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Efficient oxidative self-coupling of polystyrene bearing chain-end primary amines

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ABSTRACT

A series of well-defined linear polystyrenes (PSs) with different degree of polymerization (DP) was synthesized via atom transfer radical polymerization (ATRP) using *tert*-butyloxycarbonyl (*t*-boc)-pro-tected 4-(aminomethyl)phenyl 2-bromoisobutyrate (BAPB) as an initiator. The resulting polymers were deprotected by cleavage of the *t*-boc protecting groups via treatment with trifluoroacetic acid (TFA) to generate the chain-end primary amine functionality. The chain-end primary amine groups of the polymers were self-coupled in the presence of 2,2'-azobisisobutyronitrile (AIBN) under an oxygen atmosphere via imine bond formation. The coupling efficiency decreased slightly as the chain length of the PS increased. The imine linkages of the coupled PSs were hydrolyzed in the presence of HCl to individual PS chains.

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1. Introduction

While 'controlled/living radical polymerization' (CRP) offers the preparation of polymers with predetermined molecular weights and a narrow molecular weight distribution, functionalization of polymers synthesized by CRP methods remains an important challenge in polymer chemistry [1–4]. Functionalization of polymers is important in the field of preparation of telechelic polymers [5,6], anchoring polymers onto various surfaces [7–9], and bioconjugation [10–12]. For these applications, selective functionalization is required so that reactions take place only at specific sites of the polymer molecule.

While functionality is mostly introduced through prefunctionalized or protected monomers, the precise synthesis of polymers containing functional end groups is also important for many applications. For a successful reaction at the polymer chain end with high yield, simple, efficient, and versatile chemical reactions should be used. To these ends, "click" reactions [13,14], such as the Cucatalyzed alkyne/azide cycloaddition (CuAAC) [15,16], thiol-ene [17–19], and Diels–Alder [20,21] reactions have recently been used extensively as polymer modification techniques at α - or ω chain ends. Especially, "click" reactions can be combined with CRP techniques, such as atom transfer radical polymerization (ATRP)

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http://dx.doi.org/10.1016/j.polymer.2015.04.032 0032-3861/© 2015 Elsevier Ltd. All rights reserved [22–24], reversible addition—fragmentation chain transfer (RAFT) [25], and nitroxide mediated polymerization (NMP) [26], opening up new opportunities for postpolymerization modification at the polymer chain end. In addition to click reactions, it is important to develop more synthetic tools to engineer well-defined macromolecules with specific functionality.

As a radical initiator, azobisisobutyronitrile (AIBN) is used widely in radical polymerization with oxygen-free environments because carbon-centered radicals can easily react with oxygen to form peroxy radicals, which stop the polymer chain from propagating [27]. While oxygen is fatal for radical polymerization initiated by AIBN, peroxy radicals generated by the reaction between carbon centered radicals and oxygen were found to be useful in radical-based organic reactions [28–32]. Among them, Fu et al. reported the highly efficient AIBN initiated self-coupling reaction where primary amines can be reacted together to form imines under an oxygen environment [33].

The imine bond has a unique pH-responsive nature [34,35]. When the pH of the solution is reduced, in acidic conditions, the imine bond decomposes to form an aldehyde and an ammonium ion. Due to the pH-responsiveness of imine bond, it has been used as an important component for a dynamic covalent bond that is widely used in the controlled formation of various supramolecular systems [36].

To our knowledge, there is no report of the synthesis of selfcoupled polymers using oxidative transformation of chain-end primary amines to imines. Given this background, here, we

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report that well-defined polystyrenes with primary amine functionality at the chain end are highly versatile building blocks for the construction of self-coupled polymers via an AIBN-initiated oxidative coupling reaction. After the highly efficient selfcoupling reaction, the successful pH-driven cleavage of the imine bond was also demonstrated, resulting in the formation of individual polymers.

2. Experimental

2.1. Materials

Styrene (99%, Aldrich) was purified by passing through a column filled with basic alumina to remove inhibitors. Di-tert butyl dicarbonate (\geq 98%), triethylamine (\geq 99.5%), α -bromoisobutyryl bromide (98%), CuBr (98%), and trifluoroacetic acid (99%), were purchased from Aldrich with the highest purity and were used as received, with no further purification. 2,2'-Azobisisobutyronitrile (AIBN, Aldrich, 98%) was recrystallized from ethanol. 2,2'-Bipyridyl (\geq 99.0%) was purchased from Tokyo Chemical Industry (TCI) and used as received. 4-Hydroxybenzylamine (97%) was purchased from Matrix Scientific and used as received.

