Architecture of shell-crosslinked polymer nanoparticles via a living radical mechanism and modification to hollow nanocapsules

K. ISHIZU, J. PARK, K. TANIMURA, S. UCHIDA
Department of Organic Materials and Macromolecules, International Research Center of Macromolecular Science, Tokyo Institute of Technology, 2-12-1, Ookayama, Meguro-ku, Tokyo 152-8552, Japan
E-mail: kishizu@polymer.titech.ac.jp

T. TAMURA
Fine Chemicals & Polymers Research Laboratory, NOF Corporation, 82 Nishimon, Taketoyo-cho, Chita-gun, Aichi-ken 470-2398, Japan

Nanoparticles have been attracting much attention for wide applications because of their potential use as building blocks for a variety of nanotechnology applications [1, 2]. Ishizu's group established the preparation method for core-shell type polymer nanoparticles by crosslinking the segregated chains in the spherical microdomains of di- or triblock copolymer films or micelles [3]. The core-shell type nanoparticles synthesized by this method are composed of a crosslinked core, surrounded by a corona of shell chains attached with one end to the surface of the core. On the other hand, core-shell nanoparticles with a crosslinked shell have been prepared by shell-crosslinking block copolymer micelles [4, 5]. The core-shell particles prepared by the methods mentioned above are all in the nanometer-size range.

Hawker and coworkers reported the surface-initiated procedures for the growth of polymer chains containing reactive groups leading to functionalized core-shell nanoparticles [6]. After crosslinking of the polymer shell, dissolution of the core gave robust and hollow polymeric nanocapsules. More recently, we presented novel routes to hyperbranched polystyrene (PS) [7, 8] or poly(ethyl methacrylate) (PEMA) [9, 10] from 2-(*N*,*N*-diethyldithiocarbamyl)methylstyrene (DTCS) or 2-(*N*,*N*-diethyldithiocarbamyl)ethyl methacrylate (DTCM), respectively, as an inimer by one-pot photopolymerization. For example, photolysis of inimer DTCM leads to the initiating methacryloyl ethyl radical with inactive dithiocarbamate (DC) radical (see Scheme 1). This radical mechanism is very similar to the alkoxyamine-initiated living radical polymerization system, details of which were published by Moad and Rizzardo [11]. Such hyperbranched polymers formed a single molecule in solution due to a very high density. In fact, it was found from hydrodynamic properties that hyperbranched molecules behaved as hard spheres in solution [12]. Since the hyperbranched polymer has large amounts of photofunctional DC groups on its outside surface, we could derive amphiphilic star-hyperbranched copolymers by graft photocopolymerization of hyperbranched PS (as a macroinitiator) with amphiphilic vinyl monomers [13].

On the other hand, we also established one-pot synthesis of star polymers based on DC-mediated living free-radical procedures [14]. That is to say, the living free-radical copolymerization of inimer DTCS with 4,4′-bismaleimidediphenylmethane (BMIM) formed highly branched poly(methyl methacrylate) (PMMA) star polymers in the presence of methyl methacrylate (MMA) monomer. The key to this synthesis was the possibility of initial microgel formation by the preferential and controlled alternating copolymerization of DTCS with BMIM such as electron donor and acceptor monomers, respectively. As a result, the microgel formation was initially fast with preferential consumption of DTCS and BMIM. On the basis of the above experimental results, we speculate that the living free-radical copolymerization of hyperbranched macroinitiator with BMIM will form shell-crosslinked polymer nanoparticles in the presence of large excess of styrene as shown in Scheme 2. In this communication, we mention the architecture of shell-crosslinked nanoparticles via a living free-radical mechanism and modification for hollow nanoparticles.

