Norges miljø- og biovitenskapelige universitet
Fakultet for Veterinærmedisin og biovitenskap
Institutt for Kjemi, bioteknologi og matvitenskap

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Microporous polymer beads for chemical decontamination of organophosphorus nerve agents

Mikroporøse polymerkuler for kjemisk dekontaminering av organofosfatstridsmidler

Anette Kallekleiv Valle

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Abstract

The objective of the work presented in this thesis was the development of reactive polymer beads for use as decontaminants of organophosphorus nerve agents. The physiological mode of action of nerve agents, which is the cause of their high toxicity, is the ability to bind and inhibit the enzyme acetylcholinesterase (AChE). As organophosphorus nerve agents easily reach the active site of AChE and inhibit the enzyme, it was hoped that effective polymeric decontaminants could be prepared by mimicking the structural and functional characteristics of AChE.

In the present study, a suspension polymerization method suitable for polymerization of water-soluble monomers was developed for copolymerization of methyl acrylate and styrene. This method was used for the synthesis of cross-linked poly(methyl acrylate-*co*-styrene) beads. The established suspension polymerization technique was developed further by incorporation of acid-scavenging monomers into the polymer structure, more specifically 4-vinylpyridine and *N*-[3-(dimethylamino)propyl]methacrylamide (DMAPMA), entities which were believed to be capable of binding toxic byproducts formed during decontamination. Synthesized polymer products containing these monomers included cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) and poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads. However, due to low incorporation of DMAPMA and low yields, only cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads were used in further studies as these gave both high incorporation of monomers and consistent, high yields.

The cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) products were further functionalized with hydroxylamine to convert methyl acrylate moieties to the corresponding hydroxamate anion of hydroxamic acid. In the functionalized product, styrene constitutes the hydrophobic part of the polymer network, contributing to increased affinity of the reactive polymer beads towards the hydrophobic, organophosphorus nerve agents. The converted hydroxamate anions facilitate solvation of the polymer network in aqueous environments, in addition to providing nucleophilic functionalities capable of hydrolyzing the organophosphorus nerve agents. Successful conversion was confirmed by CHN analysis and IR spectroscopy.

Sammendrag

Formålet med arbeidet presentert i denne avhandlingen var utviklingen av reaktive polymerkuler for dekontaminering av organofosfatstridsmidler. Den fysiologiske funksjonen av organofosfatstridsmidler, årsaken til den høye toksisit, er deres evne til å binde og inhibere enzymet acetylcholinesterase (AChE). Det aktive setet i AChE er lett tilgjengelig for organofosfatstridsmidler og gjør det mulig for slike nervegasser å inhibere enzymet. På grunn av dette var det ønskelig å undersøke om effektive dekontamineringsmiddel, basert på polymerer, kunne fremstilles ved å etterligne strukturelle og funksjonelle kjennetegn ved AChE.

I dette studiet ble en suspensjonspolymeriseringsmetode for polymerisering av vannløselige monomerer utviklet og brukt i copolymerisering av metylakrylat og styren. Denne metoden ble bruk for syntese av kryssbundne poly(metylakrylat-*co*-styren)-kuler. Denne suspensjonspolymeriseringsmetoden ble utviklet videre ved å inkorporere andre funksjonelle monomerer i polymerstrukturen, nærmere bestemt 4-vinylpyridin og *N*-[3-(dimethylamino)propyl]metakrylamid (DMAPMA), monomerer som kan binde toksiske biprodukter som kan dannes gjennom dekontaminering. De syntetiserte polymerkulene med slike monomerer var kryssbundne poly(metylakrylat-*co*-4-vinylpyridin) og poly(metylakrylat-*co*-styren-*co*-DMAPMA)-kuler. På grunn av lav inkorporeringsgrad av DMAPMA og dårlig utbytte ved syntese av kryssbundne poly(metylakrylat-*co*-styrene-*co*-DMAPMA), ble bare kryssbundne poly(metylakrylat-*co*-styren) og poly(metylakrylat-*co*-4-vinylpyridin)-kuler brukt i videre forsøk da disse gav både en høy inkorporeringsgrad av monomerer og jevnt høyt utbytte.

Kryssbundne poly(metylakrylat-*co*-styren) og poly(metylakrylat-*co*-4-vinylpyridin)-kuler ble videre funksjonalisert ved bruk av hydroksylamin for å oppnå omgjøring av metylakrylatenhetene til det korresponderende hydroksamatanionet av hydroksaminsyre. I de funksjonaliserte produktene utgjør styren den hydrofobe delen av polymernettverket, og bidrar til affinitet mellom de reaktive polymerkulene og de hydrofobe organofosfatstridsmidlene. De konverterte hydroksamatanionene vil bidra til solvatisering av polymernettverket i vandig miljø, i tillegg til å bidra med en nukleofil funksjonalitet som kan hydrolysere nervegasser. Vellykket omgjøring til hydroksamatanioner ble påvist ved bruk av CHN-analyse og IR spektroskopi.

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Abbreviations

ACh	Acetylcholine
AChE	Acetylcholinesterase
ACVA	4,4′-Azobis(4-cyannovaleric acid)
AIBA	2,2′-Azobis(isobutyramidine hydrochloride)
AIBN	2,2′-Azobis(2-methylpropionitrile)
AMBN	2,2’-azobis(2-methylbutyronitrile)
BPO	Benzoyl peroxide
CWA	Chemical Warfare agent
DOP	Dioctanoyl peroxide
DMAPMA	*N*-[3-(Dimethylamino) propyl] methacrylamide
DVB	Divinylbenzene
EA	Ethyl acrylate
EGDMA	Ethylene glycol dimethacrylate
eq	Equivalent
GA	Ethyl *N*,*N*-Dimethylphosphoramidocyanidate (Tabun)
GB	Propan-2-yl methylphosphonofluoridate (Sarin)
GD	3,3-Dimethylbutan-2-yl methylphosphonofluoridate (Soman)
GF	Cyclohexyl methylphoshonofluoridate (Cyclosarin)
h	Hours
HDODA	1,6-Hexanediol diacrylate
HEC	2-Hydroxyethyl cellulose
HPMC	Hydroxypropyl methyl cellulose
IR	Infrared spectroscopy
MA	Methyl acrylate

Me	Methyl
mmol	Millimol
HRMAS	High-resolution magic angle spinning
NMR	Nuclear magnetic resonance
PVA	Poly (vinyl alcohol)
rpm	Revolutions per minute
THF	Tetrahydrofuran
VE	(*S*-(Diethylamino)ethyl *O*-ethyl ethylphosphonothioate)
VG	*O*,*O*-diethyl *S*-[2-(diethylamino)ethyl]phosphorothioate
VM	*S*-[2-(Diethylamino)ethyl] *O*-ethyl methylphosphonothioate
VR	*N*,*N*-diethyl-2-(methyl-(2-methylpropoxy)phosphoryl)sulfanylethanamine
VX	*O*-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothioate
WWI	World War I
WWII	World War II

Glossary of terms:

Chemical warfare agents: Chemical warfare agents are toxic chemical used as weapons to cause death, temporary incapacitation or permanent harm to individuals.

Decontamination: Decontamination is the removal of toxic chemicals from a contaminated area. Decontamination can either be accomplished through physical or chemical decontamination methods.

Dispersion polymerization: Dispersion polymerization is a heterogeneous polymerization method where the monomer(s) and initiator are completely soluble in the continuous phase, whereas the polymer is not. Polymers precipitate during polymerization, and further polymerization occurs in the precipitated particles by continuous absorption of monomers.

Emulsion polymerization: Emulsion polymerization is a heterogeneous polymerization method where the monomer is slightly soluble in the continuous phase. The monomer is dispersed in the continuous phase and stabilized as emulsion droplets and micelles by the use of emulsifiers. The initiator is soluble in the continuous phase. Polymerization is initiated in the continuous phase and propagated in the micelles.

Free radical polymerization: Free radical polymerization is a polymerization method where the reaction is initiated by free radicals.

Macroporous polymer beads: Macroporous polymer beads are polymer beads having large pores (usually >50 nm). The polymer beads contain a high degree of cross-linking to retain the porous structure.

Microporous polymer beads: Microporous polymer beads, or gel beads, are polymer beads having small pores (usually <2 nm). The polymer beads contain low degrees of cross-linking, which enables the polymer structure to solvate in appropriate solvents.

Phase-separation inhibitor: A phase-separation inhibitor is an inert solvent used in certain suspension polymerizations for preparation of microporous polymer beads. The phase-separation inhibitor is a good solvent for both the monomers and the polymer product.

Suspension polymerization: Suspension polymerization is a heterogeneous polymerization method where the monomer(s) and initiators are slightly soluble or insoluble in the continuous phase. The monomer(s) and initiator are suspended as droplets in the continuous phase by agitation. Polymerization is initiated and propagation occurs in the droplets, finally giving polymer beads.

1. Introduction

This thesis was carried out during the time period from August 2013 to May 2014 at the Norwegian Defense Research Establishment (Forsvarets forskningsinstitutt, FFI), Land Systems Division, at the group for Energetic Materials and Rocket Motor Propulsion Technology. The thesis was assigned by Tor Erik Kristensen and was carried out as collaboration between the group for Energetic Materials and Rocket Motor Propulsion Technology and the group for Chemical Warfare Agents. The latter group deals with issues concerning protection and preparedness against chemical warfare agents, which has been brought in focus by the resent use of nerve agents in Syria (29 August 2013).

The first nerve agent (tabun) was discovered as a result of a project on synthetic insecticides initiated by the German industrial scientist Gerhard Schrader in 1934. In 1936, Schrader discovered an organophosphorus compound exceedingly toxic to humans, as well as to insects. This discovery led to the synthesis of more than 2000 compounds, including the G-series of nerve agents. Again, in the 1950s, research on organophosphorus insecticides led to the discovery of a second group of nerve agents known as the V-series. Nerve agents have had a dominant role among chemical warfare agents since WWII, and are considered as the most potent chemical warfare agents ever developed. Due to the high toxicity of organophosphorus nerve agents, much research has been focused on appropriate decontamination systems. Several systems for decontamination exist, but many are corrosive and require continual rinsing to prevent degradation of surfaces. Because of this, the objective of this thesis was to synthesize an effective and non-corrosive decontamination system based reactive polymer beads.

The structure and reactive functionalities of the polymeric decontamination system were inspired by the mode of functional of the enzyme acetylcholinesterase (AChE). As organophosphorus nerve agents easily reaches the active site of AChE and inhibits the enzyme, it was hoped that effective polymeric decontaminants could be prepared by mimicking the structural and functional characteristics of AChE. Because possible contamination with nerve agents is most likely to occur in an aqueous environment, it was important for the polymer product to be microporous beads containing hydrophilic groups, while at the same time, the polymer beads should contain hydrophobic groups to ensure good affinity toward the nerve agents. To obtain such polymer products mimicking the structural characteristics and function of acetylcholinesterase, suitable monomers had to be found and

copolymerized through appropriate polymerization techniques. Methyl acrylate was chosen for its active ester moiety suitable for functionalization, and styrene was chosen for its chemical stability and hydrophobic properties. A suspension polymerization in brine was developed for the copolymerization of methyl acrylate and styrene due to the water-solubility of methyl acrylate. When a suitable suspension polymerization method had been established, acid-scavenging monomers contributing to binding of the decontamination byproducts was incorporated into the polymer structure.

The obtained polymer beads were further functionalized through conversion of methyl acrylate into the corresponding anion of hydroxamic acid. The hydroxamate anion was chosen as the reactive moiety of the decontamination product due to its high reactivity toward organophosphorus nerve agent and structural similarity to the active site of AChE. The conversion of methyl acrylate through reaction with hydroxylamine proved more difficult than expected, and several different procedures were developed before the polymer beads were successfully functionalized. The functionalized polymer beads were further analyzed using available methods, such as microscopy, element analysis and FTIR. Analysis of the hydrolysis of nerve agents, specifically of soman, by the polymer product was planned. However, such analysis was not carried out due to the short time period of the work presented in this thesis.

2. Theoretical background

2.1 Chemical warfare agents

2.1.1 History of chemical warfare agents

The use of chemical warfare agents (CWAs) can be documented throughout the Middle Ages and Renaissance, but the modern use of chemical warfare began in the early twentieth century during World War I (WWI) when German military forces released large amounts of chlorine on 22 April 1915 at Ypres, Belgium. This event marked the beginning of increasing efforts to develop more effective and potent chemical warfare agents [1,2]. Most of the initial chemical warfare agents used in WWI were chemicals with an existing industrial application like chlorine, phosgene and hydrogen cyanide. The toxicological effects of these chemicals were mostly discovered in the nineteenth century during the rapid advances in the chemical industry. These advances also lead to potential large-scale production of hazardous chemicals for military use in combat [1]. Chemical warfare agents were believed to be superior to explosives, bullets, and fragmentation on the battlefield in many situations, and the objective was to develop more portent and efficient agents for such situations [3]. Sulfur mustard (1,1'-thiobis[2-chloroethane]) was the first chemical warfare agent developed explicitly for use in warfare and which had no civilian applications. The first effective use of sulfur mustard was by the German army near Ypres, Belgium in 1917. Thereafter, chemical warfare agents were used extensively throughout WWI [3,4].

After World War I, significant efforts to develop new chemical warfare agents with higher efficiency continued and resulted in the development of the nerve agents. The nerve agents were discovered as a result of a project on synthetic insecticides initiated in 1934 by the German chemist Gerhard Schrader (1903–1990) at Bayer's division at IG Farben [5]. Through his research focused on organophosphorus compounds, Schrader discovered several effective insecticides (*e.g.* parathion). In 1936, Schrader discovered an organophosphorus compound exceedingly toxic to humans, as well as to insects. This chemical would later be named tabun or GA. As required by the German law at the time, Schrader sent a sample to the chemical weapons section of the German military in 1937. Soon after, the research and patent application were classified as secret, and further investigations of tabun and other organophosphate compounds were ordered [3,6]. This research led to the synthesis of more than 2000 compounds. Among them, about 200 were categorized as secret agents, including sarin, tabun and soman (Figure 2.1) [1,4]. These first nerve agents, discovered during WWII

were called G-agents (German agents). Large quantities of nerve agents were produced during WWII, yet nerve agents were never used by the German military during that conflict. The research on organophosphorus compounds by the Germans was successfully concealed from the Allies throughout WWII. At the end of WWII, the allies recovered weapons containing nerve agents, something that lead to further research into nerve agents by the USA and England [3,5].

Based on Schrader's research on organophosphates, Ranajit Ghosh, a chemist at Imperial Chemical Industries (ICI), synthesized a class of organophosphorus compounds with choline esters. Studies on the same compounds were performed by Schrader at IG Farben and Lars-Erik Tammelin (1923-1991) at the Swedish chemical warfare laboratories almost at the same time [7,8]. As they were found to be effective insecticides, one of them were put on the market by ICI under the trade name Amiton in 1954. The compound was soon withdrawn due to high toxicity and samples were sent to the British Armed Forces. This resulted in the discovery of several toxic compounds known as the V-agents (V stands for Victory, Venomous, or Viscous). The G-agents had attracted much interest for several reasons, but two of their properties were especially important as they increased the potential utility of chemical weapons enormously. The first was their high toxicity and ease of dissemination, which meant small doses of G-agents could be lethal. The second was their rapid physiological effect once inhaled, and also the lethal dose, which was significantly lower compared to agents previously available. Many of these properties were emphasized with the discovery of V-agents. The V-agents were rapidly lethal through inhalation, as the G-agents, but they were also rapid-acting through skin. Their high stability meant that they were persistent ground contaminates, greatly exciding sulfur mustard in efficiency [3]. The most well-known members of the V-agents are VE, VG, VM, VR and VX (Figure 2.2). VX was chosen as the most promising of this group, and seems to be the most effective CWA ever developed [1].

For as long as chemical warfare agents have been used, international agreements have been negotiated in order to limit use and production. The Geneva protocol for «the Prohibition of the Use in War of Asphyxiating, Poisonous or other Gases, and of Bacteriological Methods of Warfare» was signed in 1925, and entered into force in 1928 [9]. The protocol can be understood as a general prohibition on the use of chemical and biological weapons; however, it does not prohibit production, storage or transfer. In 1993, the chemical weapons convention (CWC) was opened for signatures; the CWC remained open until it entered into force on 29

April 1997 [9,10]. Unlike the Geneva protocol, the CWC also prohibits production, storage and transfer of chemical warfare agents. The parties of the convention are obligated to prohibit the production and use of chemical weapons, as well as reducing their stockpiles. Nevertheless, CWAs have been used in several conflicts; both by military forces and terrorist organizations. The most recent event was the use of the nerve agent sarin in Syria on 29 August 2013. CWAs might also be considered an ideal choice for many terrorist organizations as they are cheap, easy to transports and can readily be synthesized by a skilled chemist [4].

2.1.2 Classification of chemical warfare agents

Chemical warfare agents are defined by the CWC as toxic chemicals, which further can be defined as chemicals that cause death, temporary incapacitation or permanent harm to humans or animals through their chemical actions. However, not all toxic chemicals can be defined as CWAs; several distinct properties are required for this definition. One of these properties is the ability of the chemical to penetrate the body; either through skin or by inhalation. They should also have high toxicity, be chemically stable, and the production should be easy and inexpensive [4,10].

Several systems exist for the classification of CWAs, including classification by physical properties, toxicological effects or physiological effects. The most common classification of CWAs is based on their physiological effects on exposed individuals. Based on these properties, the CWAs can be organized into four categories: choking, blood, blister and nerve agents [4]. Choking agents injure the respiratory tract through inhalation of vapor or aerosols. One of the best known among this group is chlorine and phosgene [11]. Blood agents affect bodily functions by absorption into the blood, this occurs through inhalation or ingestion. Their toxic effect is caused by interruption of the electron transport chain in the inner membranes of the mitochondria or by inhibition of specific enzymes responsible for oxygen utilization and cell respiration. One of the main agents in this group is hydrogen cyanide (HCN). Agents classified as choking and blood agents were used during WWI and are often conventional industrial chemicals. Most of these agents have little importance in modern military scenarios [4].

Blister agents form one of the most common groups of CWAs and were extensively used during WWI. The group gets their name from the severe injuries, resembling burns and blisters, on the skin of exposed individuals. The intended function of these chemicals in

warfare is primarily to injure rather than kill, but exposure can be fatal in some cases [12]. Due to their chemical properties, blister agents are readily absorbed by skin, eyes, lungs, mucous membranes and blood-forming organs. The blister agent with the highest military significance is sulfur mustard. The fourth and most deadly group of CWAs is the nerve agents.

2.2 Nerve agents

Since WWII, nerve agents have had a dominant role among chemical warfare agents and are considered the most potent chemical warfare agents ever developed [13]. Due to different chemical and physical properties, nerve agents are usually divided into two subclasses: G-agents and V-agents. All nerve agents are organophosphorus compounds, with a general structure consisting of a tetrasubstituted phosphorus atom linked to oxygen by a double bond, a leaving group and two varying substituents. One of the chemical differences between G- and V-agents can be seen at the leaving groups. G-agents have fluorine or cyanide leaving groups (Figure 2.1), while V-agents possess a thiocholine-type leaving group (Figure 2.2) [5, 14]. The most common agents in the G-series are tabun (GA), soman (GD), sarin (GB) and cyclosarin (GF), while VX is the most studied among the V-agents.

In pure state, all nerve agents are colorless liquids with varying water solubility, but they can be dispersed as liquids, vapors or aerosols. Physical properties like volatility and persistency vary widely. Volatility is the tendency of a substance to vaporize; this is directly related to the vapor pressure of the substance. Persistency relates the ability of a substance to remain in the environment in an unchanged form; this is dependent on low water-solubility, low volatility and resistance to hydrolysis. The potential of exposure increases with persistency. G-agents are generally volatile liquids and therefore non-persistent; the main route of exposure is therefore inhalation. V-agents are more stable versions of G-agents with more lipophilic substituents; hence they are typically less volatile, more persistent and act through direct skin contact. They can remain in the environment up to several weeks after release and are mainly a liquid contact hazard. Among the nerve agents, sarin (GB) is the most volatile and VX the most persistent, the other nerve agents can be placed somewhere between these [13].

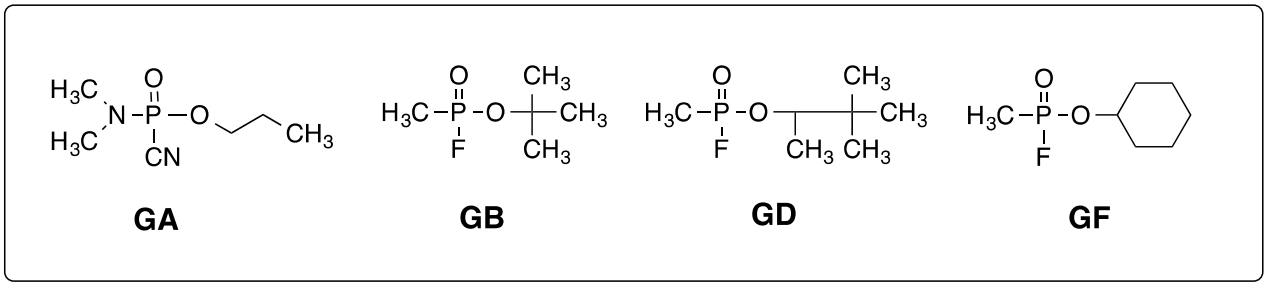


Figure 2.1: Structure of most common G-agents: tabun (GA), soman (GD), sarin (GB) and cyclosarin (GF).

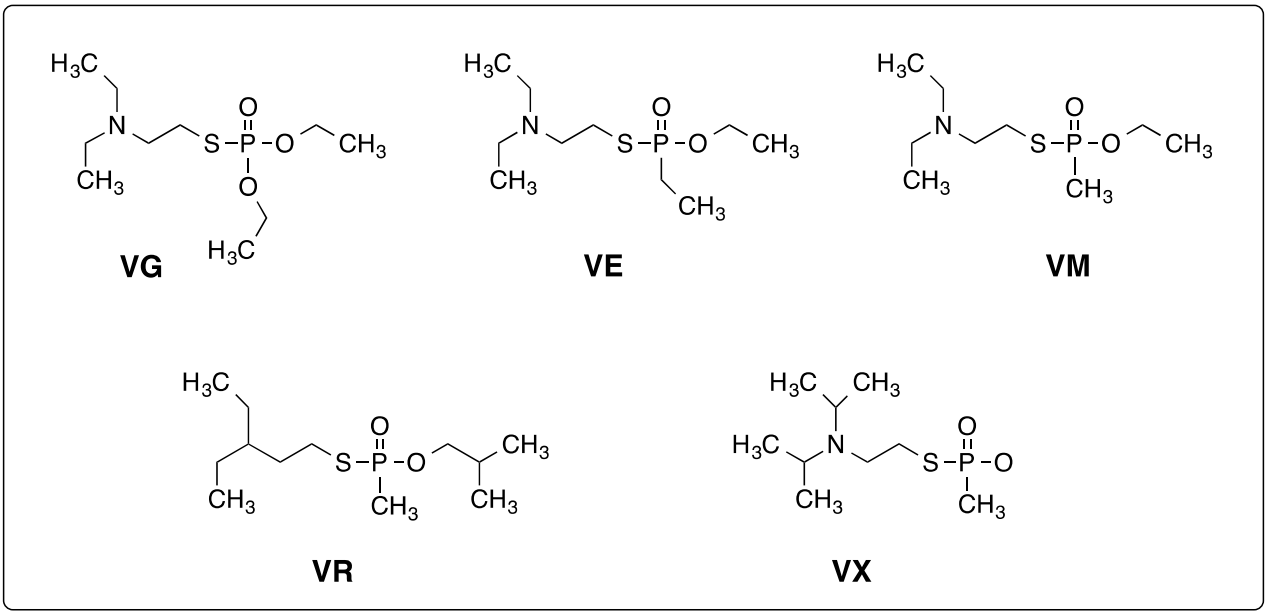
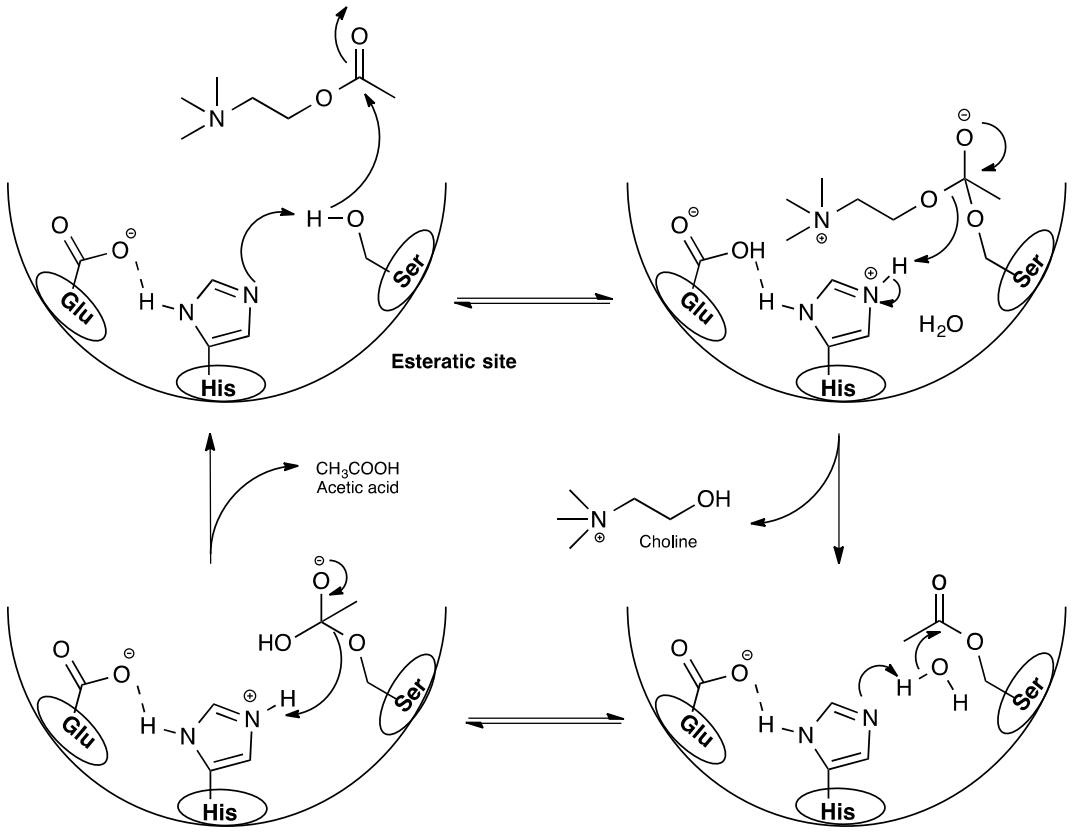


Figure 2.2: Structure of most common V-agents: VG (Amiton), VE, VM (Edemo), VR (Russian VX) and VX.

2.2.1 Physiological mode of action of nerve agents

The high toxicity of nerve agents is due to their inhibition of the enzyme acetylcholinesterase (AChE). AChE belongs to the serine esterases; a group of enzymes characterized by their possession of a reactive serine residue essential for their catalytic activity. Most serine esterases have several factors in common; one of these is the active site region. In particular, the catalytical triad containing three amino residues, one of them a serine residue, is shared by the serine esterase. In AChE, the active site consists of a serine-histidine-glutamate triad. Another common factor is a «gorge» located near the active site serine. In AChE, this gorge is approximately 20-Å deep with sides lined with side chains of aromatic residues. This provides a hydrophobic pocket for the active site in the enzyme [17,18].

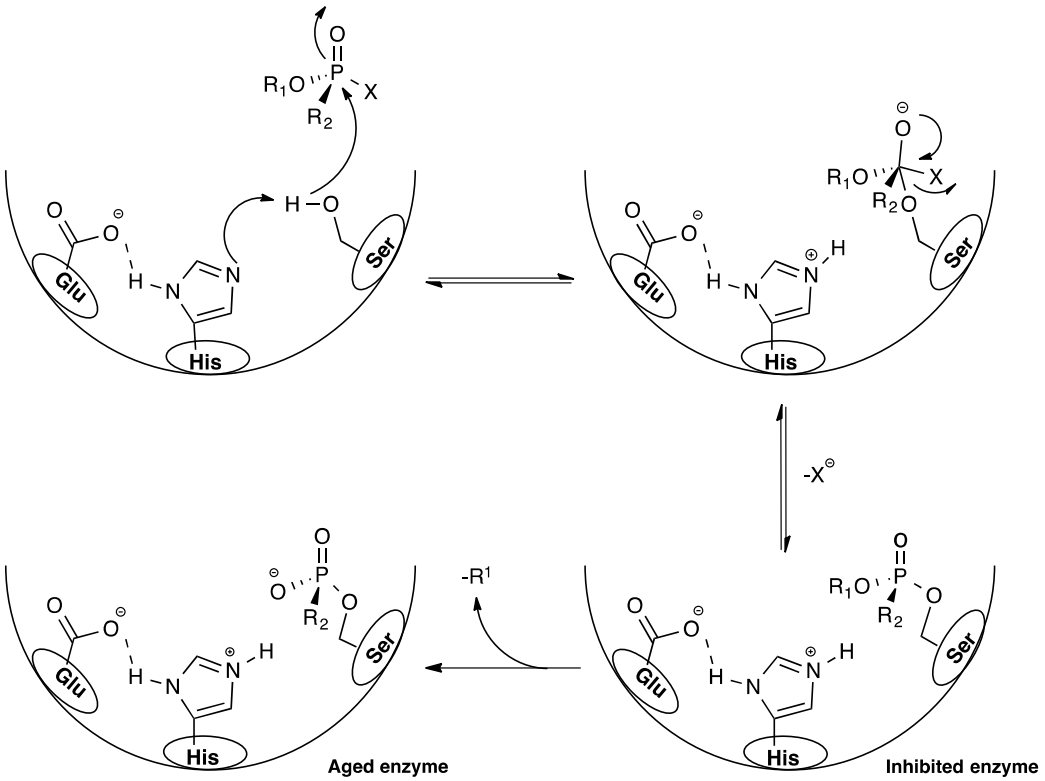
During normal function, AChE catalyzes the hydrolysis of acetylcholine (ACh) in the synaptic cleft, allowing nerve impulses to be transmitted between nerve cells. When AChE is inhibited, the otherwise rapid hydrolysis of ACh is prevented, leading to accumulation of ACh and thereby continuous stimulation of the nerve fibers [16,17]. The process of hydrolysis of ACh catalyzed by AChE starts with the formation of an enzyme-substrate complex (Scheme 2.1) [18]. Because of the close proximity of the serine and the histidine residue, the histidine ring is protonated by serine, leaving serine with a negative charge and making it a strong nucleophile. Serine carries out a nucleophilic attack on the carbonyl group of ACh, forming a complex known as the tetrahedral intermediate. The tetrahedral intermediate decomposes to an acyl-enzyme intermediate, releasing choline and replacing it with a water molecule. The water molecule then attacks the acyl-enzyme intermediate, leading to the formation of a second tetrahedral intermediate that collapses, thereby regenerating the active enzyme [19].



