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An Easy Method To Convert the Topologies of Macromolecules after Polymerization

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Supporting Information

The topology of macromolecule is an important molecular parameter that has significant influence on its properties and applications.[1] Therefore, the discovery of efficient approaches to prepare macromolecules with the same chemical components but distinct topologies is very important to tune their properties for exploitation of various applications. Currently, many synthetic approaches have successfully been developed to prepare macromolecules with different topologies but the same chemical components.[2,3] These approaches include preparing macromolecules with linear and hyperbranched topologies using living free radical polymerization,[2a−2d] preparing macromolecules with complex topologies by the polymerization of specially designed monomers,[2e] or via chain-walking catalysts,[2a] controlling over the topologies of the resultant macromolecules via Michael addition reaction.[3c] Despite the elegance and success of these approaches, most of them involve multistep organic syntheses and usually require specially designed monomers to suit each particular synthesis. Polymer chemists are hoping to find an easy method that can directly convert linear polymer into macromolecules with various topologies (such as branched, cross-linked, and dendritic) after polymerization. However, the present approaches have no capability to further tune the topologies (from linear to branched or dendritic to cross-linked structure) of resultant macromolecules because macromolecules were usually built by solid covalent bonds that are very hard to be broken and restructured. Another main limitation is that very high steric hindrance of polymer chains significantly reduces the reactivity of some active functional groups inlaid in the backbone of macromolecules. Although, recently, Davis et al. reported the synthesis of branched polymer from linear polymer via RAFT and thiol-coupling method,[2c] and Sumerlin et al. reported the synthesis of reversible gel from ABA triblock copolymer via RAFT and oxidation method,[2d] topology changes of macromolecules from linear to branched to cross-linked structures via reassembling macromolecular backbone triggered by stimuli seem impossible and have not been reported by now. To overcome the hindrances and make it possible, a key to success is to design a macromolecule that can be easily broken into active functional segments under chemical stimulus, and then these segments are able to reassemble into a new macromolecule with distinct topology. Here, we show this novel and easy method that directly polymerize common monomers into linear macromolecules first and then easily convert these linear macromolecules into macromolecules with various topologies (such as branched and cross-linked structures) under chemical stimuli.

Reversible addition−fragmentation chain transfer (RAFT) polymerization was mostly used to prepare linear macromolecules as it allows the polymerization of a large array of monomers,[4] and it also offers a facile route to prepare polymers with thiol end groups via treating the formed macromolecules with amine.[5] Poly(trithiocarbonate) (PTTC) with molecular weight of 3.0 kDa was prepared as a multifunctional RAFT agent. RAFT polymerization of *N*,*N*-dimethylacrylamide (DMA) was performed using PTTC as RAFT agent in the presence of 2-(pyridin-2-yldisulfanyl)ethyl acrylate (PDEA) at 70 °C (at or below this temperature, the free radical transferred to disulfide is little[6]), producing the linear multiblock poly(*N*,*N*-dimethylacrylamide) (PDMA) (M_n = 69.0 kDa) with pyridyl disulfide pendant units and trithiocarbonate linkages between two PDMA segments as shown in Figure 1. The number of pyridyl disulfide pendant unit in each block can be tuned by the initial ratio of PTTC to PDEA, and each block contains around one pyridyl disulfide pendant unit when the feed molar ratio of trithiocarbonate in PTTC to PDEA is around 0.85. Thus, linear multiblock PDMA with one pyridyl disulfide pendant unit in each block and one trithiocarbonate linkages between two PDMA segments was obtained; this linear macromolecule will undergo interesting reactions: the pendant pyridyl disulfide can couple thiols while trithiocarbonate units are turned into thiols in the presence of ethylenediamine. The PDMA intermediate containing two thiol ends and one pyridyl disulfide side unit was yielded when the multiblock PDMA was treated with ethylenediamine, the pendant pyridyl disulfide coupling thiol ends of PDMA intermediate,[7] which results in the formation of macromolecules (M_n = 3690.0 kDa) with branched topology since every PDMA segment containing two thiol ends (A_2) and one pyridyl disulfide side unit (B) can act as an A_2B intermediate. On the basis of the molecular weight values before and after aminolysis, ∼50 linear multiblock PDMA macromolecules formed 1 hyperbranched macromolecule; the size of the formed macromolecule only increases up to ∼100 nm from ∼19 nm (as shown in Figure 2) although the molecular weight increases by ∼50 times after aminolysis, which may result from that the formed macromolecules are of branched topology with very compact structure compared with their linear analogues as shown in Figure 1, which is similar to previous findings.[8] Further, R_g/R_h value for the PDMA with branched topology is 1.2, which is much lower than

