

Synthesis of silica-polymer hybrid particles via controlled radical polymerization in aqueous dispersed media

Xiaoguang Qiao

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SYNTHESIS OF SILICA-POLYMER HYBRID PARTICLES VIA CONTROLLED RADICAL POLYMERIZATION IN AQUEOUS DISPERSED MEDIA

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Abstract

Water-soluble brush-type polymers composed of poly(ethylene)oxide methacrylate (PEOMA) units with PEO side groups of various chain lengths ($M_n = 300$ and 950 g mol⁻¹) or of PEOMA₃₀₀ with methacrylic acid (MAA) were synthesized by nitroxide-mediated polymerization using an alkoxyamine initiator (BlocBuilder[®]) and SG1 nitroxide in the presence of a low amount of styrene. The PEOMA₃₀₀-MAA based copolymers showed a dual temperature/pH response.

The two series of macroalkoxyamines were used in aqueous emulsion copolymerization of *n*butyl methacrylate and styrene leading to the formation of particles composed of amphiphilic block copolymers through polymerization-induced self-assembly, in both the absence and presence of silica. The experiments performed in the absence of silica particles resulted in the formation of sterically or electrosterically stabilized latexes. The polymerization exhibited all the features of a controlled system with however the presence of a small proportion of dead chains. The effect of pH value, ionic strength and type and concentration of the macroalkoxyamine initiator on polymerization kinetics and latex morphologies was investigated. Depending on the reaction conditions, spherical particles, vesicles or nanofibers were successfully prepared.

The PEO-based macroalkoxyamines were shown to adsorb on the silica surface via hydrogen bond interaction between PEO and the silanol groups. This enabled block copolymers to be generated *in situ* on the silica surface leading to hybrid particles with snowman, raspberry, daisy, core-shell, "tadpole-" and "centipede-" like morphologies depending on the silica particle size, pH value and type of macroinitiator.

Keywords: Silica, surfactant-free emulsion polymerization, controlled radical polymerization, nitroxide, poly(ethylene oxide) methacrylate, methacrylic acid, block copolymers, particle morphology

RESUMÉ

Des polymères à base de méthacrylate de poly(oxyde d'éthylène) (PEOMA) avec des chaînes pendantes PEO ($M_n = 300$ ou 950 g mol⁻¹) ou des copolymères de PEOMA₃₀₀ et d'acide méthacrylique (AMA) ont été synthétisés par polymérisation radicalaire contrôlée par les nitroxydes en utilisant une alkoxyamine (BlocBuilder[®]) comme amorceur en présence de SG1 et d'une faible quantité de styrène. Les copolymères à base de PEOMA₃₀₀ et d'AMA sont thermo- et pH-sensibles. Les deux types de macroalkoxyamines ont été utilisés pour amorcer la copolymérisation en émulsion du méthacrylate de *n*-butyle et du styrène et former, par auto-assemblage induit par la polymérisation, des particules composées de copolymères à blocs amphiphiles, en absence ou présence de particules de silice. En absence de silice, des particules stabilisées de façon stérique ou électrostérique ont été formées. La polymérisation d'une faible proportion de chaînes mortes. L'effet du pH, de la force ionique et de la nature ou de la concentration des macroalkoxyamines sur la cinétique de polymérisation et la morphologie des particules a été étudié, et des sphères, des vésicules ou des nanofibres ont été obtenues.

Les macroalkoxyamines à base de PEO s'adsorbent sur la silice via la formation de liaisons hydrogène entre les chaînes PEO et les groupes silanol. La synthèse de copolymères à blocs en surface de la silice a conduit à la formation de particules hybrides de différentes morphologies (bonhomme de neige, multipodes, framboise, cœur-écorce, têtard, mille-pattes) liées à la taille de la silice, au pH et à la nature du macroamorceur.

Mots clés : Silice, polymérisation en émulsion sans tensioactif, polymérisation radicalaire contrôlée, nitroxyde, méthacrylate de poly(oxyde d'éthylène), acide méthacrylique, copolymères à blocs, morphologie

Abbreviations

AA	acrylic acid
AAm	acrylamide
AcGalEMA	methacryloyl galactose
ADIBA	2,2'-azobis(<i>N</i> , <i>N</i> '-dimethyleneisobutyramidine) dihydrochloride
ADS	adsorption
AFM	atomic force microscopy
AIBA	2,2'-azobis(2-methylpropionamide) dihydrochloride
AIBN	2,2'-azobisisobutyronitrile
AN	acrylonitrile
APS	ammonium persulfate
APTES	amino propyl triethoxysilane
APTMS	acryloxy propyl trimethoxysilane
ATRP	atom transfer radical polymerization
BA	<i>n</i> -butyl acrylate
BCP	block copolymers
BMA	<i>n</i> -butyl methacrylate
BPO	benzoyl peroxide
CMC	critical micelle concentration
CNT	carbon nanotube
CRP	controlled radical polymerization
Cryo-TEM	cryogenic transmission electron microscopy
Cryo-ET	cryogenic electron tomography
CSA	camphorsulfonic acid
CTA	chain transfer agent
CTAC	cetyltrimethylammonium chloride
$D_{\rm n}$	number-average particle diameter
$D_{ m w}$	weight-average particle diameter
DP_n	number average degree of polymerization
DCT	4-cyano-4-(dodecylsulfanylthiocarbonyl) sulfanyl pentanoic acid
DCTBAB	<i>N</i> -(4-((((dodecylthio)carbonothioyl) thio) methyl) benzyl)- <i>N</i> , <i>N</i> -dimethylethanammonium bromide
DEAAm	N,N-diethylacrylamide
DES	desorption
DLS	dynamic light scattering
DMAc	dimethylacetamide
DMAEMA	dimethylaminoethyl methacrylate
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
DVB	divinylbenzene
EA	ethyl acrylate

EtOH	ethanol
ET	electron tomography
f	molar fraction of comonomer
FTIR	Fourier-transform infrared spectroscopy
GMA	glycidyl methacrylate
HCl	hydrogen chloride
HEMA	hydroxyethyl methacrylate
HPA	2-hydroxypropyl acrylate
HPMAAm	N-(2-hydroxypropyl) methacrylamide
KPS	potassium persulfate
LCST	lower critical solution temperature
LCMs	large compound micelles
LCVs	large compound vesicles
M _n	number-average molar mass
$M_{ m w}$	weight-average molar mass
MA	methyl acrylate
MAA	methacrylic acid
MASi	tert-butyl dimethylsilyl methacrylate
MMA	methyl methacrylate
MMD	molar mass distribution
MWCNTs	multiwalled carbon nanotubes
MMT	montmorillonite
MSNs	mesoporous silica nanoparticles
MTC	2-(methacryloyl) ethyl trimethyl ammonium chloride
NaA	sodium acrylate
NIPAM	<i>N</i> -isopropyl acrylamide
NMP	nitroxide-mediated polymerization
NMR	nuclear magnetic resonance
NP ₃₀	nonyl phenol polyoxyethylenic surfactant
PCDBAB	<i>N</i> , <i>N</i> -dimethyl- <i>N</i> -(4-(((phenylcarbonothioyl) thio) methyl) benzyl) ethanammonium bromide
PDI	polydispersity index
PEO	poly(ethylene) glycol
PEOMA	poly(ethylene glycol) methyl ether methacrylate
PISA	polymerization-induced self-assembly
PRE	persistent radical effect
PSD	particle size distribution
PBA	poly(<i>n</i> -butyl acrylate)
PEA	poly(ethyl acrylate)
Poly value	Polydispersity value
PS	polystyrene
PMMA	poly(methyl methacrylate)

PAH	poly(allylamine hydrochloride)
RAFT	reversible addition-fragmentation chain transfer
S	styrene
SAXS	small angle X-ray scattering
SDBS	sodium dodecyl benzene sulfonate
SDS	sodium dodecyl sulfate
SEC	size exclusion chromatography
SEM	scanning electron microscopy
SFRP	stable free radical polymerization
SG1	N-tert-butyl-N-[1-diethylphosphono-(2,2-dimethylpropyl)] nitroxide
SiOH	silanol
SNSs	spherical silica nanoparticles
SS	4-styrene sulfonate
tBA	<i>tert</i> -butyl acrylate
tBMA	tert-butyl methacrylate
TEM	transmission electron microscopy
TEMPO	2,2,6,6-tetramethylpiperidinyl-1-oxy
TEOS	tetraethoxysilane
TGA	thermogravimetric analysis
THF	tetrahydrofuran
TiO ₂	titanium dioxide
TIPNO	N-tert-butyl-N-[1-phenyl-2-(methylpropyl)] nitroxide
VBK	9-(4-vinylbenzyl)-9H-carbazole
4VP	4-vinyl pyridine
2VP	2-vinylpyridine
1VID	1-vinyl imidazole
X_{wt}	weight conversion
\mathbf{X}_{mol}	molar conversion
Z_{av}	Z-Average size (average hydrodynamic diameter)
γ-MPS	γ-methacryloxy propyl trimethoxysilane

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General Introduction

Organic/inorganic hybrid latexes are typical examples of composite materials that combine the best attributes of inorganic solids (nanoparticles, fibers, nanotubes, etc.) with the processing and handling advantages of organic polymers. The structures obtained are of particular interest for encapsulation technologies, drug delivery, or as pigments for the paint industry.¹

Several strategies have been reported for the elaboration of such colloidal nanocomposites including heterocoagulation, layer-by-layer assembly techniques, and *in situ* polymerization.^{2,3} Among the various methods, emulsion polymerization, a free radical polymerization process widely employed industrially to manufacture a variety of products (such as paints, adhesives, and impact modifiers), has been especially well documented.¹

Emulsion polymerization requires the presence of surfactant molecules for the colloidal stability of the latex. However, there is an increasing interest in surfactant-free emulsion polymerization by removing this type of stabilizers, due not only to their detrimental effect on the film properties (surfactant migration in materials leading to the degradation of their adhesive and mechanical properties),⁴⁻⁷ but also to environmental concerns (treatment of aqueous effluents and toxicity).

Recent developments in polymer chemistry offer the synthetic chemist a wide range of tools to prepare well-defined, highly functional building blocks. Controlled radical polymerization (CRP)^{8,9} has been shown to be suitable for the preparation of organic/inorganic hybrid materials with varying structural complexity.¹⁰

As the first developed CRP method, nitroxide mediated polymerization (NMP)¹¹⁻¹⁴ has always been considered to be the simplest method with unquestionable advantages such as thermal activation, good control of the polymerization, no purification step except from a simple precipitation to remove unreacted monomer, and no environmental issues.¹⁵ First limited to the polymerization of styrenic and acrylic monomers, NMP has now become a much more mature CRP technique allowing the controlled polymerization of a wider range of monomers including methacrylic ones. So, it is no doubt that with the advantage and development of NMP, there will be more and more NMP-derived materials in many fields, such as organic/inorganic hybrid latex.¹⁵

Recently, hybrid particles were achieved in aqueous media by several groups¹⁶⁻²⁵ using another CRP technique, reversible addition–fragmentation chain transfer (RAFT). The strategy employs living amphipathic random copolymers as macromolecular RAFT agents which are able to interact with the surface of inorganic particles (i.e. titanium dioxide,^{16,17,24} gibbsite,¹⁸ clay particles,²⁵ cerium oxide nanoparticles^{19,21} or carbon nanotubes)^{22,23} and promote their encapsulation through emulsion polymerization. To the best of our knowledge, there is no example of polymer-encapsulated inorganic particles and any other hybrid morphologies using a NMP approach in aqueous dispersed media.

In this work, we will explore the synthesis of polymer/silica hybrid latexes via NMP surfactant-free emulsion polymerization under mild conditions. This work relies on the use of well-defined water-soluble brush-type polymers composed of poly(ethylene)oxide methacrylate (PEOMA) units with PEO side groups which can form hydrogen bond interactions with the silanol groups of silica particles. Taking advantage of the reactive extremity of the macroalkoxyamines adsorbed on their surface, the modified silica particles are then used in emulsion polymerization to lead to various morphologies, such as snowman, raspberry, daisy, "tadpole-" and "centipede-" like. This study clearly shows how a powerful tool such as controlled radical polymerization can be used to obtain particle morphologies which are otherwise difficult to achieve.

The manuscript is divided into five chapters.

The **Chapter 1** gives a bibliographic review of conventional and controlled radical polymerization techniques (especially NMP) and their application to the synthesis of hybrid particles in solution or in aqueous dispersed media.

The **Chapter 2** focuses on the synthesis of silica nanoparticles of various diameters and narrow size distributions. Different methods were investigated: the Stöber method was employed to synthesize silica particles in the size range from 200 to 500 nm, whereas a L-arginine-catalyzed two-phase process was employed to synthesize silica particles with diameters lower than 50 nm. A regrowth of silica seeds in ethanol/water mixture was also investigated to get silica particles with diameters comprised between 100 and 200 nm.

The **Chapter 3** deals with the synthesis of two types of PEOMA-based macroalkoxyamines. Well-defined water-soluble brush-type copolymers mainly composed of PEOMA units with PEO side groups of various chain lengths ($M_n = 300$ and 950 g mol⁻¹), or composed of

PEOMA₃₀₀ with MAA units have been prepared by NMP using a low molar mass unimolecular alkoxyamine initiator (so called BlocBuilder®) and SG1 nitroxide in the presence of a small amount of styrene. Investigation of their LCST behavior showed that the PEOMA₃₀₀/MAA based copolymers exhibited a dual temperature/pH response.

In the **Chapter 4**, two types of PEOMA-based macroalkoxyamines from Chapter 3 were used for the surfactant-free emulsion polymerization of *n*-butyl methacrylate (BMA) in the presence of a small amount of styrene. Stable particles composed of amphiphilic block copolymers were obtained, and the effect of pH value, ionic strength and type and concentration of the macroalkoxyamine initiator on polymerization kinetics and latex morphologies was investigated. Spherical particles, vesicles or nanofibers were successfully achieved according to the self-assembly of the block copolymers.

The **Chapter 5** describes the adsorption of PEO-based macroalkoxyamines on silica particles via hydrogen bond interactions between PEO and the silanol groups, and the subsequent formation of block copolymers generated *in situ* on the silica surface via emulsion polymerization, leading to hybrid particles with snowman, raspberry, daisy, core-shell, "tadpole-" and "centipede-" like morphologies depending on the silica particle size, pH value and type of macroinitiator.

We finally draw some general conclusions and perspectives for future works in the last part of the manuscript.

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Chapter 1. Bibliographic review

Introduction

In the last decades, polymer science has developed into a modern and multi-research field. Initially devoted to structural applications, polymers are indeed increasingly involved in high added-value functional materials from electronic-, optical- and biomedical-related areas.¹⁻³

To obtain a wide variety of polymers and materials, several polymerization reactions were developed such as free radical polymerization, anionic polymerization, cationic polymerization and coordination polymerization. As one of the most widely used route, free radical polymerization has attracted a lot of researchers' attention. It is a method of polymerization by which a polymer is formed from the successive addition of free radical building blocks. The nature of free radical chemical interactions makes this one of the most versatile forms of polymerization available and allows facile reactions of polymeric free radical chain ends and other chemicals or substrates. More than 60% of the polymers in the world are produced through this method.

However, the conventional free radical polymerization suffers from a major limitation: the lifetime (few seconds) of an individual radical which means it is impossible to control the molecular architecture except in a very primitive way. In other words, it is impossible to use conventional free radical polymerization to create block copolymers or polymers with controlled branches because most of the polymer chains are "dead".

This situation changed with the development of Controlled/Living Radical Polymerization (CRP), which is a form of chain polymerization where the ability of a growing polymer chain to terminate has been greatly reduced.^{4,5}

The features of a living polymerization were first reported by Michael Szwarc in 1956,⁶ for the anionic polymerization of styrene with an alkali metal/naphthalene system in tetrahydrofuran (THF). He found that after the addition of monomer to the initiating system, the increase in viscosity would eventually stop, but after the addition of a new amount of monomer the viscosity would start to increase again. This methodology indeed opened the door to well-defined polymers with precise and predetermined molar masses, compositions, topologies and functionalities. In a living polymerization, chain termination and chain transfer reactions are absent and the rate of chain initiation is also much larger than the rate of chain propagation. The result is that the polymer chains grow at a more constant rate than seen in conventional chain polymerization and their lengths remain very similar (i.e. they

have a very low molar mass dispersity). Living polymerization is a popular method for the synthesis of block copolymers as the polymer can be synthesized in stages, each stage containing a different monomer. Additional advantages are predetermined molar masses and end-groups.

Various CRP methods have been developed since the early 1990s. Each of them is based on a different mechanistic approach and has encountered more or less success over the years. The most well established methods deriving from this concept are Nitroxide-Mediated radical Polymerization (NMP),⁷⁻¹⁰Atom Transfer Radical Polymerization (ATRP)¹¹⁻¹⁴ and Reversible Addition-Fragmentation chain Transfer (RAFT)¹⁵⁻¹⁷ which will be described separately. A particular attention will be paid to NMP, which is the process used throughout this work.

Synthesis of organic/inorganic particles is another important section in this work. Organic/inorganic hybrid particles are nanocomposites meant to combine the best attributes of the organic and the inorganic parts, leading to materials with improved properties. They combine the physical properties of inorganic materials (e.g., rigidity, thermal stability) with the advantages of organic polymers (e.g., flexibility, ductility and processability). A variety of CRP techniques have been employed to generate organic/inorganic hybrid particles including NMP, ATRP, and RAFT^{18-21,22-26} but only few studies²⁷ deal with organic/inorganic hybrid particles obtained via the use of CRP in aqueous medium. As one of the most widely used inorganic materials, silica has been selected as the inorganic component in this thesis.

1. Free radical polymerization

1.1 General aspects of conventional radical polymerization

Free radical polymerization is a type of chain growth polymerization, which is suitable for most of the monomers and can be done in bulk polymerization, solution polymerization, suspension polymerization and (mini)emulsion polymerization. Basically, the traditional free radical polymerization process contains four concomitant steps: initiation, propagation, chain transfer and termination (Scheme 1.1).

Initiation is the first step of the polymerization process. During initiation, an active center is created from which a polymer chain is generated. Initiation has two steps. In the first step, one or two radicals ($R \bullet$) are created from the initiating molecules (I). In the second step, radicals are transferred from the initiator molecules to the monomer units (M) present.

During the polymerization, a polymer spends most of its time in increasing its chain length, or propagating. After the radical initiator is formed, it attacks a monomer. The free radical uses one electron to form a more stable bond with the carbon atom. The other electron returns to the second carbon atom, turning the whole molecule into another radical. This begins the polymer chain. Once a chain has been initiated, the chain propagates until there is no more monomer or until termination or chain transfer reactions occur. There may be anywhere from a few to thousands of propagation steps depending on several factors such as radical and chain reactivity, the solvent, and temperature.

Chain transfer results in the destruction of only one radical, but also the creation of another radical. Often, however, this newly created radical ($A \bullet$) is not capable of further propagation. There are several types of chain transfer mechanisms, the chain can transfer to the solvent, to the monomer, to the initiator or to the polymer. The most obvious effect of chain transfer is a decrease in the polymer chain length.

Chain termination is a reaction of a polymer chain radical with the initiator radical or with another macroradical.

$$(Initiation)$$

$$I \longrightarrow 2R \bullet$$

$$R \bullet + M \longrightarrow RM \bullet$$

$$(Propagation)$$

$$RM \bullet + M \longrightarrow RMM \bullet \stackrel{M_{n-1}}{\longrightarrow} R - (M)_n - M \bullet$$

$$(Chain transfer)$$

$$R - (M)_n - M \bullet + A \longrightarrow R - (M)_n - M + A \bullet$$

$$(Termination)$$

$$R - (M)_n - M \bullet + R \bullet \longrightarrow R - (M)_{n+1} - R$$

$$R - (M)_n - M \bullet + \bullet M - (M)_m - R \longrightarrow R - (M)_{n+m} - R$$

Scheme 1.1 Polymerization process for radical polymerization.

1.2 Kinetics

In a typical chain-growth polymerization, the reaction rates for initiation (R_i) , propagation (R_p) and termination (R_t) can be described as follows.

$$R_i = -d[M\bullet]/dt = 2k_d f[I]$$
(eq. 1.1)

$$\boldsymbol{R}_{\boldsymbol{p}} = \boldsymbol{k}_{\boldsymbol{p}}[\boldsymbol{M}][\boldsymbol{M}\bullet] \tag{eq. 1.2}$$

$$R_t = -d[M\bullet]/dt = 2k_t[M\bullet] \qquad (eq. 1.3)$$

Where *f* is the efficiency of the initiator and k_d , k_p , and k_t are the rate constants for initiator dissociation, chain propagation and termination, respectively. [I], [M] and [M[•]] are respectively the concentrations of the initiator, monomer and the active growing chains.

The concentration of active chains can be derived and expressed in terms of the other known species in the system.

$$[M\bullet] = (\frac{fk_d[I]}{k_t})^{1/2}$$
 (eq. 1.4)

In this case, the rate of chain propagation can be further described using a function of the initiator and monomer concentration.

$$R_p = k_p \left(\frac{fk_d}{k_t}\right)^{1/2} [I]^{1/2} [M]$$
 (eq. 1.5)

The kinetic chain length v is a measure of the average number of monomer units reacting with an active center during its lifetime and is related to the molar mass through the mechanism of the termination. Without chain transfer, the kinetic chain length is only the function of propagation rate and initiation rates.

$$v = \frac{R_p}{R_i} = \frac{k_p[M][M\bullet]}{2fk_d[I]} = \frac{k_p[M]}{2(fk_dk_t[I])^{1/2}}$$
(eq. 1.6)

Compared to other techniques, conventional radical polymerization has some advantages such as the relative insensitivity to impurities, the moderate reaction temperatures and the multiple polymerization processes available, e.g., bulk, solution, precipitation or emulsion polymerization. However, one of the main disadvantages related to the mechanism of free radical polymerization is the poor control of the molar mass and the molar mass distribution (MMD), and the difficulty (or even impossibility) of preparing well-defined copolymers or polymers with a predetermined functionality. The development of controlled radical polymerization techniques over the last twenty years now allows overcoming these limitations.

2. Controlled Radical Polymerization (CRP)

CRP distinguishes itself from conventional radical polymerization by involving a reversible activation/deactivation process between active and dormant species (Scheme 1.2).^{28,29}



Scheme 1.2 Reversible activation/deactivation process in CRP.²⁸

Basically, whatever the involved mechanism, the key feature for CRP is the establishment of a dynamic equilibrium between propagating radicals and various dormant species throughout the polymerization process. In order to decrease the occurrence of irreversible termination reactions to an extremely low level, the so obtained equilibrium is triggered and governed by thermal, photochemical or chemical stimuli. For the success of such an approach, a polymer chain should spend most of the polymerization time under its dormant state.

Currently, the three most effective methods of CRP include nitroxide mediated polymerization (NMP),³⁰ atom transfer radical polymerization (ATRP)³¹ and reversible addition-fragmentation chain transfer (RAFT) polymerization.^{32,33} Among these methods, NMP and ATRP operate via a reversible termination reaction whereas RAFT operates via reversible transfer reactions.

2.1 Reversible Addition-Fragmentation chain Transfer (RAFT) polymerization

RAFT polymerization is a relatively new CRP method. The first reports of radical addition-fragmentation processes appeared in the early 1970s.^{34,35} But, the direct use of

addition-fragmentation chain transfer agents, to provide a living character to radical polymerization did not appear until the late 1990s.¹⁵

RAFT has attracted much attention due to the fact that it can be applied to a broad range of monomer types and can operate under moderate conditions.³⁶ Unlike ATRP and NMP, RAFT operates on the principle of reversible chain transfer. In a RAFT mechanism, initiation occurs via the decomposition of the free radical initiator leading to the formation of propagating chains. This is followed by addition of the propagating radicals to the RAFT chain transfer agent. Further, the fragmentation of the intermediate radical occurs, giving rise to a polymeric RAFT agent and a new radical. This radical reinitiates the polymerization to form new propagating radicals. The RAFT process relies on this rapid central addition fragmentation equilibrium between propagating and intermediate radicals, and chain activity and dormancy as shown in Scheme 1.3.³⁷



Scheme 1.3 Mechanism and equilibrium in a RAFT process (from Wikipedia).

The RAFT process involves conventional free radical polymerization of a substituted monomer in the presence of a suitable chain transfer agent (CTA). The CTA typically possesses a thiocarbonylthio group (S=C-S) with substituents R and Z. A wide range of CTAs has been reported including dithioesters,³⁸ trithiocarbonates,³⁹ dithiocarbamates,^{16,40} xanthates (dithiocarbonates)^{41,42} and phosphoryl/thiophophorydithioformates.⁴³

As one of the most important CRP methods, this polymerization can be performed in a large range of solvents (including water) and within a wide range of temperatures. It is suitable for use with many different monomers and does not require highly rigorous removal of oxygen and other impurities, like conventional radical polymerization

But it also has some disadvantages: a particular RAFT agent is only suitable for limited kinds of monomers and the synthesis of a RAFT agent typically requires a multistep synthetic procedure and subsequent purification. RAFT agents will be unstable over long time periods, are highly colored and can have a pungent smell due to the small sulfur compounds. The presence of sulfur and color in the resulting polymer may also be undesirable for some applications; however, this can be eliminated with further chemical and physical purification steps.⁴⁴

2.2 Atom Transfer Radical Polymerization (ATRP)

ATRP (or transition metal-mediated living radical polymerization) was independently discovered by Mitsuo Sawamoto et al.¹¹ and by Jin-Shan Wang and Krzysztof Matyjaszewski in 1995.¹²

As the name suggests, this method is based on a reversible atom transfer reaction in which the dormant polymer P-X is activated by the catalytic action of transition metal complexes Mt^m/L , with the transition metal species in oxidation state m, L being the ligand (Scheme 1.4).³⁵ The deactivator reacts with the propagating radical in a reverse reaction (k_{deact}) to reform the dormant species and the activator.

$$P_{n}-X + Mt^{m}/L \xrightarrow{k_{act}} P_{n}^{*} + X-Mt^{m+1}/L$$

$$k_{deact} \xrightarrow{k_{deact}} P_{n}^{*} + X-Mt^{m+1}/L$$

Scheme 1.4 Activation/deactivation equilibrium in ATRP.³⁵

ATRP is a catalytic process and can be mediated by many redox-active transition metal complexes. CuI/L and X–CuII/L have been the most often used transition metal but other studied metals include Ru, Fe, Mo, Os, etc.⁴⁵

ATRP has been successfully used in living polymerizations of a wide range of monomers, such as styrenic monomers, methacrylates, methacrylamides and acrylonitrile.⁴⁶ ATRP is successful at leading to polymers of high number average molar masses and low dispersity when the concentration of the propagating radical balances the rate of radical termination. Yet, the propagating rate is unique to each individual monomer. Therefore, it is important that the other components of the polymerization (initiator, catalysts, ligands and solvents) are optimized in order for the concentration of the dormant species to be greater than the concentration of the propagating radical and yet not too great to slow down or halt the reaction.^{13,47}

2.3 Nitroxide-mediated polymerization (NMP)

NMP, also called stable free radical polymerization (SFRP), was first described by Georges et al. in 1993.⁸ In this paper, a mixture of benzoyl peroxide (BPO) and 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) (Figure 1.1) was used to initiate the bulk radical polymerization of styrene.



TEMPO

Figure 1.1 Chemical structure of TEMPO.

In NMP, the dormant species P-X is thermally or photochemically dissociated into an active/propagating radical P[•] and a stable (persistent) radical X[•] (Scheme 1.5).

$$P-X \xrightarrow{k_a} P \bullet + X \bullet$$

Scheme 1.5 Activation/deactivation equilibrium in NMP.

When the coupling of the stable free radical (nitroxide) with the polymeric radical is reversible, the propagating radical concentration can be limited to levels that allow controlled polymerization. Similar to ATRP, the equilibrium between dormant chains and active chains is designed to heavily favor the dormant state.

The living nature of ATRP and NMP is due to the persistent radical effect (PRE).⁴⁸ PRE is a general principle that explains the highly specific formation of the cross-coupling product between two radicals. When one species is persistent (long lived) and the other transient, the two radicals are formed at equal rates. The initial buildup in concentration of the persistent species is caused by the self-termination of the transient radical.

In the case of a NMP, the persistent radical is the nitroxide species and the transient radical is always the carbon radical. This leads to repeated coupling of the nitroxide to the growing end of the polymer chains, which would ordinarily be considered a termination step, but is in this case reversible. Because of the high rate of coupling of the nitroxide to the growing chain ends, there is little coupling of two active growing chains, which would be an irreversible terminating step limiting the chain length. The nitroxide binds and unbinds to the growing chain, protecting it from termination steps. This ensures that any available monomer can be easily scavenged by active chains. Because this polymerization process does not naturally self-terminate, it is described as "living," as the chains continue to grow under suitable reaction conditions whenever there is some reactive monomer to "feed" them. Because of the PRE, it can be assumed that at any given time, almost all of the growing chains are "capped" by a mediating nitroxide, meaning that they dissociate and grow at very similar rates, creating a largely uniform chain length and structure.^{49,50}

3. NMP

3.1 Mono and bicomponent initiating systems

A typical NMP can be set up following two different pathways detailed in Scheme 1.6.



Scheme 1.6 Activation–deactivation equilibrium in nitroxide-mediated polymerization. Bicomponent initiating system (a) and monocomponent initiating system (b).⁵¹

The bicomponent initiating system consists in using a conventional radical initiator in conjunction with a free nitroxide in order to form the macroalkoxyamine *in situ* (Scheme 1.6 a) whereas the monocomponent initiating system relies on the use of a preformed alkoxyamine (Scheme 1.6 b).

NMP was originally initiated by a bicomponent pathway. TEMPO was used as the stable free nitroxide in combination with a classical thermal initiator, such as 2,2'-azobisisobutyronitrile (AIBN)⁵² or benzoyl peroxide (BPO).⁸

This system has the advantage to use classical radical polymerization processes with the only addition of free nitroxides, which can be also highly desirable from both economic and practical points of views. However, the use of a bicomponent initiating system does not permit accurate control over the number of growing chains and the concentration of free nitroxide because the free radical initiator efficiency is generally ill defined. Thus, it has some strong repercussions on the kinetics and the control over the polymer characteristics.

In contrast, the monocomponent pathway allows this problem to be avoided as long as the initiation efficiency of the alkoxyamine remains close to 100%.⁵³

Compared to ATRP and RAFT, NMP has the advantage of being only governed by a thermal process and does not require any catalyst or bimolecular exchange. However, one of the weak points of this technique is its relatively limited range of controllable monomers.

3.2 NMP of methacrylic esters

Indeed, at the beginning, the selection was quite limited and only the family of styrenic monomers could be nicely controlled using TEMPO as a nitroxide.¹¹ In addition, high temperatures (125–145 °C) and long polymerization times (24–72 h) were usually required. To overcome these strong limitations, adjustments of nitroxide structure were required.

Then, with the discovery of efficient, acyclic nitroxides such as N-tert-butyl-N-(1-diethyl phosphono-2,2-dimethylpropyl nitroxide (SG1, also known as DEPN)^{53,54} and 2,2,5-trimethyl-4-phenyl-3-azahexane-3-nitroxide (TIPNO)^{55,56} (Figure 1.2), not only styrene and its derivatives^{54,55} could be polymerized in a controlled fashion but also acrylic acid,^{57,58} acrylamide,^{59,60} dienes,^{10,61} and methacrylic esters.⁶²



Figure 1.2 Chemical structures of SG1 and TIPNO.

However, most of NMP systems still need a high temperature (125–145°C), which demands more energy and solvent with higher boiling points.

Recently, Charleux et al. reported an efficient method to perform the NMP of methacrylic esters under mild conditions (70-90 °C).⁶³ It is schematically described in Figure 1.3. In their work, they studied the theoretical expression for the average activation–deactivation equilibrium constant, in a purely terminal model and in a mixed terminal model for activation–deactivation and penultimate unit effect model for propagation. The polymerizations were performed at 90 °C with an alkoxyamine initiator (SG1, Figure 1.2) able to dissociate at a sufficiently low temperature owing to the presence of a tertiary carbon radical attached to the nitroxide. By adding 4.4 or 8.8 mol % of styrene, the polymerization

could be carried out to large conversions, while exhibiting all the features of a controlled system. The existence of styrene-terminated macroradicals favors the deactivation reaction, which would not otherwise efficiently take place with a methyl methacrylate terminal unit.



Figure 1. 3 Schematic representation of the polymerization of methacrylic esters initiated by the BlocBuilder[®] SG1-based alkoxyamine with a small percentage of styrene as a comonomer. ⁶³

It was demonstrated that the system exhibited all the characteristics of a living/controlled polymerization, which was explained by the following features:

- The overall concentration of propagating radicals was strongly reduced by the copolymerization effect and the irreversible termination reactions undergone by the MMA/SG1 system were hence slowed down;
- (ii) Isolated styrene subunits were incorporated into the chains and the terminal one bearing the radical promoted the reversible deactivation by the SG1 nitroxide.
- (iii) The MMA penultimate unit effect enhanced deactivation of the so-formed styryl-SG1 alkoxyamine, which then exhibited a reduced dissociation temperature with respect to styrene homopolymerization.^{64,65} Consequently, the polymerization could be performed efficiently in the 70–90 °C temperature range.

This technique was later expanded to a series of methacrylate monomers such as methacrylic acid (MAA),⁵⁷ poly(ethylene glycol) methyl ether methacrylate (PEOMA),⁶⁶ ethyl methacrylate (EMA), *n*-butyl methacrylate (BMA),⁶⁷ tert-butyl methacrylate (tBMA),⁶⁸ glycidyl methacrylate (GMA)^{69,70} and methacryloyl galactose (AcGalEMA).⁷¹

Two other comonomers were successfully proposed for the NMP of MMA: acrylonitrile (AN) and a styrene derivative: 9-(4-vinylbenzyl)-9H-carbazole (VBK). AN yielded good control and livingness with however lower polymerization rates, most probably due to the

higher bond dissociation energy of the AN-SG1 bond.⁷² The high water-solubility of AN (solubility in water at 20 °C is 7.0 wt %) represents a strong advantage which allows potential drawbacks provided by the use of S (solubility in water at 20 °C is 0.029 wt %) to be circumvented, such as the synthesis in water-rich environments.⁷³ Concerning VBK, it was shown that as little as 1 mol% of VBK in the feed was required to obtain a controlled/living copolymerization of a MMA/VBK mixture.⁷⁴

4. NMP in aqueous dispersed media

Although CRP was successfully employed in organic media in bulk or in solution, its implementation to aqueous polymerization was plagued with numerous challenges. In particular, the compatibility of radical mediators with water, the solubility and partitioning of the radical mediators in different phases, as well as the stability of the dormant species in the presence of water have a significant influence on the loss of "living" character of the polymerization and colloidal stability of the resulting latexes.^{75,76}

Using different kinds of nitroxides, NMP has been performed in aqueous media systems such as aqueous alcoholic dispersion,^{73,77} aqueous suspension,⁷⁸ seeded emulsion,⁷⁹ ab initio emulsion⁸⁰⁻⁸² and miniemulsion.⁸³⁻⁸⁹ In the following, we will focus on the emulsion and miniemulsion processes.

4.1 Emulsion and miniemulsion polymerization

Emulsion polymerization is the most common polymerization process used in the industry for the production of dispersed polymers and has been studied in laboratories for many years. Considering a typical emulsion polymerization, there are initially four main components in the system (Figure 1.4): water, hydrophobic monomers (M), initiator and surfactant(s). Following the use of a water-soluble radical initiator, which is usually a charged molecule, stable latexes are obtained according to a complex nucleation mechanism.⁹⁰ The nucleation mechanism could be either micellar or homogeneous depending on the concentration of surfactant and the water solubility of the monomer(s). As a result of the water-soluble character of the initiator, the radicals are produced in the continuous aqueous phase in which polymerization starts. This is an important feature of emulsion polymerization. Indeed, the monomer is not polymerized in the droplets but in particles, which are created early in the process.

The latex particles obtained via emulsion polymerization are generally stabilized by a low molar mass surfactant, which can be either ionic, nonionic or a mixture of both. The stabilizer could also be amphiphilic copolymers who can offer the advantage of being better anchored at the particle surface and of providing efficient electrosteric stabilization when the hydrophilic component is a polyelectrolyte. The surfactant can also take part in the polymerization process as a part of monomers or initiator.^{91,92}



Figure 1. 4 Initial state of aqueous polymerization in emulsion (a) and in miniemulsion (b).⁵¹

The miniemulsion process is based on a high shear device such as ultrasonic or microfluidizer which can divide the starting monomer phase into submicronic droplets (50-500 nm).⁹³⁻⁹⁵ The droplets could be seen as bulk nanoreactors as they are small enough to allow radical entry and avoid the complex nucleation step existing in emulsion polymerization. To enhance the stabilization of these tiny monomer droplets, a co-surfactant (such as hexadecanol, hexdecane, decahydronaphtaline, octamethyl cyclotetrasiloxane, tetraethylsilane, etc.)⁹⁶ is initially added with the surfactant. The co-surfactant can limit the coalescence by forming a barrier at the surface of the droplets by combination with the surfactant and/or prevent Ostwald ripening by retarding monomer diffusion by building up an osmotic pressure within the monomer droplets. The choice of a suitable co-surfactant is a key issue for successful miniemulsion polymerization.

Miniemulsion polymerization has several advantages over emulsion polymerization: (i) there is no complex nucleation steps as in emulsion polymerization, (ii) the system exhibits only two phases throughout the polymerization reaction (the aqueous phase and the monomer/polymer particles), (iii) either an oil-soluble or a water-soluble initiator can be used and (iv) the final latex is theoretically a 1:1 copy of the initial droplets, allowing a direct control over the number of particles, although this is not always achieved in practice. Nevertheless, miniemulsion polymerization is hard to be applied in industrial conditions because of the limitation of the high shear devices instruments.

4.2 NMP in emulsion polymerization.

4.2.1 Emulsion polymerization with alkoxyamines and surfactant

In the beginning, NMP in true emulsion systems was rather unsuccessful due to colloidal instability and/or poor control of the polymerization, mainly assigned to nucleation of the large droplets of monomer and to nitroxide partitioning.^{30,51,97} The very first work reporting successful NMP in emulsion polymerization concerned a seeded system in order to simplify the complex nucleation step existing in ab initio batch emulsion NMP.⁹⁸ For this purpose, a PS seed latex (90 nm) stabilized by an anionic surfactant, Aerosol MA-80, was allowed to swell with S and an oil-soluble alkoxyamine based on TEMPO. Polymerization proceeded at 125 °C with some control/livingness, although the molar mass distributions (MMD) were rather large.

Later, Marestin et al.⁹⁹ studied the ab initio emulsion polymerization of styrene (S) at 130 °C with TEMPO or a variety of TEMPO derivatives in conjunction with potassium persulfate (KPS) as initiator and SDS as surfactant. In this work, only the amino-TEMPO could provide stable latexes and good control and livingness. With the other nitroxides, extremely low conversions were observed before complete coagulation of the system.

The effect of hydrophilicity of TEMPO-based nitroxides was examined in more details by Cao et al.⁸⁰ for batch emulsion polymerization of S conducted at 120 °C with potassium persulfate as an initiator and SDS as the surfactant. In this study, only the acetoxy derivative of TEMPO enabled to achieve controlled polymerization.

The development of SG1 allowed polymerization temperatures to be drastically reduced which is relevant to aqueous dispersed systems since, in the case of S, reactions can be performed at 90 °C without the need for pressurized vessels. However, by using a water-soluble redox initiator (i.e., $K_2S_2O_8/Na_2S_2O_5$) with SG1, the colloidal stability of the final latex was still imperfect as few percents of coagulum were noticed even though the polymerization process exhibited a rather good control.⁸⁴

In order to get optimized concentration of nitroxide at the polymerization locus and to prevent thermal initiation in the monomer droplets, Cunningham and co-workers used a combination of nitroxides exhibiting significant different water-solubilities. They performed a well-controlled living polymerization of S at 135 °C with sodium dodecyl benzene sulfonate (SDBS) as the surfactant, and the following combination of nitroxides: TEMPO (to

control the polymerization) and highly hydrophobic 4-stearoyl-TEMPO (to inhibit polymerization in the droplets).¹⁰⁰ Later, the same group also reported a two-step nitroxidemediated surfactant–free emulsion polymerization of S by using the water-soluble nitroxide SG1 and KPS as the initiator.¹⁰¹ In the first step, a seed of S (1.5 wt% of total S) was polymerized for 3.5 h. Then the remaining S was added over 10 min. The polymerization exhibited long induction periods as a result of the reversible termination of SG1-capped PS oligomers in the aqueous phase prior to nucleation. However, good colloidal stability with only minor coagulation as well as good livingness were obtained, but rather broad MMD was evidenced (PDI >1.7) at about 60% conversion, which was assigned to different [chains]/[SG1] ratios within the latex particles.

A significant breakthrough has been witnessed with the use of the commercially available BlocBuilder[®], a water-soluble, SG1-based alkoxyamine, in alkaline conditions.⁵¹

In order to avoid droplet nucleation that would lead to colloidal instability, a simple two-step emulsion polymerization process was developed with either monofunctional (MAMA) or difunctional (DIAMA) SG1-based alkoxyamines (Figure 1.5).⁸¹



DIAMA

Figure 1.5 Chemical structure of MAMA alkoxyamine and DIAMA dialkoxyamine.⁸¹

The first step (Figure 1.6) consisted in the synthesis of a living poly(n-butyl acrylate) (PBA) or PS seed latex with low solids content (<1 wt %) containing macroalkoxyamine chains. The seed latex with low number-average degree of polymerization (DP_n around 10) was obtained through ab initio batch emulsion polymerization from the neutralized form of the BlocBuilder[®] alkoxyamine. There was a trick here: a high amount of surfactant Dowfax 8390 was used to make a microemulsion recipe. Therefore, there was no large droplet of monomer and most of it was in the swollen micelles. The first step lasted 8 h to get well-defined and highly living SG1-capped PBA seeds. Then, for the second step, monomers such as S or BA

were added to target high solids content by chain extension. Finally, stable latexes with good colloidal properties were obtained after another 8h reaction. However, depending on the initial concentration of surfactant, the particle size distribution was rather broad with average diameters in the 260–660 nm range (Figure 1.7 a).



Figure 1.6 Two-step SG1-mediated emulsion polymerization of *n*-butyl acrylate or styrene initiated with the water-soluble SG1-based alkoxyamine. (a) Synthesis of the living seed latex initiated by the MAMA or DIAMA SG1-based alkoxyamine and (b) extension of the living seed latex after "one shot" addition of monomer.⁵¹



Figure 1.7 Transmission electron micrographs of PS latexes synthesized by two-step SG1mediated emulsion polymerization, initiated with the MAMAeNa (left) or with the DIAMAeNa (right). [Dowfax 8390] = 6.9×10^{-3} mol L⁻¹.⁵¹

This process was also applied to the synthesis of PBA-*b*-PS diblock copolymer latexes simply by adding S after the synthesis of the PBA block. Again, a stable latex with a solid content as high as 26 wt% and an average diameter of around 330 nm was recovered.⁸¹

Cunningham and co-workers¹⁰² reported NMP of BMA with a small amount of S in a surfactant-free emulsion polymerization system by using the BlocBuilder[®] alkoxyamine.

Whereas the BMA/S copolymerization system led to a bimodal particle size distribution (PSD) in the presence of surfactant (Dowfax 8390) above the critical micelle concentration (CMC), the surfactant-free emulsion polymerization counterpart conducted to monomodal PSD but suffered from poor initiation efficiencies and slow rates of polymerization as irreversible terminations occurred during nucleation.

