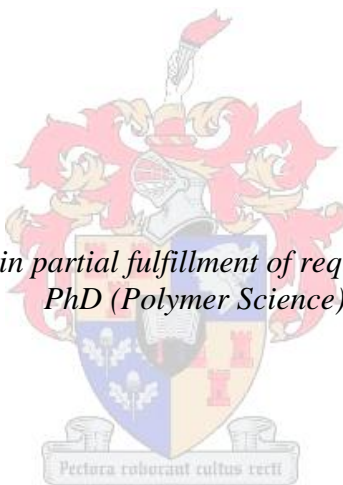# Alternating Hetero-Arm Copolymer Molecular Brushes as Scaffolds for Inorganic Nano-Wires

Dissertation presented in partial fulfillment of requirements for the degree of PhD (Polymer Science)

by

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Declaration

By submitting this dissertation electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

Waled Ajili Hadasha   Stellenbosch, **December 2012**

Abstract:

This study describes the synthesis and self-assembly of hetero-arm molecular brushes (hetero-arm MBs). These MBs consist of two polymeric side chains (SCs) of different natures, alternatingly distributed along the main chain (backbone). Two different types of hetero-arm MBs were prepared: first, **alternating amphiphlic hetero-arm MBs (AMBs)**, and second, **alternating hetero-arm MBs (AHMBs)**. **Hetero-arm AMBs** were synthesized via two strategies: (I) via a combination of "grafting through" and "grafting onto", and (II) via "grafting through".

In approach (I), poly[vinyl benzyl (polyethylene glycol)-*alt*-*N*-alkyl-maleimide)] (poly[VB-(PEG$_{12}$)-*alt*-*N*-(C$_n$H$_{2n+1}$)-MI]) was prepared via radical copolymerization of vinyl benzyl-terminated polyethylene glycol (VB-PEG$_{12}$) with maleic anhydride (MAnh) (grafting through), which produces graft copolymers with PEG SCs and reactive succinic anhydride repeat units alternatingly distributed along the backbone. These graft copolymers were then modified by nucleophilic substitution (imidization) with alkyl amines (C$_n$H$_{2n+1}$-NH$_2$) on the succinic anhydride residues (grafting onto). Three different primary amines possessing different alkyl chain lengths (n = 4, 12 and 16) were used in the modification process. In this way, hetero-arm AMBs with different hydrophilic to hydrophobic ratios were obtained.

In approach (II), similar hetero-arm AMBs were prepared in a one-step grafting through approach. In this case, poly[VB-(PEG$_{17}$)-*alt*-*N*-(C$_n$H$_{2n+1}$)-MI] (n = 10, 16 and 20) was prepared via radical copolymerization of VB-PEG$_{17}$ with *N*-dodecylmaleimide, *N*-hexadecylmaleimide and *N*-icosylmaleimide. Following the synthesis step, self-assembly of these hetero-arm AMBs in arm-selective solvents was investigated in relation to the alkyl chain length. The morphology of the obtained assemblies was characterized by Field Emission gun-Scanning Electron Microscopy (FE-SEM), Transmission Electron Microscopy (TEM) and Fluorescence Microscopy (a fluorescent dye was encapsulated). Cylindrical-like aggregates, length 10 µm and diameter ~ 250 nm, were obtained upon hetero-arm AMBs self-assembly.

The second type of hetero-arm MBs was **hetero-arm AHMBs,** in which the SCs consist of PEG and poly(*N*,*N*-dimethylamino-ethyl methacrylate) (PDMAEMA). These hetero-arm AHMBs

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were prepared via a combination of grafting through and grafting from approaches. In this case, poly[vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(poly(*N*,*N*-dimethylamino-ethyl methacrylate) maleimide] (poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI) was prepared in the following steps: (1) alternating poly[vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(4-hydroxyphenyl) maleimide] (poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI]) was synthesized via radical copolymerization of VB-PEG$_{17}$ with *N*-(4-hydroxyphenyl) maleimide (*N*-HPhMI). (grafting through), (2) the hydroxyl sites were esterified with 2-bromoisobutyryl bromide to afford poly [vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(4-(2-bromobutyryloxy)phenyl) maleimide] (poly[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI]) (macroinitiator) and (3) an atom transfer radical polymerization (ATRP) reaction of 2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMAEMA) was initiated from the obtained macroinitiator. This approach afforded poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] hetero-arm AHMBs with two water soluble SCs; however, one is water soluble at all pHs and temperatures (*i.e.* PEG), while the other is a pH- and temperature-sensitive polymer (*i.e.* PDMAEMA).

Initial attempts were made to fabricate cylindrical organo/silica hybrid materials based on these AMHBs as the organic template and *tetra*-ethylorthosilicate as the silica precursor. Preliminary results indicate the formation of silica nano-wires, ~ 8 µm in length and ~45 nm in diameter. The self-assembly behavior of these AHMBs in water at a temperature above the lower critical solution temperature of PDMAEMA (> 55 °C) was also investigated. Fibril morphology (~ 30 nm in diameter) was observed.

This study addresses initial attempts to fabricate organic/inorganic hybrid materials with controlled size and morphologies via densely grafted hetero-arm molecular brushes.

Opsomming

Hierdie studie beskryf die sintese en selfsamestelling van prototipe molekulêre borsels (prototipe MBs). Hierdie MBs bestaan uit twee polimeriese sykettings (SKs) van verskillende aard wat afwisselend langs die hoofketting (ruggraat) voorkom. Twee verskillende tipes van die prototipe MBs is gesintetiseer: eerstens, **afwisselende amfifiliese prototipe MBs (AMBs)**, en tweedens, **afwisselende hetero-arm prototipe MBs (AHMBs)**. Prototipe AMBs is gesintetiseer d.m.v. twee strategieë: (I) deur 'n kombinasie van 'enting deur' en 'enting aan' benaderings, en (II) deur middel van 'n 'enting deur' benadering.

In benadering (I) is poli[vinielbensiel(poliëtileenglikol)-*alt*-*N*-alkiel-maleïenamied)] (poli[VB-(PEG$_{12}$)-*alt*-*N*-(C$_n$H$_{2n+1}$)-MI]) gesintetiseer deur radikaalkopolimerisasie van vinielbensiel-beëindigde-poliëtileenglikol (VB-PEG$_{12}$) met maleïenanhidried ('enting deur') wat entkopolimere produseer met PEG SKs en reaktiewe suksienanhidried herhaaleenhede wat afwisselend langs die ruggraat versprei is. Daarna is die entkopolimere gewysig d.m.v. nukleofiliese substitusie (imiedisering) met alkielamiene (C$_n$H$_{2n+1}$-NH$_2$) op die oorblywende suksienanhidried ('enting op'). Drie verskillende primêre amiene met verskillende alkielkettinglengtes (n = 4, 12 en 16) is gebruik vir die wysigingsproses. So is prototipe AMBs met verskillende hidrofiliese tot hidrofobiese verhoudings verkry.

In benadering (II) is soortgelyke prototipe AMBs gesintetiseer in 'n een-stap 'enting deur' benadering. In hierdie geval is poli[VB-(PEG$_{17}$)-*alt*-*N*-(C$_n$H$_{2n+1}$)-MI] (n = 10, 16 en 20) gesintetiseer d.m.v. radikaalkopolimerisasie van VB-PEG$_{17}$ met N-dodesiel maleïenamied, N-heksadesiel maleïenamied en N-ikosiel maleïenamied. Na afloop van die sintese stap is die selfsamestelling van hierdie prototipe AMBs in spesifieke oplosmiddels in verhouding tot die alkielkettinglengtes ondersoek. Die morfologie van die versamelings is gekarakteriseer deur veld-emissie-geweer-(Eng: field emission gun-)-skandeerelektronmikroskopie (FE-SEM), transmissie-elektronmikroskopie (TEM) en fluoresserende mikroskopie ('n fluoresserende kleurstof is ingesluit). Silinderagtige versamelings (lengtes ~10 μm en deursnee ~250 nm) is deur die selfsamestelling van prototipe AMBs verkry.

Die tweede soort prototipe MBs is prototipe AHMB, waarin die SKs uit PEG en poli(N,N-dimetielaminoetiel metakrilaat) (PDMAEMA) bestaan. Hierdie prototipe AHMBs is d.m.v. 'n kombinasie van 'enting deur' en 'enting van' benaderings gesintetiseer. In hierdie geval is poli[vinielbensiel-(poliëtileenglikol)-*alt*-*N*-(poli(N,N-dimetielaminoetiel metakrilaat) maleïenamied] (poli[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI) gesintetiseer deur van die volgende stappe gebruik te maak: (1) sintese van afwisselende poli[vinielbensiel-(poliëtileenglikol)-*alt*-*N*-(4-hidroksifeniel) maleïenamied] (poli[VB-(PEG$_{17}$)-*alt*-*N*-(HPh) -MI) deur midel van radikaalkopolimerisasie van VB-PEG$_{17}$ met *N*-(4-hidroksifeniel) maleïenamied (*N*-HPhMI) ('enting deur'), **(2)** esterifikasie van die hidroksielgroepe met 2-bromoisobutiriel bromied om poli[vinielbensiel-(poliëtileenglikol)-*alt*-*N*-(4-(2-bromobutirieloksi) feniel) maleïenamied] (poli[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI]) (makro-afsetter) te berei, en **(3)** die atoomoordrag-radikaalpolimerisasie reaksie van 2-(N,N-dimetielamino)etiel metakrilaat (DMAEMA) wat begin is vanaf die gevormde makro-afsetter. Hierdie benadering gee poli[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] prototipe AHMBs met twee wateroplosbare SKs, waarvan een wateroplosbaar is by alle pHs en temperature (d.w.s. PEG), terwyl die ander tipe SK 'n pH- en temperatuur-sensitiewe polimeer is (d.w.s. PDMAEMA).

Aanvanklike pogings is aangewend om silindriese organo/silika hibriedmateriale te sintetiseer, gebaseer op hierdie AHMBs as die organiese segment en tetraëtielortosilikaat as die silika voorloper. Die voorlopige resultate dui op die vorming van silikananodrade, lengte ~8 μm en deursnit ~45 nm. Die selfsamestellingsgedrag van hierdie AHMBs is ook in water ondersoek by 'n temperatuur hoër as die laer kritieke oplossingstemperatuur van PDMAEMA (> 55 °C). 'n Draadagtige morfologie (deursnit ~30 nm) is waargeneem.

Hierdie studie beskryf aanvanklike pogings om organiese–anorganiese hibriedmateriale met beheerde groottes en morfologieë via dig-geënte hetero-arm molekulêre borsels te vervaardig.

In the memory of

my Mother & Brother (Mahmoud Hadasha),

to my father, brothers, sisters and all family

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Contents

List of Abbreviations

AA	Acrylic acid
AIBN	2,2'-azobisisobutyronitrile
AMBs	Alternating Hetero-Arm MBs
AHMBs	Alternating Hetero-Arm Molecular Brushes
ATRP	Atom transfer radical polymerization
Au	gold
$CDCl_3$	Deuterated chloroform
Co-Sh MBs	Core-shell Molecular Brusshes
DMAc	*N,N*-dimethylacetamide
DMF	*N,N*-Dimethylformamide
DMSO	Dimethylsulfoxide
DP	degree of polymerization
FE-SEM	Field Emission Scanning Electron Microscopy
FT-IR	Fourier transform infrared
$HAuCl_4$	Tetrachloroauric(III) acid
HEMA	2-Hydroxyethyl methacrylate
HMTETA	1,1,4,7,10,-10-hexamethyltriethylenetetramine
HEMA-TMS	2-(trimethylsilyloxy) ethyl methacrylate
LCST	lower critical soluble temperature
MAnh	Maleic anhydride
Me_6TREN	*Tris*-[2-(dimethylamino)ethyl]amine
MI	Maleimide
MBs	Molecular Brushes
Mw	Molecular weight
N-DMI	*N*-Decylmaleimide
N-HDMI	*N*-Hexadecylmaleimide
N-HPhMI	*N*-Hydroxyphenyl-Maleimide
N-IMI	*N*-Icosylmaleimide

NMP	Nitroxide mediated polymerization
NMR	Nuclear magnetic resonance
OMA	Octadecyl methacrylate
pBPEM	Poly(2-(2-bromopropionyloxy) ethyl methacrylate)
PNIPAAm	poly(N-isopropylacrylamide)
Pt-BA	Poly(t-butyl acrylate)
POEGMA	Poly(oligo(ethylene glycol) methacrylate)
mSt	α-methyl styrene
RAFT	Radical addition chain-transfer polymerization
ROMP	Ring-Opening Metathesis Polymerization
ROP	Ring-Opening polymerization
RT	Room temperature
PVPy	Poly-(4-vinyl pyridine) & Poly-(2-vinyl pyridine)
PS	Polystyrene
SEC	Size exclusion chromatography
TEA	triethyl amine
TEOS	Tetra Ethylorthosilicate
TEM	Transmission Electron Microscopy
THF	Tetrahydrofuran
TEMPO	2,2,6,6-Tetramethyl-1-piperidinyloxy free radical
VBC	Vinyl benzyl chloride

Short introduction & dissertation outline

Introduction

One of the daily phenomena we encounter is the formation of bubbles upon mixing of soap and water. Soap bubbles form as a thin layer of water entrapped between two layers of organized soap molecules (scientifically known as surfactant) as shown in Figure 1 (C), resulting in enclosing air as hollow sphere. Surfactant molecules consist of hydrophobic tail (*i.e.* dis-like water) and hydrophilic head (*i.e.* like water) (Figure 1 (A)). In water, surfactant molecules aggregate and form micelles (*i.e.* microscopic self-assemblies with the water-soluble head on the surface and insoluble-tail as the interior (Figure 1 (B)) in a similar way membranes of living cells are formed. The membranes of living cells are formed by the aggregation (scientifically called "self-assembly") of a special surfactant molecule known as phospholipid. Usually the aggregation (self-assembly) of surfactant molecules results in micelles with spherical morphologies, however other morphologies, like cylindrical micelles and vesicles, among others can also be formed. Such process *i.e.* self-assembly, of surfactant molecules has inspired scientists to investigate other type of natural and synthetic macromolecules of a similar nature (*i.e.* hydrophilic/hydrophobic structure).[1, 2]
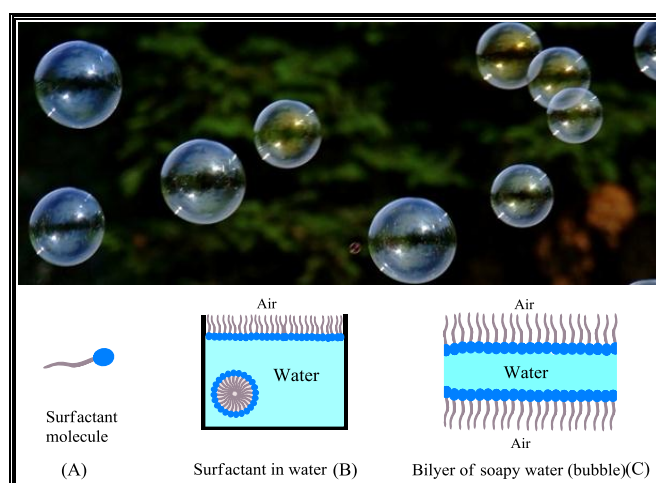
Figure 1: Schematic illustration of surfactant molecule in different mediums

In the last two decades or so, numerous macromolecules of various chemical natures, have been prepared due to the advanced developed synthetic methods. For example, a wide variety of block copolymers (BCPs), in which two polymeric segments attached at one end, were prepared.[3-5] In

solution, block copolymers form assemblies with morphologies similar to those obtained by simple surfactant molecules (as shown in Figure 2). The advantage of block copolymer assemblies over those obtained from surfactant molecules is that they are more stable and provide a wider range of functionality. Therefore, the self-assembly of block copolymers have attracted significant attention because of their potential applications in many fields, such as biomedicine, biomaterials, and microelectronics. Among all morphologies obtained via macromolecular self-assembly, cylindrical-like aggregates have gained increasing attention as they potentially can be used as a template to fabricate nano-wires with an inorganic interior (*e.g.* silica or gold).[6-9]

Block copolymer molecule

Self-assembly in solution

Micelle   Rod   Vesicle   Tube
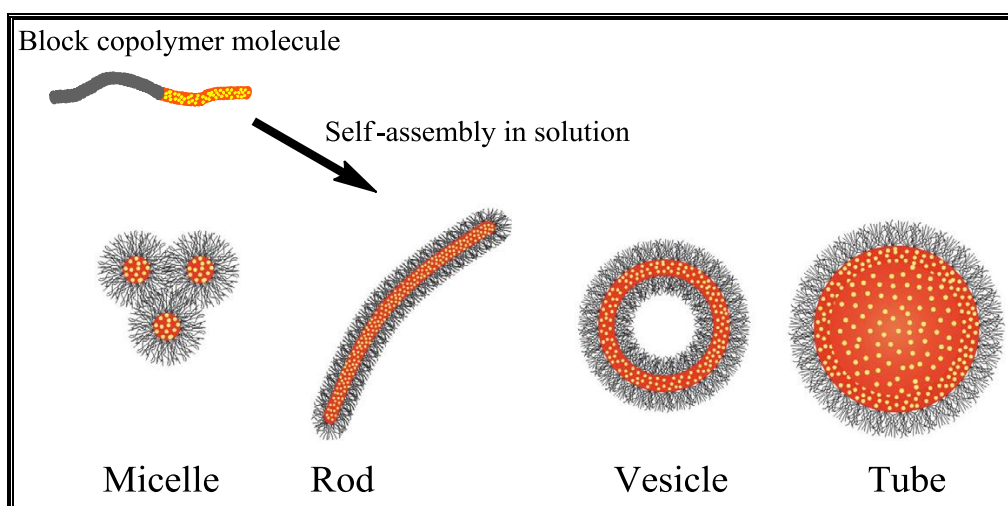
Figure 2: Some of the possible morphologies that form through the self-assembly of block copolymers[10]

Besides BCPs, many other macromolecules with even more complex structures like molecular brushes were synthesized.[11-13] Molecular brushes (MBs) are a relatively new class of macromolecules, in which a polymer backbone is densely grafted with polymeric side chains SCs, ideally, with a SC on each repeat unit of the backbone. Depending on the chemical nature of the SCs, MBs can be divided into two categories, (I) one component MBs, in which all of the SCs consist of one polymer, and (II) multi-component MBs where the SCs can be two or more homo-polymers, or block copolymers distributed along the backbone. When the SCs consist of two homopolymer of different nature, alternatingly distributed along the backbone, this MB is known as hetero-arm MB.[14, 15] In this study, hetero-arm MBs were investigated in terms of their synthesis and self-assembly in arm-selective solvents.

Layout of dissertation:

Chapter 1: An introduction to molecular brushes (MBs) is given. This chapter gives a brief definition of MBs and their different structures as well as the synthetic routes used to prepare such macromolecules.

Chapter 2: In this chapter the term 'macromolecular self-assembly' is discussed. This chapter describes some of the important aspects of macromolecular self-assembly and its potential application to fabricate novel materials of various shapes and sizes.

Chapter 3: This chapter describes the synthesis of the building blocks (monomers and macromonomers) used to prepare hetero-arm MBs. Some of the challenges faced during the course of this study are also highlighted in this chapter.

Chapter 4: This chapter discusses the results obtained during this study. It describes the approaches used to prepare hetero-arm molecular brushes of an amphiphlic nature. Furthermore, it gives the results obtained from the self-assembly of these macromolecules in an arm-selective solvent.

Chapter 5: The synthesis of a different type of hetero-arm molecular brushes is described in this chapter. It shows how hetero-arm molecular brushes were prepared. It also gives the initial results obtained when these macromolecules were used as a template to fabricate organic/inorganic materials of cylinder-like shape.

Chapter 6: This chapter gives general conclusions and remarks. It also gives some possible recommendations for future investigations.

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Chapter 1: Molecular Brushes: general aspects

Abstract

In this chapter **Molecular Brushes (MBs)** will be reviewed, to outline some important aspects and characteristic features of such interesting macromolecules. It discusses the definition of MBs and their different types, the synthetic approaches used to make such materials.

Introduction

Before the discovery of controlled or living polymerisation techniques the synthesis of well-defined macromolecules was almost impossible. As the produced polymer characteristic features such as molecular weight (*Mw*), molecular weight dispersity (*Ð*), and topology, could not be either pre-determined or controlled. With the advanced developing technologies, in many fields, the need for polymers with well-defined structures, grew bigger and bigger. In 1955 M. Szwarc[1, 2] introduced the first ever living polymerization method that was named "anionic polymerization", which produces polymers with pre-determined *Mw* and low *Ð*. Due to the sensitivity of this method towards impurities (*e.g.* oxygen) and functional monomers, its use in the synthesis of macromolecules with a wide range of chemical functionality and complexity is limited. However, the ground breaking concept of livingness, provided by anionic polymerization, inspired scientists to apply the concept on other polymerization methods such as cationic[3], group transfer[4], radical[5-9], ring-opening (RO)[10-12] and ring-opening metathesis (ROM)[13] polymerizations.

Initially, cationic and group transfer polymerizations have emerged as additional, powerful tools to synthesize well-defined macromolecules. Although these methods added a great deal in this field, the need for a more practical, and easy method was intense. At this stage scientists have shifted their focus to radical polymerization, because of its simplicity, and tolerance to a wide range of monomers of different functionalities, and to a wide range of polymerization conditions. Generally there are three approaches that rely on a radical mechanism in the synthesis of well-defined macromolecules. Two of them are based on the persistent radical effect and are either spontaneous (nitroxide mediated polymerization, NMP) or catalysed (atom transfer radical polymerization, ATRP). In these approaches the growing chains are in a reversible process between active and dormant states. In these two techniques the polymerization reaction includes two essential steps, *i.e.* activation and deactivation. In the activation step, the radicals are generated after which they propagate by adding one to a few monomer molecules. These propagating radicals are then trapped in a dormant state in a process known as the deactivation step. Controlling the rate of exchange between active and dormant species allows for virtual elimination of other chain transfer processes and reduction of the radical termination rates to a minimum. The third approach utilizes a degenerative transfer mechanism with either alkyl iodides or dithioesters (reversible addition fragmentation transfer, RAFT) as transfer agents. The

other powerful polymerization techniques, such as ROP and ROMP, have expanded the possibilities to synthesize macromolecules with an even wider range of functionality and architecture.[6, 8, 11, 13-15]

The advanced development of these controlled/living polymerization techniques opened a new avenue to precisely manipulate many aspects of macromolecular architecture in terms of topology, composition and functionality. Perhaps the most impressive achievement using these techniques is the precise control of the composition and topology of polymer brushes. [16-18] A number of different polymer brushes copolymers have been prepared and investigated in terms of their attained morphologies on surfaces and physical properties.[19-21] In the following section, polymer brushes will be reviewed but mainly focusing on one class known as molecular brushes (MBs).

Definition of polymer brushes

Polymer brushes are generally defined as a class of material of which polymeric chains are at one end tethered to a substrate. The substrate can be a surface or planar solid, a spherical particle or a linear polymer chain as illustrated in Scheme 1. 1. Depending on the substrate, polymer brushes can be classified in three categories: **1)** One-dimensional brushes (*1D*), correspond to polymer chains densely grafted on a linear polymer chain. This type is also known as molecular brush, cylindrical polymer brushes, wormlike brushes and molecular bottle brushes. **2)** Two-dimension brushes (*2D*) where the side chains (SCs) are grafted on a planar surface (*e.g.* glass plates). **3)** Three-dimension brushes (*3D*) in which the SCs are grafted on a spherical particle. The first class of these macromolecules will be the subject of this study and the term **"molecular brushes"** will be used throughout this dissertation.[17]

1D-polymer brushes
2D-polymer brushes
3D-polymer brushes
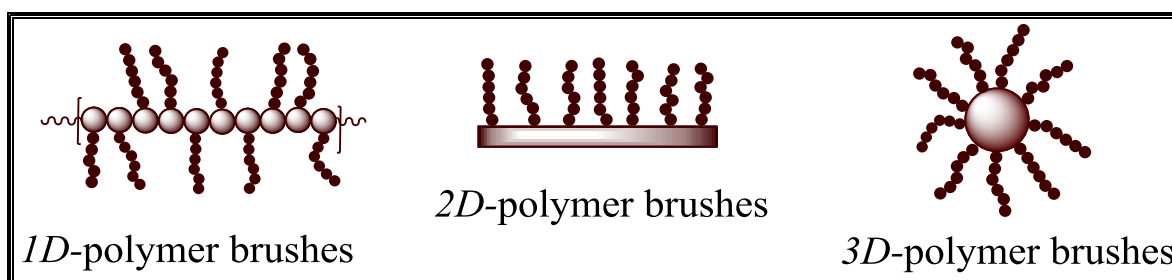
Scheme 1. 1: Schematic illustration of the possible architectures of polymer brushes.

One-dimensional brushes or molecular brushes (MBs) are a special class of graft copolymer in which the SCs are regular and densely grafted along a linear polymer chain commonly known as the backbone. Ideally, there is at least one SC on every repeat unit along the backbone (Figure 1 (a)). As a result of this high grafting density, the high steric repulsion between adjacent SCs drives the backbone to stiffen, and hence, stretch to its maximum length. Due to this high stiffness of the backbone, MBs tend to adapt a cylinder or brush like morphology that can be visualized by AFM. The morphology of such macromolecules and their properties in general, are governed by various parameters that include DP of the backbone and SCs, the grafting density, and chemical nature of the SCs.
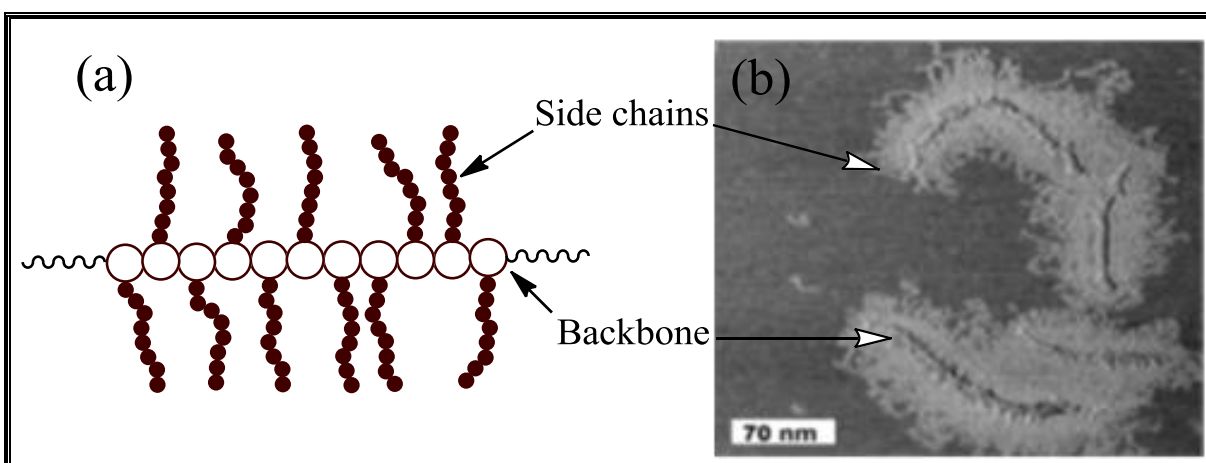
Figure 1. 1: (a) Schematic presentation of a molecular brush molecule composed of a polymeric backbone and SCs, and (b) AFM image of molecular brushes.[22]

In this chapter, MBs will be reviewed in terms of, the methods used to prepare such macromolecules, the different types of MBs prepared so far, and finally some important aspects that determine their final properties.

Synthesis of molecular brushes:

In the last two decades the synthesis of MBs has become the subject of a large number of studies. Most of these studies aimed at the synthesis of MBs with precise control over: **(i)** nature of the backbones and SCs, and **(ii)** the degree of polymerization (DP) of the backbone and SCs. Through the years, scientists have developed a variety of methods to synthesize such macromolecules. Generally there are three approaches to synthesize MBs: **"grafting through"**[23-]

[27], **"grafting onto"**[28-30], and **"grafting from"**[16, 31-33] as depicted in Scheme 1. 2. In the grafting through approach, the backbone and SCs are prepared *in-situ* though the polymerization of macromonomers. However, in the other two approaches, the backbone and the SCs are separately synthesized. These methods are discussed in the following sections.
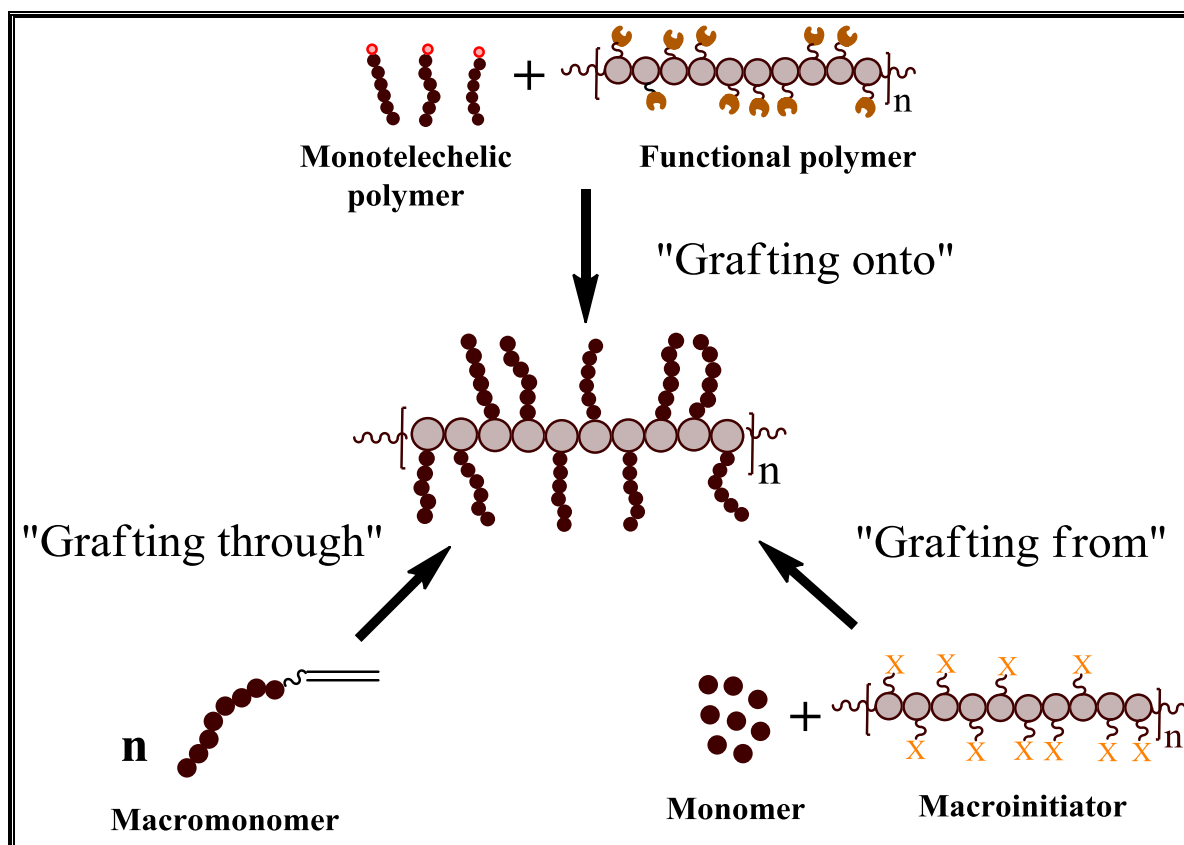
Scheme 1. 2: Schematic illustration of the strategies used for the synthesis of molecular brushes.[18]

Grafting through approach

Grafting through approach is the oldest and most used approach for the synthesis of MBs among the other approaches, in which a macromonomer is (co)polymerized through a suitable polymerization technique. The macromonomer is usually defined as a polymeric or an oligomer molecule with a polymerizable functional group at one ends. These molecules can be synthesized via any controlled polymerization (*e.g.* anionic polymerization) of a monomer *i.e.* styrene (St),[23] methyl methacrylate (MMA), ethylene glycol (EG),[34] or vinyl pyridines (VPy), and then end-functionalized with a suitable polymerizable group, such as St, methacrylate, or norbornene.[35, 36]

As a result of the wide range of macromonomers, MBs that vary in chemical nature and properties can be synthesized.