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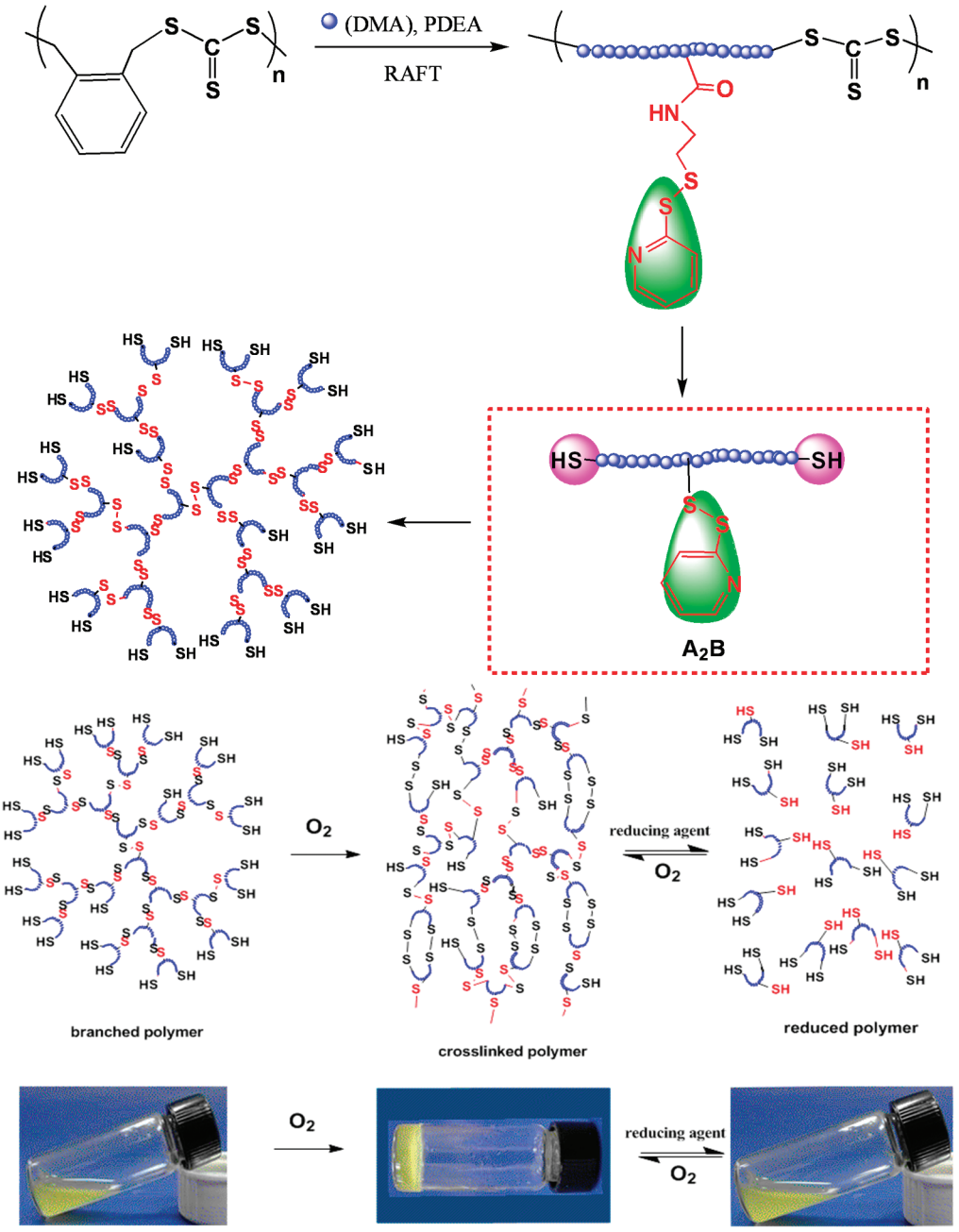

