

Smart Nanofibers from Combined Living Radical Polymerization, “Click Chemistry”, and Electrospinning

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ABSTRACT A simple method for preparing solvent-resistant nanofibers with a thermal-sensitive surface has been developed by the combined technology of reversible addition-fragmentation chain-transfer (RAFT) polymerization, atom transfer radical polymerization (ATRP), electrospinning, and “click chemistry”. Initially, well-defined block copolymers of 4-vinylbenzyl chloride (VBC) and glycidyl methacrylate (GMA) (PVBC-*b*-PGMA) were prepared via RAFT polymerization. Electrospinning of PVBC-*b*-PGMA from a solution in tetrahydrofuran gave rise to fibers with diameters in the range of 0.4–1.5 μm . Exposure to a solution of sodium azide (NaN_3) not only affords nanofibers with azido groups on the surface but also leads to a cross-linking structure in the nanofibers. One more step of “click chemistry” between the PVBC-*b*-PGMA nanofibers with azido groups on the surface (PVBC-*b*-PGMA- N_3) and alkyne-terminated polymers of *N*-isopropylacrylamide (NIPAM) (PNIPAM_{AT}), which were prepared by ATRP, allows the preparation of a PVBC-*b*-PGMA nanofiber with thermal-sensitive PNIPAM brushes on the surface (PVBC-*b*-PGMA-*g*-PNIPAM). PVBC-*b*-PGMA-*g*-PNIPAM nanofibers exhibit a good resistance to solvents and thermal-responsive character to the environment, having a hydrophobic surface at 45 °C (water contact angle $\sim 140^\circ$) and having a hydrophilic surface at 20 °C (water contact angle $\sim 30^\circ$).

KEYWORDS: thermal-sensitive • solvent-resistant • polymeric nanofibers • electrospinning • ATRP • RAFT • click chemistry • cross-linking

Functional nanofibers are of global interest for their potential applications in various areas, such as in tissue engineering (1, 2), biosensor technology (3), and drug delivery (4). Nanofibers with environmental-responsive (or smart) surfaces and cross-linked structures (or solvent resistance) are especially interesting for application to sensors (5, 6) and bioengineering (7). Poly(*N*-isopropylacrylamide) (PNIPAM) is one of the most studied synthetic responsive polymers, which undergoes a transition from a hydrophilic state to a hydrophobic state in water at 32 °C (8–10). Materials with surface-grafted PNIPAM brushes exhibit thermal-responsive properties and have wide applications in water treatment (11, 12), drug delivery (13) and biomedical (14, 15).

Electrospinning generates nanofibers by accelerating a jet of a charged polymer solution or polymer melt in an electric field (16). Wide applicability of materials, low cost, and high production rate (17, 18) make electrospinning an attractive approach for the preparation of continuous-microscale to submicrometer-scale fibers. Progress in controlled free-radical polymerization (CFRP), especially in atom-transfer radical polymerization (ATRP) (19–21) and reversible addition-fragmentation chain-transfer (RAFT) polymerization (22, 23), has provided a powerful tool for the synthesis of well-defined polymers and macromolecular architectures. The combination of electrospinning and CFRP is a promising approach to preparing functional nanofibers, attributable to the facility of the synthesis of functional macromolecules by CFRP and applicability to a wide range of materials by electrospinning. Fine works on the preparation of functional polymeric nanofibers by electrospinning of a pH-responsive triblock copolymer (24), a polymer and polypeptide conjugate (25), and a self-quaternized block copolymer (26) have been reported recently.

