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FACULTEIT INDUSTRIËLE INGENIEURSWETENSCHAPPEN
master in de industriële wetenschappen: chemie

Masterproef

Investigation and optimization of surface modification protocols to attach sequence defined oligomers onto silica substrates

Promotor :
dr. Rita DE WAELE
dr. Joke VANDENBERGH

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Prof. dr. THOMAS JUNKERS

Lowie Maes

Scriptie ingediend tot het behalen van de graad van master in de industriële wetenschappen: chemie

Gezamenlijke opleiding Universiteit Hasselt en KU Leuven

KU LEUVEN | universiteit hasselt

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Foreword and acknowledgements

As a student in chemical engineering I have little experience in the research field of controlled radical polymerization. When I first read the description of the thesis my interest was immediately agitated. Controlled polymerization is a relatively new concept and has various possibilities to change the polymer landscape. Because of my future plans to become a PhD student, working in the Polymer Reaction Design (PRD) research group of prof. dr. Thomas Junkers was a great opportunity to get an idea of what is expected from a PhD student. That being said I would like to thank prof. dr. Thomas Junkers for the warm welcome into his research group. Although he had a lot of work, he closely followed my progress and guided me through the entire project.

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Furthermore, I would like to thank the entire PRD group for supporting and helping me when needed. Special thanks to Mrs. Evelien Beaten for giving me important polymers and helping me with software problems and Mr. Joachim Laun for guiding me through the world of silica particles. Also thanks to Mr. Pieter Verstappen for the maintenance of the recycling size exclusion chromatograph, Mr. Stephan Kobben and Mrs. Erika Mertens for giving useful tips and tricks, Mr. Gijs Ramakers for assisting me with the dangerous piranha treatment and Mr. Guy Reggers for all the TGA analysis and data.

Last but not least I would like to thank my family. They supported me not only through this project but also through my entire four-year education. They taught me to carry on in difficult times and to find a good balance between labor and relaxation. Special thanks to my girlfriend for standing by my side in stressful times. She also has a lot of work but is capable to make some time for us which gives me a huge energy boost.

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List of abbreviations

Abbreviation	**Explanation**
AIBN	Azobisisobutyronitrile or 2,2'-Azobis(2-methylpropionitrile)
APTES	3-aminopropyltriethoxysilane
ATRA	Atom Transfer Radical Addition
ATRP	Atom Transfer Radical Polymerization
CPD-TTC	2-cyano-2-propyl dodecyl trithiocarbonate
CPTMO	3-chloropropyltrimethoxysilane
CRP	Controlled Radical Polymerization
CuAAC	Copper(I)-catalyzed Azide-Alkyne Cycloaddition
DCM	Dichloromethane
DMAP	4-dimethylaminopyridine
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
DoPAT	2-(Dodecylthiocarbonothioylthio)propionic acid
EA	Ethyl acrylate
Ebib	2-bromoisobutyrate
EDC	1-ethyl-3-(3-dimethylaminopropyl) carbodiimide
EHA	2-ethylhexyl acrylate
ESI-MS	Electrospray Ionization Mass Spectrometry
FRP	Free Radical Polymerization
GPC	Gel Permeation Chromatography
H-NMR	Proton Nuclear Magnetic Resonance
HPLC	High-Performance Liquid Chromatography
IEG+	Iterative Exponential Growth Plus
LRP	Living Radical Polymerization
LTQ	Linear Trap Quadrupole
MA	Methyl acrylate
ME_6TREN	Tris[2-(dimethylamino)ethyl]amine
MeOH	Methanol
MHB	Multiple Hydrogen Bond
MRFA	L-methionyl-arginyl-phenylalanyl-alanine acetate
nBuA	n-butyl acrylate
NHS	N-hydroxysuccinimide
NMP	Nitroxide-Mediated Polymerization
photo-CMP	photo-induced Copper-Mediated Polymerization

PMDETA	N,N,N',N",N"-pentamethyldiethyltriamine
PnBuA	Poly-n-butyl acrylate
PRE	Persistent Radical Effect
RAFT	Reversible Addition/Fragmentation Chain Transfer polymerization
RDRP	Reversible Deactivation Radical Polymerization
rec-SEC	recycling Size Exclusion Chromatography
RF	Radio Frequency
SD	Sequence Defined
SFRP	Stable Free Radical Polymerization
S-lens	Soft lens
SPE	Solid Phase Extraction
SUMI	Single Unit Monomer Insertion
TEMPO	2,2,6,6-tetramethylpiperidine-1-oxyl
TESPPA	N-(3-(triethoxysilyl)propyl)propiolamide
TGA	Thermogravimetric Analysis
THF	Tetrahydrofuran

Abstract

Sequence defined (SD) oligomers are synthesized by single unit monomer insertion controlled radical polymerization (SUMI-CRP) and elaborate purification which is holding back the development. Multiple hydrogen bond (MHB) SD oligomers are similar to biopolymers since they recognize their complementary part. This ability can be exploited by covalently grafting these oligomers onto silica substrates and therefore simplify the purification. For a proof of principle study grafting of SD oligomers onto silica particles is investigated.

SD acrylate trimers are obtained by RAFT or photo-CMP polymerization. The statistical mixtures are purified by column- or size exclusion chromatography. Piranha treatment proved to be unnecessary to obtain sufficient grafting densities (0.331 CPTMO groups/nm²). SD oligomers and functionalized silica particles are linked with EDC/NHS coupling or copper azide-alkyne click (CuAAC) chemistry and characterized with TGA.

The results show that synthesizing SD oligomers with the DoPAT RAFT agent is not recommended since the acid groups stick to chromatographic columns, deteriorating purification. More promising is using CPD-TTC RAFT agent, followed by trithiocarbonate modification and attachment of the alkyne SD oligomers with CuAAC onto azide-silica (0.082 oligomer groups/nm²). Also, SD oligomers synthesized by photo-CMP is successful (17.4% yield of MA-EA-EHA-Ebib). The bromides are modified into azides and grafted-to alkyne-silica (0.177 oligomer groups/nm²). As outlook, MHB SD oligomers can be investigated.

Samenvatting

Sequence defined (SD) oligomeren worden gesynthetiseerd via *single unit monomer insertion* (SUMI) gecontroleerde radicalaire polymerisatie en nauwgezette purificatie die de ontwikkeling tegenhoudt. *Multiple hydrogen bond* (MHB) SD oligomeren zijn gelijkend op biopolymeren omdat ze hun complementaire deel herkennen. Deze eigenschap kan worden uitgebuit door deze covalent te binden op silica substraten waardoor de zuivering eenvoudiger wordt. Als voorstudie wordt de *grafting* van SD oligomeren op silica partikels onderzocht.

SD-acrylaat trimeren worden gesynthetiseerd via RAFT of foto-CMP-technieken. De statistische mengsels worden gezuiverd met kolom- of *size exclusion* chromatografie. Piranha behandeling blijkt overbodig om een voldoende *surface grafting density* te realiseren (0,331 CPTMO-groepen/nm²). SD oligomeren en partikels worden aan elkaar gekoppeld via EDC/NHS-koppeling of koper azide-alkyn klikchemie (CuAAC).

De resultaten tonen aan dat het synthetiseren van SD oligomeren met DoPAT niet aangeraden is omdat de zure groepen 'kleven' op de kolom waardoor de zuivering moeilijk wordt. Een meer belovende techniek is gebruik te maken van het CPD-TTC RAFT *agent* gevolgd door een alkyn modificatie en een bevestiging aan azide-silica via CuAAC (0,082 oligomeer groepen/nm²). Het maken van SD oligomeren via foto-CMP is ook succesvol (17% opbrengst van het MA-EA-EHA-Ebib oligomeer). De bromiden worden omgevormd naar azides en bevestigd aan alkyn-silica (0,177 oligomeer groepen/nm²). In verdere experimenten kunnen MHB SD oligomeren onderzocht worden.

1 Introduction

1.1 Radical polymerization techniques

Polymerization reactions are well known to the industry and have been optimized into the smallest detail. The used polymerization technique depends on the structure of the desired product and the used monomers. One of the most employed techniques in the industry is radical polymerization. It is a kind of chain-growth polymerization that can be divided into two main subclasses: free radical polymerization (FRP) and reversible deactivation radical polymerization (RDRP). FRP is a commonly used method because of its simplicity and the wide range of monomers that can polymerized. Monomers polymerize freely with no control over the molecular weight or chain length. A variant of FRP is radical copolymerization in which multiple different monomers polymerize to form copolymers. The second technique is RDRP, also known as living radical polymerization (LRP) or controlled radical polymerization (CRP). This technique gives control over the polymerization reaction and therefore it is possible to synthesize a polymer with a specific molecular weight or chain length. An overview of all polymerization techniques is shown in Figure 1 (if a figure has no reference, it is either drawn by Edraw Max or ChemDraw Professional). [1]–[4]

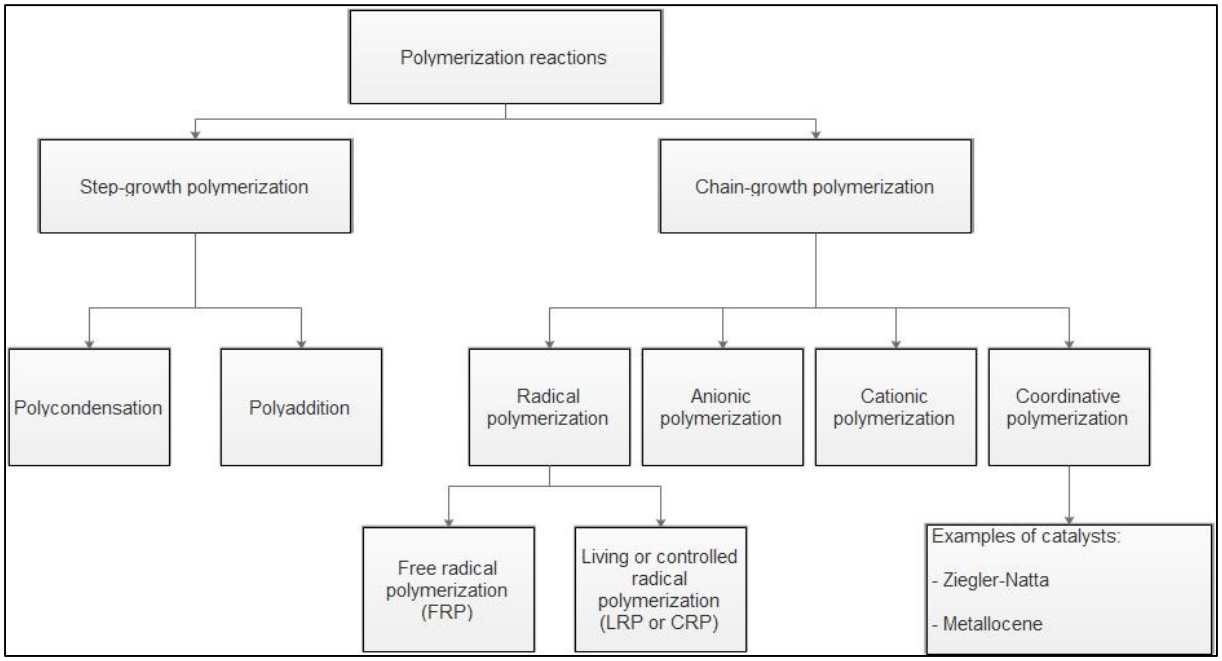

Figure 1: Overview of polymerization reactions

A radical polymerization reaction consists of 3 main steps. The first step is the initiation in which an initiator is activated into radicals with heat or a light source. These initiator radicals will react with the monomers. An electron transfer takes place which results in monomer radicals. The next step is the propagation. The monomer radicals will react with other monomers to form a polymer. Finally, termination through bimolecular termination or transfer reactions will stop the polymer chains from growing. This mechanism is illustrated in Figure 2. The initiation is a slow step contrary to the propagation. Moreover, termination occurs randomly and can happen to any chain. [5], [6]

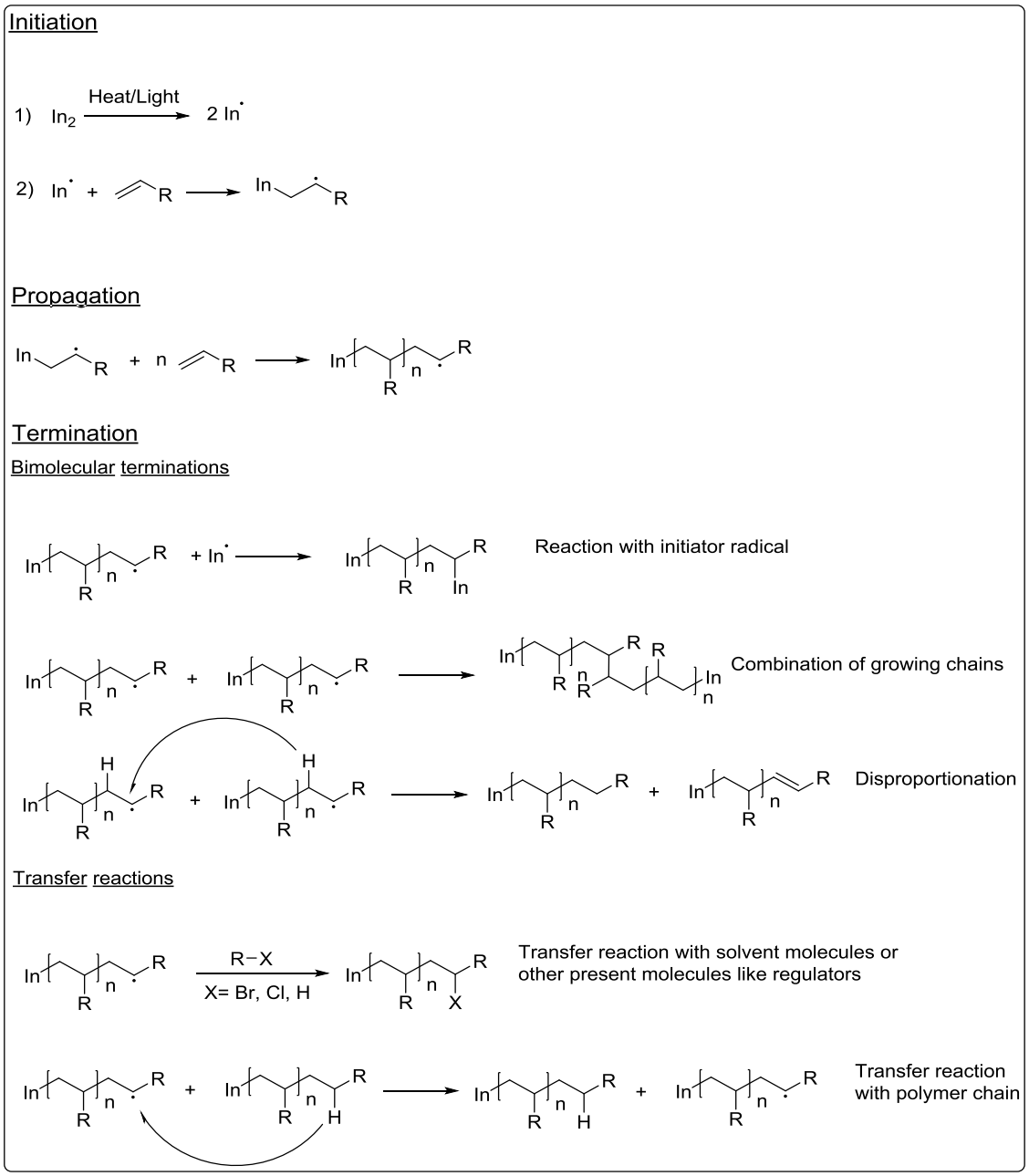

Figure 2: General mechanism of FRP

1.2 FRP versus CRP

FRP is a simple and well investigated technique and is widely employed in the chemical industry. A broad knowledge about both the thermodynamic and kinetic parameters already exists. FRP has a simple reaction mechanism, moderate reaction temperatures and can be used in different industrial processes such as emulsion and suspension polymerization. With FRP a high molecular weight is realized within a short reaction time and a wide range of different monomers can be polymerized. The biggest disadvantage of FRP is that there is no control over dispersity, molecular weight and composition because of a slow initiation, a fast non-simultaneously propagation and uncontrolled termination.[7], [8]

Controlled radical polymerization gives control over the reaction by limiting the amount of termination reactions and by obtaining an equilibrium between active chains and dormant chains. Active chains can react and polymerize while dormant chains react only when reactivated. The equilibrium between both can be achieved through two general methods. A first method is reversibly trapping radicals that can be reactivated. A second method involves a reversible transfer degenerative exchange process. A group X is exchanged to reactivate a dormant chain and deactivate an active chain. These two mechanisms are illustrated in Figure 3.[9], [10]

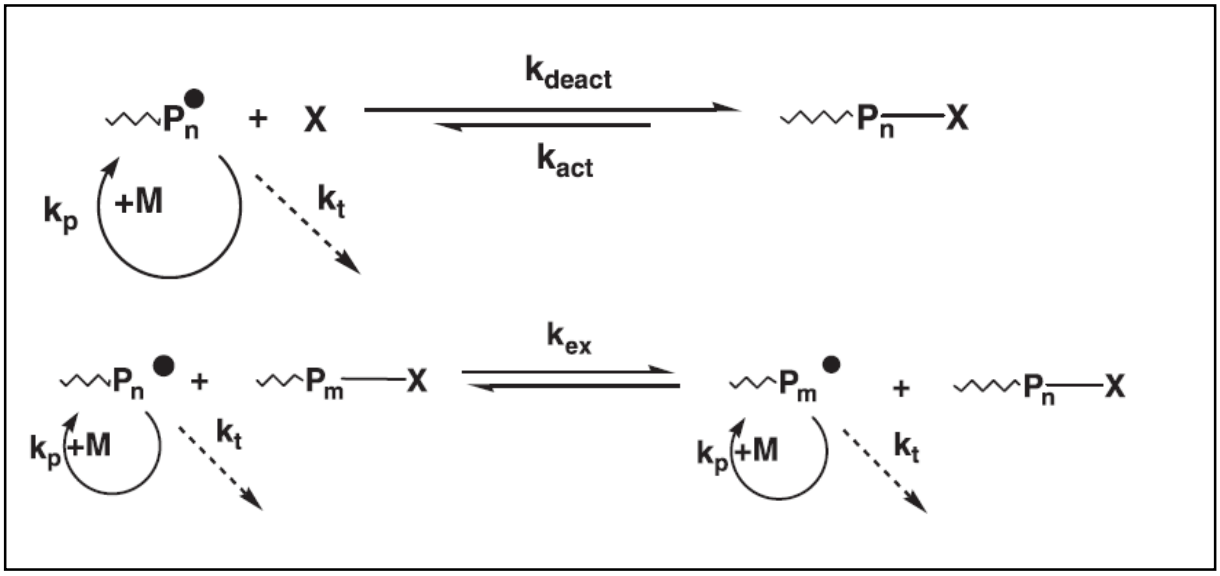

Figure 3: Reversibly trapping radicals (above) and reversible transfer degenerative exchange (below) to gain control over polymerization reactions [9]

In CRP a fast and spontaneous initiation and almost no termination gives control over the dispersity and molecular weight. Termination reactions are nearly nonexistent. Consequently, no dead chains will be formed. All polymer chains have specific end groups that can be reactivated (living). Therefore, it is possible to create block-copolymers with a well-defined sequence or to use specific monomers with reactive side groups which results in block polymers with a more complex structure. Disadvantages of CRP are more strict reaction conditions and a smaller range of possible monomers.[11], [12]

In some reactions the control over the polymerization is increased by the persistent radical effect (PRE). An active chain can be trapped by a stable radical X to form an inactive chain. This dormant chain can be reactivated spontaneously or with a catalyst. The active chain can propagate and convert back to a dormant chain or can be terminated. The stable radical X can only cross-link with an active chain but cannot terminate by itself which results in an accumulation of X. As the concentration of the stable radical increases the concentration of the active chains decreases (Le Chatelier). Because of this lower concentration of active chains there are less terminations and a steady state is achieved.[13], [14]

1.3 CRP techniques

1.3.1 Nitroxide-Mediated polymerization

Nitroxide-Mediated polymerization (NMP) is a kind of stable free radical polymerization (SFRP). The reaction mechanism is similar to FRP but control is achieved through PRE by choosing a specific molecule that will form a stable radical. The most used molecules are alkoxyamines for example 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO). This molecule was the first alkoxyamine used for NMP. Figure 4 shows the mechanism of NMP with TEMPO as a persistent radical. NMP is a simple technique that only requires a monomer, a stable radical and an initiator.[15]–[17]

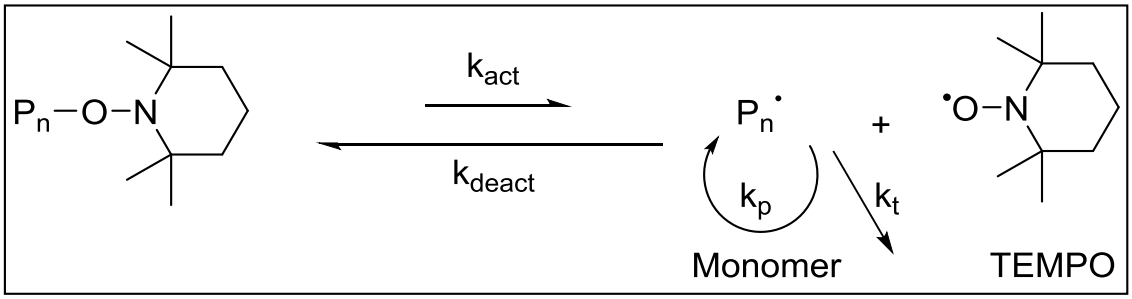

Figure 4: General mechanism of NMP with TEMPO as stable radical

1.3.2 Atom Transfer Radical polymerization

Atom Transfer Radical polymerization (ATRP) is a CRP technique based on Atom Transfer Radical Addition (ATRA). Figure 5 illustrates the general mechanism of ATRA. An initiator R-X consists of an alkyl group R and a halogen atom X. This initiator reacts with a metal catalyst, for example a complex between Cu(II) and a ligand. An electron transfer takes place with simultaneously extracting the halogen atom from the initiator. This results in a free radical and a transition metal complex M_t^{n+1}. The radical reacts with an alkene and forms a second radical. This second radical subsequently reacts with the transition metal complex and the X-group is retransferred which results in an alkylhalogenide. In ATRA an initiator is selected which produces a less stable second radical than the initial radical. Therefore, the reaction will be irreversible.[17]