Scheme 2.1. Acetylcholinesterase catalyzed hydrolysis of acetylcholine [15]

The inhibition mechanism of AChE by nerve agents on is similar to the initial step of hydrolysis (scheme 2.2). Since most of the nerve agents have hydrophobic side groups, they easily reach the active site in the hydrophobic pocket of the enzyme. Once there, the

nucleophilic serine attacks the phosphorus atom of the nerve agent, forming a trigonal-bipyramidal intermediate. The leaving group (X) departs form the intermediate, leading to the formation of a phosphylserine. The mechanism closely mimics the normal function, except that the enzyme is phosphorylated instead of acetylated. However, histidine cannot react with water and regenerate the enzyme because it is either forced into a nonproductive conformation (*e.g.* VX and tabun conjugates) or shielded from water (*e.g.* soman conjugate) [19]. The phosphorylated AChE is relatively stable but can undergo two processes. The first is spontaneous hydrolysis, leading to reactivation of the enzyme. Yet, this first reaction is slow and it is also competing with a second reaction known as "aging". This second reaction is usually a dealkylation of the second substituent (R_1) present on the phosphorus atom. Through this reaction, the enzyme is irreversibly inhibited and cannot be reactivated [15].



Scheme 2.2. Inhibition and «aging» of AChE by nerve agents [15]

2.3 Decontamination of chemical warfare agents

2.3.1 Physical and chemical decontamination

Environments, personnel and equipment contaminated with chemical warfare agents (CWAs) represent a serious health hazard to exposed individuals. These health hazards can be avoided by decontamination. Decontamination can be defined as the removal of toxic chemicals from a contaminated surface. It does not necessarily include the detoxification, but due to the hazards posed by CWAs, conversion into less toxic or non-toxic products is desirable. Decontamination can be accomplished either through physical or chemical decontamination [10,14].

The objective of physical decontamination is to remove contamination from contaminated surfaces or to absorb it to prevent exposure. Physical decontamination has the advantage of being easy and universal. However, it is less effective than chemical decontamination. Physical decontamination can be achieved through rinsing with water or the removal of contamination by other purely physical means [14]. An example of a physical decontamination system is Fuller's earth. Fuller's earth is a naturally occurring clay material, which primarily consists of the clays montmorillonite and kaolinite. It has a large absorbative capacity and is mainly used for decontamination of individuals exposed to CWAs in liquid form. The system binds the CWAs to the surface of the powder through physical absorption, but provides no destruction or detoxification of the agents. The main disadvantage of such absorption systems for decontamination is that the absorbent must be detoxified later on. Reactive sorbents, such as reactive polymers, can also be used for decontamination of surfaces. These systems can contain both physical and chemical decontaminants and therefore both remove and detoxify the CWAs [22]. Such materials are the objective of the research presented in this thesis.

In chemical decontamination, the CWAs are converted into less toxic or non-toxic products through chemical reactions. The mechanism of chemical decontamination is dependent upon the chemical properties of the CWAs. Generally, chemical decontamination can be divided into two reaction mechanisms: oxidation and hydrolysis. CWAs containing a sulfur atom are very receptive towards oxidation, *e.g.* sulfur mustard and the V-series of nerve agents. The phosphorus containing G-agents (*e.g.* tabun, sarin, soman and cyclosarin) are more receptive towards hydrolysis [15]. One of the first chemical decontaminants used was bleach powder (calcium hypochlorite). Bleach powders are strong oxidizing agents and can convert CWAs

into less toxic or non-toxic products within minutes. Unfortunately, hypochlorite solutions are highly corrosive.

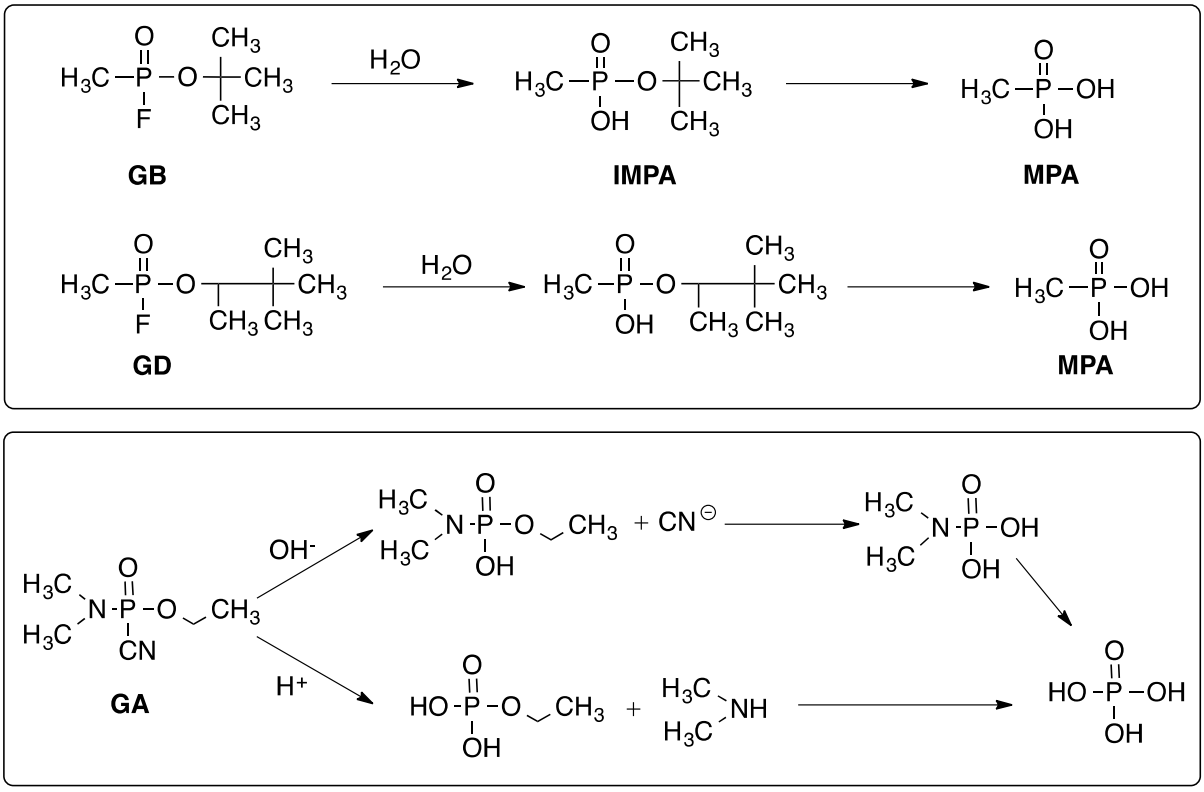
Decontamination can also be achieved through hydrolysis of the chemical warfare agents. An example of decontamination systems based on hydrolysis is DS2 (decontamination solution 2). DS2 is a general-purpose reactive decontaminant (meaning it is useful for a broad variety of CWAs). It is a polar, non-aqueous liquid composed of diethylenetriamine (70 wt%), ethylene glycol monomethyl ether (28 wt%) and sodium hydroxide (2 wt%) [21]. However, it corrodes many surfaces after prolonged exposure [14]. The Canadian decontaminant RSDL (reactive skin decontamination lotion) is another example of a decontamination system based on hydrolysis. RSDL was intended as a pre-exposure barrier skin cream, with ability to both neutralize and remove chemical warfare agents. The active component of RSDL is the potassium oximate salt potassium 2,3-butandione monooximate, which reacts rapidly with G-agents and slightly slower with V-agents. Research has shown that RSDL has low toxicity, although it may cause eye and skin irritation [49].

Not all CWAs represent a problem when it comes to decontamination. Agents like chlorine and hydrogen cyanide, both highly volatile, are quickly diluted in air. Also, very reactive agents, such as phosgene, will rapidly react with compounds available in the environment. These agents can therefore easily be removed from the environment, either by natural decomposition or by physical decontamination with water. CWAs that require decontamination are the persistent agents and agents with high toxicity in low concentrations. This includes the nerve agents, as they are highly toxic even in small quantities [4].

2.3.2 Chemical decontamination of nerve agents

Knowledge of physicochemical and toxicological properties of nerve agents is required for successful decontamination. G-agents are mainly decontaminated through hydrolysis, due to their reasonably high reactivity towards water. Both soman and sarin are relatively water-soluble, and are therefore especially receptive towards hydrolysis. Their hydrolysis has been carefully studied under different pH conditions, and hydrolysis under acidic, alkaline, and neutral conditions have been reported [21]. The hydrolysis of both nerve agents is strongly dependent on the pH. For instance, the half-life of sarin is 15 minutes at pH 1, 165 minutes at pH 5 and 0.3 seconds at pH 13 [4]. Hydrolysis of sarin and soman proceeds through nucleophilic attack on the phosphorus atom, with the end products being fluoride and a non-

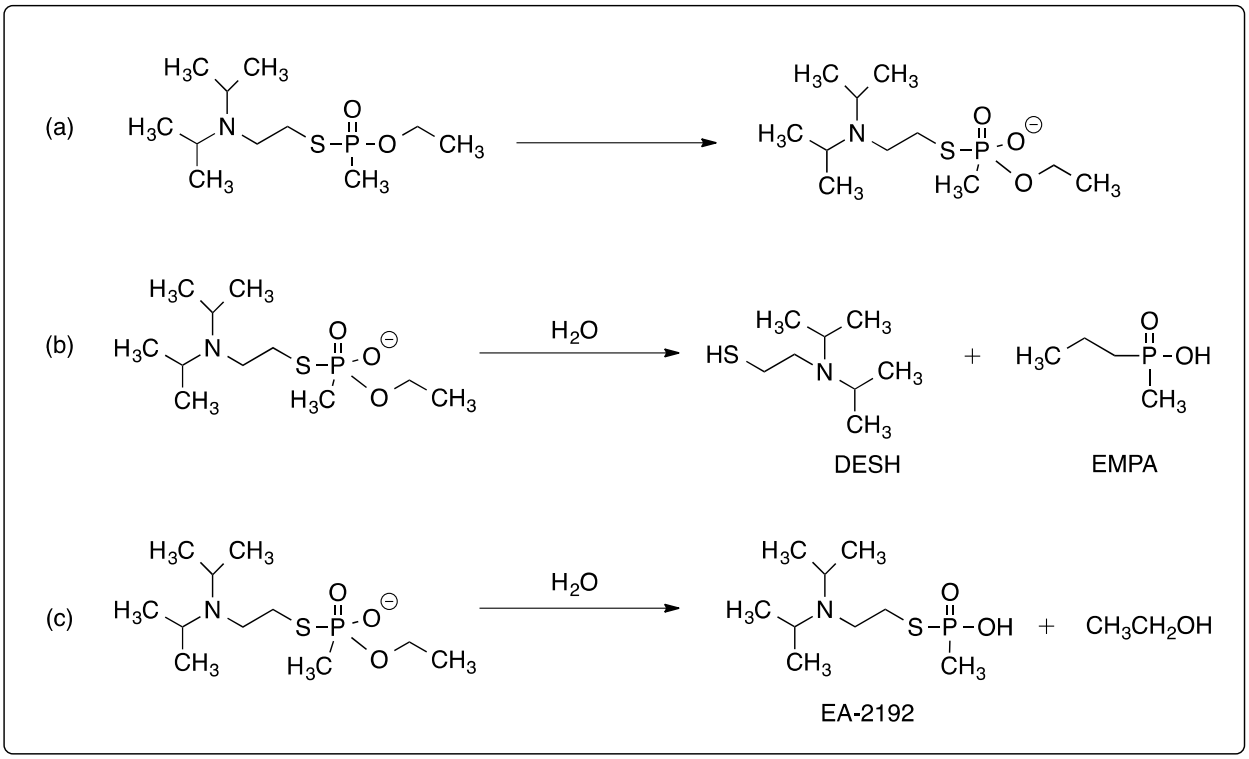
toxic phosphonic acid (Scheme 2.3). The non-toxic products are isopropyl methylphosphonic acid (IMPA) for sarin and pinacolyl methylphosphonic acid for soman. To maintain alkaline conditions throughout the hydrolysis, excess base must be added due to the formation of the acidic products (Scheme 2.3). The hydrolysis of tabun differs slightly from the hydrolysis of sarin and soman. The final hydrolysis product from tabun is phosphoric acid, but the intermediates are dependent on the reaction conditions. Hydrolysis under neutral or alkaline conditions gives formation of *O*-ethyl-*N*,*N*-dimethylamidophosphoric acid and cyanide, while hydrolysis under acidic conditions gives rise to ethylphosphoryl cyanidiate and dimethylamine (Scheme 2.3) [15].



Scheme 2.3: (a) Hydrolysis of sarin under neutral conditions. (b) Hydrolysis of soman under neutral conditions. (c) Hydrolysis of tabun under alkaline and acidic condition.

Decontamination of V-agents can also be achieved through hydrolysis. However, the rather low water-solubility of these agents makes them relatively resistant. The hydrolysis of VX is more complex than for the G-agents, and involves several pathways. When dissolved in pure water, VX forms an alkaline solution. However, the solubility will decrease as the solution becomes more alkaline. Hydrolysis of VX is initiated by the attack of hydroxide on the phosphorous atom. Following this, the intermediate formed can be hydrolyzed through two

pathways (Scheme 2.4). At pH values between 6 and 10, the predominant pathway of hydrolysis is through cleavage of the P-S bond. This results in the formation of ethyl methylphosphophonic acid (EMPA) and diisopropylethyl mercaptoamine (DESH). Hydrolysis can also occur through breakage of the P-O bond, leading to the formation of a compound called EA-2192. EA-2192 has the same toxicity as VX, and is stable towards further hydrolysis. The ratio between hydrolysis to EMPA and EA-2192 is in the range of 87% to 13% , depending on the conditions [4,15,21].



Scheme 2.4: Hydrolysis of VX. (a) Formation of intermediate. (b) The predominant way of hydrolysis. (c) Second pathway with formation of EA-2192.

2.3.3 Polymers in decontamination of chemical warfare agents

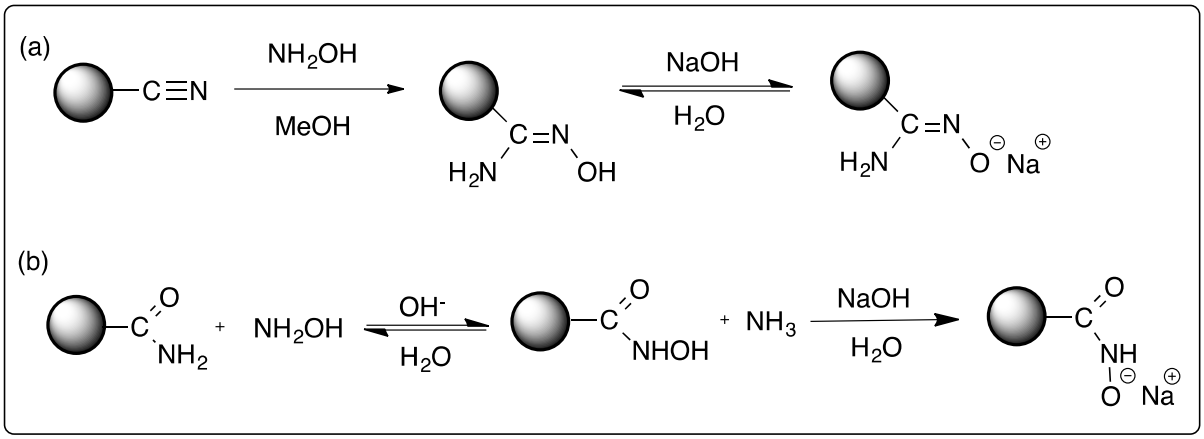
As already described, there are several different systems for decontamination of chemical warfare agents. Although most of these decontamination systems are very effective, many are corrosive and require continual rinsing to prevent degradation of surfaces. One approach to overcome these shortcomings is the use of polymer particles as solid sorbents to isolate CWAs [22]. Polymer particles for this purpose can be tailor-made with high surface area and strong affinity towards CWAs. Such solid sorbents can remove the CWAs rapidly from contaminated surfaces and thereby reduce the decontamination hazard. The main disadvantage of such physical solid sorbents is the possible off-gases after absorption, as they

don't provide any degradation of CWAs. Therefore, the contaminated polymer particles must be gathered and decontaminated [22,23].

The ideal solution to this problem would be a system composed of solid sorbents with the ability to chemically decontaminate the chemical warfare agents. This may be accomplished through different strategies. One method is through the combination of a solid sorbent with an active reagent. Such a system can be obtained by absorption of active compounds (*e.g.,* NaOH-, KOH- or hypochlorite solutions) into the solid sorbent [24]. Another method is to functionalize polymer particles by addition of reactive groups. The use of insoluble polymer in chemical synthesis was first introduced by Robert Bruce Merrifield in 1963, and have since found widespread applications in several fields. For instance, polymers are widely used for immobilization of reagents and catalysts [51-54]. Polymeric decontaminants, which are the objective of this research, can be obtained through functionalization of polymers with known reagents. An example of such a system is the skin decontaminant called the M291 kit. The M291 kit consists of pads filled with a mixture of several functional containing polymers, some containing sulfonic acid group (SO_2OH) attached and some with hydroxylamine groups. The system is intended to rapidly absorb and promote hydrolysis of the chemical warfare agents. The main advantage of reactive solid sorbent systems is the high absorptive capacity for chemical warfare agents and the reduced weight of the decontamination system.

Another example where polymer particles have been functionalized for use as decontaminants is the reactive polymers formulated by Bromberg *et al.* at Massachusetts Institute of Technology [25]. The study by Bromberg *et al.* focused on the process of degradation of CWAs by reactive polymers containing nucleophilic oximate groups; either amidoximates or hydroxamates. The reactive polymers poly(acrylamidoxime) (PANOx) and poly(*N*-hydroxyacrylamide) (PHA) were obtained by reaction of hydroxylamine with either poly(acrylonitrile) or poly(acrylamide) respectively (Scheme 2.5). Several papers have reported the hydrolytic actions of low-molecular weight oximates, such as hydroxamic acids and amidoximes, towards nerve agents [26-31]. Both hydroxamic acids and amidoximes are strong α-nucleophiles, and thereby effective deacylating and dephosphorylating agents. However, amidoximes have been reported to react more slowly with sarin in an aqueous solution than hydroxamic acids [25]. Although both are strong α-nucleophiles, their efficacy is dramatically enhanced by conversion into their corresponding amidoximate and hydroxamate anions. This enhanced reactivity is due to the presence of an unshared electron

pair adjacent to the nucleophilic center [30]. As well as being strong α-nucleophiles, hydroxamic acids and its derivatives are relatively non-toxic and biocompatible. Due to their characteristic properties, immobilized hydroxamic acid have important applications, and several papers have been published on the conversion of functional groups in polymers to hydroxamic acid. The most commonly used polymers are poly(acrylamide) [61], poly(acrylonitrile)[62], and poly(acrylate esters) such as poly(ethyl acrylate) and poly(metyl acrylate) [63-65].



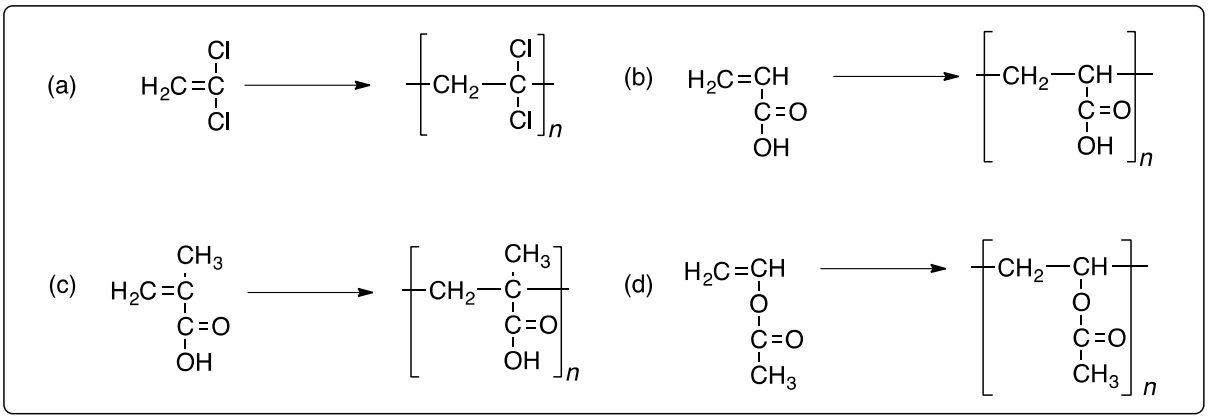
Scheme 2.5: (a) Conversion of PAN to PANOx by reaction of poly(acrylonitrile) with hydroxylamine. (b) Conversion of PAAm to PHA by reaction of poly(acrylamide) with hydroxylamine.

A decontamination system should possess a number of characteristics. A good decontamination system should be inexpensive to produce, chemically stable and readily available. It should also be environmentally compatible, non-corrosive and non-toxic. The solid sorbent system should absorb the contaminants, while keeping its decontamination activity toward the chemical warfare agents.

2.4 Polymerization

2.4.1 Free-radical polymerization

Possibly the first documented observation of polymerization can be traced to 1838 when the French chemist Henri Victor Regnault (1810–1878) reported a white precipitate obtained from boiling impure vinylidine chloride [32]. The precipitate is today easily identified as poly(vinylidene chloride), shown in Scheme 2.6. Several preparations and isolations of polymer products were reported throughout the 19th century and into the early 20th century (Scheme 2.6). However, the concept of macromolecules was not applied until described by Hermann Staudinger in 1922. His concept, that macromolecules consisted of small monomer molecules linked by covalent bonds, marked a beginning for molecular design of polymeric materials [33,34]. Furthermore, his research on macromolecules was awarded with a Nobel Prize in chemistry in 1953 [35]. In his first published paper on polymerization in 1920, Staudinger described the formation of macromolecules as repeated additions of monomers into long chain molecules. Although the mechanism of this reaction was uncertain, Staudinger proposed the participation of trivalent carbon atoms [36]. The first complete description of free radical polymerization was provided by Paul Flory in 1937. Flory was later awarded a Nobel Prize in chemistry in 1974 for *"his fundamental achievements, both theoretical and experimental, in the physical chemistry of the macromolecules"* [20]. In his paper, he described kinetics of vinyl polymerization as a chain reaction driven by free radicals [36,37].



Scheme 2.6: Examples of polymers discovered in the 19th and early 20th century. (a) Poly(vinylidine chloride). (b) Poly(acrylic acid). (c) poly (methacrylic acid). (d) Poly(vinyl acetate).

Free radical polymerization is a method of polymerization consisting of three steps: initiation, propagation and termination, as first demonstrated by Flory [37]. The first step of free radical

polymerization is initiation, and it is accomplished through the introduction of free radicals in the system. There are several different methods for achieving this; one of the most common, and the one used in this thesis, is thermal activation of suitable precursors called initiators. In thermal activation, the free radicals are produced by heating the initiator until a covalent bond is homolytically cleaved, giving rise to two primary radicals. Initiators used in thermal activation are usually azo-compounds or inorganic and organic peroxide compounds [40]. One of the most important factors when choosing an initiator for free radical polymerization is its solubility. The solubility of the initiator is dependent on the solvent in which the polymerization is carried out. If the polymerization is carried out in an organic solvent, the initiator should be oil-soluble. Likewise, if the polymerization is carried out in and aqueous solvent, the initatior should be water-soluble. Both azo- and peroxide-compounds are available as water-soluble or oil-soluble compounds, some examples are shown in scheme 6.

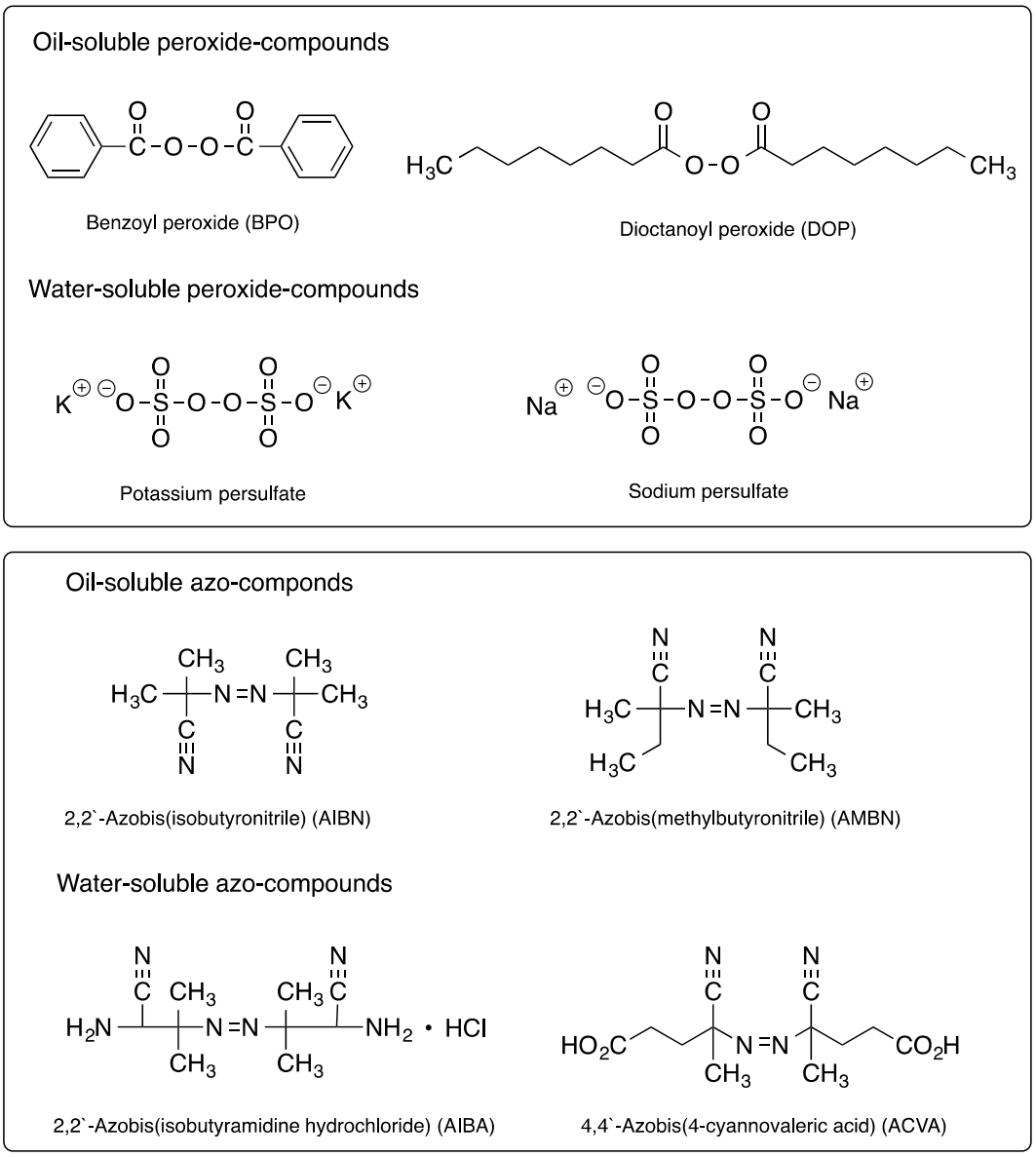


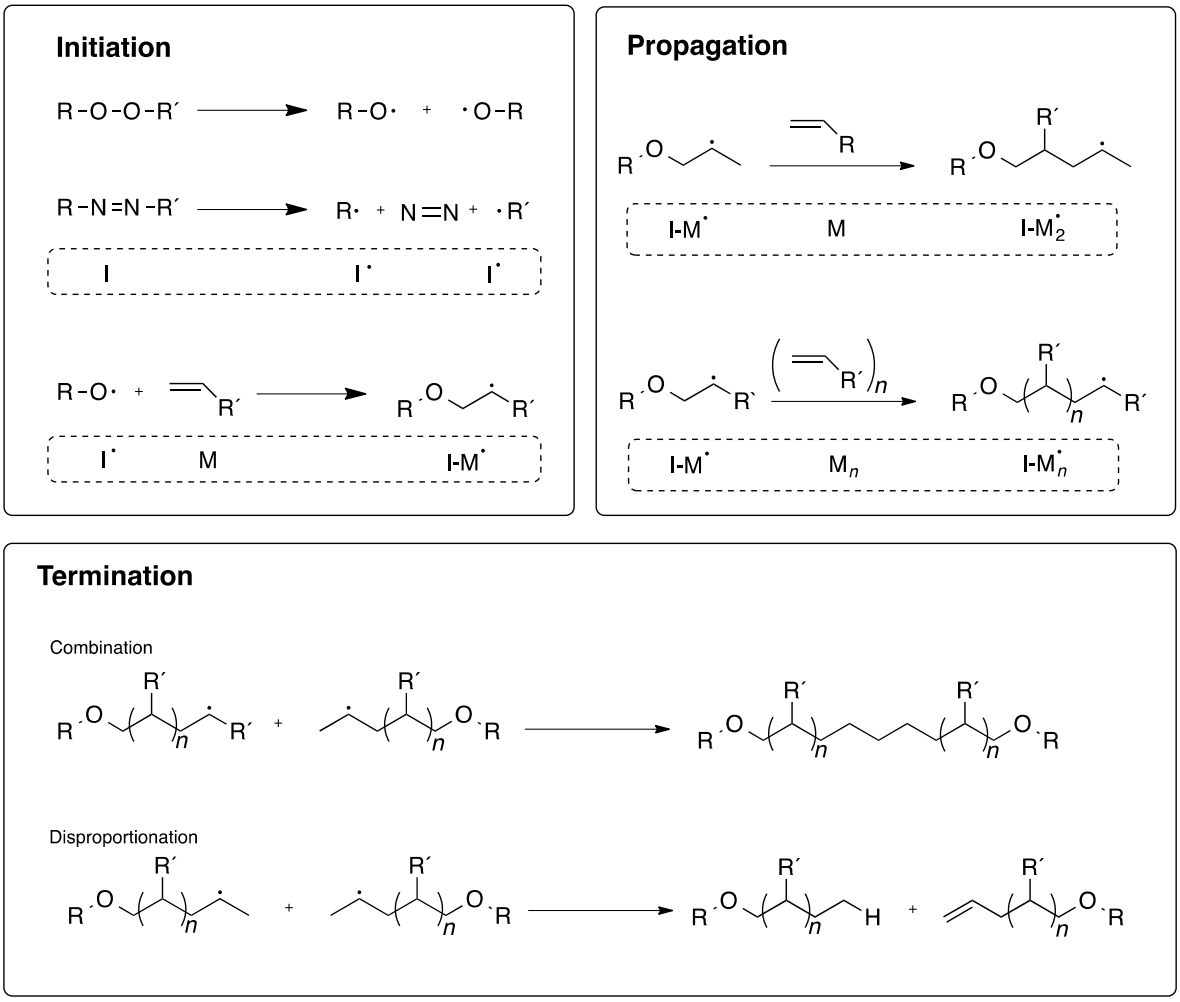
Figure 2.3: Common free radical initiators.