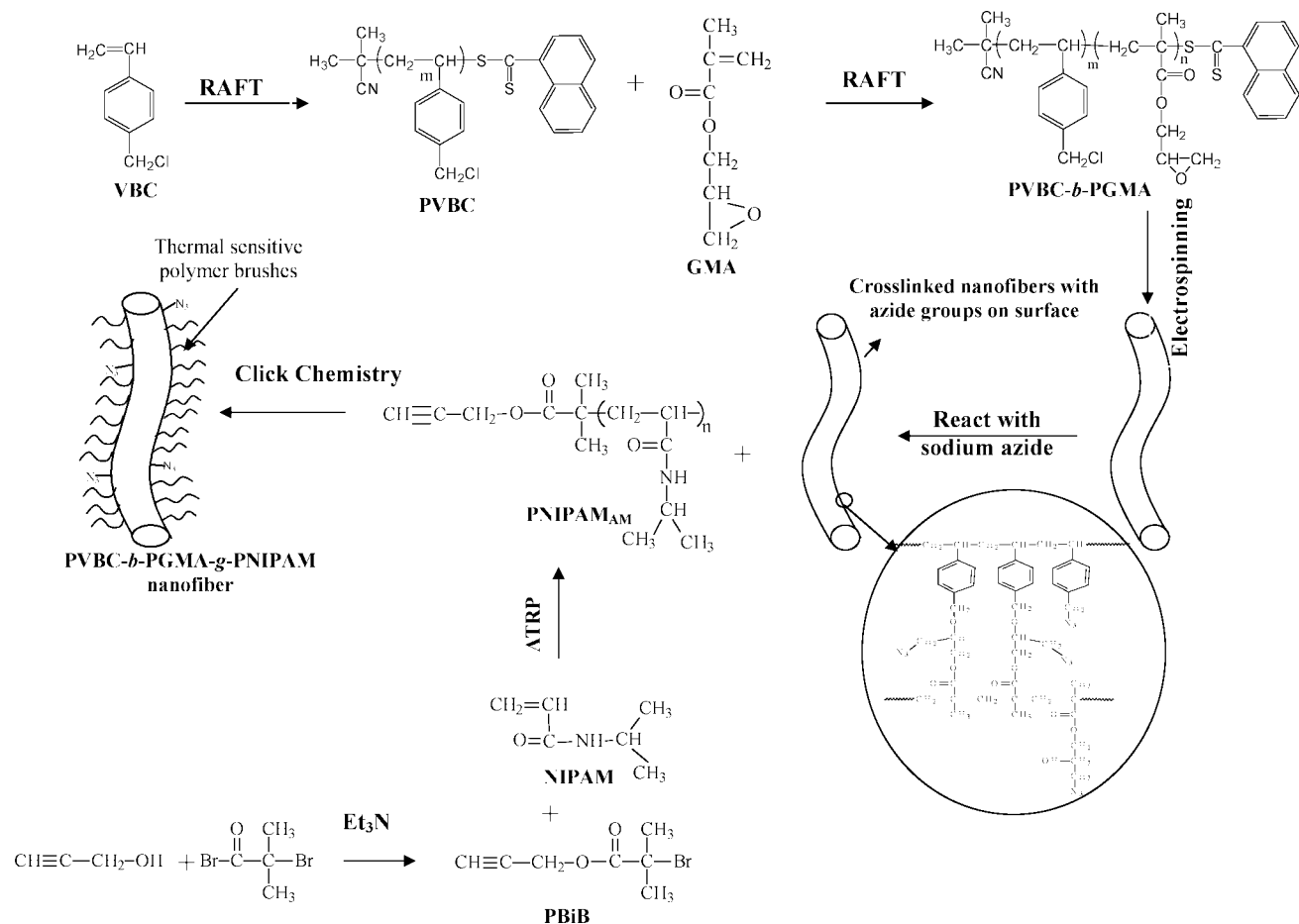
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Scheme 1. Preparation of Solvent-Resistant Nanofibers with a Thermal-Sensitive Surface by Combined ATRP, RAFT Polymerization, Electrospinning, and “Click Chemistry”^a



^a VBC = 4-vinylbenzyl chloride; PVBC = poly(4-vinylbenzyl chloride); GMA = glycidyl methacrylate; PVBC-*b*-PGMA = poly(4-vinylbenzyl chloride)-*b*-poly(glycidyl methacrylate); PNIPAM_{AM} = alkyne-terminated PNIPAM; PBiB = propargyl-2-bromoisobutyrate.

