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Tandem Synthesis of Core−Shell Brush Copolymers and Their Transformation to Peripherally Cross-Linked and Hollowed Nanostructures

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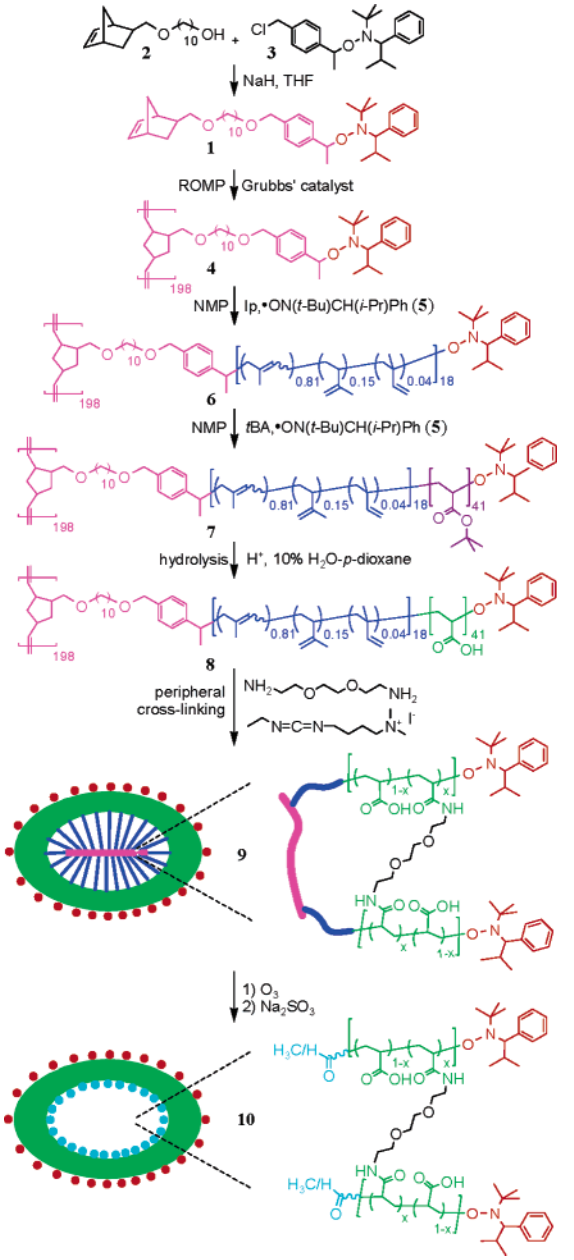
Over the past decade, the preparation and study of well-defined macromolecular core−shell nanostructures, having unique architectures and controlled dimensions, have become increasingly important. Besides those derived from dendritic polymers and self-assembly of block copolymers,[1,2] core−shell brush copolymers have also gained significant interest.[3] A variety of core−shell brush copolymers has been synthesized by sequential polymerizations using polyfunctional macroinitiators ("grafting from"),[3b−d] and by homopolymerization of diblock macromonomers ("grafting through").[3e,f] Core−shell brush copolymers have been shown to serve as carriers for encapsulation[4] and as templates for nanoparticle preparation.[5] In addition to the unique core environment imparted by the core−shell morphology of brush copolymers, the ability to conduct chemistry selectively within the peripheral or core regions allows for alteration of the macromolecular structures and their transformation to sophisticated nanoscopic objects.[1d,e] Here, we describe the synthesis of brush copolymers via a tandem living polymerization sequence and then further demonstrate the ability to transform the initial core−shell structure into an amphiphilic brush copolymer, a peripherally cross-linked nanostructure, and finally, a hollowed nanoscale framework (Scheme 1). Each transformation was designed to dramatically alter the structure and properties of the nanoscale materials.

A tandem synthetic strategy,[6] combining ring-opening metathesis polymerization (ROMP)[7] and nitroxide-mediated polymerization (NMP),[8] was utilized in the synthesis of a well-defined core−shell brush copolymer via a "grafting from" approach. A NMP−ROMP *inimer*, **1**, containing an alkoxyamine functionality (as a universal *ini*tiator for NMP)[8b] and a norbornene (NB) functionality (as a mono*mer* for ROMP),[7] was prepared in 87% yield by nucleophilic substitution of a NB-functionalized alcohol **2** with a benzylic chloride-functionalized alkoxyamine **3** (1.2 equiv) in the presence of NaH (3.0 equiv) in THF heated at reflux for 30 h. Initiated by Grubbs' catalyst $RuCl_2(CHC_6H_5)[P(C_6H_{11})_3]_2$,[7b] ROMP of **1** was conducted in toluene for 1 h at room temperature ($[\mathbf{1}]_0/[Ru]_0 = 200$). The resulting well-defined poly(**1**), i.e. **4** ($M_n^{GPC} = 122$ kDa, $PDI^{GPC} = 1.13$), has one alkoxyamine functionality per repeat unit, as determined by ^1H NMR spectroscopy. It was then used as a polyfunctional NMP macroinitiator in the sequential polymerizations of isoprene (Ip) and *tert*-butyl acrylate (*t*BA), in the presence of nitroxide **5** to suppress biradical coupling.[8b] Brush copolymer **6** ($M_n^{GPC} = 366$ kDa, $PDI^{GPC} = 1.19$) having PIp grafts with alkoxyamine termini was obtained by NMP of Ip at 120 °C for 32 h ($[Ip]_0/[\mathbf{5}]_0/[\text{alkoxyamine of } \mathbf{4}]_0 = 1550/2.71/1.00$). Using **6** as macroinitiator, NMP of *t*BA was then performed at 122 °C for 24 h ($[tBA]_0/[\mathbf{5}]_0/[\text{alkoxyamine of } \mathbf{6}]_0 = 1600/2.77/1.00$). This two-step NMP afforded the core−shell brush copolymer **7** ($M_n^{GPC} = 1410$ kDa, $PDI^{GPC} = 1.23$) having diblock PIp-*b*-P*t*BA grafts, as supported by GPC and ^1H NMR spectroscopy. The adoption of a phase-segregated cylindrical core−shell morphology was verified by atomic force microscopy (AFM) measurement on mica (Figure