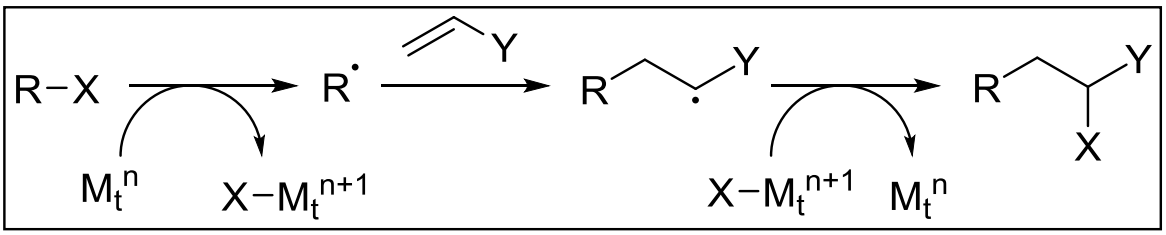

Figure 5: General mechanism of ATRA

The mechanism of ATRP is the same as the mechanism of ATRA but the reaction shown in Figure 5 is repeated n times. For ATRP a different initiator is used. The radical formed in the reaction between the initial radical and the metal catalyst is more stable. This implies that the halogen atom can be transferred back to form the radical again. This radical is capable of reacting with monomer units to form an oligomer or a polymer. The mechanism is displayed in Figure 6.[4], [17], [18]

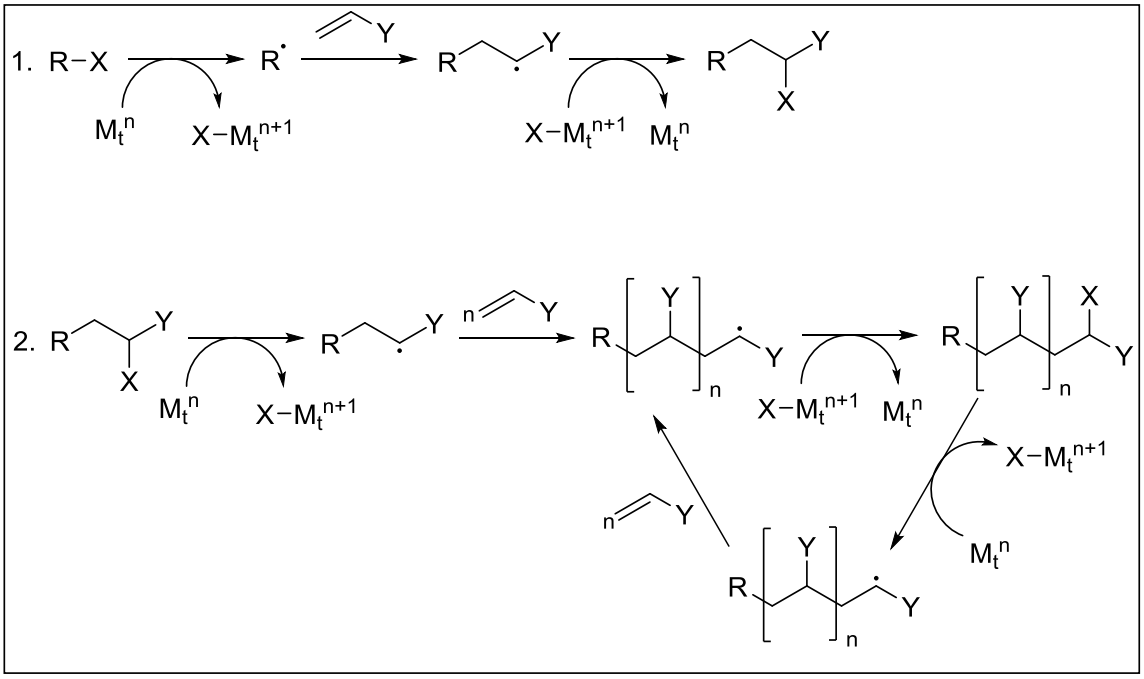

Figure 6: General mechanism of ATRP

1.3.3 Reversible Addition/Fragmentation Chain Transfer polymerization

In Reversible Addition/Fragmentation Chain Transfer polymerization (RAFT), control is achieved by creating an equilibrium between active and inactive (dormant) chains. The propagating chains are reversibly deactivated by degenerative chain transfer which results in an equilibrium between additions and fragmentations. This equilibrium is realized by choosing a specific RAFT agent which consists of two important groups. One of these groups is a good leaving group while the other group influence the rate of addition and fragmentation. Depending on which groups are used the agent has different solubility and reactivity (see Figure 7).

For RAFT polymerization a conventional initiator, a RAFT agent and a monomer is used. The mechanism is similar to FRP but with a pre-equilibrium, reinitiation and a main equilibrium to gain control over the reaction. First the conventional initiation occurs which results in a radical. Then a pre-equilibrium is achieved. The free radical leaving group will continue to react in the reinitiation step to form a propagating chain. After the reinitiation a main equilibrium between dormant and active chains is achieved. There is no limitation in termination reactions since all chains are propagating at the same time. Because of this there is control over the molecular weight distribution and chain lengths. This general mechanism with a trithiocarbonate as an example of a RAFT agent is displayed in Figure 8.[4], [10], [17], [19]–[21]

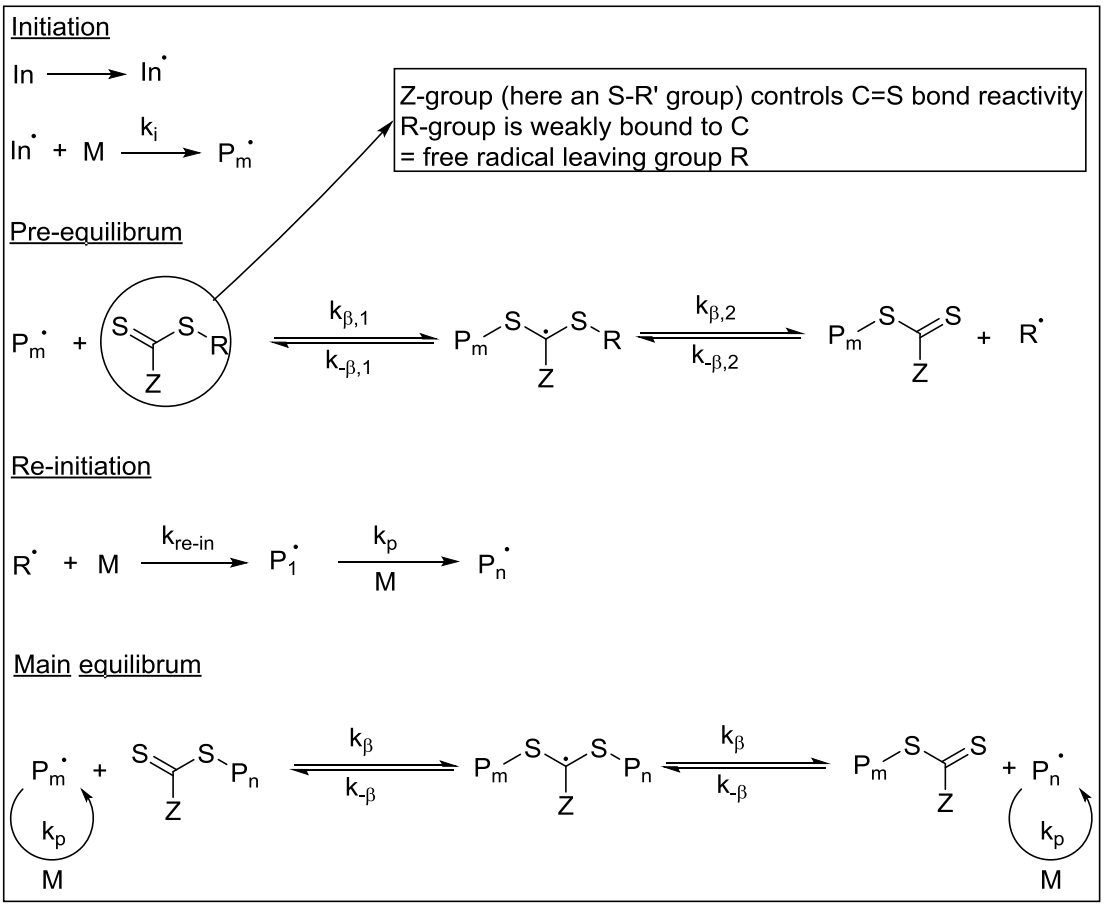

Figure 7: General mechanism of RAFT polymerization

1.4 Sequence Defined oligomers and Multiple Hydrogen Bond Sequence Defined oligomers

1.4.1 SUMI procedure to synthesize SD oligomers

With CRP techniques oligomers and polymers with specific dispersities and molecular weights can be created. It is even possible to produce an oligomer with a well-defined sequence. The synthesis of these sequence defined oligomers (SD oligomers) is illustrated in Figure 8. First a CRP method is performed which results in a statistical mixture of oligomers. The chain lengths can be shortened by using low amounts of monomer (one or two monomer equivalents) which results in a narrow molecular weight distribution. The mixture is consequently separated through recycling Size Exclusion Chromatography (rec-SEC). It is repeatedly cycled over columns that can separate molecules with different hydrodynamic volumes, until the desirable oligomer can be isolated. This process can be repeated until a specific Single Unit Monomer Insertion (SUMI) oligomer is produced. The purification through rec-SEC is intensive and time-consuming and is the Achilles' heel of the synthesis. The SUMI procedure is only possible on acrylate, acrylamide and styrene monomers.[22]–[24]

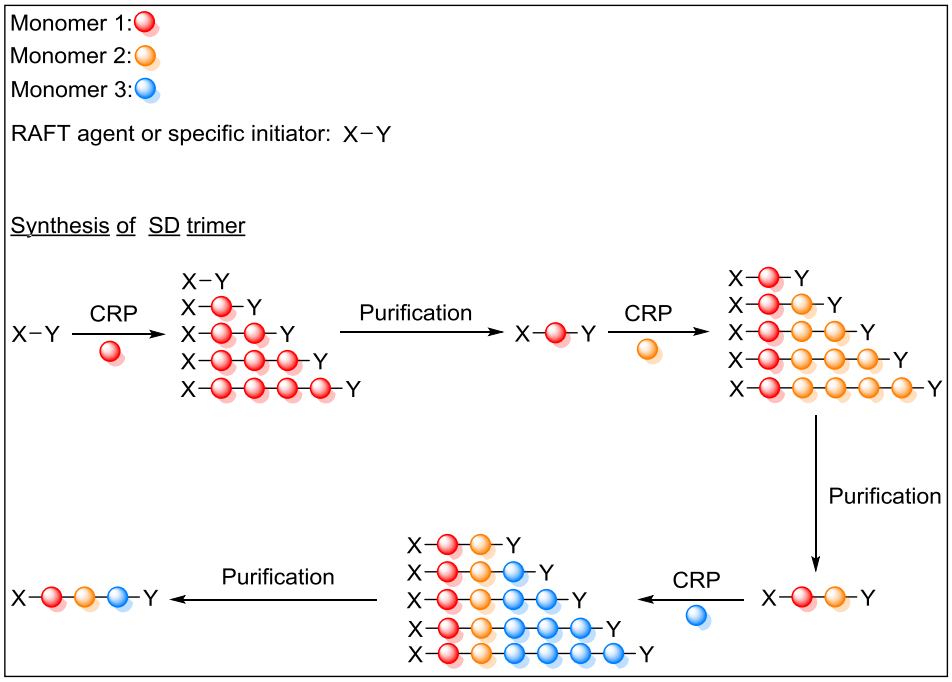

Figure 8: Synthesis of an SD trimer

SUMI-CRP is the method applied in the executed experiments but is not the only procedure to synthesize SD oligomers/polymers. SD oligomers/polymers can also be synthesized through chemoselective repeating cycles of amidification and copper-assisted alkyne-azide cycloaddition reactions. Another method is performing an iterative exponential growth plus side-chain functionalization (IEG+). With the appropriate sequence of reactions, it is possible to synthesize a large SD polymer. This last method is recently discovered. An overview of various possible synthesize routes is summarized in *Sequence-Controlled Polymers: Synthesis, Self-Assembly and Properties*.[25]–[27]

1.4.2 Difficult purification and possible solution

If acrylate monomers with nucleobases pairs as side chains are used instead of simple acrylates a Multiple Hydrogen Bond (MHB) SD oligomer can be synthesized. These oligomers are similar to biopolymers like proteins and enzymes. These biological materials are also perfectly defined and can execute tasks like selective transport or counterpart recognition. Because of this similarity the attention on the synthesis of SD oligomers and MHB SD oligomers has risen. Methods like ATRP, living ionic polymerization and RAFT are capable of synthesizing these SD oligomers and SD block copolymers. MHB SD oligomers and SD oligomers have many possibilities toward producing specific biochemical molecules but the time consuming and intensive purification is holding back the development. [22], [23], [28], [29]

A possible solution to the purification problem is attaching MHB SD oligomers onto solid substrates such as silica particles. These oligomers are capable of recognizing their counterpart in a solution and can be deployed as templates to purify mixtures of SD oligomers. When the template is added to a solution containing a mixture of oligomers produced by controlled polymerization, it binds with the specific oligomer that has to be isolated. When the template is removed from the mixture, for example by solid phase extraction (SPE), the desirable oligomer can be obtained by destroying the hydrogen bonds and separating the SD oligomer from the substrate. Because the synthesis routes for MHB SD oligomers still need to be optimized, the procedure is preferably executed with SD oligomers as a proof of principle study. These synthesis routes are optimized and the only difference with MHB SD oligomers are the functionalities of the side chains.

There are two commonly used grafting techniques to attach a polymer onto a solid substrate. In a *grafting from* technique initiator molecules are attached onto the substrate. Through addition of monomers onto these initiation points a chain can grow. When the polymers are prepared in a separate reaction and subsequently chemically or physically attached onto the substrate it is referred to as a *grafting to* procedure (see Figure 9). Attaching an SD oligomer onto a surface is always a *grafting to* procedure. If a *grafting from* procedure is executed, there is no chance to separate the desirable molecule because all different oligomers are attached to the surface.[30], [31]

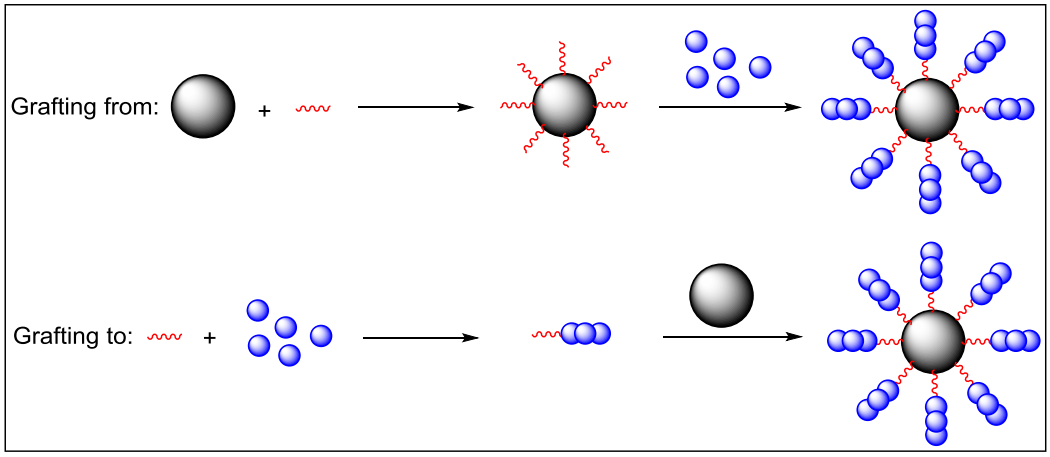

Figure 9: Grafting from and grafting to techniques

1.5 Attaching SD oligomers onto silica particles

1.5.1 Pre-treatment of silica particles

The synthesis and attaching of SD oligomers onto silica particles can be divided into four procedures. The first procedure is the pre-treatment of the silica particles. Silica particles consist of SiO_2 and can be porous, mesoporous or non-porous. The pristine particles are used in a broad range of applications such as color rubber, batteries, paint, fibers and more. On top of the SiO_2 core lies a layer of bound organic impurities. This top layer has an influence on the binding of other molecules and must be removed.[32]

A first technique that can be used to clean the surface is UV/Ozone treatment. The principle is displayed in Figure 10. UV light creates energy that is absorbed by oxygen. If the wavelength is between 184 and 189 nm oxygen will decompose into atomic oxygen which is a strong oxidizing agent. Another simultaneous reaction is the formation of ozone. This ozone decomposes into water and oxygen at a wavelength of 253 nm. The organic impurities on the surface also absorb radiation and react with the atomic oxygen. The result of this ozone treatment is a cleaned surface which can be hydroxylated, for example with NH_4OH, to create a surface with hydroxyl groups (OH-groups). After hydroxylation the surface can be silanized which will be discussed in the next paragraph.[32]–[35]

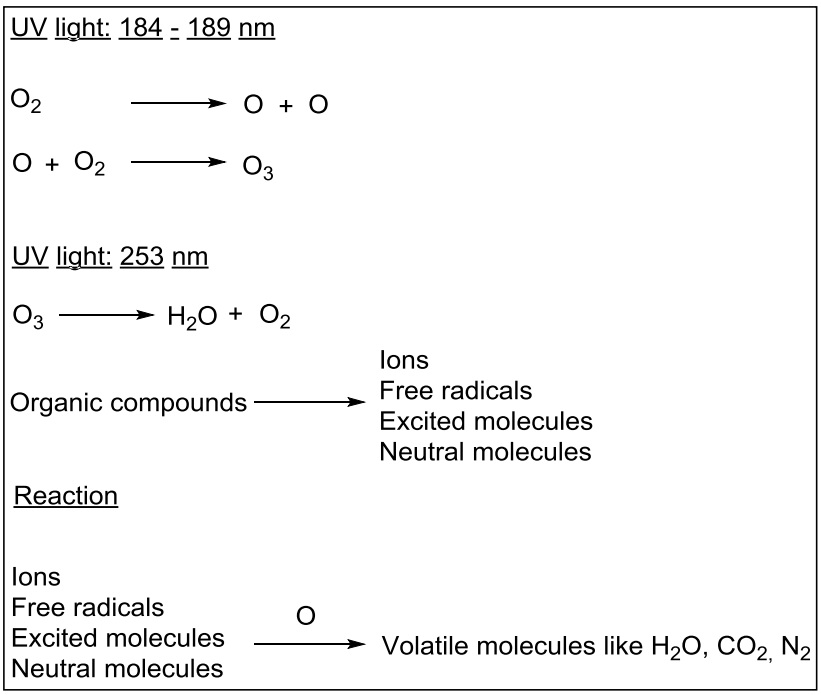

Figure 10: Reactions involved in UV/Ozone treatment

A second treatment that can be performed is piranha treatment. This is a mixture of sulfuric acid and hydrogen peroxide. When these two substances are mixed together a highly oxidizing agent is formed. This solution has the same cleaning effect as UV/Ozone treatment. After the cleaning a hydroxylation is executed. In Figure 11 the objective of the pre-treatment is illustrated.[36], [37]

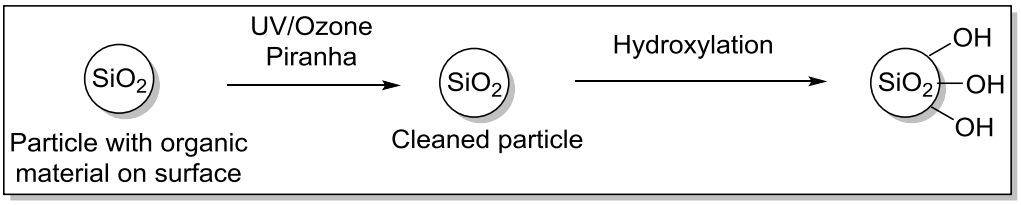

Figure 11: Objective of pre-treatment silica particles

1.5.2 Silanization of pre-treated particles

The procedure after pre-treatment is silanization of the cleaned and hydroxylated silica particles. This is the reaction between the OH-groups on the silica particles and a silane. The objective of this silanization is to convert the hydroxyl groups into another functional group that is capable of reacting with the polymer produced in the next procedure. Silanes with amino (NH_2), chloro (Cl) or alkyne end groups have the most potential to be used because the coupling reactions between these (modified) end groups and the SD oligomers are described in various articles. Examples of possible silanes are 3-aminopropyltriethoxysilane (APTES), silanes with a triple bond or 3-chloropropyltrimethoxysilane (CPTMO). CPTMO can be modified through azidation to obtain an azide functionalized silica particle. Figure 12 illustrates the objective of this procedure.[38]–[40]

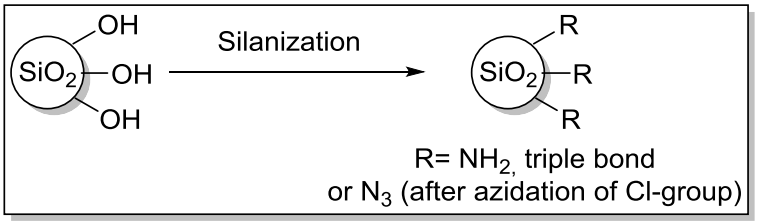

Figure 12: Objective of silanization procedure

1.5.3 Synthesis of SD oligomers

SD oligomer can be synthesized through either RAFT polymerization or photo-induced copper-mediated polymerization (photo-CMP). Photo-CMP is similar to ATRP but the reaction is stimulated with UV-light and copper(II)dibromide is added as a catalyst. In both reactions it is important to choose an initiator (photo-CMP) or chain transfer agent (RAFT) which is capable of reacting with the functionalized silica particles. This can be achieved by selecting an initiator or agent with a specific end group or through end group modification techniques. For RAFT polymerization a conventional initiator like Azobisisobutyronitrile (AIBN) is used. It is important to use a low amount of this initiator to avoid end group exchange of the RAFT agent with AIBN fragments. The result is an end mixture that contains a small fraction of oligomers with an initiator fragment instead of the specific RAFT R-end group.[40], [41]

Figure 13 illustrates two reaction procedures than can be executed to synthesize an SD oligomer. These possible techniques can be applied to monomers such as styrene derivatives, acrylates and acrylamides. Mostly AIBN is used as the initiator for RAFT polymerization because it is easy to use and has a short half-life (8 min in 100 °C). RAFT agents that could be used are 2-(Dodecylthiocarbonothioylthio) propionic acid (DoPAT) or 2-cyano-2-propyl dodecyl trithiocarbonate agent (CPD-TTC). DoPAT is a trithiocarbonate agent which contains an acid end group that can be coupled onto the silica particles. CPD-TTC is also a trithiocarbonate but with an isobutyrylnitrile group instead of an acid group. This transfer agent can be coupled onto functionalized silica particles after alkyne end group modification. Photo-CMP mainly uses alkyl halides as initiators. The halogen (X) of the initiator molecule can be transformed into another end group with a modification technique to achieve a group that can be coupled onto the functionalized silica particles.[22], [23], [40]–[44]

