Effects of Br Connected Groups on Atom Transfer Nitroxide Radical Coupling Reaction and Its Application in the Synthesis of Comb-Like Block Copolymers

GUOWEI WANG, YANNAN ZHANG, JUNLIAN HUANG

Department of Macromolecular Science, The Key Laboratory of Molecular Engineering of Polymer, State Education Ministry of China, Fudan University, Shanghai 200433, China

Received 18 November 2009; accepted 7 January 2010
DOI: 10.1002/pola.23929
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: The effects of Br connected groups on atom transfer nitroxide radical coupling (ATNRC) reaction were investigated. Two precursors methoxyl poly(ethylene oxide)-*b*-poly(ethylene oxide-*co*-2-bromoiso butyryloxy glycidyl ether) (*m*PEO-*b*-Poly(EO-*co*-BiBGE)) and methoxyl poly(ethylene oxide)-*b*-poly(2-bromoiso butyryloxy glycidyl ether) (*m*PEO-*b*-Poly(BiBGE)) with different $-C(CH_3)_2Br$ density were designed and synthesized firstly, and then ATNRC reaction were completed between these precursors and 2,2,6,6-tetramethylpiperidinyl-1-oxy poly(ε-caprolactone) (TEMPO-PCL) in the presence or absence of St monomers, respectively. The results showed that the structure of Br connected groups showed an important effect on ATNRC reaction, and the ATNRC reaction with high efficiency could be realized by transforming the higher active Br connected groups into the lower one by the addition of small amount of St monomers. The final comb-like block copolymers *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-($St_{1.8}$-*b*-PCL)] and *m*PEO-*b*-[Poly(Gly)-*g*-($St_{2.4}$-*b*-PCL)] with high coupling efficiency were obtained by this strategy. © 2010 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 48: 1633–1640, 2010

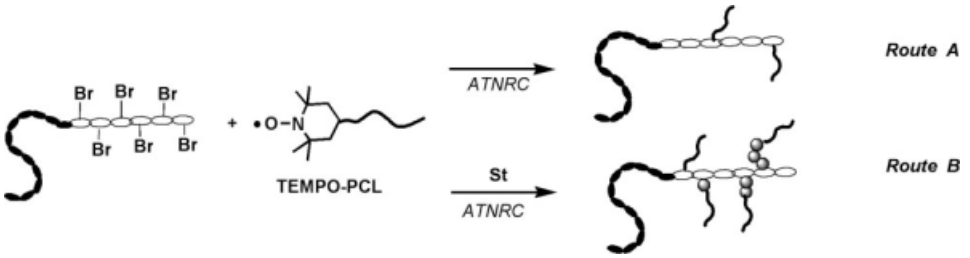
KEYWORDS: atom transfer nitroxide radical coupling (ATNRC); atom transfer radical polymerization (ATRP); block copolymers; comb-like block copolymers; graft copolymers; 2,2,6,6-tetramethylpiperidinyl-1-oxy poly(ε-caprolactone) (TEMPO-PCL)

INTRODUCTION Recently, the controlled polymerization strategies, such as the "living" anionic polymerization,[1] nitroxide mediated radical polymerization (NMRP),[2,3] atom transfer radical polymerization (ATRP),[4,5] ring-opening polymerization (ROP), and single electron transfer "living" radical polymerization (SET-LRP)[6] were widely investigated. Combining some high efficient coupling methods, such as the reaction by chlorosilane agent, the atom transfer radical coupling (ATRC)[7] and the "click" chemistry,[8] with the controlled polymerization mechanisms, some copolymers with complicated structures and compositions,[9] such as the graft,[10] hyperbranched,[11] cyclic,[12] dendritic,[13] and star-shaped copolymers[14] could be constructed. These unique copolymers were widely used in biomedical materials,[15] nanotechnology,[16] composite polymer materials,[17] and supramolecular science.[18] Specially, the synthesis of graft copolymers with different compositions by "grafting from," "grafting onto" or "grafting through" were the successful examples by combination of multiple polymerization mechanisms with coupling methods. Among them, the "grafting onto" strategy shows a promising prospect because the precursors of main chain and graft side chain could be prepared separately, and the characterization or purification of graft copolymers were quite easy. However, the low coupling efficiency was the drawback for "grafting onto" strategy. Therefore, looking for some novel coupling reactions with high efficiency would be the key to resolve this problem.

One of the widely used coupling reactions in polymer science was recently developed Cu-catalyzed azide/alkyne click (CuAAC) chemistry because of their high efficiency and tolerance to mediums.[8] However, in the "click" chemistry, the used photosensitive azide groups and possible Glaser side reaction of alkyne and alkyne should be carefully considered.[19]

In our previous works, two (co)polymer chains contained halide group and 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) group were prepared separately, then the copolymers with the complicated structures could be obtained by the coupling reaction between the halide group and TEMPO group in the presence of CuBr and ligands at elevated temperature based on the ATRP mechanism, and the reaction was termed as the atom transfer nitroxide radical coupling (ATNRC).[20] In this reaction, the terminal Br group served as oxidant was reduced to bromine anion, whereas Cu^{+} was oxidized to Cu^{2+} accordingly. Meanwhile, the formed carbon radical was immediately captured by the TEMPO radical on another (co)-polymer chain and formed an alkoxyamine between two

Additional Supporting Information may be found in the online version of this article. Correspondence to: J. Huang (E-mail: jlhuang@fudan.edu.cn)
Journal of Polymer Science: Part A: Polymer Chemistry, Vol. 48, 1633–1640 (2010)



SCHEME 1 The illustration of two synthetic routes for the comb-like block copolymers.

(co)polymers. In ATNRC reaction, CuBr participated in the reaction was served as reactant and its action was quite different from the ATRP. If some Cu(0) was added, the Cu(0) would react with the formed Cu^{2+} and the Cu^{+} was regenerated, which promoted the reaction completely. Thus, under the ATNRC conditions (such as the Cu(0)/CuBr/PMDETA system), the graft,[20] the star-shaped,[21] and the linear copolymer[22] were prepared successfully with high efficiency.

