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Polymer Nano- and Microspheres with Bumpy and Chain-Segregated Surfaces

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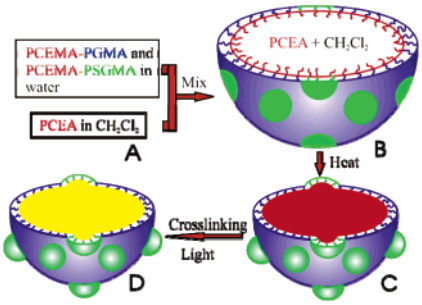
Polymer nano- and microspheres with intricate internal domain structures have been prepared from emulsion copolymerization,[1] self-assembly of block copolymers,[2] and the sol−gel process.[3] There have been, however, few reports on the preparation of polymer nano- and microspheres with surface-segregated chains. Erhardt et al.[4] prepared two-faced (Janus) nanospheres from an A−B−C triblock by chemically processing a block-segregated solid of the polymer. Gohy et al.[5] and Hu et al.[6] mixed different block copolymers that were tailor-made to contain "gluey" core blocks in a solvent to prepare mixed micelles with segregated corona chains. Spheres prepared from these approaches cannot be much larger than ∼100 nm due to difficulties associated with the synthesis of block copolymers with molar masses higher than $\sim 10^6$ g/mol. We report here a surprisingly simple method for the preparation of polymer nano- and microspheres with surface-segregated chains and with diameters between ∼30 to ∼500 nm. Even more interesting, the spheres can be produced bearing small hemispherical bumps where one type of surface chains resides predominantly.

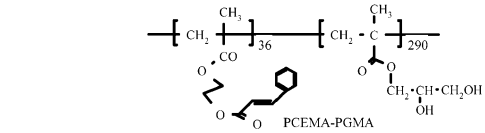
We imagined that spheres with surface-segregated chains could be prepared based on a process similar to the one depicted in Scheme 1. The process should involve, first, the preparation of an aqueous solution containing two amphiphilic diblock copolymers sharing the same water-insoluble block (A, Scheme 1). The block should also be cross-linkable to allow the structural locking of the final particles formed. In the second step, an oil phase would be added into the aqueous phase under vigorous stirring. The oil phase could be a neat solvent such as CH_2Cl_2 or CH_2Cl_2 containing a dissolved polymer. The polymer should be compatible with the water-insoluble block of the two amphiphilic diblock surfactants and should also be cross-linkable. For the fast dispersion of the oil phase inside the aqueous phase, and probably also for the fact that the two surfactants share the same water-insoluble block, we speculated that the different surfactant chains would rush to stabilize the oil droplets without attending to the identities of other surfactant molecules that had already been or were being incorporated onto an oil droplet. We further speculated that the two surfactants would be more or less randomly mixed immediately after emulsion preparation. After the droplets had been formed and stabilized by a sufficient number of surfactant chains, the different surfactant molecules would then worry about the nature of their neighbors.

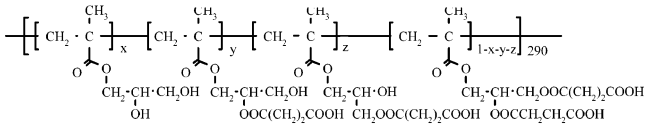
Scheme 1. Preparation of Microspheres with Bumpy and Chain-Segregated Surfaces



The fact that most polymers are incompatible would drive the position shuffling of the surfactant chains in the 2-D surface space of an oil droplet and the segregation of one type of chains from chains of the other polymer to form probably dispersed circular domains (A → B). In the third step (B → C), we would heat the system to evaporate CH_2Cl_2 to obtain solid particles. We would finally lock in the structure of the particles by cross-linking the core of the particles (C → D).