The grafting through method was introduced by Tsukahara *et al.* in 1989 to prepare MBs with very high grafting density. In this study, methacrylate-functionalized short chains polystyrene (PS-MA) macromonomers were polymerized through radical polymerization to produce MBs with uniform SCs and high grafting density.[23, 24] This method was then further employed by many other research groups to prepare MBs with different functionalities and architectures.[27, 34, 37-43] The advantage of this method is that high grafting density and SC uniformity are guaranteed.

Practically this method generally suffers from few drawbacks which limit its use. Among these drawbacks: reaching high DP, due to the polymeric nature of the macromonomer, the medium viscosity increases significantly at early stages of the polymerization, which restrict the macromonomer conversion, and hence MBs with low DP. Therefore, short chains macromonomers and low macromonomer concentration may aid in preparing MBs with high DP via grafting through approach. Also using macromonomer with highly active polymerizable end groups may enhance the monomer conversion. For example, the use of macromonomers with electron-donating and electron-accepting (such as vinyl benzyl and maleimide based macromonomers) have been reported to copolymerize to high macromonomer conversions in relatively short polymerization time.[44] The other example of highly active macromonomers is the use of norbornene-based macromonomers in ROMP, which allowed the synthesis of MBs with high DP.[45, 46]

The other difficulty associated with this method is the need of a suitable purification method to remove the unreacted macromonomers such as fractionation and dialysis which can be very effort and time consuming. [25, 47]

Grafting onto approach

The second method used to prepare MBs is grafting onto.[28, 30, 48, 49] In this approach a pre-made backbone with multifunctional groups and monotelechelic SCs are separately prepared. The MBs are then formed via a coupling reaction between the end-groups of the SCs and the pendant functional groups. For a successful grafting onto procedure, the coupling reactions must have

excellent coupling efficiency and high selectivity. For example, Deffieux and coworker employed this strategy to prepare well-defined MBs of different topologies.[28, 50-53] In this approach, polystyryl lithium (PS-Li$^+$) was reacted with poly(2-chloroethyl vinyl ether) (PCEVE) to produce MBs with a PCEVE backbone and PS SCs. This approach could potentially be used to prepare MBs with various architecture and composition. In a similar fashion Gao *et al.* have employed Sharpless' 1,3-dipolar cycloadditions ("click reactions") to prepare MBs with well-defined structure.[30] The grafting density of the obtained MBs, however, is usually affected by several factors, including the coupling efficiency, the length and the chemical structures of the SCs, as well as the initial molar ratio of SCs to the functional groups on the backbone. In general, to obtain MBs with high grafting density using this method, high molar ratio of short SCs relative to the functionality of the backbone are essential requirements.[30]

Grafting from approach

As a result of the disadvantages and limitations associated with the aforementioned methods, a new effective pathway was needed to synthesize well-defined MBs. Right after the discovery of ATRP, Matyjaszewski and coworkers have used his discovery to synthesize well-defined MBs via the method he called "grafting from".[16] Since early stages this method has proven to be the best and most efficient approach to prepare MBs among other topologies. This can be seen by the number of publications that followed the first paper by Matyjaszewski.[33, 54, 55]

In this method, a well-defined backbone is first prepared via controlled polymerization techniques, followed by attaching initiating sites to each repeat unit through well established methods *e.g.* esterification reaction with 2-bromoisobutyryl bromide. In the second step, the SCs are then generated from these initiating sites via ATRP reactions, or other polymerization techniques, of a chosen monomer. Initially, the generation of SCs was achieved solely via ATRP, however, other polymerization techniques , such as ROP[56], RAFT[49] and NMP[57], have also been used to initiate the polymerization from suitable pendants groups.

Originally the backbone was synthesized via ATRP of 2-(trimethylsilyloxy) ethyl methacrylate (HEMA-TMS), which served as a protected ATRP initiator monomer. In the first step, well-defined poly(HEMA-TMS) is synthesized followed by the deprotection and transformation of the TMS pendant groups to ATRP initiating sites to yield poly-(2-(2-bromoisobutyryloxy) ethyl

methacrylate) (PBIEM) as a macroinitiator. Moreover, in addition to ATRP, other controlled polymerization techniques, *e.g.* anionic, were also used to prepare the backbone. For example, Zhanga *et al*.[31] adapted a similar approach but used anionic polymerization, in addition to ATRP, to prepare the backbone. They showed that anionic polymerization was the better option when high Mw backbones are targeted. In addition to anionic polymerization, ROMP was also employed to prepare the backbone, which adds another powerful tool for the synthesis of well-defined MBs.[58]

Following the preparation of the backbone, the SCs can then be generated from the initiating sites along the backbone using a controlled polymerization technique. Although the majority of MBs prepared by the grafting from approach employed ATRP to form the SCs, other controlled polymerization techniques such as ROP[46, 59, 60], RAFT[61] and NMP[57] have also been used. Among all of these methods, ATRP is still the preferred choice to generate the SCs as it provide MBs with densely grafted SCs of a wide range of composition[33, 62-64] and topologies.[65, 66] With regard to the grafting efficiency in the grafting from approach when ATRP is used, Matyjaszewski and coworkers showed that the grafting efficiency of an ATRP process depends on the monomer/initiator system used and other parameters *e.g.* catalyst, reaction stoichiometry, temperature. [67] They showed that a well-designed ATRP reaction can produce MBs with grafting efficiency as high as 90%.[68]

With all of these synthetic methods in hand almost an infinite number of MBs can be prepared. The use of the above mentioned synthetic strategies, and/or their combination allowed scientists to synthesize MBs with precisely controlled backbone, and SCs of different functionalities, chemical compositions and topologies. Some examples of the MBs prepared via these will be discussed in the following section.

Structures and compositions of molecular brushes

Based on the chemical nature of the SCs, MBs can be further classified into two categories[17] **A)** one-component MBs, *i.e.* homopolymer SCs[16, 37, 53], and **B)** multi-component MBs, *i.e.* copolymer SCs.[69-73] In terms of topologies, these two classes can be further sub-divided to star-shaped MBs[65], graft-on-graft MBs[53, 59, 66], and macrocyclic MBs.[51] As illustrated in Scheme 1. 3 a

wide range of MBs with different SCs have been prepared in the last decade; these MBs will be discussed in the following section.

One-component molecular brushes

One-component MBs are the most common type found in literature. Initially this type gained great attention from both experimental and theoretical chemists, as to develop efficient methods to prepare such interesting macromolecules. Intensive studies have been performed on one-component MBs, focusing not only on their peculiar densely grafted nature but also on the different parameters that determine the conformation and properties of such materials in bulk and solution.[17-20] As shown in the synthesis section, various one-component MBs based on poly-(meth)acrylate (P(M)A), PSt, polynorbornene (PNB),[45, 58] poly(thiophene),[74] cellulose[75-77] backbone, and a wide range of SCs like PS, PMA, PEG[30], PDMAEMA[77, 78], PNIPAM[62], PVPy[79], sugar[63, 80] and polypeptide[81] among others, have been synthesized. Most of these studies concluded that MBs adapt a cylinder-like confirmations and the property of these macromolecules depends mostly on the nature of the SCs.
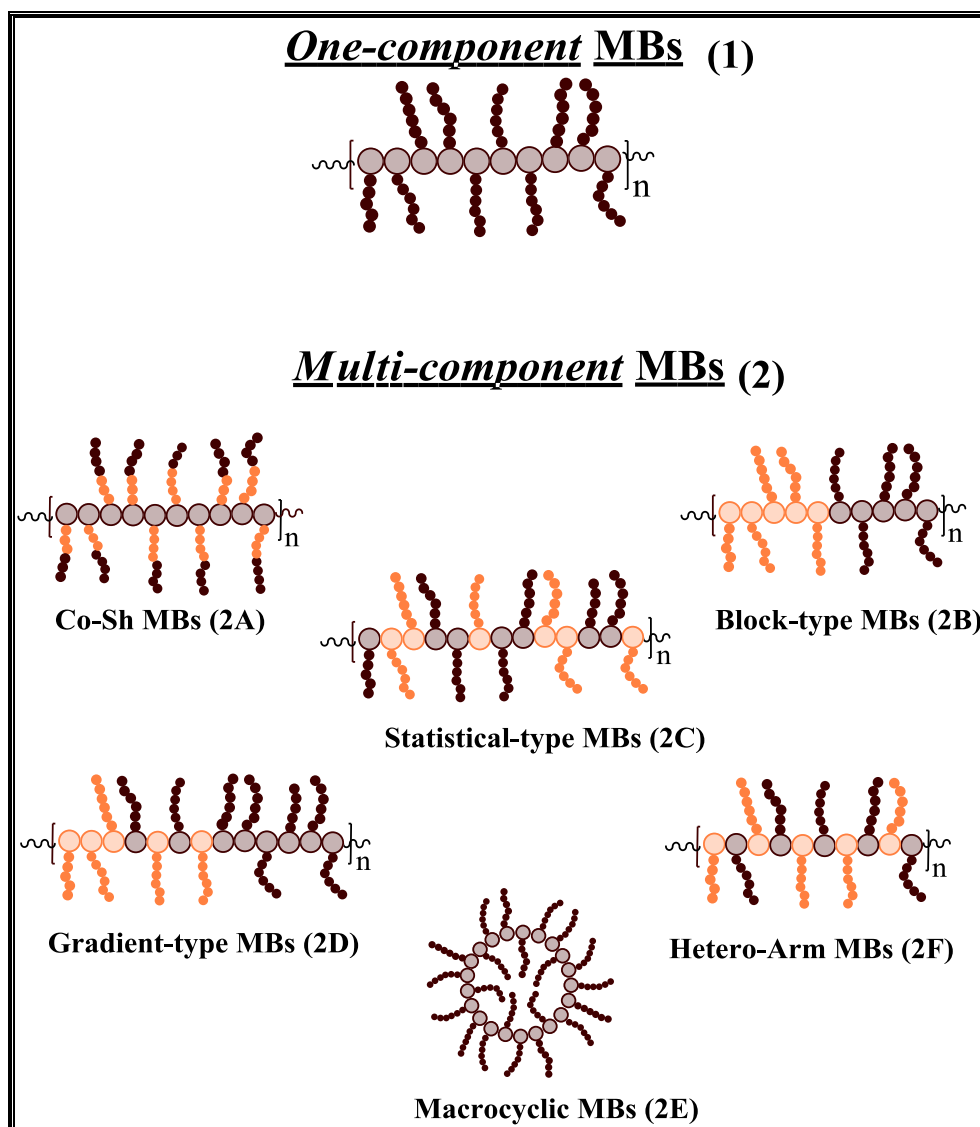
Scheme 1. 3: Various structures of MBs[17]

Multi-component molecular brushes (see Scheme 1. 3)

Depending on the chemical composition and distribution of the SCs multi-component MBs can be: (i) double cylinder type MBs or (core-shell MBs)[25, 31, 33, 54, 59], (ii) block-type MBs[45, 82, 83], (iii) hetero-arm MBs or (Janus cylinder MBs)[44, 84], or (iv) statistical (MBs).[71, 85] Core-shell MBs (Co-Sh MBs) are MBs with SCs consist of *di-* or *tri-* block copolymers.[86] The block-type MBs (AB MBs) are MBs consist of two (or more) different one-component MBs covalently bonded at one of the ends *e.g.* two different homo-polymer SCs from each extreme to the centre of the

backbone. Janus type brushes are MBs with two or more different SCs attached to the backbone. Each of these types will be briefly discussed below.

Core-shell MBs (Co-Sh MBs) (2A. Scheme 1.3)

When the SCs consist of block copolymers (*i.e. di-* or *tri-*) densely grafted along a polymeric backbone, these MBs are usually called core-shell MBs (Co-Sh MBs). To prepare Co-Sh MBs, two approaches have been used, "Grafting through" (polymerization of *di*-block macromonomer) and "Grafting from" (the sequential polymerization of two different monomers initiated from multifunctional macroinitiators).

Initially, the grafting through approach was applied to prepare Co-Sh MBs via polymerization of *di*-block macromonomer. Ishizu *et al.*[87] were the first to employ this approach to prepare Co-Sh MBs via anionic polymerization of vinyl benzyl- (poly styrene-*b*-polyisoprene) *di*-block macromonomer (VB-(PS-*b*-PIP)). However, their attempt resulted in only oligomacromonomers with low DP that adopted a globular conformation. In another attempt, norbornene-(poly(ethylene glycol)-*b*-polyisoprene) NB-(PEG)-*b*-(PS) macromonomer was polymerized using Grubbs's 1st generation catalyst was reported by Heroguez *et al.*[88] However, low DP Co-Sh MBs were also obtained. In a similar fashion Djalali, *et al.*[25] employed this approach to prepare Co-Sh MBs with amphiphilic properties. First, the *di*-block macromonomer was prepared via sequential anionic polymerizations of 2-vinylpyridine and St followed by end-functionalization with methacryloyl. The produced *di*-block macromonomer *i.e*. MA-(PVPy-*b*-PS) was polymerized via conventional radical polymerization to give Co-Sh MBs with high DP of the backbone. Since the SCs consist of PVPy coupled to PS, the obtained MBs exhibit a core of PVPy and a shell of PS which resembled an amphipolar unimolecular micelle of cylindrical shape.

Thereafter, many research groups have employed this approach aiming at Co-Sh MBs with high DP using various *di*-block macromonomers via different polymerization methods. For example, Tsubaki *et al.*[41] reported the synthesis of Co-Sh MBs via radical polymerization of vinyl benzyl-terminated and (polymethylstyrene)-*block*-(poly2-vinylpyridine) VB-(PmS-*b*-PVPy) macromonomer. This way Co-Sh MBs with high DP backbone and *di*-block copolymer SCs were obtained.

Although the "Grafting through" approach is a straightforward method to produce MBs with maximum grafting density and fixed SCs length, its use was limited because of its drawbacks as mentioned above. Because of these challenges the attention shifted to the more efficient and practical grafting from approach to prepare Co-Sh MBs.

To prepare well-defined Co-Sh MBs, *i.e.* the backbone and SCs have uniform Mw and Đ, with high DP of the backbone and high grafting density of block-copolymer SCs, the "grafting from" approach has been extensively used. As discussed earlier, "grafting from" approach consists of two steps, **i**)- synthesis of the backbone (or macroinitiator) via a controlled polymerization method, and **ii**)- synthesis of SCs. The advantage of this approach is the full control over the DP, Đ and chemical composition of both the backbone the SCs. This approach allowed the synthesis of Co-Sh MBs with SCs of various chemical nature which potential can be in wide range of applications.[89] This approach was reported, for the first time, by two independent groups: by Matyjaszewski[54] and by Müller.[33]

Followed up on their initial synthesis of well-defined MBs with PSt bearing ATRP initiator end group SCs[16], Matyjaszewski and coworkers[54] prepared Co-Sh MBs with hard-soft or soft-hard *di*-block copolymer SCs. As described earlier, well-defined PBPEM macroinitiator with multi-initiating ATRP sites was first prepare followed by sequential ATRPs of either, St and *n*-BuA (or the reversed order).[54] Similarly, Müller adopted almost identical synthetic route and prepared well-defined PBPEM macroinitiator by anionic polymerization, followed by the generation of the SCs via sequential ATRPs. The *di*-block copolymer SCs were then introduced via two sequential ATRPs of *tert*-butyl acrylate (*t*-BA) (or St) and St (or *t*-BA) to prepare well-defined Co-Sh MBs. The poly (*tert*-butyl acrylate) block was then transformed to poly acrylic acid through the hydrolysis of the *tert*-butyl groups to carboxylic acid groups to produce amphiphilic core-shell MBs.[33] In a different study, they synthesized MBs with PAA-*b*-P*n*-BA (core-shell) SCs using the same approach.[31] Following these examples many other research groups have adopted this strategy to prepare various Co-Sh MBs of different nature. For example, Ishizu and coworkers prepared Co-Sh MBs via photo-induced ATRP of *t*-BA and MMA, initiated from a pre-made poly (vinyl benzyl *N,N*-diethyldithiocarbamate) (PVBDC) backbone.[32]

In addition to ATRP, other controlled polymerization methods have also been used to prepare *di*-block copolymer SCs using the grafting from approach. For example, Cheng *et al.*[57] prepared Co-

Sh MBs by a combination of ROMP and NMP. The backbone was synthesized via ROMP of NB-based NMP macroinitiator followed by sequential NMP of isoprene (IP) and *t*-BA. In another study, Co-Sh MBs were also synthesized via a combination of anionic and RO polymerizations.[56] The backbone was first synthesized via anionic polymerization of *p-tert*-butoxystyrene followed by hydrolysis to give well-defined poly(*p*-hydroxystyrene) (PHOS). The PHOS was then utilized as the macroinitiator for two sequential ROPs of EO and PO to generate the SCs. Another Co-Sh MBs with amorphous-crystalline domains were prepared via a combination of ATRP and ROP.[59]

The combination of two different controlled polymerization methods allows the synthesis of Co-Sh MBs with two incompatible segments in the SCs. This resulted in new Co-Sh MBs with various functionalities of a controlled domain (*i.e.* in the core or the shell), and hence, new interesting morphologies and properties. For example, hydrophilic-hydrophobic could potentially be used as unimolecular micelles for medicine applications among others.

In addition to Co-Sh MBs, core-shell-corona (Co-Sh-Co) MBs have been also prepared based on the grafting from approach. In this approach three sequential polymerizations of different monomers were employed. For example, Müller and coworkers[86, 90] reported the synthesis of water-soluble Co-Sh and Co-Sh-Co MBs with P*t*-BA (core), poly(3-(trimethoxysilyl)propyl acrylate) (PAPTS) (shell), and poly(oligo(ethylene glycol) methacrylate) (POEGMA) (corona) terpolymer SCs. The obtained Co-Sh-Co MBs then served as a unimolecular cylindrical template for the *in situ* fabrication of water-soluble organo-silica hybrid nano-tubes via base-catalysed condensation of the PAPTS shell block.

Block-type MBs (2B, scheme 1.3)

Among the structural possibilities of multi-component MBs is the block-type MBs. These MBs consist of two or more densely grafted brushes attached covalently at one extreme, in which each block-brush consists of different SCs. Of all multi-component MBs, block-type MBs (AB-type MBs) have rarely been reported as only few research groups have investigated the synthesis possibilities and the attained morphology. Matyjaszewski and coworkers[83] prepared block-type MBs with *di*-block and *tri*-block brushes via combination of grafting through and grafting from strategies. The first block was prepared via ATRP of octadecyl methacrylate (ODMA) or HEMA-TMS using *mono-* or *di*-functional initiators to give MBs (with relatively short SCs, C_{18}) with

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ATRP initiator end groups (block A). The second block (B) was generated via ATRP of HEMA-TMS to produce PODMA-*b*-PBIEM, after esterification and transformation of the TMS groups to an ATRP initiator (*e.g.* -Br). The SCs on the second block were then formed by ATRP of *n*-BA initiated from the multiple initiating sites along this block to give PODMA-*b*-poly(BPEM-*g*-*n*BuA). In this case of the crystallisable PODMA segments resemble a brush block with relatively short SCs (C_{18} chains). Although the SCs of the A block of these MBs were relatively short, these MBs exhibited rod-like morphologies.

This approach inspired other researchers to synthesize block-type MBs with longer SCs on both blocks. For instance, Ishizu *et al.*[91] successfully employed this concept to prepare hetero-grafted block-type MBs with PEG and PHEMA SCs on each block. Following Matyjaszewski's approach,[83] the first block was prepared via ATRP of POEGMA (grafting through) to produce MBs with PEG SCs and ATRP initiators at the end of the backbone. In the second step, the backbone was extended through another ATRP of HEMA followed by an esterification step to give brush-*b*-PBIEM *di*-block copolymers. In the final step, the SCs on the second block were generated via ATRP of HEMA (grafting from) which gave block-type MBs of an amphiphlic nature.

In a different strategy, block-type MBs have been synthesized entirely using the grafting from approach via a combination of ROMP, to prepare the backbone, and ATRP and ROP to generate the SCs. [45] The *di*-block backbone was synthesized by two sequential ROMPs of two norbornene esters with different functionalities. The obtained *di*-block backbone displayed a macroinitiator for ATRP of St and ROP of lactide. This approach allowed the synthesis of well-defined block-type MBs with high molecular weights and low Đ for the first time. Using a similar approach, Lee *et al*. prepared well-defined block-type MBs using a combination of ATRP and ROP.[82] The *di*-block copolymer backbone was synthesized via sequential ATRP of HEMA and HEMA-TMS monomers followed by the esterification and removal of protecting TMS groups (*i.e.* from –OH to –Br (ATRP initiator) and from TMS to -OH (ROP initiator)). The SCs were then introduced via ROP of PCL from one block and ATRP of *n*-BA from the other block. This approach allowed the synthesis of well-defined block-type MBs with high Mw and low Đ.

Hetero-arm MBs (Scheme 1. 3: (2C) and (2F))

MBs with two different SCs attached to the backbone are generally called Hetero-arm MBs. If the sequence of these different SCs on the backbone is in an alternating distribution, these MBs are known as *Janus-type* MBs (Scheme 1. 3: 2F). However, for randomly distributed different SCs along the backbone, these MBs are commonly known as mixed or statistical MBs (Scheme 1. 3: 2D). Compared to other MBs, the incorporation of these two different types of SCs provides MBs with extra structural versatility and unique aggregation properties.[92, 93] When the two SCs have different nature (*i.e.* thermodynamically incompatible) unfavorable interactions between these SCs occurs leading to intramolecular phase separation.

Generally such macromolecules were synthesized using grafting through, grafting from or their combinations. For mixed MBs, the grafting through approach was initially employed by Ishizu *et al*.[26, 94] to prepare mixed MBs with PSt and PI SCs via radical copolymerization of binary vinyl benzyl terminated PSt and PI or PEG macromonomers. In a similar approach, mixed MBs with PVPy and PMMA were prepared and investigate in terms of their conformational change as a function of the SCs compatibility. In their neutral state, these MBs showed the normal cylinder-like morphology when spin-cast from chloroform onto mica. However, quaternization of the P2VP SCs with ethyl bromide induced incompatibility between the different SCs which led to intramolecular phase separation, and hence shape variation from wormlike to horseshoe or meander-like morphologies.[47] Matyjaszewski and coworkers used the grafting through approach to prepare well-defined mixed-type MBs with relatively short SCs via ATRP copolymerization of monomethacryloxypropyl poly(dimethylsilyloxane) (PDMSMA) and PEOMA. The relatively short SCs of the used macromonomers *i.e.* $DP_{PDMS} = 10$ and $DP_{PEO} = 23$ allowed the polymerization to proceed to high DP. The obtained MBs showed properties characteristic of soft gels.[71]

For well-defined mix-type MBs, the grafting from approach was employed by Wu *et al*.[69] to prepare MBs with poly-(L-lactide) (PLLA) and PSt SCs via a combination of ATRP and ROP. Initially, ATRP was used to prepare PHEMA that was partially esterified to produce macroinitiator with ATRP and ROP initiating sites. The SCs were then created simultaneously via ATRP of St and ROP of L-lactide (LLA) in a one-pot reaction.[69]

The other example of Hetero-arm MBs is the Janus-type MBs, in which the different SCs are distributed in an alternating fashion along the backbone, in this dissertation the term hetero-arm MBs will be used to describe this type of MBs. As will be discussed in Chapter 3, there are some challenges associated with the synthesis of this type of MBs. The main challenge lies in achieving the alternating distribution of the different SCs along the backbone. Many approaches were employed in an attempt to prepare such MBs.

The hetero-arm MBs can be prepared via the grafting through approach under carefully designed conditions. For example, to prepare an alternating backbone, the macromonomers used should contain electron-donating and electron-accepting polymerizable end groups, or through the addition of Lewis acid during the copolymerization reaction of the macromonomers. In this context, Ishizu *et al*. prepared hetero-arm MBs via radical copolymerization of St-(PS) with POEGMA macromonomers in the presence of a Lewis acid.[92] The behavior of the obtained hetero-arm MBs in selective solvents was investigated. In a selective solvent to one of the SCs, these MBs tend to form large cylinder-like aggregates (*i.e.* submicron size) with core-shell structure, in which the core consists of the non-soluble SCs while the soluble SCs form the shell.[92, 94, 95] In a different approach, Chen and coworkers prepared hetero-arm MBs via radical copolymerization of *N*-(poly(ε-caprolactone))-maleimide (*N*-PCL-MI) and vinyl benzyl (polyethylene glycol) (VB-PEO). Taking advantage of the well-established charge-transfer complex formation between vinyl benzyl and maleimide terminated macromonomers hetero-arm MBs with alternating PEG and PCL SCs were prepared.[44]

To overcome the challenges associated with the grafting through approach, Ishizu *et al*.[84] prepared hetero-arm MBs via the combination of grafting through and grafting from approaches. In the first step, alternating radical copolymerization of VB-PS macromonomer and *N*-(4-hydroxyphenyl) maleimide (*N*-HPhMI) was carried out to produce MBs with PS SCs and ATRP initiating moieties (after the modification step) alternatingly distributed along the backbone. The obtained copolymer was used as a macroinitiator for the ATRP of MMA to generate the other of SCs. In a different approach, Yin *et al*. combined grafting from and grafting onto approaches to prepare hetero-arm MBs with PMMA and PNIPAM SCs.[96]

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Behaviour and properties of molecular brushes

Graft copolymers with densely grafted SCs have gained significant academic interest due to their inherent properties related to the multibranched molecular structures.[17-19] Because of the high density of the SCs grafted on the backbone, MBs have the following characteristics: i) small and compact molecular dimension with high aspect ratios, ii) an extended rod-like conformation instead of the coil-like conformation that is adopted by linear polymers, and iii) high density of functional groups and chain-ends. Because of these unique features MBs provide a new class of materials with unusual properties compared to those of their linear counterparts. The properties of MBs can be tuned by a number of factors that include grafting density, length, chemical nature and architecture of the SCs. These factors and their effects on the conformation and properties of MBs will be discussed in the following section.

One of the important parameters that determine the conformation adopted by MBs, and hence their properties, is the grafting density. The grafting density parameter describes the number of SCs per repeat unit of the backbone. it is an important parameter which can determines the stiffness of the backbone and the adopted morphology of a single MB. The number of SCs on the backbone can be controlled and tuned by varying the employed synthetic method. As discussed in the synthesis section, the wide range of synthetic methods, *i.e*. radical, anionic, RO and ROM polymerizations, and approaches, *i.e*. grafting "through", "onto" and "from", allows the synthesis of MBs with almost full control over grafting densities. For example, depending on the used synthetic method and approach, MBs with a SC on every repeat unit, *i.e*. a SC on every second carbon atom (C-C)[68], or a SC on every fourth or fifth carbon atom (in the case of ROMP)[46, 88, 97], were prepared. Other abnormal MBs with two SCs on a single repeat unit[98], MBs with SCs loosely distributed along the backbone[99, 100] or MBs with SCs with gradient distribution on the backbone were also synthesized.[85]

The morphology of these MBs in solution or on surfaces (generally mica) was investigated by cryo-TEM and atomic force microscopy (AFM). Most of these studies revealed that the MBs adapt a rod-like morphology.[22] However, the attained morphology depends significantly on the chemical nature of the SCs. The effect of the chemical nature of the SCs on the morphology and properties of MBs was investigated by many research groups. Matyjaszewski and coworkers[54]

prepared three different MBs with P*n*-BA, poly(P*n*-BA-*b*-PS) and poly(PS-*b*-P*n*-BA) SCs. This variation in chemical composition and segments order resulted in a morphology change from a rod-like to globular morphologies. When the MBs consist of only P*n*-BA SCs, they adapt a rod-like shape with an almost fully extended main chain. However, when the chemical nature of the SCs changes by introducing a second block, *i.e*. PS, the adapted morphology depends significantly on the order of the different segments in the SCs. When the SCs consist of P*n*-BA as the core and PS as the shell, the MBs still adapt a rod-like shape, while MBs with the reversed order of the blocks adapted a globular morphology.

These core-shell structures of MBs represent an interesting class of MBs as they can be used as unimolecular micelles of cylindrical shape. Co-Sh MBs with amphiphilic SCs usually resemble unimolecular micelles of rod-like morphology, *i.e*. one molecule with soluble and non-soluble domains. Because of the amphiphilic nature of the SCs, these unimolecular micelles may respond to a change of the surrounding environment, *e.g.* solvent quality, temperature, solution pH, salt content, and light. For example, Müller and coworkers[33] investigated the solution behaviour of Co-Sh MBs with poly(PS-*b*-PAA) SCs using NMR in different solvents. It was found that these MBs form unimolecular micelles with a thickness that varies with the solvent quality. In CD_3OD (good solvent for PAA only), for example, the ^{1}H NMR spectrum of these MBs showed only the PAA signals, which implies that the PAA segments (shell) are fully stretched. The absence of the PS signals in this solvent indicates that these segments were completely collapsed. However, when the solvent quality changed by adding $CDCl_3$ to the solution, the PS signals were pronounced and their intensity increased with increasing the $CDCl_3$ fraction. The micelle structure in this system is very different to that obtained from *di*-block copolymers. While the micelle structure was preserved in this system, micelles obtained from *di*-block copolymer may be unstable through this transition of solvent quality. Furthermore, the micelles size (length and diameter) can easily be controlled by simply adjusting the backbone and SCs length and by adjusting the solvent quality.

The other important aspect of the influence of SCs chemical nature is that, it determines the solubility and compatibility in various mediums, *e.g* biocompatibility. For instance, Muthukrishnan *et al*. successfully prepared well-defined sugar-containing MBs by grafting sugar-carrying polymers from long macroinitiators.[63] Other biocompatible MBs based on polypeptides

were obtained by Zhang *et al*.[81] via a combination of grafting through and grafting from approaches. These biocompatible MBs may find their applications in bio-related fields such as drug delivery and tissue engineering.

Furthermore, MBs with stimuli-responsive SCs have attracted a lot of attention recently. In this regard many research groups prepare MBs with external-responsive SCs and investigated their properties as a function of external stimuli, like pH, temperature, salt, or light. Li *et al*. investigated the thermal behaviour of MBs with the temperature-responsive poly(*N*-isopropylacrylamide) (PNIPAAm) SCs in solution.[62] AFM analysis showed interesting single-molecular morphology transitions from worm-like conformation into spheres-like morphologies as the solution temperature increased above the lower critical soluble temperature (LCST). Similar results were obtained by Balamurugan *et al*.[74] who studied the morphology transition of MBs with a conducting poly(thiophene) backbone and PNIPAAm SCs.