Recently, Monteiro and coworkers also explored a rapid, selective, and reversible NRC reaction based on the SET-LRP mechanism in the presence of polar solvent of DMSO,[23] and Fu et al. prepared several diblock copolymers by using the similar NRC method in the presence of polar solvents of tetrahydrofuran (THF) or CH_3OH.[24] Thus, the NRC methods (including the SET-NRC at low temperature based on SET-LRP mechanism and ATNRC at elevated temperature based on ATRP mechanism) had exhibited their huge significance in polymer science, and these works were comprehensively reviewed by Rosen and Percec.[25] Nevertheless, there were still some questions about this NRC method should be clarified. For example, in our previous work, it was found that in the same conditions, PS-Br always shows the higher coupling efficiency than P*t*BA-Br in ATNRC.[20] To clarify this point and enlarge the application range of ATNRC reaction, in this work, the comb-like block copolymers *m*PEO-*b*-[Poly (EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] and *m*PEO-*b*-[Poly(Gly)-*g*-(St_x-*b*-PCL)] were prepared by ATNRC reaction in the presence or absence of St monomers. Two routes with the different coupling conditions were adopted as follows (Scheme 1).

EXPERIMENTAL

Materials

THF (SCR, 99%) and pyridine (SCR, 99.5%) were refluxed over sodium wire, then distilled from sodium naphthalenide and sodium wire solution, respectively. Styrene (St, Aldrich, 98%) was washed with 10% NaOH aqueous solution followed by water thrice successively, dried over CaH_2, and distilled under reduced pressure. ε-Caprolactone (ε-CL) (Aldrich, 99%) was dried over CaH_2 and distilled under reduced pressure. Cuprous bromide (CuBr, Acros, 98%) was purified by stirring overnight in acetic acid and filtered, then washed with ethanol and diethyl ether successively, and finally dried under vacuum. 2-Bromoisobutyryl bromide (98%) and *N,N,N′,N′,N″*-pentamethyldiethylenetriamine (PMDETA) were purchased from Aldrich and used as received. Nanosize copper powder (~100 nm, Aldrich, 99.9%) was used as received. All other reagents were purchased from Sinopharm Chemical Reagent Co. (SCR) and used as received, unless otherwise noted.

α-Methoxyl-ω-hydroxy-poly(ethylene oxide) [*m*PEO, $M_{n(SEC)}$ = 7800 g/mol, polydispersity index (PDI) = 1.10] was synthesized by ROP of EO using ethylene glycol monomethyl ether potassium as the initiator. 2,2,6,6-Tetramethylpiperidinyl-1-oxy poly(ε-caprolactone) (TEMPO-PCL) was synthesized according to a previously work using 4-hydroxyl-2,2,6,6-tetramethylpiperidinyl-1-oxy (HTEMPO) as initiator and tin(II)-bis(2-ethyl hexanoate) ($Sn(Oct)_2$, 0.0655 mol/L in dried toluene) as catalyst.[22] ^{1}H-NMR ($CDCl_3$, δ) (ppm) of TEMPO-PCL: 4.12–4.02 (—$CH_2C\mathbf{H}_2OC(O)$—), 3.70–3.62 (—$CH_2C\mathbf{H}_2OH$), 2.35–2.24 (—$C(O)C\mathbf{H}_2CH_2$—), 1.72–1.56 (—$CH_2C\mathbf{H}_2CH_2C\mathbf{H}_2CH_2$—), 1.42–1.33 (—$CH_2CH_2C\mathbf{H}_2CH_2CH_2$ O—), 1.28–1.17 ($C\mathbf{H}_3$, methyl protons of TEMPO). $M_{n(NMR)}$ = 3100, $M_{n(SEC)}$ = 5800, PDI = 1.19 (See Supporting Information). 1-Ethoxyethyl glycidyl ether (EEGE) was synthesized from glycidol and ethyl vinyl ether according to the literature.[26]

Measurements

The number average molecular weight and PDI were estimated by size exclusion chromatography (SEC). SEC traces were performed in THF at 35 °C with an elution rate of 1.0 mL/min on an Agilent 1100 equipped with a G1310A pump, a G1362A refractive index detector, and a G1314A variable wavelength detector, and polystyrene standard samples were used for calibration. ^{1}H-NMR spectra were obtained by a DMX 500 MHz spectrometer using tetramethylsilane (TMS) as the internal standard and $CDCl_3$ as the solvent.

Preparation of Precursors *m*PEO-*b*-poly(BiBGE) and *m*PEO-*b*-poly(EO-*co*-BiBGE)

The preparation procedures of precursors were described in details in Supporting Information. The synthesis of methoxyl poly(ethylene oxide)-*b*-poly(2-bromoiso butyryloxy glycidyl ether) (*m*PEO-*b*-Poly(BiBGE)) and methoxyl poly(ethylene oxide)-*b*-[poly(ethylene oxide-*co*-2-bromoiso butyryloxy glycidyl ether) (*m*PEO-*b*-Poly(EO-*co*-BiBGE)) were accorded to the reference,[27] and the linear *m*PEO ($M_{n(SEC)}$ = 7800 g/mol) was used as the initial macroinitiator. Taking the *m*PEO-*b*-Poly(EO-*co*-BiBGE) as example, the process involved the synthesis of methoxyl-poly(ethylene oxide)-*b*-poly(ethylene oxide-*co*-ethoxyethyl glycidyl ether) (*m*PEO-*b*-Poly(EO-*co*-EEGE)) ($M_{n(NMR)}$ = 14,300 g/mol, $M_{n(SEC)}$ = 10,500 g/mol, PDI = 1.15) by anionic ring-opening copolymerization of EO and ethoxyethyl glycidyl ether (EEGE), the methoxyl-poly (ethylene oxide)-*b*-poly(ethylene oxide-*co*-glycidyl) (*m*PEO-*b*-

Poly(EO-*co*-Gly)) ($M_{n(NMR)}$ = 13,300 g/mol) by hydrolysis of EEGE units, and the *m*PEO-*b*-Poly(EO-*co*-BiBGE) by subsequent esterification of the recovered hydroxyl groups by 2-bromoisobutyryl bromide. ^{1}H-NMR ($CDCl_3$) δ (ppm) of *m*PEO-*b*-Poly(EO-*co*-BiBGE): 1.93 (—C (CH_3)$_2$Br), 3.38(CH_3O—), 3.49–3.79 (—CH_2CH_2O— and —CH_2CH (CH_2—)O— for PEO main chain), 4.19–4.35 (—CH_2COO—), $M_{n(NMR)}$ = 15,500 g/mol.

Similarly, the *m*PEO-*b*-Poly(BiBGE) ($M_{n(NMR)}$ = 12,300 g/mol) was also synthesized by the same procedure from *m*PEO-*b*-Poly(EEGE) ($M_{n(SEC)}$ = 9,000 g/mol, PDI = 1.16, $M_{n(NMR)}$ = 12,300 g/mol.), which was obtained by the anionic ROP of EEGE. ^{1}H-NMR ($CDCl_3$) δ (ppm) of *m*PEO-*b*-Poly(BiBGE): 1.93 (—C(CH_3)$_2$Br), 3.38 (CH_3O—), 3.49–3.79 (—CH_2CH_2O— and —CH_2CH(CH_2—)O— for PEO main chain), 4.19–4.35 (—CH_2COO—), $M_{n(NMR)}$ = 12,300 g/mol.

