POLYMER MICRO-SPHERES WITH SURFACE AND INTERIOR GRAFTS

SYNTHESES OF NOVEL POLYMER MICRO-SPHERES WITH SURFACE AND INTERIOR GRAFTS

By

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A thesis

Submitted to the School of Graduate Studies

in Partial Fulfillment of the Requirement

for the Degree

Doctor of Philosophy in Chemistry

McMaster University

DOCTOR OF PHILOSOPHY (2002) McMaster University

(Chemistry) Hamilton, Ontario

TITLE: Syntheses of Novel Polymer Micro-spheres with Surface and Interior Grafts

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NUMBER OF PAGES: xix; 157

Abstract

Polymers and block copolymers have been grafted from hard and soft polymer micro-spheres by atom transfer radical polymerization (ATRP) and ring opening polymerization (ROP). The hard and soft micro-spheres were prepared by precipitation polymerization of divinylbenzene-80 (DVB80), and of DVB80/hydroxyethylmethacrylate (HEMA), respectively, in neat acetonitrile.

Residual vinyl groups in the hard, poly(DVB80) micro-spheres were hydrochlorinated to form benzyl chloride groups that subsequently served as ATRP initiators for poly(styrene) and poly(styrene-*block*-4-methylstyrene) grafts. Hydrophilic poly(HEMA) and poly(2-(dimethylamino)ethyl methacrylate) poly(DMAEMA) were also grafted from hard micro-spheres containing bromopropionates, using ATRP in the presence of CuBr/Me_4Cyclam.

Hydroxy groups in soft, poly(DVB80-*co*-HEMA) micro-spheres were used directly as initiators for ring opening polymerization of ε-caprolactone catalyzed by aluminum compounds. In the addition, they were reacted with α-bromopropionyl bromide to form ATRP initiators.

Several combinations of ATRP-ATRP and ROP-ATRP with different monomers were carried out using these initiator micro-spheres. In particular, the soft micro-spheres grafted with poly(methacrylic acid), poly(methylmethacrylate), poly(methylmethacrylate-*block*-dimethylaminoethylmethacrylate), poly(methylmethacrylate-*block*-trimethylammoniumethylmethacrylate), poly(methylmethacrylate-*block*-HEMA), poly(methylmethacrylate-*block*-glycidylmethacrylate), poly(ε-caprolactone-*block*-

methylmethacrylate), poly(ε-caprolactone-*block*-dimethylaminoethylmethacrylate).

The internal morphology of these homo and block copolymer grafted microspheres was studied using electron microscopy and x-ray microspectroscopy.

Acknowledgments

Fist of all, I would like to express my thanks to my supervisor, Professor Harald Stöver, for his valuable guidance, generous help and enthusiasm. Your experience and perspectives help me a lot in completing this thesis. He has made me a good scientist and no word can fully express my thanks.

I would also like to thank my supervisory committee members, Dr. M. Brook and Dr. Shiping Zhu, for their ideas, help and encouragement. Their chemistry/polymer expertises are deeply appreciated.

Sincere appreciation is also extended to Dr. Don Hughes, Mrs. Marcia West, Mr. Klaus Schultes, Mr. Brian Sayer, Mr. George Timmins, and Mr. Frank Gibbs for their assistance in using the TEM, ESEM, NMR, IR, and DSC facilities.

To my fellows in Dr. Stöver group, thank you for your generous help and support during my stay. Thanks go to: Wenhui, Nick, Xiangzheng , Kui, Mukkaram, Anna, Lisa, Xiangchun, Ester, Randy, Frank, Daryl, Janevieve, and Pauly.

Thanks are also due to the staff in the Department office for their help provided through many years. Especially, I am grateful to Carol Dada for her valuable help and advice.

Finally, I have to thank my family for their patience, understanding, and support. My love goes to my wife, Sai Gao; my son Mark Zheng; my parents Ri Sheng Zheng and Jing Xiang Chen. My work could not have been completed without their sacrifices.

Table of Contents

Table of Contents (continued)

Table of Contents (continued)

Table of Contents (continued)

Table of Contents (continued)

List of Figures

List of Figures (continued)

List of Figures (continued)

List of Figures (continued)

List of Tables

List of Schemes

List of Schemes (continued)

List of Abbreviations

AIBN – 2,2'-Azobisisobutyronnitrile

ATRP – Atom Transfer Radical Polymerization

Bipy – Bipyridine

CV – Coefficient of Variance

DSC – Differential Scanning Calorimetry

DMAEMA – 2-(Dimethylamino)ethyl Methacrylate

DVB80 – Mixture of Divinylbenzene Isomers and Ehtylvinylbenzene Isomer with 80 mol% of Divinyl Components

ESEM – Environmental Scanning Electron Microscope

FT-IR – Fourier Transform Infrared

GMA – Glycidal Methacrylate

GPC – Gel Permeation Chromatography

HEMA – 2-Hydroxyethyl Methacrylate

HPLC – High Performance Liquid Chromatography

MA – Methyl Acrylate

MMA – Methyl Methacrylate

Me_4Cyclam – 1,4,8,11-Tetramethyl-1,4,8,11-Tetraazacyclotetradecane

Me_6Tren – Tris[2-(dimethylamino)ethyl]amine

MEK – Methyl Ethyl Ketone

MeSt – 4-Methylstyrene

List of Abbreviations (continued)

M_n – Number Average Molecular Weight

M_w – Weight Average Molecular Weight

M_w/M_n – Molecular Weight Distributuin

MWD – Molecular Weight Distribution

NMR – Nuclear Magnetic Resonance

pcl – poly(ε-caprolactone)

PDI – Polydispersity Index

PDMS – Polydimethylsiloxane

PEG – Polyethylene Glycol

PIDS – Polarization Intensity Differential Scattering

PS – Polystyrene

psi – Pound per Square Inch

ROP – Ring Opening Polymerization

r.t. – Room Temperature

SEM – Scanning Electron Microscope

St – Styrene

TEM – Transmission Electron Microscope

THF – Tetrahydrofuran

TGA – Thermogravimetric analysis

dNbipy – 4,4'-Dinonyl-2,2'-dipyridyl

Preface – Thesis outline

This thesis has been prepared in modified "sandwich" style. The thesis starts with a general introduction to micro-spheres: their preparation, modification, and applications. Each subsequent chapter represents a published journal article or manuscript. The research aims and a brief description of the thesis chapters follow below.

Chapter 1 – Introduction to Polymer Micro-spheres: Preparations, Modifications, and Applications

Overall introduction of the thesis

The aim of the first chapter is to review relevant research background in polymer micro-sphere research and introduce general concepts relating to their preparation, modifications, and applications.

Chapter 2 - Grafting of Polystyrene from Narrow Disperse Polymer Particles by Surface-Initiated Atom Transfer Radical Polymerization

Research Objective

The aim of this research was to adapt a combination of grafting-from and living/controlled polymerization (ATRP) to modify narrow dispersed polymer micro-spheres with polymer grafts. The new modification method should provide a powerful tool to prepare micro-spheres with linear polymer chains grafted on their surfaces, which

can be used as HPLC packing materials and materials for photonic crystals.

Synopsis

In this chapter, grafting of polystyrene from narrow disperse polymer particles by surface-initiated atom transfer radical polymerization was investigated. Poly(DVB80) particles prepared by precipitation polymerization were used as starting particles. Their residual surface vinyl groups were hydrochlorinated to form chloroethylbenzene initiating sites for subsequent ATRP of styrene using CuBr/2bipy as catalyst system. Polystyrene was found grafted not only from the particle surfaces, but also from within a thin swellable shell layer, leading to particles size increases from 2.96 to 3.07 μm. This (near) surface layer of grafted polystyrene improved colloidal stability and facilitated formation of 2-dimensional colloidal arrays. Block copolymers of poly(styrene-*b*-4-methylstyrene) were grown from the particles and the livingness of surface initiated ATRP discussed.

Associated Publication

"Grafting of Polystyrene from Narrow Disperse Polymer Particles by Surface-Initiated Atom Transfer Radical Polymerization" Guodong Zheng, H. D. H. Stöver, *Macromolecule* (2002), *35*, 6828-6834.

Chapter 3 - Grafting of Poly(alkyl (meth)acrylates) from Swellable Poly(DVB80-*co*-HEMA) Micro-spheres by Atom Transfer Radical Polymerization

Research Objective

The goal of this research was to extend the method of grafting-from by ATRP to swellable polymer micro-spheres having both surface and interior initiator sites. The resulting micro-spheres should combine high swelling ability in organic solvents with high functionality, both of which are required for polymeric support reagents.

Synopsis

In this chapter, the graft polymerization of methyl acrylate (MA), methyl methacrylate (MMA), glycidyl methacrylate (GMA), hydroxyethyl methacrylate (HEMA), and 2-(dimethylamino)ethyl methacrylate (DMAEMA) by atom transfer radical polymerization (ATRP) from lightly cross-linked poly(DVB80-*co*-HEMA) microspheres. These poly(DVB80-*co*-HEMA) microspheres were prepared by precipitation copolymerization and subsequently modified by reaction with 2-bromopropionyl bromide to serve as ATRP macroinitiators. MMA, MA, and HEMA were then grafted from these initiator microspheres at room temperature using CuBr/Me_4cyclam as catalyst. The graft sites, and hence the grafted polymers, are distributed throughout the initiator microspheres. Addition of a second monomer formed grafted block copolymers, indicating that the ATRP reaction was controlled/living. The final particles represent novel, high-capacity polymer-supports comprised of swellable core particles carrying 5.82, 5.09, and 5.18 mmol/g of grafted poly(GMA), poly(DMAEMA), and poly(MMA-*b*-DMAEMA), respectively. The grafted particles were characterized using ESEM, FTIR, Coulter particle sizing and potentiometric

titration.

Associated Publication

"Grafting of Poly(alkyl (meth)acrylates) from Swellable Poly(DVB80-*co*-HEMA) Micro-spheres by Atom Transfer Radical Polymerization" Guodong Zheng, H. D. H. Stöver, *Macromolecule* (**2002**), *35*, 7612-7619.

Chapter 4 - Grafting of Poly(ε-caprolactone) and Poly(ε-caprolactone-*block*-dimethylaminoethyl methacrylate) from Polymer Micro-spheres by Ring Opening Polymerization and ATRP

Research Objective

The objective of this research was to use ring opening polymerization catalyzed by aluminum compounds to modify lightly cross-linked micro-spheres with biodegradable poly(ε-caprolactone). Furthermore, the poly(ε-caprolactone) grafted micro-spheres was converted to ATRP initiator micro-spheres and subsequently grafted with the second polymer block. Eventually, the micro-spheres will have amphiphilic block copolymer on the surfaces of the micro-spheres, comprisied of a biodegradable inner block and a functional outer block.

Synopsis

In this chapter, the ring opening polymerization (ROP) of ε-caprolactone catalyzed by $Al(Et)_3$ and $Al[OCH(CH_3)_2]$ was carried out, using lightly cross-linked

poly(DVB80-*co*-HEMA) microspheres as macroinitiators. The resulting poly(ε-caprolactone) grafted particles with active propagating ends were converted to macroinitiators for ATRP, and used to further graft dimethylaminoethylmethacrylate (DMAEMA) to produce microspheres grafted with block copolymer. The ROP of ε-caprolactone from the poly(DVB80-*co*-HEMA) initiator microspheres was carried out at both room temperature and 70 °C for different reaction times to produce grafted particles with different graft loadings. The subsequent grafting of poly(DMAEMA) blocks using ATRP led to significant particle size increases from 1.57 to 2.24 μm, and to high amine loadings of 5.10 mmol/g dry particles. The grafted particles were characterized using ESEM, FT-IR, ^{1}H-NMR, Coulter particle sizing and potentiometric titration.

Associated Publication

"Grafting of Poly(ε-caprolactone) and Poly(ε-caprolactone-*block*-dimethylaminoethyl methacrylate) from Polymer Micro-spheres by Ring Opening Polymerization and ATRP" Guodong Zheng, H. D. H. Stöver, ; *Polymeric Materials Science and Engineering* (2002), *87* 111-113. *Macromolecules, submitted.*

Chapter 5 – The Properties and Morphology of Polymers and Block Copolymers Tethered on Polymer Micro-spheres

Research Objective

The objective of this research was to study the modification of hydrophilic

poly(HEMA) and pooy(DMAEMA) on the hard (polyDVB80) and of block copolymers the soft poly(DVB-*co*-HEMA) micro-spheres. The properties and morphology of block copolymer tethered on polymer micro-spheres, as a function of length and polarity of each polymer block will be investigated for exploration of the block copolymer under confined condition.

Synopsis

In this chapter, the use of combination method of grafting from with ATRP to modify polymeric micro-spheres was reported. Residual vinyl groups on the hard poly(DVB80) micro-spheres has been converted into ATRP initiators by hydroboration/oxidation reaction followed by a esterification. The surface modification on the hard poly(DVB80) micro-spheres by grafting poly(HEMA) and poly(DMAEMA) via ATRP has generated hydrophilic micro-spheres. The surface property of the micro-spheres, IR spectrum, and acid-base titration has shown the successful modification. Swellable lightly cross-linked poly(DVB-co-HEMA) micro-spheres were modified with various block copolymers, poly(MMA-b-DMAEMA) with different length of first poly(MMA) block, poly(MMA-b-TMAEMA), and poly(MMA-b-GMA). The phase separation of the amphiphilic block copolymer occurred on the micro-spheres has been observed by electron scanning microscopy. The micro-spheres modified with poly(MMA-b-DMAEMA) and poly(MMA-b-TMAEMA) has shown electrolyte property.

Associated Publication

"The Property and Behavior of Block Copolymer Tethered on Polymer Microspheres" Guodong Zheng, H. D. H. Stöver, *Macromolecules* to be submitted

Chapter 6 Future Work in the Surface Modification of the Polymeric Microspheres

Future Work

The aim of the chapter is to find out the future work based on the discussion of the thesis work.

Chapter 1 Introduction to Polymer Micro-spheres: Preparations, Modifications, and Applications

1.0 Background

Polymeric micro-spheres have attracted much interest in academia and industry. The interest has been mainly directed to (a) the preparation of micro-spheres, (b) the modifications of the micro-spheres, and (c) their applications. Micro-spheres have demonstrated current and potential applications throughout chemical and life science, and technology. They impact on many related tasks, including separation, analysis, organic synthesis, immunological screening and diagnostics, drug and vaccine delivery, agrochemicals, food, paper coating and adhesives, as well as on precision engineering and photonics. In particular, micro-sphere based HPLC stationary phases in used the separation and analysis have been well developed. Many reversed-phase resins for separations of polycyclic aromatic hydrocarbons,[1,2] chiral stationary phases for enantiomer separation,[3,4] and specialty resins for affinity chromatography[5] have demonstrated successful applications. In polymer support reagents, micro-spheres have been widely used as solid phase protecting agents,[6] scavenging agents,[7] in the synthesis of bio-compounds[8,9,10] and in selective organic synthesis.[11,12] For these applications, micro-spheres with specific chemical composition, size, porosity, core-shell morphology, rigidity, swelling ability are desirable. The choice of methods to prepare and modify micro-spheres is critical to that end. Emulsion polymerization, for example

is an excellent technique to prepare narrow disperse micro-spheres smaller than 1 μm. Suspension polymerization is a suitable method for making large micro-spheres in the range from 10 to 1000 μm. Although the micro-spheres made by suspension polymerization are widely used as GPC and HPLC stationary phases, the size distribution of these micro-spheres is typically broad,[13] which gives impetus to develop new methods. Dispersion polymerization can provide micro-spheres that are both large in size and have narrow dispersity, but usually cannot contain more than 0.5% crosslinker. Finally, precipitation polymerization is an excellent process to prepare large and narrow disperse micro-spheres with cross-linking degrees ranging from 5 to 100%.[14] Accordingly, the correlation between methodology and size, size dispersion, porosity, morphology, and cross-linking degree should be well understood when specific micro-spheres for certain application are to be prepared. Once again, the modification of micro-spheres also requires micro-spheres having particular features such as functional group loading, accessibility, and polarity, which are closely related to the method used in the preparation of the micro-spheres.

In this chapter, a brief review of the methods for preparing and modifying micro-spheres and related characterization is provided.

1.1 The Preparation of Micro-spheres

1.1.1 Emulsion Polymerization

Emulsion polymerization was first used during World War II for manufacturing synthetic rubber.[15] This polymerization method is presently the dominant process for

commercial polymerization of many monomers used for paints, coatings, finishes, and in the rubber industries. Emulsion polymerization has several distinct advantages including ease of controlling the process due to fewer thermal and viscosity problems compared to bulk polymerization. Polymer micro-spheres generated from emulsion polymerization, referred to as latex with sizes in the 0.05 to 1 μm diameter range, can be used directly without further separation. In emulsion polymerizations, the main components are the monomer or monomers, dispersing medium, emulsifier, and water-soluble initiator. The monomer is only slightly soluble in the polymerization medium. The emulsifier or surfactant is used to help emulsify the monomer in the aqueous polymerization medium, to form 5-50 μm monomer droplets, containing typically 95 to 99% monomer. Excess emulsifier forms micelles, the volume ratio of monomer to polymerization medium is usually within about 0.1-0.5, and the polymerization is carried out at 40-80 °C.

The size of the micelles is much smaller than that of the monomer droplets, while the number of micelles is about 10^6-10^8 times greater than the number of monomer droplets. Consequently, the micelles represent a significantly larger total surface area compared with the monomer droplets. When the initiator dissolved in the continuous medium decomposes upon heating to form radicals that react with dissolved monomer, the majority of the formed oligoradicals partition into the surfactant micelles rather than into the monomer droplets, due to the difference of surface area. Hence, the polymerization mainly takes place in the micelles, and the size of the micelles increases during the polymerization upon capturing more oligoradicals and adsorbing more monomer. The monomer droplets here serve as a reservoir.

A simplified picture of an emulsion polymerization is illustrated in Figure 1.1

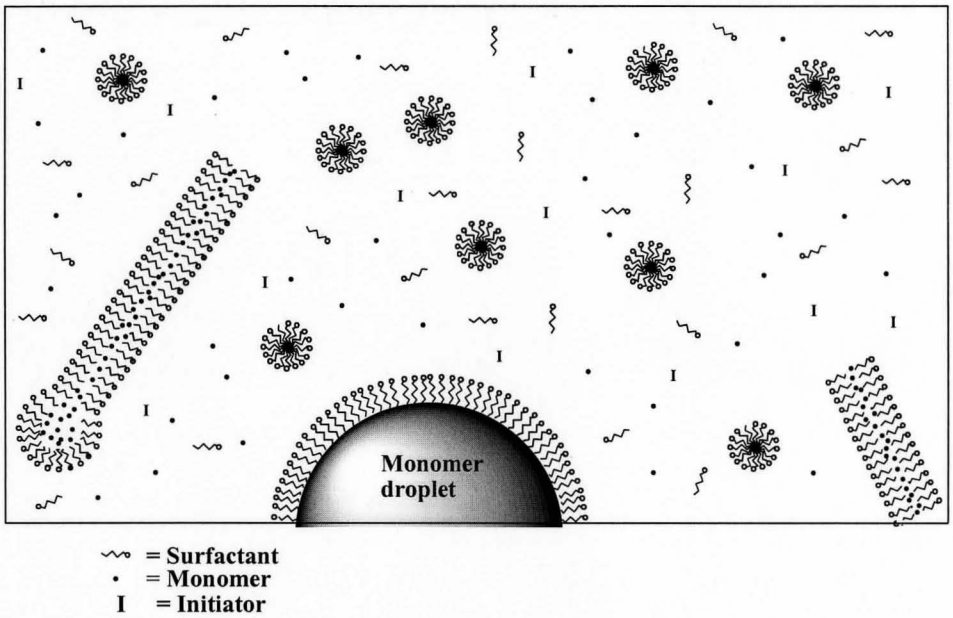


Figure 1.1 Major components in emulsion polymerization

Figure **1.2** Photographs of polystyrene latex made by emulsion polymerization

The numbers of micelles is fairly constant throughout the polymerization. Therefore, the size of micro-spheres depends on the concentration of surfactant and monomer and the size distribution is typically very narrow (CV% ~ 1%). A transmission electron micrograph of polystyrene latexes produced in our lab by emulsion polymerization using $K_2S_2O_8$ initiator is shown in Figure 1.2.

1.1.2 Suspension Polymerization

Suspension polymerization is a process that resembles emulsion polymerization but is quite different in mechanism and reaction characteristics. In suspension polymerization, oil-soluble initiators are employed and dissolved in the monomer droplets in which polymerization occurs. The size of the micro-spheres formed in suspension polymerization are typical large, in the range 10 ~ 1000 μm and their size distribution is broad.

The volume ratio of the monomer phase to the polymerization medium is typically between 0.1- 0.5, and the temperature of polymerization is usually in the range of 20 – 100 °C. The monomer phase is suspended in the polymerization medium in the form of small droplets that are stabilized by a suitable suspension stabilizer. The suspension polymerization then takes place in the droplets in which initiators decompose to form radicals upon heating. The polymerization reaction can be driven to nearly completion in the conversion of monomer. The size and size distribution of micro-spheres formed in suspension polymerization strongly depends on many parameters such as stirring rate, monomer loading, stabilizer concentration, viscosity, and temperature. The final size of micro-spheres corresponds to the size of monomer droplets formed at

the beginning.

It is worth noting that the stabilizer in a suspension polymerization plays a different role from the surfactant in an emulsion polymerization. The role of the stabilizer in suspension polymerizations is to prevent the coalescence of monomer droplets, rather than to form a hydrophobic domain suitable for polymerization. Two types of stabilizer are commonly used:

1. water-soluble polymers such as poly(vinyl alcohol), hydroxypropyl cellulose, sodium poly(styrene sulfonate), and the sodium salt of acrylic acid – acrylate ester copolymer, and

2. water-insoluble inorganic powders such as talc, hydroxyapatite, barium sulfate, magnesium carbonate, calcium phosphate, and aluminum hydroxide. The level of stabilizer used in suspension polymerization is <0.1 wt.% of the aqueous phase.

1.1.3 Dispersion Polymerization

In dispersion polymerization,[16] the reaction mixture composed of monomer, initiator, steric stabilizer, and solvent is initially homogeneous like in solution polymerization. However, the polymerization medium is a precipitant (non-solvent) for the polymer formed during the polymerization. The polymer formed in the polymerization de-solvates and coagulates to form small particle nuclei, which adsorb steric stabilizers on its surfaces and eventually become stable particle dispersions. These particles grow by absorbing both monomers and oligomer radical. Depending on the solubility parameters of polymer and solvent, polymerization may proceed largely within individual micro-spheres, or in the solution phase. In either case, mono-dispersed micro-

spheres in the range of about 0.1-10 μm can be obtained. Addition of crosslinker in amounts larger than 0.5% of total monomer usually interferes with the steric stabilization of the particles, and hence causes broader size distribution and eventually, coagulation.

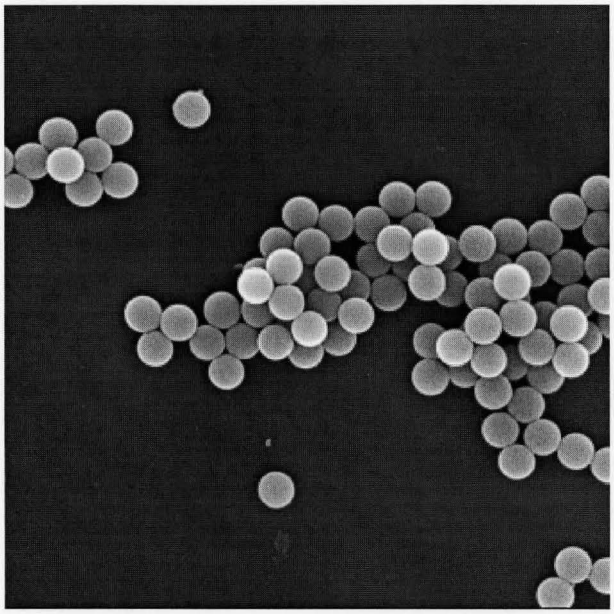


Figure 1.3 Dispersion polymerization of 4-methylstyrene micro-spheres

Dispersion polymerization is used to produce finely divided, stable dispersions that can be used directly as coating, paints, adhesives and other products. The resultant micro-spheres are large and can be easily isolated and purified by filtration and centrifugation. Figure 1.3 shows the ESEM image of about 2 micrometer diameter poly(4-methylstyrene) microspheres produced by dispersion polymerization in ethanol.

1.1.4 Precipitation Polymerization

Precipitation polymerization is essentially similar to the dispersion polymerization

except that no stabilizer is present. In precipitation polymerization, the initial state of the polymerization mixture is the same as that of dispersion polymerization and the initially formed polymer molecule collapses in the medium to form primary particles (nuclei). These nuclei gradually flocculate leading to the formation of precipitates with irregular shape and wide size distribution, and hence the term "precipitation" polymerization. Bulk polymerization of vinyl chloride and acrylonitrile, and solution polymerization of tetrafluoroethylene in water, are examples of precipitation polymerization.[17] The absence of stabilizer and additives in precipitation polymerization is very useful in the production of pure polymers.

Recently, it has been discovered that the precipitation polymerization is no longer a method to produce only irregular shaped precipitates. Our group and others have reported that the precipitation polymerization with high cross-linker concentration and proper solvency can produce mono-dispersed micro-spheres.[18, 19, 20] The reaction conditions differ from those of conventional precipitation polymerization, with low monomer loading (≤ 4 wt.%), higher cross-linker percentage (≥ 5 wt.% relative to monomer), gentle agitation, and marginal or near-*theta* solvency.[21] Under these reaction conditions, mono-disperse micro-spheres with solid, core-shell, or porous morphologies may be formed. Matching the solvent composition to the solubility parameters of the monomer allowed the preparation of functional micro-spheres such as poly(DVB-*co*-HEMA), poly(DVB-*co*-MMA), poly(DVB-*co*-MA), poly(DVB-*co*-GMA), poly(DVB-*co*-MAn), and poly(DVB-*co*-ClMeSt).[22, 23, 24]

Study of the mechanism of the precipitation polymerization has revealed that the

transient gel layer on the micro-sphere surfaces formed during polymerization serves as an auto-steric stabilizing layer, and provides colloidal stability to the growing microspheres. Another essential condition for micro-sphere formation is the presence of cross-linker that provide residual vinyl groups on micro-spheres (and oligomer) surfaces to capture oligo-radicals from the polymerization medium and hence allow the

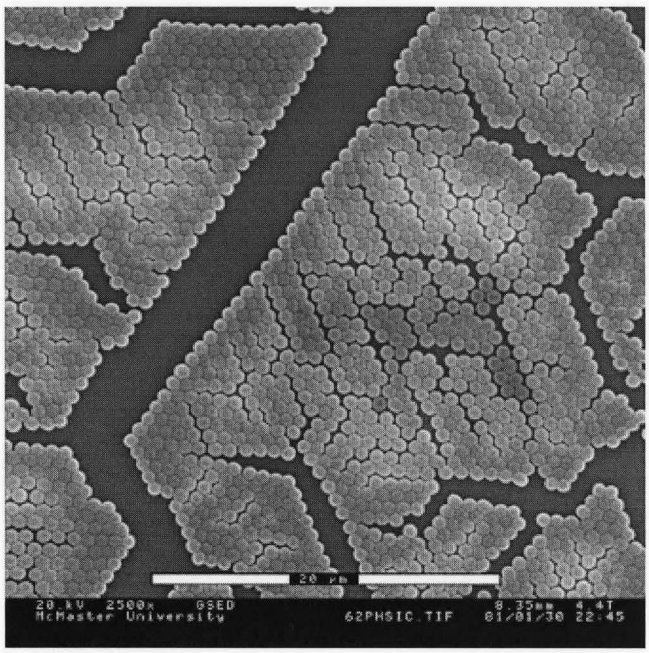


Figure 1.4 The ESEM image of micro-spheres made from the precipitation polymerization of DPDVBS

growth of the micro-spheres. Figure 1.4 shows the ESEM image of mono-dispersed micro-spheres made from the precipitation polymerization of diphenyldivinylbenzylsilane (DPDVBS).

1.1.5 Other Methods

As summarized above, each polymerization has advantages and disadvantages

concerning the size, size distribution, surface properties, mechanical strength, etc. The improvement and modification of the above methods always attracts much attention. As well, new polymerization methods for preparing polymer micro-spheres are continuously being developed. Two of these new methods, multi-step swelling polymerization and dynamic swelling polymerization, are most elegant and useful.

1.1.5.1 Multistep Swelling and Polymerization

Multistep swelling and polymerization is also called seeded and activated swelling polymerization. Preformed, mono-disperse polymer micro-spheres can be added as seeds to the polymerization mixture at the onset of the polymerization.[25,26] The seed micro-spheres serve as shape templates that retain their shape and narrow size-distribution as they are swollen by monomers and solvents. The size distribution of resultant micro-spheres strongly depends on the size distribution of the seed micro-spheres. Usually, polystyrene seed micro-spheres are prepared by an emulsifier-free emulsion polymerization, in which the micro-spheres can be mono-dispersed. [27] The process includes at least two swelling steps:

1. activating solvent swelling and
2. monomer/porogenic solvent swelling

Depending on the ratio of monomer to seed micro-spheres, the process can produce mono-dispersed micro-spheres up to 100 μm in diameter. [28] The magnitude of the enlargement of the seed micro-spheres can be calculated according to the following simple relationship:

$$d_p^3/d_{seed}^3 = (V_{monomer} + V_{seed})/V_{seed}$$

where d_p is the diameter of the final micro-spheres, d_{seed} is the diameter of the seed micro-spheres, $V_{monomer}$ is the volume of monomers used in the swelling, and V_{seed} is the volume of the seed micro-spheres.

Porogenic substances were often used to generate porous micro-spheres. When a good solvent for growing polymer chains is used as porogenic substance, relatively small pores with narrow pore size distribution would form in the micro-spheres. In contrast, a non-solvent for growing polymer chains would lead to relatively large pores with wide pore size distribution. This is particularly useful for preparing porous narrow dispersed micro-spheres used in chromatography. The micro-spheres made from this process have shown excellent column efficiency with very low back-pressure drops.[29,30]

However, the multi-step swelling and polymerization is a time consuming process and needs precise control. It is still difficult to produce high quality micro-spheres by this process, even at the pilot scale.

1.1.5.2 Dynamic Swelling Polymerization

Dynamic swelling polymerization is very similar to the multi-step swelling and polymerization.[31] The only difference between these two methods is in the swelling step: the dynamic swelling method requires only one step swelling. Seed micro-spheres are suspended in the mixture of monomer and solvent (A) in the presence of stabilizer, followed by a slow addition of solvent (B), in which the monomer does not dissolve. The monomer would accordingly be driven into the micro-spheres and swell the micro-spheres during the addition of solvent (B). Since the solvent (B) is slowly added at a controlled rate, undissolved monomer in form of tiny monomer droplets separated from

the mixture will dynamically adsorb in the seed micro-spheres. In this way, each seed micro-sphere has the same chance of taking up the same amount of monomer if the seed micro-spheres are of the same size (surface / volume ratio). An alternative procedure to swell dynamically the seed micro-spheres is to lower the temperature, to reduce the monomer solubility.[32] A very high swelling ratio of monomer to the seed micro-spheres is available to meet the requirement for making large micro-spheres. The polystyrene seed micro-spheres can adsorb about 100 times their own weight of styrene, leading to large, monodisperse micro-spheres of 8.5 μm diameter during subsequent polymerization.[33] The investigation of the thermodynamic background of the dynamic swelling method has revealed that high swelling is based on the size difference between the monomer droplets and polymer seed micro-spheres.[34,35]

In addition to preparing large micro-spheres, the dynamic swelling polymerization method is also suitable to prepare micro-spheres in highly cross-linked, hollow, and snowman shape.[36,37,38]

1.2 Modification of Micro-spheres

Micro-spheres with functional groups can be prepared by using functional monomers in polymerization, and by modifying preformed micro-spheres, as shown in Figure 1.5.