Figure 1. Illustration of topology change of poly(*N*,*N*-dimethylacrylamide) (PDMA): from linear PDMA to branched PDMA to cross-linked PDMA gel.

R_g/R_h value of 1.6 for the linear multiblock PDMA (the value is 1.5−2.0 for linear polymer and 0.8−1.5 for hyperbranched or dendritic macromolecules[9]), which further indicates the produced macromolecules have branched structure. However, the branching degree cannot be obtained from calculation.

The pyridyl disulfide can quickly couple thiols to release 2-pyridinethione byproduct that has a strong absorption at 375 nm in the UV spectrum. In a control experiment, multiblock PDMA with pyridyl disulfide side unit couples a small molecular thiol (such as 1-thio-β-D-glucose); the coupling reaction completed within 2 h via tracing the byproduct of 2-pyridinethione's absorption at 375 nm in the UV spectrum (see Supporting Information). The aminolysis of linear multiblock PDMA was also traced by the absorption of 2-pyridinethione byproduct at 375 nm in the UV spectrum. The results show that thiol coupling completed after ~5 days; the longer time is needed to complete the thiol-coupling reaction compared with small thiol molecules, which may result from high steric hindrance of macromolecular chain. The chain length of PDMA segment between two trithiocarbonates can be controlled by the feed ratio of DMA to PTTC; the longer the PDMA chain length is, the more time of thiol-coupling reaction is needed. For example, it took ~2 days for PDMA segment with MW of ~3000 to complete thiol coupling, but it took ~5 days for PDMA segment with MW of ~6000 to complete thiol coupling. In the ^{1}H NMR spectra, it is clear that the proton peaks ascribed to pyridyl pendant units were absent after aminolysis, indicating the complete aminolysis and thiol−disulfide exchange reaction as shown in

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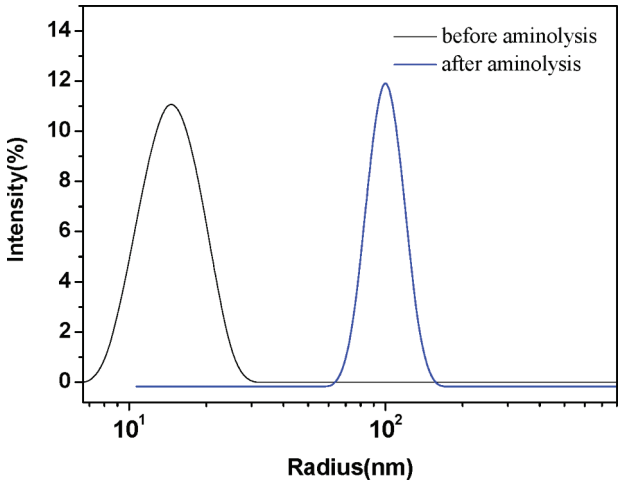

Figure 2. Size of the formed branched PDMA and linear multiblock PDMA before aminolysis.

