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Review

Metallo-supramolecular block copolymer micelles

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ABSTRACT

Supramolecular copolymers have become of increasing interest in recent years in the search for new materials with tunable properties. In particular, metallo-supramolecular block copolymers in which metal–ligand complexes are introduced in block copolymer architectures, have known important progress, allowing better control over the synthetic strategies to prepare varied architectures, and providing a better understanding of the parameters governing their self-assembly. These metallo-supramolecular block copolymers have been further considered as precursor for micellar assemblies. The introduction of metal–ligand complexes in block copolymer micelles resulted in micellar structures with unique and unprecedented structures and properties. We review here recent developments achieved in the development of such metallo-supramolecular block copolymer micelles.

1. Introduction

Inspired by nature, supramolecular chemistry has become increasingly important, and is now a major field in chemical research. Nowadays, a large variety of polymers containing supramolecular binding units are synthetically accessible. The combination of macromolecular and supramolecular chemistry paves the way towards new functional materials that can be designed to target a specific application by applying controlled and living polymerization techniques teamed up with organic synthesis for the introduction of functional moieties into the polymer architecture. Among the different possible non-covalent interactions, metal–ligand interactions are of particular interest due to their high directionality, the adjustability of their binding strength in a rather broad range (approximately between 25 and 95% of a covalent C–C bond, with a bond energy of 350 kJ/mol) and the interesting characteristic features of metal–ligand complexes, e.g. redox, photo-physical and magnetic properties [1–4].

Block copolymers are defined as polymeric architectures in which at least two different polymer segments or blocks are connected together. Due to the generally observed thermodynamic incompatibility between those different polymer blocks, phase separation occurs in block copolymers. However, since the blocks are connected together, this microphase separation process is spatially limited and results in self-assembled structures whose characteristic sizes are of the order of a few times the radius of gyration of the constituent blocks and thus range from ca. 10 to 100 nm [5]. Moreover, these self-assembled structures tend to be regularly distributed throughout the bulk material, giving rise to long-range ordering and the formation of structures such as cubic arrays of spheres or hexagonally packed cylinders. This finally results in nanostructured materials whose size and morphology depend on the degree of incompatibility between the constituent blocks, the relative volume fraction and the lengths of the blocks [5]. When a block copolymer is dissolved in a selective solvent, i.e. a good solvent for one of the block and a bad solvent for the other blocks, the

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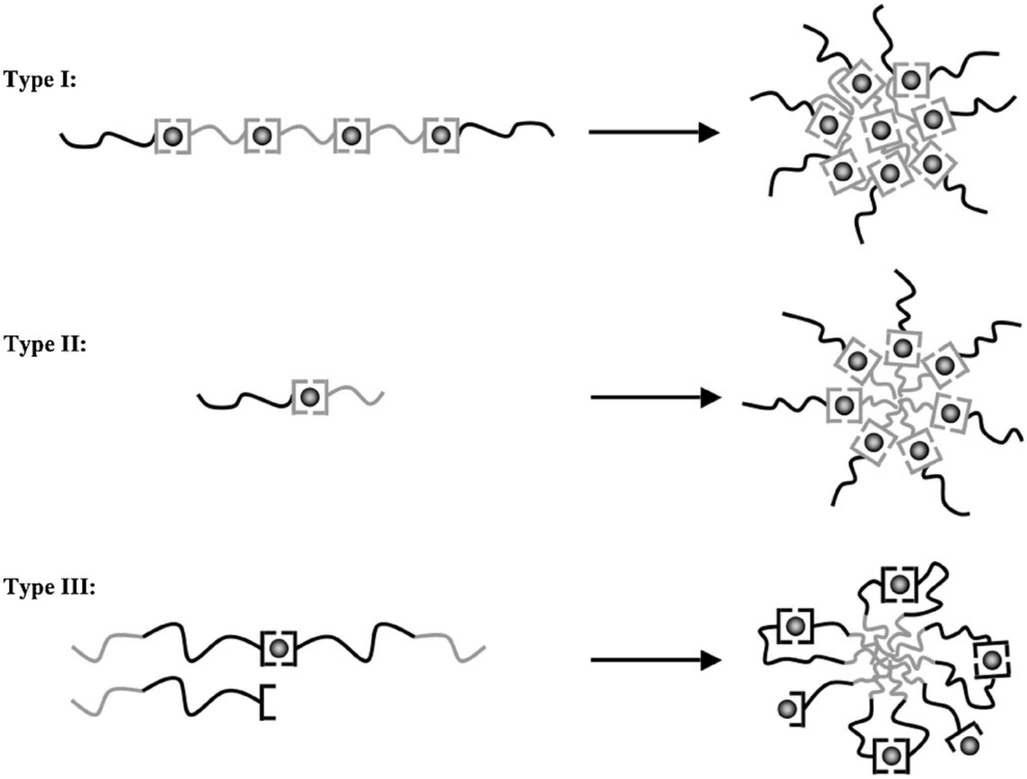

Fig. 1. Schematic representation of the three different types (I, II and III) of metallo-supramolecular block copolymer micelles that will be discussed in this review. The different architectures of the metallo-supramolecular block copolymers from which those micelles are formed are also represented. The core and coronal blocks are represented in dark grey and black, respectively; the metal–ligand complexes are depicted as [•]. Both mono- and bis complexes are shown in the case of metallo-supramolecular block copolymers of type III.

microphase separation results in the formation of micelles. Block copolymer micelles thus contain a micellar core consisting of the insoluble blocks which is surrounded by a micellar corona formed by the soluble blocks [6]. Such micellar systems have received increased attention during the past 30 years due to their numerous applications in various fields ranging from drug delivery to templates for nanoparticle synthesis [7].

A prominent example of the combination of the above-mentioned concepts is found in metallo-supramolecular block copolymers. Metallo-supramolecular block copolymers can be defined as polymeric systems combining metal–ligand complexes to block copolymer structures [8,9]. This should lead to systems combining the characteristic features of block copolymers (e.g. microphase separation between immiscible constituent blocks) with those of supramolecular polymers (e.g. reversibility and tunability of the strength of the supramolecular bonds).

Metallo-supramolecular block copolymers have been considered for the formation of micelles coined metallo-supramolecular block copolymer micelles. In this review, we will focus on three different types of metallo-supramolecular block copolymer micelles that can be distinguished by the different localization of the metal–ligand complexes in the micellar structure. In this respect, metallo-supramolecular block copolymer micelles, in which the metal–ligand complexes are located in the core (type I), at the core–corona interface (type II) or in the corona (type III) will be reviewed and discussed (see Fig. 1). Those metallo-supramolecular block copolymer micelles are originated from the self-assembly in a selective solvent of three distinct types of metallo-supramolecular block copolymers. In the following, the core-forming insoluble blocks will be denoted by A, the corona-forming soluble polymer blocks will be named B, the ligands attached on polymer blocks will be depicted as -[and the metal ions will be shown as •. For all the examples used, mono- (-[•) or bis- (-[•]-) metal–ligand complexes will be discussed.

Metallo-supramolecular micelles of type I are formed from a core in which each monomeric motif contains a metal–ligand complex (depicted as]-A-[•]-A-[•]-A-[•]-A-[, see Fig. 1). This core is surrounded by a corona of a covalent B polymer blocks. In metallo-supramolecular micelles of type II, metal–ligand complexes have been introduced at the junction between the different polymer blocks. This leads to diblock copolymers containing a supramolecular linker between the constituent blocks (A-[•]-B, see Fig. 1). When these A-[•]-B metallo-supramolecular diblock copolymers are dissolved in a solvent selective for the B blocks, metallo-supramolecular micelles of type II are formed that contain a core formed by the insoluble A blocks and a corona constituted by the soluble B blocks. The [•] metal–ligand complexes are located at the core–corona interface (Fig. 1). Metallo-supramolecular block copolymer of type III are formed by classical block copolymer structure functionalized by a ligand at one end (A-b-B-[structure, Fig. 1). Those block copolymers have been self-assembled in a B-selective solvent into block copolymer micelles prior to complexation with metal ions. This leads to block copolymer micelles containing a micellar core formed by the A blocks surrounded by B coronal chains. The extremities of those coronal chains are decorated with -[ligands that are available for complexation with metal ions (Fig. 1).