Well-defined hyperbranched PEMA was prepared by photopolymerization of DTCM in 50% benzene solution with UV irradiation for 30 min in a sealed glass ampoule under high vacuum at 30 °C (250 W high-pressure mercury lamp, UV intensity 420 W/m^2, irradiation distance 150 mm). After polymerization, the polymer was recovered by precipitation with methanol. The precipitation fractionation of hyperbranched PEMA (HB-PEMA) was carried out with a benzene-methanol system, because the hyperbranched PEMA exhibited a broad molecular weight distribution (M_w/M_n). The HB-PEMA obtained was recognized to show unimodal character ($M_w/M_n = 1.28$) on the gel permeation chromatography (GPC) profile. The details concerning the synthesis, purification and characterization were given elsewhere [9, 10]. The weight-average molecular weight ($M_w = 3.48 \times 10^4$) was derived from Zimm plot by means of static light scattering (SLS: He-Ne laser $\lambda_0 = 632.8$ nm) in benzene. The particle diameter ($D_h = 10$ nm) was determined by dynamic light scattering (DLS) with cumulant method in benzene (see Fig. 1a).

^{1}H NMR spectrum (500 MHz, in $CDCl_3$) of HB-PEMA is shown in Fig. 2a; this displays the expected resonances for the methyl protons of PEMA (*b* and

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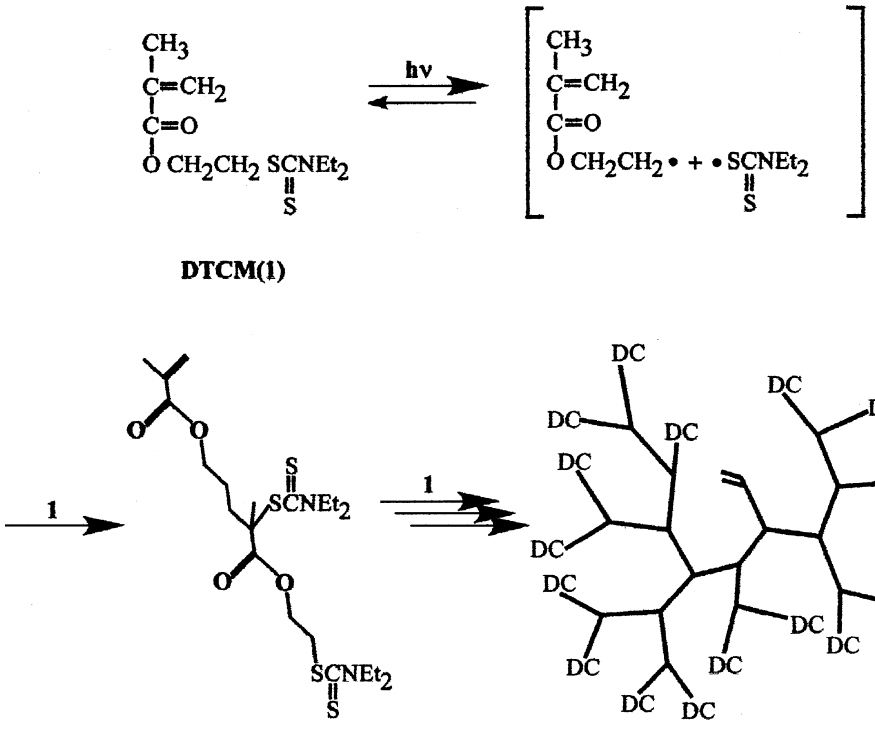
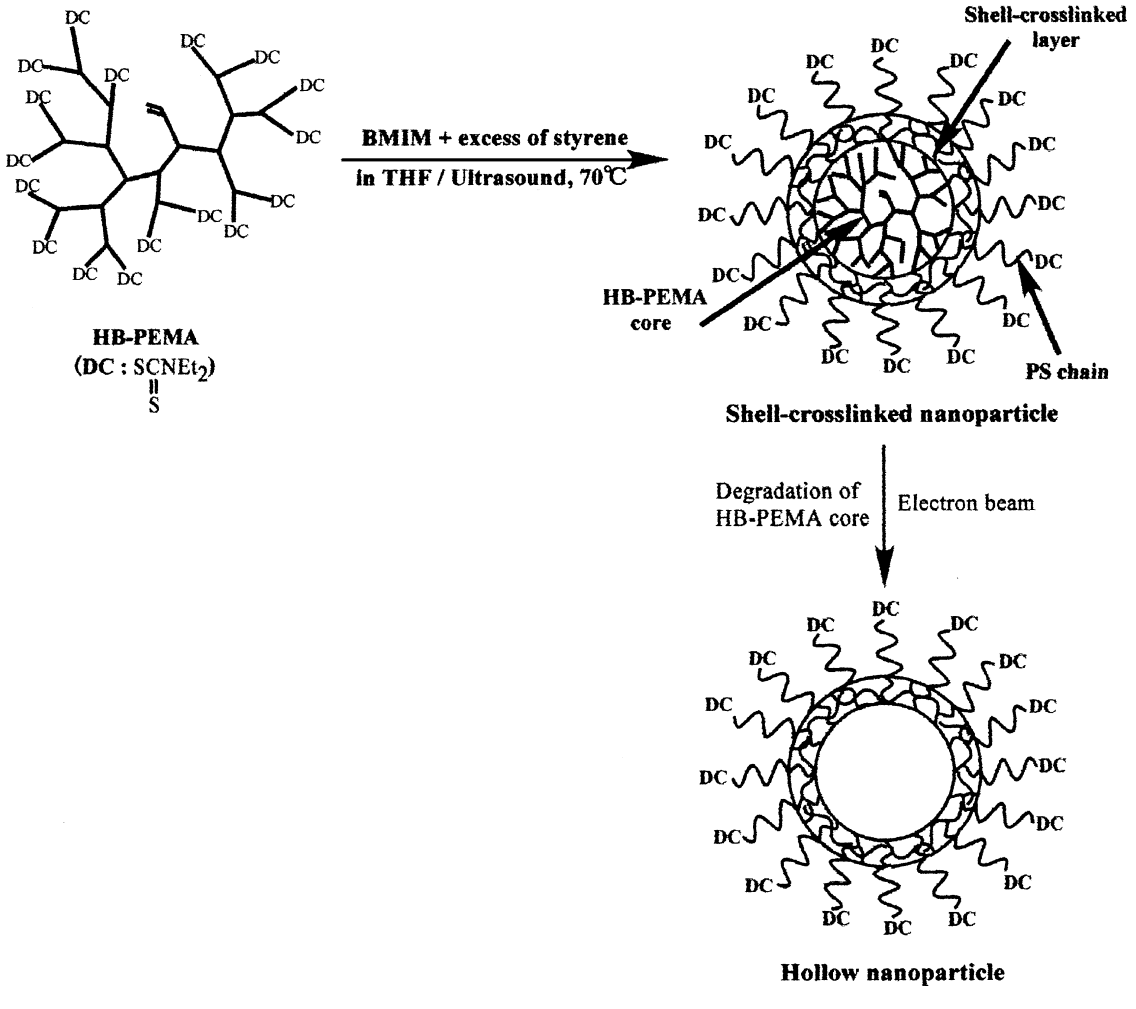