In a different approach Matyjaszewski and coworkers have prepared MBs with block copolymer SCs, in which one of the blocks is a temperature responsive polymer.[101] They investigated the effect of the chemical composition of the SCs on the solution behaviour of such macromolecules. An unusual concentration-dependent LCST behaviour was observed for molecular brushes with PDMAEMA-*co*-PMMA and PDMAA-*co*-PBA SCs. At very low concentrations ($\leq$ 0.1 w%), intramolecular collapse occurs as the temperature exceeds the LCST, however, at a concentration of 1 w% or higher, intermolecular aggregation took place. The other observation was that the LCST of these MBs can be tuned by simply changing the chemical composition of the SCs. Similar result were obtained for MBs with the pH, salt or light responsive SCs.[64, 102]

Due to this wide range of the structure of MBs types that result in some potential applications, the use of MBs as building blocks in the synthesis of nano-objects and organic-inorganic hybrid materials will be highlighted in subsequent Chapters.

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Chapter 2: From a Single Molecule to Nano-or Micro-Size Objects: The Power of Molecular Self-Assembly

Macromolecular self-assembly as a bottom-up approach to fabricate novel nano-materials is discussed in this chapter. It gives some examples of macromolecules and their structural requirements used in this field. It also shows the potential applications that these assemblies can be used for. Among the many applications, this chapter focuses on fabrication of organic/inorganic nano-materials through macromolecular self-assembly.

Introduction

In recent years, the advanced developments in medicine, electronics and optics, among other fields, demanded the synthesis and fabrication of novel materials with ever more sophisticated and unique properties and performances. Nano- and micro-size structures are of a major interest. Generally, the formation or construction of nano-size objects can be achieved via two approaches, top-down and bottom-up.[1] In the top-down approach (Figure 2.1 (A)), micro-fabrication methods such as photolithography are usually used to sculpture materials into the desired shape, order and size. However, in the bottom up approach (Figure 2.1 (B)), such structures are fabricated in the reverse order, *e.g.* starting from simple constituents to build complex architecture, in similar way many complex natural structures are formed.[2-7]
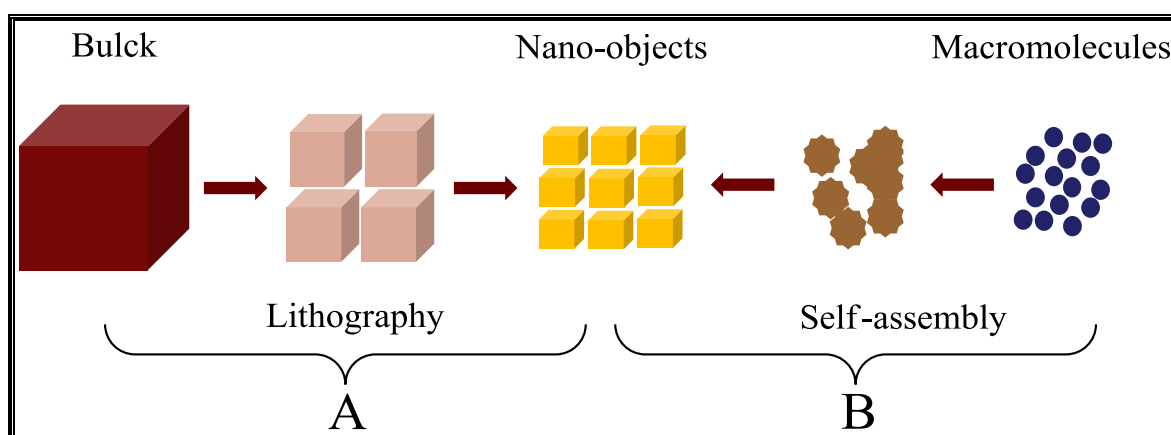
Figure 2. 1: Illustration of the approaches used to fabricate nano-objects: (A) Top-down and (B) Bottom-up.

Inspired by these examples found in nature, scientists, have shifted their attention to the bottom-up approach as it allows the fabrication of nano-objects with relatively more control and flexibility over shape and size.[3, 8] The bottom-up approach involves arranging and organizing small units, known as building blocks, into complex nanostructures of predesigned shapes and order, using physical forces operating at the nano-scale. This approach is usually termed **'self-assembly'**. The advantage of the 'bottom-up' approach, self-assembly in particular, is that the building blocks can be pre-designed and programed to direct and control the assembly process into the desired nanostructures.

In nature, various complex and diverse structures are fabricated from a rather limited choice of building blocks (*i.e.* amino acids, lipids, etc.) via self-assembly. For instance, membranes of

living cells are formed through the aqueous self-assembly of amphiphilic phospholipids.[9] Higher in complexity and diversity, proteins with different functionalities and well-defined tertiary and quaternary structures are constituted of folded peptide segments.[7] Irrespective of the complexity of these natural structures, the formation of these structures is governed and directed simply by the combination of weak interactions between the building blocks. These weak interactions include van der Waals forces, electrostatic forces, π–π interactions, metal coordination, H-bonding, and hydrophobicity.[2, 4]

Inspired by these sophisticated structures found in nature, many studies have adapted similar approaches (*i.e.* self-assembly) to fabricate novel materials starting from synthetic macromolecules. Some of these studies focused on understanding the principle of self-assembly[10-12], while others investigated potential applications.[5, 13, 14] One of the increasingly interesting applications of such approach is the synthesis of hybrid organic-inorganic nanostructures.[15] Before discussing methods used to fabricate such structures, molecular self-assembly will be briefly discussed, in terms of definition, and morphologies obtained.

Macromolecular self-assembly

Molecular self-assembly is emerging as a new and powerful approach to construct novel supramolecular architectures. Generally, the term self-assembly describes the spontaneous association of numerous individual parts into coherent and well-defined structures with unique properties. Molecular self-assembly, however, is the spontaneous organization of molecules, under specific conditions, into well-defined structures and stable arrangements through a number of weak *i.e.* non-covalent interactions, such as hydrogen bonds, electrostatic (ionic bond), hydrophobic and van der Waals interactions.[2, 7]

The self-assembly of macromolecules, in bulk and in solution, is a broad and active area of research. In bulk, block copolymers made of thermodynamically incompatible segments tend to phase separate into organized domains, which may be used to prepare impact-resistant materials, or patterned films (Figure 2. 2). However, in solution macromolecular self-assembly allows the construction of nano and micro scale objects of various morphologies, including spherical, cylinder, and tubular morphologies among others (Figure 2. 3). [16-21] Among all these morphologies, cylinder, and tubular shaped aggregates have attracted significant attention as they

potentially can be used to fabricate nano-wires. Therefore, the following discussion will focus primarily on such morphologies obtained via macromolecular self-assembly in solution.
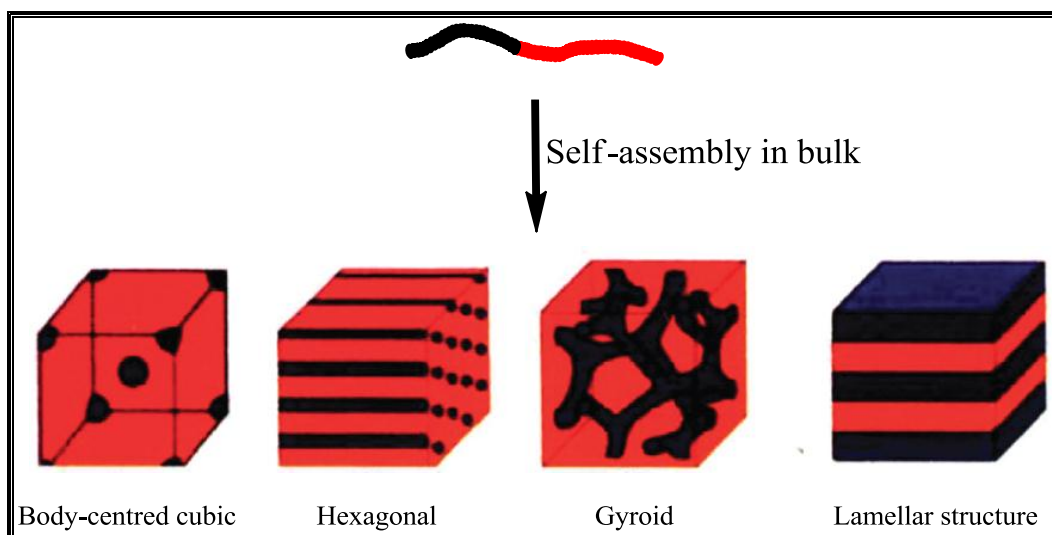
Figure 2. 2: Schematic representations of various micro-domains obtained from a linear AB BCP in bulk.[18, 20]

With the growing need for advance nano-materials, especially in fields like electronics and medicine, cylindrical shaped morphologies may represent promising candidates to fulfill these needs. Such morphology can be obtained via self-assembly of various macromolecules that includes peptides[22-24], nucleic acids[25], low molecular weight surfactants[26, 27], block copolymers (BCPs)[20, 28, 29], and MBs.[30, 31] For instance, BCPs with *tri-* or *di-*block topology, in a selective-solvent to one of the blocks, form cylindrical shape aggregates with core-shell morphologies under controlled conditions. Such morphology is governed by: (i) degree of stretching of the core-forming block, (ii) interfacial tension between the core and the solvent outside the core, and (iii) the repulsion interactions among corona-forming chains. Practically, the morphology of aggregates can be controlled and directed by, the chemical composition (*i.e.* hydrophilic/hydrophobic ratio) and concentration of the BCPs used, and by the nature of solvent and its content in the mixture, among other factors such as additive present in the solution (*e.g.* a homopolymer similar to one of the blocks).[32-34]
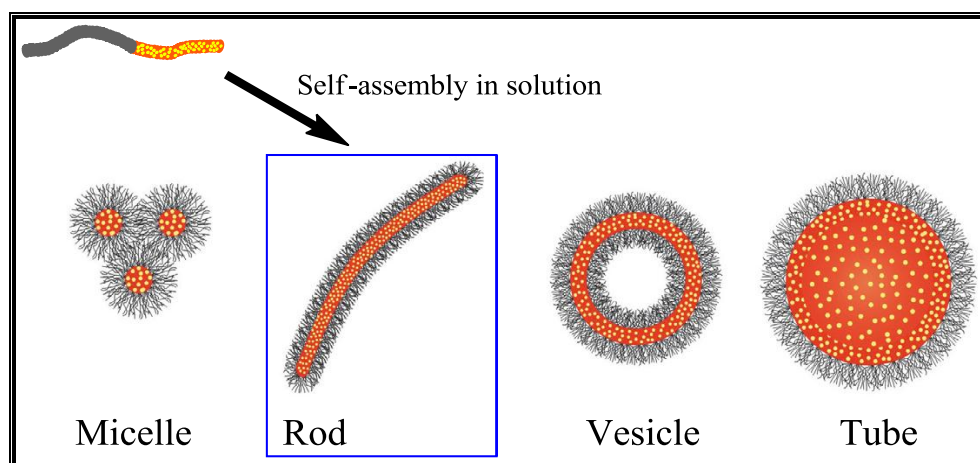
Figure 2. 3: Different morphologies formed by BCP in a block-selective solvent.[15, 18]

The advantage of using BCPs is that, they provide stable and durable aggregates that can be post-stabilized by means of crosslinking methods. In addition, the use of BCPs allows the formation of cylindrical aggregates with large diversity of functionality in either the core or the shell. This is particularly important for many applications, such as in the field of microelectronics, photoelectric materials (*i.e.* the fabrication of organic-inorganic hybrid nano-structures)[15], in the field of biomedicine drug delivery applications.[11 23, 35]

Macromolecules with even more complex architectures, such as cyclic and linear molecular brushes (MBs)[30, 36], have also been employed to construct nano-objects with cylindrical shape morphologies. The use of such complex architectures as building blocks is a relatively new approach. Compared to the investigation of BCPs self-assembly in solution, those addressing the self-assembly of MBs in either bulk or solution are very rare. This could be due to the challenges and difficulties associated with their synthesis. The self-assembly of cyclic brushes, in mixed solvents was investigated. Cyclic brushes with PS/PI CSs self-assembled into cylindrical objects with an average diameter of about 100 nm, and lengths of up to 600 nm in heptane.[36] In a different approach Biesalski *et al*. used peptide-based macrocyclic molecules to fabricate nanotubes.[37, 38]

In terms of linear MBs, most of the studies focused on their solution properties rather than on their self-assembly in selective solvents.[39] Linear MBs represent an interesting class of macromolecules. Due to the intramolecular excluded-volume interactions between SCs, MBs adapt cylindrical shape morphology in solution. This way each MB molecule represents a nano-

size cylinder which can be further assembled into larger cylindrical objects. Among all MBs types, hetero-arm MBs was recently used as building blocks to fabricate large cylindrical morphologies.[40, 41] Because of the difference in chemical nature of hetero SCs and their alternating distribution, such MBs can be considered as *di*-BCPs, *i.e.* many molecules of *di*-BCPs that are fixed together via covalent bonds at the junction point between the two blocks. Therefore, hetero-arm MBs can also be speculated to form cylindrical morphologies in a selective solvent to one of the SCs. Indeed, this phenomenon was explored by Ishizu *et al* using amphiphilic hetero-arm MBs with alternating PEG/PS SCs in THF/H_2O (1:1 v/v) solvent system. Taking advantage of the adopted conformation and incompatibility between the two SCs, large rod-like aggregates were prepared. Such aggregates exhibit rod-like morphology in the sub-micron size (*i.e.* ~4 μm in length and diameter of ~ 250 nm).

As mentioned earlier, the bottom up, self-assembly of macromolecules is a major topic in recent literature because of its promising potential as fabrication tool to build novel materials required in many fields such as biomedicine, biomaterials, microelectronics, photoelectric materials, and catalysts among other. These potential possibilities will be discussed in the following section.

Applications of macromolecular self-assembly

The self-assembly of macromolecules seems to be a promising approach to build structures in size ranging between micrometers and nanometers. Such structures may aid to first, understand the structure-properties relationship, and second, produce materials with sophisticated properties for many fields. For example, peptide-amphiphiles are known to self-assemble into nano-structures under physiological conditions and form nano-fibers with a cylindrical geometry.[23, 35] The obtained nanofibers showed high bioactivity that can potentially be used in many biomedical applications, including tissue engineering, regenerative medicine, and drug delivery.[24] Another potential application for macromolecular self-assembly is the construction of organic/inorganic hydride nano-materials that may find use in many fields like electronics, nano-sensors and optics. The following section discusses the strategies used to fabricate hybrid materials with cylindrical geometry.

The construction of organic/inorganic nano-materials has attracted considerable attention lately. Two methods have been used, first, electrospinning techniques and template-directed methods. This discussion focuses only on template-directed methods.

Template-directed synthesis is a straightforward approach for the synthesis of organic/inorganic materials. The organic phase is a natural or synthetic polymer (*i.e.* template), and the inorganic part can be *e.g.* a metal, metal oxide, or silica. This process is usually called metallization. It relies on the electrostatic interactions between the metal colloidal nanoparticles (metal precursor) and the used template. Therefore the only structural requirement for the used template is that it consists of moieties able to interact with metal precursors in specific environments (*e.g.* temperature, pH).

Generally, the metallization procedure involves three steps to fabricate the hybrid structures, *viz.* **(I)**- the mixing step, *i.e.* the metal precursor is mixed with the template to bind and complex the metal ions to specific sites on the used template, **(II)**- the reduction step, converting the metal ions into metal clusters **(III)**- the growth step, *i.e.* the growth of the metal clusters into metal particles.

Several kinds of elongated naturally produced templates have been used to fabricate hybrid nano-objects. Typical examples of such natural templates are: deoxyribonucleic acid DNA[42-46], cellulose[47], and the Tobacco Mosaic Virus (TMV)[48]. Because of its interesting structure and dimensions, DNA has regularly been used as a template for such approach. For example, Braun *et al.*[42] prepared DNA-template-based silver (Ag) in three steps. First, the DNA was localized between two electrical contacts, second introduction of an Ag^+ solution through an exchange process of the Ag^+ in solution with Na^+ associated with the DNA templates. In the third step the formed Ag^+ associated DNA was then reduced to give silver nano-wires of 100 nm thick and 15 mm long.

Synthetic peptides that mimic natural templates have also been used to prepare nano-wires. It is well known that peptide molecules self-assemble into nanofibers and nanotubes, which can be utilized to fabricate hybrid nano-materials with well-defined dimensions.[14, 49]

Similar to peptides, low-molecular weight surfactants can also self-assemble into cylinder-like nano-objects that can be used as templates for organic/inorganic hybrid materials. The use of

surfactant-based templates allowed the successful synthesis of porous hematite (α-Fe$_2$O$_3$) nano-rods.[50] Furthermore, gold nano-rods and nano-wires were synthesized via the so-called seed-mediated growth approach. This approach begins with the synthesis of metallic nanoparticles by chemical reduction of a metal salt in the presence of a capping agent such as citrate to eliminate the agglomeration of particles and to control their size. The resultant nano-particles (seeds) are added to a solution containing the metal salt, the cylinder-like template as well as a weak reducing agent. Under controlled conditions, the seeds act as a nucleation site that promotes the growth of nano-rods and nanowires. The dimensions of the obtained nano-objects can be easily controlled by simply varying the ratio of the seeds to the metal salt in the solution. Although the mechanism of growth is still not fully understood, this approach provides a relatively easy way to prepare nano-objects with well-defined geometries and dimensions.[51, 52]

Unlike low molecular weight surfactants, self-assembled block copolymers provide, more stable templates with higher function groups variety.[20] BCPs-based templates provide versatile tools to fabricate a variety of functional nanostructures with properties specifically designed for a wide range of applications. Since the metallization process is driven by electrostatic interactions, BCPs provide templates with programmable structure and high density of embedded functionality. This allows control over the spatial position of the inorganic domain within these templates (*i.e.* core, or shell). Many research groups adapted this strategy and prepared many well-defined nano-structures with different inorganic components including: noble metals (*e.g.* Au, Ag), semiconductors (*e.g.* CdSe) and magnetic materials (*i.e.* Fe$_3$O$_4$). The formation of organic-inorganic nano-cylinders is possible by treating the neat BCP-based templates or via the use of BCPs with repeat units that already contain inorganic precursor.

For example Liu *et al.*[53] were the first to explore the former approach and prepare superparamagetic nano-tubes. Initially, the templates were fabricated via bulk self-assembly of tri-BCP followed by dispersing these templates in THF containing the inorganic precursor. Then, they adopted an improved strategy that allowed the synthesis of water-dispersible Pd hybrid magnetic nanofibers.[54, 55] In this approach, they used [PI-*b*-P*t*-BA-*b*-P(CEMA-*r*-HEMA)-*b*-PSMA] tetra-BCP to form a template with core-shell-corona structure through solution self-assembly. After cross-linking of the P(CEMA-r-HEMA) layer (shell) and partial cleavage of the PI core with ozone, the Pd^{2+} was loaded and reduced to produce Pd nanoparticles. These Pd

nanoparticles could be used as a catalyst for the further electroless deposition of Pd[16] or other metals (*e.g.* Ni).[54]

The use of BCPs that already contain inorganic components was also a successful approach to prepare hybrid nano-fibers.[56] The hybrid nano-fibers are created simultaneously with the self-assembly step of the BCPs. This approach represents an interesting strategy to fabricate hybrid nano-cylinders in which the number of experimental steps is reduced. However, due to limitations associated with the synthesis of such BCPs as well as due to limited variation of the inorganic precursor, its use and versatility was restricted. In a slightly different approach, Fahmi *et al.*[57] have prepared gold nano-tubes via the self-assembly of pre-modified BCPs. In this approach, the BCPs (building blocks) were first modified with the inorganic precursor before the self-assembly step. As a consequence, the final morphology could be tuned before the reduction step, to give nano-objects of pre-programed morphology.

Other types of macromolecular assemblies with cylindrical geometry such as molecular brushes were also used to fabricate hybrids. As an example, core-shell (Co-Sh) MBs were used as a template to prepare hybrid nano-materials of well-defined dimensions (see Figure 2. 4). In this case the template represents a single macromolecule that consists of many BCPs (side chains, SCs) assembled and covalently bonded to a polymeric chain (backbone). The unique Co-Sh structure of the MBs provides nano-templates in which the core acts as host for the inorganic particles while the shell serves as an insulating layer, which prevents aggregation of the particles across different MBs.
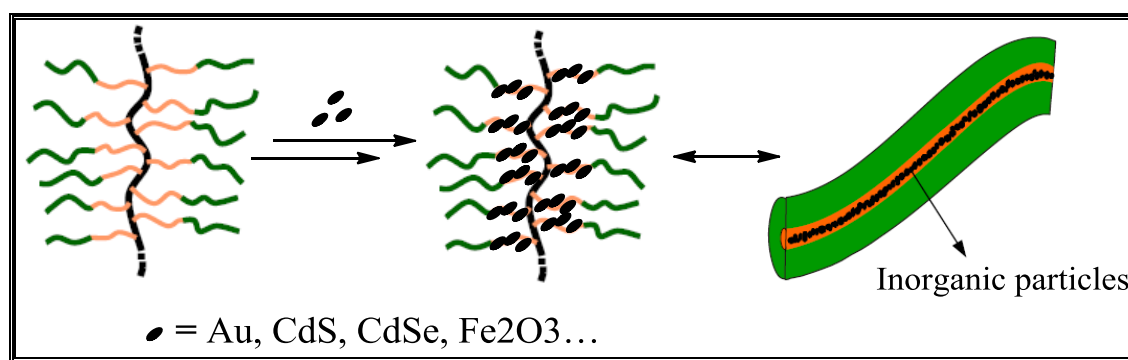
Figure 2. 4: Illustration of Co-Sh MBs forming hybrids nanoparticles.[58]

The advantage of this approach is that templates are synthesized via controlled techniques, which allow precise control over the template dimensions (*i.e.* length and diameter) as well as the position of the host-forming compartments within the templates. Consequently, the inorganic nano-particles can be easily directed towards the core or the shell.

Schmidt *et al.*[59] were the first to employ this approach to prepared hybrid nano-materials. Co-Sh MBs consisting of PVPy as the core and PSt as the shell were utilized as templates for gold (Au) nano-wires. The PVPy core can selectively be used as a nano-reactor to accommodate the gold precursor ($HAuCl_4$). Subsequent reduction of the gold salt ($Au^{3+} \rightarrow Au^{0}$) via UV irradiation produces gold nano-wires. Based on this strategy, Müller and coworkers[58, 60] have succeeded in the synthesis of various organic/inorganic hybrid nano-wires. Initially, the Co-Sh MBs templates, which consist of PAA and P*n*-BA as core and shell respectively, were synthesized. The PAA in the core was then neutralized with NaOH (*i.e.* to increase the coordination efficiency with the metal ions) followed by introduction of the metal ions through an ion exchange process and subsequent chemical treatment to produce the corresponding hybrid nano wires. The same templates have been used to fabricate hybrid nano-wires that include, semiconducting (*e.g.* CdS),[61] superparamagnetic (*e.g.* iron oxides),[50, 62] and titania[63] among others.[64]

Moreover, the same group prepared different templates, based on Co-Sh MBs for organo/silica hybrid nano-wires, via a slightly modified procedure. In this case, the MB templates are made up of poly(ε-caprolactone) (PCL) as the core and poly[2-(dimethylamino) ethyl methacrylate] (PDMAEMA) as a polycationic shell. The formation of silica nano-wires was achieved by loading the shell-forming segments with silica precursor, namely tetramethyl orthosilicate (TMOS) and by subsequent hydrolysis and condensation.[65] In addition, water-soluble MBs with silicate precursor-contain segments were also prepared, these nano-wires serve as *in situ* templates for the pyrolytic formation of purely inorganic silica nanowires in the core or shell-forming segments. The silicate-containing compartments can be converted into continuous silsesquioxane ($R–SiO_{1.5}$) domains.[66, 67]

Macromolecular self-assembly as a bottom up approach to fabricate novel nano-materials displays a powerful strategy to fulfill the need of today's advance technologies. Unlike top-down approach, which requires in some cases high temperature and pressure, bottom-up approach offers a relatively easy and efficient approach (e.g. low energy consumption) to generate

materials for a wide range of applications including nanotechnology, and drug delivery. The self-assembly of many macromolecules has become a very active and popular field of study in recent years. However, the self-assembly of some macromolecules, with interesting structure like hetero-arm MBs, has rarely been investigate. This could be due to the difficulties associated with the synthesis of such macromolecules. In this study the self-assembly of hetero-arm MBs provide was investigates. The following two chapters describe the initial approaches used in this field.

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Chapter 3: Towards Alternating Hetero-Arm MBs: Synthesis of Building Blocks

Abstract

In this chapter, the experimental methods used to synthesize the building blocks (monomers and macromonomers) of alternating hetero-arm MBs are described. It also shows the challenges and restrictions we faced during the course of this study.

Introduction

As was stated in Chapter one, MBs can be synthesized via three approaches, namely: grafting onto, grafting through and grafting from. These techniques have been used successfully to synthesize MBs with different chemical structures and grafting densities.[1, 2] Due to the limitations associated with each of these techniques, as well as due to the restrictions associated with this study, *i.e.* the desire to create an alternating backbone and hetero-grafted side chains, a combination of these techniques was essential to arrive at the desired molecular structure and hence morphology.

The challenges of this study are to synthesize **alternating** (different backbone repeat units) **hetero-arm** (different side chains) MBs. These challenges limit the choice of monomers that can be used to synthesize the alternating copolymer backbones. Apart from the alternating character, the use of monomers that allow the copolymer to be converted into the eventual MB is essential.

So, the first challenge is to synthesize MBs with an alternating backbone. Generally, alternating copolymers can be synthesized via two ways. The first option is, via copolymerization of a strong electron-acceptor (*e.g.* maleic anhydride (MAnh)) with an electron-donor (*e.g.* styrene) monomer. The second alternative is, via copolymerization of weak electron-donor and electron acceptor monomers such as methacrylates and styrene or its derivatives in the presence of a Lewis acid.[3] The Lewis acid enhances the alternating tendency through a complexation mechanism during the copolymerization reaction. In the present study, use is made of the well-established alternating tendency between vinyl benzyl and maleimide monomers, the first approach.

The other challenge is the attachment of the SCs of different nature to the alternating backbone. To overcome this challenge, two grafting strategies are used. First, a combination is used of "grafting through" with "grafting onto" approaches and second, a combination is used of "grafting through" with "grafting from". For this purpose, the monomers and/or macromonomers have to be chosen carefully. They should have a high tendency towards alternation during the copolymerization reaction, and they should have functional groups that are tolerant to the relevant polymerization conditions. The monomer pair of choice, which fulfils these requirements, is *N*-substituted maleimide and *p*-substituted styrene. This monomer combination

has extensively been studied and it has been proven that they have a strong tendency to form alternating copolymers with limited influence of their substitution moieties.[4-6]
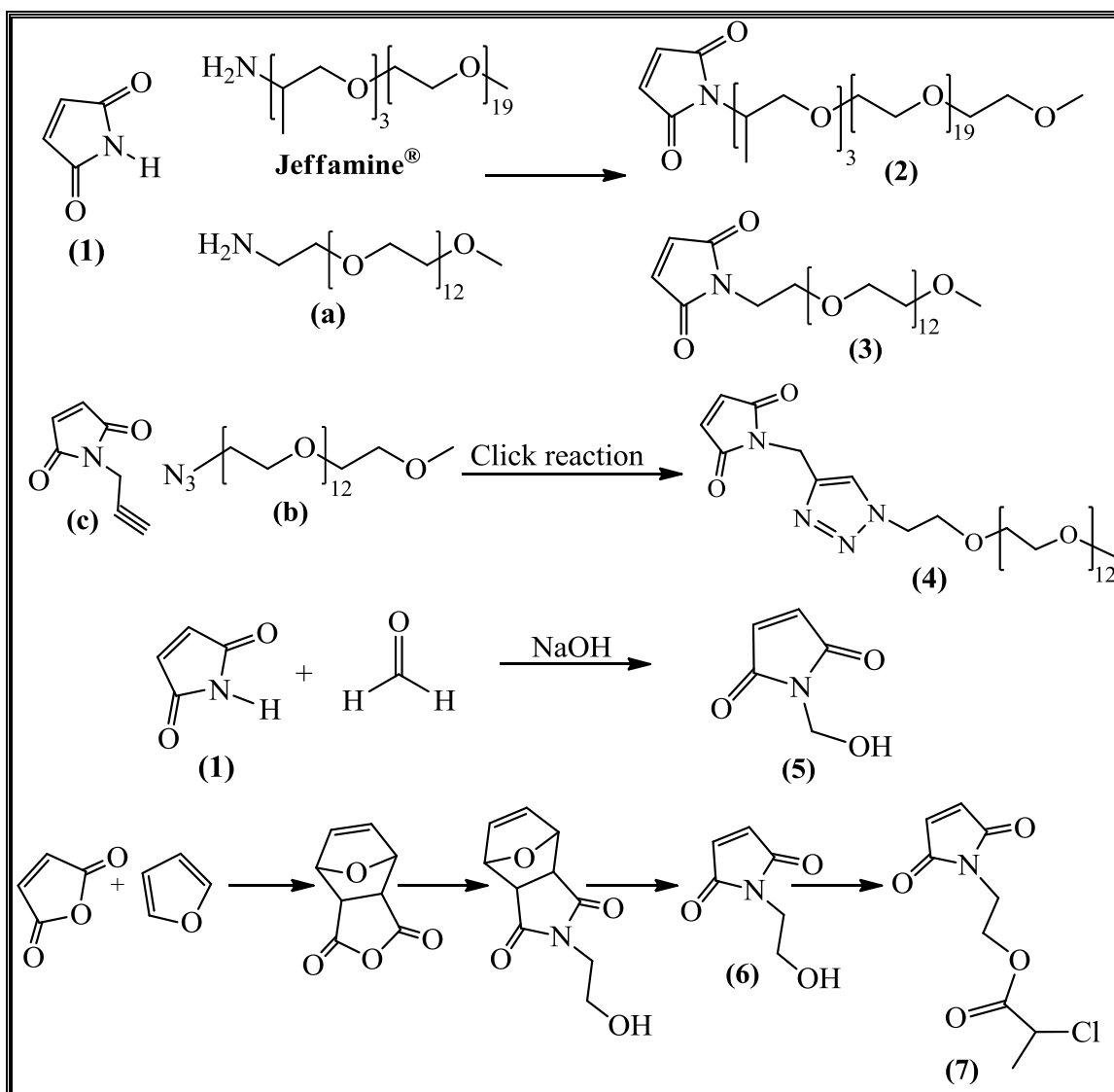
Scheme 3.1: Synthetic approaches for monomers and macromonomers used during initial stages of this study.

The initial idea was to synthesize maleimide-based macromonomers that can copolymerize with *p*-substituted styrene to give an alternating copolymer. This was expected to result in copolymers that contain SCs and sites amenable for additional grafting, alternatingly distributed along the main backbone. These latter sites can then be used to generate the second SCs. Many challenges were faced in the synthesis of the maleimide-based macromonomers. A number of different

methods were used to prepare maleimide-based monomers and macromonomers as indicated in Scheme 3.1.

For example, attempts were made to synthesize *N*-PEG-maleimide macromonomer (**2**) and (**3**) starting from maleimide and either *N*-Jeffamine® or PEG-NH$_2$ (synthesized) respectively. The yields and functionalization efficiencies were very low besides the difficulty experienced during the purification steps. The synthesis of macromonomer (**4**) was attempted, which makes use of the high efficiency of the Huisgen 1,3-dipolar cycloaddition, also called "click reaction"[7]. Although the starting materials were synthesized (*i.e*. *N*-propargyl-maleimide (a) (yield ~ 35%) and PEG-N$_3$ (b), the synthesis of the macromonomer via the click reaction failed. It seems that the click reaction in this specific case was not selective. The azide moiety seems to be quite reactive towards the maleimide ring. ^{1}H NMR spectroscopy revealed that the maleimide double bond disappeared completely.