The radical produced by decomposition of the initiator can then add to the double bond of a monomer, thereby producing an initiator-monomer radical (I-M•) with an active center (Scheme 2.7). This I-M• radical can then initiate the polymerization by reaction with monomers in the second step known as propagation [39].

In the propagation step, a polymer chain will grow through the addition of a large number of monomer molecules to the active center. In each addition, the active center is transferred to the monomer being consumed. There are two possible types of addition for monomers in the propagation step, called head-to-head or head-to-tail addition. The head-to-tail addition is

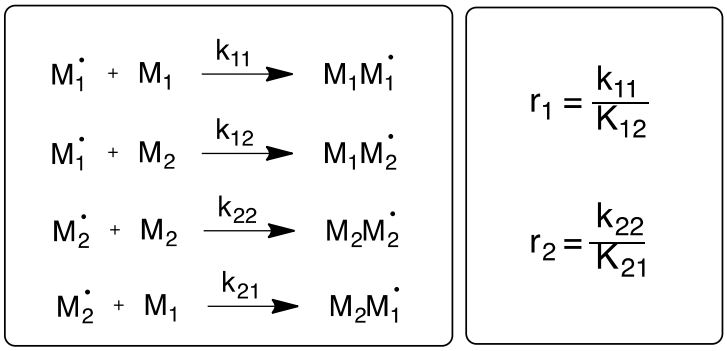
expected to be predominant based on steric considerations, as well as the possible electronic interactions between neighboring groups of certain monomers [39]. Once propagation has been initiated, the polymer chain will grow until there is no more monomer in the system or until the propagation is terminated. The mechanism of propagation is shown in Scheme 2.7.

At some point during propagation, the polymer chain is terminated due to the high reactivity of free radicals. Termination can occur through several different mechanisms; the two most common is combination and disproportionation (Scheme 2.7). Combination is simply the reaction between two radicals, forming a covalent bond and prohibiting the radicals from continuing the propagation. Combination may occur between two active centers in propagating chains or between the active center of a propagating chain and another type of free radical (*e.g.* an initiator). Disproportionation happens through the transfer of a hydrogen radical from one active center to another, resulting in a saturated and an unsaturated product [38].



Scheme 2.7: Mechanism of initiation, propagation and termination

Free radical polymerization can be carried out with a single monomer, and the synthesized polymer would then be called a homopolymer. However, free radical polymerization can also be carried out using a mixture of two or more monomers, and the product formed in such a polymerization is called a copolymer. Copolymers frequently have more desirable physical properties than homopolymers, as copolymerization can be used to modify various properties of the polymers by changing the monomer composition [41]. Copolymerization can for instance be used to improve mechanical and chemical properties of polymers for specific applications. The composition of a copolymer is dependent on the monomers in the reaction mixture, as different monomers have different tendencies to undergo copolymerization. The distribution of monomers in a copolymer can be described by the Mayo-Lewis equation or the copolymer equation [38].



Scheme 2.8: Copolymerization of two different monomers and the corresponding reactivity ratios.

The Mayo-Lewis equation describes the reactions that can occur between two monomers, M_1 and M_2, and the rate constants for these reactions (k). The copolymerization can produce two active centers, $M_1^{\bullet}$ or $M_2^{\bullet}$, with different reactivity dependent on the monomer unit. Further polymerization can yield two types of propagating species: either through reaction with M_1 or M_2. The rate constants describe the tendency of a specific active center to propagate through addition of the same monomer or the other. This is often referred to as self-propagation and cross-propagation. The monomer reactivity ratios (r) can be obtained by dividing the rate constant for self-propagation on the rate constant of cross-propagation. These two parameters (r_1 and $r_{2)}$ simply describe the ratio for the rate constants for the reaction of a propagating chain with a given monomer.

Mainly three different categories of copolymerization can be observed depending on the values of the monomer reactivity ratios, shown in Figure 2.4. These three categories of copolymerization can be classified based on whether the monomer reactivity of the monomers are unity, less than unity or greater than unity. The simplest of the three, ideal copolymerization, occurs when the relative reactivity of the monomers show the same preference towards both active centers. In other words, if $r_1 = r_2 = 1$. The arrangement of monomers units along the copolymer chain will therefore be random. The second category, alternating copolymerization, is characterized by $r_1 \ll 1$ or $r_2 \ll 1$. This means that the monomers show a preference towards the other monomer type. Block copolymerization is the third category; this applies to a copolymerization where both r_1 and r_2 are greater than 1 ($r_1 > 1$ and $r_2 > 1$). The copolymer composition will then consist of blocks of both monomers in the chain. Generally, the behavior of most known copolymerization systems will lie between the two extremes of ideal and alternating copolymerization [38].

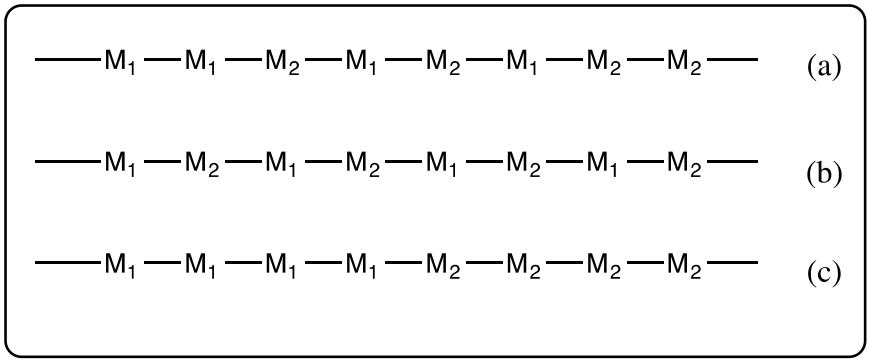


Figure 2.4: Three most common copolymerization compositions. (a) Ideal (random) copolymerization. (b) Alternating copolymerization. (c) Block copolymerization

2.4.2 Homogeneous and heterogeneous polymerization

Free radical polymerization can be classified into two types: homogeneous and heterogeneous polymerization. This classification is generally based on the initial reaction mixture, which can be either homogeneous or heterogeneous. The simplest type of homogeneous polymerization is bulk polymerization, which has the advantage of low contamination of the polymer product. However, the polymerization system provides poor heat-transfer and high viscosity, making the polymerization difficult to control [38]. These disadvantages can be overcome by carrying out the polymerization in a solvent, as the solvent will act as a diluent and provide heat-transfer. However, the purification of the polymer products can be difficult in solution polymerization. Heterogeneous polymerization usually consists of a two-phase

system, where the monomer forms fine dispersions in an immiscible liquid. This provides good control of both viscosity and heat-transfer. The monomers are usually referred to as the «monomer phase» or the «dispersed phase», while the other liquid is defined as the «polymerization medium» or «continuous phase» [42]. There are several methods for heterogeneous polymerization. The most common are suspension polymerization, emulsion polymerization and dispersion polymerization.

2.4.3 Suspension polymerization

The simplest of heterogeneous polymerization methods is suspension polymerization (also referred to as pearl, bead, or droplet polymerization). The term suspension polymerization describes a mechanism with a monomer phase dispersed in the continuous phase by agitation. The monomer(s) are almost completely insoluble in the continuous phase. The initiator is soluble in the monomer phase, and polymerization proceeds in the monomer droplets, eventually forming solid polymer particles [44]. The suspension of the monomer phase is stabilized by the addition of a non-micelle-forming emulsifier, usually referred to as a suspension stabilizer, to avoid coalescence of the droplets [38].

Suspension polymerization can usually be classified into two types, oil-in-water (O/W) and water-in-oil (W/O). The oil-in-water type is the more common of the two, and is sometimes referred to as normal suspension polymerization. In this type of suspension polymerization, the droplets consist of oil-soluble monomer(s) and initiator dispersed in an aqueous continuous phase. Water-miscible polymers, both natural and synthetic, are frequently used as suspension stabilizers in oil-in-water systems [43]. Some examples of common suspension stabilizers are poly(vinyl alcohol) and poly(vinyl pyrrolidone). Many common monomers, such as styrene, methyl methacrylate and ethyl acrylate, have low water-solubility and are therefore suitable for normal suspension polymerization. However, some monomers, such as methyl acrylate, acrylonitrile and vinyl pyridine, have significant water-solubility. If the desired monomers are highly water-soluble, water-in-oil systems (also called inverse suspension polymerization) can be carried out. In inverse suspension polymerization, a water-soluble monomer is dispersed in a non-aqueous continuous phase. The continuous phase is immiscible with the aqueous monomers, and usually consists of a liquid aliphatic hydrocarbon or mixture of aliphatic hydrocarbons [45]. For this type of suspension polymerization, a water-soluble initiator is used to ensure that the polymerization occurs inside the droplets. Non-aqueous suspension stabilizers, like ethyl cellulose and cellulose

acetate butyrate, have been developed for this type of suspension polymerization [41]. Inverted suspension polymerization is less common, due to the higher density of the monomer phase to the continuous phase, making dispersion difficult. Halogenated hydrocarbons are therefore added to the continuous phase to increase its density, and thereby stabilize the dispersion.

An alternative to inverse suspension polymerization is a modified normal suspension polymerization where the continuous phase is saturated with salt. Adding salt to the continuous phase limits the solubility of the monomer, thereby helping to stabilize the dispersed monomer droplets. Suitable salts for this purpose are water-soluble, inert inorganic salts, often belonging to the alkali metals and the alkali earth metals. Sodium chloride, calcium chloride and potassium chloride are frequently used [47,48]. The preferred concentrations of inert salt are approximately 25%. This poses a problem, as many suspension stabilizers used in normal suspension polymerization are insoluble under high salt concentrations. Examples of suspension stabilizers useful in these suspension polymerization systems are 2-hydroxyethyl cellulose, gelatin and xanthan gum (Figure 2.5).

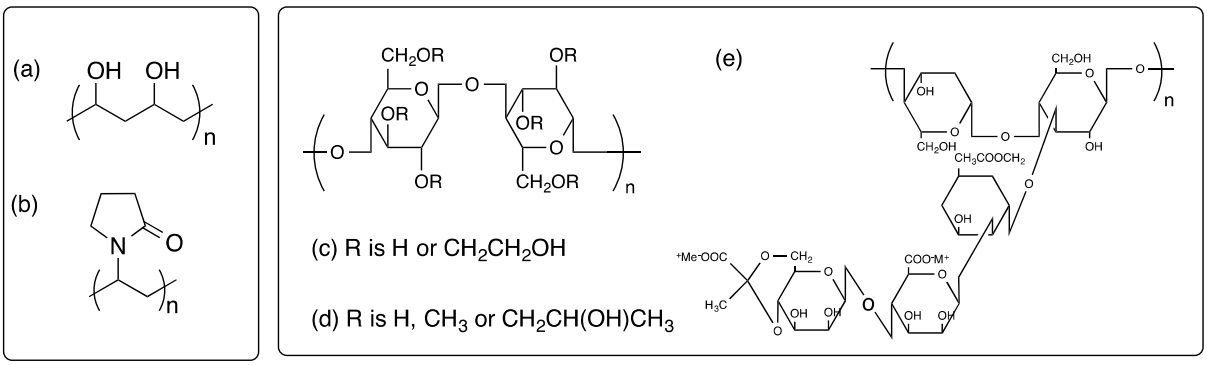


Figure 2.5: Common suspension stabilizers for normal suspension polymerization: (a) PVA and (b) PVP, and for normal suspension polymerization in brine: (c) 2-hydroxyethyl cellulose, (d) hydroxypropylmethyl cellulose and (e) xanthan gum.

The morphology of polymer beads formed in suspension polymerization can easily be regulated by adding an inert solvent to the monomer phase and the use of cross-linkers. The inert solvent is used to control the porosity of the resulting polymer beads. Generally, polymer beads can either be of a macroporous or microporous type. The main feature of macroporous beads is the large pores in the polymer structure and the high degree of cross-linking. These two main features can also be used to differentiate macroporous polymer beads from

microporous polymer beads, which contain small pores and have a low degree of cross-linking. Several different solvents can be used as the inert solvent, depending on the desired structure of the polymer product. When synthesizing macroporous polymers, the inert solvent is usually called a porogen. The porogen can be a good solvent, a non-solvent, or even solid particles. For synthesis of microporous polymers, the inert solvent can be called a phase-separation inhibitor. Both porogens and phase-separation inhibitors are soluble in the monomer phase, the difference occurs during polymerization. A porogen is a good solvent for the monomer but a poor solvent for the polymer product. At some point during the polymerization, phase-separation or perspiration of the polymer occurs. It is this phase-separation that yields the porous structure of the polymer product [56,60]. The integrity of the macroporous structure is maintained by the use of a large quantity of cross-linker. The function of a phase-separation inhibitor is completely opposite of a porogen. For an inert solvent to be used as a phase-separation inhibitor, it should be a good solvent for the monomers, as well as for the polymer product. Its function is to prevent the monomers from diffusing out of the droplets and to inhibit precipitation of the polymer. The use of a phase-separation inhibitor is often required in suspension polymerization, especially in copolymerization of monomers with different solubility. The reason for this is that the monomer rarely is a good solvent for its polymers, a phase-separation inhibior are therefore used to prevent the polymer from precipitating.

As the polymerization progresses in the dispersed monomer droplets, the size of the monomer droplets usually corresponds to the size of the resulting polymer beads. The size of the polymer beads obtained from suspension polymerization generally lies within the size range of 50–1000 μm in diameter. Often, it is desirable to obtain polymer beads within a certain size range, size control is therefore important. This can readily be controlled, as the size of monomer droplets depend on factors such as stirring speed, composition of the continuous phase, and volume ratio of continuous phase to monomer phase. By adjusting the stirring speed, the bead size can easily be regulated. At low stirring speed, the suspended monomer droplets and the polymer beads will be large. At higher stirring speed, the size of the monomer droplets and polymer beads will decrease [41,43]. Also, the use of brine generally produces larger polymer beads, due to the increased interfacial surface tension between the continuous phase and the monomer droplets. The production of monodisperesed beads, however, requires specialized systems.

2.4.4 Emulsion polymerization

Emulsion polymerization is a heterogeneous process with a superficial resemblance to suspension polymerization, but the mechanism and kinetics of the process are quite different. In emulsion polymerization, the monomer is slightly soluble in the continuous phase. One of the main components in emulsion polymerization is an emulsifier. The emulsifier is a molecule with both hydrophilic and hydrophobic parts. This allows the emulsifier to interact both with the continuous phase and the monomers. The initiator is, unlike in suspension polymerization, soluble in the reaction medium and insoluble in the monomer phase.

In the beginning, the emulsifiers will stabilize large monomer droplets (1-100 μm) in the continuous phase and the excess emulsifiers will create micelles (2-10 nm) containing smaller amounts of monomer. Upon heating of the system, the water-soluble initiator will decompose, creating radicals that react with the small amounts of monomer dissolved in the continuous phase. As the radicals propagate and become less water-soluble, they are absorbed by the micelles. The monomers rapidly polymerize in the micelles and are replenished by diffusion of monomer from the monomer droplets, gradually forming polymer particles.

The size of the finished polymer product is another difference between suspension and emulsion polymerization. Unlike the relatively large polymer beads (50-1000 μm) formed in suspension polymerization, the polymer beads formed in emulsion polymerization are much smaller (typically 50 – 300 nm) [38,42].

2.4.5 Dispersion polymerization

In dispersion polymerization, the initial reaction system is a homogeneous medium of monomer(s), an organic solvent, free radical initiator, and a particle stabilizer. The organic solvent is miscible with the monomer(s), but is a poor solvent for the polymer, which means that the reaction medium will become heterogeneous as nucleation and formation of primary particles occurs when the polymerization propagates and the polymer precipitates. When this occurs, stabilization occurs by absorption of stabilizer from the continuous phase. The polymer swell to a certain degree in the polymerization medium and/or the monomer, polymerization therefore occurs within the particle by absorption of monomer and free radicals from the continuous phase [41,42].

Polymer beads produced from dispersion polymerization typically lie in the size range of 1–10 μm, and can therefore be placed between those obtained from emulsion polymerization and suspension polymerization based on the particle size obtained. The polymer size in dispersion polymerization can be controlled through the temperature of polymerization, type of stabilizer and the concentrations of monomer, initiator and stabilizer.

3. Results and discussion

3.1 General

The objective of the work presented in this thesis was the synthesis of polymer beads containing reactive functionalities for decontamination of organophosphorus nerve agents, taking inspiration from the mode of function of the enzyme acetylcholinesterase. These reactive polymer beads should be applicable for decontamination in aqueous environments. The reason for this is that in the event of an attack with nerve agents, the contaminated area, which generally will be constituted by an outdoors urban/rural residential area or natural area, can be described as an "aqueous" environment. To obtain such reactive polymer beads, it was important to establish a balance between hydrophilic properties, in order to facilitate solvation of the polymer network in aqueous environments, and hydrophobic properties, for increased receptiveness of the polymeric decontaminant towards the hydrophobic nerve agents. For the synthesis of polymer beads containing such a balance between hydrophobic and hydrophilic properties, as well as structural characteristics mimicking acetylcholine esterase, suitable monomers and polymerization conditions had to be identified.

The experimental work presented in this thesis was initiated by copolymerization of ethyl acrylate and styrene through normal suspension polymerization. Ethyl acrylate was chosen for its active ester moiety suitable for conversion to the hydroxamate anion of hydroxamic acid, and styrene was chosen for its chemical stability and hydrophobic properties. Ethyl acrylate was soon replaced with methyl acrylate, due to the more reactive leaving group of methyl acrylate. A suspension polymerization in brine was developed for the copolymerization of methyl acrylate and styrene because of the greater water-solubility of methyl acrylate compared to ethyl acrylate. When a suitable suspension polymerization method had been established, acid-scavenging monomers contributing to binding of the decontamination byproducts were incorporated into the polymer structure.

The obtained polymer beads were functionalized further through conversion of methyl acrylate into the corresponding anion of hydroxamic acid. The conversion of methyl acrylate through reaction with hydroxylamine proved more difficult than expected, and several different procedures were developed before the polymer beads were successfully functionalized. The functionalized polymer beads were further analyzed using available methods, such as microscopy, CHN analysis and IR spectroscopy.

3.2 Choice of heterogeneous polymerization method

Before any experiments could be undertaken, a suitable heterogeneous polymerization technique had to be identified. Several potential techniques for heterogeneous polymerization were available for this purpose, the three most common being emulsion, dispersion and suspension polymerization (See theoretical background, chapter 2.4.3-2.4.6). These three techniques can be distinguished by several different properties, but for the work presented in this thesis, the size of the polymer product was the most important factor. Smaller polymer beads have better diffusion properties than larger polymer beads, due to the large surface area. However, larger polymer beads are easier to isolate and often easier to work with. Out of the three heterogeneous polymerization methods, suspension polymerization gives the largest polymer beads (50-1000 μm). Another advantage of suspension polymerization is that the size of the polymer beads is easily controlled by different factors, such as stirring speed and the adjustments of the ratio of the continuous and the dispersed phase.

3.3 Synthesis of polymer beads using suspension polymerization

When polymers are used in reaction mixtures, they normally constitute a significant portion of the reaction environment. Therefore, it is reasonable to expect that the structure and properties of the polymer will impact the chemical reaction conditions when they are applied. Hence, there cannot be a universally used polymer materials for all applications [51]. The intended application of the polymers should therefore be considered in order to synthesize suitable materials. Firstly, the polymer beads should contain a monomer containing a functional group that can be converted into the desired reactive moiety. Secondly, the polymer should be able to absorb the reaction solvent, solvating the polymer network [55]. The high degree of cross-linking in macroporous beads prevents swelling, although the presence of large pores facilitates diffusion of solvent inside the polymers. However, the high degree of cross-linking results in a rigid structure, which may reduce the reactivity of the functionalities. On the contrary, microporous beads will swell significantly in good solvents due to their low degree of cross-linking, thus providing access to functional groups located in the interior of the polymer beads [56]. As the majority of reactive groups are located in the interior through random functionalization, good absorption of solvent is essential. Microporous beads are therefore preferred over macroporous beads, and such beads were used for the work presented in this thesis.

To obtain such nonporous polymer beads, a low degree of cross-linker, traditionally between 1 and 2 mol%, is used. In the work conducted in this thesis, 2 mol% cross-linker was used throughout, unless otherwise stated. The hydrophobicity and flexibility of the cross-linker have a significant role in determining the polarity and inter-chain interactions of the polymer product. Studies have shown that flexible cross-linkers provide enhanced reactivity of the polymer resin. However, cross-linking agents used to obtain such expandables polymer beads are often difunctional acrylics, such as ethylene glycol dimethacrylate (EDGMA), 1,4-butanediol dimethacrylate and 1,6-hexanediol diacrylate (HDODA). As the functionalization of polymer in this thesis was based on reaction between active esters and hydroxylamine, the presence of esters in the cross-linking network may lead to chemical degradation of the polymer network. Thus, the use of such cross-linking agents is not ideal. Divinylbenzene (DVB) is one of the most common cross-linking agents, and is extensively used due to the high stability of the cross-links. This cross-linking agent is known to be inert during most chemical reactions due to its hydrocarbon structure. Because of this, DVB was used as the cross-linking agent throughout the work presented in this thesis.

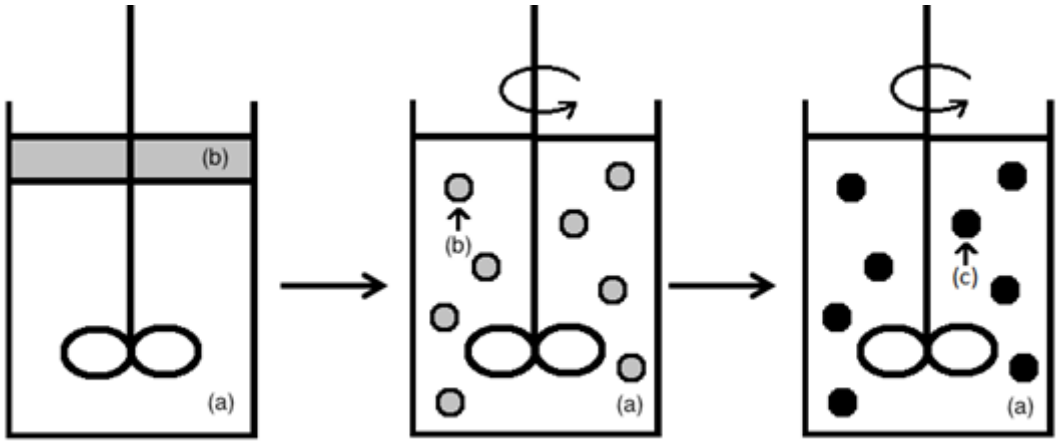


Figure 3.1: During suspension polymerization, the system comprises different phases. (a) The continuous phase, containing the suspension stabilizers. (b) The dispersed phase, containing monomers, initiator and phase-separation inhibitor. During polymerization, the monomer droplets containing the dispersed phase will form polymer beads as in (c).

3.3.1 Synthesis of cross-linked poly(methyl acrylate-*co*-styrene) beads

As the structural characteristics and properties of the polymer beads are important for the function of the finished product, the choice of monomers was considered carefully. As the polymer products synthesized in the work presented in this thesis were intended as decontaminants for organophosphorus nerve agents, the structural characteristics of the polymer were designed to mimic acetylcholine esterase (AChE) (Figure 3.2). The reason for mimicking AChE is that nerve agents easily reach the active center and inhibits the enzyme, therefore it was hoped that effective polymeric decontaminants could be prepared by mimicking the structural and functional characteristics of AChE. The active site of AChE is located in a hydrophobic pocket in the enzyme. The sides of this hydrophobic pocket are lined with side-chains of aromatic residues, which makes the active site easily reachable for the hydrophobic nerve agents. To mimic the structure of this hydrophobic pocket, styrene was used as a monomer in the backbone of the polymer particles. Styrene is a vinyl monomer derived from dehydrogenation of ethylbenzene. Because of its chemical stability, availability and low cost, it has many applications in polymer science. The active site of AChE contains three particularly important amino acids, which contributes to binding of the nerve agent and removal of the leaving group (see theoretical background, chapter 2.2.1). This is achieved through a nucleophilic attack of serine on the phosphorus atom in the nerve agent. To obtain such a nucleophilic group, the polymeric decontaminant must contain a functional group that can be converted to hydroxamate or other functionalities with a reactivity towards nerve agents. Active esters, like acrylates, are often used for subsequent conversion into other functionalities. The reaction of polymer-bound active esters with amines is possibly among the most frequently used functionalization reactions.

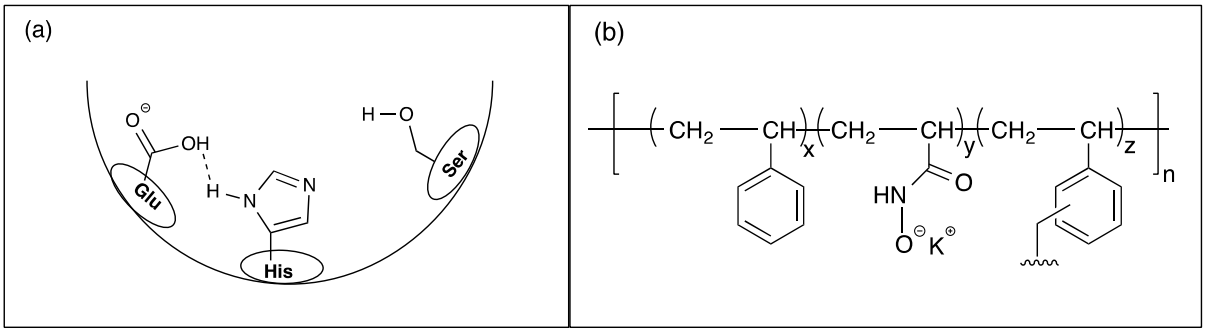
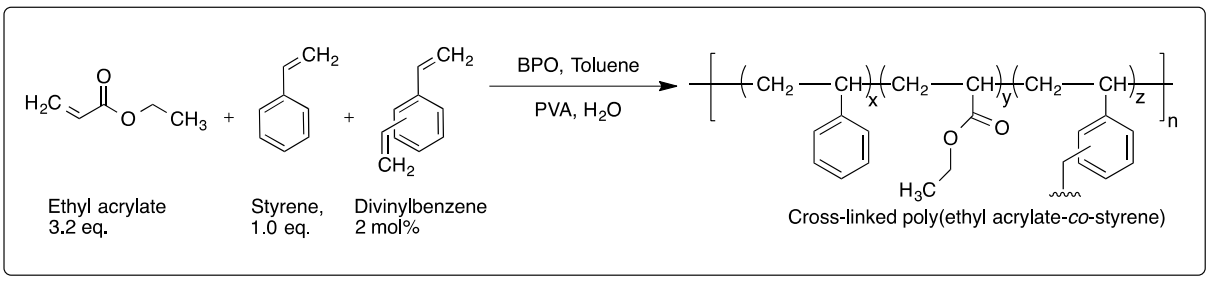


Figure 3.2: Comparison of (a) the active site of AChE and (b) the polymer backbone of the polymeric decontaminant.