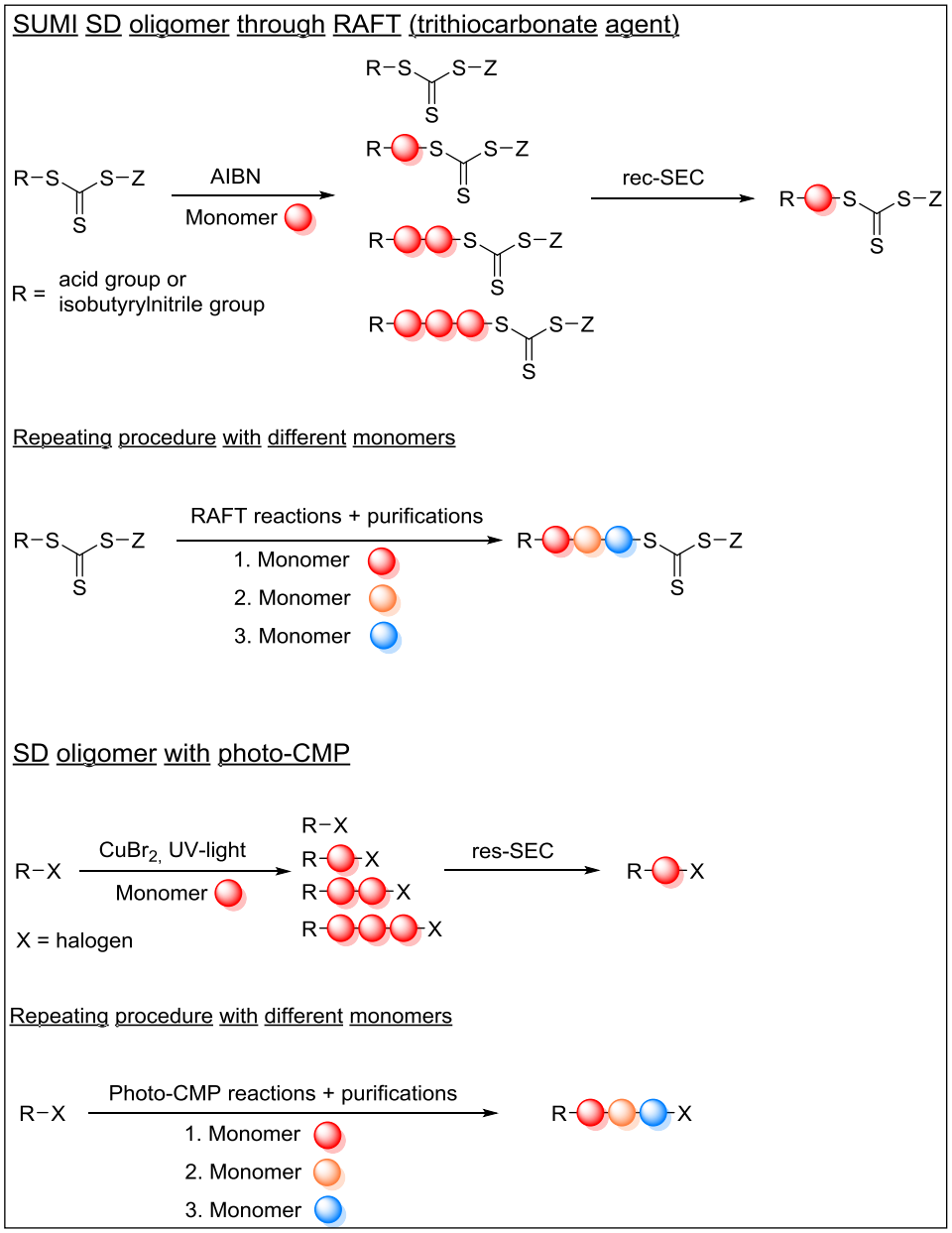

Figure 13: Synthesis of SD oligomers through RAFT polymerization and photo-CMP

1.5.4 Coupling SD oligomers onto silanized particles

The final procedure is to couple the SD oligomer onto the functionalized particles. Depending on which SD oligomer or silane was used in the previous steps, there are different coupling reactions that can be performed. A first example is a 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride and N-hydroxysuccinimide coupling (EDC/NHS coupling). This reaction is possible when the oligomer contains a carboxyl end group and the silica surface contains amino groups. The mechanism is illustrated in Figure 14.

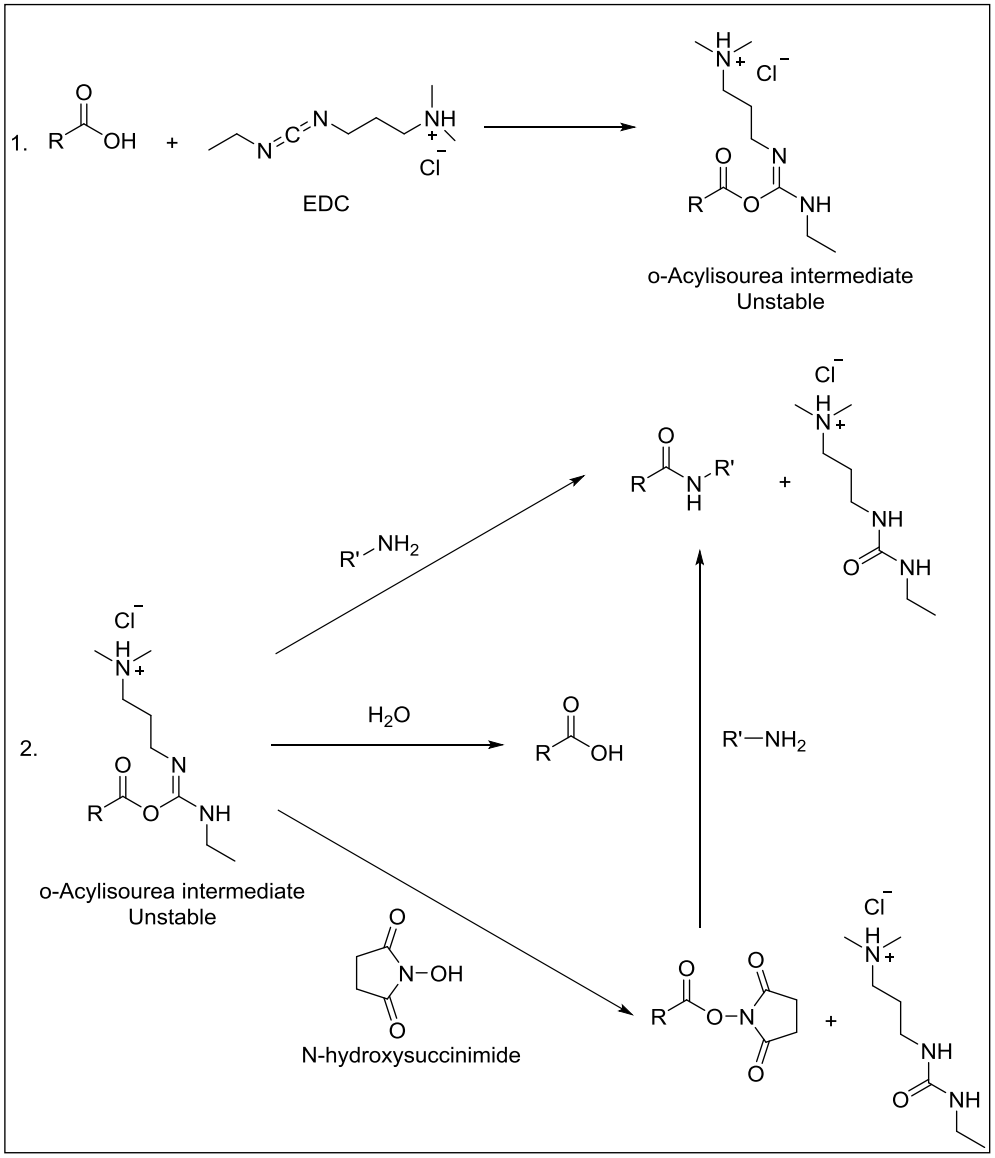

Figure 14: EDC/NHS coupling reaction

The carboxyl end group reacts with EDC to form an unstable intermediate which can react in three different ways. It can immediately react with a primary amine to form an amide bond and isourea by-product. If water is present, the ester function can hydrolyze. The last possibility is reaction of the carboxyl group with NHS to form a stable intermediate. This stable molecule can also react with a primary amine to form the amide bond.[45]–[47]

Another coupling reaction that can be performed is a Copper(I)-catalyzed Azide-Alkyne Cycloaddition click reaction (CuAAC click reaction). In order to put this reaction into effect the surface of the silica particles must consist of triple bonds. Also the end group of the SD oligomer needs to be an azide group. Figure 15 shows the mechanism of the CuAAC reaction. The copper catalyst forms a π-complex with the triple bond of the alkyne. The azide attacks this complex and eventually forms the final product through various reaction steps.[48], [49]

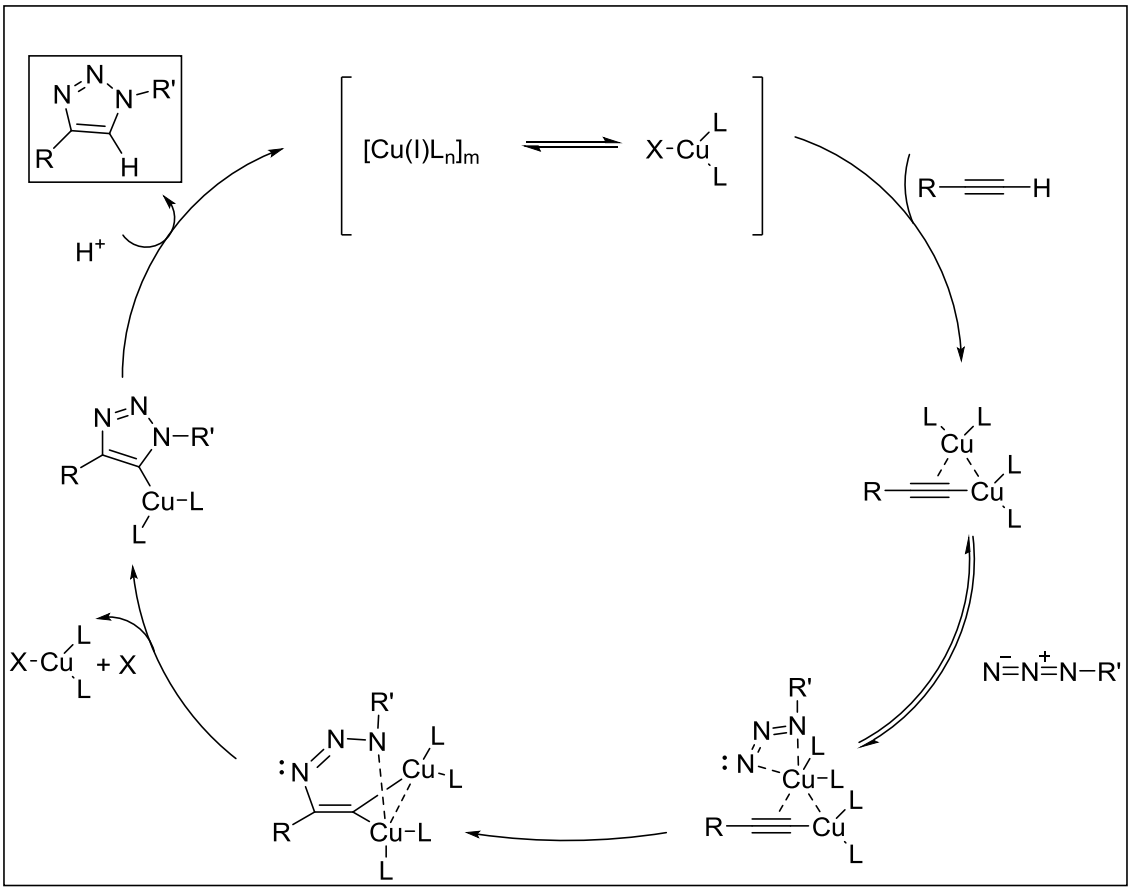

Figure 15: CuAAC reaction mechanism

1.6 Combined procedures

The previously described procedures are combined to attach the synthesized SD oligomers onto silica particles. All these combined procedures start with the piranha or UV/Ozone treatment on pristine silica particles. Three different pathways can be followed. A first pathway is functionalizing the particles with APTES to convert the hydroxyl surface groups into amino groups. The SD oligomer is synthesized through RAFT polymerization with DoPAT used as transfer agent. The particles and DoPAT SD oligomer are coupled with an EDC/NHS reaction.

A second pathway is synthesizing an SD oligomer through RAFT with CPD-TTC used as transfer agent. The dodecyl end group is modified through aminolysis and thiol-ene addition with propargyl acrylate to obtain an alkyne modified CPD-TTC SD oligomer. Silica particles are silanized with CPTMO and subsequently azidated which results in azide functionalized silica particles. Alkyne modified CPD-TTC SD oligomers414141 and azide functionalized particles are linked together with copper-click chemistry (CuAAC-click reaction).

A last pathway is functionalizing the particles with a silane, which consists of a triple bond as an end group such as N-(3-(triethoxysilyl)propyl)propiolamide (TESPPA). This silane can be synthesized through an EDC/NHS coupling between APTES and propiolic acid. The SD oligomer is synthesized through photo-CMP with a typical initiator such as ethyl 2-bromoisobutyrate (Ebib). The Br-group can be changed to an azide group with an end group modification technique. After this procedure the azide modified photo-CMP SD oligomer is coupled onto the alkyne functionalized silica particles through a CuAAC click reaction. These three combined procedures are displayed in Figure 16.[50]

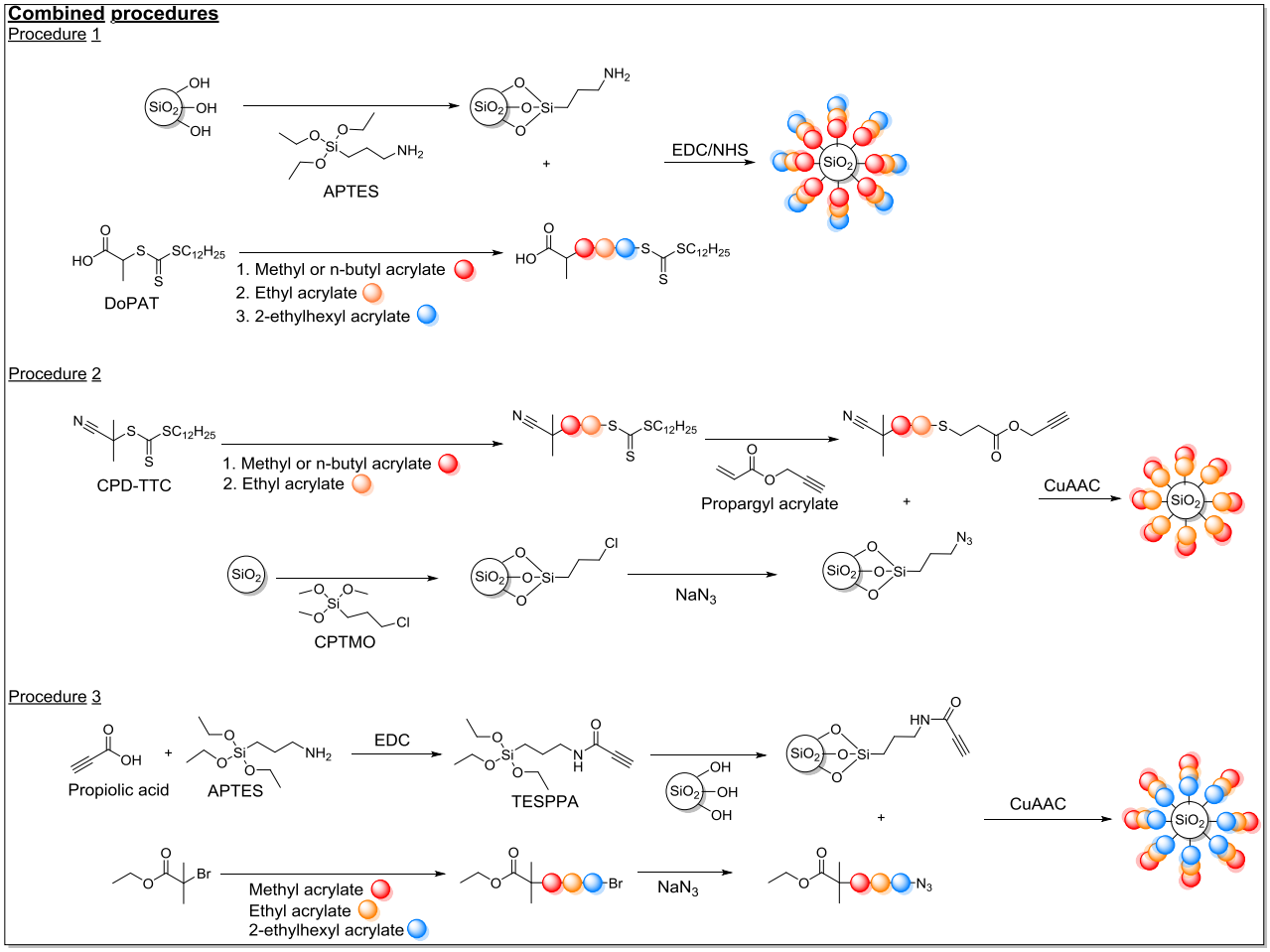

Figure 16: Combined procedures to synthesize and attach SD oligomers onto silica particles

As is illustrated in Figure 16 only SD oligomers are synthesized with CRP-techniques. Few research is done on MHB SD oligomers. Therefore, a first step is investigating the synthesis of SD oligomers with subsequently attachment onto functionalized silica particles using small monomers like methyl acrylate (MA) or ethyl acrylate (EA). If this procedure is optimized, the synthesis of MHB SD oligomers can be investigated. Finally, both investigations can be combined with the intension to simplify the difficult purification occurring when synthesizing SD oligomers.

2 Materials and experimental

2.1 Materials

For the executed experiments all solvents and the following products were used as received: 3-aminopropyltriethoxysilane (APTES, Sigma-Aldrich, 99%), 3-chloropropyltrimethoxysilane (CPTMO, Sigma-Aldrich, 97+%), 2-cyano-2-propyl dodecyltrithiocarbonate (CPD-TTC, Sigma-Aldrich, 97%), copper(II)bromide ($CuBr_2$, Sigma-Aldrich, 99%), 4-dimethylaminopyridine (DMAP, Acros, 99%), ethyl 2-bromoisobutyrate (Ebib, Sigma-Aldrich, 98%), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC, Acros, 98+%), hydrogen peroxide (H_2O_2, Acros, 35% solution water stabilized), sulfuric acid (H_2SO_4, Fisher Scientific, >95%), hexylamine (Sigma-Aldrich, 99%), sodium azide (NaN_3, Sigma-Aldrich, ≥99%), ammonium hydroxide (NH_4OH, Fisher Scientific, 25% solution), N-hydroxysuccinimide (Sigma-Aldrich, 98%), N,N,N',N'',N''-pentamethyldiethylenetriamine (PMDETA, Acros, 99%), propiolic acid (Tokyo Chemical Industry Co., >97%), pyridine (Acros, 99+%), amorphous non-porous silica nanoparticles (US Research Nanomaterials Inc., 1µm, 18m²/g), amorphous porous silica particles (Davisil Chromatic Silica, 70-200 µm, 550m²/g).

2-(Dodecylthiocarbonothioylthio) propionic acid (DoPAT)[1], propargyl acrylate[2], MA-EA-CPD-TTC RAFT agent[3] and tris[2-(dimethylamino)ethyl]amine (ME_6TREN)[4] were synthesized according to previously reported literature. Azobisisobutyronitrile (AIBN, Sigma-Aldrich, 98%) was recrystallized twice from ethanol prior to use. The monomers ethyl acrylate (EA, Acros, 99%), 2-ethylhexyl acrylate (EHA, Acros, 99%), methyl acrylate (MA, Acros, 99%) and n-butyl acrylate (nBuA, Acros, 99%) were deinhibited over a column of activated basic alumina, prior to use.

A ± 1 M HCl-solution was prepared by diluting 83,5 mL of a 35 Vol% HCl-solution with demineralized water to one liter. Copper(I) bromide (CuBr, Acros, 98%) was washed with acetic acid at 80 °C for 18 h to remove any soluble oxidized species before being filtered, washed with absolute ethanol, brought to pH 7, then washed with ethyl ether, and then vacuum dried (± 0.2 mbar).

[1] Ferguson C. J., Hughes R. J., Nguyen D., Pham B. T. T., Gilbert R. G., Serelis A. K., Such C. H. and Hawkett B. S., *Macromolecules* **2005**, *38 (6)*, 2191-2204.

[2] Lang A. S., Neubig A., Sommer M. and Thelakkat M., *Macromolecules*, 2010, 43 (17), pp 7001–7010

[3] Vandenbergh J., Reekmans G., Adriaensens P. and Junkers T., *Chem. Commun.*, 2013, 49, 10358

[4] Feng L., Hu J., Liu Z., Zhao F. and Liu G., *Polymer* **2007**, *48 (13)*, 3616-3623.

2.2 Characterization

Purification of products was performed either via silica column chromatography or on a recycling preparative HPLC LC-9210 NEXT system in the manual injection mode (3 mL) comprising a JAIGEL-1H and JAIGEL-2H column and a NEXT series UV and RI detector using chloroform ($CHCl_3$) as the eluent with a flow rate of 3.5 $mL \cdot min^{-1}$. ^1H-NMR spectra were recorded in deuterated chloroform ($CDCl_3$) with a Varian Inova 300 or 400 spectrometer at 300 or 400 MHz. An OMNICURE Series 1000 system was used as UV-light source. The OMNICURE system was equipped with a 100 W high pressure mercury vapor short arc lamp (320–500 nm) at an iris setting of 100%.

