Kinetic modeling of radical thiol-ene chemistry

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PREFACE

Before proceeding to the actual description of the performed research, I would like to thank some people in particular who helped me realizing this research project. First of all, a special thanks goes to my supervisors Professor Filip Du Prez and Professor Marie-Françoise Reyniers for giving me the opportunity and providing me the means to work on this challenging subject. Secondly, I would like to thank my coaches Milan Stamenovic and Dr. Dagmar D’hooge for teaching me some experimental and modeling skills, for the useful discussions, and for the extensive evaluation of my results.

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Finally, I would like to thank my girlfriend, my parents, my brothers, and my friends for their support during the completion of this Master thesis.
Laboratorium voor Chemische Technologie

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In this work a combined experimental and kinetic modeling study is presented for radical thiol-ene coupling reactions both involving low and high molar mass compounds. In Chapter 1, the scope of this project is highlighted, whereas in Chapter 2 an overview of the reactions denoted in literature as “click” reactions is given, particularly focusing on the features and applications of the radical thiol-ene reaction. Next, in Chapter 3 a detailed kinetic study is presented for radical thiol-ene chemistry using low molar mass compounds, and the gained knowledge is further used in the study of polymer functionalization reactions for a model system using radical thiol-ene chemistry, as discussed in Chapter 4. Finally, general conclusions and some indications for future research are given in Chapter 5.

**Key words:** Radical thiol-ene chemistry, kinetic modeling, polymer functionalization, diffusional limitations
Kinetic modeling of radical thiol-ene chemistry

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Abstract: A combined experimental and kinetic modeling study is presented for radical thiol-ene coupling reactions both involving low and high molar mass compounds. For a low molar mass model system (DVE/BT/DMPA/1,4-dioxane), based on optimal reaction conditions and a detailed product characterization ball–park kinetic parameter values are reported allowing to evaluate the importance of side reactions and diffusional limitations for the coupling reaction between DVE and thiol-functionalized polystyrene in the same solvent. Preliminary simulations indicate that the reduced coupling efficiency (70%) can be partially attributed to recombination reactions and diffusional limitations.

Keywords: Radical thiol-ene chemistry, kinetic modeling, polymer functionalization, diffusional limitations

I. INTRODUCTION

In 2001, Sharpless et al. introduced the concept of “click chemistry” as a new approach in the field of organic chemistry. The “click” concept states that organic synthesis should be focused on highly selective, simple and orthogonal reactions that results in heteroatom-linked molecular systems with high efficiency. Ever since, many reactions have been explored as “click” reactions. Recent research has indicated that in particular radical thiol-ene coupling reactions are very promising, since terminal alkene and thiol groups can be easily introduced and these reactions can be performed in the presence of UV light without a (toxic) catalyst, contrary to the initially popular Cu(I)-catalyzed azide-alkyne 1,3-dipolar cycloaddition reactions.

Figure 1 shows the principle of the radical thiol-ene coupling technique. Initially, radicals are generated by the cleavage of a photoinitiator (I$_2$; typically DMPA), and subsequent chain transfer to the thiol present leads to the formation of thyl radicals, which can in turn add to the present “ene”. Note that the desired thio-ether coupling product is formed once the resulting carbon-centered radical abstracts a hydrogen from another thiol molecule. However, it can be expected that several side phenomena, such as termination reactions, diffusional limitations and side reactions with the initiator fragments, interfere with the normal cyclic thiol-ene process leading to a lowering of the coupling efficiency, in particular in case polymer-polymer conjugation is aimed at. A detailed answer of the effect of these phenomena is though currently largely lacking.

In this Master thesis, a combined experimental and kinetic modeling study is presented for thiol-ene coupling reactions allowing to map the influence of side phenomena on the reaction rate and the coupling efficiency. In particular, a distinction is made between thiol-ene coupling reactions involving low and high molar mass compounds. First, ideal experimental conditions for parameter discrimination are determined based on a first model system, i.e., the coupling reaction between 1-dodecanethiol (DT) and dodecyl vinyl ether (DVE). Next, ball-park values of the relevant kinetic parameters are reported for a second model system (benzyl thiol (BT)/ DVE/1,4-dioxane), which are subsequently used to study the thiol-ene coupling process with thiol-functionalized polystyrene (PS-SH) in the same solvent. Detailed product characterization (on-line FTIR spectroscopy, 300/500 MHz $^1$H-NMR, (GCx)GC analysis, and GC/MS) is performed to facilitate the determination of these parameters. In addition, the effect of the “ene” reactivity on the thiol-ene coupling process is evaluated.

II. KINETIC STUDY OF RADICAL THIOL-ENE CHEMISTRY USING LOW MOLAR MASS Compounds

A. Determination of ideal experimental conditions: radical thiol-ene reaction between 1-dodecanethiol and dodecyl vinyl ether

Based on a systematic experimental study of the coupling reaction between DT and DVE, it is found that the coupling reaction is optimally performed using a 360 nm UV-lamp set-up, as contrary to 254 nm UV-lamps, a good initiation rate can be obtained and a glass flask can be safely used. Also, this study revealed that the intensity of the radiation of the UV-lamps does not reach its maximum value during the typical low reaction times, necessitating the inclusion of this effect in the kinetic model.

For bulk experiments, a high oxygen tolerance and a very fast reaction rate is observed, leading to a significant rise in temperature during reaction, due to its strong exothermicity. In addition, the reaction rate is significantly influenced by the initial amount of DMPA. Interestingly, a too high initial amount of DMPA results in a lowering of the reaction rate. On the other hand, in solution the
coupling reaction proceeds slower and the temperature rise due to reaction can be safely neglected, allowing a more straightforward determination of kinetic parameters. However, solution experiments for parameter determination should be performed under argon atmosphere, since a small influence of oxygen is observed at low reaction times.

GCxGC analysis indicated the possible occurrence of termination reactions, such as the formation of disulfides (viz. Figure 2). However, further investigation is needed to determine the actual importance of these side reactions.

**B. Kinetic study of the reaction between benzyl thiol and dodecyl vinyl ether in 1,4-dioxane: determination of kinetic parameters**

Preliminary ball-park values for the kinetic parameters for the coupling reaction between DVE and BT in 1,4-dioxane under argon atmosphere were determined assuming a limited influence of side reactions and including the intensity change of the UV-lamp. Using these values, a good agreement with the experimental conversion profiles calculated from on-line FTIR, \(^{1}H\)-NMR 300 MHz and GC measurements for different initial molar ratios of thiol to “ene” is obtained (viz. Figure 3 A, B and C).

Furthermore, in agreement with literature data kinetic modeling confirmed that the same parameter values can be used to describe the coupling reaction between DVE and DT in n-octane (viz. Figure 3 D). However, since the formation of benzyl disulfide during the reaction could be demonstrated by qualitative GC/MS, further model development requires the performance of additional experiments.

**C. Extension to other “enes”: radical thiol-ene reaction between 1-dodecane thiol and 2-norbomene in 1,4-dioxane**

Experiments indicated that 2-norbomene (Nb) is much more reactive than DVE since reaction times were ca. 10 times lower even though the same reaction conditions were applied. However, all the performed equimolar reactions between DT and Nb in 1,4-dioxane lead to a thiol conversion of approximately 50 %, for which currently no straightforward explanation could be given based on GC/MS and \(^{1}H\)-NMR 300 MHz results. Further investigation is thus necessary to understand the latter phenomenon.

**III. KINETIC STUDY OF THE COUPLING REACTION BETWEEN THIOL-FUNCTIONALIZED POLYSTYRENE AND DODECYL VINYL ETHER IN 1,4-DIOXANE: EVALUATION OF THE IMPORTANCE OF SIDE PHENOMENA**

First, PS was prepared by RAFT polymerization using dibenzyl trithiocarbonate as chain transfer agent without a conventional initiator. Subsequently, the trithiocarbonate groups were cleaved by aminolysis, resulting in required PS-SH. Finally, the UV-induced coupling between PS-SH and DVE was performed in 1,4-dioxane, and a limiting functionalization efficiency of ca. 70% (on a thiol basis) was observed both by on-line FTIR and \(^{1}H\)-NMR 500 MHz measurements.

The reduced coupling efficiency can at least be partially attributed to undesired recombination reactions, as indicated by GPC measurements, and to diffusional limitations, as indicated by preliminary simulation results (viz. Figure 4).

However, it should be emphasized that impurities, side reactions during the polymerization process and the aminolysis also can have a significant effect on the measured coupling efficiency.

**IV. CONCLUSIONS**

From the experimental study of the reaction between DT and DVE it can be concluded that the determination of ball-park values for the kinetic parameters of the involved reactions in radical thiol-ene chemistry for low molar mass compounds is best done based on experimental data in solution using the 360 nm UV-lamp set-up, and performed under argon atmosphere. In these conditions, a glass flask can be used and isothermality is guaranteed.

Ball-park values for a model system (DVE/BT/1,4-dioxane/DMPA) were obtained assuming a limited influence of recombination reactions, though a quantification of the termination products is necessary to acquire an unambiguous set of rate coefficients. A good agreement between experimental and modeling results is obtained, also for the related DVE/DT system in n-octane using the same parameters. Furthermore, a significantly faster reaction rate can be obtained by replacing DVE by Nb. However, further investigation should reveal the explanation for the unexpected conversion profile of the thiol compound.

For coupling reactions with a low molar mass “ene” and a thiol-functionalized macromolecule, it has been indicated for a PS SH/DVE/1,4-dioxane/DMPA model system that the coupling efficiency can be affected during each of the three synthesis steps. In particular, it has been demonstrated that the coupling reaction is influenced by recombination reactions and diffusional limitations.

**NOTATION**

FTIR=Fourier transform infrared radiation; RAFT = reversible addition fragmentation chain transfer; NMR = nuclear magnetic resonance; GC = gas chromatography; MS = mass spectroscopy; DMPA= 2,2-dimethoxy-2-phenylacetophenone; PS=polystyrene; GPC= gel permeation chromatography

**REFERENCES**


Nederlandstalige samenvatting: ‘Kinetische modellering van radicalaire thiol-en chemie’

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Abstract: Een gecombineerde experimentele en modellering-studie wordt toegelicht voor radicalaire thiol-en koppelings-reacties tussen zowel laagmoleculaire als hoogmoleculaire componenten. Na een gedetailleerde productkarakterisering en optimalisatie van de reactiecondities worden richtwaarden voor de kinetische parameters geraapporteerd voor een laagmoleculair modelssysteem (DVE/BT/DMPA/1,4-dioxaan), die een evaluatie van het belang van zijreacties en diffusielimiteringen voor de koppelingsreactie tussen DVE en thiol-gefuncionaliseerde polystyreen in hetzelfde solvent mogelijk maken. Preliminaire simulatieresultaten tonen aan dat de verminderde koppelings-efficiëntie (70 %) gedeeltelijk te wijten is aan recombinatiereacties en diffusielimeteringen.

Sleutelwoorden: Radicalaire thiol-en chemie, kinetische modellering, polymeerfuncionalisatie, diffusielimeteringen

I. INLEIDING


Figuur 1 toont het principe van de radicalaire thiol-en koppelingsreactie. Initieel worden radicalen gegenereerd door de dissociatie van een fotoninitiator (I₂; typisch DMPA), en een daaropvolgende transfer reactie naar het thiol resulteert in de vorming van thylradicalen, dewelke op hun beurt kunnen adderen op de aanwezige dubbele binding. Het gewenste thio-ether wordt gevormd wanneer het gegenereerde koolstofradicaal een proton abstraheert van een andere thiolmolecule. Doch, verschillende ongewenste fenomena zoals terminatiereacties, diffusielimeteringen en zijreacties met initiatorfragmenten kunnen optreden, en kunnen een verminderde koppelings-efficiëntie veroorzaken, vooral in het geval van polymerge-polymerconjugaties.⁴ Een gedetailleerde studie van het belang van deze fenomenen ontbreekt echter.

In dit afstudeerwerk wordt een gecombineerde experimentele en kinetische modelleringstudie toegelicht voor thiol-en koppelings-reacties, met als doel de invloed van neveneffecten op de reactiesnelheid en koppelings-efficiëntie in kaart te brengen voor zowel laagmoleculaire als hoogmoleculaire componenten. Eerst worden de ideale experimentele condities voor parameterisering bepaald met behulp van een eerste modelssysteem, i.e., de reactie tussen 1-dodecaanthiol (DT) en dodecylvinylether (DVE). Vervolgens worden initiële waarden voor de relevante kinetische parameters bepaald voor een tweede modelssysteem (benzythiol (BT)/DVE/1,4-dioxaan), en deze worden tot slot aangewend in de studie van de modificatie van thiol-gefuncionaliseerde polystyreen (PS-SH) met DVE in hetzelfde solvent. De bepaling van deze parameters is ondersteund door een gedetailleerde productkarakterisering (on-line FTIR spectroscopie, 300/500 MHz 1-H-NMR, (GC)xGC, en GC/MS). Tevens wordt de invloed van de reactiviteit van de dubbele binding op het thiol-en koppelingsproces geëvalueerd.

II. KINETISCHE STUDIE VAN RADICALAIRE THIOL-EN CHEMIE MET LAAGMOLECULARE COMPONENTEN

A. Bepaling van ideale experimentele condities: radicalaire thiol-en reactie tussen 1-dodecaanthiol en dodecylvinylether

Een experimentele studie van de reactie tussen DT en DVE wees uit dat de koppelingsreactie het best uitgevoerd wordt met een 360 nm UV-lamp opstelling, aangezien een goede reactiesnelheid kan verkregen worden en een glazen kolf kan worden gebruikt, in tegenstelling tot de 254 nm UV-lamp. Bovendien heeft deze studie aangetoond dat de reactietafel van de straling van de UV-lampen niet zijn maximale waarde bereikt gedurende de typisch lage reactietijden, waardoor het dus noodzakelijk is dit effect in het kinetisch model te implementeren.
Voor bulkexperimenten werd een hoge zuurstof tolerantie en een zeer snelle reactiesnelheid waargenomen. Door het sterk exotherm karakter leidt dit echter tot een aanzienlijke temperatuurstijging tijdens de reactie. Ook wordt de reactiesnelheid sterk beïnvloed door de hoeveelheid DMPA toegevoegd, waarbij een te hoge initiële concentratie aan DMPA resulteert in een lagere reactiesnelheid.

Anderzijds verloopt de koppellingsreactie in oplossing trager en is de temperatuurstijging door reactie verwaarloosbaar, zodat een meer evidente bepaling van kinetische parameters mogelijk is. Experimenten in oplossing moeten echter uitgevoerd worden onder argonatmosfeer, aangezien een beperkt effect van zuurstof werd vastgesteld.

GCGXGC analyse heeft bovendien aangetoond dat de vorming van dilsulfides (zie Figuur 2) mogelijk is. Verder onderzoek is echter nodig om het eigenlijke belang van deze zijreacties te bepalen.

B. Kinetische studie van de reactie tussen benzylthiol en 2-norborneen in 1,4-dioxaan: bepaling van kinetische parameters

Na implementatie van de intensiteitsverandering van de UV-lamp werden eerste waarden voor de kinetische parameters voor de koppeling tussen BT en DVE in 1,4-dioxaan bepaald onder de veronderstelling van een beperkte invloed van zijreacties. Simulaties met deze waarden toonden een goede overeenstemming met experimentele conversiedata uit on-line FTIR, 1H-NMR 300 MHz en GC metingen voor verschillende initiële molaire thiol tot "en" verhouding (zie Figuur 3A, B en C).

Bovendien kunnen dezelfde parameterwaarden aangewend worden om de reactie tussen DT en DVE in n-octaan te beschrijven. Bovendien kan een belangrijke efficiëntie worden verkregen door DVE te vervangen door Nb, de experimentele data resulteert, en dit ook voor het DT-DVE systeem in n-octaan. Verder onderzoek is echter nodig om het onverwachte effect te verkrijgen of deze effecten mogelijk zijn voor de functionalisatie van benzylthiol en 2-norborneen in 1,4-dioxaan.

C. Uitbreiding: radicalaire thiol-en reactie tussen 1-dodecaanthiol en 2-norborene in 1,4-dioxaan

Experimenten hebben aangetoond dat 2-norborene (Nb) veel reactiever is dan DVE, aangezien onder dezelfde reactieconders ca. 10 keer hogere reactiesnelheden werden waargenomen. Alle uitgevoerde experimentele experimenten leiden echter tot een thiolconversie van ongeveer 50 %, wat niet kan verklaard worden op basis van de huidige GC/MS) en 1H-NMR 300 MHz resultaten.

III. KINETISCHE STUDIE VAN DE KOPPELINGSREACTIE TUSSEN THIOL-GEFUNCTIONALISEERD POLYSTYREEN EN DODECYLVINYLEThHER IN 1,4-DIOXAAN: EVALUATIE VAN HET BELANG VAN RANDFENOMENEN

PS werd eerst bereid via RAFT polymerisatie met dibenzylthiociarbonnaat als ketentransfer agent zonder toevoeging van een conventionele initiator. Vervolgens werden de trithiocarbonylgruppen gesplitst via aminolyse resulterend in de vorming van PS-SH. Tenslotte werd de UV-geïnduceerde koppellingsreactie tussen PS-SH en DVE uitgevoerd in 1,4-dioxaan, en zowel on-line FTIR als 1H-NMR 500 MHz metingen leidden tot een functionalisatie-efficiëntie van ca. 70 %.

De geëvalueerde koppelingsefficiëntie kan tenminste voor een deel toegeschreven worden aan ongewenste recombinatieresfecties, zoals aangetoond door GPC metingen, en aan diffusielimiteringen, aangetoond via intrinsieke simulaties (zie Figuur 4).

Het moet echter benadrukt worden dat ook onzuiverheden en zijreacties tijdens het polymersatieproces en de aminolyse reactie een belangrijk effect kunnen hebben op de waargenomen koppelingsefficiëntie.

IV. CONCLUSIES

Op basis van de experimentele studie van de reactie tussen DT en DVE kan besloten worden dat de bepaling van richtwaarden voor de snelheidsefficiënten in de radicalaire thiol-en reactie tussen laagmoleculaire componenten het best uitgevoerd wordt uitgaand van experimentele data in oplossing onder argonatmosfeer en gebruik makend van de 360 nm UV-lamp opstelling. Onder deze conditions kan een glazen kolven worden gebruikt en is isothermiteit gegarandeerd.

Dergelijke snelheidsefficiënten werden verkregen voor een modellsysteem (DVE/BT, 1,4-dioxaan/DMPA) waarbij een beperkte invloed van recombinatieresacties werd aangenomen. Een quantitative analyse van de terminatieprodukten is echter nodig om een ondubbelzinnige set kinetische parameters te verkrijgen. Een goede overeenstemming tussen simuleringsresultaten en experimentele data resulteert, en dit ook voor het DT-DVE systeem in n-octaan. Bovendien kan een aanzienlijk snellere reactiesnelheid verkregen worden door DVE te vervangen door Nb, verder onderzoek is echter nodig om het onverwachte conversiesprofiel van het thiol te verklaaren.

Voor de functionalisatie van PS-SH en PS met DVE in 1,4-dioxaan werd aangetoond dat de koppelingsefficiëntie kan beïnvloed worden tijdens elk van de drie synthesesetten. Er werd bewezen dat een bepaald de koppellingsreactie beïnvloed wordt door recombinatieresacties en diffusielimiteringen.

NOTATIE

FTIR=Fourier transform infrarood; RAFT = reversibel additie-fragenmetaketentransfer; NMR = nucleaire magnetische resonantie; GC = gaschromatografie; MS = massaspectroscopie; DMPA= 2,2-dimethoxy-2-phenylacetophenon; PS=polystyreen; GPC= gelgolfchromatografie

REFERENTIES


Figuur 4: Vergelijking tussen intrinsieke simulaties met dezelfde intrinsieke kinetische parameters als in Figuur 3 (rode lijn), en experimentele data voor de functionalisatie-efficiëntie (zwarte bollen), i.e. \( \beta \) (product)/thiol), (A; equimolar; 0.05 w/o DMPA), en de DVE conversie (B; 3-voudige overmaat DVE; 0.05 w/o DMPA) voor de modificatie van PS-SH met DVE in 1,4-dioxaan.
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CHAPTER 1: INTRODUCTION

Recent experimental studies have demonstrated the significant potential of thiol-ene chemistry for polymer conjugation. The principle of the thiol-ene coupling technique is shown in Figure 1.

Starting from a photoinitiator initiator radicals are generated, which can undergo chain transfer to the thiol present resulting in the formation of thiol radicals, which can in turn add to the present “ene”. The coupling product is obtained once the in the addition step obtained carbon-centered radical also takes part in a chain transfer reaction. However, several side phenomena, such as termination reactions and diffusional limitations, can interfere with the normal cyclic thiol-ene process leading to a lowering of the coupling efficiency. A detailed answer of the effect of these phenomena is though currently largely lacking.

Therefore, in this Master Thesis, a systematical detailed kinetic study of radical thiol-ene chemistry is presented. The aim of the present work is to develop an intrinsic kinetic model based on experimental data for low molar mass thiol-ene systems, which allows in a next step to determine the influence of side reactions and diffusional limitations on the functionalization of polymers using radical thiol-ene chemistry. Termination products are identified based on an extensive product characterization.

In what follows, in Chapter 2 an overview of the reactions denoted in literature as “click” reactions is given, particularly focusing on the features and applications of the radical thiol-ene reaction. Next, in Chapter 3 a detailed kinetic study is presented for radical thiol-ene chemistry using low molar mass compounds, and the gained knowledge is further used in the study of polymer functionalization reactions for a model system using radical thiol-ene chemistry, as discussed in Chapter 4. Finally, general conclusions and some indications for future research are given in Chapter 5.
CHAPTER 2: LITERATURE SURVEY

1 Overview of “Click” reactions

In 2001, Sharpless et al.\textsuperscript{[2]} introduced the concept of “click chemistry” as a new approach in the field of organic chemistry. The “click” concept states that organic synthesis should be focused on highly selective, simple and orthogonal reactions that give heteroatom-linked molecular systems with high efficiency. More precisely, a successful “click” reaction is defined as a modular reaction that proceeds with nearly quantitative yields under mild reaction conditions, ideally without the formation of byproducts or when present easily removable by non-chromatographic methods. Based on this concept, in particular, a transformational effect on organic synthesis, polymer chemistry and drug discovery has been obtained \textsuperscript{[3]}.