In the formation of micro-spheres during polymerization, functional monomer can be used to produce functional polymer or copolymer micro-spheres. Generally, the methods described above are suitable to produce micro-spheres with functionality.

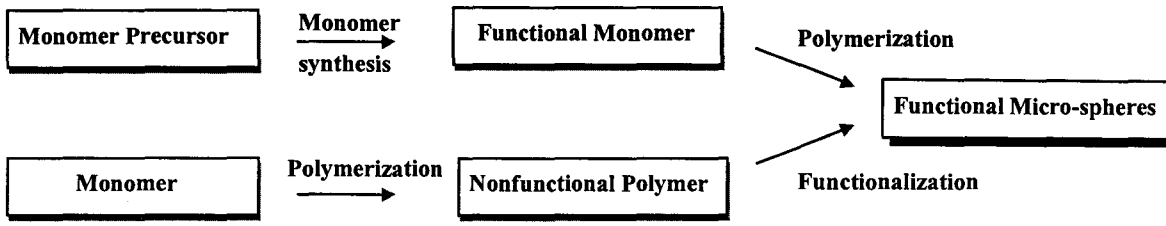


Figure 1.5 Two alternative routes conventionally employed for synthesis of functional micro-spheres

However, each method has limits to produce certain desired functional micro-spheres. Emulsion polymerization, for example, is not suitable for hydrophilic monomer since they will dissolve in the polymerization medium. Copolymerizations, especially using semi-batch type approaches, have to be used to incorporate hydrophilic comonomers. An alternative procedure for preparing hydrophilic functional emulsion micro-spheres is to modify emulsion micro-spheres after polymerization.

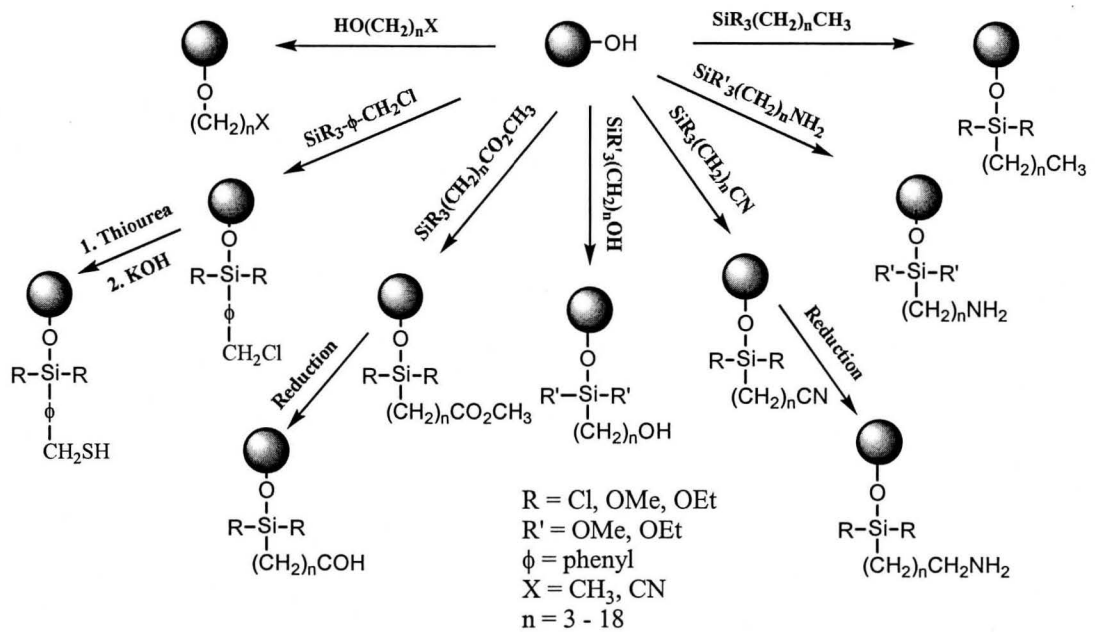
In this section, modification of micro-spheres with both functional groups and polymers will be discussed.

1.2.1 Modification of Micro-sphere for Introducing Functional Groups

Many types of inorganic and organic micro-spheres have been modified by chemical reactions. Depending on swellability and porosity, micro-spheres may be modified on their outer surface, or throughout the bulk of the particle. Active groups on preformed micro-spheres, which allow modification reaction to take place, must be taken into account. The choice of polymerization method and material to produce preformed micro-spheres is important although most modifications have been done with

commercially available micro-spheres.

Scheme 1.1 shows modification of silica micro-spheres with active silanol groups by alcohols, trichloro, and triethoxysilanes carrying various functionalities. [39]



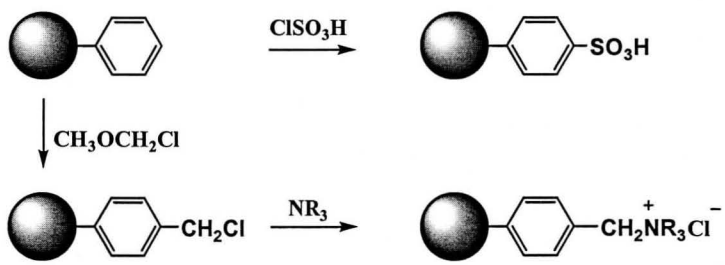
Scheme 1.1 The routes to modify silica micro-spheres

The functionalization of silica micro-spheres is based on the chemistry of surface silanol groups. The silanol group can react with active trichloro, trialkoxysilanes, and alcohols carrying various functionalities. The modification reaction on silica micro-spheres is normally straight forward and is carried out by refluxing the micro-spheres in a toluene solution of the reagent.[40,41] In some cases, the reaction takes place in toluene containing traces of water, or in aqueous media.[42,43] In either case, the chemistry of the reaction is complicated since the silanol groups may be free or H-bonded, depending on the thermal history of the micro-spheres. The efficiency of the modification strongly

depends on the starting micro-spheres (thermal history, porosity, size etc.), reagents (type of active group and chain length), solvents, and reaction temperature.

The modification using silylation reagents is also applicable to other inorganic micro-spheres such as those consisting of titania and zirconia.[44]

Polystyrene micro-spheres are the most popular organic material used as strongly acidic and strongly basic ion exchange resins.[45] Commercially important polystyrene ion exchangers are produced in one or two steps (Scheme 1.2).

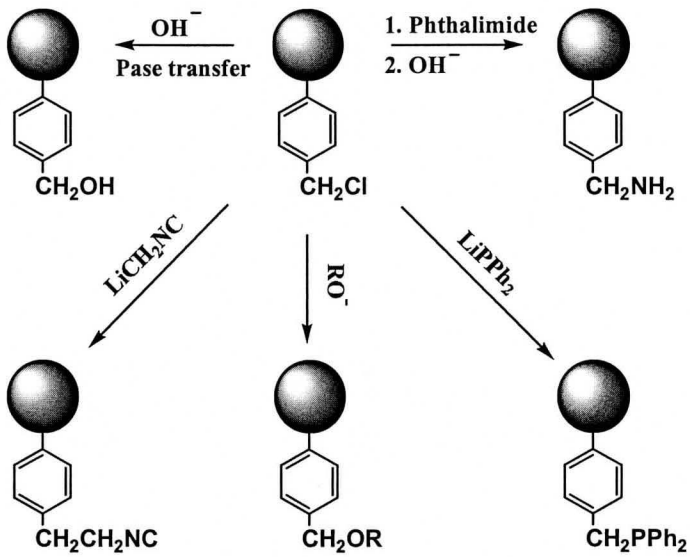


Scheme 1.2 The routes to commercial ion exchange resins

The aromatic phenyl ring in the poly(styrene-*co*-divinylbenzene) micro-spheres can be sulfonated using chlorosulfonic acid to produce strongly acidic cation exchanger. The same starting micro-spheres are able to react with chloromethyl methyl ether to generate the chloromethylated poly(styrene-*co*-divinylbenzene) that is further treated with trialkylamine to give strongly basic anion exchanger.

In addition to the chloromethylation of polystyrene-based micro-spheres, the corresponding micro-spheres also can be prepared using chloromethylstyrene monomer

through a copolymerization.[24] The chloromethylated poly(styrene-*co*-divinylbenzene) micro-spheres is the most useful intermediate for the synthesis of styrene-based functional micro-spheres. Some functional micro-spheres derived from the chloromethylated precursor are depicted in Scheme 1.3.[46]

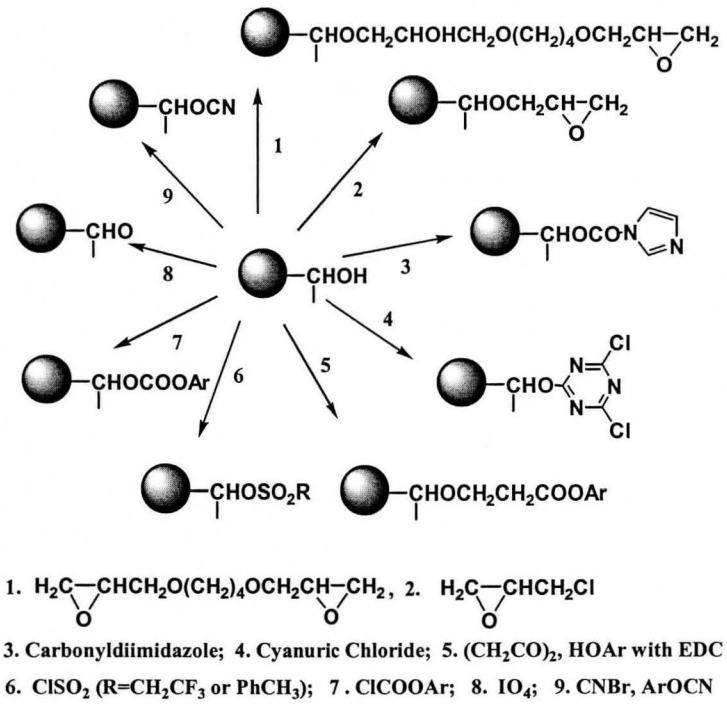


Scheme 1.3 Functional groups derived from chloromethyl styrene micro-spheres

These functional groups derived from chloromethyl groups are commonly used as chelating agents in hydrometallurgy as well as a wide range of other analytic, catalytic, and synthetic uses.[47,48]

One of the functional micro-spheres above, incorporating CH_2NH_2 groups, is particularly interesting in solid phase peptide synthesis. The micro-spheres with CH_2NH_2 groups could also be prepared by the reaction of hexamethylenetetramine with the chloromethylated poly(styrene-*co*-divinylbenzene) micro-spheres, followed by

treatment with hydrochloric acid.[49] The flexibility of such amine groups on micro-spheres used for solid state synthesis is important for accessibility, and is achieved by using a spacer arm.



1. H_2C—$CHCH_2O(CH_2)_4OCH_2CH$–CH_2 (O), 2. H_2C—$CHCH_2Cl$ (O)

3. Carbonyldiimidazole; 4. Cyanuric Chloride; 5. $(CH_2CO)_2$, HOAr with EDC

6. $ClSO_2$ (R=CH_2CF_3 or $PhCH_3$); 7. ClCOOAr; 8. IO_4; 9. CNBr, ArOCN

Scheme 1.4 The routes to modify polysaccharide micro-spheres

Many other polymeric micro-spheres such as polysaccharide and polyacrylamide have been widely functionalized. The modifications are based on the chemistry of hydroxy groups in polysaccharide and amide groups in polyacrylamide. Scheme 1.4 illustrates the routes to modify polysaccharide micro-spheres.[50]

It is noteworthy that the most of chemical reactions shown in Scheme 1.4 are also applicable to other hydroxy bearing polymers and to hydroxy derivatives of silica micro-spheres.

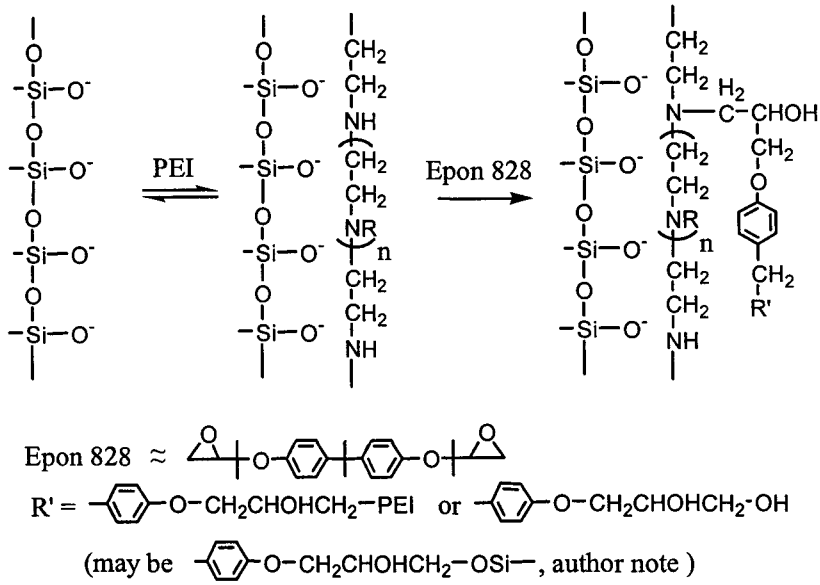
1.2.2 Modification of Micro-spheres for Tethering Polymers or Block Copolymers

Modification of micro-spheres for tethering polymers or block copolymers provides not only a way to introduce functionality, but moreover permits changing the surface properties of the micro-spheres. Such modifications can also lead to changes in micro-sphere size and morphology, depending upon the amounts of polymer grafted. The modification of micro-spheres by grafting polymers differs significantly from functionalization by chemical reactions. Many methods have been used to tether polymer chains on micro-spheres. Those modification methods can be roughly categorized into (1) Grafting-on; (2) Grafting-through; (3) Grafting-from.

Grafting-on The method of grafting-on refers to grafting preformed polymer to micro-spheres by a chemical reaction. The preformed polymer may have one or multi-functional groups that are able to react with active groups on the micro-spheres. The preformed polymer would be anchored with one, usually terminal, functional group to a micro-sphere. This grafted polymer would normally assume a coiled conformation. The number and amount of polymer grafted on the micro-sphere depends on the molecular weight and property of the graft. Normally, the polymer density on the micro-spheres does not reach a high level when using the grafting-on approach, since an already grafted polymer with a coil conformation will tend to repulse the in-coming polymer.

On the other hand, a preformed polymer with multi-functional groups would blanket the surface of the micro-spheres. Polyethyleneimine (PEI) is a multi-functional polymer and was widely used to blanket silica micro-spheres for applying HPLC packing

material. An example is shown in the Scheme 1.5.[51] PEI was first adsorbed on silica micro-spheres, followed by cross-linked with EPON 828, poly(bisphenol A-*co*-epichlorohydrin) MW=377 to form pellicular micro-spheres.



Scheme 1.5 PEI blanketed silica micro-spheres

Grafting-through The grafting-through is a method to modify micro-spheres by suspending micro-spheres in polymerization solutions, and subsequently polymerizing to embed the micro-spheres in polymer shell or matrix. The grafting-through method is often used to prepare core-shell micro-spheres by heterogeneous polymerization.[52] The structures of core-shell micro-spheres were obtained by aqueous polymerization of HEMA on polystyrene core micro-spheres and by aqueous polymerization of styrene in the presence of polyHEMA core micro-spheres. Interestingly, both polymerizations gave

a similar structure, with polystyrene cores and polyHEMA shells.[53] In the case of polystyrene seeds, polymerization of HEMA in aqueous medium led to polyHEMA deposited on the seeds. On the contrary, the polyHEMA seeds would adsorb styrene from the aqueous phase, and the polymerization of styrene occurred inside polyHEMA core.

The grafting-through approach was also used to make pore-matrix micro-spheres. Porous inorganic micro-spheres such as porous silica are soaked in a solution of an organic monomer mixture, usually containing a cross-linker and an initiator. Subsequent polymerization results in the formation of polymer distributed in pores of the inorganic micro-spheres. When large amount of organic monomer was used, many small silica micro-spheres embedded in an individual organic polymer micro-spheres was observed.[54]

Grafting-from The grafting-from refers to the modification of polymer on micro-spheres by *in situ* polymerization starting from the active sites on the micro-spheres. The difference between grafting-from and grafting-through lies mainly in the locations of initiators. In grafting-through, the polymerization initiates in solution but the active propagating sites on the micro-spheres mainly form by chain transfer unless the micro-spheres have some functional groups such as vinyl. Therefore, the polymerization takes place all the way from solution to micro-spheres. The grafting-from approach requires the starting micro-spheres to be modified with initiators, and hence polymerization initiates only on the micro-spheres. During polymerization, some of the active sites may transfer to the solution but most remain on the micro-spheres. In particular, when a combination of living polymerization and grafting-from is used, the polymer chains

formed on the micro-spheres should be of similar length.

When the surface of silica gel was modified by coating with a monolayer of covalently bound azo-initiator, the polymerization of styrene with high and controlling density on the silica surface occurred upon heating.[55]

For better control in terms of molecular weight and weight distribution, living/controlled polymerization such as an ionic one was employed for grafting-from. Living polymerization methods, on the other hand, are able to generate grafted homopolymers and block copolymers of uniform lengths.

A lithium compound is a common reagent to generate an anion for living anionic polymerization. The addition of *sec*-butyllithium (*s*-BuLi) to a layer of 4-trichlorosilylstyrene immobilized on a silica surface, and the subsequent living anionic polymerization of styrene and isoprene from the resulting surface-bound initiator groups could lead to well defined homo-polymer and block copolymer.[56] The studies of grafting-from process through ionic polymerization involved micro-spheres, based on carbon black,[57] and silica[58] were also reported.

Recently, the application of atom transfer radical polymerization (ATRP) to grafting polymers from solid surfaces[59] has generated much interest since ATRP, a controlled/living radical polymerization, has a number of advantages over both conventional free radical and ionic polymerization.[60] ATRP has a highly living nature, allowing for the synthesis of block copolymers,[61] dendrimeric polymer[62] and graft copolymers,[63] and is particularly tolerant of water[64] and functional groups.[65] Below are some examples of grafting off micro-spheres.

Spherical silica micro-spheres with an average diameter of 70 nm were tethered with surface ATRP initiator (2-(4-chloromethylphenyl)ethyl)dimethylethoxylsilane, followed by ATRP of styrene at 130 °C in presence of CuCl/dNbipy as catalyst. The size of the micro-spheres increased with conversion, consistent with the molecular weight of the grafted polymer. The grafted polymer chains were cleaved from the support particles using 5% aqueous HF and aliquat 336, and showed narrow molecular weight distribution with a PDI of about 1.3.[66]

Grafting polymer from polymeric micro-spheres is only reported very recently. Wang resin was transformed into an initiator for ATRP of methacrylates at initiator loading of 0.9 and 3.5 mmol g^{-1}. The polymers of poly(methacrylates) were harvested from the insoluble resin by cleavage using trifluoroaceticc acid. Poly(MMA) de-tethered from the resin was found to have an average number molar mass, M_n of 8200 and a polydispersity, PDI of 1.18 after surface polymerization for 3 h.[67] Potential resins for oligopeptide solid-phase synthesis were prepared by ATRP via grating-from Wang, Merrifield, and primary amino functional beads.[68]

1.3 Applications of Micro-spheres

Micro-spheres can be employed in many applications as mentioned above. Here only those applications related to the research presented in this thesis will be discussed. My work has focused on the development of HPLC packing material and solid support reagents. In this section, the discussion is not to give any examples of polymer micro-spheres in applications of HPLC and solid phase synthesis since their importance is

obvious but rather to explore the design of polymer micro-spheres for achieving a better performance.

HPLC Packing Material Many applications of modified micro-spheres, especially as packing material of HPLC, rely on the properties of the particle surface. For the development of HPLC stationary phases, several important aspects should be considered: size, size distribution, functionality, polarity, porosity, and mechanical strength. Since the precipitation polymerization will be selected for preparing micro-spheres in this thesis, the size and size distribution would be controlled. The other aspects of functionality, polarity, porosity, and mechanical strength are more important. Modified hydrophilic surface of polymeric packing material is required for the separation of bio-chemicals because inherent hydrophobic character of polymeric micro-spheres is a serious limitation that may cause the proteins to denature due to hydrophobic-hydrophobic interactions.[69] On the other hand, hydrophobic character of the surface is required for a reversed-phase column. It has turned out that higher and denser coverage of polymeric C_{18} phase has better molecular recognition for polycyclic aromatic hydrocarbons (PAH) than lower coverage of monomeric C_{18}.[70] To enhance the separation efficiency, the porosity of the stationary phase, namely high surface area is required in most cases. The micro-spheres made by precipitation polymerization could have high porosity but the pore size usually is smaller than 50 Å. This corresponds to a molecular weight cut-off of about 500 Daltons, which is too small for separation of large molecules. A series of studies has revealed that this is an inherent limitation of precipitation polymerization.[71] However, high porosity, especially large pores of the

polymeric micro-spheres will decrease the mechanical strength and may lead to deformation or destruction during use. Therefore, obtaining polymeric stationary phases with both high surface areas and high mechanical strength is a challenging subject.

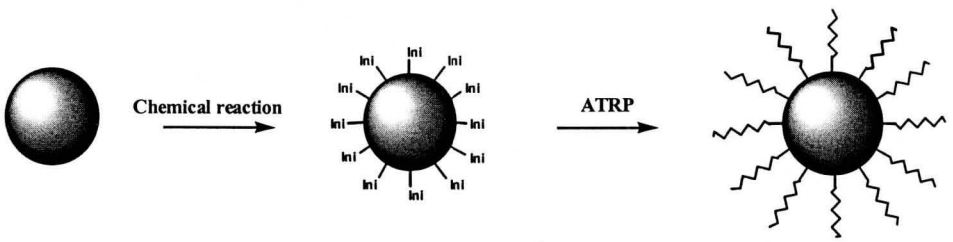
In this thesis, a new approach to develop polymeric stationary phases with both high "surface area" and high mechanical strength will be adopted. That is a three-step process:

(1) using the precipitation polymerization to provide highly cross-linked, robust micro-spheres as starting particles

(2) introducing ATRP initiators on the starting micro-spheres

(3) using a combination of ATRP and grafting-from to generate polymer chains on the micro-spheres

Scheme 1.6 illustrates the last two steps of the process.



Scheme 1.6 Introducing initiators and grafting-from polymer chains on the micro-spheres

Grafting polymer chains from highly crosslinked microsphere surfaces would enhance the interaction between the polymer chains and solutes. Therefore, the modified particles should have both high mechanical strength and high separation efficiency. The

grafted polymer chains could be either hydrophilic or hydrophobic. A block copolymer may also be grafted since the ATRP is a living/controlled polymerization. The modification of micro-sphere surfaces can be expected to achieve:

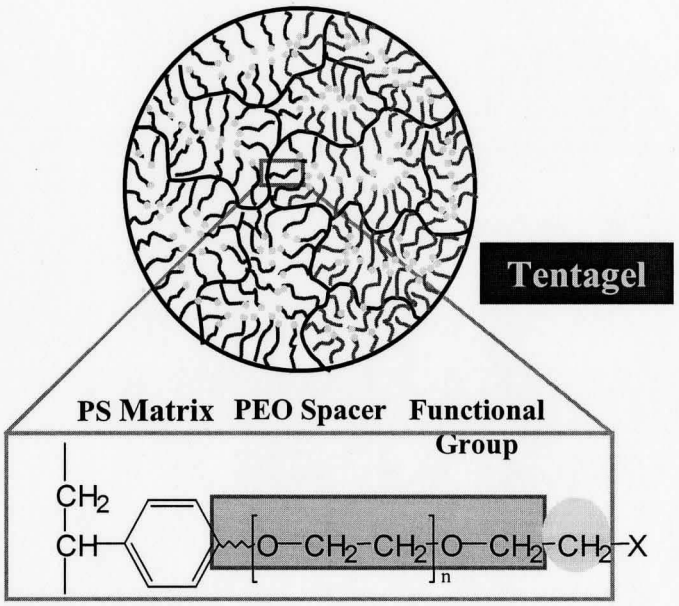
1. The different types of grafted polymers can be selected using different monomers such as hydrophilic hydroxyethyl methacylate (HEMA), dimethylaminoethyl methacrylate (DMAEMA) or hydrophobic butyl methacrylate(BMA), methyl methacrylate (MMA), etc. depending on requirements of separations.

2. Graft block copolymers may also be prepared by subsequent polymerizations since the ATRP is living.

3. The length of grafted polymers can be controlled by reaction time and monomer loading during the modification.

Polymer support reagents Functional polymeric micro-spheres used as polymer support reagents must meet some requirements. Those polymer support reagents should be mechanical stable, compatible with a range of solvents, and have high functionality. Many polymer support reagents have been commercialized, such as Pepsyn,[72] TentaGel,[73] and PolyHIPE.[74] The compatibility with various solvents was first considered for solid-phase synthesis of bio-compounds. The TentaGel, for example, are comprised of a lightly cross-linked polystyrene backbone and grafted polyethylene oxide with a functional group at end. The structure of the TentaGel is shown in Scheme 1.7.

In this structure, the lightly cross-linked polystyrene as a backbone provides the mechanical strength and the polyethylene oxide with a functional group having high percentage of the total weight predominates the property of the micro-spheres. Hence,



Scheme 1.7 The structure of the TentaGel polymer support reagent

the TentaGel will swell in any solvent that is a good solvent for polyethylene oxide. However, the TentaGel has only relatively low functional group loading, due to only one functional group being introduced at the end of each polyethylene oxide. It was found that lowering the molecular weight of polyethylene oxide increased the relative functional loading but decreased the reactivity due to decreased swelling ability and flexibility. The low functionality of the TentaGel is hence an inherent limitation of such resins.

On the other hand, lightly cross-linked polystyrene beads such as Merrifield resin have higher functionality since the functional groups are directly attached on phenyl ring of the polystyrene. The properties of the beads are dominated by polystyrene that is not very compatible with many polar solvents. The reactivity of groups on those beads was

lower than that of TentaGel. Therefore, an ideal polymer support reagent should have compatibility with various reaction solvents and high functionality having high reactivity.

In this thesis, an effort to develop polymer support reagents with both solvent compatibility and high functionality will be described. Once again, the combination of living/controlled polymerization and grafting-from will be used to prepare those materials.

The structure of new polymer support reagents will be similar to that of the TentaGel but have much higher functionality. The starting micro-spheres with a low degree of cross-linking will be prepared by precipitation polymerization. The ATRP initiators will be introduced onto the micro-spheres and polymerization of functional monomer such as dimethylaminoethyl methacrylate from the initiator micro-spheres will be performed to obtain the grafted polymer particles. The properties of the resultant micro-spheres will be determined by the grafted polymer (high weight percentage), which should swell well in all solvents dissolving the grafted polymer. The functionality of new micro-spheres should be much higher than that of TentaGel since the functional groups attach in each unit of the polymer rather than only one in each polymer.

Conclusively, a new modification method consisting of the combination of living/controlled polymerization and grafting-from will be developed and will be tested for the preparation both of ideal HPLC stationary phases, and of novel polymer support reagents with high compatibility and functionality.

1.4 Characterization of Polymeric Micro-spheres

The characterization of micro-spheres, especially modified micro-spheres can be categorized into two aspects, the determination of chemical composition and size (or/and morphology). There are many modern techniques available to characterize polymeric micro-spheres. In this thesis, only those techniques used in this study are briefly reviewed below.

1.4.1 General Characterization of Polymeric Micro-spheres

Nuclear Magnetic Resonance (NMR) Both ^{13}C and ^{1}H are excellent techniques to analyze polymer composition and structure in solution. To study polymeric micro-spheres or polymer grafted on micro-spheres, the magic angle spin technique is required. However, when linear polymer was grafted on micro-spheres, the polymer would swell in good solvent and can be studied in gel state by NMR.

Fourier Transform Infrared (FT-IR) FT-IR is a very popular technique to determine the composition of inorganic and organic compounds. It is a particular useful method to verify functional groups in organic molecules in qualitative and quantitative measure. For polymeric micro-spheres and the modified microspheres, the composition and functionality can be easily detected by using KBr pellet.

Potentiometry titration is widely used in analytic chemistry for qualitatively measuring acid, base and various other compounds. This technique is also able to determine organic acid, base, and some functional groups. The functionality of modified micro-spheres can be titrated to give information about functional loading, which may relate to modification degree.

Elemental analysis Elemental analysis is often used to determine chemical

composition of organic and polymer molecules. The change in composition reflects the modification and modification degree. Elemental analysis is a powerful method to monitor the modification of micro-spheres.

1.4.2 Characterization of Size and Morphology of Micro-spheres

Environmental Scanning Electron Microscope (ESEM) ESEM is the same technique as scanning electron microscope (SEM) except for the presence of a vapor environment, especially water vapor. The electron microscope is used to generate images of solid or soft material to provide information about surface and morphology. This is a particularly useful technique to study polymeric micro-spheres.

The electron microscope emits an electron beam that can be focused on narrow area of the sample. The beam may be scanned across the sample surface or fixed at one point and hence the machine is called a scanning electron microscope. The electrons can pass through the surface of the sample and interact with the sample to generate radiation. Different radiation e.g. auger electrons, secondary electrons, back scattered electrons, and characteristic X-rays may escape from different depths and have different spatial resolutions and energy information.

Secondary electrons are those electrons arising from inelastic collisions of the electron beam with the outer shells of atoms near the surface. Back-scattered electrons are electrons of the incident beam reflected by inelastic collisions with nuclei of atoms near the surface. Both the back scattered and secondary electrons "illuminate" the surface and are used to generate a map of surface texture.

Such high resolution maps provide important information about the size, size

distribution, and morphology of micro-spheres, which makes the technique an excellent tool to study micro-spheres.

Coulter Multisizer The Coulter multisizer is an instrument for measuring the size of micro-spheres. The principle of the instrument is based on the electric conductivity of a microsphere dispersion in a conducting solution. A special design of an electrochemical cell consists of two electrodes inserted each side of an aperture on a tube (Figure 1.6).

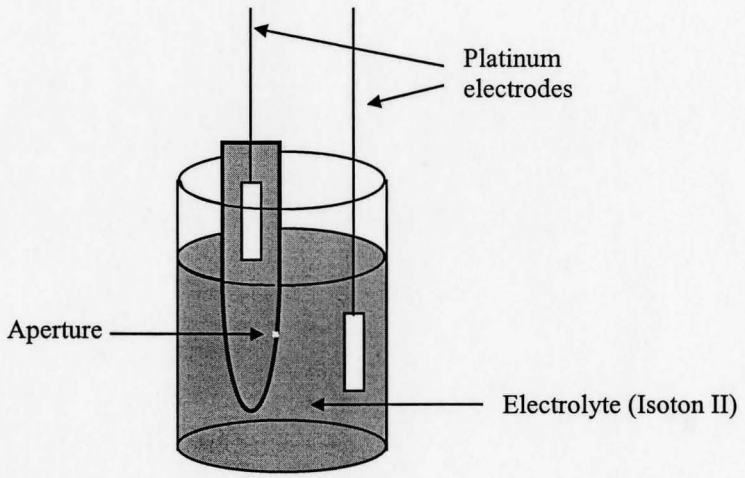


Figure 1.6 Schematic of a Coulter multi-sizer electrochemical cell

During measurement, a drop or two of dilute micro-spheres in suspension (often acetone) is added to the aqueous electrolyte, Isoton II, outside the tube and the micro-spheres in the electrolyte are carried through the aperture by a flow of the electrolyte. The electric resistance between the two electrodes changes when micro-spheres pass the aperture. The electric resistance is proportional to the volume of the electrolyte replaced

by the micro-sphere in the aperture. A profile of electric current with time will be recorded and automatically converted into a plot of size and number of micro-sphere.

Tubes with different aperture diameters can be selected for micro-spheres in certain range. The micro-spheres that are about 40% of the aperture in size lead to blockage, and the micro-spheres smaller than about 2% of the aperture do not give any signal above the noise and are effectively invisible.

It is worth mentioning that micro-spheres modified with electrolyte or polyelectrolyte will be seen as smaller micro-spheres since the micro-spheres do not increase the electric resistance as usual micro-spheres do.

