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Cross-linking the Linear Polymeric Chains in the ATRP Synthesis of Iron Oxide/Polystyrene Core/Shell Nanoparticles

Guifeng Li, Jinda Fan, Rong Jiang, and Yong Gao*

Department of Chemistry and Biochemistry,
Southern Illinois University,
Carbondale, Illinois 62901-4409

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During recent years, the synthesis of superparamagnetic iron oxide nanoparticles coated with a thin shell of organic polymeric wall has attracted a great deal of research attention due to the potential biomedical applications of these nanomaterials.[1] Because of anistropic dipolar attraction, nanometer-sized iron oxide cores intend to aggregate into larger clusters, losing the specific properties associated with their nanometer dimensions. A shell of coating materials, especially organic polymers, are often needed to cover the superparamagnetic iron oxide core to prevent such a core agglomeration. In addition, the coating materials will also provide a platform for the attachment of the functionalities such as biologically active peptide and protein molecules to improve the biospecificity of nanoparticles for their interactions to specific cells and tissues. Such core/shell nanocomposites can be used for the site-specific magnetic resonance imaging for medical diagnosis[2] and ac magnetic field-assisted cancer therapy.[3] However, the in vivo biomedical applications usually prefer these articles to have narrow size distributions for uniform physical/chemical properties and possess an overall dimension smaller than 20 nm for high tissue penetration capability.[4] Among many approaches for coating the surface of nanoparticles with a shell of organic polymers, the surface-initiated atom transfer radical polymerization (ATRP) has become a method of choice recently.[5] Several groups have reported the synthesis of the polymeric core/shell nanoparticles such as SiO_2,[6] Au,[7] $MnFe_2O_4$,[8] and Fe_2O_3[9] via ATRP. ATRP can offer polymeric shells with low polydispersity and this method is easy to control the molecular weight, thereby, the thickness of the polymeric shell wall.[10]

However, as far as we know, previous ATRP studies for the synthesis of the core/shell nanoparticles usually yielded a shell of linear polymeric molecules protecting iron oxide cores (Scheme 1A).[8,9] For example, the enlightening work recently reported by Wang et al.[9] has utilized a solvent-free ATRP approach for the synthesis of the core/shell nanoparticles in which iron oxide cores were protected with a layer of non-cross-linked polystyrene shell. These linear polymers usually attach to the surfaces of metal oxide cores through linker molecules—the initiators via, for example, a −COOH group. A simple noncovalent linkage between the iron oxide core and the polymeric chain is not sufficient to achieve a permanent linkage. Instead, a dynamic exchange between the polymeric chains and other competing molecules possessing a −COOH group such as peptides and amino acids in the biological systems could lead to the dissociation of the polymeric chains from the core surfaces. The loss of the coating material and its terminal functionalities could demolish the biospecificity of these materials. In the present paper, we would like to report our synthesis of the cross-linked polymeric core/shell structure via an ATRP approach that employed divinylbenzene (DVB) for cross-linking the linear polystyrene chains. The cross-linked polymeric shell will serve as a cage, preventing the undesired site exchange of the nanoparticle surface functionalities. Fluorescence exchange experiments were used to test the stability of our core/shell nanoparticles against the site-exchange processes.

To synthesize the core/shell maghemite/polystyrene nanoparticles, we first introduced the initiator 10-carboxydecanyl 2-bromo-2-methyl-thiopropanoate onto the surface of maghemite nanoparticles via a site-exchange process. In a typical experiment, the mixture of initiator 10-carboxydecanyl 2-bromo-2-methyl-thiopropanoate (72 mg, 0.196 mmol) and the freshly prepared maghemite nanocrystals coated with oleate (220 mg)[11] in 20 mL of $CHCl_3$ was stirred at ambient temperature for 24 h under Ar protection. The resulting maghemite nanoparticles were collected magnetically using an external permanent magnet (0.7 T) and repeatedly washed with acetonitrile. Then, these nanoparticles were added into a 20-mL xylene solution of CuBr (43 mg, 0.3 mmol), 4,4′-dinoyl-2,2′-dipyridyl (DNDP) (450 mg, 1.1 mmol), $CuBr_2$ (3.4 mg, 0.015 mmol), styrene (8 mL, 70 mmol), and variable amounts of DVB (Scheme 1). After 24 h at 135 °C under Ar, the solution was cooled to room temperature and particles were magnetically collected and repeatedly washed with toluene.