4.2.2 Surfactant-free emulsion polymerization with water-soluble macroalkoxyamines

Charleux and co-workers reported the first successful ab initio batch emulsion NMP which relied on the development of SG1-based poly(sodium acrylate) alkoxyamine (PNaA-SG1).¹⁰³ In this approach, no surfactant was required due to the multiple charges provided by PNaA. The emulsion NMP of S and BA could be performed at 120 °C. Although M_n increased linearly with conversion, the macroinitiator efficiency was below 100%. The final particles had a narrow PSD. Besides, as the PNaA formed a pH sensitive polymer shell, the size and stability of the latex particles changed under different pH values.

Then, a polyNaA-SG1 macroalkoxyamine was used by the same group to polymerize 4vinylpyridine through NMP in emulsion polymerization.¹⁰⁴ They got stable latexes with different morphologies like spherical or worm-like micelles, multicompartmented or spherical vesicles as shown in Figure 1.8. These structures were composed of well-defined block copolymers of acrylic acid (AA) and 4-vinyl pyridine (4VP) with a long hydrophobic block. The structures were found to solubilize when decreasing the pH owing to the basic nature of the P4VP block.



Figure 1.8 Classical (*left*) and cryo- (*right*) TEM images of the aggregates obtained by nitroxide-mediated emulsion polymerization of 4-vinylpyridine initiated by PNaA-SG1.¹⁰⁴
Following the discovery that methacrylic acid (MAA) could be nicely controlled with the help of a low percentage of S,^{47,50} SG1 end-capped P(MAA-*co*-S) macroalkoxyamines were synthesized and employed as initiators in the surfactant-free, ab initio batch emulsion copolymerization of MMA with a low amount of S at temperatures below 90 °C.¹⁰⁵ The polymerizations were particularly fast (> 90% conv. in less than 3 h), well-controlled and with a high initiating efficiency due to the high dissociation rate constant of the macroalkoxyamines. It led to the *in situ* formation of amphiphilic block copolymers that self-assembled into small particles with average diameters below 100 nm, according to a polymerization-induced self-assembly process in which the polymerization would allow the *in situ* creation of well-defined amphiphilic block copolymers and their self-assembly simultaneously to the growth step.¹⁰⁶

The method was further extended to the design of PEG-based macroalkoxyamines via terpolymerization of MAA, PEOMA and a few percents of S to ensure a controlled process at 80 °C.⁹⁸ Stable spherical latex particles exhibiting a very small average diameter (32 nm) and a high polydispersity factor (0.3) (due to a low fraction of aggregates), were obtained under basic conditions (pH = 8). Macroalkoxyamines with a high proportion of PEOMA units resulted in highly viscous latexes suggesting the formation of non-spherical morphologies under these conditions, although there was no experimental evidence like TEM analysis for instance, to support this assumption.

Brusseau et al.¹⁰⁷ used 4-styrene sulfonate (SS) instead of S in the copolymer chain to create a more hydrophilic macroalkoxyamine. The copolymerization was performed in DMSO at 76 °C and all characteristics of this controlled/living system indicated an efficient deactivation of the propagating radicals by the nitroxide SG1. The P(MAA-*co*-SS)-SG1 macroalkoxyamine was then used for the ab initio batch emulsion polymerization of MMA with a small amount of S. Latexes with a 20 wt% solids content were stable and exhibited small average diameters in the 29–43 nm range. Interestingly, well-defined morphologies such as hairy spherical micelles, nanofibers, or vesicles were obtained depending on the molar mass of the hydrophobic block as shown in Figure 1.9.¹⁰⁸



Figure 1.9 TEM images of the final nano-objects obtained from different hydrophobic block molar masses for a same macroinitiator $P(MAA_{41}-co-SS_{10})-SG1 (M_n = 5600 \text{ g mol}^{-1}).^{108}$

4.3 NMP in miniemulsion polymerization

Many publications were devoted to NMP in miniemulsion, using a bicomponent initiating system with TEMPO or derivatives as the nitroxide. For instance, the nature of the TEMPO substituent has been selected in order to adapt the hydrophilicity of the nitroxide to the polymerization process. These investigations were performed at elevated temperatures (typically above 100 °C), mainly with styrene as the monomer. ^{31,83,90,109,30,97,110} Due to the features of miniemulsion polymerization, both oil- and water-soluble initiators were investigated. In comparison with emulsion polymerization, the miniemulsion system usually displays improved stability.

The first successful report for NMP miniemulsion polymerization was via an oil-soluble bicomponent initiating system. TEMPO was selected as the controlling agent and BPO as the initiator for the polymerization of S. The reaction was carried out at 125 °C with Dowfax 8390 as the surfactant and hexadecane as a co-stabilizer.⁸⁷ In contrast to conventional miniemulsion polymerization, the use of TEMPO allowed the synthesis of PS chains with M_n

= 40 000 g mol⁻¹ and a narrow MMD with D = 1.14 to 1.6. The latex was stable but with a larger diameter ($D_n = 121$ nm) and a broad size distribution ($D_w/D_n = 1.58$).

Similar works with S miniemulsion polymerization were investigated by Cunningham et al.¹⁰³ who conducted a series of experiments in which the solubility of nitroxide and initiator was systematically varied. It was noticed that TEMPO offered a better control than TEMPO-OH with regards to the evolution of molar masses. The TEMPO/KPS system resulted in more polymer chains (and consequently lower M_n) than TEMPO/BPO initiation system. They also introduced camphorsulfonic acid (CSA) in the S miniemulsion polymerization to see the effect on the final conversion and molar mass, which were found to depend on the nitroxide/BPO ratio. It was shown that CSA was more effective in enhancing the rate and molar mass when the initial free-nitroxide amount was higher. Despite the differences in their water solubility, no significant differences of CSA addition were observed between TEMPO and TEMPO-OH.¹⁰⁴

Macleod and co-workers employed TEMPO/KPS for the polymerization of S at 135 °C with an optimized [TEMPO]₀/[KPS]₀ initial ratio of 2.9.¹¹¹ A very fast polymerization was achieved and polymers with low \mathcal{D} were obtained. When the hydrophobic TEMPO was replaced by the more hydrophilic TEMPO-OH, the evolution of M_n with conversion was affected.¹⁰³ Whereas with TEMPO the use of KPS led to a larger initiation efficiency than with BPO, a poor control in the early stages of the polymerization was obtained with TEMPO-OH whatever the nature of the initiator, likely due to the lack of free nitroxide in the organic phase.

A significant breakthrough appeared with the use of SG1 instead of TEMPO in miniemulsion polymerization of S.^{93,112} It allowed the polymerization to be performed at a lower temperature (i.e., 90 °C) with either AIBN or a redox system ($K_2S_2O_8/Na_2S_2O_5$) as the initiator. Though the conversion of the monomer was limited to 60 % after 24 h of reaction, the polymers exhibited rather low dispersity. The limited conversion was probably due to the persistent radical effect together with the almost negligible rate of thermal auto-initiation of S at such a temperature that caused an accumulation of SG1 in the medium.

According to simulations by Greszta and Matyjaszewski of TEMPO-mediated radical polymerization of S at 120 °C, transfer to monomer leads to a relatively small but significant increase in polydispersity.¹¹³ The number of dead chains formed by chain transfer to monomer was higher than by termination, but most dead chains were formed by alkoxyamine

decomposition. To achieve accurate control over the number of active chains, TEMPOcapped PS was used as macroinitiator.

For instance, Pan and co-workers successfully reported the polymerization of S at 125 °C using a PS-TEMPO macroinitiator ($M_n = 7050 \text{ g mol}^{-1}$) with hexadecane as a co-stabilizer and Dowfax 8390 as a surfactant.^{86,114,115} The experimental molar masses were systematically below the theoretical ones and the dispersity continuously increased with monomer conversion. This behavior was ascribed to thermal auto-polymerization of styrene at high temperature leading to the creation of new chains throughout the reaction and to concomitant irreversible terminations.

Okubo and co-workers found a strong effect of the initial concentration of PS-TEMPO on the control/livingness of S in miniemulsion polymerization.⁸⁹ The control was poor when the PS-TEMPO concentration was less than 0.02 M, which is due to the combined effect of enhanced thermal initiation of styrene polymerization and partial positioning of TEMPO at the water/oil interface. In contrast, higher initiator concentrations led to satisfying results. A PS-TEMPO was also successfully used as a macroinitiator for the cross-linking NMP miniemulsion of S with 1 % DVB at 125 °C.^{85,116}

Recently, the group of Zetterlund reported the SG1 mediated polymerization of S in miniemulsion on the basis of *in situ* surfactant formation without the use of homogenization device.⁸⁸ The method relies on the formation of a fine aqueous miniemulsion on gentle mixing of the organic phase and the aqueous phase resulting in the *in situ* formation of a surfactant (oleic acid) at the oil/water interface.

There was no real efficient water-soluble alkoxyamine until 2004. The first important step has been achieved by Charleux and co-workers who took advantage of the BlocBuilder[®] alkoxyamine structure to report the first example of a water-soluble monocomponent initiating system in NMP miniemulsion polymerization.¹¹⁷ This alkoxyamine was fully water-soluble based on the carboxylate salt form. BA and S were polymerized at 112 °C and 120 °C, respectively. In case of S, the initiation efficiency was lower than expected which was attributed to a highly pronounced persistent radical effect leading to a very slow chain growth in the aqueous phase. Moreover, the pH of the aqueous phase was shown to have a strong influence on the polymerization rate: it should remain above 5 to avoid side reactions of SG1 degradation. Besides the high control of molar mass and molar mass distribution, the charged

alkoxyamine that remained attached onto the polymer particle surface contributed in the reduction of the average particle diameter.

5. Organic/inorganic hybrids via CRP methods

In the past few decades, the interest for organic/inorganic hybrid particles with complex shapes has increased considerably due to the potential benefits of these nano-objects in multiple areas of material science.^{105,118} These hybrid particles are meant to combine the best attributes of the organic and inorganic parts. A variety of CRP techniques have been employed to generate organic/inorganic hybrid particles including NMP, ATRP, and RAFT. ^{18-21,22-26,30,110,119} Generally, all these techniques for hybrid particles are performed with a "grafting" process.

Grafting polymer chains at the surface of inorganic particles can be performed according to three main techniques: "grafting from", also called "surface-initiated polymerization"; "grafting to", which consists in the coupling of a reactive polymer chain to a functional group attached at the surface and "grafting through", by which the polymer is bound via copolymerization with attached unsaturated groups (Scheme 1.7).¹²⁰



Scheme 1.7 Scheme for grafting techniques. Redrawn from ref.¹²⁰

According to the technique employed, the polymer grafting density and the chain conformation at the surface may vary substantially, from dense brushes (high surface density and stretched conformation) to mushroom conformation at low grafting density.¹²¹ In the former case, mainly achieved via surface-initiated polymerization, the polymer layer thickness depends directly on the average molar mass of the attached chains.

In this section, we will focus on the synthesis of organic/inorganic hybrids via CRP in nonaqueous media and aqueous media.

5.1 Organic/inorganic hybrids via CRP in non-aqueous media

A lot of works on the synthesis of organic/inorganic hybrids via CRP methods performed in non-aqueous media have been reported. Some selected examples are briefly reviewed in this section.

5.1.1 ATRP

The group of Matyjaszewski reported the synthesis of a series of organic/inorganic hybrids via surface-initiated ATRP polymerization.^{122,123} As shown in Scheme 1.8, silica particles were first modified with 1-(chlorodimethylsilyl) propyl 2-bromoisobutyrate to get 2-bromoisobutyrate-functionalized silica colloids. Then, ATRP of different monomers (S, MMA or BA) was carried out from the silica surface. These polymer chains could be further extended by subsequent polymerization of different monomers to get SiO₂/block copolymers hybrids such as SiO₂-*g*-(PS-*b*-PBA), SiO₂-*g*-(PMMA-*b*-PBA) and SiO₂-*g*-(PBA-*b*-PMMA). Ultrathin films of hybrid nanoparticles were examined using TEM (Figure 1.10) and atomic force microscopy (AFM), to characterize the impact of graft composition on the nanoscale morphology.



Scheme 1.8 Synthetic methodology to prepare hybrid nanoparticles by ATRP according to Pyun et al.¹²³



Figure 1.10 TEM images of SiO₂/polymer hybrid nanoparticle cast onto carbon-coated copper grids: (a) 2-bromoisobutyrate functionalized silica colloidal initiators; (b) SiO₂-g-PS₁₇₅ hybrid nanoparticles; (c) SiO₂-g-PBA₉₄ hybrid nanoparticles; (d) SiO₂-g-PMMA₁₇₅ hybrid nanoparticles. Scale bar = 200 nm.¹²³

Based on a similar process, several groups grafted different ATRP initiators on the surface of silica particles to get hybrid particles via the "grafting from" process. For instance, Carrot et al.¹²⁴ synthesized an ATRP initiator containing a silane function that could be condensed with silica nanoparticles. PBA-*g*-SiO₂ hybrid particles were then obtained following surface initiation ATRP of BA. El Harrak et al.¹²⁵ grafted 2-bromoisobutyrate bromide onto thiol-functionalized silica nanoparticles and discussed the colloidal stability after grafting of the initiator. First, thiol-functionalization of the surface was achieved via silanization with a mercaptopropyl triethoxysilane. Second, the overgrafting of the silica surface was performed through reaction of the thiol with 2-bromoisobutyryl bromide to generate the halogen-functional ATRP initiator. From that, the polymerization of styrene was conducted.

Yu et al.¹²⁶ synthesized silica/PS and silica/PS-*b* poly(methacryloxy propyl trimethoxysilane) hybrid particles via surface-initiated ATRP from silica nanoparticles and compared their

wettabilities which were determined by water contact angle and surface roughness measurements.

Lattuada et al.¹²⁷ used iron oxide nanoparticles synthesized at high temperature and carrying surface oleic acid ligands as a starting point for generation of a range of functionalized nanoparticles after ligand exchange. An ATRP initiator, namely 2-bromo-2-methyl propionic acid, was introduced at the surface of the particles. These ATRP-initiator-containing nanoparticles were then used to grow hydrophilic polymer chains such as poly(acrylic acid), poly(methacrylic acid), poly(2-hydroxyethyl methacrylate) and poly(dimethylaminoethyl methacrylate) using organic solvents such as dimethylformamide, dimethylsulfoxide or dichlorobenzene.

Pamela et al.^{128,129} reported a surface-initiated polymerization of MMA and S via ATRP from ordered mesoporous silica particles. They grafted a silylated alkyl bromide to the silica surface and then performed the polymerization either in the presence or in the absence of free initiator ethyl-2- bromoisobutyrate in toluene.

Berge et al.¹³⁰ used "grafting from"/"grafting to" ATRP approaches to generate interesting Janus hybrid particles. As shown in Scheme 1.9, silica particles were first modified with 3-aminopropyltriethoxysilane (APS) and then used to stabilize wax droplet. An ATRP-initiator was then immobilized onto the part of the surface without protection. The first polymer, either poly(tert-butyl acrylate) (PtBA) or poly(N-isopropylacrylamide) (PNIPAM), was immobilized on one side of silica particles using surface ATRP "grafting from" approach. After dissolving the wax, the second polymer poly(2-vinylpyridine) (P2VP) was immobilized using the "grafting to" method by reaction between reactive end groups of polymer chains and functional groups on the particle surface. The authors also showed that the obtained bicomponent Janus particles (Figure 1.11) are stimuli-responsive and changes in pH resulted in the formation of hierarchically structured aggregates of the Janus particles.



Scheme 1.9 Scheme of the synthesis of bicomponent Janus particles by "grafting from" and "grafting to" approaches. The bare silica particles are coated by APS, assembled around wax colloidosomes and selectively modified by ATRP initiator at one side (upper panel). The first polymer (PtBA or PNIPAM) is grafted by surface-initiated ATRP. The carboxyl-terminated second polymer (P2VP) is grafted to free amino groups on silica particles by the "grafting to" approach.¹³⁰



Figure 1.11 SEM images of the PtBA-*b*-P2VP Janus particles. The P2VP-modified area is enclosed by a dashed line.¹³⁰

5.1.2 RAFT

Several methods of polymer grafting via the RAFT process including the "grafting from", "grafting to" and "grafting through" methods have been reported Among them, the "grafting from" and "grafting through" methods allow monomer molecules to easily diffuse to the surface of the particles, allowing higher grafting density and better control of the molar masses and dispersity of the polymer chains.^{131,132}

Chinthamanipeta et al.¹³² synthesized well-defined PMMA/silica nanocomposites via "grafting through" using the RAFT process. As illustrated in Scheme 1.10, methacrylate-functionalized colloidal silica nanoparticles were first obtained by grafting of 3-methacryloxy propyl dimethyl chlorosilane. Then the polymerization of MMA was carried out by using 4-cyano-4-(dodecylsulfanylthiocarbonyl) sulfanyl pentanoic acid (DCT) as RAFT agent leading to PMMA/silica nanocomposites with some free PMMA chains.



Scheme 1.10 Scheme for synthesis of PMMA/SiO₂ nanoparticles via grafting through using the RAFT process.¹³²

Hojjati et al.¹³³ used the "grafting from" RAFT process to obtain polymer- TiO_2 hybrid particles. The authors grew PMMA chains from solid surfaces of TiO_2 nanoparticles using

DCT as RAFT agent to form $TiO_2/PMMA$ nanocomposites. The kinetics of graft polymerization of MMA from the surface of TiO_2 was studied with two different surface densities, and it was found that the rate of reaction decreased with increasing surface density of RAFT agent anchored to the nanoparticles.

Ngo et al.¹³⁴ also used a similar process to form polymer-TiO₂ hybrid particles. In their work, 3-(trimethoxysilyl)propyl methacrylate (MPS) was used as a coupling agent to anchor the polymer chains on the inorganic surface. Core-shell TiO₂-polymers were prepared. MMA and a methacrylic monomer containing a hydrolytically labile bond such as tert-butyl dimethylsilyl methacrylate (MASi) were grafted on the nanoparticle surface. The grafting efficiency of PMMA through the surface of TiO₂ nanoparticles was 5 times less than the one obtained by Hojjati et al.¹³³ TGA measurements showed that grafted PMMA and PMASi were accounted for 10% and 4.8% of the particle mass, respectively.

In addition, various polymers such as PAA,¹³⁵ PS,¹³⁶⁻¹³⁸ PMMA,¹³⁹⁻¹⁴² and PNIPAM¹⁴³ have been successfully "grafted from" different inorganic surfaces via the RAFT process including titanium dioxide, silicate substrates, cadmium selenide, gold nanoparticles, palygorskite and carbon nanotubes.

5.1.3 NMP

Numerous functional alkoxyamines have been designed to graft polymer chains from the surface of silica particles using NMP. These alkoxyamines are based on trichlorosilane (SiCl₃), triethoxysilane (Si(OEt)₃) or trimethoxysilane (Si(OMe)₃) functional groups.¹⁴⁴⁻¹⁴⁶

For instance, in Blomberg's work,¹⁴⁷ the "grafting from" NMP was used to form silica/PS hybrid particles. In order to graft a functional alkoxyamine on the surface of the silica particles, a surface-active alkoxyamine with trichlorosilane was designed based on the alkoxyamine SG1. After grafting the alkoxyamine on the silica surface, S was introduced to obtain polymer brush-modified nanoparticles. Capsules were formed by crosslinking the PS brushes grown from the silica surface, either thermally by the incorporation of benzocyclobutene monomer or chemically by the reaction of maleic anhydride repeat units with a diamino crosslinker, followed by subsequent dissolution of the silica core.

Alkoxyamines were also synthesized *in situ* at the surface of silica nanoparticles to prepare PS-grafted silica nanoparticles by NMP of styrene.¹⁴⁵ As shown in Scheme 1.11, two routes

were investigated to graft the alkoxyamine initiator onto silica. In the first route, (acryloxypropyl)trimethoxysilane (APTMS) was covalently attached to silica and the alkoxylamine was formed *in situ* by spin trapping the acryloxy radicals produced by reaction of azobisisobutyronitrile (AIBN) with the grafted APTMS molecules using SG1 as radical trap. In the second route, the surface alkoxyamine initiator was produced in a one-step process by reacting simultaneously SG1, AIBN, and APTMS in the presence of silica.



Scheme 1.11 Reaction scheme for covalent bonding of the SG1-based alkoxyamine initiator onto silica and subsequent grafting of PS from the functionalized silica surface.¹⁴⁵

Parvole et al.¹⁴⁸⁻¹⁵⁰ also used the surface-initiated NMP strategy to grow poly(n-butyl acrylate) (PBA) and poly(ethyl acrylate) (PEA) brushes from azo-grafted silica surfaces by adding SG1, which acts as a chain growth moderator (so-called bimolecular polymerization system).

Ladmiral et al.¹⁵¹ anchored a TEMPO-based functional alkoxyamine (with triethoxysilane) on the surface of monodisperse zinc sulfide (ZnS) nanoparticles coated with a thin layer of silica. Controlled PS brushes were then grown on the particle surface to get ZnS@SiO₂/PS hybrid particles (Scheme 1.12). Hollow spheres constituted of a silica shell with well-defined, high-density PS brushes were then synthesized by selective dissolution of the ZnS core (Figure 1.12).



TAA: Thioacetamide TEOS: Tetraethoxysilane PVP: Poly(vinylpyrrolidone) PPE: 2,2,6,6-tetramethyl-1-(1-phenyl-2-(5 (triethoxysilyl)pentyloxy)ethoxy)piperidine

Scheme 1.12 Schematic representation for the synthesis of ZnS@SiO₂–PS particles by surface-initiated NMP of styrene.¹⁵¹



Figure 1.12 (a) TEM and (b) SEM images of $ZnS@SiO_2$ particles coated with a PS brush ($M_n = 64\ 200\ g\ mol^{-1}$), (c) hollow particle after selective dissolution of the ZnS core.¹⁵¹

Vinas et al.¹⁵² described the preparation of a BlocBuilder[®] derivative with an N-succinimidyl ester (MAMA–NHS, Figure 1.13), which was shown to be an excellent initiator for NMP and allowed the formation of well-defined polymers. This MAMA–NHS initiator can be particularly convenient for the post-functionalization of polymer chain ends. Recently, Chevigny et al.¹⁵³ successfully used this alkoxyamine to graft polymer chains onto primary amine-coated silica particles.



Figure 1.13 a) Initiator MAMA-SG1 (BlocBuilder[®]) and b) activated ester MAMA-NHS.¹⁵³

Charleux and co-workers¹⁵⁴ also employed the same MAMA-NHS alkoxyamine for the grafting of a variety of polymer chains (PS, PBA or PMMA) by the "grafting to" method onto primary-amine functionalized Stöber silica particles under mild conditions in different solvents including THF, DMSO and toluene. To increase the grafting density in simple experimental conditions, a direct one-step method was proposed as shown in Scheme 1.13. Core-shell particles with different thickness of the PS layer were obtained (Figure 1.14)



Scheme 1.13 Schematic representation of the grafting techniques involving the MAMA-NHS alkoxyamine: (a) "grafting to" and (b) "one-step" strategies. ($R_1 = H$ or CH_3 , $R_2 = COOCH_3$, $COOC_4H_9$, or C_6H_5).¹⁵⁴



Figure 1.14 One-step synthesis of grafted polymer chains onto primary amine-coated silica particles by NMP using a NHS-bearing alkoxyamine based on SG1: TEM pictures of the Stöber silica particles grafted with PS layer thickness of 5 nm (a), 15 nm (b) and 25 nm (c). ¹⁵⁴

Jiang et al.¹⁵⁵ reported a route to get interesting mixed P*t*BA/PS brush-grafted silica particles with high grafting density. Both ATRP and NMP were used in the process. As shown in Scheme 1.14, a triethoxysilane-terminated Y-shape initiator was immobilized onto bare silica particles. P*t*BA brush-grafted silica was first obtained via surface ATRP of *t*BA, followed by surface-initiated NMP of S. Mixed P*t*BA/PS brushes were thus grafted on the silica particles. The composites showed different morphologies when the molecular ratio of the two brushes was varied (Figure 1.15).



Scheme 1.14 Schematic illustration for the synthesis of high grafting density mixed PtBA/PS brushes with a fixed PtBA M_n and various PS molar masses by sequential ATRP and NMP from Y-initiator-functionalized silica particles.¹⁵⁵



Figure 1.15 Top-view bright field TEM micrographs of (A) $D_PPS/D_PPtBA = 0.59$, (B) $D_PPS/D_PPtBA = 0.90$, (C) $D_PPS/D_PPtBA = 1.31$, (D) $D_PPS/D_PPtBA = 1.70$, and (E) $D_PPS/D_PPtBA = 1.88$, after being cast from a CHCl₃ dispersion and annealed with CHCl₃ vapor (CHCl₃ is a good solvent for both PtBA and PS). The samples were stained with RuO₄ vapor at room temperature for 20 min. The inset in each TEM micrograph shows the enlarged area marked by the long white arrow.¹⁵⁵

The "grafting from" approach by NMP was also applied to a variety of inorganic materials such as titanium oxide (TiO₂), iron oxide nanoparticles (Fe₃O₄ or γ -Fe₂O₃) and Laponite clay platelets.

For instance, Matsuno et al.¹⁵⁶⁻¹⁵⁸ grafted TiO₂ with PS from the 4-methoxy-TEMPO-based alkoxyamine initiator whose phosphoric acid group can be absorbed on the surface of TiO₂. They also grafted Fe₃O₄ nanoparticles with PS by using the same surface-active alkoxyamine. Chen et al.¹⁵⁹ graft P4VP on the surface of Fe₃O₄ nanoparticles after modification with MPS. Binder et al.¹⁶⁰ prepared core-shell γ -Fe₂O₃ nanoparticles with a well-defined PNIPAM shell by surface initiated NMP.

Recently, Robbes et al.¹⁶¹ reported an efficient multi-step "grafting from" NMP to obtain PS/γ -Fe₂O₃ composites. After modification of the surface charges of the nanoparticles and

solvent exchange in dimethylacetamide (DMA_C), aminopropyltriethoxysilane (APTES) was grafted on the surface and further reacted with the MAMA-NHS alkoxyamine, which allowed the controlled polymerization of S from the surface.



Scheme 1.15 Scheme for grafting: the surface charge modification [I], solvent transfer [II], silanization [III], the over-grafting of the initiator [IV] and the polymerization from the particles surface [V].¹⁶¹

Konn et al.¹⁶² incorporated a SG1-based alkoxyamine terminated with an ammonium group (so called quaternary ammonium alkoxyamine initiator) onto Laponite clay platelets by ion exchange (Scheme 1.16). Well-defined PS chains were then grown from the Laponite surface in the presence of a sacrificial alkoxyamine initiator. The experiments carried out with and without clay platelets exhibited similar kinetics behaviors indicating that the inorganic part did not affect the livingness of the polymerization. The resulting PS-functionalized clay particles could be well dispersed in organic solution.



Scheme 1.16 Illustration of the intercalation of the quaternary ammonium alkoxyamine initiator (1) into Laponite by cation exchange and the subsequent formation of ionically-bonded PS chains by surface-initiated NMP of styrene using a sacrificial alkoxyamine initiator.¹⁶²

Datsyuk et al.¹⁶³ reported an *in situ* NMP of MMA onto double-wall carbon nanotubes (DWCNTs) using a two-step process. The main advantage of this two-step synthetic route is that it does not involve any CNT pre-treatment or functionalization. As illustrated in Scheme 1.17, short PAA chains were first polymerized *in situ* in the presence of NMP initiator. A pre-composite (DWCNT-PAA) was thus obtained. In the second step, the presence of the stable nitroxide radical on the CNT surface made it possible to reinitiate the polymerization of different monomers. Composite particles, namely DWCNT-PAA-PMA and DWCNT-PAA-PS were successfully obtained with CNT contents varying between 0.3 and 4.7 wt%. The same procedure was applied later to the grafting of PAA-PMA or PAA-PS to multiwall carbon nanotubes (MWCNTs) and DWCNTs resulting in enhanced electrical conductivities.¹⁶⁴ Extrapolation to emulsion polymerization was also briefly reported in this article.



Scheme 1.17 Schematic illustration of the two steps synthetic process for the elaboration of CNTs-based composite materials.

5.2 Organic/inorganic hybrids via CRP in aqueous media

Compared with non-aqueous CRP systems, works reporting the synthesis of organic/inorganic hybrids via CRP in aqueous media are relatively scarce, most of them focusing on ATRP³¹ or RAFT.²⁵

5.2.1 ATRP

Armes and co-workers investigated the grafting of silica particles with methacrylate-based polymers by aqueous ATRP.¹⁶⁵⁻¹⁶⁹ As shown in Scheme 1.18, the nano-silica particles were first turned into ATRP initiators after reaction with 3-(dimethylethoxysilyl)propyl-2-bromoisobutyrate in ethanol at 20 °C. Then the surface-initiated ATRP of PEOMA and 2-(N-morpholino) ethyl methacrylate was performed in water at 20 °C for 3h to get well-defined, polymer-grafted silica particles.



Scheme 1.18 Reaction scheme for the synthesis of polymer-grafted silica particles via aqueous ATRP.¹⁶⁶

Hu et al.¹⁷⁰ used a 4-[(chloromethyl)phenyl] trichlorosilane to modify the surface of oleicacid-stabilized iron oxide nanoparticles and then graft an ATRP initiator. A methacrylate macromonomer based on poly(ethylene glycol) (PEOMA) was then polymerized in water after a short sonication step. Polymerization was performed at 35 °C using CuCl as a Cu (I) source and bipyridine as a ligand.

5.2.2 RAFT

Nguyen et al.^{171,172} developed a method for the encapsulation of solid particulate materials with living amphiphilic copolymers acting as stabilizer of inorganic pigments. The authors used low molar mass (M_n lower than 2000 g mol⁻¹) P(AA-*co*-BA) or P(MAA-*co*-BA-*co*-MAA) amphiphilic copolymers obtained by RAFT copolymerization of BA and AA or MAA, BA and MMA in dioxane respectively. These copolymers or macroRAFT agents carried a thiocarbonyl thio end-group. TiO₂ particles were first well dispersed in water with the low molar mass copolymers through a sonication step. Then the encapsulation was performed at 70 °C with a slow monomer feeding emulsion process. The mixture of hydrophobic monomers was MMA and BA. The living ends of the macroRAFT agents allowed further growth by adding hydrophobic monomer units. The hydrophilic part of the newly formed block copolymers was pulled out towards the aqueous phase. Finally, a very nice TiO₂ encapsulation was obtained (size around 365 nm), as shown in Figure 1.16.



Figure 1.16 Encapsulated TiO_2 pigment particles with a P(BA-*co*-MMA) shell using poly(AA₁₀-*co*-BA₅) macroRAFT agent as both stabilizer and control agent of the emulsion polymerization.¹⁷¹

Daigle et al.¹⁷³ reported a general method for the synthesis of hybrid core–shell nanoparticles by using a very similar process. Instead of a copolymer incorporating hydrophobic and hydrophilic units, the authors used PAA macroRAFT agents obtained by RAFT polymerization of AA performed in ethanol and using a trithiocarbonate as a control agent.⁴⁴ The PAA macroRAFT agent was used to stabilize and disperse in water a range of inorganic compounds including oxides: BaTiO₃, TiO₂ (rutile and anatase), Al₂O₃, CuO and ZrO₂, metals (Zn, Mo) and nitrides (Si₃N₄). The polymerization of a hydrophobic monomer (styrene and/or BA) was then performed at 80 °C using ACPA as a water-soluble initiator (Figure 1.17). Compared with Nguyen's work,¹⁵³ this strategy required the use of additional surfactant (sodium dodecyl sulfate) in order to minimize secondary nucleation induced by the presence of PAA in water. Besides, the high M_n and large MMD (D = 2.2) indicated that the polymerization was not really under control.



Figure 1.17 (a) BaTiO₃, (b) TiO₂, and (c) Al_2O_3 encapsulated with a PS shell using PAA macroRAFT agent as dispersant.¹⁷³

Ali et al.¹⁷⁴ extended Nguyen's strategy to the encapsulation of gibbsite as a model plateletlike colloidal inorganic substrate. Cationically charged gibbsite platelets were first coated with anionically charged P(AA-*co*-BA) macroRAFT agents. A mixture of MMA and BA was then fed to allow chain extension of the macroRAFT agents and formation of a polymer shell around the clay platelets as illustrated in Scheme 1.19 and Figure 1.18.



Scheme 1.19 Schematic representation of the synthesis of anisotropic polymer/gibbsite nanocomposite latex particles by aqueous starved feed emulsion polymerization with the use of RAFT copolymers as stabilizers.¹⁷⁴



Figure 1.18 Encapsulated gibbsite with P(MMA-co-BA) shell using (a) $P(AA_{10}-co-BA_5)$, (b) $poly(AA_{10}-co-BA_{2.5})$, (c) $poly(AA_{10}-co-BA_{7.5})$, and (d) $poly(AA_5-co-BA_5)$ macroRAFT agents as dispersants.¹⁷⁴

As reported by Zhong et al.,¹⁷⁵ this method was then extended to the encapsulation of noncovalently modified carbon nanotubes with three different macro-RAFT copolymer dispersants: P(AA-co-BA), PAA and P(S-co-AA) (Figure 1.19). All the three dispersants led to equally successful encapsulations of the nanotubes.



Figure 1.19 Schematic representation and TEM image of the encapsulation of CNT in aqueous medium by RAFT polymerization.¹⁷⁵

Later, Nguyen et al.¹⁷⁶ reported a method to synthesise polymer-coated COOH-functionalized multiwalled carbon nanotubes (MWCNTs). As illustrated in Scheme 1.20, the stabilizing charge on the surface of the COOH-functionalized MWCNTs was first changed from negative to positive by the adsorption of poly(allylamine hydrochloride) (PAH). An amphiphilic macroRAFT copolymer (P[(4-styrenesulfonic acid)-*co*-(acrylic acid)-*co*-(butyl acrylate)]) was then adsorbed onto the surface and used as both stabilizer and controlling agent. Subsequent emulsion polymerization then resulted in a uniform coating of the tubes with MMA and BA copolymers.



Scheme 1.20 Alternative adsorption of positively charged PAH and negatively charged macro-RAFT copolymer onto negatively charged COOH-functionalized MWCNTs.¹⁷⁶

Very recently, Zgheib et al.¹⁷⁷ synthesized organic/inorganic latexes encapsulating CeO₂ nanoparticles via RAFT-mediated surfactant-free emulsion polymerization by taking advantage of the strong interaction between carboxylic acid groups of macroRAFT agents and CeO₂. The CeO₂ nanoparticles were coated with two types of macroRAFT agents (PAA-CTPPA and P(AA-*co*-BA)-CTPPA) (Scheme 1.21) and then used in the emulsion polymerization of hydrophobic monomer(s) (BA alone or a mixture of MMA and BA) to form the encapsulating shell. The use of PAA₃₈–CTPPA-coated CeO₂ in MMA–BA (80/20 wt ratio) emulsion polymerization or P(AA₁₁-co-BA₁₁)–CTPPA-coated CeO₂ in BA emulsion polymerization both led to unsuccessful encapsulation owing to a poor affinity between the modified surface of CeO₂ and the monomer(s) to polymerize. In contrast, emulsion polymerization of MMA–BA (either 80/20 or 50/50 wt ratio) in the presence of P(AA₁₁-*co*-BA₁₁)–CTPPA-coated CeO₂ led to an effective encapsulation as shown in Figure 1.20.



Scheme 1.21 Illustration of the aggregation state of CeO₂ nanoclusters after the adsorption of either PAA₃₈–CTPPA or P(AA₁₁-*co*-BA₁₁)–CTPPA.¹⁷⁷



Figure 1.20 Cryo-TEM images of the latex particles obtained after emulsion polymerization of hydrophobic monomer(s) in the presence of CeO₂ nanoclusters coated with macroRAFT agents: (a): P(AA₁₁-*co*-BA₁₁)–CTPPA and MMA–BA 80/20 (wt/wt); (b): P(AA₁₁-*co*-BA₁₁)–CTPPA and MMA–BA 50/50.¹⁷⁷

A similar process was employed by Warnant¹⁷⁸ and Garnier.^{179,180} Cerium oxide-based hybrid latexes were successfully achieved both with a phosphonated macro-RAFT agent (poly(vinylbenzylphosphonic diacid-*co*-S) RAFT agent)¹⁷⁸ and amphiphatic sulfonated macro-RAFT agents: (poly(BA-*co*-AMPS) and poly(BA-*co*-AA-*co*-AMPS) macro-RAFT agents).¹⁸⁰

Hartmann's team^{181,182} reported a controlled growth of polymer chains from the surface of clay platelets (sodium montmorillonite clay (i.e. MMT clay containing primarily Na⁺ ions in the interlayer space)) that were modified with *N*,*N*-dimethyl-*N*-(4-((((phenylcarbonothioyl) thio) methyl) benzyl) ethanammonium (PCDBAB) or *N*-(4-((((dodecylthio)carbonothioyl) thio) methyl) benzyl)-*N*,*N*-dimethylethanammonium (DCTBAB). They used a surface-active RAFT agent and performed miniemulsion polymerization of styrene at 75 °C with hexadecane as a hydrophobe, SDS as a surfactant and AIBN as an initiator. The miniemulsion polymerization process resulted in polymers with decreasing molar mass and low dispersity as the RAFT concentration increased.

6. Polymer/SiO₂ hybrid latexes obtained by conventional emulsion polymerization

Apart from controlled radical polymerization, organic/inorganic latexes can also be elaborated by conventional radical polymerization as recently reviewed.¹⁸³ A large variety of polymer/inorganic particles have been reported by varying the nature of both the polymer and the inorganic materials but silica remains the inorganic particles the most widely studied. To form polymer/silica hybrid latexes in conventional emulsion polymerization, four main strategies depicted in the following sections can be used.

6.1 Silica particles functionalized by γ-methacryloxy propyl trimethoxysilane (γ-MPS)

In the early 1990s, Espiard et al.¹⁸⁴⁻¹⁸⁶ reported the encapsulation of silica particles through emulsion polymerization by using γ -MPS as coupling agent. In this now widely applied strategy, the silica particles are first modified with γ -MPS. As shown in Figure 1.21, PS/silica particles with different morphologies could be then obtained via emulsion polymerization performed in the presence of such functionalized silica particles.^{183,187-191} The density of the

coupling agent and the silica seed diameter had a strong influence on the particle morphology.



Figure 1.21 Left: Silica/PS composite particles elaborated through emulsion polymerization using γ -MPS as silane coupling agent. Right: TEM images of some these particles reproduced (a) from,¹⁸⁷ (scale bars: 200 nm), (b) from,¹⁸⁸ (c) from,¹⁸⁹ and (d) from^{190,183}

6.2 Macromonomer-mediated synthesis of polymer-silica colloidal clusters

Besides the silane coupling agent, chemical modification of silica particles can also be performed by adsorbing some macromonomers. Reculusa et al. reported the synthesis of raspberry-like silica/PS particles after silica modification with a PEO-based macromonomer (PEOMA).¹⁹² The ethylene oxide units of the macromonomer built strong cooperative hydrogen bonding interactions with the surface silanols. Through copolymerization with the methacrylate group of the macromonomer, PS nodules were anchored on the silica surface (Figure 1.22). The morphology strongly depends on the ratio between the number and size of silica seeds and the number and size of growing nodules. Raspberry-like, snowman-like or multipod-like colloids were obtained by varying these respective factors.^{193,194} But, in contrast to γ -MPS, which forms strong covalent bonds with the silica surface, PEO-based macromonomers display only weak interactions.



Figure 1.22 Left: Elaboration of silica/PS raspberry-like colloids through emulsion polymerization using a methyl methacrylate (MMA)-terminated poly(ethylene oxide) macromonomer (PEOMA) as coupling agent. Right: SEM and TEM pictures of the raspberry-like particles.¹⁸³

6.3 Auxiliary comonomers

This strategy is based on the strong interaction between auxiliary comonomers and the surface of silica. For example, the pyridine group of 4VP displays acid-base interactions with the silanol groups of silica. Armes and coworkers first reported the synthesis of colloidal dispersions of polymer/silica nanocomposite particles in high yield by homopolymerization of 4VP in the presence of ultrafine silica particles (less than 20 nm).¹⁹⁵ In addition to vinylpyridine monomers (2VP and 4VP), 1-vinyl imidazole (1VID) (Figure 1.23) and 2-(methacryloyl) ethyl trimethyl ammonium chloride (MTC) were also shown to be efficient auxiliary comonomers.^{196,197}



Figure 1.23 *Left*: Reaction scheme for the formation of silica/PMMA raspberry-like colloids prepared using 1VID as auxiliary comonomer. *Right*: TEM images of obtained nanocomposite particles.¹⁹⁷

6.4 Cationic Initiators

Another efficient route to the formation of polymer/silica composite latexes is through electrostatic interactions. For instance, cationic initiators can strongly adsorb on the anionic surface of silica particles. As illustrated in Scheme 1.22, Luna-Xavier et al.¹⁹⁸⁻²⁰⁰ first described the synthesis of silica/PMMA nanocomposite latexes by emulsion polymerization using 2,2'-azobis (2-amidinopropane) dihydrochloride (AIBA) in combination with a nonionic polyoxyethylenic surfactant (NP₃₀). Many factors can influence particle morphology, such as the suspension pH, the type of monomer, the silica size and concentration, and the initiator concentration. Recently, Parvole et al.²⁰¹ reported a novel original synthetic route to hybrid dissymmetrical snowman- and dumbbell-like silica/polymer colloidal particles through emulsion polymerization of methyl methacrylate (MMA) or styrene using а bicationic initiator 2,2'-azobis(N,N'-dimethyleneisobutyramidine) dihydrochloride (ADIBA) previously anchored on the silica surface (Figure 1.24).



Scheme 1.22 Schematic representation of the polymerization reaction initiated with AIBA at the surface of silica beads in combination with a non-ionic surfactant.¹⁹⁸



Figure 1.24 Hybrid dissymmetrical snowman- and dumbbell-like silica/polymer colloidal particles synthesized by emulsion polymerization using a surface-adsorbed cationic initiator.²⁰¹

Conclusions

As mentioned in the beginning of this chapter, the leading actor of this story is NMP. Compared with ATRP and RAFT, it has some drawbacks such as the range of controllable monomers, the polymerization temperature or the chain-end functionalization. However, as the first CRP method to be developed, NMP has always been considered to be the simplest method with unquestionable advantages such as thermal activation, good control, no purifications, except a simple precipitation to remove unreacted monomer, and no environmental issues. In the last 15 years, a lot of work has been done to solve the main weaknesses of NMP, or at least minimize them. NMP has now become a much more mature CRP technique. So, it is no doubt that with the advantage and development of NMP, there will be more and more NMP-derived materials in many fields, such as organic/inorganic hybrid materials.

Recently, a lot of work has been done to form hybrid particles via CRP methods. ATRP, RAFT and NMP were proved to be successfully performed in non-aqueous media using the so-called "grafting from", "grafting to" and "grafting through" techniques. ATRP and RAFT were also performed in aqueous media. While ATRP was mainly used to graft hydrophilic polymers onto inorganic colloidal particles, the RAFT process was employed to encapsulate inorganic pigments. The strategy relies on the adsorption of low molar mass amphiphilic macroRAFT agents to encourage the emulsion polymerization to occur at the inorganic surface upon chain extension with hydrophobic monomers. Hybrid latexes with encapsulated morphologies were successfully achieved by this method. However, as far as we know, there is no report describing the synthesis of hybrid particles by NMP using a similar approach.