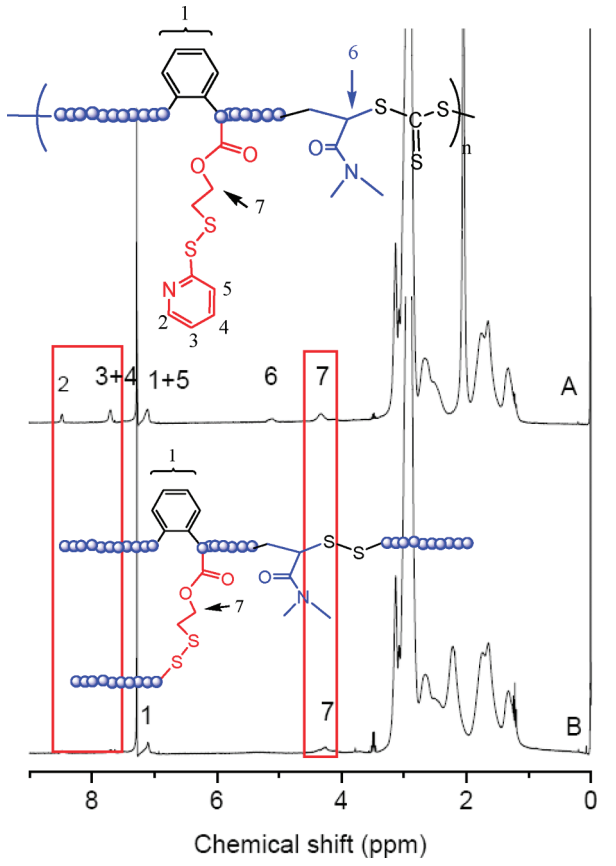

Figure 3. ^{1}H NMR spectra of linear multiblock PDMA before (A) and after (B) aminolysis.

Figure 3B. Moreover, the peak corresponding to the ester methylene units of PDEA at 4.2 ppm survived after aminolysis, and their relative integral value changed very little before and after aminolysis, indicating that ester units are stable during the aminolysis of trithiocarbonate, which is similar to previous findings.[10] Furthermore, the stability of ester unit during the aminolysis of trithiocarbonate can be verified by appearance of absorption for the ester unit of PDEA in its FT-IR spectra before and after aminolysis of trithiocarbonate, which may result from the low concentration of ethylenediamine used.

On the other hand, the linear multiblock PDMAs with 0, 0.8, 2.0, and 5.0 pyridyl disulfide units in each PDMA segment were obtained by adjusting the initial feed ratio of PTTC to PDEA. Treating the linear multiblock PDMA having no pyridyl disulfide unit in PDMA segment with ethylenediamine produces homopolymer with much lower molecular weight; treating the linear multiblock PDMA having 0.8 pyridyl disulfide units in each PDMA segment with ethylenediamine produces branched PDMA, but treating linear PDMAs having 2.0 and 5.0 pyridyl disulfide units in each PDMA segment, respectively, produces cross-linked gels (see Supporting Information). Hence, each PDMA segment has around one or less pyridyl disulfide unit is very important for the formation of branched macromolecules. The branched macromolecule is bioreducible since it contains many active thiol terminals and volatile disulfide linkages. The branched PDMA will be reduced into linear PDMA with molecular weight of ~6000 under dithiothreitol (DTT).

The branched polymer with terminal thiols was able to be further oxidized to a cross-linked and biodegradable macromolecular gel in the presence of oxygen as shown in Figure 1. The gel is bioreducible and reversible, and it can be converted to a solution under the reduction of DTT; the resulting solution can back to a macromolecular gel under oxidation of oxygen as shown in Figure 1, and this process is reversible.[11] The RAFT polymerization can be applied in the controlled polymerization of a large array of monomers; different linear multiblock macromolecules were obtained when different monomers such as styrene, methacrylate, *N*-isopropylacrylamide, etc., were used in polymerization using PTTC as RAFT agent in the presence of PDEA; these linear multiblock macromolecules can easily be transferred into branched macromolecules in the presence of ethylenediamine, and the corresponding branched macromolecules can be further transferred into bioreducible cross-linked structure in the presence of oxygen (see Supporting Information). Therefore, this is a versatile method for converting the topologies of macromolecules from linear to branched to cross-linked structures.