The aforementioned characteristics of “click” reactions are achieved by a high thermodynamic driving force, usually greater than 80 kJ mol\textsuperscript{[3]}. Besides that, the reaction has to be stereo- and regiospecific, and applicable to a wide variety of readily available starting compounds. From a practical viewpoint, it should be simple to perform the reaction in bulk or in an environmentally benign solvent (e.g. water) with a facile product isolation, and it should be water and oxygen insensitive. The following classes of chemical transitions can be designated as “click” reactions \textsuperscript{[2]}:

i. cycloadditions of unsaturated species, especially 1,3-dipolar cycloaddition reactions, but also the Diels-Alder reactions;
ii. nucleophilic substitution reactions, in particular ring-opening reactions of strained heterocyclic electrophiles such as epoxides, aziridines, aziridinium ions and episulfonium ions;
iii. “non-aldol” type carbonyl reactions, such as the formation of ureas, thioureas, aromatic heterocycles, hydrazones and amides;
iv. additions to carbon-carbon multiple bonds, especially oxidative cases such as epoxidation, dihydroxylation, aziridination and sulfenyl halide addition, but also Michael additions of Nu-H reactants (Nu = nucleophile).

An overview of the reactions, which are denoted as “click” reactions in literature, can be found in Table 1 \textsuperscript{[4-5]}. Next to the reagents and the mechanism, the main application fields of the particular reaction are included.
Table 1: Overview of reactions denoted as “click” reactions in literature.

<table>
<thead>
<tr>
<th>entry</th>
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<tr>
<td>3</td>
<td>azide</td>
<td>electron-deficient alkyne</td>
<td>[3+2] cycloaddition</td>
<td>L, PEP2</td>
</tr>
<tr>
<td>4</td>
<td>azide</td>
<td>Aryne</td>
<td>[3+2] cycloaddition</td>
<td>L</td>
</tr>
<tr>
<td>5</td>
<td>tetrazine</td>
<td>Alkene</td>
<td>Diels-Alder retro-[4+2] cycloaddition</td>
<td>L</td>
</tr>
<tr>
<td>6</td>
<td>tetrazole</td>
<td>Alkene</td>
<td>1,3-dipolar cycloaddition (photoclick)</td>
<td>L, PEP2</td>
</tr>
<tr>
<td>7</td>
<td>dithioester</td>
<td>Diene</td>
<td>hetero-Diels-Alder cycloaddition</td>
<td>P3</td>
</tr>
<tr>
<td>8</td>
<td>anthracene</td>
<td>Maleimide</td>
<td>[4+2] Diels-Alder reaction</td>
<td>P3, P1b</td>
</tr>
<tr>
<td>9</td>
<td>thiol</td>
<td>Alkene</td>
<td>radical addition (thio click)</td>
<td>P1b, P4</td>
</tr>
<tr>
<td>10</td>
<td>thiol</td>
<td>Enone</td>
<td>Michael addition</td>
<td>P1a</td>
</tr>
<tr>
<td>11</td>
<td>thiol</td>
<td>Maleimide</td>
<td>Michael addition</td>
<td>P1a, P3</td>
</tr>
<tr>
<td>12</td>
<td>thiol</td>
<td>Isocyanate</td>
<td>nucleophilic addition</td>
<td>P1a, P6, P5</td>
</tr>
<tr>
<td>13</td>
<td>thiol</td>
<td>Alkyne</td>
<td>radical addition</td>
<td>L, P1a, P2, P4</td>
</tr>
<tr>
<td>14</td>
<td>thiol</td>
<td>para-fluoro</td>
<td>nucleophilic substitution</td>
<td>P1b</td>
</tr>
<tr>
<td>15</td>
<td>amine</td>
<td>para-fluoro</td>
<td>nucleophilic substitution</td>
<td>P1b</td>
</tr>
</tbody>
</table>
A practical aspect which is in particular important for the application of “click chemistry” in polymer chemistry, is the “equimolarity feature” \(^{[4,6]}\). This property of efficient “click” reactions, although not included in its original definition, enables polymer-polymer conjugation to be performed without the necessity of a product purification step. If one polymer “click” component is used in excess, or a significant amount of side-products are formed, a complex mixture is obtained that is in the worst case non-separable. As the definition of the “click” reaction dictates that the product should be easily isolated by non-chromatographic methods, distillation and precipitation are the only available separation techniques. When dealing with polymeric reactants, distillation can be ruled out and precipitation will be difficult, if not impossible, since the solubility of the “click” polymer product and the starting compounds does not differ that much. Also, a fast “click” reaction is desirable from an industrial point of view. Hence, for the conjugation of polymers, two requirements should be added \(^{[4,6]}\) to the original definition of a “click” reaction as introduced by Sharpless et al.:

- end-group transformation without the formation of significant side-products;
- high conjugation efficiency, and more specifically, a reasonable reaction time without employing an excess of one reaction partner.

Though a large variety of reactions have been explored as “click” reactions, research has been mainly focused on the Cu(I)-catalyzed azide-alkyne 1,3-dipolar cycloaddition reaction (CuAAC). The Huisgen reaction has been successfully applied for the synthesis of biomedical libraries, functional block copolymers, uniformly structured hydrogels, the preparation of dendrimers, and
many others \cite{7-12}. This very broad applicability is due to the facile reaction conditions and strong orthogonality of the copper-mediated Huisgen reaction.

However, the use of the toxic copper catalyst and the stringent safety hazards caused by the explosive nature of azides, have encouraged researchers to evaluate the potential of other reactions to become “click” reactions. Recent research has been mainly focused on Diels-Alder reactions, metal-free dipolar cycloadditions \cite{4,13}, and a series of thiol-based reactions including thiol-ene, thiol-yne \cite{14-16}, thiol-isocyanate \cite{17}, thiol-parafluorostyrene \cite{18} and thiol-bromo processes \cite{19-20} (see Table 1). In what follows, is focused on thiol-ene click reactions, which are thought to have the strongest potential to match the popularity of the Cu(I)-catalyzed azide-alkyne cycloaddition reactions.

2 Thiol-ene “click” reaction

The relatively weak sulfur-hydrogen bond of thiols is the basis for a large number of chemical reactions that proceed with quantitative yields under mild conditions, and which can be initiated by a variety of methods. The highly efficient reaction of thiols with double bonds (“enes”) was already studied in the early 1900s, and gained a profound attention during the last century. Initially it was used to prepare near-perfect networks and films, and due to the recognition of its “click” characteristics it has been recently employed in other areas of synthesis (see section 2.2.4).

There are several features which make the thiol-ene reaction that attractive \cite{21}. Firstly, it can proceed under a variety of conditions: a radical pathway or a catalytic process mediated by nucleophiles, acids or bases (Michael addition), without a catalyst in highly polar solvents (e.g. DMF, water) or via supramolecular catalysis. Secondly, a wide range of enes serve as suitable substrates and virtually any thiol can be employed. Thirdly, the reaction is relatively insensitive to the ambient oxygen or water, and can yield a single regioselective product in a nearly quantitative fashion under very mild conditions. Also, polymeric networks can be formed when multifunctional thiols and enes are used \cite{22-25}. These features make thiol-ene chemistry amenable to applications ranging from high performance protective polymer networks to processes that are important in the optical, biomedical, sensing, and bioorganic modification fields \cite{3,26}. It should however be stressed that the reactivity strongly depends on the component structure and the reaction mechanism. In what follows, the thiol Michael addition and the radical thiol-ene reaction are discussed. Main focus is on the latter technique, since that one is investigated in this Master thesis.
2.1 Thiol-Michael addition

Catalytic reactions between a thiol and an electron-deficient ene are called thiol-Michael additions. Maleimides, (meth)acrylates, fumarate esters, α,β-unsaturated ketones, acrylonitrile, cinnamates and crotonates, can all be efficiently coupled with a thiol under base, (organo)metallic, Lewis acid or nucleophilic catalysis.

The mechanism of thiol-Michael addition is based on a nucleophilic addition of a thiolate anion on an activated carbon-carbon double bond. Since the active species are anions, no termination reactions occur, and consequently no byproducts are formed. The reaction proceeds to full conversion in typically a couple of minutes, or even seconds. As the double carbon-carbon bond has to be activated, this reaction is however less versatile than the thiol-ene radical addition reaction.

The way the thiolate anion is formed, depends on the nature of the catalyst used. Weak base catalysts, such as triethylamine (NEt₃), are usually sufficient for deprotonation of the thiol with formation of a triethylammonium cation and the corresponding thiolate anion, which can then start the anionic reaction cycle (see Figure 2): the intermediate carbon-centered anion, which is a stronger base than NEt₃, abstracts a proton from another thiol molecule (or from the triethylammonium cation) with formation of the thio-ether product and a new thiolate anion (or NEt₃ molecule).

Another possibility is the use of a nucleophile as catalyst. The reaction scheme for this strategy is shown in Figure 3. Primary or secondary amines, or even more efficient alkyl phosphine nucleophilic catalysts are used. Evidence for a nucleophile-based mechanism is for example obtained from a real-time full fourier transform infrared red (FTIR) kinetic study of the “click” reaction between hexanethiol and hexyl acrylate catalyzed by three different catalysts with very similar basicity, but different nucleophilicity [27]. The strong difference in the kinetics can only be

![Figure 2](image_url)
explained by a nucleophilic addition of the catalyst to the electron deficient carbon-carbon double bond of the acrylate (see Figure 3). The weakly basic dimethylphenylphosphine (Me₂PPh) is a very efficient nucleophilic catalyst (chemical structure is shown in Figure 4).

![Figure 3](image)

**Figure 3**: The phosphine-catalyzed mechanism for the Michael-addition of a thiol to an acrylic carbon-carbon double bond.

A particularly reactive “ene” substrate is a maleimide (Figure 4). Because of its ring-strain coupled with two electron-withdrawing carbonyl groups, the carbon-carbon double bond is strongly activated and such thiol-ene reactions proceed very rapidly. However, these reactions should be performed with care, as the most efficient maleimides are highly neurotoxic. In highly polar solvents, such as dimethylformamide (DMF) and dimethylsulfoxide (DMSO), thiol-maleimide reactions can be even conducted without a catalyst, since the dissociation of the thiol with formation of the corresponding thiolate anion is promoted by the solvent.

![Figure 4](image)

**Figure 4**: Chemical structure of Me₂PPh and maleimide

### 2.2 Radical thiol-ene “click” reaction

In 1938, Kharasch et al. showed that the addition of thiols to enes can proceed via a free-radical chain mechanism. Between 1970 and 1980, the research of Morgan, Ketley and coworkers has lead to the first large-scale use of thiol-ene photocuring in the United States. Because of the odor that accompanied thiol-ene chemistry and the rapid yellowing upon weathering of thiol-ene coatings, thiol-ene photocuring gave way to other photocurable systems. The yellowing was a result of the use of benzophenone in relatively large quantities as
photoinitiator, as degradation of the remaining initiator into colored byproducts occurred upon light exposure.

In the late 1970s Ketley and coworkers showed that also cleavage type initiators (e.g. 2,2-dimethoxy-2-phenylacetophenone (DMPA)) could be used to initiate the thiol-ene polymerization. Therefore, many efforts have been made to revive thiol-ene photopolymerizations in industrial applications \[32-34\]. Recent achievements of Bowman, Hoyle and coworkers \[26\], have highlighted the great potential of thiol-ene chemistry and have lead to the increasing interest for this type of reaction during the last years.

The great advantage of the UV light-mediated thiol-ene radical reactions over classical free radical photopolymerizations, is that they combine the classical benefits of “click” reactions with the advantages of a photoinitiated process, which mainly involve activation at specific time intervals and at desired locations (spatial control) \[26\]. For example, when the functionality of at least one of the multifunctional reactants is greater than two, uniform networks with homogeneous cross-link density as well as low shrinkage degree can be formed as a consequence of the step growth nature of the thiol-ene radical addition reaction (see section 2.2.4.2).

The mechanism of this reaction and the reactivity of both the ene and the thiol functional groups are discussed in the next sections. As the oxygen insensitivity of the thiol-ene “click” reaction has strongly enlarged its application field, this feature will also be described. Finally, the most important applications of the thiol-ene “click” reactions will be mentioned.

### 2.2.1 Mechanism

Figure 5 shows the mechanism for a radical thiol-ene reaction. In a first step, initiator radicals are generated. In principle, every process that generates free radicals can be used as initiating system. Both thermal initiation and UV-induced photoinitation are possible. In a next step, the initiator radical abstracts a hydrogen atom from the thiol group and thereby generates a thyl radical, \( RS' \). This radical can also be produced by photolysis or thermal cleavage of the sulfur-hydrogen bond from the thiol group. The generated thyl radical can rapidly add- to both electron rich and electron poor carbon-carbon double bonds, which is referred to as propagation. Depending on the chemical nature of the ene, a single propagation step or a homopolymerization can occur. Note that in case a single propagation reaction step occurs, the process can be seen as a pure coupling technique that forms after propagation an intermediate carbon-centered radical. This radical can also readily abstract a hydrogen atom from another thiol-functionalized molecule with the generation of the desired thio-ether product and another thyl radical (chain transfer step). The latter can again add to another carbon-carbon double bond and start the reaction cycle once more. The chain process will however stop if termination reactions between the free radicals occur. Note that these are considered as undesired side reactions. The three most important termination reactions are thyl-thyl radical coupling (or recombination), head-to-head coupling of the carbon-
centered radicals and cross-termination between a thyl and a carbon-centered radical. It should be reminded that in conditions leading to a significant amount of terminated species, the process might not be considered as a successful “click” reaction \([2, 4]\).

The addition of the thyl radical across the carbon-carbon double bond is exothermic, with reaction enthalpies ranging from \(-44\) kJ mol\(^{-1}\) for the electron-rich vinyl ether double bond to \(-94.6\) kJ mol\(^{-1}\) for the electron-poor double bond of an N-alkyl maleimide \([35]\). The thio-ether click product has an anti-Markovnikov orientation, as the intermediate carbon-centered radical is more stable upon addition of the thyl radical onto the less substituted carbon atom of the double bond \([36]\).

A single propagation step occurs for the reaction between a thiol and a norbornene, a vinyl ether, an allyl ether or a vinyl siloxane (typical enes). On the other hand, if (meth)acrylates are used as “ene”-reactant, the assumption that homopolymerization doesn’t occur is invalid and a binary system has to be considered consisting of two reaction cycles (see Figure 6). The first reaction cycle involves alternation of chain transfer and propagation reactions (thiol-ene click), and the second incorporates addition and chain-growth mechanisms (homopolymerization of the (meth)acrylates) \([26]\).
This binary system is often applied in acrylate network formation, since by changing the thiol-acrylate molar ratio or the reactivity of the reactants for one particular reaction cycle, the mechanical and physical properties of the network can be tailored. Compared to the conventional (meth)acrylate homopolymerizations, the presence of the thiol groups in the binary thiol-acrylate systems results in a significantly reduced oxygen inhibition, a delay of the gel point conversion and a strongly diminished shrinkage of the final polymer network \[26\]. For relatively small thiol concentrations (5-20 wt%), these benefits are achieved without a significant decrease of the modulus or glass-transition temperature of the pure (meth)acrylate \[37\]. The thiol groups thus increase the polymerization rate in the presence of oxygen \[38\] and exclude the need for a nitrogen atmosphere or extremely high light intensities to overcome oxygen inhibition. These properties enable a facile implementation of thiol-(meth)acrylate polymerization in the formation of hydrogels and tissue engineering matrices, as polymerizations are conducted in a clinical environment, where oxygen is inherently present \[39-41\]. The exact structure of the network produced by the thiol-(meth)acrylate polymerization is not known, however it is shown that the network is more homogeneous with respect to the cross-link density \[3\].

Lecamp and coworkers \[42\] have thoroughly studied the photopolymerization of a dimethacrylate polyether oligomer, containing an aromatic ether, and TetraThiol1 (chemical structure is shown in Figure 7) by a combination of full DSC and real-time FTIR. They have found that the methacrylate conversion was three times greater than the thiol conversion, as the methacrylate is consumed both by the homopolymerization and copolymerization. Furthermore, a decrease in glass transition temperature was observed relative to the dimethacrylate homopolymer, thus indicating that the presence of the thiol has a plasticizing effect.

---

**Figure 6**: Cyclic representation of the reaction mechanism of the radical thiol-ene reaction if homopolymerization of the ene does occur \[26\].
Besides the binary thiol-(meth)acrylate systems, also ternary thiol-ene-(meth)acrylate systems are possible, in which a non-homopolymerizable “ene” is added to the binary thiol-(meth)acrylate composition. This extra feature enables several opportunities to manipulate polymerization and polymer properties that are not possible with the binary systems. For instance in a thiol-allyl ether-methacrylate system, a nearly equivalent glass transition temperature is achieved as for a pure methacrylate system (80°C versus 85°C), while the width of the glass transition region is reduced with approximately a factor two \cite{43}. Furthermore, there is a better control over the network homogeneity, the gel point conversion and the cross-link density in ternary systems \cite{44}.

Finally, when two non-homopolymerizable “enes” are added to a thiol, a ternary thiol-ene-ene system is obtained. If applied to thiol-ene networks, the network properties are thus determined by the choice of the monomers: dependant on the chemical structure of the “ene” components, both thiol-ene reactions will have different rates that control the network formation. For example, thiol-allyl ether-maleimide networks have a very high thermal stability \cite{45}.

### 2.2.2 Reactivity

The overall rate of the thiol-ene radical addition reaction is strongly influenced by the chemical structure of the “ene” and thiol groups. In this section, some general rules are formulated for the overall rate as a function of the chemical structure of the reactants. A distinction is made between the chemical structure of the “ene” and the thiol.

#### 2.2.2.1 “Ene” reactivity

A comparison between the overall reaction rates for a variety of “enes” has been made by Hoyle et al. \cite{3}, and is based on their own lab results along with general reactivity trends highlighted in publications from Bowman \cite{46}, Jacobine \cite{47} and coworkers. These authors obtained the following general reactivity order for addition of a typical thiol to different “enes” \cite{3} (for chemical structures see Figure 8).
Except for norbornene, methacrylate, styrene and conjugated dienes, this ordering is in agreement with the first basic rule of Morgan and coworkers, which states that reactivity decreases with decreasing electron density of the carbon-carbon double bond [48]. The very high reactivity of norbornenes can be attributed to a combination of the significant loss of ring strain upon addition of a thiol radical to the carbon-carbon double bond, and the subsequent rapid hydrogen-abstraction rate from a thiol by the carbon-centered radical. The low overall reaction rates for methacrylates, styrenes and conjugated dienes are due to the high stability of the intermediate carbon-centered radicals, resulting in low hydrogen-abstraction rate coefficients [3, 21].

In addition, it has been indicated that also the degree of substitution of the double bond influences its reactivity in a thiol-ene free radical chain reaction. Terminal “enes” are in general more reactive than internal carbon-carbon double bonds. This was confirmed by real-time infrared (RTIR) experiments performed by Hoyle and coworkers, who showed that 1-hexene was 8 times more reactive than trans-2-hexene and 18 times more reactive than trans-3-hexene [21] (see Figure 9). This suggests that steric hindrance is an important factor for the reactivity of the “enes”.

Figure 8: Chemical structures of the “ene” components mentioned in the reactivity order [3].

Figure 9: Structure of 1-hexene, trans-2-hexene and trans-3-hexene
However, besides steric effects also cis-trans equilibria of the “ene” can significantly affect the overall rate at which the thiol-ene reaction occurs. Thiol radicals can lead to the conversion of cis C=C bonds into the less reactive trans C=C bonds, as the addition of a thiol radical to cis C=C bonds is reversible \[^{[21, 49]}\]. For example, when an excess of methanethiol is reacted with cis-2-butene at 60 °C initiated by azobisisobutyronitrile (AIBN), significant amounts of the trans diastereomer are detected \[^{[50]}\] (see Figure 4). This can be explained as a function of the values of the rate coefficients of the reactions involved. It has been reported that the rate coefficient of the beta C-S scission of the intermediate carbon-centered radical into cis-2-butene, \( k_1 \), is 20 times higher than the rate coefficient of chain transfer, \( k_{ct} \), which leads to the desired thio-ether product. On the other hand, the rate coefficient for beta C-S scission into the trans-2-butene isomer, \( k_2 \), is 80 times higher than \( k_{ct} \) \[^{[51]}\].

\[
\begin{align*}
\text{CH}_3\text{SH} + \text{H}_2\text{C} = \text{C}(\text{H})\text{CH}_3 \quad &\xrightarrow{k_1} \quad \text{H}_3\text{C}\underset{\text{H}}{\text{C}}\underset{\text{H}}{\text{C}}\text{H}_3 \quad &\xrightarrow{k_2} \quad \text{H}_3\text{C}\underset{\text{H}}{\text{C}}\underset{\text{H}}{\text{C}}\text{H}_3 + \text{RS}^- \\
&\quad \xrightarrow{k_{ct}} \quad \text{H}_3\text{C}\underset{\text{H}}{\text{C}}\underset{\text{H}}{\text{C}}\text{H}_3 \quad &\quad \text{RS}^- \quad &\quad \text{thio-ene product}
\end{align*}
\]

\textbf{Figure 10: cis-trans equilibrium competing with the desired chain transfer reaction} \[^{[21]}\]

\[2.2.2 \text{ Thiol reactivity}\]

The most widely used multifunctional thiols are Tetrahydrol1 and trimethylolpropane tri(3-mercaptopropionate) \[^{[3]}\]. The chemical structures of these compounds are shown in Figure 12. Next to these commercially available thiols, other multifunctional thiols have been reported, which are used in numerous applications \[^{[52]}\].

Morgan et al. \[^{[48]}\] have indicated that not all thiols are equally reactive toward “enes”. In particular, they compared the reactivity of alkyl thiols, thiol glycolate esters and thiol propionate esters (see Figure 11), three important thiols. It was found that propionate and glycolate esters are more reactive than alkyl thiols. For example, the radical addition rate of methyl mercaptopropionate to 1-heptene has been reported to be six times higher than for 1-pentanethiol \[^{[3]}\].

\[\text{Alkyl 3-mercaptopropionate} \quad \text{Alkylthioglycolate} \quad \text{Alkylthiol}\]

\textbf{Figure 11: General structures of the thiols used for determination of the “ene” reactivity} \[^{[3]}\].
M. C. Cole proposed that the higher reactivity of thiol glycolate esters and thiol propionate esters is caused by a weakening of the sulfur-hydrogen bond by intramolecular hydrogen bonding of the thiol hydrogen group with the ester carbonyl group \[^{[53]}\]. Alternatively, L. M. Stock suggested that this increased reactivity can be explained by polar effects \[^{[50]}\].