In this work, we will explore the synthesis of polymer/silica hybrid latexes via NMP emulsion polymerization under mild conditions. Water-soluble brush-type macroalkoxyamine initiators based on poly(ethylene glycol) methyl ether methacrylate (PEOMA) or copolymers of PEOMA with methacrylic acid (MAA) will be synthesized for that purpose. PEO are known to adsorb onto silica through strong cooperative hydrogen bonding interactions between the ether oxygen groups of PEO and the silanol groups of silica. The incorporation of MAA units in the copolymers will allow us to further tune the lower critical solution temperature (LCST) of the macroinitiator by varying the suspension pH. We expect to influence likewise the polymerization behavior and the control of particle morphology. These macroalkoxyamine initiators will be further chain-extended with hydrophobic monomers in

aqueous emulsion either in the absence or in the presence of silica to generate particles composed of self-assembled block copolymer or composite latexes, respectively. The effects of pH, salt concentration and silica particle size on the polymerization kinetics, the control over polymerization and the final particle morphology will be investigated for both series of macroalkoxyamines.

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Chapter 2. Synthesis of silica particles

Introduction

Silica has been the focus of the majority of studies on oxide-based nanostructured materials. One of the major reasons for this is its easy processability, high chemical inertness and exceptional colloidal stability. Moreover, silica can be processed as a thin film with controllable porosity and optical transparency. All these properties make silica ideal for use in model systems, and it is widely used in many industrial areas ranging from paints and drug delivery to composite materials.¹

In this chapter, we will first provide an overview of the most important methods available to synthesize monodisperse silica nanoparticles. We will emphasize in particular the effects of reaction parameters and processing conditions on the control of silica particle size and morphology. Some general considerations on the surface chemistry of silica and their surface modification with organosilane molecules and/or polymers will be also briefly introduced.

Based on this bibliographic review, three methods have been selected to synthesize silica nanoparticles of controlled sizes and narrow size distributions: the "Stöber process",² the two-phase amino acid catalyzed process,³ and the seed regrowth process. The three synthetic routes have been explored and compared in section 2. With the purpose of introducing functional groups at the silica surface, we also explored the grafting of an organosilane molecule, namely γ -methacryloxy propyl trimethoxysilane (γ -MPS) in aqueous media using the two-phase amino acid catalyzed method. Hybrid silica spheres and mesoporous silica particles have been obtained using this strategy. The results are reported in section 3.

1. Bibliographic review

1.1 Generalities on silica

Silica or silicon dioxide (SiO_2) is one of the most abundant materials in the earth's crust and exists with different crystalline forms and amorphous states. Silica is an important component for the manufacture of glasses, optical instruments, refractory materials and for the electronic industry. Consequently, considerable attention has been paid to the synthesis, functionalization and properties of silica both in industry and in academic research.



Figure 2.1 Basic structural unit of SiO₂.

As shown in Figure 2.1, the basic structural unit for SiO₂, which is also the fundamental building block of all silicate materials, is the silicon oxygen tetrahedron. It consists in a central silicon atom surrounded by 4 oxygen atoms. In each of the most thermodynamically stable crystalline forms of silica, on average, all 4 of the vertices (or oxygen atoms) of the SiO₄ tetrahedra are shared with others, yielding the net chemical formula: SiO₂. SiO₂ has a number of distinct crystalline forms (quartz, trydimite, cristobalite, ...). All of the crystalline forms involve tetrahedral SiO₄ units linked together by shared vertices in different arrangements, excepted stishovite and fibrous silica. Stishovite silica has a rutile-like structure where silicon is 6 coordinate and fibrous silica has a structure similar to that of SiS₂ with chains of edge-sharing SiO₄ tetrahedra.^{4,5}

Generally, silica nanoparticles are composed of amorphous silica and can be divided in two categories: silica nanopowders (e.g., fumed silica and precipitated silica) and colloidal silica suspensions. Silica nanopowders are mainly produced by the pyrolysis and precipitation methods in industry. *Fumed silica* (also called pyrogenic silica) is a fine, white, odorless, and tasteless amorphous powder. Pyrogenic silica is extensively used as filler and thickening agent in a variety of products for food industry, paints and adhesives. It is also frequently added to cosmetics and toothpastes due to its respective light diffusing and mild abrasive qualities. It is manufactured by a high-temperature vapor process in which SiCl₄ is hydrolyzed in a flame of oxygen-hydrogen according to the following reaction (eq. 2.1):⁶

$$SiCl_4 + 2H_2 + O_2 \rightarrow SiO_2 + 4HCl \qquad (eq. 2.1)$$

The production of *precipitated silica* starts with the reaction of an alkaline silicate solution with a mineral acid. Sulfuric acid and sodium silicate solutions are added simultaneously to water under agitation. Precipitation is carried out under alkaline conditions. The choice of agitation, duration of precipitation, the addition rate of reactants, temperature, pH and

concentration can all influence the properties of silica. For instance, the formation of a gel stage is avoided by stirring at elevated temperatures. The resulting white precipitate is filtered, washed and dried in the manufacturing process.⁷

$$Na_2O(SiO_2)_{3.3} + H_2SO_4 \rightarrow 3.3SiO_2 + Na_2SiO_4 + H_2O$$
 (eq. 2.2)

The washing and drying process can also affect the characteristics of the particles. Particle size, porosity and density can all be manipulated this way to some extent. Manufactures can prepare precipitated silica in a number of ways depending on its intended use by the customers. Precipitated silica are used in a number of applications including the food industry, pharmaceuticals and the rubber or plastic industries where they are used as additives to improve characteristics such as flexibility and durability or act as reinforcing fillers to rubber products.

Colloidal silicas are suspensions of fine amorphous, non porous, and typically spherical silica particles in a liquid phase. Usually they are suspended in an aqueous phase and are stabilized electrostatically. Colloidal silica particles are most often obtained by the sol-gel process.⁸ The sol-gel process is a versatile wet chemical method for producing solid materials.⁹ The method is used for the fabrication of metal oxides, especially the oxides of silicon and titanium. This technique involves the transition of a system from a colloidal liquid (named sol) into a solid gel phase. The precursors (typically metal alkoxides or metal salts) in the solution evolve gradually to form a gel-like three-dimensional network containing both a liquid phase and a solid phase.

The reaction is generally divided into two steps as illustrated below for tetraethoxysilane (TEOS), which is the main precursor for the synthesis of silicon dioxide:

1) Hydrolysis of TEOS to produce hydroxyl groups in the presence of small amounts of water. Usually, a mutual solvent such as alcohol is used as homogenizing agent because water and alkoxides are immiscible. The alkoxide groups (OC_2H_5) are progressively replaced by hydroxyl groups (OH) with the concomitant formation of ethanol.

$$-Si - OEt + HOH - Si - OH + EtOH (eq. 2.3)$$

2) The polycondensation reaction occurs simultaneously to the hydrolysis. The polycondensation reaction involves hydroxyl groups and residual alkoxy groups to form a three-dimensional network through the release of water (equation 4) or ethanol (equation 5).



A simplified representation of the overall process is shown in Figure 2.2.



Figure 2.2 Simplified representation of TEOS hydrolysis and condensation reactions during the sol-gel process (from Wikipedia).

Several chemical aspects play an important role in the sol-gel process. The chemical reactivity of metal alkoxides towards hydrolysis and condensation depends mainly on the electronegativity of the metal atom, its ability to increase the coordination number, the steric hindrance of the alkoxy group and on the molecular structure of the metal alkoxides (monomeric or oligomeric). The amount of added water in the hydrolysis step and how the water is added determine whether the metal alkoxides are completely hydrolyzed or not and which oligomeric intermediate species are formed.

Several techniques have been developed for colloidal silica formation based on the sol-gel process, such as the Stöber process, the amino acid-catalyzed synthesis of silica in a twophase process ³ and the microemulsion process.¹⁰ Considering the ease of implementation and the impact on the environment, the Stöber process is the most widely used to get colloidal silica nanoparticles.^{11,12} In this process, colloidal silica spheres are prepared by the hydrolysis and condensation reaction of tetraethyl orthosilicate in a water/ethanol mixture using ammonia as a base catalyst. Although various studies have been made on the Stöber method, the control of particle size and particle size distribution is still attracting much attention. Indeed controlling the size, size distribution and shape of silica particles with a high degree of precision and in a reproducible way remains a challenge. Among the large number of studies devoted to the control of silica particles size, the development of the "seed regrowth" technique is an outstanding achievement.^{13,14} The seed regrowth technique is based on the further growth of preformed silica particles used as seeds, by adding the silica precursor (e.g. TEOS). The size of the final particles depends on the amount of TEOS added to the seed dispersion and the size of the seed. The size of silica particles accessible by the Stöber process and by the seed regrowth method ranges from sub-micron to micrometers,15 but the preparation of monodisperse silica spheres with particles size below 50 nm was unsuccessful until the development of a novel two-phase method which is based on the use of amino acids as catalysts.³ All three techniques are described in more details in the following section.

1.2 Synthesis of monodisperse colloidal silica particles

1.2.1 The Stöber process

1.2.1.1 General description of the Stöber process

In 1968, Stöber and coworkers² reported a very simple and efficient method to synthesize monodisperse spherical silica particles by means of hydrolysis of a dilute solution of TEOS in

alcohol (e.g. methanol, ethanol, *n*-propanol or *n*-butanol) under basic conditions. This process first published by Kolbe in 1956,¹⁶ is known as the "Stöber process" and often considered as a pioneer work in the field.

In the "original" paper of Stöber, Fink and Bohn, the authors carefully examined the influence of different alkoxides and alcohols as well as the water and ammonia concentrations on the resulting particle size and size distribution. Usually the reaction is performed at room temperature but higher or lower temperature can also be applied.¹⁷

In general, particles will become larger when tetramethoxysilane is replaced by tetraethoxysilane. The same trend is observed when methanol is replaced by ethanol as the solvent, and/or when branched alkoxides (eg. *n*-propyl, *n*-butyl or *n*-pentyl) are used. However, in most cases, the concentration was kept around 0.2 mol L^{-1} since larger concentrations often led to non-spherical particles while smaller concentrations resulted in a lower amount of product.

The particles size is also strongly dependent on the ammonia and water concentrations as illustrated in Figure 2.3. Ammonia increases the reaction rate and promotes the formation of larger particles. Particles size also increases with increasing water concentration for low amount of water but excess water has the opposite effect as particle size then decreases with increasing water contents.



Figure 2.3 Final particle sizes as obtained by reacting 0.28 mol L^{-1} of TEOS with various concentrations of water and ammonia in ethanol.²

A few years later, Bogush et al.³ extended the work of Stöber and established empirical equations to fit their experimental data as follows:

$$D_p(nm) = A[H_2O]^2 exp(-B[H_2O]^{1/2})$$
 (eq. 2.6)

Where

$$A = [TEOS]^{1/2}(82 - 151[NH_3] + 1200[NH_3]^2 - 366[NH_3]^3)$$

and

$$\mathrm{B} = 1.05 - 0.523 [\mathrm{NH}_3] - 0.128 [\mathrm{NH}_3]^2$$

Equation 2.6 is however only valid for the following concentration ranges (in mole L^{-1}) at 25 °C: 0.1 < [TEOS] < 0.5, $0.5 < [H_2O] < 17$ and $0.5 < [NH_3] < 3$. Silica particles with diameters comprised between 20 and 800 nm and a narrow size distribution could be successfully obtained under those conditions.

Attempt to increase particle size with increasing the initial TEOS concentration was unsuccessful as this significantly increased the size distribution. Therefore a seeded growth technique was proposed to increase both the particle size and the solid content as will be illustrated later in section 1.2.1.3.

The Stöber process is usually performed in batch (also called one step process) or in semibatch (also called two-steps process) (Figure 2.4).¹⁸ In the batch process,¹⁹ the reactants (TEOS/H₂O/NH₄OH/EtOH) are initially charged into the reactor under stirring, and left to react for a certain period of time. The batch process has the advantage that high conversions can be reached by leaving the reactants in the reactor for long periods of time. In addition, it is simple and needs little supporting equipment. But it also has the disadvantages of high labor costs per unit production, and it is not efficient to obtain particles with a narrow size distribution as mentioned above. On the contrary, the semi-batch process^{19,20} in which a diluted TEOS solution (TEOS/EtOH) is slowly fed into a reactor containing water, ammonia and ethanol at a constant feed rate, allows a greater control over the resulting particle size, shape, and size distribution, because of the short nucleation time of this system. In addition, it has the advantages of good temperature control and good control of reaction rate because the reaction proceeds as reactants are added.



Mechanism for Stöber process

Figure 2.4 Batch and semi-batch Stöber processes.¹⁵

Figure 2.5 shows a typical SEM image of silica nanoparticles synthesized via the batch Stöber process with 0.17 M tetraethylorthosilicate (TEOS), 2.0 M ammonia and 6.0 M H_2O in ethanol.²¹



Figure 2.5 Typical SEM image of SiO₂ particles prepared via the Stöber method in batch. [TEOS] = 0.17 M, [H₂O] = 6.0 M and [NH₃] = 2.0 M.²¹

1.2.1.2 Nucleation and growth mechanism for the Stöber process

Several growth and formation mechanisms have been proposed for the synthesis of monodisperse Stöber silica particles. Two major models are usually considered: the La Mer model (also called the monomer addition growth model)²² and the aggregation/growth model.²³

In 1950, La Mer and Dinegar proposed a model based on classical nucleation theory, to qualitatively describe the kinetics of burst nucleation of non crystalline solids in solution.²² They proposed that, from a strong initial supersaturation, a rapid nucleation of particles would initially occur followed by the adsorption of diffusing atomic matter on the freshly nucleated particles. This model has been then widely used for qualitative interpretation of silica particles formation and growth, and proved useful in particular for understanding particle size and size distribution of silica particles made by the Stöber process.²⁴ Figure 2.6 shows how the La Mer model relates monomer concentration to reaction time.

In a homogeneous nucleation system in which no nuclei or particles are initially present, an energy barrier exists for nuclei generation,²⁵ which requires the monomer concentration to be higher than a critical value defined as C_{min} nu. Once this is achieved, the nucleation process starts, and monomers can either react with each other to generate new nuclei; or add to the surface of existing nuclei, leading to the growth of these nuclei.^{22,26} Both nucleus generation and growth consume monomers, leading to the decrease of monomer concentration in the system. When the monomer concentration decreases below C_{min} nu, nucleation stops; however, monomers continue to add to nuclei surfaces leading to growth of the particles until the monomer concentration drops below the equilibrium solubility of the monomer, $C_{s.}^{27,28}$



Reaction time

Figure 2.6 Nucleation model according to La Mer and Dinegar.²⁴

In this model, TEOS hydrolysis is the rate-determining step even for high water-to-TEOS ratios. The second reaction step, the condensation reaction was found to be faster by at least a factor of 3. Many experimental results are in favor of a LaMer type reaction mechanism. In particular the appearance of an induction period at the beginning of the reaction would indicate that it takes a certain time for the hydrolysis of TEOS to exceed the critical nucleation concentration of silicic acid in the solution, which is then followed by the precipitation of silica. However, there are also some experimental evidences that support an alternative mechanism called aggregation/growth model (Figure 2.7).

According to Bogush and Zukoshi,²³ the aggregation/growth model assumes that nanometersized silica particles (nuclei) are formed continuously during the hydrolysis and condensation of TEOS. These nuclei are colloidally unstable, and they will coagulate to form larger units. Above a critical aggregate size, they are stable. Further growth is accomplished by addition of subsequent primary nuclei to existing "particle" surface of the agglomerates. The number and size of these units will be determined not only by the reaction kinetics, but also by different parameters affecting the dispersion stability, like ionic strength of the solution, temperature, charges on the particles surface, pH and solvent properties (e.g. viscosity, dielectric constant, etc.).²⁹



Figure 2.7 Aggregation/growth model according to Bogush and Zukoski.²³

1.2.1.3 The seed regrowth process

The seed regrowth process (also called seed polymerization reaction), was developed to improve dispersity and size control (typically above 1 μ m) of silica particles by treating the

less controllable nucleation as a separate stage of formation of small seeds and then growing these seeds in well-defined conditions.¹³

The theoretical regrowth process is claimed to occur without formation of a new generation of silica particles,¹³ which means that TEOS hydrolysis and condensation reactions only happen on the preformed silica seeds.^{26,30} Once the size of the seeds is determined, the size of the final particles can be controlled precisely through the amount of seed introduced in the reactor and the amount of TEOS added to the seed dispersion. In seeded growth experiments where no new particles are formed, the seed particle diameter increases from the initial seed size, D_s , to the final size, D_f , according to the equation:

$$\left(\frac{D_f}{D_s}\right)^3 = \frac{W_s + W}{W_s}$$
 (eq. 2.7)

Where W_s is the weight of SiO₂ initially present as seeds and W is the amount of SiO₂ formed in the reaction mixture upon TEOS addition.

If regrowth conditions are unfavorable (e.g., the number of seeds is too small), new particles will be formed (also called secondary nucleation). Chen et al.²⁸ discussed the mechanism of the regrowth process under conditions where new particles are formed. Under given reaction conditions and total external surface area of seeds, the smaller the seed particles, the fewer the newly formed particles during seed growth. They also indicated that the early stages of growth of silica particles are controlled by diffusion of condensed species having electric charges, against an electrostatic repulsion, onto the surface of the silica seeds.

It is very easy to grow particles that are less than 0.2 μ m in size, but the growth of particles larger than 1.5 μ m has to be done under very carefully controlled conditions. The following general guidelines can be used in this case to avoid secondary nucleation. The ammonia concentration should be kept between 0.5 and 1.0 mol L⁻¹ and the water concentration should be kept at about 5 to 8 mol L⁻¹. The TEOS concentration can be slightly increased during the process to values of 1.0 mol L⁻¹ or even higher in some cases.

1.2.2 Amino acid-catalyzed synthesis of silica nanoparticles in a two-phase process

Recently, Yokoi et al.^{31,32} reported a simple and reproducible synthesis route for producing highly monodisperse silica nanoparticles with diameters comprised between 15 and 20 nm.

The synthesis is based on the very slow increase of the solution supersaturation. In this process, basic amino acids such as lysine and arginine are used as catalysts in aqueous media, while TEOS is delivered heterogeneously using a top inert organic layer (octane). As lysine was shown to be effective for the formation of silica particles due to its electrostatic interactions with silicic acid, D- and L-forms of lysine and their mixtures were later used to control the size of the silica nanoparticles.³

Later, by using a similar process, Hartlen et al.³³ prepared highly monodisperse silica particles ranging from 15 nm to more than 200 nm using a regrowth approach with L-arginine as a base catalyst in aqueous media. The resulting silica particles were compatible with the Stöber process and regrown further without any purification to larger sizes in ethanol/water solution using ammonia as catalyst. Fouilloux et al.^{34,35} used small angle X-ray scattering (SAXS) to determine the size distribution and concentration of silica nanoparticles synthesized by the Hartlen process (Figure 2.8). The classical La Mer nucleation growth model was used to describe the overall process. The model enabled to satisfactorily predict the nanoparticle number and size but it was not sufficient to describe correctly the size monodispersity.



Figure 2.8 TEM images and size histogram of silica nanoparticles synthesized using the Larginine process according to Fouilloux et al.³⁴

Recently, the seed regrowth was used to prepare highly monodisperse silica particles with diameters comprised between 15 and 500 nm using L-arginine as a base catalyst in a mixture of ethanol and water.³⁶ Interestingly, anisotropic silica particles with worm like morphologies

were obtained using this L-arginine-catalyzed regrowth process.³⁷ The addition of ethanol in the original aqueous sol of silica seeds may destroy colloidal stability and lead to aggregation of the silica seeds. Although the L-arginine process is gaining increasing attention as a simple waterborne process for silica seeds synthesis, the monodispersity of the regrown particles in either size or shape is however often poorly controlled which presents a major challenge, seriously restricting the use of this technique and its potential applications.

1.3 Surface modification of silica particles

1.3.1 Surface chemistry of colloidal silica particles

The properties of amorphous silica of high specific surface area, from the smallest colloidal particles to macroscopic gels, depend on the chemistry of the surface of the solid phase. The term "surface" will be understood to mean the boundary of the nonporous solid phase. The "surface" usually means the boundary that is not permeable to nitrogen, the adsorbate most commonly used to measure the surface area.

The key characteristic of the siloxane (Si-O-Si) surface of SiO₂ is that the so-called "residual valences" react with water so that at ordinary temperature, the surface becomes covered with silanol (SiOH) groups. SiOH groups can also be entrapped deep inside the structure during synthesis. External silanols can form hydrogen bonds with molecules having polar atoms, such as an oxygen atom. In all cases, there is a binding force between a specific atom of the adsorbate and an atom on the surface so that once the silica surface becomes covered, no second layer is adsorbed. In water solution, protonation and dissociation (i.e., deprotonation) of the surface hydroxyls produce a charged oxide surface. The hydroxyl groups of silica are acidic and deprotonate to create negative surface charges for pH larger than the isoelectric point (e.g. pH = 2) according to:

$$\equiv$$
SiOH \implies \equiv SiO⁻ + H⁺ (eq. 2.8)

Surface OH groups are subdivided as following (Figure 2.9): (i) isolated silanols, \equiv SiOH; (ii) geminal silanols or silanediols, =Si(OH)₂ and (iii) H-bonded vicinal OH groups (also called bridged silanols). On the SiO₂ surface there also exist surface siloxane groups or \equiv Si $-O-Si\equiv$ bridges with oxygen atoms on the surface. At last, there is structurally bound water inside the silica skeleton and very fine ultramicropores, d < 1 nm (d is the pore diameter), i.e. internal silanol groups.³⁸



Figure 2.9 Types of silanol groups and siloxane bridges on the surface of amorphous silica, and internal OH groups.³⁸

As shown in Figure 2.9, the different silanol species are usually denoted according to the conventional Q^n terminology where *n* indicates the number of bridging bonds (-O-Si) tied to the central Si atom: Q^4 , surface siloxanes; Q^3 , single silanols; Q^2 , geminal silanols (silanediols).³⁸

Calculation of silanol numbers of the silica surface can be approached in several ways. The simplest is that proposed by Iler³⁹ based purely on geometric considerations and the density of amorphous SiO₂. He concluded that that there should be 7.8 silicon atoms nm⁻² at/or very near the surface. However, Boehm⁴⁰ pointed out that since all the silicon atoms cannot be exactly at the boundary, some must be above and some below, and hence only half of the silicon atoms would bear OH groups so that there would be only 3.9 OH nm⁻². On the basis of the concept of "absolute" adsorption of properties of SiO₂, an attempt was made by Zhdanov et al. ⁴¹ to establish a value for the concentration of OH groups on the surface of amorphous completely hydroxylated silica. The most probable value was 6.9-7.5 OH nm⁻². In practice, the number of silanol groups strongly depends on the nature of the surface and may significantly vary from one type of silica to another.

1.3.2 Surface modification of colloidal silica particles

Generally, the surfaces of inorganic materials are functionalized with polymer chains either chemically (through covalent bonding) or physically (by physisorption).⁴² A drawback of physisorbed polymers is that they are thermally and solvolitically unstable due to the relatively weak van der Waals forces or hydrogen bonding that anchor them to the surface.⁴³ Covalent grafting techniques are preferred to maximize a stable interfacial compatibility between the two phases.

For the silica particles, the hydroxyl groups on the surface can be easily tailored with organic compounds or polymers. Silanol groups can be easily functionalized by different chemical procedures. The most convenient technique for silica surface functionalization is the reaction of silanol groups with suitable organosilanes (also called silane coupling agents) (Figure 2.10).⁴⁴



Figure 2.10 Surface modification of silica particles with organosilane molecules.⁴⁴

As described in Chapter 1, organosilane molecules can be further used to attach polymer chains to silica surfaces using the "grafting from" or "grafting to" approaches. In the "grafting to" method, pre-formed, end-functionalized polymer chains are reacted with a chemically activated substrate (Figure 2.11).⁴⁵ One advantage of this method is that polymer chains can be characterized before being attached to the substrate. The drawback, however, is that only relatively low grafting densities are obtained due to steric crowding of already attached chains on the surface, which hinders diffusion of additional chains to reactive sites.⁴⁶ Reactive end groups must diffuse through the barrier of these polymer chains to couple with functional groups on the surface and this diffusion barrier becomes more pronounced as more

chains are attached.⁴⁷. Though polymer brushes have been anchored to inorganic surfaces via the "grafting to" method, more densely grafted brushes may be prepared by using the "grafting from" method to circumvent the diffusion barrier problem.

The "grafting from" method involves formation of an initiator layer on the surface of the silica followed by polymerization of monomer (Figure 2.11). Different polymerization techniques can be used to modify silica surfaces. Thick brushes with a high grafting density can be formed because monomer can easily diffuse to reactive sites of the growing polymer chains. In this method, the steric barrier to incoming polymers imposed by the *in situ* grafted chains does not limit the access of smaller monomer molecules to the active initiation sites.⁴⁸ This polymerization technique is also commonly referred to as surface-initiated polymerization. Preparation of polymer brushes via the "grafting from" technique on silica nanoparticles can be accomplished by conventional free radical, controlled free radical, cationic, anionic and ring-opening metathesis polymerization techniques.⁴⁹



Figure 2.11 "Grafting to" and "grafting from" approaches of surface modification.

The main challenge in dispersing silica particles in organic solution lies in controlling their aggregation. It is necessary to stabilize the particles to prevent aggregation, which is usually performed by grafting polymer chains using the different methods mentioned above. These long polymer chains control the nanoparticle aggregation by steric repulsions. Another advantage of grafted polymer chains is that they can improve compatibility of inorganic particles with polymeric matrices, a key step in the elaboration of nanocomposite materials. It has been reported that controlling filler aggregation in composite materials may improve mechanical properties and enhance optically transparency.⁵⁰ The formation of stable dispersions in solvents or polymer matrices is an important aspect of material science affecting the final properties of formulations and coatings.

1.4 Conclusions

The Stöber process is quite likely one of the most popular method for the synthesis of colloidal silica nanoparticles. It has been widely described in literature and applied to various industries. It is a very simple and environmentally friendly process that allows synthesizing fine amorphous, non-porous, and typically spherical silica particles in the absence of surfactant.

Recently a biphasic amino acid catalyzed process has been reported as an alternative of the Stöber process to generate tiny silica particles. Compared to the Stöber process, it has the advantage of being highly reproducible while ensuring an efficient control of size and size distribution in a size range of ten to several tens nanometers. This process was also recently implemented to the synthesis of hybrid materials⁵¹ and mesoporous silica particles.⁵²

In the frame of this thesis, the Stöber process and the biphasic amino acid catalyzed process were used to synthesize silica nanoparticles of controlled sizes and size distributions in a large size range from 30 nm up to 600 nm. In addition, with the objective to functionalize the surface of the silica particles obtained, the amino acid catalyzed process was also used to introduce functional groups at the silica surface through the grafting of an organoalkoxysilane, namely γ -methacryloxy propyl trimethoxysilane in a two-phase process. The results are described in the following sections.

2. Synthesis of monodisperse silica particles

Although commercial silica sols (e.g., Klebosol silica) are available, synthetic silica particles are particularly appropriate for model colloidal studies since spherical particles can be prepared with various sizes and a narrow size distribution.

In this section, we aim to synthesize monodisperse silica particles with controlled sizes and size distributions. Based on the characteristics of the different processes described above, the classic Stöber procedure (batch and semi-batch) was employed to produce relatively large particles (0.2 μ m < D_n < 1 μ m), while the two-phase amino acid catalyzed process (L-arginine process) was employed to produce particles with diameters lower than typically 50 nm. We also tried to find favorable conditions to synthesize silica particles with intermediate sizes in a mixture of ethanol and water using ether ammonia or L-arginine as catalysts.

2.1 Synthesis of silica particles via the Stöber process

2.1.1 Experimental procedure

Synthesis

In the batch process, all the monomer, solvent and catalyst were mixed together at the beginning of the reaction. In this work, TEOS (Aldrich, 29.12 g, 0.2 mol L^{-1}), deionized water (75.6 g, 6 mol L^{-1}) and absolute ethanol (Prolabo, 450 g, 13.9 mol L^{-1}) were mixed, charged into a 1L round bottom flask and stirred for 20 min. A mixture of ammonia and ethanol (ammonia solution (Adrich, 28% wt/wt aqueous ammonia solution, diluted in 15 g of absolute ethanol, 0.5 mol L^{-1}) was introduced at once on the top of the flask and stirred for at least 24 h at room temperature.

The TEOS concentration was maintained constant in all experiments $(0.2 \text{ mol } \text{L}^{-1})$ while the ammonia and water concentrations were varied according to the recipes shown in Table 1 in order to see their effect on the final silica particle sizes and size distributions.

Exp	[EtOH] mol L ⁻¹	[H ₂ O] mol L ⁻¹	[NH ₃] mol L ⁻¹	[TEOS] mol L ⁻¹	Z _{av} (nm)	Poly (DLS)	D _n (nm) (TEM)	D _w /D _n (TEM)
SJ08	14.50	6.0	0.1	0.2	62	0.02	56	1.04
SJ09	14.46	6.0	0.2	0.2	171	0.01	125	1.03
SJ10	14.42	6.0	0.3	0.2	245	0.01	/	/
SJ11	14.37	6.0	0.4	0.2	281	0.03	/	/
SJ12	14.33	6.0	0.5	0.2	404	0.01	314	1.01
SJ13	14.30	6.0	0.6	0.2	450	0.02	441	1.01
SJ14	14.26	6.0	0.7	0.2	460	0.06	/	/
SJ15	14.22	6.0	0.8	0.2	506	0.03	/	/
SJ16	14.18	6.0	0.9	0.2	525	0.08	/	/
SJ17	14.14	6.0	1.0	0.2	665	0.02	/	/
SJ18	13.73	6.0	2.0	0.2	740	0.27	700	1.05
SJ19	14.33	4.0	0.5	0.2	257	0.02	233	1.01
SJ20	14.33	8.0	0.5	0.2	439	0.02	359	1.07
SJ21	14.33	10.0	0.5	0.2	387	0.03	338	1.10

Table 1. Experimental conditions and average diameters of all silica particles obtained by the

 Stöber process in batch.^a

^aTotal volume: 700 mL. Temperature: 25 °C

The reactor used in the semi-batch process is shown in Figure 2.12. In a typical reaction, a certain amount of ammonia, deionized water (75.6 g, 6 mol L^{-1}) and absolute ethanol (part 1, 400 g) were first mixed, and charged into the round bottom flask and stirred for 20 min. Then a mixture of TEOS (29.12 g, 0.2 mol L^{-1}) and ethanol (part 2, 50 g) was then added dropwise (10 mL h⁻¹) into the flask and kept stirring for 24 h at room temperature. All the corresponding experimental conditions are given in Table 2.



Figure 2.12 Experimental setup for the Stöber semi-batch procedure.

Table 2. Experimental conditions and average diameters of all silica particles obtained by the Stöber process in semi-batch.^a

Exp	[EtOH] mol L ⁻¹	[H ₂ O] mol L ⁻¹	[NH ₃] mol L ⁻¹	[TEOS] mol L ⁻¹	Z _{av} (nm)	Poly value (DLS)	D _n (nm) (TEM)	D _w /D _n (TEM)
SJ01	14.50	6.0	0.1	0.2	77	0.01	59.9	1.245
SJ02	14.42	6.0	0.3	0.2	299	0.07	/	/
SJ03	14.33	6.0	0.5	0.2	361	0.03	295.3	1.083
SJ04	14.30	6.0	0.6	0.2	454	0.03	/	/
SJ05	14.26	6.0	0.7	0.2	1032	0.20	890.5	1.165
SJ06	14.14	6.0	1.0	0.2	1441	0.20	/	/
SJ07	13.73	6.0	2.0	0.2	7231	0.29	/	/

^aTotal volume: 700 mL. T = 25 °C.

Characterizations

DLS (Nano ZS from Malvern Instruments) was used to measure the particle size (average hydrodynamic diameter, $Z_{av.}$) and the dispersity of the samples (indicated by the Poly value - the higher this value, the broader the size distribution). Typically, one drop of the silica suspension was diluted in pure deionized water or in pure ethanol depending on the type of silica, before analysis. The reported particle size represents an average of 3 measurements.

Transmission electron microscopy (TEM) analyses were performed at an accelerating voltage of 80 kV with a Philips CM120 transmission electron microscope (Centre Technologique des Microstructures, plate-forme de l'Université Claude Bernard, Lyon 1). Highly diluted samples were dropped on a Formvar-carbon coated copper grid and dried under air. The number-average (D_n) and the weight-average particle diameter (D_w) and polydispersity index (PDI = D_w/D_n) were calculated using $D_n = \sum n_i D_i / \sum n_i and D_w = \sum n_i D_i^4 / \sum n_i D_i^3$, where n_i is the number of particles with diameter D_i .

2.1.2 Results and discussion

2.1.2.1 Analysis of particle size and particle size distribution by DLS

In the Stöber method, the diameter of silica spheres can be increased by increasing the concentration of ammonia or TEOS, or by using an alcohol with short alkyl chains.² Figure 2.13 shows the evolution of the final silica particle size as a function of ammonia concentration in both semi-batch and batch processes. It is seen that the particle size increases significantly with increasing ammonia concentration.

For the batch process, under the given reaction conditions, the particle size increases following the trend described in the classic Stöber process.² The Poly value does not significantly vary (< 0.08) until an ammonia concentration of 1.0 mol L⁻¹. The high ammonia concentration may result in high ionic strength which was already proved to lead to the coagulation of silica particles.²³ The broad particle size distribution for the semi-batch process appeared at a lower ammonia concentration (0.7 mol L⁻¹). The feeding rate of the TEOS/ethanol solution has a great effect on the silica particle size because of the system's short nucleation time and the slow hydrolysis rate of the reaction.²⁶ Under the given conditions of this work, for the same ammonia concentration, the silica particles prepared by the batch process were smaller than the particles obtained by the semi-batch process. This may be ascribed to a longer time of growth for the silica particles in the semi-batch process.



Figure 2.13 Final particle sizes and Poly values (DLS) of silica particles synthesized by the Stöber process in batch and semi-batch as a function of ammonia concentration at room temperature: $[H_2O] = 6 \text{ M}$, [TEOS] = 0.2 M. See Table 1 for experimental details.

Figure 2.14 shows the final particle size and particle size distribution of silica particles synthesized by the Stöber process in batch for different concentrations of H₂O. It can be clearly observed that the particle size goes through a maximum as the water concentration increases. This behavior has been already observed in early works.^{2,11} The nucleation rate, and hence the final particle size, strongly depends on the ratio of the hydrolysis rate to the polymerization rate. Factors that promote nucleation must result in small particles while factors that favor growth should have the opposite effect. Increasing water concentration promotes hydrolysis for high water contents, which results in higher nucleation rate and more particles, while for low water contents, the growth process becomes predominant as the hydrolysis rate is lower than the rate of monomer consumption resulting in bigger particles.



Figure 2.14 Final particle sizes and poly values for the Stöber process in batch as a function of H_2O concentration at room temperature: [TEOS] = 0.2 M, [NH₃] = 0.5 M. See Table 1 for experimental details.

2.1.2.2 Morphologies and particle size distribution analysis with TEM

Figure 2.15 shows TEM images and size histograms of a series of silica particles synthesized by the Stöber process. As previously mentioned we fixed the TEOS concentration and varied the ammonia concentration to vary the final particle size. Silica nanoparticles with an average diameter of 56 nm was obtained at low ammonia concentration (Figure 2.16 A, $[NH_3] = 0.1$ mol L^{-1}). The particle size distribution is relatively broad (PDI = 1.04). Furthermore, the particles are not spherical but slightly elliptic. It is well known that ammonia can influence particles morphology and create spherical particles during the reaction. In the absence of ammonia, silica particles exhibit more irregular shapes.² A closer inspection of the TEM image of Figure 2.15A reveals that the particles are clustering on the grid suggesting limited colloidal stability which is likely due to the low ammonia concentration used in this particular experiment. Silica particles prepared with higher ammonia concentrations (0.5 and 0.6 M) exhibit perfect spherical morphologies and a narrow size distribution (PDI = 1.01). However, increasing further the ammonia concentration to 2M led to a broadening of the size distribution as shown in the TEM image of Figure 2.15E. Two distinct populations of particles centered around 800 and 1000 nm, respectively, can be clearly identified on this TEM image leading to a PDI of 1.05.



Figure 2.15 Selected TEM images and size histograms of a series of silica particles synthesized by the Stöber process with different particle sizes and size distributions: A: SJ08, B: SJ09, C: SJ12, D: SJ13 and E: SJ18 (Table 1).

In conclusion, the Stöber process is a simple method for the synthesis of colloidal silica particles. However, the broad size distribution and the non-spherical particle shape observed for high and low ammonia concentrations, respectively, prevent the application of the Stöber process to the synthesis of very large (> 700 nm) and small (e.g., below 150 nm) silica beads. Therefore in the following, we used the amino acid catalyzed process and the seed regrowth process to synthesize monodisperse silica nanoparticles, with very small diameters (lower than typically 100 nm) or with intermediate particle sizes (e.g., diameters comprised between 200 and 300 nm). For the sake of simplicity, the amino acid catalyzed process will be called hereafter the L-arginine process with reference to L-arginine, which is used as catalyst.

2.2 Synthesis of silica particles via the L-arginine process

2.2.1 Experimental procedure

L-arginine (Figure 2.16) is an amino acid who has been used previously as a base catalyst for silica hydrolysis and for silica particles stabilization,⁵³ which is likely due to its strong basicity and interactions with silica surfaces.

The synthetic procedure is similar to the one described in the work of Hartlen et al.,³³ with however a slight modification. No inert oil (e.g. $octane^{3,32}$ or cyclohexane³³⁻³⁵) was employed in the system. In a typical procedure, L-arginine (Aldrich, 26.3 mg, 6 mmol L⁻¹) was first diluted in deionized water (25 g), charged into the reactor (Figure 2.17) and kept stirring for several minutes with a stirring bar. Once the solution reached 60 °C, TEOS was carefully introduced on top of the reactor leading to two separate phases. The stirring rate was fixed at 250 rpm so that the top organic layer was left almost undisturbed and the water phase could be well mixed. The mixture was stirred at 60 °C for 72h. All experiments were performed with a fixed L-arginine concentration and various TEOS contents. The formed particles were characterized as reported previously for the Stöber process (section 2.1.1). The corresponding experimental conditions and results are shown in Table 3.



Figure 2.16 Chemical structure of L-arginine.



Figure 2.17 Schematic representation of the reactor used for the L-arginine process.

Table 3. Experimental conditions and average diameters of the silica particles obtained from the L-arginine process using different TEOS contents.^a

No	TEOS (mL)	[TEOS] (mol L ⁻¹)	Z _{av} (DLS) (nm)	Poly value (DLS)	Solid content (%)	D _n (TEM) (nm)	D _w /D _n (TEM)
SJLA01	0.25	0.045	17.9	0.15	0.39	13.4	1.01
SJLA02	0.50	0.09	20.2	0.13	0.51	16.7	1.02
SJLA04	1.0	0.179	29.8	0.12	1.02	17.9	1.02
SJLA05	2.0	0.358	33.9	0.06	2.00	22.0	1.01
SJLA07	3.0	0.537	43.1	0.07	2.95	26.8	1.01
SJLA06	4.0	0.717	49.0	0.04	3.93	30.1	1.01

^a H₂O = 25 mL. [L-arginine] = 6 mmol L⁻¹. Reaction time = 72 h. T = 60 °C.

2.2.2 Results and discussion

2.2.2.1 Particle size and particle size distribution

Figure 2.18 shows the evolution of the final silica particle size and Poly value determined by DLS. We observe that the particle size increases and the Poly value decreases as the TEOS content increases. The TEM images in Figure 2.19 show that the smallest particles tend to form aggregates on the TEM grid. Thus, the high Poly value for the low amount of TEOS is likely due to the strong binding interaction caused by the large specific surface area.



Figure 2.18 Final particle sizes and Poly values determined by DLS for the silica particles obtained by the L-arginine process using different TEOS contents.

The number of silica particles per liter of silica sol was calculated for different TEOS contents based on the final particle size determined by DLS and the solid content (Table 3). Figure 2.20 shows that the number of silica particles almost did not change with increasing TEOS contents. As it was already described in the literature,^{34,35} in the L-arginine process, the supersaturation increases slowly until it reaches a critical value at which a single nucleation burst creates enough particles to absorb the injected monomers. The increase of the solution supersaturation is controlled by the rate of TEOS hydrolysis and the interfacial area between the organic top layer and the aqueous phase, which only depends on the geometry of the reactor and is thus independent of the amount of TEOS. Consequently, for a fixed amount of catalyst, the number of silica nuclei is solely determined by the TEOS-water interface area and is not influenced by the amount of TEOS introduced in the top layer.

As shown in Figure 2.19, the resulting particles have a narrow size distribution (PDI < 1.02) and diameters comprised between 16 and 30 nm as determined by TEM.



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mL, B: 0.5 mL, C: 1.0 mL, D: 2.0 mL, E: 3.0 mL and F: 4.0 mL (Table 3).



Figure 2.20 Evolution of silica particle number as a function of TEOS amount during the Larginine process. Water = 25 mL [L-arginine] = 6 mmol L^{-1} . T = 60 °C. 72 h.

All the results show that the L-arginine process presents the advantage to form well-defined silica nanoparticles with diameters smaller than typically 50 nm and with a narrow particle size distribution. As there is no alcohol in the system, the final aqueous silica sol can be used directly without further purification. However, the fairly long reaction time is an obvious drawback of the L-arginine process, which is due to a very slow growth process. To avoid this drawback, the regrowth of 30 nm silica seeds (obtained from the L-arginine process) in ethanol/water mixture was also investigated in this work.

2.3 Regrowth of silica seeds in ethanol/water mixtures using ammonia or Larginine as catalysts

The 30 nm silica seeds used for the regrowth process were obtained from the L-arginine method using the experimental conditions of Table 3 and a fixed amount of TEOS (4.0 mL, SJLA06). The experiment was repeated three times to be sure that the synthesis was reproducible and the silica seeds stable. As shown in Table 4, the particle size (determined either by TEM or DLS analysis) changed within ± 1 nm. The TEM results are shown in Figure 2.21.



Figure 2.21 TEM images of the L-arginine silica seeds used in the regrowth process. A: SJLA06G, B: SJLA06H and C: SJLA06I (Table 4).

2.3.1 Seed regrowth using ammonia as catalyst in a Stöber-like process

As mentioned in the introduction, the seed regrowth using the Stöber process is usually employed to synthesize silica particles with diameters larger than typically 1 μ m, starting from relatively big seed particles (with diameters larger than typically 500 nm).⁵⁴ In this work, we employed this method to generate particles of intermediate diameters (in the range of 100 - 200 nm) using small and monodisperse silica seed particles (30 nm) obtained by the L-arginine process.
SJL-A-06	(Journey)	ine] [TE	OS] [TEO]	S H ₂ 0	\mathbf{Z}_{av} (DLS)	Poly value	$D_{\rm n}$ (TEM)	$D_{\rm w}/D_{\rm n}$	Solid content
SUL-A-U6					(IIIII) 10.01	(CLU)	(1111)		(0/1M)
		1, ,	.12	1.07	49.04	0.040	1.00	1.01	2.72
OUL-A-UU.	H 6	4	. 0.72	25.1	42.78	0.088	31.5	1.01	3.78
SJL-A-06	9 I	4	0.72	25.2	43.11	0.081	32.2	1.01	3.81
^a Reaction tir	ne = 72 h. T = 60	℃ (
Table 5. Ex	perimental conc	litions and ma	ain characterist	ics of the silic	a particles obtaii	ned by the seed	l regrowth metho	od using amn	ionia as catalyst
and SJLA0	6G as silica see	ds (see Table	4) in a Stöber-	like process. ^a					
No	Silica seeds	[NH ₃]	[H ₂ O] Total	[EtOH]	Target size ^b	Z _{av} (DLS)	Poly value	$D_{\rm n}$ (TEM)	$D_{ m w}/D_{ m n}$
	(mol L ⁻¹)	$(mol L^{-1})$	(mol L ⁻¹)	(mol L ⁻¹)	(uu)	(uu)	(DLS)	(uu)	(TEM)
SJKR 01	0.02	0.1	6	11.9	112	113	0.03	/	/
SJKR04	0.02	0.3	9	11.8	112	163	0.02	136	1.001
SJKR02	0.02	0.6	9	11.7	112	168	0.06	138	1.003
SJKR03	0.02	1.0	9	11.5	112	288	0.47	/	/
SJKR05	0.02	1.5	9	11.3	112	469	0.68	/	/

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In a typical Stöber regrowth reaction, a certain amount of silica seeds (30 nm silica particles, 0.02 M) was gently dispersed in an ethanol solution containing water and ammonia. Upon uniform mixing, 42.0 g TEOS (1.0 mol L^{-1}) was added. The concentration of ammonia was varied from 0.1 mol L^{-1} to 1.5 mol L^{-1} to see its effect on the final particles while the water concentration was maintained constant. The corresponding experimental conditions and results are given in Table 5.