“Click chemistry” is a strongly growing approach to synthesizing the well-defined and complex macromolecular structures because of its high specificity, quantitative yields, and functional group tolerance (27–29). “Click chemistry” has also been used to tune the functionality of the polymeric or nonpolymeric material surface (30–35). In this work, solvent-resistant nanofibers with an environmental-responsive surface were prepared via the combined technology of ATRP, RAFT, electrospinning, and “click chemistry”. The experimental procedure is shown in Scheme 1. Initially, block copolymers of poly(4-vinylbenzyl chloride) (PVBC) and poly(glycidyl methacrylate) (PGMA) (PVBC-*b*-PGMA) were synthesized via consecutive RAFT polymerizations. Electrospinning of PVBC-*b*-PGMA polymers gave rise to nanofibers with diameters in the range of 400 nm to 1.5 μm . Exposing the PVBC-*b*-PGMA nanofibers to a solution of sodium azide (NaN_3) not only affords nanofibers with azido groups on the surface but also leads to cross-linking in the nanofibers. Another step of “click chemistry” between these nanofibers and alkyne-terminated PNIPAM (PNIPAM_{AT}) allows the preparation of solvent-resistant nanofibers with a thermal-sensitive surface.

Previous work shows that PGMA-*b*-PVBC can be easily prepared via RAFT using 2-cyanoprop-2-yl 1-dithionaphtha-

late (CPDN) as the RAFT agents (36). In this work, PVBC was synthesized in a controlled manner via RAFT polymerization using CPDN as the chain-transfer agents. Another step of RAFT polymerization of GMA using the prepared PVBC as the macro chain-transfer agents allows the synthesis of PVBC-*b*-PGMA block copolymers. Well-defined PVBC₅₀-*b*-PGMA₁₅ (PVBC-*b*-PGMA copolymers with 50 VBC repeat units and 15 GMA repeat units on average), PVBC₅₀-*b*-PGMA₄₂, PVBC₇₄-*b*-PGMA₅₂, and PVBC₇₄-*b*-PGMA₄₆ were obtained by regulation of the polymerization times.

Factors such as the solution viscosity, solution conductivity, surface tension, and electric field intensity markedly influence the morphology of the resulting fibers (16). Figure 1a shows the scanning electron microscopy (SEM) image of nanofibers electrospun from PVBC₇₄-*b*-PGMA₄₆ at a concentration of about 20 wt % in tetrahydrofuran (THF). The fibers with an average diameter of about 800 nm are very uniform. The decrease in the concentration of electrospinning leads to a decrease in the size of the nanofibers. For PVBC₇₄-*b*-PGMA₄₆ with a concentration decreasing from 20 to 15 wt %, the average diameters of the nanofibers reduce from 800 to 400 nm. The M_n of PVBC-*b*-PGMA is another important factor influencing electrospinning. For the PVBC₅₀-*b*-PGMA₁₅ polymer, it is difficult to obtain well-defined fibers even at a

