# PREPARATION OF $CO_2$-SWITCHABLE AND WATER-REDISPERSIBLE LATEXES USING NITROXIDE-MEDIATED SURFACTANT-FREE EMULSION POLYMERIZATION

by

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# Abstract

The main objective of this research project was synthesizing $CO_2$-responsive latexes by nitroxide-mediated polymerization (NMP). Therefore, 2-(diethylamino)ethyl methacrylate (DEAEMA) as a $CO_2$-responsive monomer was chosen for the synthesis poly(DEAEMA) macroinitiator that can be used as a stabilizer for the preparation of poly(methyl methacrylate), PMMA, latexes.

NMP of DEAEMA was performed in bulk with excellent control and livingness. The synthesized poly(DEAEMA) was then used in the protonated form as a macroalkoxyamine and stabilizer for the preparation of pH-responsive and $CO_2$-switchable latexes with surfactant-free emulsion polymerization. The resultant latex particles were stable with small particle size and narrow size distribution. To simplify the process, PMMA latexes were prepared by one-pot two-step nitroxide-mediated surfactant-free emulsion polymerization. First, DEAEMA was polymerized for the first time in water and then at high conversions, MMA was added to the reaction media and amphiphilic diblock copolymers were formed, which converted to the latex particles when the hydrophobic block reached to the critical chain length based on polymerization-induced self-assembly (PISA) mechanism. However, the synthesized nanoparticles with poly(DEAEMA) shell and PMMA core were not redispersible after coagulation. It was figured out that the main reason for the irreversible coagulation of latex particles was the low glass transition temperature ($T_g$) of poly(DEAEMA) which causes the diffusion of the particles shell into each other. Also, it was demonstrated that DEAEMA is hydrolyzed very fast in the basic conditions and high temperatures suitable for NMP.

To address these issues, dimethaminopropyl methacrylamide (DMAPMA) was used as another $CO_2$-responsive monomer with higher $T_g$ and also hydraulic stability in the synthesis of MMA and styrene latexes. In this case, the synthesized nanoparticles were redispersible by the stimulation of $CO_2$.

# Statement of Co-Authorship

The content of chapter 3 has been published in *Polymer Chemistry* (*Polymer Chemistry*, **2014**, 5, 6163-6170). The content of chapters 4 and 5 have been published in *Macromolecules* (*Macromolecules*, **2015**, 48, 72-80, *Macromolecules*, **2015**, 48, 1952-1958). The material presented in chapter 7 has been submitted to *Macromolecular Reaction Engineering*. Dr. Omar García-Valdez was the co-author of chapter 7. He performed PEGylation experiments and analyzed the results. The bulk of the research was carried out independently by me, under the supervision of Dr. Michael Cunningham. The preparation and editing of this thesis and above-mentioned manuscripts was conducted under the supervision of Dr. Michael Cunningham.

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# List of Abbreviations

| | |
|---|---|
| AN | Acrylonitrile |
| ATRP | Atom transfer radical polymerization |
| BB | BlocBuilder |
| CLRP | Controlled/living radical polymerization |
| CTS | Chitosan |
| CMC | Critical micelle concentration |
| CSIRO | Commonwealth scientific and industrial research organisation |
| DEAEMA | 2-(diethylamino)ethyl methacrylate |
| DMAEMA | 2-(dimethylamino)ethyl methacrylate |
| DMAPMA | Dimethylaminopropyl methacrylamide |
| DIW | Deionized water |
| DLS | Dynamic light scattering |
| DPAIO | 2,2-diphenyl-3-phenylimino-2,3-dihydroindol-1-yloxyl nitroxide |
| FRP | Free-radical polymerization |
| GMA | Glycidyl methacrylate |
| GPC | Gel permeation chromatography |
| IUPAC | International Union of Pure and Applied Chemistry |
| LCST | Lower critical solution temperature |
| MA | Methacrylic acid |
| MMA | Methyl methacrylate |
| MWD | Molecular weight distribution |
| NHS | *N*-Hydroxysuccinimide |
| NIPAM | *N*-Isopropylacrylamide |
| NMP | Nitroxide-mediated polymerization |
| NMR | Nuclear magnetic resonance |
| PDI | Polydispersity index |
| PEGMA | Poly(ethylene glycol)methyl ether methacrylate |
| PISA | Polymerization-induced self-assembly |
| PMMA | Poly(methyl methacrylate) |
| PS | Polystyrene |
| PRE | Persistent radical effect |
| RAFT | Reversible Addition-Fragmentation chain-Transfer |
| RI | Refractive index |
| ROP | Ring-opening polymerization |
| SDS | Sodium dodecyl sulfate |
| SEC | Size exclusion chromatography |
| SEM | Scanning electron microscopy |
| SG1 | *N*-tert-butyl-*N*-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide |
| SFEP | Surfactant-free emulsion polymerization |
| SS | Sodium 4-styrene sulfonate |
| TEM | Transmission electron microscopy |
| TGA | Thermogravimetric analysis |
| THF | Tetrahydrofuran |
| TEMPO | (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl |
| TIPNO | 2,2,5-Trimethyl-4-phenyl-3-azahexane-3-nitroxide |

# Nomenclature

| | |
|---|---|
| $K_p$ | Rate constant of propagation [L·mol$^{-1}$·s$^{-1}$] |
| $K_{act}$ | Rate constant for activation [s$^{-1}$ or L.mol$^{-1}$.s$^{-1}$] |
| $K_{deact}$ | Rate constant for activation [L.mol$^{-}$1.s$^{-1}$] |
| $K_t$ | Rate of termination [L.mol$^{-1}$.s$^{-1}$] |
| $K$ | Equilibrium constant of $k_{act}/k_{deact}$ |
| $j_{crit}$ | Critical chain length |
| p$K_a$ | Acid dissociation constant |
| p$K_{ah}$ | p$K_a$ of the conjugated acid |
| $T_{10H}$ | 10 h half-life |
| $F_{MMA}$ | Weight fraction of MMA |
| $T_g$ | Glass transition temperature |
| $f_{S0}$ | Mole fraction of styrene in the monomer feed |
| $M_n$ | Number-average molecular weight [g. mol$^{-1}$] |
| $M_w$ | Wight-average molecular weight [g. mol$^{-1}$] |
| *Đ* | Dispersity |
| M | Molarity |
| X | Conversion |
| $Z_{ave}$ | $Z$-diameter (nm) |
| r | Molar ratio of nitroxide to initiator |
| $\delta$ | Chemical shift |
| $N_p$ | Number of particles |
| $D_z$ | Diameter of the particle [nm] (intensity value from DLS) |
| $\sigma$ | Particles size distribution (value from DLS) |
| $\zeta$ | Zeta potential [mV] |

# List of publications

A. Darabi, A. R. Shirin-Abadi, J. Pinaud, P. G. Jessop, and M. F. Cunningham, " Nitroxide-mediated surfactant-free emulsion copolymerization of methyl methacrylate and styrene using poly(2-(diethyl)aminoethyl methacrylate-co-styrene) as a stimuli-responsive macroalkoxyamine", *Polymer Chemistry*, **2014**, 5, 6163-6170.

A. Darabi, A. R. Shirin-Abadi, P. G. Jessop, and M. F. Cunningham, "Nitroxide-mediated polymerization of 2-(diethylamino)ethyl methacrylate (DEAEMA) in water", *Macromolecules*, **2015**, 48, 72-80.

A. Darabi, P. G. Jessop, and M. F. Cunningham, "One-pot synthesis of poly((diethylamino)ethyl methacrylate-*co*-styrene)-*b*-poly(methyl methacrylate-*co*-styrene) nanoparticles via nitroxide-mediated polymerization", *Macromolecules*, **2015**, 48, 1952-1958.

A. Darabi, O, García-Valdez**,** P. G. Jessop, and M. F. Cunningham, "Preparation of PEGylated Chitosan via nitroxide-mediated polymerization in aqueous media", *Macromolecular Reaction Engineering*, Accepted.

A. Darabi, P. G. Jessop, and M. F. Cunningham, "Comprehensive review: $CO_2$-responsive polymers", In progress.

A. Darabi, P. G. Jessop, and M. F. Cunningham, "Preparation of $CO_2$-switchable latexes using dimethylaminopropyl methacrylamide (DMAPMA)", In progress.

A. Darabi and M. F. Cunningham, "Preparation of easily water-redispersible latexes by surfactant-free emulsion polymerization", In progress.

A. Darabi and M. F. Cunningham, "Nitroxide-mediated polymerization of poly(poly(ethylene glycol methyl ether methacrylate in water)", In progress.

## Chapter 1

# Introduction

Controlled/living radical polymerization (CLRP) is an effective and versatile method for producing polymers with target molecular weight, functionality, and relatively narrow dispersity. Nitroxide-mediate polymerization (NMP) is one of the main types of CLRP, which employs a nitroxide as a mediating species to establish a reversible deactivation between growing polymer chains. Conducting NMP in aqueous media, the relatively high temperatures required for the decomposition of the alkoxyamines, and difficulty in polymerizing methacrylate monomers are the main challenges of NMP. On the other hand simplicity of the reaction is the main advantage of this technique. Also, NMP does not have issues in terms of residual catalyst as in atom transfer radical polymerization (ATRP) or the smell and colour concerns with reversible addition-fragmentation chain-transfer (RAFT) polymerization. However, there are very few reports related to the NMP of tertiary amine methacrylate-based monomers. Specifically applying NMP for producing $CO_2$-responsive polymers has been not discussed in the literature.

## 1.1 Overview

In this work, NMP in aqueous solution is investigated and different monomers are polymerized for the first time in water by NMP to expand the applicability of this technique. Water is always a preferred solvent from an industrial point of view, and performing CLRP techniques in water is very popular from a scientific point of view. Specifically in this work we focus on the synthesis of pH-responsive tertiary amine-based monomers such as 2-(diethylamino)ethyl methacrylate (DEAEMA) and also PEG-based monomers such as poly(ethylene glycol)methyl ether methacrylate (PEGMA) for producing macroinitiator by NMP that can be used as stabilizer for the preparation of latexes. To show the application of the synthesized macroinitiators, poly(DEAEMA) and poly(PEGMA), they are used as stabilizers in the synthesis of PMMA latexes and modification of chitosan (CTS), respectively. Since DEAEMA is $CO_2$-responsive, the use of this monomer in the production of $CO_2$-responsive latexes is also investigated. The main advantage of using $CO_2$ as a trigger in the synthesis of $CO_2$-responsive polymers is that $CO_2$ has low toxicity, is biocompatible, abundant, inexpensive, and is non-accumulating in the system. We will also investigate the use of dimethylaminopropyl methacrylamide (DMAPMA) as an alternative for DEAEMA in the preparation of $CO_2$-responsive latexes.

Chapter 2 of this thesis is a literature review on NMP and $CO_2$-switchable materials. In chapter 3 bulk polymerization of DEAEMA for the synthesis of PDEAEMA is investigated and then the usage of the synthesized macroinitiator for the preparation of PMMA latexes is explained. Chapter 4 explains the synthesis of PDEAEMA in water and the effect of different parameters on the kinetics of the polymerization. Chapter 5 contains the description of the one-pot synthesis of PMMA latexes using PDEAEMA stabilizer. Chapter 6 is related to the NMP of PEGMA in water and use of the synthesized poly(PEGMA) for the modification of chitosan. Using DMAPMA for producing $CO_2$-responsive latexes is demonstrated in chapter 7. Conclusions and recommendations for future work are presented in chapter 8.

## 1.2 Research objectives

The primary objectives of my doctoral research are:

- Study NMP of DEAEMA as a pH-responsive and $CO_2$-switchable monomer in different polymerization systems.
- Study NMP of PEGMA in aqueous solution.
- Perform nitroxide-mediated surfactant-free emulsion polymerization of MMA using poly(DEAEMA) macroalkoxyamine.
- Modify chitosan using poly(PEGMA) by *grafting to* and *grafting from* approaches.
- Prepare $CO_2$-responsive latexes under $CO_2$ atmosphere using DMAPMA as a $CO_2$-switchable comonomer.

## 1.3 Summary of original contributions

- The first NMPs of DEAEMA and PEGMA were performed in water with a high degree of control and livingness.
- The one-pot two-step production of PMMA latexes was conducted using NMP of DEAEMA followed by *in-situ* chain extension by MMA.
- Modification of chitosan was carried out by *grafting to* and *from* approaches using poly(PEGMA) synthesized previously by NMP in water.
- $CO_2$-switchable PS and PMMA latexes were prepared using DMAPMA as a $CO_2$-switchable comonomer.

# Chapter 2

# Literature review

The main focus of my Ph.D. was the synthesis of different polymers and latexes using DEAEMA and DMAPMA as $CO_2$-switchable comonomers. Therefore, the literature review has been divided in two main parts. The first part is related to NMP, while second part is related to $CO_2$-switchable materials, which in recent years has attracted considerable research attention.

## 2.1 Nitroxide-mediated polymerization (NMP)

In free radical polymerization (FRP) the average lifetime of polymer chains is less than 1 second and all polymer chains die very quickly. Therefore, a living polymerization system is not achievable and block copolymers cannot be synthesized by FRP.[1] Anionic polymerization, developed by Szwarc[2], had a major impact on the development of living polymers. To keep polymer chains living in this system, chain transfer and termination reactions are eliminated. This is achievable by completely eliminating any moisture or oxygen, which requires applying high vacuum and very low temperatures (~ -80 °C).[3] Furthermore, there is a limited range of monomers polymerizable by anionic polymerization. Reversible deactivation radical polymerization (the new terminology of “reversible deactivation radical polymerization” (RDRP) has been proposed by IUPAC for controlled/living radical polymerization[4]) can be used for polymerizing many different monomers at mild conditions with a high level of control over their structure. In CLRP, the initiation occurs very fast and all chains grow at the same time. Since irreversible termination reactions occur at a relatively low level, the livingness of the most of the chains is preserved and the addition of a second block, in order to prepare diblock copolymers, is possible. The fraction of dead chains in CLRP is usually less than 10%.[1] Atom transfer radical polymerization (ATRP), nitroxide-mediated polymerization (NMP), and reversible addition-fragmentation chain transfer polymerization (RAFT) are the main types of CLRP. The first two mechanisms are based on reversible termination and the third one is based on reversible chain transfer.[5] CLRP has the advantages of both free radical polymerization and living polymerization[6]: (i) flexible polymerization conditions, and (ii) a broader range of polymerizable monomers by CLRP.

NMP was used in this research in order to synthesis homopolymers and diblock copolymers in bulk, solution, and emulsion. In the 1980s, Solomon and coworkers[7] at CSRIO (Commonwealth Scientific and Industrial Research Organization) discovered that carbon-centered radicals in free radical polymerization can be trapped by nitroxides to produce controlled and living low molecular weight polymers. In 1993, Georges et al.[8] used 2,2,6,6-tetramethylpiperidinyl-*N*-oxyl (TEMPO) as a nitroxide in the RDRP of styrene. This work later became the foundation of nitroxide-mediated polymerization.

### 2.2.1 Kinetics of NMP

In NMP, a thermally unstable alkoxyamine is decomposed homolytically and produces nitroxide and initiator radicals (Figure 2.1).[9] NMP can be employed for the synthesis of polymers with relatively narrow molecular weight distributions and different polymeric structures can be made by this technique (Figure 2.2).

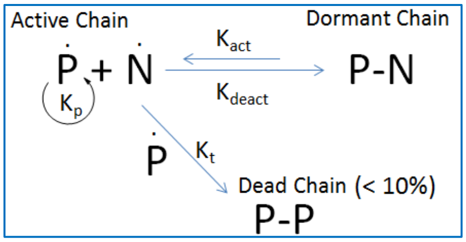


Figure 2.1 General scheme of NMP.

Nitroxides are stable radicals that usually do not self-terminate but are able to react with propagating radicals and deactivate them. Activation reaction occurs every 100 to 1000 seconds while deactivation takes place very fast (in a fraction of a second). However, during the short period time of the activation, some monomers (1 to 5 monomers) are added to the growing chains.[3] Therefore, all the chains have an almost equal chance for growing, and finally a polymer with a narrow molecular weight distribution (MWD) is produced. At the start of the polymerization, the concentration of both propagating radicals and nitroxides increases with time. Nitroxides do not undergo mutual irreversible termination reactions, but propagating radicals can terminate each other. Therefore, as conversion increases, propagating radicals have more chance to react with each other and the population of propagating radicals decreases while the concentration of nitroxide increases. Nitroxide molecules deactivate the propagating radicals (deactivation) and convert them to a dormant state. After a while the dormant chains will be activated and continue growing (activation). Finally, a balance (equilibrium) of activation-deactivation is established. This phenomenon is called persistent radical effect (PRE), which was first explained by Fischer.[10]

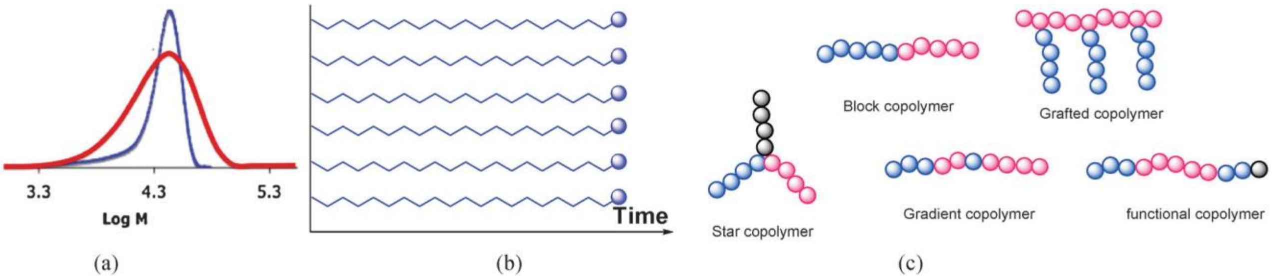


Figure 2.2 (a) PDI in FRP (bold line) and NMP (thin line). (b) live polymer chain ends. (c) Examples of polymers afforded by NMP.[9]

There are two types of initiation systems: bicomponent and monocomponent. In the bicomponent system, the initiator and the nitroxide are individually supplied for the reaction. The ratio of the initiator to the nitroxide is very important since it will affect the kinetics of the polymerization.[6] An example of this system is VA-044 (initiator) and SG1 (nitroxide), which has been used in some of the experiments of this research for the preparation of $CO_2$-switchable diblock copolymer. In the monocomponent system an alkoxyamine is used that can be homolytically decomposed by heat to produce initiator and nitroxide. An example of this system is BlocBuilder.[11] Commonly in the NMP of methacrylic monomers, a small amount of free nitroxide is used to increase the control of the reaction at the start of the polymerization. McHale et al.[12] have investigated the effect of excess nitroxide in the NMP of methyl methacrylate.

### 2.2.2 Range of monomers and nitroxides for NMP

Styrene and styrenic derivatives have been polymerized by different nitroxides. In most cases, temperatures above 100 ºC are required because of the slow polymerization rate. TEMPO-mediated polymerization is performed at high temperatures (~ 120-135 ºC) but in the case of SG1, polymerization can be carried out at much lower temperatures (~ 90-120 ºC).[3] For the methacrylic monomers, the situation is different. The only reported nitroxide that can produce homopolymer of methyl methacrylate (MMA) with good control (PDI< 1.4 up to 60% conversion) and livingness is DPAIO (2,2-diphenyl-3-phenylimino-2,3-dihydroindol-1-yloxyl).[13] This nitroxide is not available commercially. NMP of MMA with BlocBuilder™ is possible with the addition of a small amount of styrene in the monomer mixture (<10 mol %) in order to suppress the fast rate of the polymerization reaction by decreasing the average activation-deactivation equilibrium constant (*K*) and obtaining a controlled/living polymerization system.[14]

The common nitroxides for NMP are TEMPO (2,2,6,6-tetramethyl-piperidine-*N*-oxyl), TIPNO (2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide), and SG1(*N*-tert-butyl-*N*-(1-diethyl phosphono-2,2-dimethylpropyl) nitroxide). The most common alkoxyamine is BlocBuilder™ (*N*-(2-methylpropyl)-*N*-(1-diethylphosphono-2,2-dimethylpropyl)-O-(2-carboxylprop-2-yl)hydroxyl-amine). Recently new alkoxyamines such as *N*-hydroxysuccinimidyl-BlocBuilder™ (NHS-BlocBuilder™)[15] and 2,2′,5-trimethyl-3-(1-phenylethoxy)-4-tert-butyl-3-azahexane, (styryl-TITNO)[16] have been synthesized, which can be decomposed at lower temperatures. The complete list of all the synthesized nitroxides and monomers polymerized by NMP has been presented in a review paper from Charleux's group.[6]

### 2.2.3 NMP in the dispersed media

Transition of NMP from homogeneous systems to dispersed media is challenging due to partitioning effects, coagulation, exit of radicals from particles, and different loci of polymerization.[3] As the main part of the propagation reactions happen in the monomerswollen particles, solubility of the nitroxide in the monomer phase is crucial for having effective activation-deactivation cycles.[6]

### Emulsion

In a typical emulsion polymerization system, the reaction medium is liquid (usually water). A hydrophobic or slightly water-soluble monomer is dispersed in water by means of a surfactant (emulsifier). The size of the dispersed particles depends on the ratio of surfactant to monomer (more surfactant leads to smaller particles).[17] Another component in the emulsion polymerization is a water-soluble initiator which is decomposed thermally and produces the initiating radicals in water. These radicals attack a small fraction of the monomer dissolved in the aqueous phase and start the propagation. If the concentration of surfactant exceeds its critical micelle concentration (CMC), micelles are formed by the aggregation of the excess surfactant. Usually each micelle (2-10 nm in size depending on the surfactant concentration) contains 50-150 surfactant molecules.[17]

Since the concentration of dissolved monomer in the aqueous phase is very low, oligoradicals (formed by the reaction of initiator and monomer in the water phase) grow slowly, and after a while they become hydrophobic enough to enter the micelles. The total area of micelles is much larger than that of monomer droplets; therefore, radicals have a higher chance to enter the micelles.[17] Micelles become polymer particles after entering radicals, and this process is called heterogeneous nucleation (micellar nucleation). If the oligoradicals grow more than the critical length ($j_{crit}$) before entering into the micelles, they precipitate in the water phase and are stabilized by the surfactant to form polymer particles (primary particles).[1] This process is called homogeneous nucleation. Primary radicals can coagulate and form aggregate particles, which are colloidally stable. These aggregates can grow by absorbing monomer and are converted to the latex particles. This process is called coagulative nucleation.[18]

The early attempts at performing TEMPO-mediated emulsion polymerization were not successful because of the latex instability as a result of droplet nucleation[19,20] but some TEMPO derivatives such as amino-TEMPO and acetoxy-TEMPO resulted in satisfying results, which were attributed to the hydrophilic nature of those nitroxides.[20] To suppress droplet nucleation, which was found to be the main reason of the coagulation in the TEMPO-emulsion polymerization, Cunningham and co-workers[20] used a combination of 4-stearoyl-TEMPO as an inhibitor of the droplet nucleation and TEMPO as the mediating nitroxide in *ab* initio emulsion polymerization of styrene at 135 °C with SDBS as surfactant. To eliminate the coagulation, the ratio of TEMPO to 4-stearoyl-TEMPO was adjusted to 1.33.

The invention of SG1 and BlocBuilder™ improved the situation to a large extent. BlocBuilder™ can thermally decompose to produce initiator and nitroxide (Figure 2.3). BlocBuilder™ is water soluble in its ionized form, which is a great advantage for emulsion polymerization.[21]

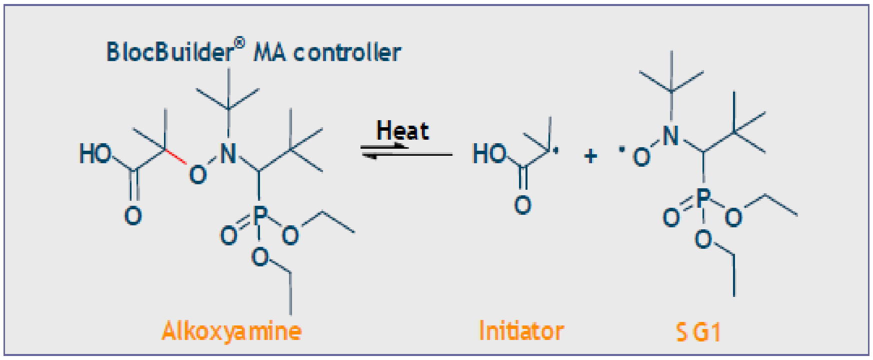


Figure 2.3 Decomposition of BlocBuilder to initiator and nitroxide SG1. Reprinted from reference [21].

In order to eliminate droplet nucleation in the early stages of the polymerization, Charleux and co-workers[22] used a two-step SG1-mediated emulsion polymerization of *n*-butyl acrylate and styrene (Figure 2.4). The polymerization was controlled and living and the latex was stable with a narrow molecular weight distribution. To be more industrially viable, the semibatch of this process was conducted by the same group.[22] In this process, monomer was added continuously during the course of the polymerization. This addition was fast compared to the polymerization time; therefore, the probability of the side reactions as a result of starved conditions was low. The final latex was stable and polymerization showed all characteristics of a controlled/living system (Figure 2.5).

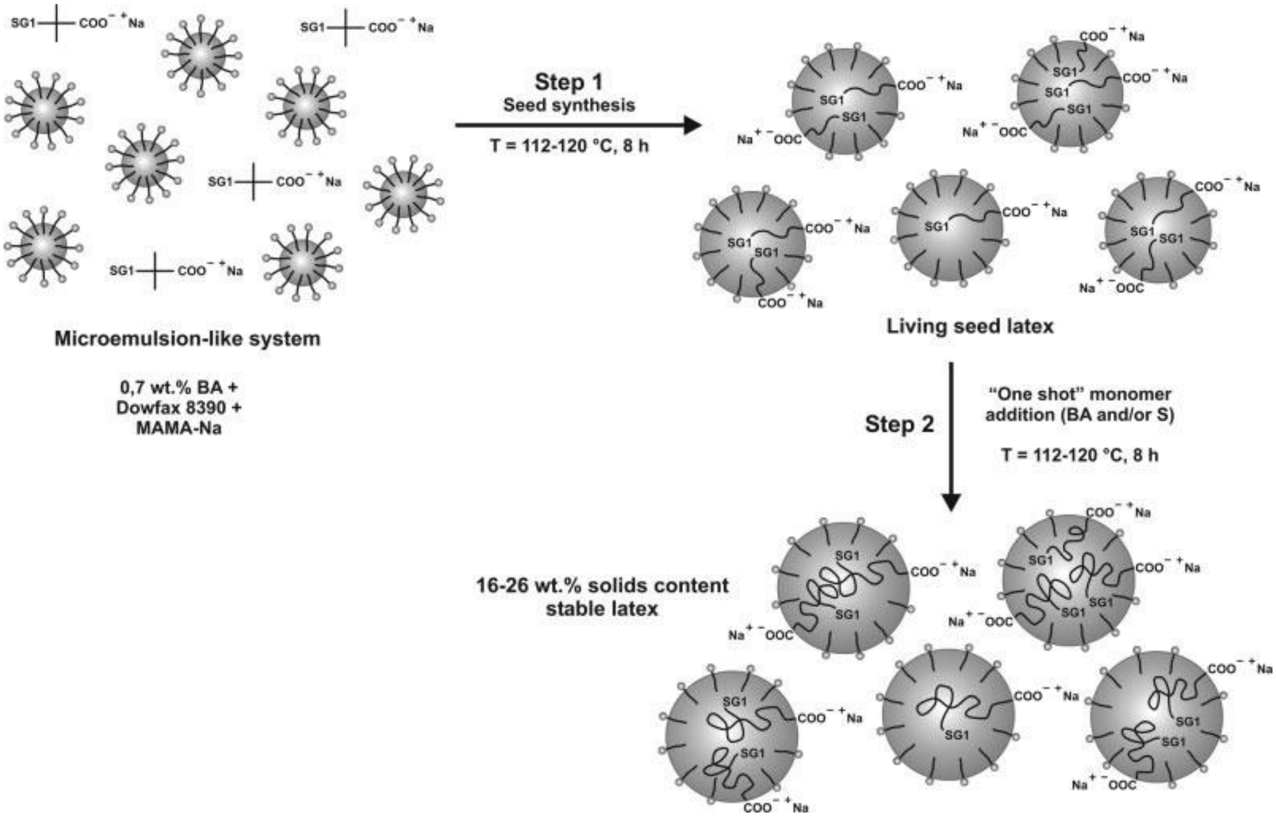


Figure 2.4 Two-step emulsion polymerization process. Reprinted from reference [22].

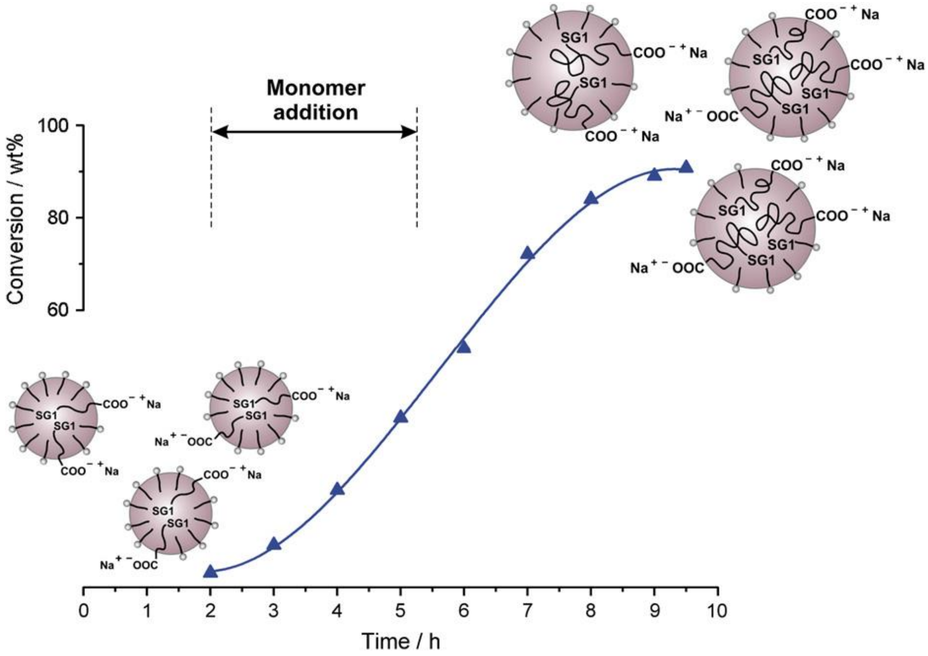


Figure 2.5 Semibatch SG1-mediated emulsion polymerization. Reprinted from reference [22].

Cunningham et al.[23] reported SG1-mediated surfactant-free emulsion polymerization of styrene. The stability of the latex was provided by the sulfate end group of potassium persulfate (KPS) which is a water-soluble initiator. One of the important parameters in the success of the polymerization was pH, which was adjusted by the amount of the $K_2CO_3$ added to the system.

## Miniemulsion

The main difference between emulsion and miniemulsion is in the particle nucleation mechanism (Figure 2.6). In miniemulsion, a high shear device such as ultrasonicator is used to produce a dispersion of monomer droplets with submicronic size (50-1000 nm). A highly hydrophobic compound such as hexadecane or a high molar mass polymer is used as a costabilizer to suppress Ostwald ripening.[24] An alkoxyamine-terminated macroinitiator can be used as costabilizer as well.[6] Contrary to emulsion polymerization, the concentration of surfactant in miniemulsion polymerization is kept below CMC to prevent micellar nucleation. The polymerization occurs in the droplets and the size of the droplets does not change during the reaction (final latex particles are a copy 1:1 of the starting droplets).[25]

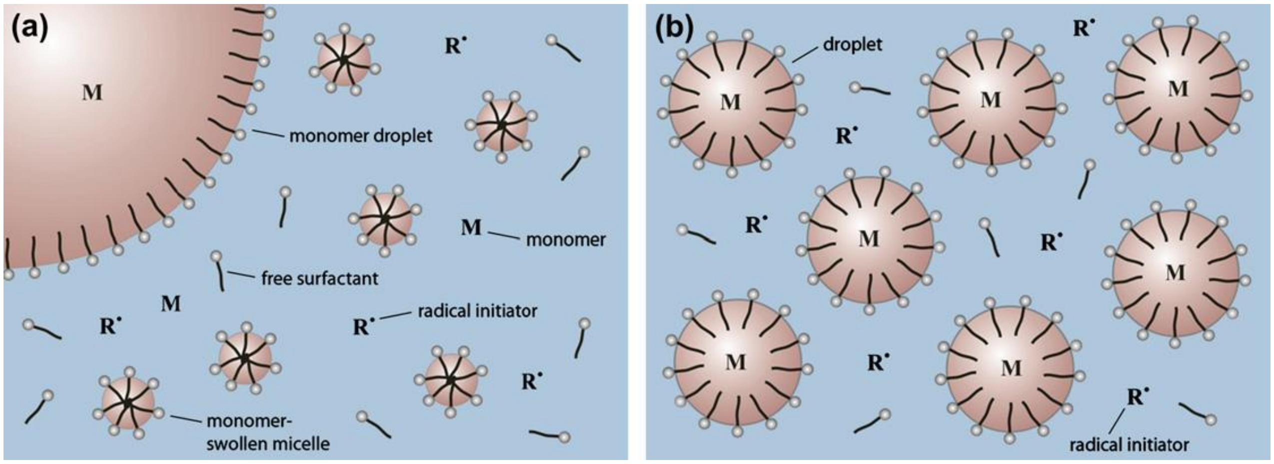


Figure 2.6 Initial state of polymerization in emulsion (a) and miniemulsion (b). Reprinted from reference [25].

The first TEMPO-mediated living radical miniemulsion polymerization of styrene with benzoyl peroxide (BPO) as the initiator was reported by El-Aasser group.[26] During the last decade many research studies have been conducted in the field of nitroxide-mediated miniemulsion polymerization with TEMPO and SG1. Cunningham[3] reviewed NMP in miniemulsion based on the nitroxide type. Conversions are limited to 60-70% in most TEMPO-mediated miniemulsion polymerization because of alkoxyamine disproportionation reactions. Cunningham and coworkers[27] performed a semibatch addition of nitroxide-scavenging additives such as ascorbic acid in TEMPO mediated styrene miniemulsion. Conversions of more than 98%

were obtained in short times (~ 2-3 h). Also, as a result of shorter polymerization time, higher livingness was achieved. SG1 is more flexible in conducting emulsion and miniemulsion polymerization since it requires lower temperature and a wider range of monomers can be polymerized by SG1.[25]

### 2.2.4 Synthesis of block copolymers by NMP

The general strategy for the preparation of a diblock copolymer is the synthesis of the first block and the extension of the second block. This method is called the sequential addition of monomers.[17] The first block can be purified by different methods before addition of the second block. In this case, the first block acts as the initiator for the polymerization of the second block. Therefore, the first block is considered as a macroinitiator. Also, the first block can be used without any purification (*in situ*). Difunctional alkoxyamines have been also employed for the synthesis of di- and triblock copolymers.[6] SG1, TIPNO, and TEMPO have been used in designing many different block copolymers by NMP.[6] Homopolymers, copolymers, diblock copolymers, graft copolymers, and cross-linked polymer particles have been prepared by NMP in emulsion.[28]

### 2.2.5 Polymerization-induced self-assembly (PISA)

If amphiphilic block copolymers are dissolved in a selective solvent (a good solvent for one block and a non-solvent for the other block), the copolymer chains associate reversibly to form micellar aggregates. Insoluble block forms the core while the soluble block forms the corona of the micelle.[29] These block copolymer micelles have lower CMC compared to the low-MW surfactants which is a great advantage in many applications such as drug delivery.[29]

Amphiphilic block copolymers can be synthesized by CLRP methods such as NMP. A relatively new method is based on the in *situ* chain extension of a hydrophilic block (prepared by CLRP in water) with a hydrophobic block and the self-assembly of the resultant diblock copolymer.[30] In fact, the hydrophilic block plays the role of the initiator for the extension of the hydrophobic block (Figure 2.7). This process is called polymerization-induced self-assembly (PISA).[30] Compared to anionic polymerization; the main advantage of synthesizing diblock copolymer by NMP or other CLRP methods is the compatibility of the reaction medium with water. Thus, block copolymers can be synthesized in aqueous media, which is more environmentally friendly. Amphiphilic block copolymers can be used as stabilizers (surfactants) in emulsion polymerization.[30] Also, other unique properties of block copolymers are their ability to be used as the emulsifier for a system of two immiscible liquids.[31] In such a condition, each of the liquids are non-solvents for one of the blocks of the block copolymer but a selective solvent for the second block.

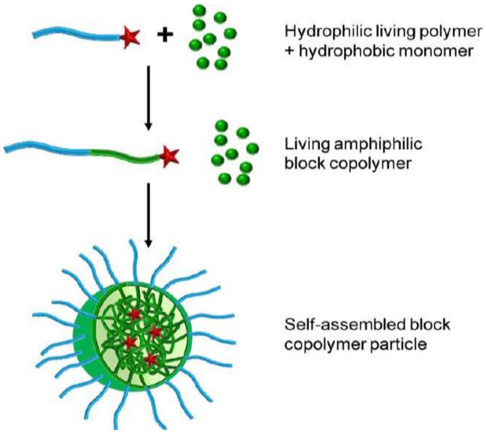


Figure 2.7 Polymerization-induced self-assembly (PISA). Reprinted from reference [30].

## 2.3 Switchable materials

Switchable materials are materials whose properties can change with the application of a trigger. There are many potential applications for these switchables in different processes in order to decrease waste, increase energy efficiency, reduce material consumption and as a result cost reduction, and finally to make processes greener. One important type of switchable materials is $CO_2$-switchable materials. $CO_2$ is an ideal trigger for switchable or stimuli-responsive materials because it is benign, inexpensive, green, abundant, and does not accumulate in the system. Many different $CO_2$-responsive materials including polymers, latexes, solvents, solutes, gels, surfactants, and catalysts have been prepared so far. In my research, I have employed DEAEMA and DMAPMA as $CO_2$-switchable comonomers and stabilizers, which acted like surfactants. I have also used VA-061 as a $CO_2$-switchable initiator for producing $CO_2$-switchable latexes. Therefore, in the following sections, $CO_2$-switchable surfactants, $CO_2$-switchable monomers, $CO_2$-switchable initiators, and $CO_2$-switchable latexes are discussed in more detail.

### 2.3.1 $CO_2$-switchable surfactants

In many applications, materials such as polymer latexes are required to react to a specific stimulus or trigger such as $CO_2$.[32] Stimuli-responsive materials exhibit reversible changes in their physical or chemical properties in response to external triggers such as temperature, pH, light, or voltage.[33] However, there are major limitations in applying these triggers including economical and environmental costs and product contamination.[33] Instead, $CO_2$ as a benign, inexpensive, abundant, and non-toxic trigger for stimuli-responsive materials has received great attention during the last decade.[34]

In 2006, $CO_2$-switchable surfactants based on the long-chain alkylamidines were introduced, which could be easily switched on and off in aqueous media in the presence of $CO_2$ (Figure 2.8).[35] In this case, bicarbonate salts rather than carbamate salts were formed upon $CO_2$-addition. Components **1a** and **1b** are protonated (switched on) by bubbling $CO_2$ in their aqueous solutions and converted to components **2a** and **2b.** In the protonated form they can stabilize latex particles due to the existence of electrostatic repulsive forces**.** When they are deprotonated (switched off) by removal of $CO_2$ from the system, the latex is destabilized and coagulated.

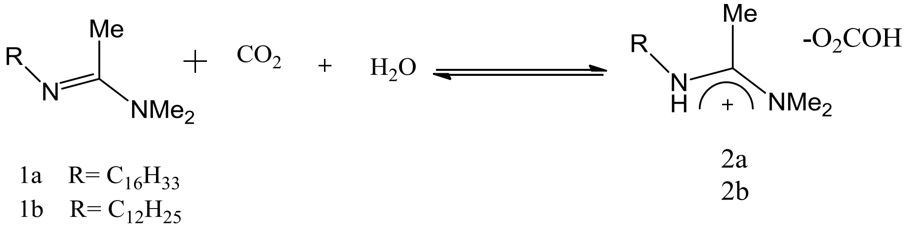


Figure 2.8 $CO_2$-switchability of amidine-based switchable surfactants. Reprinted from reference [35].

There are a few reviews related to $CO_2$-switchable materials including $CO_2$-switchable solvents and surfactants,[33] $CO_2$-responsive polymers,[34] and $CO_2$-responsive block copolymers.[36] Surfactants are essential components of emulsion, miniemulsion, microemulsion, and suspension polymerization.[37] The main role of surfactants in all these polymerization systems is stabilizing latex particles.[17] However, after polymerization, the existence of surfactant in the final product is problematic. Removal of the surfactant by washing processes is not always perfect and most often some amount of the surfactant remains in the purified polymer. In general, the better the surfactant at stabilizing latex particles, the more difficult is its removal from the system.[38] Residual surfactants can alter the properties of the final product[35]; for example, in film forming applications, migration of the residual surfactant has a negative effect on the properties of the final product.[39,40,41] Latex destabilization (for obtaining latex powder) is conventionally performed by addition of acid, base, and salt depending on the type of surfactant employed in emulsion polymerization.[32] Therefore, post-washing steps are required for removing these chemicals and a large volume of waste water is produced, which leads to the increase in the cost and environmental impact of the process.[42]

Another issue in latex production is transportation of the latex from the point of production to the point of consumption. Because a large fraction of the mass of the latex is water, moving latex from one location to another means paying extra money for the transportation of water.[43] Switchable surfactants can address all the above-mentioned concerns. These surfactants can be switched on (active state) or switched off (inactive state) as needed.[33] This is an advantage in latex production since the stability of the latex is not always necessary. So far many different types of switchable surfactants have been prepared which mainly differ in the type of the trigger that is used in the switching on and off process. Brown et al.[44] have recently reviewed stimuli-responsive surfactants. In most cases addition of acid, base, oxidant, or reductant is required, which has environmental impact due to producing wastewater in the following washing steps. In the case of light sensitive surfactants, the reaction media should be transparent,[38] which is unlikely in many polymers or latex suspensions. Also, switchable peptide surfactants (pepfactants), which are based on series of amino acids, are expensive.[45,46]

To overcome these problems, $CO_2$-switchable surfactants, as a new class of stimuli-responsive surfactants, were introduced.[35] In aqueous media, pH can change by addition of $CO_2$. The degree of change in pH depends on the concentration of dissolved $CO_2$ in the aqueous phase. However, the solubility of gases in liquids depends on temperature, pressure, and pH. As temperature increases, the solubility of $CO_2$ decreases, while as the pressure increases the solubility of $CO_2$ increases.[47]

Long-chain alkyl amidines can be protonated by bubbling $CO_2$ into their aqueous solution.[35] In this state, they can behave like surfactants because they have a charged hydrophilic head and a long hydrophobic tail. Therefore, they can be employed as stabilizers in emulsion polymerization.[35] The removal of $CO_2$ to "switch off" the surfactant can be simply performed by purging with a nonacidic gas such as nitrogen, argon, or air. Because deprotonation is an endothermic process, heat is generally required to facilitate the deprotonation reaction.

The performance of long-alkyl chain molecules as $CO_2$-switchability surfactants depends largely on the nature of their head group. The structure of the head group can change solubility, basicity, heat of protonation, and $CO_2$-switchability of the surfactant.[48]

$CO_2$-switchable surfactants have been used in emulsion polymerization for the stabilization of the original emulsion and the product latex particles.[35,38,49] However, in some cases, the surfactant is not available commercially and should be synthesized. For example, *N*,*N*-didodecylacetamidinium bicarbonate, as a double-tailed cationic surfactant, was synthesized by the reaction of dimethylacetamide dimethylacetal and dodecylamine and then reacting with dry ice.[50] (*N*-amidino)dodecyl acrylamide (DAm) was employed as a $CO_2$-switchable surfactant for the preparation of coagulatable/redispersible polystyrene latexes.[32] Redispersion of the latex was achieved by purging with $CO_2$, while coagulation was performed by purging with $N_2$ and heating to remove $CO_2$ and neutralize latex particles. However, it must be noted that the amidine group was partially hydrolyzed under basic conditions.

Poly(DMAEMA-*b*-MMA), prepared *via* two-step solution RAFT polymerization, was used in the protonated form (initial protonation was performed by addition of HCl) as a $CO_2$-switchable surfactant in emulsion polymerization of MMA.[43,51] The latex stability depended on the diblock copolymer composition, and the latex particles size decreased with increasing weight fraction of MMA ($F_{MMA}$). After neutralizing the latex with caustic soda, the coagulated latex was redispersible if $F_{MMA}$<46%. $CO_2$-switchable PS and PMMA latexes by using $CO_2$-switchable surfactants have been prepared.[52-54] Coagulation and redispersion of latex particles was achieved by removal and addition of $CO_2$. It has been shown that when both initiator and surfactant are $CO_2$-switchable, redispersion is most effective and almost full recovery of the zeta potential and size distribution of latex particles are obtained.[52] Similarly, PMMA latexes were prepared using long chain alkyl amidine $CO_2$-switchable surfactants, and the effects of several parameters including the type and amount of surfactant and initiator, and solid contents on the particle size and zeta potential were investigated.[53] The resulting latex particles were 50 to 350 nm in size and could be easily filtered to obtain dry polymer powder.