Furthermore, this method can be applied to transfer linear block copolymer into branched block copolymer to cross-linked polymer gel. The linear PDMA (M_n = 69.0 kDa) with active trithiocarbonate linkages can afford further topology modification as a macromolecular RAFT agent. Here, thermosensitive poly(*N*-isopropylacrylamide) (PNIPAM) was introduced to yield a thermosensitive linear multiblock copolymer, PDMA-*b*-PNIPAM, with molecular weight of 250.0 kDa as shown in Figure 4. The linear PDMA-*b*-PNIPAM was easily converted into a thermosensitive branched block copolymer (M_n = 617.0 kDa) via an A_2B intermediate (see Supporting Information) after the treatment of ethylenediamine with a similar mechanism described before. UV and NMR results also verified the aminolysis and thiol−disulfide exchange reaction (see Supporting Information). The branched block copolymer can be further converted into cross-linked structures under oxygen oxidation to form a bioreducible and thermosensitive gel as shown in Figure 4. The sol−gel transition is reversible with degradation to a solution of a linear triblock polymer under DTT reduction and cross-linked again to a biodegradable gel under oxygen oxidation (as shown in Figure 4). These results demonstrate our method is also able to readily tune block polymer topology from linear structures to branched and cross-linked block structures with

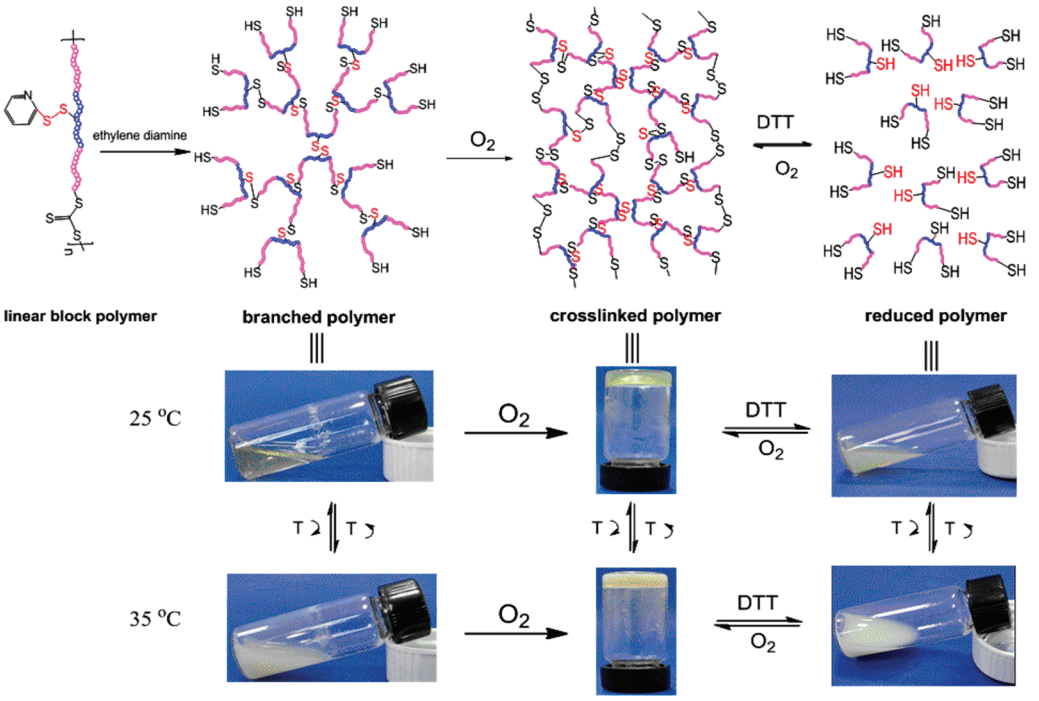

Figure 4. Illustration of topology change and temperature effect of a block copolymer of PDMA-*b*-poly(*N*-isopropylacrylamide) (PNIPAM): from linear to branched to cross-linked structures.

stimuli-responsive properties, facilitating the development of more complicated and smart functional polymers with distinct topologies.