ESI-MS was performed using an LTQ Orbitrap Velos Pro spectrometer (ThermoFischer Scientific) equipped with an atmospheric pressure ionization source operating in the nebulizer assisted electro spray mode. The instrument was calibrated in the m/z range 220-2000 using a standard solution containing caffeine, MRFA and Ultramark 1621. A constant spray voltage of 5 kV was used and nitrogen at a dimensionless auxiliary gas flow-rate of 5 and a dimensionless sheath gas flow-rate of 10 were applied. The S-lens RF level, the gate lens voltage, the front lens voltage and the capillary temperature were set to 50%, -90V,-8.5V and 275°C respectively. A 250 µL aliquot of a polymer solution with concentration of 10 µg mL^{-1} was injected. A mixture of THF and methanol (THF:MeOH = 3:2), all HPLC grade, were used as solvent. TGA was executed using a HI-Res TGA 2950 Thermogravimetrix Analyzer (TA instruments). Samples were heated at a rate of 20 °C/min until 900 °C under a nitrogen atmosphere. A Centrifuge 5702 (Eppendorf) was used for separating particles.

2.3 Synthesis

2.3.1 Coupling DoPAT RAFT SD oligomer onto amino functionalized silica particles

Synthesis of DoPAT RAFT SD oligomer

Synthesis of nBuA-DoPAT RAFT agent (1) and MA-DoPAT RAFT agent (2). Two different SD oligomers were synthesized through RAFT polymerization as shown in Figure 17. For the first oligomer (a) 1 eq. of the monomer nBuA, 1 eq. of DoPAT RAFT agent, 0.05 eq. of AIBN, 2.6 mL of butyl acetate and a stirring bar were added into a glass vial (10 mL). For the second oligomer (b) 2 eq. of the monomer MA, 1 eq. of DoPAT RAFT agent, 0.05 eq. of AIBN, 3.7 mL of butyl acetate and a stirring bar were added into a glass vial (10 mL). Both mixtures were purged with nitrogen for 10 min. The vials were subsequently transferred into a glovebox and placed in a 100 °C copper heat-block and reacted for 20 min. After the reaction, the mixtures were transferred into aluminium pans to evaporate excess solvent and monomer. The desirable products were obtained via rec-SEC to yield 0.190 g (25%) of pure nBuA-DoPAT RAFT agent **(1)** and 0.117 g (7%) of pure MA-DoPAT RAFT agent **(2)**. Supporting information of this reaction and all following reactions can be found in Appendix A.

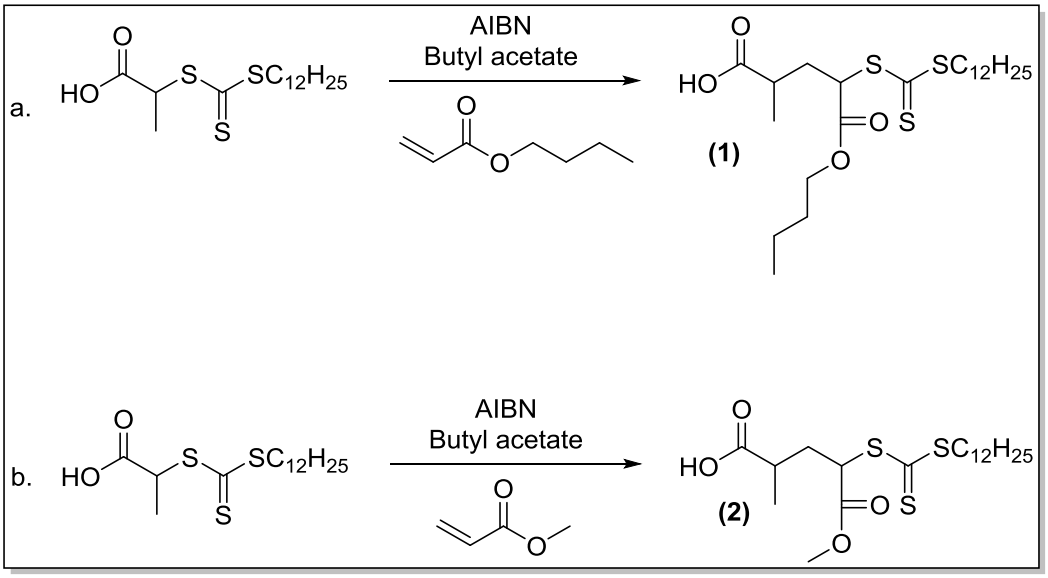

*Figure 17: Synthesis of nBuA-DoPAT RAFT agent (**1**) and MA-DoPAT RAFT agent (**2**)*

Synthesis of nBuA-EA-DoPAT RAFT agent (3). A second insertion on product **(1)** was performed with EA (Figure 18). For this reaction 1 eq. of the monomer EA, 1 eq. of nBuA-DoPAT RAFT agent, 0.05 eq. of AIBN, 1.4 mL of butyl acetate and a stirring bar were added into a glass vial (10 mL). The mixture was purged with nitrogen for 10 min and subsequently transferred into a glovebox. It was placed in a 100 °C copper heat-block and reacted for 10 min. After the reaction, the mixture was transferred into an aluminium pan to evaporate excess solvent and monomer. The desirable product was obtained via rec-SEC to yield 0.038 g (17%) of pure nBuA-EA-DoPAT RAFT agent **(3)** and 0.105 g of unreacted product **(1)**. Therefore, the procedure was repeated with 1 eq. of the unreacted nBuA-DoPAT RAFT agent, 1 eq. of the monomer EA, 0.05 eq. of AIBN and 0.1 mL of butyl acetate to obtain a final yield of 0.066 g (26%) of pure product **(3)**.

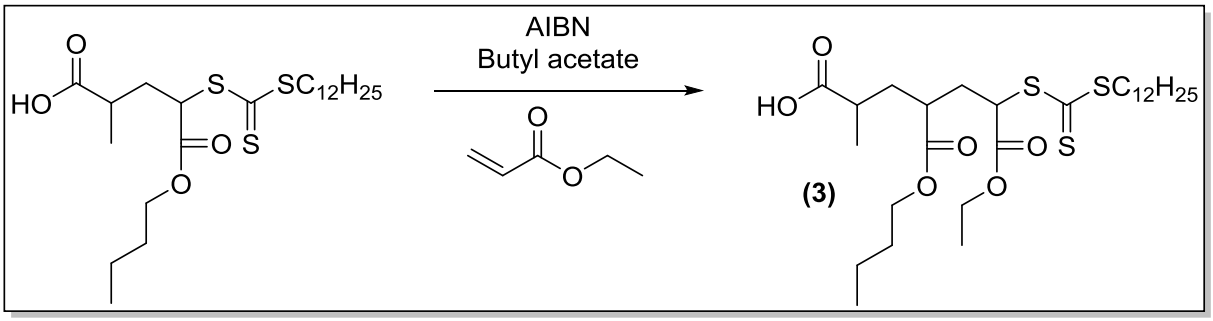

*Figure 18: Synthesis of nBuA-EA-DoPAT RAFT agent (**3**)*

Functionalization of the silica particles

Piranha treatment of silica particles. To remove impurities on the pristine silica particles a piranha treatment was executed. 2.5 g of silica particles (either small particles of 1µm, non-porous, 18m²/g or large particles of 70-200 µm, porous, 550m²/g) and a stirring bar were added in a 50 mL H_2SO_4/H_2O_2-solution (95/5 Vol%). The mixture was stirred for 20 min at room temperature and was then diluted with approximately 150 mL of water to deactivate the solution. The particles were separated by centrifuging for 15 min at 4400 rpm, washed with a ± 1 M HCl-solution and centrifuged again. The particles were then dispersed into a 50 Vol% NH_4OH/H_2O_2-solution and stirred for 20 min at room temperature. Subsequently the particles were separated by centrifuging for 15 min at 4400 rpm, washed with ethanol and centrifuged again. Finally, they were vacuum dried (± 0.2 mbar) to remove any excess moisture.

Functionalization of treated particles with APTES (4). Four different types of particles were silanized: large silica particles (70-200 µm, porous, 550 m²/g) which were treated with piranha or used pristine (without treatment) and small particles (1 µm, non-porous, 18 m²/g) which were treated with piranha or used pristine. The silanization procedure is the same for all four types of particles with exception of the large pristine particles which were already silanized at 110 °C as (Figure 19). For the silanization 1 g of particles, 1 mL of APTES, 10 mL of dry toluene and a stirring bar were added in a 50 mL round bottom flask. The mixture was refluxed overnight at 70 °C with continuous stirring. Subsequently the particles were separated by centrifuging for 15 min at 4400 rpm. After this they were washed with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. The particles were finally vacuum dried (± 0.2 mbar) before TGA analysis.

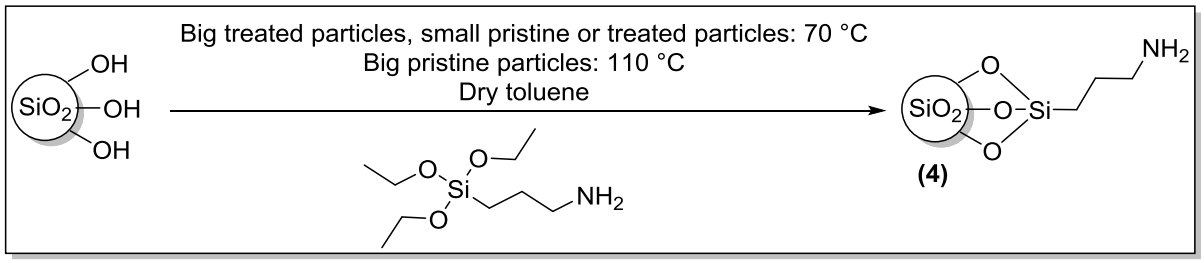

*Figure 19: Synthesis of amino functionalized silica particles (**4**)*

EDC/NHS coupling reaction between DoPAT PnBuA polymer and amino functionalized particles

The coupling reaction was executed on small non-porous (1 µm) and large porous (70-200 µm) silica particles which were treated with piranha solution and silanized with APTES. Because the DoPAT RAFT SD oligomers were not synthesized yet a 7000 g/mol and a 5223 g/mol poly-n-butyl acrylate (PnBuA) DoPAT RAFT polymer were used. The objective of the reaction on the large porous silica particles was to investigate if this coupling reaction could work as is illustrated in Figure 20. Therefore, the polymer was used in high excess (10-15 equiv).

For the large silica particles 0.1 eq. of DMAP, 1.1 eq. of NHS, 1.1 eq. of EDC, 0.100 g of amino functionalized silica particles and a stirring bar were added into a test tube. The test tube was placed in a beaker filled with ice. An excess of polymer (PnBuA DoPAT RAFT polymer, M_n = 7000 g/mol), 1.1 eq. of pyridine and 5 mL of butyl acetate were added into a glass vial (10 mL) and subsequently cooled in an ice bath. When the temperature of the mixture reached 0°C it was added into the test tube. The reaction was carried out overnight with continuous stirring. The particles were separated through centrifugation (15 min at 4400 rpm) and washed with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. Finally, they were vacuum dried (± 0.2 mbar) before TGA analysis.

For the small non-porous particles, a lower excess of the PnBuA polymer was used (3.20 equivalents). The following stock solutions were prepared and placed in an ice bath: 0.002 g of DMAP dissolved in 1 mL of butyl acetate, 0.019 g of NHS dissolved in 10 mL of butyl acetate and 0.013 g of pyridine dissolved in 1 mL of butyl acetate and placed in an ice bath. 1.1 eq. of EDC, 3.20 eq. of the PnBuA-DoPAT RAFT agent (M_n = 5223 g/mol), 0.100 g of amino functionalized silica particles and 5 mL of butyl acetate were added into a test tube and placed in a beaker filled with ice. 0.1 mL of DMAP-stock solution, 1.0 mL of NHS-stock solution and 0.1 mL of pyridine-stock solution were added into the test tube. The reaction was carried out overnight with continuous stirring. The particles were separated through centrifugation (15 min at 4400 rpm) and washed with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. The particles were finally vacuum dried (± 0.2 mbar) before TGA analysis.

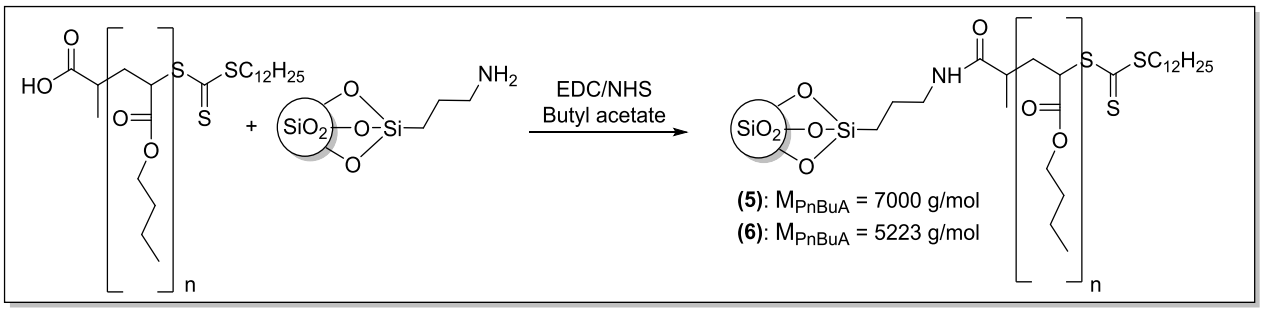

Figure 20: Coupling reaction between PnBuA-DoPAT RAFT polymer and functionalized silica particles

2.3.2 Coupling CPD-TTC RAFT SD oligomer onto functionalized silica particles

Alkyne end group modification of CPD-TTC RAFT SD oligomer

To attach the MA-EA-CPD-TTC SD oligomer onto functionalized silica particles an alkyne end group modification needs to be executed (Figure 21). 1 eq. of MA-EA-CPT-TTC SD oligomer was dissolved in 37 eq. of THF (5 times the mass of the used oligomer) and transferred into a GPC vial. 10 eq. of propargyl acrylate, 10 eq. of hexylamine and a stirring bar were added into the GPC vial and subsequently brought into a glovebox. The mixture was purged with nitrogen and reacted for 3 hours at room temperature with continuous stirring. Afterwards, the mixture was poured into an aluminium pan to evaporate excess solvent and monomer. The crude product was purified via rec-SEC to yield 0.023 g (31%) of pure alkyne modified CPD-TTC SD oligomer **(7)**.

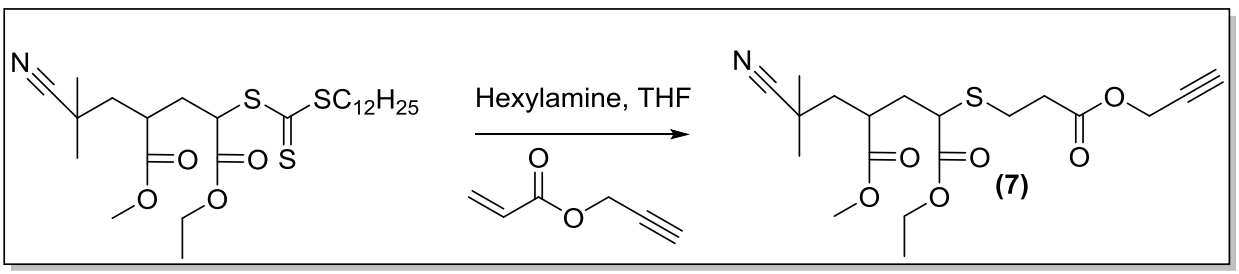

*Figure 21: Synthesis of alkyne modified CPD-TTC SD oligomer (**7**)*

Functionalization of the silica particles

Silanization with CPTMO (8). A first step in functionalizing the particles is executing a silanization with CPTMO as described in Figure 22. Pristine silica particles (1 µm) were dried for 4 hours at 120 °C. 1 g of these particles was transferred into a 50 mL round bottom flask. 4 mL of CPTMO, 20 mL of dry toluene and a stirring bar were added. The mixture was refluxed at 120 °C overnight under a nitrogen atmosphere. The next day the particles were separated by centrifuging for 15 min at 4400 rpm followed by a washing with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. Finally, the particles were vacuum dried (± 0.2 mbar) before TGA analysis.

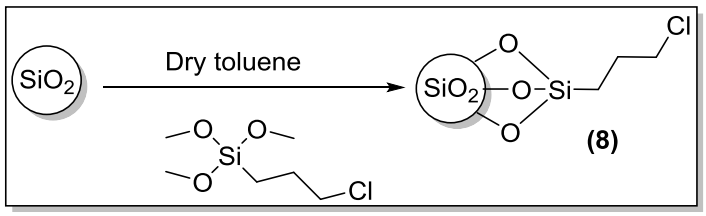

*Figure 22: Synthesis of chloro functionalized silica particles (**8**)*

Azidation of the chloro silica particles (9). The second step in functionalization of the silica particles is executing an azidation of the Cl-group as is shown in Figure 23. 1 eq. of the chloro silica particles were transferred into a glass vial (10 mL). 1.2 eq. of NaN_3, 5 mL of DMF and a stirring bar were added into the vial. The reaction mixture was stirred overnight. The next day the particles were separated by centrifugation (15 min at 4400 rpm) followed by a washing with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. Finally, the particles were vacuum dried (± 0.2 mbar).

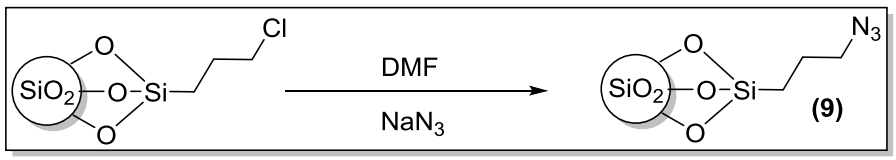

*Figure 23: Synthesis of azide functionalized silica particles (**9**)*

CuAAC-click reaction between alkyne modified CPD-TTC SD oligomer and azide functionalized particles

The azide functionalized particles and alkyne modified CPD-TTC SD oligomer were linked together by copper-click chemistry as is displayed in Figure 24. 6.4 eq. of the alkyne modified CPD-TTC SD oligomer, 1 eq. of azide functionalized particles, 4 mL of DMF and a stirring bar were added into a glass vial (10 mL). 1 eq. of CuBr, 2 eq. of PMDETA, a stirring bar and 1 mL of DMF were added into a GPC vial. Both vials were transferred into a glovebox and purged with nitrogen. After purging the CuBr/PMDETA mixture was added into the glass vial. The mixture was reacted for 3 hours at room temperature with continuous stirring. After the reaction the particles were separated by centrifugation (15 min at 4400 rpm) and washed three times with ethanol. The particles were vacuum dried (± 0.2 mbar) before TGA analysis.

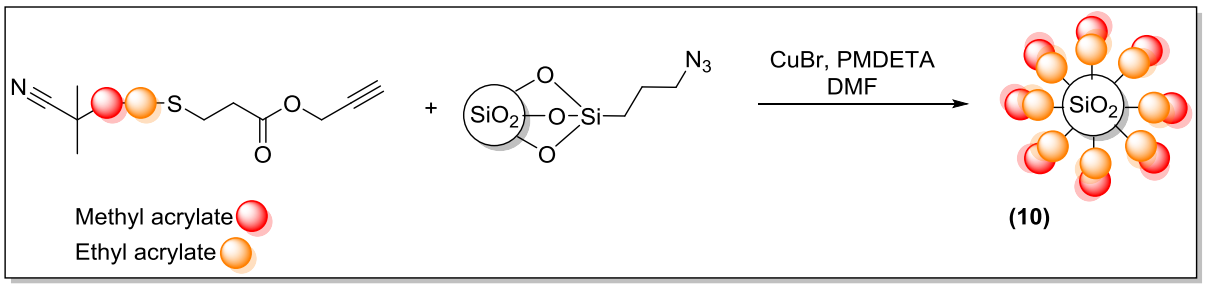

Figure 24: CuAAC-click reaction between azide functionalized silica particles and the alkyne modified CPD-TTC SD oligomer

2.3.3 Coupling photo-CMP SD oligomer onto functionalized silica particles

Synthesis of photo-CMP SD oligomer

Synthesis of MA-Ebib (11). A first monomer insertion was performed with the aim of synthesizing an SD oligomer through photo-CMP (Figure 25). 0.014 eq. of $CuBr_2$, 0.084 eq. of ME_6TREN, 1 eq. of the monomer MA, 1 eq. of the initiator Ebib, 3.000 g of DMSO (50% of the total volume) and a stirring bar were added into a sealed 50 mL 3-neck flask and placed in a cold water bath. The mixture was purged with nitrogen for 10 min. The UV source was aimed and placed at 3 cm of the bottom of the flask and switched on. After 4 h of reaction time the UV source was switched off. The solution was diluted with approximately 100 mL of deionized water and extracted with chloroform. Excess solvent in the organic fraction was evaporated and the crude product was purified with classic column chromatography to yield 1.303 g (40%) of pure MA-Ebib **(11)**.

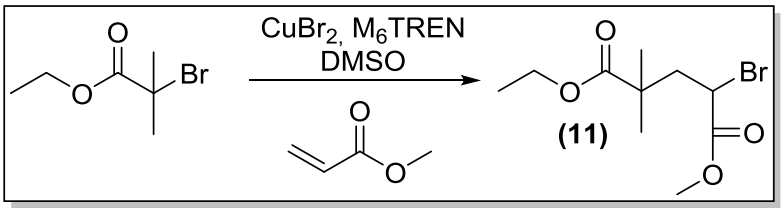

*Figure 25: Synthesis of MA-Ebib (**11**) through photo-CMP*

Synthesis of MA-EA-Ebib (12). A second monomer insertion was performed on the previous synthesized MA-Ebib **(11)** which is illustrated in Figure 26. 0.014 eq. of $CuBr_2$, 0.084 eq. of ME_6TREN, 1 eq. of the oligomer MA-Ebib, 1 eq. of the monomer EA, 1.760 g of DMSO (50% of the total volume) and a stirring bar were added into a sealed 50 mL 3-neck flask and placed in a cold water bath. The mixture was purged with nitrogen for 10 min. The UV source was aimed and placed at 3 cm of the bottom of the flask and switched on. After 1 h of reaction time the UV source was switched off. The solution was diluted with approximately 100 mL of deionized water and extracted with chloroform. Excess solvent in the organic fraction was evaporated and the crude product was purified with classic column chromatography to yield 0.640 g (36%) of pure MA-EA-Ebib **(12)**.