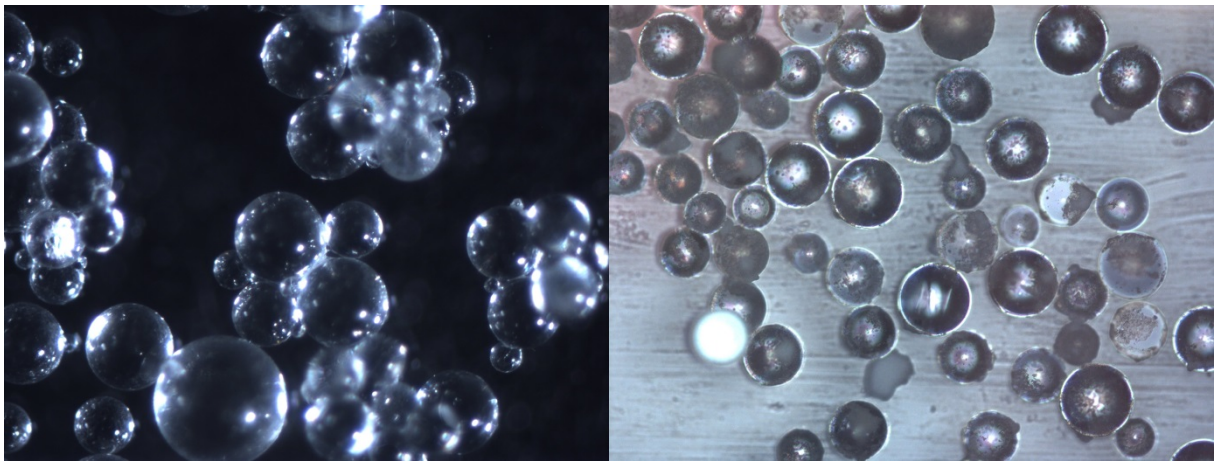
The simplest method for suspension polymerization is by normal suspension polymerization. In order to carry out normal suspension polymerization, where the monomers are dispersed in an aqueous medium, the monomers must be insoluble or have a low degree of solubility in water. Acrylates were found to be the most promising functional groups for conversion to hydroxamic acid. Acrylates are esters of acrylic acids, and contain a vinyl group directly attached to the carbonyl carbon. The alcohol moiety of the ester can be any organic alkyl chain, but preferably methyl, ethyl or propyl. Of these three, ethyl acrylate was selected as the most favorable. This was based on its alcohol moiety, which is a reactive leaving group, and its reasonably low solubility in water. Ethyl acrylate, styrene and divinylbenzene were mixed together with the oil-soluble radical initiator benzoyl peroxide (BPO), and toluene was used as the phase-separation inhibitor (Scheme 3.1). Toluene is a good solvent for most styrenes, acrylates, methacrylates and their polymer products, thus it can be used as a phase-separation inhibitor to prevent diffusion of monomers into the continuous aqueous phase and precipitation of the polymer. The monomer mixture was then suspended as droplets in the continuous phase. To stabilize the suspension during polymerization, a water-soluble suspension stabilizer was added. The continuous phase in this initial experiment consisted of a 0.5 wt% aqueous solution of poly(vinylalcohol) (PVA). PVA is a water-soluble polymer obtained by partial hydrolysis of poly(vinyl acetate) (PVAc). It is one of the most commonly used suspension stabilizers in normal suspension polymerization.



Scheme 3.1: Copolymerization of cross-linked poly(ethyl acrylate-*co*-styrene) with benzoyl peroxide as initiator, toluene as phase-separation inhibitor and an aqueous solution of 0.5 wt% PVA as the continuous phase.

After polymerization, the aqueous phase and impurities such as unreacted or partly reacted monomers and monomer diluents must be separated from the polymer beads. The suspension was therefore cooled down to room temperature before being poured into a beaker containing methanol. When the polymer beads are added to the methanol, they will collapse as toluene is

extracted from them and then sediment to the bottom of the beaker. The impurities can then usually be separated from the polymer beads as they are either soluble in the methanol or stay suspended due to their low density. This allows the impurities to be removed by decantation, while leaving the polymer product behind. This process was repeated until the added methanol remained clear. After decantation, the beads were isolated by vacuum filtration. The polymer beads were then purified with methanol, water and isopropanol. The cross-linked poly(ethyl acrylate-*co*-styrene) beads obtained using this procedure were white beads. The polymerization of these polymer beads gave a yield of 45% based on recovery of monomers. The morphology and size range of the polymer product was determined using microscopy. The polymer beads were spherical with a smooth surface, and the majority of the particles were in the size range of 100-200 μm (Picture 3.1).



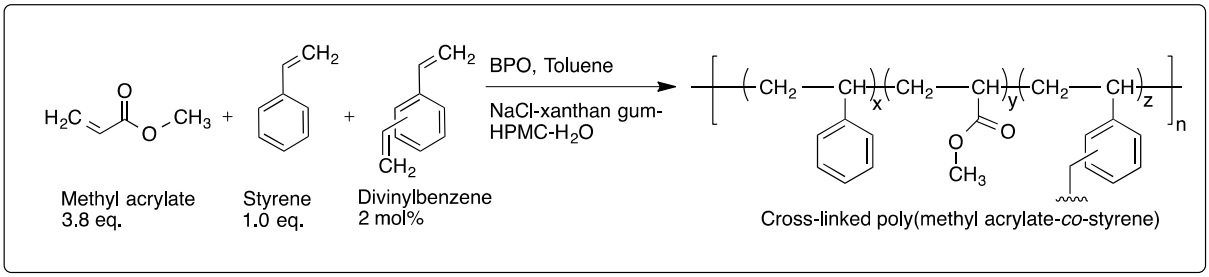
Picture 3.1: Cross-linked poly(ethyl acrylate-*co*-styrene) beads after purification.

As the polymer beads synthesized in the work presented in this thesis were to be functionalized for use as a decontaminant for organophosphorus nerve agents, it is important to find (an) appropriate solvent(s) that can promote conversion of the alcohol moiety to hydroxamic acid. Therefore, the beads` ability to absorb and swell in different solvents was tested. It is also important to find good solvent for use as phase-separation inhibitors. The solvents tested were common solvents regularly used in synthesis, such as tetrahydrofuran (THF), toluene, dichloromethane, and ethyl acetate. Ethyl acetate was the poorest of the solvents, and gave only moderate swelling of the polymer beads. The other solvents gave significantly better swelling, but THF was found to be the best of them. It was therefore decided to first use THF in the functionalization reaction of the beads described here. This work will be described later (chapter 3.4).

Although the polymer beads containing ethyl acrylate as the functional monomer gave fine, spherical particles with good swelling abilities, it was desirable to replace it with a more reactive monomer. Because the polymer beads obtained were to be functionalized, the ester group should be accessible for reaction with the hydroxylamine. Ethyl acrylate was therefore replaced with methyl acrylate. By using a methyl ester, instead of an ethyl ester, the functional group will be more receptive towards functionalization, as the methoxy group is a better and more reactive leaving group than the ethoxy group. A disadvantage with using methyl acrylate is the significantly higher degree of water solubility of this monomer compared to ethyl acrylate. This means that normal suspension polymerization is difficult, as methyl acrylate would partly diffuse into the continuous phase. To overcome this difficulty, the polymerization can be performed as a normal suspension polymerization where the continuous phase is saturated with salt (brine). By nearly saturating the continuous phase with salt, the solubility of methyl acrylate is significantly decreased. Diffusion of the monomer into the continuous phase can thereby be significantly reduced. A problem with such modified suspension polymerizations is that most suspension stabilizers are unstable or insoluble under high salt concentrations. Therefore, common stabilizers such as PVA and poly(vinylpyrrolidone) (PVP) do not stabilize the monomer droplets sufficiently. However, suspension polymerization in brine is well documented, and several known and commercially available suspension stabilizers have been found (see theoretical background, chapter 2.3.4) [45-48,57-58].

The first experiments with a continuous phase consisting of brine were based on a patent by Hamann *et al.* [48]. Haman *et al.* found that polymer beads could be produced by suspension polymerization in brine with the aid of a suspension system comprising a combination of a high molecular weight polysaccharide and a hydroxylalkylmethyl cellulose. According to the patent, the combination of these two suspending agents could produce uniformly sized and spherical polymer beads of both porous and nonporous morphology. Based on this patent, the first combination of suspension stabilizers used in this thesis was the commercially available polymers xanthan gum and hydroxypropylmethyl cellulose (HPMC). An aqueous solution with xanthan gum and HPMC was prepared, and further saturated with 25 wt% sodium chloride. The recommended concentrations of suspension stabilizer are between 0.05 to 0.5 wt% for xanthan gum and 0.007 to 0.02 wt% for HPMC. Several different aqueous solutions, with concentrations ranging from the lowest to the highest concentrations, were prepared. The suspension polymerization was performed as mentioned earlier, but with methyl acrylate as

the functional monomer and the prepared brine as the continuous phase (Scheme 3.2). When using brine as the continuous phase, interfacial surface tension between the continuous and the dispersed phase is significantly higher than in normal suspension polymerization. Stirring speed must therefore be increased to obtain polymer beads of similar sizes. However, the interfacial surface tension between the two phases will decrease with increasing temperature, and good stirring can be reached at acceptable stirring rates.

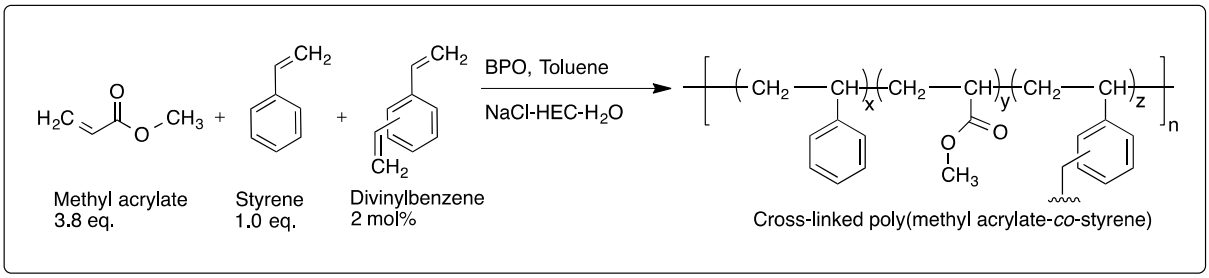


Scheme 3.2: Copolymerization of cross-linked poly(methyl acrylate-*co*-styrene) with benzoyl peroxide as initiator, toluene as phase-separation inhibitor and brine, containing the combination of xanthan gum and HPMC as stabilizers, as the continuous phase.

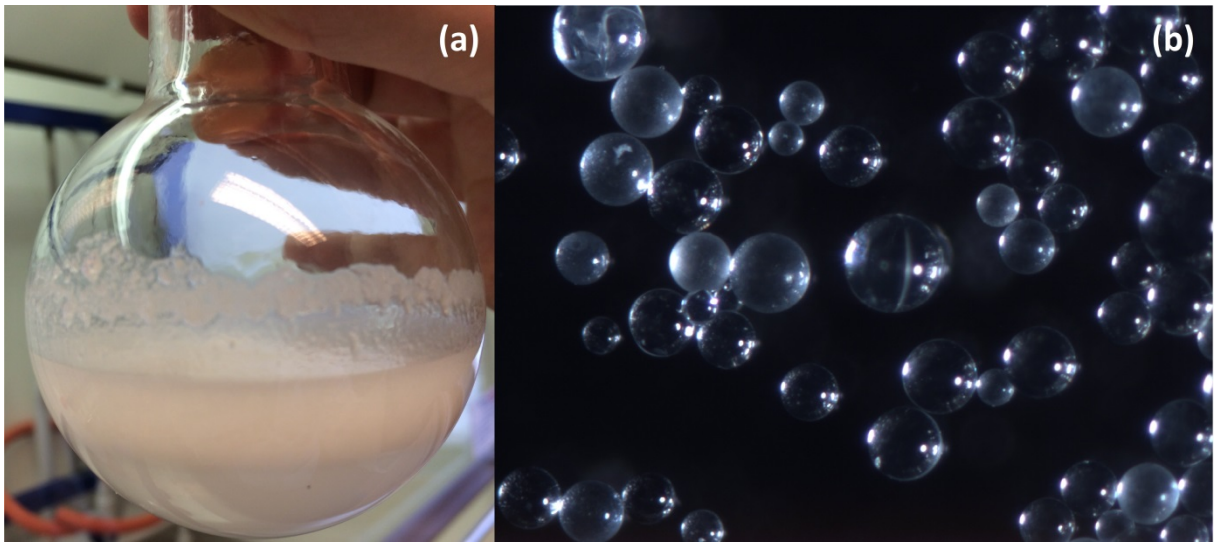
Because the brine was used as the continuous phase, the purification procedure could not be completed as described earlier. This is due to the high salt concentration, where salt will start precipitating if the suspension is added to methanol. To avoid this, the decantation step was carried out using water. Most of the salt is washed out by the decantation, allowing the purification procedure to proceed as described earlier. In the first suspension polymerization with brine, the concentrations of suspension stabilizers were 0.5 wt% for xanthan gum and 0.02 wt% for HPMC. The polymer beads obtained from this were small and varied significantly in size. The yield was less than 40%. To improve the yield, the concentrations were lowered from 0.5 to 0.25% for xanthan gum and from 0.02 to 0.01% for HPMC. With the lower concentrations of both suspension stabilizers, it was easier to obtain a good stirring rate. Stirring speed was important for the formation of monomer droplets and facilitated better size control. This polymerization gave a better yield, at 86%. A sample of the polymer products was analyzed with microscopy to evaluate the morphology and size range of the beads. Based on this analysis, the size range of the polymer beads was between 70 and 350 μm (Picture 3.3). Also, the polymer beads seemed to be spherical with a smooth surface.

Because the results of the suspension polymerizations with the suspension stabilizers xanthan gum and HPMC were rather poor, another suspension stabilizer was evaluated. This second

system for suspension polymerization in brine was based on an invention by Steffier [46]. The invention relates to a suspension polymerization conducted in the presence of a nonionic, substituted hydroxyalkyl cellulose suspension stabilizer, which effectively stabilize the monomer drops and prevent coalescence. According to the patent, the preferred stabilizer is hydroxyethyl cellulose containing between 0.1 to 10 C_{16} alkyl side chains per 100 anhydroglucose units and between 2.5 to 4 ethylene oxide groups substituting each anhydroglucose units [46]. The brine was prepared by dissolving 0.3 wt% 2-hydroxyethyl cellulose (HEC) and 25 wt% sodium chloride in water. For the polymerization, the monomer phase was prepared as mentioned earlier, and added to the brine under agitation (Scheme 3.3).

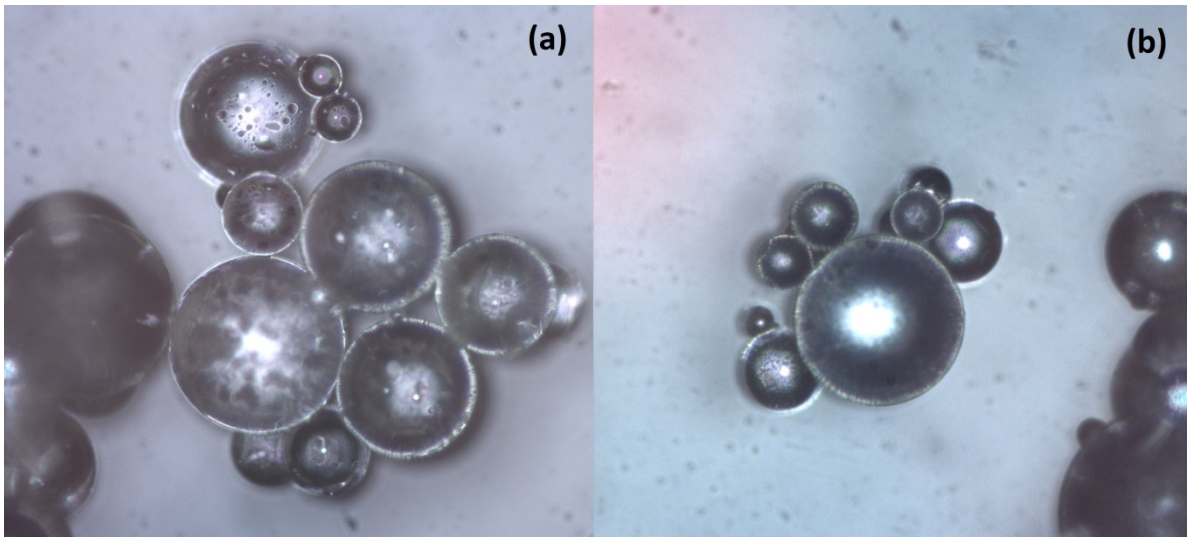


Scheme 3.3: Copolymerization of cross-linked poly(methyl acrylate-*co*-styrene) with benzoyl peroxide as initiator, toluene as phase-separation inhibitor and brine, containing 2-hydroxyethyl cellulose, as the continuous phase.



Picture 3.2:(a) Reaction mixture after suspension polymerization of styrene and methyl acrylate using 2-hydroxyethyl cellulose. (b) Cross-linked poly(methyl acrylate-*co*-styrene) beads after purification.

After polymerization, the suspension was treated using the same procedure as in the previous suspension polymerization in brine. The polymer beads obtained with this suspension polymerization system were large, clear beads varying slightly in size, with a yield of 83%. Characterization of the polymer beads using microscopy showed that these polymer products are slightly less polydisperse than the polymer beads synthesized using xanthan gum and HPMC as the suspension stabilizers (Picture 3.3). However, the size difference between the polymer products is not at large as expected. As mentioned earlier, the cross-linked poly(methyl acrylate-*co*-styrene) beads in brine using xanthan gum and HPMC as the suspension stabilizer gave beads in the size range of 70 to 350 μm. On the other hand, the polymer beads synthesized with the same monomers, but using 2-hydroxyethyl cellulose, were found to produce polymer beads in the range between 100-300 μm. This procedure therefore gave polymer beads in a slightly narrower size range and with a more consistent yield. The suspension polymerization with hydroxyethyl cellulose was therefore preferred when compared to suspension polymerization with xanthan gum and HPMC. The procedure was therefore scaled up, and the obtained polymer beads were purified further by continuous extraction using a Soxhlet apparatus with methanol as the solvent.



Picture 3.3: Isolated and purified cross-linked poly(methyl acrylate-*co*-styrene) beads obtained using (a) 2-hydroxyethyl cellulose and (b) xanthan gum and HPMC as suspending agents.

As these polymer beads were to be used for further experiments, samples of the polymer product was analyzed using CHN analysis and IR spectroscopy. Element analysis is a common technique for analysis of polymer beads. The technique can provide information

about the monomer composition of the polymer backbone and about the degree of functionalization. Element analysis can be used to detect several different atom types, and can be used to determine the total amount of the chosen elements in the total polymer structure. For instance, carbon, hydrogen, halogen, nitrogen, sulfur and phosphorus analyses are widely performed [56]. For the purpose of analyzing the untreated cross-linked poly(methyl acrylate-*co*-styrene) beads, the element analysis (CHN analysis) was used to evaluate the amount carbon, hydrogen and nitrogen in the polymer product. Based on the initial amount of monomers added to the copolymerization, the element composition would be expected to be C: 66.3%, H: 7.2% and N: <0.3% (detection limit for N) assuming full conversion. This theoretical composition is quite close to the obtained results from the CHN analysis, thus indicating that copolymerization was successful. The most pronounced absorption exhibited in the infrared spectrum obtained from the IR of the polymer beads was the C=O absorptions from methyl acrylate at 1733 cm^{-1}.

3.3.2 Synthesis of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads

The initial experiments focused on the synthesis of polymer beads suitable for further functionalization with reactive groups for decontamination. When these polymer beads were functionalized, they should therefore yield an efficient decontamination of nerve agents. However, the beads have no affinity towards the products formed during decontamination. Such decontamination byproducts can include hydrogen fluoride (HF) and hydrogen cyanide (HCN). The objective of decontamination is to convert toxic chemicals into non-toxic or less toxic compounds through chemical reactions (see theoretical background, chapter 2.3.1). Although the decontamination products are less toxic than the actual nerve agents, they may still be harmful if left in the environment. An ideal solution would be to include a functional monomer in the finished product, which can bind the products of decontamination. This functional monomer could either be included in the same polymer beads or in separate polymer beads. If the functional monomer is to be included in the same polymer beads, it is important that it stays inert during the functionalization process.

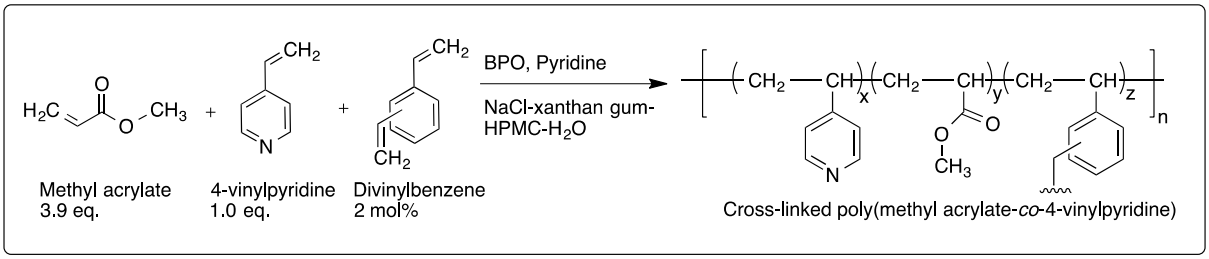
As it would be very desirable to obtain a product for both decontamination and binding of the formed decontamination products, a suitable monomer had to be identified. The monomer should be able to copolymerize with methyl acrylate, using the procedure established for methyl acrylate and styrene. The functional monomer should also have a high affinity toward the decontamination products. Because most decontamination products from nerve agents are

acidic, the functional monomer should have the ability to bind such byproducts (see theoretical background, chapter 2.3.2). The first functional monomer chosen for this purpose was 4-vinylpyridine. This monomer was presumed to be suitable for copolymerization due to its polarity and structural similarities to styrene. 4-vinylpyridine is a derivate of pyridine with a vinyl groups attached to the 4-position. The acid-binding properties of 4-vinylpyridine is due to the structural similarities to tertiary amines. Due to its structure, it is expected to be inert during the functionalization reaction. As the polymeric nerve agent decontaminant is intended for use in aqueous environments, it is important to find the right balance between the hydrophobic and the hydrophilic properties of the polymer product. Incorporation of 4-vinylpyridine is expected to increase the water-compatibility of the decontaminant, which will provide easier access to the hydroxamic acid moieties.

The first attempt of synthesizing polymer beads with 4-vinylpyridine was carried out using the same procedure as for methyl acrylate and styrene. However, it soon became apparent that the polymerization of this monomer presented certain unusual features. One of these unusual features is the solubility of the monomer in organic solvents, which was very restricted. When the monomer is added to toluene, something resembling instant polymerization occurs, resulting in the formation of a gum-like material. As toluene was unable to dissolve 4-vinylpyridine, a more suitable phase-separation inhibitor had to be identified. Several solvents were tested, including *N*-methyl-2-pyrrolidone, dichloromethane, cyclohexanone and pyridine. Dichloromethane completely dissolved the monomer, but as it is a weak chain-transfer agent and far too volatile for polymerization (bp. 40 ^{0}C), it would be a poor choice. After several attempts, pyridine was found to be the best solvent and was used in further suspension polymerizations with 4-vinylpyridine.

Even though the use of xanthan gum and HPMC as suspension stabilizers was found to give poorer results than 2-hydroxyethyl cellulose, both suspension systems were tested in the copolymerization of 4-vinylpyridine and methyl acrylate. The first polymerization was carried out in brine using xanthan gum and HPMC as suspension stabilizers. The monomer phase was prepared as before, but with pyridine as the phase-separation inhibitor instead of toluene due to the restricted solubility of 4-vinylpyridine. The monomer phase was prepared by dissolving initiator, cross-linker and monomers in pyridine (Scheme 3.4). However, the solution became opalescente with addition of methyl acrylate. The reason for this is probably the restricted solubility of 4-vinylpyridine in methyl acrylate. Acrylates are generally poor solvents, thus

small quantities of 4-vinylpyridine precipitates in the solution. As most of the 4-vinylpyridine is expected to remain dissolved in the monomer phase, the polymerization was continued. The solubility would also improve as the temperature was increased to initiate the polymerization.



Scheme 3.4: Copolymerization of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) with benzoyl peroxide as initiator, pyridine as phase-separation inhibitor and brine, containing the combination of xanthan gum and HPMC as stabilizers, as the continuous phase.

After polymerization, the suspension was treated in the same manner as with the previous suspension polymerizations in brine. After separation and purification, the size range and morphology of the particles were analyzed. Many of the beads were clustered together, but they seemed to be spherical particles, mainly in the size range of 70 to 370 µm (Picture 3.5). This is slightly larger than for the cross-linked poly(methyl acrylate-*co*-styrene) beads. The reason for this is probably that pyridine is a poorer phase-separation inhibitor, which allows the monomer to diffuse out of the monomer droplets and polymerize there.

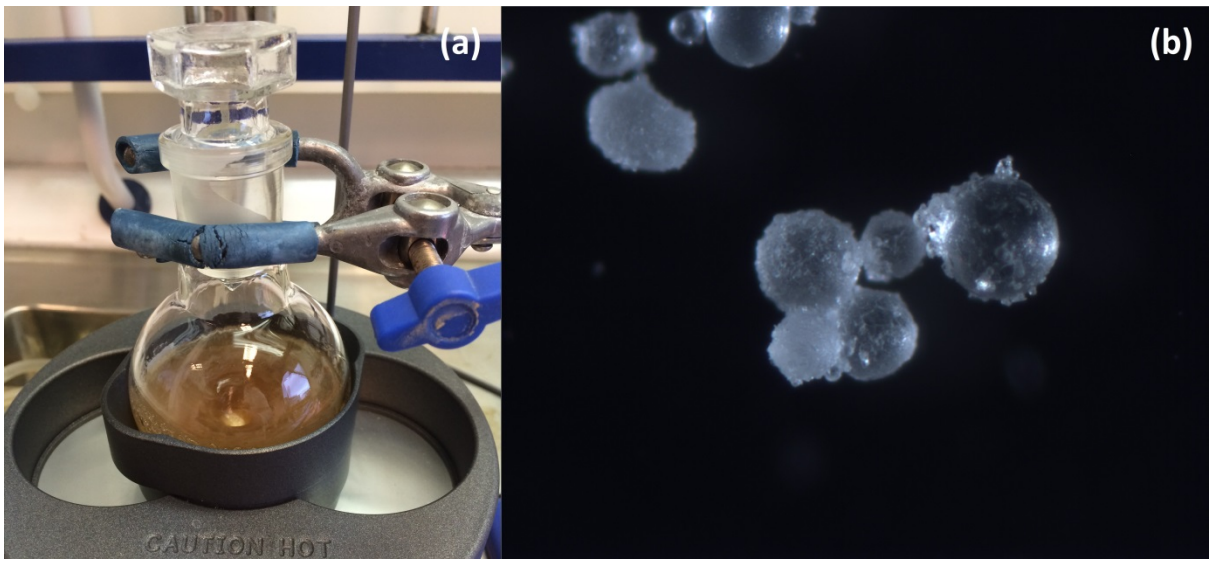
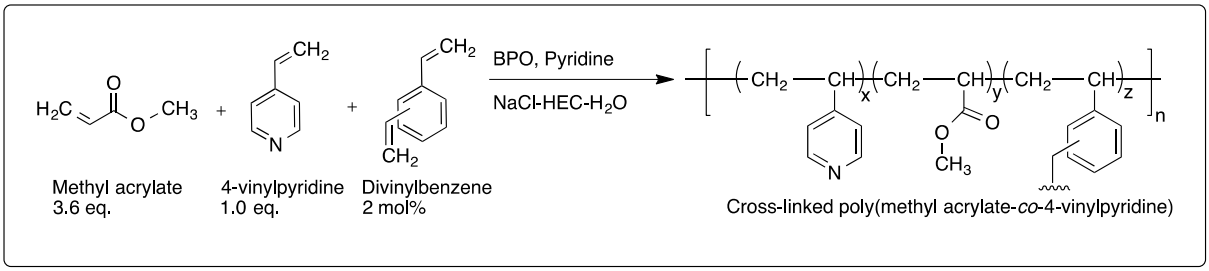


Figure 3.4: (a) Reaction mixture after suspension polymerization of 4-vinylpyridine and methyl acrylate using 2-hydroxyethyl cellulose as a suspension stabilizer. (b) Cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads after purification.

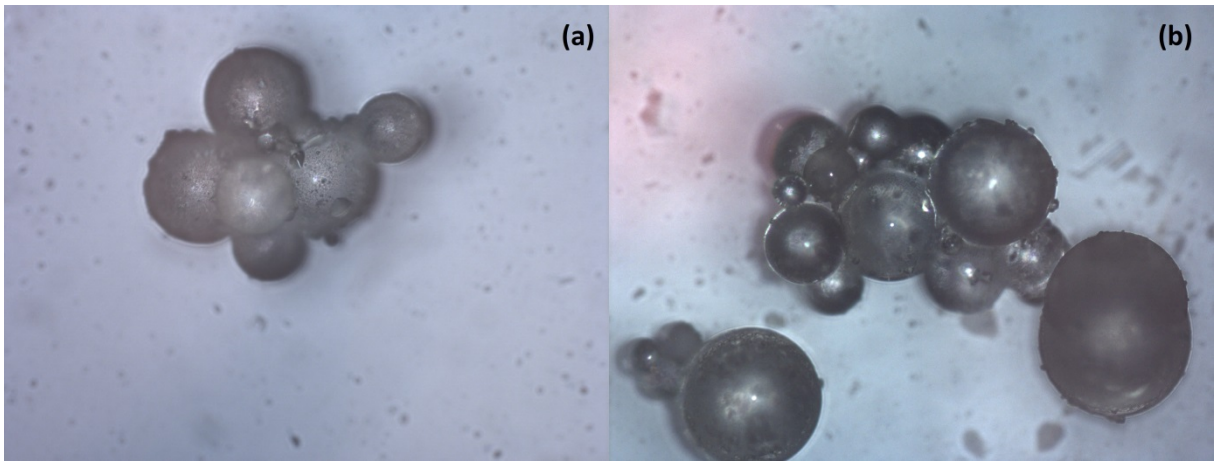
Polymerization of 4-vinylpyridine and methyl acrylate was also attempted using 2-hydroxyethyl cellulose as suspending agent. The polymerization was carried out following the general procedure, and pyridine was used as a phase-separation inhibitor. The monomer phase was prepared by dissolving initiator, cross-linking agent and 4-vinylpyridine in pyridine as the phase-separation inhibitor (Scheme 3.5). Methyl acrylate was added to the monomer phase at the end, the addition was carried out under swirling to prevent precipitation of 4-vinylpyridine. The monomer phase was then added to the continuous phase under agitation. Separation and purification of the polymer beads was carried out following the same procedure as used previously.