The infrared spectroscopy of the dried product indicates the presence of polystyrene on the surface of the formed polystyrene core/shell nanoparticles. Characteristic peaks of polystyrene at 2800−3100 and 1200−1600 cm^{-1} were observed, which were not present in the spectrum of maghemite nanoparticles coated with oleic acid and the initiator (Figure 1). Formation of polystyrene molecules was also supported by the ^1H NMR and

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* To whom correspondence should be addressed. E-mail: ygao@chem.siu.edu.

(1) *Scientific and Clinical Applications of Magnetic Carriers*; Häfeli, U., Schütt, W., Teller, J., Zborowski, M., Eds.; Plenum Press: New York, 1997.

(2) Josephson, L.; Tung, C. H.; Moore, A.; Weissleder, R. *Bioconjugate Chem.* **1999**, *10*, 186.

(3) Jordan, A.; Scholz, R.; Wust, P.; Fahling, H.; Felix, R. *J. Magn. Magn. Mater.* **1999**, *201*, 413.

(4) Portet, D.; Denizot, B.; Rump, E.; Lejeune, J. J.; Jallot, P. *J. Colloid Interface Sci.* **2001**, *238*, 37.

(5) For a recent review: Matyjaszewski, K.; Xia, J. *Chem. Rev.* **2001**, *101*, 2921.

(6) (a) Von Werne, T.; Patten, T. E. *J. Am. Chem. Soc.* **2001**, *123*, 7497. (b) Pyun, J.; Matyjaszewski, K. *Chem. Mater.* **2001**, *13*, 3436.

(7) (a) Kamata, K.; Xia, Y. *J. Am. Chem. Soc.* **2003**, *125*, 2384. (b) Mandal, T. K.; Fleming, M. S.; Walt, R. *Nano Lett.* **2002**, *2*, 3.

(8) Vestal, C. R.; Zhang, Z. J. *J. Am. Chem. Soc.* **2002**, *124*, 14312.

(9) Wang, Y.; Teng, X.; Wang, J.-S., Yang, H. *Nano Lett.* **2003**, *3*, 789.

(10) Patten, T. E.; Matyjaszewski, K. *Adv. Mater.* **1998**, *10*, 901.

(11) Hyeon, T.; Lee, S. S.; Park, J.; Chung, Y.; Na, H. B. *J. Am. Chem. Soc.* **2001**, *123*, 12798.

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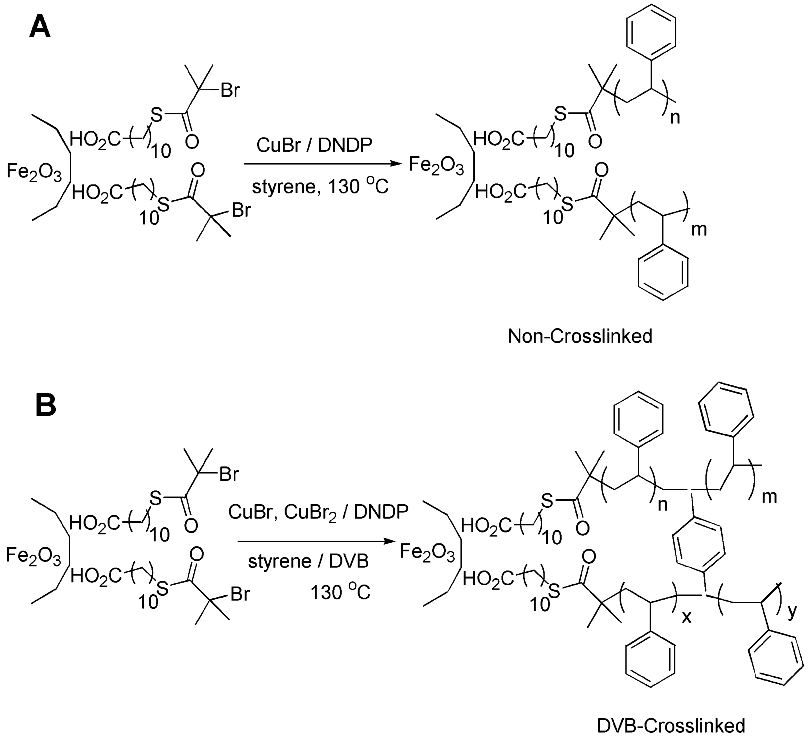
Scheme 1. (A) ATRP Synthesis of Non-cross-linked Polystyrene/Iron Oxide Nanoparticles; (B) ATRP Synthesis of DVB-cross-linked Polymeric Core/Shell Nanoparticles Using DVB as the Cross-linking Agent[a]