In the following, we will discuss in detail these three different types of metallo-supramolecular block copolymer micelles.

2. Metallo-supramolecular block copolymer micelles of type I

Metallo-supramolecular micelles of type I have been prepared from either polycondensation-type supramolecular polymers or poly(ferrocenylsilane) (PFS) containing block copoly-

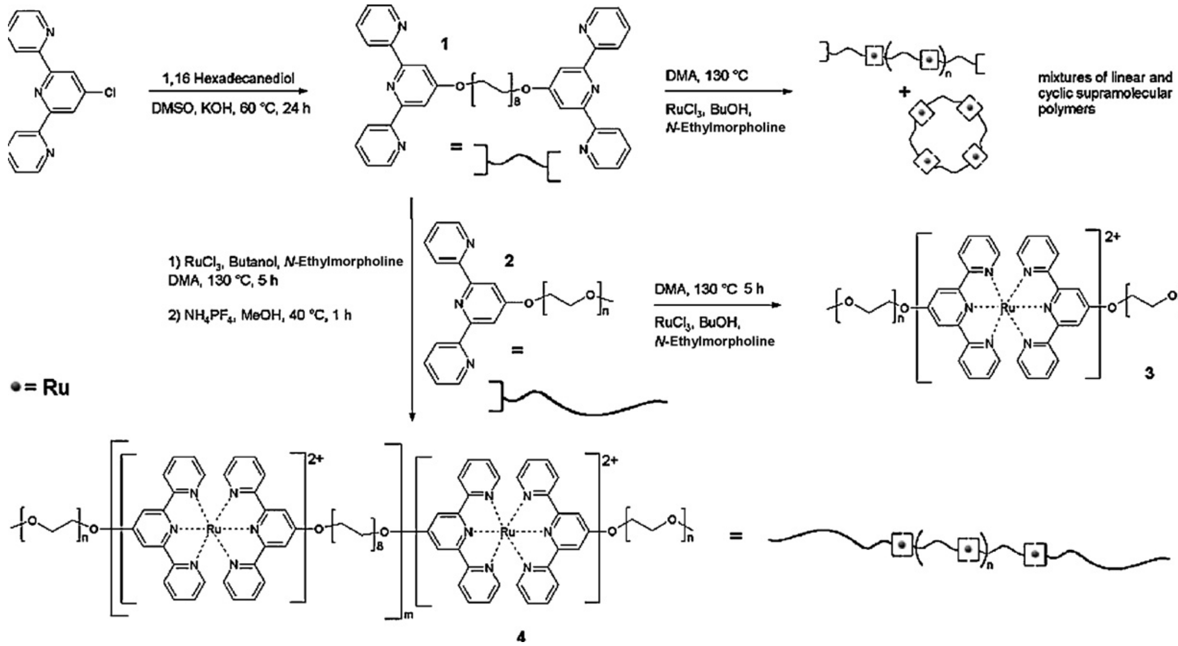

Fig. 2. Synthetic strategy and chemical structure of polycondensation-type I metallo-supramolecular block copolymers based on 1,16-bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane-ruthenium complexes and α-terpyridine-ω-methyl-poly(ethylene oxide) as chain stopper (reprinted with permission from Ref. [10]).

mers. In polycondensation-type polymers, each monomer or macromonomer is linked by non-covalent interactions. This approach requires the use of monomers or macromonomers bearing at least two binding sites (]-A-[) that could be further condensed through supramolecular interactions. This approach leads to polymers containing many supramolecular linkers along the main-chain, and has been successfully applied to the synthesis of supramolecular polymers using metal–ligand coordination complexes (e.g.]-A-[•]-A-[•]-A-[•]-A-[, see Fig. 1). When the polycondensation reaction is quenched by a polymer block bearing a single binding site (B-[), a triblock architecture is obtained (B]-A-[•]-A-[•]-A-[•]-A-[B, see Fig. 1). Dissolving such a copolymer in a selective solvent for the B block results in micelles containing a core formed by the]-A-[•]-A-[•]-A-[•]-A-[blocks and a corona formed by the B blocks (type I, Fig. 1).

This polycondensation approach has been first implemented for the polymerization of 1,16-bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane with $RuCl_3$ under reducing conditions [10]. The initial test polymerizations were conducted in a parallel fashion to optimize the reaction conditions for this polymerization process. This was necessary since known literature procedures for the polymerization of bis-terpyridine ligands require very long reaction times and/or an additional step for the activation of the ruthenium species. The screening process led to the conclusion that dimethylacetamide in combination with butanol and *N*-ethylmorpholine as reducing additives was a very capable reaction medium for the polymerization of 1,16-bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane with $RuCl_3$ under reducing conditions. However, gel permeation analysis showed that a mixture of different species was obtained, which are most likely different sizes of macromolecular rings and linear polymers (Fig. 2).

After the evaluation of the best reaction conditions for the polymerization of 1,16-bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane with $RuCl_3$, the supramolecular B]-A-[•]-A-[•]-A-[•]-A-[B triblock could be synthesized via a polycondensation approach utilizing a α-terpyridine-ω-methyl-poly(ethylene oxide) polymer (PEO) as a chain stopper during the polymerization reaction (Fig. 2). As a consequence, both ends of the synthesized polymer were capped with poly(ethylene oxide) chains resulting in the desired structure. Moreover, the utilization of a chain-stopper in the course of the polymerization avoided the formation of macrocyclic rings to a large extent.

Micelles with a supramolecular metal–ion complex containing core and a PEO corona were obtained in water from the investigated B]-A-[•]-A-[•]-A-[•]-A-[B triblock [10]. Dynamic light scattering (DLS) of the obtained micelles showed the presence of objects with a diameter of 70 nm as well as a minor population of aggregates of these micelles with a size of approximately 500 nm. The polydispersity index obtained by DLS was 0.45, indicating that the micelles

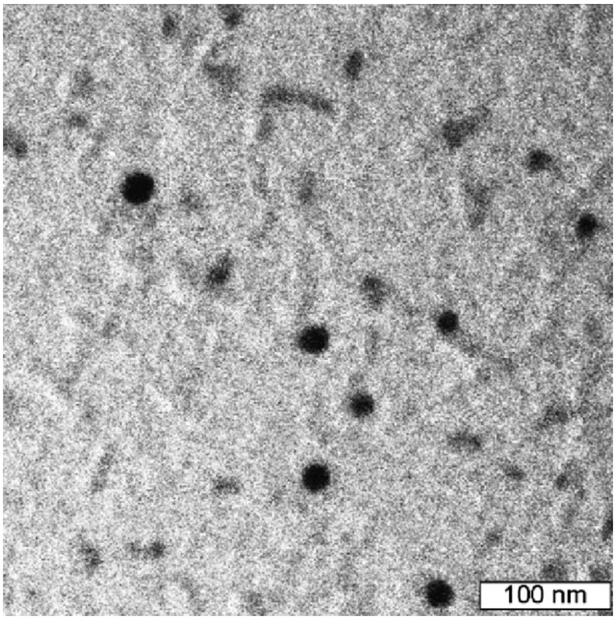

Fig. 3. Transmission electron microscopy picture of aqueous micelles made from polycondensation-type I metallo-supramolecular block copolymers based on 1,16-bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane-ruthenium complexes and α-terpyridine-ω-methyl-poly(ethylene oxide) as chain stopper (reprinted with permission from ref. [10]).

were rather polydisperse. Moreover, those micelles were imaged by resonant mode scanning probe microscopy in water. Furthermore, TEM experiments of unstained micelles revealed spherical objects with a mean diameter of 25 nm (Fig. 3). This result clearly showed that the investigated micelles have the proposed structure with the supramolecular repeat unit in the core of the micelles since a repeat unit containing no metal would show no contrast in TEM and rings would be observed in the case where the metal containing repeat units would form the corona of the micelles (Fig. 3).