Scheme 3.5: Copolymerization of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) with benzoyl peroxide as initiator, pyridine as phase-separation inhibitor and brine, containing 2-hydroxyethyl cellulose as the suspension stabilizer, as the continuous phase.

As seen with the cross-linked poly(methyl acrylate-*co*-styrene) beads, the use of 2-hydroxyethyl cellulose yielded polymer beads with a more consistent size distribution than the polymer beads prepared using xanthan gum and HPMC. This suspicion was confirmed by microscopy, as the particles prepared with 2-hydroxyethyl cellulose are in the size range of 100 to 300 μm, which is slightly narrower (Picture 3.5). The polymer beads had a light brown color and were obtained in a yield of 88%. Analysis of the morphology of the cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads showed polymer beads with rough surfaces due to adherence of small particles (Picture 3.4). The beads seemed to be spherical. However, the polymer beads are covered with small particles. This might be due to pyridine being a poor phase-separation inhibitor, which may lead to some of the monomer mixture diffusing into the continuous phase nucleating small particles there during polymerization. However, the majority of the polymer beads are large, which suggests that the beads are reasonable stabilized in the continuous phase. Because the suspension polymerization using 2-hydroxyethyl cellulose gave better results, this procedure was scaled up and the obtained

polymer beads were further purified for analysis by continuous extraction using a Soxhlet apparatus with methanol as the solvent.



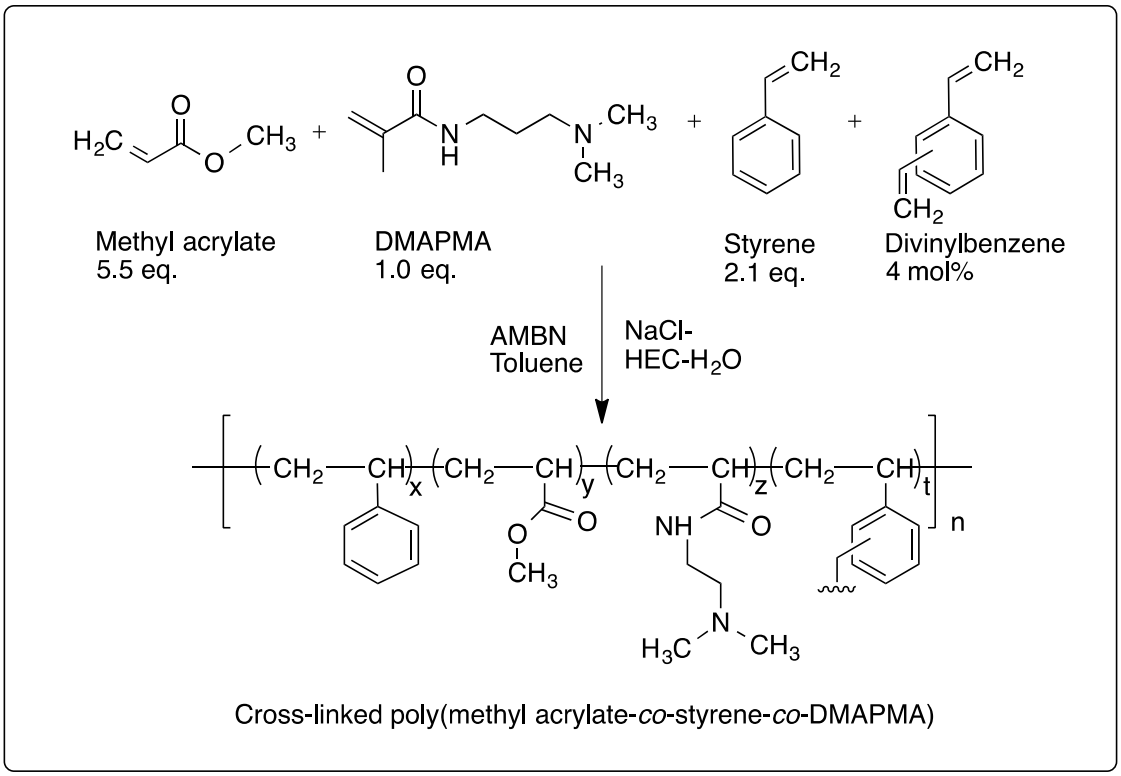
Picture 3.5: Comparison of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads prepared using (a) 2-hydroxyethyl cellulose and (b) the combination of xanthan gum and HPMC as suspending agents.

As the polymer beads were used in further work in this thesis, a sample of the polymer product was sent for CHN analysis. The CHN analysis was used to obtain information about the content of carbon, hydrogen and nitrogen in the polymer beads. This information can be used to determine how much of the initial monomers have been incorporated into the polymer product. If every monomer in the initial monomer phase had been copolymerized, the element composition would be C: 62.8%, H: 6.9% and N: 3.9%. This theoretical element composition is quite close to the obtained results from the CHN analysis, thereby indicating that copolymerization was successful. As well as CHN analysis, IR was used to analyze the cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads. Like the IR spectrum obtained from the cross-linked poly(methyl acrylate-*co*-styrene) beads, the most distinct absorption was the C=O stretching from methyl acrylate at 1733 cm^{-1}.

3.3.3 Synthesis of cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads

The second functional monomer chosen for use as an acid-scavenging monomer in the polymer beads was *N*-[3-(dimethylamino)propyl]methacrylamide (DMAPMA). Unlike 4-vinylpyridine, DMAPMA has no structural similarities to styrene. The monomer was chosen for its tertiary amino group, which is expected to have good affinity towards the acidic decontamination byproducts. The monomer has a high water-solubility, much greater than methyl acrylate. By including this monomer in the polymer backbone, it was anticipated that it would increase the hydrophilic properties of the polymer-support, thus providing easier access to the reactive moieties. To maintain the right balance of hydrophilic and hydrophobic groups in the polymer beads, styrene was included. The incorporation of styrene provides affinity towards the hydrophobic nerve agents in an aqueous environment and makes the reactive moieties reachable for them. DMAPMA is a functional monomer with a tertiary amine group and a vinyl group. The monomer may be homopolymerized, but is best suited for copolymerization with other unsaturated monomers [59]. The polymer products formed with this monomer are widely used as absorbent or flocculants in water treatment, or as water treatment agents. The monomer is soluble in water and most organic solvents. This is an advantage for the copolymerization, as toluene can be used as the phase-separation inhibitor.

The first polymerization with DMAPMA was performed in 2-hydroxyethyl cellulose using the same procedure as previously, with two exceptions (Scheme 3.6). As DMAPMA contains a tertiary amine, benzoyl peroxide was not used as an initiator. Amines and peroxides are not chemically compatible, as peroxides tend to react with amines. Instead, an oil-soluble azo-initiator is used, as they are generally more chemically inert towards amines. Because of this, the azo-initiator AMBN was used throughout all polymerizations with DMAPMA. Also, the polymer product was expected to have a high degree of solvation of the polymer network in aqueous environment due to the high water solubility of DMAPMA. The degree of cross-linking in these polymer beads was therefore increased to 4 mol% to prevent excessive swelling.



Scheme 3.6: Copolymerization of cross-linked poly(methyl acrylate-*co*-styrene-co-DMAPMA) with AMBN as initiator, toluene as phase-separation inhibitor and brine, containing 2-hydroxyethyl cellulose as the suspension stabilizer, as the continuous phase.

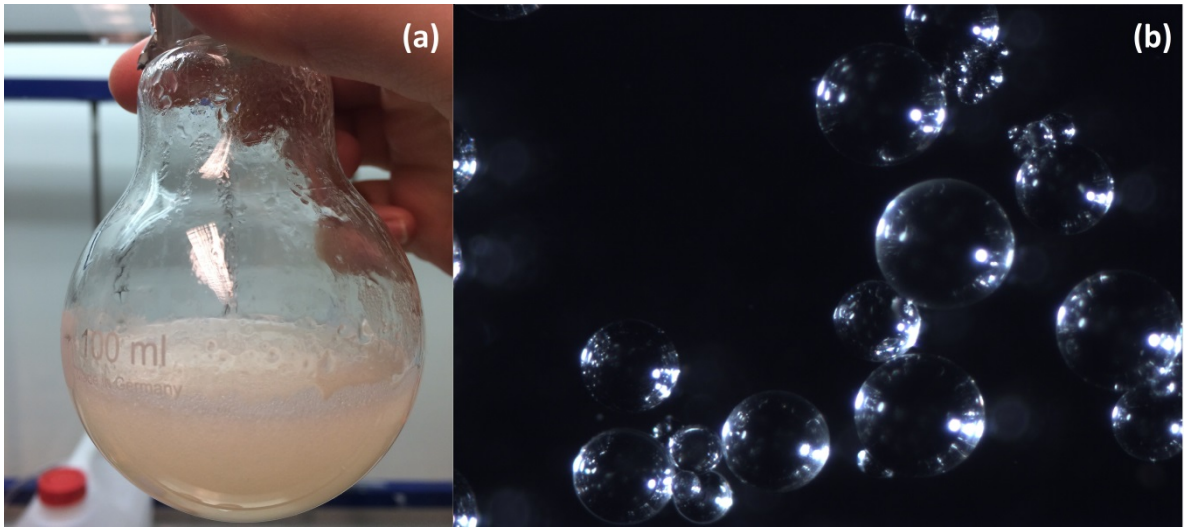
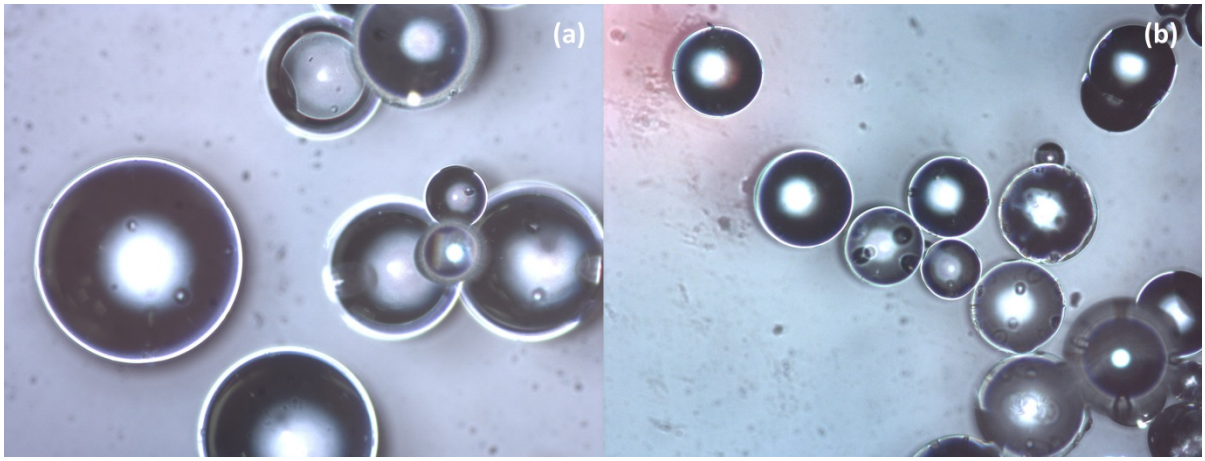


Figure 3.6: (a) Reaction mixture from suspension polymerization of DMAPMA, styrene and methyl acrylate. (b) Purified cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads after separation and purification.

Separation and purification of the polymer beads were attempted using the same procedure as described previously. However, the supernatant proved difficult to decant as portions of the

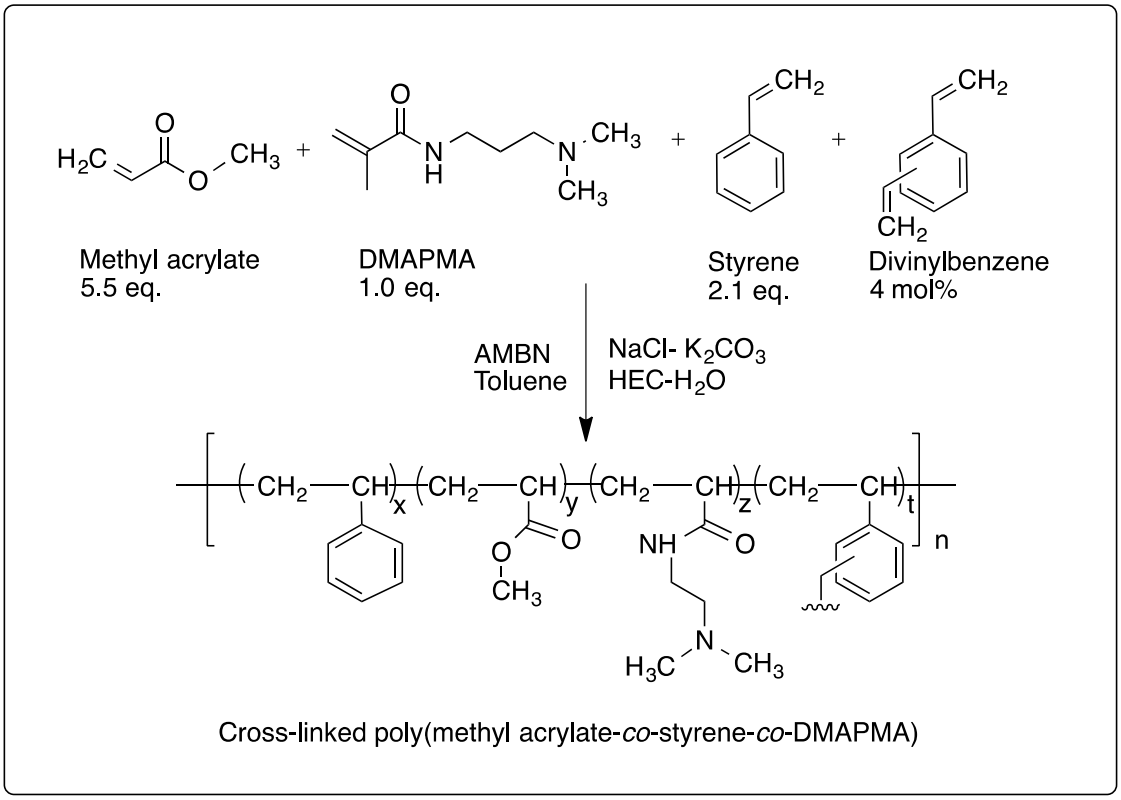
cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads seemed unable to sediment. The decantation step of the purification procedure could therefore not be applied. Due to the hydrophilic properties of DMAPMA, the polymer product was expected to be more hydrophilic and therefore to swell more in water than the other polymer beads described up to this point. However, the cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads seemed to swell less than the former polymers, not more. This is not an unknown phenomenon in polymer science, as it often happens that the desired properties of the monomer are not transmitted to the polymer product. To solve this problem, decantation was carried out in methanol. The supernatant could then be decanted, but the beads clogged the filter during vacuum filtration. As the use of methanol facilitated sedimentation of the beads, but prevented vacuum filtration, the decantation step was carried out using a mixture of water and methanol in hope that the reduced density of the solution would facilitate sedimentation of the polymer beads. This time, the supernatant was easily decanted and the purification procedure was continued.



Picture 3.7: Cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads prepared (a) with an alkaline continuous phase and (b) without an alkaline continuous phase.

The polymers obtained from the polymerization were clear, spherical beads with a smooth surface. The particles appeared smaller than other polymer beads prepared using the same procedure, stirring speed and temperature. The polymerization also gave a poor yield, typically around 40 to 50%. Microscopy of the polymer products showed that the greater part of the polymer beads were in the size range of 60-300 μm (Picture 3.7). The polymer beads were within the range of the cross-linked poly(methyl acrylate-co-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads, although the lower part of the size range had a slightly

lower limit. Although the size range of the polymer beads are approximately the same as for the previous products prepared in brine, the low yields obtained implies that the procedure is not ideal. The structure of DMAPMA slightly resembles an emulsifier, with a hydrophilic head and a hydrophobic tail. A feasible explanation could therefore be that DMAPMA acts as an emulsifier, which could cause something similar to emulsion polymerization. This can be avoided by adding an alkaline compound to the continuous phase, thereby effectively preventing diffusion of the monomer during polymerization. Further suspension polymerization with DMAPMA was therefore carried out with a small amount of potassium carbonate (giving pH=12 in the continuous phase) dissolved in the continuous phase (Scheme 3.7).



Scheme 3.7: Copolymerization of cross-linked poly(methyl acrylate-*co*-styrene-co-DMAPMA) with AMBN as initiator, toluene as phase-separation inhibitor and brine, containing some added K_2CO_3 and 2-hydroxyethyl cellulose as the suspension stabilizer as the continuous phase.

The polymer beads obtained from suspension polymerization under alkaline conditions were separated by decantation using a mixture of water and methanol, followed by vacuum filtration. The resulting polymer beads were clear, spherical and larger than the previously

synthesized beads. The polymerization also gave a better yield, at 65%. Microscopy of the polymer products obtained with this procedure revealed them to be larger than the cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads obtained previously. The majority of the polymer beads were in the range of 150-500 μm (Picture 3.7). As this procedure gave larger polymer beads, it could suggest that the DMAPMA monomer was functioning to some extent as an emulsifier during the polymerization. Based on these results, the polymerization was scaled up. Several polymerizations at larger scale were attempted using this procedure. However, polymerization resulted in low yields and small polymer beads, and the use of DMAPMA as an acid-scavenging monomer was abandoned.

Although further use of DMAPMA in the copolymerization of reactive polymer beads for decontamination of nerve agents was abandoned, a sample of the cross-linked poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) prepared in an alkaline medium was analyzed using CHN analysis. By doing this, it could be determined how much DMAPMA that had been incorporated during the polymerization. The composition of monomers present in the monomer phase at the start of the polymerization was used to estimate the element composition of the polymer product, assuming that all monomers had been copolymerized. This estimated element composition would be approximately C: 65.8%, H: 7.9% and N: 3.1%. Interpretation of the results from the CHN analysis showed that the carbon and nitrogen content of the polymer beads were significantly lower than the estimated values. This indicated that only about half of the DMAPMA initially added to the monomer phase actually have been incorporated into the polymer beads, and that a considerable amount of monomer had diffused into the continuous phase. In addition, there was a considerable variance in the measurements of nitrogen in the three parallels (N: 1.9, 1.8, 2.4). This suggests that the incorporation of DMAPMA during polymerization varies greatly, thus leading to large variations of detectable nitrogen in the CHN analysis.

3.4 Incorporation of hydroxamic acid functionalities through post-modification of polymer beads

Functionalized polymer beads are polymers beads to which functional group are either physically or chemically attached, preferably covalently bound. Functionalization of polymer beads is generally achieved through incorporation of functional monomers during polymerization or through post-modification. When functionalized monomers are used for polymerization, the functional groups can be uniformly distributed in the polymer structure,

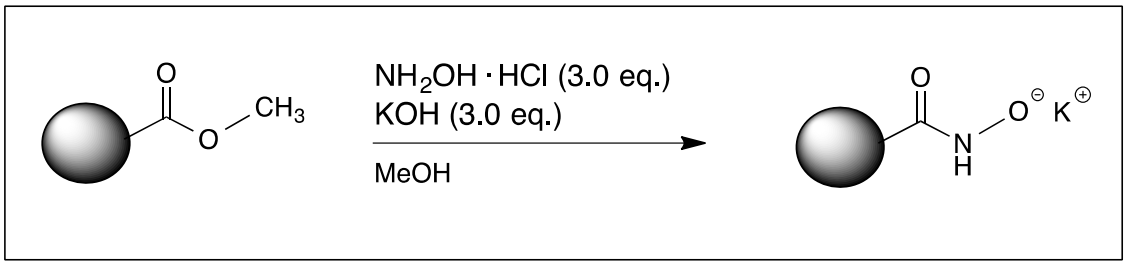
but considerable manipulation is required to obtain a good yield of the product. The reactive polymer beads in this thesis cannot be produced using this method, mainly due to two reasons. Firstly, acrylates are almost impossible to convert into hydroxamic acid directly. The reason for this is that the hydroxylamine would react as a nucleophile through 1,4-addition or Michael addition on the methyl acrylate. In the unlikely event of managing to obtain such conversion, the monomers would be impossible to copolymerize with styrene, due to the enormous difference in solubility properties. The functionalization of polymers in work presented in this thesis was therefore obtained through post-modification. Post-modification provides a non-uniform distribution of functional groups. Vinyl-type monomers can be used to produce reactive polymers of both methods, although post-modification is probably the most frequently used.

One of the most frequently used strategies for post-modifications is the functionalization of active ester polymers. Numerous examples of active acrylate ester polymers as starting materials for preparation of hydroxamic acid polymers have been described [63-65]. An example of such polymerization and functionalization was reported by T. S. Lee *et al.* [63]. In the work described in that paper, cross-linked poly(ethyl acrylate) beads were prepared by suspension polymerization. Further, the ethyl acrylate moieties in the polymer structure were converted into hydroxamic acid through reaction with hydroxylamine hydrochloride. Some of the most common acrylate monomers used for this purpose are methyl, ethyl and propyl acrylate. The reason for this is the relatively reactive leaving group of the monomers. Active ester acrylates are most commonly used in functionalization reactions with amines, as they are known to react under mild conditions and forming the corresponding amides in high yields [66-67]. The work presented in this thesis was focused on the conversion of methyl acrylate to the corresponding anion of hydroxamic acid. This was achieved through reaction with hydroxylamine. The different strategies tested to accomplish such functionalization are described below.

3.4.1 Functionalization by reaction with hydroxylamine hydrochloride

The first functionalization procedure was based on the procedure reported by T. S. Lee *et. al* [63] (Scheme 3.8). An amount of hydroxylamine hydrochloride, approximately corresponding to 3 equivalents when compared to the expected quantity of methyl acrylate in the polymer beads, was dissolved in methanol under stirring. The expected amount of methyl acrylate moieties in the polymer product was calculated based on the amount of monomer added and

the number of incorporated methyl acrylate moieties, assuming complete conversion. If all the methyl acrylate monomers dissolved in the dispersed phase is incorporated during polymerization, the functional monomer should constitute about 72% of the polymer product. The expected quantity of methyl acrylate can then be calculated and used to determine the needed amount of hydroxylamine. After dissolution of hydroxylamine hydrochloride was completed, potassium hydroxide was added to the solution. Potassium hydroxide is added to release free hydroxylamine under formation of potassium chloride, thereby leaving hydroxylamine available for reaction with the acrylate ester. When all potassium hydroxide had dissolved, the polymer beads were added. The temperature of the reaction mixture was set to 65 °C over night, to ensure that the functionalization was completed.

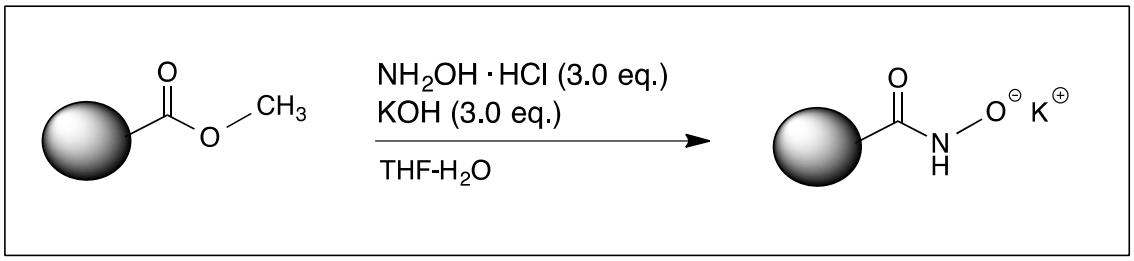


Scheme 3.8: Conversion of methyl acrylate to the hydroxamate anion of hydroxamic acid using methanol as the reaction medium.

After functionalization, the mixture was cooled down to room temperature before being vacuum filtrated. The polymer beads were washed with methanol, 0.1 M HCl and then water. The hydrochloric acid was added in order to convert hydroxamate anions to hydroxamic acid. The simplest method for determining if the ester groups had been functionalized with hydroxamic acid is to see if the polymer beads swell in neutral and/or alkaline water. If the ester groups have been converted to hydroxamic acid groups, the polymer beads should be able to swell in water as the hydroxamic acid provides better hydrophilic properties. The alkaline solution should promote conversion into the corresponding hydroxamate anion. However, no swelling could be observed which indicated that little or no reaction between the acrylates and hydroxylamine had occurred. The reason for this may be that methanol is a poor solvent for the polymer beads, thus providing insufficient swelling of the polymer network and preventing hydroxylamine access to the interior of the particles.

Because of the poor results from the first functionalization reaction, methanol as reaction solvent was replaced with a mixture of water and THF. THF was chosen as it was found to

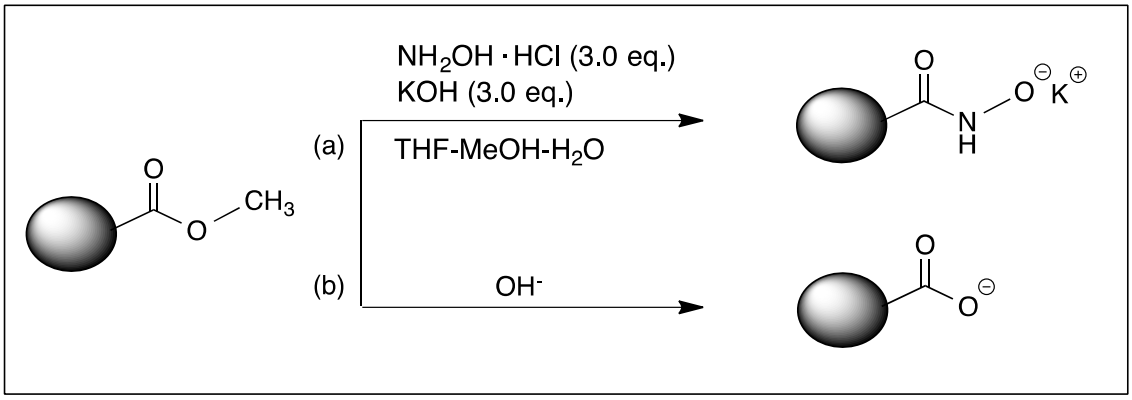
provide good swelling of the polymer beads (see chapter 3.3.1). Except for replacing the solvent, the reaction procedure was carried out as described earlier (Scheme 3.9). As before, swelling of the functionalized polymer beads was tested in both neutral and alkaline water, but the beads did not swell in either of them. During purification, the polymer beads seemed to collapse with the addition of HCl. The use of HCl during purification of the polymer beads was therefore removed. As the polymer beads obtained gave little swelling in alkaline water, a new procedure with different composition of the solvent was chosen. The poor result could also be due to the large amounts of water used in the procedure, which might inhibit completion of the reaction.



Scheme 3.9: Conversion of methyl acrylate to the hydroxamate ion of hydroxamic acid using a mixture of THF and water as the reaction medium.

The third attempted procedure for conversion of methyl acrylate to hydroxamic acid was carried out in a solution consisting of THF, methanol and water. The ratios of the solvents were 2:1:1 (Scheme 3.10). The THF should promote swelling of the unreacted polymer beads and therefore allow the reagent to access the interior of the particles. As the conversion of ester groups proceeds, the polymer beads should become more hydrophilic. Thus, the presence of water should aid swelling of the functionalized polymer beads. Also, the total volume of the solution was decreased to obtain a higher concentration of hydroxylamine. To ensure that the hydroxamic acid groups were converted to the corresponding hydroxamate ion, potassium hydroxide was added to the solution before terminating the reaction. The amount corresponded to one equivalent of the expected amount of methyl acrylate in the polymer backbone. Swelling of polymer beads functionalized with this procedure was only attempted in neutral water, as the hydroxamate anions should provide solvation of the polymer network. The functionalized polymer beads showed good swelling in water, which indicates that the functionalization had been successful. However, it could also be a result of the harsh reaction conditions, which might have led to the hydrolysis of the ester. Hydrolyzed polymer beads would also be expected to swell in water. Such harsh reaction conditions

occurs after addition of KOH to the reaction mixture, as the dissolution process is very exothermic, which leads to an increase in the temperature in the reaction mixture. A new procedure was therefore developed.



Scheme 3.10: (a) Conversion of methyl acrylate to the hydroxamate ion of hydroxamic acid using a mixture of THF and water as the reaction medium. (b) With harsh reaction conditions, hydrolysis of the ester may occur.

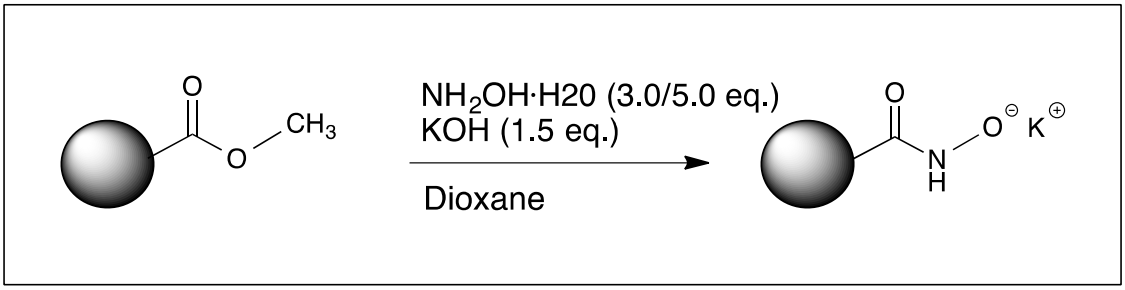
3.4.2 Functionalization of polymer beads by reaction with aqueous hydroxylamine

In further procedures, the hydroxylamine salt was replaced by an aqueous solution containing 50% hydroxylamine. By using this aqueous solution, there is no need for addition of potassium hydroxide for the removal of hydrogen chloride to make free hydroxylamine available for reaction. The aqueous hydroxylamine solution (3 or 5 equivalents relative to the expected content of methyl acrylate in the polymer structure) was mixed with THF. Polymer beads were charged directly in a round-bottom flask, and the solution of aqueous hydroxylamine and THF was added drop-wise. The use of agitation with a magnet was left out in these procedures; instead it was assumed that diffusion of hydroxylamine from the solution would ensure conversion of methyl acrylate moieties to hydroxamic acid. The reaction temperature was reduced to 40 °C, to avoid evaporation of hydroxylamine. Due to the poor miscibility of THF with aqueous hydroxylamine, the reaction mixture comprised two phases. To avoid this, an alternative solvent with better compatibility with water was used in the second attempt using this procedure. Dioxane was found to be the best alternative, as it is completely miscible with both hydroxylamine and water. The same procedure was carried out with dioxane as the reaction solvent. However, neither of the functionalized products swelled in either neutral or alkaline water.