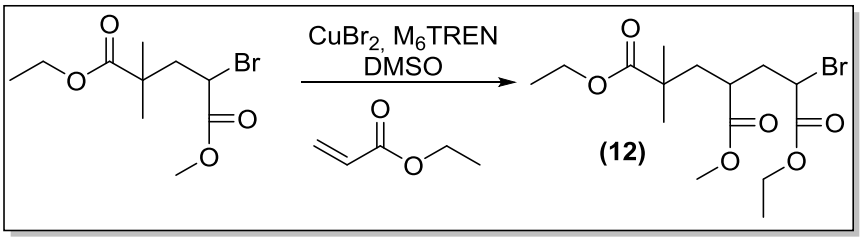

*Figure 26: Synthesis of MA-EA-Ebib (**12**) oligomer through photo-CMP*

Synthesis of MA-EA-EHA-Ebib (13). A third monomer insertion was performed on the previous synthesized MA-EA-Ebib **(12)** which is displayed in Figure 27. 0.014 eq. of $CuBr_2$, 0.084 eq. of M_6TREN, 1 eq. of the oligomer MA-EA-Ebib, 1 eq. of the monomer EHA, 4.400 g of DMSO (80% of the total volume) and a stirring bar were added into a sealed 3-neck flask and placed in a cold water bath. The mixture was purged with nitrogen for 10 min. The UV source was aimed and placed at 3 cm of the bottom of the flask and switched on. After 1 h of reaction time the UV source was switched off. The solution was diluted with approximately 100 mL of deionized water and extracted with chloroform. Excess solvent in the organic fraction was evaporated and the crude product was purified with classic column chromatography to yield 0.165 g (17%) of pure MA-EA-EHA-Ebib **(13)**.

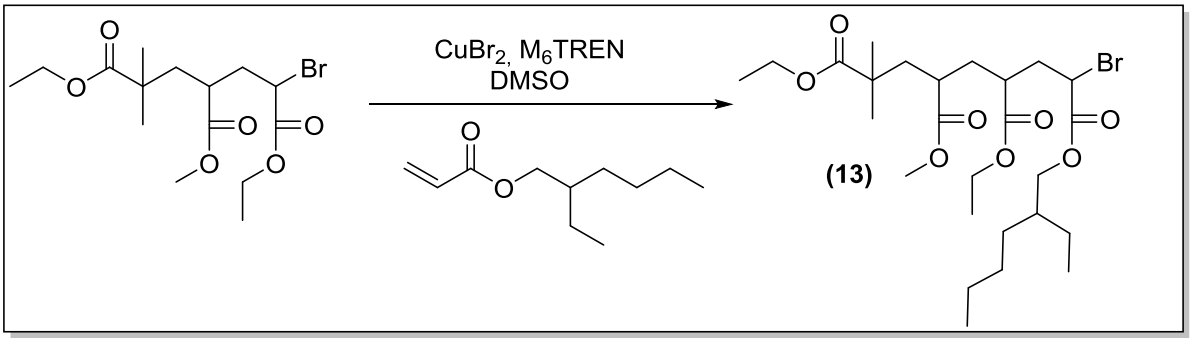

*Figure 27: Synthesis of MA-EA-EHA-Ebib (**13**) oligomer through photo-CMP*

Azide end group modification of MA-EA-EHA-Ebib (14). To make it possible to attach product **(13)** onto functionalized silica particles an azidation is performed (Figure 28). 1 eq. of MA-EA-EHA-Ebib was transferred into a glass vial (10 mL). 1.2 eq. of NaN_3, 1.5 mL of DMF and a stirring bar were added into the vial. The reaction mixture was stirred overnight. The next day the mixture was diluted with deionized water and extracted with DCM. The excess solvent in the organic fraction was evaporated and the product was finally vacuum dried (± 0.2 mbar) to yield 0.114 g (69%) of azide modified photo-CMP SD oligomer **(14)**.

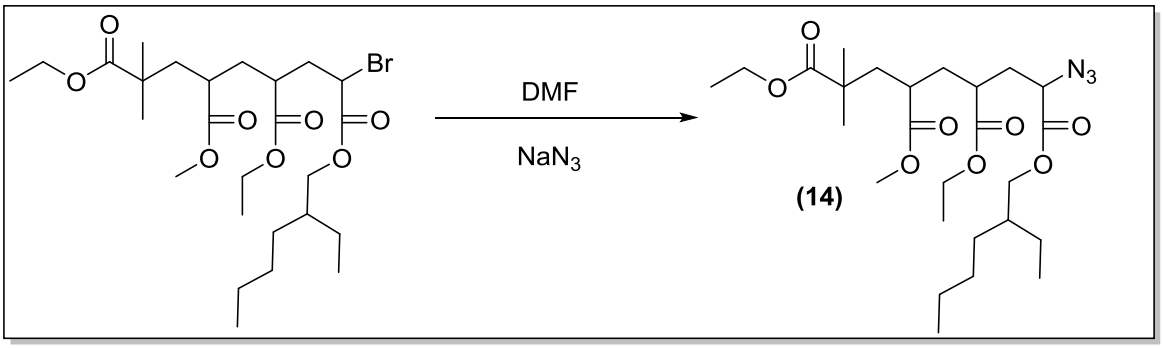

*Figure 28: Synthesis of azide modified photo-CMP SD oligomer (**14**)*

Functionalization of the silica particles

Synthesis of N-(3-(triethoxysilyl)propyl)propiolamide (TESPPA, (15)). A first step in functionalizing the silica particles is synthesizing the appropriate alkyne silane which is displayed in Figure 29. 1 eq. of APTES, 1.1 eq. of propiolic acid and 1.1 eq. of EDC were dissolved in 15 mL of DCM in a 50 mL round bottom flask. A stirring bar was added and the mixture was reacted for 1 hour at room temperature. The mixture was filtered through a syringe filter followed by a co-evaporation with 50 mL of toluene. The co-evaporation was repeated and an H-NMR sample was taken before the mixture was dissolved in 20 mL of dry toluene in a round bottom flask.

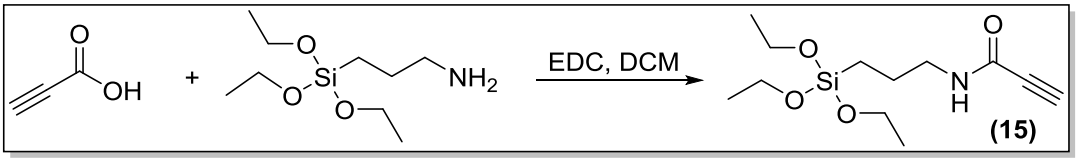

*Figure 29: Synthesis of TESPPA (**15**)*

Silanization of pristine silica particles (1 µm) with TESPPA (16). The second step of functionalizing the silica particles is silanization of pristine particles with product **(15)** as is shown in Figure 30. Pristine silica particles (1 µm) were dried for 4 hours at 120 °C. Next, 4 g of the particles and 1.5 mL of pyridine were added to the previous prepared TESPPA solution. The mixture was refluxed overnight at 110 °C under a nitrogen atmosphere. The next day the particles were separated by centrifugation for 15 min at 4400 rpm followed by a washing with toluene, ethanol, water and again ethanol. Between the washing steps the particles were separated by centrifugation. Finally, the particles were vacuum dried (± 0.2 mbar) before TGA analysis.

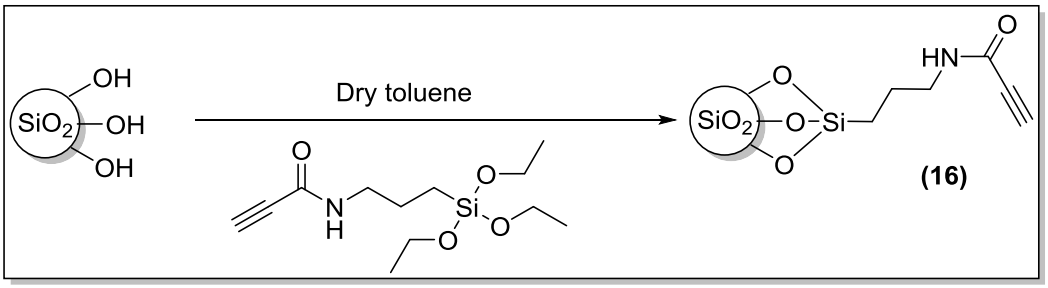

*Figure 30: Synthesis of alkyne functionalized silica particles (**16**)*

CuAAC-click reaction between azide modified photo-CMP SD oligomer and alkyne functionalized particles

The functionalized particles and azide modified SD oligomers were linked together by CuAAC-click chemistry as is displayed in Figure 31. 1.6 eq. of azide modified photo-CMP SD oligomer, 1 eq. of alkyne functionalized particles, 9 mL of DMF and a stirring bar were added into a glass vial (10 mL). 1 eq. of CuBr, 2 eq. of PMDETA, a stirring bar and 1 mL of DMF were added into a GPC vial. Both vials were transferred into a glovebox and purged with nitrogen. After purging the CuBr/PMDETA mixture was added into the glass vial. The mixture was reacted for 3 hours at room temperature. After the reaction the particles were separated by centrifugation (15 min at 4400 rpm) and washed 3 times with ethanol. The particles were vacuum dried (± 0.2 mbar) before TGA analysis.

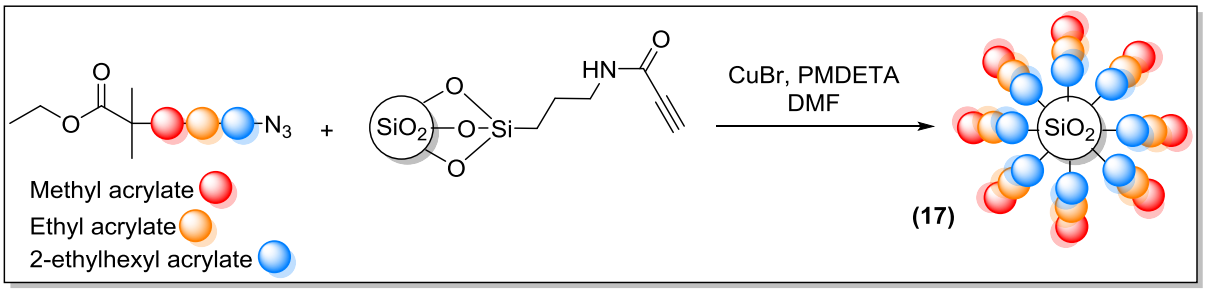

Figure 31: CuAAC-click reaction between alkyne functionalized silica particles and the azide modified photo-CMP SD oligomer

3 Results and discussion

3.1 Coupling DoPAT RAFT SD oligomer onto functionalized silica particles

3.1.1 Synthesis of DoPAT RAFT SD oligomer

SD oligomers were synthesized through SUMI-CRP. A first CRP technique used to produce these oligomers is RAFT. DoPAT was used as the transfer agent, because the acid group makes it possible to attach the SD oligomer through EDC/NHS coupling onto amino functionalized silica particles. To initiate the RAFT SUMI oligomerization, AIBN was added to the mixture. At higher temperatures (100 °C) this initiator splits into two initiator radicals. These radicals can react with monomers (nBuA and MA) to produce monomer radicals but can also participate in the polymerization itself resulting in a replacement of the acid group. Although the final oligomer distribution mainly carries both DoPAT end groups, also a small distribution is found with an AIBN-fragment in alfa position as illustrated in Figure 32(a).

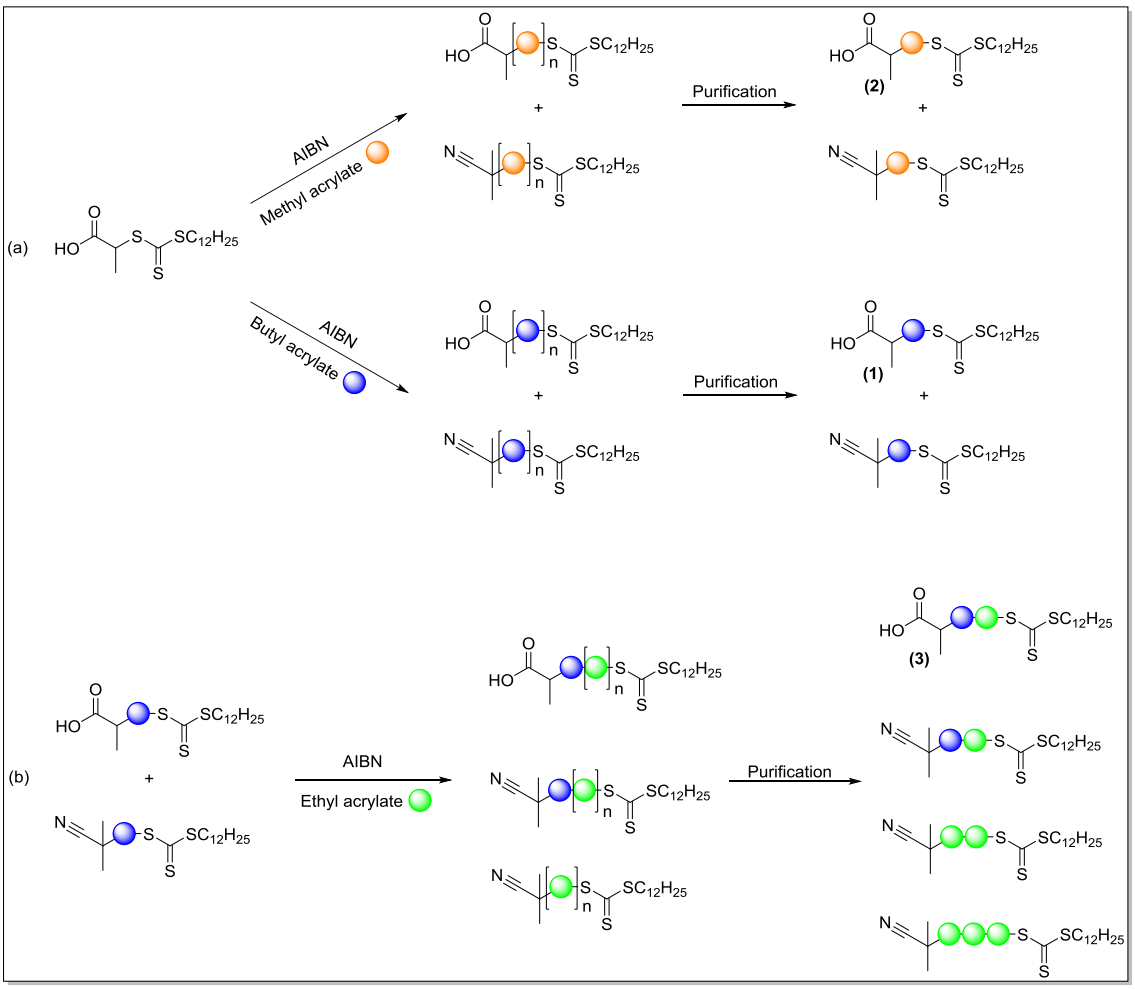

Figure 32: Distribution of oligomers synthesized via SUMI using DoPAT as transfer agent

The mass difference between the final two molecules in Figure 32 (a) is approximately 5 g/mol. This difference is too small to separate both products through rec-SEC which makes it impossible to synthesize a 100% pure SUMI-1 nBuA-DoPAT (**1**) or MA-DoPAT SD (**2**) product. Therefore, in the second insertion on product (**1**) with the monomer EA not only the oligomer with both DoPAT groups reacts, but also the oligomer with the isobutyrylnitrile group. Furthermore, the same problem with the initiator radicals and purification occurs in this second insertion resulting in a final product that mainly consist of nBuA-EA-DoPAT (**3**), but also contain inseparable isobutyrylnitrile oligomers (Figure 32 (b)). This problem is already reported in previous literature.[51]

A solution to this problem is using a low equivalent of AIBN to decrease the possibility of this end group exchange. In the performed reactions 0.05 equivalents of AIBN were used for each equivalent of DoPAT. The exchange is limited, but still present which can be seen in the mass spectrum of nBuA-DoPAT (**1**) and nBuA-EA-DoPAT (**3**) shown in Figure 33 and Figure 34 respectively. In all spectra the presence of the acid group is visible. Because the mass difference is only 5 g/mol the purification will never be perfect and the SD oligomer with the isobutyrylnitrile group will always be present in the final product. The result is a loss of SD oligomer that can be coupled onto amino functionalized particles.

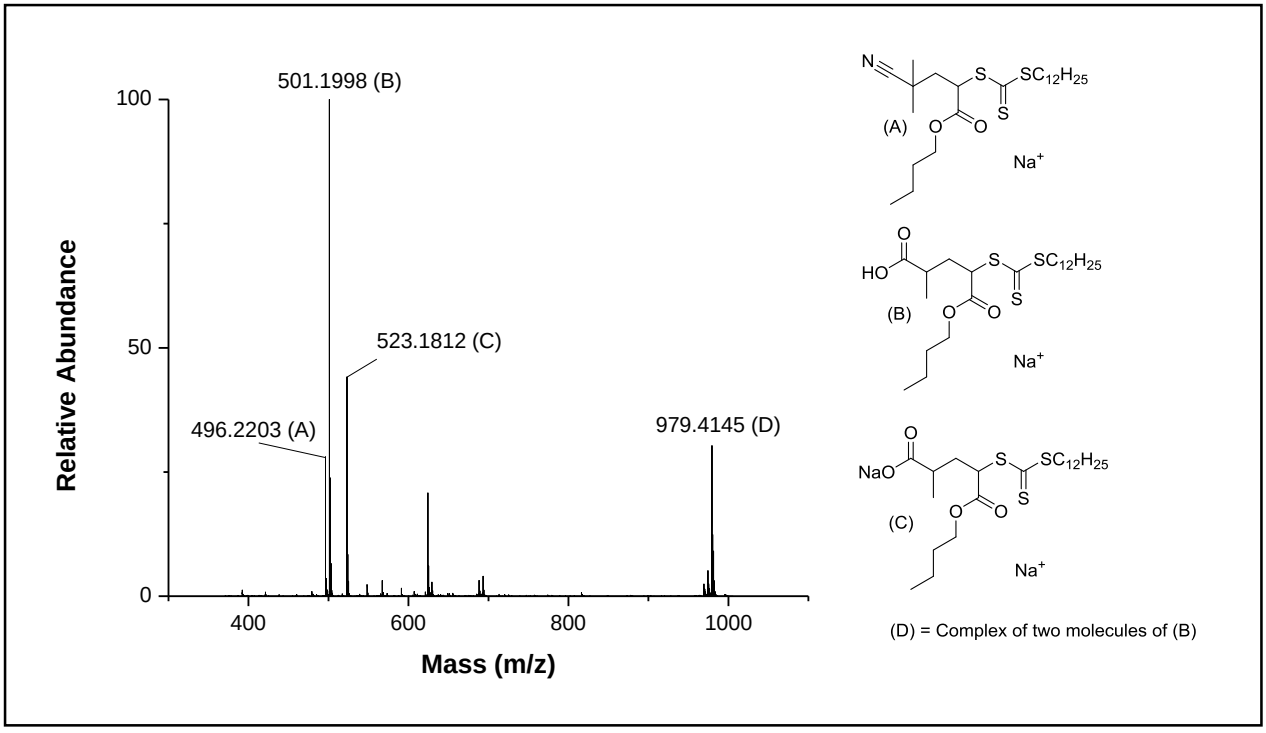

*Figure 33: ESI-MS of nBuA-DoPAT (**1**)*

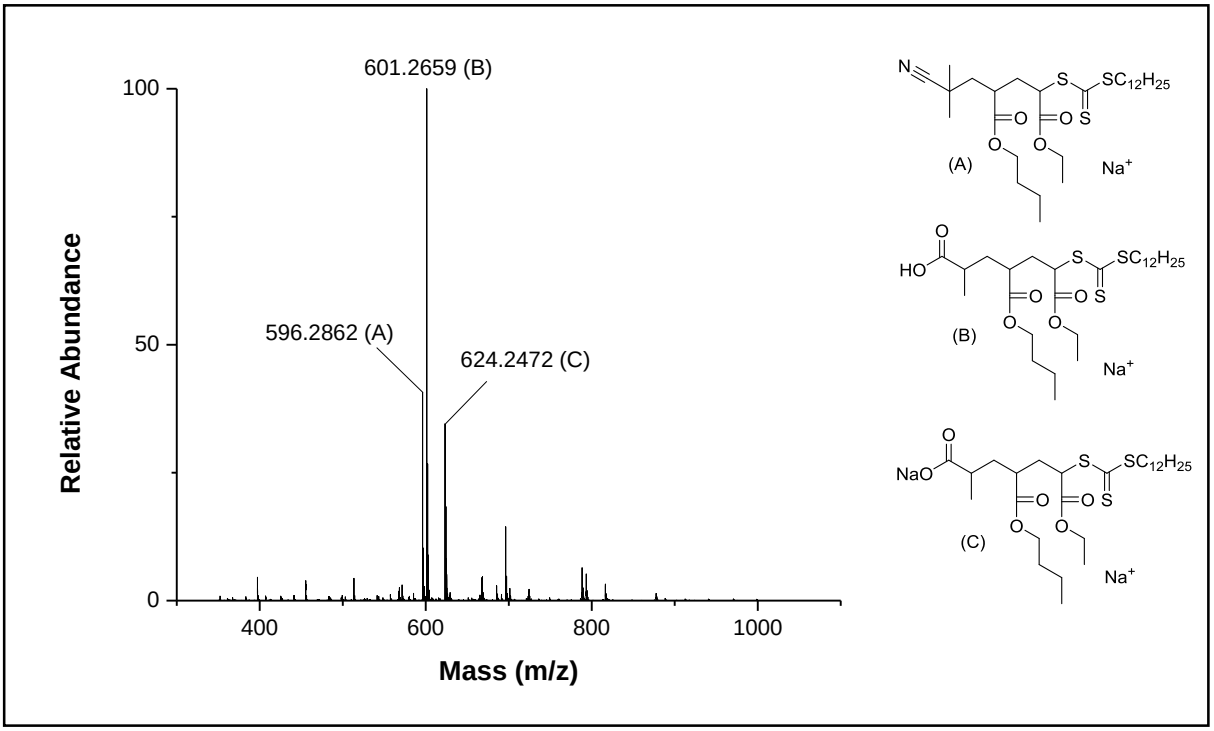

*Figure 34: ESI-MS of nBuA-EA-DoPAT (**3**)*

The first reaction with nBuA-DoPAT (**1**) and EA had a yield of 17% of pure nBuA-EA-DoPAT (**3**) and a yield of 46% of unreacted nBuA-DoPAT (**1**). Therefore, a repeated reaction with the unreacted product was executed. In this repeated reaction another effect of the presence of the isobutyrylnitrile group is highlighted (Figure 35). If the nBuA-DoPAT RAFT agent (**1**), used for the second monomer insertion, was 100% pure there should be no mass peaks of 568.2862 and 668.3082 present in the ESI-MS spectrum of nBuA-EA-DoPAT (**3**). These peaks represent an oligomer with no nBuA monomer unit, but only EA monomer units. Therefore, the nBuA-DoPAT (**1**) fraction used for this second EA RAFT polymerization also contained some pure molecules of DoPAT in which the acid group is replaced by an isobutyrylnitrile group forming the CPD-TTC RAFT transfer agent (ESI-MS (m/z) = 368.1516)). Most likely due to low ionization, this species was not previously observed in the ESI-MS spectrum of nBuA-DoPAT (**1**), although it must have been clearly present as a side product. This effect also causes a loss of product that is capable of reacting in the coupling reaction.