In a very recent paper, the same polycondensation strategy was extended to prepare similar B]-A-[•]-A-[•]-A-[•]-A-[B triblock copolymer using again bis(2,2′:6′,2″-terpyridin-4′-yloxy)hexadecane as the A units in the core and a α-terpyridine-ω-methyl-poly(ethylene oxide) polymer as a chain stopper during the polymerization reaction [11]. In contrast to the previous example, Ni(II), Co(II) and Fe(II) ions were used instead of ruthenium ions during the polymerization. The influence of the different binding strength of Ni(II), Fe(II), and Co(II) metal ions with terpyridine ligands on the metallo-polycondensation reaction was studied.

Micelles were prepared from these copolymers in acetone/water (50/50) mixtures and characterized by DLS and cryo-TEM. The analysis of the DLS results obtained on the micelles from the three copolymers revealed the presence of two different populations. The first population was attributed to isolated, non-aggregated copoly-

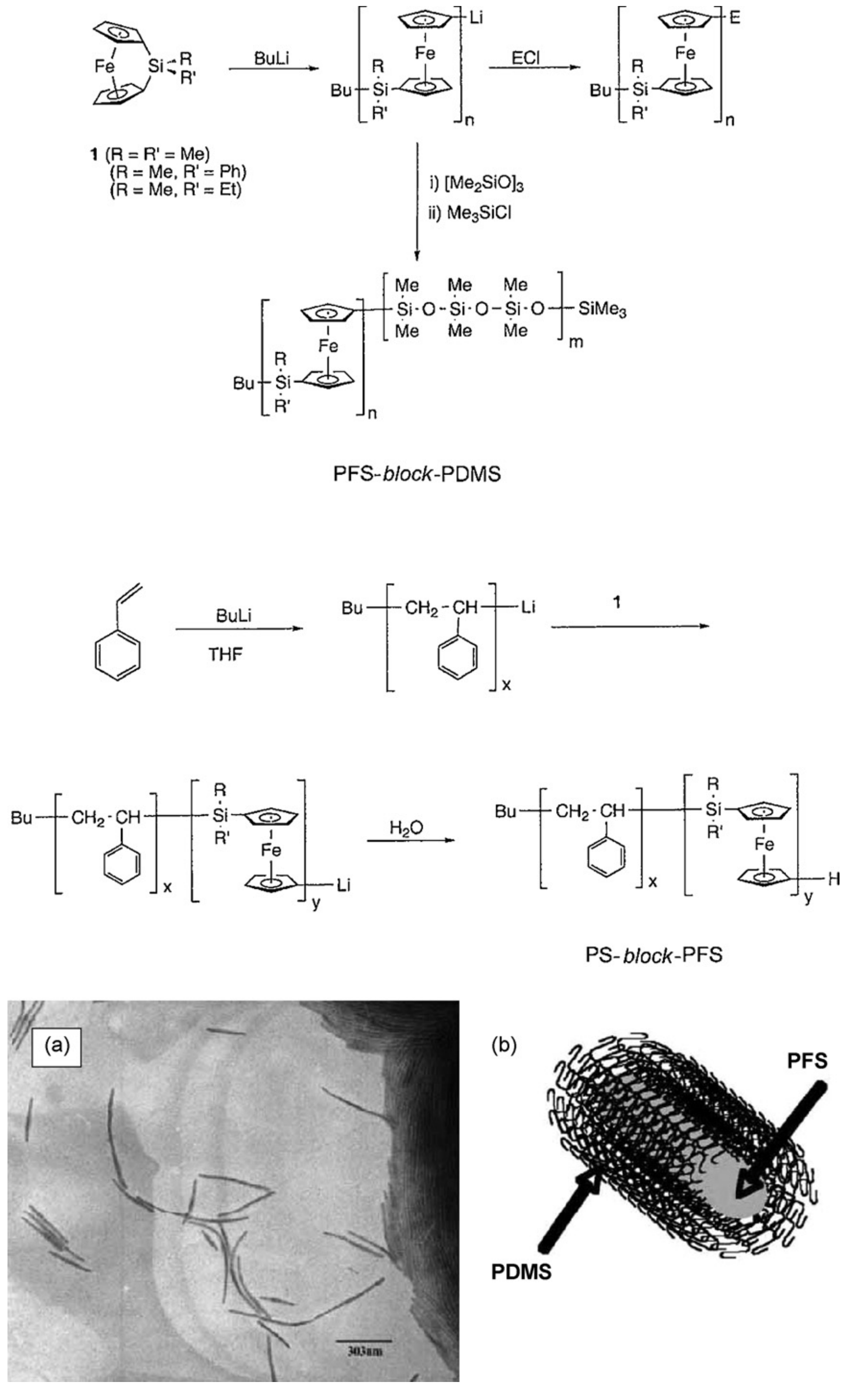

Fig. 4. Synthesis of poly(ferrocenylsilane)-containing diblock copolymers, TEM picture of rod-like micelles formed by a PFS$_{50}$-b-PDMS$_{300}$ (PFS/PDMS ratio 1:6, the numbers in subscript represent the average degree of polymerization of the corresponding block) block copolymer in hexane (A) and scheme for those rod-like micelles (B) (adapted from Ref. [14] with permission).

mer chains while the second one to micelles. The micelles formed by the supramolecular triblocks were imaged by cryo-TEM. Spherical objects with a radius in the range of 10–14 nm were observed for all copolymers together with a few larger aggregates [11].

Besides polycondensation-type metallo-supramolecular block copolymers, another approach leading to micelles of type I is based on the use of block copolymers containing a poly(ferrocenylsilane) block (PFS). In 1994, Manners and co-workers demonstrated that highly pure silicon-bridged [1]ferrocenophanes undergo living anionic ring-opening polymerization under mild conditions (25 °C, in THF) using initiators such as butyllithium [12]. This allowed the synthesis of PFS with controlled molecular weights and narrow molecular weight distributions and also allowed the synthesis of the first block copolymers containing metal–ligand complexes in one of the blocks [13].

The initial materials were block copolymers of poly(ferrocenyldimethylsilane) blocks with poly(dimethylsiloxane) (PDMS) and PS blocks (Fig. 4) [14].

Dissolution of these block copolymers in a non-solvent of the PFS blocks and a good solvent for the other block would lead to micelles containing a PFS core and a corona of the other block. Such micelles have been extensively studied by the groups of Manners and Winnik. By simply dissolving PFS-b-PDMS diblock copolymers in warm hexane, worm-like micelles (PFS/PDMS ratio 1:6) [15,16], or hollow nanotubes (PFS/PDMS ratio 1:13) [17,18], with a PFS core and a PDMS corona, have been observed. These cylindrical structures can be directly visualized by TEM due to their iron-rich core. The cylinders represent the thermodynamically preferred morphology in solution which is controlled by the crystallization of the PFS segments. Indeed, when micelles are formed above the melting temperature of the PFS block, or when an amorphous PFS block is used, spherical micelles are observed [19].

These cylindrical micelles consist of a potentially conductive core of PFS surrounded by an insulating sheath or corona of PDMS and are candidates for the formation of semiconducting nanowires. Furthermore, those well-defined micelles may be of use as etching resists for semiconducting substrates, and offer potential access to magnetic or semiconducting nanoscopic patterns [20,21].

Vancso and co-workers reported on the self-assembly of PFS-b-poly(methylmethacrylate) (PMMA) block copolymers in acetone, a PMMA-selective solvent [22]. The resulting micellar morphology depends on the block copolymer composition. For a PFS/PMMA block ratio of 1:23, monomolecular or small spherical micelles were essentially formed while only a fraction of the block copolymers associated into cylindrical micelles. As the PFS fraction increased, a larger proportion of copolymer chains aggregated into cylindrical micelles. At a block ratio of 1:6, well-defined cylindrical micelles were exclusively formed.

Aqueous micelles could also be obtained from PFS-containing block copolymers. In this respect, PFS block have been combined with poly(dimethylaminoethylmethacrylate) (PDMAEMA) to lead to amphiphilic block copolymers. In a further step, the PDMAEMA block was quaternized with methyl iodide. The micellization behavior of these two block copolymers was further investigated [23].

Poly(2-vinylpyridine) (P2VP) has been recently combined with PFS to construct PFS-b-P2VP block copolymers [24]. The micellization of these block copolymers was studied and a spherical-to-rod-like micelles morphological transition was observed that depended again on the crystallization of the PFS micellar core [25].