Scheme 1 Reaction scheme for formation of hyperbranched PEMA.



Scheme 2 Schematic illustration for syntheses of shell-crosslinked nanoparticle and nanocapsule.

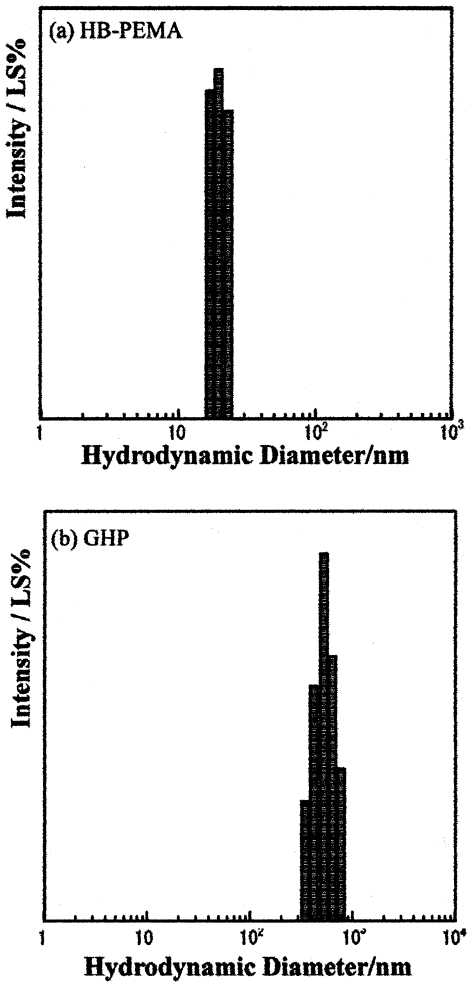


Figure 1 Particles size distributions by DLS: (a) HB-PEMA in benzene and (b) shell-crosslinked nanoparticles in $CHCl_3$.