After many unsuccessful attempts, the attention was shifted to a different approach in which maleimide-based monomers with specific functional groups were prepared, instead of macromonomers. This approach started with the synthesis of *N*-methylol-maleimide (**5**), and *N*-[2-hydroxy ethyl] maleimide (**6**) in high yield and purity. However, the copolymerization of these monomers with VB-PEG$_n$ (**11** see Scheme 3.3) macromonomer, gave an insoluble gel irrespective of the polymerization conditions (*i.e*. solvent, temperature and concentrations). The same results were obtained when (**7**) used. This phenomenon could be explained by some kind of interactions that take place alongside the polymerization process. For example, intra- or intermolecular interactions of the hydroxyl groups (-OH) with the imide fragment (O=C-N) of the maleimide ring could lead to the formation of intra- or intermolecular complexes. Such behaviour was also observed for similar systems.[8, 9]

Interestingly, when *N*-(hydroxyphenyl) maleimide *N*-(HPh)-MI (**10,** see Scheme 3.2) was copolymerized with VB-PEG$_n$ under similar conditions used for monomers (**5**) and (**6**), no gel formation was observed. It seems that the phenyl moieties block the -OH groups from reaching the imide fragments and hence no intra- or intermolecular complexation could take place. This could explain the difference in gel-formation rate of the two other monomers. For example, when the (-OH) groups move freely as in monomer (**5**) (*i.e*. only one carbon atom between the –OH and the –N-C=O) the gel starts to form within 5 minutes, whereas it takes 2 hours in the case of

Chapter 3: Towards Alternating Hetero-Arm MBs: Synthesis of Building Blocks

monomer (**6**). No gel formation was observed when the movements are restricted by the stiff phenyl groups. The following section describes the synthetic procedures used to prepare the (macro)-monomers that were used successfully to prepare alternating MBs.

Experimental section

Materials

4-Chloromethyl styrene (4-CMS, 90% Aldrich) was used as received. Poly(ethylene glycol) methyl ether (PEG-OH, $M_n \sim 550$ g/mol and $M_n \sim 750$ g/mol, Aldrich) was first azeotropically dried by toluene. Sodium hydride (60% dispersion in mineral oil, Aldrich), 1,4-dioxane (anhydrous 99.8% Aldrich); *n*-butyl amine (99.5% Aldrich), *n*-dodecyl amine (98% Aldrich), and *n*-hexadecyl amine (98% Aldrich) were used without further purification. Maleic anhydride (MAnh) (Acros organic 99%) was recrystallized from toluene and then purified further by vacuum sublimation at 55 °C and stored under argon at room temperature. 2,2'-Azobisisobutyronitrile (AIBN, Riedel de Haën) was recrystallized from methanol and dried under vacuum. Tetrahydrofuran (THF) (Aldrich) was purified first by stirring over NaOH, and then distilled from sodium/benzophenone, and stored over molecular sieves. Phosphorus pentoxide (P_2O_5) was used as received. Distilled deionized (DDI) water was obtained from a Millipore Milli-Q purification system.

Measurements

Nuclear magnetic resonance spectroscopy (NMR)

Proton NMR (^{1}HNMR) and carbon-13 NMR (^{13}CNMR) spectra were collected from Varian 300MHz VNMRS NMR instrument, Varian 400MHz UNITY INOVA NMR instrument equipped with a Varian magnet (7.0 T), or a 600 MHz Varian Unity Inova spectrometer equipped with an Oxford magnet (14.09 T). Depending on the solubility of the synthesized compounds various deuterated solvents were used including, deuterated chloroform ($CDCl_3$), deuterated *N,N*-dimethylformamide DMF-d^7, deuterated acetone-d^6, and deuterated dimthyl sulfoxide (DMSO-d^6). All chemical shifts were reported in ppm downfield from tetramethylsilane (TMS), used as an internal standard ($\delta = 0$ ppm).

Fourier transmittance infrared

Fourier transform infrared (FTIR) spectra were recorded on a Nexus FTIR spectrophotometer equipped with a Smart Golden Gate attenuated total reflectance (ATR) diamond from Thermo Nicolet with ZnSe lenses. Each spectrum was scanned 32 times with 4.0 cm^{-1} resolution and data analysis was performed with Omnic Software version.

Size Exclusion Chromatography (SEC)

N,*N*-Dimethylacetamide-size exclusion chromatography (SEC-DMAc)) analysis was carried out on a DMAc solvent system using a flow rate of 1.0 mL/min. The instrument setup consisted of a Shimadzu LC-10AD pump, a Waters 717Plus autosampler, a column system fitted with a 50x8 mm guard column in series with three 300x8 mm, 10 μm particle size GRAM columns (2 x 3000Å and 100Å) obtained from PSS, a Waters 2487 dual wavelength UV detector and a Waters 410 differential refractive index (DRI) detector all in series. 100 μL injection volumes are sampled individually with the oven temperature of the column and DRI detector kept at 40 °C. The solvent was stabilized with 0.05% BHT (w/v) and 0.03% LiCl (w/v), and samples were filtered through a 0.45 μm GHP filter to prevent any impurities entering the system. Calibration was done using PMMA standards (Polymer Laboratories) ranging from 690 to 1.2*10^6 g/mol. Data acquisition was done using Millennium32 software, version 4.

1,1,1,3,3,3-hexafluoro-2-propanol-size exclusion chromatography (SEC-HFIP) was measured on a system equipped with a Waters 1515 Isocratic HPLC pump, a Waters 2414 refractive index detector (40 ℃), a Waters 2707 autosampler, a PSS PFG guard column followed by 2 PFG-linear-XL (7 μm, 8*300 mm) columns in series at 40°C. Hexafluoroisopropanol (HFIP, Biosolve) with potassium trifluoro acetate (3 g/L) was used as eluent at a flow rate of 0.8 mL min-1. The molecular weights were calculated against polymethyl methacrylate standards (Polymer Laboratories, Mp = 580 Da up to Mp = 7.1*10^6 Da).

Scanning Electron Microscopy (SEM)

SEM analysis was carried out on a Nova NanoSEM with a Field Emission gun manufactured by FEI. The samples (on the mica or glass plates) were placed glued on the SEM grid and coated with a layer of gold-palladium or carbon to induce contrast and reduce charging of the sample.

Fluorescent Microscopy

Samples for fluorescence microscopy were observed on an Olympus Cell system attached to an IX-81 inverted fluorescence microscope. The microscope was equipped with a F-view-II cooled CCD camera (Soft Imaging Systems), using 572 nm excitation and UBG triple band pass emission filter. For the z-stack image frames, an Olympus Plan Apo N 60x/1.4 oil objective and the Cell imaging software have been used for the image acquisition and analysis.

Transmission Electron Microscopy (TEM)

The analyses were performed on a FEI Tecnai G2 20 TWIN with a Gatan Tridiem 863 energy filter with a built-in CCD camera microscope, operating with an accelerating voltage of 120 kV. Each sample was analyzed at different areas on the copper grid to obtain representative images.

Synthesis of monomers and macromonomer

Synthesis of N-hydroxyphenyl-Maleimide (N-HPh-MI) (10).[10]

N-(HPh)-MI (10) was synthesized in two steps as follows. MAnh (30 g, 0.306 mol) was dissolved in anhydrous DMF (150 mL) in a 500 mL 3-neck flask under argon atmosphere. Then, 4-amino phenol (29.76 g, 0.272 mol) in DMF (100 mL) was added over 60 min, and the mixture was allowed to stir for six hours at room temperature. Thereafter, a solution of phosphorus pentoxide P_2O_5 (15.50 g, 0.109 mol) and sulphuric acid (6.5 g, 0.066 mol) in DMF (100 mL) was added slowly. The solution was brought to 95 °C and allowed to stir for 12 hours. After cooling to room temperature, the reaction mixture was poured in ice water, followed by extraction with diethyl ether (at least 5 times). The organic layers were collected, washed with water and the solvent was removed to give the crude product as a yellow solid. The crude product was recrystallized from isopropanol to yield 35.7 g of bright yellow crystals (70 %),^{1}H NMR spectrum of *N*-(HPh)-MI is given in Appendix C.
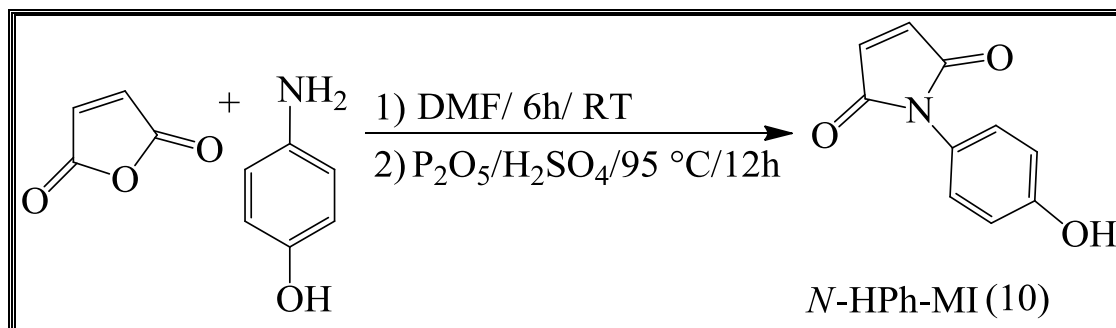
Scheme 3.2: synthesis of *N*-hydroxy phenyl maleimide (*N*-HPh-MI)

## Synthesis of 4-vinyl benzyl-(poly ethylene glycol) (VB-PEGn)

The macromonomer (VB-PEGn) was prepared according to a literature procedure.[11] A dry three-necked, 500 mL flask under argon atmosphere was charged with sodium hydride (1.31 g, 54.54 mmol) and dry THF (50 mL). The flask was placed in an ice bath before a solution of PEG-OH (10 g, 21.82 mmol) in THF (50 mL) was added drop wise over 2 hours. The mixture was stirred under argon atmosphere at room temperature for 24h. Thereafter, the mixture was cooled with an ice bath and a solution of *p*-CMS (8.31 g, 54.54 mmol) in dry THF (50 mL) was added drop wise. The mixture was stirred under argon atmosphere for 24h. The solvent was evaporated and the reaction was quenched with DDI H_2O cautiously at 0 °C. The water layer was extracted with CH_2Cl_2 (4 × 100 mL), and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated until most of the CH_2Cl_2 was removed. The residue was precipitated from cold ether three times, dried under vacuum and kept refrigerated. The product (8 g) was recovered as a pale yellow viscous liquid (yield: 80%, purity > 96 % by NMR, (^{1}H NMR spectrum of VB-PEG$_{12}$ and VB-PEG$_{17}$ are shown in Appendix A and B respectively)). ^{1}H NMR (400 MHz, CDCl$_3$) δ = 3.35 (s, 3H, OCH$_3$), 3.60 (m, OCH$_2$CH$_2$-PEG), 4.52 (s, 2H, CH$_2$O), 5.20 (d, *J* = 10.9, 1H CH$_{vinyl}$) 5.70 (d, *J* = 17.6, 1H CH$_{vinyl}$), 6.67 (dd, *J* = 10.9 and 17.6, 1H, CH$_{vinyl}$), 7.31 (dd, 4H, CH$_{aromatic}$). The degree of functionalization was determined using ^{1}H NMR and proved to be quantitative within the accuracy of the measurement.
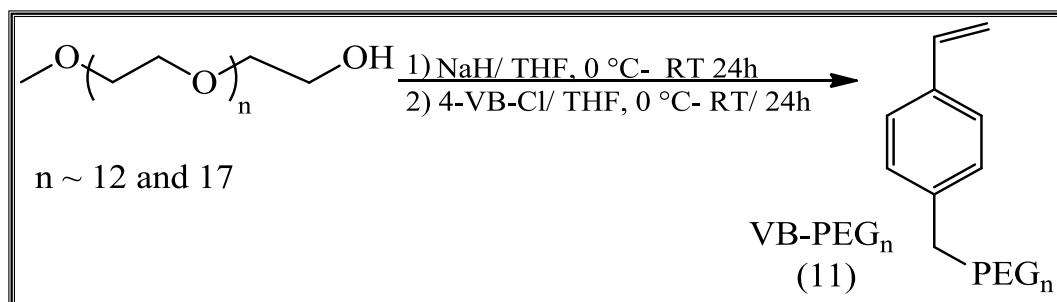
Scheme 3.3: Synthesis of VB-PEG$_n$ (**11**)

Synthesis of *N*-alkyl-maleimide (*N*-C$_n$H$_{2n+1}$-MI), n= 10, 16 and 20[12]
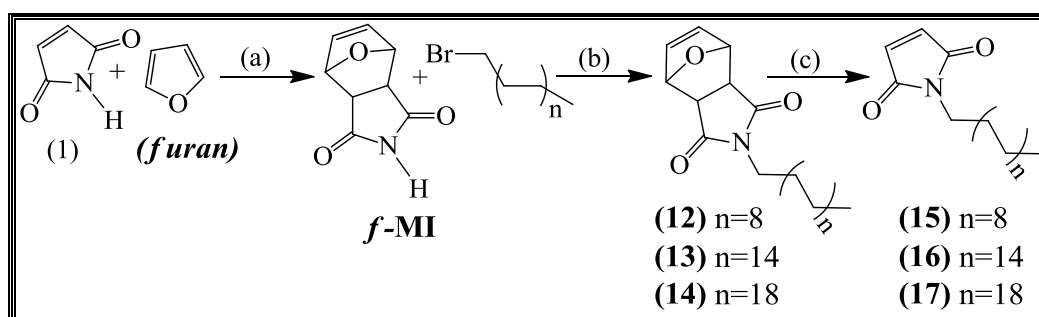
Scheme 3.4: Schematic illustrations of the synthetic routs used to prepare *N*-dodecylmaleimide (15 yield ~90%); *N*-hexadecylmaleimide (16, yield ~ 80%)) and *N*-icosylmaleimide (17, yield ~ 65%): conditions: (a) Toluene, 90 °C, 12h, (b) K$_2$CO$_3$, DMF, 50 °C, 3h, ~ 80%; (c) toluene reflux, 10 h.

Maleimide (3.00 g, 30.9 mmol) and furan (4.20 g, 46.35 mmol) were mixed in 50 mL of toluene in a 250 mL round bottom flask and heated to 90 °C for 12 hours. The product (*f*-MI) precipitated as white crystals that were collected by filtration and washed with cold diethyl ether (3×50 mL). The white crystals were then dried under vacuum for 4 hours and used without further purification (obtained 4.25 g, 82 %).

The macromonomers were prepared using different alkyl bromines *i.e*. 1-bromododecane (n=10), 1-bromohexadecane (n=16), and 1-bromoicosane (n=20). In a representative reaction

N-dodecylmaleimide (12) was synthesized as follows. In a dry 100 mL round bottom flask *f*-MI (2.8 g 16.69 mmol) and K$_2$CO$_3$ (6.0 g, 43.9 mmol) were mixed in dry DMF (50 mL) (in the case of 1-bromoicosane (n=20), toluene (15 mL) was added to assist dissolution of the bromide), before a solution of 1-dibromododecane in DMF (11.25 g 50.8 mmol in 15 mL) was added. The mixture was heated to 50 °C for 3 hours (6 hours for n=16 and 20). Thereafter, diethyl ether (150

mL) was added, followed by a careful addition of 5% HCl (50 mL). The mixture was washed with water (3×200 mL). The organic layer was collected and dried with magnesium sulphate and evaporated to dryness. The crude product was purified by liquid column chromatography (20% EtOAc/hexane) to isolate the furan-protected dodecylmaleimide (*f*-DMI) as off-white crystals (yield 3.97 g, 78%) ^{1}H NMR (400 MHz, DMSO-d^6) δ = 0.86 (m, 3H, CH$_3$); 1.15-1.34 (m, 16H, CH$_2$); 1.44 (m, 2H, CH$_2$); 2.9 (s, 2H, CH$_{ring}$); 3.33 (t, 2H, N-CH$_2$); 5.12 (s, 2H, OCH$_{ring}$); 6.55 (s, 2H, CH$_{vinyl}$).

Compound (**12**) was then dissolved in toluene (150 mL) and heated at reflux under N$_2$ flow for 12 hours. After removing most of the toluene by rotavap, the crude product was subjected to a column chromatograph using EtOAc/hexane (1:4 v/v) as the eluent, and after removing the solvents off-white crystals were obtained. ^{1}H NMR (400 MHz, CDCl$_3$, see Appendix D for the ^{1}H NMR spectrum) δ = 0.87 (m, 3H, CH$_3$); 1.24 (m, 16H, CH$_2$); 1.55 (m, 2H, CH$_2$); 3.51 (t, 2H, N-CH$_2$); 6.65(s, 2H, CH$_{vinyl}$). The *N*-hexadecylmaleimide (**16**) (yield = 4.7 g (~ 80%) ^{1}H NMR is given in Appendix E) and *N*-icosylmaleimide (**17**) (yield = 4.5 g (~ 65%) ^{1}H NMR is given in Appendix F) macromonomers were synthesized in a similar fashion.

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# Chapter 4: Amphiphilic Alternating Hetero-Arm MBs: Synthesis and Self-Assembly[a]

Abstract

This chapter describes the synthesis and self-assembly of amphiphilic alternating MBs (AMBs). These MBs consist of two different SCs, *i.e.* hydrophilic and hydrophobic. AMBs were prepared via two strategies. (I) poly[vinyl benzyl (polyethylene glycol)-*alt*-*N*-alkyl-maleimide)] [poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$))] graft copolymers were synthesized via the combination of grafting through and grafting onto approaches. This process involved the copolymerization of vinyl benzyl-terminated polyethylene glycol (VB-PEG$_{12}$) with maleic anhydride (MAnh) (*i.e.* "grafting through"). The copolymer was then modified through nucleophilic substitution (imidization) with alkyl amines (C$_n$H$_{2n+1}$-NH$_2$) on the MAnh residues (*i.e.* "grafting onto"). Three different primary amines possessing different alkyl chain lengths (*i.e.* n = 4, 12, and 16) were used. In this way, AMBs with different hydrophilic to hydrophobic ratios were obtained. (II) Similar AMBs as in approach (I) were synthesized in one step by applying the grafting through approach only. These AMBs were obtained via the copolymerization of VB-PEG$_{17}$ with *N*-(C$_n$H$_{2n+1}$)-MI where in this case n = 10, 16 and 20. The self-assembly of the obtained AMBs in selective solvents was then investigated in relation to the alkyl chain length.

[a] This chapter is largely based on the publication

Introduction

Amphiphilic molecular brushes (AMBs) are multi-component MBs possessing hydrophilic and hydrophobic SCs, densely grafted along the backbone.[1] Such macromolecules have gained significant attention because of their interesting properties in both bulk and solution, which may lead to many potential applications. The hydrophilic character is usually introduced by the presence of a water-soluble polymer as one of the SCs, e.g. PEG, while the hydrophobicity is owed to the presence of long alkyl chains or any water-insoluble polymers. When the different SCs are distributed in an alternating fashion along the backbone these MBs are generally known as hetero-arm AMBs. As a result of the high density of grafts occupying the space close by, the main chain tends to adopt an extended conformation instead of being coiled.[2, 3] In aqueous solutions, hetero-arm AMBs are expected to form cylindrical aggregates, in which the hydrophobic SCs from neighboring AMBs, aggregate to form the core of cylinders in order to hide away from aqueous environments while the hydrophilic grafts are displayed at the outside. Generally MBs are synthesized via three methods: 'grafting through', 'grafting onto' and 'grafting from'.[4, 5] However, the combination of these strategies is a common approach to overcome the complications associated with each of the individual techniques. As was mentioned in Chapter 3, the synthesis of hetero-arm AMBs is more challenging than other MBs types.
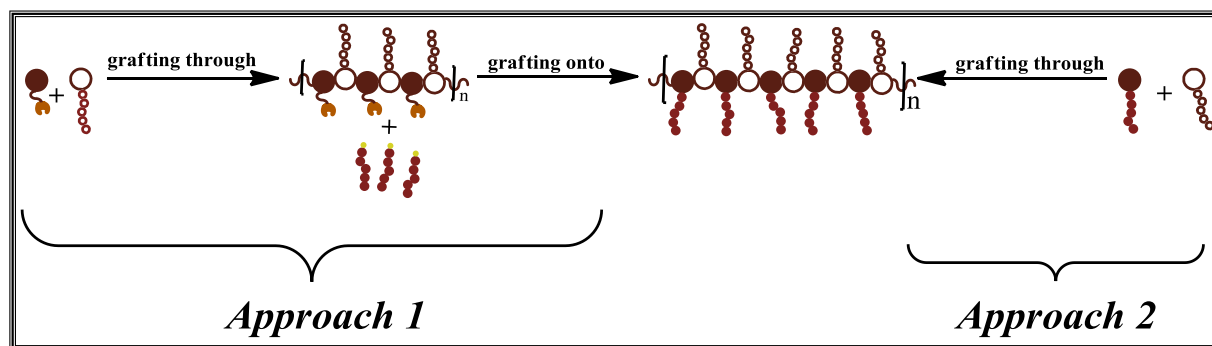

Figure 4. 1: Schematic illustration of the approaches used to prepare hetero-arm AMBs.

In this chapter, two strategies were employed to prepare hetero-arm AMBs (Figure 4.1), (1) combination of grafting through and grafting onto approaches, and (2) grafting through approach. Following the synthesis part, the self-assembly of these hetero-arm AMB in some selective solvents was investigated. The self-assembly of hetero-arm MBs is schematically illustrated in Figure 4. 2.

Approach (1): Combination of "grafting through" and "grafting onto"

As shown in Scheme 4.1, the first step involves the synthesis of MBs with hydrophilic SCs through the copolymerization of VB-PEG$_{12}$ (subscript denote the number of ethylene oxide repeat units) with MAnh. The obtained copolymer composes of water-soluble segments *i.e.* PEG, distributed on every fourth carbon atom along the backbone. In the second step, the hydrophobic SCs were introduced via nucleophilic substitution (imidization) with alkyl amines on the MAnh residues.
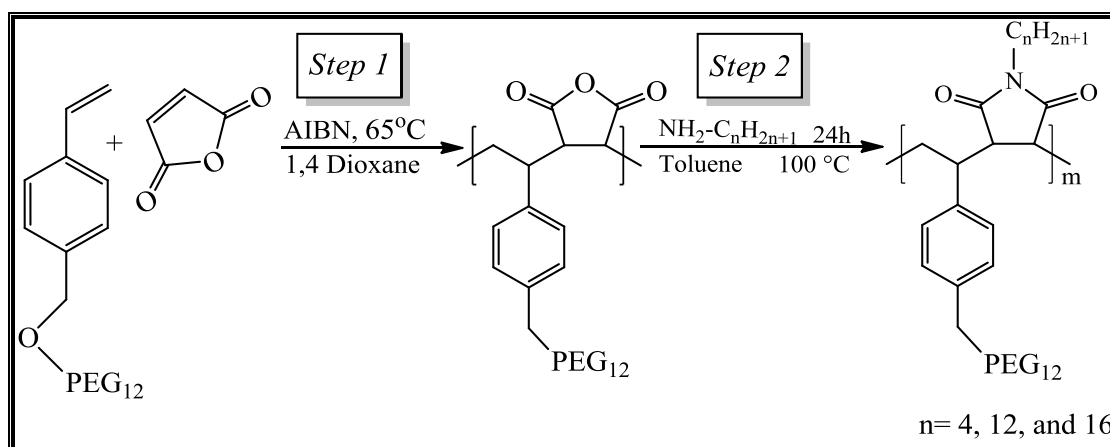
Scheme 4.1: Synthesis of hetero-arm AMBs via combination of grafting through and grafting onto approaches.

Step 1: Copolymerization of VB-PEG$_{12}$ with MAnh – "grafting through"

In a 100 mL dry Schlenk flask equipped with a stirrer bar, 1.12 g dry VB-PEG$_{12}$ (1.3 mmol), 0.13 g MAnh (1.3 mmol), AIBN (6.4 mg, 0.04 mmol) and 7 mL of dry 1,4-dioxane were charged. The mixture was degassed by three freeze-pump-thaw cycles and backfilled with argon. The flask with reaction mixture was placed in an oil bath at 65 °C with stirring for 24 h. The product was then precipitated in cold dry diethyl ether or pentane, dried under vacuum and kept as a solution in toluene, under argon atmosphere; the yield was calculated gravimetrically to be ~ 75 %. During this experiment a gel-formation was experienced after the precipitation step, which made it very challenging to characterize the obtained copolymer. Due to this phenomenon, the copolymer was used without purification in the imidization step. The gel-formation phenomenon could be attributed to the hydrolyzed of the MAnh repeat unit which generate multi-carboxylic

acid groups along the backbone. The formation of these groups enhances hydrogen bonding which causes the cross-linked polymers.

Step 2: Imidization with alkyl amines – "grafting onto"

In a dry 100 mL round bottom flask, equipped with a stirrer bar and a dropping funnel, poly(VB-(PEG$_{12}$)-*alt*-MAnh) (0.25 g, 0.26 mmol of succinic anhydride unit) was dissolved in toluene (25 mL). A solution of the primary amines (Scheme 4.1) in 10 mL toluene (2 *eq* relative to the anhydride unit) was added drop wise at RT before the flask was placed in an oil bath at 100 °C. The mixture was kept stirring for 48 h. After removing most of the toluene, the mixture was dialyzed against a water/acetone mixture (1:2 v/v%) for 1 week (*i.e.* almost every 12h on the first two days and then once a day) and then against water for 2 days. The remaining solution was then freeze-dried to give the AMBs.

Approach (2): Amphiphilic molecular brushes via "grafting through"

Copolymerization of VB-PEG$_{17}$ with N-(C_nH_{2n+1})-MI (n =10, 16, 20)

The copolymerization was carried out in a 50 mL dry Schlenk flask equipped with a stirrer bar, septum and a condenser. In a representative experiment, N-decylmaleimide (N-($C_{10}H_{21}$)-MI) (0.14 g, 0.580 mmol), VB-PEG$_{17}$ (0.50 g, 0.580 mmol), and AIBN (9.50 mg, 0.058 mmol) were dissolved in 5 mL of dry toluene. The flask was degassed by five freeze-pump-thaw cycles and refilled with Ar. The flask with reaction mixture was placed in an oil bath at 65 °C for 5 h. The polymer was then purified by precipitation from methanol before dialysis against acetone:water mixture (70:30 v/v) for 2 days, and after removing the solvents, the polymer was dried under vacuum at room temperature. After the purification process the yield was determined gravimetrically, and found to be ~ 89% for (N-($C_{10}H_{21}$)-MI) n= 10, while it was a little lower (*i.e.* ~70 %) for (N-($C_{16}H_{33}$)-MI), and (N-($C_{20}H_{41}$)-MI). The copolymerization was monitored by NMR spectroscopy to measure the monomer conversion.

R= C_9H_{19}
$C_{15}H_{31}$
$C_{19}H_{39}$
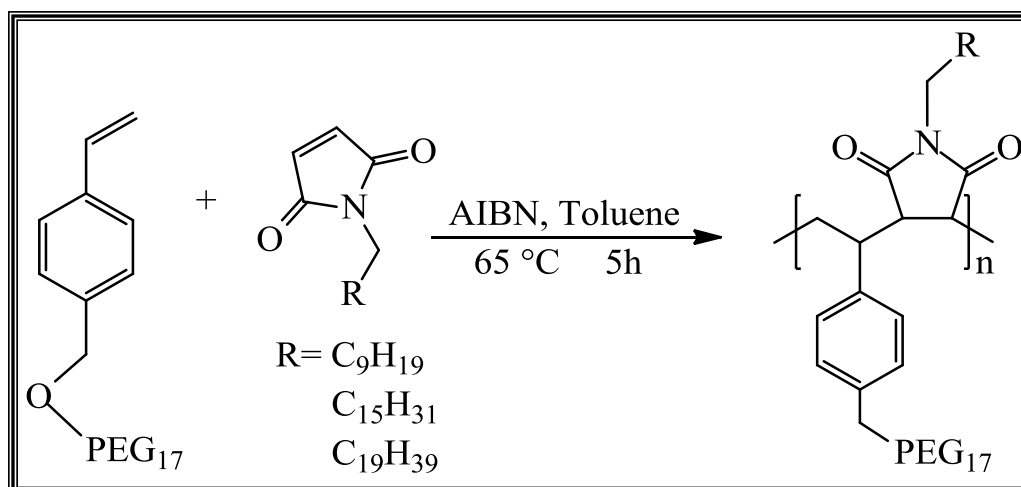
Scheme 4.2: Synthesis of hetero-arm AMBs via grafting through approach (copolymerization of macromonomers).

Self-assembly of hetero-arm AMBs in selective solvents

Two approaches have been used for the assembly of AMBs. In approach (I), the AMBs were dissolved in a good solvent for both arms, followed by the slow addition of an arm-selective solvent. This approach is similar to that used to prepare cylinder morphologies from di-block copolymers. In approach (II), the AMBs were dissolved in a solvent mixture consisting of both arm-selective and non-selective solvents followed by slow solvent evaporation. This approach was adopted by Ishizu[6] to prepare rod-like aggregates from hetero-arm MBs consisting of PEG and PSt SCs. In this approach, the good solvent should first be miscible with the non-solvent and second, should have a lower boiling point (higher vapor pressure) than the non-solvent.
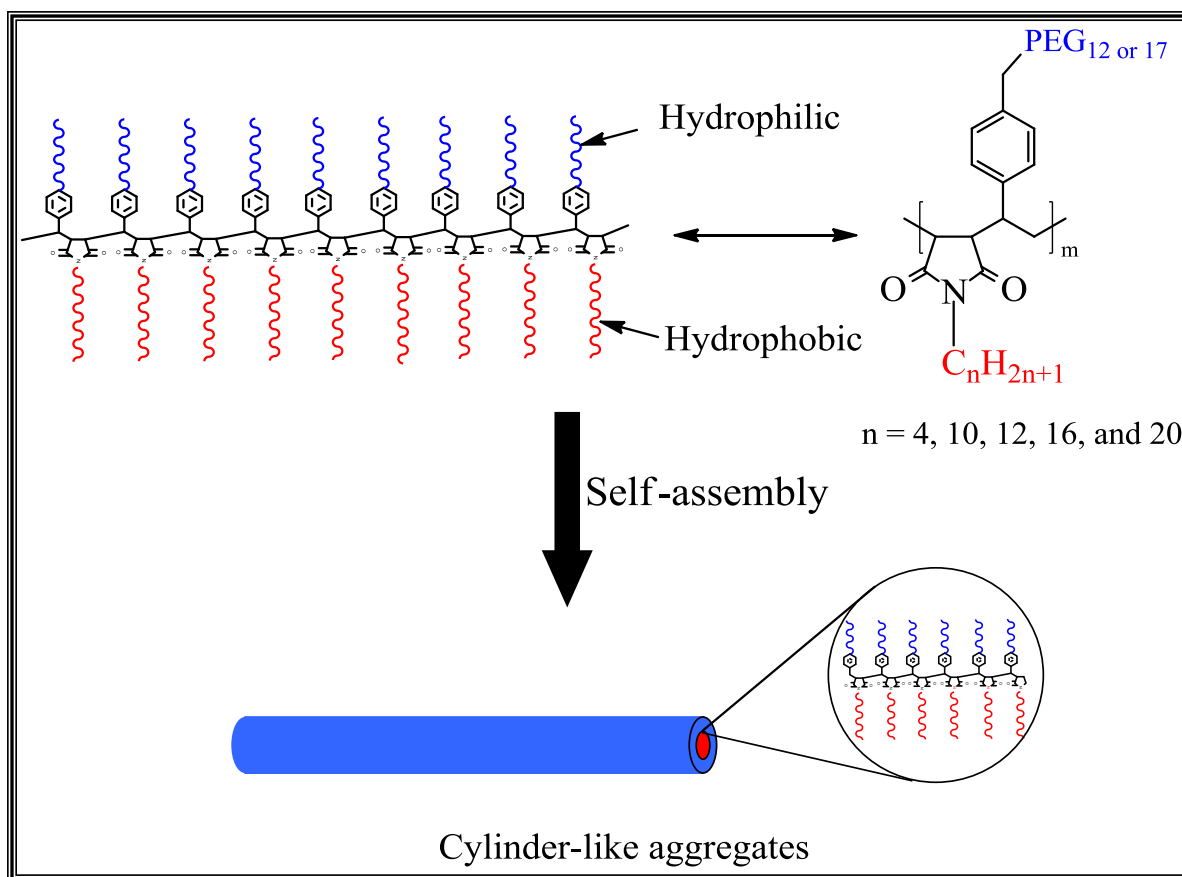
Figure 4. 2: Schematic illustration for the self-assembly of hetero-arm AMBs into cylinder-like structures

Approach (I):

In a representative experiment, a solution of AMBs in THF or DMF (good solvents) (1 mg/mL) was prepared and passed through a 0.45 µm filter. 1 mL of this solution was then added to a 20 mL glass vial, and then 4 mL of pre-filtered H_2O was added slowly with an addition rate of 0.015 mL/min. The THF was then evaporated at room temperature under N_2 flow (DMF was removed via dialysis). The SEM samples were prepared via drop casting the solution on glass plates, which were then left to dry slowly at RT under a small N_2 flow. The TEM samples were prepared by drop casting the solution (~ 20 µL) onto the carbon grid, which was allowed to sit for ~ 10 min, followed by removing the excess liquid via wicking. The remaining solvent was then let to evaporate at RT. Approximately 20 µL of solution was drop casted onto the sample, before being wicked away. The sample was allowed to air-dry overnight.