[a] The cage of the cross-linked polymeric shell prevents the loss of the polymeric chain due to the site exchange. The percentage of DVB in styrene could be varied for different cross-linking densities.

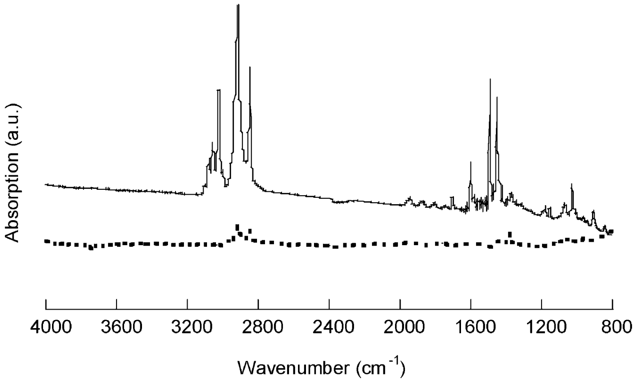


Figure 1. FT-IR spectra of iron oxide nanoparticles coated with initiator (dotted line) and with 10% DVB-cross-linked polystyrene (solid line).

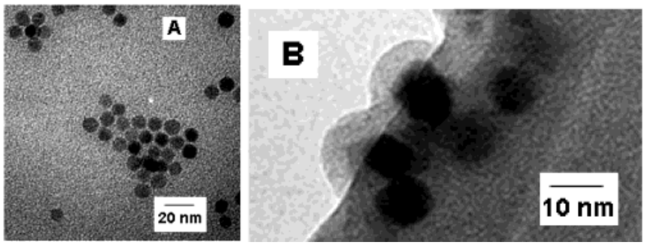


Figure 2. TEM micrographs of 10% DVB-cross-linked iron oxide/polystyrene core/shell nanoparticles on (A) the Formvar/carbon film coated copper grid (400 mesh); and (B) the lacey carbon film coated copper grid (300 mesh) consisting of woven-mesh-like holes. The polystyrene shells are visible at the edge of a hole in (B).

gel permeation chromatography (GPC) analysis of the organic polymeric shell of the nanoparticles after HCl dissolution of the maghemite cores (Supporting Information). Transmission electron microscopy (TEM) studies confirmed that these nanoparticles have very narrow size distributions with an average core dimension of 11 nm (Figure 2A) surrounded with a 4.7-nm polystyrene shell (Figure 2B).

To test the stability of these cross-linked core/shell maghemite nanoparticles against the undesired site-exchange processes, we placed 2.5 mg of the core/shell maghemite nanoparticles protected with a 10% DVB-cross-linked polystyrene shell into a $CHCl_3$ solution (10 mL) of 6-(1-pyrenyl)hexanoic acid (1 mg, 3.16 μmol). After the solution was stirred at ambient temperature for about 96 h, nanoparticles were magnetically concentrated using a permanent magnet of 0.7 T.[12] The solution was removed and nanoparticles were washed three times with $CHCl_3$ (20 mL). The organic solutions were combined, dried over anhydrous sodium sulfate, and concentrated to a final volume of 10 mL. The fluorescence spectrum (Figure 3A) of the aforementioned solution after the site-exchange reaction (line e, diluted 2500-fold) and the one of 6-(1-pyrenyl)hexanoic acid measured before the introduction of maghemite nanoparticles (line a, diluted 2500-fold) suggest that pyrene molecules were not adsorbed onto the surface of maghemite particles protected with 10% DVB-cross-linked polystyrene during the site-exchange reaction. This conclusion was also supported by the absorption spectra in Figure 3B (lines a and e). Presumably the 10% DVB-cross-linked polystyrene shell serves like a cage, preventing the competitive binding of 6-(1-pyre-

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[12] Fe_2O_3 Nanoparticles were known to quench fluorescence: Turro, N. J.; Lakshminarasimhan, P. H.; Jockusch, S.; O'Brien, S. P.; Grancharov, S. G.; Redl, F. X. *Nano Lett.* **2002**, *2*, 325.