Preparation of Comb-Like Block Copolymers *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] and *m*PEO-*b*-[Poly(Gly)-*g*-(St_x-*b*-PCL)] by ATNRC Reaction

Using the comb-like block copolymer methoxyl poly(ethylene oxide)-*b*-[poly(ethylene oxide-*co*-glycidyl)-*g*-(Styrene$_x$-b-poly (ε-caprolactone))] (*m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)]) as example. Typically, *m*PEO-*b*-Poly(EO-*co*-BiBGE) (0.50 g, 0.48 mmol of -Br groups), TEMPO-PCL (1.4880 g, 0.48 mmol), toluene (20 mL), St (0.22 mL, 1.92 mmol), Cu(0) (0.0156 g, 0.24 mmol), CuBr (0.0686 g, 0.48 mmol), and PMDETA (0.0892 mL, 0.48 mmol) were charged into a 50 mL ampoule, the reaction mixture was degassed with three cycles of freeze-pump-thaw and then purged with N_2, kept at 80 °C for 48 h. Afterward, the mixture was diluted with THF and passed through an activated neutral alumina column to remove the copper salts. After THF was removed by distillation under vacuum, the crude product was purified by fractionated precipitation to remove the remaining TEMPEO-PCL. The final *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] was collected and then dried in vacuum at 45 °C for 12 h till to a constant weight. ^{1}H-NMR ($CDCl_3$, δ) (ppm): 1.28–1.17 (CH_3, methyl protons of TEMPO), 1.42–1.33 (—$CH_2CH_2CH_2$ CH_2CH_2O—), 1.72–1.56 (—$CH_2CH_2CH_2CH_2CH_2$—), 2.35–2.24 (—C(O)CH_2CH_2—), 3.49–3.79 (—CH_2CH_2O— and —CH_2CH (CH_2—)O— for PEO main chain), 4.12–4.02 (—CH_2CH_2 OC(O)—), 6.31–7.01 (—C_6H_5—). $M_{n(NMR)}$ = 47,300 g/mol, $M_{n(SEC)}$ = 49,500 g/mol, PDI = 1.19.

Similarly, the comb-like block copolymer methoxyl poly(ethylene oxide)-*b*-[poly(glycidyl)-*g*-(Styrene$_x$-*b*-poly (ε-caprolactone))] (*m*PEO-*b*-[Poly(Gly)-*g*-(St_x-*b*-PCL)]) was obtained by ATNRC reaction between *m*PEO-*b*-Poly(BiBGE) ($M_{n(NMR)}$ = 12,300 g/mol) and TEMPO-PCL in the presence of St monomers using the same procedure. ^{1}H-NMR ($CDCl_3$, δ) (ppm): 1.28–1.17 (CH_3, methyl protons of TEMPO), 1.42–1.33 (—$CH_2CH_2CH_2$ CH_2CH_2O—), 1.72–1.56 (—$CH_2CH_2CH_2CH_2CH_2$—), 2.35–2.24 (—C(O)CH_2CH_2—), 3.49–3.79 (—CH_2CH_2O— and —CH_2CH (CH_2—)O— for PEO main chain), 4.12–4.02 (—CH_2CH_2 OC(O)—), 6.31–7.01 (—C_6H_5—). $M_{n(NMR)}$ = 51,700 g/mol, $M_{n(SEC)}$ = 48,700 g/mol, PDI = 1.24.

The ATNRC without St monomer between *m*PEO-*b*-Poly(EO-*co*-BiBGE), *m*PEO-*b*-Poly(BiBGE) and TEMPO-PCL were conducted by the similar aforementioned procedure.

Model ATNRC Reaction Between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and 4-Hydroxyl-2,2,6,6-tetramethylpiperidinyl-1-oxy (HTEMPO)

Typically, *m*PEO-*b*-Poly(EO-*co*-BiBGE) (0.80 g, 0.84 mmol of -Br groups), HTEMPO (0.1445 g, 0.84 mmol), St (0.38 mL, 3.36 mmol), toluene (6.0 mL), Cu(0) (0.0273g, 0.42 mmol), CuBr (0.1201 g, 0.84 mmol), and PMDETA (0.1563 mL, 0.84 mmol) were charged in a 50 mL ampoule. The reaction mixture was degassed with three cycles of freeze-pump-thaw and then purged with N_2, kept at 80 °C for 48 h. Afterward, the mixture was extracted with methylene dichloride to remove the copper salt and concentrated, then precipitated in ethyl ether and dried in vacuum at 45 °C for 12 h till to a constant weight. ^{1}H-NMR ($CDCl_3$, δ) (ppm): 1.62–1.17 (CH_3—, —CH_2— protons on TEMPO), 1.62–1.95 ppm (—CH_2—CH(C_6H_5)—) protons on St_x), 3.49–3.79 (—CH_2 CH_2O— and —CH_2CH(CH_2—)O— for PEO main chain), 4.12–4.02(—CH_2OC(O)—), 6.10 ppm and 5.57 ppm (—C(CH_3)= CH_2), 6.31–7.01 (—C_6H_5—).

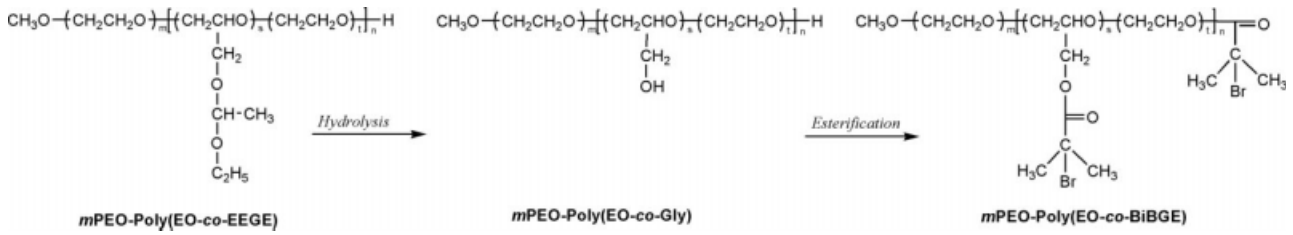
The ATNRC without St monomer was performed by the similar aforementioned procedure, and ^{1}H-NMR ($CDCl_3$, δ) (ppm) for the obtained copolymer: 1.62–1.17 (CH_3—, —CH_2— protons on TEMPO), 3.49–3.79 (—CH_2CH_2O— and —CH_2 CH(CH_2—)O— for PEO main chain), 4.12–4.02(—CH_2 OC(O)—), 6.10 ppm and 5.57 ppm (—C(CH_3)=CH_2).

