chapter 2 reviewed the main aspects of thiolactone chemistry and amine-thiol-ene conjugation for the preparation of multifunctional polymer materials. Thiolactone chemistry encompasses several advantages,

including atom efficiency, functional group variety, and sustainability. In particular, thiolactone chemistry contributes to sustainability via the use of the bio-based building blocks, including homocysteine thiolactone and other bio-based feedstock, such as fatty acids and amino acids. In addition, amine-thiol-ene conjugation is an atom efficient approach for the preparation of functionalized polymers, which can be conducted in water and at room temperature.

Chapter 3 provided an overview of thiol-ene polymerization for the preparation of coatings, which has been an actively growing research field. Thiol-ene chemistry enables the preparation of homogeneous polymer networks using a variety of bio-based building blocks and rapid UV-triggered photopolymerization. The utility of thiol-ene photopolymerization has been applied in a broad spectrum of coatings, including waterborne polyurethane dispersions, pigmented acrylate coatings, and UV-thermal thiol-ene-epoxy coatings.

Chapter 4 described the methodology and results obtained regarding thiolactone-based coatings with a variety of functional groups, ranging from a difunctional non-polar 1,10-diaminodecane to a trifunctional polar tris(2-aminoethyl)amine. The coating preparation process was optimized in terms of the solvent mixture and UV-curing process in order to obtain homogeneous films without visible defects. The resulting films demonstrated high transparency and low haze, as well as excellent impact resistance.

The follow-up question was what these coatings could be useful for? A new application of formaldehyde scavenging coatings was investigated in Chapter 5. A proof of concept was conducted by applying the formaldehyde scavenging coatings on top of urea-formaldehyde adhesives. The emissions of formaldehyde from samples coated with polymers containing different amine functional groups were evaluated according to the standard formaldehyde release test by the flask method. The thiolactone-based coatings with residual amine functionalities were highly effective in trapping formaldehyde emissions due to both the barrier effect, as well as the covalent linking of the formaldehyde to the polymer.

The next question arose, whether entirely different types of functionalities could be incorporated into polymers using thiolactone chemistry, such as cationic and anionic groups. This question formed the foundation of Chapter 6, which focused on the development of ionic polymers using thiolactone chemistry. In previous work, mostly a single type of functional side group was

incorporated into polymers without any targeted intermolecular interactions. On the other hand, ionic groups have strong intermolecular interactions that affect polymer conformation and responsiveness to the environment, including the pH, ionic strength, and temperature. Therefore, thiolactone chemistry was used to introduce carboxylic acid side groups and tertiary amine side groups in the same polymer chain. Four strategies for incorporating ionic functional groups into polymers were investigated, but the only approach that worked effectively was based on the use of the *N*-maleamic acid thiolactone monomer.

The resulting ionic polymers, called polyampholytes, exhibited alternating cation-anion arrangement in the polymer chain, which yielded high aqueous solubility and thermoresponsiveness. In addition, the versatility of the thiolactone chemistry has enabled simple incorporation of both covalent, ionic, and hydrogen bonding linkages, which are expected to yield new synergistic material properties.

Another question, as a starting point of Chapter 7, was whether the thiolactone moiety itself could be used as a functional additive rather than adding extra functional groups via thiolactone chemistry. Indeed, the thiolactone moiety could be used as a bio-based source of thiols, which can inhibit radicals. Inspired by the high effectiveness of glutathione antioxidant in cells, thiolactone chemistry was used to incorporate radical inhibitors into polymers. A variety of molecular and polymer-bound radical inhibitors were prepared using thiolactone chemistry and their antioxidant efficiency was evaluated using a standard DPPH· assay. Remarkably, thiolactone chemistry also provided a simple approach to tailor antioxidant efficiency in terms of total antioxidant capacity and kinetics. For example, radical inhibitors with several thiol groups were prepared and the DPPH· test results confirmed that their antioxidant efficiency was greater than that with monofunctional thiol compounds.

Most importantly, this work demonstrated how thiolactone chemistry can be used to prepare complex polymer structures in a simple manner and under mild reaction conditions. Thereby, bio-based building blocks, sustainable processes, and functional materials have all been enabled using the thiolactone chemistry platform.

8.3 Outlook

The quest for greater sustainability in resource and energy consumption is a global challenge that requires multidisciplinary and integrated solutions. In that respect, multifunctional materials can contribute to lower raw material requirements and reduced waste by enabling a single material to serve multiple roles, such as substrate protection, damage recovery, and sensing. Multifunctional materials could also streamline production processes, thereby reducing energy consumption and minimizing waste. For example, multiple coating layers do not need to be applied if all the necessary functionalities are integrated into a single coating, thereby reducing solvent consumption and thermal/UV-energy utilization.