![Figure 12: Chemical structures of commercially available thiols Trithiol1 and Tetrathiol1](image)

### 2.2.3 Oxygen insensitivity

The salient feature of radical thiol-ene chemistry is its relative insensitivity or high tolerance to oxygen. As shown in Figure 15, even in the presence of oxygen, thiy radicals can be continuously regenerated. When oxygen interacts with the formed carbon-centered radicals the resulting peroxides will still abstract a thiol hydrogen, leading to the formation of a slightly modified click product and the release of a thiy radical. However, it should be kept in mind that in dilute conditions, i.e., for low concentrations of thiol, a successful click reaction also requires the removal of oxygen prior to the reaction.

As in open air the thiol-ene reaction runs successfully to completion in a few seconds \[^{[3]}\] (TriThiol2 with trivinyl ether), this chemistry opens up the way for rapid curing in sunlight and air without the need of laminating the resin during sunlight exposure \[^{[3, 54]}\]. Even when no photoinitiator is present, the film can still be cured in sunlight in a few minutes by cleavage of the sulfur-hydrogen bond. Furthermore, it is worthwhile noting that in a typical conventional free radical polymerization no thiols are present and therefore the presence of oxygen can lead to an inhibition of the overall polymerization rate.

To illustrate this effect, Figure 13 shows the differential scanning calorimetry (DSC)-exotherms for the photopolymerization of (A) pure 1,6-hexanediol diacrylate (HDDA, Figure 14) and (B) a 1:1 molar mixture of TriThiol1 (Figure 12) and AE2 (Figure 14), in air and nitrogen \[^{[3]}\]. It is clear that the influence of oxygen for the thiol-ene reaction between TriThiol1 and AE2 is very limited, while a strong inhibition occurs for the homopolymerization of HDDA.

Finally for completeness, it is mentioned here that sometimes thiols are used to increase the polymerization rate and to reduce the amount of photoinitiator required. This is typically done for photocuring applications for the production of thin films and coatings.
2.2.4 Applications

Though it is only recently recognized as a “click” reaction, the radical thiol-ene addition reaction is already used for a very broad range of applications, as evidenced by the large number of recent publications and patents. The traditionally perceived disadvantages have been circumvented, and lots of progress has been made in the study and application of this reaction during the last century. As the number of applications is far too high to discuss all of them in this chapter, the most prominent features of the application field of the radical thiol-ene addition reaction will be
highlighted. First, the generation of fourth generation dendrimers by radical thiol-ene “click” reactions is discussed, followed by the description of the unique properties of thiol-ene networks. Next, the use of the features of thiol-ene networks in optical components and microfluidic devices is described. As the ultimate goal of this Master thesis is the kinetic modeling of the functionalization of polymers, finally the use of radical thiol-ene chemistry in this field will be extensively discussed.

### 2.2.4.1 Dendrimer formation

Dendrimers are symmetrically branched, spherical molecules with a very high functionality, that are often used in drug-delivery processes. The high yield and the orthogonality of the radical thiol-ene reaction allows the efficient synthesis of dendrimers with virtually any type of end-group, both by convergent and divergent synthesis routes. One recent literature example of dendrimer synthesis by radical thiol-ene “click” chemistry is highlighted below.

Hawker et al. conducted the a “click” reaction between 2,4,6-triallyloxy-1,3,5-triazine (core of the dendrimer) and thioglycerol under bulk conditions, photoinitiated by 2,2-dimethoxy-2-phenylacetophenone (DMPA), with quantitative formation of a hexahydroxy dendrimer ([G1]-OH$_6$) (ref Figure 16). In a second step, the primary and secondary alcohol functionalities are subjected to an esterification reaction with 4-pentoic anhydride catalyzed by dimethylaminopyridine (DMAP), to yield the corresponding 6-functional “ene”. Next, thioglycerol was again added and the second generation 12-functional alcohol ([G2]-OH$_{12}$) was formed under UV irradiation by radical thiol-ene coupling reactions. This process was then iterated to yield the fourth generation dendrimer ([G4]-OH$_{48}$ or [G4]-ene$_{48}$) in a divergent manner (see Figure 16). In the case of the ene-functionalized fourth generation dendrimers, the pendant carbon-carbon double bonds were reacted with a variety of thiols in a post-modification step. This resulted in the formation of dendrimers with selective chain-end functional groups.
2.2.4.2 Low shrinkage networks

The high uniformity of thiol-ene networks results in exceptional features, compared to conventional polymer materials. Due to the step-growth nature of the radical thiol-ene polymerization, networks with a uniform cross-link density and a narrow glass-transition region are obtained, in contrast to the conventional acrylate-based photocured networks that are very heterogeneous and do not exhibit the same physicomechanical properties \[^3\]. For a polymer film
of TriThiol1 and Allyl Triazine (chemical structures are shown in Figure 17) in a 1:1 molar ratio, the narrow glass transition temperature region was illustrated by Hoyle et al. by dynamic mechanical analysis (DMA) measurements. As can be seen in Figure 18, the transition from a glassy to the rubbery state is spread over a temperature range of 50 °C, whereas for conventional acrylate-based networks, this can reach up to 200 °C.

![Figure 17: Chemical structure of Allyl Triazine and TriThiol1](image)

Figure 17: Chemical structure of Allyl Triazine and TriThiol1

![Figure 18: Loss tangent (tanδ) as a function of the temperature (°C) for a polymer film of an equimolar mixture of TriThiol1 and Allyl Triazine with 1 wt% DMPA. δ is the phase shift between the applied sinusoidal stress and the resulting strain of the polymer. Tanδ reaches a maximum at the glass transition temperature of the polymer network](image)

Figure 18: Loss tangent (tanδ) as a function of the temperature (°C) for a polymer film of an equimolar mixture of TriThiol1 and Allyl Triazine with 1 wt% DMPA. δ is the phase shift between the applied sinusoidal stress and the resulting strain of the polymer. Tanδ reaches a maximum at the glass transition temperature of the polymer network.

Another advantage of thiol-ene films, compared to conventional polymer materials, is that stress development in the film due to polymerization shrinkage is reduced. This shrinkage stress occurs since the highly cross-linked polymer network resists deformation, and can cause cracking and eventually failure. The reduction of this stress is explained by a combination of two factors: the higher gel-point conversion of thiol-ene networks and the monofunctionality of the carbon-carbon double bond in radical thiol-ene reactions. The latter leads to less contraction of the Van der Waals distances between the monomer molecules when the polymer is formed (shrinkage is thus reduced). Note that in conventional free radical polymerizations the carbon-carbon double bond is bifunctional. On the other hand, polymerization shrinkage is reduced as the gel-point conversion is higher, since shrinkage prior to gelation is accommodated by viscous flow with virtually no stress development within the sample.

Bowman and coworkers measured this shrinkage stress with a tensometer for both a mixture of dimethacrylates and a mixture of a tetrafunctional thiol and a trifunctional allyl ether. By simultaneously measuring the carbon-carbon double bond (methacrylate or allyl ether) conversion with FTIR, the shrinkage stress was plotted versus the carbon-carbon double bond...
conversion. Figure 19 shows this graph for both the methacrylate and the thiol-ene polymerization. It clearly shows that the thiol-ene polymerization reaches a higher conversion and has overall a lower stress development. This reduction in stress leads to an increased adhesion of the thiol-ene films to a large variety of substrates [3], including plastics, metals [33], glass and wood, which is further promoted by the thio-ether group. Moreover, thio-ether linkages are flexible and serve as efficient antioxidants, which makes thiol-ene chemistry an evident choice for use in clear-coat applications [3].

These features of the thiol-ene network make it a high rating candidate for dental restoratives [57], for which low stress material is required and which are currently methacrylate-based.

However, for applications such as dental restoratives, a high-$T_g$ material is required. Since the thio-ether linkages are flexible, traditional thiol-ene combinations are not appropriate. Though by using norbornenes, glass transition temperatures above 80$^\circ$C can be achieved due to mobility restrictions [58].

Probably the most interesting application of thiol-ene networks involves the photoinitiated polymerization of thick thermost set materials with ultraelastic properties [3]. The polymerization process is called “frontal polymerization”, as a non-linear chemical wave front propagates through the sample by diffusion of an exothermic reaction zone. Before the front there is monomer, and behind it there is polymer. However, a thermally sensitive polymerizable medium has to be used [26]. A photoinitiator initiates the polymerization at the sample surface, followed by a thermally propagating wave sustained by a peroxide or azo thermal radical source. This is depicted on Figure 20, which shows the different zones in the sample.

![Figure 19](image1.png)

**Figure 19:** Plot of the shrinkage stress versus the carbon-carbon double bond conversion for a, the photopolymerization of a mixture of dimethacrylates, and b, the photopolymerization of a tetrafunctional thiol and a trifunctional allyl ether [22].

![Figure 20](image2.png)

**Figure 20:** Illustration of the frontal polymerization process initiated thermally or by UV light [26].
The great advantage of thiol-ene frontal polymerizations over traditional free radical frontal polymerizations, is its negligible oxygen inhibition. This is the main practical drawback of conventional frontal polymerizations, as long exposure times and high intensity sources are required to initiate the front. The production in air of thick thermosets of various thiol-acrylate mixtures initiated by UV light, has been reported by Hoyle and coworkers \cite{59}.

**2.2.4.3 Optical components**

Another application of the thiol-ene radical polymerization with a great growth potential, is its use as optical component. In this subsection, two representative examples are discussed. First, an example of the use of basic thiol-ene chemistry in the production of optical lenses is briefly discussed, followed by a more elaborate description of the profitable use of thiol-ene radical polymerization in polymer-dispersed liquid-crystalline (PDLC) materials.

Hoyle et al conducted the addition of multifunctional thiols to divinylbenzene with formation of a clear glassy material with a high refractive index. The resultant network is characterized by a high glass transition temperature (> 90°C), and is very effective for the production of excellent optical lenses \cite{3}.

When a thiol-ene mixture is copolymerized with an amount of a nonreactive small-molecule liquid crystal, a separate liquid-crystalline phase forms from the original homogeneous single-phase mixture as the polymerization proceeds \cite{60}. The liquid-crystal-rich domains align when an electric field is applied, and the originally opaque polymer film is transformed into an optically transparent film \cite{3}. The switching efficiency between those two states of the polymer film, is dictated by the nature of the basic cross-linked network.

As thiol-ene networks are characterized by a uniform cross-link density, the dispersity in the shape and size of the liquid-crystal-rich domains is relatively narrow. This uniform phase separation is also promoted by the sudden gelation in thiol-ene network formation: the liquid-crystal phase separation already occurs below the gel point conversion. The phase-separated liquid-crystal domains thus formed, are then locked in the network by cross-linkages, when gelation takes place \cite{61-62}.

Thiol-ene holographic polymer-dispersed liquid-crystalline composites (HPDLC) gained a profound interest during the last few years, as they are suitable for many optical and electronic applications \cite{60, 63}. High-intensity lasers (visible or UV) and a photoinitiator are required for processing of HPDLCs. A typical application are diffraction gratings based on thiol-ene HPDLCs, of which a tunneling electron microscope (TEM) picture is shown in Figure 21. These thiol-ene based gratings combine excellent diffraction efficiencies with high switching speeds and low switching voltages, unlike their multiacrylate-based counterparts \cite{64-66}. For example, Bunning and coworkers showed \cite{67} that in ternary thiol-ene-acrylate systems, the HPDLC network switching and diffraction efficiency decreased as the acrylate concentration increased,
since heterogeneities were introduced in the network structure by homopolymerization of the acrylates. Other applications of thiol-ene HPDLCs are photonic crystals, switchable photomasks, ferroelectric liquid-crystal devices, …

![Figure 21: TEM image of two different thiol-ene based HPDLC diffraction gratings. The white bar indicates the scale: it is a unit of 500 nm](image_url)

### 2.2.4.4 Polymer functionalization

Post-polymerization modification of polymer chains is an interesting way to tailor the chemical, physical and mechanical properties of a polymer. However, conventional techniques are often inappropriate owing to the formation of low-yield byproducts, which have to be removed afterwards and thus require long reaction times. Contrary, thiol-ene click chemistry has proven to be a rapid and efficient method to functionalize polymers with either end or side-chain “ene” functional groups under mild reaction conditions. As any functional group linked to a small molecule thiol can be coupled to either side-chain or terminal “enes” in quantitative yields and with hardly need for purification, the radical thiol-ene post-polymerization modification process is a benign method for obtaining new high-performance polymeric materials.

Both the radical thiol-ene reaction and the thiol-Michael addition reaction can be used for the functionalization process. The first use of the radical thiol-ene “click” reaction for polymer functionalization dates already from 1948, when Serhiuk and coworkers conducted the addition of aliphatic thiols to 1,2-polybutadiene (PBD). On the other hand, the nucleophile- or base-mediated thiol-ene reaction with activated substrates is not as widely examined as its radical counterpart. Nevertheless, there are some recent publications on the modification of macromolecular thiols prepared by RAFT polymerization via the thiol-Michael addition reaction

In particular, Schlaad and coworkers reported the addition of a range of functional thiols via the radical pathway (ref Figure 22) to well-defined homopolymers of polybutadiene (PBD), and AB diblock copolymers of PBD and poly(ethylene oxide) (PEO). Although a 10 fold excess of thiol was used, the degree of modification was only 70-80 %, whilst all the carbon-carbon double bonds had reacted. As shown in Figure 23, this is due to competing intramolecular cyclisation reactions. A carbon-centered radical, formed upon addition of the thiyl radical onto the carbon-carbon double bond, can also react with an adjacent “ene” functional group with formation of a five- or six-membered ring. Note that the addition of a single thiyl radical
consumes two “ene” functional groups, which explains the maximum modification yield of 80%. Furthermore, the degree of cyclisation is proved to be dependent on the size of the thiol-functional molecule. The importance of cyclisation increases as the thiol is larger and bulkier, due to steric hindrance of the chain transfer step.

Figure 22: Chemical structures of the functional thiols, used by Schlaad and coworkers to functionalize PBD[54, 63, 73]

Figure 23: Reaction scheme for the competing intramolecular cyclisation reaction in the radical thiol addition to the pending ene functional groups in PBD[21].

Generally, to eliminate the occurrence of intramolecular cyclisation, the carbon-centered radicals have to be geometrically configured in a way they cannot react with adjacent “ene” functional groups[26], which is the case for polymers consisting of a backbone with side-chain “ene” functional groups. For example, Gress et al. could synthesize a novel polyoxazoline followed by a thiol-ene functionalization (ref Figure 24), which proceeded quantitatively without any formation of cyclisation products[74].

Also Campos and coworkers performed the functionalization of a broad range of “ene”-functional polymers, using the thermal or photochemical radical thiol-ene reaction[75]. A few examples are shown in Figure 25. Another noteworthy example is the thiol-ene modification of a polysulfone derivatized with “ene” side groups[76]. The backbone of this polymer (depicted in Figure 26) has excellent mechanical and thermal properties, which makes it an appropriate material for fuel-cell membranes.
Finally, many applications in bio-organic chemistry \cite{77-80} and photo-patterning of surfaces \cite{81-83} are based on thiol-ene post polymerization. For a detailed discussion of these applications is referred to the literature.

**Figure 24:** The thiol-ene functionalization reaction of poly(2-(3-butenyl)-2-oxazoline) with hydrophilic and hydrophobic small molecule thiols \cite{26}.

**Figure 25:** Thiol-ene post-polymerization modification reaction of pendent side-chain “ene” functional groups in styrenic, methacrylic and polyester-based statistical copolymers \cite{75}.

**Figure 26:** Functionalization of a polysulfone backbone derivatized with “ene” side groups \cite{76}.
CHAPTER 3: KINETIC STUDY OF RADICAL THIOL-ENE CHEMISTRY USING LOW MOLAR MASS COMPOUNDS

In this chapter, a detailed kinetic study is presented for radical thiol-ene chemistry using low molar mass compounds. For such reaction systems, diffusional limitations can be safely neglected and therefore the observed differences can be solely attributed to chemical effects. For a series of model compounds covering the different chemical reactivity of the “ene” functional group, the coupling efficiency is studied both experimentally and by using kinetic modeling.

Main focus is on the radical thiol-ene reactions in 1,4-dioxane, allowing a direct use of the gained knowledge and obtained results in the kinetic study of radical thiol-ene chemistry involving high molar mass compounds (see Chapter 4). In particular, several experimental techniques are used for a detailed product characterization, to assess the importance of side reactions and to define optimal reaction conditions. In addition, ball-park values for the intrinsic kinetic parameters of all important reaction steps for a model system are reported based on intensive kinetic simulations. It is shown that a good description of the observed experimental trends is obtained.

1 Experimental procedure

In this section, the experimental procedure to investigate radical thiol-ene reactions between low molar mass compounds is described. It includes the specifications of the chemicals used, the conditions of the experiments performed, the description of a typical experiment in bulk and solution, and the analysis methods applied.

1.1 Materials

Dodecyl vinyl ether (DVE; 98 % pure), 1-dodecane thiol (DT; ≥ 98 % pure) and 2-norbornene (N; 99 % pure) were purchased from Sigma Aldrich. Benzyl thiol (BT; 99 % pure) and the solvent 1,4-dioxane (> 99 % pure, stabilized) were purchased from Acros Organics. The solvent n-octane (95 % pure) was obtained from Lab-Scan analytical sciences. As a radical source 2,2-dimethoxy-2-phenylacetophenone (DMPA) was used, which cleaves upon irradiation with UV-light generating benzoyl and methyl radicals. All chemicals were used as received. The chemical structures of the aforementioned components are depicted in Figure 27.
Figure 27: Chemical structures of the used compounds for the study of radical thiol-ene chemistry using low molar mass compounds.

1.2 Experimental conditions

The experimental conditions used to study radical thiol-ene reactions using low molar mass compounds are listed. From left to the right is specified: the chemical name of the reagents, the initial molar ratio of the thiol to the “ene”, the initial mass percentage of the initiator (DMPA), the ambient temperature, the indication whether the experiment is performed open to the air or under argon atmosphere, the chemical name of the solvent, the volume percentage of the solvent, the type of flask material used, and finally the wavelength at which the sample was irradiated. Note that the abbreviations used to designate the chemical compounds in the second column are defined below.
Table 2: Experimental conditions for radical thiol-ene chemistry using low molar mass compounds

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<th>components*</th>
<th>[thiol]₀/[ene]₀</th>
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<th>presence of O₂</th>
<th>solvent</th>
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*DT = 1-dodecane thiol; DVE = dodecyl vinyl ether; BT = benzylthiol; Nb = 2-norbornene (see Figure 27)
1.3 Thiol-ene experiment in bulk

For a typical bulk experiment (e.g. entry 10 in Table 2; equimolar amounts), 0.0437 g of DMPA is weighed with an analytical balance, and put into a two-necked, glass flask of 50 mL. As the main analysis technique in bulk experiments is the Mettler Toledo ReactIR 4000 on-line FTIR spectrometer (see paragraph 1.5), this flask has one neck with a large diameter that exactly fits with the adapter around the IR-probe, and another one with a much smaller diameter.

Next, 2.7 mL of DVE is added to the flask with a precise 1 mL syringe. The small diameter neck is covered with a septum and the flask is attached to the IR-probe adapter. In order to remove oxygen, a with argon filled balloon provides via a long needle a constant argon flux through the DVE liquid, which is continuously stirred at a rate of 800 rotations per minute (rpm). After 30 minutes of purging with argon, 2.5 mL of DT is added to the sample through the septum with a 1 mL syringe. Note that the total volume in the flask after this addition amounts to ca. 5mL, which is sufficient to immerse the tip of the probe, and to make proper FTIR-measurements possible.

After the addition of DT, the mixture is purged with argon for another 20 minutes to remove the remaining oxygen. Thereafter, the balloon is removed, the sensor at the tip of the IR-probe is brought in contact with the mixture and the ambient temperature is measured with a digital VWR thermometer. Subsequently, a set-up of inox steel with nine 360 nm lamps is put around the flask and IR-probe unit, and the open side of the set-up is covered with aluminum foil preventing the exit of UV-radiation.

Finally, the mixture is irradiated with UV-light during ca. 5 minutes followed by a transfer of the mixture to a small vial.

1.4 Radical thiol-ene experiment in solution

A typical thiol-ene experiment in solution (e.g. entry 22 in Table 2; equimolar amounts) is similar to the bulk reaction described above. For the same reason as aforementioned, the total volume used for the experiment is 5 mL. First, 0.00255 g DMPA is dissolved in 4.46 mL of 1,4-dioxane in the same 50 mL two-necked, glass flask. Then, 0.37 mL DVE is added and after attaching the flask to the IR-probe, the obtained mixture is purged with argon for 30 minutes and again stirred at 800 rpm. After 30 minutes, BT is added and the ventilation is switched on, since this compound produces an intense smell. The sample is purged for another 20 minutes and afterwards irradiated for 10 minutes with 360 nm UV-light. The same lamp set-up is used as in the bulk thiol-ene “click” experiment.
1.5 Analysis

In all experiments, a Mettler Toledo ReactIR 4000 on-line FTIR is used to measure the absorption of infrared radiation by the carbon-carbon double bond at 1620 cm\(^{-1}\) and the thiol group at 2570 cm\(^{-1}\). As samples are taken each 15 seconds, the disappearance of the carbon-carbon double bond and the thiol group can be simultaneously monitored during the radical thiol-ene reaction. In addition, at relatively high reaction times the obtained mixture is analyzed with \(^1\)H-NMR 500 MHz to determine the remaining amount of the starting products. For these measurements, typically, 10 mg of sample is put in a NMR-tube and dissolved in 750 µL of deuterium-doped chloroform (CDCl\(_3\)). Both for the bulk experiments and those in solution, the obtained FTIR spectra are corrected for possible thiol-ene ‘click’ reactions during the second purge period of 20 minutes caused by the thermal decomposition of DMPA. For this, a first absorption spectrum is recorded just after the thiol compound is added to the mixture and compared with the one obtained just before the UV-lamp is switched on. However, in all experiments almost identical spectra were recorded, indicating that the thermal decomposition of DMPA is negligible. Furthermore, in the bulk experiments no reference spectra are recorded and only the air background is measured, whereas in solution the measurement procedure is more extended, as an additional reference spectrum of the solvent is recorded. This solvent spectrum is subtracted from the sample absorption spectrum in order to obtain clearer absorption peaks of the thiol group and the carbon-carbon double bond.

