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Controlled synthesis of amino-acid based tadpole-shaped organic/inorganic hybrid polymers and their self-assembly in aqueous media

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ABSTRACT

Synthesis, characterization and solution behavior of tadpole-shaped amphiphilic polymers with hydrophobic polyhedral oligomeric silsesquioxane (POSS) chain-end and hydrophilic main-chain having leucine pendants were investigated. Reversible addition-fragmentation chain transfer (RAFT) polymerization technique was employed to polymerize *tert*-butyloxycarbonyl-L-leucine methacryloyloxyethyl ester (Boc-Leu-HEMA) in the presence of POSS based RAFT agent. The POSS content and molecular weight of polymers could be controlled while maintaining a narrow molecular weight distribution (<1.3). Glass transition temperature (T_g) of tadpole shaped polymers (TSP) increased with increasing content of POSS moiety in the polymer matrix. Circular dichroism (CD) spectroscopy confirmed that the POSS moiety did not perturb the higher ordered secondary conformation of TSP, attained due to the presence of pendent chiral leucine moiety. Expulsion of side chain Boc groups produced pH responsive amphiphilic cationic polymers, which exhibited self-assembly in aqueous medium, confirmed by dynamic light scattering (DLS) and field-emission scanning electron microscopy (FE-SEM). The aggregation behavior of POSS end-capped polymeric nanoparticles was further investigated through nile red encapsulation as a hydrophobic probe in aqueous medium.

1. Introduction

In the past few decades, considerable attention has been paid to the design and effortless synthesis of polymers having distinct chain topologies due to their large involvement of macromolecular properties and self-assembling behavior both in bulk as well as solute state [1,2]. Polymers having various chain architectures such as cyclic [3], sun-shaped [4], *H*-shaped [5], *Y*-shaped [6], θ-shaped [7] and tadpole-shaped [8,9] have been designed with the advent of various controlled polymerization techniques. Their self-assembling behavior in a selective solvent was found to be largely influenced by their nonlinear shape in comparison to the linear counterpart [10,11]. Among these nonlinear architectures tadpole shaped polymer is unique due to their dramatic effect on self-assembling behavior in different solvent system [12,13].

Recently, polyhedral oligomeric silsesquioxane (POSS) containing tadpole shaped polymers have been reported with the help of controlled radical polymerization (CRP) technique [14]. POSS is a special class of three dimensional (3D) cubic nanoscale building block unit with Si—O—Si

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framework having general formula $(RSiO_{3/2})_n$ (with n is commonly 6, 8, or 10), where R group contains reactive or nonreactive polymerizable organic vertex or functionality which plays a key role in controlling the reactivity and solubility in various polar/nonpolar organic solvents during the radical polymerization [15]. This particular property makes it unique and attractive in comparison to other inorganic nanocomposites like clay, carbon nanotubes, etc. POSS molecules can be easily incorporated into polymeric matrix *via* conventional chemical copolymerization, cross-linking, grafting or physical blending to enhance the mechanical as well as thermal property [16,17]. Recently, extensive research is going on organic/inorganic nanohybrid materials due to their combination of properties developed from inorganic siloxane core and organic vertex group [18]. Ohno et al. employed monofunctional POSS based initiator for the synthesis of well-defined, tadpole-shaped hybrid macromolecular architectures *via* atom transfer radical polymerization (ATRP) [19]. Using reversible addition-fragmentation chain transfer (RAFT) polymerization technique Zhang et al. applied POSS modified chain transfer agent (CTA) for the synthesis of hybrid poly(*N*-isopropylacrylamide) (PNIPAM) and poly(acrylic acid) (PAA), and explored the self-assembled core–shell nano-dimensional macromolecular architectures with uniform diameter in aqueous medium [20,21]. POSS containing tadpole shaped polystyrene has been synthesized and examined in various organic solvents to study the self-assembly behavior [22]. Müller and coworkers have developed synthetic strategy for the preparation of POSS-containing hybrid homopolymers and block copolymers, and explored solution behavior in aqueous medium to obtain interesting higher-order morphology such as spherical and ellipsoids [21,23].