In this context, thiolactone chemistry can enhance sustainability since it employs bio-based building blocks and it enables added functionality of materials via a simple and efficient route, namely, amine-thiol-ene conjugation. UV-cured coatings have been developed using thiolactone chemistry, thereby demonstrating the use of bio-based building blocks and added functionality for scavenging formaldehyde emissions. The thiolactone chemistry platform can be used in the future to prepare many types of multifunctional scavenging coatings in order to target other pollutants, such as VOC's and heavy metals. In addition, polymer materials with greater porosity would enhance scavenging performance due to a higher active surface area for the interaction with target molecules. For example, thiolactone chemistry could be used for the functionalization of silica or graphene and the development of hybrid materials for scavenging pollutants.

Thiolactone chemistry has been shown to enhance the properties of UV-cured thiol-ene coatings via the additional polymer cross-linking with multifunctional amines. The UV-triggered thiol-ene coupling is highly suitable for surface modification and patterning due to its high efficiency and lack of oxygen sensitivity. Concurrently, thiolactone chemistry is a versatile strategy for the introduction of a variety of functionalities into polymers. The combination of thiolactone and thiol-ene chemistry could be used for the functionalization of a variety of surfaces, such as nanoparticles and microfluidic channels. Thereby, new properties could be introduced on the surface, such as thermoresponsiveness.

Another aspect of sustainability is reduction in waste, where dynamic and reprocessable materials can play an important role. Since natural organic matter is constantly recycled and reused, chemical systems that can function similarly are an active area of research. Thiolactone chemistry is well suited for the preparation of dynamic materials with tunable strength of intermolecular interactions. For example, ionic interactions and thiol-disulfide interchange could be used to prepare self-healing polymers. Additional functionalities, such as hydrogen-bonding groups, could be introduced into the self-healing polymers via thiolactone chemistry in order to tune the self-healing performance.

In addition, the capability of introducing different functionalities in the polymer backbone and side-chains via thiolactone chemistry can be harnessed for the design of more complex hierarchical polymers with secondary and tertiary structures, analogous to proteins. The functionality of proteins, especially enzymes, originates from both molecular and conformational effects that are specifically tailored to their environment. Thiolactone chemistry is a synthetic enabler for the development of bio-inspired polymer materials with the synergistic effects of molecular and conformational structures.

Chapter 9. Nederlandstalige samenvatting (Dutch summary)

9.1 Samenvatting van de doelstellingen

De hoofddoelstelling van dit project was het gebruik van thiolactonchemie als platform voor de ontwikkeling van multifunctionele polymeermaterialen, waaronder UV-uithardende deklagen, formaldehyde-vangende deklagen, radicaal-inhibiterende polymeren en polyamfolyten. Daarnaast werd onderzocht hoe verschillende functionaliteiten in de hoofd- en zijketens van polymeren, alsook in vernettingen de resulterende polymeereigenschappen beïnvloeden.

Thiolactonchemie is uitgegroeid tot een belangrijk hulpmiddel ter functionalisatie en modificatie van polymeren door middel van amine-thiol-ene conjugatie. De thiolactonmolecule is een biogebaseerde bron van thiolen, dewelke zelf in een nucleofiele -, radicale - of redoxreactie kunnen deelnemen. De combinatie van zowel thiolacton- als thiol-een-chemie maken de duurzame ontwikkeling van biogeïnspireerde multifunctionele materialen mogelijk, wat tevens de focus van dit project was.

Dit doctoraatsonderzoek behandelt enkele onderzoeksvragen en mogelijkheden om thiolacton bouwstenen te incorporeren in materialen ter verbetering van hun eigenschappen of functionaliteit. De opheldering van nieuwe onderzoeksrichtingen en toepassingen van thiolactonchemie op moleculair en macromoleculair niveau was het einddoel.

9.2 Algemene conclusies

Het eindresultaat van het beschreven onderzoek is niet alleen een antwoord op een specifieke wetenschappelijke vraag, maar creëert ook nieuwe vragen naar toekomstig onderzoek. De initiële doelstelling was de ontwikkeling van multifunctionele polymeermaterialen door gebruik te maken van thiolactonchemie. In Hoofdstuk 2 werden de hoofdaspecten van thiolactonchemie en amine-thiol-een-conjugatie beoordeeld ter bereiding van multifunctionele polymeermaterialen. Thiolactonchemie kent enkele voordelen, waaronder atoomefficiëntie, functionele groep variatie en duurzaamheid. Voornamelijk de bijdrage in duurzaamheid is van belang door gebruik te

maken van biogebaseerde bouwstenen, waaronder homocysteinethiolacton en andere biogebaseerde grondstoffen, zoals vetzuren en aminozuren. Daarnaast is amine-thiol-een-conjugatie een atoomefficiënte manier voor de bereiding van gefunctionaliseerde polymeren, dat zowel in water als bij kamertemperatuur kan uitgevoerd worden.

