División Jóvenes Profesionales



Mini-Review

AMPHIPHILIC COPOLYMERS WITH DIFFERENT ARCHITECTURES AS AN ALTERNATIVE TO CONVENTIONAL SURFACTANTS

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Resumen Gráfico - Graphical Abstract



Resumen

El uso de macrosurfactantes anfifílicos como agentes emulsificantes a demostrado tener mayor eficiencia que los surfactantes de bajo peso molecular usualmente empleados. Tradicionalmente, los copolímeros en bloque han sido los primeros sistemas macromoleculares en ser probados como surfactantes. Debido a la introducción de técnicas de polimerización controlada en la década del 90, recientemente se han reportado una serie de avances en cuanto a la preparación de macromoléculas de arquitectura compleja para este tipo de aplicaciones. En este mini-review, vamos a reportar el estado del arte y los avances más recientes en la preparación de macromoléculas con especial énfasis en copolímeros con arquitecturas complejas (tipo estrella y cilindricas). También presentaremos un resumen de las posibles rutas de síntesis y monómeros que ofrecen una alternativa para obtener surfactantes novedosos.

Abstract

The use of amphiphilic macrosurfactants as emulsifying agents has shown to have higher efficiency with respect to low molecular weight surfactants. Traditionally, block copolymers have been the first macromolecular systems used for this purpose. Due to the introduction of controlled polymerization techniques in the late nineties, the last decade showed an increase in the number of papers that report the

preparation of macromolecules with complex architectures. In this mini-review, we report some advances in the preparation of amphiphilic macromolecules, with special emphasis in copolymers with complex architectures, star and cylindrical. We present a summary list about the synthetic methods and monomers employed to obtain amphiphilic systems as possible alternatives to traditional surfactant.

Palabras Clave: surfactantes macromoleculares, copolímeros anfifilicos, polimerización controlada. *Keywords:* macromolecular surfactants, amphiphilic copolymers, controlled polymerization.

1. Introduction

Surfactants are amphiphilic organic compounds that present two regions with very different polarity, these amphiphilic molecules have the ability to self-assemble in aqueous environment producing micelles. One region of surfactants are hydrophilic/lipophobic and the other is lipophilic/hydrophobic. This context gives to these chemical entities, formidable characteristics and applications. Many products that we use in our daily life are based or contain amphiphilic molecules.¹ Figure 1 shows a simple representation of a general surfactant. Commonly, these molecules have as lipophilic group large hydrocarbon moieties, such as octyl (C_8), lauryl (C_{12}), stearyl (C_{18})s hydrophilic part can contain ionic or non-ionic (polar) groups. The most common ionic groups are sulfonates, phosphates, quaternary ammonium salts; as non-ionic groups, generally, oligo ethylene glycols are used. In order to decrease the free energy, surfactants can be adsorbed at the interface water-oil or can incorporate small oil phases in the formed micelles (figure 1).



Figure 1. Schematic representation of a surfactant and its behaviour at the interface water-oil or micelle formation.

Recently, amphiphilic copolymers have been employed as macrosurfactants with good results in many areas.² Polymeric systems have some advantages compared to small molecule surfactants.

Due to their size, amphiphilic polymers produce a better control over lyophilic/lyophobic balance. This generates more thermodynamically stable structures, producing a lower critical micelle concentration (CMC) than small molecule analogues.³ Some commercially available polymeric surfactants, such as block copolymers of poly(ethylene oxide) and poly(propylene oxide), have already found a widespread use as wetting agents, emulsifiers, foam stabilizers, and detergents. These copolymers are called Poloxamers and Pluronics.

More recently, polymeric structures with complex architectures have attracted attention because these structures provide unique opportunities to control the molecular packing and the symmetry (figure 2).

In this mini-review, we describe the most recently amphiphilic copolymer systems prepared in the scientific community with a special emphasis in copolymers with complex architectures, star and cylindrical branched copolymers. Firstly, a short description about traditional block copolymers will be presented and then, a deeper description about star and cylindrical branched copolymers will be presented. Figure 2 shows a schematic illustration of cylindrical branched copolymers relative to the conventional amphiphilic block copolymer and small molecule surfactant.