RESULTS AND DISCUSSION

Synthesis of Precursors *m*PEO-*b*-Poly(EO-*co*-BiBGE) and *m*PEO-*b*-Poly(BiBGE)

In the investigation of the effect of Br connected groups structure and density on ATNRC reaction, two precursors with —C(CH_3)$_2$Br groups were designed and synthesized. The block copolymers *m*PEO-*b*-Poly(EO-*co*-EEGE) and *m*PEO-*b*-Poly (EEGE) with different numbers of EEGE units were synthesized by anionic ROP of EEGE or its copolymerization with EO using *m*PEO and DPMK as coinitiator, then *m*PEO-*b*-Poly (BiBGE) and *m*PEO-*b*-Poly(EO-*co*- BiBGE) were obtained, respectively, by the hydrolysis of EEGE units of *m*PEO-*b*-Poly (EEGE) and *m*PEO-*b*-Poly(EO-*co*-EEGE) to form *m*PEO-*b*-Poly (Gly) and *m*PEO-*b*-Poly(EO-*co*-Gly), and subsequent esterification of recovered —OH groups with 2-bromoisobutyryl bromide. The whole process was illustrated in Scheme 2.

By analyzing the ^{1}H-NMR spectrum of *m*PEO-*b*-Poly(EO-*co*-BiBGE) [Fig. 1(A)], the transformation efficiency of Gly units to BiBGE units was nearly 100% (See Supporting Information), which confirmed the esterification was really complete. The number ratio of EO units on *m*PEO segment, EO, and BiBGE units (N_{BiBGE}) on poly(EO-*co*-BiBGE) segment was 184:95:15, and the number ratio of EO on *m*PEO segment and BiBGE units (N_{BiBGE}) on poly(BiBGE) segment for block copolymer *m*PEO-*b*-PBiBGE was 184:19 (See Supporting Information).



SCHEME 2 The synthesis of precursor *m*PEO-*b*-Poly(EO-*co*-BiBGE).

Synthesis of Comb-Like Block Copolymers *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] by ATNRC Reaction

In our previous work, it was found that the ATNRC reaction efficiency between PS-Br and TEMPO-contained polymers was higher than that of P*t*BA-Br. To further confirm and explain this phenomenon, the preparation of comb-like block copolymer *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] was performed by ATNRC reaction between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and TEMPO-PCL in the presence or absence of small quantity of St monomers (4.0 equiv. of —$(CH_3)_2$Br groups), respectively (Scheme 3).

In the absence of any St monomers, there was a little product remained after the unreacted TEMPO-PCL was removed. However, once small amount of St monomers were added, the yield of graft copolymers was increased greatly as following described.

In the presence of St monomers, it was observed that the peak attributed to comb-like block copolymers *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] (C) was shifted to the higher molecular weight compared with its precursors of TEMPO-PCL and *m*PEO-*b*-Poly(EO-*co*-EEGE) from the SEC results (Fig. 2). From the ^{1}H-NMR spectrum [Fig. 1(C)], the resonance signal at 3.49–3.79 ppm for methylene protons (—C$\boldsymbol{H}_2$$CH_2O$—, —C$\boldsymbol{H}_2$$CH(CH_2$—)O—) on main chain, at 4.12–4.02 ppm for methylene protons (—CH_2C$\mathbf{H}_2$OC(O)—), and at 2.35–2.24 ppm for methylene protons (—C(O)C$\mathbf{H}_2$$CH_2$—) on PCL segment were all observed. The signal for St units was also detected at 6.31–7.01 ppm for aromatic protons (—$C_6\boldsymbol{H}_5$—). Using the following Formula 1, the efficiency of ATNRC (E.F.$_{(ATNRC-1)}$) was determined according to the already known $M_{n(NMR)}$ of TEMPO-PCL [$M_{n(NMR)(TEMPO\text{-}PCL)}$, Fig. 1(B)] and listed in Table 1:

$$\text{E.F.}_{(\text{ATNRC}-)} = \frac{A_e \Big/ \left(\frac{M_{n(\text{NMR})(\text{TEMPO}-\text{PCL})}}{115} \times 2\right)}{A_b/(N_{EO} \times 4 + N_{BiBGE} \times 3)} \div N_{BiBGE} \times 100\% \quad (1)$$

where A_b is the integral area at 3.49–3.79 ppm, A_e is the integral area at 4.12–4.02 ppm, and 115 is the molecular weight of CL units. N_{EO} and N_{BiBGE} were the numbers of EO and BiBGE units on PEO main chain, respectively.

The E.F.$_{(ATNRC-1)}$ of ATNRC was about 75.6% in the presence of St monomers, which was corresponding to 11 chains of TEMPO-PCL grafted on each main chain. The numbers of inserted St monomers could be calculated by using the Formula 2:

$$N_{St} = \frac{A_m/5}{A_b/(N_{EO} \times 4 + N_{BiBGE} \times 3)} \div N_{BiBGE} \quad (2)$$

where A_m is the integral area at 6.31–7.01 ppm, and others were the same as defined before. The obtained N_{st} value is 1.8.

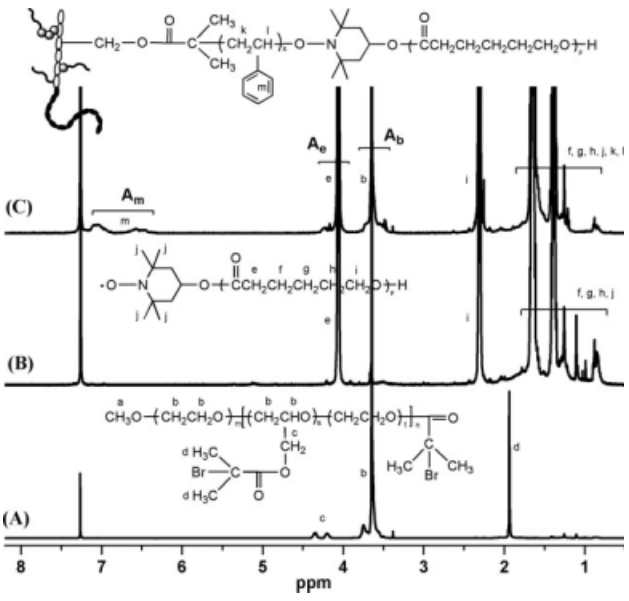
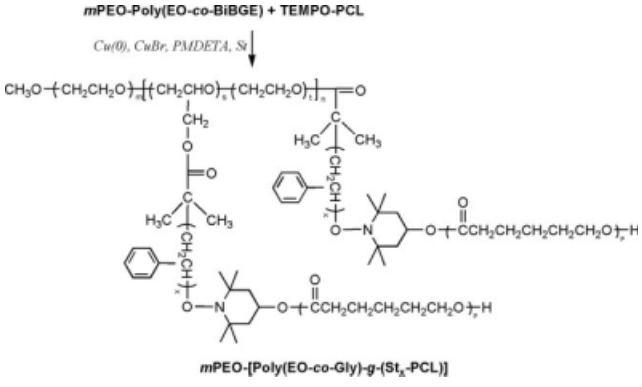