Despite the poor swelling in both neutral and alkaline water of these polymer beads, a sample of cross-linked poly(methyl acrylate-*co*-styrene) beads functionalized using the previous procedure was analyzed by with both CHN analysis and IR spectroscopy. The CHN analysis of the untreated polymer particles, as discussed earlier (chapter 3.3.1), showed no detectable nitrogen in the polymer structure. If the methyl acrylate moieties in the polymer beads had converted, a significant change in the nitrogen content in the CHN analysis is expected. When comparing the element composition from the untreated particles and the polymer beads functionalized using the combination of dioxane and aqueous hydroxylamine as the reaction medium, no significant changes could be observed. Both the carbon and hydrogen levels were nearly identical, and the nitrogen level was still below the detection limit. This indicated that the conversion of methyl acrylate to hydroxamic acid had been unsuccessful. In addition to CHN analysis, the polymer beads were analyzed with IR spectroscopy. The IR spectrum of the polymer beads functionalized using dioxane in combination with aqueous hydroxylamine as the reaction medium was compared to the spectrum of the untreated polymer particles. The IR spectrum of the functionalized polymer beads contained the same bands as the spectrum of the untreated beads. The lack of change in the bond stretches further validated that the functionalization using this procedure had been unsuccessful.

Due to the lack of conversion of methyl acrylate moieties obtained from the previous functionalization procedure, a new procedure was developed. Although there is no need for potassium hydroxide to release hydroxylamine from its hydrochloride, it was added throughout further procedures to obtain the hydroxamate anion of hydroxamic acid. The reason for the hydroxamic acid moieties being converted to the corresponding hydroxamate anions is the expected increase in efficiency of CWA decontamination achieved though such conversion as the nucleophilicity of the moieties are increased [25]. Additionally, an excess of hydroxylamine was used to ensure that the functionalization yielded full conversion. The quantity of hydroxylamine used corresponded to 3 or 5 equivalents relative to the expected quantity of methyl acrylate in the polymer product. In the previous procedures for functionalization, base was added at the end of the reaction to obtain the anion of hydroxamic acid. By doing this, the exothermic reaction occurring when potassium hydroxide is dissolved in a solvent might promote other reactions, such as hydrolysis (Scheme 3.10b). As mentioned before, hydrolyzed polymer-supports will also swell in water, which may give the impression of a successful functionalization. To avoid hydrolysis of the functional groups, the potassium hydroxide was dissolved in the reaction mixture before initiating the reaction. Therefore,

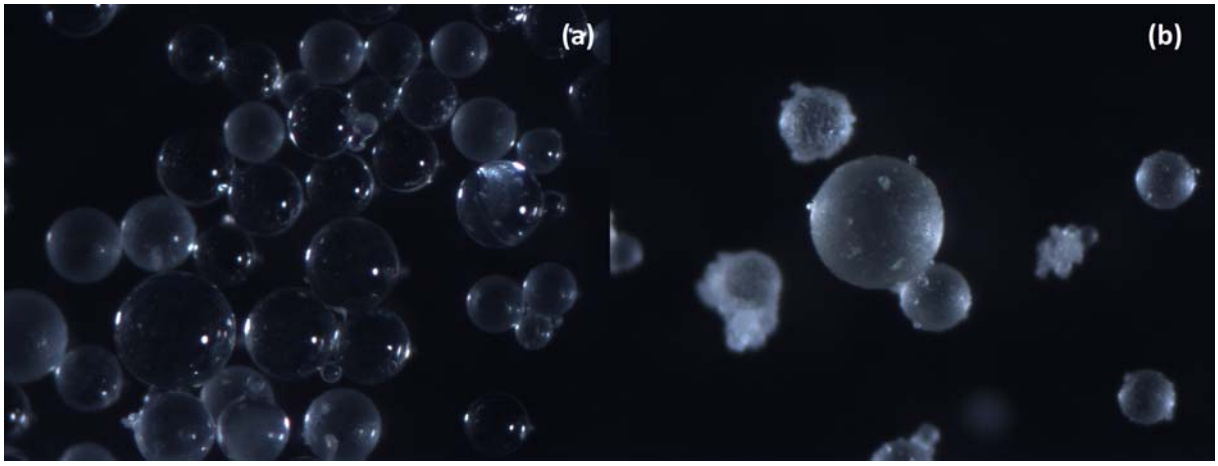
potassium hydroxide was completely dissolved in the aqueous hydroxylamine solution, before adding the dioxane. Addition of a strong base should deprotonate the hydroxylamine, thus providing a greater reactivity of the reagent. The amount of base used corresponded to 1.5 equivalents of the expected amount of methyl acrylate moieties in the polymer beads. Once potassium hydroxide was dissolved in the hydroxylamine, the solution was no longer miscible with dioxane. Nevertheless, the mixture was added drop-wise to the polymer beads and the temperature was set to 40 °C.



Scheme 3.11: Conversion of methyl acrylate into the hydroxamate anion of hydroxamic acid using a mixture of dioxane, aqueous hydroxylamine and potassium hydroxide as the reaction medium.

Initially, the polymer beads swelled in the dioxane and were therefore suspended over the aqueous hydroxylamine. However, being left in the reaction mixture over night, the polymer beads were located at the bottom. This might indicate functionalization of the methyl acrylate had occurred and that the solvation of the polymer network in dioxan had decreased. The polymer beads were purified using the same procedure as earlier. Since the functionalized beads were slightly sticky when added to methanol, it was found that soaking the polymer beads in water simplified the transfer to vacuum filtration drastically. When water was added, the polymer beads swelled significantly. To determine if the increased swelling of the polymer beads meant that functionalization had been successful or if the methyl groups were hydrolyzed, the polymer beads were analyzed using CHN analysis and IR spectroscopy. Weighting of the functionalized polymer beads also showed an increase in weight, which could indicate functionalization and incorporation of potassium, however this increase in weight would also occur after hydrolysis. Nevertheless, successful functionalization was confirmed through both CHN analysis and IR spectroscopy.

Samples of both cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads functionalized using dioxane, aqueous hydroxylamine and potassium hydroxide as the reaction mixture (Scheme 3.12), were analyzed using CHN analysis and IR spectroscopy. As the hydroxamate anion was the only moiety in the cross-linked poly(methyl acrylate-*co*-styrene) beads containing nitrogen, all nitrogen observed in the element composition was be assumed to belong to the converted moieties. The amount of nitrogen per gram polymer beads was calculated to be 3.6 mmol. As the monomers in the polymer backbone, except methyl acrylate, are expected to be inert to the functionalization reaction, the amount of methyl acrylate moieties converted into the hydroxamate anion was estimated to be approximately 40-50%.



Picture 3.8: (a) Functionalized cross-linked poly(methyl acrylate-*co*-styrene) beads. (b) Functionalized cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads.

Additionally, the cross-linked poly(methyl acrylate-*co*-styrene) beads were analyzed using IR spectroscopy. However, the absorption signal from the analyzed polymer beads was rather low compared to the untreated particles. Analysis of the spectra from both the untreated and the functionalized polymer beads showed that the absorption band at 1727 cm^{-1} detected for the untreated polymer particles, which is characteristic of an ester, disappeared after functionalization. The fact that this absorption band disappears after functionalization indicated that all methyl acrylate moieties had been converted, while the CHN analysis indicated only partial conversion of the methyl acrylate moieties. Taken together, this suggested that the degree of conversion varied in the polymer structure. As the CHN analysis showed incomplete conversion, the carbonyl absorption from the ester should be detected in both the untreated and functionalized polymer samples. However, the IR spectroscopy

analyses only the surface of the polymer beads, unlike CHN analysis, which provides an average value of the entire polymer composition. Therefore, it can be assumed that the functionalization was complete on the polymer surface, but decreased progressing into the polymer structure. This indicated that dioxane was unable to solvate the entire polymer network. In that case, dioxane would provide hydroxylamine access to the polymer surface but not to the entire interior of the polymer structure, hence giving uncompleted conversion of methyl acrylate moieties. The IR spectrum also showed the appearance of two new bands at 1627 cm^{-1} and at 1556 cm^{-1} after functionalization. Both bands are associated with the amide of the hydroxamate moiety. The bond at 1627 cm^{-1} represent the carbonyl stretch of the amide and the bond at 1556 cm^{-1} represents the N-H stretch. In addition, a stretching absorption at 3200 cm^{-1} could be observed, this is the amine stretch of the hydroxamate moiety.

The determination of converted moieties in the cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads through CHN analysis is complicated by the presence of the nitrogen atoms in the 4-vinlypyridine moieties. Through calculations of the element composition obtained after conversion, the amount of methyl acrylate moieties converted to the hydroxamate anion was estimated to be around 40-50%. The cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads were also analyzed using IR spectroscopy. As for the cross-linked poly(methyl acrylate-*co*-styrene) beads, the signal obtained from IR spectroscopy was lower for the functionalized beads than for the untreated beads. When comparing the two IR spectra, the same changes in absorptions could be observed as for the cross-linked poly(methyl acrylate-*co*-styrene) beads. After functionalization, the absorption of carbonyl stretch characteristic for the ester at 1726 cm^{-1} seemed to have disappeared. However, a small absorbance around 1700 cm^{-1} could be observed. This could be the stretching absorbance of the carbonyl belonging to the methyl acrylate, as conversion only would be expected to be around 40-50% based on the values obtained from the CHN analysis. Since the absorbance is very weak, it was assumed that conversion of methyl acrylate moieties on the polymer surface was almost complete, and that the degree of conversion decreased progressing into the polymer structure. As for the cross-linked poly(methyl acrylate-*co*-styrene) beads, this indicated that dioxane was unable to solvate the entire polymer network completely, hence limiting the reaction between hydroxylamine and the methyl acrylate moieties on the interior of the polymer beads. Also, two new bands at 1634 and 1557 cm^{-1} characteristic for the amide had appeared after functionalization. The stretching absorption of the amine, at 3200 cm^{-1}, could also be observed for the functionalized poly(methyl acrylate-*co*-4-vinylpyridine) beads.

4. Conclusion and future prospects

4.1 Conclusion

A suspension polymerization technique for copolymerization of methyl acrylate and styrene in brine, using 2-hydroxylethyl cellulose as the suspension stabilizer, was successfully developed and used for the synthesis of cross-linked poly(methyl acrylate-*co*-styrene) beads. The established suspension polymerization technique was then used to incorporate acid-scavenging monomers through copolymerization of methyl acrylate with the acid-scavenging monomers 4-vinylpyridine and DMAPMA, producing cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) and poly(methyl acrylate-*co*-styrene-*co*-DMAPMA). The incorporation of DMAPMA proved more difficult than expected due to structural characteristics similar to emulsifiers, giving a low incorporation of the monomer and low yields. The synthesis of cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads was more successful, giving high incorporation of monomers and high yields. Therefore, these two polymer products were used for further functionalization with hydroxylamine to obtain conversion of methyl acrylate to the hydroxamate anion. Suspension polymerization of cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads was also attempted in brine using the combination of xanthan gum and HPMC as suspension stabilizers. However the use of 2-hydroxyethyl cellulose as the suspension stabilizer gave slightly less polydisperse polymer particles and a more consistent yield.

The functionalization proved more difficult than expected, and several reaction conditions were tested in order to obtain a suitable procedure for conversion of methyl acrylate. The successful functionalization of cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads was confirmed through both CHN analysis and IR spectroscopy, giving a degree of conversion between 40-50 %. Unfortunately, testing of the polymer beads containing hydroxamate anion functionalities in chemical decontamination of nerve agents was not performed due to the limited time period of the work presented in this thesis.

4.2 Future prospects

For future work, it would be of interest to synthesize polymer beads containing acrylonitrile monomers, and further functionalization of such polymer beads with hydroxylamine for conversion of the acrylonitrile moiety into amideoximate anions. Polymerization of acrylonitrile was not carried out during the work presented in this thesis, due to the limited solubility of poly(acrylonitrile), which complicates the copolymerization process. However, polymer particles functionalized with amidoximate anions have been proved effective in decontamination of nerve agents by Bromberg *et al.* [25] and would therefore be of interest in further work.

In addition, further testing of the reactive polymer beads should be performed in order to obtain information about the polymers` ability to decontaminate nerve agents. Such information can be obtained by the use of ^{31}P HRMAS (High-resolution magic angle spinning) NMR to detect the degradation of nerve agents, for instance soman. If the reactive polymer beads are able to decontaminate the nerve agent, the relative intensity belonging to the initial nerve agent will decrease over time and signals belonging to degradation products will appear.

5. Experimental

5.1 Materials and methods

5.1.1 Laboratory equipment

Only standard laboratory glassware and equipment were used. Heating mantels used in this work were an all-aluminium type, coated with fluoropolymers (Heat-on® from Radleys). As heating mantels were used for all reactions, all temperatures given in the experimental procedures are mantel temperatures.

5.1.2 Solvents and reagents

Chemicals were purchased from Sigma-Aldrich Co. or other commercial sources. All chemical were used as received, unless otherwise is stated. Monomers were used without removal of inhibitors before polymerization.

Preparation of 0.5 wt% aqueous PVA solution: A 1000 mL round-bottom flask equipped with an elliptical stirring bar (40 x 20 mm) was charged with PVA (Mowiol 40-88, M_w ~ 205,000 and 86.7-88.7% hydrolysis, 5 g) and water (1000 mL). The reaction mixture was stirred at 750 rpm at 90 ^{0}C and then allowed to reach room temperature. The stirring was kept at 750 rpm until complete dissolution of PVA was accomplished.

Preparation of brine: Brine was prepared in a 600 mL beaker by dissolving 2-hydroxyethyl cellulose (M_w~1,300,000 and 2.5 mol ethoxy-functionalization, 1 g, 0.4 wt%) and NaCl (80 g, 25 wt%) in water (240 mL). The beaker was equipped with a stirring bar (57 mm x 27 mm) and the solution was stirred at 500 rpm until solution of 2-hydroxyethyl cellulose and NaCl was complete.

5.1.3 Microscopy

Pictures of polymer beads were obtained by microscopy, using in-built software (ImageAccess easyLab) for determination of beads sizes. Size and morphology of the polymer beads were estimated using a Leica DMR microscope. Pictures showing morphology of the polymer beads were obtained using a Zeiss stemi 2000-C microscope.

5.1.4 CHN analysis

CHN analysis was used to provide information about the monomer composition of the polymer backbone and the degree of functionalization. Polymer samples were sent to Eurofins Mikro kemi AB in Uppsala, Sweden, for CHN analysis. Given values for carbon, hydrogen and nitrogen content are the average value from two or three parallels for each sample.

5.1.5 IR spectroscopy

IR spectroscopy was used for detection of functional groups in the polymer samples and for evaluation of suspension polymerization and the subsequent functionalization. Spectra were recorded at Forsvarets forskningsinstitutt (FFI) on a Bruker *VERTEX 70* using a Bruker *Platinum ATR (*Attenuated total reflectance) unit.

5.1.6 Calculation of chemical yield

To estimate the chemical yield obtained from the polymerization reaction, a theoretical upper limit was calculated by assuming that all monomers added to the polymerization reaction had been incorporated during the polymerization reaction. The chemical yield from the polymerization reaction was calculated based on the obtained amount of polymer beads divided on this theoretical value the sum of monomers initially added to the polymerization reaction. Fragments from initiator have been disregarded in this calculation.

5.1.7 Calculation of polymer composition

For calculation of reagents in further functionalization of the polymer products, the polymer composition must be estimated. To estimate the polymer composition, it was assumed that the theoretical value of monomers was approximately equivalent to the actual value of monomers incorporated during the polymerization reaction. The amount of monomers incorporated was estimated by dividing the theoretical value of monomer initially added to the polymerization on the total amount of monomers.

Example:

Calculation of methyl acrylate (mmol/g polymer) in poly(methyl acrylate-*co*-styrene) beads:

$\%MA = (28.5\ g / (28.5 + 9.09 + 1.104)g) \cdot 100\% = 73.65\%$

$m_{MA}/g\ polymer = 1\ g_{MA} / g\ polymer \cdot (73.65/100) = 0.7365\ g_{MA} / g\ polymer$

$n_{MA}\ /g\ polymer = (0.7365\ g_{MA} / g\ polymer) / 86.09\ g_{MA} / mol_{MA}$

$= 0.008555\ mol_{MA} / g\ polymer \approx 8.56\ mmol_{MA} /g\ polymer$

5.1.8 Calculation of the degree of functionalization (mmol/g polymer)

To evaluate the degree of functionalization, the amount of nitrogen incorporated through conversion of methyl acrylate must be estimated. To estimate the degree of functionalization, it was assumed that the given values of nitrogen from CHN analysis originated from converted methyl acrylate only, as the other monomers are assumed to be inert during the functionalization. The degree of functionalization was estimated by calculating the amount of nitrogen incorporated through functionalization and comparing this to the estimated amount methyl acrylate in the polymer composition.

Example:

Calculation of nitrogen (mmol/g polymer) in functionalized poly(methyl acrylate-*co*-styrene) beads:

$\%N/g\ polymer = 1\ g_N / g\ polymer \cdot (3.55/100) = 0.0355\ g_N / g\ polymer$

$n_N /g\ polymer = (0.0355\ g_N / g\ polymer) / 14.01\ g_N / mol_N = 0.00253\ mol_N / g\ polymer$

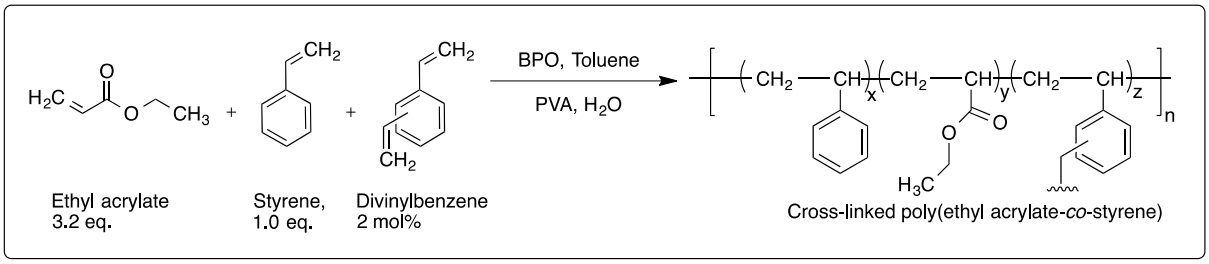
$= 2.53\ mmol_N / g\ polymer$

5.1.9 Estimation of the degree of functionalization using ChemDraw

The degree of functionalization of cross-linked poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads were estimated through element analysis in ChemDraw. The different monomers, using the appropriate molar ratios, were drawn in ChemDraw and the methyl acrylate moieties was converted one by one to the hydroxamate anion (containing the potassium salt) to identifying the polymer composition closest to the values of carbon, hydrogen and nitrogen obtained from the CHN analysis. For these estimates, it was assumed that the given increase of nitrogen from the CHN analysis originated from the conversion of methyl acrylate moieties only. All other monomers in the polymer structure were assumed to be inert during functionalization.

5.2 Experimental procedures

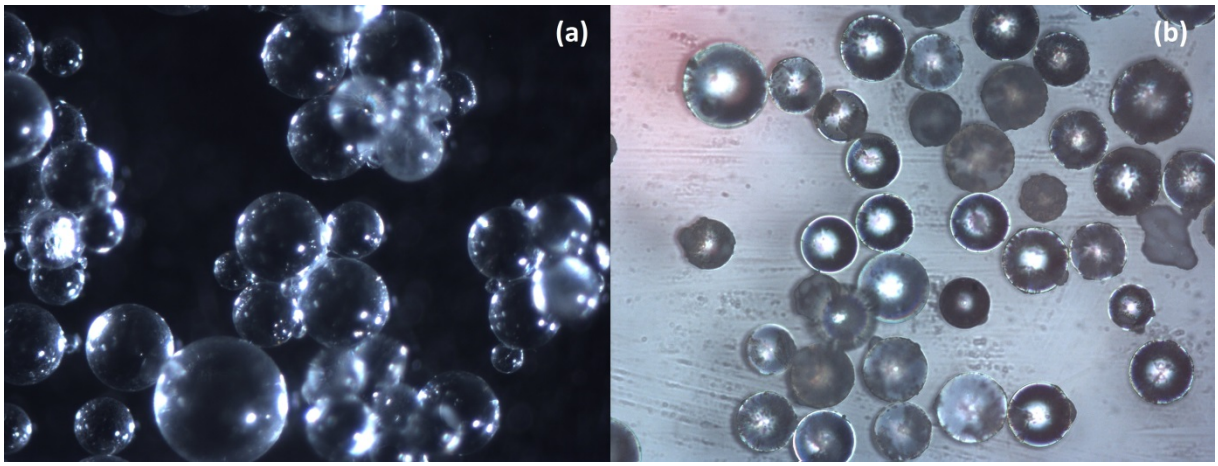
5.2.1 Synthesis of cross-linked poly(ethyl acrylate-co-styrene) beads



An aqueous solution of polyvinyl alcohol (Mowiol 40-88, 75 mL, 0.5 wt%) was added to a 250 mL round-bottom flask equipped with an elliptical stirring bar (25 mm x 14 mm), and stirring speed was set to 700 rpm. Benzoyl peroxide (0.558 g, 2.3 mmol, 2 wt%) was dissolved in toluene (15 mL), before ethyl acrylate (22.5 mL, 20.7 g, 207 mmol), styrene (7.5 mL, 6.8 g, 65 mmol) and DVB (0.355 g, 2.6 mmol, 1 mol %) were added followed by gentle stirring. The resulting monomer solution was carefully added to the aqueous PVA-solution under stirring. The stirring speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emulsion was heated to 75 ^{0}C and kept at this temperature for about 24 hours, giving a suspension of polymer particles.

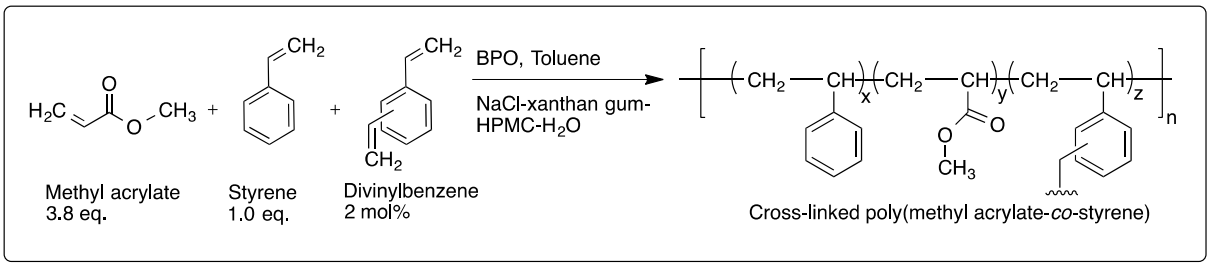
The suspension was then allowed to reach room temperature and poured into a 600 mL beaker. Water (400 mL) was added to the beaker and the beads were allowed to settle by gravity for 5 minutes. The supernatant was removed by decantation and the process was repeated with a mixture of water (200 mL) and methanol (200 mL). The polymer beads were transferred to a Büchner funnel and washed with water (1000 mL), methanol (200 mL) and isopropanol (50 mL), and then dried at room temperature.

Product: Clear polymer beads (100-200 μm)
Yield: 12.326 g (45 %)



Picture 5.1: (a) Picture of cross-linked poly(ethyl acrylate-*co*-styrene) beads obtained with Zeiss stemi 2000-C. (b) Picture of cross-linked poly(ethyl acrylate-*co*-styrene) beads obtained with Leica DMR (largest polymer bead on this picture has a diameter of 200 μm).

5.2.2 Synthesis of cross-linked poly(methyl acrylate-*co*-styrene beads using xanthan gum and HPMC

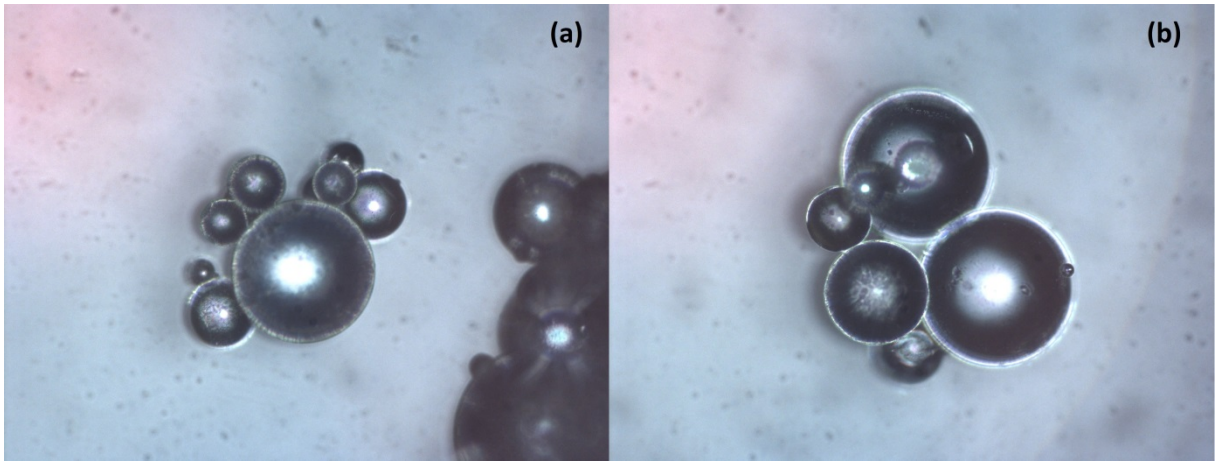


The continuous phase was prepared in a 100 mL round-bottom flask equipped with an elliptical stirring bar (25 mm x 14 mm) by dissolving NaCl (10.0 g, 25%) in 12 mL of an aqueous solution containing xanthan gum (0.2 wt%) and HPMC (hydroxypropoxyl content~ 9.1 %, 0.008%) and water (18 mL). The solution was stirred at 500 rpm until the NaCl was completely dissolved. The monomer phase was prepared by dissolving benzoyl peroxide (0.193 g, 0.80 mmol, 1 wt%) in toluene (20 mL), before methyl acrylate (7.125 g, 82.8 mmol, 3 eq.), styrene (2.273 g, 21.8 mmol, 1 eq.) and DVB (0.272 g, 2.09 mmol, 2 mol%) were added, followed by gentle stirring. The resulting monomer phase was carefully added to the brine under stirring. The stirring speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emulsion was heated to 75 ^{0}C and kept at this temperature for about 19 hours, giving a suspension of polymer particles.

The suspension was then allowed to reach room temperature and poured into a 400 mL beaker. Water (200 mL) was added to the beaker and the beads were allowed to settle by gravity for 5 minutes. The supernatant was removed by decantation and the process was repeated with a mixture of water (100 mL) and methanol (100 mL). The polymer beads were transferred to a Büchner funnel and washed with water (500 mL), methanol (100 mL) and isopropanol (50 mL), and then dried at room temperature.

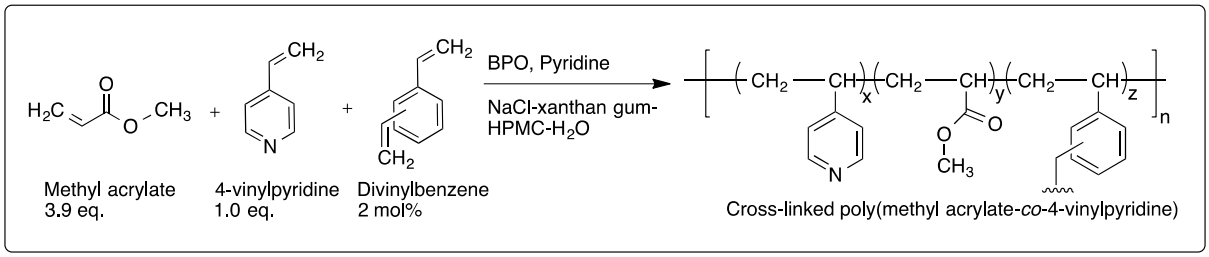
This procedure was used for several preparations of cross-linked poly(methyl acrylate-*co*-styrene) beads, varying the concentration of xanthan and HPMC.

Product: Clear polymer beads (70-350 μm)
Yield: 8.4 g (84 %)



Picture 5.2: Picture of cross-linked poly(methyl acrylate-*co*-styrene) beads prepared using xanthan gum and HPMC obtained with Leica DMR. (a) The largest polymer bead in this picture has a diameter of 300 μm. (b) The largest polymer bead in this picture has a diameter of 350 μm.