Figure 2. Schematic illustration of cylindrical branched copolymers relative to the conventional amphiphilic block copolymer and small molecule surfactant.

2. Linear copolymers

Linear copolymers can be classified based on how the units are arranged along the chain.⁴ Four are the principal and most common arranged forms, alternating copolymers, block copolymers, statistical copolymers and sequential copolymers (Figure 3). For the first case; i.e., alternating copolymers, the monomers present an alternation along the chain (*1* in figure 3). On the other

hand, block copolymers present two blocks of each monomer in the same chain (2 in figure 3). Statistical copolymers are systems in which the sequence of monomers does not present an ordered pattern (3 in figure 3) and, finally, in sequential copolymers the monomer units are arranged in a repeating sequence (4 in figure 3). All microstructures mentioned can be designed to present two regions with very different polarity. In the following sections, the strategies to provide amphiphilic characteristic to each linear copolymer microstructure will be explained.

2.1 Linear Block Copolymers

Linear block copolymers are the most common copolymers employed as amphiphilic entities. Block copolymers are heterogeneous polymer systems, different blocks from which they are built is independent of each other. As a result, block copolymers often combine the relevant properties of each homopolymer. This feature is the reason why a block copolymer formed by two monomers with very different polarity will present two regions with very different polarity.



Figure 3. Most common copolymer microstructures: alternating copolymers, block copolymers, statistical copolymers and sequential copolymers.

One of the most used and studied non-ionic hydrophilic monomer is the ethylene oxide (EO). Blocks copolymer based on EO have strong implications in many industrial processes. When propylene oxide (PO) is used as a hydrophobic entity, EO and PO produce a very used block and triblock copolymers. Moreover, triblock copolymers POE-PPO-PEO are commercially available as non-ionic macromolecular surface-active agents.⁵ An important characteristic of POE-PPO-PEO solutions is their self-assembling and thermo-gelling behaviour. Concentrated aqueous solutions of POE-PPO-PEO are liquid at low temperature and form a gel at higher temperature in a reversible process. This feature and due of their amphiphilic structures, POE-PPO-PEO copolymers have useful in many industrial applications, such as emulsification, dispersion stabilization, detergency, lubrication, separation, cosmetics, pharmaceutical applications, bioprocessing, release among others.⁶

Several ionic monomers have been employed as hydrophilic entities to obtain amphiphilic block copolymers. Sternhagen et al.⁷ synthesized amphiphilic ionic peptoid block copolymers. These copolymers have been studied in water at pH = 9 and their amphiphilic capability produced small spherical micelles with a hydrodynamic radius of ~5–10 nm and critical micellar concentration (CMC) in the 0.034–0.094 mg/mL range.

Matsuoka et al,^{8–10} obtained a diblock copolymers having sulfonic acid groups in its hydrophilic chain with poly(diethylsilacyclobutane) or polystyrene as a hydrophobic segment. These authors found that the water surface tension depends on copolymer composition and chain lengths. The micelles size were 100-200 Å and were confirmed by dynamic light scattering and small-angle X-ray scattering experiments. Due to strong ionic character of this class of amphiphilic block copolymer, these authors suggest some peculiar behaviour in the surface tension.

2.2 Linear non-block Copolymers

This class of copolymers have been employed as a new alternative to linear block copolymers. The synthetic procedures to obtain non-block copolymers use to be easier than block copolymers. In this class of macromolecules, the amphiphilic behaviour is provided by the pendant group. In the last decades, the papers about these systems have grown significantly. Figure 4 shows a schematic representation of this class of copolymers and the most common monomers used to give the amphiphilic behaviour. This class of macromolecules is also known as branched polymers or cylindrical brunched polymers (in section 3, this class of macromolecules will be explained again).

Some authors described the preparation and use of non-block copolymers with amphiphilic properties. Some of these authors have used free radical copolymerization of monomers with long polar and nonpolar pendant groups.^{11–15} This context generates linear backbones with hydrophilic and hydrophobic polymeric pendant group statistically, alternately or sequentially distributed along the backbone. More recently, the literature shows works in which controlled radical copolymerization techniques allowed to obtain this kind of systems with better composition, molecular weight, and polydispersity.