FIGURE 1 The ^{1}H-NMR of precursors *m*PEO-*b*-Poly(EO-*co*-BiBGE) (A), TEMPO-PCL (B), and *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] (C) copolymers.



SCHEME 3 The ATNRC reaction between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and TEMPO-PCL in the presence of St monomers.

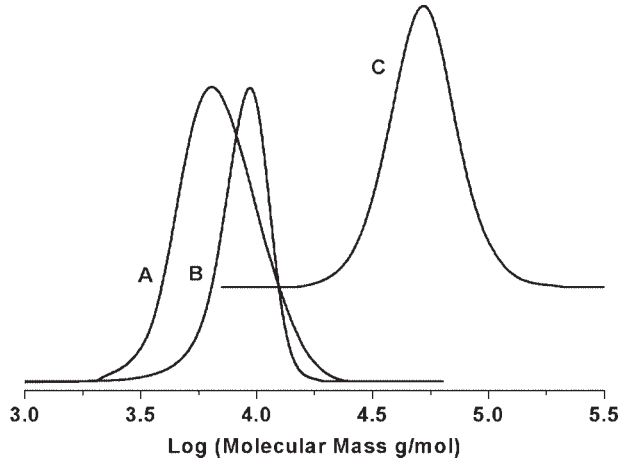


FIGURE 2 SEC curves of TEMPO-PCL (A, $M_{n(SEC)}$ = 5800 g/mol, PDI = 1.19), *m*PEO-*b*-Poly(EO-*co*-EEGE) (B, $M_{n(SEC)}$ = 10,500 g/mol, PDI = 1.15), and *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] (C, $M_{n(SEC)}$ = 47,300 g/mol, PDI = 1.19).

The molecular weight of graft copolymers *m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(St_x-*b*-PCL)] could be determined by using the Formula 3 and listed in Table 1:

$$M_{n(NMR)(mPEO\text{-}b\text{-}[Poly(EO\text{-}co\text{-}Gly)\text{-}g\text{-}(St_x\text{-}b\text{-}PCL)])} = E.F._{(ATNRC\text{-}1)} \times N_{BiBGE} \times M_{n(NMR)(TEMPO\text{-}PCL)} + M_{n(NMR)(mPEO\text{-}b\text{-}Poly(EO\text{-}co\text{-}Gly))} + N_{BiBGE} \times N_{St} \times 104 \quad (3)$$

where 104 is the molecular weight of St unit, and others were the same as defined before.

However, in the absence of any St monomers, the comb-like block copolymers were formed with a rather low $E.F._{(ATNRC-1)}$ of 20.3%, and there was about only three chains of TEMPO-PCL was grafted.

Synthesis of Comb-Like Block Copolymers *m*PEO-*b*-[Poly(Gly)-*g*-(St_x-*b*-PCL)] by ATNRC Reaction

In the copolymer *m*PEO-*b*-Poly(BiBGE), the density of —$(CH_3)_2$Br groups was higher than that in *m*PEO-*b*-Poly(EO-*co*-BiBGE). As it was well known, the coupling efficiency between different polymers was dependent on the density of functional groups on used polymers no matter "click" chemistry or ATNRC, the higher the density of functional groups, the lower the coupling efficiency.[28] In the absence of any St monomers, the graft copolymer was formed between *m*PEO-*b*-Poly(BiBGE) and TEMPO-PCL with the low $E.F._{(ATNRC-2)}$ of 10.2% (which was also calculated using the Formula 1 and listed in Table 1), and there was about only 2 chains of TEMPO-PCL grafted on the main chains. In the presence of small amount of St monomers (4.0 e.q. of —$(CH_3)_2$Br groups), the coupling reaction was preformed smoothly with the $E.F._{(ATNRC-2)}$ of 59.5%, which was about corresponding to 11 chains of grafted TEMPO-PCL on main chains, and the inserted number of St monomers (N_{st} = 2.4) could also be calculated according to the ^{1}H-NMR spectrum using the Formula 2. Similarly, the molecular weight of graft copolymers *m*PEO-*b*-[Poly(Gly)-*g*-(St_x-*b*-PCL)] could be determined by using the Formula 3 and listed in Table 1.

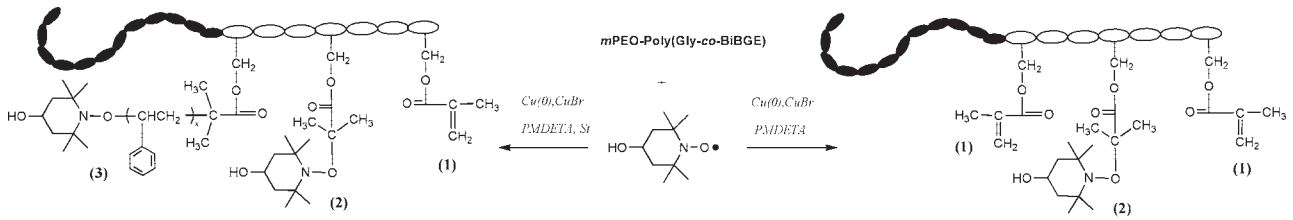
Comparing with the E.F. of ATNRC reaction in these cases, it was concluded that the main chain with higher density of —$(CH_3)_2$Br groups really exerted some effect on ATNRC reaction due to steric hindrance. However, obviously, the existence of small quantity of St monomers would largely improve the ATNRC efficiency no matter the density of —$(CH_3)_2$Br groups were dense or sparse.

Comparing with the CuAAC "click" chemistry between azide and alkynene groups under the comparable conditions (refer to the similar graft density and the molecular weight of side chains),[28] the obtained ATNRC E.F.s were all close to or higher than that of the formers.