2.2. Instrumentation

¹H NMR spectra were collected in CDCl₃ on a Bruker Avance 300 MHz NMR spectrometer. The apparent molecular weights and molecular weight distributions were measured by GPC (Agilent Technologies 1200 series) using a polystyrene standard, with DMF as the eluent at 30 °C and a flow rate of 1.00 mL/min.

2.3. Synthesis

2.3.1. t-Boc-4-hyroxy benzyl amine (2)

To a solution of the 4-hydroxybenzylamine (2.0 g, 16.2 mmol) in THF (20 mL) was added TEA (3.4 mL, 24.3 mmol), followed by the slow addition of di-tert butyl dicarbonate (5.30 g, 24.3 mmol in 20 mL of THF). The reaction mixture was stirred at room temperature for 3 h, after which time the solvent was removed *in vacuo*. The crude mixture was partitioned between H₂O and diethyl ether. The organic layer was collected and dried using anhydrous MgSO₄. The solution was filtered, concentrated, and purified by chromatography (hexane:ethyl acetate = 1:2) to provide *t*-boc-4-hyroxy benzyl amine. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 7.16–7.10 (2H, d, aromatic), 6.79–6.74 (2H, d, aromatic), 4.83–4.67 (1H, broad, $-CH_2-NH-COO-$), 4.27–4.15 (2H, d, $-C-CH_2-NH-$), and 1.46–1.42 (9H, s, $-C(CH_3)_3$).

2.3.2. t-Boc-4-(aminomethyl)phenyl 2-bromo-2-methylpropanoate initiator (**3**)

t-boc-4-hydroxy benzyl amine (2.72 g, 12.2 mmol), TEA (3.4 ml, 24.3 mmol), and THF (50 mL) were added to a 250-mL round flask equipped with a stir bar. The flask was cooled in an ice bath. α -Bromoisobutyryl bromide (3.0 mL, 24.5 mmol in 10 mL of THF) was injected slowly. The reaction mixture was allowed to proceed in the ice bath for 30 min and continued for 24 h at room temperature. The product was collected, washed with THF, and filtered. The filtrate was dried under reduced pressure and the crude product was recrystallized from hexane to yield white crystals with a yield of 58.1%. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 7.35–7.27 (2H, d, aromatic), 7.10–7.03 (2H, d, aromatic), 4.88–4.79 (1H, broad, $-CH_2-NH-COO-$), 4.33–4.25 (2H, d, $-C-CH_2-NH-$), 2.07–2.02 (6H, s, $-C-(CH_3)_2$ Br), and 1.46–1.42 (9H, s, $-C(CH_3)_3$).

2.3.3. Polymerization of styrene from 3 (A1-A3)

Styrene (30.7 mL, 268 mmol), *t*-boc-4-(aminomethyl)phenyl 2bromo-2-methylpropanoate (0.50g, 1.34mmol), 2,2'-Bipyridyl (0.21 g, 1.34 mmol), and anisole (10 mL) were added to a 50-mL Schlenk flask equipped with a magnetic stir bar. Oxygen was removed by three freeze-pump-thaw cycles, and CuBr (0.096 g, 0.67 mmol) was added under an argon atmosphere. The polymerization was conducted at 110 °C for 20 h. Samples were removed periodically by syringe to determine the molecular weight and PDI by GPC and monomer conversion by ¹H NMR spectroscopy. The polymerization was quenched by cooling and exposing the solution to air. The catalyst was removed by passing the solution through a neutral alumina column. The resulting polymer was precipitated by addition to methanol, and dried under high vacuum at room temperature overnight. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 7.30–6.24 (5H, broad, aromatic), 4.85–4.70 (1H, broad, -CH₂-NH-COO-), 4.30-4.65 (1H, broad, -CH₂-CH-Br), 4.28-4.18 (2H, d, -C-CH₂-NH-COO-), 2.70-0.80 (3H, broad, polymer backbone part), and 1.48–1.44 (9H, s, -C(CH₃)₃).