2.3.1.1 Effect of ammonia concentration

The DLS results show that when the ammonia concentration was higher than 0.6 mol L⁻¹, the Poly value was very high which indicates that the regrowth process was out of control. More information could be found in the TEM images (Figure 2.22). Figure 2.22A shows the formation of a mixture of big spherical particles and very small silica particles for $[NH_3] = 0.1 \text{ mol } L^{-1}$. The big spherical particles likely come from the regrowth silica seeds and the small ones may be due to some secondary nucleation due to the relatively lower condensation rate than hydrolysis rate for low ammonia concentration.⁵⁵ Figure 2.22B shows successful regrowth of the silica seeds for $[NH_3] = 0.3 \text{ mol } L^{-1}$. The resulting particles have a spherical morphology and a narrow size distribution ($D_w/D_n = 1.001$). Their diameter is also consistent with the theoretical particle size (see Table 5).

Both the DLS and TEM results (Figure 2.22C) show that the particle size and size distribution of SJKR02 ($[NH_3] = 0.6 \text{ mol } L^{-1}$) are similar to those of SJKR04 ($[NH_3] = 0.3 \text{ mol } L^{-1}$, Figure 2.22B). However, a closer inspection of the TEM images revealed the presence of some silica dumbbells i.e., two spherical silica particles aggregated together (see the red circles). The proportion of dumbbell particles increased with increasing the concentration of ammonia to 1.0 mol L^{-1} (Figure 2.22D and E). Increasing further the ammonia concentration to 1.5 mol L^{-1} led to silica aggregates composed of three or four spherical silica particles glued together into clusters or anisotropic worm-like structures.³⁰ Particles aggregation may be caused by two factors. First, particle stability decreases with increasing ammonia concentrations and second, the addition of ethanol to the aqueous silica sol may disturb colloidal stability and promote aggregation.

These results indicate that an optimized ammonia concentration for the Stöber regrowth process using L-arginine silica seeds would be around 0.3 mol L^{-1} . A lower ammonia concentration leads to secondary nucleation while a higher concentration leads to the formation of doublets or triplets of silica spheres.



Figure 2.22 TEM images of Stöber regrowth silica particles synthesized using 30 nm Larginine silica seeds and different concentrations of ammonia. A: 0.1 mol L⁻¹, B: 0.3 mol L⁻¹, C: 0.6 mol L⁻¹, D: 1.0 mol L⁻¹ and E: 1.5 mol L⁻¹ (Table 5).

Figure 2.23 compares silica particles obtained by the Stöber process with silica particles of similar sizes obtained by the seed regrowth process. The results show that the regrowth process leads to silica particles ($D_n = 136 \text{ nm}$, $D_w/D_n = 1.001$, SJKR04, Table 5) with a significantly narrower size distribution than the ones obtained by the conventional Stöber process ($D_n = 125 \text{ nm}$, $D_w/D_n = 1.03$, SJ09, Table 1).



Figure 2.23 TEM images of silica particles obtained by the regrowth process using the Larginine silica as seeds and ammonia as catalyst (A, SJKR04 Table 5) compared to silica particles obtained by the conventional Stöber process in batch (B, SJ09, Table 1).

2.3.2 Seed regrowth using L-arginine as catalyst in a Stöber-like process

The regrowth process using L-arginine as catalyst is different from the L-arginine process described above for the synthesis of silica seeds. Indeed, as the reaction was performed in the presence of ethanol, there was no phase separation.

In the regrowth process, an appropriate amount of the seed dispersion (SJLA06 H and I in Table 4) was added to a mixed solution of water and ethanol containing L-arginine. Subsequently, TEOS was added to the solution and the resulting mixture was stirred at 70 °C for 24 h. The concentrations of silica seeds, L-arginine, water and TEOS used in all experiments performed in this work are reported in Table 6.

A similar work has been done by Okubo et al.^{36,37} The authors investigated the effect of amino acid (type and concentration), water concentration and alcohol (type and concentration) on the seed regrowth. The diameter of the final silica particles could be finely tuned from 80 to 550 nm by varying the amounts of reagents in the recipe.. To be different from these previous works, we fixed the water, ethanol and L-arginine concentrations, and only varied the concentrations of silica seeds and TEOS to study their effect on the diameter and morphology of the final silica particles.

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Table 6. Experimental conditions and main characteristics of the silica particles obtained by the seed regrowth method using L-arginine as catalyst and SJLA06H or SJLA06I as silica seeds (see Table 4) in a Stöber like process.^a

No	Silica Seeds (mol L ⁻¹)	[TEOS] (mol L ⁻¹)	TEOS	Target size ^b (nm)	Conv. (%)	Z _{av} (DLS) (nm)	Poly value (DLS)	D _n (TEM) (nm)	$D_{\rm w}/D_{\rm n}$ (TEM)	Particle morphology
SJLR16	0.01	0.23	50	282.6	67.6	221.3	0.10	185.4	1.03	Spheres
SJLR14	0.26	0.23	50	102.0	77.1	222.6	0.13	129 ^c	/	Worms
SJLR13	0.50	0.23	50	83.6	82.5	240.9	0.25	125 ^c	/	Worms
SJLR11	1.04	0.23	50	69.69	98.1	388.9	0.50	100°	/	Worms
SJLR15	2.04	0.23	50	58.5	100	93.9	0.06	49.5	1.003	Spheres
SJLR17	0.59	0.12	25	58.7	100	89.5	0.03	50.8	1.004	Spheres
SJLR19	1.04	0.33	75	74.9	77.4	379.2	0.43	114 ^c	/	Worms
SJLR18	1.03	0.44	100	76.2	61.5	2653	0.72	116°	/	Worms
SJLR12 ^d	1.04	0.23	50	50.7	31.6	571.7	0.84	59°	/	Worms
Γ = 70 °C ex	cented for SJLR	12. Reaction t	ime = 24 h	[H,O] = 10.4 r	nol L-1. []	-arginine] = 6.5	8 mol L ⁻¹ ^b Calcı	ulated using e	duation 7 cor	.iSt

conversion given in the table.^c Width of the worm-like silica.^d Reaction performed at room temperature. Silica seeds used in the regrowth process: SJLA06H for experiments SJLR11-12 and SJLA06I for experiments SJLR13-19. a_

2.3.2.1 Effect of silica seed concentration

As the reaction was performed under basic conditions (pH was around 10), the hydrolysis rate of TEOS was not expected to be remarkably high but the condensation of silicate species should be very fast.^{39,54,56} Thus, given the large number of reactive silanol groups present on the surface of the silica seeds, the new silicate species coming from TEOS are preferentially consumed for the regrowth on the silica seeds rather than for the formation of new silica particles. This was confirmed by TEM analyses, which showed the absence of secondary nucleated spheres under our experimental conditions even for relatively low seed concentrations (Figure 2.24). Furthermore, TEM indicates the formation of a majority of spherical particles (90 %) and a few dimers for very low silica seed concentrations (Figure 2.24B-D). The morphological transition from spheres to worms is supported by DLS measurements. Indeed, most particles have a broad size distribution (Poly value higher than typically 0.1), which is likely related to the worm-like morphology of the particles. Furthermore, the average hydrodynamic diameter is significantly larger than the width of the worm-like silica particles as expected for anisotropic particles.

Similar anisotropic morphologies have already been reported in the literature by Wang et al.³⁷ The authors showed that the length-to-diameter ratio of the formed worm-like particles depends on the seed concentration. The higher the seed concentration, the larger the particle number and the higher the collision frequency between particles, which promotes the formation of worm-like morphologies through self-aggregation.

However, surprisingly, increasing further the silica seed concentration produced mainly spherical silica particles (Figure 2.24E, 2.04 mol L⁻¹, SJLR15). This may be explained by the fast condensation rate of TEOS leading to stable colloidal particles without particle aggregation or assembly. As TEOS is only consumed through condensation on the silica seed, more silica seeds should promote TEOS polymerization, and lead consequently to higher conversions. Figure 2.25 shows that as expected, the higher the concentration of silica seeds, the higher the TEOS conversion after 24 h. Faster TEOS polymerization may result in a lower TEOS concentration during the early reaction stage which would increase the dielectric constant of the suspension media and enhance consequently charge repulsions.



Figure 2.24 TEM images of the silica particles prepared with the Stöber-like regrowth process with L-arginine as catalyst, using $[TEOS] = 0.23 \text{ mol } L^{-1}$ and varying silica seed concentrations: A: 0.01, B: 0.26, C: 0.50, D: 1.04 and E: 2.0 mol L^{-1} (Table 6).



Figure 2.25 Evolution of TEOS conversion after 24h as a function of the silica seeds concentration (Table 6).

2.3.2.2 Effect of TEOS concentration

To investigate the effect of TEOS concentration on the morphology of the resulting silica particles, the initial silica concentration was fixed at 0.31 wt%. Wang et al.³⁷ has reported that the TEOS concentration only has an effect on the diameter of the worm-like anisotropic particles. However, the results in this work indicate that, under the conditions given in Table 6, the concentration of TEOS also impacts the degree of aggregation of the particles.

For low TEOS concentrations, the final particles are spherical (Figure 2.27A). Their diameters correspond to the theoretical particle size based on equation 2.7. This result can again be explained by the low TEOS concentration in the suspension medium. Indeed, as expected, increasing TEOS concentration promotes aggregation as judged by TEM and DLS analysis (Table 6). TEOS contributes to a decrease in the dielectric constant of the hydroalocoholic suspension, which decreases the effective charge repulsion between particles and favor silica self-assembly. Furthermore, Figure 2.26 shows that TEOS is not completely consumed after 24h. The higher the initial TEOS concentration, the lower the final conversion and the higher consequently the amount of residual TEOS which may promote aggregation.

Figure 2.27B-D shows the increase of aggregation degree with the increase of TEOS concentration. The same trend was also observed by DLS according to the average particle size and Poly value. Though all TEOS is consumed for the regrowth of the silica seeds without forming new particles, high TEOS concentration may destroy the colloidal stability of the system and increase the degree of the aggregation.



Figure 2.26 Evolution of TEOS conversion after 24 h as a function of the initial TEOS concentration (Table 6).



Figure 2.27 TEM images of the silica particles prepared with the Stöber-like process and Larginine as catalyst, using different TEOS concentrations with the same amount of silica seeds (0.31 wt%). A: 0.12 mol L⁻¹, B: 0.23 mol L⁻¹, C: 0.33 mol L⁻¹ and D: 0.44 mol L⁻¹ (Table 6). The conversions are 100 %, 98 %, 77 % and 61 %, respectively.

2.3.2.3 Formation of worm-like silica particles

The original silica seeds are stabilized by the negative charges present on their surface. As previously mentioned, the addition of ethanol results in a decrease of the dielectric constant of the medium, which decreases electrostatic repulsion between the charged particles.⁵⁷ The formation of the worm-like silica particles likely operates via a two-stage process³⁷ as shown in Figure 2.28: (1) assembly of the silica seeds under given ethanol and L-arginine

concentrations, (2) fixation of the self-assembled structure and 3) growth of the worm-like structure by hydrolysis and condensation of TEOS. These stages can proceed simultaneously.



Figure 2.28 Scheme illustrating the formation of worm-like anisotropic silica particles.

The experiment SJLR11 in Table 6 was considered to investigate the formation mechanism of the worm-like silica particles. Samples were withdrawn from the reactor at regular time intervals to see the evolution of TEOS conversion with reaction time (Figure 2.29) and of particles morphology with conversion (Figure 2.30). The width of the worm-like particles increased from 45 nm to 100 nm with increasing TEOS conversion while their length did not significantly change. This result indicates that TEOS is consumed for the growth of the silica seeds without forming new particles and supports the above mechanism.



Figure 2.29 Evolution of TEOS conversion with reaction time for the Exp. SJLR11 (Table 6).



Figure 2.30 TEM images of Exp. SJLR11 at different reaction times. A: 1 h, conversion = 32 %, B: 3 h, conversion = 50 %, C: 7 h, conversion = 64 % and D: 24 h, conversion = 98 % (Table 6).

2.3.2.4 Effect of reaction temperature

The effect of the reaction temperature on the L-arginine-catalyzed regrowth process was also investigated. Figure 2.22 shows the regrowth result for the experiment performed at room temperature (SJLR12). The particles obtained at low conversion (31 %) exhibit the same morphology and size distribution (Figure 2.31A) than the ones formed at 70 °C for a similar conversion (32 %, Figure 2.30A). But after 7 days at room temperature (conversion 93 %), the TEM image of Figure 2.31B shows a mixture of worm-like particles and small irregular particles originating from secondary nucleation. This secondary nucleation is likely due to the relatively lower condensation and higher hydrolysis rate of TEOS. Considering the previous results, another third step for the L-arginine regrowth process at room temperature must be considered: the silica seeds keep growing via TEOS addition until the condensation and

hydrolysis balance is broken. The hydrolysis rate becomes higher than the condensation rate leading to the appearance of the second population. It is worth mentioning that the condensation rate of TEOS at room temperature is much lower than the one at high temperature.



Figure 2.31 TEM images for the SJLR12 silica sample obtained by the L-arginine-catalyzed regrowth process at room temperature. (A) Conversion = 31 % (24 h) and (B) conversion = 93 % (7 days).

Although some researchers already employed the L-arginine regrowth method to form spherical silica nanoparticles with a wide range of particles size and narrow size distributions, the addition of ethanol in the original aqueous sol of silica seeds may destroy the colloidal stability and lead to particle aggregation through self-assembly. We showed that it is difficult to avoid 1D-assembly of the silica seeds under the experimental conditions reported in this work. Spherical silica particles were solely obtained for low amounts of TEOS or for high silica seed concentrations. We suggest that fast TEOS consumption is key in the control over particles morphology in the presence of L-arginine. Indeed TEOS contributes to decreasing the dielectric constant of the suspension medium resulting in a decrease of the electrostatic repulsions between particles. Of course, the L-arginine and ethanol concentrations also play a role in the process and the resulting morphology is controlled by a complex interplay between seed concentration, ionic strength and dielectric constant.

3. Synthesis of hybrid and mesoporous silica nanoparticles via the Larginine process

Porous materials can be classified according to their pore size. Microporous materials have pore diameters of less than 2 nm and macroporous materials have pore diameters of greater than 50 nm. The mesoporous category thus lies in the middle with diameters between 2 and 50 nm.⁵⁸

Since the discovery of mesoporous materials by Yanagisawa et al.⁵⁹ and Kresge et al.^{60,61} in the early 1990s, significant progress has been made in the synthesis of ordered mesoporous materials with various compositions, structures, and morphologies.^{62,63} Mesoporous silica materials can provide scientists with several advantages. Mesoporous silica synthesized by using a surfactant template method are highly stable, and have controlled pore sizes and narrow pore size distributions. They can be used in different fields, such separation techniques, adsorption, catalysis, drug delivery, sensors, or photonics for instance.⁶⁴⁻⁷¹

To date, many different strategies have been developed for the synthesis of mesoporous silica nanoparticles (MSNs) including self-assembly,⁷²⁻⁷⁴ emulsion templating⁷⁵ and post-etching.⁷⁶ Among them, synergetic self-assembly between a cationic surfactant and a silica precursor (e.g. TEOS) proved to be an efficient method to form uniform spherical MSNs.⁷⁷⁻⁸⁰ Suzuki et al.⁸¹ demonstrated that well-ordered MSNs with a diameter lower than 100 nm can be prepared by using cetyltrimethylammonium chloride (CTAC) with a nonionic triblock copolymer (Pluronic F127). Recently, Yokoi et al.^{52, 73} described a new method for preparing MSNs with a size of about 20 nm in a TEOS–water biphasic system containing basic amino acids as catalysts and CTAC as surfactant. As it was described before, hydrolysis rate of TEOS is quite slow in this system due to the reaction proceeding at the TEOS–water interface, which is one of the key factors for synthesizing small spherical silica nanoparticles.

In recent years, several groups^{82-85, 86,87} have reported the synthesis of submicrometer-size mesoporous silica spheres with a core-shell structure employing long chain organosilanes as porogens instead of traditional cationic surfactants. Co-condensation of TEOS and organosilane molecules allows forming an organic-inorganic hybrid shell at the surface of colloidal particles used as templates. One advantage of this method is that the shape, functionality, size, size distribution and shell thickness of the final porous particles can be easily controlled by varying the nature of the templating core and the shell composition.

In this section, we used TEOS and γ -methacryloxy propyl trimethoxysilane (γ -MPS) as a mixed silica source to synthesize hybrid silica nanoparticles via the L-arginine process. Two approaches referred hereafter to as one-step and multi-step process, were employed in this work to synthesize hybrid silica nanoparticles with different morphologies depending on the initial weight fraction of γ -MPS.

3.1 Experimental procedure

3.1.1 Synthesis of hybrid γ -MPS-functionalized silica particles via a one-step biphasic process

Hybrid γ -MPS-functionalized silica particles were synthesized using the L-arginine process in one step following a procedure similar to the one described above (paragraph 2.2.1) except that TEOS was replaced by a mixture of TEOS and γ -MPS. Typically, 25 mL of a 6 mmol L⁻¹ L-Arginine solution were first introduced in the reactor (Figure 2.17) with a stir bar and stirred for several minutes. Once the solution reached 60 °C, a mixture of TEOS and γ -MPS was added carefully to get a two-phase solution. The stirring rate was fixed at 250 rpm. The reaction was kept at 60 °C for 72 h.

3.1.2 Synthesis of core-shell γ-MPS-silica particles via a multi-steps biphasic process

Core-shell γ -MPS-silica particles were synthesized in the same reactor following three steps. In a first step, 25 mL of a 6 mmol L⁻¹ L-arginine solution was introduced in the reactor and stirred for several minutes. Once the temperature reached 60 °C, 0.5 g of TEOS was added carefully to get a two-phase solution. This step was carried out for at least 48 h to form silica nanoparticles around 15 nm in size and to reach full TEOS consumption. In the second step, a certain amount of γ -MPS was introduced in the reactor. At the same time, the stirring speed was increased to 750 rpm and kept for 30 min, then reduced to 250 rpm (like in the previously described biphasic process). For the third step, a certain amount of TEOS (5 g) was carefully added to the solution to get a two-phase solution again. The reaction then proceeded at 60°C for 96 h.

3.1.3 Characterizations

The hybrid silica spheres and the γ -MPS-silica core-shell particles were characterized by DLS and TEM using the procedure described in section 2.1.1 for pure silica.

Cryo-TEM was used to visualize the Pickering γ -MPS droplets. In a typical analysis, a drop of the suspension was deposited on a continuous carbon film, blotting the water in excess, mounting the dry specimen on the Gatan holder and quenching it in liquid nitrogen before introduction in the microscope. The holder was then cooled down and the specimen was observed at -180 °C.

Scanning electronic microscopy (SEM) was performed using a FEI QUANTA 250 FEG scanning electron microscope, at an acceleration voltage of 15kV. A drop of the particle suspension was placed on a formvar/carbon film, dried and covered by a thin layer of gold/palladium (Sputtering Au/Pd with Baltec MED020 - 10 nm) before analysis.

Fourier transform infrared (FTIR) spectra were recorded from KBr pellets at room temperature using a Nicolet Avatar FTIR spectrometer.

²⁹Si solid-state NMR was performed on a Bruker DSX-300 spectrometer operating at 59.63 MHz. The spinning rate was 10 kHz. The ²⁹Si chemical shifts were referenced to tetramethylsilane (TMS).

N₂ adsorption/desorption isotherms, pore size distributions and BET surface areas were determined on a Micromeritics ASAP2010 apparatus. Prior to analysis, the silica samples were first purged under a vacuum at 120 °C to remove surface water. For the calcination process, samples were purged under a vacuum at 550 °C for at least 24h. N₂ adsorption and desorption isotherms were then collected at 77 K. The pore size distributions (especially for the samples after calcination) and the surface areas of samples were measured using the BET model.

TGA were performed on a TGA Q50 from TA Instrument using a temperature ramp from 20 to 800 $^{\circ}$ C at a heating rate of 10 $^{\circ}$ C min⁻¹. The weight loss was used to determine the organic groups content in the particles.

Chapter 2. Synthesis of silica particles

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(TEM) $D_{\rm w}/D_{\rm n}$ 1.011.021.021.141.141.26 $D_{\rm n}$ (TEM) (um) 30 32 57 133 233 830 **Poly value** (DLS) 0.02 0.02 0.05 0.04 0.04 0.18 Z_{av} (DLS) 160.4 263.7 (um) 43.3 49.6 76.3 1020 I otal conversion at 72h (%) 9.66 98.2 96.4 94.2 10082.1 Initial fraction of γ -MPS Density of the monomer mixture (g cm⁻³) 0.9410.935 0.938 0.9330.9440.949 (mol%)10.102.09 5.01 7.49 14.81 0 SLMT03 **SLMT04** SLMT05 **SLMT06** SLMT02 SJLA01 °

^a H_2O : 25 mL; [L-arginine] = 6 mmol L⁻¹ and TEOS = 4 mL.

Table 8. Experimental conditions and main characteristics of the hybrid silica particles obtained via the multi-step method.^a

No SLMT07 SLMT08	Initial fraction of γ -MPS (mol%) 2.26 4.89	Total conversion at 96h (%) 97.6		Poly value (DLS) 0.09	D_n (TEM) (nm) 87	<i>D</i> _w / <i>D</i> _n (TEM) / 1.04
SLMT09	9.89	98.3	194	c0.0	146	1.03

^a $H_2O: 25 \text{ mL}; [L-arginine] = 6 \text{ mmol } L^{-1}.$

3.2 Results and discussion

3.2.1 Morphology and size control of hybrid silica particles

For the synthesis of the hybrid silica particles via the L-arginine process, the organic layer is a mixture of TEOS and γ -MPS. To keep this organic layer as a top layer, the density of the mixture must be lower than that of pure water (1.0 g cm⁻³). Thus, the ratio of TEOS and γ -MPS in the mixture is very important considering the respective densities of TEOS (0.933 g cm⁻³) and γ -MPS (1.055g.cm⁻³). Here, the mixture was supposed to be an ideal solution whose density (ρ_x) could be determined with the simple equation (eq. 2.9):

$$\frac{1}{\rho_x} = \sum (\frac{x_i}{\rho_i})_n \tag{eq. 2.9}$$

where x_i is the mass fraction and ρ_i is the density of component i in the mixture solution. As shown in Table 7, the density of the γ -MPS/TEOS mixture was kept at values lower than 1.0 g cm⁻³.

TEM (Figure 2.32) and SEM (Figure 2.33) were used to characterize the morphology of the hybrid silica nanoparticles synthesized in the presence of increasing amounts of γ -MPS. Figure 2.32 shows that the diameter of the particles increased from 30 nm to 830 nm as the molar fraction of γ -MPS increased from 0 to 14.8 mol%. A direct comparison of the TEM image of Figure 2.32A (without γ -MPS) with all other TEM images clearly shows that the hybrid particles have a rough surface. This was confirmed by the SEM images of Figure 2.33B and C that provide a clearer view of the surface roughness. When the molar fraction of γ -MPS increased to 10.1 mol%, the polydispersity of the particles increased to 1.14. For a γ -MPS concentration of 14.8 mol%, the two-phase solution was destroyed as the density of monomer layer increased to above the boundary point for the two-phase equilibrium. The monomer quickly diffused into the water phase to form a milky solution. The size and dispersity of the particles were no longer controlled in these conditions.



Figure 2.32 TEM images of hybrid γ -MPS-functionalized silica particles for increasing molar fractions of γ -MPS. A: SJLA01 (0). B: SLMT02 (2.09 mol%). C: SLMT03 (5.01 mol%). D: SLMT04 (7.49 mol%). E: SLMT05 (10.10 mol%). F: SLMT06 (14.81 mol%) (Table 7).





Figure 2.33 SEM images of hybrid silica/ γ -MPS particles for increasing molar fractions of γ -MPS. A: SLMT03 (5.0 mol%). B: SLMT04 (7.5 mol%). C: SLMT05 (10.1 mol%). D: SLMT06 (14.8 mol%).

3.2.2 Structural characterization of the hybrid silica particles

FTIR spectra of pure silica and silica/ γ -MPS particles are shown in Figure 2.34. All the spectra show a large band between 3100 and 3700 cm⁻¹, which is ascribed to the stretching vibration of OH groups from Si–OH groups, and residual methanol and water. The bands in the 2850–3000 cm⁻¹ region and at 1470 cm⁻¹ are from the stretching of CH₃, CH₂ and CH groups (ν and δ). The bands at 1700 cm⁻¹ and 1630 cm⁻¹ are attributed to the carbonyl (C = O) and C = C stretching vibrations of γ -MPS, respectively. Finally, the peaks at 1050–1250 cm⁻¹ are characteristic of C-O-C and Si-O-Si stretchings.⁸⁸ The band at 1700 cm⁻¹ attributed to hydrogen-bonded carbonyl groups of the silane moiety increased in intensity with increasing the initial γ -MPS concentration. Simultaneously, a new band at the same position as in pure γ -MPS, and attributed to "free" non-bonded carbonyl, appeared at 1720 cm^{-1.89} This result shows the high degree of co-condensation of the γ -MPS with TEOS at low concentrations, and a mixture of self-condensation of γ -MPS and co-condensation of γ -MPS and TEOS at higher concentrations characterized by the appearance of "free" carbonyl groups.



Figure 2.34 FTIR spectra of the silica particles obtained for increasing molar fractions of γ -MPS. A, SLMT01 (0). B, SLMT02 (2.09 mol%). C, SLMT03 (5.01 mol%). D, SLMT04 (7.49 mol%). E, SLMT05 (10.10 mol%). F, SLMT06 (14.87 mol%) (Table 7).

To gain further insight into the chemical structure of the hybrid particles, they were characterized by ²⁹Si solid-state NMR (Figure 2.35). The different species are denoted according to the conventional Q^n and T^n notation where Q and T designate tetra- and trifunctional units, respectively, and *n* is the number of bridging O atoms surrounding the silicon atom. The chemical shift of di- and tri-substituted siloxanes (T² and T³ units) appears at -57 ppm and -65.8 ppm, respectively while the chemical shift of Q³-Si and Q⁴-Si appears at -101 ppm and -110.4 ppm respectively for all the examples with γ -MPS. With a higher concentration of γ -MPS, the mono-substituted siloxane units (T¹) appear at -48.5 ppm.



Figure 2.35 ²⁹Si solid state NMR analysis of the hybrid silica particles for increasing molar fractions of γ -MPS. A, SLMT01 (0). B, SLMT03 (5.01 mol%). C, SLMT04 (7.49 mol%). D, SLMT05 (10.10 mol%). E, SLMT06 (14.87 mol%) (Table 7).

The hybrid particles were additionally characterized by thermogravimetric analysis (TGA) The TGA thermograms of all hybrid particles of Table 7 are shown in Figure 2.36. The weight loss of the hybrid particles was determined from the residual weight at 800 °C in the TGA thermograms under air atmosphere. The thermal degradation behaviors of the hybrid copolymers can be divided into two stages. The primary degradation stage could be caused by the cleavage of copolymer chains, and the secondary degradation stage could be brought about by further oxidation of silicate.⁹⁰ As it was expected, the weight loss increased as the initial fraction of γ -MPS increased. In Figure 2.37, the weight loss in TGA *vs* initial fraction of γ -MPS shows a linear increase until the system was destroyed in SLMT06. The high weight loss of SLMT06 is probably due to the unhydrolyzed γ -MPS.



Figure 2.36 TGA result of hybrid particles with different fraction of γ -MPS. A, SLMT01 (0). B, SLMT02 (2.09 mol%). C, SLMT03 (5.01 mol%). D, SLMT04 (7.49 mol%). E, SLMT05 (10.10 mol%). F, SLMT06 (14.87 mol%) (Table 7).



Figure 2.37 Evolution of weight loss with different initial molar fractions of γ -MPS

3.2.3 Mesoporous behavior of the hybrid silica particles after calcination

Three samples (SLMT03, 04, 05) with different molar fraction of γ -MPS were observed with TEM after calcination. As shown in Figure 2.38, mesopores appeared after removal of the organic fraction at 800 °C for 2h. Especially for the SLMT05 with high fraction of γ -MPS (Figure 2.38C), some hollow particles were observed.

Nitrogen adsorption-desorption technique was employed to characterize the porous structure of the particles before and after calcination. As shown in Figure 2.39, the adsorption (ADS) and desorption (DES) isotherms shift a lot before and after calcination. The great increase of the BET surface area (Table 9) shows that mesoporous particles were obtained after calcination, in agreement with the TEM observation. It is characteristic of cylindrical mesopores with a narrow pore size distribution ranging from 0.5 to 2.5 nm (Figure 2.40).

The morphology and structure analyzes of the hybrid silica particles show that the γ -MPS is not only a silicate source, but also a mesostructural template. During the formation of hybrid silica particles, γ -MPS is involved in the hydrolysis and subsequent condensation with TEOS. The hydrophobic methacryloxy chains on the γ -MPS tend to aggregate together inside the hybrid particles as a porogen. Although the BET analyzes did not show a great change of the pore size, hollow structures in the TEM image also indicate that the high initial fraction of γ -MPS can lead to the lose control of cocondensation of γ -MPS and TEOS which may form " γ -MPS rich" area in the hybrid particles which will tend to be hollow structure after calcination as illustrated in Figure 2.38C.





Figure 2.38 TEM images after calcination of hybrid silica/ γ -MPS particles prepared with different molar fractions of γ -MPS. A: SLMT03 (5.01 mol%). B: SLMT04 (7.49 mol%) and C: SLMT05 (10.10 mol%).

Table 9	BET	results	for	the	hybrid	silica/ γ -MPS	particles	prepared	with	different	molar
fractions	of γ-N	MPS bef	ore	and	after cal	lcination.					

No	γ-MPS (mol%)	BET before calcination (m ² g ⁻¹)	BET after calcination (m ² g ⁻¹)
SLMT03	5.01	114.4	460.4
SLMT04	7.49	80.7	616.7
SLMT05	10.10	27.1	657.1







Figure 2.39 Nitrogen adsorption (ADS) and desorption (DES) isotherms of SLMT03, SLMT04 and SLMT05, before and after calcination: ADS before calcination (\bullet). DES before calcination (\blacktriangle). ADS after calcination(\blacklozenge). DES after calcination (\blacksquare).



Figure 2.40 Mesoporous size distribution after calcinations: SLMT03 (\blacktriangle). SLMT04 (\blacklozenge) and SLMT05 (\blacksquare).

3.2.4 Synthesis of core-shell like hybrid particles via a multi-steps L-arginine-based process

Since we believe the high aggregation of methacryloxy chains on the γ -MPS can introduce a hollow structure, an extension of the L-arginine process (multi-steps route) was investigated to control this aggregation and to form well-ordered hollow core–porous shell particles. Figure 2.41 illustrates the different steps for the synthesis of γ -MPS/silica core-shell particles according to this process.

The process was based on a Pickering-emulsion like process.^{91,92} In classical Pickering emulsions, the emulsion is stabilized by the adsorption of small colloidal particles at the oil-water interface. In the present work, the small silica nanoparticles was employed to stabilize the γ -MPS droplets in the water phase.

As described in the experimental part, the first step consisted in the synthesis of small silica seeds. Based on the results for pure silica synthesized in Table 3, 0.09 mol L⁻¹ of TEOS was added to get nanosilica seeds with size around 15 nm at 100% conversion. In the second step, γ -MPS was added to the silica seeds. As the density of γ -MPS is higher than that of water, γ -MPS quickly sank to the bottom. The stirring speed was thus increased to a much higher speed to allow a fine dispersion of γ -MPS droplets stabilized by the silica nanoparticles (Pickering stabilization). Carefully observed by eyes, the color of the mixture changed from white opaque to light blue semi-transparent in 0.5 h. The DLS results showed that stable monodisperse droplets were obtained which was also confirmed by cryo-TEM (Figure 2.42). The γ -MPS droplets are stabilized by small silica nanoparticles adsorbed on their surface.





Figure 2.41 Schematic illustration for the synthesis of γ -MPS/silica core-shell hybrid particles via a multi-step L-arginine-based process.



Figure 2.42 TEM (left) and cryo-TEM (right) of γ -MPS droplets stabilized with small silica particles.

Finally, another addition of TEOS via the biphasic method led to the formation of a raspberrylike silica shell around the γ -MPS droplets. As shown in Figure 2.43, this step includes a secondary nucleation of new silicate source (TEOS) and aggregation of the γ -MPS droplets, which could be clearly seen by the significant change of the droplet size (from 30 nm to 100 nm) and morphologies from multipod-like to raspberry-like droplets.



Figure 2.43 Cryo-TEM of the silica-stabilized γ -MPS droplets before and after TEOS addition. The morphology evolved from multi-pod-like (left) to raspberry-like (right).

As shown in Figure 2.44, the raspberry-like shell turned to be a complete silica shell upon TEOS polymerization, the shell thickness increasing until all TEOS was consumed. As the γ -MPS core was totally "protected" by the silica shell, its size did not change during the growth process.



Figure 2.44 TEM images of the γ -MPS/silica hybrid particles formed upon further addition of TEOS. The morphology evolved from raspberry-like droplets to thin core-shell and then thick core-shell particles (from left to right).

3.2.5 Effect of γ-MPS concentration on the core-shell hybrid morphology

As shown in Table 8, different concentrations of γ -MPS were used to see its effect on the morphology of the core-shell particles. The DLS result showed that when the concentration of γ -MPS was low (e.g. 0.024 mol L⁻¹, SLMT07 in Table 8), the Poly value of the particles was very big. The corresponding TEM image of SLMT07 (Figure 2.45A) shows the presence of some core-shell particles together with many free silica particles around, which indicates γ -MPS could not adsorb all the silica seeds.

The free silica particles fade away when the concentration of γ -MPS increased (SLMT08: 0.054 mol L⁻¹; Figure 2.45B and SLMT09: 0.116 mol L⁻¹, Figure 2.45C). At the same time, core-shell hybrids exhibit quite narrow size distribution. The SEM of the SLMT09 showed that the surface of the particles is rough with some raspberry-like dots on it that are likely due to the metallic particles used for SEM analysis.



Figure 2.45 TEM images of core-shell γ -MPS/silica particles with different molar fractions of γ -MPS. A: SLMT07 (2.26 mol%). B: SLMT08 (4.89 mol%). C: SLMT09 (9.89 mol%). C1: SEM images of SLMT09 (9.89 mol%) (Table 8).

3.2.6 Porous core-hollow shell structure after calcination

Figure 2.46 shows the TEM images of SLMT08 and 09 after calcination. Porous core-hollow shell structure can be clearly seen in Figure 2.46B. Figure 2.47 displays the BET analysis of SLMT09 before and after calcination. The surface area increased from 32 m² g⁻¹ before calcination to 258 m² g⁻¹ after calcination. It should be noted that the curve for N₂ desorption has a significant hysteresis indicative of the presence of mesopores and macropores due to the

hollow structure of the particles. The mesoporous size distribution of Figure 2.48 indicates that the pore size is around 4 nm.



Figure 2.46 TEM images of the particles with different fraction of γ -MPS after calcination. A: SLMT08 (4.89 mol%) and B: SLMT09 (9.89 mol%).



Figure 2.47 Nitrogen adsorption (ADS) and desorption (DES) isotherms of SLMT09 before and after calcination: ADS before calcination (\bullet). DES before calcination (\blacktriangle). ADS after calcination(\bullet). DES after calcination (\blacksquare).



Figure 2.48 Mesoporous size distribution after calcination for SLMT09.

3.2.7 Structure characterization of core-shell hybrid silica particles

Figure 2.49 shows the TGA thermogram for core-shell hybrid particles obtained with different concentrations of γ -MPS. As it was expected, the weight loss increased as the initial fraction of γ -MPS increased.



Figure 2.49 TGA result of core-shell particles synthesized with different molar fractions of γ -MPS. SLMT10 (2.26 mol%), SLMT08 (4.89 mol%) and SLMT09 (9.89 mol%) (Table 8).

Figure 2.50 displays the FTIR spectra of pure silica and core-shell hybrids obtained for different concentrations of γ -MPS. Compared with the previous results in Figure 2.34, the band at 1700 cm⁻¹ almost disappeared. The "free" non-bonded carbonyl for self-condensation of γ -MPS appeared even for low concentration. This result shows that the self-condensation is the main choice for both γ -MPS and TEOS.



Figure 2.50 FTIR spectra of the core-shell particles synthesized with different molar fractions of γ-MPS. A, SLMT00 (0). B, SLMT10 (2.26 mol%). C, SLMT08 (4.89 mol%). D, SLMT09 (9.89 mol%) (Table 8).

Figure 2.51 shows the ²⁹Si NMR spectrum of SLMT09. The chemical shift of di- and trisubstituted siloxanes (T^2 and T^3 in the spectra) appears at -57.5 ppm and -66.6 ppm; the chemical shift of Q³-Si and Q⁴-Si appears at -101.5 ppm and -110.8 ppm and the residual TEOS was also observed at -81.1ppm.



Figure 2.51 ²⁹Si Solid NMR of SLMT09 (with 9.89 mol% γ -MPS.).

3.2.8 Conclusions

The L-arginine process and a multi-step extension of this process were investigated to synthesize hybrid silica particles with different particle sizes and morphologies. Those hybrid particles exhibited a big increasing of surface area after calcination (e.g. $27 \text{ m}^2 \text{ g}^{-1}$ before calcination and $657 \text{ m}^2 \text{ g}^{-1}$ after calcination). Including the TEM observation, we can conclude that this strategy offers a simple route for the synthesis of MSNs. In addition, this route was extended to the synthesis of core-shell like hybrids based on a Pickering growth-like approach. After calcination, silica particles with hollow core–porous shell structure were achieved.

For the L-arginine process with γ -MPS/TEOS mixture, the initial γ -MPS concentration has a great impact on the particle size and stability of the system, but less effect on the pore size and size distribution. We suspect the length of the hydrophobic chains of the organosilane may have a great effect on the control of pore size, a parameter which may be investigated in future works.

For the core-shell hybrid silica particles achieved via the multi-step process, the γ -MPS concentration was also the key to form well-ordered monodisperse core-shell hybrids, low concentration of γ -MPS leading to the formation of free silica, and high γ -MPS concentration inducing a loss of colloidal stability of the system. We also argue that the length of the hydrophobic chains of the organosilane has a great effect on the morphology of the resulting hybrid core-shell particles. What is more, this route could be potentially extended to

encapsulate monomers or drugs in pure aqueous media without any surfactant and co-solvent, which opens the door to a new class of inorganic capsules.

Conclusions

The main objective of this chapter was to synthesize monodisperse silica particles with different sizes and narrow size distributions. Different processes were employed and different parameters were adjusted to achieve the best control of both particle size and size distributions.

At first, we have investigated the classic Stöber method either in batch or in semi-batch. We discussed the effect of ammonia concentration and water concentration on the silica particle size and size distribution. Under the conditions used in our work, the Stöber method is suitable for the synthesis of silica particles with narrow size distribution in the size range from 200 nm to 500 nm.

Then the L-arginine process was employed to get silica particles smaller than 50 nm. This novel process showed significant advantages for the synthesis of small spherical silica nanoparticles due to the slow hydrolysis rate of TEOS in this system. However, the fairly long reaction time due to a very slow growth process is an obvious drawback of the L-arginine process. To avoid this drawback, the regrowth of silica seeds in ethanol/water mixtures was also investigated to get silica particles with diameters comprised between 100 and 200 nm. The regrowth of 30 nm silica seeds from L-arginine process was carried out via a Stöber-like process using either ammonia or L-arginine as catalysts. Under the conditions studied in our work, a regrown silica ($D_n = 136$ nm) with a narrow size distribution was achieved when ammonia was used as catalyst. In contrast, the regrowth of silica seeds with L-arginine as the catalyst mainly led to worm-like silica particles as the addition of ethanol and TEOS in the original aqueous dispersed silica sol would affect colloidal stability and lead to assembly or aggregation of the spherical silica particles.

Furthermore, the L-arginine process in one step or in multi-steps was investigated to synthesize hybrid silica particles and core-shell particles using TEOS and γ -MPS as the silica sources. After removal of the methacryloxy chains of γ -MPS, which also act as a pore template in the process, mesoporous silica particles with pore sizes around 2 nm and hollow core-porous shell silica particles were successfully obtained.

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Chapter 3

Synthesis of poly(ethylene oxide)- (PEO-) based macroalkoxyamine initiators

Introduction

This chapter deals with the synthesis and characterization of water-soluble macroalkoxyamine initiators based on poly(ethylene glycol) methyl ether methacrylate (PEOMA) or copolymers of PEOMA with methacrylic acid (MAA). These two series of macroalkoxyamine initiators will be used further in Chapter 4 and 5 to synthesize amphiphilic block copolymers through polymerization-induced self-assembly (PISA) in aqueous emulsion, first in the absence and then in the presence of silica. The main purpose of inserting PEOMA units in the hydrophilic block is to establish strong cooperative hydrogen bonding interactions with the silanols on the silica surface, which is the key to get hybrid particles via NMP in this thesis. The incorporation of MAA units in the copolymers will allow us tuning their LCST behavior by varying the suspension pH. Indeed, a lower LCST may promote further interaction of the hydrophobic monomers with the inorganic surface making the interface more hydrophobic, and hence more compatible with the growing polymer chains.

The chapter is divided into three parts. We first start with a short bibliography review on PEOMA-based polymers and their LCST behavior. Then, we describe the synthesis of PEOMA-based macroalkoxyamine initiators and their copolymers with MAA. Finally, in the last section we discuss the effect of pH, ionic strength, copolymer nature and composition on the cloud point temperature of the macroalkoxyamine initiators.