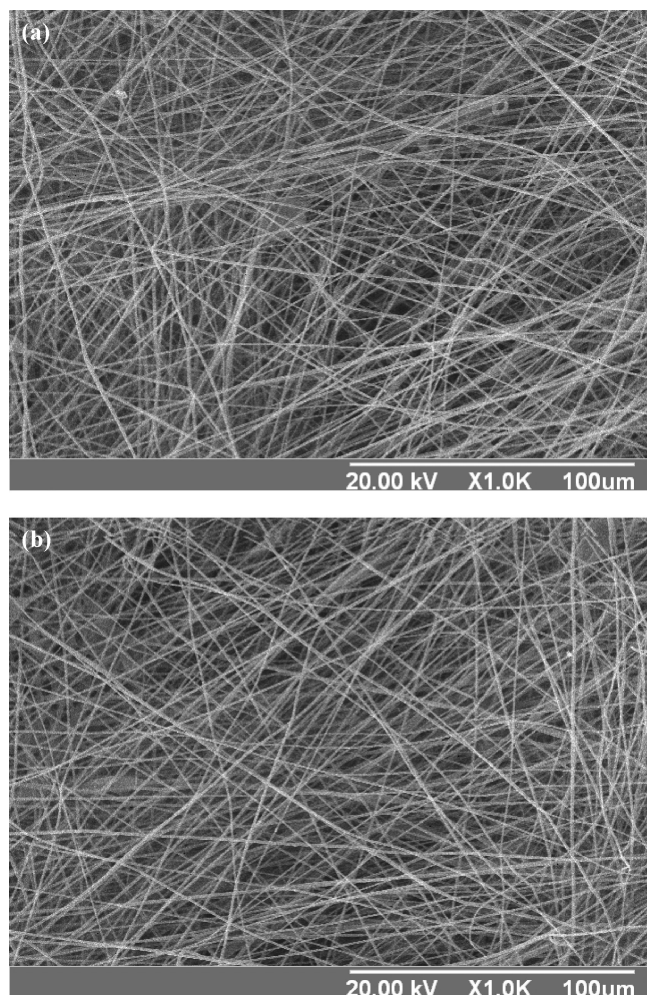


FIGURE 1. SEM surface images of the (a) nanofibers electrospun from PVBC₇₄-*b*-PGMA₄₆ (having 74 VBC repeat units and 46 GMA repeat units in each macromolecule) at a concentration of about 20 wt % in THF and (b) prepared nanofibers after reaction with sodium azide in a mixed *N,N*-dimethylformamide (DMF)/water solution (1:1 in volume ratio) and immersion in THF for 2 h.

high concentration of 25 wt %. For PVBC-*b*-PGMA polymer solutions at the same concentration, the higher the number-average molecular weight (M_n), the higher the viscosity of the polymer solution. When the viscosity of the solution is lower than a critical point, electrospinning cannot be carried out with a stable jet. Thus, beads on fibers or beads were formed.

A polymer with azido groups can be easily obtained via reaction between PVBC and sodium azide (37). Epoxy groups can also react with sodium azide to yield the corresponding 1-hydroxy-2-azido compounds (38). It is interesting to find that a cross-linked gel was obtained when PVBC-*b*-PGMA reacted with sodium azide. In order to study azidation of PVBC-*b*-PGMA copolymers, a model reaction of GMA and VBC with NaN_3 in a mixed DMF and water solvent (1:1 in volume) was carried out at 50 °C. After 8 h of reaction, about 58 % of 3-azido-2-[(4-vinylbenzyl)oxy]propyl 2-methylacrylate was obtained, except 1-(azidomethyl)-4-vinylbenzene and 3-azido-2-hydroxypropyl 2-methylacrylate. The generation of 3-azido-2-[(4-vinylbenzyl)oxy]propyl 2-methylacrylate was confirmed by mass spectrometry

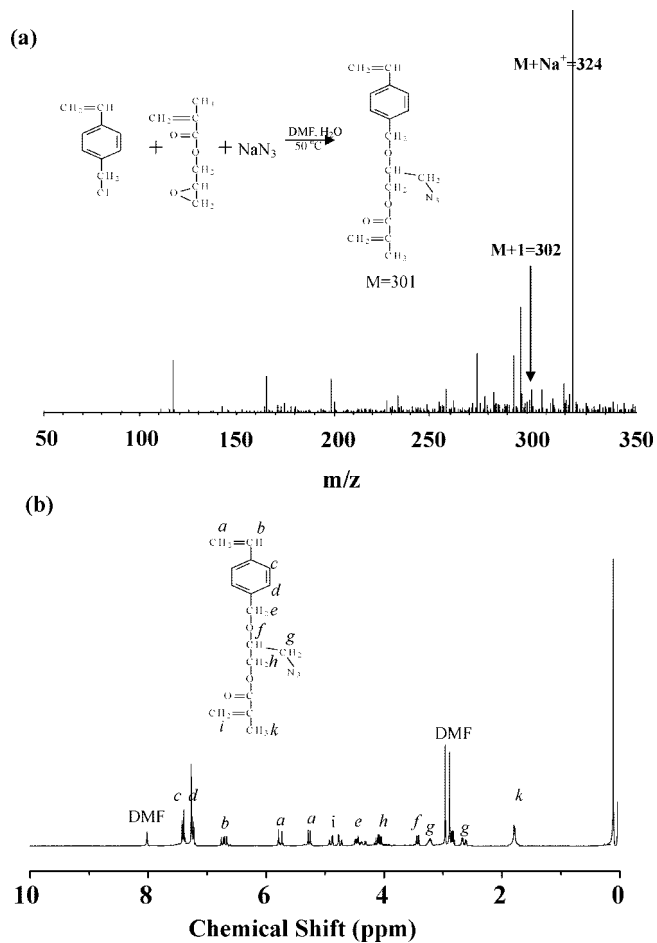


FIGURE 2. (a) Positive-ion mass spectrum and (b) ^1H NMR spectrum of 3-azido-2-[(4-vinylbenzyl)oxy]propyl 2-methylacrylate.