A dilute suspension of polymeric micro-spheres is required to reduce aggregation in aqueous electrolyte. Polymeric micro-spheres, especially those with a large hydrophobic monomer content, quite often form doublets, triplets, and aggregates, which

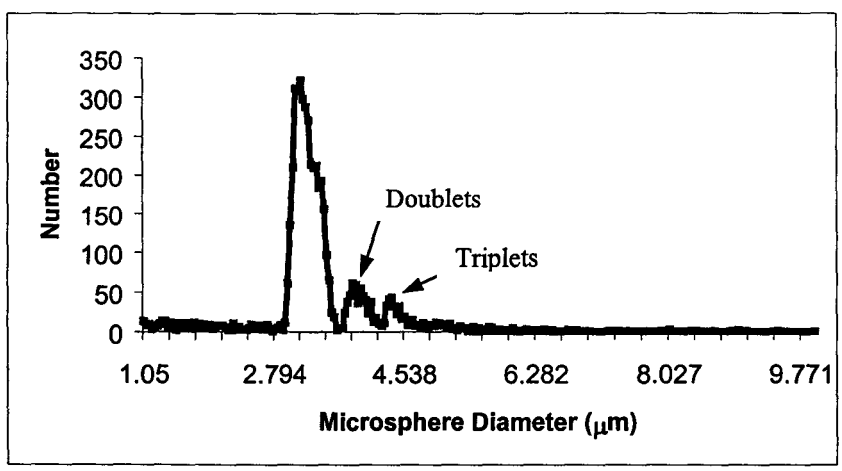


Figure 1.7 Coulter multi-sizer results of poly(DVB) micro-spheres with linear poly(HEMA) chains on their surface

would be measured as a single, larger micro-sphere. These would appear as shoulder peaks on the right hand side of the main peak, shifted by the cubic root of two or three. A typical plot of micro-spheres with doublet and triplet signals is shown in Figure 1.7.

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Chapter 2 Grafting of Polystyrene from Narrow Disperse Polymer Particles by Surface-Initiated Atom Transfer Radical Polymerization[1]

Abstract

Grafting of polystyrene from narrow disperse polymer particles by surface-initiated atom transfer radical polymerization was investigated. Poly(DVB80) particles prepared by precipitation polymerization were used as starting particles. Their residual surface vinyl groups were hydrochlorinated to form chloroethylbenzene initiating sites for subsequent ATRP of styrene using CuBr/2bipy as catalyst system. Polystyrene was found grafted not only from the particle surfaces, but also from within a thin shell layer, leading to particle size increases from 2.96 to 3.07 μm. The surface layer of polystyrene improved colloidal stability and facilitated formation of colloidal arrays. Block copolymers of poly(styrene-*b*-4-methylstyrene) were grown from the particles, and the living nature of surface initiated ATRP is discussed.

2.0 Introduction

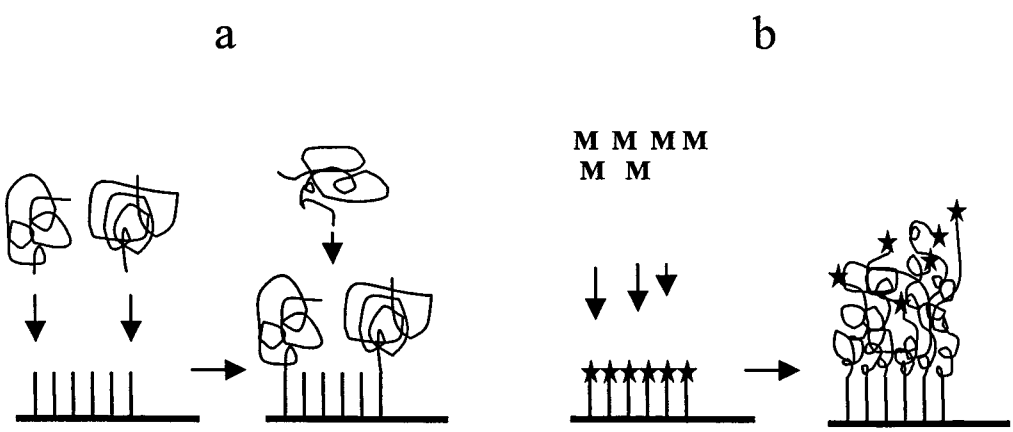
The modification of particles or planar surfaces by grafting of polymer chains has attracted much academic and industrial interest. Particular attention has been given to polymer "brush-type" layers with properties such as being able to change their swelling volume in response to changes in pH or ionic strength,[1] temperature,[2] solvent quality, or

[1] G. Zheng, H.D.H. Stöver, *Macromolecule* (**2002**), *35*, 6828-6834.

mechanical force.[3,4] The grafted surfaces may be formed by either a "grafting onto" or a "grafting from" approach.

In the former case (Scheme 2.1a), pre-formed polymer chains carrying an active terminal group are coupled onto a reactive surface. This approach allows careful control of the polymer chains, but tends to suffer both from low grafting rates[5] and from low final graft density,[6] since already tethered chains try to maintain their coil shape in good solvents, and hence hinder further grafting in their vicinity. As well, the overall amount of grafted polymer first increases with increasing molecular weight, but subsequently decreases due to the steric exclusion.

The "grafting-from" technique (Scheme 2.1b) allows polymer chains to initiate from every active site on the substrate, giving high grafting densities because monomers can easily diffuse to the propagating sites.



Scheme 2.1 Surface Grafting of Polymer Chains

Rühe et al. [7] reported the conventional free radical polymerization of styrene from the surface of silica gel coated with a monolayer of covalently bound azo-initiator. Graft polymers with high, controlled graft density could be obtained. However, conventional free radical polymerization, especially when confined to a thin layer, leads to a wide molecular weight distribution of the grafted polymers, largely due to termination reactions.[8] Moreover, this approach is not suitable for preparing block copolymers.

Living polymerization methods, on the other hand, are able to generate grafted homopolymers and block copolymers of uniform lengths. Schouten's group[9] reported the addition of *sec*-butyllithium (*s*-BuLi) to a layer of 4-trichlorosilylstyrene immobilized on a silica surface, and the subsequent living anionic polymerization of styrene and isoprene from the resulting surface-bound initiator groups.

Ulman's group[10] used self-assembled monolayers of biphenyllithium moieties on gold substrates as initiation sites for the anionic polymerization of styrene. The polymerization of styrene through this grafting-from method yielded densely grafted polymer brushes with a thickness of 18 ± 0.2 nm and a surface roughness of 0.3-0.5 nm.

In most cases, the study of grafting-from process through ionic polymerization involved planar surfaces, or particles, based on carbon black,[11] carbon fiber,[12] graphite,[13] and silica.[14] The sensitivity of ionic polymerizations to polar impurities, as well as to ionic repulsion at high initiator loading, can limit their utility for grafting polymers from solid surfaces.

Controlled/living radical polymerizations such as atom transfer radical polymerization (ATRP)[15] have a number of advantages over both conventional free

radical and ionic polymerization. ATRP has a highly living nature, allowing for the synthesis of block copolymers[16] and graft copolymers,[17] and is particularly tolerant of water[18] and functional groups.[19] Several groups have worked on applications of ATRP in grafting polymers from solid surfaces. Patten et *al.* reported the preparation of structurally well-defined polymer-nanoparticle hybrids by ATRP. [20] Spherical silica particles with an average diameter of 70 nm were tethered with surface ATRP initiator (2-(4-chloromethylphenyl)ethyl)dimethylethoxylsilane, followed by ATRP of styrene at 130 °C in presence of CuCl/dNbipy as catalyst. The size of the particles increased with conversion, consistent with the molecular weight of the grafted polymer. The grafted polymer chains were cleaved from the support particles using 5% aqueous HF and aliquot 336, and showed narrow molecular weight distribution with a PDI of about 1.3.

ATRP were also carried out on the inside of glass capillaries[21] to be used for electrophoresis, and from initiator patterned onto a gold substrate[22] for generating barriers to wet chemical etchants of gold.

The ease of attaching initiators through silyl coupling agents, and the ease of detaching the formed polymer chains to determine their molecular weight and molecular weight distribution, led to significant use of glass,[23] silicon wafers,[24] silica gel[25] and silica particles[26] as support surfaces for ATRP. In contrast, few reports deal with ATRP grafting from organic polymeric particles.[27, 28]

We report here the modification of organic polymeric particles by grafting styrene from polydivinylbenzene (PDVB80) microspheres using ATRP. The PDVB80 micro spheres are prepared by precipitation polymerization of DVB80 using AIBN as initiator

in the absence of added stabilizer or surfactant. However, they do have residual vinyl groups on their surface, which were easily converted into 1-chloroethylbenzene groups by hydrochlorination. The bulk ATRP of styrene took place from benzyl halide initiator sites in the presence of CuBr/2bipy as catalyst.

2.1 Experimental Section

2.1.1 Chemicals

DVB80 (70-85% DVB isomers, Fluka, Oakville, Canada), acetonitrile (HPLC grade, Aldrich), tetrahydrofuran (THF, 99+%, Aldrich), methyl ethyl ketone (MEK) (99+% Aldrich), 2,2'-dipyridyl (bipy) (99+% Aldrich), Cu(II)Br_2 (99%, Aldrich), and diethyl malonate (99%, Aldrich) were used as received. 2,2'-Azo-bis-(2-methylpropionitrile), (AIBN, Eastman Kodak Co.) was recrystallized from methanol. Styrene and 4-methylstyrene were purchased from Aldrich Chemical Co. and purified by distillation under vacuum prior to polymerization. Anhydrous hydrogen chloride in a steel cylinder was purchased from Matheson.

2.1.2 Methods

Preparation of Starting Particles The starting PDVB80 particles were prepared by precipitation polymerization in neat acetonitrile as described earlier.[29] Divinylbenzene-80 (DVB80) (6.0 g, 46 mmol), acetonitrile (200 ml), and AIBN (0.12 g, 2 wt% relative to monomer) were placed in a 250 ml polyethylene bottle and shaken vigorously until the initiator was completely dissolved. The bottle was placed in a reactor equipped with horizontal rollers and a programmable temperature controller. The

reactor gently agitates the sample by rolling the bottles at approximately 4 rpm. The temperature profile used for polymerization started with a 1 hour ramp from room temperature to 60 °C followed by a 1 hour and 40 min ramp to 70 °C where the temperature was kept constant for 24 hours. The resultant micro-spheres were isolated by vacuum filtration through a 0.5 μm membrane filter with three subsequent washing with THF. The clean particles were dried at room temperature under vacuum for 24 hours. The yield of particles was 3.4 g (56.7%), with the remainder being unreacted monomer.

Hydrochlorination of Particles PDVB80 particles (2.00 g) were suspended in 20 ml of THF in a 50-ml two-neck round-bottomed flask for 2 hours. Dry hydrogen chloride (HCl) was slowly passed through the suspension for 1 hr at room temperature. The flow rate of HCl was controlled such that all HCl introduced dissolved in the THF. The HCl saturated suspension was kept for 2 hours at room temperature. The resulting PDVB80-HCl particles were filtered and washed with THF. The final particles were dried at room temperature under vacuum for 24 hours. The yield of particles was 2.07 g. A blank recovery test indicated that recovery after work up was quantitative.

Preparation of CuBr Due to the low purity of CuBr purchased from Aldrich, the CuBr used in ATRP were prepared by the reduction of $CuBr_2$ with dimethyl malonate. $CuBr_2$ (10.0 g, 44.8 mmol) was added to 50 ml of dimethyl malonate/THF (1:1) and the mixture was refluxed for 3 hours. The light yellow precipitate was filtrated through a 0.5 μm membrane filter and washed with methanol followed by hexane. The precipitated CuBr was stored under nitrogen prior to use. The yield was almost quantitative (6.26 g, 43.6 mmol / 97.5%).

Grafting Polymers from Particles The ATRP took place in bulk styrene. Particles PDVB80-HCl (3.00 g) and CuBr (0.26 g, 1.81 mmol) were placed in a flask and degassed/purged with three cycles of vacuum/nitrogen. Subsequently, degassed 2,2'-bipyridine (bipy) (0.58 g, 3.71 mmol) in 10.0 g of styrene was added through a double tipped needle. The mixture was stirred with a magnetic bar, heated to 110 °C under nitrogen, and the reaction continued for 19 hours. The resulting blue-green particles were isolated by centrifugation, re-dispersed three times in THF, several times in methanol/glacial acetic acid (95/5) until the particles were almost white, and finally twice in diethylether prior to drying. The resulting particle yield was 3.34 g. The polymerization solution was very viscous due to the formation of polystyrene through thermal auto-initiation in solution. This polymer was precipitated into methanol and 4.5 g of polystyrene ($M_n = 2.65 \times 10^4$, $M_w = 4.43 \times 10^4$, and $M_w/M_n = 1.67$) were obtained.

Similar polymerizations were carried out for the preparation of grafted particles with different polymerization times, with samples taken via syringe at each time interval. These samples were centrifuged and purified as described above. The first supernatants were used for determining molecular weight of the polymer in solution.

The second grafting, of poly(4-methylstyrene), from particles previously grafted with polystyrene, used a procedure similar to the first grafting: poly(styrene) grafted particles (1.00 g) and CuBr (78 mg, 0.54 mmol) were placed in a flask with a magnetic stir bar, and degassed. Subsequently, degassed bipy (255 mg, 1.63 mmol) dissolved in 4-methylstyrene (3.4 g) was added, and the mixture reacted at 110 °C for 11 hours. The resulting particles were purified by centrifugation as described above. The final yield was

1.09g.

Particle Size Analysis The particle sizes and size distributions were measured using a 256-channel Coulter multisizer interfaced with a computer. A 30 μm aperture tube was chosen to accommodate the particle size range of 1-10 μm. A small amount of particles, dispersed in acetone, was added to 25 ml of Coulter Isoton II electrolyte solution and stirred for 1 min with a mini-stirrer provided with the instrument.

The Coulter multisizer measurements were confirmed using a Philips ElectroScan 2020 environmental scanning electron microscope (ESEM). The samples for the measurement of ESEM were prepared by dispersing particles in THF and casting a drop of this particle suspension on a piece of glass glued to an electron microscope stub with double-sided adhesive tape. The samples were dried under vacuum for 2 hours and sputter coated with 5 nm of gold. The quoted diameters are averages from 50 to 100 particles, and were measured using UTHSCSA ImageTool software.

The particle sizes in the solvent swollen state were measured on a laser light scattering instrument, a Coulter LS230 particle sizer which operates on the principle of Fraunhofer diffraction for large particles (>0.4 μm) and polarization intensity differential scattering (PIDS) for small particles (<0.4-0.8 μm). A good solvent for polystyrene, methyl ethyl ketone was used to disperse the particle samples.

Molecular weight analysis The soluble polymers were analyzed by size exclusion chromatography using a Waters Model 590 pump, equipped with three Waters 5 micron Ultrastyragel Linear columns, and with a Waters 410 Differential Refractometer set to 40°C. Tetrahydrofuran was used as mobile phase at 1 mL/minute, and narrow

disperse linear polystyrene standards were used for calibration.

FT-IR Analysis Fourier transform infrared analysis was performed on a Bio-rad FTS-40 FT-IR spectrometer. All samples were prepared as pellets using spectroscopic grade KBr in a Carver press at 15,000 psi. The spectra were scanned over the range of 4000 - 400 cm^{-1}, in the transmission mode.

Elemental Analysis Elemental analysis of the particles was carried, in triplicates, out by Guelph Chemical Laboratories Ltd., in Guelph, Ontario, Canada.

2.2 Results and Discussion

2.2.1 The Introduction of Initiator Sites on the Particles

The narrow dispersed PDVB80 particles prepared by precipitation polymerization have diameters of 2.96 μm. As a direct result of their formation mechanism,[30] they have a thin surface layer consisting of lightly crosslinked and swellable poly(divinylbenzene). This surface gel layer facilitates redispersing the particles in a range of good solvents for modification and grafting reactions. The particles contain residual vinyl groups both within, and on their surfaces, as indicated by the CH out-of-plane deformation of monosubstituted vinyl groups, seen at 990 cm^{-1} in the FT-IR spectrum. These residual vinyl groups can be hydro-chlorinated to form 1-chloroethylbenzene groups, which are typical ATRP initiators. In comparison to the native PDVB80 particles, the FT-IR spectrum of the hydro-chlorinated PDVB80 particles showed a decrease in the intensity of the peak at 990 cm^{-1} relative to an asymmetrical conjugated double bond stretch, 1603 cm^{-1}, due to the aromatic rings. The intensity ratio of the two peaks at 990/1603 cm^{-1}

changed from 0.38 to 0.22, indicating significant conversion of the residual vinyl groups. While the addition of HCl to molecular styrene can be accompanied by formation of significant amounts of dimer,[31] in our case, the residual styrenic double bonds in the particles are immobilized by the polymer backbone, which should prevent excessive dimerization during hydrochlorination.

Our hydro-chlorination of PDVB80 particles led to a weight gain of 3.5%, corresponding to the formation of PDVB80-HCl. According to the following equation:

$$\frac{X \times M_{DVBHCl}}{M_{DVB80}} + (100 - X) = 103.5$$

where X is the percentage of DVB80 units in the PDVB80 particles converted to 1-chloroethylbenzene, M_{DVBHCl} is the molecular weight of DVB-HCl, and M_{DVB80} is the average molecular weight of DVB80, this weight gain corresponds to 12.5% of DBV80 units in the starting particles having been hydrochlorinated. Elemental analysis revealed the presence of 3.19 wt% chlorine in the PDVB-HCl particles, which corresponds to 12.1% of DVB80 units converted to 1-chloroethylbenzene, using the following equation:

$$X = \frac{Y\frac{M_{DVB}}{M_{Cl}}}{100 + Y\frac{M_{DVB}}{M_{Cl}} - Y\frac{M_{DVBHCl}}{M_{Cl}}}$$

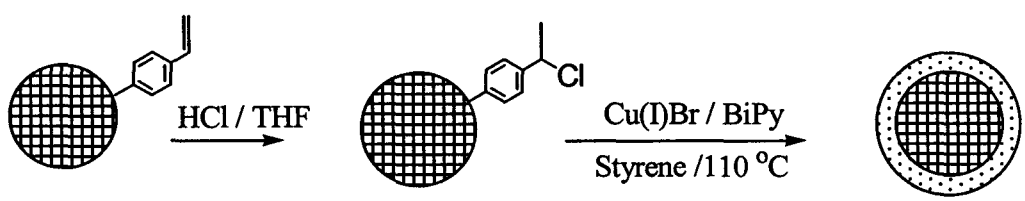
where Y is the weight percentage of chlorine in the PDVB-HCl particles, and M_{Cl} is the atomic weight of chlorine.

If the outer layer of the starting particles were not crosslinked, and if the particles had uniform density distribution, then the observed chlorine could be accounted for by a

hypothetical complete hydrochlorination of the pendant vinyl bonds, in an outer shell of the starting particles with 4.3% radial thickness. In fact, the particles have a cross-linking gradient that decreases from the core to the surface, and that ends in a partially cross-linked gel layer at the surface.[32] Correspondingly, the amount of pendant double bonds decreases from the surface towards the core of the particles. Moreover, hydrochlorination will depend on penetration of the hydrogen chloride into the particle structure. Hence, the hydrochlorinated layer in the particles should exceed 4.3% in radial thickness, and show its own gradient by favoring surface-hydrochlorination. The starting particles used in this experiment are about 3 μm in diameter. Therefore, the initiator sites in the particles should be found at least up to ~100 nm from the surface. This shell layer should become swollen with the newly formed polystyrene.

2.2.2 Graft polymerization of styrene from particles

The polymerization of styrene from these initiator sites was conducted at 110 °C in the presence of the catalyst, CuBr/2bipy (Scheme 2.2).



Scheme 2.2 ATRP from surface of particle initiators

The grafted polystyrene changed both the properties of the particle surfaces, and the size of the particles. Figure 2.1 shows the measurement of the particle sizes before and after graft polymerization, using a Coulter multi-sizer.

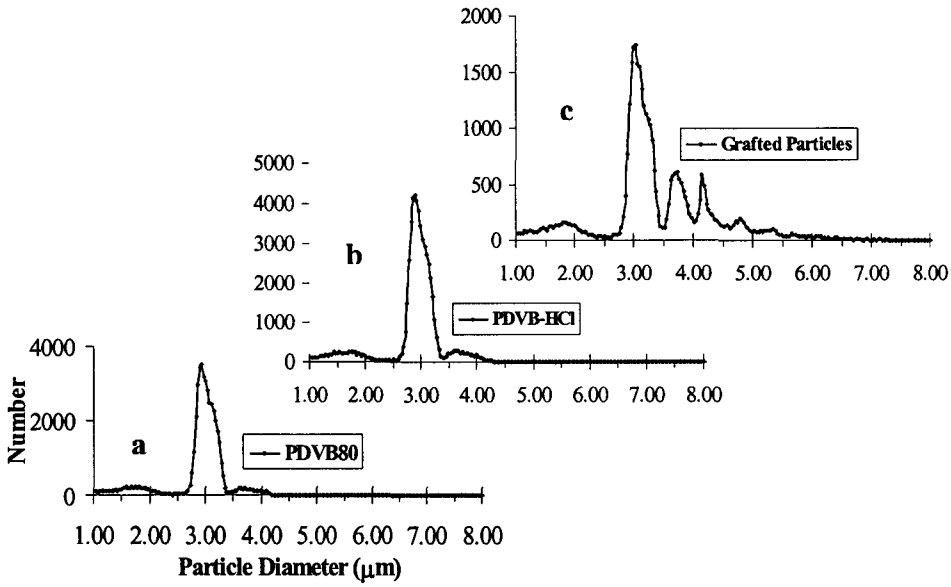
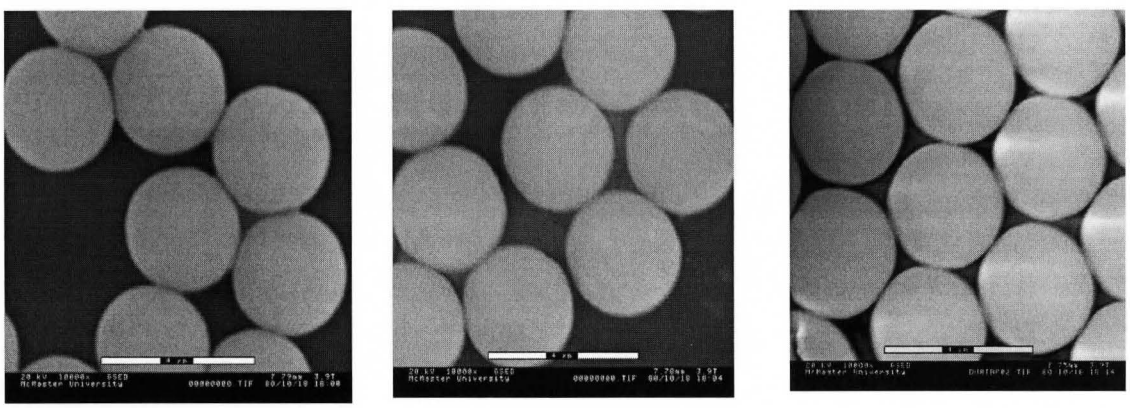


Figure 2.1 Particle size distributions of starting particles, particle initiators, and polystyrene-grafted particles

Number-average particle diameters, $\overline{Dn}$ of 2.88, 2.88 and 3.10 μm, with coefficients of variation, CV of 18, 21, and 43%, were found for PDVB80, PDVB80-HCl and grafted particles, respectively. The size of the PDVB-HCl particles remained unchanged from that of PDVB particles, which indicated that the hydrochlorination increased the density of the particles, as the total weight of the particles increased. On the other hand, the diameter of the styrene-grafted particles increased about 4% compared to both PDVB-HCl and PDVB80 particles. The 4% increase in particle diameter corresponds to a 12.5% increase in particle volume, which is consistent with the observed

weight increase of 11.3%. The density of the particles is considered to be similar to that of the grafted polystyrene, at 1.05 g/mL. The apparent coefficient of variation, CV of the grafted particles was larger than those of the PDVB80 and PDVB-HCl particles. This is due to the enhanced formation of doublets and triplets of the polystyrene coated particles during the Coulter sizing in an aqueous medium. In Figure 2.1c, on the right side of the large peak there are two smaller peaks, due to transient particle doublets and triplets that contribute significantly to the large CV. The mean particle diameters were taken from the main peak in the Coulter histogram. The sizes of the grafted particles were confirmed by ESEM (Figure 2.2).



2.96 μm
Starting particles

2.96 μm
Particle initiators

3.07 μm
PS-grafted particles

Figure 2.2 ESEM images of starting particles, particle initiators, and polystyrene-grafted particles

The images showed that all particles have very smooth surfaces and remain unagglomerated. The ESEM images were taken from dried samples, and should correspond to the diameters measured by Coulter multisizer using an aqueous medium in

which the surface chains should be collapsed. The measured of particles from these ESEM images are 2.96, 2.96 and 3.07 μm for PDVB80, PDVB80-HCl and grafted particles respectively, which is consistent with the particles diameters obtained from the Coulter multi-sizer. The ESEM size data reflect averages over about 100 particles each. It is noteworthy that the ESEM images show no large particles, which confirms that the two small peaks in Figure 2.1c correspond to transient particle doublets and triplets.

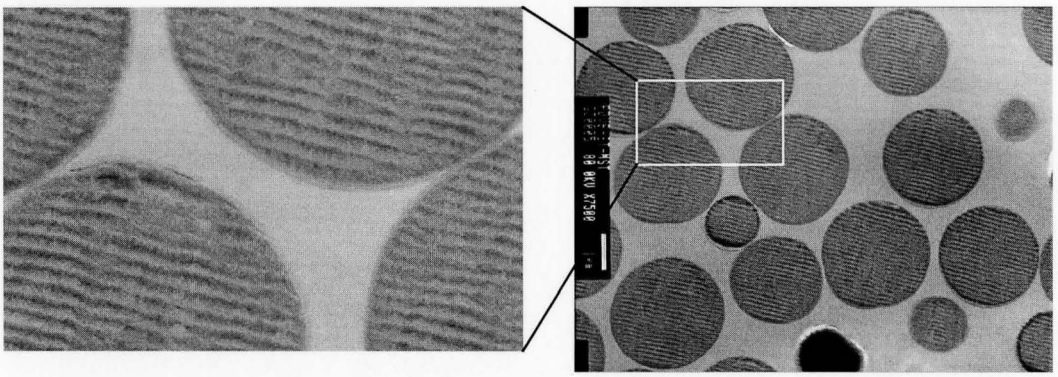


Figure 2.3 TEM images of poly(styrene-*b*-4-methylstyrene) grafted particles

The internal structure of the grafted particles was shown by TEM (Figure 2.3) to consist of a hard core and a very thin surface layer.

The reaction on the particles was also confirmed by elemental analysis. The 3.19 wt% chlorine in particle initiators was converted to 1.79 wt% chlorine and 0.33 wt% bromine in grafted particles. The bromine found in particles showed that ATRP has taken place on the particles. The bromine came from Cu(I)Br by way of an exchange equilibrium during the ARTP. The percentage of chlorine was higher than the percentage of bromine in the grafted particles. Two causes might be responsible. One is some

chlorine in the particles might be not accessible to the relatively large catalyst complex $(bipy)_2Cu(I)$, and hence would not become involved in the ATRP reaction. The other is that the Cl-C bond in benzyl chlorides (68 kcal/mol) is stronger than the Br-C bond in benzyl bromide (51 kcal/mole), which would suggest that benzylic chloride should dominate in the Cu-catalyzed benzylic halide interchange. In fact, Matyjaszewski et *al.*[33] studied the halide exchange during ATRP, using mixed halide initiation systems. Model studies of (1-chloroethyl)benzene/CuBr in the presence of two equivalents of di-nonyl-bipy showed that an equilibrium of 88% (1-chloroethyl)benzene and 12% (1-bromoethyl)benzene was reached after 40 min at 110 °C.

The decrease of the total halogen percentage in our grafted particles compared with the particle initiator, indicated that the formation of polymer grafted on the particles, as well as partial chain termination, led to an increase of the total carbon and hydrogen percentage. The fraction of polymer chain termination can be estimated based on the weight increase of the grafted particles, and the total halogen percentage. If the observed bromine weight percentage (0.33 wt%) were converted into the equivalent theoretical chlorine percentage (0.15 wt%), then the total chlorine in the grafted particles would be 1.94 wt%. The total chlorine in grafted particles should be 2.87 wt%, assuming all propagating groups survived. Hence, about 32.4% of propagating species were terminated, presumably at an early stage of reaction before the near steady-state concentration of Cu(II) was achieved.[34] Afterward, the reaction becomes a controlled/living polymerization. This has been confirmed by the subsequent addition of another polymer block to these particles, discussed below.

The hair-like polymer layer on the particle surface, which leads to the aggregation of the particles in a bad solvent, could conversely stabilize the particles in a good solvent.

Although the surface graft on the particles cannot prevent sedimentation, they do prevent particle aggregation in good solvents, and promote the formation of two or three-dimensional arrays upon deposition from a good solvent onto a surface. Asher et al.[35] used highly charged polystyrene particles to build two or three-dimensional arrays for use as photonic crystals. In their case, the charges on the particles helped the formation of arrays. Our particles are another example of the formation of particle arrays, helped by the grafted polymer on the particle surfaces.

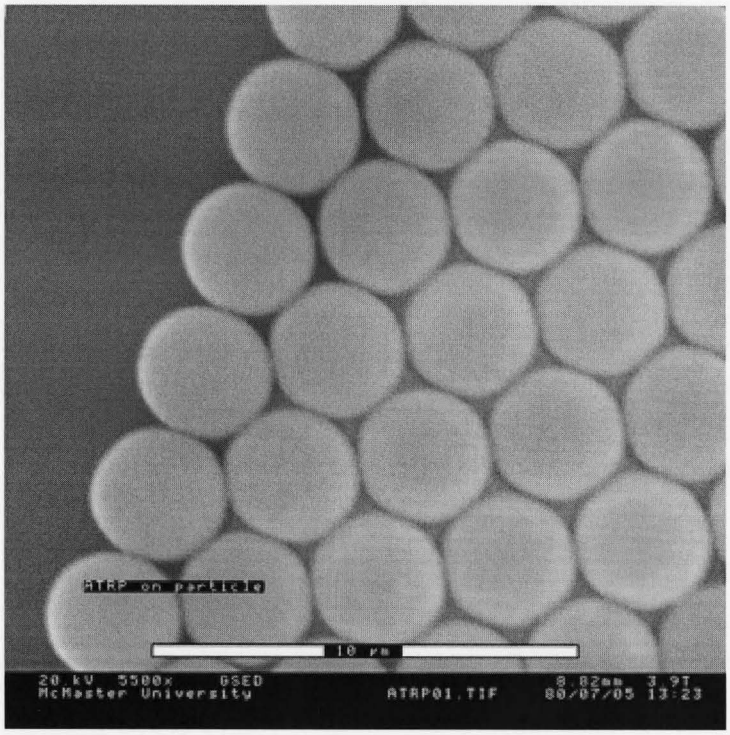


Figure 2.4 ESEM image of 2-D array of poly(styrene) grafted particles

Figure 2.4 shows a two-dimensional hexagonal array formed by adding a drop of the grafted particles dispersed in a good solvent such as THF, onto a glass plate. In contrast, non-grafted PDVB80 and PDVB-HCl particles do not generate such arrays with this procedure. The results confirmed that the grafted particles have polymer chains of significant molecular weight on their surfaces. Auroy et al.[36] pointed out that for the formation of a crystalline packing of grafted particles, two essential conditions, namely particles having polymer chains with high molecular weight and a low polydispersity, must be met.