### 2.3.2 $CO_2$-switchable monomers

DEAEMA,[36,42,55-68] DMAEMA,[55,69-75] 3-*N'*,*N'*- dimethylaminopropyl acrylamide (DMAPA),[76] *N*-(3-Dimethylaminopropyl)methacrylamide (DMAPMA),[77] and methacrylic acid (MA)[72] have been used so far for the synthesis of $CO_2$-responsive (co)polymers. DEAEMA and DMAEMA are the two most studied $CO_2$-switchable monomers, and have been used extensively in the synthesis of pH-responsive polymers.[78] DEAEMA is hydrophobic in the neutral form and hydrophilic when the tertiary amine group becomes protonated. This protonation and deprotonation can be performed reversibly by addition and removal of $CO_2$. The p$K_a$ of DEAEMA and the corresponding homopolymer is 8.8 and 7.5, respectively.[79] DEAEMA is a $CO_2$-switchable monomer and incorporating DEAEMA in the structure of (co)polymer can induce $CO_2$-switchability to the whole structure of the polymer.[55] DMAEMA is another $CO_2$-switchable monomer with the p$K_a$ of 8.3 and 7.4 for the monomer and polymer, respectively.[79] While DEAEMA and PDEAEMA are hydrophobic, DMAEMA and PDMAEMA are hydrophilic. These two monomers are prone to hydrolysis,[80] however, based on our observations, DEAEMA is more resistant to hydrolysis than DMAEMA. A good substitution for these monomers could be dimethylaminopropyl methacryalamide (DMAPMA), which is a hydrophilic, $CO_2$-switchable, and hydrolytically stable monomer.

### 2.3.3 $CO_2$-switchable initiators

2,2'-Azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044)[38,52-54] and 2,2'-azobis[2-(2-imidazolin-2-yl)propane] (VA-061)[32,38,42,52-54,81-83] are two important $CO_2$-switchable initiators. To be more precise, VA-044 is $CO_2$-switchable only after neutralization with a base to remove the chloride counter ion. The 10 h half-life decomposition temperature of VA-061 is 61 °C and decreases when protonated (~ 45 °C) which makes it suitable for initiating polymerizations under a $CO_2$ atmosphere.[81] The positively charged imidazole groups resulting from decomposition of VA-044 or protonated VA-061 are very effective in stabilizing latex particles. The Cunningham's group performed surfactant-free emulsion polymerizations of styrene using VA-061 initiator under a $CO_2$ atmosphere,[81] finding that the obtained latex particles could be coagulated by $CO_2$ removal and redispersed upon the introduction of $CO_2$ (Figure 2.9). The solid content was relatively low (~ 7%), but could be increased if a small amount of DEAEMA as a $CO_2$-switchable comonomer is included.[42]

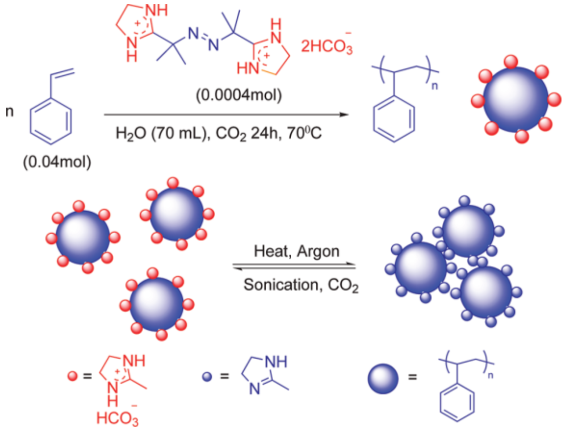


Figure 2.9 Preparation of switchable polystyrene latex using VA-061 initiator. Reprinted from reference [81.]

### 2.3.4 $CO_2$-switchable latexes

Conventional methods for breaking suspensions include the addition of a salt, an acid for a latex stabilized by anionic surfactants, or a base for a latex stabilized by cationic surfactants.[84,85] Addition of chemicals such as acids or bases causes salt accumulation in the system. To address this problem, a $CO_2$-switchable latex was reported.[35] Long-chain alkyl amidine compounds were used as $CO_2$-switchable surfactants in the emulsion polymerization of styrene. After the polymerization, removal of $CO_2$ by bubbling of Ar at 65 °C, triggered the coagulation of the PS latex. Also, $CO_2$-switchable PS and PMMA latexes employing amidine-based switchable surfactants have been prepared.[81] In each case the latexes could be coagulated by removal of the $CO_2$. It was found that initiator and surfactant selection is crucial in preparing $CO_2$-switchable latexes. For example, VA-044 causes the permanent stability of latexes even in the absence of $CO_2$.[81] Shortly after, the first time coagulatable and redispersible $CO_2$-switchable PS latexes was reported.[52] When both initiator and surfactant are $CO_2$-switchable, redispersion of latexes can be performed more effective. The aggregation and redispersion of latexes were possible for several cycles without accumulation of any background salt.[52] Aryl amidines and tertiary amines are less basic than alkyl amidines; as a result they are switched off much more rapidly.[38] Long chain tertiary amine switchable surfactants are commercially available and have lower cost compared with aryl amidine based surfactants. PMMA latexes made using tertiary amine and aryl amidine based surfactants were destabilized much more easily by bubbling Ar to remove the $CO_2$ and had lower zeta potentials than those prepared with alkyl amine based surfactants.[38] $CO_2$-switchable PS latexes were made under $CO_2$ atmosphere in surfactant-free emulsion polymerization using VA-061 as both initiator and stabilizer.[81] According to the calculations of the decomposition rate parameters, the 10 h half-life ($T_{10h}$ half-life) of VA-061 under a $CO_2$ atmosphere was estimated to be similar to the 10 h half-life of VA-044 under an Ar atmosphere.[81] Because imidazole groups created from the decomposition of VA-061 are bonded covalently to the surface of the latex particles, unlike switchable surfactant, they cannot be detached from latex particles during destabilization. Thus, upon bubbling $CO_2$ they can be protonated again and stabilize latex particles. To increase solid content, polymerization was repeated at 65 °C and 0.54 mol% DEAEMA was used as a $CO_2$-switchable comonomer to prepare a $CO_2$-switchable PS latex.[42] It was found that adding a few mole percent MMA can increase the conversion considerably because MMA is more hydrophilic than styrene and produces more hydrophobic oligomers in the aqueous phase. After destabilization and drying, the latex could be re-dispersed by $CO_2$ bubbling and sonication (Figure 2.10).

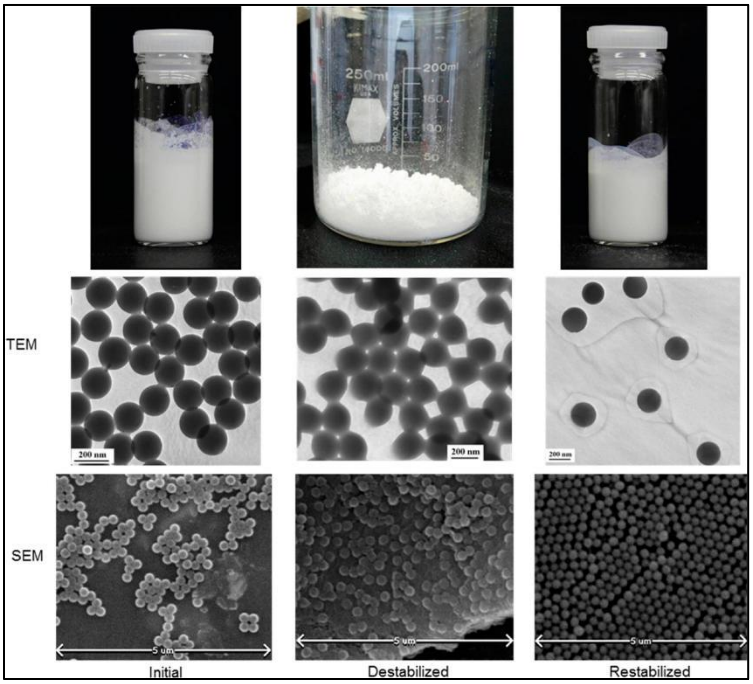


Figure 2.10 TEM and SEM of the original latex (left), after destabilization in the presence of poly(DEAEMA) (middle) and redispersed after 10 min of sonication under $CO_2$ atmosphere (right). Reprinted from reference [42].

An amidine-containing styrene derivative was synthesized and then employed as a $CO_2$-switchable comonomer in the surfactant-free emulsion polymerization of styrene.[86] Since 2,2'-azobis(2-methylpropionamidine)dihydrochloride (V-50) had been used as a positively charged initiator, destabilization of the prepared latex was only possible by addition of a small amount of a base such as NaOH. However, the coagulated latex was redispersible after $CO_2$ bubbling followed by sonication.[86] The coagulated, filtered and dried latex powder was also redispersible using $CO_2$ and ultrasound. In another study, $CO_2$-switchable PS latexes were prepared by using VA-061 as a $CO_2$-switchable initiator.[32] In this process, (*N*-amidino)dodecyl acrylamide was synthesized as a $CO_2$-switchable surfactant and then employed in the emulsion polymerization of styrene. However about 20% hydrolysis of amidine was observed in the surfactant during the reaction.[32] The PS latexes were stable against electrolytes and could be coagulated and redispersed several times. To overcome the hydrolysis problem and simplify the synthesis steps, DMAEMA as a commercially available $CO_2$-switchable monomer was employed in the preparation of PDMAEMA-*b*-PMMA via RAFT polymerization.[51] This diblock copolymer was used as a polymeric surfactant in the emulsion polymerization of MMA. To keep surfactant protonated during the reaction, protonation was done by HCl. The resultant latex could be coagulated by addition of a small amount of base. After washing with DI water, the latex could be redispersed and coagulated many times by addition and removal of $CO_{2.}$ It was found that the latex would be stable if the weight fraction of MMA ($F_{\mathrm{MMA}}$) in the surfactant was lower than 58.5%.[51] Particle size decreases when $F_{\mathrm{MMA}}$ increases.

An advantage of using polymeric surfactants is the prevention of surfactant migration in film-forming applications. When latexes are employed as film-forming polymers, physically adsorbed surfactants on the surface of the particles migrate toward the interfaces and lead to phase separation that reduces gloss and adhesion.[41] Also, they can be entrapped in pockets and increase percolation by water or water sensitivity. These are major drawbacks for paint and coating applications.[40,41] Surfactants that are covalently linked to the particles cannot desorb and migrate during film formation.

$CO_2$-switchable PMMA and PS latexes were prepared using commercially available *N*, *N*-dimethyldodecylamine (DDA), a $CO_2$-switchable surfactant, via miniemulsion polymerization.[87] The PMMA latexes could be aggregated by bubbling argon (Ar) at 60 °C and redispersed by bubbling $CO_2$ at room temperature. DDA is protonated by bubbling $CO_2$ in the solution and converted to $DDAH^+HCO_3^-$ but some deprotonation occurs after sonication or during the reaction at elevated temperatures.[87] At 80 °C, 40 % of $DDAH^+HCO_3^-$ switched back to DDA after 2 h. PS latexes were not destabilized only by bubbling Ar. The reason could be attributed to the lower density of PS latex (1.05 g $cm^{-3}$) compared to PM latex (1.18 g $cm^{-3}$).[87] However, increasing the pH to 9 resulted in the aggregation of PS latexes because of the decrease in the hydration effect of the tertiary amine. Since the PS nanoparticles contained some hexadecane with a density of 0.77 g $cm^{-3}$, the final density of the PS latex was lower than 1 and it collected on the surface of the water.[87] In dispersion of nanoparticles composed of a DDA hydrophobic core and polyvinylformal (PVF) shell, bubbling $CO_2$ converted the core from hydrophobic to hydrophilic, which was the first report of preparing water-core polymer capsules from O/W emulsions (Figure 2.11).

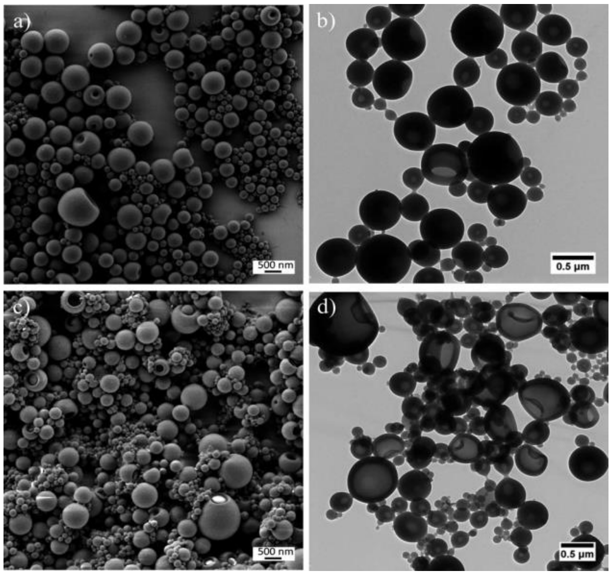


Figure 2.11 SEM and TEM images of PVF colloids: (a and b) with DDA as the core; (c) and (d) with water core. PVF capsules were prepared by using PVF and DDA (4:1 by weight). Reprinted from reference [87].

*N*-Methacryloyl-11-aminoundecanoic acid was employed as a $CO_2$-switchable comonomer and stabilizer in the preparation of PS latexes *via* surfactant-free miniemulsion polymerization.[88] Latex particles were coagulated by bubbling $CO_2$ due to protonation of carboxyl groups and redispersed by ultrasonication due to removal of $CO_2$ form the solution. According to DLS and zeta potential measurements, redispersion and coagulation processes were repeatable. Surfactant-free miniemulsion polymerization has also been used for the preparation of $CO_2$-switchable PDMAEMA-*b*-PS nanoparticles.[73] The resultant particles had a core-shell structure with 120 nm diameter.

Using a different method, a $CO_2$-switchable latex can be produced by using non-switchable components including initiator, monomer, and surfactant.[89] In this method, the stability of the latex is controlled by adding a ”switchable water” ionogen to the aqueous phase. In switchable water, the ionic strength of the aqueous solution can be switched between low and high values by addition and removal of $CO_2$.[89] This change occurs because an amine or polyamine called an ionogen is reversibly converted from a neutral to a bicarbonate salt by the action of $CO_2$. For example, sodium dodecylsulfate (SDS), in the absence of an ionogen, is not $CO_2$-switchable but the aqueous solution of SDS and *N*,*N*-dimethylethanolamine (DMEA, an ionogen) has $CO_2$-switchable air/water surface tension (Figure 2.12). Jessop and coworkers showed that a PS latex stabilized by SDS can be aggregated by bubbling $CO_2$ and redispersed by bubbling Ar (to remove $CO_2$).[89] Since the latex was prepared with potassium persulfate (KPS) initiator, the aqueous solution was acidic. Therefore, the initial pH was lower than the p$K_a$ of carbonic acid and prevented neutralization of the amine group by removal of $CO_2$. Figure 2.13 shows the results as the latex was neutralized by NaOH and then treated with DMEA ionogen, after which the latex was $CO_2$-responsive.

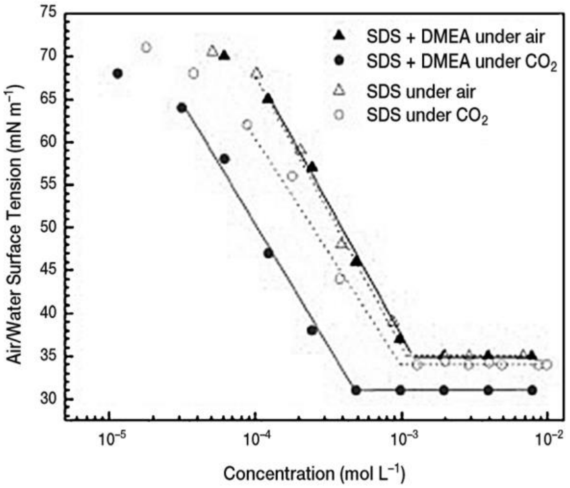
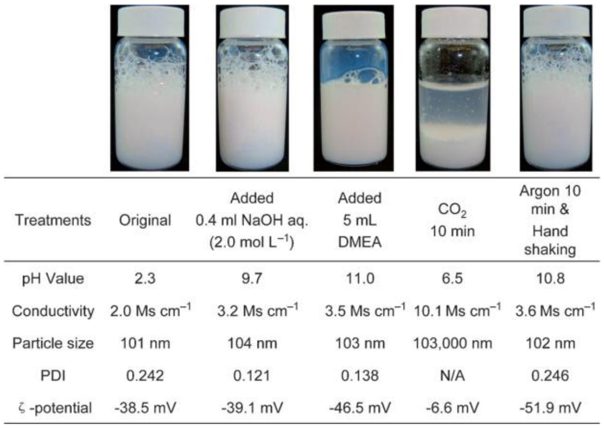


Figure 2.12 Air/water surface tension as a function of the concentration of aqueous solutions of SDS under air or $CO_2$ in the presence of DMEA (33 % v/v) under air or $CO_2$ at 25 °C. Reprinted from reference [89].



| Treatments | Original | Added 0.4 ml NaOH aq. (2.0 mol L$^{-1}$) | Added 5 mL DMEA | $CO_2$ 10 min | Argon 10 min & Hand shaking |
|---|---|---|---|---|---|
| pH Value | 2.3 | 9.7 | 11.0 | 6.5 | 10.8 |
| Conductivity | 2.0 Ms cm$^{-1}$ | 3.2 Ms cm$^{-1}$ | 3.5 Ms cm$^{-1}$ | 10.1 Ms cm$^{-1}$ | 3.6 Ms cm$^{-1}$ |
| Particle size | 101 nm | 104 nm | 103 nm | 103,000 nm | 102 nm |
| PDI | 0.242 | 0.121 | 0.138 | N/A | 0.246 |
| ζ -potential | -38.5 mV | -39.1 mV | -46.5 mV | -6.6 mV | -51.9 mV |

Figure 2.13 Reversible aggregation/redispersion of a PS latex prepared by using styrene (15 mL), SDS (0.5 g), KPS (0.1 g) and water (50 mL). Reprinted from reference [89].

$CO_2$ has also been used for tuning microemulsion aggregations.[90,91] Reactive ionic liquids were employed in the preparation of a $CO_2$-switchable microemulsion.[91] In a microemulsion system containing cyclohexane, surfactant (1-hexadecyl-3-methylimidazolium chloride ($C_{16}mimC_l$) and decanol, with mole ratio of 1:2), and ionic liquid (1-butyl-3-methylimidazolium triazolide ([bmim][tria123])), the nanodomains can be reversibly tuned by addition and removal of $CO_2$.[91] Silica particles prepared in surfactant-free emulsions using only $CO_2$-switchable chemical functional groups can stabilize oil-in-water emulsions, while particles containing both $CO_2$-switchable and hydrophobic functional groups on their surface are able to stabilize water-in oil emulsions.[92] Emulsions are broken when $CO_2$ is introduced due to the alteration of the wettability of the stabilizing particles which leads to phase separation of emulsions. The stability is re-established by bubbling air and $CO_2$ removal. $CO_2$ creates a positive charge on the surface of the responsive particles, increasing hydrophilicity and as a result the particles destabilize the emulsion.[92] Acrylic latexes with low $T_g$ were prepared in surfactant-free emulsion polymerization (SFEP) of MMA and BA with a small amount of DEAEMA as a $CO_2$-switchable comonomer.[93] The $T_g$ of the copolymer was adjusted by the combination of MMA and BA. If the $T_g$ is higher than room temperature, the latex is $CO_2$-redispersible while if the $T_g$ is lower than ambient temperature, after coagulation, latex particles are diffused to each other and they are not $CO_2$-redispersible.

As DEAEMA is one of the most investigated monomers in $CO_2$-switchablity technology, the main focus of this thesis is NMP of DEAEMA. Chapter 3 is related to the NMP of DEAEMA in bulk and then using the synthesized macroalkoxyamine as a macroinitiator for the preparation of PMMA latexes. Chapter 4 explains the NMP of DEAEMA in water and then based on the information obtained in this chapter, the one-pot synthesis of PMMA latexes using PDEAEMA macroinitiator will be explained in chapter 5. In the second half of the thesis NMP of PEGMA (chapter 6) and PEGylation of chitosan (chapter 7) are explained. Also, to address the issues (low $T_g$ and hydrolysis) related to the usage of DEAEMA for the synthesis of $CO_2$-switchable latexes, chapter 8 explains employing DMAPMA as a $CO_2$-switchable comonomer for the preparation of $CO_2$-switchable latexes. Finally, chapter 9 includes conclusion and future works.

## References

(1) Qiu, J.; Charleux, B.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, 26, 2083–2134.

(2) Szwarc, M. *Nature* **1956**, 178, 1168–1169.

(3) Cunningham, M. F. *Prog. Polym. Sci.* **2008**, 33, 365–398.

(4) Jenkins, A. D.; Jones, R. G.; Moad, G. *Pure Appl. Chem.* **2009**, 82, 483–491.

(5) Asua, J. M. *Polymer Reaction Engineering*; Blachwell Publishing Ltd, **2007**.

(6) Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux, B. *Prog. Polym. Sci.* **2013**, 38, 63–235.

(7) Solomon, D. H. *J. Polym. Sci., Part A: Polym. Chem.* **2005**, 43, 5748–5764.

(8) Georges, M.; Veregin, R. P. N.; Kazmaier, P. M.; Gordon, K. H. *Macromolecules* **1993**, 26, 2987–2988.

(9) Bertin, D.; Gigmes, D.; Marque, S. R. A; Tordo, P. *Chem. Soc. Rev.* **2011**, 40, 2189–2198.

(10) Fischer, H. *Chem. Rev.* **2001**, 101, 3581–3610.

(11) Vinas, J.; Chagneux, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D. *Polymer* **2008**, 49, 3639–3647.

(12) McHale, R.; Aldabbagh, F.; Zetterlund P, B. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, 45, 2194–203

(13) Guillaneuf, Y.; Gigmes, D.; Marque, S. R. A; Astolfi, P.; Greci, L.; Tordo, P.; Bertin, D. *Macromolecules* **2007**, 40, 3108–3114.

(14) Nicolas, J.; Mueller, L.; Dire, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules* **2009**, 42, 4470–4478.

(15) Vinas, J.; Chagneus, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D. *Polymer* **2008**, 49, 3639-3647.

(16) Cameron, N. R.; Lagrille, O.; Lovell, P. A.; Thongnuanchan, B. *Polymer* **2014**, 55, 772-781.

(17) Odian, G. *Principles of Polymerization*; Fourth Edi.; John Wiley & Sons: Hoboken, New Jersey, **2004**.

(18) Young, R. J.; Lovell, P. A. *Introduction to polymers*, Third Edi.; CRC Press, Taylor & Francis Group, **2011**.

(19) Marestin, C.; Noel, C.; Guyot, A.; Claverie, J. *Macromolecules* **1998**, 31, 4041-4044.

(20) Maehata, H.; Liu, X.; Cunningham, M.; Koeshkerian, B. *Macromol. Rapid. Commun*. **2008**, 29, 479-484.

(21) BlocBuilder$^{TM}$ data sheet from Arkema Group.

(22) Charleux, B.; Nicolas, J. *Polymer* **2007**; 48, 5813–5833.

(23) Simms, R. W.; Hoidas, M. D.; Cunningham, M. F. *Macromolecules* **2008**, 41, 1076–1079.

(24) Asua, J. M. *Prog. Polym. Sci.* **2002**, 27, 1283–346.

(25) Charleux, B.; Nicolas, J. *Polymer*, **2007**, 48, 5813-5833.

(26) Prodpran, T.; Dimonie, V. L.; Sudol, E. D.; El-Aasser, M. S. *Macromol. Symp*. 2000, 155, 1–14.

(27) Lin, M.; Cunningham, M. F.; Keoshkerian, B. *Macromol. Symp*. **2004**, 206, 263–274.

(28) Grubbs, R. B. *Polymer Reviews*, **2011**, 51, 104–137.

(29) Gohy, J. F. *Adv. Polym. Sci*., **2005**, 190, 65–136.

(30) Charleux, B.; Delaittre, G.; Rieger, J.; D'Agosto, F. *Macromolecules*, **2012**, 45, 6753−6765.

(31) Riess, G.; Labbe, C. *Macromol. Rapid. Commun*. **2004**, 25, 401-435.

(32) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Langmuir* **2012**, 28, 5940-5946.

(33) Jessop, P. G.; Mercer, S. M.; Heldebrant, D. J. *J. Energy Environ. Sci*. **2012**, 5, 7240-7253.

(34) Lin, S.; Theato, P. *Macromol. Rapid Commun.* **2013**, 34, 1118–1133.

(35) Liu, Y.; Jessop, P. G.; Cunningham, M.; Eckert, C. A; Liotta, C. L. *Science* **2006**, 313, 958–960.

(36) Yan, Q.; Zhao, Y. *Chem. Commun.* **2014**, 50, 11631–11641.

(37) Wang, Q.; Fu, S.; Yu, T. *Prog. Polym. Sci.* **1994**, 19, 703–753.

(38) Fowler, C. I.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 2955–2962.

(39) Shirakbari, N.; Ebrahimi, M.; Salehi-Mobarakeh, H.; Khorasani, M. *J. Macromolecular Science, Part B* **2014**, 53, 1286–1292.

(40) Monteiro, M. J.; Sjoberg, M.; Van der Vlist, J.; Gottgens, C. M. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, 23, 4206–4217.

(41) Aramendia, E.; Barandiaran, J.; Grade, J.; Blease, T.; Asua, M. *Langmuir* **2005**, 21, 1428–1435.

(42) Pinaud, J.; Kowal, E.; Cunningham, M.; Jessop, P. *ACS Macro Lett.* **2012**, 1, 1103–1107.

(43) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Macromolecules* **2013**, 46, 1261–1267.

(44) Brown, P.; Butts, C. P.; Eastoe, J. *Soft Matter* **2013**, 9, 2365-2374.

(45) Malcolm, A. S.; Dexter, A. F.; Middelberg, P. J. *Asia-Pac. J. Chem. Eng.* **2007**, 2, 362–367.

(46) Dexter, A. F.; Middelberg, P. J. *J. Phys. Chem. C* **2007**, 111, 10484–10492.

(47) Haynes, W. M. *Handbook of Chemistry and Physics*; 96th Edi.; CRC Press, **2015**.

(48) Scott, L. M.; Robert, T.; Harjani, J. R.; Jessop, P. G. *RSC Adv.* **2012**, 2, 4925-4931.

(49) Su, X.; Fowler, C.; O'Neill, C.; Pinaud, J.; Kowal, E.; Jessop, P.; Cunningham, M. *Macromol. Symp.* **2013**, 333, 93–101.

(50) Wang, L.; Qiao, W.; Cao, C.; Li, Z. *Colloids and Surfaces A: Physicochemical Eng. Aspects* **2008**, 320, 271–274.

(51) Zhang, Q.; Yu, G.; Wang, W. J.; Li, B. G.; Zhu, S. *Macromol. Rapid. Commun.* **2012**, 33, 916–921.

(52) Mihara, M.; Jessop, P.; Cunningham, M. *Macromolecules* **2011**, 44, 3688–3693.

(53) Fowler, C. I.; Muchemu, C. M.; Miller, R. E.; Phan, L.; O'Neill, C.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2011**, 44, 2501–2509.

(54) O'Neill, C.; Fowler, C.; Jessop, P. G.; Cunningham, M. F. *Green Materials* **2012**, 1, 27–35.

(55) Han, D.; Tong, X.; Zhao, Y. *ACS Macro Lett.* **2012**, 1, 57–61.

(56) Qian, Y.; Zhang, Q.; Qiu, X.; Zhu, S. *Green Chem.* **2014**, 16, 4963–4968.

(57) Morse, A. J.; Armes, S. P.; Thompson, K. L.; Dupin, D.; Fielding, L. A.; Mills, P.; Swart, R. *Langmuir* **2013**, 29, 5446–5475.

(58) Yan, B.; Han, D.; Boissière, O.; Ayotte, P.; Zhao, Y. *Soft Matter* **2013**, 9, 2011–2016.

(59) Feng, A.; Zhan, C.; Yan, Q.; Liu, B.; Yuan, J. *Chem. Commun.* **2014**, 50, 8958–8961.

(60) Yan, Q.; Zhao, Y. *J. Am. Chem. Soci.* **2013**, 135, 16300–16303.

(61) Liu, H.; Guo, Z.; He, S.; Yin, H.; Fei, C.; Feng, Y. *Polym. Chem.* **2014**, 5, 4756–4763.

(62) Guo, J.; Wang, N.; Wu, J.; Ye, Q.; Zhang, C.; Xing, X. H.; Yuan, J. *J. Mater. Chem. B* **2014**, 2, 437-442.

(63) Kumar, S.; Tong, X.; Dory, Y. L.; Lepage, M.; Zhao, Y. *Chem. Commun.* **2013**, 49, 90–92.

(64) Liu, H.; Zhao, Y.; Dreiss, C. A.; Feng, Y. *Soft matter* **2014**, 10, 6387–6391.

(65) Zhang, J.; Han, D.; Zhang, H.; Chaker, M.; Zhao, Y.; Ma, D. *Chem. Commun.* **2012**, 48, 11510–11512.

(66) Zhang, Q.; Zhu, S. *ACS Macro Lett.* **2014**, 3, 743–746.

(67) Su, X.; Cunningham, M. F.; Jessop, P. G. *Polym. Chem.* **2014**, 5, 940-944.

(68) Lu, H.; Zhou, Z.; Jiang, J.; Huang, Z. *J. Appl. Polym. Sci.* **2015**, 132, 41307-41314.

(69) Cai, Y.; Shen, W.; Wang, R.; Krantz, W. B.; Fane, A. G.; Hu, X. *Chem. Commun.* **2013**, 49, 8377–8379.

(70) Lu, H.; Jiang, J.; Huang, Z.; Dai, S. *J. Appl. Polym. Sci.* **2014**, 131, 40872-40878.

(71) Liu, B.; Zhou, H.; Zhou, S.; Zhang, H.; Feng, A.; Jian, C.; Hu, J.; Gao, W.; Yuan, J. *Macromolecules* **2014**, 47, 2938–2946.

(72) Han, D.; Boissiere, O.; Kumar, S.; Tong, X.; Tremblay, L.; Zhao, Y. *Macromolecules* **2012**, 45, 7440–7445.

(73) Wang, X.; Jiang, G.; Wei, Z.; Li, X.; Tang, B. *European Polymer Journal* **2013**, 49, 3165–3170.

(74) Xu, L. Q.; Zhang, B.; Sun, M.; Hong, L.; Neoh, K. G.; Kang, E. T.; Fu, G. D. *J. Mater. Chem. A* **2013**, 1, 1207–1212.

(75) Liu, P.; Zhang, Y.; Wang, W. J.; Li, B. G.; Zhu, S. *Green Materials* **2014**, 2, 82-94.

(76) Schattling, P.; Pollmann, I.; Theato, P. *Reactive and Functional Polymers* **2014**, 75, 16–21.

(77) Boniface, K.; Wang, H.; Dykeman, R.; Cormier, A.; Mercer, S. M.; Liu, G.; Cunningham, M. F.; Jessop, P. G. *Green Chem.* **2015**, DOI: 10.1039/C5GC01201E.

(78) Dai, S.; Ravi, P.; Tam, K. C. *Soft Matter* **2008**, 4, 435-449.

(79) Van de Wetering, P.; Moret, E. E.; Schuurmans-Nieuwenbroek, N. M.; van Steenbergen, M. J.; Hennink, W. E. *Bioconjugate Chem.* **1999**, 10, 589–597.

(80) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2015**, 48, 72–80.

(81) Su, X.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 666–670.

(82) Darabi, A.; Shirin-Abadi, A. R.; Pinaud, J.; Jessop, P. G.; Cunningham, M. F. *Polym. Chem.* **2014**, 5, 6163–6170.

(83) Su, X.; Jessop, P. G.; Cunningham, M. F. *Green Materials* **2014**, 2, 69–81.

(84) Gilbert, R. G. *Emulsion polymerization : A Mechanistic Approach*; Academic Press: London ; San Diego, **1995**.

(85) Lovell, P. A; El-Aasser, M. S. *Emulsion Polymerization and Emulsion Polymers*; J.Wiley: New York, **1997**.

(86) Zhang, Q.; Wang, W. J.; Lu, Y.; Li, B. G.; Zhu, S. *Macromolecules* **2011**, 44, 6539–6545.

(87) Zhao, Y.; Landfester, K.; Crespy, D. *Soft Matter* **2012**, 8, 11687-11696.

(88) Fischer, V.; Landfester, K.; Munoz-Espi, R. *ACS Mac. Lett.* **2012**, 1, 1371–1374.

(89) Su, X.; Robert, T.; Mercer, S. M.; Humphries, C.; Cunningham, M. F.; Jessop, P. G. *Chemistry* **2013**, 19, 5595–5601.

(90) Zhang, J.; Han, B. *Accounts of Chemical Research* **2013**, 46, 425–433.

(91) Brown, P.; Wasbrough, M. J.; Gurkan, B. E.; Hatton, T. A. *Langmuir* **2014**, 30, 4267–4272.

(92) Liang, C.; Liu, Q.; Xu, Z. *ACS Appl. Mater. Interfaces* **2014**, 6, 6898–6904.

(93) Gariepy, D.; Zhang, Q.; Zhu, S. *Macromolecular Chemistry and Physics*, **2015**, 5, 561–568.

# Chapter 3

# Nitroxide-mediated surfactant-free emulsion copolymerization of methyl methacrylate and styrene using poly (2-(diethyl) aminoethyl methacrylate-*co*-styrene) as a stimuli-responsive macroalkoxyamine

## Abstract

The SG1-mediated copolymerization of 2-(diethyl)aminoethyl methacrylate (DEAEMA) and a small percentage of styrene (S) was performed with different initiating systems including a monocomponent initiating system using an alkoxyamine of n-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder) at 80 °C and a bicomponent initiating system using 2,2'-azobis[2-(2-imidazolin-2-yl)propane] (VA-061) as the initiator and *N*-tertbutyl-*N*-(1- diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1) as the nitroxide at 100 °C. The resultant macroalkoxyamines, poly(DEAEMA-*co*-S)-SG1, were used as pH-sensitive macroinitiators in the nitroxide-mediated surfactant-free emulsion copolymerization of methyl methacrylate (MMA) and styrene at 90 °C, which proceeded via a polymerization-induced self-assembly (PISA) process, leading to the in-situ formation of pH-responsive amphiphilic block copolymers. The reaction was well-controlled with high initiation efficiency and exhibited excellent livingness as evidenced by evolution of

the molar mass distribution. The final latex particles were pH-sensitive with excellent colloidal stability and monomodal size distribution.

## 3.1. Introduction

Preparation of stimuli-responsive materials exhibiting reversible changes in chemical or physical properties in response to external triggers by controlled/living radical polymerization (CLRP) has been an active area of research during the last decade.[1,2] Tertiary amine-based polymers, an important category of stimuli-responsive polymers which are pH and/or temperature-responsive, have potential applications in emulsion polymerization,[3] block copolymers synthesis,[4] and the biomedical field[5] (gene or drug delivery).[6,7] In particular, the monomers 2-(diethylamino) ethyl methacrylate (DEAEMA) and 2-(dimethylamino)ethyl methacrylate (DMAEMA) have been polymerized employing different CLRP techniques. Atom transfer radical polymerizations (ATRP) of DMAEMA and 2-(dimethylamino)ethyl acrylate (DMAEA) were reported, respectively, by Matyjaszewski and Zhu groups.[8,9] Gan et al.[10] prepared well-defined poly(DEAEMA) via ATRP and then used the synthesized poly(DEAEMA) as a macroinitiator for producing poly(DEAEMA-*b*-tBMA). Reversible addition fragmentation chain transfer (RAFT) radical polymerization has been applied successfully in the synthesis of different stimuli-responsive (co)polymers.[11] RAFT of DMAEMA in water was carried out using 4,4’-azobis(4-cyanopentanoic acid) (V501) as a water-soluble initiator and 4-cyanopentanoic acid dithiobenzoate (CPADB) as a chain transfer agent.[12] D'Agosto et al.[13] investigated the effect of several parameters such as the ratio of RAFT agent to initiator, the concentration of the monomer, and the ratio of monomer to RAFT agent on the RAFT polymerization of DMAEMA.

Iodine transfer polymerization of DEAEMA has also been performed by Goto et al.[14] in bulk. In this elegant study, the control of the polymerization could be achieved by employing ammonium iodide to reversibly activate the chain-end.

In contrast, there are few reports of the NMP of functional monomers with a tertiary amine group. Lokaj et al.[15] first reported the NMP of DMAEMA using polystyrene (PS) macroinitiator in bulk. Bian and Cunningham[16] studied the effects of temperature, solvent polarity, chain transfer to polymer, and excess nitroxide on the NMP of DMAEA initiated by an SG1-based alkoxyamine. Maric and Zhang[17] performed nitroxide-mediated copolymerization of DMAEMA and styrene using *n*-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder) in bulk at 80 °C. The livingness of the poly(DMAEMA) was tested by chain extension with a DMAEMA/styrene mixture.

DMAEMA and DEAEMA can be used in their protonated form to stabilize latex particles during emulsion polymerization. When $CO_2$ is employed as a protonating agent, this allows the development of easily coagulable/redispersable latexes. Zhao et al.[18] showed that these monomers and their derived-polymers can be protonated (“switched on”) by bubbling $CO_2$ in their water solution, thus becoming highly hydrophilic. Removing of $CO_2$ from the solution, simply by air-bubbling, then allows recovery of the neutral and more hydrophobic form of the monomers or polymers. Taking advantage of the $CO_2$-switchability of these monomers, Cunningham et al. found they could considerably increase the solids content of their surfactant-free emulsion polymerization of styrene from 7%[30] to 27%.[19] Copolymers of stearyl methacrylate and DMAEMA, poly(SMA-*co*-DMAEMA), were used as polymeric surfactants in the miniemulsion polymerization of styrene.[20] Diblock copolymers containing poly(DMAEMA) or poly(DEAEMA) as a pH-sensitive block can be used as polymeric surfactants in emulsion polymerization. Zhang et al.[21,22] synthesized $CO_2$-switchable PMMA latexes using poly(DMAEMA)-*b*-poly(MMA) as a polymeric surfactant in the emulsion polymerization of MMA. poly(DEAEMA-*co*-PEGMA) was used as a pH-sensitive polymeric stabilizer in tetradecane-in-water emulsions.[23]

Compared to ATRP and RAFT, NMP has a fairly simple mechanism since it requires only the use of an alkoxyamine, which acts as an initiator and controlling agent at the same time.[24] Block copolymers comprised of hydrophilic and hydrophobic blocks are of high interest.[25,26,27] Sequential addition of monomers (i.e. synthesis of the first block and then extension of the second block) is the general strategy for the preparation of diblock copolymers.[28] Charleux's group developed the polymerization-induced self-assembly (PISA) process which is based on the in situ chain extension of a hydrophilic block (prepared by CLRP techniques) with a hydrophobic block and then the subsequent self-assembly of the resultant diblock copolymer in water.[29] One of the main advantages of this process is the absence of surfactants that can alter the properties of the final product especially in film-based applications. Interestingly, while DMEAMA, DEAEMA, or their (co)polymers are of interest to reversibly stabilize latexes, to the best of our knowledge they have never been employed for the synthesis of latexes by NMP using the PISA technique.

We have synthesized DEAEMA and DMAEMA-based macroalkoxyamines via NMP and used them as stimuli-responsive stabilizers and initiators for the nitroxide-mediated surfactant-free emulsion copolymerization of methyl methacrylate and styrene, according to the PISA process. In the first stage, poly(DEAEMA-*co*-S)-SG1 or poly(DMAEMA-*co*-S)-SG1 macroinitiators were synthesized via NMP using 2,2'-azobis[2-(2-imidazolin-2-yl)propane] (VA-061) as initiator and

SG1 as nitroxide at 100 ºC or using *n*-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder) as alkoxyamine at 80 ºC. In the second stage the protonated macroinitiator is chain extended with methyl methacrylate in a surfactant-free emulsion polymerization (SFEP). The polymerization kinetics, livingness of the polymer chains, control over molecular weight and molecular weight distribution, colloidal characteristics of the latex particles, pH-responsiveness, and $CO_2$-switchability of the final latexes are described in detail.

## 3.2. Experimental section

**Materials.** All chemicals, monomers, and inhibitor removal columns were purchased from Aldrich unless otherwise stated. 2-(diethylamino)ethyl methacrylate (DEAEMA, 99%) was passed through a column of basic aluminum oxide (~150 mesh) prior to use. Styrene (S, >99%) and methyl methacrylate (MMA, 99%) were purified by passing through columns packed with inhibitor remover. The 2-((tert-butyl-(1-(diethoxyphosphoryl)-2,2-dimethylpropyl) amino) oxy)-2-methylpropanoic acid initiator (BlocBuilder) and the *N*-tertbutyl-*N*-(1- diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1, 85%) were supplied by Arkema. 2,2'-azobis[2-(2-imidazolin-2-yl)propane] (VA-061) was purchased from Wako Pure Chemical Industries and used without further purification. Sodium hydroxide (NaOH, >97%), tetrahydrofuran (THF, >99%), methanol (>99.8%), hexane (>98.5%), hydrochloride acid (38 wt %), and carbon dioxide ($CO_2$, Praxair, medical grade) were used as received. All aqueous solutions were prepared with deionized water (DIW). N-hydroxysuccinimide BlocBuilder (NHS-BlocBuilder) was synthesized according to the reported procedure.[30]

**SG1-mediated copolymerization of DEAEMA and styrene in bulk using VA-061 as the initiator and SG1 as the nitroxide.** In a typical experiment, a mixture of DEAEMA (25.0 g, 0.135 mol), S (1.56 g, 0.015 mol) (initial molar fraction of styrene in the monomer mixture: $f_{s0}$= 0.1), VA-061 (0.18 g, 0.72 mmol), and SG1 (0.31 g, 1.08 mmol) were introduced into a 50 mL three-neck round-bottom flask immersed in an ice-water bath and the mixture was deoxygenated with a nitrogen stream for 20 min. The mixture was then introduced into a preheated oil bath at 100 °C and fitted with a reflux condenser, a nitrogen inlet and a thermometer. Time zero of the polymerization was taken when the flask was immersed in the oil bath. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and allowed to react for up to 2 h with samples withdrawn periodically for kinetic studies and raw polymer analysis. Samples were quenched by immersion in an ice-water bath and then dried under air flow for 24 h. At the end of the reaction, the flask was cooled in an ice-water bath to stop the polymerization reaction and then the polymer was purified by precipitation in 20-fold volume of cold hexane (after precipitation, the solution was kept in the freezer for 6 h and then it was decanted to leave the precipitated polymer as a paste).

**SG1-mediated copolymerization of DEAEMA and styrene in bulk using NHS-BlocBuilder.** A mixture of DEAEMA (20.0 g, 0.108 mol), S (1.12 g, 10.7 mmol) (initial molar fraction of styrene in the monomer mixture: $f_{s0}$= 0.09), NHS-BlocBuilder (1.0 g, 2.1 mmol), and SG1 (62.0 mg, 0.21 mmol) were mixed in a 50 mL three-neck round-bottom flask immersed in an ice-water bath and the mixture was deoxygenated with a nitrogen stream for 20 min. The mixture was then introduced into a preheated oil bath at 80 °C and fitted with a reflux condenser, a nitrogen inlet and a thermometer. Time zero of the polymerization was taken when the flask was immersed in the oil bath. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and continued to react for up to 2 h with samples withdrawn periodically for kinetic studies and raw polymer analysis. Samples were quenched by immersion in an ice-water bath and then dried under the flow of air for 24 h. At the end of the reaction, the polymerization medium was first cooled in an ice-water bath to stop the polymerization and then, the polymer was purified by precipitation in 20-fold volume of cold hexane (after precipitation the solution was kept in the freezer for 6 h and then it was decanted to leave the precipitated polymer as a paste).

**Surfactant-free emulsion polymerization of MMA.** In a typical experiment (experiment 1, Table 3.1), in a 50 mL three-neck round-bottom flask fitted with a reflux condenser, a nitrogen inlet and a thermometer, poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine (0.2 g, 0.034 mmol) was mixed with deionized water (22 mL), and pH was adjusted to 6.0 by addition of HCl 1M. The solution was deoxygenated by nitrogen bubbling for 20 min at room temperature. MMA (4.65 g, 0.045 moles) and S (0.53 g, 5.0 mmoles) were added to the flask and $N_2$ bubbling continued for 10 minutes more. The flask was then immersed in a preheated oil bath at 90 °C. Time zero of the polymerization was taken when the flask was immersed into the oil bath. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and the polymerization was allowed to proceed for 5 h. Samples were periodically withdrawn and quenched by immersion in an ice-water bath and the dried under the flow of air for 24 h to follow monomer conversion gravimetrically.

**Characterization.** Monomer conversion was determined gravimetrically. To determine conversion, 0.5 mL samples were removed from the reaction flask via syringe, quenched in an ice-water bath to stop polymerization, and were allowed to dry under a flow of air for 24 h. Size exclusion chromatography (SEC) was used to determine molecular weight and molar mass dispersity (*Đ*) of the polymer samples. The SEC was equipped with a Waters 2960 separation module containing three Styragel columns coupled with the separation limits between 400 and $1 \times 10^6$ g mol$^{-1}$. THF was used as the eluent with a flow rate of 0.3 mL min$^{-1}$. A differential refractive index detector (Waters 2960) was used and the average molar masses ($M_n$ and $M_w$) and molar mass dispersity (*Đ*) were derived from a calibration curve based on polystyrene (PS) standards from Polymer Standard Service. For the reactions under $CO_2$ atmosphere, samples were dried under air at least for 24 h to make sure that all the amine groups became deprotonated and poly(DEAEMA-*co*-S) became soluble in THF. For the reactions performed in the presence of HCl, at the end of the reaction all the amine groups were neutralized with base (1M sodium hydroxide) before running SEC. Particle size, size polydispersity (PDI), and zeta-potential were determined for the stable latexes using the Zetasizer Nano ZS. Before measurements of the latex particle diameters, the latex samples were diluted in deionized water. Measurements were taken in a disposable capillary cuvette. Particle size and polydispersity were taken from intensity average values.