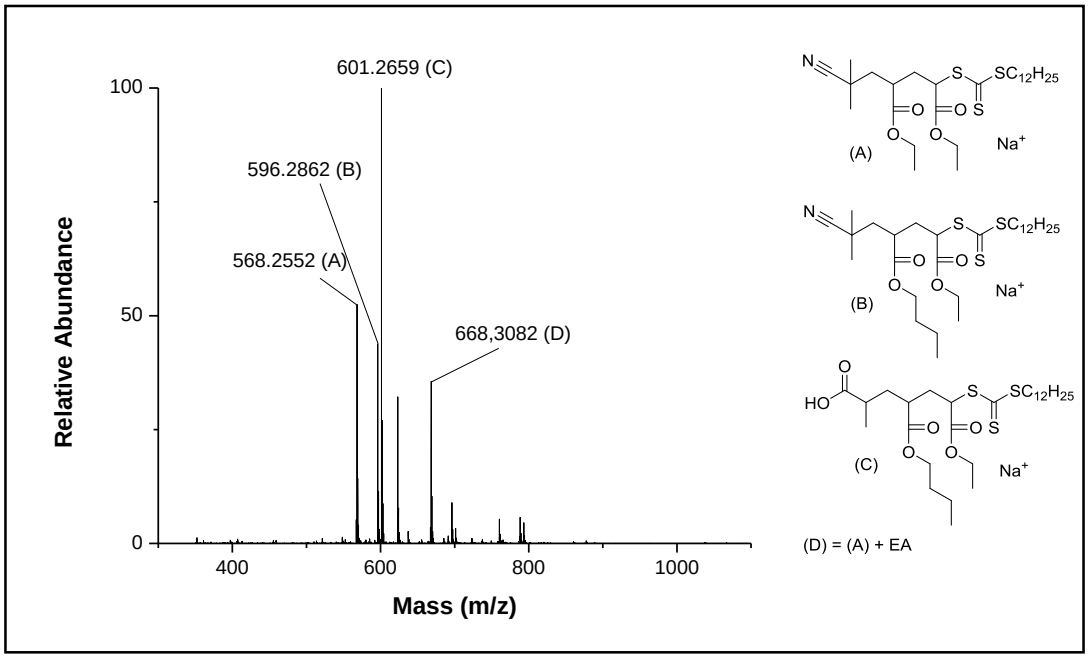

*Figure 35: ESI-MS of nBuA-EA-DoPAT (**3**) (repeated reaction)*

A last drawback is the complex purification of DoPAT RAFT SD oligomers. Figure 36 represents the chromatogram of the purification of the MA-DoPAT RAFT agent (**2**). The yield of pure product after this run was 2%. Therefore, mixed fractions were combined and a second run was performed (Figure 37). For this second run the purification took over 400 min to achieve peaks that are poorly separated and to obtain a final yield of 7% of pure MA-DoPAT (**2**). These yields are insufficient contrary to other reported yields of SD oligomers (46% for a nBuA-EHA-CPD-TTC RAFT SD oligomer).[23]

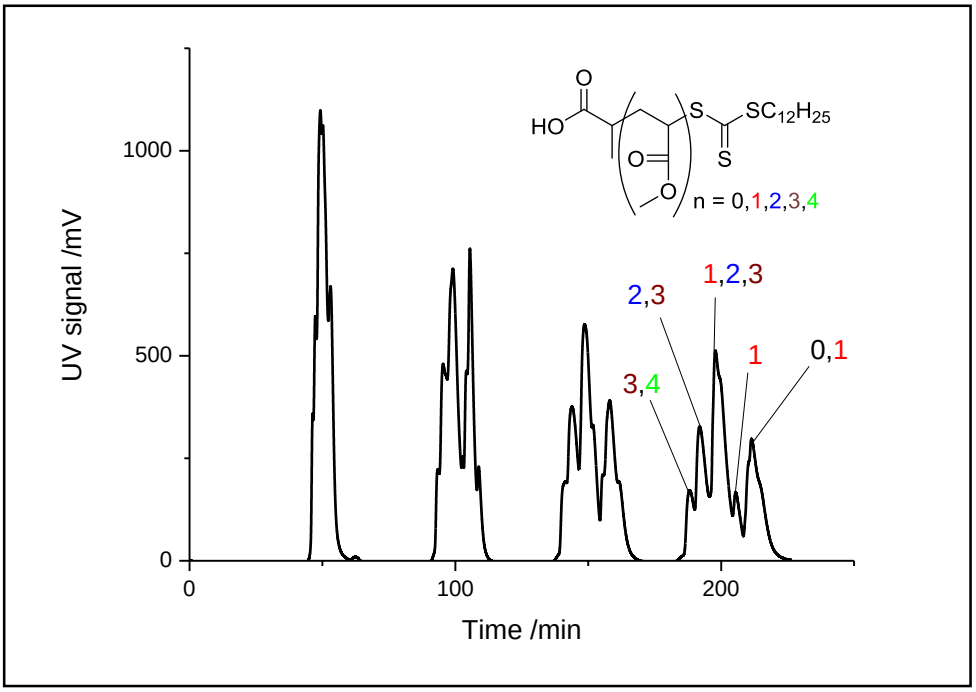

*Figure 36: rec-SEC trace recorded during consecutive purification cycles of MA-DoPAT (**2**)*

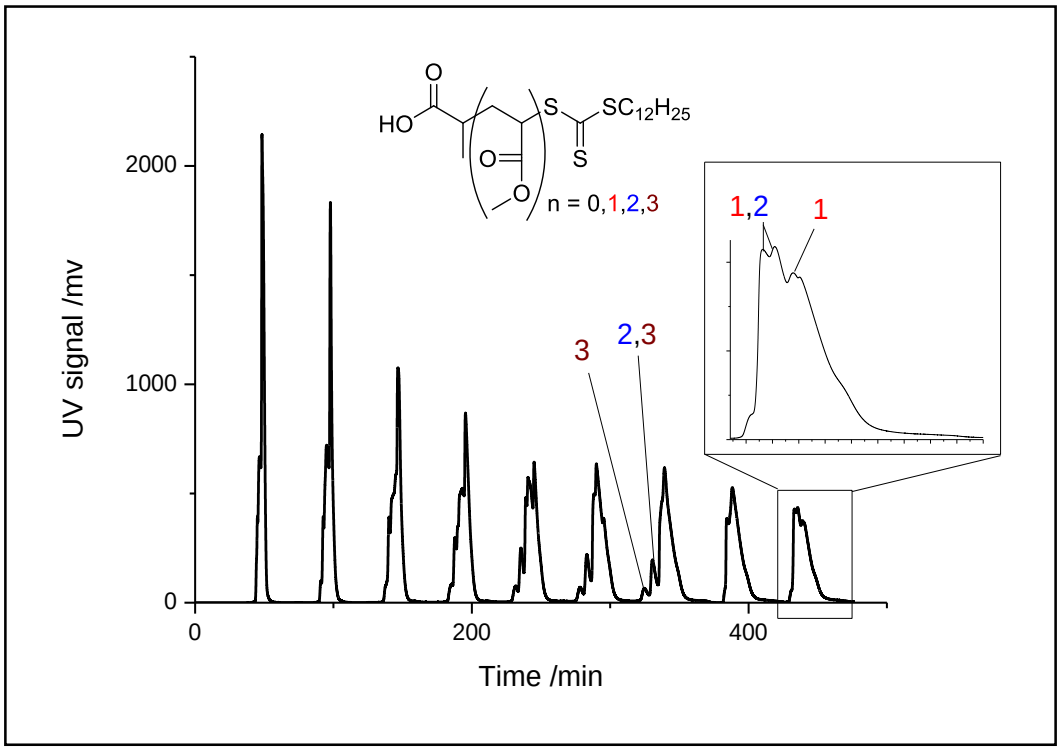

*Figure 37: rec-SEC trace recorded during consecutive purification cycles of 2 fractions from a previous run (see Figure 36) containing MA-DoPAT (**2**)*

These complex chromatograms are the result of an interaction of the acid group of DoPAT that tends to stick to the material (cross-linked polystyrene) of the column. Because of this interaction an overlap between products of different hydrodynamic volumes is created. Furthermore, due to the interaction during the cycles, peaks appear and disappear. This time consuming and almost impossible purification makes it difficult to produce a sufficient amount of pure DoPAT SD oligomers. Therefore, the experiments were stopped after the synthesis of MA-DoPAT RAFT agent (**2**) and nBuA-EA-DoPAT RAFT agent (**3**).

3.1.2 Functionalization of silica particles and EDC/NHS coupling with DoPAT RAFT SD oligomer

A silanization with APTES was performed on four different types of silica particles to synthesize amino functionalized silica particles. These particles can be linked together with DoPAT SD oligomers through EDC/NHS coupling. With TGA it is possible to determine the surface grafting density of the silane onto the particle. The results are displayed in Figure 38 and Figure 39. An example of the calculation of the surface grafting density in explained in Appendix B.

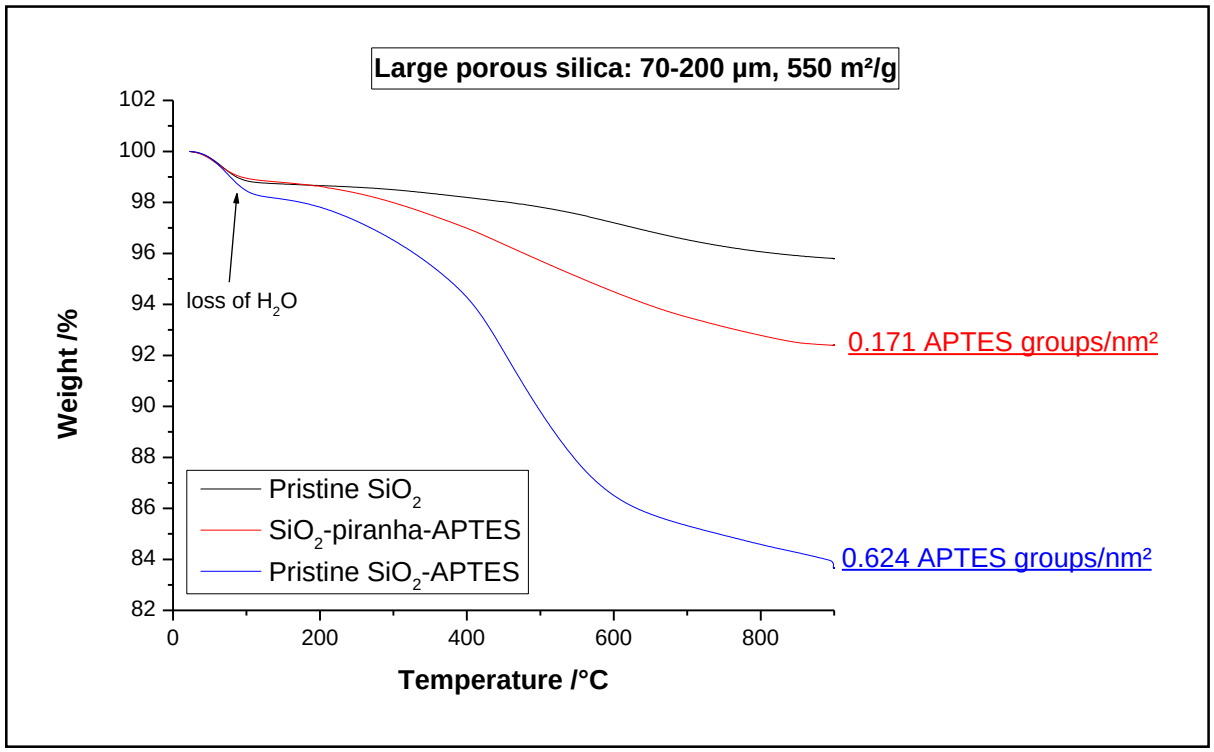

*Figure 38: TGA result of amino functionalized silica (**4**) on pristine or piranha treated large silica particles (70-200 µm)*

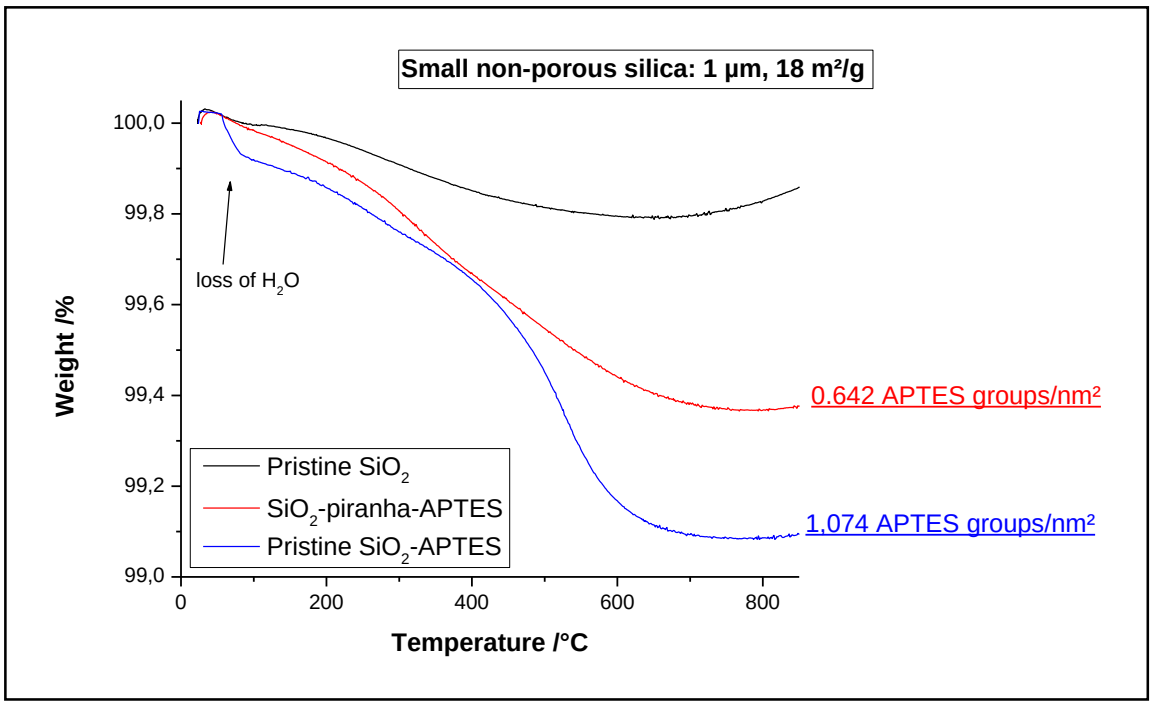

*Figure 39: TGA result of amino functionalized silica (**4**) on pristine or piranha treated small silica particles (1 µm)*

Particles treated with a piranha solution have a lower surface grafting density in comparison with particles which are used pristine. This suggest that piranha treatment is not necessary to obtain a sufficient amount of grafting. This piranha treatment is often used on silicon wafers which have a different surface structure. The surface of silicon wafers consists of a layer of organic impurities on top of a Si-H surface. To activate these wafers, a treatment with piranha solution is executed which removes the impurities and changes the Si-H surface to a Si-OH surface. This surface is then capable of reacting with a silane.[52]–[54]

Silica particles, contrary to silicon wafers, consist of a SiO_2 core below a layer of organic impurities. These organic molecules are attached onto the surface through an ether bond. When the particles are treated with piranha solution the organic layer is removed and replaced by a Si-OH layer. This layer increases the hydrophilic character of the silica particles and makes a silanization with APTES more strong (due to the possibility of binding with 3 OH surface groups per silane molecule, see Figure 40), but also more difficult because the organic APTES is, to a certain extent, repelled by the super hydrophilic silica surface. Furthermore, when a reaction with APTES is performed in the presence of water, there is a possibility that the silane will cross-link (depending on the pH of the solution) and not be able to react with the surface.

If a silanization with APTES is performed on pristine silica particles, the surface consists of organic molecules bound through an ether function. This ether function will break and be replaced by the Si-O bond of APTES. Depending on which R-groups are attached onto the surface, APTES will only be bound through two or even one Si-O bond. Also the Si-O-R bonds are not as hydrophilic in comparison with the Si-OH bounds of the piranha treated silica surface. These phenomena contribute to a higher surface grafting density. The difference between silanization with APTES on treated and untreated particles is summarized in Figure 40.

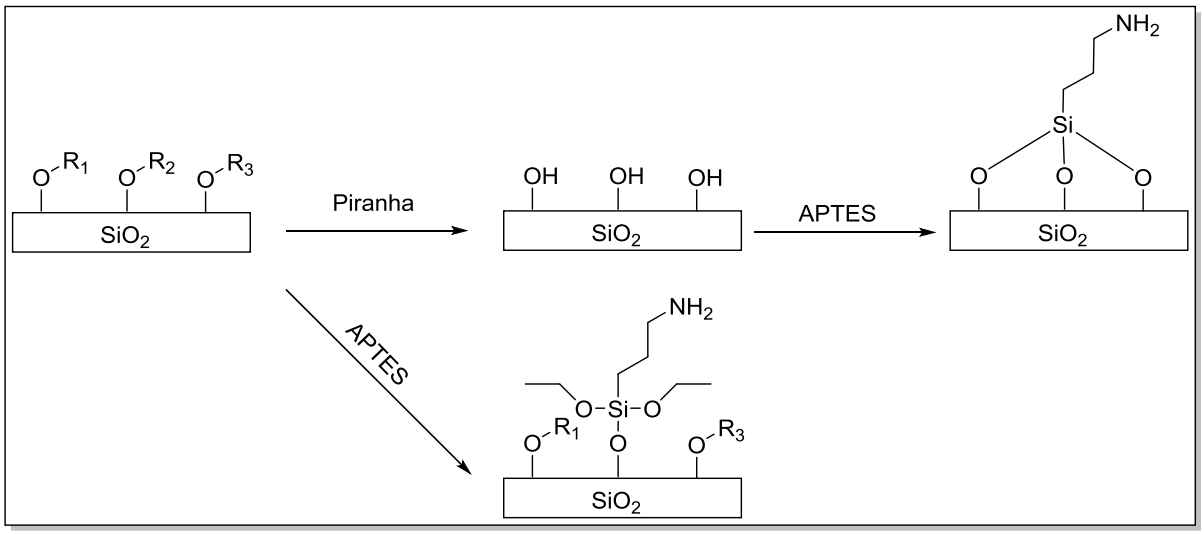

Figure 40: Difference between silanization on a silica surface treated with piranha solution and a pristine silica surface

To attach the DoPAT RAFT SD oligomer onto amino functionalized silica particles an EDC/NHS coupling was performed. For this reaction large and small piranha treated silica particles were used. Because SD oligomers were not synthesized yet, the coupling was executed with a 7000 g/mol and 5223 g/mol PnBuA-DoPAT polymer. The TGA results are displayed in Figure 41 and Figure 42 respectively. The EDC/NHS coupling on the large silica particles seemingly worked, but the results need to be interpreted with caution. Because the particles are porous, the mass loss can either be caused by outer or inner degradation. These two effects are measured at the same time which makes it difficult to make a correct interpretation of the results.

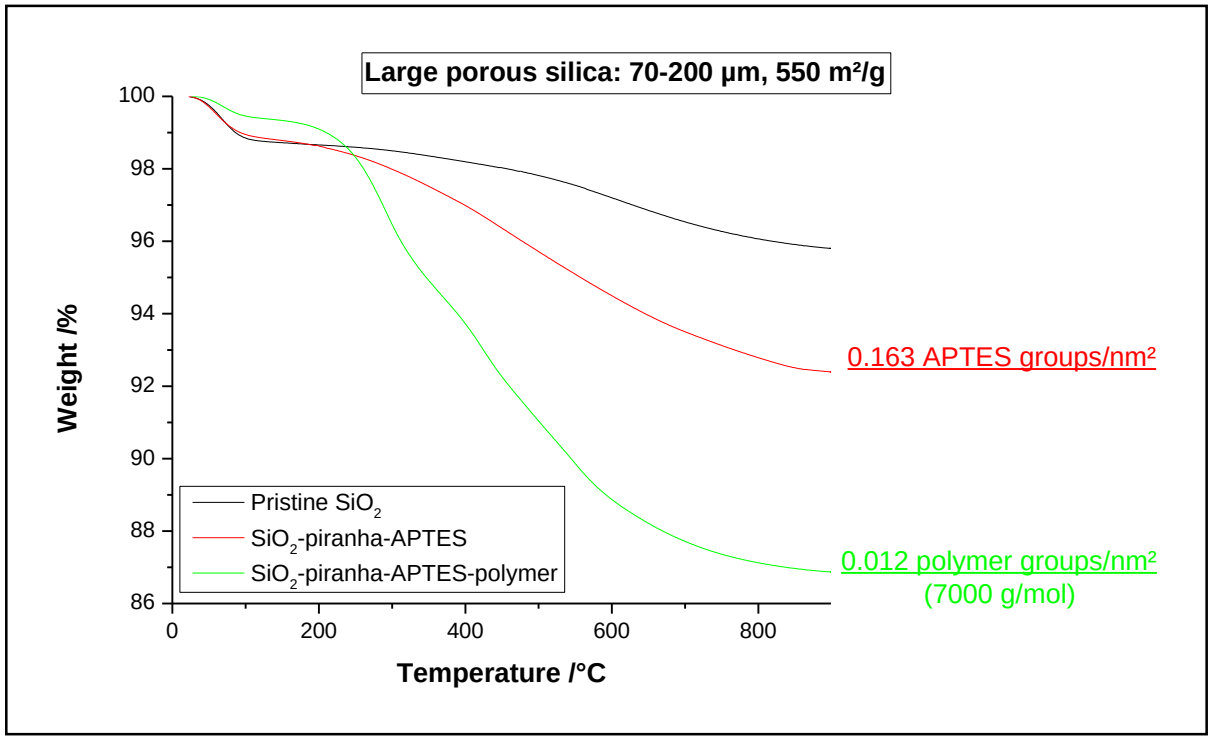

*Figure 41: TGA result of polymer attached through EDC/NHS onto large porous functionalized silica particles (**5**)*

The TGA data (Figure 42) indicate that the EDC/NHS coupling on the small particles did not work. If the coupling worked, the final particles should have a higher mass loss than the amino functionalized silica particles. Therefore, it is not possible to determine the surface grafting density of the DoPAT SD oligomer. This failure could be the result of the high amount of solvent used in comparison with the lower amounts of DMAP, NHS and EDC. However, due to the difficult procedure of synthesizing DoPAT SD oligomers this path was no longer investigated.