2.3.4. t-Boc deprotection of A1 (B1)

A1 (0.5 g) was dissolved in dichloromethane (10 mL) in a 50-mL round flask, equipped with a stir bar. To this solution trifluoroacetic acid (TFA, 5 mL) was injected slowly. The reaction mixture was stirred at room temperature for 8 h, after which time it was concentrated *in vacuo*. The crude solution was diluted with EtOAc, and washed with Na₂CO₃ and brine. The organic layer was dried using anhydrous MgSO₄, concentrated, and precipitated by addition to methanol. The resulting polymer was dried under high vacuum at room temperature overnight. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 7.30–6.24 (5H, broad, aromatic), 4.30–4.65 (1H, broad, $-CH_2-CH-Br$), 3.85–3.77 (2H, d, $-C-CH_2-NH-COO-$), and 2.70–0.80 (3H, broad, polymer backbone part).

2.3.5. Coupling of **B1** (C1)

B1 (40 mg, 0.013 mmol, assuming the molecular weight is 3000), AIBN (44 mg, 0.26 mmol), and toluene (1 mL) were added into a 50-mL round flask equipped with a magnetic stir bar. The solution was purged with oxygen for 15 min. The solution was stirred vigorously and heated at 70 °C for 12 h under an oxygen atmosphere and precipitated into methanol, and dried under vacuum at 25 °C for 24 h. ¹H NMR (300 MHz, CDCl₃, δ in ppm): 9.97–9.90 (1H, s, $-C-CH=N-CH_2-$), 8.10–6.24 (5H, broad, aromatic), 5.39–5.33 (2H, s, $-C-CH=N-CH_2-$); 4.30–4.65 (1H, broad, $-CH_2-CH-Br$), 3.85–3.77 (2H, d, $-C-CH_2-NH-COO-$), and 2.70–0.80 (3H, broad, polymer backbone part).

2.3.6. The cleavage of C1

C1 (20 mg in 1 mL DMF) was treated by 0.2 mL of 1 M HCl. The reaction mixture was stirred at 50 $^{\circ}$ C for 5 h and precipitated into methanol. The resulting polymer was dried under high vacuum at room temperature overnight.

3. Results and discussion

The synthesis of *tert*-butyloxycarbonyl (*t*-boc)-protected 4-hydroxybenzylamine (**2**) involved the reaction of di-tert butyl dicarbonate with 4-hydroxybenzylamine (**1**) in the presence of triethylamine (TEA) in THF. Compound **2** reacted with α -bromoisobutyryl bromide to yield a target initiator, **3**. ¹H NMR spectra confirmed the successful synthesis of **2** and **3** (Fig. S1).

The strategy used is illustrated schematically in Scheme 1. ATRP was used to directly prepare a series of polystyrenes (PSs) potentially containing terminal primary amine with a controlled molecular weight and low polydispersity. A CuBr/bpy catalyst system was

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Scheme 1. Synthesis of a) latent primary amine initiator, 3 and b) coupling of chain-end primary amine groups of polystyrene prepared by ATRP.

used for the ATRP of styrene using compound **3** as an initiator in anisole. Samples were removed at regular intervals during polymerization to obtain **A1–A3** polymers with different molecular weights as well as to monitor conversion and molecular weight evolution. The polymerization was stopped at 50% monomer conversion and the molecular weight and molecular weight distribution of the resulting PSs were obtained using a gel permeation chromatography (GPC) DMF line with polystyrene standards (Fig. 1, Table 1).

Deprotection of *t*-boc groups was accomplished by reacting **A1–A3** polymers with trifluoroacetic acid (TFA) in dichloromethane. ¹H NMR spectroscopy confirmed the successful deprotection of **A1**, as monitored by the disappearance of the *t*-boc peaks at 1.2–1.3 ppm and the appearance of the $-CH_2NH_2$ peak at 3.8 ppm (Fig. 2). The apparent molecular weight of **B1** did not change after deprotection, suggesting that deprotection did not lead to change in hydrodynamic volumes in DMF. **A2** and **A3** were



also deprotected successfully to yield **B2** and **B3**, respectively (Figs. S2 and S3).