TABLE 1 The Data for the Precursors and Comb-Like Block Copolymers

Sample	$M_{n(SEC)}$[a] (g/mol)	PDI[a]	$M_{n(NMR)}$[b] (g/mol)	N_{BiBGE}[c]	E.F.[d] (%)
*m*PEO	7,800	1.10	8,100		
TEMPO-PCL	5,800	1.19	3,100		
*m*PEO-*b*-Poly(EO-*co*-EEGE)	10,500	1.15	14,300		
*m*PEO-*b*-Poly(EO-*co*-BiBGE)			15,500	15	
*m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-(S_x-*b*-PCL)]	47,300	1.19	49,500		75.6
*m*PEO-*b*-[Poly(EO-*co*-Gly)-*g*-PCL]	17,400	1.19	20,700		20.3
*m*PEO-*b*-Poly(EEGE)	9,000	1.16	10,800		
*m*PEO-*b*-Poly(BiBGE)			12,300	19	
*m*PEO-*b*-[Poly(Gly)-*g*-(S_x-*b*-PCL)]	48,700	1.24	51,700		59.5
*m*PEO-*b*-[Poly(Gly)-*g*-PCL]	18,200	1.27	21,000		10.2

[a] The number average molecular weight ($M_{n(SEC)}$) and PDI were determined by SEC, calibrated against PS standards using THF as elution.
[b] $M_{n(NMR)}$ were determined by ^{1}H NMR.
[c] N_{Br} were the number of Br groups on precursors.
[d] E.F. were the coupling efficiency in ATNRC reaction.



SCHEME 4 The ATNRC reaction between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and HTEMPO in the presence or absence of St monomers.

Model ATNRC Reaction Between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and HTEMPO

In the former two cases, the effect of small amount of St monomers on ATNRC reaction was observed. However, the question, that is, what is happened for —$(CH_3)_2$Br groups in the presence of St monomers, was still unclear. Thus, a model ATNRC reaction between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and HTEMPO with or without St monomers was designed and completed, respectively, and the possible structure of the formed copolymer was shown in Scheme 4.

Figure 3 showed the ^{1}H-NMR spectrum of the formed copolymers in the presence (B) and absence (A) of St monomers. From Figure 3(A), the resonance signal at 1.95 ppm assigned to the methyl group protons (—C(C***H***$_3$)=CH_2, —C(C***H***$_3$)$_2$), the signal at 4.05–4.40 ppm assigned to the methylene protons (—C***H***$_2$OCO—), the signal at 6.10 ppm and 5.57 ppm assigned to the methylene protons (—C(CH$_3$)=C***H***$_2$), and the signal at 1.88–1.10 ppm assigned to the protons on TEMPO groups were observed. In the presence of St monomers [Fig. (B)], the signal for aromatic protons (—C$_6$***H***$_5$—) at 6.31–7.01 ppm was observed, and the signals for double bond at 6.10 and 5.57 ppm in ^{1}H-NMR spectrum[29] were also be detected. It was confirmed that the disproportionation of the radicals generated from —$C(CH_3)_2$Br in CuBr/PMDETA system could be happened in both cases. Through the ^{1}H-NMR spectra, the efficiency of disproportionation (E.F.$_{dis}$) and E.F.$_{(ATNRC-3)}$ were calculated according to the Formula 4 and Formula 5, respectively, and listed in Table 2:

$$\text{E.F.}_{\cdot\text{dis}} = \frac{A_f/2}{A_a/2} \times 100\% \quad (4)$$

$$\text{E.F.}_{\cdot(\text{ATNRC}-3)} = (1 - \text{E.F.}_{\cdot\text{dis}}) \times 100\% \quad (5)$$

where A_a is the integral area at 4.05–4.40 ppm, A_f is the sum integral area at 6.10 ppm and 5.57 ppm. The inserted number of St monomers could be calculated according to Formula 6 and listed in Table 2:

$$N_{St} = \frac{A_k/5}{A_a/2} \quad (6)$$

where A_k is the integral area at 6.31–7.01 ppm, and others were the same as defined before. The values of N_{st} were 0.9 and 1.0 for Entry B and Entry C, respectively.

By analyzing the data from Table 2, when the reaction was conducted between the *m*PEO-*b*-Poly(EO-*co*-BiBGE) and HTEMPO in the absence of St monomers, the disproportionation structure (**1**) composed the main product. When small amount of St monomers were added, TEMPO terminated structure (**2**) and (**3**) formed the main product.

According to the ATRP mechanism, the appropriate equilibrium constants ($K_{ATRP} = k_{act}/k_{deact}$) between the activation process (generation of radicals, k_{act}) and the deactivation process (formation of alkyl halides, k_{deact}) would play an important role in good control over the polymerization. Usually,

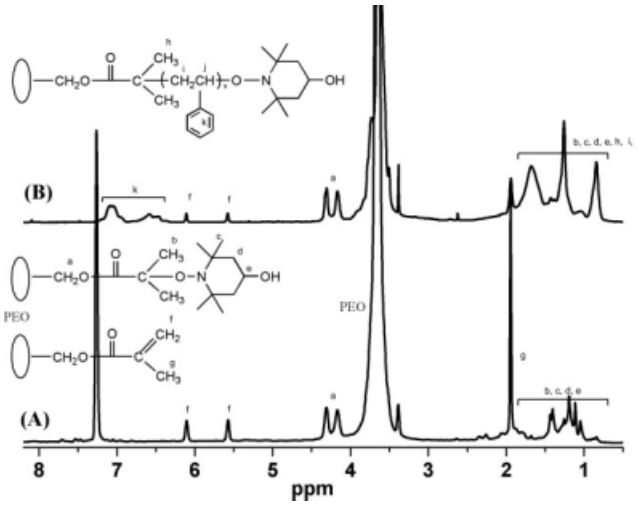
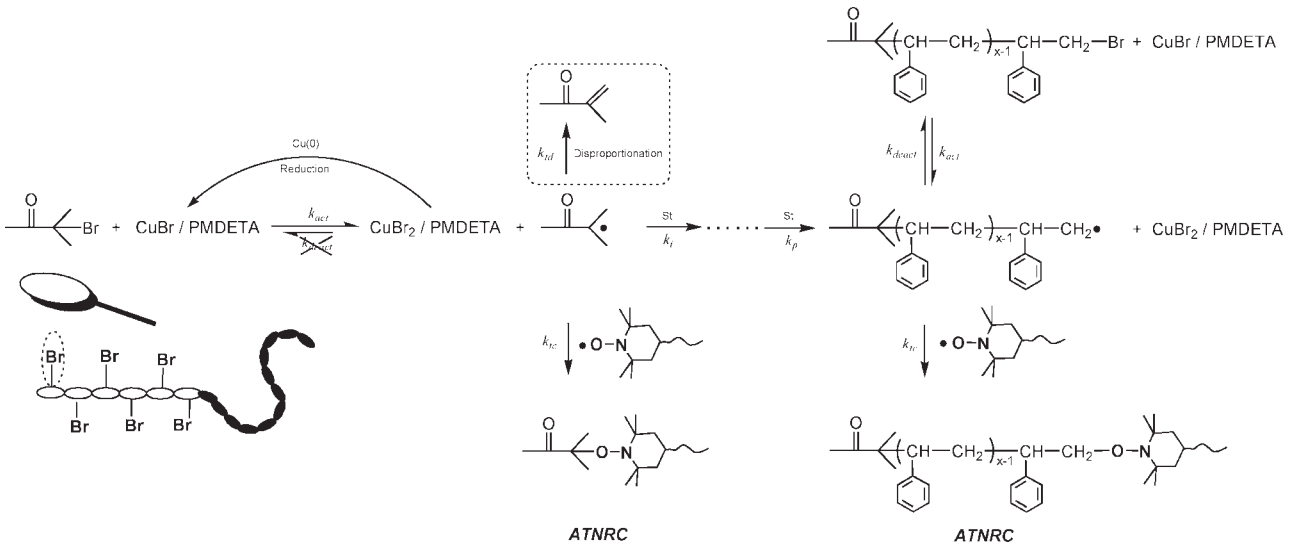