Hoofdstuk 3 bevat een overzicht van thiol-een-polymerisatie voor de bereiding van deklagen - een steeds uitbreidend onderzoeksveld. Door middel van thiol-een-chemie kunnen homogene polymeernetwerken bereid worden door gebruik te maken van een verscheidenheid aan biogebaseerde bouwstenen en snelle UV-geïnitieerde fotopolymerisatie. Het gebruik van thiol-een fotopolymerisatie werd reeds gebruikt in een breed spectrum van deklagen, waaronder watergedragen polyurethaandispersies, gepigmenteerde acrylaatdeklagen, en UV-warmte thiol-ene-epoxydeklagen.

Hoofdstuk 4 beschrijft de methodologie en resultaten omtrent thiolacton-gebaseerde deklagen met verscheidene functionele groepen, gaande van difunctionele niet-polaire 1,10-diaminodecaan tot een trifunctionele polaire tris(2-aminoethyl)amine. Het bereidingsproces van de deklagen werd geoptimaliseerd in termen van het solventmengsel en het UV-vernettingsproces, zodat een homogene laag zonder zichtbare defecten kon bekomen worden. De resulterende lagen vertoonden hoge transparantie en lage wazigheid, alsook uitstekende impactresistentie.

De vraag die men hierna zou kunnen stellen is was waar deze deklagen nuttig zouden kunnen zijn? Een nieuwe toepassing van formaldehyde-vangende deklagen werd onderzocht in Hoofdstuk 5. Dit concept werd bewezen door de fomaldehyde-vangende deklagen aan te brengen bovenop urea-formaldehyde adhesieven. De emissie van formaldehyde vanuit de samples, die bedekt werden met polymeren die verschillende amine functionaliteiten bevatten, werd geëvalueerd volgens een standaard formaldehyde-vrijgave test volgens de fles methode. De thiolacton-gebaseerde deklagen met overgebleven amine functionaliteiten waren uitermate effectief in het vangen van de vrijgestelde formaldehyde wegens het barrière effect, alsook de covalente binding van formaldehyde met het polymeer.

Een volgende vraag was of totaal verschillende functionaliteiten, zoals kationische en anionische groepen, konden geïncorporeerd worden in polymeren door gebruik te maken van thiolactonchemie. Deze vraag vormde de fundering voor Hoofdstuk 6, waar de focus ligt op de

ontwikkeling van ionische polymeren, gebruik makend van thiolactonchemie. In voorgaand onderzoek werd meestal slechts één type functionele zijgroep geïncorporeerd in polymeren zonder zich te richten op intermoleculaire interacties. Daartegenover staat het feit dat ionische groepen sterke intermoleculaire krachten kunnen ontwikkelen die een invloed zullen hebben op de polymeerconformatie en de responsiviteit naar de omgeving, zoals pH, ionische sterkte, en temperatuur. Daarom werd thiolactonchemie gebruikt ter introductie van carbonzuur zijgroepen en tertiaire amine zijgroepen in dezelfde polymeerketen. Vier strategieën voor de incorporatie van ionisch functionele groepen in polymeren werden onderzocht, maar de enige succesvolle benadering maakte gebruik van het N-maleamic acid thiolacton monomeer.

De resulterende ionisch polymeren, polyamfolyten genaamd, bevatten een alternerende kation-anion schikking in de polymeerketen, wat zorgde voor een hoge wateroplosbaarheid en thermoresponsiviteit. Daarenboven heeft de veelzijdigheid van thiolactonchemie gezorgd voor een simpele incorporatie van zowel covalente, ionische en waterstofbrug verbindingen, waarvan wordt verwacht dat ze nieuwe synergetische materiaaleigenschappen kunnen veroorzaken.

Als startpunt voor Hoofdstuk 7 was de vraag de thiolacton entiteit zelf kan gebruikt worden als functioneel additief in de plaats van de toevoeging van extra functionele groepen via thiolactonchemie. Inderdaad, thiolacton kan gebruikt worden als biogebaseerde bron van thiolen, wat zorgt voor de inhibitie van radicalen. Geïnspireerd door de hoge effectiviteit van glutathione antioxidans in cellen, werd thiolactonchemie gebruikt om radicaalinhibitoren in te bouwen in polymeren. Verscheidene moleculaire en polymeergebonden radicaalinhibitoren werden bereid gebruik makend van thiolactonchemie en hun antioxiderende effectiviteit werd geëvalueerd met de standaard DPPH• analyse. Thiolactonchemie zorgde opmerkelijk voor een eenvoudige manier om de antioxiderende effectiviteit af te stemmen in termen van totale antioxiderende capaciteit en kinetiek. Zo werden bijvoorbeeld radicaalinhibitoren met verschillende thiolgroepen bereid, waarna de DPPH• analyse bevestigde dat hun antioxiderende effectiviteit groter was dan deze van monofunctionele thiol componenten.