5.2.3 Synthesis of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine beads using xanthan gum and HPMC

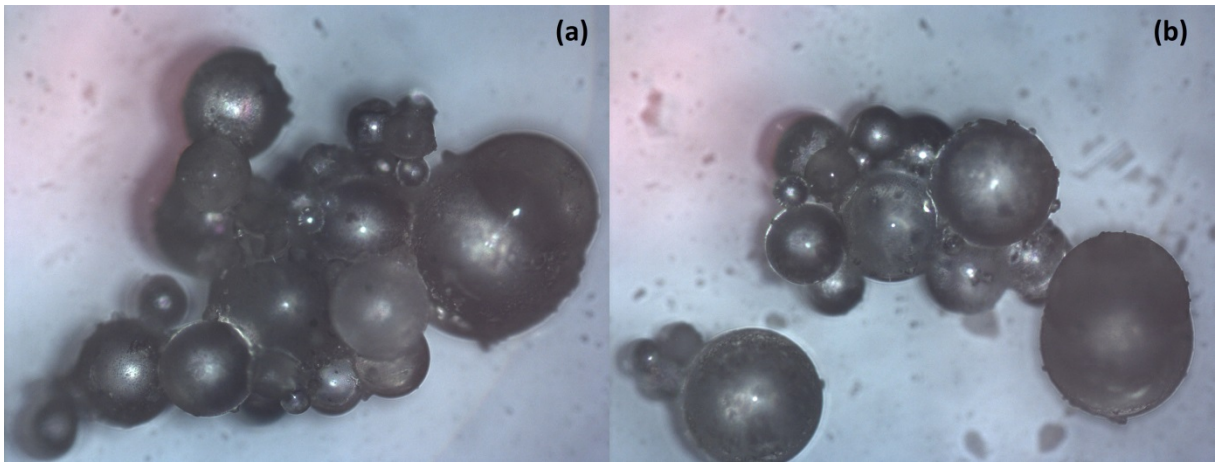


The continuous phase was prepared in a 100 mL round-bottom flask equipped with an elliptical stirring bar (25 mm x 14 mm) by dissolving NaCl (10 g, 25%) in 12 mL of an aqueous solution containing xanthan gum (0.2 wt%) and HPMC (hydroxypropoxyl content~ 9.1%, 0.008%) and water (18 mL). The solution was stirred at 500 rpm until NaCl was completely dissolved. The monomer phase was prepared by dissolving benzoyl peroxide (0.196 g, 0.81 mmol, 1 wt%) in pyridine (20 mL), before methyl acrylate (7.125 g, 82.80 mmol, 3 eq.), 4-vinylpyridine (2.438 g, 23.19 mmol, 1 eq.) and DVB (0.276 g, 2.12 mmol, 2 mol%) were added, followed by gentle stirring. The resulting monomer phase was carefully added to the brine under stirring. The stirring speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emsulsion was heated to 75 ^{0}C and kept at this temperature for about 20 hours.

The suspension was allowed to reach room temperature and poured into a 400 mL beaker. Water (200 mL) was added to the beaker and the beads were allowed to settle by gravity for 5 minutes. The supernatant was removed by decantation and the process was repeated with a mixture of water (100 mL) and methanol (100 mL). The polymer beads were transferred to a Büchner funnel and washed with water (500 mL), methanol (100 mL) and isopropanol (50 mL), and then dried at room temperature.

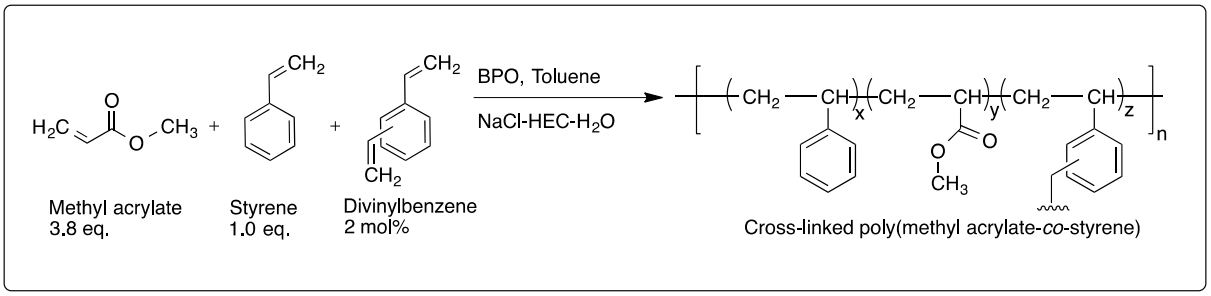
This procedure was used for several preparations of cross-linked poly(methyl acrylate-*co*-4-vinylpyridine) beads, varying the concentration of xanthan and HPMC.

Product: Light brown beads (70-370 μm)
Yield: 8.84 g (88 %)



Picture 5.2: Picture of poly(methyl acrylate-*co*-4-vinylpyridine) beads prepared using xanthan gum and HPMC obtained with Leica DMR. (a) The largest polymer bead in this picture has a diameter of 350 μm. (b) The largest polymer bead in this picture has a diameter of 370 μm.

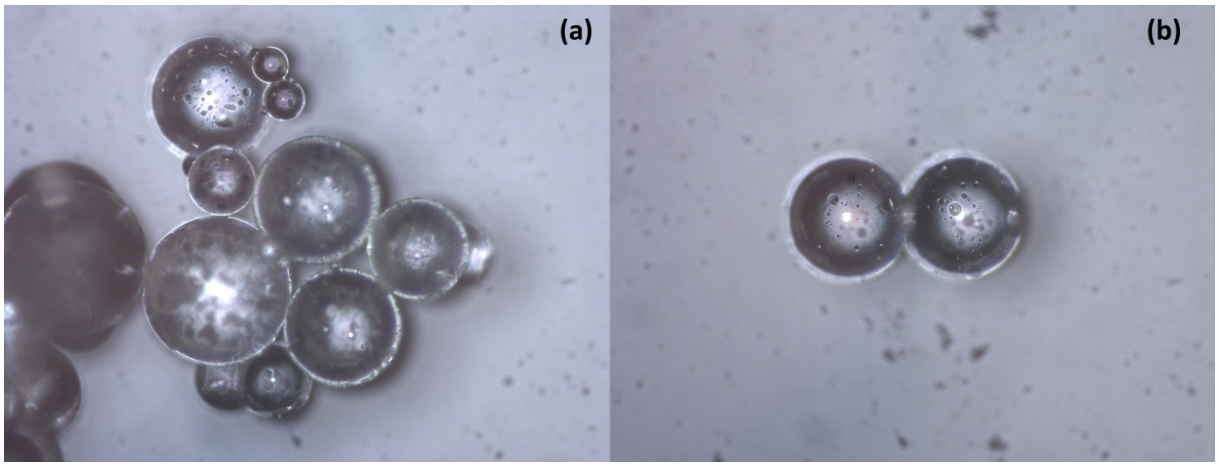
5.2.4 Synthesis of cross-linked poly (methyl acrylate-co-styrene) beads using 2-hydroxyethyl cellulose



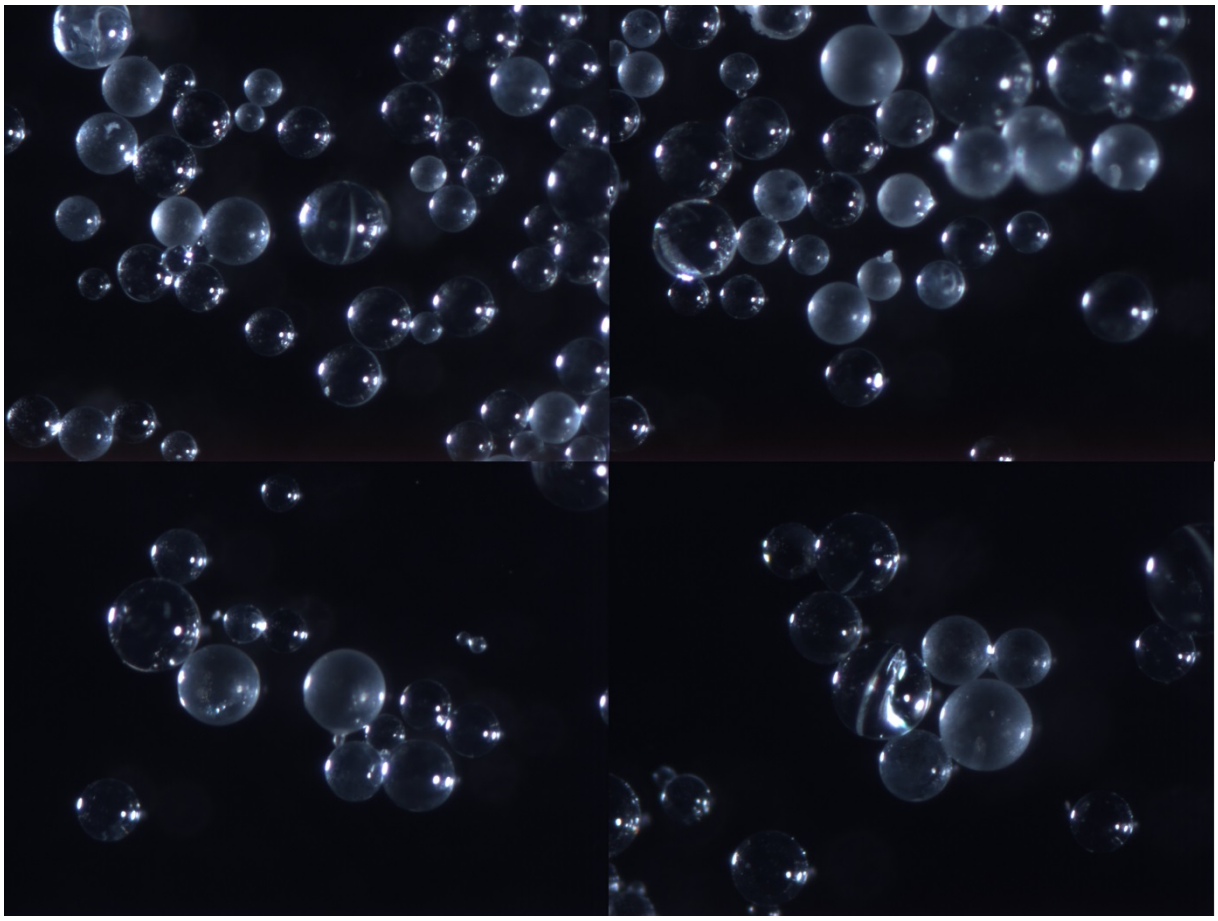
Brine containing 2-hydroxyethyl cellulose (120 mL) was added to a 250 mL round-bottom flask equipped with an oval stirring bar (40 mm x 20 mm) and stirring speed was set to 700 rpm. Benzoyl peroxide (0.772 g, 3.19 mmol, 1 wt %,) was dissolved in toluene (mL), before methyl acrylate (28.5 g, 331.05 mmol), styrene (9.09 g, 86.99 mmol) and DVB (1.104 g, 8.45 mmol, 2 mol %) were added followed by gentle stirring. The resulting monomer solution was carefully added to the brine under stirring. The stirring speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emulsion was heated to 75 ^{0}C and kept at this temperature for about 20 hours, giving a suspension of polymer particles.

The suspension was then allowed to reach room temperature and poured into a 600 mL beaker. Water (400 mL) was added to the beaker and the beads were allowed to settle by gravity for 5 minutes. The supernatant was removed by decantation and the process was repeated with a mixture of water (200 mL) and methanol (200 mL). The polymer beads were transferred to a Büchner funnel and washed with water (1000 mL), methanol (200 mL) and isopropanol (50 mL), and then dried at room temperature.

Product: Clear polymer beads (100-300 μm)
Yield: 32.995 g (82.5%)
CHN analysis: C: 65.6, H: 7.3, N: <0.3
IR: 2950 (Aromatic, C-H_2), 2360, 2341 (Benzene, provably small traces of impurities), 1727 (Carbonyl of saturated ester, C=O), 1194, 1156 (Ester, C(=O)-O and O-C=O) cm^{-1}



Picture 5.3: Picture of poly(methyl acrylate-*co*-styrene) beads prepared using 2-hydroxyethyl cellulose obtained with Leica DMR. (a) The largest polymer bead in this picture has a diameter of 300 µm. (b) The largest polymer bead in this picture has a diameter of 300 µm.



Picture 5.4: Picture of separated and purified poly(methyl acrylate-*co*-styrene) beads prepared using 2-hydroxyethyl cellulose obtained with Zeiss stemi 2000-C.

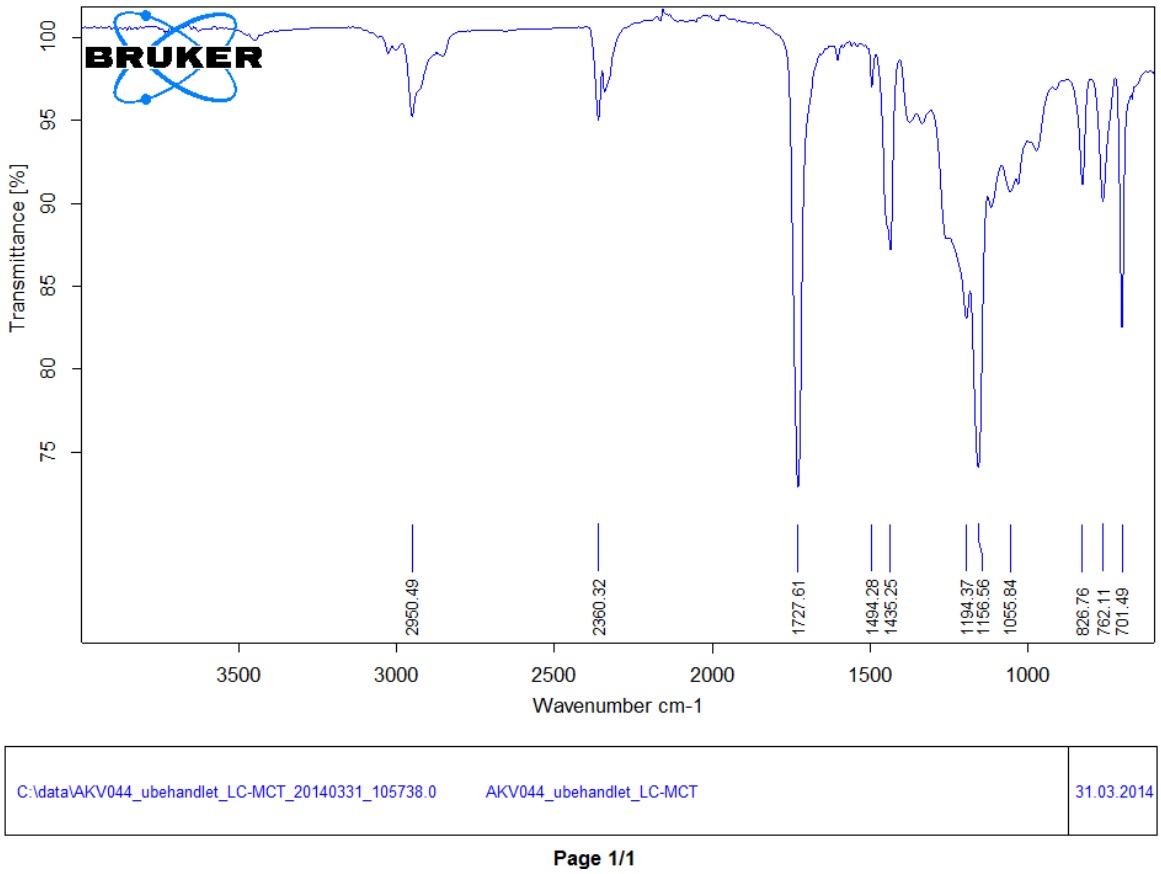
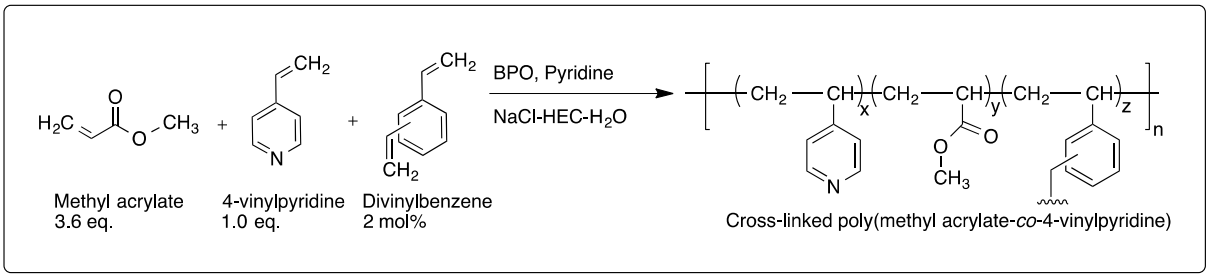


Figure 5.1: IR-spectrum obtained from poly(methyl acrylate-*co*-styrene) beads.

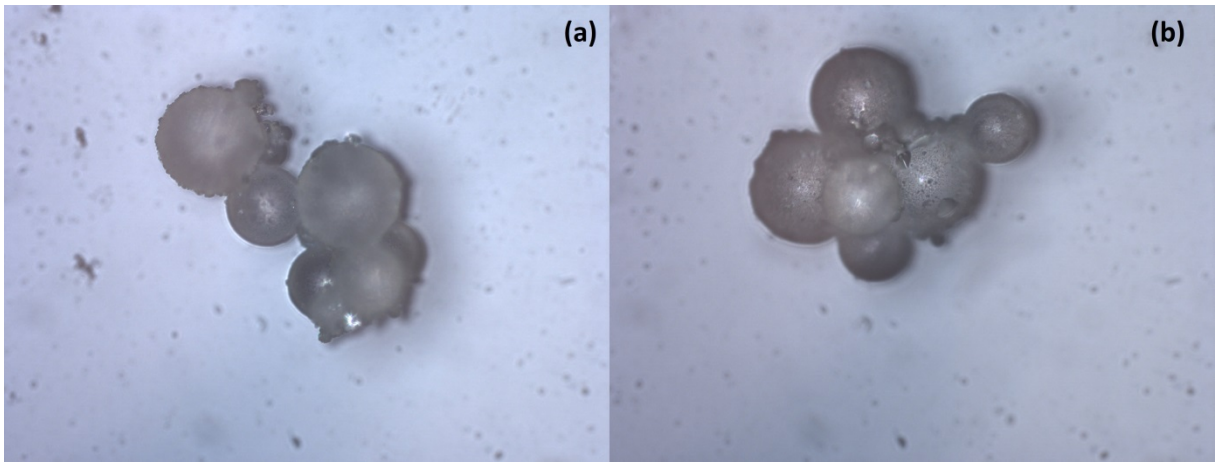
5.2.5 Synthesis of cross-linked poly(methyl acrylate-co-4-vinylpyridine) beads



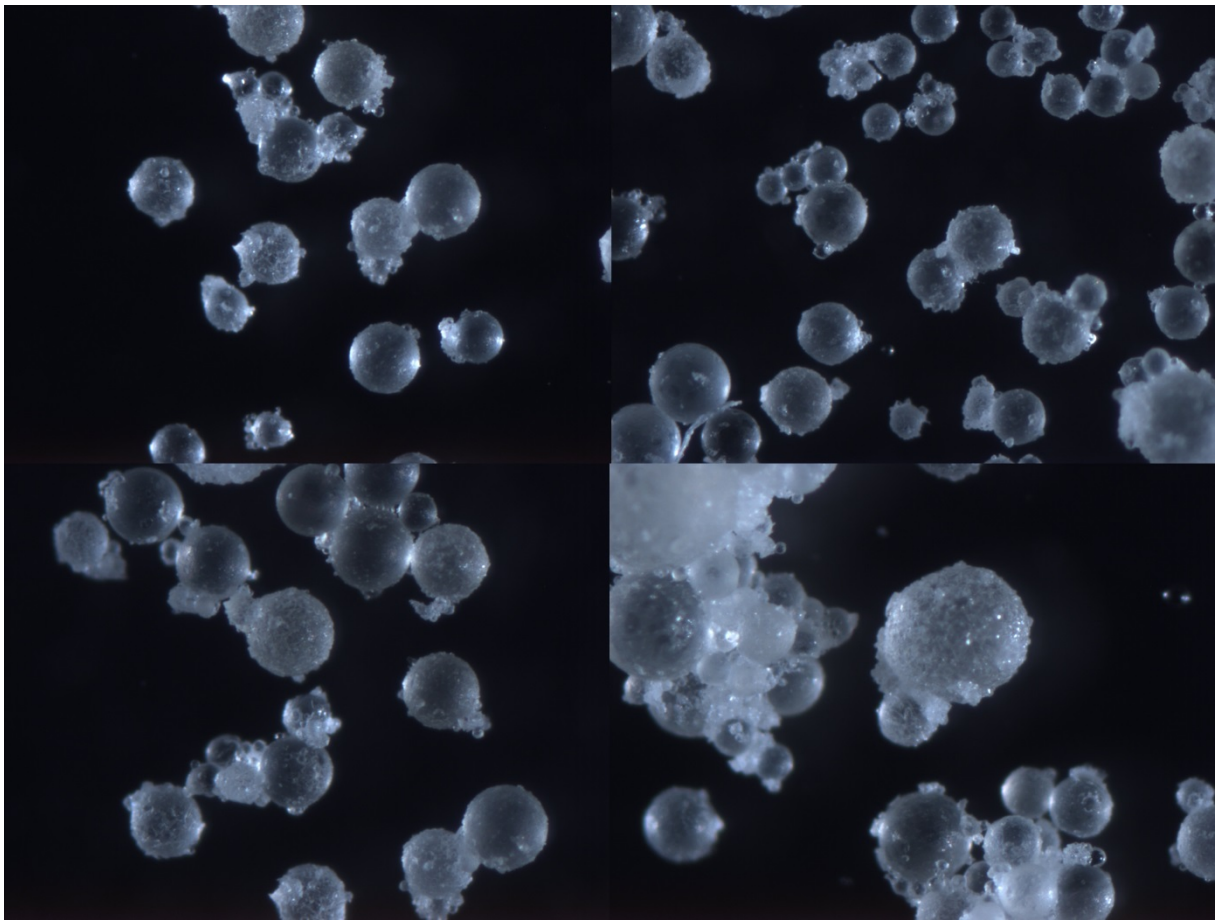
Brine containing 2-hydroxyethyl cellulose (120 mL) was added to a 250 mL round-bottom flask equipped with an oval stirring bar (40 mm x 20 mm) and stirring speed was set to 700 rpm. Benzoyl peroxide (0.784 g, 3.34 mmol, 1 wt%) was dissolved in pyridine (20 mL) before 4-vinylpyridine (9.75 g, 92.73 mmol) and DVB (1.104 g, 8.48 mmol, 2 mol%) were added followed by gentle stirring. Methyl acrylate (28.5 g, 331.05 mmol) was added drop-wise to prevent precipitation of 4-vinylpyridine. The resulting monomer solution was added to the brine under stirring. The stir speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emulsion was heated to 75 ^{0}C and kept at this temperature for about 21 hours, giving a suspension of polymer particles.

The suspension was then allowed to reach room temperature and poured into a 600 mL beaker. Water (400 mL) was added to the beaker and the beads were allowed to settle by gravity for 5 minutes. The supernatant was removed by decantation and the process was repeated until the supernatant was clear (1-2 times). The polymer beads were transferred to a Büchner funnel and washed with water (1000 mL), methanol (200 mL) and isopropanol (50 mL), and then dried at room temperature. A small portion of these polymer beads (≈ 2 g) was purified by Soxhlet-extraction for 6 h in methanol (200 mL) before element analysis.

Product: Light brown polymer beads (100-300 µm)
Yield: 29.915 g (74.8%)
CHN analysis: C: 62.7, H: 7.3, N: <0.3
IR: 3443 (Probably small traces of MeOH), 2923 (Aromatic, C-H_2), 2360 (Benzene, provably small traces of impurities), 1726 (Carbonyl of saturated ester, C=O), 1597, 1557, 1434 (Ring, C=C, C=N), 1194, 1157 (Ester, C(=O)-O and O-C=O) cm^{-1}



Picture 5.5: Picture of poly(methyl acrylate-*co*-4-vinylpyridine) beads prepared using 2-hydroxyethyl cellulose obtained with Leica DMR. (a) The largest polymer bead on this picture has a diameter of 250 μm. (b) The largest polymer bead on this picture has a diameter of 300 μm.



Picture 5.6: Picture of separated and purified poly(methyl acrylate-*co*-styrene) beads prepared using 2-hydroxyethyl cellulose obtained with Zeiss stemi 2000-C.

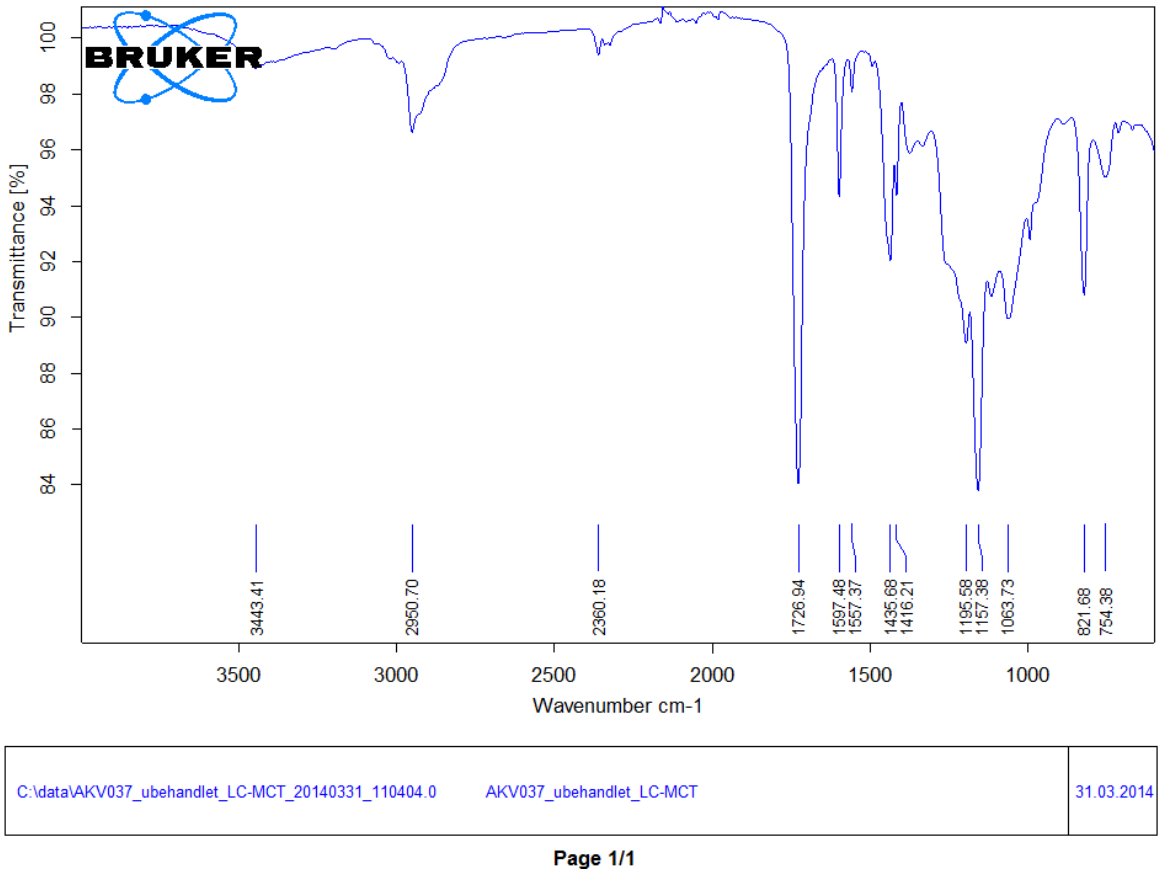
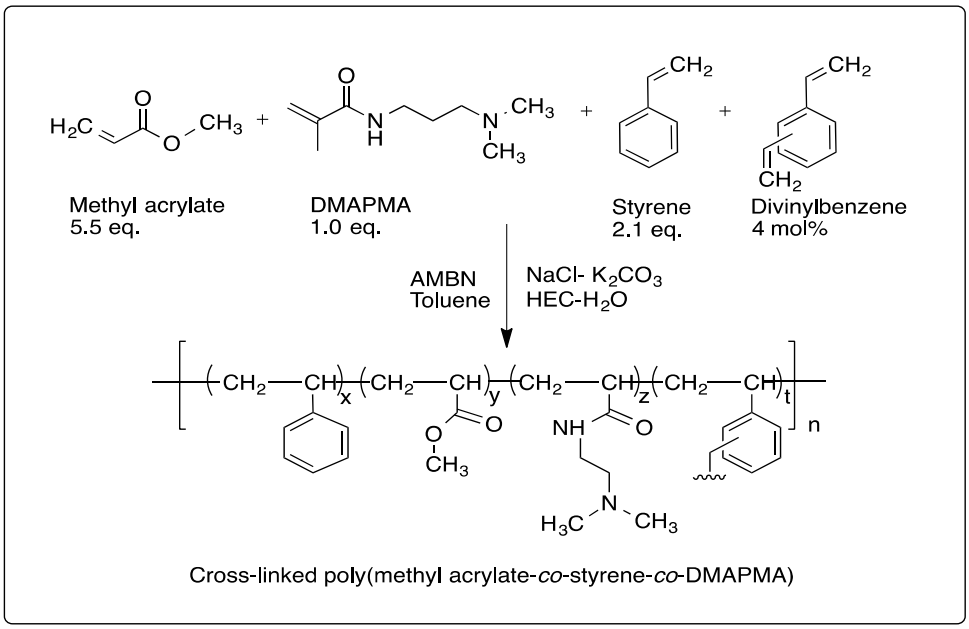


Figure 5.2: IR-spectrum obtained from poly(methyl acrylate-*co*-4-vinylpyridine) beads

5.2.6 Synthesis of cross-linked poly (methyl acrylate-co-styrene-co-DMAPMA) beads



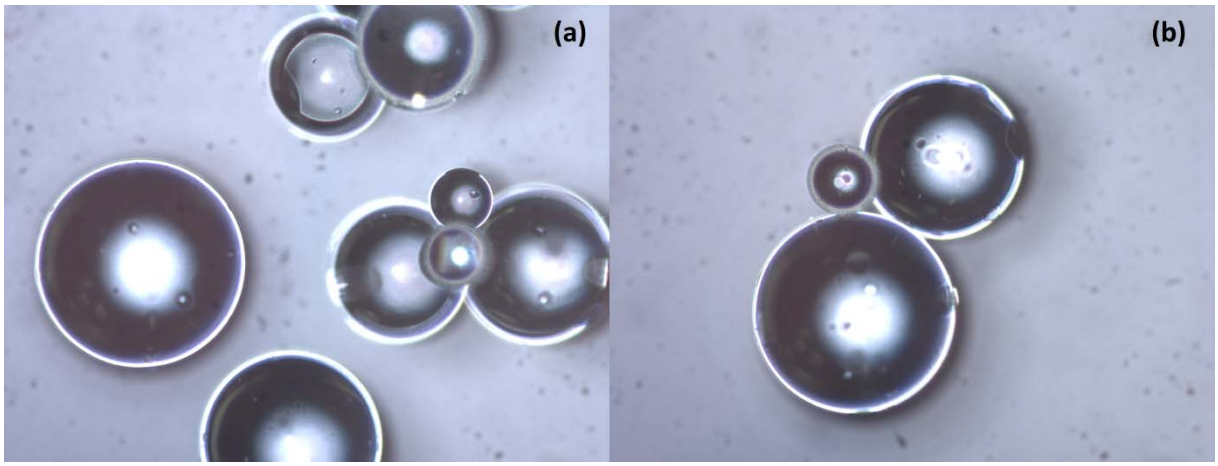
Brine containing 2-hydroxyethyl cellulose (30 mL) and K_2CO_3 (0.250 g, 1.80 mmol) was added to a 100 mL round-bottom flask equipped with an elliptical stirring bar (25 mm x 14 mm) and stirring speed was set to 700 rpm. AMBN (0.099 g, 0.52 mmol, 1 wt%) was dissolved in toluene before DMAPMA (2.35 g, 13.80 mmol), styrene (2.273 g, 21.82 mmol), methyl acrylate (4.75 g, 55.18 mmol) and DVB (0.473 g, 3.63 mmol, 4 mol%) were added followed by gentle stirring. The resulting monomer solution was added to the brine under stirring. The stirring speed was regulated to promote a stable emulsion of the monomer phase (typically 400-600 rpm). The stable emulsion was heated to 75 ^{0}C and kept at this temperature for about 19 hours, giving a suspension of polymer particles.