On the basis of the cross-linkability requirement, we decided to use the photo-cross-linkable poly(2-cinnamoyloxyethyl methacrylate) or PCEMA polymer as the water-insoluble block of the surfactants. On the basis of water solubility and the fact that our model homopolymers, poly(glyceryl methacrylate), PGMA, and succinated PGMA, PSGMA, were incompatible and underwent macrophase separation in films cast from water (Supporting Information), we decided to use PGMA and PSGMA as the water-soluble blocks of the surfactants. The specific parent diblock that we used consisted of 36 CEMA units and 290 GMA units. We prepared PCEMA−PSGMA by succinating 69% of the hydroxyl groups of the PGMA block of PCEMA−PGMA.





The polymers that were used as oil-phase additives included a homopolymer, poly(2-cinnamoyloxyethyl acrylate), PCEA, consisting of 150 units. PCEA rather than PCEMA was used because we did not have a well-defined PCEMA sample handy at that time and thought that the structural difference between PCEMA and PCEA was small enough for them to be compatible.

We started by preparing an aqueous phase containing equal weights of PCEMA−PGMA and PCEMA−PSGMA at a total concentration of 2.0 mg/mL and an oil phase containing PCEA dissolved in CH_2Cl_2 at 25 mg/mL. An emulsion was obtained by adding the oil into the aqueous phase either under mechanical stirring at 1500 rpm or under magnetic stirring followed by ultrasonication. The emulsion prepared under mechanical stirring was stirred for 1 h to allow the surface chains to reorganize before it was warmed over 1 h to 55 °C and heated at this temperature for 1 h to evaporate CH_2Cl_2. The solidified emulsion droplets were irradiated with UV light to cross-link the PCEMA block and PCEA chains, yielding "permanent" spheres.

Such an experiment produced spheres that not only had segregated surface chains but also bore hemispherical bumps. Suspecting that the bumps were developed during CH_2Cl_2 evaporation due to the gradual crowding of the surface chains and the

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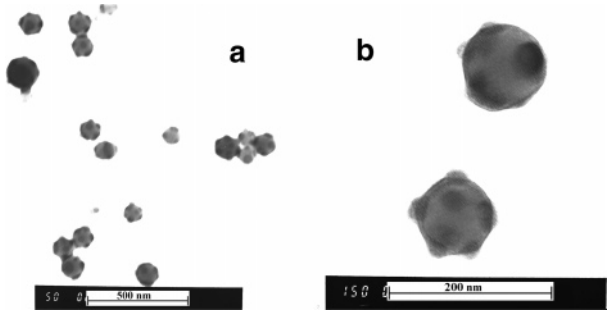

Figure 1. (a and b) TEM images of PCEA microspheres taken at low and high magnifications. The spheres were aspirated from water onto nitrocellulose-coated copper grids and stained by uranyl acetate. They were synthesized using (1) emulsion prepared under magnetic stirring followed by ultrasonication; (2) weight ratio between PCEMA−PGMA, PCEMA−PSGMA, and PCEA at 1:1:2; (3) water to CH_2Cl_2 volume ratio in the final emulsion mixture at 37.5/1; (4) PCEA concentration in CH_2Cl_2 at 25 mg/mL; and (5) $CuCl_2$ to carboxyl group molar ratio at 9%.

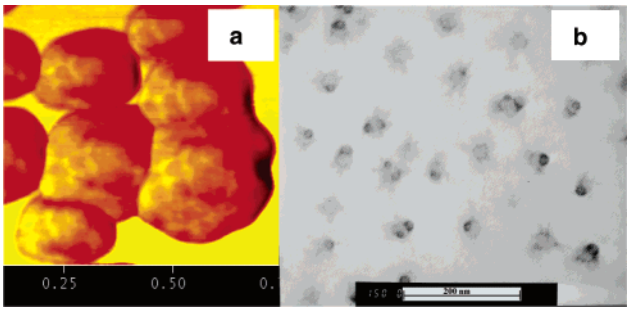

Figure 2. (a) AFM phase-contrast image of a PCEA microsphere sample. The width of the image is 0.75 μm. (b) TEM image of PCEMA−PGAM/PCEMA−PSGMA nanospheres.