Recently, Manners and co-workers reported unique behavior for rod-like micelles with a crystalline PFS core. They indeed demonstrated that these micelles were capable of growing epitaxially through the addition of more polymer, producing extended micelles with a narrow size polydispersity, in a process analogous to the growth of living polymer [26] (Fig. 5). By adding a PFS block copolymer with a different coronal block, they could form co-micelles. The authors initially prepared well-defined and stable cylindrical micelles from a PFS-b-poly(isoprene) (PFS-b-PI) diblock copolymer in hexane. However, when additional PFS-b-PI chains dissolved in a common good solvent such as tetrahydrofuran (THF) or toluene were added, the micelles appeared to become longer. Moreover, the authors noted that this growth process did not process via“self-micellization” of the free chains followed by addition to the ends of preexisting micelles (micelles fusion) but rather that the micelle growth happened via the addition of free chains on the preexisting micelles. Furthermore, this growth process was monitored to

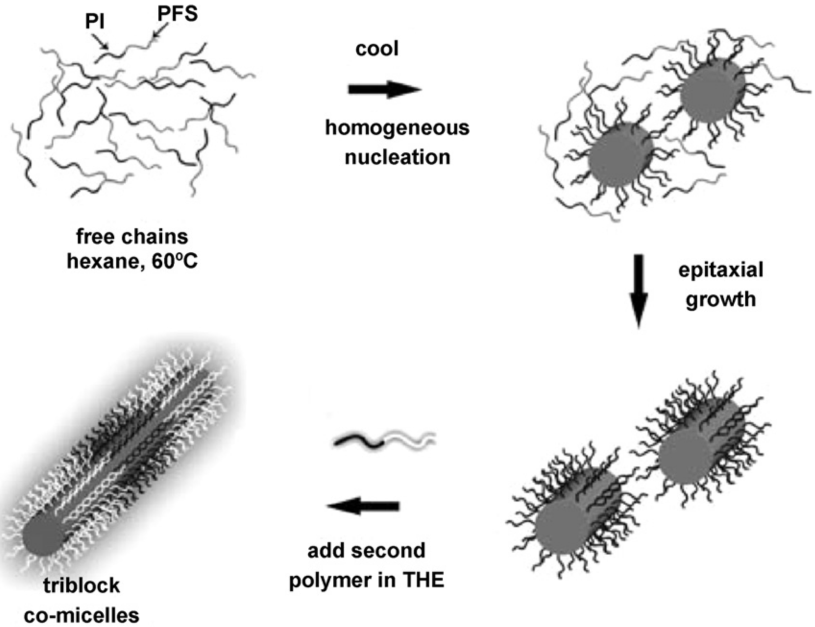

Fig. 5. Schematic representation for the formation of co-micelles from PFS-containing block copolymers via epitaxial growth process (reprinted with permission from Ref. [26]).

proceed linearly with time, in agreement with the concept of a living polymerization process. Addition of non-associated chains of another type of PFS-containing block copolymer of different coronal block to the initial PFS-b-PI micelles allowed the formation of co-micelles. The resulting rod-like micelles had a ABA-like structures since the growth process happened at both ends of the initial PFS-b-PI micelles. The same authors demonstrated that the PI coronal part of those micelles could be stabilized by cross-linking using a Pt(0)-catalyzed hydrosilylation leading to shell-cross-linked micelles [27].

These authors also selectively functionalized different parts of those co-micelles, by extending the living supramolecular polymerization approach to block copolymers with hydrophilic blocks and to polar solvents. Electrostatic interactions were indeed used to selectively functionalize the resulting co-micelles with Au and PbS nanoparticles in a spatially selective manner to afford novel composite structures (Fig. 6) [28].

Very recently, a new approach to the synthesis and encapsulation of silver and silver halide nanoparticles inside shell-cross-linked PI-b-PFS cylindrical block copolymer micelles through in situ redox reactions has been reported [29,30]. The partial preoxidation of the swollen PFS core using tris(4-bromophenyl)aminium hexachloroantimonate followed by redox reaction between the remaining Fe(II) centers in the PFS core and Ag^+ cations led to the formation of silver nanoparticles (Fig. 7). The size of those silver nanoparticles varied with different amounts of silver ions added to the micelle solution (Fig. 7).

3. Metallo-supramolecular block copolymer micelles of type II

Metallo-supramolecular block copolymer micelles of type II have been obtained from A-[•]-B metallo-supramolecular block copolymers (Figs. 1 and 8). First, the synthesis of such copolymers will be briefly discussed. The terpyridine ligand has been mainly considered in these metallo-supramolecular block copolymers. This ligand should be attached to a polymer chain end. Two main strategies have been reported so far to reach this goal. The first one involves the grafting of a terpyridine functionalized at the 4′-position on the reactive chain end of a polymer [31–33]. The commercially available 4′-chloro-2,2′:6′,2″-terpyridine is a very useful compound in that respect to react with α- or ω-hydroxyl-functionalized polymers. Recently, it has been demonstrated that the anionic polymerization of styrene could be terminated with chloro-terpyridine, avoiding thus the post-functionalization step [34]. The second synthetic strategy consists of using a terpyridine-functionalized initiator. This method has the advantage of producing polymer chains with a theoretical functionalization degree of 1. In this respect, terpyridine-functionalized initiators have been developed for nitroxide mediated radical polymerization

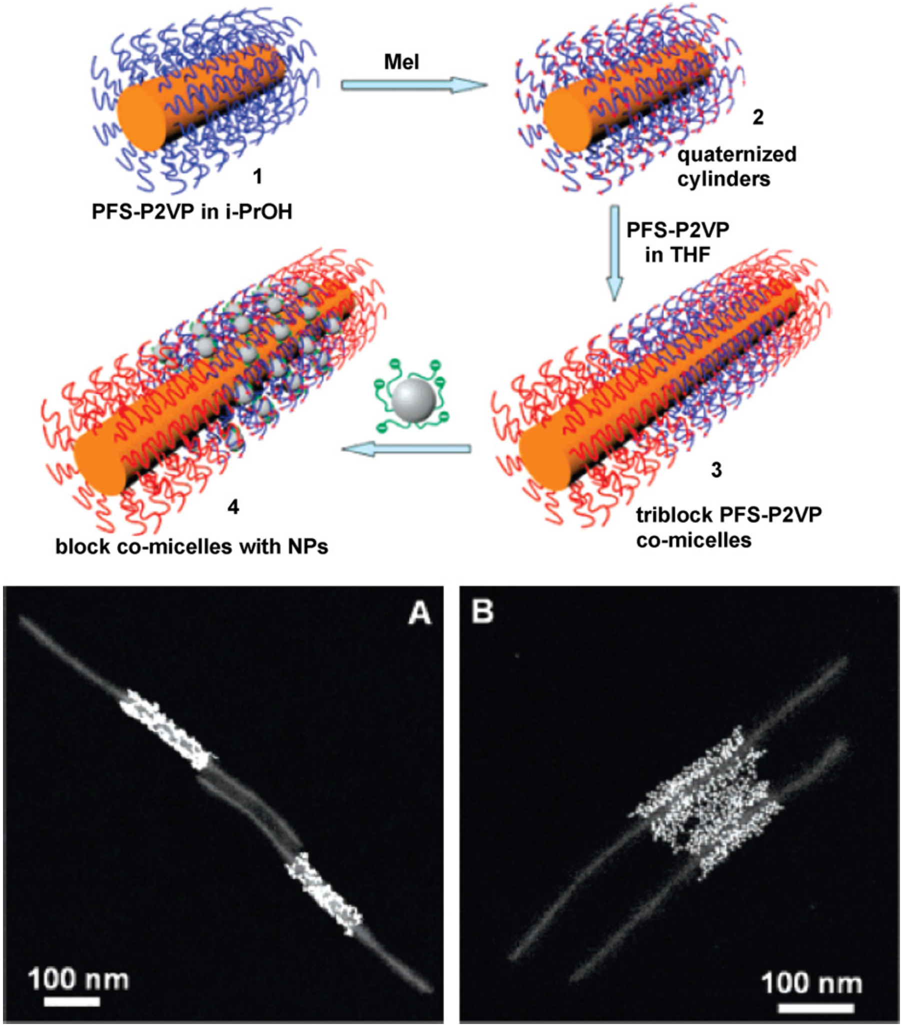

Fig. 6. Schematic representation for the formation of co-micelles from PFS-b-P2VP diblock copolymers in isopropanol (i-PrOH) and dark-field TEM images showing block co-micelles with the central block functionalized with Au nanoparticles (A) and PbS quantum dots (B) (adapted with permission from Ref. [28]).