Respect to the aforementioned non-block copolymers, block copolymers have a clear separation between hydrophobic and hydrophilic regions and this situation give good intermolecular selfassemblies and produce dispersions with monodisperse size and morphology. Although hydrophilic/hydrophobic statistical copolymers had less intermolecular self-assemblies to produce micelles, these copolymers have demonstrated potential capabilities as emulsified agents to generate disperse systems similar to the case of Pickering emulsions.

2.3 Star-branched copolymer

Star polymers are branched macromolecules consisting of several linear polymer chains connected to a central point.^{16–18} The central point called "the core", is generally a simple molecule, or macromolecule with low molecular weight. The chains, commonly called "the arms", can be linear homo- or copolymer chains. For copolymer chains, these can present their own structural characteristics previously descript, alternating, block, statistical and sequential. On the other hand, based on chains distribution anchored to the core, star polymers can be classified as homo-arm star polymers¹⁰ or mikto-arm star copolymers (figure 4).¹¹ The first category consists in a symmetrical structure with all arms containing identical chemical composition and similar chain length. Contrary, mikto-arm star polymers contain different arm species with different chemical compositions and/or chain length. This short review will focus on the first-mentioned category.



Figure 4. Schematic representation of star copolymers with homo and mikto arms (a) and the most common synthetic approaches (b)

Star polymers can be synthesized in different ways (figure 4b), (a) growing the polymer chains from a preformed core (grafting from),^{21–23} (b) coupling preformed polymer chains and preformed core^{24–26} or (grafting to) (c) generating the core from preformed polymer chains (grafting through).^{27,28}

Several authors have been prepared amphiphilic star copolymers with promising and improved properties with respect to traditional analogous. Below, synthetic strategies and emulsification properties of some amphiphilic star copolymers are mentioned.

2.4 Star Block branched Copolymers

This kind of block copolymers is a new class of water-soluble amphiphilic block copolymers. Several monomers have been combined to prepare these materials, ionic and non-ionic and the final the properties generally improve with respect to non-branches analogous. The most important contributions of this class of polymers have been in bioscience.^{29–32} Below, some relevant examples of synthesis and properties of these copolymers are mentioned.

Kreutzer et al.³³ have synthesized water-soluble, amphiphilic star block copolymers with a large number of arms based on n-butyl methacrylate (BMA) and poly-(ethylene glycol) methyl ether methacrylate (PEGMA). Using fourth-generation hyperbranched polyester (Boltorn H40, core entity) terminated in 2-bromoisobutyric acid as a macroinitiator, sequential atom transfer radical polymerization (ATRP) allowed obtaining star polymers that contained on average 20 diblock copolymer arms. The AFM image in figure 5 clearly shows the individual arms of the star polymers and allows for the determination of the exact number of arms per molecule. These authors obtained after analysis of more than 1000 molecules an average number of arms of 16, a value slightly lower than the number determined by alcoholysis of the H40 precursors.





Figure 5. (a) Atomic force microscopy height micrograph of an amphiphilic star block copolymers based on PBMA, PPEGMA and Boltorn H40. (b) Distribution of the number of arms, as evaluated from AFM images. "Reprinted with permission from (Kreutzer, G.; Ternat, C.; Nguyen, T. Q.; Plummer, C. J. G.; Månson, J. A. E.; Castelletto, V.; Hamley, I. W.; Sun, F.; Sheiko, S. S.; Herrmann, A.; Ouali, L.; Sommer, H.; Fieber, W.; Velazco, M. I.; Klok, H. A. *Macromolecules* 2006, *39* (13), 4507–4516.). Copyright (2018) American Chemical Society."

Using SAXS experiments on aqueous solutions, these authors indicated that the star block copolymers can be regarded as unimolecular micelles and through NMR spectroscopy they evaluated the ability of the polymers to encapsulate and release hydrophobic guests. These star amphiphilic block copolymers have been employed to study hydrophobic fragrances encapsulation in water. Diffusion coefficients of four different fragrance molecules in the free form and in the presence of the polymer have been determined trhought NMR spectroscopy and the degree of encapsulation depends on the hydrophobicity of the guest molecule. The fragrance molecules are mainly located in the hydrophobic core of the polymer, which is tightly packed, whereas the hydrophilic shell is flexible and takes up only a small percentage.³⁴

Carletto et al,³⁵ prepared polymethyl methacrylare-block-polystyrene arms with cross-linked divinylbenzene core. The authors observed that several factors affecting the polymer aggregation and solubility such as the length, the composition of the arms and the polymerization catalyst used. On the other hand, using ATRP strategies, Gao et al³⁶ have been prepared three-arm star block copolymers based on polystyrene and poly(ethylene oxide) chains to evaluate its amphiphilic capability.