In summary, we first report a novel method to change topologies of polymers from linear to branched to cross-linked structures. RAFT polymerization was utilized to build the functional linear polymer that can be easily restructured to the branched polymers and to the reversible cross-linked gel. The linear polymer can be further modified to the linear smart block polymer, and topology change of the block polymer from linear to branched to cross-linked block structures is also feasible. The method opens a facile and efficient route to tune polymer topology for various customized applications and enhances our ability for development of smart complicated polymer systems.

■ ASSOCIATED CONTENT

Supporting Information. Information about the experimental materials and methods as well as ^{1}H NMR and UV spectra of polymers obtained. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Hawker, C. J.; Fréchet, J. M. J. *ACS Symp. Ser.* **1996**, *624*, 132–144. (b) Sunder, A.; Heinemann, J.; Frey, H. *Chem. Eur.* **2000**, *6*, 2499–2506. (c) Bharathi, P.; Moore, J. S. *Macromolecules* **2000**, *33*, 3212–3218. (d) Hawker, C. J.; Fréchet, J. M. J.; Grubbs, R. B.; Dao, J. *J. Am. Chem. Soc.* **1995**, *117*, 10763–10764. (e) Grayson, S. M.; Fréchet, J. M. J. *Chem. Rev.* **2001**, *101*, 3819–3867. (f) Hecht, S.; Fréchet, J. M. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 74–91. (g) Feng, X.; Taton, D.; Borsali, R.; Chaikof, E. L.; Gnanou, Y. *J. Am. Chem. Soc.* **2006**, *128*, 11551–11562. (h) You, Y. Z.; Yu, Z. Q.; Meng, C. C.; Hong, C. Y. *Angew. Chem., Int. Ed.* **2010**, *49*, 1099–1102.

(2) (a) Gaynor, S.; Edelman, S. G.; Matyjaszewski, K. *Macromolecules* **1996**, *29*, 1079–1081. (b) Fréchet, J. M. J.; Henmi, M.; Gitsov, I.; Aoshima, S.; Leduc, M.; Grubbs, R. B. *Science* **1995**, *269*, 1080–1083. (c) Tao, L.; Liu, J. Q.; Tan, B. H.; Davis., T. P. *Macromolecules* **2009**, *42*, 4960–4962. (d) Vogt, A. P.; Sumerlin, B. S. *Soft Matter* **2009**, *5*, 2347–2351. (e) Saudan, C.; Balzani, V.; Gorka, M.; Lee, S.-K.; Maestri, M.; Vicinelli, V.; Vogtle, F. *J. Am. Chem. Soc.* **2003**, *125*, 4424–4425.

(3) (a) Guan, Z.; Cotts, P. M.; McCord, E. F.; McLain, S. J. *Science* **1999**, *283*, 2059–2062. (b) Wang, F.; Zhang, J. Q.; Ding, X.; Dong, S. Y.; Liu, M.; Zheng, B.; Li, S. J.; Wu, L.; Yu, Y. H.; Gibson, H. W.; Huang., F. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 1090–1094. (c) Hong, C. Y.; You, Y. Z.; Wu, D. C.; Liu, Y.; Pan, C. Y. *J. Am. Chem. Soc.* **2007**, *129*, 5354–5355. (d) Wu, D. C.; Liu, Y.; He, C. B.; Chung, T. S.; Goh, S. T. *Macromolecules* **2004**, *37*, 6763–6770. (e) Wan, W. M.; Pan., C. Y. *Chem. Commun.* **2008**, *43*, 5639–5641.