1. Bibliography review on PEOMA-based polymers and their LCST behavior

PEOs are polymers of ethylene oxide. As PEO molecular weight increases, viscosity and freezing point increases, and solubility in water decreases. Even at the highest molecular weights, PEOs are highly water-soluble. Low molecular weight PEOs (< 600 g mol⁻¹) are clear liquids above 24 °C. Due to their low toxicity, flexibility and good water-solubility, PEOs are deeply employed in the pharmaceutical area, especially for drug delivery purposes such as polymer-protein/peptide bioconjugates (termed PEGylation)¹⁻⁷ or "stealth" long circulating nanoparticles.⁸⁻¹¹ Indeed, PEO gives rise to several potential beneficial effects including increased bioavailability and plasma half-lives, biocompatibility/decreased immunogenicity, reduced proteolysis, and enhanced solubility and stability, thus being considered as a key material in this field.²

Chapter 3. Synthesis of PEO-based macroalkoxyamines

Linear PEO chains and PEO-based copolymers have also been extensively used as stabilizers and/or surface modifiers of polymer colloids and inorganic particles. The early use of PEObased copolymers was facilitated by the development of well-defined architectures via anionic polymerization. PEO segments can be introduced in a copolymer in two different manners. The first one takes advantage of the terminal hydroxyl group of the PEO chain (produced via anionic polymerization of ethylene oxide) to introduce a target functionality able to react as an initiator (hydroxy groups for ring opening polymerization,¹² alkoxyamine for NMP^{12, 14} or alkyl halide for ATRP¹⁵) or a chain transfer agent (thiols¹⁶ for conventional radical polymerization, dithioester^{17,18} or trithiocarbonate^{19,20} for RAFT). The second method relies on the use of PEO-based macromonomers based on a styrenic,²¹ an acrylate²² or a methacrylate^{13,14} polymerizable group that can be successfully polymerized via conventional radical polymerization²⁵ or introduced in a well-defined (block) copolymer via NMP,^{13,14,15,16} ATRP¹⁷⁻²¹ or RAFT.^{22,23} The latter type of macromonomer (PEOMA for poly(ethylene glycol) methyl ether methacrylate) is the most common one due to the simplicity of synthesis and availability, the stability of the ester bond to hydrolysis and the reduced extent of chain transfer reactions in free-radical polymerization. Figure 3.1 gives the chemical structure of PEOMA.



Figure 3.1 Molecular structure of PEOMA.

PEOMA-based polymers are thermoresponsive and present a lower critical solution temperature (LCST) phase transition. Below the LCST, the polymer chains are in an expanded state and fully dissolved, whereas above this temperature they are dehydrated and insoluble. This behavior is characteristic of non-ionic surfactants containing PEO chains, which exhibit reverse solubility versus temperature behavior in water and therefore "cloud out" at some point as the temperature is raised.²⁴ Typically the cloud point of a dilute polymer solution is reported as an indicator of the thermoresponsive nature of the polymer sample,

rather than the LCST of a polymer/water phase diagram. The cloud point temperature of a polymer is defined as the temperature at which a transparent polymer solution exhibits the first signs of cloudiness, the polymer chains precipitating as a second phase giving to the fluid a cloudy appearance. Experimentally, the cloud point is generally defined as the temperature at which normalized transmittance is reduced to 50 % during the phase transition.

The LCST of PEOMA-based homopolymers depends on the length of the PEO side-chains or in the case of copolymers, on the comonomer composition. Lutz et al.^{21,25-27} studied the influence of PEO chain length on the LCST behavior of a large range of poly(ethylene glycol) methacrylate polymers in aqueous solutions and showed that the LCST increases with increasing the number of ethylene glycol units in the lateral chains. For instance, the LCST of poly(2-(2'-methoxyethoxy) ethyl methacrylate) (PMEO₂MA, 2 EO units) is 26 °C while that of poly(triethylene glycol methacrylate) (PMEO₃MA, 3 EO units) is 52 °C. Finally poly(oligo (ethylene glycol) methacrylate) with 8-9 ethylene oxide units (PEOMA₄₇₅) has a LCST of 90 °C (Figure 3.2).^{21,25} Copolymers of PMEO₂MA or PMEO₃MA and PEOMA have intermediate LCST values.



Figure 3.2 Molecular structures of various oligo(ethylene glycol) methacrylates and the LCST of the corresponding homopolymers. Hydrophobic and hydrophilic molecular regions are indicated in red and blue, respectively.²⁵

Chapter 3. Synthesis of PEO-based macroalkoxyamines

The incorporation of comonomers in the polymer chain usually provides a strong change in the LCST. Generally speaking, the LCST decreases with the incorporation of hydrophobic comonomers and increases when the comonomer is hydrophilic. PEOMA has been copolymerized with many comonomers like *N*-isopropyl acrylamide, dimethyl aminoethyl methacrylate,^{28,29} alkyl methacrylates,³⁰ styrene,²³ or methacrylic acid to provide materials of various LCSTs. For instance, Becer et al.³¹ reported the LCST behavior of a variety of well-defined homopolymers and copolymers of MAA, PEOMA₄₇₅ and PEOMA₁₁₀₀. The cloud point of P(MAA-*co*-PEOMA₄₇₅) copolymers could be tuned in the 20-90°C range with increasing the PEOMA₄₇₅ mol percentage. Interestingly, P(MAA-*co*-PEOMA₁₁₀₀) copolymers showed a LCST behavior at certain compositions, although their homopolymers did not reveal any cloud point. One possible interpretation of this result is the formation of intramolecular hydrogen bonding interactions between the acid groups of MAA and the ethylene glycol units of the PEOMA chains at low pH value (pH = 2 and 4), which is an additional driving force to expel the water from the hydration shell and, which consequently tends to lower the LCST.

The LCST of PEO-based polymers are also dependent on ionic strength. Magnusson et al.³² studied the effect of the addition of salts of the Hofmeister series on the LCST behavior of brush-type statistical P(PEOMA₄-*co*-PEOMA₈) copolymers. In view of the strong interactions of PEO chains with Lewis acids, both Li⁺ and Na⁺ counterions were investigated in this work. Very marked changes in LCST occurred following the admixture of strong chaotropes (SCN⁻) or kosmotropes (SO₄²⁻), traditionally known as water-structure "breakers" and water-structure "makers," respectively. Luzon et al.³³ studied the salt effect on the LCST behavior of a series of brush-type copolymers made from di(ethylene glycol) methacrylate (DEOMA) and PEOMA (M_n = 475 g mol⁻¹, 8-9 EO units). The addition of salt (i.e., NaCl or Na₂SO₄) caused a decrease in the LCST of the copolymers. The type of salt also influenced the LCST behavior with the Na₂SO₄ salt exhibiting a stronger effect than NaCl. This influence of salt structure is known as the Hofmeister effect.^{34,35}

Finally, the nature of the end groups of the polymers was also proved to have a significant effect on the cloud point. Roth et al.³⁶ selectively modified the end groups of heterotelechelic poly[oligoethylene glycol monomethyl ether methacrylate] polymers and investigated the influence of the chemical structure of both end groups onto the LCST behavior in water. By comparing a series of polymers with the same degree of polymerization but with two end groups of variable sizes and polarities, they concluded that the introduction of hydrophobic

groups on both ends of the polymer chains decreased the LCST. The incorporation of charged end groups increased the LCST and could compensate for the effect of the hydrophobic group located at the opposite chain end. Vo et al.³⁷ compared the LCST behavior of poly(2-hydroxypropyl acrylate) (PHPA) homopolymers before and after removal of the hydrophobic dodecyl thiocarbonylthio end group coming from the RAFT agent used for their synthesis. Without the hydrophobic dodecyl end groups, the PHPA homopolymers were more hydrophilic and hence exhibited higher LCST values.

2. Synthesis of PEOMA-based brush-type macroalkoxyamine initiators

As mentioned in Chapter 1, Charleux et al.^{38,39,13} showed that the nitroxide-mediated copolymerization of methacrylate esters can be carried out under mild conditions (< 90 °C) by addition of a small amount of styrene to the reaction medium. Following this strategy, we report in the following section the NMP synthesis of P(PEOMA-*co*-S) and P(PEOMA-*co*-MAA-*co*-S) living copolymers and terpolymers, respectively.

2.1 Experimental section.

Materials

The monomers styrene (S, 99%, Acros), methacrylic acid (MAA, 99%, Aldrich) and two different poly(ethylene oxide) methyl ether methacrylate macromonomers (PEOMA₃₀₀, number-average molar mass $M_n = 300$ g mol⁻¹ and PEOMA₉₅₀, $M_n = 950$ g mol⁻¹, Aldrich) were used without further purification. The *N*-(2-methylpropyl)-*N*-(1-diethylphosphono-2,2-dimethylpropyl)-*O*-(2-carboxylprop-2-yl) hydroxylamine initiator (BlocBuilder[®], 99%) and N-tert-butyl-N-(1-diethyl phosphono- 2,2-dimethylpropyl) nitroxide (SG1, 85%) were kindly supplied by Arkema. Ethanol (Prolabo, pure) and dimethyl sulfoxide (DMSO, Aldrich) were used as received.

Synthesis

P(PEOMA-*co*-S)-SG1 brush-type macroalkoxyamine initiators of various molar masses, compositions and PEO chain lengths ($M_n = 300$ and 950 g mol⁻¹, respectively) were synthesized following the procedure previously reported by Charleux et al.^{40, 41} In a typical reaction, the monomers (PEOMA and S), SG1 and ethanol were stirred in an erlenmeyer flask and deoxygenated by nitrogen bubbling for 20 min at room temperature. The BlocBuilder[®] alkoxyamine initiator was added and nitrogen was bubbled for 10 additional minutes. The

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mixture was then introduced into a three-neck round-bottom flask (50 mL) and heated to 78.5 °C. The time zero of the reaction was triggered at 75 °C. Samples were periodically withdrawn to follow monomer conversion by using proton NMR. Scheme 3.1 shows the schematic description of the synthesis. All the corresponding experimental conditions are given in Table 1.



Scheme 3.1 Schematic representation of the synthesis of brush-type P(PEOMA-*co*-S)-SG1 macroalkoxyamine initiators using BlocBuilder[®] as alkoxyamine initiator in ethanol at 78.5 °C in the presence of a small amount of free SG1 nitroxide.

Synthesis of P(PEOMA-*co*-MAA-*co*-S)-SG1 brush-type macroalkoxyamine initiators was performed using a similar process with only slight modifications. As shown in Scheme 3.2, ethanol was replaced by DMSO and only PEOMA₃₀₀ was used, while the reaction temperature was increased to 80 °C. All the corresponding experimental conditions are given in Table 2.



Scheme 3.2 Schematic representation of the synthesis of brush-type $P(PEOMA_{300}-co-MAA-co-S)-SG1$ macroalkoxyamine initiators using BlocBuilder[®] as alkoxyamine initiator in DMSO at 80 °C in the presence of a small amount of free SG1 nitroxide.

Characterizations

¹H NMR spectroscopy for kinetic analysis was performed in 5 mm diameter tubes in DMSOd₆ at room temperature (Bruker DRX 300). The individual molar conversions of S, PEOMA and MAA (when present) ($X_{\rm S}$, $X_{\rm PEOMA}$ and $X_{\rm MAA}$, respectively) during the macroinitiator synthesis were determined by measuring the vinyl proton integrals of the monomers (three vinyl protons of S at $\delta = 6.74$ ppm, $\delta = 5.83$ ppm and $\delta = 5.25$ ppm, two CH₂ protons at $\delta =$ 6.04 ppm and $\delta = 5.69$ ppm for PEOMA and two vinyl protons at 5.84 and 5.29 ppm for MAA) using 1,3,5-trioxane as an internal reference ($\delta = 5.12$ ppm). The chemical shift scale was calibrated relative to tetramethylsilane. The overall conversion considered was the molar conversion, X_{mol}, directly accessible via the NMR analysis and calculated from the individual monomer conversions according to the relationship: $X_{\rm mol} = X_{\rm S} \times f_{\rm S,0} + X_{\rm PEOMA} \times f_{\rm PEOMA,0} + X_{\rm MAA} \times f_{\rm MAA,0}$ where $f_{\rm S,0} f_{\rm PEOMA,0}$ and $f_{\rm MAA,0}$ are, respectively, the initial molar fractions of S, PEOMA and MAA in the monomer mixture. For the plots representing $M_{\rm n}$ as a function of the overall conversion, the weight conversion was used, and calculated according to $X_{\rm wt} = X_{\rm S} \times W_{\rm S,0} + X_{\rm PEOMA} \times W_{\rm PEOMA,0} + X_{\rm MAAA,0} \times W_{\rm MAA,0}$ where $W_{\rm S,0}$, $W_{\rm PEOMA,0}$ and $W_{\rm MAA,0}$ are, respectively, the initial weight fractions of S, PEOMA and MAA in the monomer mixture.

Run	[PEOMA ₃₀₀] (mol L ⁻¹)	[PEOMA ₉₅₀] (mol L ⁻¹)	[S] (mol L ⁻¹)	[SG1] ₀ (mol L ⁻¹)	[BlocBuilder] (mol L ⁻¹)	$f_{0,\mathrm{S}}^{a}$	Target $M_n^{\rm b}$ (g mol ⁻¹)	Target DP [°] (PEOMA ₃₀₀ /PEOMA ₉₅₀ /S)
M1 M2	0.83	0 0.26	0.080 0.027	0.001	0.0087 0.0088	0.088 0.092	29 930 28 980	96/0/10 30/0/3
M3	0.20	0.20	0.039	0.001	0.0086	0.088	29 420	22/22/4
Run	[PEOMA ₃₀₀] (mol L ⁻¹)	[MAA] (mol L ⁻¹)	[S] (mol L ⁻¹)	$[SG1]_0$ (mol L ⁻¹)	[BlocBuilder] (mol L ⁻¹)	$f_{0,\mathrm{S}}^{-\mathrm{a}}$	Target <i>M</i> (g mol ⁻¹)	Target DP [°] (PEOMA ₃₀₀ /MAA/S)
M4	1.08	0.27	0.16	0.0015	0.014	0.105	26 030	77/19/11
M5	0.71	0.77	0.17	0.0017	0.015	0.103	19 560	45/50/11
9W	0.34	1.35	0.18	0.0020	0.015	0.096	14 610	20/81/11

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<u>.</u>; ÷ 2 ģ a a fraction of free SG1 versus BlocBuilder[®]: r = 0.119^a In

Size exclusion chromatography (SEC) analyses of P(PEOMA-*co*-S)-SG1 copolymers were performed in DMF (with LiBr, 0.01 mol L⁻¹) using an EcoSEC semi-micro GPC system from Tosoh equipped with a dual flow refractive index detector and a UV detector. The analyses were performed at 50 °C using a flow rate of 1 mL min⁻¹. Toluene was used as a flow rate marker. All polymers were injected at a concentration of 2 mg mL⁻¹ after filtration through a 0.45 µm pore-size membrane. Separation was performed with a guard column and three PSS GRAM columns (7 µm, 300 × 7.5 mm). The average molar masses (number-average molar mass M_n and weight-average molar mass M_w) and the molar mass dispersity (M_w/M_n) were derived from the RI signal by a calibration curve based on poly(methyl methacrylate) (PMMA) standards.

SEC analyses of P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 terpolymers were performed in THF. All polymers were injected at a concentration of 3 mg mL⁻¹ after filtration through a 0.45 μ m pore-size membrane. The separation was carried out on three Polymer Laboratories columns [3 × PLgel 5 μ m Mixed C (300 × 7.5 mm)] and a guard column (PL gel 5 μ m). Columns and detectors were maintained at 40 °C. THF was used as the mobile phase at a flow rate of 1 mL min⁻¹ and toluene served as a flow rate marker. The average molar masses and molar mass distributions were calculated with a calibration curve based on PMMA standards. Before analysis, the polymers were modified by methylation of the carboxylic acid groups using trimethylsilyl diazomethane as reported elsewhere.⁴²

2.2 Results and Discussion

2.2.1 P(PEOMA-co-S)-SG1

¹H NMR spectroscopy was used to investigate the copolymerization kinetics of PEOMA and styrene. Figure 3.3 shows the evolution of both individual and overall monomer conversions with time. Styrene is obviously consumed faster than PEOMA which implies chemical drift with polymer chain "richer" in styrene at the beginning. The overall molar conversion is nearly the same as the conversion of PEOMA.



Figure 3.3 Molar conversion *vs* time plots during the synthesis of P(PEOMA-*co*-S)-SG1 macroinitiators: a) M1 (PEOMA₃₀₀), b) M2 (PEOMA₉₅₀) and c) M3 (50 mol % PEOMA₃₀₀+ 50 mol % PEOMA₉₅₀) (Table 1).

The first-order plot of $\text{Ln}[1/(1-X_{\text{mol.}})]$ vs time of Figure 3.4 shows a linear evolution indicating a constant concentration of propagating radicals. The slope and final conversions directly depend on the type of macromonomer used, and hence on its initial molar concentration, which varies in all experiments (the initiator concentration being the same): the higher the concentration, the higher the slope. Similar results were obtained by Nicolas et al.¹³ during the homopolymerization of PEOMA₃₀₀ using BlocBuilder[®] as an initiator.



Figure 3.4 $Ln[1/(1-X_{mol.})]$ *vs.* time plots during the synthesis of P(PEOMA-*co*-S)-SG1 macroinitiators. M1 (PEOMA₃₀₀, **•**), M2 (PEOMA₉₅₀, **•**) and M3 (50 mol % PEOMA₃₀₀ + 50 mol % PEOMA₉₅₀, **•**) (Table 1).

The evolutions of M_n and M_w/M_n measured by SEC in DMF as a function of the overall weight conversion (Figure 3.5) show a linear increase and narrow molar mass distributions $(M_w/M_n < 1.4)$, indicative of a good control of the polymerization exempt of side reactions such as chain transfer reactions to the solvent. Although a PMMA calibration was applied and may not be fully appropriate, it appears that all M_n data points fall close to the theoretical line, which is the expected trend with a high initiator efficiency. The good control over chain growth is moreover corroborated by the SEC peaks, which shift toward higher molar masses with the progress of monomer conversion (Figure 3.6).



Figure 3.5 Evolutions of M_n and M_w/M_n (determined by SEC in DMF, PMMA calibration) with the weight conversion X_{wt} during the synthesis of P(PEOMA-*co*-S)-SG1 macroinitiators. M1 (PEOMA₃₀₀, \blacksquare and \Box), M2 (PEOMA₉₅₀, \bullet and \circ) and M3 (50 mol% PEOMA₃₀₀ + 50 mol% PEOMA₉₅₀, \blacktriangle and \triangle) (Table 1). The straight line corresponds to the theoretical evolution.





Figure 3.6 Evolution of the size exclusion chromatograms (SEC in DMF, PMMA calibration) with weight conversion during the synthesis of the P(PEOMA-*co*-S)-SG1 macroinitiators. M1 (PEOMA₃₀₀), M2 (PEOMA₉₅₀) and M3 (50 mol % PEOMA₃₀₀ + 50 mol % PEOMA₉₅₀) (Table 1).

In summary, the SG1-mediated copolymerization of PEOMA with a small percentage of S performed in ethanol at 78.5 °C was shown to exhibit all the characteristics of a controlled radical polymerization. A favored incorporation of S at the beginning of the copolymerization was observed, enabling an efficient deactivation of the propagating radicals by the nitroxide SG1.

2.2.2 P(PEOMA₃₀₀-co-MAA-co-S)-SG1

To allow for a faithful comparison between all P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 copolymers, we fixed their number-average degrees of polymerization (around 110) and only varied the PEOMA₃₀₀ to MAA ratio (Table 2). The individual S, MAA and PEOMA₃₀₀ molar conversions were determined by ¹H NMR as described above.

Figure 3.7 shows the evolution of monomer conversions with time. As before, S was consumed much faster than MAA or PEOMA. Furthermore, the plots also indicate a higher conversion rate for PEOMA than for MAA.⁴³



Figure 3.7 Molar conversion *vs* time plots for the synthesis of P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroinitiators with different molar ratio of PEOMA₃₀₀ and MAA: a) M4 (PEOMA₃₀₀/MAA= 4/1), b) M5 (PEOMA₃₀₀/MAA = 1/1), and c) M6 (PEOMA₃₀₀/MAA = 1/4) (Table 2).

As before, Figure 3.8 shows a linear variation of conversion with time in semi-logarithmic coordinates indicating first-order kinetics with respect to monomer and a constant concentration of the active species. The slope and final conversions directly depend on the types of monomers and concentrations. The initiator and monomer concentrations being the same for all experiments, the increase of the initial MAA fraction results in the decrease of the slope value.⁴³



Figure 3.8 Ln[1/(1- $X_{mol.}$)] *vs.* time plots for the synthesis of P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroinitiators with different molar ratio of PEOMA₃₀₀ and MAA. M4 (PEOMA₃₀₀/MAA = 4/1, •), M5 (PEOMA₃₀₀/MAA = 1/1, •) and M6 (PEOMA₃₀₀/MAA = 1/4, \checkmark) (Table 2).

The evolutions of M_n and M_w/M_n measured by SEC in THF as a function of the overall weight conversion show a linear increase and low molar mass distributions ($M_w/M_n < 1.6$) (Figure 3.9) indicating a good control of the polymerization. The good control over chain growth was corroborated by the SEC peaks, which shifted toward higher molar masses with increasing monomer conversion (Figure 3.10).



Figure 3.9 Evolutions of M_n and M_w/M_n (determined by SEC in THF, PMMA calibration) with the weight conversion X_{wt} for the synthesis of P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroinitiators with different molar ratio of PEOMA₃₀₀ and MAA. M4 (PEOMA₃₀₀/MAA = 4/1, \blacktriangle and \bigtriangleup), M5 (PEOMA₃₀₀/MAA = 1/1, \bullet and \circ), and M6 (PEOMA₃₀₀/MAA = 1/4, \checkmark and \bigtriangledown). The straight line in the M_n *vs.* conv. plot corresponds to the theoretical evolution (Table 2).







Figure 3.10 Evolution of the size exclusion chromatograms (SEC in THF, PMMA calibration) with weight conversion during the synthesis of the P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroinitiators with different molar ratio of PEOMA₃₀₀ and MAA. M4 (PEOMA₃₀₀/MAA = 4/1), M5 (PEOMA₃₀₀/MAA = 1/1) and M6 (PEOMA₃₀₀/MAA = 1/4) (Table 2).

All the results presented in this section show that the SG1-mediated copolymerization of $PEOMA_{300}$ and MAA with a small percentage of S performed in DMSO at 80 °C offers a good control of molar masses and molar mass distributions. The evolutions of individual monomer conversions with time indicate that S is consumed faster than PEOMA or MAA,

which may result in a slight composition drift. Fast S consumption at low conversions may induce a rapid depletion of S and a loss of control at very high conversions. These macroinitiators have been synthesized at a larger scale in the following section. To ensure the livingness of the macroalkoxyamine initiators, their synthesis will be stopped at relatively low conversions as reported below.

3. Synthesis of PEOMA-based macroalkoxyamine initiators for emulsion polymerization and their LCST behavior

Based on the kinetic studies presented in the previous section, we carried out a series of larger scale reactions in order to get larger amounts of macroalkoxyamine initiators of targeted molar mass and compositions (Table 3) and to study their LCST behaviors. These living polymers will be used further in Chapters 4 and 5 to synthesize polymer latex particles via surfactant-free nitroxide-mediated aqueous emulsion polymerization first in the absence and then in the presence of silica.

3.1 Experimental procedure

Larger scale syntheses of PEOMA-based macroalkoxyamine initiators were performed in a 500 mL three-neck round-bottom flask according to the recipes of Tables 1 and 2. Based on the kinetics studies, the reaction was carried out for different periods of time (2h for Ma1, Ma2 and Ma3, 50 min for Ma4 and 60 min for Ma5 and Ma6). As mentioned above, the polymerization was stopped at relatively low monomer conversions to ensure a high fraction of living chains. The final product was dried under vacuum after precipitation in diethyl ether before analysis. ¹H NMR spectroscopy was used to determine the monomer conversion and to characterize the final products after precipitation. As illustrated in Figure 3.11 for Ma2, ¹H NMR shows the absence of residual monomer after precipitation.

The cloud points of the macroinitiator solutions in water (0.5 wt %) were determined by monitoring the transmittance at 500 nm as a function of temperature using a Shimadzu (UV-1800) UV-visible spectrometer. The temperature range was from 20 to 80 °C and the heating rate was 1 °C min⁻¹. The cloud point was defined as the temperature corresponding to 50% transmittance ($T_{50\%}$).

Sodium hydroxide (0.1M and 1M aqueous solutions) was used to increase the pH value of the macroinitiator solutions in water. Sodium chloride (NaCl) was used to fix the ionic strength.



Figure 3.11 Typical ¹H NMR spectrum (in DMSO) of the final P(PEOMA-*co*-S)-SG1 copolymer synthesized on a larger scale in ethanol solution at 78.5 °C (Ma2 in Table 3), after precipitation in diethyl ether.

All purified polymers were characterized by SEC in THF. The results reported in Table 3 again show a good control of the polymerization ($M_w/M_n < 1.2$ for P(PEOMA-*co*-S) and $M_w/M_n < 1.4$ for P(PEOMA-*co*-MAA-*co*-S)). Using M_n from SEC and the average composition of the copolymers (molar fractions F_{PEOMA}, F_S and F_{MAA}) from NMR, it was possible to determine the average number of comonomer units within the chains. The number of styrene units in the P(PEOMA-*co*-S)-SG1 copolymers is relatively small, and its weight proportion is far smaller considering the high molar mass of the macromonomers, which will ensure a negligible effect of styrene on the solubility behavior of these macroalkoxyamines in water. In contrast, the number of styrene units of the P(PEOMA-*co*-S)-SG1 macroalkoxyamines is much larger which is compensated for by the incorporation of MAA units within the chains which should guarantee polymer water solubility.

experimental conditions shown in Tables 1 and 2.	

Chapter 3. Synthesis of PEO-based macroalkoxyamines

lar conv. (%) $M_{\rm n}({ m g mol}^{-1}) \ M_{\rm w}/M_{\rm n}$ Structure of the copolymers	Structure of the copolymers P[(PEOMA ₃₀₀) ₃₈ -co-S ₃] P[(PEOMA ₉₅₀) ₁₂ -co-S ₁] P[(PEOMA ₃₀₀) ₁₀ -co-(PEOMA ₉₅₀) ₁₀ -co-S ₁] P[(PEOMA ₃₀₀) ₃₄ -co-MAA _{6.7} -co-S _{7.2}] P[(PEOMA ₃₀₀) ₂₉ -co-MAA _{6.7} -co-S _{7.3}]	⁻¹) M _w /M _n 1.17 1.11 1.15 1.37 1.40	M _n (g mol 12 100 11 700 13 200 11 600 11 800	erall molar conv. (%) 33.2 25.0 29.9 43.4 57.4	0 ⁴
13.2 12 100 1.17 P[(PEOMA ₃₀₀) ₃₈ -c 12.0 1.1700 1.11 P[(PEOMA ₉₅₀) ₁₂ -c 13.0 1.15 P[(PEOMA ₃₀₀) ₁₀ -co-(PEOM 13.4 11 600 1.37 P[(PEOMA ₃₀₀) ₃₄ -co-MA	P[(PEOMA ₃₀₀) ₂₉ - <i>co</i> -MA P[(PFOMA ₃₀₀),,- <i>co</i> -MA	1.40	11 800 8500	55.0	
13.2 12 100 1.17 P[(PEOMA ₃₀₀) ₃₈ -co) 15.0 11 700 1.11 P[(PEOMA ₉₅₀) ₁₂ -co 19.9 13 200 1.15 P[(PEOMA ₃₀₀) ₁₀ -co-(PEOMA	P[(PEOMA ₃₀₀) ₃₄ <i>-co</i> -MAA P[(PEOMA ₃₀₀) ₂₉ <i>-co</i> -MAA	1.37 1.40	11 600 11 800	43.4 57.4	
13.2 12 100 1.17 P[(PEOMA ₃₀₀) ₃₈ -co-S ₃] 5.0 11 700 1.11 P[(PEOMA ₉₅₀) ₁₂ -co-S ₁]	P[(PEOMA ₃₀₀) ₁₀ -co-(PEOMA ₉₅₀) ₁₀ -co	1.15	13 200	29.9	
$[3.2 12 100 1.17 P[(PEOMA_{300})_{38}-co-S_3]$	$P[(PEOMA_{950})_{12}-co-S_1]$	1.11	11 700	25.0	
	$P[(PEOMA_{300})_{38}-co-S_3]$	1.17	12 100	33.2	

3.2 LCST behavior of the PEO-based macroalkoxyamine initiators

In this section, we investigate the thermo-responsive behavior of the PEO-based macroalkoxyamine initiators synthesized in the previous section, and whose main characteristics are summarized in Table 3. We paid particular attention to the effects of PEO chain length, copolymer composition, suspension pH and ionic strength on the LCST.

3.2.1 P(PEOMA-co-S)-SG1 macroalkoxyamine initiators

Effect of PEO chain length

Figure 3.12 shows the phase transition of the Ma1 macroinitiator (PEOMA₃₀₀, $M_n = 12\,100$ g mol⁻¹, $M_w/M_n = 1.17$, Table 3) in aqueous solution at pH = 4.3. The light transmittance profile reflects typical behavior of LCST-type phase separation, where solutions are 100% transparent at low temperature and quickly become cloudy (0% transmittance) above the critical temperature, illustrating the sudden solubility drop of the polymer in water. The cloud point determined as the 50% transmittance temperature was found equal to 51 °C.

Such aggregation behavior was not observed for Ma2 and Ma3 macroalkoxyamine initiators composed of longer PEO side chains (Ma2, PEOMA₉₅₀) or of a 50/50 molar mixture of long and short PEO chains (Ma3, 50 mol% PEOMA₉₅₀ + 50 mol% PEOMA₃₀₀) indicating good water solubility of these macroinitiators in the temperature range investigated (i.e., 20-80 °C). These results are in good agreement with previously reported literature data, and show that the hydrophilicity of the PEOMA-based polymers can be modulated by varying the length of the PEO side chains or the copolymer composition.^{25, 27, 44}



Figure 3.12 Plot of transmittance as a function of temperature for an aqueous solution (0.5 wt %, pH = 4.3) of the SG1-capped P[(PEOMA300)38-co-S3] Ma1 macroinitiator (M_n = 12 100 g mol⁻¹, M_w/M_n = 1.17, Table 3) as measured by UV/Vis spectroscopy at 500 nm (heating rate = 1 °C min⁻¹).

Effect of pH

We have plotted in Figure 3.13 the absorbance versus temperature for a series of Ma1 solutions of fixed concentrations (0.5 wt %) and different pH values. Starting from pH = 4 (the pH of pure Ma1 in water), the pH of the solution was adjusted to 8 and 10 with 0.1 M NaOH. The cloud point slightly decreased with increasing pH value, and was found equal to 51 °C, 50 °C and 48.5 °C, for pH 4, 8 and 10, respectively.



Figure 3.13 Plot of transmittance as a function of temperature (heating rate = 1 °C min⁻¹) for an aqueous solution (0.5 wt%) of the SG1-capped P[(PEOMA₃₀₀)₃₈-co-S₃] Ma1 macroinitiator ($M_n = 12 \ 100 \ \text{g mol}^{-1}$, $M_w/M_n = 1.17$, Table 3) as measured by UV/Vis spectroscopy at 500 nm for different pH values. (-) pH = 4.0, (-) pH = 8.0 and (-) pH = 10.0.

Considering that the Ma1 macroalkoxyamine contains only one terminal COOH group, it was not expected that a change in pH would affect its LCST behavior. The cloud point of P(PEOMA) macromonomers is known to depend on the nature of the end-groups on the polymer backbone but while hydrophobic end-groups tend to lower cloud points, hydrophilic end-groups usually increase LCST values. The cloud point of Ma1 should therefore increase with increasing pH as the polymer would become more hydrophilic. However, the results show on the contrary that the cloud point decreases with increasing pH suggesting that another mechanism may play a role here. We thus suspected that the cloud point shift could be due to an increase of the ionic strength of the suspension medium and we therefore chose to study its effect.

Effect of ionic strength

Figure 3.14 shows the effect of increasing ionic strength on the cloud point of Ma1. The same Ma1 solution with different concentrations of NaCl was analyzed. The transmittance curves

shift to lower temperatures as the salt concentration increases. The cloud point was found to vary from 51 to 44.5 °C with increasing the NaCl concentration from 0 to 10^{-1} mol L⁻¹. These results are consistent with previous literature reports on the effect of NaCl on the LCST behavior of PEOMA-based polymers. For instance, Luzon and coworkers³³ reported a LCST decrease of around 2 °C in the presence of 0.04 mol L⁻¹ of NaCl for P(DEOMA-*co*-PEOMA) statistical copolymers synthesized by RAFT.



Figure 3.14 Plot of transmittance as a function of temperature (heating rate = 1 °C min⁻¹) for an aqueous solution (0.5 wt %) of the SG1-capped P[(PEOMA₃₀₀)₃₈-*co*-S₃] Ma1 macroinitiator ($M_n = 12\ 100\ \text{g mol}^{-1}$, $M_w/M_n = 1.17$, Table 3) as measured by UV/Vis spectroscopy at 500 nm for different NaCl concentrations. (—) no salt, (—) 10⁻³ mol L⁻¹, (—) 10^{-2} mol L⁻¹ and (—) 10⁻¹ mol L⁻¹.

In summary, the thermoresponsive behavior of P(PEOMA₃₀₀-*co*-S)-SG1 macroalkoxyamine initiators could be tuned by varying the PEO chain length or by manipulating the copolymer composition. Ma1 with short PEO side–chains (PEOMA₃₀₀) showed a cloud point around 51 °C while Ma2 with longer PEO side chains (PEOMA₉₅₀) or Ma3 composed of 50 mol% of PEOMA₃₀₀ and 50 mol% of PEOMA₉₅₀, did not show any cloud point between 20 and 80 °C. As shown in Figure 3.15 for Ma1, the cloud point was also influenced by the ionic strength and the suspension pH and decreased with increasing NaCl concentrations or pH values. While it is known that the presence of salt lowers the LCST of non-ionic water-soluble

Chapter 3. Synthesis of PEO-based macroalkoxyamines

polymers due to the kosmotropic effect, it was not expected that the change of pH would affect the water solubility of the macroalkoxyamine initiators as the later contain only one MAA unit which should contribute to a LCST increase. The results thus suggest a salting out effect produced by the increase of ionic strength that accompanies the change of pH.



Figure 3.15 Cloud point ($T_{50\%}$) versus NaCl concentration (**■**) and suspension pH (**●**) for the P[(PEOMA₃₀₀)₃₈-*co*-S₃] Ma1 macroinitiator. The dashed lines are only guides for eyes.

In the following section, we investigate the thermoresponsive behavior of the P(PEOMA₃₀₀*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiators that contain both pH-sensitive and thermosensitive repeating units. The combination of these two components will endow the macroalkoxyamine initiators with a double responsive behavior. The effect of pH and copolymer composition on the LCST behavior of this series of copolymers is discussed below. 3.2.2 P(PEOMA-co-MAA-co-S)-SG1 macroalkoxyamine initiators

Effect of MAA content at pH = 4.4 and pH = 6.1

Figure 3.16 shows the cloud points of SG1-capped P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroalkoxyamine initiators as a function of MAA mole percentage (15 and 42 mol%) for two different pH values (pH = 4.4 and 6.1). The cloud point decreases linearly with increasing MAA content at pH = 4.4 and shows a linear increase at pH = 6.1.



Figure 3.16 Cloud points of SG1-capped P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroinitiators as a function of MAA mole percentage for different pH values estimated by 50% transmittance points of the first heating curves: pH = 4.4 (**•**) and pH = 6.1 (**•**). The dashed lines are only guides for eyes.

For pH values larger than the pKa $(5.05)^{45}$ of poly(methacrylic acid) (PMAA) (i.e. pH = 6.1), the MAA units become deprotonated and the cloud point therefore increases as the hydrophilicity of the copolymer increases. Below pKa, on the contrary, the cloud point decreases upon the incorporation of MAA units indicating decreased water solubility. Possible interpretations for this unexpected clouding behavior below pKa are the rather hydrophobic character of MAA but also the formation of intra or intermolecular interactions between the carboxylic acid groups of MAA units and the ether oxygen groups of PEO

leading to self-complexation as reported elsewhere.⁴⁶⁻⁴⁸ The LCST decreases as the degree of hydrophobicity increases consecutively to water expulsion from the hydration shell.

The water solubility of P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroinitiators also depends on the copolymer composition and decreases with increasing MAA content at low pH values. Indeed, we observed that high molar masses PMAA homopolymers (M_n larger than typically 5 000 g mol⁻¹) are insoluble in water at low pH values and that pH values higher than the pKa of PMAA are required to ensure complete and quick dissolution of the polymer chains. Consequently, as shown in Figure 3.17, the Ma6 macroalkoxyamine initiator containing 68 mol% of MAA (P[(PEOMA₃₀₀)₁₃-*co*-MAA₄₄-*co*-S₈], Table 3) was completely insoluble at room temperature and pH = 4.4 while it was fully soluble at pH = 6.1. Furthermore, it did not show any cloud point between 0 and 80 °C at both pH values. Figure 3.18 shows representative transmittance versus temperature plots of Ma6 at pH = 5.5 and 6.0. According to Figure 3.18, the Ma6 macroinitiator appeared to be solely pH-responsive even if the curve indicates a slow decrease in transmittance around 43 °C at pH = 5.5.



Figure 3.17 Picture of Ma6 in water at pH = 6.1 (left) and pH = 4.4 (right).



Figure 3.18 Plot of transmittance as a function of temperature (heating rate = 1 °C min⁻¹) for an aqueous solution (0.5 wt%) of the SG1-capped P[(PEOMA₃₀₀)₁₃-*co*-MAA₄₄-*co*-S₈] Ma6 macroinitiator ($M_n = 8500$ g mol⁻¹, $M_w/M_n = 1.37$, Table 3) as measured by UV/Vis spectroscopy at 500 nm for different pH values. (–) pH = 5.5 and (–) pH = 6.1.

Effect of pH

As previously discussed, MAA-free P(PEOMA₃₀₀-co-S)-SG1 macroalkoxyamine initiators are not pH sensitive. The clouding behavior of the suspensions with increasing pH was attributed to the concomitant increase of ionic strength upon neutralization of the alkoxyamine initiator.

In contrast, the suspension pH had a strong influence on the cloud points of the dualresponsive P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroalkoxyamine initiators. Figure 3.19 shows temperature-turbidity curves of the macroalkoxyamine initiator containing 15 mol% MAA (Ma4, P[(PEOMA₃₀₀)₃₄-*co*-MAA_{6.7}-*co*-S_{7.2}], Table 3) for increasing suspension pHs. The transmittance curves are gradually shifted to higher temperatures as the pH value increases whereas the phase transition becomes less sharp.



Figure 3.19 Plot of transmittance as a function of temperature (heating rate = 1 °C min⁻¹) for an aqueous solution (0.5 wt%) of the SG1-capped P[(PEOMA₃₀₀)₃₄-*co*-MAA_{6.7}-*co*-S_{7.2}], Ma4 macroinitiator ($M_n = 11$ 560 g.mol⁻¹, $M_w/M_n = 1.37$, Table 3) as measured by UV/Vis spectroscopy at 500 nm for different pH values. (—) pH = 4.4, (—) pH = 4.6, (—) pH = 5.1, (—) pH = 5.5, (—) pH = 6.1, (—) pH = 6.7, (—) pH = 7.2 and (—) pH = 7.8.

Figure 3.20 is a plot of transmittance as a function of temperature for the macroalkoxyamine initiator containing 42 mol% of MAA (Ma5, P[(PEOMA₃₀₀)₂₉-*co*-MAA₂₆-*co*-S_{7.3}], Table 3). Again, the cloud point temperature increases with increasing pH. The increase is more important for Ma5 than for Ma4 indicating that the former is more pH sensitive than the latter. The cloud point of Ma5 (42 mol% MAA) increased of 36 °C as the pH value increased from 4.9 to 6.0 while it increased of only 17 °C in the case of Ma4 (15 mol% MAA).



Figure 3.20 Plot of transmittance as a function of temperature (heating rate = 1 °C min⁻¹) for an aqueous solution (0.5 wt%) of the SG1-capped P[(PEOMA₃₀₀)₂₉-*co*-MAA₂₆-*co*-S_{7,3}], Ma5 macroinitiator ($M_n = 11~770~g~mol^{-1}$, $M_w/M_n = 1.40$, Table 3) as measured by UV/Vis spectroscopy at 500 nm for different pH values. (-) pH = 4.9, (-) pH = 5.5, (-) pH = 6.0 and (-) pH = 6.5.

The cloud point temperatures of Ma4 and Ma5 are plotted in Figure 3.21 as a function of pH and compared to the cloud point of Ma1, which is independent of pH (i.e., 51 °C). We observe that the slope of the cloud point *vs* pH curves depends on the MAA content in the copolymers: the larger the MAA molar fraction, the higher the slope (i.e. $slope_{Ma5} > slope_{Ma4}$). The curves also show that the range of pH values for which we observed a LCST behavior shrank as the MAA content increased, until it completely disappeared (Ma6).

In conclusion, P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroalkoxyamine initiators showed a dual temperature and pH-responsive behavior. The cloud point temperature could be tuned in a large range by varying the MAA mole percentage in the copolymer and the suspension pH. The LCST increased with increasing pH or MAA content above pKa while increasing the MAA content below pKa resulted in a LCST decrease.



Figure 3.21 Cloud point temperature ($T_{50\%}$) *versus* pH for Ma4 (15 mol% MAA , \blacktriangle) and Ma5 (42 mol% MAA, \blacksquare). The dashed lines represent the cloud point temperature of Ma4 (----), Ma5 (----) and Ma1 (0 mol% MAA) (----), respectively.

Conclusions

In this chapter, well-defined water-soluble brush-type copolymers mainly composed of PEOMA units with PEO side groups of various chain lengths ($M_n = 300$ and 950 g mol⁻¹) or of PEOMA₃₀₀ with MAA units were synthesized by nitroxide-mediated polymerization using a low molar mass unimolecular alkoxyamine initiator (so called BlocBuilder®) and SG1 nitroxide in the presence of a small amount of styrene. The resulting SG1-capped macroalkoxyamines possessed the predicted molar masses based on the monomer/initiator molar ratio and narrow molar mass distributions.

As expected, the cloud point of P(PEOMA-*co*-S)-SG1 macroinitiators increased with increasing hydrophilicity and could be tuned by varying the PEO chain length or the copolymer composition. The cloud point was also influenced by ionic strength and pH although to a much lesser extent. The cloud point decreased with increasing salt concentrations or pH due to hydrogen bonds disruption.

P(PEOMA₃₀₀-*co*-MAA-co-S)-SG1 macroalkoxyamine initiators exhibited both thermo- and pH- responsive behaviors. As a consequence, their LCST could be finely tuned from 20 to 80
°C by varying the MAA content or the pH. Unexpectedly, the LCST of the copolymers decreased with increasing MAA content below pKa likely due to intramolecular H-bonding interactions resulting in decreased solubility, while as expected it increased above pKa due to MAA ionization.

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Chapter 4. Nitroxide-mediated (NMP) surfactant-free emulsion polymerization

Introduction

PEO-based amphiphilic block copolymers such as PEO-*b*-polystyrene or PEO-*b*-poly(methyl methacrylate) have been very often used as stabilizers in emulsion polymerization.¹⁻³ With the advent of controlled/living free radical polymerization (CRP),⁴⁻⁹ novel types of hydrophilic segments are now available,¹⁰ but PEO remains a candidate of choice for many applications requiring sterically stabilized particles. Its advantages are, among others, the improved stability of the particles under freezing conditions, high shear or in the presence of polyelectrolytes,¹¹ antifouling properties,^{12,13} biocompatibility,¹⁴⁻¹⁶ and the ability to interact with inorganic surfaces.^{17,18} For instance, PEO-based macromonomers have been shown to adsorb on clays and silica and to be efficient compatibilizers for the synthesis of nanocomposite colloids through emulsion polymerization.¹⁹⁻²² Furthermore, the adjustable water-solubility of PEO-based polymers with temperature,^{23,24} polymer architecture,^{25,26} comonomer compositions,^{27,28} polymer chain length²⁹ and salt concentration,³⁰ allows manipulating their responsive behavior in water, and hence their self-assembling properties.³¹ In particular, brush-type amphiphilic block copolymers (BCP) of PEOMA and benzyl methacrylate³² or BCP of PEOMA and styrene³³ have been reported. These diblock copolymers were synthesized via consecutive ATRP or RAFT solution polymerizations and subsequently self-assembled in water by slow addition of a selective solvent for one of the two blocks in order to trigger aggregation of the dissolved chain, and hence micelle formation. Not only spherical micelles but also worms or vesicles can be formed by this method depending on the relative volume fraction of the core-forming block.