Approach (II):

5 mg of AMBs were dissolved in 10 mL of THF/H_2O (or acetone/H_2O) mixture (90:10 v/v) at room temperature. This solution was then used to prepare AMB solutions of various concentrations, *i.e.* 0.05 and 0.2 mg/mL. The solutions were passed through a 0.45 μm filter followed by drop (or spin, 3000 rpm for 5 min) casting onto a glass plate. The plates were then left to dry at room temperature over 10-14 days. The same procedure was used for all different AMBs. TEM and SEM sample were prepared in the same way as above.

Results and discussion

Synthesis of hetero-arm AMBs

Approach 1: Combination of "grafting through" and "grafting onto"

Scheme 4.1 shows the synthetic procedure used in this study to prepare AMBs. In the first step, the copolymerization of VB-PEG with MAnh was used to prepare an alternating copolymer with hydrophilic SCs and reactive MAnh units uniformly dispersed along the backbone. It is known that styrene derivatives with electron-donor groups as *para*-substituent may increase the electron density of the polymerizable double-bond, and hence favor the formation of alternating structures.[7, 8] Systems of a similar monomer pair have been reported to polymerize rapidly and alternatingly when the initial monomer ratio is equimolar. For example, Chen and coworkers[9] conducted the copolymerization of styryl macromonomers, bearing Fréchet-type dendrons, with MAnh to produce high *Mw* alternating copolymers under mild polymerization conditions.

According to the literature, the alternating sequence of the two repeat units in the copolymers can be measured by two methods. One is through determining the chemical shift of the carbon atoms of the S-MAnh repeat units along the backbones according to distortionless enhancement by polarization transfer (DEPT) spectroscopy.[10] The other method is through determining the chemical shift of the quaternary aromatic carbon "next to backbone" of the St repeat units using ^{13}C NMR spectroscopy.[11] In this study, it was very difficult to determine the alternating structure of the obtained copolymers using these methods due to the difficulty experienced in detecting the carbons on or near the backbone using ^{13}C NMR. Based on the structural similarity of VB-PEG

and the styryl macromonomers used in literature, it is most likely that the copolymerization of VB-PEG$_{12}$ macromonomer (*Mn* = 666 g/mol) with MAnh proceeds in an alternating fashion to produce strictly alternating copolymers.

The obtained alternating copolymers [poly(VB-(PEG$_{12}$)-*alt*-MAnh)] were then modified through nucleophilic substitution (imidization) with alkyl amines on the MAnh residues (Scheme 4.2, Step 2). MBs produced via the "grafting onto" approach usually suffer from low grafting density. However, it was proven to produce high grafting density in cases where an efficient coupling reaction is used and when the SCs have relatively low molecular weight.[12-14] In this study, the second SCs were introduced via the grafting onto approach through an imidization process in which the MAnh repeat units were reacted with a primary amine. Such process has been extensively studied and is known to give quantitative conversion. Three different primary amines possessing different alkyl chain lengths (*i.e. n*-butyl amine, *n*-dodecyl amine and *n*-hexadecyl amine) were used, in this way AMBs with different hydrophilic to hydrophobic ratios were obtained.

Figure 4.3 shows FT-IR spectra of the alternating copolymer before and after the modification step. The FT-IR spectrum of [poly(VB-(PEG$_{12}$)-*alt*-MAnh)] is shown in Figure 4.3 (A). The spectrum shows the expected absorbance band of both repeat units along the backbone. For example, the absorbance bands at 1784 and 1750 cm^{-1} assigned to asymmetrical and symmetrical carbonyl groups (C=O) of the MAnh. Bands at 1460, 1347, 1252 cm^{-1} were assigned to the aromatic (C=C) stretches, as well as the ether (O-C) stretch of PEG at ~ 1100 cm^{-1}. Figure 4.3 (B, C, and D) shows the FT-IR spectra of [poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$)] (n=4, 12 and 16 respectively). It can be seen that the stretch vibration signal of (C=O) (MAnh) shifts from 1750 cm^{-1} (Figure 4.3, A) to 1693 cm^{-1} (N-C=O) of MI (Figure 4.3, B, C and D). The shift to a lower wavenumber was attributed to formation of an imide bond, which confirms the successful imidization process. Figure 4.3 (B-C) also shows the appearance of a signal at around 1550 cm^{-1} (C-N) as the MAnh units were modified to MI units. The absence of absorbance at 1750 cm^{-1} in the FT-IR spectra of the modified copolymer (Figure 4.3, B-C) indicates that a high degree of imidization is achieved on the copolymer backbones.
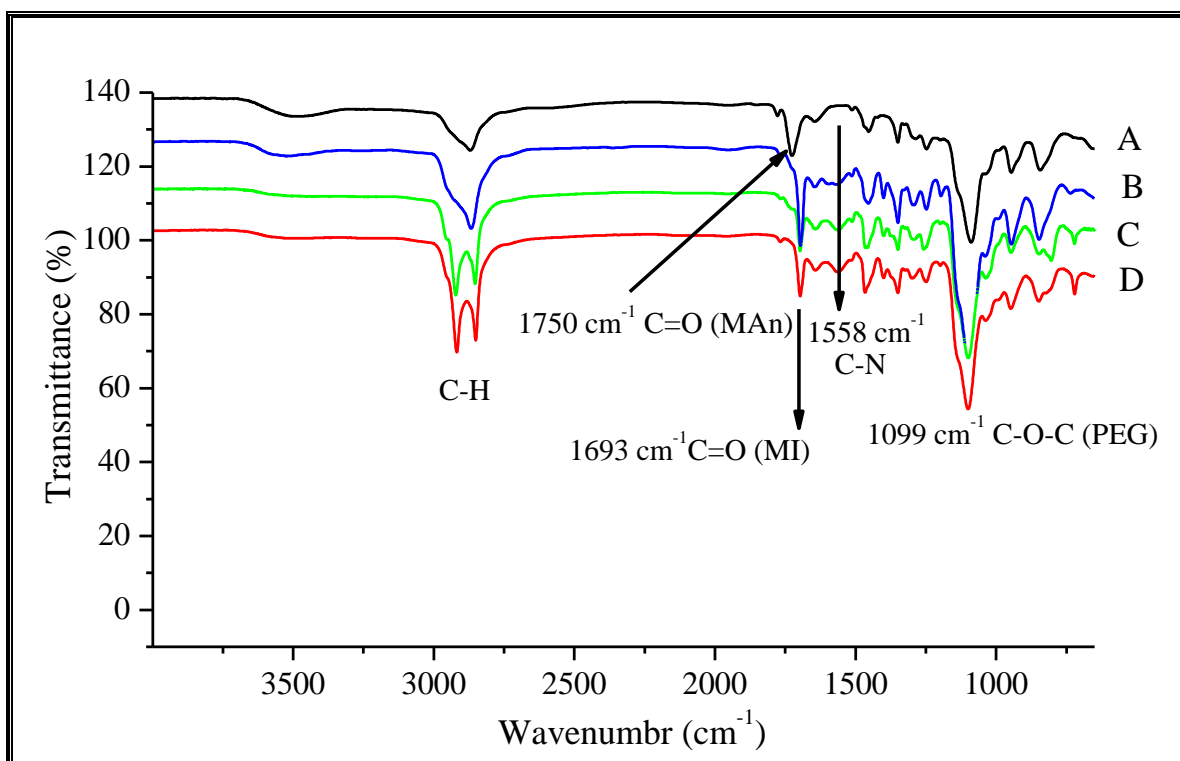
Figure 4.3: FT-IR spectra of poly(VB-(PEG$_{12}$)-*alt*-MAnh) before and after imidization with different primary amines. (A): Poly(VB-(PEG$_{12}$)-*alt*-MAnh), (B): Poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_4$H$_9$)), (C): Poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$)) and (D): Poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_{16}$H$_{33}$)).

The ^{1}H NMR spectra of alternating copolymers before and after modification are shown in Figure 4.4. In Figure 4.4 (A), no vinyl protons could be found, which is indicative of complete removal of unreacted monomers after the copolymerization. Interestingly, the protons attached to the backbone and the aromatic protons "next to the polymer chain" of VB-PEG$_{12}$ repeat units could not be detected in the ^{1}H NMR spectrum irrespective of the solvent used (acetone-*d*^{6}, DMSO-*d*^{6}, DMF-*d*^{7}), (*i.e.* only through zooming in on the spectrum, these protons could be detected as broad signals). This could be due to the stiffness of the backbone, which is a unique characteristic feature of MBs. This phenomenon is still not fully understood and still needs to be investigated further. It will be discussed briefly in the following chapter. Because of this phenomenon, NMR spectroscopy could not be used to study the microstructure of the copolymer, *i.e.* the alternating sequence of the repeat units along the backbone. However, ^{1}H NMR spectroscopy was very useful to confirm the modification process. The appearance of peaks in the region between 0.5 to the 2 ppm (Figure 4.4 B & C) indicates a successful imidization reaction and hence introduction

of the hydrophobic SCs. Once again, due to the weak peaks intensities as well as due to peak overlap, ^{1}H NMR could not be used for quantitative analysis of the obtained AMBs.
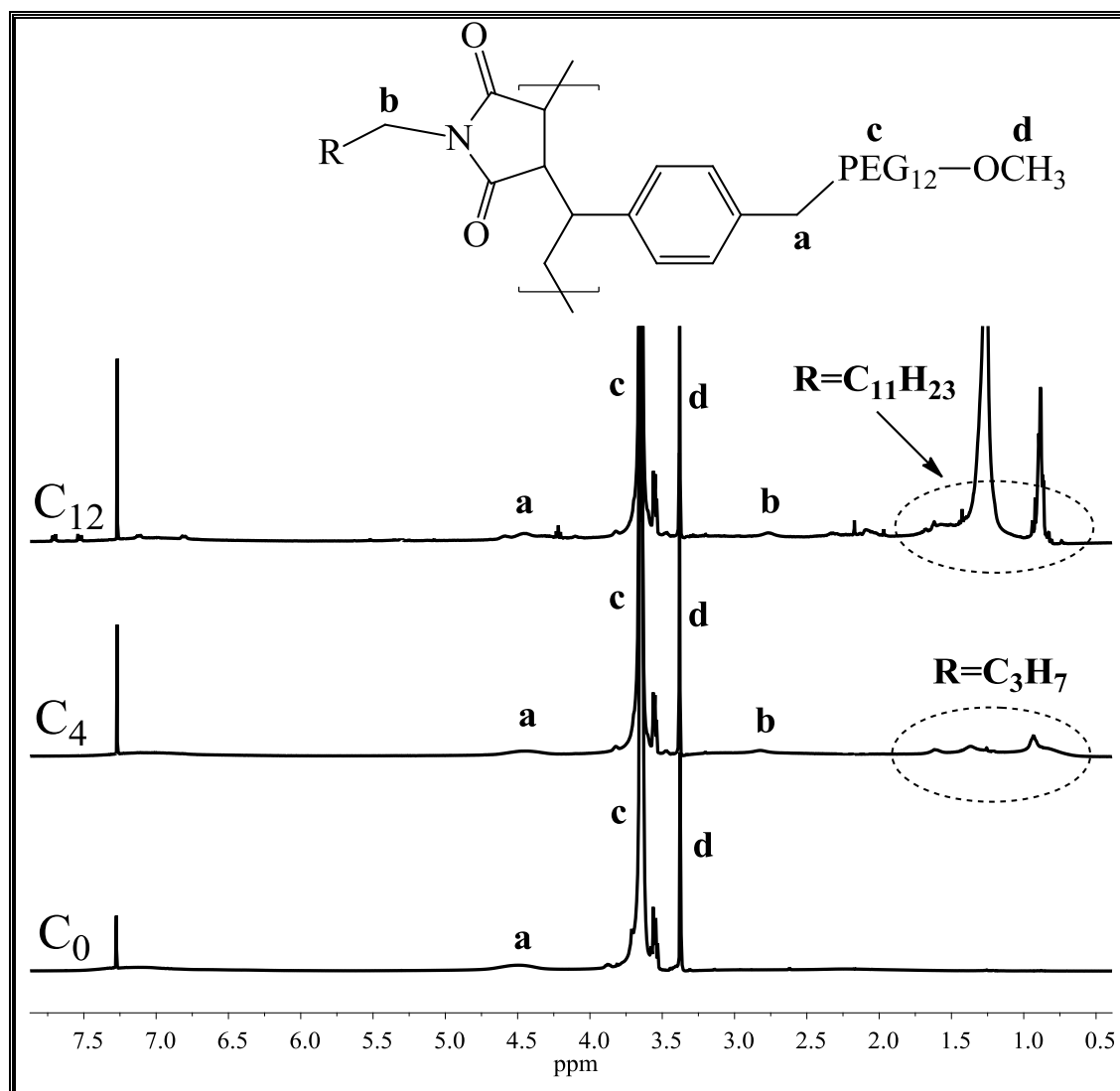
**Figure 4. 4:** ^{1}H-NMR spectra of Poly (VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$)): (C0): Poly(VB-(PEG$_{12}$)-*alt*-MAnh), C4: Poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_4$H$_9$)), C12: Poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$))

Approach (2): Amphiphilic molecular brushes via "grafting through"

Grafting through is one of the oldest and most used approaches to synthesize MBs. The advantage of this approach is that MBs with pre-determined SC length and high grafting density can be prepared in one step. However, it is generally very difficult to prepare MBs with high DP, because of the inherently low concentration of polymerizable end groups of the macromonomers and the steric hindrance of SCs. To overcome these challenges, high macromonomer

concentration may be needed to produce MBs with high DP of the backbone.[15] In addition, the use of macromonomers with short SCs and highly active polymerizable end groups may assist in producing MBs with high DP. In this study, the grafting through approach was employed to synthesize hetero-arm AMBs using styryl and maleimide-based macromonomers with relatively short SCs. This way AMBs with high DP were made in one step, which overcomes the challenges experienced when approach 1 was used. This advantage is owing to the copolymerization nature of St and MI which is well known to copolymerize rapidly and alternatingly when the initial monomer ratio is equimolar.[16, 17]

Copolymerization reactions of VB-PEO$_{17}$ with N-(C$_n$H$_{2n+1}$)-MI (n = 10, 16, and 20) were carried out in toluene under conventional conditions using AIBN as initiator. The copolymerization proceeded to high conversion ($\sim$ 89 %) within relatively short time (5 h) as indicated by NMR spectroscopy. Figure 4.5 shows the ^{1}H NMR spectra of the copolymerization of VB-PEO$_{17}$ with N-(C$_{10}$H$_{21}$)-MI before and after polymerization. The signals of each of the macromonomers before the start of the polymerization in the region of vinyl proton of the double bonds were clearly identified (proton a, b, and c) as shown in Figure 4.5 (A). However, after the copolymerization ($\sim$5 h) the signals of these protons disappeared almost completely as depicted in Figure 4.5 (B), which shows the high activity of these macromonomers in radical polymerization. The solvent signal at 2.08 ppm was used as a reference signal to measure the monomer conversion. It is noteworthy mentioning that the resonances signals of proton d (*i.e.* close to the backbone) and e (*i.e.* aliphatic SCs) in Figure 4.5 (B), were significantly broadened after the polymerization. This broadening could be explained by the high stiffness of the copolymer backbone (*i.e.* broadening of signal d) and the high Mw of the produced copolymer (*i.e.* broadening of signals e).
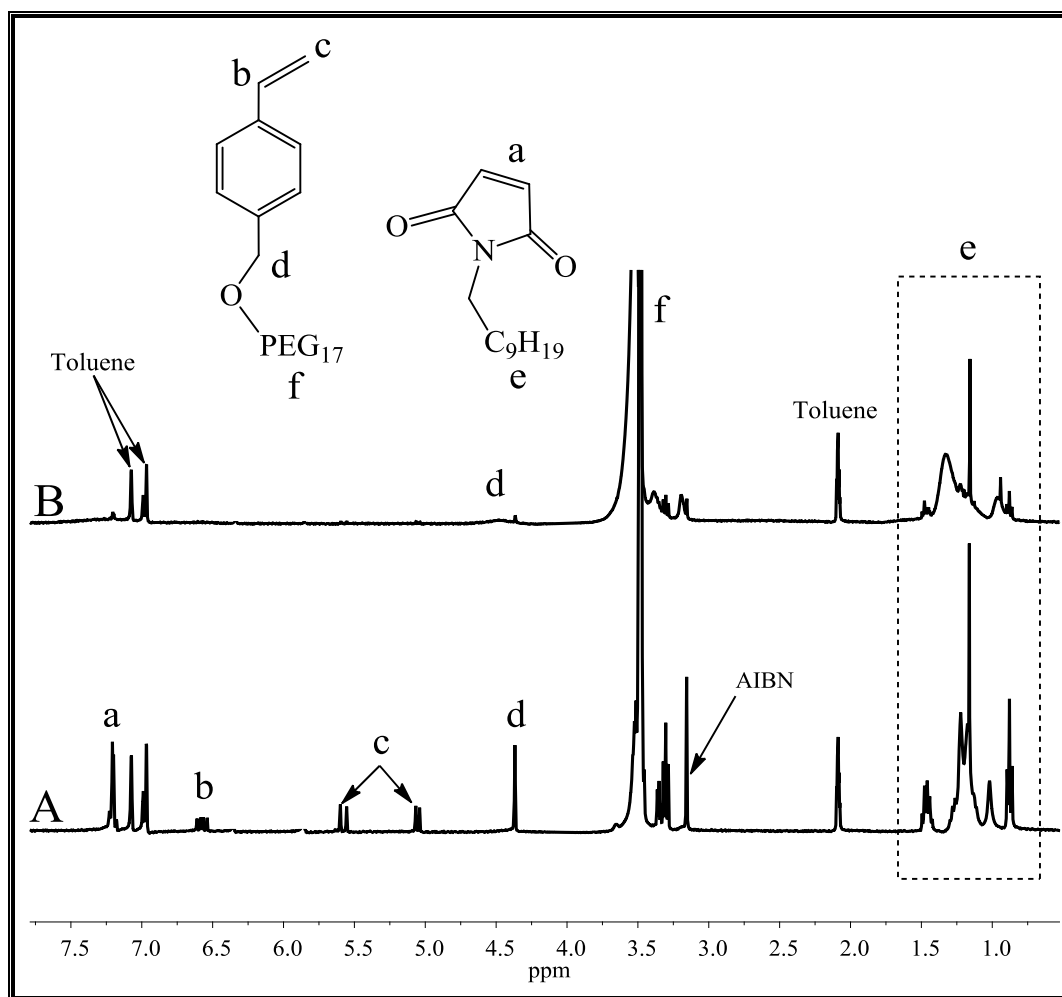
Figure 4. 5: ^{1}H-NMR spectra of the radical copolymerization VB-(PEG$_{17}$) with *N*-(C$_{10}$H$_{21}$)-MI initiated with AIBN in toluene at 65 °C, (A) before polymerization(time = 0 h), and (B) after polymerization (time = 5 h)

The obtained hetero-arm AMBs were characterized by SEC, and ^{1}H-NMR spectroscopy. NMR gave similar results to that obtained by the first approach. Once again, it was difficult to measure the microstructure of the backbone based on NMR spectroscopy due to the weak signals of protons near the backbone of the MBs. Nevertheless, the NMR spectra of all the obtained MBs show the assigned signals of both SCs (*i.e.* PEG and alkyl chains) indicating successful copolymerization of the macromonomers. During the course of this study many attempts have been made to measure the molecular weight of the AMBs obtained from both approaches using SEC in either THF or DMAc with 0.05% BHT (*w/v*) and 0.03% LiCl (*w/v*). However, in all attempts, there was clear evidence of column interaction as witnessed by peak shape and reproducibility.

This issue was one of the challenges faced during this study, and the only reliable results were obtained when SEC in HFIP was used. However, Based on the width of peaks in the ^{1}H NMR spectra as well as on the significant increase in viscosity during polymerization, there is no doubt that the polymers are of high molecular weight. The SEC results of AMBs prepared obtained in the first approach are show in Figure 4.6. The values of the obtained Mw from SEC using refractive index detection relative to PMMA standards are estimate values, and they are much lower than the real ones. The lower values of experimental Mw observed for AMBs could be due to the fact that the AMBs have lower hydrodynamic volumes than the equivalent linear standard used for calibration. As a result, the AMBs will elute later during SEC analysis compared to their linear standard.[18] As it can be seen in Figure 4. 6, the Mw values did not move to higher molecular weight significantly with increasing the aliphatic SCs. This phenomenon was reasonable, since the new aliphatic SCs were formed in the cavities of first SCs (*i.e.* PEG$_{12}$) and contributed less to the hydrodynamic volume of whole polymers.
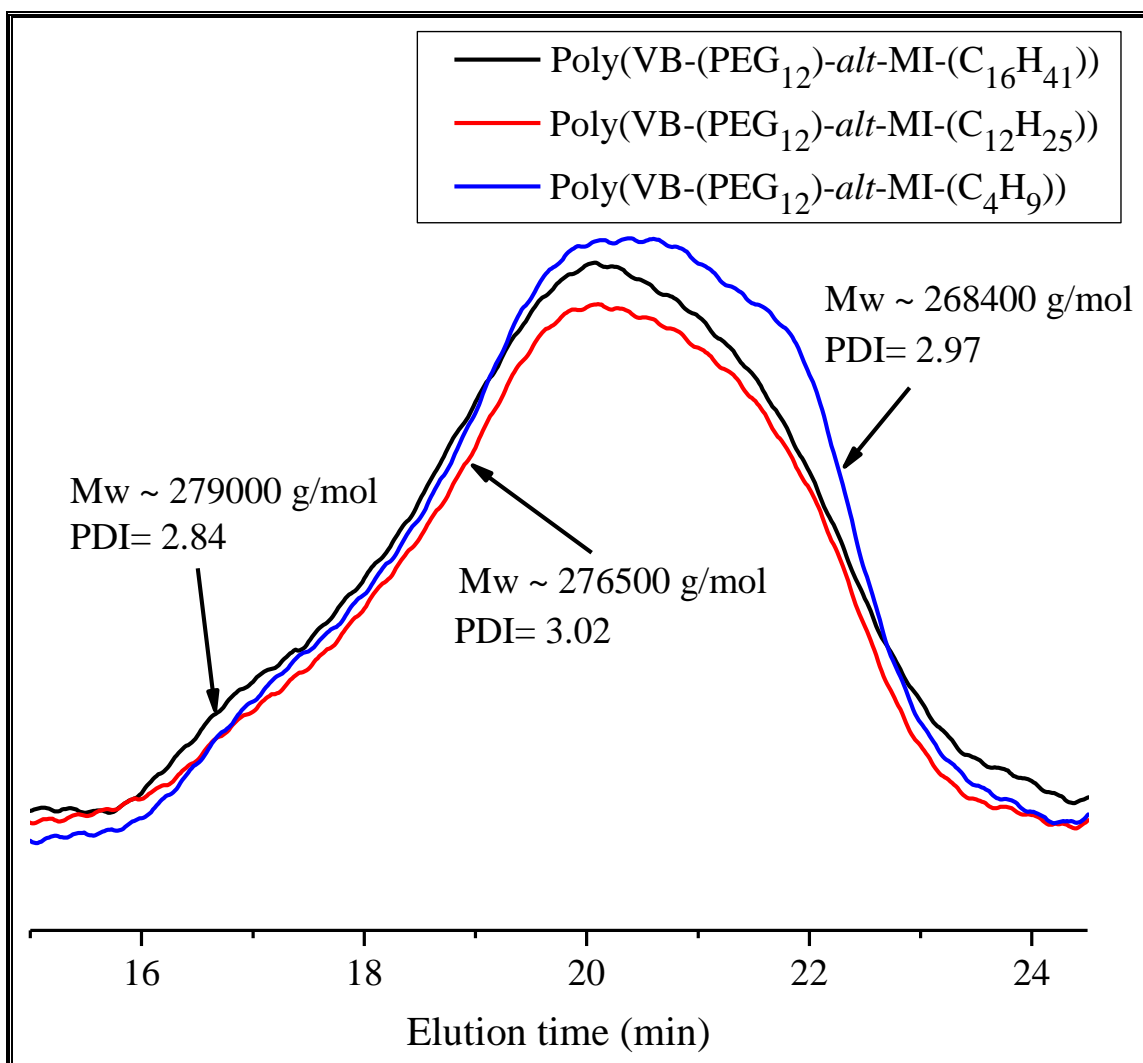
Figure 4. 6: SEC traces of poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$)): Blue: poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_4$H$_9$)), red: poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$)), and black: poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_{16}$H$_{33}$))

Self-assembly of hetero-arm AMBs in selective solvents

Despite many reports on nanotube formation from phospholipids, peptidic amphiphiles, other small-molecule surfactants and *di*-block copolymers, reports on the self-assembly of MBs in general and AMB in particular are rare. It is well known that *di*-block copolymers self-assemble into a wide range of morphologies, including spheres, cylinders, vesicles, and many other complex structures. These morphologies can usually be controlled and directed by the copolymer composition (*i.e.* ratios of the blocks) and concentration, nature and composition of the used solvents. Unlike *di*-block copolymers, the self-assembly of MBs with different SCs has rarely

been studied. In this study the self-assembly of hetero-arm AMBs in a selective solvent was investigated by the use of SEM, TEM, and fluorescence microscopy.

The synthesized hetero-arm AMBs consist of a densely grafted linear backbone with hydrophilic and hydrophobic SCs alternatingly distributed along the backbone. Based on the alternating structure of the backbone, a repeat unit can be considered to consist of one pair of the two macromonomers, with one PEO and one alkyl (between C_4 and C_{20}) SC on each repeat unit. This structure is very similar to a macromolecular brush prepared by polymerization of *di*-block copolymers (*di*-BCs) at the junction points (see Scheme 4. 3). Because of this structural similarity, it was expected that AMBs will self-assemble into interesting morphologies. Di-block copolymers self-assemble into various different morphologies. Contrarily, AMBs are expected to give cylinder like structures because of the high stiffness of the backbone as well as the limited freedom the SCs have.
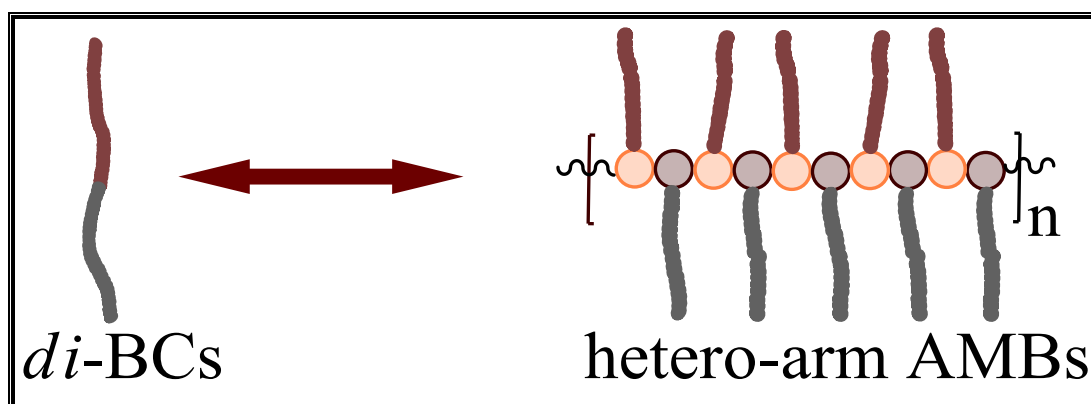
Scheme 4. 3: Schematic illustration showing the similarity between *di*-BCs and hetero-arm AMBs

Figure 4.7 gives a representation of the FE-SEM images for AMB assemblies on mica. These AMBs were prepared using the first approach (combination of grafting through and grafting onto) and consist of poly[VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$)] where n = 4, 12, and 16. Large rod-like aggregates were observed for all AMBs with different length of hydrophobic arms. These assemblies were prepared using approach (I), in which the AMBs where dissolved in THF:H$_2$O (90:10 v/v) at a concentration of 0.2 mg/mL followed by drop casting on freshly cleaved mica. AMBs seem to lead to cylindrical morphologies upon self-assembly in solution. In this system, THF is a good solvent for both arms while H$_2$O is a good solvent for only one arm *i.e.* PEG. In solution, AMBs are expected to be in their extended conformation, as both arms (hydrophilic and

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hydrophobic) are soluble. However, upon drying, the THF will evaporate at a faster rate than water, which eventually leaves the AMBs in (almost) pure water. Consequently, the hydrophobic arms of adjacent AMBs are expected to aggregate in a way that hides the hydrophobic chains from the aqueous phase. Due to the grafting density, a linear shape of the aggregates is expected. Two different morphologies would fit this criterion, *i.e.* cylindrical aggregates with a hydrophobic core (elongated micelles), and tubular aggregates with a hydrophilic inner and outer wall and a hydrophobic layer in between (elongated vesicles). A cartoon of both morphologies is depicted in Figure 4.8, where the circular (toroidal) morphology is used for clarity.
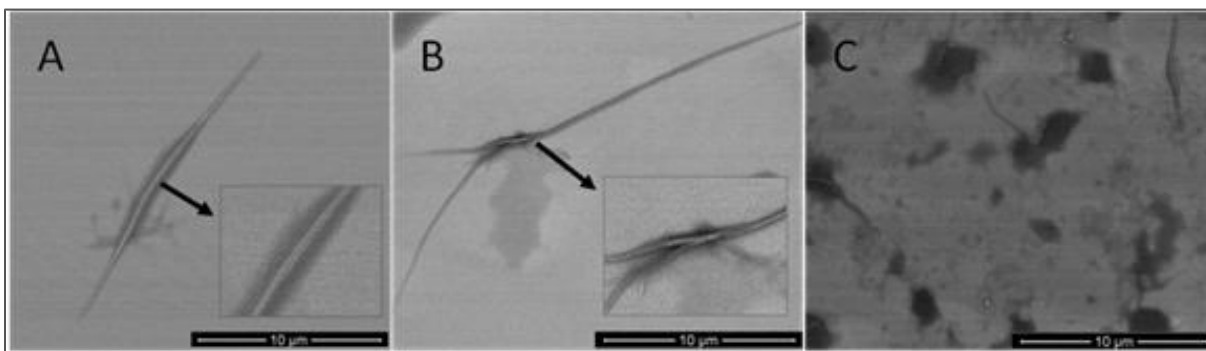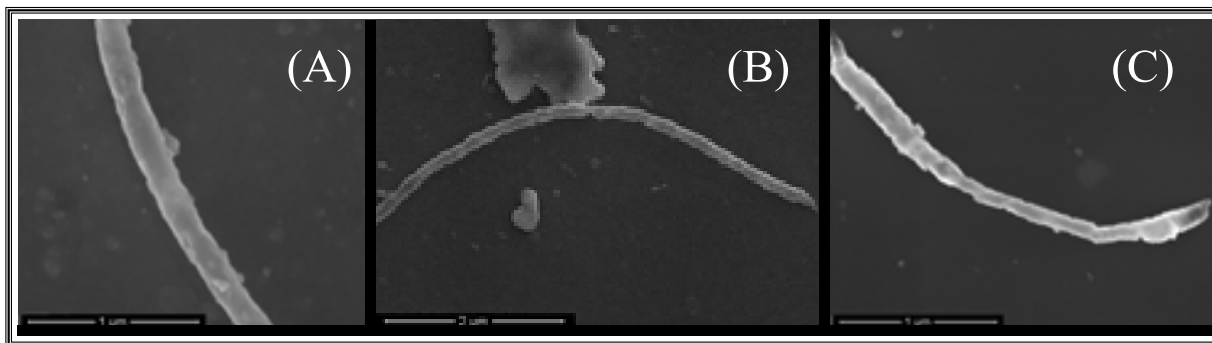

Figure 4. 7: FE-SEM photographs of aggregation products of poly(VB-(PEG$_{12}$)-*alt*-MI-(C$_n$H$_{2n+1}$)): (A) n = 4, (B) n = 12 and (C) n = 16.