Poree et al,³⁷ evaluated the transdermal drug delivery capability of star block copolymer micelles as an alternative to the more common oral and intravenous routes. For this, the authors synthesized 6- and 12-arm star amphiphilic block copolymers using sequential ATRP of polar oligo(ethylene glycol) methacrylate and nonpolar lauryl methacrylate. The polymerization was carried out using brominated macroinitiators based on 2,2-bis(hydroxymethyl) propionic acid. These star block copolymers demonstrate the ability to encapsulate polar entities in nonpolar media. Furthermore, their transdermal carrier capabilities were demonstrated, verifying penetration of the carriers into the stratum corneum.

Liu et al,³⁸ prepared amphiphilic multiarm star copolymer based on Boltorn H40, poly(L-lactide) and Poly(2-ethoxy-2-oxo-1,3,2-dioxaphospholane) (PEP) (H40-star-PLA-SS-PEP) with disulfide linkages between the hydrophobic polyester core and hydrophilic polyphosphate arms. Due to their amphiphilic structure, H40-star-PLA-SS-PEP was able to self-assemble into micelles in aqueous solution. These structures were used to evaluate the glutathione-mediated intracellular drug delivery and the micelles show potentiality to improve the antitumor efficacy of hydrophobic chemotherapeutic drugs.

To disperse an oil phase in water, Li et al.³⁴ prepared a series of well-defined amphiphilic multiarm star copolymer based on poly(ethylene oxide) and poly(butyl acrylate). These star structures produce the formation of stable water-in-oil emulsions. On the other hand, Narrainen et al.³⁹ studied the micellization behavior of amphiphilic block copolymers based on poly(*n*-butyl

methacrylate) [P(n-BMA)] and poly[(2-dimethylamino)ethyl methacrylate] (PDMAEMA) on functionalized bromo P(n-BMA) macroinitiator cores prepared from monofunctional, difunctional, and trifunctional initiators: 2-bromo-2-methylpropionic acid 4-methoxyphenyl ester, 1,4-(2-bromo-2-methyl-propionate) benzene, and 1,3,5-(2-bromo-2methylpropionato)benzene. Fluorescence spectroscopy and dynamic light scattering showed that the micellar capability and micelle size depended essentially on the molecular weight of the copolymer and arms number.

2.5 Star non-block branched Copolymers

This class of copolymer have been less study than star block branched copolymers. The amphiphilic behaviour of these copolymers is provided by selecting differentiate polarities between core entity and copolymer shell. Another alternative, as the case of linear non-block copolymers, is selecting monomer with large pendant group. Below are some relevant examples of synthesis and properties of these copolymers.

Kowalczuk et al,⁴⁰ synthesized amphiphilic star copolymers composed of a hyperbranched poly(arylene oxindole) (PArOx) core. Shells were different length arms formed by poly[di(ethylene glycol) methyl ether methacrylate] (PDEGMA) or copolymer poly [di(ethylene glycol) methyl ether methacrylate-ran-oligo(ethylene glycol) methyl ether methacrylate] P(DEGMA-ran-OEGMA). The amphiphilic behaviour of this system is due to the hydrophobic core and hydrophilic shells. These thermo-responsive star non-block branched copolymers showed good properties in solution and the amphiphilic capability was study by light scattering techniques, AFM and cryo-TEM. Different results indicate that star non-block branched copolymers obtained are prospective carriers for biomolecules.