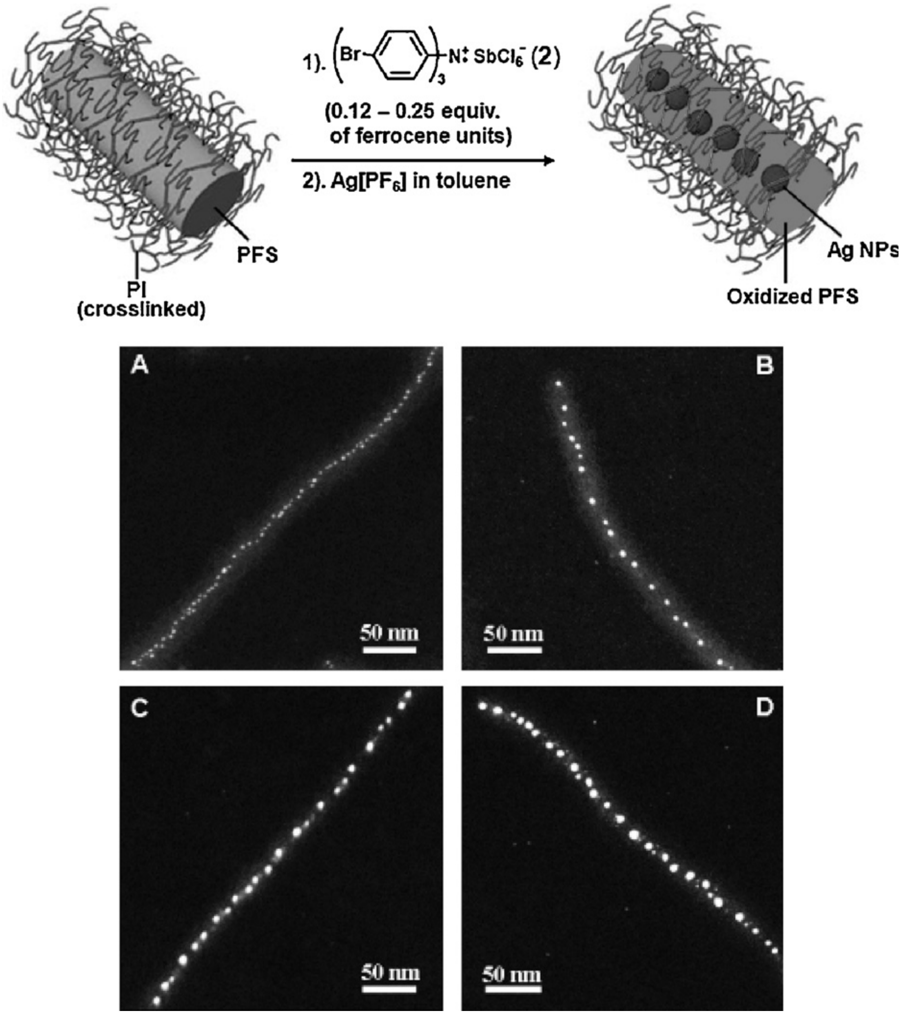

Fig. 7. Schematic representation for the formation of silver nanoparticles (NPs) in shell-cross-linked PFS-b-PI micelles and dark-field TEM images of those micelles pretreated with tris(4-bromophenyl)aminium hexachloroantimonate (0.125 equiv. of ferrocene units), followed by addition of $AgPF_6$ in different amounts: 12.5% (A), 25% (B), 50% (C), and 75% (D) for total ferrocene units (adapted with permission from Ref. [30]).

(NMRP) [35–37], and for reversible addition-fragmentation chain transfer polymerization (RAFT) [38].

The synthesis of A-[•]-B metallo-supramolecular block copolymers requires the formation of heteroleptic complexes. In other words, the reaction between A-[, B-[and • should selectively lead to A-[•]-B complexes and the formation of homoleptic A-[•]-A and B-[•]-B complexes should be avoided. Very few metals (Ru, Os, Ir, Co) are suitable for this approach, among which only ruthenium has been used for the synthesis of metallo-supramolecular block copolymers. Such a selective complexation process requires a two-step complexation procedure. Indeed, ruthenium(III) ions are known for forming a stable mono-complex with terpyridine, while ruthenium(II) ions do form a stable bis-complex with the same ligand [39]. Therefore, the synthesis of A-[Ru^{II}]-B metallo-supramolecular block copolymers can be selectively achieved by first making the A-[Ru^{III} (or B-[Ru^{III}) mono-complex, which is fur-

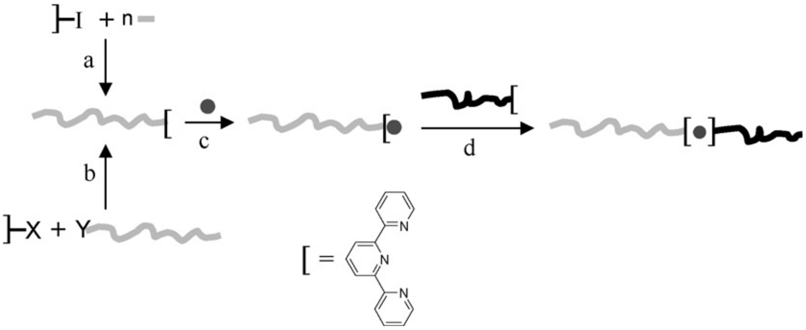

Fig. 8. Schematic representation of the synthetic strategy to prepare metallo-supramolecular block copolymers of type II. The first step is the synthesis of the macroligands by either using a functionalized (supramolecular) initiator (a), or grafting a terpyridine on a reactive chain end (b). The second step is the preparation of a mono-complex with Ru^{III} (c). Finally, the second block, bearing a free terpyridine unit, is added to form a terpyridine-ruthenium(II) bis-complex (d).

ther reacted under the appropriate reducing conditions with B-[(or A-[) to form the desired A-[Ru^{II}]-B bis-complex (Fig. 8) [40].

Poly(styrene)-[Ru]-poly(ethylene oxide) (PS-[Ru]-PEO) block copolymers, and in particular the PS_{20}-[Ru]-PEO_{70} composition, were initially studied [41]. For these copolymers, the macroligands were prepared by reacting chloro-terpyridine with the hydroxy chain end of PEO and PS (which was end-capped with one unit of ethylene oxide at the end of the anionic polymerization). Formation of micelles from these amphiphilic copolymers has been then extensively studied. The high stability of the *bis*-2,2′:6′,2″-terpyridine-ruthenium(II) complexes allows the integrity of the formed block copolymers to be kept in various environments, such as organic solvents or water, even under extreme pH and salt concentration [42]. DLS revealed the presence of two populations, one with a hydrodynamic diameter of about 65 nm, and one around 200 nm [41]. Cryo-TEM experiments enabled the identification of these two populations [43]. The first population does not correspond to individual micelles but to a mixture of micelles and small aggregates, while the population with larger size results from the clustering of a large number of micelles. The characteristic features of the micelles formed by the PS_{20}-[Ru]-PEO_{70} copolymer were also compared to the ones formed by a classical covalent block copolymer: PS_{22}-*b*-PEO_{70} [42]. The diameter of the PS core was the same for the covalent and metallo-supramolecular samples, but in the case of the covalent counterpart, only individual micelles were formed, showing that micelles formed by metallo-supramolecular copolymers have a strong tendency to aggregate. The formation of micellar aggregates could almost be totally suppressed by modifying the method of preparation of the micelles [44]. Indeed, a slow and regular addition of water, with the help of a syringe pump, to an initial DMF solution of the PS_{20}-[Ru]-PEO_{70} copolymer resulted in a well-defined micellar solution with almost no further aggregation of micelles.