analysis (Figure 2a) and ^1H NMR (Figure 2b). PVBC-*b*-PGMA_{N3} nanofibers were obtained when PVBC-*b*-PGMA nanofibers were exposed to a NaN_3 solution in mixed DMF and water. Most importantly, the resulting nanofibers have a cross-linked structure. The cross-linked structure of the nanofibers was ascertained by the well-preserved nanostructure of PVBC-*b*-PGMA_{N3} after immersion into a THF solvent for 2 h (Figure 1b).

Thermal-responsive polymers of PNIPAM_{AT} were synthesized via ATRP of NIPAM, using propargyl-2-bromoisobutyrate (PBiB) as the initiator, tris[2-(dimethylamino)ethyl]amine (Me6TREN) as the ligand, and copper(I) bromide (CuBr) as the catalyst. The polymerizations were carried out in a controlled manner, and the resulting polymers are very uniform. At a reaction time of 4 h, the prepared PNIPAM_{AT} has a M_n of about 8.3×10^5 g/mol (about 73 repeat units) and a polydispersity index of about 1.1.

Cross-linked PVBC-*b*-PGMA nanofibers with thermal-sensitive PNIPAM brushes on the surface (PVBC-*b*-PGMA-*g*-PNIPAM) were obtained by “click chemistry” between PVBC-*b*-PGMA_{N3} nanofibers and PNIPAM_{AT} polymers. The presence of the PNIPAM brushes on the PVBC-*b*-PGMA-*g*-PNIPAM nanofiber surface was studied by FTIR analysis. In comparison to a PVBC-*b*-PGMA_{N3} nanofiber, the distinct reduction in the strength of the azide group at 2102 cm^{-1} and the appearance of a peak at 1640 cm^{-1} attributable to the formation of a hydrogen bond

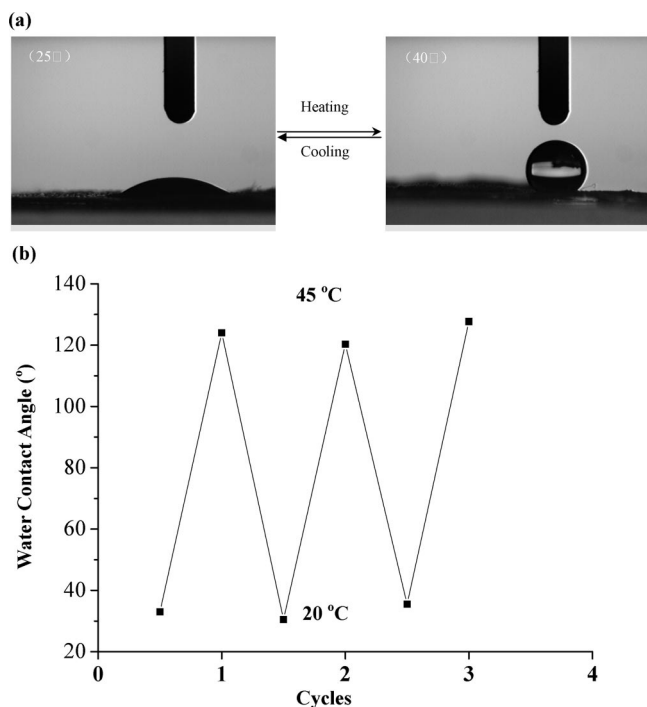


FIGURE 3. (a) Photographs of a water droplet on the surface of nanofibers of PVBC₇₄-*b*-PGMA₄₆-*g*-PNIPAM₇₃, which shows a thermal-responsive surface of the nanofiber that could switch between hydrophilicity at low temperature (20 °C) and hydrophobicity at high temperature (45 °C). (b) Reversibility of the water contact angle transition on the nanofibers of PVBC₇₄-*b*-PGMA₄₆-*g*-PNIPAM₇₃ at 20 and 45 °C, respectively. Half-cycles: 20 °C. Integral cycles: 45 °C.