Dit werk demonstreert voornamelijk hoe thiolactonchemie gebruikt kan worden om complexe polymeerstructuren op een eenvoudige manier en onder milde omstandigheden te bereiden. Hiervoor werden zowel biogebaseerde bouwstenen, duurzame processen en functionele materialen gebruikt in combinatie met het thiolactonchemie platform.

9.3 Vooruitzichten

De zoektocht naar verhoogde duurzaamheid in bron en energieconsumptie is een wereldwijde uitdaging die multidisciplinaire en geïntegreerde oplossingen vereist. In dit opzicht kunnen multifunctionele materialen bijdragen aan verminderde grondstofvereisten en verminderde hoeveelheden afval door eenzelfde materiaal meerdere functies te geven, zoals substraat bescherming, schadeherstelling en een sensorfunctie. Multifunctionele materialen zouden ook productieprocessen kunnen stroomlijnen, waardoor de energieconsumptie en afvalproductie verminderd wordt. Bijvoorbeeld, meerdere deklagen moeten niet aangebracht worden indien alle nodige functionaliteiten in één enkele coating geïntegreerd zitten, waardoor solventconsumptie en warmte/UV-energieverbruik verminderd worden.

In deze context kan thiolactonchemie de duurzaamheid verhogen, daar het gebruik maakt van biogebaseerde bouwstenen en functionaliteit aan materialen toevoegt via een simpele en efficiënte route, namelijk amine-thiol-een-conjugatie. UV-vernette deklagen werden ontwikkeld gebruik makend van thiolactonchemie als demonstratie voor het gebruik van biogebaseerde bouwstenen en toegevoegde functionaliteit voor de opvanging van formaldehyde uitstoot. Het thiolactonchemie-platform kan in de toekomst gebruikt worden om veel verschillende soorten multifunctionele vangende deklagen te bereiden om ook andere vervuilende stoffen, zoals vluchtige organische stoffen en zware metalen, op te vangen. Daarenboven zouden polymeermaterialen met grotere porositeit de vangende prestatie verhogen door de vergroting van het actieve oppervlak voor de interactie met doelwitmoleculen. Bijvoorbeeld, thiolactonchemie zou gebruikt kunnen worden voor de functionalisatie van silica of grafeen en de ontwikkeling van hybride materialen voor het vangen van vervuilende deeltjes.

Het werd bewezen dat thiolactonchemie de eigenschappen van UV-vernette thiol-een deklagen verbeterd via additionele polymeervernetting met multifunctionele amines. De UV-geïnitieerde thiol-een koppeling is uitermate geschikt voor oppervlakmodificatie en patroonvorming wegens zijn hoge efficiëntie en gebrek aan zuurstofgevoeligheid. Tegelijkertijd is thiolactonchemie een veelzijdige strategie voor de introductie van verscheidene functionaliteiten in polymeren. De combinatie van thiolacton en thiol-een-chemie kan gebruikt worden voor de functionalisatie van

verschillende oppervlakken, zoals nanopartikels en microfluidische kanalen. Daarbij kunnen nieuwe eigenschappen geïntroduceerd worden aan het oppervlak, zoals thermoresponsiviteit.

Een ander aspect van duurzaamheid is de afvalvermindering, waar dynamische en opnieuw verwerkbare materialen een belangrijke rol in spelen. Aangezien natuurlijk organische materiaal constant gerecycleerd en hergebruikt wordt, is de zoektocht naar chemische systemen met gelijkaardige mogelijkheden een actief onderzoeksveld. Thiolactonchemie is zeer geschikt voor de bereiding van dynamische materialen met aanpasbare sterkte van intermoleculaire interacties. Bijvoorbeeld, ionische interacties en thiol-disulfide uitwisseling kunnen gebruikt worden om zelfherstellende materialen te bereiden. Extra functionaliteiten, zoals waterstofbrugvormende groepen, kunnen geïntroduceerd worden in de zelfherstellende polymeren via thiolactonchemie om zodoende de zelfherstellende eigenschappen af te stemmen.

De mogelijkheid om verschillende functionaliteiten te introduceren in de polymeerhoofdketen en zijketen via thiolactonchemie kan gebruikt worden voor het ontwerpen van meer complexe hiërarchische polymeren met secundaire en tertiaire structuren, analoog aan proteïnen. De functionaliteit van proteïnen, voornamelijk enzymen, is afkomstig van zowel moleculaire als conformationele effecten die specifiek ontworpen zijn aan hun omgeving. Thiolactonchemie is een synthetische manier om biogeïnspireerde materialen met synergetische effecten te ontwikkelen op moleculair en conformationeel vlak.

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