## 3.3. Results and discussion

DEAEMA has a tertiary amine group that makes this monomer pH sensitive. This monomer is water-soluble (hydrophilic) in its protonated form and essentially water-insoluble (hydrophobic) in its neutral form. Before performing emulsion polymerizations with MMA, the kinetics of the nitroxide-mediated aqueous solution polymerization of DEAEMA was studied in different systems to compare the blocking efficiency of poly(DEAEMA) macroinitiators.

In all experiments 8-10 mol% styrene was used in the monomer mixture to reduce the irreversible deactivation of propagating radicals and increase the livingness of the polymer chains.[31] The most convenient approach to making the poly(DEAEMA) block would be to polymerize DEAEMA in water. MMA could then be added to yield a one-pot process. Therefore in the first set of experiments we conducted polymerizations in water by protonating DEAEMA with bubbling of $CO_2$ into the water solution at atmospheric pressure. In most of these experiments, the reaction was neither controlled nor living. The main problem was the very low solubility of $CO_2$ in water at high temperatures, and as a result a biphasic system existed since the monomer was not sufficiently protonated to make it water soluble. Lowering the temperature to 60 ºC increased the $CO_2$ solubility but gave a very slow reaction with poor control. Based on these observations, it was decided to prepare the poly(DEAEMA) based macroinitiator in bulk under a nitrogen atmosphere thereby allowing the reaction to be performed at higher temperatures with the neutral form of DEAEMA.

### 3.3.1 Nitroxide-mediated copolymerization of DEAEMA and styrene in bulk.

**Bicomponent system:** VA-061 as initiator and SG1 as nitroxide. DEAEMA and VA-061 are pH-responsive and $CO_2$-switchable monomer and initiator, respectively.[3] Using VA-061 as initiator in the NMP of DEAEMA causes both the head and the body of the polymer chains to become pH-sensitive (Figure 3.1).

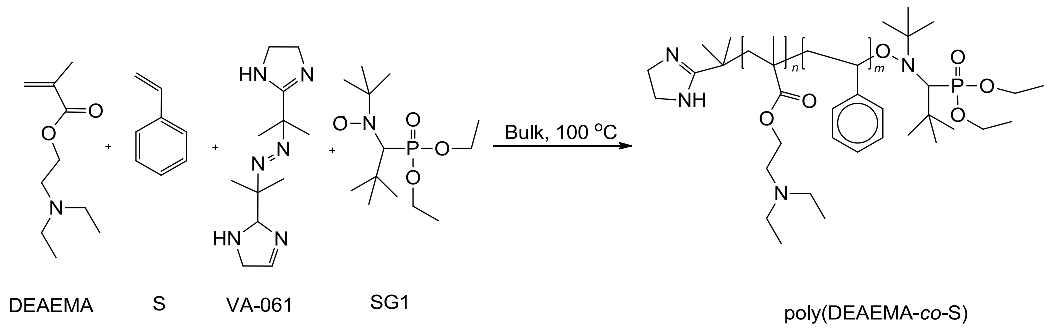


Figure 3.1 A schematic representation of the bulk copolymerization of DEAEMA and styrene initiated by VA-061 as initiator and SG1 as nitroxide.

VA-061 is not soluble in DEAEMA at room temperature, but at elevated temperatures it becomes soluble after decomposition and addition to DEAEMA. For the NMP of DEAEMA using VA-061 as the initiator and SG1 as the nitroxide, three different temperatures were investigated: 90, 100, and 110 °C. While at 90 °C complete solubilisation of VA-061 in DEAEMA took about one hour, at 110 °C it took less than 10 minutes. However the polymerization rate was very fast with poor control and high molar mass dispersity. At 100 °C, the initiator was dissolved in the monomer phase in about 20 minutes and better control was obtained. Thus, the temperature was set to 100 °C for the rest of the experiments. According to our observations, at $[SG1]_0/[VA\text{-}061]_0$ ratios higher than ~1.2, control of the reaction was improved. Also, the polymerization should not be continued beyond approximately 35% conversion since viscosity increases and irreversible termination reactions begin to noticeably affect the dispersity and chain livingness. Reactions exhibited all the features of well-controlled and living polymerizations (Figures 3.2 and 3.3): a linear increase of $M_n$ with monomer conversion; linear increase of ln[1/(1-x)] versus time; relatively narrow molecular weight distribution; and complete shifts in the molecular weight distributions (MWD) to higher molar masses (Number average molecular weights ($M_n$) were calculated based on polystyrene standards). An induction period is observed in Figure 3.2a, showing the time required for the reaction to consume free excess SG1 present at the start of the reaction. The intercept of the $M_n$ versus conversion is higher than zero probably because of the time required for the establishment of the activation-deactivation cycles of the alkoxyamine. Some experiments were also performed using DMAEMA as the pH-sensitive monomer and the results showed similar behaviour in terms of control and livingness of the reactions.

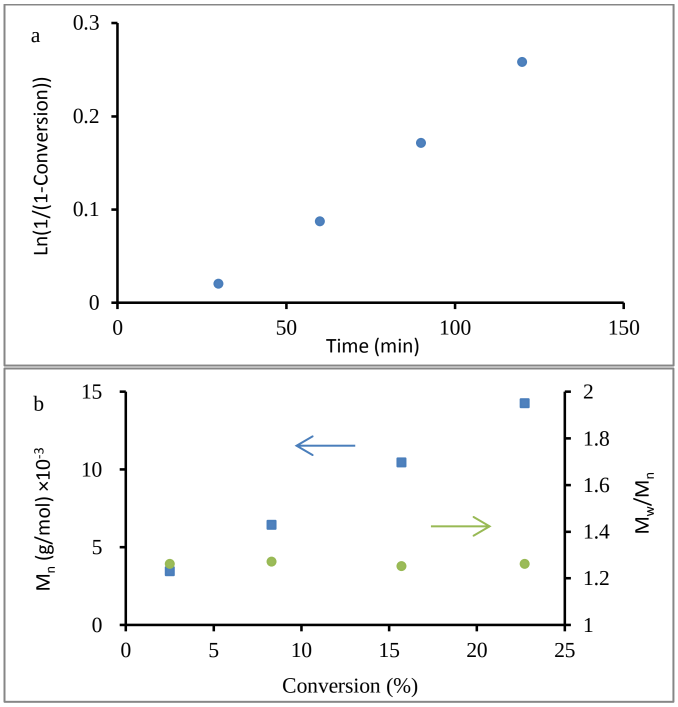


Figure 3.2 Bulk copolymerization of DEAEMA and S (initial molar fraction of styrene:$f_{S0}$=0.1) at 100 °C in the presence of VA-061 and SG1 ($[SG1]_0/[VA\text{-}061]_0$=1.5). (a) ln[1/(1-X)] vs time plot (X=conversion) (b) number-average molar mass, $M_n$, and polydispersity index, $M_w/M_n$, vs conversion.

To test the $CO_2$-switchability of the final polymer, after precipitating the polymer in cold hexane, it was dissolved in a small amount of methanol and then water was added to the solution. The poly(DEAEMA-*co*-S) precipitated in water but after $CO_2$ bubbling through the solution for a few minutes, the polymer completely dissolved in water and the solution became transparent (Figure 3.4).

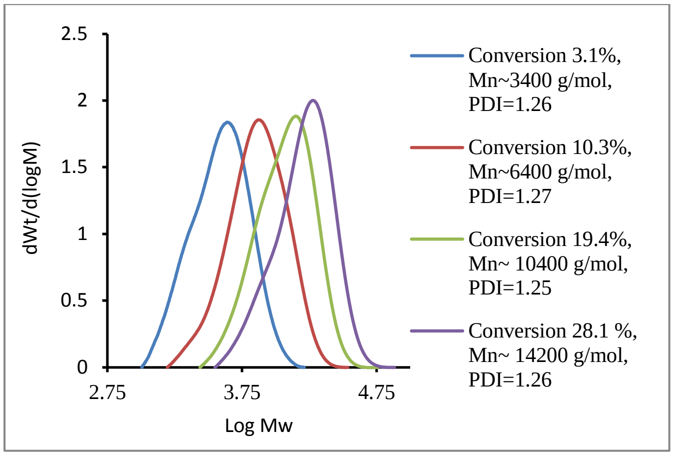


Figure 3.3 Size exclusion chromatograms at various monomer conversions for the copolymer of the DEAEMA and S in bulk at 100 ºC with $f_{S0}$=0.1 and $[SG1]_0/[VA\text{-}061]_0$=1.5.

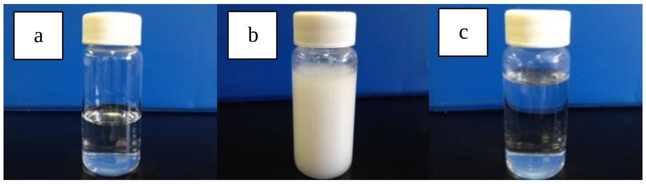


Figure 3.4 $CO_2$-switchability test of the poly(DEAEMA-*co*-S): (a) in methanol (b) after adding water (c) after bubbling $CO_2$ for 10 minutes at room temperature.

### Monocomponent system: NHS-BlocBuilder

One of the disadvantages of bicomponent initiating systems (nitroxide and initiator) is difficulty in controlling and predicting initiator efficiency. Alkoxyamines are monocomponent initiating systems which produce initiator and nitroxide in an equimolar ratio after decomposition at elevated temperatures. To compare the differences between these systems, two different alkoxyamines, BlocBuilder and *n*-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder), were used in the NMP of DEAEMA. BlocBuilder was used as the first choice of alkoxyamine because it is available commercially. Most of the reactions using BlocBuilder resulted in high polydispersity and poor livingness of the synthesized poly(DEAEMA-*co*-S) macroinitiator. BlocBuilder was not completely soluble in the monomer phase. Changing the ratio of SG1 to BlocBuilder and temperature did not improve the situation. The reason for the poor performance may be the presence of the carboxylic group on the BlocBuilder. It has been reported that NHS-BlocBuilder is able to polymerize DMAEMA (a similar monomer to DEAEMA with more hydrophilicity) with the small amount of styrene in the monomer feed without the need to add any free SG1.[17] Therefore; we employed this alkoxyamine instead of BlocBuilder for the NMP of DEAEMA (Figure 3.5).

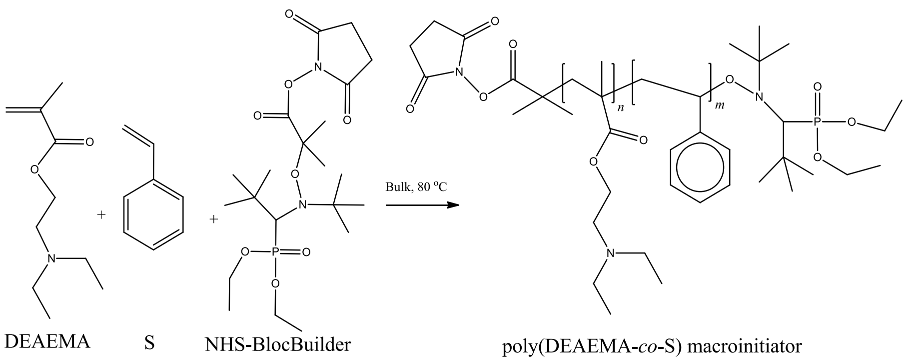


Figure 3.5 A schematic representation of the Bulk copolymerization of DEAEMA and S initiated by NHS-BlocBuilder.

The NHS-BlocBuilder is more soluble in DEAEMA at room temperature than BlocBuilder. In most experiments, reactions showed all the features of a controlled and living polymerization up to 50% conversion (Figure 3.6) as indicated by the low polydispersity index at these conversions. No trace of residual macroinitiator is observed on the SEC chromatograms (Figure 3.7), indicating a very high initiation efficiency. The clean shift of the SEC chromatograms with conversion shows the simultaneous growth of all polymer chains and indicates a good control and livingness of the polymerization.

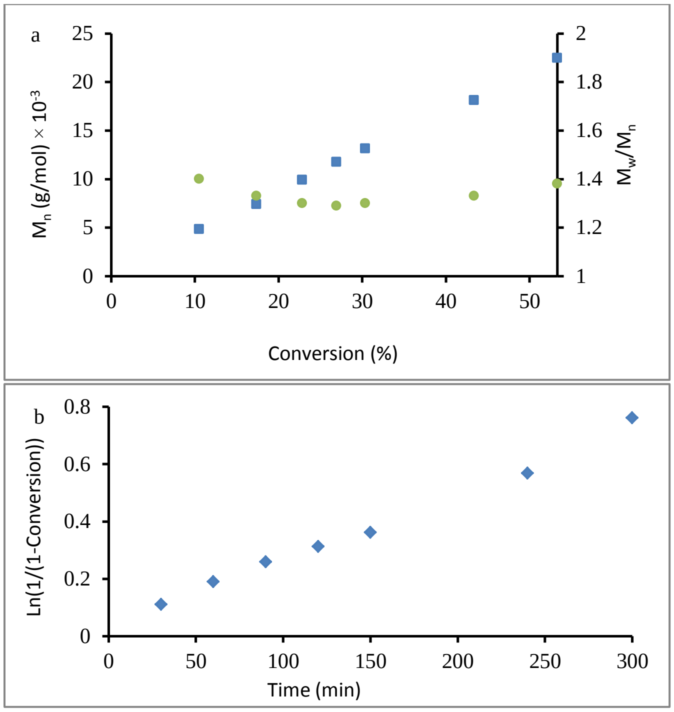


Figure 3.6 Kinetic plots of the bulk copolymerization of DEAEMA and S (initial molar fraction of styrene: $f_{s0}$=0.1) at 80 °C in the presence of NHS-BlocBuilder and SG1 ($[SG1]_0/[NHS\text{-}BlocBuilder]_0$=0.1). (a) number-average molar mass, $M_n$, and polydispersity index, PDI, vs conversion. (b) ln[1/(1-X)] vs time (X= conversion).

The initiator efficiency appeared to be very high since there is no remaining peak in the low molecular weight parts of the SEC chromatograms. The final polydispersity was less than 1.4 for a macroinitiator with $M_n$ ~ 23000 g/mol and 53 % conversion in bulk. Finally, to ensure most of the poly(DEAEMA-*co*-S)-SG1 chains were capped with an SG1 moiety, chain extension tests were performed in bulk using styrene as monomer. The temperature was chosen as 120 °C which is suitable for the NMP of styrene. The SEC chromatogram of the poly(DEAEMA-*co*-S) macroinitiator shifted to higher molecular weight without any shoulder on the low molecular side of the chromatogram, confirming a high degree of livingness of the macroinitiator (Figure 3.8).

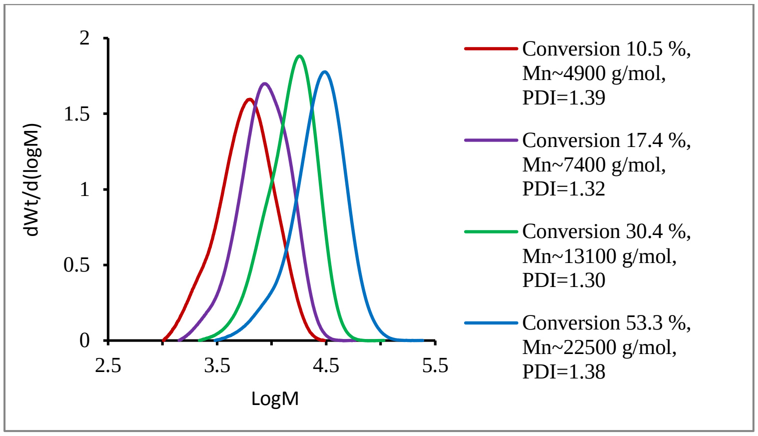


Figure 3.7 Size exclusion chromatograms of the DEAEMA and S copolymer obtained in bulk at 80 °C with $f_{s0}$=0.1 and $[SG1]_0/[NHS\text{-}BlocBuilder]_0$=0.1 at various monomer conversions for the copolymer.

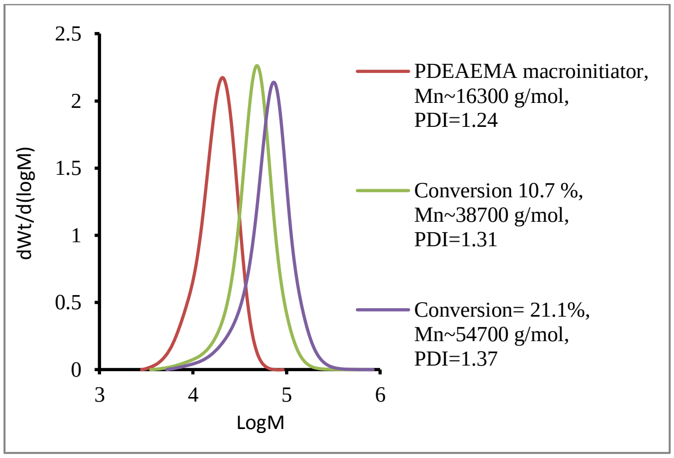


Figure 3.8 Chain extension of the poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine via nitroxide-mediated polymerization of styrene in bulk at 120 °C.

### 3.3.2 Surfactant-free emulsion polymerization of MMA

In its protonated form, poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine is expected to be water-soluble and thus to be able to stabilize latex particles obtained by a polymerization-induced self-assembly mechanism. As such, and with the aim of preparing easily coagulatable/redispersible latexes via NMP, we first tried to use $CO_2$ as a protonating agent for the macroalkoxyamine. However, protonation of the poly(DEAEMA-*co*-S)-SG1 macroinitiator with $CO_2$ appeared challenging for different reasons. Firstly, at the higher temperatures employed for NMP (T> 80 °C), the solubility of $CO_2$ in water is almost negligible and hence does not reduce the solution pH below the $pK_a$ of the polymer (i.e. $pK_a$=7.4[32]). As a result, the macroinitiator protonated at room temperature reverts to its neutral form at reaction temperature and is no longer able to stabilize latex particles. Secondly, based on our observations if the concentration of DEAEMA in water exceeds ~10 wt%, protonation requires long times at room temperature. Even after a long time, complete protonation of all the amine groups in the polymer chains is not possible using only a weak acid such as carbonic acid.[33] Therefore, HCl (strong acid) was used for protonation of the macroinitiator during the emulsion polymerization experiments (Figure 3.9).

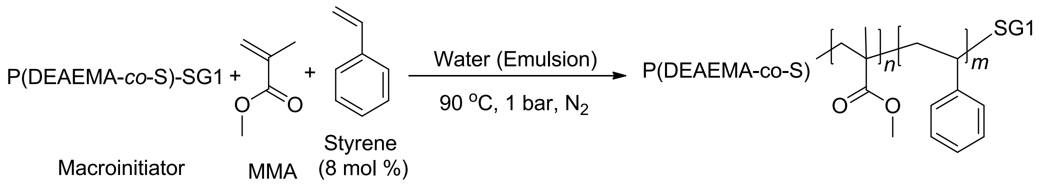


Figure 3.9 A schematic representation of emulsion copolymerization of MMA and S initiated by poly(DEAEMA-*co*-S)-SG1 macroinitiator.

Table 3.1. shows the experimental conditions employed in the polymerization-induced self-assembly (PISA) of MMA with either poly(DEAEMA-*co*-S)-SG1 or poly(DMAEMA-*co*-S)-SG1 macroinitiators.

Table 3.1 Experimental conditions for the surfactant-free emulsion copolymerization of MMA with a small percentage of styrene initiated by poly(DEAEMA-*co*-S)-SG1 or poly(DMAEMA-*co*-S)-SG1 macroinitiators.

| No. | Macroinitiator | $M_n$[a] (g mol$^{-1}$) | [Macroinitiator]$_0$ (mmol L$^{-1}$ solution) | [MMA]$_0$ (mol L$^{-1}$) | [S]$_0$ | $f_{s,0}$[b] | Target $M_n$[c] at full conversion (g mol$^{-1}$) | $Z_{ave}$ (nm) |
|---|---|---|---|---|---|---|---|---|
| 1 | $M_1$ | 5900 | 1.27 | 1.68 | 0.18 | 0.1 | 158250 | 90 |
| 2 | $M_2$ | 17530 | 1.96 | 1.46 | 0.16 | 0.1 | 100380 | 75 |
| 3 | $M_3$ | 5470 | 3.72 | 1.67 | 0.14 | 0.08 | 50000 | 61 |
| 4 | $M_4$ | 3870 | 4.46 | 0.71 | 0.06 | 0.08 | 21740 | - |

[a] Experimental $M_n$ measured by SEC, [b] Mole fraction of styrene in the monomer feed, [c] Theoretical number-average molar mass calculated according to $M_n$ = MM(macroinitiator) + conversion × initial weight of monomers/initial mol number of macroinitiator, with conversion =1.

In the first experiment (No. 1, Table 3.1) the suitability of the protonated poly(DEAEMA-*co*-S)-SG1 macroinitiator with $M_n$~5900 g mol$^{-1}$ for producing stable latex was evaluated. The reaction was stopped after 5 h and the polymer was neutralized with 1 M sodium hydroxide solution thus inducing coagulation of the latex particles that could be filtered and dried. The conversion of MMA was 40 % and the final latex was stable without any coagulum. The dried polymer had a molecular weight of 101 kDa with dispersity of 1.4. The clear shift in the SEC chromatograms (Figure 3.10) indicates the formation of poly(poly(DEAEMA-*co*-S)-*b*-poly(MMA-*co*-S)) amphiphilic block copolymers according to the PISA technique.

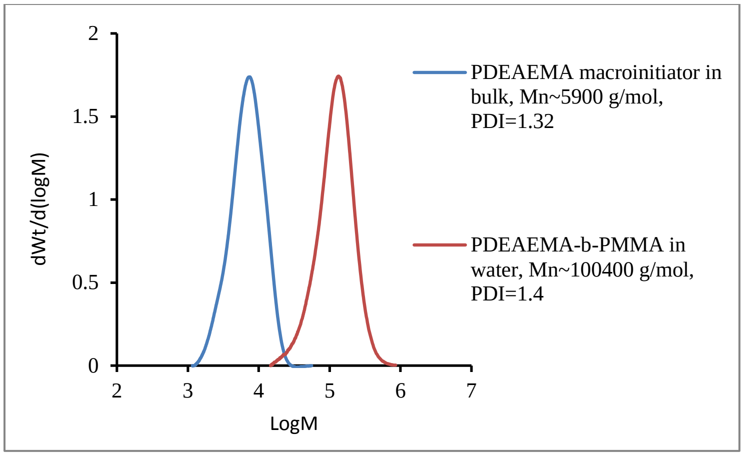


Figure 3.10 Size exclusion chromatograms at various monomer conversions for nitroxide-mediated emulsion copolymerization of MMA and S initiated with Poly(DEAEMA-*co*-S) macroinitiator at 90 °C.

To investigate the effect of the molecular weight of the macroinitiator on the pH-responsiveness of the latex, which will be discussed later, a new macroinitiator ($M_2$ in Table 3.1) with higher $M_n$ was prepared. To increase the conversion, concentration of the macroinitiator was increased in order to increase the number of generated radicals in the water phase and as a result increase the number of oligoradicals which finally leads to the increase in the number of particles. Samples were taken periodically to monitor the control and livingness of the reaction. Results are shown in Figure 3.11. Number average molecular weights were higher than theoretical values (Figure 3.11 a). SEC chromatograms shifted to higher molecular weights but small shoulders were observed at lower molecular weights, which indicate the macroinitiator contains some dead chains (Figure 3.11 b). Polydispersities are higher compared to the previous experiments which indicate decrease in the control of the reaction. The livingness of the reaction decreased at conversions higher than 40%. The intensity average particle size is monomodal with the average diameter of 75 nm (Figure 3.11 c).

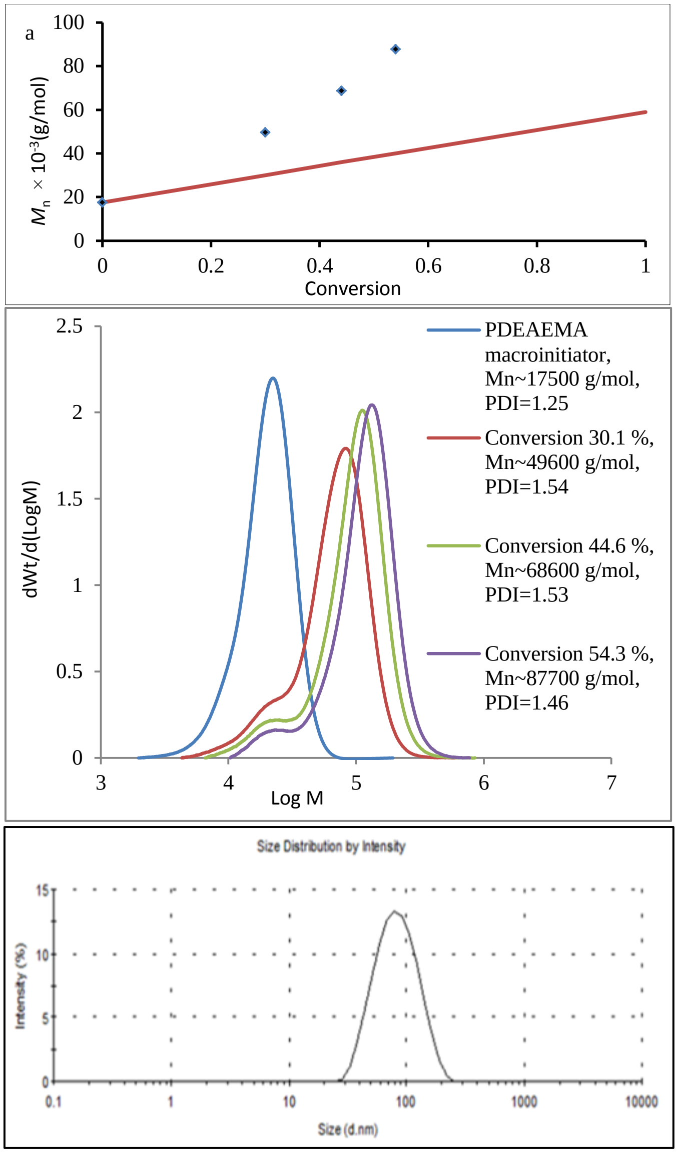


Figure 3.11 Nitroxide-mediated emulsion copolymerization of MMA and S initiated with Poly(DEAEMA-*co*-S) macroinitiator at 90 °C (No. 2, Table 3.1) (a) number average molecular weight versus conversion, (b) Size exclusion chromatograms at various monomer conversions, (c) Intensity distribution of particles size from DLS.

To increase the polymerization rate and final conversion, the amount of styrene in the monomer mixture was reduced from 10 to 8 % (No.3 Table 3.1). In this case, conversion increased from 54% in the previous experiment to more than 63% at the same reaction time. Also, decreasing the $M_n$ of the macroinitiator improved the control and livingness of the polymerization which can be seen from the lower PDIs and better shifts in the SEC chromatograms (Figure 3.12). The polydispersities decreased considerably from 1.46 to 1.23. No residuals of the macroinitiator were observed in the SEC chromatograms, indicating very efficient reinitiating ability of the polymer chains. Attempts at precipitation of poly(DEAEMA-*co*-S) with molecular weight less than 5000 g mol$^{-1}$ in hexane or diethyl ether were not successful.

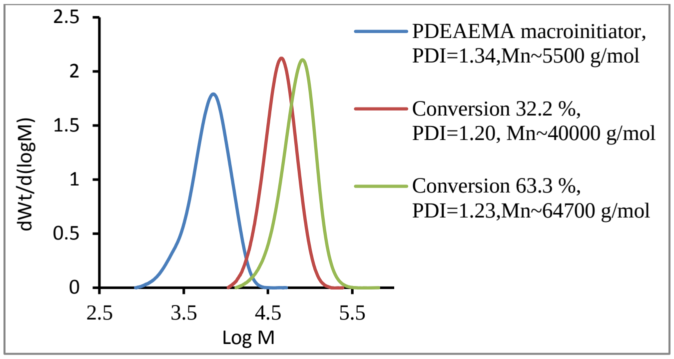


Figure 3.12 Size exclusion chromatograms at various monomer conversions for nitroxide-mediated emulsion copolymerization of DEAEMA and S at 90 °C with $f_{S0}$=0.08.

DMAEMA is another pH-sensitive monomer with a structure similar to DEAEMA. It has higher water-solubility (more hydrophilic) which can be helpful in redispersion of dried latex. Furthermore, its precipitation in hexane is considerably easier compared to DEAEMA. Thus, poly(DMAEMA-*co*-S)-SG1 macroinitiator with $M_n$=3870 g mol$^{-1}$ was synthesized and readily precipitated in hexane (No. 4, Table 3.1). It was then used as a macroinitiator instead of poly(DEAEMA-*co*-S)-SG1. The macroinitiator concentration was increased while the length of the second block decreased. Results are shown in Figure 3.13. Final conversion increased to more than 70%. Ln [1/(1-conv.)] increased almost linearly with time and the polydispersity of the latex decreased to 1.18. Size exclusion chromatograms of the macroinitiator completely shifted to the right, and there was no visible shoulder which confirms that most of the macroinitiator chains were living. In all of the synthesized latexes, coagulation occurred immediately after neutralizing the latex with sodium hydroxide. In other words, all the latexes were easily switched off. After separation of the latex particles by centrifugation, washing with DI water to remove the residual salt, drying under air for 24 h, and grinding, the dried latex powders were partially redispersible in carbonated water with $CO_2$ bubbling for 30 minutes and followed by sonication for 10 minutes. Increasing the period time of $CO_2$ bubbling and the number of sonication cycles improved the redispersibility of the latexes. Interestingly, those latexes dried under air without neutralization by NaOH, were readily redispersible by water addition with a few minutes sonication. Chain entanglements of the polymers in the particle shell may affect the $CO_2$-redispersibility of the latexes.

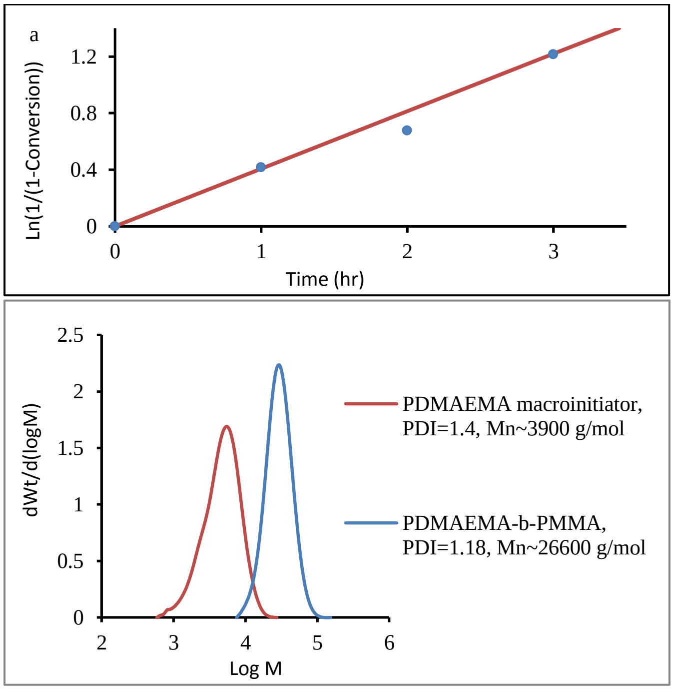


Figure 3.13 Emulsion copolymerization of MMA and S (initial molar fraction of styrene: $f_{s0}$=0.1) at 90 °C initiated by poly(DMAEMA-*co*-S)-SG1 macroinitiator (No. 4 Table 3.1), (a): Ln [1/(1-conversion)] vs time plot, (b): Size exclusion chromatograms at various monomer conversions.

## Conclusions

The nitroxide-mediated polymerization of DEAEMA and DMAEMA using either a bicomponent system of VA-061 as initiator and SG1 as nitroxide, or a monocomponent system of NHS-BlocBuilder led to excellent results in terms of control and livingness of the polymerization reactions. The synthesized poly(DEAEMA-*co*-S)-SG1 and poly(DMAEMA-*co*-S)-SG1 macroalkoxyamines were used for the first time as stabilizers and macroinitiators in their protonated form in the nitroxide-mediated surfactant-free emulsion polymerization of MMA and small amount of styrene based on the polymerization-induced self-assembly mechanism. The polymerizations showed the features of controlled and living polymerizations. The final latex displayed a monomodal particle size distribution with particle sizes between 70 and 90 nm, was pH-responsive and was easily coagulated by neutralization with NaOH. Redispersion of those NaOH-neutralized and dried latexes in carbonated water was difficult; however, latexes dried under air were easily redispersed.

To simplify the process and omitting the precipitation and purification of the macroalkoxyamine, poly(DEAEMA-*co*-S) should be synthesized in water and the hydrophobic monomer is added directly to the reaction medium to produce diblock copolymer. In chapter 4, the synthesis of DEAEMA-based macroinitiator will be explained and then in chapter 5 one-pot synthesis of PMMA latex will be studied.

## References

(1) Lin, S.; Theato, P. *Macromol. Rapid. Commun*. **2013**, 34, 1118-1133.

(2) Li, M. H.; Keller, P. *Soft Matter* **2009**, 5, 927-937.

(3) Pinaud, J.; Kowal, E.; Cunningham, M.; Jessop, P. *ACS Macro Lett.* **2012**, 1, 1103-1107.

(4) Yan, B.; Han, D.; Boissiere, O.; Ayotte, P.; Zhao, Y. *Soft Matter* **2013**, 9, 2011-2016.

(5) Kelley, E. G.; Albert, J. N. L.; Sullivan, M. O.; Epps, T. H. *Chem. Soc. Rev*. **2013**, 42, 7057-7071.

(6) Manganiello, M. J.; Cheng, C.; Convertine, A. J.; Bryers, J. D.; Stayton, P. S. *Biomaterials* **2012**, 33, 2301-2309.

(7) Tang, Y.; Liu, S. Y.; Armes, S. P.; Billingham, N. C. *Biomacromolecules* **2003**, 4, 1636-1645.

(8) Zhang, X.; Xia, J.; Matyjaszewski, K. *Macromolecules* **1998**, 31, 5167-5169.

(9) Zeng, F.; Shen, Y.; Zhu, S. *Macromol. Rapid. Commun*. **2002**, 23, 1113-1117.

(10) Gan, L.; Ravi, P.; Mao, B. W. M.; Tam, K. *J. Polym. Sci., Part A: Polym. Chem*. **2003**, 41, 2688-2695.

(11) Smith, A. E.; Xu, X.; McCormick, C. L. *Prog. Polym. Sci*. **2010**, 35, 45-93.

(12) Xiong, Q.; Ni, p.; Zhang, F.; Yu, Z. *Polymer Bull.* **2004**, 53, 1-8.

(13) Sahnoun, M.; Charreyre, M. T.; Veron, L.; Delair, T.; D'Agosto, F. *J. Polym. Sci., Part A: Polym. Chem*. **2005**, 43, 3551-3565.

(14) Goto, A.; Ohtsuki, A.; Ohfuji, H.; Tanishima, M.; Kaji, H. *J. Am. Chem. Soc*. **2013**, 135, 1131-1139.

(15) Lokaj, J.; Vlcek, P.; Kriz, J. *Macromolecules* **1997**, 47, 7644-7646.

(16) Bian, K.; Cunningham, M. F. *J. Polym. Sci., Part A: Polym. Chem*. **2006**, 44, 414-426.

(17) Zhang, C.; Maric, M. *Polymers* **2011**, 3, 1398-1422.

(18) Han, D.; Tong, X.; Zhao, Y. *ACS Macro Lett*. **2012**, 1, 57-61.

(19) Su, X.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 666-670.

(20) Zhang, M.; He, J.; Mao, J.; Liu, C.; Wang, H.; Huang, Y.; Ni, P. *Colloids and Surf., A*, **2010**, 360, 190-197.

(21) Zhang, Q.; Yu, G.; Wang, W. J.; Li, B. G.; Zhu, S. *Macromol. Rapid. Commun*. **2012**, 33, 916-921.

(22) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Macromolecules* **2013**, 46, 1261-1267.

(23) Shahalom, S.; Tong, T.; Emmett, S.; Saunders, B. R. *Langmuir* **2006**, 22, 8311-8317.

(24) Cunningham, M. F. *Prog. Polym. Sci*. **2008**, 33, 365-398.

(25) Gohy, J. *J. Adv. Polym. Sci.*, **2005**, 190, 65-136.

(26) Riess, G.; Labbe, C. *Macromol. Rapid. Commun*. **2004**, 25, 401-435.

(27) Lavasanifar, A.; Samuel, J.; Kwon, G. S. *Advanced Drug Delivery Reviews* **2002**, 54, 169-190.

(28) Odian, G. Principles of Polymerization; Fourth Edi. John Wiley & Sons: Hoboken, Ney Jersey, **2004**.

(29) Charleux, B.; Delaittre, G.; Rieger, J.; D'Agosto, F. *Macromolecules* **2012**, 45, 6753-6765.

(30) Vinas, J.; Chagneux, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D,; *Polymer*, **2008**, 49, 3639-3647.

(31) Nicolas, J.; Mueller, L.; Dire, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules*, **2009**, 42, 4470-4478.

(32) Butun, N. C. B. V.; Armes, S. P.; *Polymer*, **2001**, 42, 5993-6008.

(33) Cotanda, P.; Wright, D. B.; Tyler, M.; O'Reilly, R. K.; *J. Polym. Sci., Part A: Polym. Chem.* **2013**, 51, 3333-3338.

## Chapter 4

# Nitroxide-mediated polymerization of 2-(diethyl) aminoethyl methacrylate (DEAEMA) in water

## Abstract

The nitroxide-mediated polymerization (NMP) of 2-(diethyl)aminoethyl methacrylate (DEAEMA) with a small amount of acrylonitrile (AN) as a comonomer was performed for the first time in water at 90 °C and atmospheric pressure using *n*-hydroxysuccinimidyl BlocBuilder (NHS-BB) alkoxyamine without addition of excess nitroxide. The same reaction was carried out using the bicomponent initiating system 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044) as initiator and *N*-tert-butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1) as nitroxide. Both polymerization reactions were well-controlled and exhibited excellent livingness as evidenced by low molar dispersity and evolution of the molar mass distribution. The hydrolytic stability of DEAEMA at the polymerization conditions and the effects of several parameters including initiating system, temperature, ratio of nitroxide to initiator, initiator and monomer concentrations, and comonomer type were investigated. Chain extension of the synthesized macroinitiator with methyl methacrylate (MMA) and styrene (S) MMA in a one-pot process led to the i*n situ* formation of poly(DEAEMA-*co*-AN)-*b*-poly(MMA-*co*-S) diblock copolymers based on the polymerization-induced self-assembly (PISA) process.

## 4.1. Introduction

Development of controlled/living radical polymerization (CLRP) has had a major impact on polymer science.[1,2,3] (The new terminology of Reversible-Deactivation Radical Polymerization (RDRP) has been proposed by IUPAC for CLRP.[4]) Polymeric architectures with different composition, structures, and functionalities can be prepared in relatively mild conditions by CLRP techniques. Of the three main types of CLRPs, nitroxide-mediated polymerization (NMP) and atom-transfer radical polymerization (ATRP) are based on reversible activation-deactivation cycles of growing polymer chains while reversible-addition-fragmentation-transfer (RAFT) polymerization is based on reversible chain transfer.[3] NMP is a powerful technique with arguably the simplest mechanisms amongst all LRP techniques for preparing polymers with a narrow molecular weight distribution (MWD) and low molar dispersity ($Đ$).[5] Furthermore, there is no concern of residual catalyst, colour or toxicity in the final polymer. CLRP can be applied for the preparation of well-defined polymeric architectures in aqueous media which is not possible in ionic polymerization.[3] However, applying CLRP in aqueous media (homogeneous or dispersed) is often quite difficult due to problems such as hydrolysis and aminolysis reactions in RAFT polymerization or other side reactions in the case of ATRP.[6,7] There are a very limited number of reports related to NMP in homogeneous aqueous solution. A further difficulty for NMP is the high temperature (>100 °C) traditionally required which necessitates using pressurized vessels. However, performing NMP at lower temperatures now is possible with some nitroxide/monomer combinations. The first example of NMP conducted in homogeneous aqueous solution was with of sodium 4-styrenesulfonate in water using a 2,2,5-trimethyl-4-phenyl-3-azahexane-3-oxy (TIPNO) based carboxy-funtionalized nitroxide.[7] The alkoxyamine was synthesized by a multi-step process and was water-soluble in its basic form. NMP of the same monomer was performed at 120 °C using a bicomponent initiating system consisting of the water-soluble nitroxide (synthesized beforehand through a multi-step process) and VA-044 and V-50 initiators.[8] NMP of *n*,*n*-dimethylacrylamide, sodium 4-styrenesulfonate, and 2-(acryloyloxy)ethyl benzyldimethylammonium chloride was carried out in water using an SG1-based alkoxyamine containing a carboxylic acid group (MAMA-SG1) and free excess SG1.[6] The alkoxyamine was converted to the water-soluble state by addition of sodium hydroxide before the start of the reaction and the blocking efficiency of the synthesized polymers was assessed by chain extension experiments. Grassl et al.[9] conducted the NMP of acrylamide in water at 120 °C using a bicomponent initiating system comprised of SG1 as the nitroxide and 2,2'-azobis (2-methylpropionamidine)dihydrochloride (VAZO®56WSP). The polymerization proceeded (without significant monomer hydrolysis), yielding star-like polymer chains. The same group polymerized acrylamide in water employing a similar initiating system in microwave-assisted NMP.[10] Charleux's group[11] performed nitroxide-mediated copolymerization of methacrylic acid (MA) and sodium 4-styrenesulfonate in acidic conditions (pH=3.5) in water using the BlocBuilder alkoxyamine and SG1 at a comparatively low temperature (76 °C). The short polymerization time and low temperature were considered important parameters in enabling the successful NMP even at low pH. Chain extension experiments were then conducted in the emulsion copolymerization of methyl methacrylate (MMA) and styrene at 90 °C in the same pot.

(Diethylamino)ethyl methacrylate (DEAEMA) and (dimethylamino)ethyl methacrylate (DMAEMA) are two typical examples of tertiary amine methacrylate-based monomers. The p*K*a of DEAEMA and DMAEMA monomers are 8.8 and 8.3 while the p$K_a$ of their corresponding homopolymers are 7.5 and 7.4, respectively.[12] Recently, DEAEMA and DMAEMA have received considerable attention because of their $CO_2$-switchability.[13-24] For example, $CO_2$-switchable latex,[25] surfactant,[26] and hydrogel[17,27] have been prepared using DEAEMA and DMAEMA as $CO_2$-switchable components in the structure of the final polymers. In most of these publications, DEAEMA and/or DMAEMA were polymerized via RAFT or ATRP. There are few reports related to the NMP of functional monomers bearing a tertiary amine group. Polystyrene macroinitiator was employed for the NMP of 2-(dimethylamino)ethyl methacrylate (DMAEMA) in bulk.[28] The effect of different parameters such as solvent polarity, temperature, excess nitroxide, and chain transfer to polymer on the NMP of DMAEA was reported by Cunningham.[29] A copolymer of DMAEMA and styrene was synthesized by NMP in bulk at 80 °C employing *n*-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder) alkoxyamine.[30] The chain extension experiment with a DMAEMA/styrene mixture was performed to assess the livingness of the poly(DMAEMA-*co*-S).

In our previous publication[31] we synthesized poly(DEAEMA-*co*-S) in bulk and then employed it in the protonated form as a macroalkoxyamine for the preparation of PMMA latexes. To the best of our knowledge there is no report of NMP of methacrylate monomers containing a tertiary amine group in water. In this paper we report for the first time the NMP of DEAEMA in water using different initiating system at temperatures below the boiling point of water. The effect of parameters including temperature, comonomer type, excess nitroxide, monomer concentration, and initiator concentration on the control and livingness of the polymerization reaction are studied in detail. The livingness of the poly(DEAEMA-*co*-AN) is demonstrated by chain extension in a one-pot process using polymerization-induced self-assemble (PISA).[32]

## 4.2. Experimental section

**Materials.** All chemicals, monomers, and inhibitor removal columns were purchased from Aldrich unless otherwise stated. 2-(Diethylamino)ethyl methacrylate (DEAEMA, 99%) was passed through a column of basic aluminum oxide (mesh ~150) prior to use. Styrene (S, >99%) and methyl methacrylate (MMA, 99%) were purified by passing through columns packed with inhibitor remover. The 2-((tert-butyl-(1-(diethoxyphosphoryl)-2,2-dimethylpropyl) amino) oxy)-2-methylpropanoic acid initiator (BlocBuilder) and *N*-tertbutyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1, 85%) were supplied by Arkema. 2,2'-Azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044) was purchased from Wako Pure Chemical Industries and used without further purification. Sodium hydroxide (NaOH, >97%), tetrahydrofuran (THF, >99%), hydrochloric acid (38 wt%), and nitrogen ($N_2$, Praxair, medical grade) were used as received. All aqueous solutions were prepared with deionized water (DIW). *N*-hydroxysuccinimide BlocBuilder (NHS-BB) was synthesized according to the reported procedure.[33]

**Copolymerization of DEAEMA and AN in water.** In a typical experiment (exp. 5, Table 4.1), DEAEMA (5.0 g, 27.0 mmol), and deionized water (48 mL) were mixed in a 100 mL 3-neck round-bottom flask. The flask was immediately immersed in an ice-water bath and the pH of the solution adjusted to 6 by dropwise addition of concentrated hydrochloric acid (HCl 38 wt%). Then, AN (0.14 g, 2.7 mmol) (initial molar fraction of AN in the monomer mixture: $f_{s0}$= 0.09), NHS-BB (0.07 g, 0.15 mmol), and SG1 (8.0 mg, 0.03 mmol) were introduced into the flask and the mixture was deoxygenated with a nitrogen stream for 20 min. The mixture was then introduced into a preheated oil bath at 90 °C and fitted with a reflux condenser, a nitrogen inlet and a thermometer. Time zero of the polymerization was taken when the flask was immersed in the oil bath. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and allowed to react for 2 h with samples withdrawn periodically for kinetic studies and raw polymer analysis. Samples were quenched by immersion in ice-water bath. A portion of each sample was used for NMR analysis and the remainder neutralized with NaOH 1 M and then dried under air for 24 h for SEC analysis.