c; δ 1.5 and 1.0 ppm), the methyl (*g*; 1.3 ppm) and methylene protons (*f*; 3.72 and 4.01 ppm) of the DC groups and the ethylene protons (*e* and *d*; 3.60 and 4.21 ppm) adjacent to DC groups, and confirms the presence of hyperbranched structure. If the formation of hyperbranched PEMA proceeds by an ideal living radical mechanism, the integration ratio of ethylene protons (*d* and *e*) adjacent to DC groups to the ethylene protons (*f*) of DC groups should be 1:1. The observed ratio was close to 1:1. The number of peripheral DC groups (*N*) of HB-PEMA molecule is estimated to be 104 (numer/molecule) from the number-average molecular weight ($M_n = 2.72 \times 10^4$).

The shell-crosslinked polymer nanoparticles were prepared by graft copolymerization of HB-PEMA macroinitiator (0.1 g; DC groups = 3.82×10^{-4} mol) with BMIM (0.078 g, 2.17×10^{-4} mol) and styrene (1.26 ml, 1.1×10^{-2} mol) in tetrahydrofuran (THF, 8×10^{-6} m^3). Photopolymerization led to partial gelation after 5 min of UV irradiation. A UV beam seems to be too strong a tool to cleave the C–S bonds of HB-PEMA macroinitiator. So, we carried out such graft copolymerization under ultrasonic irradiation (28 kHz) at 70 °C to cleave the C–S bond of HB-PEMA macroinitiator. In general, intense ultrasound produces large density and pressure changes within each small wavelength. This results in large stresses, and molecules are forced to move rapidly. It also produces heat in most materials and cavitation in liquids. Cavitation is the formation of bubbles of vapor caused by the mechanical fracture of the liquid in a region where the pressure is decreasing [15]. The copolymerization solution showed turbidity after 3.5 h of ultrasonic irradiation at 70 °C. Graft polymerization product (GNP) was recovered by precipitation with methanol. Long time of irradiation also led to gelation in the copolymerization system.

The ^1H NMR spectrum (in $CDCl_3$) also supports the formation of graft copolymer (see Fig. 2b). There are not only characteristic signals of HB-PEMA but also aromatic protons (*l* and *m*; δ 6.8–7.4 ppm) of polystyrene (PS) arms. We determined the composition of graft copolymer (GHP) using the signals of *l* and *b*, *c*. The integrated ratio of $1{:}b + c$ was 35.5:672.0. Therefore, the composition of PS shell was estimated to be 7.5 mol%, i.e., $100(1/2) \div [(1/2) + (b + c)/3]$. The degree of polymerization (DP_n) of a PS grafted chain was calculated from M_n of HB-PEMA and the number of DC groups (*N*), assuming that styrene and BMIM propagated from all the DC groups on the outside surface of the hyperbranched macroinitiator. As a result, the DP_n of a PS graft chain was 8. In general, the propagation rate constant (order of 10^3 1/mol s) of alternating copolymerization is much faster than that of vinyl polymerization such as styrene [16]. The propagating radicals always proceed with homopolymerization of styrene:BMIM = 2:1 complexes formed donor and acceptor monomers in the initial stage [14]. Moreover, this alternating copolymerization leads to crosslinking and forms the shell-crosslinked layer because bifunctional monomer BMIM works as crosslinker. After BMIM is consumed perfectly, the propagating step of styrene starts from DC radicals from the shell-crosslinked layer. The DP_n of BMIM units incorporated into a grafted chain was calculated to be 0.6, i.e., $[BMIM]_0/[DC]_0$, assuming all the DC groups are initiating sites. However, it was found from kinetic studies on the formation of hyperbranched PEMA that the initiator efficiency was smaller than unity [10]. Therefore, both the DP_ns of BMIM units and PS grafted chain seem to be longer than corresponding calculated values.