Having obtained **B1–B3** polymers with chain-end primary amine functionality, self-coupling reactions of these polymers were investigated. The chain-end primary amine groups of the polymers (**B1–B3**) were reacted together to form imine bond in the presence of AIBN under an oxygen atmosphere, leading to self-coupled polymers, **C1–C3**. For all reactions, a 20-fold molar excess of AIBN over primary amine functionalized polymers (**B1–B3**) was used to ensure high conversion. ¹H NMR spectroscopy confirmed imine formation of **C1** by the appearance of the new peaks (**f** and **g**), representing protons of imine groups at 9.9 and 5.2 ppm and the complete disappearance of peak **e** at 3.8 ppm, indicating the successful conversion to **C1** (Fig. 2). Similarly, the successful syntheses of **C2** and **C3** were confirmed by ¹H NMR spectroscopy (Figs. S2 and S3).

The influence of molecular weight on the coupling efficiency was assessed by GPC (Fig. 3). As evidenced by ¹H NMR spectroscopy, the successful self-coupling reaction was further confirmed by GPC analysis, with M_n of self-coupled polymers (**C1–C3**) being increased, almost twice that of the precursor polymers (**B1–B3**).

Table 1										
Summary of DMF GPC results and efficiency of self-coupling reactions.										
	М		a (g/mol)	М	b (g/mol)	b	v			

	<i>M</i> _n , theory ^a (g/mol)	$M_{\rm n}, _{\rm app}$ (g/mol)	PDI	Ycoupling
A-1	3000	3500	1.06	_
B-1	3000	3600	1.06	-
C-1	6000	6000	1.17	80
A-2	6000	6600	1.07	-
B-2	6000	5800	1.11	-
C-2	12 000	9400	1.10	77
A-3	10 000	11 500	1.11	-
B-3	10 000	10 660	1.12	_
C-3	20 000	16 400	1.14	70

^a Theoretical molecular weight determined from monomer conversions.

^b Apparent number-average molecular weight and PDI determined by DMF GPC with PS calibration.

^c Determined by apparent number-average molecular weight.

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Fig. 3. GPC traces for a primary amine-containing polystyrenes and their self-coupled products.

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Scheme 2. Formation of individual polymers by the cleavage of the imine bond under acidic conditions.

The molecular weight distribution of the self-coupled polymers remained as narrow as $M_n/M_w = 1.1-1.17$. As seen in Fig. 3a, the self-coupling of the parent polymer **B1** ($M_n = 3600 \text{ g/mol}, M_n/$ $M_w = 1.06$) resulted in a polymer **C1** with high molecular weight $(M_n = 6000 \text{ g/mol})$ and a broad molecular weight distribution $(M_n/$ $M_w = 1.17$). As the chain length of the parent polymers was larger, a low shift towards the high molecular region in the apparent molecular weight was observed (Fig. 3b and c). Based on an increase in the apparent M_n values, the coupling efficiencies of **B1**, **B2**, and **B3** were calculated to be 80, 77, and 70%, respectively. As expected, the self-coupling efficiency decreased as the molecular weight of the polymer increased. When the primary amine-terminated linear PS had a higher molecular weight, the effect of relatively low chainend group concentration decreased the self-coupling efficiency. Table 1 summarizes the results of self-coupled polymers with differing molecular weights.

Due to the pH-responsive nature of the benzoic imine bond, the self-coupled polymers can decompose into individual polymers under acidic condition. One of the decomposed polymers has an aldehyde group in the chain end and the other has an ammonium ion (Scheme 2). After treatment with HCl, the GPC traces shifted towards lower molecular weights (Fig. 4). These results indicated the successful pH-driven cleavage of the imine bond, which, in turn, leads to the formation of individual polymers.

4. Conclusions

In summary, the synthesis of self-coupled polystyrenes based on the AIBN-initiated oxidative coupling of primary amines to imines has been described. A series of polystyrenes with different molecular weight was synthesized via ATRP from a t-boc-protected initiator with good control of the polymer molecular weight and molecular weight distribution. Deprotection of the *t*-boc groups resulted in polystyrenes with chain-end primary amine group. The self-coupling reactions of polystyrenes were demonstrated in the presence of AIBN under an oxygen atmosphere. The efficiency of coupling reaction was assessed by GPC. Regardless of the molecular



Fig. 4. DMF GPC traces of C2 and its hydrolyzed product after treatment with HCl.

weight of polystyrenes, the coupling efficiency was >70%. The acidcatalyzed decomposition of selfcoupled polymers into individual polymers was also demonstrated. This oxidative coupling and decoupling strategy, combined with ATRP and efficient postpolymerization functionalization, represents a modular route to well-defined functional polymers.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http:// dx.doi.org/10.1016/j.polymer.2015.04.032.