**Chain extension experiment.** DEAEMA (0.5 g, 0.53 mol $L^{-1}$), styrene (28 mg, 0.053 mol $L^{-1}$), SG1 (23 mg, 11 mmol $L^{-1}$), VA-044 (17 mg, 7.5 mmol $L^{-1}$), and DIW were mixed in a round bottom flask and pH was adjusted to 6 by dropwise addition of concentrated HCl. The contents of the flask were then deoxygenized by bubbling nitrogen for 20 min while immersing in an ice-water bath. Then flask was inserted into a preheated oil bath at 90 °C. After 15 min of reaction, the contents of the flask were added to a second flask containing hydrophobic monomers and the reaction continued for 2 h. For the preparation of hydrophobic monomers, MMA (10.12 g, 0.9 mol $L^{-1}$), S (1.04 g, 0.09 mol $L^{-1}$), and deionized water were mixed in a separate flask and deoxygenized for 20 min by bubbling with nitrogen, and then inserted into a preheated oil bath at 90 °C.

**Characterization.** The monomer conversion was determined by $^1H$ NMR (Bruker Advance-400) performed in 5 mm diameter tubes in $D_2O$ at room temperature. The monomer conversion was calculated by measuring the vinyl proton integrals at δ=6.11 ppm and δ=5.82 ppm using 1,3,5-trioxane as an internal reference (δ=5.26 ppm). The chemical shift scale was calibrated based on tetramethylsilane. Size exclusion chromatography (SEC) was used to determine the molecular weight and polydispersity index (*Đ*) of the polymer samples. The SEC was equipped with a Waters 2960 separation module containing three Styragel columns coupled with the separation limits between 400 and $1 \times 10^6$ g $\mathrm{mol^{-1}}$. THF was used as the eluent with a flow rate of 0.3 mL $\mathrm{min^{-1}}$. A differential refractive index detector (Waters 2960) was used and the average molar masses ($M_\mathrm{n}$ and $M_\mathrm{w}$) and molar mass dispersity (*Đ*) were derived from a calibration curve based on polystyrene (PS) standards from Polymer Standard Service. All the amine groups were neutralized with base (1 M sodium hydroxide) before running SEC.

## 4.3. Results and discussion

### 4.3.1 Hydrolysis of DEAEMA

In the previous chapter (published in *Polymer Chemistry*[31]) it was explained that poly(DEAEMA-*co*-S)-SG1 macroinitiator was synthesized in bulk and then used as a macroalkoxyamine in the preparation of PMMA latexes. DEAEMA is a $CO_2$-switchable monomer that becomes hydrophilic when protonated by purging $CO_2$ in its aqueous solution at room temperature. Our attempts at conducting NMP of DEAEMA under $CO_2$ atmosphere in aqueous solutions were not successful, primarily because of the very low solubility of $CO_2$ in water at the higher temperatures required for NMP. In fact, the reaction medium was heterogeneous and some small fraction of DEAEMA remained in the protonated form while the major part of that was deprotonated and became hydrophobic. In this work we decided to protonate DEAEMA using a strong acid (HCl) to ensure that all of the DEAEMA remains in the protonated form during reaction at high temperatures and the system is homogeneous at all times. In all of our experiments the pH was adjusted to 6, which is low enough to solubilize DEAEMA in water and prevent hydrolysis at elevated temperatures (as discussed below). For investigating the effect of pH on the hydrolysis of DEAEMA, three samples were prepared with the same concentration of DEAEMA in water (1.0 mol $L^{-1}$). The pH of the samples was adjusted to 9, 8, and 7, respectively. The samples were placed into a preheated oil bath at 90 °C for 2 h. The same experiment was repeated at 80 °C. $^1$H NMR spectra were recorded every 15 min during and also at the start the experiment (The $^1$H NMR spectra of hydrolysis experiments and calculations of hydrolysis percentage can be found in the Appendix A). Figure 4.1 shows the effect of pH and temperature on the rate of DEAEMA hydrolysis.

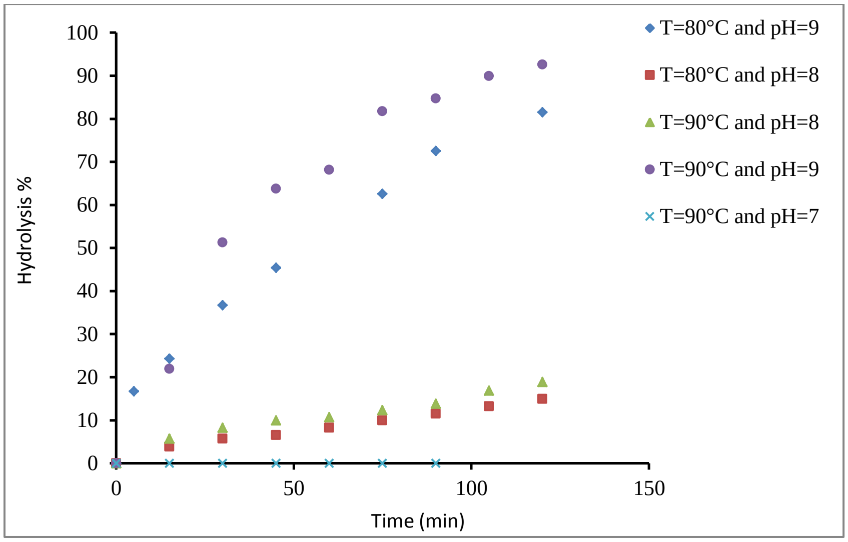


Figure 4.1 DEAEMA hydrolysis in water (1 M solution) with varying pH and temperature.

At pH 9 the rate of hydrolysis is very high; in 2 h more than 90% of the monomer is hydrolysed at 90 °C, which is the reaction temperature used for the NMP of DEAEMA in this study. While decreasing temperature to 80 °C reduced the hydrolysis percentage to some extent, reduction of pH from 9 to 8 had a much more pronounced effect on decreasing the hydrolysis percentage. At pH 7, hydrolysis was negligible during the 2 h experiment although there was still some hydrolysis observed over a longer period of time (< 10% after 5 h). All experiments in this study were performed at pH range between 6 and 6.5 and no hydrolysis was observed during the polymerization. This pH range is also high enough to be suitable for SG1 use (SG1 degradation) and low enough to prevent hydrolysis of NHS-BlocBuilder.[34,35]

### 4.3.2 Comonomer type

DEAEMA is a methacrylate monomer and therefore not effectively homopolymerized using SG1 since a high portion of propagating radicals will terminate irreversibly due to the high activation-deactivation equilibrium constant K. Hydrogen transfer between propagating radicals and the nitroxide is another concern.[36] Adding a few mole percent of a comonomer with small K in the monomer mixture can reduce the overall equilibrium constant and increases the control and livingness of the reaction.[37] Therefore, in all experiments in this study 9 mol% of a comonomer such as styrene or acrylonitrile was added to the monomer mixture (Figures 4.2 and 4.3). Table 4.1 shows experimental conditions for the NMP of DEAEMA in water.

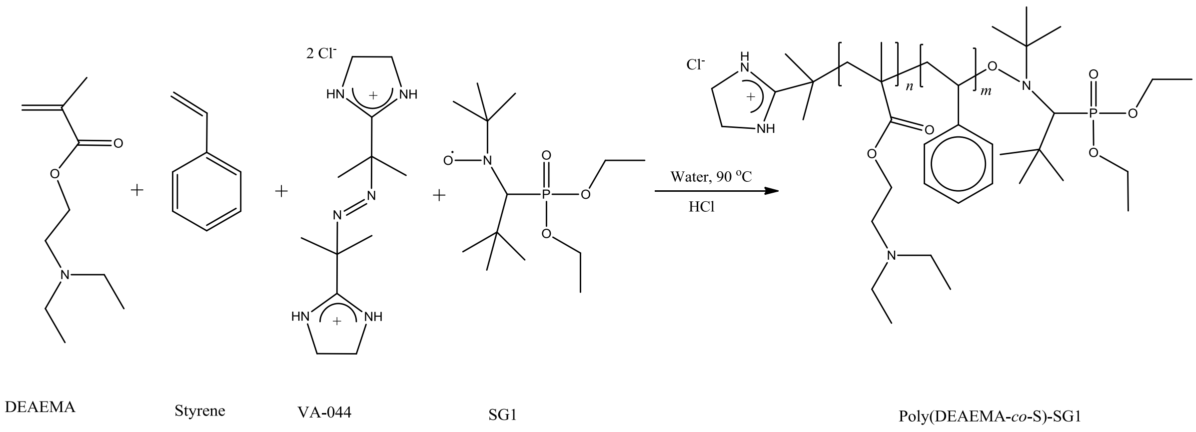


Figure 4.2 Schematic representation of the polymerization of DEAEMA with 9 mol% styrene in water initiated by VA-044.

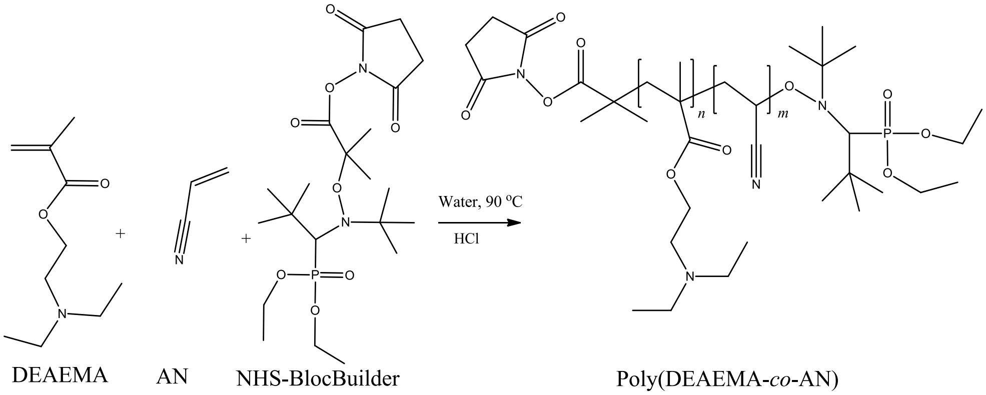


Figure 4.3 Schematic representation of the polymerization of DEAEMA with 9 mol% acrylonitrile in water initiated by NHS-BB.

Table 4.1 Experimental conditions for the NMP of DEAEMA in water.

| exp. | DEAEMA (mol L$^{-1}$) | initiator | s[a] | Comonomer | $f_{x,0}$[b] | r[c] | $M_{n,SEC}$ (g mol$^{-1}$) | $M_w/M_n$ | Time (min) | χ[d] (%) | Temp. (°C) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.5 | VA-044 | 0.005 | styrene | 0.09 | 1.5 | 19300 | 1.61 | 60 | 84.0 | 90 |
| 2 | 0.5 | VA-044 | 0.005 | styrene | 0.09 | 2 | 18000 | 1.36 | 60 | 66.0 | 90 |
| 3 | 0.5 | VA-044 | 0.005 | acrylonitrile | 0.09 | 2 | 15600 | 1.43 | 90 | 75.8 | 90 |
| 4 | 0.5 | NHS-BB | 0.005 | acrylonitrile | 0.09 | 0 | 49400 | 1.30 | 120 | 82.0 | 90 |
| 5 | 0.5 | NHS-BB | 0.005 | acrylonitrile | 0.09 | 0.1 | 45500 | 1.34 | 120 | 58.0 | 90 |
| 6 | 1.0 | NHS-BB | 0.005 | acrylonitrile | 0.09 | 0.1 | 54000 | 1.22 | 120 | 80.0 | 90 |
| 7 | 0.5 | NHS-BB | 0.005 | acrylonitrile | 0.09 | 0.2 | 39500 | 1.27 | 120 | 40.7 | 90 |
| 8 | 0.5 | NHS-BB | 0.01 | acrylonitrile | 0.09 | 0.2 | 21600 | 1.34 | 120 | 60.4 | 90 |
| 9 | 0.5 | NHS-BB | 0.005 | acrylonitrile | 0.09 | 0.2 | 42100 | 1.40 | 90 | 30.0 | 80 |
| 10 | 0.5 | VA-044 | 0.005 | acrylonitrile | 0.09 | 1.5 | 22400 | 1.35 | 300 | 90.0 | 80 |

[a] Molar ratio of initiator to monomers (s=[initiator]$_0$/([DEAEMA]$_0$+[comonomer]$_0$). [b] Initial molar fraction of comonomer in the monomer mixture ($f_{x,0}$=[comonomer]$_0$/([DEAEMA]$_0$+[comonomer]$_0$). [c] Ratio of free nitroxide to initiator (r=[SG1]$_0$/[Initiator]$_0$). [d] Conversions were Calculated by $^1$H NMR.

In the first experiment (exp. 1 Table 4.1), styrene was employed as a comonomer, VA-044 as initiator, and SG1 as nitroxide. At the start of the reaction, mixture was not completely homogeneous because of the low solubility of the styrene, but after a few minutes it became totally homogeneous. The ratio of SG1 to VA-044 was adjusted to 1.5. Although the livingness of the reaction was reasonably good according to the shift in molecular weight distributions (MWD) to higher values, the Đ of the final polymer was high (*Đ*=1.61), indicating relatively poor control over the reaction. Adding more SG1 ([SG1]$_0$/[VA-044]$_0$=2) increased the control of the reaction and lowered *Đ* to 1.36 (exp.2 Table 4.1). The addition of more SG1 did have a significant effect on the rate of the polymerization, and conversion plateaued after 40 min at 66%, likely due to nitroxide accumulation in the reaction medium. At the start of the reaction, the polymerization medium had a yellowish colour which disappeared quickly once the polymerization started and after a few minutes the solution became completely colourless.

Figure 4.4 shows the kinetic plots and Figure 4.5 shows the SEC chromatograms of experiment 2 in Table 4.1. Mild curvature can be seen in the log plot. The $M_n$ versus conversion plot shows an initially high value of $M_n$, which increases linearly but does not reflect slowly increasing number of chains during polymerization.

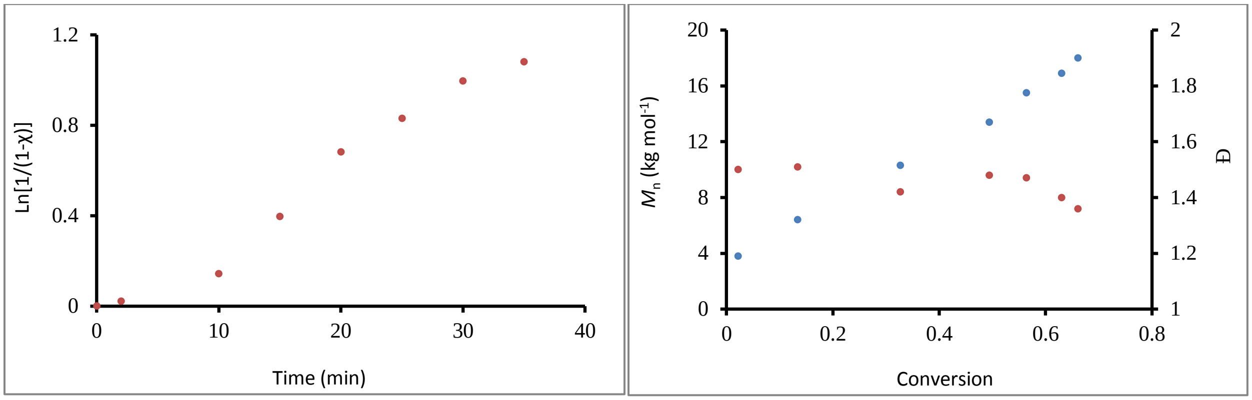


Figure 4.4 Kinetic plots of the copolymerization of DEAEMA and styrene (initial molar fraction of styrene: $f_{s0}$=0.1) at 90 °C using VA-044 as the initiator and SG1 as the nitroxide ($[SG1]_0/[VA\text{-}044]_0$=2).

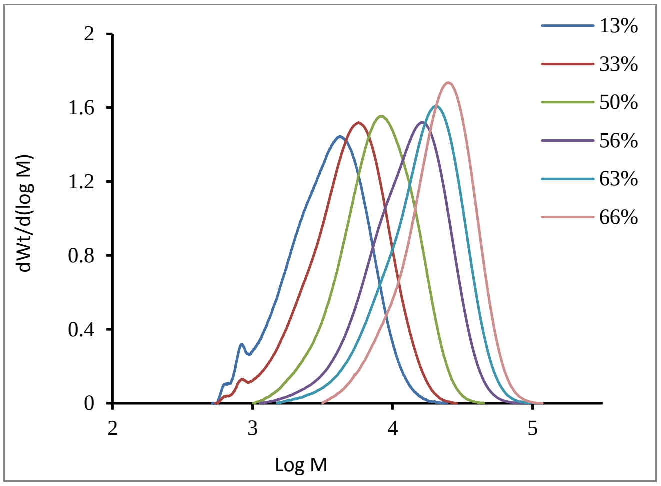


Figure 4.5 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% styrene in water at 90 °C using VA-044 as the initiator and SG1 as the nitroxide.

While DEAEMA is completely water-soluble at pH= 6, styrene is a hydrophobic monomer and its solubility in water is low. Therefore, a hydrophilic monomer such as acrylonitrile would be better choice as a comonomer (exp. 3 Table 4.1). It was previously reported that acrylonitrile is an effective comonomer for the NMP of MMA.[38] The kinetic data and SEC results showed that acrylonitrile can be also used as an effective comonomer for the NMP of DEAEMA in water (Figures 4.6 and 4.7).

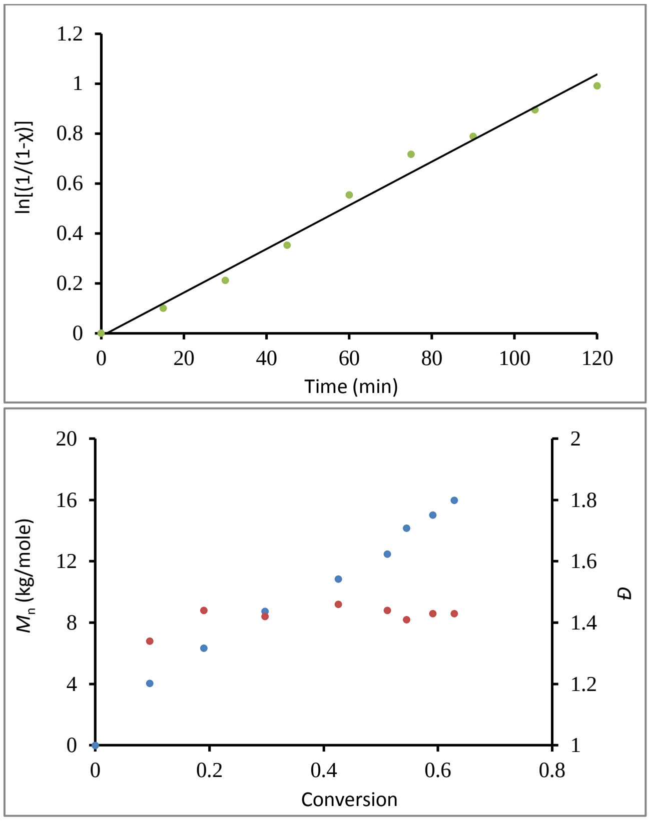


Figure 4.6 Kinetic plots of the copolymerization of DEAEMA and acrylonitrile (initial molar fraction of acrylonitrile: $f_{x0}$=0.09) at 90 °C using VA-044 as initiator and SG1 as nitroxide ($[SG1]_0/[VA\text{-}044]_0=2$): (a) ln[1/(1-χ)] versus time, (b) $M_n$ and $M_w/M_n$ versus conversion.

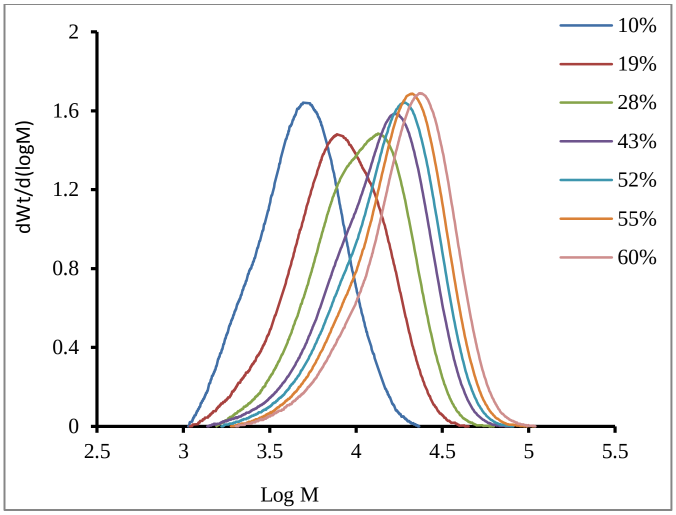


Figure 4.7 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using VA-044 as initiator and SG1 as nitroxide.

The linearity of the ln[1/(1-X)] versus time graph indicates a constant concentration of propagating radicals over the course of the polymerization. Also, the low molar mass dispersity ($Đ$ < 1.5) and the linear increase of the number-average molecular weight ($M_n$) versus conversion show good control of the reaction. The complete shift of the molecular weight distribution with increasing conversion confirms the livingness of the polymer chains.

### 4.3.3 Initiating system

To investigate the effect of the initiating system (monocomponent versus bicomponent) on the kinetic of the polymerization, NHS-BB was used as alkoxyamine in the NMP of DEAEMA in water (exp. 4 Table 4.1) using acrylonitrile as a comonomer. NHS-BlocBuilder has been applied previously in the NMP of DMAEMA in bulk using styrene as a comonomer at 80 °C.[30] To prevent hydrolysis of NHS-BlocBuilder and DEAEMA, the pH was adjusted to 6.[35] NHS-BB is not soluble in water at pH=6 but when the reaction is started at elevated temperatures; it is decomposed by heat and becomes soluble after a few minutes. Figures 4.8 and 4.9 show the kinetic plots and SEC chromatograms of the reaction.

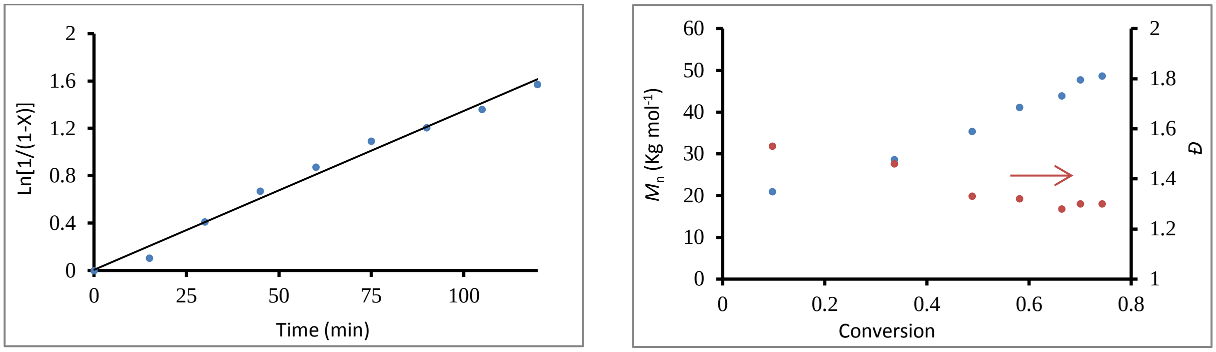


Figure 4.8 Kinetic plots of the copolymerization of DEAEMA and acrylonitrile (initial molar fraction of acrylonitrile: $f_{x0}$=0.09) in water at 90 °C using NHS-BB as alkoxyamine without adding free SG1 (a) ln[1/(1-X)] versus time, (b) $M_n$ and $M_w/M_n$ versus conversion.

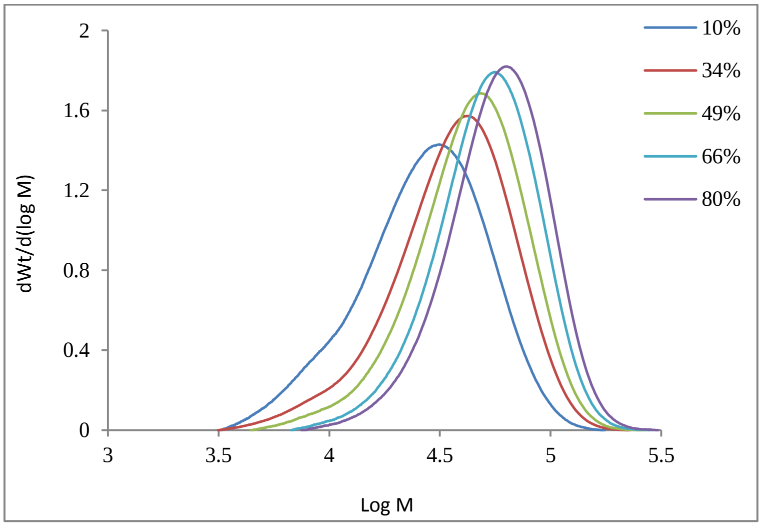


Figure 4.9 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using NHS-BB as alkoxyamine without adding free nitroxide.

$M_n$ and ln [1/(1-X)] increased linearly with conversion and time, respectively, which show the concentration of growing chains has remained constant during the reaction. The final *Đ* is 1.3 which confirms good control over the polymerization. The MWD plots show excellent livingness

(Figure 4.9). Somewhat surprisingly, good control over the reaction has been achieved using NHS-BB despite not adding free nitroxide.

### 4.3.4 Monomer concentration

To determine the effect of monomer concentration on the kinetics of the polymerization, two experiments were performed (exp. 5 and 6 in Table 4.1) with DEAEMA concentration of 0.5 and 1.0 mol $L^{-1}$, respectively, while the rest of the conditions such as comonomer concentration in the monomer mixture, the ratio of $[SG1]_0/[NHS\text{-}BB]_0$, and the temperature were kept constant (as a result, the target $M_n$ increased). The polymerization rate was much faster for the higher concentration of DEAEMA (Figure 4.10). Both reactions had a linear trend in the ln[1/(1-χ)] versus time graph but when the DEAEMA concentration was increased, the control over the reaction improved remarkably and the final Đ dropped from 1.34 to 1.22. Increasing the monomer concentration causes the polymerization medium to more closely resemble the bulk condition. The livingness of the reaction is also excellent, which can be seen in the shifts of the MWD to higher molecular weights in Figure 4.11.

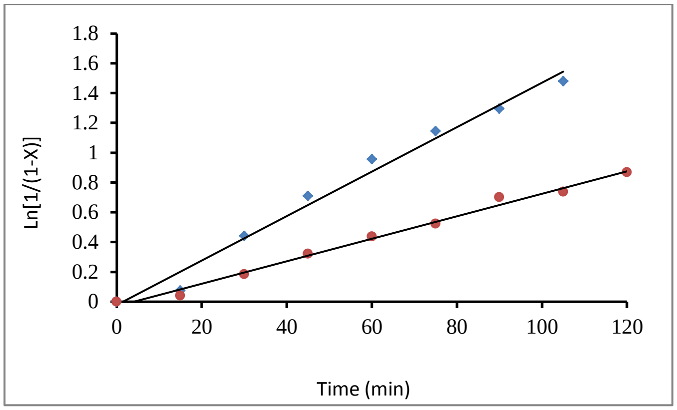


Figure 4.10 Kinetic plots of the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using NHS-BB as an alkoxyamine and SG1 as a nitroxide ($[SG1]_0/[NHS\text{-}BB]_0=0.1$); square: $[DEAEMA]_0= 1.0$ mol $L^{-1}$, and circle: [DEAEMA]0=0.5 mol $L^{-1}$.

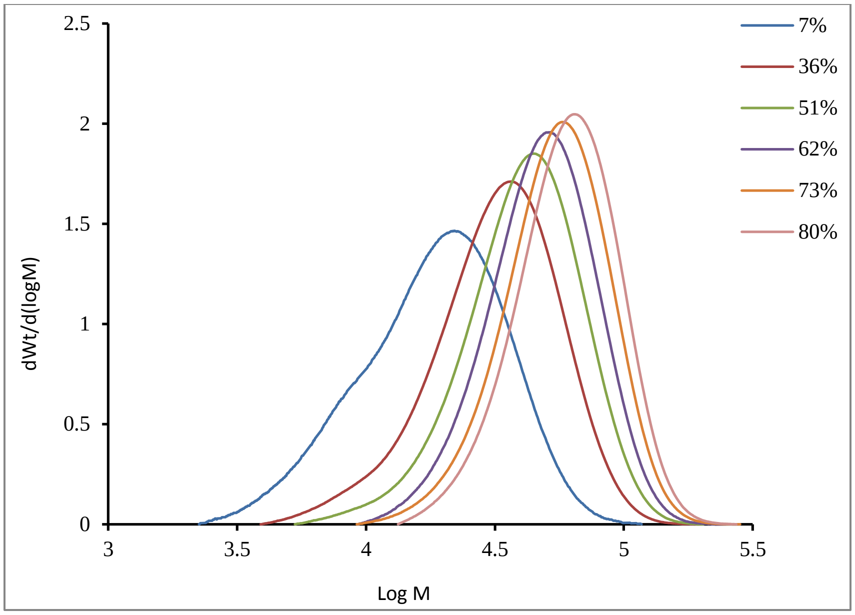


Figure 4.11 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90°using NHS-BB as an alkoxyamine and SG1 as a nitroxide ($[SG1]_0/[NHS\text{-}BB]_0=0.1$) with $[DEAEMA]_0=1.0$ mol $L^{-1}$.

### 4.3.5 Effect of SG1

It is common in NMP to add a few percent of free excess nitroxide with respect to the alkoxyamine at the start of the reaction to facilitate the establishment of the reversible activation-deactivation cycles of the dormant polymer chains. Without having free nitroxide at the start of the reaction and before establishment of the activation-deactivation equilibrium, increased termination can occur early in the polymerization. To compare the results of different experiments with variable quantities of free SG1 in the polymerization reaction, experiments 4, 5, and 7 in Table 4.1 were designed with $[SG1]_0/[NHS\text{-}BB]_0$= 0, 0.1, and 0.2, respectively. Figure 4.12 shows ln[1/(1-X)] versus time.

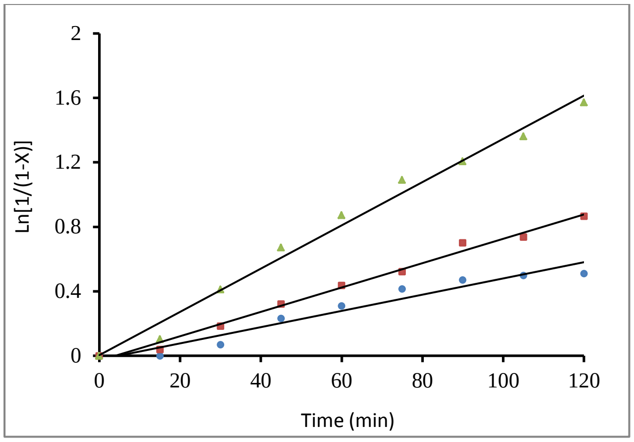


Figure 4.12 Ln[1/(1-χ)] versus time for the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using NHS-BB as an alkoxyamine and SG1 as the nitroxide; triangle: $[SG1]_0/[NHS\text{-}BB]_0=0$, square: $[SG1]_0/[NHS\text{-}BB]_0=0.1$, and circle: $[SG1]_0/[NHS\text{-}BB]_0=0.2$.

Increasing the amount of free SG1 decreases the rate of reaction which can be observed in Figure 4.13. More SG1 in the polymerization medium increase the probability of growing radicals being deactivated by SG1 before termination with other polymer chains (thereby increasing livingness) but also reduces the propagating radical concentration and therefore the polymerization rate. As a result the final conversion decreased from 82% in the experiment with $[SG1]_0/[NHS\text{-}BB]_0=0$ to 41% in the experiment with $[SG1]_0/[NHS\text{-}BB]_0=0.2$. The livingness of the reaction for all three reactions is excellent, which can be observed in Figures 4.9 and 4.13.

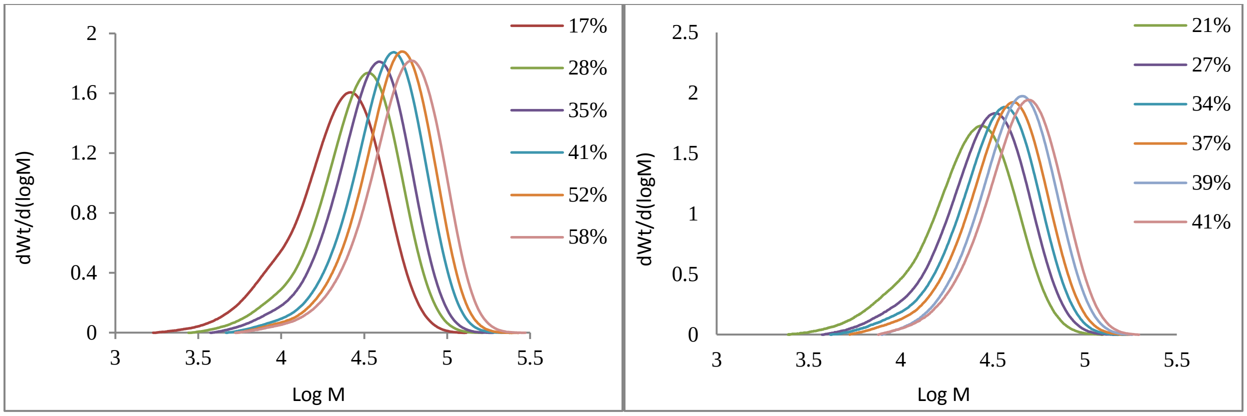


Figure 4.13 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using NHS-BB as an alkoxyamine and SG1 as a nitroxide; left: ($[SG1]_0/[NHS\text{-}BB]_0=0.1$), right: ($[SG1]_0/[NHS\text{-}BB]_0=0.2$).

### 4.3.6 Initiator concentration

To increase the conversion in experiment 7 (Table 4.1), the concentration of NHS-BB was increased (exp. 8, Table 4.1). The final conversion jumped from 40% to 60%, while linearity in the kinetic plots was preserved and clean evolution of the MWDs was observed (Figures 4.14 to 4.16).

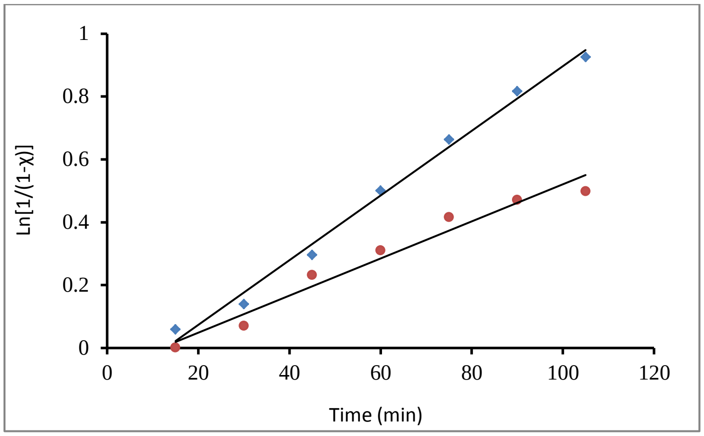


Figure 4.14 Ln[1/(1-X)] versus time for the NMP of DEAEMA with 9 mol% acrylonitrile in water using NHS-BB as an alkoxyamine and SG1 as a nitroxide ($[SG1]_0/[NHS\text{-}BB]_0=0.2$); square: $[NHS\text{-}BB]_0/[Monomers]_0=0.01$, circle: $[NHS\text{-}BB]_0/[Monomers]_0=0.005$.

$M_n$ increased linearly with conversion while the $Đ$ remained around 1.35 demonstrating good control over the polymerization (Figure 4.15). The final molecular weight in experiment 8 (Table 4.1) is approximately half of the molecular weight in experiment 7, an expected result since the number of growing chains was doubled due to doubling of the amount of initiator. In Figure 4.16 a very small amount of tailing can be seen at low molecular weights indicating a small population of dead chains. These dead chains probably form during the early stage of polymerization before the establishment of the reversible deactivation cycles of the dormant chains capped with the SG1. Another indicator of this phenomenon is the non-zero intercept of the $M_n$ versus conversion graph.

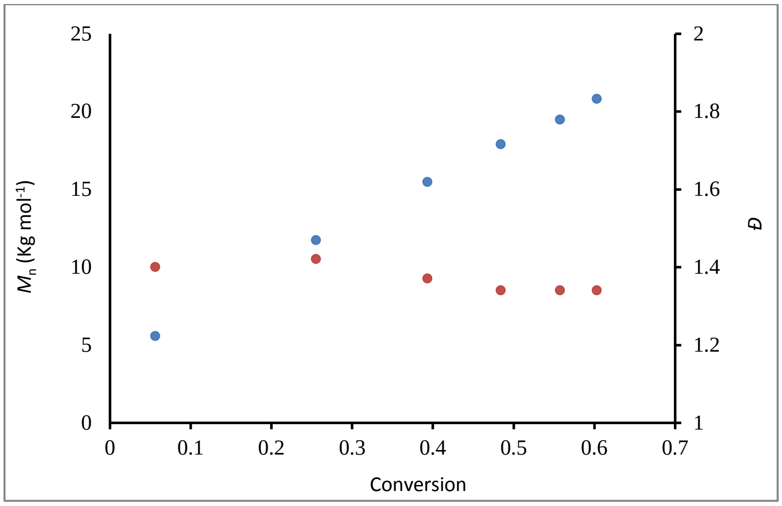


Figure 4.15 $M_n$ and $M_w/M_n$ versus conversion in the NMP of DEAEMA and a small amount of AN at 90 °C using NHS-BB alkoxyamine and SG1 nitroxide ($[SG1]_0/[VA\text{-}044]_0=2$) with $[DEAEMA]_0=0.5$ mol L$^{-1}$ and $[NHS\text{-}BB]_0/[monomers]_0=0.01$.

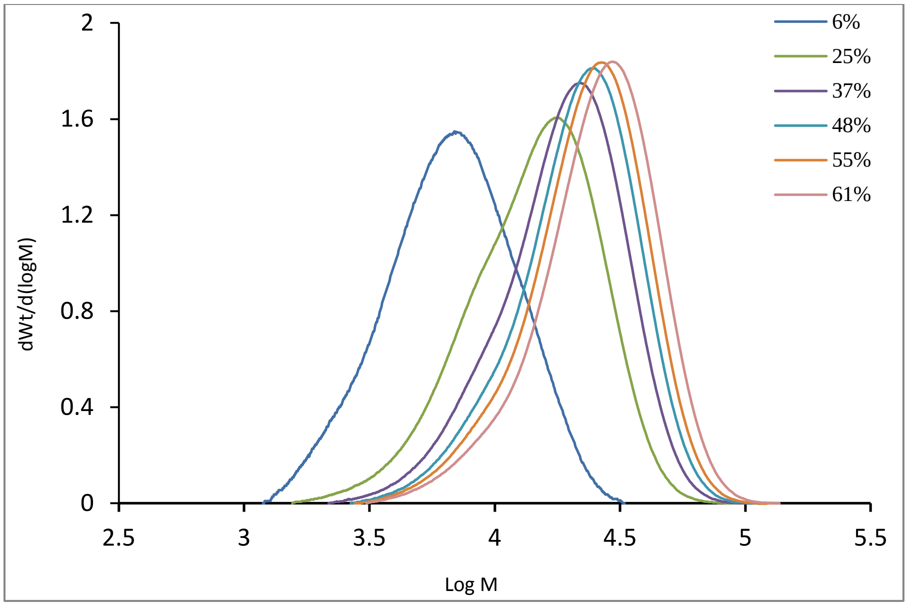


Figure 4.16 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 90 °C using NHS-BB as alkoxyamine and SG1 as nitroxide ($[SG1]_0/[NHS\text{-}BB]_0=0.2$) with [DEAEMA]0=0.5 mol $L^{-1}$ and $[NHS\text{-}BB]_0/[monomers]_0=0.01$.

### 4.3.7 Temperature

Temperature has a direct effect on the decomposition of the alkoxyamine, which can affect the rate of polymerization. To assess the effect of temperature on the NMP of DEAEMA in water, experiment 8 in Table 4.1 was repeated at 80 °C (exp. 9 Table 4.1). At lower temperature the decomposition of NHS-BB alkoxyamine is lower and polymerization is also slower compared to 90 °C (Figure 4.17). The final molar dispersity increased from 1.27 to 1.40 when lowering the temperature from 90 to 80 °C but the livingness of the reaction remained very good (Figure 4.18). Lowering the temperature increases the time of activation-deactivation cycles of the dormant chains and as a result decreases the control over the polymerization.

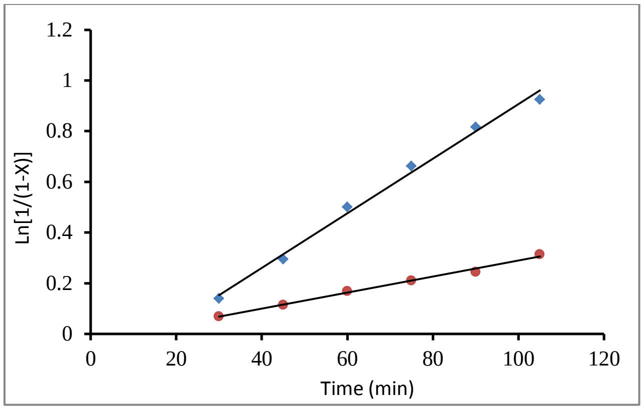


Figure 4.17 Ln[1/(1-χ)] versus time for the NMP of DEAEMA with 9 mol% acrylonitrile in water using NHS-BB as alkoxyamine and SG1 as nitroxide ($[SG1]_0/[NHS\text{-}BB]_0=0.2$); square: T= 90 °C, circle: T= 80 °C.

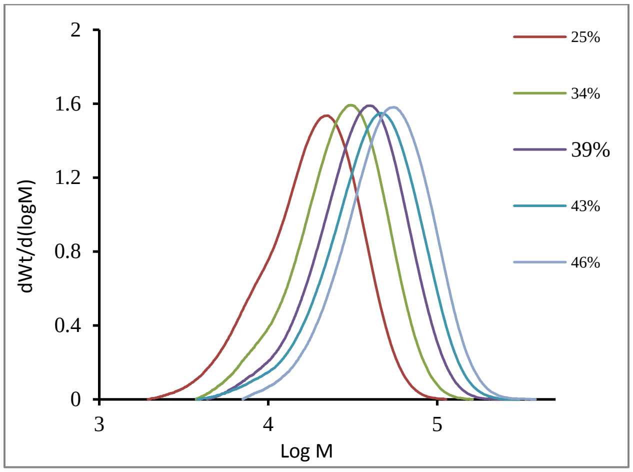


Figure 4.18 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 80 °C using NHS-BB as alkoxyamine and SG1 as nitroxide with the ratio of $[SG1]_0/[NHS\text{-}BB]_0=0.2$.

Experiment 3 (Table 4.1) was repeated at 80 °C but with less SG1 to increase the conversion (exp. 10 Table 4.1). Since the decomposition of VA-044 is slower at 80 °C compared to 90 °C, the polymerization should proceed more slowly but at the same time reducing the amount of SG1 will tend to increase the rate of polymerization. Again excellent results indicating good control over the reaction and excellent livingness were obtained. Final conversion reached to 90% in 5 h (Figures 4.19 and 4.20).

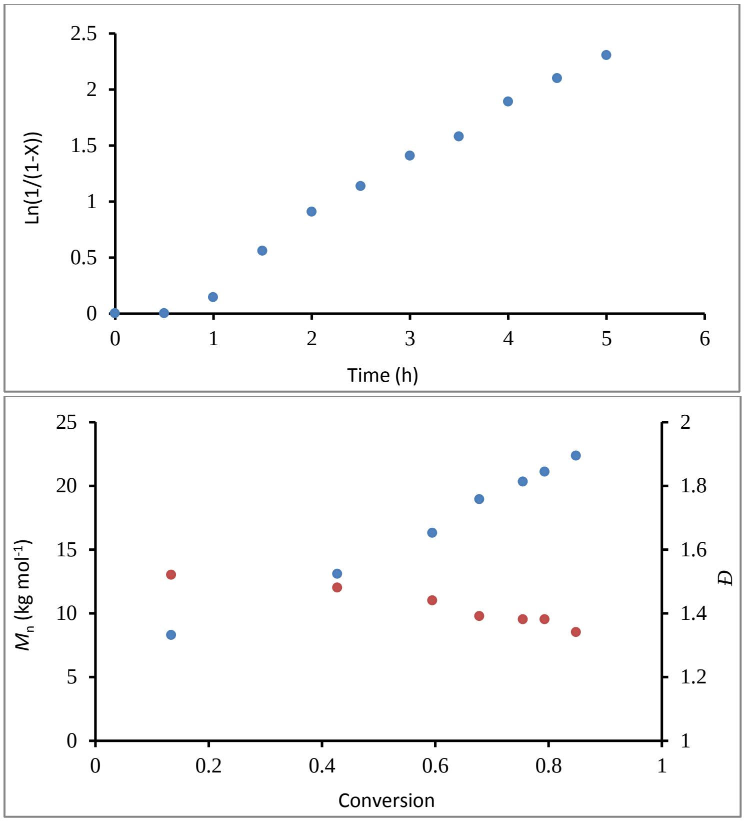


Figure 4.19 Kinetic plots of the copolymerization of DEAEMA and acrylonitrile (initial molar fraction of acrylonitrile: $f_{x0}$=0.09) in water at 80 °C using VA-044 as initiator and SG1 as nitroxide ($[SG1]_0/[VA\text{-}044]_0$)=1.5 at 80 °C (a) ln[1/(1-X)] versus time, (b) $M_n$ and $M_w/M_n$ versus conversion.