Interestingly, the morphology of the aggregates is fairly similar for all the AMB-C$_4$ and AMB-C$_{12}$. The AMB-C$_{16}$ shows a quite different morphology, as the observed cylindrical aggregates are shorter as well as thinner compared to those obtained by other AMBs. This could be due to the ability of AMB-C$_{16}$ to crystallize, which restricts the movement and mobility of these molecules and hence results in smaller aggregates. The other observation about these aggregates is that the diameter (d) decreases from the center to the sides/tips of the cylinders in all AMBs. This suggests that these AMBs aggregate in the two expected morphologies within the same cylinder. In the center, (d ~ 200 nm) the AMBs aggregate in vesicle morphology (Figure 4.8 [B]) in which the number of AMB molecules is sufficient to generate such morphologies. However, at the extremes of the aggregates, the diameter narrows down to below 50 nm. The elongated micelle (Figure 4.8 [A]) is the predominant structure where the number of AMB molecules decreases and vesicle morphology is no longer feasible. The most logical explanation for this behavior is the tendency of the AMBs to minimize contact of the hydrophobic arms with the aqueous phase.
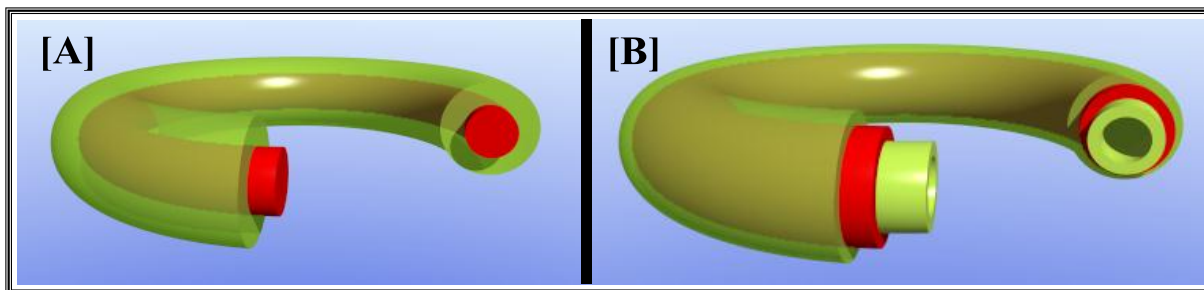
Figure 4. 8: Cartoons of self-assembled hetero-arm AMBs. [A]: elongated micelle, and [B]: elongated vesicle.

Similar elongated aggregates were obtained when hetero-arm AMBs with longer SCs were self-assembled under similar conditions as discussed above, or when approach (II) was used *i.e.* addition of the selective solvent method. Figure 4.9 shows the FE-SEM images for hetero-arm AMBs assemblies on glass.


Figure 4.9: FE-SEM photographs of aggregation products on a glass surface of poly(VB-(PEG$_{17}$)-*alt*-MI-(C$_n$H$_{2n+1}$)): (A) n = 10, (B) n = 16 and (C) n = 20.

The AMBs in Figure 4.9 consist of slightly longer CSs, *i.e.* poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_n$H$_{2n+1}$)] in which n = 10, 16 and 20. Generally, the rod-like aggregates obtained from these AMBs were shorter and less defined. For example, Figure 4.9 (C) shows the obtained structure when poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{10}$H$_{21}$)] MBs were assembled. Although the cylinder-like morphology was attained, the aggregates were less defined in diameter compared to those obtained when poly[VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$)] were used. This could be due to the mobility of AMBs during the assembly process, which facilitate and directs the assemblies into longer structures.

The obtained cylinder-like morphologies were also investigated using TEM and fluorescence microscopy. Although TEM analysis was very challenging as the samples were very difficult to prepare on the carbon coated-Cu grids as well as the poor contrast of the obtained objects as

shown in Figure 4.10, the initial images support the results obtained by SEM. Elongated aggregates were obtained from all AMBs with different SCs length. Figure 4.10 shows cylinder-like structures obtained from poly[VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$)] (image (A)), and poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{16}$H$_{33}$)] (image (B)).
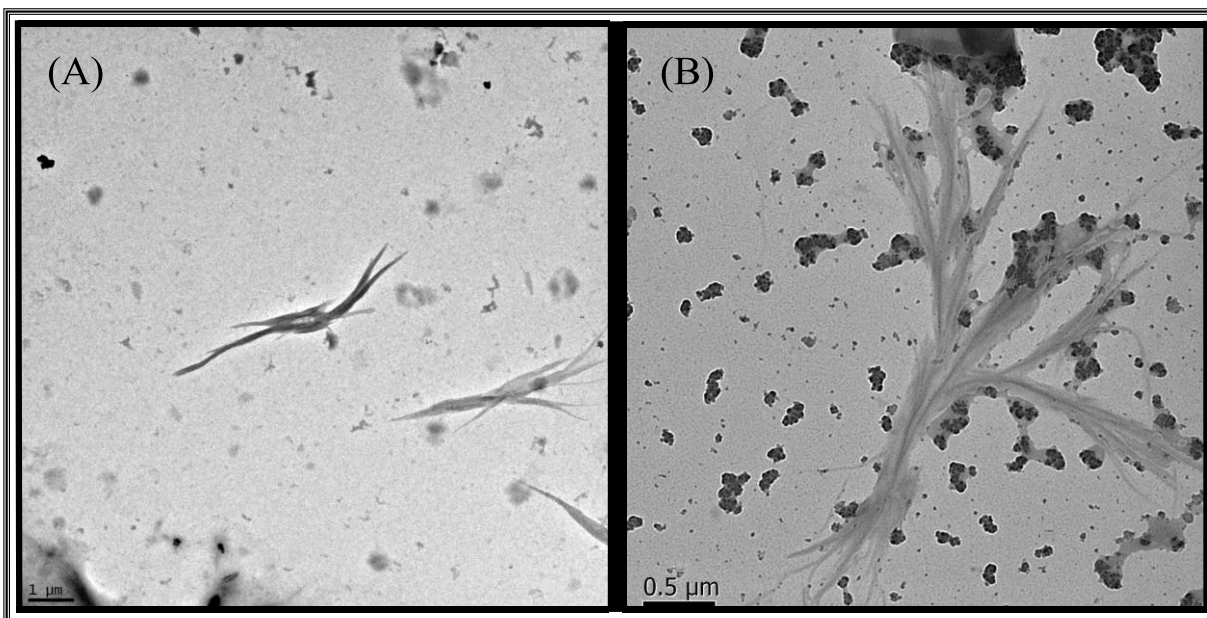

Figure 4.10: TEM images of self-assembly aggregates on mica of (A) poly[VB-(PEG$_{12}$)-*alt*-MI-(C$_{12}$H$_{25}$)], and (B) poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{16}$H$_{33}$)]

The obtained structures were also investigated using fluorescence microscopy. The purpose of this study was to investigate the position of different SCs in the aggregates. In this experiment, a solution of hydrophobic fluorescent dye (Perylene Red, Exalite 613) (15- 20 µL, 0.005 mg/mL) was added to the AMBs solutions. This mixture was left to dry slowly as mentioned earlier. During the self-assembly process, the hydrophobic dye will be encapsulated within the hydrophobic domain of the aggregates to hide away from the aqueous phase. Upon drying the fluorescent dye will be concentrated in the core of the aggregates. Imaging through the fluorescent emission of the dye will give an idea about the morphology formed. Figure 4.11 shows the result obtained from different AMB assemblies using approaches (I) and (II) *i.e.* solvent mixture or the non-solvent addition approaches.

The fluorescent microscopy experiment shows that it is possible to use AMBs assemblies as scaffolds for foreign agents making MBs promising candidates for many applications such as

drug delivery or for the synthesis of organic-inorganic hybrid materials. The latter application requires that the core-forming SCs should contain functional groups which are able to interact with an inorganic precursor; this topic will be discussed in the following chapter.
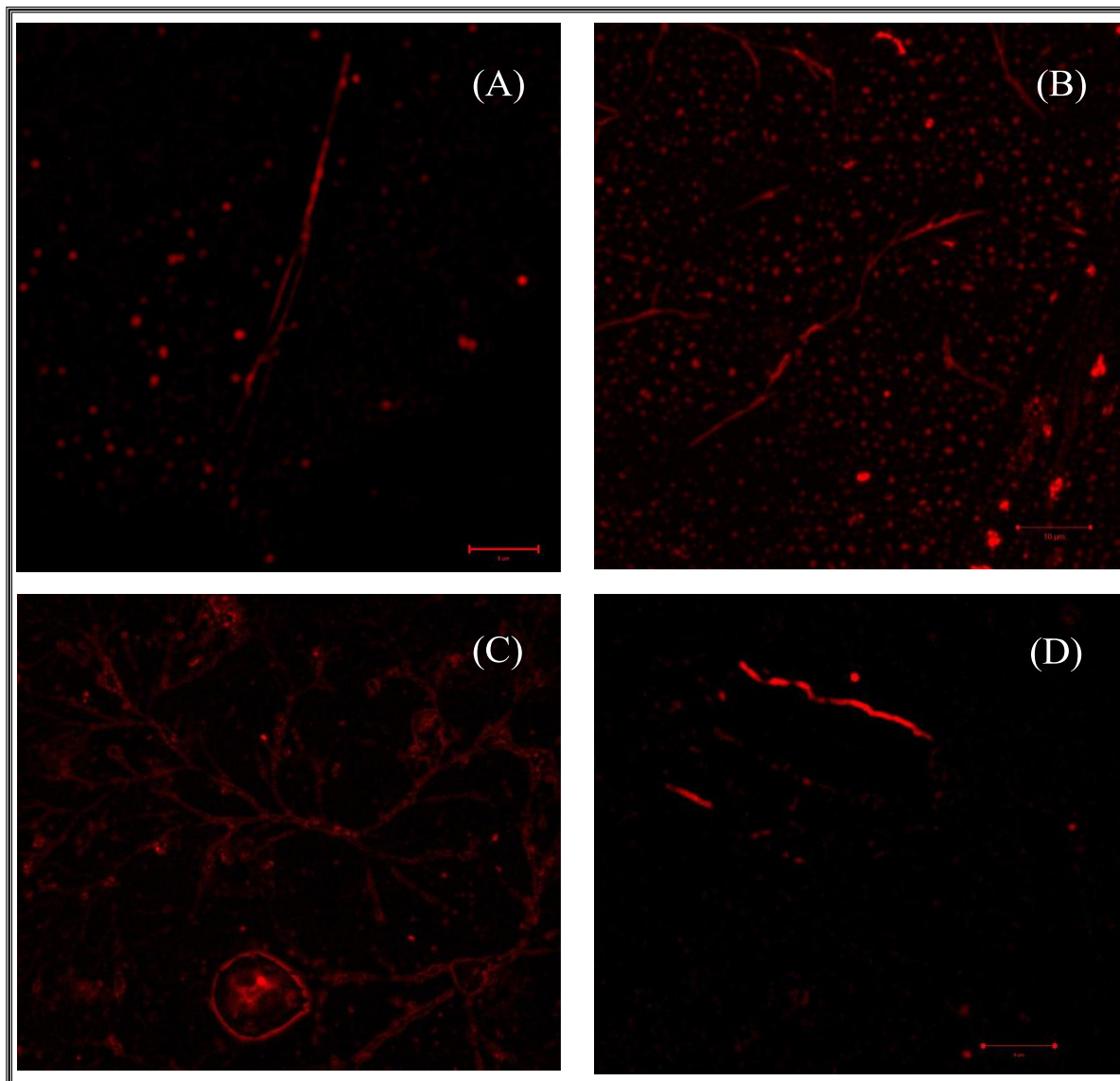
Figure 4. 11: Fluorescence micrographs of hetero-arm AMBs with Perylene Red encapsulated, (A) and (C): poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{16}$H$_{33}$)] (scale bar represents 5 and 10 µm respectively), (B): poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{10}$H$_{33}$)], and (D): poly[VB-(PEG$_{17}$)-*alt*-MI-(C$_{20}$H$_{33}$)] (scale bar represents 10 and 5 µm respectively)

There are two ways for an AMB to minimize exposure of the hydrophobic grafts to the aqueous phase. The one way is to form toroidal structures, *i.e.* the cylindrical or tubular aggregates bend to form a closed circular aggregate. In this way, the self-assembled structure has no "open ends" that would expose the hydrophobic grafts. The other way is to gradually diminish the diameter of

the tubular aggregate by reducing the number of chains in the circumference of the tube until the inner layer ceases to exist and the tube converts into a solid cylindrical aggregate (elongated micelle). It is expected that subtle differences in the primary structure of the amphiphilic molecular brush determine which one of the two scenarios is exhibited. Clearly, in the present case, the tubular aggregates are almost linear, which suggests that formation of a toroidal structure would energetically be unfavorable.

Conclusion

Amphiphilic hetero-arm molecular brushes with hydrophobic and hydrophilic side chains were synthesized by two different methods. The first method is a combination of grafting through and grafting onto approaches, and the second method by grafting through only. The first approach involves two steps. First, VB-PEG and MAnh are copolymerized in an alternating fashion (grafting through), and second, the grafting onto approach is used to introduce hydrophobic arms of different length via a nucleophilic substitution of primary amines on the MAnh units. In the second method, grafting through is used to synthesize AMBs in one step. In this approach VB-(PEG) (macromonomer 1) and MI-(C_nH_{2n+1}) where n = 10, 16 and 20 (macromonomers 2) are copolymerized to give AMBs. Among the many challenges that were faced during the course of this work, when the first method (combination of grafting through and grafting onto) was employed it was difficult to fully characterize the obtained copolymer before the modification step (grafting onto) due to gel formation. This could be due to the reactivity of the MAnh units on the backbone, which tend to hydrolyze easily in the presence of moisture. Generally it was difficult to measure the molecular weight of the obtained AMBs as there was clear evidence of column interaction as witnessed by peak shape when SEC in THF or in DMAc with 0.05% BHT (*w/v*) and 0.03% LiCl (*w/v*) was used. Reproducibility was an issue when SEC in HFIP was used.

The self-assembly behavior of the synthesized hetero-arm AMBs with various hydrophobic SCs length was investigated in selective solvent systems. The preliminary results showed that cylindrical aggregates were formed upon the self-assembly of hetero-arm AMBs. The morphology of the aggregates was to some extent influenced by the length of the hydrophobic SCs. It can be concluded that the majority of cylindrical structures consist of two morphologies,

i.e. elongated vesicle (at the center of the aggregates) and elongated micelles (at the extremes of the cylinders).

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Chapter 5: Alternating Hetero-Arm MBs: Synthesis and Self-Assembly

Abstract

A combination of grafting through and grafting from approaches was applied to prepare hetero-arm alternating hetero-arm MBs (hetero-arm AHMBs). The procedure included the following steps: (1) radical copolymerization of vinyl benzyl terminated polyethylene glycol (VB-PEG$_{17}$) macromonomer with *N*-(4-hydroxyphenyl) maleimide *N*-(HPh)-MI gave poly [vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(4-hydroxyphenyl) maleimide (poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI]) with PEG SCs and hydroxyphenyl groups alternatingly distributed along the backbone (grafting through), (2) esterification of the hydroxyl sites with 2-bromoisobutyryl bromide to produce poly [vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(4-(2-bromobutyryloxy)phenyl) maleimide (poly[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI]) (macroinitiator) and (3) atom transfer radical polymerization ATRP reaction of 4-vinyl pyridine (4-VPy) and 2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMAEMA) initiated by the obtained macroinitiator to give poly[vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(polyvinyl pyridine) maleimide], (poly[VB-(PEG$_{17}$)-*alt*-*N*-(PVPy)-MI]) and poly[vinyl benzyl-(polyethylene glycol)-*alt*-*N*-(poly(*N*,*N*-dimethylamino-ethyl methacrylate) maleimide], (poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI). The obtained hetero-arm AHMBs were then used as a templates to prepare organic/inorganic hybrid materials.

Introduction

Macromolecular self-assembly is a common process in nature. Membranes of living cells, for example, are formed by the self-assembly of phospholipids. Such processes have inspired scientists to fabricate structures with unique properties to fulfill the requirements in many advanced fields such as medicine, microelectronics and optics. One of the ways to fabricate such materials is via the self-assembly of synthetic macromolecules (building blocks) such as di-block copolymers in bulk or in solution. This approach offers a relatively easy route to build structures with controlled morphology and domain functionality. The key strategy of this approach is that the building blocks contain two or more thermodynamically incompatible segments to drive the assemblies into the final desired morphology. Therefore, the only structural requirement for molecular self-assembly is that the building blocks contain moieties able to undergo secondary interactions in specific environments.[1-5]

Among the various morphologies obtained through macromolecular self-assembly is the cylindrical aggregate[5, 6]. This morphology has attracted a great deal of attention in recent years as it can potentially be used as template for inorganic materials to prepare nano-rods, nano-wires, and nanotubes.[2, 7] Many natural templates of cylindrical shapes such as tobacco mosaic virus (TMV)[8] and DNA[9-11] have been employed to prepare hybrid materials. Cylindrical hybrid organic-inorganic materials can also be fabricated using synthetic macromolecules, either in assemblies such as in the case of block copolymers[12], or as a unimolecular template such as MBs.[13, 14] In the current approach, the polymeric template of a pre-designed shape with additional functional groups is used as a host for inorganic materials. These functional groups should be capable of coordinating with inorganic precursors (metal ions or silica). Subsequently, these metal ions can be chemically converted into the corresponding metal particles (metallization or silicification) within the template. In this study, hetero-arm AHMBs were employed as assemblies for template-directed synthesis of organo-silica nano-objects.

This chapter describes the approaches used to synthesize alternating hetero-arm molecular brushes (AHMBs) with PEG and either poly(*N,N*-dimethylamino ethyl methacrylate) (PDMAEMA) or polyvinylpyridine (PVPy) SCs. A combination of grafting through and grafting from approaches was employed to prepare these hetero-arm AHMBs. As illustrated in Figure 5.1,

the grafting through approach was used to prepare MBs with one type of SCs alternatingly distributed along the backbone. In the second step the other type of the SCs was generated via the grafting from approach. The obtained hetero-arm AHMBs were then used to prepare silica nano-cylinders via a sol-gel process (silicification).
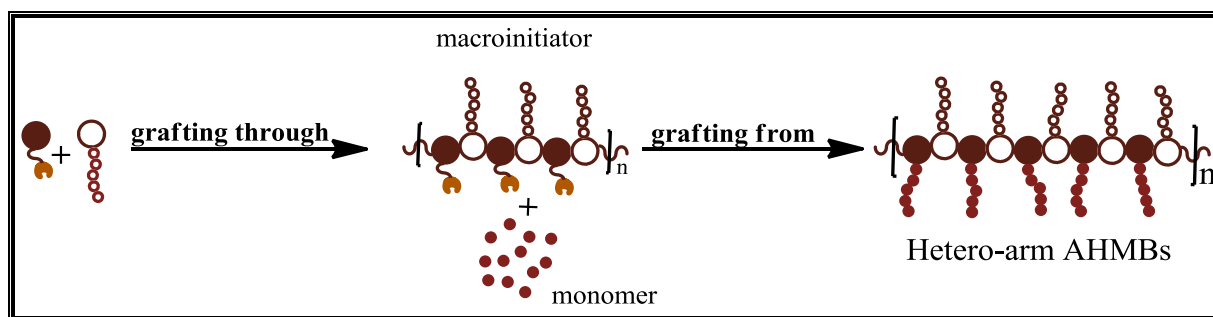
Figure 5. 1: Schematic illustration of the synthetic route used to synthesize AHMBs

The silicification process (Scheme 5.1) involves hydrolysis of silicon alkoxide precursors (such as *tetra*-ethylorthosilicate TEOS), followed by condensation, aggregation, and agglomeration, to produce silica particles. The silica formation process can be directed and catalyzed by a polymeric template (hetero-arm AHMBs in this study), which allows the synthesis of hybrid organo-silicate or different shapes.
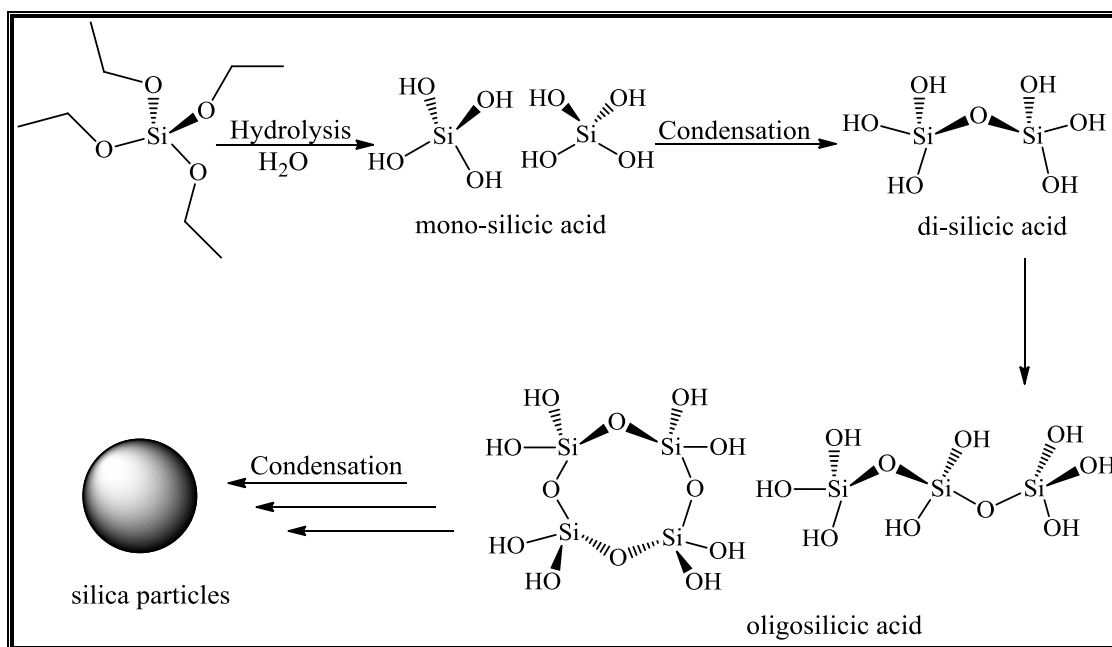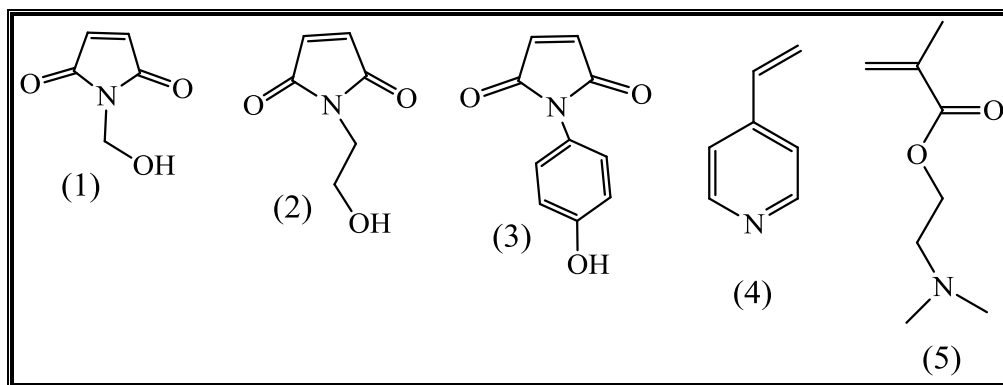
Scheme 5. 1: Schematic representation of the silicification of TEOS (sol-gel process)

Synthesis of alternating hetero-arm molecular brushes (AHMBs).

Initial approaches:

As was mentioned in **Chapter 3**, a number of different approaches were attempted to synthesize AHMBs. The challenge was to synthesize AHMBs with two different SCs alternatingly distributed along the backbone. The purpose of these different SCs is to direct and control these MBs into large assemblies, with a core that is able to host inorganic materials and a shell that solubilizes these aggregates in different mediums. Therefore the core domains of these aggregates should contain polymers with functional groups that are able to bind to an inorganic precursor under controlled conditions. Among the many polymeric materials that can be used for this purpose, poly acrylic acid (PAA), polyimides, and poly vinyl pyridines were used extensively in literature and proved to be suitable hosts for many inorganic materials including metal, metal oxides, and silica. In this study, PDMAEMA and PVPy were selected because they are relatively easy to synthesize in one step via ATRP, instead of the multi-step process required in the case of PAA.

Scheme 5. 2: Schematic representation of the *N*-functionalized maleimides used in the study

The initial focus was to synthesize MBs with two different SCs via a combination of grafting though and grafting from approaches. An alternating copolymerization of a maleimide (MI) based macromonomer *i.e.* MI-PEG and vinyl benzyl chloride (VBC) will be conducted to produce copolymers with ATRP initiating sites (macroinitiator). Subsequently, this macroinitiator could be used to initiate an ATRP reaction of functional monomers such as DMAEMA and 4-VPy to generate the second SCs. However due to the difficulty associated with the synthesis of the MI-based macromonomers (*i.e.* low yield, purification and low functionality), this approach was abandoned for another approach. This new approach was based on the reverse order of the initial approach *i.e.* vinyl benzyl-terminated poly ethylene glycol (VB-PEG$_{17}$) and *N*-functionalized MI (with ATRP initiator groups).

VB-PEG$_{17}$ macromonomer was prepared according to a literature procedure via the coupling reaction between mono-methoxy polyethylene glycol-(PEG) and VBC. This procedure afforded macromonomer with high yield and purity (up to 80%, purity > 96 % by ^{1}H NMR). (As described in chapter 3) three MI-based monomers were synthesized with high to medium yields. *N*-methylol- maleimide **(1)** was synthesized easily through the base-catalyzed reaction between maleimide and formaldehyde. Monomer **(1)** was then copolymerized with VB-PEG under different polymerization conditions in an attempt to synthesize an alternating copolymer that can be further modified to produce an ATRP macroinitiator. However, all of these attempts were unsuccessful in producing soluble copolymers, which can further be analyzed and modified. Gel formation was observed within minutes after the start of the polymerization.

After these initial attempts, the focus was turned to copolymerization of (2) with VB-PEG$_{17}$. Initially, monomer (2) was synthesized through the modification of maleic anhydride (MAnh) with ethanolamine. Protection of the MAnh with furan was essential to produce (2) in sufficient yield (between 54–60 %). Similar results to those obtained from monomer (1) were observed however, gelation started after a minimum of two hours from the start of the polymerization reaction. Isolation via precipitation of the copolymer before gelation did not work either, as the precipitated polymer formed gel-like materials in a wide range of solvents. Modification of the two monomers via esterification with acid chloride or bromide before the polymerization also resulted in insoluble materials. After these unsuccessful attempts, monomer (3) was successfully synthesized and copolymerized with VB-PEG$_{17}$ in 1,4-dioxane and gave soluble copolymers. The obtained copolymers were then modified to produce ATRP macroinitiators and used to prepare AHMBs as will be discussed in the following sections.

Synthesis of poly[VB-(PEG$_{17}$)-*alt*-(*N*-(HPh)-MI)] "grafting through"

All polymerizations were carried out under Ar atmosphere in a dry 50 mL Schlenk flask. In a typical experiment, *N*-(HPh)-MI (0.066 g, 0.350 mmol), VB-(PEG$_{17}$) (0.330 g, 0.350 mmol) and AIBN (3 mg, 0.0175 mmol) were dissolved in dry 1,4 dioxane (6 mL) in a Schlenk flask. The flask was degassed by five freeze-pump-thaw cycles and back-filled with Ar. The flask was then placed in a preheated oil-bath at 65 °C for 12 h. After polymerization, the polymer was isolated by precipitating twice from cold pentane. The precipitated polymer was then dried under vacuum for 2 h at room temperature. The polymer was dried further by azeotropic distillation from toluene before the esterification step. Some of the copolymer was purified further by dialysis against an acetone:water (1:1 v/v) mixture for ~ 3 days followed by water for 2 days. The polymer was subsequently isolated via freeze-drying.
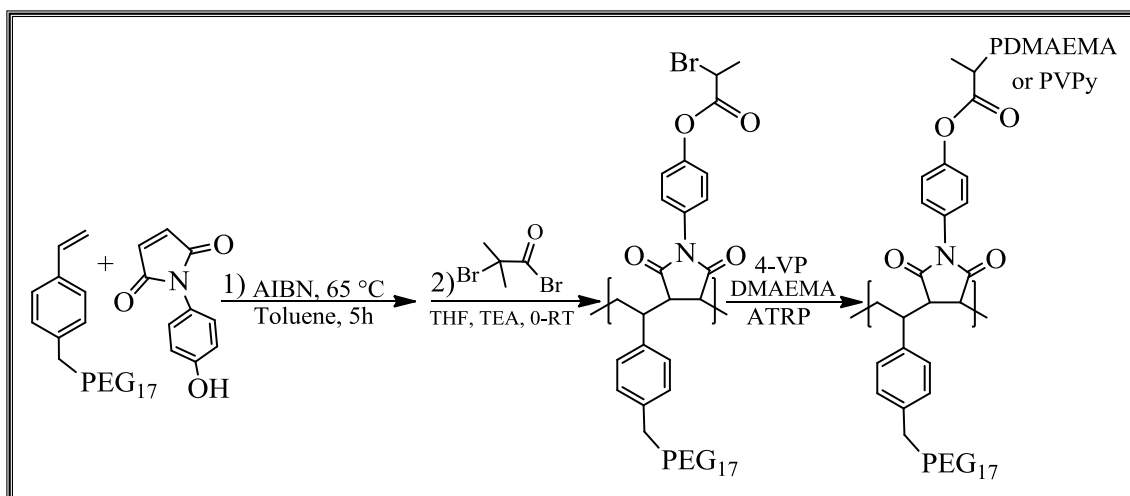
Scheme 5. 3: Synthesis of the hetero-arm AHMBs with PEG and PDMAEMA or PVPy SCs

Synthesis of poly[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI] "Esterification step"

In a dry 2-neck flask, a dry sample of poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI] (0.38 g, -OH groups, 0.359 mmol) and dry triethyl amine (TEA) (0.066 g, 0.640 mmol) were dissolved in dry THF (30 mL). The solution was allowed to stir for 30 minutes before 2-bromoisobutyryl bromide (0.140 g, 0.600 mmol) or (2-chloropropanoyl chloride (0.082 g, 0.600 mmol)) was added slowly at 0 °C. The mixture was stirred for 3 h at 0 °C followed by stirring at room temperature for 24 h. The white precipitated salt was then removed by filtration, and the solvent was removed by a rotating evaporator. The obtained polymer was dialyzed against acetone:ethanol mixture (1:1 v/v) for 3 days followed by water for 2 days (Separations MWCO 7000) and the polymer was freeze-dried (degree of esterification: 100% as was measured by FT-IR and NMR).