Analytical ultracentrifugation (AUC) has been used rarely to characterize block copolymer micelles although it allows the determination of the weight fraction of micelles, unimers and other species such as superaggregates of micelles. Although it can be argued that the unimer-micelle-aggregate equilibrium is continuously disturbed and re-established during the AUC experiment, it has been successfully applied to PS_{20}-[Ru]-PEO_{70} metallo-supramolecular block copolymer micelles [44,45]. An average molar mass of 318.000 g/mol was found, corresponding to an aggregation number of 53 copolymer chains per micelle.

These initial investigations on the nanoscale organization of the PS_{20}-[Ru]-PEO_{70} metallo-supramolecular copolymer in a selective solvent revealed a deep influence of the *bis*-terpyridine ruthenium complexes on the microphase separation between the PS and PEO blocks. Therefore, other compositions than the PS_{20}-[Ru]-PEO_{70} were also synthesized and characterized. Since the method for preparing metallo-supramolecular block copolymers relies on the coupling of two macroligands via a simple two-step synthesis, it is rather straightforward to prepare a library of block copolymers. This combinatorial approach is certainly an advantage of metallo-supramolecular block copolymers compared to classical covalent ones. A library of 13 members of PS_x-[Ru]-PEO_y block copolymers was thus prepared and the micellization behavior in water was studied [46]. Further characterization of the micelles revealed that the core size did not scale linearly with the degree of polymerization (DP) of the PS block as expected from the theory of classical covalent copolymers. Only two core sizes were observed, one around 10 nm for DP of 70 and below, and one around 20 nm for DP of 200 and above. For copolymers having a DP in the transition region between 70 and 200, two populations were observed. This unusual behavior has been attributed to electrostatic repulsions between the charged terpyridine-ruthenium bis-complexes present at the junction of the two blocks which strongly affect the self-assembly behavior. This has been demonstrated by preparing micelles in the presence of salt to screen out the repulsions. In this case, the metallo-supramolecular block copolymers behaved as their covalent counterpart, the core diameter scaling linearly with $DP^{3/5}$. The evolution of the core diameter for micelles prepared with and without salt is shown in Fig. 9.

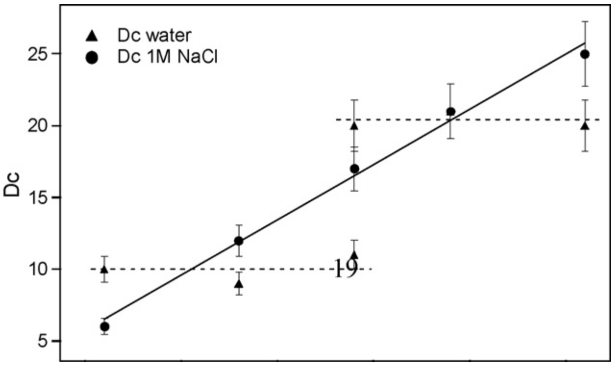

Fig. 9. Relationship between the measured core size (Dc in nm) of PS_x-[Ru]-PEO_y micelles and the 3/5th power of the PS block DP, for micelles prepared in pure water (triangles) and in 1 M NaCl (circles). The solid line represents the linear regression obtained from the data in 1 M NaCl. The dashed lines, evidencing the presence of only two sizes, are only a guide for the eyes (reprinted with permission from Ref. [46]).

Beside the formation of libraries of copolymers, another advantage of metallo-supramolecular block copolymers is the reversibility of the *bis*-terpyridine complexes. This concept has been initially demonstrated on metallo-supramolecular micelles prepared from an amphiphilic poly(ethylene-*co*-butylene)-[Ru]-PEO copolymer in water (PEB-[Ru]-PEO) [47]. Although *bis*-2,2′:6′,2″-terpyridine-ruthenium(II) complexes have proven to be extremely stable in various environments, experiments on PEB-[Ru]-PEO micelles have shown that the addition of a large excess of a competing ligand (hydroxyethyl ethylenediaminetriacetic acid, trisodic salt) (HEEDTA) did allow the opening of those complexes. However, a very large excess of the competing ligand (10^5 molar excess) was required and the sample needed to be heated at 60 °C for a few hours. This experiment was conducted directly on the aqueous micelles and resulted in the formation of original nanoobjects decorated at their surfaces with terpyridine ligands (Fig. 10). The opening of the complex was directly seen macroscopically by the disappearance of the characteristic orange color of the *bis*-2,2′:6′,2″-terpyridine-ruthenium(II) (Fig. 10). A sharp decrease in micelle diameter was also observed by AFM and DLS, as a proof of the breaking of the metal–ligand complexes, the release of the coronal chains and accordingly the formation of nanoobjects (see AFM pictures in Fig. 10) [47]. The excess of competing ligand and the released coronal chains were then eliminated by dialysis against pure water. That terpyridine ligands were still present at the surface of these nanoobjects was proven by observation of the characteristic violet color of iron-terpyridine complexes after addition of iron(II) acetate.

Very recently, the reversibility of *bis*-2,2′:6′,2″-terpyridine-ruthenium(II) complexes has been employed by O'Reilly and co-workers to create nanocapsules from a PS-[Ru]-Poly(acrylic acid) (PAA) diblock copolymer (Fig. 11) [48]. In the first step, micelles with a PS core and a PAA corona were obtained in water from this copolymer. The PAA corona was then cross-linked by using 2,2′-(ethylenedioxy)-*bis*(ethylamine) in the presence of 1-[3′-(dimethylamino)propyl]-3-ethylcarbodiimide methiodide in order to create a cross-linked shell around the PS core.

The hollowing out of these nanoparticles was investigated using HEEDTA as competitive ligand to open the *bis*-2,2′:6′,2″-terpyridine-ruthenium(II) complexes. The shell-cross-

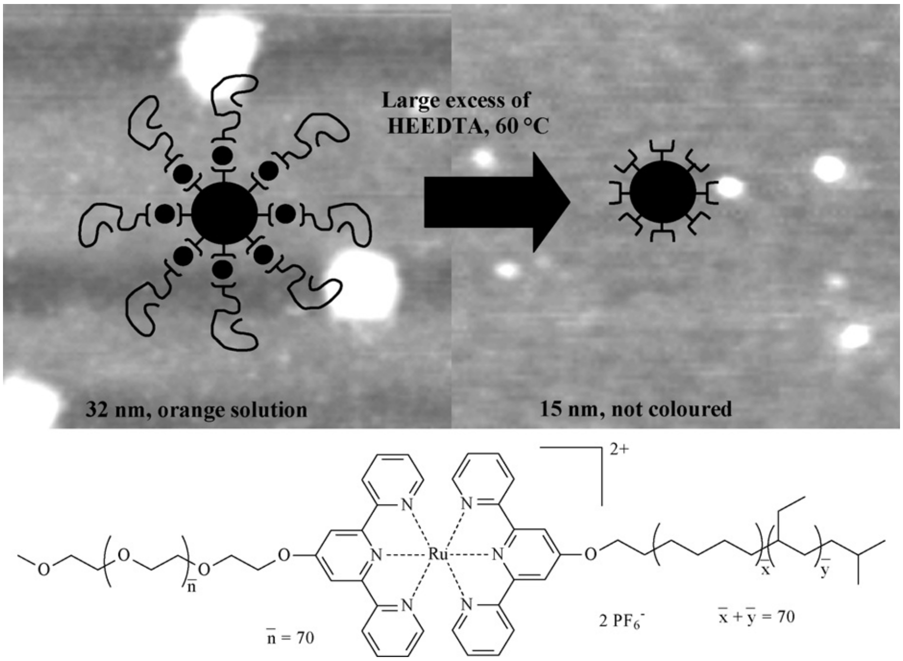

Fig. 10. Schematic representation of PEB-[Ru]-PEO metallo-supramolecular micelles. The complexes can be opened by addition of a large excess of HEEDTA. This is accompanied by a change in the color of the micellar solution which turns from orange to colorless. The AFM pictures (height contrast) obtained for the micelles before and after treatment with HEEDTA are shown in the background. The average diameter of the objects is also indicated. The chemical structure of the PEB_{70}-[Ru]-PEO_{70} used for this experiment is shown below (adapted with permission from Ref. [47]).