The recent developments achieved in controlled radical polymerization in dispersed media now allow amphiphilic block copolymers to be synthesized directly in water from hydrophilic reactive precursor polymers that self-assemble *in situ* upon growth of their hydrophobic segment. The formed polymer particles are exclusively composed of well-defined amphiphilic block copolymers and can exhibit various morphologies such as spherical micelles, cylindrical micelles (also called fibers when the length to diameter ratio is very large) and vesicles. This method is known as polymerization-induced self-assembly (*PISA*).¹⁰

In this chapter, we were particularly interested in developing *PISA* in emulsion using nitroxide-mediated polymerization (NMP). Macroalkoxyamine initiators composed of PEOMA or of copolymers of PEOMA with MAA were used for the emulsion polymerization

of a methacrylate monomer, namely *n*-butyl methacrylate (BMA), in the presence of a low proportion of styrene. Poly (*n*-butyl methacrylate) is a polymer with a glass transition temperature close to the ambient ($T_g = 20$ °C), being thus a good model for acrylic latexes used in the coating industry. Depending on the macroalkoxymine, the self-assembled nano-objects were stabilized either sterically or electrosterically, depending on the pH.

Before dealing with the experimental results, a brief literature survey on the self-assembly of amphiphilic block copolymers in selective solvents or generated *in situ* via emulsion or dispersion polymerization is presented. This will introduce the experimental work that is divided into two parts.

In the first part, our aim was to investigate PISA in aqueous emulsion using the macroalkoxyamines composed of PEOMA units (besides styrene) and thus displaying a brush-type structure. The purpose was to examine the effect of the PEO and macroalkoxyamine chain lengths, along with the effect of the experimental conditions on the emulsion polymerization kinetics, on the control of the polymerization and on the ability to form sterically stabilized nanoparticles.

In the second part, our aim was to investigate the effect of the macroalkoxyamine microstructure on the outcomes of the emulsion polymerization using SG1-capped P(PEOMA-*co*-MAA-*co*-S) macroinitiators. The purpose was to examine the stability of the resulting latex particles around and far above the cloud point temperature, along with the effects of MAA content and pH values on the emulsion polymerization kinetics and self-assembled morphologies.

1. Self-assembly of block copolymers

Since 1995, a wide range of crew-cut aggregates of different morphologies have been prepared from asymmetric amphiphilic BCP systems based on their self-assembling properties.³⁴⁻³⁸ The aggregate morphologies include spherical micelles, rods, bicontinuous structures, lamellae, vesicles, large compound micelles (LCMs), large compound vesicles (LCVs), tubules, "onions", "eggshells", baroclinic tubules, pincushions, etc. Overall, more than 20 morphologies have been identified, some of which are thermodynamically induced, while others are kinetically controlled.

Based on the BCP self-assembly behavior³⁹ in solution, the formation mechanism of the various morphologies was discussed by Eisenberg et al.⁴⁰ and was attributed to two

competing factors: interfacial energy between the two blocks (an enthalpic contribution), and chain stretching (an entropic contribution). As microphase separation occurs, the two blocks separate from each other in such a way as to minimize interfacial area in order to lower the total interfacial energy. Phase separation induces chain stretching away from the preferred coiled polymer chain conformation; the degree of stretching depends on the volume fraction of one block relative to that of the diblock. Figure 4.1 shows the well-known cone column mechanism for morphological transitions. When the diblocks are highly asymmetric, i.e. the volume fraction of one block such as block A is small, the A blocks prefer to aggregate into spherical microdomains, leaving the B blocks to surround them as "coronas" (Figure 4.1a). This way affords the system the lowest interfacial area and increases configurational entropy relative to other morphologies, and thus is energetically favourable.⁶ As f_A increases at a fixed temperature, the corona volume fraction (or the effective volume fraction of block B) decreases and less curved interfaces are formed (Figure 4.1b and c). Hence, the polymer chains have to adopt new arrangements to reduce their stretching, leading to a morphological transition from spheres to cylinders and to lamellae.



Figure 4.1 Schematic illustration of the possible polymer chain arrangements in different morphologies of AB diblocks (A block, — and B block, —) changing from sphere (a) to cylinder (b) and to lamella (c) as the volume fraction (f_A) of the A block increases. The dash curve in each morphology represents the interface between A and B domains.⁴⁰

In many cases, the processing route (e.g., solvent exchange, film rehydration, pH switch, etc.) used to produce block copolymer aggregates in solution can influence their final morphology to a similar extent as the hydrophobic/hydrophilic balance of the copolymer.⁴¹ Furthermore, such processing techniques are normally limited to dilute copolymer solutions (<1%), which is a significant disadvantage for commercial viability.

Recently, with the development of controlled/living radical polymerization, the elaboration of BCP self-assembly in aqueous media has attracted much attention not only because of the well-controlled morphologies, but also in view of their potential applications. Many studies focused on the synthesis of well-defined hydrophobic (co)polymers using miniemulsion or emulsion polymerization recipes in order to take advantage of the specific features of the heterogeneous process.⁴²⁻⁵² The next step was to develop surfactant-free emulsion polymerization by creating amphiphilic block copolymer chains *in situ*.⁴² The initial idea was that the so-formed amphiphilic block copolymers would simply stabilize classical latex particles (not necessarily under controlled conditions),⁵³⁻⁵⁸ but it then appeared that a good control of the polymerization would allow the *in situ* creation of well-defined amphiphilic block copolymers and their self-assembly simultaneously to the growth step.¹⁰ This is the socalled polymerization-induced micellization or polymerization-induced self-assembly (PISA) process. PISA can be performed under aqueous emulsion or dispersion polymerization conditions using the RAFT^{59, 60-67} or the NMP⁶⁸⁻⁷⁰ processes. Whatever the polymerization process, pure spheres, fibers or vesicles can be obtained by tuning the length of the hydrophobic block or the nature of the hydrophilic block. Armes et al.65 proposed a mechanism for the worm (or fiber) to vesicle transformation during the synthesis of poly(glycerol monomethacrylate)-*b*-poly(2-hydroxypropyl methacrylate) (PGMA-b-PHPMA) diblock copolymers by RAFT-mediated aqueous dispersion polymerization. As illustrated in Figure 4.2, increasing the PHPMA block length resulted in the formation of branched worms, partially coalesced worms, nascent bilayers, "octopi", "jellyfish" and finally pure vesicles.

Recently, P(MAA-*co*-PEOMA) macroRAFT agents have been shown to be very efficient stabilizers during the *in situ* synthesis of P(MAA-*co*-PEOMA)-*b*-PS amphiphilic block copolymers by aqueous emulsion polymerization.⁶⁶ The pH (or ionization degree of the MAA units) and the molar masses of the hydrophilic and hydrophobic blocks were found to be key parameters to control the nano-object morphologies (spherical micelles, nanofibers, and vesicles). In a similar way as that shown in Figure 4.1 for the self-assembly of preformed amphiphilic block copolymers, the morphology evolved from spheres, to fibers and finally to vesicles when the molar mass of the hydrophobic block was increased (in appropriate pH conditions and for a given hydrophilic block). This trend was observed for a variety of polymers such as styrene, *n*-butyl acrylate, methyl methacrylate and their copolymers.^{71,72}

The similar result was also observed by using P(MAA-*co*-SS)-SG1 macroalkoxyamine in NMP emulsion polymerization with P(MMA-*co*-S) as the hydrophobic block.⁷⁰



Figure 4.2 Suggested mechanism for the polymerization-induced worm-to-vesicle transformation during the synthesis of PGMA₄₇-*b*-PHPMA₂₀ diblock copolymers by RAFT aqueous dispersion polymerization.⁶⁵

2. Surfactant-free emulsion polymerization of BMA and styrene initiated by P(PEOMA-*co*-S)-SG1 macroalkoxyamines

All emulsion polymerizations were performed using the macroalkoxyamine initiators Ma1, Ma2 and Ma3 whose main characteristics are recapitulated in Table 1. In all cases, the polymerization temperature was 85 °C and the duration was 6 h. The parameters that were studied in this work are the nature of the macroinitiator and its concentration at a pH of approximately 4 (natural pH of the macroinitiator solution in the concentrations used), the pH and the salt concentration (Table 2). Their effect on the polymerization kinetics, on the control over the formation of amphiphilic block copolymers, and on the self-assembled nano-objects stability and morphology was studied.

Run	$M_{\rm n}({\rm g\ mol}^{-1})$	$M_{\rm w}/M_{\rm n}$	Structure of the copolymers
Ma1	12 100	1.17	P[(PEOMA ₃₀₀) ₃₈ -co-S ₃]
Ma2	11 700	1.11	$P[(PEOMA_{950})_{12}-co-S_1]$
Ma3	13 200	1.15	$P[(PEOMA_{300})_{10}-co-(PEOMA_{950})_{10}-co-S_{1.6}]$

 Table 1 Recapitulation of the main characteristics of the P(PEOMA-co-S)-SG1

 macroalkoxyamine initiators used in this work.

2.1 Experimental procedure

Materials

The monomers styrene (S, 99%, Acros) and *n*-butyl methacrylate (BMA, 99%, Aldrich) were used without further purification. The P(PEOMA-*co*-S)-SG1 macroalkoxyamine initiators were synthesized as described in Chapter 3.

Emulsion polymerizations

In a typical surfactant-free emulsion polymerization (experiment E2 in Table 2), a certain amount of macroinitator Ma2 (0.46 g; 0.0024 mol L^{-1}) was first dissolved in 12.5 g of water. The solution was then stirred under nitrogen bubbling for 30 min at room temperature. Then the monomers: BMA and styrene (2.35 g of BMA and 0.15 g of S) were introduced into the aqueous solution and the obtained unstable biphasic system was deoxygenated by nitrogen bubbling for another 20 min. This mixture was introduced into a 50 mL round-bottom flask and heated at 85 °C for 6h. Time zero of the polymerization was taken when the reaction temperature reached 70 °C. Samples were periodically withdrawn to follow monomer conversion by gravimetric analyses. The natural pH value of the macroinitiator solutions in deionized water was close to 4 (due to carboxylic acid end-group; depending on the concentration) and was not altered for most of the emulsion polymerizations performed in this work. To increase the pH value for the experiments E8 and E9 in Table 2, sodium hydroxide (0.1 M aqueous solution) was introduced before addition of the monomer.

Chain extension experiment

Chain extension of the SG1-capped poly(PEOMA₉₅₀-*co*-S) macroinitiator Ma2 was performed in 1,4-dioxane solution at 85 °C. For this purpose, BMA and styrene (2.35 g of

BMA, 1.071 mol L⁻¹ and 0.15 g of S, 0.093 mol L⁻¹) were introduced into 12.5 g of 1,4dioxane containing 0.46 g of Ma2 (2.4 mmol L⁻¹). The target M_n at 100% conversion was 75 500 g mol⁻¹. After nitrogen bubbling for 30 min at room temperature, the temperature was increased to 85 °C and the reaction was performed for 6 h.

The amount of unreacted macroinitiator Ma2 was determined as follows: first the weight distribution ($w(\log M)$ vs log M) derived from the SEC data was transformed into a number distribution ($n(\log M)$ vs log M) by dividing $w(\log M)$ by the molar mass. Then the obtained number distribution plot was deconvoluted into two peaks, one corresponding to the number distribution of unreacted Ma2, the other one to the number distribution of the formed block copolymer. The ratio of the peak areas finally gave access to the respective molar amount of each species.

Characterizations

For each emulsion polymerization, the monomer conversion was determined by gravimetric analysis. Samples of the latex were taken during the polymerization, put in a pre-weighted aluminum capsule and immediately put in the oven. The capsule was dried at 100 °C until constant weight was achieved. The conversion was calculated according to the following equation (4.1):

$$X_{\rm wt}(\%) = \left(\frac{M_{\rm dp}}{M_{\rm wl}} - \frac{M_{\rm np}}{M_{\rm t}}\right) \times \frac{M_{\rm t}}{M_{\rm m}} \times 100 \qquad (\rm eq.\ 4.1)$$

Where M_{dp} , M_{wl} , M_{np} , M_t and M_m are respectively the weight of the dried polymer, wet latex, non-polymerizable compounds in the recipe, total recipe weight and monomers in the recipe.

Dynamic light scattering (DLS, Nano ZS from Malvern Instruments) was used to measure the particle size (average hydrodynamic diameter, Z_{av}) and the dispersity of the samples (indicated by the Poly value – the higher this value, the broader the size distribution). Before measurements, the latex samples were diluted in deionized water.

SEC analyses of polymers were performed in THF. All polymers were injected at a concentration of 3 mg mL⁻¹ after filtration through a 0.45 μ m pore-size membrane. The separation was carried out on three Polymer Laboratories columns [3 × PLgel 5 μ m Mixed C (300 × 7.5 mm)] and a guard column (PL gel 5 μ m). Columns and detectors were maintained at 40 °C. THF was used as the mobile phase at a flow rate of 1 mL min⁻¹ and toluene served as a flow rate marker. The number and weight average molar masses (M_n and M_w ,

respectively) and molar mass distributions (M_w/M_n) were calculated with a calibration curve based on PMMA standards.

Transmission electron microscopy (TEM) was performed at an accelerating voltage of 80 kV with a Philips CM120 transmission electron microscope (Centre Technologique des Microstructures (CTµ), plate-forme de l'Université Claude Bernard Lyon 1, Villeurbanne, France). Highly diluted samples were dropped on a Formvar-carbon coated copper grid and dried under air. Phosphotungstic acid (1.5 wt %, pH = 7) was used to increase the specimen contrast. The number-average (D_n) and the weight-average particle diameter (D_w) and polydispersity index (PDI = D_w/D_n) were calculated using $D_n = \sum n_i D_i / \sum n_i n_i D_i^4 / \sum n_i D_i^3$, where n_i is the number of particles with diameter D_i .

For cryo-TEM, a drop of the suspension was deposited on a continuous carbon film, blotting the water in excess, mounting the dry specimen on the Gatan holder and quenching it in liquid nitrogen before introduction in the microscope. The holder was then cooled down and the specimen was observed at -180 °C.

2.2 Living character of the Ma2 macroalkoxyamine initiator

Before conducting emulsion polymerization experiments, it was important to assess the living character of the macroalkoxyamine initiators. To do so, a chain extension experiment was carried out in 1,4-dioxane solution using the Ma2 macroalkoxyamine in the copolymerization of *n*-butyl methacrylate with 8 mol% of styrene. Despite a good control of the polymerization observed for the synthesis of this macroalkoxyamine and even though initiation took place during the chain extension process, unreacted macroinitiator chains were clearly visible on the chromatograms of the obtained copolymers (Figure 4.3).

E1Ma12.772 2404.0//E2Ma22.475 6304.27665 700 (1.67)E3Ma32.577 6504.27568 300 (1.71)E4Ma21.2168 3503.92742 300 (2.36)E5Ma21.7104 8004.35370 100 (1.80)E6Ma24.845 4303.78340 000 (1.54)E7Ma27.234 5304.18329 900 (1.39)E8Ma22.476 0306.06655 641 (1.68)	Macroinitiat Type (mmol L	r Target M_n ⁻¹) (g mol ⁻¹) ^b	pH ^c	\mathbf{X}_{wt} (%) ^d	$M_{ m n} \left(M_{ m w}/M_{ m n} ight)^{ m e}$	Z _{av} (DLS) (nm)	Poly value (DLS)	D _n (TEM) (nm)	$D_{\rm w}/D_{\rm n}$ (TEM)	Stability
E2Ma22.475 6304.27665 700 (1.67)E3Ma32.577 6504.27568 300 (1.71)E4Ma21.2168 3503.92742 300 (2.36)E5Ma21.7104 8004.35370 100 (1.80)E6Ma24.845 4303.78340 000 (1.54)E7Ma27.234 5304.18329 900 (1.39)E8Ma22.476 0306.06655 641 (1.68)	Ma1 2.7	72 240	4.0	<u> </u>	/	/	/	/	/	Unstable ^f
E3Ma32.577 6504.27568 300 (1.71)E4Ma21.2168 3503.92742 300 (2.36)E5Ma21.7104 8004.35370 100 (1.80)E6Ma24.845 4303.78340 000 (1.54)E7Ma27.234 5304.18329 900 (1.39)E8Ma22.476 0306.06655 641 (1.68)	Ma2 2.4	75 630	4.2	76	65 700 (1.67)	132	0.21	73	1.04	Stable
E4Ma21.2168 3503.92742 300 (2.36)E5Ma21.7104 8004.35370 100 (1.80)E6Ma24.845 4303.78340 000 (1.54)E7Ma27.234 5304.18329 900 (1.39)E8Ma22.476 0306.06655 641 (1.68)	Ma3 2.5	77 650	4.2	75	68 300 (1.71)	165	0.11	130	1.05	Stable
E5Ma21.7104 8004.35370 100 (1.80)E6Ma24.845 4303.78340 000 (1.54)E7Ma27.234 5304.18329 900 (1.39)E8Ma22.476 0306.06655 641 (1.68)	Ma2 1.2	168 350	3.9	27	42 300 (2.36)	301	0.14	181	1.03	Stable
E6Ma24.84.54.303.78.34.0000(1.54)E7Ma27.23.45.304.18.32.9900(1.39)E8Ma22.4760.306.06.65.56.41(1.68)	Ma2 1.7	$104\ 800$	4.3	53	70 100 (1.80)	213	0.10	112	1.04	Stable
E7 Ma2 7.2 34 530 4.1 83 29 900 (1.39) E8 Ma2 2.4 76 030 6.0 66 55 641 (1.68)	Ma2 4.8	45 430	3.7	83	40 000 (1.54)	85	0.09	54	1.03	Stable
E8 Ma2 2.4 76 030 6.0 66 55 641 (1.68)	Ma2 7.2	34 530	4.1	83	29 900 (1.39)	58	0.19	42	1.03	Stable
	Ma2 2.4	76 030	6.0	99	55 641 (1.68)	437	0.69	/	/	Stable
E9 Ma2 2.4 72 240 6.7 43 50 100 (1.67)	Ma2 2.4	72 240	6.7	43	50 100 (1.67)	1086	0.39	/	/	Unstable

Table 2 Experimental conditions and characteristics of the polymer latex particles synthesized by surfactant-free emulsion polymerization of n -
butyl methacrylate with a low percentage of styrene using SG1-capped P(PEOMA-co-S) copolymers as macroinitiators. Effect of the nature of
the macroinitiator, of its concentration and of the pH. ^a

^b Theoretical molar mass at 100% conversion determined according to: Target $M_{\rm n}$ (g mol⁻¹) = $M_{\rm m}$ ^{alkoxyamine} + $\left(\frac{initial mas of monomer}{mass of alkoxyamine}\right) \times M_{\rm m}$ ^{alkoxyamine} ^c Initial pH determined before polymerization. ^d Weight conversion determined by gravimetric analysis. ^e Determined by SEC in THF with PMMA standards. ^a All polymerizations were carried out at 85 °C for 6 h. The total monomer concentration was 20 wt% and the initial molar fraction of styrene was $f_{s0} = 0.08$. ^fThe latex suspension turned into a gel when the temperature reached the cloud point temperature of the macroinitiator (51 °C). ^g Stirring had to be stopped because of the high viscosity of the emulsion after 6h of reaction.



Figure 4.3 Evolution of the size exclusion chromatograms (THF solution, PMMA calibration) with weight conversion for the chain extension of the SG1-capped P(PEOMA₉₅₀*co*-S) macroinitiator Ma2 in 1,4-dioxane at 85 °C. The final conversion is 62.4 wt%, $M_n = 29$ 200 g mol⁻¹ and $M_w/M_n = 1.85$.

This indicates the presence of dead chains formed either during the synthesis or during the reinitiation step. The amount of these unreacted chains was estimated to be ca. 30 mol%. This can be explained by the low number of styrene units, on average 1 per chain (see Table 1). It is thus likely that not all chains are terminated by a styrene-SG1 end-group, which is mandatory for stability of the terminal alkoxyamine and hence for the living character of the chains. However, on the basis of the possibility for the Ma2 copolymer to reinitiate the radical polymerization of a hydrophobic monomer in solution, we decided to use the P(PEOMA-*co*-S)-SG1 macroalkoxyamines of Table 4 as macroinitiators in the surfactant-free emulsion copolymerization of BMA with a low percentage of styrene, without further attempt to reduce the proportion of dead chains. Indeed, this would require an increase in the fraction of styrene in the hydrophilic macroinitiator, which would be detrimental to its water solubility and to the low activation temperature (indeed the possible formation of styrene dyads at the chain end would lead to an alkoxyamine structure with increased dissociation temperature).⁷³⁻⁷⁶ In the following sections, we were mainly interested in evaluating the

ability of the P(PEOMA-*co*-S)-SG1 copolymers to form self-assembled amphiphilic block copolymer nano-objects with good steric stability.

2.3 Effect of the nature and concentration of macroinitiator

All three macroalkoxyamines of Table 1 were engaged in emulsion polymerization experiments according to the recipe given in Table 2. As shown in Table 2, only the macrolkoxyamines Ma2 and Ma3 (with long PEO chains) were able to lead to stable latex particles. Indeed, in the case of Ma1 with short PEO side-chains, the polymerization temperature was well above the cloud point of the stabilizing chains (i.e., 51 °C, see Chapter 3). This result correlates well with the previous LCST measurements and can be attributed to the decreased solvent quality and subsequent collapse of PEO chain as temperature is increased. The collapse of the PEO chains is attributed to increased thermal motion disrupting the structured orientation of the hydrogen-bonded water molecules that surround the PEO. The layer collapse results in a decrease in the steric component of the free energy of interaction, thereby allowing the van der Waals interparticle attraction to become dominant which results in latex destabilization.

The experiments E2 (Ma2) and E3 (Ma3) compare the effect of the nature of the macroinitiator at pH = 4.2 under otherwise similar experimental conditions. Such pH might be too low for a good SG1 stability, but it was shown that acidic conditions were acceptable when the polymerizations were carried out at low temperatures over short reaction times in the water phase.⁷⁷ As shown in Figure 4.4, the polymerization kinetics and the evolution of $M_{\rm n}$ with conversion are similar for both reactions. Compared with the solution polymerization shown in Figure 4.3, the reinitiation step was even more efficient in emulsion as only a small SEC trace of unreacted macroinitiator was still visible at the final conversion (Figure 4.5) indicating less irreversible termination during chain extension in water. The obtained polymer dispersions were equally stable and contained self-stabilized spherical particles (Figure 4.6) composed of P(PEOMA-co-S)-b-P(BMA-co-S) amphiphilic diblock copolymer chains with the hydrophilic segments at the surface. The only difference between the experiments was the final particle diameter, which was almost twice smaller when Ma2 was used, indicating better stabilization ability than Ma3. As both macroinitiators exhibited similar molar masses (see Table 1), they thus contained the same number of ethylene oxide (EO) subunits, which were distributed in a different manner: 12 PEOMA₉₅₀ grafts with 19 EO subunits each for Ma2 versus 10 PEOMA₉₅₀ + 10 PEOMA₃₀₀ with respectively 19 and 4.5 EO subunits, for Ma3. In

consequence, this result confirms that long grafts are more favorable to a good stabilization than shorter ones.



Figure 4.4 a) Evolution of monomer weight conversion with time and b) evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the theoretical evolution of M_n with conversion) during the surfactant-free emulsion polymerization of S and BMA using Ma2 or Ma3 as macroinitiators. E2 (Ma2, PEOMA₉₅₀, • and \circ) and E3 (Ma3, 50 mol% PEOMA₃₀₀+ 50 mol% PEOMA₉₅₀, • and Δ) (See Table 2).



Figure 4.5 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of S and BMA using Ma2 or Ma3 as macroinitiators. E2 (Ma2, PEOMA₉₅₀) and E3 (Ma3, 50 mol% PEOMA₃₀₀ + 50 mol% PEOMA₉₅₀) (Table 1).



Figure 4.6 TEM images of the final P(PEOMA-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of S and BMA using Ma2 or Ma3 as macroinitiators. E2 (Ma2, PEOMA₉₅₀) and E3 (Ma3, 50 mol% PEOMA₃₀₀ + 50 mol% PEOMA₉₅₀) (Table 2). In both cases, phosphotungstic acid was used to increase specimen contrast.

The effect of the macroinitiator concentration was then studied using Ma2 at a pH of approximately 4. The initial concentration was varied from 1.2 mM to 7.2 mM (E2 and E4 to E7 in Table 2), while the overall amount of hydrophobic monomers was maintained the same (i.e., 20 wt%). This thus led to different target molar masses at full conversion. The polymerization kinetics shown in Figure 4.7 was strongly dependent on the initiator concentration, the highest rate being obtained for the highest concentration. This effect was more pronounced here than when P(MAA-co-S)-SG1 macroinitiators were used in the emulsion copolymerization of methyl methacrylate with styrene.⁷⁸ As compartmentalization of the propagating radicals does not affect the rate for NMP in emulsion (for large enough particles, i.e., with diameters above 50 nm),^{79,80} the difference cannot be ascribed to a difference in particle diameter, which actually significantly decreased (from 301 to 58 nm, see Table 2) when the macroinitiator concentration was increased. It is thus likely the direct consequence of the persistent radical effect and of the proportion of released SG1, which is expected to be smaller when the initial alkoxyamine concentration is increased, hence leading to a higher concentration of propagating radicals. From literature,⁸¹ the equation giving the concentration of free nitroxide released due to the persistent radical effect reads:

$$[SG1] = ([SG1]_0^3 + 3k_t K^2 [P - SG1]_0^2 t)^{1/3}$$
 (eq. 4.2)

with $[P-SG1]_0$ the initial concentration of alkoxyamine, k_t , the overall rate constant of termination and K, the activation-deactivation equilibrium constant. It then comes that:

$$[SG1]/[P-SG1]_0 = ([SG1]_0^3 [P-SG1]_0^{-3} + 3k_t K^2 [P-SG1]_0^{-1} t)^{1/3} (eq. 4.3)$$

is larger at a given time when $[P-SG1]_0$ is lower. The concentration of propagating radicals, which reads:

$$[P^{\bullet}] = K [P - SG1]_0 / [SG1]$$
(eq. 4.4)

thus decreases accordingly, although not in a linear manner.

As shown in Figure 4.8 and in Figure 4.9, the quality of control over the chain growth was also improved when the initial concentration of Ma2 was increased: better match between the

experimental values and the theoretical ones, lower molar mass dispersities and higher reinitiation efficiency. The concomitant decrease in particle diameter is related to an increase in the number of particles formed, since the initial amount of hydrophobic monomer was the same in all cases. This indicates an increase in the overall stabilized surface area, which agrees well with *in situ* formation of amphiphilic block copolymers. Particle diameters are remarkably low given the non ionic character of the P(PEOMA-*co*-S) stabilizing corona, which emphasizes the high stabilizing ability of brush type hydrophilic polymers with poly(ethylene glycol) side chains. In all cases the particles were spherical as illustrated in the TEM pictures of Figure 4.10.



Figure 4.7 Evolution of monomer weight conversion with time during the surfactant-free emulsion copolymerization of BMA with S for increasing Ma2 concentrations: E4 (1.2 mmol L^{-1} , •), E5 (1.8 mmol L^{-1} , •), E2 (2.4 mmol L^{-1} , •), E6 (4.8 mmol L^{-1} , •) and E7 (7.2 mmol L^{-1} , •) (See Table 2).



Figure 4.8 Evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the theoretical evolution of M_n with conversion) during the surfactant-free emulsion polymerizations of BMA and S for increasing Ma2 concentrations: E4 (1.2 mmol L⁻¹, $M_n \blacksquare$, $M_w/M_n \square$), E5 (1.8 mmol L⁻¹, $M_n \blacklozenge$, $M_w/M_n \diamondsuit$), E2 (2.4 mmol L⁻¹, $M_n \bullet$, $M_w/M_n \odot$), E6 (4.8 mmol L⁻¹, $M_n \blacktriangle$, $M_w/M_n \bigtriangleup$) and E7 (7.2 mmol L⁻¹, $M_n \blacktriangledown$, $M_w/M_n \bigtriangledown$) (See Table 2).





Figure 4.9 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of BMA and S for increasing Ma2 concentrations: E4 (1.2 mmol L^{-1}), E5 (1.7 mmol L^{-1}), E2 (2.4 mmol L^{-1}), E6 (4.8 mmol L^{-1}) and E7 (7.2 mmol L^{-1}) (Table 2).



Figure 4.10 TEM images of the final P(PEOMA-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of increasing Ma2 concentrations: E4 (1.2 mmol L⁻¹), E5 (1.7 mmol L⁻¹), E2 (2.4 mmol L⁻¹), E6 (4.8 mmol L⁻¹) and E7 (7.2 mmol L⁻¹) (Table 2). Phosphotungstic acid was used to increase specimen contrast.

2.4 Effect of pH

Although the macroinitiators used are not polyelectrolytes and only contain one carboxylic acid group at the chain end, the pH was increased from 4.2 (experiment E2) to 6.0 (experiment E8) and finally to 6.7 (experiment E9), in order to check whether it might affect the polymerization kinetics and the control over molar mass. Indeed, SG1 is known to degrade in acidic media.⁸² Therefore, the free SG1 concentration should increase with increasing pH (as there is less degradation), which should result in lower reaction rates, all the other parameters of the reactions remaining the same. The weight conversion vs time curves of Figure 4.11 show that the polymerization rate followed the expected trend and decreased with increasing pH, as a result of a shift of the activation-deactivation equilibrium toward a lower concentration of propagating radicals due to an accumulation of more free SG1. In contrast, the pH did not affect the evolution of M_n with conversion (Figure 4.12), neither the initiation efficiency (Figure 4.13) in a too significant manner. More surprising was the effect of pH on the final particle morphology, as illustrated in Figure 4.14, which shows the cryo-TEM images of the final dispersions. At the lowest pH (E2), spherical particles were observed, as already shown in Figure 4.10, and like in all the previously described experiments performed at the same pH. However, when the pH was increased, totally different morphologies were seen, including worm-like micelles and vesicles. Similar nanoobjects have already been observed under various conditions using NMP⁶⁸⁻⁷⁰ or RAFT^{59,60-67} processes. In all cases however the macroalkoxyamines or the macroRAFT agents contained weak acid, pH-sensitive, monomer units (acrylic or methacrylic acid). It was not expected that a change in pH would affect the behavior of PEO-based macroalkoxyamines. Even though the α end-group is a methacrylic acid unit coming from the BlocBuilder® initiator, the effect of a single terminal unit is quite surprising. We then suspected that an increase in the ionic strength would better explain the trend and decided to study the effect of an inert salt (NaCl) concentration.



Figure 4.11 Evolution of monomer weight conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma2 macroinitiator for increasing pH values: E2 (pH = 4.2, •), E8 (pH = 6.0, \checkmark) and E9 (pH = 6.7, \blacktriangle) (Table 2).



Figure 4.12 Evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the theoretical M_n evolution with conversion) during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma2 macroinitiator for increasing pH values: E2 (pH = 4.2, $M_n \bullet$, $M_w/M_n \circ$), E8 (pH = 6.0, $M_n \blacktriangledown$, $M_w/M_n \bigtriangledown$) and E9 (pH = 6.7, $M_n \blacktriangle$, $M_w/M_n \bigtriangleup$) (Table 2).



Figure 4.13 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma2 macroinitiator for increasing pH values: E2 (pH = 4.2), E8 (pH = 6.0) and E9 (pH = 6.7) (Table 2).



Figure 4.14 Cryo-TEM images of the final P(PEOMA₉₅₀-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the Ma2 macroinitiator for increasing pH values: E2 (pH = 4.2), E8 (pH = 6.0) and E9 (pH = 6.7) (Table 2).

2.5 Effect of salt concentration

NaCl was chosen as a salt for direct comparison with NaOH to check the effect of ionic strength without modification of the pH. The chosen concentrations were 10^{-3} , 10^{-2} , 10^{-1} and 0.5 mol L⁻¹, to allow a good comparison with NaOH concentrations used in the previous experiments: E8, $[NaOH] = 1.9 \times 10^{-3} \text{ mol } L^{-1}$ and E9, $[NaOH] = 3.9 \times 10^{-3} \text{ mol } L^{-1}$, while the pH remained close to 4.2 - 4.3. As shown in Table 3 and in Figure 4.15, the polymerization rate decreased with the increase in NaCl concentration. Moreover, the crossover efficiency and the quality of control over chain growth were gradually lost (Table 3, Figure 4.16 and Figure 4.17). This could be due to changes in the conformation of the PEO chains upon salt addition impacting the rate constants of activation/deactivation. However, to the best of our knowledge, there is so far no study in the literature dealing with these aspects. More interesting was the effect of NaCl concentration on the final morphology and stability of the self-assembled structures. At low salt concentration (0 or 1 mM), stable, spherical particles were obtained (E2, Figure 4.14 and E10, Figure 4.18, respectively). At 10 mM the system remained stable and started to form elongated micelles (E11, Figure 4.18), while at 100 mM, simple and multi-compartmented vesicles also appeared (E12, Figure 4.18). At 0.5 M, the system was highly unstable, from the beginning of the reaction. The change in morphology appeared in the same salt concentration range for NaOH and NaCl, corroborating the dominating effect of the ionic strength over the pH. Such change in morphology and in colloidal stability may be ascribed to the behavior of the PEO chains in water. As shown in Chapter 3, the addition of salt influences the lower critical solution temperature of PEO-based polymers. We remind here that the cloud point of Ma1 decreased from 51 to 44.5 °C with increasing NaCl concentrations from 0 to 0.1 M (Figure 3.16 in Chapter 3). To confirm this assumption, we examined the influence of NaCl on the cloud point of Ma2 at a fixed pH value of 4.2. Unfortunately, the Ma2 macroinitiator did not exhibit any cloud point over the 20-80 °C range at pH 4.2 in the presence of 0.5 M of NaCl. This is likely related to the high molar mass of the PEO side chains that shifts the cloud point temperature to values that are outside the measuring range. However, a visual inspection of the macroinitiator solutions indicates that they are becoming turbid for temperatures close to 90-100 °C. This therefore supports the assumption that the morphologies shown in Figure 4.14 are induced by the increase of ionic strength of the suspension medium upon increasing pH, in a salt concentration window, which however has to remain below that inducing phase separation, to avoid complete instability. Such effect of the ionic strength has already been observed in the

case of poly(acrylic acid-*co*-PEO acrylate) macroRAFT agents used in the emulsion polymerization of styrene,⁶¹ but to the best of our knowledge, this is the first time that it is reported for NMP.

Table 3 Experimental conditions and characteristics of the latex particles synthesized by surfactant-free emulsion polymerization of *n*-butyl methacrylate with a low percentage of styrene using the Ma2 macroinitiator. Effect of NaCl concentration.^a

Entry	[Ma2] (mmol L ⁻¹)	Target M _n (g mol ⁻¹)	pН	[NaCl] (mol L ⁻¹)	X _{wt} (%)	$M_{\rm n} \left(M_{\rm w}/M_{\rm n} \right)$	Z _{av} (DLS) (nm)	Poly value (DLS)
E2	2.4	75 630	4.2	0	76	65 700 (1.67)	132	0.21
E10	2.5	75 600	4.3	10^{-3}	51	33 900 (1.89)	182	0.15
E11	2.5	75 800	4.3	10 ⁻²	46	25 030 (2.08)	/	/
E12	2.3	80 200	4.1	10 ⁻¹	37	20 100 (1.83)	/	/
E13 ^b	2.4	79 850	4.2	0.5	/	/	/	/

^aAll polymerizations were carried out at 85 °C for 6 h. The total monomer concentration was 20 wt% and the initial molar fraction of styrene was $f_{S0} = 0.08$. ^b Unstable latex.



Figure 4.15 Evolution of monomer weight conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of the P(PEOMA₉₅₀-*co*-S)-SG1 macroinitiator (Ma2) for increasing NaCl concentrations: E2 (0 mol L⁻¹, •), E10 (10⁻³ mol L⁻¹, \checkmark), E11 (10⁻² mol L⁻¹, \blacktriangle) and E12 (10⁻¹ mol L⁻¹, \blacksquare) (Table 3).



Figure 4.16 Evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the evolution of theoretical M_n with conversion) during the surfactant-free emulsion polymerization of BMA and S in the presence of the P(PEOMA₉₅₀-*co*-S)-SG1 macroinitiator (Ma2) for increasing NaCl concentrations: E2 (0 mol L⁻¹, $M_n \bullet$, $M_w/M_n \circ$), E10 (10⁻³ mol L⁻¹, $M_n \blacktriangledown$, $M_w/M_n \circ$), E11 (10⁻² mol L⁻¹, $M_n \blacktriangle$, $M_w/M_n \bigtriangleup$) and E12 (10⁻¹ mol L⁻¹, $M_n \blacksquare$, $M_w/M_n \Box$) (Table 3).



Figure 4.17 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of BMA and S in the presence of the P(PEOMA₉₅₀-*co*-S)-SG1 macroinitiator (Ma2) for increasing NaCl concentrations: E10 (10^{-3} mol L⁻¹), E11 (10^{-2} mol L⁻¹) and E12 (10^{-1} mol L⁻¹) (Table 3).



Figure 4.18 Cryo-TEM images of the final P(PEOMA₉₅₀-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the macroinitiator Ma2 for increasing NaCl concentrations: E10 (10^{-3} mol L⁻¹), E11 (10^{-2} mol L⁻¹) and E12 (10^{-1} mol L⁻¹) (Table 3).

2.6 Conclusions

In summary, brush-type SG1-capped P(PEOMA-*co*-S) alkoxyamine macroinitiators with PEO side chains of various chain lengths and one terminal methacrylic acid unit, were used to initiate the aqueous nitroxide-mediated emulsion polymerization of *n*-butyl methacrylate and styrene under low temperature conditions. Only the macroinitiators with long PEO side groups, and whose cloud points were above the reaction temperature, led to stable latex suspensions. Despite the presence of a small proportion of dead chains indicating the occurrence of irreversible termination reactions, molar masses evolved linearly with

conversion as expected for controlled radical polymerization. Sterically stabilized selfassembled diblock copolymer particles with film-forming properties were obtained *in situ* upon chain extension of the P(PEOMA₉₅₀-*co*-S) hydrophilic block. While spherical latex particles were obtained at pH = 4.2 regardless of the molar mass of the hydrophobic block over the entire range studied, vesicles and elongated particles were obtained at pH = 6.0 and 6.7. As an increase of pH should not directly affect the properties of PEO in water, these results suggest a salting out effect produced by the increase of ionic strength that accompanies the change of pH in agreement with LCST measurements. This provides an unprecedented way to control the morphology of self-assembled diblock copolymers obtained through nitroxide-mediated polymerization independently of the degree of polymerization of each block.

3. Surfactant-free emulsion polymerizations of BMA and styrene initiated by P(PEOMA-*co*-MAA-*co*-S)-SG1 macroalkoxyamines

We have shown in the previous section that the solubility behavior of P(PEOMA-*co*-S)-SG1 macroinitiators had a great effect on the latex stability and particle morphology. The polymerization initiated by Ma1 (cloud point = 51 °C) did not produce a colloidally-stable latex as phase separation occurred when the reaction temperature exceeded the cloud point of the macroinitiator owing to the desolvation of the PEO chains. In the following, we want to investigate in more depth the effect of macroalkoxyamine's composition and cloud point on kinetics and particle morphology. P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroinitiators were used for that purpose. Indeed, as shown in Chapter 3, the cloud point of these dual pH/temperature responsive macroalkoxyamines could be easily varied over a wide range through a simple change of the pH value.

3.1 Experimental procedure

All emulsion polymerization experiments with P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiators were conducted using the same process as the one described in section 2.1. The molar mass and structures of these macroalkoxyamine initiators are recapitulated in Table 4 (Ma4, Ma5 and Ma6) while the various experimental conditions are reported in Table 5 and Table 6. Sodium hydroxide (NaOH, 1M) was used to fix the pH of the macroalkoxyamine solutions before monomer addition.

Run	$M_{\rm n}({\rm g\ mol}^{-1})$	$M_{\rm w}/M_{\rm n}$	Structure of the copolymers	MAA molar fraction (%)
Ma4	11 600	1.37	P[(PEOMA ₃₀₀) ₃₄ -co-MAA _{6~7} -co-S _{7.2}]	15
Ma5	11 800	1.40	P[(PEOMA ₃₀₀) ₂₉ -co-MAA ₂₆ -co-S _{7.3}]	42
Ma6	8 500	1.32	P[(PEOMA ₃₀₀) ₁₃ - <i>co</i> -MAA ₄₄ - <i>co</i> -S ₈]	68

Table 4 Recapitulation of the main characteristics of the P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiators used in this work.

3.2 Effect of MAA content at pH = 7.5

In order to assess the effect of the MAA content on both the kinetics and the control of the emulsion copolymerization of BMA with a small percentage of S, three experiments were carried out at a fixed pH of 7.5 using Ma4 (E14, 15 mol% MAA), Ma5 (E17, 42 mol% MAA) and Ma6 (E19, 68 mol% MAA) macroalkoxyamine initiators (Table 5). Under such pH conditions, these macroalkoxyamine initiators are fully water-soluble and do not exhibit any cloud point below 80 °C as shown in Chapter 3. Thus, in the polymerization medium, those hydrophilic macroalkoxyamines are composed of PEOMA and NaMA subunits (ionization of the MAA units) in various proportions that can efficiently contribute to the electrosteric stabilization of the particles. All polymerizations reached maximal conversion within 1.5 h (Figure 4.19). As shown in Figure 4.19, the polymerization rate decreased with increasing MAA molar fraction in the copolymer, which is likely due to the increase of the ionic strength. Actually, in order to achieve the same pH value, the amount of 1M NaOH solution added increased with the MAA percentage, leading to an increase of the ionic strength in the system. A similar decrease of the polymerization rate was observed when the ionic strength was increased in the presence of Ma2 macroinitiator (Figure 4.15). In the present case, it is however difficult to de-correlate the influence of the macroinitiator architecture from that of the ionic strength, on the conformation in water of the PEO-based macroalkoxyamines. However, it is very likely that the initial state may be different between the three experiments, which may impact the activation/deactivation rate constants.



Figure 4.19 Evolution of monomer weight conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of P(PEOMA-*co*-MAA-*co*-S) macroalkoxyamine initiators of increasing MAA molar fractions at pH = 7.5. E14: Ma4 (\blacksquare , 15 mol% MAA); E17: Ma5 (\bullet , 42 mol% MAA) and E19: Ma6 (\blacktriangledown , 68 mol% MAA) (Table 5).



Figure 4.20 Evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the evolution of theoretical M_n with conversion) during the surfactant-free emulsion polymerization of BMA and S in the presence of P(PEOMA-*co*-MAA-*co*-S) macroalkoxyamine initiators of increasing MAA molar fractions at pH = 7.5. E14: Ma4 (\blacksquare , 15 mol% MAA); E17: Ma5 (\bullet , 42 mol% MAA) and E19: Ma6 (\blacktriangledown , 68 mol% MAA) (Table 5).
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The controlled character of the polymerization is illustrated in Figure 4.20 with the linear increase of M_n with monomer conversion before the conversion reached its maximum value. In the same way as for the salt effect described above for the P(PEOMA₉₅₀-co-S)-SG1 macroalkoxyamine initiator, the crossover efficiency and the quality of control over chain growth were gradually lost. Nevertheless, the shift of the SEC peaks (Figure 4.21) indicates an efficient reinitiation step and the effective synthesis of amphiphilic block copolymers. Figure 4.21 however clearly indicates the presence of dead chains, the amount of which was not quantified.