References

- [1] Braunecker WA, Matyjaszewski K. Prog Polym Sci 2007;32(1):93-146.
- [2] Coessens V, Pintauer T, Matyjaszewski K, Prog Polym Sci 2001;26(3):337–77.
- Goto A, Fukuda T. Prog Polym Sci 2004;29(4):329–85. [3]
- [4] Matyjaszewski K. Prog Polym Sci 2005;30(8-9):858-75.
- [5] Tasdelen MA, Kahveci MU, Yagci Y. Prog Polym Sci 2011;36(4):455-567.
- [6] Tsarevsky NV, Sumerlin BS, Matyjaszewski K. Macromolecules 2005;38(9): 3558-61.
- [7] Barbey R, Lavanant L, Paripovic D, Schüwer N, Sugnaux C, Tugulu S, et al. Chem Rev 2009;109(11):5437-527.
- [8] Edmondson S, Osborne VL, Huck WTS. Chem Soc Rev 2004;33(1):14-22.
- [9] Zhao B, Brittain WJ. Prog Polym Sci 2000;25(5):677-710.
- [10] Lutz J-F, Börner HG. Prog Polym Sci 2008;33(1):1–39.
- [11] Lutz J-F, Börner HG, Weichenhan K. Macromolecules 2006;39(19):6376-83.
- Siegwart DJ, Oh JK, Matyjaszewski K. Prog Polym Sci 2012;37(1):18-37. [12]
- [13] Fournier D, Hoogenboom R, Schubert US. Chem Soc Rev 2007;36(8):1369-80.
- [14] Sumerlin BS, Vogt AP, Macromolecules 2010:43(1):1–13.
- [15] Lutz J-F. Angew Chem Int Ed 2007;46(7):1018-25.
- [16] Lutz J-F, Börner HG, Weichenhan K. Macromol Rapid Commun 2005;26(7): 514-8.
- [17] Hoyle CE, Bowman CN. Angew Chem Int Ed 2010;49(9):1540-73.
- [18] Killops KL, Campos LM, Hawker CJ. J Am Chem Soc 2008;130(15):5062-4.
- Lowe AB. Polym Chem 2010:1(1):17-36. [19]
- Kim T-D, Luo J, Tian Y, Ka J-W, Tucker NM, Haller M, et al. Macromolecules [20] 2006:39(5):1676-80.
- Tasdelen MA. Polym Chem 2011;2(10):2133-45. [21]
- Matyjaszewski K, Xia J. Chem Rev 2001;101(9):2921-90.
- Wang J-S, Matyjaszewski K. J Am Chem Soc 1995;117(20):5614-5. [23]
- [24] Matyjaszewski K, Tsarevsky NV. Nat Chem 2009;1(4):276-88.
- [25] Lowe AB, McCormick CL. Prog Polym Sci 2007;32(3):283-351.
- [26] Hawker CJ, Bosman AW, Harth E. Chem Rev 2001;101(12):3661-88.
- [27] Hammond GS, Sen JN, Boozer CE. J Am Chem Soc 1955;77(12):3244-8.
- [28] Aoki Y, Sakaguchi S, Ishii Y. Adv Synth Cat 2004;346:199-202.
- [29] Iwahama T, Sakaguchi S, Nishiyama Y, Ishii Y. Tetrahed Lett 1995;36(38): 6923-6
- Ishii Y, Iwahama T, Sakaguchi S, Nakayama K, Nishiyama Y. J Org Chem [30] 1996;61(14):4520-6.
- Biffis A, Minati L. J Cat 2005;236(2):405-9. [31]
- Konnick MM, Stahl SS. J Am Chem Soc 2008;130(17):5753-62. [32]
- [33] Liu L, Wang Z, Fu X, Yan C-H. Org Lett 2012;14(22):5692-5.
- Xu S, Luo Y, Graeser R, Warnecke A, Kratz F, Hauff P, et al. Bioorg Med Chem [34] Lett 2009:19(3):1030-4.
- Xu S, Luo Y, Haag R. Macromol Biosci 2007;7(8):968-74. [35]
- [36] Wang C, Wang G, Wang Z, Zhang X. Chem. A Eur J 2011;17(12):3322-5.

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