Combining self-condensing vinyl polymerization (SCVP) and reversible addition–fragmentation chain transfer (RAFT), Narrainen et al,³⁹ designed and synthesized amino acid-based hyperbranched polymers based on tert-butyl carbamate (Boc)-L-valine acryloyloxyethyl ester (Boc-Val-HEA) and S-(4-vinyl)benzyl S'-butyltrithiocarbonate (VBBT) with variable degrees of branching (DB), molecular weights (Mn), and chainend functionalities. Removing Boc groups from the polymers results in water-soluble pH-responsive cationic hyperbranched architectures with tunable pH responsiveness. Dynamic light scattering (DLS), atomic force microscopy (AFM) and scanning electron microscopy (SEM) reveal the interesting self-assembly of star polymers in aqueous media with amino acid-based cores and water-soluble thermo-responsive arms.

2.6 Cylindrical branched copolymers

Cylindrical brunched copolymers are branched polymers consisting of several linear polymer chains connected to a linear polymeric backbone (figure 6).^{41,42} This kind of structures are involved in various biological functions, including the lung and particular processing.

The linear polymeric backbone is generally a functional polymer chain and the bonded chains can be linear homo- or copolymers structures. In the case of copolymers, these can present their own microstructure, such as alternating, block, statistical and sequential (figure 6a). On the other hand, based on chains distribution anchored to the backbone, linear branched copolymers can be classified as random brush copolymers and gradient brush copolymers (figure 6a). In the first category, a uniform density of chains are bonding along the backbone and in the second category; the polymeric chains are forming a gradient along the backbone. the first-mentioned category.

Cylindrical branched copolymers can be prepared principally by three synthetic approaches, grafting from, grafting through and grafting to. In grafting from reactions, the backbone polymer contains reactive sites to initiate the polymerization of the side copolymer chains (figure 6b). Grafting to reactions connect an end functional of preformed copolymer chains with a backbone polymer with reactive sites for connecting side copolymer chains (figure 6b). Finally, in Grafting through reactions, a typical copolymerization occurs with macromonomer precursors (figure 6b). In order to prepare structures with cylindrical shapes, in the synthetic procedures, the backbone should be much longer than the lateral anchored chains.



Figure 6. Schematic representation of cilindrical copolymers with random- and gradient-branched distribution (a) and the most common synthetic approaches (b)

In the literature, the number of monomers employed to obtain cylindrical brunched polymers is not very extent and these macromolecules have been prepared in general to produce functional materials. Based on our consideration, below are listed the most relevant examples. A distinctive observation of this class of macromolecules with densely grafted polymeric side chains, is that According to the above characteristic Li et al,⁴⁶ reported the synthesis, characterization, and properties of cylindrical-brush polymers based on poly-N-isopropyl-acrylamide (PNIPAM) side chains, in which the side-chain repulsion can be controlled easily by variation of the temperature due to the well-known lower critical solution temperature in aqueous solution. PNIPAM brushes were grafting from the macroinitiator poly-2-bromoisobutyryloxyethyl methacrylate (PBIEM). This macroinitiator can be prepared by ATRP of hydroxyethylmethacrylate and subsequent reaction with a-bromoisobutyric acid bromide. The AFM image in figure 7 clearly shows the cylindrical structure of the obtained copolymer by Li.



Figure 7. AFM image of the cylindrical PNIPAM brush polymers spin casted from a dilute solution in acetone. "Reprinted with permission from (Li, C.; Gunari, N.; Fischer, K.; Janshoff, A.; Schmidt, M. Angew. Chemie - Int. Ed. 2004, 43 (9), 1101–1104). Copyright (2018) John Wiley & Sons Inc."

In cylindrical brunched polymers, the conformational degree and physical-chemical properties can be controlled by steric repulsion of grafted side chains. In this context, the polymers can be either flexible or stiff, depending on the length of the side chains and their grafting density. Cylindrical brunched polymers can be designed to switch their conformation in response to environmental changes, e.g. solvent, temperature, pH, ionic strength. Gunari et al,⁴⁷ reported the complex formation of cylindrical brush polymers with poly(L-lysine) (PLL) side chains and sodium dodecylsulfate (SDS). These authors found that due to the hydrophobicity of the b-sheets formed by the PLL side chain–SDS complexes, increasing amount of added surfactant the cylindrical polymers first adopt a helical conformation followed by a spherically collapsed

structure. Additionally, Cong et al,⁴⁸ systematically investigated the influence of surfactant, salt, and pH on the supramolecular structure of cylindrical brush polymers with poly(L-lysine) (PLL). These authors found that salt additions destroy the helical structures as do pH conditions below 4 and above 6. The most probable reason is that the polymer surfactant complexes start to disintegrate. Finally, Cong et al,⁴⁹ reported the synthesis of a core-shell cylindrical brush copolymer with poly(2-hydroxyethyl methacrylate) (PHEMA) backbone and polystyrene-block-poly(ε-caprolactone) (PS-b-PCL) diblock side chains with ATRP grafting from method.