The suspension was allowed to reach room temperature and poured into a 400 mL beaker. A mixture of water (100 mL) and methanol (100 mL) was added to the beaker and the beads were allowed to settle by gravity for 10 minutes. The supernatant was removed by decantation and the process was repeated with water (200 mL). The polymer beads were then transferred to a Büchner funnel and washed with water (600 mL), methanol (100 mL) and isopropanol (50 mL).

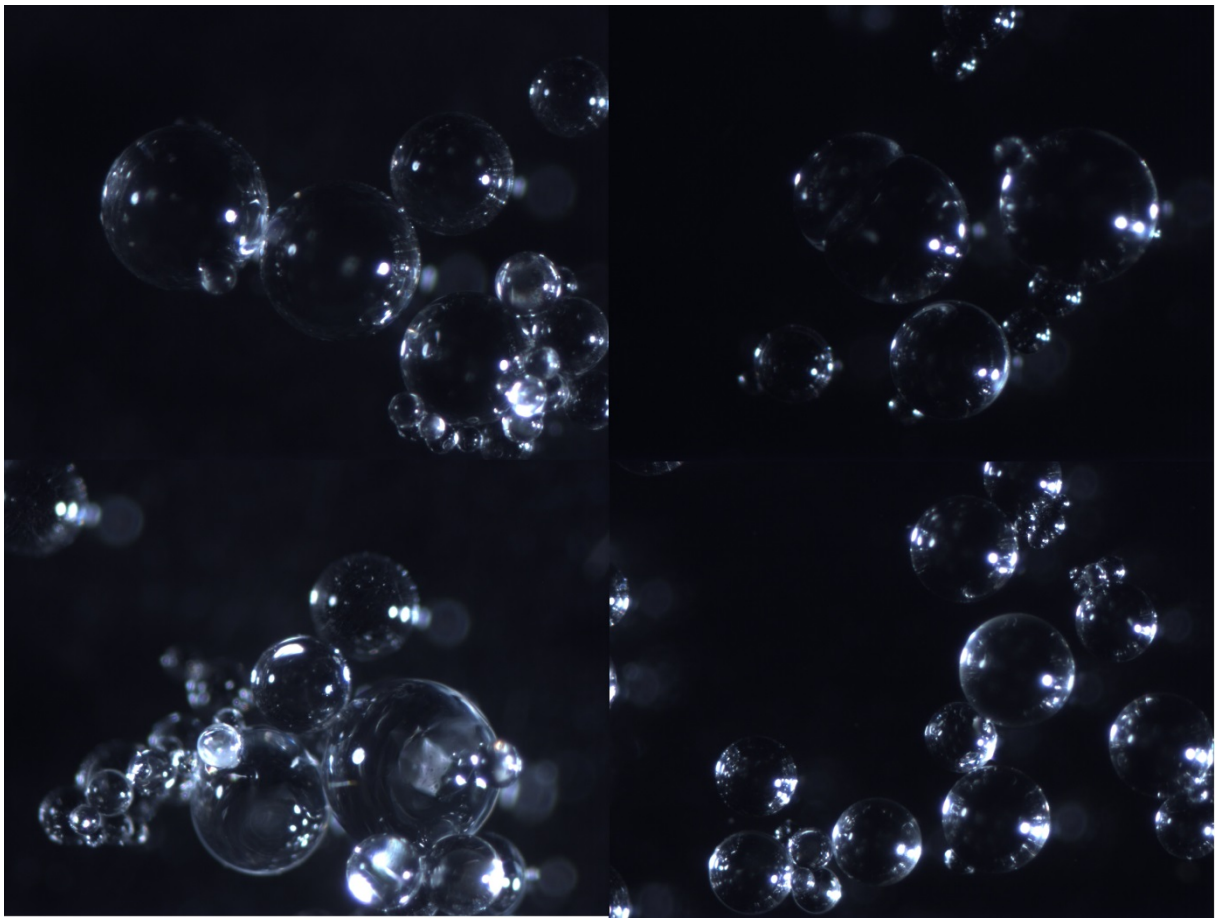
Product: Clear polymer beads (150-500 μm)

Yield: 6.573 g (65.7%)

CHN analysis: C: 70.2, H: 7.7, N: 2.0

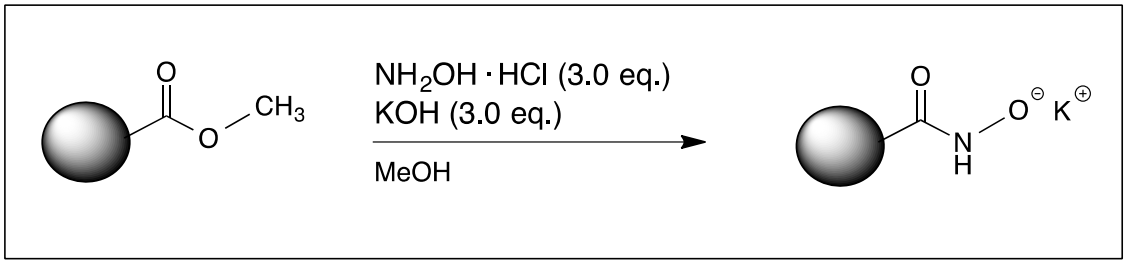


Picture 5.7: Picture of poly(methyl acrylate-*co*-styrene-*co*-DMAPMA) beads prepared using 2-hydroxyethyl cellulose obtained with Leica DMR. (a) The largest polymer bead on this picture has a diameter of 480 μm. (b) The largest polymer beads on this picture has a diameter of 460 μm.



Picture 5.8: Picture of separated and purified poly(methyl acrylate-*co*-styrene-co-DMAPMA) beads prepared using 2-hydroxyethyl cellulose obtained with Zeiss stemi 2000-C.

5.2.7 Functionalization of cross-linked polymer beads by reaction with hydroxylamine hydrochloride



Polymer beads were functionalized by reaction with hydroxylamine hydrochloride in an attempt to obtain hydroxamate moieties through conversion of methyl acrylate. Hydroxylamine hydrochloride (10 g, 143.9 mmol, 3 eq.) was added to a 250 mL round-bottom flask equipped with an elliptical stirring bar (25 mm x 14 mm) and dissolved in MeOH (150 mL) by gentle stirring. After completed dissolution of $NH_2OH \cdot HCl$, KOH (86%, 8.48 g, 151.1 mmol, 3 eq.) was added to the solution under stirring. The temperature was set to 65 ^{0}C and the reaction was left over night.

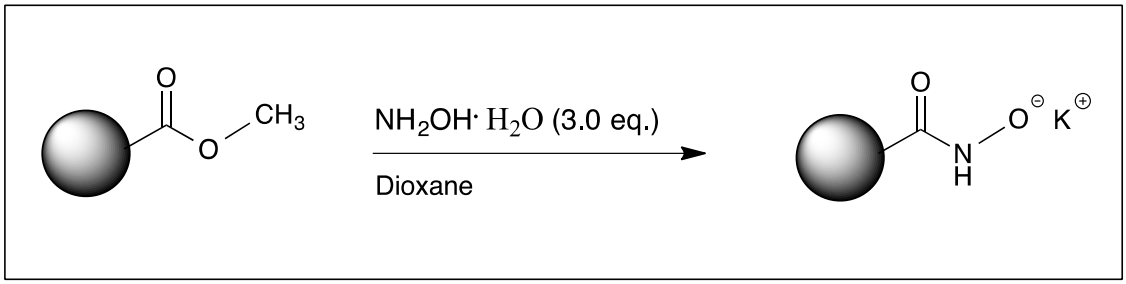
After functionalization, the reaction mixture was allowed to reach room temperature before being transferred to a Büchner funnel and washed with methanol (100 mL), 0.1 M HCl (200 mL) and water (200 mL), and then dried at room temperature.

This procedure was used functionalization of both poly(methyl acrylate-*co*-styrene) and poly(methyl acrylate-*co*-4-vinylpyridine) beads. The procedure was repeated for both type of polymer beads, but different solvent mixtures were utilized (Table 5.1)

Table 5.1: Different solvent mixtures used for functionalization reactions in procedure 5.2.7

Functionalization reaction nr.	Solvent 1	Solvent 2	Solvent 3
1	THF	-	-
2	THF (1.0 eq.)	Water (1.0 eq.)	-
3	THF (2.0 eq.)	Water (1.0 eq.)	MeOH (1.0 eq.)

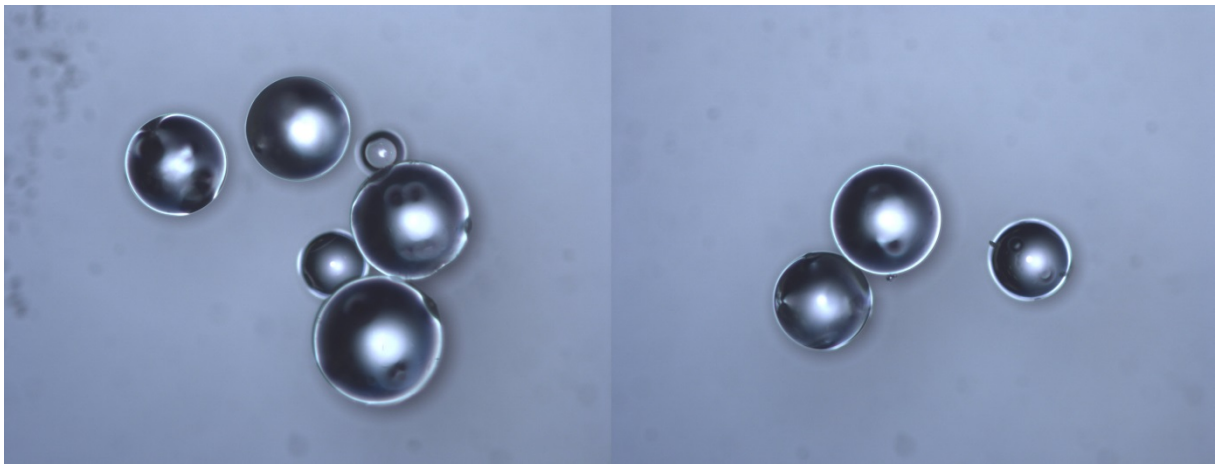
5.2.8 Functionalization of cross-linked poly(methyl acrylate-co-styrene) beads with aqueous hydroxylamine



Polymer beads were modified to obtain poly (hydroxamic acid) resins via reaction with excess of aqueous hydroxylamine in dioxan. An aqueous solution of hydroxylamine (50%, 5.087 g, 77 mmol, 3 eq.) was added to dioxan (12 mL). A 250 mL round-bottom flask was charged with polymer beads (3 g) followed by swelling of the polymer beads in the solution containing hydroxylamine (50%) and dioxane. The reaction mixture was heated to 45 ^{0}C (mantel temperature) and kept at this temperature for 23 h without stirring.

The beads were allowed to reach room temperature and poured into a beaker containing methanol (100 mL). The polymer beads were allowed to settle by gravity for 5 min before the supernatant was removed by decantation. Water (100 mL) was added before the polymer beads were transferred to a Büchner funnel and washed with methanol (100 mL), water (100 mL) and isopropanol (50 mL), and then dried at room temperature. A portion of the functionalized polymer beads were purified by Soxhlet-extraction for 6 h with MeOH (200 mL) prior to further analysis.

Product: Clear polymer beads (100 - 300 µm)
Yield: 2.548 g (85%)
CHN analysis: C: 66.9, H: 7.3, N: <0.3
IR: 2950 (Aromatic, C-H_2), 1729 (Carbonyl of saturated ester, C=O), 1435 (Alkane, C-H_2), 1156 (Ester, O-C=O) cm^{-1}



Picture 5.9: Picture of poly(methyl acrylate-*co*-styrene) beads functionalized in a solution containing dioxane and aqueous hydroxylamine, obtained with Leica DMR. (a) The largest polymer bead on the picture has a diameter of 270 µm. (b) The largest polymer beads on this picture has a diameter of 250 µm.

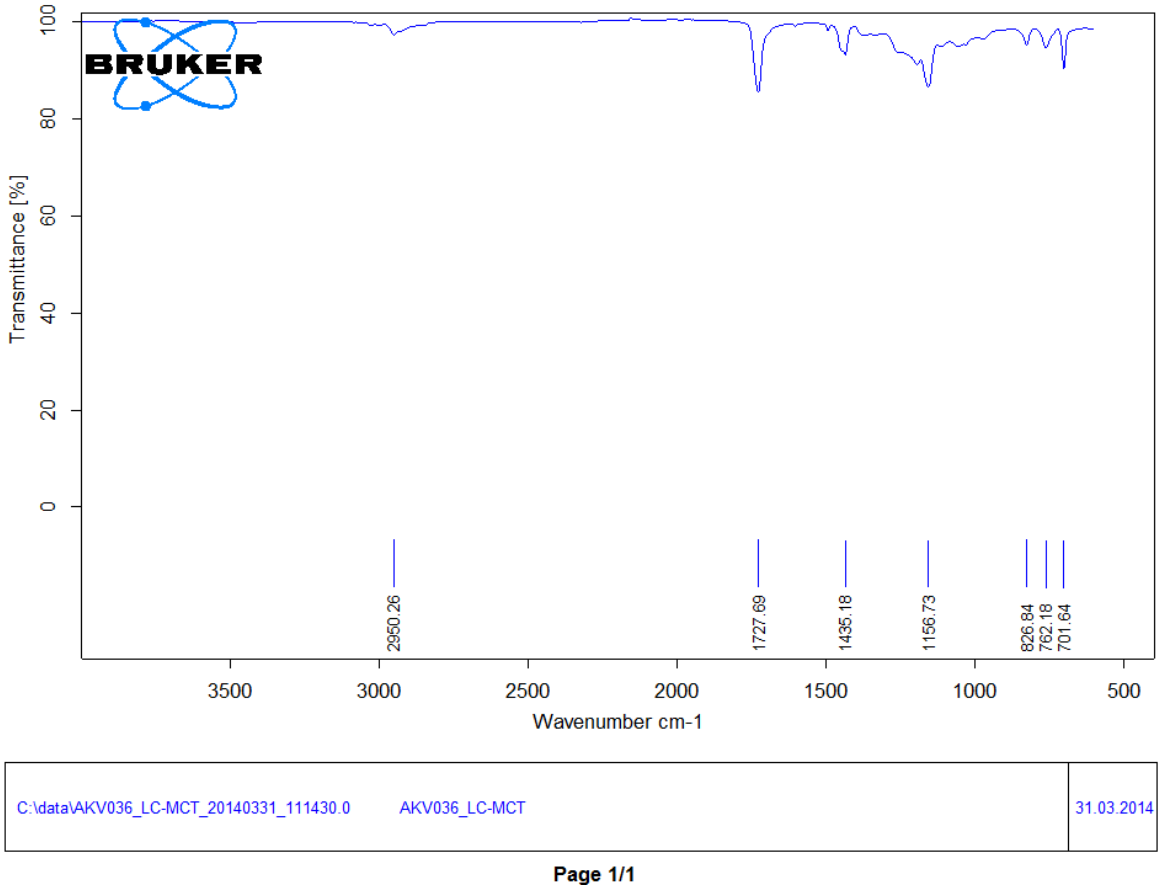
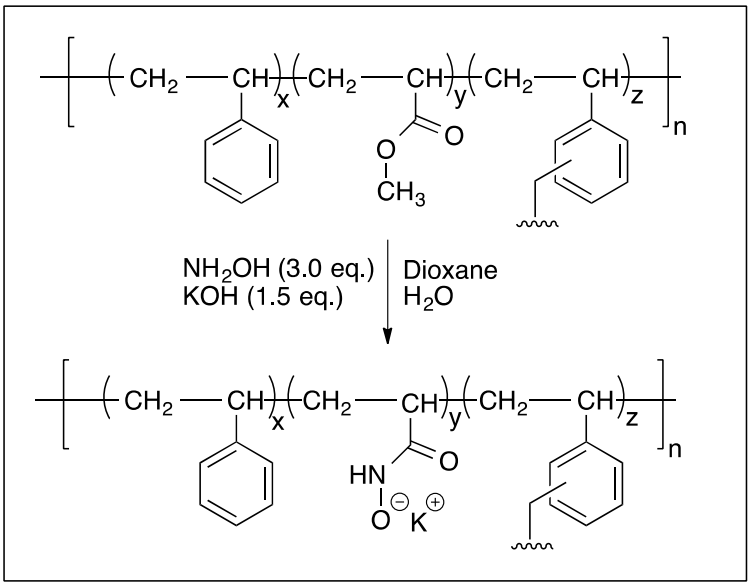


Figure 5.3: IR-spectrum obtained from poly(methyl acrylate-*co*-styrene) beads functionalized in a solution containing Dioxane and aqueous hydroxylamine.

5.2.9 Functionalization of cross-linked poly(methyl acrylate-co-styrene) beads with aqueous hydroxylamine:



Polymer beads were modified to obtain poly(hydroxamate) resins via reaction with excess of hydroxylamine in dioxan. KOH (86%, 10.8 g, 165 mmol, 1.5 eq.) was dissolved in an aqueous solution of hydroxylamine (50%, 25.4 g, 384 mmol, 3 eq.), before adding dioxan (60 mL) to the solution. A 250 mL round-bottom flask was charged with polymer beads (15 g) followed by swelling of the polymer beads in the solution containing KOH (86%), hydroxylamine (50%) and dioxan. The reaction mixture was heated to 45 ^{0}C (mantel temperature) and kept at this temperature for 24 h without stirring.

The beads were allowed to reach room temperature and poured into a beaker containing methanol (150 mL). The polymer beads were allowed to settle by gravity for 5 min before the supernatant was removed by decantation. Water (150 mL) was added before the polymer beads were transferred to a Büchner funnel and washed with methanol (200 mL) and isopropanol (50 mL), and then dried at room temperature. A portion of the functionalized polymer beads were purified by Soxhlet-extraction for 6 h with MeOH (200 mL) prior to further analysis.

Product: Clear polymer beads (100-300 μm)

Yield: 21.767 g (145 %)

CHN analysis: C: 43, H: 5.6, N: 5.1

IR: 3200 (Amine, N-H), 2950 (Aromatic, C-H_2), 1627 (Amide, C=O), 1556 (Amide, N-H), 1449, 1395 (Ring, C=C, C=N)

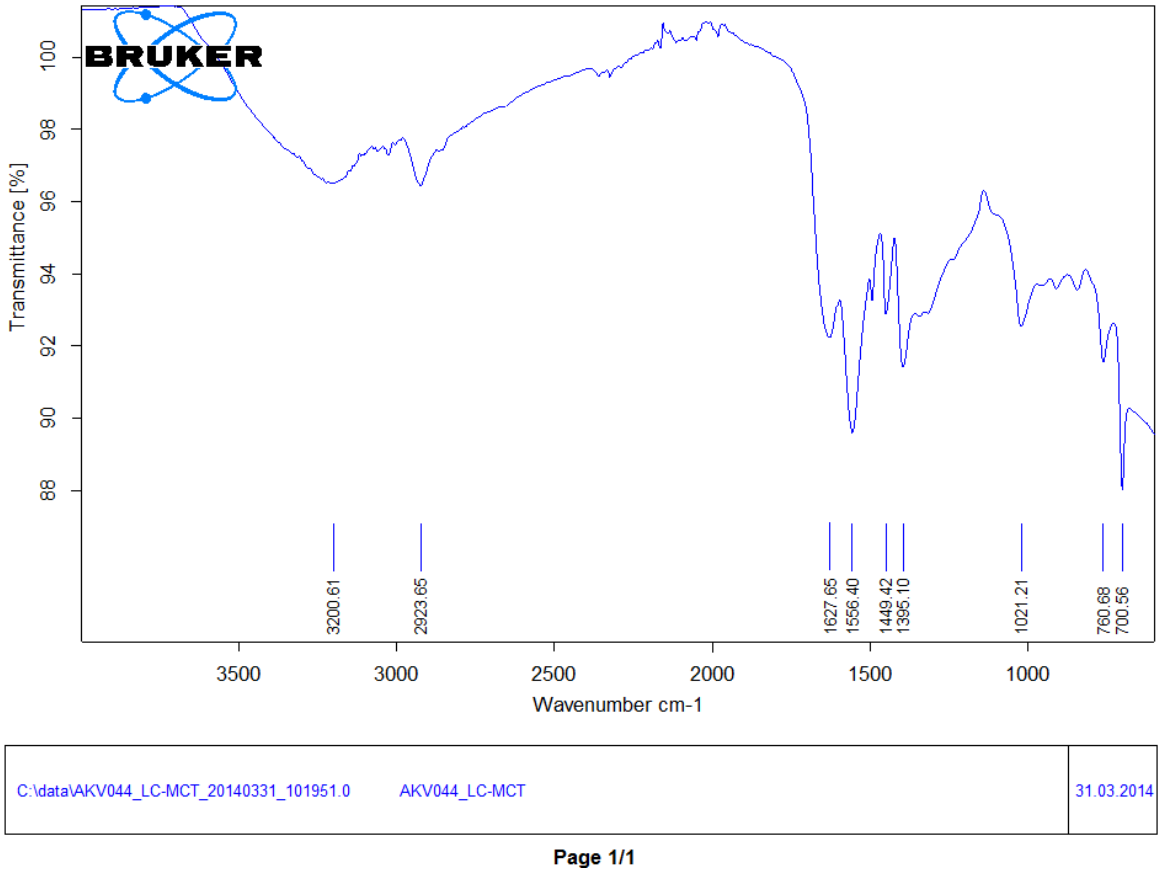
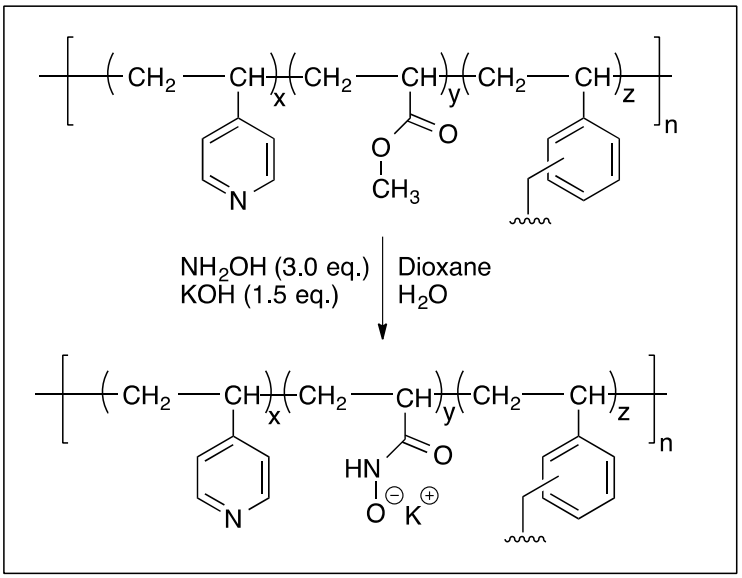


Figure 5.4: IR-spectrum obtained from poly(methyl acrylate-*co*-styrene) beads functionalized in a solution containing KOH, aqueous hydroxylamine and dioxane.

5.2.10 Functionalization of cross-linked poly (methyl acrylate-co-4-vinylpyridine) beads with aqueous hydroxylamine:



Polymer beads were modified to obtain poly (hydroxamate) resins via reaction with excess of aqueous hydroxylamine in dioxan. KOH (86%, 10.8 g, 165 mmol, 1.5 eq.) was dissolved in an aqueous solution of hydroxylamine (50%, 25.4 g, 384 mmol, 3 eq.), before adding dioxan (60 mL) to the solution. A 250 mL round-bottom flask was charged with polymer beads (15 g) followed by swelling of the polymer beads in the solution containing KOH (86%), hydroxylamine (50%) and dioxan. The reaction was heated to 45 ^{0}C (mantel temperature) and kept at this temperature for about 24 h without stirring.

The beads were allowed to reach room temperature and poured into a beaker containing methanol (150 mL). The polymer beads were allowed to settle by gravity for 5 min before the supernatant was removed by decantation. MeOH (150 mL) was added before the polymer beads were transferred to a Büchner funnel and washed with MeOH (200 mL) and isopropanol (50 mL), and then dried at room temperature. A portion of the functionalized polymer beads was purified by Soxhlet-extraction for 6 h with MeOH (200 mL) prior to further analysis.

Product: Clear polymer beads (100-300 μm)

Yield: 21.394 g (142.6 %)

CHN analysis: C: 42.5, H: 5.6, N: 7.6

IR: 3200 (Amine, N-H), 2923 (Aromatic, C-H_2), 2359 (Benzene, provably small traces of impurities), 1634 (Amide, C=O), 1557 (Amide, N-H), 1600, 1446 (Ring, C=C, C=N)

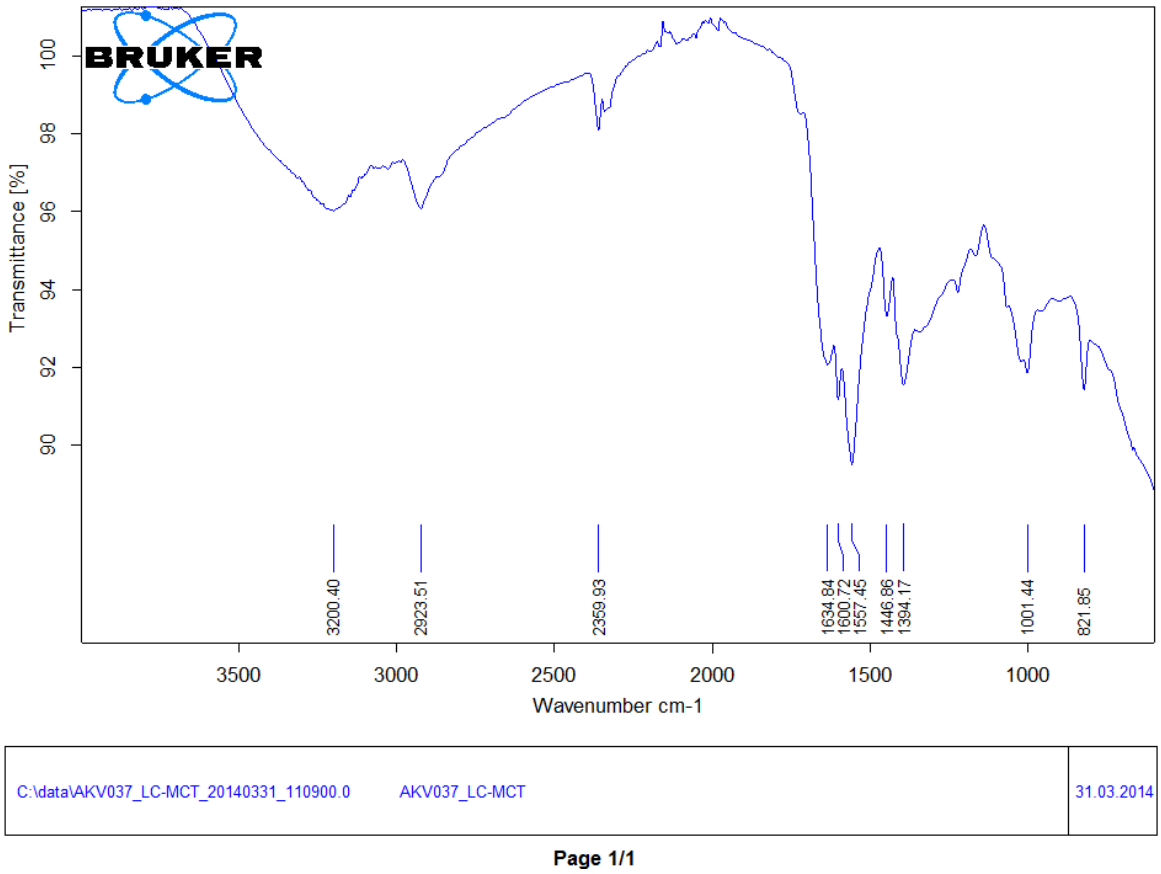


Figure 5.5: IR-spectrum obtained from poly(methyl acrylate-*co*-4-vinylpyridine) beads functionalized in a solution containing KOH, aqueous hydroxylamine and dioxane.

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