between $>N-$ and $-C=O$ in the FTIR results (39) reveal that PVBC-*b*-PGMA-*g*-PNIPAM nanofibers were successfully prepared (see the Supporting Information). FTIR results also indicate that a small number of azido groups were left on the PVBC-*b*-PGMA-*g*-PNIPAM nanofiber surface even after reaction with an excess amount of PNIPAM_{AT} polymers over azido groups. The incomplete conversion of azido to triazole groups may be due to the steric hindrance of PNIPAM brushes grafted onto the fiber surface.

To explore the thermal-sensitive behavior of the surface, water contact angles were measured at different temperatures. Figure 3a shows photographs of water-drop profiles on nanofibers of PVBC₇₄-*b*-PGMA₄₆-*g*-PNIPAM₇₃ at 20 and 45 °C, respectively. PVBC₇₄-*b*-PGMA₄₆-*g*-PNIPAM₇₃ nanofibers exhibited a hydrophobic surface property at 45 °C, having a water contact angle of about 140°. When the temperature dropped to 20 °C, the nanofibers changed to a hydrophilic surface and water contact angle decreased to less than 30°. The temperature-responsive properties of the nanofibers are attributable to the competition between the inter- and intramolecular hydrogen bonding of PNIPAM brushes below and above the critical solution temperature (CST) of 32 °C (40, 41). At a temperature below CST, the hydrophilic C=O and N-H groups in the PNIPAM brushes form intermolecular hydrogen bonding and interact easily with water molecules. Thus, the PVBC-*b*-PGMA-*g*-PNIPAM nanofibers exhibit a hydrophilic surface. When the temperature increased to a temperature above CST, intramolecular hydrogen bonding between the C=O and N-H groups in the PNIPAM brushes was generated, resulting in a compact and collapsed

conformation of the PNIPAM brushes, which is difficult for water molecules accessing the C=O and N-H groups. Besides the enthalpic change (or the formation of hydrogen bonds), the conformation change of the PNIPAM brushes could also be attributed to the entropic change of the PNIPAM polymers, which is associated with the so-called hydrophobic effect, leading to the release of water molecules around the hydrophobic side group of PNIPAM. Therefore, PVBC-*b*-PGMA-*g*-PNIPAM nanofibers exhibit a hydrophobic surface. The permanence of surface thermal-sensitive properties of PVBC-*b*-PGMA-*g*-PNIPAM nanofibers was also demonstrated by several repeated temperature-changing cycles from 20 to 45 °C. A switch character from hydrophilic to hydrophobic indicates a good reversibility of the surface wettability of PVBC-*b*-PGMA-*g*-PNIPAM nanofibers.

In summary, a simple method for preparing solvent-resistant nanofibers with a thermal-sensitive surface has been developed by the combined technology of RAFT polymerization, ATRP, electrospinning, and “click chemistry”. It is interesting to find that the reaction between the PVBC-*b*-PGMA nanofibers and sodium azide not only produces nanofibers with a high density of azide groups on the surface but also gives rise to cross-linked nanofibers. One more step of “click chemistry” between the PVBC-*b*-PGMA-_{N3} nanofibers and PNIPAM_{AT} allows the preparation of PVBC-*b*-PGMA-*g*-PNIPAM nanofibers. PVBC-*b*-PGMA-*g*-PNIPAM nanofibers exhibit a good resistance to solvents and thermal-responsive character to the environment. The prepared cross-linked nanofibers with smart surface can be potentially used as biosensors, in scaffold-supported cell therapy for tissue engineering, and as carrying materials for drug and gene delivery.

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Supporting Information Available: Experimental conditions, tables of polymer and nanofiber characterization, and NMR and FTIR spectra of polymers. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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