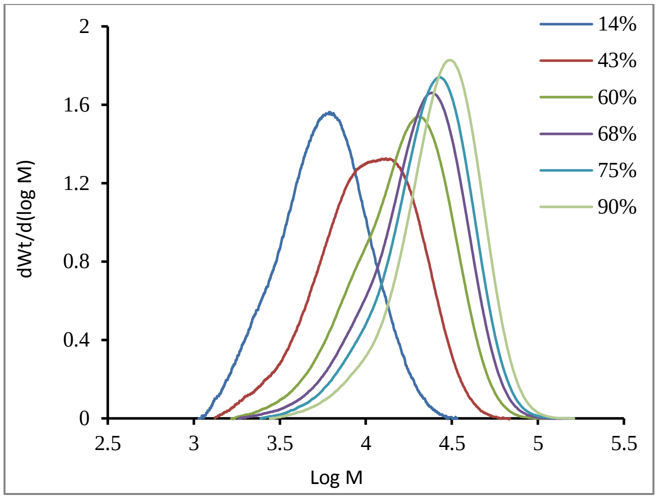


Figure 4.20 Evolution of MWDs with conversion during the NMP of DEAEMA with 9 mol% acrylonitrile in water at 80 °C using VA-044 as initiator and SG1 as nitroxide ($[SG1]_0/[VA\text{-}044]_0=1.5$).

### 4.3.8 Chain extension

To check the ability of the poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine to be extended by a second block, a chain extension experiment was performed. Experiment 1 in Table 4.1 was repeated but with a higher amount of initiator ($[VA\text{-}044]_0/[monomers]_0=0.02$). (VA-044 was chosen because it decomposes to radicals containing positively charged imidazole groups, which can help stabilize particles in emulsion.) Then after 15 min (corresponding to 60% conversion based on $^1H$ NMR observation) the contents of the reaction were added to the hydrophobic monomers (MMA and S). Styrene was used as a comonomer in both the first and second blocks. When the hydrophobic block attains a certain chain length which is no longer soluble in water, the diblock copolymer forms a particle based on a PISA process. In this situation, the hydrophilic poly(DEAEMA-*co*-S) containing the stabilizing moieties forms the shell of the particle and hydrophobic poly(MMA-*co*-S) forms the core of the particle. Unreacted monomers from the first step will be consumed at the start of the second step and thus a gradient copolymer will be formed between the hydrophilic and hydrophobic blocks. Figure 4.21 shows the SEC chromatograms of the macroinitiator and latex. The complete shift of the MWD to the right confirms the livingness of the macroinitiator.

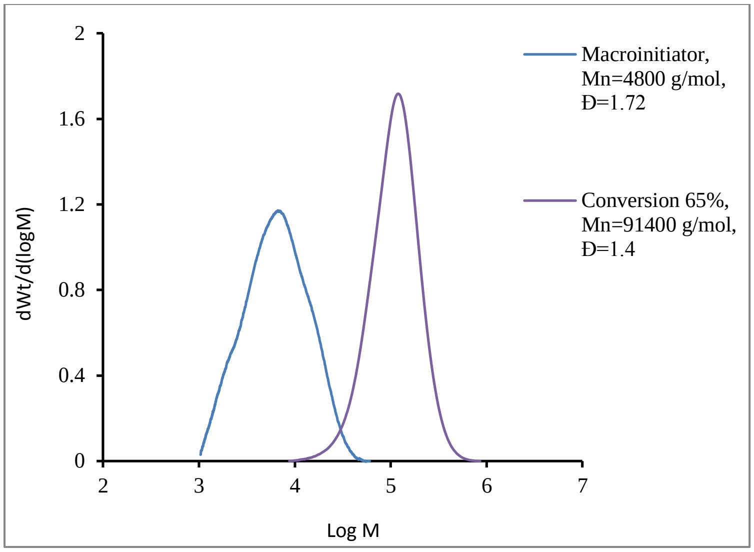


Figure 4.21 Evolution of MWDs with conversion during the chain extension experiment.

## Conclusion

Nitroxide-mediated polymerization of DEAEMA with a small amount of acrylonitrile was performed for the first time in water, an environmentally-friendly and inexpensive solvent, using NHS-BB alkoxyamine without addition of free nitroxide. Results of the detailed kinetic study were presented, examining the effects of several parameters including initiating system, comonomer type, initiator concentration, DEAEMA concentration, temperature, and the ratio of free excess nitroxide to alkoxyamine. The polymerization reaction showed all the features of a well-controlled and living polymerization; linearity in the plots of ln[1/(1-X) versus time, linear increase of Mn with conversion, and clear shifts of the MWD with conversion. Successful chain extension of poly(DEAEMA-*co*-AN) with MMA and S in water led to the in-situ creation of poly(DEAEMA-*co*-AN)-*b*-poly(MMA-*co*-S) diblock copolymer nanoparticles via the PISA process. Since the chain extension experiment in water showed promising results, we decided to investigate in detail the synthesis of PMMA latex by surfactant-free emulsion polymerization (SFEP) based on the PISA technique using poly(DEAEMA-*co*-AN) or poly(DEAEMA-*co*-S) macroalkoxyamine synthesized in water, followed chain extension with MMA in a one-pot process. This will be the subject of the next chapter.

## References

(1) Cunningham, M. F. *Prog. Polym. Sci*. **2008**, 33, 365-398.

(2) Zetterlund, P. B.; Kagawa, Y.; Okubo, M. *Chem. Rev*. **2008**, 108, 3747-3794.

(3) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci*. **2007**, 32, 93-146.

(4) Jenkins, A. D.; Jones, R. G.; Moad, G. *Pure Appl. Chem*. **2009**, 82, 483-491.

(5) Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux, B. *Prog. Polym. Sci*. **2013**, 38, 63-235.

(6) Phan, T. N. T.; Bertin, D. *Macromolecules* **2008**, 41, 1886-1895.

(7) Nicolay, R.; Marx, L.; He, P. *Macromolecules* **2007**, 40, 6067-6075.

(8) Mannan, M. A.; Fukuda, K.; Miura, Y. *Polym. J.* **2007**, 39, 500-501.

(9) Grassl, B.; Clisson, G.; Khoukh, A.; Billon, L, L. *Eur. Polym. J.* **2008**, 44, 50-58.

(10) Rigolini, J.; Grassl, B.; Billon, L,; Reynaud, S.; Donard, O. F. X. J. *Polym. Sci.; Part A: Polym. Chem.* **2009**, 47, 6919-6931.

(11) Brusseau, S.; D'Agosto, F.; Magnet, S.; Couvreur, L.; Chamigton, C.; Charleux, B. *Macromolecules* **2011**, 44, 5590-5598.

(12) Van de Wetering, P,; Moret, E. E.; Schuurmans-Nieuwenbroek, N. M.; Van Steenbergen, M. J.; Hennink, W, E. *Bioconjugate Chem*. **1999**, 10, 589-597.

(13) Feng, A.; Zhan, C.; Yan, Q.; Liu, B.; Yuan, J. *Chem. Commun*. **2014**, 50, 8958-8961.

(14) Kumar, S.; Tong, X.; Dory, Y. L.; Lepage, M.; Zhao, Y. *Chem. Commun*. **2013**, 49, 90-92.

(15) Yan, B.; Han, D.; Boissiere, O.; Ayotte, P.; Zhao, Y. *Soft Matter* **2013**, 9, 2011-2016.

(16) Liu, H.; Guo, Z.; He, S.; Yin, H.; Fei, C.; Feng, Y. *Polym. Chem*. **2014**, 5, 4756-4763.

(17) Han, D.; Tong, X.; Zhao, Y. *ACS Macro Lett*. **2012**, 1, 57-61.

(18) Yan, Q.; Zhao, Y, *J. Am. Chem. Soc*. **2013**, 135, 16300-16303.

(19) Cai, Y.; Shen, W.; Wang, R.; Krantz, W. B.; Fane, A. G.; Hu, X. *Chem. Commun*. **2013**, 49, 8377-8379.

(20) Liu, H.; Zhao, Y.; Dreiss, C. A.; Feng, Y. *Soft Matter* **2014**, 10, 6387-6391.

(21) Xu, L. Q.; Zhang, B.; Sun, M.; Hong, L.; Neoh, K. G.; Kang, E. T.; Fu, G. D. *J. Mater. Hem*. A **2013**, 1, 1207-1212.

(22) Liu, P.; Lu, W.; Wang, W. J.; Li, B. G.; Zhu, S. *Langmuir* **2014**, 30, 10248-10255.

(23) Zhang, J.; Han, D.; Zhang, H.; Chaker, M.; Zhao, Y.; Ma, D. *Chem. Commun*. **2012**, 48, 11510-11512.

(24) Zhang, Q.; Zhu, S. *ACS Macro Lett*. **2014**, 3, 743-746.

(25) Pinaud, J.; Kowal, E.; Cunningham, M.; Jessop, P. *ACS Macro Lett*. **2012**, 1, 1103-1107.

(26) Zhang, Q.; Yu, G.; Wang, W, J.; Li, B. G.; Zhu, S. *Macromol. Rapid, Commun*. **2012**, 33, 916-921.

(27) Morse, A. J. Armes, S. P.; Thompson, K. L.; Dupin, D.; Fielding, L. A.; Mills, P.; Swart, R. *Langmuir* **2013**, 29, 5446-5447.

(28) Lokaj, J.; Vlcek, P.; Kriz, J. *Macromolecules* **1997**, 47, 7644-7646.

(29) Bian, K.; Cunningham, M. F. *J. Polym. Sci., Part A: Polym. Chem*. **2006**, 44, 414-426.

(30) Zhang, C.; Maric, M. *Polymers* **2011**, 3, 1398-1422.

(31) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Pinaud, J.; Cunningham, M. F. *Polym. Chem*. **2014**, 6163-6170.

(32) Charleux, B.; Delaittre, G.; Rieger, J.; D'Agosto, F. *Macromolecules* **2012**, 45, 6753-6765.

(33) Vinas, J.; Chagneux, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D. *Polymer* **2008**, 49, 3639-3647.

(34) Belleney, L.; Nicolas, J.; Bertin, D.; Dire, C. *J. Polym. Sci., Part A: Polym. Chem*. **2008**, 46, 6333-6345.

(35) Chenal, M.; Mura, S.; Marchal, C.; Gigmes, D.; Charleux, B.; Fattal, E.; Couvreur, P.; Nicolas, J. *Macromolecules* **2010**, 43, 9291-9303.

(36) Cotanda, P.; Wright, D. B.; Tyler, M.; O'Reilly, R. K. *J. Polym. Sci., Part A: Polym. Chem*. **2013**, 51, 3333-3338.

(37) Van der Houwen, O. A. AG. J.; Underberg, W. J. M.; Hennink, W. E. *Macromolecules* **1998**, 31, 8063-8068.

(38) Charleux, B.; Nicolas, J. *Polymer* **2007**, 48, 5813-5833.

(39) Chenal, M.; Boursier, C.; Gillaneuf, Y.; Taverna, M.; Couvreur, P.; Nicolas, *J. Polym. Chem*. **2011**, 2, 1523-1530.

(40) Nicolas, j.; Mueller, l.; Dire, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules* **2009**, 42, 4470-4478.

(41) Nicolas, J.; Dire, C.; Muller, l.; Belleney, J.; Charleux, B.; Marque, S. R. A.; Bertin, D.; Magnet, S.; Couvreur, L. *Macromolecules* **2006**, 39, 8274-8282.

(42) Nicolas, J.; Brusseau, S.; Charleux, B. *J. Polym. Sci., Part A: polym. Chem*. **2010**. 48, 34-47.

## Chapter 5

# One-pot synthesis of poly((diethylamino)ethyl methacrylate-*co*-styrene)-*b*-poly(methyl methacrylate-*co*-styrene) nanoparticles via nitroxide-mediated polymerization

## Abstract

Poly((diethylamino)ethyl methacrylate-*co*-styrene)-*b*-poly(methyl methacrylate-*co*-styrene) nanoparticles were prepared by one-pot process via nitroxide-mediated polymerization (NMP). For synthesizing the first block, the SG1-mediated copolymerization of 2-(diethylamino)ethyl methacrylate (DEAEMA), a pH-sensitive monomer, and a small percentage of styrene (S) was performed in water at 90 °C using 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride, (VA-044) , as a positively charged stabilizer and initiator. The resultant macroalkoxyamine was then employed without any purification in the protonated form as both macroinitiator and stabilizer in the same pot for the surfactant-free emulsion copolymerization of methyl methacrylate (MMA) and styrene at 90 °C, which proceeded via polymerization-induced self-assembly (PISA). Latex particles had monomodal size distribution, narrow size distribution and small average size. The polymerization kinetics, the control over molar mass and molar mass distribution, the effect of the charge density on the particles size and latex stability, and the colloidal characteristics of the *in situ*-formed block copolymer micelles were studied in detail.

## 5.1. Introduction

Emulsion polymerization is an environmentally-friendly and industrially viable technique for producing polymeric latexes.[1,2] Latexes are applied in different areas such as coatings, rubber, textiles, paints, and the biomedical and pharmaceutical fields.[3,4] The surfactant type and concentration plays a critical role in determining the mean particle size and colloidal stability of the latex, with particle stabilization being achieved by electrostatic and/or steric repulsive forces. The size of the dispersed particles depends strongly on the ratio of surfactant to monomer (more surfactant leads to smaller particles).[5]

2-(Diethylamino)ethyl methacrylate (DEAEMA) and 2-(dimethylamino)ethyl methacrylate (DMAEMA) are two methacrylic monomers with a tertiary amine group, which results in the pH-sensitivity of both monomers and polymers. Emulsion copolymerization of DEAEMA has been reported for the preparation of pH-sensitive latexes (convertible to microgels)[6] and highly responsive $CO_2$-switchable zwitterionic crosslinked particles.[7] DEAEMA and DMAEMA have both been used as stabilizers in their protonated form in emulsion polymerization.[8,9] $CO_2$-switchable latexes that are easily coagulated and redispersed (upon addition and removal of $CO_2$ respectively) can be prepared using as little as 0.5 mol% DEAEMA.[30] It has been shown that incorporating DEAEMA or DMAEMA in the structure of (co)polymer induces $CO_2$-switchability to the whole structure.[10]

A limited number of publications exist reporting the use of living radical polymerization (LRP) with DEAEMA and DMAEMA. Zhu's group prepared well-defined poly(DMAEMA-*co*-MMA) copolymers by RAFT and used them as polymeric surfactant in the emulsion polymerization of

MMA to yield $CO_2$-switchable latexes.[8,11] Charleux et al.[12] reported the synthesis of poly(DEAEMA) by performing reversible addition-fragmentation chain transfer (RAFT) polymerization in ethanol using (4-cyanopentanoic acid)-4-dithiobenzoate as a chain transfer agent. The macro-RAFT agent was then used in the protonated form as a stabilizer in the emulsion polymerization of styrene. Sahnoun et al.[13] prepared poly(DMAEMA) by RAFT polymerization in dioxane at 90 °C using 2-cyanoprop-2-yl dithiobenzoate (CPDB) RAFT agent and investigated the polymerization kinetics. RAFT of DMAEMA in water was performed using 4-cyanopentanoic acid dithiobenzoate (CPADB) as a chain transfer agent.[14] Atom transfer radical polymerizations (ATRP) of DMAEMA and 2-(dimethylamino)ethyl acrylate (DMAEA) were reported, respectively, by Matyjaszewski and Zhu.[15,16] Gan et al.[17] prepared well-defined poly(DEAEMA) via ATRP and then used the synthesized poly(DEAEMA) as a macroinitiator for producing poly(DEAEMA-*b*-tBMA). Aqueous RAFT polymerization of DEAEMA was performed using 4-cyano-4-(ethylsulfanylthiocarbonyl) sulfanylpentanoic acid (CEP) RAFT agent and the resultant poly(DEAEMA) purified and chain extended with *N*-isopropyl acrylamide (NIPAM) to prepare dually responsive poly(DEAEMA-*b*-NIPAM) block copolymer.[18]

There are even fewer publications on the NMP of tertiary amine methacrylate-based monomers, although NMP is among the simplest LRP techniques for the preparation of diblock copolymers.[19] NMP of methacrylate monomers is usually carried out by adding a few mole percent of a styrenic monomer to increase the control and livingness of the polymerization.[20] Lokaj et al.[21] reported nitroxide-mediated bulk polymerization of DMAEMA employing polystyrene (PS) macroinitiator. The effects of different parameters such as solvent polarity, temperature, chain transfer to polymer, and excess nitroxide on the SG1-mediated polymerization of DMAEA was reported by Bian and Cunningham.[22] Maric and Zhang[23] prepared poly(DMAEMA-*co*-S) copolymer by nitroxide-mediated bulk copolymerization using *n*-hydroxysuccinimidyl BlocBuilder (NHS-BlocBuilder) and tested the livingness of the resultant copolymer by chain extension with a DMAEMA/styrene mixture.

We have prepared poly(DEAEMA-*co*-S) in bulk using different initiating systems.[24] The resultant copolymer was purified and then it was employed in its protonated form in the emulsion polymerization of MMA. We have reported the detailed kinetic study of the NMP of DEAEMA in aqueous media.[25] Given the excellent control and livingness obtained in the NMP of DEAEMA in water, it was decided to prepare poly(MMA) latexes in a one-pot process using poly(DEAEMA) as initiator and stabilizer. To do so, first poly(DEAEMA-*co*-S)-SG1 is prepared in water at 90 °C using *N*-tertbutyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1) as the nitroxide. The synthesized macroalkoxyamine is then used directly in the same pot as both initiator and stabilizer in the emulsion copolymerization of methyl methacrylate (MMA) and styrene (S) via a PISA[26-29] mechanism, which eliminates the need for purification and isolation of the macroinitiator. This one-pot process is more environmentally benign since there is no need to use organic solvent for the preparation and purification of the macroinitiator. Furthermore, the absence of surfactant is another advantage since the residual surfactant can alter the properties of the final product. Using PISA approach, different morphologies are also achievable by the precise control over the polymerization of the two blocks. The polymerization kinetics, control over molar mass and molar mass distribution, livingness of the polymer chains, effect of the charge density on the particles size, and the colloidal characteristics of the in *situ*-formed block copolymer micelles are studied in detail.

## 5.2. Experimental section

**Materials.** All chemicals, monomers, and inhibitor removal columns were purchased from Aldrich unless otherwise stated. 2-(Diethylamino)ethyl methacrylate (DEAEMA, 99%) was passed through a column of basic aluminum oxide (~ 150 mesh) prior to use. Styrene (S, >99%) and methyl methacrylate (MMA, 99%) were purified by passing through columns packed with inhibitor remover. The *N*-tertbutyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1, 85%) was supplied by Arkema. 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044) was purchased from Wako Pure Chemical Industries and was used without further purification. Sodium hydroxide (NaOH, >97%), tetrahydrofuran (THF), hydrochloride acid (38 wt%), and nitrogen ($N_2$, Praxair, medical grade) were used as received. All aqueous solutions were prepared with deionized water (DIW).

**SG1-mediated copolymerization of DEAEMA with styrene in water.** The polymerization reactions were performed in deionized water. In a typical experiment, DEAEMA (2.0 g, 0.53 mol $L^{-1}$) was mixed with deionized water (18 mL) in a 50 mL three-neck round-bottom flask and the pH was adjusted to 6 by the addition of concentrated HCl. Then, styrene (0.055 g, 0.026 mol $L^{-1}$, initial molar fraction of styrene in the comonomer mixture: $f_{S0}$=0.09), SG1 (0.047 g, 8 mmol $L^{-1}$), trioxane (20 mg, 0.01 mol $L^{-1}$), and VA-044 (0.035 g, 5.4 mmol $L^{-1}$) were added and nitrogen bubbling was performed for 20 minutes at room temperature. The mixture was then immersed in an oil bath heated at 90 °C. The time zero of polymerization was taken when the flask was immersed in the oil bath. Samples were withdrawn at regular time intervals and quenched by cooling in an ice-water bath. Monomers conversion was determined by $^1$H NMR analysis. Gel permeation chromatography (GPC) was used for measuring molecular weight and molar dispersity (*Đ*). Samples were neutralized by 1 M NaOH and then centrifuged to separate the polymer precipitate. The polymers were washed with deionized water and then dried under air flow for 24 h before GPC measurements. Monomer conversion was calculated on the basis of the integration of trioxane protons (5.11 ppm) as an internal reference and the integration of the vinylic proton of DEAEMA (6.11 ppm).

**Emulsion copolymerization of methyl methacrylate and a small percentage of styrene initiated by the protonated poly(DEAEMA-*co*-S) macroalkoxyamine.** Emulsion copolymerizations were performed in a one-pot two-step process. In the first step, the copolymerization of DEAEMA and styrene was carried out at 90 ºC in deionized water (as explained in the previous section). In a separate flask, the mixture of hydrophobic monomers and water including MMA (10.12 g, 0.1 mol), S (1.04 g, 0.01 mol, initial molar fraction of styrene in the comonomer mixture; $f_{S0}$=0.09), and water (100 g) were mixed and deoxygenated by bubbling nitrogen for 20 min at room temperature. After 15 min of the DEAEMA/S NMP reaction in the first step, the contents of this reaction were added to the second flask containing the mixture of MMA, S, and water at 90 ºC (all at atmospheric pressure). The solids content was 10% based on the overall mass of the reaction medium. Reactions were allowed to proceed for 3-5 hours. 1 mL samples were withdrawn at regular time intervals and quenched by cooling in an ice-water bath and then dried under air flow for 24 h. Monomers conversion was measured gravimetrically.

**Analytical techniques.** $^1$H NMR spectroscopy was used for the measurements of the monomer conversion in the first step. Analyses were performed in 5 mm diameter tubes in $D_2O$ at 25 ºC using an automated Bruker Advance 400 MHz spectrometer. The chemical shift scale was calibrated based on the solvent peak ($\delta = 4.79$ ppm). The GPC was equipped with a Waters 2960 separation module containing three Styragel columns coupled with the separation limits between 400 and $1 \times 10^6$ g mol$^{-1}$. THF was used as the eluent with a flow rate of 0.3 mL min$^{-1}$. A differential refractive index (RI) detector (Waters 2960) was used and molar mass distributions were derived from a calibration curve based on poly(methyl methacrylate) standards from Polymer Standard Service. All polymers were analyzed at a concentration of 5 mg mL$^{-1}$ after filtration through a 0.2 µm pore-size membrane. The software used for data collection and calculation was Empower Pro version 5.0 from Waters. The intensity-average diameters ($D_z$) of the latex particles and the dispersity factor ($\sigma$) were measured by dynamic light scattering (DLS) at a temperature of 25 °C using a Zetasizer Nano Series (Nano ZS) from Malvern Instrument using the Zetasizer 6.2 software. Before measurements, the latex samples were diluted in deionized water. The particles images were taken using transmission electron microscopy (TEM, Hitachi H-7000).

## 5.3. Results and discussion

### 5.3.1 SG1-mediated copolymerization of DEAEMA with styrene in water

In our previous publication[24] we synthesized poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine in bulk using either a bicomponent initiating system (VA-061 as the initiator and SG1 as the nitroxide) or monocomponent initiating system (NHS-BlocBuilder as alkoxyamine). This macroalkoxyamine was then purified by precipitating in cold hexane and employed in the protonated form in the preparation of PMMA latex in surfactant-free emulsion polymerization. To take advantage of the $CO_2$-switchability of DEAEMA, we attempted to synthesize poly(DEAEMA-*co*-S) macroinitiator in water under $CO_2$; however, because of the high temperatures required for the NMP step, the $CO_2$ concentration in the aqueous phase was low, and as a result DEAEMA was only partially protonated. The polymerization medium became heterogeneous with ensuing loss control and livingness. We recently showed the NMP of DEAEMA in water with excellent control and livingness[25] and therefore decided to explore the one-pot synthesis of PMMA latexes using poly(DEAEMA-*co*-S)-SG1 macroinitiator that is prepared *in situ*. First water-soluble macroinitiator is prepared and then added directly to the flask containing hydrophobic monomers. To study the kinetics of the polymerization reaction in the first step for the *in situ* preparation of the macroalkoxyamine, and also to determine the best time for starting the second step while preserving a high degree of livingness in the macroalkoxyamine chains, SG1-mediated copolymerization of DEAEMA with a small percentage of styrene using VA-044 as the inisurf (initiator and surfactant) was carried out in water at 90 °C

(Figure 5.1). To solubilize DEAEMA in water, hydrochloric acid was used as a protonating agent. Therefore, DEAEMA remained in the protonated form during the reaction.

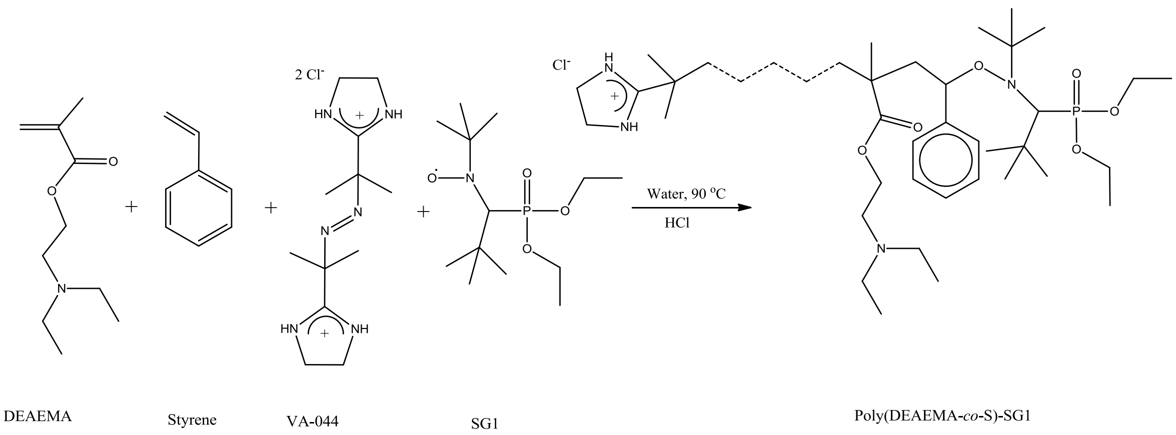


Figure 5.1 Schematic representation of the polymerization of DEAEMA with 9 mol% styrene in water initiated by VA-044 at 90 °C; $[\text{DEAEMA}]_0$= 0.5 mol $L^{-1}$, $[\text{VA-044}]_0$=0.01 mol $L^{-1}$, $f_{S,0}{}^{a}$=0.09, $[\text{SG1}]_0/[\text{VA-044}]_0$=1.5, and pH= 6.

Since DEAEMA is a methacrylate monomer, in all experiments 9 mol% styrene was used in the monomer mixture to reduce the irreversible termination reactions and maintain the livingness of the polymer chains.[20] DEAEMA is a pH-responsive monomer that is hydrophilic in its protonated form and hydrophobic in its neutral form. To convert DEAEMA to its water-soluble form at the start of the reaction, pH was adjusted to 6 in all experiments by addition of concentrated HCl. At this pH, the amine groups of the DEAEMA monomer may not be totally protonated but the pH is sufficiently low enough to solubilize DEAEMA in water.[36] More importantly, this pH is sufficiently high to prevent the degradation of SG1,[31] and at the same time it is low enough to protect the DEAEMA from hydrolysis.[25] The initiator used in this step was 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044), which is a water-soluble initiator with positively charged fragments. Based on our previous experiments with 2,2'-azobis[2-(2-imidazolin-2-yl)propane (VA-061) under a $CO_2$ atmosphere,[8,32] we know the charged imidazole groups are able to provide additional stabilization of the latex particles in emulsion polymerization. At 90 °C the half-life of VA-044 in water is less than 2 minutes.[32] Therefore, most of the initiator is decomposed very quickly at the start of the reaction and the majority of polymer chains are initiated at nearly the same time. The target $M_n$ of the poly(DEAEMA-*co*-S)-SG1 at full conversion was 9700 g $mol^{-1}$. An advantage of the one-pot emulsion polymerization process is that we can target different molecular weights of the macroinitiator without experiencing difficulties in the purification of polymer, specifically low molecular weight polymers which have proven very difficult to isolate. For example, based on our observations, precipitation of low-molecular weight poly(DEAEMA) (i.e. molecular weights less than ~5000 g $mol^{-1}$) prepared via bulk polymerization in normal hexane (a good non-solvent for poly(DEAEMA)) is difficult, although precipitation is easier with poly(DMAEMA) because of its higher polarity. According to $^1H$ NMR results, the conversion of the DEAEMA increased very fast and in less than 15 minutes, reached about 70% (Figure 5.2).

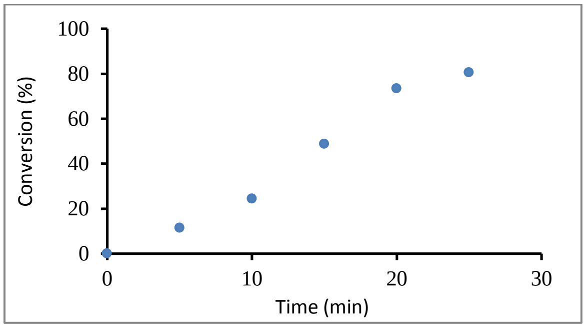


Figure 5.2 Overall conversion vs time for the SG1-mediated copolymerization of DEAEMA and 9 mol% S in water at 90 °C.

The high rate of nitroxide-mediated polymerization of other methacrylate monomers in water has been reported previously.[33,34] To keep most of the macroinitiator living during the second step, the addition of the macroinitiator to the second batch of monomers should be done after ~17 min reaction time (about 60% conversion) in the first step. The remainder of the unreacted monomers from the first step are then copolymerized with the hydrophobic monomers in the emulsion polymerization step, although most of them are expected to be incorporated into the polymer chains very quickly at the start of the emulsion polymerization because of their high water solubility in the reaction medium. Scheme 1 shows the experimental conditions for the polymerization of DEAEMA with 9 mol% styrene in water initiated by VA-044 at 90 °C. The molar dispersity of the produced macroinitiator was relatively high ($M_w/M_n > 1.65$) but based on our observations, which are discussed in the next section, this macroinitiator was quite living and able to initiate the emulsion copolymerization of MMA and styrene. Detailed study of the NMP of DEAEMA in water has been presented in the previous paper.[25]

### 5.3.2 Emulsion copolymerization of MMA with a low percentage of styrene initiated by the protonated poly(DEAEMA-co-S) macroalkoxyamine

The poly(DEAEMAH$^+$Cl$^-$-*co*-S)-SG1 macroalkoxyamine prepared in the first step was used without any purification as a macroinitiator in the emulsion copolymerization of MMA and styrene in the second step (Figure 5.3). Table 5.1 shows the experimental conditions for conducting emulsion polymerization of MMA with 9 mol% of styrene initiated by poly(DEAEMAH$^+$Cl$^-$-*co*-S)-SG1, and colloidal characteristics of the resultant latex particles.

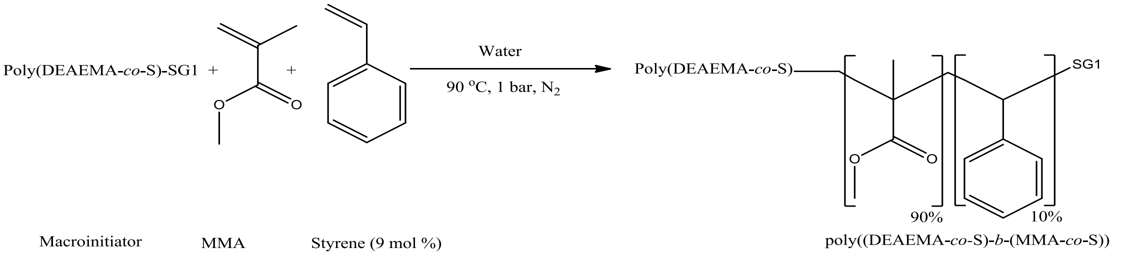


Figure 5.3 Schematic representation of surfactant-free batch emulsion of methyl methacrylate with 9 mol% styrene at 90 °C initiated by poly(DEAEMA-*co*-S) macroalkoxyamine synthesized *in situ* in water at 90 °C.

Table 5.1 Experimental conditions and characteristics of PMMA latexes prepared by emulsion polymerization of methyl methacrylate (MMA) with 9 mol% of styrene (S) at 90 °C initiated by poly(DEAEMA-*co*-S)-SG1 macroalkoxyamine in a one-pot process.

| entry | DEAEMA (mmol L$^{-1}$) | VA-044 (mmol L$^{-1}$) | $f_{St,0}$[a] | Time (h) | X[b] | Latex $M_{n,GPC}$ (g mol$^{-1}$) | $M_w/M_n$ | $D_z$ (nm)[c] | $N_p$ ($10^{18}$/L)[d] | $\sigma$[e] |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.08 | 0.0016 | 0.09 | 5 | 87 | 38100 | 1.43 | 48 | 1.35 | 0.09 |
| 2 | 0.04 | 0.0008 | 0.09 | 4 | 85 | 92300 | 1.40 | 51 | 1.2 | 0.11 |
| 3 | 0.02 | 0.0004 | 0.09 | 2.25 | 53 | 103500 | 1.26 | 57 | 0.85 | 0.04 |
| 4 | 0.01 | 0.0002 | 0.09 | 5 | 30 | 142700 | 1.21 | 65 | 0.57 | 0.10 |

[a] Initial molar fraction of styrene in the monomer mixture. [b] Conversions calculated gravimetrically. [c] Intensity-average diameter of the final latex measured by DLS. [d] Number of latex particles, calculated according to $N_p = (6\times\tau)/(\phi\times\pi\times D_z^3)$ in which τ= solids content, ϕ= polymer density, $D_z$= *Z*-average diameter of the latex. [e] Dispersity obtained from DLS.
Note: Concentrations of DEAEMA and VA-044 were calculated based on the initial values added at the start of the first step and the total volume of the reaction in the second step.

Poly(DEAEMAH$^+$Cl$^-$-*co*-S)-SG1 macroalkoxyamine acted as both initiator and stabilizer in the emulsion polymerization reaction. The positive charges on the initiator fragments at the end of the polymer chains and also positive charges on the amine groups of the DEAEMA units of the macroinitiator provide sufficient electrostatic repulsion forces between latex particles to stabilize them. To investigate the effect of the number of positive charges on the size and dispersity of the latex particles, the amount of poly(DEAEMA) macroinitiator that was used for the initiation of the emulsion polymerization of the second batch was varied while the amount of hydrophobic monomer remained constant. Macroinitiator was kept in the protonated form; therefore, it was water-soluble and the addition of the hydrophobic monomers resulted in the *in situ* formation of amphiphilic block copolymers based on the PISA process.

In the first step of the reaction different batches of macroinitiator solution with the same recipe were prepared. The only difference in these batches was the volume of the reaction. As a result, the smaller batch contained a lower number amount of protonated DEAEMA units and VA-044 initiator. The number of particles increased with increasing DEAEMA content in the first step of the polymerization while the size of particles correspondingly decreased (see $D_z$ and $N_p$ in Table 5.1). This is an expected behavior in emulsion polymerization that confirms a higher number of charges available in the polymerization medium can stabilize more particles. All latexes had low size dispersity (relatively narrow particle size distribution) with fairly small intensity-average diameter (48-65 nm), indicating that poly(DEAEMA-*co*-S) was an effective stabilizer in the surfactant-free emulsion polymerization of MMA (Figure 5.4).

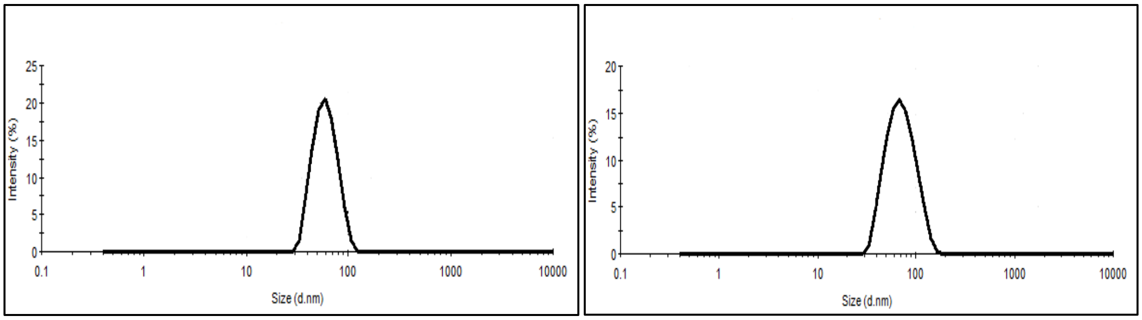


Figure 5.4 Graphs of the intensity average particle diameter. Left graph: entry 3 Table 5.1, right graph: entry 4 Table 5.1.

While most of the stabilization of the particles resulted from the DEAEMA, an important portion of the colloidal stability may also be related to the initiator (VA-044). Furthermore, the pH of the reaction in the first step has a significant effect on the number of the charged DEAEMA units in the reaction (the lower the pH, the higher the number of charged DEAEMA units in the system). All the latexes had a translucent bluish colour which is indicative of the small particle size. The stability of all latexes was excellent in all cases (latexes were stable for a few weeks with no settling), and with negligible coagulum.

There is a reduction in the final conversion with a decrease in the amount of macroinitiator. Decreasing the amount of macroinitiator also decreases the number of oligoradicals formed during the initial stages of the emulsion polymerization and as a result reduction in the number of loci of polymerization. Fewer loci leads to fewer particles ($N_p$ in Table 5.1) which then results in lower overall rates of polymerization and final conversion.

Figure 5.5 shows kinetic plots of the emulsion polymerization of MMA and styrene initiated by poly(DEAEMA-*co*-S) macroinitiator. Number average molecular weight increased linearly with conversion, which shows good control over chain growth. The dispersities decreased continuously with conversion.

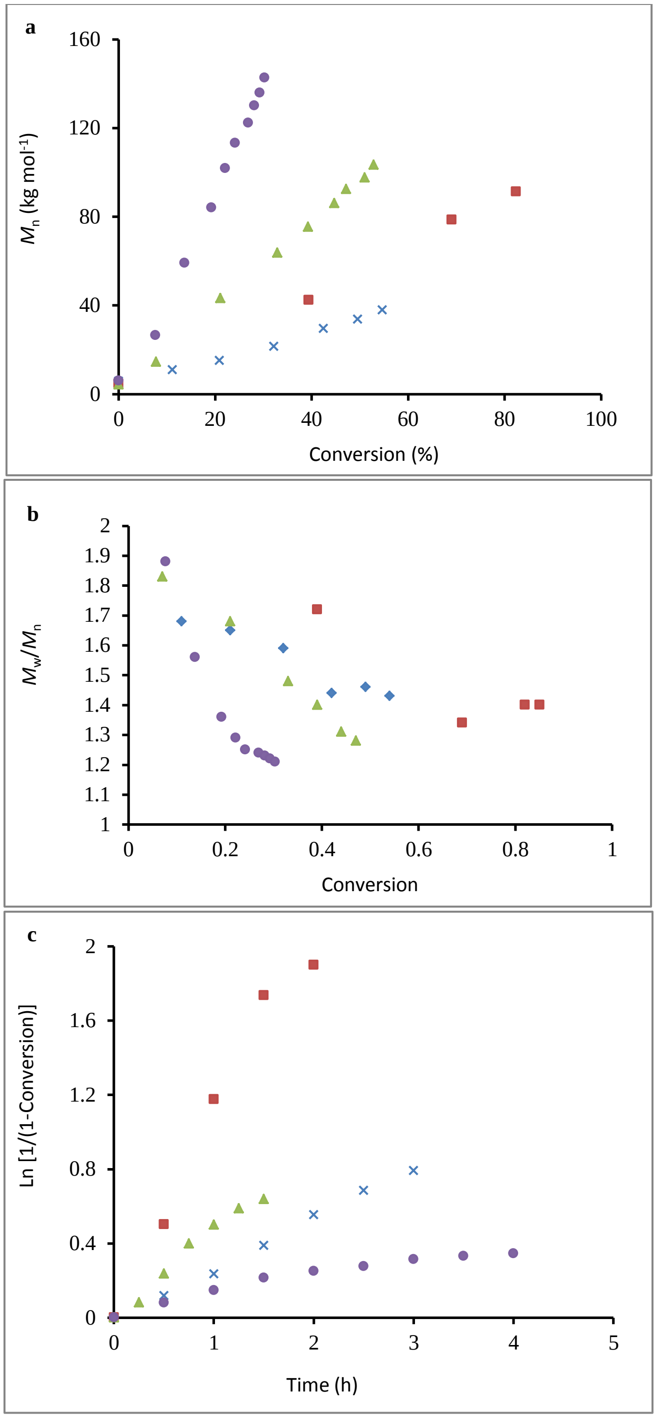


Figure 5.5 Kinetic plots of the emulsion polymerization of methyl methacrylate with 9 mol % styrene at 90 °C initiated by poly(DEAEMA-*co*-S) macroinitiator synthesized in water at 90 ºC in the same pot: experiment 1 (red ■ entry 1 Table 5.1), 2 (green ▲ entry 2 Table 5.1), 3 (blue × entry 3 Table 5.1), 4 (purple ● entry 4 Table 5.1). (a) $M_n$ versus conversion (b) $M_w/M_n$ versus conversion (c) Ln[1/(1-conversion)] versus time.

The concentration of propagating radicals remained approximately constant during the polymerization, as can be seen from the near linearity in the plot of the ln [1/ (1-conversion)] versus time. Figure 5.6 shows the GPC chromatograms of experiments 3 and 4 in Table 5.1.

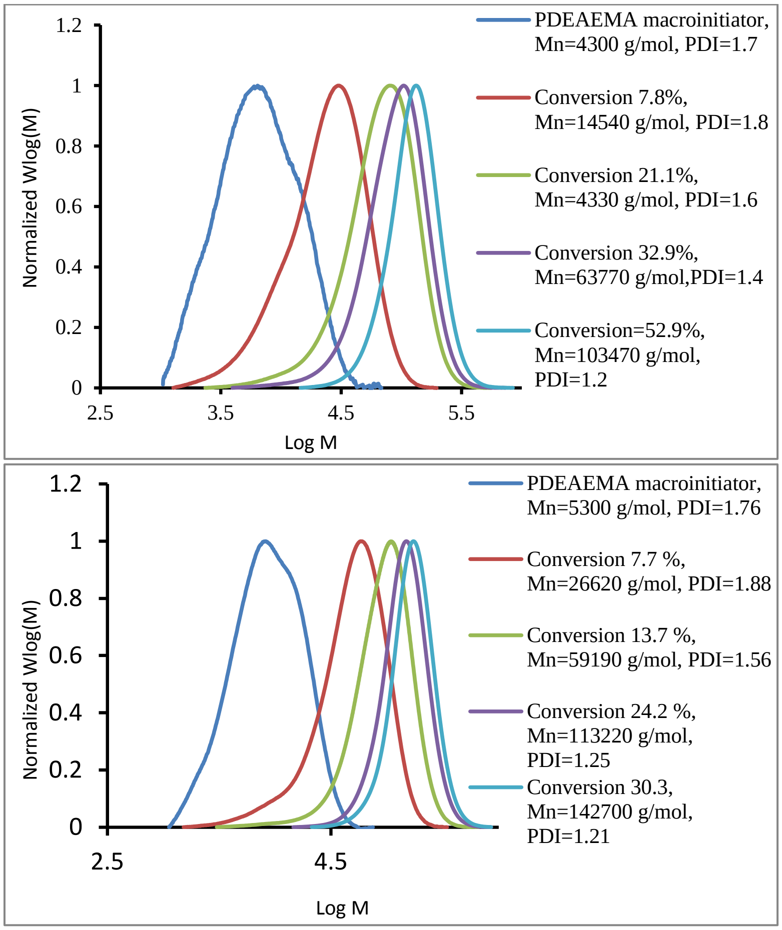


Figure 5.6 GPC chromatograms of emulsion polymerization of methyl methacrylate with 9 mol % styrene at 90 °C initiated by poly(DEAEMA-*co*-S) macroinitiator synthesized in water at 90 °C in the same pot: (a) entry 3 Table 5.1 (b) entry 4 Table 5.1.

The complete shift of the whole body of the GPC curves indicates a high degree of livingness of the polymer chains. The same trend was observed in all the experiments performed with different amounts of macroinitiator. The shifts of the GPC chromatograms to higher molecular weight confirmed the formation of *in situ* amphiphilic block copolymer.

Since the stability of the latex particles was imparted primarily by the protonated poly(DEAEMA-*co*-S) macroinitiator, all latexes were pH-sensitive and could easily be coagulated by adding equimolar NaOH based on the acid added at the start of the first step to neutralize the positive charges on the amine groups of the DEAEMA units in the macroinitiator.

Figure 5.7 shows TEM image of the latex particles. As was previously observed by DLS, the latex particles have a narrow size distribution. Also, the size of the latex particles in the TEM image is in a good agreement with the intensity-diameter obtained from DLS (Table 5.1). The TEM image confirmed the spherical structure of the latex particles. The shell of the particles is believed to be formed by the DEAEMAH$^+$ block and the core of the particles are primarily the MMA block. After neutralizing with NaOH, DEAEMAH$^+$ is converted to the DEAEMA which is not soluble in water, and; therefore, the polymer particles aggregate.