electrostatic repulsion between the dissociated carboxyl groups of PSGMA, we added NaCl at 0.10 M to the aqueous phase to screen out the electrostatic interaction. This recipe change reduced, indeed, the bumpiness. We then asked if we could purposely promote bump formation. Divalent cations were known to bind with carboxyl groups of different poly(acrylic acid) chains to effect "physical cross-linking" of the polymer,[7] and we thought they might help PSGMA clustering as well. After some optimization, we found that $CuCl_2$ at ∼9 mol % relative to the PSGMA carboxyl groups helped produce the bumpiest spheres. Figure 1 shows transmission electron microscopy (TEM) images for a batch of microspheres prepared with use of $CuCl_2$ and no NaCl. Figure 1a shows that the bumpy spheres have a mean size of ∼100 nm. At a higher magnification, we see in Figure 1b that the darker bumps have a size of ∼30 nm on the surfaces of the microspheres. Since uranyl acetate was used to stain the sample and it is known to stain carboxyl groups selectively,[8] this suggests the concentration of the PSGMA chains at the surfaces of the bumps. The hemispherical shape of the bumps is evident in Figure 1b as one compares the top-down and side views of the different bumps.

To further confirm the segregation of the PSGMA and PGMA surface chains, we have studied by atomic force microscopy (AFM) a sample that was prepared without the use of $CuCl_2$ but with NaCl. These spheres were not very bumpy. Figure 2a shows an AFM phase-contrast image of several spheres of this sample. Since this imaging mode maps viscoelasticity property differences of a surface, the fact that we are able to see a contrast in the lighter regions of the spheres suggests PSGMA and PGMA segregation. Further substantiation of this claim was rendered by the agreement between the sizes of the circular dark domains determined from AFM and TEM, which were both at ∼30 nm.

We further determined that we could increase or decrease the size of the spheres prepared by decreasing or increasing the stirring speed used during emulsion formation. To decrease the size of the prepared spheres further, we decreased the use of polymer in the oil phase. Without using any polymer in CH_2Cl_2 and using conditions otherwise identical to those described for the spheres of Figure 1, except the use of NaCl at 0.100 M, we produced PCEMA−PGMA spheres that were ∼30 nm in diameter bearing zero, one, or two PCEMA−PSGMA bumps (Figure 2b). The diameter of these bumps is ∼20 nm.

We have so far performed only preliminary experiments to test the hypothesized model for formation of the particles. We have, for example, determined by dynamic light scattering (DLS) a substantial size decrease for the oil droplets after CH_2Cl_2 evaporation. We have also shown by DLS that the size of the polymer spheres produced varied depending on the amount of CH_2Cl_2 used under otherwise identical preparation conditions, despite the fact that CH_2Cl_2 was eventually removed from the system. This thus suggests the kinetic control of the sizes of the resultant particles. Furthermore, we found that the PGMA and PSGMA chains segregated only if the initial polymer concentration in CH_2Cl_2 and, thus, the viscosity of the oil phase was sufficiently low to facilitate surfactant chain position reshuffling on the oil droplet surfaces after droplet formation.

In summary, we have established a new method for the production of nano- and microspheres with segregated surface chains. While a complete understanding of this process remains elusive, the spheres produced may have many applications. The spheres may, for example, self-assemble under controlled conditions, for example, via the addition of a selective solvent or divalent cations, into superlattices.[9] Superlattices of this type may find applications in photonics and catalysis, etc. The spheres should also allow the attachment of different biopolymers to facilitate their use in targeted drug delivery. The spheres will be useful in our group mainly in directing attachment of block copolymer nanotubes to microspheres when we perform the chemical coupling of nano- or microspheres with nanotubes to make superstructures and nanodevices.[10]

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Supporting Information Available: Experimental details for the syntheses. Evidence for incompatibility of PGMA and PSGMA. DLS characterization results. TEM image for microspheres with segregated cores. This material is available free of charge via the Internet at http://pubs.acs.org.

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