Synthesis of poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI], "grafting from"

The catalyst solution was first prepared separately, by stirring Cu$^{(I)}$Cl (0.008 g, 0.083 mmol), Cu$^{(II)}$Cl$_2$ (0.002 g, 0.017 mmol), and HMTETA (0.019 g, 0.083 mmol) in a degassed solvent mixture consisting of 2-propanol/butanone or acetone/anisole (1:1 v/v, 8 mL). This mixture turned homogenous and green in color upon stirring (about 30 min). Then, in a 50 mL Schlenk flask, poly[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI] (macroinitiator, 0.100 g, -Br groups, 0.083 mmol), DMAEMA (3.91 g, 24.90 mmol), and the solvent mixture 7.5 mL) were added. This solution was subjected to five freeze-pump-thaw cycles. After equilibration at room temperature, the catalyst

solution was added via a degassed syringe. The flask was placed in a preheated oil bath at 30 °C. THF was added to dilute the solution. After passing through a basic alumina column, the solution was concentrated by a rotary evaporator. Afterwards, it was precipitated into cold pentane to remove the residual monomer and other impurities. The precipitate was then dissolved in 1,4-dioxane and dialyzed against 1,4-dioxane for two days followed by dialysis against water for 4 days before it was freeze-dried. Attempts were made to measure the monomer conversion using ^{1}H NMR. However, due to signals overlapping as well as base line problems, it was very difficult to obtain conclusive results. The conversion was then estimated based on the final polymer mass to be ~ 10 %.

A similar procedure was employed to prepare poly[VB-(PEG$_{17}$)-*alt*-*N*-(PVPy)-MI] hetero-arm AHMBs. However, TEMPO solution (0.025 mg/mL) was added to the polymerization mixture after 18h (conversion ~ 9%) in an attempt to remove the halogen groups at the SC ends. The mixture was left to stir for an additional 6h at 55 °C before the polymer was precipitated and purified in a similar way as for poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] mentioned above.

Fabrication of organo-silica hybrid nanowires.

A solution of TEOS (25 μL in 2 mL ethanol) was added drop wise to a solution of poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] solution (0.2 mg/mL) in acidic water at room temperature (RT) and a pH of 4. The homogeneous solution was vigorously stirred for 20 min at RT before it was headed slowly to 80 °C (~ 2 °C/min). The mixture was then kept stirring at this temperature (i.e. 80 °C) for 12h (to remove the ethanol) and at 65 °C for 48h. TEM samples were then prepared from this solution.

Self-assembly of hetero-arm AMBs:

A solution of poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] in DDI water (neutral pH) with a concentration of 0.3 mg/mL was prepared at RT. The solution was filtered through 0.45 μm filter before it was place in an oven at RT. The temperature was increased slowly to 70 °C (~ 2 °C/min). The solution was stirred at this temperature for 36h before the TEM samples prepared. The TEM samples where prepare under the same conditions.

Results and discussion

Synthesis of hetero-arm AHMBs

Highly alternating copolymers can usually be prepared by copolymerization of electron-accepting monomers such as maleic anhydride or MI with electron-donating monomers such as styrene. In this study, *N*-(HPh)-MI (**3**) was copolymerized with VB-PEG$_{17}$ to produce MBs, which consist of an alternating backbone with PEG SCs and reactive functional groups. The copolymerization of (**3**) with many styrene derivatives has been reported to give exclusively alternating copolymers when equimolar ratios are used.[15-19] The monomer conversion was measured gravimetrically, using purified copolymers, and was found to be ~ 75% assuming all of the macromonomer was removed during the purification process. The chemical composition of the obtained copolymers was measured using ^{1}H NMR spectroscopy and was found to be 49 % and 51% *N*-(HPh)-MI and VB-PEG$_{17}$ respectively. This ration was measured from the integration intensity of signal proton (a) and (d) in Figure 5.3 (B).

One of the used methods to determine the alternating sequence of the repeat units in S-MAnh (or MI) copolymers is by determining the triad sequence of the repeat units by ^{13}C NMR.[20, 21, 22] Usually the chemical shift of the aromatic carbon "next to polymer chain" of the styrene repeat units is used to determine sequence the repeat unit, however this method could not be used in this study due to due to the poor signal intensity obtained for this carbon. However, based on the results reported in literature of similar monomers,[16, 19, 23, 24] and based on the chemical composition of the copolymer (~ 1:1 ration of both repeat units) the obtained copolymerization (**3**) with VB-PEG$_{17}$ was assumed to produce primarily alternating copolymers.

During the course of the study, an interesting observation was made regarding the NMR (^{1}H & ^{13}C) spectra of all the obtained alternating MBs with PEG SCs. In all of these spectra, the signals of the protons near or on the backbone (*i.e.* aromatic and methylene protons) were undetectable although these protons (*i.e.* vinyl and aromatic ring protons in VB-PEG$_{17}$) were observable in the macromonomer NMR spectrum before the copolymerization. Although the ratio of these protons to the protons of the PEG in VB-PEG$_{17}$ (*i.e.* macromonomer) is very small, they were clearly seen in the NMR spectrum as shown in Figure 5. 2 (A). However, after the copolymerization, these protons were undetectable (Figure 5.2 (B)). This phenomenon was attributed to the high

stiffness of the backbone. In an attempt to quantify the stiffness of the backbone, NMR analysis of poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI] was performed at different temperatures *e.g.* 25°C- 120 °C in DMSO-*d*^{6}. The solution of these MBs was extensively purified by filtration (through 0.25 µm filters) and centrifuged to eliminate any assemblies that might take place in the solution. Similar results were obtained irrespective of the used solvent (acetone-*d*^{6}, or CDCl$_3$ or DMF-*d*^{7} at room temperature) and number of scans. Figure 5.3 shows ^{1}H NMR spectra obtained from poly[VB-(PEG$_{17}$)-*alt*-(*N*-(HPh)-MI)] in DMSO-*d*^{6} at different temperatures.

Figure 5.3 (A) represents the obtained NMR spectra recorded at different temperatures, processed with MestReNova software. As mentioned earlier, the spectra only show the signals assigned for the PEG SCs (including the methoxy end groups of the SCs). No signals of other protons *i.e.* backbone or aromatic protons of VB repeat units were observed in the entire temperature range used. By expanding **(zoom in)** the spectra, almost all protons could be observed as shown in Figure 5.3 (B), the intensity of the signals slightly improved as the temperature increased. This can be seen when signals (b) and (d) at different temperatures were compared, however this slight increase could not be quantified based on these spectra due to the overlapping of the signals of the PEG (*i.e.* as reference signals) and water signals

Although the NMR spectra of the copolymer at different temperatures could not be used for quantitative analysis of the backbone stiffness, they were useful in measuring the chemical composition of the copolymer. As shown in Figure 5.3 (B), the resonances of protons close to the backbone, like the aromatic protons of both repeat units (b, and c), methylene protons (d) and protons (a) which were assigned to the hydroxyl groups in the copolymer are observed. All of these resonances are greatly broadened which indicates that the backbone of copolymer is quite stiff due to the presence of the PEG SCs. The ratio of the two repeat units in the copolymer was calculated by using the integration peak area of signals (a) (-OH of *N*-(HPh)-MI repeat units) and signal (d) (methylene of VB-PEG$_{17}$ repeat units). The ratio was found to be: ~ 1: 1.05, which indicates that the copolymer contains almost the same number of the two different repeat units.
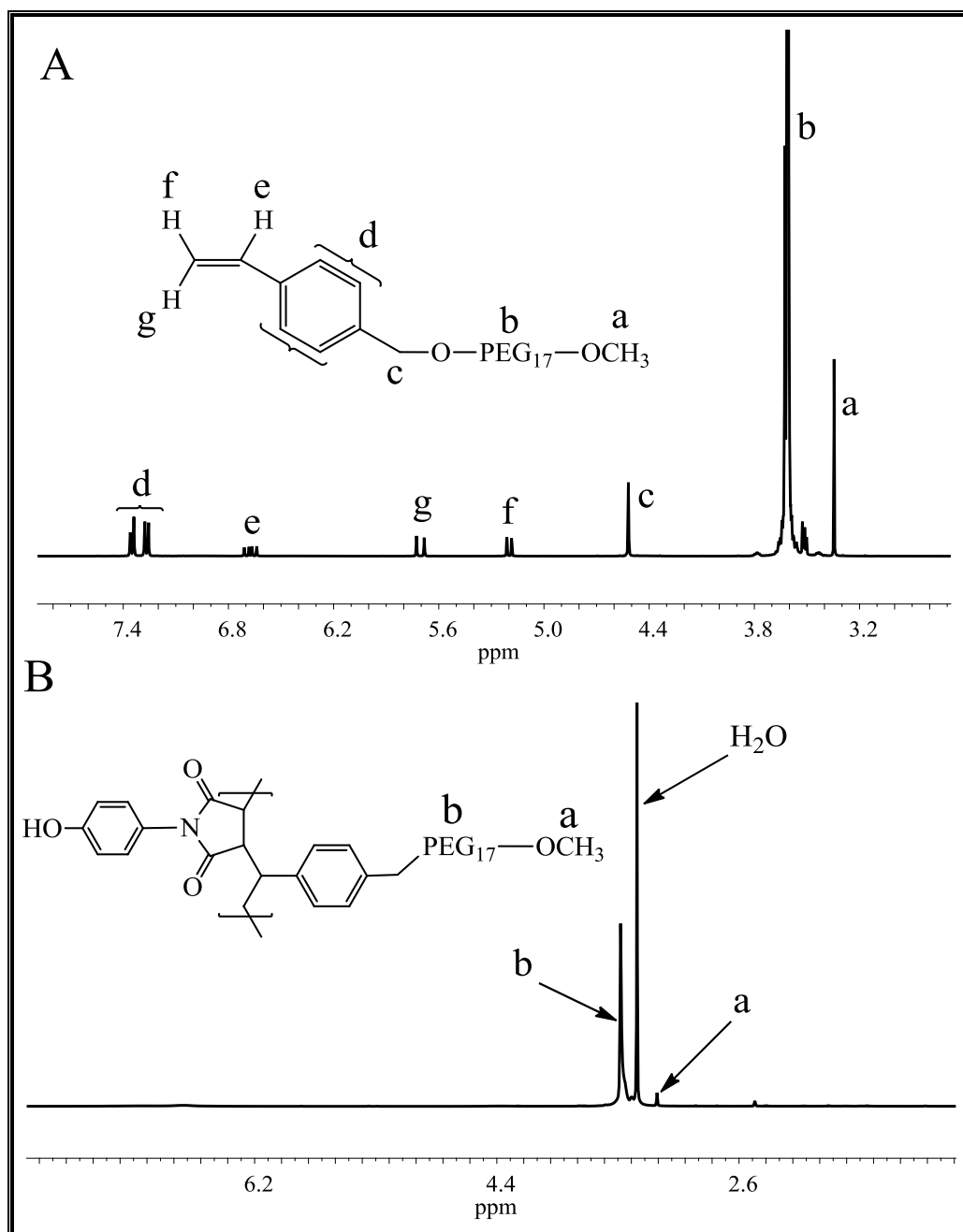
Figure 5. 2: ^{1}H NMR spectra of VB-PEG$_{17}$ (A) and poly[VB-(PEG$_{17}$)-*alt-N*-(HPh)-MI] (B) at room temperature
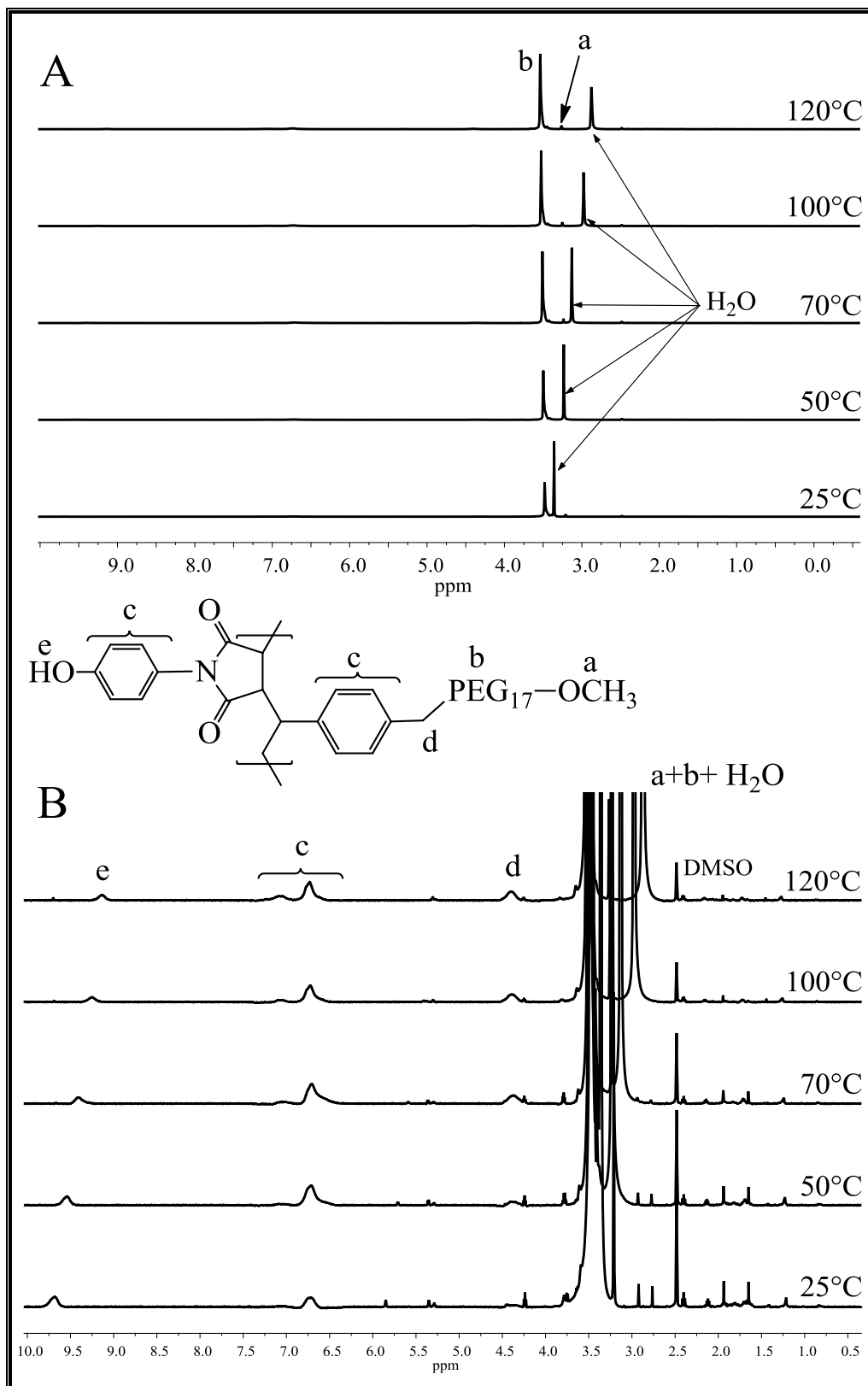
Figure 5. 3: ^{1}H NMR of poly[VB-(PEG$_{17}$)-*alt-N*-(HPh)-MI] in DMSO-*d^6* at different temperatures, (A) as received (without zooming in using MestReNova software, and (B) zoomed in as processed with MestReNova software.

Following these investigations, the copolymer was modified through esterification of the phenolic hydroxy group in the alternating copolymers with 2-bromoisobutyryl bromide (or 2-chloroisobutyryl chloride) in THF. Figure 5.4 shows ^{1}H NMR spectra of the copolymers before and after the modification reaction. As can be seen, the proton signal of the hydroxy groups (a) (in Figure 5.4 (A)) disappeared completely and new signals appeared in the region between 1.4 and 1.8 ppm (in Figure 5.4 (B)) after the esterification reaction. This indicates that, within the detection limit, all of the –OH groups were transformed to 2-bromoisobutyryl groups (ATRP initiator sites).
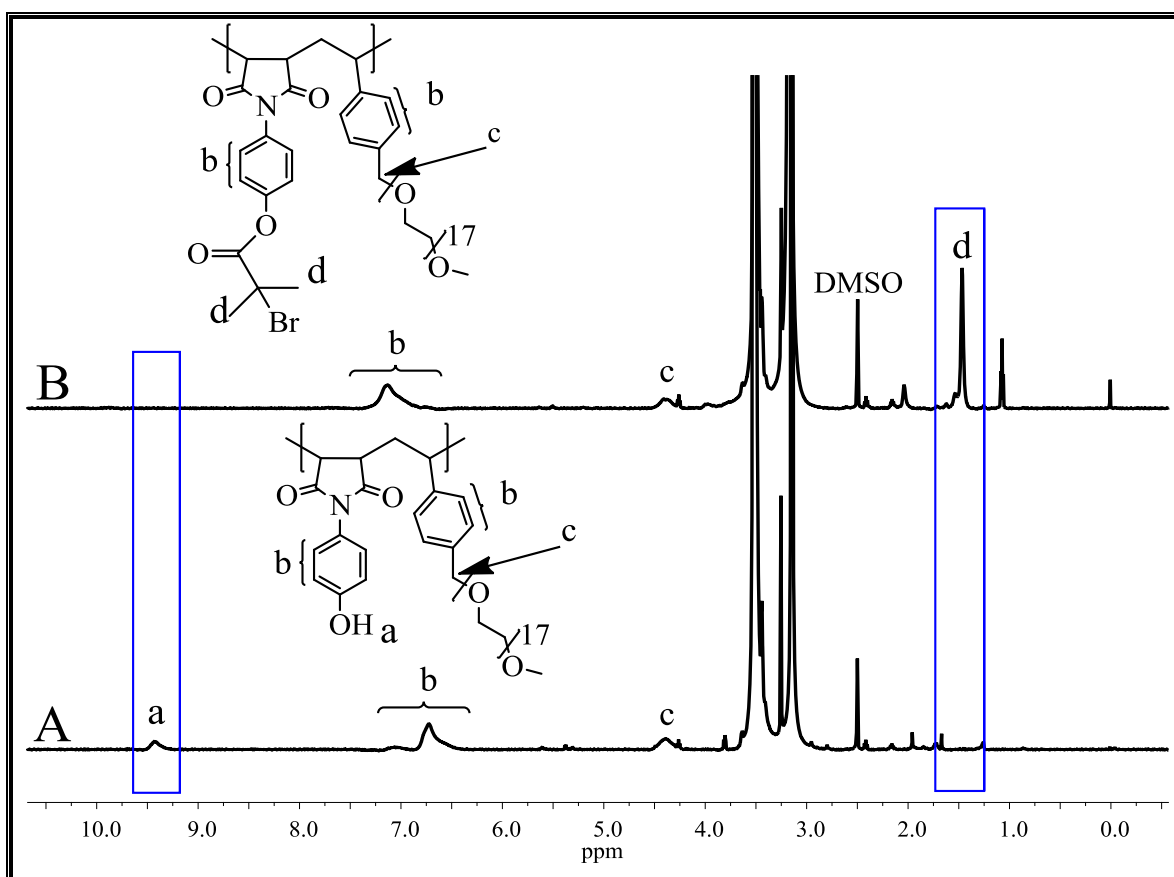
Figure 5. 4: ^{1}H NMR spectrum of poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI] (A) before, and (B) after modification of the phenolic –OH into an ATRP initiator.

The formation of poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI] as well as its transformation to poly[VB-(PEG$_{17}$)-*alt*-*N*-(BrPh)-MI] was further confirmed by FT-IR spectroscopy. As shown in Figure 5.5, the expected absorbance stretches of both repeat units were observed. For example, Figure 5.5 (A) gives the characteristic absorbance for *N*-(HPh)-MI repeat units (*e.g.* the (-OH) groups

(stretching) between (3100- 3530 cm^{-1}) and for the carbonyl groups at (1700 cm^{-1})) and for VB-(PEG$_{17}$) repeat units (*e.g.* the ether stretch (C-O-C) of PEG at (1115 cm^{-1})) which confirms the copolymer formation. Figure 5.5 (B) shows the FT-IR spectrum of the copolymer after the esterification reaction. The disappearance of the (-OH) stretching absorbance at 3310 cm^{-1}, and the appearance of carbonyl groups stretching of ester bonds at 1755 cm^{-1} indicate a successful complete esterification reaction and hence successful synthesis of the ATRP macroinitiator. The obtained macroinitiator was then used to prepare hetero-arm AHMBs by initiating either 4-VPy or DMAEMA polymerization from the ATRP initiating sites along the backbone.
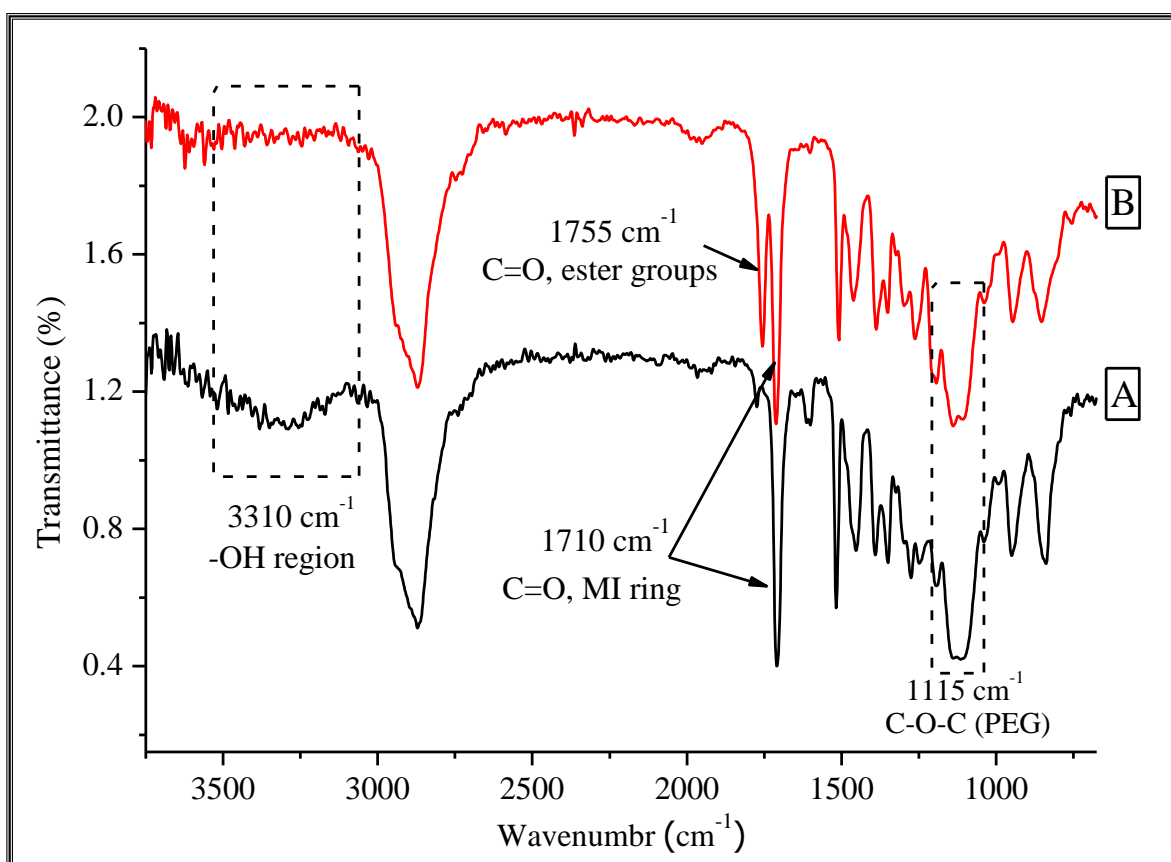
Figure 5. 5: FT-IR spectrum of poly[VB-(PEG$_{17}$)-*alt*-*N*-(HPh)-MI]: (A) before, and (B) after modification of the phenolic –OH into an ATRP initiator.

Due to the intended applications of these hetero-arm AHMBs *i.e.* construction of organic/inorganic hybrid materials, the second of SCs (besides PEG SCs) should contain functional groups that are able to (I)- spontaneously drive and direct these brushes to form assemblies, and (II) should be able to bind or react with an inorganic precursor. In this context,

many functional monomers have already been employed in literature, including AA, (2- or 4-) VPy, and DMAEMA. Initially, 4-vinyl pyridine was chosen to generate PVPy as the second SCs using ATRP, due to its nature as a pH-responsive polymer and its strong affinity to bind to a wide range of inorganic precursors such as *tetra*-ethylorthosilicate or $HAuCl_3$. For this purpose the ATRP of 4-VPy was investigated.

The ATRP of 4-VPy is not a straightforward polymerization in contrast to ATRP of other monomer classes. Due to the ability of 4-VPy (or the polymer) to complex with the copper catalyst and reaction with the halide at the chain ends (quaternization), special treatment and attention should be given to such polymerization. To overcome these challenges, a strong multidentate ligand such as hexamethyl *tris*(2-aminoethyl)amine (Me$_6$-TREN) with $Cu^{(I)}Cl/Cu^{(II)}Cl_2$ should be used to form the catalyst. This ligand forms strong complexes with the copper ions and thus favorably competes with the pyridine units. One of the other challenges of this polymerization is a significant dissociation process of the deactivating $Cu^{(II)}$ halide complex in protic solvents, leading to uncontrolled polymerization. The addition of a sufficient amount of the deactivator (~ 30 % of $Cu^{(I)}$) improves the degree of control of the produced polymer.[25, 26]

Initially, a chloride-based ATRP macroinitiator (*e.g.* poly[VB-(PEG$_{17}$)-*alt*-*N*-(ClPh)-MI] was used in combination with Me$_6$TREN/$Cu^{(I)}Cl/Cu^{(II)}Cl_2$ under different conditions (*i.e.* temperature, solvents). However, these attempts produced cross-linked polymers within short polymerization times. Because of the large number of initiation sites on a macroinitiator chain, termination via chain-chain coupling might take place. This could be mainly due to the fast exchange equilibrium between the active and dormant species since a very active Me$_6$TREN-based complex was used. To overcome these challenges a slower ATRP was designed by using *N,N,N',N'',N''',N'''-*hexamethyltriethylenetetramine/$Cu^{(I)}Cl/Cu^{(II)}Cl_2$ catalyst system in combination with a bromine-based macroinitiator in isopropanol/methyl ethyl ketone (1/1 v/v) at 30 °C. The chlorine at the end of the SCs were then transformed to alkoxyamines via the addition of TEMPO to the polymerization mixture in an attempt to minimize possible post-polymerization quaternization reactions.[26] Although poly[VB-(PEG$_{17}$)-*alt*-*N*-(PVPy)-MI] was successfully prepared under these conditions, as indicated by NMR, this polymer could not be used further as cross-linking took place upon storage.