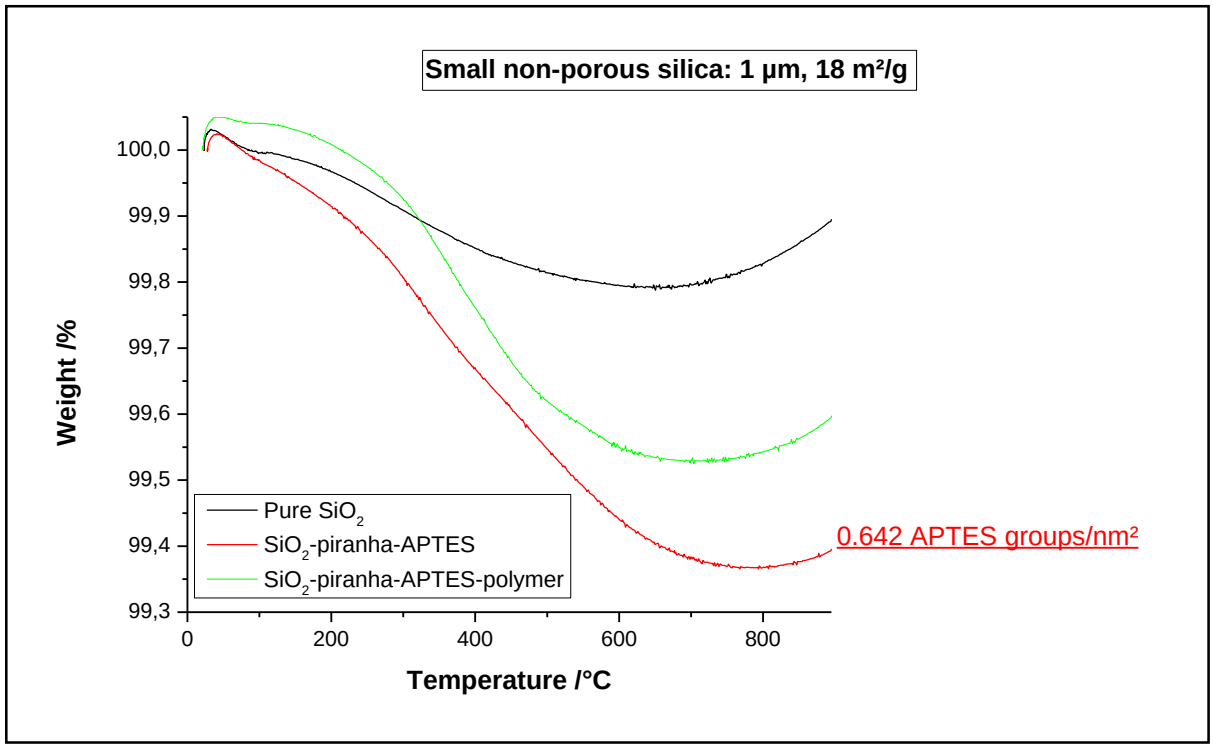

*Figure 42: TGA result of polymer attached through EDC/NHS onto small non-porous functionalized silica particles (**6**)*

Another effect that is clearly present in Figure 42 is the rising slope at the end of the TGA curve. This effect can also be seen in other TGA curves but, does not always occur. When TGA is executed, a continuous nitrogen flow is applied above the sample. This flow can push the sample down or up resulting in lower or higher measured mass. This effect becomes more predominant when the measured masses are close to the detection limit of the balance (small particles) or when the temperature rises. Because of this phenomenon the surface grafting density is always calculated based on the lowest measured mass during the analysis and not the final mass.

3.2 Coupling CPD-TTC RAFT SD oligomer onto functionalized silica particles

3.2.1 Alkyne end group modification of CPD-TTC RAFT SD oligomer

Synthesizing DoPAT RAFT SD oligomers with subsequent attachment onto amino functionalized silica particles proved to be a difficult and almost impossible pathway. Another method is synthesizing a CPD-TTC RAFT SD oligomer with an alkyne modified end group and attaching it onto azide functionalized silica particles (See Figure 17). An alkyne end group modification was performed on the MA-EA-CPD-TTC RAFT agent. The ESI-MS of the alkyne modified SD oligomer (**7**) synthesized through aminolysis and thiol-ene addition is illustrated in Figure 43. The end group modification was successful, but the used MA-EA-CPD-TTC RAFT agent was not 100% pure. It also contained MA-EA-EA-CPD-TTC besides the desirable oligomer, but in a significant smaller amount. Also, because of the high eq. of hexylamine, another side product was formed (B). Both impurities do not react through CuAAC coupling. Therefore, the mass loss measured with TGA is only due to the alkyne modified CPD-TTC SD oligomer.

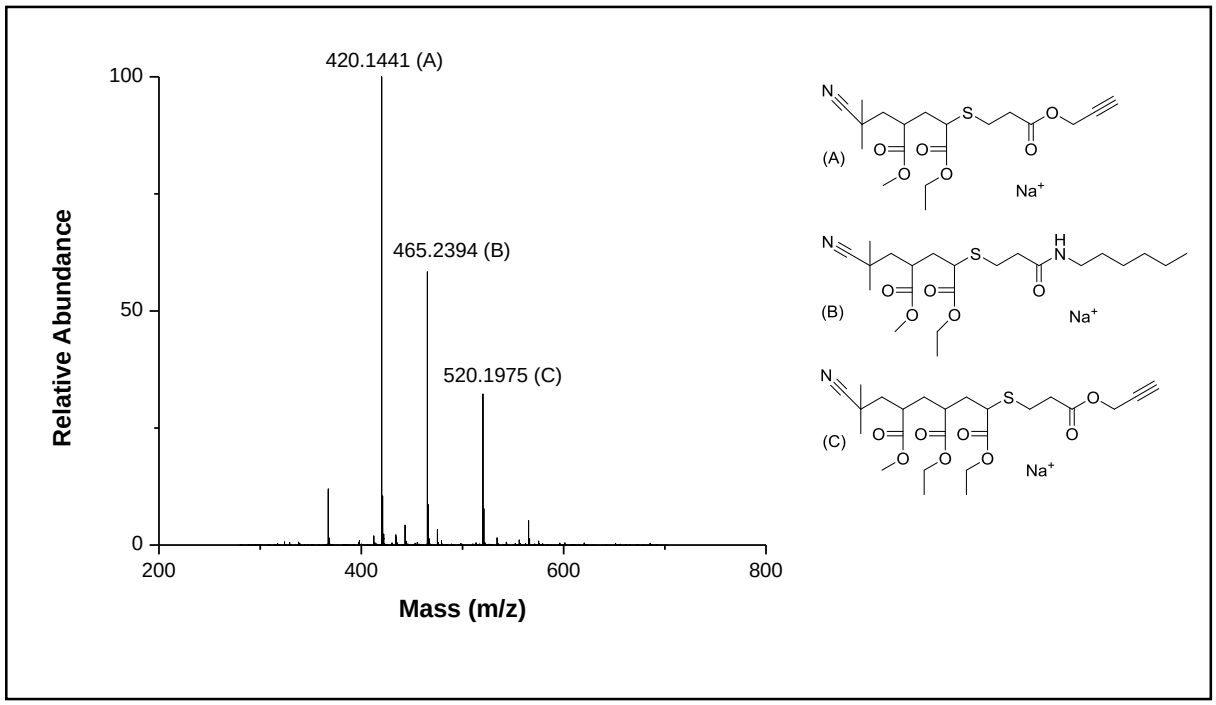

*Figure 43: ESI-MS of alkyne modified MA-EA-CPD-TTC (**7**)*

With CPD-TTC as a RAFT agent the problem with the AIBN initiator does not occur, because the alfa end group is already an isobutyrylnitrile group. Both groups are the same, so there is no change in structure of the final SD oligomer. This makes the purification of these SD oligomers mixtures less complex contrary to the purification of SD oligomers synthesized with DoPAT. Furthermore, the purification of CPD-TTC oligomers is more straightforward (products do not interact with the cross-linked polystyrene material of the column). The loss of product is far less which results in a more profitable approach in comparison with DoPAT.

3.2.2 Functionalization of silica particles and CuAAC-click coupling

For this method pristine silica particles (1 µm) were silanized with CPTMO. After this reaction the Cl-group was azidated to obtain functionalized silica particles with N_3-groups on the surface. This group is capable of reacting with the previous synthesized alkyne modified CPD-TTC RAFT SD oligomer through copper-click chemistry. The TGA results of the chloro functionalized silica particles (**8**) and silica particles with attached alkyne modified MA-EA-CPD-TTC oligomer (**10**) are shown in Figure 44.

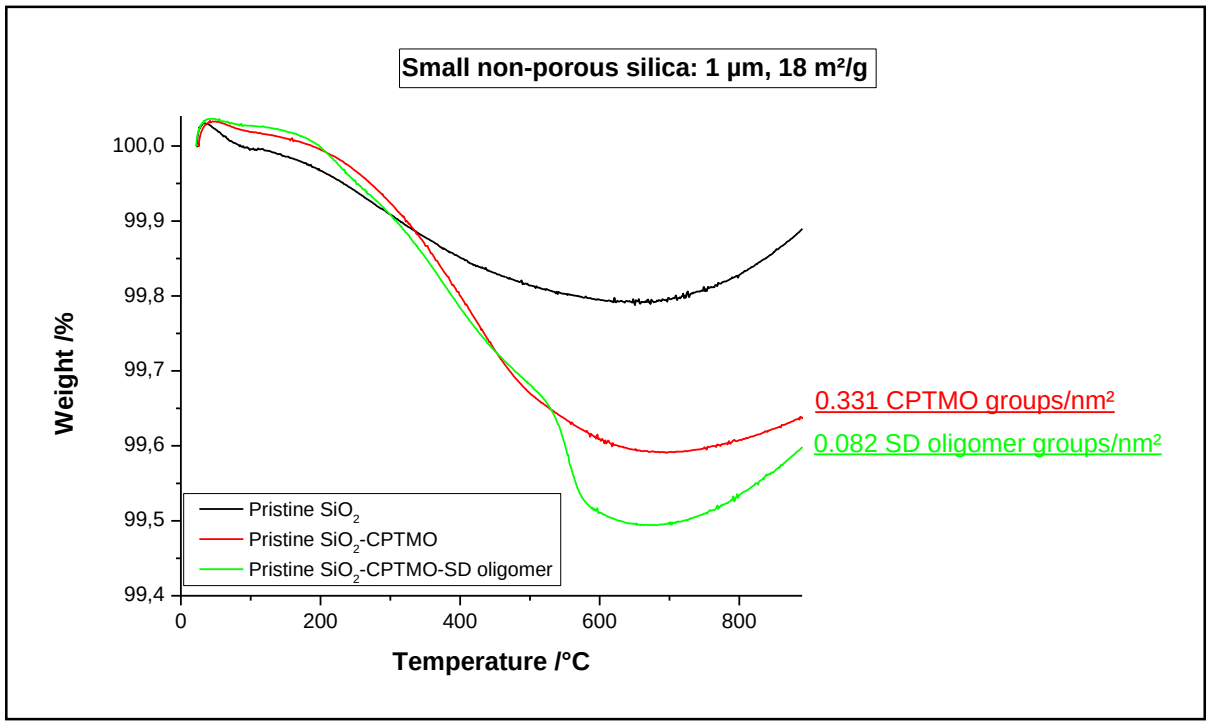

*Figure 44: TGA result of chloro functionalized silica particles (**8**) and silica particles with attached MA-EA-CPD-TTC oligomer (**10**)*

These TGA data indicates that both silanization and coupling were successful. The surface grafting density of the SD oligomer is lower compared to CPTMO. This means that only 25% of the CPTMO groups reacted with the SD oligomer. The reason for this relatively low conversion is steric hindrance. When two attached azidated CPTMO molecules are right next to each other a first approaching SD oligomer has no problem to find a suitable group. If a second SD oligomer wants to bind, the first attached SD oligomer causes steric hindrance which results in a more complex approach of the second molecule and a lower surface grafting density.

3.3 Coupling photo-CMP oligomer onto functionalized silica particles

3.3.1 Synthesis of photo-CMP SD oligomer

A last method to attach SD oligomers onto silica particles starts with the synthesis of a photo-CMP SD oligomer. MA-EA-EHA-Ebib (**13**) was synthesized through three consecutive photo-CMP reactions. After each monomer insertion the mixture was purified through either classic column chromatography (first and second monomer insertion) or rec-SEC (third monomer insertion). Figure 45-47 displays the ESI-MS spectra obtained after every purification step. Contrary to the DoPAT SD oligomers no end group replacement occurs. Therefore, the purification is much simpler and a pure SUMI end product can be obtained.

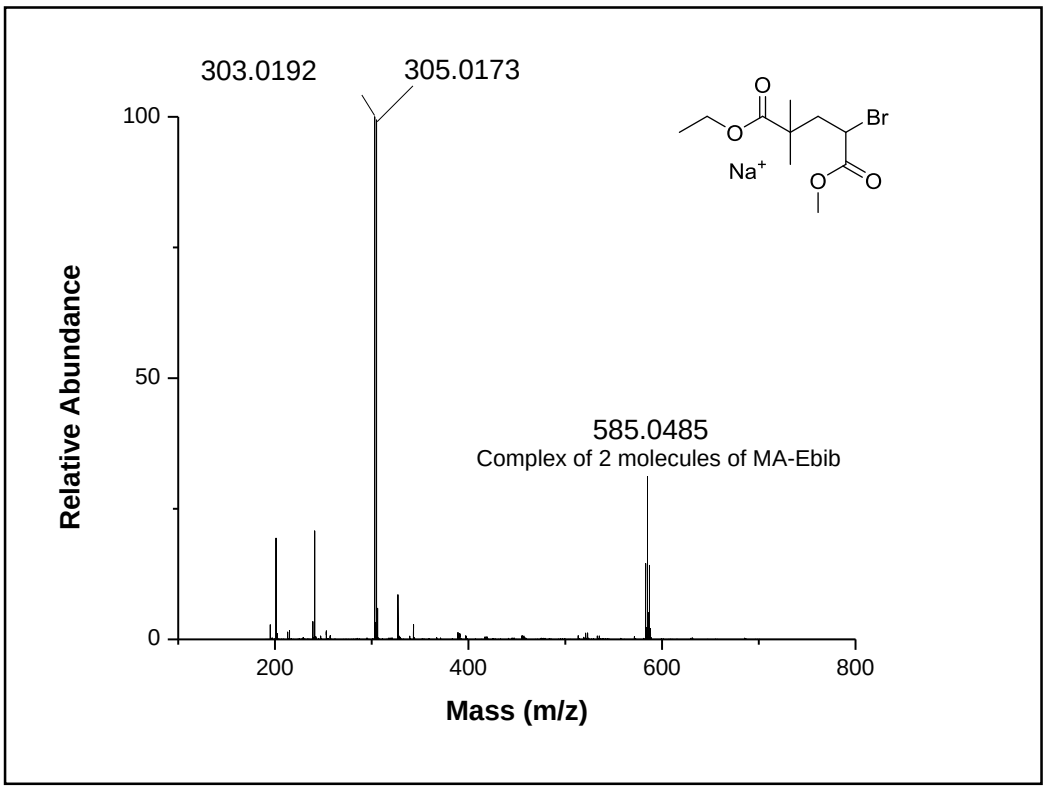

*Figure 45: ESI-MS of MA-Ebib (**11**)*

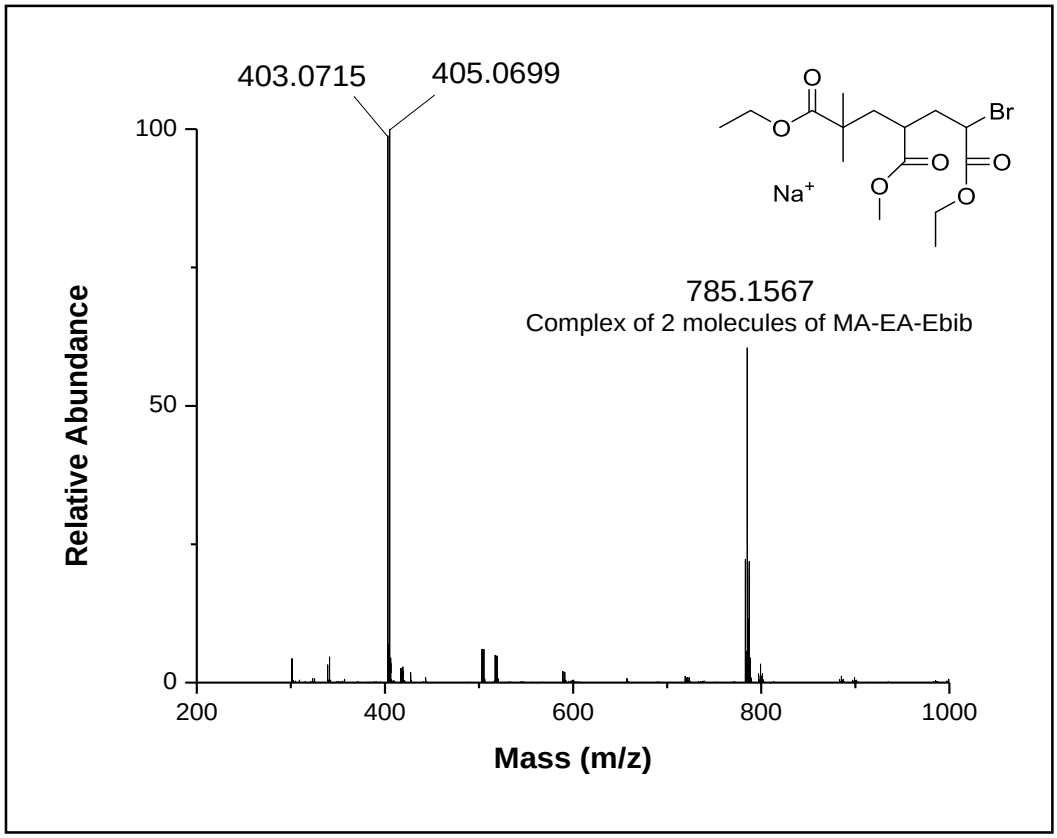

*Figure 46: ESI-MS of MA-EA-Ebib (**12**)*

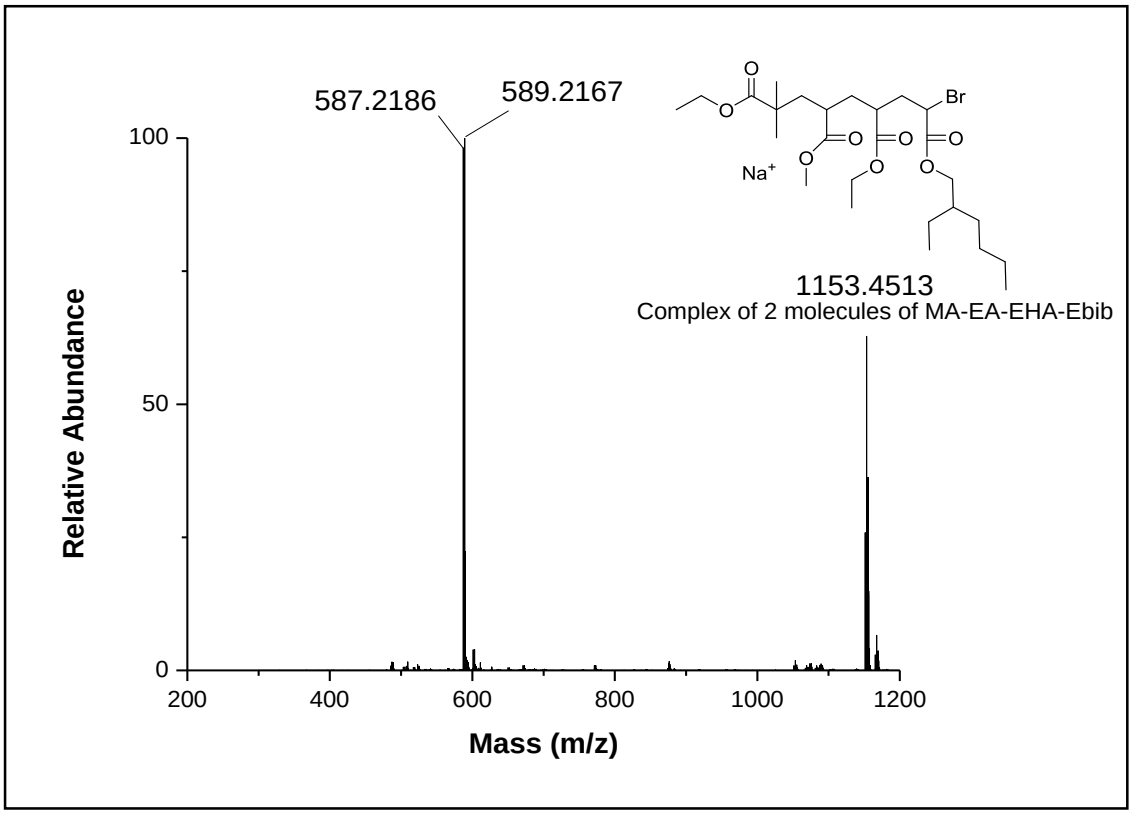

*Figure 47: ESI-MS of MA-EA-EHA-Ebib (**13**)*

Because SUMI oligomers with a different number of acrylate insertions have a different polarity, the first two insertions can be purified with classical column chromatography instead of rec-SEC. This technique is easier to perform and does not take much time contrary to rec-SEC purification. Another advantage is less loss of product with isolated yields of 40% for MA-Ebib (**11**) where the yield of MA-DoPAT (**2**) only was 7%. To make grafting onto alkyne functionalized silica particles possible an azide end group modification on MA-EA-EHA-Ebib (**13**) was performed. The Br-group is transformed into an N_3-group through azidation with a yield of 69%. The ESI-MS of this product is shown in Figure 48.