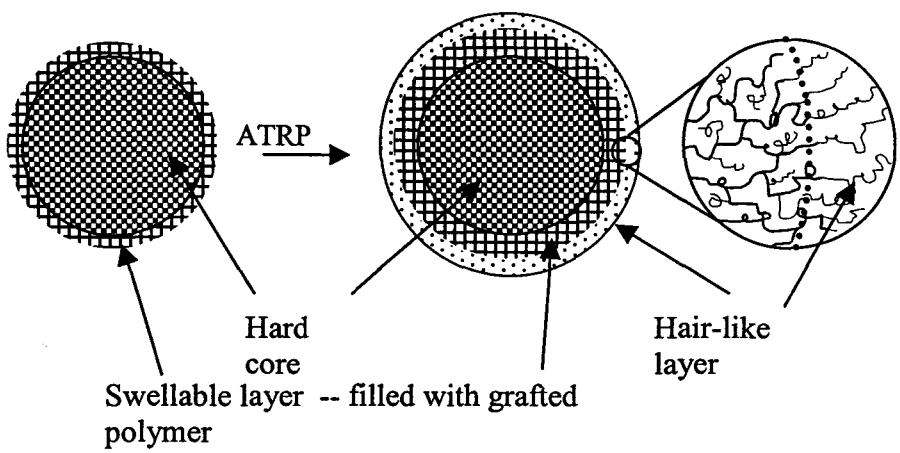
Interestingly, the grafted particles dispersed in a good solvent can be induced to aggregate by adding a poor solvent such as hexanes. The resulting particle aggregates prepared from a poor solvent were very easy to re-disperse in a good solvent. On the other hand, the grafted particles dried from a good solvent formed hard clusters that were difficult to re-disperse in a good solvent, likely due to entangling of the grafted polymer between particles.

The surface grafts were also confirmed by measuring the particle size in the swollen state by light scattering in MEK suspension. The sizes of PDVB80, PDVB80HCl and grafted-particles were 3.26, 3.26, and 3.70 μm, respectively. Compared with their dry diameters of 2.96, 2.96, and 3.07 μm, the size of the polystyrene grafted particles increased much more than the other two particles, which demonstrates both the effects of particles swelling and of the graft layer on the particle surface expanding in a good solvent.

2.2.3 The size growth of particles

In terms of the growth of polymer chains on the surface, polymer grown on planar surfaces is much easier to study than polymer on spherical particles. This is because certain surface techniques with high precision, such as ellipsometry, are only suitable to measure the thickness of coatings on planar surface.

Fortunately, our grafted particles gave high enough increases in particle size, and their sizes are easy to measure by Coulter multi-sizer and ESEM. The size increase is attributed to two contributions: grafted polymer grown on particle surfaces and grafted polymer grown within the outer layer of the particle initiators. In other words, graft polymerization in the outer layer of particles amplified the size increase by filling polymers into the relatively lightly cross-linked network. As discussed above, initiator sites may be located as deep as 100 nm below the particle surface, and ATRP of styrene should take place mainly within this layer of the particles.



Scheme 2.3 Surface and outer layer grafting of polystyrene by ATRP

Scheme 2.3 shows the increase of particle sizes contributed by polymers grown on the surface and in this outer layer.

2.2.4 Controlled/living polymerization properties

The concentration of initiators on solid surfaces usually is lower than in solution polymerization. It will produce an extremely low concentration of Cu(II) species that are needed to generate dormant species in a controlling equilibrium. Inadequate Cu(II) levels will result in loss of control of the polymerization. In order to help control the polymerization, free initiators[37] or Cu(II) compounds[38] may be added to help establish the required equilibrium between active and dormant species in grafting polymerizations from solid surface. However, a well-controlled system will have a relatively slow polymerization. In the case of our large particles, a slow grafting polymerization might not generate a thick enough polymer layer to detect. Hence we used Cu(I)Br as the only cupper source without the addition of Cu(II) or free initiators. The amount of catalyst CuBr/2bipy was 65% equivalent to the total initiating sites (0.94 mmol/g) in particles calculated from the chlorine elemental analysis. The molecular weight and molecular weight distribution of grafted polymer could not be determined in these reactions because of their covalent linkage to the particle. However, the molecular weight and perhaps the molecular weight distribution of grafted polymer may be roughly estimated by measuring the polymer formed in solution. The molecular weight and molecular weight distribution of soluble polymer was M_n = 2.65x 10^4, M_w = 4.43 x 10^4, and M_w/M_n = 1.67. This soluble polymer would be initiated thermally, but would then be terminated by reaction with Cu(II) present in the system. A detailed comparison of surface grafted and soluble

polymer, however, is beyond the scope of this paper.[35]

The living nature of the polymerization should improve as soon as the Cu(II) levels increase due to some early stage termination. As elemental analysis showed the existence of halogen, the grafted particles could still be used as particle initiators to form block copolymer. A second grafting polymerization of 4-methylstyrene on polystyrene grafted particles was accordingly carried out for 11 hours, at similar polymerization conditions as in the first grafting. Successful growth of poly(4-methylstyrene) was confirmed by the increase of the particles to 3.17 μm as measured by Coulter multi-sizer.

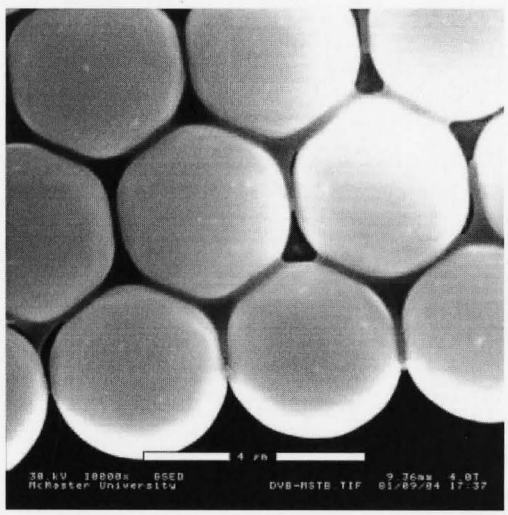


Figure 2.5 ESEM image of poly(styrene-*b*-4-methylstyrene) grafted particles

The size increase was confirmed by ESEM. The Figure 2.5 shows the image of the second grafted particles. The particles deformed at contact points, which implies that the surface layers of the particles are soft and consist largely of linear polymer.

Conclusion

Grafting of polystyrene from narrow dispersed polymer particles by surface-initiated atom transfer radical polymerization can generate a brushy polymer layer. The residual surface vinyl groups on the particles poly(DVB80) particles prepared by precipitation polymerization could be hydrochlorinated to form chloroethylbenzene initiating sites for subsequent ATRP of styrene using CuBr/2bipy as catalyst system. The initiating sites and polystyrene grafts were found not only on the particle surfaces, but also from within a thin shell layer, leading to particles size increases from 2.96 to 3.07 μm. The surface layer of polystyrene improved colloidal stability and facilitated formation of colloidal arrays. Block copolymers of poly(styrene-*b*-4-methylstyrene) were grown from the particles, which indicated the significant poly(styrene) chains were reactivated .

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Chapter 3 Grafting of Poly(alkyl (meth)acrylates) from Swellable Poly(DVB80-*co*-HEMA) Micro-spheres by Atom Transfer Radical Polymerization[1]

Abstract

We report the graft polymerization of methyl acrylate (MA), methyl methacrylate (MMA), hydroxyethyl methacrylate (HEMA), and 2-(dimethylamino)ethyl methacrylate (DMAEMA) by atom transfer radical polymerization (ATRP) from lightly cross-linked poly(DVB80-*co*-HEMA) microspheres. These poly(DVB80-*co*-HEMA) microspheres were prepared by precipitation copolymerization and subsequently modified by reaction with 2-bromopropionyl bromide to serve as ATRP macroinitiators. MMA, MA, and HEMA were then grafted from these initiator microspheres at room temperature using CuBr/Me_4cyclam as catalyst. The graft sites, and hence the grafted polymers, are distributed throughout the initiator microspheres. Addition of a second monomer formed grafted block copolymers, indicating that a significant portion of the first grafts could be reactivated. The final particles represent novel, high-capacity polymer-supports comprised of swellable core particles carrying 5.09 and 5.18 mmol/g of grafted poly(DMAEMA) and poly(MMA-*b*-DMAEMA), respectively. The grafted particles were characterized using ESEM, FTIR, Coulter particle sizing and potentiometric titration.

[1] G. Zheng, H.D.H. Stöver, *Macromolecule* (**2002**), *35*, 7612-7619.

3.0 Introduction

Polymer supported reagents, scavengers, and catalysts have been successfully used in organic synthesis.[1] Advantages such as high product purity, and simplification of work-up in high-throughput parallel synthesis, continue to drive the development of new polymer-supported reagents.[2] The majority of supported reagents are based on divinylbenzene (DVB) cross-linked polystyrene (PS), which is very stable in both basic and acidic media, and in all organic solvents.[3] However, lightly cross-linked polystyrene resins must be swollen in good solvents before use to allow penetration by the reactant. They perform badly in poor solvents for PS, which are required in some syntheses. Bayer[4] grafted polyethylene glycol (PEG) onto lightly cross-linked polystyrene beads by anionic polymerization, forming the so-called TentaGels. At high PEG loadings, these TentaGel beads swell in all solvents dissolving PEG. The resulting PEG-grafted polymer-supported reagents are suitable for reactions in a wide range of solvents, including the solid-phase supported synthesis of peptides and nucleotides. Due to the use of anionic polymerization in the graft polymerization, the desired functional groups could only be introduced at the termini of the PEG chains, and consequently, the functional capacity of TentaGel resins are fairly low.

If the functional groups were present in every monomer unit of the grafted polymer, the capacity of the resulting polymer-supported reagents would be greatly increased, and could lead to polymer-supported reagents combining a high swelling factor and a high functional capacity. So far, polymer-supported reagents with such combined properties are unavailable. Bradley et *al.*[5] tried to enhance the functional

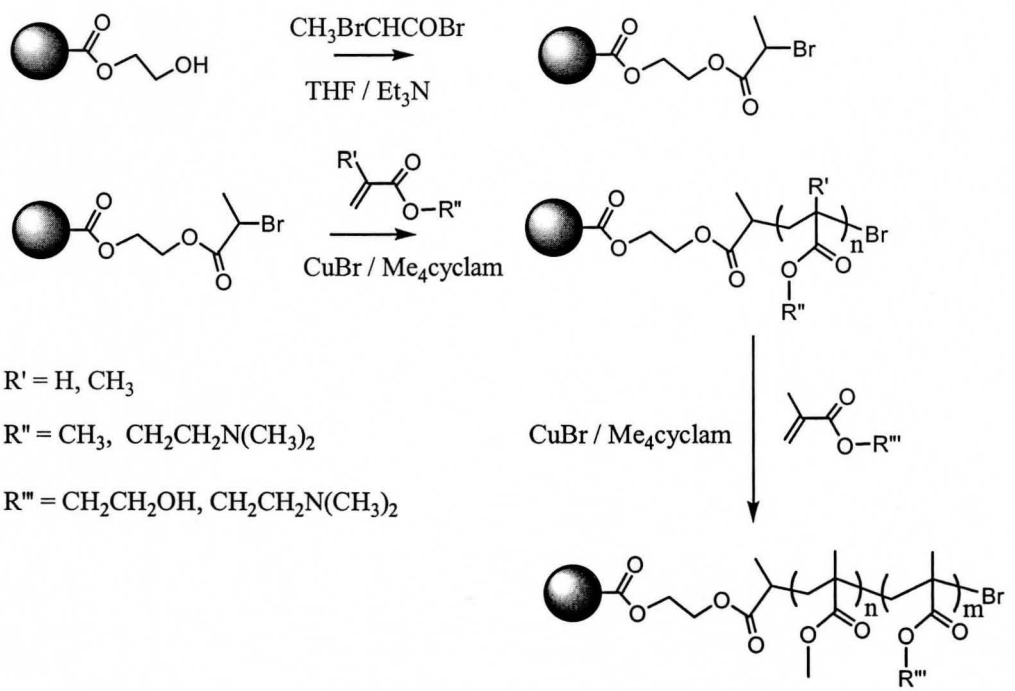
capacity of solid supports using a dendrimerization process. Three generations of amidoamino dendrimers were built on a TentaGel base with a modest increase in amine loading from 0.85 nmol/bead to 4.0 nmol/bead.

Recently, atom transfer radical polymerization (ATRP), a controlled/living polymerization has been developed[6]. The livingness of ATRP allows sequential polymerization of monomers to produce block copolymers. Matyjaszewski et *al.*[7] have demonstrated the controlled ATRP of (meth)acrylates from monofunctional narrow-disperse poly(dimethylsiloxane) (PDMS) macroinitiators. The resulting polymers showed linear increases in number-average molecular weight (M_n) with conversion, demonstrating the effectiveness of ATRP in synthesizing a variety of inorganic/organic polymer hybrids. Jérôme et *al.*[8] used difunctional poly(*n*-butyl acrylate) as a macroinitiator for the polymerization of methyl methacrylate (MMA) to produce poly(MMA-*b*-BA-*b*-MMA) triblock copolymers with a polydispersity index of 1.15.

Typically, ATRP initiators are halide compounds, such as benzyl halides and α-halo carboxylates, which convert into stabilized radicals upon halide transfer. The growth of polymer chains from the initiator is activated by metal complexes. The ability to grow polymer chains from halide initiators has been used for grafting polymer off solid surfaces. Porous silica gel coated with a self-assembled monolayer from 1-trichlorosilyl-2-(*m/p*-chloromethylphenyl)ethane successfully initiated polymerization of acrylamide. The number-average molecular weights of the grafted polymers were up to 13-15 kDa, with PDI's below 1.3.[9] Polystyrene with M_n = 26500 and PDI = 1.33 was also grafted from silica nanoparticles via ATRP, leading to an increase in the diameter of the

nanoparticles by about 20 nm.[10] We recently introduced 1-chloroethylbenzene initiators onto polyDVB particles by hydrochlorination of residual vinyl groups, and conducted ARTP of styrene from the initiator sites located on and below the particle surface, to produce polystyrene grafted particles with a greater than 100 nm increase in diameter.[11]

Another advantage of ATRP is its tolerance to water and many functional groups[12], which makes it ideal for use with functional monomers. We hence planned to introduce functional groups in every monomer unit in a grafted polymer, in order to



Scheme 3.1 Reaction of bromopropionyl bromide with precursor particles H_i to produce initiator particles H_iBr, and the subsequent graft-polymerization and graft-block copolymerization of alky(meth)acrylates from H_iBr

prepare high capacity polymer-supported reagents.

A key aspect of this plan was to graft polymer from lightly cross-linked particles. These precursor particles could be prepared by a precipitation copolymerization of divinylbenzene (DVB) and hydroxyethyl methacrylate (HEMA). These particles can be designed to have a relatively highly cross-linked core and a lightly cross-linked outer layer, due to the difference in reactivity between DVB and HEMA. The hydroxyl group in HEMA would be reacted with α-bromopropionyl bromide to generate an ATRP initiator. Polymer chains could then be grown from the initiator sites located in the outer layers and at the surface of the particles (Scheme 3.1).

3.1 Experimental Section

3.1.1 Chemicals

DVB80 (70-85% DVB isomers, Fluka, Oakville, Canada), 1,4,8,11-tetramethyl-1,4,8,11-tetraazcyclotetradecane (Me_4cyclam) (98% Aldrich), acetonitrile (HPLC grade, Aldrich), 2-bromopropionyl bromide (97% Aldrich) and triethylamine (99% Aldrich) were used as received. 2,2'-Azo-bis-(2-methylpropionitrile), AIBN, (Eastman Kodak Co.) was recrystallized from methanol. Hydroxyethyl methacrylate (HEMA) (97%), methyl methacrylate (MMA) (99%), and 2-(dimethylamino)ethyl methacrylate (DMAEMA) (98%) were purchased from Aldrich Chemical Co. and purified by distillation under vacuum prior to polymerization. THF (99+% Aldrich) was refluxed over K-Na alloy and distilled under nitrogen. CuBr was prepared by the reaction of $CuBr_2$ with dimethyl malonate.[11]

3.1.2 Methods

Preparation of Precursor Particles Precursor particles, poly(DVB80-*co*-HEMA) were prepared by precipitation polymerization in neat acetonitrile. DVB80 (1.05 g, 8 mmol), HEMA (4.95 g, 38 mmol), acetonitrile (200 ml), and AIBN (0.12 g) were placed in a 250 ml polyethylene bottle and shaken vigorously to ensure complete dissolution of the initiator. The bottle was placed in a reactor equipped with horizontal rollers and a programmable temperature controller. The reactor gently agitates the sample by rolling the bottles at approximately 4 rpm. The temperature profile used for polymerization started with a 1 h ramp from room temperature to 60 °C followed by a 100 min ramp to 70 °C and then a further 24 h at 70 °C. The resulting particles were isolated by vacuum filtration over a 0.5 μm membrane filter with three subsequent washings with THF. The yield of clean particles was 3.04 g (50.7%) after drying at room temperature under vacuum for 24 h.

The Preparation of Initiator Particles Precursor particles (2.00 g) were suspended for 2 h in 20 ml of THF containing 0.95 g (9.39 mmol) of triethylamine in a 50-ml two-necked round-bottomed flask, followed by dropwise addition of 2.0 g (9.26 mmol) 2-bromopropionyl bromide to the suspension, which was cooled with an ice-water bath. The mixture was stirred at room temperature overnight. The initiator particles were filtered and washed with THF and methanol thoroughly. The yield of the resultant particles was 3.08 g after drying at room temperature under vacuum for 24 h.

Grafting Polymers from Particles The ATRP was carried out in THF solution. Initiator particles (H_IBr, 0.3 g) and methyl methacrylate (2.0 g, 20 mmol) were added in

8 ml of THF in a 25 ml flask purged with THF saturated nitrogen for 1hr and then a degassed 2 ml THF solution of CuBr (26 mg, 0.18 mmol) / Me_4cyclam (46 mg, 0.18 mmol) was added via a cannula. The mixture was stirred with a magnetic bar at room temperature under nitrogen for 15 h. The resulting blue particles were centrifuged and re-dispersed at least three times in THF and then repeatedly in methanol until the particles became almost white. The yield of Poly(MMA) grafted particles was 1.24 g.

The progress of the polymerization was tracked by removing aliquot samples with a syringe at various time intervals. The samples were centrifuged and purified as described above.

Grafting Block Copolymers from Particles A similar procedure was used to graft the second generation poly(DMEAMA) or poly(HEMA) from particles already grafted with the first generation poly(MMA). The poly(MMA) grafted particles (H_1Br-*g*-poly(MMA), 0.3 g) and HEMA (1.5 g, 11.5 mmol) were dissolved in 8 ml of THF in a 25 ml flask purged with THF saturated nitrogen for 1hr and then a degassed 2 ml THF solution of CuBr (5.8 mg, 0.04 mmol) / Me_4cyclam (10.2 mg, 0.04 mmol) was added via a cannula. The polymerization was conducted at room temperature for 23 h. The yield of block copolymer grafted particles was 1.03 g.

Particle Size Analysis The particle sizes and size distributions were measured using a 256-channel Coulter Multi-Sizer II interfaced with a computer. A 50 μm aperture tube was chosen to accommodate the particle size range of 1-7 μm. A small amount of particles dispersed in acetone was added to 25 ml of Coulter Isoton II electrolyte solution and stirred for 1 min. The Coulter Multi-Sizer II measurements were confirmed using a

Philips ElectroScan 2020 environmental scanning electron microscope (ESEM). The samples for ESEM were prepared by dispersing particles in THF and casting a drop of particle suspension onto pieces of glass. The samples were dried under vacuum for 2 h and sputter coated with 5 nm of gold.

TEM analysis The internal structure of the grafted particles was studied using a JEOL 1200EX transmission electron microscope. Here, the samples were embedded in Spurr epoxy resin and microtomed to generate 40-60 nm thick slices.

FT-IR Analysis Fourier transform infrared analysis was performed on a Bio-Rad FTS-40 FT-IR spectrometer. All samples were prepared as pellets using spectroscopic grade KBr in a Carver press at 15,000 psi. The spectra were scanned over the range 4000 - 400 cm^{-1}, in the transmission mode, at a resolution of 2 cm^{-1}.

3.2 Results and Discussion

3.2.1 Preparing precursor particles with hydroxyl groups and initiator particles

Particles with hydroxyl groups were prepared by a precipitation copolymerization of DVB80 and HEMA in acetonitrile. The formation of particles and their size and size distribution is strongly dependent on the monomer loading and cross-linker ratio. As we wish to prepare lightly cross-linked particles, different ratios of cross-linker (DVB80) to HEMA were selected to optimize the polymerization conditions to reach mono-dispersed particles with low cross-link degrees. The different cross-linker ratios led to differences in the size and size distribution of the particles. Figure 3.1 shows the size distributions

for four different samples as measured by a Coulter Multi-Sizer II. The lowest

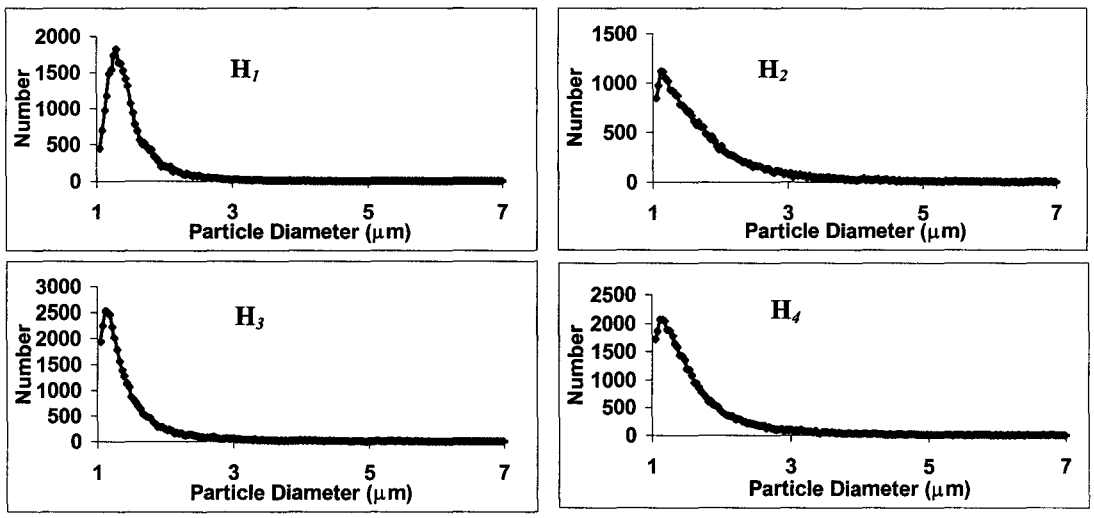


Figure 3.1 Size and size distribution of precursor particles having different ratios of HEMA to DVB80. H_1 (82.5 mol% HEMA); H_2 (73.2 mol% HEMA); H_3 (63.8 mol% HEMA); H_4 (54.0 mol% HEMA)

cross-linker ratio (sample H_1, 82.5 mol% HEMA) gave large particles with narrow size distribution. Further decreasing the cross-linker content resulted in the formation of coagulum instead of particles.

The particles H_1 with 82.5 mol% fraction of HEMA should have the highest swelling ratio and the highest hydroxyl groups content, which should allow the introduction of more initiators per particle. The efficiency of cross-linking in precipitation polymerization usually is much lower than in emulsion or suspension polymerization, due to the low total monomer loadings used here. This results in an actual cross-linking degree up to an order of magnitude lower than the cross-linker fraction in the monomer. In the present case, the residual pendant vinyl groups may lead to secondary crosslinking during the subsequent graft polymerization. The overall cross-

linking degree should decrease from the particle center to the shell, due to the tendency of styrenic and methacrylic monomers to form alternating copolymers. Although the monomer reactivity ratios for copolymerization of DVB and HEMA are not available, comparison with the parent comonomer pair of styrene and methyl methacrylate, which have monomer reactivity ratios of r_1=0.52 and r_2=0.46,[13] is instructive. It implies that the particles H_1 have a higher DVB content in the center, and a lower DVB content in the outer layer of the particles. Such particles with lower cross-linker density in the outer layer might be expected to swell more in good solvents than particles with uniform structure.

For comparison, 2 g each of two types of particles H_1 (82.5 mol% HEMA) and H_3 (63.8 mol% HEMA) were used to prepare initiators by esterification of the hydroxyl groups with 2-bromopropionyl bromides. The yields of the two initiator particles H_1Br and H_3Br were 3.08 g and 2.42 g respectively, which indicated higher initiator concentration in H_1Br than that in H_3Br. The efficiency of these esterifications in precursor particles H_1 and H_3 can be estimated as 81.2% and 65.2%, respectively, assuming that the precursor particles have compositions equal to the comonomer ratio used to prepare the particles, 82.5% and 63.8% HEMA. In fact, due to the moderate conversion to polymer particles of about 50% commonly seen in the precipitation polymerization, and the slight tendency towards alternating copolymerization of the two monomers, the HEMA fraction in the precursor particles might be slightly lower than in the feed. Therefore, the efficiency of the esterification may have been even higher. The higher conversion observed for H1 is attributed to easier diffusion of bromopropionyl

bromide into the more lightly cross-linked particles.

3.2.2 Grafting MMA and MA from the initiator particles

The CuBr/Me_4cyclam catalyst system has proven very effective for the ATRP of N,N-dimethylacrylamide at room temperature.[14] It should hence also act as a catalyst for (meth)acrylate polymerization as the activation in ATRP depends on the redox reaction of the initiator with the Cu(I) complex. Specifically, 2-bromo-2-methylpropionate should be easier to reduce than 2-bromo-2-methylpropionamide since the ester is a stronger electron-withdrawing group than amide. The initiator particles H_1Br and H_3Br were therefore used to initiate polymerization of MMA and MA. The polymerizations took place in THF solution at room temperature and the results are shown in Table 3.1. The

Table 3.1 The ATRP polymerization of MMA or MA on Initiator Particles

	Inititor Particles [0.3 g]	**CuBr / Me_4cyclam**	**Monomer**[a]	**Yield**[b]
H_1Br-*g*-poly(MMA)	H_1Br	26 mg/46 mg	MMA	1.24 g
H_1Br-*g*-poly(MA)	H_1Br	26 mg/46 mg	MA	0.77 g
H_2Br-*g*-poly(MMA)	H_3Br	26 mg/46 mg	MMA	0.36 g
H_2Br-*g*-poly(MA)	H_3Br	26 mg/46 mg	MA	0.33 g

a: 2 g of monomer in 10 mL tetrahydrofuran

b: Reaction time, temp.: 15 hr, r.t.

ATRP of MMA from 0.3 g each of H_1Br and H_3Br initiator particles caused weight increases to 1.24 g and 0.36 g, or by 313% and 20%, respectively. This result is

consistent with the higher initiator loading and accessibility of H_1Br compared with H_3Br. The ATRP of MA from H_1Br and H_3Br gave weight increases of only 157% and 10%, respectively, indicating that the ATRP of MMA is more efficient than that of MA. The dormant 2-bromo-2-methylpropionate end-group formed in the polymerization of MMA is easier to activate than the 2-bromopropionate formed in the polymerization of MA because a more stable tertiary radical is formed. Faster polymerization of MMA was also indicated by a faster change in solution color from gray [Cu(I)] to faint blue [Cu(II)], since the concentration of [Cu(II)] is directly proportional to the concentration of radicals, and builds up during the reaction through radical coupling or disproportionation.

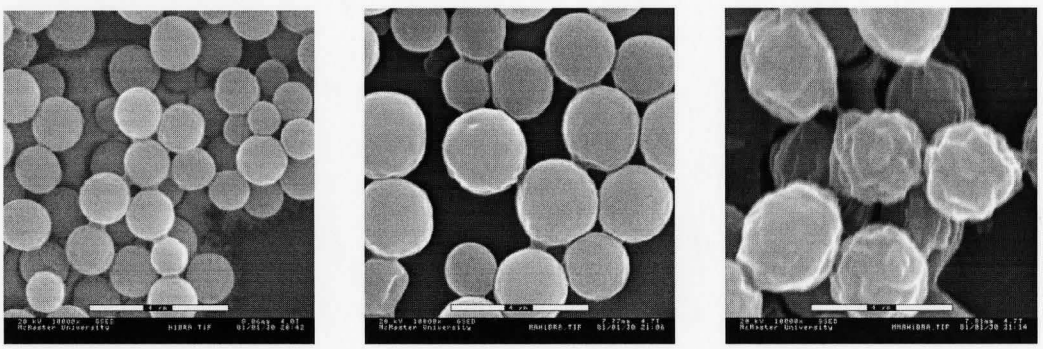


Figure 3.2 ESEM images of ATRP particles made from initiator particles H_1Br
a: particles H_1Br; b: poly(MA) grafted particles H_1Br-*g*-poly(MA);
c: poly(MMA) grafted particles H_1Br-*g*-poly(MMA)
The scale bar is 4 μm

The size and morphology of the particles was studied by ESEM. Three typical images of grafted particles H_1Br-*g*-poly(MMA), H_1Br-*g*-poly(MA) and H_1Br are shown in Figure 3.2 After grafting with MMA and MA, the sizes of the particles increased from

1.4 μm to 2.7 μm and 2.2 μm, respectively. These large size increases confirm that polymer chains not only grow from the surface, but predominantly grow from initiator sites within the particles, as expected from the swellable nature of the initiator particles. Polymerization just of the surface initiator sites would lead to much smaller size increases, on the order of 50 to 100nm.

As discussed above, the initiator particles should have a gradient of initiator concentration, increasing from the inside to the surface. As a result, the grafted polymer grown from initiator sites distributed within the initiator particles would form an interpenetrating network with the DVB/HEMA of the original initiator particle, and lead to a substantial overall size increase. This interpenetrating network would also show a compositional gradient, based on higher initiator concentration and accessibility near the particle surface.

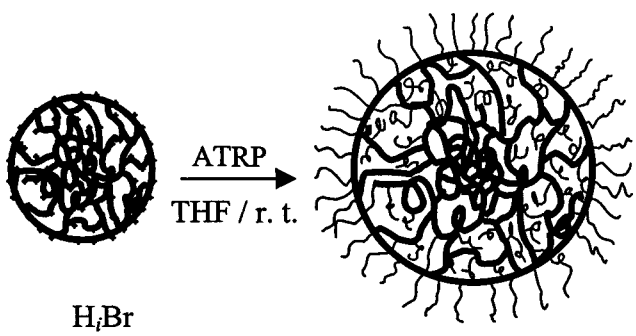


Figure 3.3 Illustration of internal structure of initiator particles H_iBr and polymer grafted particles

These features are illustrated in Figure 3.3 for an initiator particle grafted with

PMMA. We are currently studying these compositional gradients using scanning transmission x-ray microscopy (STXM).

The final sizes of the particles H_IBr-*g*-poly(MMA) and H_IBr-g-poly(MA) correspond to about 620% and 290% increases in particle volume. However, the weight increases of the particles H_IBr-*g*-poly(MMA) and H_IBr-*g*-poly(MA) were only 313% and 157%. The difference between weight and volume increases suggests that the grafted particles have much lower densities than the initiator particles. Since PMMA and PMA both have inherent densities similar to those of poly(DVB-*co*-HEMA), the difference between weight increase and volume increase must be attributed to an increase in porosity of the resultant particles.

The H_IBr-*g*-poly(MMA) particles have very rough surfaces compared with the H_IBr-g-poly(MA) particles. Since PMMA is radiation sensitive,[15] it may depropagate under the electron beam during an ESEM measurement. This would selectively cleave the grafted PMMA from the interpenetrating network, and cause the observed rough surfaces. Careful ESEM observation indeed showed that the PMMA-grafted particles do have smooth surfaces when the electron beam is first focused on the particles, but that the surface rapidly becomes rough during image acquisition. This depropagation of PMMA in the network also caused a decrease in size and particle volume where the electron beam was focused on the particles, especially at high magnification, suggesting a collapse of the internal pore structure as well. In contrast to PMMA, the PMA-grafted particles were relatively resistant to e-beam damage, and showed smooth particle surfaces. This agrees with the results of Cook et *al.*,[16] who found the monomer concentration of MMA to be 10^6 times higher than that of MA in polymerization-depolymerization equilibria at

25 °C.