FIGURE 3 ^{1}H-NMR for the model ATNRC reaction between *m*PEO-*b*-Poly(EO-*co*-BiBGE) and HTEMPO in the absence of St ([—$(CH_3)_2$Br]:[TEMPO]:[St] = 1.0:1.0:0) (A) and in the presence of St ([—$(CH_3)_2$Br]:[TEMPO]:[St] = 1.0:1.0:4.0) (B).

TABLE 2 The Data for Model ATNRC Reaction

	*m*PEO-*b*-Poly(EO-*co*-BiBGE) + HTEMPO			
Entry	[—$(CH_3)_2$Br]:[TEMPO]:[St]	E.F.$_{dis.}$ (%)[a]	E.F.$_{(ATNRC-3)}$ (%)[b]	N_{st}[c]
A	1.0:1.0:0	67.8	32.2	
B	1.0:1.0:4.0	7.8	92.2	0.9
C	1.0:1.0:10.0	6.2	93.8	1.0

[a] The E.F.$_{dis.}$ were calculated according to the ^{1}H NMR spectra using Formula 4.
[b] The E.F.$_{(ATNRC-3)}$ were calculated according to the ^{1}H NMR spectra using Formula 5.
[c] The N_{st} were calculated according to the ^{1}H NMR spectra using Formula 6.



SCHEME 5 The mechanism of ATNRC reaction between —$C(CH_3)_2Br$ appended on main chain and TEMPO-PCL in the presence St monomers.

the solvents, ligand, structure of initiator, and the temperature would affect the k_{act} and k_{deact}, and finally the K_{ATRP}.[30] Similarly, the structure of the Br connected groups such as the isobutyl-bromide [—$C(CH_3)_2Br$, which used as the model of poly(methyl acrylate)] and phenylethyl-bromide [—$CH(C_6H_5)$—CH_2Br, which act the model of polystyrene] would also affect the ATNRC process. Tang and Matyjaszewski have reported that the k_{act} of —$C(CH_3)_2Br$ was about 16 times higher than that of —$CH(C_6H_5)$—CH_2Br under the same conditions.[31] It means that the higher activity for the former structure would lead to the easier termination via disproportionation during the ATRP,[29] as well as in the ATNRC procedure (Scheme 5).

Especially, in our ATNRC reaction, the TEMPO group was connected at the end of PCL, the steric hindrance resulted from the higher molecular weight of main chain or side chains, and the denser grafting sites on main chain would restrict the contact probability between TEMPO groups and the generated radicals on main chain. In the absence of St monomers, once the radical generated from —$C(CH_3)_2Br$, it might not be trapped by TEMPO immediately through the ATNRC (k_{tc}), the radicals would prefer to terminate by disproportionation (k_{td}) instead of forming the dormant radical. However, in the presence of St monomers, if the radical generated from —$C(CH_3)_2Br$ was not trapped by TEMPO, the radicals could initiate the oligomerization (k_i or/and k_{td})) of St monomers to form —[$CH(C_6H_5)$—CH_2]x—Br. Then, the radicals formed by the latter could be captured by TEMPO in the next cycle (k_{tc}). Thus, the disproportionation was largely prevented, and the E.F. of ATNRC was significantly increased.

Usually, the versatile —$C(CH_3)_2Br$ groups could be introduced into various copolymers by the easily esterification of hydroxyl groups on (co)polymer chains. Thus, based the above results, it may be useful to transform the higher active —$C(CH_3)_2Br$ on various polymer chains into the lower active —$CH(C_6H_5)$—CH_2Br by the addition of small amount of St monomer, and the ATNRC reaction with higher efficiency could be completed.

CONCLUSIONS

The effect of Br connected groups variation on ATNRC reaction was investigated. It was found that when the —$(CH_3)_2Br$ was transformed to —$CH(C_6H_5)$—CH_2Br, the ATNRC reaction was carried out in high efficiency, and the transformation could be easily completed by addition of small quantity of St monomers.

We appreciate the financial support to this research by Natural Science Foundation of Shanghai (No. 08ZR1400800) and the Natural Science Foundation of China (No. 20874013).

REFERENCES AND NOTES

1 Vazaios, A.; Lohse, D. J.; Hadjichristidis, N. Macromolecules 2005, 38, 5468–5474.

2 Andruzzi, L.; Hexemer, A.; Li, X. F.; Ober, C. K.; Kramer, E. J.; Galli, G.; Chiellini, E.; Fischer, D. A. Langmuir 2004, 20, 10498–10506.

3 Li, J.; Chen, X. R.; Chang, Y. C. Langmuir 2005, 21, 9562–9567.

4 Xu, F. J.; Song, Y.; Cheng, Z. P.; Zhu, X. L.; Zhu, C. X.; Kang, E. T.; Neoh, K. G. Macromolecules 2005, 38, 6254–6258.

5 Save, M.; Granvorka, G.; Bernard, J.; Charleux, B.; Boissiere, C.; Grosso, D.; Sanchez, C. Macromol Rapid Commun 2006, 27, 393–398.

