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Solution behavior of star polymers with oligo(ethylene glycol) methyl ether methacrylate arms

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ABSTRACT

Star polymers composed of a hyperbranched poly(arylene oxindole) (PArOx) core and arms of different length 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) were obtained via atom transfer radical polymerization. The stars obtained were thermoresponsive. The cloud point temperatures (T_{cp}) depended upon the composition of the arms and the concentration of stars in solution. Comparison of the sizes determined using light scattering techniques in acetone and water below T_{cp} confirmed that the stars existed in water as isolated macromolecules. The unimolecular structure of the stars below T_{cp} was proved by AFM and cryo-TEM. Above T_{cp}, a significant increase in particle size with the concentration was observed. Encapsulation of a hydrophobic dye in stars was studied by UV–VIS and fluorescence spectroscopy. The results indicate that stars obtained are prospective carriers for biomolecules.

1. Introduction

Oligo(ethylene glycol) methacrylates (OEGMAs) are the class of monomers that have from one to dozens ethylene glycol units bonded to a methacrylate backbone. In the last years (co)polymers based upon these compounds became an alternative for poly(N-isopropylacrylamide) because of their thermosensitive properties. The thermosensitivity of poly[oligo(ethylene glycol) methacrylates] might be tuned easily over a broad temperature range by copolymerization of (ethylene glycol) methacrylates with different lengths of ethylene glycol units in the backbone [1]. The phase transition is reversible without any hysteresis. Moreover OEGMA-based polymers have anti-fouling properties and are inert to biological materials [2].

OEGMA monomers may be (co)polymerized by different methods such as living anionic [3], group transfer [4] and free radical polymerization [5,6]. Nowadays various types of controlled radical polymerization (e.g., nitroxide-mediated, reversible addition-fragmentation chain transfer or atom transfer radical polymerization) are also applied [7–10]. Those methods became a powerful and versatile tool to access different polymethacrylates of well-defined structure [2,11,12]. Poly[oligo(ethylene glycol) methacrylate] segments were used to prepare polymers of different topologies such as gradient and block copolymers [1,13,14], brushes [15,16], hyperbranched and star polymers [17–19] and to obtain microgels [20,21], polymer-modified inorganic nanoparticles [22] and bioactive surfaces [2].

Core–shell stars with a shell made of different poly(oligo(-ethylene glycol) methacrylates) were synthesized interalia by Chen et al. [23], Sun and Guan [24] and Zhang et al. [19] by "core-first" methods. The authors used chain walking polymerization to obtain a dendritic or hyperbranched polyethylene core, which was applied as a macroinitiator in atom transfer radical polymerization (ATRP) of oligo(ethylene glycol) methacrylates yielding the arms of the target star polymers [19,23,24]. Such stars with many arms ($f > 45$) were investigated as carriers for hydrophobic small macromolecules [24] or in conjugation processes, for example, with protein [23]. Kreutzer et al. obtained stars with approximately 20 copolymer arms based on poly(*n*-butyl methacrylate)-block-poly(oligo(ethylene glycol) methacrylate) and hyperbranched core (Boltorn H40) [25], which were found to be able to encapsulate and release hydrophobic guest molecules [25]. Ring opening polymerization of ε-caprolactone and ATRP of poly(ethylene glycol)

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methacrylates with long ethylene glycol chains (M_n = 475 and 1100 g/mol) led to amphiphilic star polymers with 4, 6, 8 and 12 arms, respectively [26]. The solubilization ability of the star polymers was investigated using fat brown RR [26]. Li et al. have used inorganic functionalized cores to obtain poly(diethylene glycol monomethyl ether) methacrylate and poly(triethylene glycol monomethyl ether) methacrylate nanoparticles by surface-initiated ATRP [27]. For all stars mentioned above, the solution behavior was investigated in water below and above LCST [23–25,27]. The group of Sawamoto used the "arm first" method to synthesize star polymers with copolymer arms made of poly(oligo(ethylene glycol) methyl ether methacrylate)-block-poly(methyl metacrylate) and a microgel ruthenium (II) core. Such stars are soluble in water and exhibit an upper critical solution temperature (UCST) in 2-propanol [22]. Star polymers based on poly[oligo(ethylene glycol) methacrylates] are being investigated as potential carriers for hydrophobic drugs [28,29], dyes or fragrances [24–26] or for the removal of organic impurities from water [18].

Amphiphilic core–shell structures are known to be able to self-assemble in selective solvents forming aggregates of different morphologies. In selective solvents and dilute solution, amphiphilic core–shell structures exist as isolated macromolecules, often called unimolecular micelles [30]. For some of them, if the concentration increases over a critical threshold (critical micelle concentration – cmc), aggregation of macromolecules is observed similar to linear amphiphilic block copolymers. The resulting spherical structures with the aggregated cores of the stars are called multimolecular micelles (MMM) [31]. The mechanism of the star aggregation based on secondary aggregation of unimolecular micelles via intermolecular interactions has also been described [31–33]. MMM or stars with a large number of arms may self-assemble, forming so-called multimicelle aggregates (MMA) – structures with many cores surrounded by the arms contained not only in the shell but also inside the interior of the aggregate [31,34–36].