Figure 4.21 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of BMA and S in the presence of P(PEOMA-*co*-MAA-*co*-S) macroalkoxyamine initiators of increasing MAA molar fractions at pH = 7.5. E14: Ma4 (a, 15 mol% MAA); E17: Ma5 (b, 42 mol% MAA) and E19: Ma6 (c, 68 mol% MAA) (Table 5).

4.5

5.0

log M

5.5

6.0

6.5

54.1%

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butyl methacrylate with a low percentage of styrene using SG1-capped P(PEOMA₃₀₀-co-MAA-co-S) copolymers as macroinitiators. Effect of **Table 5** Experimental conditions and characteristics of the polymer latex particles synthesized by surfactant-free emulsion polymerization of *n*the nature of the macroinitiator and of the pH.^a

Entry	Macroi Type (m	nitiator mol L ⁻¹)	Target <i>M</i> _n (g mol ⁻¹) ^b	рН ^с	Cloud point (°C) ^d	\mathbf{X}_{wf} (%) ^e	$M_{ m n} \left(M_{ m w}/M_{ m n} ight)^{ m f}$	Z _{av} (DLS) (nm)	Poly value (DLS)	D_{n}^{g} (nm)	$D_{\rm w}/D_{\rm n}^{ m g}$ (TEM)	[NaOH] (mol L ⁻¹) ^h
E14	Ma4	5.2	43 258	7.5	/	78.2	55 661 (2.17)	429	0.64	59	1.32	1.74×10^{-2}
E15	Ma5	5.3	41 745	5.0	34	52.5	27 257(1.91)	607	0.38	/	/	/
E16	Ma5	5.5	42 158	6.0	67	60.7	36 586 (1.90)	527	0.61	/	/	3.21×10^{-2}
E17	Ma5	5.4	42 134	7.5	/	54.0	38 662 (1.99)	468	0.33	78	1.09	5.10×10^{-2}
E18	Ma5	5.4	42 235	9.1	/	48.6	30 555 (2.08)	387	0.31	70	1.07	5.44×10^{-2}
E19	Ma6	5.1	41 477	7.5	/	40.8	44 069 (1.77)	361	0.24	108	1.06	6.41×10^{-2}
^a All pc	olymerizatic	ons were ca	arried out at 85	°C for a	t least 2h. The tots	al monom	her concentration v	vas 20 wt% ar	nd the initial mo	lar fractic	on of styren	e was $f_{\rm S0}$ =

0.08.^b Theoretical molar mass at 100% conversion determined according to:

 $1 \times M_{\rm m}^{~alkoxyamine}$ Target $M_{\rm n}({\rm g\,mol}^{-1}) = M_{\rm m}^{alkoxyamine} + \left(\frac{initial\,mas\,of\,monomer}{mass\,of\,alkoxyamine}\right)$

analysis.¹ Determined by SEC in THF with PMMA standards.² For spheres in the TEM images.¹ The concentration of NaOH in the system was calculated ^c Initial pH determined before polymerization. ^d Determined by UV/Vis spectroscopy (see Chapter 3). ^e Weight conversion determined by gravimetric based on the added amount of 1M NaOH solution.

The final obtained amphiphilic P(PEOMA₃₀₀-co-MAA-co-S)-b-P(BMA-co-S) diblock copolymer dispersions are colloidally stable with however the formation of some aggregates as indicated by the discrepancy between DLS and TEM particle sizes and the high Poly values (Table 5). The particles exhibit different morphologies as illustrated in Figure 4.22. For low MAA contents (E14, 15 mol %) in the first block, the final latex is composed of a mixture of small spherical particles ($D_n = 59 \text{ nm}$, $D_w/D_n = 1.32$) and fibers ($D_n = 65 \text{ nm}$) as determined by statistical analysis of TEM images over a large number of particles. When the MAA content increased to 42 mol% (E17), only spherical particles were obtained which indicates a better stabilization of the macroalkoxyamine initiator with higher MAA percentage. Their diameter was slightly bigger ($D_n = 78$ nm) and their size distribution narrower ($D_w/D_n = 1.09$). Finally, a mixture of spherical particles ($D_n = 108$ nm, $D_w/D_n =$ 1.06), elongated spheres, fibers and vesicles was obtained when the MAA percentage increased to 68 mol% (E19). This result is likely due to a competition between increasing hydrophilicity (upon increasing MAA content) and salting out effect as the NaOH concentrations used to adjust the pH value was increased from 17 to 64 mM when increasing MAA molar fraction from 15 to 68 mol% (Table 5).



Figure 4.22 TEM images of the final P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-poly(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of P(PEOMA-*co*-MAA-*co*-S) macroalkoxyamine initiators of increasing MAA molar fractions at pH = 7.5. E14: Ma4 (a, 15 mol% MAA); E17: Ma5 (b, 42 mol% MAA) and E19: Ma6 (c, 68 mol% MAA) (Table 5). Phosphotungstic acid was used to increase specimen contrast.

3.3 Effect of pH

To investigate the effect of pH on the emulsion polymerization kinetics, the control over molar mass and on the final morphology of the latex particles, four experiments were conducted at pH = 5.0, 6.0, 7.5 and 9.1, respectively, using Ma5 as macroinitiator (42 mol% MAA, Table 5, E15 to E18). As it was mentioned before, the ionization degree of the MAA subunits in the P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiator is very high at pH = 7.5 and 9.1. At low pH (pH = 6.0 and 5.0), the situation is different and the macroalkoxyamine initiator becomes only partially ionized.⁶⁶ It should be noted that the Ma5 water solution at pH = 5.0 was still turbid after 1 h of treatment with ultrasounds. As mentioned before, the free SG1 concentration should increase with increasing pH (as there is less degradation), which should result in lower reaction rates. The weight conversion *vs* time curves of Figure 4.23 show that the polymerization rate followed the expected trend and decreased with increasing pH except for pH = 5.0. The low polymerization rate observed in this case may be due to the poor water solubility of Ma5 under these pH conditions as already mentioned.

Figure 4.24, Figure 4.25 and Table 5 show that the pH did not affect the evolution of M_n with conversion and the initiation efficiency to a significant extent. TEM images in Figure 4.25 clearly show a transition from mainly vesicles (pH = 5.0), fibers/vesicles (pH = 6.0), and spheres ($D_n = 78 \text{ nm}$, $D_w/D_n = 1.09$, pH = 7.5) toward smaller spheres ($D_n = 70 \text{ nm}$, $D_w/D_n = 1.07$, pH = 9.1) upon increasing pH. This trend shows that as expected, increasing pH value increases the stabilization ability of the macroalkoxyamine initiator.



Figure 4.23 Evolution of monomer weight conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma5 macroalkoxyamine initiator (42 mol% MAA) for increasing pH values. E15: pH = $5.0 (\blacktriangle)$; E16, pH = $6.0 (\blacksquare)$; E17, pH = $7.5 (\bullet)$ and E18, pH = $9.1 (\blacktriangledown)$.



Figure 4.24 Evolution of M_n and $M_w/M_n vs$ weight conversion (the full lines represent the evolution of theoretical M_n with conversion) during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma5 macroalkoxyamine initiator (42 mol% MAA) for increasing pH values. E15, pH = 5.0 ($M_n \blacktriangle$, $M_w/M_n \bigtriangleup$); E16, pH = 6.0 (M_n \blacksquare , $M_w/M_n \Box$); E17, pH = 7.5 ($M_n \bullet$, $M_w/M_n \odot$) and E18, pH = 9.1 ($M_n \blacktriangledown$, $M_w/M_n \bigtriangledown$).



Figure 4.25 Evolution of the size exclusion chromatograms and TEM images (phosphotungstic acid was used to increase specimen contrast) of the final P(PEOMA-co-MAA-co-S)-b-P(BMA-co-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the Ma5 macroalkoxyamine initiator (42 mol% MAA) for increasing pH values. A: E15, pH = 5.0; B: E16, pH = 6.0; C: E17, pH = 7.5 and D: E18, pH = 9.1.

More surprising was the stability of the latex suspensions above the cloud point of the macroalkoxyamine initiators at pH = 5.0 and 6.0. During polymerization, the medium suddenly became milky when the temperature reached the cloud point temperature but the colloidal stability was maintained during and after the polymerization (Figure 4.26). We recall here that under similar conditions, the emulsion was broken in a short period of time when Ma1 (without MAA subunits, Table 1) was used as macroinitiator. This points to the determinant role of MAA in imparting colloidal stability to the formed latex particles even for reaction temperatures exceeding cloud points.



Figure 4.26 Pictures of the final latexes obtained at different pH values (after 2 months). pH = 5.0 (E15) and pH = 6.0 (E16).

3.4 Effect of macroinitiator concentration

Besides the pH value and the MAA molar fraction, the molar mass of the hydrophobic and hydrophilic blocks are also of high importance in controlling the morphology of the final latex particles as already demonstrated in previous works using NMP⁶⁸⁻⁷⁰ or RAFT.^{59, 60-67}

The effect of the macroinitiator concentration was studied using Ma4 at different pH (pH = 6.0, 7.5 and 9.0, E20 to E27, Table 6). For each pH value, the initial concentration of Ma4 was varied from 2.6 mM to 9.0 mM, while the overall amount and composition of the hydrophobic monomers (BMA and S) were maintained the same as before (20 wt%). As for the PEOMA-based macroalkoxyamine initiators, the polymerization kinetics curves shown in Figure 4.27 were strongly dependent on the initiator concentration, the highest reaction rate

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being obtained for the highest concentration. Figure 4.28 shows that for each pH value with different concentrations of Ma4, the experimental M_n increased linearly with monomer conversion, even if the experimental molar masses did not always fit with the predicted ones.



Figure 4.27 Evolution of monomer weight conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma4 macroalkoxyamine initiator for different concentrations (2.6 mM, 5.2 mM and 9.0 mM) and different pH values. A: E20, E23, E25, pH = 6.0; B: E21, E14, E26, pH = 7.5 and C: E22, E24, E27, pH = 9.0 (See Table 6).

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Table 6 Experimental conditions and characteristics of the polymer latex particles synthesized by surfactant-free emulsion polymerization of *n*butyl methacrylate with a low percentage of styrene using the SG1-capped P(PEOMA₃₀₀-co-MAA-co-S) Ma4 macroalkoxyamine initiator. Effects of the macroinitiator concentration and of the pH.^a

Entry	Macroin Type (mn	itiator nol L ⁻¹)	Target $M_{\rm n}$ (g mol ⁻¹) ^b	рН°	Cloud point (°C) ^d	\mathbf{X}_{wt} (%) ^e	$M_{ m n} \left(M_{ m w}/M_{ m n} ight)^{ m f}$	Z _{av} (DLS) (nm)	Poly value (DLS)	[NaOH] (mol L ⁻¹) ^g
E20	Ma4	2.6	74 679	6.0	59	73.1	70 056 (1.77)	378	0.28	1.31×10^{-2}
E21	Ma4	2.6	75 091	7.5	/	71.3	87 865 (1.95)	276	0.37	1.74×10^{-2}
E22	Ma4	2.6	72 804	9.0	/	75.1	88 974 (1.89)	235	0.33	1.91×10^{-2}
E23	Ma4	5.2	43 322	6.0	59	75.5	41 324 (1.79)	332	0.22	2.60×10^{-2}
E14	Ma4	5.2	43 258	7.5	/	78.2	55 661 (2.17)	429	0.64	3.49×10^{-3}
E24	Ma4	5.2	43 310	9.0	/	70.7	45 898 (2.27)	383	0.54	3.93×10^{-3}
E25	Ma4	9.0	29 687	6.0	59	86.5	41 723 (2.18)	387	0.57	4.54×10^{-2}
E26	Ma4	9.1	29 786	7.5	/	88.7	45 487 (2.16)	516	0.30	6.04×10^{-2}
E27	Ma4	8.9	29 635	9.0	/	80.7	42 732 (2.25)	268	0.53	6.62×10^{-2}

All polymerizations were carried out at δ^{-1} for at least 2 n. The total monomer concentration was 20 wt% and the initial motal flaction of stytene was S_{80} $= 0.08^{\circ}$ ^bTheoretical molar mass at 100% conversion determined according to:

Target $M_n(g \text{ mol}^{-1}) = M_m^{\text{ alkoxyamine}} + \left(\frac{\text{initial mas of monomer}}{\max \text{ of alkoxyamine}}\right) \times M_m^{\text{ alkoxyamine}}$

^c Initial pH determined before polymerization. ^d Determined by UV/Vis spectroscopy (see Chapter 3). ^e Weight conversion determined by gravimetric analysis. ^TDetermined by SEC in THF with PMMA standards.^g The concentration of NaOH in the system was calculated based on the added amount of 1M NaOH solution.



Figure 4.28 Evolution of M_n and M_w/M_n vs weight conversion (the full lines represent the evolution of theoretical M_n with conversion) during the surfactant-free emulsion polymerization of BMA and S in the presence of the Ma4 macroalkoxyamine initiator for different concentrations (2.6 mM ■, 5.2 mM ▼ and 9.0 mM •) and different pH values. A: E20, E23, E25, pH = 6.0; B: E21, E14, E26, pH = 7.5 and C: E22, E24, E27, pH = 9.0 (See Table 6).

Figure 4.29 shows for each experiment the evolution of the size exclusion chromatograms with conversion. A complete shift of the SEC traces towards higher molar masses illustrates the controlled growth of the hydrophobic block with the formation of amphiphilic block copolymers. However, a small shoulder on the low molar mass side was observed for the highest Ma4 concentration, whatever the pH, indicating the presence of unreacted (and likely dead) Ma4 chains. In most cases, there was also a shoulder on the high molar mass side. For all these reasons, the final molar mass distributions were quite broad ($M_w/M_n > 1.7$).

In all experiments, stable amphiphilic P(PEOMA-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) diblock copolymers were formed and self-assembled during the emulsion polymerization. Figure 4.30 shows the cryo-TEM pictures of the different latex obtained. A clear relationship between the polymerization parameters (pH value and Ma4 concentration) and the final particle morphology could be observed. For a same pH (pH = 9.0 or 7.5), the morphology changed from spheres to fibers and then to vesicles when the macroinitiator concentration decreases (i.e., when the length of the hydrophobic block increases) (from E27 to E22, and also from E26 to E21 in Figure 4.30). It should be noted that the cloud point of Ma4 (59 °C) is lower than the reaction temperature at pH = 6.0, and only vesicles were obtained with 2.6 mM and 5.2 mM Ma4 (E20 and E23, respectively, in Figure 4.30). A mixture of elongated and "onion"-like particles was obtained with 9.0 mM of Ma4 at pH = 6.0 (E25 in Figure 4.30).

The effect of pH value for a given macroinitiator concentration is similar to the trend observed with Ma5 in the previous section. Decreasing the pH value decreases the stabilization ability of the macroalkoxyamine initiator (by changing its hydrophilicity), which leads to an increasing fraction of fibers and vesicles instead of spheres for the final latex particles.



Figure 4.29 Evolution of the size exclusion chromatograms of the final P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the Ma4 macroalkoxyamine initiator for different pH values and macroinitiator concentrations (see Table 6).



Figure 4.30 Cryo-TEM images of the final P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the Ma4 macroalkoxyamine initiator for different pH values and macroinitiator concentrations (see Table 6).

3.5 Conclusions

In summary, SG1-capped P(PEOMA₃₀₀-*co*-MAA-*co*-S) macroalkoxyamine initiators with a dual thermo/pH sensitive behavior have been used to initiate the aqueous nitroxide-mediated emulsion polymerization of *n*-butyl methacrylate and styrene. The linear increase of molar masses with monomer conversion and the shift of the SEC traces towards higher molar

masses illustrate the controlled growth of the hydrophobic block with the formation of amphiphilic block copolymers. However, in most of the cases, the presence of dead chains was observed (in variable amounts). Both the pH value and initial MAA molar fraction in the macroalkoxyamine had a great effect on the polymerization kinetics and particle morphology. Whatever the pH, even for reaction temperatures exceeding the cloud point of the macroalkoxyamine initiator, stable amphiphilic P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*- P(BMA-*co*-S) diblock copolymers were formed and self-assembled during the emulsion polymerization. The morphologies of the latex particles were dependent on the MAA fractions in the macroalkoxyamine, and on the initial concentration of the macroalkoxyamines, which leads to varying molar mass ratio of the hydrophilic and hydrophobic blocks in the copolymer.

Conclusions

In this chapter, PEOMA- and PEOMA/MAA-based macroalkoxyamines whose characteristics were described in Chapter 3 have been used to initiate the aqueous emulsion polymerization of BMA with a small fraction of S under moderate temperature conditions. Despite the presence of a small proportion of dead chains indicating the occurrence of irreversible termination reactions, molar masses evolved linearly with conversion as expected for controlled radical polymerization. (Electro)sterically stabilized self-assembled diblock copolymer particles with film-forming properties were obtained *in situ* upon chain extension of the hydrophilic block.

Macroalkoxyamine initiators mainly composed of PEOMA units (except for styrene) resulted in the formation of latex particles with different morphologies such as spheres, fibers and vesicles according to polymerization–induced self-assembly of amphiphilic block copolymers in water. While spherical latex particles were obtained at pH = 4.2 regardless of the molar mass of the hydrophobic block over the entire range studied, vesicles and elongated particles were obtained at pH = 6.0 and 6.7. This was interpreted in terms of a salting out effect produced by the increase of ionic strength that accompanies the change of pH. This provides an unprecedented way to control the morphology of self-assembled diblock copolymers obtained through nitroxide-mediated polymerization independently of the degree of polymerization of each block. The effect of pH on particle morphology was further studied by investigating the dual pH/temperature responsive P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiators. Changing the pH value allowed controlling the cloud point temperature of this series of macroalkoxyamines and hence tuning the final morphologies (spherical micelles, nanofibers, and vesicles). Stable amphiphilic P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) diblock copolymers were formed and self-assembled during the emulsion polymerization even for reaction temperatures exceeding the cloud point of the macroalkoxyamine initiator. The morphologies of the latex particles were dependent on the MAA fractions in the macroalkoxyamine, and on the initial concentration of the macroalkoxyamines, which leads to varying molar mass ratio of the hydrophilic and hydrophobic blocks in the copolymer.

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Chapter 5.

NMP-mediated synthesis of polymer/silica hybrid particles

Introduction

In recent years, there has been an increasing interest for the grafting of polymers to inorganic surfaces. As described in the bibliographic chapter, grafting can be done in various ways using anionic, cationic or free radical processes.¹⁻⁷ In order to achieve a high density of grafts with well-defined architectures and controlled molar masses, living polymerization techniques are preferred. These techniques usually involve growth of the polymer from the solid surface by means of immobilized initiators using the so-called "grafting from" method.^{8,9} All three major CRP processes (i.e., ATRP, RAFT and NMP) have been reported for that purpose resulting in the synthesis of highly dense polymer brushes from various inorganic particles.⁹⁻¹¹ However, the developed systems mainly rely on solvent-borne strategies and less attention has been paid to waterborne approaches.

On the other hand, the formation and assembly in aqueous media of amphiphilic block copolymers have recently attracted much attention.¹² Indeed, apart from conventional spheres, more complex morphologies like fibers, vesicles or worms can be obtained directly in water upon the chain extension of preformed hydrosoluble controlling agents with hydrophobic monomers. Very recently, CRP has also been employed to synthesize hybrid latex particles in aqueous dispersed media.¹³⁻¹⁷ Although the main purpose of these works was to encapsulate inorganic pigments and thus generate core-shell structures, it can be anticipated that block copolymers self-assembly on inorganic surfaces could lead to hybrid particles with new interesting morphologies.

In this chapter, we aim to perform a "growth through" NMP in aqueous dispersed media to synthesize polymer/silica hybrid particles. The envisioned strategy mainly relies on the use of well-defined hydrophilic PEOMA-based macroalkoxyamines previously adsorbed on the surface of silica particles, and does not require any chemical modification. The adsorbed macroinitiators will be further chain-extended in water to generate composite particles relying on the PISA process described in Chapter 4.

In the first part, the $P[(PEOMA_{950})_{12}$ -*co*-S₁]-SG1 macroalkoxyamine with long PEO side chains (i.e. Ma2 - see Chapter 3) was employed to generate silica/polymer particles by surfactant-free emulsion polymerization of BMA and S in the presence of silica nanoparticles. The purpose was to investigate the self-assembly behavior of the so-formed block copolymers in the presence of silica particles and the polymerization kinetics as a

function of the experimental conditions such as the pH value, the macroalkoxyamine concentration and the silica particle size.

In the second part, we propose to enhance the interaction between the growing polymer chains and the silica surface by using $P[(PEOMA_{300})_{34}$ -*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 macroalkoxyamine as initiator (i.e. Ma4 - see Chapter 3). This macroalkoxyamine has a cloud point below the reaction temperature (i.e. 59 °C), and is also pH sensitive. This gives it an amphipathic character that can be advantageously used to encapsulate silica particles or lead to new unexpected morphologies using the suspension pH as an external trigger.

1. Polymerization-induced self-assembly of P[(PEOMA₉₅₀)₁₂-*co*-S₁]-*b*-P(BMA-*co*-S) block copolymers in the presence of silica particles

1.1 Experimental procedure

Materials

The experimental conditions and main characteristics of the silica particles used in this section are given in Table 1. The aqueous commercial silica sol (Klebosol 30N50) was kindly supplied by Clariant (France) and the other samples were synthesized as reported in Chapter 2. The monomers: *n*-butyl methacrylate (BMA, 99%, Aldrich), styrene (S, 99%, Acros) and the coupling agent: γ -methacryloxy propyl trimethoxysilane (γ -MPS, Acros Organics) were all used as received. The P[(PEOMA₉₅₀)₁₂-*co*-S₁]-SG1 macroalkoxyamine initiator was synthesized as reported in Chapter 3 (Ma2: $M_n = 11700$ g mol⁻¹ and $M_w/M_n = 1.11$).

Macroinitiator adsorption on the silica surface

Macroalkoxyamine solutions of various concentrations were mixed with a stock dispersion of the commercial Klebosol silica sol (S2 in Table 1) at pH = 5.0 to cover a final macroinitiator concentration range between 0.2 and 8 mol L⁻¹ (i.e., 0.02 - 3.2 μ mol m⁻²) while maintaining a fixed silica concentration of 50 g L⁻¹. The dispersion was stirred for one hour and further ultracentrifuged at 18 000 rpm for 30 min (Beckman Coulter Allegra 64R centrifuge). The recovered solid was dried under room temperature for 3 days before analysis. The density of adsorbed polymer chains, A (μ mol m⁻²), was determined by thermogravimetric analysis (TGA) using equation (5.1):

A (µmol m⁻²) =
$$\frac{\left(\frac{W_{50-400}}{100 - W_{50-400}}\right) \times 100 - W_{silica}}{M_n \times S_{spec} \times 100} \times 10^6$$
 (eq. 5.1)

where W_{50-400} is the weight loss between 50 and 400 °C corresponding to the thermal decomposition of the macroalkoxyamine initiator, M_n is the molar mass of the macroinitiator, $S_{spec.}$ is the specific surface area of silica ($S_{spec.} = 50 \text{ m}^2 \text{ g}^{-1}$, supplier data record for Klebosol colloidal silica sol) and W_{silica} is the weight loss of bare silica.

Grafting of γ -MPS onto the silica particles

The 30 nm silica nanoparticles (S1 in Table 1) was modified with γ -MPS using a Stöber-like process. Typically, the original aqueous silica dispersion was diluted with water down to 3.7 wt% and mixed with analytical grade absolute ethanol and ammonia (0.2 mol L⁻¹) up to the desired solid content (0.9 wt%) to ensure colloidal stability of the silica particles. Then, a predetermined amount of γ -MPS (0.5 g, 22.9 µmol m⁻²) was added to the diluted silica suspension. Grafting was carried out at room temperature for 24 h under continuous stirring. The γ -MPS-modified silica was extensively washed with absolute ethanol via a series of centrifugation/redispersion cycles to remove non-reacted species, dried in an oven at 90 °C prior to analysis and redispersed in water before use. The grafting density G (µmol m⁻²) was determined by thermogravimetric analysis (TGA) using equation (5.2):

G (µmol m⁻²) =
$$\frac{\left(\frac{W_{50-800}}{100 - W_{50-800}}\right) \times 100 - W_{silica}}{M \times S_{spec} \times 100} \times 10^{6}$$
 (eq. 5.2)

where W_{50-800} (wt%) is the weight loss between 50 and 800 °C corresponding to the thermal decomposition of the silane molecule, M is the molar mass of the decomposition part of grafted silane (127 g mol⁻¹), W_{silica} is the weight loss of silica determined before grafting and S_{spec} (m² g⁻¹) is the specific surface area of silica which was calculated according to the equation (5.3):

$$S_{\text{spec}} = \frac{6 \times 10^3}{\rho \times D_{\text{n}}} \tag{eq. 5.3}$$

where ρ (2.1 g cm³) is the density and D_n (30 nm) is the diameter of the silica particles, respectively.

Surfactant-free emulsion polymerization

In a typical emulsion polymerization experiment (entry EH02 in Table 2), a known quantity of macroinitiator (Ma2, 0.88 g; 2.3 mmol L^{-1}) was introduced in the silica suspension (25 g). The size and concentration of the silica particles were varied as reported in Table 2. The mixture was then stirred under nitrogen bubbling for 30 min at room temperature. Then, the monomers, a mixture of BMA and S (2.35 g of BMA and 0.15 g of S), were introduced in the suspension and the obtained unstable biphasic system was deoxygenated by nitrogen bubbling for another 20 min. This mixture was introduced into a 50 mL round flask, and heated at 85 °C for 6h. Time zero of the polymerization was taken when the reaction temperature reached 70 °C. Samples were periodically withdrawn to follow monomer conversion by gravimetric analysis. Hydrochloric acid (0.1 M aqueous solution) was used to control the pH value before addition of the monomers. The experimental conditions and main characteristics of the resulting latex particles are listed in Table 2.

The number ratio of polymer latex particles to silica particles, N_{Latex}/N_{Silica} , was determined by two different ways. The first way was based on statistical analysis of the cryo-TEM images by counting manually the number of latex particles and the number of silica particles and making the ratio. Silica and polymer particles show significantly different contrasts and can be thus unambiguously identified on the micrographs.

In the second method, N_{Latex}/N_{Silica}, was determined according to the equation (5.4) below:

$$\frac{N_{latex}}{N_{silica}} = \left(\frac{C_{polymer}}{C_{silica}}\right) \left(\frac{d_{silica}}{d_{polymer}}\right) \left(\frac{D_{n \ silica}}{D_{n \ latex}}\right)^{3} \quad (eq. 5.4)$$

where C_{silica} (g L⁻¹) is the silica concentration, $C_{polymer}$ (g L⁻¹) is the polymer concentration determined by the monomer conversion; d_{silica} and $d_{polymer}$ (g cm⁻³) are the silica and polymer mass densities, respectively; and D_n _{Silica} and D_n _{Latex} (nm) are the diameters of the silica and latex particles determined by cryo-TEM, respectively. A minimum of 150 particles was counted for each batch.

Characterizations

For each emulsion polymerization, the monomer conversion was determined by gravimetric analysis. Samples of the hybrid latex were taken during the polymerization, put in a preweighted aluminum capsule and immediately put in the oven. The capsule was dried at 100 °C until constant weight was achieved. The conversion was calculated according to the following equation (5.5):

$$X_{\rm wt} = \left(\frac{M_{\rm dp}}{M_{\rm wl}} - \frac{M_{\rm np}}{M_{\rm t}}\right) \times \frac{M_{\rm t}}{M_{\rm m}} \times 100 \qquad (eq. 5.5)$$

Where M_{dp} , M_{wl} , M_{np} , M_t and M_m are the weight of the dried hybrid latex, wet hybrid latex, non-polymerizable compounds in the recipe, total recipe weight and monomers in the recipe.

Dynamic light scattering (DLS, Nano ZS from Malvern Instruments) was used to measure the particle size (average hydrodynamic diameter, Z_{av}) and the dispersity of the samples (indicated by the Poly value – the higher this value, the broader the size distribution). Before measurements, the latex samples were diluted in deionized water.

SEC analyses of polymers were performed in THF. All hybrid samples were first dissolved in THF and then centrifuged to remove the silica particles. The supernatant incorporating the polymer chains was dried and then redissolved in THF and injected at a concentration of 3 mg mL⁻¹ after filtration through a 0.45 μ m pore-size membrane. The separation was carried out on three Polymer Laboratories columns [3 × PLgel 5 μ m Mixed C (300 × 7.5 mm)] and a guard column (PL gel 5 μ m). Columns and detectors were maintained at 40 °C. THF was used as the mobile phase at a flow rate of 1 mL min⁻¹ and toluene served as a flow rate marker. The number and weight-average molar masses (M_n and M_w , respectively) and molar mass distributions (M_w/M_n) were calculated with a calibration curve based on PMMA standards.

Transmission electron microscopy (TEM) was performed at an accelerating voltage of 80 kV with a Philips CM120 transmission electron microscope (Centre Technologique des Microstructures (CTµ), plate-forme de l'Université Claude Bernard Lyon 1, Villeurbanne, France). Highly diluted samples were dropped on a Formvar-carbon coated copper grid and dried under air. Phosphotungstic acid (1.5 wt %, pH = 7) was used to increase the specimen contrast. The number-average weight-average particle diameter (D_n and D_w , respectively) and the polydispersity index (PDI = D_w/D_n) were calculated using $D_n = \Sigma n_i D_i / \Sigma n_i$ and $D_w = \Sigma n_i D_i^4 / \Sigma n_i D_i^3$, where n_i is the number of particles with diameter D_i .

Chapter 5. NMP-mediated synthesis of polymer/silica hybrid particles

For cryo-TEM experiments, a drop of the suspension was deposited on a continuous carbon film, blotting the water in excess, mounting the dry specimen on the Gatan holder and quenching it in liquid nitrogen before introduction in the microscope. The holder was then cooled down and the specimen was observed at -180 °C.

Cryo-electron tomography (cryo-ET) experiments were performed at the CBMN (Chimie et Biologie des Membranes et des Nanoobjets, UMR 5248, Bordeaux) by Jean-Christophe Taveau and Olivier Lambert. Tilt-series were collected automatically from -60° to +60° at 2° intervals along the tilt axis using the FEI tomography software. The defocus was ~10 μ m, and the magnification was set such that each CCD pixel corresponded to 1.08 nm at the specimen level. For image processing, using colloidal gold particles as fiducial markers, the 2D projection images, binned 2-fold, were aligned with the IMOD software package images,¹⁸ and then tomographic reconstructions were calculated by weighted back-projection using Priism package.¹⁹

Cryo-scanning electron microscopy (SEM) was performed in a FEI QUANTA 250 FEG scanning electron microscope, at an acceleration voltage of 15 kV. The specimen was first mounted on an appropriate holder – a wide variety is available to suit most sample types – which was itself mounted onto a cleverly designed freezing/vacuum transfer rod. The sample was plunge frozen in slushy nitrogen and then transferred under vacuum onto the cooled stage of the cryo-SEM preparation chamber. The preparation chamber was pumped by a rotary pump. Finally the simple-to-use gate valve between the preparation chamber and the SEM could be raised and the specimen transferred onto the cooled stage of the SEM for observation.

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$\begin{array}{c} W) & D_{w}/D_{n} \\ (TEM) \end{array}$	1.01	1.08	1.01	1.01	1.01
D _n (TEN (nm)	30	LL	140	230	440
Poly value (DLS)	0.04	0.04	0.02	0.02	0.06
Z _{av} (DLS) (nm)	43	86	163	257	460
Hd	8.9	7.3	9.5	9.3	9.0
Solids content (%)	3.9	23.7	11.3	5.3	10.0
[TEOS] (mol L ⁻¹)	0.717	/	0.2	0.4	0.6
[Catalyst] (mol L ⁻¹)	6.0×10^{-3}	/	0.1	0.2	0.3
Catalyst	L-Arginine	/	$\rm NH_3$	$\rm NH_3$	$\rm NH_3$
Synthetic procedure	Hartlen	Commercial product ^a	Stöber batch ^b	Seed regrowth ^b	Stöber batch ^b
Sample name	S1	S2	S3	S4	S5

Table 1 Experimental conditions and main characteristics of the silica particles used in this work.

^aAqueous commercial silica sol (Klebosol 30N50) from Clariant (France). ^b All Stöber silica suspensions were characterized after redispersion in water through successive centrifugation/redispersion cycles.





Chapter 5. NMP-mediated synthesis of polymer/silica hybrid particles

Table 2 Experimental conditions and characteristics of all silica/polymer latex particles synthesized by surfactant-free emulsion polymerization of *n*-butyl methacrylate and styrene using the SG1-capped $P[(PEOMA_{950})_{12}-co-S_1]$ -SG1 copolymer (Ma2 in chapter 3) as macroinitiator and different silica particles sizes.^a

Entry	Silica	D_{n} Silica (nm) ^b	[Silica] (g L ⁻¹)	pH ^c	[Macroinitiator] (mmol L ⁻¹)	Target $M_{\rm n}$ (g mol ⁻¹) ^d	Conv. (%) ^e	$M_{\rm n} \left(M_{\rm w}/M_{\rm n} \right)^{\rm f}$ (g mol ⁻¹)	Z _{av} (DLS) (nm)	Poly (DLS)	$D_{\rm n}({ m TEM})$ (nm) ^g	$D_{\rm w}/D_{\rm n}$ (TEM)
EH01	S1	30	25	5.0	1.2	14 1176	35.3	24 000 (2.3)	154	0.242	60	1.03
EH02	$\mathbf{S1}$	30	22	5.4	2.3	72 606	75.7	39 900 (1.7)	136	0.130	64	1.04
EH03	S2	LL	50	6.0	2.4	$80\ 180$	74.4	33 000 (1.7)	219	0.117	88	1.06
EH04	S3	140	50	5.8(+)	2.4	80 015	52.8	57 300 (1.8)	218	0.574	86	1.03
EH05	$\mathbf{S4}$	230	50	5.7(+)	2.4	80 235	50.5	27 500 (2.2)	167	0.276	85	1.06
EH06	S5	440	50	(+)0.9	2.4	80 149	45.8	45 200 (1.7)	235	0.409	93	1.03
EH07	S3	140	50	2.2(+)	2.4	79 266	53.4	58 300 (1.9)	232	0.555	80	1.03
EH08	S3	140	50	6.7(+)	2.4	80 513	74.9	56 900 (2.3)	636	0.279	/	/
EH09	S3	140	50	7.7	2.1	90 229	80.3	51 300 (2.2)	651	0.284	/	/
EH10	$\mathbf{S4}$	230	50	8.2	2.4	$80 \ 940$	65.3	42 300 (1.9)	2569	0.487	/	/
EH11	$\mathbf{S1}$	30	25	8.0(-)	2.4	78 241	69.7	60 300 (1.8)	1020	0.505	/	/
EH12	$\mathrm{S1}^{\mathrm{h}}$	30	25	5.2(+)	2.4	79 632	72.1	47 600 (1.8)	166	0.043	/	/
EH13	${ m S1}^{ m h}$	30	25	8.1(-)	2.4	79 632	63.5	47 600 (1.1)	206	0.123	/	/
^a All pol	ymerizati	ons were cari	ried out at	85 °C foi	r 6 h. The total mono	mer concentra	ation was	20 wt% and the i	initial molar fra	ction of st	yrene was $f_{\rm S0}$ =	= 0.08.
^b Detern	ined by 7	TEM (see Tal	ble 1). [°] In	itial pH c	letermined before po	lymerization,	natural o	r adjusted with H	CI (+) or NaO	H (-). ^d The	eoretical mola	ır mass at
100% ca	onversion	determined a	according t	to: Targe	$ {\rm et}M_{\rm n}({\rm gmol^{-1}})=M$	r alkoxyamine m	$+\left(\frac{initio}{mas}\right)$	<u>il mas of monomer</u> s of alkoxyamine	$\left(\right) \times M_{\mathrm{m}}^{alkoxyc}$	ımine		

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 $^{\circ}$ Determined by gravimetric analysis. ^f Determined by SEC in THF with PMMA standards. ^g Diameter of latex particles in the TEM images. ^h γ -MPS-

functionalized silica particles.

1.2 Macroalkoxyamine adsorption on the silica surface

Studying the adsorption of the PEO-based macroalkoxyamine is of primary importance for an accurate understanding of the mechanism of hybrid particles formation. The adsorbed amounts were determined according to the TGA results in Figure 5.2 using the weight loss reported in Table 3 and equation (5.1). Figure 5.3 gives the isotherm for adsorption of the $P[(PEOMA_{950})_{12}$ -*co*-S₁]-SG1 macroalkoxyamine onto the silica sol (S2) at a fixed concentration of 50 g L⁻¹ and pH = 5.0.



Figure 5.2 TGA analysis of Ma2 adsorption on the Klebosol silica sol (S2, Table 1) for different Ma2 concentrations at 25 °C and pH = 5.3. [Silica] = 50 g L⁻¹.

Table 3 Weight loss (50 - 400 °C) and adsorbed amounts of the Ma2 macroalkoxyamin	ie or
the Klebosol silica sol (S2, Table 1) determined by TGA for various Ma2 concentrations.	

Ma2 concentration (mmol L ⁻¹)	Weight loss 50-400 °C (wt%)	Free Ma2 (mmol L ⁻¹)	Adsorbed amount (µmol m ⁻²) ^a
0	3.5	0	0
0.46	5.3	0.38	0.03
0.98	10.5	0.66	0.13
2.00	17.8	1.29	0.27
4.09	20.5	3.22	0.35
6.14	21.7	5.19	0.38
8.19	22.4	7.19	0.40

^a Determined using equation (5.1). [Silica] = 50 g L^{-1} . pH = 5.3.



Figure 5.3 Adsorption isotherm of the $P[(PEOMA_{950})_{12}$ -*co*-S₁]-SG1 macroalkoxyamine initiator (Ma2) onto the Klebosol silica sol (S2, Table 1) at 25 °C and pH = 5.3. [Silica] = 50 g L⁻¹.

As shown in Figure 5.3 and Table 3, the adsorbed amount of macroalkoxyamine on the silica surface increases as the Ma2 initial concentration increases, until a plateau is reached for a concentration close to 4 mmol L^{-1} . Free macroalkoxyamine can be found even for very low Ma2 concentration (0.46 mmol L^{-1}). The maximal adsorption capacity is around 0.4 µmol m⁻².

The maximum concentration of PEO-based macroalkoxyamine on the silica surface is less than reported^{20,21} for adsorption of linear PEO-based bottle brush polymers carrying cationic groups, namely (methacryloxyethyl trimethylammonium chloride)-*b*-(PEOMA₂₀₀₀) on silica (1.32 µmol m⁻² equivalent to 2.75 mg m⁻²).²¹ This may be due to different driving forces for adsorption of the polymer on silica. For the macroalkoxyamine P[(PEOMA₉₅₀)₁₂-*co*-S₁]-SG1, the interaction between the polymer and silica occurs only through the PEO side chains. The addition of charged segments^{20,21} can provide a stronger driving force for adsorption. Comblike polymers are known to adopt a stiff rod-like conformation in dilute solutions, the stiff nature of the polymer originating from the repulsions between PEO side chains.^{22,23} As macroinitiator adsorption occurs though the PEO chains, the adsorbed layer can be thus envisaged as rods lying flat along the silica surface to maximize the interaction between PEO and the surface silanol groups (Figure 5.4). Although many of the PEO side chains interact with the surface, some of them must for geometrical reasons be extended into solution.

Figure 5.5 shows the different mechanisms envisioned for the adsorption of the macroalkoxyamines on the silica surface for low and high Ma2 concentrations. For low Ma2 concentration, the adsorption occurs with a preferential orientation parallel to the surface even though there is a low amount of free Ma2. When the Ma2 concentration increases, the adsorbed fraction decreases for a same polymer chain and the PEO brush chains are extended away from the surface to make room for more polymer chains. Once the maximum adsorption capacity is reached, the amount of free polymer chains steadily increases.



Figure 5.4 Scheme for adsorption of brush-like polymers on the silica surface.





1.3 Synthesis of silica/polymer hybrid particles

In this section, we took advantage of the successful interaction of the macroalkoxyamine initiator with the silica surface to synthesize polymer/silica hybrid particles through NMP in

Chapter 5. NMP-mediated synthesis of polymer/silica hybrid particles

aqueous dispersed media. The role of the living polymer in the system is threefold: a coupling agent, an initiator and a stabilizer (thus avoiding the need for any external molecular surfactant). Figure 5.1 shows the TEM images and size histograms of the silica particles used for that purpose. Their diameters are comprised between 30 and 440 nm (as determined by TEM) and their size distribution is very narrow (D_w/D_n lower than 1.01) with the exception of the commercial Klebosol silica sol ($D_w/D_n = 1.08$). As shown in Table 2, the parameters that were studied in this section were the macroinitiator concentration for a fixed silica particle size of 30 nm, the silica particle size and the pH. As before, we have investigated their effect on the polymerization kinetics, on the control over the formation of amphiphilic block copolymers, and on the self-assembled nano-objects stability and morphology.

1.3.1 Effect of macroinitiator concentration

1.3.1.1 Kinetics

The effect of the macroinitiator concentration on kinetics was studied for the 30 nm silica particles (S1), using either 1.2 mmol L^{-1} or 2.3 mmol L^{-1} of Ma2 (EH01 and EH02, respectively, in Table 2). The pH was adjusted to 5, whereas the pH of the silica dispersion was initially close to 9. The polymerization kinetics shown in Figure 5.6 exhibits a trend similar to that observed for the blank emulsion polymerization without silica particles: the higher the concentration of macroinitiator, the higher the polymerization rate. As already mentioned in Chapter 4, these observations can be related to the persistent radical effect and of the proportion of released SG1, expected to be smaller when the initial alkoxyamine concentration is increased, hence leading to a higher concentration of propagating radicals. Figure 5.7 and Figure 5.8 show the evolution of the molar mass and molar mass dispersity with conversion. The control over chain growth is gradually lost which is similar to the results of blank emulsion polymerization for high ionic strengths (Figure 4.15 in Chapter 4). In the present system, the overall ionic strength is due predominantly to the surface charge of the particles, the compensating counterions and the salt generated upon addition of hydrochloric acid in order to reach a pH close to 5.



Figure 5.6 Evolution of monomer conversion with time during the surfactant-free emulsion polymerization of BMA with S in the presence of 30 nm diameter silica particles (S1, [Silica] = 25 g L⁻¹) for two different macroinitiator concentrations. EH01 (1.2 mmol L⁻¹, \blacksquare) and EH02 (2.3 mmol L⁻¹, \blacktriangle) (Table 2).



Figure 5.7 Evolution of M_n and M_w/M_n vs weight conversion (the full lines represent the theoretical M_n) for the surfactant-free emulsion polymerizations of BMA and S in the presence of 30 nm diameter silica particles (S1) for two different macroinitiator (Ma2) concentrations. EH01 (1.2 mmol L⁻¹, $M_n \blacksquare$, $M_w/M_n \square$) and EH02 (2.3 mmol L⁻¹, $M_n \blacktriangle$, $M_w/M_n \bigtriangleup$) (Table 2).



Figure 5.8 Evolution of the size exclusion chromatograms with weight conversion during the surfactant-free emulsion polymerization of BMA and S in the presence of 30 nm diameter silica particles (S1) and for two different macroinitiator (Ma2) concentrations. EH01 (1.2 mmol L^{-1}) and EH02 (2.3 mmol L^{-1}) (Table 2).