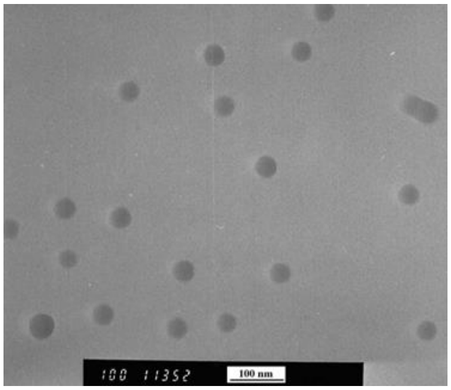


Figure 5.7 TEM image of the PMMA latex particles produced by surfactant-free emulsion polymerization of MMA with 9 mol% styrene at 90 °C initiated by poly(DEAEMA-*co*-S)-SG1 macroinitiator synthesized in water at 90 °C.

## Conclusions

The nitroxide-mediated polymerization of 2-(diethylamino)ethyl methacrylate (DEAEMA) with a few mole percent of styrene was successfully performed in acidic conditions (pH=6) in water at

90 °C and atmospheric pressure.  The polymerization rate was very fast, with the conversion increasing to more than 70% in less than 20 min based on NMR measurements. To keep most of the polymer chains living for use in the second step (emulsion polymerization), the macroinitiator should be added to the hydrophobic monomers after 17 min of the start of the first reaction.

The synthesized macroalkoxyamine, poly(DEAEMA-*co*-S)-SG1, was used without any purification as a macroinitiator in the surfactant-free emulsion polymerization of methyl methacrylate (MMA) and styrene at 90 °C. The emulsion polymerization proceeded via polymerization-induced self-assembly (PISA) and exhibited the features of a well-controlled and living radical polymerization. The final latexes had narrow molecular weight distribution. The latex particles had narrow size distribution as measured by DLS with small diameter and excellent colloidal stability. The final latexes were pH-sensitive and coagulated easily by neutralization with stoichiometric amounts of sodium hydroxide (NaOH). This one-pot process is simple to conduct, economical, and environmentally-friendly since there is no need to use any solvent for purification of the macroinitiator.

In the previous chapters, DEAEMA was employed for the formation of the shell of the latex particles. It was interesting for us to prepared diblock copolymer nanoparticles comprised of poly(DEAEMA) cores. For stabilization of the particles, poly(ethylene glycol) methyl ether methacrylate (PEGMA) can be used. This subject will be studied in the next chapter.

## References

(1) Lovell, P. A.; El-Aasser, M. S. *Emulsion Polymerization and Emulsion Polymers*; John Wiley: New York, **1997**.

(2) Gilbert, R. G. *Emulsion Polymerization: A Mechanistic Approach*; Academic Press: London, **1995**.

(3) Fitch, R. M. *Polymer Colloid: A Comprehensive Introduction*; Academic Press: San Diego, **1997**.

(4) Nomura, M.; Tobita, H.; Suzuki, K. *Emulsion Polymerization: Kinetics and Mechanistic Aspects in Polymer Particles*; Spring: Berlin, **2005**.

(5) Odian, G. *Principles of Polymerization*, 4th ed.; John Wiley & Sons: Hoboken, NJ, **2004**.

(6) Morse, A. J.; Armes, S. P.; Thompson, K. L.; Dupin, D.; Fielding, L. A.; Mills, P.; Swart, R. *Langmuir* **2013**, 29, 5446-5475.

(7) Liu, P.; Lu, W.; Wang, W. J.; Li, B. G.; Zhu, S. *Langmuir* **2014**, 30, 10248-10255.

(8) Pinaud, J.; Kowal, E.; Cunningham, M.; Jessop, P. *ACS Macro Lett*. **2012**, 1, 1103-1107.

(9) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Macromolecules* **2013**, 46, 1261-1267.

(10) Han, D.; Tong, X.; Zhao, Y. *ACS Macro Lett*. **2012**, 1, 57-61.

(11) Zhang, Q.; Yu, G.; Wang, W. J.; Li, B. G.; Zhu, S. *Macromol. Rapid. Commun*. **2012**, 33, 916-921.

(12) Manguian, M.; Save, M.; Charleux, B. *Macromol. Rapid. Commun*. **2006**, 27, 399-404.

(13) Sahnoun, M.; Charreyre, M. T.; Veron, L.; Delair, T.; D'Agosto, F. *J. Polym. Sci., Part A: Polym. Chem*. **2005**, 43, 3551-3565.

(14) Xiong, Q.; Ni, P.; Zhang, F.; Yu, Z, *Polym. Bull*. **2004**, 53, 1-8.

(15) Zhang, X.; Xia, J.; Matyjaszewski, K. *Macromolecules* **1998**, 31, 5167-5169.

(16) Zeng, F.; Shen, Y.; Zhu, S. *Macromol. Rapid. Commun*. **2002**, 23, 1113-1117.

(17) Gan, L.; Ravi, P.; Mao, B. W. M.; Tam, K. *J. Polym. Sci., Part A: Polym. Chem*. **2003**, 41, 2688-2695.

(18) Smith, A. E.; Xu, X.; Kirkland-York, S. E.; Savin, D. A.; McCormick, C. L. *Macromolecules* **2010**, 43, 1210-1217.

(19) Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux, B. *Prog. Polym. Sci.* **2013**, 38, 63-235.

(20) Nicolas, J.; Mueller, L.; Dire, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules* **2009**, 42, 4470-4478.

(21) Lokaj, J.; Vlcek, P.; Kriz, J. *Macromolecules* **1997**, 47, 7644-7646.

(22) Bian, K.; Cunningham, M. F. *J. Polym. Sci., Part A: Polym. Chem*. **2006**, 44, 414-426.

(23) Zhang, C.; Maric, M. *Polymers* **2011**, 3, 1398-1422.

(24) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Pinaud, J.; Cunningham, M. F. *Polym. Chem*. **2014**, 5, 6163-6380.

(25) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2015**, 48, 72-80.

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

(27) Sprong, E.; Leswin, J. S. K.; Lamb, D. J.; Ferguson, C. J.; Hawkett, B. S. *Macromol. Symp*. **2006**, 231, 84-93.

(28) Ganeva, D. E.; Sprong, E.; De Bruyn, H.; Warr, G. G.; Such, C. H. Hawkett, B. S. *Macromolecules* **2007**, 40, 6181-6189.

(29) Charleux, B.; Delaittre, G.; Rieger, J.; D'Agosto, F. F. *Macromolecules* **2012**, 45, 6753-6765.

(30) Lee, A. S.; Gast, A. P.; Butun, V.; Armes, S. P. *Macromolecules*, **1999**, 32, 4302-4310.

(31) Charleux, B.; Nicolas, *J. Polymer* **2007**, 48, 5813-5833.

(32) Su, X.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 666-670.

(33) Brusseau, S.; D'Agosto, F.; Magnet, S.; Couvreur, L.; Chamignon, C.; Charleux, B. *Macromol. Rapid, Commun*. **2011**, 44, 5590-5598.

(34) Chenal, M.; Mura, S.; Marchal, C.; Gigmes, D.; Charleux, B.; Fattal, E.; Couvreur, P.; Nicolas, J. *Macromolecules* **2010**, 43, 9291-9303.

## Chapter 6

# Preparation of poly(poly(ethylene glycol)methyl ether methacrylate-*co*-styrene)-*b*-poly(2-(diethylamino)ethyl methacrylate-*co*-acrylonitrile) by nitroxide-mediated polymerization in water

### Abstract

The nitroxide-mediated polymerization (NMP) of poly(ethylene glycol) methyl ether methacrylate (PEGMA) with a small amount of styrene (S) as a comonomer was performed in water at 90 °C using 2,2'-azobis[2-(2-imidazolin-2-yl)propane]dihydrochloride (VA-044) as initiator and *N*-tert-butyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1) as nitroxide. The reaction was well-controlled and exhibited excellent livingness as evidenced by low molar dispersity and evolution of the molar mass distribution. The resultant macroalkoxyamine was then employed in the nitroxide-mediated polymerization of 2-(diethylamino)ethyl methacrylate hydrochloride (DEAEMAH$^+$Cl$^-$) with a small amount of acrylonitrile (AN) in water at 90 °C. The resulting poly(PEGMA-*co*-S)-*b*-poly(DEAEMAH$^+$Cl$^-$-*co*-AN) polymer chains were converted to diblock copolymer nanoparticles after neutralizing with base.

### 6.1 Introduction

Nitroxide-mediated polymerization (NMP) is one of the simpler techniques among controlled/living radical polymerizations (CLRPs), for preparing polymers with different composition, structures, and functionalities and with low molar dispersity (*Đ*).[1-4] (IUPAC has introduced the terminology "Reversible-Deactivation Radical Polymerization" (RDRP).[5]) Because of inherent difficulties in achieving control with NMP in water-based systems, there are only a few reports of NMP in homogeneous aqueous solution, for the monomers sodium 4-styrenesulfonate,[6-8] n,n-dimethacrylamide,[8] 2-(acryloyloxy)ethyl benzyldimethylammonium chloride,[8] acrylamide,[9,10] methacrylic acid,[11] and DEAEMA.[12] In the NMP of methacrylate monomers, disproportionation between propagating radical and nitroxide and a high activation-deactivation equilibrium constant (*K*), which causes irreversible termination reactions, often leads to uncontrolled polymerizations.[13] To address this problem, the common solution is addition of a small amount of a comonomer with a lower *K* value (such as styrene, acrylonitrile, or 9-(4-vinylbenzyl)-9H-carbazole) to reduce the average *K* and therefore decrease the overall concentration of propagating radicals.[14-16] As a water-soluble, methacrylate-based monomer, PEGMA (poly(ethylene glycol) methyl ether methacrylate) is of interest for a broad range of applications. PEGylation has been used in drug delivery,[17] for modification of chitosan copolymers in medical applications,[18] and peptide and protein modification.[19] The NMP of PEGMA has been reported by Charleux in pure ethanol and also in ethanol/water solutions.[20-23]

As water is considered a green, inexpensive, abundant, and safe solvent, performing chemical reactions in water is appealing. In this paper we report the NMP of PEGMA in water using a small amount of styrene or acrylonitrile as comonomer at 90 °C. While NMP has been applied in the polymerization of PEGMA in alcoholic mixtures,[20-22] to the best of our knowledge there is no report of preparation of poly(PEGMA) by NMP in water. The SG1-terminated poly(PEGMA) chains were then chain extended with DEAEMA (2-(diethylamino)ethyl methacrylate), a tertiary amine methacrylate-based and pH-responsive monomer. The p$K_a$ of DEAEMA is 8.8, while the p$K_a$ of its polymer PDEAEMA is 7.4.[24] At the pH used in our reactions (~6.5), DEAEMA is hydrophilic (water-soluble) and the synthesized poly(PEGMA-*co*-S)-b-poly(DEAEMAH$^+$Cl$^-$-*co*-AN) polymer chains are water-soluble, while after neutralizing with a base the PDEAEMA-rich block becomes hydrophobic, leading to the formation of diblock copolymer nanoparticles.

## 6.2 Experimental section

### Material

Poly(ethylene glycol) methyl ether methacrylate (PEGMA, $M_n$=950 g mol$^{-1}$), acrylonitrile (AN, >99%), and inhibitor removal columns were purchased from Aldrich and used as received. 2-(Diethylamino)ethyl methacrylate (DEAEMA, 99%) was passed through a column of basic aluminium oxide (mesh ~150) prior to use. Styrene (S, >99%) was purified by passing through columns packed with inhibitor remover. Sodium 4-styrenesulfonate (SS, > 90%) was purchased from Fluka. The 2-((tert-butyl-(1-(diethoxyphosphoryl)-2,2-dimethylpropyl) amino) oxy)-2-methylpropanoic acid initiator (BlocBuilder) and *N*-tertbutyl-*N*-(1-diethylphosphono-2,2-dimethylpropyl) nitroxide (SG1, 85%) were supplied by Arkema. 2,2'-azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044) was purchased from Wako Pure Chemical Industries and used without further purification. Sodium hydroxide (NaOH, >97%), tetrahydrofuran (THF, >99%), ethyl ether (>99.9%), ethanol anhydrous (GreenField Ethanol Inc.), hydrochloric acid (38 wt%) and nitrogen ($N_2$, Praxair) were used as received. All aqueous solutions were prepared with deionized water (DIW). N-hydroxysuccinimide BlocBuilder (NHS-BB) was synthesized according to the reported procedure.[25]

### Copolymerization of poly(ethylene glycol) methyl ether methacrylate (PEGMA) and styrene (S) in water

In a typical experiment (exp.1, Table 6.1) PEGMA (10.0 g, 0.011 mol), S (0.12 g, 0.001 mole) (initial molar fraction of S in the monomer mixture: $f_{s0}$= 0.09), trioxane (500 mg), SG1 (123 mg, 0.42 mmol), and deionized water (35 mL) were mixed in a 100 mL, 3-neck round-bottom flask. In a second flask immersed in an ice-water bath, VA-044 (68 mg, 0.21 mmole) was dissolved in 5 mL DI water. The contents of both flasks were deoxygenized for 20 min by purging nitrogen. The first flask was then introduced into a preheated oil bath at 90 °C and fitted with a reflux condenser, a nitrogen inlet and a thermometer. After 2 min the initiator solution was added. Time zero of the polymerization was taken when the initiator solution was added to the reaction mixture. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and allowed to react for 2 h with samples withdrawn periodically for kinetic studies and polymer analysis. Samples were quenched by immersion an in ice-water bath. A portion of each sample was used for NMR analysis and the remainder first neutralized with 0.005 M NaOH to convert the charged imidazole group (resulting from VA-044 initiator decomposition) to its neutral form and then dried under air for 24 h for SEC analysis. All experiments and corresponding results for the NMP of PEGMA with a small amount of a comonomer are given in Table 6.1.

### Synthesis of poly(PEGMA-*co*-S)-*b*-poly(DEAEMA-*co*-AN)

First, poly(PEGMA-*co*-S)-SG1 macroalkoxyamine was synthesized according to the procedure described above. To preserve the livingness of the macroinitiator, the reaction was stopped at

~60% monomer conversion. The solution was then dried under air. The dried polymer was dissolved in a minimum amount of ethanol and then precipitated in diethyl ether to remove unreacted monomers. To prepare poly(PEGMA-*co*-S)-*b*-poly(DEAEMA-*co*-AN), DEAEMA (3.0 g, 0.016 mol) was mixed with water (30 mL) and then pH was adjusted to 6.5 by addition of concentrated HCl. Acrylonitrile (0.1 g, 0.0018 mol) and poly(PEGMA-*co*-S) macroinitiator (1 g, 0.091 mmol) were added to the flask and mixture deoxygenated with $N_2$ for 20 min. The flask was then introduced into the preheated oil-bath at 90 °C and the reaction continued for 2 h. Samples were taken periodically for kinetic studies and polymer analysis.

### Characterization

The monomer conversion was determined by $^1$H NMR (Bruker Avance-400) performed in 5 mm diameter tubes in $D_2O$ at room temperature. The monomer conversion was calculated by measuring the vinyl proton integrals at $\delta$=6.11 ppm and $\delta$=5.82 ppm using 1,3,5-trioxane as an internal reference ($\delta$=5.26 ppm). The chemical shift scale was calibrated based on tetramethylsilane. Size exclusion chromatography (SEC) was used to determine molecular weight and dispersity (*Đ*) of the polymer samples. The SEC was equipped with a Waters 2960 separation module containing three Styragel columns coupled with separation limits between 400 and 1 × 106 g mol$^{-1}$. THF was used as the eluent with a flow rate of 0.3 mL min$^{-1}$. A differential refractive index detector (Waters 2960) was used and the average molar masses ($M_n$ and $M_w$) and molar mass dispersity (*Đ*) were derived from a calibration curve based on polystyrene (PS) standards from Polymer Standard Service. At the end of the reaction all amine groups were neutralized with base (1M NaOH) prior to running SEC.

## 6.3 Results and discussion

### 6.3.1 Copolymerization of poly(ethylene glycol) methyl ether methacrylate (PEGMA) and styrene (S) in water

The first NMP of PEGMA ($M_n$ = 300 g mol$^{-1}$) was reported by Nicolas et al.20 The polymerization was performed in bulk using styrene as a comonomer; however, molar dispersity (*Đ*) of the polymer was high (>2.2 at 60% conversion) because of the fast polymerization and poor control over the reaction. Ethanol was added to the mixture to decrease the concentration of the monomer and as a result reduce the rate of polymerization. The same group performed the NMP of PEGMA ($M_n$ = 300 g mol$^{-1}$) using acrylonitrile (highly water-soluble monomer) instead of styrene as a comonomer. The polymerization was performed in an alcoholic mixture (ethanol/water); however, due to the LCST of the PEGMA (~60 °C) conducting the reaction in pure water was not possible at temperatures suitable for NMP. Recently Charleux's group reported the synthesis of poly(poly(ethylene oxide) methyl ether methacrylate-co-styrene)-b‑poly(n‑butyl methacrylate-co-styrene) amphiphilic block copolymers.[22] To overcome the LCST problem, polymerization was conducted in an ethanol/water mixture. Although good control over the reaction was obtained for the first block, ~30% dead chains were observed in the chain extension experiment.[22]

High molecular weight PEGMA ($M_n$=950 g mol$^{-1}$) is hydrophilic at temperatures high enough for NMP.[22] Therefore, we decided to take advantage of the water-solubility of PEGMA at high temperatures and run the NMP of PEGMA in water (Figure 6.1). As PEGMA is a methacrylate monomer, a small amount of styrene (S), sodium 4-styrenesulfonate (SS) or acrylonitrile (AN) was added to reduce the concentration of propagating radicals and increase the control and livingness of the reaction.[13]

Table 6.1 Experimental conditions for the NMP of PEGMA in water.

| exp. | PEGMA (mol $L^{-1}$) | initiator | $s^a$ | Comonomer | $f_{x,0}$ [b] | $r^c$ | $M_{n,SEC}$ (g $mol^{-1}$) | $Đ$ | Time (h) | $X^d$ (%) | Temp. (°C) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.2 | VA-044 | 0.02 | S | 0.09 | 2 | 20700 | 1.17 | 3 | 80 | 90 |
| 2 | 0.2 | VA-044 | 0.02 | SS | 0.09 | 2 | 22900 | 1.21 | 2 | 73 | 90 |
| 3 | 0.2 | VA-044 | 0.02 | AN | 0.09 | 2 | 19400 | 1.19 | 3 | 54 | 90 |
| 4 | 0.2 | VA-044 | 0.02 | AN | 0.09 | 2 | 15200 | 1.14 | 3 | 32 | 80 |
| 5 | 0.2 | VA-044 | 0.02 | AN | 0.09 | 1.5 | 21900 | 1.16 | 3 | 91 | 80 |
| 6 | 0.2 | NHS-BB | 0.01 | AN | 0.09 | 0.1 | 40800 | 1.09 | 4.5 | 33 | 90 |

[a] Molar ratio of initiator to monomers ($s=[\text{initiator}]_0/([\text{PEGMA}]_0+[\text{comonomer}]_0)$). [b] Initial molar fraction of comonomer in the monomer mixture ($f_{x,0}=[\text{comonomer}]_0/([\text{PEGMA}]_0+[\text{comonomer}]_0)$). [c] Ratio of free nitroxide to initiator ($r=[\text{SG1}]_0/[\text{Initiator}]_0$). [d] Conversions were calculated by $^1H$ NMR.

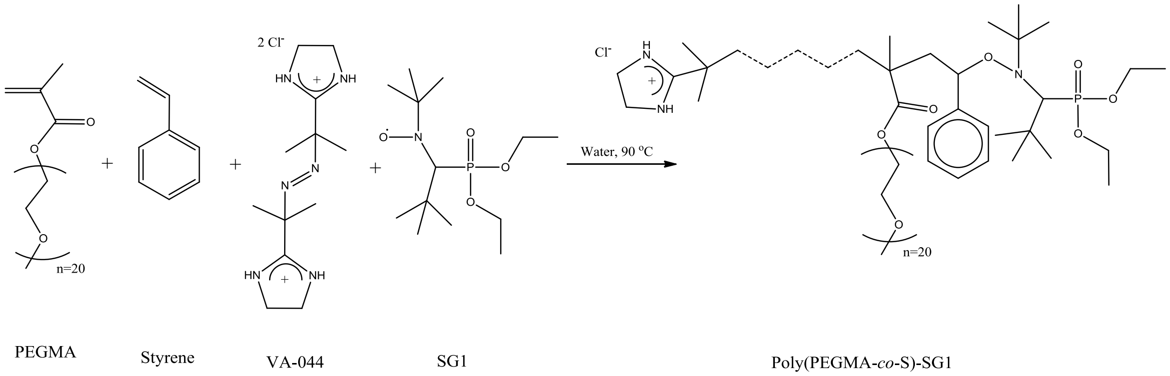


Figure 6.1 Schematic representation of the polymerization of PEGMA with 9 mol% styrene in water at 90 °C initiated by VA-044.

When styrene (exp.1, Table 6.1) or sodium 4-styrenesulfonate (exp.2, Table 6.1) was added as a comonomer the rate of reaction was considerably higher compared to the case when acrylonitrile was employed in the reaction as a comonomer at similar experimental conditions (exp.3, Table 6.1). This was expected behavior according to previously published reports.[21] In most cases a linear trend up to high conversions is observed in the plots of ln [1/(1-conversion)] versus time (Figure 6.2) and molar dispersities are less than 1.2 (Table 6.1), which confirm good control over the course of the polymerization. Styrene is an effective comonomer as it controls the reaction very well, which can be seen from the linear increase of the $M_n$ versus conversion and low molar dispersities (Figure 6.3). Therefore, for making a batch of macroinitiator for use in the synthesis of diblock copolymer, styrene was used as a comonomer in the first block. Temperature also has a significant effect on the rate of polymerization (see experiments 3 and 4 Table 6.1). However, the effect of free SG1 in the system is even more important than temperature (compare experiments 4 and 5, Table 6.1). Also, *n*-hydroxysuccinimidyl BlocBuilder (NHS-BB) was evaluated (exp. 6, Table 6.1), and the results showed excellent control over the polymerization. In all experiments, molecular weight distributions (MWDs) were clearly shifted to higher values with conversions, confirming excellent livingness of the polymer chains during the reaction (Figure 6.4).

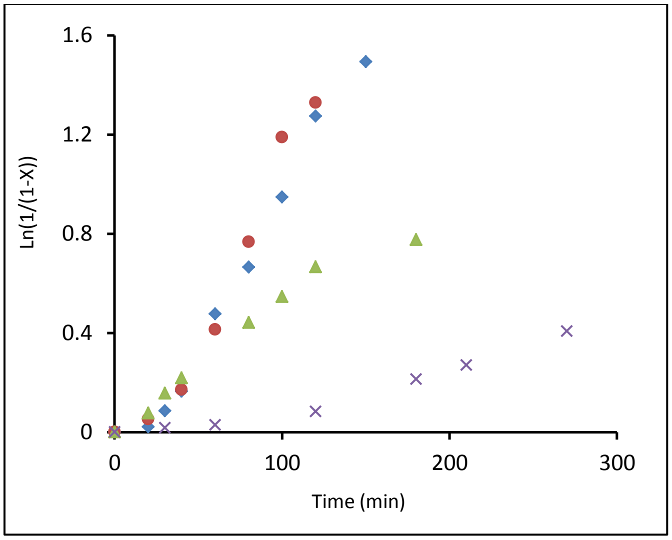


Figure 6.02 Kinetic plots of the NMP of PEGMA in water with 9 mol% of different comonomers and initiators: ● sodium 4-styrenesulfonate comonomer, T=90 °C, and $[\text{VA-044}]_0/[\text{Monomers}]_0=0.02$, ♦ styrene comonomer, T=90 °C, $[\text{VA-044}]_0/[\text{Monomers}]_0=0.02$, ▲ acrylonitrile comonomer, T= 80 °C, $[\text{VA-044}]_0/[\text{Monomers}]_0=0.02$, × acrylonitrile comonomer, T=90 °C, $[\text{NHS-BB}]_0/[\text{Monomers}]_0=0.01$.

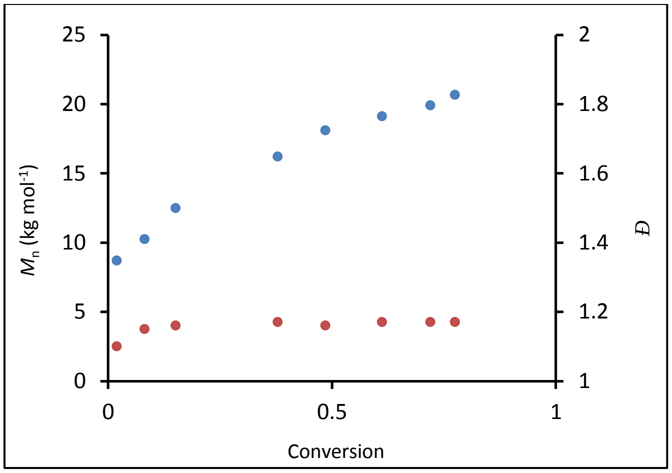


Figure 6.03 Evolution of number average molecular weight ($M_n$) and molar dispersity (*Đ*) (determined by SEC in THF using PMMA calibration) with conversion for the NMP of PEGMA with 9 mol% styrene as a comonomer in water at 90 °C employing VA-044 as the initiator and SG1 as the nitroxide ($[VA\text{-}044]_0/([PEGMA]_0+[styrene]_0)=0.02$ and $[SG1]_0/[VA\text{-}044]_0=2$).

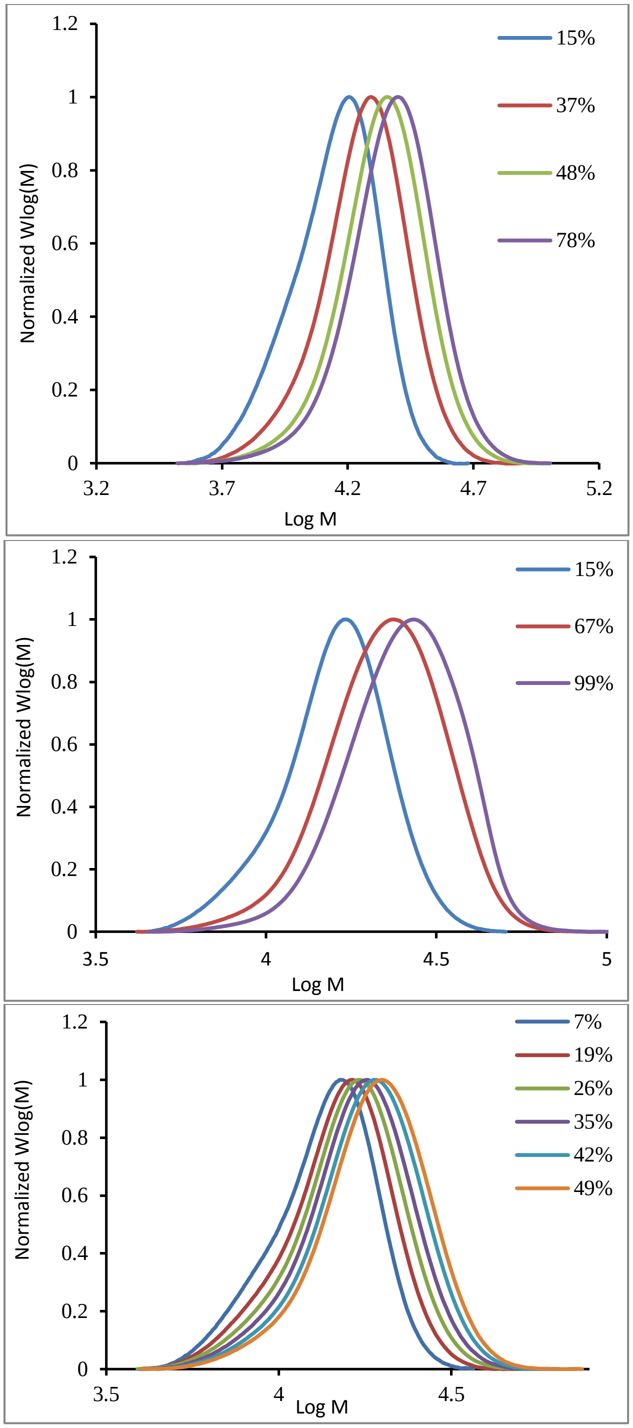


Figure 6.04 Evolution of MWDs with conversion during the NMP of PEGMA ($[PEGMA]_0$=0.2 mol L-1) in water using VA-044 as initiator and SG1 as a nitroxide, (a): with 9 mol% styrene, T= 90 °C, ($[SG1]_0/[VA\text{-}044]_0$=2), (b) with 9 mol% acrylonitrile, T= 80 °C, ($[SG1]_0/[VA\text{-}044]_0$=1.5), and (c) with 9 mol% acrylonitrile, T=90 °C, ($[SG1]_0/[VA\text{-}044]_0$=2).

### 6.3.2 Synthesis of poly(PEGMA-*co*-S)-*b*-poly(DEAEMA-*co*-AN)

Chain extension was performed using poly(PEGMA-*co*-S)-SG1 as a macroinitiator in the nitroxide-mediated polymerization of DEAEMA with a small amount of acrylonitrile (AN) at 90 °C. To solubilize the DEAEMA in water, it was protonated before the start of the experiment by reducing the pH to 6.5 using HCl. At this pH, DEAEMA is not readily hydrolyzed.12 To prepare the macroinitiator, the copolymerization of PEGMA and styrene was performed as described in the previous sections. The polymerization was stopped at ~60 % to ensure a high degree of livingness in the macroinitiator. After purification the macroinitiator was employed to initiate the polymerization of DEAEMA with a small amount of AN at 90 °C. The $M_n$ increased linearly with conversion; however molar dispersities were somewhat high at ~1.5 (Figure 6.5). The livingness of the reaction however was excellent as evidenced by the clear shift in the MWDs (Figure 6.6).

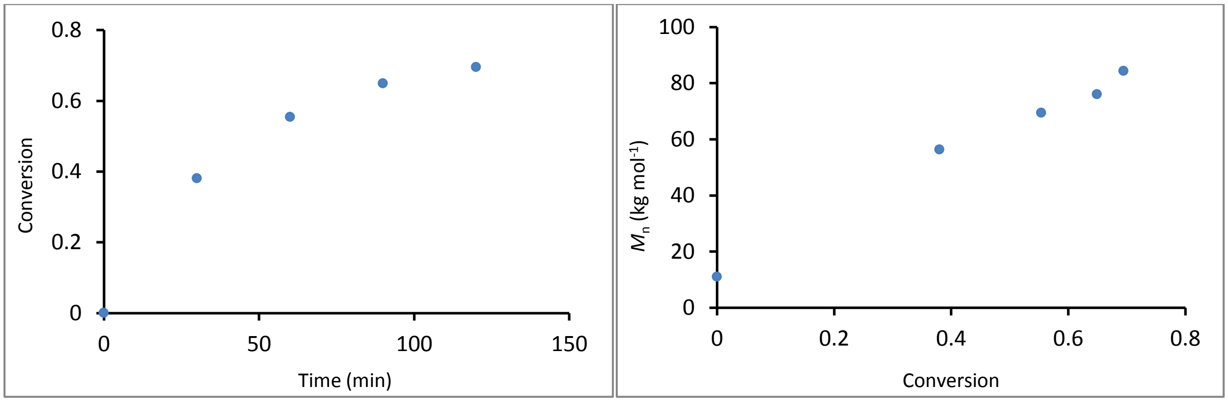


Figure 6.5 Nitroxide-mediated polymerization of DEAEMA (protonated with HCl) and 9 mol% of AN in water at 90 °C initiated by poly(PEGMA-*co*-S) macroinitiator: (left) conversion versus time (right) $M_n$ versus conversion.

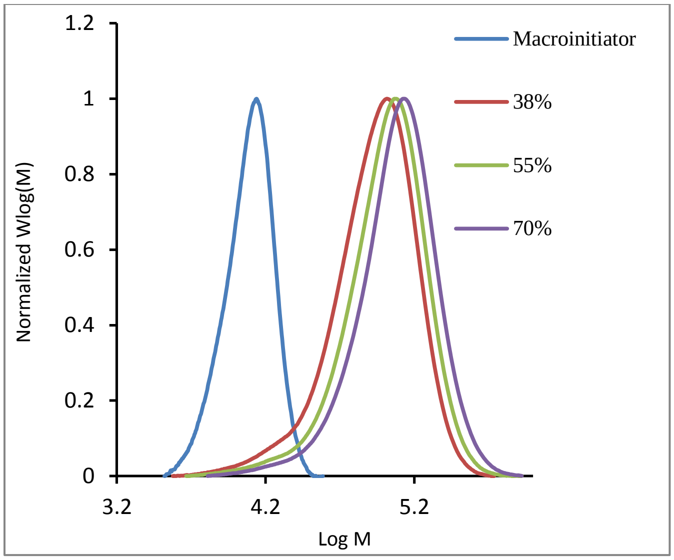


Figure 6.06 Evolution of MWDs with conversion during the nitroxide-mediated polymerization of DEAEMA (protonated with HCl) and 9 mol% of AN in water at 90 °C initiated by poly(PEGMA-*co*-S) macroinitiator.

DEAEMA is a pH-responsive monomer that is hydrophobic in the neutral form and hydrophilic in its protonated form. At the end of the reaction, when the polymer was neutralized with NaOH, latex particles with small size ($D_z$= 41 nm) were immediately formed, which were likely comprised of poly(PEGMA-*co*-S) shells and poly(DEAEMA-*co*-AN) cores. However, a very small percentage of large particles were also observed is the intensity size distribution (not visible in the volume distribution) of the particles (Figure 6.7), which may be attributable to a small amount of coagulation.

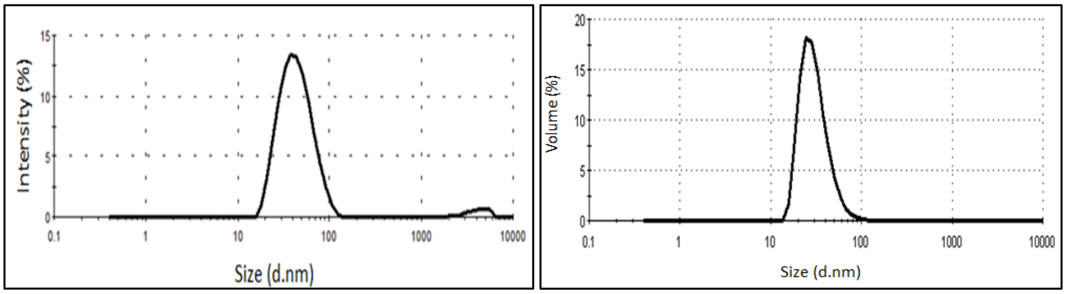


Figure 6.07 Particle size distributions by intensity (left) and volume (right) of poly(PEGMA-*co*-S)-*b*-poly(DEAEMA-*co*-AN) nanoparticles.

## Conclusions

Nitroxide-mediated polymerization of poly(ethylene glycol) methyl ether methacrylate (PEGMA) was performed for the first time in water using SG1 as nitroxide and VA-044 as initiator with a small amount of a comonomer with a low activation-deactivation equilibrium constant (*K*) including styrene, acrylonitrile, and sodium 4-styrenesulfonate. The reaction was well-controlled as evidenced by low molar mass dispersity. The resultant macroalkoxyamine was used after purification as a macroinitiator in the NMP of DEAEMAH+Cl-, which led to the formation of poly(PEGMA-*co*-S)-b-poly(DEAEMAH$^+$Cl$^-$-*co*-AN). The clear shift of the GPC curves of the macroinitiator to the right showed excellent livingness of the macroalkoxyamine. After neutralizing with NaOH, the free polymer chains were converted to diblock copolymer nanoparticles. Our results demonstrate that NMP may be successfully applied in aqueous media to prepare PEGMA-containing homopolymers or block copolymers, and nanoparticles stabilized with poly(PEGMA) moieties.

Considering living character of the poly(PEGMA) synthesized by NMP, this macroinitiator can be used in the synthesis and functionalization of other polymers. For example, in the next chapter it will be shown that PEGylation of chitosan can be achieved in water using poly(PEGMA) macroalkoxyamine synthesized by NMP.

## References

(1) Cunningham, M. F. *Prog. Polym. Sci.* **2008**, 33, 365-398.

(2) Zetterlund, P. B.; Kagawa, Y.; Okubo, M. *Chem. Reviews*, **2008**, 108, 3747-3794.

(3) Braunecker, W. A.; Matyjaszewski, K. *Prog. Polym. Sci.* **2007**, 32, 93-146.

(4) Nicolas, J.; Guillaneuf, Y.; Lefay, C.; Bertin, D.; Gigmes, D.; Charleux. B. *Prog. Polym. Sci.* **2013**, 38, 63-235.

(5) Jenkins, A, D.; Jones, R. G.; Moad, G. *Pure Appl. Chem.* **2009**, 82, 483-491.

(6) Nicolay, R.; Marx. L.; He, P. *Macromolecules*, **2007**, 40, 6067-6075.

(7) Mannan, M. A.; Fukuda, K.; Miura, Y. *Polymer*, **2007**, 39, 500-501.

(8) Phan, T. N. T.; Bertin, D. *Macromolecules*, **2008**, 41, 1886-1895.

(9) Grassl, B.; Clisson, G.; Khoukh, A.; Billon, L. *Eur. Polym. J*, **2008**, 44, 50-58.

(10) Rigolini, J.; Grassl, B.; Billon, L.; Reynaud, S.; Donard, O. F. X.; *J. Polym. Sci., Part A: Polym. Chem.*, **2009**, 47, 6919-6931.

(11) Brusseau, B.; D'Agosto, F.; Magnet, S.; Couvreur, L.; Chamignon, C.; Charleux, C.; *Macromol. Rapid. Commun*. **2011**, 44, 5590-5598.

(12) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Cunningham, M. F. *Macromolecules*, **2015**, 48, 72-80.

(13) Nicolas, J.; Mueller, C.; Matyjaszewski, K.; Charleux, B. *Macromolecules*, **2009**, 42, 4470-4478.

(14) Dire, L. C. C.; Charleux, B.; Magnet, S. *Macromolecules*, **2007**, 40, 1897-1903.

(15) Nicolas, J.; Brusseau. S.; Charleux, B. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, 48, 34-47.

(16) Lessard, B.; Ling, E. J. E.; Morin, M. S. T.; Maric, M. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, 49, 1033-1045.

(17) Veronese. F. M.; Pasut, G.; *Drug Discov. Today*, **2005**, 10, 1451-1458.

(18) Casettari, L.; Vllasaliu, D.; Castangnino, E.; Stolnik, S.; Howdle, S.; Illum, L. *Prog. Polym. Sci.*, **2012**, 37, 659-685.

(19) Veronese, F. M. *Biomaterials* **2001**, 5, 405-417.

(20) Nicolas, J.; Couvreur, P.; Charleux, B. *Macromolecules*, **2008**, 41, 3785-3761.

(21) Chenal, M.; Mura, S.; Marchal, D.; Gigmes, D.; Charleux, B.; Fattal, E.; Couvreur, P.; Nicolas, J. *Macromolecules*, **2010**, 43, 9291-9303.

(22) Qiao, B.; Lansalot, X. X.; Lami, E. B.; Charleux, B. *Macromolecules*, **2013**, 46, 4285-4295.

(23) Qiao, X. G.; Dugas, P. Y.; Charleux, B.; Lansalot, M. Lami, E. B. *Macromolecules*, **2015**, 48, 545-556.

(24) Van de Watering, P.; Moret, E. E.; Schuurmans-Nieuwenbroek, N. M.; Van Steenbergen, M. J.; Hennink, W. E. *Bioconjugate Chem.* **1999**, 589-597.

(25) Vinas, J.; Chagneux, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D. *Polymer*, **2008**, 49, 3639-3647.

## Chapter 7

# PEGylation of chitosan via nitroxide-mediated polymerization in aqueous media

## Abstract

Chitosan (CTS), valued for its biocompatibility, biodegradability, and biological tolerance finds applications in the biomedical and pharmacy fields. CTS properties can be improved if polymer chains are grafted to the CTS backbone. PEGylation of CTS is often carried out in order to obtain materials suitable for medical applications. The PEGlytation of CTS with poly(poly(ethylene glycol) methyl ether methacrylate-*co*-styrene), poly(PEGMA-*co*-S), via nitroxide-mediated polymerization (NMP) using both *grafting to* and *from* approaches has been performed. To conduct PEGylation of CTS via *grafting to*, CTS was first functionalized with glycidyl methacrylate (GMA) yielding CTS-*g*-GMA macromer. Poly(PEGMA-*co*-S), synthesized via NMP, was then grafted to the CTS-*g*-GMA yielding CTS-*g*-GMA-poly(PEGMA-*co*-S). For PEGylation via *grafting from*, CTS-g-GMA was first converted into a macroalkoxyamine using an SG1-based alkoxyamine. Graft copolymerization of PEGMA-*co*-S was then performed, yielding CTS-*g*-GMA-poly(PEGMA-*co*-S). The synthesis of CTS-*g*-GMA-poly(PEGMA-*co*-S) carried out in aqueous media either via *grafting to* or *from* was confirmed by $^1$H NMR and TGA.

## 7.1 Introduction

In the past few decades, chitosan (CTS) has been one of the most studied and/or modified biopolymers, mainly due to its biocompatibility, biodegradability, biological tolerance, and its potential for widespread applications in the biomedical and pharmacy fields, specifically in drug delivery systems,[1] water and wastewater treatment, agriculture, biopharmaceutics, cosmetics and beverage industries.[2] CTS is obtained from the partial alkaline deacetylation of chitin. Chitin is a biopolymer found in a large number of living organisms such as shellfish and insects, and is the second most abundant polymer on earth after cellulose. The main difference between CTS and chitin is that chitin possess an acetyl group on the second position (C-2) of the glycosidic ring and CTS (β (1→4)-links to 2-amino-2-deoxy-D-glucopyranose and to 2-acetamido-2-deoxy-D-glucopyranose) an amino functionality in the same position (Figure 7.1).[2]

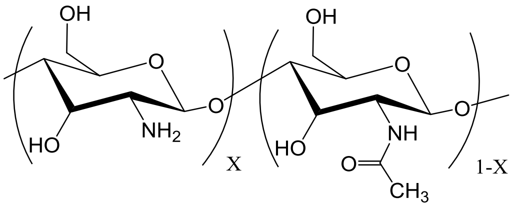


Figure 7.01 Structure of partial deacetylated chitosan.

In order to increase its suitability for a broader range of applications, CTS has been widely modified with graft synthetic (co)polymers. Such modifications have been achieved via free radical polymerization (FRP),[3-6] ring-opening polymerization (ROP),[7] γ-radiation or cationic polymerization,[8] but relatively few studies involving living/controlled radical polymerization (CLRP) or variations have been reported.[9-11] The modification of CTS with synthetic polymers often represents a challenge due to its insolubility in common organic solvents, which is attributed to its rigid D-glucosamine structure (Figure 7.1), ability to hydrogen bond intermolecularly, and high crystallinity.[2] CTS solubilization occurs only by the protonation of the $–NH_2$ of the D-glucosamine monomeric unit in acidic media ($pH < 6.5$).[12] Another important issue that should be considered in the modification of CTS is that some of the valuable CTS bioproperties are attributed to the presence of the $–NH_2$ group; therefore preserving this functional group is crucial for many applications. PEGylation of CTS, the covalent attachment of polyethylene glycol (PEG) or derivatives to CTS backbone chain, has been one of the most common modifications of CTS in order to obtain materials suitable for medical applications since PEG is soluble in both water and organic solvents and has low toxicity and good biocompatibility.[1] It is well-known that PEG groups covalently attached to CTS improve the biocompatibility of CTS.[13] PEGylation of CTS is also carried out in order to improve its solubility properties and could improve its affinity to water or organic solvents.[14] PEGylated CTS has been mainly used in the biomedical field, a few examples include; as a carrier/delivery vehicle since it may form polycomplexes with anionic drugs; in DNA delivery PEGylated CTS improve storage stability of chitosan-DNA complex nanoparticles, decrease the toxicity of chitosan nanoparticles.[1,13-15] Introduction of PEG groups onto the CTS backbone chain is commonly performed on the $-NH_2$ group at C-2,[1] mainly due to its higher reactivity in comparison with the hydroxyl groups (-OH) at C-6 and C-3.[15] One of the most commonly used methodologies for the PEGylation of CTS is end-group functionalization of the α-monomethoxy and ω-hydroxy-PEG with different functional groups such as aldehyde, carboxylic acid, carbonate, iodide, epoxide, NHS-ester, or sulfonates, which are able to react with the amino group of CTS yielding PEGylated-CTS based materials.[15] Despite the fact the PEGylation of CTS on the $–NH_2$ groups is easier than on the –OH groups, some researchers have investigated the modification of the –OH groups of CTS with PEG chains. To achieve modification of the –OH groups, the –$NH_2$ groups were typically first functionalized with phthalic anhydride yielding *N*-phthaloylchitosan (which swells in pyridine, *N*,*N*-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO))[16] followed by the introduction of PEG by esterification[17,18] or "click chemistry" reactions.[19] Also sodium dodecylsulfate (SDS)/chitosan complexes (SCC), which are soluble in DMSO,[20] have been modified with PEG on the hydroxyl groups via click chemistry.[19]

Macromonomers composed of a vinyl moiety, either styrenic, acrylic or methacrylic, connected to short (PEG) chains with variable chain length has allowed the synthesis of well-defined PEG-based macromolecular architectures via CLRP or FRP.[21-25] Different molecular weight PEGMA, which implies a different number of ethylene glycol units, has been one of the most commonly used macromonomers for the synthesis of PEG-based materials, largely due to its commercial availability. PEGMA is soluble in water and in organic solvents and it is possible to polymerize it via NMP in bulk[25] or in water/ethanol systems.[26] Very recently, our research group reported the nitroxide-mediated copolymerization of PEGMA with a small amount of styrene in water at 90 °C using VA-044 as initiator and SG1 as nitroxide.[27] Performing polymerization reactions in water is always appealing since water is a green, nontoxic, and inexpensive solvent.