(4) (a) Moad, G.; Rizzardo, E.; Thang, S. H. *Acc. Chem. Res.* **2008**, *41*, 1133–1142. (b) Boyer, C.; Bulmus, V.; Davis, T. P.; Ladmiral, V.; Liu, J. Q.; Perrier, S. *Chem. Rev.* **2009**, *109*, 5402–5436. (c) You, Y. Z.; Oupicky, D. *Biomacromolecules* **2007**, *8*, 98–105. (d) Benaglia, M.; Chiefari, J.; Chong, Y. K.; Moad, G.; Rizzardo, E.; Thang, S. H. *J. Am. Chem. Soc.* **2009**, *131*, 6914–6915. (e) Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379–410. (f) You, Y. Z.; Hong, C. Y.; Pan, C. Y. *Adv. Mater.* **2004**, *16*, 1953–1957. (g) Boyer, C.; Stenzel, M. H.; Davis, T. P. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 551–595.

(5) (a) You, Y. Z.; Kalebaila, K. K.; Brock, S. L.; Oupicky, D. *Chem. Mater.* **2008**, *20*, 3354–3359. (b) Qiu, X. P.; Winnik, F. M. *Macromol.*

Rapid Commun. **2006**, *27*, 1648–1653. (c) Boyer, C.; Davis, T. P. *Chem Commun.* **2009**, *40*, 6029–6031.

(6) (a) Boyer, C.; Liu, J. Q.; Wong, L. J.; Tippett, M.; Bulmus, V.; Davis, T. P. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 7207–7224. (b) Liu, J. Q.; Bulmus, V.; Barner-Kowollik, C.; Stenzel, M. H.; Davis, T. P. *Macromol. Rapid Commun.* **2007**, *28*, 305–314.

(7) (a) Zugates, G. T.; Anderson, D. G.; Little, S. R.; Lawhorn, I. E. B.; Langer, R. *J. Am. Chem. Soc.* **2006**, *128*, 12726–12734. (b) Bontempo, D.; Heredia, K. L.; Fish, B. A.; Maynard, H. D. *J. Am. Chem. Soc.* **2004**, *126*, 15372–15373. (c) Xu., J. T.; Tao, L.; Liu, J. Q.; Bulmus, V.; Davis, T. P. *Macromolecules* **2009**, *42*, 6893–6901. (d) Wong, L. J.; Boyer, C.; Jia, Z. F.; Zareie, H. M.; Davis, T. P.; Bulmus, V. *Biomacromolecules* **2008**, *9*, 1934–1944.

(8) Hong, C. Y.; Pan, C. Y.; Huang, Y.; Xu, Z. D. *Polymer* **2001**, *42*, 6733–6740.

(9) (a) Burchard, W. *Adv. Polym. Sci.* **1983**, *48*, 1–120. (b) You, Y. Z.; Pan, C. Y. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 1730–1737.

(10) (a) Mayadunne, R. T. A.; Rizzardo, E.; Chiefari, J.; Krstina, J.; Moad, G.; Postma, A.; Thang, S. H. *Macromolecules* **2000**, *33*, 243–245. (b) You, Y. Z.; Manickam, D. S.; Zhou, Q. H.; Oupicky, D. *Biomacromolecules* **2007**, *8*, 2038–2044. (c) Wu, D. C.; Liu, Y.; Chen, L.; He, C. B.; Chung, T. S.; Goh, S. H. *Macromolecules* **2005**, *38*, 5519–5525.

(11) (a) You, Y. Z.; Manickam, D. S.; Zhou, Q. H.; Oupický, D. *Macromolecules* **2007**, *40*, 8617–8624. (b) Jia, Z. F.; Liu, J. Q.; Boyer, C.; Davis, T. P.; Bulmus, V. *Biomacromolecules* **2009**, *10*, 3253–3258. (c) Tsarevsky, N. V.; Matyjaszewski, K. *Macromolecules* **2005**, *38*, 3087–3092. (d) Li, C. M.; Madsen, J.; Armes, S. P.; Lewis, A. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 3510–3513.