1.3.1.1 Particle morphology

The hybrid particles synthesized in the presence of 30 nm diameter silica particles (25 g L⁻¹) and a low concentration of Ma2 (EH01, 1.2 mmol L⁻¹), have been observed by cryo-TEM (Figure 5.9). In such conditions, the affinity between the polymer and the silica is confirmed as almost every polymer nodule (in light grey) is in contact with one silica particle (in dark grey). Some isolated silica beads and free latex particles can also be occasionally seen together with a few trimers (i.e. two polymer nodules adsorbed on one silica particle). A statistical calculation of the respective number of polymer nodules and silica particles leads to a ratio close to 1. A similar analysis was performed for the polymerization carried out with a higher macroinitiator concentration (EH02, 2.3 mmol L⁻¹). As shown in Figure 5.9, hybrid structures resulting from the growth of three latex particles on one silica particle are mainly obtained in this case. Based on the equation (5.4) and by setting d_{silica} to 2.1 g cm⁻³ and d_{polymer} to 1.0 g cm⁻³, we found that N_{Latex}/N_{silica} is 0.7 and 1.5 for EH01 and EH02, respectively. Furthermore, it is worth noting the absence of a significant number of free

polymer latex particles indicating that the polymerization mainly took place at the silica surface.

Table 4 compares the diameters and numbers of the latex particles synthesized in the absence and presence of silica particles. It is seen that the particle size is smaller and the particle number larger when the emulsion polymerization was carried out in the presence of silica particles. This is particularly evident for the lowest macroalkoxyamine concentration (EH01, 1.2 mmol L^{-1}). As free macroinitiator is present in the aqueous phase whatever the macroalcoxyamine concentration, the polymerization likely starts both in water and on the silica surface as schematically represented in Figure 5.10. The resulting block copolymers may coagulate to form free polymer latex particles in water or coagulate on the ones generated at the silica surface. However, the low fraction of free latex particles suggests that they prefer to self-assemble with the ones generated at the silica surface to stabilize them. Furthermore, the fact that the latex particle size decreases in the presence of silica for the lowest initiator concentration suggests that the silica particles also contribute in this case to the stabilization of the self-assembled block copolymers. Indeed, for low macroinitiator concentration, the surface coverage is low and the remaining dissociated silanol groups of silica may provide extra colloidal stability to the growing polymer spheres resulting in smaller particle sizes.



Figure 5.9 Cryo-TEM images of the final multipod-like hybrid latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of 30 nm diameter silica particles (S1, [Silica] = 25 g L⁻¹) for two different macroinitiator (P[(PEOMA₉₅₀)₁₂-*co*-S₁]-SG1) concentrations. EH01 (1.2 mmol L⁻¹) and EH02 (2.3 mmol L⁻¹) (Table 2).


Figure 5.10 Schematic for the nucleation of polymer latex particles in the water phase and on the silica surface.

Table 4 Diameters (D_n) and numbers (N_p) of the self-assembled block copolymer particles synthesized in the absence (blank emulsion polymerization) and presence (hybrid) of 30 nm silica particles.

	Ma2 (mmol L ⁻¹)	Blank e	xperiment	Hybrid latex		
Entry		D _{n Latex} (nm)	N _{p Latex} ×10 ¹⁷ L ⁻¹	D _{n Latex} (nm)	N _{p Latex} ×10 ¹⁷ L ⁻¹	
EH01	1.2	181	0.18	60	6.2	
EH02	2.3	73	7.5	64	11.0	

1.3.2 Effect of silica particle size

1.3.2.1 Kinetics

Figure 5.11 shows the evolution of monomer conversion with time for polymerizations performed in the presence of silica particles with increasing diameters and a fixed macroinitiator concentration (Ma2, 2.4 mmol L^{-1}) over a pH range of 5.4 - 6.0. It is clearly seen that the curves can be divided into two groups with different polymerization rates depending on the amount of hydrochloric acid used to achieve the target pH value, or in other words, on the ionic strength. For EH02 (prepared with silica S1 obtained from the L-arginine

process, pH = 9) and EH03 (prepared with the commercial silica S2, pH = 7.3), the pH value of the mixture of macroalkoxyamine and silica sol was 5.4 and 6.0, respectively. In contrast, the use of Stöber silica particles (EH04, EH05 and EH06) required some hydrochloric acid in order to neutralize the residual amount of ammonia and adjust the pH value to 6.0, which resulted in a higher ionic strength and hence, in a lower polymerization rate. Within a group of experiments (EH02/EH03 and EH04/EH05/EH06), the size of the silica particles has no significant effect on the polymerization rate.



Figure 5.11 Evolution of monomer conversion with time for the surfactant-free emulsion polymerizations of BMA and S in the presence of silica particles with different particle diameters using Ma2 as macroinitiator (2.4 mmol L⁻¹). EH02 (S1, 30 nm, 25 g L⁻¹, \blacktriangle), EH03 (S2, 77 nm, 50 g L⁻¹, \bullet), EH04 (S3, 130 nm, 50 g L⁻¹, \blacksquare), EH05 (S4, 230 nm, 50 g L⁻¹, \triangleright) and EH06 (S5, 440 nm, 50 g L⁻¹, \bigtriangledown).

1.3.2.2 Particle morphology

Figure 5.12 shows that daisy-shaped particles are obtained with 77 nm silica particles (EH03, Table 2). Each silica particle is surrounded by in average 5/6 latex particles. Calculation of $N_{\text{Latex}}/N_{\text{silica}}$ based on equation (5.4) gives a ratio of 4.2. A closer inspection of the cryo-TEM images shows that the latex particles may be located in the equatorial plane of the silica spheres. Indeed, if there were one latex particle above the silica particles, one should be able to distinguish it as the size of the latex particles is around 88 nm, which is larger than the

silica particle size. Perro et al. has reported similar planar arrangements during the synthesis of silica/polystyrene particles though seeded emulsion polymerization using PEOMA-functionalized silica particles as seeds.^{25,26} The observed 2D arrangement was attributed to the falling-in of the PS nodules on the TEM grid. Cryo-electron tomography images indeed showed that the arrangement of the biphasic particles was not planar, but in polyhedral shapes such as square antiprisms.²⁵ Similar 3D analyses would be also helpful in the present situation to assess the exact morphology of the observed daisy structure.

Furthermore, a closer look at the composite particles allows one to note that there is a tiny distance (black arrow) between the central silica core and the polymer latex particles. This region of lower contrast (i.e. of lower electronic density) could be reasonably attributed to the brush-type macroalkoxyamine initiator that is physically entrapped at the interface between the silica particles and the polymer nodules as schematically illustrated above Figure 5.10.



Figure 5.12 Cryo-TEM images of the final multipod-like hybrid latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of 77 nm silica (EH03 in Table 2) using $P[(PEOMA_{950})_{12}$ -co-S₁]-SG1 as macroinitiator (2.4 mmol L⁻¹).

Figure 5.13 shows the TEM images of the composite particles obtained for larger silica particle size and a fixed Ma2 concentration of 2.4 mmol L⁻¹. The morphology evolved from daisy-like to raspberry-like upon increasing the silica particle size from 140 nm to 440 nm. As the silica concentration was maintained constant in all experiments ([Silica] = 50 g L⁻¹,

except for EH02), increasing the silica particle size leads to a diminution of the silica particle number and of the total available surface area. When the number of silica particles is much smaller than the number of self-assembled latex particles (Table 5), the polymer nodules cover the entire silica surface and raspberry-like particles are obtained as shown in Figure 5.13. This assumption was confirmed by cryo-SEM observation (Figure 5.14) that provided a clear evidence of the presence of latex particles all around the silica spheres. Concomitantly, the amount of free latex particles is expected to increase with increasing the size of the silica particles as there will be obviously more free Ma2 in water and less surface area to capture all the resulting block copolymers.

Table 5 shows that as expected for high Ma2 concentration (i.e. for high macroinitiator surface coverage), there is no significant influence of the silica diameter on the sizes of the polymer nodules neither on that of the free latex particles. Consequently, the maximum number of latex particles that can be accommodated around each silica particle solely depends on the silica particle size and increases with increasing silica diameter. As shown in Table 5, for the hybrid particles obtained with 230 nm and 440 nm silica particles, N_{p Latex}/N_{p Silica} is much higher than the theoretical number of latex particles that can be close packed (with hexagonal symmetry) on each silica sphere.^{27,28} This, together with the important concentration of free Ma2 in these two experiments, explains the high amount of free latex particles observed on the TEM images of Figure 5.13 B, B1 and 5.13 C, C1.

Entry	D _{n Silica} (nm)	N _{p Silica} ×10 ¹⁷ L ⁻¹	D _{n Latex} (nm)	N _{p Latex} ×10 ¹⁷ L ⁻¹	$ m N_{p\ Latex}/ m N_{p\ Silica}$	D _{n Silica} / D _{n Latex}	N _{max} ^a
EH02	30	7.4	64	11.0	1.5	0.5	/
EH03	77	0.9	88	4.2	4.2	0.9	/
EH04	140	0.17	86	3.2	19.1	1.6	25
EH05	230	0.037	85	3.1	84	2.7	50
EH06	440	0.0053	93	2.2	407	4.7	119

Table 5 Particle diameters and numbers of latex particles obtained in the presence of silica

 particles of different sizes, and corresponding latex-to-silica number ratios.

^a Maximum number of latex particles that can be close-packed around each silica sphere calculated according to: $N_{max} = \frac{2\pi}{\sqrt{3}} \left(\frac{D_{n\,Silica} + D_{n\,Latex}}{D_{n\,Silica}} \right)^2$. This equation only holds for $D_{n\,Silica}/D_{n\,Latex} > 1.2$.^{27,28}



Figure 5.13 Cryo-TEM images of the final multipod-like hybrid latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of a fixed amount of silica particles with increasing particles diameters using $P[(PEOMA_{950})_{12}$ -*co*-S₁]-SG1 as macroinitiator (2.4 mmol L⁻¹). (A, A1) EH04 (S3, 140 nm), (B, B1) EH05 (S4, 230 nm) and (C, C1) EH06 (S5, 440 nm). The images corresponding to 30 nm and 77 nm silica particles are shown in Figure 5.9 and Figure 5.12, respectively.



Figure 5.14 Cryo-SEM image of the raspberry-like composite particles synthesized in the presence of 440 nm diameter silica particles (EH06 in Table 2).

1.3.3 Effect of pH

1.3.3.1 Kinetics

We have shown in Chapter 4 that the pH and ionic strength had great effects on the kinetics of emulsion polymerizations initiated by PEOMA-based macroalkoxyamines. In this section, the 140 nm silica particles (S3, Table 1) were used to investigate the effect of pH (and indirectly ionic strength) on kinetics. It should be noted here that the natural pH of the silica suspension (50 g L^{-1}) containing Ma2 (2.4 mmol L^{-1}) was approximately 8.0. The pH was decreased from 7.7 (experiment EH09) to 6.7 (experiment EH08), then to 5.8 (experiment EH04) and finally to 2.2 (experiment EH07) through the addition of hydrochloric acid which was accompanied by an increase of ionic strength. Consequently, as shown in Figure 5.15, the polymerization rate followed the expected trend and decreased with decreasing pH value (i.e. with increasing ionic strength). As pH and ionic strength evolve oppositely, the curves overlapped for EH07 and EH04.



Figure 5.15 Evolution of monomer conversion with time for the surfactant-free emulsion polymerizations of BMA and S in the presence of 140 nm diameter silica particles (S3, Table 1, [Silica] = 50 g L⁻¹) for different pH values: EH07 (pH = 2.2, \checkmark), EH04 (pH = 5.8, \blacksquare), EH08 (pH = 6.7, •) and EH09 (pH = 7.7, \blacktriangle).

1.3.3.2 Particle morphology

Before describing the effect of pH on composite particle morphology, it is worth showing again the morphologies of the pure latex particles under similar pH conditions. Figure 5.16 provides a recap of the self-assembled morphologies obtained in the absence of silica particles as a function of the pH. As discussed in Chapter 4, the morphology evolved from spheres, to vesicles and finally to fibers when the pH increased from 4.2 to 6.7. Actually, the PISA process always led to a mixture of morphologies, and spheres could sometimes be observed together with fibers or vesicles. We report in the following the hybrid morphologies observed when the self-assembly process was carried out in the presence of silica particles for different pH values. In addition to the 140 nm silica particles previously described in the kinetics experiments, we also imaged the composite latexes obtained for smaller (S1, 30 nm) and larger (S4, 230 nm) silica particles sizes at pH = 8.0 and 8.2, respectively (EH11 and EH10 in Table 2).



Figure 5.16 Recap of the typical morphologies of the final P(PEOMA₉₅₀-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion polymerization of BMA and S for increasing pH values. (E2, pH = 4.2; E8, pH = 6.0 and E9, pH = 6.7 in Chapter 4).

Low pH values (pH = 2.2 and 5.8): daisy-like hybrids

Figure 5.17 shows cryo-TEM images of the hybrid particles synthesized at low pH(pH = 2.2)and 5.8, respectively). As described before, daisy-like hybrids are observed under such pH conditions. Although the ionic strength increased with decreasing pH, surprisingly, this had no significant effect on the morphology, although the ionic strength had a strong influence in the absence of silica (Figure 4.18 in Chapter 4). This corroborates well with the kinetics results and suggests that the adsorption of the macroinitiator on the silica surface has some influence on the evolution of the particle morphology. Indeed, in the presence of silica, multipod-like particles are likely formed in the early steps of the PISA process (i.e. at very low monomer conversions). The self-assembled latexes could aggregate together to form new assemblies such as vesicles, fibers or jellyfish like particles at higher monomer conversion as reported in the literature for RAFT or NMP, and as shown in Chapter 4 in the absence of silica for high ionic strengths. However, macroinitiator adsorption on the silica surface may stabilize the assembly and retard the onset at which such morphology transition would occur. Furthermore, although we do not have any experimental evidence for that, the adsorbed amount should increase with decreasing pH as the silanol groups density increases, which should promote adsorption. This may contribute to decreasing molecular mobility at the silica polymer interface, which would further stabilize the assembled block copolymers.



Figure 5.17 Cryo-TEM images of silica/polymer composite particles obtained by surfactantfree emulsion polymerization of BMA and S in the presence of the 140 nm diameter silica particles (S3, Table 1, [Silica] = 50 g L⁻¹) for different pH values. (A) EH07, pH = 2.2, (B) EH04, pH = 5.8.

Intermediate pH values (pH = 6.7): snowman-like hybrid vesicles

Figure 5.18 shows the cryo-TEM images of the hybrid particles synthesized in the presence of 140 nm silica particles at pH = 6.7. Snowman particles and snowman-like vesicles constitute the primary morphologies at this pH. The vesicular morphology likely originates from the fusion of the polymer nodules into short worms, which evolved into longer worms and finally vesicles upon increasing monomer to polymer conversions. Again, such vesicular morphologies were previously observed at lower pH values in the absence of silica. It is worth mentioning here again that, in the presence of silica, higher pH values correspond to lower ionic strengths (as there is less HCl added), which should promote the formation of spherical morphologies. However, as mentioned above, macroinitiator adsorption depends on pH, and decreases with increasing pH. Decreasing adsorption may allow the system to evolve in a similar way as in the absence of silica resulting in similar morphologies. Besides, in the presence of silica, the ionic strength is likely high enough to account for the observed morphology transition upon increasing pH value. The system is obviously very complex, and discussing further the impact of ionic strength and silica particles on the mechanism leading to the observed morphologies would be very risky.



Figure 5.18 Cryo-TEM images of snowman-like silica/polymer vesicles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the 140 nm diameter silica particles (S3, Table 1, [Silica] = 50 g L⁻¹) at pH = 6.7 (EH08).

High pH values (pH = 7.7 and 8.2): core-shell particles and other intermediate morphologies

As shown in Figure 5.16, linear worm-like micelles and vesicles were the main morphologies obtained at pH = 6.0 and 6.7 in the absence of silica. As described in the literature,²⁹ polymer worms originate from the gradual evolution of spheres into dimers and trimers that evolve further to linear fibers and vesicles. Intermediate morphologies like octopi or jellyfish structures can also be visualized under some specific conditions. The jellyfish structure was shown to be the final stage prior to vesicles formation. The jellyfish "tentacles" undergo fusion to form predominantly a vesicular phase, but some vesicles may remain interconnected via residual "tentacles". As stated above for pH = 6.7, Figure 5.19 shows that a similar phase rearrangement can also take place at the silica surface resulting in various hybrid morphologies. Fusion of the polymer nodules formed at the silica surface result in three intrinsically different morphologies at pH 7.7 with 140 nm silica (EH09): i) "perfect" coreshell particles (pointed to by yellow arrows in Figure 5.19 B and B1), ii) half-capped particles (red arrow in Figure 5.19 A1 and B1) and iii) janus vesicles (green arrow in Figure 5.19 A1). Interestingly, the thickness of the polymer bilayer is almost the same in all directions whatever the morphology which supports the assumption that the observed self-assembled structures originate from the fusion of the polymer nodules formed in the early stages of the polymerization. It is also worth emphasizing that under given conditions (EH09), some

tentacles wrapped around the silica spheres to form hybrid particles with a "tadpole"-like morphology characterized by silica particles connected to a tentacle or vesicle tail originating from incomplete worm and/or bilayer fusion (black arrow in Figure 5.19 A). At pH = 8.2, where the interaction between the macroinitiator and the silica surface is expected to be low, "perfect" core-shell composite particles are predominantly formed in the presence of 230 nm silica particles (Figure 5.19 B and B1). It is worth reminding that these experimental conditions mainly led to polymer fibers in the absence of silica whose presence can also be identified on the TEM images of the composite particles.



Figure 5.19 Cryo-TEM images of silica/polymer composites particles obtained by surfactantfree emulsion polymerization of BMA and S in the presence of silica particles for high pH values. (A, A1) EH09, pH = 7.7 (D_n silica = 140 nm, [Silica] = 50 g L⁻¹), (B, B1) EH10, pH = 8.2 (D_n silica = 230 nm, [Silica] = 50 g L⁻¹).

High pH values (pH = 8.1): centipede-like hybrids

Another interesting morphology was observed with 30 nm silica particles at pH = 8.1 (EH11). As shown in Figure 5.20, centipede-like hybrid particles consisting of polymer fibers surrounded by silica particles were formed in this case. In addition, spherical polymer particles were also adsorbed on the external part of the silica particles in contact with water. It is also worth noting the presence of silica-decorated vesicles in the same sample, indicating significant affinity of the growing polymer chains for the silica particles. Again, the silica particles are most of the time surrounded by one or two spherical latex particles located on the external side of the composite vesicles in contact with water. As vesicles and worms are formed by the fusion of spherical latex particles formed at low conversions, some of the spherical polymer particles may have escaped the fusion process and left aside during the sphere-to-worm and worm-to-vesicle transitions resulting in two-scale hybrid morphologies.





Figure 5.20 Cryo-TEM images of silica/polymer composite latex particles (entry EH11 in Table 2) obtained by surfactant-free emulsion polymerization of BMA and S in the presence of the 30 nm diameter silica particles (S1, Table 1, [Silica] = 25 g L⁻¹). (A, A1) Silica-decorated worm-like micelles and (B) silica-decorated vesicles.

1.3.3.3 Cryo-electron tomography (cryo-ET) analyses

Cryo-electron tomography (cryo-ET) is a leading method for 3D imaging of single objects. This technique involves the acquisition of a series of cryo-TEM images under different tilt angles and the subsequent computer-assisted reconstruction of the original 3D volume. In materials science, this approach was promoted by the studies of mesoporous materials,³⁰⁻³³ nanocomposite particles,³⁴ carbon nanotubes,³⁵ dispersions of silica particles in natural rubber,³⁶ and self-assembled aggregates.³⁷

In order to gain a deeper insight into the structure of the polymer/silica hybrid particles described above, especially those with a core-shell morphology, sample EH09 (Silica S3, 140 nm, pH = 7.7) was observed with the cryo-ET technique. These experiments were performed at the CBMN (Chimie et Biologie des Membranes et des Nanoobjets, UMR 5248, Bordeaux) by Jean-Christophe Taveau and Olivier Lambert (see experimental section for details).

Sample EH09 was first observed by cryo-TEM. The brush-like surface of the latex can be clearly observed in Figure 5.21 (red arrows).



Figure 5.21 Typical cryo-TEM images of silica/polymer composite latex particles (entry EH09, Table 2) obtained by surfactant-free emulsion polymerization of BMA and S in the presence of 140 nm diameter silica particles at pH = 7.7 (S3, Table 1, [Silica] = 50 g L⁻¹). Courtesy of Jean-Christophe Taveau and Olivier Lambert (CBMN, UMR 5248, Bordeaux).

A rough estimation of the shell thickness gives a brush layer of around 10 nm. As mentioned above, a separation distance (pointed by the orange arrow) is also clearly visible at the polymer/silica interface. Compared with the length of the brushes (around 10 nm), this distance is much smaller (around 3.5 nm) in agreement with the conformation of the adsorbed polymer chains.

To elucidate the accurate structure of the "perfect" core/shell particles obtained in experiment EH09, the particles in the red square (in Figure 5.22A) were selected to perform cryo-ET. Analysis of the x-y cross sections (Figure 5.22B) shows that the silica particles (dark in the images) are fully covered by polymer (grey in the images). The z slices of the reconstruction also show the brush-like surface (red arrow in Figure 5.22C) of the polymer and the interfacial layer (orange arrow in Figure 5.22C) between silica and the polymer particles.



Figure 5.22 Cryo-ET analysis of "perfect" core-shell hybrid particles (EH09). (A) Cryo-TEM image showing the nano-object that has been selected for the reconstruction map. (B) Map of z slices showing different cross-sections of a 3D volume reconstructed from a tomographic series recorded from the particle in red square in image A. (C) Selected image of the red square in image B.

The composite particle with a "tadpole" morphology (purple rectangle in Figure 5.23A, particle No. 1) was also analyzed by cryo-ET. Inspection of the reconstruction volume of the "tadpole"-like particle in the purple rectangle reveals that the silica particle (particle No.1, Figure 5.23B) is fully encapsulated by polymer (grey in the images). To gain further insight into particle morphology, segmentation was used to generate graphical representations that remarkably demonstrate the 3D structure of the particles (Figure 5.23C), which was not straightforward from the x-y cross sections of the 3D volume only (Figure 5.23B). The visualization of the segmented volume was observed from three directions (Figure 5.23C). The structure of the protruding tentacle (green arrows) connecting the encapsulated silica with the nascent bilayer vesicle (red arrows) and the brush-like surface (orange arrows) of the polymer can be clearly seen in these 3D images.

This cryo-ET analysis also remarkably shows the wrapping-up of the octopus tentacles to form the jellyfish that will evolve further into a vesicle. Such a transient morphology is difficult to be confirmed with cryo-TEM only. This highlights the benefits and the necessity of advanced techniques like cryo-ET for more accurate characterization of particles with complex shapes as the ones elaborated in this work (Figure 5.23A).

Finally, although this was not the predominant morphology at high pH values, the snowmanlike composite particles were also characterized by cryo-ET. Figure 5.24 shows a series of cryo-TEM images at different tilt angles. Surprisingly, the polymer particle (pointed to by red arrows) does not appear spherical but as an elongated sphere. However, this comment results from the observation of one single hybrid particle selected from only one sample, and obviously cannot be extrapolated to any snowman particles formed in the presence of our PEO-based macroalkoxyamines. Further analyses should be undertaken to confirm the aboveunexpected result.





Figure 5.24 Morphology of the snowman-like composite particle (EH09) observed by cryo-TEM. (A) Cryo-TEM image. (B) Gallery of the selected particle observed at different tilt angles.

1.3.4 γ-MPS functionalized silica particles

Our aim in this section was to encapsulate silica particles into polymer fibers. As nonfunctionalized silica particles only led to silica-decorated fibers and/or vesicles, the silica surface was functionalized by γ -methacryloxypropyl trimethoxysilane (γ -MPS) in order to promote encapsulation.

The grafting was performed as reported in the experimental section using the 30 nm silica particles (S1, Table 1). The grafted amount was calculated from the weight loss of γ -MPS determined by TGA using equation (5.2) (Figure 5.25). We found a grafting density of 4.2 μ mol m⁻², whose value is of the same order of magnitude than the highest values previously reported for similar grafting reactions.³⁷



Figure 5.25 TGA results of non-functionalized and γ -MPS functionalized silica particles (D_n SiO₂ = 30 nm, S1 in Table 1).

An experiment (EH13 in Table 2) was first carried out in the presence of the γ -MPS-functionalized silica particles at pH = 8.1 which should favour the formation of worm-like particles (Figure 4.14, Chapter 4). However, as shown in Figure 5.26 A and A1, polymer-encapsulated silica particles with spherical core/shell or muti-core/shell morphologies were mainly observed under these conditions. Similar morphologies were obtained at lower pH (Figure 5.26 B and B1, EH12, pH = 5.2). On close inspection of Figure 5.26 A, a few polymer fibers could also be occasionally seen but these fibers did not contain any silica particles.

One possible explanation for the observed spherical "core/shell" morphology of the composite particles is the formation of covalent bonds between the silica particles and the growing polymer chains, which would decrease the mobility of the self-assembled block copolymers and would consequently prevent them from fusing to generate elongated morphologies and/or vesicles. The silica particles would somehow play the role of a crosslinker in the system.



Figure 5.26 Cryo-TEM images of polymer-encapsulated silica particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of γ -MPS-functionalized silida particles (S1*, $D_n = 30$ nm, Table 1) using Ma2 as macroinitiator (Table 2) at different pH values. (A, A1) pH = 8.1 (EH13) and (B, B1) pH = 5.2 (EH12).

1.3.5 Conclusions

In summary, we have investigated the self-assembly behavior of P(PEOMA-*co*-S)-*b*-P(BMA*co*-S) brush-like block copolymers at the surface of silica particles. PEO-based macroalkoxyamines were previously adsorbed at the silica surface and used to initiate the growth of the hydrophobic block through aqueous NMP emulsion polymerization. The polymerization was however poorly controlled (high molar mass dispersities) although the shift of the SEC traces indicated successful formation of block copolymers. Cryo-TEM and cryo-electron tomography techniques were employed to assess with more accuracy the structure of the composite particles. As summarized in Figure 5.27, composite particles with

snowman, raspberry, daisy-shaped, "perfect" core/shell, snowman-like vesicles, "tadpole" and "centipede"-like morphologies were successfully achieved depending on the silica particle size and the suspension pH. To the best of our knowledge, this is the first report on the synthesis of composite particles by NMP-mediated aqueous emulsion polymerization.

The experimental results seem to indicate that the presence of silica strongly impacts the composite particle morphologies at low pH values and their evolution, by impacting both the amount of macroinitiator adsorbed (which depends on the pH) and by participating to the stabilization. At high pH values, the effect of silica on the self-assembled morphologies seems to be less pronounced as the morphology evolved as expected according to the results obtained in the absence of silica under similar conditions. However, further systematic studies on the separate effect of pH and ionic strength on the adsorption isotherms and the resulting nanostructures are needed to give a clear picture of the mechanisms leading to the formation of the various morphologies and draw firm conclusions.



Figure 5.27 Morphology map for the PISA process performed in the presence of silica particles with adsorbed P(PEOMA-*co*-S)-SG1 brush-like macroalkoxyamine initiators.

2. Polymerization-induced self-assembly of P[(PEOMA₃₀₀)₃₄-*co*-MAA_{6.7}-*co*-S_{7.2}]-*b*-P(BMA-*co*-S) block copolymers in the presence of silica particles

The aim of this section was to tune the silica/polymer interfacial properties by changing the nature of the macroalkoxyamine initiator. Indeed, by choosing a macroalkoxyamine with a cloud point lower than the reaction temperature (85 °C), we expect the hydrophilicity of the macroalkoxyamine to be reduced and thus bring more hydrophobicity to the silica surface, which may favor the polymerization of the hydrophobic monomers and influence particle morphology.

The P[(PEOMA₃₀₀)₃₆-*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 macroalkoxyamine (Ma4 in Chapter 3, cloud point = 59 °C) with short PEO side chains was selected for this study.

2.1 Experimental procedure

The experimental procedure is the same as the one depicted for the emulsion polymerizations performed with Ma2 in the presence of silica particles (section 1.1). The commercial Klebosol silica sol (S2, $D_n = 77$ nm, Table 1) was used as the silica source. A 1M NaOH standard solution was used to adjust the pH value. The experimental conditions and the main characteristics of the composite particles are given in Table 6. The characterization techniques are the same as the ones depicted in section 1.1.

2.2 Kinetic analysis

Figure 5.28 shows the evolution of monomer conversion with time for different pH values in the presence of 77 nm silica particles (S2 in Table 1). It is seen that the polymerization rate is almost the same. Compared to the blank emulsion polymerization without silica (Figure 4.27, Chapter 4), the polymerization rate is lower which may be due to the increase of ionic strength imparted by the use of the silica sol.



Figure 5.28 Evolution of monomer conversion with time during the surfactant-free emulsion polymerization of BMA and S in the presence of 77 nm silica using $P[(PEOMA_{300})_{34}$ -*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 as macroinitiator (5.2 mmol L⁻¹) for increasing pH values. EMPS01 (pH = 6.0, **■**), EMPS02 (pH = 7.5, **▲**) and EMPS03 (pH = 9.0, **●**).

Figure 5.29 shows the SEC traces of Ma4 and of the final samples (after getting rid of the silica particles) for the different pH values. The nice shift of the SEC peaks indicates a better control of the livingness than those with Ma2 macroalkoxyamine, with still, however, the presence of unreacted Ma4 chains.



Figure 5.29 Evolution of the size exclusion chromatograms with weight conversion for the surfactant-free emulsion polymerization of BMA and S in the presence of 77 nm silica particles using $P[(PEOMA_{300})_{34}$ -*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 as macroinitiator (Ma4, 5.2 mmol L⁻¹) for different pH values.

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Table 6 Experimental conditions and characteristics of the multipod-like silica/polymer latex particles synthesized by surfactant-free emulsion polymerization of n-butyl methacrylate and styrene using the SG1-capped P[(PEOMA₃₀₀)₃₆-co-MAA_{6.7}-co-S_{7.2}]-SG1 copolymer as macroinitiator (Ma4) in the presence of 77 nm silica particles (S2) for different pH values.^a

 $^{b}M_{n} = 11700$ g mol⁻¹, $M_{w}/M_{n} = 1.4$, 15 mol% MAA. ^c Determined by TEM (see Table 1). ^d Initial pH determined before polymerization. ^e Theoretical molar mass at 100% conversion determined according to: Target $M_{\rm n}({\rm g\,mol}^{-1}) = M_{\rm m}{}^{alkoxyamine} + \left(\frac{initial\,mas\,of\,monomer}{mass\,of\,alkoxyamine}\right) \times M_{\rm m}{}^{alkoxyamine}$. F Determined by ^a All polymerizations were carried out at 85 °C for 6 h. The total monomer concentration was 20 wt% and the initial molar fraction of styrene was $f_{s0} = 0.08$. gravimetric analysis. ² Determined by SEC in THF with PMMA standards.

2.3 Particle morphology

Before describing the effect of pH on composite particle morphology, it is worth showing again the morphologies of the pure latex particles under similar pH conditions. Figure 5.30 shows the blank emulsion polymerizations performed with Ma4 (Chapter 4, section 3.4). The increase in the hydrophilicity of the P(PEOMA₃₀₀-*co*-MAA-*co*-S) block with increasing pH accounts for the observed morphological evolution from mainly vesicles, vesicles and fibers to mainly spheres.



Figure 5.30 Cryo-TEM images of the P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) latex particles obtained by surfactant-free emulsion using P[(PEOMA₃₀₀)₃₄-*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 as macroinitiator (Ma4, 5.2 mmol L⁻¹) in the absence of silica for different pH values (E23, E14 and 24 in Chapter 4).

The final composite particles obtained for different pH values were observed by cryo-TEM (Figure 5.31). The latex morphology evolved from vesicles/fibers to vesicles/rods/spheres and then mainly spheres with elongated spheres (or short rods) upon increasing pH. These results corroborate well with those obtained in the absence of silica.

All composite particles have a multipod-like structure independently of experimental conditions (Figure 5.31). The number of polymer particles adsorbed on the silica surface increases with increasing pH. As shown in Figure 5.31A and A1 for composite particles formed at pH = 6.0, the silica beads (red circles) have one or two polymer nodules on their surface. Free silica particles are also present. At pH = 7.5 (Figure 5.31B, B1), two or three polymer nodules can be found on one silica particle, and there is no free silica. Fused latex

particles and short adjacent rods can also be occasionally seen close to the silica spheres. Figure 5.31C, C1 show that more polymer nodules are present on the silica surface at pH = 9.0. A very interesting and unusual morphology can be observed in this case. Some silica particles are surrounded by elongated particles or short rods (black arrows), forming a star-like structure (yellow circles). In addition, it is worth noting the presence of a significant amount of free polymer particles at pH = 7.5 and 9, which may attributed to the high amount of free macroinitiator in the water phase likely due to poor affinity of the MAA-based macroalkoxyamine for the silica surface under high pH conditions.

Unexpectedly, the interaction seems to be even lower at lower pH as evidenced by the presence of free silica particles. If one considers that protonated MAA units are still present at pH = 6.0, the formed carboxylic acid/ethylene oxide complex between MAA units and PEO side chain^{38,39} could compete with the formation of hydrogen bonds between PEO and the silanol groups of silica. This competition may disappear at high pH when the carboxylic acid groups are fully ionized which can explain why more polymer particles are adsorbed on the silica surface at pH = 9.0. Compared with the composite particles obtained for PEOMA₉₅₀-based macroalkoxyamines, the combination of the polymer and silica particles seems in any case weaker for the P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine.

Conclusions

Silica-P(PEOMA₉₅₀-*co*-S₁)-*b*-poly(BMA-*co*-S) composite particles were synthesized through NMP-mediated surfactant-free emulsion polymerization using a well-defined PEOMA₉₅₀-based macroalkoxyamine. A rich variety of morphologies like snowman, raspberry, daisy-shaped, "perfect" core/shell, Janus vesicles, "tadpole"- and "centipede"-like, was achieved by varying the silica particle size and/or the pH value. In each case, the obtained morphologies result from the polymerization-induced self-assembly of the block copolymers at the silica surface. The poly(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine with short PEO side chains was then investigated. By decreasing the LCST of the macroalkoxyamine initiator, we expected to promote better interactions of the growing polymer chains with the silica surface and favor encapsulation. However, unfortunately, this did not lead to the expected result. We suspect that the incorporation of MAA units in the copolymer drastically affected macroinitiator adsorption, which is a key factor in the control of particle morphology.



Figure 5.31 Cryo-TEM images of the hybrid latex particles obtained by surfactant-free emulsion polymerization of BMA and S in the presence of 77 nm silica particles using $P[(PEOMA_{300})_{34}$ -*co*-MAA_{6.7}-*co*-S_{7.2}]-SG1 as macroinitiator (Ma4, 5.2 mmol L⁻¹) for different pH values. (A, A1) EMPS01, pH = 6.0, (B, B1) EMPS02 pH = 7.5 and (C, C1) EMPS03, pH = 9.0.

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General conclusion and perspectives

The aim of this PhD thesis was to produce polymer/silica nanocomposites via nitroxidemediated emulsion polymerization. To accomplish this aim, the project was divided into four main parts:

- 1. Synthesis of silica particles,
- 2. Synthesis of PEOMA-based macroalkoxyamines,
- Nitroxyde-mediated surfactant-free emulsion polymerization in the absence of silica particles and,
- 4. Surfactant-free emulsion polymerization in the presence of silica particles.

In the first part, the sol-gel process was used for the synthesis of silica particles of various diameters. First, the classical Stöber method was investigated using batch and semi-batch processes. Under the conditions used in our work, the Stöber method was suitable for the synthesis of silica particles with narrow size distribution in the size range from 200 nm to 500 nm. However, the broad size distribution and the aggregation between particles for high and low ammonia concentrations, prevented the application of the Stöber process to the synthesis of large particles (> 700 nm) and small nanoparticles (< 100 nm). Therefore, the amino acid catalysis process was studied for the synthesis of small silica nanoparticles, with a size typically lower than 100 nm. This novel process showed significant advantages for the synthesis of small spherical silica nanoparticles due to the slow hydrolysis rate of TEOS in this system. However, the fairly long reaction time due to a very slow growth process was an obvious drawback of the L-arginine process. To avoid this drawback, the regrowth of silica seeds in ethanol/water mixture was investigated to get silica particles ranging from 100 to 200 nm. The regrowth of 30 nm silica seed was carried out via a Stöber-like process with either ammonia or L-arginine as catalysts. Under the conditions studied in our work, a regrown silica ($D_n = 136 \text{ nm}$) with a narrow size distribution was achieved when ammonia was used as the catalyst. However, the regrowth method with L-arginine as the catalyst was unable to form spherical silica nanoparticles in most of the cases except for high silica seeds fraction or for low TEOS concentrations. The addition of ethanol in the original aqueous silica sol was detrimental to the colloidal stability and led to assembly or aggregation of the particles. We expect to improve our results in further works, by varying in particular the ratio of ethanol and water or the reaction temperature.

In addition, the L-arginine process and a multi-step extension process were investigated to synthesize hybrid silica particles and core/shell hybrids with TEOS and γ -MPS as silicate sources. After removal of the methacryloxy chains of the γ -MPS, which also act as a pore template in the hybrids, mesoporous silica particles with pore sizes of around 2 nm and hollow core-porous shell silica particles were successfully obtained. This new process could be potentially extended in a future work to organosilane molecules of higher chain lenghts in order to tune the porous properties of the resulting hybrid particles.

In the second part, well-defined water-soluble brush-type copolymers mainly composed of PEOMA units with PEO side groups of various chain lengths ($M_n = 300$ and 950 g mol⁻¹) or of PEOMA₃₀₀ with MAA units were synthesized by nitroxide-mediated polymerization using a low molar mass unimolecular alkoxyamine initiator (so called BlocBuilder®) and SG1 nitroxide in the presence of a small amount of styrene. The resulting SG1-capped macroalkoxyamines possessed the predicted molar masses based on the monomer/initiator molar ratio and narrow molar mass distributions. As expected, the cloud point of P(PEOMAco-S)-SG1 macroinitiators increased with increasing hydrophilicity and could be tuned by varying the PEO chain length or the copolymer composition. The cloud point was also influenced by ionic strength and suspension pH although to a much lesser extent. The cloud point decreased with increasing salt concentrations or suspension pH due to hydrogen bonds disruption. P(PEOMA₃₀₀-co-MAA-co-S)-SG1 macroalkoxyamine initiators exhibited both thermo- and pH- responsive behaviors. As a consequence, their LCST could be finely tuned from 20 to 80 °C by varying the MAA content or the suspension pH. Unexpectedly, the LCST of the copolymers decreased with increasing MAA content below the pKa likely due to intramolecular H-bonding interactions resulting in decreased solubility, while as expected it increased above the pKa.

Before investigating emulsion polymerization in the presence of silica particles, the behavior of the P(PEOMA-*co*-S)-SG1 macroalkoxyamines in the aqueous nitroxide-mediated emulsion polymerization of *n*-butyl methacrylate and styrene under low temperature conditions was studied. Despite the presence of a small proportion of dead chains indicating the occurrence of irreversible termination reactions, molar masses evolved linearly with conversion as expected for controlled radical polymerization. Sterically stabilized self-assembled diblock copolymer particles with film-forming properties were obtained in situ upon chain extension of the P(PEOMA₉₅₀-*co*-S) hydrophilic block, consistent with a PISA process. While spherical latex particles were obtained at pH = 4.2 regardless of the molar mass of the hydrophobic block

over the entire range studied, vesicles and elongated particles were obtained at pH = 6.0 and 6.7. As an increase of pH should not directly affect the properties of PEO in water, these results suggest a salting out effect produced by the increase of ionic strength that accompanies the change of pH as attested by turbidimetry measurements. This provides an unprecedented way to control the morphology of self-assembled diblock copolymers obtained through nitroxide-mediated polymerization independently of the degree of polymerization of each block.

The effect of pH on particle morphology was further studied by investigating the dual pH/temperature response of P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 macroalkoxyamine initiators. Changing the pH value allowed controlling the cloud point temperature of this series of macroalkoxyamines and hence tuning the final morphologies (spherical micelles, nanofibers and vesicles). Stable amphiphilic P(PEOMA₃₀₀-*co*-MAA-*co*-S)-*b*-P(BMA-*co*-S) diblock copolymers were formed and self-assembled during the emulsion polymerization even for reaction temperatures exceeding the cloud point of the macroalkoxyamine initiator. This result is suprising and further work would no doubt be necessary to fully understand the mechanisms operating during the polymerization, in particular during the nucleation step.

The morphologies of the latex particles were dependent on the MAA fractions in the macroalkoxyamines, but even more on the pH, which enables changing the hydrophilicity of the macroalkoxyamine, and on the initial concentration of the macroalkoxyamines, which leads to varying molar mass ratio of the hydrophilic and hydrophobic blocks in the copolymer.

Several silica particles with different sizes (30 nm, 77 nm, 140 nm, 230 nm and 440 nm) were finally modified by the adsorption of PEO-based macroalkoxyamines via hydrogen bond interactions between PEO and the silanol groups, and subsequently used in BMA/styrene emulsion polymerization. The aim was the formation of block copolymers generated *in situ* on the silica surface to form silica/polymer hybrid particles. Depending on the silica particle diameter and on the pH value, composite particles with snowman, raspberry, daisy, "perfect" core/shell, snowman-like vesicles, "tadpole"- and "centipede"- like morphologies were successfully achieved through NMP emulsion polymerization using P[(PEOMA₉₅₀)₁₂-*co*-S₁]-SG1 as macroalkoxyamine. To the best of our knowledge, this is the first work reporting the synthesis of composite particles with such morphologies through a "growth through" approach via NMP emulsion polymerization. The cryo-ET technique was employed to analyze the accurate structure of the composite latexes. The reason for the poor living control

of the chain growth was considered to be the high ionic strength (introduced by the silica sol and the salt generated by adjusting the pH) which was also a parameter of great importance for the self-assembly of the block copolymers. However, the particle morphology evolved in an unexpected direction based on the later parameter indicating that the silica particles also have some influence on the self-assembly process. We suggest that they participate to the stabilization of the self-assembled block copolymers by means of the adsorbed hydrophilic block and their surface charges, which both strongly depends on pH. However, this is clearly a complex system and further systematic studies on the separate effect of pH and ionic strength on the adsorption isotherms and the resulting nanostructures would have to be carried out in order to give a clear picture of the mechanisms leading to the formation of the various morphologies.

P(PEOMA₃₀₀-*co*-MAA-*co*-S)-SG1 was further investigated to enhance the hydrophobic character of the macroalkoxyamine initiator. Indeed, the later display a cloud point temperature (51 °C) well below the reaction temperature (85 °C). However, compared with the composite particles obtained with the PEOMA₉₅₀-based macroalkoxyamine, the combination of the polymer and silica particles seems weaker in this case resulting in a higher proportion of pure silica beads and/or free latex particles. This may be due to inter- or intramolecular complexations between MAA and PEO at low pH and to charge repulsions at larger pH, which would both contribute to decrease macroinitiator adsorption. Such low adsorption would counterbalance the expected hydrophobic effect. However, further work should be pursued to study the adsorption behavior of this series of macroalkoxyamine initiators in order to gain a better understanding and a clearer picture of the underlaying mechanism.

The results obtained in the frame of this PhD thesis also opened up new perspectives in the field of NMP-mediated emulsion polymerization and hybrid latexes. In particular, future work could be focused on the synthesis of new PEOMA-based macroinitiators incorporating functional comonomers which could enhance macroalkoxyamine adsorption on the silica surface and strenghen interfacial interaction like for instance 4-vinylpyridine. The incorporation of hydrophobic units into the PEO₉₅₀-based copolymers (such as BMA or MMA) could also be envisaged. Indeed such copolymers may promote silica encapsulation as was previously reported in the literature for RAFT-mediated polymerizations performed in the presence of inorganic particles.