In this paper, we report the PEGylation of CTS by the introduction of PEGMA-based copolymers via NMP and the *grafting to* and *from* approaches in aqueous media. For the PEGylation of CTS via *grafting to* and NMP, firstly CTS was functionalized with GMA yielding CTS-*g*-GMA following previous reports,[8,28,29] then poly(PEGMA-*co*-S), synthesized via NMP, was grafted to CTS-*g*-GMA using the double bond of the GMA unit as anchor group. In the grafting *from* approach, CTS-*g*-GMA was converted SG1-based macroalkoxyamine, CTS-*g*-GMA-NBB, which enabled grafting copolymerizations of PEGMA and S in aqueous media. The synthesis of CTS-*g*-GMA-poly(PEGMA-*co*-S) either via *grafting to* or *from* was confirmed by $^1$H NMR and TGA. To the best of our knowledge, this is the first report of the PEGylation of CTS using poly(PEGMA-*co*-S) via NMP.

## 7.2 Experimental Section

### Materials

Chitosan (CTS, Aldrich, degree of deacetylation of 85%), glycidyl methacrylate (GMA, Aldrich, 97%), potassium hydroxide (KOH, Aldrich, 90%) hydroquinone (Fisher), acetic acid (Fisher, 99.7%), tetrahydrofuran (THF, ACP, 99+%), deuterium oxide (Cambridge Isotope Laboratories, D 99.9%), poly(ethylene glycol) methyl ether methacrylate (PEGMA, Aldrich, $M_n$=950 g mol$^{-1}$), chloroform-d (CDCl3, Aldrich, 99.8%), 2,2'-Azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044, Wako Pure Chemical Industries), sodium hydroxide (NaOH, >97%), tetrahydrofuran (THF, >99%), and nitrogen ($N_2$, Praxair) were used as received. Styrene (S, Aldrich, > 99%) was passed over a column containing basic aluminium oxide (Aldrich, ~150 mesh) to remove the inhibitor and stored below 5 °C prior to polymerization. All aqueous solutions were prepared with deionized water (DIW). BlocBuilder (2-methyl-2-(*N*-tert-butyl-*N*-(1-diethoxyphosphoryl-2,2-dimethylpropyl)aminoxy)-propionic acid alkoxyamine) (BB, 99%) and SG1 (4-(diethoxyphosphinyl)-2,2,5,5-tetramethyl-3-azahexane-*N*-oxyl) (85%) were kindly supplied by

Arkema. 2-Methyl-2-[*N*-tert-butyl-*N*-(1-diethoxyphosphoryl-2,2-dimethylpropyl)aminoxy]-*N*-propionyloxysuccinimide (NHS-BB) was synthesized from BB according to previous reports.[30]

### Characterization

$^1$H NMR spectroscopy was performed on an FT-NMR Bruker Avance 400 MHz spectrometer with a total of 256 scans, at room temperature using $D_2O$, $D_2O/CH_3COOH$ or $CDCl_3$ as solvent at 5 mg/mL. Thermogravimetric analyses (TGA) were performed using a TA Instruments Q500 TGA analyzer by heating the sample using the following ramp: 10 °C min$^{-1}$ from 30 to 75 °C, held for 30 min at a plateau of 75 °C, and 10 °C min$^{-1}$ to 600 °C. Gel Permeation Chromatography (GPC) analysis was performed with a Waters 2690 Separation Module and Waters 410 Differential Refractometer with THF as the eluent. The column bank consisted of Waters Styragel HR (4.6x300 mm) 4, 3, 1, and 0.5 separation columns at 40 °C.

### Synthesis of CTS-*g*-GMA

CTS was functionalized with GMA following previous reports.[8,28,29] CTS (1 g) was dissolved in 100 mL 0.4 M acetic acid solution in a three neck round bottom flask, then 5 mL of 0.05 M KOH and a hydroquinone solution (0.09 mmol in 10 mL of $H_2O$) were added to the reaction mixture. Finally, GMA (0.024 mol, 3.53 g, and 3.30 mL) was added to the system dropwise. The reaction mixture was previously degassed for 30 minutes under $N_2$ atmosphere prior to increasing the temperature to 65 °C and magnetically stirred for 2 h. The final pH of the mixture was 3.8. After reaction water was removed from the system by vacuum at room temperature. Finally CTS-*g*-GMA was washed three times in clean THF, and dried under vacuum. CTS-*g*-GMA was analyzed by $^1$H NMR in $D_2O/CH_3COOH$ (0.4 M).

### Synthesis of poly(PEGMA-*co*-S) via NMP in water

The copolymerization of PEGMA and S in water was carried out according to the method previously reported from our group.[27] In a typical experiment PEGMA (10.0 g, 0.011 mol), S (0.12 g, 0.001 mole), trioxane (500 mg), SG1 (123 mg, 0.42 mmol), and DIW (35 mL) were mixed in a 100 mL 3-neck round-bottom flask. In a second flask immersed in an ice-water bath, VA-044 (68 mg, 0.21 mmol) was dissolved in 5 mL DIW. The contents of both flasks were deoxygenized for 20 min by purging nitrogen. The first flask was then introduced into a preheated oil bath at 90ºC and fitted with a reflux condenser, a nitrogen inlet and a thermometer after 2 min the initiator solution was added. Time zero of the polymerization was taken when the initiator solution was added to the reaction mixture. The reaction mixture, while remaining under $N_2$, was stirred at a speed of 300 rpm and allowed to react for 2 h. At the end of the reaction a sample was taken a portion of the sample was used for NMR analysis and the remainder was neutralized with 0.005 M NaOH to convert the charged imidazole group (resulting from VA-044 initiator decomposition) to its neutral form and then dried under air for 24 h. Finally the product poly(PEGMA-*co*-S) was analyzed by GPC using PMMA calibration.

### Synthesis of CTS-*g*-GMA-poly(PEGMA-*co*-S) via *grafting to*

CTS-*g*-GMA (0.50 g) was dissolved in 50 mL of 0.1 M acetic acid in a three neck round bottom flask. KOH (0.05 M, 50 mL) was added to the CTS-*g*-GMA solution to increase pH to 5 and magnetically stirred under nitrogen for 30 minutes before increasing the temperature to 90 ºC. Separately, poly(PEGMA-*co*-S) (1 g) was dissolved in 30 mL of DIW under $N_2$ atmosphere. When CTS-*g*-GMA solution reached the desired temperature, 10 mL of the poly(PEGMA-*co*-S) solution was added  into the reaction system every 30 min for 1 h, and the system was then kept under these conditions for a further 2 h.  At the end of the reaction, water was removed from the system using a rotary evaporator and CTS-*g*-GMA-poly(PEGMA-*co*-S) was washed with water and THF (three times each) in order to remove free polymer. The synthesized CTS-*g*-GMA-poly(PEGMA-*co*-S) was analyzed by $^1$H NMR and TGA.

### Synthesis of CTS-*g*-GMA-NBB macroalkoxyamine

CTS-*g*-GMA (1 g) was dissolved in 100 mL of 0.1 M acetic acid in a three neck round bottom flask. 0.05 M KOH (50 mL) was added to CTS-*g*-GMA solution to increase the pH to 5.1. NHS-BB (1 g) was dispersed in 30 mL of DIW and added to CTS-*g*-GMA solution. The solution was then deoxygenated for 30 minutes under nitrogen atmosphere prior to increasing the temperature to 85°C and magnetically stirred for 1.5 h. After reaction, the flask was cooled, and the DIW was removed from the system using a rotary evaporator. Finally, CTS-*g*-GMA-NBB macroalkoxyamine was washed with THF two times in order to remove free NHS-BB. CTS-*g*-GMA-NBB was analyzed by $^1$H NMR.

### *Grafting from* polymerization using CTS-*g*-GMA-NBB macroalkoxyamine: CTS-*g*-GMA-poly(PEGMA-*co*-S)

In a typical experiment**,** CTS-*g*-GMA-NBB (0.17 g) was dissolved in 17 ml of 0.1 M acetic acid solution in a three neck round bottom flask. 0.05 M KOH (10 mL) was added to CTS-*g*-GMA-NBB solution to increase the pH to 5. PEGMA (3 g, 3.15 mmol), S (0.3 mmol) and SG1 (0.015 mmol) were added to CTS-*g*-GMA-NBB. The solution was then deoxygenated for 30 minutes under nitrogen atmosphere before increasing the temperature to 85 °C and magnetically stirred for

0.5, 1 or 2 h. Finally the DIW was removed from the system using a rotary evaporator. CTS-*g*-GMA-poly(PEGMA-*co*-S) was washed with THF and DIW in order to remove free monomer. The product was dried for 24 h prior to being analyzed by $^1$H NMR in $D_2O/CH_3COOH$ and TGA.

## 7.3 Results and Discussion

PEGylation of CTS by two different approaches (*grafting to* and *from*) using NMP was conducted for the first time in aqueous media (Figure 7.2). In the case of the *grafting to* approach, poly(PEGMA-*co*-S) chains with low molar dispersities ($Đ < 1.2$) were grafted to the CTS backbone, and in the *grafting from* approach, poly(PEGMA-*co*-S) chains were grown from the CTS-macroalkoxyamine. For the *grafting to* approach, poly(PEGMA-*co*-S), synthesized via NMP, was grafted to CTS-*g*-GMA through the reaction of the vinyl bond of the CTS-*g*-GMA and the free radical end-group of the poly(PEGMA-*co*-S) after thermal dissociation of the SG1 nitroxide in aqueous media (pH=5.1) yielding CTS-*g*-GMA-poly(PEGMA-*co*-S). For the *grafting from* approach, CTS-*g*-GMA was converted into macroalkoxyamine by intermolecular 1,2 radical addition of 2-methyl-2-[*N*-tert-butyl-*N*-(1-diethoxyphosphoryl-2,2-dimethylpropyl)aminoxy]-N-propionyloxysuccinimide (NHS-BB) in aqueous media (pH=5.1), yielding CTS-*g*-GMA-NBB. The resulting macroalkoxyamine, CTS-*g*-GMA-NBB, was then employed in the *grafting from* polymerization reaction of PEGMA in the presence of a small amount of S and free SG1 at 85 °C.

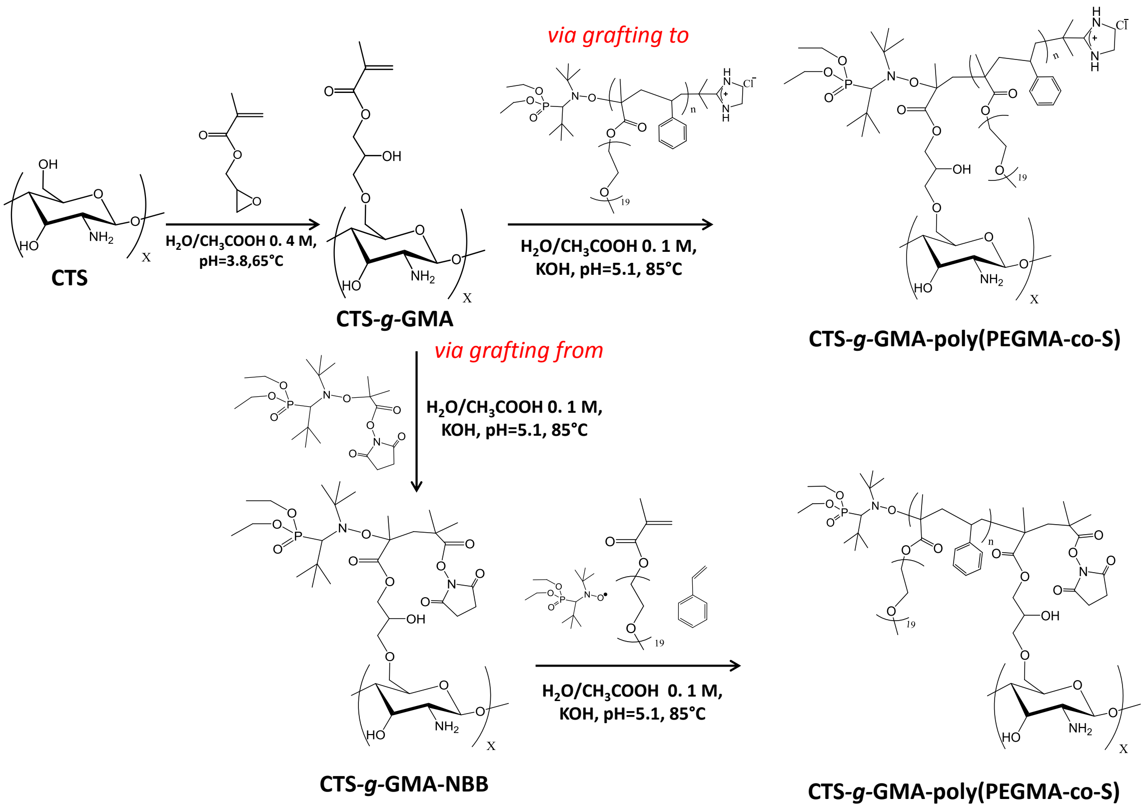


Figure 7.2 General procedure for the PEGylation of CTS via NMP and grafting to and from approaches.

### 7.3.1 Grafting to: synthesis of CTS-*g*-GMA

Employing $^1$H NMR we confirmed the synthesis of CTS-*g*-GMA (Figure 7.3). The spectra for CTS exhibits peaks at 3.09, 3.67, 3.83, and 4.52 ppm attributed to $H_2$, $H_{5\text{-}6}$, $H_{3\text{-}6}$, and $H_1$, respectively. The spectra for CTS-*g*-GMA, besides the characteristic displacements of CTS, shows new signals at 4.24 ppm attributed to the $H_7$ and $H_8$ protons of GMA, which are closest to the ether linkage with CTS. Finally the displacements observed at 5.71 and 6.11 ppm are attributed to the $H_{10,\ 11}$ vinyl protons of the GMA unit. The degree of functionalization of CTS with GMA was estimated to be 11 mol%, which was calculated from the integral ratio between the GMA vinyl proton peak at 6.1 ppm and the CTS proton peak at 3.1 ppm.

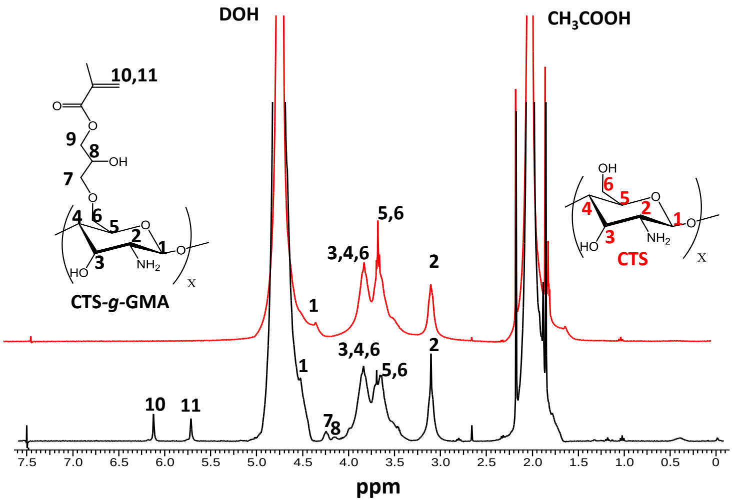


Figure 7.03 $^1$H NMR spectra of CTS (red line) and CTS-*g*-GMA (black line) in 0.4 M $D_2O$+$CH_3COOH$.

### 7.3.2 Grafting to: synthesis of poly(PEGMA-*co*-S) via NMP in water

The copolymerization of PEGMA and S was carried out in DIW. In the case of the polymerization of methacrylates via NMP with SG1, it is necessary to add small amounts (8-10 mol% respect with the methacrylate monomer) of monomers with a low activation-deactivation equilibrium constant ($K$) such as S or acrylonitrile (AN)[31,32] in order to obtain good control over the polymerization. According to previous reports from our group,[27] S is a good choice of comonomer for the polymerization of PEGMA in DIW since it affords control over the polymerization (linear increase of the $M_n$ versus conversion and narrow molecular weight distributions).[27] From our GPC traces (Figure 7.4) it was determined that poly(PEGMA-*co*-S) with $M_n$~10900 g/mol (PMMA equivalent molecular weights), and $Đ$=1.2 was produced , which subsequently was grafted to the CTS-*g*-GMA.

### 7.3.3 Grafting poly(PEGMA-*co*-S) to CTS-*g*-GMA

The process of grafting well-defined (co)polymers to the CTS backbone chain via NMP chemistry as well as the reaction conditions needed were previously reported by our group,[28] and is based on the thermal dissociation of SG1 from the copolymer chain (previously synthesized via SG1-mediated polymerization) resulting in two radicals: the stable SG1-nitroxide radical and a free radical at the end of the copolymer chain. This chain-end radical is able to react with the double bond of CTS-*g*-GMA before being deactivated by the SG1, covalently linking the copolymer chain to CTS (Figure 7.4).

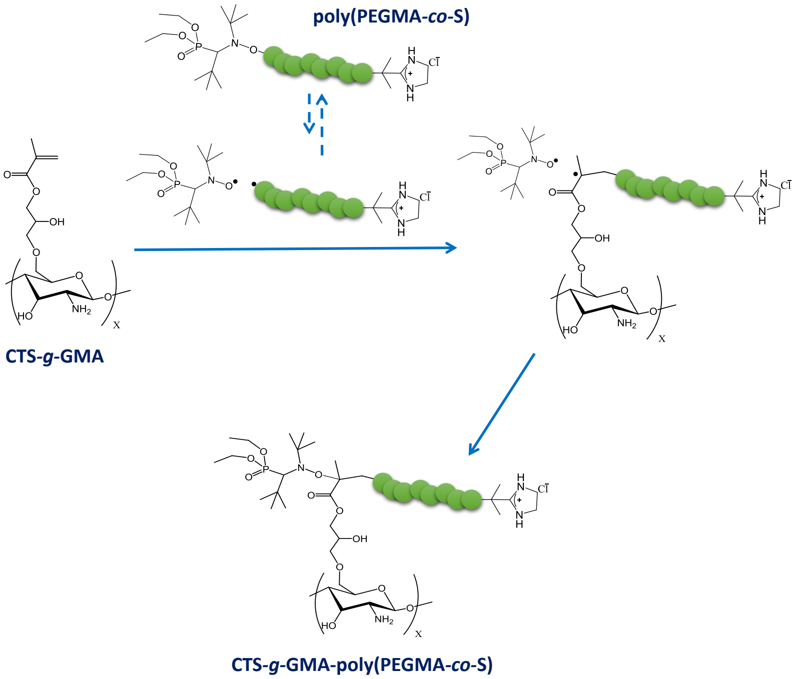


Figure 7.04 Proposed mechanism for the reaction between chain-end radical of poly(PEGMA-*co*-S) chain and a double bond of CTS-*g*-GMA.

The synthesis of CTS-*g*-GMA-poly(PEGMA-*co*-S) was confirmed by $^1$H NMR (Figure 7.5). The corresponding spectra shows the characteristic peaks of the glycosydic ring of CTS previously explained and the characteristic signals of poly(PEGMA-*co*-S) at 3.4-4 ppm ($H_{17}$, $H_{18}$), at 4.23 ppm ($H_{16}$), 3.5 ppm ($H_{19}$). Unreacted vinyl bond of the GMA can be seen at 5.7 and 6.1 ppm. From the integral ratio between the GMA vinyl proton peak at 5.7 ppm and the CTS proton peak at 3.1 ppm ($H_2$), it was determined that for every 100 units of CTS, there are approximately 7 chains of poly(PEGMA-*co*-S), indicating a grafting efficiency value (GMA unites/grafted polymer chains) of 64%.

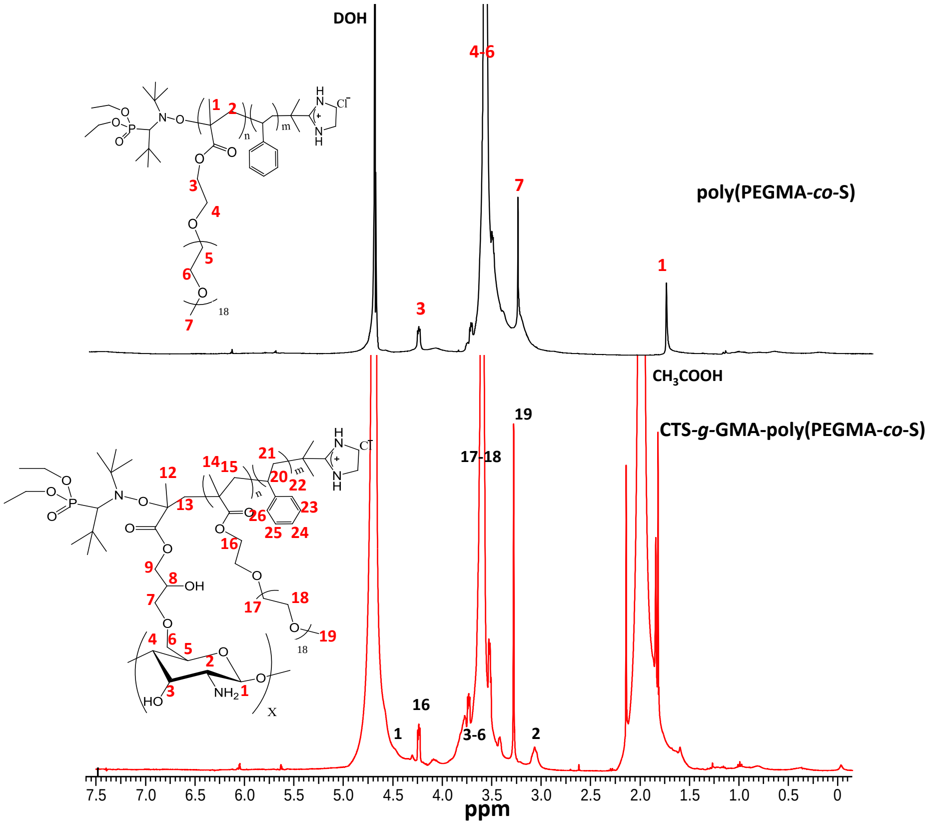


Figure 7.5 $^1$H NMR spectra of CTS-*g*-poly(PEGMA-*co*-S) in 0.4 M $D_2O$+$CH_3COOH$ and poly(PEGMA-*co*-S) in $D_2O$.

The corresponding TGAs of CTS, poly(PEGMA-*co*-S) and CTS-g-GMA-poly(PEGMA-*co*-S) are shown in Figure 7.6. The TGA of CTS shows a first weight loss attributed to the loss of physisorbed water and a second weight loss (250 to 350 °C) related to the pyrolysis of the biopolymer, which begins with the rupture of the glycosidic bonds followed by the degradation of CTS.[33] The TGA for poly(PEGMA-*co*-S) shows the complete decomposition of the methacrylic polymer between 320 and 420 °C. In the TGA for CTS-*g*-GMA-poly(PEGMA-*co*-S) are observed two decomposition steps, the first one between 250 and 350°C attributed to the degradation of CTS, and the second one related to the decomposition of the grafted chains between 350 and 450 ºC. CTS-*g*-GMA-poly(PEGMA-*co*-S) showed better thermal stability compared to CTS which is common in PEGylated-chitosan, and may be attributed to the weakening the hydrogen bonds between the CTS chains and parts of the CTS domains near the new PEG chains.[1,34]

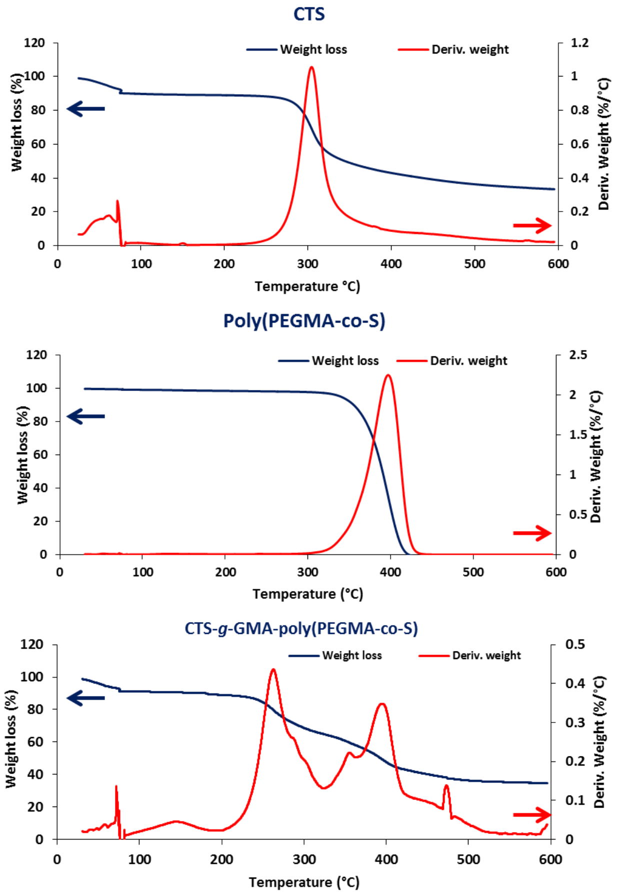


Figure 7.6 Thermogravimetric analyses of CTS, poly(PEGMA-*co*-S) and CTS-*g*-GMA-poly(PEGMA-*co*-S).

### 7.3.4 Grafting from: synthesis of CTS-*g*-GMA-NBB macroalkoxyamine

NHS-BB was introduced to the CTS-*g*-GMA (previously synthesized) by an intermolecular 1,2 radical addition process, yielding CTS-*g*-GMA-NBB macroalkoxyamine. The $^1$H NMR spectra of NHS-BB and CTS-*g*-GMA-NBB are shown in Figure 7.7. The spectrum for CTS-*g*-GMA-NBB shows, in addition to the characteristic signals of CTS-*g*-GMA, new peaks attributed mainly to the NHS-BB linked to GMA. From 0.9 to 1.40 ppm ($H_{12\text{-}13}$, $H_{18,20}$) are the signals attributed to some of the -$CH_3$ groups, from 2.3 to 2.7 ppm ($H_{14\text{-}15}$, $H_{17}$) are peaks attributed to –$CH_2$ and –CH-N groups, and from 4.1 to 4.4 ppm ($H_{12}$) are signals attributed to the -$CH_2$-O- groups. The degree of functionalization of CTS with alkoxyamine groups was determined from the integral ratio between the NHS-BB signals at 0.9-1.4 ppm and the CTS proton peak at 3.1 ppm and was estimated to be 10 mol%, which would indicate that approximately 90% of the GMA units were functionalized with the alkoxyamine.

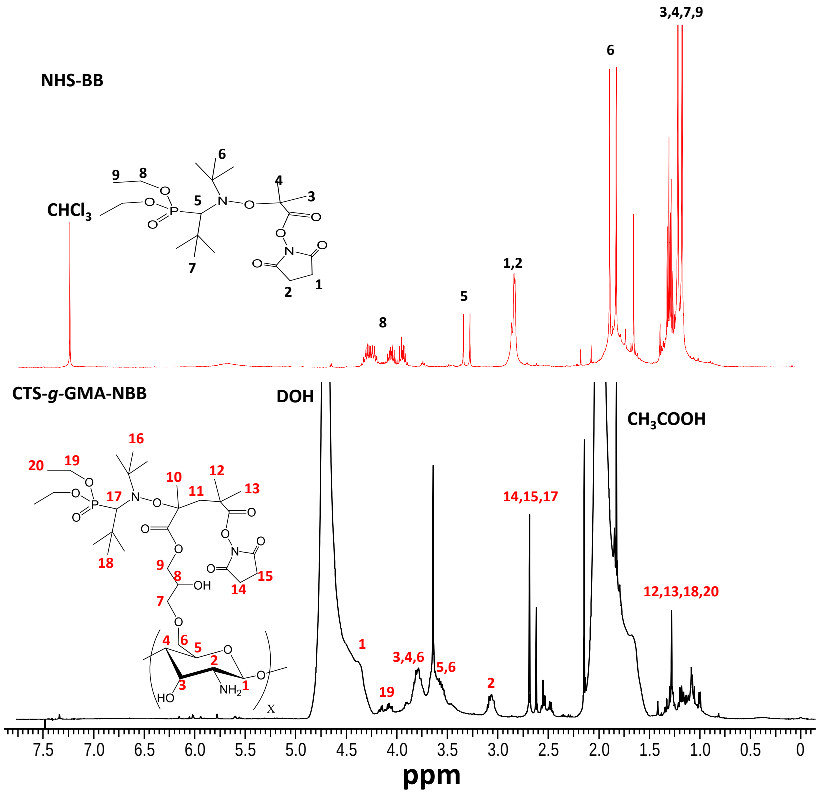


Figure 7.07 $^{1}$H NMR spectra of NHS-BB in $CDCl_3$ and CTS-*g*-GMA-NBB in 0.1 M $D_2O/CH_3COOH$.

### 7.3.5 *Grafting from* polymerizations

CTS-*g*-GMA-poly(PEGMA-*co*-S) was also synthesized via a grafting from approach using CTS-*g*-GMA-NBB. Grafting from polymerizations of PEGMA in the presence of small amounts of S and free SG1 (in order to decrease the concentration of propagating radicals and leading to a better controlled polymerization) were performed under light acidic conditions (pH~5) at 90 °C and at different reaction times. The fraction of monomers converted into graft copolymer was calculated by gravimetry method, and the composition of the resulting materials was determined. By gravimetry method it was determined that the monomer conversion and therefore the composition changed according to the reaction time. The monomer conversions at 0.5, 1 and 2 h were approximately 2.0, 2.3 and 2.8% respectively. From these conversion values the compositions (CTS:poly(PEGMA-*co*-S)) at 0.5, 1 and 2 h can be calculated as 73:27%, 70:30% and 65:35% respectively. Although the monomer conversion was low, this was enough to achieve high degrees of grafting. Short reaction times were used since the polymerization of methacrylate monomers is considerably faster than styrenic or acrylic monomers. It has been established that in grafting from polymerizations, low initiation efficiency is a common issue, and therefore it was decided to use a large excess of monomers to promote the grafting reaction.[8,10]

TGA analysis of CTS-*g*-GMA-poly(PEGMA-*co*-S) (Figure 7.8) obtained via *grafting from* at 0.5, 1 and 2 h show an initial weight loss from 220 to 300 °C due to CTS pyrolysis. From 300 to 500°C it is shown a continuous weight loss (with two changes in the slope) attributed to the decomposition of the grafted poly(PEGMA-*co*-S). Assuming that mostCTS-*g*-GMA is decomposed by 350°C and poly(PEGMA-*co*-S) decomposes after 300°C, the percentages of poly(PEGMA-*co*-S) grafted to the CTS backbone chain were estimated to be 25, 28 and 31% of the total graft polymer mass at 0.5, 1, and 2 h respectively which is in good agreement with the values determined by gravimetry. TGA measurements also confirmed that grafting poly(PEGMA-*co*-S) to CTS via *grafting from* improved the thermal stability compared to CTS-*g*-GMA-poly(PEGMA-*co*-S) obtained via a *grafting to* approach. This unexpected improvement in the thermal stability may be attributed to the higher graft density achieved with the *grafting from* approach, or some termination of the growing chains leading to crosslinking, as it has been previously observed.[8]

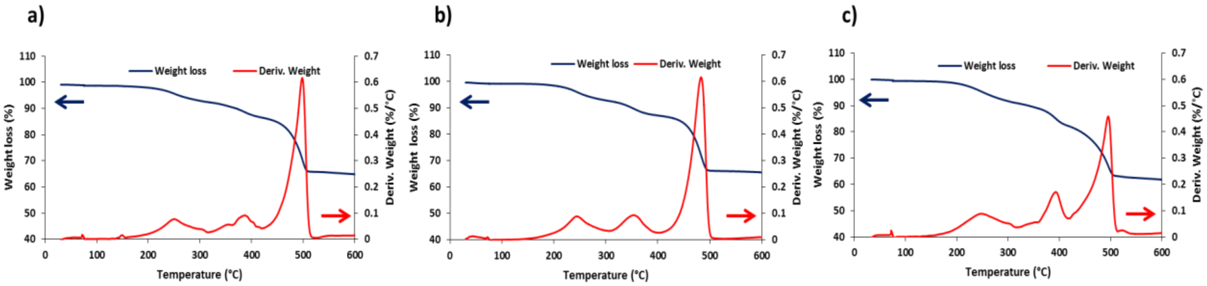


Figure 7.08 TGA of CTS-*g*-GMA-poly(PEGMA-*co*-S) obtained at 0.5h (a), 1h (b) and 2 h (c) via a *grafting from* approach.

By $^1$H NMR analysis the synthesis of CTS-*g*-GMA-poly(PEGMA-*co*-S) was confirmed. Figure 7.9 shows the $^1$H NMR spectra of CTS-*g*-GMA-poly(PEGMA-*co*-S) at 0.5, 1 and 2 h. The spectra show new signals that confirm the grow of poly(PEGMA-*co*-S) from the CTS backbone chain: 0.9 to 1.40 ppm ($H_{12-13}$, $H_{29,31}$) are the signals attributed to -$CH_3$ groups of the SG1-end group; between 3.4 and 4 ppm appears a strong signal (overlapped with the CTS signal) is attributed to the protons of the ethylene glycol unit ($H_{24}$, $H_{25}$). At 4.23 ppm the peak is attributed to protons in the α-position to the methacrylic unit of PEGMA ($H_{23}$). The methyl group of PEGMA is shown at 3.5 ppm.

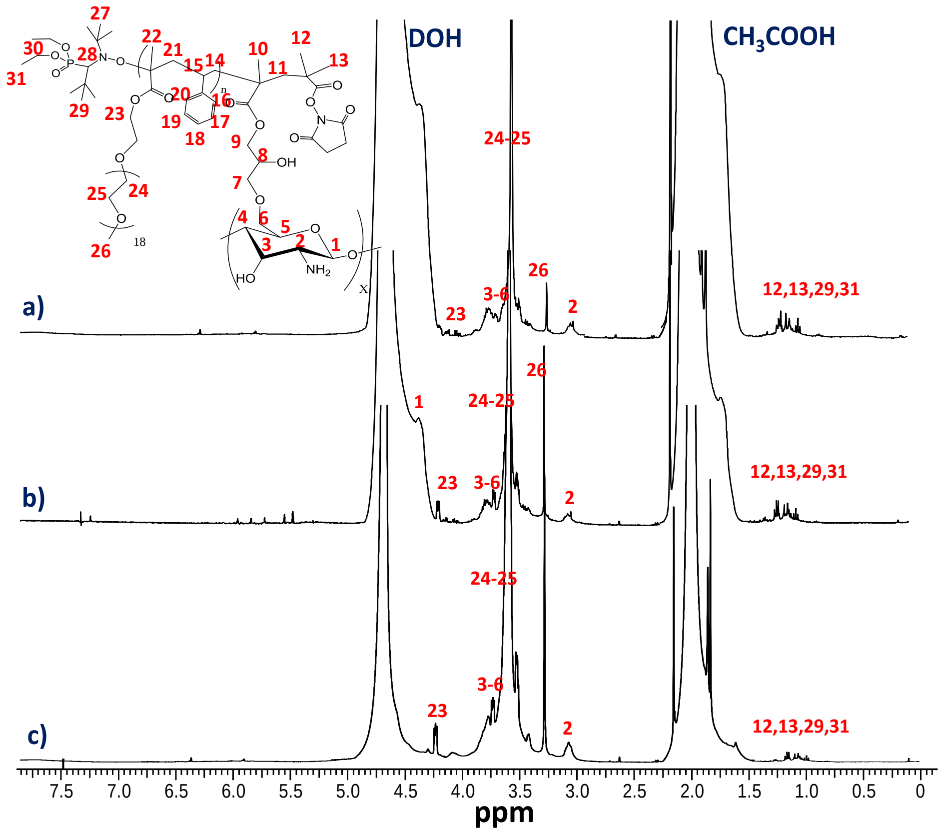


Figure 7.9 $^1$H NMR spectra of CTS-*g*-GMA-poly(PEGMA-*co*-S) in 0.4 M $D_2O$+$CH_3COOH$ obtained via a *grafting from* approach at 0.5 h (a), 1 h (b) and 2 h (c).

## Conclusions

The PEGylation of CTS using NMP via both grafting to and from approaches was conducted in aqueous media. The PEGylation of CTS was carried out on the OH groups on the CTS molecule, preserving the amino functionality. The grafting to procedure enabled grafting well-defined poly(PEGMA-*co*-S) using a novel strategy. The resulting properties of the PEGylated chitosan (obtained via grafting to) may be modified simply by the changing the molecular weight of the poly(PEGMA-*co*-S) made via NMP. Using a grafting from approach, the PEGylation of CTS is possible and reasonable amounts of PEG groups can be introduced to the CTS backbone chain. The advantage of the grafting to procedure over the grafting from approach is that in the grafting to procedure well-defined poly(PEGMA-*co*-S) chains are grafted ($M_n$, composition) whereas for the grafting from approach, a process to effectively cleave the grafted chains must be developed to determine the $M_n$ of the grafted chains. The grafting from procedure can be useful when high graft density or high molecular weight poly(PEGMA-*co*-S) chains are desired. Using these methodologies is possible to manipulate the amount of PEG incorporated to CTS therefore it is possible to manipulate the properties according to the needs for every specific potential application. PEGylated CTS has been widely used in biomedical field due to PEG groups increase/improve the biocompatibility of the resulting materials and also such groups can improve CTS biocompatibility, hydrophilicity/hydrophobicity, etc. Due to its unique properties, PEGylated CTS could find applications in different areas such as biomedical and biopharmaceutics, water and wastewater treatment and agriculture.

In all previous chapters, DEAEMA was used as a pH-responsive monomer in the synthesis of pH-responsive polymers by NMP. In the next chapter it will be explained that dimethylaminopropyl methacrylamide (DMAPMA) can also be used in the preparation of pH-responsive polymer, which has several advantages compared to DEAEMA.

## References

(1) Casettari, L.; Vllasaliu, D.; Castagnino, E.; Stolnik, S.; Howdle, S.; Illum, L. *Prog. Polym. Sci.* **2012**, 37, 659-685.

(2) Rinaudo, M.; *Prog. Polym. Sci.* **2006**, *31*, 603-632.

(3) Mourya, V.K.; Inamdar, N. N. *React. Funct. Polym.* **2008**, *68*, 1013-1051.

(4) Jayakumar, R.; Prabaharan, M.; Reis, R. L.; Mano, J. F. *Carbohydr. Polym.* **2005**, *62*, 142-158.

(5) Jenkins, D. W.; Hudson, S. M. *Chem. Rev.* **2001**, *101*, 3245-3273.

(6) Elizalde-Peña, E. A.; Flores-Ramirez, N.; Luna-Barcenas, G.; Vásquez-García, S. R.; Arámbula-Villa, G.; García-Gaitán, B.; Rutiaga-Quiñones, J. G.; González-Hernández, J. *Eur. Polym. J.* **2007**, *43*, 3963-3969.

(7) Liu, L.; Li, Y.; Liu, H.; Fang, Y. E. *Eur. Polym. J.* **2004**, *40*, 2739-2744.

(8) Yoshikawa, S.; Takayama, T.; Tsubokawa, N. *J. Appl. Polym. Sci.* **1998**, *68*, 1883-1889.

(9) Garcia-Valdez, O.; Champagne-Hartley, R.; Saldivar-Guerra, E.; Champagne, P.; Cunningham, M. F. *Polym. Chem.* **2015**, *6*, 2827-2836.

(10) Tizzotti, M.; Charlot, A.; Fleury, E.; Stenzel, M.; Bernard, J. *Macromol. Rapid Commun.* **2010**, 31, 1751-1772.

(11) García-Valdez, O.; Ramírez-Wong, D. G.; Saldívar-Guerra, E.; Luna-Bárcenas, G. *Macromol. Chem. Phys.* **2013**, 214, 1396-1404.

(12) Rinaudo, M.; Pavlov, G.; Desbrières, J. *Polymer,* **1999**, 40, 7029-7032.

(13) Prego, C.; Torres, D.; Fernandez-Megia, E.; Novoa-Carballal, R.; Quiñoá, E.; Alonso, M. *J. Controlled Release,* **2006**, 111, 299-308.

(14) Du, J.; Hsieh, Y. L. *Cellulose,* **2007**, 14, 543-552.

(15) Kurita, K. *Prog. Polym. Sci.* **2001**, *26*, 1921-1971.

(16) Kurita, K.; Ikeda, H.; Yoshida, Y.; Shimojoh, M.; Harata, M. *Biomacromolecules,* **2002**, 3, 1-4.

(17) Makuška, R.; Gorochovceva, N. *Carbohydr. Polym.* **2006**, 64, 319-327.

(18) Gorochovceva, N.; Makuška, R. *Eur. Polym. J.* **2004**, 40, 685-691.

(19) Gruškienė, R.; Čiuta, G.; Makuška, R. *Chemija,* **2009**, 20, 241-249.

(20) Cai, G.; Jiang, H.; Tu, K.; Wang, L.; Zhu, K. *Macromol. Biosci.* **2009**, 9, 256-261.

(21) Lutz, J. F. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, 46, 3459-3470.

(22) Zhao, B.; Li, D.; Hua, F.; Green, D. R. *Macromolecules,* **2005**, 38, 9509-9517.

(23) Tan, B.; Hussain, H.; Liu, Y.; He, C.; Davis, T. *Langmuir,* **2009**, 26, 2361-2368.

(24) Hua, F.; Jiang, X.; Li, D.; Zhao, B. *J. Polym. Sci., Part A: Polym. Chem.* **2006**, 44, 2454-2467.

(25) Nicolas, J.; Couvreur, P.; Charleux, B. *Macromolecules* **2008**, 41, 3758-3761.

(26) Chenal, M.; Mura, S.; Marchal, C.; Gigmes, D.; Charleux, B.; Fattal, E.; Couvreur, B.; Nicolas, J. *Macromolecules* **2010**, 43, 9291-9303.

(27) Darabi, A.; Jessop, P. G.; Cunningham, M. F. Unpublished.

(28) García-Valdez, O.; George, S.; Champagne-Hartley, R.; Saldívar-Guerra, E.; Champagne, P.; Cunningham, M. F. *Polymer* **2015**, 67, 139-147.

(29) Flores-Ramírez, N.; Elizalde-Peña, E. A.; Vásquez-García, S. R.; González-Hernández, J.; Martinez-Ruvalcaba, A.; Sanchez, I. C.; Luna-Bárcenas, G.; Gupta, R. B. *J. Biomater. Sci. Polym. Ed.* **2005**, 16, 473-488.

(30) Vinas, J.; Chagneux, N.; Gigmes, D.; Trimaille, T.; Favier, A.; Bertin, D. *Polymer,* **2008**, 49, 3639-3647.

(31) Nicolas, J.; Dire, C.; Mueller, L.; Belleney, J.; Charleux, B.; Marque, S. R. A.; Bertin, D.; Magnet, S.; Couvreur, L. *Macromolecules,* **2006**, 39, 8274-8282.

(32) Nicolas, J.; Brusseau, S.; Charleux, B. *J. Polym. Sci., Part A: Polym. Chem.* **2010**, 48, 34-47.

(33) Qu, X.; Wirsen, A.; Albertsson, A. C. *Polymer,* **2000**, 41, 4589-4598.

(34) Deng, L.; Qi, H.; Yao, C.; Feng, M.; Dong, A. *J. Biomater. Sci. Polym. Ed.* **2007**, 18, 1575-1589.

## Chapter 8

# Preparation of $CO_2$-switchable latexes using dimethylaminopropyl methacrylamide (DMAPMA)

## Abstract

$CO_2$-switchable polystyrene (PS) and poly(methyl methacrylate) (PMMA) latexes were prepared via a surfactant-free emulsion polymerization (SFEP) under a $CO_2$ atmosphere, employing dimethylaminopropyl methacrylamide (DMAPMA) as a $CO_2$-switchable and hydrolytically stable comonomer. The conversion of SFEP of styrene reached to > 95% in less than 5 h. The resulting latexes had near monodisperse particles ($Đ \leq 0.04$), as confirmed by DLS and TEM. The latexes could be destabilized by bubbling nitrogen ($N_2$) and heating at 80 ºC for 30 min and easily redispersed by only bubbling $CO_2$ for a short period of time without using sonication.

## 8.1 Introduction

Emulsion polymerization is an industrially viable process for producing polymer latexes yielding high molecular weights can be achieved at fast polymerization rates, and providing effective heat transfer due to the use of water as an environmentally-friendly solvent for the polymerization medium. The colloidal stability of the latex particles is provided by surfactant; however, residual surfactant can be detrimental to the properties of the final latex specifically in film-forming applications due to the migration of the surfactant to the surface of the film.