For the experiments using the DT-DVE system, i.e. entry 1 to 21 in Table 2, analysis by other conventional analytical techniques, such as gas chromatography (GC), liquid chromatography (LC) or UV-VIS spectrometry is unfortunately not possible, since both components have a similar chemical structure, are not UV-active and generate after reaction a high-boiling coupling product (for comparison: tetracosane, C\(_{24}\)H\(_{50}\), has a boiling point of 391°C). However, the samples can be analyzed by off-line GCXGC (Thermo Scientific TRACE GCXGC set-up). A flame ionization detector (FID) is used for quantitative analysis and a sensitive qualitative characterization of the sample is provided by a Thermo Scientific TEMPUS Time Of Flight-Mass Spectrometer (TOF-MS).

On the other hand, for the BT-DVE and DT-N systems, i.e. entry 22 to 24 in Table 2, analysis by GC is also possible since the reagents are chemically more different and the “click” product has a lower molar mass than for the DT-DVE system. For the sake of comparison, extra repeating experiments are performed for these compounds, in which samples are manually taken with 1 mL syringes each 15 second. A Hewlett Packard (Agilent) 5890 GC with a 7673 autosampler and FID is used for the analysis using vials containing approximately 1 mg sample per mL dichloromethane. In parallel, a few droplets of the samples are put into NMR-tubes, dissolved in CDCl\(_3\) and analyzed by \(^1\)H-NMR 300 MHz. For each such experiment, two independent analyses are thus performed. For completeness, it is mentioned here that the first sample is taken before
the thiol is added and the second just before the UV-lamp is switched on, allowing an easy
determination which peak(s) in the chromatogram/NMR-spectrum correspond(s) to the “ene” and
which to the thiol. Furthermore, a Hewlett-Packard GCD-Plus GC/MS (G1800B), which is based
on a HP 5890 Series II GC with a 5971 Mass Spectrometer Detector, is used for a qualitative
characterization of the sample after completion of the reaction.

Also, a VLX365 radiometer (bandwidth: 355-375 nm) is used to measure the intensity profile of
the used UV lamps, of which, the temperature profiles are monitored with a digital VWR
thermometer. The measurements are performed at the same position relative to the lamp as the
mixture is positioned.

Finally, for the specifications and a detailed description of the working principle of the used
analysis instruments and UV-lamps, is referred to Appendix C.

2 Kinetic model

An overview of the considered reactions in the kinetic model is given in Table 3. A distinction is
made between initiation, addition, chain transfer and termination by recombination reactions.
Based on literature data, homopolymerization of the ene functional groups studied can be safely
neglected [84-85]. Note that termination by disproportionation is neglected and an initiator
efficiency is used in such way that it accounts for the fraction of initiator radicals leading to chain
transfer and propagation, i.e., all other reactions with the initiator radicals are included in the
initiator efficiency.

The continuity equations that correspond with the reactions in Table 3, are listed in Appendix A.
It is assumed that no volume change occurs during the reaction, which is valid at least to a first
approximation. The expression for the initiation rate is adapted from literature [85-87], and its
derivation and assumptions are discussed in Appendix B. Contrary to literature models [86], no
quasi-steady-state assumption is used to integrate this set of differential equations. All the
continuity equations in Appendix A are simultaneously integrated using the numeric LSODA
solver (i.e., Livermore Solver for Ordinary Differential Equations). This subroutine uses [88] the
Adams method for non-stiff ordinary differential equations (ODE) and a backward differential
formula method for stiff ODE’s, and automatically switches between both.

Table 3: Overview of reactions for the kinetic modeling of radical thiol-ene chemistry using low molar mass compounds

| Initiation | $I_1I_2 \overset{f, h, \nu}{\rightarrow} I_1 + I_2$ |


### Addition

\[ I_1' + R'CH=CH_2 \xrightarrow{k_{p1}} I_1CH_3R'CH \]
\[ I_2' + R'CH=CH_2 \xrightarrow{k_{p2}} I_2CH_2R'CH \]
\[ RS' + R'CH=CH_2 \xrightarrow{k_{CT1}} RSCH_2CHR' \]

### Chain Transfer

\[ I_1' + RSH \xrightarrow{k_{CT1}} I_1H + RS' \]
\[ I_2' + RSH \xrightarrow{k_{CT2}} I_2H + RS' \]
\[ R'CHCH_2SR + RSH \xrightarrow{k_{CT3}} R'CH_2CH_2SR + RS' \]
\[ I_1CH_3R'CH + RSH \xrightarrow{k_{CT4}} I_1CH_2CH_2R' + RS' \]
\[ I_2CH_3R'CH + RSH \xrightarrow{k_{CT5}} I_2CH_2CH_2R' + RS' \]

### Termination by Recombination

\[ 2RS \xrightarrow{k_1} RS-SR \]
\[ RS + R'CHCH_2SR \xrightarrow{k_2} RSC R'HCH_2SR \]
\[ 2R'CHCH_2J_1 \xrightarrow{k_3} I_1CH_2CHR'CHR'CH_2 \]
\[ 2R'CHCH_2J_2 \xrightarrow{k_4} I_2CH_2CHR'CHR'CH_2 \]
\[ R'CHH_2J_1 + R'CHCH_2J_2 \xrightarrow{k_5} I_1CH_2CHR'CHR'CH_2 \]
\[ RS' + R'CHCH_2J_1 \xrightarrow{k_6} RSCHR'CH_2J_1 \]
\[ RS' + R'CHCH_2J_2 \xrightarrow{k_7} RSCHR'CH_2J_2 \]
\[ RSCH_2CHR' + R'CHCH_2J_1 \xrightarrow{k_8} RSCH_2CHR'CHR'CH_2 \]
\[ RSCH_2CHR' + R'CHCH_2J_2 \xrightarrow{k_9} RSCH_2CHR'CHR'CH_2 \]

Furthermore, it is assumed that the initiator radicals have equal reactivity regarding both the addition onto the carbon-carbon double bond, and the abstraction of the thiol hydrogen, which implies equal values for \( k_{p1} \) and \( k_{p2} \), and \( k_{CT1} \) and \( k_{CT2} \), respectively.

Similarly, the values for the chain transfer rate coefficients \( k_{CT3}, k_{CT4} \) and \( k_{CT5} \) are assumed identical, since the immediate chemical surroundings (\( \alpha \)-positions) of the carbon-centered radicals in the chain transfer reactions are the same.

Finally, all the rate coefficients of the recombination reactions are also taken the same, i.e., \( k_{t1} = k_{t2} = \ldots = k_{t10} \).
3 Results and discussion

In this section, first the importance of the UV lamp intensity change during reaction is highlighted and the temperature change due to reaction is discussed for bulk and solution experiments. Next, a detailed experimental kinetic study is presented for a model system (DVE and DT), in which the effect of the most important reaction and process conditions on the thiol-ene coupling process is discussed. In this study, not only the disappearance of the “ene” and the thiol or the formation of the coupling product is investigated, but also attention is paid to influence of side reactions on the coupling efficiency.

Next, based on the formulated insights, optimal reaction conditions are selected for the determination of ball-park values of kinetic parameters required to understand radical thiol-ene reactions involving high molar mass compounds. As model system the thiol-ene coupling reaction between BT and DVE in 1,4-dioxane is used to illustrate the kinetic modeling approach.

3.1 Intensity profile of the UV-lamps

An important feature of the UV-lamps used is that the intensity of the radiation does not reach its maximum value immediately. For one side of the 360 nm lamp set-up, the corresponding profile measured with the VLX365 radiometer is shown in Figure 28. Note that the intensity that reaches the sample is actually three times higher than the values shown in Figure 28, since the sensor of the VLX365 radiometer was directed to only three of the nine identical UV-lamps when monitoring the intensity. The symmetrical configuration of the nine lamps (see Appendix C) thus results in a three times higher intensity than measured at the sample position.

Since the intensity build-up has a range of about 3 minutes, which is comparable to the reaction times in solution and much longer than those in bulk, it can be expected that the observed reaction rate is strongly affected by this phenomenon. It will be shown in section 3.4.5 that including this effect is indeed essential for a good description of the recorded experimental data and consequently crucial for a good determination of the related kinetic parameters.
Interestingly, measurements with the same radiometer, which is designed for the range of 355 to 375 nm, revealed that the 254 nm lamp is also characterized by a clear intensity build-up spread over approximately 3 minutes, as shown in Figure 29. Note that this means that the 254 nm lamp also emits at \textit{ca.} 365 nm, though with a rather small intensity. The maximum intensity is in this case \textit{ca.} 0.09 W cm\(^{-2}\), whereas for the 360 nm lamp set-up a higher intensity of \textit{ca.} 0.6 W cm\(^{-2}\) per lamp is obtained.

![Figure 28: Intensity profile of the 360 nm UV-lamp set-up measured with a VLX365 radiometer in the middle of the box. (3 of 9 lamps)](image)

### 3.2 Verification of isothermicity during the reaction

To assess whether during the reaction isothermal conditions can be assumed for the kinetic modeling study, the temperature increase of the ambient air caused by the UV-lamps has been
first measured with a digital VWR thermometer as a function of time. The obtained temperature profiles of the 360 nm and 254 nm UV-lamps are shown in Figure 30.

Since reactions are completed after approximately 5 minutes in bulk and about 10 minutes in solution (see further), it can be expected that the temperature rise that will be caused by the UV-lamp during an actual experiment is negligible (see also Table 4).

![Figure 30: Temperature versus time profile of the 360 nm UV-lamp (black triangles; measured in middle of the box) and the 254 nm UV-lamp (black squares; measured at 5 cm from the lamp), measured with a digital VWR thermometer](image)

<table>
<thead>
<tr>
<th></th>
<th>254 nm</th>
<th>360 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>time (min)</td>
<td>temperature (°C)</td>
<td>time (min)</td>
</tr>
<tr>
<td>0</td>
<td>20.2</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>20.5</td>
<td>2</td>
</tr>
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<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14</td>
</tr>
</tbody>
</table>

Table 4: Temperature values of ambient air for the first 15 minutes for both the 254 nm and the 360 nm UV-lamp, conditions are the same as in Error! Reference source not found..

However, the reaction heat produced by the radical thiol-ene reaction should also be taken into account to verify the isothermicity. Both in bulk and in solution the temperature of the sample during the reaction was therefore measured with the same digital VWR thermometer as mentioned above. For the bulk experiments (entry 1 to 14 in Table 2), a temperature rise of 15 °C
during the first two minutes of the reaction was observed, even when a two-fold excess of one compound was used. Note that this means that kinetic modeling of bulk experiments is extremely complicated, since it requires the consideration of Arrhenius parameters for each reaction. However, based on the bulk experimental data some general insights can be obtained.

On the other hand, for the radical thiol-ene reactions performed in solution, no significant temperature rise of the sample was measured for the conditions applied (entry 18 to 24 in Table 2). In this Master thesis, therefore the kinetic modeling was limited to solution systems, which are also used in case a high molar mass compound is involved.

3.3 Experimental model system: radical thiol-ene reaction between 1-dodecane thiol and dodecyl vinyl ether

Based on a first screening of low molar compounds taking into account availability, price, solubility and in-house experimental data, DT and DVE are chosen as model compounds (entry 1 to 21 in Table 2). From the chemical nature of these compounds, it is clear that the only possible UV-induced reaction in this system is that between the thiol and the ene functional group. Note that dodecyl vinyl ether can only homopolymerize via a cationic mechanism\(^{84}\), so this can be excluded in the system under consideration. As a result, every side-product formed is inherent to the radical thiol-ene reaction, which is necessary to draw unambiguous conclusions. Furthermore, DT has a rather high molar mass, which reduces odor annoyance and in turn makes the experiments easier to perform.

In what follows, first the experimental results are discussed for a reference case, which corresponds to a bulk experiment irradiated at 254 nm using a glass flask with equimolar amounts of thiol and “ene”. Next, the effect of the flask type, the initial molar ratio of the “ene” to the thiol, the initial initiator concentration, the wavelength and the presence of oxygen is discussed while keeping for each case the other conditions as for the reference case. Finally, experimental results are presented if solvent is added (n-octane) using the 360 nm UV-lamp set-up.

3.3.1 Reference case

Figure 31 presents the on-line FTIR absorption spectra versus time for entry 1 in Table 2, i.e., the reference case conditions. Clearly, the IR-absorption peak of the carbon-carbon double bond at 1620 cm\(^{-1}\)\(^{85, 89-90}\) decreases upon irradiation. However, the disappearance of thiol groups cannot be directly derived due to the very low absorbance of the thiol, though its absorption peak becomes clear after a more detailed analysis, as will be discussed further on. Note that also the formation of the “click” product gives rise to a peak at 1110 cm\(^{-1}\), caused by the strong IR-absorption of the thio-ether group. Unfortunately this peak is superimposed on two smaller peaks.
(see Figure 31), which makes it only useful as a qualitative indication that the desired click-product is formed.

The change of the peak area for the carbon-carbon double bond is shown in Figure 32 for 3 repeating experiments. Note that this area is relative to a single point baseline taken at a stable point of the spectrum, i.e., at a wave number where the IR-absorbance does not change during the reaction. Figure 32 clearly shows that the obtained reaction profiles are very reproducible. However, it is remarkable that the peak area of the carbon-carbon double bond absorption peak does not go to zero, although an IR-spectrum of a sample containing only DT and DMPA showed no absorption peak at the wavelength considered. Furthermore, \(^1\)H-NMR 500 MHz measurements of the DT-DVE mixture after the reaction for two repeating experiments (entry 1 in Table 2) showed that all the DVE had reacted. Hence, the remaining IR-absorption at 1620 cm\(^{-1}\) can be very likely attributed to impurities present in the DVE used, which do not react. Note that for the calculation of conversions, this additional absorption is taken into account.

![Figure 31: 3D FTIR-absorption spectrum as a function of reaction time obtained with the iCIR 3.0 software (entry 1 in Table 2). For a better view of the absorption peak corresponding to the thiol group, see Figure 34.](image)

![Figure 32: Area of the carbon-carbon double bond IR-absorption peak at 1620 cm\(^{-1}\) versus time for 3 repeating experiments (conditions: entry 1 in Table 2)](image)
The conversion of the carbon-carbon double bond is calculated by relating the peak area to the initial peak area, i.e. considering a linear relation between concentration and peak area. Note that a constant volume can be assumed along the complete reaction time. The average conversion profile of the carbon-carbon double bond is presented in Figure 33.

![Conversion profile of the carbon-carbon double bond](image)

**Figure 33:** Conversion profile of the carbon-carbon double bond (conditions: entry 1 in Table 2)

The conversion of the thiol group is calculated in a similar way. Note that the thiol functional group absorbs at 2570 cm\(^{-1}\) [86, 89], and the resulting absorption peak lies on a shoulder of a much bigger neighboring peak at 3000 cm\(^{-1}\) (absorption of C-H). The peak is therefore integrated relative to a two point baseline, as shown in Figure 34, and the corresponding conversion change is depicted in Figure 35, which illustrates that nearly 100 percent conversion of the thiol groups is reached after 200 seconds.

![Absorption peak of the thiol functional group at 2570 cm\(^{-1}\)](image)

**Figure 34:** Absorption peak of the thiol functional group at 2570 cm\(^{-1}\). Since it lies on a shoulder of a larger neighboring peak, it is integrated relative to a two point baseline (conditions: entry 1 in Table 2; 15 sec).
3.3.2 Effect of the used flask material

Since glass blocks over 90 percent of the radiation with a wavelength lower than 300 nm[^91] only a minor part of the radiation emitted by the 254 nm UV-lamp penetrates through the glass and initiates reaction, i.e. the 360 nm UV-radiation (see section 3.1). If quartz is used instead of glass, the major 254 nm emitted radiation is not attenuated by the flask and reaches the sample completely. A large difference in reaction rate should thus be expected at first sight, as the effective irradiation intensity of the sample is now much larger. However, the reaction profile does not differ much from the one obtained with a glass flask as depicted in Figure 36, though it is somewhat steeper. This can be understood from a measurement of the UV-absorption profile of DMPA in a mixture of DT and DVE, which showed that DMPA has in this chemical environment a maximal absorption at 350 nm (very broad peak), whereas at 254 nm the absorption is nearly zero.

3.3.3 Effect of the initial molar ratio of thiol to “ene”

The aforementioned results all correspond to a molar ratio of thiol to ene functional groups of 1:1 (see entry 1 in Table 2). However, bulk reactions between DT and DVE using the 254 nm UV-lamp were also carried out in 2:1 (entry 2 in Table 2) and 1:2 (entry 3 in Table 2) molar ratios. The corresponding average conversion versus time profiles of the carbon-carbon double bond are compared with that for an equimolar ratio in Figure 37. As expected, the carbon-carbon double bond reaches approximately 100 % conversion when an excess of the thiol compound is used (entry 2 in Table 2), and nearly 50 % in case of an excess of DVE. Note that the reaction proceeds somewhat faster in case an excess of DT or DVE is used, which indicates that the overall reaction rate is dependant both on the thiol and the “ene” concentration, in agreement with observations of Bowman et al. [85].

Figure 36: Area of the carbon-carbon double bond IR-absorption peak at 1620 cm$^{-1}$ versus time for 3 repeating experiments with a glass flask (black dots), and two repeating experiments with a flask made of quartz (blue and purple dots). Conditions: entry 1 in Table 2.
3.3.4 Effect of initial initiator concentration

To study the effect of the added amount of initiator on the reaction rate, reactions between DT and DVE were conducted in bulk using different initial amounts of initiator, i.e., 1 w%, 2 w%, 4 w%, 6 w% and 8 w% of DMPA (see entry 1 and entry 4-7 in Table 2). The corresponding conversion profiles of DVE based on on-line FTIR measurements are shown in Figure 38, and are similar to those of DT in Figure 39. Note that only for the experiments using 1 w% of DMPA the reproducibility of the results is verified, however the data for 6 and 8 w% of DMPA clearly indicate that a higher initiator concentration does not necessarily result in a higher reaction rate, but in contrary, will slow down the reaction when it exceeds a certain threshold value. This can be explained by assuming that termination reactions become more important when the amount of radicals in the mixture increases. It should be emphasized that this still has to be confirmed by repeating experiments and kinetic modeling.
3.3.5 Effect of the wavelength

From the discussion above it is clear that for experiments using a glass flask, switching between the available 254 nm UV-lamp and 360 nm UV-lamp set-up is in fact equivalent to switching between two different UV-radiation intensities at ca. 360 nm. Since the intensity of each 360 nm UV-lamp is more than 7 times higher than that of the 254 nm UV-lamp, a much higher reaction rate of the radical thiol-ene reaction between DT and DVE is expected, as DMPA will decompose more quickly. Two bulk experiments using the 254 nm UV-lamp, i.e. entry 1 and 2 in Table 2, are repeated using the more intense 360 nm UV-lamp, i.e. entry 9 and 12 in Table 2. A
comparison between the reaction profiles of the carbon-carbon double bond monitored by on-line FTIR for both set-ups is shown in Figure 40 (conditions: entry 1 and entry 9 in Table 2) and Figure 41 (conditions: entry 2 and entry 12 in Table 2). From these figures it can be derived that the reaction using the 360 nm UV-lamp set-up proceeds more than 5 times faster than if the 254 nm lamp were used.

![Figure 40: Area of the carbon-carbon double bond IR-absorption peak at 1620 cm$^{-1}$ versus time using the 254 nm UV-lamp (black dots; condition: entry 1 in Table 2) and the more intense 360 nm UV-lamp set-up (dotted blue line; entry 9 in Table 2).](image)

![Figure 41: Area of the carbon-carbon double bond IR-absorption peak at 1620 cm$^{-1}$ versus time using the 254 nm UV-lamp (black dots; condition: entry 2 in Table 2) and the more intense 360 nm UV-lamp set-up (dotted blue line; entry 12 in Table 2).](image)

### 3.3.6 Influence of the presence of oxygen

In the literature survey (see Chapter 2) it was already highlighted that the radical thiol-ene reaction is mostly highly tolerant to oxygen. In this Master thesis, the oxygen sensitivity was attested for the DT-DVE system, based on on-line FTIR measurements. For the bulk reactions
between DT and DVE, no difference in reaction rate is observed if oxygen is excluded from the sample. This is illustrated by Figure 42, in which the reaction profiles of the carbon-carbon double bond using conditions of entry 10 in Table 2 (oxygen excluded) are compared to the profiles of entry 9 in Table 2 (oxygen present).

![Figure 42](image)

**Figure 42:** Area of the carbon-carbon double bond IR-absorption peak at 1620 cm\(^{-1}\) versus time when oxygen is excluded (two repeating experiments; black dots; condition: entry 10 in Table 2) and when oxygen is present (blue dots; condition: entry 9 in Table 2).

### 3.3.7 Effect of side reactions: side product identification

In order to identify termination products, GCXGC analysis was performed of samples taken at three different times after completion of the radical thiol-ene reaction between DT and DVE using a two-fold excess of DT and irradiated by the 360 nm UV-lamp (i.e., entry 12 in Table 2). Under these conditions, the formation of disulfides should be promoted by the excess of DT, in particular when after completion of the thiol-ene reaction all DVE molecules have reacted and still initiator radicals are present in the mixture.

First, a GCXGC/TOF-MS analysis of one of the collected samples was conducted in order to assign the peaks appearing in the 2D-chromatogram, by comparison of the obtained mass spectra with data from the National Institute of Standards and Technology (NIST) database. Next, the three samples were subsequently analyzed with GCXGC using the FID, to make a more quantitative analysis possible. Four compounds, i.e., DT, DMPA, dodecyl disulfide and the coupling product, were identified in the FID chromatograms (see Figure 43), based on comparison with the data obtained via GCXGC/TOF-MS, and peak volumes were calculated with the GCImage software. Note that the obtained peak volumes have to be corrected by multiplication with a response factor for the FID. All peak volumes were normalized by the volume of the peak corresponding to the thiol-ene coupling product, since its concentration should remain constant after completion of the reaction.
Figure 43: 2D FID-chromatogram after 620 seconds of irradiation of a mixture of DT and DVE using a two-fold excess of DT (conditions: entry 12 in Table 2).