2.7 Cylindrical Branched Block Copolymers

Cylindrical branched block copolymers are the most studied cylindrical branched copolymer. Several authors have described the preparation and uses of cylindrical branched block copolymers. Based in our consideration, below are listed the most relevant examples. Wooley et al. developed the synthesis of cylindrical branched block copolymers based on poly(acrylic acid) with core-shell and block distribution. These authors investigated their self-assembly in aqueous solutions.^{50,51} In some articles, cylindrical branched block copolymers produced spherical aggregates often characterized in the dried state.^{50,52} In this state, the information obtained on the micellar composition and morphology is not representative of the actual state. On the other hand, Fenyves et al.⁵³ explore a new class of giant polymeric surfactants with cylindrical branched architecture. These amphiphilic block copolymers containing polylactide (PLA) and poly(ethylene oxide) (PEO) side chains were synthesized by a grafting-from method. Critical micelle concentration of these materials was determined to be approx. 1 nM indicating an enhanced thermodynamic stability of the produced micelle aggregates.

Gromadzki et al,⁵⁴ synthesized amphiphilic methacrylate-based cylindrical branched block copolymers using grafting-from ATRP. For this, the authors firstly prepare poly(2-(2-bromoisobutyryloxy)ethyl methacrylate) PBIEM as the macroinitiator and next tert-butyl methacrylate (tBuMA) was polymerized from PBIEM. After the chlorine-terminated PBIEM-graft-P(tBuMA)-Cl macroinitiators were subsequently copolymerized with 2-(dimethylamino ethyl) methacrylate (DMAEMA) yielding densely grafted copolymers with diblock copolymer side chains PBIEM-graft-P(tBuMA)-block-PDMAEMA. The hydrolysis of tert-butyl groups produce the ionic amphiphilic methacrylate-based cylindrical branched block copolymers.

Chenet al,⁵⁵ combining step-growth polymerization and reversible addition fragmentation chain transfer (RAFT) polymerization in a "grafting from" methodology to produce amphiphilic cylindrical branched block copolymers based on styrene and tert-butyl acrylate block copolymer arms from poly(N-alkyl urea peptoid) backbone. The tert-butyl groups were removed using

trifluoroacetic acid affording hydrophilic polyacrylic acid segments. The molecular brushes were observed to generate stable micelles in aqueous solution.

Radzinski et al,⁵⁶ produced amphiphilic cylindrical branched block copolymers via ring-opening metathesis polymerization using grafting through process. These authors studied different parameters on the grafting process and they optimized conditions yielded amphiphilic cylindrical branched block copolymers with controllable molecular weights, polydispersity and high conversions. These authors,⁵⁷ also studied the kinetics parameters on the polymerization and the lifetime of the catalyst.

Tang et al,⁵⁸ synthesized amphiphilic cylindrical branched block copolymers based on helical polypeptide backbone and polylactide-b-poly-(ethylene glycol) block copolymer side chains via a grafting-to method. This complex structure has been synthesized by ring-opening polymerization (ROP). Using Langmuir-Blodgett (LB) technique and atomic force microscopy (AFM), the authors have allowed for direct imaging of the synthesized copolymer and the characterization of their molecular weight (MW) distribution. These authors observed that temperature variation can cause partial and reversible unfolding of the helical backbones and the temperature effect is greatly diminished for the copolymers with longer side chains.

Tang et al,⁵⁹ also prepared PNIPAM lateral chains integrated to poly[oligo(ethylene glycol) methacrylate] (POEGMA) as the core using successive atom transfer radical polymerization (ATRP). These authors found that POEGMA core existence gives double phase transition temperature to the unimolecular micelle formed.