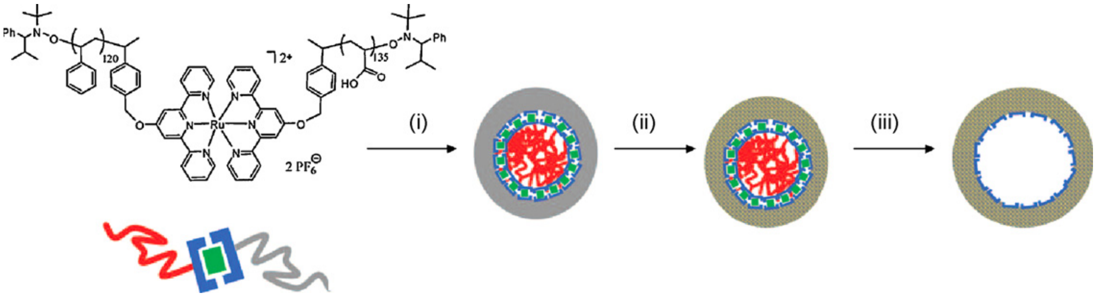

Fig. 11. Formation of hollow nanocapsules from a PS-[Ru]-PAA metallo-supramolecular block copolymer (PS blocks in red, PAA blocks in grey, ruthenium(II) as a green square). The PS-[Ru]-PAA copolymer is self-assembled into micelles (i); the PAA shell is cross-linked (ii); the [Ru] complexes are opened by treatment with HEEDTA and the released PS blocks are removed by repeated dialysis in THF/water mixtures (iii) (adapted with permission from Ref. [48]).

linked micelles were then extensively dialyzed into a THF/water (2:1) mixture in order to remove the uncomplexed PS chains from the core. To confirm the hollow nature of the nanostructures, and thus complete removal of the hydrophobic PS core domain, sequestration studies were performed using a hydrophobic dye molecule. The response of the accordingly obtained nanocages to pH-changes was also investigated. A reversible pH-dependent change in size was demonstrated. Indeed, the size of those nanocages could be readily cycled between ca. 90 and 240 nm by changing the pH between 5 and 9.

Interestingly enough, another approach towards similar hollow polymeric nanocages has been reported, again by Moughton and O'Reilly [49]. This strategy relies on both a SCS "pincer"-based nitroxy-mediated radical polymerization (NMP) initiator and a pyridine-functionalized NMP initiator which were employed for the polymerization of styrene and *tert*-butyl acrylate, respectively. After deprotection of the *tert*-butyl group, the two polymers were connected to form a metallo-supramolecular amphiphilic block copolymer using relatively weak coordination of the pyridine to a palladium(II) metal center and strong non-covalent interaction to the SCS "pincer" ligand (Fig. 12). Shell-cross-linked micelles were then prepared by cross-linking of the PAA chains as described above. The hollowing of the micellar core was achieved at low pH by repeated dialysis. As a result, polymeric nanocages with well-defined interior chemical functionality were obtained.

Besides micelles with spherical morphology, rod-like micelles were obtained from a PFS-[Ru]-PEO copolymer in water [50]. Those

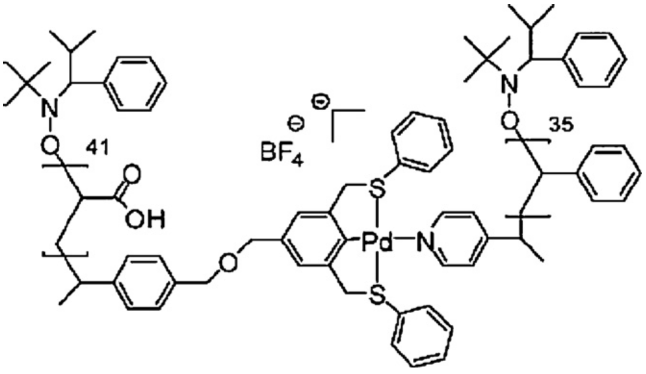

Fig. 12. Chemical structure of metallo-supramolecular block copolymer of type II based on a SCS pincer.

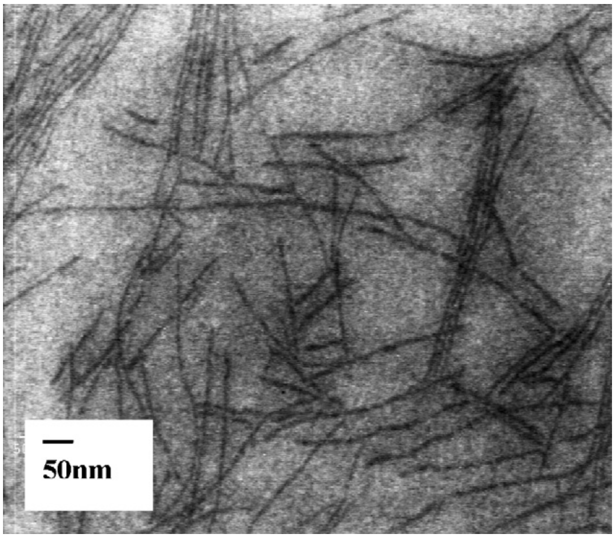

Fig. 13. TEM picture of cylindrical micelles formed by a PFS$_{12}$-[Ru]-PEO$_{70}$ metallo-supramolecular copolymer in water. No contrasting agent has been added for the visualization of these micelles because they contain iron atoms in the core. Reprinted with permission from Ref. [50].

micelles actually combine the characteristic features of metallo-supramolecular micelles of types I and II. The micelles had a constant diameter but were rather polydisperse in length, and DLS indicated that they were rather flexible. Crystallization of the PFS in these micelles was observed by differential scanning calorimetry (DSC), and is thought to be responsible for the formation of these rod-like structures. A typical TEM image of those rod-like micelles is shown in Fig. 13.

Harruna et al. reported the synthesis of an amphiphilic PS-[Ru]-poly(*N*-isopropylacrylamide) using RAFT polymerization with a terpyridine functionalized chain transfer agent [38]. Such an approach is very interesting since it allows the introduction of thermoresponsive poly(*N*-isopropylacrylamide) with lower critical solubility behavior in metallo-supramolecular block copolymer micelles. Beside temperature-responsive polymer blocks, pH-responsive ones have proven to be useful for dedicated applications including, e.g. pH-controlled drug release. In this respect, a terpyridine-functionalized PS-b-P2VP copolymer has been complexed with a terpyridine-functionalized PEO to lead to a PS-b-P2VP-[Ru]-PEO ABC triblock copolymer [51]. This copolymer was further used to prepare core-shell-corona micelles consisting of a PS core, a P2VP shell and a PEO corona. This kind of micelle has the capability to respond to pH via the protonation/deprotonation of the P2VP shell. The pH-response of these micelles can be advantageously used for the encapsulation or release of active species reversibly trapped in the P2VP shell. Moreover, the P2VP shell can serve as a nanoreactor for the production of metal nanocapsules [52].

4. Metallo-supramolecular block copolymer micelles of type III

Metallo-supramolecular micelles of type III consist of a core formed by insoluble A blocks and a corona of soluble B blocks. Ligands are introduced at the extremity of the coronal B blocks. In such systems, micellization of an A-b-B-[copolymer is realized prior to the addition of metal ions. The bare micelles are first characterized and the changes occurring after the addition of metal ions are then monitored. Whenever sufficiently diluted solutions of micelles are considered, the addition of metal ions only results in intra-micellar complexation. In sharp contrast, the addition of metal ions to more concentrated solutions of these micelles results in inter-micellar complexation that further allows the formation of micellar gels.