Direct morphological observation for graft copolymer (GHP) was performed on a transmission electron microscope (TEM) at an accelerating voltage of 75 kV. The specimens were prepared by placing of 0.1 wt% THF solutions of GHP on copper grids coated with a thin carbon film, and allowing them to dry freely and sputtering with Pt. The particle size (D_n) and size distribution (D_w/D_n) were determined from a survey of 300 samples picked out from the photographs that were obtained. A typical TEM photograph of the GHP is shown in Fig. 3a. All of the products obtained are spherical nanoparticles (D_n = ca. 12 nm). It is also found from this photograph that the particle size distribution ($D_w/D_n = 1.02$) is very narrow. These nanoparticles formed partially the aggregates by intermolecular reaction because the THF solution of GHP exhibited turbidity as mentioned earlier. In fact, the particle diameter of GHP product was ca. 180 nm in $CHCl_3$ and its size distribution was relatively broad (see Fig. 1b).

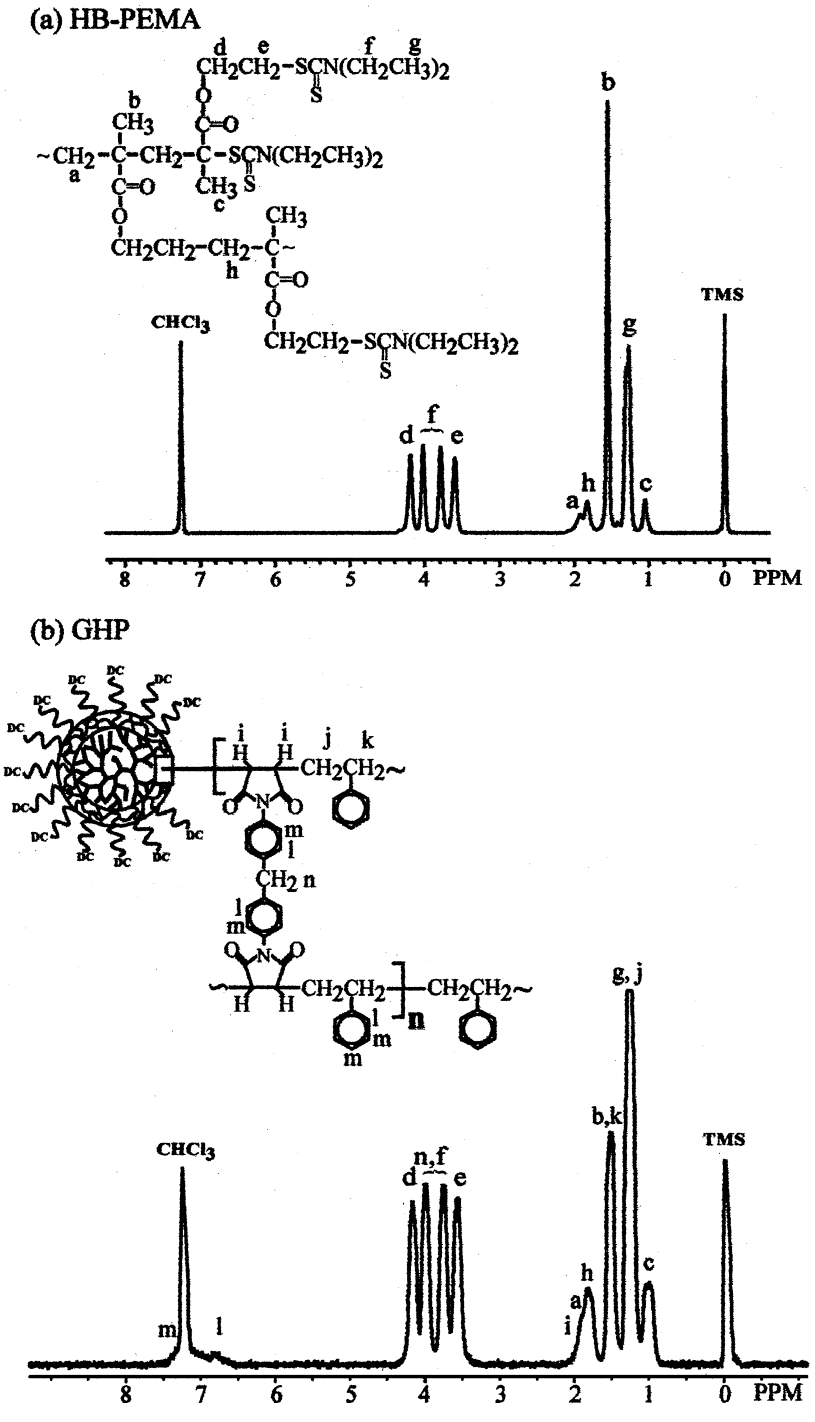


Figure 2 ^{1}H NMR spectra in $CDCl_3$: (a) HB-PEMA and (b) shell-crosslinked nanoparticles.

Subsequently, we investigated the possibility of application for hollow nanocapsules using such shell-crosslinked polymer nanoparticles. The etching of HB-PEMA cores is possible to perform by the following two methods: (1) hydrolysis of HB-PEMA cores and (2) degradation of PEMA cores by electron beam or deep-UV irradiation [17]. In this work, we employed the degradation of HB-PEMA cores by electron beam. The specimens were prepared by placing of 0.1 wt% THF solutions of