Scheme 1



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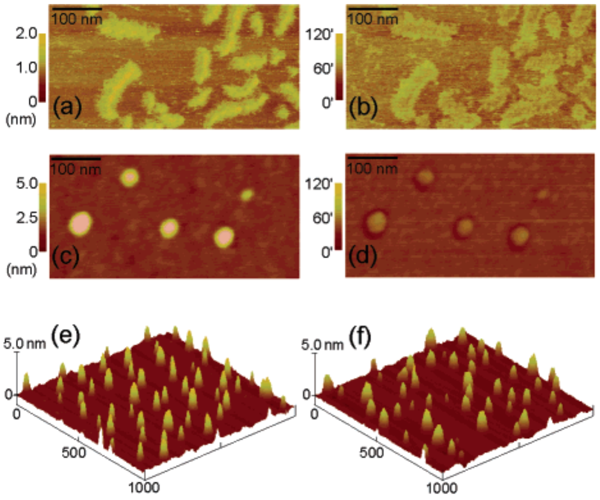

Figure 1. Tapping mode AFM images of **7**−**10**: (a) height image of brush copolymer **7** on mica, (b) phase image of brush copolymer **7** on mica, (c) height image of brush copolymer **8** on silicon, (d) phase image of brush copolymer **8** on silicon, (e) 3D height image of peripherally cross-linked brush copolymer **9** on mica, (f) 3D height image of hollowed nanostructure **10** on mica. AFM samples were prepared by spin casting the corresponding sample solution (in THF for **7**, **8** and water for **9**, **10**) on freshly cleaved mica or precleaned silicon substrates.

1 a and b). Complete conversion of the *t*BA units of **7** into acrylic acid (AA) units was achieved by hydrolysis of **7** in the presence of 0.2 M HCl in 10% water-*p*-dioxane heated at reflux for 12 h. With less steric hindrance and stronger interchain attraction among the shell block segments for the resulting amphiphilic core−shell brush copolymer (in comparison to **7**), **8** exhibited aggregated structures on mica but presented as collapsed, globular micelles on silicon, as detected by AFM measurement (Figure 1 c and d).

Following a typical procedure,[9] cross-linking of **8** was performed to afford peripherally cross-linked brush copolymer **9**. Cross-linking of **8** was accomplished in water using 0.11 equiv of 2,2′-(ethylenedioxy)bis(ethylamine) (a diamino cross-linker) and 0.22 equiv of 1-[3′-(dimethylamino)propyl]-3-ethylcarbodiimide methiodide (a catalyst), relative to the amount of AA units of **8**. Upon cross-linking in water, the nanostructures underwent an increase in the volume-average hydrodynamic diameter (D_h), from **8** having a D_h of 11.5 ± 0.3 nm (by DLS) to **9** with an increased D_h of 17.2 ± 1.6 nm, presumably due to a combination of the hydrophilicity change of the peripheral block segments and the volume occupied by the cross-linking units. As a soft material, **9** collapsed when deposited from water onto mica and appeared as flattened globules with an average diameter (D_{av}) of 36.1 ± 8.5 nm and an average height (H_{av}) of 2.22 ± 0.32 nm (Figure 1e).

Subsequently, hollowed nanostructures **10** were prepared by selective degradation of the PIp-based core of **9**, using ozone followed by reduction with Na_2SO_3.[10] DLS measurement of **10** suggested that it experienced some extent of aggregation in water, but the hollowed architecture of **10** was supported by AFM imaging (Figure 1f). Compared with **9**, **10** had a 10% increase in D_{av} (39.7 ± 10.6 nm) and an 11% decrease in H_{av} (1.98 ± 0.39 nm). These data indicate that **10** was significantly more flexible than **9** and flattened more substantially upon absorption onto mica. As a control experiment, selective degradation of the PIp-based core of brush copolymer **8** was also performed following the same procedure, and no nanostructure retention could be detected by either DLS or AFM. Such results further verified the effectiveness of the combined peripheral cross-linking, in creating a robust nanoscale structure, **9**, and core degradation, for the production of the hollowed nanoscale framework of **10**.

In summary, we have demonstrated the preparation of core−shell brush copolymers, based on a tandem-controlled polymerization synthetic route. These macromolecules were then used as unimolecular templates to prepare peripherally cross-linked nanoparticles and hollowed nanoscale frameworks. Because there are many functionalities (including carboxylic acid, alkoxyamine, aldehyde, and ketone) presented, these types of materials can be further utilized to construct nanoscale objects in aqueous solutions for a variety of interesting applications.[11]

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Supporting Information Available: Detailed Experimental Section, including histograms for the AFM data. This material is available free of charge via the Internet at http://pubs.acs.org.

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