Transportation cost is another problem in the latex industry since most often the locations where the product are used are far removed from production sites. Considerable energy and cost savings could be realized if latexes could be aggregated, shipped as concentrated wet cakes or dry powder, and then redispersed on site. In applications where aggregation of the latex is required to obtain resins, coagulation is commonly achieved by the addition of large amount of salts, acids, or bases to break the emulsion and destabilize the latex. To address these issues, the concept of switchable surfactants was introduced for the preparation of $CO_2$-switchable latexes.[1] Different types of switchable surfactants have been reported that are triggered by acids, bases, redox reagents, and light, but these triggers are not suitable for the preparation of switchable latexes for various reasons including environmental impact, cost, and toxicity.[2]

$CO_2$ as an inexpensive, non-accumulating, benign, biocompatible, and easily applied and removed trigger offers a unique and promising route for the preparation of switchable latexes.[3] Therefore, development of $CO_2$-redispersible latexes has attracted significant attention during the past few years.[4] In our first papers the redispersibility of the synthesized $CO_2$-switchable latexes were not investigated.[1,5] To produce redispersible latexes, the common practice is to use large amounts of protective colloid or employ a comonomer containing acid groups.[6] However theses redispersible latexes are not suitable for coating applications because surface charges are preserved during film drying. The first $CO_2$-switchable and redispersible latex, reported by Mihara et al.[7] demonstrated the capability of undergoing multiple coagulation and redispersion cycles without salt accumulation. Employing amidine-functionalized comonomer has also been reported for the preparation of $CO_2$-switchable PS latexes.[8] However in both cases, the $CO_2$-switchable group was synthesized in a multistep process. An acyclic amidine-containing comonomer, (*N*-amidino)dodecyl acrylamide, has also been employed as a $CO_2$-switchable surfactant for the preparation of reversibly coagulatable and redispersible PS latexes.[9] Unfortunately hydrolysis of the amidine group occurred during the emulsion polymerization. Zhu's group reported the preparation of redispersible PMMA latexes using a $CO_2$-switchable polymeric surfactant.[10,11] Poly(2-(dimethylamino)ethyl methacrylate)-*block*-poly(methyl methacrylate, PDMAEMA-*b*-PMMA , as a polymeric surfactant, was synthesized *via* a two-step solution reversible addition-fragmentation chain transfer (RAFT) polymerization. This surfactant was protonated by HCl before the start of the polymerization and thus at the end the reaction, the first cycle of coagulation was performed by the addition of a base. The amidine-containing initiator, VA-061 was used as both the initiator and positively charged stabilizer in the surfactant-free emulsion polymerization (SFEP) of styrene.[2] However, the solid content was low (~ 6%) and reaction time was relatively long (~ 24 h). To increase the solid content, 2-(diethylamino)ethyl methacrylate, DEAEMA, was employed as a $CO_2$-switchable comonomer in the SFEP of styrene.[12] Despite considerable progress in preparing $CO_2$-switchable latexes, two issues have not been satisfactorily addressed. First is that redispersion of aggregated latexes is often difficult, requiring high energy input such as sonication to effectively redisperse the particles. Second is that the stabilizing moieties (especially comonomers such as DEAEMA and (*N*-amidino)dodecyl acrylamide) are often prone to hydrolysis.

In this paper we report the synthesis of reversibly coagulatable and redispersible PS and PMMA latexes by SFEP under $CO_2$ atmosphere using DMAPMA, which has not previously been used to make $CO_2$-switchable latexes. DMAPMA is inexpensive, commercially available, and its tertiary amine groups are readily $CO_2$-switchable. Employing DMAPMA as a $CO_2$-switchable comonomer in the preparation of $CO_2$-switchable latexes has several advantages since this monomer has high glass transition temperature ($T_g$~96 °C), higher $pK_{aH}$ (~9.2[15]) than DEAEMA (~8.8[13]) and DMAEMA (~8.3[13]), and is hydrolytically stable. We demonstrate that $CO_2$-switchable latexes made using DMAPMA are near monodisperse, readily redispersed without requiring any high energy input due to the high $T_g$ of the DMAPMA-containing stabilizing moieties, and hydrolytically stable during polymerization. The colloidal characteristics of the resultant latexes and redispersibility of the synthesized latexes without using sonication are investigated in detail.

## 8.2 Experimental section

**Materials.** $CO_2$ and $N_2$ (Praxair, Medical grade) were used as received. 2,2'-azobis[2-(2-imidazolin-2-yl)propane] (VA-061) was purchased from Wako Pure Chemical Industries Ltd. Styrene (S, >99%), methyl methacrylate (MMA, 99%), and dimethylaminopropyl methacrylamide (DMAPMA, 99%) were purchased from Sigma Aldrich and purified by passing through columns packed with inhibitor remover (Sigma Aldrich).

**Preparation of $CO_2$-switchable PS and PMMA latexes**. In a typical experiment (exp 1 Table 8.1), DMAPMA (0.04 g, 0.24 mmol) and VA-061 (0.06 g, 0.024 mmol) were added into a flask containing deionized water (45 mL) and $CO_2$ was bubbled into the solution at room temperature for 30 min to switch on (protonate) initiator and monomer. Then, styrene (5 g, 0.05 mol) was added to the flask and $CO_2$ bubbling continued for an additional 10 min. The flask was then inserted into a preheated oil bath at 65 °C and the reaction carried out for 4 h under $CO_2$ atmosphere (Figure 8.1). Time zero of polymerization was taken at the moment that the flask was inserted into a pre-heated oil bath at 65 °C. PMMA latexes were prepared in a similar manner. The $CO_2$-switchable behaviour of DMAPMA and VA-061 is shown in Figure 8.2.

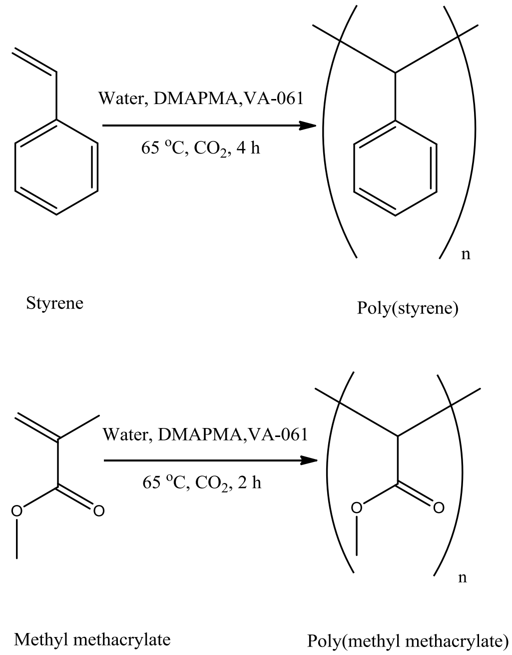


Figure 8.1 Preparation of $CO_2$-switchable polystyrene and poly(methyl methacrylate) latexes by free-radical polymerization.

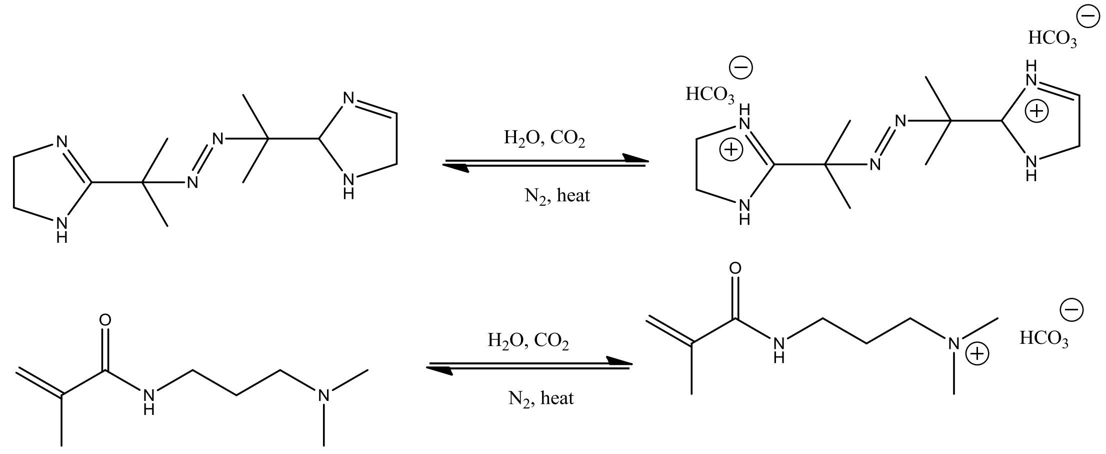


Figure 8.2 The $CO_2$-switchablity behavior of VA-061 (top) and DMAPMA (bottom).

**Characterization.** Monomer conversion was determined gravimetrically. During polymerization, 1-2 g samples were withdrawn from the reaction mixture and immersed immediately in an ice/water bath to stop polymerization and then dried under air for 2 days.

Particle size, dispersity index (*Đ*), and zeta-potential were measured using a Zetasizer Nano ZS (size range from 0.6 nm to 9 µm). Samples were diluted with carbonated, deionized water. All measurements were performed in disposable capillary cuvettes.

## 8.3 Results and discussion

### 8.3.1 DMAPMA as a $CO_2$-switchable comonomer

We previously reported the use of DEAEMA as a $CO_2$-switchable comonomer in the SFEP of styrene.[12] However, the final monomer conversion was consistently low. DMAEMA has also been used in the synthesis of $CO_2$-switchable surfactant for further use in the emulsion polymerization of MMA.[11] However, polymerizations runs under $CO_2$ atmosphere were not successful probably because of the rapid increase in the particle size and creaming of the latex.[10] Recently we investigated the hydrolytic stability of DEAEMA and showed that this monomer hydrolyses rapidly at pH higher than 7.[13] Using DEAEMA or DMAEMA for the preparation of redispersible latexes under a $CO_2$ atmosphere is challenging for two reasons: (1) hydrolysis of these monomers during polymerization; and (2) relatively low extent protonation of the tertiary amine groups under polymerization temperatures,[14] which is a consequence of comparatively low $pK_{aH}$ values compared to amidines for example. Both of these phenomena result in decreasing positive charge on the surface of the particles (charge density) and thus reduced colloidal stability and possibly aggregation. Hydrolysis of DEAEMA or DMAEMA leads to the formation of methacrylic acid-groups. The number of $CO_2$-switchable groups on the surface of the particles decreases. Furthermore, the existence of absorbed or covalently bonded acid compounds on the surface of the particles with negative charges will counter the cationic charges and may even lead to the formation of complexes, consequently further decreasing the stability of the latex particles. We hypothesized that using a hydrolytically stable monomer such as DMAPMA instead of DEAEMA or DMAEMA should lead to better colloidal stability, higher polymerization rates and final conversions and improved reversible switchability. To study the hydrolytic stability of the DMAPMA, 0.5 M solution of this monomer in water was prepared (which resulted in pH=11.5), then it was left at room temperature for 4 h and then heated at 40 and 60 ºC for 4 h at each of those temperatures. As it is shown in Figure 8.3, the corresponding peaks in the NMR spectra have not changed during the time at different temperatures, which mean DMAPMA is stable against hydrolysis at the experimental conditions of this study.

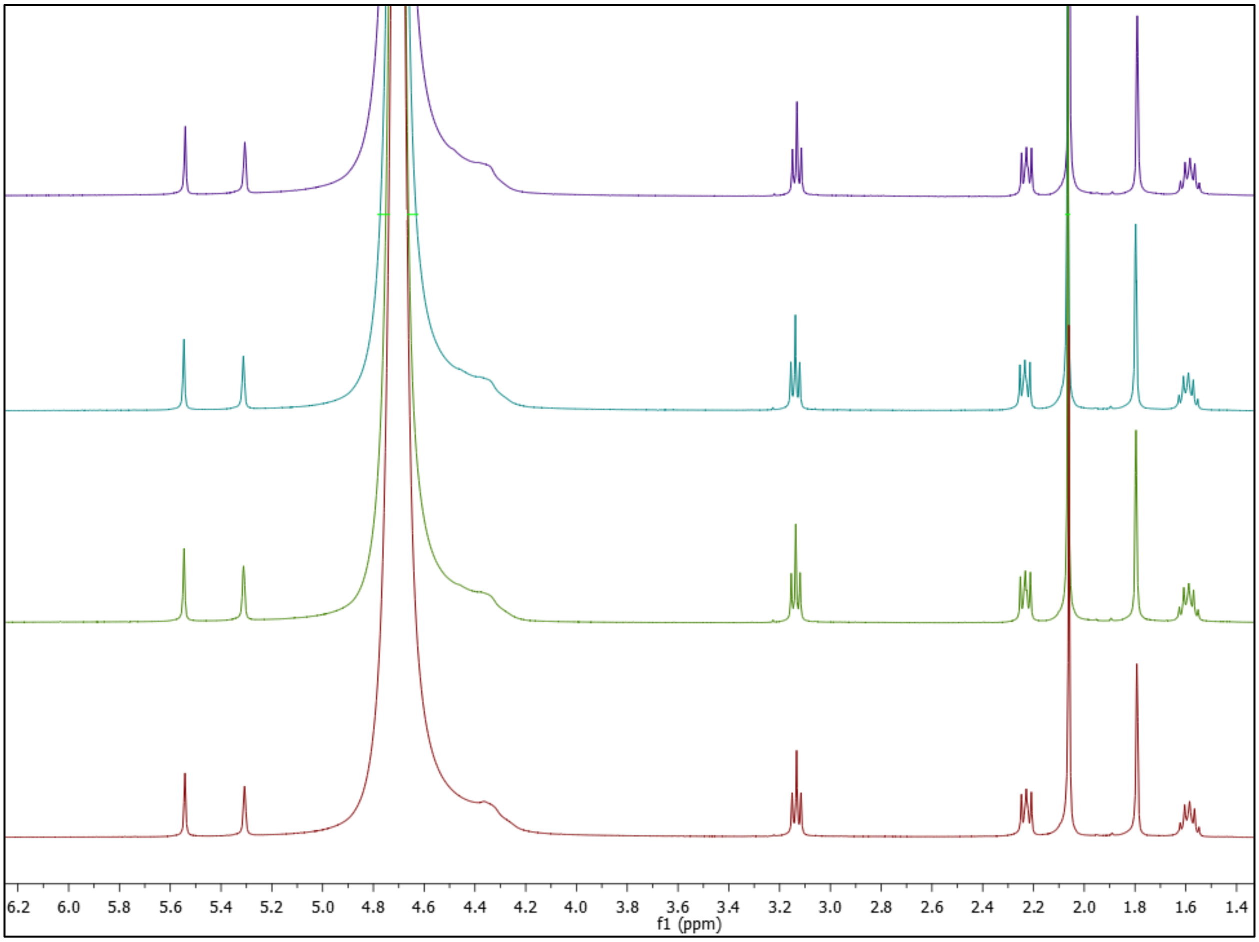


Figure 8.3 NMR spectra of the 0.5 M solution of DMAPMA in $D_2O$ solvent at different temperatures. From bottom to top: initial solution at room temperature, after 4 h at room temperature, after 4 h at 40 °C, and after 4 h at 60 °C.

DMAPMA has fairly high basicity (p$K_{aH}$=9.2[15]) and as a result remains in the protonated form under reaction conditions (Figure 8.4). To calculate the degree of protonation of the DMAPMA in our reaction conditions, three experiments were conducted. In the first experiment the solution of DMAPMA (0.5 M) was prepared and its NMR spectrum was taken as a reference (red curve in Figure 8.4). Then an equimolar solution of HCl with 10% added excess HCl was added and again the NMR was taken (green curve in Figure 8.4). Then, in a similar solution of DAMPMA (0.5 M), $CO_2$ was purged for 30 min and then the flask was inserted into a preheated oil bath at 65 °C; after 1 h heating, the last NMR was taken (purple curve in Figure 8.4). Based on analyses of these NMR spectra, the protonation efficiency (1-(Δδ/δ)) of the DMAPMA at 65 °C after 1 h heating was more than 88%, which is excellent for providing the positive charges required for stabilization of the latex particles.

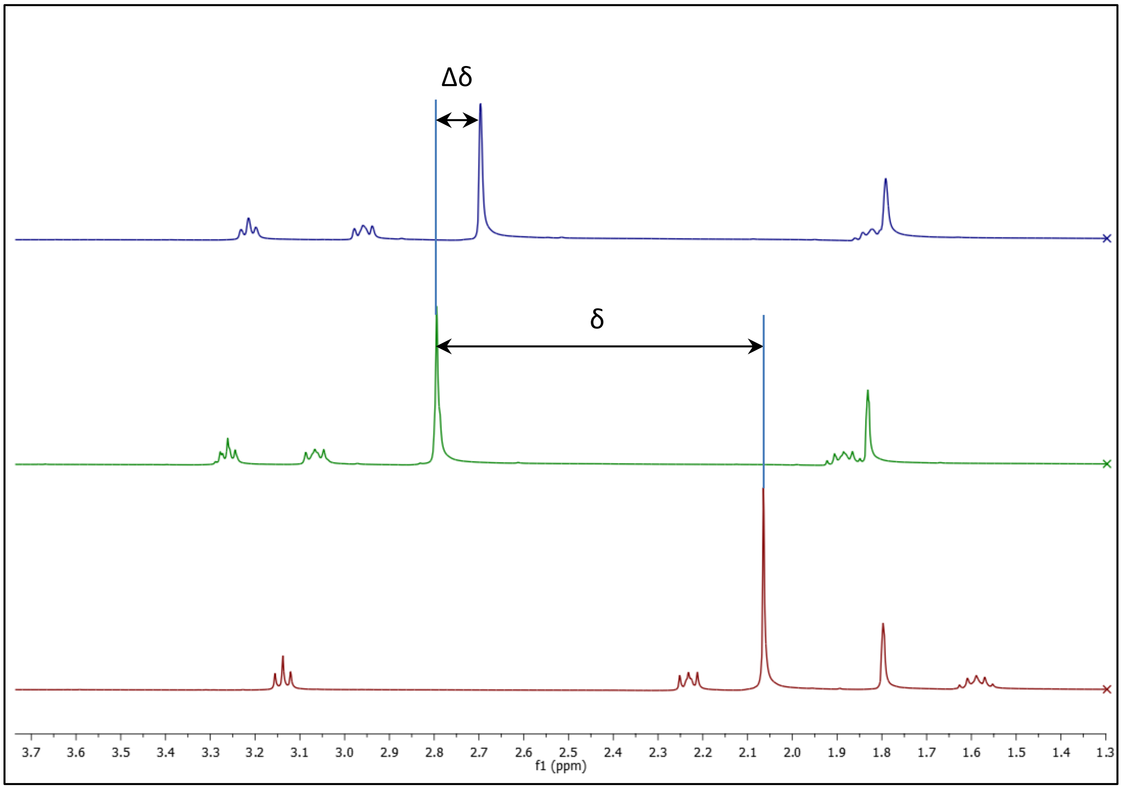


Figure 8.4 NMR spectra for the calculation of protonation efficiency of the DMAPMA under $CO_2$ purging conditions at 65 °C for 1 h; bottom spectrum: 0.5 M DMAPMA at room temperature, middle spectrum: 0.5 M DMAPMA with 10 mol% excess HCl above equimolar, and top spectrum: 0.5 DMAPMA under $CO_2$ purging at 65 °C for 1 h.

The glass transition temperature of poly(DMAPMA) ($T_g$=96 °C[16]) is also higher than poly(DEAEMA) ($T_g$=20 °C[17]) or poly(DMAEMA) ($T_g$=19 °C[18]). We hypothesized that during aggregation, the particles would effectively have a harder shell layer and consequently mutually diffusion of chains from neighbouring particles would be less likely, and as result redispersion of the latex might easily be achieved without using sonication (as is usually required for $CO_2$ switchable latexes).

### 8.3.2 Emulsion polymerization of S and MMA under $CO_2$ atmosphere

As the solubility of $CO_2$ in water decreases with increasing temperature, most tertiary amine groups belonging to DEAEMA or DMAEMA are probably converted to their neutral form during emulsion polymerization. Therefore, it is often preferable to use a strong acid such as HCl to achieve near complete protonation of these monomers to ensure that there is enough positive charge for stabilizing particles during polymerization.[11,19] However, based on the results obtained from the emulsion polymerization of styrene or MMA using DMAPMA as a $CO_2$-switchable comonomer, very stable latexes with monodisperse particle size distribution can be obtained under only $CO_2$ atmosphere (exp. 1, Table 8.1).

Table 8.1 Surfactant-free emulsion polymerization (SFEP) of S and MMA at 65 °C using DMAPMA as a $CO_2$-switchable comonomer and VA-061 as initiator.

| Exp. | M | $[VA\text{-}061]_0/[M]_0$ (% mol) | $[DMAPMA]_0/[M]_0$ (% mol) | Conversion (%) | Particle size (nm) | PDI | ζ–potential (mV) |
|---|---|---|---|---|---|---|---|
| 1 | S | 0.5 | 0.5 | 96 | 244 | 0.01 | 46 |
| 2 | MMA | 0.5 | 0.5 | 100 | 456 | 0.03 | 45 |
| 3[a] | S | 1 | 0 | 35[b] | 230 | 0.02 | 46 |
| 4 | S | 0.5 | 1 | 95 | 210 | 0.01 | 60 |

[a] In this experiment VA-044 was used instead of VA-061. [b] Conversion after 20 h.

High conversion (96 %) was attained in less than 5 h for the emulsion polymerization of styrene (Figure 8.5). We believe the primary reason for achieving high conversion in a relatively short time (compared to the situation where no $CO_2$-switchable monomer is used) is the high percentage of charged $CO_2$-switchable groups during polymerization that act as stabilizing moieties and increase the number of loci of polymerization (i.e. particles) and as a result the rate of polymerization. At similar reaction conditions (exp.2, Table 8.1), the rate of reaction for the emulsion polymerization of MMA is faster than styrene possibly due to the higher hydrophilicity of the MMA compared with styrene and consequently formation of more oligomers at the start of the reaction that are then converted to particles.

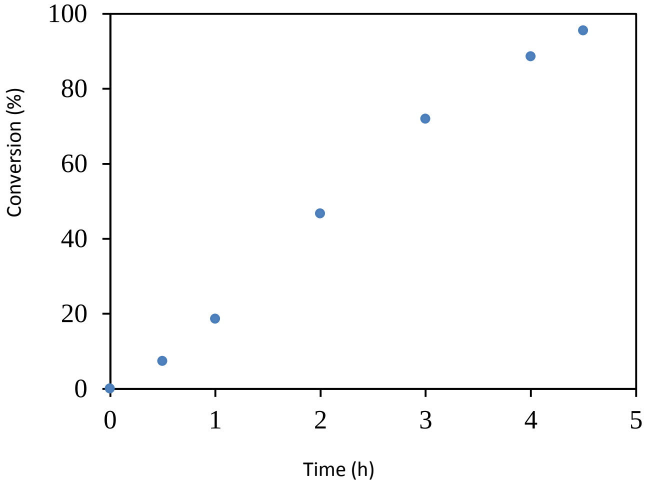


Figure 8.5 Conversion curve for emulsion polymerization of styrene at 65 $^0$C using VA-061 as initiator and DMAPMA as $CO_2$-switchable comonomer. $[VA\text{-}601]_0/[S]_0=0.005$ and $[DMAPMA]_0/[S]_0=0.005$. Weight ration of water: styrene is 5:45.

The mechanism of particle formation is based on SFEP. The main advantage of this mechanism is that no added surfactant is used in the system and positively charged polymer chains containing protonated tertiary amine groups (from DMAPMA) as well as imidazole group (from VA-061 decomposition) are chemically bounded to the surface of the latex particles. Therefore, surfactant migration does not occur during purification of the latex nor upon drying of films. After heating the reagents at the start of the reaction, the initiator begins decomposing and the resultant radicals react with the monomer present in the water phase. Since DMAPMA is a water-soluble monomer and styrene is a hydrophobic monomer, the amount of DMAPMA monomer accessible for the initiator is much higher than styrene. Therefore, the composition of the oligomers forming at the start of the reaction is expected to be mostly consist of gradient polymer chains starting with DMAPMA units and gradually continued with the addition of styrene units until they become sufficiently hydrophobic to be converted to the latex particles. To highlight the effect of the addition of the DMAPMA on the reaction, a similar reaction without using DMAPMA was performed. In this case, VA-041(1 mole %) was used and the reaction was performed under nitrogen. After 20 h, the final conversion was only 35%.

Interestingly monodisperse particles were formed in the emulsion polymerizations of both S and MMA as indicated by the low PDI obtained from DLS measurements (Table 8.1). As it can be seen in TEM images (Figure 8.6), the particles are spherical and monodisperse.

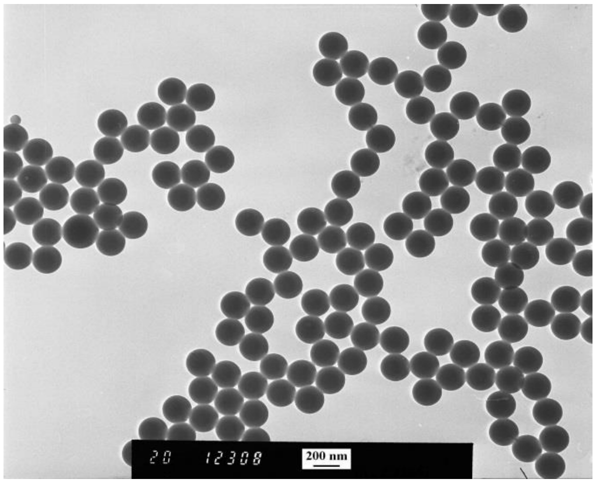


Figure 8.6 TEM image of the PS latex prepared by SFEP of styrene at 65 °C using DMAPMA as $CO_2$-switchable comonomer and VA-061 as initiator under $CO_2$ atmosphere.

To investigate the effect of the DMAPMA concentration of the colloidal properties of the latex particles, the concentration of DMAPMA was increased to 1 mol% with respect to monomer (styrene). As expected, the zeta potential of the latex increased to 60 mV because of the increase in positive charges on the surface of the latex particles. The particle size decreased from 244 nm (exp. 1, Table 8.1) to 210 nm (exp. 4, Table 8.1). Increasing DMAPMA concentration leads to an increase in the number of particles due to the increase in the loci of polymerization (more positive charges presence in the reaction medium can stabilize more particles) and therefore decreases the size of the particles. Monodispersed latex particles were again obtained as confirmed by the low PDI (0.01) from DLS measurements.

### 8.3.3 Aggregation and redispersion

When the switchable groups on $CO_2$-switchable particles are switched off, the latex particles coagulate rapidly. PS latex (exp. 1 Table 8.1) was switched off (ζ-potential close to from DLS measurements) by bubbling $N_2$ at 80 °C for 30 min. However, because of similar densities of PS and water (density of PS is 1.05 g $cm^{-3}$), settling of the PS particles took a long time and separation was difficult to achieve even with zero ζ-potential and using centrifugation at 6000 rpm. Switched off PMMA latexes could however be easily separated by centrifugation because of the greater density difference with water (density of PMMA is 1.18 g $cm^{-3}$). Even without using a centrifuge, the PMMA latexes settled after a few hours and two separated phases were clearly formed with PMMA particles at the bottom and water at the top. While coagulation typically proceeds readily, redispersion of aggregated $CO_2$-switchable particles (by switching on the stabilizing moieties *via* $CO_2$ bubbling) has often proven very difficult, typically requiring sonication if redispersion can be achieved at all (frequently it is not possible). However using DMAPMA as a comonomer, in both PS and PMMA latexes that had been coagulated were easily redispersed by bubbling $CO_2$. If latexes were dried, then sonication was also needed in addition to the $CO_2$ bubbling for redispersion. The latex prepared without using $CO_2$-switchable functional group (exp. 3, Table 8.1) could not be coagulated because the surface of the latex particles was permanently charged. Industrially, acid and /or base are added to coagulate such latexes, which results in the production of an additional wastewater stream.

## Conclusion

Monodisperse $CO_2$-switchable PS and PMMA latexes were synthesized by emulsion polymerization using a simple recipe composed of monomer and 0.5 mol% of the comonomer DMAPMA. All reactions were conducted at 65 °C under $CO_2$ atmosphere. DMAPMA was employed as a $CO_2$-switchable monomer and also acted as a surfactant, which increased the conversion and stabilization of the latex. DMAPMA is resistant to hydrolysis and thus it does not produce methacrylic acid with negative charge to make a complex with positive charges created from decomposition of the initiator. DMAPMA is hydrophilic and therefore it remains outside the particle during polymerization and positive charges are not buried inside the particles. Since the $pK_{aH}$ of the DMAPMA is higher than DEAEMA or DMAEMA, its positive charges are better preserved at high temperatures during polymerization compared with DEAEMA or DMAEMA, which leads to the higher conversion during polymerization of styrene at relatively short polymerization time. The synthesized PMMA latexes could be easily coagulated by bubbling $N_2$ and applying heat and redispersed readily by bubbling $CO_2$ without using sonication. While facile redispersion of PS latexes were also achievable by only bubbling $CO_2$, coagulation of them were challenging probably because of the close density of the PS to water. However, if the PS latex in the switched off for (zero zeta potential) remains for a few days, it will be coagulated. For styrene polymerization, the reaction reached to near full conversion at relatively short times (~ 5 h).

## References

(1) Liu, Y. Jessop, P. G.; Cunningham, M. F.; Eckert, C. A.; Liotta, C. L. *Science*, **2006**, 313, 958-960.

(2) Su, X.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 666-670.

(3) Jessop, P. G.; Mercer, S. M.; Heldebrant, D. *J. Energy & Environmental Science* **2012**, 5, 7240.

(4) Lin, S.; Theato, P. *Macromol. Rapid. Commun*. **2013**, 1118-1133.

(5) Fowler, C. I.; Muchemu, C. M.; Miller, R. E.; Phan, L.; O'Neill, C.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2011**, 44, 2501-2509.

(6) Shirin-Abadi, A. R.; Darabi, A.; Jessop, P. G.; Cunningham, M. F. *Polymer* **2015**, 60, 1-8.

(7) Mihara, M.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2011**, 44, 3688-3693.

(8) Zhang, Q.; Wang, W. L.; Lu, Y.; Li, B. G.; Zhu, S. *Macromolecules* **2011**, 44, 6539-6545.

(9) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Langmuir* **2012**, 28, 5940-5946.

(10) Zhang, Q.; Yu, G.; Wang, W. J.; Li, B. G.; Zhu, S. *Macromol. Rapid. Commun*. **2012**, 33, 916-921.

(11) Zhang, Q.; Yu, G.; Wang, W.; Yuan, H.; Li, B.; Zhu, S. *Macromolecules* 2013, 46, 1261-1267.

(12) Pinaud, J.; Kowal, E.; Cunningham, M. F.; Jessop, P. G. *ACS Macro Lett*. **2012**, 1, 1103-1107.

(13) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2015**, 48, 72-80.

(14) Fowler, C. I.; Jessop, P. G.; Cunningham, M. F. *Macromolecules* **2012**, 45, 2955-2962.

(15) Wetering, P. Van De.; Moret, E. E.; Schuurmans-nieuwenbroek, N. M. E.; Steenbergen, M. J. Van.; Hennink, W. E. *Insight* **1999**, 589-597.

(16) Cited, R. *Hydrophilic Ampholytic Polymer*. US Patent, US 6,361, 768 B1, 2003.

(17) BASF Technical Information for DEAEMA available at: http://www.specialty-monomers.basf.com/portal/streamer?fid=235727

(18) BASF Technical Information for DMAEMA available at: http://www.specialty-monomers.basf.com/portal/streamer?fid=235729

(19) Darabi, A.; Shirin-Abadi, A. R.; Jessop, P. G.; Pinaud, J.; Cunningham, M. F. *Polym. Chem*., **2014**, 5, 6163-6170.

## Chapter 9

# Conclusion and recommendations for future work

### 8.1. Conclusions

Conducting polymerization reactions in water is appealing due to several advantages in using water as a solvent including biocompatibility, availability, low price, and safey. However, performing controlled/living radical polymerization specifically nitroxide-mediated polymerization (NMP) in water is challenging because of the polarity of the water which affects the behaviour of the nitroxide. NMP of methacrylate monomers is also difficult because of the disproportionation reaction (H-transfer )between nitroxide and growing radicals or a too large activation-deactivation equilibrium constant (high concentratuion of propagating radicals and as a result irreversible termination). 2-(diethylamino)ethyl methacrylate is a methacrylate-based pH-sensitive and $CO_2$-switchable monomer, which hase been used in several studies for the preparation of $CO_2$-responsive polymers. Poly(ethylene glycol)methyl ether methacrylate (PEGMA) is another methacrylate-based monoemer, which has been used frequently in the PEGylation process.

In this Ph.D. reseach project, the NMP of DEAEMA and PEGMA was succefully performed in water for the first time. In both cases a few mole percent of styrene or acrylonitrile was employed to get control and livingness in the final polymer. After synthezing poly(DEAEMA-*co*-S), it was used in the protonated form as both macroinitiator and stabilizer in the preparation of PMMA latex nanoparticles. It was shown that poly(DEAEMA-*co*-S), synthesized in bulk, is an effective stabilizer for preparting latex by surfactant-free emulsion polymerization of MMA. Utilizing NHS-BlocBuilder leads to the formation of a living macroinitiator that is able to initiate the polymerization of MMA. However, polymerizing DEAEMA in water is not possible due to fast hydrolysis of this monomer in aqueous solution at pH higher than 7. Therefore, to achieve control and living radical polymerization of DEAEMA in water, it is important to reduce the pH to the values lower than the p$K_a$ of this monomer in order to protect the tertiary amine group. In this situation it is also possible to polymerize DEAEMA in water, which creats an interetsing option for the preparation of PMMA latexes in a one-pot two step process. In this process, first , DEAEMA in the presence of a few mole percent comonomer such as acrylonitrile is polymerized in water and then at high conversions MMA monomer is added to the same pot to produce PMMA latex. It wa shown that VA-044 (water-soluble initiator) and SG1 (nitroxide) are an ideal initiating system for polymerization of DEAEMA in water. Using NHS-BlocBuilder as a monocomponent initiating system also resulted in a polymerization with good control and livingness as evidened by the kinetic plots and GPC curves. To understand the role of the positive charges of initiator radicals produced for decomposition of VA-044, emulsion polymerization of styrene and/or MMA was performed in surfactant-free mode using VA-044 as both initiator and stabilizer. It was shown that VA-044 is a very effective stabilzer and latexes with close to 20 % soilds content could be produced without coagulation.

PEGMA as another methacrylated-based monomer was also polymerized in water by NMP for the first time in water. Using the similar initiating system (SG1 as nitroxide and VA-044 as initiaor), and employing a few mole percent of styrene resulted in a controlled/living radical polymerization. The synthesized poly(PEGMA-*co*-S) was then employed in the PEGylation of chitosan in water by both *grafting to* and *grafting from* approaches.

When DEAEMA is used as a $CO_2$-responsive comonomer in the preparation of $CO_2$-swicthable latex, polymeric nanoparticles are not redispersible after coagulation probably due to the low Tg of DEAEMA and diffusion of the shell of the particles into each other. To address this problem and also the hydrolysis issue, dimethylaminopropyl methacrylamide (DMAPMA) was employed in the preparation of $CO_2$-swictahble latexes under $CO_2$ atmosphere in a surfactant-free emulsion polymerization (SFEP). This mononer is hydrolitically stable and also with higher $pK_a$ than DEAEMA stays mostly in its protonated form at the high temperatures required for polymerization. The $T_g$ of this monomer is also close to the Tg of styrene and therefore latex nanoprticles comprised of PS core and PDMAPMA shell are redispersible after coagulation by bubbling $CO_2$.

## 8.2. Recommendations for future work

Based on many different experiments that were performed by NMP in this research project, it seems that synthesizing low temperature nitroxides is still the main challenge for many applications specifically preparing $CO_2$-switchable latexes under $CO_2$ atmosphere.

Increasing $CO_2$ pressure can increase $CO_2$ solubility and reduce pH, which could be helpful in the preparation of $CO_2$-switchable latexes under a $CO_2$ atmosphere. Based on the promising results obtained for free-radical emulsion polymerization of DMAPMA for the preparation of $CO_2$-switchable latexes, it is recommended that this monomer is also tested for the preparation of $CO_2$-switchable latexes by NMP under $CO_2$ atmosphere. Because of the higher pKa of

DMAPMA than DEAEMA, this monomer and the corresponding polymer remains more in the protonated form at high temperature than dos DEAEMA, which it means there would be fewer problems in terms of the stability of the latex particles during surfactant-free emulsion polymerization.

It is recommended that if a $CO_2$-switchable polymer is to made by NMP, polymerization is performed under $N_2$ atmosphere in bulk or solution and then the final product is used as a $CO_2$-switchable material. In this case there is no concern about $CO_2$-solubility or other side reactions in the aqueous phase.

I think the most important work that could be done for the future work in the area of $CO_2$-switchability is trying to expand the application of $CO_2$-switchable materials. From a synthetic point of view, it seems that they can be made by very different methods including controlled/living radical polymerization or free radical polymerization, but in terms of the application, there are many opportunities such as water-treatment, biomedical applications, $CO_2$-capture, sensors, and hydrogels.

## Appendix A

# Hydrolysis of DEAEMA

Due to hydrolysis, DEAEMA is decomposed to methacrylic acid and dimethylaminoethanol (Figure S1).

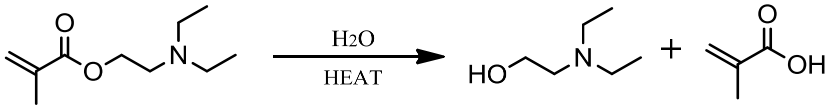


Figure S1. Hydrolysis of 2-(diethylamino) ethyl methacrylate (DEAEMA)

For investigating the effect of pH on the hydrolysis of DEAEMA, three samples were prepared with the same concentration of DEAEMA in water (1 mol $L^{-1}$). The pH of the samples was adjusted to 9, 8, and 7, respectively. The samples were placed into a preheated oil bath at 90 °C for 2 h. The same experiment was repeated at 80 °C. $^1$H NMR spectra were recorded every 15 min during and also at the start the experiment. Figure S1 shows the effect of pH and temperature on the rate of DEAEMA hydrolysis.

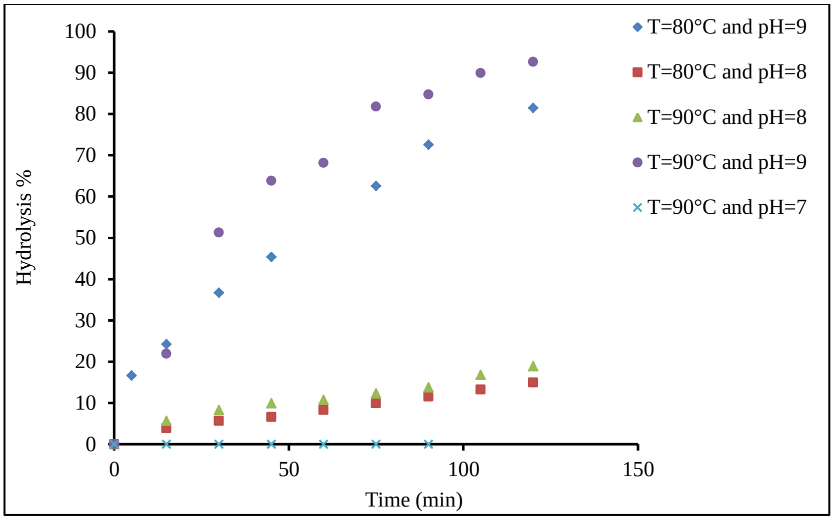


Figure S2. DEAEMA hydrolysis in water (1 M solution) with varying pH and temperature.

BY knowing the initial concentration of DEAEMA and the ratio of characteristic peaks of DEAEMA and methacrylic acid, the hydrolysis percentage can be easily calculated. Figures S2 and S3 show the selected view of the $^1$H NMR of DEAEMA in $D_2O$ at 90 $^o$C at pH 7 and 9, respectively.

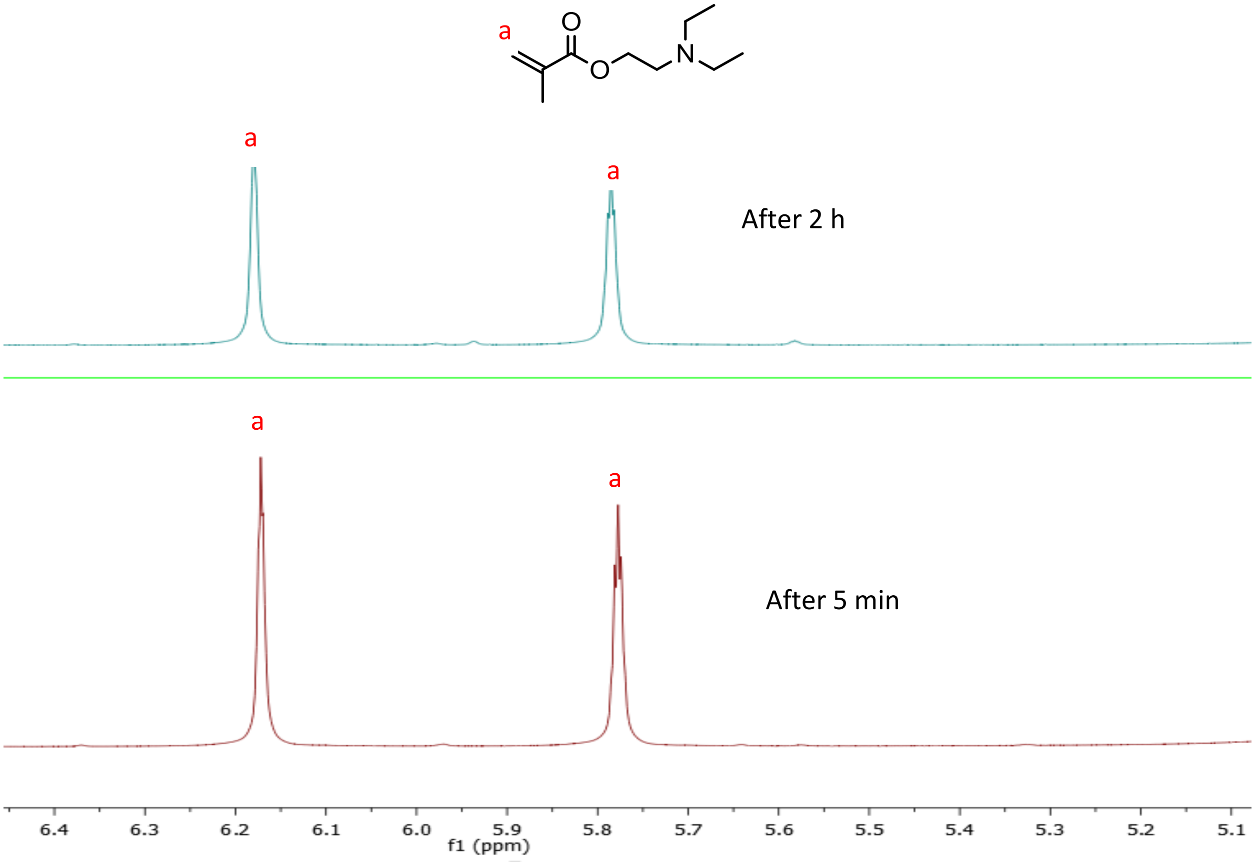


Figure S3. Selected view of the $^1$H NMR spectra of DEAEMA in $D_2O$ at pH=7 and T=90 °C.

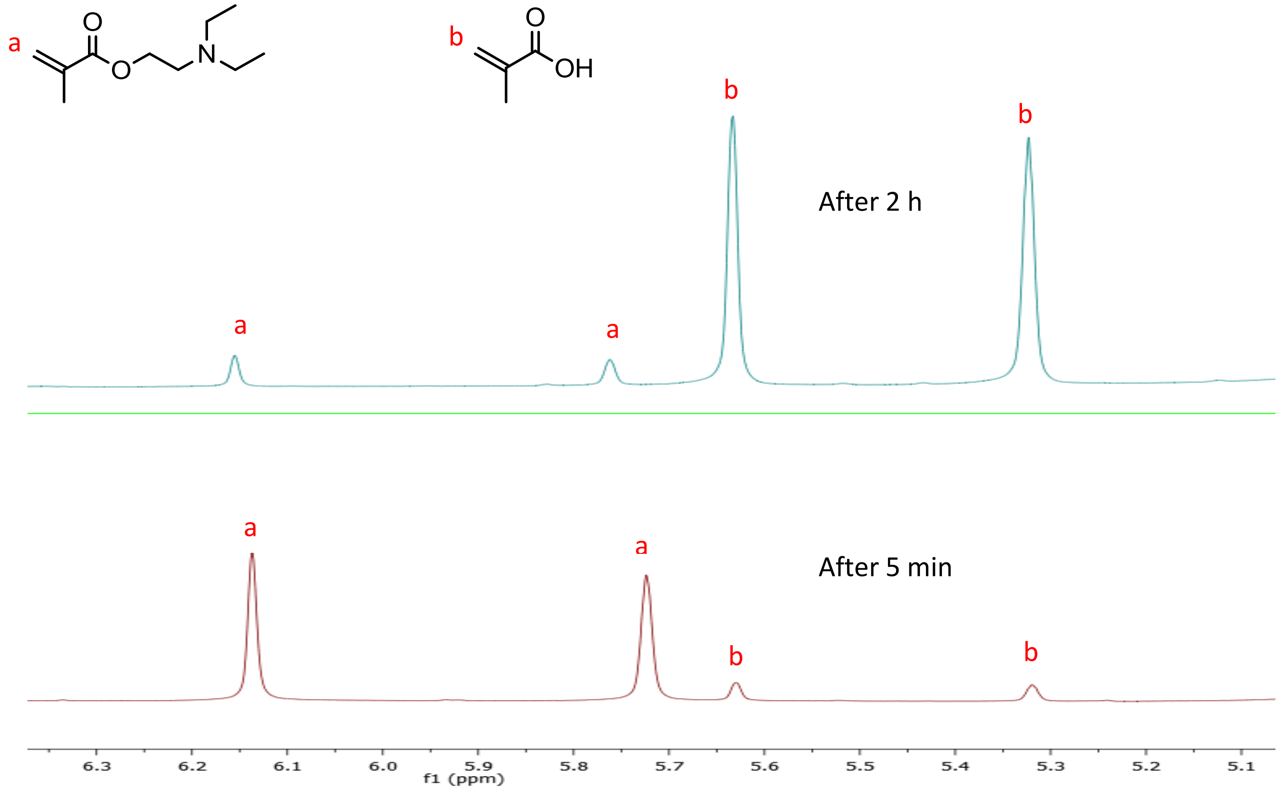


Figure S3. Selected view of the $^1$H NMR spectra of DEAEMA in $D_2O$ at pH=9 and T=90 °C.