Zehm et al,⁶⁰ prepared amphiphilic cylindrical branched block copolymers coupling RAFT and NMP (nitroxide-mediated polymerization) techniques. This combination allows to prepared complex amphiphilic polymers. The resulting polymers were composed of a thermosensitive poly(N-isopropylacrylamide) brush as hydrophilic block and a polystyrene brush as hydrophobic block.

2.8 Cylindrical Branched Statistic Copolymers

This class of copolymer can be prepared by grafting from, grafting thought and grafting to methods. This copolymers are the easiest to prepare and can be obtained by controlled and uncontrolled methods.

Iborra et al,⁶¹ using grafting to method, obtained a copolymer based on lauryl methacrylate and poly(ethylene glycol) methyl ether methacrylate, prepared by solution radical copolymerization. Emulsification studies thought DLS showed different sizes of the formed micelles depending on solvent polarity due to polymer-polymer or polymer-solvent interactions and rheological characterization was undertaken to study the viscoelastic properties of the dispersed systems.

Additionally, this copolymer allowed to disperse small amounts of an organic solvent in water forming only one phase. Finally, due to the amphiphilic properties of this macrosurfactant, highly stable dispersions of carbon nanotubes in water were prepared.

Xia et al,⁶² synthesized polylactide (PLA) and poly(*n*-butyl acrylate) (P*n*BA) side chains at similar MWs. In contrast, brush block copolymers containing approximately equal volume fractions of these MMs self-assembled into highly ordered lamellae with domain spacing over 100 nm. Their assemblies suggested that the block structure adopted an extended conformation in the ordered state.

Yamamoto et al,^{63,64} obtained dual responsive cylindrical branched statistic copolymers based on di(ethylene glycol) methyl ether methacrylate (MEO2MA), tri(ethylene glycol) methyl ether methacrylate (MEO3MA) and MAA grafting from poly(2-(2-bromoisobutyroyloxy)ethyl methacrylate (PBIEM) macroinitiators using atom transfer radical polymerization (ATRP). The authors observed that the lower critical solution temperature (LCST) of this system decreased with the increasing molar fraction of MAA in the copolymer and the responsive nature of the copolymer is enhanced by the dense graft structure of a brush copolymer.

Gromadzki et al,⁵⁴ aforementioned in before section, also synthesized amphiphilic methacrylatebased cylindrical branched statistical copolymers using grafting-from ATRP. These authors did not find clear differences between PBIEM-graft-P(MAA)-block-PDMAEMA and PBIEM-graft-P(MAA)-stat-PDMAEMA.

Using grafting-from via ATRP, Pietrasik et al,⁶⁵ synthesized amphiphilic cylindrical branched statistic copolymers with side chains consisting of two copolymers: 2-(dimethylamino)ethyl methacrylate with methyl methacrylate, and N,N-dimethylacrylamide with butyl acrylate. Poly(2-(2-bromoisobutyryloxy) ethyl methacrylate) and poly(2-(2-bromopropionyloxy)ethyl methacrylate) were used as macroinitiators. These authors found thought DLS studies in water an unusual concentration-dependent LCST suggesting that, due to the compact structure of molecular brushes, an intramolecular collapse can occur.

3. Conclusions

In this mini-review, we have discussed some advances in the preparation of amphiphilic macromolecules, with special emphasis in copolymers with complex architectures, star and cylindrical. Their controlled compositions and architectures are produced by sequential addition of controlled/living polymerization techniques and the combination of controlled polymerization techniques with facile coupling chemistry. One of the most fascinating features of amphiphilic copolymers with complex architectures is their ability to self-assemble into nanoscale ordered structures with various morphologies and behaviours. Amphiphilic copolymers have been

employed as macrosurfactants with good results in many areas and the polymeric systems have some advantages compared to small molecule surfactants, amphiphilic polymers produce a better control over lyophilic/lyophobic balance and this context generates more thermodynamically stable structures, producing a lower critical micelle concentration (CMC) than small molecule analogues. When the polymer architecture presents more complexity, generally their amphiphilic capability produced small spherical micelles and less critical micellar concentration (CMC). In the last decade increase the number of papers that report the preparation of amphiphilic macromolecules with complex architectures and for the future will be crucial the design and synthesis of complex material to replace the materials known today.

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