The thus obtained normalized volumes of the DMPA and dodecyl disulfide peaks are shown versus time in Figure 44 and as expected, the signal of DMPA decreases and that of dodecyl disulfide increases in time. Furthermore, the normalized volume of the DT peak also decreases in time and is depicted in Figure 45. Note that Figure 43 shows next to the four assigned peaks, many other small peaks (e.g. even recombination products of initiator radicals were detected), which can be identified by extensive comparison with GCXGC/TOF-MS chromatograms, though more GCXGC experiments should be performed to do this thoroughly, and to obtain reliable results.
3.3.8 Effect of the presence of n-octane as solvent

As indicated in section 3.2, the determination of absolute ball-park values for intrinsic rate coefficients is in practice limited to experiments in solution, since only then isothermicity is guaranteed. In this Master thesis, based on the initial results in bulk, reactions in solution were carried out using solely the 360 nm UV-lamp set-up, as it has a well-defined radiation intensity at 360 nm (without the issue whether the radiation is blocked or not) and its set-up provides a safe and easy way of working, in particular when manually samples have to be taken.

First it is important to bear in mind that an appropriate degree of dilution has to be selected, that allows a proper identification and integration of the carbon-carbon double bond IR-absorption peak and also induces a reaction time that is long enough to have sufficient FTIR measurement.
points in the steep region of the reaction profiles. The latter is of great importance for an unambiguous comparison between simulation results and experimental data, enabling a proper optimization of kinetic rate coefficients. Initially n-pentane was used as a solvent to search for the optimal starting concentration of the reagents (entry 15 to 17 in Table 2). Unfortunately it evaporates when an argon flux is provided through the sample to remove oxygen. To resolve this, the higher boiling solvent n-octane was used instead (entry 18 to 21 in Table 2). The reaction profile of the carbon-carbon double bond monitored with on-line FTIR for the optimal starting concentration of the reagents (0.2 M; i.e. entry 19 in Table 2) is shown in Figure 46. Note that also less initiator is added (0.1 w% compared to 1 w% used for the bulk experiments) to further decrease the reaction rate, and thus obtain more FTIR measurement points.

![Figure 46](image)

**Figure 46:** Conversion profile of the carbon-carbon double bond based on on-line FTIR measurements for the optimal dilution conditions (equimolar ratio of DT and DVE; condition: entry 19 in Table 2).

Similarly to the bulk case (see 3.3.6), the reaction between DT and DVE in n-octane was also conducted without exclusion of oxygen by argon purge, in order to investigate the influence of oxygen on the reaction rate. In agreement with the observations of Hoyle et al. and Sivertz et al. [3, 92], a small effect was observed as demonstrated by Figure 47, which shows the change of the area of the carbon-carbon double bond absorption peak monitored by on-line FTIR. After the 360 nm UV-lamps are switched on, an induction period of ca. 1 minute appears before the reaction starts.
The determination of ball-park values for the kinetic parameters of the involved reactions in radical thiol-ene chemistry for low molar mass compounds is best done based on experimental data in solution using the 360 nm UV-lamp set-up, and conducted under argon atmosphere. In these conditions a glass flask can be used and a sufficient effect on reaction rate for parameters discrimination results when studying initial molar ratios of thiol to ene from 0.5 up to 2.

In what follows, a detailed kinetic study of the radical thiol-ene coupling reaction between BT and DVE in 1,4-dioxane is presented, for which both experimental and kinetic modeling results are compared using the above conditions. Note that based on the bulk experimental model system it can be expected that the coupling reaction is influenced by the impurity of DVE and by disulfide formation.

3.4 Kinetic study of radical thiol-ene reaction between benzyl thiol and dodecyl vinyl ether in 1,4-dioxane: comparison of experimental and modeling results

Since no extensive characterization of the samples was possible in the DT-DVE system due to practical issues (GCXGC) and analytical limitations (see section 1.5), only one experimental response was used to calculate thiol and “ene” conversions, i.e., on-line FTIR measurements. However, as the intrinsic rate coefficients in the kinetic model have to be adjusted to obtain a good agreement between the simulated and the experimental conversion profiles, a verification of
the latter by another analytical technique is very beneficial. Therefore, DT was replaced by BT in order to make analysis by GC and GC/MS possible, as the coupling product now has a lower molar mass and thus a lower boiling point. 1,4-Dioxane was used as a solvent, since the aim is to apply the gained knowledge on the BT-DVE system to polymer modification reactions, which are mainly conducted in the same solvent. For samples taken during the reaction, conversion profiles of both BT and DVE can be calculated from the obtained gas chromatograms, and peak assignment is possible due to the gained mass spectrum of each peak. Furthermore, $^1$H-NMR 300 MHz spectra provide a third way to monitor the conversion of the samples taken (see also section 1.5). Note that BT is also an alkyl thiol and, hence, it can be expected that its reactivity is similar to that of DT. Therefore, the values of the intrinsic rate coefficients for which the BT-DVE reaction in 1,4-dioxane is well described, should also provide a good agreement with the previously determined conversion profiles for the DT-DVE system in n-octane.

Unfortunately in this Master thesis only for the reaction between BT and DVE in equimolar amounts, i.e., entry 22 in Table 2, the conversion could be measured based on the three separate responses described above. The reaction in the experiments using a molar ratio of BT to DVE of 2 and 0.5, i.e., entry 24 and 23 in Table 2, could only be followed by on-line FTIR, though samples are taken after the reaction for characterization by GC/MS analysis. In the following, the experimental results are discussed for the three molar ratios of BT to DVE previously mentioned. Next, since GC/MS allows a very sensitive characterization of the reaction mixture, the identification of termination products in the samples taken after completion of the reaction, is described. Finally, simulation results are presented and the agreement with experimental data is discussed.

### 3.4.1 Results for equimolar amounts of BT and DVE

According to the experimental procedure described in section 1.5, GC- and $^1$H-NMR 300 MHz samples were taken each 15 seconds. Note that the analysis of a reference sample, which only contains DVE and the initiator DMPA dissolved in 1,4-dioxane, allows an easy identification of the reagent and product peak(s) in both GC-chromatograms and $^1$H-NMR 300 MHz spectra (see also section 1.5). This peak assignment is discussed below.

Figure 48 shows the GC-chromatograms of the reference sample (A), the sample taken just before the 360 nm UV-lamps are switched on (B), and the sample after 45 seconds of reaction (C). The peaks corresponding to 1,4-dioxane, BT and DVE can be easily identified based on the chromatograms shown, and are labeled in Figure 48.
Figure 48: Overlay of 3 FID-chromatograms for the equimolar reaction between BT and DVE in 1,4-dioxane (i.e., entry 22 in Table 2), in which A represents the reference sample, B the starting mixture of BT and DVE in 1,4-dioxane, and C the sample mixture after 45 seconds of reaction.

For the collected $^1$H-NMR 300 MHz results, a similar figure is presented (Figure 49), in which an overlay is shown of the reference spectrum (A), the spectrum just before reaction (B), and the spectrum at 45 seconds of reaction (C). Again, the peaks corresponding to 1,4-dioxane, BT and DVE are identified and labeled.
Figure 49: Overlay of the $^1$H-NMR 300 MHz reference spectrum (A), the spectrum just before reaction (B), and the spectrum after 45 seconds of reaction (C). (Conditions: entry 22 in Table 2)

To calculate conversions of both BT and DVE based on the collected GC- and $^1$H-NMR 300 MHz-results at various reaction times, the corresponding peaks have to be integrated against an internal standard, of which the concentration in the sample remains constant during the reaction. Most convenient the solvent 1,4-dioxane can be used, if no significant volume change of the sample during the reaction occurs (e.g. due to density changes or evaporation of the solvent), which was experimentally verified. The peak areas after integration of the GC-chromatograms are thus divided by the area of the peak corresponding to 1,4-dioxane. Since the FID is mass dependent and not concentration dependent, no absolute concentrations of the compounds in the sample can be determined, however calculation of conversions is possible by relating the peak area of the compound at a certain time with its peak area prior to reaction. Both the conversion of BT and DVE are determined in this way. For the analysis of the $^1$H-NMR 300 MHz spectra, peaks are integrated relative to the area of the $^{13}$C satellite peak of 1,4-dioxane at 3.44 ppm. Conversions are again calculated by taking ratios of peak areas. Contrary to the GC-results, only the conversion of DVE can be derived from integration of the $^1$H-NMR 300 MHz spectra.

The conversion profiles of DVE obtained from both GC- and $^1$H-NMR 300 MHz results for two repeating experiments according to entry 22 in Table 2, are shown in Figure 50. A good agreement for the conversion profiles between the two different analytical methods is obtained.

*Conversions are calculated based on the disappearance of the peak at ca. 9.7 ppm, although this peak cannot be assigned. The peak that was expected to decrease at ca. 6.5 ppm (proton of the double bond) did not appear in the spectrum. A further investigation is necessary, but unfortunately goes beyond the timeframe of this master thesis.
and furthermore, the results of each technique are reproducible. For benzyl thiol, the conversion profiles derived from GC peak areas in both repeating experiments are depicted in Figure 51.

**Figure 50:** Conversion profiles of DVE calculated based on $^1$H-NMR 300 MHz data (blue and purple dots) and GC-results (black dots).

**Figure 51:** Conversion profiles of BT calculated based on GC-results

Next to conversion data of the starting compounds, also the formation of the coupling product can be monitored, however as indicate above only qualitative information can be obtained. With $^1$H-NMR 300 MHz, the reaction profile of the product can be monitored by using the area of peak a, b or c (see Figure 49), corresponding to three different sets of protons of the coupling product, which is shown in Figure 52 for one of the two performed experiments. A similar product profile can be obtained from the GC peak areas (see Figure 53).

In agreement with the bulk experimental reference case, in this figure, also the profile for an unidentified impurity of DVE can be registered (at retention time 10.57 minutes). Note that this impurity does not influence the radical thiol-ene reaction, since its concentration does not change.
during the reaction. However it does have a significant effect on the conversion profile of BT and DVE. As seen in Figure 50 and Figure 51, only 73 % BT has reacted, while the conversion of DVE reached 90 % within 200 seconds. This higher conversion of DVE can hence be partly explained by the impurities present in DVE, since in this way there is actually a small excess of BT (the impurity level wasn’t taken into account when DVE was added). GC measurements indicated an impurity level of DVE of approximately 10 mol %.

\[ \text{Figure 52: Reaction profile of the coupling product determined by the areas of peak a (green dots), peak b (blue dots) and peak c (brown dots) in the } ^1\text{H-NMR 300 MHz spectrum.} \]

\[ \text{Figure 53: Reaction profile of the coupling product (black squares) and an impurity of DVE (black triangles) obtained from the corresponding peak areas in the GC-chromatogram.} \]

Unfortunately, the data gained with on-line FTIR were subject to drift because the strong ventilation necessary to prevent odor annoyance from the benzyl thiol disturbed the purging of the instrument with dry nitrogen. A good third verification of the conversion profile could thus not be obtained.
3.4.2 Results for initial molar ratio of BT to DVE of 2

The practical issues above mentioned were overcome by switching off the ventilation after benzyl thiol was added and opening a window in the lab during the purging of the mixture with argon. In the meantime, the IR-signal could stabilize and after approximately half an hour the FTIR-measurements could start. The strong influence of the ventilation on the carbon-carbon double bond absorption peak in the IR-spectrum is illustrated in Figure 54. In this experiment (entry 24 in Table 2) the ventilation is switched on after the thiol-ene reaction is completed (i.e., at ca. one hour in Figure 54) to show its disturbance of the IR-signal.

The conversion profile of the carbon-carbon double bond and the thiol functional group, based on the areas of the IR-absorption peaks at 1620 cm\(^{-1}\) and 2570 cm\(^{-1}\) respectively (see section 3.2.1) for the reaction between BT and DVE in a molar ratio of 2 (entry 24 in Table 2), are shown in Figure 55. As expected, DVE reaches nearly 100 % conversion, whereas the thiol only approximately 50 %. In addition, GC measurements of samples taken at different times after the reaction showed that no full conversion of the DVE was indeed obtained, since a small DVE peak remained in the chromatogram. A very small fraction of DVE did not react, even when 360 nm UV-irradiation was held on for 30 minutes, although an excess of BT is present. This can be explained by assuming a full conversion of the initiator (only 0.05 w% added), which causes the propagation-chain transfer cycle of the thiol-ene process to stop on condition that some termination occurred (see section 3.4.5).
3.4.3 Results for initial molar ratio of BT to DVE of 0.5

For an initial molar ratio of BT to DVE of 0.5, i.e. entry 23 in Table 2, a DVE conversion of approximately 55 % was obtained. Note that this in agreement with an impurity level of DVE of ca. 10 mol %, however not all BT molecules have reacted according to GC/MS-measurements, although an excess of DVE is used (see total ion chromatogram in Figure 57). This is a similar result as the one described in section 3.4.2. The lack of initiator radicals at the end of the reaction and the occurrence of termination reactions could thus be a valid explanation.
3.4.4 Identification of termination products

Since a reaction cannot be assigned to as a “click” reaction if termination occurs and furthermore when the termination products are not easy to separate \(^{2,4}\), some sensitive GC/MS measurement were performed for the reaction between BT and DVE using an excess of DVE (conditions: entry 23 in Table 2) to study in particular the formation of benzyl disulfide. Note that under these reaction conditions, no disulfide formation can occur due to coupling of thiyl radicals after all the DVE has reacted since an excess of DVE is present. In order to do so the split ratio of the injection on the column was lowered, thus a more concentrated sample was injected.

A zoom of the obtained chromatogram is depicted in Figure 58, and shows a variety of small peaks, next to the large reagent and product peaks. Some of them are just impurities of the chemical products used, while others correspond to side products formed during the reaction. Unfortunately, not all peaks can be assigned since many mass spectra are not completely resolved due to the low abundance of the peaks. However, based on its mass spectrum the peak at a retention time of 14.36 minutes is clearly identified as corresponding to benzyl disulfide (according to the NIST-database \(^{93}\); see Figure 59). The peaks close to the product peak at a retention time of 16.68 minutes will probably also correspond to side products, though they are not identified yet and further investigation is necessary. Furthermore, a GC/MS-analysis of pure BT demonstrated that no disulfide is present in the BT used, so it follows that that the benzyl disulfide, which is detected in the sample taken after 10 minutes of irradiation of a BT-DVE mixture (see Figure 58), is formed by recombination of the benzyl thiyl radicals during the radical thiol-ene reaction. Hence, it can be concluded that the studied system is not a perfect ideal coupling system.

Figure 57: GC/MS total ion chromatogram of a sample taken after 10 minutes of UV-irradiation (conditions: entry 23 in Table 2).
3.4.5 Preliminary kinetic modeling results

3.4.5.1 BT-DVE system

Figure 61 presents the comparison between the preliminary simulation results (dotted lines) and the experimental data (black dots) for a molar ratio of BT to DVE of 0.5 (A), 2 (B) and 1 (C), i.e., entry 22-24 in Table 2. For all simulations the changing intensity profile of the 360 nm UV-lamp set-up has been implemented according to Figure 28, while accounting for the three times higher actual intensity. A typical literature value of 0.75 is considered for the initiator efficiency $\eta$ and the molar absorptivity $\varepsilon$ of DMPA, necessary to calculate the initiation rate, is taken equal to the
one as measured in tetrahydrofurane (THF), a similar solvent to 1,4-dioxane (190 L mol\(^{-1}\) cm\(^{-1}\); see Figure 60).

Figure 60: Determination of the molar absorptivity of DMPA in THF at 360 nm\(^{[95]}\).

Also, due to current lack of quantitative data on the presence of disulfides, the kinetic parameters are optimized in this Master thesis aiming at a limited influence of disulfide formation. The effect of this assumption is illustrated further on.

It is derived from Figure 61 that a good description of the experimental data is obtained, except at high conversion. However, it should be reminded that it has been experimentally demonstrated that the used DVE is not pure, explaining the mismatch at high conversions. (see section 3.4.3).

Table 5 shows the corresponding ball-park values of the optimized kinetic parameters. The order of magnitude of these ball-park values is in agreement with literature data of related systems. However, it should be stressed that there are other sets of the parameter values, which also lead to the same simulated conversion profiles. Therefore, additional responses to which one single parameter can be adjusted (ideally a termination rate coefficient), are necessary to obtain an unambiguous set of rate coefficients.

Note that the very sensitive GC/(MS) and the more extended GCXGC analysis methods are well-suited (see section 3.3.7 and 3.4.4) to obtain concentration profiles of the termination products by manually taking samples during the reaction, and adding a low-concentration internal standard to enable quantitative analysis. The low concentration of the internal standard is necessary to have a clearly resolved standard peak in the chromatogram against which the peaks corresponding to the termination products can be integrated, as the injector split ratio should be lowered to obtain a proper detection of the recombination products. Unfortunately, this measurements could not be performed in this Master thesis. For completeness it should also be reminded that the experimentally obtained conversion profiles of the non-equimolar reactions between BT and DVE in 1,4-dioxane (Figure 61 A and B) have to be still verified by repeating experiments.
Figure 61: Comparison between simulated and experimentally determined conversion profiles of the carbon-carbon double bond (red line in A, B and C) and the thiol group (green line in B). The profiles were experimentally determined by on-line FTIR in A and B, and by both GC and $^1$H-NMR 300 MHz in C. Conditions: A = entry 23, B = entry 24 and C = entry 22 in Table 2); no correction for impurities.

Table 5: Preliminary intrinsic rate coefficients obtained by optimization of model simulations to experimental data (see Figure 61) for BT + DVE in 1,4-dioxane.

<table>
<thead>
<tr>
<th>kinetic parameter</th>
<th>value (L mol$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{p1-2}$</td>
<td>$3.0 \times 10^6$ [96]</td>
</tr>
<tr>
<td>$k_p3$</td>
<td>$4.9 \times 10^6$</td>
</tr>
<tr>
<td>$k_{CT1-2}$</td>
<td>$1.5 \times 10^6$ [97]</td>
</tr>
<tr>
<td>$k_{CT3-5}$</td>
<td>$4.1 \times 10^6$</td>
</tr>
<tr>
<td>$k_{t1-18}$</td>
<td>$6.0 \times 10^{10}$</td>
</tr>
</tbody>
</table>

Using the preliminary ball-park values for the kinetic rate coefficients, the concentration profile of each component in the reaction mixture can be simulated by the kinetic model for a given set of reaction conditions, as illustrated in Figure 62 and Figure 63. Figure 62 shows the simulated
concentration profiles of BT, DVE and the coupling product for the equimolar reaction between BT and DVE (A; condition: entry 22 in Table 2), and those for the three main recombination products in the reaction between BT and DVE (B; condition: entry 22 in Table 2). It can be seen that the concentration profiles of BT and DVE coincide (Figure 62 A), indicating an equal consumption of both products, and furthermore that ca.0.2 % of the starting compounds will undergo one of the three main termination reactions.

Finally, Figure 63 presents the concentration profile of DMPA in the equimolar reaction between BT and DVE (entry 22 in Table 2). Note that nearly all the initiator molecules have disappeared after 10 minutes.
3.4.5.2 Validity of kinetic parameters for other thiol-ene systems

Based on literature data it can be expected that the kinetic model is extendable to some other thiol-ene systems, which is illustrated in this Master thesis for the DT-DVE system in n-octane. Since DT has a similar reactivity as BT (both alkyl thiols), it is very likely that the same rate coefficients can be used (see Table 5) to simulate the thiol-ene reaction between DT and DVE in n-octane. However, for the kinetic modeling the molar absorptivity $\varepsilon$ of DMPA has to be changed, since a different chemical environment is present.

Based on the results of McMahon et al., who observed a very low UV-absorbance of DMPA at 360 nm in methylcyclohexane $^{[98]}$, a molar absorptivity which is ten times less than that in 1,4-dioxane is assumed (i.e., $\varepsilon = 19 \text{ L mol}^{-1} \text{ cm}^{-1}$). A good agreement is obtained between the model and the experimental data described in 3.3.8, as shown in Figure 64, supporting the preliminary kinetic model results.

![Figure 64: Comparison between simulated (red line) and experimentally determined conversion profile of the carbon-carbon double bond by on-line FTIR measurements (conditions: entry 19 in Table 2).](image)

3.4.5.3 Coupling efficiency

Since a reaction cannot be assigned to a “click” reaction if undesired side reactions occur that generate products which are not easily separated, a mathematical function is introduced in order to quantify to which extent side reactions occur, i.e., the coupling efficiency $F$. It is defined as the root mean square of two ratios $f_1$ and $f_2$ which account for undesired reactions of the “ene” and the thiol functional group respectively, as they relate the amount of coupling product formed to the quantity of “ene” or thiol that has reacted:

$$F = \sqrt{f_1 f_2} = \sqrt{\frac{[\text{thio-ether}] V}{([\text{ene}]_0 V_0-[\text{ene}] V)} \frac{[\text{thio-ether}] V}{([\text{thiol}]_0 V_0-[\text{thiol}] V)}}$$

If assumed that product isolation is not straightforward, the coupling efficiency $F$ should be very close to 1 in order to assign the thiol-ene reaction as a “click” reaction. For the reaction between BT and DVE in 1,4-dioxane using an excess of DVE, the variation of the coupling efficiency $F$ during the reaction is shown in Figure 6539, along with the ratios $f_1$ and $f_2$. Note that $F$ is
different from 1 at the end of the radical thiol-ene reaction, and this will always be the case since termination is inherent to the radical thiol-ene mechanism: in every addition or chain transfer reaction the number of radicals remains constant, which will eventually lead to a total concentration of recombination products that is equal to the initial initiator concentration multiplied with the initiation efficiency.

Finally, the definition of the coupling efficiency can be extended to other “click” reactions between a component A and B in order to study the importance of side reactions, and again a value very close to 1 is necessary to assign the particular reaction as a “click” reaction if the product is not easily isolated:

\[ F = \frac{[\text{product}]}{\sqrt{[\text{reactant A}]_0 V_0 - [\text{reactant A}] V}} \frac{[\text{product}]}{[\text{reactant B}]_0 V_0 - [\text{reactant B}] V} \]

Figure 65: Variation of the coupling efficiency F (blue line) and the ratios \( f_1 \) (red line) and \( f_2 \) (green line) during the reaction between BT and DVE in 1,4-dioxane using equimolar conditions (conditions: entry 22 in Table 2).