3.2.3 Study of Grafted Particles by FT-IR

FT-IR was used to follow the chemical changes occurring during introduction of initiators and the grafting polymerization. Figure 3.4 shows the FT-IR spectra of precursor particles H_1, initiator particles H_1Br, and the PMMA-grafted particles H_1Br-*g*-poly(MMA). The hydroxyl groups in H_1 give a broad stretching band at 3445 cm^{-1} and the ester groups give rise to a strong stretching band at 1725 cm^{-1}. In addition, absorptions at 1605 and 1511 cm^{-1} are due to aromatic carbon-carbon double bond stretching.

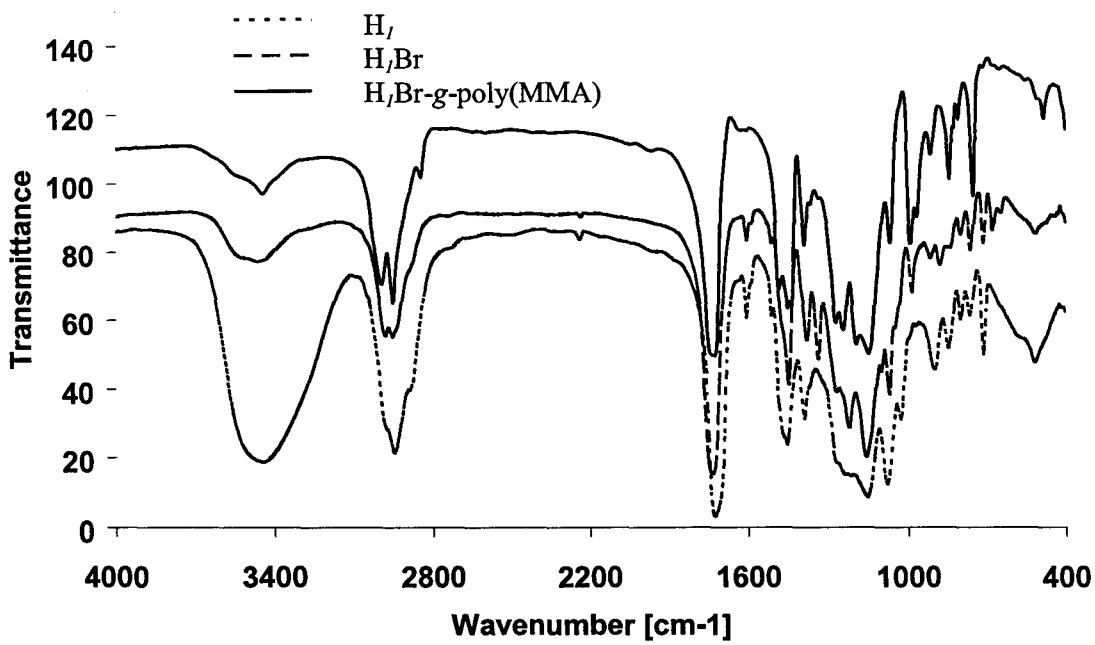


Figure 3.4 FT-IR spectra of particles. H_1: poly(DVB80-*co*-HEMA) particles made from 82.5mol% HEMA; H_1Br: initiator particles made from H_1; H_1Br-*g*-poly(MMA): poly(MMA) grafted from particles H_1Br

In the spectrum of H_1Br, the band at 3445 cm^{-1} due to hydroxyl is dramatically decreased as a result of esterification. The residual hydroxyl absorption, still visible after vacuum drying the particles for 24 h, indicates that some hydroxyl groups inside particles were not available for reaction with 2-bromopropionyl bromide. Meanwhile, the characteristic ester carbonyl peak shifted from 1725 cm^{-1} (HEMA) to 1736 cm^{-1} as expected for a α-bromo substituted ester. The electron-withdrawing bromine at the α-position of the ester in the initiator shifts the carbonyl band to higher wave numbers, compared with the carbonyl band in HEMA. The new absorption at 1339 cm^{-1} was attributed to the methyl group in the initiator,[17] which could be an indicator for ATRP since it should decrease or disappear after polymerization.

After grafting, the carbonyl stretching band in the spectrum of H_1Br-*g*-poly(MMA) is dominated by PMMA, and the peak shifts back to 1727 cm^{-1}. Although grafted PMMA has similar spectral characteristics to the core PHEMA in H_1Br, the changes in relative intensities demonstrate that grafting was successful: 1) the hydroxyl stretching band becomes even smaller as the relative concentration of residual OH groups decreases upon grafting of PMMA, and 2) the aromatic carbon-carbon double bond stretch at 1605 and 1511 cm^{-1} disappeared in the noise after grafting.

The FT-IR spectra of H_3, H_3Br, and H_3Br-*g*-poly(MMA) shown in Figure 3.5 show similar trends. However, the intensity of the hydroxyl group absorption in H_3Br was larger compared with that of H_1Br, indicating a higher concentration of residual hydroxyl groups in H_3Br. This is likely a result of reduced swelling in the more highly cross-linked H_3, which directly affects the accessibility of reagents.

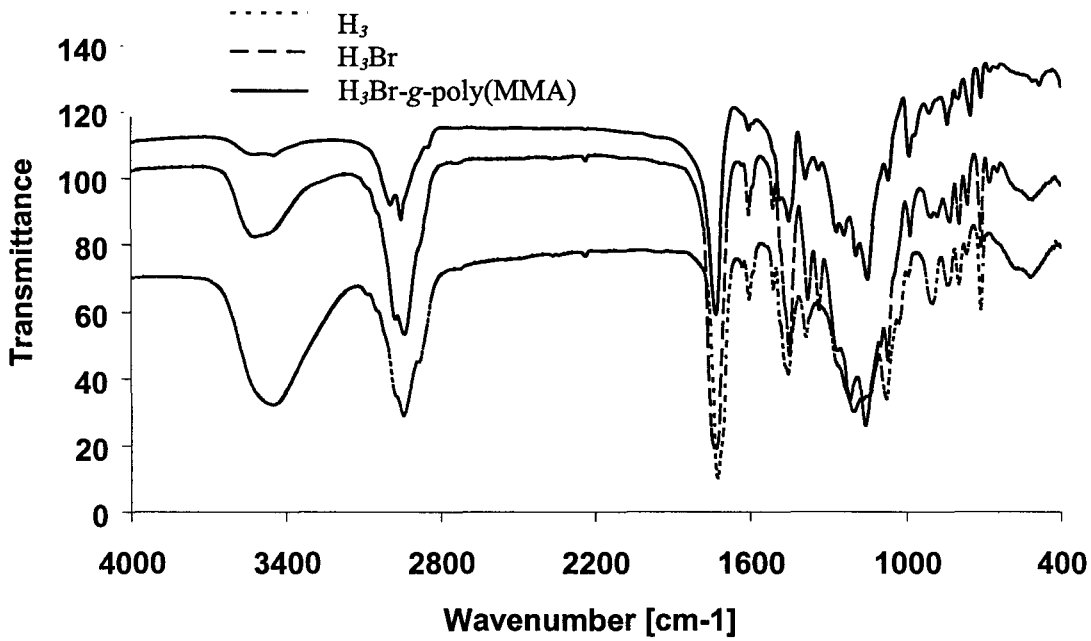


Figure 3.5 FT-IR spectra of particles. H_3: poly(DVB80-*co*-HEMA) particles made from 63.8 mol% HEMA; H_3Br: initiator particles made from H_3; H_3Br-*g*-poly(MMA): poly(MMA) grafted from particles H_3Br

Absorption due to the benzene rings in the core of the particle is evident in the H_3Br-*g*-poly(MMA) spectrum and is stronger still in the H_3Br-*g*-poly(MA) spectrum. The intensities of the benzene adsorption bands are related to the shell thickness of the particles, which vary in the order of H_1Br-*g*-poly(MMA) > H_1Br-*g*-poly(MA) > H_3Br-*g*-poly(MMA) > H_3Br-*g*-poly(MA), as determined by both diameter and weight increases.

3.2.4 The living nature of Graft-ATRP from particles

The living nature of ATRP allows controlled polymer growth and the production of block copolymers. The living nature of the ATRP in the present graft system was determined by monitoring particle size changes, both with reaction time, and with

different monomer loadings at constant reaction time. The preparation of block copolymers on particles grafted with poly(MMA) was also used to show the living nature.

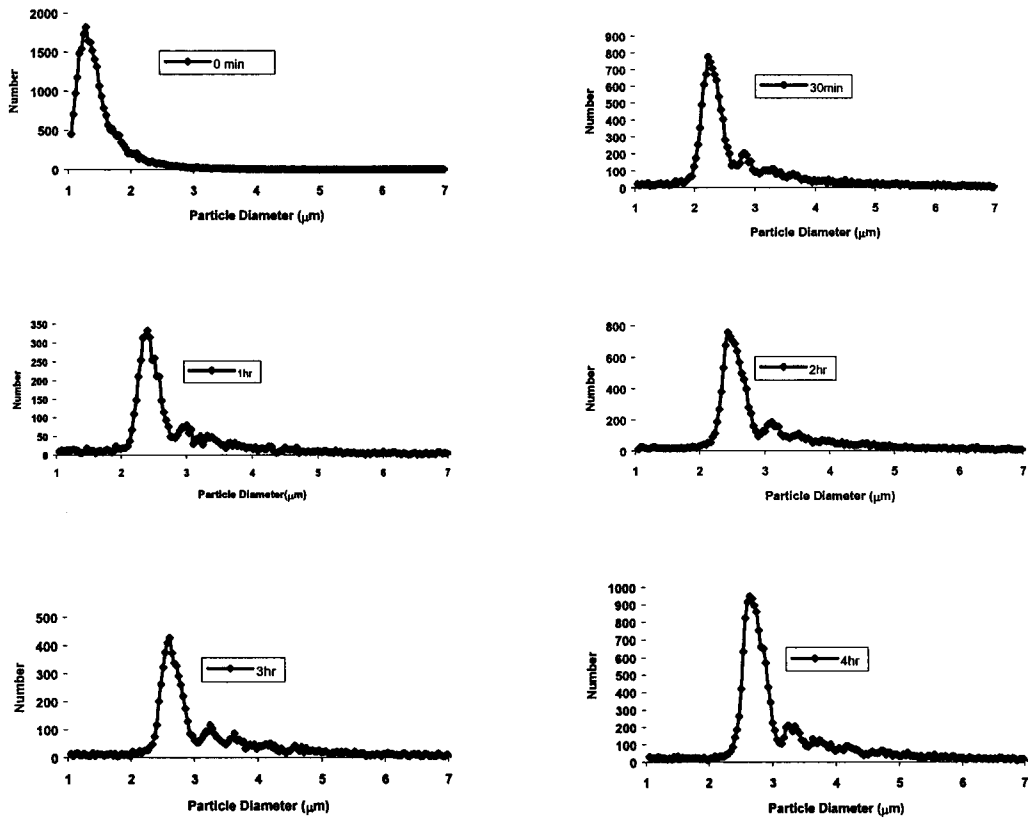


Figure 3.6 Size and size distribution of H_1Br-*g*-poly(MMA) particles formed by grafting polymerization of MMA for different times

The ATRP of MMA from initiator particles H_1Br leads to an increase of particle size with reaction time. Figure 3.6 shows the size distributions of grafted particles over time. The particle size changed significantly with the reaction time. The small peaks appearing to the right of the main peaks during the reaction are attributed to temporary

aggregates of 2, 3, or more particles during passage through the Coulter Multisizer orifice, and hence the size and size distributions were calculated using only the main peak. Similarly, the particle volumes were calculated from the main particle diameter. They are plotted as a function of reaction time in Figure 3.7a.

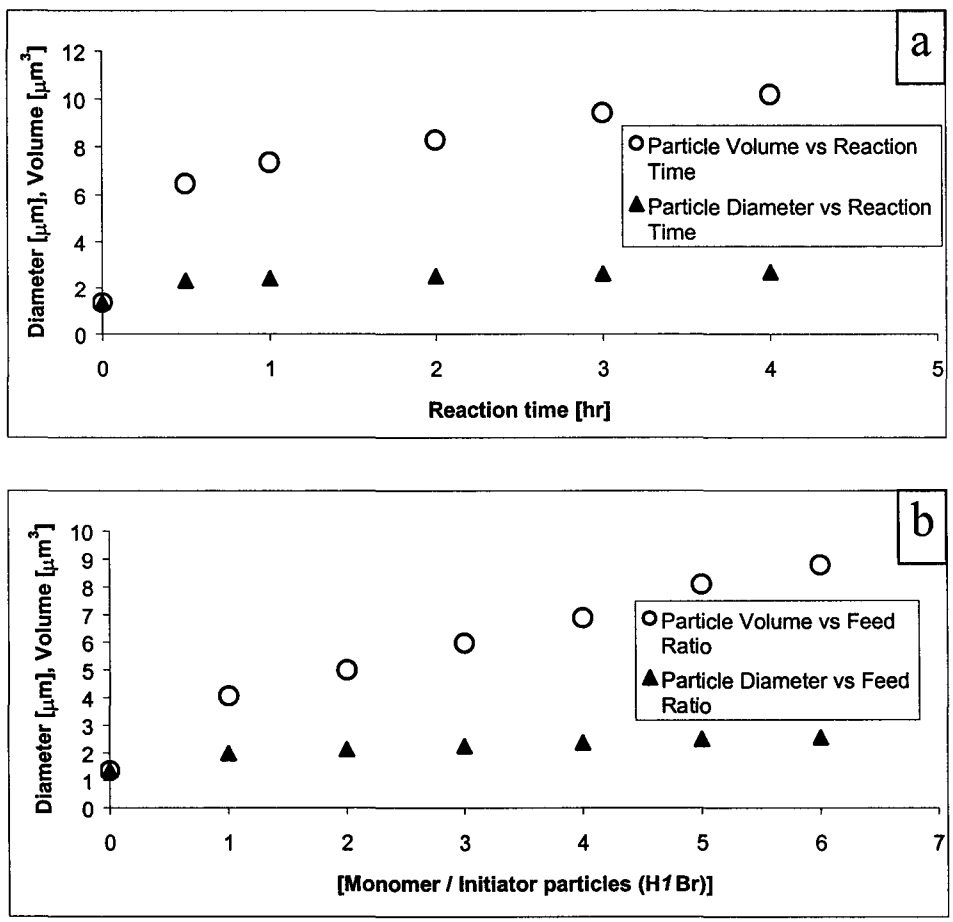


Figure 3.7 The growth of grafted particles: a) with different polymerization times at constant monomer feed concentration, and b) with different monomer loading for 15 hr. The particle volumes were calculated from the radii using $V=4/3\pi r^3$

The average particle volume increased rapidly from 1.35 to 4.06 μm^3 during the early stages of polymerization, followed by a slower, linear increase with reaction time. This demonstrates that the size of particles could be controlled through reaction time, especially after the early stages. As discussed above, polymer chains grow from both the surface and interior of the particles. Most polymer chains should be inside the network. The size jump at early stages might be due to the rapid polymerization of monomer within the network of the swollen particle initiator, followed by rapid swelling by solvent. The CuBr/Me_4cyclam catalyst used in this experiment is very efficient and some polymerizations are complete within minutes.[18] When monomers within the network were consumed, the polymerization rate might be determined by the diffusion of monomer into the network. In addition, the Cu(II)Br concentration would increase after the early stages and promote the formation of dormant species, which would slow the polymerization.

Similarly, particle size could be controlled through monomer loading. The growth of particles with different monomer loading over 15 h reaction time is plotted in Figure 3.7b. The sizes of the grafted particles at all monomer loadings are significantly larger than that of the initiator particles. The size increase of grafted particles with monomer loading is linear.

Figure 3.8 shows ESEM images of grafted particles with increase of monomer loadings. No outsized particles were observed in the images, which confirmed the peaks to the right of the main peak in Figure 6 were due to temporary particle aggregates in aqueous solution during measurement. The observed particle surfaces became rougher

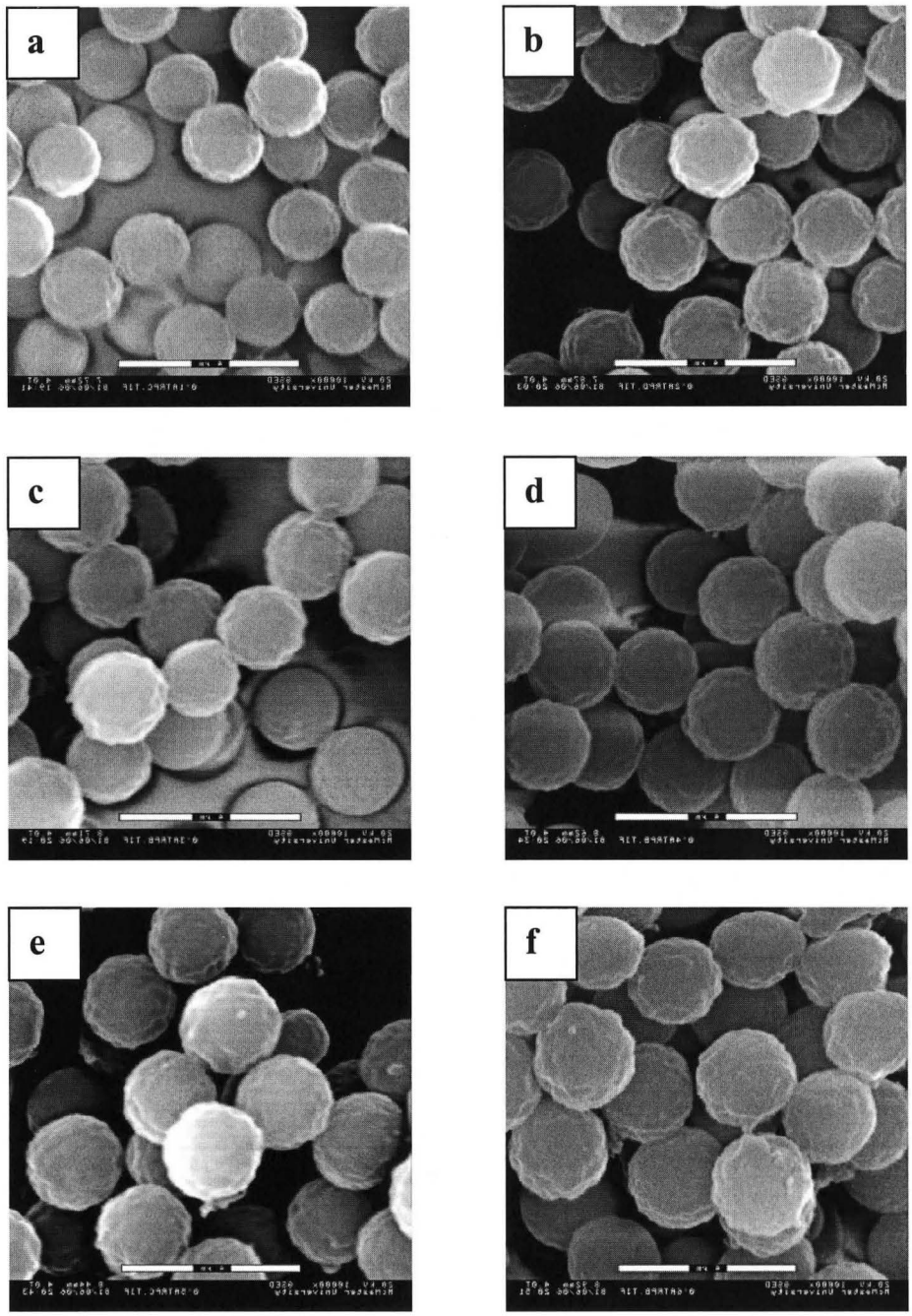


Figure 3.8 ESEM images of ATRP grafted particles from initiators H_iBr with different monomer loading for 15 hr. Grafting polymerization condition: a) 0.1 g MMA; b) 0.2 g MMA; c) 0.3 g MMA; d) 0.4 g MMA; e) 0.5 g MMA; f) 0.6 g MMA. The scale bar is 4 μm

with higher monomer loading, and with longer reaction time, either due to loss of MMA under the e-beam, or due to an amplification of small inhomogeneities of the initiator particles during grafting.

The internal structure originally proposed for the grafted particles, and illustrated in Figure 3.3, was confirmed by TEM images of microtomed particles (Figure 3.9). The surface layer of the particles, which consists of almost pure linear PMMA, decomposed under the electron beam and left a void indicated by a white ring. Decomposition was

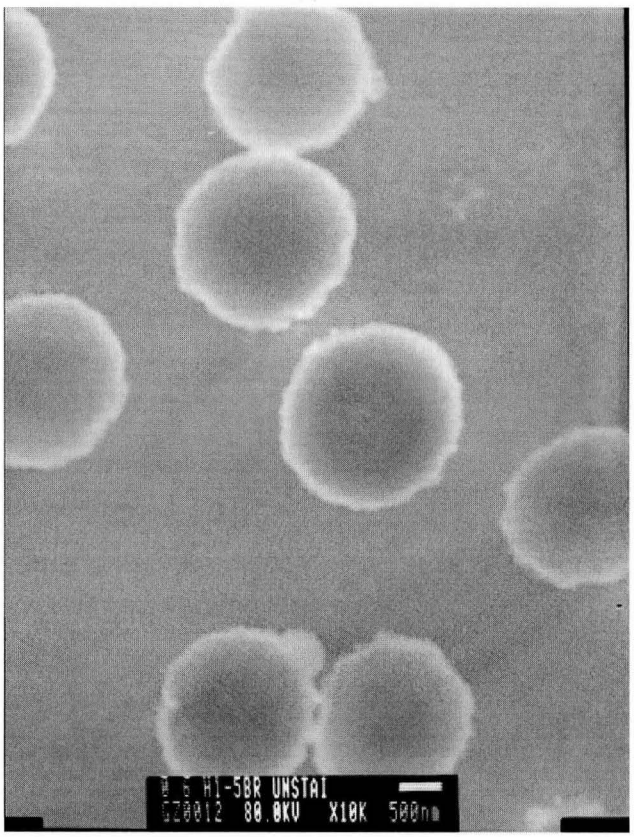


Figure 3.9 TEM images of poly(MMA) grafted particles from initiators H_1Br
The scale bar is 500 nm

observed when the electron beam was focused on the particle slices. The white rings were present at the beginning but grew with exposure to the electron beam. Also, the white ring was hard to detect for particles with a low degree of MMA grafting.

3.2.5 Grafting block copolymer onto particles

The poly(MMA)-grafted particles obtained after 4 h of polymerization, isolation and purification, were used as initiator particles for a second ATRP of HEMA and DMAEMA. The particle weights increased by 243% (48% conversion of monomer) and 435% (87% conversion of monomer) respectively, upon this second generation grafting at room temperature for 23 h, while the size of the particles increased from 2.7 μm to ca 4.1 and 4.7 μm. This result confirmed that a significant portion of the first grafts can be reactivated using ATRP catalysts.

3.2.6 Grafting functional polymer onto particles

Functional polymers containing basic groups were prepared by grafting poly(DMAEMA) onto 0.4 g of H_IBr particles. A procedure similar to that used to graft MMA and MA onto particles was used. The resulting particles H_IBr-*g*-poly(DMAEMA) showed weight increases of 398% (1.99 g, 80% monomer conversion). The loading of tertiary amine groups on the particles can be calculated from the weight increase after grafting. The functional loading of H_IBr-*g*-poly(DMAEMA) and H_IBr-*g*-poly(MMA)-*b*-poly(DMAEMA) particles was also measured by potentiometric titration with acid. Table 3.2 compares the functional loadings calculated from the particle weight increase upon grafting, with those obtained by potentiometric titrations. The titrations were carried out in aqueous phase, and were complete within 10 minutes. These results confirm the

high functional loadings expected from grafting functional monomers off a swellable support resin. In addition, the agreement between weight gain and titration, especially for the graft-block copolymer, indicate that most of the functional groups are highly accessible.

Table 3.2 Functional Loading of Grafted Particles

	H_1Br-*g*-poly(DMAEMA)	**H_1Br-*g*-[poly(MMA)-*b*-poly(DMAEMA)]**
Weight Increase [g][a]	1.59	0.87
Functional Loading [mmol/g][b]	5.09	5.18
Capacity mmol/g][c]	4.60	5.30

a: weight of H_1Br initiator particles: 0.4 g;

b: based on weight increase;

c: based on potentiometric titration

Several factors such as high functional group loading, high polarity, and narrow size distribution should make these particles compatible with proteins and other biomaterials. In the future, we will explore applications in binding and separation of proteins and other biomolecules.

3.3 Conclusion

Grafting functional acrylates and methacrylates by controlled/living ATRP from

swellable microsphere initiators can lead to novel, highly functional polymer supports. Cu(I)/Me4cyclam serves as active catalyst of these monomers in THF at room temperature, and suitable for the formation of grafted block copolymer. The original, lightly crosslinked core particles are converted into swellable, interpenetrating network microspheres comprised mainly of the grafted polymer.

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Chapter 4 Grafting of Poly(ε-caprolactone) and Poly(ε-caprolactone-*block*-dimethylaminoethyl methacrylate) from Polymer Microspheres by Ring Opening Polymerization and ATRP[1]

Abstract

We report the ring opening polymerization (ROP) of ε-caprolactone catalyzed by $Al(Et)_3$ and $Al[OCH(CH_3)_2]$, from lightly cross-linked poly(DVB80-*co*-HEMA) microspheres. The resulting poly(ε-caprolactone) grafted particles with active propagating ends were converted to macroinitiators for ATRP, and used further to graft dimethylaminoethylmethacrylate (DMAEMA) to produce microspheres grafted with block copolymer. The ROP of ε-caprolactone from the poly(DVB80-*co*-HEMA) microspheres was carried out at both room temperature and 70 °C for different reaction times to produce particles with different graft loadings. The subsequent grafting of poly(DMAEMA) blocks using ATRP led to significant particle size increases from 1.57 to 2.24 μm, and to high amine loadings of 5.10 mmol/g dry particles. The grafted particles were characterized using ESEM, FT-IR, ^{1}H-NMR, Coulter particle sizing and potentiometric titration.

4.0 Introduction

Polymers grafted on solid surfaces are being extensively studied, with a range of

[1] G.Zheng, H.D.H. Stöver, Macromolecules, submitted.

the objectives including improved wetting, friction, adsorption, and adhesion. The effects of grafting on the properties of surfaces mainly depend on the type, density, and chain length of the grafted polymer, that are sensitive to the choice of polymerization techniques. A number of papers have reported on the grafting of polymers onto and from solid surface.[1] The grafting-from method has fundamental advantages over the grafting-onto method, especially in terms of maximum grafting density. In order to graft polymers from solid surface, the initiators must be covalently bound onto the surface and living/controlled polymerization is required to ensure polymer growing from these surface sites.

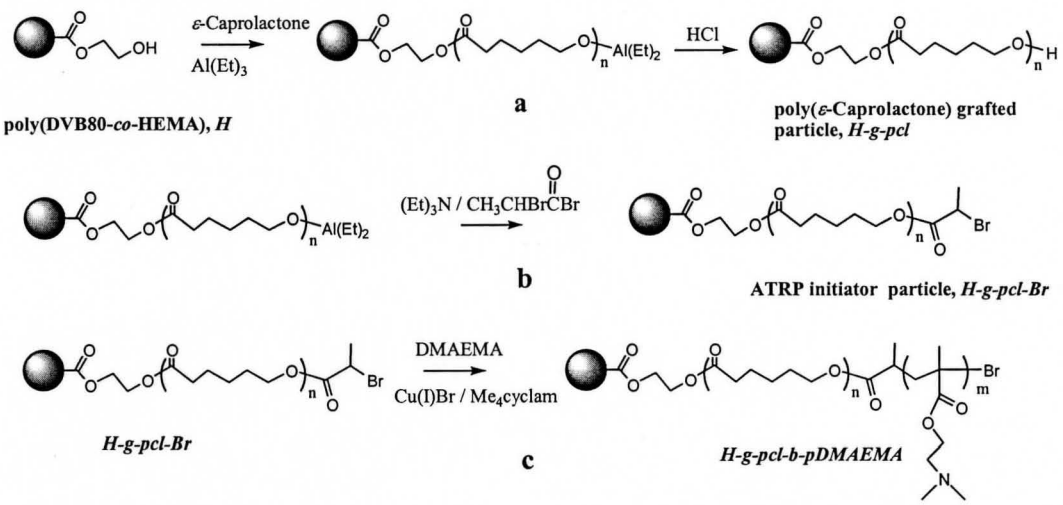
Several living/controlled polymerizations were used for grafting polymers from solid surfaces. Recently, the most popular living/controlled polymerization used in grafting polymer from solid surface has been the atom transfer radical polymerization (ATRP). ATRP[2] has a number of advantages over both conventional free radical and ionic polymerization, allows the synthesis of block copolymers[3] and grafting copolymers,[4] and is particularly tolerant of water[5] and functional groups. Several groups have reported ATRP grafting from solid surfaces.[6]

The ring opening polymerization (ROP) of cyclic esters and related compounds is another living/controlled method suitable for grafting polymer from solid surface. The polyester prepared by ROP of ε-caprolactone is biodegradable, which is potentially important to different applications. The ROP of cyclic esters can be catalyzed or initiated by organometallic derivatives, with different mechanisms.[7] When metal alkoxides containing free p-, d-, or f- orbitals of a favorable energy are used as initiators, polymer

chains grow from the alkoxy group in the initiators, by a two-step "coordination-insertion" mechanism.[8] Among metal alkoxides, aluminum alkoxides such as $Al(OiPr)_3$[9] and $AlOR(Et)_2$[10] have been reported to be efficient initiators toward polymerization and copolymerization of cyclic esters with narrow molecular weight distribution. $AlOR(Et)_2$, prepared by the reaction of $AlEt_3$ with alcohol ROH, was often used to synthesize α,ω functional polymer.[11] Using a similar route, Hamaide et al.[12] have reported the heterogeneous catalytic coordination ROP by Si-O-$Al(OR)_2$ covalently attached to porous silica. This immobilized $Al(OR)_2$ was prepared by reacting Si-OH with $Al(iBu)_3$, followed by replacing the *i*Bu groups with excess ROH. In the heterogeneous ROP process, polymer chains propagated through monomers inserting into the bonds of Al-OR rather than Al-OSi at the roots of the polymers. However, the linkage of SiO-Al-$[(O(CH_2)_5CO)_nOR]_2$ is labile to bases such as water and alcohol. The heterogeneous catalytic coordination ROP process was only useful for producing tailor-made ω-functionalized (oligo)copolymer and recycling of the catalyst. For permanently grafting polymer on particles, a robust linkage for tethering ROP catalyst on the particle surface is required.

In this paper, we report on ROP of ε-caprolactone from the surface of polymeric micro-spheres. The polymeric micro-spheres of poly(DVB80-*co*-HEMA) were prepared by precipitation polymerization in neat acetonitrile. Their hydroxyl groups were then reacted with $Al(Et)_3$ to form $AlOR(Et)_2$ initiating sites. The polyester could then propagate from these initiator sites to produce polyester grafted surfaces, with monomers always inserting at the heads of the polymers (Scheme 4.1a). A subsequent change of

initiating groups by reaction with bromopropionylbromide would allow ATRP of different methacrylates, resulting in a series of amphiphilic block copolymer grafts combining bio-degradable and functional blocks.(Scheme 4.1b). Both ROP and ATRP polymerizations took place at room (Scheme 4.1c).



Scheme 4.1 Grafting poly(ε-caprolactone-*b*-DMAEMA) from poly(DVB80-*co*-HEMA) micro-spheres by subsequent polymerizations

4.1 Experimental Section

4.1.1 Chemicals

Solvents were purchased from Aldrich and used as received unless otherwise specified. 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (Me_4cyclam) (98 % Aldrich), 2-bromopropionyl bromide (97 %, Aldrich), triethylaluminum (1.0 M in hexanes), aluminum isopropoxide (98+ %, Aldrich), DVB80 (70-85 % divinylbenzene isomers, Fluka, Oakville, Canada), and triethylamine (99 %, Aldrich) were used as

received. Hydroxyethyl methacrylate (HEMA, 97 %), methyl methacrylate (MMA, 99 %), and 2-(dimethylamino)ethyl methacrylate (DMAEMA, 98 %) were purchased from Aldrich Chemical Co. and purified by distillation under vacuum prior to polymerization. ε-caprolactone (99+ %, Aldrich) was dried by keeping it over active 4 Å molecular sieves. Tetrahydrofuran (THF, 99+ % Aldrich) was refluxed over potassium-sodium alloy and distilled under nitrogen. CuBr was prepared by the reaction of $CuBr_2$ with dimethyl malonate.