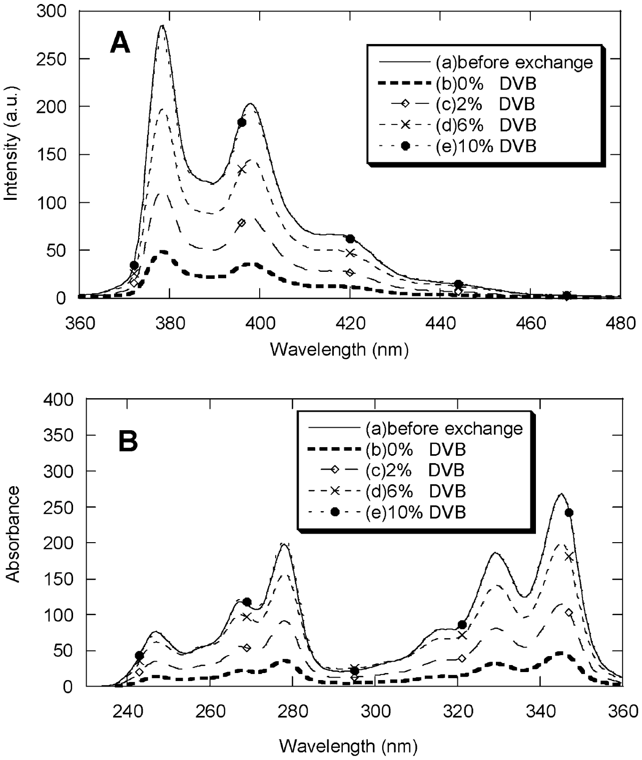

Figure 3. (A) Fluorescent spectra of 6-(1-pyrenyl)hexanoic acid in $CHCl_3$ (a) before and after site-exchange reactions with core/shell Fe_2O_3 nanoparticles protected with (b) non-cross-linked (0% DVB), (c) 2%, (d) 6%, and (e) 10% DVB-cross-linked polystyrene, respectively. The excitation wavelength was 378 nm. (B) Absorption spectra of 6-(1-pyrenyl)hexanoic acid in $CHCl_3$ (a) before and after site-exchange reactions with core/shell iron oxide nanoparticles protected with (b) non-cross-linked (0% DVB), (c) 2%, (d) 6%, and (e) 10% DVB-cross-linked polystyrene, respectively.

nyl)hexanoic acid onto the surface of maghemite cores. However, lighter DVB-cross-linked polystyrene shells are less effective at shielding the adsorption of the pyrene probes onto the surface of metal oxide cores. The calculations based on the fluorescent intensities at 378 nm in Figure 3A suggested that about 83%, 61%, and 31% of 6-(1-pyrenyl)hexanoic acid molecules were exchanged onto the surfaces of nanoparticles for the 0%, 2%, and 6% DVB-cross-linked polystyrene shells, respectively. This was also supported by similar calculations from the absorption spectra in Figure 3B.

In summary, we reported an ATRP synthesis of monodisperse core/shell maghemite nanoparticles protected with a thin layer of DVB-cross-linked polystyrene molecules. The 10% DVB-cross-linked polymeric shell could prevent the undesired site exchange of the coating materials with competing ligands in solution, leading to the improvement of the stability of core/shell nanomaterials. Nanoparticles coated with a thin shell offer tremendous application potentiality in organic synthesis and biological applications, and our progress for the applications of the core/shell nanoparticles in these areas will be reported in due course.

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Supporting Information Available: The experimental procedures for the synthesis of 10-carboxydecanyl 2-bromo-2-methyl-thiopropanoate and HCl dissolution of the cores of the Fe_2O_3 nanoparticles protected with DVB-cross-linked polystyrene. ^1H NMR and GPC spectra of the 10% DVB-cross-linked polystyrene shells after HCl dissolution of the Fe_2O_3 cores (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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