In the case of core–shell nanoparticles made of thermoresponsive polymers, the temperature also influences their aggregation behavior. Below LCST, stars exist as unimolecular micelles or form MMMs [18,19,26,37]. Above LCST, core–shell structures exist either as micelles (only shrinking in size) or as aggregates to bigger structures [19,37,38].

The solution behavior of stars is a phenomenon which, despite the amount of data presented above, still calls for further investigation. The relationship between the star structure, its solution properties and possible aggregation is critical because the hydrodynamic properties of stars are essential in their future applications as delivery vehicles for bioactive species.

The aim of our study is to follow the behavior of poly[oligo(ethylene glycol) methacrylate] stars in a good solvent where the core and the arms are soluble and the macromolecules are isolated and to compare the results with those in the selective solvents (e.g., water), including results below and above their phase transition temperature. Such a systematic overview of the influence of carefully determined parameters of star structures and their solution properties is needed and will be helpful in obtaining efficient and safe nanocontainers for the encapsulation of guest molecules. In this paper, we describe the "core-first" synthesis via ATRP of star polymers consisting of a hyperbranched poly(arylene oxindole) core and a shell created by a homopolymer of di(ethylene glycol) methyl ether methacrylate (PDEGMA) or a copolymer of poly[di(ethylene glycol) methyl ether methacrylate]-*ran*-poly[oligo(ethylene glycol) methyl ether methacrylate] (P(DEGMA-*ran*-OEGMA)).

The hyperbranched poly(arylene oxindole) used as the core has a large number of reactive functional groups, 100% degree of branching and is strongly hydrophobic. The subsequent introduction of thermosensitive arms opened the possibility to create a nanoparticle, where hydrophobic core surrounded by hydrophilic shell forms a container separated from the external environment. Therefore, active molecules of the similar philicity as the core (e.g., dyes and drugs) may be entrapped inside yielding thermo-switchable nanoparticles for controlled transport and delivery applications.

The stars obtained were characterized by gel permeation chromatography with multiangle laser light scattering detection (GPC-MALLS). Their thermosensitivity and encapsulation of a selected dye was studied by UV–Vis and fluorescence spectroscopy. Using light scattering, the solution behavior of the stars in a good and selective solvent was monitored. The shape and size of the stars on a glass surface were studied by AFM and cryo-TEM imaging techniques.

2. Experimental

2.1. Materials

Di(ethylene glycol) monomethyl ether methacrylate (DEGMA, 95%), oligo(ethylene glycol) monomethyl ether methacrylate (OEGMA, M_n = 300 g/mol), *N,N,N',N',N"*-pentamethyl diethylenetriamine (PMDETA, 99%), 2,2′-bipyridyl (Bpy ≥ 98%), copper (I) bromide (CuBr, 99.999%), copper (II) bromide ($CuBr_2$, 99%), copper (I) chloride (CuCl 98%), ethyl α-bromoisobutyrate (EBIB, 98%) were purchased from Aldrich and used as received. Anisole (99%) was purchased from Aldrich and purified by distillation prior to use. DOWEX MARATHON MSC ion exchange resin (Aldrich) was transformed into the H^+ type using 1.6 M HNO_3. *n*-Hexane (99%), chloroform (98.5%) were purchased from POCh and used as received. Acetone (99.5%) and toluene (99%) were purchased from POCh and filtered through membrane filters with pore size 0.02 μm prior to use. Pyrene (98%, Aldrich) and 4-(dicyanomethylene)-2-methyl-6-(4-dimethylaminostyryl)-4H-pyran (4HP, 98%, Aldrich) were used as received.

2.2. Synthesis of poly(arylene oxindole) core

The synthesis and characterization of the poly(arylene oxindole) (PArOx) was described in our previous paper [39]. The molar mass of poly(arylene oxindole) (PArOx) was M_n = 20 000 g/mol and M_w/M_n = 1.7.

2.3. Synthesis of star polymers with poly[di(ethylene glycol) monomethyl ether methacrylate] arms

The PArOx (15×10^{-3} g, 7.5×10^{-7} mol) was dissolved in 2 mL of anisole under nitrogen in a Schlenk flask with magnetic stirrer. CuBr (3.2×10^{-3} g, 2.23×10^{-5} mol), $CuBr_2$ (1×10^{-3} g, 4.5×10^{-6} mol) and di(ethylene glycol) monomethyl ether methacrylate (DEGMA 0.42 g, 2.22×10^{-3} mol, 0.41 mL) (monomer to anisole ∼1:5 v/v) were added to the solution. The mixture was degassed using freeze–vacuum–thaw cycles. After first degassing, PMDETA (9.13×10^{-3} g, 5.27×10^{-5} mol, 1.1×10^{-2} mL) was added to the stirred mixture. The solution was degassed twice using freeze–vacuum–thaw cycles. The flask was placed in an oil bath and thermostated at 40 °C. The monomer conversion was measured by gel permeation chromatography with polystyrene (Polymer Laboratories) (M_n = 1990 g/mol and M_w/M_n = 1.05) as internal standard. At regular intervals of time samples (stars S1–S5, Table 1) of the reaction mixture were taken and injected into GPC chromatograph. Integration of the signals of the unreacted DEGMA and of the polystyrene yielded the amount of the reacted monomer.