On the other hand, amino-acid incorporated non-biological synthetic polymers exhibit better biocompatibility, solubility in aqueous medium, and have been shown as ideal candidate for bio-medical applications such as in drug delivery, tissue engineering, biosensors and gene carriers [24,25]. The presence of amino-acid moieties as pendant groups in the synthetic polymers gave rise to stimuli-responsive properties such pH, temperature and ionic strength responsiveness [26]. Amino acids can be modified at amine or carboxyl site to generate *N*-terminus or *C*-terminus vinyl monomers, respectively. These monomers can be polymerized *via* conventional free radical polymerization or CRP techniques to obtain free carboxyl or amino group pendant polymers [27,28]. Therefore, we combined POSS and amino acid, and in the present work tadpole shaped POSS-containing hybrid polymers were prepared *via* RAFT polymerization of Boc-L-leucine methacryloyloxyethyl ester (Boc-Leu-HEMA). As a representative amino acid, we have chosen naturally occurring L-leucine due to its large availability, established role in the formation of α-helices structures, ability to provide biocompatibility and chiral character. Boc group expulsion gave pH responsiveness and cationic surface charge and attained different kinds of morphology in aqueous medium.

2. Experimental section

2.1. Materials

Aminoisobutyl polyhedral oligomeric silsesquioxane (POSS) was purchased from Hybrid Plastics, MS, USA. Boc-L-leucine (Boc-L-Leu-OH, 99%, Sisco Research Laboratories Pvt. Ltd., India), trifluoroacetic acid (TFA, 99.5%, Sisco Research Laboratories Pvt. Ltd.), 2-hydroxyethyl methacrylate (HEMA, 97%, Sigma), 4-dimethylaminopyridine (DMAP, 99%, Sigma), dicyclohexylcarbodiimide (DCC, 99%, Sigma), nile red (NR, Sigma) and 1-hydroxybenzotriazole (HOBt, spectrochem, India) were used without any further purification. The 2,2′-azobisisobutyronitrile (AIBN, Sigma, 98%) initiator was purified by recrystallization from methanol, stored in the refrigerator. 1,4-Dioxane was purified through a basic alumina column prior to polymerization. The NMR solvents such as $CDCl_3$ (99.8% D), methanol-d_4 (CD_3OD, 99.8% D) and D_2O (99% D) were purchased from Cambridge Isotope Laboratories, Inc., USA. The synthesis of 4-cyano-4-(dodecylsulfanylthiocarbonyl)sulfanyl pentanoic acid (CDP) was conducted according to the earlier reported procedure [29]. Solvents such as hexanes (mixture of isomers), acetone, ethyl acetate, tetrahydrofuran (THF) and dichloromethane (DCM) were purified by standard procedures. The leucine containing vinyl monomer, Boc-Leu-HEMA, was synthesized as reported previously by our group [30].

2.2. Characterization techniques

The ^1H and ^{13}C NMR spectroscopic measurements were carried out on a Bruker Avance^{III} 500 spectrometer at 298 K. The ^{29}Si NMR study was performed on a JEOL 400 MHz spectrometer at 298 K. The FT-IR spectrum was recorded on KBr pellets using a Perkin–Elmer Spectrum 100 FT-IR spectrometer. The UV–visible spectroscopic measurements were carried out on a HITACHI U-4100 UV–vis spectrometer, with a scan rate of 240 nm/min. Fluorescence spectra were recorded on a Horiba Jobin Yvon FluoroMax-4 spectrofluorometer. The number average molecular weight (M_n) and molecular weight distribution (dispersity, $Đ$) of various tadpole shaped polymers were determined by gel permeation chromatography (GPC) in *N,N*-dimethylformamide (DMF) at 35 °C using a flow rate of 1.0 mL min^{-1} (Viscotek GPC pump; columns: two Visco Gel I-Series G4000). Detection consisted of a Viscotek refractive index (RI) detector operating at 660 nm, and a Viscotek model 270 series platform consisting of a laser light scattering detector (detection angles of 7° and 90°) and a four-capillary viscometer. Narrow molecular weight polystyrene standards were used to develop the calibration curve. Thermal behaviors of synthesized polymers were characterized by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) at a heating rate of 10 °C/min under N_2 atmosphere by using Mettler Toledo DSC1 STRe and TG/SDTA 851e instruments, respectively. During DSC measurement, tadpole shaped polymers were first cooled from room