4.1.2 Syntheses

The poly(DVB-*co*-HEMA) (H_j) starting particles composed of different ratios of DVB80 to HEMA were prepared by precipitation polymerization as reported previously.[13] The particles made with the comonomer ratios $R_{DVB/HEMA}$ of 4.7, 2.7 1.8, and 1.2 were designated as H_1, H_2, H_3, and H_4.

Initiator Particles (H_1-Al(Et)$_2$) for ROP. The starting particles, H_1 (2.0 g), were dispersed in 50 ml of dry THF for 2 h and then 2.5 ml of $(Et)_3Al$ (2.5 mmol) in hexanes (1.0 M) were slowly added. The reaction solution was stirred at room temperature for 4 h and the resultant particles were isolated by centrifugation followed by three washings each with dry THF and diethyl ether. The particles were dried under vacuum for 12 h.

Grafting Polymers from Initiator Particles (H_1-Al(Et)$_2$) by ROP. The graft ROP of ε-caprolactone to form H_1-*g*-*pcl* was conducted in two ways.

Method A Poly(DVB-*co*-HEMA) particles H_1 (0.3 g) suspended in 8 ml of dry THF in the presence of $(Et)_3Al$ (2 ml, 2.0 mmol) or $[(CH_3)_2CHO]_3Al$ (0.41 g, 2.0 mmol) in a 25 ml flask were stirred for 1 h. ε-Caprolactone (2.0 g, 17.5 mmol) was rapidly

added into the suspension and the polymerization was continued at room temperature or 70 °C for 5 h. The resulting grafted particles were filtered on 0.5 μm Teflon filter paper, followed by triple sequential washings with acidic methanol (5 % HCl) and THF. The yield of the modified particles was 0.64 g.

Method B The initiator particles H_1-$Al(Et)_2$ (0.30 g) were suspended in 8 ml of dry THF in a 25 ml flask were stirred for 1 h. ε-Caprolactone (2.0 g, 17.5 mmol) was rapidly added into the suspension and the polymerization was continued at room temperature for 5.5 h. The resulting grafted particles were filtered on 0.5 μm Teflon filter paper, followed by triple sequential washings with acidic methanol (5 % HCl) and THF. The yield of the modified particles was 0.32 g.

Initiator particles (H_1-g-pcl-Br) for ATRP. Active poly(ε-caprolactone) grafted particles made from 1.00 g of H_1 and 5 h ROP were suspended for 2 h in 10 ml of THF containing 0.45 g (4.4 mmol) of triethylamine in a 50-ml two-neck round-bottom flask. Bromopropionyl bromide (0.95 g, 4.4 mmol) was added dropwise into the suspension through a dropping funnel. An ice-water bath was used during the addition of bromopropionyl bromide and the resulting mixture was slowly allowed to warm and stirred with a magnetic stirrer at room temperature for 16 hours. The particle initiators were filtered and washed three times each with THF and methanol. The resulting particles were dried at room temperature under vacuum for 24 h.

Grafting Block Copolymer from Microspheres H_1-g-pcl by ATRP The particles H_1-g-pcl-Br (0.50 g) were suspended in 5 ml of THF containing 2.0 g (12.7 mmol) of

DMAEMA and purged by passing THF-saturated nitrogen through the solution for 30 minutes. A degassed solution of CuBr (35 mg, 244 μmol) and Me_4cyclam (62.6 mg, 244 μmol) in 2 mL CH_3CN was transferred into the suspension through a cannula. The mixture was stirred with a magnetic bar at room temperature under nitrogen for 10 h. The resulting grafted particles were centrifuged and re-dispersed three or more times in THF, and several times in NH_4OH/methanol (1/20 by volume), until the particles became almost white. The particles were finally washed with ether and dried at room temperature under vacuum for 24 h. The yield of resultant particles was 2.44 g.

Particle Size Analysis The particle sizes and size distributions were measured using a 256-channel Coulter Multisizer interfaced with a computer. A 30 μm-aperture tube was chosen to accommodate the particles size range of 1-10 μm. A small amount of particles, dispersed in acetone, was added to 25 ml of Coulter Isoton II electrolyte solution and stirred for 1 min with the mini-stirrer supplied with the instrument. The Coulter Multisizer measurements were confirmed using a Philips ElectroScan 2020 environmental scanning electron microscope (ESEM).

ESEM analysis The ESEM samples were prepared by dispersing the particles in THF and casting a drop of the resulting particle suspension on a piece of microscopy cover glass glued onto an ESEM stub. The samples were dried under vacuum for 2 hours and sputter-coated with 5 nm gold.

TEM Analysis The internal structure of the grafted particles was studied using a JEOL 1200EX transmission electron microscope. Here, the samples were embedded in Spurr's epoxy resin and ultramicrotomed to generate 40-60 nm thick slices. The samples

gave sufficient contrast without staining.

FT-IR Analysis Fourier transform infrared analysis was performed on a Bio-Rad FTS-40 FT-IR spectrometer. All samples were prepared as pellets using spectroscopic grade KBr in a Carver press at 15,000 psi. The spectra were scanned over the range 4000 - 400 cm^{-1}, in the transmission mode.

4.2 Results and Discussion

The starting microspheres containing hydroxy groups were prepared by precipitation polymerization of divinylbenzene-80 (DVB80) and hydroxyethylmethacrylate (HEMA) in neat acetonitrile as described earlier.[13] Different ratios $R_{DVB/HEMA}$ of DVB80 to HEMA were used to explore the effects of cross-linking degree and hydroxy loading. Both presence and availability of hydroxy groups in the particles particles should depend strongly on this monomer ratio, since at high values for $R_{DVB/HEMA}$ the remaining HEMA groups would be less accessible due to the lower degree of swelling.

Preliminary experiments showed significant differences in the efficiency of grafting poly(ε-caprolactone) from particles having different monomer composition. The particles H_1, H_2, H_3, and H_4 having $R_{DVB/HEMA}$ values of 4.7, 2.7 1.8, and 1.2 respectively, were used to initiate the ROP of ε-caprolactone in the presence of $Al(Et)_3$. The weights of particles H_1, H_2, H_3, and H_4 after the polymerization at 70 °C for 10 h have increased by 107, 70, 37, and 37 %, respectively. These results demonstrated that the particles H_1, with the lowest crosslinker level and the highest HEMA level, permit the

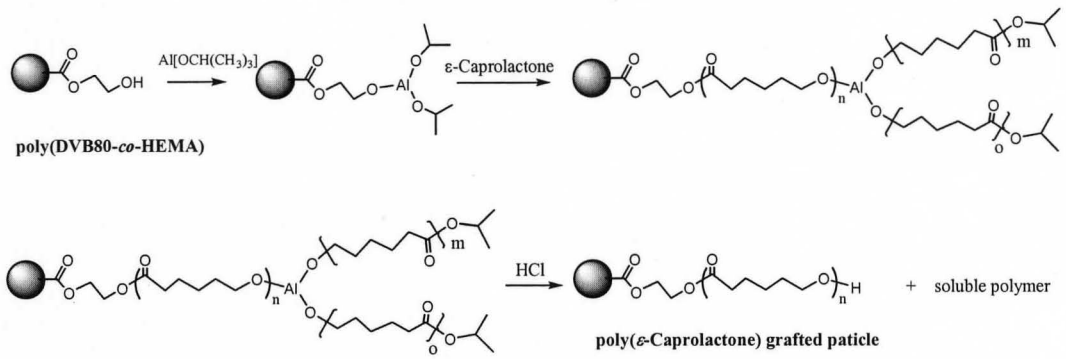
most efficient grafting polymerization. Accordingly, we subsequently used only particles H_1 as seeds for grafting poly(ε-caprolactone) and poly(ε-caprolactone-*block*-DMAEMA).

4.2.1 ROP of ε-caprolactone catalyzed by $Al(Et)_3$ and $Al(i\text{-}PrO)_3$

Two types of catalysts, triisopropoxyaluminum $Al[OCH(CH_3)_2]_3$ and triethylaluminum $Al(Et)_3$, were used for the grafting ROP of ε-caprolactone. As mentioned above, ε-caprolactone can be activated by Al-O bonds in aluminum alkoxides. When triethylaluminum $Al(Et)_3$ was used as a catalyst, hydroxy groups on the particles first reacted with it to form aluminum alkoxides. Subsequently, the resulting particle-bound aluminum alkoxides started polymer chains growing from the particle. Any excess of triethylaluminum $Al(Et)_3$ in the solution should not affect the grafting ROP polymerization, and could in fact be used to remove trace water, if needed. However, the resulting aluminum hydroxides might also initiate ROP of ε-caprolactone since a few percent of soluble poly(ε-caprolactone) was observed in the present grafting reactions.

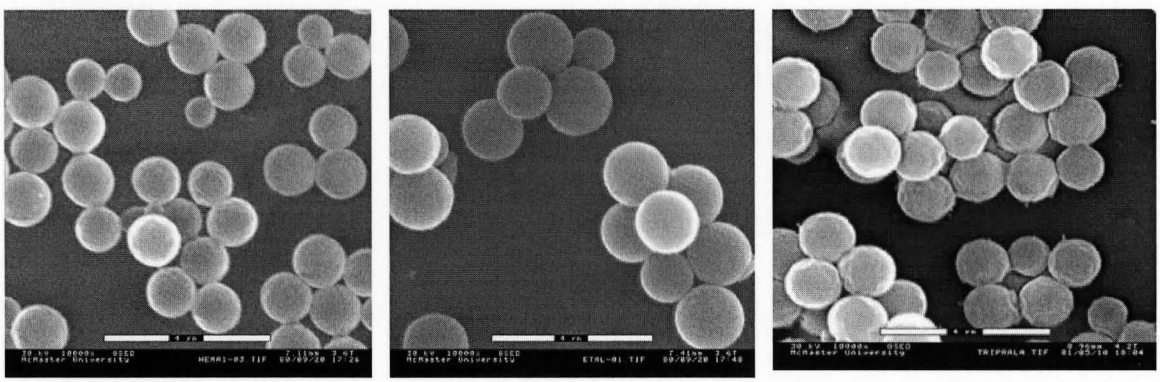
In contrast, the catalyst triisopropoxyaluminum $Al[OCH(CH_3)_2]_3$ proved to be more complicated. Triisopropoxyaluminum can react with primary hydroxy groups on the particles through an alkoxide exchange reaction, resulting in particle bound aluminum alkoxides. Polymer chains could then grow both from these particle bound, primary alkoxides, but also from the remaining aluminum isopropoxy moieties, both particle bound and free. The poly(ε-caprolactone) chains originating from isopropoxy groups would become detached from the particles or the free catalyst, upon washing with hydrogen chloride (Scheme 4.2). This side reaction would account for the significant amount of soluble polymer observed. Therefore, triisopropoxyaluminum

$Al[OCH(CH_3)_2]_3$ is less efficient than $Al(Et)_3$ in terms of grafting polymer from particles.



Scheme 4.2 Grafting poly(ε-caprolactone) from poly(DVB80-*co*-HEMA) micro-spheres catalyzed by triisopropoxyaluminum

The ESEM images show that grafting using $Al(Et)_3$ results in larger particle sizes compared to grafting using $Al[OCH(CH_3)_2]_3$ (Figure 4.1). The particle diameter increased by about 31 % and 15 %, and the weight increased by 82 % and 40 %, respectively.



H_1 **H_1 -g-pcl using $Al(Et)_3$** **H_1 -g-pcl using $Al[OCH(CH_3)_2]_3$**

Figure 4.1 ESEM Images of starting particles H_i and of the poly(ε-caprolactone) grafted particles

In addition to using the starting particles H_1 directly to initiate ring opening polymerization via *in situ* formation of initiators in the presence of $Al(Et)_3$, the particles H_1 were also converted to initiator particles H_1-$Al(Et)_2$ by the reaction with $Al(Et)_3$, in order to study the polymerization in absence of free $Al(Et)_3$. The results of grafting poly(ε-caprolactone) from these initiator particles, H_1-$Al(Et)_2$, are reported in the next section.

4.2.2 The effect of temperature, monomer loading and reaction time

The grafting efficiency for the particles H_1 increased when the ROP of ε-caprolactone from the particles was carried out at 70 °C. However, for longer polymerization times at elevated temperature, both weight and size of the grafted particles reached a maximum and subsequently decreased (Table 4.1). The polymerization of ε-caprolactone is an equilibrium reaction between forward and depolymerization reactions. At 70 °C the polymerization could quickly reach an equilibrium state. If the depolymerization or backbiting reaction generates not only 7-membered ring ε-caprolactone but also cyclic dimers or oligomers, then the equilibrium could shift towards lower molecular weights as it populates these species.

In addition to the change of particle size and weight with reaction time, the ESEM images also show morphology changes of the particles (Figure 4.2).

The particles studied after 5 h reaction time had fuzzy surfaces, indicating long polymer chains on the surfaces. At longer reaction times the particle sizes decreased slightly, and the particles showed a smoother surface, suggesting a more narrow chain length distribution due to the equilibrium between polymerization and de-

polymerization.

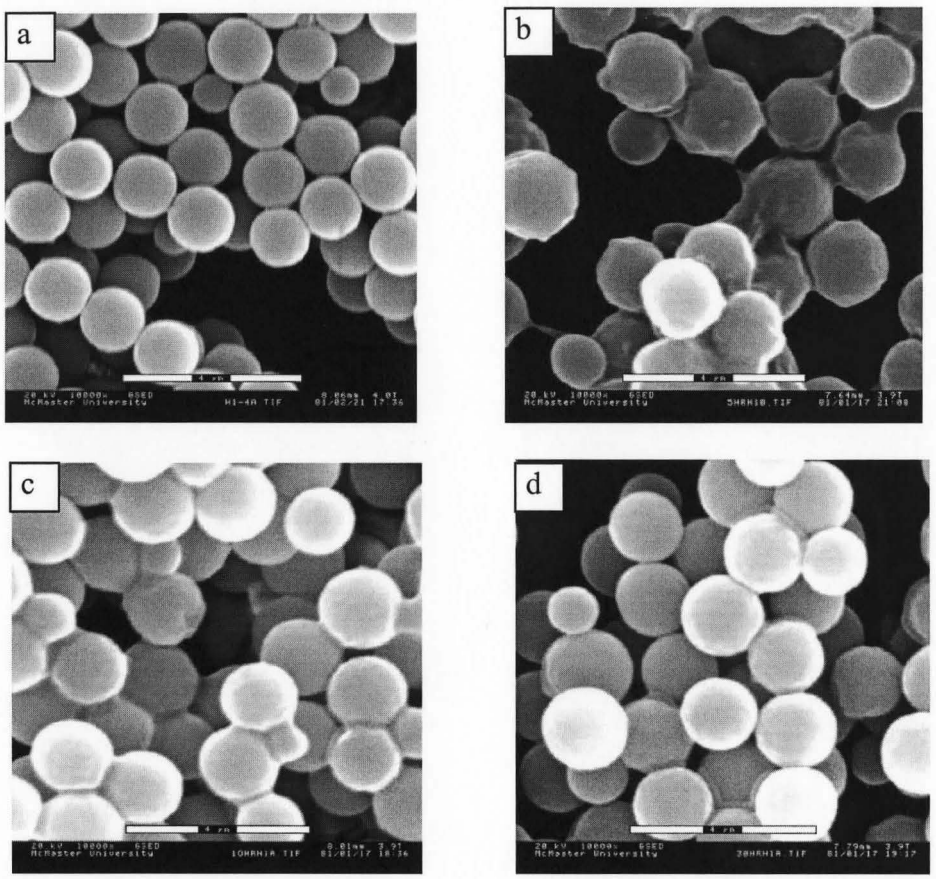


Figure 4.2 ESEM images of the poly(ε-caprolactone) grafted particles made in different reaction time at 70 °C. a. H_I b. 5 h c. 10 h d. 30 h

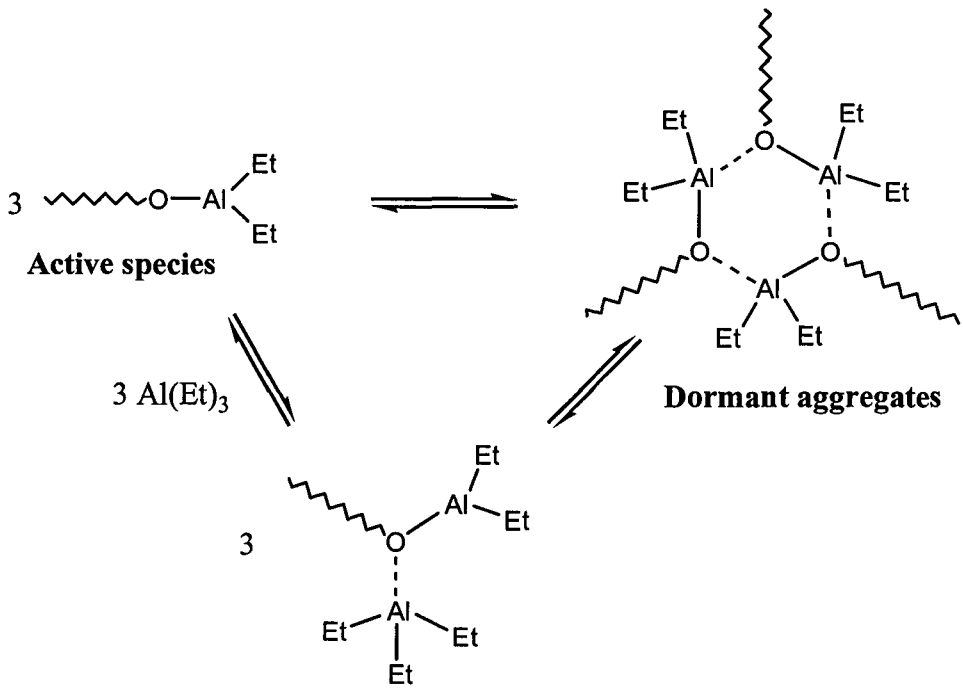
The grafting ROP of ε-caprolactone from the particles was found to proceed at room temperature, though at a much slower rate (Table 4.1). In contrast to the reaction carried out at 70 °C, the size of the particles grafted at room temperature increased with the reaction time. The largest particles were obtained at the longest reaction time, which indicates the backbiting reaction is much less effective at room temperature.

Table 4.1 The weight increase and size of poly(ε-caprolactone) grafted particles from H_1

Entry[a]	70 °C	R. T.	Wt increase %	Size[c] (μm)
1	1 h		3	1.40
2	2 h		65	1.72
3	3 h		100	1.81
4	5 h		113	1.89
5	10 h		106	1.85
6	20 h		71	1.77
7	30 h		73	1.77
8[b]		30 min	0	1.56
9[b]		1.5 h	0	1.56
10[b]		2.5 h	1	1.56
11[b]		3.5 h	1.5	1.56
12[b]		4.5 h	3	1.60
13[b]		5.5 h	6	1.60
14		30 min	0	1.56
15		1.5 h	5	1.60
16		2.5 h	8	1.64
17		3.5 h	26	1.68
18		4.5 h	30	1.72
29		5.5 h	40	1.74
20		6.5 h	43	1.74
22		8.5h	50	1.82

[a] H_1 was used as initiator in the presence of excess $Al(Et)_3$. [b] H_1-$Al(Et)_2$ was used as initiator. [c] 1.40 μm particles were used for polymerization at 70 °C; 1.56 μm particles were used for polymerization at r. t.

In order to investigate the effect of excess $Al(Et)_3$ on the ROP, initiator particles were prepared by reaction of particles H_1 with $Al(Et)_3$, and isolated following thorough washings with dry THF. The initiator particles showed much less activity than the reaction in presence of excessive $Al(Et)_3$ (Table 4.1). The particle size increased slowly with the reaction time. The lower activity of these preformed initiator particles may be attributed to the formation of non-active complexes (Scheme 4.3). Duda et al. reported the formation of the non-active aggregates in solution ROP of (di)lactones catalyzed by



Scheme 4.3 The structure of aggregated catalyst

aluminum alkoxides.[14] In fact, only a small fraction of dissociated aluminum alkoxides are active in ROP of (di)lactones. In our case, aluminum alkoxides were tethered on particles and the local concentration of the aluminum complex should be very high, leading to an even smaller fraction of active complex. The excess $Al(Et)_3$ might prevent the association of the tethered aluminum alkoxides, by coordinating to electron pairs on the aluminum alkoxide oxygens. During the preparation of the initiator particles the excess $Al(Et)_3$ was washed away, and the equilibrium would shift to the dormant, aggregated side.

Interestingly, an induction period for solution ROP of lactones was observed by

Teyssié *et al.* with aluminum isopropoxide as the initiator in stoichiometric conditions.[15] The induction period was interpreted in term of the aggregates that required some time to dissociate. The induction period was also found in this study and could be shortened by addition of excessive $Al(Et)_3$.

4.2.3 The conversion of the propagating end into initiator for ATRP, and ATRP of DMAEMA to form block copolymer

The subsequent grafting of a different polymer using ATRP, off the particles grafted with poly(ε-caprolactone), was attempted in order to prepare block copolymer grafted particles having hydrophilic shells.

To this end, the propagating aluminum alkoxide ends were directly converted to ATRP initiator groups by reaction with bromopropionyl bromide in the presence of pyridine.

The hydrophilic monomer dimethylaminoethyl methacrylate (DMAEMA) was then grafted off the resulting bromopropionate terminated poly(ε-caprolactone) grafts, converting the originally hydrophobic particles into polar, ionizable particles well dispersable in water.

The poly(ε-caprolactone) grafted particles prepared at room temperature for 5.75 h, were used for the conversion of initiating groups from ROP to ATRP. The formation of bromopropionate was determined by the weight increase and by FT-IR. The bromopropionate groups on particles showed a characteristic peak of methyl groups at 1380 cm^{-1}.[16] The intensity of the peak became weaker during ATRP due to the decrease in relative concentration of the bromopropionate group.

The ATRP of DMAEMA from the initiator particle *H_1-g-pcl-Br* was carried out at room temperature, using CuBr/Me_4cyclam as catalyst. THF was used as solvent for the ATRP because it is good solvent for both initiator particles and poly(DMAEMA). The ATRP of DMAEMA catalyzed by CuBr/Me_4cyclam was very effective. Polymers were grafted off the particles *H_1-g-pcl-Br in* 97.0 % and 98.4 % of monomer conversion, for ratios of DMAEMA to the initiator particles of 2 : 0.5 and 1.3 : 0.5 by weight, resulting in block-grafted particles *H_1-g-pcl-b-pDMAEMA(A)* and *(B)*. These particles *H_1-g-pcl-b-pDMAEMA* showed hydrophilic properties. They dispersed easily in polar organic solvents and water. The grafted particles tended to aggregate upon drying, likely due to the long, polar chains grafted on their surfaces.

Due to the high swellability of the original particles, we expect that the block grafts will be distributed both within and on the surface of the particles, in analogy to similar particle morphologies discussed earlier.[16]

Aggregation in solution was also observed when a non-polar solvent such as hexane was added to the suspension of the grafted particles in a good solvent such as THF. The long, surface grafts function as steric stabilizer in good solvents but collapse in poor solvents.

The ESEM images of the block-grafted particles *H_1-g-pcl-b-pDMAEMA* demonstrated the morphologies and sizes of the particles (Figure 4.3). The size of the particles increased dramatically compared to the initiator particles *H_1-g-pcl-Br*. When the particles *H_1-g-pcl-b-pDMAEMA* were cast on a glass piece from a THF suspension, the particles fused into a polymer matrix upon drying, presenting clearly the particle cores

and a matrix formed from the surface grafts. Individual, relatively spherical particles were observed when aggregates of the particles made by addition of non-solvent to a suspension cast on a glass piece. This observation indicates that the grafted polymer shrinks upon the addition of a non-solvent, and collapses down onto the particle surface.

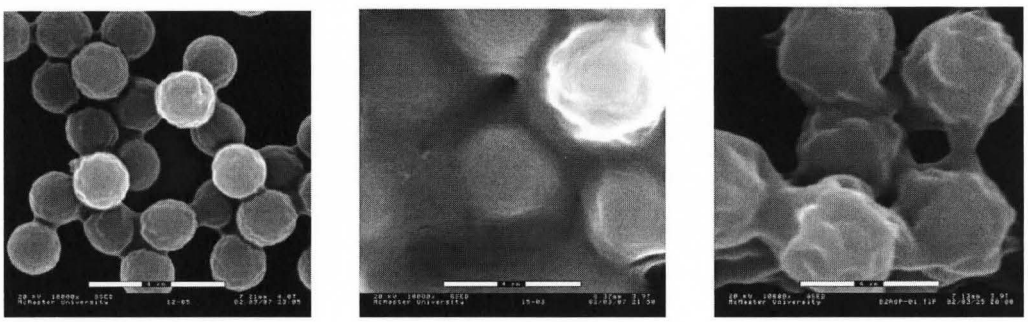
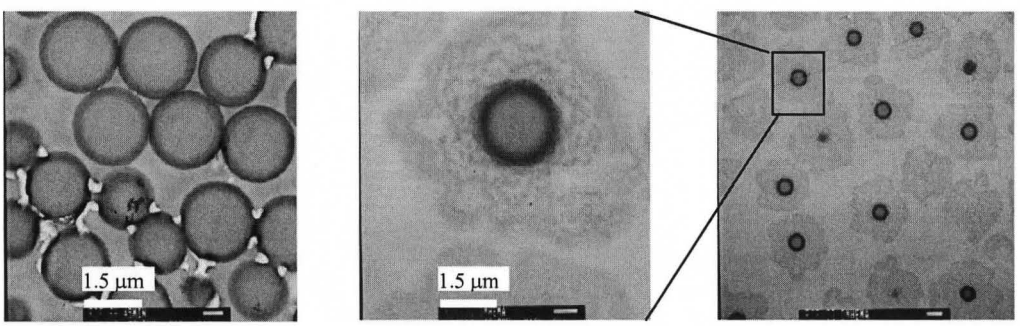


Figure 4.3 ESEM images of grafted particles A. poly(ε-caprolactone) grafted particles B. poly(ε-caprolactone-b-DMAEMA) grafted particles cast from THF C. poly(ε-caprolactone-b-DMAEMA) grafted particles cast from ether The scal bar is 4 μm

The internal structure of the grafted micro-spheres was studied using transmission electron microscope. The TEM image of sliced samples is shown in Figure 4.4.



H_1-g-pcl *H_1-g-pcl-b-pDMAEMA*

Figure 4.4 TEM image of sectioned samples of *H_1-g-pcl* and *H_1-g-pcl-b-pDMAEMA*

The particles grafted with poly(ε-caprolactone) show a core-shell structure with a dark ring of poly(ε-caprolactone) and a light core representing the particle H_1. After the core-shell particles were grafted with poly(DMAEMA), a cloudy contour comprised of linear poly(DMAEMA) surrounds each core-shell particle. The matrix of poly(DMAEMA) was presumably swollen by the epoxy resin, as indicated by some region having similar contrast to interstitial epoxy resin.

The amount of grafted poly(DMAEMA) on the particles was confirmed by acid-base titration. The functional polymer with tertiary amine was titrated with aqueous hydrochloride and demonstrated a very sharp jump at the equivalent point, similar to the behavior expected for free tertiary amine (Figure 4.5).

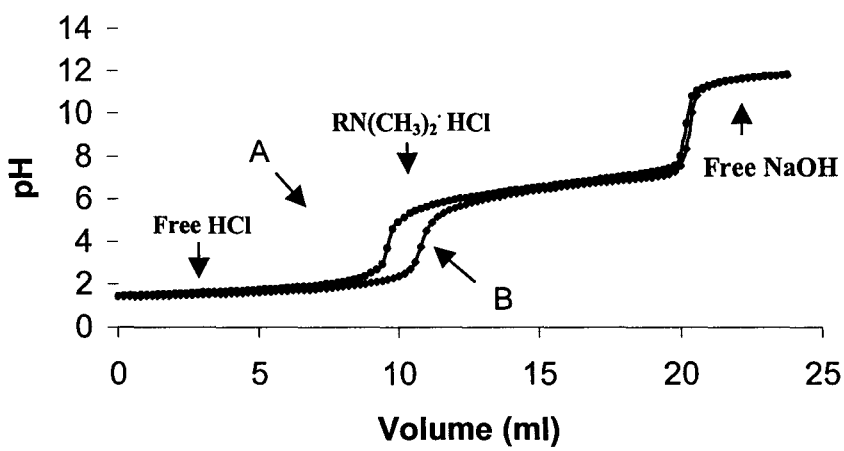


Figure 4.5 Acid–base titration on the grafted particles

This result shows that all of the poly(DMAEMA) on the particles was easily accessible. The amount of grafted poly(DMAEMA) on the particles H_1-g-pcl-b-pDMAEMA (A) and (B) was calculated based on the consumed hydrochloride. Functional

amine loadings of 5.10 mmol/g and 4.53 mmol/g, corresponding to 80.2 wt% and 71.1 wt%, were found, consistent with the weight increase from initiator particles after grafting polymerization.

4.2.4 The study by FT-IR and NMR on the grafted particles

The surface modification and grafted polymer was determined by FT-IR. The starting particles H_1 composed of poly(DVB80-co-HEMA) were showed the expected hydroxy stretch at 3445 cm^{-1}, plus an ester group at 1725 cm^{-1} (Figure 4.6). The ROP of

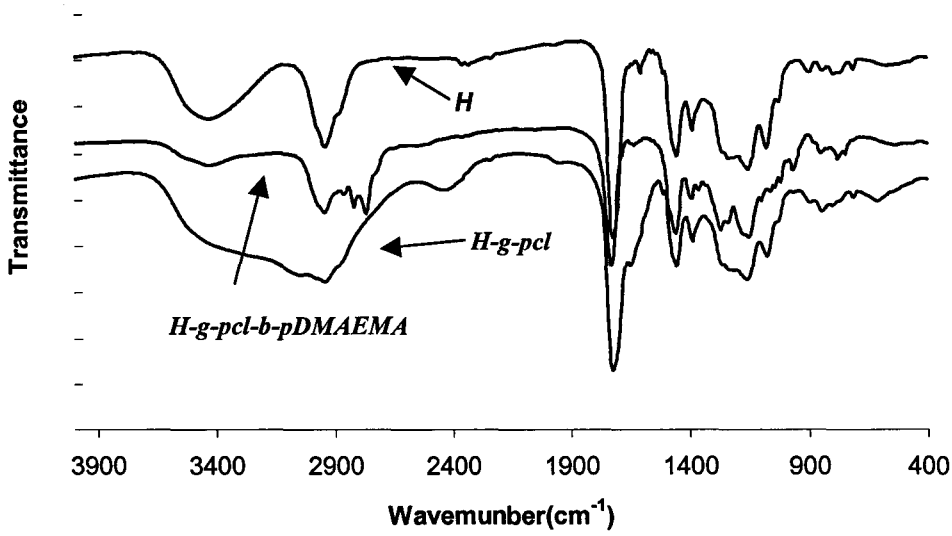


Figure 4.6 FT-IR spectra of grafted particles

ε-caprolactone on the DVB80-HEMA particles H_1 changed the relative ratios, but not the nature of the functional groups. For example, the ratio of (residual) hydroxy to ester groups decreased with polymerization, as seen from the a gradual decline in intensity at 3445 cm^{-1} in the samples of grafted particles H_1-*g*-*pcl* generated at increasing reaction time. In addition, the absorptions at 1605 and 1511 cm^{-1} due to aromatic carbon-carbon

double bond decreased during polymerizations. Moreover, the stretch corresponding to the C-H bond in poly(ε-caprolactone) gave rise to strong, broad band at *ca* 3000 cm^{-1}.