Because of these challenges, DMAEMA was used as a functional monomer to generate the second type of the SCs. The ATRP of DMAEMA was relatively easier than that of 4-VPy. Generally, in order to prepare well-defined MBs with relatively high grafting density using grafting from approach (*e.g.* ATRP), some points have to be taken into consideration. For example, the catalyst/ligand system, initiator, and solvent-to-monomer ratio all influence the initiating efficiencies which in turn affect the final grafting density.[27, 28] High initiation efficiency can be achieved by reducing the monomer concentration and increasing the deactivator (*i.e.* $Cu^{(II)}$ halide) concentration in the mixture. For methacrylate monomers the initiation is more efficient when bromine is exchanged to chlorine by the use of $Cu^{(I)}Cl/Cu^{(II)}Cl_2$ as demonstrated by Matyjaszewski *et al.*[29]

In this study, the ATRP of DMAEMA was initiated from poly[VB-(PEG_{17})-*alt*-*N*-(BrPh)-MI] macroinitiator. Halogen exchange, where the bromine of the macroinitiator (*i.e.* *N*-(BrPh)-MI repeat units) was replaced by chlorine from $Cu^{(I)}Cl/Cu^{(II)}Cl_2$, was employed. This will ensure fast initiation from the backbone and also ensures to produce hetero-arm AHMBs with sufficient PDMAEMA SCs. Among the different polymerization conditions used, the best results were obtained when the ratio of the ATRP components was [DMAEMA]:[macro-I]:$[Cu^{(I)}Cl]$:$[Cu^{(II)}Cl_2]$:[HMTETA] = [300]:[1]:[1]:[0.2]:[1] in acetone/anisole solvent mixture, where [macro-I] is based on the concentration initiation sites.[30, 31]
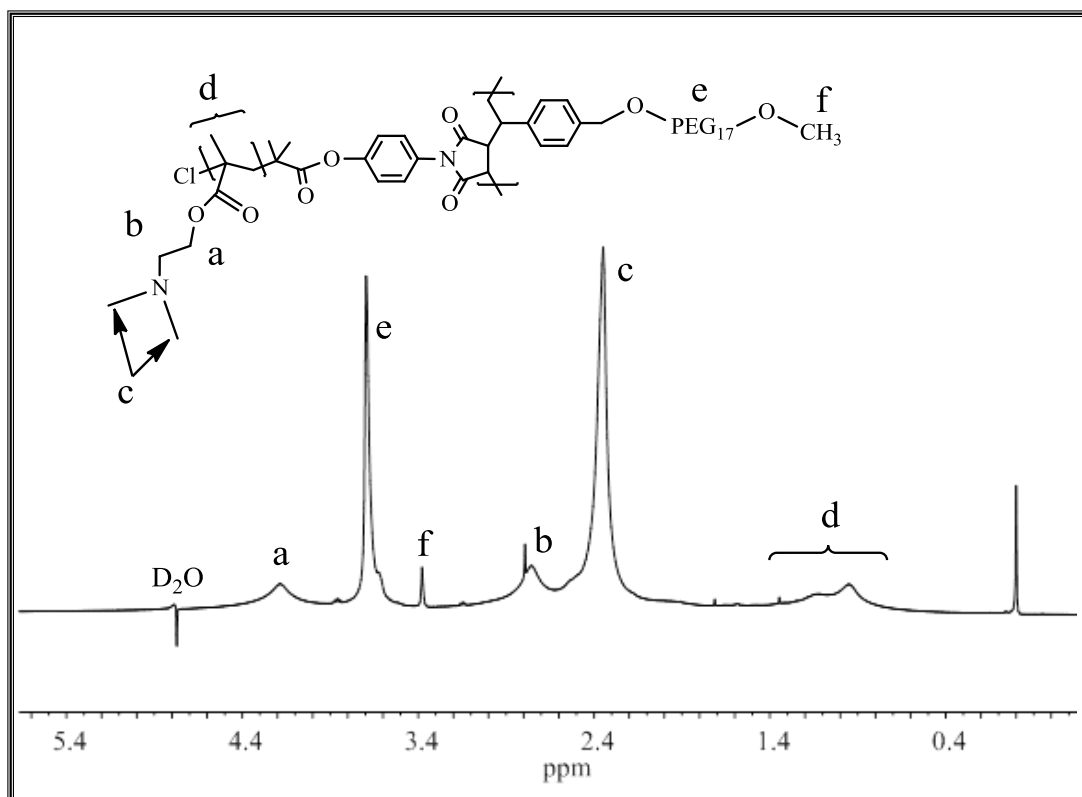
Figure 5. 6: NMR spectrum of poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI] (hetero-arm AHMBs) in D$_2$O

^{1}H NMR was used to analyze the structure of the prepared hetero-arm AHMBs. Comparison of the NMR spectrum of poly[VB-(PEG$_{17}$)-*alt-N*-(BrPh)-MI] (Spectrum (B) in Figure 5.4) to that of poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI] (Figure 5.6), confirms the successful incorporation of PDMAEMA. As can be seen in Figure 5.4 (B), the proton signals between 1.4- 1.8 (signal d) of the methyl groups, adjacent to the ester group in *N*-(BrPh)-MI repeat units, have disappeared after the ATRP reaction of DMAEMA. New signals assigned to PDMAEMA protons have appeared (*i.e.* signals a, b, and c in Figure 5.6). It is worth mentioning that the signals of protons a, b, and d of the PDMAEMA SCs are broader than that of the PEG SCs signals (peak e). This indicates that the PDMAEMA SCs are much stiffer compared to that of the PEG SCs.
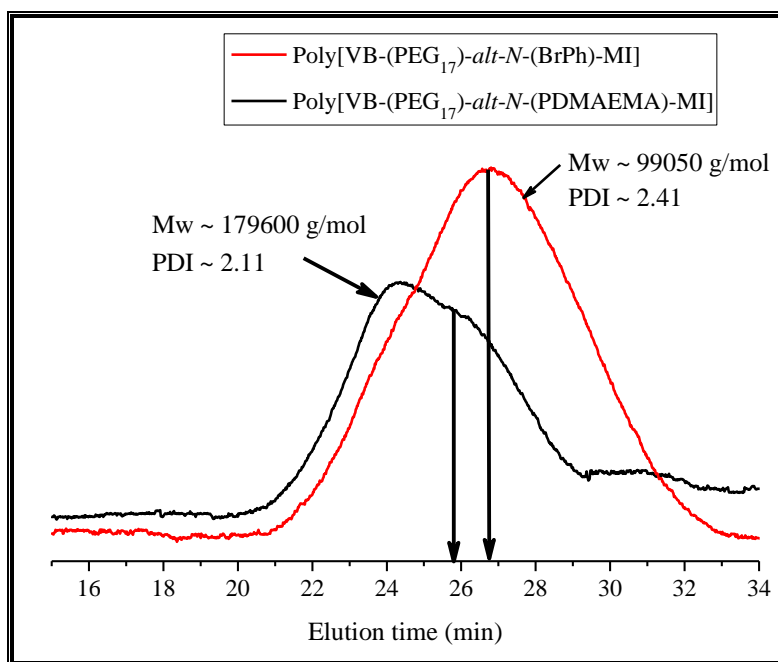
Figure 5. 7: SEC traces of poly[VB-(PEG$_{17}$)-*alt-N*-(BrPh)-MI] (red curve) and poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI] (black curve) measured in DMAc.

The molecular weights (Mw) of the macroinitiator and hetero-arm AHMBs were determined by conventional SEC in DMAc. Figure 5.7 shows the SEC traces of the macroinitiator (poly[VB-(PEG$_{17}$)-*alt-N*-(BrPh)-MI]) (red curve) and the hetero-arm AHMBs (poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI]) (black curve). The SEC curve of poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI] shifts to the high molecular- weight side compared to that of the poly[VB-(PEG$_{17}$)-*alt-N*-(BrPh)-MI] precursor. It is noteworthy to mention that the Mw of the poly[VB-(PEG$_{17}$)-*alt-N*-(PDMAEMA)-MI] and poly[VB-(PEG$_{17}$)-*alt-N*-(BrPh)-MI] obtained from SEC analysis using refractive index detector relative to PMMA standards, were an estimate Mw and not the true Mw. This difference was due to the fact that the hydrodynamic volume of these highly branched polymers is not the same as the hydrodynamic volume of PMMA standards at similar molar masses. Although conventional SEC cannot give the true Mw of the AHMBs, it still can show the difference of the elution time between the hetero-arm AHMBs and the macroinitiator. The SEC traces of hetero-arm AHMBs show a shoulder peak elute at higher elution time, this peak could be due to the presence of a small fraction of unreacted macroinitiator, which is very unlikely in this case due to the high concentration of initiation sites or it could also be due to presence of small fraction AHMBs with shorter PDMAEMA SCs. Since these AHMBs were soluble in a

wide range of solvents and the absence of gelation during the preparation of these MBs it can be safely concluded that there was no evidence of brush-brush coupling products.

Based on these results, hetero-arm AHMBs with PEG and PDMAEMA SCs were successfully prepared via a combination of grafting through and grafting from approaches. The following discussion briefly describes the strategies adopted to conduct the self-assembly of the prepared hetero-arm AHMBs.

Fabrication of organic-inorganic hybrid materials

The prepared hetero-arm AHMBs consist of two different water-soluble SCs, one of which is a water soluble at all pH and temperature range (*i.e.* PEG)[32], while the type of the SCs is pH- and temperature-sensitive polymer (*i.e.* PDMAEMA). Its solubility in water depends on the temperature and pH of the solution. In water, the hydrophobicity of PDMAEMA can be tuned by the solution pH and temperature.[33-35] Due to this different nature of the two SCs, these hetero-arm AHMBs can be assembled into larger structures by tuning, either, the pH or temperature of the solution. These assemblies can further be used as templates for inorganic materials. In this study the prepared hetero-arm AHMBs were used to fabricate organo-silica nano-structures in solution. As mentioned in the experimental section, two methods were employed to prepare these nano-structures, by temperature and pH.

This experiment is similar to the of fluorescence dye encapsulation in AMBs experiments discussed in Chapter 4 in which a fluorescent dye was encapsulated within the hydrophobic domain of assembled AMBs. In the current experiments, a silica precursor (*i.e.* TEOS) was used instead of the fluorescent dye. Figure 5.8 shows TEM images of the nano-structures obtained via the self-assembly of hetero-arm ATHMs in presence of TEOS [(A) and (B)] and without TEOS [(C) and (D)].
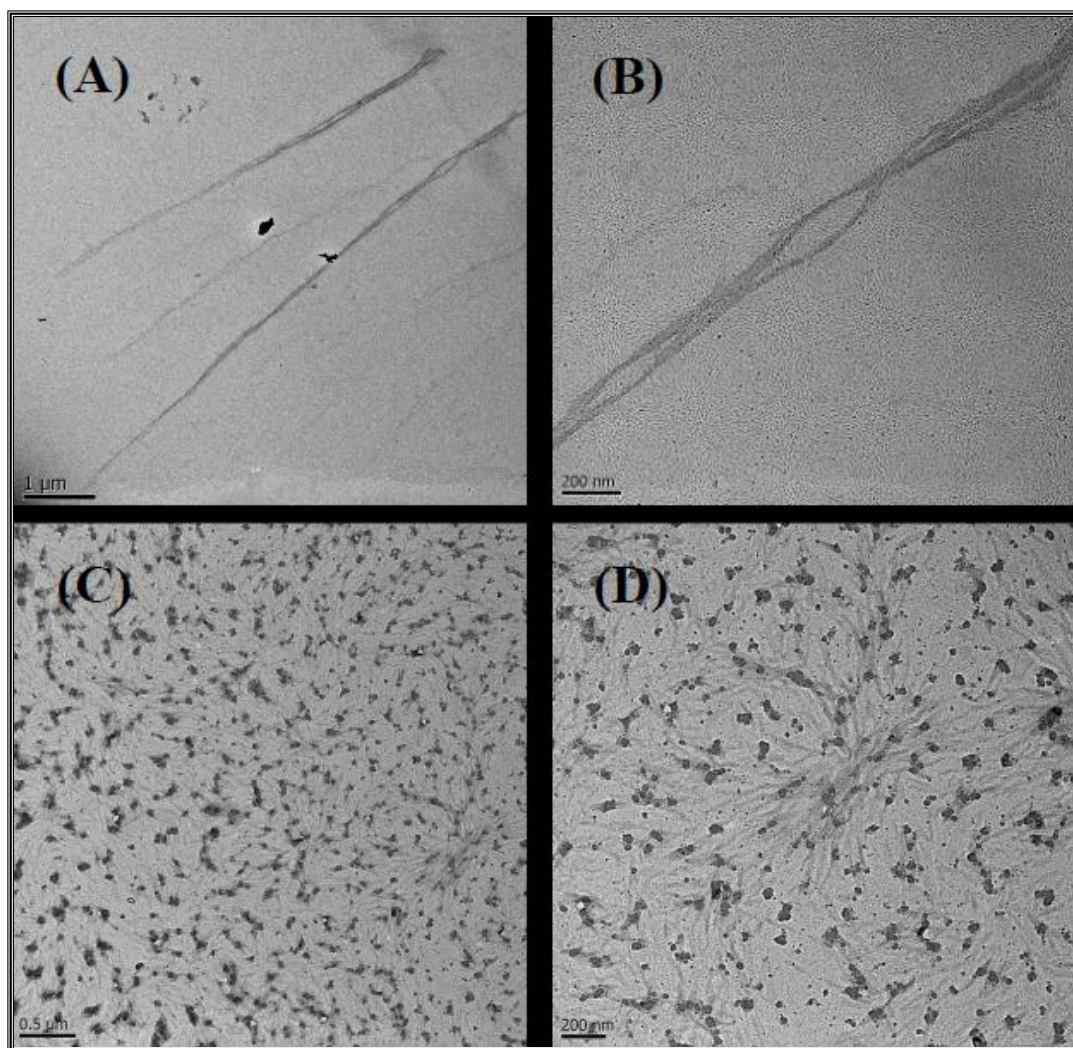
Figure 5. 8: TEM images of, (A, B): poly[VB-(PEG$_{17}$)-*alt*-(*N*-PDMAEMA)-MI] assemblies in water (0.2 mg/mL) in the presence of TEOS (25 µL) and (C, D): poly[VB-(PEG$_{17}$)-*alt*-*N*-(PDMAEMA)-MI] assemblies in DDI water (0.3 mg/mL) at 70 °C

In the presence of the silica precursor, cylinder-like structures with a diameter of ~ 45 nm and a length of ~ 8 µm were obtained. The mechanism of formation of these structures is slightly different from that explained in Chapter 4. In this case, the structures were formed in a multi-step process. Initially the hetero-arm AHMBs were dissolved in water at pH of 4 at RT. Under these conditions the PDMAEMA SCs exhibit positively charged sites due to the tertiary amine groups. These sites attract selectively the negatively charged silica (silica deposition step) that forms via the sol-gel mechanism, followed by silica growth. As the temperature increases and silica growth seems to create intra-molecular phase separation within the AHMBs, where by the PEG SCs stay dissolved while the PDMAEMA SCs start to collapse. Because of the presence of PEG SCs (*i.e.*

very weak interactions between PEG and silica precursor within the pH range 2.0-7.0)[36, 37] and the stiffness of the backbone, these AHMBs aggregate enter-molecularly to form cylinder-like structures with a silica core and PEG shell.

In the absence of the silica precursor, hetero-arm AHMBs self-assemble into fibrillar structures upon increasing solution temperature as shown in Figure 5.8, [(C) and (D)]. In this case, the hetero-arm AHMBs were molecularly soluble in water at neutral pH (6.5) at RT. However, as the temperature increases the PDMAEMA SCs start to collapse at a temperature close to their LCST (~ 55 °C). Continuous temperature increase leads to the intra-molecular phase separation of the two SCs, in a similar way as for AMBs discussed in Chapter 4, *i.e.* collapsed PDMAEMA hides away from water, while PEG forms a protective shell around them. The diameter of the obtained cylindrical aggregates was ~ 30 nm and length of ~1 µm.

In conclusion, hetero-arm AHMBs with two different SCs were prepared via a combination of grafting through and grafting from approaches. Grafting through involves the radical copolymerization of well-chosen functional monomers with macromonomer to produce high molecular weight, soluble MBs with one type of SC. The transformation of these functional groups allows the generation the second SC via the grafting from approach. The obtained hetero-arm AHMBs were then employed as template to fabricate organic-silica hybrid nano-structures.

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Chapter 6: General conclusions and possibilities for further work

Abstract

Throughout the course of this study, different types of hetero-arm MBs were investigated in terms of their synthesis and characterization as well as potential applications. The preliminary results of these investigations and recommendations of future work are presented in this chapter.

General conclusions

This dissertation focuses on the development of a new bottom-up approach to prepare nano-structures of cylindrical shapes using hetero-arm MBs with alternating hetro-arms (SCs). Two types of hetero-arm MBs were synthesized via combination of different grafting approaches commonly used to prepare MBs. The combination of these approaches provides an efficient route to prepare different type of MBs with high molecular weight and high grafting density. A combination of grafting through and grafting onto approaches allowed the synthesis of amphiphlic alternating MBs, with PEG and different alkyl SCs. The self-assembly of these hetero-arm MBs in selective solvents was then investigated. In a different combination strategy, alternating hetero-arm MBs (hetero-arm AHMBs) were also prepared via the combination of grafting through and grafting from approaches. The obtained hetero-arm AHMBs were then employed as a template to prepare organic/inorganic hybrid materials.

In this dissertation, an introduction to MBs is given in **Chapter 1**. This chapter gives a brief definition to MBs and their different structures as well as the synthetic routes used to prepare such macromolecules. In **Chapter 2** the term self-assembly is discussed. This chapter describes some of important aspects of macromolecular self-assembly and their employment in construction of novel materials of various shapes and sizes. **Chapter 3** describes the synthesis of the monomers and macromonomers used to prepare the hetero-arm MBs. Because of the alternating nature of the backbone required to synthesis hetero-arm MBs, monomers and macromonomers with electron donating/accepting nature were synthesized. The challenges faced to synthesize these molecules were also highlights in this chapter.

Chapter 4 illustrates the successful synthesis of amphiphilic hetero-arm hetero-arm molecular brushes (AMBs) with hydrophobic and hydrophilic side chains (SCs). The synthetic route involves a combination of two grafting approaches, "grafting through" and "grafting onto". In the first approach, the grafting through approach was used to synthesize MBs with hydrophilic SCs and reactive sites alternatingly distributed along the backbone. In this step, VB-PEG$_{12}$ macromonomer was polymerized with MAnh in an alternating fashion. In the second approach, the grafting onto approach was used to introduce hydrophobic arms via a nucleophilic substitution of primary amines on the MAnh units. The grafting efficiency was satisfactory high

as indicated by FT-IR analysis. A number of AMBs with varied hydrophobic side-chain length were synthesized to investigate the self-assembly behavior of these AMBs in THF/water mixtures. The preliminary results indicate these AMB assembled into cylindrical aggregates, as shown in the FE-SEM and TEM images. The morphology and size of the aggregates was to some extent influenced by the length of the hydrophobic side chains. Generally, these cylindrical aggregates may consist of two morphologies, *i.e.* elongated vesicle (at the center of the aggregates) and elongated micelles (at the extremes of the cylinders). The ability of the longer side chains to crystallize during the formation of these aggregates may restrict further growth.

Chapter 5 describes the synthesis of a different type of hetero-arm MBs. Alternating hetero-arm molecular brushes were successfully synthesized in two steps. Grafting through approach was used to prepare one type of the SCs, while grafting from was used to generate the other type of SCs. Grafting through involves the radical copolymerization of well-chosen functional monomers with macromonomer to produce high molecular weight, soluble MBs with one type of SC. The transformation of these functional groups allows the generation the second SC via the grafting from approach. The obtained hetero-arm AHMBs were then employed to fabricate nano-objects of cylindrical morphology. The initial experiments showed that hetero-arm AHMBs can self-assemble into fibril structures of various sizes. Furthermore these hetero-arm AHMBs were also used as templates to build organic-silica hybrid nano-structures. In the presence of an inorganic precursor these MBs formed organo-silica nano-wires with a diameter of ~ 45 nm and length in range of 5 µm.

Recommendations:

Chapter 2 of this dissertation described the importance of self-assembly of many macromolecular in fabricating novel and sophisticated materials of different shape and size for many applications. However, the self-assembly of some macromolecules with complex architecture, like hetero-arm MBs, is still at its first and infancy stages. This dissertation provides an initial approach in the field hetero-arm MBs that can be extended to almost limitless investigations, mechanistic investigation, molecular composition investigations, and potential application. In terms of mechanistic investigation, one should focus on the parameter that govern the self-assembly of these macromolecules such as the SCs length and ratios. Investigation in terms varying the
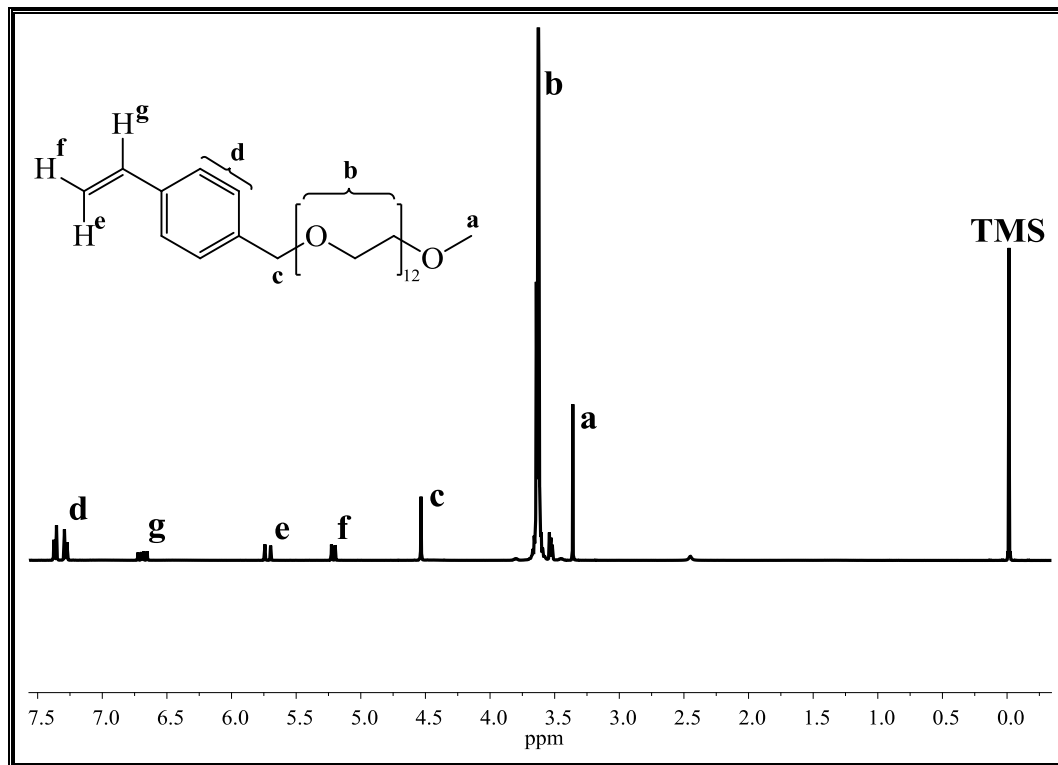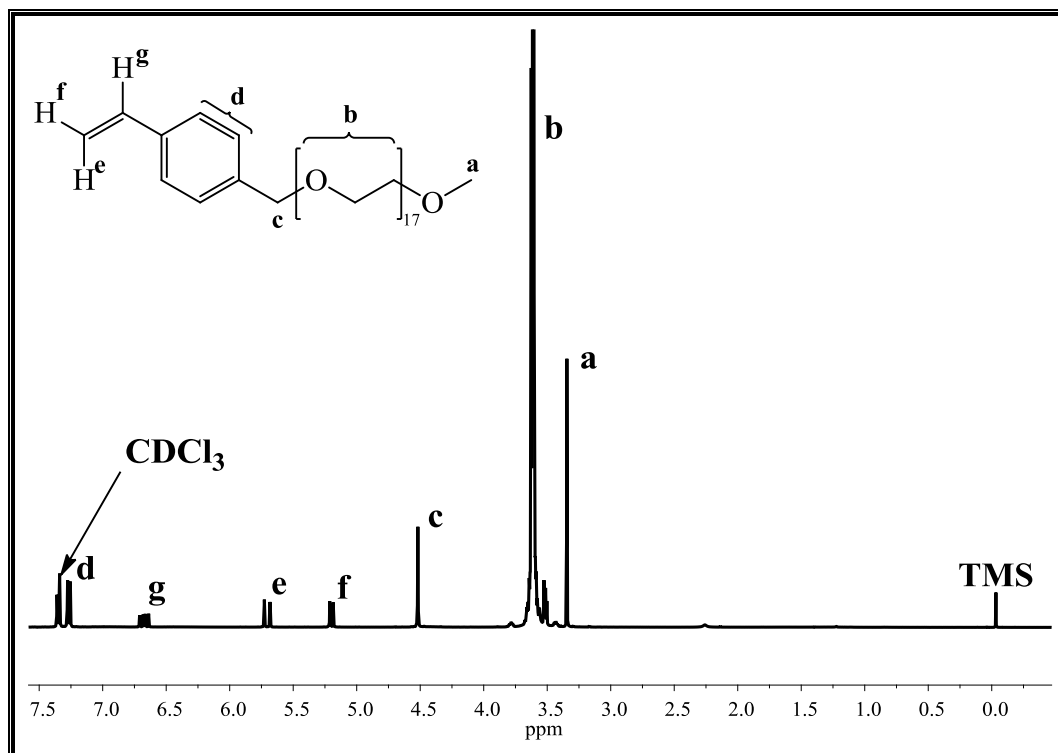
chemical composition, *e.g.* other type of SCs that can be used for suitable applications are also needed. Finally investigating other possible synthetic routs is also important to provide easy access to hetero-arm MBs.

Appendixes: NMR spectra of the (macro)monomers

Appendix A: ^{1}H NMR spectrum of VB-(PEG$_{12}$) in CDCl$_3$.

Appendix B: ^{1}H NMR spectrum of (VB-PEG$_{17}$) CDCl$_3$.

Appendix C: ^{1}H NMR spectrum *N*-hydroxyphenyl-Maleimide (*N*-HPh-MI) in DMSO.
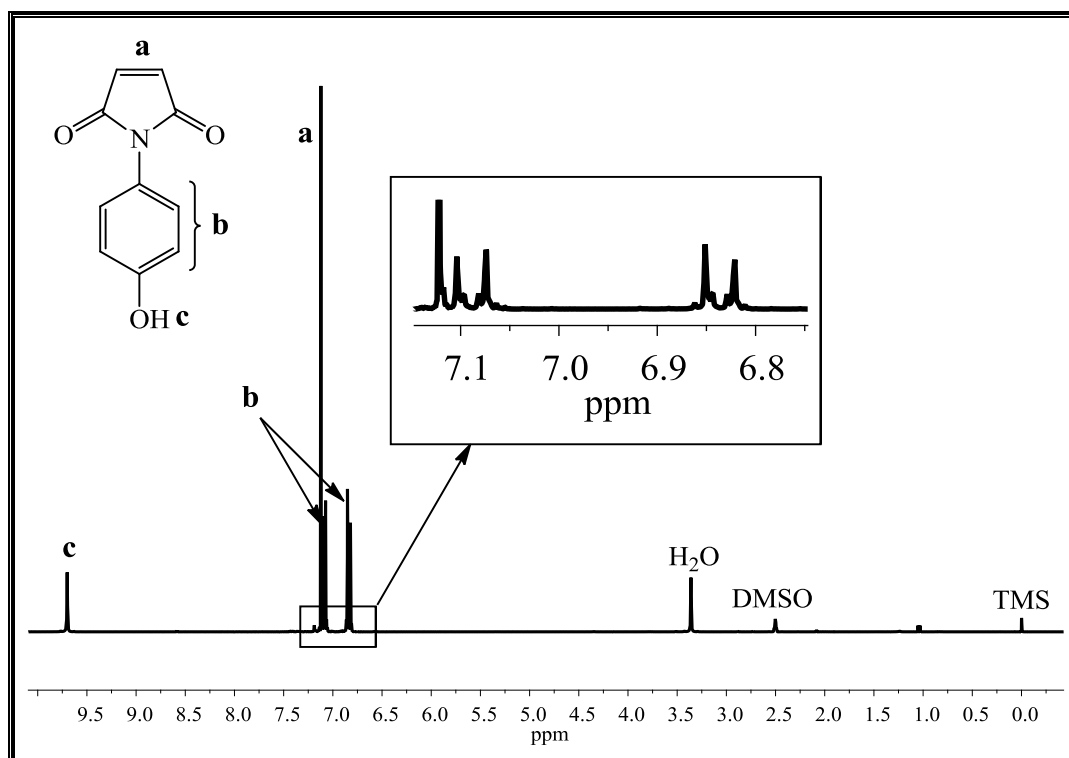
Appendix D: ^{1}H NMR spectrum *N*-dodecylmaleimide (*N*-C$_{10}$H$_{21}$-MI) in DMSO.
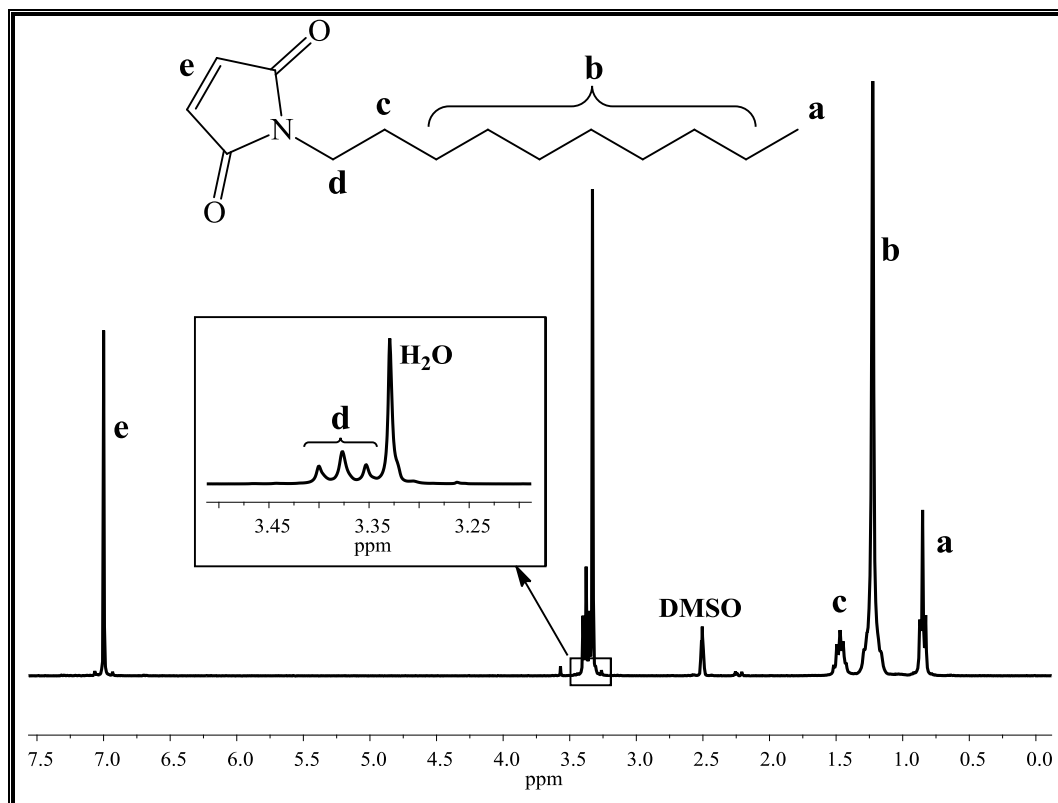
Appendix E: ^{1}H NMR spectrum *N*-hexadecylmaleimide (*N*-C$_{16}$H$_{33}$-MI) in CDCl$_3$

100
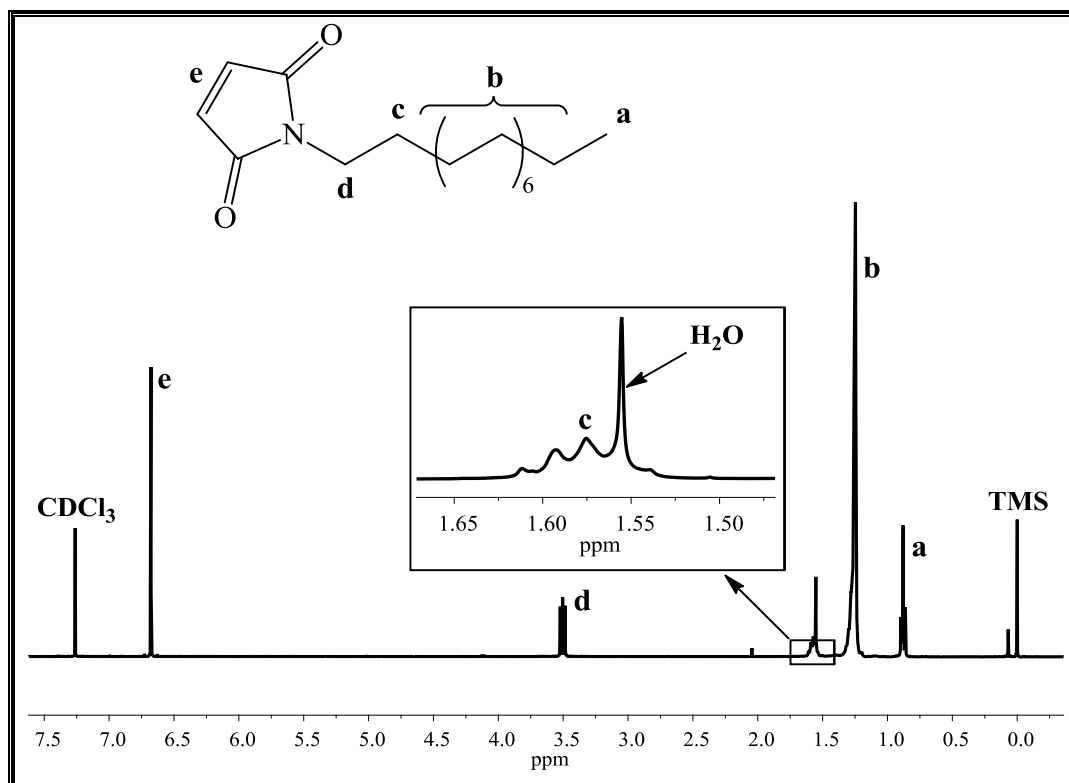
Appendix F: ^{1}H NMR spectrum *N*-icosylmaleimide (*N*-C$_{20}$H$_{41}$-MI) in CDCl$_3$