3.4.5.4 Importance of implementation of the intensity profile

Importantly, simulations revealed that the consideration of the intensity change of the UV-lamp with increasing time is crucial, since only in that case the experimentally observed S-shaped conversion profiles (e.g. Figure 56) can be obtained, and proper parameter adjustment is possible. This is shown in Figure 66, in which a comparison is made between the simulated conversion profiles of the carbon-carbon double bond if the intensity change is implemented in the model (red line) and if it is neglected, using the same kinetic parameters (Table 5). It is clear that the intensity change of the used UV-lamp does have a significant effect on the conversion profile, and should thus be implemented in the model in order to obtain reliable kinetic parameters.
3.4.5.5 Theoretical assessment of disulfide formation on the coupling reaction

Since the formation of disulfides during the radical thiol-ene reaction was experimentally verified (see sections 3.3.7 and 3.4.4), a theoretical study of the effect of the corresponding rate coefficient, i.e. $k_{t1}$, on the conversion and the coupling efficiency was performed, using the preliminary ball-park values for the other kinetic parameters listed in Table 5. $k_{t1}$ was varied between $5.0 \times 10^9$ and $5.0 \times 10^{11}$ L mol$^{-1}$ s$^{-1}$ and the results are shown in Figure 40 A (effect on conversion) and B (effect on coupling efficiency) for the equimolar reaction between BT and DVE (i.e., entry 22 in Table 2). As expected, a higher value of $k_{t1}$ results in a lower reaction rate and coupling efficiency, and vice versa. However, in all cases the coupling efficiency is relatively high. Note that a ten-fold increase of $k_{t1}$ results in a much higher proportional decrease of the reaction rate, than in case $k_{t1}$ is decreased. These results indicate that the extent to which disulfide formation occurs, mainly has a significant effect on the reaction rate. A quantification of the termination products is therefore an absolute necessity in order to determine reliable kinetic parameters and to subsequently understand thiol-ene coupling reactions involving polymeric species.
Figure 67: Simulations of the carbon-carbon double bond conversion (A) and the coupling efficiency (B) for different values of $k_{t_1}$, while the other kinetic parameters are held constant (Table 5). $k_{t_1}$ was varied between $5.0 \times 10^9$ (blue dotted line) and $5.0 \times 10^{11}$ L mol$^{-1}$ s$^{-1}$ (dark blue full line) (conditions: entry 22 in Table 2).

3.5 Radical thiol-ene reaction between 1-dodecane thiol and 2-norbornene in 1,4-dioxane

As mentioned in the introduction of this chapter, experiments were also performed using an “ene” compound with a different reactivity than DVE, i.e. 2-norbornene (Nb). Due to the alleviation of ring strain upon reaction with a thiol group, the carbon-carbon double bond in Nb is much more reactive than that in DVE (10 times$^{[99]}$; see Chapter 2). Note that this very high reactivity of Nb and, hence, the lower reaction times of the radical thiol-ene reactions using this compound, highlight its potential not only for polymer modification reactions, but also polymer-polymer conjugation.

Similarly as for DVE, the coupling reaction was studied in 1,4-dioxane. Contrary, DT was used instead of BT because of practical reasons (smell annoyance). However the latter is very likely to have no effect on the obtained rate coefficients, as shown in paragraph 3.4. In the following, the results using equimolar amounts of “ene” and thiol are discussed (i.e., entry 25 and 26 in Table 2).

Since the carbon-carbon double bond of Nb absorbs IR-radiation at 713 cm$^{-1}$, initially the disappearance of the Nb carbon-carbon double bond was followed with on-line FTIR. However, a continuously varying noise on the IR-signal starting from approximately 900 cm$^{-1}$ makes a proper measurement impossible. This noise is always present, even if the probe is perfectly clean, as illustrated in Figure 68. Note that the variation of the area of the carbon-carbon double bond absorption peak (see Figure 69), although disturbed, does give a qualitative indication that Nb disappears very quickly.
In order to obtain proper conversion profiles, samples were manually taken during the reaction and analyzed by GC and $^1$H-NMR 300 MHz. In a first experiment, the same conditions as those used for the BT-DVE system were applied (entry 25 in Table 2) and a similar analysis procedure was followed: the first sample is a reference sample that only contains Nb and DMPA dissolved in 1,4-dioxane, while the second sample is taken just before the 360 nm UV-light is switched on, and the next samples are collected each 15 seconds during the reaction.

Figure 70 shows the GC-chromatograms of the reference sample, the sample taken just before starting the UV-irradiation, and the sample taken after 15 seconds of reaction. Assignment of the reagent, solvent and product peaks is in this way straightforward, and the corresponding peaks are labeled in Figure 70.
Figure 70: Overlay of 3 FID-chromatograms for the equimolar reaction between DT and Nb in 1,4-dioxane (i.e., entry 25 in Table 2), in which A represents the reference sample, B the starting mixture of DT and Nb in 1,4-dioxane, and C the sample mixture after 15 seconds of reaction.

An overlay of the $^1$H-NMR 300 MHz spectra of the same three samples is shown in Figure 71, and the peaks corresponding to Nb and the coupling product are labeled. Again 1,4-dioxane is used as an internal standard, relative to which peak areas in the $^1$H-NMR 300 MHz spectra and the GC chromatograms are determined according to the method described in section 3.4.1. By taking ratios of peak areas, conversions of both DT and Nb have been calculated. Note that only conversions of Nb can be derived from the $^1$H-NMR 300 MHz spectra (based on the area of the peaks at 5.95 ppm and 2.82 ppm), since the shift of the protons bonded to the carbon atom adjacent to the sulfur is very small. Conversion profiles of Nb, based on both GC- and $^1$H-NMR 300 MHz results, and of DT, calculated from GC-data, are shown together in Figure 72.
Figure 71: Overlay of the $^1$H-NMR 300 MHz reference spectrum (A), the spectrum just before reaction (B), and the spectrum after 15 seconds of reaction (C). (Conditions: entry 25 in Table 2)

Figure 72: Conversion profiles of DT (black squares) and Nb based on GC (black triangles) and $^1$H-NMR 300 MHz (blue dots, blue line is eye catcher) results (conditions: entry 25 in Table 2).

It is clear that Nb disappears very fast and reaches 100% conversion in less than 15 seconds, since that is the time at which the first sample was taken and analysis showed that full conversion of Nb was already obtained. However, the conversion profile of DT is very remarkable, as only
half of the DT molecules are consumed while equimolar amounts of DT and Nb were used. This observation is also confirmed by a GC/MS characterization of the mixture after reaction for the on-line FTIR experiment previously described (also according to entry 25 in Table 2), as shown in Figure 73.

![Figure 73: GC/MS total ion chromatogram taken after the reaction between N and DT in equimolar amounts in 1,4-dioxane (condition: entry 25 in Table 2).](image)

In order to verify this unexpected result, a second experiment was performed (i.e., entry 26 in Table 2), in which equimolar amounts of DT and Nb were used, and the reaction was monitored with GC and $^1$H-NMR 300 MHz. However, four times more DMPA was added to investigate the effect of initiation on the thiol conversion. The first sample during the reaction was now taken after 5 seconds. Similar conversion profiles of Nb and DT were obtained, though DT was now consumed for ca. 55 %, as illustrated in Figure 74, however this difference of 5 % is too small to draw any conclusions. Furthermore, since no additional peaks appear in the GC-chromatogram within the temperature range scanned (ref Appendix C), no straightforward mechanistic explanation can be put forward in this Master thesis. Further investigation of this phenomenon is thus necessary. Note that from the GC-chromatograms it can however be concluded that Nb reaches 100 percent conversion in approximately 5 seconds, since after 5 seconds still a minuscule, but clearly resolved 2-norbornene peak is present in the chromatogram (after 20 seconds of reaction this peak has disappeared).
4 Conclusions

The coupling reaction between low molar mass compounds is optimally performed using the 360 nm UV-lamp set-up. Contrary to the 254 nm lamp a good initiation rate can be obtained and a glass flask can be safely used.

Due to a fast reaction rate, the coupling between DVE/Nb and DT/BT is strongly influenced by the change of the intensity profile of the 360 nm UV-lamp set-up. Good ball-park values for the kinetic parameters can thus only be obtained in case the intensity profile of the UV-lamp(s) is explicitly accounted for.

Bulk experiments are characterized by a significant rise in temperature during reaction and are characterized by a high oxygen tolerance. On the other hand, in solution the temperature rise can be safely neglected allowing a more straightforward determination of kinetic parameters. However, solution experiments for parameter determination should be performed under argon atmosphere, since a small influence of oxygen is observed at low reaction times.

For a bulk model coupling reaction between DVE and DT, it is shown that the oxygen tolerance is very high and the reaction rate is strongly influenced by the initial molar ratio of the starting compounds and the initial DMPA amount. Interestingly, a too high initial amount of DMPA results in a lowering of the reaction rate. Similar trends were obtained or can be expected for the related DVE/BT system in 1,4-dioxane.

Detailed product characterization revealed that the used DVE contains ca. 10 mol% of impurity, which leads to a coupling efficiency lower than expected both in bulk and solution experiments.
Furthermore, GCxGC and GC/MS analysis are shown to be powerful tools for the identification of termination products, such as the formation of disulfides. Based on qualitative GCXGC and GC analysis, it can be concluded that the bulk model coupling reaction (1 w% DPMA) and the coupling reaction between DVE and BT (0.05 wt% DPMA) in 1,4-dioxane cannot be assigned as a pure “click” reaction, since termination products could be identified. Further investigation is needed to determine the actual importance of these side reactions.

Preliminary ball-park values are reported for the coupling reaction of DVE and BT in 1,4-dioxane under argon atmosphere assuming a limited influence of side reactions. These parameters can be used to a first approximation for coupling reactions involving high molar mass compounds. A good agreement with the experimental data for different initial molar ratios of monomer to initiator is obtained and in agreement with literature data the same parameters could be used to describe the coupling reaction between DVE and DT in n-octane.

Finally, it was observed that Nb was much more reactive than DVE since reaction times were ca. 10 times lower even though the same reaction conditions were applied. However, all the performed equimolar reactions between DT and Nb in 1,4-dioxane lead to a thiol conversion of approximately 50 %, for which currently no straightforward explanation could be given based on GC/(MS) and $^1$H-NMR 300 MHz results. Further investigation is thus necessary to understand the latter phenomenon.
CHAPTER 4 : KINETIC STUDY OF POLYMER FUNCTIONALIZATION USING RADICAL THIOL-ENE CHEMISTRY

In this chapter, a kinetic study of polymer end-group modification with low molar mass compounds is presented. Analogously as in Chapter 3, a model system is defined, which considers the coupling reaction between dodecyl vinyl ether and thiol-functionalized polystyrene in 1,4-dioxane. In particular, attention is paid to the potential loss of the functionalization efficiency in each synthesis step. Also, a preliminary evaluation of the importance of diffusional limitations on the functionalization efficiency is presented using the kinetic parameters as obtained in Chapter 3. Finally, a strategy for a more detailed kinetic investigation of polymer functionalization reactions using radical thiol-ene chemistry is proposed.

1 Experimental procedure

In this section, the experimental procedure to study the modification of thiol-functionalized polystyrene (PS-SH) with dodecyl vinyl ether (DVE) as low molar mass compound is described. It includes the specifications of the chemicals used, the description of the synthesis of the thiol-functionalized polystyrene (PS), the conditions of the coupling experiments performed, the description of a typical thiol-ene functionalization experiment, and the analysis methods applied for both synthesis steps.

1.1 Materials

Dodecyl vinyl ether (DVE; 98 % pure(*)), the eluens tetrahydrofuran (THF; > 99.9 % pure, inhibitor free), the reducing agent tributylphosphine (TBP; 97 % pure) and trichloroacetyl isocyanate (TAIC) were purchased from Sigma Aldrich. Propylamine (98 % pure), the solvent 1,4-dioxane (> 99 % pure, stabilized) and the initiator 2,2-dimethoxy-2-phenylacetophenone (DMPA; 99 % pure) were purchased from Acros Organics. Methanol (99 % pure) was obtained from Chem-Lab. All chemicals above were used as received. Styrene (99 %, extra pure), purchased from Acros Organics, was passed through a column of basic alumina to remove the inhibitor before use. The chain transfer agent (CTA) dibenzyl trithiocarbonate (DBTTC) was
obtained from Arkema and used as received. The chemical structures of the aforementioned compounds are depicted in Figure 75.

(*) It has been demonstrated in Chapter 3 that DVE contains, however, an impurity inreactive with respect to the thiol, which in fact necessitates the use of a small excess of DVE.

![Figure 75: Chemical structures of the used compounds in the kinetic study of polymer functionalization using radical thiol-ene chemistry](image)

### 1.2 Aminolysis of polystyrene

First, 1 g of PS prepared by reversible addition fragmentation chain transfer (RAFT) polymerization (CTA: DBTTC) is put into a two-necked 25 mL flask and is dissolved in 5 mL of THF. The two necks are covered with a septum and to remove oxygen a constant flux of argon is provided by an argon filled balloon through a long needle, which is put into the sample liquid. After 40 minutes of purging, a twenty-fold excess of TBP relative to the amount of trithiocarbonyl groups (ca. 0.5 mL) and an excess of amine (3 mL) are added to the polymer solution through the septum by means of an argon purged syringe. The reaction is allowed for one hour and afterwards the obtained PS-SH is precipitated two times by dropwise addition to cold methanol and subsequent filtration in order to remove all the remaining low molar mass compounds. Finally, the purified functionalized PS (PS-SH; \(M_n\) number average molar mass = 4700 g mol\(^{-1}\) (see further)) is dried overnight in a vacuum oven. However, it should be beared in mind that it has been indicated that not all polymer chains prepared by RAFT polymerization and cleaved by aminolysis will exhibit thiol end-groups \(^{100}\) (see further).
1.3 Experimental conditions for the coupling reactions

The experimental conditions used to study the coupling reaction between the thiol-functionalized polystyrene and DVE are listed in Table 6 (entry 1-5). From left to the right is specified: the chemical name of the reagents, the equivalents of thiol with respect to the “ene”, the initial mass percentage of the initiator (DMPA) with respect to the total sample mass, the ambient temperature and finally the time span of the UV irradiation. All reactions are conducted in 1,4-dioxane, using ca. 1 ml of solvent for each 50 mg of PS-SH added. Furthermore, the 360 nm UV-lamp set-up is used as irradiation source and in principle an amount of 100 mg PS-SH is initially present, except for entry 4 in Table 6, in which an excess of “ene” is used. In addition to the thiol-ene coupling reactions, also an experiment without the presence of DVE has been performed to study the importance of disulfide formation for PS-SH (entry 6 in Table 6).

Table 6: Experimental conditions used to study the thiol-ene reaction between PS-SH and DVE. The number average molar mass of PS-SH is 4700 g mol⁻¹ (determined by GPC; gel permeation chromatography)

<table>
<thead>
<tr>
<th>entry</th>
<th>components</th>
<th>[thiol]₀/[ene]₀</th>
<th>initial w% DMPA of total sample mass</th>
<th>t (°C)</th>
<th>irradiation time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PS-SH + DVE</td>
<td>1</td>
<td>0.05</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>PS-SH + DVE</td>
<td>1</td>
<td>0.05</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>PS-SH + DVE</td>
<td>1</td>
<td>0.05</td>
<td>23</td>
<td>32</td>
</tr>
<tr>
<td>4</td>
<td>PS-SH + DVE</td>
<td>0.2</td>
<td>0.05</td>
<td>21</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>PS-SH + DVE</td>
<td>1</td>
<td>0.5</td>
<td>22</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>PS-SH</td>
<td>-</td>
<td>0.05</td>
<td>22</td>
<td>30</td>
</tr>
</tbody>
</table>

1.4 Typical functionalization experiment of PS-SH with DVE

For a typical polymer functionalization experiment (e.g. entry 2 in Table 6) 0.00109 g of DMPA is weighed with an analytical balance, and put into a two-necked 25 ml flask. Next, 0.100 g of PS-SH is added and subsequently ca. 2 mL of 1,4-dioxane in order to obtain a clear solution. The two necks are sealed with a septum and the mixture is purged for 40 minutes with argon to remove oxygen, by means of an argon filled balloon attached to a long needle. Afterwards 5.5 µL
of DVE is added to the sample solution through the septum and the mixture is purged for another 10 minutes. Thereafter, the balloon is removed and the flask is put in the middle of the 360 nm UV-lamp set-up, covering the open side of the set-up with aluminum foil to prevent the exit of UV-radiation, and it is irradiated with UV-light during 15 minutes. During all the steps described above, the sample mixture is continuously stirred at a rate of 800 rpm. Finally, the resulting polymer is precipitated two times in cold methanol and dried overnight in a vacuum oven.

1.5 Analysis

In all PS-SH functionalization experiments with DVE, the dried polymers are analyzed by gel permeation chromatography (GPC). A PL GPC50plus (PolymerLabs/Agilent) equipped with a PL AS RT autosampler and refractive index (RI) detector is used for the determination of the number average molar mass \( M_n \) and the polydispersity index (PDI) of the polymer samples using THF as eluens. Absolute molar masses are obtained, since the GPC is calibrated with PS standards.

In order to study the efficiency of the cleavage of the trithiocarbonate group, UV-VIS absorption spectra of the PS prepared by RAFT polymerization before and after the aminolysis are recorded with a Specord 200 double-beam spectrophotometer with two large-area photodiodes.

In order to quantify the functionalization efficiency between the thiol-functionalized PS and DVE, \(^1\)H-NMR 500 MHz measurements are performed by putting 10 mg of polymer in a NMR-tube and dissolving it in \( \text{ca. 750 } \mu \text{L of deuterium-doped chloroform (CDCl}_3 \)\. In parallel, a second set of \(^1\)H-NMR 500 MHz samples is prepared, however in addition one droplet of TAIC is added, which in principle quantitatively converts the thiol groups (see Figure 76) leading to the formation of imidic hydrogens, which show a resonance peak in the range 8-11 ppm. It should however be noted that the in situ derivatization of thiol end-groups of polymers by TAIC is not as effective as hydroxy, amino or carboxy end-groups \[^{101}\].

![Figure 76: Reaction scheme for the in situ derivatization of thiol end-groups with TAIC \[^{101}\].](image)

For the experiment using a five-fold excess of DVE, i.e., entry 4 in Table 6, next to the off-line characterization with \(^1\)H-NMR 500 MHz and GPC described above, the radical thiol-ene reaction is monitored with on-line FTIR spectroscopy by recording the disappearance of the carbon-carbon double bond absorption peak at 1620 cm\(^{-1}\). Note that first an IR-absorption spectrum of
the solvent 1,4-dioxane is recorded, which is subtracted from the sample spectrum in order to obtain a more resolved carbon-carbon double bond absorption peak.

Finally, for detailed information about the specifications and the working principle of the used analytical techniques is referred to Appendix C.

2 Results and discussion

In this section, first the synthesis and characterization of the thiol-functionalized polystyrene (PS-SH) is highlighted, since the efficiency of this synthesis reaction can have a major impact on further functionalization results. Next, an experimental kinetic study of the modification of the thiol end-groups with DVE using UV-induced radical thiol-ene chemistry is presented, in which the functionalization efficiency is determined by on-line FTIR and $^1$H-NMR 500 MHz measurements. In this study, the importance of side reactions is evaluated by GPC characterization of the resulting polymers. Finally, preliminary kinetic modeling results are presented and discussed in comparison with experimental data to assess the possible influence of diffusional limitations on the functionalization efficiency.

2.1 Characterization of thiol-functionalized polystyrene: efficiency of the synthesis strategy

In a first step, polystyrene (PS) was synthesized by a 6 hour RAFT polymerization using DBTTC as chain transfer agent, of which the symmetric chemical structure leads to a PS polymer characterized by a trithiocarbonyl group in the middle of the chain, as shown in Figure 77. The RAFT polymerization was solely self-initiated, i.e., no conventional initiator was added.

![Figure 77](image)

Figure 77: Reaction scheme for the RAFT polymerization of PS with DBTTC as CTA

GPC analysis showed that the resulting PS has a $M_n$ of 10000 g mol$^{-1}$ and a PDI of 1.2 (see Figure 78). However, a comparison between the areas of the resonance $^1$H-NMR 500 MHz peaks corresponding to remaining styrene monomer and PS, indicated a molar mass of ca. 9000 g mol$^{-1}$, though the exact value is of no great importance for the further experiments.
Figure 78: Derivative of the molar mass distribution of the PS prepared by RAFT polymerization with DBTTC as chain transfer agent.

Note that $M_n$ is relatively low and a high livingness is to be expected. On the other hand, termination reactions cannot be excluded in the RAFT polymerization and a least part of the loss of functionalization efficiency is very likely caused already in the PS synthesis step. Unfortunately, the end-group fidelity of the PS could not be determined.

In a second step, the trithiocarbonyl group was reduced to a thiol via aminolysis at ambient temperature in the presence of propylamine as a nucleophile (see Figure 79). Since it is known from literature [100] that some disulfide formation cannot be suppressed, a large excess of the reducing agent TBP was used to minimize this effect. However, Lima et al. also reported the presence of hydrogen terminated polymer chains as additional side-products [100] and, hence, it can be expected that in this second step again still part of the functionalization efficiency is affected.

Figure 79: Reaction scheme for the aminolysis of PS prepared by RAFT with propylamine. Note that also possible side-reactions are indicated by dashed lines.
To verify whether the aminolysis was successful, UV-absorption experiments were performed, since the trithiocarbonyl groups exhibit a strong absorbance of UV-light between 290 and 350 nm. Figure 80 clearly shows that the strong absorbance of the trithiocarbonate moiety as recorded before the aminolysis reaction (purple line) is completely disappeared afterwards (PS-SH; blue line), indicating that the cleavage of the trithiocarbonyl groups was very effective. However the importance of side-product formation (see Figure 79) cannot be assessed by this method, as a quantitative analysis of the amount of thiol end-groups should be performed.

Furthermore, GPC analysis (Figure 81) showed that the number average molar mass of PS-SH is approximately half that of the PS as synthesized according to the RAFT polymerization scheme in Figure 77, i.e., 4700 g mol\(^{-1}\), which supports an effective cleavage of the trithiocarbonyl groups.

**Figure 80:** UV-absorption spectrum of the PS prepared by RAFT polymerization with DBTTC as chain transfer agent before (purple line) and after (PS-SH; blue line) aminolysis.