When the ATRP initiator was introduced onto the particles *H_1-g-pcl*, the characteristic methyl stretch of bromopropionate at 1380 cm^{-1} was observed (not shown). The adsorption could be used as a probe to monitor the ATRP, with the peak decreasing during ATRP of DMAEMA due to a relative reduction in the methyl group concentration. The new functional groups arising from the tertiary amine in DMAEMA show a doublet of C-N stretching at 1272 and 1239 cm^{-1}. As well, the hydroxyl and aromatic stretches diminished compared with the starting particles *H_1*.

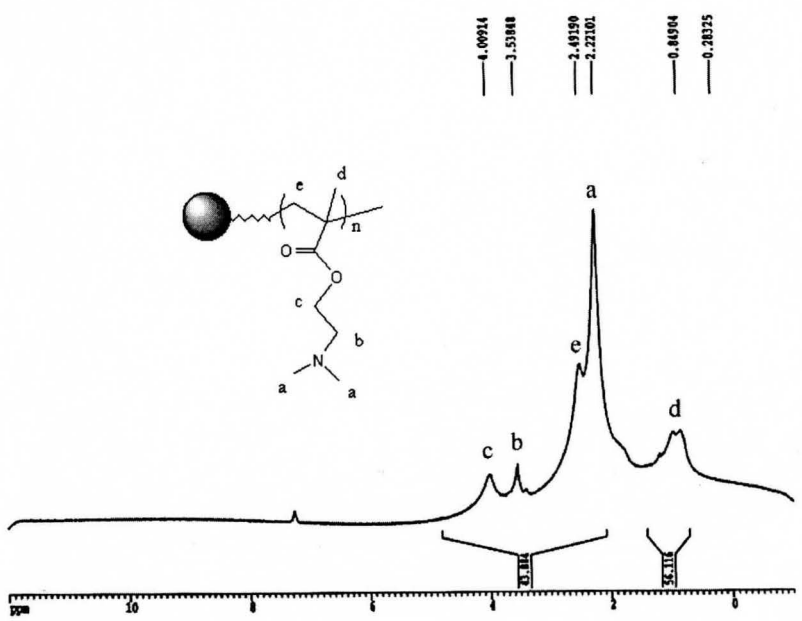


Figure 4.7 Gel-^{1}H NMR of *H_1-g-pcl-b-pDMAEMA*

A gel ^{1}H-NMR of the grafted particles *H_1-g-pcl-b-pDMAEMA* , swollen in $CDCl_3$ is

shown in Figure 4.7. The chemical shift at 2.2 ppm was attributed to the methyl groups on the tertiary amine. The shape of peak was very typical for soluble polymer, which indicated that the grafted particles dispersed well in CD_3OD and the grafted polymer on the particles behaved like soluble polymer.

4.3 Conclusion

Poly(*ε*-caprolactone) was grafted from lightly cross-linked poly(DVB80-*co*-HEMA) particles using ring opening polymerization (ROP) catalyzed by $Al(Et)_3$. The poly(*ε*-caprolactone) grafted particles with active propagating ends were subsequently converted to ATRP initiators, followed by the ATRP of DMAEMA to generate grafted block copolymer. The grafting of a hydrophilic polymer block from hydrophobic polymer blocks on the particles poly(DVB80-*co*-HEMA) led to dramatically particle size increases from 1.57 to 2.24 μm, and high amine functional loading of 5.10 mmol/g. The grafted particles were characterized using ESEM, FT-IR, ^{1}H-NMR, Coulter particle sizing and potentiometric titration.

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Chapter 5 The Property and Behavior of Polymers and Block Copolymer Tethered on Polymer Micro-spheres[1]

Abstract

We report the use of ATRP to graft off polymeric micro-spheres. Residual vinyl groups on non-swellable poly(DVB80) micro-spheres were converted into ATRP initiators by hydroboration/oxidation followed by esterification. Subsequent grafting by ATRP of poly(HEMA) and poly(DMAEMA) generated hydrophilically modified micro-spheres. The surface properties of these micro-spheres, FT-IR spectra, and potentiometric titration reflect the successful modification. In addition, swellable, lightly cross-linked poly(DVB-*co*-HEMA) micro-spheres were modified in a similar manner by grafting block copolymers, poly(MMA-*b*-DMAEMA), poly(MMA-*b*-TMAEMA), and poly(MMA-*b*-GMA). Microphase separation of the grafted amphiphilic block copolymers was studied by scanning electron microscopy. The micro-spheres modified with poly(MMA-*b*-DMAEMA) and poly(MMA-*b*-TMAEMA) show polyelectrolyte properties.

5.0 Introduction

Solid supports have found application in research areas including analytic and synthetic chemistry, biotechnology, and precision engineering. In particular, they are

[1] G.Zheng, H.D.H. Stöver, Macromolecules, to be submitted.

used in the analytic and preparative HPLC columns, as polymer support reagents, catalyst supports, and as functional resins for combinatorial synthesis, drug and vaccine delivery, and photonic crystals.[1]

All applications require solid supports with specific morphologies and surface properties. Polymer support reagents, for example, need to combine proper functionality with sufficient accessibility to reactants. Good compatibility with and swellability in reaction solvents will also enhance the reactivity of the functional groups. DentaGel, a popular polymeric support reagent, has excellent compatibility with both polar and non-polar solvents, since these supports are comprised of lightly cross-linked polystyrene grafted with a large amount of poly(ethylene glycol).[2] Chromatography stationary phases have to additionally withstand high column back pressures, and maintain high column flow rates. They may need to be modified to have hydrophilic, hydrophobic, amphiphilic properties, and even contain selective binding sites for affinity chromatography. In some case such as direct analyses of drugs in serum or plasma, the selective modification of interior and exterior surfaces of stationary phase is needed. Tanaka et al. describes the size-selective modification of porous silica to contain both hydrophilic exteriors and hydrophobic interiors.[3] Another porous polymer-based packing material, the highly cross-linked polystyrene called Styrosorb, was recently employed as a restricted-access stationary phase in sample clean-up for HPLC.[4] In this stationary phase, the outer surface is Tris-modified to become hydrophilic, while the unmodified internal surface remains hydrophobic. When these stationary phases were used in the direct analysis of drugs in the presence of polypeptides, the small drug molecules were retained in the hydrophobic

micro-pores, while the polypeptides were excluded from these micro-pores, and did not bind to the hydrophilic exterior either.[5]

This chapter deals with the modification of polymer micro-spheres by grafting polymers and block copolymers. It also concerns the properties of polymers and block copolymers tethered on polymer micro-spheres. It will demonstrate a new method for modification of mono-dispersed polymeric micro-spheres with hydrophilic and hydrophobic polymers, which may lead to potentially useful chromatography stationary phases and polymeric support reagents. The polymer grafted polymeric micro-spheres may overcome the drawback of other porous polymer-based micro-spheres, i.e. their limited mechanical strength. Highly cross-linked non-porous micro-spheres prepared by precipitation polymerization can withstand column backpressures of over 10,000 psi.[6] If such micro-spheres are modified by grafting a dense layer of long polymer chains off their surfaces, the chromatographic separation efficiency would be improved in comparison to porous or swellable microspheres, and the capacity enhanced in comparison to non-grafted, surface functionalized supports. Therefore, the modified particles will have both high mechanical strength and high separation efficiency. In addition, block copolymer grafted micro-spheres with hydrophobic blocks attached near the micro-sphere surface and hydrophilic blocks extended beyond the surface may perform as stationary phase for direct analyses of drugs in serum.

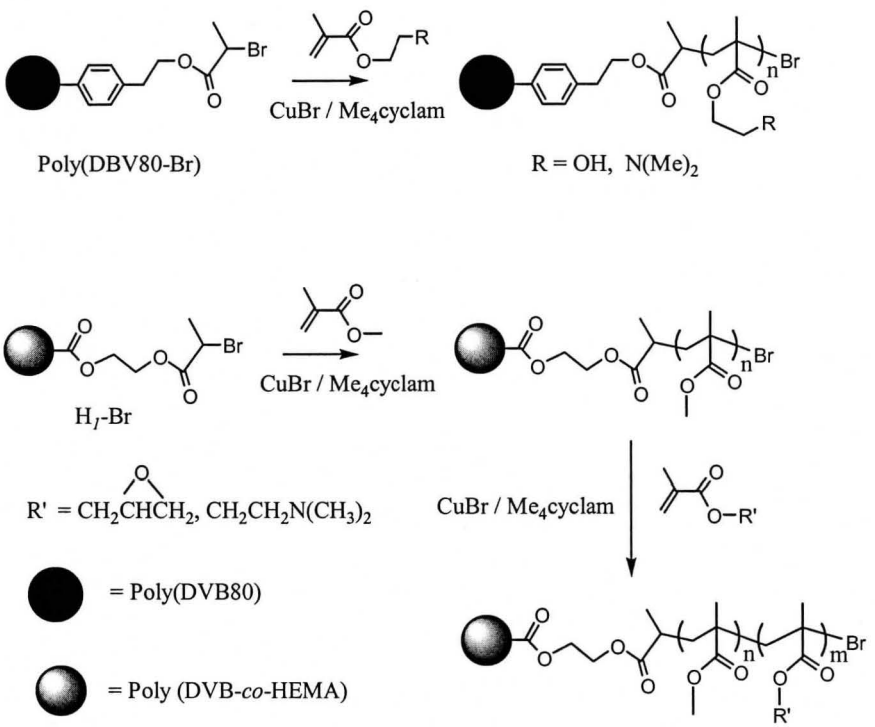
ATRP has been widely used to prepare homo-polymers,[7] block copolymers,[8] highly branched polymers,[9] and dendrimers.[10] Recently, it has been used to modify surfaces including planar surfaces,[11] spherical surfaces,[12] and the internal surface of a

capillary.[13] Most of these experiments benefited from the excellent properties of ATRP including:

1) a living/controlled polymerization
2) its tolerance for water[14] and functional groups[15]
3) polymerization occurring at designed sites

Surface modification by ATRP mainly includes two steps: introducing ATRP initiators onto the surface, and initiating polymerization from these initiator sites in the presence of ATRP catalyst. Haddleton's group[16,17] has successfully demonstrated the surface modification on polymer spheres by ATRP. A series of cross-linked polystyrene-based beads including Wang, Merrifield, and primary amino functional resins were converted into ATRP initiators. Subsequently, poly(methyl methacrylate), poly(benzyl methacrylate), and hydrophilic poly(N,N-dimethylacrylamide) was grafted from those polystyrene-based beads. Patten[18] has reported that 70 nm spherical silica particles were tethered with surface ATRP initiator (2-(4-chloromethylphenyl)ethyl)-dimethylethoxysilane, followed by ATRP of styrene at 130 °C in presence of CuCl/2dNbipy as catalyst. Well-defined polymer-inorganic nano-particle hybrids formed and the size of the particles increased with conversion, consistent with the molecular weight of the grafted polymer. We recently reported the hydrochlorination of highly cross-linked polystyrene micro-spheres made from precipitation polymerization into ATRP initiator particles and grafting polymerization of styrene and 4-methylstyrene from their surface.[19] The micro-spheres with hydroxy groups were also used to prepare ATRP initiator micro-spheres by reaction with α-bromopropionyl bromide.[20] Homo-polymers

and block copolymers were grafted on these initiator micro-spheres. This chapter is a continuation of our efforts at surface modification by ATRP as shown as follow (Scheme 5.1).



Scheme 5.1 Surface modification of micro-spheres by ATRP

5.1 Experimental Section

5.1.1 Chemicals

Solvents were purchased from Aldrich and used as received unless otherwise specified. 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (Me_4cyclam, 98 % Aldrich), 2-bromopropionyl bromide (97 % Aldrich), methyl iodide (99 % Aldrich),

sodium borohydride (98 %, Aldrich), born trifluoride diethyl etherate (Aldrich), DVB80 (70-85 % divinylbenzene isomers, Fluka, Oakville, Canada), and triethylamine (99 % Aldrich) were used as received. Hydroxyethyl methacrylate (HEMA, 97 %), methyl methacrylate (MMA, 99 %), glycidyl methacrylate (97 %), and 2-(dimethylamino)ethyl methacrylate (DMAEMA, 98 %) were purchased from Aldrich Chemical Co. and purified by distillation under vacuum prior to polymerization. THF (99+ %, Aldrich) was refluxed over K-Na alloy and distilled under nitrogen. CuBr was prepared by the reaction of $CuBr_2$ with dimethyl malonate.

5.1.2 Syntheses

Preparation of hydroxy-functional micro-spheres (poly(DVB80)-OH) Micro-spheres poly(DVB80) were prepared by precipitation polymerization using DVB80 in neat acetonitrile as reported previously.[21] Micro-spheres poly(DVB80) (5.00 g) were suspended in dry THF (50 ml) in a dry 100 ml flask for 2 h and 0.5 g (13 mmol) of sodium borohydride was added. The suspension was cooled in a cold-water bath and 1.88 g (13 mmol) boron trifluoride diethyl etherate dissolved in 5 ml THF was added dropwise via a syringe to the suspension. The temperature of the reaction suspension was maintained at 20 °C during the addition of BF_3 and further for 3 h. At the end of this period, the flask was immersed in an ice bath and 5 ml of cold water was added slowly to destroy any residual $NaBH_4$.

Hydrogen peroxide (4 ml 30 % in water, 35 mmol) was slowly added to the reaction mixture. During the addition, the pH of the solution was maintained near 8 by adding 3 M sodium hydroxide as needed. The final solution were filtered through a 0.5

μm membrane filter and washed with water (pH = 8) followed by methanol. The resultant micro-spheres were dried under vacuum at room temperature for 24 h. The yield of the hydroxy micro-spheres was 5.07 g.

Preparation of initiator micro-spheres (poly(DVB80-Br)) Hydroxy micro-spheres, poly(DVB80-OH) (2.00 g) were suspended for 2 h in 20 ml of THF containing 0.4 g (4.0 mmol) of triethylamine in a 50-ml two-necked round-bottomed flask, followed by dropwise addition of 0.8 g (3.7 mmol) 2-bromopropionyl bromide to the suspension, which was cooled with an ice-water bath. The mixture was stirred at room temperature overnight. The initiator particles were filtered and washed with THF and methanol thoroughly. The yield of the resultant particles was 2.04 g after drying at room temperature under vacuum for 24 h.

Conversion of micro-spheres poly(DVB-co-HEMA) (H_1) into initiator micro-spheres (H_1-Br) Precursor micro-spheres (H_1) comprised of DVB80 and HEMA (molar ratio of 17.5/82.5) were prepared by precipitation polymerization reported previously. [22] The precursor micro-spheres H_1 (2.0 g) were dispersed in 20 ml of dry THF for 2 h in a dry flask and 0.95 g (9.39 mmol) of triethylamine was added followed by dropwise addition of 2.0 g (9.26 mmol) 2-bromopropionyl bromide to the mixture. The mixture was stirred at r. t. overnight. The initiator micro-spheres were filtered and washed with THF and methanol thoroughly. The yield of the resultant particles was 3.08 g after drying at room temperature under vacuum for 24 h.

Grafting Poly(HEMA) or Poly(DMAEHA) from micro-spheres poly(DVB80-Br) by ATRP Initiator micro-spheres poly(DVB80-Br) (2.00 g) and HEMA (2.0 g, 20

mmol) were added in 8 ml of THF in a 25 ml flask purged with THF saturated nitrogen for 1hr and then a degassed 5 ml THF solution of CuBr (39 mg, 0.27 mmol) / Me_4cyclam (69 mg, 0.27 mmol) was added via a cannula. The mixture was stirred with a magnetic bar at room temperature under nitrogen for 10 h. The resulting micro-spheres were centrifuged and re-dispersed at least three times in THF and then repeatedly in methanol. The yield of poly(HEMA) grafted micro-spheres was 2.26 g.

When monomer DMAEMA was used to grafting poly(DMAEMA) from the same initiator micro-spheres, all other conditions was kept the same except using 2.0 g of DAMEA instead of HEMA. The yield of poly(DMAEMA) grafted micro-sphere were 2.30 g.

Grafting poly(MMA) from micro-spheres H_1-Br by ATRP Initiator particles (H_1-Br, 1.20 g) and methyl methacrylate (8.0 g, 80 mmol) were added in 32 ml of THF in a 100 ml flask purged with THF saturated nitrogen for 1 hr and then a degassed 4 ml acetonitrile solution of CuBr (103 mg, 0.72 mmol) / Me_4cyclam (184 mg, 0.72 mmol) was added via a cannula. The mixture was stirred with a magnetic bar at room temperature under nitrogen for 15 h. The resulting blue particles were centrifuged and re-dispersed at least three times in THF and then repeatedly in methanol until the particles became almost white. The yield of Poly(MMA) grafted particles was 4.80 g.

Other ratios (1:3 and 1:1) of initiator micro-spheres to MMA were used to prepare micro-spheres with different grafted poly(MMA) loading, under the same conditions. The yield of there two other grafted micro-spheres were 3.72 g and 2.88 g respectively. These three different grafted micro-spheres have poly(MMA) loading 0.75,

0.68, and 0.58 g/g micro-spheres respectively.

Grafting Second Block poly(DMAEMA) from micro-spheres H_1-g-polyMMA-Br by ATRP The micro-spheres *H_1-g-polyMMA-Br* (0.50 g, poly(MMA) loading 0.75 g/g micro-spheres) were suspended in 5ml of THF containing 2.0 g of DMAEMA and purged by passing THF-saturated nitrogen for 30 min. Pre-degassed CH_3CN solution (2 ml) containing CuBr (35 mg, 244 μmol) / Me_4cyclam (62.6 mg, 244 μmol) was added to the suspension through a cannula. The mixture was stirred with a magnetic stir bar at room temperature under nitrogen and the reaction took place for 10 h. The resulting particles were centrifuged and re-dispersed with THF at least three times and with NH_4OH/methanol (1/20 by volume) many times until the particles became almost white. The particles were finally washed with ether and dried at room temperature under vacuum for 24 h. The yield of resultant micro-spheres was 2.06 g.

Other two poly(MMA) grafted micro-spheres with poly(MMA) loadings of 0.68 and 0.58 g/g micro-spheres, produced 2.10 and 2.14 g of poly(MMA-*b*-DEMEMA) grafted micro-spheres respectively, at the same reaction condition.

Grafting poly(GMA) from micro-spheres H_1-g-polyMMA-Br by ATRP The micro-spheres *H_1-g-polyMMA-Br* (0.50 g, poly(MMA) loading 0.68 g/g micro-spheres) were suspended in 5ml of THF containing 2.0 g of GMA and purged by passing THF-saturated nitrogen for 30 min. Pre-degassed CH_3CN solution (2 ml) containing CuBr (35 mg, 244 μmol) / Me_4cyclam (62.6 mg, 244 μmol) was added to the suspension through a cannula. The mixture was stirred with a magnetic stir bar at room temperature under nitrogen and the reaction took place for 10 h. The resulting particles were centrifuged

and re-dispersed with THF at least three times. 2.40 g of the resultant micro-spheres, H_1-*g*-poly(MMA-*b*-GMA) was obtained.

Conversion of poly(MMA-b-DEMEMA) grafted micro-spheres into poly(MMA-b-TEMEMA) grafted micro-spheres Poly(MMA-b-DEMEMA) grafted micro-spheres (1.0 g) made from H_1-g-polyMMA-Br with poly(MMA) loading of 0.75 g/g micro-spheres were suspended in acetonitrile (10 ml) and 1.0 g of iodomethane was added to the mixture. The mixture was stirred at room temperature for 15 h. The resulting micro-spheres were centrifuged and re-dispersed with acetonitrile at least three times. The yield of the micro-spheres was 1.52 g.

Particle Size Analysis The particle sizes and size distributions were measured using a 256-channel Coulter multisizer interfaced with a computer. A 30 μm-aperture tube was chosen to accommodate the particles size range of 1-10 μm. A small amount of particles, dispersed in acetone or in water, was added to 25 ml of Coulter Isoton II electrolyte solution and stirred for 1 min with a mini-stirrer attached to the instrument. The Coulter multi-sizer measurements were confirmed using a Philips ElectroScan 2020 environmental scanning electron microscope (ESEM). The samples for ESEM measurement were prepared by dispersing the particles in THF and casting a drop of the particle suspension on a pieces of glass stuck on a microscopy stub. The samples were dried under vacuum for 2 h and sputter coated with 5 nm gold.

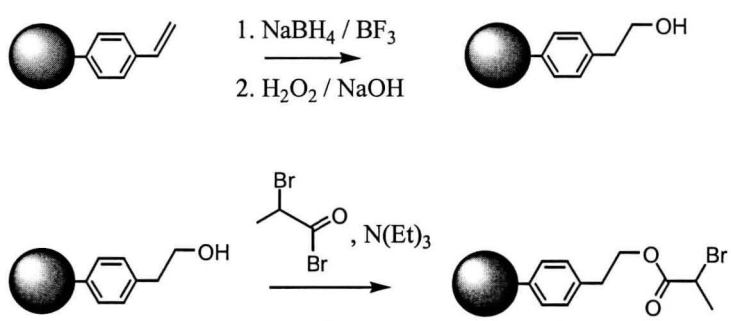
TEM analysis The internal structure of the grafted particles was studied using a JEOL 1200EX transmission electron microscope. Here, the samples were embedded in Spurr's epoxy resin and microtomed to generate 40-60 nm thick slices.

FT-IR Analysis Fourier transform infrared analysis was performed on a Bio-Rad FTS-40 FT-IR spectrometer. All samples were prepared as pellets using spectroscopic grade KBr in a Carver press at 15,000 psi. The spectra were scanned over the range 4000 - 400 cm^{-1}, in the transmission mode.

5.2 Results and Discussion

5.2.1 Preparation of Initiator Micro-spheres PDVB80-Br

Highly cross-linked polystyrene micros-spheres made from the precipitation polymerization contain a considerable amount of residual vinyl groups.[23] Hydroboration/oxidation was used to transform these vinyl groups into hydroxyl groups at β position of ethylbenzene, followed by the esterification with bromopropionyl bromide to produce ATRP initiators (Scheme 5.2).



Scheme 5.2 The formation of initiator micro-spheres from highly cross-linked polystyrene

In the first two reactions, hydroxy groups were introduced into the surfaces of polystyrene micro-spheres and the resulting micro-spheres were much polar than the

starting micro-spheres. These micro-spheres could suspend in water but some micro-spheres were still aggregated in water. On the contrary, the starting micro-spheres did not suspend in water at all, but rather floated on water. This result indicated the hydroxy groups were introduced on the microspheres but their density on the surface of micro-spheres may not be very high.

Earlier, we reported that hydrochlorination of similar poly(DVB80) microspheres may penetrate about 100 nm into the particle. The hydroxy groups in the present micro-spheres should have similar functional group depth profile as the earlier, hydrochlorinated micro-spheres, since both modifications are based on residual vinyl groups on the micro-spheres. In hydration modification, the reactants are $(BH_3)_2$ formed by *in situ* reaction of $NaBH_4$ and BF_3 in the first modification and H_2O_2 in the second modification respectively. These molecules are a little larger than HCl and hence may penetrate less into the the micro-spheres. The hydroxy loading in the modified micro-spheres may therefore be less than the 0.9 mmol/g found for hydrochlorination (see Chapter 2). The sizes of micro-spheres before and after the hydration were measured and found not to show any change, similar to the case of the hydrochlorinated micro-spheres. After incorporating the ATRP initiators, the surface properties changed back to hydrophobic, and the micro-spheres were not suspendable in water any more. The hydration and formation of initiators on the micro-spheres were monitored by FT-IR (Figure 5.1). When hydration on the micro-spheres took place, the characteristic hydroxy peak at 3454 cm^{-1} got larger than that of the starting micro-spheres. Meanwhile, the intensity of the peaks at 992 cm^{-1} corresponding to the vinyl group completely

disappeared. The hydroxy peak at 2454 cm^{-1} found in the starting micro-spheres may be

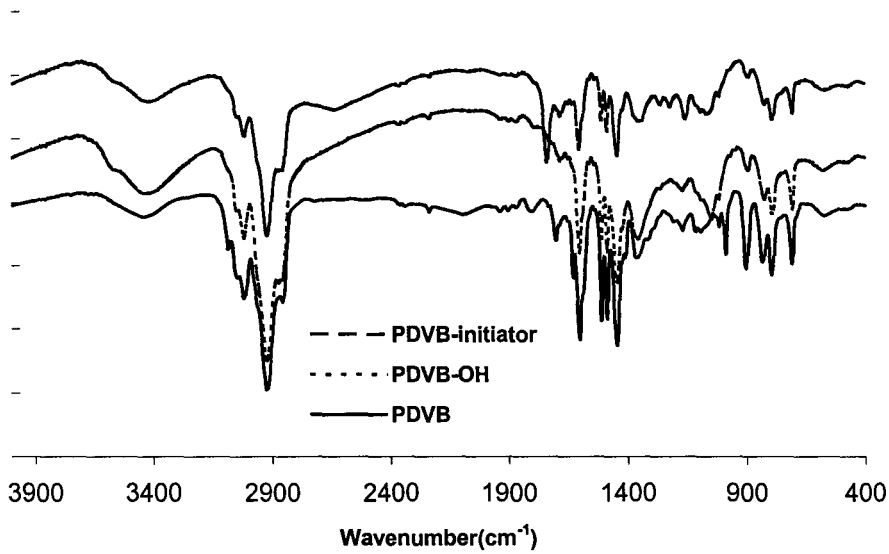


Figure 5.1 FT-IR spectra of poly(DVB80), poly(DVB80-OH) and initiator poly(DVB80-Br)

attributed to the oxidation of some vinyl groups during the formation of the micro-spheres. Water was carefully kept away from the starting micro-spheres by using dried solvents for preparation and purification and the micro-spheres were dried under vacuum for 24 h. The oxidation of the vinyl group was not caused by storage since a fresh sample also showed the hydroxy peak. After the esterification to introduce the initiator functionality, the characteristic carbonyl stretching at 1725 cm^{-1} appeared in the initiator micro-spheres and the hydroxy peak at 3454 cm^{-1} decreased back to about the same intensity as in the starting micro-spheres. The results indicated the formation of the ester groups and the disappearance of the (accessible) hydoxy groups. In the spectrum of the

initiator micro-spheres, another characteristic peak at 1373 cm^{-1} is assigned to the stretching of methyl group at α-position of bromine.

5.2.2 Grafted poly(HEMA) and poly(DMAEMA) on the micro-spheres poly(DVB80)

The grafting polymerization of HEMA from the initiator micro-spheres was catalyzed by Cu(I)Br/Me_4Cyclam at room temperature. Although the livingness of solution polymerization catalyzed by this catalyst system was not very good, as indicated by poor control over molecular weight distribution,[24] grafting polyMMA from micro-spheres H_I-Br using the same catalyst system showed the ability to prepare block copolymer (see below). That result indicated that a significant portion of propagating sites was still active. In the current grafting polymerization of HEMA, the polymerization was carried out for 10 h and the size of the micro-spheres increased from 3.04 to 3.14 μm as measured using the Coulter multisizer.

Figure 5.2 shows the size and size distribution of micro-spheres before and after grafting with poly(HEMA). The sizes of the starting and initiator micro-spheres show no notable difference. The grafted micro-spheres demonstrated that not only the size increased but also that the size distribution increased. However, the appearance of a broader size distribution is attributed to the micro-spheres aggregating in the aqueous phase used for the Coulter multisizer measurements. The two small peaks at the right side of the large peak are doublets and triplets, which is confirmed by calculation of the volume based on the diameters of these two small peaks.

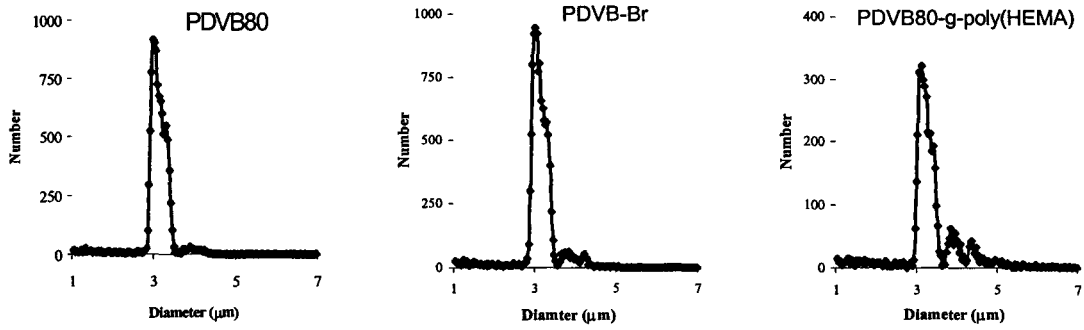


Figure 5.2 The size and size distribution of micro-spheres before and after grafting with poly(HEMA)

The surface properties of grafted micro-spheres were changed from those of the initiator micro-spheres, and the micro-spheres were now wetable by water. Surprisingly, the micro-spheres strongly aggregated in water and only dispersed well in acidic aqueous media. We believe that the grafted poly(HEMA) chains on the micro-spheres were closely arranged and there is strong hydrogen bonding in and between the micro-spheres. In acidic aqueous solution, these hydrogen bonds were interrupted and the micro-spheres could be dispersed due to the better salvation of the grafted polymer chains.

Grafting of poly(DMAEMA) from the same initiator micro-spheres was carried out in a similar fashion. The grafted micro-spheres were easily dispersable in water. The amount of grafted poly(DMAEMA) was measured by acid-base titration. An amine loading on the micro-spheres of 0.81 mmol/g was found, which is consistent with the weight increase of 15 %.

The micro-spheres grafted with poly(HEMA) and poly(DMAEMA) were characterized by FT-IR and the spectra of the two grafted micro-spheres are shown in Figure 5.3.

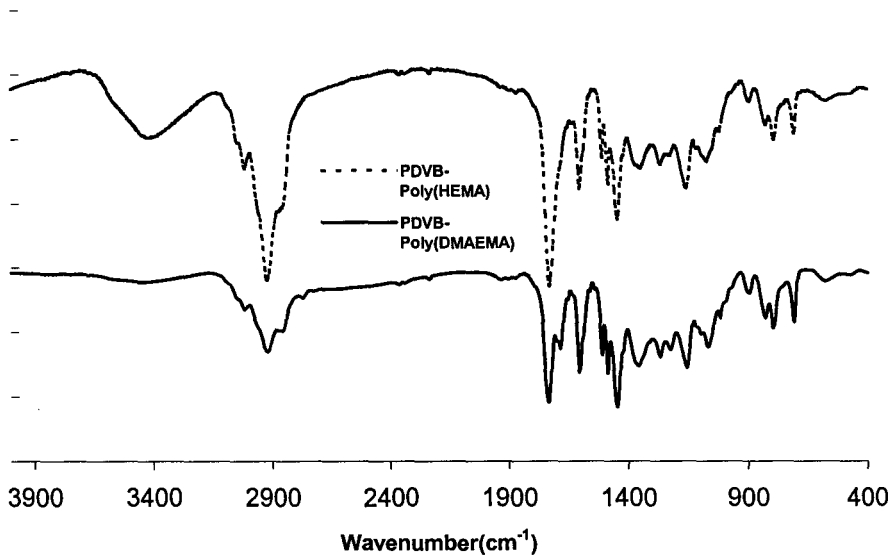


Figure 5.3 FT-IR spectra of micro-spheres grafted with poly(HEMA) and poly(DMAEMA)

The micro-spheres grafted with poly(HEMA) show two signals at 3442 and 1732 cm^{-1}, corresponding to hydroxy and ester groups respectively. These two signals are increased significantly over the non-grafted precursor. In contrast, grafting the micro-spheres with poly(DMAEMA) leads to a stronger band at 1740 cm^{-1}, and a weaker peak at 3400 cm^{-1}. These results confirmed the micro-spheres have been modified with the two hydrophilic polymers.