6 (a) Percec, V.; Barboiu, B.; Bera, T. K.; van der Sluis, M.; Grubbs, R. B.; Jean, M. J.; Frechet, J. M. J Polym Sci Part A: Polym Chem 2000, 38, 4776–4791; (b) Percec, V.; Barboiu, B. Macromolecules 1995, 28, 7970–7972; (c) Percec, V.; Guliashvili, T.; Ladislaw, J. S.; Wistrand, A.; Stjerndahl, A.; Sienkowska, M.

J.; Monteiro, M. J.; Sahoo, S. J Am Chem Soc 2006, 128, 14156–14165; (d) Percec, V.; Barboiu, B.; Grigoras, C.; Bera, T. K. J Am Chem Soc 2003, 125, 6503–6516.

7 (a) Sarbu, T.; Lin, K. Y.; Ell, J.; Siegwart, D. J.; Spanswick, J.; Matyjaszewski, K. Macromolecules 2004, 37, 3120–3127; (b) Sarbu, T.; Lin, K. Y.; Spanswick, J.; Gil, R. R.; Siegwart, D. J.; Matyjaszewski, K. Macromolecules 2004, 37, 9694–9700; (c) Kopping, J. T.; Tolstyka, Z. P.; Maynard, H. D. Macromolecules 2007, 40, 8593–8599; (d) Tolstyka, Z. P.; Kopping, J. T.; Maynard, H. D. Macromolecules 2008, 41, 599–606.

8 (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. Angew Chem Int Ed Engl 2001, 40, 2004–2021; (b) Binder, W. H.; Sachsenhofer, R. Macromol Rapid Commun 2007, 28, 15–54; (c) Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. Macromolecules 2005, 38, 7540–7545; (d) Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. Macromolecules 2005, 38, 3558–3561; (e) Malkoch, M.; Schleicher, K.; Drockenmuller, E.; Hawker, C. J.; Russell, T. P.; Wu, P.; Fokin, V. V. Macromolecules 2005, 38, 3663–3678; (f) Helms, B.; Mynar, J. L.; Hawker, C. J.; Frechet, J. M. J. J Am Chem Soc 2004, 126, 15020–15021; (g) Durmaz, H.; Dag, A.; Altintas, O.; Erdogan, T.; Hizal, G.; Tunca, U. Macromolecules 2007, 40, 191–198; (h) Gao, H.; Matyjaszewski, K. Macromolecules 2006, 39, 4960–4965; (i) Gao, H. F.; Matyjaszewski, K. J Am Chem Soc 2007, 129, 6633–6639.

9 Yagci, Y.; Tasdelen, M. A. Prog Polym Sci 2006, 31, 1133–1170.

10 (a) Zhang, H.; Ruckenstein, E. Macromolecules 2000, 33, 814–819; (b) Se, K.; Yamazaki, H.; Shibamoto, T.; Takano, A.; Fujimoto, T. Macromolecules 1997, 30, 1570–1576.

11 Gauthier, M.; Tichagwa, L.; Downey, J. S.; Gao, S. Macromolecules 1996, 29, 519–527.

12 Lee, C.; Lee, H.; Lee, W.; Chang, T.; Roovers, J. Macromolecules 2000, 33, 8119–8121.

13 Teng, J.; Zubarev, E. R. J Am Chem Soc 2003, 125, 11840–11841.

14 Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. Chem Rev 2001, 101, 3747–3792.

15 (a) Trubetskoy, V. S. Adv Drug Delivery Rev 1999, 37, 81–88; (b) Stiriba, S. E.; Kautz, H.; Frey, H. J Am Chem Soc 2002, 124, 9698–9699.

16 Djalali, R.; Li, S. Y.; Schmidt, M. Macromolecules 2002, 35, 4282–4288.

17 Zhang, M.; Drechsler, M.; Muller, A. H. E. Chem Mater 2004, 16, 537–543.

18 He, L.; Huang, J.; Chen, Y.; Xu, X.; Liu, L. Macromolecules 2005, 38, 3845–3851.

19 (a) Siemsen, P.; Livingston, R. C.; Diederich, F. Angew Chem Int Ed Engl 2000, 39, 2632–2657; (b) Duxbury, C. J.; Cummins, D.; Heise, A. J Polym Sci Part A: Polym Chem 2009, 47, 3795–3802; (c) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. Angew Chem Int Ed Engl 2005, 44, 5188–5240.

20 (a) Sun, R. M.; Wang, G. W.; Liu, C.; Huang, J. L. J Polym Sci Part A: Polym Chem 2009, 47, 1930–1938; (b) Fu, Q.; Liu, C.; Lin, W. C.; Huang, J. L. J Polym Sci Part A: Polym Chem 2008, 46, 6770–6779.

21 (a) Fu, Q.; Wang, G. W.; Lin, W. C.; Huang, J. L. J Polym Sci Part A: Polym Chem 2009, 47, 986–990; (b) Liu, C.; Pan, M. G.; Zhang, Y.; Huang, J. L. J Polym Sci Part A: Polym Chem 2008, 46, 6754–6761.

22 Lin, W. C.; Fu, Q.; Zhang, Y.; Huang, J. L. Macromolecules 2008, 41, 4127–4135.

23 Kulis, J.; Bell, C. A.; Micallef, A. S.; Jia, Z. F.; Monteiro, M. J. Macromolecules 2009, 42, 8218–8227.

24 Fu, Q.; Lin, W. C.; Huang, J. L. Macromolecules 2008, 41, 2381–2387.

25 Rosen, B. M.; Percec, V. Chem Rev 2009, 109, 5069–5119.

26 Fitton, A. O.; Hill, J.; Jane, D. E.; Millar, R. Synthesis 1987, 12, 1140–1142.

27 Li, Z. Y.; Li, P. P.; Huang, J. L. J Polym Sci Part A: Polym Chem 2006, 44, 4361–4371.

28 (a) Riva, R.; Schmeits, S.; Jerome, C.; Jerome, R.; Lecomte, P. Macromolecules 2007, 40, 796–803; (b) Li, H.; Riva, R.; Jerome, R.; Lecomte, P. Macromolecules 2007, 40, 824–831; (c) Tsarevsky, N. V.; Bencherif, S. A.; Matyjaszewski, K. Macromolecules 2007, 40, 4439–4445; (d) Parrish, B.; Breitenkamp, R. B.; Emrick, T. J Am Chem Soc 2005, 127, 7404–7410.

29 Schellekens, M. A. J.; Wit, F.; Klumperma, B. Macromolecules 2001, 34, 7961–7966.

30 Nanda, A. K.; Matyjaszewski, K. Macromolecules 2003, 36, 599–604.

31 Tang, W.; Matyjaszewski, K. Macromolecules 2007, 40, 1858–1863.