**Figure 81:** Derivative of the molar mass distribution of the PS prepared by RAFT polymerization with DBTTC as chain transfer agent before (PS; dotted line) and after (PS-SH; full line) aminolysis.
2.2 Functionalization of PS-SH with DVE: evaluation of functionalization efficiency

Initially, in order to study the functionalization of PS-SH with DVE, the absorbance of the DVE carbon-carbon double bond was monitored with on-line FTIR using 0.15 g PS-SH and a five-fold excess of DVE (entry 4 in Table 6). Such excess was used to obtain a well-defined absorption peak at 1620 cm\(^{-1}\), and to benchmark the experimental results with those reported by Stamenovic et al. (\(M_n = 4000\) g mol\(^{-1}\); 0.2 equivalents of DMPA; five-fold excess of DVE). However, it should be reminded that the use of an excess of one of the starting compounds should be avoided, since even for a 100\% functionalization efficiency, in this case the reaction cannot be assigned as a true polymer modification.

The DVE conversion was calculated based on the corresponding peak area (see Chapter 3) and is shown versus time in Figure 82. For a ‘perfect’ coupling reaction, a conversion of 20\% is to be expected. However, from this figure it follows that the conversion stagnates around 30 minutes at a value of circa 14\%, which indicates a functionalization efficiency of 70 \%, which was in turn verified by \(^1\)H-NMR 500 MHz analysis (Figure 85; both with and without addition of TAIC, see further). Interestingly, a 20\% lower functionalization efficiency than reported by Stamenovic et al. \(^6\) (i.e., 90 \%) is obtained. However, to assess whether the results are inherently different, a quantitative analysis of the thiol end-groups should still be performed. Furthermore, it should be noted that the signal is somewhat unstable due to the low concentration of the DVE carbon-carbon double bonds in the sample, even though a five-fold excess was used.

![Figure 82: Conversion versus time of the carbon-carbon double bond based on on-line FTIR measurements (five-fold excess DVE; conditions: entry 4 in Table 6).](image)

Unfortunately, under equimolar conditions, no on-line characterization of the sample by FTIR spectroscopy could be performed, since the carbon-carbon double bond absorption peak was too weak to obtain a proper signal. Instead, the conversion of the functionalization reaction was
calculated based on off-line $^1$H-NMR 500 MHz results of samples taken at different reaction times. Separate experiments were performed using different UV-irradiation times, according to entry 1 to 5 in Table 6, and $^1$H-NMR 500 MHz spectra of PS-SH before coupling with DVE, both with and without in situ derivatization with TAIC (see section 1.5), were recorded to allow an easy peak identification and to obtain a well-defined starting point of the reaction. The peak assignment and integration for both NMR analysis procedures is discussed below.

Figure 83 shows an overlay of the $^1$H-NMR 500 MHz spectra of PS-SH (A) and the DVE-functionalized PS (PS-DVE) after 5 minutes of reaction (B) with the peaks corresponding to PS (i.e., 6-7 ppm (c); B) and DVE (i.e., 0.85 ppm (a) and 3.25 ppm (b); B) labeled. In order to calculate the conversion of the coupling reaction, the peaks corresponding to DVE were integrated against the area of the PS-peak between 6 and 7 ppm, since the amount of PS does not change during the functionalization reaction. The functionalization efficiency was determined by relating the peak area of the DVE peaks to the expected peak area if equimolar amounts of DVE and PS with a molar mass of 4700 g mol$^{-1}$ were present.

In case the NMR-samples were subject to an in situ derivatization with TAIC, the conversions were calculated based on the decrease of the resonance peak at ca. 10.2 ppm corresponding to the imidic hydrogen (see section 1.5). Note that again peak areas are determined relative to the area of the PS-peak between 6 and 7 ppm. In Figure 84, an overlay is shown of the $^1$H-NMR 500 MHz spectra of PS-SH (A) and PS-DVE after 5 minutes of reaction (B), both modified with TAIC, with the imidic hydrogen and PS-peaks labeled.
Figure 84: Overlay of the $^1$H-NMR 500 MHz spectra of PS-SH (A) and PS-DVE after 5 minutes of reaction (B), both after in situ derivatization with TAIC.

The resulting conversion profiles based on both NMR analysis procedures are shown in Figure 85 (black, blue and purple dots). In the same figure, also the functionalization efficiency after 30 minutes for the previous cases (5-fold excess of DVE) is shown (red and orange points). Each analysis was performed twice in order to check the reproducibility, and in general it can be concluded that both analysis methods provide reproducible results. However a third verification of the results is recommended. Clearly, with increasing reaction time the functionalization efficiency increases until a limiting value of circa 70% is obtained after one hour.

Figure 85: Conversion versus time of the functionalization reaction of PS-SH with DVE, calculated based on $^1$H-NMR 500 MHz measurements of the resulting polymer with (black dots) and without (blue en purple dots, lines serve as eye catcher) in situ derivatization by TAIC (conditions: entry 1,2 and 5 in Table 6). Also the functionalization efficiency of the functionalization reaction of PS-SH with DVE using a five-fold excess of DVE (conditions: entry 4 in Table 6) are shown (red dots: without addition of TAIC; orange dots: with addition of TAIC); the experiment according to entry 3 in Table 6 (equimolar amounts of PS-SH and DVE, 32 minutes of reaction) did not provide representative $^1$H-NMR 500 MHz results (see further) and was therefore excluded from this figure.
As indicated in paragraph 1.5, all obtained polymers with different degrees of DVE end-group functionalization were also analyzed by GPC in order to characterize the molar mass distributions. The reaction time, the number average molar mass and the PDI of the analyzed polymers are listed in Table 7, in which the entry is in accordance with the experimental conditions given in Table 6. The corresponding derivatives of the molar mass distributions are depicted in Figure 86.

Both from Table 7 and Figure 86 it is clear that the number average molar masses of the obtained polymers after the UV-induced functionalization reaction with DVE are much higher than expected assuming a perfect coupling. Values around 6000 g mol\(^{-1}\) are obtained, which are too high taking into account that the molar mass of DVE is only 212.38 g mol\(^{-1}\), suggesting the occurrence of coupling reactions, e.g. thiol-thiol, thiol-carbon or carbon-carbon (see Chapter 3; kinetic model: reactions).

However, no general trend can be observed between the number average molar masses or the PDI’s of the polymer and the irradiation time. On the other hand, the occurrence of thiol-thiol recombination has been indicated by an experiment in which no DVE is present (entry 6 in Table 2; Figure 7: black dashed line). Similar to the coupling reactions with DVE, a clear shift to higher molar masses is observed after the UV-irradiation, together with a significant increase of the PDI.

Table 7: Number average molar mass and PDI for the PS with different degrees of DVE end-group functionalization (conditions: same entry in Table 6)

<table>
<thead>
<tr>
<th>entry</th>
<th>components</th>
<th>(M_n) (g mol(^{-1}))</th>
<th>PDI</th>
<th>irradiation time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>PS-SH</td>
<td>4700</td>
<td>1.23</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>PS-SH + DVE</td>
<td>6000</td>
<td>1.24</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>PS-SH + DVE</td>
<td>6200</td>
<td>1.26</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>PS-SH + DVE</td>
<td>6100</td>
<td>1.25</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>PS-SH + DVE</td>
<td>5700</td>
<td>1.24</td>
<td>62</td>
</tr>
<tr>
<td>6</td>
<td>PS-SH</td>
<td>6100</td>
<td>1.29</td>
<td>30</td>
</tr>
</tbody>
</table>
2.3 Kinetic modeling results

In order to assess the importance of diffusional limitations for the coupling reaction between PS-SH and DVE, the conversion profile obtained by on-line FTIR analysis (5-fold DVE excess) and the functionalization efficiencies calculated from $^1$H-NMR 500 MHz analysis (equimolar and 5-fold excess DVE) were compared with intrinsic simulations using the kinetic parameters reported in Chapter 3 for the corresponding low molar mass BT-DVE model system.

Clearly, it follows from Figure 87 A and B that in case intrinsic kinetics would apply, a much faster reaction rate would be obtained, indicating a significant influence of diffusional limitations on the coupling reaction. However, it should be kept in mind that the loss of functionalization efficiency in the synthesis steps prior to the coupling reactions is not accounted for in the kinetic model making a real assessment of the importance of diffusional limitations at this stage very difficult.
Figure 87: Comparison between intrinsic simulations using same intrinsic kinetic parameters as obtained in Chapter 3 (red line), and experimental data (black dots) for the functionalization efficiency, i.e. \( \frac{[\text{product}]}{[\text{thiol}]} \) (A; equimolar; 0.05 w% DMPA; based on \(^1\)H-NMR 500 MHz data), and the “ene” conversion (B; five-fold excess of DVE; 0.05 w% DMPA; based on on-line FTIR data) of the modification of PS-SH with DVE in 1,4-dioxane.

It should be stressed that diffusional limitations can only be important on those reactions steps, which involve a macromolecule, since it is well-known that the translational diffusion of non-macromolecules is fast, especially in media characterized by a low viscosity, as is the case in the present work.

Finally, it should be noted that in case diffusional limitations are important for the functionalization efficiency, the chain transfer reaction (blue dashed arrow in Figure 88) is the only one leading to a lowering of this efficiency.

Figure 88: Addition and chain transfer step for the radical thiol-ene reaction between PS-SH and DVE.
3 Conclusions and future work

For the DVE/PS-SH model system in 1-4 dioxane, it is demonstrated that for both using an excess and an equimolar amount of DVE, a limiting functionalization efficiency of circa 70% (on a thiol basis) exists.

The reduced functionalization efficiency can partially be explained by the impurity of DVE, the loss of end-group fidelity during the PS synthesis, the influence of side reactions during the aminolysis and the occurrence of recombination reactions during the coupling reaction. In particular, it has been indicated in this chapter that disulfide formation takes place during the coupling reaction based on experimental GPC data obtained in case no DVE is present. Furthermore, kinetic modeling of the coupling reaction assuming intrinsic kinetics, i.e., neglecting diffusional limitations, using the kinetic parameters obtained in Chapter 3, suggest the possible influence of diffusional limitations on the functionalization efficiency.

In order to obtain reliable results of the functionalization efficiency for the modification of PS-SH with DVE, a quantification of the thiol end-groups after cleavage of the trithiocarbonyl groups by aminolysis, is necessary as this would allow to assess the imperfections corresponding to both the RAFT polymerization process and the aminolysis reaction.

The Ellman test [102], which is widely used for characterization of cysteinyl thiols in proteins, can provide such a quantitative analysis of the thiol-end groups and could be used in future work. In this test, the thiol-functionalized polymer is added to a dilute solution of Ellman’s reagent (see Figure 89), which is basified to a pH of 8. The disulfide reagent reacts with the thiol end-groups and produces an anion (see Figure 89), which is characterized by a strong visible absorbance maximum at 412 nm. A simple measurement of the absorbance allows the determination of the concentration of the thiol groups after calibration.

![Figure 89: Reaction of Ellman’s reagent with a thiol end-group](102)
CHAPTER 5: GENERAL CONCLUSIONS

In this Master thesis, a detailed kinetic study of thiol-ene coupling reactions is presented allowing to better understand the influence of reaction conditions and side reactions on the coupling efficiency both for systems involving low and high molar mass compounds.

Experiments revealed that to optimally benefit from the potential of the thiol-ene coupling method, a good radiation source should be selected. Clearly, better results are obtained in case 360 nm lamps are used instead of 254 nm lamps. Also, depending on the purity of the starting compounds, slightly modified initial conditions have to be used.

For the coupling reactions with a low molar mass “ene” and thiol, the kinetics are fast and influenced significantly by the non-instantaneous build-up of the intensity profile of the UV-lamp. Moreover, if the coupling reaction is performed in bulk a temperature rise up to 15°C is to be expected, prohibiting an accurate kinetic modeling of such systems. Contrary in solution, isothermal conditions can be safely assumed, although it is recommended to perform such reactions under argon atmosphere. Detailed currently qualitative product characterization (GCxGC/MS, GC/MS) revealed that the coupling efficiency is lowered by the occurrence of termination reactions, in particular by disulfide formation. In particular, ball-park values for a model system (DVE/BT/1,4-dioxane/DMPA) were obtained assuming a limited influence of these reactions, though a quantification of the termination products is necessary to acquire an unambiguous set of rate coefficients. A good agreement between experimental and modeling results is obtained, also using the same parameters for the related DVE/DT system in n-octane. Furthermore, a significantly faster reaction rate can be obtained by replacing DVE by Nb, however further investigation should reveal the explanation for the unexpected conversion profile of the thiol compound.

For the coupling reactions with a low molar mass “ene” and a thiol-functionalized macro-molecule, it has been indicated for a PS-SH/DVE/1,4-dioxane/DMPA model system that the coupling efficiency can be affected during each synthesis step: (i) PS synthesis (ii) PS-SH synthesis (iii) coupling PS-SH with DVE. A limiting coupling efficiency of 70% is reported and in particular further research is necessary to determine the loss during the PS synthesis and aminolysis step. Kinetic simulations using the parameters obtained for the analogous low molar mass system indicate that diffusional limitations might also contribute to this loss.
APPENDIX A : CONTINUITY EQUATIONS

In this appendix the continuity equations corresponding to the considered reaction steps in Table 3 in Chapter 3 are listed. A short notation is used and no concentration change due to a volume change is considered.

\[
\frac{d[I_1I_2]}{dt} = -R_i = -\frac{2.303f\varepsilon[I_1I_2]l_0\lambda}{N_A h c}
\]

\[
\frac{d[C_\text{=}]}{dt} = -k_{p1}[I_1][C_\text{=}] - k_{p2}[I_2][C_\text{=}] - k_{p3}[RS][C_\text{=}]
\]

\[
\frac{d[RSH]}{dt} = -k_{ct1}[I_1][RSH] - k_{ct2}[I_2][RSH] - k_{ct3}[C3][RSH] - k_{ct4}[C1'][RSH]
\]

\[
- k_{ct5}[C2'][RSH]
\]

\[
\frac{d[RS]}{dt} = -k_{p3}[RS][C_\text{=}] + k_{ct1}[I_1][RSH] + k_{ct2}[I_2][RSH] + k_{ct3}[C3][RSH]
\]

\[
+ k_{ct4}[C1'][RSH] + k_{ct5}[C2'][RSH] - 2k_{t1}[RS]^2 - k_{t2}[RS'][C3']
\]

\[
- k_{t7}[RS'][C1] - k_{t8}[RS'][C2]
\]

\[
\frac{d[C1']}{dt} = k_{p1}[I_1][C_\text{=}] - k_{ct4}[C1'][RSH] - 2k_{t4}[C1']^2 - k_{t6}[C1'][C2'] - k_{t7}[RS'][C1']
\]

\[
- k_{t9}[C1'][C3]
\]

\[
\frac{d[C2']}{dt} = k_{p2}[I_2][C_\text{=}] - k_{ct5}[C2'][RSH] - 2k_{t5}[C2']^2 - k_{t6}[C1'][C2'] - k_{t8}[RS'][C2']
\]

\[
- k_{t10}[C2'][C3']
\]

\[
\frac{d[C3']}{dt} = k_{p3}[RS][C_\text{=}] - k_{ct3}[C3'][RSH] - k_{t2}[RS'][C3'] - 2k_{t3}[C3']^2 - k_{t9}[C1'][C3']
\]

\[
- k_{t10}[C2'][C3']
\]

\[
\frac{d[I_1]}{dt} = R_i - k_{p1}[I_1][C_\text{=}] - k_{ct1}[I_1'][RSH]
\]

\[
\frac{d[I_2]}{dt} = R_i - k_{p2}[I_2][C_\text{=}] - k_{ct2}[I_2'][RSH]
\]

\[
\frac{d[I_1H]}{dt} = k_{ct1}[I_1'][RSH]
\]
\[
\frac{d[L_2H]}{dt} = k_{CR2}[L_2][RSH]
\]
\[
\frac{d[C1]}{dt} = k_{CT4}[C1][RSH]
\]
\[
\frac{d[C2]}{dt} = k_{CT5}[C2][RSH]
\]
\[
\frac{d[C3]}{dt} = k_{CT3}[C3][RSH]
\]
\[
\frac{d[RSRR]}{dt} = k_{t1}[RS]^2
\]
\[
\frac{d[RS - C3]}{dt} = k_{t2}[RS][C3]
\]
\[
\frac{d[C3 - C3]}{dt} = k_{t3}[C3]^2
\]
\[
\frac{d[C1 - C1]}{dt} = k_{t4}[C1]^2
\]
\[
\frac{d[C2 - C2]}{dt} = k_{t5}[C2]^2
\]
\[
\frac{d[C1 - C2]}{dt} = k_{t6}[C1][C2]
\]
\[
\frac{d[RS - C1]}{dt} = k_{t7}[RS][C1]
\]
\[
\frac{d[RS - C2]}{dt} = k_{t8}[RS][C2]
\]
\[
\frac{d[C1 - C3]}{dt} = k_{t9}[C1][C3]
\]
\[
\frac{d[C2 - C3]}{dt} = k_{t10}[C2][C3]
\]

in which:

\[ [C_\neq] = [R'CH=CH_2] \]

\[ [C_1'] = [I_2CH_2R'CH] \]
\[ [C1] = [I_1CH_2CH_2R'] \]
\[ [C2'] = [I_2CH_2R'C'H] \]
\[ [C2] = [I_2CH_2CH_2R'] \]
\[ [C3'] = [R'CHCH_2SR] \]
\[ [C3] = [R'CH_2CH_2SR] \]
\[ [RS-C3] = [RSC'R'HCH_2SR] \]
\[ [C3-C3] = [RSCH_2CHR'CHR'CH_2SR] \]
\[ [C1-C1] = [I_1CH_2CHR'CHR'CH_2I_1] \]
\[ [C1-C2] = [I_1CH_2CHR'CHR'CH_2I_2] \]
\[ [C2-C2] = [I_2CH_2CHR'CHR'CH_2I_2] \]
\[ [RS-C1] = [RSCHR'CH_2I_1] \]
\[ [RS-C2] = [RSCHR'CH_2I_2] \]
\[ [C3-C1] = [RSCH_2CHR'CHR'CH_2I_1] \]
\[ [C3-C2] = [RSCH_2CHR'CHR'CH_2I_2] \]
\[ [C4] = [I_1R'CHCH_2I_1] \]
\[ [C5] = [I_1R'CHCH_2I_2] \]
\[ [C6] = [I_2R'CHCH_2I_1] \]
\[ [C7] = [I_2R'CHCH_2I_2] \]
\[ [C8] = [I_2R'CHCH_2SR] \]
\[ [C9] = [I_2R'CHCH_2SR] \]
APPENDIX B: KINETICS OF PHOTOINITIATION

Photoinitiation is a process, in which radicals are generated by visible or ultraviolet light irradiation. One particular compound in the reaction system, i.e., the ‘photoinitiator’, undergoes excitation by absorption of a photon and decomposes subsequently into radicals \[^{103}\].

There are several advantages associated with photoinitiation in polymerization processes, e.g. polymerization can be confined to specific regions, and turned on and off by switching the light source on and off. Furthermore, a fast initiation can be obtained since the source of radicals can be controlled by the temperature and the light intensity. However, photoinitiation has one strong limitation: the penetration of the light energy through a sufficiently thick material is low. Hence, photopolymerizations are mainly only well-suited for surface and thin-layer applications, such as coatings.

In this appendix, the commonly used rate equation describing the photoinitiation process is derived, while discussing its inherent assumptions.

As explained by G. Odeon \[^{103}\], the (volumetric) photoinitiation rate \( R_i' \) (mol m\(^{-3}\) s\(^{-1}\)) can be calculated by:

\[
R_i' = \frac{d[I]}{dt} = 2 f I_a,
\]

in which \([I]\) is the initiator radical concentration at a time \(t\), \(f\) an efficiency factor accounting for side reactions involving the initiator fragments, and \(I_a\) the intensity of the absorbed light in moles of photons per unit of volume and time, i.e., a volumetric light intensity. The maximum value of \(f\) is 1, corresponding to the case in which all radicals produced by dissociation of the initiator molecules, initiate the reaction. In particular, for the radical thiol-ene reaction, \(f\) corresponds to the fraction of initiator radicals leading to chain transfer and propagation. The factor of 2 in Equation (1) is necessary to reflect that two radicals are obtained per molecule undergoing photolysis.

The volumetric intensity of the absorbed light \(I_a\), can be related to the intensity of the absorbed light on a layer at distance \(D\) in the reaction system (mol m\(^{-2}\) s\(^{-1}\)) \(I_a'\):

\[
I_a(D) = \frac{dI_a'}{dD},
\]

in which \(I_a'\) can be calculated using the Beer-Lambert law \[^{104}\]:

\[
I_a' = I_0 \left( 1 - e^{-\alpha[A]D} \right),
\]
in which \( I_0 \) is the incident light intensity at the outer surface (mol m\(^{-2}\) s\(^{-1}\)), \([A]\) is the molar concentration of light-absorbing photoinitiator A (mol m\(^{-3}\)), and \( \alpha \) is the absorption coefficient of A. The latter is a function of the wavelength of the incident light and the temperature, and its units are mol\(^{-1}\) m\(^2\). It should be noted that alternatively, the molar absorptivity \( \varepsilon \) can be used which is related to \( \alpha \) by:

\[
\alpha = \varepsilon \ln 10 = 2,303 \varepsilon.
\]

Hence, by combining Equation (2) and (3), and using the molar absorptivity, \( I_a \) follows from:

\[
I_a = \frac{d[I']}{dD} = 2,303 \varepsilon [A] I_0 e^{-2,303 \varepsilon [A] D} \tag{4}
\]

However, in general the light intensity delivered by the light source is expressed in J m\(^{-2}\) s\(^{-1}\) (\( I_0' \)), which can be accounted for by insertion of a conversion factor into Equation (4), i.e., \( N_A h\nu = N_A h c / \lambda \), the energy of a mole of light photons, in which \( h \) is the constant of Planck (J s\(^{-1}\)), \( c \) is the speed of light (m s\(^{-1}\)), \( \lambda \) is the wavelength of the incident light (m), and \( N_A \) (mol\(^{-1}\)) is the constant of Avogadro:

\[
I_a = \frac{d[I']}{dD} = 2,303 \varepsilon [A] I_0'e^{-2,303 \varepsilon [A] D \lambda} \tag{5}
\]

Note that if 2,303 \( \varepsilon [A] D \) is sufficiently small, the exponential term in Equation (5) is approximately equal to 1, and \( I_a \) can assumed to be independent of the penetration depth leading to:

\[
I_a = \frac{2,303 \varepsilon [A] I_0' \lambda}{N_A h c} \tag{6}
\]

and finally:

\[
R_i = -\frac{d[I]}{dt} = \frac{2,303 f \varepsilon [A] I_0' \lambda}{N_A h c} \tag{7}
\]

The latter assumption is in particular valid for reaction systems using low initiator concentrations, and which are characterized by a small \( \varepsilon \) value, as can be expected in this work, at least to a first approximation.
APPENDIX C: EXTENDED INSTRUMENT DESCRIPTION

In this appendix, a more extended description is given of the working principle and the technical specifications of the analytical instruments used.