5.2.3 Grafted block copolymer poly(MMA-*b*-DMAEMA) on the micro-spheres poly(DBV80-*co*-HEMA)

The study of block copolymers in solution and matrix has shown many different forms and morphologies.[25] However, little work on block copolymer under confined condition such as grafted off surfaces, has been reported.[26] One of the most significant feature of living radical polymerization is its ability to produce block copolymer. The initiator micro-spheres, H_I-Br were previously used to prepare micro-spheres grafted with block copolymer of poly (MMA-*co*-DMAEMA). Here, the study of grafting block copolymers with different block lengths from the initiator micro-spheres should give very interesting information about the behavior of block copolymers under confined condition. The length of the polymer block could be controlled through different polymerization times and different monomer loadings. Under the same reaction conditions, the polymerization time and monomer loading has shown a linear relationship with the weight (micro-sphere volume) increase of grafted polymer, providing the opportunity to prepare first block polymer of controlled length (see Chapter 3).

The micro-spheres, H_IBr were grafted with poly(MMA) by ATRP at monomer loadings (monomer/initiator micro-sphere weight ratios) of 1.0, 3.0, and 6.7 to produce new initiator micro-spheres H_I-*g*-poly(MMA)-Br. The new initiator micro-spheres with weight ratios of grafted poly(MMA) to the micro-spheres of 1.4; 2.1; and 3.0 (namely poly(MMA) loading 0.58, 0.68, and 0.75 g/g micro-spheres) were obtained. According to the mechanism of ARTP, these polymer-grafted micro-spheres should have a 2-bromoisobutyrate group at end of each living polymer chain, which can be used for the

second polymerization. The second polymerization of N, N-dimethylaminoethyl methacrylate from the poly(MMA) grafted micro-spheres in the presence of CuBr/Me_4Cyclam generated the second block poly(DMAEMA). Three types of micro-spheres comprised of different weight ratios of core to first block poly(MMA) to second block poly(DMAEMA) were prepared. These ratios for the three type of micro-spheres were 1.0 : 1.4 : 7.7; 1.0 : 2.1 : 10.2; and 1.0 : 3.0 : 12.5 respectively. Although the catalyst of CuBr/Me_4Cyclam used in the grafting polymerization has shown a poor control in solution polymerization, it has demonstrated better control in the preparation of block copolymer.[27] This result implies that slow diffusion of radicals on propagating species such as on a preformed polymer or in confined state, may reduce the radical combination rate and could produce well-defined polymers and block copolymers. The heterogeneous polymerization of grafting polymer from the micro-spheres should have a better control indicated by the observed linear weight increase with the polymerization time, and the ability to generate block copolymer. Therefore, the weight ratios in each type of micro-sphere may reflect the length ratios of the two blocks.

Each of the block copolymer grafted micro-spheres has a significant size increase from the starting micro-spheres, and there are difference in diameter and morphology between these three micro-spheres (Figure 5.4). Interestingly, the micro-spheres with different lengths of block copolymer show significantly different morphologies. The micro-spheres (Figure 5.4a and b) without and with the shortest first block poly(MMA) is spherical. With the length of first block polymer increasing, some of the micro-spheres changed their shape from spherical to doughnut shaped. The

population of the microspheres with this changed morphology increased with the length of the first block, as shown in Figure 5.4d relative to Figure 5.4c.

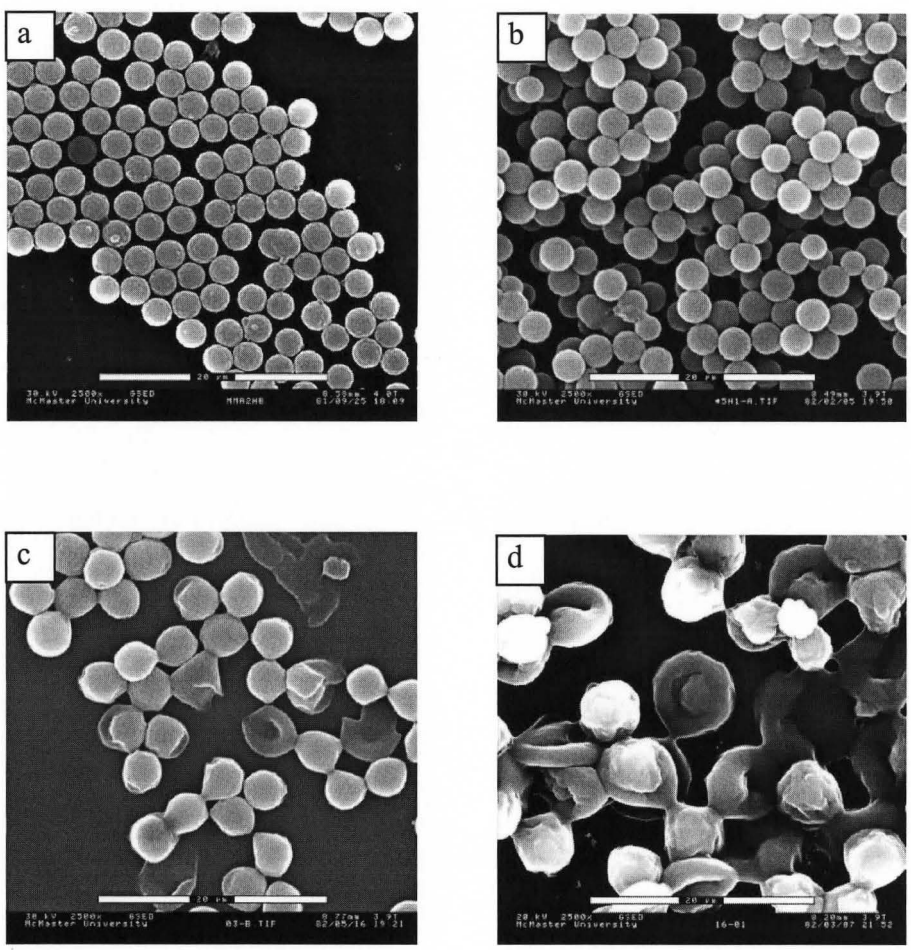
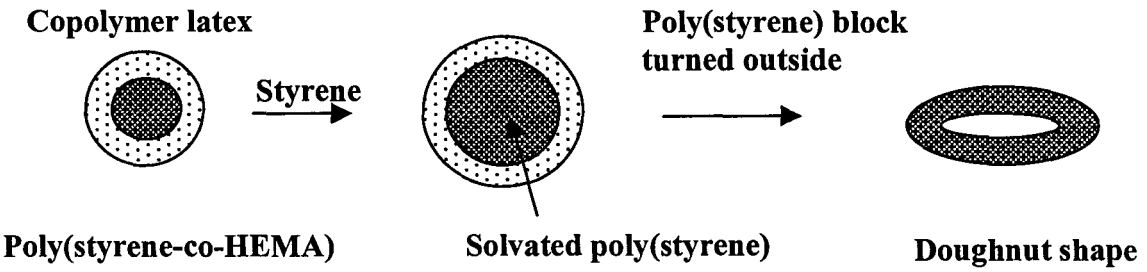


Figure 5.4 ESEM images of grafted micro-spheres with different length of polymer blocks The weight ratio of first bock poly(MMA) to the second block of poly(DMAEMA): a. 1 : 0; b. 1.4 : 7.7; c. 2.1 : 10.2; d. 3.0 : 12.5

A tentative explanation for this phenomenon is that the block copolymer with one hydrophobic poly(MMA) block and one hydrophilic, block poly(DMAEMA) underwent

phase separation, and that the two phases reversed between external layer and internal layer. Chen[28] has reported that amphiphilic poly(St-*co*-HEMA)) formed latex and changed morphology upon the addition of styrene or toluene as shown in Scheme 5.3.

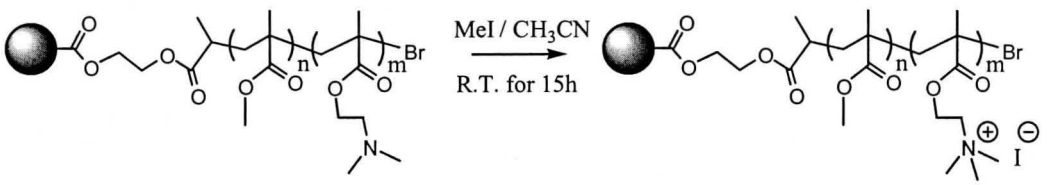


Scheme 5.3 The morphologies of amphiphilic block copolymer latex in different solvents

Initially, the hydrophilic poly(HEMA) faces outside and the hydrophobic polystyrene stays inside the latex. When a non-polar solvent such as styrene or toluene is added in the form of vapor, the polystyrene core swells until finally the morphology changes when the solvency of the environment becomes favorable to polystyrene. The block copolymer grafted micro-spheres may behave similarly in a environment with variable solvency, except for the restriction the that the crosslinked core places on their rearrangement. Therefore, when the micro-spheres were suspended in THF to prepare samples for ESEM imaging, the poly(MMA) block likely moved the outside to form the donut-like shape, held together by the central cores. The longer the first block of poly(MMA) is, the easier the change of morphology is.

5.2.4 Grafted block copolymer poly(MMA-*b*-TMAEMA) on the micro-spheres poly(DBV80-*co*-HEMA)

The block copolymer, poly(MMA-*b*-DMAEMA) grafted micro-spheres were further modified to form a ionic block copolymer, poly(MMA-*b*-TMAEMA) by methylation with methyl iodide (Scheme 5.4).



poly(MMA-*b*-DMAEMA) poly(MMA-*b*-TMAEMA)

Scheme 5.4 The methylation of tertiary amine into quaternary amine in the block copolymer grafted micro-spheres

The methylation of the micro-spheres lead to charged micro-spheres that are much more polar and even easier to disperse in water. The degree of methylation was measured by titrating the remaining tertiary amine, and found to be quantitative. Acid-base titration has shown no remaining amine on the micro-spheres. This result confirmed that the tertiary amines of poly(DMAEMA) on the micro-spheres are easily accessible. Both of the micro-spheres having poly(DMAEMA) and poly(TMAEMA) are poly-electrolytes. The tertiary amines in poly(DMAEMA) are strong bases, which can be protonated by water based on the equation: $H_2O + \text{-}NMe_2 = \text{-}NHMe_2^+ + OH^-$ to form charges on the polymer chains. An interesting experiment of size measurement by Coulter multisizer has shown that the sizes of the micro-spheres grafted with poly(MMA-

b-DMAEMA) and poly(MMA-*b*-TMAEMA) were much smaller than expected. According to the principle of the Coulter multisizer, the size of polymer micro-spheres is measured by determining the electric resistance between two electrodes placed at each side of an aperture. The size (volume) of a micro-sphere correlates to the increase of electric resistance due to the volume of electrolyte solution that is replaced by a micro-sphere passing through the aperture. If micro-spheres are ionic conductors, the increase of the electric resistance by micro-sphere passage will be smaller than that of normal micro-spheres. For micro-spheres modified with polyelectrolyte, the apparent size of the micro-sphere may be smaller than that of the micro-spheres without modification. Figure 5.5 shows the size and size distribution of micro-spheres with and without the polyelectrolyte modification.

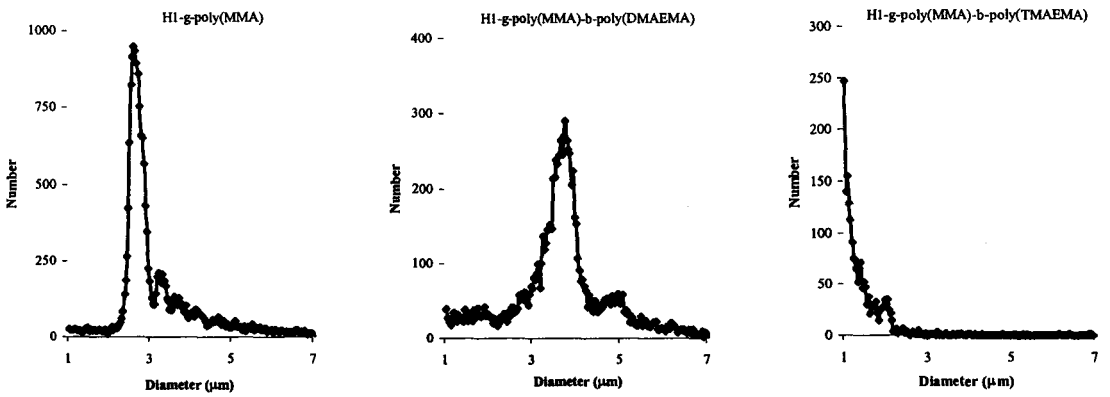


Figure 5.5 The size and size distribution of the micro-spheres grafted with and without electrolyte

The microsphere sizes as measured by the Coulter Multisizer in Figure 5.5 are 2.69, 3.80 and <1.0 μm, for H_1-*g*-poly(MMA), H_1-*g*-poly(MMA)-*b*-poly(DMAEMA),

and H_1-*g*-poly(MMA)-*b*-poly(TMAEMA), respectively. In fact, H_1-*g*-poly(MMA)-*b*-poly(DMAEMA) and H_1-*g*-poly(MMA)-*b*-poly(TMAEMA) should be much larger than H_1-*g*-poly(MMA) since a large amount of second block polymer has been added.

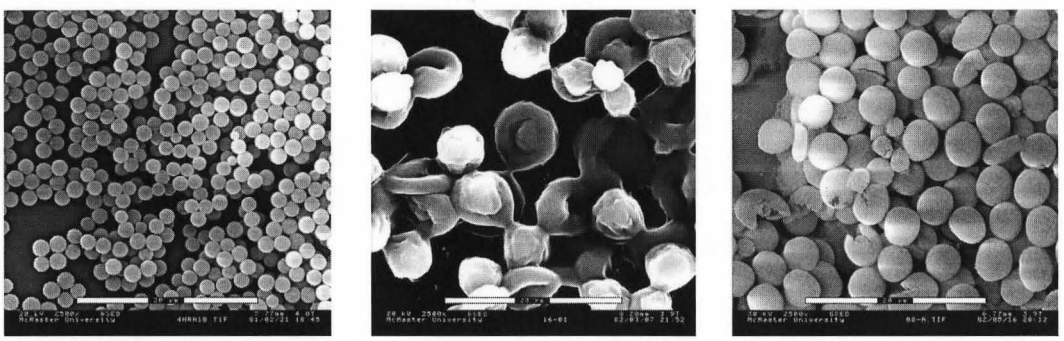


Figure 5.6 ESEM images of the polymer grafted micro-spheres

From ESEM images (Figure 5.6), the order of these micro-spheres should be H_1-*g*-poly(MMA)-*b*-poly(TMAEMA) ≅ H_1-*g*-poly(MMA)-*b*-poly(DMAEMA) >> H_1-*g*-poly(MMA). These results indicated the polyelectrolyte effect on the size measurement scales in the order of H_1-*g*-poly(MMA)-*b*-poly(TMAEMA) > H_1-*g*-poly(MMA)-*b*-poly(DMAEMA) > H_1-*g*-poly(MMA), in accordance with their charge densities. The morphologies of these micro-spheres show significant differences as well. H_1-*g*-poly(MMA) micro-spheres were spherical as expected. The H_1-*g*-poly(MMA)-*b*-poly(DMAEMA) micro-spheres showed morphologies effected by phase separation of the block copolymer as mentioned above. The micro-spheres H_1-*g*-poly(MMA)-*b*-poly(TMAEMA) were found to have broken shells and oval shapes. Some small micro-spheres, about 1.2-1.4 μm in diameter as measured in the image, in the center of the image are likely original cores separated from their shells. This may be caused by the

charge repulsion of the poly(TMAEMA). The micro-spheres of H_1-*g*-poly(MMA)-*b*-poly(TMAEMA) also showed damaged morphologies when the electron beam was focused for a few minutes on the sample during the imaging, as shown in Figure 5.7. The micro-spheres expanded and finally broke. This morphology may be caused by both charge repulsion and the depolymerization of either the poly(TMAEMA) or poly(MMA) via electron beams passing through the surface layer. The depolymerization of poly(MMA) under the electron beam[29] would produce methyl methacrylate that could vapourize under the localized heating, and both plasticize and expand the outer shell.

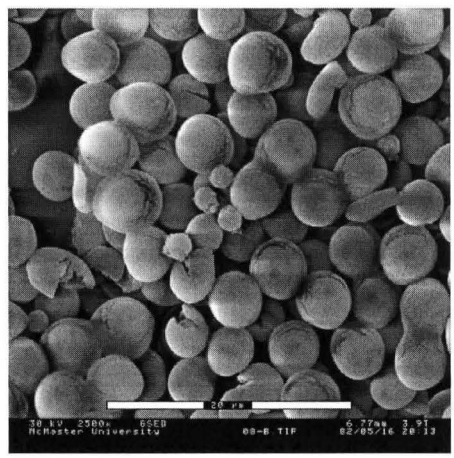


Figure 5.7 The damaged micro-spheres of H_1-*g*-poly(MMA)-*b*-poly(TMAEMA)

5.2.5 Grafted block copolymer poly(MMA-*b*-GMA) on the micro-spheres poly(DBV80-*co*-HEMA)

Poly(glycidyl methacrylate), poly(GMA) as a second block polymer was grafted from the micro-spheres grafted with a first block of poly(MMA), using a similar procedure as described above. The grafting polymerization of GMA was found to be

very effective and the conversion of monomer was much higher than that of other monomers. The initiator micro-spheres, H_I-*g*-poly(MMA)-Br (0.5 g, poly(MMA) loading 0.68 g/g micro-spheres) were reacted with 2.0 g of GMA in presence of CuBr/Me_4Cyclam for 15 h at room temperature, resulting in 2.4 g of the grafted micro-spheres, H_I-*g*-poly(MMA-*b*-GMA). Figure 5.8 shows the ESEM images of H_I-*g*-poly(MMA)-Br and the poly(MMA-*b*-GMA) grafted micro-spheres. The block copolymer, poly(MMA-*b*-GMA) grafted micro-spheres showed large size and relatively smooth surfaces (Figure 5.8b). Several micro-spheres in the center of the image showed shrunken surfaces which demonstrated the decomposition of first block poly(MMA) inside the micro-sphere due to electron beam damage. The micro-spheres in the center area were irradiated at high magnification for two minutes. The results indicated that the

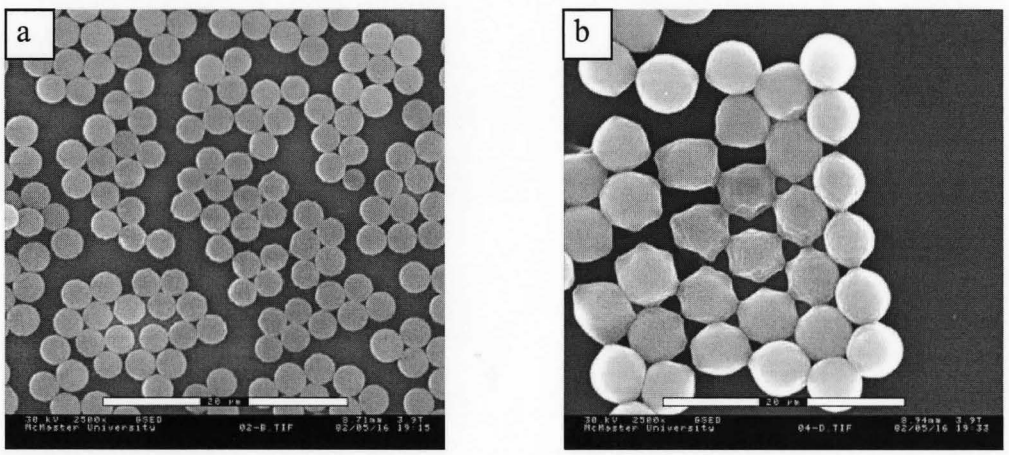


Figure 5.8 The ESEM images of the H_I-*g*-poly(MMA)-Br (a) and H_I-*g*-poly(MMA)-*b*-poly(GMA) micro-spheres (b) The scale bar is 20 μm

surfaces of these micro-spheres is stronger than that of poly(MMA)-b-poly(TMAEMA) grafted micro-spheres described above.

The resultant micro-spheres were reacted with butylamine without catalyst at room temperature for 20 h to determine the reactivity of glycidyl groups on the micro-spheres. Some reaction did occur, but no weight gain was observed after recovery. In a parallel experiment, the microspheres were reacted with 10 % sulfuric acid under the same conditions, a 7.0 % weight gain was observed, corresponding to a 70 % hydrolysis of the glycidyl groups. Investigation into this limited reactivity of the grafted poly(GMA) will be done in future.

The internal structure of the grafted micro-spheres was studied by TEM (Figure 5.9). The small dark cores represent the poly(DVB-*co*-HEMA) starting micro-spheres,

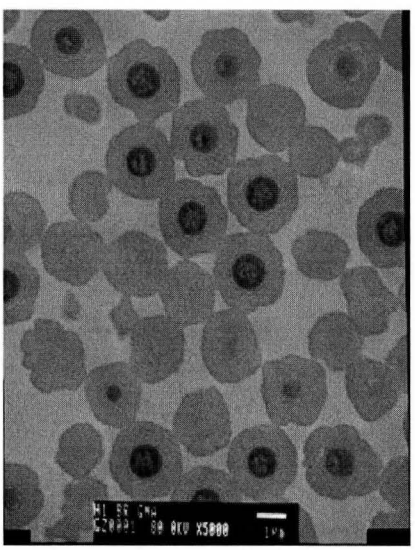


Figure 5.9 TEM image of the section of poly(MMA-*b*-GMA) grafted micro-spheres. The scale bar is 1.0 μm

and the larger outer rings are block copolymer poly(MMA-*b*-GMA). These large rings were apparently swollen by the Spurr's epoxy resin used for embedding. The surface of the micro-spheres (outer perimeter of the large ring) appears denser than the interior of the large ring. This may be a reason why the glycidyl groups in the micro-spheres are not very reactive. This question is being pursued using Scanning Transmission X-ray Microspectroscopy (STXM).

5.3 Conclusion

Grafting polymer and block copolymer by ATRP from polymeric micro-spheres has successfully demonstrated the surface modification. Residual vinyl groups on hard poly(DVB80) micro-spheres have been converted into ATRP initiators by hydroboration/oxidation reaction followed by esterification. The surface modification on the hard poly(DVB80) micro-spheres by grafting poly(HEMA) and poly(DMAEMA) via ATRP has generated hydrophilic micro-spheres, which may be useful as chromatographic stationary phases. Swellable lightly cross-linked poly(DVB-*co*-HEMA) micro-spheres were modified with various block copolymers, poly(MMA-*b*-DMAEMA) with different length of the first poly(MMA) block, poly(MMA-*b*-TMAEMA), and poly(MMA-*b*-GMA). The phase separation of the amphiphilic block copolymer occurring on the micro-spheres was studied using scanning electron microscopy.

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(23) The bromination test by the addition of bromine to micro-spheres suspension in THF showed the considerable amount of bromine consumed. Nevertheless, the amount of surface vinyl groups could not to determines since bromine was continuously consumed by diffusion in the micro-spheres. A control test showed the micro-spheres made from suspension polymerization has much less residual vinyl groups.

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Chapter 6 Summary and Future Work in the Surface Modification of the Polymeric Micro-spheres

Precipitation polymerization is an excellent method for preparing polymeric micro-spheres. This method has several advantages over other preparation methods, namely, 1) the ability to generate narrow or mono dispersed micro-spheres in one step; 2) the micro-spheres have clean surfaces without any surfactant or stabilizer; 3) a wide range of monomers from water soluble to non-polar may be utilized; and 4) a large amount of residual vinyl groups is available for modification at or near the particle surface. In addition, micro-spheres may be prepared with a variety of properties, such as cross-linking degree (from 5 to 100%), or size (0.1 to 10 μm diameter). Both homo and copolymer compositions can be prepared by precipitation polymerization and this leads to a wide range of potential applications.

In this thesis, the grafting modification of micro-spheres made from precipitation polymerization was explored with the goal of extending and improving the application of the micro-spheres. The resulting contributions and the outcome of the efforts are summarized as follows:

1. The hard polymeric micro-spheres of polyDVB80 have been converted to ATRP initiator micro-spheres with benzyl chloride surface groups and subsequently poly(styrene) or poly(styrene-*co*-4-methylstyrene) were grafted from the micro-spheres using ATRP. The resultant micro-spheres with polymer grafts could be used for reversed

phase-HPLC. The same starting micro-spheres have been grafted with poly(HEMA) or poly(DMAEMA), and might be used for normal phase-HPLC.

2. The swellable micro-spheres of poly(DVB-*co*-HEMA) have been grafted with a variety of polymers or block copolymers including poly(MA), poly(MMA), poly(HEMA), poly(DMAEMA), poly(GMA), poly(MMA-*b*-HEMA), poly(MMA-*b*-DMAEMA), and poly(MMA-*b*-TMAEMA) using ATRP. The resultant micro-spheres with functional polymer demonstrated high accessibility and functionality and could be used as polymer support reagents. The combination of ROP and ATRP was also successfully applied for grafting polymer or copolymer from the swellable micro-spheres.

3. This thesis work has demonstrated practical ways to produce hard polymeric micro-spheres modified with surface polymer grafts, and soft polymeric micro-spheres modified with both surface and interior polymer grafts. Highly dense polymer and block copolymer modified microsphere surfaces and interiors have been prepared and the phase separation of block copolymer on the micro-spheres has been observed.

A number of aspects of this research could be further developed in the future, both from a fundamental and a practical perspective:

1. Fundamental studies:

a) The choice of proper catalyst system In surface grafting using ATRP, a high degree of livingness is important for precisely controlling the length of the grafted polymer and block copolymers. The degree of livingness is very much dependant on the catalyst system. In our work, at least some grafted block copolymers were successfully prepared using the very active catalyst system of CuBr/Me_4Cyclam, even though this

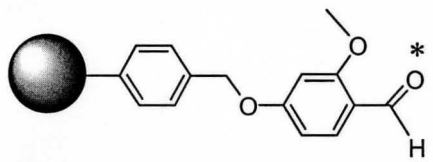
catalyst system showed a poor control in solution polymerization. Some other catalyst systems showed very good control in solution polymerization but may not be able to produce block copolymer on solid surfaces. For example, Haddleton[1] reported that a catalyst system comprised of CuBr/N-(*n*-propyl)-2-pyridylmethanimine, which gave good control in solution polymerization of MMA, was used for surface modification of Wang resin. However, attempts to prepare true block copolymers via a two-stage process involving isolation of the resin with the first block and subsequent reuse to attach the second block were not satisfactory.

This discrepancy is likely related to the different mobilities of propagating sites in grafting environments, as compared to solutions. Therefore, the specific requirements for catalysts used for grafting ATRP, as opposed to solution ATRP, have to be evaluated, and proper catalyst systems able to graft well-defined block copolymer from surfaces need to be found.

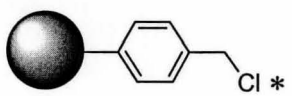
b) *The use of a cleavable linker for attaching initiator on the micro-spheres* In our work, the grafted polymers were covalently bound on the micro-spheres, such that it is not possible to selectively cleave the grafted polymer to determine its molecular weight. In order to determine the molecular weight and molecular weight index of grafted polymer, a cleavable linker for the attached initiators must be used.

Polymer grafted off solid surfaces via a cleavable linker has already been reported. Silica micro-spheres were surface-modified using ATRP initiator attached to the surface via labile Si-O bond. The grafted polymers were subsequently cleaved using fluoride ions.[2] Wang resin with benzyl alcohol groups was used by Haddleton for

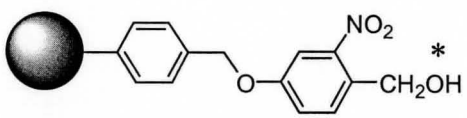
preparing ATRP initiator linked by a cleavable ester.[1] Many other cleavable linkers have been widely used in solid phase synthesis. Some of these linkers are illustrated below (Scheme 6.1). The first three of these are easily accessible through copolymerization of chloromethylstyrene in the precipitation polymerization.



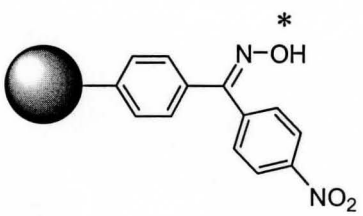
Attaching point: *
Attachment: Amines
Cleavage reagent: TFA



Attaching point: *
Attachment: Carboxylic acids, Alcohols, Amines
Cleavage reagent: HF, $SnCl_4$, MeONa, H_2/PdTFA



Attaching point: *
Attachment: Acids
Cleavage reagent: *hv* (photolabile)

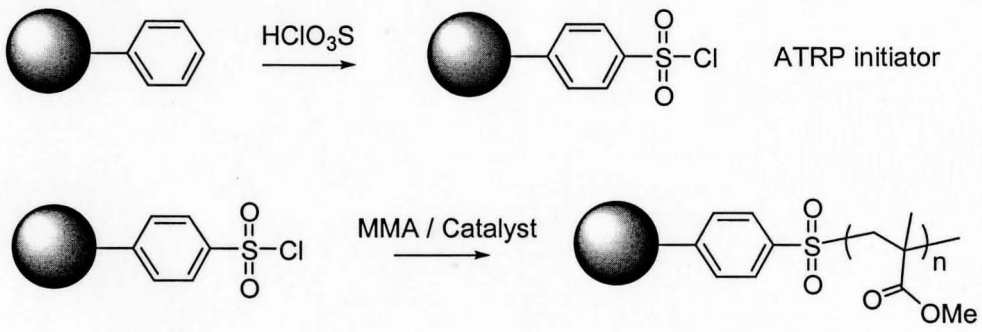


Attaching point: *
Attachment: Acids
Cleavage reagent: 25% TFA, hydrazine, and Amine

Scheme 6.1 The structure of cleavable linker for attaching ATRP initiator

c) *The use of a robust linker for attaching initiator on the micro-spheres* For certain applications such as HPLC stationary phase and polymer support scavenger, the

grafted polymer should be permanently linked. A linker such as an ester group may not be strong enough to resist hydrolysis in some conditions. In our work, some polymer such as poly(styrene) was linked through stable carbon-carbon bonds. The poly(meth(acrylate)) was linked with an ester, which is not a selectively cleavable group but may be hydrolyzed in use under certain condition. The common initiators for ATRP of (meth)acrylate, 2-bromopropionate and 2-bromoisobutyrate, contain potentially labile ester groups. The poly(meth(acrylate)) could be functionalized with various substituents to serve as HPLC stationary phases and as polymer support scavenger To graft poly(meth)acrylates)) off micro-spheres using a robust link, other initiators must be used. The benzenesulfonyl chloride should be a good choice since it is a good initiator for polymerization of (meth)acrylate, and moreover the resulting benzenesulfone link is much more stable than ester groups. This grafting chemistry is illustrated in Scheme 6.2.

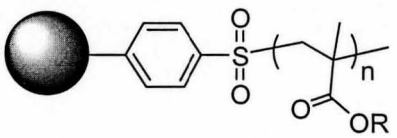


Scheme 6.2 Grafting poly(MMA) from a robust linker

2) Practical studies:

a) *The test of chromatographic separation efficiency of polymer grafted stationary phases.* In our current work, the hard poly(DVB80) micro-spheres have been modified with poly(styrene), poly(HEMA), and poly(DMAEMA) to give materials with potential uses as reversed and normal phase HPLC resins. These three materials should be packed into columns and tested for the separation of organic and bioorganic compounds.

b) *The introduction of other functional groups for preparing polymer support scavengers.* The formation of poly(DVB-*co*-HEMA) micro-spheres grafted with very high poly(DMAEMA) loading was demonstrated. These materials can be used as acid scavengers. In future work, other functional monomers can be used to modify micro-spheres to prepare other reagents such as base scavenger, nucleophile, electrophile, and catalyst. Some possible monomer are list as below:



1. R = $CH_2CH_2\overset{+}{N}(Me)_3\,X^-$ X = Br^-, Cl^-, CN^-, HCO_3^-, Br_3^-
2. R = CH_2CH_2NCO, CH_2CH_2NCS
3. R = $CH_2CH_2N{=}C{=}N$–⬡
4. R = CH_2CH_2–N⬡NH

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