shell-crosslinked nanoparticles GHP on copper grids followed as described above. These specimens were exposed to the electron beam (100 kV) for 5 min and sputtered with Pt. Fig. 3b shows in TEM photograph of GHP nanoparticles after the irradiation treatment of the electron beam. The texture shows discrete particles and any kind of deformation of the nanocapsules was not observed. Individual particles were difficult to discern because of significant loss of shape due to their small size and hollow nature. Since PEMA chains easily degrade under an electron beam, shell-crosslinked nanocapsules seem to be provided by this etching procedure.

In conclusion, shell-crosslinked polymer nanoparticles were synthesized by DC-mediated living free-radical copolymerization of BMIM and styrene initiated by hyperbranched PEMA macroinitiator. The key to this synthesis was the initial network formation of shell-crosslinked layers by the preferential and controlled alternating copolymerization of styrene and BMIM such as electron donor and

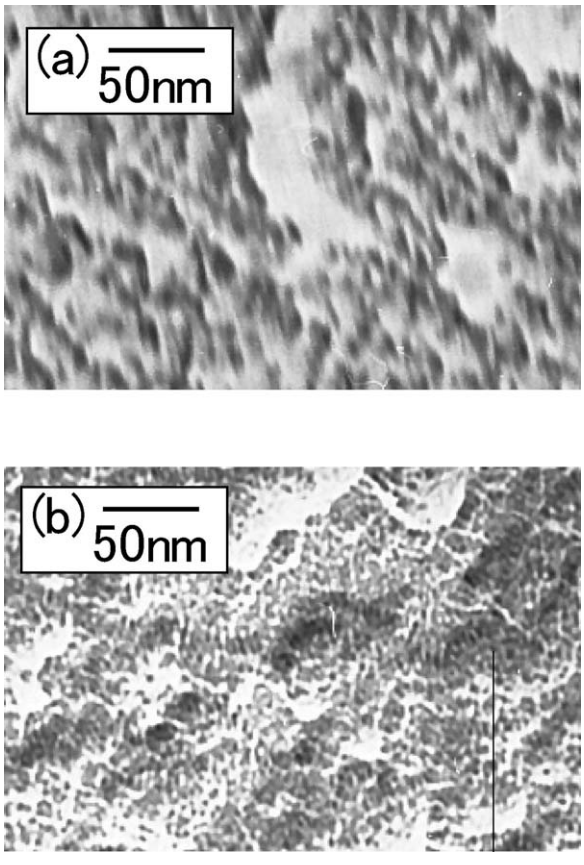


Figure 3 TEM photographs: (a) shell-crosslinked nanoparticles and (b) shell-crosslinked nanocapsules.

acceptor monomers. Since hyperbranched PEMA cores easily degraded under an electron beam, we could produce shell-crosslinked nanocapsules from shell-crosslinked nanoparticles. Such nanocapsules hold significant promise for a variety of applications because of their potential for the encapsulation of active substances such as drugs and dyes.

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Received 23 September
and accepted 30 October 2003