Although such micelles sound very interesting allowing the formation of nanoobjects with “sticky end-groups” through

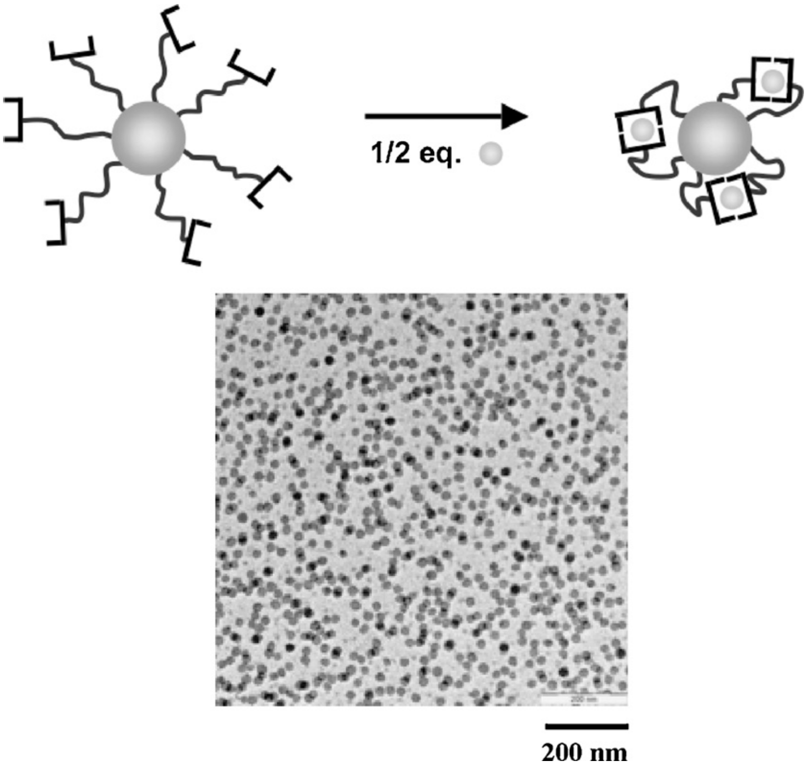

Fig. 14. Schematic representation of the effect of added metal ions (metal ion/terpyridine molar ratio of 1/2) on metallo-supramolecular micelles of type III prepared from a PS$_{47}$-b-PtBA$_{55}$-[copolymer in ethanol and TEM picture of the initial PS$_{47}$-b-PtBA$_{55}$-[micelles (adapted from Ref. [53] with permission).

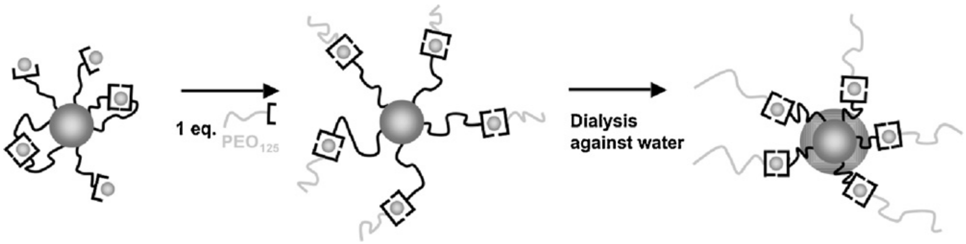

Fig. 15. Effect of the addition of a PEO_{125}-[block on PS_{47}-b-$PtBA_{55}$-[micelles loaded with 1 equiv. of Fe^{2+}, and collapse of the PtBA layer after transfer of the micelles into water.

metal–ligand complexation, they have been scarcely reported in literature. Very recently, we reported on this strategy, i.e. the use of metallo-supramolecular interactions to tune the size of micelles by changing the conformation of the coronal chains [53]. This approach was based on the use of a diblock copolymer PS-b-poly(*tert*-butylacrylate) (PtBA) end-functionalized with a terpyridine moiety on the PtBA block. Micelles were obtained in ethanol, a selective solvent for the PtBA blocks, that consist of a PS core and a PtBA corona with terpyridine ligands located at the extremity of the PtBA chains. Well-defined spherical micelles with a hydrodynamic radius (R_h) of 22 nm were obtained (Fig. 14). The second step was the addition of metal ions (Zn^{2+}, Ni^{2+} and Fe^{2+}) to the micelles in order to induce the formation of complexes with the terpyridine terminal groups. For a metal ion/terpyridine molar ratio of 1/2, formation of *bis*-terpyridine-metal ion complexes in the micellar corona is essentially expected as depicted in Fig. 14.

This should result in a looping of the coronal chains inducing the formation of flower-like micelles and a decrease of the overall R_h. The extent of this decrease depended on the metal ion used. The largest decrease was observed for Ni^{2+} ions and the smallest for Zn^{2+} ions. This decrease was attributed to a strong contraction of the PtBA coronal chains. Nevertheless, the micelles were stable over weeks and did not display any secondary aggregation, proving that the looped PtBA coronal chains still enable a good micellar stability. In a second step, another 1/2 equiv. of metal ion was added to the micelles in order to reach a final metal ion/terpyridine molar ratio of 1/1. This may trigger the formation of mono-complexes leading to the disappearance of the PtBA loops and hence to an expansion of the corona. The obtained DLS results showed no change in the micellar dimension for the Ni^{2+} and Fe^{2+} containing samples, while the R_h increased from 14 to 17 nm in case of the Zn^{2+} containing sample. A metal ion/terpyridine molar ratio of 1/1 was also achieved by directly adding the proper amount of metal ions to the initial PS_{47}-*b*-$PtBA_{55}$-[micelles. Similar results were obtained for the twofold addition of 1/2 equiv. of metal salts. These results indicated that flower-like micelles containing bis-terpyridine metal complexes were essentially observed for Ni^{2+} and Fe^{2+} although the metal ion/terpyridine molar ratio points towards mono-complexes. In case of Zn^{2+}, the formation of mono-complexes was observed when the metal ion/terpyridine molar ratio was 1/1. To further trigger the formation of mono-complexes a large excess of metal ions (final metal ion/terpyridine molar ratio of at least 5/1) was added. Under these conditions, the Ni^{2+} containing sample still formed flower-like micelles since no increase in the size of the micelle was observed. The Fe^{2+} containing sample showed an increased R_h to 18 nm that could be due to the disappearance of looped PtBA chains concomitant with the replacement of bis-complexes by mono-complexes. In the case of Zn^{2+}, the R_h of the micelles further increased to reach 22 nm, i.e., the size of the initial micelles. These experimental observations are in agreement with the corresponding stability constants of the complexes from terpyridine and Ni^{2+}, Fe^{2+} and Zn^{2+}. Indeed, Ni^{2+} forms the most stable complexes and the Zn^{2+} the least stable, with the Fe^{2+} in between.

In addition to tuning the micellar size by changing the conformation of the coronal chains, this strategy could also be used to build more complex objects, going from the core-shell initial system to a core-shell-corona one. This has been achieved by complexing a third terpyridine-functionalized polymer block on the PS-b-PtBA-[micelles decorated with metal ions. An equimolar amount, with respect to the copolymer chains, of a terpyridine end-functionalized poly(ethylene oxide), PEO-[, has been added to the PS-b-PtBA-[micelles previously loaded with 1 equiv. of Fe^{2+} ions, and should thus yield PS-b-PtBA-[Fe]-PEO micelles. To further prove that the additional PEO layer has been grafted to the initial micelles, the PS-b-PtBA-[Fe]-PEO micelles were transferred into water, a selective solvent for the PEO block. Stable micelles with a PS core, a PtBA shell and a PEO corona were obtained (Fig. 15), proving the success of the transfer in water and thereby the efficiency of the grafting of the additional PEO layer through formation of Fe^{2+}/terpyridine complexes.

5. Conclusions

As shown by the results already available in the literature, important progress has been made in the development of synthetic strategies towards amphiphilic metallo-supramolecular block copolymers. The combination of a highly modular synthetic approach, enabling the preparation of various architectures, in the presence of a metal center having particular properties, make metallo-supramolecular block copolymers ideal candidates for the assembly of new, stimuli-responsive, functional materials.

In this respect, amphiphilic metallo-supramolecular block copolymers have been further used to prepare micelles. Indeed, metal–ligand complexes have been incorporated in the core, corona and at the core–corona interface of block copolymer micelles. From these reports, it is clear that the presence of metal–ligand complexes in these micelles has a deep impact at several levels, ranging from the structural features to the functionality of the accordingly obtained materials.

However, it is still an emerging field and a lot of work still need to be done in order to gain better understanding and control over the parameters governing the self-assembly and nanostructure formation.

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