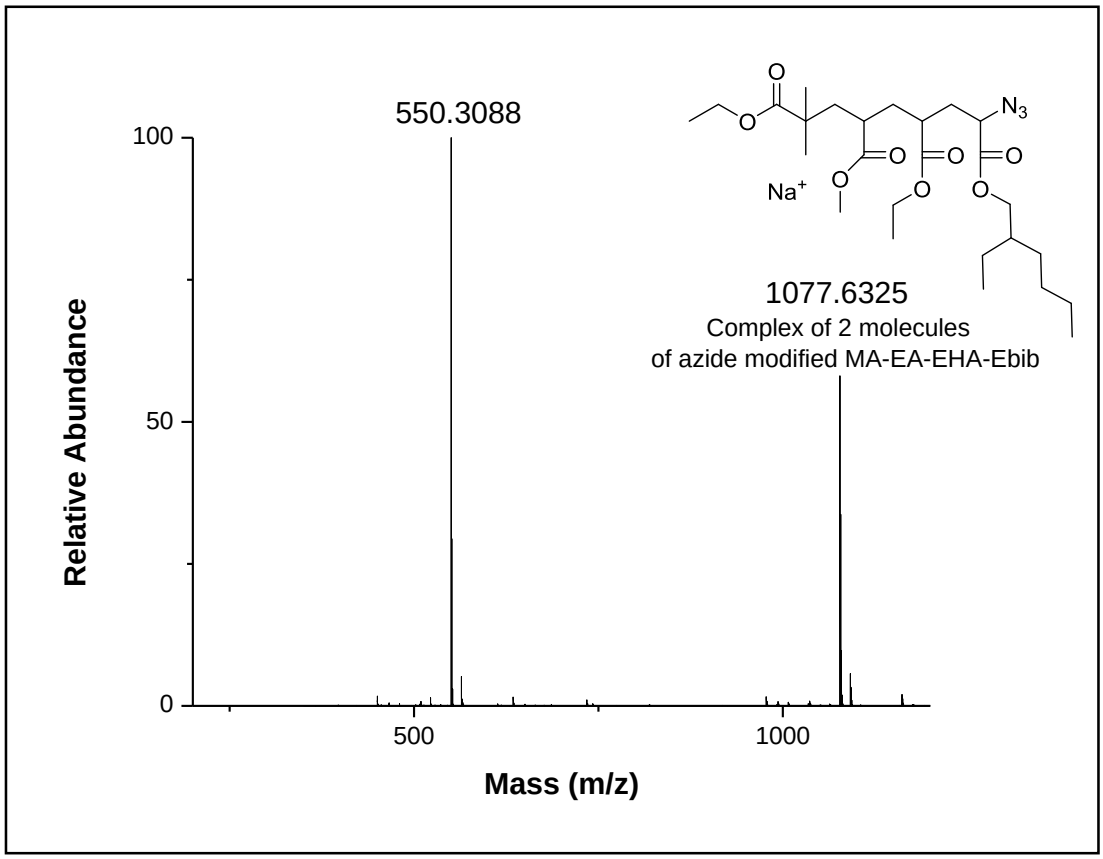

*Figure 48: ESI-MS of azide modified MA-EA-EHA-Ebib (**14**)*

3.3.2 Functionalization of silica particles

To attach the azide modified photo-CMP SD oligomer onto silica particles these particles need to be functionalized. This functionalization consisted of two steps. In a first step TESPPA (**15**) was synthesized through EDC coupling of propiolic acid and APTES. In a second step silica particles (1 µm) were silanized with product (**15**). No piranha treatment on the particles was performed, because of the negative influence on the silanization. Figure 49 displays the TGA results of the alkyne functionalized silica particles (**16**). TGA data indicate that the attachment of TESPPA (**15**) onto the pristine particles was successful. It also confirms that piranha treatment is not necessary.

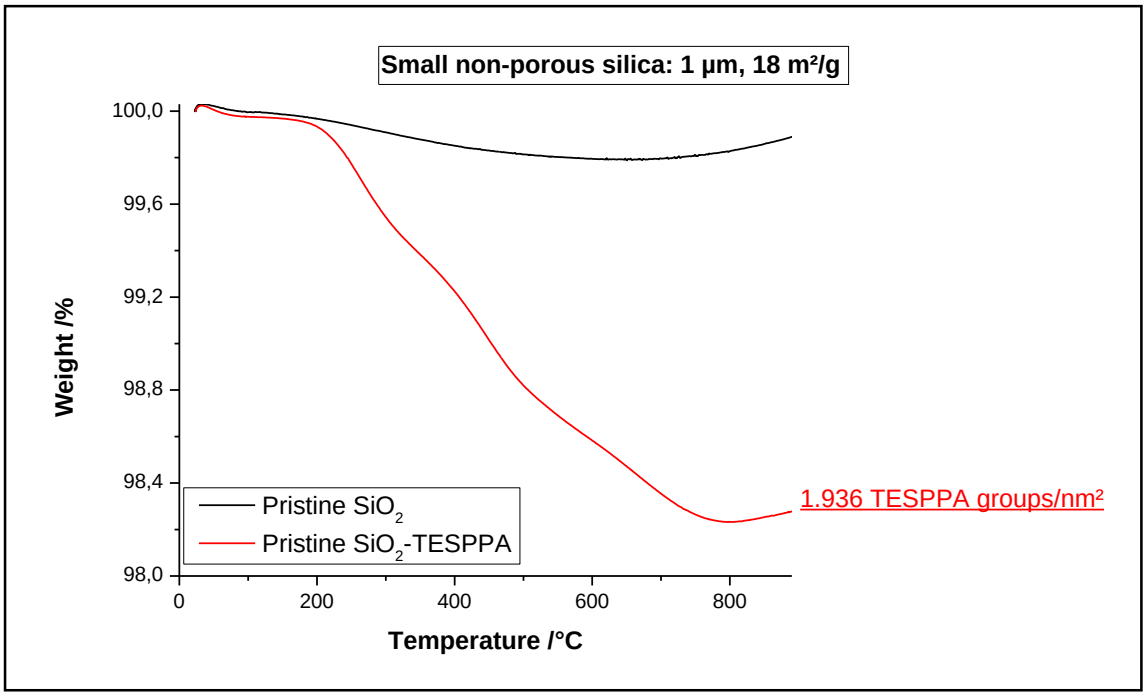

*Figure 49: TGA result of alkyne functionalized silica particles (**16**)*

3.2.3 CuAAC-click coupling

The functionalized particles and azide modified photo-CMP SD oligomer are coupled together through copper-click chemistry. The TGA results are shown in Figure 50. With this approach the highest surface grafting density of both silane and SD oligomer was achieved in this research. With CPD-TTC RAFT polymerization only a surface grafting density of 0.082 SD oligomer groups/nm² was obtained. With photo-CMP the surface grafting density increased more than 2-fold (0.1777/0.082 = 2.16).

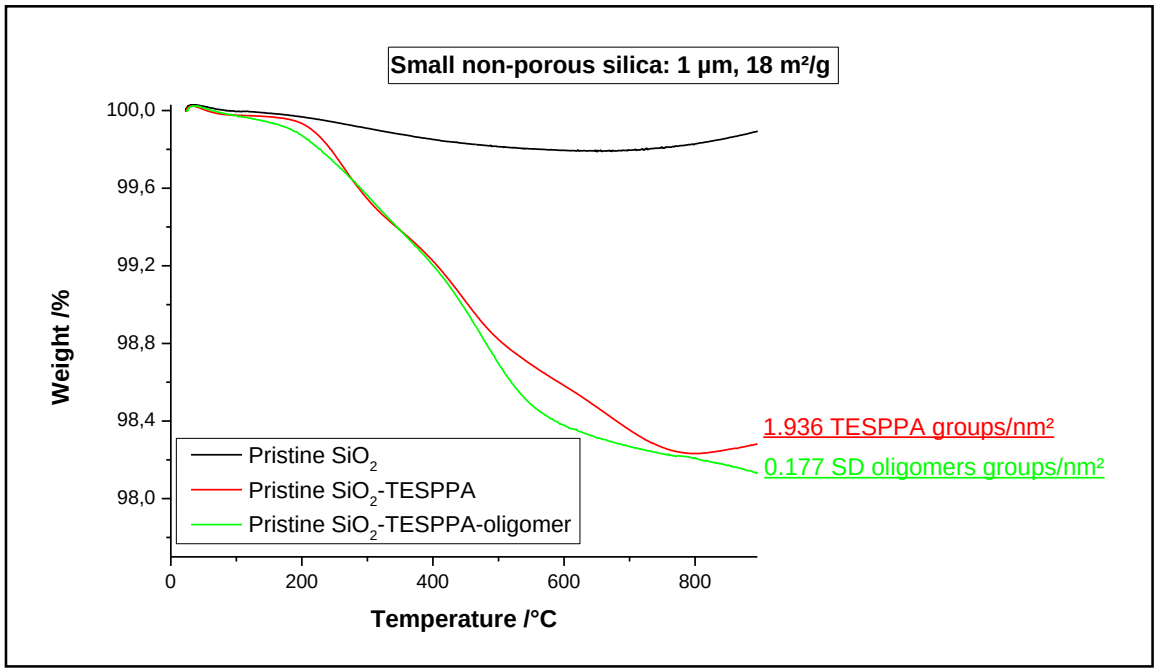

*Figure 50: TGA result of alkyne functionalized silica particles (**16**) and alkyne functionalized silica particles with attached MA-EA-EHA-Ebib oligomer (**17**)*

There are significant differences between the photo-CMP procedure and the DoPAT RAFT procedure. Because of the group exchange between AIBN and the DoPAT RAFT agent the purification of the SD oligomer mixtures is almost impossible. The yields are low contrary to the yields achieved with photo-CMP. The purification in the photo-CMP procedure is easier, because classic column chromatography can be applied. There is also no exchange of the Br-group which results in pure end products.

For silanization with TESPPA (APTES-derivate) a surface grafting density of 1.936 groups/nm² (Figure 49) was achieved. This is within the expected range according to previous studies (1.69 to 2.5 APTES groups/nm²) which indicates a successful silanization. Silanization with CPTMO resulted in a surface grafting density of 0.331 groups/nm² (Figure 44). In comparison with TESPPA silanization this is a decrease of 83%. Therefore, it can be concluded that in these experiments silanization with TESPPA is preferred and the procedure with CPTMO need to be optimized.[39]

In the CuAAC-click reactions surface grafting densities of 0.082 alkyne modified CPD-TTC SD oligomer groups/nm² (Figure 44) and 0.177 azide modified Ebib SD oligomer groups/nm² (Figure 50) were obtained. Previous studies report surface grafting densities of 0.27 to 0.29 polystyrene or polyacrylamide groups/nm². A reason for the lower SGD could be the amount of solvent used in the performed experiments. Therefore, a higher SGD is possibly achieved if the reaction is executed with a lower amount of solvent. Another suggestion is using $CuSO_4$ and ascorbic acid instead of Cu(I)Br and PMDETA as catalysts. [55], [56]

Synthesizing SD oligomers through CPD-TTC RAFT followed by alkyne modification and attachment onto azide functionalized silica particles is possible but the photo-CMP procedure shows the most promising results. Both procedures could be optimized in a further project to achieve higher surface grafting densities of both silanes and SD oligomers. Also synthesizing MHB SD oligomers could be investigated. If the optimization of the attachment procedures is completed and the synthesis of MHB SD oligomers is possible, both methods can be combined to simplify the purification and open pathways to the future.

4 Conclusion

Synthesizing SD oligomers through RAFT polymerization with DoPAT as a transfer agent is not recommended. DoPAT RAFT agent carries an acid group that makes the purification difficult and insufficient. This acid group causes two main problems. A first problem is that the acid group can be exchanged by an isobutyrylnitrile group derived from AIBN. This problem can be partially solved by using a low amount of initiator, but the initiator will still be present. This results in a loss of final product, because these AIBN groups cannot be used in EDC/NHS graftings. A second problem is the interaction of the acid group with the material (cross-linked polystyrene) of the rec-SEC column. Complex chromatograms are achieved and the seemingly pure end fractions are not pure at all. Therefore, it can be concluded that DoPAT is not preferred as a transfer agent for synthesizing RAFT SD oligomers with the aim of attachment onto functionalized particles.

A more promising approach is synthesizing SD oligomers with CPD-TTC as a transfer agent followed by trithiocarbonate modification and attachment of the resulting alkyne SD oligomers with CuAAC onto azide-silica. The group exchange that causes problems with the purification of DoPAT RAFT SD oligomer mixtures does not occur. This results in a simpler purification with less loss of desired product. Further experimenting with different types of monomers is suggested to discover the boundaries of this procedure.

Piranha treatment of silica particles is unnecessary to obtain a sufficient surface grafting density of silanes. Treating particles with piranha solution makes them more hydrophilic which results in repelling of the silane. Also, silanes can cross-link in the presence of water.

Synthesizing SD oligomers through photo-CMP is also a promising procedure. The simple purification method of SD oligomer mixtures resulted in higher yields. The bromide groups can be modified into azides and can be grafted to alkyne-silica. With this approach a surface grafting density of 0.177 SD oligomer groups/nm² can be achieved which is an increase of 116% in comparison with the CPD-TTC RAFT procedure (0.082 SD groups/nm²). The higher surface grafting density and good yields make photo-CMP suitable for further experimenting.

The CPD-TTC RAFT and photo-CMP procedure proved successful, but can be optimized to achieve higher surface grafting densities. Also MHB SD oligomers could be used instead of SD oligomers. The synthesis of MHB SD oligomers and subsequently coupling onto functionalized silica particles can be investigated.

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Appendices

Appendix A: Supporting information of materials and experimental

Coupling DoPAT RAFT SD oligomer onto amino functionalized silica particles

Synthesis of DoPAT RAFT SD oligomer

Synthesis of nBuA-DoPAT RAFT agent

Product	Quantity	Eq.	mmol
nBuA	0.200 g	1	1.560
DoPAT RAFT agent	0.547 g	1	1.560
AIBN	0.013 g	0.05	0.079
Butyl acetate	2.600 mL	/	/

ESI-MS (m/z): 501.1998 (nBuA-DoPAT RAFT + Na^+), 496.2205 (nBuA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group).

Synthesis of MA-DoPAT RAFT agent

Product	Quantity	Eq.	mmol
MA	0.500 g	2	5.808
DoPAT RAFT agent	1.018 g	1	2.904
AIBN	0.024 g	0.05	0.146
Butyl acetate	3.700 mL	/	/

ESI-MS (m/z): 459.1664 (MA-DoPAT RAFT + Na^+), 454.1830 (MA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group).

Synthesis of nBuA-EA-DoPAT RAFT agent

Product	Quantity	Eq.	mmol
EA	0.039 g	1	0.389
nBuA-DoPAT RAFT agent	0.190	1	0.396
AIBN	0.003	0.05	0.018
Butyl acetate	1.400 mL	/	/

ESI-MS (m/z): 568.2548 (EA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group), 596.2860 (nBuA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group), 601.2659 (nBuA-EA-DoPAT RAFT + Na^+), 668.3085 (EA-EA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group).

Synthesis of nBuA-EA-DoPAT RAFT agent with unreacted nBuA-DoPAT RAFT agent from previous reaction

Product	Quantity	Eq.	mmol
EA	0.022 g	1	0.219
nBuA-DoPAT RAFT agent	0.105 g	1	0.219
AIBN	0.002	0.05	0.011
Butyl acetate	0.100 mL	/	/

ESI-MS (m/z): 568.2548 (EA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group), 596.2860 (nBuA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group), 601.2659 (nBuA-EA-DoPAT RAFT + Na^+), 668.3085 (EA-EA-EA-DoPAT RAFT + Na^+ with isobutyrylnitrile group instead of acid group).

EDC/NHS coupling reaction between DoPAT PnBuA polymer and amino functionalized particles

Large particles

Product	Quantity	Eq.	mmol
DMAP	0.004 g	0.1	0.033
NHS	0.040 g	1.1	0.347
EDC	0.066 g	1.1	0.344
Amino functionalized particles	0.100 g	/	/
PnBuA polymer (M_n = 7000 g/mol)	/	10-15	/
Pyridine	0.027 g	1.1	0.341

Butyl acetate	5.000 mL	/	/

Small particles

Product	Quantity	Eq.	mmol
DMAP	0.0002 g (0.1 mL out of stock solution)	0.1	0.002
NHS	0.0019 g (1.0 mL out of stock solution)	1.1	0.017
EDC	0.0030 g	1.1	0.017
Amino functionalized particles	0.1000 g	/	/
PnBuA polymer (M_n = 5223 g/mol)	0.2510 g	3.20	0.048
Pyridine	0.0013 g (0.1 mL out of stock solution	1.1	0.016
Butyl acetate	5.000 mL	/	/

Coupling CPD-TTC RAFT SD oligomer onto functionalized silica particles

Alkyne end group modification of CPD-TTC RAFT SD oligomer

Product	Quantity	Eq.	mmol
MA-EA-CPD-TTC SD oligomer	0.064 g	1	0.120
THF	0.320 g	5 times mass of polymer	4.438
Propargyl acrylate	0.132 g	10	1.203
Hexylamine	0.121 g	10	1.198

ESI-MS (m/z): 420.1441 (alkyne modified MA-EA-CPD-TTC + Na^+).

Functionalization of the silica particles

Azidation of the chloro silica particles

Product	Quantity	Eq.	mmol
Chloro functionalized silica particles	0.5590 g	1	0.083*
NaN_3	0.0065 g	1.2	0.100
DMF	5.0 mL	/	/

* Estimation based on following data: Normal surface grafting density of OH-groups = 5 groups/nm². Silica particles have a surface area of 18 m²/g particles. Estimation: $9x10^{19}$ CPTMO-groups/g or 0.149 mmol/g

CuAAC-click reaction between alkyne modified CPD-TTC SD oligomer and azide functionalized particles

Product	**Quantity**	**Eq.**	**mmol**
Alkyne modified CPD-TTC SD oligomer	0.0115 g	6.4	0.0289
Azide functionalized silica particles	0.4543 g	1	0.0045*
CuBr	0.0007	1	0.0049
PMDETA	0.0015	2	0.0087
DMF	5.0 mL	/	/

* Surface grafting density: 0.3325 N_3-groups/nm² (TGA result) = 0.01 mmol/g (surface area of 18 m²/g)

Coupling Ebib photo-CMP SD oligomer onto functionalized silica particles

Synthesis of Photo-CMP SD oligomer

Synthesis of MA-Ebib

Product	**Quantity**	**Eq.**	**mmol**
$CuBr_2$	0.036 g	0.014	0.161
ME_6TREN	0.225 g	0.084	0.977
MA	1.000 g	1	11.616
Ebib	2.270 g	1	11.638
DMSO	3.000 g	50 Vol%	38.397

ESI-MS (m/z): 303.0189 and 305.0169 (MA-Ebib + Na^+)

Synthesis of MA-EA-Ebib Photo-CMP SD oligomer

Product	**Quantity**	**Eq.**	**mmol**
$CuBr_2$	0.014 g	0.014	0.063
ME_6TREN	0.090 g	0.084	0.391
EA	0.463 g	1	4.624
MA-Ebib	1.303 g	1	4.635
DMSO	1.760 g	50 Vol%	22.527

ESI-MS (m/z): 403.0717 and 405.0700 (MA-EA-Ebib + Na^+)

Synthesis of MA-EA-EHA-Ebib Photo-CMP SD oligomer

Product	Quantity	Eq.	mmol
$CuBr_2$	0.0051 g	0.014	0.023
ME_6TREN	0.0325 g	0.084	0.141
EHA	0.3093 g	1	1.678
MA-EA-Ebib	0.6400 g	1	1.679
DMSO	4.4000 g	80 Vol%	56.316

ESI-MS (m/z): 587.2189 and 589.2169 (MA-EA-EHA-Ebib + Na^+)

Azide end group modification of MA-EA-EHA-Ebib

Product	Quantity	Eq.	mmol
MA-EA-EHA-Ebib	0.165 g	1	0.292
NaN_3	0.023 g	1.2	0.354
DMF	1.5 mL	/	/

ESI-MS (m/z): 550.3080 (azide modified MA-EA-EHA-Ebib + Na^+).

Functionalization of the silica particles

Synthesis of N-(3-(triethoxysilyl)propyl)propiolamide (TESPPA)

Product	Quantity	Eq.	mmol
APTES	1.500 g	1	6.776
Propiolic acid	0.522 g	1.1	7.452
EDC	1.429 g	1.1	7.454
DCM	15.0 mL	/	/

1H NMR (400 MHz, CDCl3): δ 8.73 (t, J = 5.5 Hz, 1H), 3.81 (q, J = 14.0, 7.0 Hz, 2H), 3.29 (t, J = 15.3 Hz, 2H), 2.70 (s, 1H), 1.92 (t, J = 13.2, 6.4 Hz, 2H), 1.73 – 1.62 (m, 2H), 1.22 (t, J = 11.7, 5.2, 3.2 Hz, 3H).

CuAAC-click reaction between azide modified Photo-CMP SD oligomer and alkyne functionalized particles

Product	**Quantity**	**Eq.**	**mmol**
Azide modified Photo-CMP SD oligomer	0.0574 g	1.6	0.1089
Alkyne functionalized silica particles	1.0000 g	1	0.0684*
CuBr	0.0097 g	1	0.0676
PMDETA	0.0236 g	2	0.1362
DMF	10 mL	/	/

* Surface grafting density: 2.2884 TESPPA groups/nm² (TGA result) = 0.0684 mmol/g (surface area of 18 m²/g)

Appendix B: Example of surface grafting density calculation

TGA data of large silica particles (70-200 µm, 550 m²/g)

Particle	Weight loss (%)	Weight loss (mg)	Molar mass organic residue (g/mol)
Pristine SiO_2	4.21	0.67407	/
SiO_2-piranha-APTES	7.41	1.09919	221,37

1 g of pristine SiO_2 → Weight loss = 1000 mg x 4.21% = 42.10 mg

1 g of SiO_2-piranha-APTES → Weight loss = 1000 mg x 7.41% = 74.10 mg

↓

For each gram of SiO_2-piranha-APTES there is 32.00 mg of APTES (74.10 mg – 42.10 mg) or **0.144 mmol** (0.032 (g) / 221.37 (g/mol))

Therefore, for each gram of pristine SiO_2 there is **0.156 mmol** of APTES (0.144/ (100%-7.41 %))

0.156 mmol of APTES = **$9.391*10^{19}$ APTES groups for each gram of pristine SiO_2** ($0.156*10^{-3}$ (mol) x $6.02*10^{23}$)

↓

SGD = 0.171 APTES groups/nm² ($9.391*10^{19}$ (groups/g) / $550*10^{18}$ (nm^2/g))

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Ik/wij verlenen het wereldwijde auteursrecht voor de ingediende eindverhandeling:
Investigation and optimization of surface modification protocols to attach sequence defined oligomers onto silica substrates

Richting: **master in de industriële wetenschappen: chemie**
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