C.1 On-line FTIR spectrometer

*Working principle:*

An on-line fourier transform infrared (FTIR) instrument monitors absorption spectra in the infrared range, and is a powerful tool to record conversion profiles of specific functional groups. The spectra can be obtained in two different ways depending on the set-up used: (i) in transmission mode or (ii) based on the principle of attenuated total reflectance (ATR). The spectrometer available in the PCR-group and used in this project, is based on ATR.

By means of a ZnSe crystal, the incident IR-radiation beam is directed towards a single crystal silicon sensor, which is in contact with the sample at a single side. At the edges of this sensor, total reflection of the IR-radiation beam takes place, though it is attenuated at the sample side by which the functional groups present in the sample absorb IR-radiation at specific frequencies (Figure 90). Absorption only takes place when the frequency of the incident radiation matches that of the group or bond that vibrates, and if there is a change in the dipole moment during this vibration. Upon absorption of the photon the nature of the vibration can be different, e.g. stretching, scissoring, rocking, wagging and twisting.

*Figure 90:* Schematic view of the probe of the on-line FTIR. The path followed by an IR-radiation beam in the probe is marked red.[1]
The corresponding interferogram is recorded by means of a Michelson interferometer. In the Michelson interferometer, the incoming collimated beam is split into two halves and these are led to a fixed, respectively moving mirror assembly (see Figure 91). For each position of the moving mirror a difference in optical path length between the split beams is established. The light absorption of functional groups in the sample is monitored versus the position of the moving mirror, and thus an interferogram is generated. Computer software converts this interferogram by Fourier transformation into a regular absorption spectrum, which shows the light absorption at each wavelength of the spectral range.

![Figure 91: Schematic view of a Michelson interferometer](image)

**Specifications:**

The on-line FTIR spectrometer used in this Master thesis is a Mettler Toledo ReactIR 4000. It consist of four basic units: a system unit, which contains the interferometer, a secondary computer and the optical interface; a conduit; sampling technology and a computer. The laser is a Class I device in regards to laser emission from the instrument’s interface and provides a spectral range from 4800 cm\(^{-1}\) to 400 cm\(^{-1}\). The instrument’s probe has a jacket of hasteloy steel, and a pure gold seal separates the optical crystal from the sample, as can be seen in Figure 92. The sensor at the end of the probe is a sensitive 16 mm silicon component (R-6103). The instrument is purged continuously with dry nitrogen at a rate of 8 liter per minute. The light absorption is detected by a liquid nitrogen cooled mercury cadmium telluride detector (MCT), which is characterized by a high sensitivity. Finally, the recorded spectra are analyzed with the iC IR software (version 3.0).
C.2 300 MHz and 500 MHz H-NMR instrumentation

Working principle:

Nuclear magnetic resonance spectroscopy (NMR) is one of the main techniques to obtain physical, chemical and structural information about molecules, and is based on the phenomenon that a spinning charge generates a magnetic field, resulting in a magnetic moment. The NMR-spectrometer has to be tuned for a specific nucleus, which is the proton in the case of H-NMR.

When an external magnetic field is applied two spin states can exist \[^{106}\] , as the magnetic moment of the spinning charge can be aligned with or opposed to the external magnetic field. Between both states a small difference in energy exist, which increases for a stronger external magnetic field. For H-NMR spectroscopy, powerful magnets are necessary having fields strengths of 1 to 20 T. However, the energy difference is still very small and is therefore usually expressed as a frequency in units of MHz.

In the H-NMR spectrometer, the sample is irradiated with a radio frequent wave with an energy corresponding exactly to the gap between the two spin states of the proton (e.g. 300 MHz). The radio frequency energy is absorbed and this causes excitation of the protons to their higher spin state, in which the magnetic moment is opposed to the external magnetic field. However, not all the proton nuclei absorb at the same magnitude of the external magnetic field depending on their electronic environment allowing identification and quantification of functional groups. Hence,
dedicated electronic devices monitor the absorption of radio frequency energy for each value of the external magnetic field strength, and in that way allow to generate a full NMR-spectrum.

It should be noted that the electron(s) in the immediate surroundings of the proton concerned will also move in response to the external magnetic field, so as to generate a much smaller secondary field, which opposes the applied field and shields the proton nucleus. The external magnetic field thus has to be increased to compensate for this contribution.

Specifications:

In this Master thesis a $^1$H NMR 300 and 500 MHz are used. The $^1$H-NMR 300 MHz is a Bruker Avance 300 and it is a three-channel spectrometer, equipped with a 5 mm BBO probe with ATM. The instrument has a BACS-60 Sample changer for 60 samples, and is controlled by Topspin 2.1 and ICONNMR software. The set-up is shown in Figure 93.

![Figure 93: Photo image of the Bruker Avance 300 NMR.](image)

The $^1$H-NMR 500 MHz is a Bruker DRX500, which is an upgrade from the AM500 (1987) with reuse of the Oxford magnet. It is a three-channel spectrometer, equipped with 5 mm probes with Z-gradient (50 g/cm):

i. 5 mm TBI probe inverse type ($^1$H, $^{31}$P, BB)

ii. 5 mm DUAL probe direct type ($^1$H, $^{13}$C with high signal to noise ratio)

iii. 5 mm SEI probe inverse type ($^1$H, $^{13}$C)

The instrument has a NMRCASE Sample changer for 24 samples, and is controlled by Topspin 1.3 and ICONNMR software. Temperature control of the instrument is provided by a BVT-2000 Eurotherm controller and a BCU-05 precooler for stable temperature operation. The set-up is shown in Figure 94.
C.3 UV-lamps

Two different UV-lamp types are used in this Master thesis (see Chapter 3), the specifications of which are listed below. The first lamp type is a VL-100C lamp with a power of 100 Watt. A Grid tube emits UV-light with a wavelength of 254 nm. A photo image of this lamp is shown in Figure 95.

The second lamp type used is a 360 nm lamp. Contrary, to the other lamp type these lamps are used in an in-house PCR set up consisting of a box of inox steel with nine 360 nm lamps in a configuration as shown in Figure 96. Each lamp has a power of 9 Watt, and they are ordered in such a way that a maximum UV light intensity is achieved in the middle of the box. The box shields the operator from the harmful UV radiation.
C.4 Radiometer for intensity measurement

The UV light intensity is measured with a VLX365 radiometer (Figure 97) developed by Vilber Lourmat. It uses a quartz diffuser and a silicon photo-electric sensor for an accurate and direct measurement of the UV intensity, without converting it first into visible light. The VLX series are in principle designed to measure the UV intensity for a single wavelength, in this case 365 nm. However, the bandwidth ranges from 355 to 375 nm. The selection of the small wavelength range is accomplished by an interference filter. Intensities up to 200 mW cm\(^{-2}\) can be measured with an accuracy of approximately 5 %.

C.5 Thermometer

The temperature during reaction or in open air is measured with a digital VWR thermometer (EU 620-0919). By means of a small sensor connected to a flexible cable (see Figure 98), it is able to
monitor both ambient temperature as well as sample liquid temperatures. Temperatures between -50°C and 70°C can be measured.

![Photo image of the digital VWR thermometer](image)

**Figure 98: Photo image of the digital VWR thermometer**

### C.6 Gas chromatography GC

**Working principle:**

Gas chromatography (GC) is a chemical analysis technique to separate volatile components in a complex mixture. Samples are injected in a column with a microsyringe, in which separation takes place based on their interaction with a stationary phase, i.e., adsorption. Chemical compounds which interact strongly with the stationary phase will elute at higher retention times than components with only a small affinity for the stationary phase in the column. A simplified set-up of a gas chromatograph is shown in Figure 99.

The mobile phase is a carrier gas, which moves the sample components through the column. Mostly, helium is used as the carrier gas, since it is non-flammable, compatible with most detectors, and provides a good separation for a large range of flow rates. However, the best separation is obtained with hydrogen as the mobile phase.

There are two types of columns used in gas chromatography: packed columns and capillary columns. The former are glass or stainless steel tubes filled with a packing of inert, solid support material which is coated with a liquid or solid stationary phase. Capillary columns have a diameter that is ten times smaller than that of packed columns, and are much longer and often wound into coils increasing the flexibility of this approach. The inner walls of the columns are coated with active material to stimulate absorption. The choice of the stationary phase is very important with regard to the separation efficiency. As rule of thumb it can be stated that the polarity of the stationary phase should be similar to that of the sample analyzed. Furthermore, the column is placed in an oven, which is temperature controlled. Note that, if a temperature program for the oven is applied, there is a second driving force for the separation of the chemicals, i.e., their difference in volatility.
Finally, a detector monitors the time at which each component elutes and the amount of that component. The electrical signal of this detector is converted to a chromatogram by computer software. Flame ionization detectors (FID) and thermal conductivity detectors (TCD) are the most commonly used, and are briefly described below.

A flame ionization detector is a destructive detector that uses an air-hydrogen flame to produce ions. As components elute from the column of the GC, they are injected into the flame, burned and thus generating ions which are then collected on a collector plate. A very sensitive ammeter detects these ions and generates an electrical current, which is the signal output of the detector. A sensitivity of $10^{-13} \text{ g s}^{-1}$ is achieved for hydrocarbons with a dynamic range of $10^8$. The signal of the detector is mass dependent, as more ions are generated when the component consists of a greater number of carbon atoms. Components that cannot be burned, however, will not be detected. Hence, H$_2$O, CO$_2$, SO$_x$ and NO$_x$ will not give rise to any output signal.

A thermal conductivity detector (TCD), on the other hand, is a non-destructive detector which is less sensitive than a FID ($10^{-8} \text{ g s}^{-1}$) and is characterized by a smaller dynamic range ($10^5$). However, the aforementioned gases which cannot be detected by FID, will generate a proper output signal with TCD. Via a heated filament the thermal conductivity of the vapor that elutes from the column is compared with that of a reference gas, and via a Wheatstone bridge circuit an output signal is obtained. After all, the thermal conductivity of the column effluent (when an analyte elutes) is lower than that of the reference gas, which decreases the heat transfer of the filament to its surroundings and thus increases the filament’s temperature. This temperature change results in a change of resistance of the filament, which is monitored with the Wheatstone bridge circuit. Note that the output signal of the TCD is concentration dependent.

Fig. 99: Schematic set-up of a gas chromatograph \cite{107}

Specifications:

In this Master thesis, a Hewlett Packard (Agilent) 5890 gas chromatograph is used equipped with a 7673 autosampler, a capillary split/splitless injector, capillary column and an FID detector. This GC is controlled by one computer with HPIB connection and Chemstation B.03.02 software.
The carrier gas is hydrogen provided by a Parker-Balston hydrogen generator. The 7673 autosampler injects 1 µL solution with a 10 µL microsyringe through a rubber septum into a flash vaporizer glass liner at the head of the column. To avoid contamination of previous samples, the autosampler automatically rinses the syringe three times with methanol, three times with dichloromethane and three times with the current sample between every two injections. As the for the capillary column a low sample amount is sufficient, a split injection with a ratio of 1:50 is applied in such way that only a small part of the injected volume is mixed with the carrier gas and enters the column. The column is a XTI-5 column purchased from Restek. It has a length of 30 m and an internal diameter of 0.25 mm. The stationary phase is a 5 % diphenyl 95 % dimethyl polysiloxane, which mainly interacts with non polar compounds. The pressure in the column is set at 0.965 bar and sample flows through it at 1.4 ml min\(^{-1}\). The temperature program of the oven, in which the column is placed, starts at 50° C for three minutes, followed by a fast temperature gradient to 315° C at a rate of 20° C min\(^{-1}\). The eluted components are ionized and detected by a FID. Note that the temperature of the detector block should be higher than the highest column temperature to prevent condensation effects.

### C.7 GC/MS

**Working principle:**

Gas chromatography-mass spectroscopy (GC/MS) is a so-called hyphenated analytical technique. It combines in one single method the ability to separate the components by gas chromatography with the individual characterization of each chemical compound by mass spectroscopy. Both qualitative and quantitative analysis of a complex mixture is thus possible.

The instrument consists of two major building blocks: the gas chromatograph, which is discussed in paragraph A.6, followed by the mass spectrometer. As the components in the sample have different retention times, they can be analyzed separately by mass spectroscopy after they elute from the GC’s column. A schematic drawing of an electron ionization source is shown in Figure 100. The components first enter an electron ionization (EI) source, where electrons are produced by heating a wire filament (thermionic emission). The filament is made of tungsten or rhenium, fabricated as a wire, a coil, or sometimes a ribbon. The generated electrons are accelerated to 70 eV in the region between the filament and the entrance to the ion source block. Next, attraction to a trap electrode results in the formation of an electron beam. The sample molecules are introduced to the ion source in a direction perpendicular to the electron beam, and become ionized and fragmented depending on the electron energy. Low energy electrons will not cause fragmentation and will therefore lead to molecular ions. At around an electron energy of 70 eV, the strongest possible ionization is achieved, as the de Broglie wavelength of the electrons matches the typical bond length in organic molecules, which maximizes the energy transfer. The
mass of the fragment ion divided by its charge, is called the mass to charge ratio (m/z). However, since most fragments have a single positive charge, m/z usually represents the molar mass of the fragment. Finally, a repeller electrode guides the positively charged fragments to the entrance slit of the quadrupole detector to determine their individual mass.

![Figure 100: Schematic representation of an electron ionization source][108]

A quadrupole detector consists of four parallel metal rods, to which an oscillating electric field is applied. Ions travel down the quadrupole between the rods towards the electron multiplier detector. Only fragments with a certain m/z ratio will go through the entrance slit of the electron multiplier detector, whereas other ions have unstable trajectories and collide with the rods. By varying the electric field of the quadrupoles, a range of m/z ratios is scanned. This occurs many times per second. The mass spectrum thus obtained can be used as a fingerprint for the analyzed compound.

**Specifications:**

In this Master thesis, a Hewlett-Packard GCD-Plus GC/MS (G1800B) is used, which is based on a HP 5890 Series II GC with a 5971 Mass Spectrometer Detector. The GC’s have electronic pressure control and split/splitless injectors. The MSD’s are equipped with a heated ion source, a heated transfer line and a Single Quadrupole Mass Analyzer, furthermore Single Ion Monitoring (SIM) is possible.

Using a split ratio of 1:120, samples were injected on the GC/MS with the 5971 MSD, which scans a mass range from 10 to 450 amu. A Total Ion Chromatogram (TIC) is thus generated. The GC column is an Agilent DB-5ms column purchased from J&W Scientific. It is a non-polar column with a length of 30 m and an internal diameter of 0,25 mm. The stationary phase is a Phenyl Arylene polymer, which is virtually equivalent to the 5 % -Phenyl-95 % methylpolysiloxane. The flow through the column is 0,7 mL min\(^{-1}\) and helium is used as a carrier gas. The column is placed in an oven, which is temperature controlled: the temperature starts for 3 min at 70° C, then increases to 315° C at a rate of 17,5° C min\(^{-1}\), and remains at 315° C for
another 3 min. As is the case for the GC (see paragraph A.6), separation is based on two distinct driving forces: interaction with the stationary phase and difference in volatility.

**C.8 GC X GC**

*Working principle:*

Comprehensive gas chromatography (GC×GC) is an advanced technique to characterize the detailed chemical composition of samples, both qualitatively and quantitatively. GC×GC differs from two-dimensional GC, as not only a few fractions of the eluent from the first column but the entire sample is separated on two different columns. Compared to one-dimensional GC (see C.6, C.7), GC×GC offers an improved resolution and enhancement of the signal-to-noise ratio, without loss of time.

The standard GC×GC set-up is shown in Figure 101. Two different separation columns are used, based on two statistically independent separation mechanisms. The first column contains a non-polar stationary phase and hence, separation in this column is based on volatility differences between the sample components. The second column is much shorter and narrower and separates the compounds based on their interaction with a (medium) polar stationary phase.

*Figure 101:* Schematic overview of the GC×GC-FID/TOF-MS setup (1: split/splitless injector, 2: 1st dimension apolar column, 3: 2nd dimension polar column, 4: manual 4-port 2-way valve, 5: solenoid valves, 6: two jet cryogenic CO2 modulator, 7: protective helium flow) [109]

Between the two columns an interface, i.e., a cryogenic modulator, is present. Its main role is to trap adjacent fractions of the analyte eluting from the first-dimension column by cryogenic cooling, and heating-up these cold spots rapidly to release them as refocused analyte pulses into
the second-dimension column. To prevent leakage of the first column material, two jets are used that each by turn collect the first-dimension eluent. The second-dimension separation must be completed before the next fraction is injected to avoid wrap-around, the phenomenon that second-dimension peaks show up in a later modulation than in which they were injected. This explains the shorter and narrower second-dimension column compared to the first one.

In order to maintain the separation obtained in the first-dimension column, the narrow fractions trapped by the modulator and released in the second column, should be no wider than one quarter of the peak width in the first dimension. Hence, second-dimension separations should be very fast, in the order of 2 to 8 seconds. An illustration of the visualization principle of the GCXGC output is shown in Figure 102. Detailed qualitative analysis can be performed using the time of flight-mass spectrometer (TOF-MS) and for quantification an FID is used.

![Figure 102: Visualization of GC×GC output](image)

**Specifications:**

The set-up (see Figure 103) was built from a Thermo Scientific TRACE GC×GC, obtained from Interscience Belgium and fine-tuned at the LCT. It contains a split/splitless injector and a cold on-column injector. The specifications for both GCXGC/FID and GCXGC/TOF-MS are summarized in Table 8. Thermo Scientific’s Xcalibur software was used to acquire the data obtained with TOF-MS and to perform detailed peak identification by comparison of the mass spectra with the NIST database. HyperChrom and GCIImage were used to process the data obtained with the Thermo Scientific’s Xcalibur software, and conduct peak integrations.
Table 8: GCXGC settings

<table>
<thead>
<tr>
<th>Detector</th>
<th>FID, 300°C</th>
<th>TOF-MS, 35-450 amu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection</td>
<td>0.2 µL, split flow 10 mL min⁻¹, 300 °C</td>
<td>0.2 µL, split flow 10 mL min⁻¹, 300 °C</td>
</tr>
<tr>
<td>Carrier gas</td>
<td>He, constant flow (2.1 mL min⁻¹)</td>
<td>He, constant flow (1.8 mL min⁻¹)</td>
</tr>
<tr>
<td>First column</td>
<td>MXT-1 (60 m × 0.25 mm × 0.25 µm)</td>
<td>MXT-1 (60 m × 0.25 mm × 0.25 µm)</td>
</tr>
<tr>
<td>Second column</td>
<td>BPX-50 (2 m × 0.15 mm × 0.15 µm)</td>
<td>BPX-50 (2 m × 0.15 mm × 0.15 µm)</td>
</tr>
<tr>
<td>Oven temperature</td>
<td>40 → 300 °C (3 °C min⁻¹) (20 min hold)</td>
<td>40 → 300 °C (3 °C min⁻¹) (20 min hold)</td>
</tr>
<tr>
<td>Modulation period</td>
<td>5s</td>
<td>5s</td>
</tr>
</tbody>
</table>

**C.9 UV-VIS spectrometer**

**Working principle:**

A UV-VIS spectrometer measures the absorbance of chemical compounds in a sample mixture for a range of wavelengths, and can be used for both qualitative and quantitative analysis. The instrument available at the PCR-group and used in this Master thesis, is a double-beam spectrophotometer with two large-area photodiodes (see Figure 104). The radiation of a deuterium lamp for the UV region, and a halogen lamp for the VIS region of the spectrum is sent to the entrance slit of a monochromator, which consists of a filter and a subsequent concave grating that focuses light with a specific wavelength on the exit slit. After exiting from the monochromator, the beam is split into a sample and a reference beam, which are guided through the sample compartment. Two Peltier temperature-controlled photodiodes detect the transmitted radiation for both the reference and the actual sample. Note that the photometer section is protected against dust by a cover. Finally, concentrations of absorbing species can be determined based on the Beer-Lambert law, which states a proportional relation between the absorbance and the concentration of the absorbing compound.
Specifications:

The SPECORD 200 spectrophotometer (see Figure 105) was obtained from Analytik Jena AG. It has a wavelength range of 190-1100 nm and can make scans up to 6000 nm/min. WinASPECT software is used to process the acquired data.

C.10 Gel permeation chromatography (GPC)

Working principle:

GPC is a well-known technique to determine the molar mass distribution of polymers, as polymer molecules are separated based on their molecular size in solution. A GPC system consists of four major building blocks, i.e., a reciprocating piston pump, a two position injection valve, a packed column and a detector. The pump delivers a constant volumetric flow rate of eluent to the
column, whereas the injection valve permits the introduction of sample on the column without interrupting the eluent flow. The GPC columns are packed with cross-linked, insoluble beads with a rigid pore structure and controlled particle size, typically co-polymers of styrene and divinyl benzene. Large polymer molecules will not be able to permeate all of the pores and will thus have lower column residence times than small molecules which permeate deep into the porous matrix (see Figure 106). Note that the separation is purely a physical separation based on the hydrodynamic volume of the polymers in solution, as no interaction or binding with the column packing takes place. The concentration of the polymer in the eluens can be detected based on differences in refractive index (RI) and ultraviolet absorbance (UV), or via evaporative light scattering (ELS) or mass detector (EMD).

![Figure 106: Illustration of the separation principle of GPC](image1)

**Specifications:**

The GPC set-up (see Figure 107) used in this Master thesis is a PL GPC50plus obtained from PolymerLabs/Agilent with 5 detectors, however since polystyrene (PS) was only analyzed, the refractive index (RI) detector calibrated with PS standards is sufficient for the current analysis. The GPC is equipped with a PL AS RT autosampler and contains two Plgel 5 µm MIXED-D columns. Measurements were performed with THF as eluens.

![Figure 107: Photo image of the GPC set-up.](image2)
1. www.mt.com/ReactIR.


106. [http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm](http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm).


111. [www.bouman.chem.georgetown.edu](http://www.bouman.chem.georgetown.edu).

112. [http://followchemistry.files.wordpress.com](http://followchemistry.files.wordpress.com).